June 2017 Volume 76 Supplement 2

Annals of the Rheumatic Diseases

The EULAR Journal



Annual European Congress of RHEUMATOLOGY

EULAR 2017

Madrid, 14–17 June 2017

Abstracts

ard.bmj.com

eular
fighting rheumatic & musculoskeletal diseases together
70 anniversary 1947 - 2017
BMJ

Annals of the Rheumatic Diseases

Annual European Congress of Rheumatology

14 – 17 June, 2017

Madrid, Spain

Abstracts

The EULAR Journal

ARD
The EULAR Journal

Editor
Tore K Kvien (Norway)

Associate Editors
Francis Berenbaum (France)
Johannes Bijlsma (The Netherlands)
Dimitrios Boumpas (Greece)
Gerd Burmester (Germany)
Mary Crow (USA)
Iain McInnes (UK)
David Pisetsky (USA)

Methodological and Statistical Advisor
Stian Lydersen (Norway)

Graphical Advisor
Maarten Boers (The Netherlands)

Social Media Advisors
Alessia Alunno (Italy)
Mary Canavan (Ireland)
Meghna Jani (UK)
Elena Nikiphorou (UK)
Paul Studenic (Austria)

Guidelines for Authors and Reviewers

Full instructions are available online at http://ard.bmj.com/pages/authors. Articles must be submitted electronically at http://mc.manuscriptcentral.com/ard. Authors retain copyright but are required to grant ARD an exclusive licence to publish. (http://authors.bmj.com/submitting-your-paper/copyright-and-authors-rights).

Annals of the Rheumatic Diseases publishes original work on all aspects of rheumatology and disorders of connective tissue. Laboratory and clinical studies are equally welcome

Editorial Board

Daniel Aletaha (Austria)
Matthew Brown (Australia)
Loreto Carmona (Spain)
Carlo Chizzolini (Switzerland)
Bernard Combe (France)
Philip Conaghan (UK)
Maurizio Cutolo (Italy)
László Czirják (Hungary)
Nicola Dalbeth (New Zealand)
Oliver Distler (Switzerland)
Thomas Dörner (Germany)
Dirk Elewaut (Belgium)
Gary Firestein (USA)
David Fox (USA)
Sherine Gabriel (USA)
Mary Goldring (USA)
Juan Gómez-Reino (Spain)
Walter Grassi (Italy)
Wolfgang Gross (Germany)
Francis Guillemin (France)
Ahmet Gül (Turkey)
Kåre Birger Hagen (Norway)
Frederic Houssiau (Belgium)
Tom Huizinga (The Netherlands)
Roland Jonsson (Norway)
Mariana Kaplan (USA)
George Kollias (Greece)
Robert Landewé (The Netherlands)
Zhan-Guo Li (China)
Rik Lories (Belgium)
Ingrid Lundberg (Sweden)
Gary MacFarlane (UK)
Xavier Mariette (France)
Alberto Martini (Italy)
Wlodzimierz Maslinski (Poland)
Marco Mattuci Cerinic (Italy)
Dennis McGonagle (UK)
Pier-Luigi Meroni (Italy)
Pierre Miossec (France)
Timothy Niewold (USA)
Mike Nurmohamed (The Netherlands)
Monika Østensen (Switzerland)
Mikkel Østergaard (Denmark)
Constatino Pitzalis (UK)
Berent Prakken (The Netherlands)
Lars Rönnblom (Sweden)
Jane Salmon (USA)
Georg Schett (Germany)
José da Silva (Portugal)
Hendrik Schulze-Koops (Germany)
Nan Shen (China)
Alexander So (Switzerland)
Tuulikki Sokka (Finland)
Deborah Symmons (UK)
Tsutomu Takeuchi (Japan)
Yoshiya Tanaka (Japan)
Alan Tyndall (Switzerland)
John Varga (USA)
Dimitrios Vassilopoulos (Greece)
Douglas Veale (Ireland)
Jiri Vencovsky (Czech Republic)
Ronald van Vollenhoven (Sweden)
Michael Ward (USA)
Kevin Winthrop (USA)
Kazuhiko Yamamoto (Japan)

Advisory Committee

Wim van den Berg (The Netherlands)
Stefano Bombardieri (Italy)
Ferdinand Breedveld (The Netherlands)
Leslie Crofford (USA)
Michael Doherty (UK)
Maxime Dougados (France)
Paul Emery (UK)
Daniel Furst (USA)
Steffen Gay (Switzerland)
Désirée van der Heijde (The Netherlands)
Marc Hochberg (USA)
Joachim Kalden (Germany)
Edward Keystone (Canada)
Lars Klareskog (Sweden)
Peter Lipsky (USA)
Stefan Lohmander (Sweden)
Sir Ravinder Maini (UK)
Emilio Martín-Mola (Spain)
Haralampos Moutsopoulos (Greece)
James O'Dell (USA)
Karel Pavelka (Czech Republic)
Leo van de Putte (The Netherlands)
Jozef Rovensky (Slovakia)
Yehuda Shoenfeld (Israel)
Josef Smolen (Austria)
Walther van Venrooij (The Netherlands)
Michael Weinblatt (USA)
Frank Wollheim (Sweden)
Anthony Woolf (UK)

Subscription Information

ARD is published monthly; subscribers receive all supplements
ISSN 0003-4967 (print); 1468-2060 (online)

Institutional Rates 2017

Print
£939; US$1832; €1268

Online
Site licences are priced on FTE basis and allow access by the whole institution. Details available online at http://journals.bmj.com/content/subscribers or contact the Subscription Manager in the UK (see above right)

Personal Rates 2017

Print (includes online access at no additional cost)
£387; US$755; €523

Online only
£164; US$320; €222

EULAR congress delegates
Delegates receive a Continuous Professional Development package that includes a 12 month complimentary subscription to *ARD* in print and/or online

Personal print or online only and institutional print subscriptions may be purchased online at http://journals.bmj.com/content/subscribers (payment by Visa/Mastercard only)

Residents of some EC countries must pay VAT; for details, call us or visit http://journals.bmj.com/content/subscribers

Contact Details

Editorial Office
Annals of the Rheumatic Diseases
BMJ Publishing Group Ltd
BMA House
Tavistock Square
London WCIH 9JR,UK
T: **+44 (0)20 7383 6250**
E: **ard@bmj.com**

Permissions
http://www.bmj.com/company/products-services/rights-and-licensing/permissions

Supplement Enquiries
T: **+44 (0)20 7383 6057**
E: **journals@bmj.com**

Subscriptions
For all subscription enquiries and orders
T: **+44 (0)20 7111 1105**
E: **http://ard.bmj.com/pages/subscribe**

Display Advertising Sales
Sophie Fitzsimmons
T: **+44 (0)20 7383 6783**
E: **sfitzsimmons@bmj.com**
http://www.bmj.com/company/raise-visibility-and-reach

Online Advertising Sales
Marc Clifford
T: **+44 (0) 20 7383 6161**
E: **mclifford@bmj.com**
http://www.bmj.com/company/raise-visibility-and-reach

Display & Online Advertising Sales (USA)
American Medical Communications (AMC)
T: **+1 732 490 5530**
E: **jloughran@americanmedicalcomm.com**

Author Reprints
Reprints Administrator
E: **admin.reprints@bmj.com**

Commercial Reprints (except USA & Canada)
Nadia Gurney-Randall
T: **+44 (0)20 8445 5825**
M: **+44 07866 262344**
E: **ngurneyrandall@bmj.com**

Commercial Reprints (USA & Canada)
Ray Thibodeau
T: **+1 267 895 1758**
M: **+1 215 933 8484**
E: **ray.thibodeau@contentednet.com**

EULAR
EULAR Executive Secretariat
Seestrasse 240, 8802 Kilchberg, Switzerland
E: **eular@eular.org**
www.eular.org

For all other ARD contacts
http://ard.bmj.com/contact-us

Welcome Address

Dear Colleagues,

Welcome to this EULAR Annual European Congress of Rheumatology in Madrid!
Welcome to the 70th anniversary of EULAR!

The annual EULAR Congresses, which began in 2000, are today a major event in the calendar of world rheumatology. This meeting, which marks the 70th anniversary of our very active society, will once again provide a unique occasion for the exchange of scientific and clinical information. It will facilitate interaction between patients, medical doctors, scientists, health professionals and professionals representing the pharmaceutical industry from Europe and from around the world. Participating in the congress is just one element of the annual educational package provided by EULAR: Almost all oral presentations will be available online after signing up and participants will be provided with a complimentary, one-year subscription to the latest developments and publications in the field of rheumatic and musculoskeletal diseases (RMDs). This is in line with a new, exciting event taking place in Madrid this year – the launch of the EULAR School of Rheumatology, which will be unique in providing education in rheumatology throughout the world.

EULAR has grown rapidly in terms of the number of participants and the quality of the submissions. A record number of more than 4'850 abstracts have been submitted to this year's congress in Madrid, and 180 sessions and poster tours are offered. This tremendous success continues to reflect the increasing interest in RMDs; it also reflects the availability of increased information on the size, burden and cost of these diseases for society – and a significantly improved ability to diagnose and treat them. The incorporation of health professional and patient organisations within EULAR has been a considerable stimulus for these advances.

The EULAR Congress 2017 in Madrid will provide a wide range of topics including clinical innovations, clinical translational and basic science. In addition, there will be significant contributions made by People with Arthritis and Rheumatism (PARE), by Health Professionals in Rheumatology (HPR) and by the health care industry. The core science and central activity of the congress will be the poster presentations and poster tours with their highly interactive exchanges between participants. The Madrid meeting will further promote the reputation of the EULAR Congress as a most innovative and informative venue for clinical research for the practising physician and health professionals. Meanwhile, the EULAR EMEUNET organisation of young rheumatologists aims to attract young colleagues to the meeting and will disseminate the message that rheumatology is one of the most attractive and successful disciplines of medicine.

We are back in the vibrant city of Madrid with its remarkable history, architecture, galleries, museums and ambience, all of which will once again provide an excellent background for clinical exchanges, international collaborations and renewal of friendships. "No pierdas tu tren" and in international language "Don't Delay, Connect Today!" marks the first general EULAR Campaign to be launched in Madrid aiming at early recognition and treatment of RMDs.

It is our great pleasure and a real joy in welcoming medical doctors, patients, health professionals and representatives of the pharmaceutical industry and we hope their stay in Madrid will be delightful, informative, and educational. We wish you a great time, good science, good discussions, good meetings and most of all good memories to take home when you are heading back from Madrid and from our 70th anniversary congress.



Gerd R. Burmester
President of EULAR

EULAR 2017 Abstracts Reviewers

ABISHEK, Abishek (United Kingdom)
ADACHI, Jonathan D. (Canada)
ALIJOTAS, Jaume (Spain)
ALLANORE, Yannick (France)
AMITAL, Howard (Israel)
AMOURA, Zahir (France)
ARINGER, Martin (Germany)
ASKLING, Johan (Sweden)
ATZENI, Fabiola (Italy)
AVCIN, Tadej (Slovenia)
BAILDAM, Eileen (United Kingdom)
BARALIAKOS, Xenophon (Germany)
BASU, Neil (United Kingdom)
BECKER, Mike O. (Switzerland)
BERESFORD, Michael (United Kingdom)
BERGMAN, Stefan (Sweden)
BERTSIAS, Georges (Greece)
BIERMA-ZEINSTRA, Sita (Netherlands)
BIJLSMA, Johannes W. J. (Netherlands)
BILYY, Rostyslav (Ukraine)
BLANCO, Francisco J. (Spain)
BLÜML, Stephan (Austria)
BODE, Christina (Netherlands)
BOONEN, Annelies (Netherlands)
BOSTRÖM, Carina (Sweden)
BOUMPAS, Dimitrios (Greece)
BREBAN, Maxime (France)
BROWN, Matthew (Australia)
BRUCE, Ian (United Kingdom)
BUCKLEY, Chris (United Kingdom)
CAEYERS, Nele (Belgium)
CALABRESE, Leonard (United States)
CARMONA, Loreto (Spain)
CARREIRA, Patricia (Spain)
CATRINA, Anca (Sweden)
CERVERA, Ricardo (Spain)
CHAPURLAT, Roland D. (France)
CHEVALIER, Xavier (France)
CHIZZOLINI, Carlo (Switzerland)
CHOY, Ernest (United Kingdom)
CIKES, Nada (Croatia)
CLAUDEPIERRE, Pascal (France)
COMBE, Bernard (France)
CONAGHAN, Philip (United Kingdom)
CONSOLARO, Alessandro (Italy)
CONTI, Fabrizio (Italy)
COSTEDOAT, Nathalie (France)
CUTOLO, Maurizio (Italy)
CZIRJÁK, László (Hungary)
DA SILVA, José Antonio P. (Portugal)
D'AGOSTINO, Maria-Antonietta (France)
DALBETH, Nicola (New Zealand)
DAMJANOV, Nemanja (Serbia)
DE KEYSER, Filip (Belgium)
DE PABLO, Paola (United Kingdom)
DE THURAH, Annette (Denmark)
DE WIT, Maarten (Netherlands)
DISTLER, Oliver (Switzerland)
DIXON, William G. (United Kingdom)
DOHERTY, Michael (United Kingdom)
DORIA, Andrea (Italy)
DÖRNER, Thomas (Germany)
EA, Hang-Korng (France)
EHRENSTEIN, Michael (United Kingdom)
ELEWAUT, Dirk (Belgium)
EMERY, Paul (United Kingdom)
ERNESTAM, Sofia (Sweden)
FERREIRA, Ricardo (Portugal)
FILIPPUCCI, Emilio (Italy)
FINCKH, Axel (Switzerland)
FITZGERALD, Oliver (Ireland)
FLEISCHMANN, Roy (United States)
FONSECA, João (Portugal)
FONTES, Francisca (Portugal)
GARROOD, Toby (United Kingdom)
GENSLER, Lianne (United States)
GERLI, Roberto (Italy)
GOBBO MONTOYA, Milena (Spain)
GONZALEZ-GAY, Miguel Angel (Spain)
GOTTENBERG, Jacques-Eric (France)
GUDU, Tania Elena (Romania)
GUILLEMIN, Francis (France)
GÜL, Ahmet (Turkey)
HACHULLA, Eric (France)
HAHN, Bevra (United States)
HAROON, Nigil (Canada)
HAUGEN, Ida Kristin (Norway)
HAY, Elaine (United Kingdom)
HERNANDEZ-RODRIGUEZ, Jose (Spain)
HERRICK, Ariane L. (United Kingdom)
HERRMANN, Martin (Germany)
HETLAND, Merete (Denmark)
HIEPE, Falk (Germany)
HOUSSIAU, Frederic (Belgium)
HUPPERTZ, Hans-Iko (Germany)
HURKMANS, Emalie (Netherlands)
IAGNOCCO, Annamaria (Italy)
INGEGNOLI, Francesca (Italy)
INMAN, Robert (Canada)
IOAN-FACSINAY, Andreea (Netherlands)
IONESCU, Ruxandra (Romania)
ISAACS, John D. (United Kingdom)
ISENBERG, David (United Kingdom)
JACOBSSON, Lennart (Sweden)
JUHL PEDERSEN, Susanne (Denmark)
KAVANAUGH, Arthur (United States)
KAY, Jonathan (United States)
KHANNA, Dinesh (United States)
KILTZ, Uta (Germany)
KIRKHAM, Bruce (United Kingdom)
KITAS, George (United Kingdom)
KJEKEN, Ingvild (Norway)
KLOPPENBURG, Margreet (Netherlands)
KOULOUMAS, Marios (Cyprus)
KOVÁCS, Laszlo (Hungary)
KOWAL-BIELECKA, Otylia (Poland)
KRIEG, Thomas (Germany)
KRISTENSEN, Lars Erik (Denmark)
LANDEWÉ, Robert B. M. (Netherlands)
LEMS, Willem F. (Netherlands)
LEÓN VÁZQUEZ, Fernando (Spain)
LIPMAN, Marc (United Kingdom)
LOZA, Estibaliz (Spain)
LUNDBERG, Ingrid (Sweden)
LUQMANI, Raashid (United Kingdom)
MACFARLANE, Gary J. (United Kingdom)
MACHADO, Pedro (United Kingdom)
MAHLER, Elien (Netherlands)
MAKSYMOWYCH, Walter (Canada)
MALFAIT, Anne-Marie (United States)
MALLEN, Christian D. (United Kingdom)
MANFREDI, Angelo (Italy)
MANNERKORPI, Kaisa (Sweden)
MARIETTE, Xavier (France)
MARTIN IBANEZ, Javier (Spain)
MARZO-ORTEGA, Helena (United Kingdom)
MATUCCI-CERINIC, Marco (Italy)
MCGONAGLE, Dennis (United Kingdom)
MCINNES, Iain B. (United Kingdom)
MEASE, Philip (United States)
MEIER, Florian (Germany)
MOLLOY, Eamonn S. (Ireland)
MOLTÓ, Anna (France)
MÜLLER-LADNER, Ulf (Germany)
MUNOZ, Luis (Germany)
MUNUERA, Pedro (Spain)
NAGY, Gyorgy (Hungary)
NAVARRO-COMPÁN, Victoria (Spain)
NDOSI, Mwidimi (United Kingdom)
NEOGI, Tuhina (United States)
NEUMANN, Elena (Germany)
NURMOHAMED, Michael (Netherlands)
OLOFSSON, Tor (Sweden)
PAGNOUX, Christian (Canada)
PASCUAL, Eliseo (Spain)
PAVELKA, Karel (Czech Republic)
PEREZ-RUIZ, Fernando (Spain)
PERROT, Serge (France)
PETER, Wilfred F. (Netherlands)
PETERSSON, Ingemar (Sweden)
PITZALIS, Costantino (United Kingdom)
PODDUBNYY, Denis (Germany)
PRODINGER, Birgit (Switzerland)
PUTRIK, Polina (Netherlands)
QUARTIER, Pierre (France)

RAHMAN, Anisur (United Kingdom)
RAMIRO, Sofia (Netherlands)
RAMMING, Andreas (Germany)
RANNOU, François (France)
RIEMEKASTEN, Gabriela (Germany)
RITCHLIN, Christopher T. (United States)
RODDY, Edward (United Kingdom)
ROGGE, Lars (France)
ROVERE-QUERINI, Patrizia (Italy)
RUBBERT-ROTH, Andrea (Germany)
RUDWALEIT, Martin (Germany)
SCHETT, Georg (Germany)
SCHIFF, Michael (United States)
SEPRIANO, Alexandre (Portugal)
SHAHRARA, Shiva (United States)
SIEBERT, Stefan (United Kingdom)
SILVA-FERNÁNDEZ, Lucía (Spain)
SMITH, Vanessa (Belgium)
SO, Alexander (Switzerland)
SOKKA-ISLER, Tuulikki (Finland)
SORIANO, Alessandra (Italy)
SOUSA, Elsa (Portugal)
STEEN-CARLSSON, Katarina (Sweden)
SULLI, Alberto (Italy)
SVENUNGSSON, Elisabet (Sweden)
SYRBE, Uta (Germany)
SZEKANECZ, Zoltán (Hungary)
TAAMS, Leonie (United Kingdom)
TAKEUCHI, Tsutomu (Japan)
TAM, Lai-Shan (People's Republic of China)
TAS, Sander W. (Netherlands)
TAYLOR, Peter C. (United Kingdom)
TEN CATE, Rebecca (Netherlands)
TERSLEV, Lene (Denmark)
TINCANI, Angela (Italy)
TROUW, Leendert (Netherlands)
TURESSON, Carl (Sweden)
UHLIG, Till (Norway)
UROWITZ, Murray (Canada)
VALESINI, Guido (Italy)
VAN DEN BOSCH, Filip (Belgium)
VAN DER HEIJDE, Désirée (Netherlands)
VAN DER KRAAN, Peter (Netherlands)
VAN DER LAKEN, Conny (Netherlands)
VAN DER WOUDE, Diane (Netherlands)
VAN GAALEN, Floris A. (Netherlands)
VAN RIEL, Piet L. C. M. (Netherlands)
VAN WIJK, Femke (Netherlands)
VASSILOPOULOS, Dimitrios (Greece)
VEALE, Douglas (Ireland)
VENCOVSKY, Jiri (Czech Republic)
VERSTAPPEN, Suzanne (United Kingdom)
VLIET VLIELAND, Thea (Netherlands)
VOJINOVIC, Jelena (Serbia)
WEDDERBURN, Lucy (United Kingdom)
WIEK, Dieter (Germany)
WINTHROP, Kevin (United States)
WITTOEK, Ruth (Belgium)
WOUTERS, Carine (Belgium)
ZHANG, Weiya (United Kingdom)
ZULIAN, Francesco (Italy)

EULAR wishes to express its sincerest thanks to all abstracts reviewers for their most appreciated collaboration.

Contents

Welcome Address iii
EULAR 2017 Abstracts Reviewers iv

Speakers Abstracts

Speaker Presentations

Wednesday, 14 June 2017

SP0001–SP0004 Joint EULAR - APLAR session: novel animal models - where no researcher has gone before... ... 2
SP0005–SP0008 Health professional welcome session 2
SP0009 WIN & HOT session 3
SP0010–SP0012 Moving towards new criteria in SLE, Sjögren's and APS 4
SP0013–SP0016 The differential diagnosis of diffuse skin sclerosis and of Raynaud's phenomenon and a practical approach to assessment 5
SP0017–SP0018 Controling the balance between cancer and autoimmunity 5
SP0019–SP0021 Fibromyalgia: a disease of the peripheral or central nervous system 6
SP0022 Chondrocyte channels (role in mechanotransduction)or "channeling the chondrocyte" 6
SP0023–SP0024 Wearable technologies in 21st century healthcare 7
SP0025–SP0027 Assessment and management of osteoporosis 7
SP0028–SP0030 Systematic literature review: the link from science to clinical practice 8
SP0031–SP0033 EULAR Campaign: Don't Delay, Connect Today 8
SP0034–SP0036 Standing Committee session on paediatric rheumatology 9
SP0037–SP0040 Ultrasound basic I & II 10
SP0041–SP0043 Rehabilitation and modern drug treatment - needs and challenges 10
SP0044–SP0046 Comorbidities: having one RMD is enough - we don't need anything else 11

Thursday, 15 June 2017

SP0047–SP0049 Cytokines and chemokines 11
SP0050–SP0052 Bringing rheumatology research to the next level: addressing the main challenges of patient partnerships in research and health care service design 12
SP0053 WIN & HOT session 13
SP0054–SP0056 Treat-to-target in axSpA: reality or utopy? 13
SP0057–SP0058 Calcium crystal deposition in rheumatic diseases 14
SP0059–SP0060 Fifty shades of remission in RA 15
SP0061–SP0063 Innate immunity 15
SP0064–SP0066 To be and to become: transition from paediatric to adult care 16
SP0067–SP0068 Heterogeneity in JIA 16
SP0069–SP0070 EULAR - EMA session 17
SP0071–SP0073 Barrier free employment for young people with RMDs 17
SP0074 Epidemiology of rheumatic and musculoskeletal diseases - a critical appraisal 18
SP0075–SP0077 Ultrasound advanced I & II 19
SP0078–SP0079 PsA: an integrated perspective 19
SP0080 Autoinflammatory diseases in children and adults 20
SP0081–SP0083 Immunogenicity of biologics; myth or reality? 20
SP0084–SP0085 Which target / outcome is more relevant in the management of SLE? 21
SP0086–SP0087 Joint EULAR - EFIS session: Tilting the balance: from disease to tolerance induction 21
SP0088–SP0090 What to do about comorbidity? 22
SP0091 Data visualisation: tables and graphs for publication and presentation I & II 23
SP0092–SP0094 Difficult to reach patient groups 23
SP0095–SP0097 EULAR Projects in musculoskeletal imaging 24

SP0098–SP0100	Capillaroscopy I & II	24
SP0101–SP0103	Ultrasound, clinical, diagnostic and therapeutic skills I & II	25
SP0104–SP0105	Macrophage M2 polarization: implications in fibrotizing diseases	26
Friday, 16 June 2017		
SP0106	Mucosal B cells: gatekeepers of immune function	26
SP0107	WIN & HOT session	27
SP0108	Comorbidities in rheumatoid arthritis	27
SP0109–SP0110	Life-threatening presentation of rheumatic diseases	27
SP0111	AxSpA: From bug to gut and to disease phenotype	28
SP0112–SP0114	Pregnancy meets rheumatic patients	28
SP0115–SP0116	Neuronal and hormonal alterations in arthritis	29
SP0117–SP0120	Fighting osteoporosis fragilities	29
SP0121–SP0122	Biological agents in juvenile idiopathic arthritis: open issues	30
SP0123–SP0124	Health equity and economy - a vital relationship	31
SP0125–SP0127	Biomarkers in cardiovascular rheumatology - state-of-the-art 2017	31
SP0128–SP0129	MRI I & II	32
SP0130	WIN & HOT session	32
SP0131–SP0133	What is behind vasculitis?	33
SP0134	Cytokine taxonomy: reflection in the therapy of arthritides and other IMIDs	33
SP0135–SP0137	Regulatory molecules in connective tissue	33
SP0138–SP0140	Patient engagement in research: best practices, benefits, and challenges	34
SP0141–SP0142	RA treatment in patients wanting to become pregnant - interactive session	35
SP0143–SP0144	Latest advances in the treatment and management of psoriatic arthritis and the latest news on the use of Biosimilars in RMDs	35
SP0145–SP0148	From pre-RA to established RA	35
SP0149	Laboratory course - from the clinic to the lab and back II	36
SP0150–SP0151	Switching T on and off: how T cells drive and regulate chronic inflammation	36
Saturday, 17 June 2017		
SP0152–SP0153	Reverse translation - learning from clinical trials in SLE, Sjögren's and APS	37
SP0154–SP0156	Genomic imprinting and post-translational modifications	37
SP0157–SP0158	Optimizing treatment for osteoarthritis: take the phenotype in account "one size does not fit all"	38
SP0159–SP0162	Targeting adipose tissue inflammation	38
SP0163–SP0165	Trials and tribulations of medication adherence	39
SP0166	Outcome in juvenile idiopathic arthritis	40
SP0167	Getting financial support to research in RMDs through horizon 2020: opportunities, good practices, and successful experiences	41
SP0168–SP0171	EULAR Projects - challenging projects in education and training	41
SP0172–SP0174	Workshop: strengthening your organisation - how to manage volunteers	42
SP0175	WIN & HOT session	42
SP0176–SP0177	Systemic sclerosis	42
SP0178	How diet influences musculoskeletal diseases	43
SP0179–SP0180	Can targeting disease activity in hand osteoarthritis improve our treatment in the 21st century	43
SP0181–SP0184	Why we do develop autoimmunity	44
SP0185–SP0188	Closing the gap between objective measures and self-report in fibromyalgia	45
SP0189	Interactive cases from the HOT and WIN sessions	45
SP0190	Suffering in silence. Optimizing the management of psychological well-being for people with RMDs	46
SP0191–SP0194	Showcasing the EULAR Online Course for Health Professionals	46
SP0195	HPR Highlight session	47

Scientific Abstracts

Oral Presentations

Wednesday, 14 June 2017

OP0001–OP0002	Moving towards new criteria in SLE, Sjögren's and APS	50
OP0003–OP0004	Controlling the balance between cancer and autoimmunity	51
OP0005–OP0006	Fibromyalgia: a disease of the peripheral or central nervous system	52
OP0007–OP0008	Chondrocyte channels (role in mechanotransduction) or "channeling the chondrocyte"	53
OP0009-HPR	Wearable technologies in 21st century healthcare	53
OP0010	Assessment and management of osteoporosis	54
OP0011	Systematic literature review: the link from science to clinical practice	54
OP0012-PARE	EULAR Campaign: Don't Delay, Connect Today	55
OP0013–OP0014	Standing Committee session on paediatric rheumatology	55
OP0015–OP0022	Still breaking news on TNF inhibitors in rheumatoid arthritis	56
OP0023–OP0030	Progress in managment of SpA	60
OP0031–OP0038	Early diagnosis of systemic sclerosis and myositis: biomarkers and diagnostic tool	64
OP0039–OP0046	SLE, Sjögren's and APS - clinical aspects	67
OP0047–OP0054	Osteoporosis treatment gap, new options and new strategies	70
OP0055-HPR	Rehabilitation and modern drug treatment - needs and challenges	73
OP0056–OP0063	Basic and clinical science in paediatric rheumatology	74
OP0064–OP0071	Impact of rheumatic diseases	78
OP0072-PARE	Comorbidities: having one RMD is enough - we don't need anything else	81
OP0073–OP0080	Risk factors for developing diseases or comorbidities	82
OP0081–OP0088	Scleroderma, myositis and related syndromes, etiology, pathogenesis	85
OP0089–OP0096	Novel insights in inflammatory mediators	89

Thursday, 15 June 2017

OP0097	Cytokines and chemokines	92
OP0098–OP0105	Progress in biological treatment of RA	92
OP0106–OP0113	PsA: a fascinating disease	96
OP0114–OP0121	More or less imaging in axial SpA?	100
OP0122–OP0129	Clinical and therapeutical news in systemic sclerosis	103
OP0130–OP0137	Vasculitis clinical and pathogenic highlights	107
OP0138-HPR–OP0145-HPR	HPR mind over matter - patients perspectives	110
OP0146–OP0153	RA: really a systemic disease?	113
OP0154–OP0161	Advances in RA and SpA pathophysiology	116
OP0162-PARE–OP0163-PARE	Bringing rheumatology research to the next level: addressing the main challenges of patient partnerships in research and health care service design	119
OP0164–OP0171	Osteoarthritis: new horizons for treatment	119
OP0172–OP0179	Cellular drivers of inflammation in rheumatic disease	123
OP0180–OP0187	Joint health & joint damage: a tale of three tissues	126
OP0188–OP0189	Treat-to-target in axSpA: reality or utopy?	129
OP0190–OP0191	Calcium crystal deposition in rheumatic diseases	130
OP0192	Fifty shades of remission in RA	131
OP0193–OP0194	Innate immunity	131
OP0195	To be and to become: transition from paediatric to adult care	132
OP0196–OP0197	Heterogeneity in JIA	132
OP0198-PARE–OP0199-PARE	Barrier free employment for young people with RMDs	133
OP0200	Epidemiology of rheumatic and musculoskeletal diseases - a critical appraisal	134
OP0201–OP0202	PsA: an integrated perspective	135
OP0203–OP0204	Immunogenicity of biologics; myth or reality?	136
OP0205–OP0206	Which target / outcome is more relevant in the management of SLE?	137
OP0207–OP0208	Joint EULAR - EFIS session: tilting the balance: from disease to tolerance induction	138
OP0209-HPR	What to do about comorbidity?	139
OP0210-PARE–OP0211-PARE	Difficult to reach patient groups	139
OP0212–OP0213	Macrophage M2 polarization: implications in fibrotizing diseases	140

Friday, 16 June 2017

OP0214–OP0215	Mucosal B cells: gatekeepers of immune function	141
OP0216–OP0223	PsA: the options grow!	141
OP0224–LB0003	From classics to new: synthetic DMARDs in RA	146
OP0231–LB0002	New treatments in SLE, Sjögren's and APS	150
OP0238–OP0245	Axial spondyloarthritis from risk factors to clinical outcomes	153
OP0246–OP0253	RA - causes and courses	157
OP0254-HPR–OP0261-HPR	HPR move to improve	161
OP0262–OP0269	Gout: advances in diagnosis and management	164
OP0270–LB0001	Low back pain and fibromyalgia	168
OP0276-PARE–OP0282-PARE	PARE abstract session	171
OP0283–OP0290	Imaging and treamtent response in rheumatology	173
OP0291–OP0298	From genetics through epigenetics to proteomics: understanding disease mechanisms	177
OP0299–OP0306	Innovative insights into mechanism of SLE, Sjögren's and APS	180
OP0307–OP0308	Comorbidities in rheumatoid arthritis	182
OP0309	AxSpA: from bug to gut and to disease phenotype	183
OP0310–OP0311	Pregnancy meets rheumatic patients	184
OP0312–OP0313	Neuronal and hormonal alterations in arthritis	184
OP0314-HPR	Fighting osteoporosis fragilities	185
OP0315–OP0316	Biological agents in juvenile idiopathic arthritis: open issues	186
OP0317-PARE–OP0318-PARE	Health equity and economy - a vital relationship	186
OP0319	Biomarkers in cardiovascular rheumatology - state-of-the-art 2017	187
OP0320–OP0321	What is behind vasculitis?	187
OP0322	Cytokine taxonomy: reflection in the therapy of arthritides and other IMIDs	188
OP0323–OP0324	Personalised care for back pain	188
OP0325–OP0326	Regulatory molecules in connective tissue	189
OP0327-PARE	Patient engagement in research: best practices, benefits and challenges	190
OP0328-PARE	Latest advances in the treatment and management of psoriatic arthritis and the latest news on the use of biosimilars in RMDs	190
OP0329–OP0330	Switching T on and off: how T cells drive and regulate chronic inflammation	191

Saturday, 17 June 2017

OP0331	Reverse translation - learning from clinical trials in SLE, Sjögren's and APS	192
OP0332–OP0333	Genomic imprinting and post-translational modifications	192
OP0334–OP0335	Optimizing treatment for osteoarthritis: take the phenotype in account "one size does not fit all"	193
OP0336	Targeting adipose tissue inflammation	194
OP0337-HPR	Trials and tribulations of medication adherence	194
OP0338	Outcome in juvenile idiopathic arthritis	195
OP0339	Systemic sclerosis	195
OP0340	How diet influences musculoskeletal diseases	196
OP0341–OP0342	Can targeting disease activity in hand osteoarthritis improve our treatment in the 21st century	196
OP0343	Why we do develop autoimmunity	197
OP0344-HPR	Closing the gap between objective measures and self-report in fibromyalgia	198
OP0345-PARE–OP0346-PARE	Suffering in silence. Optimizing the management of psychological well-being for people with RMDs	198
OP0347-HPR	Showcasing the EULAR Online Course for Health Professionals	199

Late Breaking Abstracts

Friday, 16 June 2017

LB0001	Low back pain and fibromyalgia	170
LB0002	New treatments in SLE, Sjögren's and APS	153
LB0003	From classics to new: synthetic DMARDs in RA	149

Poster Presentations

Thursday, 15 June 2017

Guided Poster Tours

T1:	THU0001–THU0010	Genetic basis, egpigenetics an genomics in disease	200
T2:	THU0025–THU0034	Inflammatory mediators in rheumatic disease	208
T3:	THU0068–THU0077	RA disease course and prognosis	224
T4:	THU0168–THU0176	MTX, GCs and JAK inhibitors in RA	265
T5:	THU0216–THU0225	Pathomechanism in SLE, SS, APS	286
T6:	THU0246–THU0257	Novelty in the clinical approach to SLE, Sjögren's and APS I	297
T7:	THU0294–THU0303	Vasculities clinical aspects I	314
T8:	THU0345–THU0354	Progress in managment of spondyloarthritis	334
T9:	THU0401–THU0410	A stroll among the crystals	359
T10:	THU0486–THU0495	Paediatric rheumatology	390
T11:	THU0538–THU0547	Clinicial features and treatment of orphan diseases	410
T12:	THU0596–THU0605	Rheumatology training and disease burden	431
T13:	THU0648–THU0657	Economical impact of biosimilars and sicussing risks with patients	450
T14:	THU0695–THU0704	Outcomes across all rheumatology	470

Posters

THU0001–THU0024	Genomics, genetic basis of disease and HLA / T cell recognition	200
THU0025–THU0067	Cytokines and inflammatory mediators	208
THU0068–THU0115	Rheumatoid arthritis - prognosis, predictors and outcome	224
THU0116–THU0167	Rheumatoid arthritis - comorbidity and clinical aspects	245
THU0168–THU0215	Rheumatoid arthritis - non biologic treatment	265
THU0216–THU0245	SLE, Sjögren's and APS - etiology, pathogenesis and animal models	286
THU0246–THU0293	SLE, Sjögren's and APS - clinical aspects (other than treatment)	297
THU0294–THU0344	Vasculitis	314
THU0345–THU0400	Spondyloarthritis - treatment	334
THU0401–THU0467	Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis	359
THU0468–THU0483	Fibromyalgia	384
THU0484–THU0485	Basic science in paediatric rheumatology	389
THU0486–THU0537	Paediatric rheumatology	390
THU0538–THU0579	Other orphan diseases	410
THU0580–THU0598	Education	425
THU0599–THU0657	Public health, health services research and health economics	432
THU0658–THU0704	Validation of outcome measures and biomarkers	455
THU0705–THU0719	Rehabilitation	474

Friday, 16 June 2017

Guided Poster Tours

F1:	FRI0022–FRI0031	RA stromal cells - reloaded	487
F2:	FRI0129–FRI0138	RA all over the body	529
F3:	FRI0179–FRI0190	TNF inhibitors in RA = always and again	548
F4:	FRI0212–FRI0222, FRI0178	Trends in non-TNF alpha bilogicals for RA I	562, 548
F5:	FRI0255–FRI0265	Novelty in the clinical approach to SLE, Sjögren's and APS II	582
F6:	FRI0303–FRI0312	Vasculities clinical aspects II	601
F7:	FRI0353–FRI0362	Scleroderma and myositis: etiology	620
F8:	FRI0363–FRI0372	Indexes and predictors in systemic sclerosis and myositis	624
F9:	FRI0420–FRI0423, FRI0080–FRI0084	New drivers in RA and SpA pathophysiology	645, 507
F10:	FRI0472–FRI0481	Outcome in AxSpA: does it matter?	665
F11:	FRI0524–FRI0533	Osteoporosis risk assessment and treatment: new tools and new strategies	689
F12:	FRI0582–FRI0591	What's new in orphan diseases	709
F13:	FRI0623–FRI0632	Imaging advances in arthritis - what is new?	724
F14:	FRI0683–FRI0692	Risk factors for RMDs or comorbid conditions	748

Posters

FRI0001–FRI0021	Cartilage, synovium and osteoimmunology	480
FRI0022–FRI0084	Rheumatoid arthritis - etiology, pathogenesis and animal models	487
FRI0085–FRI0128	Rheumatoid arthritis - prognosis, predictors and outcome	509
FRI0129–FRI0177	Rheumatoid arthritis - comorbidity and clinical aspects	529
FRI0178–FRI0211	Rheumatoid arthritis - anti-TNF therapy	548
FRI0212–FRI0254	Rheumatoid arthritis - other biologic treatment	562
FRI0255–FRI0302	SLE, Sjögren's and APS - clinical aspects (other than treatment)	582
FRI0303–FRI0352	Vasculitis	601
FRI0353–FRI0362	Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models	620
FRI0363–FRI0419	Scleroderma, myositis and related syndromes	624
FRI0420–FRI0429, FRI0431	Spondyloarthritis - etiology, pathogenesis and animal models	645, 649
FRI0430–FRI0481	Spondyloarthritis - clinical aspects (other than treatment)	649
FRI0482–FRI0523	Psoriatic arthritis	670
FRI0524–FRI0581	Osteoporosis	689
FRI0582–FRI0622	Other orphan diseases	709
FRI0623–FRI0682	Diagnostics and imaging procedures	724
FRI0683–FRI0731	Epidemiology, risk factors for disease or disease progression	748

Saturday, 17 June 2017

Guided Poster Tours

S1: SAT0010–SAT0019	Innate mediators and autoantibodies in rhematic disease	772
S2: SAT0027–SAT0036	How B and T cells contribute to rheumatic disease	777
S3: SAT0037–SAT0046	RA - risk factors and consequences	781
S4: SAT0088–SAT0097	From the heart of rheumatology	802
S5: SAT0176–SAT0187	Trends in non-TNF alpha bilogicals for RA II	836
S6: SAT0219–SAT0230	New treatment options in SLE, Sjögren's and APS	856
S7: SAT0312–SAT0321	SSc, myositis and rare diseases: etiology and animal models	890
S8: SAT0372–SAT0381	Last news on systemic sclerosis and myositis	911
S9: SAT0433–SAT0441	A walk through PsA progress	935
S10: SAT0483–SAT0494	Steps forward in osteoarthritis research	958
S11: SAT0556–SAT0565	Infection related rheumatic disease: clinical and epidemiologic aspects	987
S12: SAT0609–SAT0618	Imaging advances in vasculitis, crystal and connective tissue disease	1004
S13: SAT0669–SAT0678	Comorbidities and outcomes in RMDs	1027

Posters

SAT0001–SAT0016	Innate immunity in rheumatic diseases	769
SAT0017–SAT0036	Adaptive immunity (T cells and B cells) in rheumatic diseases	774
SAT0037–SAT0087	Rheumatoid arthritis - prognosis, predictors and outcome	781
SAT0088–SAT0139	Rheumatoid arthritis - comorbidity and clinical aspects	802
SAT0140–SAT0175	Rheumatoid arthritis - anti-TNF therapy	821
SAT0176–SAT0218	Rheumatoid arthritis - other biologic treatment	836
SAT0219–SAT0261	SLE, Sjögren's and APS - treatment	856
SAT0262–SAT0311	SLE, Sjögren's and APS - clinical aspects (other than treatment)	873
SAT0312–SAT0324	Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models	890
SAT0325–SAT0381	Scleroderma, myositis and related syndromes	895
SAT0382–SAT0432	Spondyloarthritis - clinical aspects (other than treatment)	916
SAT0433–SAT0482	Psoriatic arthritis	935
SAT0483–SAT0555	Osteoarthritis	958
SAT0556–SAT0582	Infection-related rheumatic diseases	987
SAT0583–SAT0608	Back pain, mechanical musculoskeletal problems, local soft tissue disorders	996
SAT0609–SAT0668	Diagnostics and imaging procedures	1004
SAT0669–SAT0716	Epidemiology, risk factors for disease or disease progression	1027

Abstracts Accepted for Publication

AB0001–AB0009	Genomics, genetic basis of disease and HLA / T cell recognition	1047
AB0010–AB0020	Adaptive immunity (T cells and B cells) in rheumatic diseases	1050

AB0021–AB0025	Innate immunity in rheumatic diseases	1054
AB0026–AB0058	Cytokines and inflammatory mediators	1055
AB0059–AB0075	Cartilage, synovium and osteoimmunology	1067
AB0076–AB0111	Rheumatoid arthritis - etiology, pathogenesis and animal models	1073
AB0112–AB0120	Spondyloarthritis - etiology, pathogenesis and animal models	1085
AB0121–AB0163	SLE, Sjögren's and APS - etiology, pathogenesis and animal models	1089
AB0164–AB0186	Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models	1104
AB0187–AB0188	Basic science in paediatric rheumatology	1112
AB0189–AB0289	Rheumatoid arthritis - prognosis, predictors and outcome	1113
AB0290–AB0373	Rheumatoid arthritis - comorbidity and clinical aspects	1149
AB0374–AB0394	Rheumatoid arthritis - anti-TNF therapy	1179
AB0395–AB0416	Rheumatoid arthritis - other biologic treatment	1186
AB0417–AB0441	Rheumatoid arthritis - non biologic treatment	1196
AB0442–AB0470	SLE, Sjögren's and APS - treatment	1204
AB0471–AB0548	SLE, Sjögren's and APS - clinical aspects (other than treatment)	1215
AB0549–AB0597	Vasculitis	1243
AB0598–AB0682	Scleroderma, myositis and related syndromes	1260
AB0683–AB0708	Spondyloarthritis - treatment	1292
AB0709–AB0736	Spondyloarthritis - clinical aspects (other than treatment)	1302
AB0737–AB0794	Psoriatic arthritis	1312
AB0795–AB0819	Osteoarthritis	1336
AB0820–AB0860	Osteoporosis	1345
AB0861–AB0901	Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis	1357
AB0902–AB0922	Infection-related rheumatic diseases	1371
AB0923–AB0932	Fibromyalgia	1378
AB0933–AB0943	Back pain, mechanical musculoskeletal problems, local soft tissue disorders	1382
AB0944–AB0975	Paediatric rheumatology	1385
AB0976–AB0996	Other orphan diseases	1396
AB0997–AB1074	Diagnostics and imaging procedures	1403
AB1075–AB1115	Public health, health services research and health economics	1431
AB1116–AB1160	Epidemiology, risk factors for disease or disease progression	1446
AB1161–AB1176	Validation of outcome measures and biomarkers	1461
AB1177–AB1182	Rehabilitation	1467
AB1183–AB1194	Education	1469

Health Professionals in Rheumatology Abstracts

Oral Presentations

Wednesday, 14 June 2017

OP0009-HPR	Wearable technologies in 21st century healthcare	53
OP0055-HPR	Rehabilitation and modern drug treatment - needs and challenges	73

Thursday, 15 June 2017

OP0138-HPR–OP0145-HPR	HPR mind over matter - patients perspectives	110
OP0209-HPR	What to do about comorbidity?	139

Friday, 16 June 2017

OP0254-HPR–OP0261-HPR	HPR move to improve	161
OP0314-HPR	Fighting osteoporosis fragilities	185

Saturday, 17 June 2017

OP0337-HPR	Trials and tribulations of medication adherence	194
OP0344-HPR	Closing the gap between objective measures and self-report in fibromyalgia	198
OP0347-HPR	Showcasing the EULAR Online Course for Health Professionals	199

Poster Presentations

Thursday, 15 June 2017

Guided Poster Tours

T15: THU0750-HPR–THU0759-HPR HPR from top to toe; health professional practice 1486

Posters

THU0720-HPR–THU0751-HPR HPR interventions (educational, physical, social and psychological) 1476
THU0752-HPR HPR measuring health (development and measurement properties of PROs, tests, devices) 1487
THU0753-HPR–THU0755-HPR HPR epidemiology and public health (including prevention) 1487
THU0756-HPR–THU0757-HPR HPR patients' perspectives, functioning and health (descriptive: qualitative or quantitative) 1488
THU0758-HPR HPR professional education, training and competencies 1489
THU0759-HPR HPR interventions (educational, physical, social and psychological) 1489
THU0760-HPR–THU0772-HPR HPR service developments, innovation and economics in healthcare 1490

Friday, 16 June 2017

Posters

FRI0732-HPR–FRI0750-HPR HPR measuring health (development and measurement properties of PROs, tests, devices) 1495
FRI0751-HPR–FRI0765-HPR HPR epidemiology and public health (including prevention) 1502
FRI0766-HPR–FRI0772-HPR HPR professional education, training and competencies 1507

Saturday, 17 June 2017

Guided Poster Tours

S14: SAT0717-HPR–SAT0725-HPR Nursing and daily practice 1510

Posters

SAT0717-HPR, SAT0719-HPR, SAT0723-HPR–SAT0724-HPR, SAT0726-HPR–SAT0770-HPR HPR patients' perspectives, functioning and health (descriptive: qualitative or quantitative) 1510, 1511, 1512, 1513
SAT0718-HPR HPR measuring health (development and measurement properties of PROs, tests, devices) 1510
SAT0720-HPR HPR service developments, innovation and economics in healthcare 1511
SAT0721-HPR–SAT0722-HPR HPR epidemiology and public health (including prevention) 1511
SAT0725-HPR HPR interventions (educational, physical, social and psychological) 1513

Abstracts Accepted for Publication

AB1195-HPR–AB1207-HPR HPR measuring health (development and measurement properties of PROs, tests, devices) 1530
AB1208-HPR–AB1214-HPR HPR epidemiology and public health (including prevention) 1534
AB1215-HPR–AB1230-HPR HPR interventions (educational, physical, social and psychological) 1536
AB1231-HPR–AB1241-HPR HPR patients' perspectives, functioning and health (descriptive: qualitative or quantitative) 1542
AB1242-HPR–AB1246-HPR HPR service developments, innovation and economics in healthcare 1546
AB1247-HPR–AB1249-HPR HPR professional education, training and competencies 1548

People with Arthritis and Rheumatism in Europe Abstracts

Oral Presentations

Wednesday, 14 June 2017

OP0012-PARE EULAR Campaign: Don't Delay, Connect Today 55
OP0072-PARE Comorbidities: having one RMD is enough - we don't need anything else 81

Thursday, 15 June 2017

OP0162-PARE–OP0163-PARE Bringing rheumatology research to the next level: addressing the main challenges of patient partnerships in research and health care service design 119

OP0198-PARE–OP0199-PARE Barrier free employment for young people with RMDs 133
OP0210-PARE–OP0211-PARE Difficult to reach patient groups 139

Friday, 16 June 2017

OP0276-PARE–OP0282-PARE PARE abstract session 171
OP0317-PARE–OP0318-PARE Health equity and economy - a vital relationship 186
OP0327-PARE Patient engagement in research: best practices, benefits and challenges 190
OP0328-PARE Latest advances in the treatment and management of psoriatic arthritis and the latest news on the use of biosimilars in RMDs 190

Saturday, 17 June 2017

OP0345-PARE–OP0346-PARE Suffering in silence. Optimizing the management of psychological well-being for people with RMDs 198

Poster Presentations

Thursday, 15 June 2017

Guided Poster Tours

T16: PARE0001–PARE0011 PARE - Poster tour I 1552

Friday, 16 June 2017

Guided Poster Tours

F17: PARE0012–PARE0022 PARE - Poster tour II 1556

Thursday, 15 June to Saturday, 17 June 2017

Posters

PARE0001 Building patient led organisations 1552
PARE0002 Arthritis research 1552
PARE0003 Work and rehabilitation 1552
PARE0004–PARE0007 Patient information and education 1553
PARE0008 Best practice campaigning 1554
PARE0009 Psychosocial support 1555
PARE0010 Arthritis research 1555
PARE0011 Best practice campaigning 1555
PARE0012–PARE0019 Patient information and education 1556
PARE0020–PARE0022 Building patient led organisations 1559

Abstracts Accepted for Publication

AB1250-PARE–AB1251-PARE Patient information and education 1560
AB1252-PARE–AB1253-PARE Best practice campaigning 1560

Author Index 1563

Speakers Abstracts

Speaker Presentations

WEDNESDAY, 14 JUNE 2017

Joint EULAR - APLAR session: novel animal models - where no researcher has gone before...

SP0001 RELEVANCE OF ANIMAL MODELS IN OSTEOARTHRITIS

T. Pap. *Institute of Experimental Musculoskeletal Medicine (IEMM), University Münster, Münster, Germany*

Osteoarthritis (OA) is the most frequent joint disease and a leading cause of disability in the Western world. Currently, we do not have a cure for this degenerative disorder and despite a high individual and socioeconomic demand, available therapeutic strategies have not changed substantially within the last 40 to 50 years, largely involving basic symptomatic control using analgesics and NSAIDS, physiotherapy and behavioural changes, and eventual prosthetic replacement in end-stage disease. While prosthetic joint replacement constitutes an effective surgical treatment option for patients whose joints are irreversibly damaged by OA, demographic development together with altered physical activities in our aging society increasingly demonstrate the limitations of joint replacement surgery as the only real treatment modality. There is, therefore, an urgent requirement for disease modifying drugs that aim to halt OA disease progression during the early stages and potentially to kick start cartilage regeneration. This need is contrasted, however, by a sustained "translational roadblock" in OA research with very few conceptually novel therapeutic approaches on the horizon. Amongst others, this "translational roadblock" results from a general lack in our understanding of how articular chondrocytes as the only cells in joint cartilage acquire and maintain their specific and highly specialised phenotype and how this phenotype changes during OA onset and progression. Investigation of this developmental aspect of disease pathology in OA patients and using human samples has many limitations, which is why animal models remain to constitute a key element of cartilage and OA research. This lecture summarizes the relevance of different animal models for understanding fundamental principles of cartilage homeostasis and remodelling in health and osteoarthritic cartilage degeneration. By focusing on the analysis of chrondrocyte phenotypic stability, it provides examples for how the use of such models can contribute to understanding OA and to the development of new therapeutic strategies for the disease.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7260

SP0002 NOVEL ANIMAL MODELS IN SYSTEMIC SCLEROSIS

X. Yu. *Research Center Borstel, Borstel, Germany*

Systemic sclerosis (SSc) is a severe autoimmune disease with a considerable reduction of life expectancy. Autoimmunity, vasculopathy and fibrosis are three hallmarks of SSc, while the pathogenesis of the disease is largely unknown. Animal models of SSc provide an excellent tool to for exploring the disease pathogenesis of the disease. Aiming to provide a concise and curate updates in the field of animal models of SSc, this lecture will concentrate on emerging novel animal models and highlight new development and their impact on understanding pathogenesis of SSc.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7128

SP0003 NOVEL ANIMAL MODEL IN ARTHRITIS

Y. Iwakura. *Research Institute for Biomedical Sciences, Tokyo University of Science, Chiba, Japan*

We have generated two rheumatoid arthritis (RA) models, human T-cell leukemia virus type I (HTLV-I) transgenic mice and IL-1 receptor antagonist (Ra)-deficient (KO) mice, to elucidate the pathogenic mechanisms of the disease. Both models spontaneously developed arthritis that closely resembles RA in humans. We found that TNF-, but not IL-6-, deficiency suppressed development of arthritis in IL-1Ra KO mice, while IL-6 but not TNF was involved in the development of arthritis in HTLV-I transgenic mouse model. IL-17 plays an important role in both models, suggesting the central role of IL-17 in these RA models.

We found that the expression of C-type lectin receptor (CLR) genes was augmented in the affected joints of these models using DNA microarrays. Dendritic cell immunoreceptor (DCIR) is one of such CLRs with a carbohydrate recognition domain in their extracellular carboxy terminus and an ITIM in its intracellular amino terminus. Because human syntenic locus for the CLR genes is linked to several autoimmune diseases including RA and SNPs in the *Dcir* gene is associated with RA, we have generated *Dcir* KO mice to examine the roles of this gene in the immune system. We found that aged *Dcir* KO mice spontaneously developed autoimmune enthesitis and ankyloses accompanied by fibrocartilage proliferation and ectopic ossification. DCs were excessively expanded in *Dcir* KO mice, causing these mice autoimmunity and also highly susceptible to induced-autoimmune diseases. *Dcir* KO mouse–derived bone marrow cells differentiated into DCs more efficiently than did wild-type BMCs upon treatment with GM-CSF, due to enhanced STAT-5 phosphorylation. Furthermore, we found that IFN-g producing T cells were increased in *Dcir* KO mice and IFN-g enhanced bone and cartilage formation, resulting in the increase of bone volume and aberrant ossification in joints. DCIR is also expressed in osteoclasts and suppresses osteoclastogenesis upon activation. These findings suggest that DCIR plays important roles in both immune system and bone metabolism.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7154

SP0004 PEPTIDYL ARGININE DEIMINASE 4 AND RHEUMATOID ARTHRITIS: FROM HUMAN GENETICS TO MURINE MODELS

K. Yamamoto[1,2]. [1]*The University of Tokyo, Tokyo;* [2]*RIKEN, Yokohama, Japan*

We have previously reported that functional haplotypes of peptidyl arginine deiminase 4 *(PADI4*) are associated with rheumatoid arthritis (RA). We found that transcripts of the risk haplotype of *PADI4* are more stable than those of the non-risk haplotypes, suggesting that increased expression and function of PAD4 (encoded by *PADI4* gene) increase the risk of RA. The association has been confirmed by several studies with different ethnics. Further, we also reported *PADI4* polymorphisms highly predispose male smokers to RA. Since PAD4 catalyzes an arginine residue in a protein to citrulline and anti-citrullinated protein antibodies (ACPA) are highly specific in RA, it has been reasonable to speculate that increased PAD4 is associated with increased citrullinated proteins, leading to the initiations of tolerance breakdown or inflammatory arthritis.

However, the mechanisms of PAD4 involvement turned out to be more complex than previously thought in animal models. In order to investigate the pathological process in detail, we made *Padi4* knockout mice. Decreased severity of experimental autoimmune arthritis wad observed in these mice. Further, we found PAD4 regulates the pro-apoptotic fate of neutrophils, and promotes the expression of pro-inflammatory cytokines in macrophages. These actions could result in the pro-arthritic roles of *PADI4*. Recently, neutrophil extracellular traps (NETs) were reported as an important immune stimulator in RA and SLE, and PADI4 is required for the generation of NETs. Especially, NET-containing immune complex (IC) stimulated plasmacytoid dendritic cells to accelerate the interferon secretion in SLE. Therefore, *PADI4* could play several different roles in the immune system and also in the pathogenesis of autoimmune diseases.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7136

WEDNESDAY, 14 JUNE 2017

Health professional welcome session

SP0005 LOOKING BACK AT 70 YEARS OF EULAR AND 30 YEARS OF HP INVOLVEMENT: A REHABILITATION PERSPECTIVE

T. Vliet Vlieland. *Orthopaedics J11-R, Leiden University Medical Center, Leiden, Netherlands*

The medical treatment of people with rheumatic and musculoskeletal diseases (RMDs) has improved enormously over the past decades. As medical treatment is not completely successful or available for all rheumatic conditions or individual patients, and the demands society imposes on people to participate fully are increasing, there is a substantial proportion of people with RMDs who have functional disabilities.

Health professionals (HPs) play an essential role in the management of people with RMDs with disabilities by enabling to reach and maintain their optimal physical, sensory, intellectual, psychological and social functional levels. They provide people with the tools they need to attain independence and self-determination. As such, their contribution is in line with the World Health Organisation definition of rehabilitation [http://www.who.int/topics/rehabilitation/en/]. An important feature of rehabilitation is its multidisciplinarity. Over the past decades, it has been more and more acknowledged that HPs' role in the management of people with RMDs concerns a team effort rather than the summation of single interventions by individual HPs or specific professions. This view is reflected in multiple guidelines and standards of care for the clinical management of RMDs, where the need for people with RMDs to have access to a multidisciplinary team of HPs is underlined.

The acknowledgement of the importance of the team of HPs runs in parallel with developments in the organization and activities of HPs within EULAR over the past years.
In connection with EULAR, there is a growing network of HPs from multiple professions across Europe. By working together, and collaborating with patients and rheumatologists and other physicians, EULAR HPs have achieved multiple milestones with respect to the quality of clinical care, education, and research over the past years and are equipped to encounter future challenges.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7181

SP0006 LOOKING BACK AT 70 YEARS OF EULAR AND 30 YEARS OF HP INVOLVEMENT: A NURSING PERSPECTIVE

J. Hill[1,1]. *Retired, -Harrogate, United Kingdom*

At the 1987 EULAR Congress held in Athens, a British nurse, Vicky Stephenson, arranged a meeting that was attended by about 30 health professionals. The meeting decided that a working group of Health Professionals from different professions and countries should work towards establishing a Standing Committee within EULAR. This was achieved in 1989 and since that time, the role of Health Professionals within EULAR has changed dramatically.
In this lecture, I will describe the evolution of rheumatology nursing over the past thirty years, and the part that EULAR has played in the dissemination, education and facilitation of best nursing practice and experiences within Europe. This will be illustrated by two pieces of work. In late 2009, EULAR part funded a Web-based survey to evaluate the status of extended roles undertaken by health professionals in Europe. The data from this survey relating to nursing has been extracted and analysed separately and will be presented. The following year, EULAR also funded a study to investigate the role of the nurse in the management of chronic inflammatory arthritis. The important recommendations resulting from this piece of work will also be shown.
Following the recommendations project, a number of other important nursing initiatives have been launched under the auspices of EULAR. These will be highlighted to enable delegates to understand how far rheumatology nursing has developed and how far it still has to go.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7130

SP0007 70 YEARS PAST AND A VIEW OF THE FUTURE: LOOKING BACK AND LOOKING FORWARD

H.W. Bijlsma. *Department of Rheumatology & Clinical Immunology, University Medical Center, Utrecht, Netherlands*

In 1913 the Dutch general practitioner Jan van Breemen, moved by the needs of the many disabled people in his practice, started an international cooperation to fight rheumatic and musculoskeletal diseases. His initiative led to the formation of the International League Against Rheumatism (ILAR), and subsequently to the formation of regional Leagues, such as EULAR in 1947.
EULAR has in the following 70 years developed into a unique organisation of rheumatologists, scientists, health professionals and patients, who together are aiming *to reduce the burden of rheumatic diseases on the individual and society and to improve the treatment, prevention and rehabilitation of musculoskeletal diseases. To this end, EULAR fosters excellence in education and research in the field of rheumatology. It promotes translation of research advances into daily care and fights for the recognition of the needs of people with RMDs by the governing bodies in Europe* (EULAR mission statement 2005).
The first European Rheumatology Congress was held in September 1947 in Copenhagen and was attended by 200 delegates from 16 countries. At the EULAR 2017 Madrid Congress over 14.000 attendees are expected, coming from more than 120 countries.
EULAR is unique in the sense that three pillars work closely together in one organization: rheumatologists, health professionals and patients. Today, I want to focus a bit on the health professionals pillar, since this pillar has its formal 30 years jubilee in 2017 as well. At the American celebration of 50 years of non-physician health professionals in Rheumatology (2015), Brady described three science-driven practice paradigm shifts that play an important role in managing patients with RMDs: 1.The widely used “Self-management programs”, that were developed from information giving and ’patient education’. 2.The positive and intensive use of “Exercise and physical activity”, that were developed from previous acclaimed bed rest and assisted range of motion exercises. 3. The OMERACT initiated definitions and applications of Patient-reported outcome measures, instead of only biomedical assessment of disease activity.
In addition, she recognized two “evolutions in practice”: 1.Understanding Psychological Factors, from accepting “the arthritic personality” to actively addressing depression, anxiety, coping skills, sense of control and confidence. 2. The development of the important role that nurses and other health professionals can play in the treatment of patients with RMDs.
The EULAR health professionals can be very proud of the important part that Europeans have played in these worldwide developments.
My priorities as president-elect of EULAR for the coming two years are:
- Further development of the School of Rheumatology
- Large public awareness campaign: Don’t delay, Connect today
- New EULAR Strategy 2018–2023

I hope and expect that the pillar of health professionals will take an active role in the cooperation that is necessary to reach our common goals.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7105

SP0008 THE FUTURE FOR HEALTH PROFESSIONALS IN RHEUMATOLOGY

A. De Thurah[1,2]. *[1]Department of Clinical Medicine, Aarhus University; [2]Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark*

In recent years the prevalence of rheumatic diseases has raised leading to increased outpatient activity; at the same time, a general lack of rheumatologists has been described (1). This has created new demands from patients and the health care system towards innovative models of care, e.g. nurse-led follow-up (2), direct access strategies (3) and tele-health interventions (1). In the future this will call for extended and specialized roles for health-professionals within rheumatology, and for future development of compatibility of training of health professionals within the European countries.
Further, the current health-service development is confronting the population with increasing demands to understand and utilize health information and to navigate through this increasingly complex healthcare system. It requires that patients are capable of understanding and managing their health, and calls upon a strong focus on health-literate (HL) skills, and the formation of so-called HL organizations (4). In the future, health professionals within rheumatology will have a key role in supporting the development of HL responsive organizations through self-management strategies and patient centered care.
The present presentation will address some of these future demands for health professionals in Rheumatology
References:
[1] Ward IM, Schmidt TW, Lappan C, Battafarano DF. How critical is tele-medicine to the rheumatology workforce? Arthritis Care Res (Hoboken). 2016 Feb 11.
[2] Primdahl J, Sorensen J, Horn HC, et al. Shared care or nursing consultations as an alternative to rheumatologist follow-up for rheumatoid arthritis outpatients with low disease activity–patient outcomes from a 2-year, randomised controlled trial. Ann Rheum Dis. 2014 Feb;73(2):357–64.
[3] Hewlett S, Kirwan J, Pollock J, et al. Patient initiated outpatient follow up in rheumatoid arthritis: six year randomised controlled trial. BMJ. 2005 Jan 22;330(7484):171.
[4] Health Literacy; the solid facts. World health Organization, Regional Office [Internet]. 2013. Available from: http://www.euro.who.int/__data/assets/pdf_file/0008/190655/e96854.pdf.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7155

WEDNESDAY, 14 JUNE 2017

WIN & HOT session

SP0009 WHAT IS NEW (WIN) IN PSORIATIC ARTHRITIS

R. Lories. *Skeletal Biology and Engineering Research Center, Dept. of Development & Regeneration, KU Leuven, Leuven, Belgium*

Novel therapies and targets have transformed the management of psoriatic arthritis and related skin disease psoriasis. The successful introduction and widespread use of anti-IL17, anti-IL12/23 and anti-PDE4 strategies have joined the ranks of TNF inhibitors. Novel biological insights into specific disease mechanisms are co-emerging with this new wave of treatment options. The different available treatments allow the community to further focus on optimal patient management aiming at remission or minimal disease activity. Yet, the assessment of the patient and his/her satisfaction with current health status remains challenging. Treat to target initiatives are trying to define optimal care and cure adapted to the specific characteristics of the disease. Molecular knowledge of the disease processes remains scattered and insufficient to build a comprehensive view on the disease for the individual patient that would allow the personalized definition of effective strategies.
Disclosure of Interest: R. Lories Grant/research support from: Celgene, Boehringer-Ingelheim, UCB, Consultant for: Janssen, Celgene, Novartis, Pfizer, UCB, Abbvie, Speakers bureau: Janssen, Celgene, Novartis, Pfizer, Merck, UCB, Abbvie
DOI: 10.1136/annrheumdis-2017-eular.7259

WEDNESDAY, 14 JUNE 2017

Moving towards new criteria in SLE, Sjögren's and APS

SP0010 CLASSIFICATION OF SLE – CHALLENGES AND POTENTIAL SOLUTIONS

M. Aringer on behalf of SLE Classification Criteria Steering Committee. *Medicine III, University Medical Center TU Dresden, Dresden, Germany*

Systemic lupus erythematosus is characterized by a wide variety of autoantibodies, which, if pathogenic, can lead to inflammation, damage, thrombosis or functional defects of essentially all organ systems. The 1982 American College of Rheumatology classification criteria and their 1997 revision have greatly influence the disease concept over the last decades. With the at least 4 out of 11 criteria to be present, they essentially depict the concept of multiple autoantibodies and multiple organs systems. Putting all items on equal weight made the system relatively easy to use and to memorize, but this approach was not entirely intuitive. Dermatologists have criticized that patients could meet the criteria based on fulfilling all 4 mucocutaneous criteria only. Importantly, sensitivity was felt to be suboptimal, reaching 83% in the cohort of the SLE International Collaborating Clinics (SLICC) group, and lower values in very early disease.

The 2012 SLICC SLE classification criteria introduced two new concepts. First, patients have to be positive for autoantibodies, namely for anti-nuclear antibodies (ANA) or antibodies to double-stranded DNA. Second, if patients are autoantibody-positive, classification criteria can be fulfilled by nephritis on histology without any other items. The SLICC groups also introduced large lists of skin and neuropsychiatric symptoms and refined some of the definitions. While many of these ideas are intuitively correct, not all were derived in a pre-defined scientific way. These criteria managed to increase sensitivity to 97% in their own validation data and to a range of 92–99% in other cohorts. At the same time, however, the SLICC set lost specificity, falling to 84% as compared to the 96% of the ACR criteria. This trade-off was presumably influenced by the SLICC group's choice to keep the overall structure the same. Early disease sensitivity was still not optimal.

In a large transatlantic project jointly supported by EULAR and the ACR, we have over the last years tried to develop (even) better SLE classification criteria. The main goals are to have a relatively intuitive set that helps in teaching, increase sensitivity as compared to the ACR criteria, but maintain specificity in the same range, improve the performance in early SLE, involve the larger SLE community as far as possible, and do this in a strictly scientific way. Given that ANA often are the door to SLE in the diagnostic approach, and that ANA have very high sensitivity, but modest specificity for SLE, we explored whether ANA could be used as an entry criterion. Meta-regression, after compiling ANA data of 13,080 SLE patients from a systemic literature search, gave a sensitivity of 97.8% (CI 96.8–98.5%) for a titer of at least 1:80 on HEp2-ANA immunofluorescence. It was therefore decided that HEp2-ANA of $\geq$1:80 would be used as an entry criterion.

Three different approaches were used to maximize the overview on potential items, namely an SLE expert Delphi exercise involving 123 SLE experts, an international early disease cohort with 389 SLE patients and 227 patients with conditions mimicking SLE, and a patient survey, which 339 SLE patients filled out and mailed anonymously. The resulting 41 items were then reduced in a nominal group technique exercise with 7 international SLE experts, resulting in a list of 20 items plus ANA as an entry criterion. These items were then submitted to multi-criteria decision analysis in a two day conference with 6 international experts together with the steering committee. This approach under the same moderator (Dr. Ray Naden) had already been successfully used for the rheumatoid arthritis and systemic sclerosis criteria.

The present results are 20 weighted items, which can be additively used within a continous scale, and a cut-off for classification. Weights for class III or IV lupus nephritis are much higher than for leukopenia or unexplained fever. This candidate system will now be tested against both the ACR and the SLICC criteria in a large cohort of SLE patients and patients with mimicking conditions. If successful, ANA of $\geq$1:80 and weighted criteria will lead to better performance, particularly in early disease, and give us a system that is hopefully intuitive enough to convey an idea of the disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7303

SP0011 SJÖGREN'S CRITERIA REVISITED!

S.J. Bowman. *University Hospital Birmingham Rheumatology Dept, Birmingham, United Kingdom*

In clinical practice it is up to the clinician to use their judgement in making a diagnosis of pSS. In research it is essential to have agreed classification criteria so that there is confidence that participants in a study have the specified condition. During the 1980's a number of classification criteria were proposed with a major debate as to the advantages and disadvantages of each of these criteria.

In 1988 a working group of 29 experts from 12 European countries initiated a study to develop consensus criteria. They published their initial findings in 1993 and in 2002 Vitali et al published the American European Consensus Group Criteria (AECG). The AECG criteria have been the most widely used "gold-standard" criteria for the classification of pSS in research studies. Criteria are never fixed in perpetuity, however, and as new technology such as ultrasound becomes more widely used or new data becomes available further revision is likely. In 2013, an International Collaboration, the Sjögren's International Clinical Collaborative Alliance (SICCA) funded by the National Institutes for Health in the USA collected data from 1618 participants to devise the American College of Rheumatology (ACR) preliminary criteria for SS and in 2016 following a further international consensus group exercise the American College of Rheumatology – European League against Rheumatism (EULAR) consensus criteria for Sjögren's syndrome have been published.

In this presentation I will go through the development of these criteria, the underlying rationale and by the end of the talk attendees should have a better understanding of how these criteria can be used in research and to support clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7290

SP0012 ADVANCED APS CRITERIA 2016/2017

P.L. Meroni. *Rheumatology, ASST G Pini - Res. Lab Immunorheumatology, Ist. Auxologico Italiano, University of Milan, Milan, Italy*

The classification of the anti-phospholipid syndrome (APS) is based on the occurrence of arterial/venous thrombotic events and/or pregnancy complications with no identifiable causes in the persistent presence of medium/high titres of anti-phospholipid antibodies (aPL) detectable by solid phase (anti-cardiolipin – aCL or anti-beta2 glycoprotein I – ab2GPI) tests and/or PL-dependent functional coagulation assays (lupus anticoagulant – LA). These classification criteria are currently also used as diagnostic tools.

aPL represent a risk factor, consequently the presence of two/three positive diagnostic laboratory tests is a valuable parameter to stratify the patients at highest risk for developing the syndrome/recurrences.

The syndrome displays a protean clinical picture depending on the involved tissue/organ. The majority of the clinical (criteria) manifestations are clearly related to vascular ischemic events. However some manifestations apparently cannot be supported by a thrombotic mechanism and alternative pathogenic pathways have been suggested. This is the case for thrombocytopenia, central nervous system involvement such as movement disorders and cognitive abnormalities, and APS nephropathy. Heart valve disease, skin ulcers and livedo reticularis are also frequent events in APS patients and their relationship with vascular thrombosis is unclear. Still debated is the suggestion to include these manifestations as additional clinical diagnostic criteria. The possibility to use all these criteria for ranking the patients as having a definite (standard clinical criteria) or probable APS (non classification criteria) is also debated.

The revised criteria for obstetric morbidity comprise otherwise unexplained pregnancy loss. Some of the obstetric criteria might display low sensitivity/specificity for APS. In particular the attribution to aPL of a pregnancy wastage early on gestational course requires the exclusion of a myriad of ethiologies. Conversely, the rate of late foetal losses is very low, making this criterion rather specific. Placenta-mediated obstetric complications provide another critical field: pre-eclampsia and intra-uterine growth restriction are relatively common. To enhance the specificity for APS, the classification criterion included only cases requiring delivery before 34 weeks of gestation. Medium/high aPL titres and double/triple laboratory tests positivities confer a higher risk for pregnancy complications but recent data seem to suggest that also persistent low aPL titres can be predictive for a negative pregnancy outcome. This finding has been recently explained by the availability of large amounts of b2GPI in tissues of the reproductive system. Even though classification criteria have allowed uniformity in APS diagnosis, there still remain some controversies.

The field of the laboratory classification criteria is even more in progress. Epitope profiling for anti-b2GPI antibodies is quite promising since the characterization of reactivity against the domain 1 of the molecule appears to display a higher specificity for APS and stronger predictive value than the antibodies against the whole molecule. However, anti-domain 1 assay is less sensitive and cannot replace the standard test at the moment. Antibodies against prothrombin (PT) have been reported to be associated with both the vascular and the obstetric APS, in particular when the antibodies are detectable against a solid phase complex of PT with phosphatidylserine (PS) (the so called anti-PS/PT assay). However a clear evidence for their usefulness in the clinical diagnosis and risk stratification for APS patients as well as their true pathogenic role is still debated.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7276

WEDNESDAY, 14 JUNE 2017

The differential diagnosis of diffuse skin sclerosis and of Raynaud's phenomenon and a practical approach to assessment

SP0013 WIDESPREAD CUTANEOUS THICKENING – COULD THIS BE EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS?

A. Suarez. *Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom*

A case of diffuse sclerosing skin disease shall be presented. The features that initially led the treating team to consider a diagnosis of systemic sclerosis shall be discussed, alongside subsequent features that emerged that cast doubt over this diagnosis and led the team to undertake additional investigative studies. The presentation shall provide a chronological description of the clinical features, laboratory studies, microvascular imaging and histological studies that helped the team to reach a definitive diagnosis and plan management accordingly.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7183

SP0014 THE DIFFERENTIAL DIAGNOSIS OF DIFFUSE SCLEROSING SKIN DISEASE AND A PRACTICAL APPROACH TO ASSESSMENT

J. Pauling[1,2]. *[1]Pharmacy and Pharmacology, University of Bath; [2]Rheumatology, Royal National Hospital for Rheumatic Diseases (Royal United Hospitals), Bath, United Kingdom*

The differential diagnosis for sclerosing skin disease is broad but there are clinical and laboratory features that can help guide clinicians to the correct diagnosis. This presentation shall provide a comprehensive review of the spectrum of sclerosing skin disease. A practical approach to interpreting the clinical, serological, microvascular imaging and histological features that can help differentiate disease states shall be presented to provide rheumatologists with a practical approach to the assessment of patients with sclerosing skin disease. Case histories shall be used to illustrate the pertinent clinical features and investigative approaches that can help distinguish systemic sclerosis from other sclerosing skin conditions such as scleroedema, pan-sclerotic morphoea, lipodermatosclerosis and chronic graft versus host disease. A specific focus shall be placed on the role of autoantibodies in the diagnosis of systemic sclerosis, including recent work reporting the presence of novel systemic sclerosis-specific autoantibodies in patients with antinuclear antibody-negative diffuse cutaneous systemic sclerosis.
Disclosure of Interest: J. Pauling Grant/research support from: Actelion pharmaceuticals, Consultant for: Actelion pharmaceuticals, Speakers bureau: Actelion pharmaceuticals
DOI: 10.1136/annrheumdis-2017-eular.7132

SP0015 NEW ONSET RAYNAUD'S PHENOMENON – COULD THIS BE EARLY LIMITED CUTANEOUS SYSTEMIC SCLEROSIS?

M. Hughes. *The University of Manchester, Greater Manchester, United Kingdom*

A case shall be presented of a patient with Raynaud's phenomenon and whether this could be early limited cutaenous systemic sclerosis. The presentation shall describe the clinical features and investigative approaches that helped us reach a diagnosis, with a particular focus on the role for microvascular imaging and the detection of SSc-associated autoantibodies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7173

SP0016 THE DIFFERENTIAL DIAGNOSIS OF RAYNAUD'S PHENOMENON AND PRACTICAL APPROACH TO ASSESSMENT WITH A FOCUS ON IMAGING

A.L. Herrick. *University of Manchester, Manchester, United Kingdom*

Raynaud's phenomenon is the term used to describes episodic vasospasm of the digital vasculature in response to cold exposure and/or emotional distress. The majority of people with Raynaud's phenomenon have primary (idiopathic) Raynaud's phenomenon which is 'benign' in that it does not progress to irreversible digital ischaemia, and is not associated with any underlying disease. Conversely, when Raynaud's phenomenon is secondary to an underlying disease/condition (for example to a systemic sclerosis-spectrum disorder), it can be severe, sometimes progressing to digital ulceration and/or gangrene. Raynaud's phenomenon is often the presenting feature of connective tissue disease and therefore provides a window of opportunity for early diagnosis.
The first step in management of Raynaud's phenemenon is establishing the diagnosis. Is this primary or secondary Raynaud's, and if secondary, then to what? While a careful history and examination are always the first steps, different laboratory tests and vascular imaging studies can be used to reach the correct diagnosis. This presentation will provide practicing rheumatologists with a practical approach to the diagnosis and assessment of Raynaud's phenomenon, focussing on the diagnostic and prognostic role of vascular imaging (including nailfold capillaroscopy and thermography).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7190

WEDNESDAY, 14 JUNE 2017

Controling the balance between cancer and autoimmunity

SP0017 SHARED MECHANISMS IN CANCER AND AUTOIMMUNITY

A. Rosen. *Medicine/Rheumatology, Johns Hopkins University School of Medicine, Baltimore, Md 21205, United States*

Some rheumatic disease autoantibodies are powerful markers of subgroups of patients who have distinct disease phenotypes and trajectories. Of particular interest are markers of several disease subgroups in whom cancer and rheumatic disease onset are clustered together in time. For example, a subgroup of scleroderma patients have coincident onset of cancer and scleroderma. This is observed in scleroderma patients with autoantibodies against the RNA polymerase-3 (POLR3), and more recently with autoantibodies recognizing the minor spliceosome. In autoimmune myopathies, temporal clustering of diagnosis of cancer and myositis is associated with autoantibodies to NXP2 and components of the TIF1 complex. Interestingly, although the incidence of cancer is higher in patients with these autoantibodies, most patients with these autoantibodies manifest cancer, even with extended periods of follow-up. These observations provide an important opportunity to investigate the potential mechanisms which operate at the cancer-immune interface during development of rheumatic diseases.
We have investigated such mechanisms in scleroderma patients with autoantibodies to POLR3 who also had a cancer diagnosed an average of -2.6 years from scleroderma onset. In cancers from these patients, we found genetic alterations of the POLR3A locus in six of eight patients with antibodies to POLR3 but not in eight patients without these antibodies. 3 antibody-positive patients had somatic mutations in POLR3A; 5 patients had loss of heterozygosity at the POLR3A locus. Analyses of peripheral blood lymphocytes and serum suggested that POLR3A mutations sparked cellular immunity and cross-reactive humoral immune responses. These results offer insight into the pathogenesis of scleroderma, and potentially other autoimmune syndromes. They suggest that somatic mutations in autoantigens in different cancers might initiate an immune response to the mutated autoantigen, which spreads to include the wild type version. Tissues (e.g. blood vessels, regenerating muscle) in which specific autoantigens are expressed at high levels, or potentially play critical functional roles, may be particularly susceptible to immune-mediated dysfunction. The results also provide support for the idea that acquired immunity helps to control naturally occurring cancers in patients with autoimmune rheumatic diseases; it is possible that this immune response may sometimes be fully effective, preventing the emergence of cancer.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7165

SP0018 CONTROLING THE BALANCE BETWEEN CANCER AND AUTOIMMUNITY

A. Marabelle[1,2]. *[1]Drug Development Department; [2]INSERM U1015, Gustave roussy, Villejuif, France*

Immunotherapy is revolutionizing cancer therapy with a paradigm shift: antibodies are now designed to target immune cells rather than cancer cells with the aim of stimulating the anti-tumor immune response. Monoclonal antibodies targeted against CTLA-4, PD-1 or PD-L1 and anti-CTLA-4 + anti-PD-1 combinations have shown potent activity with significant improvements in the overall survival of patients. Multiple other immunomodulatory drugs are currently in development. These novel therapies generate immune related adverse events that mimick auto-immune diseases. These side effects represent a major challenge for the implementation of immunotherapy in oncology. The aim of this talk will be to provide an update on the clinical results of combination therapies and discuss the current challenges and perspectives for the future of immuno-oncology.
Disclosure of Interest: A. Marabelle Grant/research support from: BMS, MERUS, Consultant for: ROCHE, GENMAB, PIERRE FABRE, LYTIX, PFIZER, Speakers bureau: ROCHE, MSD, BMS, ASTRA ZENECA
DOI: 10.1136/annrheumdis-2017-eular.7299

WEDNESDAY, 14 JUNE 2017

Fibromyalgia: a disease of the peripheral or central nervous system

SP0019 SIGNS, SYMPTOMS AND CO-MORBIDITIES OF FIBROMYALGIA

R.-D. Treede. *Medical Faculty Mannheim, Heidelberg University, Heidelberg, Germany*

In the beta browser version of ICD11, fibromyalgia is listed as a chronic primary pain syndrome (Treede et al. 2015). It is categorized as chronic widespread pain, and is distinguished from other chronic widespread pain by a) tender point counts (American College of Rheumatology 1990 criteria), or b) psychosocial distress (ACR 2010). Both ACR definitions are problematic for research purposes: mechanisms of tender points are poorly understood, and using distress as inclusion criterion may lead to circular arguments.

Chronic primary pain is characterized by significant emotional distress and functional disability. It is multifactorial: biological, psychological and social factors contribute to the pain syndrome. The diagnosis is appropriate independently of identified biological or psychological contributors unless another diagnosis would better account for the presenting symptoms. Chronic Primary Pain can occur in any body site (face, low back, neck, upper limb, thorax, abdominal, pelvis, urogenital region), or in a combination of body sites (Widespread pain). In general, multiple sites of pain are associated with higher distress and disability than single sites. Chronic Primary Pain is also often associated with sleep disturbance, adverse side effects of treatments (such as medication dependence), and comorbidities (such as depression, anxiety, anger, guilt, fear, and a range of chronic medical conditions).

As part of the research consortium LOGIN we have compared the pathophysiology of fibromyalgia, other chronic widespread pain and chronic localized pain in the lower back. In those datasets, fibromyalgia patients showed higher comorbidity of anxiety and depression and more functional impairment than the other groups (Gerhardt et al. 2016). A deficit in conditioned pain modulation (CPM) was related to the spatial spread of ongoing pain, consistent with the neurobiology of endogenous pain control systems. FMS differed from CWP with respect to psychosocial burden, consistent with the shift in clinical diagnostic criteria. Tender point counts (an evoked pain measure) were still useful to identify the FMS patients (Gerhardt et al. 2017). A study using the childhood trauma questionnaire suggests that early stress exposure is associated nonspecifically with lowered pressure pain thresholds which may be related to tender points (Tesarz et al. 2016).

Experimental sleep deprivation in healthy subjects or rodents leads to symptom profiles reminiscent of fibromyalgia (e.g. widespread hyperalgesia, anxiety), suggesting a potential vicious circle of pain, hyperalgesia and sleep disturbance in fibromyalgia.

In summary, fibromyalgia is a chronic primary pain syndrome characterized by widespread pain and major comorbidities. A combination of predisposition plus an initiating painful event seem to play a role in its genesis; according to the dual hit hypothesis, traumatic events during childhood may contribute to the predisposition.

Supported by the German Federal Ministry of Education and Research (BMBF; LOGIN consortium, FKZ: 01EC1010A and 01EC1010B) and the German Research Foundation (DFG: SFB 1158 Subproject S01).

References:

[1] Gerhardt A, et al. (2016) Clin J Pain 32: 568–579.
[2] Gerhardt A, et al. (2017) Pain: in press.
[3] Schuh-Hofer S, et al. (2013) Pain 154: 1613–1621.
[4] Tesarz J, et al. (2016) Pain 157: 1799–1809.
[5] Treede RD, et al. (2015) Pain 156: 1003–1007.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7289

SP0020 PERIPHERAL PATHOLOGY IN FIBROMYALGIA

C. Sommer. *Department of Neurology, Universitätsklinikum Würzburg, Würzburg, Germany*

The pathophysiology of pain in fibromyalgia is complex. In recent years, an involvement of the thinly myelinated nerve fibers of the A-delta type and the unmyelinated C-fibers has been reported in fibromyalgia patients. Independent research groups have published consistent findings of objective injury to these "small nerve fibers". These included disturbances in function, electrical properties, and morphological integrity of these nerve fibers. While the reasons for this small fiber pathology and its contribution to FMS pain are still unclear, a new research field has emerged that will focus on uncovering the underlying pathophysiology. In this talk, I will summarize current findings and discuss their significance for the understanding of the fibromyalgia syndrome.

Disclosure of Interest: C. Sommer Grant/research support from: Kedrion, Speakers bureau: Baxalta, CSL Behring, Genzyme, Grifols, Pfizer

DOI: 10.1136/annrheumdis-2017-eular.7088

SP0021 CENTRAL PATHOLOGIES IN FIBROMYALGIA

E. Kosek. *Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden*

Fibromyalgia is characterized by widespread, mainly muscular pain that is exacerbated during and following physical activity. Although mechanisms such as muscle ischemia and peripheral nerve fibre pathology have been implicated in fibromyalgia, currently no known peripheral pathology can fully account for the pain. Therefore, the pain in fibromyalgia is most likely explained by a complex interaction between peripheral and central mechanisms. Fibromyalgia patients are characterized by a multimodal, widespread, increase in pain sensitivity and a dysfunction of endogenous pain inhibitory mechanisms. Imaging studies have revealed functional as well as structural cerebral abnormalities in fibromyalgia. During painful stimulation, fibromyalgia patients exhibited an inability to activate cerebral structures associated with the descending pain inhibitory system, i.e., rostral anterior cingulate (rACC) and thalamus[1]. There was no association between depression or anxiety and cerebral processing of evoked pain, indicating segregated mechanisms for mood and pain processing[2]. Furthermore, FM patients had less pain related functional connectivity within the brain's pain inhibitory network and structural changes such as decreased cortical thickness and reduced brain volumes[3]. Longer duration of FM pain was associated with more pronounced functional and structural abnormalities suggesting a time-dependent progress of cerebral pathology, even when controlled for age and mood[3]. In addition, FM patients had elevated interleukin-8 in the cerebrospinal fluid indicating neuro-inflammation[4], possibly due to glia cell activation. Interleukin (IL)-8 is co-localized with translocator protein (TSPO) in glia cells. During glia activation, the production of TSPO is increased and TSPO agonists are involved in the regulation of the expression of IL-8 and it's receptor, thus affecting glia to neuron signalling and central sensitisation. We have recently documented that FM patients who are carriers of the genetic functional polymorphism associated with high TSPO binding affinity report higher pain intensity and more severe fibromyalgia symptoms compared to genetically inferred TSPO low affinity binders and that this genetic polymorphism also affects cerebral pain processing[5]. To our knowledge, this is the first finding of genetic mechanisms associated with symptom severity in FM.

Finally, the effect of different treatments on central pathology in FM will be discussed. Short pain duration was predictive of a positive response to a 12 weeks treatment with a serotonin-noradrenalin re-uptake inhibitor (SNRI)[6]. The degree of symptom improvement and reduced pain sensitivity in SNRI treated FM patients corresponded to the degree of increased pain related activation of cerebral areas associated with pain modulation and the default mode network[6]. In contrast, cognitive behaviour therapy did not affect clinical pain or pain sensitivity but increased activations of cerebral regions implicated in executive cognitive control during painful stimulation and thus likely reappraisal of painful stimuli[7]. Finally, 15 weeks of physical exercise partially normalized resting state activity in FM[8]. The results demonstrated that different treatment modalities affected specific brain mechanisms, indicating that at least some of the cerebral abnormalities in FM are reversible.

References:

[1] Jensen et al. Pain 2009;144:95–100.
[2] Jensen et al. Arthritis Rheum 2010;62(11):3488–3495.
[3] Jensen et al. Arthritis Rheum. 2013 Dec;65(12):3293–303.
[4] Kosek et al. J Neuroimmunology, 2015 Mar 15;280:49–55.
[5] Kosek et al. Brain Behav Immun. 2016 Nov;58:218–227.
[6] Jensen et al. J Pain, 2014 Dec;15(12):1328–37.
[7] Jensen et al. Pain 2012:153(7):1495–503.
[8] Brain Connect, 2015 Aug 18;9:134–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7142

WEDNESDAY, 14 JUNE 2017

Chondrocyte channels (role in mechanotransduction)or "channeling the chondrocyte"

SP0022 TRPA1 CHANNELS IN OSTEOARTHRITIS

E. Moilanen. *The Immunopharmacology Research Group, University of Tampere, Tampere, Finland*

Osteoarthritis (OA) has long been viewed as a degenerative "wear-and-tear" disease of cartilage. There is, however, increasing evidence to confirm that inflammation has a critical role in the pathogenesis and symptoms of the disease. Inflammation in osteoarthritis is distinct from that typical for rheumatoid arthritis; it is generally low-grade in its nature but characterized by exacerbations with joint effusions and more severe symptoms. Osteoarthritis shares many features of innate immunity but the inflammatory mechanisms eventually leading to anatomical and functional changes and symptoms typical for osteoarthritis are not known in detail; but their further understanding is essential for the development of disease-modifying treatments for osteoarthritis.

Transient receptor potential ankyrin 1 (TRPA1) is a ligand-gated membrane-bound cation channel. It has been widely studied in sensory neurons where it acts

as a chemosensor for harmful exogenous compounds and mediates pain and neurogenic inflammation. More recently, TRPA1 has been found to be activated also by endogenous compounds formed in inflammation, such as reactive oxygen and nitrogen species. That prompted us to investigate the role of TRPA1 in inflammatory conditions including osteoarthritis.
Monosodium iodoacetate (MIA) -induced arthritis is a widely used animal model of osteoarthritis. We found that MIA evoked acute inflammation, degenerative cartilage changes and joint pain in wild type mice; but interestingly, those responses were significantly attenuated in TRPA1 deficient animals. Furthermore, TRPA1 was found to be expressed and inducible by inflammatory factors including IL-1 and IL-17 in primary human OA chondrocytes; and the TRPA1 channel was shown to be functional based on calcium influx assays. Pharmacological inhibition and genetic depletion of TRPA1 downregulated the production of inflammatory factors and MMP enzymes in mouse cartilage and primary human OA chondrocytes.
The present results introduce TRPA1 as a plausible factor involved in the pathogenesis of OA and provide a novel target for analgesic and anti-inflammatory drugs with disease modifying potential in OA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7275

WEDNESDAY, 14 JUNE 2017

Wearable technologies in 21st century healthcare

SP0023 REVIEW OF WEARABLE TECHNOLOGIES

A.M. Clarke-Cornwell. *School of Health Sciences, The University of Salford, Manchester, United Kingdom*

Working environments have in recent times become less physical with the increase in sedentary, computer-based occupations. Sedentary time is known to be associated with a number of health-related outcomes, including obesity, heart disease, diabetes, cardiometabolic risk factors, some cancers and early mortality, independent of physical activity. There is limited research that has examined sedentary time and physical activity and associations with musculoskeletal conditions, despite these being responsible for the majority of work-related ill health and days absent from work.
The validity and practicality of objective and subjective techniques to measure physical behaviour have been widely reported; however, there is no gold standard that is valid, accurate, reliable and also practical. Self-reported methods can be practical and low-cost, but are subject to recall and social desirability bias; whereas objective devices, such as accelerometers, can be expensive, but allow for information on intensity, frequency and duration of activity to be measured.
The Health Survey for England 2008 used both subjective and objective measures of physical activity: they found that 39% of men and 29% of women were meeting the recommended levels of physical activity when asked via a questionnaire. In comparison, when physical activity was objectively measured using an accelerometer, it was found that only 6% of men and 4% of women met these targets.
Wearable technologies, including research grade accelerometers (e.g. activPAL™) and consumer wearables (e.g. FitBit), are increasingly being used in research, not only to measure physical behaviours but may also be useful in facilitating and monitoring behaviour change. This work will present an overview of wearable technologies used in research, what they can (and can't) measure, and in particular their application in musculoskeletal research.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7177

SP0024 WEARABLE TECHNOLOGIES IN RESEARCH AND CLINICAL TRIALS

M. Mc Carthy. *IT Innovation, Icon Plc, Dublin, Ireland*

The use of wearable technology in clinical trials has the potential to be one of the most disruptive innovations in drug development. The cost and duration of the current clinical trial design has been under scrutiny for a number of years with the sustainability of the exiting model under question. A critical success factor is adequate patient recruitment and retention. Recent initiatives to redesign the clinical trial process have focused on the creation of trials that are more patient focused. A wealth of medical grade physiological data is now readily available from wearable technology, with the potential to create a new future where patients no longer have to visit research sites and where real-time data are available remotely.
However, integrating wearables into a clinical trial is more complex than simply giving the patient a smartwatch and spontaneously generating clinically relevant data. Focusing on technology and sandwiching it into a trial is not a best practice. Wearables need to be viewed as a component of an overall patient-centric strategy rather than solutions in themselves. When creating a remote trial, simply shifting the burden from the sites to the patients, requiring them to carry out a number of tasks in an unsupported, uncontrolled environment is neither welcome nor sustainable. The process for successful selection and integration of wearables needs to take a number of criteria into consideration; clinical hypotheses, the value that is gained by the inclusion of wearables, the robustness of the data generated by the devices, and ensuring that the data adds clarity not additional complexity to the trial.
The re-engineering of the clinical trial to create a patient focused trial goes beyond mere convenience. Wearables and sensor have the potential to generate digital maps of individual's physical behaviours. Wearable technology is facilitating the remote capture of real life data but also has the potential to create new end points and outcome measures that are meaningful to the patient and could hold the key to a new clinical trials paradigm.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7160

WEDNESDAY, 14 JUNE 2017

Assessment and management of osteoporosis

SP0025 THE USE OF BIOMARKERS FOR OSTEOPOROSIS CLINICS

K. Akesson. *Clinical Sciences Malmö, Lund University, Malmö, Sweden*

The balance between bone resorption and bone formation is maintained through a complex regulatory system of systemic and local factors acting on bone cells, such as calcium regulating and sex hormones, growth factors and cytokins. Furthermore, the competence of the bone cells and the number of active cells will determine the production of bone matrix proteins, while other incompletely understood intrinsic mechanisms will determine mineralization and micro-structure. Exposure of the matrix after osteoclastic activation allows for proteolytic enzymes to commence the degradation of the collagenous structure. The signals responsible for termination of bone resorption and initiation of bone formation (coupling) are not yet completely understood. Nevertheless, a tight coupling between resorption and formation is required to maintain bone mass and to preserve the micro-architectural integrity of bone.
Based on this knowledge markers of bone metabolism have been developed. These markers have been evaluated in terms of their ability to predict fracture, change in bone mass, and response to pharmacological treatments in clinical trials and additionally to monitor treatment in clinic.
The lecture will cover the use of markers in clinical trial, interpretation of change in markers from currently available and potential new drugs and to what extent and how to best apply in clinic.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7296

SP0026 NOVEL IMAGING TECHNIQUES FOR ASSESSING OSTEOPOROTIC FRACTURE RISK

R. Chapurlat[1,2]. [1]*Université de Lyon;* [2]*Medicine, INSERM UMR 1033, Lyon, France*

The measurement of areal bone mineral density (aBMD) by dual x-ray absorptiometry (DXA) has been the mainstay for the diagnosis of osteoporosis for at least two decades. The sensitivity and specificity of this test, however, remains suboptimal. For example, more than 50% of postmenopausal women with fragility fracture are not identified with DXA. A great deal of research has been performed recently to develop alternative or complementary imaging techniques to overcome DXA predictive limitations. These techniques are based on the non invasive analysis of bone microarchitecture and estimation of bone strength by finite element analysis (FEA).
Texture analysis uses mathematical models based on fractal analysis to evaluate bone microarchitecture using various types of bone images. The trabecular bone score (TBS) has emerged as an approach that may improve fracture risk prediction. The TBS is based on the texture analysis of the DXA lumbar spine image to quantify bone microarchitecture. Several cohort studies have shown that a subset of individuals could be reclassified with TBS. A meta-analysis results have allowed for incorporation of the TBS in the FRAX score calculation, that is widely available.
The measurement of volumetric BMD with quantitative computerized tomography (QCT) at the hip has been shown to predict fracture risk. These images can also be used to perform FEA that may increase the fracture risk prediction. The additional value of this technique compared with DXA remains to be established in a clinical setting.
Bone microarchitecture can also be assessed at peripheral sites such as the distal radius and tibia using high resolution peripheral quantitative tomography (HRpQCT). Numerous cross-sectional and case-control studies have shown a significant association between prevalent fracture and bone microarchitecture and estimated bone strength assessed with FEA. The bone parameters measured at distal sites are also associated with fractures at distant sites, e.g., the vertebrae and the femoral neck. In a recent prospective study, bone microarchitecture at the distal radius - especially the trabecular vBMD - has been associated with incident osteoporotic fracture. The FEA models were also predictive of fragility fracture. The best models and the most appropriate architectural parameters - whether they are trabecular of cortical - remain to be dissected out and their comparative diagnostic value with aBMD by DXA remains to be established.
The measurement of the TBS may allow for reclassification of a subset of

postmenopausal women at higher risk for fracture whereas they display a moderately reduced aBMD. Hip QCT and HRpQCT may also improve the prediction for fracture, but they are still research techniques.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7232

SP0027 EMERGING THERAPIES FOR OSTEOPOROSIS

P. Geusens. *Rheumatology, MaastrichtUMC and UHasselt, Genk, Netherlands*

Currently, anti-resorptive drug therapy is the cornerstone of fracture prevention. Anti-resorptive drugs decrease bone remodelling, allowing the remaining bone to increase secondary mineralisation, and, with denosumab, also allowing periosteal bone modelling.
Teriparatide is currently the only available bone-forming drug, which increases bone formation more than bone resorption, and has been shown to reduce the risk of vertebral and non-vertebral fractures.
Recently, two randomized clinical trials have been published on the effect of new bone forming agents on the risk of fracture.
Abaloparatide is a 1–34 fragment of PTHrP, with different pharmacokinetics and potential different signalling mechanisms compared to teriparatide. It increases bone formation more than bone resorption, both to a lesser degree than teriparatide. In the double blind, randomised placebo-controlled 18-month ACTIVE study, abaloparatide significantly reduced the risk of vertebral (-86%), clinical (-43%), non-vertebral (-43%) and major fractures (-70%). In a parallel randomised exploratory open-label comparison with teriparatide, bone density increased significantly more with abaloparatide, but the anti-fracture effect was similar, except for a significantly better result on prevention of major fractures.
Romosozumab is a monoclonal antibody that binds sclerostin, which is an inhibitor of bone formation. In contrast to other bone forming agents, it disconnects the increase in bone formation from a decrease in bone resorption. In the double-blind placebo-controlled FRAME study, romosozumab significantly reduced the risk of vertebral (-63%) and clinical fractures (-36%) during the first year, an effect that was maintained by transitioning to one-year denosumab treatment.
The effect on non-vertebral fractures was not significant, but geographic interaction was found. When excluding patients from South America, in whom fracture risk was low, one-year treatment with romosozumab significantly decreased the risk of non-vertebral fractures by 42%.
Abaloparatide and romosozumab are new bone forming agents, with different effects on bone remodelling and remodelling and early effects on clinical fractures. This opens new perspectives in individualised treatment of patients with high fracture risk and for fracture prevention in patients with low bone turnover, multiple vertebral fractures, very low BMD and fractures or bone loss during anti-resorptive treatment.
Disclosure of Interest: P. Geusens Grant/research support from: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Roche, UCB, BMS, Novartis, Consultant for: Amgen
DOI: 10.1136/annrheumdis-2017-eular.7265

WEDNESDAY, 14 JUNE 2017

Systematic literature review: the link from science to clinical practice

SP0028 SYSTEMATIC LITERATURE REVIEW: WHERE TO START

S. Ramiro. *Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

Starting a systematic literature review (SLR), particularly for the first time, may be an overwhelming task. As its designation indicates, it requires a systematic approach, in order to ensure that all the relevant literature addressing the research question at hand is covered and appropriately summarized.
SLRs are particularly helpful for clinicians, who have a question based on their clinical practice and want to obtain the best evidence based answer. The large and increasing amount of existing literature makes the life of a clinician difficult when trying to search by him/herself for the answer based on the original studies. An SLR may thus be an efficient way to get the answer, by condensing hundreds of studies into a good summary. They are also of the basis, together with expert opinion, of diagnostic and/or management/treatment recommendations.
The first step of an SLR is always to properly formulate the research question, in a way that the literature covering the topic can be searched. The classic approach is the PICO framework, in which the formulated question includes the different elements guiding the literature search, namely the Population of interest, the Intervention to which patients are exposed, the Comparator against which the effect of the intervention is to be compared and the Outcomes on which the assessment of the intervention will rely and in which the SLR will focus (e.g. efficacy, safety outcomes, etc).
A crucial aspect when reviewing the literature is the risk of bias assessment. Studies should be judged for their methodological quality so that one can interpret their findings accordingly. If a study is methodologically not sound, then we know that it will not be very helpful in answering the research question and, most important, this cannot be ignored when performing an SLR. This risk of bias assessment also requires some knowledge of important epidemiology and biostatistics concepts, which are needed to correctly understand how a study is conducted.
These and other steps contribute to shaping an SLR. Challenges involved when performing an SLR will be discussed in detail in this presentation, as well as the different steps of an SLR and the most critical aspects that should be considered. Tips from experiences with SLRs will be shared. This should ultimately encourage (young) clinicians and researchers on where to start when embarking on an SLR challenge, but hopefully also on how proceed with and bring to an end a successful and informative SLR.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7140

SP0029 LINKING SCIENCE TO CLINICAL PRACTICE: FROM THE SYSTEMATIC LITERATURE REVIEW TO THE FORMULATION OF RECOMMENDATIONS

R. Landewe. *Rheumatology & clinical immunology, Amsterdam Rheumatology & immunology center, Amsterdam, Netherlands*

Systematic literature review (SLR) is a scientific method to collect the available data in the literature regarding a specific research question, and to compare the quality of different studies, in order to arrive at the best possible answer. SLR is not the same as data-pooling. In contrast to what many clinicians think, SLR is clinical science and not “easy going”, it takes a lot of time and effort, you can make mistakes, and you need to practice and obtain experience. A proper SLR is all but “low hanging fruit”.
Nevertheless, SLRs from the evidence base of guidelines, and as such are integral parts of them.
This lecture will describe how SLRs should be translated into guidelines, and what pitfalls may prevent that the appropriate evidence will be enclosed in recommendations, or that too weak evidence gets a too prominent place.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7212

SP0030 BEYOND THE RECOMMENDATIONS: EXAMPLES OF SYSTEMATIC LITERATURE REVIEW IN DAILY CLINICAL PRACTICE

K. Visser[1,2]. *[1]VU Medical Center; [2]Academic Medical Center, Amsterdam, Netherlands*

Recommendations and guidelines for management and treatment of rheumatic diseases exist to help rheumatologists deliver optimal care for their patients in an evidence-based way. However, not all practical questions and medical difficulties encountered by rheumatologists in daily clinical practice can be addressed using these existing guidelines. Moreover, time in practice is limited and usually does not allow for extensive systematic literature research to find evidence regarding a specific medical question that needs answering in due time. Therefore, an essential skill for doctors and those in training, besides medical knowledge and examination skills, is to be able to search for, withdraw and appraise published evidence applicable to a confined topic. A so called CAT – critically appraised topic – is a compact systematic literature research following a strictly formulated PICO to answer a clinical question encountered in daily practice. Results can be presented in department meetings and stored in a database for education purposes and use in daily practice. This presentation will address the structure, the carrying out, as well as important pros and cons of the CAT. Examples will be given drawn from the experience of young rheumatologists in training in the Netherlands.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7307

WEDNESDAY, 14 JUNE 2017

EULAR Campaign: Don’t Delay, Connect Today

SP0031 HOW COULD GPS ENHANCE THE EARLY DIAGNOSIS OF RHEUMATIC DISEASES

C.D. Mallen. *Arthritis Research UK Primary Care Centre, Primary Care and Health Science, Keele, United Kingdom*

Primary care and general practice has a key role to play in the early and accurate detection of patients with rheumatoid arthritis.
This talk will explore some of the current barriers to best practice, highlighting the workload associated with musculoskeletal problems in primary care and the challenges in making a prompt diagnosis. Possible solutions will be explored, highlighting the importance of strong patient and professional partnerships
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7239

SP0032 THE CONTRIBUTION OF PHYSIOTHERAPISTS TO EARLY DETECTION OF INFLAMMATORY ARTHRITIS

P. Kirwan[1,2]. [1]*Physiotherapy Dept, Connolly Hospital;* [2]*School of Physiotherapy, Royal College of Surgeons in Ireland, Dublin, Ireland*

Early recognition of inflammatory arthritis is of utmost importance, as failure to do so can delay appropriate treatment and result in permanent joint damage and disability. This presentation will set out to explore the role a Physiotherapist/Healthcare Professional can play in recognition of inflammatory joint disease. Healthcare Professionals/Physiotherapists are often the first point of contact for patients suffering from joint/musculoskeletal pain. They are therefore very well positioned to be the first to identify possible inflammatory sources of pain versus non-inflammatory sources. Useful clinical tools which aid in this decision making process will be discussed. The question as to whether a physiotherapist can recognise inflammatory joint disease versus non-inflammatory joint conditions will be explored with the aim being to highlight the important role a physiotherapist can play in this important diagnostic challenge. With reference to ongoing clinical and research work in this field, this presentation will set out to ask whether or not a Healthcare Professional/Physiotherapist can accurately recognise/diagnose inflammatory arthritis and whether they miss inflammatory arthritis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7168

SP0033 THE EULAR CAMPAIGN "DONT DELAY CONNECT TODAY" AND HOW ORGANISATIONS CAN GET INVOLVED

J. Church. *Arthritis Ireland, Dublin, Ireland*

Arthritis is a chronic disease with multiple co-morbidities. With the development of powerful biologic drugs, improvements in care pathways for patients and very effective self-management interventions, early diagnosis and intervention can lead to significant improvements in liefstyle, physical movement, incerased well-being and work force participation. Despite its significant impact on the population and the cost to the economy, Arthritis still remains an underfunded subspecialty within the health systems and one that is shrouded in public myth. The EULAR campaign "Done Delay, Connect Today", aims to promote early intervention by encouraging those with typical symptoms to take action and consult their doctor at the earliest possible opportunity. The campaign which will be adopted and executted across all PARE members also aims to dispel the myths and educate the public about the seriosness of arthritis and the need to taek action.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7175

WEDNESDAY, 14 JUNE 2017

Standing Committee session on paediatric rheumatology

SP0034 SHARE RECOMMENDATIONS ON SYSTEMIC VASCULITIDES

M.W. Beresford on behalf of SHARE Systemic Vasculitis Working Group.
Paediatric Rheumatology, Alder Hey children's NHS Foundation Trust, Institute of Translational Medicine, University of Liverpool, Liverpool, United Kingdom

Background: Primary systemic vasculitides (PSV) are very rare in children and consequently, little evidence exists. Evidence-based guidelines are lacking; this is an important and unmet need. The European initiative SHARE (Single Hub and Access point for paediatric Rheumatology in Europe) aims to optimize care for children with rheumatic diseases.
Objectives: To provide recommendations for diagnosis and treatment for children with rare forms of PSV.
Methods: Recommendations were developed by a consensus process in accordance with the European League Against rheumatism standard operating procedures. An extensive systematic literature was performed and evidence-based or evidence-informed recommendations were extrapolated from the included papers. These were evaluated by a panel of 16 experts via an online survey and subsequently in two consensus meetings, using nominal group technique. Recommendations were accepted when $\geq$80% of experts agreed.
Results: A total of 78 recommendations were accepted in the two consensus meetings. Recommendations pertained to general cross-cutting recommendations for diagnosis and treatment of PSV, as well as disease-specific statements for childhood-onset Polyarteritis Nodosa, Granulomatosis with Polyangiitis, Microscopic Polyangiitis, Eosinophilic Granulomatosis with Polyangiitis, and Takayasu Arteritis.
Conclusions: European-wide recommendations for the diagnosis and treatment of rare forms of paediatric PSV have been formulated through an evidence-based consensus process. The SHARE project aims to provide international recommendations and significantly improve the standard of care for children with rheumatic diseases.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7205

SP0035 CONSENSUS-BASED RECOMMENDATIONS (SHARE) FOR THE MANAGEMENT OF JUVENILE SCLERODERMA

F. Zulian. *Department of Woman and Child Health, University of Padova, Padova, Italy*

Background: In 2012, a European initiative called Single Hub and Access point for pediatric Rheumatology in Europe (SHARE) was launched to optimise and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases. Juvenile Scleroderma in its two variety, localized scleroderma (JLS) and systemic sclerosis (JSS) is a rare disease within the group of paediatric rheumatic diseases (PRDs) and can lead to significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physicians' experience. Consequently, treatment regimens differ throughout Europe.
Objectives: To provide recommendations for diagnosis and treatment of both JLS and JSS.
Methods: Recommendations were developed by an evidence-informed consensus process using the EULAR standard operating procedures. A committee was constituted, consisting of 16 experienced paediatric rheumatologists, mainly from Europe. Recommendations derived from a validated systematic literature review were evaluated by an online survey and subsequently discussed at two consensus meetings using nominal group technique. Recommendations were accepted if $>$80% agreement was reached.
Results: In total, 1 overarching principle, 17 recommendations on diagnosis and 13 recommendations on therapy were accepted with $>$80% agreement among experts. Topics covered include assessment of skin and major organ involvement and suggested treatment pathways.
Conclusions: The SHARE initiative aims to identify best practices for treatment of patients suffering from PRD. Within this remit, recommendations for the diagnosis and treatment of JLS and JSS have been formulated by an evidence informed consensus process to produce a standard of care throughout Europe.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7184

SP0036 SHARE RECOMMENDATIONS ON JUVENILE DERMATOMYOSITIS

A. Van Royen-Kerkhof. *Wilhelmina Children Hospital, Utrecht, Netherlands*

Background: In 2012, a European initiative called Single Hub and Access point for pediatric Rheumatology in Europe (SHARE) was launched to optimise and disseminate diagnostic and management regimens in Europe for children and young adults with rheumatic diseases.
Juvenile Dermatomyositis is a rare *Pediatric Rheumatic Disease (PRD)*, associated with significant morbidity. Evidence-based guidelines are sparse and management is mostly based on physicians' experience. Consequently, treatment regimens differ throughout Europe.
Objectives: To provide recommendations for diagnosis and treatment of JDM based on evidence-informed consensus.
Methods: Recommendations were developed by an evidence-informed consensus process using the European League Against Rheumatism standard operating procedures. A committee was constituted, consisting of 19 experienced paediatric rheumatologists and 2 experts in paediatric exercise physiology and physical therapy, mainly from Europe. Recommendations derived from a validated systematic literature review were evaluated by an online survey and subsequently discussed at two consensus meetings using nominal group technique. Recommendations were accepted if $>$80% agreement was reached.
Results: In total, 7 overarching principles, 33 recommendations on diagnosis and 19 recommendations on therapy were accepted with $>$80% agreement among experts. Topics covered include assessment of skin, muscle and major organ involvement and suggested treatment pathways.
Conclusions: The SHARE initiative aims to identify best practices for treatment of patients suffering from PRD. Within this remit, recommendations for the diagnosis and treatment of JDM have been formulated by an evidence-informed consensus process to produce a standard of care for patients with JDM throughout Europe.
SHARE – JDM Working Group: B. Bader-Meunier (Department for Immunology, Hematology and Pediatric Rheumatology, Necker Hospital, Paris, France), E. Baildam (Alder Hey Children's NHS Foundation Trust, Eaton Road, Liverpool, UK), T. Constantin (Semmelweis Hospital, Budapest, Hungary), B. Feldman (Department of Rheumatology, The Hospital for Sick Children, Toronto, Ontario, Canada.), P. Lahdenne (Department of Pediatric Rheumatology, Children's Hospital, Helsinki University Central Hospital, Helsinki), B. Magnusson (Astrid Lindgren Children's Hospital, Department for Pediatric Rheumatology, Karolinska University HospitalStockholm, Sweden), K. Nistala (Centre for Rheumatology, University College London, UK), C. Pilkington (Centre for Rheumatology, University College London, UK), A. Ravelli (Istituto Giannina Gaslini, Pediatria II, Reumatologia, Paediatric Rheumatology International Trials Organisation (PRINTO) Coordinating Center, Genoa, Italy), R. Russo (Service of Immunology and Rheumatology, Hospital de Pediatría Garrahan, Buenos Aires, Argentina), M. van Brussel (Child Development and Exercise Center, Division of Pediatrics, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands), JJ. van der Net (Child Development and Exercise Center, Division of Pediatrics, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands), L. Wed-

derburn (Centre for Rheumatology, University College London, UK), N. Wulffraat (Department of Pediatric Immunology, University Medical Centre Utrecht, Utrecht, The Netherlands), B. Bader-Meunier (Department for Immunology, Hematology and Pediatric Rheumatology, Necker Hospital, Paris, France), E. Baildam (Alder Hey Children's NHS Foundation Trust, Eaton Road, Liverpool, UK), T. Constantin (Semmelweis Hospital, Budapest, Hungary), B. Feldman (Department of Rheumatology, The Hospital for Sick Children, Toronto, Ontario, Canada), P. Lahdenne (Department of Pediatric Rheumatology, Children's Hospital, Helsinki University Central Hospital, Helsinki), B. Magnusson (Astrid Lindgren Children's Hospital, Department for Pediatric Rheumatology, Karolinska University HospitalStockholm, Sweden), K. Nistala (Centre for Rheumatology, University College London, UK), C. Pilkington (Centre for Rheumatology, University College London, UK), A. Ravelli (Istituto Giannina Gaslini, Pediatria II, Reumatologia, Paediatric Rheumatology International Trials Organisation (PRINTO) Coordinating Center, Genoa, Italy), R. Russo (Service of Immunology and Rheumatology, Hospital de Pediatría Garrahan, Buenos Aires, Argentina).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7286

WEDNESDAY, 14 JUNE 2017

Ultrasound basic I & II

SP0037 HOW TO ASSESS US ELEMENTARY LESIONS IN CPPD

G. Filippou. *University of Siena, Siena, Italy*

Ultrasonography has been increasingly used the last years for the identification of calcium pyrophosphate dihydrate crystal deposition (CPPD) in joints and on 2011 has been considered by the EULAR task force on CPPD as a promising tool for the diagnosis of the disease. However, it is common experience between sonographers that in daily clinical practice CPP identification by US is rather challenging as crystal deposits are not always numerous and diffuse. Furthermore, other conditions can mimic CPP deposition leading to a wrong diagnosis. The recently created OMERACT US for CPPD subtask force has created for the first time a set of criteria for identification of CPP deposition and assessed their reliability trying to address some of the issues that impede a wider use of US for CPPD diagnosis. During this section will be exposed the main US features of CPP deposition according to the new criteria as well as the principal pitfals that could mislead diagnosis. The scanning techique and some tips and tricks that could help sonographers to identify correctly CPP deposition will also be explained.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7251

SP0038 HOW TO ASSESS CARTILAGE IN RA AND PITFALLS + DEMO

P. Mandl. *Rheumatology, Medical University of Vienna, Vienna, Austria*

Cartilage damage is a key process in rheumatoid arthritis which appears to be more clearly associated with irreversible physical disability than bony damage. While conventional radiography only allows the evaluation of joint space narrowing, a proxy measure of cartilage loss, musculoskeletal ultrasound is a reliable tool for evaluating cartilage damage. The presentation will introduce the pitfalls and challenges associated with visualizing cartilage in rheumatic diseases in general and rheumatoid arthritis in particular. It will also review recent studies in the filed which have validated sonography for both the quantitative measurement of cartilage thickness and for the semiquantitative scoring of cartilage change. A practical demonstration will also be provided.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7274

SP0039 HOW TO EVALUATE THE SUBTALAR JOINT

A. Iagnocco. *Università degli Studi di Torino, Torino, Italy*

The subtalar joint, also known as the talocalcaneal joint, is a synovial joint of the foot, that occurs between the talus and the calcaneus with the talus that is oriented slightly obliquely on the anterior surface of the calcaneus. The two bones articulate at two different sites (i.e. one anteriorly and one posteriorly). The *anterior talocalcaneal joint* is a convex area of the talus that fits on a concave surface of the calcaneus. The *posterior talocalcaneal joint* is formed by a concave surface of the talus and a convex surface of the calcaneus.
The subtalar joint contributes to the dorsiflexion of the ankle. Three articulating facets (anterior, middle and posterior) are present between the talus and the calcaneus. The sustentaculum tali forms the floor of middle facet, and the anterior facet articulates with the head of the talus, and sits lateral and congruent to the middle facet. The posterior facet is the largest of the three, and separated from the others by the tarsal canal. The most relevant actions done by the joint are inversion and eversion of the foot. The subtalar joint can also be considered a combination of the anatomic subtalar joint discussed above, and the talocalcaneal part of the talocalcaneonavicular joint. When both those joints are accounted together, it allows for pronation and supination to occur.
The subtalar joint is frequently involved in arthritis and, particularly in patients with previous sprains, secondary osteoarthritis can also occur. Symptoms of subtalar joint arthritis include pain, loss of motion through the joint's range of motion, and difficulty walking on uneven surfaces.
Among the imaging techniques that are appropriate for the assessment of the subtalar joint, ultrasound (US) has been increasingly used over the last years. Indeed it is able to image different abnormalities, including both inflammatory and structural changes, and it is helpful in guiding local procedures that can be easily and safely performed with optimal patient's tolerance.
The US scanning technique is quite complex, and the whole joint area should be scanned in the longitudinal (sagittal or coronal) plane with pathology that should be confirmed in the orthogonal (perpendicular) plane. By using a standardised scanning technique and agreed definitions of pathology, US allows an optimal assessment of inflammatory and structural abnormalities, thus filling the gap between clinical and radiographic evaluations of the subtalar joint.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7292

SP0040 HOW TO SCAN THE HIP, NEW APPROACH AND DEMO

I. Möller on behalf of EULAR Working Group Anatomy for the IMAGE.
Rheumatology; anatomy; sonoanatomy-sonopathology, Instituto Poal de Reumatología; University of Barcelona, Hospitalet de Llobregat, Spain

The exploration of the hip includes not only intraarticular findings such as synovitis or lesions of the labrum but also the dynamic exploration of the tendons and muscles surrounding it as well as of the neurovascular bundles of interest. All this is an essential complement in the differential diagnosis of the rheumatic patient. The iliopsoas tendon as well as the hip adductors will be demonstrated during the presentation. The anterior and antero internal part of the groin region constitute a relatively frequent consultation and study of the tendinous snapping and its differential diagnosis with the snapping of intraarticular origin can be made by means of the musculoskeletal ultrasound. It requires systematization and knowledge of the regional anatomy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7156

WEDNESDAY, 14 JUNE 2017

Rehabilitation and modern drug treatment - needs and challenges

SP0041 CURRENT NEEDS FOR REHABILITATION

M. Björk. *Department of social and welfare studies, Linköping University, Norrköping, Sweden*

New biological medications and earlier multi professional interventions have led to a reduction in the extent of disability for patients with rheumatic diseases. However disability still remains a key problem for many patients and patients may experience participation restrictions even though they are achieving "remission". To be able to engage in the things we want or need to do is crucial to our health and sometimes a challenge to meet for health professionals. Also, there is an on going discussion of whether today's patients have new rehabilitation needs and if they are met by the health care. This session summarizes both qualitative and quantitative evidence of the disability in today's patients with arthritis. It will further discuss the current needs of rehabilitation in today's patient in relation to existing standards and guidelines. Rehabilitation interventions and patient reported strategies in relation to pain, fatigue and affected activity balance will be highlighted since they are common disabilities among today's patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7269

SP0042 THE ART OF JUGGLING - A PATIENT'S PERSPECTIVE

F.M. Catrina. *LRR, Bucharest, Romania*

Diagnosed with ankylosing spondylitis since 2006, when just turned 24 years old. I was very demoralized and could not understand why I have rheumatic pains bigger than my grandmother 70 years old. I did not understand why I can not go, just do anything wrong to anyone. Slowly, slowly I began to understand the disease and help doctors started to move again.But my secret to healthy aging, was family. Therefore we understand that positive thinking can help me more than any drug, and how you can have a more positive attitude as if in a nice family environment?
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7139

SP0043 **WORK RETENTION REHABILITATION IN PRACTICE**

Y. Prior[1,2] on behalf of Rehabilitation Research Group, University of Salford. [1]*Health Sciences, University of Salford, Manchester;* [2]*Rheumatology, Mid Cheshire NHS Trust Leighton Hospital, Crewe, United Kingdom*

This session aims to meet health professionals' needs in recognising, examining, and identifying problems that patients with inflammatory arthritis (IA) face at work. We know that one in five people with inflammatory arthritis lose their job within five years of diagnosis and, once work disabled, they are unlikely to return to work. Therefore, preventive interventions targeted at work retention, which aim to help people to stay at work, are needed to avoid the transition from work instability to work disability. Rheumatology health professionals play an important role in identifying patients' work problems at an earlier stage and helping them to stay at work. Currently, there are no set pathways to outline health professionals' approach to identifying people with work problems and/or work rehabilitation interventions in the UK. Further, there is a need to train health professionals in the importance of the early recognition of these problems and evidence-based interventions to address work instability.

This session will focus specifically on the rheumatology occupational therapy-led work rehabilitation taken place in a NHS setting in the UK. Using real life case studies, Dr Prior will discuss the standardised assessments used in identifying work problems, collaborative goal setting and work interventions to provide a snapshot of work rehabilitation in the context of clinical practice.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7240

WEDNESDAY, 14 JUNE 2017

Comorbidities: having one RMD is enough - we don't need anything else

SP0044 **SCREENING FOR COMORBIDITIES IN DAILY PRACTICE: WHO AND HOW?**

L. Gossec. *Paris 06 University, Pitié-Salpétrière Hospital, Paris, France*

Comorbidities are frequent in RMDs, as in many other chronic diseases. In inflammatory rheumatic diseases, the most frequent comorbidities are cardio-vascular diseases, depression, infections and cancers. Some of these diseases are more frequent than in persons without RMDs, some are not more frequent but are more often under-assessed and under-treated. These comorbidities and their risk factors need to be screened for. Screening in daily practice is not so simple since it necessitates time, physician expertise and patient cooperation. In this talk, we will address recent recommendations on how to screen for comorbidities, how often and in which setting this should be performed, and the respective roles in screening of rheumatologists, rheumatology nurses and persons with RMDs.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7135

SP0045 **DO PATIENT ORGANISATIONS HAVE A ROLE TO PLAY IN PREVENTING CO-MORBIDITIES?**

A.M. Bosworth. *n/a, National Rheumatoid Arthritis Society, Maidenhead, United Kingdom*

My talk will look in detail at how patient organisations can play a role in preventing co-morbidities. NRAS is currently engaged in two major projects which are both directly concerned with the prevention of co-morbidities. During RA Awareness Week in the UK, 19–26 June, NRAS will launch "Love your Heart" an on-line, interactive video programme to educate people with RA about their increased risk of heart disease and atherosclerosis. This programme explains in simple terms why people with RA are at increased risk of cardiovascular disease. The programme provides the opportunity to appraise individual risk factors, complete a QRISK2 assessment with their GP and provides a cognitive-behavioural framework to empower people to change their behaviours and achieve a healthier lifestyle, thereby reducing risk of heart disease. Baseline and 6 months evaluations are built into the programme. It has been developed with input from a consultant rheumatologist, GP, and other health experts as well as patients. If time permits I will also a describe a research study we are undertaking with 3 hospitals in the UK whereby we will randomly assign newly diagnosed patients to receive a targeted support fprogramme rom NRAS or be in a control group which does not receive this support for a period of 6 months. Our aim is to show that the group receiving the targetted support has less anxiety and depression, although other outcomes will also be measured.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7230

SP0046 **PREVENTION AND THE PROTECTIVE ROLE OF EXERCISE AND LIFESTYLE INTERVENTIONS ON COMORBIDITIES IN RHEUMATIC DISEASES**

S. Garcia Diaz. *Rheumatology, Consorci Sanitari Integral, Hospital Moises Broggi Sant Joan Despi, Sant Joan Despi, Spain*

Background: It has been recognised that patients with rheumatic diseases are at increased risk of developing comorbid conditions such as cardiovascular disease (CVD), malignancies, infections and osteoporosis (among others). Lifestyle interventions (non smoking, non alcohol, healthy diet and exercise) may play an important role to reduce comorbidities in these patients.
Objective: To find if lifestyle interventions and especially exercise play a vital role in preventing comorbidities in rheumatic diseases through an extensive review of recent literature.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7223

THURSDAY, 15 JUNE 2017

Cytokines and chemokines

SP0047 **TYPE I INTERFERON SYSTEM IN AUTOIMMUNITY**

L. Rönnblom. *Department of Medical Sciences, Uppsala University, Uppsala, Sweden*

The type I interferon (IFN) system is our main defense against viral infections and can be activated by a large number of sensors of nucleic acid, triggering the production of more than 15 different proteins with antiviral and immunostimulatory capacity. There are several observations suggesting an important role for this system in the etiopathogenesis of SLE and other autoimmune diseases. Among these are the reported development of autoimmune diseases during treatment with IFN-alpha, a prominent increase in the expression of type I IFN regulated genes (an IFN signature) in a number of rheumatic diseases, the existence of endogenous or self derived IFN inducers in SLE patients and a genetic association between autoimmune diseases and gene variants within the type I IFN signaling pathway.

The type I IFN system is closely connected to a number of cytokine and chemokine pathways, which all can contribute to both the IFN signature and the type I IFN effects. Important type I IFN effects are maturation and differentiation of dendritic cells, activation of T and B cells with enhanced antibody production and induction of increased expression of autoantigens. Consequently, type I IFNs can act as an immune adjuvant and promote an autoimmune process. Recent data have also shown that the regulation of the type I IFN system is abnormal in SLE, which all together suggests that inhibition of the type I IFN system could be beneficial in SLE and possible also other autoimmune diseases. Many different therapeutic targets exists and several studies are in progress aiming to block, or down-regulate, the activated type I IFN system in SLE. A number of studies with monoclonal anti-IFN-alpha antibodies have been reported, and a small study investigating vaccination with an interferon-alpha-kinoid against IFN-alpha has been published. Recently, a phase IIb study targeting the type I IFN receptor in moderate to severe SLE was published, reporting substantially reduced disease activity. Other therapeutic possibilities include elimination of the endogenous IFN inducers and inhibition of key molecules in the type I IFN signaling pathway. The results so far shows that it's possible to suppress the IFN signature and improve several biomarkers in SLE patients without major safety problems. The challenge for the future is to modulate the interferon system in autoimmune diseases more precisely and realize that different treatments may be appropriate in various patients.

Disclosure of Interest: L. Rönnblom Grant/research support from: AstraZeneca
DOI: 10.1136/annrheumdis-2017-eular.7134

SP0048 **TARGETING OF ANGIOGENESIS**

S. Tas on behalf of European Synovitis Study Group. *AMC Clinical Immunology & Rheumatology, Amsterdam Rheumatology and immunology Center, Amsterdam, Netherlands*

Angiogenesis is de novo capillary outgrowth from pre-existing blood vessels. This process not only is crucial for normal development, but also has an important role in supplying oxygen and nutrients to inflamed tissues, as well as in facilitating the migration of inflammatory cells to the synovium in rheumatoid arthritis, spondyloarthritis, and other tissues in systemic autoimmune diseases. Neovascularization is dependent on the balance of proangiogenic and antiangiogenic mediators, including growth factors, cytokines, chemokines, cell adhesion molecules and matrix metalloproteinases. In this lecture I will provide an overview of the various pathways that govern these angiogenic processes and discusses potential approaches to interfere with pathological angiogenesis, and thereby ameliorate inflammatory disease, by targeting these pathways specifically in endothelial cells.

Key Messages:

- In chronic inflammatory diseases, angiogenesis enables increased delivery of oxygen and nutrients to immune cell populations accumulating in inflamed tissues, and contributes to further immune cell infiltration

- Angiogenesis is driven not only by hypoxia, but also by proinflammatory mediators produced by immune and stromal cells
- Many pathways downstream of these proinflammatory stimuli contribute to various cellular processes involved in angiogenesis
- Targeting proangiogenic pathways to inhibit neovascularization has been successfully exploited in several cancers, and may also prove beneficial in the treatment of chronic inflammatory diseases

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7153

SP0049 DNA AGGREGATES AS ALARMINS

D. Pisetsky. *Medicine, Duke University Medical Center, Durham, North Carolina, United States*

DNA is a large polymeric molecule that displays powerful immunological activities and operates in the context of multi-component aggregates to alarm the immune system and stimulate innate immunity. Although DNA has important roles in normal host defense, DNA can serve as an autoantigen and autoimmunogen by itself or in association with other immunologically active nuclear molecules. In the setting of systemic lupus erythematosus (SLE), DNA is a key target antigen; while antibodies to pure DNA double stranded DNA serve as important biomarkers, the relevant antigenic form of DNA during disease is the nucleosome in which DNA is bound to histones. Furthermore, nucleosomes can be components of microparticles which are small membrane-bound structures that are released from dead and dying cells. MPs can stimulate immune responses and serve as a nidus for immune complex formation. In normal immunity, DNA can interact with nucleic acid sensors in the cytoplasm of cells to stimulate responses including production of type 1 interferon. These sensors respond to DNA from intracellular organisms such as bacteria and viruses although damaged DNA and DNA from mitochondria can also interact with these receptors. While these sensors are intracellular, they can interact with extracellular DNA that is introduced or transfected into the cell; this translocation event occurs with DNA bound with other molecules. In another facet of host defense, DNA can be released from neutrophils during a process termed NETosis. A NET or neutrophil extracellular trap is a mesh-like structure comprised of DNA as well as granule proteins that have antibacterial activity. NETs can trap and kill bacteria. Thus, in its diverse immunological roles, DNA interacts with other molecules to form aggregates or sub-cellular structures that alarm the immune system, promote host defense or drive critical events in autoimmunity.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7271

THURSDAY, 15 JUNE 2017

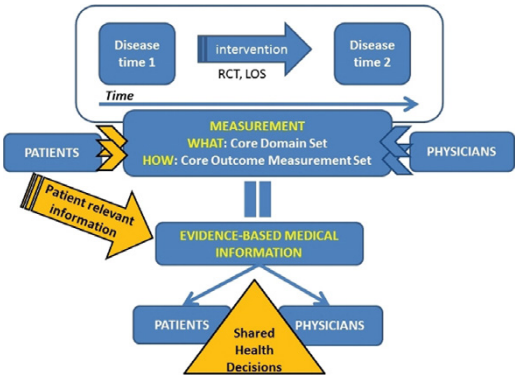
Bringing rheumatology research to the next level: addressing the main challenges of patient partnerships in research and health care service design

SP0050 ENSURING REPRESENTATIVENESS OF THE PATIENTS' PERSPECTIVES IN THE FINAL RESULTS GENERATED FROM CLINICAL RESEARCH – CHALLENGES FROM THE PERSPECTIVE OF RESEARCHERS

A.-M. Orbai on behalf of GRAPPA-OMERACT Psoriatic Arthritis Core Set Working Group. *Rheumatology, Johns Hopkins University School of Medicine, Baltimore, United States*

Now more than ever, patients are increasingly taking part in shared healthcare decisions with their physicians. Information from clinical research, on which evidence-based medicine draws upon, ideally needs to make sense to patients and not only physicians.

Representativeness of the patients' perspectives in the final results of clinical research is therefore critical for shaping the content and quality of medical knowledge and for shared clinical decision-making. As a result there is increased emphasis and even requirement from organizations around the world to include patient research partners (PRPs) as equal members in the medical research team. PRP inclusion means participation in research question generation, study design, data analysis/interpretation, authorship and results dissemination. Several questions remain: 1) How can we maximize the impact of the perspective patients bring to the table? 2) How can we ensure we capture the patients' perspective accurately and carry it forward into the final product of research? We can maximize impact and reach by including the patients' perspective in research that defines the way we assess disease and disease targeted interventions. Randomized controlled trials (RCTs) and longitudinal observational studies (LOS) are currently our main source of clinical information regarding efficacy of disease targeted interventions. Outcomes assessed in RCTs and LOS, as well as the health measurement tools used to assess these outcomes need to include the patient perspective in order for the information generated from these studies to be valid and usable. A conceptual diagram to illustrate how the patients' perspective is critical in generating health information for patient and physician shared decision making is represented in the Figure.



Case study: the updated Psoriatic Arthritis (PsA) Core Domain Set patient domains. A core domain set is the minimum set of outcomes that need to be assessed to evaluate the effect of disease targeted interventions. The first PsA core domain set was developed in 2006 by physicians and methodologists. The core set update study identified clinical trial outcomes important for patients as a group and for physicians as a group and reconciled both perspectives to recommend an updated PsA core domain set that represents the perspective of both patients and physicians. Five PRPs were members of the working group and contributed during all stages of the project. The perspective of patients was included as follows: a) domain generation through qualitative data collection and analysis from international focus groups; b) first domain prioritization exercise in electronic surveys with patients and physicians; c) a face to face nominal group technique meeting with 12 patients and 12 physicians to prioritize domains; d) second domain prioritization exercise through electronic surveys with patients and physicians; e) discussion and voting at the 2016 Outcome Measures in Rheumatology conference. During the process of achieving consensus we observed the following dynamic for patient prioritized domains (percentages represent proportions of patients ranking each domain important in the first survey and then the second survey): 1) Pain was rated important by 76% of patients in the first survey and 82% in the second survey and remained a core domain; 2) Fatigue 78% then 71% and became core domain; 3) Physical function 72% then 80% and remained a core domain; 4) Participation (daily activities and employment/work) was important to 72–76% of patients in the first survey and to 78% in the second survey and became a middle circle domain (important, not required); 5) Emotional well-being 60% then 57% and was placed in the middle circle; 6) Independence 82% then 63% and placed on the research agenda. In each of these situations the trend in the patient's vote as a group followed the physician's vote with one exception: the domain participation.

Summary of challenges and solutions for ensuring representativeness of the patients' perspective in the final results: Patients may change their views and align with physicians during the course of a research project. PRPs can help increase awareness of the patients' perspective throughout all stages of the research process. Special attention should be given to: 1) use of methods that adequately capture the patient perspective in the initial stages of a research project, and 2) allowing a robust patient perspective to take shape from patients as a group, before the consensus process with additional stakeholders begins. In addition, supporting patients with adequate information and materials and involving PRPs in their development will maximize understanding of the task for patients and their full participation.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7245

SP0051 BECOMING A PATIENT RESEARCH PARTNER IN THE FIELD OF RHEUMATOLOGY. MY EXPECTATIONS AND THE CHALLENGES OF BEING EDUCATED AND TAKEN SERIOUSLY

E.F. Mateus[1,2,3]. [1]*LIGA PORTUGUESA CONTRA AS DOENÇAS REUMÁTICAS, Lisbon, Portugal;* [2]*Patient Research Partner, EULAR, Zurich, Switzerland;* [3]*ENP, EUPATI Portugal, Lisbon, Portugal*

Patients often feel that their experience of illness is not valued nor understood by others. However, there has been a growing recognition of the importance of the patient perspective and involvement in research, improving its methodology and outcomes. The European Medicines Agency has been involving patients' and consumers' representatives on their work since 2005. The "European League Against Rheumatism recommendations for the inclusion of patient representatives in scientific projects" have been published in the "Annals of the rheumatic diseases" in 2011.

I was diagnosed with Juvenile Idiopathic Arthritis when I was 5 years old, back in 1977. Therefore, I have 40 years of experience of living with a Rheumatic and Musculoskeletal Disease (RMD), but no recollection of what my life was like "before" and "after" the diagnosis. I have learned to live and cope with my RMD, with a sense of being different from my peers. This sense of "uniqueness" was

only disrupted when I realised that my experience of illness was quite common to other persons with a RMD. I can still remember my fascination, in a Patient Reported Outcomes workshop, by discovering that our experience as patients had a bigger relevance that the one we usually conceive.

Then, I felt the need of understanding the research process and specific jargon, so I could relate them with my knowledge on living with a RMD. Otherwise, any insight on the patient perspective would be "lost in translation", due to an inability to establish a correspondence between the scientific terminology and mindset regarding the disease, and the experience of illness and sickness by the individuals. Training opportunities were also recognised as desirable by the above mentioned EULAR recommendations, to increase expertise and understanding of research methods and to promote the patients' self-confidence on their contribution to research.

The *Patient Research Partners* (PRP) training by EULAR, in 2013, was the first step towards a better understanding of what could be the role of patients and on how to provide a meaningful input from the patients' perspective into research processes. It was followed in 2014 by the training provided by European Patients' Academy on Therapeutic Innovation (EUPATI) for *Patient Expert on the Medicines Research and Development Process*. This expert-level training was organized in a mixture of independent e-learning coursework and face-to-face training events over a 14-month period. The syllabus involved six modules: Discovery of Medicines & Planning of Medicine Development, Non-Clinical Testing and Pharmaceutical Development, Exploratory and Confirmatory Clinical Development, Clinical Trials, Regulatory Affairs, Medicinal Product Safety, Pharmacovigilance and Pharmaco-epidemiology, HTA principles and practices. Additionally, in 2016, I have attended the 1st EULAR course on Health Economics in Rheumatology.

In the meantime, my background as an anthropologist led me to become interested in Medical Anthropology. Between 2007–2015 my academic research (MA Phil. and PhD) was oriented towards a specialization in Anthropology of Health, with a special interest in Anthropology of Pharmaceuticals.

Based on my personal experience, on this lecture I will focus on the challenges of the role of the PRP trying to fill the gap between the mindsets and practices of different stakeholders.

Navigating through different meanings of symptoms and treatments, the educated patient representative must act like a translator, decodifying the biologic impact of the disease and intervention over the experience of illness on the everyday aspects of living with a RMD. The biggest expectation and challenge might be to bring these aspects forward, as relevant for the other stakeholders, since they shape individual values and patient's preferences.

Although recognised as having a pivotal role, patient's involvement in research may be limited by tokenism or by ineffective patients' participation. Patients' involvement is now a requirement and an added value to any project. But, is the project team ready and willing to listen to patients? Are PRP duly involved in the project, or are they just expected to be recipients without any input of their perspectives into the development and implementation of the research?

The knowledge and education acquired to perform our task enables us to understand science enough to communicate the patient experience in a meaningful way, improving the research. Our added value is, undoubtedly, our experience with the disease, our understanding of the individual values and preferences shaped by the everyday aspects of living with a RMD. We should be taken more seriously, for the benefit of science and patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7243

SP0052 BUILDING PATIENT PARTNERSHIP IN HEALTH CARE SERVICE DESIGN AND DELIVERY

H. Lempp. *Rheumatology, Kings College London, London, United Kingdom*

This paper will present details of the approach to patient and public involvement in health service delivery, health service research and health care education in England. The presentation will be based upon a Logical Framework with the following key elements: inputs, processes, outputs, and outcomes/impacts. Key barrier acting to minimise the impact of building patient partnerships will be discussed, illustrated by examples from our experience in the preparatory stages for our departmental strategy to formalise close Patient Partnership for our research portfolio: (i) establish honorary contracts for patients for the academic Institution and local Hospital Trust; (ii) include patients on the interview panels to appoint project researchers (iii) build in a separate funding within the overall project budget for the costs associated with patient partnership and (iv) manage patient expectations of rapid implementation of the results of research after the completion of projects. Patient Partnership is essential and feasible to make health care service and design relevant.

References:

[1] Otto AK, Novielli K, Morahan PS.(2006) Implementing the logic model for measuring the value of faculty affairs activities. Acad Med. 2006 Mar;81(3):280–5.
[2] Mockford C, Staniszewska S, Grifiths F, Herron–Marx S. The impact of patient and public involvement on UK NHS health care: a systematic review. International Journal for Quality in Health Care, 2012; 24:28–38.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7123

THURSDAY, 15 JUNE 2017

WIN & HOT session

SP0053 HOT SESSION: VASCULITIS TREATMENT

R.A. Luqmani. *University of Oxford, Oxford, United Kingdom*

The systemic vasculitides are characterized by inflammation of blood vessels, which if untreated, results in tissue or end organ damage or death. Chapel Hill nomenclature is widely used to define different forms of vasculitis according to the size of the predominantly affected vessels. Other forms of vasculitis are not defined by a predominant vessel size (e.g. Behcet's syndrome). Vasculitis associated with the presence of anti-neutrophil cytoplasm antibody (ANCA), termed AAV, is less common than giant cell arteritis (GCA), but considerable advances have been made in understanding the pathogenesis and evidence based treatment for AAV. AAV is divided into three major forms: granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss syndrome). ANCA are implicated in their pathogenesis but not all patients with AAV are ANCA positive.

We will review recent EULAR guidelines on therapy for AAV, based on careful structured clinical evaluation of patients, with stratification according to severity. Cyclophosphamide or rituximab (plus glucocorticoid) is used for severe disease, followed by maintenance with azathioprine (AZA) or methotrexate (MTX), and reducing doses of glucocorticoids; or maintenance rituximab. Additional plasmapheresis is indicated for very severe disease; by contrast for less severe disease, MTX or AZA or mycophenolate (plus glucocorticoids) can be used. The evidence for effectiveness is clear for MPA and GPA. A number of studies are underway to improve our use of these existing agents and to test newer, mechanism based treatments such as inhibition CTLA4Ig or of the C5 complement pathway in GPA and MPA. For EGPA with severe manifestations, cyclophosphamide and glucocorticoids are recommended. A trial of mepolizumab (inhibitor of interleukin 5, a potent driver of eosinophil production) in EGPA has recently been completed. IL-6 inhibition with tocilizumab is a significant advance over glucocorticoid monotherapy in treatment of GCA. Apremilast is effective in treating mucocutaneous manifestations of Behcet's syndrome. Relapse is a common feature of many forms of vasculitis and needs to be monitored by structured clinical evaluation. Monitoring of ANCA titres in AAV or the acute phase response in most forms of vasculitis can be misleading and should not serve as sole guide to therapy in the absence of clinical evidence of active disease. Early survival is over 94% of patients with most forms of vasculitis. Five year survival is 70–75% for AAV with current therapy. However, if the condition is more severe disease, especially with significant renal impairment, mortality is worse.

Vasculitis remains a challenge. Whilst mortality has dramatically reduced as a result of effective immunosuppression, relapse and chronic damage are significant problems for all forms of vasculitis. We need a better understanding of how to manage and limit the long term chronic effects of vasculitis and its therapy.

Disclosure of Interest: R. Luqmani Grant/research support from: Arthritis Research UK, GSK, MRC, UCSF/OIF, Canadian Institutes of Health Research, The Vasculitis Foundation; Consultant for: GSK, Medpace, MedImmune, Roche

DOI: 10.1136/annrheumdis-2017-eular.7162

THURSDAY, 15 JUNE 2017

Treat-to-target in axSpA: reality or utopy?

SP0054 THE CONCEPT OF TREAT-TO-TARGET

J. Braun. *Rheumazentrum Ruhrgebiet, 44649 Herne, Germany*

Many illnesses including most rheumatic diseases have substantial effects on well-being and quality of life, including deterioration of physical and mental function and a reduced life expectancy, since they can cause damage to organs and cells. If healing and regeneration cannot be achieved an impairment of organ function can be expected. In acute diseases this may occur rapidly over hours to days and weeks, while it often takes months to years in chronic diseases. However, if treatment is instituted early enough, organ damage may be prevented or diminished.

Critical for an optimal management of diseases with potentially severe outcomes is to determine the responsible thresholds for, for example, disease activity or to define the maximum level of a surrogate marker at which damage is unlikely to occur and, thus, will not be harmful in the long term. Although the optimal aim of therapy is cure, and appropriate therapy may even normalize life expectancy, many chronic diseases such as hypertension, diabetes, rheumatoid arthritis (RA) and ankylosing spondylitis (AS) have remained without curative therapies in the last decades – even though considerable progress has been made. Thus, a strategic therapeutic approach should aim for prevention of future damage, and maximal improvement of compromised organ function. Therefore, a clearly defined threshold of a validated measure that predicts future harm or no or minimal harm, is a target of critical importance for chronic diseases with potentially severe outcomes. Treat-to-target strategies having been developed to achieve this have widespread implications. They should be routinely followed - as long as the potential harm from treatment is carefully balanced against its benefit. Clearly, if inappropriately managed, the consequences of diabetes and hypertension in

the long run include, myocardial infarction, stroke, renal failure, blindness, etc. Therefore, target values for biological markers have been determined below which organ damage does usually not occur and life expectancy is normalised. Examples for domains in which such thresholds have been defined are blood pressure, glycosylated haemoglobin (HbA1c), and others.
Inflammatory rheumatic diseases lead to organ damage not only in the musculoskeletal system but they may also harm internal organs. A target level of a measure related to its long-term outcome, can be a surrogate measure like the cholesterol level for cardiovascular diseases, or a composite measure of disease activity as used in RA (DAS28) or in AS (ASDAS). The treat-to-target strategy can be reduced to a simple algorithm of, on the one hand measuring activity and on the other hand, in consequence, adapting treatment. Treatment adaptation does not necessarily mean changing a medication or increasing the dosage of a drug but may even also mean life style changes, as long as the therapeutic target is attained or nearly attained - importantly within a prespecified time frame. Therapeutic adaptations should always take patient factors, including comorbidities, adverse events and patient preferences, into account.
However, the musculoskeletal system can mostly not be assessed by using a simple surrogate or direct “gold standard” measures, since rheumatic diseasese with multiple signs and symptoms are mostly rather complex. In RA information derived from physical examination using a quantitative joint count is considered very important. This is different in AS. Additionally, information from the history, which can be collected through patient self-report multifaceted questionnaires, has proven effective in determining patient status and its change. This is even more important in AS. However, functional impairment has reversible and irreversible components. Damage is a consequence of high and/or persisting disease activity. The most important variables contributing to joint damage in RA are swollen joint counts and C-reactive protein (CRP). The latter in combination with questions on back pain is also important in AS, while in RA the use of composite measures of disease activity that comprise joint counts is critical. There is good evidence that, if this strategy is consequently followed, physical function will improve and joint damage be reduced in patients with RA. To determine optimal treatment targets in RA it is necessary to define the thresholds of disease activity measures at which progression of joint destruction is halted. Of note, only remission is associated with maximal reversal of functional impairment and a stop of progression of damage as well as work disability. However, it needs to be realized that some remission criteria are more stringent than others.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7129

SP0055 WHAT ARE THE CHALLENGES FOR APPLYING TREAT TO TARGET IN AXIAL SPONDYLOARTHRITIS?

M. Dougados. *rheumatology Hopital Cochin, René Descartes University, paris, France*

The concept of Treat to Target (T2T) applied in rheumatoid arthritis has been evaluated in psoriatic arthritis and is currently under investigation in two different strategy trials in patients suffering from axial spondyloarthritis (axSpA). Whatever le results of these trials will be, the acceptation of this concept and consequently its implementation in daily practice might be challenging for several reasons.
The concept of T2T necessitates 3 different steps and also the close collaboration of the patient and the availability of different treatment modalities.
The three different steps consist in:
a) the choice of the most relevant outcome measure (e.g. a measure evaluating a domain recognized as predisposing to subsequent clinically relevant damage (either structural damage or important comorbidities such as cardiovascular diseases)).
b) the determination of the threshold of the outcome measure to reach (threshold below which the risk of subsequent damage is abolished or significantly decreased).
c) The time to reach the target is usually related to the treatment modality (a few days for NSAIDs and several weeks for DMARDs).
A part these different steps, two points have to be considered a) this T2T approach is impossible without embarking the patient in a true share decision b) this T2T strategy requires the possibility to adapt/increase the treatment in case the target is not reached after one or several “conventional” treatment modalities.
For each of these different points we will consider past-on ongoing initiatives proposing to resolve the different encountered issues in order to facilitate the elaboration and the implementation of a T2T strategy in AxSpA.
Disclosure of Interest: M. Dougados Grant/research support from: UCB,ABBVIE,PFIZER,MERCK, Consultant for: UCB,ABBVIE,PFIZER,MERCK
DOI: 10.1136/annrheumdis-2017-eular.7119

SP0056 UPDATE OF THE T2T RECOMMENDATIONS IN SPA

D. Van Der Heijde on behalf of T2T in SpA working group. *Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

In 2013 the first recommendations for treating spondyloarthritis to target (T2T) were published. These followed the reasoning for the T2T recommendations for rheumatoid arthritis. Although the systematic literature review at that time did not provide evidence to support the recommendations, five overarching principles and 11 recommendations were formulated. There were 9 commen recommendations for axial SpA, peripheral SpA and psoriatic arthritis and 2 additional recommendations for each subgroup specifically. In 2017 the T2T working group met again to update the recommendations. This was based on an updated systematic literature review. Data had been published that there is indeed a clear link between inflammation and subsequent longterm outcomes, which is the basis for the T2T principles.
SpA is characterised by musculoskeletal signs and symptoms (arthritis, enthesitis, dactylitis, axial disease) but also extra-articular manifestations (psoriasis, inflammatory bowel disease, anterior uveitis) are important manifestations. Moreover, comborbidities (such as osteoporosis, cardiovascular disease). All these manifestations are taken into account in the formulation of the recommendations. The overarching principles were kept largely identical. Some changes in the wording were made for a better understanding, but no fundamental changes were made. A total of 11 recommendations were formulated. These are now for all subgroups of SpA and no specific recommendations are proposed. In principle, the treatment target is remission or inactive disease of musculoskeletal and extra-articulaur manifestations, and the target should be individualised. It is important that remission/inactive disease should be based on a combination of clinical and laboratory parameters, and disease activity should be measured on the basis of clinical signs and symptoms as well as acute phase reactants. This is important to realise, e.g. in axial SpA as patient reported outcomes only are at best weakly correlated with structural damage. In certain circumstances, low disease activity may be an alternative target. Because of the heterogeneous presentation of SpA, not only the target, but also the assessments should be individualised. Both in the overarching principles and in the recommendation the shared decision between patient and rheumatologist is listed as the basis of the T2T management.
The updated recommendations will be presented.
Disclosure of Interest: D. Van Der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, Employee of: Imaging Rheumatology
DOI: 10.1136/annrheumdis-2017-eular.7158

THURSDAY, 15 JUNE 2017

Calcium crystal deposition in rheumatic diseases —

SP0057 CALCIUM CRYSTALS AND THEIR LINK TO OSTEOARTHRITIS

J. Bertrand. *Department of Orthopeadic Surgery, Otto-von-Guericke University Magdeburg, Magdeburg, Germany*

Calcification of cartilage is a common finding during osteoarthritis (OA). We have shown that it is mainly of the BCP type and not the CPPD type of crystal formation. BCP cartilage calcification is directly linked to the severity of cartilage degradation and, therefore, OA severity. We have also shown that with increasing hypertrophic differentiation of chondrocytes, the amount of calcification increases in vivo and in vitro. This indicates a link between chondrocyte hypertrophy andcartilage calcification. The pyrophosphate pathway is known to be involved in tissue calcification. It functions to keep the sensitive balance of pyrophosphate (PPi) and phosphate (Pi), thereby preventing the generation of calcium-phosphate crystals. One key player in this pathway is the nucleotide pyrophosphatase phosphodiesterase (NPP1), which has been demonstrated to be regulated by inflammatory mediators such as IL-1. In our cohort of OA patients, the expression of collagen X and NPP1, but not ANK and TNAP, correlated with cartilage calcification and also with the Mankin-Score. NPP1 expression inverse correlated with the calcification, whereas collagen X was upregulated. This finding was confirmed in experimental murine OA using the DMM mouse model. Furthermore, NPP1mut/mut mice (ttw/ttw) exhibit more calcification activity than wild type controls in joints as well as in cartilage of non weight bearing areas, including ear cartilage, suggesting that mechanical stress is not required for the induction of calcification. NPP1mut/mut (ttw/ttw) mice developed typical OA-like changes as evaluated by histological analysis as well as in vivo imaging and histological stainings. Intriguingly, calcification was associated with increased expression of the hypertrophic cartilage marker collagen X and the bone marker collagen I. Additionally, BCP crystals are able to activate chondrocyte differentiation via the WNT signaling pathway.
NPP1 is an important player in OA-associated cartilage calcification. Pathologic calcification of cartilage resembles in many aspects cartilage transformation into bone. Taken together, the data suggest that OA is characterized by the re-activation of molecular signalling cascades that at least in part resemble endochondral ossification.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7192

SP0058 REVIEW OF THE DIFFERENT IMAGING MODALITIES TO DETECT CALCIUM DEPOSITION DISEASES

P. Omoumi. *Lausanne University Hospital, Lausanne, Switzerland*

Crystal deposits in and around the joints are common and most often encountered

as incidental imaging findings in asymptomatic patients.
However, they can also cause chronic or acute arthropathy, generating symptoms. In the chronic setting, imaging features are usually characteristic and allow the differentiation of the type of crystal arthropathy. In the acute phase and in the early stages of the crystal deposition, the signs are often non-specific, and the final diagnosis still relies on the analysis of synovial fluid.
Radiography is the main imaging modality for the workup of these conditions. It can confirm the diagnosis and often characterizes the type of crystal arthropathy. In recent years, US has played an increasingly important role in this setting, and is a useful tool in superficially located crystal-induced arthropathies. CT nicely complements radiography for deeper sites, especially the axial skeleton. DECT is a promising tool for the characterization of crystal arthropathies, in particular gout as it permits a quantitative assessment of deposits, and may help in the follow up of patients.
When performed in the acute stage, MRI may show severe inflammatory changes that could be misleading and correlation to radiographs or CT should help to distinguish crystal arthropathies from infectious or tumoral conditions.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7263

THURSDAY, 15 JUNE 2017

Fifty shades of remission in RA

SP0059 REMISSION: MORE THAN CLINICAL ...?

M. Boers. *Epidemiology & Biostatistics; Amsterdam Rheumatology and immunology Center, VU University Medical Center, Amsterdam, Netherlands*

This session is about defining remission. Most examples will be about rheumatoid arthritis (RA) because most experience has been gathered in that disease. But the concept of remission should be viewed from a wider perspective than one disease. The session includes two pro-con debates (on the utility of including imaging and biomarkers in a definition of remission).
As in all things, when embarking on a scientific project, one must ask:
"Why are we doing this?"
To even begin with answering the question, we must first agree on a clear conceptual definition of remission. When we started on the development of the ACR-EULAR definition of remission in RA, we used dictionary sources and discussions to settle on this:
"The state of absence of disease activity in patients with a chronic illness, with the possibility of return of disease activity." [1]
It is clear that choices are made from the beginning, especially with the concept "disease activity", and the possibility that disease activity returns (as opposed to "healing", where this possibility does not exist). Disease activity is a tangible concept adequately defined in RA, but less so in many other rheumatological diseases. Also, disease activity is conceptually separate from (mostly irreversible) consequences of the disease, such as damage. Finally, note that the above concept does not contain the elements "duration" or "treatment".
If we continue with the above concept, why do we want to proceed to operationalize the remission definition? The two main reasons are research and patient care. For both, it is clear that we are defining a very good, perhaps even the best state a patient can be in, given that we are talking about chronic disease, i.e. the root cause of the disease cannot be taken away to heal the patient. Being in such a good state has immediate benefits (minimal disease impact) and probably also future benefits, if lack of disease activity translates to less consequences (damage etc). In both research and patient care, we want a definition that is both valid (favorable test characteristics; links to prognosis) and feasible (time, costs, interpretability). Validity and feasibility oppose each other to a certain extent (eg, definitions with better sensitivity and specificity are usually more expensive). Research and patient care differ in their use of the definition. In research, validity and feasibility can be lower than in patient care, because research is about groups, and cost and interpretability are less of an issue than in patient care.
Most of the people criticizing the current ACR-EULAR remission definition of RA are confused over its purpose: whereas it was intended for use in trials, they criticize it for lack of validity in the clinic. For instance, it is felt that the patient global criterion is too strict, so that patients with no apparent inflammatory activity but a patient global score of 2 or higher (scale 0–10) are "unjustly" not classified as in remission. Also, the lack of a duration or treatment criterion is felt to be a problem, but this is not an issue in research.
In the following pro-con debates, please consider the following:
Proposals to change existing criteria for remission must also be held to the question: "Why are we doing this?"
References:
[1] Remission. (Accessed 21–02–2017, at http://en.wikipedia.org/wiki/Remission.)
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7124

SP0060 BIOMARKERS ARE REQUIRED FOR REMISSION: PRO

R. Van Vollenhoven. *Amsterdam Rheumatology and Immunology Center Arc, Amsterdam, Netherlands*

1. Conceptually, remission is thought of as a state where the disease is absent. As we approach a better understanding of the underlying pathophysiological process of a disease, it becomes more and more relevant to include in a definition of remission appropriate biochemical markers of that process.
2. From a practical point of view, definitions of remission in RA have been built upon clinical parameters of disease activity, supplemented in some cases with a single biomarker. However, it is clear that in practice these definitions are insufficiently precise: held against a gold standard of expert opinion, they perform at around 80–90%, misidentifying one or two out of every ten patients. And while there is an understandable and in many ways desiriable development of more patient-reported emphasis in outcomes, it has considerable practical value to be able to objectify an important disease state such as remission.
3. There is convincing evidence to show that biomarkers can be employed succesfully to predict some aspects of RA. In the day-to-day care of patients with this disease, the most important prediction may be whether the effective drug can be tapered or not. Current evidence indicates that biomarkers may be invaluable at helping clinicians and their patients make this important decision.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7288

THURSDAY, 15 JUNE 2017

Innate immunity

SP0061 A DAY IN THE NEUTROPHIL'S LIFE

A. Hidalgo. *Cell & Developmental Biology, Fundación CNIC, Madrid, Spain*

Immunity is essential for life, yet the strength of immune responses are not constant throughout the day. This oscillatory immunity reflects an adaptation of organisms to environmental changes that occur through day-night cycles, so as to optimize and concentrate effective responses to the times of maximal environmental threat. In my talk I will discuss our ongoing efforts to uncover the mechanisms by which neutrophils, the most abundant and aggressive of all immune cells, orchestrate temporal immunity. These mechanisms are reflected in diurnal changes in phenotype and function of neutrophils, which we refer to as neutrophil aging. We propose that the existence of a timed response of neutrophils governed by cell-intrinsic and –extrinsic mechanisms suggests that inflammatory disease co-opts ancestral processes to damage tissues.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7054

SP0062 DIFFERENTIAL SCAVENGING OF APOPTOTIC CELLS AND BACTERIA

G. Krönke. *Internal Medicine 3, University of Erlangen-Nuremberg, Erlangen, Germany*

During inflammation and infection, we are simultaneously confronted with both self and non-self in form of dying cells and microbes, respectively. Mechanisms that facilitate the non-immunogenic clearance of self-antigens derived from apoptotic and necrotic cells and that, in parallel, allow the initiation of an immune response against invading pathogens are incompletely understood. Recent data from our laboratory show that the immune system actively sorts apoptotic cells (ACs) and bacteria into distinct subspecies of phagocytes thereby enabling a segregated processing of self and non-self as well as a differential immune response against these two entities. During inflammation, ACs were cleared by tissue resident macrophages (resMφ) that performed a non-immunogenic disposal of self antigens, whereas bacteria were preferentially ingested by monocyte-derived inflammatory macrophages. We identified the enzyme 12/15-lipoxygenase and the nuclear receptor Nr4a1, both specifically expressed by resMφ, as key factors that control the coordinated and non-immunogenic phagocytosis of ACs by these specialized macrophage subset. Incorrect sorting and aberrant uptake of AC-derived self-antigens by pro-inflammatory and immunocompetent phagocytes, however, resulted in the break of self-tolerance and autoimmunity. Our data thus demonstrate the importance of a sorted clearance of ACs for the maintenance of immunologic self-tolerance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7198

SP0063 THE ROLE OF MUSCLE IN INNATE IMMUNE RESPONSES

P. Rovere-Querini. *Immunology, Transplantation and Infectious Disease, San Raffaele Scientific Institute and Vita-Salute San Raffaele University, Milano, Italy*

The skeletal muscle represents a unique site from the immunological point of view. Leukocytes are virtually absent in healthy conditions. However they are quickly recruited upon muscle injury, persist during the regenerative phases to disappear again after tissue healing. Thus, it represents and ideal scenario to study the

involvement of the innate immune system in the homeostatic response either to the conventional programmed death of multinucleated myofibers and to the parallel occurrence of "non-canonical" cell death and survival programs, including necrosis and autophagy. Recruited phagocytes are responsible of the clearance of damaged myofibers and of dying muscle stem/progenitor cells, stromal cells and leukocytes. Muscle macrophages in particular are endowed with remarkable plasticity throughout regeneration and healing, switching from activated cells that generate inflammatory cytokines to reparative assets, that play a non redundant role during the resolution phases of the damage and regulate the termination of the inflammatory responses. This dynamic transition between is increasingly felt to be the key to muscle homeostasis. Conversely defects in the process favour maladaptive remodeling with deposition of collagen and fat accumulation and in predisposed individuals autoimmunity leading to inflammatory idiopathic myopathies. A specialized population of regulatory T (Treg) cells, which control the inflammatory response by promoting the M1-to-M2 switch, and the activation of the muscle stem cells, satellite cells is receiving increasing attention for their central role in tissue homeostasis. Thus, the immunological perception of muscle cell death and regeneration – in turn influenced by environmental cues, including mitophagy and alteration of the redox balance - determines whether these events foster successful tissue healing or persisting inflammatory myopathies. The insights that are progressively become available on this original scenario hold promises to develop new approaches for disease treatment. Thus, immunologic perception of death and regeneration of muscle cells determine whether these events promote healing of tissues or persistent inflammatory myopathies. The insights that are becoming increasingly available on this original scenario hold promise for the development of new approaches to the treatment of persistent human muscle disease.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7279

THURSDAY, 15 JUNE 2017

To be and to become: transition from paediatric to adult care

SP0064 TO BE AND TO BECOME: REFLECTIONS ON MY TRANSITION

W. Olsder. *YOUTH-R-WELL.COM, Groningen, Netherlands*

The importance of successfully transitioning pediatric patients to adult care is increasingly recognized across a wide range of health care providers. However, there are still many challenges occurring during the transition phase. This presentation will contribute to these challenges by sharing the journey of a young person with arthritis on the transition to adult care.

As a young patient with arthritis, I made the journey from pediatric care to adult care a couple of years ago. I am diagnosed with arthritis since I was 14 years old. In this presentation, I will show the experiences of my own transition. Furthermore, as the chair of Youth-R-Well.com, an organization for young people with RMDs in the Netherlands, I will share some of the main points around transition I learned from other young patients. For every person, the transition to adult care is experienced different. Therefore, I will try to give some main answers from personal journeys on the questions: How is the transition experienced by a young patient? What are the current challenges faced by a young patient during the transition? What should be the role of the parents during the transition? What are best practices for the transition to adult care?

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7193

SP0065 ARE WE ASKING THE RIGHT QUESTIONS IN TRANSITION RESEARCH?

K. Minden[1,2]. [1]*Epidemiology unit, German Rheumatism Research Centre;* [2]*Charite Universitätsmedizin, Berlin, Germany*

Already in 1991 Robert Blum pointed to the diverse set of issues of which the clinicians need to be cognisant to successfully care for youth with chronic illness. Since then, the special health care needs of adolescents and young adults with chronic diseases, including rheumatic diseases, have been on the agenda. Despite efforts to develop holistic services and programmes for youth, there are still inconsistencies in service delivery and practice standards. This revealed a survey among paediatric rheumatologists from 115 centres in 22 European countries in 2016. A minority of European paediatric rheumatology centres have a written transition policy, follow a standardised, structured approach in transitioning patients and measure the success of their interventions with evaluated instruments. To overcome these deficits and existing practice variation, key elements of transitional care, frameworks and pathways to implement and assess transition programmes have been recommended by EULAR and PRES.

However, as long as we don't have robust evidence upon best practice for transition, on the best metrics for measuring "success" and "outcome" of transitional care services and on the impact of interventions on the young people with rheumatic diseases will the service planning and delivery for transition aged youth remain suboptimal and result in adverse long-term outcomes.

The literature about transitional care is exponentially increasing each year and comprises among others assessments of experience of care and clinical outcomes, evaluations of different services and processes of care. What we have learned so far from transition research in the field of rheumatology, which research priorities are currently set on the agenda by health care providers and whether they meet those of young people will be in the focus of this lecture.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7264

SP0066 IMPLEMENTATION OF A BRIEF TRANSITION PROGRAMME FOR ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

L.R. Knudsen. *Department of Rheumatology, Aarhus University Hospital, Aarhus, Denmark*

Background: It is well described that adolescents and parents find transition between the children's and adult ward challenging (1–2) because they feel inadequate prepared, and find communication and cultural differences between child and adult care challenging. Thus, transitional care programmes becomes essential for a successful process (3).

Objectives: We aimed to develop a brief transition programme for adolescents with juvenile idiopathic arthritis (JIA), suitable for daily clinical practice in the children's and adult ward of rheumatology at Aarhus University Hospital, Denmark.

Methods: The development was based upon studies of transitional care programmes and qualitative studies of the patient, parent, and health professionals perspective in the transition process. Needs in the transition process from the perspective of both adolescents and parents were further investigated through semi-structured interviews. We used studies by Janet McDonagh and colleagues (3) as a theoretical framework for the programme development.

Results: The programme focuses on the final part of the transition process by including the adolescent from the children's ward at the age of 14. It runs for two years in the children's ward and continues the first year in the adult ward. The programme focuses on preparing the adolescent and parents for transition by enhancing the adolescent's knowledge and skills in coping with JIA. The programme further focuses on the relation between the adolescents and parents by bringing attention to the need for a gradually separation, and to placing more self-dependence on the adolescents. A guideline, describing the programme, containing concrete instructions to health professionals has been developed. The programme was primarily initiated by the adult ward, but nurses and physicians in both wards have been involved throughout the process.

The programme consists of the following elements;

- Assigned contact persons.
- Information leaflets about transitional care, transfer to adult care and differences between the children's and adult ward, i.e. in ways of working and treatment procedures.
- Independent consultations with health professionals.
- Materials for educational sessions.
- Educational sessions dealing with JIA and treatment, dialogue on adherence and challenges in adolescence.
- Arrangements of visits to the adult ward before transfer.

Conclusions: Our experiences with the programme in practise are generally positive. However, we have experienced that successful implementation calls for good collaboration and continuous involvement of the health professionals involved in the programme on a daily basis. Hence, ongoing meetings and communication have been essential to promote collaboration between the children's and adult ward.

References:

[1] Shaw KL, Southwood TR, McDonagh JE. User perspectives of transitional care for adolescents with juvenile idiopathic arthritis. Rheumatology 2004; 43:770–78.
[2] Reiss JG, Gibson RW, Walker LR. Health care transition: youth, family, and provider perspectives. Pediatrics 2005; 115:112–20.
[3] McDonagh JE, Shaw KL, Southwood TR. Growing up and moving on in rheumatology: development and preliminary evaluation of a transitional care programme for a multicentre cohort of adolescents with juvenile idiopathic arthritis. J Child Health Care 2006; 10:22–42.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1784

THURSDAY, 15 JUNE 2017

Heterogeneity in JIA

SP0067 CYTOKINES IN JUVENILE IDIOPATHIC ARTHRITIS

W. de Jager. *Pediatric Immunology, University Medical Center Utrecht, Utrecht, Netherlands*

The importance of cytokines in the pathogenesis of inflammatory diseases is highlighted by the success of therapeutic approaches directed against cytokines and cytokine receptors. Cytokines are characterized by their redundancy and pleyotropy: multiple cytokines can target the same receptor, while on the other hand a single cytokine can have multiple, even contradictory immunological effects.

Linking a cytokine/protein biomarker signature with clinical outcome may help to identify and classify patient cohorts. Thus "intelligent" cytokine signatures can be used as biomarkers in human inflammatory diseases. There are however various risks associated with this approach; often it is impossible to obtain material from the site of inflammation and there are various often not well-known technical aspects crucial to obtain reliable and usable results. Although standardization has been prominent in day to day clinical practice, standardization of sample collection and laboratory assessments remains suboptimal. Inconsistency in sample collection can affect the results of biological assays and thus several characteristics require thorough evaluation and standardization. This standardization is not limited to assay validity and reproducibility but also pre-analytical treatment and appropriate specimen types.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7203

SP0068 CLINICAL INSIGHTS INTO JIA HETEROGENEITY

A. Consolaro on behalf of EPOCA Study Group. *Istituto Giannina Gaslini, Genova, Italy*

Several epidemiologic surveys have documented a remarkable, yet unexplained, disparity in the prevalence of juvenile idiopathic arthritis (JIA) subtypes among different geographic areas or ethnic groups. Moreover, the therapeutic approach to JIA is not standardized and the availability of the novel and costly biologic medications is not uniform throughout the world. This disparity may have significant impact on disease outcome. The multinational study of the EPidemiology, treatment and Outcome of Childhood Arthritis (EPOCA study) is aimed to obtain information on the variability of JIA phenotypes in different geographic areas, the therapeutic approaches of pediatric rheumatologists practicing in diverse countries, and the disease status and outcome of children with JIA currently followed worldwide. Participation in the study was proposed to all pediatric rheumatology centers that are part of the Pediatric Rheumatology International Trials Organization (PRINTO), and to several centers in the US and Canada. Each center was asked to enroll 100 consecutive JIA patients or all consecutive patients seen within 6 months. Each patient received a retrospective and cross-sectional assessment. Parent- and child-reported outcomes were recorded through the administration of the Juvenile Arthritis Multidimensional Assessment Report (JAMAR). Participating countries were grouped into 6 geographic areas. Patients were then grouped according to their country's gross domestic product per capita (GDP) and the total expenditure on health per capita (HE) (source www.who.org). Currently, 8,325 patients from 44 countries have been entered in the web database. Comparison of main epidemiology, treatment, and outcome features across the different geographic areas was performed. Patients living in countries with GDP or HE below the median had lower frequency of remission, higher median cJADAS, higher frequency of damage, and were less frequently prescribed biologic DMARDs. These results were confirmed when analyses were conducted only in oligoarthritis or polyarthritis patients. These results provide further evidence of the wide difference of JIA characteristics across geographic areas in terms of age at disease onset, subtype prevalence, and frequency of anterior uveitis. Overall, patients living in non-Western countries had higher levels of disease activity and cumulative damage than patients followed in North America and Western Europe. This disparity in disease outcomes may be partially due to differences in the availability or affordability of biologics, as confirmed by the evidence of worst outcomes in countries with lower GDP or HE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7236

THURSDAY, 15 JUNE 2017

EULAR - EMA session

SP0069 REGISTRIES IN MUSCULOSKELETAL DISEASES AND THEIR REGULATORY USE

R. Vesely. *Rheumatology, Respiratory, Gastroenterology and Immunology Office, European Medicines Agency, London, United Kingdom*

Patient registries collect information about individuals sharing health-related characteristics, for example, a particular disorder, a treatment or a procedure. While randomised controlled trials typically provide the primary evidence supporting marketing authorisations for new medicines, the patients studied may not be fully representative of everyone ultimately receiving the medicine and the trials may provide limited information about the natural history of the disorder. Information collected in patient registries is potentially of value for filling these evidence gaps in certain situations and for providing post-marketing safety and effectiveness information. Multiple stakeholders stand to benefit from using registry information in this way including patients, healthcare providers, policy makers, manufacturers and healthcare regulators.

In 2014, the EMA commenced a Registry Initiative aiming to optimise the use of registries in supporting medicines authorisations. Establishing a strategy of early engagement between marketing authorisation applicants and registry holders and a task force to support activities, a pilot phase was undertaken aiming to understand the barriers and enablers in using registries to support marketing authorisation applications and to inform the development of recommendations to optimise their use.

On 28 October 2016 the Agency organised Patient Registries Workshop to collect and discuss the information about experience from different patient registries in various therapeutic areas. The topics included:

- Benefits of registries for regulators
- Benefits of registries for HTA and payers
- Benefits for industry
- Benefits for clinicians and researchers
- Benefits for patients
- Challenges in collaboration between registries
- Technical challenges
- Governance
- Sustainability

Conclusions of the pilot and the workshop have been utilised in the following activities including workshops to support registries in individual diseases.

There are multiple advanced registries in RA and JIA. Utilisation of outcomes of these and other existing or newly planned registries in other musculoskeletal diseases for regulatory purposes current environment offers new opportunities that require further analyses and collaboration.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7159

SP0070 NEWS FROM OMERACT – IMAGING AND MORE

V. Strand. *Stanford University School of Medicine, Portola Valley, United States*

Objective In rheumatoid arthritis (RA), MRI provides earlier detection of structural damage than radiography (X-ray) and more sensitive detection of intra-articular inflammation than clinical examination. This analysis was designed to evaluate the ability of early MRI findings to predict subsequent structural damage by X-ray.

Methods Pooled data from four randomised controlled trials (RCTs) involving 1022 RA hands and wrists in early and established RA were analysed. X-rays were scored using van der Heijde-modified or Genant-modified Sharp methods. MRIs were scored using Outcome Measures in Rheumatology (OMERACT) RA MRI Score (RAMRIS). Data were analysed at the patient level using multivariable logistic regression and receiver operating characteristic curve analyses.

Results Progression of MRI erosion scores at Weeks 12 and 24 predicted progression of X-ray erosions at Weeks 24 and 52, with areas under the curve (AUCs) of 0.64 and 0.74, respectively. 12-week and 24-week changes in MRI osteitis scores were similarly predictive of 24- week and 52-week X-ray erosion progressions; pooled AUCs were 0.78 and 0.77, respectively. MRI changes in synovitis at Weeks 12 and 24 also predicted progression of X-ray joint damage (erosion and joint-spacenarrowing) at Weeks 24 and 52 (AUCs=0.72 and 0.65, respectively).

Conclusions Early changes in joint damage and inflammation detected with MRI predict changes in joint damage evident on subsequent X-rays. These findings support the use of MRI as a valid method for monitoring structural damage in short-duration RCTs.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7189

THURSDAY, 15 JUNE 2017

Barrier free employment for young people with RMDs

SP0071 YOUNG PATIENTS: READY, BRILLIANT AND ABLE TO WORK!

L. Kullamaa. *European Patients' Forum, Brussels, Belgium*

In May 2016, European Young Patients Group, an initiative representing young patients from the European Patients' Forum (EPF) and the European Multiple Sclerosis Platform (EMSP), organised a workshop in the framework of the European Youth Event (EYE) 2016 in Strasbourg that corresponded with one of the five main programme themes titled, Exclusion or Access: Crackdown on Youth Unemployment.

The physical and emotional symptoms of chronic conditions, together with social stigma and attitude, create significant barriers to young patients in the job market. With appropriate support, they, like all enthusiastic young people, can be assets for employers. Through interactive discussion, creative expression, education and open dialogue, the workshop aimed to challenge expectations and inaccurate perceptions about the abilities of young people with chronic conditions, tackle societal beliefs and stereotypes of individuals with chronic conditions, stimulate discussion to explore concrete solutions and develop practical actions for young people and their allies accessing employment and steer change to ensure young patients benefit from equal opportunities and treatment at work. By addressing these specific objectives, the workshop was to ultimately raise awareness of the extra burdens faced by young people with chronic conditions transitioning from education to employment, as well as bringing public attention to the stigma and discrimination that exists at both the recruitment stage and in relation to employees disclosing their health conditions. It also was to compliment and

strengthen the EPF and EMSP's wider initiatives on tackling the multiple forms of discrimination faced by patients with chronic conditions.
The workshop demonstrated how many issues surrounding young people with chronic conditions transitioning into the labour market are still prevalent. The expectation of discrimination and stigma in the workplace, along with the unwillingness to disclose their condition when applying for a job for fear of rejection are confounded by young patients' experiences of negative employer attitudes. Moreover, the concept of quota systems and giving people with chronic conditions and/or disabilities preference among applicants for certain jobs possibly suggests that they are employed because they have a chronic condition and/or disability, not because of their abilities. This unambiguous form of positive discrimination also affects how young people manage information about their health. They feel forced to share about their condition to get an interview, however by doing so they risk being subjected to negative reactions in the interview or at the workplace.
Young people with chronic conditions have a great deal to contribute to the workplace and more action should be taken to encourage and support employers with hiring them. Training and resources should be provided to managers and employees to raise awareness of the impact that chronic conditions can have on an individual, and how they can be assisted through small adjustments or specific care requirements. Employees should not assume what someone can or cannot do and how their condition affects them, therefore a place for an open discussion should be created. In addition, where quota systems apply, they should be re-evaluated and designed to recruit young patients on merit, in competition with other workers without a chronic condition and/or disability.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7262

SP0072 CHALLENGES AND POTENTIAL SOLUTIONS ABOUT STAYING IN WORK AS A YOUNG PERSON WITH AN RMD

J. Andersen[1,2,3]. *[1]Lupus Europe, Romford, Essex, United Kingdom; [2]EULAR Young PARE, Zürich, Switzerland; [3]Lupus Dk, Gigtforeningen, Copenhagen, Denmark*

Introduction: A lot of young people with RMDs experience difficulties when it comes to staying in work after diagnosis. Some employers see a young person with an RMD-diagnosis as a liability. They are afraid it will cause a lot of difficulties with sick leaves and less work effort and in the end cost them a lot of money. Often the young person hasn't worked in the company for that many years (because of the age) and hasn't had the chance to make themselves indispensable/a valued work force yet, which makes it easy/obvious for the employer to terminate their employment.
The process of getting a diagnosis can often cause long periods of sick leave in the beginning and many employers don't understand that this will get better over time as the person gets used to having the disease and the medication has a chance to work properly.
Some young people choose not to tell their employer, that they have an illness at all, which can also be a big problem. When the employer and the work colleges don't know about the diagnosis, they cannot take special consideration to the person with the illness. Sometimes, you might a little extra break to be able to work an entire day and without it you risk wearing yourself down and having to quit the job yourself. If you choose to take the breaks yourself or perhaps fail at your job, because you try to do as much as the healthy persons, you risk getting fired, because nobody knows there is a good reason why you cannot do as much as you "should". Young and inexperienced persons can have difficulties demanding special treatment. They are often too insecure to stand their own ground and demand special consideration.
Objectives: I aim to examine the problems young people with RMDs face, when they want to stay in work and find potential solutions to these problems. How big is the problem? What can be done by the young people themselves? How can national patient organisations help them? How can EULAR PARE or other united European patient organisations help? Do we need new regulations? How do we make each country follow the EU-legislation?
Methods: I have asked young people with RMDs from all across Europe about their experiences with staying in work through social media and email. I have also asked patient organisations from all of Europe through email and personal meetings about their experiences, when it comes to young people with RMDs and work.
Results: The challenges differ from country to country. In some countries having an RMD is seen as a taboo, a sign of weakness. In other countries, an RMD-diagnosis makes you no different than the rest of society and the expectations to what you can do are often too high. I will attempt to make a presentation of potential solutions to the different issues. How it could help, if patient organisations spread awareness about RMDs among employers all across Europe. How, if the young person told their employer, that they have an RMD, it might help them in the long run. There are several places where young people with RMDs can get help and advise on how to act, when they want to stay in work. There already exists EU-legislation on the area, but not all EU-states respect them and adhere to them – this has to be changed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7167

SP0073 PRACTICAL EMPLOYABILITY SUPPORT FOR YOUNG PEOPLE WITH RMDS

M. Mcallister. *Working Well with Arthritis Joint Working Service, Arthritis Care, Glasgow, United Kingdom*

Background: Arthritis Care is a UK national charity providing a range of support through three services;
Working Well with Arthritis - Joint Working employability service (Scotland only).
87% of Arthritis and Work Scotland 2016 survey respondents' state arthritis has a high or very high impact on work. Joint Working (JW) service aims to address this by:
Providing holistic employability support to individuals of working age to improve their capacity to manage their condition in work.
Providing employers support to increase understanding of arthritis within the workplace
Offering employers free Arthritis Awareness training.
Young People and Families Service (YPFS) for age 10 - 25 years.
Series of free, one day or weekend workshops, to help reduce social isolation, increase confidence and management of condition.
Living Well with Arthritis offers adults access to self management support such as:
Managing pain/symptoms; activity/exercise; health walks, Tai chi for arthritis; peer support.
Objectives: Joint Working (JW) service aims to help individuals of working age with arthritis make informed decisions about work, support them to remain in, return to, or explore suitable work, training or alternative employability opportunities.
1 in every 1,000 young people in the UK has arthritis, YPFS complements medical treatment by providing additional social and emotional support, to help reduce isolation and increase resilience. With all services being delivered by Arthritis Care there is a natural crossover and support network for young people around transitioning from education to work.
The services aim to provide individuals with the knowledge, confidence, skills and support to empower them to make informed life and work decisions and access key support services - with the aim of improving their chances of remaining in work.
Method: There is a partnership and referral process to JW via NHS Rheumatology Occupational Therapy staff, within specific NHS areas, though referral to JW is open to anyone with arthritis.
Partnership working with; NHS, employability networks and Arthritis Care YPFS is key to the success of JW service.
Individuals with arthritis often find; communicating their needs, understanding their rights and navigating the system can be complex and overwhelming.
Joint Working provides support through a range of mediums; 1 to 1 meetings (where practical), email and/or phone. Exploring areas of concern, improving understanding of rights, awareness of, and access to national employment support schemes, mainstream or disability employability services.
Results: Young people who have used Joint Working service have been supported to access a range of services; obtaining specialist equipment or travel support to remain in work, returning to work after many years unemployed, work placement to support university course, volunteering or specialist employability opportunities,
Conclusions: The employability interventions have positive psychosocial benefits, reducing feelings of isolation, increasing confidence and raising aspirations.
People with arthritis value the opportunity to discuss any issues they have remaining in, returning to or embarking on a career path.
The ongoing access to all Arthritis Cares services, ensure young people have a long-term support network.
Maureenm@arthritiscare.org.uk
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7149

THURSDAY, 15 JUNE 2017

Epidemiology of rheumatic and musculoskeletal diseases - a critical appraisal

SP0074 THE FUTURE OF EPIDEMIOLOGICAL RESEARCH IN RHEUMATIC AND MUSCULOSKELETAL DISORDERS

L. Gossec. *Rheumatology Department, Paris 06 University, Pitié-Salpétrière Hospital, Paris, France*

Epidemiological research has gone through a very exciting time over the past years in rheumatic and musculoskeletal disorders (RMDs). The future is just as exciting. Although 'traditional' epidemiology in terms of prevalence and incidence of diseases is quite well-known now, there are many gaps to our knowledge in particular in the field of outcomes research (what to assess, when and how?) but also in the field of predictive factors (e.g. predictive factors of severity and of treatment response). Better knowledge in outcomes assessment is key to feasibility of standardised assessments and is the basis of shared decision making. Better knowledge of predictive factors will open the door to truly personalised medicine. Some future directions will be discussed in this talk.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7122

THURSDAY, 15 JUNE 2017

Ultrasound advanced I & II

SP0075 ULTRASOUND AND MAGNETIC RESONANCE IMAGING FUSION OF IMAGES EVALUATION OF TENOSYNOVITIS – A PILOT STUDY ON A NEW IMAGING TECHNIQUE IN RHEUMATOID ARTHRITIS PATIENTS

M.A. Danielsen[1,2]. *[1]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup; [2]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark*

Background/Purpose: Image fusion is an advanced imaging technology, which enables fusion of ultrasound (US) and magnetic resonance imaging (MRI). This fusion gives for each US probe position an exact projection of the corresponding anatomical area on a previously obtained MR image, during a live US assessment. This study is the first to address image fusion of US and MRI tenosynovitis.
The aim of this study was to assess and compare US and MRI visualisation of tenosynovitis using image fusion technique.
Methods: Fifteen rheumatoid arthritis patients with US verified tenosynovitis in the wrist or hand had an MRI performed of the affected wrist or hand. A subsequent image fusion was performed, i.e. the MR images and a live US assessment of one tendon sheath were fused. In order to compare the two imaging modalities quantitatively, the area of the tendon and tendon sheath in the transverse axis was measured on US and MRI for each image fusion. Due to partial volume artefacts (voxel containing two different tissues and therefore possessing a signal average of tendon and tendon sheath) on MRI two measures were performed; area 1) the circumference of the black tendon, i.e. excluding voxels containing two types of tissue 2) the circumference of the grey line that surrounds the black tendon, i.e. including voxels containing two types of tissue. Tenosynovitis was assessed using the proposed OMERACT semi-quantitative scoring system for US and MRI. US scoring was therefore based on both grey scale and Doppler, whereas MRI scoring was based only on post-contrast tenosynovial enhancement, measured as distance from the tendon to end of the enhanced tendon sheath.
Results: The median circumference area of the tendons and tendon sheaths on US and MRI 1 and 2 were respectively 0.16 (25;75 pctl: 0.10;0.25), 0.9 (0.06–0.18) and 0.13 of (0.10;0.25) for the tendons and 0.18 (0.13–0.26), 0.27 (0.20–0.45) and 0.23 (0.16–0.40) for the tendon sheaths. Statistically significant differences were found for all measured areas between US and MRI, except for the US tendon area and the MRI tendon area 2 (Wilcoxon's test; p=0.47). Overall agreement between US and MRI tenosynovitis scoring systems was good (see table 1).
Conclusion: In conclusion, we found that US and MRI have good agreement for quantitative assessment of tendons and scoring of tenosynovitis, when comparing the two modalities using image fusion, if the partial volume artefacts on MRI are included in the measure.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7204

SP0076 HOW AND WHEN TO ASSESS THE CERVICAL FACET JOINTS + DEMO

D.A. Bong[1,2] on behalf of EULAR Working Group Anatomy for the IMAGE.
[1]Instituto Poal de Reumatologia; [2]University of Barcelona, Barcelona, Spain

At any given time, 10% of the adult population will be affected by neck pain. Although similar in incidence to low back pain, its has less of a socio-economic impact and uncommonly progresses to neurologic deficit. Pain may result from degenerative, traumatic or inflammatory processes involving the diarthrodial facet (zygapophyseal) joints and/or the facet (medial branch of the dorsal dorsal rami) nerves. Although routinely evaluated by radiography, magnetic resonance imaging and computed tomography, high-resolution musculoskeletal ultrasound (MSKUS) imaging and guidance has become increasingly popular, particularly among pain management specialists, in the evaluation and treatment of these structures owing to its safety, portability, superior resolution and direct real-time visualization. This presentation will discuss the unique anatomy and sonoanatomy of the cervical spine and its innervation/vascularization with particular focus on the facet joints and nerves and the use of MSKUS in the evaluation and treatment of the facet joint/nerve with review of available evidence. Examination technique and sonoanatomic findings will be demonstrated.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7170

SP0077 HOW TO EVALUATE JOINTS IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

J. Vojinovic. *Pediatric Rheumatology, Clinical Centre, Medical Faculty, University of Nis, Nis, Serbia*

Ultrasound (US) has numerous advantages when used to examine joints in children compared to other imaging modalities. This include non-invasiveness, rapidity of performance, easy repeatability, high patient acceptability and lack of exposure to ionizing radiation. In addition, it does not require sedation for scanning in younger children. US is more sensitive than physical examination and may detect early disease that is not evident on physical examination. Lack of standardized precise definitions of grey scale (GS) and Power Doppler (PD) US findings in different age groups was the biggest limitation for its use. Additional difficulty is age dependent variability of normal sonoanatomy, due to maturation and ossification in children. That is why acquisition, interpretation and comparison of US images are completely different than in adults and had to be addressed specifically. All this may affect the validity of the technique, and without defined standardized examination technique, US can be a challenge in the childhood population. On the other hand, US as an imaging technique is considered to be examiner and equipment dependent. Studies resulting in good intra and inter-reader reliability and validity, based on specific definitions, are essential for its application as a diagnostic tool. Recently developed standardized image acquisition methodology, definitions of joint components in healthy children, as well as, definitions for synovitis components and its grading in GS and PD in children will be presented in details.
US allow precise and thorough visualization of inflammatory and destructive joint abnormalities, including synovial hyperplasia, joint effusion, cartilage damage, bone erosion, tenosynovitis and enthesopathy. In JIA ultrasound is considered particularly useful for its ability to detect subclinical synovitis and improve classification of JIA patients into the subtypes. Current evidences about application of ultrasound in JIA can improve definition of remission necessary to optimize treatment strategies. Due to peculiarities of US examination and image acquisition in children additional educational efforts among pediatric rheumatologists are required for expanding this imaging modality in daily practice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7186

THURSDAY, 15 JUNE 2017

PsA: an integrated perspective

SP0078 CAN IMAGING BE A PREDICTOR OF PSORIATIC DISEASE?

M. Østergaard. *Copenhagen Center for Arthritis Research, Copenhagen University Hospital Rigshospitalet, Glostrup, Denmark*

Early detection of inflammatory joint diseases is very important to allow prompt initiation of effective therapies. Identifying patients with early arthritic disease can be challenging by conventional clinical, laboratory and radiographic methods, and more advanced imaging modalities such as computed tomography (CT), magnetic resonance imaging, ultrasonography (US) and various nuclear medicine techniques can provide additional information.
This talk describes the current knowledge on the value of different imaging modalities for 1) predicting development of psoriatic disease in undifferentiated patients 2) predicting development of psoriatic arthritis (PsA) in patients with psoriasis with and without musculoskeletal pain and 3) predicting the disease course in patients with PsA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7188

SP0079 PATHOLOGIES ACROSS THE TISSUES IN PSA

R. Lories. *Skeletal Biology and Engineering Research Center - Dept. Development & Regeneration, KU Leuven, Leuven, Belgium*

The psoriatic disease concept includes the skin disease psoriasis and joint disease psoriatic arthritis. Increasingly, prevalent comorbidities such as obesity and cardiovascular disease are considered to be an integral part of the psoriatic disease concept in many patients.
Within this disease concept, accumulating evidence indicates molecular and cellular cross talk between affected organs and tissues. Skin inflammation affects the bone; nail disease is associated with specific types of arthritis; inflammation links to cardiovascular disease; skin or joint disease may contribute to depression. Novel therapeutic strategies are reaching psoriatic disease patients as never before. Their global impact could be envisioned from a holistic perspective, optimizing the strategy chosen as determined by the active molecular and cellular network that triggers and sustains disease.
Thus, linking the joints with the skin and other organs involved is proposed as an entry point towards personalized medicine in a complex disease.
Disclosure of Interest: R. Lories Grant/research support from: Celgene, Boehringer-Ingelheim, UCB, Consultant for: Janssen, Celgene, Novartis, Pfizer, UCB, Abbvie, Speakers bureau: Janssen, Celgene, Novartis, Pfizer, Merck, UCB, Abbvie

DOI: 10.1136/annrheumdis-2017-eular.7258

THURSDAY, 15 JUNE 2017

Autoinflammatory diseases in children and adults

SP0080 RECURRENT EPISODES OF FEVER AND ARTHRITIS IN ADULT PATIENT

C. Deaconu. *Department of Rheumatology and Internal Medicine, Sfanta Maria Hospital, Bucharest, Romania*

Background: Familial Mediterranean Fever (FMF) is a relatively rare condition that belongs to the more recent group of autoinflammatory diseases (AIDs)[1]. It primarily affects patients with Mediterranean or Middle Eastern origins and its clinical setting includes short, recurrent episodes of fever, serositis, skin rash and a high risk of amyloidosis[2]. FMF is an autosomal recessive transmitted disease and several mutations of the Mediterranean fever gene (*MEFV*) on chromosome 16 have been identified[3]. Patients respond well to colchicine therapy or if necessary, biological therapy with anti-IL 1, IL6 or anti-TNF could be initiated[4]. Establishing the right diagnosis might raise difficulties for rheumatologists who are not fully accustomed to this condition.
Objectives: To evaluate the clinical course, specific features and treatment difficulties of a male patient diagnosed with FMF in adulthood, based on the description of a case report.
Methods: Case-description using patient's medical records and investigations.
Results: This is the case report of a 37-year old male patient currently admitted for right knee arthritis and high grade fever (39.1℃). His medical history dates back at age 16 when he presented in the Pediatric Department with recurrent episodes of prolonged fever (up to 40℃), diffuse abdominal pain together with myalgia, arthralgia accompanied by increased acute phase reactants; after various sources of infection and hematological malignancies were excluded, physicians noted positive low titer ANA (1/20) but normal complement fractions, absent lupus (LE) cells. Further medical investigations showed a negative rheumatoid factor, ACPA, negative antibodies' panel (dsDNA, Sm, Ro, U1-RNP) and absent cryoglobulins but a positive HLA B27. No signs of sacroiliitis were detected on the x-ray. Patients' repeated complaints of knee or ankle arthritis together with later finding of positive anti-Salmonella and anti-Shigella antibodies leaded to establishing the diagnosis of reactive arthritis. Due to symptoms' persistence and reoccurrence under non-steroidal anti-inflammatory drugs, he was prescribed high dose corticosteroids and sulfasalazine. At age 20 the patient presented with recurrent arthritis of the knees and ankles, fever (38.5℃) and abdominal pain with markedly elevated inflammatory markers. The abdominal ultrasound highlighted a splenomegaly and peritonitis. Colchicine treatment was initiated and his favorable response led to MEFV genetic testing that revealed a mutation of the 10.1 exon, thus confirming the diagnosis of FMF by fulfilling two major criteria of the Tel-Hashomer diagnostic set. Subsequently, he performed a gingival biopsy that excluded the presence of amyloid deposits. Patient's partial response to colchicine with repeated incomplete attacks of FMF and persistent inflammatory syndrome led to the initiation of biological therapy with Etanercept along with Sulfasalazine and glucocorticoids, due to temporary unavailability of an anti-IL1 agent. Patient's delay in diagnosis and longstanding corticosteroid therapy led to major articular consequences (bilateral aseptic osteonecrosis of the femoral head with requiring hip arthroplasty).
Conclusions: This case presentation depicts the hardships of setting the right diagnosis in a case of late onset FMF due to unusual geographical setting, absence of suggestive family history and heterogeneous clinical presentation together with possibilities in therapeutic approach if patients are non or partially responsive to traditional therapies. Furthermore it points out possible drug side effects and comorbidities that require the same quality medical care as the main rheumatic disease.
References:
[1] Livneh A, Langevitz P, Zemer D, et al. Criteria for the diagnosis of familial Mediterranean fever. Arthritis Rheum. 1997;40(10):1879–1885. doi:10.1002/1529–0131(199710)40:10<1879::AID-ART23>3.0.CO;2-M.
[2] Yalcinkaya F, Ozen S, Ozcakar ZB, et al. A new set of criteria for the diagnosis of familial Mediterranean fever in childhood. Rheumatology. 2009;48(4):395–398. doi: 10.1093/rheumatology/ken509.
[3] Dogan H, Akdemir F, Tasdemir S, et al. A novel insertion mutation identified in exon 10 of the MEFV gene associated with Familial Mediterranean Fever. BMC Med Genet. 2014;15:74. doi:10.1186/1471–2350–15–74.
[4] Ozen S, Demirkaya E, Erer B, et al. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis. 2016;75(4):644–651. doi:10.1136/annrheumdis-2015–208690.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7171

THURSDAY, 15 JUNE 2017

Immunogenicity of biologics; myth or reality?

SP0081 THE T CELL RESPONSE TO THERAPEUTIC ANTIBODIES

B. Maillere. *Institute Frederic Joliot, CEA, gif sur Yvette, France*

Therapeutic antibodies (TMabs) are part of the best successful therapeutic products of the last decades. They are currently used to treat many inflammatory diseases such as rheumatoid arthritis (RA) and bowel diseases and represent worldwide a market of several billions of dollars. However they have the major drawback to be potentially immunogenic and therefore might elicit anti-drug antibodies (ADA). ADA could dramatically reduce the efficacy of the drugs or might provoke allergic reactions. Because generally self-proteins are less immunogenic than foreign proteins, the sequence of therapeutic antibodies has been humanized. However humanization even at the highest level does not fully guarantee the lack of immune responses demonstrating the important need to know more about ADA response. Because T cells are known to initiate the ADA response, we are currently investigating the T cell response to immunogenic therapeutic antibodies. With the perspective of immunogenicity prediction, we quantified the number of very rare T cells specific for therapeutic antibodies in the blood of normal donors and found a good concordance between the number of T cells specific to them and their respective clinical immunogenicity level. We then identified the CD4 T cell epitopes of four immunogenic TMabs with different levels of humanization, namely the chimeric antibodies Infliximab (Ifx) and Rituximab (Rtx), the humanized antibody Natalizumab (Ntz) and the fully human Adalimumab (Adm). CD4 T lymphocytes were expanded by several weekly rounds of stimulation with autologous dendritic cells loaded with each of the investigated antibodies and the T cell specificity was assessed by IFNg ELISPOT using overlapping peptides encompassing the whole sequence of their variable parts. Nine epitopes were identified in the VL and VH chains of Rituximab and Infliximab. They overlap CDR or FR regions of both chimeric antibodies and some of them are shared by multiple donors. As inferred from binding experiments, T cell epitopes often exhibited a good affinity for HLA-DR molecules found in the responding donors. Nine CD4 T cell epitopes were found in the VH and VL parts of the humanized therapeutic antibody Natalizumab while the fully human antibody Adalimumab hosted 10 T cell epitopes. As a result, the number of T cell epitopes is very similar across the different therapeutic antibodies but their location is highly variable from one antibody to another one. Finally to assess the clinical relevance of the identified T cell epitopes, we evaluated the ability of Ifx and Rtx T cell epitopes to stimulate T cells of patients having developed ADA. Two third of the T cell epitopes identified from the healthy donors stimulated PBMCs from ADA+ patients and promoted the secretion of a diversity of cytokines. These data emphasize the predictive value of evaluating the T cell repertoire of healthy donors to anticipate and prevent immunogenicity of therapeutic antibodies. Together our data provide new insights on the origin of immunogenicity of chimeric, humanized and human therapeutic antibodies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7250

SP0082 IMMUNOGENICITY OF BIOLOGICS IN INFLAMMATORY BOWEL DISEASES

A. Gils. *Dept of Pharmaceutical Sciences, KU Leuven, Leuven, Belgium*

Anti-tumor necrosis factor-alpha and anti-integrin monoclonal antibodies show great benefits for inducing and maintaining remission, healing the mucosa and restoring the quality of life of patients with inflammatory bowel diseases. The therapeutic potential of these intrinsically powerful biologicals is tempered by a high variability in clinical response. Whereas primary non-response is defined as the lack of clinical response to treatment, assessed 8–12 weeks after initiation, secondary loss of response is defined as loss of clinical benefit after initially responding which can be attributed to disease-related or drug-related factors. Assays have been developed to determine the concentration of the therapeutic antibody in serum of the treated patient. The trough concentration is the concentration just before the next administration and for practical reasons therapeutic drug monitoring is mainly based on measurement of these trough concentrations. Several studies have reported correlations between through concentration of infliximab, adalimumab, golimumab, vedolizumab and clinical outcome. Optimal therapeutic windows have been defined for both infliximab and adalimumab. A panel of prospective studies in which dosage regimens are adapted in order to achieve target trough infliximab concentrations that correlate with beneficial therapeutic outcomes have been initiated.
Immunogenicity is the capability of biologicals to elicit an unwanted immune response that results in the formation of anti-drug antibodies. Anti-drug antibodies can be non-neutralizing or neutralizing. Non-neutralizing antibodies do not impair the drug-target interaction but may increase clearance of the drug resulting in lower serum concentrations. Neutralizing anti-drug antibodies compete with the target for the antigen-binding site and modulate directly the activity of the drug in addition to the enhanced clearance of the drug. A number of anti-drug antibody assays to quantify the immunogenicity of biologicals have been developed. Most of the assays quantify the total amount of anti-drug antibodies but comparing anti-drug antibody concentrations between different assays is hampered by the

use of different calibrators and by the fact that drug tolerance differs among assays ranging from extreme drug sensitive over various forms of drug tolerant to drug resistant anti-drug antibody asssays. The clinical relevance of the different type of anti-drug antibody assays remains to be proven.
Combining therapeutic drug concentrations and anti-drug antibody concentrations with relevant patient, disease and drug information will lead to optimal dosing of patients aiming at optimal clinical, biochemical and endoscopic outcomes.
Disclosure of Interest: A. Gils Grant/research support from: IIR grants from pfizer, Speakers bureau: speakers fee by Pfizer, MSD, Abbvie, Takeda, JnJ
DOI: 10.1136/annrheumdis-2017-eular.7210

SP0083 AS A RHEUMATOLOGIST, DOES IT HAVE ANY CONSEQUENCE IN MY DAILY PRACTICE?

J.W. Bijlsma. *Rheumatology & Clinical Immunology, UMCU, Utrecht, UTRECHT, Netherlands*

It is nearly inevitable that when we administer foreign (even humanised) proteins intravenously or subcutaneously to a person, that said person will develop antibodies to that (foreign) protein. This happens to most of our patients when we administer biologicals; depending on the sensitivity of our methods, we can measure these anti-bodies easily or not at all. These antibodies start becoming a problem when they are actually binding the administered biological, thus making the active drug less available for its targeted function. We can evaluate this by measuring the actual drug-level, so called trough level. Numerous reports have been published, showing that there is indeed a negative correlation between e.g. anti-tumor necrosis factor (TNF) drug antibodies and the efficacy of anti TNF in the treatment of RA. It has also been shown that adding methotrexate (MTX) to the anti-TNF treatment improves its efficacy and reduces the level of anti-drug antibodies. Probably only 10 mg MTX weekly would be enough to obtain this effect.
So what do I do as a clinician when I observe that a patient, who originally did very well, loses response to her biological? Do I measure possible anti-drug antibodies? No, the consequences are zero: When the patient is not responding to the given drug anymore, I need to adapt the treatment; the drug she is using is not effective anymore, so we should change. Would the presence of anti-drug antibodies influence my decision? No, there is no cross-reactivity to other biologicals (even from the same class of action), except to its biosimilar (underscoring that it is a real biosimilar!). In case there is doubt whether a patient is actually using the biological we could better measure the drug-trough level; but –in my practice- this question seldom arises in patients with active arthritis, being treated with a biological.
Measuring drug-trough levels is a completely other item, and perhaps more relevant. Biologicals are in general given in a standard fixed dosage, while there are clear differences in patients characteristics, that could influence bioavailability of the biological. In addition when the disease is more active, it could be that more biological is needed to temper the inflammation compared to low disease activity, where perhaps a lower dosage would be more than effective. To guide physician and patient in personalizing and optimizing treatment with biologicals measuring drug-trough levels might be helpful. Different studies have been performed trying to use through level of the drug in adapting the dosage, and even in predicting possibility to stop the drug treatment. This area is still being evaluated and it is too early to make firm statements, but with a look at cost-effectiveness this will certainly become relevant.
Coming back to the original question: do I use anti-drug antibodies in my daily practice to guide treatment: no, it doesn't influence my decisions. Will I use in the future drug trough levels to guide treatment decisions: this could well be, but it is too early to make a final decision yet.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7118

THURSDAY, 15 JUNE 2017

Which target / outcome is more relevant in the management of SLE?

SP0084 BIOLOGICAL TARGETS IN SLE

C. Chizzolini on behalf of Swiss SLE Cohort Study and PRECISESADS consortium. *Immunology & Allergy, Geneva University Hospital, Geneva, Switzerland*

SLE is a prototypical condition characterized by the complete subversion of immunological tolerance and the generation of autoantibodies directed against a wide array of ubiquitous and tissue-specific antigens. This is possible because the joint dysregulation of the innate and adaptive arms of the immune system; which results from multiple gene polymorphisms, each contributing marginally, distinct epigenetic regulation, alteration of the threshold of activation for T and B cells, enhanced responses of antigen-presenting cells resulting from the altered disposal of apoptotic cells, as well as dysregulation of cytokine circuitries including regulatory networks.
Pathogenic mechanisms resulting in clinically overt SLE very likely are heterogeneous among individuals. Thus, the identification of biological targets in SLE goes also with the identification of selected modules of gene activation in distinct individuals. Very strong signals indicate that type I interferon (IFN) may contribute to autoimmunity in a large proportion of SLE individuals and therapeutic trials targeting IFN signaling suggest the clinical relevance of this mediator. B cells/plasmablasts are also relevant and obvious targets. Refinements in our understanding in B cell sub setting and/or the timing in disease development in which they play a relevant role should result in defining the appropriate targets specific to this cell lineage. Gene modules activated during flares suggest that neutrophils in a subset of individuals may also be relevant targets. Cytokine affecting T cell differentiation, in particular T follicular helper cells, represent additional relevant targets.
Within the last several years a number of novel biological targets have been identified in SLE. However, a single biological agent has been approved for SLE treatment in the last five decades. This underlies the difficulties encountered when translating validated targets in efficacious therapeutic agents. This stress the need for careful preclinical evaluation. It further emphasizes the need of small phase II clinical trials based on stringent inclusion criteria aiming at precisely identifying individual groups more likely to respond to validate the target. Current progress made in the identification of molecular signatures in individuals with SLE will offer the tools for the requested accurate selection.
Disclosure of Interest: C. Chizzolini Grant/research support from: Unrestricted reserach grant form GSK
DOI: 10.1136/annrheumdis-2017-eular.7228

SP0085 PATIENT REPORTED OUTCOMES

M. Schneider. *Policlinic & Hiller Research Unit for Rheumatology, HHUD, Duesseldorf, Germany*

In SLE as in other rheumatic diseases, the most relevant target of intervention should be a status with controlled disease process assuring no further accrual of damage. If actual expert discussions like DORIS define the frame of such a status, clinical activity measured by a validated lupus disease activity instrument, serologic activity and therapy – because of harm - are the dimensions of remission with its duration as additional factor for outcome. Patient reported outcomes (PROs) were not included. Otherwise, if payers and reimbursement system decide about relevance, patient outcomes are clear of highest importance as target.
Looking on the evidence of PROs for outcome in SLE, PROs were never used as primary endpoint in clinical trials. In RCTs, PROs were often collected and mostly explorative analysed. There is no evidence that PROs can validly define the above described status of controlled disease. But from systematic analyses in RA, we know that pure PRO like VAS of general health status and semi PRO like tender joints are at least as relevant as more "objective" criteria like swollen joints or CRP as clearly exhibited by the ACR/Eular remission criteria for RA.
The challenge in SLE is that the discrepancies between patients' and physicians' perception and perspectives are even more distinct than in RA. Sometimes, there is the expression that physicians and patients are describing different diseases. The burden of illness in lupus is better defined by pain than by organ manifestations; the overall survival in SLE is more related to lupus nephritis than to fatigue. It is obvious that physicians should analyse the actual clinical symptoms and integrate the future consequences of their actual management in their decision, and patients are more focused on release of their actual burden.
Until today, these different and divers perspectives are no integrated, neither in RCTs nor in daily care. But such integration is mandatory, because no side imagines the complete picture of lupus, which may also produce to the poor results of clinical trials. In routine care, this behaviour causes frustration and mental distress, optimal results are prohibited.
So, the answer to what is more relevant in the management of SLE patients - clinical targets, biological targets or PROs – is the integration of all important aspects of lupus. This implies more than the statistical evaluation of the best items of all three aspects, it is the active involvement of patients in their care: patient empowerment in SLE, a fruitful process, in which both sides have to learn a lot from and about each other.
Disclosure of Interest: M. Schneider Shareholder of: no, Grant/research support from: GSK; UCB, Consultant for: Astra-Zeneca; GSK; Lilly; Roche; Suppremol; UCB, Employee of: no, Paid instructor for: no, Speakers bureau: Astra-Zeneca; GSK; Roche; Pfizer; UCB
DOI: 10.1136/annrheumdis-2017-eular.7248

THURSDAY, 15 JUNE 2017

Joint EULAR - EFIS session: Tilting the balance: from disease to tolerance induction

SP0086 PATHOGENIC MEMORY CELLS: ROAD BLOCKS TO TOLERANCE INDUCTION?

H.-D. Chang. *German Rheumatism Research Center Berlin, Berlin, Germany*

While conventional state-of-the-art immunosuppression can lead to significant

improvement for patients suffering from rheumatic diseases, only in rare cases a therapy-free remission is achieved. In most cases stopping of treatment results in disease relapse. Apparently, components of the immune system are refractory to conventional immunosuppression and can drive the inflammation. Experimental and clinical evidence suggests that cells of the immunological memory persist despite immunosuppression and if pathogenic play a major role in the chronification of the disease. In particular long-lived memory plasma cells secreting autoantibodies represent a major therapeutic challenge. Once generated, they are not subject to physiological and even conventional therapeutic immune regulation. Their elimination may be prerequisite to curative therapies. A detailed understanding the lifestyle of long-lived memory plasma cells will be important to address this cell type therapeutically.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7257

SP0087 HOW ANTIGEN PRESENTING CELLS CAN BE TURNED INTO TOLEROGENIC CELLS

J.D. Isaacs. *Insitute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom*

Antigen presenting cells (APCs) lay at the heart of all immune responses. Whereas we generally consider APCs as cells that stimulate immune reactivity, they are also critically important for avoiding autoreactivity. Thus in health our tissues are patrolled by cells such as immature dendritic cells, which downregulate responses to self-antigens. Corruption of this process is a central factor in autoimmunity.

A number of groups have developed methods to generate "tolerogenic" antigen presenting cells, that mimic the cells which regulate self-tolerance in health. It is hypothesised that administration of such cells, loaded with autoantigens, to patients with autoimmune disease should be able to overcome autoreactivity and re-establish immune regulation. Our own group has developed a therapeutic approach based upon autologous tolerogenic dendritic cells, which we derive from circulating peripheral blood monocytes. Unlike conventional mature DC, which produce IL-12p70 and other pro-inflammatory cytokines, tolDC produce no IL-12p70 but high levels of IL-10. They deviate naïve T-cells towards an IL-10-producing, anti-inflammatory phenotype and induce hyporesponsiveness in memory T-cells. In mixed cultures they dominate mature, pro-inflammatory DC and down-regulate T-cell activation. Their phenotype is stable in the presence of pro-inflammatory stimuli. Equivalent murine tolDC switch off collagen-induced arthritis, with immune deviation from IL-17 to IL-10 production by CD4+ T cells and a reduction in type II collagen-specific T cell responses.

In a phase 1 trial (AuToDeCRA), we demonstrated that these cells are safe when administered into a recently inflamed target knee joint of patients with inflammatory arthritis. However, in that safety study we were unable to demonstrate a tolerogenic effect in vivo. Furthermore, we have reason to believe that administered cells may remain in the target joint, whereas a disease-modifying effect is likely to require migration to secondary lymphoid tissues. Moving forwards we are designing a study that will address the optimal administration route for tolDC, based on a technique to track the cells in vivo and to measure their effect on autoreactivity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7253

THURSDAY, 15 JUNE 2017

What to do about comorbidity?

SP0088 NEW DRUGS, BUT STILL COMORBIDITY

A. Häkkinen. *Health Sciences, University of Jyväskylä, 40014 Jyväskylä University, Finland*

As the population ages the simultaneous presence of multiple pathological conditions in the form of comorbidity and multimorbidity is more a rule than an exception. Comorbidity is reported in 35 to 80% of all ill people (Taylor et al. 2010). Comorbidity and multimorbidity are challenging researchers, clinicians and policy makers as these persons require more frequent appointments and hospitalizations and are at a greater risk for drug interactions, disability and mortality (Slater 2011).

Although numerous chronic disease prevention strategies and treatment guidelines have been developed, they mainly address single conditions and ignore the presence of co-existing conditions (van der Noyen 2016). Especially physical activity in its different forms has numerous preventive and curative effects in most of the diseases in addition to drugs. These benefits are such as increased muscle force and aerobic capacity, maintenance of bone and cardiovascular health, decreased inflammation and pain, improved function and well-being.

Studies reveal that more than 80% of rheumatoid arthritis (RA) patients carry two or more comorbid conditions (Krisnan et al. 2005). However, according to the QUEST-RA study (5,235 patients from 21 countries), only 14% of all patients reported to perform physical exercise at least 3 times weekly. Physical inactivity was associated with female sex, older age, obesity, comorbidity, disability, disease activity, pain and fatigue (Sokka et al. 2008). Traditionally, patients with RA were advised to limit physical exercises due to a fear that exercises might increase disease activity and be harmful for joints but more recent studies show that they benefit from exercise (Baillet et al. 2012).

Compared to RA, osteoarthritis (OA) is more common with prevalence of ∼150 million people world-wide. In OA comorbidity rates vary between 68–85% in different studies. The most frequently occurring co-morbidities are diabetes, hypertension, cardiovascular disorders, obesity and back pain. De Rooij et al. (2016) have developed tailored exercise therapy for knee OA and comorbidity. In their study during the 20-week program 76% of the participants needed adaptations to frequency, type, intensity or duration of exercise sessions. In addition, 96% needed education and coaching related to comorbidities.

In our study group-based strength and balance training for two years was offered for community-dwelling participants aged >75 years. The results showed that those who did not start in the group had more comorbidities, lower cognition, higher sedative load, higher risk of malnutrition, and poorer self-reported health than those who started in the gym. Despite of multimorbidity and hospital admissions, many older adults were capable of long-term regular training (Aartolahti et al. 2015).

With multimorbidity multi-drug therapies are common and they increase the risk of side effects. Exercise is also beneficial for health and it should be considered as a non-pharmacological drug. As for any other drugs, individual dosing of exercise is very important as well.

References:

[1] Aartolahti E et al. Gerontol Geriatr.2015;61:452–7.
[2] Baillet A et al. Rheumatology 2012;51:519–527.
[3] de Rooij M et al. Arthritis Care Res. 2016 Aug 26.
[4] Krishnan E et al Ann Rheum Dis. 2005;64:1350–2.
[5] Slater M, BMC Public Health 2011:11:77.
[6] Sokka T et al Arthritis Rheum. 2008:15;59:42–50.
[7] Taylor A et al. BMC Public Health 2010;10:718.
[8] van der Zee-Neuen A Arthritis Care & Research 2016:68,1823–183.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7061

SP0089 HOW TO PREVENT AND TREAT CARDIOVASCULAR COMORBIDITY WITH EXERCISE?

H. Dagfinrud. *Diakonhjemmet Hospital, Oslo, Norway*

Low cardiorespiratory fitness is a strong predictor of cardiovascular disease and all-cause mortality in healthy people as well as in patient groups. Unfit individuals have twice the risk of death from all causes, and tailored exercise is important to improve fitness.

It is well established that patients with inflammatory rheumatic diseases have increased risk for cardiovascular disease compared with healthy population, and it is therefore particularly important that these patients benefit from the risk-reducing effect of exercise. Exercise has traditionally been recommended as part of the treatment for patients with rheumatic diseases, but exercise programs has mainly focused on improving mobility and reducing pain. Further, patients with active disease has been recommended to exercise with low intensity. To increase cardiorespiratory fitness, however, high intensity exercise is needed. It is therefore encouraging that recent studies show that patients with active rheumatic disease tolerate intensive cardiorespiratory- and strength exercises and can benefit from such health-enhancing training. Recent research in this field will be presented and discussed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7287

SP0090 COMORBIDITY-ADAPTED EXERCISE FOR PATIENTS WITH KNEE OSTEOARTHRITIS

M. De Rooij. *READE, Center for Rehabilitation and Rheumatology, Amsterdam, Netherlands*

Exercise therapy is a key intervention in the management of patients with knee OA[1]. However, comorbidity is present in 68 to 85% of patients with OA (e.g. cardiac disease, diabetes type 2, obesity)[2,3]. Comorbidity interferes with exercise therapy. In clinical practice, comorbidity is a frequent reason to exclude patients from exercise therapy. If accepted into an exercise program, both therapists and patients tend to reduce exercise intensity to a level unlikely to be effective, because of fear of aggravating symptoms of the comorbid disease. Further, the effect of exercise therapy in patients with knee OA and severe comorbidity is not known. Patients with unstable medical conditions, precluding safe participation in an exercise program, are excluded from clinical trials. In view of the effectiveness of exercise therapy in knee OA and the high prevalence of comorbidity, there is a great need for comorbidity-related adaptations to exercise therapy. In this lecture a strategy (i3-S strategy) will be presented on how to develop comorbidity-related adaptations to exercise therapy in an index disease (e.g osteoarthritis)[4]. According this strategy we have developed a tailored exercise program for patients with knee OA and comorbidity. Subsequently, to evaluate the efficacy of the tailored exercise program for patients with knee OA and comorbidity (cardiac disease, diabetes type 2, COPD and obesity (body mass index $\geq$30kg/m^2) a randomized controlled trial (n=126) was performed in a secondary care setting. The results showed that tailored exercise therapy greatly improved physical functioning, reduced pain and

was also safe for patients with knee OA and (severe) comorbidity[5]. At present we are implementing and evaluating the protocol in primary care.

References:
[1] Fransen M, McConnell S, Harmer AR, Van der Esch M, Simic M, Bennell KL. Exercise for osteoarthritis of the knee. Cochrane Database Syst Rev 2015; 1:CD004376.
[2] Tuominen U, Blom M, Hirvonen J, Seitsalo S, Lehto M, Paavolainen P et al. The effect of co-morbidities on health-related quality of life in patients placed on the waiting list for total joint replacement. Health Qual Life Outcomes 2007; 5:16.
[3] van Dijk GM, Veenhof C, Schellevis F, Hulsmans H, Bakker JP, Arwert H et al. Comorbidity, limitations in activities and pain in patients with osteoarthritis of the hip or knee. BMC Musculoskelet Disord 2008; 9:95.
[4] Dekker J, de Rooij M, van der Leeden M. The i3-S strategy for developing comorbidity-related adaptations to exercise therapy. Disability and Rehabilitation 2016; 38:905–9.
[5] de Rooij M, van der Leeden M, van der Esch M, Cheung J, Häkkinen A, Haverkamp D, Roorda LD, Twisk J, Vollebregt J, Lems WF, Dekker J. Efficacy of tailored exercise therapy in patients with knee osteoarthritis and comorbidity: a randomized controlled trial. Accepted for publication in Arthritis Care & Research (Hoboken), 2016.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7077

THURSDAY, 15 JUNE 2017

Data visualisation: tables and graphs for publication and presentation I & II

SP0091 DATA VISUALISATION: TABLES AND GRAPHS FOR PUBLICATION AND PRESENTATION

M. Boers. *Epidemiology & Biostatistics; Amsterdam Rheumatology and immunology Center, VU University Medical Center, Amsterdam, Netherlands*

This workshop (held both on Thursday and on Friday) is an introduction to the principles of good graph and table design as pioneered by Cleveland[1] and Tufte[2] and updated by Few[3] so that the participant can better answer the following questions:

Which of the messages in my research results requires a graph or table? Recognizing how graphs improve on simple statistics and convey much more information. Knowing when a table is better, or keeping the data in the body text.

How can I best convey the message? Striving for clear vision by choice of graph, scaling, discrimination of data series, minimizing non-data ink, avoiding chart junk. Striving for clear understanding through a balance between data and explanation. Using order, subheadings, formatting and rules to guide your reader through your table data.

Is my graph/table truthful? Creating a direct proportion between graph and data quantities, avoiding forms prone to misinterpretation, labels to prevent ambiguity; keeping data in context, avoiding more dimensions in the graph than in the data.

This year's course will extend introductory material available via YouTube clips on the ARD website (ard.com)!

Direct link: https://www.youtube.com/playlist?list=PLXU14EQbU_V9JpmolAKsaCC0VjJzbxzAN

Note that you can also sign up for a special lecture followed by a poster tour after the session, devoted to poster design!

References:
[1] Cleveland WS. The elements of graphing data: Hobart Press, Summit, NJ, USA; 1994.
[2] Tufte E. The visual display of quantitative information. 2nd ed: Graphics Press, Cheshire, CT, USA; 2001.
[3] Few S. Show me the numbers. Designing tables and graphs to enlighten. 2nd ed: Analytics Press, Oakland, CA, USA; 2012.

Disclosure of Interest: M. Boers Consultant for: Director of Epiconsult BV that offers training in data visualization
DOI: 10.1136/annrheumdis-2017-eular.7125

THURSDAY, 15 JUNE 2017

Difficult to reach patient groups

SP0092 THE VICIOUS CIRCLE OF EDUCATIONAL LEVEL AND RISK OF POVERTY IN RHEUMATOID ARTHRITIS - RESULTS OF A CROSS-SECTIONAL MULTICENTER STUDY IN GERMANY

M. Zaenker[1,2]. *[1]Rheumatology Dept., Immanuel Klinikum Bernau & Heart Center Brandenburg, Bernau; [2]Brandenburg Medical School, Neuruppin, Germany*

This lecture will provide an overview on the dimensions of poverty in general and describe methods of assessing the risk of poverty in patients with rheumatoid arthritis (RA).

Based on results of a cross-sectional multicenter study of RA-patients from outpatient-clinics in Brandenburg and Saarland, Germany, this talk will give a rationale for how patients with RA are threatened by poverty due to treatment-related expenses, disability and early retirement compared to the general population.

It will be highlighted, that the equalized disposable income of RA patients is significantly lower than in general population and RA patients share a doubled risk of poverty, even in social-welfare well-secured countries such as Germany.

Further, the talk will demonstrate that both lower educational level and socio-economic state are associated with more severe disease course of RA and various underlying mechanisms will be discussed.

Disclosure of Interest: M. Zaenker Consultant for: Celgene, Hospira, MSD, Roche
DOI: 10.1136/annrheumdis-2017-eular.7247

SP0093 THE CHALLENGES AND SOLUTIONS FOR ENGAGING PATIENTS FROM ETHNIC BACKGROUNDS IN RHEUMATOLOGY CARE

K. Kumar. *University of Manchester, Manchester, United Kingdom*

Rheumatoid Arthritis (RA) is a condition with no cure and can cause disability[1]. RA affects nearly 1 in 100 adults. Early disease is characterised by pain and other features of inflammation, such as heat, swelling of joints, and loss of function. RA is associated with increased costs of co-morbid conditions (such as cardiovascular (CVD) associated with RA[2]. CVD associated with RA is the most common cause of death in RA patients. The risk of developing CVD is worse in some ethnic groups[3;3;4]. Furthermore, RA causes physical damage and social, economic, psychological and cultural problems that impact on all aspects of patient life.

There are effective treatments available for RA[5]; however, non-adherence to medicines (not taking medicines as prescribed) is a significant issue in RA[6]. Patients' perceptions play an important role in adherence to medicines. Our research in the UK, has showed differences between individuals from ethnic groups on how they view their medicines[7]. These views can potentially impact on medication adherence and patients' satisfaction with information they receive in clinic.

In the UK, we have recently shown that patients from different ethnic backgrounds with RA were disstaified with the information they receive about medicines[7]. Patients beliefs about medicines and illness pereceptions were found to be associated with satisfaction with information received by clinicans. Furthermore, the British Society of Rheumatology (BSR) led a national audit to investigate the delivery of care across UK rheumatology services. In this audit of early inflammatory arthritis service, we found patients from different ethnic backgrounds expressed greater impact of the disease on functional disability, fatigue, emotional well-being, physical well-being and coping and worse in older patients. This can impact on the way patients perceive their disease activity and information received on treatments. If we understand the needs of patients from ethnic backgrounds we can help improve the health outcomes. This session will provide the audience with insight into some solutions from the UK that might be helpful in order to improve satisfaction with information, disease enagement and treatment adherence.

References:
[1] Emery P. Evidence supporting the benefit of early intervention in rheumatoid arthritis. J Rheumatol, 2002;29 (2):3–8.
[2] John H, Kitas G, Toms T, Goodson N. Cardiovascular co-morbidity in early rheumatoid arthritis. Best Pract Res Clin Rheumatol 2009; 23(1):71–82.
[3] Grover S, Sinha RP, Singh U, Tewari S, Aggarwal A, Misra R. Subclinical atherosclerosis in rheumatoid arthritis in India. J Rheumatol 2006; 33(2):244–247.
[4] Chung CP, Giles JT, Petri M, Szklo M, Post W, Blumenthal RS et al. Prevalence of traditional modifiable cardiovascular risk factors in patients with rheumatoid arthritis: comparison with control subjects from the multi-ethnic study of atherosclerosis. Semin Arthritis Rheum 2012; 41(4):535–544.
[5] Smolen JS, Landewe R, Breedveld FC, Buch M, Burmester G, Dougados M et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis 2014; 73(3):492–509.
[6] Pasma A, Schenk CV, Timman R, Busschbach J, van den bemt B, Molenaar E et al. Non-adherence to disease-modifying antirheumatic drugs is associated with higher disease activity in early arthritis patients in the first year of the disease. Arthritis Research & Therapy 2015; 17:doi:10.1186/s13075–015–0801–4.
[7] Kumar K, Raza K, Nightingale P, Horne R, Chapman S, Greenfield S et al. Determinants of adherence to disease modifying anti-rheumatic drugs in White British and South Asian patients with rheumatoid arthritis: a cross sectional study. BMC Musculoskelet Disord 2015; 16(1):396.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7086

SP0094 **THE SWEDISH EXPERIENCE - HOW A PATIENT ORGANISATION COULD REACH OUT TO IMMIGRANTS AND DEVELOP THROUGH INTEGRATION**

T. Diao. *The Swedish Rheumatism Association (SRA), Stockholm, Sweden*

Bakground: in the early years of the new millennium many European countries faced an increased number of immigrants due to the second Iraqi war that affected the whole sub region. Some of these immigrants reached the Swedish shores and many of them have RMDs.
In an attempt to help integrate them to the Swedish society, the SRA reached out to these immigrants with RMDs to give them the tools and the knowledge of how to live a decent life with RMDs and also to inform them about how the Swedish healthcare system works. By informing them and giving them the tools to live their lives to the fullest in Sweden the SRA participated indirectly to reduce the burden of the welfare system and also increased the number of our members and embraced the diversity in the organisation.
Objectives: By running some tests with our local chapters the SRA noticed that the lack of knowledge about the RMDs was immense among these minorities. So the SRA decided to act together with other actors to facilitate the inclusiveness of these minorities into the society.
Methods: To achieve this giant task the SRA applied and received financial support from the Swedish General inheritance fund and collaborated with several health providers, the employment office, some Folk High Schools, ABF (Adult Liberal Education Association) and our local chapters and joinders in 5 of the biggest cities: Stockholm, Örebro, Gothenburg, Norrköping and Umeå.
Results: This experience was a breakthrough for the SRA. The SRA was the firth patient organisation that walked this new path. The iconoclastic experience enriched the SRA and gave it a great knowledge of how to reach out to minority groups and giving them the tools to be a fully part of the society despite the burden of the RMDs.
Conclusion: The SRA increased it's knowledge, capacity and flexibility during this experience. Today the SRA is cited as a reference in Sweden when it comes to reaching out to different minorities suffering of RMDs. Many organisations are now lining up to work with the SRA in these matters. In 2007 the SRA received the price for best project from the Swedish General Inheritance Fund.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7298

THURSDAY, 15 JUNE 2017

EULAR Projects in musculoskeletal imaging

SP0095 **EULAR RECOMMENDATIONS FOR THE USE OF IMAGING IN THE DIAGNOSIS AND MANAGEMENT OF LARGE VESSEL VASCULITIS IN CLINICAL PRACTICE**

C. Dejaco [1,2] on behalf of Taks force to develop the EULAR recommendations for the use of imaging in LVV. [1] *Rheumatology, Medical University Graz, Graz, Austria;* [2] *Rheumatology Service, Hospital of Bruneck, Bruneck, Italy*

Large vessel vasculitis (LVV) is the most common form of primary vasculitis comprising giant cell arteritis (GCA) and Takayasu arteritis (TA).
Although temporal artery biopsy and conventional angiography are still the golden standard diagnostic tests for GCA and TA, respectively, modern imaging methods including ultrasound, magnetic resonance imaging, computed tomography (CT) and ^{18}F-FDG positron emission tomography - CT are increasingly used. In clinical practice however, these methods are inconsistently applied and rheumatologists and other specialists are still uncertain about the specific value of these modalities. This project has been conducted with the aim to provide user-friendly, evidence-based recommendations for the use of modern imaging methods for diagnosis, monitoring and outcome prediction of primary LVV. Specifically, we give advice on 1) when to use these imaging techniques, 2) what specialists might conclude from imaging results and 3) what technical standards are required to achieve high quality imaging results.
These recommendations aim at an early and specific diagnosis as well as an improved assessment of LVV, thus ultimately leading to better outcomes of patients with LVV.
Disclosure of Interest: C. Dejaco Grant/research support from: Pfizer, MSD, Esaote, Speakers bureau: Pfizer, MSD, AbVie, Celgene, UCB, Roche, BMS, GSK, Novartis, Sandoz
DOI: 10.1136/annrheumdis-2017-eular.7221

SP0096 **EULAR/PRES STANDARDISED PROCEDURES FOR MUSCULOSKELETAL ULTRASOUND (MSUS) IMAGING IN PEDIATRIC RHEUMATOLOGY**

P. Collado. *Rheumatology, Hospital Universitario Severo Ochoa, Madrid, Spain*

Musculoskeletal ultrasound (MSUS) is a readily available and suitable imaging technique to asses the immature skeleton of paediatrics in different musculoskeletal rheumatic diseases (MSRD). Besides the potential operator –dependent feature of this technique, the age-related variation of normal sonoanatomy due to the child's growth makes more difficult acquisition, interpretation and comparison of images than in adults. Hence, to use MSUS as a valid technique for diagnosis of MSRD, it is needed to develop specifically evidence-based recommendations for paediatrics. Additionally, the variability in background and experience of ultrasonographers in different countries requires an international multidisciplinary contribution for an optimal standardization of MSUS performance in paediatric MSRD.
Reflecting the perceived need for developing recommendations on the standardization of procedures for performing MSUS examination in MSRD, a collaborative international EULAR/PReS task force was convened. In the talk, it is going to summarize the original proposed specific aims and update on work for each aim previously mentioned. A systematic literature search was performed in Medline and Embase from databases inception to 1st June 2016 as the first step. One hundred and eighty-eight articles were finally included after reviewing 6059 records identified. The scanning for the knee and the ankle joint was the most common reported, whereas the paediatric wrist was uncommon.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7074

SP0097 **REPORT OF ANATOMY FOR THE IMAGE REPORT OF THE EULAR WORKING GROUP OF ANATOMY FOR THE IMAGE**

I. Möller on behalf of EULAR Working Group Anatomy for the IMAGE. *Rheumatology; anatomy; sonoanatomy-sonopathology, Instituto Poal de Reumatología; University of Barcelona, Hospitalet de Llobregat, Spain*

The EULAR Working Group for the Image became an official "working group" 2 years ago with the purpose of furthering anatomic study and education related to the human musculoskeletal system and relevant non-musculoskeletal structures important in the practice of rheumatology and, more specifically, rheumatologic imaging including but not limited the high-resolution musculoskeletal ultrasound and MRI.
Studies performed:
- "Sonographic and anatomical description of the subtalar joint" – submitted for publication.
- "The anterior rotator cuff – a link between anatomy and ultrasound" – submitted for publication.
- "Learning model for successful ultrasound-guided synovial biopsy": pending submission.

New/Ongoing projects:
- Deep layer of the abdominal subcutaneous fat pad and cardiovascular risk: ultrasound measurement and relationship with visceral fat
- The mechanical function of the Hoffa fat pad as seen in a dynamic musculoskeletal ultrasound study.
- Ultrasound study of the neurovascular supply to the joints.
- The relevance of ligaments in inflammatory disorders of the articulations of the hand and wrist.
- The principles of anatomy as seen in musculoskeletal ultrasound.

Activities promoted by the group:
- Barcelona Sonoanatomy IX and X under scientific endorsement of EULAR.

Support:
- OMERACT: "Reliability exercise of synovitis at the subtalar joint".

In collaboration with the University of Barcelona:
- Certificate Course "Expert in Musculoskeletal Ultrasound".

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7157

THURSDAY, 15 JUNE 2017

Capillaroscopy I & II

SP0098 **THE IMPORTANCE TO DIFFERENTIATE NORMAL FROM ABNORMAL CAPILLAROSCOPIC IMAGES FOR AN EARLY DIAGNOSIS OF DISEASE**

V. Smith. *Department of Rheumatology, Faculty of Internal Medicine, Ghent University Hospital, Ghent University, Gent, Belgium*

Medical doctors frequently get patients with Raynaud's phenomenon (RP), a frequent symptom in the general population, referred. The importance of distinguishing normal capillaroscopic findings from (pathognomonic) abnormal (pathological) findings, lies in the fact that this distinction allows the differentiation between a primary RP (not connected to any connective tissue disease [CTD]) from a secondary RP due to systemic sclerosis (SSc) and diseases of the scleroderma spectrum.
What is normal in primary RP? A normal capillaroscopic pattern, by qualitative assessment, is characterized by a homogeneous distribution of hairpin shaped capillaries as a "comb-like structure", with a density of between 9–14 capillaries per mm. Yet, there exists a wide intra- and inter-individual variety in a normal population which will be discussed in this session.
What is pathognomonic abnormal in patients with RP due to SSc? Patients with the RP who have an underlying clinically recognizable (= with skin involvement) SSc show a very characteristic combination of capillary abnormalities in the nailfold, which can easily be assessed through qualitative assessment (= pattern

recognition). Maricq et al. described last centrury, with the widefield technique (magnification X12–14) the scleroderma pattern. This pathognomonic combination contains the following: a striking widening of all three segments of the capillary loop (arterial, venous and intermediate), loss of capillaries, disorganization of the nailfold capillary bed. Many branched "bushy" capillaries may also be observed.
In 2000, Cutolo et al. qualitatively assessed the nailfolds of an SSc cohort with patients fulfilling the American College of Rheumatology (ACR) criteria for SSc with the nailfold videocapillaroscopic (NVC) technique (magnification X200). According to the different proportions of the hallmark parameters of the scleroderma pattern (giants, capillary loss, hemorrhages and (neo)angiogenesis Cutolo et al. defined three patterns "early", "active" and "late".
The central role of capillaroscopy in distinction between a primary and secondary RP due to SSc is reflected by the fact that capillaroscopy is one of the new ACR/EULAR criteria for classifying a patient as having SSc.
Besides playing a paramount role in distinguishing a primary from secondary RP, capillaroscopy has an additional role. It can inform the rheumatologist dealing with a patient population with merely the RP and no other signs of a CTD, who will futurely develop SSc. This role is reflected by capillaroscopy playing a central role in the LeRoy and VEDOSS criteria for (very) early diagnosis of SSc.
What about capillaroscopic morphology in connective tissue diseases other than SSc?
No large scale prospective cohorts exist describing capillaroscopic morphology in connective tissue diseases other than SSc. Moreover, several morphologic defintions exist across literature of different schools. The EULAR Study Group on microcirculation in Rheumatic diseases was set up in 2014 to tackle, in between others these working points.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7161

SP0099 WHY CAPILLAROSCOPY CAN PREDICT DISEASE SEVERITY AND PROGNOSIS

M. Cutolo on behalf of EULAR Study Group on Microcirculation. *Internal Medicine, Research Lab Division Rheumatology University of Genova, genova, Italy*

Nailfold capillaroscopy (NVC) is today considered to be safe biomarker in order to make an early diagnosis of slected Connective Tissue Diseases (CTDs) in presence of Raynaud' phenomenon, and to measure progressive microvascular and tissues damage including response to long term treatment,
Systemic sclerosis is the only CTD to date in which prognostic indices have been described to predict clinical complications. Predictions have been made based on baseline capillaroscopic images and based on sequential capillaroscopic follow-up.
Baseline qualitative-assessed scleroderma patterns have been described to be linked with future organ involvement in any of the nine organ systems affected by SSc according to the disease severity scale of Medsger (general, peripheral vascular, skin, joint, muscle, gastrointestinal tract, lung, heart and kidney) (1). Additionally, baseline capillaroscopic evaluations have been linked to future development of digital trophic lesions in SSc. A simple scoring system has been used recently in the largest pan-European study evaluating the role of capillaroscopy in predicting digital ulcers in SSc (2). More specifically, in this study, simply the number of capillaries per linear mm had been evaluated. Besides counting the number of capillaries/capillary alterations, dimensions can also be measured. The latter has also been used in prediction of patients with RP whether, because of SSc, there will be a possibility for them to develop a secondary RP. Similarly, it has recently been attested that if the average capillary diameter (average of the largest apical, efferent and afferent limb in 16 fields, more specifically 2 fields per finger, fingers 2–5 from each hand) is less than 30 μm in a group of patients with RP but without scleroderma characteristic findings on nailfold videocapillaroscopy (NVC), the patient has a low chance of developing SSc, while if $>$30 μm, then the patient has 50% chance to develop SSc (3). Concerning the ability of capillaroscopy to measure response to treatment, there are yet no prospective randomized, double-blind, placebo-controlled trials, evaluating the ability of capillaroscopy to monitor response to therapy concerning RP-related outcome measures. It is noteworthy and promising that in small studies showing response of immunosuppressive/vasomodulating treatment on disease severity, outcome measures are available (4–6).
References:
[1] V. Smith et al. J Rheumatol 40,2013,52–7.
[2] M. Cutolo et al. Arthritis Rheumatol 68,2016,2527–39.
[3] A. Trombetta et al. J Rheumatol 43,2016, 599–606.
[4] I. Miniati et al. Ann Rheum Dis 68, 2009;94–8.
[5] V. Smith et al. J Rheumatol 43, 2016,995–6 6.
[6] A. Trombetta, C et al. J Rheumatol. 2016;43:2033–41.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7295

SP0100 HOW TO SELECT THE MOST APPROPRIATE CAPILLAROSCOPIC DEVICE: PROS AND CONS

W. Hermann. *Department of Rheumatology and Clincial Immunology, Kerckhoff-Klinik, Bad Nauheim, Germany*

One of the most important indications for performing capillaroscopy is to differentiate between primary and secondary Raynaud's syndrome. Different kinds of microscopes are at hand and generally vary in terms of picture quality or price. Before purchasing a microscope and capillaroscopy software, several considerations about the required standards of examination should be made; some of which are summarized as follows:

- The region of interest (ROI). Normal capillaries have a mean diameter of about 8 μm. For an accurate assessment a magnification of 100–200x is recommended, for an overview the magnification of 50x is sufficient.
- Measurement. Beside qualitative measures like changes in vessel architecture, there should be the possibility of quantifying the number of capillaries/mm or vessel diameters.
- Documentation. All parts of the examination have to be stored and assigned to patient and case.
- Practical aspects and handling of the device.
- Different kinds of microscopes are on the market of which three will be discussed in detail. Briefly summarized:
- Stereo microscopes.

Advantages: Very good image quality, zooming in and out without problems, relatively easy to use.
Disadvantages: device is not mobile, in patients with finger contractures examinations are difficult to perform, relatively high costs.

- Videocapillaroscopes:

Advantages: Very good image quality, easy to use, "gold standard" for capillaroscopy.
Disadvantages: No overview, zooming in and out not applicable (change of lenses required), relatively high costs.

- USB microscopes:

Advantages: low costs, zooming in and out without problems, easy to use.
Disadvantages: limited picture quality, documentation laborious.
Selecting a capillaroscopic device depends on the conditions of use ("quick look" vs. "academic evaluation and follow up"), which should be clarified before buying a device. The price range is significant and usually differs between 100€ for USB microscopes and up to 10,000€ for stereo and videocapillaroscopes
Literature:
[1] Cutolo M et al. How to perform and interpret capillaroscopy. Best Pract Res Clin Rheumatol. 2013;27(2):237–48.
[2] Cutolo M et al. State of the art on nailfold capillaroscopy: a reliable diagnostic tool and putative biomarker in rheumatology? Rheumatology (Oxford). 2013;52(11):1933–40.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7206

THURSDAY, 15 JUNE 2017

Ultrasound, clinical, diagnostic and therapeutic skills I & II

SP0101 DIAGNOSTIC AND THERAPEUTIC ULTRASOUND-GUIDED PROCEDURES

P. Mandl. *Rheumatology, Medical University of Vienna, Vienna, Austria*

The lecture will provide an overview of sonography-guided musculoskeletal interventions which can be grouped broadly as diagnostic and therapeutic procedures. Primarily diagnostic procedures include arthrocentesis, biopsy from various musculoskeletal tissues (synovial, bone, muscle etc.), aspiration of fluid from cystic lesions, tendon sheaths and bursae. The therapeutic group features joint and soft tissue injections, needling of periarticular calcification, including barbotage. Both indirect and direct-guidance techniques will be detailed and published literature on accuracy, outcome and safety of sonographic-guided interventions will be reviewed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7272

SP0102 HOW TO PERFORM A QUICK AND EFFICIENT PHYSICAL EXAMINATION

M. Doherty. *Academic Rheumatology, University of Nottingham, Nottingham, United Kingdom*

The GALS (Gait, Arms, Legs, Spine) screen is a quick and reasonably sensitive way to detect common musculoskeletal (MSK) abnormalities as part of a general medical assessment (1). However, for a person with MSK complaints a detailed assessment is required to determine the diagnosis and the impact of the condition on that person. The key starting point is the history. This needs to be holistic and individualised as the enquiry proceeds since the impact of any condition is

person specific and influenced by many factors (e.g. psychosocial factors, illness perceptions, sleep, comorbidity etc.). A thorough history alone usually suggests the single most likely cause for the patient's problem(s). The history should then guide the subsequent physical examination – an efficient targeted "rapier" approach is recommended in which the practitioner selects the appropriate skills from a range of competencies according to specific elements in the history. This contrasts with a more lengthy hypothesis-free "general screen" in which the same set of uniform procedures is undertaken in each patient.
This presentation will cover key principles and considerations of assessment and illustrate how the history guides the subsequent "rapier" examination (2). Examples include:
(1) in the *history:* determination of pain localisation and features that associate with radiated pain; important pain and stiffness characteristics that differentiate mechanical usage-related pain, inflammatory pain, acute crystal synovitis pain, destructive bone pain and neurogenic pain; non-specific symptoms of inflammation (2) in the *examination:* usual order of inspection at rest, inspection during movement, then palpation at rest and during movement of symptomatic regions; contrasting clinical findings that quickly differentiate joint and peri-articular problems; initial selection of the movement(s) that is affected first and most severely by arthropathy - the tight pack position(s); detection of "stress pain" (pain worse in tight-pack positions but reduced/absent in loose-pack positions - the most sensitive sign of inflammation); examination for effusion, soft-tissue and firm swelling; use of resisted active movements and stress tests for peri-articular lesions; a targeted screen for asymptomatic disease prompted by main diagnosis.
EULAR learning resources available at http://www.eular.org/edu_training_dvd.cfm include: (1) The "GALS" screen and (2) Principles of the musculoskeletal history and examination.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2947

SP0103 **HOW TO ASSESS US COMPETENCY SKILLS**

H.B. Hammer. *Dept of Rheumatolgy, Diakonhjemmet Hospital, OSLO, Norway*

To optimize and standardize musculoskeletal ultrasonography education for rheumatologists, there is a need for competency assessments addressing the required training and practical and theoretical skills. Because of the increasing use of MSUS in rheumatology, there has been a focus over the past years on training.
A minimum training requirements are described by The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) where a 3 levels competency assessment (COMPASS) has been developed for rheumatologists, including an in-detail description of what theoretical and practical competencies to be acquired at each level with a related log book (1). The rheumatology-COMPASS levels are closely related to the levels of the EULAR MSUS courses, thereby ensuring that the content is supported by already provided courses such as the EULAR and EULAR-endorsed MSUS courses to facilitate the implementation of the rheumatology-COMPASS. In COMPASS level 1 the course contents resemble the EULAR MSUS basic and intermediate courses, level 2 resembles the EULAR MSUS advanced course whereas level 3 requires attendance in a "teach-the-teachers course" or experience as a teacher in at least 2 international MSUS courses. Level 3 also includes an academic level requiring research activity and acceptance of level 1 and 2 sonographers for training.
The EULAR MSUS courses have been organized since 1998 and the interest in these courses has been increasing. In 2007, the first 3 level EULAR MSUS course was conducted with great success and the 3 level courses (basic, intermediate and advanced) have been running ever since in relation to the EULAR congress, focusing mainly on the relevant content on the individual levels and the distribution between practical and theoretical skills.
EULAR has developed the following competence levels; level 1 and 2. The EULAR level 1 competency includes the performance of EULAR Online MSUS course and attendance to basic, intermediate and advanced MSUS courses, where attending the intermediate and advanced courses require a certain number of US examinations (however, if already reached COMPASS level 1, 2 or 3, there is no need of images for the EULAR courses), and the advanced course requires in addition to pass a practical examination. The EULAR level 2 competency is organized to ensure a minimum level of US knowledge for teachers in MSUS courses (2). This level includes the EULAR Teach the Teachers course as well as passing a theoretical and practical examination. Since there is a growing number of EULAR endorsed MSUS courses, it is of highly importance that the teachers in these courses have equal qualifications thereby providing comparable training and competencies beneficial for the clinical use of US. Information about the competence requirements is found at the EULAR website (http://www.EULAR.org).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7147

THURSDAY, 15 JUNE 2017

Macrophage M2 polarization: implications in fibrotizing diseases

SP0104 **REPROGRAMMING OF MYELOID CELLS IN CANCER: MECHANISMS AND SIGNIFICANCE**

A. Sica. *Pharmacological Sciences, University of Eastern Piedmont, NOvara, Italy*

Chronic inflammation mediates tumor development by promoting a constant influx of inflammatory cells capable of modulating genes involved in cancerogenesis and creating micro and macroenvironments that support cancer growth. A major side effects of cancer inflammation is the pathological expansion and recruitment of myeloid cells endowed with immunosuppressive activity, to control the unresolved inflammation. Tumors reprogram myeloid cell differentiation and functions through various mechanisms, including altered metabolism, cancer-related inflammation andalteration of the hematopoietic output. These events govern the expansion of myeloid suppressor populations, mainly myeloid-derived suppressor cells (MDSCs) and tumor associated macrophages (TAMs). MDSCs and TAMs orchestrate tumor immunosuppression in concert with regulatory T cells, inhibitory cytokines and immune check points receptors, and act to subvert anti-tumor immunity, hence causing that eventually support immune evasion establishing a bottleneck for cancer immunotherapy. I will discuss inflammatory circuits and epigenetic events sustaining the expansion and the tumor-promoting reprogramming of myeloid cells in cancer bearers.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7285

SP0105 **MACROPHAGES, METABOLISM AND INFLAMMATION**

N.O.S. Camara. *Immunology, University of Sao Paulo, Sao Paulo, Brazil*

Macrophages are a heterogeneity population implicated in several diseases and correlated with distinct tissue outcomes after injury. M2 macrophages have been associated with tissue repair whereas M1 macrophages participate in early phase of tissue damage. Recent works have also suggested that upon activation, macrophages can use distinguished nutrients as source of energy and these metabolic pathways lead to their activation and differentiation. Nutrient sensors are intimae associated with innate receptors and therefore connected with inflammatory response. Uric acid is a damage-associated molecular pattern (DAMP), released from ischemic tissues and dying cells which, when crystalized, is able to activate the NLRP3 inflammasome through frustrated phagocytosis. Soluble uric acid (sUA) is found in high concentrations in the serum of great apes, and even higher levels in some diseases, before the appearance of crystals. sUA can be released in a hypoxic environment and triggers NLRP3 through the production of mitochondrial ROS, with increased maximum and reserve oxygen consumption ratio (OCR) and higher VDAC protein levels. This process is followed by ASC speck formation, caspase-1 activation and IL-1β release. These findings may have profound implications for inflammatory-related diseases.
Support: FAPESP and CNPq.
Disclosure of Interest: N. Camara Grant/research support from: FAPESP, CNPq
DOI: 10.1136/annrheumdis-2017-eular.7283

FRIDAY, 16 JUNE 2017

Mucosal B cells: gatekeepers of immune function

SP0106 **THE LUNG AS A DRIVER OF RA-ASSOCIATED AUTOIMMUNITY**

A. Catrina. *Department of Medicine, Rheumatology Unit, Karolinska University Hospital and Institutet, Stockholm, Sweden*

Rheumatoid arthritis (RA) is a chronic inflammatory disease resulting from the complex interaction between genes and environment. In a large majority of patients this interaction leads to formation of disease-specific anti-citrullinated proteins antibodies (ACPA). Systemic autoimmunity may be triggered at mucosal sites (such as the lungs) long before the first signs of inflammation are starting in the joints. According to this model, smoking (and others environmental triggers) induces subclinical inflammation in the lungs, leading to increased local citrullination and formation of ACPA in genetically susceptible individuals. Lung changes on high-resolution computer tomography are present in both early-untreated ACPA positive RA and ACPA positive individuals at risk for but not yet having disease. Further, signs of subclinical inflammation and immune activation with germinal centers formation and ACPA enrichment is present in early untreated RA. Shared citrullinated targets have been described in the lungs and joints of patients with RA and more recent data unravels novel mechanisms showing how this extra-articular triggered autoimmunity progresses to joint-specific inflammation. Beside an initiating role, the lung might also be a secondary target for antibodies, especially in longstanding seropositive RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7293

FRIDAY, 16 JUNE 2017

WIN & HOT session

SP0107 HOT SESSION: SCLERODERMA TREATMENT

C.P. Denton. *Centre for Rheumatology, Royal Free Hospital and Ucl Medical School, London, United Kingdom*

This presentation will provide an up to date summary of current management of SSc that can be applied across the disease spectrum. Systemic sclerosis (SSc) remains a challenging multifaceted rheumatic disease with high mortality and morbidity. However, treatments are emerging for some aspects of the disease and long term survival has improved significantly over the past decades. This session will review the clinical challenge and current therapeutic landscape of SSc focusing on practical aspects of management such as identifying and treating significant organ based complications in the lung, heart, kidney and gastrointestinal tract. Current approaches to overall disease management will be summarized including the use of haemopoietic stem cell transplant in selected poor prognosis cases. Recently updated EULAR/EUSTAR treatment recommendations will be reviewed and other evidence based management guidelines will be considered within a practical patient-focused framework.

Disclosure of Interest: C. Denton Grant/research support from: Inventiva, CSL Behring, GSK, Bayer, Consultant for: GSK, Actelion, Inventiva, Roche

DOI: 10.1136/annrheumdis-2017-eular.2534

FRIDAY, 16 JUNE 2017

Comorbidities in rheumatoid arthritis

SP0108 HERPES ZOSTER: HOW TO PREVENT, TO DIAGNOSE AND TO TREAT

L. Calabrese. *Rheumatology, Cleveland Clinic, -Cleveland, United States*

Herpes Zoster is a major public health problem and is an infection that results from re-activation of latent varicella infection acquired most commonly naturally or more recently through immunization. The incidence of HZ is approximately twice that of the general population in patients with immune mediated inflammatory diseases (IMIDs). Underlying mechanisms are largely those which compromise cell mediated immunity and epidemiologic risks largely follow immunosenescent patterns (i.e. aging). Rheumatologists use a large variety of immunosuppressive drugs which further increase the risk of HZ and are obliged to recognize the clinical syndrome, its complications, apply effective therapy and be actively engaged in strategies to maximize immunization and prevention. This discussion will focus on recent advances in each of these areas highlighting newly described complications of HZ such as stroke and advances in vaccine development.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7214

FRIDAY, 16 JUNE 2017

Life-threatening presentation of rheumatic diseases

SP0109 ACUTE RESPIRATORY FAILURE, MACULO-PAPULAR RASH, INDURATIVE EDEMA OF THE EXTREMITIES AND CERVICAL LYMPHADENOPATHY IN A 6-WEEK-OLD INFANT

C. Birolo. *Pediatric Rheumatology Unit, Department for Woman and Child Health, University of Padua, Italy, Padua, Italy*

Case report: A previously healthy 40-days-old male infant, from non-consanguineous parents from Morocco, presented in a peripheral hospital with fever for 48 hours, associated with rhinorrhea, mild diarrhea and progressive irritability during the last 24 hours. Initial laboratory studies revealed elevated acute phase reactants (CRP 116 mg/L), mild neutrophilia, elevated liver enzymes (AST 315, ALT 174 U/L), direct hyperbilirubinemia, discoagulopathy. Cerebral spinal fluid analysis and microbiology cultural workup resulted negative. A wide-spectrum antibiotic and antiviral therapy was initiated. On the 6th day of illness he developed diffuse maculo-papular rash, indurative edema of the extremities, right cervical lymphadenopathy and bilateral conjunctival injection. On the basis of a certain clinical diagnosis of Kawasaki disease and the infant was treated with IGIV 2 g/kg. An echocardiography performed prior to the IGIV infusion showed homogeneously dilated coronary arteries (left coronary artery 3.2 mm, right coronary artery 2.2 mm). Twelve hours after the end of IVIG infusion, the child presented a rapidly progressive, severe respiratory failure requiring endotracheal intubation and was transferred to our ICU. On admission (day 7th), physical examination revealed a feverish, critically ill-infant with hepatomegaly (5–6 cm below the right costal margin), diffuse maculo-papular rash, “sock-like” erythema and swelling of the feet, cheilitis, bilateral conjunctival injection and right cervical adenopathy. The urine output was markedly decreased; he rapidly developed hemodynamic instability with hypotension and tachycardia. Complete blood count showed anemia (6.8 g/dl), thrombocytopenia (16.000/mmc), elevated CRP (240 mg/L), hypoalbuminemia (18 g/dl) and hypofibrinogenemia (0.83 g/L); liver enzymes were normal. Intensive ventilatory and hemodynamic support therapy were started, in addition to a massive transfusional regimen.

Given the clinical and hematological picture, the diagnosis of MAS was considered and subsequently confirmed by high ferritin level (2197 mcg/L), AST above the normal value (61 U/L) and hypertriglyceridemia (181 mg/dl) [2]. The clinical suspicion was supported by persistent cytopenia despite daily transfusions, low erythrocyte sedimentation rate (3 mm/h) with concomitant rising CRP, elevated IL2-R level (28.320 KU/L) and decreased NK function. The patient was treated with high dose methylprednisolone pulse therapy (25 mg/kg) for 3 consecutive days 12–14), followed by a maintenance of 1 mg/kg/daily. By day 15th, a progressive decrease in inflammatory markers and a concomitant improvement of general conditions was observed, with the possibility to discontinue inotropic support on day 12th and invasive ventilation on day 25th. Since day 17th, a diffuse cutaneous desquamation was noted. The fever settled on day 35th.

Echocardiography follow-up revealed an increasing, irregular dilation of left (max 5 mm) and right (max 3.5 mm) coronary arteries, with a progressive left ventricular apex hypocinesis, but a stable ejection fraction (55%). ECG showed persistent repolarization abnormalities.

Of note, Adenovirus-PCR was found positive in the bronchoalveolar washing performed on admission.

The differential diagnosis included: Kawasaki disease complicated by respiratory distress syndrome and MAS, familiar hemophagocytic lymphohistiocytosis, autoimmune lymphoproliferative syndrome, criopyrinopathies and immunodeficiency.

Comment: Kawasaki disease can be catastrophic in the early infancy, due to atypical presentation and resistance to the conventional therapy. Despite typical in its presentation, this case was complicated by two challenging conditions, respiratory distress syndrome and MAS, which hampered the diagnostic and therapeutic management during the course of the disease and required massive intensive support.These two complication are rarely associated to KD. In this particular case, respiratory failure can probably be explained by a combination of causes: fluid overload, systemic vasculitis and the concomitant and probably triggering Adenovirus infection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7176

SP0110 LIFE-THREATENING COMPLICATIONS IN SYSTEMIC VASCULITIS

M.C. Cid on behalf of G. Espigol-Frigolé, S. Prieto-González, J. Hernández-Rodríguez, A. García-Martínez. *Systemic Autoimmune Diseases, Hospital Clinic. University of Barcelona, Idibaps, Barcelona, Spain*

Systemic vasculitis may present with life-threatening complications that need to be promptly recognized and appropriately managed to ensure patient survival and minimize irreversible organ damage.

The most common life-threatening events differ between large and medium or small-vessel vasculitis. In large-vessel vasculitis, particularly giant-cell artertis (GCA), vascular remodelling in response to inflammation may lead to severe stenosis leading to ischemic stroke in 3–6% of patients and, rarely, myocardial infarction, mesenteric ischemia or critical extremity ischemia. For these complications, particularly when happening in treated patients, intensifying immunosuppressive therapy is not the best or only option and additional interventions may be required. Stroke occurs as a consequence of carotid or vertebral stenosis. Stenosis of the carotid siphon has been repeatedly reported. In necropsy studies, vasculitic involvement and thrombosis of proximal intracranial branches has been observed. Infarcts are usually multiple, usually happen shortly after the initiation of glucocorticoid therapy, convey a 30% mortality or lead to remarkable disability. If critical stenosis is suspected before irreversible infarction, percutaneous intraluminal angioplasty may be function and life saving.

Acute aortic syndrome (aortic dissection or intramural haematoma) is an increasingly recognized hurdle in patients with GCA. It is usually a delayed complication occurring months and frequently years after diagnosis. Its frequency has not been delimitated but in a recent prospective follow-up study it was demonstrated to affect at least 2% of patients. Emergency open surgery repair, when feasible, is the best option for ascending aorta involvement (type A) and endovascular repair for involvement of the descending aorta (type B).

In small-vessel vasculitis, life-threatening presentations include rapidly progressive glomerulonephritis leading to kidney failure, alveolar haemorrhage, alithiasic colecistitis with perforation and intestinal ischemia. Rapidly progressive glomerulonephritis and alveolar haemorrhage are more frequently seen in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and anti glomerular basement membrane disease. Alveolar haemorrhage can be occasionally seen in cryoglobulinemic or IgA vasculitis. In addition to supportive measures, these patients are usually treated with high-dose methyl-prednisolone, cyclophosphamide or rituximab and plasma exchange. Plasma exchange has been found superior to IV methyl prednisolone mega-doses in preserving or recovering renal function but this advantage do not seem to persist over long-term follow-up. This approach is usually applied also to alveolar haemorrhage although there is not strong evidence supporting it.

Gastrointestinal complications, particularly intestinal ischemia and intestinal or gallbladder perforation are life-threatening complications which may require emer-

gent surgery. These may be observed in polyarteritis nodosa, cryoglobulinemic vasculitis, eosinophilic granulomatosis with polyangiitis and other AAV. High-dose glucocorticoids and cyclophosphamide are usually applied.Children with IgA vasculitis may develop bowel intussusception
Deep venous thrombosis and pulmonary embolisms are significantly more frequent in AAV and Behçet disease than in the general population, especially during active disease. Anti-coagulation may be needed in AAV, although this approach is controversial in Behçet's disease. By contrast, aneurysm formation is typical in polyarteritis nodosa and Behçet's disease and may be occasionally seen in AAV. Massive bleeding derived form aneurysm rupture usually requires arterial embolization.
It is important to keep in mind that during the early course of diagnosed vasculitis, intense immunosuppressive therapy may favour life-threatening infections including opportunistic infections such as pneumocystis jiroveci pneumonia or disseminated CMV.
In summary, systemic vasculitis may present with a variety of severe complications and other may develop during follow-up. These complications are heterogeneous, vary according to the size of vessels involved, and usually require specific procedures or treatments in addition to immunosuppressive therapy. Due to the life-threatening nature of these complications their immediate recognition and management are crucial to patient survival.
Supported by SAF 577–8R and Marató TV3 2014/201507
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7166

FRIDAY, 16 JUNE 2017

AxSpA: From bug to gut and to disease phenotype –

SP0111 INHIBITING BONE FORMATION IN THE CLINIC. ARE WE THERE YET?

R. Landewe. *Rheumatology& immunology, Amsterdam Rheumatology & immunology Center, Amsterdam, Netherlands*

One of the most characteristic features of axial spondyloarthritis (axSpA) is bone formation in the spine (syndesmophytes). Syndesmophytes may occur at any time during the course of the disease, are more frequent in patients with radiographic axSpA (AS) than in those with non-radiographic axSpA, and are best seen on conventional X-rays of the spine. Currently, it is suggested that (low-radiation) CT-scanning of the spine provides a better (more sensitive) picture of developing syndesmophytes than conventional X-rays.
Syndesmophytes matter in that they interfere with spinal mobility and physical function independent of inflammation. As such, it makes sens to try and prevent their occurrence or to inhibit their progression.
It is a matter of debate whether current available treatments are able to inhibit syndesmophyte growth or occurrence. Part of the debate is the methodological challenges related to measuring syndesmophyte progression properly.
In this lecture I will address current issues related to inhibition of syndesmophyte formation in patients with axial SpA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7211

FRIDAY, 16 JUNE 2017

Pregnancy meets rheumatic patients

SP0112 WHICH DRUGS IN PREGNANT PATIENTS?

M. Ostensen. *Department of Rheumatology, St.Olavs Hospital, Trondheim, Norway*

Management of rheumatic disease during pregnancy starts with prepregnancy counselling.Assessment of maternal and fetal risks is necessary for adjusting therapy before and during pregnancy. The aim of therapy is to keep the disease in remission or at least at low activity throughout pregnancy.
Immunosuppressive drugs requiring withdrawal before conception are methotrexate, cyclophosphamide,and mycophenolate which are known teratogenic drugs. Other drugs like leflunomide, tofacitinib and several biological should be discontinued because pregnancy experience is at present insufficient and safety for the fetus has not been proven.Flares of rheumatic disease showing be treated immediately and with pregnancy compatible drugs.For patients with inflammatory arthritis like rheumatoid arthritis,spondyloarthritis and juvenile idioipathic arthritis disease activity during pregnancy can be controlled with antimalarials, sulfasalazine and TNF inhibitors. Women with systemic lupus erythematosus should continue basic therapy with hydroxychloroquine, and azathioprine, ciclosporine or tacrolimus added when necessary due to organ manifestations. Severe flares during pregnancy may require biologics like rituximab,abatacept,tocilizumab or Anakonda, in SLE corticoid pulses or, if life threatening, intravenous gamma globulin or cyclophosphamide.
Treatment during pregnancy demands balancing suppression of maternal disease and no harm to the child. Selecting the adequate type, the right dose and the right timing of medications for optimal care of pregnant patients remains a challenge.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7246

SP0113 PREGNANCY IN SLE: STILL CHALLENGING FETAL AND MATERNAL ISSUES

R. Fischer-Betz. *Rheumatology, Heinrich-Heine-University, Duesseldorf, Germany*

Patients with SLE are mostly young women diagnosed during their childbearing years. Several "unmet needs" in the management of reproductive health issues may impact on the decision to have children. Because of earlier recognition of disease and advances in medical treatment, family planning has gained greater importance. Concerns include the effect of pregnancy on maternal disease, the impact of disease activity on fetal health, and the safety of medications during pregnancy and breastfeeding. Preconception counselling and risk stratification (including life style, disease activity, autoantibody profile, previous vascular and pregnancy morbidity, hypertension and the use of drugs with emphasis on benefits from hydroxychloroquine and antiplatelets/anticoagulants) are essential for prevention of unwanted complications during pregnancy. Recommendations for the management of family planning and antirheumatic treatment during pregnancy and lactation have been published recently by EULAR. However, many lupus patients still do not feel that their family planning concerns are adequately addressed in current clinical practice and report that they receive inconsistent advice from the various healthcare professionals. There is a clear need for provision of up-to-date and consistent information/support to our patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7091

SP0114 CHILDREN OF PATIENTS WITH RHEUMATIC DISEASES: ISSUES RELATED TO MATERNAL DISEASE AND TREATMENT

L. Andreoli. *Rheumatology and Clinical Immunology, University of Brescia, Brescia, Italy*

A major source of anxiety for women with systemic autoimmune diseases (SADs) who wish to become pregnant is the possible impact of maternal disease and medications on the offspring, in terms of physical and mental development. A recent multicenter survey conducted in 24 Italian Rheumatology Centers showed that more than 50% women affected by SADs restricted their family size mainly because they were afraid that children could get an autoimmune disease or could be harmed by intrauterine exposure to maternal autoantibodies and anti-rheumatic drugs (Dall'Ara, ACR abstract, Arthritis Rheumatol 2016; 68, suppl 10). Therefore, the long-term follow-up children born to mothers with SADs is a topic of major relevance for the counselling on family planning.
First of all, it should be emphasized that preterm birth and other foetal complications, such as low birth weight and babies small for gestational age, are more common in patients with systemic autoimmune diseases as compared to the general population. These conditions carry themselves an increased risk for poorer physical and neuropsychiatric development. Therefore, the prevention of foetal complications should be operated by means of close obstetrical monitoring and tight control of maternal disease activity, which would be detrimental for foetal wellbeing. In this context, the use of "safe" anti-rheumatic drugs is of paramount importance for pregnant women with SADs.
Recently, a dedicated EULAR Task Force has released points to consider for the use of anti-rheumatic drugs during pregnancy and lactation (Gotestam Skorpen, Ann Rheum Dis 2016). The work of this Task Force was focused on updating the information about the use of "conventional synthetic" (cs) DMARDs but also to provide for the first time evidence-base indications on the use of "biologic" (b) DMARDs, mainly anti-TNFalfa agents.
No significant impairment in the maturation and functioning of the child's immune system has been observed for several csDMARDs, supporting their safety of use during pregnancy (Andreoli, J Autoimm 2012).
Turning to bDMARDs, a case-control study on the long-term follow-up of children exposed in utero to anti-TNFalfa drugs showed the safety of use either until the positive pregnancy index or during the second and third trimester of gestation (Dall'Ara, EULAR abstract, Ann Rheum Dis 2016; 75, Suppl 2:493). No differences between exposed and non-exposed children were found in terms of congenital defects, developmental milestones, response to vaccinations and major health problems. No particular problems were also observed in children who were breastfed while maternal anti-TNFalfa intake. The use of anti-TNFalfa agents during breastfeeding had been proposed to women who were strongly motivated based on the following considerations: 1) these drugs are poorly or absolutely not excreted into breast milk as recently demonstrated for certolizumab pegol (Clowse, ACR abstract, Arthritis Rheumatol 2016; 68, suppl 10); 2) even this was the case, the drug will be degraded in the baby's gastrointestinal tract and absorption could not be possible.
Regarding maternal disease, major concerns are linked to fetal exposure to maternal autoantibodies, mainly anti-Ro/SSA (for the development of Neonatal Lupus) and antiphospholipid antibodies (aPL). Therefore, the evaluation of these autoantibodies with potential negative impact on pregnancy and neonatal outcome should be part of the preconception work-up of women with SADs in order to provide adequate counselling and preventative strategies (Andreoli, Ann Rheum Dis 2017).

The transplacental passage of maternal aPL does not generally produce any thrombotic complication in the neonate. The registry of infants born to mothers with APS, started by the European Forum on aPL in 2003, is collecting precious information for the assessment of neonatal outcome and subsequent development. The exposure to maternal aPL was linked to learning disabilities (LD) in children born to both mothers with SLE and with APS, based on the experimental observation that aPL can affect neural cells functioning. A recent study on the long-term neurodevelopment of children exposed in utero to aPL was reassuring for a normal neurological functioning and intelligence level, but found a higher rate of LD as compared to the general population (19% vs 3%) (Nalli, Lupus 2017). These affected children were all born at term to triple aPL positive mothers.

Although systemic autoimmune diseases are not hereditary, newborns may receive from the mother a genetic background that may predispose to the emergence of autoimmunity and, possibly, of related symptoms. However, the incidence of autoimmune diseases in the offspring was rather low (1%) among 269 children with a mean age of 15 years collected in the previously cited survey of Italian Rheumatology Centers.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7174

FRIDAY, 16 JUNE 2017

Neuronal and hormonal alterations in arthritis

SP0115 NEUROTRANSMITTERS AND INNERVATION IN SYNOVIUM

R.H. Straub. *Dept. of Internal Medicine, University Hospital, Regensburg, Germany*

The synovial tissue is innervated by nociceptive sensory nerve fibers and sympathetic postganglionic nerve fibers. While sensory nerve fibers have afferent (by transmitting pain to the CNS) and efferent functions (by local release of neuropeptides), sympathetic nerve fibers exert mainly efferent vasoregulatory, energy-regulating and immunomodulating roles. In synovial tissue of patients with rheumatoid arthritis (RA), the major proinflammatory neuropeptide of sensory nerve fibers is substance P, which is upregulated relative to anti-inflammatory calcitonin gene-regulated peptide (CGRP). In addition, sensory nerve fibers undergo a sprouting response leading to sensory hyperinnervation of RA synovial tissue. Removal of sensory nerve fibers exerts anti-inflammatory effects, and it is thought that this elimination is beneficial during hemiplegia, which can spare the paralytic limb from developing RA. Therapeutic neutralization of substance P was not successful, most probably due to vast receptor redundancy. Furthermore, the sensory nervous system undergoes a sensitization response (aggravation of pain and inflammation) in the synovial tissue, the dorsal root ganglion, the spinal cord, and more central in the brain. Chemical sympathectomy or suppression of adrenergic signaling significantly reduce inflammatory processes in the initial acute state of inflammation whereas the same procedures may increase inflammation at later stages. These findings indicate that the sympathetic nervous system supports the development of inflammation but can reduce inflammation at more chronic stages. During chronic inflammation, the density of sympathetic nerve fibers in synovial tissue is reduced but other tyrosine hydroxylase-positive cells secreting noradrenaline appear in the inflamed joint. In addition to local vascular effects in the joint, the sympathetic nervous system influences numerous immune processes in the joint and in lymphoid organs. Hence the net effect of the sympathetic nervous system on inflamed tissue results from local sympathetic effects in the joint as well as from sympathetic influences on major systemic immune processes and energy regulation. This lecture summarize the central aspects of the two nervous systems.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1256

SP0116 HOW TO TARGET NEURONAL AND HORMONAL ALTERATIONS IN ARTHRITIS

M. Cutolo on behalf of ACR and EULAR Study Groups on Neuro Endocrine Immunology of Rheumatic Diseases (NEIRD). *Internal Medicine, Research Lab Division Rheumatology University of Genova, genova, Italy*

Neuroendocrine pathways link the central nervous system (CNS) with the periphery by means of hormones and nerve fibres. Neuroendocrine connections are important for integrating signals throughout the body. Hormones are soluble factors circulating in the blood and lymph, while nerve fibres are solid cables connecting brain centres with distinct anatomical sites in the periphery.

Several network connecting the NeuroEndocrine Immune (NEI) system are target for the treatment of chronic immune inflammatory diseases, including arthritis in RMD (1).

The hypothalamic–pituitary–adrenal (HPA) axis is the best studied connection between the CNS and peripheral sites of inflammation. The HPA axis hormones comprise CRH, adrenocorticotropic hormone (ACTH) and several steroid hormones of the adrenal gland, including cortisol and adrenal androgens such as dehydroepiandrosterone (DHEA), its biologically inactive degradation product DHEA sulfate (DHEAS), and androstenedione (ASD). The adrenal gland synthesises glucocorticoids (GCs) following a circadian rhythm and the exogenous administration of GCs in chronic arthritis should be regarded as a replacement therapy for adrenal gland hypofuntion (2).

The hypothalamic–pituitary–gonadal (HPG) axis has been linked to rheumatic diseases because we observe a female preponderance in the prevalence and incidence of rheumatic diseases, which is most probably linked to sex hormones. Hormones of the HPG axis comprise gonadotropin-releasing hormone, luteinising hormone/follicle-stimulating hormone and the two major bioactive steroid hormones of the gonadal glands, testosterone and oestrogens. Increased peripheral metabolism of sex hormones is seen in chronic arthritis (ie. synovial tissue).

The hypothalamic–pituitary–prolactin axis is important since Prolactin is thought to have proinflammatory effects in RMD. Blood levels rise sharply at the beginning of sleep so this hormone can be a regulatory element in the circadian rhythms of the immune system (1).

Similar condition for the melatonin pathway, that in addition is increased I rheumatoid arthritis patients. Blood levels rise sharply at the beginning of sleep and melatonin might, thus, be a regulatory element in the circadian rhythms of the immune system. Melatonin at normal concentrations has proinflammatory effects. Finally, the vitamin D endocrine system, which is one of the most complex and diffuse systems controlling bone mass and also the immune response in autoimmune rheumatic diseases. Vitamnin D deficiancy is common in chronic RMD and decreased in winter with related flares of RMD.

Finally, vitamin D, via its active hormonal metabolite 1,25(OH)2D3 (D hormone), regulates both innate and adaptive immunity, potentiating the innate response (monocytes/macrophages with antimicrobial activity and antigen presentation) but suppressing adaptive immunity (T and B lymphocyte functions). D hormone deficiency is a risk factor for autoimmunity and for infections and cancer.

By considering that all steroid hormones before mentioned, are also produced *via* intracrine synthesis by the inflammatory cells (ie. macrophages) at the site of arthritis, it is increasing in presence of localized inflammatory conditions the local treatment (ie injection of GCs in joints). On the other hands, the immune stimulating action of estrogens should noy suggest their use in pathological conditions. Same caution with the use of melatonin in presence of arthritis, whereas 1,25(OH)2D3 is considered an adhiuvant in immune system suppression at dosages over 2,000 IU/day.

References:

[1] Straub R et Cutolo M. EULAR Textbook, chapt e MBJ 2015 2. Straub RH, Cutolo M. Rheumatology (Oxford). 2016;55:ii6-ii14.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7300

FRIDAY, 16 JUNE 2017

Fighting osteoporosis fragilities

SP0117 OSTEOPOROTIC FRACTURES IN EUROPE: ARE WE DOING ENOUGH

J.A. Kanis. *University of Sheffield & Australian Catholic University, Melbourne, Cobham, Surrey, United Kingdom*

The past 30 years has seen significant milestones in assessment and management of osteoporosis. These include the development of DXA and FRAX to identify individuals at high risk of fragility fracture and the development of interventions that have been shown to significantly decrease the risk of fracture in well-designed clinical trials. A major challenge has been how to apply these treatments. Measurements of bone mineral density (BMD) are used for diagnosis and for fracture risk prediction. Facilities for BMD testing are patchy and many European countries have inadequate resources to service the societal needs. In addition, BMD has poor sensitivity for the prediction of fracture so that the majority of fractures occur in individuals with T-scores >-2.5 SD. The development of FRAX has improved the sensitivity of fracture risk prediction and is now adopted in many assessment guidelins.

Despite these advances, there are a number of challenges to be faced. Of paramount importance is that few patients with a prior fracture and even less with osteoporosis alone actually receive treatment. In Europe, there is wide inter-country variation in the treatment of women at high risk for osteoporotic fractures. The treatment gap varies from 25% in Spain to 95% in Bulgaria. Large treatment gaps were identified in countries with populations at both high and low risk of fracture. In total in the EU, it is estimated that, out of the 18.4 million women that exceed the risk level in 2010, 10.6 million were untreated. These figures are conservative since an undetermined proportion of low-risk women will have received treatment. Moreover, the treatment gap is increasing in many countries. Thus the disease is under-recognised by the medical community.

Urgent action is required to address the under-recognition of osteoporosis and fragility fracture. Simple measures include:

- The development of country-specific guidelines,
- Piloting screening strategies in the elderly,
- Identifying the determinants of imminent risk,
- The development of fracture liaison services.

Whereas osteoporosis is recognized, worldwide, as a major Public Health issue, with one in two women and one in five men over the age of 50 years presenting

a fragility fracture, a vast proportion of women at high risk remain untreated. Case-finding strategies prioritizing assessment of men and women with prior fracture are required to alleviate this problem.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1859

SP0118 ESTABLISHING AND IMPLEMENTING A FRACTURE LIAISON SERVICE

S. Stephenson on behalf of National Osteoporosis Society. *Service Development - Operations, National Osteoporosis Society, Bath, United Kingdom*

Objectives: The objective of the National Osteoporosis Society (NOS) is to establish a Fracture Liaison Service (FLS) in every NHS Trust in the United Kingdom (UK). The Service Delivery Manager supports sites to establish, implement and develop a new FLS, as well as to improve the quality of existing services. The FLS model enables secondary fracture prevention through identification of fragility fractures in every person who breaks a bone aged over 50 using dedicated case-finding, with assessment and appropriate management of osteoporosis where necessary. The object of FLS is to prevent secondary fractures, in particular expensive hip and vertebral fractures, thereby providing both clinical and cost effectiveness for patients and payers. The NOS has developed a unique service to support FLS across the UK.
Developments: A team of specialist development managers with clinical and commissioning experience support providers and payers in the process of establishing new FLS's by offering consultation and guidance at every step of the process from pathway development to successful funding of services. This model has been replicated across the UK since April 2015 with the support and expertise of the NOS. Once an FLS is established the NOS provides support with service improvement, whether through additional commissioning of funds, Peer review or Gap analysis.
Results: Results from a range of analyses show that FLS has a positive impact on fracture rate and in particular hip fractures.
At the time of writing, the NOS is currently supporting 166 sites across the UK. 83 sites are improving the quality of their service; 58 sites are developing new services. 13 new services have been commissioned since commencement of the work programme, delivering new FLS provision to an additional 1.6 million people over 50, preventing 1,482 hip fractures over a 5-year period. Figures have been calculated from the NOS FLS Benefits Calculator https://benefits.nos.org.uk
Challenges: The primary challenge in establishing an FLS is identifying a clinical champion - this maybe a nurse, an allied health professional, rheumatologist or ortho-geriatrician in the hospital, or a representative from Public Health or from a Clinical Commissioning Group (CCG). The champion can lead and take the FLS from an idea to implementation.
To support the establishment and implementation of FLS the NOS has developed the FLS Implementation Toolkit as well as the Clinical Standards for FLS. The Clinical Standards will shortly be supported with a supplementation - New Clinical Guidance on the identification of Vertebral Fractures.
Furthermore, the Charity has developed the Fracture Prevention Practitioner (FPP) training for those wishing to implement an FLS. This is backed by the Competency Framework for Nurses, allied health professional and doctors to ensure best practice in fracture prevention.
Conclusion: The NOS service development model of support is successful in driving the establishment, implementation and improvement of FLS across the UK. This is tough in an economic climate where health budgets are constrained. However, there is strong evidence that investment in FLS improves the quality of care as well as illustrating financial savings in health and social care. NHS England recommends that every patient with/or at risk of osteoporosis and fragility fractures should have access to a commissioned service.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7217

SP0119 PREDICTING FRACTURE RISK: ACCURACY AND FEASIBILITY OF TOOLS

A.A. Marques. *Rheumatology, Centro Hospitalar e Universitario de Coimbra, Coimbra, Portugal*

Several therapeutic options and screening strategies are available to effectively decrease fracture risk. However the main clinical challenge still consists in accurately identifying and selecting individuals for bone densitometry and for pharmacological treatment, in order to increase efficiency and minimize individual and societal costs.
The World Health Organization provided an operational definition of osteoporosis as a bone mineral density (BMD) that lies 2.5 or more standard deviations below the average value for young healthy women of the same gender and ethnical background [T-score $\leq$-2.5]. However, BMD has limited sensitivity and specificity in the prediction of fracture. In fact, a large number of conditions have been firmly established as risk factors for the occurrence of fragility fractures, independently from BMD. These have been combined into prediction algorithms to estimate fracture probability and are currently available for calculate the risk of fractures. However, the existing tools differ in many relevant aspects: from their own feasibility, to the number and availability of clinical risk factors included, the accessibility of BMD measurements and, finally, their performance in different settings.
With this session we aim to identify and synthesize the best available evidence on the accuracy and feasibility of the currently available tools designed to predict fracture risk.
Several therapeutic options and screening strategies are available to effectively decrease fracture risk. However the main clinical challenge still consists in accurately identifying and selecting individuals for bone densitometry and for pharmacological treatment, in order to increase efficiency and minimize individual and societal costs.The World Health Organization provided an operational definition of osteoporosis as a bone mineral density (BMD) that lies 2.5 or more standard deviations below the average value for young healthy women of the same gender and ethnical background [T-score $\leq$-2.5]. However, BMD has limited sensitivity and specificity in the prediction of fracture. In fact, a large number of conditions have been firmly established as risk factors for the occurrence of fragility fractures, independently from BMD. These have been combined into prediction algorithms to estimate fracture probability and are currently available for calculate the risk of fractures. However, theexisting tools differ in many relevant aspects: from their own feasibility, to the number and availability of clinical risk factors included, the accessibility of BMD measurements and, finally, their performance in different settings.With this session we aim to identify and synthesize the best available evidence on the accuracy and feasibility of the currently available tools designed to predict fracture risk.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7255

SP0120 PREDICTING THE RISK OF FALLS AND PROMOTING BALANCE IN OLDER ADULTS

D. Rose. *Kinesiology, California State University, Fullerton, Fullerton, United States*

Falls are the leading cause of injury and death due to injury among the older adult population in the United States. Of those who fall, 24% will sustain serious injuries and 6% will experience fractures. In addition to injury, older adults who fall may experience decreased functional ability, loss of independence, a poorer quality of life, or premature mortality. At a global level, these statistics are similar among developed countries. It is important to first identify the intrinsic and extrinsic risk factors that contribute to falls and then intervene appropriately once the level of fall risk has been identified. It is important to understand that there is no one size suits all fall risk reduction program and that the type of program will vary as a function of the level of risk. Core components of successful fall risk reduction programs include exercise, environmental modifications, and behavior change techniques aimed at fostering long-term adherence to engaging in fall risk reducing behaviors. The purpose of this presentation will be to describe appropriate methods for identifying fall risk, and intervention strategies that have been shown to significantly reduce fall risk and/or fall incidence rates across the continuum of fall risk.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7244

FRIDAY, 16 JUNE 2017

Biological agents in juvenile idiopathic arthritis: open issues

SP0121 LONG TERM SIDE EFFECTS OF BIOLOGICAL AGENTS IN JIA

J.F. Swart on behalf of Pharmachild and Foreum (Comorbidity in JIA). *Pediatric Rheumatology, UMC Utrecht, Utrecht, Netherlands*

In the last years, the interest in the concept of comorbidity and its societal as well as individual impact has increased. Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease starting in childhood which often persists into adulthood. Clinicians are facing an aging population with multiple morbid conditions occurring in one individual. Long term outcome studies show the high prevalence and the potential interaction of coexisting diseases. For JIA recent studies reported that uveitis, asthma/atopic diseases and diabetes mellitus are prevalent comorbidities in JIA with 11.6–30%, 10.8% and 3.5% respectively, followed by cardiovascular disease, malignancies and inflammatory bowel diseases. Childhood long term outcome studies and Pharmacovigilance registries already revealed associations of co-existing diseases and the role of used medication (especially biologicals). It is important to plan preventive and screening strategies in order to prevent or early detect and treat comorbidities and integrated follow up once comorbidity exists.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7172

SP0122 **AUTOIMMUNE PHENOMENA ASSOCIATED WITH BIOLOGICAL AGENTS**

P. Quartier[1,2]. [1]*Pediatric Immunology-Hematology and Rheumatology Unit, Necker-Enfants Malades Hospital;* [2]*IMAGINE Institute, Paris-Descartes University, Paris, France*

Biologic agents are being increasingly used in pediatric rheumatology, particularly TNF antagonists but also abatacept, tocilizumab, interleukin (IL)-1 antagonists and some other drugs. In Juvenile Idiopathic Arthritis (JIA) and some autoinflammatory diseases, data from phase 3 and extension trials or from cohorts such as Pharmachild allow to prospectively collect information on adverse events "of special interest", including autoimmune complications. A few patients develop autoimmune/dysimmune features while on biologics, as seen in adults, including central nervous system lesions, inflammatory bowel disease or psoriasis. In addition, in patients with systemic-onset JIA, anti- IL-1 treatment is usually associated with the appearance of a type 1 interferon signature (gene expression analyses) which might in some cases favour lupus-like autoimmune features.
On the other hand, among patients with early-onset arthritis, vasculitis, recurrent fever or other inflammatory manifestations, an increased number of children are diagnosed with complex monogenic diseases resulting in auto-inflammation, immune deficiency and autoimmunity. In such cases, biologics might not be responsible for the occurrence of autoimmune features that may sometimes be diagnosed on treatment. This distinction is important as biologics are useful treatments also in some of these patients, as was shown in patients with a diagnosis of Systemic-onset JIA and ANCA-associated glomerulonephritis in whom anti-IL-1 treatment was beneficial. It was also more recently shown in patients with *lipopolysaccharide-responsive beige-like anchor* (*LRBA)* mutations associated with autoimmunity and inflammation, including polyarthritis: as LRBA is a partner of cytotoxic-T lymphocyte antigen-4 (CTLA4),. abatacept has been used as a targeted treatment and shown efficacy.
We hence aim to discuss the way to explore patients who develop autoimmune features while on biologics in order to take the right decisions regarding treatment maintenance, withdrawal or modification and regarding patients follow-up.
Disclosure of Interest: P. Quartier Grant/research support from: Abbvie, Novartis, Pfizer, Roche, Consultant for: Abbvie, Novartis, Sanofi, SOBI, Speakers bureau: Abbvie, BMS, Novartis, PfiZer, Roche, SOBI
DOI: 10.1136/annrheumdis-2017-eular.7231

FRIDAY, 16 JUNE 2017

Health equity and economy - a vital relationship

SP0123 **UNCOVERING THE EQUITY GAP IN RHEUMATIC AND MUSCULOSKELETAL DISEASES**

P. Putrik. *Rheumatology, Maastricht University Medical Center (MUMC), Maastricht, Netherlands*

The aim of this lecture is to discuss the current evidence on the socio-economic inequities in disease outcomes in RMDs. Socio-economic determinants at the individual and country level will be considered, as well as the interplay between these factors. In particular, attention will be given to the role of different socio-economic factors in the access to biologic DMARDs in rheumatoid arthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7164

SP0124 **HEALTH ECONOMICS AND HEALTH EQUITY: TWO COMPLEMENTARY DISCIPLINES**

B. Fautrel[1,2,3]. [1]*Rheumatology, APHP - CHU Pitié Salpétrière;* [2]*Rheumatology, UPMC - Pierre and Marie Curie University;* [3]*CRI-IMIDIATE Clinical Research Network, FCRIN Clinical Research Infrastructure Networks, Paris, France*

Health equity in the one hand refers to the absence of systematic disparities in health between different social groups in a given Society, a province, a country or a group of country. Health inequity thus corresponds to a situation in which health services are not similarly available to all people with the same health conditions and health needs, due to individual personal or socioeconomic characteristics.
Health economics in the other hand focuses on how to allocate health budgets in order to maximize the general health of the population as a whole. With regards to this, no specific attention is dedicated to socially disadvantaged subgroups. In addition, the most visible action in the field of health economics was the valorization of therapeutic innovation, i.e., the determination of its price not on production costs but on the value associated with this innovation.
Economic evaluation – i.e., determination of incremental cost-effectiveness ration – has lead during the last 20 years to substantial financial pressure on health care systems with dramatic increase in health expenditures mainly due to the costs of therapeutic innovation. Several studies have shown that such a process may increase health inequities within a country or a group of countries if specific actions are not taken to maintain or improve treatment availability and access to care to all the population members whatever their social, educational and economic characteristics.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7280

FRIDAY, 16 JUNE 2017

Biomarkers in cardiovascular rheumatology - state-of-the-art 2017

SP0125 **INFLAMMATION AND CARDIOVASCULAR DISEASE – RELEVANT METABOLIC BIOMARKERS**

E. Choy. *Section of Rheumatology, Cardiff University, Cardiff, United Kingdom*

Patients with RA have increased mortality compared with the general population mostly due to higher cardiovascular disease (CVD), which is up to 50% more frequent [1]. Even after adjusting for traditional cardiovascular risk factors such as smoking, diabetes and hypertension, the risk for CVD is increased by up to twofold compared with the normal population [2]. Whilst traditional cardiovascular risk factors, contribute to the increased risk of mortality in RA patients, they do not fully explain increase in cardiovascular risk [3,4]. European League Against Rheumatism (EULAR) recommend regular assessment of cardiovascular risk in patients with RA [5]. Since traditional cardiovascular risk factor assessment equations, such as Framingham and the Systematic Coronary Risk Evaluation Score (SCORE) models, underestimate cardiovascular risk in RA, EULAR recommends multiplying such traditional cardiovascular risk scores by 1.5 for patients with RA. Such adjustment operates at the population level. Ideally, cardiovascular biomarkers that can predict future cardiovascular event in the individual patient will improve screening and management.
Biomarkers of cardiovascular disease can be divided into five major categories: lipids, inflammation, endocrine, vascular and prothrombotic [7]. HDL and LDL are used in routine clinical practice. However, they do not predict future cardiovascular events in patients with RA as the levels of HDL and LDL are suppressed during inflammation [8]. The ratio of HDL/LDL or total cholesterol/HDL is less affected by inflammation. Other lipid biomarkers include apolipoprotein A-1, apolipoprotein B, cholesterol ester transfer protein lipoprotein-associated phospholipase A2, small-dense LDL and paraxonase-1. They have been measured in patients with RA but their precise value in predicting cardiovascular risk in RA has not been determined.
High level of inflammation as measured by ESR and CRP is associated with increased cardiovascular risk in patients with RA. EULAR recommended adequate suppression of inflammation as a key strategy to reduce cardiovascular events [5]. Disease flares increased cumulative cardiovascular risk [9]. Many inflammatory mediators are elevated in RA, whether they can add to traditional cardiovascular risk score to improve individual risk prediction should be evaluated.
The vascular biomarker of cardiovascular disease, VCAM-1, has also been shown to elevated in patients with RA. High level of VCAM-1 was associated with high cardiovascular risk score[ix].
Metabolic syndrome is common in patients with inflammatory arthritis. Insulin resistance is a feature of metabolic syndrome. Fibrinogen and other prothrombotic molecules are part of the acute phase response, their levels are elevated in RA. Neither endocrine nor prothrombotic factors have been studied systematically in RA.
References:
[1] Meune C, Touze E, Trinquart L, Allanore Y. Rheumatology 2009 Oct; 48(10):1309–13.
[2] Gabriel SE. The American Journal of Medicine 2008 Oct;121(10 Suppl 1):S9–14.
[3] Dessein PH, Joffe BI, Veller MG, Stevens BA, Tobias M, Reddi K, et al. The Journal of rheumatology 2005 Mar;32(3):435–42.
[4] del Rincon ID, Williams K, Stern MP, et al. Arthritis Rheum. 2001;44:2737–2745.
[5] Agca R, Heslinga SC, Rollefstad S et al. Ann Rheum Dis. 2017 Jan;76(1):17–28.
[6] Montgomery JE and Brown JR. Vascular Health and Risk Management. 2013:9 37–45
[7] Choy E and Sattar N. Ann Rheum Dis. 2009 Apr;68(4):460–9.
[8] Myasoedova E, et al. Ann Rheum Dis. 2016 Mar;75(3):560–5.
[9] Davies RD et al ACR 2016 abstract no 1447.
Disclosure of Interest: E. Choy Grant/research support from: Roche, UCB, Pfizer, Biocancer, Consultant for: Amgen, Biogen, BMS, Boehringer Ingelheim, Celgene, Chugai Pharma, Eli Lilly, Hospita, I Janssen, Napp, Novimmune, Novartis, Pfizer, Regeneron, Roche, R-Pharm, Sanofi-Aventis, Tonix and UCB., Speakers bureau: Amgen, BMS, Boehringer Ingelheim, Chugai Pharma, Eli Lilly, Hospira, MSD, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, and UCB.
DOI: 10.1136/annrheumdis-2017-eular.7237

SP0126 **THE VESSEL WALL IN IMIDS – NEW EMERGING VASCULAR MARKERS**

Z. Szekanecz. *Department of Rheumatology, University of Debrecen, Faculty of Medicine, Debrecen, Hungary*

Cardiovascular disease dependent on inflammatory accelerated atherosclerosis

leads to increased mortality in rheumatoid arthritis (RA). In addition to traditional, Framingham risk factors, several immuno-inflammatory cells, mediators and molecules may link atherosclerosis to arthritis. Among immune cells, primarily TH1 cells, as well as endothelial cells play a crucial role in synovial and vascular inflammation. Various cell surface molecules, such as adhesion receptors, CD40-CD40 ligand or members of the RANK-RANK ligand-osteoprotegerin system, as well as soluble pro-inflammatory cytokines, chemokines, autoantibodies and proteases have been implicated in RA and vascular damage. The early assessment of atherosclerosis and early intervention would decrease cardiovascular risk in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7197

SP0127 TAPERING BIOLOGICS INDUCES A PROTHROMBOTIC STATE IN RHEUMATOID ARTHRITIS?

M.T. Nurmohamed on behalf of M. Heslinga, J. Meijers & M. Nurmohamed. *Rheumatology, Amsterdam Rheumatology immunology Center | VUmc & Reade, Amsterdam, Netherlands*

In addition to the "traditional" risk factors for venous trombo-embolism (VTE), like age, trauma and immobilisation, inflammation could also be regarded a risk factor for VTE. For example, patients with acute inflammatory conditions (sepsis), but also patients with chronic inflammation, like inflammatory bowel disease (IBD) and rheumatoid arthritis (RA), have an increased risk of thrombosis.

Inflammation can lead to activation of coagulation, and vice-versa, coagulation also has considerable effects on overall inflammatory activity. First, the inflammatory cytokine network induces several pro-thrombotic conditions including insulin resistance, dyslipidaemia, endothelial dysfunction and alteration of coagulation and fibrinolysis. Second, activation of the extrinsic coagulation system and impairment of the fibrinolytic pathway may contribute to amplify and perpetuate the inflammatory response. Previous studies have reported several blood parameters that reflect a prothrombotic state in RA. These include increased levels of thrombin-antithrombin complex, prothrombin fragment F1+2, von Willebrand factor, plasmin-alpha2-antiplasmin complex and D-dimer, as well as an increased platelet count. Impaired fibrinolysis combined with increased antithrombin levels have also been reported in RA. An important mediator in the inflammatory pathway is tumor necrosis factor-α (TNF-α). In the general population, TNF-α induces a disbalance between clotting and fibrinolysis, resulting in a hypercoagulable state. Since TNF-α is the key player in RA, RA is an ideal "human model" to study the interplay between inflammation and coagulation. Hence, RA can be considered as a pro-thrombotic state, which explains partly why patients with RA are at increased risk of thrombo-embolic cardiovascular events.(1)

Only one small study suggested that TNF-inhibitors (TNFi) is accompanied with normalization of thrombotic biomarkers: an improvement of clinical and laboratory parameters as well as a reduction in the activation of coagulation and endothelial dysfunction was found in RA patients treated with a TNFi. In addition, we previously demonstrated that combination therapy with corticosteroids improves the procoagulant state that exists in early RA. (2)

Nowadays, tapering of biological therapies is becoming more and more standard of care. However, the effects on the coagulation status in RA are unknown. In light of the growing evidence of an increased cardiovascular morbidity and mortality in RA, mostly independent of traditional risk factors, treatment strategies in RA should not only aim at relieving symptoms and inhibiting joint destruction but should have a beneficial effect on the vasculature and haemostasis to reduce cardiovascular events. Although modest, there is evidence suggesting a beneficial effect of TNFi on the haemostatic status in RA. Unfavourable changes in haemostatic markers, such as TAT, F1+2, vWF, PAP, D-dimer and thrombin generation, which indicate a pro-thrombotic state, may therefore (re)occur when RA patients stop with TNFi treatment. We first assessed arterial wall inflammation with 18F-FDG PET scans in RA patients in remission under TNFi therapy or DMARD therapy versus controls. The FDG uptake in the aorta in DMARD remission patients was similar to the controls, whereas the uptake in RA patients in remission under antiTNF was significantly higher than in controls either when looking at the overall aortic uptake or the most diseased segment. Theoretically, stopping TNF blockade in these patients might lead to increased inflammation and thus coagulation activation. Therefore, we are presently investigating it and to what extent tapering/stopping TNFi therapy induces a pro-thrombotic state in RA patients.

References:

[1] Van den Oever et al. Ann Rheum Dis. 2014;73:954–7.
[2] Van Den Oever et al Ann Rheum Dis 2012;71(Suppl3):348.
[3] Bernelot Moens et al Arthritis Res Therapy 2016;18: 115.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7143

FRIDAY, 16 JUNE 2017

MRI I & II

SP0128 MRI OF ENTHESITIS – BY CONVENTIONAL AND WHOLE-BODY MRI - INCLUDING QUIZ CASES

I. Eshed[1,2]. *[1]Diagnostic Imaging, Tel Aviv University, Tel Aviv; [2]Diagnostic Imaging, Sheba Medical Center, Ramat Gan, Israel*

Entheses are sites of attachment of tendons, ligaments, fascia, or capsule into bone, providing a mechanism for reducing stress at the bony interface. Entheses dissipate biomechanical stress and, in doing so, are thought to be subjected to repeated micro traumas.

Inflammation of the entheses, enthesitis, is a well-known hallmark of spondyloarthritis (SpA), playing a central role in disease pathogenesis. It can also be associated with degenerative, endocrinologic, metabolic and traumatic conditions. Magnetic resonance imaging (MRI) is a sensitive tool for the detection of early signs of enthesitis in patients with SpA. The MRI features of enthesitis are well described, and include thickened enthesis with altered signal intensity and perientheseal soft tissue edema. Bone marrow edema and erosions at the adjacent bone appear mainly in SpA-associated enthesitis. Contrast material administration improves the reliability, sensitivity and specificity of detecting enthesitis on an MRI.

Whole-body (WB) MRI allows assessment of all peripheral and axial joints and entheses from "head-to-toe" in one examination. The promising role of WBMRI in the evaluation of enthesitis in SpA and other rheumatic diseases was evaluated in several cross sectional and prospective studies. Indeed WB MRI was shown to be sensitive in the detection of inflammatory lesions, including enthesitis, on multiple sites, potentially serving as a one stop shop for the estimate of active disease load.

In the current presentation, the typical imaging properties of enthesitis on conventional and WB-MRI will be presented along with several challenging quiz cases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1911

SP0129 CLASSIFICATION, DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS BY MRI - INCLUDING QUIZ CASES

M. Østergaard. *Copenhagen Center for Arthritis Research, Copenhagen University Hospital Rigshospitalet, Glostrup, Denmark*

Magnetic resonance imaging (MRI) is essential in the process of diagnosis of axial spondyloarthritis (axSpA) in clinical practice, as described in recent EULAR recommendations (1). However, several important differential diagnoses need to be considered. MRI is also key in the Assessment in SpondyloArthritis International Society (ASAS) classification criteria for axSpA (2), for which a consensus definition of a positive MRI was made in 2009 (3). The ASAS MRI working group has recently provided an updated definition of what is needed to fulfill the MRI-criterion in the ASAS criteria (4), based on a consensus excercise. This talk will describe the evidence behind the use of MRI for diagnosis of axSpA, describe the current ASAS consensus on how to use MRI for classification of axSpA, and examples of the most important differential diagnoses will be shown. The presentation will include patient cases for audience review.

References:

[1] Mandl P, Navarro-Compan V, Terslev L et al. EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. Ann Rheum Dis (Published online) 2015.
[2] Rudwaleit M, Landewe R, van der Heijde D et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. Ann Rheum Dis 2009; 68(6):770–776.
[3] Rudwaleit M, Jurik AG, Hermann KG, et al. Defining active sacroiliitis on magnetic resonance imaging (MRI) for classification of axial spondyloarthritis: a consensual approach by the ASAS/OMERACT MRI group. Ann Rheum Dis 2009; 68(10):1520–1527.
[4] Lambert RG, Bakker PA, van der Heijde D et al. Defining active sacroiliitis on MRI for classification of axial spondyloarthritis: update by the ASAS MRI working group. Ann Rheum Dis (Published online) 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7169

FRIDAY, 16 JUNE 2017

WIN & HOT session

SP0130 WIN SESSION: OSTEOPOROSIS

P. Geusens. *Rheumatology, MaastrichtUMC and UHasselt, Genk, Belgium*

The clinical pathway for fracture prevention consists of a 5-step approach: case finding, risk evaluation, differential diagnosis, treatment and follow up. For each of these steps new insights have emerged during the last year.

Epidemiologic studies have shown that not only fracture risk, but also mortality is increased after fracture, and that adequate therapy can not only decrease fracture risk but also increase survival.
Fracture risk is not constant over time. It is highest the years following a fracture, and immediately increases in some instances, such as after starting glucocorticoids or androgen deprivation therapy. This has raised the concept of "imminent" fracture risk, in contrast to long-term fracture risk as included in FRAX. In this context, we present the the EULAR initiative, in collaboration with EFORT, that published recommendations for multidisciplinary acute fracture care, including orthogeriatric care after hip fracture, and subsequent fracture prevention at the Fracture Liaison Service.
The presence, number and severity of vertebral fractures contribute to fracture risk, independent of BMD. Most vertebral fractures are subclinical and can therefore only be diagnosed by imaging of the spine. The role of vertebral fracture assessment (VFA) using DXA will be discussed.
New treatment insights will be reviewed, including for glucocorticoid users, combined and sequential treatments with anti-resorptive and bone forming drugs, real world data and the role of fall prevention.
Prescription of and adherence to treatment are still major issues. In patients adherent to therapy, new insights and recommendations will be reviewed on the need for early treatment, duration of treatment and the clinical approach when considering stopping drug therapy.
Disclosure of Interest: P. Geusens Grant/research support from: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Roche, UCB, BMS, Novartis, Consultant for: Amgen
DOI: 10.1136/annrheumdis-2017-eular.7267

FRIDAY, 16 JUNE 2017

What is behind vasculitis?

SP0131 AUTOIMMUNE ATHEROSCLEROSIS

Z. Szekanecz. *Department of Rheumatology, University of Debrecen, Faculty of Medicine, Debrecen, Hungary*

Arthritides have been associated with accelerated atherosclerosis to increased vascular disease risk. Traditional risk factors, as well as the role of systemic inflammation including cytokines, chamokines, proteases, autoantibodies, adhesion receptors and others have been implicated in the development of these vascular diseases. Accelerated atherosclerosis and increased cardio- and cerebrovascular morbidity and mortality have been observed in rheumatoid arthritis (RA) and spondyloarthropathies (SpA).
Endothelial dysfunction, overt atherosclerosis and vascular stiffness may be indicated by brachial artery flow-mediated vasodilation (FMD), common carotid intima-media thickness (ccIMT) and aortic pulse-wave velocity (PWV), respectively. These abnormalities have been described in most inflammatory rheumatic diseases. While ccIMT and stiffness are relatively stable, FMD may be influenced by many confounding factors.
In addition to traditional vasculoprotection, immunosuppressive agents including corticosteroids, traditional and biologic DMARDs may have significant vascular and metabolic effects. The official EULAR recommendations on the assessment and management of cardiovascular disease in arthritides have been published.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7194

SP0132 VIRUSES DRIVING VASCULITIS

L. Calabrese. *Rheumatology, Cleveland Clinic, Cleveland, United States*

Viruses have long been associated with varying forms of vasculitis in both pre-clinical models and human diseases. Immunopathogenic mechanisms have varied and include direct vascular invasion, immune complex mediated and more recently novel mechanisms which include autoinflammatory like responses. This discussion will review major advances in the field of medical virology as it applies to rheumatic diseases, especially vascular inflammatory disease, including an introduction to the human and more specifically vascular microviromes. Major forms of virally mediated vasculitis will be discussed with an emphasis on new viral vasculitis syndromes largely defined by next generation sequencing and their potential clinical impact.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7216

SP0133 ANCA AND THEIR ENVIRONMENT

R.A. Luqmani. *University of Oxford, Oxford, United Kingdom*

The association between antibodies to neutrophil cytoplasm (ANCA) and systemic vasculitis has transformed our understanding of granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). ANCA undoubtedly play a major role in their pathogenesis. There are different forms of ANCA, but only two of direct clinical relevance: cytoplasmic c-ANCA (usually directed against proteinase 3, PR3), and perinuclear p-ANCA (usually directed against myeloperoxidase, MPO). P-ANCA can also be directed against other antigens including bactericidal/permeability-increasing protein, lactoferrin, human neutrophil elastase, cathepsin G and azurocidin, but their clinical significance is not clear.
Transfer of MPO ANCA in humans (maternal-foetal route) and animal models (necrotizing pauci-immune glomerulonephritis after passive transfer of purified antibody or splenocytes from MPO-deficient mice immunized with murine MPO) has resulted in features of MPA. By contrast, the pathogenicity of anti-PR3 antibodies is less well-established. There is a significant genetic predisposition to disease in patients with AAV. Patients with PR3-ANCA have a strong association with HLA-DP and genes encoding alpha-1-antitrypsin and proteinase 3; by contrast, patients with MPO-ANCA have an association with HLA-DQ. Other factors that could interact with ANCA include: loss of B cell and T cell tolerance; direct involvement by neutrophils and their mediators in vascular injury and damage, degranulation and cytokine production; environmental exposure to silica or certain strains of Staphylococcus aureus, coupled with a lack of effective T cell regulation to prevent inflammation. Neutrophils spontaneously release of neutrophil extracellular traps (NETS), which directly cause endothelial cell damage and complement activation. NETS retain proteinase 3 and myeloperoxidase, helping to break immune tolerance and inducing antibody formation. The alternative complement pathway plays a crucial role in the pathogenesis of AAV. Activated neutrophils produce C5a, which in addition to recruitment, primes additional neutrophils for further activation by ANCA. C3a, C5a, soluble C5b-9 are elevated in active disease and plasma levels of complement factor H, a regulator of the alternative complement pathway is significantly lower in patients with active AAV.
Central to the pathogenesis of AAV is a dysregulated immune response to ANCA and aberrant expression of their target autoantigens, MPO and PR3. Environmental exposure to silica may inactivates α1-antitrypsin, whilst activating monocytes and macrophages releasing cytokines such as interleukin-1 and TNF-α, oxygen radicals and lysosomal enzymes (such as PR3 and MPO). Other environmental interactions include CpG-ODN, a short synthetic DNA containing unmethylated CpG and several drugs, especially propylthiouracil and levamisole-adulterated cocaine. Some of these associations could provide a better insight into the development of ANCA associated disease.
ANCA play a central role in the pathogenesis of systemic vasculitis, supported by a dysregulated immune system, with significant interactions with micro-organisms, environmental toxins and drugs, all of which can contribute to the development and severity of disease.
Disclosure of Interest: R. Luqmani Grant/research support from: Arthritis Research UK, GSK, MRC, UCSF/OIF, Canadian Institutes of Health Research, The Vasculitis Foundation, Consultant for: GSK, Medpace, MedImmune, Roche
DOI: 10.1136/annrheumdis-2017-eular.7151

FRIDAY, 16 JUNE 2017

Cytokine taxonomy: reflection in the therapy of arthritides and other IMIDs

SP0134 INTERLEUKIN-2 THERAPY IN SLE

J.Y. Humrich. *Department of Rheumatology and Clinical Immunology, University Hospital Schleswig-Holstein, Campus Lübeck, Lübeck, Germany*

There is an unmet need for more effective and selective therapeutics in severe autoimmune diseases such as systemic lupus erythematosus (SLE). A deeper understanding of the pathogenic mechanisms in the past has led to the clinical translation of low-dose interleukin-2 (IL-2) therapy which primarily aims to restore the activity of regulatory T cells. First results from phase I/II studies are promising by proving the selective expansion of regulatory T cells *in vivo* and by providing first evidence for the clinical efficacy of low-dose IL-2 therapy in SLE. Here we will summarize key findings which led to the development of this novel therapeutic concept and will highlight the main rationales for the clinical translation of low-dose IL-2 therapy in SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7305

FRIDAY, 16 JUNE 2017

Regulatory molecules in connective tissue

SP0135 MYOSTATIN, SCLEROSTIN, SYNDECAN AND MORE

T. Pap. *Institute of Experimental Musculoskeletal Medicine (IEMM), University Münster, Münster, Germany*

Rheumatoid arthritis (RA) is the prototype of an inflammatory arthritis that is characterized by chronic inflammation, progressive cartilage destruction and bone erosion. Development of RA is marked by the hyperplasia of the synovial membrane as caused by an infiltration and accumulation of inflammatory cells such as macrophages and lymphocytes as well as an increase in the number of resident mesenchymal cells. These fibroblast-like synoviocytes (FLS) are a key part of the local immune system in the joints and integrate signals

form different sources into a pathological tissue response. Resorption of the juxtaarticular bone is part of this pathological tissue response and is denoted as focal bone erosion which occurs early in this disease and over time is associated with significant morbidity. Focal bone erosions are observed at the interface of pannus and bone tissue both marginally, where pannus invades cortical bone, and in the immediate subchondral bone, where the pannus invades the marrow space. Many of the cytokines and growth factors implicated in the inflammatory processes are secreted by FLS and have also been demonstrated to impact directly or indirectly on osteoblast and/or osteoclast differentiation and function. However, research of the last years has also identified some novel pathways by which i) osteoclast- mediated bone resorption is regulated and fine-tuned under inflammatory conditions such as in RA and that ii) link inflammatory bone resorption to other features of systemic autoimmunity such as the activation of developmental pathways or muscle weakness. This lecture will review some of these novel mediators and pathways, including members of the Wnt- signalling pathway (e.g. sclerostin), members of the GDF- family of growth differentiation factors (e.g. myostatin) and cells surface anchored proteoglycans (e.g., syndecans). Focusing on the role of these molecules in the FLS-mediated regulation of osteoclastic bone resorption, the lecture will point to general principles of inflammatory bone remodelling and discuss potential therapeutic implications for RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7261

SP0136 MULTIFACTORIAL TISSUE GROWTH FACTORS

C.P. Denton. *Centre for Rheumatology, Royal Free Hospital and Ucl Medical School, London, United Kingdom*

Connective tissue is a critical component of all organs and has special importance in the musculoskeletal system. In specialist tissues, such as bone, cartilage of muscle an in vascular structures and internal organs there is a mixture of less specialized connective tissue together with the specific tissue and organ specific cellular components. In addition to physiological function there are two other areas in which it plays a central role. Normal embryonic an postnatal growth and development, and tissue repair in response to injury. It has emerged that there are shared pathways, mediators and mechanisms in these different processes and that multifactorial tissue growth factors have an important role. In this way, these proteins can have a profound influence on multiple cell types and provide a mechanistic link in many complex chronic diseases. It is notable that pathways that are perturbed in one chronic disease, such as atherosclerosis or osteoarthritis may be similarly disrupted in different context in conditions such as lung fibrosis or scleroderma. Transforming growth factor beta family members are prototypic examples of this class of protein. This included TGFbeta isoforms but also the related bone morphogenetic (BMP) and activin family of proteins. They share chemical structure and an ability to regulate multiple cell types in a context specific way. In addition, there is remarkable complexity in their regulation with intrinsic inhibitory mechanisms to protect from inappropriate biological activity. Their role in repair means that activation of preformed protein may regulate biological effects. Proteins regulated by the TGFbeta family, such as the CCN family of matricellular proteins and some for the cardinal growth factors and cytokines share properties. There is functional and signaling redundancy and cross talk. Conceptually it is interesting to envisage dysfunctional networks of cytokines in disease that may be attenuated by extracellular blocking or antagonism. Insights for many areas of developmental biology and pathology have informed about this challenging area of molecular medicine.

Disclosure of Interest: C. Denton Grant/research support from: Inventiva, CSL Behring, GSK, Bayer, Consultant for: GSK, Actelion, Inventiva, Roche
DOI: 10.1136/annrheumdis-2017-eular.2532

SP0137 FROM GLYCOSYLATION TO INFLAMMATION

M. Herrmann. *University Hospital Erlangen, Erlangen, Germany*

One of the best studied posttranslational modification of immunoglobulin G (IgG) is the addition of a complex glycan to asparagine 297, which is required for IgG to bind to Fc-receptors and for the activation of complement via the classical activation pathway. In the absence of the glycan the IgG usually behave like a lame duck unable to execute its effector functions. The sugar tree is polymorphic and there are several functional consequences related to the glycan. The terminal sialylation, the presence of galactose, the core fucosylalation and the insertion of a bisecting third sugar chain all reportedly modify the biological and functional activities of IgG.

As examples for the impact of Asp-297 associated glycans to the activity I will present (I) the sialylation of anti-histon autoantibodies in patients with systemic lupus erythematosus (II) the exposure of sugar epitopes by random IgG isolated from patients with rheumatoid arthritis (III) the molecular analysis of the glycan of random IgG isolated from patients with inflammatory diseases and controls and (IV) and finally the glycosylation of IgG-anti-phospholipid autoantibodies in healthy children.

(I) The autoantibodies are mainly found in the non-sialyated fraction of the anti-histon autoantibodies which can be considered inflammatory IgG.

(II) The circulating random IgG from patients with rheumatoid arthritis show an increased exposure of the Asp-297 associated glycans.

(III) The molecular analysis of the glycan of random IgG isolated from patients with systemic lupus erythematosus, rheumatoid arthritis, sepsis showed disease-specific glycans.

(IV) The non-pathogenic IgG-anti-phospholipid autoantibodies isolated from healthy children displayed an increased sialylation when compared to the pathogenic autoantibodies from adults with anti-phospholipid syndrome.

The examples point to a strong impact of IgG glycosylation in the etiopathogenesis of chronic inflammatory rheumatic diseases. One should consider to include IgG glycan analyses into the diagnostic repertoire for autoantibodies.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7291

FRIDAY, 16 JUNE 2017

Patient engagement in research: best practices, benefits, and challenges

SP0138 THE CHALLENGES OF PATIENT INVOLVEMENT IN SCIENTIFIC RESEARCH. HOW TO ACHIEVE TRUE REPRESENTATION OF THE PATIENTS' VOICE?

M. De Wit on behalf of the EULAR Working group for Collaborative Research. *Dept. Medical Humanities, EMGO+ research institute, VU University Medical Centre, Amsterdam, Netherlands*

There is a strong call in the western world for collaborative research. Rheumatology is one of the disciplines that has explored best practices and paved the way to implement lessons learned. Although good methodologies for evaluating the impact of patient participation stay behind, we have been able to develop expert-based recommendations for collaboration. They are helpful for both researchers and patient representatives, but they do not address all concerns that occur in daily practice. In this lecture current challenges of integrating the perspectives of patients in clinical research will be discussed: 1. Defining the role and complementary value of patient research partners; How can patients in the role of collaborative partner contribute to research in addition to the data that patients provide as respondent or study participant? 2. Facilitating and guiding researchers in collaborative research; We have experience in preparing and educating patient representatives for their role in research, but how should researchers be trained and supported? 3. Preserving the patients' voice throughout the research process; Qualitative research may elicit patients' experiences with health care or health interventions, but what is needed to guarantee that these findings are not lost in the rigorous process of producing scientific knowledge? 4. Demonstrating impact of collaborative research to funders and the public; Despite many case studies reporting a great variety of patient participation methods, there are no clinical trials nor consensus on a validated methodology for assessing the outcomes of patient involvement in research.

For each challenge we will try to propose a way forward. These challenges will also be discussed at the newly established EULAR working group for collaborative research.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7249

SP0139 MEANINGFUL PATIENT AND PUBLIC INVOLVEMENT IN PLANNING RESEARCH

A. Redmond. *Leeds Institute for Rheumatic and Musculoskeletal medicine, University of Leeds, Leeds, United Kingdom*

Historically, services providing care for people with long term conditions (LTCs), together with any associated research agendas, have been driven entirely by clinicians. In many cases this is well meaning and is done with some consideration of what patients need, but almost always the end result relies on the clinicians' interpretation of what *they* think patients need.

Recently it has become more usual to involve patents in planning research projects and service changes directly. Initial attempts to give patients genuine input were *ad hoc* in nature and so patient contributions could be lacking, ignored or misinterpreted.

In many cases having poor patient input is worse than no input at all as it lends false credibility to the process. Lately a range of formal requirements, arrangements and methods have become adopted and this presentation will focus on how these can be brought to bear to ensure meaningful patient and public involvement in planning research. From national guidance such as the UK's INVOLVE initiative, to local standard operating procedures we will share experiences and lessons learned.

The session will close with a practical summary of how to make PPI contributions genuine and meaningful, and some insights into possible future developments as this aspect of the research process matures and consolidates.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7220

SP0140 **PATIENT ENGAGEMENT IN RESEARCH: A PCORI EXEMPLAR**

J. Poole. *Occupational Therapy Program, University of New Mexico, Albuquerque, United States*

This session will discuss patient and stakeholder involvement as members of the research team on a grant funded by the Patient Centered Outcomes Research Institute (PCORI). Patients with a rare chronic disease, systemic sclerosis, and members from key stakeholder organizations were involved in evaluating, revising and testing the effectiveness of an internet self-management program. They participated at several levels of engagement including planning the study, conducting the study, and disseminating the results. This session will discuss how engagement occurred at each of these levels through different opportunities such as creating interventions, identifying outcomes, recruiting, presenting findings, and planning dissemination efforts. The benefits and challenges for both researchers and patient research partners will also be described.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7294

FRIDAY, 16 JUNE 2017

RA treatment in patients wanting to become pregnant - interactive session

SP0141 **NEW RA, BUT WHAT ABOUT A NEW BABY?**

A. Willemze. *Rheumatology, LUMC, Leiden, Netherlands*

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease affecting women often in their childbearing years. In this case presentation a 35 year old female patient is illustrated with a recently diagnosed rheumatoid arthritis with active disease and a wish to conceive in the nearby future. Management of disease activity in patients who wish to conceive or during pregnancy might be a challenge due to limited treatment options. How should we treat this patient taking into account her wish to conceive in the nearby future? Should the patient postpone her wish to conceive because of active disease?
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7182

SP0142 **FOREPLAY AND FINALE: FACTORS AFFECTING FERTILITY, BIRTH AND LACTATION IN RHEUMATOID ARTHRITIS PATIENTS. CLINICAL CASE**

P. Nero. *Rheumatology, Hospital CUF Descobertas, Lisboa, Portugal*

We present the clinical case of a 38 year old woman diagnosed with rheumatoid arthritis at the age of 32. She went into remission of her disease during treatment with subcutaneous methotrexate (25 mg/week) for 2 years. She decided to become pregnant and stoped treatment. RA relapses 4 months later and she has no response to classic DMARD's (sulphassalazine and hydroxychloroquine) and starts etanercept (50mg/week). She gets pregnant and achieves remission at week 16 of her pregnancy. At week 36 she is still in remission and stops etanercept. 2 months after giving birth the disease relapses but she wants to breastfeed and would like to restart etanercept. We agreed and 3 months after restarting anti-TNF RA is again in remission. In January 2017 her RA is inremission for 15 months and keeps her medication with etanercept every other week because she plans another pregnancy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7144

FRIDAY, 16 JUNE 2017

Latest advances in the treatment and management of psoriatic arthritis and the latest news on the use of Biosimilars in RMDs

SP0143 **A NEW DAY FOR PEOPLE WITH PSORIATIC ARTHRITIS: A HETEROGENEOUS DISEASE THAT CAN BE TREATED WELL?**

L.C. Coates. *Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom*

This talk will summarise recent advances in research around the treatment of psoriatic arthritis (PsA). Firstly there will be an update on research that shows the importance of treating patients promptly when they are diagnosed. Then results from studies of new therapies for both psoriasis and psoriatic arthritis will be shown to highlight the drugs that have recently become available in the clinic or are likely to be become available in the next few years. This will include new biologic disease modifying drugs with different targets including those that target interleukin 17 and interleukin 23 as well as new oral medications that are part of a family called small molecules. The role of these new therapies and how they compare to existing therapies in the clinic will be addressed. Finally there will be a summary on the research of how to use the existing and new therapies in the clinic including the use of the "treat to target" strategy.
Disclosure of Interest: L. Coates Grant/research support from: Abbvie, Janssen, Consultant for: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, UCB
DOI: 10.1136/annrheumdis-2017-eular.7145

SP0144 **BIOSIMILARS IN RHEUMATIC DISEASES: SOCIETY CHANCES VERSUS PATIENT CONCERNS**

A.A. Den Broeder. *Rheumatology, St. Maartenskliniek, Ubbergen, Netherlands*

Biosimilars are biologically but also in clinical practice for all intents and purposes identical to the original drug, as has been shown in blinded trials. But the perception amongst patients and sometimes physicians is one of possible inferiority, therefore they are often reluctant to transition to a biosimilar. However, although the listed prices of biosimilars and original products are the same, discounts are often higher for biosimilars, and widespread adoption of biosimilars drives the mean discount opt. So, society, hospitals, insurance companies and governments have preference for introduction of biosimilars to drive costs down.
Starting in new patients with a biosimilar is not controversial. Transitioning existing users from originator to biosimilar however is. This field has some interesting aspects, two of which will be elaborated on:
1/ balance of power, interests and ethics: different approaches are used by hospitals, insurance companies and governments to get biosimilars in use (collective buy e.g.). Big pharma are sometimes using campaigns to discredit biosimilars (create FUD, Fear Uncertainty and Doubt) towards patients and doctors, although some pharmaceutical companies are making original biologicals as well as biosimilars. Scientific societies of doctors have different recommendations, based on different beliefs towards biosimilars. In Most countries, Patients freedom of choice and right for best care are seen as paramount, but the other side of the coin might be that patients can be asked to adhere to a "social contract" to help in making healthcare financially sustainable for all.
2/ nocebo and attribution in open label transitioning: blinded research has shown that tansitioning to a biosimilar is not different with regard to safety and effect than continuing the original biological. However, in clinical practice a patient and physician knows that the patient has changed to a biosimilar. This may lead to nocebo effects (due to the perceived inferiority of the drug, experiences of subjective adverse effects and loss of efficacy are induced). In addition, adverse events of loss of efficacy that occurs independent of drug switch might be attributed to the biosimilar, called incorrect causal attribution. Both effects lead to more patient stopping a biosimilar after unblinded switch than in blinded studies. Prevention of nocebo and attribution in daily care is perhaps possible using a variety of techniques (e.g. restriction of fall back to originator, n=1 blinded provocation test, biobetter communication, patient incentive, patient/physician education), but this requires more research.
In summary, the use of biosimilars is a chance for society to maintain healthcare affordable, but it represents a challenge to maximise this potential.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7222

FRIDAY, 16 JUNE 2017

From pre-RA to established RA

SP0145 **PATHOPHYSIOLOGIC PROCESSES LEADING TO THE DEVELOPMENT OF AUTOIMMUNITY**

R. Toes. *Rheumatology, Leiden University Medical center, -Leiden, Netherlands*

Rheumatoid arthritis (RA) is a common complex disease characterized by chronic inflammation which results in joint destruction and significant disability in those affected. According to the World Health Organisation, within 10 years of onset, at least 50% of patients in western countries are unable to sustain a full-time job bringing about detrimental consequences to patients as well as exorbitant societal costs. The cause of RA remains unknown. Human genetic studies have provided valuable insight with over 100 genetic risk factors identified to date. Genetic variants at the human leucocyte antigen (HLA) locus remain the most prominent genetic risk factor. Smoking is the best known environmental factor to date. Microbial triggers have also long been postulated in RA although specific microbes involved in disease pathogenesis remain to be identified.
The majority of RA patients (60–70%) harbors autoantibodies, including Rheumatoid factors (RF) and autoantibodies against modified self-antigens, commonly termed Anti-Modified Protein Antibodies (AMPA). A prominent example of AMPA are Anti-Citrullinated Protein Antibodies (ACPA). ACPA are highly disease-specific biomarkers of important diagnostic and prognostic value, with ACPA-positive patients being at risk for rapidly progressive, destructive and systemic disease. The strongest genetic risk factors for RA, the so-called HLA-shared epitope (SE) alleles, associate only with ACPA-positive-disease, indicating that ACPA define a specific disease entity within the complex group of symptoms clinically defined as RA. Current concepts of RA pathogenesis hold that a sequence of events leads to the development of ACPA-positive disease. Environmental factors are thought to cause an initial break of tolerance leading to the generation

of ACPA. This initial development of auto-immunity appears to be independent of the disease-predisposing HLA-molecules. In most patients, this early event generates a polyclonal yet limited, mostly low-level autoantibody response that can be present for many years in the absence of clinical symptoms. Upon a putative second trigger, the ACPA epitope recognition repertoire broadens, more isotypes are being used, and ACPA serum levels rise. This is followed by precipitation of disease and is likely associated with the presence of the predisposing HLA-molecules. While the nature of this second trigger is presently unknown, the second event that initiates the broadening of the auto-immune response, in particular the citrulline-specific immune response, could mark a crucial moment upon which the auto-immune response becomes self-perpetuating and, potentially, irreversible.

Despite the many facets of ACPA revealed in the past two decades summarized above, it is not known how a breach of tolerance towards citrullinated proteins is mediated, or how ACPA-producing B-cells emerge.

Provision of T-cell help is crucial to convey the ability to B cells to modify the B cell receptor through somatic hypermutation. At present, it is unknown how ACPA- or other Anti-Modified Protein Antibody (AMPA)-producing B cells are "helped" by CD4+ Thelper cells, but it is often speculated that an auto-reactive T-cell response is crucial for their appearance. Our recent data show that such help could be provided by T-cells recognizing foreign proteins that have undergone a post-translational modification. In mice, AMPA-responses recognizing modified self-proteins are readily induced by immunization with modified proteins of non-selforigin. This is explained by the observation that the murine AMPA-response was, both at the monoclonal- and polyclonal level, highly cross-reactive towards multiple modified proteins, including proteins of self- and foreign origin. A similar observation was made analyzing the AMPA response in sera from RA patients. These data are important as the cross-reactive nature of AMPA could explain how autoreactive B-cell responses against PTM self-proteins can be induced by exposure to PTM foreign proteins thereby providing new insights on the breach of autoreactive B-cell tolerance.

Taken together, the analysis of the fine-specificity and recognition pattern of antibodies against modified proteins in RA during different phases of disease, together with detailed studies on the the identification, isolation and phenotypic characterization of auto-reactive B cells that express AMPA starts to shed light on the earliest phases of autoimmunity in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7218

SP0146 CAN WE PREDICT WHO IS GOING TO DEVELOP RHEUMATOID ARTHRITIS?

D. Van Der Woude. *Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

To accurately predict disease development can be considered the "holy grail" of risk factor research. It holds the potential to employ preventive treatment thereby nipping RA in the bud.

This presentation will review familial risk in RA and the underlying genetic risk factors, as well as environmental risk factors for disease. Autoantibodies are a potent prognostic marker when it comes to the risk of developing RA, and play a key role in current pathophysiological hypotheses. The newest players in the autoantibody field, and latest concepts of how the various risk factors contribute to disease onset will be discussed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7141

SP0147 CAN WE PREVENT THE ONSET OF RHEUMATOID ARTHRITIS IN HIGH RISK INDIVIDUALS?

K.D. Deane. *Division of Rheumatology, University of Colorado Denver, Aurora, United States*

Multiple studies have demonstrated that rheumatoid arthritis (RA) related biomarkers can identify individuals without inflammatory arthritis who are at high-risk for the future development of clinically apparent synovitis and classified RA. These findings have led to the development of several prevention trials in RA that have either been completed, or are underway. With these exciting developments as background, this lecture will discuss multiple aspects of RA prevention including the role of biomarkers and other factors in developing robust prediction models for future RA, and methods to identify individuals before they develop RA. In addition, this lecture will discuss specific preventive approaches to RA such as clinical trial design and choice of preventive interventions that are based on our growing understanding of the mechanisms of RA development.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7235

SP0148 PATHOPHYSIOLOGY OF ESTABLISHED RA SYNOVITIS

B. Lauwerys. *Department of Rheumatology, Université catolique de Louvain, Brussels, Belgium*

Access to synovial tissue through - minimally invasive - synovial biopsy procedures led to the implementation of new translational approaches to our understanding of established RA. In this lecture, we will illustrate how the identification of different synovial pathotypes and related molecular pathways translated into clinically relevant phenotypes, such as disease severity or response to therapy. Validation of these concepts in ongoing large-scale multi-centric trials will be key to the integration of synovial assessment tools in clinical practice.

Disclosure of Interest: B. Lauwerys Shareholder of: DNALytics

DOI: 10.1136/annrheumdis-2017-eular.7282

FRIDAY, 16 JUNE 2017

Laboratory course - from the clinic to the lab and back II

SP0149 NEW TRENDS IN BIOMARKERS IN INFLAMMATORY JOINT DISEASES

E. Feist. *Rheumatology, Charite University Hospital, Berlin, Germany*

This lecture provides an overview on new developments in biomarker research and standardization in inflammatory joint diseases. The presentation includes an introduction of established and new biomarkers in serum and synovial fluid as well as methods for their detection. Furthermore, an overview on different modifications of auto-antigens (including citrullinated and carbamylated isoforms) and their role in immune response and pathogenesis of disease will be given. The diagnostic performance of new and established biomarkers will be discussed including antibodies against modified antigens also illustrated by difficult to diagnose cases. In this context, special attention will be attributed to the predictive value of biomarkers for diagnosis of disease and treatment response.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7200

FRIDAY, 16 JUNE 2017

Switching T on and off: how T cells drive and regulate chronic inflammation

SP0150 TH17 CELLS DRIVE AND REGULATE TISSUE INFLAMMATION

V. Kuchroo on behalf of Basic and Translation Science. *Evergrande Center for Immunologic Diseases, Harvard Medical School, Boston, United States*

Recently a subset of interleukin (IL)-17-producing T cells (T_H17) distinct from T_H1 or T_H2 cells was described and shown to have a crucial role in the induction of autoimmune tissue injury. Accumulating data suggests that there are three distinct steps in Th17 differentiation: *Induction*, *Amplification* and *Stabilization* mediated by distinct cytokines. Whereas TGF-b + IL-6 or IL-1 + IL-6 induces them, IL-21 amplifies Th17 cells, IL-23 stabilizes the phenotype of Th17 cells. Loss of any of the cytokines (TGF-β, IL-1, IL-6, IL-21 or IL-23) in the pathway results in a defect in generation of Th17. However not all Th17 cells are pathogenic and induce autoimmunity, IL-23 is a key cytokine that induces pathogenicity in Th17 cells (Lee et al., 2012). Using expression profiling at very high temporal resolution, novel computational algorithms and innovative nano-wire based "knock-down" approaches, we have developed a regulatory network that governs the development of Th17 cells. In addition to high-density temporal microarray analysis, we have performed single-cell RNA-seq of Th17 cells in order to characterize cellular heterogeneity, identify subpopulations, functional states and learn how gene expression variation affects Th17 effector functions. We have identified novel regulators of Th17 cells both *in vivo* and *in vitro* that do not affect Th17 differentiation but affect pathogenic vs. non-pathogenic functional states of Th17 cells. Some of the regulators that make Th17 cells non-pathogenic are also utilized by CD8+ T cells to induce T cell "exhaustion" or "dysfunction". These novel inhibitory molecules cooperate with other known "check-point" co-inhibitory receptors to suppress anti-tumor immunity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7254

SP0151 SWITCHING OFF UNWANTED IMMUNE RESPONSES: THE MECHANISM OF ANTIGEN-SPECIFIC IMMUNOTHERAPY WITH T CELL EPITOPES

D.C. Wraith. *Institute of Immunology & Immunotherapy, University of Birmingham, Birmingham, United Kingdom*

Control of autoimmune and allergic conditions can be reinforced by tolerance induction with peptide epitopes; this presentation will focus on the mechanisms involved. Peptides must mimic naturally processed epitopes. Peptide induced peripheral tolerance is characterised by the generation of anergic, IL-10 secreting $CD4^+$ T-cells with regulatory function. $CD4^+$ T-cells become anergic following their first encounter with peptide. The loss of proliferative capacity correlates with a cytokine switch from a pro-inflammatory to a phenotype characterised by secretion

of the anti-inflammatory cytokine IL-10. IL-10 Treg/Tr1 cells suppress dendritic cell maturation, prevent Th cell differentiation and create a negative feedback loop for Th driven immune pathology. Tolerance induction involves upregulation of transcription factors controlling IL-10 and inhibitory receptors limiting T cell signalling. Results from clinical trials of peptide immunotherapy will be discussed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7209

SATURDAY, 17 JUNE 2017

Reverse translation - learning from clinical trials in SLE, Sjögren's and APS

SP0152 LEARNING FROM CLINICAL TRIALS IN SYSTEMIC LUPUS ERYTHEMATOSUS

D.A. Isenberg. *University College London/University College Hospital London, London, United Kingdom*

An enormous sense of frustration has surrounded the results of clinical trials in patients with systemic lupus erythematosus (SLE). A steady stream of trials including those studying the effects of Epratuzumab, Abatacept, Rituximab, Tabalumab and Silfalimumab have failed to meet their endpoints. Even though Benlysta (which blocks the B-cell activating factor BAFF) did meet its endpoints, it only demonstrated a difference of around 10% between the Benlysta-treated and placebo-treated arms in trials involving over 800 patients.
However, there are some bright spots on the horizon. Trials comparing the use of Mycophenolate with other classic immunosuppressive drugs clearly showed it to be as good as Cyclophosphamide in getting patients into renal remission and demonstrated its superiority in maintaining that remission compared to Azathioprine[(1)]. The use of Atacicept which blocks two B-cell activating factors has shown some extremely promising results[(2)] as have trials of both Rontalizumab and Anifrolumab[(3)] (which block interferon-alpha).
Some key messages learnt from the running of the lupus trials include the importance of minimising the concomitant steroids and immunosuppression; ensuring the quality of those assessors participating in the clinical trials and the utility of employing an independent peer-review panel to monitor data as it is collected from the participating centres during the course of the trial. It is also evident that selecting patients who are more serologically active is likely to be of benefit both in clinical trials and in the clinic. However, we still need better biomarkers to help guide us; the identification of individuals expressing a high interferon alpha signature (and who thus might better benefit from an interferon alpha blocker) is one such example.
It remains ironic that Rituximab, the most widely used monoclonal antibody in SLE, failed its endpoint in two clinical trials. However, detailed analyses of data from those trials have shown some encouraging trends including falls in dsDNA antibodies and improvement in some clinical parameters.
References:
[1] Dooley MA et al. N Engl J Med 2011; 365; 188.
[2] Isenberg et al. Ann Rheum Dis 2015; 74; 2006–18.
[3] Furie R et al. Arthritis Rheum 2015; 67 (suppl 10) (abstract).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7196

SP0153 LESSONS FROM APS TRIALS

M. Khamashta[1,2]. *[1]Rheumatology Dept, Dubai Hospital, Dubai, United Arab Emirates; [2]Lupus Research Unit, St Thomas Hospital, London, United Kingdom*

Prevention of thrombosis in patients with APS remains a vexing clinical problem. In patients with a history of thrombosis, there is considerable risk of recurrence, and long-term anticoagulation treatment with warfarin is effective in most cases. Existing evidence suggest that the use of DOACs for secondary thromboprophylaxis for APS patients with previous VTE is promising. Until new data from ongoing clinical trials are available, there is not enough evidence to consider using DOACs in patients with APS and previous arterial events. The efficacy of heparin and low-dose aspirin in APS patients with previous pregnancy losses is supported by 3 meta-analysis available on the topic. In patients with antiphospholipid antibodies but without a previous thrombotic event, most physicians in the field recommend thromboprophylaxis with low-dose aspirin. Given the diversity of clinical presentations and medical specialties involved, it is not surprising that treatment of APS has been subject of intense debate. Due to the difficulty in conducting trials in the setting of a relatively rare condition, well designed multicenter studies (such as registries) using actual classification criteria and standardized tests should be performed in the future to answer all the opened questions regarding management of APS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7284

SATURDAY, 17 JUNE 2017

Genomic imprinting and post-translational modifications

SP0154 RATIONALE TO TARGET IMMUNE MEMORY RESIDING IN INFLAMED TISSUES

H.-D. Chang. *German Rheumatism Research Center Berlin, Berlin, Germany*

T helper (Th) lymphocytes play a major role in the regulation of immune responses and are thought to initiate and drive chronic rheumatic inflammation. Memory Th lymphocytes persist in the inflamed tissue and are refractory to therapeutic intervention. In chronic inflammation Th lymphocytes have undergone molecular adaptations, such as the upregulation of Twist1 and the microRNA miR-148a, which are not found in circulating Th lymphocytes, and support the survival of the Th cells within the inflamed tissue. Within the inflamed tissue, the Th lymphocytes constantly recruit and activate inflammatory cells, such as monocytes/macrophages and granulocytes through the secretion of particular chemokines and interleukins. The monocytes/macrophages in turn can recruit more Th cells into the inflamed tissue. Disrupting this vicious circle by specifically targeting the memory Th cells resident in the inflamed tissue by interfering with their molecular adaptations could be an interesting therapeutic option.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7278

SP0155 THE ROLE OF POST-TRANSLATIONAL MODIFICATION AND AUTOREACTIVITY

R. Toes. *Rheumatology, Leiden University Medical Center, -Leiden, Netherlands*

Rheumatoid arthritis (RA) is a prototype autoimmune disease, with the hallmark signs of synovial inflammation and the presence of autoantibodies. Of the different autoantibody systems present in RA, rheumatoid factors (RF) are probably the best studied. Their presence was first detected >70 years and it was in the late 1950s when it was realized that RF reacted to gamma globulins. Since the discovery of RF several other autoantibody systems have been discovered in RA, many of them directed against post-translationally modified protein antigens. The most prominent example of such autoantibodies are anti-citrullinated protein antibodies (ACPA), which are directed against a wide-array of citrullinated proteins. Now RF and ACPA determination are the two major diagnostic laboratory tests for RA and part of the EULAR and ACR criteria for RA.
In the past few years, it has become clear that the autoantibody response present in RA extends towards several other modified proteins, such as proteins modified by acetylation or carbamylation. As all these auto-antibodies recognize Post-Translationally Modified (PTM) proteins, these antibodies are collectively called Anti-Modified Protein Antibodies (AMPA). In the context of this presentation, I will focus on the auto-antibody response against citrullinated, carbamylated and acetylated proteins.
Carbamylation leads to the formation of homocitrulline. Structurally, homocitrulline greatly resembles citrulline but is one methylene group longer. Citrulline is generated when PAD enzymes modify the amino acid arginine. In contrast, the amino acid homocitrulline is generated by a chemical reaction in which cyanate reacts with the amino acid lysine. Arginine and lysine are located at different positions in the amino acid sequence of proteins, and therefore these modifications occur at different positions in proteins with different flanking amino acids. Intriguingly, although homocitrulline residues can also be recognised by auto-antibodies, these auto-antibodies often do not crossreact with citrulline. Acetylation is a process where acetyl groups are added to free amines of lysine residues by acetyl transferases. Acetylated lysine does not resemble citrulline but bears similarity to homocitrulline except at the side chain terminal amine, which is replaced by a methyl moiety.
By now it is clear that AMPA consist of different auto-antibody families that are largely distinct, but that can also display a certain degree of cross-reactivity. Therefore, the notion is emerging that, although cross-reactivity exist, different classes of AMPAs are generally seen as distinct auto-antibody families that target different antigens, but intriguingly often co-occur. As the AMPA-responses in RA are often found together, it indicates that –somehow- AMPA-reactivity has a commonality that is currently not understood.
Although, the reason why an immune response starts against PTM proteins is not known, it appears crucial to obtain understanding on the breach of tolerance towards PTM proteins as the immune response against these proteins has been intimately implicated in disease-pathogenesis. Understanding the full AMPA response, the triggers that drive AMPA production, their mutual crosstalk and the pathways by which AMPA and/or AMPA-expressing B cells possibly contribute to RA will be important for the development of curative interventions in RA. In the context of this presentation, some of these aspects will be discussed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7219

SP0156 **HOW BIG DATA HELP US UNDERSTAND NEW AND OLD THERAPY TARGETS**

P.E. Lipsky. *Ampel Biosolutions, Charlottesville, United States*

Gene expression profiling is a valuable tool to identify the altered cellular status of cells or tissues. Metaanalysis of available gene expression profiles from numerous sources provides a means to assess the molecular alterations characteristic of autoimmune diseases, such as systemic lupus erythematosus (SLE) and to develop insights into possible new therapies. Toward this end, all of the publicly available gene expression datasets from SLE blood and tissue were assembled and a variety of analytic algorithms were employed to identify differentially expressed genes, gene modules associated with clinical features, molecular pathways associated with SLE and potential upstream regulators. This information was employed to cross-reference a variety of databases to predict novel molecular pathways and potential drug candidates. Specifially, gene expression profiles obtained from lupus affected skin, synovium and kidney were obtained, compared to metaanalyzed data obtained from active lupus B cells, T cells and myeloid cells, and cross-referenced to various pathway analytic tools including Molecular Signature (MS©)-Scoring, Ingenuity Pathway Analysis© Upstream Regulator (IPA©-UR) and Library of Integrated Network Based Cellular Signatures (LINCS). More than 300 arrays from lupus patients and appropriate controls were analyzed to determine differentially expressed (DE) genes [8279 discoid skin, 5465 lupus synovium, 6381 lupus nephritis glomerulus, 5587 lupus nephritis tubulointerstitum]. Notably, the majority of lupus affected tissue DE genes were detected in more than one tissue and 439 were differentially expressed in all tissues. Tissue inflammatory/immune cell infiltration was documented by genes encoding specific cell markers as well as by unique gene expression signatures (Biologically Informed Gene Clustering, BIG-C©). Examination of curated predicted functional groups from the STRING (Search Tool for Retreaval of Interacting Genes/Proteins) output of common up-regulated transcripts in lupus tissue predicted therapeutic targets and drugs using STITCH (Search Tool for Interacting Chemicals) and IPA's BioProfiler© that were confirmed by connectivity using LINCS. Analysis of gene expression datasets for the presence of specific gene modules using GSVA (Gene Set Variation Analysis) documented the overall similarity of active lupus gene sets as well as the uniqueness of individual patient samples.These results demonstrate the value of comprehensive application of orthogonal curated bioinformatics tools in identifying the role of inflammatory/immune cells in lupus pathogenesis and tissue damage. This approach demonstrated that there are molecular pathways common to all lupus patients and tissues, and there are pathways involved in inflammatory response of some but not all patients and tissues. Further analysis should generate a molecular model of lupus immunopathogenesis and could identify therapies that may be useful in all lupus patients versus those with involvement of specific tissues and treatments specifically targeted to individual lupus patients.

Grammer AC et al. Lupus (2016) 25:1150–1170.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7234

SATURDAY, 17 JUNE 2017

Optimizing treatment for osteoarthritis: take the phenotype in account "one size does not fit all"

SP0157 **METABOLIC PHENOTYPE: THE TWO FACES OF OBESITY IN OSTEOARTHRITIS**

F. Berenbaum[1,2,3]. *[1]Department of Rheumatology, Sorbonne University; [2]INSERM; [3]AP-HP Hospital Saint-Antoine, Paris, France*

Osteoarthritis (OA) has long been considered as the consequence of tear and wear due to mechanical triggers. In that paradigm, the increased risk of OA in obese patients can be explained by overload on weight-bearing joints. The discovery of an increased risk of hand OA in obese patients has changed the paradigm by opening up an additional hypothesis (not ruling out the mechanical hypothesis) based on systemic factors secreted by the adipose tissue (even the central one or/and the intraarticular one), which could have a deleterious effect on joints. More recently, cohorts data have suggested that obese patients with a metabolic syndrome (MetS) (an association of cardiometabolic factors that increase the risk of cardiovascular events i.e. diabetes, hypertension, dyslipidemia) have an increased risk of OA compared to obese patients without MetS. The most recent researches in that field highlight the role of metabolic-triggered inflammation (called meta-inflammation) on the initiation/progression of OA and the role of each of the components of the MetS independently (hyperglycemia, insulinoresistance, oxLDL, endothelial dysfunction, etc.). A better understanding of this newly defined OA phenotype, namely the MetS-associated OA, should lead to the discovery of new drugs specifically targeting this phenotype or/and to assess the efficacy of drugs in OA already on the market for diabetes, hypertension or dyslipidemia.

Disclosure of Interest: F. Berenbaum Grant/research support from: Servier, TRB Chemedica, Consultant for: Pfizer, AbbVie, GSK, Flexion Therapeutics, Nordic Bioscience, MerckSerono, Jansen, Expanscience

DOI: 10.1136/annrheumdis-2017-eular.7120

SP0158 **PAIN PHENOTYPE: CAN WE TAKE ADVANTAGE OF THE PLACEBO EFFECT**

A. Abhishek. *Academic Rheumatology, University of Nottingham, Nottingham, United Kingdom*

The discordance between pain and structural changes in osteoarthritis has been recognised for over two decades. Recent research has also identified different pain phenotypes in people with osteoarthritis. This suggests that the changes in the peripheral and central nervous system may affect both the severity and character of pain and associated features in osteoarthritis. Placebo response, the improvement in symptoms in those in the placebo arm of a randomized controlled trial, and placebo effect, the difference in improvement in those treated with placebo (in placebo arm of a randomized controlled trial) and those who have had no treatment (e.g. in the observation only arm of a three arm randomized controlled trial) are mediated by complex neural mechanisms and are especially relevant to the management of osteoarthritis. Indeed, the placebo response associated with most osteoarthritis treatments is stronger than their treatment effects. While a large placebo response is a significant obstacle to the development of new drugs and non-drug interventions for the treatment of osteoarthritis, it can be utilised as a "friend" in the day to day and long-term management of a person with osteoarthritis. This lecture will outline the pain phenotypes associated with osteoarthritis and describe the potential for placebo effect in improving osteoarthritis pain. The pain phenotypes associated with osteoarthritis that are most likely to be improved by optimizing placebo response and the underlying mechanisms will be discussed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7224

SATURDAY, 17 JUNE 2017

Targeting adipose tissue inflammation

SP0159 **ADIPOSE TISSUE – BYSTANDER OR THERAPEUTIC TARGET?**

M.I. Bokarewa. *Rheumatology and Inflammation Research, University of Gothenburg, Gothenburg, Sweden*

Adipose tissue (AT) is a complex endocrine organ with profound effects on body physiology. Research of recent years generated remarkable volume of information on metabolic and immune functions of AT. The lecture will focus on topics of AT biology that shed light on areas of interest linking metabolic, immune and rheumatic conditions.

AT is a recognized master regulator of energy balance and nutritional homeostasis. Cells of AT are active part in establishment of autoimmunity, and also osteoarthritis and osteoporosis. Macrophages enrich AT, change its phenotype and mediate inflammation, enhance antigen presentation. Th17 and regulatory T cells reside and operate in AT, having distinct transcriptional and functional characteristics from counterparts of the lymphoid organs. IL6 and IL33 signaling contribute to this distinction. Adipocytes communicate with other cell types by means of signal molecules adipokines, interleukins, and fatty acids and may affect blood pressure, muscle functions, wound healing, bone formation, hematopoiesis and tumor growth. Localization of AT plays important role for its properties including cellular composition, their gene expression profile and secretome, response to external forces and their therapeutic potential. Subcutaneous AT and bone marrow AT are most available and studied in humans.

Adiposity has been revealed as a risk factor for development of multiple autoimmune conditions including type 1 diabetes, rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, psoriasis and thyroiditis. It also associates with low response rate to both biologic and non-biologic anti-rheumatic treatment. Notably, cumulative evidence show a surprising protective action of AT for radiographic joint damage in arthritis.

Antirheumatic drugs have remarkable effect on the body fat composition and serum lipid profiles, and could therefore be considered as AT-targeting agents. Impact of these drugs on the composition and function of AT localized subcutaneously and in the bone marrow remains in focus of research and will provide new insights in mechanisms of insulin resistance, cardiovascular risk, bone metabolism and autoantibody production.

Production of adipokines has been proposed a mechanism through which AT fuels inflammation and severity of autoimmune diseases however direct evidence still awaits. Several adipokine targeting and adipokine stimulating therapies have been designed and experimentally tested in the models of collagen-induced arthritis, autoimmune diabetes and insulin resistance, encephalitis, and osteoporosis induced by estrogen-deficiency. In human settings, the experience of leptin substitution in anorexia neurosa and in lipodistrophy revealed positive effects on bone metabolism and improved cognition.

In conclusion, AT attracts increasing attention as an active contributor of inflammation and autoimmunity. Further studies are needed to confirm and specify the effects and pathogenic links within AT. Novel insights in mechanisms regulating the diversity of AT composition and functions may assist conversion of AT into a teammate of anti-rheumatic processes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7064

SP0160 IS DIABETES AN INFLAMMATORY DISEASE AND SHOULD BE TREATED LIKE THAT?

A. Schaeffler. *Department of Internal Medicine-III, Endocrinology and Diabetes, University of Giessen, Germany, Giessen, Germany*

It is a well-known clinical observation that inflammatory diseases are accompanied by metabolic implications such as hyperglycemia, insulin resistance and increased fatty acids. On the other hand, metabolic diseases have inflammatory implications. There is a chronic and low-grade state of inflammation in obesity and type 2 diabetes. Physiological insulin resistance during infection or inflammation re-distributes glucose and fatty acids to immune cells. On the basis of systemic and adipose tissue inflammation such as MCP-1/TLR-4-driven macrophage infiltration and pro-inflammatory polarization of these cells, this lecture will give a summary of anti-diabetic effects of anti-inflammatory drugs used in rheumatology.

What is the evidence from clinical studies using anti-inflammatory approaches to treat patients with type 2 diabetes mellitus?

Basically, TNF plays an important role in insulin resistance in rodents. Blocking TNF in rodents reverses obesity-related diabetes. There are no state of the art clinical studies showing convincing evidence of an anti-diabetic potential due to underpowered cohorts and short duration of the studies. Only one single study over 6 months showed a 10% improvement of fasting glucose levels in 40 prediabetic obese patients.

Diacerein belongs to the chemical group of anthranoids. Although the mechanism of action is unknown, diacerein decreases the levels of TNF and of IL1b and has therefore been used in rheumatic diseases. Diacerein has potent effects on insulin secretion and glycemic control with a reduction of HBA1c level by 1.6%.

IL-1 receptor antagonists such as anakinra (a recombinant human IL-1 receptor antagonist) have also been studied in diabetes. Anakinra was able to improve glycemia, inflammation and insulin secretion. Two additional studies in patients with impaired glucose tolerance or prediabetes demonstrated positive effects of anakinra on beta cell secretory capacity. Since anakinra requires daily injections and often causes adverse effects at the injection site, humanized antibodies against IL1b have been developed. Each of these antibodies had beneficial effects in patients with type 2 diabetes. However, studies were either underpowered or showed only little improvements of glycosylated HBA1c levels, probably due to low pre-study levels.

Inhibition of the IKK/NFkB pathway might also be of benefit in insulin resistance. Salsalate improves insulin sensitivity, insulin secretion and glycemic control to a moderate extent of 0.4–0.5%. Salsalate also has effects in prediabetic patients and in drug-naive type 2 diabetic patients.

There is upcoming evidence of potential benefical effects of CCR2 antagonism in diabetes.

Obesity causes an increased flux of fatty acids into muscle and liver with an accumulation of DAG in these organs. DAG activates specific isoforms of protein kinases, that is PKC T in muscle and PKC E in the liver. These isoforms cause an inhibitory phosphorylation of IRS-1 and the insulin receptor itself leading to insulin resistance. Weight reduction by diet, physical activity and bariatric surgery remove ectopic fat and are able reverse diabetes. Most interestingly, PKC-isoform specific inhibitors such as FGF-21 might represent new drug targets.

Finally, targeting ectopic fat is more close to the pathophysiology of diabetes than anti-inflammatory therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7055

SP0161 THE ROLE OF ADIPOSE TISSUE IN OSTEOARTHRITIS

A. Ioan-Facsinay. *Leiden University Medical Center, Leiden, Netherlands*

The association between obesity and osteoarthritis (OA) is nowadays well-accepted. This association is present both in weight-bearing and non-weight-bearing joints, indicating that next to local effects, systemic effects associated with obesity could play a role in disease. The relative contribution of local and systemic effects could be different in each joint. In this presentation, I will summarize the current knowledge about the contribution of local and systemic adipose tissues to osteoarthritis in different joints, with emphasis on knee OA. Moreover, obesity-associated changes and their role in OA will be highlighted.

The key messages I would like to convey are:

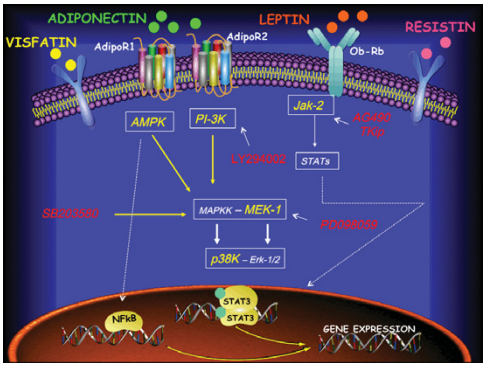
- Mechanical stress is a major contributor to knee OA
- The infrapatellar fat pad (IFP), an intra-articular adipose tissue in the knee, is dostinct from other adipose tissues and could play a role in knee OA
- Only few obesity-related features have been described in IFP in OA

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7207

SP0162 ADIPOKINES IN THE PATHOPHYSIOLOGY OF CARTILAGE

O. Gualillo. *NEIRID Lab (Laboratory of NeuroEndocrine Interactions In Rheumatology and Inflammatory Diseases), Sergas Idis, Santiago de Compostela, Spain*

Fat mass dysregulation is a marked characteristic of overweight and obesity. Obesity is, historically, a classic risk factor for osteoarthritis development and progression and shares with osteoarthritis a huge societal impact but also several common biochemical features that are strongly related to the low-grade inflammatory status. Even though OA has been considered during decades a disabling degenerative disease related to mechanical, age and genetic factors with poor inflammatory component, the current consensus is that OA, in particular OA associated with metabolic alterations, is a global muscle-skeletal diseases in which pro-inflammatory and catabolic mediators, most of them produced by a dysregulated visceral or periarticular white adipose tissue (WAT), are at play. The coexistence of obesity and OA is a clinical reality and is changing the traditional view of this degenerative disorder. Thus, chronic low-grade inflammation is a common characteristic shared by both obesity and OA. It has been demonstrated that obesity increases the incidence of OA, particularly in weight-bearing joints such as knees. However, the fact that obese individuals have an increased risk of developing OA in non-weight bearing joints such as hands and wrists suggests that factors produced by WAT play a role in the onset and/or progression of OA. In addition to a growing body of evidence demonstrating that obesity has a direct mechanical effect joint cartilage, recent research shows that pro-inflammatory factors produced by WAT (collectively known as adipokines) promote further inflammation and degradation of cartilage, also influencing the whole joint environment (i.e. synovium, muscle, bone and immune cells). Accumulating evidence shows another potential source of inflammatory adipokines in the joint is the Hoffa infrapatellar fat pad. Adipokines including leptin adiponectin, visfatin and lipocalin 2 have been demonstrated to exhibit a wide spectrum of biological activity including the activation of pro-inflammatory and catabolic pathways mediated by elevated levels of NO, ROS, MMPs and PGE2. The discovery of adipokines has made a major contribution to our understanding of the complex relationship between diabesity and OA, encompassing a variety of factors that include the immune system, metabolism and biomechanics. A critical aspect that must constantly be borne in mind is that diabesity and OA share a low-grade inflammatory state that heavily influences the course of OA progression. Therefore, the prevention and correction of diabesity should be the first line approach for tackling the detrimental effects of weight gain, adiposity and altered metabolic WAT function in OA. The aim of this lecture is to summarize the role of adipokines in bone and cartilage function, as well as in inflammatory and degenerative joint disease. We discuss clinical implications and then survey attempts to exploit this role for therapeutic gain, which holds potential as a novel approach for drug development in bone and joint disease.



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7199

SATURDAY, 17 JUNE 2017

Trials and tribulations of medication adherence

SP0163 INTERVENTIONS TO IMPROVE MEDICATION ADHERENCE IN PATIENTS WITH INFLAMMATORY ARTHRITIS

J.E. Vriezekolk. *Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands*

Non-adherence to medication in rheumatic diseases is a major concern for patient's health, because incorrect use can result in *less* therapeutic benefits of treatment, including more disease activity and increased radiological damage. As a consequence, non-adherence may lead to more disability and lower health-related quality of life. Using Lowe's taxonomy[1], the current state of evidence around medication adherence interventions will be presented. Examples of promising intervention strategies will be highlighted.

References:

[1] Lowe et al. (2011) Development of a taxonomy of interventions to organise the evidence on consumers' medicine use.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7081

SP0164 **BARRIERS AND FACILITATORS TO ADHERENCE TO MEDICATION IN PATIENTS WITH INFLAMMATORY ARTHRITIS**

K. Koutsogianni. *The Arthritis Foundation of Crete, Heraklion, Crete, Greece*

Background: Inflammatory arthritis can cause pain, stiffness, joint damage and even disability without proper and early guided treatment. The full benefits of several treatments recommended, can be achieved if patients strictly follow drug regimens. However, rates of adherence to prescribed medications in patients with inflammatory arthritis seem to be suboptimal.
Objectives: To identify the barriers and facilitators for adherence to medication on patient's perspective and to suggest ways to facilitate the patients with chronic conditions as the inflammatory arthritis are, to understand the value of compliance to treatment.
Methods: The problem of poor patient compliance was detected about 2,000 years ago when Hippocrates taught his students to pay particular attention to the analysis of the causes that led their patients to lie regarding compliance with medical instructions given to them. The adherence to medication of patients suffering from chronic diseases reaches only 50% (WHO-2003) while the rate of compliance to prescribed medicines for patients with rheumatoid arthritis tend to be quite low and range from 30–80%.
Fear and insecurity about the side effects of the medicines, the doubt of efficacy of medications, the refusal to accept the IA diagnosis and the long term treatments, the desire to stop treatment to be free of the ongoing dependency on medication, the lack of competence by some physicians to involve the patient in the treatment procedure and the large amount of patients co-payment are the most significant barriers to patients adherence. A survey conducted among patients of the Arthritis Foundation of Crete aiming to assess the degree of their adherence to MTX showed that 1 in 4 patients reported missing at least one dose of MTX on their own initiative during the last 6 months without referring to their doctor and the main reason was due to side-effects.
Experiencing beneficial effects of the medications and being able to maintain autonomy and social participation, receiving clear and understandable information about the treatment options, having support from family and friends, having a good relationship with the treating physician and being involved in shared decision making process are the keys for leading the patients to better adherence.
Conclusion: A good patient-health professional relationship, knowledge about treatment options and appropriate amount of information provided by HCPs as well as the patients' acceptance of their health condition and understanding of the necessity of long term therapy appear to improve adherence to medication for patients with inflammatory arthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7133

SP0165 **CAN MUSCULOSKELETAL ULTRASOUND INFORM HEALTH BELIEFS AND PLAY A ROLE FOR MEDICATION ADHERENCE?**

K. Kumar. *University of Manchester, Manchester, United Kingdom*

Rheumatoid Arthritis (RA) is a condition with no cure and can cause disability[1]. RA affects nearly 1 in 100 adults. Early disease is characterised by pain and other features of inflammation, such as heat, swelling of joints, and loss of function. RA is associated with increased costs of co-morbid conditions (such as cardiovascular (CVD) associated with RA[2].
Medication can ease symptoms and limit disease progression in RA[3]. Despite this, nonadherence to medication is common in RA[4]. In the UK, we found that showing patients their joint swelling via musculoskeletal ultrasound scan as an educational tool helped to increase beliefs about the necessity of treatment[5]. Our study provided a deeper understanding of adherence to disease modifying anti-rheumatic drugs (DMARDs) in patients with RA. Improving adherence is likely to be facilitated by incorporating visual representations of the disease process and better explanations of the consequences of poorly controlled RA into the consultation. This session will uncover some suggestions around the use of musculoskeletal ultrasound in improving adherence to DMARDs.
References:
[1] Emery P. Evidence supporting the benefit of early intervention in rheumatoid arthritis. J Rheumatol, 2002;29 (2):3–8.
[2] John H, Kitas G, Toms T, Goodson N. Cardiovascular co-morbidity in early rheumatoid arthritis. Best Pract Res Clin Rheumatol 2009; 23(1):71–82.
[3] Smolen JS, Landewe R, Breedveld FC, Dougados M, Emery P, Gaujoux-Viala C et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. Ann Rheum Dis 2010; 69(6):964–975.
[4] Pasma A, Schenk CV, Timman R, Busschbach J, van den bemt B, Molenaar E et al. Non-adherence to disease-modifying antirheumatic drugs is associated with higher disease activity in early arthritis patients in the first year of the disease. Arthritis Research & Therapy 2015; 17:doi:10.1186/s13075-015-0801-4.
[5] Kumar K, Raza K, Gill P, Greenfield S. The impact of using musculoskeletal ultrasound imaging and other influencing factors on medication adherence in patients with rheumatoid arthritis: a qualitative study. Patient Prefer Adherence 2016; 10:1091–1100.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7085

SATURDAY, 17 JUNE 2017

Outcome in juvenile idiopathic arthritis

SP0166 **LONG-TERM OUTCOME OF JIA INTO ADULTHOOD**

B. Flato[1,2]. *[1]Institute of clinical medicine, University of Oslo; [2]Dep of Rheumatology, Oslo University Hospital, Oslo, Norway*

Background: In patients with juvenile idiopathic arthritis (JIA), scarce information on disease outcomes into adulthood are available.
Objectives: To review the long-term outcome and possible time trends in adult JIA and discuss how JIA in adulthood is similar to or different from adult onset rheumatic diseases.
Results: JIA is a heterogeneous group of diseases, but across different categories patients with JIA share some clinical, prognostic and genetic characteristics different from those found in adult onset arthritis (i.e. growth disturbances, more varying prognoses, and HLA-DRB1*08). The most common categories of JIA, oligoarthritis and RF-negative polyarthritis, do not have any adult counterpart. On the other hand, 82–96% of patients with systemic, RF-positive polyarticular, psoriasis related, and enthesitis related JIA were recently found to fulfil the criteria for adult Stills, RA, psoriatic arthritis, and adult spondylarthropathy, respectively. Furhermore, recent analyses of large patient groups show that patients with oligoarticular and RF-negative polyarticular JIA share HLA associations with seronegative RA (HLA-DRB1 amino acid at position 13).
At transition to adult care, about half of the JIA patients (range 42–67%) have active disease or are on anti-rheumatic medication. In adult JIA patients, active disease after more than 20 years of disease duration occured in 40 percent (range 37–43%). Differences in definitions of remission, classification criteria and/or selection of patient may explain these variations.
Within a cohort, no reduction were found in the proportion of patients with active JIA from childhood to adulthood in 3 long-term longitudinal studies; 62% at 5- and 60% at 17-year followup, 42% at 10- and 37% at 26-year followup) and 45% at 15- and 41% at 30-year followup.
Limitation in physical functioning has been found in 45–50% of adult JIA patients. The proportion with severe disability has increased with increased disease duration in several cross sectional and one longitudinal study. However, no definite trends towards detoriation of physical functioning over time were found in two recent longitudinal studies. The proportion of JIA patients with severe disability was low in long-term studies from this century, 3% to 11%, compared to 15–48% in studies from 1960 to 1990.
Up to 90% of the patients with childhood polyarthritis had radiographic damage in studies from 1966–76, compared to about 40% in studies from this century. In the total group of JIA patients, 24%>36% developed erosive disease, most frequently in wrists and hips. However, the use of radiographic scoring systems in JIA has been hindered by growth disturbances and varying joint distributions. Thus radiographic progression has never been investigated in clinical trials.
Several studies have shown that adults with JIA experience more pain, poorer health related quality of life and lower employment rates than age and sex matched controls from the general population, in spite of similar or higher education levels. A new study shows that JIA has a detrimental effect on HRQOL both in patients with and without clinical remission, and physical, but not mental, HRQOL deteriorate slightly from adolescence to adult life.
Ongoing active uveitis into adulthood has been found in half of the patients with JIA associated uveitis. One third of them have visual impairment and 40% need ocular surgery in early adult life. Recent studies indicate that adult JIA patients have increased rates of subclinical atherosclerosis and malignancies.
The use of arthroplasties in JIA patients decreased dramatically from 1990 to 2005, while the rates were stable in RA and increased in spondylarthropathy and osteoarthritis patients. Joint surgery now occurs in less than 15% of adult JIA patients.
Previous long-term followup studies have mainly been performed before biologic agents were available or early methotrexate was used. Long-term outcomes in JIA patients treated with biologic agents have been described in two registry based studies. Inactive disease was achieved in 24–67% of the adult JIA patients and 52–74% were still on a biologic agent at last followup. It has been found that biologics improve physical HRQOL in children with JIA, and that most of the acquired improvement is maintained in adult life. However, biologics were started several years after disease onset in these studies. Only 38–56% of adult JIA patients with long-term active disease were on synthetic or biological DMARDs according to recent followup studies.
Conclusion: About half of JIA patients have active disease into adulthood. JIA affects physical outcome, HRQOL and visual outcome, but adult patients with long-term active JIA seems to receive inadequate therapy. So far, the long-term outcome in patients receiving early biologic and/or synthetic DMARDs is not known.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7138

SATURDAY, 17 JUNE 2017

Getting financial support to research in RMDs through horizon 2020: opportunities, good practices, and successful experiences

SP0167 HORIZON 2020: OPPORTUNITIES FOR MEDICAL RESEARCH AND INNOVATION

S. Hogan. *DG Research, Directorate Health, European Commission, Brussels, Belgium*

Horizon 2020 is the largest EU Research and Innovation programme ever with nearly €80 billion of funding available over 7 years (2014 to 2020). It is an opportunity for supporting excellence and collaboration in research, on a scale and scope that is seldom feasible at global level.
Horizon 2020 contributes to the Innovation Union, a Europe 2020 flagship initiative aimed at securing Europe's global competitiveness. By coupling research and innovation, Horizon 2020 is helping to achieve this with its emphasis on excellent science, industrial leadership and tackling societal challenges. The goal is to ensure Europe produces world-class science, removes barriers to innovation and makes it easier for the public and private sectors to work together in delivering innovation. This it is seen as a means to drive economic growth and create jobs, Horizon 2020 has the political backing of Europe's leaders and the Members of the European Parliament.
Horizon 2020 is open to everyone, with simplified and more rapid application and reporting procedures.
The next work programme for the period 2018 – 2020 will be published in Autumn 2017.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7225

SATURDAY, 17 JUNE 2017

EULAR Projects - challenging projects in education and training

SP0168 THEORY OF POSTER DESIGN AND PRESENTATION

M. Boers. *Epidemiology & Biostatistics; Amsterdam Rheumatology and immunology Center, VU University Medical Center, Amsterdam, Netherlands*

This lecture introduces basic elements of poster design, and is followed after the session by a special poster tour devoted to design. It strongly links to the concepts discussed in my workshop on data visualization.
To design an effective poster, its message and the intended audience must be clear. Effective posters stand out because they convey their main message almost instantly, and then seduce participants to stay longer and learn more. Much more than oral presentations, posters are about selling your work in competition with all those other people presenting in your session.
In a good poster, all elements work together like a symphony orchestra:
Title, headings, text, tables, graphs, format, colors, layout, handouts, gimmicks, and ... you!
For the design process, you need a good plan (including timelines!), good tools (templates, software!) and a ruthless editor. Editing is about throwing out more and more stuff, until finally you reach the point where throwing out more destroys understanding. So the "orchestra" has single instrumentation, and is wonderfully transparent.
Posters are not "comprehensive"! All the details you love can go into a specially designed handout (NOT an exact replica of your poster).
Your role as presenter is special: you must be visible but unobtrusive, and flexible to accommodate different viewer styles, and have different modes of presentation (eg. walkthrough, answer questions, respond to critique). Also make sure your contact details are visible and correct (if no handout, be sure to have business cards). If you are playful you can use gimmicks to increase your visibility: match your clothes to your color scheme, make something in real 3D on your poster, use sound, etc. But don't overdo it: this is just the icing on the cake: this is a science, not a commercial exhibit.
When we go to assess posters in the upcoming poster tour, we will be looking for the following elements:
1. Overall message clear?
2. Text quality: brevity, clarity
3. Table quality: clear vision, clear understanding
4. Graph quality: clear vision, clear understanding
5. Design elements: layout, choice of font, color
6. Handout: not a replica, elements 1–5 repeated
7. Presenter: style, contact details

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7127

SP0169 EULAR SCHOOL OF RHEUMATOLOGY. A CHALLENGING EDUCATIONAL EULAR PROJECT. WHERE ARE WE NOW?

J.W. Bijlsma. *Rheumatology & Clinical Immunology, UMCU, Utrecht, UTRECHT, Netherlands*

In the last decade EULAR has further developed its educational portfolio. Apart from very educational tracks in the EULAR Congress, EULAR offers:
- on-line courses (Rheumatology, Connective Tissue Diseases, Scleroderma, Paediatrics, Ultrasound, Health Professionals), that are being followed by thousands of students all over the world
- text-books, based on the on-line courses
- live courses, such as the Postgraduate Course, Ultrasound courses, capillaroscopy, epidemiology, immunology, teach the teachers
- exchange programs, for trainees, scientists, health professionals and patients
- on-line image library, on-line outcome registry
- learning DVDs for medical students
- scientific endorsement of other courses

To bring all these offerings under one umbrella, EULAR decided to found the School of Rheumatology.
But the School is doing substantially more: we identified 7 areas (classrooms) where we bring enthusiastic and involved people together to evaluate the present needs in those areas and to prioritize new educational activities for those unmet needs. The following classrooms are actively developing new products:
Classroom medical students: formulating standard curriculum for musculoskeletal diseases and providing video-materials to support teachers and students.
Classroom trainees in rheumatology: start of a journal club, evaluating possibilities to install a European (EULAR) examination to become a rheumatologist, imaging on-line course.
Classroom teachers: course on assessment questions was already held, a teach the teachers event is planned.
Classroom rheumatologists: development of a pocket primer on rheumatic diseases, to be used as an app.
Classroom scientist: preparing a possible on-line course on epidemiology and clinical (trial) research, evaluating possible webinars for basic science methodology.
Classroom health professionals: preparing an accreditation system for health professionals; expanding on-line courses.
Classroom patients: implementing and distributing lays versions of recommendation; development of a patient partner program in research; webinars on actual items in the form of questions and answers (eg biosimilars).
Some of the items on this agenda can be organised within one year, for some others many years are foreseen; it will be a dynamic process. Ideas and support are very welcome via the EULAR Standing Committee on Education, or directly to the EULAR office, attention of the education program manager.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7108

SP0170 ASSESSING RHEUMATOLOGY SKILLS

C. Haines. *The Medical School, The University of Nottingham, Nottingham, United Kingdom*

Medical Education is making great advances in understanding the power of assessment. Modern learners seek frequent, faster feedback on their learning to study more effectively. It is now common for examinations to be statistically monitored in order to show that acceptable levels of reliability have been reached. But, a test is only as good as its questions. Clinicians are not often trained in how to create valid and reliable test questions. This session will describe some basic principles for creating valid and reliable tests for the knowledge, skills and attitudes which are required by practising rheumatologists. The speaker is currently the Eular Educationalist, who advises Eular on how to continually enhance assessment processes for the online courses and the new trainee examination.
As a result of the session participants will be better able to:
- Describe how face validity and reliability apply to Eular assessments
- Describe the differences between formative assessment for learning and summative assessment for grading
- Identify improvements which they could make to test questions
- Identify improvements which they could make to tests

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7202

SP0171 HOW TO SELECT THE MOST APPROPRIATE CAPILLAROSCOPIC DEVICE: PROS AND CONS

F. Ingegnoli. *Dept. of Clinical Sciences and Community Health, Università degli Studi di Milano, ASST Gaetano Pini, MILANO, Italy*

Nailfold capillaroscopy is a simple noninvasive imaging technique mainly used to observe capillaries within the first few micrometers from the skin surface. After application of a drop of immersion oil, capillaries can be observed with a magnification lens because they run parallel to the epidermis at the nail bed area. The study of the morphology of superficial nailfold capillaries provides clinically

relevant information in the management of patients with scleroderma-spectrum diseases.
Recently, an international survey on non-invasive techniques to assess the microcirculation performed under the aegis of members of the European League Against Rheumatism (EULAR) Study Group on Microcirculation in Rheumatic diseases (SG_MC/RD) showed that nailfold capillaroscopy was the one most used technique in both clinical and research settings by adult physicians and paediatric rheumatologists to assess patients with Raynaud's phenomenon.
A number of different instruments are available to perform the exam. They have different characteristics in terms of their cost, quality of images, magnifications, training period, portability, software for image analysis and storage.
Some of these instruments can be used both in clinical and research settings such as the stereomicroscope and the videocapillaroscope. The stereomicroscope allows the widefield visualization of the nailfold with low magnifications, the training is relatively short, but the examination is difficult to perform in patients with digital flexion contractures.
There appears to be consensus regarding the use of videocapillaroscopy that allows a detailed visualisation of capillary morphology using higher magnifications (100–300x). Contact probe with polarized light microscopy permits easier observation of the skin surface, and the training period is briefer. Specific softwares are available for images analysis, storage, and complete medical reports (text + images) can be produced.
By contrast, in a clinical setting, nailfold capillaries can generally be visualised using more simple but also efficient tools such as a dermatoscope, USB microscope, ophtamloscope or smartphone device. The quality of images can be quite good, although the lower magnification means that some details are unlikely to be seen, and they often lack the possibility of image storage and measurement. In particular, the dermatoscope with magnification of the order of x10 is a small, inexpensive and easily portable piece of equipment that has been suggested to be comparable to videocapillaroscopy in routine clinical practice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3247

SATURDAY, 17 JUNE 2017

Workshop: strengthening your organisation - how to manage volunteers

SP0172 MANAGING VOLUNTEERS- A UK PERSPECTIVE

C.B. Jacklin. *External Affairs, National Rheumatoid Arthritis Society, Maidenhead, United Kingdom*

Volunteers are an integral part of any charity and it would be impossible to run a charitable organisation without the support of volunteers. Like paid staff they need to be trained, nurtured and rewarded but as volunteers they need to be handled in a very different way to employees.
People who volunteer do so for many differernt reasons and not always perhaps for the right reasons so managing volunteers takes great skill and diplomacy.
My talk will cover how to value volunteers, lessons we have learned from managing volunteers over many years as well as how to manage issues with volunteers and the lessons I've learned from my mistakes!
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7227

SP0173 THE CHALLENGES OF A SMALL ORGANIZATION

M. Kosanovic. *Association of Rheumatic Diseases Patients of the Republic of Serbia (ORS), Belgrade, Serbia*

When a group of citizens establishes a non-profit and a non-government organisation in our country, those volunteers are carried by great enthusiasm. At the beginning when founding an NGO the main problems are lack of experience and financial resources. Those deficiencies can be overcome by some other qualities such as the personal competencies of volunteers.
As NGOs are seen by the public rather critically in our country, our organization had to face several additional challenges. In my presentation I will illustrate the following aspects: the non-attractiveness of NGOs for volunteers, the lack of awareness how volunteering is important for a society, the lack of knowledge how to attract volunteers and how to manage them, the lack of knowledge how to define the volunteers' positions and how to monitor their work, the lack of their systemic, continuing education and the lack of rewards, recognition and appreciation to acknowledge the most dedicated volunteers.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7187

SP0174 WAYS OF SUPPORTING VOLUNTEERS

S. Ssymank. *Rheuma-Liga Baden-Württemberg E.V., 76646 Bruchsal, Germany*

The promotion of volunteer workers is an indispensable part of the human resources policy of self-help organizations and requires specific concepts. Using the example of the rheumatism league Baden-Württemberg -an organization with 65,000 members, 3,000 volunteers and 10 fulltime employees- there will be shown best- practice examples.
A successful concept covers the areas of recruitment, training, support and integration.
The support of volunteers should include four key areas:
1. Transfer of knowledge and professional competences
2. Individual support for personal development
3. Promotion of teamwork and social skills
4. Framework conditions (insurance cover, reimbursement of expenses)

The implementation of these requirements should be carried out by specifically trained volunteer managers on the basis of a strong and motivating personal relationship.
This strategy can be seen as a precondition for establishing a long-term relationship of the volunteer with the association, a successful local work, satisfied members and volunteers who perceive their work as satisfying and fulfilling.
Silke Ssymank
Deputy managing director
Rheumatism League Baden-Württemberg e.V., Germany
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7084

SATURDAY, 17 JUNE 2017

WIN & HOT session

SP0175 WHAT IS NEW IN JUVENILE IDIOPATHIC ARTHRITIS

N.M. Wulffraat. *Dept. of Paediatrics, University Medical Center Utrecht, Dept. Pediatric Rheumatology, Utrecht, Netherlands*

Juvenile Idiopathic Arthritis comprises 7 subcategories. As the insights in pathogenesis progress so does the need for reclassification that is based more on biology than on clinical phenotypes. After a series of clinical trials for new biologicals, now trials are started that test specific treatment strategies such as treat to target an d step down studies. Especially rapid induction of remission is currently a major aim, followed by biomarked guided tapering of medication.
The expending number of potential biomarkers forms the basis for the creation of personalized medicin, a strategy aimed at providing individualized medication choices. Since most pediatric rheumatic conditions are rare, international collaboration is vital. The recently created European Reference Networks (ERN) will prove instrumental here.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7281

SATURDAY, 17 JUNE 2017

Systemic sclerosis

SP0176 TARGETING VASCULOPATHY FROM THE BEGINNING

M. Cutolo on behalf of EULAR Study Group on Microcirculation in Rheumatic Diseases. *Internal Medicine, Research Lab Division Rheumatology University of Genova, genova, Italy*

In systemic sclerosis (SSc), the natural history of microvascular damage progresses from capillary dilation to capillary loss and reactive angiogenesis, as detectable by nailfold videocapillaroscopy (NVC) [1]. The process is systemic and determines multiple clinical manifestations, from the early appearance of Raynaud's phenomenon, trough formation of digital ulcers (DUs), until severe organ involvement, impairing patient's quality of life or leading to main death causes, including interstitial lung disease and pulmonary arterial hypertension (PAH), hearth involvement, scleroderma renal crisis [2,3]. Although microvascular and macrovascular abnormalities frequently coexist in disease such as diabetes mellitus and other vascular diseases, the possible association between microvascular failure and macrovasculopathy in SSc patients has not been deeply investigated. However, significant correlations seem to exist between increased Intima-Media Thickness (IMT) of periferic small-caliber arteries (macrocirculation) and altered peripheral BP (LASCA) at the level of hand microvessels (microcirculation) in SSc patients.
SiIn addition, sgnificant capillary loss, observed at NVC, is peculiar of the "Late" scleroderma pattern of microangiopathy and is mainly preceded by progressive capillary enlargement, microhemorrhages and their collapse, leeding to presence of large avascular areas [4]. The importance of capillary loss was already demonstrated by a simple and reliable prognostic index, capable to predict digital trophic lesion development in SSc-related microvascular disease, when evaluated as part of the semi-quantitative NVC scoring [5]. Moreover, microvascular function and its alterations in SSc, can be reliably assessed by laser-doppler flowmetry (LDF) and laser speckled contrast analysis (LASCA), evaluating blood perfusion at fingertips or at larger body areas [6–9].
The most frequently used drugs for treatment of complications in SSc patients, approved with evidence grade Ia, are vasoactive drugs. In particular, for severe

RP and for prevention of DUs onset and treatment of PAH, both intravenous prostanoid iloprost (ILO), and the dual endothelin-1 receptor antagonist (ERA) BOSE are used, respectively [10]. Bosentan seems to block pathogenic activities of Endothelin-1, the endothelial derived mediator determining both vasoconstriction and also the fibrosis genes induction [11–14].
Previous long-term follow up studies, showed that treatment with BOSE in combination with ILO interferes with progression of nailfold microvascular damage, evaluated through both capillary number semi-quantitative scoring at NVC and fingertip blood perfusion (FBP) at LDF [15,16].
In particular, an open label, prospective study of 4 follow up years showed that long-term treatment with BOSE added to ILO infusions administered quarterly in SSc patients, exerts a remodelling effect on structural and functional microvascular alterations and on stabilization of lung function, compared to ILO mono-therapy [17].

References:
[1] Cutolo M et al. Nature Rev Rheumatol 2010;6:578–87.
[2] Berezne A et al. Arthritis Care Res 2011;63:277–85.
[3] Wigley FM. Clin Rev Allergy Immunol. 2009;36:150–75.
[4] Cutolo M et al. J Rheumatol. 2000;27:155–60.
[5] Smith V et al. Ann Rheum Dis. 2011;70:180–3
[6] Cutolo M, et al. J Rheumatol 2010;37:1174–80.
[7] Ruaro B et al. Ann Rheum Dis 2014;73:1181–5.
[8] Sulli A et al. Ann Rheum Dis, 2014;73:2059–61.
[9] Lambrecht V, et al. Ann Rheum Dis. 2016 pii: annrheumdis-2015–208857.
[10] Kowal-Bielecka O, et al. Ann Rheum Dis, 2009;68:620–628.
[11] Herrick AL. urr Opin Rheumatol 2011;23:555–61.
[12] Abraham D et al. Arthritis Res Ther. 2007;9 Suppl 2:S2.
[13] Sulli A et al. J Rheumatol. 2009;36:1235–9.
[14] Maurizio CutoloJ Rheumatol 2015;42;456–463.
[15] M Cutolo et al. J Rheumatol. 2013;40:40–5.
[16] M Cutolo et al. J Rheumatol 2014;41;881–886.
[17] Trombetta et al. J Rheumatol. 2016;43:2033–41.

Disclosure of Interest: M. Cutolo Grant/research support from: actelion, italfarmaco
DOI: 10.1136/annrheumdis-2017-eular.7302

SP0177 NEW APPROACHES BY TARGETING SOLUBLE MEDIATORS

C.P. Denton. *Centre for Rheumatology, Royal Free Hospital and Ucl Medical School, London, United Kingdom*

Although the aetiopathogenesis of systemic sclerosis (SSc) remains incompletely understood there is now sufficient knowledge about the pathobiology of the disease and mechanisms underlying development of fibrosis, autoimmunity and vasculopathy to permit informed selection of candidate soluble mediators that may be important drivers of the disease. This has permitted testing of potential targeting approaches in preclinical models and in vitro tissue culture systems. The data from these studies has informed understanding of the disease and has started to be translated into clinical trials that test hypotheses in vivo in patients. This approach has in turn fueled the concepts of reverse translation that are being applied to further understand SSc mechanisms in model systems and observational cohort studies. Soluble mediators that have emerged as strong targets for therapeutic intervention include TGFbeta superfamily members, connective tissue growth factor, IL13, IL4 and IL6. Studies of agents that target these proteins have been proposed or undertaken. Targeting TGF-beta appears to have benefit for skin thickening and attenuate some of the characteristic TGF-beta regulated genes and proteins in skin. However, the most encouraging data have emerged from targeting the IL6 axis using anti-IL6R neutralizing antibodies. This approach was promising in a Phase II study and further trials are ongoing. Interestingly this approach appears to attenuate macrophage gene expression signatures in the skin, may prevent worsening of lung fibrosis and showed significant benefit in the skin by biomarker analysis and a strong trend of benefit over 48 weeks for skin sclerosis score. Other small clinical trials testing TNF-alpha blockade have been more disappointing. Finally, it is possible that soluble mediators may be identified that directly attenuate the fibroproliferative mechanism of SSc. Experimental studies have suggested that increasing alpha-MSH may have benefit for skin fibrosis in a small controlled clinical trial. Clinical trial design is critical to the success and interpretation of studies targeting soluble mediators to define target engagement, mechanism of action, and possible clinical benefit. Advances in trial design are facilitating progress and it seems likely that, as in other rheumatic diseases, targeting key soluble mediators will become a therapeutic reality of the next few years. Defining the place of such approaches compared to other emerging treatment strategies will remain challenging.

Disclosure of Interest: C. Denton Grant/research support from: Inventiva, CSL Behring, GSK, Bayer, Consultant for: GSK, Actelion, Inventiva, Roche
DOI: 10.1136/annrheumdis-2017-eular.2533

SATURDAY, 17 JUNE 2017

How diet influences musculoskeletal diseases

SP0178 GUT DYSBIOSIS AND OTHER CHALLENGES PRECIPITATE ARTHRITIS

C. Mackay. *Biodiscovery Research Institute, Monash University, Clayton, Australia*

Environmental factors contribute to development of autoimmune diseases. For instance, human autoimmune arthritis can associate with intestinal inflammation, cigarette smoking, periodontal disease, and various infections. The cellular and molecular pathways whereby such remote challenges might precipitate arthritis or flares remain unclear. We have defined many of the pathways in the gut that contribute to homeostasis, particularly GPCRs such as GPR43 and their ligands the short chain fatty acids. Such receptors and their ligands are anti-inflammatory. To probe peripheral inflammation connections to arthritis, we used a transfer model of self-reactive arthritis-inducing CD4 cells from KRNtg mice that, upon transfer, induce a very mild form of auto-inflammatory arthritis in recipient animals. This model enabled us to identify external factors that greatly aggravated disease, such as microbiota effects or disruption of gut homeostasis. We show that several distinct challenges precipitated full-blown arthritis, including intestinal inflammation through DSS-induced colitis, and bronchial stress through Influenza infection. Both triggers induced strong IL-17 expression primarily in self-reactive CD4 cells in lymph nodes draining the site of inflammation. Moreover, treatment of mice with IL-1b greatly exacerbated arthritis, while transfer of KRNtg CD4 cells lacking IL-1R significantly reduced disease and IL-17 expression. Thus, IL-1b enhances the autoaggressive potential of self-reactive CD4 cells, through increased Th17 differentiation, and this influences inflammatory events in the joints. We propose that diverse challenges that cause remote inflammation (lung infection, colitis, gut dysbiosis) result in IL-1b -driven Th17 differentiation, and this precipitates arthritis in genetically susceptible individuals. Thus the etiology of autoimmune inflammatory arthritis likely relates to diverse triggers that converge to a common pathway involving IL-1b production and Th17 cell distribution.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7301

SATURDAY, 17 JUNE 2017

Can targeting disease activity in hand osteoarthritis improve our treatment in the 21st century

SP0179 WHAT IS DISEASE ACTIVITY IN FINGER OA?

R. Wittoek. *Rheumatology, University Hospital Ghent, Gent, Belgium*

Osteoarthritis of the interphalangeal finger joints constitutes one of the most prevalent musculoskeletal diseases with variable clinical impact ranging from nearly asymptomatic to severe inflammatory pain in and around affected joints, presence of soft tissue and bony swelling, stiffness and gradual loss of function. Current therapeutic options are limited to analgesic treatment but research on targeted therapies is increasing.
In order to improve the current treatments, a critical appraisal of the needs for improvement in finger OA is needed and how disease activity is best defined.
Assessing disease activity or joint activity in finger OA is challenging: disease activity can comprise pain, inflammatory activity and structural damage.
In clinical practice, a combination of patient-reported (e.g. visual analogue scale or Likert scale pain), more objective and performance-based measures (e.g. grip strength) are used to assess and follow disease activity. In clinical research, pharmacological trials and epidemiological studies, a standardized approach to assess the disease activity is necessary to estimate the burden of disease and to evaluate the efficacy of potential new treatments. The instruments being used, depend mostly on the aim of the study or research question. In case structural disease progression is being studied, imaging-based outcome measures are mostly used. Structural changes can be assessed on joint level or on patient level, both by conventional radiographs, ultrasound and magnetic resonance imaging. Several imaging based outcome measures and scoring systems are being suggested but true consensus about the instruments of preference is still lacking. Therefore, further validation of these instruments is warranted.
This lecture will give an overview of the current instruments to measure activity in finger OA in several domains and discuss its strengths and limitations.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7071

SP0180 BIOLOGICS AND OTHER INFLAMMATORY THERAPIES IN FINGER OA. WHAT HAVE WE LEARNED?

X. Chevalier. *Dept. of Rheumatology, University Paris XII, UPEC, Créteil, France*

Hand osteoarthritis (HOA) is the most frequent form of osteoarthritis. A subset of digital hand OA is marked by an “inflammatory” like presentation with painful interphalangeal joints, refractory to NSAIDS and analgesics.

This clinical form of OA may be associated with a so called "erosive" radiographic aspect marked by subchondral erosions of the finger joints and ankylosis. Many mediators of inflammation have been involved in the pathogenesis of osteoarthritis such as prostaglandin E2, free radicals and main cytokines (IL1B, IL6, and TNFa). Using Doppler power ultrasonography and magnetic resonance imaging, it has been shown that synovitis is frequently associated with HOA and correlates with pain and with disease progression.
Taking all those considerations together, it appears logical to target synovitis in HOA, especially with an erosive form.
Because erosive hand OA is a polyarticular disease, the treatment is more systemic than local.
Local or oral NSAIDS are out of scope because this presentation focuses on patients with HOA non responders to analgesics and NSAIDS. So far, none of the disease modifying drugs such as methotrexate has proved its efficacy.
Regarding biologics, several strategies have been approached. The first biotherapy used in HOA was IL2 receptor plus hydroxychloroquine in a very limited number of patients. Then and more recently, anti-TNFa strategy has been tested in well done RCT, in painful hand OA: one with adalimumab over a year, one with adalimumab 40 mg with 2 sub-cutaneous injections, one using Etanercept (50 mg/week 24 weeks and then 25 mg/week the next 24 weeks). None of those anti-TNFa blockers demonstrated a structural or an analgesic effect. However in the long term trial published by Verbruggen G, the incidence of new erosive lesions was decreased in Adalimumab group compared to placebo, only in a subgroup of patient with clinically inflamed IP joints.
Using anti-IL1B strategy, a decrease in pain has been observed in 3 patients using daily subcutaneous injection of Anakinra (100mg) over 3 months ( ).
In this Eular meeting a double inhibition of IL-1 Beta and IL-1 Alpha (using a monoclonal antibody directed against both cytokine) failed to demonstrate any benefit compared to placebo injection over 26 weeks.
Finally anti-IL6 strategy has been presented in this 2017 Eular meeting in a limited number of patients (n=18) with erosive HOA. Using monthly IV perfusion, the authors showed an improvement in pain level and functional status.
Conclusion: though anti-inflammatory strategy in painful HOA is logical, no treatment so far has been able to demonstrate a beneficial effect. Further studies should contemplate either news targets, or new modalities of repeated injections and should be adapted according to the phenotype of pain.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7304

SATURDAY, 17 JUNE 2017

Why we do develop autoimmunity

SP0181 FAILURE OF NATURAL REGULATORY AUTOANTIBODY NETWORK AS CAUSE OF AUTOIMUNITY

O.C. Marques on behalf of Lubeck University. Prof. Riemekasten. *Reumathology, University of Lübeck, 23562 Lübeck, Germany*

The role of autoantibodies in normal physiology is under debate. In investigating autoantibody (aab) concentrations against G protein-coupled receptors (GPCR) in different autoimmune diseases, we found both increased and decreased aab concentrations, which suggests physiological anti-GPCR aab levels may be dysregulated in autoimmune diseases. During our analysis of healthy donor antibodies to 16 GPCR and 15 growth factors and related signaling molecules, we discovered several clusters of correlations in these antibody concentrations. Possible functional interactions of these 31 autoantibody target molecules were studied by STRING, DAVID, and enriched Gene Ontology analyses. Through these analyses, a network of GPCR, growth factors, and signaling molecules with endothelin receptor type A (ETAR) in the center was revealed. Migration and locomotion were suggested to be the most significant functions regulated by the antibody network. Accordingly, IgG from healthy donors induced both IL-8 expression by peripheral blood mononuclear cells (PBMCs) as well as migration of neutrophils and tumor cells, which was specifically diminished by the ETAR inhibition. These data supports a change of paradigm from the notion that autoantibodies are an exclusive autoimmune phenomenon to the concept that they are part of the normal human physiology, which become dysregulated under the influence of different factors and subsequently cause autoimmune diseases.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2218

SP0182 ALTERATIONS IN THE ANTIBODY REPERTOIRE AND SUGAR MODULATION AS CAUSE FOR AUTOIMMUNITY

H.U. Scherer. *Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

Many auto-immune diseases are hallmarked by the presence of auto-reactive B cells that can develop into autoantibody-secreting plasma cells. In most cases, the secreted autoantibodies have extensively been studied in their role as disease-associated biomarkers, and for some, specific pathogenic effector functions have been demonstrated supporting the use of interventions that target the plasma cell compartment. In other cases such as rheumatoid arthritis (RA), however, the pathogenicity of specific autoantibodies is less clear, and the therapeutic efficacy of B cell depleting therapy that spares the plasma cell compartment indicates that auto-reactive B cells themselves can have pathogenic effector functions that contribute to disease. In this context, it is of great interest to understand the mechanisms that allow auto-reactive B cells to emerge from the naïve repertoire, a process that marks the onset of systemic autoimmunity and frequently precedes the clinical onset of disease.
RA is characterized by a remarkable appearance of autoantibodies that target post-translational modifications of proteins, of which anti-citrullinated protein antibodies (ACPA) display the highest specificity for disease. In addition, ACPA associate with active destructive RA and pose individuals with arthralgia at-risk for progression towards arthritis. We recently found that ACPA display significant alterations with regard to the glycosylation of both the Fc-tail as well as the F(ab)-domain. While the ACPA-IgG Fc-tail loses galactose and sialic acid residues prior to the onset of arthritis, a process associated with enhanced inflammatory antibody activity that occurs potentially under the influence of IL-17 producing T cells, ACPA also carry abundant glycans in the antigen-binding region of the F(ab) domain. These latter glycans are reminiscent of F(ab)-glycans found in follicular lymphoma B cells, and were here identified as N-linked, biantennary glycans composed of a remarkably high frequency of sialic acid residues. Notably, N-glycosylation requires the presence of glycosylation consensus sequences in the protein. As such sequences are normally scarce in the germline encoded variable regions of B cell receptors (BCR), the acquisition of F(ab)-glycans requires mutations of the amino-acid sequence to generate N-glycosylation sites. This process is mediated by somatic hypermutation, which is mainly induced by T cells that provide help to B cells. As >90% of all ACPA-IgG molecules carry such F(ab)-linked N-glycans, and as protective antibodies in the same individuals and many autoantibodies in other diseases do not show this feature, it is conceivable that the acquisition of F(ab)-glycans by ACPA-IgG is a T cell –mediated process that provides a selective advantage to ACPA-expressing B cells. This notion is supported by the observation that additional F(ab)-glycans are not found on ACPA-IgM. How F(ab)-glycans facilitate the emergence and/or expansion of auto-reactive B cells in this context, however, remains unclear. Using recently developed technology to identify and isolate citrullinated antigen-specific B cells from patients, we can now address this question by studying the frequency and localisation of N-glycosylation sites in the antibody repertoire and by studying the phenotype and functional characteristics of ACPA-expressing B cells. Together with our investigations on the modulation of ACPA Fc-glycans, these studies provide a deeper understanding of mechanisms that allow the development of autoimmunity as such, and of the mechanisms that underlie the progression from systemic autoimmunity towards overt autoimmune disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7179

SP0183 FAILURE OF TREG CONTROL TO UNDERSTAND AUTOIMMUNITY

J.Y. Humrich. *Department of Rheumatology and Clinical Immunology, University Hospital Schleswig-Holstein, Campus Lübeck, Lübeck, Germany*

Regulatory T cells (Treg) expressing the transcription factor FoxP3 are crucial for the maintenance of immunological tolerance to self and thus for the control of autoimmunity. There is strong evidence that numeric or functional defects in Treg cell biology are involved in the pathogenesis of particular autoimmune diseases. Here we will focus on the fundamental role of Treg cells in diverse autoimmune and rheumatic diseases and will explain how a failure of the Treg cell system can evolve and contribute to the development of such diseases. Furthermore, therapeutic approaches aiming to overcome these Treg cell defects and to restore Treg cell activity in the patients will be discussed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7306

SP0184 ROLE OF MICROENVIRONMENT AND ENDOGENOUS PATHWAYS TO BREAK TOLERANCE

P. Lamprecht. *Universität Zu Lübeck, Lübeck, Germany*

Break of tolerance driving autoimmune disease is initiated by a combination of predisposing genetic and environmental factors resulting in self-perpetuating chronic inflammation and tissue damage. Effector molecules and cells targeting tissues housing the inciting autoantigen(s) maintain tissue damage and the autoimmune response. Granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis) is a prototypical autoimmune disease characterized by extravascular necrotizing granulomatous inflammation and a systemic autoimmune vasculitis associated with anti-neutrophil cytoplasmic autoantibodies specific for the neutrophil- and monocyte-derived serine-protease proteinase 3 (PR3-ANCA). GPA is strongly associated with *HLA-DPB1*0401* polymorphisms. Its association with the *R620W* variant of the *PTPN22* gene has been linked to reduced immune-regulatory interleukin (IL)-10 transcription. Epidemiological studies and molecular analysis of immune cells suggests a multifactorial pathogenesis of GPA, in which a potentially metachronous and individually varying sequence of infectious agents contributes to the break of tolerance and chronic inflammation sustaining autoimmunity in GPA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6407

SATURDAY, 17 JUNE 2017

Closing the gap between objective measures and self-report in fibromyalgia

SP0185 DIVERGENCES BETWEEN OBJECTIVE AND SELF-REPORTED PHYSICAL FUNCTION IN FIBROMYALGIA

M. Henriksen. *Parker Instituttet Frederiksberg Hospital, Copenhagen, Denmark*

In fibromyalgia (FM), intolerance to physical activity, with increased pain and experience of early muscle fatigue, is a predominant feature. Furthermore, shorter endurance times and higher perceived effort during physical activity compared with healthy controls are characteristic. However, there are discrepancies between physical functioning as perceived by the patients and as measured objectively or during performance tests. For example, in 840 FM patients and 122 healthy controls, we found reduced muscle strength in approximately 50% of the FM patients. However, the patients with subnormal muscle strength did not self-report worse symptoms or more physical disablement than those with normal muscle strength. Much like central sensitization of pain, it has been suggested that impaired sensory-motor interaction is present in FM, which may be a cause for observed discrepancies between perceived and objective signs of muscle fatigue. That is, the sensory inputs to the central nervous system during a physical activity are over-interpreted, leading to amplified sensations of fatigue and discomfort normally associated with exhausting muscle work.
To illuminate this we conducted a controlled experiment, in which FM patients and health controls completed a muscle exhaustion test, while objective measures of muscle fatigue were collected by electromyography in parallel with reporting of perceived muscle fatigue. The results suggest that among FM patients, central nervous system processes normally associated with muscular fatigue were present, yet without any evidence of peripheral muscle fatigue. The study supports a hypothesis about abnormal sensory-motor interaction among FM patients that can explain the discrepancies between perceived and observed physical disability in FM.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7148

SP0186 COGNITIVE FOG: SUBJECTIVE AND OBJECTIVE UNDERSTANDINGS OF THE SYMPTOM OF DYSCOGNITION

B. Walitt. *National Institute of Nursing Research, National Institutes of Health, Bethesda, United States*

Dyscognition refers to the complaint that a person's ability to perform thinking tasks is impaired. This complaint is colloquially known as "brain fog". It is a major symptom of a variety of disorders and associated with considerable work and social disability for those experiencing it. However, attempts to demonstrate objective cognitive impairment in persons reporting "brain fog" have not been straightforward. In this lecture, the symptom of cognitive dysfunction will be described from the patient's point of view, using fibromyalgia as a disease model. The cognitive tests used to determine objective alterations in cognitive ability will be reviewed, the amount of objective impairment demonstrated in fibromyalgia will be placed into clinical context, and the "disconnect" between what the experience of dyscognition is and the cognitive content measured by modern testing will be discussed. The poor relationship between the magnitude of subjective dyscognition and objective cognitive performance will be examined, including evidence gleaned from neurological imaging studies. In conclusion, the experience of cognitive fog is not well captured by current testing paradigms. Subjective complaint is a poor predictor of objective cognitive performance. The neuronal mechanisms responsible for the experience of cognitive fog may be separate from those required to perform cognitive tasks.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7215

SP0187 ASSOCIATIONS OF PAIN-RELATED COGNITIONS WITH THE DISCORDANCE BETWEEN SUBJECTIVE AND OBJECTIVE PHYSICAL FUNCTION IN FIBROMYALGIA: THE AL-ÁNDALUS PROJECT

F. Estévez-López[1,2]. *[1]Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Granada, Spain; [2]Department of Psychology, Faculty of Social and Behavioural Sciences, Utrecht University, Utrecht, Netherlands*

Background: In fibromyalgia, there is a disagreement between patients' self-reports and performances; i.e., subjective and objective status, respectively.
Objectives: First, to test the discordance between subjective and objective measures of physical function. Second, to determine whether catastrophizing and self-efficacy are independently associated with this discordance.
Methods: Four hundred and five fibromyalgia females and 193 age-matched female controls. Participants filled out the Pain Catastrophizing Scale, Chronic Pain Self-efficacy Scale, and physical functioning subscales of the Revised Fibromyalgia Impact Questionnaire (FIQR) and Short Form-36 (SF-36) health survey. Objective physical function was measured with a battery of performance-based tests (e.g., 6-min walk test). Subjective and objective physical function were expressed as deviation from the general population in standard deviation (*SD*) units using means and *SD* of the control group.
Results: Fibromyalgia participants reported a worse physical function than performed ($p<.001$). We found a consistent association of higher catastrophizing with greater discordance between subjective and objective physical function. A significant association of higher self-efficacy with lower discordance was only found when subjective physical function was reported on the SF-36 but not on the FIQR.
Conclusions: Although both are markedly impaired, subjective physical function is more impaired than objective physical function in fibromyalgia. Catastrophizing is associated with this discordance. In rehabilitation settings, physical function of fibromyalgia females should be evaluated by both subjective and objective assessments to fully understand their physical function.
Acknowledgements: This work was supported by the Spanish Ministry of Economy and Competitiveness [I+D+i DEP2010–15639, I+D+i DEP2013–40908-R, and BES-2014–067612].
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7185

SP0188 THE DRUGS DON'T WORK

L. Piggott. *Fibromyalgia, Nantwich, United Kingdom*

This presentation will depict the journey of Louise, a previous school teacher and a single mother of two, living with Fibromyalgia as well as multiple other diagnoses. Louise will discuss her feelings around being diagnosed with Fibromyalgia, how this was communicated to her and what this meant for her career and family life. Following this, Louise will share her journey through the secondary care as a Fibromyalgia patient, and her own search for answers and cure to Fibromyalgia in an attempt to salvage her life and independence, prior to accepting that this is a long-term condition which will require self-management and perseverance. In addition, Louise will share her thoughts on pain and fatigue in Fibromyalgia, and how the "drugs don't work".
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7191

SATURDAY, 17 JUNE 2017

Interactive cases from the HOT and WIN sessions

SP0189 HOT SESSION: INTERACTIVE CLINICAL ASPECTS AND CASES ON VASCULITIS TREATMENT

R.A. Luqmani. *University of Oxford, Oxford, United Kingdom*

The systemic vasculitides are characterized by inflammation of blood vessels resulting in end organ, or tissue damage or necrosis. They are defined by the Chapel Hill nomenclature according to the calibre of the predominantly affected vessels. Other forms of vasculitis not defined by a predominant vessel size are also recognized (e.g. Behcet's syndrome). Large vessel vasculitides include giant cell arteritis and Takayasu arteritis; medium vessel vasculitides includes Kawasaki disease and PAN; small vessel vasculitides are divided into: immune complex small vessel vasculitis and anti-neutrophil cytoplasm antibody (ANCA) - associated vasculitis (AAV). The immune complex group, with moderate to marked vessel wall deposits of immunoglobulin and/or complement, is represented by anti-glomerular basement membrane disease, cryobulinaemic vasculitis, hypocomplementaemic urticarial vasculitis (anti-C1q vasculitis) and IgA vasculitis (Henoch–Schönlein). By contrast, AAV has few or no immune deposits and is associated with (in most cases) the presence of ANCA specific for myeloperoxidase (MPO-ANCA) or proteinase 3 (PR3-ANCA). Depending on their clinical presentation and ANCA specificity, AAV is divided into three major variants: granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) (Churg–Strauss syndrome). In some cases, vasculitis is relatively trivial and may lead to minor, often asymptomatic clinical features such as splinter haemorrhages. However, in severe forms of ANCA associated vasculitis, the consequences of rapid onset of ischaemia and occlusion of blood vessels can lead to organ failure and death.
The multisystem involvement in most forms of vasculitis can be a real challenge. Patients may present to different specialists resulting in diagnostic delay. The investigation of patients with suspected vasculitis should follow on from a careful history and examination to determine the likely diagnosis. The differential diagnosis is very wide. It is important to correctly identify patients with vasculitis as early as possible, but it is also important to rule out more common causes. In acutely unwell patients, the differential diagnosis depends on the combination of clinical features. Vasculitides tend to involve multiple organ systems. In fact, the more organ systems affected, the more likely it is that the patient has vasculitis.

We will review some examples of cases with what might appear to be unusual clinical features which form a more consistent pattern. Initial treatment is generally straightforward, but the evaluation of patients during the course of their illness is often difficult due to variation in disease, as well as drug toxicity, damage and co-morbidity. We will discuss examples of patients where relapse is suspected but not always confirmed.
In this overview we will summarise current practice in vasculitis, illustrated by cases to provide a clinical context in which to interpret and implement evidence based management of vasculitis
Disclosure of Interest: R. Luqmani Grant/research support from: Arthritis Research UK, GSK, MRC, UCSF/OIF, Canadian Institutes of Health Research, The Vasculitis Foundation;, Consultant for: GSK, Medpace, MedImmune, Roche
DOI: 10.1136/annrheumdis-2017-eular.7152

SATURDAY, 17 JUNE 2017

Suffering in silence. Optimizing the management of psychological well-being for people with RMDs

SP0190 FACTS AND FIGURES: HOW MENTAL HEALTH CARE ADDRESSES THE PSYCHOLOGICAL BURDEN OF RMD'S IN EUROPE

E. Dures. *University of the West of England, BRISTOL, Bristol, United Kingdom*

It is recognised that patients have to make behaviour changes and psychological adjustments to address the impact of inflammatory arthritis on their lives. Challenges include fluctuating pain, fatigue and flares of disease activity, and emotional consequences. Meeting these challenges effectively requires patients to engage in medical management, role management, and emotional management. For some patients this can be a struggle, and the rheumatology team can be a valued source of support.
This session will examine patient perspectives on the psychological impact of inflammatory arthritis and the role of the rheumatology team in meeting the associated support needs. It will look at the relationship between psychological distress, well-being and self-management, and will highlight patients' views on the characteristics of patient-centred, collaborative care. It will look at factors that influence psychological impact, adaptation and self-management; present data from patients on ways in which well-being and self-management can be enhanced or diminished through clinical interactions with the rheumatology team; and will consider the implications for clinical practice, including the training needs of the rheumatology team.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7121

SATURDAY, 17 JUNE 2017

Showcasing the EULAR Online Course for Health Professionals

SP0191 PRINCIPLES OF NON-PHARMACOLOGICAL MANAGEMENT OF REGIONAL MUSCULOSKELETAL DISORDERS

P. Oesch. *Physiotherapy, Kliniken Valens, Valens, Switzerland*

The two main components of non-pharmacological management of regional musculoskeletal disorders are a thorough assessment followed by rehabilitative care.
Assessment includes a careful history, level of daily activities and participation, including occupation, rehabilitative care to date, possible presence of psychosocial problems, sports and hobbies. Special attention must be given to patient's expectations and personal objectives. A systemic enquiry is also important, as regional pain may be due to an underlying medical condition. Clinical examination consists of observation of posture, mobility, and whether there is evidence of wasting, asymmetry, deformity, or muscle imbalances. Palpation of soft tissue and bony structures follows to identify areas of tenderness, lumps, myofascial trigger points, tendon crepitus. Assessment of active and passive movements in all planes follows looking for specific restrictions. Examination is not restricted to the site of pain; as for example upper limb pain syndromes may be referred from the neck. In some patients further medical investigation is necessary when a thorough history, examination, and ultrasonography do not provide sufficient diagnostic information. This may involve blood tests, plain radiography, CT or MRI.
Rehabilitative care is a customized process, which aims to achieve an optimal functional outcome and participation in all aspects of life. Active rehabilitation and a gradual return to normal activities are key points in successful treatment of regional pain syndromes. Progressive exercise is a fundamental part of the treatment of most regional musculoskeletal complaints. The goal is to work towards full, specific, pain free functional activity. In myofascial pain syndromes and non specific arm pain in particular, there is a need for review of postural issues and ergonomics and building aerobic fitness. In addition, providing information to the patient about the nature of the condition, beneficial and negative habits and activities, self help exercises, expected response to treatment and outcome should all be part of the approach to these patients. Psychological interventions may complement rehabilitative care. Cognitive and behavioral methods focus on changing the patient's interpretation and reaction to pain. The main assumption of a behavioral approach is that pain and pain disability are influenced by somatic pathology and also by psychosocial factors (eg, patient's attitudes and beliefs, psychological distress and illness behavior). Consequently, the behavioral treatment of regional musculoskeletal disorders does not primarily focus on removing an underlying organic pathology, but on the reduction of disability through modification of environmental contingencies and cognitive processes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7137

SP0192 PRINCIPLES OF NON-PHARMACOLOGICAL MANAGEMENT OF RHEUMATIC DISEASES

T. Vliet Vlieland on behalf of Dr. Keegan Knittle, Professor Jo Adams and Dr. Mwidmi Ndosi. *Orthopaedics J11-R, Leiden University Medical Center, Leiden, Netherlands*

Background and aims: Rheumatic and musculoskeletal diseases (RMDs) have a major impact on patients' lives. Apart from symptoms such as pain, stiffness and fatigue, many patients may experience limitations in daily activities and participation in society. Rheumatology health professionals (HPs) play a pivotal role in the improvement and maintenance of patients' functioning, a crucial aspect of patients' quality of life. To ensure the quality of care, HPs need to be appropriately trained. For this purpose, one module of the EULAR online course for HPs is dedicated to HPs' interventions related to various RMDs.
Methods: Using the same methodology, expertise and technology used in other EULAR online courses, the following components of the module were developed: A Main Text, Interactive Clinical Cases, Indepth Discussions and two Assessment sets.
Results: First, 4 learning aims were formulated: After completing the module, the student a. Has an overview of interventions commonly provided by HPs in the treatment of patients with RMDs; b. Demonstrates appropriate understanding of opportunities and limitations of the various interventions employed by HPs on the individual patient level; c. Can properly advise and support patients regarding self-management strategies including e.g., appropriate medication usage, exercises, the application of joint protection and energy conservation, the usage of orthoses and adaptive equipment or other; and d. Can make a substantiated decision on when to refer a patient to another health professional, a physician or a multidisciplinary team. Second, a wide range of modalities, such as exercise therapy, self-management support, cognitive behavioural therapy, the provision of orthoses, assistive devices or physical modalities were described. These were further applied and/or explained by means of Interactive Clinical Cases and Indepth Discussions (Patient education and Physical Activity Interventions).
Conclusions: A module of the EULAR Online course for HPs specifically describes and explains HPs' interventions employed in the management of people with various RMDs. Its contents will be updated according to new clinical and scientific insights. Moreover, it will be adapted to the educational needs of HPs, by taking into account the comments of the students and perspectives from HPs across Europe.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7180

SP0193 PRINCIPLES OF NON-PHARMACOLOGICAL MANAGEMENT OF FIBROMYALGIA

J.E. Vriezekolk. *Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands*

Having fibromyalgia greatly impacts person's mental and physical wellbeing, his activities of daily living, and the society at large. Despite scientific progress to unravel the aetiology of fibromyalgia syndrome, no cure is yet available. The management of fibromyalgia comprises both pharmacological and non-pharmacological treatment option to alleviate the symptom burden of the disease. The recently published EULAR revised recommendations for the management of fibromyalgia[1], proposes that the management of fibromyalgia should take the form of a graduated approach with the aim of improving health-related quality of life. It should focus first on non-pharmacological treatment, including education, self-management and physical therapy with graded physical exercises. In this talk a brief overview of the current evidence regarding non-pharmacological care in fibromyalgia will be given. The importance of patients' self-management, (tailored) interventions to support self-management, and its dissemination and implementation in clinical practice will be highlighted.
References:
[1] Macfarlane GJ, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis 2017;76:318–328.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7163

SP0194 **PRINCIPLES OF ASSESSMENT IN CLINICAL PRACTICE**

R. Hilfiker. *Physiotherapy, HES-SO Valais-Wallis, Leukerbad, Switzerland*

In clinical practice, assessment is important for the selection of intervention strategies, goal setting, prognosis and the evaluation of the progression made towards the treatment goals. For example, we need to assess the patients' perceptions on how the disease, functioning and disability interferes with their life situation. Furthermore, we should assess how they can cope with stressful events, what social support they experience and how they adjust to living with a chronic disease. The assessment should provide information on problems, needs and priorities of the patients, as well as on strengths and resources. Based on the initial assessment, mutually agreed treatment goals and treatment strategies can be defined together with the patients.

We need to be aware of the differences, strengths and weaknesses of observations (e.g. Barthel Index), measures (walking speed) and self-reported questionnaires (patient-reported outcomes) or individualised, patient specific measures (e.g. the Patient-Specific Functional Scale).

In most situations, it is recommended to combine generic and specific measures to cover general as well as specific issues of health, functioning and disability or contextual factors. This will also allow the comparison across groups of patients.

Each tool used in the assessment should serve a clear objective and should be able to achieve this objective in the given situation. We need to know the relevant measurement properties on reproducibility and validity for the instrument in a given situation. The agreement or the measurement error will tell us, for example, how small a change can be to be detected (i.e. smallest detectable change). This is important when we want to monitor change (evaluation). Reliability indices will tell us how good we can distinguish groups of patients and whether we can use an instrument in a group setting (i.e. in a study; the ICC should be at least 0.7) or for the use with individuals in clinical practice (ICC should be at least 0.9).

We can distinguish three types of validity, content validity, construct validity and criterion validity. The content validity informs on how good a tool covers all relevant aspects of the construct to be measured and whether all items cover relevant aspects. An instrument has a good criterion validity if its results are similar to a so-called gold standard (instrument that is known to be valid). The construct validity tells us whether the scores of the measurement instrument are associated with instruments that measure a similar construct and are not associated with scores from instruments that measure non-related concepts.

Other important aspects are responsiveness and interpretability. Responsiveness is the ability of an instrument to detect change over time in the construct to be measured. Interpretability means that the scores are understandable and meaningful. Aspects of interpretability are floor and ceiling effects, and whether the smallest detectable change and the minimal important change are known.

Of course, the application of an instrument has to be feasible. Therefore, there is often a trade-off between measurement properties and feasibility, i.e. the perfectly reliable and valid instrument might be too expensive or too time consuming. Therefore, a less "perfect" instrument might be chosen.

All the mentioned aspects need to be considered when defining an individual assessment strategy for a patient. The assessment and evaluation should be an integrated part of the treatment process. It verifies that the treatment is in line with the needs and priorities of the patients; the documentation of changes might motivate both patients and health professionals and it might increase adherence to the recommended treatments.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7226

SATURDAY, 17 JUNE 2017

HPR Highlight session

SP0195 **HIGHLIGHTS FROM THE HEALTH PROFESSIONAL SESSIONS**

R.J.O. Ferreira[1,2]. [1]*Health Sciences Research Unit: Nursing (UICiSA:E), Escola Superior de Enfermagem de Coimbra;* [2]*Rheumatology department, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal*

EULAR congress is one on the biggest events in the world of rheumatology. To accommodate all the diversity of topics, several sessions take place at same time, in different rooms. It is very hard, even impossible, to be in all sessions, poster tours, social meetings and other learning events of your interest. It often happens that one want to be at 3 or 4 places at same time.

This "Highlights" session is designed to summarize the most important conclusions of the talks given in all sessions from Health Professionals programme. By this way you can catch on what you missed to be in other places. Of course you can also read the abstracts in the EULAR app or Annals of Rheumatic Diseases Suplement or even to watch the podcasts after the event. However, this highlights session will provide you an integrated view of the different contents in a more appealing and interactive perspective.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7256

Scientific Abstracts

Oral Presentations

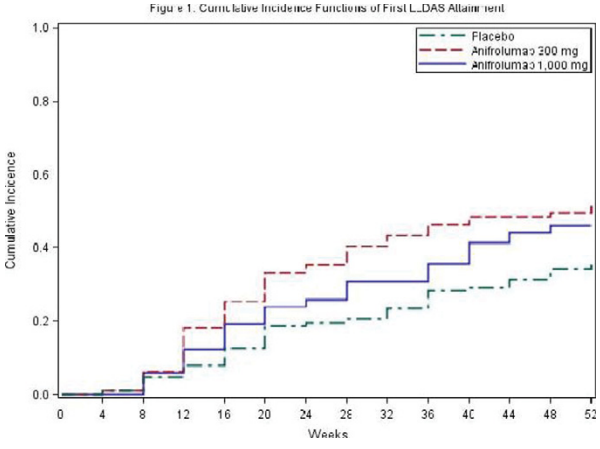
WEDNESDAY, 14 JUNE 2017

Moving towards new criteria in SLE, Sjögren's and APS

OP0001 THE LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) DEFINITION DISCRIMINATES RESPONDERS IN A SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) TRIAL: POST-HOC ANALYSIS OF THE PHASE IIB MUSE TRIAL OF ANIFROLUMAB

E. Morand[1], A. Berglind[2], T. Sheytanova[2], R. Tummala[3], G. Illei[4]. *[1]Monash University, Melbourne, Australia; [2]AstraZeneca, Mölndal, Sweden; [3]AstraZeneca; [4]MedImmune LLC, Gaithersburg, United States*

Background: A LLDAS definition has received preliminarily validation. Achieving low disease activity by this definition is associated with protection from damage accrual for patients (pts) with SLE.[1] However, it has not been evaluated as an endpoint in randomized controlled trials (RCTs).
Objectives: We evaluated LLDAS as an RCT endpoint in a *post-hoc* analysis of the MUSE trial of anifrolumab in pts with moderate to severe SLE.[2]
Methods: During the 52-week MUSE study, pts with active SLE received intravenous placebo, anifrolumab 300 mg, or 1,000 mg, in addition to standard of care, every 4 weeks for 48 weeks. LLDAS requires all of the following: SLEDAI–2K $\leq$4 without major organ activity, no new disease activity, PGA (0–3) $\leq$1, prednisolone $\leq$7.5 mg/day, and tolerance of standard immunosuppressant dosages.[1] LLDAS utility, its association with other endpoints, and discrimination between anifrolumab- and placebo-treated pts, were explored using descriptive statistics, logistic regression, and Gray's test. All randomized pts in MUSE were included in the analyses, and non-response imputation was performed after dropout.
Results: For pts receiving placebo (n=102), anifrolumab 300 mg (n=99), or anifrolumab 1,000 mg (n=104), LLDAS criteria were met at least once by 35%, 52%, and 46% of pts, respectively (odds ratio [OR] vs. placebo; 300 mg: 1.97, 95% CI 1.08, 3.58; p=0.027; 1,000 mg: 1.63, 95% CI 0.90, 2.95; p=0.103). Positive associations were observed between LLDAS and both the SLE Responder Index (SRI[4]) and BILAG-based Composite Lupus Assessment (BICLA), with 87% and 74% of pts attaining LLDAS at Week 52 also being SRI(4) and BICLA responders, respectively (χ^2=57.61 and 55.18; both $p<0.0001$). However, only 47% and 51% of SRI(4) and BICLA responders reached LLDAS. Increased LLDAS attainment from Week 12 (300 mg) or 28 (1,000 mg) was associated with anifrolumab treatment, compared with placebo (OR range; 300 mg: 1.7–3.6; 1,000 mg: 1.7–2.5). LLDAS was attained earlier (300 mg: χ^2=6.39, p=0.012; 1,000 mg: χ^2=2.44, p=0.119) in anifrolumab-treated pts (Figure 1). At Week 52, more anifrolumab-treated pts attained a LLDAS (OR vs. placebo; 300 mg: 3.41, 95% CI 1.73, 6.76, $p<0.001$; 1,000 mg: 2.03, 95% CI 1.01, 4.07, p=0.046). More anifrolumab-treated pts spent $\geq$50% of observed time in LLDAS (OR vs. placebo; 300 mg: 3.04, 95% CI 1.34, 6.92; p=0.008; 1,000 mg: 2.17, 95% CI 0.93, 5.03; p=0.072), and the OR of sustained LLDAS for at least six consecutive visits from Week 12 to 52 were 4.02 (95% CI 1.38, 11.73; p=0.011) (300 mg) and 2.95 (95% CI 0.99, 8.78; p=0.052) (1,000 mg).
Conclusions: LLDAS is associated with validated treatment response measures, SRI(4) and BICLA, but is more stringent than either. Anifrolumab was associated with $\leq$3.6-fold OR increases in LLDAS attainment, as well as greater aggregate and sustained time in LLDAS. This LLDAS definition should be considered as a study endpoint in SLE RCTs.



References:
[1] Franklyn K, et al. Ann Rheum Dis. 2015;75:1615–21.
[2] Furie R, et al. Arthritis Rheumatol. 2017;69:376–86.
Acknowledgements: Funded by MedImmune. Medical writing support: R Plant, QXV Comms, an Ashfield company, funded by MedImmune.
Disclosure of Interest: E. Morand Grant/research support from: Astra Zeneca, Janssen, UCB, BristoMyersSquibb, Consultant for: AstraZeneca, Pfizer, Merganser, Baxalta, BristoMyersSquibb, UCB, A. Berglind Shareholder of: AstraZeneca, Employee of: AstraZeneca, T. Sheytanova Employee of: AstraZeneca, R. Tummala Employee of: AstraZeneca, G. Illei Shareholder of: AstraZeneca, Employee of: MedImmune LLC
DOI: 10.1136/annrheumdis-2017-eular.2464

OP0002 MULTICRITERIA DECISION ANALYSIS FOR DEVELOPING NEW CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS

S. Tedeschi[1], S. Johnson[2], D. Boumpas[3], D. Daikh[4], B. Diamond[5], T. Dorner[6], S. Jacobsen[7], D. Kamen[8], W. McCune[9], M. Mosca[10], R. Ramsey-Goldman[11], G. Ruiz-Irastorza[12], M. Schneider[13], J. Smolen[14], M. Urowitz[2], D. Wofsy[4], M. Aringer[15], R. Naden[16], K. Costenbader[1]. *[1]Harvard Medical School, Boston, United States; [2]Univ. Toronto, Ontario, Canada; [3]Univ. Athens, Athens, Greece; [4]Univ. California, San Francisco; [5]Feinstein Institute, Manhasset, United States; [6]Charite Univ. Hospitals, Berlin, Germany; [7]Copenhagen Univ. Hospital, Copenhagen, Denmark; [8]Medical Univ. S. Carolina, Charleston; [9]Univ. Michigan, Ann Arbor, United States; [10]Univ. Pisa, Pisa, Italy; [11]Northwestern Univ., Chicago, United States; [12]Biocruces Institute, Barakaldo, Spain; [13]Univ. Dusseldorf, Dusseldorf, Germany; [14]Medical Univ. Vienna, Vienna, Austria; [15]Univ. Medical Center Carl Gustav Carus, Dresden, Germany; [16]McMaster Univ., Hamilton, Canada*

Background: EULAR and ACR are supporting multi-phase development of SLE classification criteria based on weighted criteria and a continuous probability scale. Prior steps included criteria generation, criteria reduction through Delphi and Nominal Group Technique exercises, literature review for sensitivity/specificity of candidate criteria, and organization of candidate criteria into seven clinical and three immunologic domains.
Objectives: To refine definitions of candidate criteria, determine relative weights using multicriteria decision analysis, and determine a threshold score for SLE classification.
Methods: An SLE Expert Panel (9 North American, 8 European) submitted 167 unique cases with a range of SLE probability. Experts scored 20 representative cases using the candidate criteria and rank-ordered them. In a 2-day meeting, experts reviewed inter-rater reliability of scoring, refined criteria definitions, and participated in a multicriteria decision analysis (MCDA) exercise using 1000Minds™ software. Experts were presented a series of decisions between two cases, each with different criteria from two domains (e.g. oral ulcers [cutaneous] and acute pericarditis [serositis] vs. alopecia [cutaneous] and pleural effusion [serositis]) and anonymously voted for the case more likely to be classified as SLE. Votes were discussed until consensus was reached for each decision. Using the consensus decisions, 1000Minds™ calculated criteria weights, assigned a total score to each of remaining 147 cases and rank-ordered the cases. Experts voted on whether each case should be classified as SLE. MCDA was repeated for criteria whose calculated weights were inconsistent with expert opinion until group consensus was achieved. 1000Minds™ then re-calculated criteria weights and re-ranked cases once. The score of the last case for which expert consensus was achieved was the threshold score.
Results: Inter-rater reliability was good; human data entry error, not following instructions, and differing interpretations of criteria definitions accounted for discrepancies. Arthritis and pericarditis definitions were modified through group discussion. The MCDA involved 74 pairwise decisions. Cranial neuropathy and Class VI lupus nephritis were removed as they added little to SLE classification. MCDA was repeated for the arthritis and cutaneous domains as initial weights did not match expert opinion. After criteria weights and scores were re-calculated once, experts reached consensus for SLE classification for case score $>$83.
Conclusions: Using an iterative process, the expert panel refined definitions, weighted candidate criteria and determined a threshold score of $>$83 for SLE classification, which will undergo validation.
Acknowledgements: Joint support from EULAR and ACR
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5464

WEDNESDAY, 14 JUNE 2017

Controlling the balance between cancer and autoimmunity

OP0003 RHEUMATIC IMMUNE RELATED ADVERSE EVENTS OF CHECKPOINT THERAPY FOR CANCER: CASE SERIES OF AN EMERGING NOSOLOGIC ENTITY

C. Calabrese[1], E. Kirchner[1], A. Kontzias[1], V. Velcheti[2], L. Calabrese[1].
[1]Rheumatologic and Immunologic Diseases; [2]Hematology and Oncology, Cleveland Clinic, Cleveland, United States

Background: Immune checkpoint therapy is a major advance in the field of oncology. Agents targeting CTLA-4, programmed cell death protein 1 (PD-1) and PD-ligand 1 have produced significant survival benefits in patients with malignancies. With these therapies have come a unique spectrum of adverse events related to over-activation of the immune system with resultant autoimmune disease. To date reports of rheumatic immune related AEs (irAEs) have not been adequately characterized, as they are infrequently reported in clinical trials. We describe the largest series of rheumatic irAEs secondary to checkpoint inhibitors to date.
Objectives: To report our 22 month experience with 19 patients evaluated in the Cleveland Clinic Rheumatology department.
Methods: A retrospective chart review was performed on 19 patients, 16 without pre-existing autoimmune disease (AID) and 3 with pre-existing AID, seen in our rheumatology department February 2015-December 2016. 2 designated rheumatologists evaluated all patients. Recorded information included gender, age, age at malignancy diagnosis, malignancy details, checkpoint inhibitor, nature of rheumatic irAE, time of onset, diagnostic data, treatment of irAE and response to treatment.
Results: In the group without pre-existing AID 56% developed a rheumatic irAE within 16 weeks of starting immunotherapy, with median time to onset of 14.5 weeks (table 1). Of the 3 patients with pre-existing AID, 1 experienced a disease flare after starting immunotherapy.
Conclusions: Rheumatic irAEs is a new field that will continue to grow. At this stage we have more questions than answers regarding their epidemiology, natural history and pathophysiology. Our findings reinforce that rheumatic irAEs are complex, at times require aggressive immunosuppression and can impact checkpoint inhibitor therapy for the underlying malignancy.
Disclosure of Interest: C. Calabrese: None declared, E. Kirchner: None declared, A. Kontzias: None declared, V. Velcheti Grant/research support from: Genentech, Bristol-Myers Squibb, Merck, Astra Zeneca, Genoptix, Consultant for: Genentech, Bristol-Myers Squibb, Merck, Astra Zeneca, Celgene, Genoptix, Foundation Medicine, L. Calabrese Consultant for: Bristol-Myers Squibb
DOI: 10.1136/annrheumdis-2017-eular.1628

OP0004 RHEUMATOID ARTHRITIS OCCURING AFTER IMMUNE CHECKPOINT INHIBITORS

R. Belkhir[1] pagebreak, S. Le Burel[1], O. Lambotte[1], G. Mouterde[2], E. Pertuiset[3], L. Dunogeant[4], A. Marabelle[5], A. Leary[6], A.-L. Voisin[7], X. Mariette[1]. *[1]Hôpitaux Universitaires Paris-Sud, Université Paris-Sud, AP-HP, le Kremlin Bicêtre; [2]Lapeyronie Hospital, Montpellier; [3]CH René Dubos, Pontoise; [4]Centre Hospitalier du Pays d'Aix, Aix-en-Provence; [5]Drug Development; [6]Université Paris-Saclay; [7]Unité Fonctionnelle de Pharmacovigilance, Université Paris Saclay, Gustave Roussy Cancer Center, Villejuif, France*

Background: Immune checkpoints inhibitors (ICIs) targeting cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and Programmed cell death protein 1 (PD-1) have demonstrated survival improvement in multiple cancers. Immune Related Adverse Events (IrAE) have been described with ipilimumab and anti PD1. Relapse or flare of preexisting auto-immune diseases has been reported but occurrence of new auto-immune diseases seems to be less frequent. A series of 13 patients with non-classified rheumatic IrAE has been published: 9 patients developed non-specific inflammatory arthritis but no seropositive rheumatoid arthritis (RA) and 4 presented with sicca symptoms but did not fulfill criteria for Sjögren syndrome [1].
Objectives: We did a retrospective study for collecting patients who developed seropositive rheumatoid arthritis (RA) after exposition to ICIs.
Methods: We used the "Club Rhumatismes et Inflammation (CRI)" network, a section of the French Society of Rheumatology and the Gustave Roussy Cancer

Abstract OP0003 – Table 1. Demographic features, cancer types, immunotherapy and rheumatic irAEs

Patient	Age	Sex	Malignancy	Immunotherapy	irAE	Serology	Time to onset (weeks)	Treatment	Improvement	Immunotherapy held for irAE
1	74	F	NSCL	Nivo	Arthritis	ANA 1:160 Anti-dsDNA 77	7.3	Prednisone 40 mg	Significant	Y
2	49	F	Melanoma	Ipi Pembrolizumab	Arthritis		52.7	Prednisone 20 mg HCQ	Moderate	Y
3	42	F	RCC	Ipi/Nivo	Arthritis		3	Prednisone Infliximab, MTX Etanercept	Moderate	N
4	57	M	RCC	Ipi/Nivo	Arthritis	RF 214	48.4	Prednisone, MTX Etanercept Adalimumab	Significant	N
5	59	F	Melanoma	Ipi/Nivo	Arthritis		21.7	Prednisone 60 mg	Minimal	N
6	81	M	Melanoma	Ipi/Nivo	Arthritis	ANA 1.5	13.1	Prednisone 15 mg	Moderate	Y
7	59	M	RCC	Ipi/Nivo	Arthritis	ANA 1.8	56	Prednisone 10 mg	Minimal	N
8	53	M	Melanoma	Ipi/Nivo	Arthritis		16	Methylprednisolone 80 mg IM	Minimal	Y
9	63	59	NSCL	Nivo	Arthritis	ANA 1:160	38	Prednisone 30 mg Methorexate	Minimal	Y
10	57	F	Melanoma	Ipi/Nivo	Arthritis Sicca	ANA 1:320 6.7	6.7	Prednisone 30 mg	Significant	Y
11	61	M	Melanoma	Ipi/Nivo	Sicca		5.3	Prednisone 60 mg*	Significant	Y^
12	63	M	RCC	Atezolizumab	Sicca		21.9	Prednisone 60 mg*	Significant	Y^
13	68	M	Melanoma	Ipi/Nivo	Sicca PMR	ANA 1:1280 SSA	8.1	Prednisone 30 mg	Significant	Y
14	79	M	Melanoma	Nivo	PMR Sicca		2	Prednisone 20 mg	Moderate	Y
15	63	M	RCC	Nivo	PMR		213	Prednisone 40 mg Infliximab Tocilizumab	Moderate	Y
16	68	M	NSCL	Tremelimumab Durvalumab	Myositis		4.6	IV methylpred 60 mg Prednisone 60 mg	Moderate	Y

NSCL non-small cell lung cancer, RCC renal cell carcinoma, Ipi ipilimumab, Nivo nivolimumab, RF rheumatoid factor HCQ hydroxychloroquine, MTX methotrexate, *Prednisone given for hypophysitis. ^Immunotherapy held for hypophysitis.

Abstract OP0004 – Table 1

Patients	Sex/age	Type of cancer	ICI	Date of first ICI exposure	Date of IrAE	Type of rheumatic IrAE	IrAE response to treatment	Autoantibody results
1	F 55 y	Squamous cell carcinoma of the vagina	nivolumab	October 2015	October 2015	RA	resolution with NSAIDS	anti-CCP: 671 U/ml RF: 18 UI/ml
2	F 66 y	Endometrial adenocarcinoma	pembrolizumab	March 2016	April 2016	RA	resolution with corticosteroids prednisone 10 mg/day	anti-CCP: 233 U/ml RF:180 UI/ml
3	M 59 y	Lung adenocarcinoma	nivolumab	May 2016	July 2016	RA	resolution with prednisone 10 mg/d tapered to 5 mg/d 1 months later	anti-CCP: 61 U/ml RF: 47 UI/ml
4	F 56 y	Metastatic melanoma	pembrolizumab	August 2015	September 2015	RA	resolution with hydroxychloroquine 400mg/day and NSAIDS	anti-CCP: 22UI/ml
5	M 80 y	Metastatic melanoma	nivolumab	April 2016	April 2016	RA	Resolution with prednisone 15mg/day (tapered) and hydroxychloroquine 200mg/day	anti-CCP:42 UI/ml
6	M 68 y	Lung adenocarcinoma	nivolumab	June 2015	July 2015	RA	Resolution after stopping nivolumab and after 1 month of methotrexate 10 mg/w (maintained 3 months)	anti-CCP >300U/ml RF: 246 UI/ml

Center register of safety of ICI for collecting patients treated with an ICI and who developed symptoms of arthritis with diagnosis of RA.
Results: We report 6 patients without any previous rheumatic disease, who developed seropositive rheumatoid arthritis (RA) after exposition to ICIs, all of them after anti-PD1.
Conclusions: This is the first description of RA occurring after anti-PD1 treatment for cancer. All cases responded to corticosteroids or with immunosuppressive therapy. This suggests that the PD1/PDL1 axis plays a role in RA pathophysiology. The combined expertise of oncologists, immunologists and rheumatologists is crucial in the successful management of these patients.
References:
[1] Cappelli LC, Gutierrez AK, Baer AN, et al. Inflammatory arthritis and sicca syndrome induced by nivolumab and ipilimumab. Ann Rheum Dis 2017;76:43–50.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3768

WEDNESDAY, 14 JUNE 2017

Fibromyalgia: a disease of the peripheral or central nervous system

OP0005 FIBROMYALGIA IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A 10-YEAR PERSPECTIVE

S.A. Provan, C. Austad, V. Halsaa, H.B. Hammer, T.K. Kvien, T. Uhlig.
Rheumatology, Diakonhjemmet Hospital, Oslo Norway, Oslo, Norway

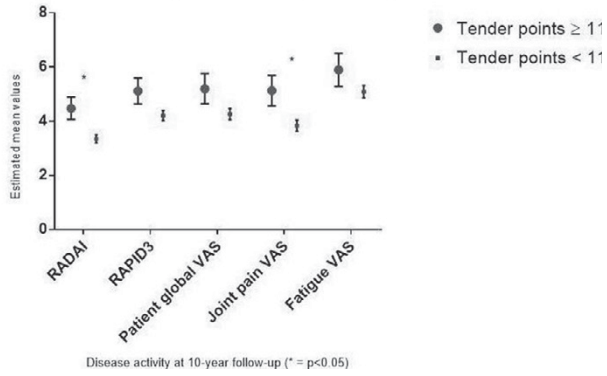
Background: Approximately 10% of patients with rheumatoid arthritis (RA) have coexisting fibromyalgia (FM). Little is known of the cross-sectional and longitudinal relationship between FM and RA disease activity.
Objectives: To examine the cross-sectional and longitudinal relationship between FM and RA disease activity.
Methods: Oslo RA register (ORAR) was established in 1994 as a prospective, observational, longitudinal nested cohort study. The inclusion criteria were RA according to the 1987-ACR classification criteria and a residential address in Oslo. 636 patients in ORAR were asked to participate in a clinical examination in 1999. A trained study-nurse systematically assessed the 18-tender point count and performed 28-tender and 28-swollen joint counts (TJC/SJC). Patients self-reported disease activity and pain related to RA, and completed the Stanford Health Assessment Questionnaire (HAQ). RA disease activity was calculated as DAS28. Fibromyalgia was diagnosed if $\geq$11 tender points were reported. FM associated variables; fatigue, muscular tenderness, headache, abdominal pain and difficulties concentrating were also scored (0–10 VAS).
At the 10-year follow-up patients completed a questionnaire that included RA Disease Activity Index (RADAI) and Routine Assessment of Patient Index Data (RAPID-3).
In cross-sectional and longitudinal analyses RA disease activity, FM associated variables and health status were compared between patients with $\geq$11 and $<$11 tender points. Level of significance was calculated using ANCOVA models corrected for age, gender, BMI and level of education. The FM associated variables at baseline were also corrected for baseline SJC 28 and C-reactive protein (CRP). The variables in the longitudinal study were corrected for the same variables as the cross-sectional analyses, but additionally for baseline values of the dependent variable when available.
Results: 488 patients agreed to participate in the baseline data-collection and 192 participated at the 10-year follow-up. The mean (SD) age was 59.5 (12.5) years, and 87% were female. There were no significant differences in age, disease duration or participation at follow-up between patients with and without FM, but only women had FM.
Patients with FM in addition to RA had higher DAS28, SJC, TJC, pain and patient global VAS, but also higher levels of fatigue, abdominal pain and concentration difficulties (table 1).

Table 1. Baseline cross-sectional associations

Variables Tender points $\geq$11 Mean (SD)	Tender joint count $<$11 n=40	Adj. Bivariate n=440	p
RA disease activity			
RA disease duration (years)	16.3 (8.9)	14.9 (9.3)	0.31
CRP (mg/L)	17.4 (24.4)	14.5 (13.4)	0.08
DAS28	5.3 (1.0)	4.4 (1.3)	0.002
PainVAS	4.5 (2.2)	3.5 (2.3)	0.03
SJC	9.8 (5.7)	6.8 (5.1)	0.04
TJC	13.3 (5.6)	7.4 (6.5)	$<$0.001
Patient disease activity VAS	4.7 (2.2)	3.7 (2.3)	0.03
Fibromyalgia related variables			
Muscular tenderness VAS	5.9 (2.7)	3.2 (2.6)	$<$0.001
Fatigue VAS	6.6 (2.7)	4.4 (2.7)	$<$0.001
Headache VAS	2.0 (2.4)	1.4 (2.1)	0.25
Abdominal pain VAS	3.7 (3.5)	1.9 (2.3)	$<$0.001
Difficulty concentrating VAS	2.9 (2.7)	1.7 (1.1)	0.003
Health Status			
HAQ	1.2 (0.1)	1.0 (0.0)	0.09

At the 10-year follow-up patient with FM had significantly higher levels of RA disease activity and pain (figure 1).

Figure 1 Longitudinal analyses
Disease activity at 10-year follow-up grouped according to baseline presence of FM



Conclusions: Presence of FM in patients with RA was associated with significantly higher levels of RA disease activity both in the cross-sectional and longitudinal perspectives. Secondary FM should be considered in patients with RA not reaching remission.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2972

OP0006 INFLUENCE OF AUTONOMIC NERVOUS SYSTEM DYSFUNCTION IN THE GENESIS OF SLEEP DISORDERS IN FIBROMYALGIA PATIENTS

M. Rizzi[1], D. Radovanovic[2], P. Santus[2], A. Airoldi[1], F. Frassanito[1], S. Vanni[1], A. Cristiano[1], R. Casale[3], R. Furlan[4], F. Atzeni[5], P. Sarzi-Puttini[5]. *[1]Respiratory Unit, Center for Sleep and Respiratory Disorders "Luigi Sacco" University Hospital; [2]Department of Biomedical Sciencies L. Sacco, University of Milan, Milan; [3]Habilita, Care & Research Rehabilitation Institutes, EFIC Pain School, Department of High Technology Rehabilitation & Pain Rehabilitation Unit, Zingonia di Ciserano, Bergamo; [4]CNR Institute of Neuroscience, Milano, Italy; IRCCS Humanitas, Rozzano; [5]Rheumatology Unit, University Hospital L. Sacco, Milan, Italy*

Background: Fibromyalgia (FM) is characterised by chronic musculoskeletal pain, autonomic nervous system (ANS) dysfunction, and disturbed sleep.
Objectives: The aim of this study was to evaluate the influence of ANS dysfunction on the genesis of sleep disorders.
Methods: Fifty consecutive Caucasian women (age 51.2±7.3 years) whose FM had been diagnosed on the basis of the 2010 ACR classification criteria were compared with 45 healthy female controls matched for age and body mass index.All of the FM patients underwent a clinical, polysomnographic and autonomic profile evaluation at rest and during a tilt test to determine muscle sympathetic nerve activity (MSNA), plasma catecholamine levels, and the spectral indices of cardiac sympathetic (LF_{RR}) and vagal (HF_{RR}) modulation computed by means of the spectrum analysis of RR during sleep.
Results: The FM patients had more tender points ($p<0.001$), a higher ESS score ($p<0.001$), and more signs and symptoms of orthostatic intolerance ($p<0.001$) than the controls. They also had a higher heart rate (HR), more MSNA and a higher LF/HF ratio, and lower HF_{RR} values at rest. The increase in tilting-induced MSNA was less in the FM patients (2±1 *vs* 16±3.1 bursts/min, $p<0.05$; 2±1 *vs* 12±2.8 bursts/100 $p<0.05$), whereas the trend in the spectral indices of the cardiac autonomic profile (LF_{RR} and the LF/HF ratio) and plasma catecholamine levels were similar in the two groups; furthermore, the decrease in the index of cardiac vagal modulation (HF_{RR}) was also less in the patients (HF_{RR}NU -17.3±3.2 *vs* -32.4±4.8, $p<0.05$; $HF_{RR}ms^2$ -148±50 *vs* -857±374, $p<0.05$). The stepwise tilt induced syncope or pre-syncope in 23 of the 50 patients (46%) and two of the 45 controls (5%) ($p<0.001$),Their sleep was less efficient ($p<0.01$), and they had a higher proportion of stage 1 non-REM sleep ($p<0.001$), experienced many arousals and periodic limb movements (PLMs) per hour of sleep ($p<0.001$) and a high proportion of periodic breathing (PB%) ($p<0.0001$). Their cyclic alternating pattern (CAP) rate was significantly increased ($p<0.001$).During sleep, the patients had a higher HR, and LF/HF ratio, and lower HF_{RR}, differences that were more marked during non-REM sleep, as were the presence of CAP, PB and PLMs. PLMs were mainly observed during CAP subtype A2 and A3. As in the tilt test, there was also a decrease in the index of cardiac vagal modulation during sleep: the decrease in HR_{RR} during sleep and in comparison when awake was less in the FMS patients than the controls (11.6±4.2 *vs* 31.1±5.3 NUs, $p<0.01$; 45±38 *vs* 403±281 ms^2, $p<0.0001$)
The number of tender points, pain VAS, the CAP rate, the PB% of sleeping time and the PLMI all seemed to correlate positively with HR and the LF/HF ratio, and negatively with HF_{RR} during sleep
Conclusions: Our data confirm that the FM patients have an autonomic nervous system dysfunction that is consistent with sympathetic over-activity due to the

intensity of chronic pain when awake and during sleep. These findings explain the excessive rate of syncope observed in the FM population during wakefulness, and the increased presence of CAP, PB and PLMs during sleep.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3365

WEDNESDAY, 14 JUNE 2017

Chondrocyte channels (role in mechanotransduction) or "channeling the chondrocyte"

OP0007 CCR2 INHIBITION ABROGATES IL-6–INDUCED ACTIVATION OF MATRIX METALLOPROTEINASES IN CARTILAGE

A. Latourte[1,2], J. Maillet[1,2], J. Goossens[1], H.-K. Ea[1,2], M. Cohen-Solal[1,2], E. Haÿ[1], P. Richette[1,2]. [1]*Inserm U1132 BIOSCAR, Hôpital Lariboisière;* [2]*Rheumatology Department, Hôpital Lariboisière, University Paris Diderot, Paris, France*

Background: Interleukin 6 (IL-6) plays a crucial role in many rheumatic diseases, including osteoarthritis (OA) [1]. In cartilage, IL-6 activates chondrocyte catabolism by increasing the production of matrix-degrading enzymes, including matrix metalloproteinase 3 (MMP-3) and MMP-13, but it could have other roles.
Objectives: We aimed to identify new biological processes regulated by IL-6 in cartilage.
Methods: RNA-seq analysis (Illumina HiSeq platform) was used to determine biological pathways associated with IL-6/IL-6R (100 ng/ml) stimulation in mouse primary articular chondrocytes. Results were further validated by qPCR and western blot analysis. The effect of stimulation with CC chemokine ligand 2 (CCL2; 10 ng/ml), CCL7 and CCL8 (100 ng/ml) was investigated *in vitro* and *ex vivo* in mouse femoral head cartilage explants. The impact of targeted inhibition of CCL2 or CCL7 by siRNA or blockade of their common receptor CCR2 by a specific antagonist (RS-504393) was determined in IL-6–treated chondrocytes and/or cartilage explants.
Results: Transcriptomic analysis revealed overrepresentation of multiple functional clusters of genes in IL-6–stimulated chondrocytes, with strongly increased expression of signalling molecules and especially cytokines. Two of the 10 top genes upregulated by IL-6 were *Ccl7* (log2 fold change [FC] 2.33, adjusted p-value [p_{adj}] =3.35x10^{-62}) and *Ccl2* (log2 FC 1.85, p_{adj} =9.10x10^{-26}), which encode for CCR2 ligands. qPCR and western blot validations confirmed these results and revealed that IL-6 stimulation also increased the mRNA level of *Ccl8*, another CCR2 ligand not identified by RNA-seq analysis. CCL2 and CCL7 but not CCL8 activated extracellular signal-regulated kinase 1/2 and c-Jun N-terminal kinase signalling and increased MMP-3 and MMP-13 production and activation. CCR2 blockade but not the specific inhibition of CCL2 or CCL7 by siRNA, greatly abrogated the IL-6–induced catabolism *in vitro* and *ex vivo*.
Conclusions: We identified 2 chemokines, CCL2 and CCL7, as key targets of IL-6 in chondrocytes. Although their main role is to mediate monocyte/macrophage recruitment to the joint, their receptor, CCR2, is also strongly involved in IL-6–induced cartilage catabolism. These results suggest a novel mechanism by which CCL2/CCR2 and CCL7/CCR2 signalling could be involved in rheumatic diseases, especially OA [2].
References:
[1] Latourte A, Cherifi C, Maillet J, et al. Systemic inhibition of IL-6/Stat3 signalling protects against experimental osteoarthritis. Ann Rheum Dis Published Online First: 27 Oct 2016. doi:10.1136/annrheumdis-2016–209757.
[2] Raghu H, Lepus CM, Wang Q, et al. CCL2/CCR2, but not CCL5/CCR5, mediates monocyte recruitment, inflammation and cartilage destruction in osteoarthritis. Ann Rheum Dis Published Online First: 13 Dec 2016. doi:10.1136/annrheumdis-2016–210426.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3359

OP0008 DEFICIENT AUTOPHAGY INDUCES CHONDROCYTE DYSFUNCTION THROUGH LAMIN A/C ACCUMULATION IN AGING AND OSTEOARTHRITIS

P. López de Figueroa[1], U. Nogueira-Recalde[1], V. Calamia[2], F.G. Osorio[3], M. Lotz[4], C. López-Otín[3], F.J. Blanco[5], B. Carames[1]. [1]*Rheumatology Division. Cartilage Biology Group;* [2]*Plataforma de Proteómica, Servicio de Reumatología, The Institute of Biomedical Research of A Coruña (INIBIC), A coruña;* [3]*Departamento de Bioquímica y Biología Molecular, Facultad de Medicina, Instituto Universitario de Oncología (IUOPA), Universidad de Oviedo, Oviedo, Spain;* [4]*Department of Molecular and Experimental Medicine, The Scripps Research Institute, la Jolla, CA, United States;* [5]*Division Reumatología, The Institute of Biomedical Research of A Coruña (INIBIC), A coruña, Spain*

Background: Aging-related Osteoarthritis (OA) is characterized by insufficient extracellular matrix synthesis and articular cartilage degradation. Autophagy is essential to maintain chondrocyte homeostasis by regulating the intracellular macromolecule and organelle turnover (1). Previous findings indicated that autophagy is defective in Aging and OA articular cartilage (2,3). However, the specific target/-s that regulates this homeostatic mechanism and affect cartilage integrity are still unknown.
Objectives: The objective of study is to identify targets regulating autophagy in human chondrocytes.
Methods: We performed quantitative proteomic analysis of Atg5 knockdown primary uman chondrocytes using iTRAQ (isobaric tags for relative and absolute quantitation) labeling coupled with on-line 2D LC/MS/MS. Protein identification and quantification were performed using Protein Pilot Software v 4.0. Each MS/MS spectrum was searched in the Uniprot/Swissprot database for *Homo sapiens*. Human chondrocytes and human cartilage from healthy, aged and OA patients were employed to confirm the role of the identified target by Western Blot (WB), Inmunofluorescence (IF) and Inmunohistochemistry (IHC). Importanly, CRISPR/Cas9 genome editing technology was used for mechanism of action studies.
Results: 24 out of 487 proteins were significantly altered ($p<0.05$) in response to defective autophagy. Cytoskeleton organization, collagen catabolism, oxidative stress, and aging pathways were affected. Interestingly, Lamin A/C, a nuclear protein implicated in cell senescence, was found upregulated under defective autophagy. Increased Lamin A/C expression was found in human chondrocytes with reduced autophagy. Furthermore, aged and OA human cartilage showed increased Lamin A/C expression. Induction of chondrocyte senescence by genetic deletion of Zinc Metalloproteinase STE24 (Zmpste24) via CRISPR-Cas9, lead to Lamin A/C accumulation, accompanied by a reduction of LC3 and increased chondrocyte death and mitochondrial dysfunction, suggesting that deficient autophagy is correlated with senescence of human articular cartilage.
Conclusions: Lamin A/C, a nuclear protein contributing to structural integrity to the nucleus and matrix was identified as candidate target for regulating cartilage function under defective autophagy, such as aging and OA. These results support the hypothesis that autophagy is decreased with aging. Therefore, targeting Lamin A/C might be a promising strategy to find novel therapeutics for cartilage aging and OA.
References:
[1] Lotz MK and Caramés B. Autophagy and cartilage homeostasis mechanisms in joint health, aging and OA. Nat Rev Rheumatol 2011;7:579–587.
[2] Caramés B, Olmer M, Kiosses WB, Lotz MK. The relationship of autophagy defects to cartilage damage during joint aging in a mouse model. Arthritis Rheumatol 2015;67:1568–76.
Acknowledgements: This study was supported by Instituto de Salud Carlos III-Ministerio de Economía y Competitividad, Spain-CP11/00095 and Fondo Europeo de Desarrollo Regional (FEDER).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3819

WEDNESDAY, 14 JUNE 2017

Wearable technologies in 21st century healthcare

OP0009-HPR THE EFFECT OF AN 8-WEEK WATER EXERCISE PROGRAM ON ANAEROBIC EXERCISE CAPACITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

D. Bayraktar[1], S. Savci[2], O. Altug-Gucenmez[3], E. Manci[4], B. Makay[3], N. Ilcin[2], S.E. Unsal[3]. [1]*Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Izmir Katip Celebi University;* [2]*School of Physical Therapy and Rehabilitation;* [3]*Faculty of Medicine, Division of Pediatric Rheumatology;* [4]*Instute of Health Sciences, Dokuz Eylul University, Izmir, Turkey*

Background: Anaerobic exercise capacity was reported to be lower in children with juvenile idiopathic arthritis (JIA) than healthy children. However, to our knowledge, there is no study focusing on improving anaerobic exercise capacity in JIA.
Objectives: To investigate the effect of an 8-week water exercise program, which was performed at the weekends, on anaerobic exercise capacity in children with JIA.
Methods: Forty-two children with JIA were divided into two groups as exercise and control. Prior to the study, anaerobic exercise capacity was measured performing a 30-second Wingate test. Deep water running was employed as the progressive water exercise program for the exercise group. Control group did not receive any additional treatment other than their usual care. Weekends were chosen for the exercise sessions considering the educational program of the children. Exercise intensity was set as moderate. Exercise intensity was determined with a wearable heart rate tracking system during the exercises. All children were reassessed regarding to anaerobic exercise capacity two months after the first assessment.
Results: All children completed the study without any adverse effects. Twenty-one children were in the exercise group, others were assessed as controls. No significant differences were determined between groups prior the study regarding to age, disease duration, height, weight, body-mass index, and anaerobic exercise capacity related parameters ($p<0.05$). While all anaerobic exercise capacity parameters improved in the exercise group, no improvement were seen in the control group. The in-group comparisons were shown at Table 1. The comparison of the changes between groups after 8 weeks were demonstrated at Table 2.

Table 1. In-group comparison before and after the study

	Before Median (IQR 25/75)	After Median (IQR 25/75)	p
Exercise Group (n=21)			
Peak Power (W)	354.73 (267.59/471.55)	441.3 (295.2/636.9)	**0.002***
Peak Power (W/kg)	6.74 (5.44/8.94)	7.7 (6.4/9.7)	**0.001***
Average Power (W)	291.5 (188.78/359.61)	360.0 (220.4/446.4)	**0.001***
Average Power (W/kg)	5.54 (4.07/6.88)	6.0 (4.8/7.4)	**0.002***
Control Group (n=21)			
Peak Power (W)	355.57 (225.43/463.62)	366.7 (236.3/447.8)	0.259
Peak Power (W/kg)	6.69 (5.80/7.83)	7.3 (6.1/8.1)	0.232
Average Power (W)	261.04 (181.68/351.27)	284.8 (187.8/373.0)	0.050
Average Power (W/kg)	5.29 (4.75/5.85)	5.5 (5.0/6.1)	0.076

Wilcoxon Test. IQR: Interquartile Range; W: watt; W/kg: watt/kilogram; *p<0.05.

Table 2. The differences in the groups after 8 weeks

	Exercise Group (n=21) Median (IQR 25/75)	Control Group (n=21) Median (IQR 25/75)	p
ΔPeak Power (W)	65.1 (23.8/107.1)	24.5 (-15.6/39.4)	**0.009***
ΔPeak Power (W/kg)	0.9 (0.3/1.6)	0.3 (-0.3/0.6)	**0.007***
ΔAverage Power (W)	41.4 (9.9/78.7)	17.3 (5/31.3)	**0.019***
ΔAverage Power (W/kg)	0.6 (0.3/1.3)	0.2 (-0.1/0.5)	**0.024***

Mann-Whitney U Test. IQR: Interquartile Range; Δ: Delta; W: watt; W/kg: watt/kilogram; *p<0.05.

Conclusions: The present study is the first study focusing on improving anaerobic capacity in children with JIA. According to our results, an 8-week water exercise program which is performed at the weekends might be beneficial to improve anaerobic exercise capacity in children with JIA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5670

WEDNESDAY, 14 JUNE 2017

Assessment and management of osteoporosis

OP0010 EFFECT OF DENOSUMAB COMPARED WITH RISEDRONATE IN GLUCOCORTICOID-TREATED INDIVIDUALS: RESULTS FROM THE 12-MONTH PRIMARY ANALYSIS OF A RANDOMIZED, DOUBLE-BLIND, ACTIVE-CONTROLLED STUDY

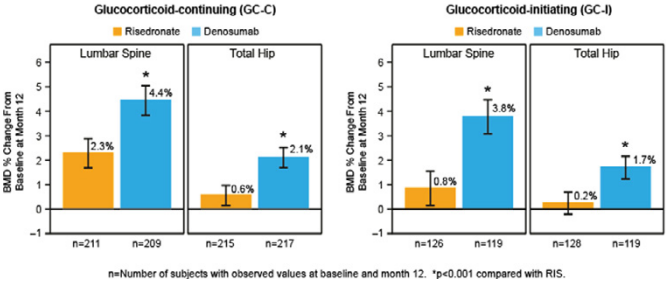
K. Saag[1], R.B. Wagman[2], P. Geusens[3], J. Adachi[4], O. Messina[5], R. Emkey[6], R. Chapurlat[7], N. Daizadeh[2], N. Pannacciulli[2], W. Lems[8]. *[1]University of Alabama, Birmingham, AL; [2]Amgen Inc., Thousand Oaks, CA, United States; [3]Maastricht University, Maastricht, Netherlands; [4]McMaster University, Hamilton, ON, Canada; [5]Cosme Argerich Hospital, Buenos Aires, Argentina; [6]Emkey Arthritis & Osteoporosis Clinic, Wyomissing, PA, United States; [7]Hôpital Edouard Herriot, Lyon, France; [8]VU University Medical Centre, Amsterdam, Netherlands*

Background: Glucocorticoid (GC)-induced osteoporosis (GIOP) remains the most common secondary cause of osteoporosis. Despite approved therapies, many subjects do not receive GIOP prevention or treatment. There is increased RANKL and decreased osteoprotegerin (OPG) expression in patients with GIOP. Denosumab (DMAb) is a monoclonal antibody to RANKL. This study was designed to assess the safety and efficacy of DMAb compared with risedronate (RIS) in GC-treated individuals, in whom treatment guidelines advocate a GIOP intervention.
Objectives: The primary objective was to demonstrate, in separate GC-continuing (GC-C) and GC-initiating (GC-I) subpopulations, that DMAb was not inferior to RIS with respect to percentage change from baseline (%Δ) in lumbar spine (LS) bone mineral density (BMD) at 12 months. Secondary objectives were to assess superiority of DMAb over RIS with respect to %Δ in LS and total hip (TH) BMD at 12 months.
Methods: This was a phase 3, randomized, double-blind, double-dummy, active-controlled study to evaluate DMAb vs. RIS in GC-treated individuals for 24 months. Eligible subjects were women and men ≥18 yrs receiving GC therapy at a dose ≥7.5 mg prednisone daily or its equivalent for ≥3 months or <3 months prior to screening (GC-C and GC-I, respectively). All subjects <50 yrs were required to have a history of osteoporotic fracture. GC-C subjects ≥50 yrs were required to have a LS, TH, or femoral neck BMD T-score ≤-2.0; or a T-score ≤-1.0 with a history of osteoporotic fracture. Subjects were randomized 1:1 to SC DMAb 60 mg every 6 months or oral RIS 5 mg daily for 24 months. Subjects were to receive daily calcium (≥1000 mg) and vitamin D (≥800 IU) supplementation. Primary outcome was %Δ in LS BMD at 12 months (non-inferiority in GC-C and GC-I). Secondary outcomes included %Δ in LS and TH BMD at 12 months (superiority). The study remains blinded and is ongoing.
Results: A total of 795 subjects (505 GC-C and 290 GC-I) enrolled in the study. Baseline characteristics were balanced between treatment groups (Table). Non-inferiority and superiority with DMAb were demonstrated for both the GC-C and GC-I subpopulations, as indicated by significantly greater BMD gains compared with RIS at the LS and TH in both subpopulations (Figure). The incidences of adverse events (AEs) and serious AEs, including serious AEs of infection, as well as fracture, were similar between treatment groups and consistent with the known safety profile of DMAb.

Table. Baseline Characteristics

	Glucocorticoid-continuing (GC-C)		Glucocorticoid-initiating (GC-I)	
	Risedronate N=252	Denosumab N=253	Risedronate N=145	Denosumab N=145
Sex – n (%)				
Male	67 (26.6)	68 (26.9)	52 (35.9)	52 (35.9)
Female	185 (73.4)	185 (73.1)	93 (64.1)	93 (64.1)
Age (years) – mean (SD)	61.3 (11.1)	61.5 (11.6)	64.4 (10.0)	67.5 (10.1)
Medical conditions of interest – n (%)				
Rheumatoid arthritis	118 (46.8)	96 (37.9)	43 (29.7)	48 (33.1)
Polymyalgia rheumatic	18 (7.1)	20 (7.9)	52 (35.9)	50 (34.5)
Systemic lupus erythematosus	16 (6.3)	15 (5.9)	4 (2.8)	2 (1.4)
Daily prednisone-equivalent dose (mg) – mean (SD)	11.13 (7.69)	12.29 (8.09)	15.61 (10.25)	16.57 (13.01)
25 (OH) vitamin D (ng/mL) – median (Q1, Q3)	28.0 (23.6, 36.3)	29.2 (24.2, 37.6)	28.6 (24.2, 36.4)	28.8 (23.6, 36.0)
BMD T-score – mean (SD)				
Lumbar spine	-1.96 (1.38)	-1.92 (1.39)	-1.06 (1.57)	-0.92 (1.86)
Total hip	-1.56 (0.96)	-1.66 (0.96)	-0.98 (1.07)	-1.14 (1.00)

Figure. BMD Percentage Change From Baseline at Month 12



n=Number of subjects with observed values at baseline and month 12. *p<0.001 compared with RIS.

Conclusions: DMAb significantly increased BMD more than RIS at the spine and hip at 12 months. The overall safety profile was similar between treatment groups. DMAb has the potential to become another treatment option for patients newly initiating or continuing GC who are at risk for fracture.
Acknowledgements: The study was funded by Amgen. C Desborough (Amgen [Europe] GmbH) provided editorial support.
Disclosure of Interest: K. Saag Grant/research support from: Amgen, Merck, Consultant for: Amgen, Merck, Radius, R. B. Wagman Shareholder of: Amgen, Employee of: Amgen, P. Geusens Grant/research support from: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Roche, UCB, BMS, Novartis, J. Adachi Grant/research support from: Amgen, Eli Lilly, Merck, Pfizer, Consultant for: Amgen, Eli Lilly, Merck, International Osteoporosis Foundation, Speakers bureau: Amgen, Eli Lilly, O. Messina Grant/research support from: Amgen, GSK, R. Emkey Speakers bureau: Amgen, R. Chapurlat Grant/research support from: Amgen, Merck, Chugai, Consultant for: Amgen, Eli Lilly, BMS, AbbVie, Pfizer, Chugai, UCB, N. Daizadeh Shareholder of: Amgen, Employee of: Amgen, N. Pannacciulli Shareholder of: Amgen, Employee of: Amgen, W. Lems Grant/research support from: Eli Lilly, Amgen, MSD, Novartis.
DOI: 10.1136/annrheumdis-2017-eular.3164

WEDNESDAY, 14 JUNE 2017

Systematic literature review: the link from science to clinical practice

OP0011 DOES A VERY EARLY THERAPEUTIC INTERVENTION IN VERY EARLY ARTHRITIS / PRE-RHEUMATOID ARTHRITIS PATIENTS PREVENT THE ONSET OF RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND METANALYSIS

B. Hugues, S. Hilliquin, S. Mitrovic, L. Gossec, B. Fautrel. *Paris 06 University (UPMC); AP-HP, Pitié Salpêtrière Hospital, Paris, France*

Background: Recent progress in the understanding of rheumatoid arthritis (RA) pathogenesis leads to growing interest in the concept of pre-RA, a clinical stage in which very early intervention could be more efficacious.
Objectives: To assess the efficacy of very early therapeutic interventions in pre-RA patients, i.e., with either undifferentiated arthritis, or ACPA-positive arthralgia/arthritis (ie, very early RA, VERA), through a systematic literature review (SLR) and meta-analysis (MA).
Methods: The SLR was performed following Cochrane guidelines. The search used "undifferentiated arthritis" or "very early rheumatoid arthritis" (VERA) associated with "therapy" or "treatment", and was limited to randomized controlled trials (RCTs) published in English over the last five years. It was conducted in Pubmed, Embase and Cochrane RCT databases, as well as EULAR and ACR congress abstracts of the last two years. Two independent readers (SH, BH) extracted the following data through a standardized form: study quality, patient status at baseline (either undifferentiated arthritis or VERA), the type of intervention, and disease characteristics over time as well as occurrence of RA.

The main outcomes that were analysed for the meta-analysis were RA occurrence at 52 weeks and beyond and the absence of radiographic progression at week 52. The meta-analysis was performed using RevMan with Mantel-Haenszel method.

Results: The search identified 595 abstracts, of which 9 RCTs were finally selected (including 2 congress abstracts). Eight were related to undifferentiated arthritis; 1 to VERA. The studies included 1156 patients, weighted mean age 45.8+/-15.2 years, mean symptoms duration 16.2+/-12.6 weeks; 66.0+/-17.7% were female.

The occurrence of RA at week 52 or more was available in 7 studies (assessing 800 patients). Early therapeutic intervention – either methylprednisolone (80 to 120mg IM), methotrexate, TNF-blocker, abatacept or rituximab -reduced the risk of occurrence of RA with a pooled odds ratio (OR) of 0.72 (95% CI [0.54; 0.96]), p 0.02 (Figure).

There was no statistically significant difference between the treatments or placebo, for the absence of radiographic progression (pooled OR 1.36 [0.82;2.27])

The outcome was assessed at Week 52 for all studies, except for Van Dongen 2007 (PROMPT), where it was assessed at Week 120. MethylPDN, methylprednisolone; MTX, methotrexate.

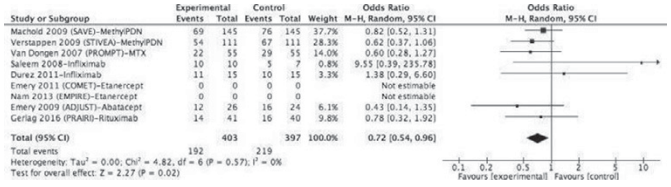


Figure 1. RA appearance at week 52 or more.

Conclusions: This meta-analysis demonstrates that early therapeutic intervention significantly reduces the risk of RA onset in pre-RA patients. The benefit /risk balance and feasibility in clinical practice remain to be further assessed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5323

WEDNESDAY, 14 JUNE 2017

EULAR Campaign: Don't Delay, Connect Today

OP0012-PARE RHEUMATOSPHERE: REACH NEW HEIGHTS IN DIAGNOSIS AND TREATMENT OF ARTHRITIS BY ENGAGING, EMPOWERING AND INSPIRING

L.A. Bennett, J.S. Nijjar, G. Fragoulis, S. Siebert, I.B. McInnes. *Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom*

Background: We aim to reach new heights in diagnosis and treatment of arthritis through research and we believe that part of this encompasses public engagement. Engaging the public is an essential part of scientific life, as the majority of work carried about by researchers is publically funded. Therefore the public are entitled to and should be encouraged to see the conclusions of this work in an easily accessible manner.

Objectives: 1) *Engage* the public about rheumatic disease, what it is, what it does to the body and how we, as scientists and clinicians, address unmet needs in this field.

2) *Empower* patients in order to help them understand their disease and treatments thereby improving patient satisfaction and compliance to therapy.

3) *Inspire* the next generation of scientist by encouraging children to study science at school and raise the profile of these subjects with education authorities and the government.

Methods: Rheumatosphere was established to address public engagement needs in the arthritis research field. We have used a variety of techniques to capture the attention of small and large audiences of all ages. Techniques include: Ultrasound scanning, coffee with a scientist at our cell cafe, posters displays, multidisciplinary classroom lessons in a school environment and comic book drawing. These resources and activities have been deployed at 5 major science events across Scotland in the last 3 years, and at the British society for rheumatology's annual conference in 2016. Further to this we have also attended regular events at the Glasgow science centre and schools across Scotland.

Results: During our first three major events we have had approximately 3000 encounters with the median age of participants being 33 years. Over half (51%) of the people that we engage with directly knew someone affected by rheumatoid arthritis. Engaging the public and patients with visualisation of their own joints using ultrasound is effective in demonstrating how joints function. This then serves as a starting point to highlight current research and celebrate the newer treatment strategies which have resulted in better outcomes for our patients. Feedback from our events show that people are keen to engage and learn more about arthritis, with 80% wanting to know more about autoimmunity and 83% wanting to know more about the clinical work going on throughout Glasgow.

Children at these events and in the classroom are encouraged to learn about the immune system and it's role in health and disease through the medium of comic books and art. Allowing the children to relate scientific topics to an already established and popular media has proven to be an effective learning tool. In 2016, 94% of school pupils who interacted with Rheumatosphere said that they had learned something new about arthritis, including careers options through which they could become involved in helping to better understand and treat disease.

Our future plans include partnering with Government and National Science Centre stakeholders to further develop educational curricula in the arena of musculoskeletal science and immunology.

Conclusions: We feel that engaging with the public and patients is an essential part of our vocation as scientists and clinicians and only by empowering them will we be able to reach new heights in diagnosis and treatment of arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5044

WEDNESDAY, 14 JUNE 2017

Standing Committee session on paediatric rheumatology

OP0013 PULMONARY MANIFESTATIONS IN JUVENILE ONSET MIXED CONNECTIVE TISSUE DISEASE AFTER LONG-TERM DISEASE DURATION – A NORWEGIAN CASE-CONTROL STUDY

S.O. Hetlevik[1], T.M. Aaløkken[2], M.B. Lund[3], B. Flatø[1], E.B. Nordal[4], M. Rygg[5], V. Lilleby[1]. *[1]Rheumatology; [2]Radiology; [3]Respiratory medicine, Oslo University Hospital, Oslo; [4]Pediatrics, University hospital of North Norway, Tromsø; [5]Pediatrics, St. Olavs University Hospital, Trondheim, Norway*

Background: Pulmonary manifestations in mixed connective tissue disease (MCTD) are common and a major cause of morbidity and mortality [1]. Data on lung involvement in patients with juvenile onset MCTD (JMCTD) are scarce.

Objectives: The aim of this study was 1) to compare pulmonary function abnormalities in a nationwide representative Norwegian JMCTD cohort with that of matched controls, 2) investigate occurrence of interstitial lung disease (ILD) in JMCTD and 3) to evaluate possible associations between pulmonary findings and disease related variables.

Methods: Inclusion criteria were fulfillment of the Kasukawa or Alarcon-Segovia criteria and symptom-onset before 18 years. The control group was randomly drawn from the national population register, after matching for age and gender. Fifty-two patients with JMCTD were examined after mean disease duration 16.2 years, 44 (85%) were female. Patients and controls performed pulmonary function tests (PFT) and a 6 min walk test (6MWT). The patients had a high-resolution CT (HRCT) of the lungs.

Results: Abnormal PFT were found in 24 patients (46%) and in 12 controls (23%) (p=0.01) (table 1).

Variable	JMCTD patients	Controls	P value
Age at examination, years	28.0 (10.3)	29.0 (10.1)	0.61
BMI, kg/m^2	22.7 (3.5)	23.4 (3.0)	0.29
Current smokers daily/occasionally, n (%)	7 (14)	9 (17)	0.59
Never smokers, n (%)	35 (67)	34 (65)	0.83
6MWD, meters	634.3 (76.5)	698.9 (86.6)	<0.01
FVC, litre	3.4 (0.6)	4.3 (1.0)	<0.01
FVC (% of predicted)	89 (14)	109 (11)	<0.01
FEV1, litre	2.9 (0.5)	3.5 (0.8)	<0.01
FEV1 (% of predicted)	89 (13)	102 (11)	<0.01
FEV1/FVC	0.86 (0.06)	0.82 (0.07)	<0.01
DLCO/VA (mmol/kPa min/l)	1.6 (0.2)	1.8 (1.0)	0.26
DLCO/VA (% of predicted)	88 (12)	92 (13)	0.14

More patients than controls had abnormal FVC (11 patients and 0 controls, p<0.01) and FEV1 (12 patients and 2 controls, p<0.01). Diffusing capacity for carbon monoxide adjusted for alveolar volume was abnormal in 12 patients and 8 controls (p=0.34). One patient and 3 controls had a pathological FEV1/FVC (less than 70% of predicted, p 0.62). HRCT showed ILD in 15 patients (29%). The extent of lung parenchyma involved was median 2% (range 1–75) in the patients with ILD. Two patients had more than 20% of lung parenchyma involved (graph 1). The most common abnormalities were reticular patterns, being present in 13 patients (25%). 2 patients (4%) had ground glass attenuation.We could not find correlations between the extent of ILD and PFT or 6MWT. There were no significant differences in PFT values or other disease related variables between the patients with and without ILD.

Conclusions: Patients with JMCTD had significantly reduced pulmonary function after mean 16.2 years disease duration compared to matched controls. However, overall lung function was only moderately reduced. The occurrence of ILD assessed with HRCT was 29%, but the majority of patients with ILD had mild disease. To our knowledge, this is the first systematic case-control study of pulmonary manifestations in JMCTD.

References:

[1] Gunnarsson R, Aalokken TM, Molberg O, et al. Prevalence and severity of interstitial lung disease in mixed connective tissue disease: a nationwide, cross-sectional study. Ann Rheum Dis 2012;71:1966–72.

Disclosure of Interest: None declared

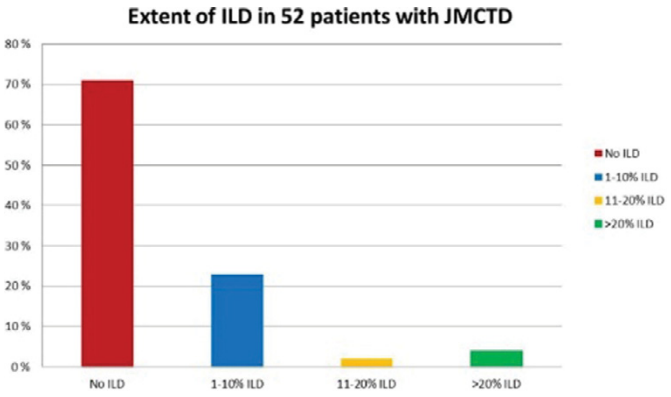


Figure 1

DOI: 10.1136/annrheumdis-2017-eular.1366

OP0014 **CONVENTIONAL RADIOGRAPHY IN JUVENILE IDIOPATHIC ARTHRITIS: JOINED RECOMMENDATIONS FROM THE FRENCH SOCIETIES FOR RHEUMATOLOGY, RADIOLOGY AND PEDIATRIC RHEUMATOLOGY**

P. Marteau [1], C. Adamsbaum [2], L. Rossi-Semerano [3], M. De Bandt [4], I. Lemelle [5], J. Wipff [6], C. Deslandre [6,7], T.A. Tran [8], A. Lohse [9], E. Solau-Gervais [10], C. Sordet [11], P. Pillet [12], B. Bader-Meunier [7], C. Gaujoux-Viala [13], S. Breton [14], V. Devauchelle-Pensec [1,15,16]. *[1]Rheumatology, CHU Brest, BREST; [2]Pediatric Radiology, Bicêtre Hospital, Paris; [3]Pediatric Rheumatology, Bicêtre Hospital, le Kremlin-Bicêtre; [4]Rheumatology, Pierre Zobda Quitman University Hospital, Fort de France; [5]Pediatric Rheumatology, Nancy University Hospital, Nancy; [6]Rheumatology A, Cochin University Hospital; [7]Pediatric Rheumatology, Necker Hospital, Paris; [8]Pediatrics, Nîmes University Hospital, Nîmes; [9]Rheumatology, Nord Franche Comté Hospital, Belfort; [10]Rheumatology, Poitiers University Hospital, Poitiers; [11]Rheumatology, Hautepierre Hospital, Strasbourg; [12]Pediatrics, Pellegrin-enfants Hospital, Bordeaux; [13]Rheumatology, Carémeau University Hospital, Nîmes; [14]Pediatric Radiology, Necker Hospital, Paris; [15]Pediatrics, CHU Brest; [16]UMR 1227, Inserm, BREST, France*

Background: Juvenile idiopathic arthritis (JIA) may lead to structural damage. Yet radiographic assessment is seldom considered in studies.
Objectives: To provide pragmatic guidelines concerning conventional radiography (CR) in each subtype of JIA (exclusion of systemic JIA).
Methods: A multidisciplinary task force of 15 French experts (rheumatologists, pediatricians, radiologists) plus one patient's representative, was convened. Following the GRADE[1] method, they formulated a series of research questions concerning CR assessment, at diagnosis and follow-up of each subtype of JIA. Systemic JIA was ruled out. A systematic literature review was conducted, considering articles in which structural damage was detailed (erosion, joint space narrowing, bone deformities). A series of recommendations was elaborated, following evidence-based data, and expert opinion. It underwent an evaluation from an independant committee (including patient's representative), and a final round of Delphi-voting process from the whole expert group.
Results: Of 646 publications identified, 73 original articles were included. The task force produced 4 principles and 31 recommendations. Level of evidence ranked from B to D, level of agreement was high. The experts insisted on weighing indication of CR considering structural risk. The importance of assessing structural progression, the need for constant attention to radioprotection were asserted. Systematic CR of hands and feet are thus recommended in polyarthritis JIA rheumatoid factor positive, and in polyarticular JIA with pejorative prognostic factors. Systematic CR are not recommended in oligoarticular JIA. CR is not the prime imaging technique of the axial skeleton.
Conclusions: These are the first pragmatic recommendations upon CR in JIA. They mostly rely on experts' opinion, due to lack of evidence-based data. CR is still relevant in many situations in JIA, but should not be overlooked, while non-irradiating imagine techniques are developing.
References:

[1] Brożek JL, Akl EA, Compalati E, Kreis J, Terracciano L, Fiocchi A, et al. Grading quality of evidence and strength of recommendations in clinical practice guidelines part 3 of 3. The GRADE approach to developing recommendations. Allergy. 2011 May;66(5):588–95.

Acknowledgements: Dr Bouchra Amine, Pr Nathalie Boutry, Pr Rolando Cimaz, Pr Bernard Combe, Dr Véronique Despert, M William Fahy and Mrs Céline Obert (association KOURIR), Dr Laurence Goumy, Pr Michael Hofer, Dr Laëtitia Houx, Dr Sylvie Jean, Dr Valérie Merzoug, Pr Michel Panuel, Pr Samira Rostom, Pr Jean Sibilia; the French Society for Rheumatology, the French Society for Radiology, The French Society for Pediatric and antenatal Imaging.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3862

WEDNESDAY, 14 JUNE 2017

Still breaking news on TNF inhibitors in rheumatoid arthritis

OP0015 **INDUCTION OF REMISSION AND MAINTENANCE IN EARLY, AGGRESSIVE RHEUMATOID ARTHRITIS USING ADALIMUMAB IN COMBINATION WITH METHOTREXATE WITH OR WITHOUT SHORT-TERM HIGH-DOSE GLUCOCORTICOIDS: RESULTS OF A PHASE IV MULTICENTER, RANDOMIZED, DOUBLE BLIND STUDY (CLINTRIAL.GOV: NCT00480272)**

R. Caporali [1], C. Montecucco [1], E. Bartoloni Bocci [2], B. Vitolo [1], E. Prisco [1], C. Klersy [3], R. Giacomelli [4], G. Triolo [5], M. Cutolo [6], A. Marchesoni [7], E. Gremese [8], C. Iannuccelli [9], R. Tirri [10], W. Grassi [11], G. Lopalco [12], M. Galeazzi [13], M. Matucci Cerinic [14], L. Punzi [15], G. Ferraccioli [8]. *[1]IRCCS San Matteo, Pavia; [2]University of Perugia; [3]Biometry Unit, IRCCS San Matteo, Pavia; [4]University of L'Aquila, L'Aquila; [5]University of Palermo, Palermo; [6]University of Genoa, Genoa; [7]ASST G Pini, Milano; [8]Policlinico Gemelli, Roma; [9]University la Sapienza, Rome; [10]Seconda Università, Napoli; [11]Università delle Marche, Ancona; [12]Azienda Policlinico, Bari; [13]Azienda Ospedaliera Universitaria, Siena; [14]Azienda Ospedaliera Universitaria, Firenze; [15]Azienda Ospedaliera, Padova, Italy*

Background: Remission is the current aim of early RA treatment. In patients with early, aggressive RA, combination with adalimumab (ADA) plus methotrexate (MTX) was superior to either MTX or ADA alone in obtaining clinical remission. Moreover, it has been demonstrated that a short-term aggressive treatment with high-dose glucocorticoids (GC) plus conventional DMARDs lead to long-term (up to 5 years) benefits.
Objectives: To compare the proportion of patients who achieve remission at 12 months, between two groups of subjects treated with ADA + MTX + high dose GC (intensive) and ADA + MTX + placebo (standard), and to evaluate the proportion of those maintaining remission at 24 months, after discontinuation of GC at 6 and ADA at 12 months.
Methods: The main inclusion criteria were: active RA, disease duration ≤1 year, GC and MTX-naïvity, at least one predictor of aggressive disease. All subjects received ADA for 12 months and MTX (20 mg/w) to the end of month 24. Subjects were randomized to receive prednisone (orally, 50 mg/d, progressively tapered to 6.25 mg and stopped at month 6) or placebo. Response was evaluated using DAS28, CDAI, SDAI and ACR response criteria. The difference in rate and 95% CI will be computed with a binomial regression model and identity link, while clustering on center. An intention-to-treat analysis was performed.
Results: 118 patients were assigned to standard and 115 patients to intensive group. Remission (DAS28<2.6, SDAI≤3.3, CDAI≤2.8) at 1 year in standard vs intensive group were: 56.25% vs 45.28% (RD= -11%, 95% CI -23 to1, p=0.07), 30.36% vs 21.69% (RD= -9%, 95% CI -20 to 3, p=0.14), and 28.57% vs 22.64% (RD= -6%, 95% CI -18 to 6, p=0.34). DAS28 remission at 2 years was 36.84% in standard vs 30.93% in intensive (RD= -6%, 95% CI -17 to 5, p=0.28). No superiority of the intensive group was seen in ACR20–50–70 response rates at 4, 8, 12, 24 months. The overall frequency of adverse events (AE) in patients that completed the trial was comparable between groups. The percentage of patients who discontinued for AE was higher in the intensive group (9.32% in standard vs 16.52% in intensive, RD=7%, 95% CI 1 to 13, p=0.01).

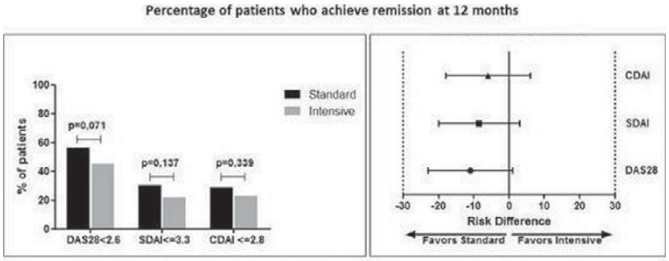


Figure 1. The percentage of patients who achieve DAS28 remission at 12 months was 56,25% in standard vs 45,28% in intensive, with RD of -11% (-23 to 1, p=0,07); SDAI remission of 30,36% in standard vs 21,69% in intensive, with RD of -9% (-20 to 3, p=0,14); CDAI remission of 28,57% in standard vs 22,64% in intensive, with RD of -6% (-18 to 6, p= 0,34).
RD= Risk Difference

Conclusions: Our results confirm that intensive treatment with biologics in early, aggressive RA might be considered to induce and maintain clinical remission. The addition of high-dose GC to a first line treatment with ADA and MTX did not prove to induce a further improvement in efficacy. Although these results should be tested with other biologic therapies, the high rate of drop out for AE in the intensive group should be carefully considered in the risk-benefit ratio.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2362

OP0016 COMPARATIVE EFFECTIVENESS AT 1 YEAR OF DIFFERENT ANTI-TNF DRUGS AS FIRST BIOLOGIC DMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS – RESULTS FROM THE NATIONWIDE SWEDISH REGISTER

C. Turesson[1,2], T. Frisell[3], M. Dehlin[4], D. Di Giuseppe[3], N. Feltelius[5], A. Kastbom[6], J. Askling[3] on behalf of ARTIS study group. *[1]Department of Rheumatology, Skåne University Hospital; [2]Rheumatology, Department of Clinical Sciences, Malmö, Lund University, Malmö; [3]Department of Medicine, Karolinska Institutet, Stockholm; [4]Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, Gothenburg University, Gothenburg; [5]Medical Products Agency, Uppsala; [6]Rheumatology/AIR, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden*

Background: Treatment with TNF inhibitors is part of the management of patients with severe rheumatoid arthritis (RA). There is limited data on the comparative effectiveness of different TNF inhibitors from clinical trials and observational studies of patients treated in clinical practice.
Objectives: To compare effectiveness of different TNF inhibitors in a large, population representative, sample of bionaïve patients with RA.
Methods: The study was based on the Swedish Rheumatology Quality register, in which clinical data are prospectively recorded at treatment initiation and at subsequent visits. Patients with RA initiating a TNF inhibitor as their first ever biologic DMARD in 2010–2014 were included and followed through 2015. The proportion remaining on drug at 1 year (±90 days) after starting therapy was compared. Furthermore, effectiveness at 1 year was assessed as the proportions with EULAR good response, remission (DAS28 <2.6), HAQ improvement (>0.2) and swollen and tender joint counts of 0, all corrected for drug survival (1). The relative response was estimated with log-binomial regression, adjusting for potential confounders and using the largest group (etanercept) as reference.
Results: A total of 5568 patients were included. There was a significant difference in the adjusted chance of drug survival across TNF inhibitors (Table). Patients treated with certolizumab or infliximab were less likely to remain on treatment compared to those started on etanercept. The chance of achieving each of the clinical response measures was significantly lower for those initiating infliximab compared to patients treated with etanercept. There were no significant differences in these outcomes compared to etanercept for any of the other TNF inhibitors.
Conclusions: Patients with RA starting infliximab as their first biologic DMARD were less likely to remain on treatment with significant improvement at 1 year compared to those initiating etanercept. There was a similar trend for certolizumab vs. etanercept, but there were no consistent differences in clinical effectiveness between etanercept and adalimumab or golimumab. Treatment context may affect these patterns.
References:
[1] Kristensen A&R 2006; 54: 600–6.
Disclosure of Interest: C. Turesson Grant/research support from: Abbvie, Pfizer, Roche, Consultant for: MSD, Pfizer, Roche, Paid instructor for: Abbvie, Bristol-Myers Squibb, Janssen, MSD, Pfizer, Roche and UCB, T. Frisell: None declared, M. Dehlin: None declared, D. Di Giuseppe: None declared, N. Feltelius: None declared, A. Kastbom Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, Paid instructor for: Bristol-Myers Squibb, Pfizer, Roche, UCB, J. Askling Grant/research support from: Abbvie, UCB, Pfizer, Merck, Samsung, Roche, Lilly
DOI: 10.1136/annrheumdis-2017-eular.2760

OP0017 LACK OF PLACENTAL TRANSFER OF CERTOLIZUMAB PEGOL DURING PREGNANCY: RESULTS FROM CRIB, A PROSPECTIVE, POSTMARKETING, MULTICENTER, PHARMACOKINETIC STUDY

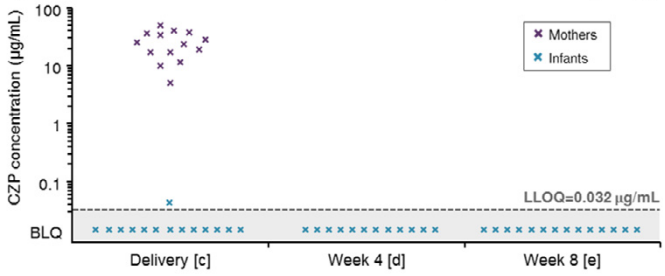
X. Mariette[1], A. Flynn[2], F. Förger[3], A. Moltó[4], R.-M. Flipo[5], A. van Tubergen[6], L. Shaughnessy[7], J. Simpson[7], M. Teil[8], E. Helmer[9], M. Wang[7], E. Chakravarty[10]. *[1]Université Paris-Sud, le Kremlin-Bicêtre, France; [2]University of Utah, Salt Lake City, United States; [3]Inselspital, University of Bern, Bern, Switzerland; [4]Groupe Hospitalier Cochin, AP-HP, Paris; [5]Centre Hospitalier Régional Universitaire de Lille, Lille, France; [6]Maastricht University Medical Center, Maastricht, Netherlands; [7]UCB Pharma, Raleigh, United States; [8]UCB Pharma, Slough, United Kingdom; [9]UCB Pharma, Brussels, Belgium; [10]Oklahoma Medical Research Foundation, Oklahoma City, United States*

Background: There is a need for effective and safe treatment during pregnancy in women affected by chronic active inflammatory diseases, such as rheumatoid arthritis. Adequate disease control is crucial to ensure the best fetal and maternal health, and reduce adverse pregnancy outcomes.[1,2] Anti-TNFs are an effective therapeutic option, but because most cross the placenta, they are often stopped during pregnancy.[3,4] Certolizumab pegol (CZP), due to its Fc-free molecular structure, has no active placental transfer compared to other anti-TNFs.[5,6]
Objectives: To accurately measure the potential level of placental transfer of CZP from mothers to infants using a highly sensitive, CZP-specific assay.
Methods: CRIB (NCT02019602) was a pharmacokinetic (PK) study of pregnant women (≥30 weeks [wks] gestation) receiving commercial CZP (maintenance dose) for an approved indication; last dose was within 35 days prior to delivery. Blood samples were collected from the mothers, umbilical cords, and infants at delivery, and infants again at Wks 4 and 8 post-delivery. CZP concentration was measured with a sensitive, CZP-specific electrochemiluminescence immunoassay validated in plasma (LLOQ=0.032 μg/mL; 10-fold lower than assay used in prior CZP PK studies[6,7]).
Results: 21 CZP-treated pregnant women were screened; 16 entered the study (Table). Maternal CZP plasma levels at delivery were within the expected therapeutic range (median [range]: 24.4 [5.0–49.4] μg/mL). Of the 16 infants delivered, 2 samples were excluded: 1 due to missing data, 1 due to implausible PK data. 13/14 infants had no quantifiable CZP levels at birth (<0.032 μg/mL); 1 infant had a minimal CZP level of 0.042 μg/mL (infant/mother plasma ratio: 0.09%); no infants had quantifiable levels at Wks 4 and 8 (Figure). 3/15 umbilical cord samples had quantifiable CZP levels (maximum: 0.048 μg/mL); 1 umbilical cord collapsed and was excluded. No anti-CZP antibodies were detected in mothers, umbilical cords, or infants. The infants of CZP-exposed mothers had a safety profile consistent with that of unexposed similar-age infants.

Table: Baseline characteristics of mothers and infants

Median (min, max), unless stated otherwise	All mothers (n=16) [a]
Age, years	31 (18, 40)
Mother's indication for CZP treatment, n	
Rheumatoid arthritis	11
Crohn's disease	3
Psoriatic arthritis	1
Axial spondyloarthritis/ankylosing spondylitis	1
Median (min, max), unless stated otherwise	**All infants (n=16)**
Female, n (%)	10 (62.5)
Gestational age at birth, weeks	39.9 (37.7, 41.7)
Weight at birth, kg	3.3 (2.6, 4.0)

Figure: Plasma CZP concentrations in mothers and infants (n=14 mother-infant pairs [b])



[a] Mothers who entered the study; [b] 2/16 infant samples were excluded: 1 due to missing data, and 1 due to implausible PK data (ie. data not consistent with a paediatric CZP PK model, based on the expected range of clearance, volume of distribution, and subsequent elimination half-life); [c] ±24 hours; [d] ±7 days (2 samples not collected); [e] ±7 days. Min: minimum; Max: maximum; BLQ: below the LLOQ (<0.032 μg/mL); LLOQ: lower limit of quantitation.

Conclusions: Using a highly sensitive assay, CZP levels were below LLOQ in 13/14 infant blood samples at birth, and all samples at Wks 4 and 8. This indicates no to negligible placental transfer of CZP from mothers to infants, suggesting lack

Abstract OP0016 – Table 1. Status at the 1-year evaluation visit among patients with RA initiating a TNF inhibitor as their first ever biologic DMARD

	Etanercept *N*=1651	Infliximab *N*-1366	Adalimumab *N*=1004	Certolizumab *N*-921	Golimumab *N*=626	*P*
Observed percentage						
On drug	70.6	66.4	69.2	65.2	68.0	
EULAR good response*	28.0	23.9	25.9	24.3	27.8	
DAS28 remission*	25.9	21.3	26.0	22.4	27.7	
HAQ improvement*	28.0	24.5	29.0	25.0	24.8	
28 Joint counts = 0*	23.3	16.8	20.4	19.0	21.6	
Adjusted† relative risk (95% CI)						
On drug	*Ref.*	0.94 (0.89–1.00)	0.98 (0.92–1.04)	0.90 (0.84–0.96)	0.97 (0.90–1.04)	0.02
EULAR good response*	*Ref.*	0.82 (0.70–0.96)	0.95 (0.80–1.12)	0.84 (0.70–1.01)	0.96 (0.79–1.17)	0.10
DAS28 remission*	*Ref.*	0.83 (0.70–0.98)	1.02 (0.85–1.21)	0.89 (0.74–1.08)	1.00 (0.82–1.23)	0.12
HAQ Improvement*	*Ref.*	0.82 (0.70–0.96)	1.04 (0.89–1.21)	0.86 (0.73–1.03)	0.86 (0.71–1.05)	0.02
28 Joint count = 0*	*Ref.*	0.74 (0.61–0.89)	0.91 (0.75–1.11)	0.85 (0.69–1.04)	0.91 (0.73–1.13)	0.03

*LUNDEX corrected (1). †Sex, age, disease duration, RF, co-treatment (methotrexate, glucocorticoids.)

of *in utero* fetus exposure during the second and third trimesters. These results support continuation of CZP treatment during pregnancy.

References:
[1] de Man Y. Arthritis Rheum 2009;60:3196–206.
[2] Morales M. Hepatogastroenterology 2000;47:1595–8.
[3] Ng S. Expert Rev Clin Immunol 2013;9:161–73.
[4] Østensen M. Curr Opin Pharmacol 2013;13:470–5.
[5] Porter C. J Reprod Immunol 2016;116:7–12.
[6] Mahadevan U. Clin Gastroenterol Hepatol 2013;11:286–92.
[7] Lacroix B. Gastroenterol 2010;138:S163–4.

Acknowledgements: This study was funded by UCB Pharma. We are indebted to the mothers and their infants for their altruistic participation. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: X. Mariette Grant/research support from: Biogen, Pfizer, UCB Pharma, Consultant for: Bristol-Myers Squibb, GlaxoSmithKline, LFB, Pfizer, UCB Pharma, A. Flynn Grant/research support from: UCB Pharma, F. Förger Grant/research support from: UCB Pharma, Speakers bureau: Mepha, Roche, UCB Pharma, A. Moltó Grant/research support from: MSD, AbbVie, Pfizer, UCB Pharma, Consultant for: MSD, AbbVie, Pfizer, UCB Pharma, R.-M. Flipo Consultant for: UCB Pharma, A. van Tubergen Grant/research support from: Pfizer, AbbVie, UCB Pharma, Janssen-Cilag, Celgene, Novartis, MSD, Consultant for: AbbVie, Novartis, Janssen-Cilag, Pfizer, Speakers bureau: MSD, Janssen-Cilag, Pfizer, L. Shaughnessy Employee of: UCB Pharma, J. Simpson Employee of: UCB Pharma, M. Teil Employee of: UCB Pharma, E. Helmer Employee of: UCB Pharma, M. Wang Employee of: UCB Pharma, E. Chakravarty Grant/research support from: UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.1640

OP0018 TOOL AND THRESHOLD PREDICTING A SUCCESSFUL BIOLOGICAL DMARDS TAPERING IN PATIENTS WITH RA REMISSION DETERMINATION

C. Barral[1], D. Hajage[2], B. Fautrel[2], P. Lafforgue[3], F. Tubach[2], T. Pham[3]. *[1]Aix Marseille University, APHM, Marseille; [2]Univ. Paris Diderot, Sorbonne, APHP, Paris; [3]Aix Marseille University, APHM, Marseille, France*

Background: Tapering trials confirmed the feasibility of TNF inhibitors (TNFi) tapering for a relevant proportion of patients in remission and/or low disease activity. However, there are no consensual predictors of a good response to therapeutic spacing among patients with rheumatoid arthritis (RA) in remission.

Objectives: To determine the most predictive tool and threshold of a successful TNFi tapering.

Methods: *Population:* The Spacing of TNF-blocker injections in Rheumatoid Arthritis Study (STRASS) trial included 137 RA patients fulfilled the ACR 1987 criteria with sustained (at least 6 months) DAS28 <2.6. Patients were randomly assigned to one of the two following strategies: in the Maintain arm, patients continued to receive TNFi at the standard full regimen and in the Spacing arm, the strategy applied progressive spacing of ADA or ETN subcutaneous injections up to discontinuation at the forth step in the spacing arm. We used the data of the Spacing arm.

Analysis: The performances of several variables (DAS28, SDAI, CDAI, CRP, ACPA status, HAQ, patient/physician global assessment, and booleen remission criteria) were assessed for the prediction of successful TNFi tapering, defined as reaching at least 25% tapering of the full regimen during at least 6 months, using sensitivity and specificity for dichotomous variables, or the area under the ROC curve (AUC) and its 95% confidence interval for continuous variables. A predictive score of successful tapering was constructed using LASSO regression modeling technique to avoid overfitting (R software version 3.2.1).

Results: The main characteristic of the 64 patients of the Spacing arm were the following (mean ± SD): age 54.3±10.7 years, disease duration 8.3±5.4 years, and DAS 28 1.9±0.6.

The baseline variables were similar between patients who failed or succeeded at TNFi spacing, except for the HAQ score (0.30 in the group success and 0.89 in the failure group, p=0.01) and the CRP (2.35 mg/l versus 3.48 mg/l, respectively, p=0.02).

Baseline variables performance in predicting successful TNFi spacing: None of the tested variables was able to predict successful TNFi spacing, except the HAQ score and the CRP. A HAQ threshold $\geq$1.125 had a specificity (Spe) of 93% and an AUC: 0.713 (CI95%: 0.540–0.886). A CRP threshold $\geq$6.8 mg/l had a Spe of 0.97 and an AUC: 0.689 (CI95%: 0.547–0.831).

Composite criteria: A composite criteria able to predict successful TNFi spacing has been elaborated, including ACPA status, Boolean criteria, SDAI, CRP and HAQ. A composite score lower than 0.502 was able to predict a successful TNFi spacing: Spe: 100%; Se: 54%; AUC: 0.829 (CI95%: 0.671 - 0.986).

Conclusions: The remission maintenance in rheumatoid arthritis after TNFi spacing is possible. Our results showed that in a population of RA patients in remission with TNFi, baseline HAQ and CRP are independent predictor factors of successful tapering. We have developed a composite index able to predict successful TNFi spacing, with an AUC of 0.829 and a specificity of 100%. A validation study will be needed to confirm its ability to select patients for treatment decrease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5786

OP0019 DMARD WITHDRAWAL IN RA PATIENTS ACHIEVING THERAPEUTIC RESPONSE WITH CERTOLIZUMAB PEGOL COMBINED WITH DMARDS: INTERIM RESULTS FROM A CANADIAN OBSERVATIONAL RANDOMIZED STUDY

J. Pope[1], E. Rampakakis[2], E. Grant[3], L. Bessette[4], J. Lazovskis[5], B. Haraoui[6], J.S. Sampalis[2,7]. *[1]Medicine, University of Western Ontario, London; [2]JSS Medical Research, St-Laurent; [3]Private Practice, Saint John; [4]Medicine, Laval University, Quebec; [5]Riverside Professional Centre, Sydney; [6]Institut de Rhumatologie de Montréal; [7]McGill University, Montreal, Canada*

Background: The efficacy and safety of certolizumab pegol in the treatment of adult patients with moderate to severe rheumatoid arthritis (RA), when administered either in combination with methotrexate (MTX) or as monotherapy, has been previously shown in several controlled clinical trials. However, a detailed assessment of certolizumab pegol in combination with a wide range of non-biologic disease-modifying drugs (nbDMARDs) used in real-life routine clinical practice is lacking compared to switching to monotherapy after achieving a response when added to nbDMARD(s).

Objectives: The objective is to compare the effectiveness and tolerability of certolizumab pegol given as add-on to nbDMARDs, including MTX and others, or as monotherapy after achieving a DAS28(ESR) improvement of $\geq$1.2 In this descriptive interim analysis, preliminary data on the effectiveness of certolizumab pegol given in combination nbDMARDs or monotherapy, are presented.

Methods: RA patients who had certolizumab pegol added to their existing DMARD regimen due to inadequate response to their nbDMARD(s) were eligible. At 3 or 6 months, those patients who achieved a change in DAS28 of $\geq$1.2 were randomized to continue combination therapy (Combination group) or withdraw nbDMARD therapy (Monotherapy group) and be followed for 18 months. A sample size of 125 randomized patients per group was calculated to have 100 randomized (50 per group) to find a difference of 15% in response.

Results: A total of 121 patients were enrolled, of whom 79 were randomized to continue combination therapy (n=35) or withdraw nbDMARDs (n=44). No significant differences were observed between-groups in baseline age, gender (83% vs. 71% female), race (89% vs. 91% Caucasian), rheumatoid factor status (56% vs. 60% positive), or prior biologic experience (17% vs. 11%).

At 18 months, upon adjusting for baseline scores, similar improvements were observed between groups in DAS28 ESR (-2.1 vs. -2.0). Furthermore, the odds of achieving DAS28 LDA (OR [95% CI]: 0.96 [0.28–3.31]), ΔDAS28$>$1.2 (0.97 [0.29–3.26]), or both (1.00 [0.29–1.49]), were not different between the Combination and Monotherapy groups. Similarly, no differences were observed between groups at 12 months of treatment with respect to these outcomes.

Conclusions: The results of this interim analysis suggest that, among RA patients achieving a therapeutic response when on combination therapy with certolizumab pegol and nbDMARDs, nbDMARDs could be withdrawn without impact on treatment effectiveness over the next year. Additional analyses with the full number of patients will be conducted to confirm this finding.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6654

OP0020 ASSESSMENT OF 3-MONTH CHANGES IN BONE MICROSTRUCTURE UNDER ANTI-TNFα THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS USING HR-PQCT

T. Shimizu[1], H.J. Choi[1], U. Heilmeier[1], M. Tanaka[1], A.J. Burghardt[1], J. Gong[1], N. Chanchek[1], T.M. Link[1], J. Graf[2], J.B. Imboden[2], X. Li[1]. *[1]Department of Radiology & Biomedical Imaging, Musculoskeletal Quantitative Imaging Research; [2]Department of Medicine, Division of Rheumatology, University of California San Francisco, San Francisco, United States*

Background: Bone erosions are usually thought to be irreversible and occur in the first few months of RA onset. With its resolution of up to 81 μm, HR-pQCT has emerged as valuable tool to assess bone changes in RA[(1,2)]. Although one previous study showed minimal erosive progression in patients with RA one year after TNFα inhibition therapy [(3)], no studies have investigated yet the very early bone changes after the initiation of anti-TNFα treatment.

Objectives: To investigate the early changes in bone erosion progression and bone microarchitecture in the MCP joints and wrist of RA patients using HR-pQCT, radiographs, and 3T MRI after 3 months of anti-TNFα treatment.

Methods: 26 RA patients underwent 3T MRI wrist scans and HR-pQCT scans of the MCP and wrist joints at baseline (BL) and at 3 months (3M). Radiographs were obtained at the baseline time point only. DAS28 was assessed at BL and 3M. Patients were divided into two groups: the anti-TNFα group and the MTX-only group.HR-pQCT-derived erosion volume, joint volume/width and bone microarchitectural parameters were computed using methods previously developed[(4–6)], and the joint destruction was assessed via Sharp and RAMRIS scorings using radiographs and MR images respectively.

Results: Patients in the Anti-TNFα group were slightly younger than patients in the MTX only group and had a higher initial DAS28 score,but otherwise displayed similar anthropometerics and demographics (Table).

DAS scores significantly improved in the anti-TNFα group from BL to 3M (Fig. A). 75 erosions were identified at BL by HR-pQCT. The anti-TNFα group showed a significant decrease of erosion volume from BL to 3M at MCH3 (with decreasing trend at MCH2 and wrist). The MTX-only group in contrast, displayed significant

Table 1. Characteristics of patients

	All patients (n=26)	MTX only (n=9)	Anti-TNFα (n=17)	*p*
Age (years)	51.9±15.4	60.0±15.1	47.7±13.8	0.056
Sex (Female :Male)	21:5	6:3	15:2	0.331
Disease duration (years)	6.5±5.4	7.5±5.0	5.7±5.6	0.518
BMI (kg/m^2)	28.3±7.1	25.2±5.1	30.1±7.6	0.109
DAS28 -ESR	4.27±2.03	2.17±0.53	5.79±1.08	<0.001
DAS28 -CRP	3.82±1.88	1.93±0.61	5.19±1.09	<0.001

increases in erosion volume at MCH2 and wrist despite low disease activity (Fig. B). In the anti-TNFα group, joint space width and volume of the MCP joints decreased significantly from BL to 3M and were positively correlated with erosion volume changes. Although microstructural parameters at the wrist and MCP remained largely unchanged, erosion volume changes were significantly negatively correlated with changes of trabecular BMD in the anti-TNFα group (Fig. C). No significant correlations were observed between HR-pQCT parameters and RAMRIS and DAS scores.

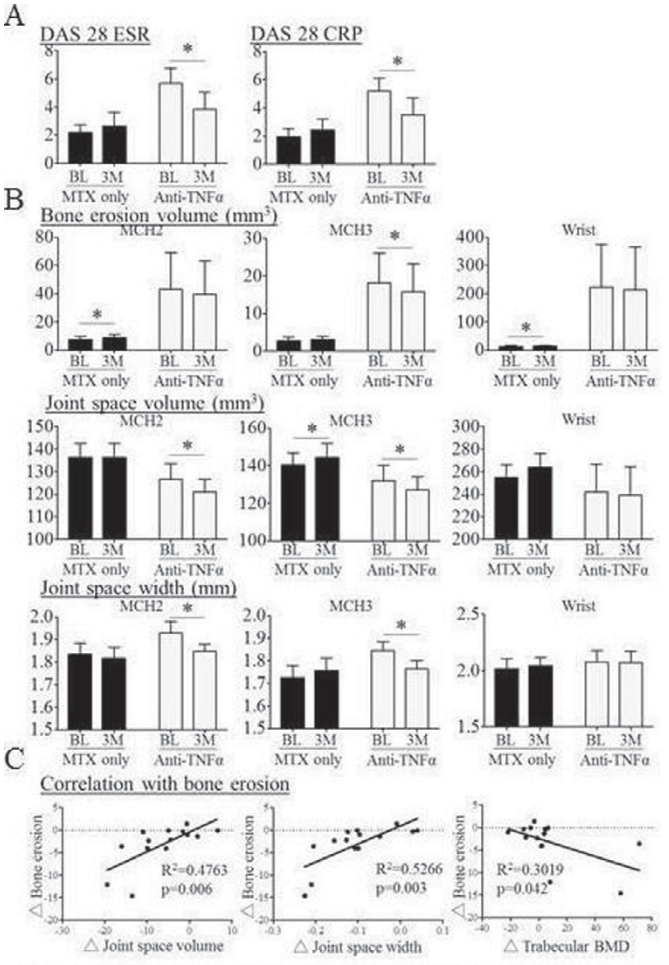


Figure. (A) Comparisons of changes of DAS 28 ESR and CRP from baseline (BL) to 3-months (3M). (B) Comparisons of changes of bone microarchitecture parameters from BL to 3M. *p<0.05; paired T test .(C) Spearman correlations between changes of erosion volume and each bone parameter in MCP in the anti-TNFα group

Conclusions: We found that anti-TNFα treatment can prevent erosion progression and deterioration of bone microarchitecture within the first 3 months of treatment. HR-pQCT can serve as a sensitive and powerful tool to quantify bone changes and monitor RA treatment even over short time periods.

References:
[1] Barnabe C et al. Nat Rev Rheumatol. 2015.
[2] Tam LS et al. J Rheumatol. 2016.
[3] Moller U et al. Ann Rheum Dis. 2009.
[4] Srikhum W et al. J Rheumatol. 2013.
[5] Yang H et al. Int J Rheum Dis. 2015.
[6] Burghardt AJ et al. Ann Biomed Eng. 2013.

Acknowledgements: The study was supported by UCB Pharma Inc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5321

OP0021 EFFICACY AND SAFETY RESULTS OF A PHASE III STUDY COMPARING FKB327, AN ADALIMUMAB BIOSIMILAR, WITH THE ADALIMUMAB REFERENCE PRODUCT IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

R. Alten[1], J. Glover[2], N. Matsunaga[3], D. Chisholm[4], M. Genovese[5]. *[1]University Medicine Berlin, Berlin, Germany; [2]Coephycient Pharmaceutical Consultancy, Guildford, United Kingdom; [3]Fujifilm Kyowa Kirin Biologics, Chiyoda-ku, Tokyo, Japan; [4]Fujifilm Kyowa Kirin Biologics, Galashiels, United Kingdom; [5]Stanford University, Palo Alto, CA, United States*

Background: FKB327 is a proposed biosimilar of the adalimumab reference product (ADL). This randomised, double-blind, Phase III study (NCT02260791; FKB327-002) evaluated the therapeutic equivalence of FKB327 and ADL in patients (pts) with active rheumatoid arthritis (RA) inadequately controlled on methotrexate (MTX).

Objectives: To assess the efficacy, safety, pharmacokinetics (PK) and immunogenicity of FKB327 compared with ADL in pts with active RA.

Methods: Pts aged ≥18 years with moderate to severe, active RA for ≥3 months and taking MTX for ≥3 months (10–25 mg/week [wk] stable dose for ≥8 wks) were enrolled. Pts were randomised 1:1 to receive FKB327 or ADL (40 mg subcutaneous injection) every 2 wks with continuing MTX, stratified by prior biologic treatment (yes/no) and screening disease activity (Disease Activity Score 28 using C-reactive protein [DAS28-CRP] ≤5.1/>5.1). The primary efficacy endpoint was American College of Rheumatology (ACR) 20 response rate at Wk 24; equivalence margins of ±13% were prespecified for a two-sided 95% confidence interval (CI) based on ADL treatment effect in previous studies. Secondary endpoints included ACR20 response rate over time, DAS28-CRP at Wk 24 and over time. Safety was assessed by the incidence/severity of adverse events (AEs) and laboratory abnormalities.

Results: 730 pts from 105 sites in 12 countries were randomised; 728 pts were treated with either FKB327 (n=366) or ADL (n=362). Demographics and baseline RA characteristics were comparable between the groups, with overall mean age of 55.3 years, mean DAS28-CRP score of 6.1 and mean MTX dose of 15.7 mg/wk. ACR20 response rates at Wk 24 (full analysis set) were comparable between the FKB327 (270/363; 74.4%) and ADL groups (271/358; 75.7%). 95% CIs for treatment difference (FKB327 – ADL: –7.6 to 5.0) fell within the ±13% equivalence margins, meeting the primary study objective. ACR20 response rates over time overlapped during Wks 4–24 (Figure 1). Least squares mean DAS28-CRP at Wk 24 were 3.43 on FKB327 and 3.42 on ADL and were equivalent using prespecified margins; changes in scores over time were also comparable. The proportions of pts reporting treatment-emergent AEs (TEAEs) on FKB327 or ADL were similar (FKB327 55.5% vs ADL 61.6%); AEs were mainly mild or moderate. The most common TEAEs (≥5%) were nasopharyngitis (7.1% vs 8.0%) and upper respiratory tract infection (3.6% vs 5.0%). Incidences of serious AEs were similar (4.1% vs 5.2%). One death due to treatment-related disseminated tuberculosis (TB) was reported in the FKB327 group; reports of active TB were slightly higher with ADL (1 vs 3 pts). Mean serum trough concentration-time profiles of the two groups were comparable. The prevalence and titres of antidrug antibodies (ADA) were similar, including at final sampling (57.9% vs 55.8%).

Figure 1. ACR20 response rate by time (full analysis set)

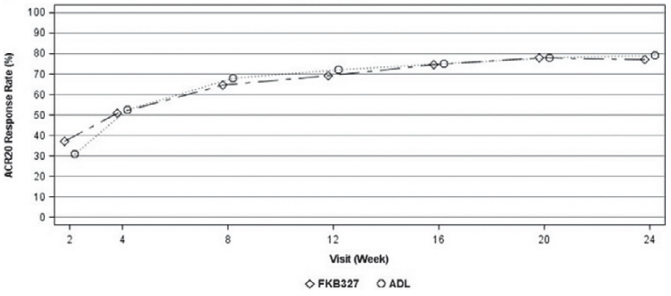


Figure 1

Conclusions: The study met its prespecified equivalency endpoint for ACR20 response rate at Wk 24, with comparable rates over time. Safety profiles, ADA formation and PK were also similar, supporting the comparability of FKB327 and ADL in pts with active RA.

Disclosure of Interest: R. Alten Consultant for: Fujifilm Kyowa Kirin Biologics Co., Ltd, J. Glover Consultant for: Fujifilm Kyowa Kirin Biologics Co., Ltd, N. Matsunaga Employee of: Fujifilm Kyowa Kirin Biologics Co., Ltd, D. Chisholm Employee of: Fujifilm Kyowa Kirin Biologics Co., Ltd, M. Genovese Consultant for: Fujifilm Kyowa Kirin Biologics Co., Ltd, Abbvie, Amgen, Boehringer Ingelheim, Pfizer, Samsung Bioepis

DOI: 10.1136/annrheumdis-2017-eular.2220

OP0022 TNFI AND TOFACITINIB MONOTHERAPY AND COMPARATIVE EFFECTIVENESS IN CLINICAL PRACTICE: RESULTS FROM CORRONA REGISTRY

G.W. Reed[1,2], R.A. Gerber[3], Y. Shan[1], L. Takiya[4], K.J. Dandreo[1], D. Gruben[3], J.M. Kremer[5], G.V. Wallenstein[3]. *[1]Corrona, LLC, Southborough; [2]UMass Medical School, Worcester; [3]Pfizer, Inc., Groton; [4]Pfizer, Inc., Collegeville; [5]Albany Medical College, Albany, United States*

Background: TNF inhibitors (TNFi) can be used as monotherapy (mono) or in combination (combo) with conventional DMARDS (cDMARDS). Data from randomized clinical trials and European registries suggest there is evidence of better effectiveness of TNFi combo therapy than mono. Effectiveness of TNFi mono vs combo in US clinical practice, in particular among biologic naïve and experienced patients, has not been assessed. There have also been no assessments of tofacitinib (tofa) mono vs tofa combo nor tofa mono vs TNFi combo in US clinical practice. Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA.
Objectives: This study quantifies the prevalence and effectiveness of TNFi monotherapy use compared to TNFi combination therapy by line of therapy in US clinical practice. Secondary objectives were to compare tofa monotherapy use and effectiveness separately to tofa combo and to TNFi combo therapies.
Methods: RA patients initiating a TNFi (adalimumab, etanercept, infliximab, golimumab, certolizumab pegol) or tofa with a six month follow-up in Corrona US were identified. A subcohort of TNFi initiations after 11/6/2012 (market approval of tofa) were used for comparisons with tofa initiators. We defined combo therapy as TNFi or tofa used with MTX only and mono as no use of any cDMARD. The primary outcome was achieving LDA (low disease activity) or remission based on CDAI ($\leq$10) at 6 months. Patients switching to another biologic prior to 6 months were defined as non-responders. Secondary outcomes included modified ACR20/50/70 and mean change in CDAI. Combo and mono initiators were matched within line of therapy using a propensity score. Covariates for the model were selected if the standardized mean difference between the groups $>$0.1.
Results: From 10/2001 to 8/2016 there were 7976 eligible TNFi initiations in Corrona, with 2511 (31%) mono initiations. Mono by line of therapy was 21%, 36% and 42% for 2nd, 3rd and 4th line therapy, respectively. There were 555 tofa initiations with 338 (61%) mono and mono rates of 47%, 58% and 63% for 2nd, 3rd and 4th line therapy, respectively. In the matched populations, across outcome measures (Table 1), TNFi combo was more effective than TNFi mono in 2nd line therapy (55.6% LDA vs 47.1% LDA) and differences diminished with 3rd line (43.2% vs 36.6%) and 4th line (32.0% vs 34.0%). Tofa combo therapy was similar to mono in the matched 3rd and 4th + line populations combined (35.2% LDA vs 31.1% LDA). Tofa mono was similar to TNFi combo therapy in the matched 3rd and 4th + line populations combined (33.6% LDA vs 37.5% LDA).

Table 1 Matched Patients		TNF Combo vs TNF Mono			Tofa Combo vs Tofa Mono	TNFi Combo vs Tofa Mono
		2nd line* (n=1206)	3rd line* (n=1180)	4th line* (n=800)	3rd and 4th line (n=244)	3rd and 4th line (n=304)
LDA	OR [95% CI]	1.3 [1.0-1.6]	1.3 [1.0-1.7]	0.9 [0.7-1.2]	1.2 [0.7-2.1]	1.2 [0.7 – 1.9]
mACR20	OR [95% CI]	1.2 [1.0-1.6]	1.2 [0.9-1.6]	1.2 [0.9-1.7]	0.8 [0.4-1.6]	0.8 [0.5 – 1.4]
ΔCDAI	meanΔ [95% CI]	-0.7 [-2.2–0.8]	-1.1 [-2.6 - 0.3]	-1.5 [-3.5- 0.4]	-0.3 [-3.9 –3.3]	0.6 [-2.6 – 3.7]

*Line of Therapy defined as follows: 2nd line = prior use of at least one cDMARD and no prior use of any biologic; 3rd line = prior use of at least one cDMARD and prior use of 1 biologic; 4th line+ = prior use of at least one cDMARD and prior use of 2+ biologics

Conclusions: TNFi monotherapy is common in U.S. clinical practice. TNFi monotherapy is less effective than combination therapy especially in biologic naïve patients or with one prior biologic. There is no evidence that tofacitinib monotherapy is less effective than tofa combination therapy or TNFi combination therapy in the outcome measures reported.
Acknowledgements: This study is sponsored by Corrona, LLC. The Corrona RA registry has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, Astra Zeneca, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.
Disclosure of Interest: G. Reed Shareholder of: Corrona, LLC, Employee of: Corrona, LLC, R. Gerber Shareholder of: Pfizer, Employee of: Pfizer, Y. Shan Employee of: Corrona, LLC, L. Takiya Shareholder of: Pfizer, Employee of: Pfizer, K. Dandreo Employee of: Corrona, LLC, D. Gruben Shareholder of: Pfizer, Employee of: Pfizer, J. Kremer Shareholder of: Corrona, LLC, Grant/research support from: AbbVie, Genentech, Lilly, Novartis, Pfizer, Consultant for: AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, Employee of: Corrona, LLC, G. Wallenstein Shareholder of: Pfizer, Employee of: Pfizer
DOI: 10.1136/annrheumdis-2017-eular.1939

WEDNESDAY, 14 JUNE 2017

Progress in managment of SpA

OP0023 FOUR-YEAR IMAGING OUTCOMES IN AXIAL SPONDYLOARTHRITIS PATIENTS TREATED WITH CERTOLIZUMAB PEGOL, INCLUDING PATIENTS WITH ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

D. van der Heijde[1], X. Baraliakos[2], K.G. Hermann[3], R. Landewé[4], P.M. Machado[5], W. Maksymowych[6], O. Davies[7], N. de Peyrecave[7], B. Hoepken[8], L. Bauer[8], T. Nurminen[8], J. Braun[9]. *[1]Leiden University Medical Center, Leiden, Netherlands; [2]Ruhr-University Bochum, Herne; [3]Charité Medical School, Berlin, Germany; [4]Academic Medical Center, Amsterdam & Atrium Medical Center Heerlen, Amsterdam, Netherlands; [5]University College London, London, United Kingdom; [6]University of Alberta, Edmonton, Canada; [7]UCB Pharma, Slough, United Kingdom; [8]UCB Pharma, Monheim; [9]Rheumazentrum Ruhrgebiet, Herne, Germany*

Background: RAPID-axSpA (NCT01087762) was a long-term study in patients (pts) with axial spondyloarthritis (axSpA) treated with certolizumab pegol (CZP). This is the first report of 4-year imaging results in CZP-treated axSpA pts, including ankylosing spondylitis (AS) and non-radiographic (nr-)axSpA.
Objectives: To report 4-year X-ray and MRI data in CZP-treated axSpA pts.
Methods: RAPID-axSpA[1] was double-blind and placebo (PBO)-controlled to Wk24, dose-blind to Wk48, and open-label to Wk204. Pts fulfilling ASAS axSpA criteria were stratified using a local read according to presence/absence of radiographic sacroiliitis (AS/nr-axSpA) at randomization and had active disease. Wk0 CZP-randomized pts (200mg Q2W/400mg Q4W) continued assigned dose; PBO pts received CZP after Wk16/24. Centrally-read lateral X-rays of cervical/lumbar spine at baseline (BL), Wk96, and Wk204 were assessed using the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). Sacroiliac (SI) joint X-rays were scored for sacroiliitis at BL and Wk204. MRI scans performed at BL, Wks12, 48, 96, and 204 were assessed using Spondyloarthritis Research Consortium of Canada (SPARCC) score for SI joints and Berlin score for spine. Data are shown for CZP-treated pts including those starting on PBO. SI joint X-rays (recorded at BL and Wk204) and magnetic resonance imaging (MRI) observed data are presented for pts with valid assessments. mSASSS data were estimated for all pts using observed data and by mixed model for repeated measures (MMRM) analysis.
Results: Of 315 CZP-treated pts, 196 had available spinal X-rays and were included in MMRM analyses (BL mean mSASSS: 9.47). 158 pts had MRI assessments (BL mean SPARCC: 8.17 [n=151]; Berlin score: 6.10 [n=153]) and 137 pts had SI joint X-rays at BL and Wk204 (BL: 67.9% radiographic sacroiliitis). In AS pts, mean mSASSS change between BL and Wk204 was 0.98; 0.67 from BL to Wk96, and 0.31 from Wk96 to Wk204 (0.06, -0.01, and 0.07 respectively for nr-axSpA) (Table A). MMRM estimates were similar to observed values (0.62 and 0.70, respectively [axSpA Wk204 mean change]). Limited changes in SI joint X-ray grading were observed to Wk204: only 4.5% of pts progressed to AS, whilst 4.3% moved from an AS classification to nr-axSpA. MRI assessments showed sustained improvement (Table B).

Table A: Mixed model for repeated measures (MMRM) estimates of mSASSS to Week 204 of the RAPID-axSpA study for all patients treated with CZP

	Baseline	Week 96		Week 204	
	LS mean score (95% CI)	LS mean score (95% CI)	LS mean change from BL (95% CI)	LS mean score (95% CI)	LS mean change from BL (95% CI)
axSpA (n=196)	9.47 (7.20–11.73)	9.86 (7.52–12.21)	0.40 (0.11–0.69)	10.08 (7.71–12.46)	0.62 (0.22–1.01)
AS (n=113)	13.17 (9.79–16.56)	13.84 (10.35–17.34)	0.67 (0.21–1.13)	14.16 (10.61–17.71)	0.98 (0.34–1.63)
nr-axSpA (n=83)	4.42 (2.02–6.82)	4.41 (1.97–6.84)	-0.01 (-0.19–0.17)	4.47 (2.06–6.88)	0.06 (-0.17–0.28)

Table B: MRI outcomes to Week 204 of the RAPID-axSpA study for all patients treated with CZP (observed values)

	Baseline		Week 204		
	n	Mean score (SD)	n	Mean score (SD)	Mean change from BL (SD)
SI Joint Inflammation (SPARCC)					
axSpA	151	8.17 (13.08)	72	1.90 (5.00)	-4.70 (9.40)
AS	91	8.50 (13.83)	41	1.84 (5.60)	-4.35 (8.49)
nr-axSpA	60	7.66 (11.93)	31	1.97 (4.18)	-5.16 (10.60)
Spinal Inflammation (Berlin)					
axSpA	153	6.10 (8.68)	82	2.13 (4.46)	-4.84 (8.33)
AS	92	7.38 (8.80)	50	2.62 (5.23)	-5.51 (7.61)
nr-axSpA	61	4.17 (8.21)	32	1.36 (2.75)	-3.78 (9.38)

Data shown for all CZP-treated patients with valid assessments (including patients re-randomized from PBO at Week 16 or 24). mSASSS: modified Stokes Ankylosing Spondylitis Spine Score; SPARCC: Spondyloarthritis Research Consortium of Canada; LS: least squares. SI: sacroiliac.

Conclusions: This is the first trial to report imaging data in both AS and nr-axSpA pts over 4 years. Limited spinal radiographic progression was observed in CZP-treated pts with lower progression between Wks96 and 204 compared with the first 96 wks. Limited change in radiographic sacroiliitis was observed. Early reductions in MRI inflammation were maintained to Wk204.

References:

[1] Landewé R. Ann Rheum Dis 2014;73:39–47.

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB Pharma, Employee of: Director of Imaging Rheumatology BV, X. Baraliakos Grant/research support from: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen, MSD, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen, MSD, Novartis, Pfizer, UCB Pharma, K. G. Hermann Speakers bureau: AbbVie, MSD, Pfizer, UCB Pharma, R. Landewé Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, Consultant for: Abbott, Ablynx, Amgen, Astra-Zeneca, Bristol-Myers Squibb, Centocor, GlaxoSmithKline, Novartis, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, Speakers bureau: Abbott, Amgen, Bristol-Myers Squibb, Centocor, Merck, Pfizer, Roche, Schering-Plough, UCB Pharma, Wyeth, P. Machado Consultant for: AbbVie, Centocor, Janssen, MSD, Novartis, Pfizer, Speakers bureau: AbbVie, Centocor, Janssen, MSD, Novartis, Pfizer, W. Maksymowych Grant/research support from: AbbVie, Amgen, Eli-Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, UCB Pharma, Consultant for: AbbVie, Amgen, Eli-Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, UCB Pharma, Speakers bureau: AbbVie, Amgen, Eli-Lilly, Janssen, Merck, Pfizer, Synarc, Sanofi, UCB Pharma, O. Davies Shareholder of: UCB Pharma, Employee of: UCB Pharma, N. de Peyrecave Employee of: UCB Pharma, B. Hoepken Employee of: UCB Pharma, L. Bauer Shareholder of: UCB Pharma, Employee of: UCB Pharma, T. Nurminen Employee of: UCB Pharma, J. Braun Grant/research support from: Abbott, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, Consultant for: Abbott, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.1741

OP0024 DRUG TROUGH LEVELS AND ANTIDRUG ANTIBODIES IN NONSELECTED ANKYLOSING SPONDYLITIS PATIENTS USING SELF-INJECTED ANTITNF DRUGS

J. Hiltunen[1], P. Parmanne[1], T. Sokka-Isler[2], T. Lamberg[3], O. Kaipiainen-Seppänen[4], P. Isomäki[5], M. Kauppi[6], L. Pirilä[7], T. Uutela[8], R. Tuompo[1], H. Relas[1], T. Yli-Kerttula[9], H. Valleala[1], M. Romu[1], T. Rannio[2], K. Paalanen[2], A. Juha[2], P. Ekman[9], K. Tadesse[1], J. Borodina[2], P. Elfving[4], R. Peltomaa[1], M. Leirisalo-repo[1], H. Kautiainen[10], S. Jokiranta[11], K.K. Eklund[12]. *[1]Rheumatology, Helsinki University Hospital, Helsinki; [2]Rheumatology, Central Finland Central Hospital, Jyväskylä; [3]Immunobiology, United Medix Laboratories Ltd, Helsinki; [4]Rheumatology, Kuopio University Hospital, Kuopio; [5]Rheumatology, Tampere University Hospital, Tampere; [6]Rheumatology, Päijät-Hämeen Central Hospital, Helsinki; [7]Rheumatology, Turku University Hospital, Turku; [8]Rheumatology, Central Hospital of Lapland, Rovaniemi; [9]Rheumatology, Satakunta Central Hospital, Pori; [10]Unit of Primary Health Care, Helsinki University Central Hospital; [11]Research Programs Unit, Immunobiology, Helsinki University; [12]Rheumatology, Helsinki University Central Hospital, Helsinki, Finland*

Background: Immunization to biological drugs can reduce the treatment efficacy and increase the risk of adverse events.

Objectives: To determine the drug trough concentrations and anti-drug antibody (ADAb) levels of self-injected TNF-inhibitors, in non-selected patients with ankylosing spondylitis (AS) attending the rheumatological outpatient clinic, and to study the patient related factors affecting the immunization to antiTNF drugs.

Methods: A total of 313 patients with AS were recruited. A blood sample, taken 1–2 days prior to next drug injection, was obtained from 273 patients. Trough concentration of the anti-TNF drugs were measured with capture-ELISA (Promonitor EIA, Progenica), the levels of ADAb with radioimmunoassay (Sanquin Laboratories, The Netherlands), and the serum TNF-blocking capacity by using an in-house reporter gene assay. The clinical activity of AS was assessed using the Bath AS Disease Activity Index (BASDAI), the Bath AS Functional Index (BASFI), and the Maastricht AS Entheses Score (MASES).

Results: ADAbs were observed in 21% of patients on adalimumab (n=99), in 0% of those on etanercept (n=83), in 3% of those on golimumab (n=79) and in 50% of those on certolizumab pegol (n=12). The BASDAI in ADAb positive patients was 1.4 (sd 1.4) and in the ADAb negative patients 2.0 (sd 1.8 p=0.060). Factors affecting the immunization to biological drug could be further analyzed in patients using adalimumab. Trough drug concentrations of adalimumab correlated with the presence of ADAb (r=-0.54, rp<0.0001). In adalimumab users higher BMI was associated with the presence ADAb (p=0.019, adjusted for gender, age, and the time of biological use). Of patients who used methotrexate (MTX) 12% were ADAb positive and of those who did not use MTX 28% were ADAb positive (p=0.048 adjusted for gender, age, weight, and the time of biological use). The use of sulphasalazine was not associated with lower number of ADAb positive patients. Of adalimumab users with ADAb+ the mean BASDAI was 1.2 (sd 1.4) and of those without ADAb 1.9 (sd 1.9) (p=0.091). Of adalimumab users the drug concentration was in the target range (5–10 mg/l) in only 33% of patients.

Conclusions: The disease activity of AS patients using self injected antiTNF drugs was low. The immunization to adalimumab was relatively common in nonselected AS patient population. However, no clear association was observed between the presense of ADAb and the disease activity.

Acknowledgements: The study was financially supported by Pfizer

Disclosure of Interest: J. Hiltunen: None declared, P. Parmanne: None declared, T. Sokka-Isler: None declared, T. Lamberg: None declared, O. Kaipiainen-Seppänen: None declared, P. Isomäki: None declared, M. Kauppi: None declared, L. Pirilä: None declared, T. Uutela: None declared, R. Tuompo: None declared, H. Relas: None declared, T. Yli-Kerttula: None declared, H. Valleala: None declared, M. Romu: None declared, T. Rannio: None declared, K. Paalanen: None declared, A. Juha: None declared, P. Ekman: None declared, K. Tadesse: None declared, J. Borodina: None declared, P. Elfving: None declared, R. Peltomaa: None declared, M. Leirisalo-repo: None declared, H. Kautiainen: None declared, S. Jokiranta: None declared, K. Eklund Grant/research support from: Pfizer has supported the study financially, Consultant for: Advisory board meetings BMS, MSD, Pfizer, Abbvie, Speakers bureau: Lectures: BMS, Roche, Pfizer, Novartis

DOI: 10.1136/annrheumdis-2017-eular.5342

OP0025 ANTIDRUG ANTIBODIES DETECTION IS STRONGLY INFLUENCED BY THE TYPE OF ASSAY USED

J. Ruwaard[1], A.F. Marsman[1], M.T. Nurmohamed[1,2], H. te Velthuis[3], K. Bloem[3], T. Rispens[3], G.J. Wolbink[1,3]. *[1]Amsterdam Rheumatology and immunology Center | Reade; [2]Amsterdam Rheumatology and immunology Center | VU medical center; [3]Department of Immunopathology, Sanquin Research and Landsteiner Laboratory Academic Medical Center, Amsterdam, Netherlands*

Background: Direct comparison of immunogenicity data is hampered due to different assays used with different sensitivity for drug interference. This is the first study to compare detection of antidrug antibodies (ADA) with different assays in ankylosing spondylitis (AS) patients. Studying immunogenicity in AS patients with a drug tolerant assay may contribute to a better understanding of development of ADA.

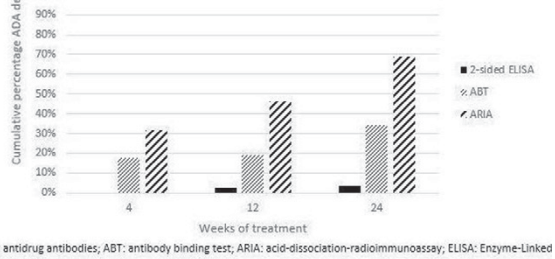
Objectives: To compare the detection of ADA in different assay techniques with differences in drug interference, acid-dissociation-radioimmunoassay (ARIA) antidrug binding test (ABT) and the more frequently used 2-sided Enzyme-linked Immuno Sorbent Assay (ELISA) in AS patients. Second, to study the relation of adalimumab drug levels with the detection of ADA.

Methods: In this study, the detection of the ADA in ARIA and ABT was compared with the detection of ADA in the 2-sided ELISA in 84 consecutive AS patient over a period of 24 weeks; at 4, 12 and 24 weeks of treatment. Adalimumab drug levels were measured using an ELISA. The assays were designed by Sanquin, Amsterdam. For the difference in drug levels we divided the patients in four different groups; all assays negative (group 0), only ARIA positive (group 1), ARIA and ABT positive, 2-sided ELISA negative (group 2) and all assays positive (group 3). We used last observation carried forward to imputate missing data.

Results: As shown in Figure 1, 26% of the patients tested positive for ADA in the ARIA compared to 14% in the ABT and no detection in the 2-sided ELISA at week 4. At weeks 12 and 24 respectively, cumulative 46% and 69% of patients, tested positive in the ARIA for ADA, compared to 19% and 35% in the ABT and 2% and 4% with the 2-sided ELISA.

Median adalimumab levels at week 24 in group 0, 1, 2 and 3 were 9.5 (5.3–13.3), 8.4 (5.3–11.0), 2.8 (0.9–4.3) and 0.002 (0.0–1.3) respectively. No significant differences were found in median adalimumab levels between patients with no ADA detection and patients tested positive in only the ARIA, respectively, 8.4 (5.3–11.0) and 9.5 (5.3–13.3) p=0.385. However, when both ARIA and ABT tested positive, drug levels significantly differed from patients with no ADA detection, 2.8

Figure 1. Cumulative percentages of ADA detection per assay type at different time points



ADA: antidrug antibodies; ABT: antibody binding test; ARIA: acid-dissociation-radioimmunoassay; ELISA: Enzyme-Linked Immuno Sorbent Assay

(0.9–4.3) and 9.5 (5.3–13.3), p=0.000. When patients tested positive in the ARIA, ABT and the 2-sided ELISA almost all patients had undetectable drug levels.
Conclusions: The fast majority of the AS patients develop ADA. The ARIA detects more ADA compared to the assays susceptible for drug interference, the ABT and the more frequently used 2-sided ELISA. Immunogenicity data should be interpreted with the knowledge of the assay and in context of drug levels.
Disclosure of Interest: J. Ruwaard: None declared, A. Marsman: None declared, M. Nurmohamed: None declared, H. te Velthuis: None declared, K. Bloem: None declared, T. Rispens Speakers bureau: Pfizer, AbbVie, G. J. Wolbink Grant/research support from: Pfizer, Speakers bureau: Pfizer, AbbVie, UCB
DOI: 10.1136/annrheumdis-2017-eular.6149

OP0026 HIGH DRUG-FREE REMISSION IN EARLY PERIPHERAL SPONDYLOARTHRITIS AFTER INDUCTION THERAPY WITH GOLIMUMAB

P. Carron[1,2], G. Varkas[1,2], H. Cypers[1,2], L. Van Praet[1], D. Elewaut[1,2], F. Van den Bosch[1,2]. *[1]Rheumatology, Univeristy of Ghent; [2]VIB Inflammation Research Center, Ghent University, Gent, Belgium*

Background: In rheumatoid arthritis there is accumulating evidence for a so-called "window of opportunity" remission induction treatment at an early stage of the disease. Whether a similar concept also applies to Spondyloarthritis is currently unknown. Given the higher chance of obtaining remission or low disease activity with early aggressive (biologic) treatment in early axial SpA, one could speculate that there is at least also a possibility of a "window of opportunity" for drug-free remission in peripheral SpA (pSpA).
Objectives: To evaluate sustained drug-free clinical remission after induction therapy with golimumab in patients with active peripheral Spondyloarthritis in a very early stage of the disease.
Methods: CRESPA (Clinical REmission in peripheral SPondyloArthritis) is an ongoing monocentric study of golimumab treatment in pSpA patients. Eligible patients were $\geq$18 years and fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for pSpA. All patients had a symptom duration $<$12 weeks. Patients were randomized 2:1 to receive golimumab 50 mg every 4 weeks or matching placebo for 24 weeks. The primary endpoint was the percentage of patients achieving clinical remission at week 24, defined as the absence of arthritis, enthesitis and dactylitis on clinical examination. If patients were in clinical remission at two consecutive visits (major evaluations at week 12, 24, 36 and 48) treatment was stopped.
These patients were prospectively followed to assess the percentage of patients in sustained drug-free clinical remission, compared to those experiencing a clinical relapse of arthritis, dactylitis or enthesitis. In case of clinical relapse patients were retreated with open-label golimumab in the extension part of this trial.
Results: In total 60 patients were randomized of whom 20 received placebo and 40 golimumab. Baseline demographics and disease characteristics were generally similar between the 2 groups. At week 24 a significantly higher percentage of patients receiving golimumab achieved clinical remission compared to patients receiving placebo (75% (30/40) versus 20% (4/20); $P<0.001$). At week 12 similar results were observed (70% (28/40) versus 15% (3/20); $P<0.001$). In 49 out of the 60 patients treatment could be stopped because they fulfilled sustained clinical remission at 2 major consecutive visits. All patients had at least a follow up of 12 months after discontinuation of treatment with a maximum of follow-up of 58 months. 53% (26/49) of these patients are still in drug-free sustained clinical remission and 47% (23/49) had a clinical relapse after withdrawal. The majority of relapsed patients experienced their flare within 6 months after discontinuation.
Conclusions: In patients with active, very early peripheral spondyloarthritis, treatment with golimumab led to high percentages of clinical remission at week 12 and 24. A remarkably high percentage of patients are still in sustained drug-free clinical remission after induction therapy with golimumab which indicates a window of opportunity for drug-free remission in this disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1656

OP0027

WITHDRAWN

WITHDRAWN

OP0028 LOW DOSE IL-2 THERAPY CAN RECOVERY TH17/TREG CELL BALANCE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

D. Xu[1], J. Fan[1], Q. Chen[1], K. Qin[1], X. Li[1], C. Gao[2]. *[1]The Department of Rheumatology, The Second Hospital of Shanxi Medical University, Taiyuan, China; [2]Department of Pathology, Joint Program in Transfusion Medicine, Brigham and Women's Hospital/Children's Hospital Boston, Harvard Medical School, Boston, United States*

Background: Recent studies have shown that increased number of Th17 cells and decreased number of Treg cells in the peripheral blood contribute to ankylosing spondylitis (AS). However, current therapy for AS, including biological agents, immunosuppressant and glucocorticoid, can not correct the imbalance of Th17 and Regulatory T (Treg) cells in AS patients effectively. It has been reported that low dose IL-2 can selectively expand Treg cells and had a critical effect on homeostatic balance between the Th17 and Treg cells.
Objectives: The study is to explore the effect of low dose IL-2 therapy on the balance of Treg and Th17 cells in patients with AS and observe the efficiency and side effects of the therapy.
Methods: Seventeen patients, who met the 1984 modified New York criteria and had evidence of active inflammatory spondylitis (defined as Bath AS Disease Activity Index (BASDAI) score >4) despite of receiving standard therapy including glucocorticoid, immune-suppressants, biological agents or combination of them, were enrolled. These patients were not only given traditional treatment, but also injected subcutaneously low-dose IL-2 (50 WIU/day for 5 days). Clinical and laboratory indicators were compared before and after IL-2 treatment. The side effects were observed in the course of therapy.
Results: The number of Treg cells significantly increased after the treatment by 1 week (22.58±12.80 vs. 73.46±33.79, p<0.001). At the same time, there was a significantly decrease in the ratio of Th17/Treg cells (0.67±0.70 vs. 0.32±0.33, p=0.068). Besides, Th17 cells were also increased (12.83±9.24 vs. 19.26±13.24, p=0.054). Clinical manifestations were improved after the combination treatment of IL-2 and traditional drugs, especially BASDAI was decreased (4.57±0.61 vs. 1.98±0.83, P<0.001). No obvious adverse reactions were observed.
Conclusions: Low dose IL-2 therapy can restore and maintain the balance of Th17 and Treg cells in the active patients with AS. Manifestation improved after the combination therapy. The therapy is safe. Further research is needed to investigate long term benefits of low-dose IL-2 therapy.
References:
[1] Wright P, Utriainen L, Milling S. Dendritic cells and regulatory T cells in spondyloarthritis. Curr Opin Rheumatol. 2013; 25(4):440–7.
[2] Zambrano-Zaragoza JF, Agraz-Cibrian JM, González-Reyes C, et al. Ankylosing spondylitis: from cells to genes. Int J Inflam. 2013; 2013:501653.
[3] Klatzmann D, Abbas AK. The promise of low-dose interleukin-2 therapy for autoimmune and inflammatory diseases. Nat Rev Immunol. 2015;15(5):283–94.
[4] He J, Zhang X, Wei Y, et al. Low-dose interleukin-2 treatment selectively modulates CD4(+) T cell subsets in patients with systemic lupus erythematosus. Nat Med. 2016;22(9):991–3.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2564

OP0029 EVALUATION OF THE EFFICIENCY OF SACROILIAC JOINTS CORTICOID INJECTIONS UNDER SCAN CONTROL AND ITS RELATIONSHIP WITH THE PRESENCE OR ABSENCE OF SACROILIITIS LESIONS SEEN ON MRI OF PATIENTS WITH SPONDYLOARTHRITIS

A.M. Devauchelle[1], O. Vittecoq[1], T. Lequerre[1], P. Michelin[2], F. Vincent[2]. *[1]Rheumatology department of Rouen; [2]Radiology department of Rouen, rouen, France*

Background: Sacroiliitis is a common symptom for patients suffering from axial and/or peripheral spondyloarthritis. Several studies have demonstrated that long standing corticosteroid injections of the sacroiliac joints can reduce significantly sacroiliitis pain. However, it is difficult to identify predictive factors of good response to the infiltration.
Objectives: Hence, our purposes were to evaluate the benefit from sacroiliac long standing corticosteroid injections and to determine if MRI sacroiliac images could predict infiltration's response.
Methods: This monocentric study was conducted in real-life circumstances between January 2013 and June 2016 from a standardized procedure. Thirty-one patients having inflammatory pain originating from the sacroiliac joints were infiltrated with a long acting corticosteroid (cortivazol) under CT scan guidance. Hence, 56 sacroiliac joints were injected. To be included, patients had to suffer mainly from low back and/or buttock region in the context of axial or peripheral spondyloarthritis defined by the 2009 ASAS criteria. A contrast enhanced MRI was performed if the last MRI dated more than six months before the infiltration. The main clinical outcome was a global benefit expressed by the patient at day 15 after the infiltration (D15), 1 month (M1), 3 months (M3) and 6 months (M6).
Results: 44.1% of patients had a global benefit of at least 50% at D15, 63.6% at M1, 48.3% at M3 and 35.7% at M6. Besides, there was a decrease of the spontaneous Visual Analog Scale for pain (VAS) of the sacroiliac joint at D15, M1 and M3. Likewise, there was a decrease of the provoked VAS of the sacroiliac at D15, M1, M3 and M6. The decrease of the spontaneous VAS was at least of 50% for 35.2% of patients at D15, 41.5% at M1, 25.6% at M3 and 33.3% at M6. There was no decrease of the BASDAI, BASFI, ESR, CRP, ASDAS ESR and ASDAS CRP. Moreover, no relationship was found between the efficiency of sacroiliac infiltrations in terms of global benefit as well as of decrease of the VAS of at least 50% and the presence of sacroiliitis images on the MRI. Neither when looking at the different subtypes of sacroiliitis lesions (bone marrow oedema, synovitis, osteitis). Among the non active sacroiliitis structural lesions (erosions, subchondral sclerosis, bone brigdes...), only fatty involution was statistically more present in the group with a global improvement or a VAS of less than 50%.
Conclusions: Long acting corticosteroid infiltrations of the sacroiliac joints are useful in patients suffering from inflammatory sacroiliitis pain. However, the majority of sacroiliac joints images found on a concomitant MRI does not predict the treatment response except fatty involution that seems to be associated with a lower response. Likewise, composite indexes/scores as well as parameters of systemic inflammation are not relevant for the patients follow up in that indication.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2303

OP0030 INEQUITY IN BIOLOGIC DMARD PRESCRIPTION FOR SPA ACROSS THE GLOBE. RESULTS FROM THE ASAS COMOSPA STUDY

E. Nikiphorou[1], D. van der Heijde[2], S. Norton[1], R. Landewé[3], A. Moltó[4], M. Dougados[4], F. van den Bosch[5], S. Ramiro[2]. *[1]KCL, London, United Kingdom; [2]LUMC, Leiden; [3]ARC, Amsterdam, Netherlands; [4]Paris Descartes University, Paris, France; [5]Ghent University Hospital, Ghent, Belgium*

Background: The value of biologic DMARDs (bDMARDs) in SpA is well recognized but global access to these treatments can be limited due to high cost and other factors.
Objectives: This study explores variation in the use of bDMARDs in SpA across countries and to what extent socio-economic (SE) factors may explain variation.
Methods: Patients fulfilling the ASAS SpA criteria in the multi-national, cross-sectional ASAS COMOSPA study were studied. Multi-level logistic regression models with random intercept for country were constructed with current use of bDMARDs as the dependent variable. Contribution of socio-economic factors using country health expenditures and gross domestic product (GDP) (all low vs medium/high tertiles) as independent country-level factors, was explored in models adjusted for socio-demographic as well as clinical variables known to determine bDMARD-use in SpA.
Results: In total, 3370 patients from 22 countries were included (mean [SD] age 43 [14] years; 66% male; 88% axial disease). Across countries, 1275 (38%) were bDMARD users. Crude mean bDMARD-use varied between 5% (China) to 74% (Belgium). After adjustment for relevant socio-demographic and clinical variables, important variation in bDMARD-use across countries remained (Figure, p<0.001). Country-level socio-economic factors, specifically higher health

Figure. bDMARD uptake (%) by country. Adjusted percentage use shown along with 95% CI, based on models with socio-economic, socio-demographic and clinical variables. Crude bDMARD uptake indicated by the orange squares.

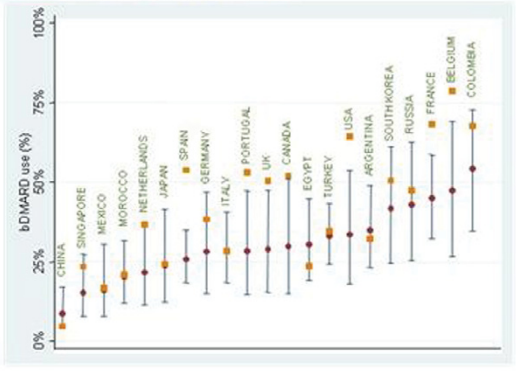


Table. Impact of country socio-economic factors on the use of bDMARDs in a model adjusting for socio-demographic and clinical variables (country included as random effects).

Independent predictors	bDMARD use OR (95% CI) (n=2758)
Country health expenditure (US dollars)	1.91(0.93,3.92)
Age (years)	1.00(0.99,1.01)
Male gender (vs females)	1.25(1.03,1.52)
Axial (vs peripheral)disease	1.55(1.09,2.22)
ASDAS (CRP based)	0.80(0.73,0.87)
Sacroiliitis on X-ray	1.38(1.09,1.74)
History of extra-articular manifestations	1.36(1.13,1.65)
BMI (kg/m²)	1.02(1.00,1.04)
Total NSAID score (0-100) in last 3 months	0.99(0.99,1.00)
Current csDMARD use	0.71(0.58,0.87)
Past csDMARD use	1.98(1.63,2.41)
Past bDMARD use	2.53(1.96,3.25)
Education (secondary/university vs primary)	0.75(0.51,1.10

expenditures were related to higher bDMARD uptake (Table), though not meeting statistical significance (OR 1.91; 95% CI 0.93,3.92). Similar findings were found with country GDP (OR 1.72;95% CI 0.83,3.57).
Conclusions: There remains important residual variation across countries in bDMARD uptake of patients with SpA followed in specialized SpA centers. This is despite adjustment of well-known factors for bDMARD use such as clinical and country-level socio-economic factors.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4480

WEDNESDAY, 14 JUNE 2017

Early diagnosis of systemic sclerosis and myositis: biomarkers and diagnostic tool

OP0031 DEVELOPMENT OF A NOVEL EPITOPE-BASED DIAGNOSTIC ASSAY FOR SYSTEMIC SCLEROSIS

G. Moroncini[1], M. Mozzicafreddo[2], M. Cuccioloni[2], A. Grieco[1], C. Paolini[1], C. Tonnini[1], S. Salvucci[1], E. Avvedimento[3], A. Funaro[4], A. Gabrielli[1].
[1]Department of Molecular and Clinical Sciences, Università Politecnica Marche, Ancona; [2]School of Biosciences and Veterinary Medicine, University of Camerino, Camerino; [3]Department of Molecular Medicine, Università Federico II, Napoli; [4]Department of Medical Sciences, University of Torino, Torino, Italy

Background: We described the conformational PDGFRα epitope of V_HPAM–Vκ16F4 agonistic autoantibody[1], cloned from memory B cells of a SSc patient, that can induce fibrosis in vivo[2]. We showed that peptides composing this epitope may be specifically recognized by serum IgG of patients with systemic sclerosis (SSc), but not of controls.
Objectives: i. To identify the immunodominant peptide within the discontinuous PDGFRα epitope of V_HPAM–Vκ16F4; ii. to identify other immunodominant epitopes recognized by agonistic autoantibodies; iii. to use these immunodominant peptides to develop an epitope-based assay for diagnosis of SSc and classification of SSc clinical subtypes.
Methods: i.The large PDGFRα peptide library used for epitope mapping of monoclonal anti-PDGFRα antibodies[1] was screened with 25 SSc (12 limited, 13 diffuse) and 25 healthy control (HC) serum samples. ii. A smaller PDGFRα peptide library containing only the top 20 conformational binders plus 20 linear and 20 conformational controls was synthesized. 60 conformational and linear peptides of a cognate protein forming a molecular complex with PDGFRα were included in the array. 20 scrambled peptides were added as negative controls. This library was screened with the same 50 serum samples. iii. A third library was synthesized, retaining the top cognate protein peptide binders, and 15 chimeric PDGFRα/cognate protein peptides, chosen among the best binders, with some nonbinding controls. This library was tested as before. Libraries were synthesized by Pepscan Presto, Netherlands. Statistical analysis was performed by Wilcoxon-Mann-Whitney test. Correlations between serological results and clinical status were made.
Results: i. An immunodominant peptide discriminating SSc from HC serum samples was identified in the first library. ii. This was confirmed by the second library, which highlighted also one immunodominant epitope from the cognate protein. Statistical analysis identified two cohorts of SSc samples (reactive vs nonreactive, the latter undistinguishable from HC) each composed by limited and diffuse SSc subtypes. iii. The third peptide library identified the chimeric peptide recognized exclusively by the reactive SSc serum samples, which were taken from patients with active, progressive disease regardless of limited vs diffuse classification, whereas the nonreactive SSc samples were taken from subjects with less active, non progressive disease.
Conclusions: We developed a conformational epitope-based assay detecting SSc-specific, agonistic, serum autoantibodies. The preliminary results suggest that this novel array may identify SSc patients with active disease, regardless of the canonical classification criteria. We propose this assay for prospective screening of large cohorts of patients affected by, or suspected for, SSc, to validate it as a tool for disease activity assessment and/or early diagnosis.
References:
[1] Moroncini G et al. Epitope specificity determines pathogenicity and detectability of anti-PDGFRα autoantibodies in systemic sclerosis. Arthritis and Rheumatology. 2015; 67(7):1891–1903.
[2] Luchetti MM et al. Induction of Scleroderma Fibrosis in Skin-Humanized Mice by Administration of Anti-Platelet-Derived Growth Factor Receptor Agonistic Autoantibodies. Arthritis & Rheumatology. 2016; 68(9):2263–73.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6009

OP0032 IS IMMUNOHISTOCHEMISTRY USEFUL TO PREDICT RESPONSE TO TREATMENT IN NECROTIZING MYOPATHIES?

S. Fernandes[1], B. Lopez[2], P. Gordon[2], S. Al-Sarraj[3]. *[1]Rheumatology, Instituto Português de Reumatologia, Lisbon, Portugal; [2]Rheumatology; [3]Clinical Neuropathology, King's College Hospital, London, United Kingdom*

Background: Muscle biopsy is the gold standard for the diagnosis of inflammatory myopathies, but the role of immunohistochemistry in Necrotizing Myopathies (NM) has not been fully characterized yet.
Objectives: To determine if MHC-I expression and pattern of C5b-9 deposition in capillaries correlate with clinical phenotype and response to treatment in NM.
Methods: The Neuropathology Departmental database was searched to identify patients with a histological diagnosis of NM and follow up data for at least 6 months (30 patients). Electronic patient records were reviewed retrospectively to record demographics, autoantibodies, treatment, proximal muscle power at 3, 6 and 12 months by Manual Muscle Testing (MMT) (2), levels of CK and flares. Patients were classified as responders when there was improvement of MMT $\geq$20% and non-responders when MMT improvement was $<$20% (3). All biopsies were reviewed blindly by an experienced neuropathologist. MHC-I expression was classified as positive only if over expressed in all fibers. The patterns of C5b-9 deposition in endomysial capillaries were classified as specific (solid), non-specific (granular) or negative.
Results: MHC-I positive group (n=16/30) had a higher proportion of responders (62,5% vs 7,7%, p=0.002), higher number of patients with total recovery of muscle power (66,7 vs. 15,4%) and were more commonly positive for autoantibodies (75% vs. 35.7%, p=0.030) when compared to the MHC-I negative group (n=14). 17 patients were positive for auto-antibodies of which 9 were myositis specific antibodies [SRP (n=6), HMG-CoA reductase (n=1), Jo-1 (n=1), P155/140 (n=1)] and 4 were myositis associated antibodies [Ro-52 (n=2), Ku (n=1), Pm/Scl (n=1)]. 13/30 patients had C5b-9 deposition, with a specific pattern in 5 and non-specific in 8. The specific pattern group had a greater reduction of CK after 6 months compared to non-specific and negative respectively (98% vs. 77% vs. 56.8%, p=0.006), greater reduction in CK after 12 months (96.6% vs. 68.9% vs. 59.6%, p=0.024) and higher rates of responders (80% vs. 60% vs. 18,8%, p=0.001). Six patients were on immunosuppressants (azathioprine/hydroxychloroquine, n=2), steroids (n=3) or both (n=1) for a minimum of 4 weeks when the biopsy was performed. Differences in age, gender, clinical features or treatment were not found to be statistically significant.
Conclusions: Upregulation of MHC I and solid staining pattern of C5b-9 in the capillaries of NM patients appears to be associated with a better outcome.
References:
[1] Cong L, Pu CQ, Shi Q, Wang Q, Lu X, Complement membrane attack complex is related with immune-mediated necrotizing myopathy, Int J Clin Exp Pathol 2014;7(7):4143–41499.
[2] Rider LG, Koziol D, Giannini EH, Jain MS, Smith MR, Whitney-Mahoney K, Feldman BM, Wright SJ, Lindsley CB, Pachman LM, Villalba ML, Lovell DJ, Bowyer SL, Plotz PH, Miller FW, Hicks JE.
[3] Vencovsky J, New ACR/EULAR Criteria for Myositis, Ann Rheum Dis 2015;74:42–43.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6814

OP0033 SPECT- AND PET/CT IMAGING IN NEWLY ONSET IDIOPATHIC INFLAMMATORY MYOPATHY

J. Simonsen[1], S. Hvidsten[1], P.F. Høilund-Carlsen[1], K.F. Thøgersen[1,2], O. Gerke[1], S. Jacobsen[3], L.P. Diederichsen[4,5]. *[1]Nuclear Medicine, Odense University Hospital, Odense C; [2]Aalborg University Hospital, Aalborg; [3]Copenhagen Lupus and Vasculitis Clinic, Center for Rheumatology and Spine Diseases, Copenhagen University Hospital, Rigshospitalet, Copenhagen; [4]Reumatology, Odense University Hospital, Odense C; [5]Clinical Research, University of Southern Denmark, Odense, Denmark*

Background: Diagnosis of idiopathic inflammatory myopathies (IIMs) is challenging and so far no pathognomonic signs exist by imaging. Few radionuclide imaging techniques have been tested for this purpose, mainly ^{99m}Tc-pyrophosphate planar imaging and ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography ($^{18F-}$FDG-PET/CT). However, ^{99m}Tc-PYP uptake has been assessed visually and at best graded semi-quantitatively.
Objectives: We aimed for quantitative ^{99m}Tc-pyrophosphate single photon emission computed tomography/computed tomography (^{99m}Tc-PYP-SPECT/CT) as well as ^{18F}-FDG-PET/CT imaging in a group of newly onset IIM patients.
Methods: Thirteen patients (mean age 62 years) with newly diagnosed, untreated IIM underwent ^{99m}Tc-PYP SPECT/CT of the thorax, pelvis, and thighs. Seven of the patients also had a whole-body ^{18}F-FDG PET/CT scan. Forty-nine healthy controls (mean age 59 years) underwent ^{99m}Tc-PYP SPECT/CT and 26 healthy controls (mean age 57 years) had a ^{18}F-FDG PET/CT scan done. Volumes of interest (VOIs) covering the right biceps, triceps, and quadriceps muscles were drawn manually on each series. Registered ^{99m}Tc-PYP counts, respectively standardized uptake values (SUVs) of ^{18}F-FDG were obtained from all VOIs. Registered counts were decay- and attenuation-corrected and adjusted for body weight and administered dose of ^{99m}Tc-PYP, yielding a parameter similar to the SUV [g mL^{-1}].

Results: IIM patients had visible tracer uptake in the skeletal muscles of the extremities. The muscular ^{99m}Tc-PYP uptake was significantly higher in upper limbs of patients than the uptake in the same muscle groups in healthy controls (uptake[biceps] 0.46 vs. 0.33 g mL^{-1}, p=0.01; uptake[triceps] 0.40 vs. 0.27 g mL^{-1}, p=0.003). The ^{99m}Tc-PYP uptake tended to be higher in the lower limbs of patients than in the lower limbs of controls (uptake[quadriceps] 0.59 vs. 0.48 g mL^{-1}, p=0.06). The muscular FDG uptake was significantly higher in patients than in controls in both upper limbs (SUV_{mean}[biceps] 1.35 vs. 0.72 g mL^{-1}, p=0.006; SUV_{mean}[triceps] 0.91 vs. 0.44 g mL^{-1}, p=0.0008) and lower limbs (SUV_{mean}[quadriceps] 0.84 vs. 0.62 g mL^{-1}, p=0.0001). The muscular FDG uptake values were consequently higher than the ^{99m}Tc-PYP uptake values, although not by a constant factor.
Conclusions: Quantitative ^{99m}Tc-PYP SPECT/CT as well as ^{18}F-FDG PET/CT imaging revealed muscular inflammation in patients with newly onset, untreated IIM. Patients had higher tracer uptake in skeletal muscles groups than healthy controls. Quantification of muscular tracer uptake with the potential to objectively distinguish physiology from pathophysiology could be a valuable tool in the challenging diagnosis of IIMs.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6000

OP0034 FACTORS ASSOCIATED WITH DISEASE PROGRESSION IN EARLY-DIAGNOSED PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS: LONGITUDINAL DATA FROM THE DETECT COHORT

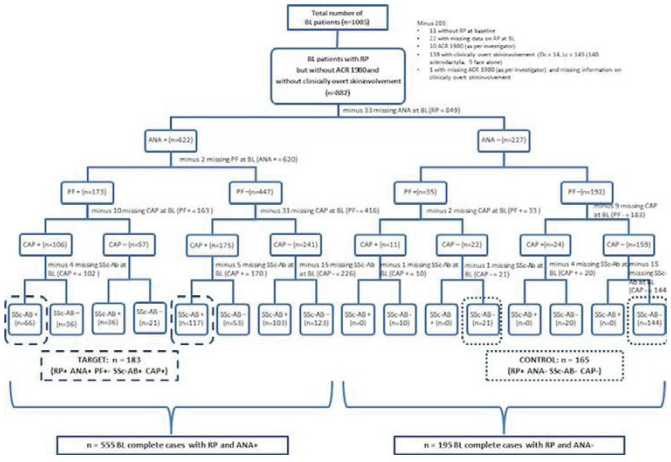
C. Mihai[1], M. Antic[2], R. Dobrota[1,2], D. Bondermann[3], H. Chadha-Boreham[4], G. Coghlan[5], C.P. Denton[6], M. Doelberg[4], E. Grünig[7], D. Khanna[8], V.V. McLaughlin[9], U. Müller-Ladner[10], J.E. Pope[11], D.M. Rosenberg[4], J.R. Seibold[12], M.C. Vonk[13], O. Distler[2]. *[1]Internal Medicine and Rheumatology, Cantacuzino Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [2]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [3]Department of Internal Medicine II, Division of Cardiology, Medical University of Vienna, Vienna, Austria; [4]Actelion Pharmaceuticals Ltd, Allschwil, Switzerland; [5]Cardiology Department; [6]Centre of Rheumatology, Royal Free Hospital, London, United Kingdom; [7]Centre for Pulmonary Hypertension, Thoraxclinic, University Hospital Heidelberg, Heidelberg, Germany; [8]Division of Rheumatology, Department of Medicine; [9]Division of Cardiology, Department of Medicine, University of Michigan, Ann Arbor, MI, United States; [10]Department of Rheumatology and Clinical Immunology, Justus-Liebig University, Giessen, Germany; [11]Division of Rheumatology, Department of Medicine, Western University of Canada, London, Ontario, Canada; [12]Scleroderma Research Consultants LLC, Litchfield, CT, United States; [13]Department of Rheumatology, Radboud University Medical Centre, Nijmegen, Netherlands*

Background: Pulmonary arterial hypertension (PAH) is a severe complication of systemic sclerosis (SSc).
Objectives: In this longitudinal study we aimed to identify factors associated with an unfavourable outcome in SSc patients with early PAH (SSc-PAH) from the DETECT cohort.
Methods: DETECT enrolled patients with SSc fulfilling the 1980 ACR classification criteria, with a minimal disease duration of 3 years since the first non-Raynaud symptom, and with a lung diffusion capacity for CO (DLCO) <60% of the predicted value. A broad range of clinical and laboratory parameters potentially associated with PAH were assessed, and right heart catheterisation (RHC) was performed in all patients at baseline. Patients diagnosed with PAH were followed up for up to 3 years in centers that agreed for the longitudinal part of the DETECT study, collecting data on survival, World Health Organization (WHO) Functional Class (FC), hospitalization, and PAH-specific treatment. Disease progression was defined as the occurrence of any of the following: WHO-FC worsening, PAH therapy with a drug combination, hospitalization, or death. Associations between baseline variables and disease progression were assessed by univariable logistic regression.
Results: Of the 145 SSc patients with PH enrolled in DETECT, 87 patients were diagnosed with PAH, of whom 57 participated in the longitudinal study (median follow-up time 12.6 months, interquartile range 10.7–21.7 months). Among these 57 patients, 33/57 (57.9%) had mild PAH, in WHO FC I or II. During follow-up, 25/57 (43.9%) patients had disease progression (4 deaths, 11 hospitalizations for PAH, 14 with worsening in WHO FC, and 8 received PAH-specific combination treatment), with a 1-year survival rate of 93%. The following factors [odds ratio, (95% confidence interval)] were associated with disease progression: male gender [4.1 (1.2–14.1)], high Forced Vital Capacity (FVC) % predicted/ DLCO % predicted ratio [3.6 (1.2–10.7)], and high Borg dyspnoea index [1.7 (1.1–2.6)]. Low DLCO (% predicted) was also significantly associated with progression [area under the curve (95% CI) 0.8 (0.6–0.9)], but the relationship was not linear.
Conclusions: More than 40% of early-diagnosed SSc-PAH patients in the DETECT cohort who were followed over time had disease progression during a rather short follow-up time, with male gender, functional capacity, and pulmonary function tests (low DLCO, high FVC%/DLCO % predicted ratio) at PAH diagnosis being associated with progression. This suggests that even mild and early detected PAH should be regarded as a high-risk complication of SSc, and every effort to make an early diagnosis is valuable.
Acknowledgements: The authors thank all investigators and patients involved in DETECT.
Disclosure of Interest: C. Mihai Grant/research support from: Actelion, Geneva Romfarm, Abbvie, Speakers bureau: Actelion, Geneva-Romfarm, Roche-Genentech, M. Antic: None declared, R. Dobrota Grant/research support from: Pfizer, Actelion, Speakers bureau: Actelion, D. Bondermann Consultant for: Actelion, GSK, MSD, Bayer, Pfizer, AOP Orphan, United Therapeutics, H. Chadha-Boreham Employee of: Actelion, G. Coghlan Consultant for: Actelion, GSK, Bayer, United Therapeutics, Endotronics, Speakers bureau: Actelion, GSK, Bayer, United Therapeutics, C. Denton Consultant for: Actelion, M. Doelberg Employee of: Actelion, E. Grünig Grant/research support from: United Therapeutics, Actelion, MSD/Bayer, GSK, Consultant for: United Therapeutics, Actelion, MSD/Bayer, GSK, Speakers bureau: United Therapeutics, Actelion, MSD/Bayer, GSK, D. Khanna Grant/research support from: Bayer, BMS, Genentech/Roche, Sanofi-Aventis, NIH K24AR063120, Consultant for: Actelion, Bayer, Covis, Cytori, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis, V. McLaughlin Consultant for: Actelion, U. Müller-Ladner Consultant for: Actelion, Speakers bureau: Actelion, J. Pope Consultant for: Actelion, Bayer, BMS, Merck, Roche, D. Rosenberg Employee of: Actelion, J. Seibold Consultant for: Acer, Actelion, Anthera, arGen-X, aTyr, Bayer, Blade, Boehringer-Ingelheim, Bristol Myers Squibb, Biogen Idec, Covis, Eiger, EMD Serono, Genkyotex, Gilead, Ironwood, Medac, MedImmune, Mitsubishi, Octapharma, Roche-Genentech, Sanofi, Teva and United Therapeutics., M. Vonk Consultant for: Actelion, O. Distler Grant/research support from: 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK,Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacyclics, Pfizer, Sanofi, Serodapharm and Sinoxa, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, Biogen Idec, Boehringer Ingelheim Pharma, BMS, ChemomAb, EpiPharm, Ergonex, espeRare foundation, GSK,Roche-Genentech, Inventiva, Lilly, medac, MedImmune, Mitsubishi Tanabe, Pharmacyclics, Pfizer, Sanofi, Serodapharm and Sinoxa
DOI: 10.1136/annrheumdis-2017-eular.2866

OP0035 PRELIMINARY ANALYSIS OF NAILFOLD CAPILLAROSCOPY IN THE VERY EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS (VEDOSS): THE CAPI-VEDOSS EXPERIENCE

M. Cutolo[1], V. Smith[2,3], O. Distler[4], O. Kowal-Bielecka[5], Y. Allanore[6], M. Matucci-Cerinic[7] on behalf of EUSTAR coworkers. *[1]Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genova, Italy; [2]Department of Internal Medicine, University of Ghent; [3]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium; [4]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [5]Department of Rheumatology and Internal Medicine, Medical University of Bialystok, Bialystok, Poland; [6]Department of Rheumatology, Paris Descartes University, Cochin Hospital, Paris, France; [7]Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Florence, Italy*

Background: In Systemic Sclerosis (SSc), before the onset of clinical signs of fibrosis, puffy fingers, specific autoantibodies and microcirculatory modifications are present and are identified in the VEDOSS criteria for "(very) early" disease. No large scale studies are available indicating the prevalence of nailfold video-capillaroscopic (NVC) SSc patterns or quantitated capillaroscopic characteristics in a "(very) early" cohort.
Objectives: Evaluation of the prevalence of SSc patterns and quantitated capillaroscopic characteristics in a "(very) early" crossectional SSc cohort.
Methods: Multicentre observational cohort study of patients with two strata (Figure): 1.Raynaud's phenomenon (RP), Anti Nuclear Antibody (ANA) positive (+), 2. RP+, ANA negative (-). "Target" (RP+, ANA+, puffy finger [PF] +/-, SSc- antibody (SSc-AB)+, NVC+) and "control" (RP+, ANA-, SSc-AB-, NVC-) subsets were described. NVC patterns (normal/non-specific alterations; non-specific abnormalities; SSc-patterns ("Early", "Active";"Late"; "Sclerodermalike") and quantitative ("absent (="none" or "rare") and "present" (="moderate" or "extensive") capillaroscopic alterations for giants, haemorrhages, capillary loss and abnormally shaped (=bushy capillaries) were evaluated). Generalized Estimating Equations (GEE) were used to assess differences in prevalences of NVC patterns between strata, taking clusters of patients within centers into account.
Results: 1085 RP patients from 40 centres (median number [n°] of pt 12 (minimum [min] 1-maximum [max] 393) per centre were enrolled in the VEDOSS online database. Due to erroneous included/missing data (e.g. erroneous: absence/missing information on RP, presence of former ACR criteria for SSc, skin involvement at baseline; missing info on: ANA positivity, PF, Cap, SSc-AB) 750 patients (median n° of 7 (min:1-max:271) were retained for the analysis. SSc nailfold videocapillaroscopic (NVC) patterns ("Early", "Active", "Late", "Scleroderma like" were present in 79%,13%,0%, 8%) as well as presence of "moderate" or "extensive" giants (49%), hemorrhages (32%), capillary loss (11%) and abnormal shapes (11%) of "target" patients and per definition in 0% of "controls". Estimated distribution of SSc patterns differed in the ANA+/- stratum: 49%/15% ($p \leq 0.001$) ("Early" 40/13%; "Active" 5/2%; "Late" 0/0%; "Scleroderma like" 3/0%). For the quantitative capillaroscopic characteristics a statistically significant difference in the presence of "moderate" or "extensive" giants (23/5%, p=0.027) between the ANA+/- stratum was found, hemorrhages (18/9%, p=0.200), capillary loss (5/2%, p=0.798) and abnormal (ramified) shapes (7/2%,p=0.445).



Conclusions: The VEDOSS cohort presents predominantly an "Early" NVC SSc pattern. Notably the prevalence of NVC SSc patterns was higher in the ANA+ than ANA- stratum. This evidence further reflects the pivotal role of NVC in the very early diagnosis of SSc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2932

OP0036 SEROLOGICAL BIOMARKERS OF ECM TURNOVER ARE ASSOCIATED WITH SKIN FIBROSIS AND LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS

S. Kubo[1], A.S. Siebuhr[2], A.-C. Bay-Jensen[2], P. Juhl[2], M.A. Karsdal[2], K. Nakano[1], S. Nakayamada[1], Y. Tanaka[1]. *[1]The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Fukuoka, Japan; [2]Nordic Bioscience, Biomarkers and Research, Herlev, Denmark*

Background: Extracellular matrix (ECM) unbalance of the skin is a hallmark of systemic sclerosis (SSc). However, currently there is no objective tool to monitor the ECM unbalance in SSc patients allowing for better understanding of the disease stage and activity.
Objectives: We investigated the potential of serological biomarkers of ECM turnover (collagen formation and degradation) as biomarkers of skin fibrosis and internal organ involvement in SSc patients.
Methods: Peripheral blood obtained from 79 SSc patients and 19 healthy subjects was included in the study. Type I, III, IV, V and VI collagen formation (P1NP, PRO-C3, P4NP7S, PRO-C5, PRO-C6) and degradation (C3M, C4M2, C5M, C6M) biomarkers were detected by ELISA in serum. Modified Rodnan skin score (mRSS) and extent of internal organ involvement (renal, lung, vasculopathy and gastrointestinal) were recorded for SSc patients with a scoring between 0 and 4, with 0 being no involvement and 4 being severe involvement. Mann-Whitney t-test was used to test difference in the biomarker levels between the patient groups and in groups with and without internal organ involvement. Spearman's correlation coefficient investigated the association between biomarkers and clinical manifestations.
Results: SSc patients had a mean age of 63.0 years, mean disease duration of 98.3 months and a mean mRSS of 11.1. SSc patients compared to healthy individuals had higher levels of C5M, C6M and PRO-C6 ($p=0.0001$, $p<0.0001$, $p<0.0001$, respectively). The levels of type VI collagen formation and degradation (PRO-C6 and C6M) were twice as that of healthy controls (12.6 vs. 5.4 and 26.0 vs 16.7 ng/ml, respectively). C4M2, PRO-C3 and PRO-C6 was associated with skin fibrosis assessed by mRSS (Spearman's rho=0.24, 0.39 and 0.29, respectively). Patients with signs and manifestation of lower gastrointestinal lesion compared to patients without lesion had higher levels of C3M (median 10.7 vs 13.8ng/mL, $p=0.017$; figure). PRO-C6 was higher in patients with pulmonary hypertension compared to patients without any signs of pulmonary hypertension (median 9.6 vs 14.3ng/mL, $p=0.006$) with a Spearman's correlation coefficient of 0.31. C6M was higher in patients with definite pulmonary hypertension (>1) compared to patients with signs of or no pulmonary hypertension (median 22.1 vs 29.9ng/mL, $p=0.026$). P1NP was lower in patients with interstitial pneumonia, whereas C6M was higher. There was no difference in the biomarker levels with and without upper gastrointestinal lesions, renal dysfunction or vasculopathy.

	Healthy	SSc	P-value	Spearman's correlation to mRSS Rho (p-value)
C3M	12.8	13.4	–	0.21 (0.06)
C4M2	31.1	34.0	–	0.24 (0.03)
C5M	2.6	3.9	0.0001	0.03 (0.81)
C6M	16.7	26.0	<0.0001	0.18 (0.11)
P1NP	136.9	130.4	–	0.03 (0.80)
PRO-C3	14.2	20.8	–	0.39 (<0.001)
P4NP7S	286.8	290.3	–	0.19 (0.10)
PRO-C5	525.2	484.4	–	0.07 (0.52)
PRO-C6	5.4	12.6	<0.0001	0.29 (0.01)

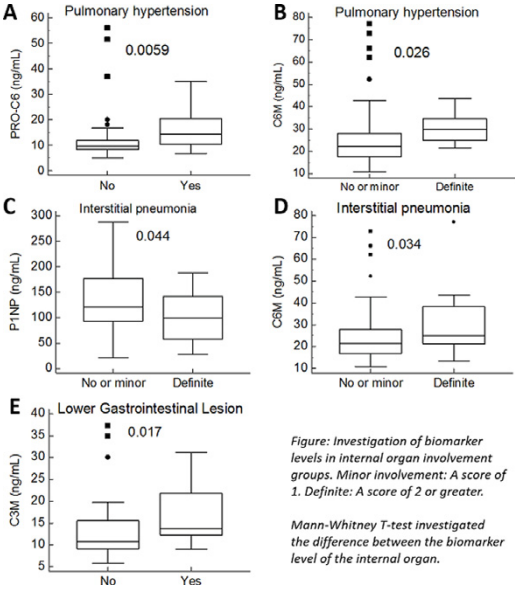


Figure: Investigation of biomarker levels in internal organ involvement groups. Minor involvement: A score of 1. Definite: A score of 2 or greater.

Mann-Whitney T-test investigated the difference between the biomarker level of the internal organ.

Conclusions: Serological biomarkers of type V and VI turnover (C5M, C6M, PRO-C6) were associated with SSc, but not serological biomarkers of type I, III and IV collagen. Especially, turnover of type VI collagen was associated with skin sclerosis, pulmonary hypertension, interstitial pneumonia and renal dysfunction. This study indicates that biomarkers of collagen turnover have a potential as new objective tool of skin fibrosis and internal organ involvement in SSc.
Disclosure of Interest: S. Kubo Speakers bureau: Bristol-Myers, A. S. Siebuhr Employee of: Nordic Bioscience, A.-C. Bay-Jensen Employee of: Nordic Bioscience, P. Juhl Employee of: Nordic Bioscience, M. A. Karsdal Employee of: Nordic Bioscience, K. Nakano: None declared, S. Nakayamada: None declared, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, MitsubishiTanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, GlaxoSmithKline
DOI: 10.1136/annrheumdis-2017-eular.4855

OP0037 EVALUATION OF SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS BY USING TWO ULTRASOUND TRANSDUCERS WITH DIFFERENT FREQUENCY

B. Ruaro, A. Sulli, S. Paolino, C. Pizzorni, M. Ghio, E. Alessandri, A.C. Trombetta, C. Cosso, M. Cutolo. *Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS AOU San Martino, Genoa, Italy*

Background: The modified Rodnan skin score (mRSS) is the validated method to evaluate the extension of skin involvement in systemic sclerosis (SSc) and to distinguish between patients with limited cutaneous skin involvement (lcSSc, skin involvement is confined to the extremities) or diffuse (dcSSc) (1,2). Recently several studies have demonstrated that skin high frequency ultrasound (US) is a valid and reproducible technique to measure dermal thickness (DT) in patients with SSc (3–6).
Objectives: To compare the values of DT obtained by two ultrasound transducers with different frequency (18 MHz and 22 MHz) in evaluating the DT in lcSSc patients and healthy controls.
Methods: Thirty-seven lcSSc patients (mean age 62±13SD years, mean disease duration 5±5SD years) and 37 healthy controls (CNT) sex and age matched were enrolled after informed consent. Both US transducers of 18 and 22 MHz (Esaote, Genova) were used to evaluate DT in the seventeen areas of the skin (zygoma, fingers, dorsum of hands, forearms, arms, chest, abdomen, thighs, legs, feet) of SSc patients where Rodnan skin score (mRSS) is usually assessed. Skin US was also performed in the same seventeen areas of CNT, looking for DT differences in comparison with lcSSc patients. Statistical analysis was carried out by non parametric tests.
Results: DT evaluated with the 22 MHz probe was found significantly higher in all body areas in comparison with the 18 MHz transducer, both in lcSSc patients ($p<0.01$) and in CNT ($p=0.05$). The median difference of DT values between the two probes was of 0.11 millimetres in lcSSc patients (minimum 0.0023, maximum 0.28 mm) and 0.01 millimetres in CNT (minimum 0.0029, maximum 0.03 mm). Of interest, in lcSSc DT evaluated by 18 MHz transducer was recognized significantly higher ($p<0.001$) also in four out of six skin areas where the mRSS was found normal (score=0) (upper-arms, chest and abdomen), with exclusion of thighs ($p=0.08$), in contrast with the classification of lcSSc. However, by using the 22

MHz transducer a statistically significantly higher median DT was showed in all skin areas, included thighs ($p<0.01$). Finally, a positive statistically significant correlation was observed between the two transducers in the evaluation of DT ($p<0.0001$), as well as between both probes and mRSS ($p<0.0001$ for both).
Conclusions: This study suggests that subclinical dermal involvement may be detectable by skin high frequency US already in patients with limited cutaneous SSc. This study confirms that DT can be better assessed in SSc patients by using a 22 MHz US probe, and suggests that DT might be underestimated by using US probes of lower frequency (18 MHz). However, the DT values obtained using both probes resulted significantly correlated together and with the mRSS.
References:
[1] Clements PJ, et al. Arthritis Rheum 2000;43:2445–54.
[2] Moore TL, et al. Rheumatology 2003;42:1559–63.
[3] Sulli A, et al. Ann Rheum Dis. 2014;73:247–51.
[4] Czirják L, et al. Ann Rheum Dis. 2007;66:966–9.
[5] Hesselstrand R, et al. Rheumatology 2008;47:84–7.
[6] Kaloudi O, et al. AnnRheum Dis.2010;69:1140–3.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2718

OP0038 MYOSITIS AUTOANTIBODIES OUTPERFORM CLINICAL SUBGROUP CLASSIFICATION IN PREDICTING MUSCLE WEAKNESS IN MYOSITIS PATIENTS

I. Pinal-Fernandez[1], W. Huang[1], M. Casal-Dominguez[1], E. Tiniakou[2], C. Parks[1], K. Pak[1], J. Albayda[2], J.J. Paik[2], S.K. Danoff[3], L. Christopher-Stine[2], A.L. Mammen[1]. *[1]Muscle Disease Unit, NIAMS/NIH, Bethesda; [2]Rheumatology; [3]Pulmonology, Johns Hopkins University, Baltimore, United States*

Background: Myositis patients may be classified as belonging to one of four clinical groups: dermatomyositis (DM), polymyositis (PM), clinically amyopathic dermatomyositis (CADM) or necrotizing myositis (NM). Alternatively, myositis patients may be classified according to myositis autoantibody status.
Objectives: The aim of this study was to determine whether clinical groups or myositis autoantibodies provide better prognostic categories with regard to muscle involvement in these patients.
Methods: All Johns Hopkins Myositis Center patients from 2002 to 2015 with a myositis specific autoantibody confirmed by two different immunologic techniques were included. Autoantibody groups accounting for less than 2% of the final sample size were excluded. Strength (analyzed as the average of deltoid and hip flexor strength using Kendall's scale) and log transformed CK levels were compared between the different autoantibody groups using multilevel regression models adjusted for age, time from disease onset, sex, race and treatments. Models with different combinations of key variables were compared using the likelihood ratio test to ascertain if autoantibody groups and clinical subgroups provided the same amount of information regarding muscle weakness and CK levels over time.
Results: 483 patients with 4181 visits were included and 10 different autoantibody groups were identified. Muscle weakness and CK levels followed a gradient among both antibody and clinical groups. Anti-SRP patients had the greatest weakness, followed by anti-HMGCR, anti-Mi2 and anti-NXP2, and then anti-Jo1. CK levels were highest in anti-HMGCR patients, followed by anti-SRP, anti-PL7, anti-Jo1 and anti-Mi2. Interestingly, strength and CK levels were dissociated in two groups: anti-NXP2 patients had significant weakness with low CK levels and anti-PL7 patients were relatively strong despite high CK levels. Multilevel regression models showed autoantibody groups explained the strength and the CK variability better than the clinical groups (AIC difference>20). Indeed, adding clinical groups to a model using only autoantibodies did not improve the model's ability to predict strength (p=0.2) and only mildly improved its ability to predict CK (p=0.01). In comparison, adding the autoantibodies to a model using the clinical groups resulted in a marked improvement in predicting both CK and strength (both $p<0.001$).
Conclusions: In patients with myositis, autoantibody status predicts strength and CK levels better than clinical grouping.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3476

WEDNESDAY, 14 JUNE 2017

SLE, Sjögren's and APS - clinical aspects

OP0039 A POPULATION-BASED STUDY ON MORTALITY AND THE INFLUENCE OF MEDICATION USE IN 4356 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND 21845 MATCHED CONTROLS FROM THE UNITED KINGDOM

I.E. Bultink[1], A. Lalmohamed[2,3], F. de Vries[3,4]. *[1]Rheumatology, Amsterdam Rheumatology and immunology Center, VU University Medical Center, Amsterdam; [2]Clinical Pharmacy, University Medical Center Utrecht; [3]Pharmacoepidemiology and Clinical Pharmacology, Utrecht University, Utrecht; [4]Clinical Pharmacy and Toxicology, Maastricht University Medical Centre, Maastricht, Netherlands*

Background: Systemic lupus erythematosus (SLE) has been associated with an increased mortality rate. However, population-based data on all-cause, age-specific and sex-specific mortality risk are limited and data on the influence of medication exposure on mortality risk in SLE are scarce.
Objectives: To estimate the magnitude of the risk from all-cause, age-specific, and sex-specific mortality in patients with SLE and relative risks compared with matched controls, and to evaluate the influence of medication exposure on mortality risk in SLE.
Methods: We conducted a population-based cohort study using the Clinical Practice Research Datalink (from 1987 to 2012). Each SLE patient (n=4356) was matched with up to 6 controls (n=21845) by age and sex. Multivariate Cox regression analysis estimated adjusted relative rates (RR) of mortality, and time interaction terms to evaluate mortality timing patterns. Time-dependent Cox models were used to evaluate the association of glucocorticoid use and hydroxychloroquine use on mortality and were adjusted for age, sex, lifestyle parameters, comorbidities and comedication.
Results: A total of 442 out of 4356 SLE patients died during the study period. Patients with SLE had an increased mortality rate for all-cause mortality compared with age- and sex-matched subjects, after adjustment for confounders (adjusted RR 1.80, 95% CI 1.57–2.08). Glucocorticoid use in the previous six months raised the mortality rate while the adjusted RR was 45% decreased with low dose hydroxychloroquine use. The RR was highest in patients aged 18–39 years (adjusted RR 4.87, 95% CI 1.93–12.3) and slightly higher in females (adjusted RR 1.82, 95% CI 1.56–2.13) compared to male patients (adjusted RR 1.68, 95% CI 1.19–2.39). The mortality rate was significantly increased for patients with a history of dementia, seizures, diabetes, cancer, and renal disease (Table 1).

Table 1. Risk of all-cause mortality within SLE patients (n=4356), stratified according to organ damage (reference = no risk factor)

	Person years (x1000)	Deaths	IR (/1000)	Adjusted RR* (95% CI)
Dementia	0.1	14	140.0	2.99 (1.74–5.14)
Seizures	1.4	37	26.4	2.33 (1.66–3.28)
Cerebrovascular event	1.9	73	38.4	1.28 (0.99–1.65
Renal disease	2.0	86	43.0	1.40 (1.09–1.78)
Osteoporotic fracture	5.1	110	21.6	1.06 (0.85–1.32)
Diabetes mellitus	0.9	45	50.0	1.90 (1.39–2.59)
Malignancy	2.0	95	47.5	1.90 (1.50–2.40)

*Adjusted for: recent use of corticosteroids, recent use of antimalarials, recent use of benzodiazepines.

Conclusions: Patients with SLE have a 1.8-fold increased mortality rate compared with the general population. Glucocorticoid use, female sex and young age are associated with an increased mortality risk while low dose hydroxychloroquine use significantly reduces the mortality rate. In addition, special attention should be paid to lupus patients with neuropsychiatric complications, diabetes, malignancy or renal disease since these subgroups of patients are at high risk of death.
Disclosure of Interest: I. Bultink Grant/research support from: Lilly Netherlands, MSD, Amgen, UCB, A. Lalmohamed: None declared, F. de Vries: None declared
DOI: 10.1136/annrheumdis-2017-eular.2458

OP0040 INTEGRATION OF SALIVARY-GLAND ULTRASONOGRAPHY IN CLASSIFICATION CRITERIA FOR PRIMARY SJÖGREN'S SYNDROME: AN INTERNATIONAL VIGNETTE-BASED STUDY

S. Jousse-Joulin[1], F. Gatineau[2], C. Baldini[3], S. Arends[4], F. Barone[5], A. Baer[6], H. Bootsma[4], S. Bowman[7], P. Brito-Zeron[8], D. Cornec[9], T. Dorner[10], S. De Vita[11], B. Fisher[12], D. Hammenfors[13], M. Jonsson[14], X. Mariette[15], V. Milic[16], T. Nakamura[17], W.-F. Ng[18], E. Nowak[2], A. Rasmussen[19], R. Seror[20], C. Shiboski[21], T. Nakamura[22], M. Ramos-Casals[23], A. Vissink[4], A. Saraux[24], V. Devauchelle-Pensec[24]. *[1]Rheumatology; [2]CIC, CHU Brest, BREST, France; [3]Rheumatology, University of Pisa, Pisa, Italy; [4]Rheumatology, University Medical Center Groningen, Groningen, Netherlands; [5]Rheumatology, University, Birmingham, United Kingdom; [6]Department of Rheumatology, Johns Hopkins University School, Baltimore, United States; [7]Rheumatology, university of Birmingham, Birmingham, United Kingdom; [8]Department of Rheumatology, Hospital CIMA-Sanitas, Barcelona, Spain; [9]Thoracic Disease Research Unit, Mayo Clinic Rochester, Rochester, United States; [10]Rheumatology, Charité Universitätsmedizin Berlin, Berlin, Germany; [11]Rheumatology, Santa Maria della Misericordia University-Hospital, Udine, Italy; [12]Rheumatology Research Group and Arthritis Research UK Rheumatoid Arthritis RACE, University of Birmingham, Birmingham, United Kingdom; [13]Rheumatology; [14]Clinical Science, university of Bergen, Bergen, Norway; [15]Rheumatology, INSERM U1184, Center Autoimmune Diseases, Paris-Sud, le Kremlin Bicetre, France; [16]Rheumatology, university of Belgrade, Belgrade, Serbia; [17]Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; [18]Rheumatology, University of New Castle, New Castle, United Kingdom; [19]Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma, United States; [20]Rheumatology, INSERM U1184, Center for Autoimmune Diseases, Paris-Sud, le Kremlin Bicetre, France; [21]Department of Dentistry, University of California, San Francisco, United States; [22]Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; [23]Hospital Clinic, university of Barcelona, Barcelona, Spain; [24]Rheumatology, Brest University and INSERMU1227, BREST, France*

Background: The recent classification criteria sets for primary Sjögren's syn-

drome (AECG 2002 and ACR/EULAR 2017) did not include major salivary glands ultrasononography (SGUS).
Objectives: The UTOPIA study was undertaken to determine if and how SGUS may improve the ACR/EULAR criteria.
Methods: Twenty four international experts in pSS evaluated on an internet-secure relational database 512 randomly realistic vignettes derived from 150 patients with suspected pSS included in the french DiapSS cohort. Each vignette contained sections on "history" (duration of the symptoms, gender, age), clinical symptoms (dry mouth, dry eyes and systemic manifestations), results of the SGUS evaluation (score > ou < to 2), and results of the major tests to diagnose pSS (Schirmer's test, ocular staining score (OSS), salivary flow, focus score on salivary biopsy, presence of anti-SSA antibodies). Each expert had to score the diagnosis of pSS as absent, unlikely, likely or present for 64 vignettes. Each vignette was evaluated by 3 experts. Diagnosis of pSS was obtained when at least 2 of 3 considered it as likely or present. Univariate and multivariate analysis (Wald test) were performed to evaluate the association between the SGUS criteria, the ACR/EULAR criteria and its different individual items with the diagnosis of pSS as defined by the experts. Data were then replicated on independent cohorts of suspicion of pSS.
Results: Univariate and multivariate analyses confirmed that ACR/EULAR criteria and SGUS were independently associated with the diagnosis of pSS. Disease duration, OSS and ocular dryness were not associated with the diagnosis of pSS. Only 6 variables were selected by logistic regression analysis: presence of anti-SSA (weight:4), focus score (weight:3), SGUS (weight:2), Schirmer's test (weight:1), dry mouth (weight:1) and salivary flow rate (weight:1). According to ROC curve analysis, a score of ≥5 had 96% Se and 84% Sp, compared with 90% Se and 84% Sp for the ACR/EULAR criteria. The corrected C statistic (AUC) for the new weighted score was 0.98.
Conclusions: Inclusion of the SGUS item in the ACR/EULAR criteria improves their diagnostic performance.
Disclosure of Interest: S. Jousse-Joulin: None declared, F. Gatineau: None declared, C. Baldini: None declared, S. Arends: None declared, F. Barone: None declared, A. Baer: None declared, H. Bootsma: None declared, S. Bowman: None declared, P. Brito-Zeron: None declared, D. Cornec: None declared, T. Dorner: None declared, S. De Vita: None declared, B. Fisher: None declared, D. Hammenfors: None declared, M. Jonsson: None declared, X. Mariette: None declared, V. Milic: None declared, T. Nakamura: None declared, W.-F. Ng: None declared, E. Nowak: None declared, A. Rasmussen: None declared, R. Seror: None declared, C. Shiboski: None declared, T. Nakamura: None declared, M. Ramos-Casals: None declared, A. Vissink: None declared, A. saraux: None declared, V. Devauchelle-Pensec Grant/research support from: ROCHE-CHUGAI
DOI: 10.1136/annrheumdis-2017-eular.3204

OP0041 ALL-CAUSE, CARDIOVASCULAR AND MALIGNANCY RELATED MORTALITY IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A POPULATION-BASED STUDY

B. Moghaddam[1], J.A. Avina-Zubieta[2,3], E.C. Sayre[2]. *[1]Division of Medicine, University of British Columbia, Vancouver; [2]Arthritis Research Canada, Richmond; [3]Division of Rheumatology, University of British Columbia, Vancouver, Canada*

Background: SLE is associated with increased risk of overall mortality; however morality trends due to specific causes including cardiovascular disease (CVD), malignancies or other causes are largely unknown.
Objectives: Our objective was to assess trends in cause-specific mortality among SLE patients between January 1, 1997 and December 31, 2012 in a general population-based context.
Methods: We conducted a population-based matched cohort on SLE patients diagnosed between January 1,1997 and December 31,2012 using an administrative health database from the province of British Columbia, Canada. We identified all incident cases of SLE and up to 10 non-SLE controls matched on sex, age, and calendar year of study entry. The cohort was divided into two cohorts based on year of SLE diagnosis (1997–2004 and 2005–2012). All-cause mortality and cause-specific incidence of death rates (IR) were calculated. Cox proportional hazard regression models were used to estimate the mortality hazard ratios (HR), adjusting for possible confounders (i.e. Charlson Comorbidity Index, number of outpatient visits, hospitalization, cardiovascular medications, glucocorticoids and NSAIDs at baseline).
Results: 4238 SLE and 42380 matched controls were studied. SLE patients had significantly increased all-cause mortality with HR 1.29 (95% CI, 1.15–1.46) and increased cause-specific mortality from CVD and other causes with HRs of 1.43 (95% CI, 1.15 -1.79) and 1.74 (95% CI, 1.46–2.09), respectively. The cohorts did not differ in the rate of death from malignancy. SLE patients had an approximately 2-fold increase in death from other causes in both early (HR 1.86 (95% CI 1.33–2.60)) and recent cohorts (HR 1.90 (95% CI 1.42–2.56)). There was no significant improvement in all-cause and cause-specific mortality trends between the two cohorts.
Conclusions: This study demonstrates that despite advances in therapy with novel biologic agents, there are no significant differences in all-cause and CVD mortality from SLE between early and recent cohorts. Death from other causes, which includes a composite of death related to for example renal disease and infections, remains high suggesting areas for future targeted research and therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4451

OP0042 BACTEREMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS FROM RELESSER REGISTRY: RISK FACTORS, CLINICAL AND MICROBIOLOGICAL CHARACTERISTICS AND OUTCOMES

I. Rua-Figueroa[1], J. López-Longo[2], M. Galindo-Izquierdo[3], V. Del Campo[4], J. De la Torre Cisneros[5], E. Uriarte[6], P. Vela[7], E. Tomero[8], J. Pego-Reigosa[4]. *[1]Rheumatology, Hospital Dr. Negrin, Las Palmas GC; [2]Gregorio Marañón Hospital; [3]Doce de Octubre Hospital, Madrid (Spain), Madrid; [4]Hospital Complex of Vigo and IISGS, Vigo; [5]Reina Sofía Hospital, Córdoba; [6]Donosti Hospital, Guipúzcoa; [7]Alicante G Hospital, Alicante; [8]La Princesa Hospital, Madrid, Spain*

Background: According to RELESSER (Spanish Society of Rheumatology Lupus Registry) data, bacteremia is the main cause of death by infection in systemic lupus erythematosus (SLE). However, the available information about this severe infection in SLE patients remains scarce.
Methods: Retrospective, nested case-control study of SLE patients (ACR-97 criteria) with at least one bacteremic episode and random controls from RELESSER Registry. Descriptive, bivariate and multivariate analysis (logistic regression)
Results: 114 bacteremic episodes in 83 patients were recorded. Incidence rate: 2,7/ 1,000 patient-years (n total: 3658). At the time of the bacteremia: median age: 40.5 (8–90) years, 88.6% female, disease duration: 9.7 (IR16.7), median SELENA-SLEDAI: 4 (IR8), 66% with severe flare (SFI criteria), active nephritis: 16.7%, median SLICC/ACR DI: 3 (IR4), any comorbidity: 64% (McCabe-Jackson criteria: 28.1% rapidly or ultimately fatal), more frequently renal failure (15.8%) or diabetes (11.4%). SLE treatment at the time of bacteraemia: 88.6% corticosteroids (68,6%>10mg/day), 57% immunosuppressors (mycophenolate 17.5% and cyclophosphamide 12.3%), 27% antimalarials. 44.7% suffered invasive procedures, more frequently intravascular catheter (24.6%). The bacteremia was nosocomial in 35.1% and the source was more frequently urinary (27.2%). 64% developed systemic inflammatory response syndrome and 35% needed intensive care unit admission, with multiorganic failure in 22.8%. The most frequent microorganism was *E.coli* (29.8%) followed by *Staphylococcus aureus* (16.7%) (22% methicillin-resistant) and *Salmonella spp.* (10.5%). 16% of the gram-negative enteric bacilli were extended-spectrum b-lactamase positive. 17.5% were multidrug resistant. 68,4% started the antibiotherapy before blood culture results, resulting finally active in susceptibility testing in 56 cases (71.8%), indicating an appropriate empirical antibiotic therapy in 49%. The bacteremia-related mortality was 14%. The risk of death was higher in patients with severe sepsis (Pitt index >8) (OR: 13 (IC95%: 3.71–45.17). The bacteremia was recurrent in 26.3%. Associations with bacteremia in bivariate analysis (114 bacteremias vs 688 controls) are shown in Table 1. Antimalarials were protective. In the multivariate analysis (adjusted for disease duration), only elevated creatinine (OR 1.31 (95% CI 1.01–1.70), p=0.045), diabetes (OR 6.01 (95% CI 2.26–15.95), p=0.000), cancer (OR 5.32 (95% CI 2.23–12.70), p=0.000), immunosuppressors (OR 6.35 (95% CI 3.42–11.77), p=0.000), cyclophosphamide (OR 9.37 (95% CI 5.12–17.14), p=0.000) and SLICC/ACR DI (OR 1.65 (95% CI 1.31–2.09), p=0.000) remained statistically significant.
Conclusions: Bacteremia occurred mostly in active SLE, frequently in the context of a severe flare. Gram negative bacilli predominated, with high rate of multidrug resistance. The empiric treatment was inappropriate in a half of the cases. The

Abstract OP0041 – Table 1. Overall and cause-specific mortality in SLE patients compared to general population; HR, hazard ratio

Cohorts		All-Cause Deaths		CVD Deaths		Malignancy Deaths		Other Causes	
		Deaths	HR (95% CI)	Deaths	HR (95% CI)	Deaths	HR (95% CI)	Deaths	HR (95% CI)
Overall Cohort	SLE (n=4238)	411	1.29 (1.15–1.46)	104	1.43 (1.15–1.79)	95	0.80 (0.63–1.00)	212	1.74 (1.46–2.09)
	Non-SLE (n=42380)	2226	1	622	1	795	1	809	1
Female Cohort	SLE (n=3643)	323	1.34 (1.17–1.54)	75	1.40 (1.08–1.81)	77	0.81 (0.62–1.05)	171	2.05 (1.68–2.50)
	Non-SLE (n=36430)	1697	1	469	1	618	1	610	1
Male Cohort	SLE (n=595)	88	1.06 (0.81–1.39)	29	1.73 (1.10–2.71)	18	0.76 (0.44–1.30)	41	1.06 (0.70–1.62)
	Non-SLE (n=5950)	529	1	153	1	177	1	199	1
Early Cohort (1997–2004)	SLE (n=1678)	98	1.20 (0.96–1.51)	25	1.18 (0.76–1.82)	22	0.68 (0.42–1.09)	51	1.86 (1.33–2.60)
	Non-SLE (n=16780)	508	1	163	1	173	1	172	1
Recent Cohort (2005–2012)	SLE (n=2560)	137	1.13 (0.92–1.39)	25	0.89 (0.57–1.39)	33	0.66 (0.45–0.98)	79	1.90 (1.42–2.56)
	Non-SLE (n=25600)	622	1	179	1	260	1	223	1

TABLE 1		
	OR	*p*
SELENA-SLEDAI	1.10 (1.06-1.14)	<0.001
SLICC/ACR DI	1.27 (1.16-1.38)	<0.001
Elevated creatinine	2.08 (1.66-2.61)	<0.001
Active nephritis	3.52 (1.94-6.37)	=0.001
Hepatitis C	4.82 (1.89-12.27)	=0.002
Diabetes	3.87 (2.06-7.26)	=0.0001
Cancer	3.60 (2.01-6.42)	=0.000
Corticosteroids (Prednisone > 10mg/day)	1.81 (1.07-3.09)	=0.023
Immunosuppressors	11.44 (7.31-17.92)	=0.000
Antimalarials	0.39 (0.25-0.61)	=0.000
Renal Transplant	5.64 (2.63-12.1)	=0.000
Dialysis	0.39 (0.25-0.61)	=0.000

recurrence and mortality were high. Immunosuppressors use, comorbidity and damage were all associated to bacteraemia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4138

OP0043 THE NUMBER OF CIRCULATING REGULATORY T CELLS IS REDUCED AND LOW-DOSE IL-2 SELECTIVELY STIMULATES ITS PROLIFERATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

X. Liu[1], X. Jing[1], X. Wu[1], J. Wang[1], Z. Liang[1], M. Hao[1], J. Chen[1], C. Gao[2], X. Li[1]. *[1]Rheumatology, The Second Hospital of Shanxi Medical University, Taiyuan, China; [2]Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, United States*

Background: The imbalance of T help 17 cells (Th17)/regulatory T cells (Tregs) is considered to be a pivotal cause of autoimmune diseases[1], including systemic lupus erythematosus (SLE). However, previous reports[1,2] describing the respective changes of Tregs and Th17 cells in SLE patients were controversial because a few samples or diverse markers were used to identify Tregs with little consensus.

Objectives: To clarify the status of Tregs and Th17 in SLE, we investigated the frequencies of Tregs and Th17 cells on a large scale and whether those defects can be corrected by the supplementation of low-dose human recombinant interleukin-2 (IL-2).

Methods: Two hundred and thirty-five SLE patients (219 women and 16 men), with mean age of 37.80±14.00 years, were enrolled. The disease activity using European League Against Rheumatism (EULAR) criteria was judged for SLE patients with erythrocyte sedimentation rate (ESR) and SLEDAI scores. The frequencies of CD3+CD4+FOXP3+Treg cells and Th17 cells in peripheral blood from these patients were measured by flow cytometry. And low-dose IL-2 was used among 127 patients at a dosage of fifty WIU every day for five days. Immunological and clinical assessments were performed again at the end of IL-2 treatment. Ninety healthy volunteers, matched for patients' age and gender, were also included for the estimation of CD4+ T cell subsets.

Results: As compared to healthy controls (median of Treg cells: 33.09 cells/ul), the frequencies of circulating CD4+CD25+FOXP3+Treg cells were significantly decreased in SLE patients (median: 15.49 cells/ul, $P<0.001$). The median ratios of Th17/Tregs cells in patients were greatly higher than those of healthy volunteers [0.42 (0.19, 0.88) vs. 0.21 (0.15, 0.34), $P<0.001$]. There was not significantly different in circulating Th17 cell between two groups. Moreover, CD4+CD25+FOXP3+Treg cells were negatively correlated with ESR and SLEDAI score (r=-0.198, $P=0.01$; r=-0.25, $P=0.002$).While no obvious correlation was seen between Th17 cells and SLEDAI score. After IL-2 therapy in SLE, there was a four-fold increase in circulating CD4+CD25+FOXP3+Treg cells [43.73 (24.08,74.22) vs. 11.95 (7.51,20.34),$P<0.001$], whereas Th17 cells were increased slightly. The ratio of Th17/Tregs was decreased significantly in patients with IL-2 treatment [0.19 (0.09,0.41) vs. 0.52 (0.23,0.95),$P<0.001$], tended to balance and had no difference with healthy individual ($P=0.275$).

Conclusions: With the increase of disease activity,CD4+CD25+FOXP3+Treg cells were gradually reducing, while Th17 cells did not show a significant change, indicating that the reduction of Tregs but not the elevation of Th17 cells may be the major reason for imbalance of Th17/Tregs. It is speculated that SLE is an autoimmune disease triggered by the defect of immunotolerance. More importantly, low-dose IL-2 selectively modulated the abundance of Tregs, which effectively induced autoimmune tolerance and further improved clinical symptoms.

References:

[1] Ji Y, Xue Y, Hejian Z, et al.Recovery of the immune balance betweenTh17 and regulatory T cells as a treatment for systemic lupus erythematosus[J]. Rheumatology 2011;50:1366–1372.

[2] Steinmetz OM, Turner JE, Paust HJ et al. CXCR3 mediates renal Th1 and Th17 immune response in murine lupus nephritis[J]. J Immunol 2009;183:4693–704.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4221

OP0044 ANTIBODIES ANTI-SACCHAROMYCES CEREVISIAE IN PRIMARY SJÖGREN'S SYNDROME: PREVALENCE, CLINICAL ASSOCIATIONS AND POSSIBLE CROSS-REACTIVITY WITH DISEASE SPECIFIC AUTOANTIGENS

A. Alunno[1], O. Bistoni[1], F. Carubbi[2,3], G. Cafaro[1], E. Valentini[4], R. Giacomelli[2], R. Gerli[1]. *[1]Department of Medicine, Rheumatology Unit, University of Perugia, Perugia; [2]Department of Biotechnological and Applied Clinical Sciences, Rheumatology Unit, University of L'Aquila; [3]Department of Medicine, ASL 1 Avezzano-L'Aquila-Sulmona, L'Aquila; [4]Department of Medicine, Rheumatology Unit, University di Perugia, Perugia, Italy*

Background: Saccharomyces cerevisiae is a common yeast used in the food industry. Antibodies against the phosphopeptidomannan part of the cell wall of S. cerevisiae (ASCA) are a well established biomarker of Crohn's disease and have been assessed in several organ-specific and systemic autoimmune diseases (ADs) (1–2) Although the pathogenic significance of ASCA is not yet fully understood, the molecular mimicry of self-antigens in several associated ADs has been suggested as putative mechanism.

Objectives: Since to date ASCA have not been tested in primary Sjogren's syndrome (pSS), the purpose of this study was to assess these antibodies in a large cohort of pSS patients and investigate their significance as potentially helpful biomarker in a clinical setting.

Methods: One hundred and four patients with pSS according to the 2002 American European Consensus criteria and 30 healthy donors (HD) were enrolled. ASCA IgG+IgA were assessed in serum samples with ASCA screen dot (Alphadia sa/nv). T cell phenotyping was performed in paired peripheral blood samples by flow cytometry. To compare the aminoacid sequence of mannan of Saccharomyces cerevisiae and well characterized auto-antigens peculiar of pSS (52kD and 60kD Ro/SSA, La/SSB) we browsed the protein database of the National Center for Biotechnology Information (NCBI) and run the Basic Local Alignment Search Tool (BLAST).

Results: ASCA were detected in 5 out of 104 pSS patients, therefore the prevalence in our cohort is 4.8%. None of the ASCA$^+$ pSS patients displayed IBD or other autoimmune conditions that could account for ASCA positivity. ASCA$^+$ pSS patients displayed more frequently a reduction of C3 and C4 complement fractions as well as pulmonary, articular and cutaneous involvement (all $p<0.05$). Binary logistic regression revealed that ASCA$^+$ pSS patients display an odds ratio of 14 ($p=0.006$) to have cutaneous manifestations of pSS. All ASCA+ patients but only 39% of ASCA- patients displayed anti-Ro52, anti-Ro60 and anti-La autoantibodies together ($p=0.01$). No differences concerning T regulatory and Th17 cell proportion could be observed in ASCA$^+$ compared to ASCA$^-$ pSS patients. S. cerevisiae mannan displays a consistent similarity with 52kD and 60kD Ro/SSA, La/SSB autoantigens. The highest similarity was observed when aligning the mannan with 60kD Ro/SSA (identities 7/11, 64%; positives 8/11, 72%, E value 2.2.).

Conclusions: Our study assessed for the first time ASCA IgG+IgA with a highly specific immunoblot assay in a large cohort of pSS patients, showing that ASCA positivity identifies a peculiar clinical and serological pSS phenotype. In particular, ASCA$^+$ pSS patients display anti-Ro52, anti-Ro60 and anti-La antibodies, low complement and cutaneous involvement. The high similarity between S. cerevisiae mannan and Ro60/SSA autoantigen may suggest that: i. ASCA may bind pSS autoantigens, such as anti-Ro, as already postulated for other autoantigens (2); ii. ASCA may bind more likely Ro60 autoantigen rather than the Ro52 or La autoantigens in pSS. A possible pathogenic/prognostic significance of ASCA in pSS may therefore be speculated.

References:

[1] Inflamm Bowel Dis 2012;18:1340–1355.

[2] Clin Rev Allergy Immunol 2013; 45: 152–61.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3163

OP0045 PREDICTORS OF PERSISTENT DISEASE ACTIVITY AND PERSISTENT LONG QUIESCENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS – RESULTS FROM THE HOPKINS LUPUS COHORT

I. Giannakou[1], K. Chatzidionysiou[1], L. Magder[2], R. van Vollenhoven[1], M. Petri[3]. *[1]ClinTRID - Unit for Clinical Therapy Research, Inflammatory Diseases, Department of Medicine, Karolinska Institutet, Stockholm, Sweden; [2]University of Maryland School of Medicine; [3]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, United States*

Background: Systemic lupus erythematosus (SLE) is characterized by a diversity of disease activity.

Objectives: The aim of this study was to identify prognostic factors of persistent disease activity and persistent long quiescence using baseline demographics and clinical characteristics.

Methods: Patients enrolled in the Hopkins Lupus Cohort from 1987 to 2014, who had at least 3 visits per year during 3 years following cohort inclusion and available information on disease activity were included. Three major patterns of SLE disease activity over time (1 year intervals) based on the modified SLE Disease Activity Index have been previously described: long quiescent (LQ), chronic active (CA) and relapsing-remitting (RR) *(1)*. Based on maintenance of the aforementioned

patterns over 3 consecutive years, patterns have been defined as: Persistent Long Quiescent (pLQ), Persistent Relapsing-Remitting (pRR), Persistent Chronic Active (pCA) and Mixed, at least 2 different pattern types. Predictors of pCA (vs. pLQ, pRR and mixed) and pLQ (vs. pCA, pRR and mixed) were identified by univariate and multivariate logistic regression analyses. Several baseline demographics (age, sex, ethnicity, disease duration, tobacco use, years of education and combined annual family income), disease characteristics at baseline (SLEDAI, PGA) and treatment categories (hydroxychloroquine, prednisolone and cytotoxic treatment followed at ≥75% of visits vs <75% of visits) were used as independent variables.
Results: 916 patients were identified. The results of the univariate analyses for pCA are shown in table 1. In the multivariate model, African American ethnicity (OR: 2.43, 95% CI: 1.19–4.94, p: 0.01) and high baseline SLEDAI (OR: 1.09, 95% CI: 1.03–1.16, p: 0.004) remained significant predictors of pCA. Higher education (>12 years; OR. 2.16, 95% CI: 1.11–4.20, p: 0.02) and low baseline SLEDAI (OR: 0.62, 95% CI: 0.52–0.75, p:<0.001) were significant predictors of pLQ in the multivariate analysis while African American ethnicity (OR: 0.36, 95% CI: 0.16–0.78, p:0.01) and female patients (OR: 0.26, 95% CI: 0.12–0.56, p:0.001) were less likely to achieve persistent long quiescence.

Table 1. pCA (vs. pLQ, RR and mixed)

	OR (95% CI)	p-value
Sex (female vs. male)	1.6 (0.4–6.7)	0.54
Age (>40 vs. ≤40 yrs)	1.4 (0.7–2.8)	0.32
Disease Duration	1.0 (0.9–1.1)	0.17
African American (vs. other)	2.6 (1.3–5.3)	0.007
Years of education (>12 vs. ≤ yrs)	0.7 (0.3–1.4)	0.27
Income		
<30000$	Ref	
30000–65000$	0.4 (0.2–1.0)	0.06
≥65000$	0.5 (0.2–1.2)	0.12
Smoking baseline (yes vs. no)	2.1 (1.0–4.6)	0.06
SLEDAI baseline	1.1 (1.0–1.2)	0.002
PGA baseline	1.5 (1.0–2.2)	0.04
Cytotoxic therapy (≥75% vs. <75% of visits)	1.1 (0.5–2.3)	0.85
Antimalaria therapy (≥75% vs. <75% of visits)	0.5 (0.3–1.0)	0.06
Prednisolone therapy (≥75% vs. <75% of visits)	1.1 (0.6–2.2)	0.82

Conclusions: In this large SLE cohort, African American ethnicity and high disease activity at the time of diagnosis are predictors of chronic activity, regardless of treatment, even after adjustment for education years and income, while higher education and low disease activity at baseline predict long-term quiescence.
References:
[1] Györi N, et al. Disease activity patterns over time in patients with systemic lupus erythematosus – Analysis of the Hopkins Lupus Cohort. Lupus Sci Med. 2017. In press.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6861

OP0046 RISK FACTORS FOR ADVERSE PREGNANCY OUTCOME IN ANTIPHOSPHOLIPID ANTIBODIES CARRIERS: RESULTS FROM A MULTICENTER ITALIAN COHORT OVER 20 YEARS OF EXPERIENCE

M.G. Lazzaroni[1], L. Andreoli[1], C.B. Chighizola[2], T. Del Ross[3], M. Gerosa[2], A. Kuzenko[3], M.-G. Raimondo[2], A. Lojacono[1], F. Ramazzotto[1], S. Zatti[1], L. Trespidi[2], P.L. Meroni[2], V. Pengo[3], A. Ruffatti[3], A. Tincani[1]. *[1]-, Brescia; [2]-, Milano; [3]-, Padova, Italy*

Background: Antiphospholipid antibodies (aPL) are risk factors for Adverse Pregnancy Outcome (APO). In particular, for aPL carriers (patients with aPL positivity with no thrombotic or obstetric history) pregnancy outcome and treatment are still undefined.
Objectives: To review pregnancy outcome in a large multicenter cohort of aPL carriers patients, according to different serological profile and treatment protocols.
Methods: We reviewed 69 pregnancies in 61 patients, prospectively followed in 3 Italian centers (1994–2015). Patients with any complication in previous pregnancies or concomitant autoimmune diseases were excluded. aPL profile was defined as the combination of the 3 criteria tests for aPL (Lupus Anticoagulant, anti-cardiolipin, anti-Beta2 Glycoprotein I). APO was defined as: miscarriage (<10w), fetal death (≥10w), severe preterm delivery (≤34w) with or without preeclampsia (PE), HELLP syndrome or perinatal death.
Results: Regarding aPL profile: 44 (64%) were single positive, 16 (23%) were double and 9 (13%) were triple. aPL non-criteria manifestations were present in 6 (9%) and lupus-like manifestations in 5 (7%). Eight pregnancies had a combination treatment with prophylactic low molecular weight heparin (LMWH) plus low dose aspirin (LDA), 37 had LDA alone and 24 had no treatment. We observed 2 thrombotic events (3%, 1 deep venous thrombosis and 1 ischemic stroke) and 6 APO (9%): 3 fetal deaths and 3 pre-term birth ≤34w with PE. We compared 8 complicated (6 APO,2 thrombosis) with 61 non-complicated pregnancies (Table 1). Acquired risk factors (p:0.006), non-criteria aPL (p:0.018) and lupus-like manifestation (p:0.010), triple positive aPL profile (p:0.001) were associated with APO. The combination treatment was also more frequent in APO pregnancies (p:0.005).

	Complicated pregnancies (n=8)	Non-complicated pregnancies (n=61)	P-value ^	OR (95% CI)
Mean age at pregnancy (mean (SD))	28.3 (5.8)	32.7(4.6)	0.015 §	
Acquired risk factors #	6 (75%)	14 (23%)	0.006	10.7 (1.55-82.4)
Congenital thrombophilia	2 (25%)	4 (7%)	0.140	
Non criteria aPL manifestations *	3 (38%)	3 (5%)	0.018	11.6 (1.37-108)
Lupus-like manifestations	3 (38%)	2 (3%)	0.010	17.7 (1.77-213)
Single positive	3 (38%)	41 (67%)	0.128	
Double positive	0 (0%)	16 (26%)	0.183	
Triple positive	5 (63%)	4 (7%)	0.001	23.7 (3.22-211)
No treatment	1 (13%)	23 (38%)	0.246	
LDA	3 (38%)	34 (56%)	0.457	
LDA+LMWH	4 (50%)	4 (7%)	0.005	14.2 (1.98-116)

Table 1. Complicated pregnancies (APO and thrombosis) compared with non-complicated pregnancies – univariate analysis
^ Fisher's exact test, except otherwise indicated; p significant <0.05
§ Student's T- test
# Acquired risk factors. Obesity (BMI>30w), hypertension (>140/90), hyper-cholesterolemia, hyper-triglyceridemia, hyper-homocysteinemia, diabetes mellitus
* Non-criteria aPL manifestations were defined as the presence of at least one of the followings: (livaedo reticularis, thrombocytopenia, headache, hemolytic anemia, cardiac valvulopathy, epilepsy)

Conclusions: Acquired risk factors,aPL profile (triple positivity), lupus-like and non-criteria aPL manifestations could represent risk factors for pregnancy complications and could determine failure to conventional treatment.These patients may deserve additional treatment, for example LMWH at higher/anti-coagulant dose or immunomodulatory treatment (e.g.hydroxychloroquine, also considering its anti-platelet/anti-thrombotic effects).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2260

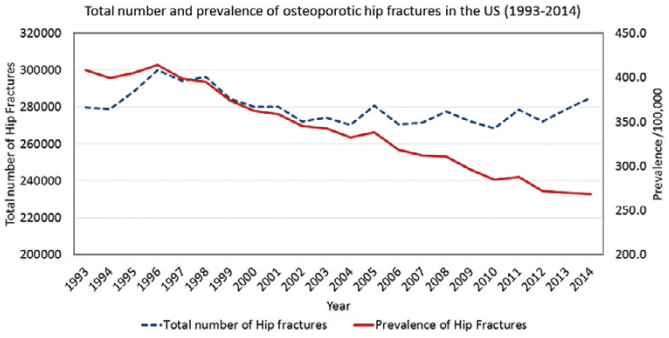
WEDNESDAY, 14 JUNE 2017

Osteoporosis treatment gap, new options and new strategies

OP0047 OSTEOPOROTIC HIP FRACTURE PREVENTION: ARE WE IN A CRISIS?

M. Sehgal[1], A. Mithal[2], A. Mithal[3], G. Singh[4]. *[1]Student, Menlo Atherton High School, Atherton, United States; [2]Student, IIIT Delhi, Delhi, India; [3]Epidemiology, ICORE, Woodside; [4]Gastroenterology and Hepatology, Stanford University, Stanford, United States*

Background: Osteoporotic hip fractures are a significant cause of morbidity and mortality in the elderly. With the aging of the US population, it was expected that there would be a nationwide "epidemic" of osteoporotic fractures; however, Medicare reimbursement for osteoporosis screening and the rapid uptake of bisphosphonate therapy in the late 1990s and early 2000s probably forestalled this epidemic. In fact, osteoporotic hip fractures numbers *declined* during this time, despite the dramatic growth of the elderly population (1). However, bisphosphonate prescriptions have dropped precipitously by over 50% from their peak in 2008 (2), likely because of concerns regarding their adverse events. In this era of "crisis" in osteoporosis prevention, has the pendulum swung back on hip fracture numbers?
Objectives: To study the number and prevalence of osteoporotic hip fractures in patients 50 years and older over the last 22 years (1993–2014) in the US?
Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in NIS from 1993 to 2014 with a primary diagnosis of non-traumatic hip fractures, and calculated age-adjusted prevalence rates. We excluded patients with concomitant diagnosis of major trauma, primary or secondary tumors locally, osteopetrosis and procedures for revision surgery or surgery for complications.
US population estimates and projections for the resident US population were obtained from the US Census Bureau.
Results: There were 407 million all-cause hospitalizations in 1.88 billion person-years of observation among people 50 years of older from 1993 to 2014 (21,626 hospitalizations per 100,000 person-years). During this time-period, there were 6.15 million hospitalizations for osteoporotic hip fractures in this population (327 per 100,000 person-years). After an initial increase in hip fractures from 1993 to 1996, there was a decline of 10.6% in total number of hip fractures from 300,154 in 1996 to 268,356 in 2010 even though population of 50 years and older increased from 69.9 million to 99.6 million in the same time. After bottoming out in 2010, the total number of hip fractures increased by 6.2% to 285,050 in 2014 (Figure, blue broken line). However, the age-standardized prevalence rate of hip fractures declined steadily (from 414/100,000 in 1996 to 269/100,000 in 2014, p<0.0001, Figure solid red line), although the rate of decline has ameliorated somewhat from 2010 onwards (not statistically significant).
Conclusions: The total number of osteoporotic hip fractures in 50 years and



older declined since 1996, bottomed out in 2010 but has started increasing again. It is critical to evaluate risks and benefits of preventive treatments for optimal management of this potentially serious problem.

References:

[1] Sehgal, A., et al., A victory in the war on osteoporosis? Declining prevalence of hospitalizations for non-traumatic hip fractures in the US. Ann Rheum Dis 2008;67(Suppl II):55.

[2] Wysowski, D.K. and P. Greene, Trends in osteoporosis treatment with oral and intravenous bisphosphonates in the United States, 2002–2012. Bone, 2013. 57(2): p. 423–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5685

OP0048 ROMOSOZUMAB RAPIDLY REDUCES CLINICAL VERTEBRAL FRACTURE INCIDENCE: RESULTS FROM THE FRAME STUDY

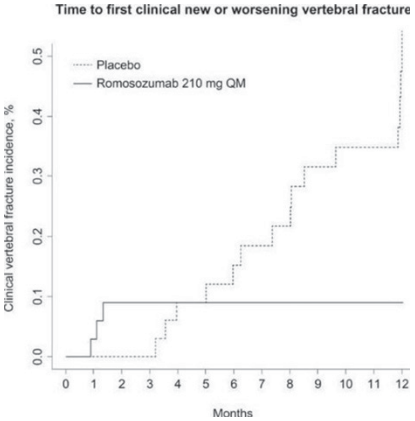
P. Geusens [1,2], M. Oates [3], A. Miyauchi [4], J. Adachi [5], M. Lazaretti-Castro [6], P.R. Ebeling [7], C.A. Perez Nino [8], C.J. Milmont [9], A. Grauer [9], C. Libanati [10]. *[1] Maastricht UMC, Maastricht, Netherlands; [2] UHasselt and ReumaClinic, Genk, Belgium; [3] Pacific Central Coast Health Center, Santa Maria, United States; [4] Miyauchi Medical Center, Osaka, Japan; [5] McMaster University, Hamilton, Canada; [6] IMA Brazil, São Paulo, Brazil; [7] Monash University, Clayton, Australia; [8] UNIENDO, Bogota, Colombia; [9] Amgen, Thousand Oaks, United States; [10] UCB, Brussels, Belgium*

Background: Romosozumab (ROMO) inhibits sclerostin and has a dual effect on bone, increasing formation while decreasing resorption, resulting in significant increases in bone mineral density (BMD) at 6 months (m), which at 12m reach 13.3% vs placebo (PBO) at the spine.[1] Using high resolution quantitative computed tomography, BMD increases were observed at both trabecular and cortical compartments of the spine, explaining the significant reductions in radiographic vertebral fracture (VFx) risk in women with osteoporosis (OP) enrolled in the FRAME trial (NCT01575834).

Objectives: Here, we report the effect of ROMO on clinical (clin) VFx incidence over 12m in women in FRAME with back pain.

Methods: FRAME enrolled 7180 postmenopausal women with OP, mean age 70.9 yrs (total hip T-score –2.5 to –3.5) and no severe VFx. Patients received monthly ROMO (n=3589; 210mg) or PBO (n=3591) for 12m. At monthly visits, women with back pain consistent with a clin VFx had a confirmatory spinal X-ray. Clin VFx risk (ROMO vs PBO) was calculated by Cox-proportional hazards model.

Results: Of 119 women reporting back pain over 12m, 20 women were diagnosed with a new or worsening VFx. With ROMO, 3 clin VFx (<0.1%; all at <2m) were identified vs 17 (0.5% at 12m) with PBO (Figure). Clin VFx risk was 83% lower in the ROMO group vs PBO at 12m (hazard ratio 0.17; 95% CI, 0.05–0.58; p=0.001). In women with clin VFx vs no clin VFx, the lumbar spine T-score was numerically lower and the FRAX score higher at baseline; other baseline characteristics were comparable among all women who reported back pain.



Conclusions: ROMO treatment for 12m was associated with rapid and large reductions in clin VFx risk vs PBO. In the ROMO group, all clin VFx occurred <2m; clin VFx risk was ≥5 times higher with PBO vs ROMO. Monthly study visits in FRAME allowed for timely radiologic confirmation of a suspected clin VFx.

References:

[1] Cosman F et al. N Engl J Med 2016;375:1532–43.

Acknowledgements: Funded by Amgen Inc. and UCB Pharma.

Disclosure of Interest: P. Geusens Grant/research support from: Amgen, Pfizer, MSD, UCS, Abbott, Eli Lilly, BMS, Novartis, Roche, Will-Pharma, Consultant for: Amgen, Speakers bureau: Amgen, M. Oates Grant/research support from: Amgen, Speakers bureau: Amgen, Eli Lilly, A. Miyauchi Consultant for: Amgen, Astellas BioPharma, J. Adachi Grant/research support from: AbbVie, Amgen, Eli Lilly, Merck, Pfizer, Consultant for: Amgen, Merck, Speakers bureau: Amgen, M. Lazaretti-Castro Grant/research support from: Amgen, Consultant for: Amgen, Eli Lilly, Sanofi, Speakers bureau: Sanofi, P. Ebeling Grant/research support from: Amgen, Merck, Eli Lilly, Consultant for: Amgen, Eli Lilly, Radius, C. A. Perez Nino Shareholder of: UNIENDO – Clinical Research, Employee of: UNIENDO – Clinical Research, C. Milmont Shareholder of: Amgen, Employee of: Amgen, A. Grauer Shareholder of: Amgen, Employee of: Amgen, C. Libanati Shareholder of: UCB Pharma, Employee of: UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.5796

OP0049 SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS EVALUATING BISPHOSPHONATES FOR THE PREVENTION AND TREATMENT OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS

A. Makhzoum [1], L. Petriw [2], M. Sattin [3], T. Towheed [4]. *[1] Department of Rheuamtology; [2] Department of Internal medicine, Queen's University, Kingston; [3] Department of Internal medicine, University of Western Ontario, London; [4] Department of Rheumatology, Queen's University, Kingston, Canada*

Background: Glucocorticoid therapy is a major risk factor for osteoporosis related fractures. A previous meta-analysis conducted by Homik et al reported that bisphosphonates therapy increased BMD in glucocorticoid- induced osteoporosis (GIO) when compared to placebo, whereas results for incident vertebral fracture did not reach statistical significance

Objectives: To evaluate the efficacy of bisphosphonates in GIO based on randomized controlled trials (RCTs). Both placebo controlled and active comparator trials were analyzed.

Methods: Two authors screened citations from the following electronic databases: Medline (1998–2015), EMBASE (1998–2015), Cochrane Library (1998–2015). A manual search was completed for conference proceedings from the ACR (2010–2015), CRA (2009–2015), and ASBMR (2009–2014). We used the study by Homik et al to identify RCTs published prior to 1998. Only RCTs that had a minimum prednisone dosage of 5 mg/day or equivalent and treatment duration of at least 3 months were included. Primary outcomes were changes in BMD and incident fractures. Two authors abstracted data using a standardized data abstraction form. We used the Cochrane Risk of Bias Tool to evaluate the quality of the selected RCTs and devised a quality score ranging from 0 to 6, where 6 represents the highest quality.

Results: A total of 466 citations were identified (239 Medline, 217 EMBASE, and 10 Cochrane Library). Fourteen RCTs met the inclusion criteria. An additional two RCTs were identified from conference proceedings. Eleven RCTs compared bisphosphonates to a placebo, three RCTs compared bisphosphonates to a vitamin D derivative, one RCT compared alendronate to teriparatide, and one RCT compared zoledronic acid to risedronate. The RCTs were of reasonably good quality with a mean quality score of 4.

Overall, of the 11 RCTs that compared bisphosphonates to a placebo, all found that the bisphosphonates were superior. Nine RCTs were pooled for mean percentage change in lumbar spine BMD (bisphosphonates n=667, placebo n=654). The pooled mean percentage change was in favor of bisphosphonates compared to placebo [weighted mean difference (WMD) of 4.03%, 95% CI (1.59–6.47), p=0.001]. Six RCTs were pooled for mean percentage change in femoral neck BMD (bisphosphonates n=486, placebo n=481) and the results favored bisphosphonates compared to placebo [WMD of 2.95%, 95% CI (0.09 -5.82), P=0.04]. Seven RCTs were pooled for outcome of incident fractures (bisphosphonates n=613, placebo n=469) and the results favored bisphosphonates compared to placebo [RR of 0.65, 95% CI (0.48–0.88), P=0.006] (Figure 1). Results were pooled using RevMan (version 5.3).

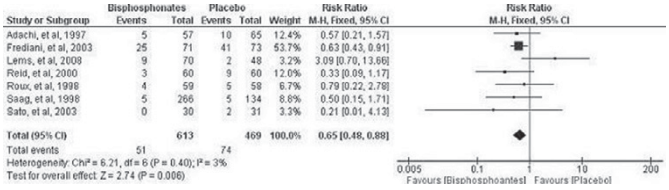


Figure 1

Conclusions: Bisphosphonates mitigate adverse changes in BMD and lower fracture risk in patients treated with glucocorticoids.

References:
[1] Homik JE, Cranney A, Shea B, et al. Bisphosphonates for steroid induced osteoporosis. Cochrane Database of Systematic Reviews 1999, Issue 1. Art. No.: CD001347.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1571

OP0050 THE TREATMENT GAP AFTER FRACTURE IN OSTEOPOROSIS PATIENTS IN SWEDEN

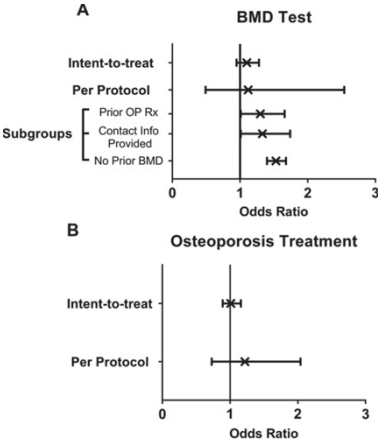
A. Spångéus[1], K. Åkesson[2], Ö. Ljunggren[3], J. Banefelt[4], L. Karlsson[4], G. Ortsäter[4], C. Libanati[5], E. Toth[5], O. Ström[4,6]. *[1]Linköping University Hospital, Linköping; [2]Lund University, Skåne University Hospital, Malmö; [3]Uppsala University Hospital, Uppsala; [4]Quantify Research, Stockholm, Sweden; [5]UCB Pharma, Brussels, Belgium; [6]Karolinska Institutet, Stockholm, Sweden*

Background: In Sweden, ~50% of women and ~25% of men are expected to suffer an osteoporosis (OP)-related fracture (Fx) during their lifetime, and hip Fx incidence in Sweden is one of the highest worldwide. Despite this, nationally only 12% of patients with Fx are prescribed an OP treatment following Fx.[1] Understanding the reasons for the marked under-treatment of patients with Fx may provide insights into how to improve deficiencies in the management of OP.
Objectives: To assess rates of OP treatment initiation within 1 year (<1 yr) following first Fx in treatment-naïve patients with fracture in Sweden and to evaluate the determinants of treatment initiation.
Methods: Patients aged ≥50 yrs with any type of Fx were identified from Swedish national registers between 2006–2012 and followed from time of first Fx. Patients who were treatment-naïve at the time of first Fx were included in the analysis. Here, we report OP treatment initiation <1 yr after Fx in the different baseline subgroups considering gender, age, Fx type, steroid use and comorbidities.
Results: 258,827 treatment-naïve patients with a first Fx (68% female; mean age 72.7 [SD 12.9] yrs) were included. Overall, 6.6% of patients initiated OP treatment <1 yr; the proportion was higher in females (8.5%) than in males (2.3%), and was highest in patients aged 70–80 yrs (10.7%) vs other ten-year age groups (mean 5.5%). Patients with a diagnosed vertebral Fx were more likely to start OP treatment (21.2%) compared with non-vertebral Fx (5.6%). The proportion of patients starting OP treatment was higher in patients receiving glucocorticoid (GC) treatment (17%) compared with those not treated with glucocorticoids (6.1%). In general, comorbidities were not positively associated with treatment initiation, except for those indirectly connected to known contributors of Fx risk, i.e. chronic pulmonary disease (GC use) and rheumatoid arthritis (FRAX-algorithm risk factor), which were associated with increased treatment initiation. Although both dementia and dependency are known to be associated with increased risk of Fx, the tendency to initiate treatment was lower in patients with these conditions compared with those without (1.5% vs 6.9% and 2.3% vs 7.4%, respectively).
Conclusions: This study confirms the large treatment gap in OP treatment initiation following a first Fx in Sweden; rate of OP treatment initiation was below the post-Fx treatment initiation rate goal of 30% and also lower than the 12% published national indicator for treatment exposure (2015).[1] The proportion of patients initiating OP treatment appears to be somewhat influenced by gender, age, Fx type, GC use, rheumatic disease, dependency and dementia; nevertheless, treatment initiation rates were low. These data highlight the need for significant efforts to improve OP management post Fx in Sweden.
References:
[1] Swedish Association of Local Authorities and Regions (SKL) and The National Board of Health and Welfare (2015) Öppna Jämförelser 2015, Hälso- och sjukvård vid kroniska sjukdomar.
Acknowledgements: Funded by UCB Pharma.
Disclosure of Interest: A. Spångéus Consultant for: Amgen, Speakers bureau: Amgen; Eli Lilly, K. Åkesson Grant/research support from: Amgen, Eli Lilly, Ö. Ljunggren Grant/research support from: Amgen, Eli Lilly, J. Banefelt Consultant for: Quantify Research, funded by UCB to conduct this study, Employee of: Quantify Research, funded by UCB to conduct this study, L. Karlsson Consultant for: Quantify Research, funded by UCB to conduct this study, Employee of: Quantify Research, funded by UCB to conduct this study, G. Ortsäter Consultant for: Quantify Research, funded by UCB to conduct this study, Employee of: Quantify Research, funded by UCB to conduct this study, C. Libanati Shareholder of: UCB Pharma, Employee of: UCB Pharma, E. Toth Shareholder of: UCB Pharma, Employee of: UCB Pharma, O. Ström Grant/research support from: Quantify Research, funded by UCB to conduct this study, Consultant for: Quantify Research, funded by UCB to conduct this study
DOI: 10.1136/annrheumdis-2017-eular.3397

OP0051 THE ACTIVATING PATIENTS AT RISK FOR OSTEOPOROSIS STUDY: A RANDOMIZED TRIAL WITHIN THE GLOBAL LONGITUDINAL STUDY OF OSTEOPOROSIS IN WOMEN COHORT

M. Danila[1], F. Anderson[2], S. Greenspan[3], A. LaCroix[4,5], J. Nieves[6], S. Silverman[7], N. Watts[8], J. Curtis[1], K. Saag[1]. *[1]University of Alabama at Birmingham, Birmingham; [2]University of Massachusetts Medical School, Worcester; [3]University of Pittsburgh, Pittsburgh; [4]Group Health Cooperative, Seattle; [5]University of California San Diego, la Jolla; [6]Helen Hayes Hospital, West Haverstraw; [7]Cedars-Sinai Medical Center, Los Angeles; [8]Mercy Health Osteoporosis and Bone Health Services, Cincinnati, United States*

Background: Osteoporosis treatment rates are declining, even among those with past fractures. Novel, low cost approaches engaging and activating patients are needed to improve care.
Objectives: To test a multi-modal, tailored, direct-to-patient, behavioral, video intervention aimed at improving rates of osteoporosis medication use.
Methods: We conducted a controlled, randomized clinical trial of our novel intervention among US women in the Global Longitudinal Study of Osteoporosis in Women cohort with self-reported fracture history who were not currently using osteoporosis therapy. The primary outcome at 6-months was self-report of osteoporosis medication use. Secondary and exploratory outcomes included starting calcium and vitamin D, bone mineral density (BMD) testing, readiness for behavioral change, and barriers to treatment.
Results: We randomized 2684 women to receive the intervention materials or usual care. Study participants were 92.6% Caucasian, with a mean (SD) age 74.9 (8.0) years, and a self-reported lower than average risk for osteoporosis (40.0%). In the 12 months prior to randomization, 1390 women reported talking with their doctor regarding osteoporosis, 7.4% reported a fracture, vitamin D or calcium supplementation were reported as 83.5% and 68.6%, respectively. We observed no differences in sociodemographic characteristics and no significant differences in the primary (11.7% vs 11.4%) and secondary (calcium, 31.8% vs 32.6%; vitamin D, 41.3% vs 41.9%; bone density, 61.8% vs 57.1%) end points between the intervention and usual care groups. Exploratory post-hoc analyses demonstrated that women in the intervention arm had more favorable views towards osteoporosis medications compared with the usual care arm and a lower proportion were in the unaware and uninvolved stages of behavior change regarding osteoporosis medications (OR=1.57, CI[1.11, 2.23]). We found that barriers to treatment were higher in the intervention, as compared to usual care arm at 6 months: concerns regarding osteonecrosis of the jaw (OR=1.58[1.14, 2.18]). We found significant differences in self-report BMD testing among the subgroup of women with no history of osteoporosis medication use (OR=1.30 [1.01, 1.66]), among those who provided a contact phone number or email address (OR=1.33 [1.01, 1.74]), and among those who did not report past BMD testing on the baseline survey (OR=1.53 [1.40, 1.68]) (Figure A). The proportion of self-reported osteoporosis treatment was similar between those with appreciable exposure to the online intervention compared with the control group (adjusted OR=1.22 [0.73, 2.04]) (Figure B).



Conclusions: This randomized study testing a novel, personalized educational intervention, did not increase the use of osteoporosis therapy at 6 months. The intervention appeared to have influenced participants' readiness for behavior change.
Acknowledgements: National Institute of Arthritis and Musculoskeletal and Skin Diseases R01 AR060240 (KS) and K23 AR062100 (MD).
Disclosure of Interest: M. Danila: None declared, F. Anderson Consultant for: Millennium Pharmaceuticals, S. Greenspan Grant/research support from: Amgen, Lilly, Consultant for: Merck, A. LaCroix Consultant for: Amgen, Pfizer, Sermonix, J. Nieves: None declared, S. Silverman Grant/research support from: Amgen, Lilly, Consultant for: Amgen, N. Watts Shareholder of: OsteoDynamics, Grant/research support from: Shire, Consultant for: AbbVie, Amgen, Janssen, Merck, Radius, Sanofi, Paid instructor for: Amgen, Shire, J. Curtis Grant/research support from: Amgen, Consultant for: Amgen, K. Saag Grant/research support from: Amgen, Lilly, Merck, Consultant for: Amgen, Lilly, Merck
DOI: 10.1136/annrheumdis-2017-eular.6591

OP0052 CORTICAL BONE LOSS IS AN EARLY FEATURE OF AXIAL SPONDYLOARTHRITIS

J. Haschka[1,2], A. Neumann[1], A. Kleyer[1], L. Schuster[1], M. Englbrecht[1], C.P. Figueiredo[1,3], C. Muschitz[2], R. Kocijan[2], H. Resch[2], J. Rech[1], G. Schett[1]. *[1]Department of Internal Medicine 3, University of Erlangen-Nuremberg, Erlangen, Germany; [2]Department of Internal Medicine II, St. Vincent Hospital, VINFORCE Study Group, Vienna, Austria; [3]Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil*

Background: Systemic bone loss is a well-known and severe consequence in axial spondyloarthritis (axSpA). To date deterioration of bone microstructure has only been described in patients with long-standing ankylosing spondylitis while bone microstructure has not been assessed in axSpA.
Objectives: The aim of the present study was to investigate bone microstructure, geometry and volumetric bone mineral density (vBMD) using high resolution peripheral quantitative CT (HR-pQCT) in a cohort of axSpA patients at an early stage of disease and to search for potential factors for deterioration of bone microstructure.
Methods: An inception cohort of 101 axSpA patients and 50 healthy controls of similar age and sex was assessed for geometric, volumetric and microstructural parameters of bone using HR-pQCT scanning of the radius. Additionally, demographic and disease specific characteristics of SpA patients were recorded.
Results: SpA patients and controls were comparable in age (median (IQR) 45.0 (15.0) vs. 44.76 (26.0) years, p=0.917), sex (female 41.6% vs. 40%, p=0.852) and BMI (median (IQR) 26.3 (6.5) vs. 23.8 (5.2), p=0.118). 75% of patients showed HLA-B27 positivity. Median disease duration was 6.5 (9.0) years, 58.4% of patients were on biological treatment and 14.9% of patients in disease remission according to ASDAS-CRP. Geometric and microstructural analysis by HR-pQCT revealed a significantly reduced cortical area (p=0.022) and cortical thickness (p=0.006) in SpA patients compared to controls. No differences in cortical porosity (p=0.685), trabecular geometry or microstructure were detected. Total and cortical vBMD were significantly reduced in SpA patients (p=0.042 and p=0.007), while there was no difference in trabecular vBMD (p=0.376). Patients with a short disease duration <2 years (n=46) showed a significant reduction of cortical thickness and cortical area (p=0.050 and p=0.032) compared to controls. Patients with a disease duration >2 years (n=55) additionally developed a decrease of cortical and total vBMD (p=0.004 and p=0.036). Multivariate regression models identified male sex to be associated with lower cortical vBMD and female sex with lower trabecular vBMD. History of prednisolone treatment (>5mg >3months) was associated with lower trabecular vBMD, and disease duration with higher trabecular vBMD. Remission status, treatment with TNF inhibitors, HLA-B27 status and presence of peripheral arthritis did not influence bone microstructure independently.
Conclusions: Bone microstructure in SpA patients is primarily characterized by deterioration of cortical bone. Cortical bone loss starts early and is evident within the first 2 years of disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3888

OP0053 BONE LOSS AND CARDIOVASCULAR RISK IN PATIENTS WITH EROSIVE AND NON-EROSIVE HAND OSTEOARTHRITIS

O. Ruzickova, O. Sleglova, K. Pavelka, L. Senolt. *Revmatology, Institute of revmatology, Prague 2, Czech Republic*

Background: Hand osteoarthritis (OA) and its more severe subset erosive hand OA are common causes of pain and morbidity. Some metabolic factors were suggested to be implicated in erosive disease. Furthermore, few studies investigated differences in systemic bone loss and cardiovascular risk factors between erosive and non-erosive hand OA.
Objectives: To compare bone mineral density (BMD) and major cardiovascular risk factors between patients with erosive and non-erosive hand OA in a cross-sectional study.
Methods: Patients with symptomatic disease fulfilling the American College of Rheumatology (ACR) criteria for hand OA were included in this study. Erosive hand OA was defined by at least one erosive interphalangeal joint. All patients underwent clinical assessments of joint swelling and radiographs of both hands. DEXA examination of lumbar spine, total femur and femur neck was performed. Metabolic risk factors (body mass index, hypertension, diabetes, dyslipidaemia) were collected. Patients were examined at baseline, one-year and two years follow-up.
Results: Altogether, 129 patients (12 male) with symptomatic nodal hand OA were included in this study and followed between April 2012 and January 2017. Out of these patients, 72 had erosive disease. The disease duration (p<0.01) was significantly higher in patients with erosive compared with non-erosive disease at baseline. Patients were taking symptomatic slow acting drugs (SYSADOA) twice a year, non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics on demand. Baseline population characteristics did not differ between both groups. Osteoporosis (T-score <-2.5 SD) was diagnosed in 12.5% (9/72) of patients with erosive hand OA and in 8.06% (5/57) of patients with non-erosive hand OA. Although bone mineral density did not significantly differ between the groups, T-scores of lumbar spine (-0.46 vs. -1.04 SD, p<0.001), total femur (-0.36 vs. -1.20 SD, p<0.001) and femur neck (-0.92 vs. -1.20 SD, p<0.01) were significantly lower in patients with erosive compared with non-erosive disease. After two years, the decrease in T- score of lumbar spine was significantly higher in patients with erosive compared with non-erosive hand OA (-0.08 SD vs. 0.07SD, p<0.01; total difference between groups is 10.92%). The decrease of T-score in femur neck, total femur and the decrease of BMD (g/cm^2) in all regions were also higher, although not significantly, in patients with erosive compared with non-erosive hand OA. In addition, more patients with erosive compared with non-erosive hand OA were treated for dyslipidaemia at baseline and after two years (32% vs. 28% and 32% vs.30%, p<0.01 for both comparisons).
Conclusions: These results suggest that patients with erosive hand OA are at risk for development of general bone loss and cardiovascular diseases.
Acknowledgements: This work was supported by the project MHCR No. 023728.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6064

OP0054 INCIDENCE OF VERTEBRAL FRACTURES IN EARLY SPONDYLOARTHRITIS: 5-YEAR PROSPECTIVE DATA OF THE DESIR COHORT

J. Sahuguet[1], J. Fechtenbaum[1], A. Molto[1], A. Etcheto[1], P. Richette[2], M. Dougados[1], C. Roux[1], K. Briot[1]. *[1]Rheumatology department, Hôpital Cochin; [2]Rheumatology department, Hôpital Lariboisière, Paris, France*

Background: Osteoporosis is a well-recognized feature of axial spondyloartyhritis (ax-SpA) and an increased risk of vertebral fractures (VFs) has been reported in patients with SpA. The prevalence of VFs is highly variable across studies, up to 30%. These data are unexpected in a disease affecting a young population, predominantly males. These results could be related to differences in methods of diagnoses of VFs and in populations with highly variable duration of the disease. We hypothesized that the prevalence and incidence of VFs be lower than the ones previously reported, especially in early spondyloarthritis.
Objectives: Our primary aim was to assess the prevalence of VFs in a cohort of early inflammatory back pain suggestive of early axial SpA and their incidence over 5 years.
Methods: Study population: patients from the DESIR (DEvenir des Spondylarthropathies Indifférenciées Récentes) cohort, which is a french national longitudinal prospective cohort including adults between 18 and 50 years old, and presenting with inflammatory back pain suggestive of axSpA for less than 3 years. Follow-up is still ongoing, but the data presented here includes the first 5 years of follow-up. All patients had thoracic and lumbar spine X-rays at baseline, 2 years and 5 years. For this particular study, all radiographs of the DESIR cohort were centrally read by one reader, an expert in the field of the diagnosis of VFs according to Genant's method. Careful assessment was used to distinguish true VFs not to be mistaken with deformities. Using a temporal sequence of reading (i.e. unblinded for chronological order), an incident VF was defined as a change in the score of a vertebra from grade 0 to a subsequent grade 1 or more. All vertebrae between T4 and L4 were evaluated. In doubtful cases, an adjudication by two other senior experts was performed. Prevalence at inclusion and the incidence of VFs over the first 5 years of follow-up were described.
Results: A total of 708 patients with inflammatory back pain were included in the DESIR cohort. Plain dorsolumbar spine X-rays were available for 694 patients, and thoracic and/or lumbar X-rays were available for 643 patients at baseline. Twenty eight VFs were identified in 21 patients (19 grade 1 VFs and 9 Grade 2 or 3 VFs); therefore, the prevalence of VFs was 4.5%.
Complete X-ray follow up between baseline and M60 was available for 433 patients. Seven incident VFs were identified in 6 patients: at 2 years 3 grade 1 VFs and 1 grade 2 VF were identified; and at 5 years, 2 grade 1 VF and 1 grade 2 or more VF were identified. The 5-year incidence of VFs was 1.6%.
Conclusions: In this study focused on a population of early spondyloarthritis, the reported low prevalence of VFs of 4.5% and incidence of 1.6% confirm our hypothesis that the real prevalence and incidence of VF in SpA is probably much lower than what was reported in previous studies. These discrepancies might be explained by the variability in the methods of vertebral fracture's assessment as vertebral deformations might be inappropriately considered as fracture.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6324

WEDNESDAY, 14 JUNE 2017

Rehabilitation and modern drug treatment - needs and challenges

OP0055-HPR PREFERENCES FOR SELF-MANAGEMENT AND SUPPORT SERVICES IN PATIENTS WITH INFLAMMATORY ARTHRITIS: A DANISH NATIONWIDE CROSS-SECTIONAL STUDY

N.M. Hammer[1], C. Flurey[2], K.V. Jensen[1], L. Andersen[1], B.A. Esbensen[1,3]. *[1]Rigshospitalet - Glostrup, COPECARE, Centre for Rheumatology and Spine Diseases & Research Unit, Glostrup, Denmark; [2]Rheumatology Unit, Bristol Royal Infirmary, Bristol, West England, United Kingdom; [3]Department of Clinical Medicine, Faculty of Health and Medical, University of Copenhagen, Copenhagen, Denmark*

Background: During recent years the medical treatment of inflammatory arthritis

(IA) has improved and become more efficient. However, many patients still continue to experience serious negative impact on both their physical and psychosocial health and wellbeing. Therefore, it is essential to identify patients' needs for support for managing IA in everyday life.
Objectives: To explore preferences for self-management and support services in patients with inflammatory arthritis.
Methods: Adult patients with IA (rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA)) were invited through The Danish Rheumatism Organization, arthritis networks, and hospitals' rheumatology departments across the country to participate in a cross-sectional study using online survey methodology. The questionnaire included questions on patient's interest in participation (requiring an answer of yes or no) in a total of 30 different self-management and support services within eight overall categories (i.e. discussion groups, one-to-one sessions, question and answer sessions, organised talks, physical activity, education sessions, raising arthritis awareness events, and online services), and preferences regarding practical issues of taking part. Descriptive statistics were applied.
Results: In total, 664 patients (85% female) responded, of which 53% had RA, 27% had PsA and 20% had axSpA. Respondents' mean age was 50 years (SD=13), and median disease duration was 10 years (IQR=4–16). Of the 30 different self-management and support services, the most popular was *Online service: Website for information (about symptoms, treatment and self-management of arthritis)* with 91% of the respondents indicating interest. This was followed by *One-to-one session with a rheumatologist (about coping with arthritis)* (89%) and *Organised talks by researchers (about current rheumatology research)* (83%). Also, *One-to-one session with a nurse*, *One-to-one session with a physiotherapist*, and *Education session on managing symptoms* were all chosen by more than 80% of the respondents. The vast majority of respondents (81%) indicated to prefer a group with no fixed commitments and an advertised time table. Regarding timing of support, the majority (70%) indicated that self-management and support services should optimally be offered whenever needed. However, respondents also stated it would be helpful within the first six months of being diagnosed (49%) as well as during flares (30%).
Conclusions: Patients with IA show high overall interest in taking part in self-management and support services. Especially, websites for finding disease related information, one-to-one sessions with health professionals, organised talks about rheumatology research and education on symptom management are requested. The preference regarding practical issues seems to be for a flexible delivery according to the patients' fluctuating needs during their illness course.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5002

WEDNESDAY, 14 JUNE 2017

Basic and clinical science in paediatric rheumatology

OP0056 IL-23P19 IS UP-REGULATED IN MONOCYTE-DERIVED MACROPHAGES FROM HLA B27 POSITIVE PATIENTS WITH ENTHESITIS RELATED ARTHRITIS

C. Fisher, D. Eleftheriou, D. Sen, Y. Ioannou. *Arthritis Research UK Centre for Adolescent Rheumatology, University College London, London, United Kingdom*

Background: Enthesitis related arthritis (ERA) is an HLAB27-associated subtype of JIA most similar to the adult spondyloarthropathies (SpA). The innate immune system, intracellular stress response (the unfolded protein response (UPR)) and IL23/IL17 pathway are strongly implicated in the pathogenesis of adult SpA. However, these systems remain relatively unexplored in ERA.
Objectives: To compare levels of the IL23 subunit, IL23p19, produced by monocyte-derived macrophages (MDMs) in the presence of lipopolysaccharide (LPS) and an inducer of the UPR (tunicamycin (TM)) from patients with ERA and healthy controls. Other pro-inflammatory cytokines and markers of the UPR were also studied.
Methods: Peripheral blood monocytes isolated from 30 patients with ERA (20 HLAB27 positive, 10 HLAB27 negative, median age 16yrs 4mths, median disease duration 3yrs 9mths, M:F 7:1) and 16 age and gender-matched healthy controls were differentiated in vitro with macrophage-colony stimulating factor. Cells were treated with IFNγ and then stimulated with LPS alone or LPS with TM for 24 hours. Pro-inflammatory cytokines and markers of the UPR were measured by expression of mRNA using qPCR and normalised against GAPDH.
Results: IL23p19 expression was higher in MDMs from HLAB27 positive patients with ERA compared to healthy controls treated with LPS [median relative expression 384.7 (IQR 179.2–1340) vs 90.5 (49.9–455.9), p=0.02]. With the addition of the UPR inducer, TM, enhanced IL23p19 mRNA expression was also seen in HLAB27 positive patients compared to those who were HLAB27 negative and healthy controls [median relative expression 608.9 (IQR 282–3286) vs 283.0 (IQR 20.1–928.2) vs 195.1 (IQR 9.8–853.7); p=0.02]. When the groups were divided in to males and females, significantly higher IL23p19 expression was seen in MDMs treated with LPS from male HLAB27 positive patients with ERA compared to male healthy controls [661.7 (IQR 169.7–1531) vs 78.3 (39.01–139.6), p=0.0095] (figure 1). This was also the case for MDMs treated with LPS and TM [537.5 (IQR 295.3–3054) vs 93.05 (IQR 2.7–1109); p=0.02]. To investigate the effect of UPR induction on IL23p19 mRNA expression, percentage increase was calculated for each patient between MDMs treated with LPS alone and MDMs treated with LPS and TM. Interestingly, median percentage increase for HLAB27 positive patients with ERA was 63% but a decrease was seen in IL23p19 mRNA expression for in HLAB27 negative patients (-3.8%) with the addition of TM. When HLAB27 positive patients not oh TNF inhibitors were compared to those on treatment, the median percentage increase between LPS and LPS + TM treated MDMs was significantly modulated [78.7% vs 10.1%, p-0.049]. mRNA expression for other pro-inflammatory cytokines including TNF, IL1 and IL6, in addition to markers of the UPR (XBP1, CHOP and BiP) demonstrated no significant differences between patients and healthy controls.
Conclusions: Expression of IL23p19 mRNA in MDMs is significantly enhanced in HLAB27 positive patients with ERA. In this group, the induction of the UPR appears to further enhance IL23p19 expression but this effect is modulated by treatment with TNF inhibitors. These results suggest a potential role for IL23 and the UPR in the pathogenesis of ERA, particularly in those who are HLAB27 positive and may have implications for treatment stratification, indicating a subgroup of patients who may respond to IL23 blockade.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5004

OP0057 FLUORESCENCE OPTICAL IMAGING IN JUVENILE IDIOPATHIC POLYARTICULAR DISEASE BEFORE AND DURING ANTIRHEUMATIC TREATMENT

A. Klein[1], G.-W. Just[1], S.G. Werner[2], I. Becker[3], P. Oommen[4], K. Minden[5], H.-E. Langer[2], G. Horneff[1]. *[1]Asklepios, Sankt Augustin; [2]RHIO, Duesseldorf; [3]University Cologne, Cologne; [4]University, Duesseldorf; [5]Charite, Berlin, Germany*

Background: Valid detection of inflamed joints is essential for correct classification, therapeutic decisions and assessment of treatment efficacy in juvenile idiopathic arthritis (JIA).
Objectives: Fluorescence optical imaging (FOI) enables visualization of inflammation in arthritis of finger and hand joints and might be used in JIA.
Methods: A 24-week observational study in polyarticular JIA patients newly starting treatment with either methotrexate or a biologic was performed. Patients were evaluated clinically, by ultrasound B–mode, power-Doppler and FOI at baseline, week 12 and 24.
Results: Of 37 patients enrolled, 24 patients started MTX and 13 a biologic for the first time (Etanercept n=11, Adalimumab and Tocilizumab one 1). Composite measures, mean JADAS 10 decreased significantly from 17.7 at baseline to 12.2 and 7.2 at week 12 and 24 respectively and JIA-ACR 30/50/70/100 response rates at week 24 were 85%/73%/50%/27%. In total 1110 joints were examined clinically, 990 by US/PD and 990 by FOI. At baseline/week12/week24 23.6%/16.4%/9.0% joints on hand and fingers were clinically active joints, by US 19.4%/16.1%/11.5% joints showed effusions, 18.8%/12.7% and 9.6% showed synovial thickening and by PD 6.9%/1.8%/5% joints showed hyperperfusion. Any sign of arthritis was detected by US/PD in 24.5%/19.2%and17%. By FOI at 38.7%/29.2%/27.6% showed a signal enhancement in at least one phase. Summarizing all 3 points

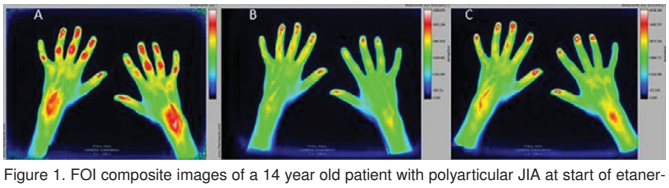


Figure 1. FOI composite images of a 14 year old patient with polyarticular JIA at start of etanercept treatment (left), after 3 (middle) and 6 months (right).

Abstract OP0057 – Table 1. Numbers of joints of a total of 2970 evaluated joints at 3 different points of time and comparison of number of joints with increased FOI signal and detection by US according to detection by clinical examination. Data on US examination were available for 2550 joints in total

	FOI					US/PD			
n (%)	Any signal 947	Composite image 530	Phase 1 396	Phase 2 783	Phase 3 180	Any signal 527	Effusion 430	Synovitis 375	Hyper-perfusion 120
Signal in clinically active joints (n=519)	320 (33.8%/61.7%)* r	205 (38.7%/39.5%)	161 (40.7%/31.0%)	277 (35.4%/ 53.4%)	81 (45.0%/15.6%)	239 (45.4%/46.0%)	211 par (49.1%/40.7%)	164 (43.7%/31.6%)	47 (39.2%/9.0%)
Signal in clinically inactive joints	627 (66.2%/25.6%)	325 (61.3%/13.3%)	235 (59.3%/9.6%9)	506 (64.6%/20.6%)	99 (55.0%/4.0%)	288 (54.6%/ 11.8%) (54.6%/11.8%)	219 (51.0%/8.9%)	211 (56.2%/8.6%)	73 (60.8%/3.0%)

*First percentage refers to columns, second to rows.

of time, the highest numbers of signals were detected by FOI with 32% of joints, especially in phase 2 while by US/PD 20.7% and by clinical examination 17.5% were active. A high number of joints (21.1%) had FOI signals but were clinically inactive. 20.1% of joints with signals in FOI did not show effusion, synovial thickening or hyperperfusion by US/PD. Due to the high number of negative results specificity of FOI compared to clinical examination/US/PD was high (84–95%), sensitivity was moderate only.
Conclusions: Improvement upon treatment with either methotrexate or a biologic can be visualized by FOI. FOI and US/PD could detect clinical but also subclinical inflammation. FOI detected subclinical inflammation in higher extent than US.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2293

OP0058 IMPROVEMENT IN PATIENT-REPORTED OUTCOMES IN PATIENTS WITH POLYARTICULAR-COURSE JUVENILE IDIOPATHIC ARTHRITIS AND INADEQUATE RESPONSE TO BIOLOGIC OR NON-BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS TREATED WITH SC ABATACEPT

N. Ruperto[1], H. Brunner[2], N. Tzaribachev[1], G. Vega-Cornejo[1], I. Louw[1], J. Anton[1], D. Viola[1], I. Foeldvari[1], V. Keltsev[1], D. Kingsbury[2], C. Wouters[1], B. Lauwerys[1], E. Alemao[3], R. Wong[3], M. Nys[4], S. Banerjee[3], A. Martini[1], D. Lovell[2]. *[1]PRINTO, Istituto Gaslini, Genoa, Italy; [2]PRCSG, CHMC, Cincinnati; [3]Bristol-Myers Squibb, Princeton, United States; [4]Bristol-Myers Squibb, Braine L'Alleud, Belgium*

Background: In patients (pts) with polyarticular-course juvenile idiopathic arthritis (pJIA), SC abatacept (ABA) 125 mg weekly has a similar pharmacokinetic profile, therapeutically equivalent efficacy and comparable safety to IV ABA 10 mg/kg every 4 weeks.[1] Although some data on paediatric pt-reported outcomes (PRO) have been published for IV ABA,[2] PRO data following treatment with SC ABA have not.
Objectives: This analysis examined the effect of SC ABA treatment on PROs (activities of daily living [ADL] limitation questionnaire of parent/caregiver, childhood HAQ [CHAQ]-DI, and parent global assessment of overall pt well-being [PaGA]) in 6–17-year pts with active pJIA in a Phase III trial (NCT01844518).
Methods: Pts with pJIA aged 2–17 years with an inadequate response/intolerance to $\geq$1 DMARD were enrolled in this single-arm, open-label study and received SC ABA weekly for 4 months based on body weight tier (10–<25 kg [50 mg ABA], 25–50 kg [87.5 mg ABA] and >50 kg [125 mg ABA]). JIA-ACR 30 criteria (ACR Pediatric 30) responders at Month 4 could receive ABA for another 20 months. For the 6–17-year cohort reported here, ADL limitation questionnaire of parent/caregiver (mean [SD] number of days [D] of parental/caregiver missed activity, paid care and missed school [absolute values per month and percentage of D missed per month relative to an assumed average of 20 school D/month]); CHAQ-DI (0–3 scale across 8 domains of disability component); and PaGA (0–100 mm visual analogue scale) were evaluated.
Results: Baseline characteristics of the 173 pts with pJIA from the 6–17-year cohort were: median (min, max) age, 13.0 (6.0, 17.0) years; median (min, max) number of active joints, 10.0 (2.0, 42.0); 78.6% of pts used MTX (median dose: 11.6 mg/m^2/week); and 26.6% were with prior biologic failure. All ADL limitation components improved from baseline to D113 (Month 4); these improvements were largely maintained at D309 (Figure). Relative percentage D missed from school decreased from 15% (D1) to 5.5% (D309, Figure D). CHAQ-DI and PaGA improved from baseline to D309 (Table). Further 2-year data are pending.

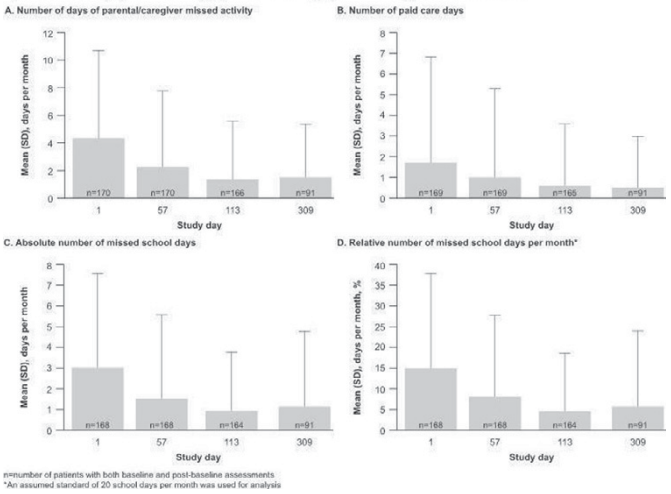
Table 1. CHAQ-DI and PaGA scores over time in the 6–17-year cohort

	Day						
	1 (n=170)	29 (n=170)	57 (n=170)	85 (n=167)	113 (n=166)	197 (n=144)	309 (n=89)
CHAQ-DI	0.99 (0.69)	0.82 (0.71)	0.73 (0.65)	0.63 (0.65)	0.61 (0.64)	0.52 (0.57)	0.46 (0.56)
PaGA (mm)	45.6 (25.97)	32.2 (24.56)	28.7 (24.58)	23.8 (23.59)	23.6 (24.32)	20.0 (23.04)	21.7 (23.58)

Data are mean (SD). For CHAQ-DI (scale 0–3) and PaGA (0–100 mm visual analogue scale), higher scores indicate greater dysfunction and lower well-being, respectively.

Conclusions: In this analysis of patients with pJIA aged 6–17 years, SC abatacept demonstrated a beneficial effect on PROs including reductions in activity limitation and disability (CHAQ-DI) and improvement in well-being (PaGA) up to D309.
References:
[1] Lovell D, et al. Arthritis Rheumatol 2016;68(suppl 10): Abstract 948.
[2] Ruperto N, et al. Arthritis Care Res 2010;62:1542–51.
Disclosure of Interest: N. Ruperto Grant/research support from: The G. Gaslini Hospital has received contributions from the following industries for the coordination activity of the PRINTO network: Bristol-Myers Squibb, GlaxoSmithKline, Hoffman-La Roche, Novartis, Pfizer,sanofi-aventis, Schwarz Biosciences, Abbott, Francesco Angelini S.P.A., Sobi, Merck Serono, Consultant for: AbbVie, Amgen, Biogen Idec, Alter, AstraZeneca, Baxalta Biosimilars, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, EMD Serono, Hoffman-La Roche, Italfarmaco, Janssen, MedImmune, Medac, Novartis, Novo Nordisk, Pfizer, sanofi-aventis, Servier, Takeda, UCB Biosciences GmbH, Speakers bureau: AbbVie, Amgen, Biogen Idec, Alter, AstraZeneca, Baxalta Biosimilars, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, EMD Serono, Hoffman-La Roche, Italfarmaco, Janssen, MedImmune, Medac, Novartis, Novo Nordisk, Pfizer, sanofi-aventis, Servier, Takeda, UCB Biosciences GmbH, H. Brunner: None declared, N. Tzaribachev: None declared, G. Vega-Cornejo: None declared, I. Louw: None declared, J. Anton Grant/research support from: Bristol-Myers Squibb, Novartis, Pfizer, AbbVie, GSK, Sobi, Roche, Alexion, Sanofi, Genzyme, Consultant for: Novartis, Sobi, Roche, Gebro, Pfizer, AbbVie, Alexion, Speakers bureau: Novartis, AbbVie, Pfizer, Sobi, Roche, Gebro, D. Viola: None declared, I. Foeldvari: None declared, V. Keltsev: None declared, D. Kingsbury: None declared, C. Wouters: None declared, B. Lauwerys: None declared, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, R. Wong Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Nys Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Banerjee Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, A. Martini: None declared, D. Lovell Grant/research support from: National Institutes of Health, NIAMS, Consultant for: AstraZeneca, Bristol-Myers Squibb, AbbVie, Pfizer, Roche, Novartis, UBC, Forest Research Institute, Horizon, Johnson & Johnson, Biogen, Takeda, Genentech, GlaxoSmithKline, Boehringer Ingelheim, Celgene, Janssen, Speakers bureau: Genentech
DOI: 10.1136/annrheumdis-2017-eular.2236

Figure. Change Over Time in Activities of Daily Living Limitation (A, Days of Parental/Caregiver Missed Activity; B, Paid Care Days; C, Missed School Days [Absolute Values]; D, Missed School Days [Relative Values]) in 6–17-Year Patients



n=number of patients with both baseline and post-baseline assessments
*An assumed standard of 20 school days per month was used for analysis

OP0059 GOLIMUMAB VERSUS TOCILIZUMAB FOR SEVERE AND REFRACTORY JUVENILE IDIOPATHIC ARTHRITIS-UVEITIS. MULTICENTER STUDY OF 33 PATIENTS

L. Domínguez Casas[1], V. Calvo-Río[1], I. Calvo[2], M. González-Fernández[2], B. López-Montesinos[2], M. Mesquida[3], A. Adán[3], M. Hernández[3], O. Maíz[4], A. Blanco[4], A. Atanes[5], B. Bravo[6], C. Modesto[7], G. Díaz-Soriano[8], M. Cordero Coma[9], D. Díaz-Valle[10], C. Fernández-Cid[11], J. Cruz[11], O. Ruiz Moreno[12], M. González-Vela[1], R. Demetrio-Pablo[1], N. Vegas-Revenga[1], C. Fernández-Díaz[1], J. Hernández[1], M. González-Gay[1], N. Palmou-Fontana[1], R. Blanco[1]. *[1]HUMV, Santander; [2]H Fe, Valencia; [3]H Clinic, Barcelona; [4]H, Donostia; [5]HUAC, A Coruña; [6]H Nieves, Granada; [7]H V d'Hebron, Barcelona; [8]H Regional Universitario, Málaga; [9]H, León; [10]H S Carlos, Madrid; [11]H, Pontevedra; [12]H Servet, Zaragoza, Spain*

Background: Uveitis is a severe manifestation of Juvenil Idiopathic Arthritis (JIA). Anti-TNFa are recommended in refractory cases, mainly infliximab (IFX) or adalimumab (ADA) (Levy-Clarke et al. Ophthalmology 2014; 121: 785–796). However, sometimes they are ineffective, contraindicated or not tolerated. The next therapeutic step is not defined.
Objectives: To compare the efficacy of Golimumab (GLM) and Tocilizumab (TCZ) in related AIJ uveitis refractory to conventional immunosuppressive drugs and anti-TNFα.
Methods: Multicenter study of 33 patients with uveitis associated-JIA. They were refractory to conventional treatment with high dose of corticosteroids and at least a) one conventional immunosuppressive drug and b) one anti-TNFa. For this reason it was decided to iniciate TCZ or GLM. TCZ was used in 25 patients: 8 mg/kg/4 w iv (n=21), 8 mg/kg/2 w (n=2); 8 mg/kg/8 w (n=1) and 2.9 mg/kg sc/w (n=1). GLM was used in 8 patients (50 mg/sc/month). We assessed visual acuity (VA), degree of intraocular inflammation, vitreous inflammation and macular thickening (with OCT). Quantitative variables were expressed with mean±SD or median [IQR], according to its distribution. They were compared with the Student t or the Mann-Whitney U test, respectively. Dichotomous variables were expressed as percentages and compared by the chi-square test.
Results: We studied 33 patients/61 affected eyes. There were no significant differences between TCZ and GLM at baseline in sex (♂/♀;4/21 vs 3/5; p=0.19), mean age (18.5±8.3 vs 19.9±8.7; p=0.55), positive ANA (95% vs 100%; p=0.7), uveitis duration before TCZ or GLM onset (116.4±93.6 vs 142.3±74.7

p=0.46), number of previous biological treatments (1.9±1.1 vs 2±1.4; p=0.84), VA (0.57±0.35 vs 0.5±0.37; p=0.42), combined immunosuppressive therapy (88% vs 75%; p=0.37), presence of cells in the anterior chamber (median, 1 [0–1] vs 1 [0.25–1.5]; p=0.6), vitritis (0 [0–0] vs 0 [0–1]; p=0.7), macular thickening (358.7±92.2 vs 313.6±77.1; p=0.32).
There were no significant difference in the efficacy between TCZ and GLM (TABLE).
After a mean follow-up of 20.48±11.7 months with TCZ and 24.25±17 months with GLM the following side effects were observed: TCZ: viral conjunctivitis plus bullous impetigo (n=1), severe thrombocytopenia and pneumonia. This last patient showed hemolytic anemia, thrombocytopenia and splenomegaly, for this reason treatment with TCZ was discontinued. With GLM cutaneous reaction was observed in 2 patients.

Table. Evolution of ocular parameters with TCZ and GLM

	TCZ (n=25)	GLM (n=8)	p
BASELINE			
VA	0.57±0.35	0.5±0.36	0.43
Cells in the anterior chamber	0.92±0.81	2.79±4.82	0.63
Vitritis	0,43±0,91	0.33±0.5	0.78
OCT	358.69±92.17	313.60±77.05	0.31
1ST MONTH			
VA	0.59±0.33	0.56±0.32	0.75
Cells in the anterior chamber	0.26±0.52	2.33±4.57	0.083
Vitritis	0.31±0.71	0±0	0.32
OCT	313.40±91.28	292.50±111.42	0.57
6TH MONTH			
VA	0.63 ±0.32	0.62 ±0.33	0.85
Cells in the anterior chamber	0,1±0,34	0±3,28	0.43
Vitritis	0,07±0,33	0,25±0,62	0.62
OCT	274,91±101,32	261,37±75,15	0.94
1ST YEAR			
VA	0.63 ±0.34	0.54 ±0.31	0.35
Cells in the anterior chamber	0±0.2	0±0	0.71
Vitritis	0.058±0.23	0±0	0.81
OCT	245.45±29.34	255±120.8	0.74

Results are expressed as mean±SD

Conclusions: TCZ and GLM seem to be equally effective and safe for refractory uveitis associated-JIA. The superiority of one or the other should be established with prospective randomized studies "Head to Head"
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3496

OP0060 HEALTH BEHAVIOR IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS- RESULTS OF THE INCEPTION COHORT OF NEWLY DIAGNOSED PATIENTS (ICON)

M. Listing[1], I. Liedmann[1], M. Niewerth[1], J. Klotsche[1], K. Mönkemöller[2], I. Foeldvari[3], J. Kümmerle-Deschner[4], T. Hospach[5], K. Minden[1]. *[1]Deutsches Rheuma-Forschungszentrum Berlin, Berlin; [2]Klinik für Kinder- und Jugendmedizin, des Kinderkrankenhauses der Stadt Köln, Köln; [3]Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg; [4]Universitätsklinik für Kinder- und Jugendmedizin Tübingen, Tübingen; [5]Zentrum für pädiatrische Rheumatologie, Klinikum Stuttgart, Stuttgart, Germany*

Background: Knowledge concerning health behavior in adolescents with juvenile idiopathic arthritis (JIA) is essential for assessing their health risks. Although there is some evidence about a relationship between low socioeconomic status (SES) and health risk behavior in adulthood, it is less clear whether this association is also true for adolescents with JIA.
Objectives: To compare the health behavior between adolescents with JIA and healthy peers and to examine the association with sex and SES.
Methods: Data of adolescents (aged 13 to 17) with JIA and healthy peers enrolled in ICON were considered for this analysis. Health behavior was assessed via questionnaire within the first years of disease. SES- Score (low, moderate, high) was determined by using an established German multidimensional aggregated index and based on the parents' education level as well as household net income.
Results: A total of 334 adolescents with JIA (61% female, mean age 15.1 (SD 1.1), mean disease duration 1.3 (SD 1.7)) and 181 healthy peers (57% female, mean age 15.3 (SD 1.3)) were included. Adolescents with JIA were less physically active and reported less consumption of alcohol compared with healthy peers (see Table). In both groups, boys were more frequently physically active and spent more time in playing video games than girls. Whereas girls with and without JIA used more often mobile phones than boys. No gender specific differences in both groups were found in consumption of illicit and legal drugs.
After stratification in groups according to the SES- Scores, socioeconomic differences were the same in adolescents with JIA and healthy peers. Teenagers with low social background (n=200) spent significantly more time in consumption of TV, mobile phones and video games than those from families with high SES (n=122). No significant relationship was found between parental SES and alcohol, nicotine and drug consumption by adolescents. The parental SES- Score was strongly associated with the education level of adolescents.

	Adolescents with JIA (n=334)	Healthy peers (n=181)	p-value
Watching TV <1h/day, n (%)	110 (33%)	68 (38%)	0.3
Playing games and computer use <1h/day, n (%)	121 (37%)	61 (34%)	0.6
Mobile phone use <1h/day, n (%)	159 (48%)	94 (52%)	0.4
Physical activity ≥ once per week, n (%)	226 (80%)	169 (94%)	<0.001
No smoking, n (%)	313 (94%)	173 (96%)	0.3
No consumption of alcohol, n (%)	168 (52%)	70 (40%)	<0.01
No consumption of illicit drugs in the last 12 months, n (%)	301 (96%)	162 (96%)	0.9
Ever sexual intercourse, n (%)	27 (8%)	13 (7%)	0.7

Conclusions: Adolescents with JIA have a similar health behavior as healthy peers, except for alcohol consumption and physical activity level. Gender and socioeconomic status are associated with health behavior of adolescents with and without JIA. Parental SES may affect adolescents' educational outcomes.
Acknowledgements: ICON is supported by a grant from the Federal Ministry of Education and Research (FKZ: 01ER0812).
Disclosure of Interest: M. Listing: None declared, I. Liedmann: None declared, M. Niewerth: None declared, J. Klotsche: None declared, K. Mönkemöller: None declared, I. Foeldvari: None declared, J. Kümmerle-Deschner: None declared, T. Hospach: None declared, K. Minden Speakers bureau: Pfizer, Roche, Pharm-Allergan
DOI: 10.1136/annrheumdis-2017-eular.4720

OP0061 DIFFUSE ALVEOLAR HEMORRHAGE: A MULTICENTER STUDY IN 847 CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

C.A. Silva[1], G. Blay[2], J.C. Rodrigues[3], G.N. Leal[2], J.C. Ferreira[2], G. Novak[2], R.M.R. Pereira[4], M.T. Terreri[5], C.S. Magalhães[6], B.C. Molinari[2], A.P. Sakamoto[5], N.E. Aikawa[2,4], L.M.A. Campos[2], T.A.P. Fernandes[6], G. Clemente[5], O.A.B. Peracchi[5], V. Bugni[5], R. Marini[7], S.B. Sacchetti[8], L.M. Carvalho[9], M.M. Fraga[10], T.C.M. Castro[11], V.C. Ramos[12], E. Bonfá[2], C.A. Silva[2,3] on behalf of Brazilian Childhood-onset Systemic Lupus Erythematosus Group. *[1]Pediatric Rheumatology Divisions, Brazilian Childhood-onset Systemic Lupus Erythematosus Group, São Paulo state; [2]Pediatric Rheumatology Unit, Children's Institute, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo; [3]Pediatric Pulmonology Unit, Children's Institute, FMUSP; [4]Division of Rheumatology, FMUSP; [5]Pediatric Rheumatology Unit, Universidade Federal de São Paulo; [6]São Paulo State University (UNESP), Faculdade de Medicina de Botucatu; [7]São Paulo State University of Campinas (UNICAMP); [8]Irmandade da Santa Casa de Misericórdia de São Paulo; [9]Ribeirão Preto Medical School – University of São Paulo; [10]Hospital Darcy Vargas; [11]Hospital Menino Jesus; [12]Pontifical Catholic University of Sorocaba, São Paulo, Brazil*

Background: Data of diffuse alveolar hemorrhage (DAH) in childhood-onset systemic lupus erythematosus (cSLE) patients are limited due to the small representation of this complication in previous case series or the focus on the comparison to adult SLE, precluding an accurate analysis of associated factors and outcomes in patients with and without this severe complication.
Objectives: To evaluate prevalence, clinical manifestations, laboratory abnormalities and treatment in a multicenter cohort study including 847 cSLE patients with and without diffuse DAH, as well as concomitant parameters of severity.
Methods: DAH was defined as the presence of at least three respiratory symptoms or signs associated with diffuse interstitial/alveolar infiltrates on chest x-ray or high-resolution computer tomography and sudden drop in hemoglobin levels with no other source of bleeding. Holm-Bonferroni correction for multiple comparisons was performed adjusting the significance level ($p<0.0022$).
Results: DAH was evidenced in 19/847 (2.2%) cSLE patients. Cough/dyspnea/tachycardia/hypoxemia occurred in all cSLE patients with DAH. Concomitant parameters of severity observed were: mechanical ventilation in 14/19 (74%), hemoptysis 12/19 (63%), macrophage activation syndrome 2/19 (10%) and death 9/19 (47%). Further analysis of cSLE patients at DAH diagnosis compared to 76 cSLE control patients without DAH with same disease duration [3 (1–151) vs. 4 (1–151) months, p=0.335], showed higher frequencies of constitutional involvement (74% vs. 10%, $p<0.0001$), serositis (63% vs. 6%, $p<0.0001$) and sepsis (53% vs. 9%, $p<0.0001$) in the DAH group. The median of disease activity score (SLEDAI-2K) was significantly higher in cSLE patients with DAH [18 (5–40) vs. 6 (0–44), $p<0.0001$]. The frequencies of thrombocytopenia (53% vs. 12%, $p<0.0001$), intravenous methylprednisolone (95% vs. 16%, $p<0.0001$) and intravenous cyclophosphamide (47% vs. 8%, $p<0.0001$) were also significantly higher in DAH patients.
Conclusions: This is the largest study to evaluate DAH. This complication, although not a disease activity score descriptor, occurs in the context of significant moderate/severe cSLE flare. Importantly, we identified that this condition is associated with serious disease flare complicated by sepsis and with high mortality rate.
Acknowledgements: This study was supported by research grants from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq 301805/2013-0 to RMRP, 303752/2015-7 to MTT, 301479/2015-1 to CSM, 305068/2014-8 to EB and 303422/2015-7 to CAS), Federico Foundation (to EB, RMRP and CAS) and by Núcleo de Apoio à Pesquisa "Saúde da Criança e do Adolescente" da USP (NAP-CriAd) to CAS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4826

OP0062 ASSESSMENT OF BIOTHERAPIES' EFFICACY IN BLAU SYNDROME: DATA FROM AN INTERNATIONAL RETROSPECTIVE COHORT OF 23 CASES

O. Fogel[1], A. Cantagrel[2], K. Ikeda[3], P. Sève[4], E. Hachulla[5], R. Cimaz[6], P. Sfriso[7], L. Punzi[7], C. Pajot[8], E. Grouteau[8], S. Tellier[8], C. Galeotti[9], S. Grotto[10], J. Sibilia[11], B. Bodaghi[12], I. Touitou[13], C. Miceli-Richard[1]. *[1]Hopital Cochin, paris; [2]Hôpital Purpan, Toulouse, France; [3]Chiba University Hospital, Chiba, Japan; [4]Hopital de la Croix Rousse, Lyon; [5]CHRU Lille, Lille, France; [6]Anna Meyer Children's Hospital, Florence; [7]University of Padova, Padova, Italy; [8]Hopital des Enfants, Toulouse; [9]CHU Bicetre, le Kremlin Bicetre; [10]CHU Rouen, Rouen; [11]CHRU Strasbourg, Strasbourg; [12]CHU pitié Salpetriere, Paris; [13]CHU Montpellier, Montpellier, France*

Background: Blau Syndrome (BS) is a rare autosomal dominant inflammatory disease characterized by early-onset granulomatous arthritis, dermatitis and recurrent uveitis (1). Mutations in the nucleotide-binding domain (NBD) of *CARD15/NOD2* gene (mainly R334W, R334Q and L469F) have been identified in Blau syndrome (2). Despite advances in BS knowledge, patients' functional prognosis remains uncertain, BS potentially leading to visual impairment or joint deformities. Optimal treatments have not been determinated yet.
Objectives: To assess the efficacy of several biologic agents in this affection
Methods: We conduct an observational, international, retrospective cohort of BS collecting clinical, biological and histological data.
Results: Among the twenty-three patients included in the cohort, 14 patients were treated by one or several lines of biologic agents, mostly by TNF blockers (80%), IL1 blockers (16%) or treatment targeting CTLA-4 (4%). Fifty-seven percent of patients achieved remission after almost two lines of treatment (1.75 lines; [0.8–2.7]). Association with csDMARDs did not significantly improved response to biologics. Considering the 3 mains symptoms independently, TNF blockers were associated with a better response in case of articular or skin features but less effective in case of ocular involvement, a clinical situation in which IL-1 targeting should be preferentially chosen.
Conclusions: Biologic treatments appeared to be effective in BS but additional data prospectively collected are still needed in order to define their place in the therapeutic strategy in order to minimize functional consequences.
References:
[1] Blau EB. Familial granulomatous arthritis, iritis, and rash. The Journal of pediatrics. 1985 Nov;107(5):689–93. PubMed PMID: 4056967. Epub 1985/11/01. eng.
[2] Miceli-Richard C, Lesage S, Rybojad M, Prieur AM, Manouvrier-Hanu S, Hafner R, et al. CARD15 mutations in Blau syndrome. Nature genetics. 2001 Sep;29(1):19–20. PubMed PMID: 11528384. Epub 2001/08/31. eng.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6660

OP0063 CANAKINUMAB TREATMENT IN PATIENTS WITH COLCHICINE-RESISTANT FMF (CRFMF), HIDS/MKD AND TRAPS: EFFICACY IN THE 16 WEEKS RANDOMISED CONTROLLED PHASE AND MAINTENANCE OF DISEASE CONTROL AND SAFETY AT WEEK 40

F. De Benedetti[1], M. Gattorno[2], J. Frenkel[3], I. Calvo[4], M. Moutschen[5], P. Quartier[6], O. Kasapcopur[7], S. Ozen[8], A. Gül[9], J. Anton[10], I. Koné-Paut[11], H. Lachmann[12], H.M. Hoffman[13], E. Ben-Chetrit[14], A. Zeft[15], Y. Gong[16], E. Vritzali[17], G. Junge[17]. *[1]IRCCS Ospedale Pediatrico Bambino Gesú, Rome; [2]G. Gaslini Institute, Genoa, Italy; [3]University Medical Center, Utrecht, Netherlands; [4]Hospital Universitario i Politecnic la Fe, Valencia, Spain; [5]CHU de Liège/University of Liège, Liège, Belgium; [6]Necker-Enfants Malades Hospital, Paris, France; [7]Department of Pediatric Rheumatology, Istanbul University Cerrahpasa Medical Faculty, Istanbul; [8]Hacettepe University, Ankara; [9]Department of Internal Medicine, Rheumatology Division, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey; [10]Hospital Sant Joan de Déu, Barcelona, Spain; [11]Hôpital Kremlin Bicetre, Paris, France; [12]UK National Amyloidosis Centre, London, United Kingdom; [13]University of California, la Jolla, United States; [14]Rheumatology Unit, Hadassah–Hebrew University Medical Center, Jerusalem, Israel; [15]Pediatrics Rheumatology, Cleveland Clinic, Cleveland, United States; [16]Novartis Pharma, Shanghai, China; [17]Novartis Pharma AG, Basel, Switzerland*

Background: Canakinumab (CAN) is a fully human monoclonal antibody targeting IL-1β, a key cytokine in the pathogenesis of periodic fever syndromes (PFS) including familial Mediterranean fever (FMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and TNF receptor-associated periodic syndrome (TRAPS).
Objectives: The CLUSTER trial (NCT02059291) studied efficacy and safety of CAN in crFMF, HIDS/MKD and TRAPS. The primary objective was to demonstrate that CAN150 mg every 4 weeks (q4w) is superior to placebo (PBO) in resolving the flare by Day 15 with no new flares over 16 weeks (wks). Secondary objectives included the proportion of patients (pts) who maintained optimal control of disease activity (absence of new flares) between Wk 16 and Wk 40 after dose reduction.
Methods: The study comprised 4 epochs (E1-E4).[1] After lead-in E1, in E2 patients at time of an active fever flare were randomised to CAN 150mg q4w or PBO for 16 wks. Responders in E2 were re-randomised to PBO or 150 mg q8w for 24 wks. During E3, pts who escaped to open-label CAN in E2, were similarly down-titrated to open-label CAN q8w to gain additional information on the long-term maintenance dose. In pts with a flare, dose could be escalated up to 300 mg q4w. Safety assessments included adverse events (AEs) and serious AEs.
Results: The proportion of responders at Wk 16 was statistically higher with CAN vs PBO (Table). In E3, among the 41 re-randomised pts (PBO vs CAN 150 mg q8w) the proportion of pts who did not present new flares was numerically higher in the CAN vs PBO group (Table). Overall at Wk 40 (end of E3), including re-randomised pts and pts treated in open-label, 46% of the crFMF pts, 53% of the TRAPS pts and 23% of the HIDS/MKD pts maintained disease control with 150 mg q8w. Conversely, up-titration to 300 mg q4w was required in 28.8% of HIDS/MKD pts, and in 10.2% and 8.3% of pts with crFMF and TRAPS, respectively. In E3, the majority of pts who received CAN had PGA <2, normal CRP and SAA levels in all 3 cohorts. No new safety findings nor death were reported in CAN-treated pts through E3 (Table).

Table. Efficacy results and summary of safety

Efficacy

	Cohort	CAN 150 mg q4w N=90	PBO N=91	OR (95% CI)	p-value
Proportion of responders at Week 16 (E2), n/m (%)	crFMF	19/31 (61.3)	2/32 (6.3)	23.8 (4.4, 227.5)	<0.0001*
	HIDS/MKD	13/37 (35.1)	2/35 (5.7)	8.9 (1.7, 86.4)	<0.002*
	TRAPS	10/22 (45.5)	2/24 (8.3)	9.2 (1.5, 94.6)	0.005*
	Cohort	CAN 150 mg q8w N=19	PBO N=22	OR (95% CI)	p-value
Proportion of pts with no new flare at Week 40 (E3), n/m (%)	crFMF	7/9 (77.8)	3/10 (30.0)	8.2 (0.8, 113.4)	0.0513
	HIDS/MKD	3/6 (50.0)	1/7 (14.3)	6.0 (0.3, 366.2)	0.2168
	TRAPS	3/4 (75.0)	2/5 (40.0)	4.5 (0.15, 313.5)	0.3571

Safety: Summary of AEs and SAEs

	All	crFMF		HIDS/MKD		TRAPS	
	PBO N=24	Any CAN* E2 N=58	Any CAN* E2+E3 N=61	Any CAN* E2 N=68	Any CAN* E2+E3 N=71	Any CAN* E2 N=43	Any CAN* E2+E3 N=61
Exposure to CAN, PY	2.0	16.4	45.6	19.1	51.0	12.1	39.2
Number of AEs	34	134	332	251	613	112	265
AE rate/100 PY	1698.8	816.7	728.2	1313.6	1201.2	925.7	676.2
Number of SAEs	1	7	17	11	20	3	5
SAE rate/ 100 PY	50.0	42.7	37.3	57.6	39.2	24.8	12.8

*Indicates statistical significance (one-sided) at the 0.025 level. *Any patient who received a dose of CAN during E2 or 3. n=number of patients who responded; m=number of patients evaluated for response; AE, adverse event; CAN, canakinumab; CI, confidence interval; E, epoch; OR, odds ratio; PBO, placebo; PY, patient-years; q4w, every 4 weeks; q8w, every 8 weeks; SAE, serious adverse event

Conclusions: Canakinumab (150 mg q4w) was efficacious in resolving flare at Day 15 and preventing new flares over 16 wks. In the longer term (40 wks), absence of flares was maintained in more than half patients at the extended dosing interval (150 mg q8w) in the crFMF and TRAPS cohorts. A higher dose was needed in HIDS/MKD patients. No unexpected safety issues were reported over 40 wks of canakinumab treatment.
References:
[1] De Benedetti F, et al. Ann Rheum Dis. 2016;75:615–6.
Disclosure of Interest: F. De Benedetti Grant/research support from: Pfizer, AbbVie, Roche, Novartis, Novimmune and BMS, M. Gattorno Grant/research support from: Novartis and SOBI, Consultant for: Novartis and SOBI, J. Frenkel Grant/research support from: Novartis and SOBI, I. Calvo Grant/research support from: Novartis, Pfizer, AbbVie and Roche, Speakers bureau: Novartis, AbbVie, Gebro and Roche, M. Moutschen: None declared, P. Quartier Grant/research support from: AbbVie, BMS, Chugai-Roche, Novartis and Pfizer, Consultant for: AbbVie, Novartis, Servier and SOBI, Speakers bureau: AbbVie, BMS, Chugai-Roche, Medimmune, Novartis, Pfizer and SOBI, O. Kasapcopur Consultant for: Novartis, Speakers bureau: Novartis and Pfizer, S. Ozen Speakers bureau: Novartis and SOBI, A. Gül Grant/research support from: Novartis, J. Anton Grant/research support from: Novartis, Consultant for: Novartis, I. Koné-Paut Grant/research support from: Novartis, SOBI and Roche, Consultant for: Novartis, SOBI, Pfizer, AbbVie and Roche, H. Lachmann Consultant for: Novartis, SOBI, Takeda and GSK, Speakers bureau: Novartis and SOBI, H. Hoffman Consultant for: Novartis, Speakers bureau: Novartis, E. Ben-Chetrit Consultant for: Novartis, A. Zeft Shareholder of: Merck, Opko Health and Arno therapeutics, Consultant for: Novartis, Y. Gong Employee of: Novartis, E. Vritzali Employee of: Novartis, G. Junge Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.2194

WEDNESDAY, 14 JUNE 2017

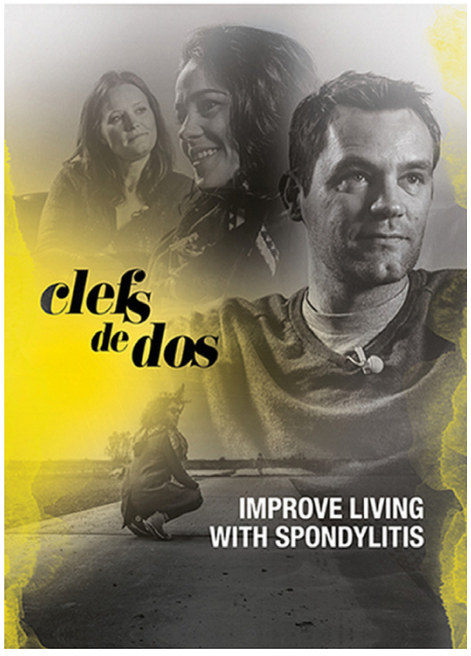
Impact of rheumatic diseases

OP0064 CLEFS DE DOS: A UNIQUE PARE-LED VIDEO PROGRAM TO IMPROVE COPING SKILLS OF PEOPLE LIVING WITH AXIAL SPONDYLOARTHRITIS

C. Beauvais[1], C. Sordet[2], A. Leboime[3], D. Vandame[4], C. Saadoun[4], G. Genin[5], F. Gerald[6]. *[1]Hôpital Saint Antoine, Paris; [2]CHU de Strasbourg, Strasbourg; [3]Hôpital Amboise-Paré, Paris; [4]UCB Pharma, Colombes; [5]Agence Catalpa, Paris; [6]Association Action contre les Spondylarthropathies - ACS, Nice, France*

Background: Diagnosis of axial spondyloarthritis (axSpA) is often delayed, with an estimated time to diagnosis of 6 years,[1] leading to patient (pt) anxiety and difficulties in coping with daily life. Many fears and beliefs have been identified,[2] including unpredictability of the disease course and concerns for the future. A survey revealed that 61% of pts want to share such experiences with other pts.[3]
Objectives: The goals were to: 1) create a video program to help pts share experiences and promote coping strategies; 2) establish the program on the internet and social networks; 3) assess the usefulness of the program for pts and healthcare professionals (HCPs).
Methods: Clefs de dos is a national French program initiated in 2015. It is led by a pt organisation, ACS-France (Action Contre les Spondyloarthropathies), Catalpa (conducted interviews, made visuals) and UCB Pharma (co-creation and promotion). Pts with axSpA were recruited by ACS on a voluntary basis to participate in focus groups; pts were selected according to their level of disease acceptance (denial [Gp1] or acceptance [Gp2]). 4 steps were planned: 1) Gp1 focus group interviews to collect feelings, words and voices; 2) Gp2 interviews to describe the pt pathway and stages in the process of disease acceptance; 3) face-to-face Gp1+Gp2 meetings for pts to share their own experiences and confront their own views; 4) rheumatologist interviews to evaluate the impact of pt testimonies on their own practice.
Results: 13 axSpA pts (10 Gp1, 3 Gp2) participated, aged 25–65 years (yrs), with 5–17 yrs disease duration; 10 were female. An animated visual was produced using Gp1 pt interviews; analysis revealed feelings of loss prior to diagnosis. Photographs and audio testimonies were used to create 3 documentary portraits of Gp2 pts, illustrating the process of disease acceptance and acquisition of coping skills (Figure). Videos of Gp1+Gp2 meetings emphasised interpersonal help and counselling between pts. 3 rheumatologists participated in step 4. They identified the importance of pt interaction to develop positive strategies, pt perspective and removal of barriers in the physician-pt relationship, and use of videos in self-management programs. By December 2016, >5,000 people had visited the website (www.clefsdedos.com), with ~500 Facebook followers from March–December 2016 (www.facebook.com/Clefsdedos/) reaching ~30,000 people via link sharing.

Figure: Example of a Clefs de dos visual creation



Conclusions: Clefs de dos was developed by and for axSpA pts. The program answers unmet needs by sharing pt experiences, particularly in situations of delayed diagnosis and lack of disease acceptance. Online access reflects good acceptability of the program, which can also be used as an educational tool in self-management. The next step is to involve other HCPs (eg. nurses, physiotherapists, psychologists).

References:
[1] Wendling D. Joint Bone Spine 2014;81(1):6–14.
[2] Berenbaum F. PLoS One 2014;9(12):e114350.
[3] Bolla G. Presentation O13, SFR 2014; Paris, France.
Acknowledgements: The authors acknowledge all patients who participated in the Clefs de dos program, and L Epivent and A Martra for contributions in co-building the communication plan. This program was conducted in partnership with ACS-France and Catalpa, and co-created and funded by UCB Pharma.
Disclosure of Interest: C. Beauvais Speakers bureau: UCB Pharma, C. Sordet: None declared, A. Leboime: None declared, D. Vandame Employee of: UCB Pharma, C. Saadoun Employee of: UCB Pharma, G. Genin: None declared, F. Gerald: None declared
DOI: 10.1136/annrheumdis-2017-eular.1987

OP0065 NURSE-LED VACCINATION PROGRAM DRAMATICALLY IMPROVES PNEUMOCOCCAL VACCINATION COVERAGE AMONG PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: A PROSPECTIVE PILOT STUDY

T. Goulenok, J. Serre, C. Francois, M.-C. Van der Haegen, J.-F. Alexandra, T. Papo, K. Sacre. *Paris-7 University, APHP, Bichat Hospital, Paris, France*

Background: Patients with chronic inflammatory rheumatic diseases (IRD) receiving immunosuppressive therapy are at high risk for invasive pneumococcal disease. Despite national recommendations regarding pneumococcal vaccination, vaccination rate remains low in this population.
Objectives: We aimed to determine whether a nurse-led vaccination program improve pneumococcal vaccination coverage among patients with chronic IRD.
Methods: From April to August 2015, all consecutive adult patients with a chronic IRD admitted in our day hospital unit (Department of Internal Medicine, Bichat Hospital, Paris, France) were screened. Eligibility for pneumococcal vaccination was assessed according to French national recommendations. Patients were identified as candidate for pneumococcal vaccination, informed on the benefice and risk of vaccination and vaccinated by nurses. Pre-intervention (i.e. percentage of patients candidate for vaccination vaccinated before the intervention program) and post-intervention (i.e. percentage of patients candidate for vaccination vaccinated after the intervention program) pneumococcal vaccination rate were compared using Chi2 test.
Results: 126 consecutive patients (43 [24–89] years, 61.9% females) with a chronic IRD were admitted in our day hospital unit during a 4 months period. Among them, 76 (60.3%) patients were candidate for pneumococcal vaccination because receiving prednisone, immunosuppressive drugs and/or biotherapy. The pre-intervention pneumococcal vaccination rate was 17.1 (13/76) %. Among patients candidate for pneumococcal infection but not vaccinated (n=63), 56 (88.9%) were accurately identified by nurses. Ten patients refused to be vaccinated and 46 eventually received pneumococcal vaccination. The post-intervention pneumococcal vaccination was 77.6 (59/76) % ($p<0.001$ as compared to the pre-intervention rate).
Conclusions: Nurse-led vaccination program dramatically improves pneumococcal vaccination coverage among patients with chronic IRD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2706

OP0066 THE PROBLEM BASED LEARNING APPLIED TO TEACHING RHEUMATOLOGICAL TOPICS AMONG NON RHEUMATOLOGY RESIDENTS

C.A. Guillen-Astete[1], A. Braña-Cardeñosa[2], M. Zamorano-Serrano[2], P. Gallego-Rodriguez[2], C. De la Casa-Resino[2]. *[1]Rheumatology Department; [2]Urgency Department, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Many pedagogical models have been included to the teaching strategies available in almost all fields of knowledge in the last 20th years. In the field of medicine teaching, the traditional teaching (TT) model based on an expert speech aid by a multimedia slide projection is now only one of many strategies. One of them is the Problem-Based learning (BPL) model, which is one of the most applied in undergraduate education; however the documented experience on residents education with rheumatologic contents in Spain is inexistent. BPL model consist in a lecture based in a clinical case or cases that the students must affront using several tools, most of them provided previously by the teacher, and the opinion of their classmates. Groups are encouraged to try to solve the medical problem while the teacher leads debates among the groups.
Objectives: Our goal is to test the impact of PBL model compared to TT among non rheumatology residents who participated in an rheumatology educational program using long term measures in their clinical practice.
Methods: We developed an educational program for second year residents of all medical specialties in our teaching hospital. The topic included the assessment and treatment of lumbar acute pain and was programmed in two separated dates using both the TT and PBL models. Students were unaware of the teaching strategy. Contents of both courses were the same and were prepared by two different experts. We reviewed the registries of medical attention performed by all residents for patients who consulted due to acute lumbar pain, and collected data about three aspects: Adherence to image test recommendations (AITR),

adherence to treatment recommendation (ATR) and recidivism before the 15th day after the day of consultation (need of further consultation due to the same medical problem). Registries included those generated along the first 12 months after the end of the courses.
Results: The TT group generated 175 registries while PBL generated 219. Both groups were formed by 20 non rheumatology second year residents. Proportion of AITR were 73.3 and 60.2% for BLT and TT groups, respectively ($P<0.001$). Considering only the registries generated in the first trimester after the courses, those proportions were respectively 80.2 and 79.5%. Proportion of ATR were 69.9 and 55.7%, respectively ($P<0.001$), however when considering only registries generated in the first trimester those proportions were 77.1 and 76.9%, respectively. Global recidivism rate (number of patients who need a further consultation due to the same medical problem or due to the side effects of their treatment among all patients attended) at the first 15th day since the first assessment was 8.7% in the PBL group and 17.5% in the TT group ($P<0.001$). At the end of both courses a survey to the students were performed. The satisfaction index –measured by a 0–10 progressive ordinal scale- were 9.1 SD 1.3 for the PBL model and 8.2 SD 1.4 for the TT model ($P<0.05$).
Conclusions: The pedagogical PBL teaching method shows a better academic impact in terms of concept retention and appliance into the medical practice along the time. In our opinion and according to our experience, most programs of education on transversal topics of rheumatology should be taught using the PBL method.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3984

OP0067 DEVELOPMENT AND VALIDATION OF A MODEL TO FACILITATE RECOGNITION OF ARTHRITIS BY GENERAL PRACTITIONERS

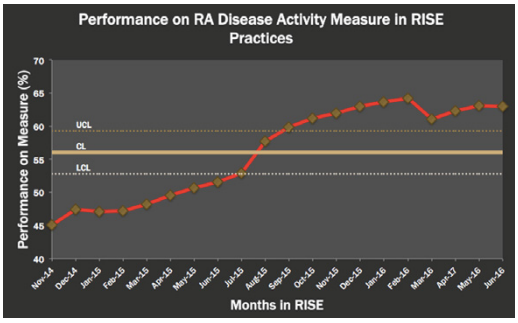
B.T. van Dijk, R.M. ten Brinck, H.W. van Steenbergen, A.H. van der Helm-van Mil. *Rheumatology, Leiden University Medical Centre, Leiden, Netherlands*

Background: Early initiation of treatment of rheumatoid arthritis is strongly associated with an improved outcome, but requires the early identification of arthritis. Physical examination of joints is crucial to this end, but is difficult for general practitioners (GPs) who have little experience. Another difficulty is that GPs see many persons with musculoskeletal symptoms per year but only few patients with clinical arthritis. To promote early recognition of arthritis, the Early Arthritis *Recognition* Clinic (EA*R*C) was initiated in Leiden, the Netherlands in 2010. GPs were instructed to refer to this clinic in case of doubt on the presence of arthritis (and not to wait and see, or to perform additional laboratory tests). At this clinic, patients filled out a form with questions on their symptoms and were seen by a rheumatologist in a short visit that comprised a full joint examination. As reported previously, this clinic importantly improved the early identification of arthritis and RA (1), but this approach may not be easily implemented in other centres or regions.
Objectives: To assess if a combination of symptoms and signs that are easy to assess can differentiate patients with and without clinical arthritis at joint examination.
Methods: 1,288 patients in whom GPs doubted on the presence of arthritis visited the EA*R*C between 2010 and 2015. Reported symptoms and signs were studied with the presence of synovitis (joint examination by experienced rheumatologist) as outcome. Multivariable logistic regression was used. A model was derived in 644 patients, and validated in the second set of 644 patients.
Results: 41% of the patients who visited the EARC had arthritis at examination. Age (per year OR 1.02; 95% CI 1.01–1.03), male sex (OR 1.8; 95% CI 1.3–2.7), symptom duration (4–12 weeks OR 3.83; 95% CI 2.22–6.60), morning stiffness >60 min (OR 1.7; 95% CI 0.9–2.9), difficulty with making a fist (OR 1.6; 95% CI 0.97–2.5), number of tender joints (1–3 tender joints OR 9.7; 95% CI 1.1–81.8) and self-reported swollen joints (OR 3.5; 95% CI 1.8–7.0) were associated with the presence of arthritis in multivariable analysis. The AUC was 0.75 (SE 0.02) in the derivation set and 0.71 (SE 0.02) in the validation set. To facilitate application in practice, a simplified model was made. This consisted of 7 variables and the total score ranged between 0–7. The AUC was 0.73 (SE 0.02). Depending on the cut-off, the PPV of the simplified model ranged between 41 and 74% and the NPV between 100 and 62%. With a cut-off of 4, the NPV was 86%, PPV 49%, specificity 35%, and sensitivity 91%.
Conclusions: A set of clinical characteristics that can be easily assessed by GPs had a reasonable discriminative ability for clinical arthritis, and can be applied by GPs in case of doubt on the presence of arthritis. This model requires further validation in general practices, but may lead to a tool that could assist GPs in their decision making regarding referral or ordering additional tests for patients with suspected early arthritis.
References:
[1] van Nies JA, et al. Ann Rheum Dis. 2013;72(8):1295–301.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2981

OP0068 PRACTICES PARTICIPATING IN THE ACR'S RHEUMATOLOGY INFORMATICS SYSTEM FOR EFFECTIVENESS (RISE) NATIONAL REGISTRY SHOW IMPROVEMENTS IN QUALITY OF CARE

J. Yazdany[1], R. Myslinski[2], T. Johansson[2], S. Kazi[3]. [1]*Medicine/Rheumatology, University of California, San Francisco, San Francisco;* [2]*American College of Rheumatology, Atlanta;* [3]*University of Texas Southwestern, Dallas, United States*

Background: The ACR launched the RISE registry in 2014 to facilitate quality improvement on a national scale. The registry passively extracts electronic health record (EHR) data from rheumatology practices, aggregates and analyzes these data centrally, and feeds performance on quality measures back to clinicians using a web-based dashboard.
Objectives: We used data from RISE to 1) examine variation in performance on quality measures across practices, and 2) evaluate trends in measure performance over time.
Methods: RISE's informatics platform continuously collects data from the EHRs of participating practices, allowing centralized aggregation and analysis of quality measures. We analyzed data collected between July 1, 2014-July 1, 2016 on all patients seen by 294 clinicians across 63 practices. Measures in the areas of rheumatoid arthritis, drug safety, preventive care and gout were examined. Performance on quality measures, defined as the percentage of eligible patients receiving recommended care, was examined at the practice level. To examine trends in performance over time, we took the subset of practices that continuously participated in RISE since its inception (n=44), and developed 1) control charts and 2) logistic regression models, in which the outcome was practice-level performance each month and the predictor was time.
Results: Data from 289,812 patients was examined. Mean (SD) age was 59 (16) years, 75% were female, 21% were racial/ethnic minorities, and 37% had public insurance. Most rheumatologists were in a group practice (73%); 25% were in solo practice and 2% part of a larger health system. Performance on measures varied significantly across practices (Table). The largest gaps were observed for gout and preventive care. For 4 of 5 measures for which the Medicare program has set national benchmarks, average performance of RISE practices exceeded targets. Of 11 measures, performance improved over time on 5 measures ($p<0.05$ in logistic models; see Figure for example control chart), was at goal on 4 measures, and saw no improvement on 2 measures (BMI screening and urate target).



Conclusions: We found significant variation in performance on quality measures across RISE practices, with the largest gaps seen in gout care and preventive care. Some practices have achieved a very high level of performance. Over time, RISE practices demonstrated improvement in over half of the measures

Abstract OP0068 – Table 1

Electronic Quality Measure (eCQM)	Measure denominator (N)	Average performance across patients (%)	Average practice-level performance (percentile)		CMS benchmark
			50th	100th	
RA: Assessment of Disease Activity	63,472	52.1	56.1	100	
RA: Functional Status Assessment	63,472	50.0	56.1	100	
RA: DMARD	63,472	90.1	91.4	98.2	9.0
Drug Safety: TB screening pre-biologic	7,842	61.1	66.6	95.7	9.0
Drug Safety: ≥1 High-Risk Medication in Elderly*	101,820	4.7	2.8	0	89.7
Drug Safety: ≥2 High-Risk Medications in Elderly*	101,820	0.1	0	0	57.8
Preventive Care: Tobacco screening and counseling	219,415	85.3	89.3	99.8	68.5
Preventive Care: BMI documentation, follow-up plan	154,501	26.4	26.7	50.7	
Preventive Care: Blood pressure management	30,607	70.0	63.2	100	

*Lower number indicates higher performance.

examined. As rheumatologists aim to improve quality of care, RISE will, by design, allow participants to measure, benchmark, and continuously monitor performance improvement.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5640

OP0069 THE BURDEN OF ANKYLOSING SPONDYLITIS: A POPULATION BASED STUDY

J.S. Lee [1], H.Y. Lee [2], E.E. Lee [1], Y.W. Song [1], E.Y. Lee [1]. *[1]Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul; [2]Center for Preventive Medicine and Public health, Seoul National University Bundang Hospital, Seongnam, Gyeonggi-do, Korea, Republic Of*

Background: Ankylosing spondylitis (AS) is an inflammatory rheumatic disease with musculoskeletal and systemic manifestations. Because AS is typically diagnosed before the age of 40 years and follows a chronic progressive course, its impact on the patient is life-long. In addition to the burden on the individual patient, that on the society is also increasing cumulatively every year [1]. The burden of AS is not confined to healthcare cost spent due to back pain and stiffness of the disease itself [2–4], but also encompass extra-articular manifestation (EAM), comorbidities, disability, and mortality contributed from AS [5].
Objectives: This study aimed to evaluate the disability, mortality, and healthcare cost for quantifying the burden of AS.
Methods: We conducted a nationwide population-based study based on national health insurance data in Korea. The patients with incident AS (n=1111) were identified with controls (n=5555) who were matched by age, sex, income, and geographic region from the year 2003 to 2013. EAMs, comorbidities, mortality and type and severity of disabilities were presented as incidence rate and compared to the controls as incidence rate ratios (IRRs). Annual health expenditure per patient was analyzed by the year and relation to AS.
Results: During the follow-up, 28% of patients in this cohort experienced any kind of EAM. More comorbidities with Charlson comorbidity index ≥3 (OR 2.18, 95% CI 1.91 to 2.48) were significantly associated. Disability rate was higher than controls regardless of causes and severity (OR 2.94, 95% CI 2.48 to 3.48). Crude IRRs for mortality was not significantly increased, but by multivariate analysis, older age at diagnosis (≥45 years old) (OR 10.53, 95% CI 4.31 to 25.68) was most strongly related to increased disability and mortality rates (Fig.1). Biologic agents elevated annual health expenditures of AS but decreased AS unrelated costs (mean 1112 vs 877 USD, p=0.0068) (Fig.2).

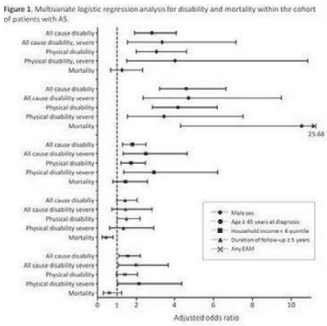


Figure 1. Multivariate logistic regression analysis for disability and mortality within the cohort of patients with AS.

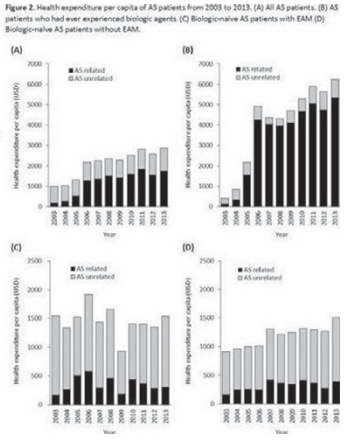


Figure 2. Health expenditure per capita of AS patients from 2003 to 2013. (A) All AS patients. (B) AS patients who had ever experienced biologic agents (C) Biologic-naive AS patients with EAM (D) Biologic-naive AS patients without EAM.

Conclusions: Along with demographic factors, systemic consequences such as EAMs and other comorbidities were associated with increased disabilities and healthcare expenditures in AS. Older age at diagnosis was significantly associated with increased mortality rates.

References:

[1] The Korean center for disease classification and information, disease statistics section, http://www.koicd.kr/stat/diseaseStats.do (Page in Korean).
[2] Huscher D, Merkesdal S, Thiele K, et al. Cost of illness in rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and systemic lupus erythematosus in Germany. Annals of the rheumatic diseases 2006;65(9):1175–83 doi: 10.1136/ard.2005.046367[published Online First: Epub Date]|.
[3] Franke LC, Ament AJ, van de Laar MA, et al. Cost-of-illness of rheumatoid arthritis and ankylosing spondylitis. Clinical and experimental rheumatology 2009;27(4 Suppl 55):S118–23.
[4] Cooksey R, Husain MJ, Brophy S, et al. The Cost of Ankylosing Spondylitis in the UK Using Linked Routine and Patient-Reported Survey Data. PloS one 2015;10(7):e0126105 doi: 10.1371/journal.pone.0126105[published Online First: Epub Date]|.
[5] Boonen A, van der Linden SM. The burden of ankylosing spondylitis. The Journal of rheumatology Supplement 2006;78:4–11.

Acknowledgements: None.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4020

OP0070 THE ROLE OF INDIVIDUAL AND COUNTRY-LEVEL SOCIO-ECONOMIC FACTORS IN WORK PARTICIPATION IN PATIENTS WITH SPONDYLOARTHRITIS ACROSS 22 COUNTRIES WORLDWIDE: RESULTS FROM THE COMOSPA STUDY

S. Rodrigues Manica [1,2], A. Sepriano [2,3], S. Ramiro [3], F.M. Pimentel-Santos [1,2], P. Putrik [4], E. Nikiphorou [5], A. Moltó [6,7], M. Dougados [6,7], D. van der Heijde [3], R. Landewé [8], F. Van den Bosch [9], A. Boonen [4]. *[1]Rheumatology Department, Centro Hospitalar de Lisboa Ocidental; [2]CEDOC - NOVA Medical School | Faculdade de Ciências Médicas, NOVA University of Lisbon, Lisbon, Portugal; [3]Leiden University Medical Center, Leiden; [4]Department Internal Medicine, Division of Rheumatology, Maastricht University Medical Center, Maastricht, Netherlands; [5]KCL, London, United Kingdom; [6]Rheumatology B Department, Paris Descartes University, Cochin Hospital, AP-HP; [7]INSERM (U1153), Clinical Epidemiology and Biostatistics, PRES Sorbonne Paris-Cité, Paris, France; [8]ARC, Amsterdam & Atrium MC Heerlen, Amsterdam, Netherlands; [9]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium*

Background: Spondyloarthritis (SpA) carries substantial financial costs, including direct costs (use of medical services and treatments) and indirect costs (loss of work productivity). While disease related factors have been repeatedly shown to be associated with work outcomes, information on the role of educational attainment and the economic wealth of the patients' country of residence is scarce.
Objectives: To explore the role of individual and country level socio-economic (SE) factors on employment, absenteeism and presenteeism across 22 countries.
Methods: Patients with a clinical diagnosis of SpA, fulfilling the ASAS SpA criteria and in working age (≤65 years old) from COMOSPA were included. Outcomes explored were employment-status, absenteeism and presenteeism according to the Work Productivity and Activity Impairment Specific Health Problem (WPAI-SHP) questionnaire. Absenteeism and presenteeism were assessed in employed patients. Multilevel logistic (for work status) and linear (for absenteeism and presenteeism) regression models with random intercept for country were constructed. Independent contribution of individual (education) and country level socio-economic factors (country healthcare expenditures and gross domestic product (GDP) (all low vs medium/high tertiles) were assessed in models adjusted for clinical factors.
Results: In total 3,114 patients from 22 countries were included (mean (SD) age 40.9 (11.8) years; 66% males; and 63% employed). Of these, 89% had axial SpA and 11% a peripheral SpA. Unadjusted employment rates ranged from 28% (Colombia) to 83% (Canada). After adjustment for relevant socio-demographic and clinical variables, differences between countries in work status persisted (Figure).

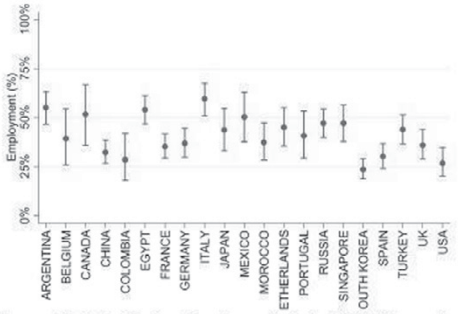


Figure – Adjusted estimates of employment rate (and 95%CI) by country derived from final multivariable, two-level model for work status, adjusted for health expenditure per capita (in USD), socio-demographic and clinical

Table – Impact of individual and country SE factors on work outcomes, in two-level models adjusted for socio-demographic and clinical variables

Independent predictors	Outcome		
	Work status (employed vs not) (N=2,897)	Absenteeism (0-100%) (N=1,619)	Presenteeism (0-100%) (N=1,497)
	OR (95% CI)	β (95% CI)	β (95% CI)
Country health expenditure per capita (US dollars)	2.42 (1.53;3.81)	-3.42 (-13.07;6.23)	-4.53 (-8.90;-0.17)
Age (years)	0.98 (0.97;0.99)	-0.04 (-0.17;0.09)**	-0.20 (-0.31;-0.10)
Gender (ref: Female)	2.26 (1.88;2.72)	-4.38 (-7.28;-1.49)	-4.30 (-6.59;-2.01)
Education (ref: Primary school or less)			
-Secondary	2.35 (1.77;3.11)	-5.42 (-10.45;-0.40)	-3.09 (-7.03;0.85)
-University	3.90 (2.91;5.24)	-7.25 (-12.33;-2.27)	-7.48 (-11.44;-3.51)
Marital status (ref: single)			
-married/living together;	2.28 (1.83;2.85)	¥	£
-divorced	2.37 (1.54;3.67)		
-widower	2.00 (0.84;4.73)		
RDCI (0-9)	0.83 (0.84;0.91)	¥	2.43 (1.21;3.66)
ASDAS-CRP	¥	3.83 (2.17;5.50)	7.43 (6.12;8.74)
BASFI (0-10)	0.98 (0.98;0.98)	0.13 (0.05;0.20)	0.45 (0.39;0.51)

RDCI=Rheumatic Disease Comorbidity Index; ASDAS-CRP= Ankylosing Spondylitis Disease Activity Score; BASFI=Bath Ankylosing Spondylitis Functional Index;
¥ Not selected during multivariable regression analysis (p ≥0.05).
£ Not selected during univariable analysis (p>0.20)

High healthcare expenditures were associated with higher employment (OR=2.42; 95% CI=1.53;3.81) and lower presenteeism (β=-4.53;CI=-8.90;-0.17). Similarly, higher GDP was associated with higher employment (OR=1.70; 95% CI=1.02;2.83), and in the same direction with presenteeism but without reaching statistical significance (β=-3.42;CI=-13.07;6.23). No significant association between any country SE indicators and absenteeism was found. At individual level, higher education was positively associated with employment-status, presenteeism and absenteeism.

Conclusions: Individual- and country-level SE factors affect work participation in SpA, and this varies significantly across countries. Better socio-economic welfare seems to support SpA patients to stay employed and productive.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3926

OP0071 SICK LEAVE AFTER SIX MONTHS IN 664 PATIENTS WITH RECENT-ONSET INFLAMMATORY ARTHRITIS

E.S. Norli[1,2], G. Hetland Brinkmann[2,3], T.K. Kvien[2], S. Lillegraven[2], O. Bjørneboe[1], A. Julsrud Haugen[3], H. Nygaard[4], C. Thunem[5], E. Lie[2], M.D. Mjaavatten[2]. *[1]Rheumatology, Martina Hansens Hospital, Sandvika; [2]Rheumatology, Diakonhjemmet Hospital, Oslo; [3]Rheumatology, Østfold Hospital Trust, Grålum; [4]Rheumatology, Lillehammer Hospital of Rheumatic diseases, Lillehammer; [5]Rheumatology, Betanien Hospital, Skien, Norway*

Background: Musculoskeletal disorders, including inflammatory arthritis (IA), are among the most common reasons for work disability and sick leave. Early IA patients with risk factors for persistent and/or erosive disease, such as high swollen joint count (SJC), acute-phase reactants, RF- or ACPA-positivity, are treated aggressively to prevent joint damage and disability.

Objectives: To study the rate of sick leave according to clinical diagnosis in an unselected very early IA cohort, and to investigate whether the predictors for sick leave are the same as the known predictors for persistent and/or erosive disease.

Methods: Data from the Norwegian Very Early Arthritis Clinic (NOR-VEAC), a longitudinal observational study of adults with IA of ≤16 weeks' duration, were used. Exclusion criteria were arthritis due to crystal deposits, trauma, osteoarthritis and septic arthritis. For the present study we included patients eligible for work participation, i.e. <65 years with no retirement or disability pension, who had information about work in the baseline and six-month case report forms. Independent samples t-test, Mann-Whitney-U test or chi-square test were used as appropriate to compare patients on sick leave after 6 months with patients not reporting sick leave. Clinically relevant baseline variables with univariate p-value <0.2, as well as age and sex, were included in the multivariable logistic regression analyses with manual backwards selection to find predictors for sick leave after six months.

Results: Of 880 patients eligible for analysis (<65 years, no retirement or disability pension), 664 (75.5%) had complete work participation data. Duration of joint swelling before inclusion [median (25–75 perc.)] was 35 (14–69) days, mean (SD) age 42.1 (12.1) years, 56.0% were females, 27.3% current smokers, and 22.4% anti-CCP and/or RF positive. The most common final clinical diagnoses were undifferentiated arthritis (35.2%), rheumatoid arthritis (22.1%) and reactive arthritis (19.7%).

The overall rate of sick leave at presentation was 37.7% and after 6 months 23.2%. More than one-third of the patients reported sick leave at first visit, regardless of diagnosis (Figure 1). At six months >20% sick leave was still reported in all groups except sarcoid arthritis and reactive arthritis. Smoking, low education (≤ high school), longer duration of joint swelling, ACPA and RF positivity, joint pain, fatigue, patient's global assessment, SF-36 (physical and mental component summary scores), HAQ-DI and tender joint count at baseline were univariably associated with sick leave after six months, whereas SJC, ESR and CRP were not. Independent predictors were current smoking (OR 2.1 (95% CI 1.4–3.2)), low education (OR 1.7 (95% CI 1.1–2.5)), longer duration of joint swelling and low SF-36 (physical and mental component summary scores).

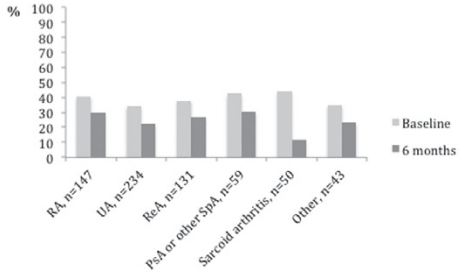


Figure 1. Proportion of patients with sick leave at baseline and after six months according to diagnosis
RA, rheumatoid arthritis; UA, undifferentiated arthritis; ReA, Reactive arthritis; PsA, psoriatic arthritis; SpA, spondyloarthritis.

Conclusions: Sick leave in IA is common, even six months after diagnosis. Predictors for sick leave after six months were associated with lifestyle and level of education rather than factors commonly considered to be predictive for unfavourable arthritis outcomes. In early IA care, health care providers should focus not only on disease activity, but also on work ability and early facilitation efforts at work.

Disclosure of Interest: E. S. Norli: None declared, G. Hetland Brinkmann: None declared, T. K. Kvien Consultant for: Tore K Kvien has received fees for speaking and/or consulting from AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, S. Lillegraven: None declared, O. Bjørneboe: None declared, A. Julsrud Haugen: None declared, H. Nygaard: None declared, C. Thunem: None declared, E. Lie: None declared, M. Mjaavatten: None declared

DOI: 10.1136/annrheumdis-2017-eular.1986

WEDNESDAY, 14 JUNE 2017

Comorbidities: having one RMD is enough - we don't need anything else

OP0072-PARE PREGNANCY AND PARENTING WITH ARTHRITIS – DEVELOPING AN EDUCATIONAL RESOURCE FOR PATIENT BY PATIENTS

L. Proulx, N. Robertson, D.P. Richards, L. Wilhelm, J. Gunderson, C. Reece, A. Sirois, A. McKinnon. *Canadian Arthritis Patient Alliance, Ottawa, Canada*

Background: For any individual, the decision to start a family is an important one. For individuals with arthritis, the decision to start a family is even more difficult. Many decisions need to be taken, including the risks of taking or not taking medication while trying to conceive and during pregnancy, and the ability to carry out their role as a parent. Few resources exist to help individuals navigate these important, life-changing decisions[1,2]. It is for this reason and through our collective experience as people living with arthritis that the Canadian Arthritis Patient Alliance (CAPA) launched a project on pregnancy and parenting with arthritis. The first phase of the project involved a survey[3] to identify patient information needs as it relates to pregnancy and parenting. The second phase focused on the creation of a medically-reviewed resource for people living with arthritis.

Objectives: An educational resource was developed for patients by patients living with inflammatory arthritis. The resource was medically reviewed by healthcare professionals.

Methods: Priority was placed on developing content for the topics identified as "very important" and "important" from the pregnancy and parenting survey. One Board member acted as project manager to develop the resource content and obtain input from people living with arthritis, researchers and rheumatologists. Methods to obtain input include software tools, e-mails and in person meetings. The educational resource was reviewed by medical experts to improve overall reliability and uptake.

Results: The educational resource is divided in two sections – one focused on pregnancy and the other on parenting. The pregnancy section includes information on fertility and family planning, talking to your partner about parenting, medication use during pregnancy and breastfeeding, managing arthritis during pregnancy and labour and delivery. The parenting section provides a variety of "life hacks" or tips for the physical care of children and dealing with fatigue and flares as well as impact of living with arthritis on a patient's children. Ongoing efforts will be made to promote the resource and use will be monitored through social media, website metrics and surveys.

Conclusions: CAPA developed a resource for people living with arthritis regarding pregnancy and parenting. CAPA aims to raise the profile of this issue and help people living with arthritis engage in dialogue with their healthcare providers during these critical life events. It is expected that use of the resource will enable shared decision-making, improve communication with health care professionals, and reduce overall stress for people living with arthritis and their families.

References:

[1] Ackerman IN, Ngian GS, Van Doornum S, Briggs AM (2015). A systematic review of interventions to improve knowledge and self-management skills concerning contraception, pregnancy and breastfeeding in people with rheumatoid arthritis. (Clin Rheumatol).

[2] Backman, C.L., Del Fabro Smith, L., Smith, S., Montie, P.L. & Suto, M. (2007). Experiences of mothers living with inflammatory arthritis. Arthritis & Rheumatism (Arthritis Care & Research), 57, 381–388.

[3] Poster from the Canadian Rheumatology Association meeting, February 2015 – Pregnancy and Parenting with Arthritis: Bridging the Information Gap.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2563

WEDNESDAY, 14 JUNE 2017

Risk factors for developing diseases or comorbidities

OP0073 PERFORMANCE OF THE EULAR DEFINITION OF ARTHRALGIA SUSPICIOUS FOR PROGRESSION TO RHEUMATOID ARTHRITIS – A LONGITUDINAL STUDY

L.E. Burgers[1], F. Siljehult[2], R.M. ten Brinck[1], H.W. van Steenbergen[1], R.B. Landewé[3,4], S. Rantapää-Dahlqvist[2], A.H. van der Helm-van Mil[5]. *[1]Rheumatology, Leiden University Medical Centre, Leiden, Netherlands; [2]Public health and clinical medicine/rheumatology, Umea University Sweden, Umea, Sweden; [3]Rheumatology, Atrium Medical Center, Heerlen; [4]Clinical immunology and rheumatology, Academical Medical Center, University of Amsterdam, Amsterdam; [5]Rheumatology, Umea University Sweden, Leiden, Netherlands*

Background: Recently a European League Against Rheumatology (EULAR)-taskforce has defined arthralgia suspicious for progression to rheumatoid arthritis (RA)[1], in order to allow inclusion of homogeneous sets of arthralgia patients in clinical studies. This was done as the field is currently shifting towards performing trials in very early disease phases as there is growing evidence that very early treatment initiation allows better disease modification and treatment of arthralgia may even prevent the development of RA. The definition was developed with the clinical expertise as reference. It is intended for use in arthralgia patient that rheumatologists' consider to be at risk for progression to RA

Objectives: To longitudinally evaluate the EULAR definition of arthralgia suspicious for progression to RA in: (1) patients in whom rheumatologists felt that imminent RA was more likely than other arthralgia's (Clinically Suspect Arthralgia, CSA); this target population fulfils the entry criterion and (2) in arthralgia patients referred to secondary care prior to rheumatologic evaluation; in these patients the entry criterion was ignored.

Methods: The definition was assessed in 241 Dutch CSA-patients and 113 patients referred to the Umeå university hospital with recent-onset arthralgia in small joints. The external reference was arthritis development <2-years follow-up.

Results: CSA-patients with a positive definition (≥3/7 parameters present) had an increased risk on arthritis development compared to definition-negative CSA-patients (HR 2.1, 95% CI 0.9–4.7). The sensitivity of a positive definition was 84% and the positive predictive value (PPV) 30%. In arthralgia patients in whom the definition was applied prior to rheumatologic evaluation, a positive definition was neither sensitive (10%) nor predictive (PPV 3%). Sensitivity analyses with fulfilment of the 2010 criteria for RA or initiation of DMARDs <2-years of follow-up as external reference showed similar results.

Conclusions: The EULAR definition of arthralgia suspicious for progression to RA is sensitive when used to support the expert's opinion on imminent RA. It was not discriminative in patients without prior rheumatologic evaluation. These data suggest that the definition should be used as designed and serves to further homogenize patients that rheumatologists consider at risk for RA.

References:

[1] van Steenbergen HW, Aletaha D, Beaart-van de Voorde LJJB de, et al. EULAR definition of arthralgia suspicious for progression to rheumatoid arthritis. Ann Rheum Dis 2016; annrheumdis-2016–209846. doi:10.1136/annrheumdis-2016–209846.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3109

OP0074 ASSOCIATION BETWEEN A HISTORY OF MYCOBACTERIAL INFECTION AND THE RISK OF SJÖGREN'S SYNDROME: A NATIONWIDE, POPULATION-BASED CASE-CONTROL STUDY

H.-H. Chen[1,2], W.-C. Chao[1], T.-L. Liao[1], Y.-M. Chen[1,2], C.-H. Lin[1], D.-Y. Chen[2,3]. *[1]Department of Medical Research; [2]Division of Allergy, Immunology and Rheumatology; [3]Department of Medical Education, Taichung Veterans General Hospital, Taichung, Taiwan, Province of China*

Background: An increased risk of tuberculosis (TB) has been found in subjects with Sjögren's syndrome (SS); however, whether TB or nontuberculous mycobacteria (NTM) infection is associated with the risk of SS is still unknown.

Objectives: To explore the association between a history of mycobacterial infection and the risk of newly diagnosed SS.

Methods: After excluding those who had rheumatoid arthritis and systemic lupus erythematosus, we identified 5,751 newly diagnosed SS cases and 86,265 non-SS patients matched (1:15) for age, sex, and the year of first diagnosis date as controls using nationwide, population-based, claims data. The association between the risk of incident SS and a history of treated mycobacterial infection, including TB and NTM, was quantified by odds ratios (ORs) with 95% confidence intervals (CIs) using conditional logistic regression analysis after adjusting for Charlson comorbidity index (CCI) and bronchiectasis.

Results: The mean ± SD age was 55±14 years and the proportion of female gender was 87.8% in newly diagnosed SS cases and non-SS controls. An association was observed between NTM infection (OR, 11.24; 95% CI, 2.37–53.24) and incident SS, but not between TB infection and incident SS (OR, 1.29; 95% CI, 0.97–1.71) after adjustment for CCI and bronchiectasis. The magnitude of the association between NTM and SS risk was greatest among those aged between 45 and 65 years (OR, 39.24; 95% CI, 3.97–387.75).

	Univariable analysis OR (95% CI)	Multivariable analysis OR (95% CI)
Nontuberculous mycobacteria	20.00 (4.48–89.36)	11.24 (2.37–53.24)
Tuberculosis	1.86 (1.41–2.45)	1.29 (0.97–1.71)
CCI ≥1	1.89 (1.77–2.01)	1.83 (1.71–1.94)
Bronchiectasis	3.19 (2.76–3.69)	2.74 (2.36–3.18)

Conclusions: The present study demonstrates a statistically significant association of newly-diagnosed SS with a history of NTM, but not TB infection.

References:

[1] Peri Y, Agmon-Levin N, Theodor E, et al. Sjogren's syndrome, the old and the new. Best practice & research Clinical rheumatology 2012;26(1):105–17.
[2] Mavragani CP, Moutsopoulos HM. The geoepidemiology of Sjogren's syndrome. Autoimmunity reviews 2010;9(5):A305–10.
[3] Elkington P, Tebruegge M, Mansour S. Tuberculosis: An Infection-Initiated Autoimmune Disease? Trends in immunology 2016.

Acknowledgements: The authors would like to thank the Biostatistics Task Force of Taichung Veterans General Hospital, Taichung, Taiwan, ROC for statistical support.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1288

OP0075 OSTEOPOROTIC FRACTURE RISK ASSESSMENT USING FRAX FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

H. Lu, W.A. Murphy Jr., C. Ebede, E. Karim, S. Manocha, D. Don-Pedro, G. Rondon, L.C. Hong, L. Suyu, R.E. Champlin, X. Pundole. *The University of Texas MD Anderson Cancer Center, Houston, TX, United States*

Background: Bone loss and fractures following hematopoietic stem cell transplantation (HSCT) is common,(1, 2) and identifying patients at high risk for osteoporotic fractures following HSCT remains challenging. In the general population, the World Health Organization fracture risk assessment tool - FRAX is utilized to estimate a patient's 10-year probability of developing a major osteoporotic fracture and hip fracture.(3) However, the utility of the FRAX model in predicting fractures following HSCT has not been evaluated.

Objectives: To assess the predictive value of FRAX in osteoporotic fracture risk assessment following HSCT.

Methods: We conducted a retrospective cohort study of patients >18 years that received a HSCT at The University of Texas MD Anderson Cancer Center, from January 1, 2001 to December 31, 2010. Patients were considered to have entered the cohort at the time of HSCT. All patients were retrospectively followed until December 31, 2013 for assessment of osteoporotic fracture. Osteoporotic fractures following HSCT were identified using ICD-9 codes, and confirmed by radiology and physician documentation. FRAX probabilities were calculated from baseline information obtained by chart review.

Results: A total of 5,170 patients underwent a HSCT during the 10-year study period. During an average of 3.3 years of follow up, 10% of patients developed a fracture. Fracture rates were higher (14%) in patients that underwent an autologous HSCT in comparison to those that received an allogeneic HSCT (6%). Mean major osteoporotic fracture FRAX scores were significantly higher in individuals who sustained an osteoporotic fracture compared to individuals who did not. The area under the receiver operating characteristic curve at 5 and 10 years following the HSCT were 0.61 and 0.66 respectively (Figure). We assessed the ability of the FRAX model for prediction of osteoporotic fracture with and without considering death as a competing risk. The hazard ratios were similar for both models (HR, 2.63, 95% CI, 1.93, 3.59; HR, 2.54, 95% CI, 1.86, 3.47, respectively).

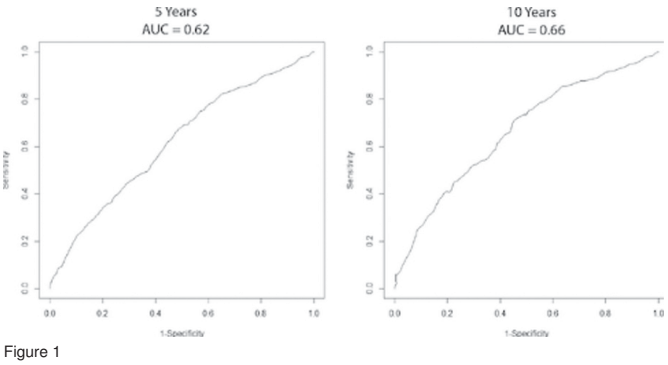


Figure 1

Conclusions: To the best of our knowledge, this is the first study to demonstrate that the FRAX model has modest discriminative ability in predicting osteoporotic fractures following HSCT. Further independent validation of our findings is necessary, before routinely using the FRAX model in clinical practice.

References:
[1] Pundole XN, Barbo AG, Lin H, Champlin RE, Lu H. Increased incidence of fractures in recipients of hematopoietic stem-cell transplantation. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2015;33(12):1364–70.
[2] Schimmer AD, Minden MD, Keating A. Osteoporosis after blood and marrow transplantation: clinical aspects. Biology of blood and marrow transplantation: journal of the American Society for Blood and Marrow Transplantation. 2000;6(2A):175–81.
[3] Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. Osteoporosis international: a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2008;19(4):385–97.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2543

OP0076 RISK OF DEVELOPING ADDITIONAL IMMUNE MEDIATED MANIFESTATIONS FOR PATIENTS WITH SYSTEMIC ARTHRITIDES

D. Aletaha[1], R. Panaccione[2], M. Davis[3], S. Johnson[3], M. Skup[4], V. Garg[4]. *[1]Medical University of Vienna, Vienna, Austria; [2]Univerity of Calgary, Calgary, Canada; [3]Medicus Economics, LLC, Milton; [4]AbbVie Inc., North Chicago, United States*

Background: Patients with the systemic arthritides ankylosing spondylitis [AS], psoriatic arthritis [PsA], rheumatoid arthritis [RA] may develop additional, non-musculoskeletal immune mediated manifestations (nms-IMMs).
Objectives: To compare the risk of developing nms-IMMs between patients with and without an existing AS, PsA, or RA.
Methods: Risk for nms-IMMs was estimated in the MarketScan Commercial Claims and Encounters database (1/2006–9/2015) for case patients with AS, PsA, RA (the "systemic arthritides"). Up to 1,000 controls were matched with replacement by age, sex, state of residence and insurance type to case patients aged 18–64. The systemic arthritides ("cases") were identified by ICD-9 diagnosis codes on ≥2 medical claims ≥30 days apart. A case patient's earliest nms-IMM claim was designated as the index date for the case and all matched controls. Onset of 6 nms-IMDs was identified by the first post-index claim: celiac disease [CE], hidradenitis suppurativa [HS], inflammatory bowel disease [IBD], lupus [SLE], psoriasis [PsO], uveitis [UV]; some of these are well-known manifestations of seronegative spondylarthropathies, like PsA and AS; some are not. All subjects had continuous health plan enrollment for ≥365 days before and after index date. Cumulative incidence of nms-IMMs was assessed at 5 years. Their risk was analyzed with stratified Cox proportional hazards models. Standard errors were adjusted for clustering by case-control match group.
Results: Among 117,794 cases, mean age was 49 years and 71% were female. Mean number of matched controls per case was 664. Across the 3 initial cohorts of patients with AS, PsA, or RA, median follow-up ranged 939–972 days for cases and 931–950 days for controls. Among case patients, 5-year cumulative incidence of any nms-IMM occurrence was 17.5% for AS, 41.8% for PsA, and 14.4% for RA. Patients with nms-IMMs had significantly higher risk than matched controls of developing each, any 1, or any 2 of the 6 manifestations (P≤0.002) (Table).

Initial IMID		Secondary IMID							
		CE	HS	SLE	PsO	UV	IBD	1st of Any 1	2nd of Any 2
AS	N Cases	6,339	6,344	6,282	6,275	6,103	6,263	6,352	6,352
	5-yr Incidence	0.9	0.2	2.9	4.2	7.7	3.4	17.5	1.2
	Hazard Ratio	11.2	3.3	23.7	8.6	54.9	16.0	17.9	24.6
PsA	N Cases	8,382	8,389	8,311	6,111	8,351	8,347	8,406	8,406
	5-yr Incidence	0.5	0.6	2.1	51.0	1.8	1.7	41.8	2.5
	Hazard Ratio	5.3	10.5	14.1	163.2	10.0	7.3	50.9	43.3
RA	N Cases	102,708	102,810	100,414	101,965	102,424	102,318	103,036	103,036
	5-yr Incidence	1.0	0.5	7.5	3.4	1.5	1.8	14.4	1.0
	Hazard Ratio	10.3	8.1	55.3	7.2	8.2	7.6	14.1	14.3

Notes: Hazard ratios from Cox proportional hazards models. Hazard ratios >1 indicate higher risk for case patients relative to controls. All hazard ratios are significant at P<0.002.

Conclusions: The risk of developing non-musculoskeletal manifestations was significantly higher for patients with AS, PsA, and RA than for matched controls. These included not only the well-known manifestations of PsA and AS but also others like manifestations leading to claims for SLE, celiac disease or HS. When managing these systemic arthritides, surveillance for additional immune mediated manifestation is warranted.
Acknowledgements: Design, study conduct, and financial support for the study were provided by AbbVie Inc. AbbVie participated in the interpretation of data, review, and approval of the abstract; all authors contributed to the development of the abstract and maintained control over the final content. Medical writing services were provided by Andrew Epstein of Medicus Economics and were funded by AbbVie.
Disclosure of Interest: D. Aletaha Grant/research support from: AbbVie, AstraZeneca, BMS, Eli Lilly, Grünenthal, Jansen, Medac, Merck, Mitsubishi Tanabe, Novo Nordisk, Pfizer, and Sanofi/Regeneron, Consultant for: AbbVie, AstraZeneca, BMS, Eli Lilly, Grünenthal, Jansen, Medac, Merck, Mitsubishi Tanabe, Novo Nordisk, Pfizer, and Sanofi/Regeneron, Speakers bureau: AbbVie, AstraZeneca, BMS, Eli Lilly, Grünenthal, Jansen, Medac, Merck, Mitsubishi Tanabe, Novo Nordisk, Pfizer, and Sanofi/Regeneron, R. Panaccione Consultant for: AbbVie, Amgen, AstraZeneca, Axcan Pharma (now Aptalis), Biogen Idec, Bristol-Myers Squibb, Centocor, ChemoCentryx, Eisai Medical Research Inc, Elan Pharmaceuticals, Ferring, Genentech, GlaxoSmithKline, Janssen, Merck Sharp & Dohme Corp, Millennium Pharmaceuticals Inc (now Takeda), Ocera Therapeutics Inc, Otsuka America Pharmaceutical, Pfizer, Shire Pharmaceuticals, Prometheus Laboratories, Schering-Plough Corporation, Synta Pharmaceuticals Corp, Teva, UCB Pharma, and Warner Chilcott, Speakers bureau: AbbVie, Amgen, AstraZeneca, Axcan Pharma (now Aptalis), Biogen Idec, Bristol-Myers Squibb, Centocor, ChemoCentryx, Eisai Medical Research Inc, Elan Pharmaceuticals, Ferring, Genentech, GlaxoSmithKline, Janssen, Merck Sharp & Dohme Corp, Millennium Pharmaceuticals Inc (now Takeda), Ocera Therapeutics Inc, Otsuka America Pharmaceutical, Pfizer, Shire Pharmaceuticals, Prometheus Laboratories, Schering-Plough Corporation, Synta Pharmaceuticals Corp, Teva, UCB Pharma, and Warner Chilcott, M. Davis Employee of: Medicus, which has received payment from AbbVie to assist with data analysis, S. Johnson Employee of: Medicus, which has received payment from AbbVie to assist with data analysis, M. Skup Shareholder of: AbbVie, Employee of: AbbVie, V. Garg Shareholder of: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.3772

OP0077 PRIMARY PROPHYLAXIS FOR PNEUMOCYSTIS PNEUMONIA IN PATIENTS WITH RHEUMATIC DISEASE AND TREATED WITH PROLONGED, HIGH-DOSE STEROID: A RETROSPECTIVE COHORT STUDY WITH 12-YEAR OBSERVATION

J.W. Park[1], J. Moon[1], J.R. Curtis[2], J.K. Park[1], E.Y. Lee[1], Y.W. Song[1], E.B. Lee[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic Of; [2]Division of Clinical Immunology & Rheumatology, University of Alabama at Birmingham, Birmingham, United States*

Background: Pneumocystis pneumonia (PCP) is a significant cause of morbidity and mortality in patients with rheumatic diseases, especially in the case of patients receiving high-dose steroid treatment.
Objectives: To investigate the efficacy and safety of PCP prophylaxis using trimethoprim/sulfamethoxazole (TMP-SMX) in patients with rheumatic disease receiving prolonged, high-dose steroids
Methods: This study includes 1522 cases of prolonged (≥4 weeks), high-dose (≥30mg/day prednisone or equivalent) steroid treatment from 1092 patients with any rheumatic diseases during a 12-year period in a single tertiary referral center in South Korea. Of them, prophylactic TMP-SMX was administered in 262 cases (prophylaxis group) with a mean (SD) duration of 229.0 (272.7) days whereas other 1260 cases received no prophylaxis (control group). Primary outcome was 1-year incidence of PCP between the two groups. Secondary outcomes included PCP-related mortality, ICU admission rate, all-cause in-hospital mortality and incidence of any adverse drug reactions (ADRs) of TMP-SMX. To minimize the baseline imbalance between the two groups, we introduced propensity-score matching and performed the same analysis in the post-matched population as a sensitivity analysis.
Results: Patients in the prophylaxis group were treated more often with secondary immunosuppressive drugs and had a higher proportion of patients with PCP high-risk diseases (ANCA-associated vasculitis and dermatomyositis) and lymphopenia at baseline. Overall, 30 cases of PCP occurred and resulted in death in 11 cases (36.7%). In the prophylaxis group, only one non-fatal case of PCP occurred. One-year PCP incidence was significantly lower in the prophylaxis group (adjusted HRs=0.096 [0.013–0.719]) (Figure). TMP-SMX also significantly reduced the PCP-related mortality (adjusted HR=0.101 [0.001–0.809]) whereas

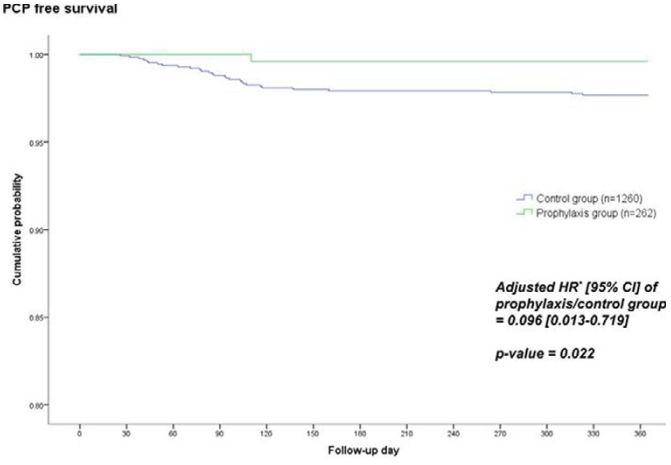


Figure. Kaplan-Meier curve of 1-year incidence of PCP between the two groups

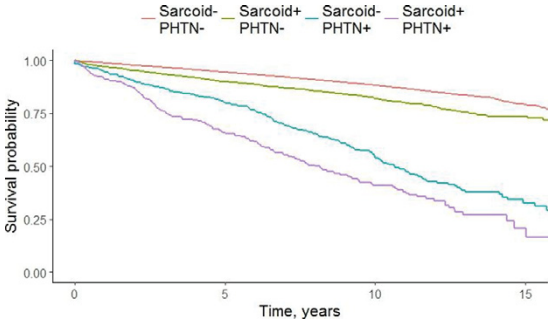
*, HR was adjusted for patient's age, concomitant cyclophosphamide pulse and baseline lymphopenia

ICU admission rate and in-hospital mortality rate were not different between the two groups during the observation. This result was consistent in the sensitivity analysis where same analysis was performed in the post-matched population.
Thirty-four cases of ADRs of TMP-SMX occurred, with an incidence rate (95% CI) of 24.2 (17.3–33.0) per 100 person-year. There were two cases of serious ADR (one pancytopenia and one Steven's Johnson syndrome) but they all recovered shortly after the discontinuation of TMP-SMX. The number needed to harm (NNH) of serious ADR was 109 whereas the number needed to treat (NNT) to prevent one case of PCP in the whole population was 52.
Conclusions: In patients with rheumatic disease receiving prolonged, high-dose steroid treatment, TMP-SMX prophylaxis significantly lower the incidence of PCP with favorable safety.
References:
[1] Stern A, Green H, Paul M, Vidal L, Leibovici L. Prophylaxis for Pneumocystis pneumonia (PCP) in non-HIV immunocompromised patients. The Cochrane database of systematic reviews. 2014(10):CD005590.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2803

OP0078 THE LONG TERM PROGNOSTIC SIGNIFICANCE OF PULMONARY HYPERTENSION IN SARCOIDOSIS - A BIG DATA ANALYSIS

S. Tiosano[1,2], O. Gendelman[1,2], A. Watad[1,2], D. Comaneshter[3], A. Cohen[3,4], H. Amital[1,2]. *[1]Internal Medicine 'B', Sheba Medical Center, Ramat-Gan; [2]Sackler School of Medicine, Tel-Aviv University; [3]Chief physician's office, Clalit Health Services, Tel-Aviv; [4]Siaal Research Center for Family Medicine and Primary Care, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel*

Background: Sarcoidosis is a multisystem, chronic, progressive, granulomatous disease. Sarcoidosis-associated pulmonary hypertension is well described, but not common complication of sarcoidosis[1]. In small scale studies, it has been previously described as a manifestation of advanced disease and was found to be associated with increased morbidity and mortality[2]. Previous studies have shown that treatment may be safe and improve pulmonary hemodynamics in sarcoidosis-associated pulmonary hypertension[3,4]. However, big data analyses regarding the exact magnitude and prognosis of sarcoidosis-associated pulmonary hypertension are lacking.
Objectives: To assess the long-term prognostic significance of sarcoidosis-associated pulmonary hypertension using a big data registry with a 15-year follow-up period.
Methods: Utilizing the medical records of Clalit Health Services, the largest HMO in Israel, we extracted a cohort consisted of sarcoidosis patients along with their age-and-sex matched controls. Dates of registration in the medical records of sarcoidosis, pulmonary hypertension and death, as well as anthropometric information and medical comorbidities were extracted from the database. To compare the distribution of variables across the cohort strata, univariate analysis was performed using Chi-square and student t-test. Multivariate analysis using a logistic regression model was used to find variables associated with pulmonary hypertension. Survival analysis using cox proportional hazards method and log-rank test was performed to find variables associated with increased risk of all-cause mortality.
Results: The cohort included 3,993 sarcoidosis patients and 19,856 age-and-sex matched controls. The mean age of both groups was 56, and both consisted about 63% females. Pulmonary hypertension was observed among 269 sarcoidosis patients (6.74%) vs. 400 controls (2.01%), $p<0.001$. In multivariate analysis, sarcoidosis was found to be independently associated with diagnosis of pulmonary hypertension (OR 3.09, 95% CI 2.6–3.67). After more than 15 years of follow-up, 710 (17.8%) of the sarcoidosis patients had died, compared to 2121 (10.7%) of the controls ($p<0.001$). In multivariate survival analysis, both sarcoidosis and pulmonary hypertension were found to be significantly associated with increased risk to all-cause mortality (HR 1.83, 95% CI 1.66–2.02 and HR 2.32, 95% CI 2.05–2.63, respectively).



Conclusions: Sarcoidosis-associated pulmonary hypertension is associated with poor prognosis. Proper screening methods are recommended to assess whether early identification and treatment may improve life expectancy.

References:
[1] Baughman, R. P., Culver, D. A. & Judson, M. A. A Concise Review of Pulmonary Sarcoidosis. Am. J. Respir. Crit. Care Med. 183, 573–581 (2011).
[2] Baughman, R. P., Engel, P. J., Taylor, L. & Lower, E. E. Survival in Sarcoidosis-Associated Pulmonary Hypertension. Chest 138, 1078–1085 (2010).
[3] Baughman, R. P. et al. Bosentan for Sarcoidosis-Associated Pulmonary Hypertension. Chest 145, 810–817 (2014).
[4] Keir, G. J. et al. Treatment of sarcoidosis-associated pulmonary hypertension: A single centre retrospective experience using targeted therapies. Sarcoidosis Vasc. Diffuse Lung Dis. 31, 82–90 (2014).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4464

OP0079 BODY FAT PERCENTAGE AND WAIST CIRCUMFERENCE WERE ASSOCIATED WITH THE DEVELOPMENT OF RHEUMATOID ARTHRITIS – A DANISH FOLLOW-UP STUDY

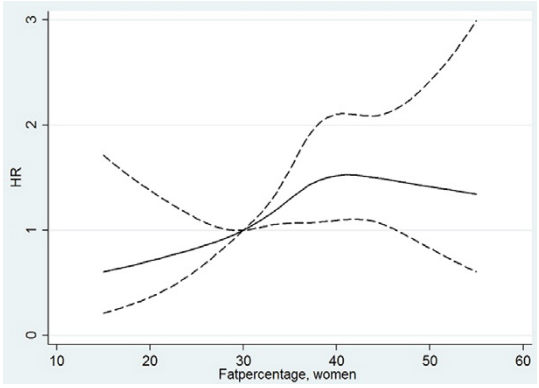
A. Linauskas[1], A.L. de Thurah[1], K. Overvad[2], M.B. Johansen[3], K. Stengaard-Pedersen[1]. *[1]Department of Rheumatology, Aarhus University Hospital; [2]Depatment of Public Health, Section of Epidemiology, Aarhus University, Aarhus; [3]Unit of Clinical Biostatistics, Aalborg Univeristy Hospital, Aalborg, Denmark*

Background: Several studies have investigated the association between overweight and the development of rheumatoid arthritis (RA) and have come out with conflicting results. Body Mass Index (BMI) has been the preferred surrogate measure for overweight in these studies. However, BMI correlates only modestly with total amount of body fat and does not reflect fat distribution.
Objectives: To investigate the association between BMI, waist circumference, bio-impedance-derived total body fat percentage and the incidence of RA.
Methods: A population-based cohort study conducted within the Danish Diet, Cancer and Health cohort, which included individuals aged 50 to 64 years at the recruitment in the period between 1993 and 1997. Body fat composition measurements and data on lifestyle factors were collected at the enrolment into the cohort. The participants who subsequently developed RA were identified via linkage to The Danish National Patient Registry. The participants were followed until development of RA, death, loss to follow-up or October 2016, whichever came first. Data were analyzed by Cox proportional hazards regression model with delayed entry and age as the underlying time variable. Analyses were stratified by gender. Cox regression analyses with restricted cubic spline were carried out to elucidate the dose-response association between anthropometric measures and risk of RA. Smoking, socio-economic status, alcohol consumption, physical activity and intake of n-3 fatty acids were included in multivariate analyses as potential confounders.

Table 1. Cox proportional hazard ratios for association between body composition measurements and incidence of RA

Variable	Hazard ratio (95% confidence interval)) Multivariable adjusted*	
	Men	Women
BMI <18.5 kg/m^2	N/A	0.86 (0.21 -3.48)
BMI 18.5–24.99 kg/m^2	1 (ref)	1 (ref)
BMI 25–29.99 kg/m^2	0.83 (0.55–1.24)	1.48 (1.14 – 1.91)
BMI >30 kg/m^2	0.69 (0.37–1.30)	1.54 (1.09 – 2.17)
Abdominal obesity (waist circumference >102 cm for men, >88 cm for women)		
No	1 (ref)	1 (ref)
Yes	1.16 (0.75–1.80)	1.24 (0.96–1.61)
	Hazard ratio (95% confidence interval) per 1% increment of body fat Multivariable adjusted*	
	Men	Women
Fat percentage	0.99 (0.96–1.03)	1.03 (1.01–1.05)

*Adjusted for age, smoking status, total tobacco consumption (g/day), smoking duration, alcohol consumption (g/day), socio-economic status, physical activity (Metabolic Equivalent of Task, MET), total intake of n-3 fatty acids.



Results: Data were available on 54 284 subjects (52% female). During follow-up (median 21 years), 283 women and 110 men developed RA. The median (IQR) time to onset of RA was 7 (4–11) years. The adjusted hazard ratio's (HR) for developing RA are presented in Table 1. Restricted cubic spline analysis of body fat percentage displayed a positive slope in women (Image). There was no linear association between amount of fat and incidence of RA among men.
Conclusions: Overweight and obesity, defined by BMI, abdominal obesity and higher body fat percentage, especially above 30%, were in women associated with a higher risk for the development of RA. In men the associations were not consistent.
Acknowledgements: The Danish Rheumatism Association, The Danish Heart Foundation, Central Denmark Region, North Denmark Regional Hospital, Scandinavian Rheumatology Research Foundation
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1526

OP0080 RISK OF AUTISM SPECTRUM DISORDER IN CHILDREN BORN TO MOTHERS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS IN TAIWAN

P.-H. Tsai, C.-F. Kuo, L.-H. Huang, S.-F. Luo. *Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan, Province of China*

Background: There is emerging evidence suggesting that offspring born to patients with rheumatic diseases has higher risk of neuropsychiatric diseases. Previous data from Quebec showed children born to women with SLE have an increased risk of autism spectrum disorder (ASD) but data regarding risk of ASD in offspring of mothers with systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) mothers have not been reported in other population.
Objectives: We aimed to examine whether offspring of mothers with SLE and RA in Taiwan has a higher risk of developing ASD using data from a linkage between National Health Insurance (NHI) database and National Birth Registry in Taiwan.
Methods: We established a birth cohort of all live-births between 2001 and 2012 in Taiwan established using the National Health Insurance database and the National Birth Registry. Children born to mothers with SLE or RA were identified and matched up to 8 controls by maternal age, 1-minute Apgar score, 5-minute Apgar score, mode of delivery, sex of child, gestational age, birth weight, socioeconomic status (place of residence, income level, occupation). A marginal Cox proportional hazard models were used to estimate the relative risk (RR; 95% confidence interval [CI]) for ASD in newborns with affected mothers.
Results: Of 1,893,244 newborns, 0.08% (n=1,594) were born to mothers with SLE (mean age 30.43±4.37 years old) and 0.04% (n=673) were born to mothers with RA (31.97±4.51 years old). Overall, 5 of 673 (0.74%) RA offspring developed ASD, 7 of 1594 (0.44%) SLE offspring developed ASD and 10,631 of 1,893,244 (0.56%) all infants developed ASD. The incidence of ASD was 140.39 (95% CI, 45.58–327.62) per 100,000 person-years for RA group, 76.19 (95% CI, 30.63–156.97) per 100,000 person-years for SLE group, 89.85 (95% CI, 88.15–91.57) per 100,000 person-years for non-RA group and 89.87 (95% CI, 88.17–91.60) per 100,000 person-years for non-SLE group. The children born to RA and SLE mothers did not have higher risk of ASD with a HR (95% CI) of 1.42 (0.60–3.40) and 0.76 (0.36–1.59) for ASD, respectively.
Conclusions: Children born to women with SLE and RA do not have higher risk of developing ASD.
References:
[1] Lahita, R.G., Systemic lupus erythematosus: learning disability in the male offspring of female patients and relationship to laterality. Psychoneuroendocrinology, 1988. 13(5): p. 385–96.
[2] Vinet, E., et al., Increased Risk of Autism Spectrum Disorders in Children Born to Women With Systemic Lupus Erythematosus: Results From a Large Population-Based Cohort. Arthritis Rheumatol, 2015. 67(12): p. 3201–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2882

WEDNESDAY, 14 JUNE 2017

Scleroderma, myositis and related ethology

OP0081 PAN-PPAR AGONIST IVA337 IS EFFECTIVE IN THE PREVENTION OF EXPERIMENTAL LUNG FIBROSIS AND PULMONARY HYPERTENSION

J. Avouac[1], I. Konstantinova[2], C. Guignabert[3], J. Sadoine[4], G. Thomas[5], S. Pezet[5], A. Cauvet[5], L. Tu[3], J.M. Luccarini[2], J.L. Junien[2], P. Broqua[2], Y. Allanore[1]. [1]*Rheumatology A and INSERMU1016, Paris Descartes University, Cochin Hospital, Paris;* [2]*Inventiva, Daix;* [3]*INSERM UMR_s 999, le Plessis Robinson;* [4]*Université Paris Descartes, Montrouge;* [5]*INSERM U1016, Paris, France*

Background: Peroxisome proliferator-activated receptors (PPARs) are nuclear receptors known to modulate fibrosis. The pan-PPAR agonist IVA337 recently demonstrated efficacy in prevention and treatment of experimental skin fibrosis [1].
Objectives: Our objective was to evaluate the antifibrotic effects of IVA337 in preclinical mouse models of pulmonary fibrosis and related pulmonary hypertension (PH).
Methods: IVA337 has been evaluated in the mouse model of bleomycin-induced pulmonary fibrosis and in Fra-2 transgenic mice, this latter being characterized by non-specific interstitial pneumonia and severe vascular remodeling of pulmonary arteries leading to PH. Mice received 2 doses of IVA337 (30 mg/kg or 100 mg/kg) or vehicle administered by daily oral gavage up to 4 weeks.
Results: Both 30 mg/kg and 100 mg/kg doses of IVA337 were well tolerated in all mouse models.
IVA337 demonstrated at a dose of 100 mg/kg a marked protection from the development of lung fibrosis induced by bleomycin compared to mice receiving 30 mg/kg of IVA337 or vehicle. Indeed, IVA337 (100 mg/kg) strongly reduced by 61% and 28% tissue density on histological measurements and total lung hydroxyproline concentrations, respectively, as compared to vehicle. IVA337 at 100 mg/kg also significantly decreased col1, col3 and fibronectin in lesional lungs.
Similarly, Fra-2 transgenic mice treated with 100 mg/kg of IVA337 displayed reduced lung density (20% *vs.* vehicle) and significant increase of functional residual capacity (30% *vs.* vehicle) when assessed by chest micro-CT imaging. These results were emphasized by a 50% reduction of the Ascroft fibrosis score (Figure 1A) and by a 48% reduction of hydroxyproline concentrations upon IVA337 (100 mg/kg) compared to vehicle treated mice.
Successful targeting of the TGF-b signaling axis was observed in both mouse models upon treatment with 100 mg/kg of IVA337. 100 mg/kg IVA337 also significantly reduced T cell and B cell infiltration in lesional lungs of Fra-2 transgenic mice.
Regarding vessel remodeling and related pulmonary hypertension, treatment with 100 mg/kg of IVA337 led to a substantial attenuation of right ventricular systolic pressure and right ventricular hypertrophy compared to mice receiving the vehicle (Figure 1B and 1C). Furthermore, IVA337 given at 100 mg/kg markedly reduced medial wall thickness (Figure 1D) and the number of muscularized distal pulmonary arteries.
In vitro in primary human lung fibroblasts, IVA337 inhibited in a dose-dependent manner TGFβ-mediated fibroblasts to myofibroblasts transition and PDGF-mediated proliferation.

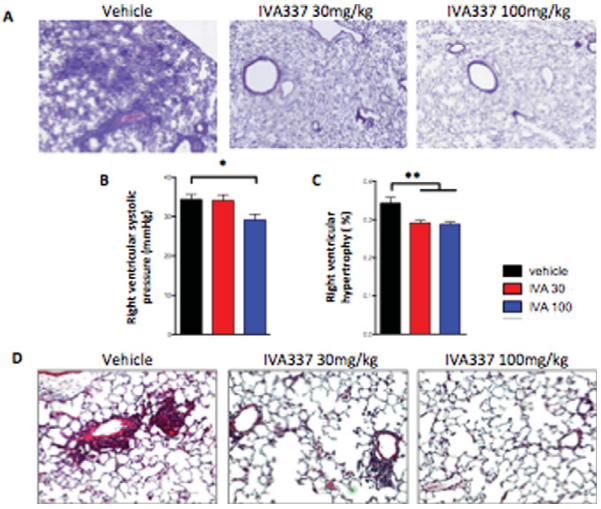


Figure 1

Conclusions: We demonstrate that treatment with 100 mg/kg IVA337 prevents lung fibrosis in two complementary animal models and substantially attenuates PH in the Fra-2 mouse model. These findings confirm that the pan-PPAR agonist IVA337 is an appealing therapeutic candidate for systemic sclerosis both, for skin and key cardiovascular complications.
References:
[1] Ruzehaji et al, Ann Rheum Dis 2016;75(12):2175–2183.
Disclosure of Interest: J. Avouac: None declared, I. Konstantinova Employee of: INVENTIVA, C. Guignabert: None declared, J. Sadoine: None declared, G. Thomas: None declared, S. Pezet: None declared, A. Cauvet: None declared, L. Tu: None declared, J. M. Luccarini Employee of: INVENTIVA, J. L. Junien Consultant for: INVENTIVA, P. Broqua Employee of: INVENTIVA, Y. Allanore Grant/research support from: Inventiva
DOI: 10.1136/annrheumdis-2017-eular.3805

OP0082 FIBROSIS AND MICROANGIOPATHY ARE THE MAIN HISTOPATHOLOGICAL HALLMARKS OF SCLERODERMA-RELATED MYOPATHY

C. Corallo[1], M. Cutolo[2], S. Soldano[2], N. Volpi[1], D. Franci[1], A. Montella[1], C. Chirico[1], R. Nuti[1], N. Giordano[1]. *[1]Medicine, Surgery and Neurosciences, University of Siena, Siena; [2]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa, Italy*

Background: Systemic sclerosis (scleroderma, SSc) is an autoimmune connective tissue disease characterized by skin and internal organ fibrosis, coupled with widespread vascular pathology. Skeletal muscle involvement in SSc has often been considered as a minor component of the disease associated with disuse.
Objectives: The goal of this study is to identify specific histopathological hallmarks of skeletal muscle involvement in SSc.
Methods: A total of 50 SSc patients presenting clinical, serological and electromyographic (EMG) features of muscle weakness, were enrolled. Patients underwent vastus lateralis biopsy, assessed for individual pathologic features including fibrosis [type I collagen (Coll-I), transforming growth factor β (TGF-β)], microangiopathy [cluster of differentiation 31 (CD31), pro-angiogenic vascular endothelial growth factor A (VEGF-A), anti-angiogenic VEGF-A165b], immune/inflammatory response [CD4, CD8, CD20, human leucocyte antigens ABC (HLA-ABC)], and membranolytic attack complex (MAC). SSc biopsies were compared to biopsies of (n =50) idiopathic inflammatory myopathies (IIMs) and to (n =50) noninflammatory myopathies (NIMs). Ultrastructural abnormalities of SSc myopathy were also analyzed by transmission electron microscopy (TEM).
Results: Fibrosis in SSc myopathy (90%) is higher compared to IIM (30%, p <0.05) and to NIM (15%, p <0.05). Vascular involvement is dominant in SSc muscle (95%), and in IIM (75%) compared to NIM (20%, p <0.05). In particular, CD31 shows loss of endomysial vessels in SSc myopathy with respect to IIM (p <0.05) and to NIM (p <0.01). VEGF-A is downregulated in SSc myopathy compared to IIM (p <0.05) and to NIM (p <0.05), while VEGF-A165b is upregulated in SSc myopathy. The SSc immune/inflammatory response suggested humoral process with majority (80%) HLA-ABC fibral neoexpression and complement deposits on endomysial capillaries MAC, compared to IIM (p <0.05), characterized by CD4+/CD8+/B-cell infiltrate, and to NIM (p <0.05). TEM analysis showed SSc vascular alterations consisting of thickening and lamination of basement membrane and endothelial cell 'swelling' coupled to endomysial/perimysial fibrosis.
Conclusions: The predominat features of SSc-related myopathy are fibrosis, microangiopathy and humoral immunity. However, it is difficult to identify specific histopathological hallmarks of muscle involvement in SSc, since they could be present also in other (IIM/NIM) myopathies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4070

OP0083 MOLECULAR TARGETED IMAGING BIOMARKERS FOR PERSONALIZED MEDICINE STRATEGIES IN SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE

J. Schniering[1], M. Benešová[2], M. Brunner[1], C. Feghali-Bostwick[3], R. Schibli[2], O. Distler[1], C. Müller[2], B. Maurer[1]. *[1]Department of Rheumatology, University Hospital Zurich, Zurich; [2]Center for Radiopharmaceutical Sciences, Paul Scherrer Insitute, Villigen-PSI, Switzerland; [3]Division of Rheumatology & Immunology, Medical University of South Carolina, Charleston, SC, United States*

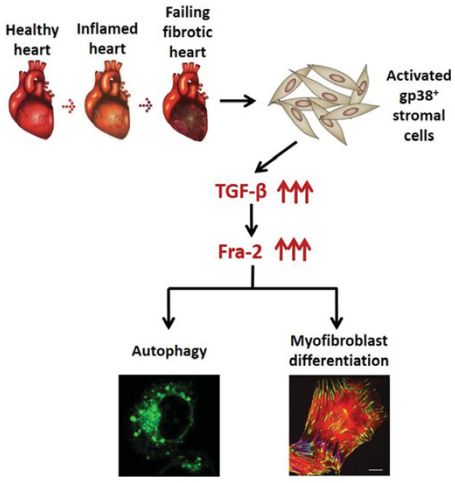
Background: Interstitial lung disease (ILD) is a life-threatening complication in systemic sclerosis (SSc). Substantial research progress has identified distinct genomic and molecular subtypes in SSc-ILD and brought molecular targeted therapies within reach. However, personalized medicine approaches are still lacking since clinically applicable tools for individualized patient stratification are not yet available.
Objectives: To assess the possibility of imaging molecular targets as a biomarker for stage-dependent assessment of ILD in the mouse model of bleomycin-induced lung fibrosis.
Methods: Expression of integrin $\alpha_v\beta_3$ and folate receptor β (FR-β) was analyzed in lung tissues from patients with idiopathic pulmonary fibrosis (IPF), SSc-ILD, and healthy controls as well as from bleomycin treated mice and saline treated controls using immunohistochemistry and qPCR (n=5–11). SPECT (Single Photon Emission Computed Tomography) or PET (Positron Emission Tomography) was performed at days 3, 7, and 14 after bleomycin instillation using the integrin $\alpha_v\beta_3$-specific ^{177}Lu-c(RGDfK)-ligand and the FR-β-specific ^{18}F-Azafol. Additionally, ^{18}F-FDG-PET and high resolution CT (HRCT) scans were performed. The specific lung uptake of the radiotracers over time was assessed by *ex vivo* SPECT or PET/CT scans and biodistribution studies.
Results: Expression of FR-β was significantly increased at the mRNA and protein level of SSc-ILD patients as compared to healthy subjects (p<0.05), whereas only its gene expression was upregulated in IPF patients (p<0.01). Integrin $\alpha_v\beta_3$ was increased at the protein level of both SSc-ILD and IPF patients (p<0.05), while its mRNA expression was not significantly altered.
Similarly, in lungs of bleomycin treated mice, but not of controls, FR-β expression was increased time-dependently at the mRNA and protein level with higher expression at day 3 and day 7, the inflammatory stages of bleomycin-induced lung fibrosis (p<0.05). In contrast, expression of integrin $\alpha_v\beta_3$ was upregulated at day 7 and day 14 at the protein, but not at the mRNA level in bleomycin treated mice, and thus not only in the inflammatory but also in the fibrotic stages (p<0.05). ^{18}F-FDG-PET and HRCT detected time-dependent changes of metabolic activity and ILD morphology in bleomycin treated mice. However, compared with these routinely employed unselective imaging techniques, molecular targeted imaging of integrin $\alpha_v\beta_3$ and FR-β successfully visualized ILD and discriminated lung inflammation and/or fibrosis in a time-dependent manner and in correspondence with the expression changes at the tissue level. The specific lung uptake of ^{177}Lu-c(RGDfK)-ligand and ^{18}F-Azafol as compared with the unspecific uptake of ^{18}F-FDG in diseased lungs over time was demonstrated by biodistribution studies and *ex vivo* SPECT or PET/CT scans.
Conclusions: Our data suggest that stage-dependent visualization of ILD with radiotracers that target key markers of lung inflammation and/or fibrosis shows promise for clinical application. As opposed to unselective imaging techniques such as ^{18}F-FDG-PET and HRCT, the introduction of specific imaging biomarkers for individualized management of SSc-ILD patients could represent the first step towards precision medicine.
Disclosure of Interest: J. Schniering Grant/research support from: Swiss National Science Foundation (S-85605–02–01), M. Benešová Grant/research support from: Swiss National Science Foundation (S-85605–02–01), M. Brunner: None declared, C. Feghali-Bostwick: None declared, R. Schibli Grant/research support from: Merck & Cie, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi; Patent licensed: mir-29 for the treatment of systemic sclerosis, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha, C. Müller Grant/research support from: Merck & Cie, B. Maurer Grant/research support from: AbbVie, Protagen, EMDO, Novartis, Pfizer, Roche, Actelion; Patent licensed: mir-29 for the treatment of systemic sclerosis
DOI: 10.1136/annrheumdis-2017-eular.1871

OP0084 RESCUE FROM THE FAILING HEART IN SYSTEMIC SCLEROSIS, A NOVEL INSIGHT: TARGETING TGF-β/FRA2-DEPENDENT AUTOPHAGY

M. Stellato[1], M. Rudnik[1], F. Renoux[1], E. Pachera[1], D. Kayalar[1], K. Sotlar[2], K. Klingel[3], J. Henes[4], P. Blyszczuk[5], O. Distler[1], G. Kania[1]. *[1]Department of Rheumatology, University Hospital, Zurich, Switzerland; [2]Institute of Pathology, Ludwig Maximilians University, Munich; [3]Department of Molecular Pathology; [4]Division of Rheumatology, University Hospital, Tubingen, Germany; [5]Department of Clinical Immunology, Jagiellonian University Medical College, Krakow, Poland*

Background: The majority of Systemic Sclerosis (SSc) patients have subclinical primary cardiac involvement, which resembles the inflammatory dilated cardiomyopathy (iDCM) with inflammation and fibrosis. Firstly, cellular progenitors of pathological myofibroblasts remain undescribed.
Secondly, autophagy may favor fibrosis through enhanced differentiation of fibroblasts in myofibroblasts
Objectives: To unravel the role of Fos-related antigen 2 (Fra2)/autophagy crosstalk in TGF-β-driven myocardial fibrosis in SSc
Methods: Genetically modified mice overexpressing Fra2 were used. Endomyocardial biopsies (EMBs) from SSc/iDCM patients and hearts from Fra2 tg and control mice were analysed by immunohistochemistry (IHC) and immunofluorescence (IF). Murine myocardial gp38$^+$ (podoplanin$^+$) stromal cells were sorted and stimulated *in vitro* with TGF-β. The cellular phenotype was assessed by qPCR, IF, stress fiber staining, SIRCOL and contraction assay on sorted cells. The antisense oligonucleotide GapmeR was used to knock-down Fra2
Results: The myocardium of SSc/iDCM patients (n=10) showed the typical phenotype of iDCM: increased fibrotic area with extended collagen deposition and enlarged number of pathological myofibroblasts, expressing Fra2 and, interestingly, the autophagy markers LC3B and Atg5. Similarly, Fra2 tg mice showed higher expression of profibrotic markers: αSMA, vimentin and collagen I compared to control mice (n=5), as well as the expression of the autophagy markers LC3B and Beclin in fibrotic regions.
Among cardiac stromal cells (Ter119$^-$CD45$^-$CD31$^-$Sca1$^+$CD29$^+$) the frequency of gp38$^+$ cells was significantly higher in Fra2 myocardium compared to control mice. The majority of gp38$^+$ cells co-expressed αSMA, vimentin and collagen I together with autophagy markers (LC3B and Beclin, n=3). Following *in vitro* stimulation with TGF-β, gp38$^+$ cells entered fibroblast-to-myofibroblast transition characterized by increased mRNA and protein levels of αSMA, collagen I, fibronectin (n=3–6), αSMA-fiber and stress-fiber formation (n=3), increased cell proliferation (n=4; p=0.04) and contraction capability (n=2; p<0.05) and enhanced collagen secretion (n=3; p=0.04). Importantly, Fra2 tg gp38$^+$ cells showed the presence of αSMA and stress fibers even without TGF-β stimulation as well as an increased contraction capability compared to control cells.
TGF-β stimulation of control gp38$^+$ cells induced the expression of LC3B, Beclin and Atg5 at mRNA and protein level (n=3–5). In contrast, TGF-β inhibition caused the downregulation of these markers (n=3).
In addition, Fra2 silencing resulted in a decreased differentiation capability of

gp38+ cells: mRNA and protein levels of the profibrotic genes αSMA and collagen I were significantly downregulated (n=5; p=0.007). Moreover, Fra2 downregulation impaired the secretion of collagens (n=4; $p<0.05$) and the formation of αSMA fibers (n=3) in addition to a significant downregulation of mRNA and protein expression of LC3B, Beclin and Atg5 (n=3)



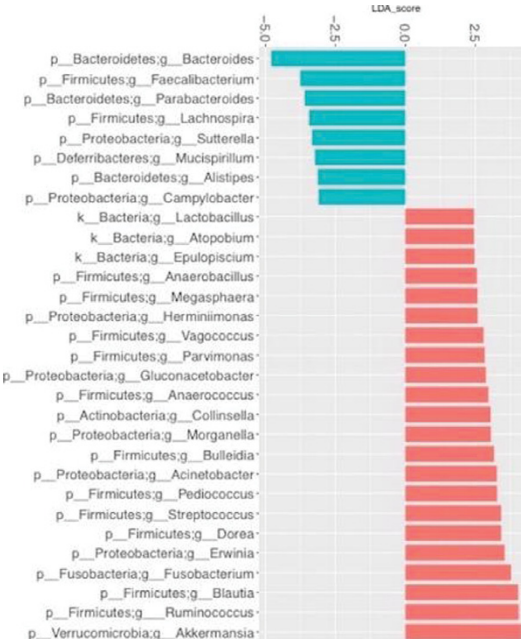
Conclusions: The TGF-β/Fra2 axis fosters an enhanced autophagy flow, leading in turn to the stromal-to-myofibroblast transition. Therefore, targeting this process might be a therapeutic strategy to abrogate fatal cardiac remodeling in SSc

Disclosure of Interest: M. Stellato: None declared, M. Rudnik: None declared, F. Renoux: None declared, E. Pachera: None declared, D. Kayalar: None declared, K. Sotlar: None declared, K. Klingel: None declared, J. Henes: None declared, P. Blyszczuk: None declared, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha, G. Kania Grant/research support from: Bayer AG
DOI: 10.1136/annrheumdis-2017-eular.3760

OP0085 LONGITUDINAL ANALYSIS OF THE GASTROINTESTINAL MICROBIOTA IN SYSTEMIC SCLEROSIS

E.R. Volkmann[1], A.-M. Hoffmann-Vold[2], Y.-L. Chang[1], J. Jacobs[1], K. Tillisch[1], E. Mayer[1], P.J. Clements[1], J. Hov[2], M. Kummen[2], Ø. Midtvedt[2], V. Lagishetty[1], Ø. Molberg[2], J. Braun[1]. *[1]University of California, Los Angeles, Los Angeles, United States; [2]Oslo University Hospital, Oslo, Norway*

Background: Gastrointestinal tract (GIT) dysfunction affects the majority of patients with systemic sclerosis (SSc). While the etiology of SSc-related lower GIT dysfunction remains elusive, we have recently demonstrated that the SSc disease state is associated with a distinct colonic microbial consortium and that specific genera are associated with SSc-GIT symptoms in a cross-sectional analysis using colonic lavage specimens.[1]
Objectives: To evaluate changes in GIT microbial composition over time in relation to GIT symptoms in SSc patients.
Methods: Adults SSc patients not on chronic antibiotic therapy were eligible to participate. Stool specimens were collected at 0, 3, 6, 9, and 12 months. Healthy controls were matched to SSc patients in a 1:1 ratio at baseline. SSc patients completed the GIT 2.0 questionnaire to assess GIT symptom severity at each collection time. The microbiota from these samples were determined by Illumina HiSeq 2500 16S sequencing. Linear Discriminant Analysis Effect Size was used to identify the genera that showed differential expression in SSc versus controls. Mixed models evaluated changes in GIT symptoms and microbial composition over time.
Results: Among 17 patients with SSc (88% Female; Median age 52.1 years), the mean (SD) baseline total GIT 2.0 score was 0.7 (0.6). The majority of participants (71%) provided at least 4 stool samples over the course of the 12-month study. Principal coordinate analysis illustrated significant microbial community differences in SSc versus healthy controls (p=0.001). Consistent with the results of our prior study using colonic lavage specimens,[1] SSc patients had decreased commensal genera, such as *Faecalibacterium* and *Bacteroides* and increased pathobiont genera, such as *Fusobacterium* and *Erwinia* compared with healthy controls (Figure 1). GIT 2.0 scores did not change significantly over the course of the 12-month study for each subject. However, patients with longer disease durations had increased GIT symptoms over time for the total score (P=0.0038), and the following domains: fecal soilage (P=0.0217), social functioning (P=0.0116), emotional well-being (P=0.0474), and constipation (P=0.0039). There was no difference in the course of GIT symptoms over time between patients with limited versus diffuse cutaneous disease. Both the absolute and relative abundances of specific genera did not change over time within individual subjects. After controlling for age, gender, ethnicity, disease duration and SSc subtype (i.e. limited vs. diffuse), low abundance of *Bacteroides* was associated with increased GIT symptoms over time.
Figure 1. Genus level taxa associated with UCLA-SSc patients versus healthy subjects. Negative and positive effect sizes denote genera decreased (blue) or increased (red) in SSc patients, respectively.



Conclusions: This study is the first to characterize lower GIT microbiota in SSc patients at multiple time points. The findings provide further evidence that lower GIT dysbiosis is a feature of the SSc disease state and that specific genera may contribute to GIT symptoms and serve as potential targets for therapeutic intervention.

References:
[1] Volkmann et al. Arthritis Rheumatol 2016;68:1483.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2077

OP0086 LONG NONCODING RNA H19X AS A NEW THERAPEUTIC TARGET FOR FIBROSIS

E. Pachera[1], A. Wunderlin[1], S. Assassi[2], G. Salazar[2], M. Frank-Bertoncelj[1], R. Dobrota[1], M. Brock[3], C. Feghali-Bostwick[4], G. Gerhard Rogler[5], G. Dijkstra[6], T. van Haaften[5], J. Distler[7], G. Kania[1], O. Distler[1]. *[1]Center of Experimental Rheumatology, University Hospital Zurich, Zurich, Switzerland; [2]Department of Internal Medicine, University of Texas, Houston, United States; [3]Department of Pulmonology, University Hospital Zurich, Zurich, Switzerland; [4]Division of Rheumatology, Medical University of South Carolina, Charleston, United States; [5]Department of Gastroenterology and Hepatology, University Hospital Zurich, Zurich, Switzerland; [6]Department of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, Netherlands; [7]Department of Internal Medicine 3, University of Erlangen, Erlangen, Germany*

Background: Long noncoding RNAs (lncRNAs) are an emerging class of transcripts involved in the regulation of gene expression. We have recently identified a novel lncRNA, H19X, to be upregulated in systemic sclerosis (SSc). We also demonstrated that H19X is a key mediator of TGFβ-driven myofibroblast development and extracellular matrix synthesis.
Objectives: To assess whether (1) H19X upregulation in SSc fibroblast is anti-apoptotic and pro-proliferative thereby favoring fibrosis (2) H19X is a regulator of fibrotic diseases in general.
Methods: To study the function of H19X in apoptosis and proliferation of of dermal fibroblasts we silenced H19X using locked nucleic acid oligonucleotides (LNA GapmeRs followed by microarray analysis, qPCR, BrdU cell proliferation assay, Caspase 3/7 apoptosis assay and scratch assay. Cells were treated with 10 ng/ml TGFβ. Lung tissues were obtained from patients with SSc and idiopathic pulmonary fibrosis (IPF) undergoing transplantation, and from healthy controls (HC). Resected gut tissue from fibrotic and non-fibrotic areas was obtained from Crohn's disease patients. Non-cancer-affected gut tissue from resections because of adenocarcinoma was used as control. Expression of H19X was analyzed by quantitative (q)PCR.
Results: H19X knockdown followed by microarray analysis (n=5) showed that FAS signaling pathway, cyclins and cell cycle regulation, regulation of cell cycle progression by Plk3, and free radical induced apoptosis were among the

pathways with the highest number of significantly enriched genes (n=5; $p<0.005$). Apoptosis markers like BCL2, IGFBP3 and FAF1 (n=5, $p<0.05$) were upregulated in H19X-silenced fibroblasts. This indicated that targeting H19X might have a pro-apoptotic effect on fibroblasts thereby protecting from fibrosis. Functional studies showed enhanced fibroblast apoptosis after H19X silencing and TGFβ stimulation (n=5, $p<0.05$). In addition to decreased apoptosis, increased fibroblast proliferation might also favor fibrosis. Indeed, H19X downregulation led to reduced cell proliferation as measured by BrdU assay (n=5, $p<0.05$). Scratch assay (n=5) showed that H19X knockdown decreases TGFβ reduced wound healing. H19X expression was significantly increased in SSc interstitial lung disease and IPF patients versus HC (n=11 each, $p<0.05$). A significant H19X overexpression was also detected in fibrotic tissue from Crohn's disease patients (n=4–10, $p<0.05$).

Conclusions: H19X supports TGFβ driven fibrosis not only by favoring myofibroblast development and extracellular matrix synthesis, but also by inducing proliferation and reducing apoptosis of dermal fibroblasts. These effects are not limited to SSc, but appear operative in a wider range of fibrotic diseases. Our results highlight the lncRNA H19X as a potent new therapeutic target in fibrotic diseases opening thereby new possibilities for the treatment of TGFβ driven fibrosis.

Disclosure of Interest: E. Pachera: None declared, A. Wunderlin: None declared, S. Assassi Consultant for: Boehringer Ingelheim, Genentech and Biogen IDEC Inc., Bayer HealthCare, G. Salazar: None declared, M. Frank-Bertoncelj: None declared, R. Dobrota: None declared, M. Brock: None declared, C. Feghali-Bostwick: None declared, G. Gerhard Rogler: None declared, G. Dijkstra: None declared, T. van Haaften: None declared, J. Distler Shareholder of: 4D Science, Grant/research support from: from Anamar, Active Biotech, Array Biopharma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, Consultant for: Actelion, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB., G. Kania Grant/research support from: Bayer, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha

DOI: 10.1136/annrheumdis-2017-eular.4877

OP0087 PLATELET-SPECIFIC FLI1-KNOCKOUT MICE SHOW ACCELERATED WOUND CLOSURE ASSOCIATED WITH INCREASED MYOFIBROBLAST FORMATION IN THE INFLAMMATORY PHASE

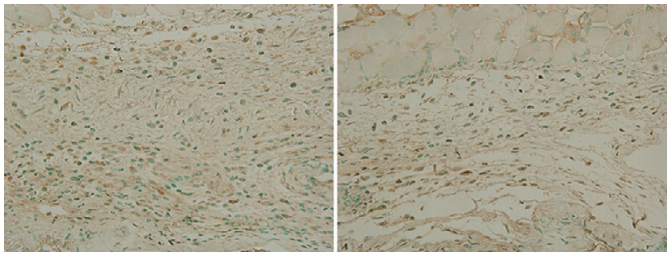
M. Hirabayashi, Y. Asano, T. Yamashita, R. Saigusa, S. Miura, K. Nakamura, T. Miyagawa, Y. Ichimura, T. Taniguchi, A. Yoshizaki, S. Sato. *Dermatology, University of Tokyo, Graduate School of Medicine, Tokyo, Japan*

Background: Systemic sclerosis (SSc) is a systemic connective tissue disease characterised by autoimmunity, vascular disorder and fibrosis of skin and other organs (1). Although substantial reports have been hitherto provided upon its pathogenesis in relation to microvasculature, among which are on endothelial and fibroblastic Fli1 deficiencies (1, 2), adequate investigation into hemocytic involvement is yet to be attained. Platelets are well known for its function in hematostasis whereas they also play a part in inflammation, immunity and cellular proliferation (3), thus prompting us to speculate their cardinal role in the development of the disease.

Objectives: Here we aim to unravel the role of platelets in the pathogenesis of SSc, with generation of platelet-specific conditional *Fli1* knockout (*Fli1* PcKO) mice to scrutinise its dermal wound healing process.

Methods: We generated *Fli1* PcKO mice using the Cre-Lox system along with *PfCre* +/- mice as an appropriate control. We made two excisional wounds on the dorsal skin of each mouse (three months old) using an eight-millimeter-diameter punch and traced the wound surfaces every other day to measure their areas using Image J until all the wounds were epithelised. On a separate experiment, perilesional skin was harvested on the day two, from which we extracted mRNA for the measurement of proinflammatory and profibrotic cytokines. An immunostaining for α-SMA was performed on the skin samples.

Results: The areas of the wounds were calculated and shown in ratio to their initial areas (day 0). *Fli1* PcKO mice showed a significant decrease in the areas compared to the control on day 2. mRNA measurement revealed a significant increase in *Mmp13* and significant decreases in *Tgfb1*, *Ifng* and *Il13* for *Fli1* PcKO. In histopathology, α-SMA positive fusiform-shaped cells were abundant in the granulation tissue of *Fli1* PcKO mice (Figure; left, *PfCre* +/-; right, *Fli1* PcKO; original magnification, ×400).



Conclusions: In dermal injuries on *Fli1* PcKO mice, inflammatory disturbances precipitate myofibroblast formation in the granulation tissue, thus anticipating wound closure by mechanical contraction.

References:

[1] Asano Y et al., Curr Rheumatol Rep. 2013; 15(12):382.
[2] Asano Y et al. Am J Pathol. 2010; 176(4):1983–98.
[3] Ramirez GA et al., Front Immunol. 2012; 3:160.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1350

OP0088 THE ROLE AND FUNCTION OF MONOCYTE-DERIVED FIBROBLAST-LIKE CELLS IN MULTI-ORGAN FIBROSIS IN SYSTEMIC SCLEROSIS

M. Rudnik[1], M. Stellato[1], V. Milleret[2], P. Błyszczuk[3], B. Maurer[1], K. Klingel[4], J. Henes[5], K. Sotlar[6], M. Ehrbar[2], O. Distler[1], G. Kania[1]. *[1]Department of Rheumatology; [2]Department of Obstetrics, Univeristy Hospital Zurich, Zurich, Switzerland; [3]Department of Clinical Immunology, Jagiellonian University Medical College, Krakow, Poland; [4]Department of Molecular Pathology; [5]Department of Rheumatology, University Hospital Tuebingen, Tuebingen; [6]Institute of Pathology, Ludwig Maximilian University, Munich, Germany*

Background: Animal studies indicated bone marrow-derived cells as a source of pathological myofibroblasts in multiple organ fibrosis such as lungs, heart, skin and kidney. Monocytes are implicated in the pathogenesis of systemic sclerosis (SSc), however detailed role of specific monocyte subsets in multi-organ fibrogenesis in SSc remains unclear.

Objectives: We aimed to determine the role and the contribution of circulating monocytes in the onset and progression of multi-organ fibrosis in SSc.

Methods: Endomyocardial biopsies (n=10) from SSc patients and healthy controls were screened by immunohistochemistry. $CD14^+$ monocytes isolated from peripheral blood of SSc patients and healthy donors were differentiated towards a myofibroblast phenotype by stimulation with TGF-β1, IL-4, IL-10 and IL-13. In addition, $CD14^+$ monocytes were co-cultured in 2D and 3D models with dermal fibroblasts originating from SSc patients or healthy subjects, or with adult cardiac fibroblasts. TGF-β signalling was blocked by SD208 and A83–01 inhibitors. Profibrotic gene expression and protein secretion were evaluated by qPCR, Western blot, protein array, immunofluorescence and ELISA.

Results: The myocardia of SSc patients revealed the presence of CD45-expressing infiltrates, an extended collagen I deposition and the presence of CD14-expressing elongated cells in the fibrotic tissue. Stimulated monocytes acquired a myofibroblast-like phenotype with increased expression of collagen I ($p<0.0001$), fibronectin ($p<0.05$), and α smooth muscle actin (α-SMA) in comparison to untreated cells. Similarly, $CD14^+$ monocytes exposed to dermal or cardiac fibroblasts acquired spindle shape and expressed higher levels of profibrotic genes. The process of monocyte-to-myofibroblast differentiation employed TGF-β/SMAD signalling. Blocking of the TGF-β receptor I and canonical SMAD-dependent pathway with inhibitors resulted in the abrogation of collagen I secretion by monocytes ($p=0.002$). $CD14^+$ monocytes from SSc patients were characterised by higher secretion of CXCL10 ($p<0.001$), which was significantly decreased after cytokine stimulation ($p<0.001$). Additionally, a tendency towards higher secretion of CCL20, CCL22, Leukemia Inhibitory Factor and neurotrophin-3 was observed for SSc monocytes.

Conclusions: Here we demonstrated the capability of peripheral blood monocytes to differentiate towards the functional myofibroblast phenotype, designating these cells as one of the potential sources of pathological tissue myofibroblasts in SSc. Additionally, these cells sustained pro-fibrotic cytokines secretion, highlighting their important regulatory functions in the fibrogenesis in SSc. Further studies of monocytes involvement in SSc might lead to novel treatment strategies.

Disclosure of Interest: M. Rudnik: None declared, M. Stellato: None declared, V. Milleret: None declared, P. Błyszczuk: None declared, B. Maurer Grant/research support from: AbbVie, Protagen, EMDO, Novartis. Congress support from Pfizer, Roche, Actelion. Patent licensed: mir-29 for the treatment of systemic sclerosis, K. Klingel: None declared, J. Henes: None declared, K. Sotlar: None declared, M. Ehrbar: None declared, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi. Patent licensed: mir-29 for the treatment of systemic sclerosis, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha, G. Kania Grant/research support from: Bayer

DOI: 10.1136/annrheumdis-2017-eular.3800

WEDNESDAY, 14 JUNE 2017

Novel insights in inflammatory mediators

OP0089 COMBINATION THERAPY OF SELECTIVE MMP9 AND TNF INHIBITORS ARE EFFICACIOUS IN THE MOUSE CIA MODEL OF RHEUMATOID ARTHRITIS

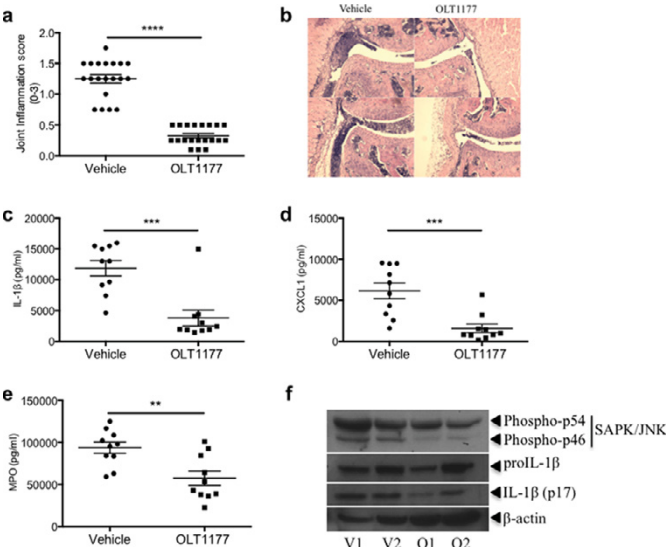
S. Kim, B. Carr, L. Tong, D. Jin, R. Wang, D. Marshall, D. Gossage, V. Smith.
Gilead sciences, Inc., Foster city, United States

Background: Matrix metalloproteinase-9 (MMP9) is highly expressed by infiltrating inflammatory cells, pannus tissue, and multinucleated cells in the synovium and subchondral bone tissue, including osteoclasts. MMP9 is implicated in rheumatoid arthritis (RA) by its involvement in joint destruction, activation of cytokines and chemokines, and promotion of tissue destruction by degrading the basement membrane of epithelia and vasculature. MMP9 knockout mice are protected from collagen-induced arthritis (CIA) disease progression. A potent, allosteric antibody inhibitor of MMP9 is currently being investigated in clinical trials. The ability of a functional murine analog of this antibody to reduce disease signs and symptoms in established, chronic mouse CIA model both as a single agent and in combination with anti-TNF, was investigated.
Objectives: We evaluated the efficacy and safety of selective MMP9 inhibition both alone and in combination with anti-TNF (etanercept), in CIA models of RA.
Methods: CIA was induced in male DBA/1J mice (n=15/group) and treatments were administered after disease establishment. Efficacy was assessed via metrics of joint injury including clinical score (erythema/ paw swelling, score 0–4) in addition to histopathological assessment of destructive joint remodeling (soft tissue changes: edema, necrosis, inflammatory cell infiltration, and fibroplasia, sum score 0–16; bone changes: cartilage damage, bone erosion, periosteal bone formation, synovitis, pannus formation, and joint destruction, sum score 0–24).
Results: All animals were included in the evaluation. In all endpoints assessed, treatment with each therapeutic agent, on its own or in combination, resulted in improvement with respect to body weight change, clinical score, and histopathological measures. The combination group provided the best overall trend for therapeutic benefit, although statistical significance as compared to each single agent alone was not met in most parameters. Body weight recovery was superior in combination as compared to single agent therapies (52% vs. 12–34%, relative to sham; $p<0.05$ combination vs. single agents). Clinical score and histopathology measures in soft tissue and bone changes were most improved in the combination therapy group, although it did not achieve statistical significance as compared to each single agent (26% vs. 17–21%; 1.5 vs. 1.5–1.8; and 7 vs. 7–9, respectively). Importantly, combination therapy resulted in a significant number of limbs with zero or mild disease as compared to single agents (no disease sign: 256% vs. 172–223%; mild disease sign: 178% vs. 138–141%). Analysis of complete blood count at the end of study revealed no abnormalities in any treatment group.
Conclusions: Selective inhibition of MMP9 was active in reducing disease severity in CIA models of RA. The combination of anti-MMP9 with anti-TNF was well tolerated and increased the number of limbs with no or mild disease compared to anti-TNF alone. Further studies are required to examine combination therapy of selective anti-MMP9 and anti-TNF therapies in a clinical setting.
Disclosure of Interest: S. Kim Shareholder of: Gilead sciences, Inc, Employee of: Gilead sciences, Inc, B. Carr Shareholder of: Gilead sciences, Inc, Employee of: Gilead sciences, Inc, L. Tong Shareholder of: Gilead sciences, Inc, Employee of: Gilead sciences, Inc, D. Jin Shareholder of: Gilead sciences, Inc, Employee of: Gilead sciences, Inc, R. Wang Shareholder of: Gilead sciences, Inc, Employee of: Gilead sciences, Inc, D. Marshall Shareholder of: Gilead sciences, Inc, Employee of: Gilead sciences, Inc, D. Gossage Shareholder of: Gilead sciences, Inc, Employee of: Gilead sciences, Inc, V. Smith Shareholder of: Gilead sciences, Inc, Employee of: Gilead sciences, Inc
DOI: 10.1136/annrheumdis-2017-eular.1941

OP0090 THE HUMAN SAFE NLRP3 INFLAMMASOME INHIBITOR OLT1177 SUPPRESSES JOINT INFLAMMATION IN MURINE MODELS OF EXPERIMENTAL ARTHRITIS

C. Marchetti[1], B. Swartzwelter[1], M.I. Koenders[2], C.A. Dinarello[1], L.A. Joosten[3].
[1]Department of Medicine, University of Colorado, Aurora, United States; [2]Department of Rheumatology; [3]Department of Medicine, Radboud University Medical Center, Nijmegen, Netherlands

Background: NLRP3 is an essential component of the inflammasome, an intracellular macromolecular complex, which activates caspase-1 for the processing and release of active IL-1β and IL-18. Activation of the NLRP3 inflammasome takes place in inflammatory joint diseases, including gout. Although inhibition of IL-1β with either the IL-1 receptor antagonist anakinra or canakinumab, a neutralizing monoclonal antibody for IL-1β is highly effective for reducing the gout flares, a clinical need remains for a safe, oral treatment of recurrent gout flares refractory to standard of care. The small orally active and safe β-sulfonyl nitrile molecule OLT1177 is a specific inhibitor of the NLRP3 inflammasome, and currently being evaluated in a Phase 2 study for the treatment of acute gout flares.
Objectives: To investigate the anti-inflammatory effect of NLRP3 inflammasome inhibitor OLT1177 in mouse models of acute joint inflammation.
Methods: Two models of experimental arthritis were used in mice: zymosan- and monosodium urate (MSU)-induced arthritis. Knee joints of male C57BL/6 mice were injected intraarticularly with 180 μg heat-killed Zymosan or 300 μg of monosodium urate (MSU) crystals mixed with 200 μM C16.0 fatty acid and bovine serum albumin. Joints were assessed 24 and 4 hours after the zymosan or MSU/C16.0 injection, respectively, for clinical, histological and cytokine analyses.
Results: Intraarticular Zymosan induced a severe joint swelling with neutrophil infiltration, high levels of synovial IL-1β, IL-6 and the neutrophil chemokine CXCL1. Treatment with OLT1177 induced reduction of joint swelling and neutrophil infiltration ($P<0.0001$ and $P=0.006$ respectively) and suppression of IL-1β and IL-6 by 55% and CXCL1 by 30% compared to mice treated with the vehicle. Four hours following intra-articular injection of MSU crystals, an elevated clinical score for knee joint inflammation was observed in vehicle-treated mice (Fig. 1). Oral treatment with OLT1177 showed reduction in joint inflammation as depicted in Fig. 1a when compared to the vehicle group ($P<0.0001$). Histological analysis of the knee revealed suppression of the influx of inflammatory cells in the articular space with OLT1177 treatment ($P<0.05$; Fig. 1b). Treatment with OLT1177 showed significant reduction in synovial tissue extracts for IL-1β (69%; $P<0.001$; Fig. 1c); IL-6 (70%; $P<0.001$); CXCL1 (75%; $P<0.001$; Fig.1d) and MPO (39%; $P=0.006$; Fig. 1e). Mice were also treated with a single dose of OLT1177 1 hour after of intraarticular MSU and reduced joint swelling and IL-1β levels ($P<0.05$) were observed. OLT1177 treatment suppressed activation of the mitogen-activated protein kinases (MAPK) family, c-jun N-terminal kinase (JNK), which is implicated in the pathophysiology of rheumatoid arthritis and gout (Fig. 1f).



Conclusions: The orally active molecule OLT1177 is a potent inhibitor of IL-1β-driven inflammatory arthritis, particularly in a model of acute gout. Considering the outstanding safety profile in humans, OLT1177 is a potential therapeutic strategy to target NLRP3-driven IL-1β-mediated disorders.
Disclosure of Interest: C. Marchetti: None declared, B. Swartzwelter: None declared, M. Koenders: None declared, C. Dinarello Grant/research support from: Charles A. Dinarello serves on the Scientific Advisory Board of Olatec and receive compensation, L. Joosten Grant/research support from: Leo A. B. Joosten serves on the Scientific Advisory Board of Olatec and receive compensation
DOI: 10.1136/annrheumdis-2017-eular.2775

OP0091 S100A8 TRIGGERS A NOVEL IMMUNE-REGULATORY MECHANISM IN DEVELOPING DENDRITIC CELLS

D. Popp[1], F. Rühle[2], W. de Jager[3], T. Vogl[1], J. Roth[1]. *[1]Institute of Immunology; [2]Institute of Human Genetics, Münster, Germany; [3]Multiplex Core Facility, Wilhelmina Children's Hospital (UMC Utrecht), Utrecht, Netherlands*

Background: S100A8/A9 heterodimers are well-known alarmins that, upon release from activated or necrotic phagocytes, promote inflammation by binding to Toll-like receptor 4 (TLR4). These proteins are highly expressed in synovial phagocytes during arthritis and proved to be reliable biomarkers for monitoring disease activity in RA. Interestingly, we now identify a novel immune-regulatory mechanism of S100A8 in human monocyte-derived dendritic cells (moDCs).
Objectives: This study aims to analyze immune-regulatory functions of S100 proteins in human DCs.
Methods: MoDCs are differentiated with or without exposure to S100A8 prior to maturation with LPS. After characterization of the activation status using flow cytometry, the ability of these cells to induce autologous $CD4^+$, $CD8^+$, and γδ T-cell proliferation is investigated. Cytokines, secreted during development are analyzed by Luminex cytokine arrays. The metabolic state of DCs is examined by using Seahorse XFp Analyzer assays. Finally, to identify molecular mechanisms leading to an immune-regulatory phenotype, the mRNA expression of moDCs is analyzed by genome-wide gene expression arrays.

Results: Our results demonstrate that early exposure to S100A8 interferes with *in-vitro* differentiation of moDCs. Compared to controls S100A8-exposed moDCs show dramatically reduced surface expression of co-stimulatory molecules upon LPS-induced maturation. In addition, early treatment of moDCs with S100A8 alters the secretion of immune-regulatory cytokines and chemokines depending on the developmental state of moDCs. S100A8-induced effects on moDC maturation are not limited to TLR4 stimulation but rather trigger a common state of unresponsiveness. Furthermore, mitochondrial respiration and glycolytic function is diminished in S100A8-treated moDCs.

As a consequence, S100A8-exposed moDCs have a reduced potential to induce autologous T-cell proliferation. We can show that these differences are mainly caused by reduced surface expression of co-stimulatory molecules on S100A8-treated moDCs.

Mechanistically, genome-wide gene expression analysis reveals dramatic differences in gene expression between S100A8-exposed and conventionally differentiated moDCs. We demonstrate that S100A8 pre-treatment of moDCs significantly blocks LPS-induced gene expression during moDC activation. Interestingly, *in-silico* analysis of transcription factor networks predicts NFκB and C/EBPδ as master regulators of S100A8-induced effects in developing moDCs. C/EBPδ on protein level, indeed, shows reduced expression in S100A8-differentiated moDCs prior and after LPS-induced maturation when compared to conventionally differentiated moDCs.

Conclusions: Taken together, our results demonstrate a novel regulatory mechanism of innate immunity to prevent overwhelming immune responses. Dysregulated repression of detrimental adaptive immune responses might very well contribute to the disease phenotype in auto-immune disorders with high systemic S100A8/A9 levels. Therefore, S100A8-differentiated immune-suppressive DCs potentially represent a promising therapeutic tool to treat auto-immune diseases in the future.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4960

OP0092 INTERLEUKIN 37 REVERSES THE METABOLIC COST OF INFLAMMATION, INCREASES OXIDATIVE RESPIRATION AND IMPROVES EXERCISE TOLERANCE

G. Cavalli[1], D. Ballak[2], J.J. Justice[2], K. Boyle[3], A. D'Alessandro[3], L.A. Joosten[4], L. Dagna[1], C.A. Dinarello[5]. *[1]Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UniRAR), Vita-Salute San Raffaele University, Milan, Italy; [2]University of Colorado Boulder, Boulder, CO; [3]University of Colorado Denver, Aurora, CO, United States; [4]Radboud University Medical Center, Nijmegen, Netherlands; [5]Medicine, University of Colorado Denver, Aurora, CO, United States*

Background: The IL-1 family cytokine interleukin 37 (IL-37) has broad anti-inflammatory effects and functions as a natural suppressor of innate inflammation and acquired immunity (1). We have reported that administration of recombinant human IL-37 to wild type mice or expression in mice transgenic for human IL-37 suppress proinflammatory cytokines and curb excessive inflammation in various conditions including inflammatory arthritis (2). Besides these anti-inflammatory effects, IL-37 also induces complex effects on metabolism. In particular, IL-37 can directly activate AMP-activated protein kinase (AMPK), a central regulator of cellular energy homeostasis and exercise-regulated metabolism (3).

Objectives: In this study, we evaluate the effects of IL-37 treatment on exercise tolerance in mice with systemic inflammation induced by LPS injection. We further investigate the effects of IL-37 on exercise tolerance in healthy mice, with specific focus on the metabolic changes induced by IL-37 administration and possibly responsible for a reduction in the metabolic costs of inflammation.

Results: Exogenous administration of IL-37 to healthy mice, not subjected to an inflammatory challenge, also improved exercise performance by 82% compared to vehicle-treated mice (p=0.01). Treatment with 8 daily doses of IL-37 resulted in a further 326% increase in endurance running time compared to the performance level of mice receiving vehicle (p=0.001). These properties required the engagement of the IL-1 decoy receptor 8 (IL-1R8) and the activation of AMP-activated protein kinase (AMPK), since both inhibition of AMPK and IL-1R8 deficiency abrogated the positive effects of IL-37 on exercise performance. Mechanistically, treatment with IL-37 induced marked metabolic changes with higher levels of muscle AMPK, greater rates of oxygen consumption and increased oxidative phosphorylation. Metabolomic analyses of plasma and muscles of mice treated with IL-37 revealed an increase in AMP/ATP ratio, reduced levels of pro-inflammatory mediator succinate and oxidative stress-related metabolites as well as changes in amino acid and purine metabolism.

Conclusions: These effects of IL-37 to limit the metabolic costs of chronic inflammation and to foster exercise tolerance provide a rationale for therapeutic use of IL-37 in the treatment of inflammation-mediated fatigue.

References:

[1] Dinarello CA, et al. (2016) Suppression of innate inflammation and immunity by interleukin-37. Eur J Immunol.
[2] Cavalli G, et al. (2016) Treating experimental arthritis with the innate immune inhibitor interleukin-37 reduces joint and systemic inflammation. Rheumatology (Oxford).
[3] Ballak DB, et al. (2014) IL-37 protects against obesity-induced inflammation and insulin resistance. Nature communications.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1789

OP0093 IL-38 OVEREXPRESSION INDUCES ANTI-INFLAMMATORY EFFECTS IN MICE ARTHRITIS MODELS AND IN HUMAN MACROPHAGES IN VITRO

M.-A. Boutet[1], A. Najm[2], G. Bart[2], R. Brion[1], S. Touchais[2], V. Trichet[1], P. Layrolle[1], C. Gabay[3], G. Palmer-Lourenco[3], F. Blanchard[1], B. Le Goff[2]. *[1]Inserm UMR957, Université de Nantes; [2]Rheumatology Unit, Nantes University Hospital, Nantes, France; [3]Department of pathology and immunology, University of Geneva school of medicine, Geneva, Switzerland*

Background: IL-38 is a newly characterized cytokine that belongs to the IL-1 family. This cytokine is expressed in the rheumatoid arthritis (RA) synovial tissue (1) and IL-38 deficient mice have exacerbated arthritis (2).

Objectives: This work aims to analyze the effect of IL-38 overexpression in the joints of arthritic mice, in human macrophages and synovial fibroblasts *in vitro*.

Methods: Articular injections of an adeno-associated virus (AAV2/8) encoding IL-38 were performed in Collagen-Induced Arthritis (CIA), K/BxN Serum Transfer-Induced Arthritis (STIA) and Antigen-Induced Arthritis (AIA) in mice. The effect of IL-38 overexpression was evaluated through clinical scores, immunohistochemistry, microCT, Luminex and RT-qPCR analysis. THP-1 monocytes/macrophages were transduced with a lentiviral vector to overexpress IL-38. Effect of conditioned media from these transduced THP-1 cells was also tested on primary culture: M1 macrophages and fibroblast-like synoviocytes from RA patients (RA-FLS).

Results: Clinical inflammatory scores were significantly decreased after AAV IL-38 injection in joints of mice with CIA and STIA, but not AIA. This decrease was accompanied by reduced macrophage infiltration and a decreased expression of Th17 expressed cytokines (IL-17, IL-23, IL-22, TNFα). However, IL-38 overexpression had no effect on cartilage or bone destruction. *In vitro*, the THP-1 monocytic cell line expressed less IL-6, TNFα and IL-23 after IL-38 overexpression. Conditioned media from these cells, containing released IL-38, was also able to exert an anti-inflammatory effect on human primary M1 macrophages and RA-FLS by reducing their IL-23 (M1) and IL-6 (M1 and RA-FLS) expression.

Conclusions: This study shows for the first time that IL-38 overexpression attenuates the severity of experimental arthritis in two mice arthritis models. IL-38 may exert its anti-inflammatory effects by decreasing the production of pro-inflammatory cytokines by macrophages and synovial fibroblasts. This effect can lead to the development of novel treatment strategies in arthritis.

References:

[1] Boutet MA, Bart G, Gahier M, Amiaud J, Brulin B, Charrier C, Morel F, Lecron JC, RolliDerkinderen M, Boureille A, et al. Distinct expression of IL-36α, β, γ and their antagonists IL-36Ra and IL-38 in Psoriasis, Rheumatoid Arthritis and Crohn's disease. Clin Exp Immunol, 2015. doi: 10.1111/cei.12761.
[2] Takenaka, S., Kaieda, S., Kawayama, T., Matsuoka, M., Kaku, Y., Kinoshita, T., Sakazaki, Y., Okamoto, M., Tominaga, M., Kanesaki, K., et al. (2015). IL-38: A new factor in rheumatoid arthritis. Biochem. Biophys. Rep. 4, 386–391.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2257

OP0094 DEVELOPMENT OF A 37-CHANNEL MASS CYTOMETRY (CYTOF) PANEL TO PREDICT TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS

B. Mulhearn[1,2,3], S. Viatte[3], T. Hussell[1], A. Barton[2,3]. *[1]Manchester Collaborative Centre for Inflammation Research (MCCIR), University of Manchester; [2]Kellgren Centre for Rheumatology, Central Manchester University Hospitals NHS Foundation Trust; [3]Centre for Musculoskeletal Research, Division of Musculoskeletal & Dermatological Sciences, University of Manchester, Manchester, United Kingdom*

Background: It is well-established that reducing the inflammation of rheumatoid arthritis (RA) early leads to improved patient outcomes. Patients who fail to respond to conventional DMARDs move on to biologic drugs, however 30% will fail to respond to the first drug tried. Biologics are trialled for at least 3 months before their efficacy can be assessed, during which time irreversible joint damage may occur.

Currently there is no way to predict which drug will be effective in individual patients. It is therefore a research priority to develop a method to predict response to each class of biologic drug. I hypothesise that the immune phenotype of a patient will influence treatment response.

Objectives: This study aims to immunophenotype T cells using mass cytometry and to test novel unbiased methods of analysing high-dimensional data.

Methods: Ten healthy controls (HC) and 10 RA patients with established disease were included. T cells were isolated and stimulated for 4 hours using anti-CD3/anti-CD28 beads in the presence of monensin and brefeldin A. Cells were stained with a 37-channel mass cytometry panel including surface markers, intracellular antigens and transcription factors.

Analysis was performed by conventional biaxial gating alongside tools available on the MRC Cytobank platform, namely Visual t-distributed stochastic neighbour embedding (viSNE), and Cluster identification, characterization, and regression (CITRUS). The CITRUS analysis compared stimulated HC with RA T cells. To

compare abundances of cell clusters, the association model Prediction Analysis for Microarrays (PAMR) was applied with a minimum cluster size of 2.2%, 5 cross-validation folds and a false discovery rate of 1%.

Results: Conventional biaxial gating showed that there were large differences in the proportions of both IFNγ^+ CD4 T cells (1–15%) and IL-17A$^+$ CD4 T cells (0–9%) within and between RA and HC. The proportion of IFNγ^+ CD4 T cells (Th1) did not correlate with that of IL-17A $^+$ T cells (Th17), leading to the generation of 4 immunophenotypes: "Th1", "Th17", "double-hi", and "low", determined by cytokine expression.

Using CITRUS we identified 3 clusters of cells which differed significantly in abundance between HC and RA. Cluster 1 was CD4$^+$CD38$^+$, had characteristics of regulatory T cells and was more abundant in HC. Cluster 2 was CD28^{low}CD8$^+$ expressing perforin and Tbet, and cluster 3 a CD127^{high}CCR6$^+$population, both of which were more abundant in RA.

Conclusions: Cytokine expression of *ex vivo* stimulated T cells from RA and HC is highly variable and can be detected using mass cytometry. Cytokine signatures of this kind may be informative when predicting treatment response.

CITRUS identified 3 cell clusters which may have been missed using conventional methods of analysis. Importantly, CITRUS allowed inspection of the phenotype of each cluster.

Our next step is to compare RA responders to non-responders using the methods described. The function of these clusters will be further investigated by cell isolation with fluorescence-activated cell sorting (FACS) and may go some way in predicting treatment response. Finally we recommend the use of both automated clustering algorithms alongside conventional gating methods when analysing high-dimensional data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2067

OP0095 PREDICTION OF CONNECTIVE TISSUE DISEASE IN AN AT-RISK COHORT USING A NOVEL INTERFERON STIMULATED GENE EXPRESSION SCORE

M.Y. Md Yusof, Y. El-Sherbiny, A. Psarras, E. Hensor, A. Alase, A. Mohamed, M. Wittmann, P. Emery, E.M. Vital. *Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*

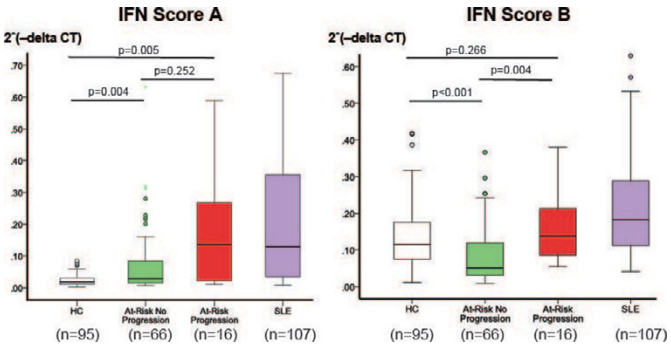
Background: A period of ANA positivity and other immune dysregulation precedes connective tissue disease, providing a potential opportunity for disease prevention. Type I interferons (IFN-I) play a role in pathogenesis but their role in disease initiation is unclear.

Objectives: To develop biomarkers of progression to systemic autoimmunity, with a view to enabling early intervention for disease prevention.

Methods: A prospective observational study was conducted in 125 patients At Risk of CTD defined by (i) ANA; (ii) $\leq$1 clinical SLE criteria; (iii) symptom duration $<$12 months and (iv) treatment-naïve. Progression was defined by meeting 2012 ACR/SLICC SLE, 2016 ACR/EULAR Primary Sjogren's, or other diagnostic criteria. Expression of 30 selected="selected" ISGs was measured using Taqman. Factor analysis was used to reduce the gene expression data to a limited set of factors, which were compared between patient groups using Mann Whitney U Test. Two factor scores explained 80% of the data variance; "Score A" (composed of IFN-α responsive genes) and "Score B" (genes responsive to IFN-α and γ). 95 healthy controls and 107 SLE patients were used as negative and positive controls.

Results: 82 patients with 1-year follow-up data were studied. 71 were female with mean age 48±15 years. 16 (20%) patients progressed to CTD (SLE=12, Sjogren's=4) in the following 12 months. At baseline, only IFN Score A was increased in both At Risk-CTD and SLE vs healthy controls; p$<$0.001. IFN Score B was only increased in true established SLE.

In At-Risk patients, IFN Score B was low in patients who did not progress and increased in those who did progress; p=0.004. However, there was no difference in IFN Score A between these two groups; p=0.252 (Figure 1). Although complement levels and lymphocyte counts were lower in SLE, these were not different between the At-Risk progression and non-progression groups. Anti-dsDNA titres were higher in SLE but not different between the progression groups; all p$>$0.10.



Conclusions: A novel ISG score predicts progression from ANA+ to clinical autoimmune disease. This may allow early intervention to prevent CTD. Analysis of other clinical, immunological and imaging biomarkers are in progress as well as a validation cohort.

Disclosure of Interest: M. Y. Md Yusof: None declared, Y. El-Sherbiny Grant/research support from: AstraZeneca, A. Psarras: None declared, E. Hensor: None declared, A. Alase: None declared, A. Mohamed: None declared, M. Wittmann: None declared, P. Emery Grant/research support from: AstraZeneca, E. Vital Grant/research support from: AstraZeneca

DOI: 10.1136/annrheumdis-2017-eular.6925

OP0096 INTERFERON SIGNATURE IN SYSTEMIC SCLEROSIS LUNG MICROVASCULAR ENDOTHELIAL CELLS

F.A. Mendoza [1], S. Piera-Velazquez [2], P. Wermuth [2], S. Addya [3], C. Feghali-Bostwick [4], S.A. Jimenez [2]. *[1]Division of Rheumatology and Scleroderma Center; [2]Jefferson Institute of Molecular Medicine and Scleroderma Center; [3]Kimmel Cancer Center, Thomas Jefferson University, Philadelphia; [4]Division of Rheumatology & Immunology, Medical University of South Carolina, Charleston, United States*

Background: Systemic Sclerosis (SSc) is characterized by severe fibroproliferative vasculopathy, exaggerated deposition of extracellular matrix molecules (ECM) in skin and multiple internal organs, and alterations of humoral, cellular and innate immunity. Vascular changes are responsible for the earliest and most severe SSc clinical manifestations, however, the mechanisms responsible have not been elucidated.

Objectives: The goal of this study was to analyze the gene expression differences between normal and SSc lung microvascular endothelial cells (EC) to improve the understanding of SSc vasculopathy pathophysiology.

Methods: Pulmonary microvascular EC were isolated employing immunomagnetic procedures from lungs from patients with SSc undergoing lung transplantation. Control pulmonary microvascular EC were isolated from autopsies of individuals who died from non-pulmonary causes. Following isolation, microarrays were performed in EC from each group. Expression of genes with the highest differential expression was validated with RT-PCR and Western blots.

Results: Interferon-stimulated genes (ISGs) including IFI44L, IFI44, IFI6, IFIH1, IFIT1 displayed the highest differential expression; being overexpressed in EC obtained from the three SSc donors (Figure 1). Other genes such as those encoding ECM production related proteins, genes associated with post-translational methylation, and genes for numerous chemokines and cytokines were also differentially overexpressed in SSc EC. Increased gene expression and increased protein levels of selected ISGs were confirmed by Western blots.

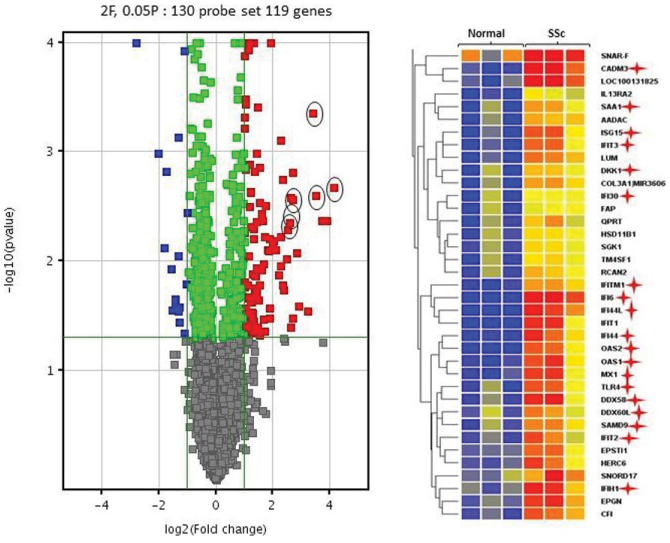


Figure 1. A: Volcano Plot showing differentially expressed transcripts with 2 fold or greater difference (p$<$0.05) in expression between SSc and normal control microvascular ECs (130 transcripts corresponding to119 genes). Selected ISGs are encircled (IFI-6, IFIT1, IFI-44,IFI44L,IFIT-3, OAS-1) B: Detail of the resulting heat map of a dendrogram (hierarchically clustered) reveals groups of genes with high expression levels (red squares), low expression levels (blue squares) or background expression levels (yellow squares). Interferon related genes are marked with a red star.

Conclusions: Numerous ISGs are differentially overexpressed in SSc pulmonary microvascular EC in comparison with normal control EC. These results suggest that events leading to an interferon response in these cells may play a role in the pathogenesis of SSc lung vasculopathy.

References:

[1] Kahaleh B. Vascular Disease in Scleroderma: Mechanisms of Vascular Injury. Rheumatic Disease Clinics of North America 2008; 34(1):57–71.

[2] Trojanowska M. Cellular and molecular aspects of vascular dysfunction in systemic sclerosis. Nat Rev Rheumatol 2010; 6(8):453–60.

[3] Matucci-Cerinic M, Kahaleh B, Wigley FM. Review: evidence that systemic sclerosis is a vascular disease. Arthritis and rheumatism 2013; 65(8):1953–62.
[4] Pattanaik D, Brown M, Postlethwaite BC, Postlethwaite AE. Pathogenesis of Systemic Sclerosis. Frontiers in immunology 2015; 6:272.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3739

THURSDAY, 15 JUNE 2017

Cytokines and chemokines

OP0097 SYSTEMIC IFN TYPE I AND TYPE II SIGNATURES IN PRIMARY SJÖGREN'S SYNDROME REVEAL DIFFERENCES IN DISEASE SEVERITY

I. Bodewes[1], S. Al-Ali[2,3], C.G. van Helden[1], N.I. Maria[1], J. Tarn[2], D. Lendrem[2], M.W. Schreurs[1], E.C. Steenwijk[1], P.L.A. van Daele[1,4], T. Both[4], S. Bowman[5], B. Griffiths[6], W.-F. Ng[2,7], M.A. Versnel[1]. *[1]Immunology, Erasmus MC, Rotterdam, Netherlands; [2]Musculoskeletal Research group, Newcastle University, Newcastle upon Tyne, United Kingdom; [3]University of Basrah, Basrah, Iraq; [4]Internal Medicine, Erasmus MC, Rotterdam, Netherlands; [5]Rheumatology, University Hospital Birmingham, Birmingham; [6]Newcastle upon Tyne Hospitals NHS Foundation Trust; [7]National Institute for Health Research, Newcastle Biomedical Research Centre, Newcastle upon Tyne, United Kingdom*

Background: Local and systemic activation of interferons (IFNs) has been demonstrated in primary Sjögren's syndrome (pSS).[1–4] Type I IFNs are associated with higher disease activity and autoantibody levels.[5] Recent findings also show activation of interferon type II (IFNγ) induced gene expression in salivary glands of pSS patients.[6, 7] Although IFN type I and II bind to different receptors they induce partially overlapping gene expression patterns. Understanding the relative contribution of IFN type I and type II may deepen our knowledge in pSS pathogenesis and promote a stratified approach to therapeutic development.
Objectives: Determine IFN type I and II inducible gene expression in patients with pSS and correlate this to disease manifestations.
Methods: In whole blood of 50 pSS patients modular IFN scores were determined using real-time quantitative PCR followed by principal component analysis. Subsequently, five indicator genes per module were analysed in two independent European cohorts with a total of 141 patients.
Results: Three groups were distinguished: without IFN activation (19–47%), with IFN type I (53–81%) and with IFN type I+II activation (35–55%). Patients with IFN activation (I or I+II) have a higher presence of auto-antibodies, IgG levels and lower lymphocyte counts compared to IFN negative patients. The biological domain of the EULAR Sjögren's Syndrome Disease Activity Index (biological-ESSDAI) was higher in patients with IFN activation, while total-ESSDAI scores were not significantly different.
66–67% of the IFN type I positive patients had an additional IFN type II inducible gene expression. Patients with IFN type I+II activation have significantly higher IgG levels and lower lymphocyte counts compared to patients with only IFN type I activation. There were no differences in fatigue or dryness, but pain scores were lower.
Conclusions: pSS patients can be stratified according to their systemic IFN activation patterns. IFN activation (I or I+II) is present in patients with the highest activity of the biological-ESSDAI. These data raise the possibility that the biological-ESSDAI rather than total-ESSDAI score may be a more sensitive endpoint for trials targeting either type I or type II IFN pathways.
References:
[1] Wildenberg, et al. EJI. 2008; 38(7):2024–2033.
[2] Gottenberg, et al. PNAS. 2006; 103(8):2770–2775.
[3] Hjelmervik, et al. A&R. 2005; 52(5):1534–1544.
[4] Emamian, et al. Genes Immun. 2009; 10(4):285–296.
[5] Brkic, et al. ARD. 2013; 72(5):728–735.
[6] Hall, et al. PNAS. 2013; 72(5):728–735.
[7] Hall, et al. A&R. 2012; 109(43):17609–17614.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3688

THURSDAY, 15 JUNE 2017

Progress in biological treatment of RA

OP0098 REMISSION AND MAINTENANCE OF EFFICACY IN A PHASE 2B STUDY OF VOBARILIZUMAB, AN ANTI-INTERLEUKIN 6 RECEPTOR NANOBODY, IN PATIENTS WITH MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS DESPITE TREATMENT WITH METHOTREXATE

T. Dörner[1], M. Weinblatt[2], P. Durez[3], R. Alten[4], K. Van Beneden[5], E.J. Dombrecht[5], K. De Beuf[5], P. Schoen[5], R.K. Zeldin[5]. *[1]Rheumatology and Clinical Immunology, Charité University Hospitals, Berlin, Germany; [2]Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, United States; [3]Department Rheumatology, Cliniques Universitaires St-Luc, Sint-Lambrechts-Woluwe, Belgium; [4]Schlosspark-Klinik, Berlin, Germany; [5]Ablynx NV, Zwijnaarde, Belgium*

Background: Vobarilizumab is a Nanobody® consisting of an anti-IL-6R domain and an anti-human serum albumin domain in development for treatment of RA. The efficacy and safety were assessed in a 24-week double-blind global phase 2b study in patients with active RA on a stable background of MTX. Main efficacy and safety results were previously reported [1].
Objectives: To report the impact of treatment with vobarilizumab on secondary efficacy endpoints including SDAI and CDAI remission and the sustained response at 4 consecutive visits based on ACR50, ACR70 and $DAS28_{CRP}$.
Methods: Patients were randomized to receive subcutaneously administered placebo or 1 of 4 dose regimens of vobarilizumab in addition to MTX. SDAI and CDAI remission at Week 24 was evaluated, as was maintenance of efficacy as defined by sustained $DAS28_{CRP} < 2.6$ responses at 4 consecutive visits (i.e., at Weeks 12, 16, 20 and 24). In addition, a post-hoc analysis was performed on sustained ACR50 and ACR70 responses from Week 12 through Week 24. Proportions of patients achieving response for these endpoints were summarized by treatment group. Subjects with missing values were analyzed as non-responders.
Results: A total of 345 patients were randomized. Demographics and baseline characteristics were similar across groups with mean baseline $DAS28_{CRP}$ between 5.8 and 6.2. At Week 24, up to 19% and 20% in the vobarilizumab groups reached CDAI and SDAI remission, respectively vs. 10% and 9% who received placebo (Table 1).

Table 1. Percentage of patients with CDAI and SDAI remission at Week 24

	Placebo (N=69)	Vobarilizumab 75mg q4w (N=69)	Vobarilizumab 150mg q4w (N=70)	Vobarilizumab 150mg q2w (N=68)	Vobarilizumab 225mg q2w (N=69)
CDAI remission (≤2.8)	10	15	19	12	19
SDAI remission (≤3.3)	9	10	19	15	20

At Week 24, up to 61% and 45% of the patients in the vobarilizumab groups achieved an ACR50 or ACR70 response, respectively (39% and 17% on placebo). Approximately one third of the randomized patients in the 3 highest treatment groups had a sustained ACR50 response from Week 12 through Week 24 (Table 2). Sustained remission defined by $DAS28_{CRP} < 2.6$ at 4 consecutive visits, i.e. at weeks 12, 16, 20 and 24, was observed in 20% to 25% of the patients in the 3 highest dosing arms compared with 3% of those receiving placebo.

Table 2. Percentage of patients with sustained efficacy response at 4 consecutive visits (Weeks 12, 16, 20 and 24)

	Placebo (N=69)	Vobarilizumab 75mg q4w (N=69)	Vobarilizumab 150mg q4w (N=70)	Vobarilizumab 150mg q2w (N=68)	Vobarilizumab 225mg q2w (N=69)
$DAS28_{CRP}$ <2.6	3	4	20	25	20
ACR50	16	14	29	31	39
ACR70	4	7	11	13	13

Conclusions: In patients with active RA, treatment with vobarilizumab at the 3 highest dose regimens in addition to MTX had a positive and sustained impact on disease activity through Week 24 as defined by clinically relevant efficacy endpoints.
References:
[1] Weinblatt et al. (Annual Scientific Meeting, Canadian Rheumatology Association, 2017).
Disclosure of Interest: T. Dörner Consultant for: Ablynx, M. Weinblatt Consultant for: Ablynx, P. Durez Consultant for: Ablynx, R. Alten Consultant for: Ablynx, K. Van Beneden Employee of: Ablynx, E. Dombrecht Employee of: Ablynx, K. De Beuf Employee of: Ablynx, P. Schoen Employee of: Ablynx, R. Zeldin Employee of: Ablynx
DOI: 10.1136/annrheumdis-2017-eular.3732

OP0099 SAFETY, TOLERABILITY AND INITIAL SIGNS OF EFFICACY OF THE FULLY HUMAN IMMUNOCYTOKINE DEKAVIL (F8IL10): A NOVEL THERAPEUTIC APPROACH FOR RHEUMATOID ARTHRITIS

M. Galeazzi[1], G. Sebastiani[2], R. Voll[3], J. Wollenhaupt[4], O. Viapiana[5], J. Dudler[6], E. Selvi[1], C. Baldi[1], M. Bardelli[1], B. Bannert[3], S. Finzel[3], C. Specker[7], P. Sarzi Puttini[8], F. Bootz[9], D. Neri[10] on behalf of the DEKAVIL Study Group. *[1]University Hospital, Siena; [2]San Camillo-Forlanini Hospital, Rome, Italy; [3]University Medical Center, Freiburg; [4]Schoen-Klinik, Hamburg Eilbek, Germany; [5]University Hospital, Verona, Italy; [6]Cantonal Hospital, Fribourg, Switzerland; [7]University Hospital, Essen, Germany; [8]Luigi Sacco Hospital, Milan, Italy; [9]Philochem AG, Otelfingen, Switzerland; [10]Philogen SpA, Siena, Italy*

Background: The antibody-based targeted pharmacodelivery of cytokines by means of immunocytokines has the potential to enhance therapeutic activity at the site of disease while sparing healthy tissues. Dekavil (F8IL10) is a fully human immunocytokine composed of the vascular targeting antibody F8 (specific to

EDA) fused to the cytokine interleukin-10. Dekavil is currently in phase II clinical development for the treatment of rheumatoid arthritis (RA).
Objectives: In the phase Ib dose escalation study, the primary objective was to explore safety, tolerability and the maximum tolerated dose of Dekavil when administered in combination with methotrexate (MTX). The aim of the currently ongoing phase II study is to assess therapeutic activity of Dekavil plus MTX over MTX alone by measuring the mean change from baseline of DAS28-CRP. Immunogenicity of F8IL10 and its PK and PD profile will also be explored.
Methods: Patients with active RA despite MTX therapy and who failed anti-TNF treatment are the target population of both studies. In the phase Ib trial, cohorts of 3–6 patients were treated with escalating doses of Dekavil (6, 15, 30, 60, 110, 160, 210, 300, 450 and 600 μg/kg) in combination with a fixed dose of MTX (10–15 mg). In the multicenter, double-blind, placebo-controlled phase 2 study, patients are randomized into two treatment groups (Dekavil 30 or 160 μg/kg plus MTX) and one placebo group (placebo plus MTX). Dekavil is administered once weekly by *s.c.* injection for a maximum of 8 weeks in both studies.
Results: Dekavil has been shown to be well tolerated up to the highest investigated dose (600 μg/kg) and an MTD was not reached. In 33 out of 34 patients treated in the phase 1 study, no DLTs, no SAEs and no SUSARs have been reported. One patient in cohort 9 (450 μg/kg) experienced a DLT (G2 purpura) and a SAE (G2 dyspnea, not drug related). The patient received corticosteroids and fully recovered within one week. Mild injection site reactions were the most frequently observed adverse events and occurred in 62% of the patients. Furthermore, two cases of drug related anemia (G2 and G3) were reported in this study. All adverse reactions resolved completely. At the first efficacy assessment after 4 cycles of treatment, 48% of evaluable patients (16/33) revealed ACR and/or EULAR responses. The fraction of responding patients increased to 57.7% (15/26) after 8 cycles of treatment. Two patients benefited from ACR70 responses for more than 12 months after the last drug administration. As of January 2017, 22 out of 87 patients have been treated in the phase 2 clinical study and neither SUSAR nor treatment-related deaths were recorded.
Conclusions: The currently available data suggest that Dekavil is a safe and promising novel therapeutic for the treatments of RA.
Disclosure of Interest: M. Galeazzi: None declared, G. Sebastiani: None declared, R. Voll: None declared, J. Wollenhaupt: None declared, O. Viapiana: None declared, J. Dudler: None declared, E. Selvi: None declared, C. Baldi: None declared, M. Bardelli: None declared, B. Bannert: None declared, S. Finzel: None declared, C. Specker: None declared, P. Sarzi Puttini: None declared, F. Bootz Employee of: Philochem AG, D. Neri Shareholder of: Philogen SpA
DOI: 10.1136/annrheumdis-2017-eular.4840

OP0100 OVERALL CANCER RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TNF INHIBITORS, TOCILIZUMAB, ABATACEPT, OR RITUXIMAB

H. Wadström, T. Frisell, J. Askling on behalf of The ARTIS study group.
Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden

Background: Immune incompetence may lower host surveillance against incipient tumours. Conversely, immune therapies have emerged as a promising therapeutic approach to cancer. Malignancies thus constitute an important aspect of the safety of biologics as used in Rheumatology, including agents targeting TNF, CD20 and IL6, and immunomodulation using CTLA4. Whereas previous reports concerning TNF inhibitors (TNFi) and risk of malignancies in rheumatoid arthritis (RA) have mostly been reassuring, risks with other biological disease modifying anti-rheumatic drugs (bDMARDs) are less studied.
Objectives: To assess the risk of malignancies in patients with RA treated with bDMARDs.
Methods: Through linkages of Swedish national and population-based registers we assembled cohorts of patients with RA initiating (Jan 2006 through Dec 2014) a first ever treatment of tocilizumab, abatacept, rituximab, or a TNFi, one cohort of patients initiating a second TNFi, one cohort of biologics-naïve csDMARD treated RA. Through linkage with the Swedish Cancer Register information on incident cancers was collected. Outcomes were defined as a first ever solid or hematologic malignancy excluding non-melanoma skin cancer (NMSC) during follow-up. Patients with a previous malignancy were excluded. Patients were followed from treatment start until death, emigration, outcome or end of follow up (Dec 2014). Hazard ratios were calculated using Cox-regression adjusted for age, sex, educational level, comorbidities, sero-positivity, number of hospitalizations and days spent in inpatient care, use of prednisolone at baseline, use of non-steroidal anti-inflammatory drugs (NSAIDs) at baseline, number of prescription drugs at baseline, and sick leave and disability (yes/no) the year before cohort entry.
Results: Adjusted for age, sex, disease- and treatment characteristics (see above), and educational level, there were no statistically significant differences in risk of a first solid or hematologic malignancy between initiators of tocilizumab, abatacept, rituximab, or a first- or second TNFi, and RA patients treated with csDMARDs.

Table 1. Number of persons, events, crude incidence, and hazard ratios for a first invasive solid or hematologic malignancy excluding NMSC

Outcome definition Cohort	Number of persons at risk	Number of events	Crude incidence per 10,000 pys	HR*
First invasive solid or hematologic malignancy excluding NMSC				
Tocilizumab	1408	30	80	0.78 (0.54–1.12)
Abatacept	1565	45	104	0.95 (0.70–1.28)
Rituximab	2793	108	103	0.86 (0.70–1.04)
First TNFi	9355	369	93	0.91 (0.82–1.01)
Second TNFi	3610	129	87	0.88 (0.73–1.05)
csDMARD RA	40071	2797	131	1 (reference)

*Adjusted for age, sex, disease- and treatment characteristics, and educational level.

Conclusions: The overall risk of malignancies among RA patients initiating, tocilizumab, abatacept, rituximab, or a first- or second TNFi in clinical practice did not differ substantially from that of RA patients treated with csDMARDs. Increased risk of tumours at specific sites, or with longer latency, cannot be excluded.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4048

OP0101 RISK OF OPPORTUNISTIC INFECTIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING ABATACEPT: ANALYSIS OF ALL AVAILABLE CLINICAL TRIAL DATA

T. Simon[1], T. Gelarden[1], E. Nkhoma[1], M. Zhou[1], S. Banerjee[1], K. Winthrop[2].
[1]*Bristol-Myers Squibb, Princeton;* [2]*Oregon Health & Science University, Portland, United States*

Background: Opportunistic infections (OI) during treatment with abatacept (ABA) have been previously reported but are lacking a comprehensive analysis.
Objectives: To present the overall incidence rates of OI and herpes infections observed in patients (pts) receiving ABA using combined clinical trial data.
Methods: OI adverse events were summarized from 16 clinical trials (both placebo-controlled and cumulative abatacept exposure); all pts randomized to placebo were on a non-biologic DMARD. Incidence rates (per 100 person-years [p-y]) were calculated by the number of pts experiencing the first event divided by the total number of p-y of exposure. The p-y of exposure was censored at the time of the first event, death, discontinuation or end of study. Random effects meta-regression was performed across the trials to estimate the frequency of OI after adjusting for between-study heterogeneity. OI were identified using a pre-specified list in the setting of biologic therapy for patients with RA. Criteria for consideration were based on type, location of the infection and causing organism. Excluded from the list were non-specific infections caused by organisms considered to be opportunistic, but common in the general population.
Results: A total of 7044 pts with RA with ~21,330 p-y of ABA exposure were included in the cumulative randomized trial data (Table). The frequency of OI

Abstract OP0101 – Table 1

Infection Outcome	Abatacept (N=2653) p-y=2355		Placebo (N=1485) p-y=1253		Cumulative abatacept (N=7044) p-y=21,330	
	N (%)	IR/100 p-y (95% CI)	N (%)	IR/100 p-y (95% CI)	N (%)	IR/100 p-y (95% CI)
Opportunistic infections*	4 (0.2)	0.17 (0.05, 0.43)	7 (0.5)	0.56 (0.22, 1.15)	45 (0.6)†	0.21 (0.15, 0.28)†
Bronchopulmonary aspergillosis	1 (<0.1)	0.04 (0, 0.2)	0	0	2 (<0.1)	0.01 (0.00, 0.03)
Eye infection fungal	1 (<0.1)	0.04 (0, 0.2)	0	0	3 (<0.1)	0.01 (0.00, 0.04)
Gastrointestinal candidiasis	0	0	1 (<0.1)	0.08 (0, 0.4)	–	–
Fungal oesophagitis	0	0	1 (<0.1)	0.08 (0, 0.4)	1 (<0.1)	0.00 (0.00, 0.03)
Meningitis cryptococcal	0	0	1 (<0.1)	0.08 (0, 0.4)	–	–
Oesophageal candidiasis	0	0	1 (<0.1)	0.08 (0, 0.4)	7 (0.1)	0.03 (0.01, 0.07)
Pneumocystis jirovecii pneumonia	0	0	1 (<0.1)	0.08 (0, 0.4)	1 (<0.1)	0.00 (0.00, 0.03)
Pneumonia pseudomonal	1 (<0.1)	0.04 (0, 0.2)	0	0	1 (<0.1)	0.00 (0.00, 0.03)
Respiratory moniliasis	0	0	1 (<0.1)	0.08 (0, 0.4)	2 (<0.1)	0.01 (0.00, 0.03)
Tuberculosis	1 (<0.1)	0.04 (0, 0.2)	1 (0.1)	0.08 (0, 0.4)	17 (0.2)‡	0.08 (0.05, 0.13)‡
Herpes						
Herpes simplex	57 (2.1)	2.5 (1.9, 3.2)	22 (1.5)	1.8 (1.1, 2.7)	60 (0.9)	0.28 (0.22, 0.37)
Herpes zoster	44 (1.7)	1.9 (1.4, 2.5)	21 (1.4)	1.7 (1.1, 2.6)	284 (4)	1.38 (1.22, 1.55)
Herpes virus infection	5 (0.2)	0.2 (0.1, 0.5)	4 (0.3)	0.3 (0.1, 0.8)	–	–

*Except herpes; †n (%) for SAE was 19 and IR/100 p-y was 0.1 (95% CI 0.05, 0.14); ‡n (%) for SAE was 11 and IR/100 p-y was 0.05 (95% CI 0.03, 0.09); '–' indicates value is not available. SAE = serious AE.

was 64% lower among pts treated with ABA vs placebo. After adjusting for heterogeneity across studies, the frequency (95% CI) of OI remained lower for the ABA group (0.15% [0.06, 0.42] vs the placebo group (0.48% [0.22, 1.04]).

Conclusions: Abatacept-treated pts had a lower incidence rate of OI compared with placebo. The OI and herpes infection incidence rates in the cumulative data are similar or lower to those reported in the literature.[1–3]

References:
[1] Curtis JR, et al. Ann Rheum Dis 2016;75:1843–7.
[2] Yun H, et al. Arthritis Care Res (Hoboken) 2015;67:731–6.
[3] Winthrop KL, et al. Ann Rheum Dis 2015;74:2107–16.

Disclosure of Interest: T. Simon Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, T. Gelarden Employee of: Alpha Consulting, E. Nkhoma Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Zhou Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Banerjee: None declared, K. Winthrop Consultant for: Pfizer, AbbVie, Bristol-Myers Squibb, UCB, Roche/Genentech, Amgen, Galapagos, Lilly
DOI: 10.1136/annrheumdis-2017-eular.2306

OP0102 PATIENT REPORTED BENEFITS OF SARILUMAB MONOTHERAPY VERSUS ADALIMUMAB MONOTHERAPY IN ADULT PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

V. Strand[1], L. Gossec[2], C. Proudfoot[3], C. Chen[4], M. Reaney[3], S. Guillonneau[5], T. Kimura[4], J. van Adelsberg[4], Y. Lin[6], E. Mangan[4], H. van Hoogstraten[6], G.R. Burmester[7]. *[1]Stanford University, Palo Alto, United States; [2]Universite Pierre et Marie Curie and Hopital Pitie-Salpetriere, Paris, France; [3]Sanofi, Guildford, United Kingdom; [4]Regeneron Pharmaceuticals, Inc., Tarrytown, United States; [5]Sanofi, Paris, France; [6]Sanofi, Bridgewater, United States; [7]Charité - University Medicine, Berlin, Germany*

Background: The phase 3 MONARCH superiority study (NCT02332590) compared efficacy and safety of sarilumab (a human anti-IL-6Rα monoclonal antibody [mAb]) 200 mg administered subcutaneously every 2 weeks (q2w), with adalimumab (an anti-TNF-α mAb) 40 mg administered q2w, in patients with active rheumatoid arthritis (RA) who were either intolerant of, or inadequate responders to methotrexate treatment. Sarilumab monotherapy demonstrated superiority to adalimumab monotherapy in reduction of disease activity and improvements in physical function and signs and symptoms of RA, with safety and tolerability consistent with IL-6R or TNF blockade.

Objectives: To compare patient-reported outcomes (PROs) with sarilumab vs adalimumab from MONARCH.

Methods: PROs assessed at baseline, weeks 12 and 24 included ACR components (Patient Global Assessment of Disease Activity [PtGA], Pain visual analog scale [VAS], Health Assessment Questionnaire Disability Index [HAQ-DI]), Medical Outcomes Study Short Form-36 (SF-36), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Morning Stiffness VAS, RA Impact of Disease (RAID) and RA-specific Work Productivity Survey (WPS-RA). Least-squares mean (LSM) between-group differences were determined by mixed-model for repeated measures with treatment, visit, treatment-by-visit interaction and region as fixed effects, and the corresponding baseline PRO scores as continuous covariates. A *P*-value <0.05 was considered statistically significant for PROs in a predefined hierarchy (ACR components, SF-36 physical component summary [PCS], FACIT-F and SF-36 mental component summary [MCS] scores). For PROs not in the hierarchy, significance is not claimed. Changes from baseline were compared with published values for minimum clinically important differences (MCIDs).

Results: Baseline demographics, disease characteristics and PROs were generally balanced between treatment groups (n=184 sarilumab; n=185 adalimumab). Improvements from baseline to week 24 were greater with sarilumab vs adalimumab across PtGA, Pain VAS, HAQ-DI, SF-36 PCS, Morning Stiffness VAS, RAID and WPS-RA global scores (all $P<0.05$, statistical significance is claimed only for PROs in the hierarchy; see table). Between-group differences in FACIT-F and SF-36 MCS scores were not significant. Improvements ≥MCID were reported by a greater percentage of patients with sarilumab than adalimumab for HAQ-DI (≥0.22 units), RAID (≥3 units), SF-36 PCS (≥2.5), and Morning Stiffness VAS (≥10) (all nominal $P<0.05$).

Table. Mean change from baseline to week 24 with sarilumab 200 mg q2w or adalimumab 40 mg q2w

PRO	Mean (SD) Baseline score		LSM Changes (SE) from Baseline to Week 24		Least-Squares Mean Between-Group Difference (95% CI)	*P*-value*
	Sarilumab 200 mg q2w (n=184)	Adalimumab 40 mg q2w (n=185)	Sarilumab 200 mg q2w (n=184)	Adalimumab 40 mg q2w (n=185)		
ACR components						
HAQ-DI	1.64 (0.54)	1.62 (0.64)	-0.61 (0.05)	-0.43 (0.05)	-0.18 (-0.31, -0.06)	<0.005
Pain VAS	70.93 (18.77)	70.32 (19.31)	-36.19 (1.78)	-27.41 (1.80)	-8.78 (-13.66, -3.90)	<0.001
PtGA	68.22 (17.38)	67.51 (18.27)	-33.30 (1.73)	-24.82 (1.75)	-8.48 (-13.24, -3.72)	<0.001
SF-36						
PCS	30.77 (6.09)	31.53 (6.48)	8.74 (0.56)	6.09 (0.56)	2.65 (1.15, 4.15)	<0.001
MCS	36.43 (10.43)	36.93 (11.59)	7.86 (0.77)	6.83 (0.77)	1.04 (-1.06, 3.13)	0.332
Physical functioning	33.26 (19.68)	35.53 (22.01)	22.38 (1.64)	15.01 (1.65)	7.37 (2.91, 11.83)	<0.005
Role-physical	34.31 (18.03)	34.89 (20.51)	20.80 (1.61)	16.23 (1.63)	4.57 (0.18, 8.96)	<0.05
Bodily pain	36.77 (15.84)	39.15 (16.87)	25.69 (1.46)	19.40 (1.47)	6.28 (2.32, 10.25)	<0.005
General health	34.00 (16.03)	36.45 (15.85)	13.96 (1.18)	11.05 (1.19)	2.91 (-0.30, 6.12)	0.076
Vitality	33.29 (16.35)	35.51 (17.39)	17.95 (1.42)	14.39 (1.43)	3.56 (-0.31, 7.43)	0.071
Social functioning	46.27 (23.18)	47.55 (26.18)	21.41 (1.81)	15.04 (1.83)	6.37 (1.43, 11.30)	<0.05
Role emotional	47.15 (24.38)	47.57 (27.15)	18.04 (1.79)	14.10 (1.81)	3.94 (-0.94, 8.82)	0.113
Mental health	48.16 (18.01)	49.81 (19.44)	14.29 (1.31)	13.26 (1.32)	1.02 (-2.54, 4.58)	0.572
FACIT-F	23.59 (8.92)	24.43 (10.26)	10.18 (0.70)	8.41 (0.71)	1.77 (-0.14, 3.67)	0.069
Morning stiffness VAS	70.76 (18.93)	68.95 (21.42)	-36.08 (1.95)	-29.29 (1.97)	-6.80 (-11.10, -0.50)	<0.05
RAID	6.89 (1.69)	6.28 (2.06)	-3.08 (0.17)	-2.30 (0.17)	-0.78 (-1.23, -0.32)	<0.001
WPS-RA (global)†	N/A	N/A	N/A	N/A	N/A	<0.005

*Least-squares mean between-group differences (sarilumab vs adalimumab).
Items above the dotted line were part of the hierarchy and thus statistical significance may be claimed. Between-group differences were not significant for FACIT-F and SF-36 MCS. Items below the dotted line are outside of the hierarchy and thus statistical significance is not claimed and nominal *P*-values are provided.
†Global test for the chance from baseline in the eight WPS-RA scores.

Conclusions: Sarilumab monotherapy compared with adalimumab monotherapy resulted in greater and clinically meaningful improvements in many PROs, including patient-reported disease activity, pain, physical function, morning stiffness, productivity, health related quality of life and health status.

Acknowledgements: This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: V. Strand Consultant for: AbbVie, Amgen, AstraZeneca, Biogen, BMS, Celltrion, CORRONA, Crescendo, Genentech/Roche, GSK, Janssen, Eli Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, Sandoz, Sanofi, and UCB, L. Gossec Grant/research support from: Member of institution that received research funding for the current study, C. Proudfoot Shareholder of: Sanofi, Employee of: Sanofi, C. Chen Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., M. Reaney Shareholder of: Sanofi, Employee of: Sanofi, S. Guillonneau Shareholder of: Sanofi, Employee of: Sanofi, T. Kimura Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., J. van Adelsberg Shareholder of: Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., Y. Lin Shareholder of: Sanofi, Employee of: Sanofi, E. Mangan Shareholder of: Pfizer Inc. and Regeneron Pharmaceuticals, Inc., Employee of: Regeneron Pharmaceuticals, Inc., H. van Hoogstraten Shareholder of: Sanofi, Employee of: Sanofi, G. R. Burmester Grant/research support from: Member of institution that received research funding for the current study
DOI: 10.1136/annrheumdis-2017-eular.2955

OP0103 THE EFFECT OF SIRUKUMAB PLUS METHOTREXATE ON CIRCULATING BIOMARKERS OF JOINT DESTRUCTION IN MODERATE TO SEVERE RHEUMATOID ARTHRITIS PATIENTS FROM THE SIRROUND-D PHASE 3 STUDY

B. Dasgupta[1], K. Campbell[1], A.-C. Bay-Jensen[2], M. Karsdal[2], K. Sweet[1], M. Sims[3], M.J. Loza[1]. *[1]Janssen Research & Development, LLC, Spring House, PA, United States; [2]Nordic Bioscience, Herlev, Denmark; [3]GlaxoSmithKline, Stevenage, United Kingdom*

Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation that can lead to progressive bone and joint damage. The cytokine interleukin-6 (IL-6) is implicated in inflammatory pathways associated with bone and cartilage degradation in RA. Inhibition of IL-6 signaling by sirukumab (SIR), an anti-IL6 cytokine monoclonal antibody, was shown to significantly reduce structural damage progression, relative to placebo (pbo), in disease-modifying antirheumatic drug inadequate responder (DMARD-IR) RA patients (pts) in the Phase 3 SIRROUND-D study.

Objectives: To investigate the mechanism of SIR on joint tissue remodeling, a panel of serum biomarkers associated with matrix metalloproteinase (MMP)-driven interstitial matrix and basement membrane degradation (C1M, C3M, C4M), bone turnover (β-isomerized C-terminal telopeptides of type I collagen, CTX-I), osteoblast formation (osteocalcin/NMID), synovial destruction (MMP-3), and tissue inflammation (MMP-mediated destruction of CRP/CRPM) were assessed in pts with moderate to severe RA from SIRROUND-D.

Methods: Serum samples from a sub-cohort of SIRROUND-D (for whom radiographic data were available) were analyzed ad hoc for the following biomarkers: C1M, C3M, C4M, CRPM, MMP-3, CTX, and osteocalcin. Samples from 100 pts treated with pbo and methotrexate (MTX) and 100 pts treated with SIR 50mg q4w + MTX were tested. Biomarkers were measured in all pts at baseline (BL) and Wk 4; samples from SIR and pbo-treated pts (50/group) were tested at Wk 52. Differences between groups were evaluated by comparing within-subject $\log_2$ ratio of Wk 4 or Wk 52 over BL values between treatment groups. Structural damage progressors versus non-progressors were defined based on changes from BL in Sharp/van der Heijde score (SHS) at Wk 52 (≥5 vs <5). Differences between groups were tested using General Linear Models.

Results: SIR significantly reduced serum levels of C1M (-48%), C3M (-30%), C4M2 (-42%), and CRPM (-22%) by Wk 4 vs pbo ($P<0.001$), with similar reductions observed at Wk 52; MMP-3 levels were more substantially decreased by SIR at Wk 52 (-39%) vs Wk 4 (-20%). In contrast, treatment with SIR resulted in increased levels of CTX-I (+20%) and osteocalcin (+12%) by Wk 4 ($P<0.001$; Figure 1). As 95% of the total study population included in this biomarker analysis did not progress (defined as ≥5 Wk 52 change in SHS), we were unable to demonstrate an association between changes in pharmacodynamic markers and radiographic progression. Nor were significant associations with pharmacodynamic changes with SIR treatment observed for comparisons among patients grouped by Wk 52 changes in SHS of ≥5 (n=5), <5 to ≥0.5 (n=41),

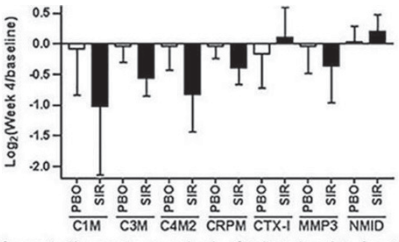


Figure 1. Changes in serum levels of indicated analyte (x-axis), displayed as mean ± SD of log2-transform of within-subject week 4/baseline ratios, stratified by treatment group (PBO, placebo; SIR, sirukumab 50mg q4w). P<0.05 for SIR vs. PBO for each analyte.

and <0.5 (n=51). BL or Wk 4 changes in levels of individual analytes were not associated with Wk 24 ACR50 or DAS28-CRP responses.
Conclusions: SIR 50mg q4w + MTX, vs pbo + MTX, inhibited radiographic progression in RA pts in SIRROUND-D and strongly inhibited biomarkers of joint and tissue destruction while enhancing markers of bone formation. These data suggest SIR may actively suppress inflammatory pathways implicated in joint destruction in RA pts.
Disclosure of Interest: B. Dasgupta Employee of: Janssen Research & Development, LLC, K. Campbell Employee of: Janssen Research & Development, LLC, A.-C. Bay-Jensen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, M. Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, K. Sweet Employee of: Janssen Research & Development, LLC, M. Sims Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, M. Loza Employee of: Janssen Research & Development, LLC
DOI: 10.1136/annrheumdis-2017-eular.3588

OP0104 TOCILIZUMAB: DOSE REDUCTION OR INTERVAL SPACING – WHICH PROVES A BETTER TAPERING STRATEGY FOR RHEUMATOID ARTHRITIS IN CLINICAL REMISSION?

Y. Urata[1], S. Abe[2], B. Devers[3], Y. Nakamura[4], H. Takemoto[5], K.-I. Furukawa[6].
[1]Department of Rheumatology, Tsugaru General Hospital, Gosyogawara; [2]Marketing Department; [3]Marketing Department, Diagnostics Division, Sekisui Medical Co., Ltd., Tokyo; [4]Departments of Orthopaedic Surgery; [5]Departments of Dermatology, Tsugaru General Hospital, Gosyogawara; [6]Department of Pharmacology, Hirosaki University Graduate School of Medicine, Hirosaki, Japan

Background: A number of studies have revealed that reduction of biological disease-modifying anti-rheumatic drugs (bDMARDs) is possible for some rheumatoid arthritis (RA) patients in whom bDMARD treatment has induced clinical remission or low disease activity.
For tocilizumab (TCZ), while there have been studies concerning tapering, there have been no studies regarding which tapering option is better in RA after clinical remission has been achieved: a dose reduction strategy (DRS) or an interval spacing strategy (ISS).
We previously demonstrated that a twin target strategy [targeting both a simplified disease activity index (SDAI) score of less than 3.3 and normalization of matrix metalloproteinase (MMP) 3 levels] can achieve effects non-inferior to standard care with regard to maintaining clinical remission in the rT-4study.
Objectives: To evaluate any significant differences that may be present between the two strategies (DRS and ISS) while tapering TCZ in RA patients who satisfied the SDAI remission and MMP-3 normalization targets under the twin target scheme.
Methods: DRS was used in patients treated with intravenous (IV) TCZ, whereas ISS was used for those treated by subcutaneous injection (SC). 57 RA patients who demonstrated SDAI remission and MMP-3 normalization using TCZ (IV, n=42; SC, n=15) participated. Dose reduction methodology (every 3 months): DRS- dose reduced by 80mg; ISS- period between injections increased by one week; up to a minimum dose of: DRS- 80 mg every 4 weeks; ISS-162 mg every 6 weeks. The dose was reverted to the previous level in the event that the target scores were exceeded, and the lower dose was eventually reattempted after the target was re-achieved. The primary outcome was the difference in the number of the times when a patient's SDAI exceeded 3.3 across the four time points.
Results: Fifty-five patients completed the observation period of 12 months and were analyzed (ITT). There were differences in the number of the times which SDAI scores exceed the target over the 12 months in the DRS group vs the ISS group: 2.4±1.7 and 0.9±1.2, respectively (p=0.0027). DRS had a duration (months) of maintained SDAI remission significantly shorter than that of ISS (3.9±5.0 vs 7.4±5.1, p=0.0213). At month 12, the proportions for DRS and ISS, respectively, for ΔmTTS$\leq$0.5 were 71.4 and 66.7% (p=0.7293); for maintained HAQDI=0 were 83.3 and 66.7 (p=0.4227) and for AE were 81.0 and 46.7 (p=0.0112). The total dose for TCZ in DRS tended to be lower than that for ISS (1367±840vs 1626±583mg, p=0.0824). The rate of total TCZ reduction showed a significant difference between DRS and ISS (29.3±15.2% vs41.8±15.0%, p=0.0037). Comparing three groups consisting of 400mg<, 401<<500mg and 500mg< across the DRS with ISS groups, there were significantly greater number of times when SDAI exceeded 3.3 in the DRS vs the ISS group; 2.3±1.6, 2.7±1.8 and 2.4±1.9, p=0.0395.
Conclusions: ISS using the twin targets as defined by the rT-4 study is an excellent strategy that is both safe and cost-effective for RA patients who are both being treated with TCZ and have reached said targets.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2501

OP0105 LONG-TERM SAFETY OF TOCILIZUMAB FROM LARGE CLINICAL TRIAL AND POSTMARKETING POPULATIONS

S. Mohan, M. Michalska, J. Yourish, J. Pei, S. Gale, C. Birchwood, E. Berber.
Genentech, Inc., South San Francisco, CA, United States

Background: Tocilizumab (TCZ) is a recombinant humanized monoclonal antibody targeted against the interleukin-6 receptor that was approved to treat rheumatoid arthritis (RA) in the EU in 2009 and in the US in 2010. TCZ has now completed long-term extension (LTE) follow-ups in a number of intravenous and subcutaneous RA trials.
Objectives: To provide an updated report on the incidence of safety events during TCZ treatment in patients with RA using data from multiple completed clinical trials and their LTEs, as well as to provide an update from the global TCZ postmarketing safety database.
Methods: Incidence and reporting rates of adverse events (AEs) of special interest, including infections, malignancies, anaphylaxis, bleeding events, myocardial infarctions, gastrointestinal perforations, strokes, hepatic events and demyelination, were estimated from 2 distinct patient data sets. Incidence rates were calculated from 12 completed TCZ RA clinical trials and their LTE periods and are reported as events per 100 patient-years (PY). Reporting rates were also estimated from the global TCZ postmarketing safety database (Oct 2008 to Oct 2015), which includes information from all spontaneously reported cases and non-interventional programs as well as literature cases, and are reported as cases per 100 patients.
Results: The clinical trial all-exposure population consisted of 7647 TCZ-treated patients with RA (81.6% female; mean [SD] age, 52 [12.6] years), constituting 22,394 PY (mean follow-up, 2.93 years) of exposure. The overall rate (95% CI) of serious AEs in the clinical trial population was 14.16 (13.67–14.66) per 100 PY. Overall incidence rates for individual events for the clinical trial population are reported in the Table and were consistent in each 6-month period over the 5-year duration. The global postmarketing population included 606,937 patients. The overall spontaneous reporting rate (range) of AEs of special interest in the postmarketing population was 9.37 (7.35–10.56) cases per 100 patients. Reporting rates of individual safety events of interest in the global postmarketing population are shown in the Table and were consistent in each 6-month period over the 7-year duration.

Table. Adverse Events Across 12 RA Clinical Trials and the Global Postmarketing Safety Database in Patients Who Received TCZ

	RA Clinical Trial All-Exposure Population (N = 7647; 22,394 PY)		Global Postmarketing Safety Database Population* (N = 606,937)	
Adverse Event of Special Interest	Patients With ≥ 1 AE, n (%)	Incidence Rate (95% CI), Events/100 PY	Cases, n	Reporting Rate (range), Cases/100 Pts
Serious infections	730 (9.5)	4.29 (4.02-4.57)	17,350	2.86 (2.11-3.62)
Malignancies†	242 (3.2)	1.18 (1.05-1.33)	1560	0.26 (0.18-0.51)
Injection site reactions	444 (5.8)	6.51 (6.18-6.85)	NA	NA
Strokes/cerebrovascular disorders	130 (1.7)	0.67 (0.56-0.78)	2069	0.34 (0.22-0.94)
Serious bleeding events	89 (1.2)	0.43 (0.35-0.52)	2440‡	0.40‡ (0.28-0.76)
Myocardial infarction	72 (0.9)	0.33 (0.26-0.42)	1946	0.32 (0.21-0.88)
Gastrointestinal perforations†	39 (0.5)	0.20 (0.15-0.27)	632	0.10 (0.06-0.30)
Serious hypersensitivity reactions§	56 (0.7)	0.26 (0.20-0.33)	NA	NA
Anaphylaxis	21 (0.3)	0.09 (0.06-0.14)	1222	0.20 (0.09-0.38)
Serious hepatic events	9 (0.1)	0.04 (0.02-0.08)	3567‡	0. 59‡ (0.34-1.21)
Demyelination	8 (0.1)	0.04 (0.02-0.07)	66	0.01 (0.00-0.02)

AE, adverse event; NA, not available; pt, patient; PY, patient year; RA, rheumatoid arthritis; TCZ, tocilizumab.
* Data are for multiple indications and from several sources (spontaneous reports, non-interventional programs, literature cases) reported following market authorization.
† Events of malignancies and gastrointestinal perforations were medically confirmed.
‡ Includes both serious and non-serious cases.
§ Serious hypersensitivity was defined as a serious adverse event occurring during or within 24 hours of the injection or infusion, excluding injection site reactions, and not judged unrelated to study treatment by the investigator.

Conclusions: The safety profile of TCZ in the current analysis, which includes information about safety events from 12 clinical trials and their LTEs and across 7 years of real-world postmarketing reports encompassing ≈ 600,000 patients, was consistent with previous safety reports. These findings are consistent with the previously reported profile of TCZ and indicate that there is no evidence of increased safety risk with increasing exposure to TCZ.
Acknowledgements: This study was funded by F. Hoffmann-La Roche/Genentech, Inc.
Disclosure of Interest: S. Mohan Employee of: Genentech, Inc., M. Michalska Employee of: Genentech, Inc., J. Yourish Employee of: Genentech, Inc., J. Pei Employee of: Genentech, Inc., S. Gale Employee of: Genentech, Inc., C. Birchwood Employee of: Genentech, Inc., E. Berber Employee of: Genentech, Inc.
DOI: 10.1136/annrheumdis-2017-eular.3573

THURSDAY, 15 JUNE 2017

PsA: a fascinating disease

OP0106 THE IMPACT OF COMORBIDITIES ON EFFECT AND DISCONTINUATION OF TUMOUR NECROSIS FACTOR INHIBITOR THERAPY IN PSORIATIC ARTHRITIS: A POPULATION-BASED COHORT STUDY

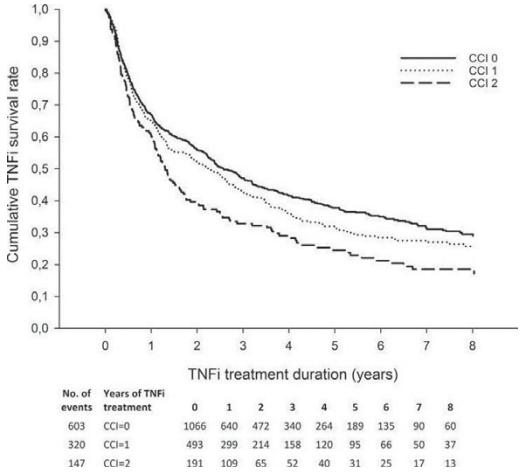
C. Ballegaard[1], P. Højgaard[1], L. Dreyer[2], R. Cordtz[2], T.S. Jørgensen[1], M. Skougaard[1], S. Tarp[1], L.E. Kristensen[1]. *[1]The Parker Institute, Copenhagen University Hospital, Bispebjerg and Frederiksberg; [2]Gentofte Hospital, Department of Rheumatology, Copenhagen University Hospital, Copenhagen, Denmark*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory disorder associated with several severe comorbidities such as cardiovascular diseases, diabetes, and depression. Tumour necrosis factor inhibitor (TNFi) therapy fails among half of patients with PsA treated in routine care.
Objectives: The objective of this population-based cohort study was to investigate if the presence of comorbidities were associated with disease activity, treatment response and adherence to therapy in patients with PsA treated with their first TNFi.
Methods: Data on patient characteristics, disease activity and treatment adherence was obtained from the DANBIO register. Information on comorbidities according to the Charlson Comorbidity Index (CCI) and psychiatric comorbidities was obtained through linkage with the Danish National Patient Register. We performed Kaplan-Meier plots and multivariate Cox proportional hazard regression analyses adjusted for sex, age, disease duration, DAS28-CRP, obesity, smoking, concurrent methotrexate treatment, calendar period, and diagnosis with depression and/or anxiety. Percentages of patients achieving relevant clinical responses were calculated.
Results: We identified 1750 patients eligible for analyses. Patients with higher CCI scores had statistically significantly higher disease activity measures at baseline compared with patients without comorbidities (Table 1). Kaplan–Meier curves showed shorter adherence to treatment for patients with CCI ≥2 compared with patients with lower CCI scores (CCI =0: 2.6 years [2.2 to 2.9], CCI =1: 2.2 years [1.7 to 2.8], CCI ≥2: 1.3 years [1.0 to 1.6], p<0.001) (Figure). Also, for patients with depression and/or anxiety the adherence to treatment was shorter compared with patients without depression and/or anxiety (absence of depression and/or anxiety: 2.4 years [2.1 to 2.6], presence of depression and/or anxiety: 1.7 years [0.26 to 3.0], p<0.027). In the multivariate Cox regression analysis a CCI score ≥2 was associated with increased risk of TNFi treatment discontinuation compared with patients without comorbidities (HR 1.72, [95% CI 1.26 to 2.37], p=0.001). A statistically significantly smaller proportion of patients with a CCI score ≥2 achieved EULAR good response (CCI =0: 41%; CCI ≥2: 23%) and EULAR good-or-moderate response (CCI =0: 54%; CCI ≥2: 47%) at 6 months compared with patients without comorbidities.

Table 1. Baseline characteristics according to Charlson Comorbidity Index (CCI)

	CCI =0 (n=1066)	CCI =1 (n=493)	CCI ≥2 (n=191)	p value
Tender joint count (28) (no.)	6 (2–11)	6 (3–12)	8 (3–15)	0.001
Swollen joint count (28) (no.)	2 (0–5)	3 (0–6)	2 (0–6)	0.016
DAS28-CRP (0 – 10)	4.4 (3.5–5.2)	4.6 (3.8–5.4)	4.9 (3.9–5.7)	<0.001
HAQ score (0 – 3)	0.88 (0.5–1.4)	1.1 (0.6–1.5)	1.4 (0.88–2.0)	<0.001
VAS patient global (0 – 100)	68 (48–84)	69 (52–84)	75 (58–88)	0.021
Depression and/or anxiety, n (%)	46 (4.3)	33 (6.7)	15 (7.9)	0.042

Values are the median/interquartile range except where stated otherwise. Comparisons were assessed by χ^2/Kruskal-Wallis test.



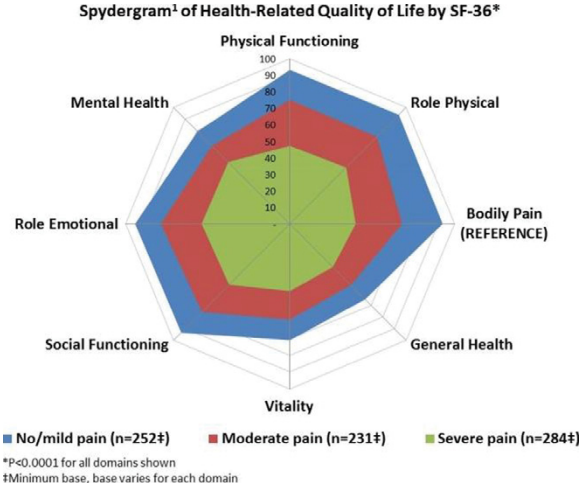
Conclusions: Presence of comorbidities was associated with higher baseline disease activity, increased risk of TNFi treatment discontinuation and reduced clinical response rates in a cohort of Danish patients with PsA.

Disclosure of Interest: C. Ballegaard Speakers bureau: Janssen Pharmaceuticals, P. Højgaard Speakers bureau: Celgene, UCB, L. Dreyer Speakers bureau: UCB, MSD, Janssen, R. Cordtz: None declared, T. Jørgensen Speakers bureau: Abbvie, Roche, UCB, Novartis, M. Skougaard: None declared, S. Tarp Grant/research support from: Abbvie, Roche, Consultant for: MSD, L. Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, MSD, Novartis, Eli Lilly, Janssen Pharmaceuticals
DOI: 10.1136/annrheumdis-2017-eular.1500

OP0107 PAIN STILL REMAINS A HIGH UNMET NEED AMONG PSORIATIC ARTHRITIS PATIENTS RECEIVING EXISTING BIOLOGIC TREATMENT: RESULTS FROM A MULTI NATIONAL REAL-WORLD SURVEY

P.G. Conaghan[1], V. Strand[2], R. Alten[3], E. Sullivan[4], S. Blackburn[4], L. Huneault[5], H. Tian[6], K. Gandhi[7], S. Jugl[8]. *[1]University of Leeds, Leeds, United Kingdom; [2]Division of Immunology/Rheumatology, Stanford University, Palo Alto, United States; [3]Internal Medicine, University Medicine Berlin, Berlin, Germany; [4]Adelphi Real World, Manchester, United Kingdom; [5]Global Patient Relations, I&D Global Communications & Advocacy, Novartis Pharma AG, Basel, Switzerland; [6]Real World Evidence; [7]Global Market Access, Novartis Pharmaceuticals Corporation, East Hanover, United States; [8]Global Patient Access Immunology & Dermatology, Novartis Pharma AG, Basel, Switzerland*

Background: Many patients diagnosed with Psoriatic Arthritis (PsA) experience pain which can persist during treatment and may impair health related quality of life (HRQOL) and the ability to work.
Objectives: To assess self-reported pain in patients with PsA receiving biologic therapy, and evaluate the association of increasing severity of pain with HRQOL and employment status.
Methods: Cross-sectional survey data from Rheumatologists and Dermatologists (specialists) treating PsA and their patients in 13 countries spanning the Americas, Asia Pacific, EU, Turkey and the Middle East were analyzed. A geographically diverse sample of specialists in each country completed a detailed form for consecutive consulting PsA patients recording information such as demographics, clinical state and treatment details. Patients voluntarily completed questionnaires providing demographics, self-reported intake of non-prescription pain medication, work status, HRQoL (EQ-5D, SF-36), impairment in physical function (HAQ-DI), and impairment in work productivity and activity (WPAI). Patient reported pain was stratified using tertiles of the SF-36 "Bodily Pain" (BP) subdomain.
Results: Results are presented from 782 patients with PsA receiving traditional biologic treatment (mainly anti-TNF) for ≥3 months who completed SF-36 questionnaires. SF-36 BP domain tertiles were: no/mild pain: BP: >75 to 100: 33.1%; moderate: BP: >52 to ≤75: 30.1%; and severe: BP: 0 to ≤52: 36.8%. A strong positive linear relationship between BP tertiles and EQ-5D pain was observed (correlation coefficient: 0.6678). More severe pain was associated with increased use of prescription NSAIDS (p=0.0026) and opioids (p=0.0065), as well as non-prescription pain medication (p<0.0001).
The level of HRQOL impairment among PsA patients increased as pain increased: SF-36 domains (excluding BP) were lower, all differences were clinically[1] and statistically significant (all p<0.0001); EQ-5D domains (excluding pain/discomfort) were also lower (p<0.0001). More severe pain was associated with greater disability (higher HAQ-DI scores), and greater activity impairment, overall work impairment, work time missed and impairment while working due to PsA (all p<0.0001). Among patients of working age (≤65), the likelihood of unemployment or retirement due to PsA was higher among patients reporting severe pain: Mild (n=21): 19.0%, Mod (n=30): 10.0%, Severe (n=36): 58.3%; p<0.0001.
Conclusions: This analysis of real world patient reported data suggests that pain is common among PsA patients receiving biologic therapy. Increasing severity of pain is associated with more impaired HRQOL, physical functioning, engagement



in activities and work productivity. These results suggest there is a need for treatments that provide fast and sustained improvement in pain to reduce the impact pain has on patients' daily life as well as societal costs.

References:
[1] Ware J, et al. User's Manual for the SF-36v2® Health Survey. Lincoln (RI): QualityMetric Incorporated; 2007:125–133.
[2] Strand et al. Ann Rheum Dis. 2009 Dec; 68(12): 1800–1804.

Disclosure of Interest: P. Conaghan Consultant for: Abbvie, Eli Lilly, Novartis, Pfizer, Speakers bureau: Abbvie, BMS, Roche, V. Strand Consultant for: AbbVie, Amgen, BMS, Celgene, Celltrion, CORRONA, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi, UCB, R. Alten Grant/research support from: Novartis Pharma AG, Speakers bureau: Novartis Pharma AG, E. Sullivan: None declared, S. Blackburn: None declared, L. Huneault Shareholder of: Novartis Pharma AG, Employee of: Novartis Pharma AG, H. Tian Shareholder of: Novartis Pharmaceuticals Corporation, Employee of: Novartis Pharmaceuticals Corporation, K. Gandhi Shareholder of: Novartis Pharmaceuticals Corporation, Employee of: Novartis Pharmaceuticals Corporation, S. Jugl Shareholder of: Novartis Pharma AG, Employee of: Novartis Pharma AG
DOI: 10.1136/annrheumdis-2017-eular.2881

OP0108 INHIBITION OF RADIOGRAPHIC PROGRESSION IN PSORIATIC ARTHRITIS BY ADALIMUMAB INDEPENDENT OF THE CONTROL OF CLINICAL DISEASE ACTIVITY

R. Landewé[1], C.T. Ritchlin[2], L.C. Coates[3], D. Aletaha[4], B. Guérette[5], Y. Zhang[5], F. Ganz[6], M. Hojnik[7]. *[1]University of Amsterdam, Amsterdam, Netherlands; [2]University of Rochester Medical Center, Rochester, United States; [3]University of Leeds and Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; [4]Medical University of Vienna, Vienna, Austria; [5]AbbVie Inc, N Chicago, United States; [6]AbbVie AG, Baar, Switzerland; [7]AbbVie, Ljubljana, Slovenia*

Background: Patients (pts) with psoriatic arthritis (PsA) may experience structural damage and irreversible functional impairment if not treated appropriately. Treatment with TNF inhibitors in rheumatoid arthritis (RA) pts showed inhibition of radiographic progression larger than expected based on the control of clinical disease activity.[1] Preliminary results showed that such a disconnect phenomenon may also be observed in PsA pts following treatment with adalimumab (ADA).[2]
Objectives: The objective of this analysis was to further examine the relationship between inhibition of radiographic progression and control of clinical disease activity using different disease activity measures following treatment with originator ADA versus placebo (PBO) in pts with active PsA.
Methods: ADEPT[3] was a 24-week (wk), randomized, double-blind trial comparing the safety and efficacy of ADA with PBO in pts with active PsA. In this post hoc analysis, radiographic progression, defined as change from baseline (BL) to wk 24 in modified total Sharp score (ΔmTSS) >0.5, was calculated in pts with evaluable radiographs at both time points. Pts were classified based on achieving minimal disease activity (MDA) and different subcategories of disease activity (remission, low, moderate, or high) based on time-averaged (TA) DAS28(CRP), DAPSA, and PASDAS. The associations between ΔmTSS and disease activity were assessed by Pearson (r_p) or Phi (r_φ) correlation coefficients.
Results: Of the 296 pts (ADA, N=144; PBO, N=152) included in this analysis, higher proportions of pts receiving ADA compared with PBO achieved MDA and remission/low disease activity status across all the outcome measures.

Table Change from Baseline to Week 24 in modified Total Sharp Score (ΔmTSS) categorized by Disease Activity Status Across Each Outcome Measure in ADA and PBO Treated Patients.

Outcome measure Mean (SD)	ΔmTSS		P-value*
	ADA	PBO	
TA-DAS28 (CRP)†	n = 144	n = 152	
Remission (≤2.6)	-0.3 (1.3)	0.1 (0.7)	.135
Low disease activity (>2.6–3.2)	-0.2 (1.3)	0.6 (1.7)	.054
Moderate disease activity (>3.2–5.1)	0.2 (1.3)	1.5 (3.6)	.085
High disease activity (>5.2)	1.7 (2.9)	4.9 (8.2)	.893
TA-DAPSA†	n = 144	n = 152	
Remission (≤4)	-0.1 (0.5)	0.0 (0.0)	.824
Low disease activity (>4–14)	-0.2 (1.0)	0.0 (0.0)	.741
Moderate disease activity (>14–28)	-0.2 (1.4)	0.4 (1.0)	**.044**
High disease activity (>28)	-0.1 (1.8)	1.4 (3.5)	**.002**
TA-PASDAS†	n = 136	n = 150	
Low disease activity (≤3.2)	-0.1 (0.9)	0.2 (0.4)	.373
Moderate disease activity (>3.2–<5.4)	-0.4 (1.5)	0.4 (1.3)	**.001**
High disease activity (≥5.4)	0.2 (1.9)	2.0 (4.3)	**.039**
MDA‡	n = 139	n = 146	
Yes	-0.2 (1.6)	0.0 (0.0)	.884
No	-0.2 (1.3)	1.1 (3.1)	**<.001**

*P-value for difference between treatment groups is based on ANCOVA.
†Time averaged (TA) variable is calculated as area under the curve (AUC) of that variable and standardized by length of study (24 weeks).
‡Minimal disease activity (MDA) was calculated in patients with at least 5 out of 7 MDA components available.
ADA = adalimumab, PBO = placebo; TA = time-averaged; DAS28(CRP) = 28-joint disease activity score based on C-reactive protein, DAPSA = disease activity index for psoriatic arthritis, PASDAS = psoriatic arthritis disease activity score; index, MDA = minimal disease activity; ANCOVA = analysis of covariance.

There was a significant interaction between treatment and disease activity status with respect to radiographic progression (P<.001 for all outcome measures). In addition, treatment with ADA for 24 wks compared with PBO resulted in significantly lower mean ΔmTSS even in pts with moderate or high disease activity (TA-DAPSA or TA-PASDAS) or not achieving MDA (Table). Radiographic progression showed a weak, but significant correlation with disease activity status in pts treated with PBO ($r_p \geq 0.3$, P<.001 for TA-DAS[CRP], TA-DAPSA, and TA-PASDAS; $r_\varphi = -0.14$ [95% CI:–0.20 to –0.09 for MDA), but not ADA.
Conclusions: The results showed that the relationship between disease activity as determined by various outcome measures differed between ADA and PBO treated pts. ADA provided inhibition of radiographic progression which was somewhat larger and independent of the control of clinical disease activity. This supports the disconnect phenomenon in PsA following ADA treatment.

References:
[1] Landewé R, et al. Arthritis Rheum. 2006; 54:3119–25.
[2] Mease PJ, et al. Arthritis Rheum. 2010; 62 (suppl 10).
[3] Mease PJ, et al. Arthritis Rheum. 2005; 52:3279–89.

Acknowledgements: AbbVie funded the study (NCT00646386), contributed to its design, and participated in data collection, analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.
Disclosure of Interest: R. Landewé Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB and Wyeth, Consultant for: Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, BMS, Janssen (formerly Centocor), GSK, Merck, Novo-Nordisk, Novartis, Pfizer, Roche, Schering-Plough, TiGenics, UCB, and Wyeth; is Director of Rheumatology Consultancy BV, Speakers bureau: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB and Wyeth, C. Ritchlin Grant/research support from: Amgen, Janssen, Pfizer, and UCB, Consultant for: AbbVie, Amgen, Janssen, Lilly, Pfizer, and UCB, L. Coates Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, and UCB, Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, and UCB, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, and UCB, D. Aletaha Grant/research support from: AbbVie, BMS, Janssen, Lilly, Merck, Medac, Mitsubishi/Tanabe, Pfizer, Roche, and UCB, Consultant for: AbbVie, BMS, Janssen, Lilly, Merck, Medac, Mitsubishi/Tanabe, Pfizer, Roche, and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Medac, Mitsubishi/Tanabe, Pfizer, Roche, and UCB, B. Guérette Shareholder of: AbbVie, Employee of: AbbVie, Y. Zhang Shareholder of: AbbVie, Employee of: AbbVie, F. Ganz Shareholder of: AbbVie, Employee of: AbbVie, M. Hojnik Shareholder of: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.1337

OP0109 IS MENTAL HEALTH COMPARABALE IN RHEUMATOID AND PSORIATIC ARTHRITIS PATIENTS? A COMPARATIVE ANALYSIS OF REAL LIFE LONGITUDINAL DATA FROM THE NOR-DMARD STUDY

B. Michelsen[1,2], E. Lie[1], K.M. Fagerli[1], E.K. Kristianslund[1], H.B. Hammer[1], G. Haugeberg[2,3,4], T.K. Kvien[1]. *[1]Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo; [2]Dept. of Rheumatology, Hospital of Southern Norway Trust, Kristiansand; [3]Dept. of Rheumatology, Martina Hansens Hospital, Bærum; [4]Norwegian University of Science and Technology, Trondheim, Norway*

Background: Only few studies have compared health related quality of life (HRQoL) between rheumatoid arthritis (RA) and psoriatic arthritis (PsA) patients.
Objectives: To compare the Medical Outcomes Survey Short Form-36 (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS) in RA and PsA patients from a large prospective observational registry.
Methods: We included RA and PsA patients from the prospective observational multicenter Norwegian-Disease-Modifying Antirheumatic Drug (NOR-DMARD) study, who started first-time tumour necrosis factor inhibitors or DMARD naïve patients starting methotrexate between year 2000 and 2012. Continuous variables were compared using independent t-test (normally distributed data). Prespecified ANCOVA analyses adjusted for age, gender and years since diagnosis were performed to compare SF-36 PCS and MCS between the RA and PsA patients at baseline and after 3 and 6 months follow-up.
Results: A total of 2735 RA and 1236 PsA patients were included. Mean (SD) age was 55.0 (13.5)/ 48.3 (12.4) years, median (25th-75th percentile) years since diagnosis 0.7 (0.02–6.4)/ 1.3 (0.09–7.7), 69.7/48.4% were women and 31.7/29.8% current smokers. Mean (SD) 28-joint Disease Activity Score was higher in RA vs. PsA patients at baseline (4.9 (1.4)/ 4.2 (1.3)) and at 3 (3.6 (1.5)/ (3.1 (1.4)) and 6 months follow-up (3.3 (1.4)/ 3.0 (1.3)), respectively ($p \leq 0.001$). Unadjusted means (SD) of SF-36 PCS and MCS were similar between the RA and PsA patients (Table 1).
In adjusted analyses SF-36 PCS was slightly higher and SF-36 MCS similar between RA and PsA patients at 3 and 6 months follow-up (Table 2).
Conclusions: Mental HRQoL reflected through SF-36 MCS was similar between RA and PsA patients at all time points, in spite of slightly worse physical HRQoL reflected through lower SF-36 PCS in the PsA group at 3 and 6 months follow-up.
Disclosure of Interest: B. Michelsen: None declared, E. Lie Consultant for: Hospira, Pfizer, UCB, Speakers bureau: AbbVie, Celgene, K. Fagerli: None declared, E. Kristianslund: None declared, H. Hammer Consultant for: AbbVie,

Table 1. Unadjusted means (SD) of SF-36 PCS and MCS

	Months	RA (mean (SD))	PsA (mean (SD))	p-value
SF-36 PCS	0	31.3 (10.0)	31.6 (9.7)	0.31
	3	36.7 (11.1)	37.3 (11.1)	0.16
	6	37.9 (11.3)	38.1 (10.9)	0.64
SF-36 MCS	0	45.6 (11.6)	46.3 (11.7)	0.08
	3	48.1 (10.9)	48.3 (10.9)	0.60
	6	48.8 (10.8)	49.1 (10.7)	0.49

Table 2. ANCOVA analyses with adjustment for age, gender and years since diagnosis

	Months	Estimated marginal means (95% CI)		P value
		RA	PsA	
SF-36 PCS	0	32.3 (31.9–32.7)	31.6 (31.0–32.2)	0.06
	3	37.9 (37.4–38.4)	36.8 (36.1–37.6)	0.02
	6	39.3 (38.8–39.9)	37.6 (36.9–38.4)	0.001
SF-36 MCS	0	46.3 (45.8–46.8)	46.2 (45.5–46.9)	0.90
	3	48.3 (47.8–48.9)	48.3 (47.6–49.0)	0.92
	6	49.5 (49.0–50.0)	48.9 (48.1–49.7)	0.21

Pfizer, UCB, Roche, MSD, BMS and Novartis., Speakers bureau: AbbVie, Pfizer, UCB, Roche, MSD, BMS and Novartis., G. Haugeberg: None declared, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB

DOI: 10.1136/annrheumdis-2017-eular.3154

OP0110 ASSOCIATION OF PHARMACOLOGICAL BIOMARKERS WITH TREATMENT RESPONSE AND LONG-TERM DISABILITY IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM OUTPASS

M. Jani [1,2], H. Chinoy [1,2], A. Barton [1,2] on behalf of Outcomes of Psoriatic Arthritis Study Syndicate (OUTPASS). *[1]NIHR Manchester Musculoskeletal Biomedical Research Unit, Manchester Academic Health Science Centre, Central Manchester Foundation Trust and University of Manchester; [2]Centre for Musculoskeletal Research, University of Manchester, Manchester, United Kingdom*

Background: Up to 40% of patients with inflammatory arthritis on TNF-α inhibitor (TNFi) treatment fail to respond either due to primary inefficacy or loss of response. One explanation is immunogenicity leading to the development of anti-drug antibodies (ADAb) and subsequent low drug levels. Few data exist on whether such pharmacological tests correlate with treatment response in psoriatic arthritis (PsA). The clinical utility of whether such tests should be incorporated into practice is in question.
Objectives: To identify (i) whether the presence of ADAbs/drug levels predict treatment response and disability in TNFi-treated PsA patients (ii) the factors associated with drug levels (iii) a drug level threshold for optimal therapeutic response.
Methods: 75 patients were available from the Outcomes of Treatment in PsA Study Syndicate (OUTPASS) [n=49 adalimumab; n=26 etanercept], a national UK prospective observational cohort. Serum samples were collected at 3, 6 and 12 months following initiation of TNFi therapy. ADAbs were measured using radioimmunoassay (RIA) and random (non-trough) drug levels using ELISA assays at 3, 6 and 12 months. Disease activity (DAS28) scores were measured at each visit. Patient self-reported adherence to TNFi was measured at each time-point. Generalised estimating equation (GEE) was used to test the association between ADAbs and drug levels, both biomarkers and treatment response [as assessed by change in DAS28 score between pre-treatment and 12 months post-treatment (ΔDAS28)], Health assessment Questionnaire (HAQ) and the association between longitudinal/baseline factors with drug levels.
Results: 264 serial samples were suitable for pharmacological testing (n=174 adalimumab; n=90 etanercept). Mean age was 51±12 years; 61% were female; median BMI 28.9 (IQR 26.0–34.9). 20% (n=10/49) of adalimumab-treated patients were positive for ADAbs, but none were detected in etanercept-treated patients. There was no significant association between etanercept drug levels and ΔDAS over 12 months [β= -0.039 (95% CI -0.31, 0.23), p=0.77]. Using GEE, adalimumab drug levels were significantly associated with ΔDAS28 over 12 months [β=0.055 (95% CI: 0.011, 0.099) p=0.014] and inversely with HAQ scores over 12 months [β= -0.022 (95% CI: -0.043, -0.00063]. ΔDAS28 was not independently associated with ADAb level [β=-0.0015 (95% CI: -0.0031, 0.000047), p=0.057]. Adalimumab concentrations between 4.5–8.5 mg/L were associated with an optimal treatment response at 6 months using concentration-effect curves. Factors that were significantly associated with adalimumab drug levels were ADAb level [β=-0.0073 (95% CI: -0.0014, 0.18), p<0.0001] and BMI [β=-0.15 (-0.29, -0.00450, p=0.043] in the final GEE model (adjusting for age, gender, adherence, BMI).
Conclusions: TNFi drug-level testing in adalimumab-initiated PsA patients may be useful in determining treatment response and disability over 12 months; interestingly, both the presence of ADAbs and BMI were inversely associated with drug levels. Identification of a drug level threshold for optimal response may help tailor adalimumab therapy for PsA patients in the future.
Acknowledgements: This work was funded from a grant awarded by the National Institute of Health and Research, Manchester Musculoskeletal BRU to MJ, AB.
Disclosure of Interest: M. Jani Grant/research support from: Abbvie, UCB, Pfizer, H. Chinoy Grant/research support from: Novartis, Abbvie, Consultant for: Eli-Lilly and Novartis, Speakers bureau: UCB, A. Barton Grant/research support from: Eli-Lilly, Speakers bureau: Roche Chugai and Pfizer
DOI: 10.1136/annrheumdis-2017-eular.2030

OP0111 THE ASSOCIATION BETWEEN SONOGRAPHIC ENTHESITIS AND RADIOGRAPHIC JOINT DAMAGE IN PSORIATIC ARTHRITIS

A. Polachek [1], R. Cook [2], V. Chandran [1,3], D. Gladman [1,3], L. Eder [3,4]. *[1]Centre for Prognosis Studies in the Rheumatic Diseases, University Health Network, Toronto; [2]Department of Statistics and Actuarial Science, University of Waterloo, Waterloo; [3]Department of Medicine, University of Toronto; [4]Women's College Research Institute, Women's College Hospital, Toronto, Canada*

Background: Enthesitis is a common clinical finding and a key pathogenic feature in psoriatic arthritis (PsA). Ultrasound is emerging as a preferred method to assess enthesitis. Little is known about the relation between the presence of enthesitis and the severity of joint damage in patients with PsA.
Objectives: Our objective was to examine the association between sonographic enthesitis and the severity of radiographic features of damage in the peripheral and axial joints in PsA.
Methods: A cross-sectional study was conducted in consecutive patients with PsA. The MAdrid Sonography Enthesitis Index (MASEI) scoring system was used to quantify the extent of sonographic entheseal abnormalities in 12 entheseal sites. Total MASEI was further categorized into: bone scores (enthesophytes, erosions) and soft tissue scores (structural changes, vascularization, bursitis). Radiographic joint damage in the peripheral joints and spine was assessed independently of the ultrasound results using the modified Steinbrocker score, Modified New York Criteria for sacroiliitis and the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Additionally, the presence of ankylosis, arthritis mutilans and periostitis in the hands or feet was determined. Linear and logistic regression models were used to assess the association between MASEI score and the radiographic features of joint damage after controlling for age, sex, BMI, PsA duration and the use of DMARDs and biologic medications.
Results: 222 patients were included (58% men) with mean (s.d.) age of 55.9 (12.9) years and PsA duration of 16.7 (12.4) years. The mean MASEI score was 15.6 (12.6). The mean modified Steinbrocker score was 18.1 (32.3), *mSASSS* was 1.7 (7.3) and 37% had sacroiliitis. Multivariate regression analyses found an association between higher scores of MASEI scores and peripheral joint damage: modified Steinbrocker score (β 9.26, p<0.0001), joint ankylosis (Odds Ration (OR) 2.09, p=0.0001) and arthritis mutilans (OR 1.73, p=0.005). The association between MASEI scores and periostitis was of borderline statistical significance (OR 1.29, p=0.06). Similarly, an association was found in multivariate analyses between higher MASEI scores and axial damage as measured by mSASSS (β 1.55, p$\leq$0.0001) and sacroiliitis (OR 1.36, p=0.02). Sub-analysis showed that the MASEI bone score were more strongly associated with radiographic damage outcomes than the MASEI soft tissue score.
Conclusions: The severity of sonographic enthesitis is a marker of radiographic peripheral and axial joint damage in PsA. The association was found with both erosive and bone formation lesions. These findings highlight the potential role of enthesitis in the pathogenesis of articular damage in PsA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5007

OP0112 IN PSORIATIC ARTHRITIS FATIGUE IS DRIVEN BY INFLAMMATION, DISEASE DURATION, AND CHRONIC PAIN: AN OBSERVATIONAL DANBIO REGISTRY STUDY

M. Skougaard [1], T.S. Jørgensen [1], S. Rifbjerg-Madsen [1], L. Coates [2], A. Egeberg [3], K. Amris [1], L. Dreyer [1], P. Højgaard [1], J. Guldberg-Møller [1], J.F. Merola [4], P. Frederiksen [1], H. Gudbergsen [1], L.E. Kristensen [1]. *[1]The Parker Institute, Copenhagen University Bispebjerg and Frederiksberg, Copenhagen F, Denmark; [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom; [3]Department of Dermatology and Allergy, Copenhagen University Hospital Gentofte and Herlev, Hellerup, Denmark; [4]Department of Dermatology and Department of Medicine, Devisions of Rheumatology, Brigham and Woman's Hospital, Boston, Massachusetts, United States*

Background: Fatigue has been identified as one of the most significant symptoms and an outcome of great importance to patients with psoriatic arthritis (PsA), but the association between underlying components of experienced fatigue and the disease has been sparsely investigated. [1]
Objectives: To describe the degree of fatigue in a PsA population. Secondly, to explore which components of inflammation and non-inflammatory factors contribute to experienced fatigue.
Methods: The study was designed as a cross-sectional survey including patients

registered in DANBIO, the Danish nationwide rheumatologic registry, from December 2013 to June 2014. Principal component analysis was used to identify clustering factors associated with fatigue

Results: A total of 1,062 PsA patients were included in the study. The median Visual Analog Scale (VAS) fatigue score was 57mm. Patients with moderate to severe fatigue (VAS score ≥57) had higher scores of pain, DAS28, HAQ, patient global assessment, and more tender and swollen joints ($p<0.001$) (Table 1). In the principal component analysis the clinical co-variables were reduced to 3 components explaining 63% of experienced fatigue (figure 1); The first component, contributing to 31%, was mainly constituted by inflammatory factors as swollen and tender joints, doctors-global evaluation, higher CRP, and pain score, whereas the second component mainly consisted of contributions from age and disease duration, explaining 17% of experienced fatigue. The third component, contributing to 15%, consisted of patient pain, tender joint count, increasing age, and by concomitant low CRP. The remaining 37% was considered residuals.

Table 1

Characteristics	Fatigue Non to mild VAS score <57 n=520		Fatigue Moderate to severe VAS score >57 n=542		p-value
		n		n	
Female, n (%)	253 (48.7%)	520	358 (66.1%)	542	<0.001
Age, yrs	53.0 (44.0–62.0)	520	52.0 (42.8–60.0)	542	0.070
Disease duration, yrs	6.0 (3.0–11.5)	449	5.0 (2.0–10.0)	456	0.022
C-reactive protein, mg/L	3.0 (1.0–6.0)	421	4.0 (2.0–7.0)	464	0.008
Patient global assessment, 0–100 mmVAS	27.0 (15.0–43.0)	520	75.5 (61.0–86.0)	542	<0.001
Doctors global assessment, 5-grade Likert scale	7.0 (3.0–15.0)	432	14.0 (7.0–14.0)	438	<0.001
PDQ pain score	9.0 (6.0–14.0)	520	17.0 (13.0–23.0)	542	<0.001
DAS28-CRP	2.3 (1.8–2.9)	400	3.5 (2.6–4.4)	418	<0.001
HAQ, 0–3	0.4 (0.1–0.8)	507	1.1 (0.8–1.6)	530	<0.001

All values are median (Q1-Q3) unless otherwise indicated. VAS; visual analogue scale, PDQ; pain assessment questionnaire, DAS28-CRP; disease activity score-C-reactive protein, HAQ; health assessment questionnaire.

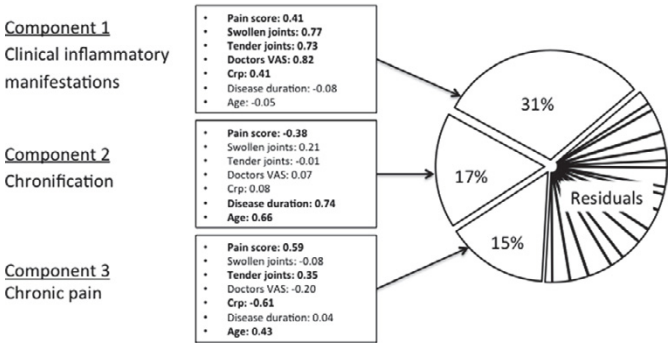


Figure 1

Conclusions: Clinical inflammatory disease activity, chronification, as well as pain in the absence of inflammation were all identified as important factors explaining 63% of moderate to severe fatigue in the current PsA population.

References:

[1] Orbai AM, Mease PJ, de WM et al. Report of the GRAPPA-OMERACT Psoriatic Arthritis Working Group from the GRAPPA 2015 Annual Meeting. J Rheumatol 43; 965–9.

Acknowledgements: This study was supported by the Oak Foundation. Data was extracted from the DANBIO Registry.

Disclosure of Interest: M. Skougaard: None declared, T. Jørgensen Speakers bureau: Abbvie, Roche, UCB, Novartis, Biogen, S. Rifbjerg-Madsen: None declared, L. Coates Grant/research support from: Abbvie, BMS, Celgene, Jannsen Pharmaceuticals, Lilly, MSD, Novartis, Pfizer, Sun Pharma, UCB, A. Egeberg Grant/research support from: Pfizer, Eli Lilly, Speakers bureau: Pfizer, Eli Lilly, Novartis, Galderma, Janssen Pharmaceuticals, K. Amris: None declared, L. Dreyer: None declared, P. Højgaard Speakers bureau: Celgene, UCB, J. Guldberg-Møller Paid instructor for: Abbvie, J. Merola Grant/research support from: Biogen IDEC, Amgen, Pfizer, Boehringer Ingelheim, Consultant for: Biogen IDEC, Eli Lilly, Novartis, Momenta, UCB, Kiniksa, AbbVie, Amgen, Pfizer, Janssen Pharmaceuticals, Momenta, Mallinckrodt, Speakers bureau: AbbVie, Eli Lilly, P. Frederiksen: None declared, H. Gudbergsen Speakers bureau: MSD, Pfizer, L. E. Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, MSD, Novartis, Eli Lilly, Janssen Pharmaceuticals.

DOI: 10.1136/annrheumdis-2017-eular.3487

OP0113 METABOLIC SYNDROME AND LIVER STIFFNESS IN PSORIATIC ARTHRITIS AND PSORIASIS PATIENTS: A CASE-CONTROL STUDY

A. Ortolan[1], M. Lorenzin[1], G. Tadiotto[1], F. Oliviero[1], A. Hoxha[1], S. Piaserico[2], L. Punzi[1], R. Ramonda[1]. *[1]Rheumatology Unit, Department of Medicine DIMED; [2]Dermatological Clinic, University of Padova, Padova, Italy*

Background: Psoriatic arthritis (PsA) and psoriasis (PsO) are commonly associated to various comorbidities, among which metabolic syndrome (MetS) has been demonstrated to be more prevalent in these groups with respect to the general population. However, few data are available regarding the comparison between PsA/PsO. Besides, a possible consequence of MetS is the development of a non-alcoholic fatty liver disease (NAFLD), which can progress to fibrosis, the latter rarely assessed in PsA/PsO.

Objectives: The aim of this case-control study was: 1) to compare prevalence of MetS in PsA and PsO 2) to evaluate the presence of liver fibrosis in these two groups using hepatic elastography.

Methods: Forty-three consecutive PsA patients classified according to CIASsification criteria for Psoriatic ARtritis (CASPAR), and 33 consecutive PsO patients without history/manifestations of arthritis, attending the Rheumatology and Dermatology Units of University of Padua, were studied. Exclusion criteria were: conditions which may cause liver fibrosis other than NALFD (eg viral hepatitis, autoimmune or genetic liver disease), alcohol consumption >20 grams/day, active smoking, daily use of non-steroidal anti-inflammatory drugs. Anamnestic, laboratory (cholesterol, triglycerides, uric acid, fasting glucose, insulin, albumin, transaminase) and metrological (blood pressure, waist circumference, height, weight) data were collected. MetS was defined according to the criteria of National Cholesterol Education Program's Adult Treatment Panel III report. Insuline resistance was quantified through HOMA (Homeostatic Model Assessement). All patients underwent hepatic elastography to evaluate liver stiffness; values >7 kPa were taken as indicator of liver fibrosis. PsO severity was assessed through Psoriasis area severity index (PASI). Differences in variables between PsA/PsO were compared through non parametric Mann-Whitney test, and Chi-square test for categorical variables. Correlations between variables were evaluated through Spearman test.

Results: PsA and PsO patients showed similar characteristics (mean age 60,2±8,4 vs 54,5±19,6 years, 74,4% vs 63% males, artritis/PsO duration 12,6±8,5 vs 18,2±14,2 years). The only variables which differ in PsA/PsO groups were Body Mass Index (BMI) (25,7±3,4vs 29,1±6,3), PASI (5±4,6 e 1,5±2,5) and serum uric acid (4,9±1,5 vs 5,7±1,4 mg/dL), all higher in PsO (p-values 0,0092, 0,0355 and 0,0001 respectively). Prevalence of MetS and liver fibrosis in the 2 groups were was similar: 34,9% and 30,8% in PsA vs 33,3% and 27,6% in PsO (p=ns). Among all correlation studied, only serum uric acid, liver stiffness and PASI correlated with other variables (Table). Most interestingly, liver stiffness very well correlated with serum uric acid in PsO ($p<0,0001$ r=0,73).

Table. Correlations found between serum uric acid, liver stiffness and PASI with other variables studied

Uric acid			Liver Stiffness			PASI	
Variables	**PsA**	**PsO**	**Variables**	**PsA**	**PsO**	**Variables**	**PsA**
BMI	n.s	p=0,019 r=0,41	**BMI**	n.s	p=0,020 ρ=0,43	**Waist circumference**	p=0,019 r=0,36
Waist circumference	n.s	p<0,0001 r=0,59	**Waist circumference**	n.s	p<0,0001 ρ=0,69	**HDL cholesterol**	p=0,012 r=-0,38
PASI	p=0,001 r= 0,47	n.s	**Fasting glucose**	p=0,037 ρ=0,33	n.s	**HOMA**	p=0,044 r=0,31
HDL cholesterol	p=0,004 r=-0,42	p=0,015 r=-0,42	**Glycated hemoglobin**	p=0,027 ρ=0,35	p=0,022 ρ=0,42	**Serum uric acid**	p=0,001 r=0,47
Triglycerides	n.s	p=0,005 r=0,48	**Insulin**	p=0,014 ρ=0,38	p<0,0001 ρ=0,64		
Fasting glucose	n.s	p<0,0001 r=0,66	**HOMA**	p=0,018 ρ=0,37	p<0,0001 ρ=0,71		
Serum insulin	n.s	p<0,0001 r=0,74	**Serum uric acid**	n.s	p<0,0001 ρ=0,73		
Glycated hemoglobin	n.s	p<0,0001 r=0,63	**Triglycerides**	n.s	p=0,016 ρ=0,44		
HOMA	p=0,025 r=0,34	p<0,0001 r=0,80					
Liver stiffness	n.s	p<0,0001 r=0,73					

BMI=Body mass Index; HDL=High Density Lipoprotein; PASI= Psoriasis area severity index; HOMA= homeostatic model assessment

Conclusions: We observed a similar prevalence of MetS and hepatic stiffness in PsA and PsO. The correlation found between uric acid level and hepatic stiffness could lie on the fact that uric acid seems to favour insulin resistance, hypertension, dyslipidemia and other MetS risk factors. MetS could be therefore one of the major determinants to liver fibrosis in PsA and PsO, thus highlighting how comorbidities are not only coexhisting conditions, but are strongly linked to each other and need to be treated as well as the skin and joint aspect.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5520

THURSDAY, 15 JUNE 2017

More or less imaging in axial SpA?

OP0114 LOW DOSE COMPUTED TOMOGRAPHY DETECTS MORE PROGRESSION OF BONE FORMATION IN COMPARISON TO CONVENTIONAL RADIOGRAPHY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULTS FROM THE SIAS COHORT

A. de Koning[1], F. de Bruin[1], R. van den Berg[2], S. Ramiro[1], X. Baraliakos[3], J. Braun[3], F.A. van Gaalen[1], M. Reijnierse[1], D. van der Heijde[1]. *[1]LUMC, Leiden; [2]Erasmus MC, Rotterdam, Netherlands; [3]Rheumazentrum, Herne, Germany*

Background: Recently we presented the good interreader reliability and sensitivity to detect changes with a newly developed scoring method of bone formation on low dose computed tomography (LD-CT) of the whole spine in patients (pts) with Ankylosing Spondylitis (AS)[1]. Next step in the validation is the comparison with conventional radiographs (CR).
Objectives: To compare the assessment of syndesmophyte formation and growth on CR and LD-CT in pts with AS.
Methods: Pts from the SIAS (Sensitive Imaging of Axial Spondyloarthritis) cohort from Leiden and Herne were analysed. Inclusion criteria were modified NY criteria, ≥1 syndesmophytes on either the cervical and/or lumbar spine on CR, and ≥1 inflammatory lesion on MRI-spine. Pts had CR of the lateral cervical and lumbar spine and LD-CT (approximately 2–3mSV) of the entire spine at baseline and two years. Two readers independently assessed both CR and CT in separate sessions. Images were paired per patient, blinded to time order, patient information, and result of the other imaging technique. CR was assessed using the mSASSS scoring method. On CT, syndesmophytes were scored in the coronal and sagittal planes for all "corners" per view, thus scoring 8 "corners" per vertebral unit. Syndesmophytes were scored as absent (score 0), <50% of the intervertebral disc height (IVDH) (score 1), ≥50% of the IVDH but no bridging (score 2) or as bridging the IVDH (score 3)[1]. The formation of new syndesmophytes (CR score 0 or 1→2 or 3, CT 0→1 or 2 or 3) and growth of existing syndesmophytes (CR score 2→3, CT 1→2 or 3, or 2→3) and the combination of both was calculated per vertebral corner. Consensus about each of these outcomes was defined by agreement of both readers on the same vertebral level. Data of CR and CT was compared per reader and for the consensus score.
Results: 50 patients (mean age 48.6 years; 84% male; 80% HLA-B27) were included in the analysis. The number (%) of pts with newly formed, growth or combined newly formed and growth of syndesmophytes for separate readers and consensus score are presented in table 1. In all comparisons, CT detected more patients with progression. This is especially apparent in case of growth and for cut-offs of a higher number of (newly formed or growth of) syndesmophytes per patient. E.g. with the strictest comparison of the consensus score for both CR and CT, 30% of the patients show bony proliferation (newly formed and growth) at ≥3 sites on CT compared with only 6% on CR.

Table 1. Comparison of CR and CT per reader and consensus* for the formation and/or growth of syndesmophytes in 50 patients with ankylosing spondylitis.

New syndesmophytes	Reader 1		Reader 2		Consensus	
	CR	CT	CR	CT	CR	CT
≥1	27 (54)	43 (86)	30 (60)	44 (88)	19 (38)	21 (42)
≥2	14 (28)	38 (76)	14 (28)	41 (82)	7 (14)	15 (30)
≥3	6 (12)	32 (64)	8 (16)	30 (60)	2 (4)	10 (20)
Growth of syndesmophytes						
≥1	10 (20)	35 (70)	7 (14)	32 (64)	3 (6)	16 (32)
≥2	8 (16)	36 (52)	6 (12)	27 (54)	3 (6)	11 (22)
≥3	2 (4)	23 (46)	4 (8)	18 (36)	1 (2)	6 (12)
New syndesmophytes or growth of syndesmophytes						
≥1	28 (56)	45 (90)	33 (66)	48 (96)	21 (42)	25 (50)
≥2	18 (36)	42 (82)	19 (38)	44 (88)	9 (18)	20 (40)
≥3	12 (24)	36 (72)	12 (24)	38 (76)	3 (6)	15 (30)

Results are presented as the number (%) of patients with ≥1, ≥2 and ≥3 newly formed syndesmophytes and syndesmophytes that grew, as well as for the combination of new formation and growth.
*Both readers agree about the formation or growth of a syndesmophyte at the same vertebral corner.
CR: conventional radiography, CT: computed tomography

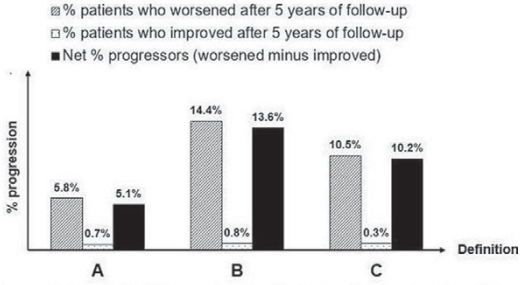
Conclusions: LD-CT covering the whole spine, is a more sensitive method for assessing the formation and growth of syndesmophytes than CR which is limited to cervical and lumbar spine in pts with AS and is a promising method of assessment for clinical research.
References:
[1] de Bruin F et al. A&R 2016; 68 (suppl 10).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5908

OP0115 EVALUATION OF THE CHANGES IN STRUCTURAL DAMAGE IN AXIAL SPONDYLOARTHRITIS ON PLAIN PELVIC RADIOGRAPHS: THE 5 YEARS DATA OF THE DESIR COHORT

M. Dougados[1], A. Sepriano[2], A. Molto[3], S. Ramiro[4], M. De Hooge[4], R. Van Den Berg[4], V. Navarro Compan[4], C. De Mattei[5], R. LandewÉ[4], D. Van Der Heijde[4]. *[1]Department of Rheumatology, Paris, France; [2]Rheumatology, Lisbon, Portugal; [3]Hopital Cochin, Paris, France; [4]Department of Rheumatology, Leiden, Netherlands; [5]Department of Biostatistics, Nimes, France*

Background: The structural damage of axial spondyloarthritis can be evaluated either at the spine or at the Sacroiliac Joint (SIJ) level and by using either plain X-Rays or MRI. So far, the evaluation of the changes in structural damage at the SIJ level has referred mainly to plain X-Rays and to a binary variable (e.g. fulfillment of the modified New York (mNY) criteria yes/no).
Objectives: To evaluate the reliability and the sensitivity to change of different outcome measures of SIJ structural damage observed at pelvic X-Rays.
Methods: *Study design:* Prospective longitudinal (5 years) follow-up of patients with recent onset (≤3 years) axial SpA (according to the treating rheumatologist) enrolled in the DESIR cohort. *Data collected:* Pelvic X-Rays at baseline and after 2 and 5 years of follow-up. *Reading procedure:* The films were evaluated by 3 trained readers unaware of their chronology according to the 0–4 mNY grading scale (from 0 = normal to 4 = fusion) for each SIJ (left and right). *Outcome measures:* One continuous variable: change in the total score (from 0 to 8) and 3 dichotomous variables: A/ Switch from non-radiographic (nr) to radiographic (r) axial SpA according to the mNY definition (e.g. at least unilateral grade III or bilateral grade II), B/ Change of at least one grade in at least one SIJ C/ Change of at least one grade in at least one SIJ and an absolute final value of the worsened joint of at least 2. *Statistical analysis:* a) inter-reader reliability of the changes in the outcome measures (intra-class correlation coefficient for the continuous outcome and Kappa statistics for the dichotomous outcomes) b) sensitivity to change by evaluating the % of net progressors (e.g. worsened minus improved) on both the completer population and the patients with at least one post baseline radiological evaluation using different missing data handling technics (Last Observation Carried Forward, Linear Extrapolation).
Results: The number of patients with available readings from all 3 readers were: 416 (baseline and 5 years), 378 (all time points) and 557 (baseline and at least one post baseline). The results were similar whatever the technic of data missing handling.
In the completer population, (a) The inter-reader reliability was low to modest: 0.21 (0.15–0.28) for the continuous variable and 0.23 (0.10–0.41), 0.24 (0.16–0.34) and 0.23 (0.13–0.35) for the dichotomous variables A, B and C, respectively.
(b) The changes in the total continuous score (from 1.41±1.68 to 1.60±1.83) was modest but highly significant (e.g. 0. 19±0.55 $p<0.0001$). The percentage of net progressors are summarized in the figure. These were 5.1%, 13.6% and 10.2% for the dichotomus variables A, B and C respectively.

Fig: changes in different binary SIJ-Plain X-Rays outcome measures



A = Switch from nr to r-axSpA according to the mNY criteria (worsened) *minus* switch from r to nr-axSpA
B = Change in at least one grade in at least one SIJ
C = Change in at least one grade in at least one SIJ and a final (at year 5) absolute value of at least 2 in the worsened joint (worsened) *minus* change in at least one grade in at least 1 SIJ and a baseline (year 0) absolute value of at least 2 in the improved joint

Conclusions: These data suggest that the structural progression at the SIJ level in recent onset SpA does exist but is modest. Different definitions of changes (e.g. at least one grade in at least one SIJ) seem to be more sensitive than the conventional definition (e.g. switch from nr to r) while reliability was similar. Therefore, these definitions might be useful to evaluate the natural history of the disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1625

OP0116 SWITCH FROM NON-RADIOGRAPHIC TO RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IS HIGHLY DEPENDENT OF BASELINE OBJECTIVE SIGNS OF INFLAMMATION: 5 YEAR DATA OF THE DESIR COHORT

M. Dougados[1], A. Sepriano[2], A. Molto[3], S. Ramiro[4], M. De Hooge[5], R. Van Den Berg[5], V. Navarro Compan[5], C. De Mattei[6], R. LandewÉ[5], D. Van Der Heijde[5]. *[1]Department of Rheumatology, Paris, France; [2]Rheumatology, Lisbon, Portugal; [3]Hopital Cochin, Paris, France; [4]Department of Rheuamtology; [5]Department of Rheumatology, Leiden, Netherlands; [6]Department of biostatistics, Nimes, France*

Background: The natural history (e.g. appearance of structural damage) of non-radiographic (nr) axial (ax) Spondyloarthritis (SpA) is not well known.
Objectives: To evaluate the switch from nr- to radiographic (r) status of recent onset axSpA after 5 years of follow-up and its predisposing factors.
Methods: *Patients:* Recent onset axial SpA (DESIR Cohort). *Outcome measure:* Radiographic SIJ status according to the mNY criteria after 5 years follow-up. *Reading of the SIJ-X-Rays:* 3 trained readers unaware of the chronology of the films. *Potential predisposing factors:* Demographics, smoking status, HLA-B27, Bone Marrow Edema (BME) at MRI of the SIJ, CRP, disease activity and

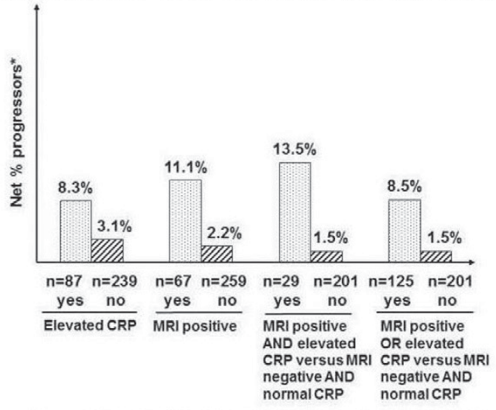
treatment. *Statistical analysis:* The radiographic progression has been evaluated in both the completers and after Linear Extrapolation (LE) and Last Observation Carried Forward (LOCF) technique in case of missing data. The predictive factors of radiographic progression were evaluated on the completer population using multilevel binomial GEE analysis incorporating measurements from all readers at 5-years and taking into account the within-reader correlation.Moreover, the progression rate was assessed in subgroups of patients according to CRP status and MRI-SIJ status at baseline.

Results: At baseline, 62 out of the 416 patients (14.9%) were considered r-ax-SpA. Out of these 416 patients, 24 (5.8%) changed from mNY negative to mNY positive after 5-years. Conversely, 3 patients changed from mNY positive at baseline to negative at year 5 (e.g. 0.7%) resulting in a net progression of 5.1%. These results were similar when applying LOCF and LE (4.1% and 3.8% net progression).

In the multivariate analysis, presence of BME at MRI-SIJ was highly predictive of radiographic progression (OR=4.85 [95% CI: 2.95–7.97]) together with a younger age (OR=0.97 [95% CI: 0.94–0.99]) and longer symptom duration (OR=1.40 [95% CI: 1.04–1.89]).

Of the 383 patients with complete data, the net % patients who switched from nr-axSpA to r-axSpA after 5 years ranged from 2.0% to 13.5% according to the presence of objective signs of inflammation at baseline (see figure).

Fig: Net % patients who switched from nr to r-axSpA after 5 years of follow-up



*% patients who switched from nr to r-axSpA *minus* % patients who switched from r to nr-axSpA according to the mNY criteria

Conclusions: This is the first cohort in early axSpA with 5-year follow-up demonstrating the importance of presence of objective signs of inflammation as predisposing factors of development of radiographic sacroiliitis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1637

OP0117 BONE MARROW OEDEMA IN SACROILIAC JOINTS OF YOUNG ATHLETES SHOWS MOST FREQUENTLY IN THE POSTERIOR INFERIOR ILIUM

U. Weber[1], A.G. Jurik[2], A. Zejden[2], E. Larsen[3], S.H. Jørgensen[3], K. Rufibach[4], C. Schioldan[3], S. Schmidt-Olsen[3]. *[1]University of Southern Denmark, Odense; [2]Aarhus University, Aarhus; [3]North Denmark Regional Hospital, Hjørring, Denmark; [4]F. Hoffmann-La Roche, Basel, Switzerland*

Background: Low grade bone marrow oedema (BMO) was reported in the sacroiliac joints (SIJ) of up to 25% of healthy individuals and mechanical back pain patients, challenging the imaging discrimination from early spondyloarthritis (SpA) [1]. Potential explanations range from mechanical stress lesions to vascular signals and anatomical SIJ variants.

Objectives: To determine BMO frequency and anatomical distribution in 8 SIJ regions in hobby and professional athletes.

Methods: The sample consisted of 2 cohorts of 20 healthy hobby runners (HR) before and after running and 22 professional ice hockey players (IP) from the Danish premier league: HR/IP 40%/100% men; mean age (SD) 27.2 (5.4)/25.9 (4.6) years; mean BMI (SD) 22.6 (1.5)/25.7 (1.6) kg/m^2. Semicoronal MRI scans of the SIJ with T1SE and STIR sequences were obtained in HR before and 24 hours after a running competition over 6.2 kilometers (mean duration 35.4 minutes, mean speed 10.4 km/h), and in IP during the competitive season. The scans were assessed for BMO independently by 3 blinded readers (AGJ, AZ, UW) according to the quadrant based MORPHO module (www.carearthritis.com). Paired images of HR were read blinded to timepoint. 7 MRI scans (2 paired images) of SpA patients under TNF treatment served to mask readers. A pre-test reader calibration used MRI scans from 11 patients with active sacroiliitis and 9 healthy volunteers. Reader agreement was assessed by ICC (3, 1). Descriptive analysis comprised mean frequency of SIJ quadrants with BMO and distribution of BMO quadrants in 8 anatomical SIJ regions: upper/lower ilium and sacrum, subdivided in anterior and posterior slices, as concordantly recorded by the majority (≥2/3) of readers.

Results: Agreement among 3 readers for SIJ BMO was excellent in calibration (ICC 0.93) and moderate in athletes (ICC 0.59) due to low frequency of BMO. The mean number (SD) of SIJ quadrants showing BMO was 3.1 (4.2)/3.1 (4.5) in HR before/after running, and 3.6 (3.0) in IP. The posterior inferior ilium was the single most affected region, followed by the upper anterior sacrum, consistently across 2 cohorts of athletes.

Table 1. Frequency and anatomical distribution of SIJ quadrants with BMO in 2 cohorts of athletes

Cohort	SIJ quadrants	Upper Ilium		Lower Ilium		Upper Sacrum		Lower Sacrum	
		Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
HR before									
	Mean (SD)	0.1 (0.4)	0.1 (0.3)	0.2 (0.7)	1.4 (1.9)	0.5 (0.9)	0.1 (0.4)	0.3 (0.6)	0.5 (1.6)
	≥1 Q (n)	3	0	1	8	4	2	3	1
	≥2 Q (n)	0	0	1	6	3	0	0	1
	≥3 Q (n)	0	0	1	2	1	0	0	1
	≥4 Q (n)	0	0	0	1	0	0	0	1
HR after									
	Mean (SD)	0.2 (0.4)	0 (0.1)	0.3 (0.8)	1.2 (1.7)	0.5 (1.0)	0.2 (0.7)	0.3 (0.7)	0.5 (1.6)
	≥1 Q (n)	2	0	2	9	3	2	3	1
	≥2 Q (n)	0	0	1	6	2	1	0	1
	≥3 Q (n)	0	0	1	3	2	0	0	1
	≥4 Q (n)	0	0	1	1	0	0	0	1
IP	Mean (SD)	0.1 (0.4)	0.1 (0.3)	0.5 (0.8)	1.9 (1.9)	0.6 (1.1)	0.1 (0.4)	0.2 (0.6)	0.1 (0.6)
	≥1 Q (n)	0	1	7	13	3	0	3	0
	≥2 Q (n)	0	0	4	11	2	0	1	0
	≥3 Q (n)	0	0	0	6	2	0	0	0
	≥4 Q (n)	0	0	0	3	1	0	0	0

Abbreviations. Q: SIJ quadrants with BMO. ≥1/2/3/4 Q (n): number of subjects (n) with ≥2/3 readers indicating ≥1/2/3/4 SIJ quadrants with BMO.

Conclusions: In hobby and professional athletes, BMO showed on average in 3–4 SIJ quadrants. The posterior lower ilium was the SIJ region most frequently affected by BMO. These findings in healthy controls may help refine thresholds for a positive SIJ MRI in early SpA.

References:

[1] Weber U et al. Curr Rheumatol Rep 2016;18:58.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4352

OP0118 IMPACT OF RADIOGRAPHIC DAMAGE IN THE SACROILIAC JOINTS ON FUNCTION AND SPINAL MOBILITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

M. Protopopov[1], J. Sieper[1], H. Haibel[1], J. Listing[2], M. Rudwaleit[3], D. Poddubnyy[1]. *[1]Department of Gastroenterology, Infectiology and Rheumatology, Charité Universitätsmedizin Berlin; [2]German Rheumatism Research Centre, Berlin; [3]Klinikum Bielefeld Rosenhöhe, Bielefeld, Germany*

Background: It has been shown in the past that the spinal mobility in patients with axial spondyloarthritis (AxSpA) is associated with spinal structural damage, disease activity parameters and spinal inflammation [1]. The impact of radiographic damage in the sacroiliac joints on functional parameters in patients with axial spondyloarthritis has not been investigated so far.

Objectives: To analyze the association between radiographic sacroiliitis and parameters of the functional status and spinal mobility in patients with axSpA.

Methods: Altogether 210 patients with definite axSpA (115 with radiographic and 95 with non-radiographic axSpA) from the German Spondyloarthritis Inception Cohort (GESPIC) were included in the current study. Radiographs of sacroiliac joints were obtained at baseline and after 2 years of the follow up and were scored by two trained readers according to the conventional grading system of the modified New York criteria (grade 0 to 4 per joint). A mean of two readers score for each joint and a sum score for both SIJ were calculated for each patient, giving a total sacroiliitis score between 0 and 8. Functional status and spinal mobility were assessed by means of the Bath Ankylosing Spondylitis Functional Index (BASFI) and the Bath Ankylosing Spondylitis Metrology Index (BASMI), respectively. Both baseline and year 2 data were included in the longitudinal mixed models analysis that was corrected for the dependencies between the two time-point values of each individual and adjusted for the structural damage in the spine (modified Stoke Ankylosing Spondylitis Spine Score - mSASSS), disease activity (the Bath Ankylosing Spondylitis Disease Activity Index – BASDAI and level of C-reactive protein – CRP), and sex.

Results: In the longitudinal mixed model analysis adjusted for the presence of structural damage in the spine (mSASSS), disease activity (BASDAI and CRP) and sex, radiographic sacroiliitis demonstrated an independent association with the BASFI: β=0.10 (95% CI 0.01–0.19) and the BASMI: β=0.12 (95% CI 0.03–0.21), respectively – table. These data indicate that change by one radiographic sacroiliitis grade in one sacroiliac joint is associated with a BASFI/BASMI worsening by 0.10/0.12 points independently of structural damage in the spine and disease activity. Assuming linear association, progression of radiographic sacroiliitis from grade 0 bilaterally to grade 4 bilaterally would result in a worsening by 0.8 points in BASFI and 0.96 points in BASMI. Sensitivity analysis performed in radiographic and non-radiographic axSpA subgroups provided similar results for both outcomes.

Conclusions: Radiographic damage in the sacroiliac joints might have an impact,

Table. Association between the sum radiographic sacroiliitis score and functional status / spinal mobility in patients with axial spondyloarthritis.

Parameters	Unadjusted mixed model analysis β (95% CI)	Adjusted mixed model analysis β (95% CI)
Outcome: BASFI		
Sacroiliitis sum score (0-8)	**0.09 (-0.05 to 0.22)**	**0.10 (0.01 to 0.19)**
mSASSS, points (0-72)	-	0.05 (0.03 to 0.07)
BASDAI, points NRS (0-10)	-	0.81 (0.74 to 0.88)
CRP, mg/l	-	0.00 (-0.01 to 0.01)
Male vs. Female sex	-	-0.02 (-0.40 to 0.37)
Outcome: BASMI		
Sacroiliitis sum score (0-8)	**0.20 (0.11 to 0.30)**	**0.12 (0.03 to 0.21)**
mSASSS, points (0-72)	-	0.07 (0.05 to 0.09)
BASDAI, points NRS (0-10)	-	0.22 (0.15 to 0.29)
CRP, mg/l	-	0.01 (0.00 to 0.02)
Male vs. Female sex	-	0.00 (-0.39 to 0.39)

mSASSS - modified Stoke Ankylosing Spondylitis Spine Score; AS - Ankylosing Spondylitis; nr-axSpA - non-radiographic axial spondyloarthritis; BASFI – Bath Ankylosing Spondylitis Functional Index; CRP - C-reactive protein; BASDAI – Bath Ankylosing Spondylitis Disease Activity Index; BASMI – Bath Ankylosing Spondylitis Metrology Index.

although small, on spinal mobility and physical function in patients with axial SpA independently of structural damage in the spine and disease activity.

References:

[1] Machado P. et al. Ann Rheum Dis 2010; 69:1465–1470.

Acknowledgements: GESPIC has been financially supported by the German Federal Ministry of Education and Research (BMBF). As funding by BMBF was reduced in 2005 and stopped in 2007, complementary financial support has been obtained also from Abbott/Abbvie, Amgen, Centocor, Schering-Plough, and Wyeth. Since 2010 GESPIC is supported by Abbvie.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3453

OP0119 EVALUATION OF THE PREDICTIVE VALIDITY OF THE ASAS AXIAL SPONDYLOARTHRITIS CRITERIA IN THE DESIR COHORT

B. Meghnathi[1], A. Etcheto[1], A. Saraux[2], M. Dougados[1], A. Moltó[1]. *[1]Paris Descartes University, Medicine Faculty; APHP, Rheumatology B Department, Cochin Hospital, Paris; [2]La Cavale Blanche Hospital, Rheumatology and Université Bretagne Occidentale, Brest, France*

Background: The face validity[1] and cross-sectional external validity[2] of the Assessment of SpondyloArthritis international Society (ASAS) criteria for axial spondyloarthritis (axSpA), and its arms has been already confirmed in previous studies. However, so far, only one study[3] has reported data regarding the predictive validity of such criteria after 4 years of follow-up.

Objectives: To evaluate the predictive validity of the ASAS criteria and its arms after 5 years of follow-up. The predictive validity of the other axSpA sets of criteria (Amor, ESSG and mNY) was also evaluated.

Methods: Patients: This analysis was performed on the DESIR cohort. A total of 708 adult (>18 and <50 years) patients presented with inflammatory back pain suggestive of axSpA (according to the rheumatologist's conviction of ≥5/10) for >3 months but <3 years duration. They were followed up every 6 months for the first 2 years and then yearly up to 5 years. Starting from month 24, as per protocol, patients could be excluded from the cohort in case another diagnosis (different from SpA) was made.

Methods: The gold standard for this analysis was the diagnosis of axSpA according to the rheumatologist at 5 years of follow-up. For this analysis, patients were considered as axSpA, if the rheumatologist at 5 years with a conviction of ≥7/10 for an axSpA diagnosis. Conversely, patients excluded as per protocol due to another diagnosis or patients with a rheumatologist conviction at 5 years of ≤3/10 for axSpA were considered as Non-axSpA. The set of criteria collected at baseline (ASAS, and its arms, Amor, ESSG and mNY: fulfilled/not fulfilled) were tested against the Rheumatologist's axSpA diagnosis (fulfilled/not fulfilled) after 5 years of follow-up. Predictive validity of all sets of criteria at baseline was evaluated by the positive predictive value (PPV).

Results: In total, among the 708 patients included in the DESIR cohort at baseline, data on Rheumatologists diagnosis at 5 years was available in 454 patients; amongst them, 352 (77.5%) had an axSpA diagnosis according to the rheumatologist. Among these 352 patients, 245, 300, 291 and 88 patients fulfilled the ASAS criteria for axSpA, Amor, ESSG and modified NY criteria's respectively. Figure 1 shows the PPV (95% CI) of the different sets of criteria below.

Conclusions: Predictive validity of the ASAS criteria for axSpA (including both arms) at 5 years was excellent; it is worth noting that the performances of the other criteria were also very good.

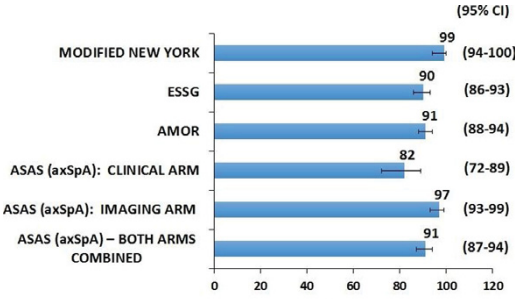


Figure 1. Bar diagram representing Positive Predictive Value (95% Confidence Interval) of various axSpA criterias

References:

[1] Molto A et al. Performances of the Assessment of SpondyloArthritis International Society Axial Spondyloarthritis Criteria for Diagnostic and Classification Purposes in Patients Visiting a Rheumatologist Because of Chronic Back Pain: Results From a Multicenter, Cross-Sectional Study. Arthritis Care & Research 2013;65:1472–81.

[2] Molto A et al. Evaluation of the validity of the different arms of the ASAS set of criteria for axial spondyloarthritis and description of the different imaging abnormalities suggestive of spondyloarthritis: data from the DESIR cohort. Ann Rheum Dis 2015;74:746–51.

[3] Sepriano A et al. Predictive validity of the ASAS classification criteria for axial and peripheral spondyloarthritis after follow-up in the ASAS cohort: a final analysis. Ann Rheum Dis. 2016;75:1034–42.

Acknowledgements: The DESIR cohort is financially supported by unrestricted grants from the French Society of Rheumatology and Pfizer France.

Disclosure of Interest: B. Meghnathi Grant/research support from: ASAS Society (ASAS FELLOW), A. Etcheto: None declared, A. Saraux: None declared, M. Dougados: None declared, A. Moltó: None declared

DOI: 10.1136/annrheumdis-2017-eular.3490

OP0120 THE ROLE OF SMOKING IN THE DEVELOPMENT AND PROGRESSION OF STRUCTURAL DAMAGE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: THE PRELIMINARY RESULTS OF A SYSTEMATIC REVIEW AND META-ANALYSIS

S. Akar[1], Y.C. Kaplan[2], S. Ecemis[1], E.K. Arslan[2], O. Gercik[1], D. Solmaz[1]. *[1]Rheumatology; [2]Pharmacology, Izmir Katip Celebi University Faculty of Medicine, Izmir, Turkey*

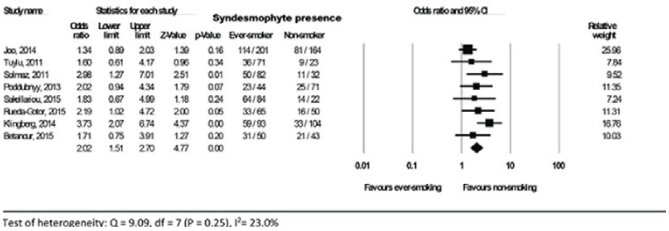
Background: Smoking may constitute a major risk factor for not only disease susceptibility but also disease severity in patients with ankylosing spondylitis (AS). Some previous cross-sectional and longitudinal studies suggested that smoking may be associated with cumulative spinal radiographic damage and regarded it as an independent predictor of spinal radiographic progression.

Objectives: The objective of this study is to determine whether smoking is associated with the cumulative radiographic spinal structural damage and radiographic progression in AS patients. In order to reach this objective, we conducted a systematic review and meta-analysis of the available studies to-date.

Methods: An electronic search was conducted from inception to June 21 2016 in EMBASE, MEDLINE/PubMed Cochrane Central Register of Controlled Trials databases. Cross-sectional and longitudinal cohort studies investigating the association between smoking and cumulative spinal structural damage or radiographic progression were included. The outcome of interest were the presence of syndesmophytes in cross-sectional studies and radiographic progression in longitudinal studies. Two independent reviewers carried out the screening process. The Quality assessment was done using The Agency for Healthcare Research and Quality (ARHQ) checklist and Newcastle-Ottawa scale. Authors of potential relevant studies were contacted for the unpublished data. Data from eligible cross-sectional studies were extracted and arranged in a 2x2 table. The odds ratios (ORs) and 95% confidence intervals (CIs) for the dichotomous outcome of interest were computed. Random-effects method was used to combine the outcome data in Comprehensive Meta Analysis Software Version 3.3.070.

Results: The combined data of eight eligible cross-sectional studies for the assessment of association between smoking and cumulative spinal structural damage suggested a significant association (OR, 2.02; 95% CI 1.51–2.70)

Figure 1. Forest plot of the association between ever-smoking and cumulative spinal structural damage in AS patients



Test of heterogeneity: Q = 9.09, df = 7 (P = 0.25), I^2 = 23.0%

(Figure 1). No significant heterogeneity was detected between studies (P=0.25, I^2=23.0%). The data from the longitudinal studies investigating the association between smoking and spinal radiographic progression is still been assessed.
Conclusions: The preliminary results of our meta-analysis showed that smoking is associated with increased cumulative spinal structural damage in patients with AS. Rheumatologists should encourage AS patients to quit smoking.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4659

OP0121 VALIDATION OF MRI STRUCTURAL LESIONS USING COMPUTED TOMOGRAPHY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

W.P. Maksymowych[1,2], D. Loeuille[3], M. Raynal[4], J. Melchior[5], M.-A. D'Agostino[6], J. Paschke[2], R.G. Lambert[7]. *[1]Medicine, University of Alberta; [2]CaRE Arthritis, Edmonton, Canada; [3]Rheumatology, CHRU de Nancy; [4]Rheumatology, CHRU de Nancy, Vandœuvre-lès-Nancy; [5]Rheumatology, CHRU de Nancy, Vandoeuvre les Nancy; [6]Rheumatology, Université Paris Ouest, Paris, France; [7]Radiology, University of Alberta, Edmonton, Canada*

Background: MRI can detect both inflammatory and structural lesions in the sacroiliac joints (SIJ) of patients with axial SpA. However, standard MRI sequences do not directly depict bone and the appearance of erosion may vary according to the presence/absence of inflammation. Consequently, further validation using an accepted gold standard, namely, computed tomography (CT), is essential.
Objectives: We aimed to assess the detection of structural lesions in the SIJ by MRI using CT as the gold standard.
Methods: CT scans from 44 patients (26 females, mean age 49.4 years, mean symptom duration 9.1 years) were reconstructed in the semicoronal plane parallel to the superior border of the sacrum, as for conventional MRI evaluation of the SIJ, and scoring of lesions by CT was confined to this plane. Structural lesions were scored in consecutive slices in SIJ quadrants (erosion, sclerosis) or SIJ halves (ankylosis) on a dichotomous basis (present/absent) using the same anatomical principles for defining SIJ quadrants as developed for the SPARCC MRI SIJ inflammation and structural scores. T1W MRI scans of the SIJ from the same cases conducted at the same time as CT were assessed independently for structural lesions (erosion, fat, backfill, ankylosis, sclerosis) blinded to CT assessments using the SPARCC method. Agreement between CT and MRI was assessed by kappa statistics. Sensitivity/specificity of MRI for CT lesions was calculated. The primary analysis was based on lesions detected concordantly by both readers at the level of the individual iliac/sacral joint surface (erosion, sclerosis) or the individual joint (ankylosis, backfill).
Results: With CT as gold standard and a lesion defined as being present when recorded in the same location on at least 1 coronal slice by both readers, MRI-defined ankylosis had 56.3% sensitivity and 100% specificity for CT ankylosis (Table). For erosion, sensitivity and specificity of MRI was 81.3% and 96.2%, and for sclerosis, sensitivity and specificity of MRI was 50% and 97%, respectively. Agreement between CT and MRI for erosion increased when the cut-off for presence of a lesion was set at 2 slices but only marginally for sclerosis, even when the cut-off for presence of a lesion was set at 3 slices. Lesions observed on CT corresponding to backfill on MRI were ankylosis, erosion, and sclerosis, in 66.7%, 66.7%, and 80% of backfill lesions, respectively.

Concordance for 2 readers		Type of Lesion	K value	Sensitivity of MRI	Specificity of MRI
MRI lesion +	CT lesion +				
≥1 slice	≥1 slice	Ankylosis	0.67	56.3%	100%
		Erosion	0.76	81.3%	96.2%
		Sclerosis	0.47	50.0%	97%
≥2 slices	≥2 slices	Ankylosis	0.71	60.0%	100%
		Erosion	0.83	84.6%	98.1%
		Sclerosis	0.53	42.9%	99.2%
≥2 slices	≥3 slices	Ankylosis	0.83	75.0%	100%
		Erosion	0.84	90%	98.1%
		Sclerosis	0.53	42.9%	99.2%

Conclusions: Ankylosis and erosion on MRI correspond closely with the same type of lesion observed on CT. Both new bone formation and erosion are frequently evident on CT at locations where backfill is observed on MRI supporting the hypothesis that backfill is an intermediary tissue between erosion and ankylosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5427

THURSDAY, 15 JUNE 2017

Clinical and therapeutical news in systemic sclerosis

OP0122 VENOUS THROMBOEMBOLISM IN SYSTEMIC SCLEROSIS: PREVALENCE, RISK FACTORS AND IMPACT ON SURVIVAL

S.R. Johnson[1], N. Hakami[2], Z. Ahmad[1], D.N. Wijeysundera[3]. *[1]University of Toronto, Toronto, Canada; [2]King Fahad Central Hospital, Jizan, Saudi Arabia; [3]Anesthesia, University of Toronto, Toronto, Canada*

Background: Systemic sclerosis (SSc) is characterized endothelial dysfunction and vasculopathy, which may result in thrombosis. Venous thromboembolism (VTE) is a vascular phenomenon that includes deep vein thrombosis (DVT) and pulmonary embolism (PE).
Objectives: To evaluate the epidemiology of VTE in SSc, specifically cumulative incidence, risk factors and impact of VTE on survival.
Methods: We conducted a cohort study of patients who fulfilled the ACR–EULAR classification criteria for SSc attending the Toronto Scleroderma Program 1970–2017. DVT was defined as the presence of thrombus on doppler ultrasound of either upper or lower extremity. PE was defined as the presence of thrombus on CT angiogram of the thorax. Time to all-cause mortality was evaluated in Kaplan Meier and Cox models.
Results: 1181 subjects (971 (82%) female, 210 (18%) male) were included. There were 40 (3.4%) VTE events. The cumulative incidence of VTE was 2.7 (95% CI 1.9, 3.7) per 1000 patient years. The presence of ILD, PAH, ScL70 antibody, anticardiolipin antibody, coronary artery disease, diabetes mellitus and PVD occurred more frequently in subjects who developed VTE.

Table 1. Venous Thromboembolism in SSc

Characteristics	VTE (N=40)	No VTE (N=1141)	Relative Risk (95% CI)
Diffuse subtype	12 (30%)	382 (33%)	1.04 (0.84, 1.30)
Male sex	9 (23%)	201 (18%)	1.28 (0.71, 2.30)
Raynaud's phenomenon	39 (98%)	1087 (95%)	1.02 (0.97, 1.08)
Esophageal dysmotility	35 (88%)	981 (86%)	1.02 (0.90, 1.15)
Interstitial lung disease	23 (58%)	393 (34%)	1.67 (1.26, 2.20)*
Pulmonary arterial hypertension	28 (70%)	367 (32%)	2.18 (1.75, 2.71)*
Abnormal nailfold capillaries	14 (35%)	354 (31%)	1.13 (0.73, 1.74)
Digital ulcers	13 (33%)	386 (34%)	0.96 (0.61, 1.51)
Scl 70 antibody	11 (28%)	186 (16%)	1.73 (1.03, 2.91)*
Anticentromere antibody	5 (13%)	215 (19%)	0.68 (0.30, 1.56)
Anticardiolipin	3 (8%)	14 (1%)	6.27 (1.88, 20.9)*
Coronary artery disease	9 (23%)	98 (9%)	2.69 (1.47, 4.92)*
Hypertension	11 (28%)	237 (21%)	1.32 (0.79, 2.22)
Diabetes mellitus	6 (15%)	61 (5%)	2.81 (1.29, 6.10)*
Hyperlipidemia	5 (13%)	78 (7%)	1.83 (0.78, 4.27)
Peripheral vascular disease	8 (20%)	41 (4%)	5.57 (2.79, 11.08)*
Cancer	7 (8%)	127 (11%)	1.57 (0.79, 3.14)
Atrial fibrillation	6 (15%)	45 (4%)	3.80 (1.72, 8.39)*

*Denotes statistical significance.

On multivariate logistic regression PAH (OR 3.77 (96%CI 1.83, 8.17), ScL70 antibodies (OR 2.45 95% CI 1.07, 5.30), anticardiolipin antibodies (OR 5.70 (95% CI 1.16, 21.2) and PVD (OR 5.31 (95% CI 1.99, 12.92) were independent predictors of VTE. Subjects with ILD more frequently experienced DVT (RR 2.85 95% CI (1.08, 7.54) but not PE (RR 1.82 (95% CI 0.89, 3.70). There were 440 deaths. There was no significant difference in survival between those with and without VTE (HR 1.6 (95% CI 0.70, 1.92). Only the presence of ILD (HR 1.54 (95% CI 1.27, 1.88) or PAH (HR 1.35 (95% CI 1.10, 1.65) remained independent predictors of mortality.

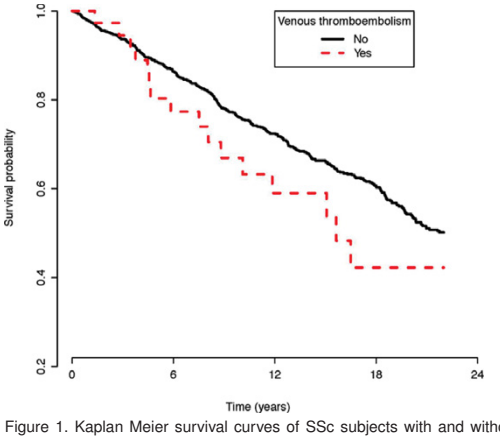


Figure 1. Kaplan Meier survival curves of SSc subjects with and without venous thromboembolism. Log rank test p=0.54

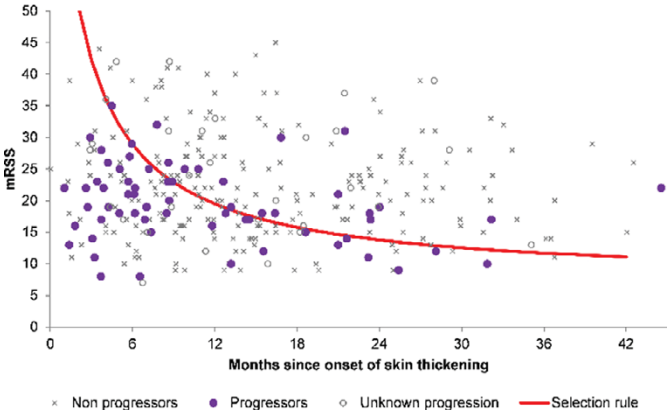
Conclusions: The risk of VTE in SSc is not increased, as the incidence of VTE in SSc is comparable to the general population. The presence of PAH, PVD, ScL70 and anticardiolipin antibodies are risk factors for VTE in SSc. VTE does not independently affect SSc survival.
Acknowledgements: Dr. Johnson is supported by the Canadian Institutes of Health Research.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5629

OP0123 PREDICTION OF PROGRESSIVE SKIN THICKENING IN EARLY DIFFUSE SYSTEMIC SCLEROSIS USING THREE-MONTHLY SKIN SCORES FROM THE EUROPEAN SCLERODERMA OBSERVATIONAL STUDY (ESOS)

A. Herrick[1], S. Peytrignet[1], X. Pan[1], R. Hesselstrand[2], L. Mouthon[3], E. Brown[1], L. Czirják[4], J.H. Distler[5], O. Distler[6], K. Fligelstone[1], W. Gregory[1], R. Ochiel[7], A. Silman[8], M. Vonk[9], M. Lunt[1], C. Denton[7]. *[1]University of Manchester, Manchester, United Kingdom; [2]Lund University, Lund, Sweden; [3]Université Paris Descartes, Paris, France; [4]University of Pécs, Pécs, Hungary; [5]University of Erlangen-Nuremberg, Erlangen, Germany; [6]University Hospital Zurich, Zurich, Switzerland; [7]University College London, London; [8]University of Oxford, Oxford, United Kingdom; [9]Nijmegen University, Nijmegen, Netherlands*

Background: ESOS (European Scleroderma Observational Study) was a prospective observational study of early diffuse cutaneous systemic sclerosis, recruiting from 50 centres in 19 countries and thus providing a unique opportunity to study parameters of disease progression at regular intervals.
Objectives: To describe the characteristics of patients with progressive skin thickening and derive prediction models for progression over 12 months.
Methods: Duration of skin thickening and autoantibody status (anti-topoisomerase-1[anti-Scl-70, TOPO], anti-RNA polymerase III[Pol3], anticentromere[ACA]) were documented. The modified Rodnan skin score (mRSS) was recorded 3-monthly for up to two years after baseline. The main outcome was the progression of mRSS. Progressive patients ("progressors") had to meet a 5-unit and 25% increase in their mRSS within the first 12 monthsof follow-up. Features of progressors vs. non-progressors were compared using the Fisher or Kruskal-Wallis test (for categorical and continuous variables), as were progression parameters between autoantibody groups. Logistic models were fitted to predict progression and, using ROC curves, were compared based on AUC, accuracy and positive predictive value (PPV).
Results: 326 patients were recruited, with median disease duration of 11.9 months. During the first 12 months, 66 patients (20.3%) progressed, 227 (69.6%) did not and 33 (10.1%) could not have their status assessed. At baseline, progressors had shorter disease duration than non-progressors: 8.1 months vs. 12.6 months (p=0.001). Progressors started with a lower mRSS, median 19 units vs. 21 for non-progressors (p=0.030).
124 patients were TOPO+, 50 were Pol3+, 20 were ACA+, 2 were TOPO+/ACA+ and 68 had none. Pol3+ patients had a higher mRSS peak (35 units vs. 27 overall[p=0.001]) and did so earlier (median 17.9 months vs. 23.1 months overall[p=0.214]).
Using an mRSS 22 cutoff point to predict progression in the ESOS cohort (as suggested in the literature) would yield a PPV of 24.3%, a weak improvement from the observed 20.3% share of progressors. A first model (Model A, with mRSS, duration of skin thickening and their interaction) had an accuracy of 60.9%, AUC of 0.67 and PPV of 33.8%. Figure 1summarizes the prediction rule, with patients under the curved line predicted to progress. By adding a variable for being Pol3+ (Model B), the model reached an accuracy of 71%, AUC of 0.71 and PPV of 41%.

Figure 1. Trade-off at baseline between mRSS and disease duration and prediction rule to select progressors (Model A)



Conclusions: 1. Patients with shorter disease duration and a lower mRSS have a higher likelihood of being progressors, with a trade-off between the two.
2. Pol3+ patients experience higher mRSS peaks and tend to reach them earlier.
3. Two prediction models for progressive thickening were derived. The advantage of having two is that Model B, while more accurate and useful in identifying high-risk patients in clinical practice, risks being too restrictive for patient selection into trials and may over-represent Pol3+ patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1869

OP0124 TREATMENT WITH CYCLOPHOSPHAMIDE FOR SYSTEMIC SCLEROSIS-RELATED INTERSTITIAL LUNG DISEASE DOES NOT IMPROVE SURVIVAL AFTER 12 YEARS OF FOLLOW UP

E.R. Volkmann[1], M. Sim[1], D.P. Tashkin[1], D. Khanna[2], P.J. Clements[1], M. Roth[1], D. Furst[1], A. Pickney[3], E. Goldmuntz[4], L. Keyes-Elstein[3], R. Elashoff[1], K. Sullivan[5] on behalf of SLS I working group. *[1]University of California, Los Angeles, Los Angeles; [2]University of Michigan, Ann Arbor; [3]Rho Federal Systems, Inc., Chapel Hill; [4]DAIT, Niaid/Nih, Bethesda; [5]Duke University, Durham, United States*

Background: Treatment with cyclophosphamide (CYC) is associated with short-term improvements in lung function, dyspnea, and radiographic fibrosis in patients with systemic sclerosis-related interstitial lung disease (SSc-ILD).[1] However, the effects of CYC therapy on long-term morbidity and mortality outcomes are unknown.
Objectives: To determine whether 1 year of treatment with CYC for SSc-ILD affects long-term morbidity and mortality in patients who participated in the Scleroderma Lung Study (SLS) I.[1]
Methods: SLS I randomized 158 SSc-ILD patients from 13 US SSc centers to 1 year of oral CYC versus placebo. The primary endpoint was the change in FVC%>predicted over 1 year. Twelve years after the study commenced, each study center contacted enrolled patients or designated surrogates to assess the following: mortality, cause of mortality, development of organ failure, need for transplant and functional status. We used counting process cox proportional hazard modeling to determine the variables associated with survival. The model findings were validated using a joint model of longitudinal and survival data. We also tested the model using long-term follow-up data from SLS II (CYC vs. Mycophenolate).
Results: Nearly half of all SLS I patients (43%) died during the follow-up period, and only 24% remained alive in the absence of organ failure. The median follow up period for all patients was 8 years. Where known, the cause of death was attributable most often to SSc. Among patients who developed malignancy (N=13), a similar proportion were treated with CYC compared with placebo. The most common type of organ failure was respiratory failure (N=31 of 33 organ failures) defined as the need for supplemental oxygen therapy (N=29) and/or lung transplantation (N=3). There was no difference in the time to death (Figure 1), or time to organ failure, or time to malignancy in patients randomized to CYC versus placebo. The Cox model identified the following variables as the most important predictors of mortality: baseline skin score (HR 1.033; P=0.0038), age at randomization (HR 1.056; $P<0.0001$), and the course of the FVC from baseline to 24 months (HR 0.975; P=0.0215). The course of the FVC was a better predictor of mortality than the baseline FVC. The joint model identified the same variables associated with mortality.

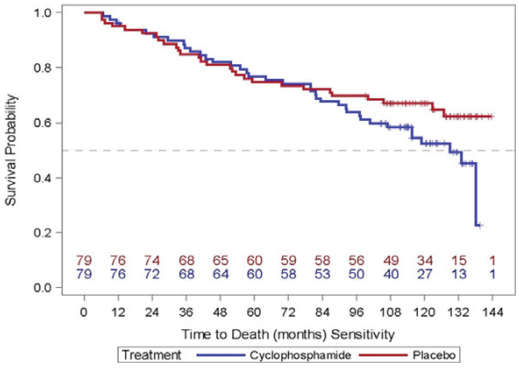


Figure 1. Time to death in patients randomized to CYC (blue line) and placebo (red line).

Conclusions: Treatment with 1-year of oral CYC for SSc-ILD does not decrease long-term mortality, organ failure or malignancy compared with placebo. In addition to identifying traditional mortality risk factors in SSc (i.e. increased skin score and advanced age), this study found that progression of the FVC over 2 years was a more important predictor of mortality than the baseline FVC. These findings suggest that early changes in surrogate measures of SSc-ILD progression may have important effects on long-term outcomes.
References:
[1] Tashkin et al. NEJM 2006;354:2655.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2488

OP0125 MORTALITY IN PATIENTS WITH DERMATOMYOSITIS/POLYMYOSITIS IN A CHINESE MEDICAL CENTRE

X. Yang. *Peking University First Hospital, Beijing, China*

Objectives: To investigate the mortality and the causes of death in Chinese patients with dermatomyositis (DM) or polymyositis (PM).
Methods: We collected the clinical data of all DM/PM patients in Rheumatology

department of Peking University First Hospital from January 2007 to May 2016.The primary causes of death were identified, the standardised mortality ratio (SMR) and years of life lost (YLL) were calculated based on the National Bureau of Statistics of China for the general population, the survival in the first decade was performed using Kaplan-Meier analysis, and the predictors of mortality were evaluated by multivariable cox regression.

Results: A total of 226 DM and 54 PM cases were included and the mean age of onset was 49.9±14.8 years for DM and 48.1±17.1 years for PM. The median follow-up duration was 40.6 (11.6–77.6) months. Among 267 patients who were successfully traced, 66 patients died. Infection (50.0%) was the leading cause of death followed by malignancy (19.7%), and interstitial lung disease (ILD) (9.1%). The overall age and sex adjusted SMR was 9.0 (95% CI 6.8–11.2) for DM, and 5.0 (95% CI 2.4–7.5) for PM. The overall age and sex adjusted SMR of DM/PM patients with ILD was 8.4 (95% CI 5.8–11.0), and the SMR of the patients with malignancy was 14.9 (95% CI 8.5–21.2). The YLL of women and men were 37.5 and 28.4 years respectively for DM, and 24.3 and 12.0 years respectively for PM (Table1). The 10-year survival of patients with ILD or malignancy was significantly worse than those without ILD or malignancy respectively (Figure 1 and 2). The independent predictors of mortality for DM were age of disease onset, respiratory muscle involvement and malignancy; and the independent predictor of mortality for PM was age at disease onset (Table2).

Table 1. The standardized mortality ratio (SMR), life expectancy (LE) and years of life lost (YLL)

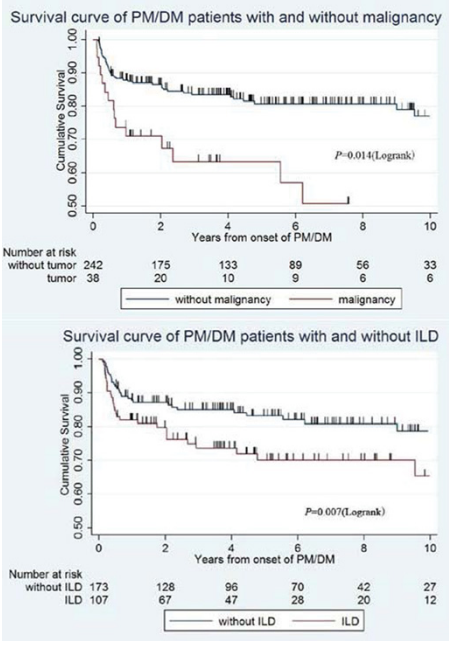
	Overall (n=280)	Females (n=201)	Males (n=79)
Dermatomyositis	226	163	63
Death number	55	37	18
SMR (95% CI)	9.0 (6.8–11.2)	12.0 (6.8–11.2)	6.0 (3.2–8.7)
LE of general population (years)	–	80.8	75.8
LE of DM patients (years)	–	43.3	47.4
YLL (years)	–	37.5 8	28.4
Polymyositis	54	38	16
Death number	11	8	3
SMR (95% CI)	5.0 (2.4–7.5)	4.2 (1.3–7.2)	9.3 (-1.2–19.8)
LE of general population (years)	–	80.8	75.8
LE of PM patients (years)	–	56.5	63.8
YLL (years)	–	24.3	12.0

Abbreviations: DM: dermatomyositis; SMR: standardised mortality ratio; CI: confidence interval; LE: life expectancy; YLL: years of life lost; PM: polymyositis.

Table 2. Multivariable cox regression analyses of risk factors in the DM/PM patients

Variables	HR	95% CI	*P* value
Dermatomyositis			
Age*	1.04	1.01–1.06	<0.001
ILD	1.35	0.74–2.48	0.319
Respiratory muscle involvement	2.58	1.19–5.58	0.016
Malignancy	3.12	1.49–6.58	0.003
Polymyositis			
Age*	1.08	1.00–1.16	0.044
ILD	2.47	0.18–34.00	0.500
ESR	1.02	0.99–1.04	0.174

*Age: Age at disease onset. Abbreviations: HR: Hazard Ratio; CI: confidence interval; ILD: interstitial lung disease; ESR: erythrocyte sedimentation rate.



Conclusions: Mortality of DM/PM patients in China is substantial, especially in females, and those with ILD or malignancy. Infection was the leading cause of death. Patients with older age at onset, respiratory muscle involvement, ILD, and malignancy need to be paid more attention.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2873

OP0126 A PHASE 2 STUDY OF SAFETY AND EFFICACY OF ANABASUM (JBT-101) IN SYSTEMIC SCLEROSIS

R. Spiera[1], L. Hummers[2], L. Chung[3], T. Frech[4], R. Domsic[5], D. Furst[6], J. Gordon[1], M. Mayes[7], R. Simms[8], S. Constantine[9], B. White[9]. *[1]Hospital for Special Surgery, New York City; [2]Johns Hopkins, Baltimore; [3]Stanford, Palo Alto; [4]University of Utah, Salt Lake City; [5]University of Pittsburgh, Pittsburgh; [6]Arthritis Association of Southern California, Los Angeles; [7]University of Texas, Houston; [8]Boston University, Boston; [9]Corbus Pharmaceuticals, Inc., Norwood, United States*

Background: Anabasum (JBT-101) is a synthetic, oral, non-immunosuppressive, preferential CB2 agonist. It inhibits onset and activates resolution of innate immune responses in animal models of systemic sclerosis (SSc).

Objectives: Evaluate safety and efficacy of anabasum in SSc

Methods: A double-blind, randomized, placebo (PBO)-controlled Phase 2 trial dosed 42 diffuse cutaneous SSc subjects with disease duration ≤6 years on stable medication including immunosuppressive drugs. Subjects received anabasum 5 mg QD, 20 mg QD, or 20 mg BID on Days 1–28, then 20 mg BID on Days 29–84, or PBO on Days 1–84. Subjects were followed off study drug on Days 85–113. The primary safety outcome was treatment-emergent adverse events (TEAEs). The primary efficacy outcome was improvement in ACR Combined Response Index in diffuse cutaneous Systemic Sclerosis (CRISS) score, combined anabasum group vs PBO, Days 29–113 (end of Weeks 4–16). The five domains of the ACR CRISS are the modified Rodnan skin score, HAQ-DI, patient and physician global assessments, and FVC % predicted.

Results: Of 42 dosed subjects, 27 (64%) received anabasum and 15 (36%) received PBO. Three anabasum subjects withdrew: 1 (3.7%) for a TEAE of moderate dizziness; 1 withdrew consent; and 1 by physician decision. One PBO subject withdrew consent. Baseline demographic and CRISS domain scores were similar except slightly more anabasum subjects used background immunosuppressive drugs (93% versus 80%, anabasum vs PBO). Seventeen (63%) anabasum subjects had 66 TEAEs, and 9 (60%) PBO subjects had 35 TEAEs. There were no serious, severe, or unexpected TEAEs related to anabasum. Severity and relationship of TEAEs to study drug were similar in both groups. The most frequent TEAEs by MedDRA system (% anabasum vs % PBO) were: nervous system (37% vs 27%); general disorders (30% vs 7%); gastrointestinal (22% vs 20%); infections (22% vs 20%); musculoskeletal (22% vs 13%); and investigations (0% vs 20%). The most frequent TEAEs in anabasum subjects were dizziness (22%) and fatigue (19%) which were usually mild. Anabasum subjects had greater improvement in ACR CRISS scores than PBO subjects (mixed model repeated measures analysis, p=0.044, 1-sided). The median ACR CRISS scores at the end of Weeks 4, 8, 12, and 16 (anabasum vs PBO) were 3.0% vs 1.0%, 19.0% vs 1.0%, 27.5% vs 1.0%, and 33.0% vs 1.0%, respectively. Among anabasum subjects, ∼50% had ACR CRISS ≥20% after 8 weeks of dosing. The individual domains of the ACR CRISS score showed greater improvement, improvement that reached minimal important differences in several domains, and less worsening in anabasum vs PBO groups. Anabasum subjects had greater improvement in SSc skin symptoms and itch. Plasma metabolipidomic profiles showed anabasum, not PBO, shifted lipid mediator production to increase pro-resolving vs pro-inflammatory lipid mediators.

Conclusions: Anabasum provided significant and medically meaningful efficacy in SSc as assessed by the ACR CRISS score and its individual domains and had acceptable safety and tolerability in this Phase 2 trial. These data support continued clinical development of anabasum for the treatment of SSc.

Disclosure of Interest: R. Spiera: None declared, L. Hummers: None declared, L. Chung: None declared, T. Frech: None declared, R. Domsic: None declared, D. Furst: None declared, J. Gordon: None declared, M. Mayes: None declared, R. Simms: None declared, S. Constantine Employee of: Corbus Pharmaceuticals, Inc., B. White Employee of: Corbus Pharmaceuticals, Inc.

DOI: 10.1136/annrheumdis-2017-eular.2712

OP0127 TEN YEARS FOLLOW-UP OF GASTROINTESTINAL INVOLVEMENT BY THE SMALL INTESTINAL CLEARANCE IN PATIENTS WITH SYSTEMIC SCLEROSIS

N. Hashimoto[1], M. Kitano[2], T. Nakazawa[3], T. Iwasaki[4], T. Hashimoto[1]. *[1]Hashimoto Rheumatology Clinic, Osaka; [2]Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya; [3]Osaka Saiseikai Nakatsu Hospital, Osaka; [4]Department of Pharmacy, Hyogo University of Health Sciences, Kobe, Japan*

Background: Systemic sclerosis (SSc) is an inflammatory autoimmune disease characterized by fibrosis and small vascular involvement in the skin, lungs, heart and gastrointestinal (GI) tract. The esophagus is the most frequently involved GI tract disorder. Although the small intestinal involvement such as malabsorption and pseudo-obstruction is less common, it has been related to morbidity and mortality of SSc patients. We previously reported a close correlation between the

esophageal diameter and the small intestinal clearance (SIC) (EULAR 2011). We also suggested that anti-centromere antibodies (ACA) are an important factor of esophageal dilatation in SSc patients (EULAR 2010). However, changes of small intestinal involvement during long-term follow-up have not yet been defined.

Objectives: The aim of this study was to evaluate a correlation between the small intestinal involvement and clinical features in SSc patients during ten years follow-up.

Methods: Fifty-five patients with a definite diagnosis of SSc [52 female and 3male with mean age of 59.4 years (range 29–77 years)] were included in the study. Thirteen (23.6%) patients were classified as diffuse SSc and 42 (76.4%) as limited SSc. The SIC grade was classified according to barium meal reach at 30 min after intake; grade 1 (>2/3 of the whole small intestine), grade 2 (1/3~2/3), grade 3 (<1/3), grade 4 (the duodenum). The SIC change was classified as follows; grade 1 and 2 or grade non-increase during follow-up was classified as "non-progressive", grade 3 and 4 or grade increase as "progressive". All SSc patients were evaluated the items as used for 2013 ACR/EULAR criteria.

Results: The mean durations of follow-up period were 9.5±0.6 years. The number of SSc patients in each SIC grade at the initial evaluation and the end of follow-up were as follows; grade 1: initial vs end; 23 vs 24, grade 2: 20 vs 9, grade 3: 10 vs 16, grade 4: 2 vs 6. The SIC change "progressive" was 40.0% of SSc patients. Positive correlation between the esophageal diameters and the SIC grade was observed in SSc patients at the initial evaluation ($r=0.61$ $p<0.01$) and the end of follow-up ($r=0.71$ $p<0.01$). The esophageal diameters at the initial evaluation were significantly wider in SIC "progressive" group than in "non-progressive" group (non-progressive vs progressive; 21.8±6.5 vs 30.9±8.6 mm, $p<0.0001$). The frequencies of SSc patients with ACA-positive and sclerodactyly were higher but with puffy fingers were lower in SIC "progressive" group than in "non-progressive" group (non-progressive vs progressive; 24.2 vs 59.1%, p=0.009; 33.3 vs 63.6%, p=0.03; 72.7 vs 45.5%, p=0.03). The prevalence of pitting scar and Interstitial lung disease were tended to be higher in SIC "progressive" compared to SIC "non-progressive" group (non-progressive vs progressive; 15.6 vs 36.4%, p=0.07; 21.1 vs 45.5%, p=0.06).

Conclusions: The present study demonstrated that the progression of small intestinal involvement was associated with esophageal dilatation at the initial evaluation during long-term follow-up of SSc patients. Our findings also suggested that ACA and skin thickening of the fingers were important factors of small intestinal involvement in SSc patients. The SIC may be a useful tool for the assessment of GI tract involvement in SSc patients during long-term follow-up.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2353

OP0128 DETECTION OF SUB-CLINICAL DIFFUSE MYOCARDIAL FIBROSIS BY NATIVE T1 MAPPING MAGNETIC RESONANCE IMAGING IN A PROSPECTIVE SYSTEMIC SCLEROSIS COHORT

V. Poindron, E. Chatelus, M. Canuet, P. Germain, S. El Ghannudi, T. Martin.
National Referral Center for Systemic Autoimmune Diseases, Hôpitaux Universitaires de Strasbourg, Strasbourg, France

Background: Cardiac involvement in systemic sclerosis (SSc) is the second most frequent SSc-related cause of death. It remains mostly asymptomatic in early stages and is underdiagnosed with routine non-invasive screening. Cardiac magnetic resonance imaging (CMR) is becoming a key actor as it has a better sensitivity than echocardiography (echo). CMR can detect diffuse myocardial fibrosis (DMF) by native T1 mapping, myocardial edema (ME) by T2 mapping and focal fibrosis by late gadolinium enhancement (LGE). Ntusi *et al.* reported an increase of 5% of T1 value suggestive of DMF in 10 of 19 SSc patients[1].

Objectives: To determine the prevalence of cardiac involvement by CMR native T1 and T2 mapping and its correlation with echo data and non-cardiac manifestations in SSc patients.

Methods: 72 patients fulfilling ACR/EULAR classification criteria were prospectively included between 2013–2016. They underwent CMR at 1.5T, including native T1 and T2 mapping, and LGE. Normal T1 value determined in our center was 1032±39 msec. In the present study an elevated native T1>1082 msec was likely representing ventricle (especially left) DMF and T2>55 msec representing ME [2].

Results: Patients characteristics: mean age: 56±14.8; diffuse disease: 38 (52.8%); anti-Scl70 positivity: 29 (40.3%); anti-RNApolIII positivity: 6 (8.3%); 21 (29.2%) patients had early disease (<2 years from first non-Raynaud symptom). The mean T1 was 1064±41.6 msec and T2 was 51.8±2.9 msec. 36 patients (50%) had DMF but only 6 (8.3%) had ME. The mean T1 in DMF cases was 1097±14, and the T2 in ME cases was 58.2±1.6 msec. LGE was reported in 25.7% of patients. Although LGE was more frequent in patients with DMF than in those without DMF (13 vs 5, p=0.024), only 13 (36.1%) DMF patients had LGE. Left ventricular ejection fraction (L-VEF), left ventricular telediastolic volume (L-VTDV), Right-VEF and Right-VTDV were similar in DMF and non-DMF (N-DMF) groups. Echo was normal in 18 (50%) patients with DMF and in 25 (69.4%) of N-DMF group (p=0.09). DMF and N-DMF groups were similar for sex ratio, age, cardiovascular risk factors and ischemic heart disease. DMF was more frequent in patients with late disease (27 vs 9, p=0.05). T1 value was positively correlated to pulmonary arterial hypertension and digital ulcerations together ($r=0.31$, p=0.008) but not with Rodnan skin score. Six patients (8.3%) died during the inclusion period: 5 were in DMF group (p=0.09). The alterations of L-VEF and R-VEF were correlated ($r=0.45$, p=0.009). DMF was not associated with skin subsets, interstitial lung disease, auto-antibody profile, all echo parameters, CRP and BNP.

Conclusions: Native T1 mapping detects left ventricular DMF in 50% of patients with SSc including 43% (9/21) of the patients with early disease. Among them, 36% had normal echocardiography and CMR L-VEF and no LGE.

References:

[1] Ntusi NA, Piechnik SK, Francis JM, et al. Subclinical myocardial inflammation and diffuse fibrosis are common in systemic sclerosis a clinical study using myocardial T1-mapping and extracellular volume quantification.J Cardiovasc Magn Reson 2014;16:21.
[2] Germain P, El Ghannudi S, Jeung MY et al. Native T1 mapping of the heart - a pictorial review. Clin Med Insights Cardiol 2014;8:1.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4955

OP0129 MYCOPHENOLATE MOFETIL VERSUS CYCLOPHOSPHAMIDE IN SCLERODERMA-RELATED INTERSTITIAL LUNG DISEASE IN A REAL LIFE SCENARIO

H. Fretheim[1], Ø. Midtvedt[1], E. Volkmann[2], T. Garen[1], M.B. Lund[1], T. Aaløkken[1], Ø. Molberg[1], A.-M. Hoffmann-Vold[1]. *[1]Oslo University Hospital, Oslo, Norway; [2]UCLA, LA, United States*

Background: Systemic sclerosis (SSc) is a serious disease with high risk of interstitial lung disease (ILD); a feared complication with poor prognosis. The SLS 2[1] supported the clinical effectiveness of Mycophenolate Mofetil (MMF) and Cyclophosphamide (Cyc).

Objectives: Evaluate the effect of MMF and Cyc on SSc-ILD in a population based cohort.

Methods: All SSc patients at Oslo University Hospital (OUH) are included in an prospective, observational SSc cohort. All patients are followed annually by rheumatologists and data are recorded in the Norwegian systemic connective tissue disease registry (NOSVAR). Here, we assessed patients diagnosed after the year 2000 (n=433). Longitudinal pulmonary function tests (PFTs), HRCT lung image results, pulmonary hypertension (PH), clinical and demographic data, antibodies and vital status were obtained from NOSVAR. Outcome measures were vital status in December 2016, extent of fibrosis measured on HRCT, FVC and DLCO development.

Results: Among 262 patients with complete data on treatment and ILD, 21 (8%) patients received treatment with Cyc, 14 (5.3%) with MMF and 17 (6.5%) with combination therapy of MMF and Cyc. 55.7% of patients did not receive any treatment for ILD. Baseline characteristics, lung fibrosis and function did not differ significantly between the MMF and Cyc (Table 1). Patients treated with Cyc show a trend of higher mortality. Treatment with Cyc resulted in a significant improvement of lung fibrosis; whereas treatment with MMF resulted in significant progression in lung fibrosis (-1.3% (SD 9.3) and 7.5% (SD 11.1), p=0.024) (Table 1). MMF treatment showed a significant improvement in the DLCO% (1.8% [SD 4.6]); whereas Cyc had a significant decline in the DLCO% (-2.1% [SD 3.5], p=0.14). Less patients treated with MMF developed PH compared with Cyc treatment (1[7.7%] compared to 8[42.1%], p=0.038) (Table 1).

Table 1. Demographics and clinical characteristics of the OUH cohort

	Total cohort (n=262)	Cyc (n=21)	MMF (n=14)	p-value
Age at diagnosis, yrs (SD)	51.4 (15.5)	52.6 (12.1)	43.5 (18.5)	–
Follow-up period, yrs (SD)	6.4 (4.0)	5.5 (3.9)	4.1 (2.3)	–
Male, n (%)	42 (16.0)	6 (28.6)	2 (14.3)	–
dcSSc, n (%)	68 (26.0)	8 (38.1)	10 (71.4)	–
Deceased, n (%)	54 (20.6)	8 (38.1)	4 (28.6)	–
PH, n (%)	35 (14)	8 (42.1)	1 (7.7)	0.038
BL FVC%,(SD)	96.4 (19.5)	83.8 (16.5)	81.5 (13.3)	–
BL DLCO%,(SD)	70.4 (19.5)	54.2 (16.2)	61.8 (14.9)	–
BL fibrosis%,(SD)	6.1 (11.3)	19.1 (15.8)	10.8 (10.3)	–
FVC% decline,(SD)	-0.9 (14.4)	-3.3 (14.3)	2.6 (11.3)	–
Annual FVC% decline,(SD)	-0.02 (6.1)	-0.3 (9.1)	2.3 (4.1)	–
DLCO% decline,(SD)	-9.1 (13.5)	-9 (14.1)	0.7 (12.4)	–
Annual DLCO% decline,(SD)	-2 (5.1)	-2.1 (3.5)	1.8 (4.6)	0.014
Fibrosis% progression,(SD)	1.2 (5.7)	-1.3 (9.3)	7.5 (11.1)	0.024
Annual fibrosis% progression,(SD)	0.5 (2.8)	-0.3 (4.9)	2.3 (4.7)	–

n: number; BL:baseline, SD: standard deviation; FVC: Forced vital capacity; DLCO: diffusing lung capacity for carbon monoxide; dcSSc: diffuse cutaneous SSc; PH: pulmonary hypertension.

Conclusions: Preliminary data from our population based cohort indicate that in a real-life scenario treatment effects of Cyc and MMF appear comparable to randomized clinical trials, but there are some potentially important nuances. Cyc seems to halt fibrosis progression, but toxicity is a major concern, while MMF could have effects on DLCO decline and the development of PH.

References:

[1] Tashkin DP et al. Mycophenolate mofetil versus oral cyclophosphamide in SLS II. Lancet Respir Med. 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4819

THURSDAY, 15 JUNE 2017

Vasculitis clinical and pathogenic highlights

OP0130 MEPOLIZUMAB FOR THE TREATMENT OF PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: A PHASE III RANDOMISED, PLACEBO-CONTROLLED TRIAL

M.E. Wechsler[1], P. Akuthota[2], D. Jayne[3], P. Khoury[4], A. Klion[4], C. Langford[5], P.A. Merkel[6], F. Moosig[7], U. Specks[8], M.C. Cid[9], R. Luqmani[10], J. Brown[11], S. Mallett[11], R. Philipson[12], S.W. Yancey[13], J. Steinfeld[13], P.F. Weller[14], G. Gleich[15]. *[1]National Jewish Health, Denver; [2]UC San Diego Health, la Jolla, United States; [3]University of Cambridge, Cambridge, United Kingdom; [4]NIAID, Bethesda; [5]Cleveland Clinic, Cleveland; [6]University of Pennsylvania, Philadelphia, United States; [7]Schleswig-Holstein Mitte, Neumünster, Germany; [8]Mayo Clinic, Rochester, United States; [9]Hospital Clinic University of Barcelona, Barcelona, Spain; [10]University of Oxford, Oxford; [11]GSK, Uxbridge; [12]Trizell Ltd, Oxford, United Kingdom; [13]GSK, Research Triangle Park; [14]Beth Israel Deaconess Medical Center, Boston; [15]University of Utah Hospital, Salt Lake City, United States*

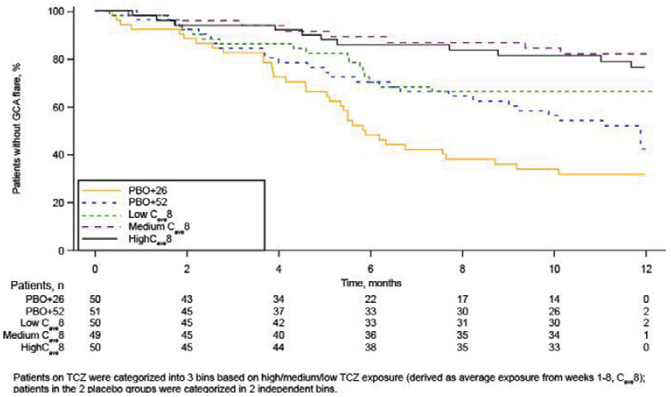
Background: Mepolizumab reduces blood eosinophils with concomitant clinical improvement in some hypereosinophilic syndromes and eosinophilic asthma.
Objectives: To investigate the efficacy and safety of mepolizumab in patients with eosinophilic granulomatosis with polyangiitis (EGPA, Churg-Strauss).
Methods: We conducted a Phase III, randomised, placebo-controlled, double-blind, parallel group, multi-centre study (NCT02020889) in patients with EGPA and a history of relapsing or refractory disease on stable therapy with prednisolone/prednisone ≥7.5–≤50mg/day with or without additional immunosuppressive therapy for ≥4 weeks. Patients were randomised 1:1 to receive mepolizumab 300mg or placebo subcutaneously, in addition to standard of care, every 4 weeks for 52 weeks. After Week 4, glucocorticoid dose could be tapered, per physician judgment, according to a suggested standard of care protocol. Co-primary endpoints (intent-to-treat [ITT] analysis) were accrued duration of remission (Birmingham Vasculitis Activity Score [BVAS]=0, prednisolone/prednisone dose ≤4mg/day) over 52 weeks; and the proportion of patients in remission at both Weeks 36 and 48. Secondary endpoints included average glucocorticoid dose during Weeks 49–52 and time to first EGPA relapse. Safety was also assessed.
Results: The ITT population included 136 randomised patients (mepolizumab n=68, placebo n=68). Baseline characteristics were similar between groups. Duration of remission accrued over 52 weeks was significantly prolonged with mepolizumab vs placebo (odds ratio: 5.91 [95% confidence interval [CI]: 2.68,13.03]; p<0.001); a significantly higher proportion of patients were in remission at Weeks 36 and 48 (32% vs 3%, odds ratio: 16.74 [95% CI: 3.61,77.56]; p<0.001). Significant reductions in average daily prednisolone/prednisone dose during Weeks 49–52 were seen with mepolizumab vs placebo (odds ratio: 0.20[95% CI: 0.09,0.41]; p<0.001). Median (range) prednisolone/prednisone dose during Weeks 49–52 was 5.0 (0.0–113.4)mg/day in the mepolizumab group and 10.0 (0.0–46.3)mg/day in the placebo group. Time to first EGPA relapse was significantly longer with mepolizumab vs placebo (hazard ratio: 0.32[95% CI: 0.21,0.50] ;p<0.001). Rates of adverse events (AEs) and serious AEs were similar for mepolizumab and placebo.
Conclusions: Treatment with mepolizumab significantly increased the likelihood and duration of remission, while reducing glucocorticoid use, in patients with EGPA, with a safety profile consistent with previous studies in severe asthma and EGPA. This demonstrates consistent and meaningful clinical benefits of mepolizumab in patients with EGPA.
Acknowledgements: Funding: GSK [115921] in collaboration with NIAID [U01 AI097073] and the Division of Intramural Research, NIAID, NIH). Abstract submitted to ATS 2017.
Disclosure of Interest: M. Wechsler Consultant for: Teva, AstraZeneca, BSCI, GSK, Novartis, sanofi, Vectura, Sunovion, Regeneron, Ambit bioscience, Meda, Mylan, Gliacure, Tunitas, Genentech, Theravance, Neurotronic, Sentien, P. Akuthota Grant/research support from: National Institutes of Health, Consultant for: Ambrx, Employee of: University of California San Diego, D. Jayne Grant/research support from: GSK, Consultant for: GSK, P. Khoury: None declared, A. Klion: None declared, C. Langford Grant/research support from: GlaxoSmithKline, Bristol-Myers Squibb, Genentech, P. Merkel: None declared, F. Moosig Grant/research support from: Roche, Consultant for: Roche, Chuagi, Lilly, GSK, U. Specks: None declared, M. Cid Consultant for: GSK, Novartis, Roche, Boehringer-Inhelheim, R. Luqmani Grant/research support from: Roche, GSK, Consultant for: Roche, GSK, J. Brown Shareholder of: GSK, Employee of: GSK, S. Mallett Shareholder of: GSK, Employee of: GSK, R. Philipson Employee of: Trizell Ltd, S. Yancey Shareholder of: GSK, Employee of: GSK, J. Steinfeld Shareholder of: GSK, Employee of: GSK, P. Weller: None declared, G. Gleich Shareholder of: Mutual funds, Grant/research support from: NIH, Consultant for: Genentech, Employee of: VAH, U Utah
DOI: 10.1136/annrheumdis-2017-eular.5610

OP0131 OPTIMAL DOSE OF TOCILIZUMAB FOR THE TREATMENT OF GIANT CELL ARTERITIS: EFFICACY, SAFETY, AND EXPOSURE-EFFICACY ANALYSIS FROM GIACTA

J.H. Stone[1], K. Tuckwell[2], S. Dimonaco[2], M. Klearman[3], N.L. Mallalieu[4], M. Aringer[5], D. Blockmans[6], E. Brouwer[7], M.C. Cid[8], B. Dasgupta[9], J. Rech[10], C. Salvarani[11], G. Schett[12], H. Schulze-Koops[13], R. Spiera[14], S.H. Unizony[1], N. Collinson[2] on behalf of GiACTA Investigators. *[1]Harvard Med Sch, Boston, United States; [2]Roche Products Ltd, Welwyn Garden City, United Kingdom; [3]Genentech, S San Francisco; [4]Roche Innovation Ctr, New York, United States; [5]Abteilung für Rheumatologie, Dresden, Germany; [6]U Hosp Gasthuisberg, Leuven, Belgium; [7]U Groningen Med Ctr, Groningen, Netherlands; [8]Hosp Clínic, U Barcelona, IDIBAPS, Barcelona, Spain; [9]Southend U Hosp, Westcliff-on-Sea, United Kingdom; [10]Friedrich-Alexander-U Erlangen-Nürnberg, Erlangen, Germany; [11]Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy; [12]Inst Clin Immunol, Erlangen; [13]Div Rheum Clin Immunol, U Munich, Munich, Germany; [14]Hosp Special Surg/Cornell, New York, United States*

Background: GiACTA, a randomized, double-blind, placebo-controlled trial, evaluated the efficacy and safety of tocilizumab (TCZ), an IL-6 receptor-α inhibitor, in patients with giant cell arteritis (GCA).[1,2]
Objectives: Secondary analyses to evaluate the differential efficacy and safety of TCZ between patients with new-onset and relapsing GCA and to evaluate the TCZ exposure-efficacy relationship at week 52 of the trial.
Methods: Patients aged ≥50 years with active GCA were randomly assigned 1:1:2:1 to short-course prednisone (PBO+26), long-course prednisone (PBO+52) (26-week or 52-week prednisone taper + weekly subcutaneous [SC] placebo, respectively), weekly (TCZ-QW) or every-other-week (TCZ-Q2W) SC TCZ 162 mg + 26-week prednisone taper. Subgroup analysis was performed by disease-onset status (new-onset vs relapsing) to evaluate the proportions of patients in sustained remission at week 52 and time to flare. The impact of TCZ exposure, categorized into high, medium and low tertiles, on time to flare was evaluated across all patients in all treatment arms.
Results: Randomization included 251 patients, 119 (47%) with new-onset and 132 (53%) with relapsing GCA, distributed evenly across groups. Higher proportions of patients achieved sustained remission in the TCZ vs placebo groups regardless of disease onset (new-onset, relapsing–TCZ-QW: 59.6%, 52.8%; TCZ-Q2W: 57.7%, 47.8%; PBO+26: 21.7%, 7.4%; PBO+52: 21.7%, 14.3%, respectively). Patients with relapsing disease at baseline were in relapse-free remission longer and thus had lower risk for flare (hazard ratio) when treated with TCZ-QW than TCZ-Q2W. Hazard ratio (99% CI) for flare vs PBO+26 was 0.23 (0.09–0.61) for TCZ-QW and 0.42 (0.14–1.28) for TCZ-Q2W; vs PBO+52 it was 0.36 (0.13–1.00) for TCZ-QW and 0.67 (0.21–2.10) for TCZ-Q2W. TCZ exposure-efficacy analysis showed that most patients in the low exposure tertile had been treated with TCZ-Q2W (80%) whereas those with medium and high exposure primarily received TCZ-QW (84% and 98%, respectively). Kaplan-Meier analysis demonstrated that patients with higher exposure benefited from a longer time to flare (Figure). Adverse events (AEs) were similar across groups. Serious AEs were reported in 15.0% TCZ-QW, 14.3% TCZ-Q2W, 22.0% PBO+26 and 25.5% PBO+52 patients; rates were similar between new-onset and relapsing patients.

Figure. Time to first GCA flare after clinical remission by exposure (tertile of $C_{ave}8$)



Patients, n						
PBO+26	50	43	34	22	17	14	0
PBO+52	51	45	37	33	30	26	2
Low $C_{ave}8$	50	45	42	33	31	30	2
Medium $C_{ave}8$	49	45	40	36	35	34	1
High $C_{ave}8$	50	45	44	38	35	33	0

Patients on TCZ were categorized into 3 bins based on high/medium/low TCZ exposure (derived as average exposure from weeks 1-8, $C_{ave}8$); patients in the 2 placebo groups were categorized in 2 independent bins.

Conclusions: The compelling treatment effect of TCZ in GCA patients as measured by sustained remission to 52 weeks was consistent regardless of disease-onset status. Duration of relapse-free remission until flare was longer in patients with higher TCZ exposure, most notably in relapsing patients treated with TCZ-QW.
References:
[1] Unizony SH et al. Int J Rheumatol. 2013;2013:912562.
[2] Stone JH et al. 2016 ACR/ARHP Annual Mtg; Washington, DC; A911.
Disclosure of Interest: J. Stone Grant/research support from: Roche, Genentech, Xencor, Consultant for: Roche, Genentech, Xencor, K. Tuckwell Shareholder of: Roche, Employee of: Roche, S. Dimonaco Employee of: Roche Products Ltd., M. Klearman Employee of: Genentech, N. Mallalieu Shareholder of: Roche, Employee of: Roche, M. Aringer Speakers bureau: Roche, Chugai, D. Blockmans:

None declared, E. Brouwer Consultant for: Roche, M. Cid Speakers bureau: Roche, Novartis, B. Dasgupta Speakers bureau: Roche, GlaxoSmithKline, J. Rech: None declared, C. Salvarani: None declared, G. Schett Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Lilly, Novartis, Roche, Sanofi, UCB, H. Schulze-Koops: None declared, R. Spiera Grant/research support from: Roche, Genentech, Consultant for: Roche, Genentech, S. Unizony: None declared, N. Collinson Employee of: Roche Products Ltd.
DOI: 10.1136/annrheumdis-2017-eular.2381

OP0132 LOW-DOSE INTERLEUKIN-2 SELECTIVELY RESTORE REGULATORY T CELL NUMBERS IN PATIENTS WITH BEHCET'S DISEASE

X. Fu[1], J. Li[2], X. Li[2], J. Luo[2], C. Gao[2], Q. Chen[2]. *[1]Department of Rheumatism; [2]The Second Hospital of Shanxi Medical University, Taiyuan, China*

Background: The lack of $CD4^+CD25^+Foxp3^+$ T regulatory cell (Treg) has been associated with human systemic autoimmune diseases, such as Behcet's disease (BD). IL-2, an essential growth and survival factor for Treg cells.However, the significance of Treg cells in the pathogenesis and the effect of low dose of IL-2 on BD are remain to investigate.
Objectives: The lack of $CD4^+CD25^+Foxp3^+$ T regulatory cell (Treg) has been associated with human systemic autoimmune diseases, such as Behcet's disease (BD). IL-2, an essential growth and survival factor for Treg cells.However, the significance of Treg cells in the pathogenesis and the effect of low dose of IL-2 on BD are remain to investigate.
Methods: Eighty patients with BD and seventy healthy donors were enrolled. $CD4^+$T cell subsets in peripheral blood mononuclear cells from these people were measured by multicolour flow cytometry. Twenty-six patients were treated daily with subcutaneous injections of 0.5 million IU of human IL-2 for five consecutive days, $CD4^+$T cell subsets were analysed before and after treatment by flow cytometry.
Results: Compared to health control,the absolute counts of circulating Treg cells were significantanty decreased in patients with BD (median:29.93 cell/uL VS median:33.16 cell/uL; p=0.039) and it is negative correlation with disease activity. While the ratios of Th17/Treg in patients with BD (median:0.29;n=80,p=0.034) were significantly higher than those of health control (median:0.2;n=70).No diffrernce in the absolute counts of circulating Th17 cells ($CD4^+IL\text{-}17^+$) between patients with BD and health control. Treatment of patients with BD with a low-dose of IL-2 regimen selectively increased the absolute counts of Treg cells, from a median of 18.97cell/uL to 74.68 cell/uL (at 5 days) (p=0.000). No significant difference was observed in the absolute counts of circulating Th17, Th1 and Th2 cells after IL-2 treatment.
Conclusions: Th17/Treg cells may play a role in the pathogenesis of Patients with BD, low-dose of IL-2 proposes a selective biological treatment strategy by restoring immune tolerance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4047

OP0133 COLOUR DOPPLER ULTRASONOGRAPHY OF FACIAL AND OCCIPITAL ARTERIES IN PATIENTS WITH GIANT CELL ARTERITIS: THE FREQUENCY OF INVOLVEMENT AND THE ROLE OF THEIR ASSESSMENT IN DAILY PRACTICE: A PROSPECTIVE STUDY

R. Jese, Ž. Rotar, M. Tomšič, A. Hočevar. *Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia*

Background: Giant cell arteritis (GCA) is the most common systemic large and medium size artery vasculitis in Western countries. Colour Doppler Sonography (CDS) allows us to study the involvement of the cranial arteries other than the temporal arteries in GCA which cannot be safely biopsied such as the facial (FaA), and occipital (OcA) arteries.
Objectives: We aimed to estimate the frequency of the FaA, and OcA involvement in GCA; and to explore the clinical characteristics of these subgroups of patients.
Methods: From 1 January 2014 to 31 December 2016, we prospectively performed a CDS of the FaA, and OcA in addition to the temporal (TA), and the extracranial supra-aortic arteries in all newly diagnosed patients suspected of having GCA. We used a Philips IU22 with a 5–17.5 MHz multi-frequency linear probe from January 2014 to August 2016 and a Philips Epiq 7 with a 5–18 MHz multi-frequency linear probe from September 2016 to December 2016. All the arteries were evaluated in two planes for the highly specific *halo*-sign.
Results: During the 36-month observation period we performed a CDS of the cranial and extra-cranial arteries in 93 GCA (66.7% female) patients. The patients' median (IQR) age was 73.7 (66.1–79.1) years, and they had a median (IQR) symptom duration of 30 (21–90) days. We observed the *halo*-sign on the FaA, and OcA in 38 (40.9%), and 29 (31.2%) cases, respectively. The FaA, and OcA were simultaneously affected in 18/93 (19.4%) cases. The FaA, or OcA were affected in 4/22 (18.2%) patients with a negative TA CDS. Patients with an FaA involvement had the highest frequency of severe visual manifestations, with permanent visual loss representing 70% of all visual manifestations. Patients with an OcA involvement least commonly had extracranial large vessel disease.
Conclusions: A fifth of patients with a negative CDS of the TAs had signs of vasculitis only on the CDS of the FaA, or OcA. The CDS of the FaA, and OcA identified approximately 5% more patients with GCA than the CDS of the TA alone.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6073

OP0134 LONG TERM OUTCOME AND PROGNOSIS FACTORS OF COMPLICATIONS IN TAKAYASU'S ARTERITIS: MULTICENTER STUDY OF 318 PATIENTS

C. Comarmond[1], L. Biard[2], M. Lambert[3], A. Mekinian[4], Y. Ferfar[1], J.-E. Kahn[5], Y. Benhamou[6], L. Chiche[7], F. Koskas[7], P. Cluzel[8], E. Hachulla[3], E. Messas[9], M. Resche-Rigon[10], T. Mirault[9], P. Cacoub[1], D. Saadoun[1] on behalf of French Takayasu network. *[1]Internal Medicine and Clinical Immunology, GROUPE HOSPITALIER PITIÉ-SALPÊTRIÈRE; [2]Saint-Louis, Paris; [3]Internal Medicine, CHU Lille, Lille; [4]Internal Medicine, CHU Saint-Antoine, Paris; [5]Internal Medicine, Foch, Suresnes; [6]Internal Medicine, CHU Rouen, Rouen; [7]Vascular surgery; [8]Imagerie CardioVasculaire et de Radiologie Interventionnelle, GROUPE HOSPITALIER PITIÉ-SALPÊTRIÈRE; [9]Vascular Medicine, HEGP; [10]SBIM, Saint-Louis, Paris, France*

Objectives: To assess long term outcome and to elaborate a prognostic score for vascular complications in patients with Takayasu arteritis (TA).
Methods: Retrospective multicenter study of characteristics and outcome of 318 TA patients [86% of females; median age 36 [25–47] years; median follow-up of 6.1 years] fulfilling ACR and/or Ishikawa criteria. Factors associated with the event free survival (EFS), relapse free survival (RFS) and incidence of vascular complications were assessed. A prognostic score for vascular complications was elaborated based on a multivariate model.
Results: The 5- and 10-years event free survival (EFS), relapse free survival (RFS) and complication free survival were 48.2% (42.2;54.9) and 36.4% (30.3;43.9), 58.6% (52.7;65.1) and 47.7% (41.2;55.1), and 69.9% (64.3;76) and 53.7% (46.8;61.7), respectively. Progressive disease course (p=0.018) and carotidodynia (p=0.036) were independently associated with EFS. Male gender (p=0.048), elevated C reactive protein level (p=0.013), and carotidodynia (p=0.003) were associated with RFS. Progressive disease course (p=0.017), thoracic aorta involvement (p=0.009), and retinopathy (p=0.002) were associated with complication free survival. We define high risk patients for vascular complications according to the presence of two of the following factors (i.e a progressive clinical course, thoracic aorta involvement and/or retinopathy). The probability of complication free survival at five years was 78.4% (69.4;88.6) and 51.5% (38.3;69.2) in the low risk and high risk group, respectively.
Conclusions: This nationwide study shows that 50% of TA patients will relapse and experience a vascular complication at 10 years. We could define high risk TA patients for vascular complications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3579

OP0135 TOCILIZUMAB IN GIANT CELL ARTERITIS: GIACTA TRIAL VERSUS A SERIES OF PATIENTS FROM CLINICAL PRACTISE

L.C. Domínguez-Casas[1], J. Loricera[1], A. Mera[2], E. Pérez-Pampín[2], J.L. Hernández[3], S. Castañeda[4], N. Vegas-Revenga[1], E. Pons[1], M.Á. González-Gay[1], R. Blanco[1]. *[1]Rheumatology, Hospital Universitario Marqués de Valdecilla. IDIVAL, Santander; [2]Rheumatology, Complejo Hospitalario Universitario de Santiago, Santiago de Compostela; [3]Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL, Santander; [4]Rheumatology, Hospital Universitario de la Princesa, Madrid, Spain*

Background: Baseline characteristics of patients from GiACTA trial have been recently reported at the ACR-2016 conference (1). GiACTA trial is a randomized, phase III controlled clinical trial evaluating the efficacy of tocilizumab (TCZ) in giant cell arteritis (GCA) (2). We had previously published a multicenter study on the use of TCZ in refractory GCA in a clinical practice setting (3).
Objectives: Our aim was to compare both studies, emphasizing on the baseline characteristics of the patients.
Methods: Comparative study between the GiACTA trial and our multicenter clinical practice study. In the latter, the diagnosis of GCA was established by the ACR-1990 criteria and in the GiACTA trial by the ACR modified criteria. In the clinical practice study, TCZ was used at standard IV dose (8 mg/kg/month), while in the GiACTA trial it was given subcutaneously (162 mg every 1 or 2 weeks, depending on the therapeutic arm). Quantitative variables were expressed as mean ± SD and were compared with the Student's t-test. Dichotomous variables were expressed as percentages and compared using the chi-square test.
Results: In the GiACTA trial, 47.4% were newly diagnosed GCAs, while in the clinical practice study were all refractory to conventional treatment. The TABLE summarizes the main baseline characteristics of both studies. Compared with the GiACTA trial, in the clinical practice study were significantly greater: a) the mean time between the diagnosis of GCA and the onset of TCZ, b) the proportion of patients with polymyalgia rheumatica and ischemic optic neuritis, c) the proportion of positive PET/CT scans, d) the mean value of ESR, and e) the proportion of patients who had received conventional immunosuppressant agents (mainly MTX) before starting TCZ. There was also a significant lower proportion of sustained remission in the clinical practice study. When only GiACTA patients with

relapsing-GCA were analyzed, these differences were maintained, except for the mean time from GCA diagnosis and the prevalence of ischemic optic neuropathy. Data on remissions were not available in this subgroup of GiACTA patients.

	GiACTA overall (n= 251)	GiACTA (only relapsing-GCA; n=132)	Clinical Practice (n= 22)	GiACTA (overall) vs Clinical Practice p	GiACTA (relapsing) vs Clinical Practice p
Women / men	188/63	99/33	17/5	0.99	0.97
Age, mean (SD)	69 (8.2)	69.1 (8)	69 (8)	1	0.
Inclusion criteria	ACR 1990 modified	ACR 1990 modified	ACR 1990	-	-
Newly diagnosed GCA/ recurrent GCA	119/132	0/132	0/22	**< 0.0001**	-
Time (months) from GCA diagnosis, mean (SD)	9.1 (16.8)	16.9 (20.3)	32,1 (39.6)	**0.01**	0.09
Signs/symptoms of GCA at TCZ onset#	98 (39)	59 (44.7)	9 (41.0)	0.96	0.92
PMR, n (%)	49 (19.5)	40 (30.3)	16 (72.7)	**< 0.0001**	**0.0003**
Unilateral blindness, n (%)	4 (1.6)	4 (3)	1 (4.5)	0.87	0.78
Bilateral blindness, n (%)	1 (0.4)	1 (0.8)	1 (4.5)	0.38	0.66
Ischemic optic neuropathy, n (%)	2 (0.8)	2 (1.5)	2 (9.1)	**0.003**	0.18
Amaurosis fugax, n (%)	2 (0.8)	1 (0.8)	0 (0)	0.38	0.31
Blurred vision, n (%)	14 (5.6)	10 (7.6)	0 (0)	0.53	0.68
ESR, mean (SD)	24 (19.4); n= 246	26.8 (19.6)	51.7 (35.4)	**0.002**	**0.004**
CRP, mean (SD)	7.5 (13.4); n= 250	8.4 (15.4)	4.1 (5.9)	**0.03**	**0.02**
Positive TAB, n (%)	156/172 (90.7)	82 (62.1)	16 (72.7)	**0.03**	0.47
Imaging techniques, n (%)	138 (55)	70 (53)	16 (72.7)	0.17	0.14
Positive MRA, n (%)	8 (3.2)	4 (3)	1 (4.5)	0.77	
Positive CT scan, n (%)	13 (5.2)	7 (5.3)	1 (4.5)	0.71	0.78
Positive PET/CT scan, n (%)	97 (38.7)	42 (31.8)	14 (63.6)	**0.004**	**0.008**
Patients on corticosteroids at study onset, n (%)	251 (100)	132 (100)	21 (95.4)	0.12	0.31
Dosage of prednisone at TCZ onset, mean (SD)	Recent ACG : 40 (13.1) Relapsing ACG: 30.2 (12)	30.2 (12)	26.2 (19.5)	-	0.36
Patients who had received traditional immunosuppressant agents, n (%)	27 (10.8)	23 (17)	19 (86.4)	**< 0.0001**	**< 0.0001**
Patients who had received biologic therapy, n (%)	-	-	2 (9.1)	-	-
TCZ route	SC	SC	IV	-	-
Sustained remission, n (%) §	82 (54.6)	-	6 (27.3)	**0.029**	-
Severe infection, n (%)§	9/150 (6)	-	3 (13.6)	0.39	-

includes localized headache, TA, or scalp tenderness, jaw claudication, new or worsened extremity claudication.
§ In RCT patients with active TCZ therapy were only considered; *p<0.05

Conclusions: Patients receiving TCZ in the clinical practice study have several baseline clinical and laboratory differences with regard to those included in the GiACTA trial and, therefore, data of this trial should be taken cautiously when applied in a real-world scenario.

References:

[1] Stone J et al. Arthritis Rheumatol.2016; 68 (suppl 10). http://acrabstracts.org/abstract/efficacy-and-safety-of-tocilizumab-in-patients-with-giant-cell-arteritis-primary-and-secondary-outcomes-from-a-phase-3-randomized-double-blind-placebo-controlled-trial/.
[2] Tuckwell K et al. Semin Arthritis Rheum. 2016 Nov 15. pii: S0049–0172(16)30275-X.
[3] Loricera J et al. Semin Arthritis Rheum. 2015; 44: 717–23.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3489

OP0136 MICRORNA-223-3P EXPRESSION IN AFFECTED SKIN OF ADULT IGA VASCULITIS CORRELATES WITH THE SEVERITY OF SKIN INVOLVEMENT

A. Hocevar[1], J. Pizem[2], M. Tomsic[1], D. Glavac[2]. *[1]Department of Rheumatology, University Medical Centre Ljubljana; [2]Institute of Pathology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia*

Background: IgA vasculitis (IgAV) represents a common systemic vasculitis in paediatric and adult population. Our current knowledge of disease pathogenesis is still very limited and there is no information on miRNAs profile in IgAV.
Objectives: The aim of our study was to determine the expression of three miRNAs (miR-148–3p, miR-155–5p and miR-223–3p) in the affected skin of adult IgAV patients.
Methods: The study included 65 skin samples from consecutive, untreated IgAV patients (61% male, median age 67.6 years, range 29–91), diagnosed between October 2014 and September 2016, and 10 control skin samples. Total RNA was isolated from tissue section of formalin-fixed, paraffin-embedded samples of biopsied IgAV vasculitic skin lesions and normal skin samples. Expression of miR-148–3p, miR-155–5p and miR-223–3p was measured using qRT-PCR. Skin miRNAs expression was then correlated to clinical characteristics of adult IgAV patients. To present relative miRNA expression the ΔΔCT method was used.
Results: We found significantly higher expression levels of miR-223–3p in the affected skin compared to controls (14-fold; $p<0.001$). The expression of the 148b-3p and miR-155–5p was near normal levels (1.05-fold and 1.13-fold increase, respectively). The differences in the expression of miR-223–3p depending on clinical parameters of IgAV are presented in Table 1. Patients with necrotic skin lesions had significantly higher miR-223 tissue expression than those with non-necrotic purpura (p=0.020). Gastrointestinal tract (GIT) involvement inversely correlated with the level of skin miR-223 expression (p=0.024). No significant relationship between renal involvement and skin miR-223 was found.
Conclusions: miR-223 expression was increased in the affected skin of IgAV in comparison to normal skin. Levels of miR-223 expression correlated with severity of skin involvement and inversely with GIT involvement.

Table 1. miR-223–3p expression in IgAV

Characteristics		Number of cases	ΔΔCT miR223–3p median	IQR1	IQR2	P value
General symptoms	YES	10	3.11	1.86	5.55	0.683
	NO	55	3.72	2.53	5.38	
Arthritis	YES	6	3.04	2.67	4.60	0.482
	NO	59	3.72	2.48	4.60	
Generalized purpura	YES	37	3.72	2.46	5.87	0.615
	NO	28	3.63	2.56	5.10	
Skin necroses	YES	32	4.68	2.94	5.84	0.020
	NO	33	3.19	1.97	4.76	
GIT involvement	YES	16	2.78	1.69	3.90	0.024
	NO	49	4.29	2.69	5.62	
Severe GIT involvement	YES	5	2.67	1.88	3.07	0.078
	NO	60	4.22	2.56	5.57	
Renal involvement	YES	28	4.29	2.69	5.72	0.260
	NO	37	3.20	1.82	5.41	
Severe renal involvement	YES	9	4.50	2.44	5.13	0.955
	NO	56	3.60	2.49	5.50	
Elevated serum IgA level	YES	30	4.63	2.71	5.93	0.041
	NO	35	3.19	1.75	4.80	

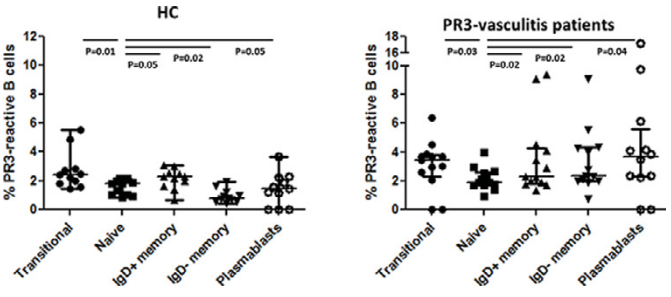
Legend: generalized purpura - purpura above the waist; GIT - gastrointestinal tract; severe GIT involvement - bloody diarrhoea or ileus or surgical intervention; severe renal involvement - acute kidney injury or nephrotic syndrome.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2250

OP0137 AUTO-REACTIVE B CELLS ESCAPE PERIPHERAL TOLERANCE CHECKPOINTS IN PATIENTS WITH PR3-ANCA ASSOCIATED VASCULITIS

D. Cornec[1,2], A. Hummel[1], T. Peikert[1], J.-O. Pers[2], U. Specks[1]. *[1]Mayo Clinic, Rochester MN, United States; [2]CHRU and University, Brest, France*

Background: While extensive studies have been performed to characterize ANCA, little is known about the auto-reactive B cells that produce these autoantibodies. Indirect evidence previously suggested the presence of circulating PR3-specific B cells in patients with PR3-ANCA-associated vasculitis (AAV).
Objectives: To develop a method to detect circulating PR3-specific B cells in patients with PR3-AAV, to study their proportion among the different B-cell subsets and to assess their relationship with disease activity.
Methods: An enzymatically inactive, conformationally mature, recombinant PR3 (rPR3) was tagged using FITC or biotin. To study the ability of this rPR3 to bind specifically to cells expressing PR3-specific immunoglobulins on their surface, we used two hybridoma cell lines, MCPR3–2 (producing an anti-human PR3 monoclonal antibody) and MCPR3–13 (producing an anti-mouse PR3 monoclonal antibody, with no cross-reactivity with human PR3). We measured the proportion of PR3-FITC positive B cells among PBMCs in 13 patients with PR3-AAV and 14 healthy controls (HCs) by flow cytometry. We then developed a multi-color flow cytometry including CD19, IgD, CD27, CD38, CD24 and biotinylated rPR3 to measure the proportion of PR3-specific B cells among different B-cell subsets in an independent group of 13 patients with PR3-AAV and 11 HCs.
Results: rPR3 efficiently bound MCPR3–2 hybridoma cells but not MCPR3–13. Specificity of the staining was confirmed by competition experiments: pre-incubation of MCPR3–2 cells with untagged human rPR3 totally abrogated rPR3-FITC staining, whereas pre-incubation with mouse rPR3 had no effect. Dose-ranging experiments defined the optimal concentration of rPR3 to stain cells expressing anti-PR3 immunoglobulin. The mean (SEM) proportion of rPR3-FITC-stained B cells was higher in patients with PR3-AAV compared to HCs: 2.10% (2.33) vs 0.45% (0.19) respectively, $p<0.001$. Patients with active disease had numerically higher proportions of PR3-specific B cells than patients in remission: 3.66% (3.28) vs 1.10% (0.52), p=0.09. In HCs, the proportion of PR3-specific B cells was highest among the transitional B-cell subset, and decreased along with the maturation of B cells (figure). Conversely, in patients, the proportion of PR3-specific B cells progressively increased with the maturation of B cells (median 1.9% of naïve B cells, 2.30% of IgD+ memory B cells, 2.37% of IgD- memory B cells, and 3.68% of plasmablasts, $p<0.05$ for all comparisons with the naïve subset).



Conclusions: This study describes an original method to detect and study

circulating auto-reactive B cells in patients with PR3-AAV, and suggests that PR3-specific B cells are associated with disease activity and may represent a promising biomarker to predict relapse risk in patients in clinical remission. The progressive enrichment in PR3-specific B cells during the B-cell maturation steps in patients suggest that auto-reactive B cells are actively selected and escape peripheral tolerance checkpoints.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6505

THURSDAY, 15 JUNE 2017

HPR mind over matter - patients perspectives

OP0138-HPR DO PATIENTS' TREATMENT BELIEFS AFFECT TREATMENT CHOICES IN KNEE AND HIP OSTEOARTHRITIS?

E.M. Selten[1], R. Geenen[2], H.J. Schers[3], F.H. van den Hoogen[1], R.G. van der Meulen-Dilling[4], W.H. van der Laan[5], M.W. Nijhof[6], C.H. van den Ende[1], J.E. Vriezekolk[1]. *[1]Rheumatology, Sint Maartenskliniek, Nijmegen; [2]Psychology, Utrecht University, Utrecht; [3]Primary and Community Care, Radboud University Nijmegen Medical Centre, Nijmegen; [4]Physical Therapy and Manual Therapy, Partnership Velperweg, Arnhem; [5]Rheumatology, Sint Maartenskliniek, Woerden; [6]Orthopaedics, Sint Maartenskliniek, Nijmegen, Netherlands*

Background: Patients' beliefs about treatment modalities for knee/hip osteoarthritis (OA) might influence their treatment choices. The Theory of Planned Behavior predicts that patients' beliefs, the norms and values of one's social environment (subjective norm) and one's perceived self-efficacy influence behaviour[1]. Moreover, symptom severity may influence treatment choices[2]. However, these relationships have not been studied yet in the context of treatment decision-making.

Objectives: To test whether treatment beliefs, subjective norm, perceived self-efficacy and symptom severity were associated with intended treatment choices in OA.

Methods: Patients with knee/hip OA who visited the Sint Maartenskliniek in 2015 and 2016 (N=700) were invited to fill out a booklet. The Treatment beliefs in OsteoArthritis questionnaire was used to assess positive and negative treatment beliefs regarding five treatment modalities: physical activities, pain medication, physiotherapy, injections and arthroplasty. Other measures were demographic and clinical variables, self-efficacy (ASES), and symptom severity (WOMAC). Associations between variables were assessed in three models (Figure 1): 1) whether treatment beliefs are associated with intended treatment choice (model 1); 2) whether treatment beliefs, subjective norm and perceived self-efficacy are associated with intended treatment choice (model 2); 3) whether treatment beliefs, subjective norm, perceived self-efficacy and symptom severity are associated with intended treatment choice (model 3). Path analyses were conducted to examine the hypothesized associations.

Results: 289 patients filled out the booklet. Model 2 had the highest explained variance for each of the treatment modalities (range 32–45%). Positive treatment beliefs and subjective norm were consistently associated with intended treatment choice across all treatment modalities. Negative treatment beliefs were associated with intended treatment choices for pain medication and arthroplasty. Perceived symptom severity was not related to intended treatment choices. No other associations were found.

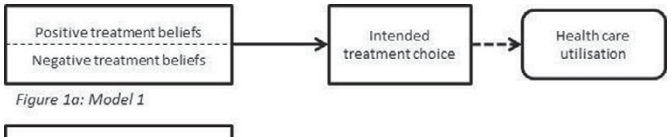


Figure 1a: Model 1

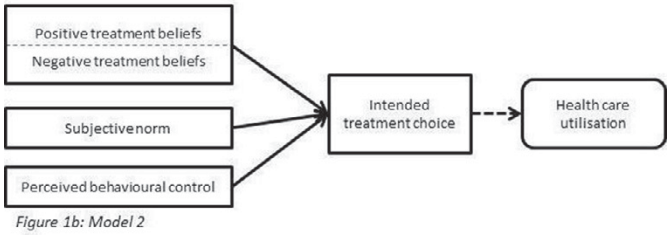


Figure 1b: Model 2

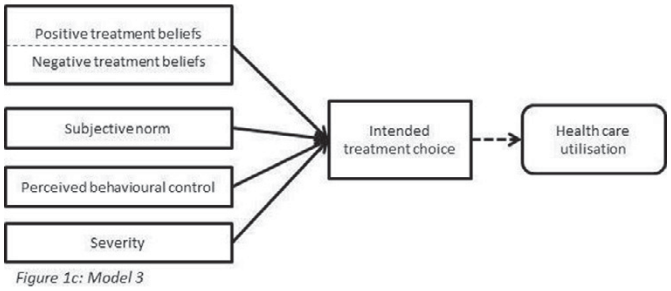


Figure 1c: Model 3

Conclusions: This is the first study that found empirical support for the relationship between treatment beliefs and treatment choices. The findings suggest that positive beliefs about treatment modalities and the norms and values of one's social environment are related to a specific treatment choice for knee/hip OA and should be addressed in the clinician's consulting room.

References:
[1] Ajzen, I. (1991). The Theory of Planned Behavior. Organ Behav Hum Dec 50. 179–211.
[2] Rosemann (2007). Health service utilization patterns of primary care patients with osteoarthritis. BMC Health Serv Res 7: 167.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4834

OP0139-HPR REDUCING ARTHRITIS FATIGUE - CLINICAL TEAMS (RAFT) USING COGNITIVE-BEHAVIOURAL APPROACHES: AN RCT

S. Hewlett[1], N. Ambler[2], C. Almeida[1], P. Blair[3], E. Choy[4], E. Dures[1], W. Hollingworth[3], B. Kadir[3], J. Kirwan[3], Z. Plummer[1], C. Rooke[5], J. Thorn[3], J. Pollock[1] on behalf of RAFT Study Group. *[1]University of the West of England, Bristol; [2]Southmead Hospital; [3]University of Bristol, Bristol; [4]University of Cardiff, Cardiff; [5]Bristol Royal Infirmary, Bristol, United Kingdom*

Background: RA fatigue is common. Group Cognitive Behavioural Therapy by CBT therapists is effective[1] but few rheumatology teams have psychologists, thus we trained rheumatology teams to deliver RAFT, a cognitive behavioural approach (CBA).

Objectives: To test if usual care plus a group CBA course for RA fatigue delivered by rheumatology teams reduces fatigue impact more than usual care alone, in a randomised controlled trial.

Methods: A pair of rheumatology nurses/OTs in each of 7 UK hospitals were trained in RAFT. RAFT is 6, weekly 2hr group sessions and a consolidation session (wk 14). Links between thoughts, feelings and behaviours (pacing, communication, sleep, stress) are addressed, with daily diaries of energy expenditure and weekly goal-setting. Usual care was a 5min discussion of the Arthritis Research UK fatigue booklet. Entry criteria were RA, Bristol RA Fatigue (BRAF-NRS) severity $\geq$6/10 and no recent major medication change. Primary outcome was fatigue impact (BRAF-NRS impact, 0–10) at 26 wks; plus wider aspects of fatigue (BRAF-Multi-Dimensional Questionnaire), pain, disability, sleep, quality of life, mood, self-efficacy, patient global opinion, valued life activities & disease activity. Intention-to-treat regression analysis involved adjustment for baseline scores and centre.

Results: 308/333 randomized patients completed 26 wks. The 25 who withdrew had similar (10yr) disease duration but were older (69 vs 62.4 yrs). Baseline fatigue impact was similar for RAFT (n=156, BRAF-NRS 7.10, SD 1.7) and controls (n=152, 7.23, SD 1.6), as were all clinical variables. At 26 wks the RAFT arm had significantly less fatigue impact than controls (BRAF-NRS 5.74, SD 2.4 vs 6.36, SD 2.4). Mean BRAF-NRS impact was reduced by -1.36 ($p<0.001$) in RAFT vs -0.88 in controls ($p<0.004$). Regression analysis showed the difference between changes in fatigue impact NRS was -0.59 in favour of RAFT (CI -1.11, -0.06). Regression analysis also showed significant differences in secondary outcomes in favour of RAFT: BRAF-MDQ total fatigue -3.42 (CI -6.44, -0.39); Living with Fatigue -1.19 (CI -2.17, -0.21); Emotional Fatigue -0.91 (CI -1.58, -0.23); and RA self-efficacy (RASE, +3.05, CI 0.43, 5.66). There were no differences between arms for changes in fatigue severity or other clinical variables.

99% of RAFT patients would definitely recommend the course to others compared to 50% controls ($p<0.001$). 90% of RAFT patients rated satisfaction $\geq$8/10 (including 62% rating 10/10); in comparison 50% controls rated satisfaction $\geq$8/10 (including 26% rating 10/10, ($p<0.0001$). Over 26 weeks 20 control patients sought extra appointments for fatigue help compared to 8 RAFT patients (14.2% vs 5.3%, $p<0.01$).

Conclusions: Rheumatology teams delivering a manualized CBA group intervention addressing fatigue impact, not only improve RA fatigue impact, but also emotional & overall fatigue, living with fatigue and self-efficacy, with very high patient satisfaction. Providing rheumatology teams with CBA skills is a potential new therapeutic approach to change practice and improve patient outcome.

References:
[1] Hewlett et al, ARD 2011;70:1060–7.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1877

OP0140-HPR ACCEPTANCE AND COMMITMENT THERAPY: A RETROSPECTIVE STUDY OF OUTCOMES FROM A HOSPITAL-BASED, GROUP, PAIN REHABILITATION PROGRAMME IN RHEUMATOLOGY SERVICES IN THE SOUTH EAST OF IRELAND

N. Nealon Lennox[1,2], S. O'Neill[2], A. Hannigan[1]. *[1]GEMS, University Limerick, Limerick; [2]Psychology, Ulster University, Derry, Ireland*

Background: Acceptance and Commitment Therapy (ACT) is a form of cognitive

behavioural therapy (CBT), which focuses on psychological flexibility and behavior change. ACT has been advocated for the treatment of Persistent Pain. A systematic review concluded that ACT is efficacious for enhancing physical functioning and decreasing distress amongst adults with chronic pain attending Pain Rehabilitation Programmes (Hann & McCracken 2014). A call was made for further studies to examine outcomes from more homogenous groups.

Objectives: To assess the effects of an eight-week group ACT, Rheumatology based programme, for people with persistent pain, on pain acceptance, activity engagement, psychological distress and self-efficacy.

Methods: Patients were referred to the programme by three Consultant Rheumatologists over a five-year period. Over one hundred patients' outcome measures were available for this retrospective study from a convenience sample. Consent had been sought routinely from patients who attended the ACT programme and ethical approval was granted from the Hospital Research Ethics Committee (REC) and Ulster University REC. Baseline measures were taken at assessment, on the final day of the programme and at the follow up six-month review. Data was analysed with One Way Repeated Measures ANOVA using SPSSv20. Effect sizes were calculated using Partial Eta Squared and interpreted using the guidelines proposed by Cohen (1998).

Results: For those with scores at all three time points, mean depression scores, anxiety scores and self-efficacy scores were statistically significantly different over time. In addition, for those with activity engagement and pain willingness scores at all three time points, scores were statistically significantly different over time.

Table 1. Change from assessment to the 6-month review

Measure (n)	Mean (SD) at assessment	Mean (SD) at 6-month review	Mean change[2] (95% CI)	P-value	Cohen's d
Depression (n=91)	8.6 (3.62)	5.9 (3.62)	-2.7 (-3.47, -1.99)	<0.001	0.76
Anxiety (n=91)	11.0 (3.81)	8.1 (3.95)	-2.9 (-3.66, -2.14)	<0.001	0.79
Self-efficacy (n=89)	37.0 (12.72)	49.6 (13.20)	12.6 (9.48, 15.80)	<0.001	0.84
Activity engagement (n=78)	32.5 (12.27)	43.8 (10.26)	11.3 (8.59, 14.03)	<0.001	0.94
Pain willingness (n=78)	16.8 (7.46)	23.6 (8.52)	6.8 (4.84, 8.73)	<0.001	0.79

Conclusions: The ACT Pain Rehabilitation Programme at University Hospital Waterford in Ireland has provided significant outcomes for reducing depression and anxiety amongst its participants as measured by the Hospital Anxiety and Depression Scale (HADS). Increases in self-efficacy were also found to be statistically significant. Increases in activity engagement & pain acceptance, as measured by the Chronic Pain Acceptance Questionnaire (CPAQ) also showed statistically significant increases. A number of limitations should be noted i.e. this was a retrospective study and depended on self report measures only. However, positive outcomes suggest ACT is a helpful intervention for people with persistent pain.

References:

[1] Hann, K.E.J., McCracken, L.M. (2014). A systematic review of randomized controlled trials of Acceptance and Commitment Therapy for adults with chronic pain: Outcome domains, design quality, and efficacy. Jounal of Contextual Behavioural Science 3, 217–222.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7008

OP0141-HPR AN INNOVATE MEASUREMENT INSTRUMENT TO ASSESS ACTIVITY LIMITATIONS IN HIP AND KNEE OSTEOARTHRITIS: THE COMPUTERIZED ANIMATED ACTIVITY QUESTIONNAIRE (AAQ) AND ITS PSYCHOMETRIC PROPERTIES

W. Peter[1,2], R. de Vet[2], M. Boers[2], J. Harlaar[2], L. Roorda[1], R. Poolman[3], V. Scholtes[3], M. Steultjens[4], E. Roos[5], F. Guillemin[6], M.G. Benedetti[7], A. Escobar Martinez[8], H. Dagfinrud[9], H. Buitelaar[10], J. Boogaard[10], C. Terwee[2]. *[1]READE; [2]VU University Mediacal Center; [3]OLVG, Amsterdam, Netherlands; [4]Glasgow Caledonian University, Glasgow, United Kingdom; [5]University of Southern Denmark, Odense, Denmark; [6]University of Lorraine, Nancy, France; [7]Istituto Ortopedico Rizzoli, Bologna, Italy; [8]Basurto University Hospital, Bizkaia, Spain; [9]Diakonhjemmet Hospital, Oslo, Norway; [10]Patient Research Partner, Amsterdam, Netherlands*

Background: The Animated Activity Questionnaire (AAQ) measures activity limitations in hip and knee osteoarthritis (HKOA), and was developed in close collaboration with patients[1]. Previously we showed an adequate construct- and cross-cultural validity of the AAQ[2]

Objectives: To determine the reliability, responsiveness and interpretability of the AAQ.

Methods: In 6 European countries the AAQ was completed twice on a computer with a 7 days interval by 238 patients (DK (36), FR (37), IT (51), NL (39), SP (36), UK (39)). Reliability was assessed by calculating internal consistency (Cronbach's alpha), the intra-class correlation coefficient (ICC), the Standard Error of Measurement (SEM) and the Smallest Detectable Change (SDC). In the Netherlands, an additional group of 92 patients were followed for 6 months in order to assess responsiveness. Data from the AAQ, a PROM (the Hip disability or Knee injury Osteoarthritis Outcome Score, ADL subscore), and performance-based tests (the Timed Up and Go test, Stair Climbing Test and 30 seconds Chair Stands Test) were collected. To estimate the Minimal Important Change (MIC) of the AAQ an anchor-based MIC distribution method was used with a Global Rating of Change (GRC) as anchor. The Receiver Operating Characteristic (ROC) method was used to find the AAQ change score that best discriminates between patients who improved in activity limitations and who are not. The MIC was compared to the SDC in order to facilitate the interpretation of change scores.

Results: Cronbach's alpha was o.94. ICC for test-retest reliability was 0.93 (95% CI: 0.91–0.95). SEM and SDC were 4.9% and 13.5%, respectively. With regard to responsiveness the change scores of the AAQ after 6 months correlated 0.58 with the PROM, 0.42–0.55 with the performance based tests, and 0.46 with GRC. The ROC curve showed an area under the curve of 0.72 with a sensitivity of 63% and a specificity of 81% for the optimal MIC of 9.1 for discrimination. The MIC was smaller than the SDC meaning that the change is important but cannot be distinguished from measurement error in individual patients.

Conclusions: The AAQ, measuring a new construct in the domain physical functioning in addition to a PROM and performance-based tests, showed good construct validity, cross-cultural validity, internal consistency and test-retest reliability. A change in AAQ score over 13.5% indicates a real improvement in activity limitations in HKOA patients. The AAQ seems to have great potential for international use in research but the application in clinical practice needs caution.

References:

[1] Peter WF et al. Arthritis Care Res (Hoboken). 2015 Jan;67(1):32–9.
[2] Peter WF et al. Arthritis Care Res (Hoboken). 2016 Oct 16.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4050

OP0142-HPR THE POTENTIAL BUFFERING ROLE OF SELF-EFFICACY AND PAIN ACCEPTANCE AGAINST INVALIDATION IN RHEUMATIC DISEASES

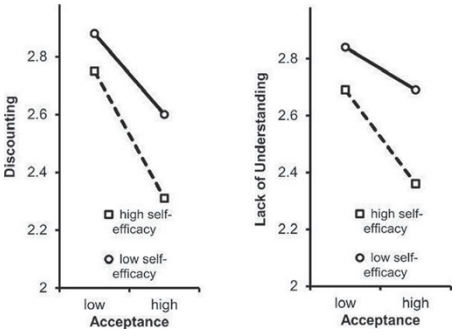
R. Geenen[1], N. Cameron[1], M.B. Kool[1], F. Estévez-López[2], I. López-Chicheri[3]. *[1]Psychology, Utrecht University, Utrecht, Netherlands; [2]Department of Physical Education and Sport, Faculty of Sport Sciences, University of Granada, Granada; [3]Health Sciences, UCAM Catholic University of Murcia, Murcia, Spain*

Background: A substantial number of people with a rheumatic disease perceive invalidation consisting of "lack of understanding" and "discounting" (negative social responses) [1]. Our study was guided by the notion that high self-efficacy will make people feel competent to deal with situations in which control of invalidation is possible and likely to be successful. In other situations, high acceptance will help people to actively and in full awareness experience even adverse situations such as invalidation without unnecessary attempts to change their frequency or form, which is considered a core aspect of acceptance.

Objectives: To get insight into the potential buffering role of self-efficacy and pain acceptance against invalidation, we examined the association of self-efficacy and pain acceptance with invalidation in people with diverse rheumatic diseases.

Methods: The design was cross-sectional. Spanish speaking people (N=1153, 91% female, mean age 45±11 years) with one or multiple rheumatic diseases completed online versions of the Illness Invalidation Inventory [2], the Chronic Pain Acceptance Questionnaire, and the Chronic Disease Self-Efficacy Scale.

Results: Before and after adjustment for age, gender, education, and fibromyalgia diagnosis, higher self-efficacy and higher pain acceptance were independently associated with discounting and lower lack of understanding ($P<0.001$, see Figure). The combined occurrence of high self-efficacy and high acceptance was associated most clearly with lower lack of understanding (interaction: $P=0.03$) and with discounting (interaction: $P=0.07$, not reaching statistical significance): see Figure.



Conclusions: The present study convincingly shows that self-efficacy and pain acceptance are associated with less invalidation. This suggests the usefulness of examining in prospective studies whether interventions aimed at increasing self-efficacy and pain acceptance can help people with rheumatic diseases for whom invalidation is a considerable burden. A cognitive-behavioral model including self-efficacy and acceptance to deal with invalidation is proposed.

References:

[1] Kool MB, van Middendorp H, Boeije HR, Geenen R. Understanding the lack of understanding: invalidation from the perspective of the patient with fibromyalgia. Arthritis Rheum-Arthritis Care Res 2009;61:1650–6.
[2] Kool MB, van Middendorp H, Lumley MA, Schenk Y, Jacobs JW, Bijlsma JW,

Geenen R. Lack of understanding in fibromyalgia and rheumatoid arthritis: the Illness Invalidation Inventory (3*I). Ann Rheum Dis 2010;69:1990–5.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2472

OP0143-HPR DISABILITY IN THE FEET RELATED TO PARTICIPATION IN DAILY LIFE IN PATIENTS WITH EARLY RA – AN INTERVIEW STUDY IN THE SWEDISH TIRA PROJECT

M. Björk[1,2], I. Thyberg[3], E. Valtersson[4], G. Östlund[5], B. Stenström[3], A. Sverker[6]. *[1]Department of Social and Welfare Studies, Linköping University, Norrköping; [2]Rheumatology clinic, Linköping university hospital; [3]Department of Rheumatology; [4]Department of Activity and Health and Department of Medical and Health Sciences, Linköping University, Linköping; [5]School of Health Care and Social Welfare, Mälardalen University, Eskilstuna; [6]Department of Activity and Health, Department of Rehabilitation Medicine, Department of Social and Welfare studies, Linköping university, Linköping, Sweden*

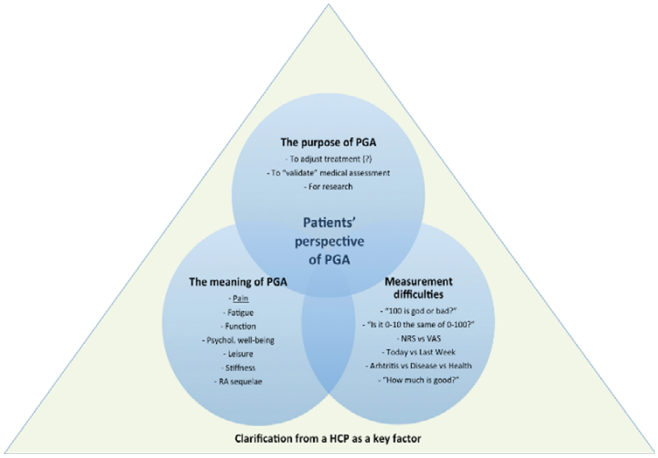
Background: Pain, stiffness and deformity of the feet are related to reduced mobility and participation restrictions in daily activities in patients with established rheumatoid arthritis (RA). The new biological medications are effective and reduce disease activity, but not disability to the same extent. Foot problems are assumed to be related to participation restrictions also in patients with early RA, diagnosed after the introduction of biological medications, hindering for example physical activity. Hence, there is a need for more knowledge about foot problems in order to identify possible needs for rehabilitative interventions.
Objectives: To explore disability related to foot problems in women and men with early rheumatoid arthritis and its relation to participation in daily life.
Methods: 59 patients (58% women, 20–63 years) with early RA were interviewed about participation dilemmas in daily life related to RA, using Critical Incident Technique. The interviews were audio-recorded and transcribed. Data related to foot problems were extracted and analysed thematically. A research partner with RA validated the retrieved categories. The study was approved by the Regional Ethics Committee.
Results: More than 2/3 of the patients mentioned that they had participation restrictions related to foot problems. The analysis revealed 5 categories concerning foot problems and the relation to participation restrictions: 1) foot problems as an early indicator of the disease, 2) hindrance in managing the daily routine and house hold activities, 3) struggling to be mobile, 4) difficulties in doing a god job at work and 5) difficulties in participating in recreation and leisure activities. Both women and men shared many experiences, as difficulties to be physically active. Several women expressed difficulties to use the shoes they wanted. Being able to move on uneven ground in, for example, the forest was something that many men expressed as difficult.
Conclusions: Patients with early RA with access to effective medications and multi professional interventions based on their individual needs still experience a wide range of foot related disability in major life arenas as work, in the household and during leisure time. This indicates a need to pay attention also in today's early RA patients to foot problems in the multi professional rehabilitation to prevent further disabilities and enable physical activity for men and women with RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3294

OP0144-HPR "IT CAN'T BE ZERO": A QUALITATIVE STUDY OF PATIENTS' PERSPECTIVE ON PATIENT GLOBAL ASSESSMENT IN RHEUMATOID ARTHRITIS

M. Henriques[1], C. Duarte[1,2], M. Ndosi[3], A. Marques[2], J.A.P. da Silva[1,2], R.J.O. Ferreira[2,4]. *[1]Faculdade de Medicina da Universidade de Coimbra; [2]Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal; [3]University of the West of England, Bristol, United Kingdom; [4]UICiSA:E, ESEnfC, Coimbra, Portugal*

Background: Patient Global Assessment (PGA) plays an important role in disease activity assessment and treatment decisions in rheumatoid arthritis (RA). However, the meaning of PGA is open to patient interpretation and this may affect the validity and reliability of clinical assessments.
Objectives: We aimed to explore: (i) patients' perspective on PGA and its different formulations (ii) how patients' perspective may be improved by a brief explanation from a health care professional (HCP).
Methods: This was a qualitative study including consecutive patients with RA attending a day hospital and an outpatient department of a university hospital in Portugal. Data collection included 4 focus-groups (FGD) and 3 individual interviews to determine patients' perspectives. To help the discussions, patients completed 3 different PGA formulations consecutively and then a HCP explained what information was expected to inform their PGA. The 3 PGA formulations and their implications were then discussed between the patient and the HCP. Data from the FGDs and the interviews were transcribed verbatim and inductive content analysis was undertaken by two independent researchers. Data were coded and categorised in themes, which were agreed upon with patients, HCP and patient research partners.
Results: Fourteen patients (12 women) with RA participated. Their age ranged from 49 to 72 years, disease duration 4 to 30 years and 11 were on biologic DMARDs. Four main themes emerged (Figure 1): (1) The purpose of PGA. Some patients did not know whether PGA affects their treatment decisions in the same way as the objective measures do: "*if the answer is not in somehow according to the exams we make (...) obviously they might ignore me*". Some believed that PGA was only used for research purposes. (2) The meaning of PGA. Pain was by far the main meaning of PGA, but also fatigue, function and other dimensions including RA sequelae; (3) Measurement difficulties. Many of these difficulties arose from the presentation of the three different PGA formulations, anchor points and their presentations: *"I always think that 100 is great: you feel 100%", "Usually the scale is 0 to 10, here I can see 0 to 100"; "Usually it has the numbers, I answer 2, it's not like a straight line like this one"; "Today is different (...) when they ask the last week, we have to go back in time and the pain isn't the same anymore*". Also cultural issues and the subjectivity of the concept were expressed: *"We, the patients, can't really assess the intensity of the pain, what could be a 9 for her, for me it might be a 5"; "I can never answer 0, because I always have something that affects me"*. (4) Clarification from a HCP as a key factor for global understanding: ["*Sometimes I just give a random number. (...) now maybe I will think more carefully and try to be as accurate as possible*".

Figure 1. Main themes of Patients' perspective of PGA



Conclusions: Our results suggest that patients' interpretation of PGA is diverse and may reflect different symptoms such as pain or psychological well-being and comorbidities. Standardization of PGA is warranted and dedicated patient debriefing is likely to improve the reliability of this assessment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6214

OP0145-HPR RHEUMATOID ARTHRITIS PATIENTS' SUPPORT NEEDS REGARDING MEDICATION USE AND THEIR PERSPECTIVES ON THE APPLICABILITY OF EHEALTH INTERVENTIONS TO ADDRESS THOSE NEEDS: A FOCUS GROUP STUDY

E. Mathijssen[1], J. Vriezekolk[1], A. Eijsbouts[1], B. van den Bemt[1,2]. *[1]Rheumatology; [2]Pharmacy, Sint Maartenskliniek, Nijmegen, Netherlands*

Background: Patients with rheumatoid arthritis (RA) encounter various problems with their medication use, including poor knowledge about disease-modifying antirheumatic drugs (DMARDs)[1], concerns about potential adverse consequences of their medication use[2] and struggles with opening the medication's packaging[3]. Additional support might decrease those problems by targeting RA patients with (eHealth) interventions that address their needs. To date, no studies have explored RA patients' support needs regarding medication use from their own perspectives, and it remains largely unknown if, and to what extent, they perceive a need for eHealth interventions.
Objectives: The objective of this study was twofold: 1) to explore RA patients' support needs regarding medication use; and 2) to gain insight into their perspectives on the applicability of eHealth interventions to address those needs.
Methods: Three focus groups with 28 RA patients (mean age: 65 years, mean disease duration: 19 years) were conducted. All focus groups were audio-recorded and subsequently transcribed verbatim. Two researchers independently conducted an inductive, thematic analysis on the transcripts.
Results: Three themes that described RA patients' support needs regarding medication use were identified: 1) Informational support; 2) Practical support; and 3) Emotional and behavioral support. Informational support refers to the provision of knowledge and facts, including advice, suggestions and feedback from healthcare providers. Practical support includes the strengthening of technical skills (e.g. administering subcutaneous injections), as well as the provision of goods and services. Emotional and behavioral support refers to the interventions enabling RA patients to better cope with their medication use. Their perspectives on the applicability of eHealth interventions to address those needs were also identified. RA patients recognized potential advantages of eHealth interventions, such as being less time consuming and easily accessible. However, concerns

on matters such as privacy, the quality and trustworthiness of information and personal interaction with healthcare providers prevailed.
Conclusions: For most RA patients, informational support regarding medication use is the most important (unmet) need. High-quality, unambiguous information about their medication use was emphasised. Moreover, this information should be provided by healthcare providers on an ongoing basis and tailored to their personal situation. Eliminating RA patients' concerns regarding eHealth interventions should be a first priority before such interventions are applicable to address these informational needs. These findings need to be confirmed in a sample of younger RA patients.
References:
[1] Fayet F, Savel C, Rodere M et al. The development of a questionnaire to evaluate rheumatoid arthritis patient's knowledge about methotrexate. J Clin Nurs 2016;25:682–9.
[2] Neame R, Hammond A. Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis. Rheumatology 2005;44:762–7.
[3] Beckman A, Bernsten C, Parker MG et al. The difficulty of opening medicine containers in old age: a population-based study. Pharm World Sci 2005;27:393–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6344

THURSDAY, 15 JUNE 2017

RA: really a systemic disease?

OP0146 DECREASE IN CARDIOVASCULAR EVENT EXCESS RISK IN RHEUMATOID ARTHRITIS SINCE 2000': A META- ANALYSIS OF CONTROLLED STUDIES

E. Filhol[1], C. Gaujoux-Viala[2], B. Combe[1], J. Morel[1], C. Hua[1], A. Nutz[2], C. Lukas[1], F. Flaisler[2]. [1]*Lapeyronie Hospital, Montpellier;* [2]*Nimes Hospital, Nimes, France*

Background: Compared with the general population, patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular disease or events (CE): stroke, Myocardial Infarction (MI), Congestive Heart Failure (CHF) and Cardiovascular Mortality (CVM). Systemic inflammation is the cornerstone of both RA and atherosclerosis. Over the past fifteen years, new treatment strategies such as tight control, treat to target, methotrexate optimization, biologic DMARDs use has allowed a better control of this inflammation.
Objectives: The aim of this systematic review was to assess the excess risk of presenting a CE in RA patients as compared to general population, before and after the 2000s.
Methods: We systematically searched literature (via Pubmed, Cochrane and abstracts from recent ACR and EULAR congresses) up to March 2016 for observational studies providing data about the occurrence of a CE (among stroke, MI, CHF, CVM) in patients with RA and in a control group. A meta-analysis of the relative risk (RR) concerning patients with RA in relation to the control group was performed for each cardiovascular event and for each period (before and after the 2000s).
Results: Out of 5714 screened references, 28 studies were included. For studies published before 2000, an increased risk of CEs was observed in RA patients:
– RR=1.12 [95% CI 1.04; 1.21], p=0.002 for stroke
– RR=1.25 [1.14; 1.37], p<0.00001 for CHF
– RR=1.21 [1.15; 1.26], p<0.00001 for CVM
– RR=1.32 [1.24; 1.41], p<0.00001) for MI.
For all studies published after the year 2000, the increased risk was not retrieved for CHF (RR=0.58 [0.11; 3.55], p=0.52) and CVM (RR=1.07 [0.74; 1.56], p=0.71). The excess risk of MI was reduced in comparison with the period before 2000: RR=1.18 [1.14; 1.23], p<0.00001.The excess risk of stroke was stable: RR=1.23 [1.06; 1.43], p=0.006.
Discussion: This meta-analysis confirms an increased risk of CEs among people with RA relative to the general population. It also appears that this excess risk is less prevalent than prior to 2000s. This might have two explanations: a better management of the cardiovascular risk in patients with RA and a better control of chronic systemic inflammation thanks to new therapeutic strategies.
Conclusions: The cardiovascular excess risk of RA patients relative to the general population has decreased since 2000s. This suggests that the recent improvements in RA management may have a positive impact on cardiovascular comorbidities.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4415

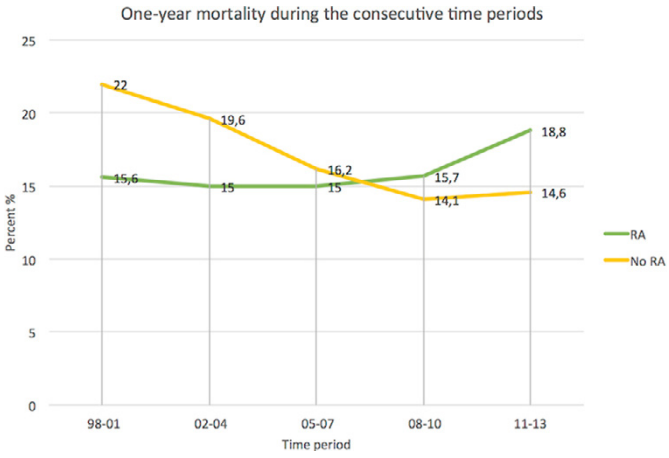
OP0147 TRENDS IN MORTALITY, CO-MORBIDITY AND TREATMENT AFTER ACUTE MYOCARDIAL INFARCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS 1998-2013

M. Skielta[1], L. Söderström[2], S. Rantapää Dahlqvist[3], S. Wållberg Jonsson[3], T. Mooe[4]. [1]*Department of Public Health and Clinical medicine, Rheumatology, Umeå University;* [2]*Unit of Research, Östersund Hospital, Östersund;* [3]*Department of Public Health and Clinical Medicine, Rheumatology, Umeå University, Umeå;* [4]*Department of Public Health and Clinical Medicine, Östersund, Umeå University, Östersund, Sweden*

Background: Rheumatoid arthritis (RA) patients have increased mortality due to cardiovascular disease (CVD). Case fatality after an acute myocardial infarction (AMI) has been reported to be increased. Whether the prognosis after AMI has changed over time in RA is unknown.
Objectives: To study the one-year mortality after a first AMI in RA versus non-RA patients during the time period 1998–2013. To identify time trends in mortality, co-morbidities and secondary preventive treatments and to explore any characteristics associated with mortality.
Methods: We identified all patients with a first time AMI in the Swedish Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA) between 1998–2013. We used the National Patient Register (NPR) to identify AMI patients with RA (RA defined as ≥2 visits to a Rheumatology or Internal Medicine department with a diagnosis of RA). In total 245376 AMI patients were identified, 4268 of them had RA. To study trends over time, the study period was divided into five consecutive time periods. Multivariate Cox regression analysis was used to identify variables associated with mortality.
Results: The one-year mortality in RA patients was stable and lower compared to non-RA patients during the first time periods but thereafter increased above the non-RA patients. In non-RA patients, mortality decreased over time and stabilised during the last time period (Figure). In RA patients the mean age at admission increased from 69 to 73 years, whilst in non-RA patients it was unchanged, 71 years. Atrial fibrillation (AF) was initially more common in non-RA patients but the prevalence decreased over time (from 19.2% to 17.5%). In RA patients, AF increased over time from 15.6% to 21.4%. The prevalence of congestive heart failure (CHF) during hospitalisation decreased markedly more in non-RA (from 41.5% to 22.7%) than in RA patients (from 36.0% to 29.2%). The most important secondary preventive treatments were similar in RA and non-RA patients. In a multivariate Cox model including data from the last time period, 2011–2013, age, CHF during hospitalisation, ST-elevation AMI (STEMI), AF, prior diabetes mellitus, a diagnosis of RA and oral anticoagulation were significantly associated with higher one-year mortality (Table).

Multivariate Cox analysis for the last time period 2011–2013

		P<0,05	95% CI
Age	1,042	0,000	1,039–1,046
CHF	2,101	0,000	1,998–2,220
STEMI	1,848	0,000	1,738–1,965
Prior diabetes	1,370	0,000	1,294–1,450
AF	1,321	0,000	1,248–1,398
RA diagnose	1,257	0,012	1,051–1,502
Oral anticoagulation	1,120	0,000	1,096–1,145



Conclusions: The marked decrease in one-year mortality after AMI seen over time in non-RA patients was not applicable in RA patients. Our finding might to some extent be explained by an increased age at AMI onset and unfavourable trends for AF and CHF in RA. However, RA *per se* was significantly associated with a worse prognosis during the last years of the study period. Secondary preventive treatment was similar in RA and non-RA patients. Further analyses including RA treatments are necessary to gain further insight into reasons behind the discrepant prognosis in RA vs. non-RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4481

OP0148 IMPACT OF A CARDIOVASCULAR EVENT ON DMARD TREATMENT AMONG PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, OR PSORIASIS

J.A. Sparks[1], T. Lesperance[2], N.A. Accortt[2], D.H. Solomon[1]. [1]*Harvard Medical School, Brigham and Women's Hospital, Boston;* [2]*Amgen, Inc, Thousand Oaks, United States*

Background: Chronic inflammatory diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), and psoriasis (PsO) increase the risk of cardiovascular (CV) disease. However, a gap in knowledge exists regarding detailed information on changes in immunosuppressive (DMARD) treatments after a CV event.
Objectives: We describe treatment patterns among patients with RA, PsA, or PsO who were being treated with DMARDs prior to a CV event.
Methods: Patients with RA, PsA, or PsO, who experienced a CV event (acute myocardial infarction, stroke, or cardiac revascularization) between 1/1/2006 and 6/30/2015 were identified in an administrative claims database. Index date was defined as the hospital discharge date for the first CV event during the study period. Patients were required to: be continuously enrolled for 12 months prior to index date; have ≥1 TNFi claim, or a conventional synthetic (cs)DMARD claim, or another biologic DMARD claim within 6 months prior to the index date; and have ≥30 days of follow-up after index date. Treatment patterns were assessed after index date and patients were classified as remaining on ("persistent"), switching, or discontinuing pre-index DMARD medication.
Results: We identified 9,529 patients with RA, PsA, or PsO; prior to the index date, 3,274 (34.4%) patients were on TNFi, 5,177 (54.3%) were on only csDMARDs as monotherapy or combination, and 1,078 (11.3%) were on non-TNFi biologics. Patients on csDMARDs at index date were older (69.4 yrs) than those on TNFi (64.1 yrs) or other biologic DMARDs (66.0 yrs). Approximately 73% of patients were persistent on their pre-CV event treatment, with higher persistence among csDMARD alone (76.0%) and TNFi + csDMARD combo (76.7%) groups and lower in the non-TNFi biologic + csDMARD combo group (60.8%, Table 1). Across all treatment groups, 95% of persistent patients resumed treatment within 90 days after the index CV event. Combination therapy users switched their pre-CV event treatment more than monotherapy users, with non-TNFi biologic users more likely to discontinue all therapy after index CV event. Patients that discontinued all therapy after an index CV event tended to be slightly older females (68.7 yrs vs 67.1 yrs), with a history of PsO (24.4% vs 16.1%), and stroke as index event (49.3% vs 41.3%) compared to those that continued therapy.
Conclusions: In a large US database reflective of typical clinical practice, nearly one-quarter of patients with RA, PsA, or PsO discontinued or switched the pre-event DMARD treatment after a CV event. Further research is needed on whether these DMARD treatment patterns after initial CV event affect risk of repeat CV event.
Disclosure of Interest: J. Sparks Grant/research support from: Amgen, Inc., T. Lesperance Consultant for: Amgen, Inc., N. Accortt Shareholder of: Amgen, Inc., Employee of: Amgen, Inc., D. Solomon Grant/research support from: Amgen, Inc.
DOI: 10.1136/annrheumdis-2017-eular.2324

OP0149 MORTALITY IN NEW-ONSET RHEUMATOID ARTHRITIS - HAS MODERN RHEUMATOLOGY HAD AN IMPACT?

M. Holmqvist[1], L. Ljung[2], J. Askling[1]. [1]*Karolinska Institutet, Stockholm;* [2]*Umeå University, Umeå, Sweden*

Background: A wealth of studies have linked rheumatoid arthritis (RA) with an excess mortality compared to the general population. With increasingly effective anti-rheumatic treatment strategies there is, however, considerable uncertainty whether this mortality gap still exists and, if so, how soon after RA onset it occurs.
Objectives: To assess the mortality in RA compared to the general population with specific focus on when during the course of the disease the risk is increased and if it also applies to patients diagnosed in recent years.
Methods: We performed a population-based cohort study of 17,512 patients with new-onset RA (identified from the Swedish Rheumatology Quality Register) 1997 through 2015, and 78,847 individually matched general population comparator subjects. We followed all individuals using nationwide census registers with full coverage to identify all deaths through 2015. We calculated mortality rates with 95% confidence intervals (CI) and compared the mortality in RA to that in the general population using Cox proportional hazards models adjusted for age, sex, year of diagnosis, and residential area.
Results: During a mean follow-up from RA diagnosis of 7 years, 2,386 RA patients and 9,850 population comparator subjects died (crude incidence: 19 per 1000 in RA and 18 per 1000 in the general population), with only a marginal decline (in the RA and in the general population cohort) during the study period. The overall HR was 0.99 (0.95–1.04), but whereas there was no increase in mortality during the first five years after RA diagnosis; the HR ≥10 years after RA onset was 40% increased. The overall pattern of HRs was similar for patients diagnosed 1997–2001, 2002–2006, and 2007–2011 (table).
Conclusions: The five-year mortality in RA is not increased, neither for patients diagnosed in the past nor for those diagnosed during the most recent five years. By contrast, at least in the most recent inception cohort for which ten-year mortality currently can be calculated (those diagnosed up to 2006), RA is still associated with an increased risk of death.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2580

OP0150 PARADOXICAL EFFECT OF BIOLOGICAL DMARDS IN RHEUMATOID ARTHRITIS PATIENTS WITH OVERWEIGHT AND OBESITY: LESS OFTEN CLINICAL REMISSION, BUT ALSO LESS RADIOLOGICAL DAMAGE

A.V. de Jonge[1], M.M. ter Wee[1,2], I.E. Bultink[1], W.F. Lems[1]. [1]*VU University medical centre, Amsterdam Rheumatology and immunology centre;* [2]*Epidemiology and Biostatistics, VU University medical center, Amsterdam, Netherlands*

Background: The relationship between treatment with biological disease-modifying antirheumatic drugs (DMARDs), including TNF-blocking agents, and disease activity in overweight and obese rheumatoid arthritis (RA) patients has not been clarified yet.
Objectives: The aim of this review is to assess the effect of overweight/obesity on the therapeutic efficacy of these drugs. Secondly, we aimed to assess the influence of overweight/obesity on the occurrence of joint destruction.
Methods: A systematic review of all articles published on these subjects using PubMed and EMBASE was executed. For the first research question, studies were eligible when focused on the clinical efficacy of biological DMARDs only in overweight/obese RA patients versus patients with normal body weight. For the second research question studies were eligible when questioning the relation between overweight and joint destruction in patients with RA. Overweight and obesity were defined according to the following body mass index (BMI) categories; BMI <20 kg/m^2 for underweight, BMI 20–25 kg/m^2 for normal weight, BMI 25–30 kg/m^2 and BMI >30 kg/m^2 for overweight.
Results: A total of 6782 articles were found, of which 12 were eligible for this review. A total of 3647 RA patients were treated with adalimumab, etanercept, infliximab, golimumab, or certolizumab pegol, or TNF blockers, rituximab, or tocilizumab.
Ten studies used disease activity as outcome. In general, these studies showed that higher BMI is associated with poor response, based on either outcome or percentages on remission or improvement defined according to EULAR guidelines. In addition, four studies showed that higher BMI is also associated with higher Health Assessment Questionnaire (HAQ)-scores.
Two articles (of which one article described the results of studies in two different RA cohorts) focused on the association between BMI and joint destruction. These articles showed that higher BMI values were associated with lower odds for having joint destruction. One study also showed that having a BMI <20 kg/m^2 was associated with a higher odds ratio (OR =4.12) for joint destruction.
Conclusions: Higher BMI levels in RA patients treated with biological DMARDs

Abstract OP0148 – Table 1. DMARD treatment patterns for RA, PsA, or PsO patients following an initial CV event (N=9,529)

Treatment prior to CV event	N	DMARD treatment persisted, n (%)	DMARD treatment switched, n (%)	All DMARDs treatment discontinued, n (%)
Entire study sample	9,529	6,985 (73.3%)	1,498 (15.7%)	1,046 (11.0%)
TNFi monotherapy	1,760	1,323 (75.2%)	232 (13.2%)	205 (11.6%)
TNFi + csDMARD combination therapy	1,514	1,160 (76.7%)	299 (19.7%)	55 (3.6%)
csDMARD monotherapy	4,369	3,320 (76.0%)	528 (12.1%)	521 (11.9%)
≥2 csDMARDs combination therapy	808	518 (64.1%)	248 (30.7%)	42 (5.2%)
Non-TNFi biologic monotherapy	718	445 (62.0%)	63 (8.8%)	210 (29.2%)
Non-TNFi biologic + csDMARD combination therapy	360	219 (60.8%)	128 (35.6%)	13 (3.6%)

Abstract OP0149 – Table 1. Hazard ratio (HR) and 95% confidence intervals (CI) adjusted for sex, residential area, year of diagnosis, and age. Overall and stratified by calendar period of RA diagnosis and time since RA diagnosis

		RA duration categories HR (95% CI)			
Calendar period of RA diagnosis	Total follow-up	<1 year	1-<5 years	5–10 years	>10 years
Total study period	1.01 (0.96–1.06)	0.57 (0.48–0.67)	0.90 (0.83–0.97)	1.11 (1.02–1.20)	1.43 (1.28–1.59)
1997–2001	1.09 (1.01–1.18)	0.58 (0.39–0.87)	0.81 (0.68–0.96)	1.06 (0.92–1.21)	1.41 (1.25–1.60)
2002–2006	1.02 (0.94–1.10)	0.37 (0.24–0.57)	0.88 (0.76–1.01)	1.15 (1.03–1.30)	1.48 (1.20–1.82)
2007–2011	0.95 (0.86–1.05)	0.65 (0.49–0.87)	0.98 (0.86–1.11)	1.09 (0.90–1.31)	–
2012–2015	0.77 (0.63–0.95)	0.63 (0.46–0.88)	0.87 (0.67–1.12)	–	–

are associated with reduced therapeutic efficacy as compared to RA patients with normal body composition. The unfavourable effect of body weight on disease activity was paralleled by a favourable, protective effect on joint destruction. This uncoupling is not fully elucidated yet, and should be further investigated.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4694

OP0151 DOCOSAHEXAENOIC ACID TREATMENT OF RHEUMATOID ARTHRITIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSS-OVER STUDY

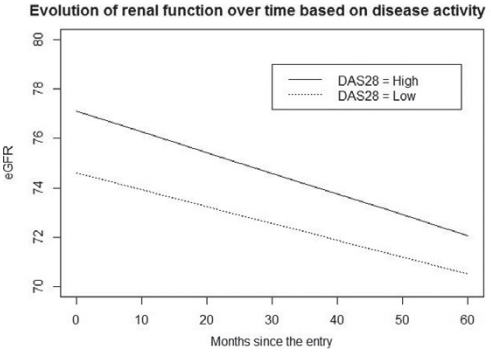
T. Neumann[1,2], C. Dawczynski[3,4], M. Dittrich[5], K. Goetze[6], A. Welzel[1], P. Oelzner[1], S. Voelker[7], A.M. Schaible[7], F. Troisi[7], L. Thomas[7], S. Pace[7], A. Koeberle[7], O. Werz[7], P. Schlattmann[8], S. Lorkowski[3,4], G. Jahreis[3,4].
[1]Department of Internal Medicine III, Jena University Hospital, Jena, Germany; [2]Department of Rheumatology, Kantonsspital St. Gallen, St. Gallen, Switzerland; [3]Competence Cluster for Nutrition and Cardiovascular Health (nutriCARD); [4]Department of Nutritional Biochemistry and Physiology, Institute of Nutrition; [5]Department of Nutritional Physiology, Institute of Nutrition, Friedrich Schiller University of Jena; [6]Department of Rheumatology, Jena University Hospital; [7]Department of Pharmaceutical/Medicinal Chemistry; [8]Department of Medical Statistics, Informatics and Documentation, Friedrich Schiller University of Jena, Jena, Germany

Background: Epidemiological studies and clinical investigations indicate a beneficial impact of long-chain n-3 polyunsaturated fatty acids (n-3 PUFA) on the inflammatory activity of rheumatoid arthritis (RA). However, the knowledge about the physiological effects of the individual compounds eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is limited.
Objectives: In our pilot study presented here, we investigated the clinical benefit of daily intake of foods enriched with microalgae oil as source of DHA in RA patients. In particular, the influence on disease activity and changes in the profile of pro-inflammatory/non-resolving and anti-inflammatory/pro-resolving lipid mediators was examined.
Methods: This is a randomized, double-blind, cross-over study on 38 patients (32 females/ 6 males) with active RA (DAS28$\geq$2.4). They were allocated to consume foods enriched with microalgae oil from *Schizochytrium sp.* (2.1 g DHA/day) or sunflower oil (placebo) for 10 weeks while maintaining stable immunosuppressive treatment.
Results: Thirty-two patients finished the study but seven patients were excluded from analysis because their DHA increase in erythrocyte lipids (EL) was less than 25% after 10 weeks of intervention indicating insufficient adherence to the intervention. Supplementation of DHA led to a decline in tender joints (TJ68) 8.4±5.6 to 6.0±5.0 (p=0.03), swollen joints (SJ66) 5.6±3.5 to 3.9±3.5 (p=0.07) and DAS28 4.3±1.0 to 3.9±1.2 (p=0.07). Joint counts in the placebo arm remained stable (TJ68) 6.7±4.9 to 8.8±8.0 (p=0.12), swollen joints (SJ66) 3.5±3.0 to 4.2±3.7 (p=0.40) and DAS28 4.0±0.9 to 4.1±1.2 (p=0.45). Ultrasound score (US-7) remained stable (15.1±9.5 to 12.4±7.0; p=0.160) while it increased in the placebo arm (11.4±7.0 to 14.0±8.8; p=0.03).
The amount of n-3 PUFA in erythrocyte increased in supplemented patients (7.0±1.2% to 10.6±1.4%; p$<$0.001) and the ratios of aracidonic acid (AA) /EPA (18.5±6.3 to 12.6±5.5; p$<$0.001) and AA/DHA (3.8±1.0 to 1.8±0.6; p$<$0.001) dropped significantly. Fatty acid distribution in erythrocyte lipids (n-3 PUFA, AA/EPA and AA/DHA) remained stable in the control arm.
Conclusions: The study shows that microalgae DHA supplements can ameliorate disease activity in patients with active RA along with a shift in the balance of AA- and DHA-derived lipid mediators towards an anti-inflammatory/pro-resolving state.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6759

OP0152 A LONGITUDINAL STUDY OF THE EFFECTS OF DISEASE ACTIVITY ON RENAL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS UTILIZING LINEAR MIXED EFFECT MODELS - ANSWER COHORT STUDY -

A. Onishi[1], K. Akashi[1], M. Hashimoto[2], M. Furu[2], W. Yamamoto[2], M. Katayama[3], R. Hara[4], T. Fujimura[4], S. Yoshida[5], K. Nagai[5], T. Hirano[6], K. Ebina[7], Y. Son[8], H. Amuro[8], H. Yamada[1], Y. Ichise[1], D. Waki[1], I. Naka[1], K. Tsuda[1], T. Okano[1], S. Takahashi[1], S. Sendo[1], Y. Ueda[1], Y. Kogata[1], J. Saegusa[1], A. Morinobu[1]. *[1]Department of Rheumatology, Kobe University Hospital, Kobe; [2]Department of the Control for Rheumatic diseases, Graduate School of Medicine, Kyoto University, Kyoto; [3]Department of Rheumatology and Clinical Immunology, Osaka Red Cross Hospital, Osaka; [4]The Center for Rheumatic Diseases, Nara Medical University, Nara; [5]Department of Internal Medicine (I), Osaka Medical College; [6]Department of Respiratory Medicine, Allergy and Rheumatic Disease, Graduate School of Medicine, Osaka University; [7]Department of Orthopaedic Surgery, Osaka University, Graduate School of Medicine; [8]First Department of Internal Medicine, Kansai Medical University, Osaka, Japan*

Background: Patients with RA have higher risk of developing chronic kidney disease compared to the general population. Although some causes of renal impairment in RA include nephrotoxic medications, amyloidosis, and glomerulonephritis, specific causes are not determined among most patients with RA. While experimental researches showed inflammatory process per se might also contribute to renal dysfunction, the results of previous clinical studies that assessed the effects of disease activity or C-reactive protein on renal function were inconsistent. This inconsistency might be attributable to their cross-sectional design, small sample size, and assessment of association between only baseline characteristics and renal outcomes without consideration for the fact that disease activity and medications had changed over time.
Objectives: To identify the effects of disease activity on renal function in RA in a multi-center cohort study.
Methods: RA patients with a sampling interval of less than 150 days were enrolled because wide sampling intervals could not take into consideration changes in disease activity and medications during their follow-up. An estimated glomerular filtration rate (eGFR) was calculated using an equation approved by the Japanese Society of Nephrology and used as an outcome variable. Linear mixed effect models were used to evaluate the renal trajectories of patients. Time from baseline (months), disease activity, and their interaction were included as fixed effects while participant identification number and time from baseline were included as random factors. Age, sex, disease duration, RF, ACPA, NSAIDs, and DMARDs that were known as a cause of renal impairment, such as tacrolimus, iguratimod, and tofacitinib, were included as covariates.
Results: A total of 25661 samples (mean sampling interval: 2.0 months) from 2104 patients was included. Patients with lower DAS28-CRP had worse renal function at inclusion, but a significantly better longitudinal trajectory on eGFR (0.0079 ml/min/1.73m^2 per month, P=0.025). Although all RA patients had naturally progressive renal impairment as they got older, patients who achieved remission or low disease activity had slower renal impairment rate of -0.068 ml/min/1.73m^2 per month compared to patients with moderate or high disease activity (-0.084 ml/min/1.73m^2 per month; P=0.037). These results were also similar using SDAI or CDAI.



Conclusions: Lower disease activity results in slower renal impairment. Because the effects of disease activity on renal function are mild, additional measures to protect renal function, such as avoiding nephrotoxic medications and treating cardiovascular risk factors are important.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4544

OP0153 RECURRENT INFECTIONS IN RHEUMATOID ARTHRITIS PATIENTS, RESULTS FROM THE BSRBR

S. Subesinghe[1], A.I. Rutherford[1], R. Byng-Maddick[2], J.B. Galloway[1].
[1]Rheumatology, King's College London; [2]Homerton Hospital, London, United Kingdom

Background: Rheumatoid arthritis (RA) patients have an increased susceptibility to infection.
Objectives: 1.To establish the rate of recurrent infection in RA patients recruited to the British Society of Rheumatology Biologics Registry Rheumatoid Arthritis (BSRBR-RA).2.To establish whether the organ class of index infection predicted future serious infection.
Methods: The BSRBR-RA is a prospective observational cohort, previously described. Patients with at least one episode of serious infection requiring hospitalisation were included if they occurred whilst on anti-rheumatic drug therapy or within 5 drug half-lives of stopping. Infections were coded by MedDRA classification in to 7 categories. Infections occurring over 14 days after the first index infection were considered as new events. Event rates were calculated and compared using a Cox proportional hazards model with adjustments made for age, gender, disease duration, baseline DAS28 score, smoking status and seropositivity.
Results: See Table 1.
In total, 21,943 subjects with 115,423 patient-years follow up were studied, 5365 subjects reported at least one serious infection. Comparing organ classes of prior infection at baseline, each group had comparable age, disease duration, baseline DAS28 and HAQ scores. The cohort characteristics are tabulated. The baseline annual rate of first serious infection was 4.6% (95% CI 4.5–4.7). Following an

Abstract OP0153 – Table 1

	Overall	Patients with infection	Respiratory	Gastrointestinal	Genitourinary	Musculoskeletal	Sepsis	Skin/Soft Tissue	Other
Age, years (SD)	57.3 (12.5)	61.5 (11.7)	60.0 (11.5)	61.7 (11.1)	59.8 (11.9)	58.7 (10.5)	63.5 (11.2)	57.9 (11.9)	55.3 (11.4)
Female (%)	75.7	72.6	74.8	77.4	89.2	70.2	76.6	79.5	83.3
Baseline DAS28 (SD)	6.2 (1.2)	6.4 (1.2)	6.3 (1.2)	6.3 (1.1)	6.3 (1.2)	6.5 (1.2)	6.4 (1.1)	6.4 (1.1)	6.3 (1.1)
Baseline HAQ (SD)	1.9 (0.7)	2.1 (0.6)	2.0 (0.6)	2.1 (0.6)	2.1 (0.6)	2.1 (0.6)	2.2 (0.5)	2.0 (0.6)	1.9 (0.6)
Steroid use,n (%)	8346 (38.2)	2632 (49.4)	2832 (43.8)	493 (51.5)	1226 (44.5)	390 (51.6)	316 (57.3)	1583 (45.2)	1267 (39.6)
Current smoker, n (%)	4682 (21.7)	1159 (21.9)	1422 (22.1)	165 (17.3)	452 (16.4)	186 (24.8)	122 (22.4)	692 (19.9)	573 (18.0)
RhFactor positive, n (%)	13,340 (63.2)	3533 (67.5)	4176 (66.1)	626 (66.2)	1737 (64.6)	527 (71.4)	361 (66.1)	2241 (65.6)	2003 (64.0)
Recurrent infection rate, % per annum (95% CI)	–	12.7 (12.1–13.2)	15.0 (13.9–16.2)	10.8 (9.2–12.8)	14.5 (12.7–16.5)	10.1 (8.7–11.8)	19.7 (15.1–25.7)	11.2 (10.1–12.5)	9.1 (7.3 -11.4)
Adjusted Hazard Ratio for annual incidence of recurrent infection (95% CI)	–	–	REF	0.79 (0.65–0.95)	0.97 (0.83–1.14)	0.81 (0.67–0.96)	1.33 (1.01–1.76)	0.87 (0.77–1.0)	0.70 (0.54–0.91)

index infection, the annual rate of serious infection was 12.7% (95% CI 12.1–13.3). Respiratory infections were the most common (41.4% of all events). The system class of index infection was associated with the risk of a recurrent event; subjects who experienced sepsis had the highest risk of subsequent serious infection within 12 months:19.7%. Compared to an index respiratory tract infection, sepsis conferred a 33% increased hazard for recurrent serious infection within a year (HR 1.33, 95% CI 1.01–1.76). Increasing age was a significant predictor of infection recurrence.

Conclusions: There is a high risk of recurrent infection in RA patients with past serious infection. Work is ongoing to determine whether organ class of recurrent infection event mirrors index events and the impact of biologic treatment decisions following the index infection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1501

THURSDAY, 15 JUNE 2017

Advances in RA and SpA pathophysiology

OP0154 ALTERED LYMPH NODE STROMAL CELLS DURING THE EARLIEST PHASES OF RHEUMATOID ARTHRITIS

C. Ospelt[1], E. Karouzakis[1], J. Hähnlein[2], J.F. Semmelink[2], R.E. Gay[1], P.P. Tak[2,3], D.M. Gerlag[2,4], S. Gay[1], L.G. van Baarsen[2]. *[1]Center of Experimental Rheumatology, University Hospital of Zurich, Zurich, Switzerland; [2]Academic Medical Center, Amsterdam, Netherlands; [3]Cambridge and GlaxoSmithKline, University of Cambridge, Stevenage; [4]R&D Projects Clinical Platforms & Sciences, GSK Clinical Unit Cambridge, Cambridge, United Kingdom*

Background: Lymph node stromal cells (LNSC) play a crucial role in shaping the immune response and maintaining peripheral tolerance. We developed an experimental model for studying the functional capacities of human LNSC during the earliest phases of RA and compared their cellular and molecular characteristics to LNSC from healthy volunteers.

Methods: ACPA+ RA patients (n=24), ACPA+ RA-risk individuals (n=23) and seronegative healthy controls (n=14;HC) underwent ultrasound-guided inguinal lymph node biopsy. Human LNSCs were isolated and expanded *in vitro* for cellular (flow cytometry), molecular (methylome, transcriptome and microRNA) and functional (contraction) analyses.

Results: RNA sequencing was performed on LNSC of HC (n=5), ACPA+ RA-risk individuals (n=6) and ACPA+ RA patients (n=4). Of interest, LNSC from ACPA+ RA-risk individuals and ACPA+ RA patients were more similar to each other compared with HC. Pathway analysis of commonly increased genes in RA (-risk) LNSC showed, among others, significant enrichment of pathways affecting actin cytoskeleton, focal adhesion and cell junction.

DNA methylation (Illumina HumanMethylation450 array) analyses revealed 459 differentially methylated CpG sites (DMS) in LNSC from ACPA+ RA patients (n=5) versus HC (n=4), 504 DMS between ACPA+ RA-risk individuals (n=3) versus HC and 665 DMS when comparing RA patients with RA-risk individuals (delta β-value >0.1, $p<0.05$). 34 DMS were different in both RA and RA-risk LNSC compared to healthy LNSC. 80% of these DMS were significantly hypomethylated and associated with antigen processing and presentation (HLA-DRB1), immune response and regulation of actin cytoskeleton.

Accordingly, in a gel contraction assay LNSC from ACPA+ RA-risk individuals and RA patients showed impaired collagen contraction compared to healthy LNSC. Healthy LNSC (n=5) covered 26.5% +/-2.5 of the well, while RA-risk (n=4) and RA (n=5) LNSC only covered 33.9% +/-5.9 and 30.6% +/-6.5.

Conclusions: This data point towards alterations in the cytoskeleton and antigen-processing and presentation in LNSC from ACPA+ RA-risk individuals and RA patients. Further studies are required to investigate the influence of this LNSC abnormality on immune responses.

Disclosure of Interest: C. Ospelt: None declared, E. Karouzakis: None declared, J. Hähnlein: None declared, J. Semmelink: None declared, R. Gay: None declared, P. Tak Employee of: GSK, D. Gerlag Employee of: GSK, S. Gay: None declared, L. van Baarsen: None declared

DOI: 10.1136/annrheumdis-2017-eular.6208

OP0155 MDM2-MEDIATED SUMOYLATION OF P53 CONTRIBUTES TO THE MIGRATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES FROM PATIENTS WITH RHEUMATOID ARTHRITIS

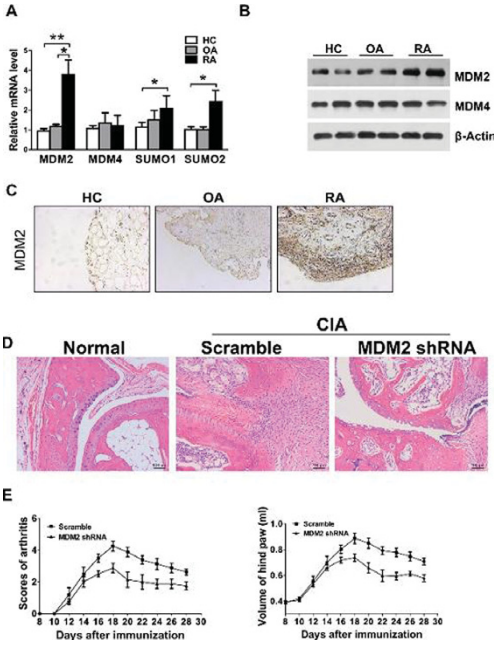
M. Shi[1,2], H. Xu[1], G. Chen[2]. *[1]Department of Rheumatology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou; [2]Department of Rheumatology, The First People's Hospital of Foshan, Foshan, China*

Background: Fibroblast-like synoviocytes (FLSs) in the synovial intimal lining are essential in the maintenance of synovial inflammation and progressive joint destruction in the development of Rheumatoid arthritis (RA). However, the precise molecular mechanisms by which this pathogenic process is regulated are not clearly defined.

Objectives: Increasing evidence indicates that p53 plays a critical role in the invasion and metastasis of cancer cells. This study aims to investigate the role of MDM2-mediated sumoylation of p53 in regulating the migration and invasion of fibroblast-like synoviocytes (FLSs) from patients with RA.

Methods: Synovial tissues were obtained from OA and RA patients, and then FLSs were separated from synovial tissues. Protein expression was measured by Western bloting or IHC staining. The sumoylation of p53 in cells was determined by immunoprecipitation. A specific inhibitor of MDM2-p53 interaction was used to inhibit the sumoylation of p53. Migration and invasion of FLSs in vitro were measured by the Boyden chamber assay.

Results: MDM2, SUMO1, and SUMO2 expression was significantly increased in the synovial tissue and FLSs of RA patients. Stimulation with TNF-α increased MDM2 expression and p53 sumoylation in RA FLSs. MDM2 shRNA inhibited p53 sumoylation, pro-inflammatory cytokines and MMPs expression, and capacity of in vitro migration and invasion in RA FLSs. Inhibition of p53 sumoylation by MDM2 shRNA promoted apotosis and reduced prolifeaation of RA FLSs. p38 MAPK signal pathway was involved in the downstream signal transduction in RA FLSs. Administration of MDM2 shRNA expressiong lentivirus attenuate the severity of rats with collagen-induced arthritis (CIA).



Conclusions: Increased MDM2-mediated p53 sumoylation contributes to aberrant aggressive behaviours of RA FLSs. Our findings suggests inhibition of MDM2 or p53 sumoylation might be a a novel therapeutic strategy to prevent synovial invasiveness and joint destruction in RA.

References:

[1] Bottini N, Firestein GS. Duality of fibroblast-like synoviocytes in RA: passive

responders and imprinted aggressors. Nat Rev Rheumatol. 2013 Jan;9(1):24–33.
[2] Ren Z, Aerts JL, Vandenplas H, et al. Phosphorylated STAT5 regulates p53 expression via BRCA1/BARD1-NPM1 and MDM2. Cell Death Dis. 2016 Dec 22;7(12):e2560.
[3] Lu M, Breyssens H, Salter V, et al. Restoring p53 Function in Human Melanoma Cells by Inhibiting MDM2 and Cyclin B1/CDK1-Phosphorylated Nuclear iASPP. Cancer Cell. 2016 Nov 14;30(5):822–823.
[4] Park JS, Lim MA, Cho ML, et al. p53 controls autoimmune arthritis via STAT-mediated regulation of the Th17 cell/Treg cell balance in mice. Arthritis Rheum. 2013 Apr;65(4):949–59.
Acknowledgements: This work is supported by grants from the National Natural Science Foundation of China (Grant number 81373182, 81373194, 8150060222 and U1401222). We would like to thank Jinjin Fan for her technical assistance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1554

OP0156 METHOTREXATE INCREASES EXPRESSION OF THE CELL CYCLE REGULATORS LBH AND P21 AND REDUCES FIBROBLAST-LIKE SYNOVIOCYTE PROLIFERATION AFTER MITOGEN STIMULATION

B. Bergström, H. Carlsten, A.-K.H. Ekwall. *Rheumatology and Inflammation Research, Gothenburg University, Gothenburg, Sweden*

Background: Activated fibroblast-like synoviocytes (FLS) are key effector cells in the joint in rheumatoid arthritis (RA). Local FLS proliferation is responsible for synovial hyperplasia, a key feature of the RA synovium correlating with disease activity. PDGF and IL-1b are known FLS mitogens. LBH is a transcription regulator and tumor suppressor, recently identified as a RA risk gene. We have demonstrated that LBH regulates FLS proliferation and that LBH expression is regulated by growth factors and by epigenetic mechanisms[1]. Methotrexate (MTX) is still the first-line treatment of RA but the target cells and mechanism of action of the low dose used in rheumatic diseases is largely unknown. Increased expression of cell cycle checkpoint genes[2] and modified DNA methylation[3] in immune cells have recently been described.
Objectives: The aim of this study was to investigate the effects of MTX on PDGF and IL1b-induced FLS proliferation *in vitro* and in particular on the expression of LBH, cell cycle genes (CDKN1A/p21 and CCND1/cyclinD1) and on genes regulating DNA methylation (DNMTs) in order to further understand the pharmacodynamics of this drug in RA and to identify novel markers for drug response.
Methods: Primary FLS from RA patients and from patients with osteoarthritis (OA) were plated on day 0 in DMEM complete, pre-treated 24 hours with MTX or control medium day 1, and stimulated with 20ng/ml PDGF+2 ng/ml IL-1b with or without 1 uM MTX in DMEM with 1% FBS for 24–48 hours starting day 2. Cells were then harvested for qPCR for gene expression and flowcytometry for cell cycle analysis.
Results: Stimulating RA-FLS cultures (n=3) with PDGF+IL-1b for 24 hours, pushed 24,5±3,5% cells into G2/M phase compared to 3,4±0,8% in unstimulated controls. Interestingly, treating PDGF+IL1b stimulated FLS with MTX, significantly inhibited cell cycle progression (4,6±1,9% in G2/M phase, p=0,02). PDGF+IL-1b stimulation of FLS for 24 hours reduced LBH mRNA expression. However, in the presence of 1uM MTX the LBH mRNA expression was significantly higher in RA-FLS (3,2±0,5 fold, p=0.002, n=5) and in OA-FLS (2,2±0,5 fold, p=0,02, n=5) after PDGF+IL-1b stimulation compared to untreated controls. In addition, MTX treatment strikingly increased the CDKN1A expression 14,3±4,4 fold (p=0,006) of treated vs untreated stimulated FLS. Furthermore, we found that 1 uM MTX restored and increased a lowered DNMT1 mRNA expression to 144±12% after PDGF+IL1b stimulation. There were no significant effects of MTX on CCND1 or DNMT3a expression at investigated time points.
Conclusions: Therapeutic doses of MTX reduce mitogen induced FLS proliferation and significantly revert mitogen-induced reduction of LBH and p21 expression in RA FLS. MTX restores expression of DNMT1 suggesting that MTX might regulate gene expression and proliferation by affecting the epigenome.
References:
[1] Ekwall, A.K., et al., The Rheumatoid Arthritis Risk Gene LBH Regulates Growth in Fibroblast-like Synoviocytes. Arthritis Rheumatol, 2015. 67(5): p. 1193–202.
[2] Spurlock, C.F., 3rd, et al., Methotrexate increases expression of cell cycle checkpoint genes via JNK activation. Arthritis Rheum, 2012. 64(6): p. 1780–9.
[3] Cribbs, A.P., et al., Methotrexate Restores Regulatory T Cell Function Through Demethylation of the FoxP3 Upstream Enhancer in Patients With Rheumatoid Arthritis. Arthritis Rheumatol, 2015. 67(5): p. 1182–92.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5079

OP0157 APOPTOSIS RESISTANCE OF SYNOVIAL FIBROBLASTS OF PATIENTS WITH RHEUMATOID ARTHRITIS IS REGULATED BY THE LONG NON-CODING RNA FAS-AS1

A. Pajak[1], Y. Horai[2], E. Pachera[1], M. Brock[2], S. Gay[1], M. Neidhart[1], O. Distler[1], A. Jungel[1] on behalf of yes. *[1]Department of Rheumatology; [2]Division of Pulmonology, University Hospital Zurich, Zurich, Switzerland*

Background: Apoptosis resistance is thought to contribute to the accumulation of synoviocytes in the affected joints of patients with rheumatoid arthritis (RA). Of particular interest, the Fas receptor (FasR) - Fas ligand (FasL) apoptotic pathway appears altered in RA[1]. Long non-coding RNAs (lncRNAs) are emerging as key regulators of gene expression. Their role in disease, however, is still poorly understood. The recently described lncRNA FAS-AS1 has been implicated in alternative splicing of FasR. This results in increased amounts of soluble FasR (sFasR) and thereby prevents FasL-induced cell death[2,3]. Whether lncRNA FAS-AS1 is involved in the apoptosis resistance of synovial fibroblasts in RA is unknown.
Objectives: To assess the regulatory role of lncRNA FAS-AS1 in the apoptosis resistance of synovial fibroblasts from patients with RA (RASF).
Methods: Levels of expression of lncRNA FAS-AS1 were measured in RASF and synovial fibroblasts from patients with osteoarthritis (OASF) by qPCR using SYBRGreen detection. Cells were treated with TNFα (10ng/ml, 24h) and/or with FasL (50ng/ml, 18h) to assess the secreted amount of sFasR by ELISA and the induction of apoptosis by Annexin V staining followed by flow cytometry. LncRNA FAS-AS1 was silenced using locked nucleic acid antisense oligonucleotides (GapmeR).
Results: There was no significant difference in basal levels of lncRNA FAS-AS1 expression between RASF and OASF (n=4 each). TNFα stimulation of synovial fibroblasts, regardless of the disease context (RA or OA), resulted in higher than 6-fold induction of lncRNA FAS-AS1 expression (6.45±1.39; $p<0,05$; n=4 for RASF and 6.26±1.47; p=0.05; n=4 for OASF). In addition, TNFα stimulation induced secretion of sFasR in RASF from 107±74 to 390±274pg/ml ($p<0.05$; n=6) and OASF from 69±54 to 249±134pg/ml ($p<0.05$; n=6). FasL induced apoptosis in both RASF and OASF (55–75±13%). However, pretreatment with TNFα reduced the FasL-induced apoptosis in RASF by 25±19% and in OASF by 15±10%. Silencing with GapmeR successfully decreased the expression of lncRNA FAS-AS1 by 40±22% SEM. Most interestingly, silencing of lncRNA FAS-AS1 reverted the TNFα inhibitory effect on FasL-induced apoptosis by 37±11% (n=4).
Conclusions: Our data revealed a novel mechanism, which may underlie apoptosis resistance in RASF. We showed that in a pro-inflammatory cytokine milieu, lncRNA FAS-AS1 up-regulates the release of sFasR and thereby may lower the responsiveness of cells to death signals. Thus, targeting lncRNA FAS-AS1 might prevent apoptosis resistance and synovial hyperplasia in RA.
References:
[1] Hong et al., Life Sciences. 2015; Feb 1; 122:37–41.
[2] Seghal et al., Leukemia. 2014; Dec 28(12); 2376–87.
[3] Villamizar et al., Oncotarget. 2016; Mar 22; 7(12):13810–26.
Disclosure of Interest: A. Pajak: None declared, Y. Horai: None declared, E. Pachera: None declared, M. Brock: None declared, S. Gay Grant/research support from: EU project BTCure, IAR, Consultant for: GSK, M. Neidhart Grant/research support from: Baugartenstiftung, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha, A. Jungel: None declared
DOI: 10.1136/annrheumdis-2017-eular.2677

OP0158 PREVALENCE OF IMMUNIZATION OF PATIENTS WITH AUTOIMMUNE DISEASE IN MEXICO

A. Arellano-Martinez, V. Gonzalez-Diaz, G.E. Martinez-Bonilla, S. Cerpa-Cruz, S.R. Gutierrez-Ureña, J. Reyes-Rueda, K.M. Garcia-Osuna, E. Gonzalez-Diaz. *Rheumatology Service, Hospital Civil Fray Antonio Alcalde, Guadalajara, Mexico*

Background: Current guidelines recommend immunization in patients with autoimmune diseases and use of immunosuppressants including biological treatment. Despite the above, the frequency of immunization is unknown in our population.
Objectives: To identify the prevalence of immunization in patients with autoimmune disease in a Rheumatology Service of a third level hospital in Mexico.
Methods: Observational, descriptive, cross-sectional study. Consecutive outpatients with autoimmune diseases who attended the Rheumatology Service of the Hospital Civil of Guadalajara during a period of 2 months (Dec. and Jan.) were included. A questionnaire was carried out to obtain demographic and immunization data. Descriptive statistical analysis was performed.
Results: 1208 patients were surveyed, 484 (40%) had a diagnosis of autoimmune disease; of whom 286 (59%) were on immunosuppressant therapy. 321 patients had a complete immunization during childhood. None of the patients knew what vaccines should by received with their diagnosis. When asked if they had been invited for immunization and from whom, 24 reported that their

general practitioner, 126 immunization campaign, 19 nurse, 9 rheumatologist, 4 pulmonologist, 1 infectious disease specialist, 1 family doctor and 1 internist. 260 (54%) reported having their immunization records. Only 37 had been vaccinated with influenza, 27 pneumococcus, 4 human papilloma virus and 2 Hepatitis B in the past. 372 (77%) accepted the invitation to be vaccinated on the day of their interview, but only 72 (19%) went to get the immunization; 41 of whom were given anti-influenza vaccines and 34 Pneumococcus (PPSV 23). The main causes for which the patient considers not to be vaccinated are: 85% "Because *my* treating doctor has not recommended me to go get vaccinated", 36% "They often do not have the vaccine to apply", 36% "I forget to get the vaccine on time", 31% "I think the application of the vaccine can make me sick", 14% "A vaccination center is not accessible", 7% "I think it is not useful to get vaccinated", and 5% "My doctor recommended me not to get vaccinated". These patients presented a total of 172 recurrent infections that included: upper airway infection 55, pneumonia 4 and others; 90 hospitalizations were required due to infection of which the main were due to: pneumonia 29, pulmonary tuberculosis 4, kidney 3, bone 1 and meningitis 1.

Conclusions: Immunization in this group of patients is low and rarely accepted mainly because their rheumatologist does not provide them with this information and due in general to a lack of information. This action is extremely important as it might reduce some serious infectious processes that lead to hospitalizations and increase the mortality in these immunosuppressed patients.

References:

[1] Singh Jec. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis and Rheumatology. 2015;: p. 1–26.

[2] Zimmerman Rec. Barriers and facilitators of pneumococcal vaccination among the elderly. Vaccine. 2003;: p. 1510–1517.

[3] Cardiel Mec. Actualización de la Guía Mexicana para el Tratamiento Farmacológico de la Artritis Reumatoide del Colegio Mexicano de Reumatología. Reumatología Clínica. 2013;: p. 1–14.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6721

OP0159 THE INITIATION, BUT NOT THE PERSISTENCE, OF EXPERIMENTAL SPONDYLOARTHRITIS IN HLA-B27/HUβ2M TRANSGENIC RATS IS CRUCIALLY DEPENDENT ON THE IL-23 AXIS

M. Van Tok[1], S. Na[2], J. Taurog[3], D. Baeten[1], L. van Duivenvoorde[1]. *[1]Clinical Immunology and Rheumatology/Experimental immunology, Academic Medical Center, Amsterdam, Netherlands; [2]Eli Lilly and Co, San diego, CA; [3]Rheumatic Diseases Division, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX, United States*

Background: The pro-inflammatory cytokine IL-17A is a central driver of pathology in human spondyloarthritis (SpA). IL-17A production was originally proposed to be dependent on the upstream cytokine, IL-23. Emerging preclinical and clinical evidence from SpA-related diseases suggest, however, that IL-17A and IL-23 have a partially overlapping but distinct biology.

Objectives: Here, we aimed to assess to what extend pathogenic IL-17A is dependent on IL-23 in SpA by selectively targeting the IL-23R in the HLA-B27/Huβ2m transgenic rat model of SpA, which we showed previously to be IL-17A-dependent.

Methods: HLA-B27/Huβ2m tg rats were immunized with low dose heat-inactivated *M. tuberculosis*/IFA. Rats were treated with a depleting anti-mouse/rat chimeric IL-23R antibody or PBS in a prophylactic (treatment initiation after immunization, before disease onset) or therapeutic (treatment initiation after disease onset) experiment. Clinical measurements included spondylitis and arthritis scores and hind paw swelling (plethysmometry). At the end of the study spleen and lymph nodes were used to assess cytokine expression, serum samples were analyzed for exposure to anti-IL23R.

Results: In the prophylactic treatment strategy, 58% and 67% of the rats in the control group developed spondylitis and arthritis, respectively. The average arthritis score at the end of the study was 3.9±1.1 and the average hind paw swelling was 0.35±0.09 cm^3. Prophylactic treatment with anti-IL-23R completely protected the rats against the development of spondylitis as well as arthritis. In the therapeutic treatment strategy, however, anti-IL23R treatment failed to reduce the incidence or decrease the severity of experimental SpA (fig. 1). With an average increase in arthritis score after the start of treatment of 1.6±2.8 versus 2.1±2.5 and an increase in paw swelling of 0.6±0.7 versus 0.3±0.6 cm^3in anti-IL23R treated versus control animals. The differential effect of IL-23R targeting in the initiation phase versus established disease could not be explained by pharmacokinetic differences as serum analyses revealed similar exposure levels. Mechanistically, the expression of presumably downstream effector cytokines such as IL-17A ($p<0.05$) and IL-22 ($p<0.01$) was reduced in the popliteal lymph nodes of rats treated prophylactically with anti-IL23R versus controls, with a similar trend in spleen. Accordingly, IL-17A production upon ex vivo re-stimulation was reduced in samples from prophylactically treated rats. In contrast, similar popliteal lymph node expression data in samples from the therapeutic experiment indicate a twofold increase in IL-17A expression and no difference in IL-22 expression in the anti-IL23R treated rats compared to controls.

Conclusions: IL-17A expression and production is dependent on the IL-23 axis in the initiation phase of experimental SpA but not in established disease. Accordingly, targeting of this axis with an anti-IL23R antibody completely prevented the onset of arthritis and spondylitis in HLA-B27/Huβ2m transgenic rats, but failed to reduce axial and peripheral joint inflammation in established disease. The cellular origin of IL-23-independent IL-17A production in established disease and the relevance to human SpA remains to be further investigated.

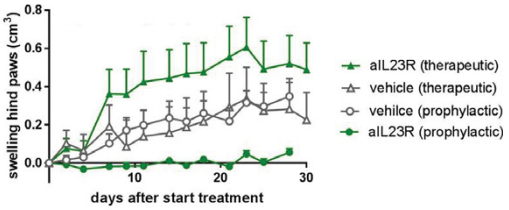


Figure 1: Swelling of the hind paws during follow up in prophylactic versus therapeutic treatment with anti-IL-23R or vehicle control (data are means +/- SEM)

Disclosure of Interest: M. Van Tok: None declared, S. Na Employee of: Eli Lilly and Co, J. Taurog Grant/research support from: AbbVie, Anges, Inc, and Celgene, D. Baeten Grant/research support from: AbbVie, Pfizer, UCB, MSD, Roche, BMS, Novartis, Eli Lilly, Janssen, Glenmark, Boehringer-Ingelheim, Employee of: part-time employee of UCB, L. van Duivenvoorde Grant/research support from: Abbvie, Boehringer-Ingelheim

DOI: 10.1136/annrheumdis-2017-eular.5248

OP0160 GUT-DERIVED TNF AS RISK FACTOR FOR THE DEVELOPMENT OF SACROILIAC INFLAMMATION

K. Debusschere[1], H. Cypers[2], P. Jacques[2], F. Van den Bosch[2], D. Souza[3], M. Brown[3], G. Nabozny[3], D. Dove[3], A. Klimowicz[3], D. Elewaut[1]. *[1]Ghent University - VIB; [2]Ghent University Hospital, Gent, Belgium; [3]Boehringer Ingelheim, Ridgefield, United States*

Background: An intruiging link exists between gut and joint inflammation in spondyloarthritis (SpA). About 50% of patients has subclinical (eg. microscopic) gut inflammation, which represents a risk factor for development of Crohn's disease, sacroiliac inflammation and evolution in to Ankylosing Spondylitis. However, the underlying mechanisms are still relatively poorly understood.

Objectives: Our goal was to examine the relationship between TNF, microscopic gut inflammation and axial inflammation using human samples and a novel mouse model. We speculated that TNF in the gut represents an important risk factor for disease severity and progression in SpA.

Methods: We examined in situ expression of TNF, TNFR1 and TNFR2 using triple in situ hybridisation in gut biopsies of human SpA patients. Furthermore, we generated intestinal specific human TNF transgenic mice, in which hTNF is under control of a rat iFABP (fatty acid binding protein) promoter, generating a mouse-model over-expressing human TNF in the ileum. These mice, together with wild type littermates, were evaluated for the development of arthritis up until the age of 13 weeks after which they were euthanized and ankle and sacroiliac joints as well as ileum were processed for histology.

Results: There was a marked upregulation of TNF in inflamed versus non-inflamed gut biopsies of human SpA patients. We also noted a predominant upregulation of TNFR1 on intestinal epithelium and TNFR2 in lamina propria respectively. Of interest, IL-17 and IL-23 were also markedly increased while IL-22 was most abundant in chronically inflamed samples. In line with this, we found that patients with gut inflammation had a higher need for anti-TNF therapy and their degree of clinical response after anti-TNF was also markedly higher.

Our transgenic mice exhibited a runt phenotype and hallmarks of inflammatory bowel disease, including increased intestinal permeability and inflammation compared to their wild-type littermates. While in peripheral joints no clear signs of arthritis were observed, the sacroiliac joints in transgenic mice, by contrast, showed marked signs of inflammation as well as bone erosion and destruction.

Conclusions: These data propose a new paradigm that gut-derived TNF is sufficient to trigger sacroiliitis and provide an alternate explanation on the relationship between gut inflammation, evolution to inflammatory bowel disease and axial inflammation in SpA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4999

OP0161 THE JAK1 SELECTIVE INHIBITOR FILGOTINIB REGULATES BOTH ENTHESIS AND COLON INFLAMMATION IN A MOUSE MODEL OF PSORIATIC ARTHRITIS

C. Robin-Jagerschmidt, S. Lavazais, F. Marsais, A. Monjardet, A. Cauvin, C. Saccomani, I. Parent, D. Merciris, E. Chanudet, M. Borgonovi, L. Lepescheux, M. Auberval, S. Dupont, P. Clement-Lacroix, R. Galien. *Galapagos SASU, Romainville, France*

Background: Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory disease characterized by the association of musculoskeletal involvement and extra-skeletal symptoms such as psoriasis and Inflammatory Bowel Disease

(IBD) with a variable clinical course. Common findings include enthesitis and dactylitis. Current treatments include anti-TNFa and anti-IL-12/IL-23 antibodies with varying success rates but the involvement of several pro-inflammatory cytokines suggests that other targeted therapies may be effective. Notably, the JAKs (a family of 4 non-receptor tyrosine kinases) are crucial for the signaling of many pro-inflammatory cytokines. In this regard, the JAK1-selective inhibitor filgotinib (GLPG0634, GS-6034) demonstrated clinical efficacy in patients with rheumatoid arthritis, a disease that shares some hallmarks with PsA and Crohn's disease, making this molecule a potential therapeutic tool for the treatment of PsA.

Objectives: Filgotinib was evaluated at the dose of 30 mg/kg/d (*per os*) in a mouse model of PsA induced by overexpression of IL-23.

Methods: Overexpression of IL-23 was induced by hydrodynamic delivery of mIL-23 enhanced Episomal Expression Vector (SBI) to male B10.RIII mice[1]. Evolution of inflammation of the paws and fingers was assessed by clinical scoring as well as *in vivo* molecular imaging (Bruker In-Vivo Xtreme imaging system). Enthesis and fingers were collected for expression analysis of inflammatory genes and target-related biomarkers. Neutrophil infiltrate, as well as pSTAT3 positive cells, were analyzed using immunohistochemistry in Achilles' enthesis and subcutaneous area, respectively. Colon was collected for lesion score determination as well as inflammatory and target-related biomarker gene expression.

Results: High levels of IL-23 were maintained during the time-course of the study and were correlated with severity of finger and paw swelling. Localization of the fluorescent signal using ProSense^{TM} imaging was asscociated with inflammation of enthesis and finger reported in PsA. Moderate inflammation of the colon was also observed. Filgotinib significantly improved clinical scoring and tended to prevent neutrophil/granulocyte infiltrate in paw (with significant effect being showed at earlier time point). Filgotinib reversed some up-regulated inflammatory genes in enthesis and/or fingers (CCL20, CXCL1, IL-22, MMP9 and TNFa) and reduced the target-related gene Mx2. Filgotinib significantly counteracted pSTAT3 induction in the subcutaneous area further demonstrating target engagement in the diseased tissue. Finally in line with previous findings[2], Mx2 expression in colon was slightly reversed by filgotinib.

Conclusions: In a mouse model of PsA, filgotinib improved global clinical score and decreased signs of inflammation in hindlimbs. Target engagement both in hindlimbs and colon was also demonstrated. These data support the evaluation of filgotinib in patients with PsA.

References:

[1] Sherlock et al. 2012 Nature Med 7:1069–1076.
[2] Van Rompaey et al. 2013 J Immunol. 191:3568–3577.

Disclosure of Interest: C. Robin-Jagerschmidt Employee of: Galapagos SASU, S. Lavazais Employee of: Galapagos SASU, F. Marsais Employee of: Galapagos SASU, A. Monjardet Employee of: Galapagos SASU, A. Cauvin Employee of: Galapagos SASU, C. Saccomani Employee of: Galapagos SASU, I. Parent Employee of: Galapagos SASU, D. Merciris Employee of: Galapagos SASU, E. Chanudet Employee of: Galapagos SASU, M. Borgonovi Employee of: Galapagos SASU, L. Lepescheux Employee of: Galapagos SASU, M. Auberval Employee of: Galapagos SASU, S. Dupont Employee of: Galapagos SASU, P. Clement-Lacroix Employee of: Galapagos SASU, R. Galien Employee of: Galapagos SASU

DOI: 10.1136/annrheumdis-2017-eular.1977

THURSDAY, 15 JUNE 2017

Bringing rheumatology research to the next level: addressing the main challenges of patient partnerships in research and health care service design

OP0162-PARE AN EXPLORATION OF LIVED EXPERIENCES AMONGST ADULTS WITH RHEUMATOID ARTHRITIS USING AN ONLINE RESEARCH COMMUNITY PLATFORM: A PILOT STUDY

S.R. Stones[1,2,3], S. Bull[1], S. Becerra[1]. *[1]Double Helix Consulting, Macclesfield; [2]Faculty of Life Sciences, The University of Manchester, Manchester; [3]School of Healthcare, University of Leeds, Leeds, United Kingdom*

Background: Online technology has revolutionised the way in which people connect and share their experiences. It also brings new opportunities to engage patients in health and social care research through the use of an online research community platform (ORCP). For example, it can improve the accuracy and usefulness of information gathered about research priorities, and it can be used to understand behaviours and preferences. Given an increasing prevalence of long-term conditions including rheumatoid arthritis, online technology represents a novel route for participation and engagement in research.

Objectives: To explore the benefits and limitations of an ORCP through understanding lived experiences of adults with rheumatoid arthritis.

Methods: We used a purposive sampling approach to ensure variation of key attributes amongst people with rheumatoid arthritis. A total of eight individuals used the ORCP during the pilot study. Qualitative data were collected through online focus groups, conducted as semi-structured interviews and asynchronous threaded discussions. The study was conducted in line with fieldwork guidelines, and written informed consent was obtained.

Results: The closed ORCP enabled a physically disconnected group to share their experiences of living with rheumatoid arthritis, describing the symptoms, diagnostic experience and support they received. In addition, participants shared their experiences and opinions about treatment delivery and adherence, the impact of rheumatoid arthritis, and the experiences of transitional care from paediatric to adult health services, where appropriate. Reasons and feeling about research participants and drug development processes were also discussed.

Conclusions: Our pilot study provided important accounts from people living with rheumatoid arthritis, highlighting the substantial impact of the disease on their daily lives. The ORCP removed physical contact between the researcher and participants, the absence of which may enable a richer data collection. However, it also has its limitations, primarily because the researcher is less able to gauge participants' attitudes and concerns. ORCPs represent a novel route of data collection, enabling researchers to immerse themselves into a community of individuals, whether they be patients, carers or professionals.

Acknowledgements: The authors would like to thank the individuals who contributed their thoughts and experiences to the pilot study.

Disclosure of Interest: S. Stones Employee of: McCann Complete Medical., S. Bull Employee of: McCann Complete Medical., S. Becerra Employee of: McCann Complete Medical.

DOI: 10.1136/annrheumdis-2017-eular.1029

OP0163-PARE INVIGORATING THE PRINCIPLE OF PARTICIPATORY RESEARCH IN GERMANY - SETUP OF A TRAINING COURSE FOR PATIENT REPRESENTATIVES

J. Clausen. *Deutsche Rheuma-Liga Bundesverband, Bonn, Germany*

Background: Patient participation in research projects is important because it enhances the legitimacy of research projects and facilitates the implementation of research results after completion of the respective projects. Since 2009, patient representatives have been actively involved in EULAR projects, and the first EULAR training course for patient representatives was conducted in 2010.

Objectives: The aim of the project was to create a training course for German-speaking patient representatives and thereby to invigorate the principle of participatory research in Germany. The training course is supposed to enable patients to make valuable contributions in research projects. In addition the training course aimed at lowering barriers and strengthening the patients' self-confidence, in order to facilitate their integration in the unfamiliar environment among researchers.

Methods: Participants were trained during a two-day interactive training course. For evaluation of the course, each participant anonymously answered 14 questions in a questionnaire.

Results: The training course consists of seven modules. In the first module (I), the history of the EULAR "patient research partners" is described and the tasks of the future German patient research partners are outlined. In the following modules, various types of research and study designs (II), the generation of research questions and hypotheses (III), various scientific tools (IV), the detailed sequence of steps in a typical research project (V), literature research in scientific databases (VI) and the process of reviewing grant applications (VII) are explained. Each module is subdivided in an explanatory section, an exercise section (where the participants have to apply the newly achieved skills) and a final discussion section.

So far, two courses have been conducted. The training course was rated either "very good" or "good" by 77% and 23% of the participants, respectively. Those patients, already actively involved in research projects, acclaim participatory research as interesting and enriching.

Conclusions: The training course was perceived very well by the participants. In future follow-up meetings, the usefulness of the various modules and any missing items will be discussed and the training course adapted accordingly.

Acknowledgements: We thank Dr. C. Sander for her contribution to the training course.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1923

THURSDAY, 15 JUNE 2017

Osteoarthritis: new horizons for treatment

OP0164 OPTIMIZING RECRUITMENT CRITERIA FOR AN OSTEOARTHRITIS STRUCTURE MODIFICATION TRIAL: DATA FROM THE OAI

M.A. Bowes[1], G. Guillard[1], A. Brett[1], G.R. Vincent[1], P.G. Conaghan[2]. *[1]Imorphics, Manchester; [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*

Background: The design of clinical trials for osteoarthritis is challenging; structural changes in tissues are quantitatively small and proceed very slowly. No clear guidance exists on how to optimise recruitment. KL grade is a poor recruitment criterion as centres interpret KL differently. Quantitative measures should be

better, and metric radiographic joint space width (rJSW) is related to subsequent risk of radiographic progression. Although new MRI measures provide increased responsiveness in DMOAD trials, it is unknown whether selecting for recruitment based on radiographic criteria are well suited for responsiveness of these new measures.

Objectives: (1) To determine which baseline rJSW values are associated with most subsequent progression for rJSW, MRI cartilage and bone outcomes (2) Explore baseline covariates that influence progression rates (3) Estimate the trial numbers needed using the criteria determined by steps (1) and (2).

Methods: We used all knees from the Osteoarthritis Initiative which had all 3 measures recorded (rJSW – Duryea method; MRI cartilage thickness & bone area, Imorphics) at baseline, 1 and 2 years. We categorised knees into bins of 1mm rJSW, and assessed the 2 year changes of each bin, and characterised the distribution of rJSW in KL 0 knees. We used ANCOVA models to consider which covariates (including gender, height, weight, alignment, age, pain severity) affected 2-year slope of change, and responsiveness using SRM. For the final optimised recruitment groups, we calculated SRMs (CIs assessed using the bootstrap method of Efron) and derived the number of patients per arm in a putative trial.

Results: 4796 knees were included (2789 females, mean age 61.45). The lower 95th percentile values for rJSW in women and men were 3.9 and 4.5mm respectively. The mean changes at 2-years for all 3 outcomes were greatest for the categories of 2–3 and 3–4mm baseline rJSW (Figure 1A) with notably little change in knees with rJSW<2mm. Of the covariates, only pain improved responsiveness. Using a total WOMAC pain criterion; ≥3/20 reduced numbers from 726 knees to 331 knees, and improved 1 year SRM (95% CI) from 0.27 (0.17,0.34) to 0.41 (0.29,0.51) in rJSW, from 0.45 (0.37,0.51) to 0.55 (0.45,0.65) in MRI cartilage and from 0.60 (0.52,0.66) to 0.73 (0.62,0.83) in MRI bone. Figure 1B shows the relative SRMs for the 3 outcomes based on 2 inclusion criteria (rJSW 2–4mm and pain ≥3/20; n=331) and demonstrates the required trial numbers (with confidence intervals) based on the SRMs.

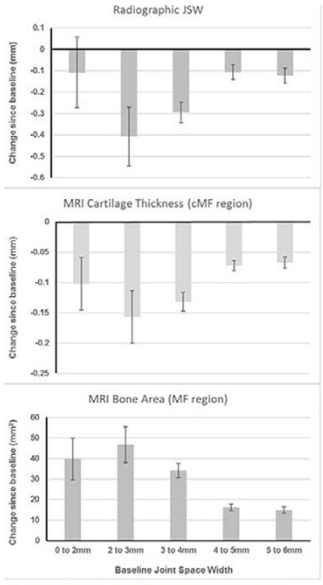


Figure 1A: *Mean 2-year change for 3 imaging outcomes by baseline rJSW*

Units are in mm for rJSW and MRI cartilage thickness, and in mm² for MRI bone area (95% confidence limits for change since baseline in brackets)

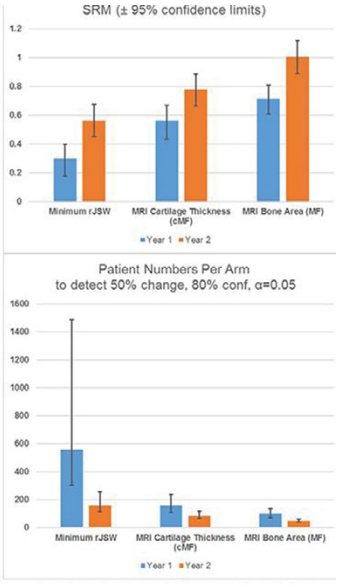


Figure 1B: *Responsiveness of knees selected for JSW 2-4 and pain ≥3 (n=331)*

Top figure shows SRMs plus 95% confidence limits, bottom figure calculates numbers required to identify change from SRMs in top figure

Conclusions: Selecting patients based on 2 simple criteria will improve responsiveness in clinical trials for all 3 imaging outcomes using standard imaging outcomes. Selecting for rJSW of 2–4mm is most important while adding a pain criteria further improves responsiveness; no other covariates improved this. Caution should be applied when using SRM to power a study because of the inherent difficulties in calculating standard deviations; Fig 1B shows for example that the confidence limits for rJSW at 12 months vary from 302 to 1489. This analysis also confirms the advantages of MRI outcomes over rJSW in terms of study size and duration: a 12-month study with cartilage thickness or bone area endpoints needs no more than 238 or 137 patients (including the upper 95th percentile confidence limit).

Disclosure of Interest: M. Bowes Employee of: Imorphics Ltd, G. Guillard Employee of: Imorphics Ltd, A. Brett Employee of: Imorphics Ltd, G. Vincent Employee of: Imorphics Ltd, P. Conaghan: None declared

DOI: 10.1136/annrheumdis-2017-eular.6860

OP0165 A NEOEPITOPE FRAGMENT OF C-REACTIVE PROTEIN IS PROGNOSTIC OF RADIOGRAPHIC KNEE OA

A.C. Bay-Jensen [1], A. Bihlet [2], I. Byrjalsen [2], J.R. Andersen [2], Y. He [1], A.S. Siebuhr [1], C.S. Thudium [1], B.J. Riis [2], C.H. Christiansen [2], M.A. Karsdal [1].
[1] Rheumatology, Nordic Bioscience Biomarkers and Research; [2] Clinical development, Nordic Bioscience, Herlev, Denmark

Background: There are two major needs in clinical development of DMOADs: 1) Identifying a suitable population with an active and progressive disease in order to demonstrate significant improvements by an efficacious intervention; and 2) Phenotyping patients and linking them to a corresponding treatment mode-of-action (e.g. anti-inflammatory). The biochemical marker CRPM is a neoepitope of C-reactive protein (CRP) and is released from the local inflamed tissue when CRP is degraded by proteases such as matrix metalloproteinases

Objectives: The purpose of this study was to translate the CRPM, from rheumatoid arthritis (RA), where it has been extensively tested, to OA, and to test whether it is predictive of radiographic OA.

Methods: The placebo arms of two phase III OA trial (clinicaltrial.gov: NCT00486434 and NCT00704847), a phase III RA study (the LITHE study, N=490), which included patients with active, moderate-severe RA (NCT00106535), as well as in an early RA cohort (N=92) were used. Subjects with symptomatic and radiographic knee OA: WOMAC pain ≥150mm and/or WOMAC function ≥510mm, and Kellgren-Lawrence grade (KLG) 2 or 3. KLG were scored for both knees at baseline and year 2 (Y2). Serum CRPM and hsCRP were measured at baseline. The association between serum CRPM levels and disease activity score (DAS28) and hsCRP was investigated by Spearman's correlations. Quartile ranges of CRPM in the early RA cohort were used to define the cut-off between inflammatory OA and non-inflammatory OA. OA knees were divided into cases and controls based on a terminology proposed by the FNIH-OAI consortium (1); knees with KLG≥2 at BL were excluded, and incidence OA at Y2 was defined KLG≥2. Logistic regression was used to compare cases and controls.

Results: There was a significant correlation between disease activity measures and CRPM in both RA studies. Seventy-five percent of the LITHE patients had high or very high levels of CRPM at BL, which was changed to a pattern similar to early RA after treatment. The mean CRPM levels were significantly lower in OA (8.5 [95% CI 8.3–8.8] ng/mL) compared to the RA patients (15.6 [9.5–21.6] ng/mL); however, a significant subset of OA patients (41% and 31% in SMC2301 and SMC2302) had CRPM levels ≥9ng/mL, as 75% of patients with early RA. Patients with BL or Y2 CRPM levels ≥9ng/mL were more likely to develop knee OA than patients with low level of CRPM. Overall, moderate to very high levels of CRPM at BL and Y2 were predictive of incidence OA with odds ratio of 4.6 [1.2–17] and 2.5 [1.2–4.8].

Table		Early RA	Moderate-Severe RA	SMC2301	SMC2302
hsCRP	Rho (p-value)	0.54 (<0.0001)	0.66 (<0.0001)		
DAS28	Rho (p-value)	0.43 (<0.0001)	0.24 (<0.0001)		
CRPM level	Quartile range	No. of patients (%)			
		Before treatment	*After treatment*	*n_1*	*n_2*
Low	<9 ng/mL	49 (8.2%)	87 (18%)	267 (59%)	233 (69%)
Moderate	9-12	100 (17%)	123 (25%)	137 (31%)	71 (21%)
High	12 – 15	132 (22%)	105 (21%)	26 (6%)	23 (7%)
Very high	>=15	318 (53%)	175 (36%)	19 (4%)	11 (3%)

Conclusions: A subset of OA patients, up to 41%, appear to have tissue inflammation comparable to that of RA, reflected by the level of CRPM. Furthermore, high CRPM levels was prognostic of incident knee OA. These data suggest that CRPM is blood-based biochemical marker for finding OA patients with an inflammatory phenotype.

References:

[1] Longitudinal validation of periarticular bone area and 3D shape as biomarkers for knee OA progression? Data from the FNIH OA Biomarkers Consortium.Hunter D et al.Ann Rheum Dis. 2016 Sep;75(9):1607–14.

Disclosure of Interest: A. Bay-Jensen Shareholder of: Nordic Bioscience, Grant/research support from: DBOARD, Employee of: Nordic Bioscience, A. Bihlet Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, I. Byrjalsen Employee of: Nordic Bioscience, J. Andersen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, Y. He Employee of: Nordic Bioscience, A. S. Siebuhr Employee of: Nordic Bioscience, C. Thudium Employee of: Nordic Bioscience, B. Riis Shareholder of: Nordic Bioscience, C. Christiansen Shareholder of: Nordic Bioscience, M. Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience

DOI: 10.1136/annrheumdis-2017-eular.6290

OP0166 RADIOGRAPHIC OUTCOMES FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF A NOVEL, INTRA-ARTICULAR, INJECTABLE, WNT PATHWAY INHIBITOR (SM04690) IN THE TREATMENT OF OSTEOARTHRITIS OF THE KNEE: WEEK 26 INTERIM ANALYSIS

Y. Yazici[1], T.E. McAlindon[2], A. Gibofsky[3], N.E. Lane[4], N. Skrepnik[5], E. Armas[6], C.J. Swearingen[1], A. DiFrancesco[1], J.R. Tambiah[1], M.C. Hochberg[7].
[1]Samumed, LLC, San Diego, CA; [2]Tufts Medical Center, Boston, MA; [3]Weill Cornell Medical College and Hospital for Special Surgery, New York, NY; [4]UC Davis Medical Center, Davis, CA; [5]Tucson Orthopedic Institute, Tucson, AZ; [6]Well Pharma, Miami, FL; [7]University of Maryland School of Medicine, Baltimore, MD, United States

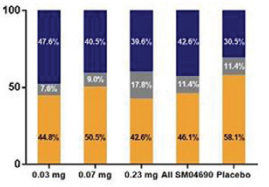
Background: Knee osteoarthritis (OA) is characterized by pain, functional impairment, and joint space narrowing due to degradation of articular cartilage and bone remodeling. The Wnt pathway plays a central role in the formation of joint tissues, and altered Wnt signaling has been associated with cartilage loss in preclinical studies. SM04690 is a small molecule Wnt pathway inhibitor in development as a disease modifying OA drug (DMOAD) and administered as an intra-articular (IA) knee injection. A phase 2, multicenter, 52-week, single-dose, randomized controlled trial of SM04690 is ongoing in subjects with moderate to severe knee OA. Radiographic results from an interim analysis at 26 weeks are reported.
Objectives: To evaluate the safety and efficacy of SM04690 IA injection for the treatment of OA.
Methods: Subjects were randomized to receive a single, 2 mL, IA injection of 0.03 mg, 0.07 mg, 0.23 mg SM04690 or placebo into the target knee on Treatment Day 1. Safety, tolerability and efficacy outcomes were assessed at Weeks 4, 13 and 26. Target knee radiographs were taken at baseline and Week 26; change in medial joint space width (mJSW) was analyzed using an intention-to-treat analysis of covariance (ANCOVA) adjusting for baseline mJSW.
Results: 455 subjects (average age 60.3 [±8.7] years, 268 [58.9%] female, mean BMI 29.9 [±4.6] kg/m^2, 293 [64.4%] Kellgren-Lawrence Grade 3, 291 [64.0%] bilateral OA) were enrolled. At Week 26, 8 serious adverse events (SAEs) in 7 subjects were reported; these were deemed unrelated to drug by the investigators. Mean mJSW change from baseline was -0.22 [±0.64] mm in placebo cohort (table 1). Compared to placebo, mean mJSW change from baseline was -0.07 [±0.62] mm in the 0.03 mg (p=0.069), -0.16 [±0.95] mm in 0.07 mg (p=0.489), and -0.03 [±0.59] mm in 0.23 mg (p=0.019) cohorts, respectively. Increase in mean mJSW was observed in 50 (47.6%) subjects in 0.03 mg, 45 (40.5%) subjects in 0.07 mg, 40 (39.6%) subjects in 0.23 mg and 32 (30.5%) subjects in placebo cohorts, respectively (figure 1). Odds of mJSW improvement, defined as change in mJSW >0, were increased 107% in 0.03 mg cohort compared to placebo (OR=2.1, 95% CI [1.2, 3.7], p=0.011), and odds of mJSW improvement were increased 69% for all SM04690 doses combined compared to placebo (OR=1.7, 95% CI [1.1, 2.7], P=0.029). Additionally, in *a priori* subanalyses, each treatment cohort, and all SM04690 doses combined, had higher probability of improving mJSW in the unilateral OA subgroup, with a 420% increase in odds of JSW response compared to placebo (all SM04690 groups combined OR=5.2, 95% CI [2.1, 12.8], p<0.001).

Table 1. Medial joint space width at baseline and week 26

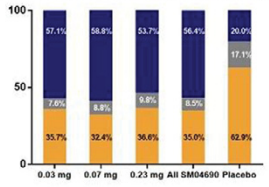
	0.03 mg	0.07 mg	0.23 mg	All SM04690	Placebo
N	111	117	109	337	116
Baseline (mm) [Mean (SD)]	3.41 (1.28)	3.45 (1.11)	3.08 (1.26)	3.34 (1.24)	3.33 (1.36)
Week 26 (mm) [Mean (SD)]					
Actual	3.38 (1.38)	3.30 (1.40)	3.06 (1.38)	3.25 (1.39)	3.10 (1.52)
Change from baseline	-0.07 (0.62)*	-0.16 (0.95)	-0.03 (0.59)**	-0.09 (0.74)	-0.22 (0.64)

*0.03 mg vs PBO, p=0.069; **0.23 mg vs PBO, p=0.019

Figure 1. JSW Change at 26 weeks: All subjects



JSW Change at 26 weeks: Unilateral subjects





Conclusions: Radiographic outcomes from this interim analysis demonstrated that treatment with SM04690 maintained or increased JSW compared to placebo. These data support the continued development of SM04690 as a potential DMOAD for the treatment of knee OA. Further studies are ongoing.

Disclosure of Interest: Y. Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, T. McAlindon Grant/research support from: Samumed, Consultant for: Astellas, Flexion, Pfizer, Regeneron, Samumed,and Seikugaku, A. Gibofsky Shareholder of: AbbVie, Amgen, J&J, GSK, Regeneron, Consultant for: AbbVie, Pfizer, Horizon, Iroko, Celgene, Novartis/Sandoz, Samumed, Speakers bureau: AbbVie, Amgen, Celgene, Pfizer, N. Lane Consultant for: Samumed, LLC, N. Skrepnik Grant/research support from: Samumed, LLC, Consultant for: Orthofix and Sanofi, E. Armas Grant/research support from: Samumed, LLC, C. Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, A. DiFrancesco Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, J. Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, M. Hochberg Consultant for: Bioberica, EMD Serono, Novartis Pharma AG, Plexxicon, Pfizer, Proximagen, Regeneron, Samumed, and Theralogix LLC
DOI: 10.1136/annrheumdis-2017-eular.3845

OP0167 EFFICACY AND SAFETY OF CNTX-4975 IN SUBJECTS WITH MODERATE TO SEVERE OSTEOARTHRITIS KNEE PAIN: 24-WEEK, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

R. Stevens[1], D. Petersen[2], J. Ervin[3], J. Nezzer[4], Y. Nieves[4], J. Campbell[1], K. Guedes[1], R. Burges[1], P. Hanson[1]. *[1]Centrexion Therapeutics, Boston; [2]Noble Clinical Research, LLC, Tucson; [3]The Center for Pharmaceutical Research, Kansas City; [4]Premier Research, Durham, United States*

Background: Osteoarthritis causes joint pain, stiffness, and reduced function, leading to disability. CNTX-4975, a highly purified, synthetic *trans*-capsaicin, targets the transient receptor potential vanilloid 1, producing analgesia via reversible deactivation of end terminals of primary afferent pain fibers within the joint and capsule.
Objectives: This 24-week dose-ranging study evaluated CNTX-4975 efficacy and safety in subjects with chronic, moderate to severe osteoarthritis-associated knee pain.
Methods: Subjects aged 45–80 years with chronic knee osteoarthritis, stable moderate to severe knee pain, and intolerability to oral or intra-articular analgesics were randomized to a single injection of placebo, CNTX-4975 0.5 mg, or CNTX-4975 1.0 mg. The primary efficacy endpoint was the area under the curve (AUC) for change from baseline in daily Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) A1 score through week 12. Least squares mean differences (LSMD) for CNTX-4975 vs placebo were calculated for the primary endpoint and the average weekly AUC WOMAC A1 scores using analysis of covariance. Additional efficacy endpoints, mean change from baseline in weekly WOMAC A1 score, WOMAC B stiffness subscale, and WOMAC C physical function subscale through week 24, were analyzed using a mixed model for repeated measures (MMRM). Statistical tests were 2-sided (alpha, P=0.10). Safety assessments included treatment-emergent adverse events (TEAEs).
Results: Efficacy was evaluated in 172 subjects (placebo, n=69; CNTX-4975 0.5 mg, n=33; CNTX-4975 1.0 mg, n=70). Mean WOMAC A1 pain scores at baseline were 7.4 (placebo), 7.2 (CNTX-4975 0.5 mg), and 7.2 (CNTX-4975 1.0 mg). In the primary efficacy analysis, significant improvements vs placebo in WOMAC A1 scores were observed at week 12 with CNTX-4975 0.5 mg (LSMD: –0.8; P=0.07) and CTNX-4975 1.0 mg (LSMD: –1.6; P<0.0001). Significant improvements vs placebo were also observed at week 24 with CNTX-4975 1.0 mg (LSMD: –1.35; P=0.0002). In the MMRM analysis, significant improvements in WOMAC A1 scores vs placebo were demonstrated with CNTX-4975 0.5 mg at week 12 (LSMD: –0.9; P=0.087) but not week 24 (LSMD: –0.5; P=0.41), and with CNTX-4975 1.0 mg at weeks 12 (LSMD: –1.5; P=0.0003) and 24 (LSMD: –0.9; P=0.067). CNTX-4975 1.0 mg significantly improved WOMAC B (LSMD: –2.5; P=0.0013) and WOMAC C scores vs placebo (LSMD: –18.3; P=0.004) at week 12. Numerically greater improvements were observed in WOMAC B and C at week 24, but differences were not significant (WOMAC B LSMD: –1.2; P=0.14; WOMAC C LSMD: –7.2; P=0.28). In the safety population, the incidence of TEAEs was 30% for placebo or CNTX-4975 1.0 mg, and 47% for CNTX-4975 0.5 mg at week 24. Most TEAEs were considered unrelated to study treatment. Arthralgia was the most common TEAE with CNTX-4975 1.0 mg (placebo, 5.7%; CNTX-4975 1.0 mg, 7.0%).
Conclusions: A single injection of CNTX-4975 1.0 mg improved pain with walking, knee stiffness, and physical function, and was well tolerated in subjects with moderate to severe osteoarthritis-associated knee pain.

Disclosure of Interest: R. Stevens Shareholder of: Centrexion Therapeutics, Employee of: Centrexion Therapeutics, D. Petersen: None declared, J. Ervin: None declared, J. Nezzer Consultant for: Centrexion Therapeutics, Y. Nieves Consultant for: Centrexion Therapeutics, J. Campbell Shareholder of: Centrexion Therapeutics, Employee of: Centrexion Therapeutics, K. Guedes Shareholder of: Centrexion Therapeutics, Employee of: Centrexion Therapeutics, R. Burges Shareholder of: Centrexion Therapeutics, Employee of: Centrexion Therapeutics, P. Hanson Shareholder of: Centrexion Therapeutics, Employee of: Centrexion Therapeutics
DOI: 10.1136/annrheumdis-2017-eular.5309

OP0168 A PHASE 2A, PLACEBO-CONTROLLED, RANDOMIZED STUDY OF ABT-981, AN ANTI-INTERLEUKIN-1ALPHA AND -1BETA DUAL VARIABLE DOMAIN IMMUNOGLOBULIN, TO TREAT EROSIVE HAND OSTEOARTHRITIS (EHOA)

M. Kloppenburg[1], C. Peterfy[2], I.K. Haugen[3], F. Kroon[1], S. Chen[4], L. Wang[4], W. Liu[4], G. Levy[4], R. Fleischmann[5], F. Berenbaum[6], D. van der Heijde[1], J. Medema[4], M.C. Levesque[4]. *[1]Leiden University Medical Center, Leiden, Netherlands; [2]Spire Sciences, Inc., Boca Raton, FL, United States; [3]Diakonhjemmet Hospital, Oslo, Norway; [4]AbbVie Inc., North Chicago, IL; [5]University of Texas Southwestern Medical Center at Dallas, Metroplex Clinical Research Center, Dallas, TX, United States; [6]University Pierre & Marie Curie and Inserm, DHU i2B, APHP, Hospital Saint-Antoine, Paris, France*

Background: No approved OA therapies reduce pain and slow joint damage. Mouse data suggested that inhibiting IL-1α and -1β with ABT-981 would reduce pain and slow structural progression in EHOA.
Objectives: To test the efficacy and safety of ABT-981 in EHOA.
Methods: Subjects with HOA per ACR criteria, ≥3 inflamed IP joints (tender, swollen, or both), hand pain ≥6 (scale 0–10), and ≥1 erosive IP joint on X-ray (Verbruggen-Veys) were randomized to placebo (PBO) or ABT-981 200 mg SC every 2 wk for 26 wk. The primary outcome was AUSCAN hand pain at 16 wk. Subjects had radiographs of both hands and MRI of the index hand at baseline and 26 wk. Both radiographs (Verbruggen-Veys, GUSS™, OARSI, Kellgren-Lawrence [KL]) and MRIs (HOAMRIS) were read by 2 independent central readers. A modified intent-to-treat population (ie, randomized and treated) was analyzed. Continuous efficacy endpoints were assessed using ANCOVA models with treatment and country as main factors and baseline measurements as covariates with LOCF imputation for the primary endpoint.
Results: Of 131 treated subjects (85% women; mean age 66 y), 61/67 randomized to PBO and 49/64 to ABT-981 completed the study; subject characteristics were well matched. AUSCAN pain was not significantly different vs PBO at wk 16 (*P*=0.39; Table 1, Figure); X-ray data and other endpoints also were not statistically different vs PBO (Table 1). ABT-981 significantly decreased hsCRP, neutrophils, IL-1α, and IL-1β. Immunogenicity had no impact on ABT-981 pharmacokinetics. Besides injection site reactions and neutropenia, ABT-981 was well tolerated and safety was similar vs PBO, with no serious infections (Table 2).

Table 1

	PBO	ABT-981	PBO	ABT-981	*P*
1° Endpoint	Baseline, mean±SD		LS, mean change±SE at Wk 16		
AUSCAN pain (0–50)	39±7	38±6	–10.7±2.4	–9.2±2.3	0.39
2° Endpoints	Baseline, mean±SD		LS, mean change±SE at Wk 26		
AUSCAN function (0–90)	69±15	71±13	–14.3±4.2	–16.4±4.0	0.49
Tender joints (0–30)	12±6	12±7	–4.7±1.2	–5.8±1.2	0.32
Swollen joints (0–30)	6±6	6±5	–1.8±0.8	–2.2±0.9	0.64
X-ray erosive joints (0–16)	2±2*	3±2*	0.26±0.08†	0.18±0.08†	0.33
KL score (0–80)	41±13	46±13	0.13±0.19	0.10±0.19	0.87
OARSI JSN (0–58)	28±10	32±9	0.14±0.19	0.03±0.19	0.51
OARSI osteophytes (0–58)	23±11	26±10	0.25±0.15	0.14±0.16	0.45
HOAMRIS synovitis (sum score; 0–52.5)	11±4	10±4	0.92±0.48	0.85±0.51	0.89
HOAMRIS erosive damage (sum score; 0–105)	18±9	17±10	0.26±0.64	0.10±0.67	0.80
HOAMRIS BML (sum score, 0–105)	7±5	5±4	0.11±0.64	0.44±0.66	0.60

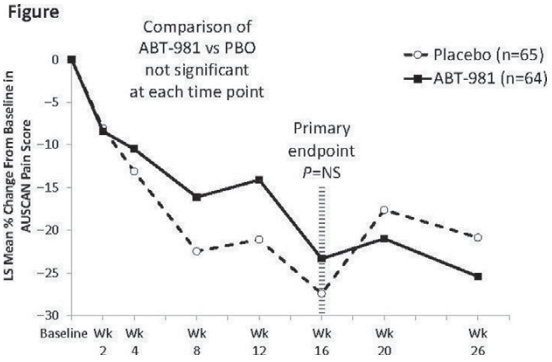
*Verbruggen-Veys, erosive phase (E) + erosive with remodeling (E/R) or† new E or E/R or R.

Table 2

	PBO (n=67)	ABT-981 (n=64)
Any AE/serious AE, %	88/3	91/3
Death, %	0	0
Infection/serious infection, %	51/0	41/0
Injection site reaction, %	16	36
Neutropenia by NCI CTCAE grade, n		
G2 (1000 to <1500/mm^3)	0	9
G3 (500 to <1000/mm^3)	0	3
G4 (<500/mm^3)	0	0

Conclusions: Despite adequate pharmacodynamics results, targeting IL-1 may be ineffective in EHOA, as ABT-981 did not improve outcomes.
Acknowledgements: AbbVie funded the study (NCT02384538); participated in study design, data collection, analysis, and interpretation and in abstract writing, review, and approval; and funded writing support by M. Theisen of CPS.
Disclosure of Interest: M. Kloppenburg Grant/research support from: Pfizer, Consultant for: AbbVie, GlaxoSmithKline, Merck, Levicept, C. Peterfy Shareholder of: Spire Sciences, Inc. (which provides imaging services for clinical trials to multiple pharmaceutical companies), Employee of: Spire Sciences, Inc. (which provides imaging services for clinical trials to multiple pharmaceutical companies), Speakers bureau: Amgen, I. Haugen Consultant for: AbbVie, F. Kroon: None declared, S. Chen Shareholder of: AbbVie, Employee of: AbbVie, L. Wang Shareholder of: AbbVie, Employee of: AbbVie, W. Liu Shareholder of: AbbVie, Employee of: AbbVie, G. Levy Shareholder of: AbbVie, Employee of: AbbVie, R. Fleischmann Grant/research support from: AbbVie, Consultant for: AbbVie, F. Berenbaum Consultant for: AbbVie, Pfizer, Regeneron, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, Employee of: Director of Imaging Rheumatology bv., J. Medema Shareholder of: AbbVie, Employee of: AbbVie, M. Levesque Shareholder of: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.4947

Figure



OP0169 EARLY OSTEOPHYTES DETECTED BY MRI ARE ASSOCIATED WITH CHANGES IN KNEE PAIN AND STRUCTURES IN OLDER ADULTS: A POPULATION-BASED COHORT STUDY

Z. Zhu[1], L.L. Laslett[1], W. Han[1], B. Antony[1], F. Cicuttini[2], G. Jones[3], C. Ding[3]. *[1]12779, Hobart; [2]Department of Epidemiology and Preventive Medicine, Monash University, Melbourne; [3]Musculoskeletal Unit, 12779, Hobart, Australia*

Background: Early stage of osteophyte (OP) formations are hard to be detected by radiography, but can be detected by magnetic resonance imaging (MRI). Their subsequent developments on structural and clinical abnormalities are still unknown.
Objectives: To describe the prevalence of early osteophytes (OPs) that were detected by magnetic resonance imaging (MRI) but not by X-ray in older adults and to evaluate the longitudinal associations with knee pain and structural changes.
Methods: 837 participants (mean age 62 years, 50% female) were randomly selected from local community at baseline. T1- or T2-weighted fat suppressed MRI was used to assess knee OPs, cartilage volume, cartilage defects and bone marrow lesions (BMLs) at baseline and after 2.6 years. Knee pain was assessed by self-administered Western Ontario and McMaster Osteoarthritis (WOMAC) Index questionnaire at baseline and after 5 years. X-ray-detected OPs were assessed at baseline using the Osteoarthritis Research Society International atlas. OPs detected only by MRI but not by standard X-ray were defined as early OPs. OPs detected by both MRI and X-ray were defined as definite OPs.
Results: The prevalence of early OPs was 75% while the prevalence of definite OPs was 10% in total knee at baseline. Compared with participants without any OPs, participants with early OPs and with definite OPs had greater cartilage volume loss and increased cartilage defects and BMLs over 2.6 years. Presence of early medial tibiofemoral OPs predicted decreases in total knee pain over 5 years, while definite OPs predicted increases in total knee pain, after adjustment for relevant covariates.

Table 1. Longitudinal associations of OP phenotype status and WOMAC knee pain changes

	Adjusted* β (95% CI)	Adjusted** β (95% CI)
Total		
No OPs (n=103)	*Ref.*	*Ref.*
Early OPs (n=481)	-0.23 (-1.33, 0.88)	-0.28 (-1.40, 0.84)
Definite OPs (n=62)	2.20 (0.51, 3.89)	1.96 (0.17, 3.76)
Medial tibiofemoral		
No OPs (n=447)	*Ref.*	*Ref.*
Early OPs (n=155)	-1.25 (-2.2, -0.30)	-1.51 (-2.50, -0.52)
Definite OPs (n=43)	2.91 (1.21, 4.60)	2.54 (0.74, 4.35)
Lateral tibiofemoral		
No OPs (n=287)	*Ref.*	*Ref.*
Early OPs (n=332)	0.12 (-0.70, 0.94)	-0.05 (-0.91, 0.81)
Definite OPs (n=27)	1.08 (-1.11, 3.27)	0.35 (-1.95, 2.66)

Results of this table are generated from a linear regression model. *Adjusted for age, sex and BMI. **Further adjusted for BMLs and cartilage defects.

Conclusions: Although early OPs are associated with knee abnormal structural changes, they predict decreases in knee pain over time suggesting an adaptive response.
References:
[1] Centers for Disease C, Prevention. Public health and aging: projected prevalence of self-reported arthritis or chronic joint symptoms among persons aged >65 years–United States, 2005–2030. MMWR Morb Mortal Wkly Rep 2003; 52: 489–491.
Acknowledgements: The authors thank the participants who made this study possible, and acknowledge the role of the staff and volunteers in collecting the data, particularly research nurses Boon C and Boon P. Warren R assessed MRIs and Dr Srikanth V and Dr Cooley H assessed radiographs.

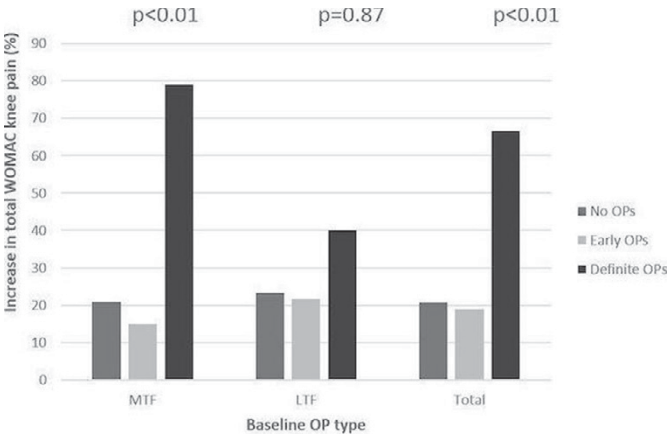


Figure 1

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1060

OP0170 LEPTIN AND ADIPONECTIN MEDIATE THE ASSOCIATION BETWEEN BODY MASS INDEX AND HAND AND KNEE OSTEOARTHRITIS

A. Veenbrink[1], F. Kroon[2], R. de Mutsert[3], W. Visser[2], S. le Cessie[3], F. Rosendaal[3], M. Kloppenburg[2]. *[1]Medicine, Universiteit Utrecht, Utrecht; [2]Rheumatology; [3]Clinical Epidemiology, Leids Universitair Medisch Centrum, Leiden, Netherlands*

Background: Associations between adiposity and osteoarthritis (OA) in non-weight-bearing joints suggest that besides mechanical factors also systemic influences contribute to OA. Systemically active substances secreted by adipose tissue, including leptin and adiponectin, are hypothesized to play a role in OA.
Objectives: To examine whether leptin and adiponectin mediate the association between body mass index (BMI) and hand and knee OA.
Methods: Cross-sectional data of a population-based study were used. Participants completed questionnaires and underwent standardized physical examination of hands and knees to define OA according to clinical American College of Rheumatology criteria. Fasting serum leptin and adiponectin were measured with immunoassays. Potential mediation was investigated using the Baron and Kenny framework. Four assumptions were investigated: associations between (1) BMI and OA (pathway *C*), (2) BMI and adipokines (pathway *A*), (3) adipokines and OA (pathway *B*), and (4) attenuation of the total association between BMI and OA after including adipokines (pathway *C'*). No exposure-mediator interaction and mediator-outcome confounding was assumed. Assumptions were investigated using logistic and linear regression analyses as appropriate. Odds Ratios (ORs) were calculated per standard deviation (SD) difference in BMI, and per ten and five units difference in leptin and adiponectin, respectively. Percentage mediation with 95% confidence intervals (CIs) was estimated, only when all four assumptions were fulfilled. Models were adjusted for age, ethnicity and education, and stratified by sex.
Results: In 6462 participants (56% women, median age 56 years (range 45–65), mean BMI 26.3 kg/m^2), prevalence of hand OA, knee OA and combined hand and knee OA were 8%, 10% and 4%, respectively. Median leptin and adiponectin concentrations were 7.1 ug/L (range 0.9–60.9) and 6.0 mg/L (0.5–23.7) in men, and 19.1 ug/L (0.5–262.0) and 10.5 mg/L (0.5–98.6) in women. BMI was positively associated with OA presence and serum leptin in both men and women (Table). A negative association was observed between BMI and serum adiponectin (-0.73 mg/L per SD BMI, 95% CI -0.55;-0.91). Leptin was positively associated with most OA types, except knee OA in men. Leptin partially mediated the association of BMI with hand OA in men (9% mediation, 95% CI 5;17) and women (30%, 13;198), and the association of BMI with knee OA in women (15%, 12;21). Similar analyses for adiponectin revealed a negative association of adiponectin with hand OA in men and partial mediation of the association of BMI with hand OA in men (19%, 12;37), whereas mediation was absent in other subgroups.
Conclusions: Leptin partially mediated the association of BMI and hand OA in both men and women, as did adiponectin in men. In addition, mediation by leptin for the association of BMI and knee OA was demonstrated in women. These findings suggest that systemic mediators contribute to hand OA, and to a lesser extent to knee OA.

Table. Associations of BMI with leptin and different types of OA (OR, 95% CI)

MEN	Pathway A BMI – log leptin* β (95% CI)		Pathway B Leptin – OA OR (95% CI)	Pathway C BMI – OA OR (95% CI)	Pathway C' BMI – OA OR (95% CI)	Mediation % % (95% CI)
SD BMI: 3.72	1.70 (1.64 – 1.77)	Hand OA	1.30 (1.13 – 1.50)	1.39 (1.18 – 1.64)	1.34 (1.06 – 1.70)	8.6 (5.4 – 17.2)
		Knee OA	1.14 (0.98 – 1.43)	1.25 (1.06 – 1.48)	^	^
		Hand and knee OA	1.28 (1.07 – 1.52)	1.59 (1.31 – 1.93)	1.82 (1.39 – 2.39)	^
WOMEN	Pathway A BMI – log leptin* β (95% CI)		Pathway B Leptin – OA OR (95% CI)	Pathway C BMI – OA OR (95% CI)	Pathway C' BMI – OA OR (95% CI)	Mediation % % (95% CI)
SD BMI: 4.88	1.82 (1.77 – 1.88)	Hand OA	1.08 (1.01 – 1.15)	1.18 (1.01 – 1.37)	1.12 (0.89 – 1.40)	30.3 (13.3 – 198.2)
		Knee OA	1.21 (1.14 – 1.29)	1.62 (1.42 – 1.85)	1.50 (1.25 – 1.81)	15.4 (11.7 – 21.3)
		Hand and knee OA	1.13 (1.05 – 1.22)	1.48 (1.26 – 1.74)	1.55 (1.25 – 1.93)	^

BMI, body mass index; CI, confidence interval; OA, osteoarthritis; OR, Odds Ratio; SD, standard deviation. Adjusted for age, ethnicity and education. *logarithmic transformation performed to obtain normal distribution. ^Mediation not calculated (no association within pathway B). ^Mediation not calculated (no attenuation of the total association of BMI and OA after including leptin in the model).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3394

OP0171 SIGNAL INTENSITY ALTERATION WITHIN INFRAPATELLAR FAT PAD PREDICTS TOTAL KNEE ARTHROPLASTY WITHIN FOUR YEARS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

K. Wang[1,2], C. Ding[1,2,3,4], M.J. Hannon[5], Z. Chen[2,6], C. Kwoh[7], D.J. Hunter[8]. *[1]Department of Rheumatology, Arthritis Research Institute, 1st Affiliated Hospital of Anhui Medical University, Hefei, China; [2]Menzies Institute for Medical Research, Hobart; [3]Royal North Shore Hospital and Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Sydney, Australia; [4]Translational Research Centre, Academy of Orthopedics, School of Basic Medical Sciences, Southern Medical University, Guangzhou, China; [5]Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, United States; [6]School of Mathematics and Information Science, Nanjing Normal University of Special Education, Nanjing, China; [7]University of Arizona Arthritis Center& Division of Rheumatology, University of Arizona College of Medicine, Tucson, United States; [8]Department of Rheumatology, Royal North Shore Hospital and Institute of Bone and Joint Research, Kolling Institute, University of Sydney, Sydney, Australia*

Background: Osteoarthritis (OA) is a common joint disease that frequently affects the knee and is the leading cause of total knee arthroplasty (TKA) in Western countries. The most common reason for TKA is to ease pain and disability. Investigation on prognostic factors associated with TKA could be a possible way to find therapeutic targets to slow disease progression and delay the time for knee replacement.
Objectives: To investigate whether infrapatellar fat pad (IPFP) signal intensity (SI) alteration predicts the occurrence of TKA in patients with knee OA over 4 years.
Methods: Participants with symptomatic knee OA were selected from the Osteoarthritis Initiative (OAI) study. Case knees (n=127) were defined as those that received TKA during 4 years follow-up visit. They were matched by gender, age and radiographic status measured at baseline with a control knee. We used T2 weighted MR images to measure IPFP SI alteration using a newly developed algorithm in MATLAB. The measurements were assessed at OAI baseline (BL), T0 (the visit when TKA was reported), 1 year prior to T0 (T1). Conditional logistic regression was used to assess the relationship between cases and control knees and assess the risk of TKA in regard to SI alteration.
Results: Participants (n=237) were mostly female (57%), with average age of 63.7±8.5 years old and mean BMI of 29.5±4.7 kg/m^2. In multivariable analysis, standard deviation of IPFP SI [sDev (IPFP)] and the ratio of high SI region volume to whole IPFP volume [Percentage (H)] measured at BL were significantly associated with TKA after adjustment for BMI, knee bending activities, self-reported knee injury and surgery history (HR: 3.5, 95% CI 1.1 to 11.4; HR: 8.9, 95% CI 1.2 to 67.2). IPFP SI alterations measured at T1 including sDev (IPFP), Percentage (H) and clustering effect of high SI [Clustering factor (H)] were significantly associated with TKA (HR: 4.0, 95% CI 1.2 to 13.2; HR 10.9, 95% CI 1.9, 63.6; HR: 1.8, 95% CI 1.1 to 2.9). All measurements including mean value of IPFP SI [Mean (IPFP)], sDev (IPFP), mean value of IPFP high SI [Mean (H)], standard deviation of IPFP high SI [sDev (H)], median value of IPFP high SI [Median (H)], upper quartile value of IPFP high SI [UQ (H)], Percentage (H), Clustering factor (H) were significantly associated with TKA at T0.
Conclusions: IPFP SI is an important predictor for TKA in knee OA patients. Targeting IPFP SI could be a potential way to reduce the need for future TKA.
Acknowledgements: Special thanks go to the participants who made this study possible, the OAI investigators, staff, participants and the funding of POMA study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1163

THURSDAY, 15 JUNE 2017

Cellular drivers of inflammation in rheumatic disease

OP0172 EXPANDED T-CELL CLONES PRESENT IN SYNOVIUM AT ONSET OF RHEUMATOID ARTHRITIS ARE ALREADY PRESENT IN THE SYNOVIUM IN THE SEROPOSITIVE "AT RISK" STAGE

G. Balzaretti[1,2], P. Klarenbeek[1], M. de Hair[1], M. Doorenspleet[1], B. van Schaik[3], M. van de Sande[1], D. Gerlag[1,4], A. van Kampen[3], F. Baas[5], P.P. Tak[1,6], N. de Vries[1]. *[1]Clinical Immunology and Rheumatology; [2]Experimental Immunology; [3]Clinical Epidemiology, Biostatistics and Bioinformatics, AMC, Amsterdam, Netherlands; [4]Clinical Unit Cambridge, GlaxoSmithKline, Cambridge, United Kingdom; [5]Genome Analysis, AMC, Amsterdam, Netherlands; [6]GlaxoSmithKline, Stevenage, United Kingdom*

Background: T-cells are thought to be key players in the initiation and progression

of rheumatoid arthritis (RA). Earlier we showed that already at the seropositive "at risk" stage uninflamed synovial tissue contains T-cell infiltrates[1]. In another study we showed that inflamed synovium selectively harbours expanded T-cell clones that are hardly present in paired blood samples[2].

Objectives: Following up on these observations, we longitudinally investigated whether the same expanded T-cell clones found in the inflamed synovial tissue at onset of RA are already present in the synovium in the seropositive "at risk" stage.

Methods: Fifty-five individuals without arthritis but seropositive for IgM rheumatoid factor and/or anti-citrullinated protein antibody (ACPA) were prospectively followed. In five aCCP+ individuals synovial biopsies and paired blood samples at inclusion ("at risk" stage) and after development of RA (ACR2010 criteria; mean time to arthritis 27 months (range 11.7–47.3)) were available for analysis. T-cell clones were identified by their unique TCRβ sequence using RNA-based next generation sequencing[3]. For each sample, 3570 TCRβ sequences were analysed. Clones with a frequency of ≥0.5% were arbitrarily considered as highly expanded clones (HECs). ANOVA and t-test were used for statistical analysis.

Results: T-cell repertoires in "at risk" and RA synovium were similar (mean (± SD) number of clones 488±70 vs 567±204 respectively, p=0.46), number of HECs (37±7 vs 31±18, p=0.41) and the impact of HECs collectively on the TCR repertoire (mean 48% ± 13% vs 50% ± 20%, p=0.84). Interestingly, of the HECs present in the synovium at onset of arthritis 23% (±9%) were already present as HECs in the synovium at the seropositive "at risk" stage. This overlap was significantly higher than that with paired blood samples taken at the arthritis (3% ± 3%; p=0.01) or at the seropositive "at risk" stage (5% ± 7%; p=0.01; Figure 1a-c patient example; Figure 1d summary of results). Further characterization of the synovial CDR3 sequences (length, total charge, polar, aromatic and aliphatic side chains) showed no significant differences between RA HECs that were and those that were not expanded in the seropositive "at risk" stage.

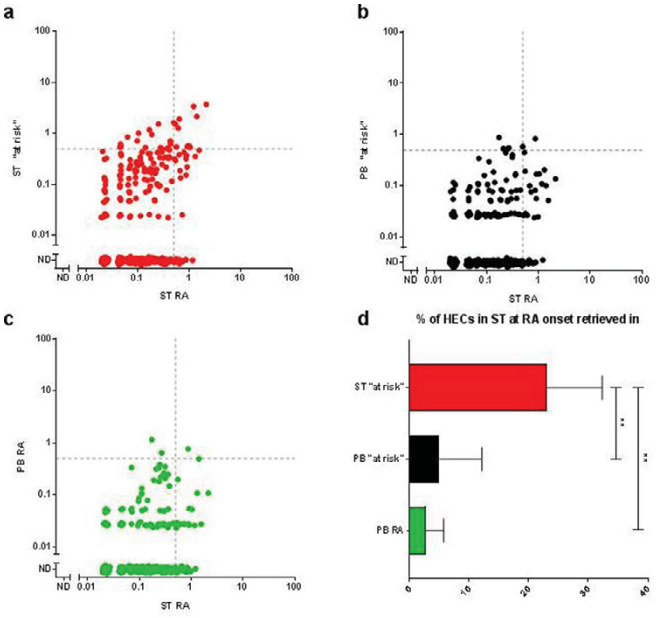


Figure 1: (a-c) Axes show the frequency of the TCR clones in the depicted samples for one patient. ND = non-detected. **(d)** Summary of results from 5 patients, **p=0.01

Conclusions: Many T-cell clones found in early RA synovial tissue are already present in the pre-clinical "at risk" phase. The resemblance in TCR repertoires indicates that the process leading to disease – at least at the T-cell level – constitutes a smooth development. These clones, being already present in the very early stage of this disease and persisting as dominant clones during contraction of active arthritis, form attractive candidates for further characterization.

References:

[1] de Hair MJ et al. Arthritis Rheum. 2014.
[2] Klarenbeek PL et al. Ann Rheum Dis. 2012.
[3] Klarenbeek PL et al. Immunol Lett. 2010.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6318

OP0173 DOMINANT B-CELL RECEPTOR CLONES IN PERIPHERAL BLOOD PREDICT ONSET OF ARTHRITIS IN INDIVIDUALS AT RISK FOR RHEUMATOID ARTHRITIS

P.-P. Tak[1], M.E. Doorenspleet[2,3], M. de Hair[4], P. Klarenbeek[2,3], M. van Beers-Tas[5], A. van Kampen[6], D. van Schaardenburg[5], D. Gerlag[4], F. Baas[3], N. de Vries[2]. *[1]Department of Clinical Immunology and Rheumatology; [2]Amsterdam Rheumatology and Immunology Center; [3]Department of Genome Analysis;[4]Clinical Immunology and Rheumatology, Academic Medical Center; [5]Amsterdam Rheumatology and Immunology Center, Reade; [6]Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, Amsterdam, Netherlands*

Background: The onset of seropositive rheumatoid arthritis (RA) is preceded by the presence of specific autoantibodies in the absence of synovial inflammation. Only a subset of these *at-risk* individuals will develop clinical disease. This impedes efforts to implement early interventions that may prevent onset of clinical disease.

Objectives: Here we analyze whether clonal changes in the B-cell receptor (BCR) repertoire can reliably predict onset of clinical disease.

Methods: In a prospective cohort study in 21 individuals *at-risk* for RA, the BCR repertoire of paired peripheral blood and synovial tissue samples was analyzed using next-generation BCR sequencing. BCR clones that were expanded beyond 0.5% of the total repertoire were labeled dominant. The relative risk for onset of arthritis was assessed, using a cut-off of presence of ≥5 dominant BCR clones. Findings in peripheral blood were validated in an independent prospective cohort of 50 *at-risk* individuals. Based on the test cohort, individuals in the validation cohort were considered positive if peripheral blood at study entry showed ≥5 dominant BCR clones.

Results: Both in the test and validation cohort, the presence of ≥5 dominant BCR clones in peripheral blood was significantly associated with arthritis development (validation cohort relative risk (RR) 6.3, 95% confidence interval (CI) 2.7 - 15, $p<1*10^{-4}$). Even when adjusted for the recently described clinical prediction rule the association remained intact (relative risk 5.0, 95% CI 1.2 - 20, p=0.024). When individuals developed arthritis, dominant BCR clones disappeared from peripheral blood and appeared in synovial tissue, suggesting a direct role of these clones in disease pathogenesis.

Conclusions: Dominant BCR clones in peripheral blood predict onset of clinical symptoms of RA in *at-risk* individuals with high accuracy. Our data suggest that during onset of RA these clones shift from peripheral blood to target tissue.

Disclosure of Interest: P.-P. Tak Employee of: GlaxoSmithKline, Stevenage, United Kingdom, M. Doorenspleet: None declared, M. de Hair: None declared, P. Klarenbeek: None declared, M. van Beers-Tas: None declared, A. van Kampen: None declared, D. van Schaardenburg: None declared, D. Gerlag Employee of: Clinical Unit Cambridge, GlaxoSmithKline, Cambridge, United Kingdom, F. Baas: None declared, N. de Vries: None declared

DOI: 10.1136/annrheumdis-2017-eular.4323

OP0174 NEW PROTEIN ARRAY TECHNOLOGY IDENTIFIES RITUXIMAB TREATED NON RESPONDER RHEUMATOID ARTHRITIS PATIENTS ARE GENERATING A NEW AUTOANTIBODY REPERTOIRE

Z. Konthur[1], M. Wiemkes[2], T. Häupl[2], G. Burmester[1], K. Skriner[2]. *[1]Max Planck Institute, Max Planck Institute; [2]Department of Rheumatology and Clinical Immunology, Charité University Medicine, Berlin, Germany*

Objectives: Rituximab (RTX) has shown clinical efficacy but up to 40% of RTX treated rheumatoid arthritis (RA) patients are poor responders (Ann-Rheum-Dis. 2005 Feb;64(2):246–52) and the commonly used RA biomarkers (*RF/ACPA)* are poor predictors for therapy response. In this study the autoantibody repertoire analysed on protein macorarrays from RA patients under RTX treatment was correlated to clinical DAS28 response.

Methods: Screening of RA sera was conducted on 37.830 unique human proteins on protein marcoarrays (http://www.engine-gmbh.de) with sera taken before and 24 weeks after treatment. The autoantibody response of different immunoglobulin classes IgD, IgA, and IgG was recorded and bioinformatically evaluated. Response was determined according to DAS28 criteria. DAS 28 scores in the responder group before treatment was from 5.4 – 7.8 and in the non-responder group 5,6 – 6,8. We analyzed 26 RA patient sera (9 responder, 7 non-responder and 10 patients with blinded response classification) investigated the data of found autoantigens *in-silico* and by hierarchical clustering

Results: In the cohort of 26 patients 1292 different autoantigens (IgD,IgA,IgG) were detected. Using protein array we investigated clusters of autoantigen responses that disappeared or developed during RTX treatment of RA patients. RA autoantigenic patterns before and 6 month after RTX treatment were patient-specific and no relevant autoantigenic cluster was found that was shared between patients or associated with response. However, RTX reduced the repertoire of autoantibodies after 24 weeks of treatment in the tested RA patient cohort on average by 60%. RA patients which do not respond are generating on average 63% new autoantibodies. In good responders to RTX only 5,5% (+/-3%) new autoantibodies can be detected. The IgA and IgG autoantibody repertoire in the serum after 24 weeks of RTX treatment is reduced (IgA: 41%, IgG: 31%) in good responders whereas it is increased (IgA: 1,3%, IgG: 24%) in non responders to RTX.

Conclusions: After 6 month of RTX treatment the autoantibody repertoire in all good responding RA patients is reduced and non responders to RTX change their autoantibody repertoire directed against new but patient specific antigens. The fast rebuilding of functional B cells is only detected in non-responders to rituximab.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6978

OP0175 CHARACTERIZATION OF NOVEL STROMAL-DERIVED AUTOANTIGENS RECOGNIZED BY RA SYNOVIAL MONOCLONAL ANTIBODIES

E. Corsiero, L. Jagemann, E. Prediletto, C. Pitzalis, M. Bombardieri. *Centre for Experimental Medicine & Rheumatology, William Harvey Research Institute, London, United Kingdom*

Background: We previously showed that up to 40% of RA synovial recombinant monoclonal antibodies (RA-rmAbs) generated from germinal center-like structure (GC-LS+) RA synovium recognize citrullinated antigens contained in neutrophils extracellular traps (NET) (1). The cellular source of other potential autoantigens targeted by the majority of locally differentiated B cells remains undefined. Recently, RA-fibroblast-like synoviocytes (RA-FLS) have been implicated in the release of citrullinated antigens (2, 3). However, whether these cells are targeted by RA-rmAbs is still unknown.
Objectives: Here, we aimed to define the RA-rmAbs immunoreactivity towards i) RA-FLS and ii) identify potential stromal-derived autoantigens.
Methods: 67 RA-rmAbs were generated from single CD19+ B cells FACS-sorted from fresh synovial cell suspensions following IgV_H+V_L genes cloning (1). RA-rmAbs were tested by means of i) cell-based immunofluorescence assays with FLS of RA patients and controls (osteoarthritis (OA)-FLS and RA-dermal fibroblast (RA-DF)), ii) co-localization with stromal specific markers and iii) immunoenzymatic tests with co-localizing antigens. Control rmAbs were also used (Sjögren's syndrome/healthy donor-IgG rmAbs).
Results: Immunofluorescence on RA-FLS demonstrated reactivity of 21% of RA-rmAbs (14/67 rmAbs) towards cytoplasmic components of FLS. Only 4 rmAbs out of 14 were binding both FLS and NET components. For some rmAbs this reactivity was not specific to RA-FLS since it was also observed for OA-FLS and RA-DF. Interestingly, strong co-localization was observed with calreticulin (CRT) which in its citrullinated (cit-CRT) form has been previously shown to recognize the RA "shared epitope" HLA domain sequence (3). When tested in ELISA for native vs cit-CRT, 57% (8/14 rmAbs) of the FLS-reactive RA clones showed binding to CRT with 4 out of 8 rmAbs displaying increased immunoreactivity towards cit-CRT. Controls rmAbs showed no reactivity to either FLS or CRT. Preliminary data suggest that RA patient serum preferentially recognize the lectin-like N-terminal domain of CRT (4).
Conclusions: Here, we provide novel evidence that a subset of locally differentiated B cells within RA synovial GC-LS can react towards RA-FLS derived antigens. Preliminary data suggest that part of this reactivity is directed towards CRT. Identification of immunodominant epitopes within CRT is under investigations.
References:
[1] Corsiero et al, ARD 2015.
[2] Sorice et al, Rheumatology 2016.
[3] Ling et al, AR 2013.
[4] Hong et al, JI 2010.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3870

OP0176 THE PARACASPASE MALT1 PLAYS A CENTRAL ROLE IN THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

E. Gilis[1,2], J. Staal[3,4], R. Beyaert[4,5], D. Elewaut[1,6]. *[1]Department of Internal Medicine, Ghent University; [2]Molecular Immunology and Inflammation Unit, VIB Inflammation Research Center; [3]Department of Biomedical Molecular Biology, Ghent University; [4]Molecular Signal Transduction in Inflammation; [5]Department of Biomedical Molecular Biology; [6]Molecular Immunology and Inflammation Unit, VIB Inflamamtion Research Center, Ghent, Belgium*

Background: One of the hallmarks of many inflammatory arthritides is their strong linkage with MHC-signalling, which is mirrored by the marked role for adaptive immunity. Accordingly, rheumatoid arthritis (RA) is characterized by the activation of auto-reactive T-cells and the development of auto-antibodies. T-cells may additionally respond to non-TCR mediated signals, which are essential in driving their effector functions. Pathways leading to the modulation of both innate and adaptive signals are therefore of marked interest to study in arthritic diseases.
Objectives: The paracaspase MALT1 is a key player in the activation and proliferation of immune and non-immune cells. These cells include the lymphoid, myeloid and mast cells, indicating MALT1's crucial role in both innate and adaptive signaling (1). Therefore, MALT1 is regarded a promising target for the treatment of autoimmune diseases and defining its role in the pathogenesis of inflammatory arthritis is a critical first step.
Methods: To unravel MALT1's role in inflammatory arthritis, we initially assessed MALT1-activation in mice that were challenged with collagen-induced arthritis (CIA), the prototype model for antigen-induced RA. We then addressed the role of MALT1 in the pathogenesis of inflammatory arthritis by challenging MALT1-deficient mice to distinct models of arthritis (CIA and CAIA) or by backcrossing MALT1-deficient mice to TNF^{DARE} mice, representing an SpA-like model. Additionally, CIA was induced in CD4-specific MALT1-deficient mice to determine the importance of MALT1 in T-cells.
Results: We provide evidence that MALT1 plays a crucial role in the pathogenesis of RA as MALT1-deficent mice were completely protected against CIA. This complete protection was additionally observed in CD4-specific MALT1-deficient mice, indicating that the selective ablation of MALT1 in CD4-positive cells is sufficient for the observed resistance against CIA. CAIA on the other hand, which is a T- and B-cell independent model of RA, did not depend on the presence of MALT1, since both $MALT1^{+/+}$ and $MALT1^{-/-}$ mice showed comparable symptoms of RA. Interestingly, TNF^{DARE} mice that were deficient for MALT1 also showed a reduced enthesitis and ileitis phenotype, although TNF-concentration in the serum of these mice was higher compared to $MALT1^{+/+}xTNF^{DARE}$ mice.
Conclusions: Overall, our data highlight that MALT1 plays a crucial role in the pathogenesis of inflammatory arthritis and represents an interesting candidate to target therapeutically.
References:
[1] Thome M. Multifunctional roles for MALT1 in T-cell activation. Nat Rev Immunol 2008; 8 (7): 495–500.
Acknowledgements: We thank Chris Vercruysse (Department of Basic Medical Sciences, University of Ghent, Belgium) for exerting the three-point-bending tests of the femurs and the lab of Prof. Dr. Luc Van Hoorebeke (Department of Physics and Astronomy) for the use of the μCT-scanner.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4924

OP0177 N-GLYCOSYLATION SITES IN THE VARIABLE DOMAIN OF B CELL RECEPTORS SPECIFIC FOR CITRULLINATED ANTIGENS

L.M. Slot[1], R.D. Vergroesen[1], L. Hafkenscheid[1], M.T. Koning[2], T. Rispens[3], H. Veelken[2], R.E. Toes[1], H.U. Scherer[1]. *[1]Department of Rheumatology; [2]Department of Hematology, Leiden University Medical Center, Leiden; [3]Department of Immunopathology, Sanquin Research, Amsterdam, Netherlands*

Background: Recent structural analysis of anti citrullinated protein antibodies (ACPA) in serum and synovial fluid of patients with rheumatoid arthritis (RA) revealed that the vast majority (>90%) of secreted ACPA IgG molecules carry N-glycans in the variable (Fab) domain. This remarkable degree of Fab-glycosylation is absent from ACPA-depleted control IgG and from autoantibodies in other diseases. So far, it is unclear why ACPA carry this feature and which biological effects these glycans mediate in the context of RA. Of note, however, N-glycosylation requires a specific amino acid consensus sequence in the protein backbone, which is very rare in germline-encoded variable region genes.
Objectives: To study the B cell receptor (BCR) repertoire of ACPA-expressing B cells to determine the frequency, origin and localisation of N-glycosylation sites in ACPA Fab domains.
Methods: Citrullinated antigen-specific and non citrulline-reactive control B cells were identified in peripheral blood of ACPA-positive RA patients by antigen-specific tetramer staining and isolated by fluorescence activated cell sorting. Cells were either sorted in pools and directly lysed, or sorted as single cells and cultured for two weeks followed by the detection of ACPA-positive culture wells by ELISA. Full-length immunoglobulin (Ig) rearrangements were identified by anchoring reverse transcription of Ig sequences, amplification by nested PCR and either next generation sequencing (NGS, PacBio platform) or, for single cell transcripts, Sanger sequencing (scSeq). Sequence reads were analysed using IMGT V-QUEST tools.
Results: The mean number of nucleotide mutations in heavy chains (HC) of IgG BCRs derived from ACPA-expressing B cells was high (33 in NGS, 48 in scSeq samples; similarity to germline: 88% in NGS, 84% in scSeq). NGS identified 12 unique IgG clones derived from 4 donors, of which 10 (83%) had at least one N-glycosylation site in the HC or light chain (LC). scSeq identified 86 unique IgG clones derived from 6 donors, of which 68 (79%) had N-glycosylation sites. For 57/86 IgG clones, we could determine the combination of HC and LC sequences. In these, only 7 (12%) clones had no sites, while 19 (33%) had one, 23 (41%) had two, 5 (9%) had three and 3 (4%) clones had four sites. 57 sites were found in the HC and 34 in the LC. All N-glycosylation sites were created by somatic mutations and not encoded in the germline sequence. Several sites were located in antigen-engaging regions. No correlation was found between the number of N-glycosylation sites and the number of somatic mutations.
Conclusions: We demonstrate that B cell surface-expressed ACPA-IgG molecules carry a remarkably high frequency of N-glycosylation sites in the Fab domain, all of which are generated by somatic mutation. This could indicate that ACPA-expressing B cells acquire a selective survival advantage by introducing N-glycosylation consensus sequences in the Fab domain, a process that is likely to occur under the influence of T cell help and that could facilitate the break of tolerance to citrullinated antigens.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5904

OP0178 FIBROBLAST PRIMING IS COMMON TO MANY SITES, AND PSORIATIC SKIN FIBROBLASTS MAY ACQUIRE INFLAMMATORY MEMORY

T. Crowley[1], J.D. O'Neil[1], H.R. Adams[1], T.W. Kragstrup[2], A. Filer[1], C.D. Buckley[1], A.R. Clark[1]. *[1]Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom; [2]Biomedicine, Health, Aarhus University, Aarhus, Denmark*

Background: Rheumatoid arthritis (RA) is a common chronic inflammatory

disease of the joints. Whilst the autoimmune element continues to be studied intensely, it is evident that the innate inflammatory response propagates the disease. Fibroblast-like synoviocytes (FLS) are the most abundant stromal cell in the synovium. FLS from RA joints are markedly different from their healthy counterparts in their inflammatory characteristics.

RA FLS exhibit a form of inflammatory memory named priming. Prolonged exposure to TNFα induces an augmented chemokine response to challenges with interferons [1]. Fibroblast priming leads to significantly augmented IL6, CCL5 and CXCL10 responses to a second challenge by TNFα, with a coincident prolonged NFκB nuclear localization (manuscript in press).

Objectives: We wished to assess whether fibroblasts from sites other than the synovial joint would also exhibit this primed response to second challenge.

Methods: Fibroblasts from the joint, skin, lung, tonsil, bone marrow and gum were stimulated with 10ng/ml TNFα for 24h, before the conditioned medium was removed and the cells were washed free of stimulus. Cells were rested for 24h before once again being washed and stimulated with 10ng/ml TNFα for a further 24h. The conditioned medium was removed and secreted mediators compared between first and second response to stimulus. Transcription and intracellular signalling at time points within each challenge were also determined.

Results: Synovial, lung and tonsil fibroblasts augmented IL6 secretion in response to the second TNFα challenge. RA bone marrow-derived fibroblasts varied in their exhibition of priming. Skin fibroblasts from patients undergoing cosmetic surgery and a gingival sample from non-chronic inflammation displayed no evidence of IL6 priming.

Fibroblasts from the skin of psoriasis (Ps) patients mounted a primed response that was significantly augmented compared to their first response to TNFα, and significantly higher than the second response of healthy skin. This augmented response matches that of FLS, as IL6 but not IL8 was increased. This pattern was also matched by gum fibroblasts from periodontitis.

Mechanistically the Ps skin fibroblasts match FLS, in that NFκB nuclear localization is prolonged in the second challenge compared to the first.

Conclusions: We have shown that inflammatory memory in the form of IL6 priming occurs in fibroblasts from a variety of anatomical sites with diverse functions. Its prevalence implies a shared phenomenon, but the variation between sites suggests a specific role required in some tissues and not others.

The finding that Ps skin fibroblasts acquire this memory response may point towards a pro inflammatory mechanism that contributes to psoriatic diseases, including psoriatic arthritis. Our data may help to explain why an estimated 30% of psoriasis patients go on to develop psoriatic arthritis [2].

References:

[1] Sohn, C., et al., Prolonged TNFαprimes fibroblast-like synoviocytes in a gene-specific manner by altering chromatin. Arthritis Rheumatol, 2014.
[2] Mease, P.J., et al., Prevalence of rheumatologist-diagnosed psoriatic arthritis in patients with psoriasis in European/North American dermatology clinics. J Am Acad Dermatol, 2013. 69(5): p. 729–35.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5179

OP0179 BRAFV600E PROMOTES MYELOID SKEWING IN MULTISYSTEMIC LANGERHANS CELL HISTIOCYTOSIS HUMANIZED MOUSE MODEL

R. Biavasco[1], M. Norelli[2], B. Camisa[2], D. Cesana[1], P. Gallina[1], B. Gentner[1], M. Ponzoni[3], L. Dagna[4], A. Bondanza[2], E. Montini[1]. *[1]Sr-Tiget; [2]Innovative immunotherapy; [3]Pathology Unit; [4]Clinical immunology and rheumatology, San Raffaele Scientific Institute, Milan, Italy*

Background: Multisystemic Langerhans cell histiocytosis (mLCH) is an aggressive disease characterized by the accumulation of mononuclear phagocytes with immunohistochemical features of dendritic cell (histiocytes)[1]. Histiocytes infiltrate mostly the skin, bone marrow (BM), lung and spleen, and produce high levels of proinflammatory cyto/chemokines, leading to organ dysfunction[2,3]. In patients, around 10% of cells in lesions carries an oncogenic mutation in the MAPK pathway, mostly $BRAF^{V600E}$ (70% of cases). $BRAF^{V600E}$ can be detected also in monocytes and BM progenitors (HSPC) from these patients, whereas only a fraction of them carries a mutation in B cells and none in T cells[4].

Objectives: To study the role of $BRAF^{V600E}$ in the pathogenesis of mLCH, we set up a humanized mouse model of mLCH based on the transplantation into immunodeficient mice (NSG) of human HSPC expressing $BRAF^{V600E}$.

Methods: We isolated HSPC from human cord blood and transduced them at two different levels (50% and 20%) with lentiviral vectors that ubiquitously express $BRAF^{V600E}$, $BRAF^{WT}$ or GFP.

Results: All $BRAF^{V600E}$ mice manifested severe weight loss within 7 weeks with a median of 3 and 5 weeks for 50% and 20% transduction groups, respectively. Mice showed dysplastic bone marrow (BM) with infiltration of histiocytes; lesions were present also in lungs, kidneys, CNS, spleen and liver. Immunophenotype of infiltrating histiocytes closely resembles mLCH, staining positive for CD14, CD68, S-100 and langerin. None of the control mice lost weight nor displayed organ alteration. Flow cytometry analyses of BM showed 5- to 7-fold reduction in engraftment of human cells in $BRAF^{V600E}$ vs GFP groups ($p<0,001$). Percentage of myeloid cells increased by 3- to 4-fold in $BRAF^{V600E}$ vs GFP groups ($p<0,001$). On the contrary, percentage of B cells was reduced by 3- to 6,5-fold in $BRAF^{V600E}$ vs GFP groups ($p<0,001$). Moreover, there was no difference in the percentage of GFP-positive cells between myeloid cells, whole BM and *in vitro* sample, suggesting a non-cell autonomous mechanism underlying this myeloid phenotype.

Conclusions: In summary, we generated for the first time a human xenogeneic transplantation mouse model of mLCH, showing that $BRAF^{V600E}$ in human HSPC promotes myeloid skewing rather than proliferation.

References:

[1] Wilejto et al. Curr Opin Rheumatol 2012. DOI: 10.1097/BOR. 0b013e32834db53e.
[2] Donadieu et al. Histiocytic Disorders of Children and Adults 2005.
[3] Kannourakis et al. Br J Cancer 1994, Sep;23:S37–40.
[4] Berres et al. J Exp Med 2014, DOI: 10.1084/jem.20130977.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1840

THURSDAY, 15 JUNE 2017

Joint health & joint damage: a tale of three tissues –

OP0180 PHARMACOLOGICAL CHARACTERIZATION OF THE ADAMTS-5 INHIBITOR GLPG1972: AN ORAL ANTI-CATABOLIC AGENT FOR THE TREATMENT OF OSTEOARTHRITIS

P. Clement-Lacroix[1], C. Little[2], R. Blanqué[1], S. Meurisse[1], P. Mollat[1], F. Brebion[1], R. Gosmini[1], F. De Ceuninck[3], I. Botez[3], L. Lepescheux[1], E. van der Aar[4], T. Christophe[4], N. Vandervoort[4], C. Cottereaux[1], D. Comas[1], P. Deprez[1], D. Amantini[1]. *[1]Galapagos SASU, Romainville, France; [2]Raymond Purves Bone and Joint Research Laboratories, University of Sydney, Kolling Institute, Northern Sydney Local Health District, Sydney, Australia; [3]Institut de Recherches Servier, Suresnes, France; [4]Galapagos NV, Mechelen, Belgium*

Background: Degradation of articular cartilage and alterations of the underlying subchondral bone are hallmarks of osteoarthritis (OA)[1]. A disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5) is a key aggrecan-cleaving enzyme involved in this pathogenic process from the earliest stages of cartilage degradation[2] and as such, is an attractive drug target for the development of a disease-modifying OA drug (DMOAD)[3].

Objectives: In this report we describe the *in vitro* and *in vivo* characterization of the small molecule GLPG1972, an inhibitor of ADAMTS-5. GLPG1972 anti-catabolic activity was evaluated in murine and human cartilage explants and DMOAD activity was investigated in the destabilization of the medial meniscus (DMM) mouse model[4].

Methods: The ADAMTS-5 biochemical assay is based on the cleavage of a fluorescent substrate by recombinant ADAMTS-5. Mouse femoral head cartilage explants were stimulated by interleukin-1a (IL-1a) for 3 days and GAG release quantified[2b]. Human articular cartilage explants were stimulated with IL-1β for 12 or 19 days and the NITEGE epitope quantified using the AGNx1 assay. Unilateral OA was induced in C57BL6 mice by DMM[4]. Mice were treated with vehicle or GLPG1972 at 30, 60 or 120 mg/kg, b.i.d. for 8 weeks. Medial femorotibial joint sections were scored by an evaluator blinded to treatment.

Results: GLPG1972 showed potent inhibition of human ADAMTS-5 (IC_{50}=20 nM). Inhibition of ADAMTS-4 was moderate (IC_{50}=57 nM), and selectivity over 100-fold was observed against a large panel of zinc metalloproteinases. GLPG1972 displayed potent anti-catabolic activity in cartilage explants, with IC_{50} values being 2 μM and <1 μM in mouse and human, respectively. In the DMM mouse model, GLPG1972 demonstrated DMOAD activity, as shown by significant reduction of femorotibial cartilage proteoglycan loss and cartilage damage score, as well as significant impact on subchondral bone sclerosis.

Conclusions: GLPG1972 is an orally bioavailable, potent and selective ADAMTS-5 inhibitor showing significant anti-catabolic activity in cartilage explants. In the DMM model, treatment with GLPG1972 resulted in significant protective effects on both cartilage and subchondral bone pathology. Taken together these results provide support to progress GLPG1972 into the clinic as an oral treatment for OA.

References:

[1] Hunter, D.J., et al. Curr. Opin. Rheumatol. 2009, 21,110–117.
[2] a) Glasson, S.S., et al Nature. 2005, Vol 434: 644–8; b) Stanton, H., et al. Nature. 2005, Vol 434: 648–5; c) Little, C.B., et al. Journal of Clinical Investigation. 2007, Vol 117(6):1627–36.
[3] Larkin, J. et al. Osteoarthritis Cartilage. 2015, 23 (8): 1254–1266.
[4] Little, C.B. and Hunter, D.J. Nat. Rev. Rheumatol. 2013, 9(8):485–497.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3775

OP0181 DELETION OF THE PROSTAGLANDIN D2 RECEPTOR DP1 EXACERBATES AGING-ASSOCIATED AND INSTABILITY-INDUCED OSTEOARTHRITIS

Y. Ouhaddi, L. Habouri, J.-P. Pelletier, J. Martel-Pelletier, M. Benderdour, H. Fahmi. *Medicine, CRCHUM, Montreal, Canada*

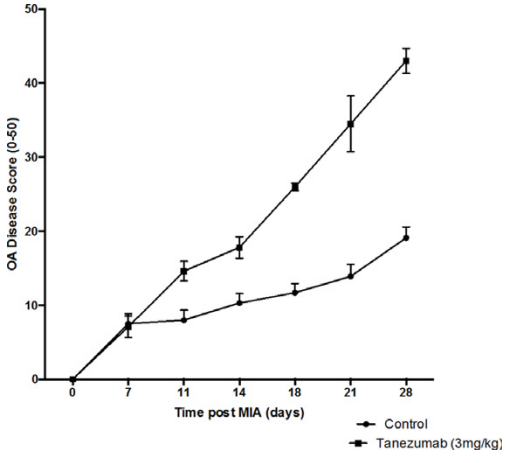
Background: *The D prostanoid receptor 1* (D*P1*), a *receptor* for prostaglandin D_2 (PGD_2) plays important roles in inflammation and cartilage metabolism. However, its role in the pathogenesis of osteoarthritis (OA) remains unknown.

Objectives: We undertook this study to explore the roles of DP1 in the development of OA and to evaluate the efficacy of a DP1 selective agonist in the treatment of OA.
Methods: We compared the development of aging-associated OA and destabilization of the medial meniscus (DMM)-induced OA in DP1-deficient (DP1-/-) and wild-type (WT) mice. The progression of OA was assessed by histology, immunohistochemistry, and microcomputed tomography (micro-CT). Cartilage explants from DP1-/- and WT mice were treated with interleukin-1α (IL-1α) ex vivo, to evaluate proteoglycan degradation. The effect of intra-peritoneal administration of the DP1 selective agonist BW245C on OA progression was evaluated in WT mice.
Results: Compared to WT mice, DP1-/- mice had exacerbated cartilage degradation in both models of OA and this was associated with increased expression of MMP-13, and ADAMTS-5. In addition, DP1-/- mice demonstrated enhanced subchondral bone changes. Cartilage explants from DP1-/- mice showed enhanced proteoglycan degradation following treatment with IL-1α. Intraperitoneal injection of BW245C attenuated the severity of DMM-induced cartilage degradation and bony changes in WT mice.
Conclusions: These findings indicate a critical role for DP1 signaling in OA pathogenesis. Modulation of DP1 functions may constitute a potential therapeutic target for the development of novel OA treatments.
Acknowledgements: This work was supported by the Canadian Institutes of Health Research (CIHR) Grant MOP-130293, the Arthritis Society, and the Fonds de la Recherche du Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6132

OP0182 CONVERGENCE OF JOINT REPAIR AND PAIN PATHWAYS VIA NERVE GROWTH FACTOR AND P75 EXPRESSING MESENCHYMAL STEM CELLS- A NOVEL EXPLANATION FOR OSTEOARTHRITIS PROGRESSION WITH ANTI-NGF IN OSTEOARTHRITIS

T. Baboolal[1], S. Al Hinai[1], E. Jones[1], J. Reckless[2], M. Foster[3], R. Doyle[4], K. af Forselles[3], S. Westbrook[3], D. McGonagle[1]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds; [2]Rxcelerate Ltd, Cambridge; [3]Levicept Ltd; [4]Tetrad Discovery Ltd, Ramsgate, United Kingdom*

Background: Nerve growth factor (NGF) is a key regulator of pain and anti-NGF therapy reduces osteoarthritis (OA) associated pain. However, anti-NGF therapy is associated with rapidly progressive OA (RPOA) [1]. In hip OA there is a 5-fold increase in mesenchymal stem cells (MSCs) from MRI bone marrow (BM) lesions, areas associated with OA progression [2]. MSCs in such lesions are uniformly positive for the NGF receptor, p75, which is also linked to chemotaxis and proliferation in other stromal cell compartments [3].
Objectives: Evaluate anti-NGF treatment in monoiodoacetate (MIA) induced OA and test whether NGF influences human BM-MSC function.
Methods: Human tibial plateau (TP) bone was isolated from patients undergoing total knee replacement. OA was induced in male Wistar rats (n=6) by intra-articular injection of 0.3 mg MIA. Each animal was treated with subcutaneous injection of control human IgG or anti-NGF (3 mg/kg) at Days 5, 10 and 15. Human and animal tissues sections were prepared for histological analysis using H&E staining and immunohistochemistry (IHC) using anti-p75 and anti-NGF antibodies. BM-MSCs were isolated from iliac crest aspirates and cultured under normal conditions. Expression of p75 was induced following overnight incubation with 400mM ethanol (EtOH) and confirmed by flow cytometry. Proliferation was assessed ± EtOH and 0–1 μg/ml NGF.
Results: Regions adjacent to cartilage loss in human TP showed abundant stromal proliferation, NGF and p75 immunoreactivity. In MIA model, by Day 18 there was substantial loss of cartilage, bone remodelling and stromal proliferation mimicking human disease. By Week 4 animals demonstrated unequal weight-bearing ($p<0.05$). Anti-NGF provided sufficient analgesia to normalise weight-bearing. Compared to IgG control, arthropathy progression was faster (Fig) with complete cartilage loss, bone marrow necrosis and cyst formation by Day 21. p75 immunoreactivity was greatly reduced in MIA-injected rats receiving anti-NGF compared with IgG. NGF positive staining was widespread in naïve and MIA-injected knees, but almost absent from MIA-treated knees of anti-NGF treated rats.



To investigate increased p75 positivity in knee OA, we restored p75 expression loss in expanded cell, to 97% of BM-MSCs (n=3) using EtOH. Increased MSC proliferation was seen at Days 6 and 9 (26%, p=0.03 and 30%, p=0.01 increase respectively, n=7) for 1 μg/ml NGF in the presence of EtOH compared to control (no NGF). In cultures without EtOH induction (absent p75) NGF had no effect.
Conclusions: TP bone from OA patients and rat MIA-treated subchondral bone contains p75 positive staining in regions of cartilage destruction and associated NGF positivity. Anti-NGF treatment exacerbated MIA-induced OA and reduced NGF and p75 expression. In vitro, NGF increased BM-MSC proliferation, suggesting NGF may be involved in the stromal proliferation seen at sites of OA damage. Thus, NGF may regulate MSC function. Complete blockade represents a novel mechanism for accelerated joint destruction in OA.
References:
[1] Hochberg MC et al. Arthritis Rheumatol 2016.
[2] Campbell TM et al Arthritis Rheumatol 2016.
[3] Jiang Y, et al. Cartilag Arthritis Res Ther 2015.
Disclosure of Interest: T. Baboolal: None declared, S. Al Hinai: None declared, E. Jones: None declared, J. Reckless Employee of: Rxcelerate Ltd, M. Foster Consultant for: Levicept Ltd, R. Doyle Employee of: Tetrad Discovery Ltd, K. af Forselles Consultant for: Levicept Ltd, S. Westbrook Shareholder of: Levicept Ltd, Employee of: Levicept Ltd, D. McGonagle: None declared
DOI: 10.1136/annrheumdis-2017-eular.6258

OP0183 CORDYCEPIN, A NOVEL COMPOUND, REDUCES KNEE JOINT PATHOLOGY AND PAIN IN THE MONOSODIUM IODOACETATE (MIA) RAT MODEL OF OSTEOARTHRITIS

S. Ashraf[1], J. Burston[2], V. Chapman[2], C. de Moor[1]. *[1]Pharmacy; [2]Arthritis Research UK Pain Centre, University of Nottingham, Nottingham, United Kingdom*

Background: Cordycepin (3' deoxyadenosine) is a popular traditional medicine in Asia, taken for conditions associated with ageing. Osteoarthritis (OA) is a common cause of pain and disability in the ageing population. Inflammation is a key component of osteoarthritic pain. Cordycepin is thought to act by inhibiting polyadenylation, the last step of mRNA synthesis, and can potentially have increased therapeutic benefit in OA (anti-inflammatory and analgesic) with fewer side effects than currently available therapies.
Objectives: The aim of this study was to determine whether cordycepin treatment alters osteoarthritic pain and pathology, and to decipher the mechanisms of action by which cordycepin exerts any potential beneficial actions.
Methods: OA was induced in male Sprague Dawley rats by intra-articular injection of mono-sodium iodoacetate (MIA; 1mg/50μl) on day 0. Cordycepin was administered orally (2mg/rat mixed in 1g of wet mash) every other day for 2 weeks (pre-emptive study: day 0 to day 14, therapeutic study: day 14 to day 28). Pain behaviour was measured as hind-limb weight-bearing asymmetry and mechanical paw withdrawal thresholds. Joint tissues were collected at days 14 and 28. Joint changes were quantified using histology and immunohistochemistry techniques. Synovial inflammation was quantified as extent of CD68 positive macrophage and cellular infiltration. Synovial angiogenesis was measured as endothelial cells positive for proliferating cell nuclear antigen (PCNA). Safranin-O staining was used to score cartilage damage and bone changes (osteophytes and channels crossing the osteochondral junction [OCJ]). Tartrate-resistant acid phosphatase (TRAP) positive osteoclasts and ADAMTS-5 and MMP13 positive chondrocytes were quantified as additional markers to detect bone and cartilage changes.
Results: The MIA rodent model of OA pain exhibited significant pain behaviour, synovial inflammation and angiogenesis, cartilage damage, osteophyte formation and subchondral bone changes, compared with non-arthritic controls. A two week pre-emptive and therapeutic treatment with cordycepin reduced MIA-induced pain behaviour and synovial changes (inflammation and angiogenesis). Pre-emptive cordycepin treatment reduced cartilage damage and the level of ADAMTS-5 and MMP13 from the chondrocytes. Pre-emptive and therapeutic cordycepin treatment reduced the number of channels crossing the OCJ and TRAP positive osteoclasts in the subchondral bone, but had no effect on numbers of osteophytes. Therapeutic cordycepin treatment did not alter cartilage damage score or the level of ADAMTS-5 and MMP13 positive chondrocytes.
Conclusions: Our data show that the analgesic effects of orally administered cordycepin in a pre-emptive and therapeutic protocol are associated with synovial changes (inflammation and angiogenesis) and bone remodelling. Administration of cordycepin before the onset of MIA-induced OA reduced cartilage damage and had a chondroprotective effect. Whereas therapeutically administered cordycepin did not alter cartilage damage. Further studies will investigate whether cordycepin mediated reduction in MIA-induced pathology and pain behaviour is as a result of its direct action on polyadenylation inhibition. Polyadenylation inhibitors could therefore be a novel class of drugs for treating OA.
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4867

OP0184 IMSYC IMMUNOLOGIC SYNOVITIS SCORE: A NEW HISTOLOGICAL SCORE FOR DISCRIMINATING INFLAMMATORY AND NON-INFLAMMATORY ARTHRITIS

A. Najm[1,2], B. Le Goff[1,2], F. Blanchard[1], J. Amiaud[1], C. Charrier[1], V. Krenn[3]. *[1]Inserm UMR 957; [2]Rheumatology, Nantes University Hospital, Nantes, France; [3]MVZ-Zentrum für Histologie, Zytologie und Molekulare Diagnostik, Trier, Germany*

Background: General Synovitis score (GSS) has been developed by Krenn *et al.* in order to discriminate inflammatory arthritis (IA) and non-inflammatory arthritis (NIA) (1). This score assesses 3 major components of synovitis: lining layer hyperplasia, activation of resident cells (stroma) and inflammatory infiltrate. All components are graded semi-quantitatively from 0 to 3 and the total score is on 9. High-grade synovitis is highly associated with IA and is defined by a score upper than 5 with a sensitivity of 61.7% and a specificity of 96.1%. As immunohistochemistry (IHC) is frequently used to better characterize synovitis, we propose to create a new IMmunologic SYnovitis SCore (IMSYC) adding 5 components to the GSS: CD68, CD3, CD20, CD31 and Ki67 immunostaining.
Objectives: Our work aimed to evaluate the diagnostic performance of this new score including IHC, to define the best cut off for inflammatory arthritis recognition, and to compare its diagnostic performance with the GSS.
Methods: 53 synovial samples from patients were obtained during surgery (arthroplasty or synovectomy). All patients gave written consent prior surgery. Samples were cut and Hematoxylin and eosin stained. CD68, CD3, CD20, CD31 and KI67 Immunohistochemistry were performed. GSS was assessed for each slide and semi-quantitative 4 scale scores (0–3) were given for each immunostaining, in a blind manner. The score is calculated on 24 (GSS 0–9 points, and 0–3 score for each of the 5 immunostaining). A representative amount of slides was read by 2 observers with a good interobserver variability (spearman correlation coefficient of 0.95, $p<0.0005$). They then defined a consensual and reproducible scoring atlas.
Results: 53 patients were included. 25 were females (47,2%), mean age was 62.1 years [Standard deviation (SD) 13.2 years]. 36 had inflammatory arthritis reparsed as follows: 28 Rheumatoid arthritis (RA), 5 had Psoriatic arthritis, 3 had Undifferentiated arthritis. “Non inflammatory” arthritis group included 10 patients with Osteoarthritis and 7 with ligaments or meniscus injuries. Mean GSS was significantly higher in the IA group 5.70 [SD 0.321] vs.3.51 [SD 0.351]; $p<0.001$). Mean IMSYC was significantly superior in the IA group 14.94 [SD 0.747] vs. 8.50 [SD 0.639]; $p<0.001$). In univariate analysis by logistic regression, GSS (Odd Ratio (OR) 2.27; $p<0.001$), CD3 (OR 4.3; p=0.002), CD68 (OR 4.5; p=0.002), Ki67 (OR 11.8; $p<0.001$), and CD31 scores (OR 6.5; p=0.001) were significantly associated with IA, however CD20 score was not (OR 0.9; p=0.34). ROC curve analysis determined the score of 10.5 out of 24 as the best cut off for discrimination between IA and non-IA with a sensitivity of 74.3% and specificity of 100%. The area under ROC curves was statistically superior with IMSYC (0.93) compared to GSS (0.81) (p=0.05).
Conclusions: We hereby propose a new synovitis score including IHC. This score has a better sensitivity and specificity than the Global synovitis score for discrimination between IA and non-IA. Moreover, this score accurately describes synovial membrane immunophenotype and could therefore give a basis for tissue driven therapies in rheumatic diseases, especially in RA.
References:
[1] Krenn V et al. Synovitis score: discrimination between chronic low-grade and high-grade synovitis.Histopathology. 2006 Oct;49(4):358–64.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2547

OP0185 IMMUNOHISTOLOGIC STUDY OF SYNOVITIS FROM PATIENTS WITH UNDIFFERENTIATED ARTHRITIS WHO EVOLVED TO RHEUMATOID ARTRHITIS OR PSORIATIC ARTHRITIS AFTER FOLLOW-UP

A. Cuervo Aguilera, R. Celis, J. Ramírez, M.V. Hernández, V. Ruíz-Esquide, J. Inciarte-Mundo, R. Sanmartí, J.D. Cañete. *Rheumatology, Hospital Clínic Barcelona, Barcelona, Spain*

Background: Undifferentiated Arthritis (UA) is defined as an inflammatory oligo/poly arthritis that does not fulfil criteria for a definitive diagnosis.Delay in diagnosis and treatment leads to poor prognosis. Previous studies have found differences in the cellular infiltrate between the synovitis of Rheumatoid Arthritis (RA) and Spondyloarthritis, including psoriatic arthritis (PsA)
Objectives: To identify synovial biomarkers that may be useful to diagnose patients with early UA
Methods: Retrospective longitudinal study.Patients with UA followed in our Arthritis Unit,who underwent arthroscopy between 2000 and 2014.Synovial biopsy were stained by immunohistochemistry with the following antibodies:CD3 for T cells,CD20 for B cells,CD79 for B cells,CD138 for plasma cells,CD31 for vessels,CD68 for macrophages,CD15 for neutrophils,CD117 for mast cells and hsp47 for fibroblasts, and quantified by Digital Image Analysis (Olympus).The same antibodies were evaluated in RA and PsA control groups
Results: 55 UA and 78 controls were included.Table 1 shows the clinical, serological and demographic characteristics.Among patients with UA, 23 (42%) patients met criteria for RA and 32 (58%) for PsA during follow-up.Synovitis of patients with UA had higher macrophage (CD68+) density in total tissue (p=0.008) and sublining (SL) (p=0.012) than the control group.The UA that evolved to RA had a higher density of CD3 T lymphocytes than the control RA group (p=0.014). No differences were observed in cells of adaptive immunity (CD20 B lymphocytes, CD138 plasma cells), innate immunity (CD117 mast cells, CD15 neutrophils), vessels (CD31) between the 4 groups.The area (%) stained by anti-hsp47 (synovial fibroblasts) in SL was higher in the RA control group than in the PsA (p=0.003)

Table 1. Data are expressed as mean±SD

	UA n=55	UA-RA n=23	UA-PsA n=32	p	RA n=40	PsA n=38	p
Age (years)	47±13	51±13	44±12	0.058	60±12	54±13	0.065
Sex (male)n (%)	22 (40)	6 (26)	16 (50)	0.074	17 (43)	23 (61)	0.111
Disease duration (years)	3±4	3±2	3±4	0.114	3±6	2±2	0.851
Time of follow-up (years)	7±4	8±4	6±4	0.038	7±3	5±3	0.008
CRP (mg/dL)	2.7±3.9	2.4±1.9	3.0±4.9	0.189	3.8±3.2	3.0±3.8	0.102
DAS28 (ESR)	4.17±1.05	4,83±1,06	3,63±0,94	0.000	5,15±1,51	4,02±1,04	0.002
ACPA n (%)	4 (22)	4 (22)	0 (0)	0.000	30 (77)	0 (0)	0.000
RF n (%)	10 (7)	9 (41)	1 (3)	0.000	28 (70)	1 (3)	0.000
csDMARD n (%)	21 (41)	7 (35)	14 (45)	0.472	29 (73)	19 (50)	0.041
bDMARD n (%)	2 (4)	0 (0)	2 (6)	0.243	8 (20)	6 (16)	0.628
PDN n (%)	7 (13)	3 (14)	4 (13)	0.851	11 (28)	5 (13)	0.117

Conclusions: This is the first immunohistological study of synovitis in a significant group of patients with UA who developed AR or PsA during follow-up. Although there are some differences between the UA and control groups in the density of CD68+ macrophages and lymphocytes T CD3+, these do not appear to be useful for an early diagnosis of UA. On the other hand, unlike the results of some previous studies, we not found differences between the cellular infiltrate (adaptive immunity, innate immunity or vessels) in patients with RA and PsA. The fact that some patients with UA were undergoing treatment prior to synovial biopsy and its retrospective character limit the results of this study
Acknowledgements: Financed: “Fondo de Investigación Sanitaria” (PI14/00785. JD Cañete) del Instituto de Salud Carlos III (ISCIII). Co-financed by BECA FER-2015. Premis “Emili Letang”, Hospital Clínic. BECA MSD-Sociedad Catalana de Reumatología
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4850

OP0186 TENOFOVIR, A NUCLEOSIDE ANALOG REVERSE TRANSCRIPTASE INHIBITOR FOR TREATMENT OF HIV, PROMOTES OSTEOCLAST DIFFERENTIATION AND BONE LOST IN VIVO IN A MECHANISM DEPENDING ON ATP RELEASE AND ADENOSINE, AND DIPYRIDAMOLE MAY BE A USEFUL TREATMENT TO REVERT THE EFFECTS

F.M. Conesa[1], P. Llamas[1], T. Wilder[2], P. Atencio[3], A. Cabello[3], M. Górgolas[3], B. Cronstein[2], R. Largo[1], G. Herrero-Beaumont[1], A. Mediero[1,2]. *[1]Joint and Bone Research Unit, Iis-Fundacion Jimenez Diaz, Madrid, Spain; [2]Division of Translational Medicine, Department of Medicine, NYU School of Medicine, New York, United States; [3]Internal Medicine Department, Iis-Fundacion Jimenez Diaz, Madrid, Spain*

Background: HIV infection devastates the immune system but also affects other tissues and organs Bone alterations have been observed in HIV disease for nearly two decades, in particular a higher risk of low bone mineral density (BMD) and fragility fractures. Treatment with Tenofovir alone or as part of HAART, leads to changes in bone catabolism markers and significant reductions in BMD in children and young adults. Tenofovir is taken up by cells and phosphorylatedand inhibits HIV-reverse transcriptase by mimicking AMP. We have recently found that Tenofovir inhibits Pannexin-1/Connexin-43-mediated ATP release from cells and decreases extracellular adenosine levels and fibrosis in murine models. Inhibition of osteoclast formation *via* adenosine A2A receptor stimulation or increasing local adenosine concentration stimulates new bone formation as well as rhBMP-2.
Objectives: As adenosine and ATP are key regulators of bone homeostasis, we determined whether Tenofovir directly affects bone by an adenosine- or ATP-dependent mechanism and if treatment with Dipyridamole, an agent that increases extracellular adenosine by blocking cellular adenosine uptake, may be a useful treatment to counteract Tenofovir effects.
Methods: M-CSF/RANKL-induced osteoclast (OC) was studied in primary murine bone marrow culture as the number of TRAP-positive cells after challenge with Tenofovir (1nM-100μM) alone or in combination with Dipyridamole (1nM-100μM). OC markers were measured by RT-PCR. Pannexin-1 and Connexin-43 expression were permanently knocked down by lentiviral infection with appropriate shRNA or scrambled shRNA and these cells were induced to differentiate into OC by RANKL. Male C57Bl/6 mice received Tenofovir 75mg/Kg/day alone or in combination with Dipyridamole 1mg/Kg/day for 4 weeks. Double labelling of bone with calcein/Alizarin Red to analized bone formation was performed and long bones prepared for microCT and histology.
Results: Tenofovir produced a dose-dependent increase in OC differentia-

tion (EC50=44.5nM) that was reversed by Dipyridamole (IC50=0.3μM). When Pannexin-1 and Connexin-43 were absent, Tenofovir did not increase OC number. Tenofovir increases Cathepsin K and NFATc1 mRNA levels during OC differentiation, and the effect was reverted by Dipyridamole. Tenofovir reduced bone formation *in vivo* (19±2μm bone aposition vs 35±4μ m untreated $p<0.05$) and this effect was reverted in the presence of Dipyridamole (30±3μm, $p<0.05$ vs Tenofovir alone). microCT revealed decrease BMD and altered trabecular bone in Tenofovir-treated mice, been reverted in the presence of Dipyridamole. TRAP-staining showed increased OC *in vivo* in Tenofovir-treated mice (21±1 vs 16±1 OC/hpf in untreated, $p<0.005$) that was reverted with Dipyridamole. Similar results were obtained for Cathepsin K.

Conclusions: These results indicate that Tenofovir enhances OC differentiation and inhibits osteoblast differentiation by an adenosine-dependent mechanism and suggests that treatment with agents that increase local adenosine concentrations, like Dipyridamole, might prevent bone loss following Tenofovir treatment.

Disclosure of Interest: F. Conesa: None declared, P. Llamas: None declared, T. Wilder: None declared, P. Atencio: None declared, A. Cabello: None declared, M. Górgolas: None declared, B. Cronstein: None declared, R. Largo: None declared, G. Herrero-Beaumont: None declared, A. Mediero Grant/research support from: Instituto de Salud Carlos III, Fondos FEDER

DOI: 10.1136/annrheumdis-2017-eular.3207

OP0187 TRANSGENIC DISRUPTION OF GLUCOCORTICOID-SIGNALING IN MATURE OSTEOBLASTS AND OSTEOCYTES ATTENUATES STRUCTURAL BONE DAMAGE IN A LONG-TERM MURINE K/BXN SERUM-INDUCED ARTHRITIS MODEL

E. Wiebe[1,2], C. Spies[1,2], J. Tu[2], T. Maleitzke[1,2], Y. Zhang[2], M. Seibel[2,3], H. Zhou[2], F. Buttgereit[4]. *[1]Department of Rheumatology and Clinical Immunology, Charité University Hospital, Berlin, Germany; [2]Bone Research Program, ANZAC Research Institute, University of Sydney; [3]Department of Endocrinology and Metabolism, Concord Repatriation Hospital, University of Sydney, Sydney, New South Wales, Australia; [4]Department of Rheumatology and Clinical Immunology, Charité Universitätsmedizin Berlin, Berlin, Germany*

Background: The role of endogenous glucocorticoids (GC) in bone metabolism in chronic inflammatory arthritis remains unclear. We have previously shown that disruption of GC-signaling in osteoblasts results in a marked attenuation of arthritis in the K/BxN serum-induced and CAIA mouse model with preservation of bone volume and structure[1,2].

Objectives: In order to investigate the impact of endogenous GCs on bone erosion and turnover in chronic inflammatory arthritis, we now studied the effects of disrupted osteoblastic GC-signaling in a *long-term* murine arthritis model.

Methods: Intracellular GC-signaling in osteoblasts was disrupted by transgenic overexpression of 11beta-hydroxysteroid dehydrogenase type 2 (11β-HSD type 2) under the control of a type 1 collagen promoter. Arthritis was induced in 5-week old male transgenic (tg) mice and their wild-type (WT) littermates. In order to maintain a chronically active arthritis, mice were boosted on day 14 and 28 by subcutaneous injection of K/BxN serum, controls (CTR) received PBS, respectively. Severity of arthritis was assessed daily by clinical scoring and ankle size measurements until the endpoint (day 42). Ankle joints were assessed by a histopathologic score and microfocal computed tomography (micro-CT). Systemic effects of inflammation on bone metabolism were quantified by histomorphometry and micro-CT of the tibia.

Results: Acute Arthritis developed in both tg and WT mice and remained active over the period of 42 days, with a reduced, yet non-significant, severity in tg compared to WT mice. Histological indices of inflammation, cartilage damage and especially bone erosion, additionally assessed by micro-CT, tended to be overall reduced in tg mice, yet not reaching a level of significance. Bone volume and bone turnover did not differ between tg and WT arthritic mice.

Conclusions: The modulating effect of disrupted GC-signaling in osteoblasts in serum-induced autoimmune-arthritis prevails in a chronic inflammatory setting, leading to less severe local inflammation and bone destruction. This supports the important role of endogenous GCs for an intact bone metabolism in inflammatory bone disease.

References:

[1] Tu J, Zhang Y, Kim S, Wiebe E, Spies CM, Buttgereit F, et al. Transgenic Disruption of Glucocorticoid Signaling in Osteoblasts Attenuates Joint Inflammation in Collagen Antibody-Induced Arthritis. Am J Pathol. 2016;186(5):1293–301.

[2] Buttgereit F, Zhou H, Kalak R, Gaber T, Spies CM, Huscher D, et al. Transgenic disruption of glucocorticoid signaling in mature osteoblasts and osteocytes attenuates K/BxN mouse serum-induced arthritis in vivo. Arthritis Rheum. 2009;60(7):1998–2007.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5806

THURSDAY, 15 JUNE 2017

Treat-to-target in axSpA: reality or utopy?

OP0188 DEFINING CLINICALLY IMPORTANT WORSENING BASED ON ASDAS-CRP FOR AXIAL SPONDYLOARTHRITIS: A DATA-BASED CONSENSUS BY THE ASSESSMENT IN SPONDYLOARTHRITIS INTERNATIONAL SOCIETY (ASAS)

A. Moltó[1], L. Gossec[2], R. Landewé[3], D. van der Heijde[4], M. Dougados[1]. *[1]Rheumatology B Department, Cochin Hospital; [2]Pitié Salpêtrière Hospital, Department of rheumatology, Paris, France; [3]Department of Clinical Immunology & Rheumatology, Amsterdam Rheumatology Center, Amsterdam and Zuyderland Medical Center, Heerlen; [4]Department of Rheumatology, Leiden University Medical Centre, Leiden, Netherlands*

Background: Disease flares are increasingly used as outcomes in axial spondyloarthritis (axSpA) trials or observational studies.

Objectives: The objective of this initiative was to define a cutoff for the ASDAS score that best defines the concept of "worsening in axSpA", to be used in the context of clinical trials and longitudinal observational studies.

Methods: Various steps were followed between 2014 and 2017. (a) Initial expert opinion within the steering group to define the scope of the project; (b) systematic literature review to collect cutoffs used for worsening in published studies; (c) vignette-exercise among ASAS members: a theoretical 'paper' patient-vignette, in whom an initial and a final value of an outcome was provided, was judged by the physicians on whether or not the patient had worsened (defining phy-worsening) (ref); (d) real-life multicenter international study: data necessary to calculate different outcomes were collected from real patients at 2 consecutive visits (spaced 7 days to 6 months): external standard was defined as a patient's report that he/she had worsened and he/she felt there was a need for treatment intensification. (e) Testing of different changes in the outcomes against both external standards for worsening (phy-worsening and pt-worsening) followed by a consensus and voting procedure among ASAS members in January 2017.

Results: (a) There was consensus about worsening being an absolute change between 2 time-points (without defining time between the 2 time-points) and about exploring cutoffs for 3 outcomes: ASDAS-CRP, BASDAI and pain. (b) The literature review had yielded 27 different cutoffs in 38 studies indicating important heterogeneity (c) The vignette-exercise yielded 12 preliminary definitions for worsening to be tested (as previously reported). (d) In the prospective study the sensitivity and specificity of each cutoff was tested against pt-worsening and judged by the ASAS-community. (e) No consensus was reached for a BASDAI-based definition due to limited performance of all cut-offs, and it was decided to not define a value for a pain-based definition for worsening. Based on aggregated data (Table), a consensus was reached among the ASAS-members to define worsening as a deterioration in ASDAS of at least 0.9 points. While this cutoff led to only moderate sensitivity when tested against pt-worsening, the overall balance of sensitivity and specificity as well as the overall face validity of this cut-off value for ASDAS was deemed most acceptable.

Table. Sensitivity and specificity of different ASDAS cutoffs to define worsening, against phy-worsening and pt-worsening considered as external standards.

Cutoff values for change in ASDAS	Vignette exercise study (N=1150 physician judgments) against the external standard 'phy-worsening' (worsening in N=591)		Prospective real-life study (N=1169 patients), against the external standard 'pt-worsening' (worsening in N=127)	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
>=0.6	97	65	55	91
>=0.9	85	87	38	96
>=1.1	60	94	33	98

Conclusions: This data-driven ASAS consensus process has allowed to propose an ASDAS-based cutoff value defining worsening in axSpA. As has been observed in other settings, the change defining worsening (at least 0.9) is smaller than the change defining improvement which is 1.2 for ASDAS. This definition should now be applied in trials.

References:

[1] Gossec L, et al. Preliminary definitions of 'flare' in axial spondyloarthritis, based on pain, BASDAI and ASDAS-CRP: an ASAS initiative. Ann Rheum Dis. 2016;75:991–6.

Acknowledgements: This study was supported by ASAS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4786

OP0189 TUMOR NECROSIS FACTOR INHIBITOR TREATMENT REDUCES SPINAL RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS BY DECREASING DISEASE ACTIVITY: A LONGITUDINAL ANALYSIS IN A LARGE PROSPECTIVE COHORT

C. Molnar[1], A. Scherer[1], X. Baraliakos[2], M. de Hooge[3], R. Micheroli[4], P. Exer[5], R. Kissling[6], G. Tamborrini[5], L. Wildi[4], M. Nissen[7], P. Zufferey[8], J. Bernhard[9], U. Weber[10], R. Landewé[11], D. van der Heijde[3], A. Ciurea[4]. *[1]SCQM, Zurich, Switzerland; [2]Rheumazentrum, Herne, Germany; [3]LUMC, Leiden, Netherlands; [4]USZ, Zurich; [5]Private Practice, Basel; [6]Balgrist, Zurich; [7]HCUGE, Geneva; [8]CHUV, Lausanne; [9]Bürgerspital, Solothurn, Switzerland; [10]Univ Southern Denmark, Odense, Denmark; [11]AMC, Amsterdam, Netherlands*

Background: Whether tumor necrosis factor inhibitors (TNFi) have an influence on radiographic progression in ankylosing spondylitis (AS) remains controversial.
Objectives: To investigate the impact of TNFi use on spinal radiographic progression in AS.
Methods: Patients fulfilling the modified NY Criteria for AS (as assessed by central reading) in the Swiss Clinical Quality Management Cohort with at least 2 years of clinical and radiographic follow-up were included. Spinal X-rays were taken every 2 years and scored independently by 2 blinded readers according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) in chronological time order. Average score of the readers was used. Radiographic progression was defined as an increase by $\geq$2 mSASSS units over 2 years. The relationship between TNFi use before a 2 year X-ray interval and progression within the interval was investigated using binomial generalized estimating equation models with adjustment for potential confounding and multiple imputation of missing covariate data. Ankylosing Spondylitis Disease Activity Score (ASDAS) was regarded as a potential intermediate variable mediating the effect of TNFi on radiographic progression. It was added to the model as a time-varying variable in a sensitivity analysis.
Results: A total of 420 patients with AS contributed to data for 597 x-ray intervals in adjusted analyses (1–5 intervals per patient); BL characteristics: male sex 66%, HLA-B27 81%, mean (SD) age 40.4 (10.9) years, disease duration 13.9 (9.8) years, mSASSS 6.4 (12.4), ASDAS 2.8 (1.1)). 39% of the patients were already on TNFi at first X-ray. Mean mSASSS progression in 2 years was 0.9 (2.7) units. The multivariable model (Table) shows that prior use of TNFi reduced the odds of progression in the next 2 year interval by 49% (odds ratio (OR) 0.51, 95% confidence interval (CI) 0.28–0.92, p=0.03). BL mSASSS and male sex also significantly affected progression. Adding ASDAS as a covariate to the model decreased the estimated effect of TNFi on progression: OR 0.65, 95% CI 0.36–1.17, p=0.15. In this model, a decrease in ASDAS by 1 unit would lower the odds for progression by 0.62 (p=0.001).

Table 1. Longitudinal multivariable analysis of radiographic progression

Variable	OR	95% CI	P value
TNFi use prior to X-ray interval	0.51	0.28–0.92	0.03
NSAID use at start X-ray interval	0.81	0.40–1.63	0.55
mSASSS at start X-ray interval	1.06	1.04–1.07	<0.001
Male gender	3.01	1.56–5.77	0.001
Disease duration	1.01	0.99–1.04	0.38
Current smoking	0.94	0.55–1.61	0.83
HLA-B27	0.99	0.46–2.12	0.98
Nb of exercise sessions per week	0.93	0.80–1.08	0.35
Peripheral arthritis	1.00	0.56–1.79	1.00

Conclusions: TNFi seem to reduce radiographic progression in patients with AS and this effect is mediated, at least in part, by a decrease in disease activity.
Acknowledgements: Supported by the Stiftung für Rheumaforschung and a research grant from the investigator initiated studies program of MSD.
Disclosure of Interest: C. Molnar: None declared, A. Scherer: None declared, X. Baraliakos: None declared, M. de Hooge: None declared, R. Micheroli: None declared, P. Exer: None declared, R. Kissling: None declared, G. Tamborrini: None declared, L. Wildi: None declared, M. Nissen: None declared, P. Zufferey: None declared, J. Bernhard Consultant for: Merck Sharp & Dohme, Pfizer, Roche, U. Weber Consultant for: Abbvie, R. Landewé: None declared, D. van der Heijde: None declared, A. Ciurea Consultant for: Abbvie, Celgene, Eli Lilly, Janssen-Cilag, Merck Sharp & Dohme, Novartis, Pfizer, UCB
DOI: 10.1136/annrheumdis-2017-eular.2571

THURSDAY, 15 JUNE 2017

Calcium crystal deposition in rheumatic diseases

OP0190 HISTOLOGICAL CHARACTERIZATION OF ROTATOR CUFF CALCIFIC TENDINOPATHY

C. Darrieutort-Laffite[1,2], A. Najm[1,2], T. Garraud[1,2], P. Layrolle[2], F. Blanchard[2], B. Le Goff[1,2]. *[1]Rheumatology, CHU Hotel Dieu Nantes; [2]Laboratoire Phy-OS, INSERM U1238, Nantes, France*

Background: Calcific tendinopathy is one of the most frequent causes of shoulder pain. Calcific deposits lead to chronic discomfort in daily and professional activity. These deposits are composed of carbonated apatite. Although the disease is frequent, its origin stays still largely unknown. Molecular and cellular mechanisms involved in this pathological mineralization process are not clearly identified.
Objectives: The objective of the study was to analyze calcified tendinous samples to understand the organization of the deposits and to characterize the cells potentially involved in their formation.
Methods: Samples were collected from cadaveric subjects. Ultrasound was first used to detect calcified tendons. Then, tendons were collected and fixed in formalin 4% during 48h. They were first analyzed with micro-CT to know the distribution of the calcific deposits. Samples were then decalcified in EDTA, dehydrated and embedded in paraffin. Some samples were not decalcified to allow a better characterization of the calcific deposits. Several histological staining were performed: hematoxylin and eosin (HE), Safranin O/Fast Green (SO/FG) and Von Kossa (no decalcified samples). Immunohistochemistry using anti-Runx2, anti-Sox9, anti-Collagen II and anti-caspase III antibodies has been performed to characterize the cells and tissue around the calcifications.
Results: Six samples were collected (1 normal and 5 calcified). On HE staining, three different histological patterns were observed. Little calcifications disseminated between tendinous fibers (N=2), voluminous ones encapsulated by a fibrous tissue (N=2) and in one sample an intra-tendinous osseous metaplasia. In the fibrous peripheral area of larger calcifications, we observed cells with round nuclei, different from tenocytes. These cells expressed Runx2 and Sox9 suggesting a chondrocyte phenotype. On SO/FG staining, this peripheral area presented a red coloration (proteoglycan specific) as the fibrocartilage at the tendon attachment. However, collagen II clearly present in the fibrocartilage was not present in these areas. As pathological calcification in cartilage can be associated with chondrocytes apoptosis, we sought for anti-Caspase III expression in the cells of the peripheral area. None of the chondrocyte-like cells located around the larger calcifications expressed Caspase III. Finally, one sample had an osseous metaplasia within the tendon with Runx2 positive cells.
Conclusions: Histological analyses of whole calcified tendon tissues showed three different patterns of calcific deposits. We can hypothesize that these patterns correspond to different stages of the disease. Chondrocyte-like cells were observed around larger deposits and could be involved in the mineralization process. Interestingly, they differ from the cells of the fibrocartilage as they did not express collagen II. Further analyses are necessary to characterize their phenotype and understand the steps leading to these deposits within the tendon.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4682

OP0191 COMPARISON OF ULTRASONOGRAPHY AND RADIOGRAPHY OF THE WRIST FOR DIAGNOSIS OF CALCIUM PYROPHOSPHATE DEPOSITION

A. Combier, M. Forien, A. Gardette, E. Palazzo, P. Dieudé, S. Ottaviani. *Rheumatology Departement, Bichat Hospital, Paris, France*

Background: The gold standard for diagnosis of calcium pyrophosphate (CPP) deposition (CPPD) is the identification of CPP crystals in synovial fluid. However, aspiration of synovial fluid can be challenging in small joints such as the wrist, a usual location of arthritis in CPPD. Despite its low sensitivity, the most widely used imaging modality is conventional radiography but ultrasound (US) seems a useful tool for diagnosis of CPPD.
Objectives: We aimed to compare the performance of US and conventional radiography of the wrist for diagnosis of CPPD.
Methods: Patients with joint effusion (knee, hip, shoulder, ankle or wrist) were consecutively included. CPPD was diagnosed by CPP crystals identified in synovial fluid. Patients without CPP crystals in synovial fluid were controls. As recommended, we used the term chondrocalcinosis (CC) to assess imaging features suggesting CPPD. Two blinded operators assessed CC in all patients by US and conventional radiography of the wrist. The presence of CC in triangular fibrocartilage (TFC) and wrist hyaline cartilage in US and TFC and radiocarpal (RC) joint in radiography was noted. A patient was considered to have CC if at least one wrist had imaging features of CC.
Results: We included 58 patients with joint effusion (32 with CPPD). The remaining 26 patients, controls, had rheumatoid arthritis (n=13), spondyloarthritis (n=6), gout (n=6), and osteoarthritis (n=1). The mean age was 67.1±16.3 years. Location of joint effusion was as follows: 34 knees, 15 wrists, 3 shoulders, 2 ankles, 3 hips and 1 elbow. Among CPPD patients, US revealed CC in 30 (93.7%) and radiography in 17 (53.1%) ($p<0.001$). The sensitivity (Se) and specificity (Sp) of US for the diagnosis of CPPD were 94% and 85%, respectively; the positive likelihood ratio was 6.1. When analyzing US features of CC separately, US Se was higher at the TFC than RC joint, 81% and 50% respectively. The Se and Sp of radiography were 53.1% and 100%, respectively. Intraobserver reliabilities for US and radiographic CC were almost perfect: κ coefficient 0.832 [95% confidence interval 0.651–1.0] and 0.880 [0.314–0.880], respectively. In all 58 patients, 113 joints were analyzed (3 patients had radiography of only one wrist). The κ coefficient between US and radiography for CC was moderate: 0.33 [0.171–0.408].
Conclusions: Our study suggests that wrist US should be considered a relevant tool for the diagnosis of CPPD, with higher sensitivity than radiography.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3987

THURSDAY, 15 JUNE 2017

Fifty shades of remission in RA

OP0192 ADDING ULTRASOUND TO THE TREAT-TO-TARGET STRATEGY SHOWS NO BENEFIT IN ACHIEVEMENT OF REMISSION: RESULTS FROM THE BIODAM COHORT

A. Sepriano[1], S. Ramiro[1], R. Landewé[2], D. van der Heijde[1], S. Ohrndorf[3], O. FitzGerald[4], M. Backhaus[3], M. Larché[5], J. Homik[6], A. Saraux[7], H. Hammer[8], L. Terslev[9], M. Østergaard[10], G. Burmester[3], B. Combe[11], M. Dougados[12], C. Hitchon[13], G. Boire[14], R. Dadashova[15], J. Paschke[15], E. Hutchings[15], W. Maksymowych[6]. *[1]LUMC, Leiden; [2]ARC, Amsterdam, Netherlands; [3]Charité, Berlin, Germany; [4]SVUH, Dublin, Ireland; [5]McMaster University, Hamilton; [6]University of Alberta, Edmonton, Canada; [7]CHU, Brest, France; [8]Diakonhjemmet Hospital, Oslo, Norway; [9]Copenhagen UH, Copenhagen; [10]Copenhagen UH, Copenhagen, Denmark; [11]CHU, Montpellier; [12]Descartes University, Paris, France; [13]University of Manitoba, Winnipeg; [14]University of Sherbrooke, Quebec; [15]CaRE Arthritis Ltd, Edmonton, Canada*

Background: While, a Treat-to-Target strategy (T2T), treating patients with rheumatoid arthritis (RA) towards a certain target (eg. clinical remission; T2T-REM), is highly recommended, several patients in clinical remission often have residual synovitis on ultrasound-imaging (US). This may result in silent radiographic progression and clinical flare. It is arguable whether targeting US-synovitis may result in "deeper" remission in clinical practice.
Objectives: To assess whether using US in a T2T strategy leads to more patients meeting clinical remission than using only clinical information.
Methods: Patients with RA who started or changed csDMARD and/or anti-TNF treatment followed in centers with expertise in US and participating in BIODAM (2-year multicenter prospective observational cohort) were included. Clinical and US data [by the US7-score that includes 7 joints of the clinically dominant hand and foot for synovitis and tenosynovitis on gray-scale US (GSUS) and power-doppler US (PDUS) and erosions on GSUS] were collected every 3 months. Per visit was decided whether the patient was treated according to the clinical definition of T2T with remission as benchmark (T2T-CLIN-REM). Though not mandatory, US-data could also be used for this purpose. T2T-CLIN-REM was considered correctly applied if: either i) a patient already had a disease activity score below the remission target (i.e. ACR/EULAR boolean remission) or ii) if not, treatment was intensified. A T2T strategy taking also US data into account (T2T-CLIN-US-REM) was considered correctly applied if: either i) both clinical and US remission (all joints included in the US7-score with GSUS synovitis <2 and PDUS synovitis=0) were present; or ii) if not, the treatment was intensified. The main outcome was ACR/EULAR boolean remission. The effect of adding US to T2T (T2T-CLIN-US-REM) on clinical remission 3 months later compared to a clinical remission benchmark only (T2T-CLIN-REM) was analyzed using generalized estimating equations with auto-regression.
Results: In total 963 visits of 130 patients were included. T2T-CLIN-US-REM was correctly followed in 33% of the visits, T2T-CLIN-REM in 14%, and any of these in 52%. Remission according to the ACR/EULAR-boolean definition was achieved in 19.6% of the visits. Compared to the conventional T2T-CLIN-REM strategy, using a combined clinical and US benchmark for T2T led to a lower – instead of higher - likelihood of ACR/EULAR-boolean remission 3 months later [OR (95% CI): 0.39 (0.24; 0.63] (table).

Table. Effect of following a T2T strategy taking both clinical and US data into account (T2T-CLIN-US-REM) compared to the clinical definition of T2T (T2T-CLIN-REM; reference) in meeting the targets 3 months later and over a period of 2 years.

T2T approach / Outcome	ACR/EULAR boolean remission aOR* (95% CI)
No T2T *vs* T2T-CLIN-REM alone§	0.49 (0.27; 0.88)
T2T-CLIN-US-REM *vs* T2T-CLIN-REM alone§	0.39 (0.24; 0.63)

*Adjusted for age, gender, HAQ-score, RF, ACPA, previous use of DMARDs, smoking-status, education and number of comorbidities. § Clinical definition of T2T (T2T-CLIN-REM) was used as the comparator for each of the presented treatment strategies.

Conclusions: Our results, from a non-randomized study, did not suggest an advantage of using US of 7 joints in addition to clinical examination as a T2T benchmark as compared to clinical examination alone in getting RA patients into clinical remission.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1613

THURSDAY, 15 JUNE 2017

Innate immunity

OP0193 INFLAMMATION OF ADVENTITIAL NERVES OCCURS IN GIANT CELL ARTERITIS PATIENTS AND IT IS CHARACTERIZED BY INFLAMMASOMES, UPR AND AUTOPHAGY ACTIVATION

F. Ciccia[1], A. Rizzo[1], R. Alessandro[1], S. Raimondo[1], G. Guggino[1], A. Cavazza[2], C. Salvarani[2], G. Triolo[1]. *[1]University of Palermo, Palermo; [2]Arcispedale Santa Maria Nuova, Reggio Emilia, Italy*

Background: Vascular adventitia is a major site of immune surveillance and inflammatory cell trafficking and is the most complex compartment of the vessel wall comprising fibroblasts, dendritic cells and macrophages, progenitor cells, vasa vasorum, pericytes and adrenergic nerves. It has been proposed that activation of adventitial nerves and release of sensory neuropeptides from their peripheral terminals may leads to neurogenic inflammation. Giant cell arteritis (GCA) is an immune-mediated disease of unknown etiology in which the inflammatory process seems to start from the adventitia of affected arteries.
Objectives: aim of the study was to evaluate the occurrence of adventitial nerves inflammation and to immunologically characterize the adventitial neuritis occurring in GCA patients.
Methods: Immunohistochemistry and RT-PCR were used to study the presence of neuritis in temporal artery samples obtained from 30 patients with temporal artery (TAB) positive GCA, 20 TAB negative GCA and 20 controls. Laser capture microdissection (LCM) was used to isolate adventitial nerves and nerve expression of pro-inflammatory cytokines involved in the pathogenesis of GCA such as IL-6, IL-17, IL-32, IL-9, IL-33 was assessed by RT-PCR. Expression of pro-inflammatory cytokines by adventitial nerves was further studied by immunohistochemistry and confocal microscopy. Autophagy, unfoled protein response (UPR) and inflammasomes pathways were also studied by RT-PCR and immunohistochemistry.
Results: Adventitial nerves showed infiltration of $CD3^+$ T cells in all the TAB positive and in 12 out of 20 TAB negative arteries but were never observed in control arteries. RT-PCR expression analysis of different pro-inflammatory cytokines clearly demonstrated specific over-expression of IL-33 in LCM isolated inflamed nerves. Immunohistochemical and confocal microscopy analysis confirmed nerve IL-33 expression. RT-PCR and immunoistochemistry demonstrated that AIM2 and NLRP3, but not NLCR4, inflammasomes were activated in inflamed nerves of GCA patients. According to inflammasomes activation, increased IL-18 expression was observed. Autophagy-related genes such as ATG16L1 and LC3 and UPR-related genes such as XBP-1 and CHOP were also over-expressed in GCA adventitial nerves as demonstrated by RT-PCR and immunohistochemistry. Finally, increased expression of AIM2 and NLRP3 inflammasomes, autophagy and UPR was also observed outside the nerves, in the context of inflamed artery wall.
Conclusions: here we demonstrated that adventitial neuritis is present in both inflamed and non-inflamed arteries of GCA patients. GCA inflamed nerves specifically produce IL-33 a cytokine of the innate immunity that has been demonstrated to be involved in the pathogenesis of GCA. AIM2 and NLRP3 inflammasomes activation was also observed in GCA arteries and in particular in the inflamed adventitial nerves being accompanied by the increased expression of IL-18. Specific activation of autophagy and UPR pathways was also observed in the inflamed GCA nerves. Altogheter these findings seem to suggest a complex immune activation of adventitial nerves in GCA, suggesting a possible role of arterial neuritis in the initiation and perpetuation of GCA artery inflammation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4345

OP0194 INVOLVEMENT OF TOLL-LIKE RECEPTOR 9 IN THE PATHOGENESIS OF EROSIVE AUTOIMMUNE ARTHRITIS AND DURING OSTEOCLASTOGENESIS

A. Fischer, B. Meyer, B. Niederreiter, G. Steiner. *Internal Medicine III-Rheumatology, Medical University Vienna, Vienna, Austria*

Background: Release and insufficient removal of endogenous nucleic acids may be involved in triggering harmful autoimmune reactions important in the initiation of systemic autoimmune diseases including rheumatoid arthritis (RA). Nucleic acid sensing molecules, such as the endosomal Toll-like receptors (TLRs) 7 and 9, have been linked to pathogenic autoimmune processes, particularly in systemic lupus erythematosus, but their role in RA is less clear. Results previously obtained in rats with pristane-induced arthrits (PIA) suggested involvement of TLR9 in the pathogenesis of this arthritis model (1). Interestingly, rats with PIA develop autoantibodies associated with RA including rheumatoid factor, anti-RA33 and antibodies to carbamylated proteins (2).
Objectives: To gain more insight into the role of TLR9 in the pathogenesis of autoimmune arthritis by investigating the effects of TLR9 inhibition in rats with PIA.
Methods: Arthritis was induced in DA rats with the mineral oil pristane. Rats were treated with a TLR9 antagonist every other day, starting one before disease induction. Arthritis was scored using established scoring systems, inflammation and bone erosion were quantified by histological analysis. Expression of TLR9

and other nucleic acid sensing TLRs was quantified by RT-PCR and Western blotting; activation (phosphorylation) of various signal transduction molecules was determined by Western blotting. Furthermore, the role of TLR9 in osteoclast differentiation and activation was investigated *in vitro*.

Results: The TLR9 antagonist significantly reduced clinical signs of arthritis by approximately 50%. Histological analyses revealed diminshed inflammation, cartilage degradation, bone erosion and significantly reduced numbers of osteoclasts in animals treated with the TLR9 antagonist. However, when treatment was started after onset of arthritis TLR9 inhibition had no effect on arthritis development and severity. IL-6 serum levels were greatly diminished in animals treated with the TLR9 antagonist and expression and activation of NF-kB in lymph nodes was reduced. Remarkably, mRNA levels of TLR7 and TLR9 strongly differed in the course of *in vitro* osteoclastogenesis. Whereas TLR7 expression did not change throughout osteoclastogenesis, expression of TLR9 was higher in precursor cells than in mature osteoclasts and stimulation with a TLR9 agonist (CpG) completely inhibited osteoclastogenesis.

Conclusions: Taken together, the results suggest an important role for TLR9 in the T cell-dependent initiation phase of PIA and thus important involvement of endogenous DNA released during apoptosis, necrosis or netosis in the initiation of autoimmune arthritis and during osteoclastogenesis. The possible relevance of these findings for human RA needs to be further elucidated in future experiments.

References:

[1] Hoffmann MH, Skriner K, Herman S, Baumann C, Steiner CW, Ospelt C, Meyer B, Gleiss A, Pfatschbacher J, Niederreiter B, Tuncel J, Zanoni G, Steiner G. Nucleic acid-stimulated antigen presenting cells trigger T cells to induce disease in a rat transfer model of inflammatory arthritis. J Autoimmun. 2011; 36:288–300.

[2] Stoop JN, Fischer A, Hayer S, Hegen M, Huizinga TW, Steiner G, Trouw LA, Toes RE. Anticarbamylated protein antibodies can be detected in animal models of arthritis that require active involvement of the adaptive immune system.Ann Rheum Dis. 2015; 74(5):949–50.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5260

THURSDAY, 15 JUNE 2017

To be and to become: transition from paediatric to adult care

OP0195 WHAT IS THE IMPACT OF JUVENILE IDIOPATHIC ARTHRITIS IN ADULTHOOD? THE MONOCENTRIC EXPERIENCE OF 240 PATIENTS FOLLOWED IN A TRANSITION TERTIARY CLINIC OF RHEUMATOLOGY

I. Pontikaki[1], L.M. Argolini[2], C. Artusi[2], P.L. Meroni[3]. *[1]Unit of Pediatric Rheumatology-Department of Rheumatology; [2]Department of Rheumatology; [3]Department of Rheumatology, Chair of Rheumatology, Gaetano Pini Institute, University of Milan, Milan, Italy*

Background: There are many differences in clinical manifestations, assessment and management of Juvenile Idiopathic Arthritis (JIA) between childhood and adults' arthritis onset. The transition from pediatric to the adult care emphasizes a lot of aspects that need to be addressed.

Objectives: To describe the long-term outcome of JIA.

Methods: Two-hundred and forty patients affected by JIA and referred to a transition care rheumatology tertiary centre were considered between 1999 and 2016. The outcome assessment included disease activity, medications, number of prosthesis implantation, pregnancy, mortality, social integration (mobility, employment status and educational level).

Results: Seventy-four (30.8%) males and 166 (69.2%) females were included; 53 (22.1%) patients were lost in follow up. Subtypes of JIA at disease onset included 101 oligoarthirtis (42.1%), 67 polyarthritis (27.9%), 43 systemic arthritis (17.9%), 7 psoriatic arthritis (2.9%), 22 enthesitis related arthritis (9.2%). Forty-eight (20%) patients had persistent uveitis. Ninety-three implant prosthesis and 14 arthodesis were recordered. The average disease duration was 20 years, the median age of the patients was 27 (18–57) years. Five deaths (2.1%) occurred in this cohort. At follow up 117 (48.7%) had low active disease activity, 70 (29.2%) had moderate disease activity, 14 (5.8%) had a high disease activity, 24 (10%) were on remission ON medication and 15 (6.3%) OFF medication. Among patients still on medication, 59 (24.6%) were treated with oral steroids, 18 (7.5%) with csDMARDs and 169 (70.4%) with bDMARDs. Seventy-five (31.3%) patients had a higher educational level (university), 195 (81.3%) had an employment, 128 (53.3%) had a driving license. Twenty-one (8.8%) pregnancies were registered. The transition age was considered after age of sixteen years old. In this contest, it was important the multidisciplinary approach of each patient that was realized with the collaboration of other specialists (ophthalmologist, orthopedic, dermatologist, obstetric, psychologist).

Conclusions: In the era of biologic therapy there was an important improvement in a lot variables of the long-term outcome of JIA. One-hundred-eighty-seven (77.9%) patients were still in tight control, not only because of the continuation of the biological therapy but also because of the multidisciplinary care carried out even during remission. JIA often persists over the adulthood. The long term follow up and care of these patients has to be conducted by a rheumatologist expertized in JIA in collaboration with other specialists.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3797

THURSDAY, 15 JUNE 2017

Heterogeneity in JIA

OP0196 CHANGING PATTERNS OF JUVENILE IDIOPATHIC ARTHRITIS PATIENTS TREATED WITH ETANERCEPT FROM 2000 TO 2016 IN THE GERMAN BIKER REGISTRY POPULATION

G. Horneff[1], K. Minden[2], I. Foeldvari[3], G. Ganser[4], J.P. Haas[5], J. Brunner[6], I. Becker[7] on behalf of BIKER collaborative group. *[1]Paediatrics, Asklepios, Sankt Augustin; [2]Charité, Berlin; [3]Private office, Hamburg; [4]Ped Rheumatol, Sendenhorst; [5]German Ped Rheum Centre, Garmisch-Partenkirchen, Germany; [6]University, Innsbruck, Austria; [7]University, Cologne, Germany*

Background: There is increasing experience with Etanercept (ETA) in juvenile idiopathic arthritis in the BIKER Registry.

Objectives: To report on practice changes ETA utilization and outcome over a period of 16 years.

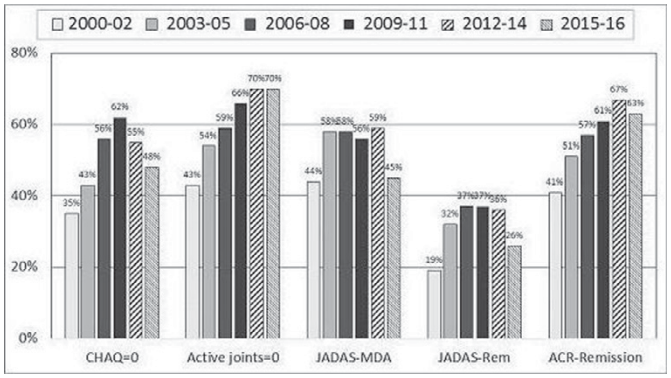
Methods: 6 cohorts of pts were created according to inclusion period. Patients' and disease characteristics,the utilization of DMARDs, steroids, NSAIDs were analysed. Efficacy was judged by PedACR30/50/70/90, JADAS and ACR-remission.

Results: Records from 2105 JIA pts treated with etanercept with at least a baseline and one follow up form were analysed. Most pts were females (67%). The median age of disease onset increased from 5.9 years in the early to 9.3 years in the later cohorts while age at start of treatment remained stable (about 13 years). Median disease duration markedly decreased from 5.3 to about 2 years. Most pts had RF neg. polyJIA followed by extended oligoarthritis. In the more recent cohorts the rate of enthesitis related arthritis increased and the rate f systemic JIA decreased (table). At registry start, 20% of newly enrolled pts belonged to the systemic JIA category compared to <1% in 2016. During the study period, the overall utilization of glucocorticoids at baseline decreased from 54% to 19% ($P<0.0001$), NSAID from 90% to 72% ($P<0.0001$), MTX from 78% to 64% ($P=0.004$). ACR30/50%70/90 response rates at month 12 were 80%/74%/59%/40% and did not vary over time while the rate of patients reaching no active joint/CHAQ DI=0/JADAS-MDA/JADAS-Remission/ACR-Remission increased from 43%/35%/44%/19%/41% to 69%/48%/45%/26%/63%.

Abstract OP0196 – Table 1

Year	2000–2002 N=248	2003–2005 N=337	2006–2008 N=444	2009–2011 N=462	2012–2014 N=436	2015–2016 N=178
Disease duration (y)	6.1±4.0	5.1±4.0	4.2±3.7	3.7±3.0	3.3±3.1	3.4±3.0
JIA category (%)	20.6	12.2	4.3	3	1.4	0.6
Sys JIA	25.8	31.8	32.9	36.6	33	33.7
RFneg PA	12.5	11.0	8.1	8	3.7	9.0
RFpos PA	2.4	4.5	6.1	6.1	3.4	5.1
PersOA	18.1	13.1	21.4	22.3	21.3	21.9
Ext OA	9.7	14.7	16.4	13.6	26.1	22.5
ERA	4.8	8.9	7.7	7.8	8	4.5
PsA unclass JIA	6	3.6	3.2	2.6	3	2.8
Uveitis	12.1	5.7	10.2	5.4	4.1	2.3
Baseline concom. NSAID/steroids/MTX/other DMARDS (%)	90.3/53.2/77.8/5.2	88.7/42.7/76.3/5	84.9/32.4/69.1/3.8	71/31/68.4/3.7	78.7/27.3/61/6.7	74.2/18.5/62.9/4.5
Active joints	10.3±9.8	9.0±9.4	7.8±9.0	6.2±8.0	4.9±6.5	4.6±5.5
Phy VAS (0–10)	6.8±2.4	5.8±2.6	5.2±2.6	4.9±2.9	5.0±2.6	4.8±2.5
Pat VAS (0–10)	5.7±2.7	5.4±2.7	4.8±2.6	3.7±2.7	3.7±2.6	3.7±2.3
CHAQ	1.0±0.8	0.8±0.7	0.7±0.6	0.6±0.6	0.5±0.6	0.5±0.5
CRP in mg/l	44.6±56.8	25.2±32.2	18.2±32.1	10.6±19.1	9.8±29.1	8.9±18.1
JADAS10	21.4±7.7	18.5±7.5	16.6±6.7	14.1±8.7	13.3±6.8	13.3±8.7

Changes in all parameters were significant ($p<0.001$) in Kruskal-Wallis-Test/Chi-quare.



Conclusions: In recent years, children have been treated earlier, received less concomitant treatment with NSAIDS, corticosteroids as well as DMARDs. More recent cohort of patients had less severe disease at baseline, but also showed a markedly better outcome already at one year of treatment reflected by higher rates of patients with no active joint, a CHAQ DI of 0, a JADAS-MDA, and ACR-Remission. These data suggest that early disease control and better pre-selection of patients who need biologics are important to improve outcome and safety in children with JIA.

Disclosure of Interest: G. Horneff Speakers bureau: Abbvie, Pfizer, Roche, Novartis, MSD, K. Minden Speakers bureau: Abbvie, Pfizer, Roche, Genzyme, Pharm-Allergan, I. Foeldvari: None declared, G. Ganser: None declared, J. Haas: None declared, J. Brunner: None declared, I. Becker: None declared

DOI: 10.1136/annrheumdis-2017-eular.1866

OP0197 **EVALUATION OF A DOSING REGIMEN FOR TOCILIZUMAB IN PATIENTS YOUNGER THAN TWO YEARS OF AGE WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS**

N.L. Mallalieu[1], J. Hsu[1], K. Wang[1], S. Wimalasundera[2], C. Wells[2], I. Calvo Penades[3], R. Cuttica[4], H.I. Huppertz[5], R. Joos[6], Y. Kimura[7], D. Milojevic[8], M. Rosenkranz[9], K. Schikler[10], T. Constantin[11], C. Wouters[12]. *[1]Roche Innovation Ctr, New York, United States; [2]Roche Products Ltd, Welwyn Garden City, United Kingdom; [3]Hosp Universitario y Politécnico la Fe, Valencia, Spain; [4]Hosp General de Niños Pedro de Elizalde, Buenos Aires, Argentina; [5]Professor Hess Children's Hosp, Bremen, Germany; [6]ZNA Jan Palfijn Antwerpen, Antwerp, Belgium; [7]Hackensack U Med Ctr, Hackensack; [8]Tufts Med Ctr, Boston; [9]Children's Hosp Pittsburgh UPMC, Pittsburgh; [10]U Louisville Hosp, Louisville, United States; [11]Semmelweis U, Budapest, Hungary; [12]U Hosp Gasthuisberg, Leuven, Belgium*

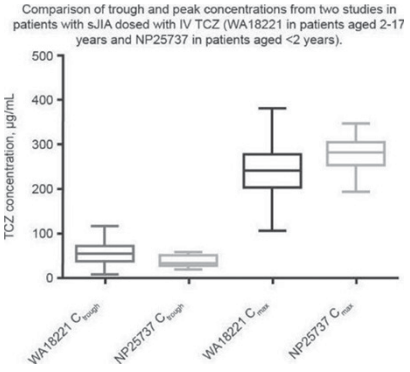
Background: Tocilizumab (TCZ) is approved for the treatment of systemic juvenile idiopathic arthritis (sJIA) based on clinical trials in patients (pts) ≥2 years of age. This study (NP25737) is the first for a biologic in sJIA pts <2 years of age.

Objectives: To evaluate the pharmacokinetics (PK), pharmacodynamics (PD), efficacy, and safety of TCZ in sJIA pts <2 years of age in a phase 1 trial.

Methods: Pts with uncontrolled sJIA and symptoms for ≥1 month prescreening who failed treatment with corticosteroids and NSAIDs and had no history of allergy to TCZ or other biologics received open-label TCZ 12 mg/kg intravenously (IV) every 2 weeks (dose calculated at each visit based on body weight). Pts were treated up to week 12 and could continue until the age of 2 years or were treated for 1 year from baseline. End points included PK (primary) at week 12, PD and efficacy (exploratory), and safety. Comparison was made to exposures from a previous trial in sJIA pts ≥2 years of age (WA18221) that was the basis for approval of TCZ in sJIA.

Results: Eleven pts were enrolled; median (range) age was 16 (10–22) months and weight was 10.40 (6.8–11.5) kg. Serum TCZ concentrations, estimated using population PK analysis, peaked immediately after infusion; median (range) maximum concentration was 282 (195–347) μg/mL (steady state reached by week 12), and median (range) trough concentration was 34.3 (19.2–59.7) μg/mL. Peak and trough exposures were within the exposure range in older children (244 [109–382] to 54.3 [10.9–117] μg/mL; Figure). Observed mean±SD soluble IL-6 receptor levels were 47.65±16.40 ng/mL at baseline and 927.83±148.07 ng/mL at day 71. CRP levels were 250.81±425.11 mg/L and 2.80±3.56 mg/L, respectively. ESR levels were 59.40±27.47 mm/h and 2.00±1.00 mm/h, respectively. Mean±SD Juvenile Arthritis Disease Activity Score-71 improved from 22.27±10.09 at baseline to 3.66±4.66 at day 71. By week 12, 10 pts had 32 adverse events (AEs) and 4 withdrew due to AEs. Infections or infestations were the most frequently reported AEs (10 events, 9 pts). Five serious AEs (SAEs) occurred; 3 pts had SAEs of hypersensitivity that led to withdrawal; 1 of these pts then experienced SAEs of foot and mouth disease and sJIA flare after study withdrawal. No actual cases of MAS were reported, but 2 pts had laboratory abnormalities indicative of MAS according to 2016 criteria.[1] No deaths occurred during the study.

Conclusions: TCZ exposures achieved in this study fell within the range of the previous trial in sJIA pts ≥2 years of age. This study provides evidence that TCZ is effective in sJIA pts <2 years of age, achieves PK and efficacy similar to those



demonstrated previously in older pts, and has a similar AE safety profile, but there was a higher incidence of serious hypersensitivity events and suspected MAS.

References:

[1] Ravelli A et al. Ann Rheum Dis. 2016;75:481–9.

Disclosure of Interest: N. Mallalieu Shareholder of: Roche, Employee of: Roche, J. Hsu Employee of: Roche, K. Wang Employee of: Roche, S. Wimalasundera Employee of: Roche Products Ltd., C. Wells Employee of: Roche Products Ltd., I. Calvo Penades: None declared, R. Cuttica Consultant for: Roche, Novartis, Lilly, GlaxoSmithKline, Bristol-Myers Squibb, Janssen, Speakers bureau: Roche, Novartis, Lilly, GlaxoSmithKline, Bristol-Myers Squibb, Janssen, H. Huppertz: None declared, R. Joos: None declared, Y. Kimura Consultant for: Novartis, SOBI, D. Milojevic: None declared, M. Rosenkranz: None declared, K. Schikler: None declared, T. Constantin: None declared, C. Wouters: None declared

DOI: 10.1136/annrheumdis-2017-eular.2386

THURSDAY, 15 JUNE 2017

Barrier free employment for young people with RMDs

OP0198-PARE **FIT FOR WORK ONLINE: SUPPORTING EMPLOYEES WITH RMDS, EMPLOYERS AND HEALTHCARE PROFESSIONALS**

G. OLeary. *Arthritis Ireland, Dublin 2, Ireland*

Background: Seven million working days are lost each year in Ireland due to RMDs, such as back & neck pain or stiffness, arthritis, and limb pain. This is therefore a significant problem which obviously impacts on both employers, employees and healthcare professionals. That is why Arthritis Ireland has developed *Fit for Work Online* - an eLearning programme which focuses on the issues that face these three groups.

Objectives: The objective of the project was to develop an online educational programme to provide information, guidance and support to employees, employers and healthcare professionals on working with RMDs.

Methods: In 2015 Arthritis Ireland began its developments of an online education programme "*Fit for Work Online*" which focuses on the tripartite relationship between the employee, employer and healthcare professional.

3 video lessons were developed as part of this eLearning programme.

- The first lesson is aimed at employees who are living with an RMD
- The second lesson is aimed at employers who have a staff member who is living with an RMD (and finally)
- The third has been developed for health professionals to update them on current guidance around RMDs and ongoing employment

A key message in all 3 videos is that *working is good for your health.*

Since employment has been shown to boost health and happiness, it is crucial, whenever possible, that people who are living with an RMD, remain in employment, or return to work, as soon as they can. That is the central message of this eLearning programme.

A number of issues were addressed in the development of this programme in order to convey these important issues:

- Firstly, employees who are living with an RMD are encouraged to take control of their condition. People living with an RMD are encouraged to consider practical steps and issues which would support them in staying in, or returning to, work.
- Secondly, from an employer's perspective, in addition to concerns about the welfare of their employees, there are other issues to consider, and it is natural for instance to be concerned about the possible impact of any health condition on their employees' performance & reliability, and consequently on their business. Adaptations, supports, flexibility and so on need to be considered.
- Finally, health professionals need to encourage, advise and facilitate people who are living with RMDs to remain in, or return to work.

Results: The *Fit for Work Online* programme will go live in February 2015. It is planned that a report on the first four months of the programme's delivery and implementation will be available at EULAR 2017 in Madrid.

Conclusions: The direct cost of RMDs at work in Ireland is estimated to be

Arthritis Ireland
Little Things make a Big Difference

at least €750 million a year. Ensuring that people who have been recently diagnosed with an RMD (or who have been living with one for a long time), have the opportunity to remain in or return to work, is central to the ideas behind *Fit-for-Work*. Everyone has a role to play to make this happen, and everyone needs to be flexible & realistic, because in the end of the day, everyone stands to benefit.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6281

OP0199-PARE **SUPPORT TO STAY EMPLOYED AND SOCIAL SECURITY ARRANGEMENTS FOR WORK DISABILITY DUE TO RA – PERCEPTIONS OF PATIENTS WITH RA AND RHEUMATOLOGISTS IN 31 EUROPEAN COUNTRIES**

P. Putrik[1], S. Ramiro[2], F. Guillemin[3], B. Rojkovich[4], F. Sivera[5], M. de Wit[6], A. Woolf[7], A. Zink[8], T. Sokka[9], A. Boonen[1] on behalf of Working Group Access to Social Security for patients with RA across Europe. *[1]Rheumatology, MUMC, Maastricht; [2]Rheumatology, Leiden University Medical Center, Leiden, Netherlands; [3]University of Lorraine, Nancy, France; [4]Polyclicic of the Hospitaller Brothers of St. John of God, Budapest, Hungary; [5]Hospital General Universitario de Elda, Alicante, Spain; [6]VU University Medical Centre, Nijmegen, Netherlands; [7]Royal Cornwall Hospital, Truro, United Kingdom; [8]DRFZ, Berlin, Germany; [9]Jyväskylä Central Hospital, Jyväskylä, Finland*

Background: Despite demonstrated influence of country of residence on labour force participation among patients with RA, little attempt has been made to understand the users' perceptions of support and social security (SS) systems.
Objectives: To explore the patterns in perceptions among patients with RA and rheumatologists from different European countries across five domains (1) importance and support to remain employed, (2) process of applying for WD, (3) obtaining and living with WD pension, (4) role of the rheumatologists in support to remain employed or apply for WD pension and (5) performance of the system.
Methods: A survey among RA patients and rheumatologists was conducted in 44 countries of European WHO Region. For each domain, several questions (4 to 6 questions per domain, each on a 1–5 Likert answer scale, dichotomized as 1 ("totally (agree)") and 0 ("not agree, not disagree", "totally (disagree)") were asked (Table). Next, sum scores were calculated for each domain and averaged per country. The domain "remaining employed" was assessed in patients who currently have or ever had work. Analyses in domains "process of applying for WD" and "obtaining and living with WD" were limited to patients who currently have or ever considered applying for WD. Comparisons of scores in all domains were explored by: EU-15, new EU member states and non-EU countries, the five types of social welfare system (Anglo-Saxon, Bismarckian, Mediterranean, Post-Communist, and Scandinavian) and by countries' wealth (GDP per capita adjusted for purchasing power parity [PPP]) using ANOVA or Pearson correlation, as appropriate.

Table. Differences in perceptions of the social security system among patients and rheumatologists by GDP, system type and EU membership status.

		Perceptions among patients¥			Perceptions among rheumatologists¥	
		Importance and support to remain employed (0-4)	Process of applying for WD (0-6)	Obtaining and living with WD (0-4)	Performance of SS system (0-4)	Role of rheumatologist (0-4)
		Mean (SD)				
GDP	GDP < 27,000 USD PPP per capita (n=16)	1.68 (0.48)ξ	2.10 (0.98)£	1.22 (0.61)£	1.39 (0.51)£	2.38 (0.53)α
	GDP ≥ 27,000 USD PPP per capita (n=15)	1.85 (0.60)ξ	2.67 (1.03)£	1.27 (0.57)£	1.74 (0.71)£	1.91 (0.51)α
Type of system	Anglo-Saxon (n =1)	**0.75 (.)***	**0.92 (.)***	**0.67 (.)***	**0.83 (.)***	2.00 (.)
	Bismarckian (n =5 (patients); n=6 (rheumatologists))	1.77 (0.29)	2.35 (0.34)	1.26 (0.70)	1.91 (0.36)	1.71 (0.23)
	Mediterranean (n =7)	1.88 (0.54)	2.12 (0.79)	1.17 (0.51)	1.35 (0.87)	2.12 (0.74)
	Post-Communist (n =15)	1.71 (0.52)	2.24 (0.94)	1.22 (0.63)	1.44 (0.52)	2.32 (0.53)
	Scandinavian (n =3)	**2.86 (0.48)***	**4.18 (1.14)***	**1.66 (0.35)***	**2.36 (0.07)***	2.11 (0.55)
EU status	EU-15 (N=12)	1.97 (0.66)	1.18 (0.59)	2.24 (0.88)	1.59 (0.73)	**1.84 (0.50)***
	EU new member states (n =11)	1.83 (0.53)	1.24 (0.62)	2.25 (1.05)	1.59 (0.60)	2.22 (0.43)
	Non-EU (n =8)	1.66 (0.65)	1.34 (0.58)	2.76 (1.23)	1.54 (0.64)	**2.42 (0.64)***

¥ score on each domain implies the higher, the better *statistically significant differences (p<0.05);
Relationship between GDP (as continuous variable) and each domain was tested with Pearson correlation coefficient ξ 0.41(p<0.05); £ not significant; α -0.44(p<0.05);

Results: Of 44 countries, 31 (70%) and 30 (68%) have provided data for patients and rheumatologists, respectively. In total, 646 patients (mean age (SD) 53 (12), 76% female, 519 (78%) ever worked) and 500 rheumatologists filled in the questionnaires. Overall, positive weak to no relationships were present between the *GDP per capita* and perceptions from rheumatologists or patients about SS arrangements. However, significant differences were observed across the *systems type* with the Scandinavian type (Finland, Norway, Sweden) consistently scoring higher than the others on most domains (table). Remarkably, rheumatologists in less wealthy and non-EU countries felt more confident in their role related to WD pension.
Conclusions: Patients'a nd rheumatologists' perceptions of systems to support persons with RA encountering work restrictions varied mostly according to the type of the social welfare system, while remarkably little differences were related to country's wealth and membership in EU. Scandinavian employment support and social security system appeared to most adequately meet the expectations of patients and rheumatologists in questions of remaining at work and application to WD pension.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4319

THURSDAY, 15 JUNE 2017

Epidemiology of rheumatic and musculoskeletal diseases - a critical appraisal

OP0200 **CONFOUNDING BY INDICATION WILL MAKE NON-TNFI BDMARDS APPEAR MORE HARMFUL THAN TNFI BDMARDS - A NATIONWIDE STUDY OF CHANNELING IN SWEDEN 2010-2014**

T. Frisell[1], E. Baecklund[2], K. Bengtsson[3], D. Di Giuseppe[1], H. Forsblad-d'Elia[4], J. Askling[1] on behalf of the ARTIS Study Group. *[1]Karolinska Institutet, Stockholm; [2]Uppsala University, Uppsala; [3]Sahlgrenska Academy, Göteborg; [4]Umeå University, Umeå, Sweden*

Background: Confounding by indication occurs when factors associated with the choice of therapy are also predictors of the studied outcome, and is generally considered the major limitation of non-randomized comparisons of different therapies. In RA, age, sociodemographic factors, disease activity, and medical history may influence the choice of e.g. a non-TNFi over a TNFi bDMARD. The degree of bias is difficult to assess since most studies have limited data on potential confounders, and residual confounding cannot be separated from true treatment effects.
Objectives: To quantify the expected confounding by indication caused by baseline differences in patient characteristics at initiation of different bDMARDs in RA.
Methods: All RA patients in the Swedish Rheumatology Register (SRQ) were linked to nationwide registers to assess whether a comprehensive list of covariates predicted the choice of bDMARD to such a degree that different rates of adverse events (AEs) would be expected. Among considered confounders were demographic variables, RA related factors (including RF, disease duration, HAQ, DAS28 w. components) and medical history (health care utilization and 20 specific conditions).
We used historical data on the 5 year risk of several AEs among RA patients starting any bDMARD 2005–2009 to predict the risk among RA patients (bionaïve and switching from a first TNFi) starting specific bDMARDs 2010–2014. Risk was modelled in logistic regressions, as a function of baseline characteristics but assuming no effect from the therapy itself.
Results: Patients starting non-TNFi were older than those starting a TNFi, had lower socioeconomic status, higher disease activity and more often a history of diseases including malignancy, serious infections, and diabetes. These factors were in general also significant predictors of AEs, and the predicted proportions of all AEs were substantially higher for non-TNFi compared to TNFi bDMARDs, highest for rituximab. Within the TNFi-group, only minor differences were seen. Age was a strong confounder, and standardizing to the age/sex-distribution of the TNFi group reduced the group difference dramatically.

Predicted percentage with AE within 5 years, based on observed baseline characteristics. Crude and standardized to age-sex distribution of TNFi as first bDMARD

	All-cause mortality		All-cause hospitalization		Malignancy		MACE		Serious infection	
	Crude	Std	Crude	Std	Crude	Std	Crude	Std	Crude	Std
First bDMARD										
TNFi	4.9		60.3		5.4		6.2		15.3	
Rit.	12.8	6.7	74.0	67.6	7.7	5.7	11.9	7.3	25.6	18.9
Toc.	8.5	7.7	63.6	64.2	5.8	5.2	8.4	8.8	19.4	18.8
Aba.	11.6	6.9	67.5	61.5	6.2	5.0	12.4	7.1	22.1	17.3
Switch from TNFi										
TNFi	5.3	5.5	68.8	68.6	5.0	5.1	7.0	7.2	17.8	18.0
Rit.	7.8	6.4	74.6	71.7	5.7	4.9	9.3	7.3	22.4	20.1
Toc.	6.5	6.8	72.3	68.3	5.3	5.0	8.4	8.0	19.8	18.8
Aba.	7.5	5.6	71.1	71.4	5.5	5.0	8.8	7.6	20.7	18.9

Conclusions: Even if there are no true differences in risk by bDMARD,

confounding by indication will make the non-TNFi drugs appear less safe than the TNFi. A simple adjustment for age and sex will reduce this confounding dramatically, but residual confounding is still expected to give higher rates of AEs, and comparisons should be adjusted for medical history and comorbidities when possible.

Acknowledgements: The ARTIS registry has been, or is, supported by agreements with Abbvie, BMS, MSD, Pfizer, Roche, Samsung Bioepis, and UCB.

Disclosure of Interest: T. Frisell: None declared, E. Baecklund: None declared, K. Bengtsson: None declared, D. Di Giuseppe: None declared, H. Forsblad-d'Elia: None declared, J. Askling Grant/research support from: Abbvie, UCB, Pfizer, Merck, Samsung, Roche, Lilly

DOI: 10.1136/annrheumdis-2017-eular.1319

THURSDAY, 15 JUNE 2017

PsA: an integrated perspective

OP0201 A PHASE 3 STUDY OF THE EFFICACY AND SAFETY OF IXEKIZUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITOR(S)

P. Nash[1], B. Kirkham[2], M. Okada[3], P. Rahman[4], B. Combe[5], D.H. Adams[6], L.N. Kerr[6], C.H. Lee[6], C.L. Shuler[6], M.C. Genovese[7]. *[1]Univ of Queensland, Brisbane, Australia; [2]Guy's Hospital, London, United Kingdom; [3]St Luke's International Univ, Tokyo, Japan; [4]Memorial Univ of Newfoundland, St. John's, Canada; [5]Lapeyrnie Hospital, Montpellier Univ, Montpellier, France; [6]Eli Lilly and Company, Indianapolis; [7]Stanford Univ, Palo Alto, United States*

Background: Tumour necrosis factor inhibitors (TNF-i) have revolutionised the management of psoriatic arthritis (PsA) yet some patients (pts) have an inadequate response (IR) or intolerance. Ixekizumab (IXE), a monoclonal high affinity antibody that selectively targets IL-17, has shown efficacy in TNF-naïve PsA pts.[1]

Objectives: To compare efficacy and safety of IXE with placebo in pts with active PsA who are TNFi-IR.

Methods: In the 24 week (wk), double-blind, placebo-controlled period of a Phase 3 PsA study (SPIRIT-P2; NCT02349295), pts with prior IR or intolerance to 1 or 2 TNF-i were randomised to SC placebo or IXE 80 mg every 2 (Q2W) or 4 wks (Q4W), following a 160 mg initial dose at Wk 0. Pts with IR to treatment (protocol defined) received rescue therapy at Wk 16. Primary endpoint was ACR20 at Wk 24. Continuous data were analyzed using mixed-effects model for repeated measures; categorical data, using a logistic regression model with missing values imputed by non-responder imputation, which treats IR as non-responders.

Results: 363 pts were randomized: ~52 yrs old on average, female (53%), white (~92%), and IR to 1 or 2 TNF-i (204 [56.2%], 128 [35.3%], respectively) or TNF-intolerant (31 [8.5%]). Most pts had current psoriasis (93.4%) and BSA≥3 (62.5%). The majority (87%) completed the 24-wk, double-blind period. A significantly higher proportion of IXE- vs placebo-treated pts at Wk 24 achieved ACR20 (65 [53.3%], 59 [48%] vs. 23 [19.5%]; Q4W, Q2W, placebo, respectively), ACR50 (43 [35.2%], 41 [33.3%] vs 6 [5.1%]; Q4W, Q2W, placebo, respectively), ACR70 (27 [22.1%], 15 [12.2%] vs 0; Q4W, Q2W, placebo, respectively), MDA (34 [27.9%], 29 [23.6%] vs 4 [3.4%]; Q4W, Q2W, placebo, respectively), DAS28-CRP, and reductions in functional disability (HAQ-DI) (Table). A significantly higher proportion of IXE-Q4W- vs placebo-treated pts reached complete resolution of dactylitis (LDI-B=0). Although enthesitis improved from baseline with both IXE doses, rates of complete resolution (LEI=0) were not significantly different compared to placebo. At Wk 24, significantly greater proportions of IXE-treated pts with ≥3% BSA achieved PASI 75 than placebo-treated patients. The incidence of treatment-emergent adverse events (TEAE) was similar across groups (83 [68%], 90 [73.2%] vs 76 [64.4%]; Q4W, Q2W, placebo, respectively). A numerically higher proportion of IXE-treated pts reported infection and a significantly higher proportion reported injection site reactions (the majority were mild) (Table). Serious infection (0, 3 [2.4%], 0; Q4W, Q2W, placebo respectively), serious AE, and oral candidiasis were numerically higher with Q2W vs placebo. No deaths or cases of inflammatory bowel disease, uveitis, TB reactivation, or grade ≥3 neutropenia were reported.

	Week 12			Week 24		
Outcomes	Placebo (N=118)	IXEQ4W (N=122)	IXEQ2W (N=123)	Placebo (N=118)	IXEQ4W (N=122)	IXEQ2W (N=123)
ACR20 n (%)	26 (22.0)	61 (50.0)**	59 (48.0)**	23 (19.5)	65 (53.3)**	59 (48.0)**
ACR50 n (%)	4 (3.4)	38 (31.1)**	41 (33.3)**	6 (5.1)	43 (35.2)**	41 (33.3)**
ACR70 n (%)	2 (1.7)	18 (14.8)*	13 (10.6)*	0	27 (22.1)**	15 (12.2)**
HAQ-DI CFB LSM (SE)	-0.1 (0.06)	-0.4 (0.06)**	-0.4 (0.06)**	-0.2 (0.08)	-0.6 (0.07)**	-0.4 (0.07)**
DAS28-CRP CFB LSM (SE)	-0.6 (0.17)	-1.8 (0.17)**	-1.5 (0.16)**	-0.8 (0.20)	-2.1 (0.19)**	-1.8 (0.18) **
LEI (0)[a] n/N (%)	20/69 (29.0)	19/68 (27.9)	29/84 (34.5)	15/69 (21.7)	24/68 (35.3)	26/84 (31.0)
LDI-B (0)[b] n/N (%)	5/14 (35.7)	19/28 (67.9)	12/20 (60.0)	3/14 (21.4)	21/28 (75.0)*	10/20 (50.0)
PASI 75[c] n/N (%)	7/67 (10.4)	39/68 (57.4)**	42/68 (61.8)**	10/67 (14.9)	38/68 (55.9)**	41/68 (60.3)**
Minimal disease activity (MDA) n (%)	6 (5.1)	31 (25.4)**	21 (17.1)*	4 (3.4)	34 (27.9)**	29 (23.6)**
Safety, n (%)						
TEAE	--	--	--	76 (64.4)	83 (68.0)	90 (73.2)
SAE	--	--	--	4 (3.4)	3 (2.5)	8 (6.5)
Discontinued from AE	--	--	--	6 (5.1)	5 (4.1)	8 (6.5)
Infections	--	--	--	35 (29.7)	47 (38.5)	47 (38.2)
Serious	--	--	--	0	0	3 (2.4)
Oral candida	--	--	--	0	0	4 (3.3)
Injection site reactions[d]	--	--	--	5 (4.2)	14 (11.5)**	29 (23.6)**

Abbreviations: CFB=change from baseline; SAE=serious adverse event.
[a]Only pts with enthesitis at baseline (LEI >0) were included in the analysis.
[b]Only pts with dactylitis (LDI-B>0) at baseline were included.
[c]Only pts with psoriatic lesions ≥3% of BSA at baseline were included.
[d]Injection site reactions is a high-level term consisting of multiple lower-level terms.
*P<0.05,**P <0.001.

Conclusions: IXE improved arthritis[1], physical function, and psoriasis[2,3] vs placebo with no unexpected safety findings in patients with active PsA and prior IR or intolerance to TNF-inhibitor(s).

References:
[1] Mease PJ et al. Ann Rheum Dis 2016;0:1–9.
[2] Gordon BK et al. N Engl J Med 2016;375:345–56.
[3] Griffiths CE et al. Lancet 2015; 386:541–51.

Disclosure of Interest: P. Nash Grant/research support from: AbbVie, Amgen, BMG, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, Roche, Sanofi, USB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Eli Lilly and Company, Hospira, Janssen, MSD, Novartis, Pfizer, UCB, Roche, Sanofi, B. Kirkham Grant/research support from: Arthritis Research UK, AbbVie, Eli Lilly and Company, Roche, UCB, Consultant for: AbbVie, Celgene, Eli Lilly and Company, Janssen, Pfizer, Novartis, M. Okada Consultant for: Eli Lilly and Company, P. Rahman Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, Novartis, Pfizer, B. Combe Grant/research support from: Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche-Chugai, UCB Pharma, Speakers bureau: Bristol-Myers Squibb, Janssen, Merck, Pfizer, Roche-Chugai, UCB PHarma, D. Adams Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, L. Kerr Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, C. Lee Shareholder of: Eli Lilly and, Employee of: E, C. Shuler Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, M. Genovese Grant/research support from: AbbVie, Astellas, Eli Lilly and Company, Galapagos, Pfizer, Vertex, Consultant for: AbbVie, Astellas, Eli LIlly and Company, Galapagos, Pfizer, Vertex

DOI: 10.1136/annrheumdis-2017-eular.1576

OP0202 EFFICACY AND SAFETY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS: OPAL BEYOND, A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 3 TRIAL

D.D. Gladman[1], W.F.C. Rigby[2], V.F. Azevedo[3], F. Behrens[4], R. Blanco[5], A. Kaszuba[6], E. Kudlacz[7], C. Wang[7], S. Menon[7], T. Hendrikx[8], K.S. Kanik[7]. *[1]Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, Canada; [2]Geisel School of Medicine at Dartmouth, School of Medicine, Lebanon, United States; [3]Universidade Federal do Paraná, Curitiba, Brazil; [4]Johann Wolfgang Goethe University & Fraunhofer IME-TMP, Frankfurt, Germany; [5]Hospital Universitario Marques de Valdecilla, Santander, Spain; [6]Specjalistyczne Gabinety Lekarskie "DERMED", Lodz, Poland; [7]Pfizer Inc, Groton, CT; [8]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for treatment of PsA.

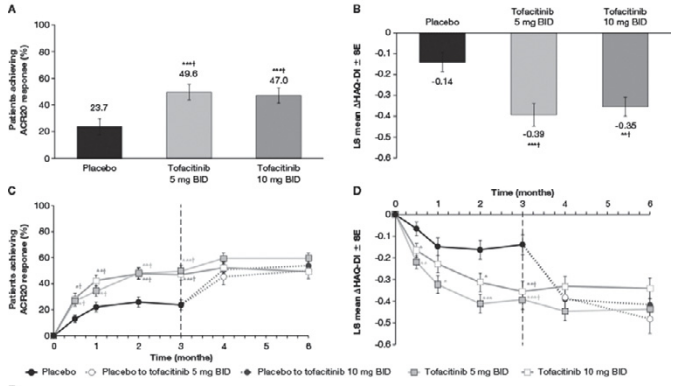
Objectives: Evaluation of efficacy and safety of tofacitinib vs placebo (PBO) in adult patients (pts) with active PsA and an inadequate response (IR) to TNF inhibitors (TNFi).

Methods: Eligible pts in this 6-month, randomised, PBO-controlled, double-blind, multicentre, Phase 3 study had ≥6 months' PsA diagnosis, met CASPAR criteria, had active arthritis (≥3 tender/painful and ≥3 swollen joints) at screening and baseline, active plaque psoriasis at screening and IR to ≥1 TNFi (discontinued due to inadequate efficacy or adverse event [AE]). Pts were randomised 2:2:1:1 to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID or PBO (advancing to tofacitinib 5 or 10 mg BID in a blinded manner at Month [M]3). Ongoing treatment with 1 conventional synthetic DMARD was required. Pts were followed through M6. Primary endpoints were ACR20 response rate and change (Δ) from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) at M3.

Results: Pts were 92.1% white, 55.3% female and mean age was 50.0 years. At baseline, mean swollen and tender/painful joint counts were 22.0 and 11.8 respectively; mean HAQ-DI score was 1.3; 69.8% of pts had LEI >0; 49.2% had Dactylitis Severity Score (DSS) >0. Most patients (62.7%) had ≥3% BSA affected by psoriasis, for whom median PASI score was 7.9. Discontinuation rate at M3 was 7.6%, and 87.6% completed M6. ACR20 response and ΔHAQ-DI significantly improved with both tofacitinib doses vs PBO at M3 (Fig 1A,B) and were maintained to M6 (Fig 1C,D). Tofacitinib 5 mg and 10 mg BID demonstrated superior ACR20 response vs PBO as early as Week 2 (26.7% [p≤0.05] and

28.8% [p≤0.05] vs 13.0%). Secondary endpoints at M3 for tofacitinib 5 mg and 10 mg respectively were: ACR50 response, 29.8% (p≤0.05), 28.0% (p≤0.05); ACR70 response, 16.8% (not significant [NS]), 14.4% (NS); ≥75% improvement of PASI in pts with baseline BSA ≥3% and PASI >0, 21.3% (NS), 43.2% (p<0.0001); ΔLEI and ΔDSS in pts with baseline score >0: ΔLEI, -1.3 (p≤0.05) and -1.3 (p≤0.05) (least squares mean [LSM]); ΔDSS, -5.2 (p≤0.05) and -5.4 (p≤0.05) (LSM). Effects were maintained to M6. Frequency of serious AEs and discontinuations due to AEs was low and similar across treatment groups (Fig 1E). The most common AEs were upper respiratory tract infection (5.3–10.8%), nasopharyngitis (1.5–10.7%) and headache (4.5–9.1%).

Figure 1. A. ACR20 response rates with tofacitinib vs placebo at M3, B. ΔHAQ-DI with tofacitinib vs placebo at M3, C. ACR20 response rates up to M6, D. ΔHAQ-DI up to M6, E. Safety summary (safety analysis set;[a] all causality)



E

	Up to M3	Up to M6			
	Placebo (N=131)	Placebo → tofacitinib 5 mg BID (N=66)	Placebo → tofacitinib 10 mg BID (N=65)	Tofacitinib 5 mg BID (N=131)	Tofacitinib 10 mg BID (N=132)
AEs, n (%)	58 (44.3)	40 (60.6)	38 (58.5)	93 (71.0)	96 (72.7)
SAEs, n (%)	3 (2.3)	2 (3.0)	1 (1.5)	5 (3.8)	8 (6.1)
Discontinuation due to AEs, n (%)	5 (3.8)	2 (3.0)	3 (4.6)	5 (3.8)	11 (8.3)
Deathe, n (%)	0	0	0	0	0
AEs of special interest, n (%) [day of onset]					
Serious infection	0	0	0	2 (1.5) [135, 166]	2 (1.5) [10, 69]
Herpes zoster (all non-serious)	0	0	0	1 (0.8) [77]	2 (1.5) [8, 156]
Malignancy[b]	0	0	0	0	0
MACE[c]	0	0	0	1 (0.8) [245]	1 (0.8) [94]

Nominal *p≤0.05, **p<0.001, ***p<0.0001 vs placebo; [a]Achieved statistical significance at p≤0.05 per the pre-specified step-down testing procedure; dashed line indicates the end of the placebo-controlled period; [b]All patients who received ≥1 dose of study medication; [c]Including non-melanoma skin cancer; [d]For this trial, MACE included one myocardial infarction and one cerebrovascular event (stroke)
ACR, American College of Rheumatology; AE, adverse event; BID, twice daily; HAQ-DI, Health Assessment Questionnaire-Disability Index; M, month; MACE, major adverse cardiovascular event; n, number of patients with event; SAE, serious adverse event; SE, standard error

Conclusions: In this study restricted to PsA pts with TNFi-IR, both tofacitinib doses appeared efficacious on musculoskeletal endpoints for treatment of PsA. No new safety risks were identified vs previous studies in other indications.

Acknowledgements: Previously presented at ACR 2016, to be presented at AAD 2017 and reproduced with permissions. This study was sponsored by Pfizer Inc. Editorial support was provided by AG McCluskey of CMC and was funded by Pfizer Inc.

Disclosure of Interest: D. Gladman Grant/research support from: Amgen, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer Inc, Novartis, UCB, Consultant for: Amgen, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer Inc, Novartis, UCB, Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer Inc, Novartis, UCB, W. F. Rigby Grant/research support from: Amgen, Pfizer Inc, Roche, Consultant for: Bristol-Meyers Squibb, Eli Lilly, Pfizer Inc, Roche, V. Azevedo Grant/research support from: Bristol-Myers Squibb, GSK, Pfizer Inc, UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Novartis, Pfizer Inc, Serono, F. Behrens Grant/research support from: Abbvie, Pfizer Inc, Roche, Chugai, Prophylix, Bioline, Novartis, Consultant for: Abbvie, Pfizer Inc, Roche, Chugai, UCB, BMS, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Lilly, R. Blanco: None declared, A. Kaszuba Consultant for: Janssen, Eli Lilly, Novartis, E. Kudlacz Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Menon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Hendrikx Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.2443

THURSDAY, 15 JUNE 2017

Immunogenicity of biologics; myth or reality?

OP0203 IMPACT OF ADALIMUMAB SERUM CONCENTRATION ON EFFICACY AND ASSOCIATION BETWEEN ANTI-DRUG ANTIBODIES AND SERUM CONCENTRATION: 24 WEEK RESULTS FROM A PHASE III STUDY COMPARING SB5 (AN ADALIMUMAB BIOSIMILAR) WITH REFERENCE ADALIMUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

J. Kay[1], M. Weinblatt[2], E. Keystone[3], M. Genovese[4], J. Ghil[5], S.Y. Cheong[5], E.E. Hong[5,5]. *[1]UMass Memorial Medical Center, Worcester;[2]Brigham and Women's Hospital, Boston, United States;[3]Mount Sinai Hospital, Toronto, Canada;[4]Stanford University, Palo Alto, United States;[5]Samsung Bioepis Co., Ltd., Incheon, Korea, Republic Of*

Background: SB5 has been developed as a biosimilar of reference adalimumab (ADL). The 24-week efficacy and safety results comparing SB5 and ADL were reported previously.[1] Here we report results of subgroup analyses of efficacy by adalimumab serum trough concentration (C_{trough}) and association between anti-drug antibodies (ADA) and C_{trough}.

Objectives: To investigate the impact of C_{trough} on efficacy and the association between ADA and C_{trough} in patients with rheumatoid arthritis (RA) treated with SB5 or ADL.

Methods: Patients with moderate to severe RA despite methotrexate treatment were randomly assigned to receive 40 mg of either SB5 or ADL administered subcutaneously every other week up to week 24. Blood samples were taken prior to study drug administration at weeks 0, 4, 8, 12, 16, and 24 to measure C_{trough}. The optimal C_{trough} cut-off point of adalimumab for good EULAR response at week 24 is reported to be 1.274 μg/mL.[2] Efficacy and immunogenicity were analysed in patients with C_{trough} <1.274 μg/mL and ≥1.274 μg/mL.

Results: C_{trough} was measured in 178 patients each from SB5 and ADL group. The post-dose mean C_{trough} was comparable up to week 24 for SB5 (range: 3.850 to 6.761 μg/mL) and ADL (range: 3.892 to 6.773 μg/mL). Generally, efficacy was higher in patients with C_{trough} ≥1.274 μg/mL for both SB5 and ADL but it was comparable between SB5 and ADL regardless of C_{trough} level. At week 24, the proportion of patients achieving good EULAR response, remission or low disease activity based on DAS28 was higher in patients with C_{trough} ≥1.274 μg/mL than in those with C_{trough} <1.274 μg/mL for both treatment groups (Figure). Other efficacy parameters, including ACR responses, DAS28, simplified disease activity index, and clinical disease activity index, showed similar results.

C_{trough} was higher for patients without detectable ADA, compared to those with ADA. Among patients with ADA, the proportion of patients with C_{trough} ≥1.274 μg/mL was 58.0% (29/50) for SB5 and 52.1% (25/48) for ADL. Among patients without detectable ADA, the proportion of patients with C_{trough} ≥1.274 μg/mL was 100.0% (121/121) for SB5 and 97.4% (114/117) for ADL.

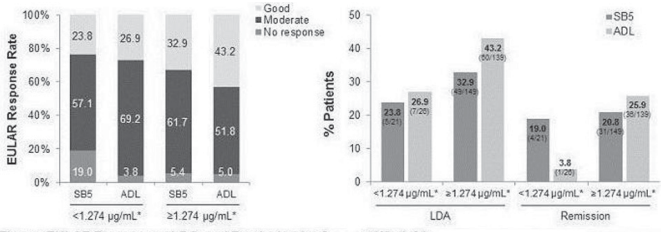


Figure. EULAR Responses, LDA, and Remission by C_{trough} at Week 24
*C_{trough} level; LDA, low disease activity
LDA defined as DAS28 ≤ 3.2 and remission defined as DAS28 < 2.6.

Conclusions: The presence of ADA reduces C_{trough} for both SB5 and ADL. In both treatment groups, almost all patients without detectable ADA, but only slightly more than half of patients with ADA, had C_{trough} ≥1.274 μg/mL at week 24. Efficacy and ADA incidence were generally comparable between SB5 and ADL regardless of C_{trough} level. However, patients with C_{trough} ≥1.274 μg/mL generally experienced greater efficacy of both SB5 and ADL than that in patients with C_{trough} <1.274 μg/mL.

References:

[1] Weinblatt ME et al. Arthritis Rheumatol. 2015; 67 (suppl 10), 8L.
[2] Chen DY et al., Ann Rheum Dis. 2015; Mar;74(3):e16.

Disclosure of Interest: J. Kay Grant/research support from: Abbvie, Ardea Biosciences, Eli Lilly, Pfizer, Genentech, Roche, UCB, Consultant for: Alexion, Amgen, AbbVie, AstraZeneca, BI, BMS, Crescendo Bioscience, Eli Lilly, Epirus, Genentech, GSK, Hospira, Janssen, MSD, Novartis, Pfizer, Samsung Bioepis, Sandoz, Roche, UCB, M. Weinblatt Consultant for: Abbvie, Amgen, Samsung Bioepis, E. Keystone Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Janssen, Lilly, Novartis, Pfizer, Consultant for: Abbott, AstraZeneca, Biotest, BMS, Genentech, Janssen, Lilly, Merck, Pfizer, Samsung Bioepis, Speakers bureau: Abbott, AstraZeneca, BMS Canada, Janssen, M. Genovese Grant/research support from: Abbvie, Consultant for: Abbvie, Amgen, FkB, BI, Merck, Samsung Bioepis, J. Ghil Employee of: Samsung Bioepis Co., Ltd., S. Y. Cheong Employee of: Samsung Bioepis Co., Ltd., E. Hong Employee of: Samsung Bioepis Co., Ltd.

DOI: 10.1136/annrheumdis-2017-eular.3348

OP0204 **IMPACT OF ANTI-DRUG ANTIBODY AND INJECTION SITE REACTION ON EFFICACY: 24-WEEK RESULTS FROM A PHASE III STUDY COMPARING SB4 (ETANERCEPT BIOSIMILAR) WITH REFERENCE ETANERCEPT IN PATIENTS WITH RHEUMATOID ARTHRITIS**

J. Vencovsky[1], P. Emery[2], E. Keystone[3], J. Ghil[4], S.Y. Cheong[4], E.E. Hong[4]. *[1]Institute of Rheumatology, Prague, Czech Republic; [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; [3]Mount Sinai Hospital, Toronto, Canada; [4]Samsung Bioepis Co., Ltd., Incheon, Korea, Republic Of*

Background: SB4 is approved by the European Commission as a biosimilar of the reference etanercept (ETN). The phase III clinical study results have been reported previously.[1,2] Data to date shows no correlation between the development of anti-drug antibody (ADA) and clinical response or adverse events with etanercept treatment.
Objectives: To investigate the impact of the presence of ADA or injection site reaction (ISR) on efficacy in patients with rheumatoid arthritis (RA) treated with SB4 or ETN up to week 24.
Methods: In this phase III randomised, double blind study, patients with moderate to severe RA received 50 mg/week of either SB4 or ETN with background methotrexate (MTX) for 52 weeks. Efficacy, safety and immunogenicity were assessed.
Results: Up to week 24, the incidence of ADA (2 patients [0.4%] in SB4 vs 39 patients [13.1%] in ETN, $p < 0.001$) and the incidence of ISR (9 patients [3.0%] in SB4 vs 48 patients [16.2%] in ETN, $p < 0.001$) were significantly lower in SB4 compared to ETN. Due to the low incidence of ADA in the SB4 treatment group, the impact of ADA on efficacy could not be evaluated. Within the ETN treatment group at week 24, there was a trend towards increased efficacy (ACR20, ACR-N, change in DAS28, remission and low disease activity based on DAS28, SDAI, or CDAI) in patients without detectable ADA compared to patients with ADA (Table). In regards to ISR, efficacy tended to be higher in patients who did not experience ISR compared to those who did within each treatment group.
There was no correlation between the presence of ADA and incidence of ISR. In patients without detectable ADA and patients with ADA, respectively, 3.0% (9/297) vs. 0.0% (0/2) of patients from SB4 group and 16.3% (42/248) vs. 15.4% (6/39) of patients from the ETN group experienced ISR.

Table. Efficacy at week 24 by presence of ADA and ISR

	SB4 50 mg		ETN 50 mg	
	(+) ADA (n=2)	(−) ADA (n=297)	(+) ADA (n=39)	(−) ADA (n=257)
ACR20	2/2 (100.0%)	218/285 (76.5%)	24/36 (66.7%)	189/236 (80.1%)
ACR50	1/2 (50.0%)	127/285 (44.6%)	15/36 (41.7%)	101/236 (42.8%)
ACR70	0/2 (0.0%)	69/285 (24.2%)	9/36 (25.0%)	50/236 (21.2%)
ACR-N	48.8±19.38	45.0±29.14	40.3±30.33	44.3±27.70
Change in DAS28	−2.98±1.063	−2.57±1.375	−2.09±1.407	−2.57±1.295
Change in SDAI	−33.50±3.394	−25.69±14.641	−23.78±15.230	−25.37±12.831
Change in CDAI	−32.65±4.596	−24.73±14.120	−22.45±14.396	−24.57±12.750
	(+) ISR (n=9)	(−) ISR (n=290)	(+) ISR (n=48)	(−) ISR (n=249)
ACR20	5/7 (71.4%)	215/280 (76.8%)	30/39 (76.9%)	183/233 (78.5%)
ACR50	1/7 (14.3%)	127/280 (45.4%)	14/39 (35.9%)	102/233 (43.8%)
ACR70	1/7 (14.3%)	68/280 (24.3%)	7/39 (17.9%)	52/233 (22.3%)
ACR-N	32.6±28.18	45.3±29.06	41.8±28.80	44.1±27.95
Change in DAS28	−1.81±1.282	−2.59±1.371	−2.31±1.280	−2.54±1.324
Change in SDAI	−20.55±11.986	−25.86±14.654	−21.56±12.233	−25.77±13.216
Change in CDAI	−20.17±11.462	−24.88±14.140	−20.74±12.062	−24.89±13.036

Data are presented in either n' (%) or mean ± standard deviation.
ACR20/50/70: American College of Rheumatology 20%/50%/70% response rate; ACR-N: numeric index of the ACR response; ADA: anti-drug antibody; CDAI: clinical disease activity index; DAS28: disease activity score measured by 28 joints; ISR: injection site reaction; LDA: low disease activity; SDAI: simplified disease activity index.
ADA and ISR status defined positive for patients with at least one ADA or ISR up to week 24 regardless of the result at week 0.
ISR counted by treatment-emergent adverse event with high-level group term of administration site reactions.

Conclusions: Significantly fewer patients from SB4 developed ADA or experienced ISR compared to ETN, however the efficacy was still comparable between SB4 and ETN in patients without detectable ADA and in patients who did not experience ISR. Within the ETN group, there was a trend towards increased efficacy in patients without detectable ADA compared to patients with ADA. In both SB4 and ETN group, patients with ISR tended to have higher efficacy than patients without ISR. There was no correlation between the presence of ADA and ISR.

References:
[1] Emery P et al. Ann Rheum Dis. 2015 Jul 07.
[2] Vencovsky J et al. Arthritis Rheumatol. 2015; 67 (suppl 10).

Disclosure of Interest: J. Vencovsky Consultant for: Samsung Bioepis Co., Ltd., Biogen, P. Emery Grant/research support from: Abbvie, BMS, Pifzer, USB, MSD, Novartis, Lilly, Consultant for: Samsung Bioepis Co., Ltd., E. Keystone Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Janssen, Lilly, Novartis, Pfizer, Consultant for: Abbott, AstraZeneca, Biotest, BMS, Genentech, Janssen, Lilly, Merck, Pfizer, Samsung Bioepis, Speakers bureau: Abbott, AstraZeneca, BMS Canada, Janssen, J. Ghil Employee of: Samsung Bioepis Co., Ltd., S. Y. Cheong Employee of: Samsung Bioepis Co., Ltd., E. Hong Employee of: Samsung Bioepis Co., Ltd.
DOI: 10.1136/annrheumdis-2017-eular.3043

THURSDAY, 15 JUNE 2017

Which target / outcome is more relevant in the management of SLE?

OP0205 **ASSOCIATION BETWEEN T FOLLICULAR HELPER CELL AND PLASMABLAST CORRELATES WITH DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

S. Nakayamada, S. Kubo, M. Yoshikawa, Y. Miyazaki, S. Iwata, I. Miyagawa, K. Nakano, K. Saito, Y. Tanaka. *The First Department of Internal Medicine, Universitiy of Occupational and Environmental Health, Japan, Kitakyushu, Japan*

Background: Various immunological abnormalities contribute to the development and perpetuation of systemic lupus erythematosus (SLE). Since SLE is a molecularly heterogeneous disease, targeted therapy has not yet been fully established. It seems to be important to explore the characteristic and interaction among the immune cell phenotypes in this disease.
Objectives: The aim of this study was to assess the relationship between the peripheral immune cell phenotypes with clinical manifestations and responsiveness to immunosuppressive therapy in patients with SLE.
Methods: Peripheral blood mononuclear cells were obtained from 143 SLE patients and 26 healthy donors (HD). The blood samples were taken at baseline and week 24 after treatment. The subset of circulating B, T and dendritic cells was defined based on comprehensive 8-color flow cytometric analysis for human immune system termed "the Human Immunology Project" proposed by the National Institutes of Health (NIH) and the Federation of Clinical Immunology Societies (FOCIS). The correlation of immune cell phenotypes with clinical characteristics and responsiveness to immunosuppressive therapies, such as cyclophosphamide, mycophenolate mofetil, or calcineurin, in addition to high-dose glucocorticoids, were evaluated. Patients who were required more than two different immunosuppressant therapies in addition to glucocorticoids were considered treatment resistant.
Results: The frequency of $CD3^+CD4^+CXCR5^+ICOS^+$ T follicular helper (Tfh) cell, but not $CD3^+CD4^+CXCR3^+CCR6^-$ Th1 cell and $CD3^+CD4^+CXCR3^-CCR6^+$ Th17 cell, were higher in SLE than that in HD (mean 1.1 vs 0.8, p=0.01). The frequency of $CD19^+CD20^+IgD^+CD27^+$ central memory B cell and $CD19^+CD20^+IgD^-CD27^-$ effector B cell were higher in SLE than that in HD (mean 23.6 vs 15.1 and 10.7 vs 5.2, $p \leq 0.001$ and $p < 0.001$, respectively). The largest difference relative to the HD was observed in the proportion of $CD19^+CD20^-CD27^+CD38^+$ plasmablast, which was higher in SLE (mean 16.2 vs 3.7, $p < 0001$) and correlated with BILAG index ($r=0.24$, $p < 0.001$). The proportion of Tfh cell significantly correlated with serum IgG level ($r=0.35$, $p < 0.001$), and the proportion of $CD3^+CD4^+CXCR5^+ICOS^+CD69^+$ activated Tfh cell correlated with serum anti-Sm antibody level ($r=0.26$, p=0.01). Among helper T cell subsets (Th1, Th17, Treg and Tfh), the proportion of Tfh cell only showed positive correlation with that of plasmablast ($r=0.24$, p=0.02). Treatment resulted in marked improvement in disease activity scores, such as SLEDAI and BILAG and resulted in significant decreased proportions of plasmablast and Tfh cell (plasmablast; mean 17.6 to 10.1, $p < 0.01$, Tfh; mean 1.1 to 0.7, $p < 0.01$). The percentage of patients who showed treatment resistance was highest among patients with high percentage of Tfh cell (p=0.03).
Conclusions: Peripheral immuno-phenotyping confirmed the importance of Tfh cell and plasmablast in patients with SLE, *i.e.* activation of Tfh cell correlated with autoantibody production while plasmablast did with disease activity of SLE. Our findings supported the relevance of Tfh cell-plasmablast axis as a potential therapeutic target for SLE. The peripheral immunophenotyping might be useful in evaluating the pathogenesis and in determining the therapeutic target of each patient.
Disclosure of Interest: S. Nakayamada: None declared, S. Kubo Speakers bureau: Bristol-Myers, M. Yoshikawa: None declared, Y. Miyazaki: None declared, S. Iwata: None declared, I. Miyagawa: None declared, K. Nakano: None declared, K. Saito: None declared, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, GlaxoSmithKline
DOI: 10.1136/annrheumdis-2017-eular.4165

OP0206 **PERFORMANCE OF SLEDAI-2K TO DETECT A CLINICALLY MEANINGFUL CHANGE IN SLE DISEASE ACTIVITY: A 36-MONTH PROSPECTIVE COHORT STUDY OF 334 PATIENTS**

D. Jesus[1], M. Rodrigues[1], A. Matos[2,3], C. Henriques[2,3,4], J. da Silva[5,6], L. Inês[1,6,7]. *[1]CHUC Lupus Clinic, Rheumatology Department, Centro Hospitalar e Universitário de Coimbra, Coimbra; [2]School of Technology and Management, Polytechnic Institute of Viseu; [3]Centre for the Study of Education, Technologies and Health, Viseu; [4]Centre for Mathematics; [5]CHUC Lupus Clinic, Rheumatology Department; [6]Faculty of Medicine, University of Coimbra, Coimbra; [7]Faculty of Health Sciences, University of Beira Interior, Covilhã, Portugal*

Background: The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is the core determinant of response in the SLE Responder Index (SRI), a primary efficacy outcome in SLE clinical trials. However, SLEDAI is unable to discriminate partial improvement/worsening, as it scores each item

categorically. Furthermore, potentially severe lupus manifestations, such as hemolytic anemia are not scored in SLEDAI.
Objectives: To evaluate the performance of SLEDAI-2K to detect a clinically meaningful change in SLE disease activity.
Methods: Prospective cohort study of SLE patients followed at a tertiary care lupus clinic from January 2014 to December 2016. Consecutive patients fulfilling the ACR'97 and/or the SLICC'12 classification criteria were included. At each outpatient visit, disease activity from the last 30 days was scored in the Physician Global Assessment (PGA) (0–3 cm scale) and in SLEDAI-2k. The association between PGA and SLEDAI-2K at each visit was tested with Spearman's Correlation. A clinically meaningful change in SLE disease activity was defined as difference in PGA $\geq$0.3 cm at follow-up compared to the baseline visit. Performance of change in SLEDAI-2K was tested in two models: against worsening and improvement in PGA $\geq$0.3 cm from baseline using Receiver Operating Characteristic (ROC) curve analysis. Sensitivity, specificity, positive and negative predictive values (PPV, NPV) of SLEDAI-2k to change in PGA was calculated. Statistical significance was set at 0.05.
Results: We included 334 patients (87.1% female, mean age at baseline - 44.8±14.5 years). At baseline, median PGA and SLEDAI-2k score was 0.2 points (range 0–2.5) and 2 points (range 0–19), respectively. Eighty-three patients (24.8%) had a PGA $\geq$0.4 points at baseline. During follow-up of 36 months, 2129 visits were performed. PGA and SLEDAI-2K scores presented a high correlation (rho=0.82, $p<0.0001$) (fig. 1). Reductions in SLEDAI-2K presented in ROC analysis an area under curve (AUC) of 0.697 [95% CI (0.628–0.766), $p<0.0001$] for an improvement in PGA$\geq$0.3. For a worsening of PGA$\geq$0.3 points, increase in SLEDAI-2K presented an AUC of 0.877 [95% CI (0.822–0.932), $p<0.0001$]. Estimated sensitivities, specificities, PPV and NPV are presented in table 1.

Table 1. Performance of Sledai-2K to detect a clinically meaningful change in PGA, using cut-offs of decrease and increase (for a clinical improvement and worsening, respectively) in SLEDAI-2K $\geq$1 and $\geq$4 points

	Δ SLEDAI-2K≥1				Δ SLEDAI-2K≥4			
	Sens.	Spec.	PPV	NPV	Sens.	Spec.	PPV	NPV
Improvement PGA≥0.3	0.7	0.571	0.397	0.825	0.288	0.929	0.622	0.763
Worsening PGA≥0.3	0.725	0.903	0.627	0.936	0.353	0.996	0.947	0.873

Sens: Sensitivity; Spec: Specificity; PPV: Positive predictive value; NPV: Non predictive value.

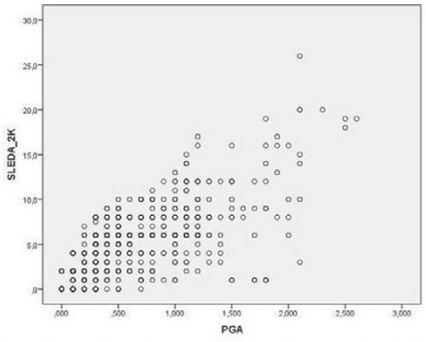


Fig. 1 Scatter diagram showing linear positive correlation between PGA and SLEDAI-2K scores (Spearman's correlation coefficient (rho) = 0.82, p <0.0001).

Conclusions: SLEDAI-2K presents a limited performance in detecting a clinically meaningful change in SLE disease activity, failing to identify more than a quarter of cases with clinically meaningful improvement or worsening. There is a need to optimize SLE disease activity measures.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3895

THURSDAY, 15 JUNE 2017

Joint EULAR - EFIS session: tilting the balance: from disease to tolerance induction

OP0207 B CELL DEPLETION INCREASES REGULATORY T CELLS AND AMELIORATES SKIN AND LUNG FIBROSIS IN A BLEOMYCIN-INDUCED SYSTEMIC SCLEROSIS MODEL MOUSE

H. Numajiri, A. Yoshizaki, T. Fukasawa, S. Ebata, Y. Asano, S. Sato. *Department of Dermatology, The University of Tokyo Graduate School of Medicine, Hongo, Bunkyo-ku, Tokyo, Japan*

Background: B cells play a critical role in systemic autoimmunity and disease expression through various functions such as cytokine production and induction of other immune cell activation. Recently, some clinical studies have shown that the efficacy of B cell depletion therapy with rituximab, a chimeric monoclonal antibody against human CD20, in systemic sclerosis (SSc) patients. However, it still remains unclear why B cell depletion can be an effective treatment for SSc.
Objectives: The purpose of this study is to assess the role of B cell depletion in SSc. We evaluated the skin and lung fibrosis of bleomycin (BLM)-induced SSc model mice treated with B cell depletion. Furthermore, we investigated the effect of B cell depletion on T cell cytokine profile.
Methods: To generate BLM-induced SSc model mice, 300 μg of BLM was injected subcutaneously into the shaved backs of the C57BL/6 mice every other day for 4 weeks. Anti-mouse CD20 monoclonal antibodies, which can deplete mouse B cells, were also injected every 2 weeks from 2 weeks later starting BLM treatment. After 4 weeks of BLM treatment, skin and lung fibrosis were assessed histopathologically. T cells and B cells were isolated from spleen using magnetic cell sorting system. Purified T cells ($5x10^5$ cells) were cultured with B cells ($5x10^5$ cells) in the presence of phorbol 12-myristate 13-acetate, ionomycin, and anti-CD3/CD28 antibodies. Cytokine expressions in the fibrotic skin and lung were quantified by real-time polymerase chain reaction. Cytokine production of T cells and B cells were analyzed by flow cytometric analysis.
Results: Dermal thickness and lung fibrosis score increased in BLM-treated mice compared with phosphate buffer saline (PBS)-treated control mice. Frequencies of interleukin (IL)-10 producing splenic B cells significantly decreased in BLM-treated mice compared with PBS-treated mice, while IL-6 producing B cell frequencies increased. Moreover, interferon (IFN)-γ, IL-4, or IL-17 producing T cell frequencies increased in BLM-treated mice. There were no significant differences in regulatory T cell frequencies between BLM-treated and PBS-treated mice. B cell depletion increased IL-10 producing regulatory T cell frequencies in BLM-treated mice. By contrast, frequencies of IFN-γ, IL-4, or IL-17 producing T cells were significantly decreased by B cell depletion in BLM-treated mice. In addition, fibrogenic cytokine mRNA expression levels of skin and lung decreased in BLM-treated mice with B cell depletion. To assess the role of B cells on T cell cytokine production, purified splenic B cells from BLM- or PBS-treated mice were cultured with naive T cells. T cells which were cultured with B cells from BLM-treated mice produced greater amounts of INF-γ, IL-4, and IL-17 than those cultured with PBS-treated mouse B cells. By contrast, B cells from PBS-treated mice induced a higher amount of IL-10 production from T cells than those from BLM-treated mice.
Conclusions: B cell depletion inhibited skin and lung fibrosis in BLM-treated mice. Furthermore, B cell depletion increased regulatory T cell frequencies in BLM-treated mice, though INF-γ, IL-4, and IL-17 producing T cell frequencies were decreased by B cell depletion. These results suggest that B cell depletion alters T cell cytokine profile, which results in inhibition of fibrosis in this model.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4189

OP0208 SYNOVIAL TISSUE OF RA PATIENTS IN REMISSION CONTAINS A UNIQUE POPULATION OF REGULATORY MACROPHAGES

A. Elmesmari[1], S. Alivernini[2], B. Tolusso[2], D. Vaughan[1], G. Di Sante[2], L. Petricca[2], E. Gremese[2], G. Ferraccioli[2], I.B. McInnes[1], M. Kurowska-Stolarska[1]. *[1]Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom; [2]Division of Rheumatology, Fondazione Policlinico Universitario A. Gemelli, Catholic University of the Sacred Heart, Rome, Italy*

Background: The majority of RA treatments target inflammation or the adaptive immune response. Partial- or non-response is common and only a minority have sustained remission. There is a knowledge gap in understanding the mechanisms that could reinstate synovial homeostasis in RA. Tissue macrophages may have a role in this process; they are present in healthy synovium and aid resolution of the inflammation in experimental models of RA. However, little is known about the regulatory properties of human synovial tissue macrophages.
Objectives: Our hypothesis is that healthy and RA synovium in remission contain macrophages with anti-inflammatory/repair properties and identifying the effector pathways that drive their function could facilitate therapeutic restoration of synovial homeostasis in RA.
Methods: We developed a flow cytometry sorting strategy for harvesting tissue-resident macrophages obtained from digested synovial biopsies of RA patients (n=21, including in remission n=5; and active RA n=16). Cells were labelled with cell lineage-specific antibodies; then macrophages were gated based on their expression of $CD64^{pos}CD11b^{pos}MHCII^{pos}Lineage^{neg}$. The potential homeostatic/repair macrophage was preliminary identified by the presence of CD206 marker. $CD206^{pos}$ and $CD206^{neg}$ macrophages were sorted using a FACS Aria III and RNAseq performed to characterise their functional signature. In some experiment, macrophages were seeded on collagen-coated plates and production of TNFa evaluated.
Results: All synovial tissue macrophages from RA in remission were $CD206^{pos}$ whereas a substantial number of synovial macrophages from active RA tissue were $CD206^{neg}$. Gene expression analyses and functional assays suggest that these populations represent distinct phenotypes in the activation spectrum. $CD206^{neg}$ macrophages have high expression of microRNA-155, which drives production of inflammatory mediators *e.g.* TNFa. In contrast, $CD206^{pos}$ macrophages showed regulatory properties characterised by increased expression of soluble (*e.g. IL10, TGFB*), surface (*e.g. IL4/14R, TGFBR1/2*) and cellular (*e.g. SHIP1, TAM, SMAD2, STAT6*) inhibitors of inflammatory activation, and increased expression of repair markers (*e.g. ARG2 and CCL18*).
Conclusions: We propose therefore that anti-inflammatory/repair macrophages may be present in human synovial tissues in remission representing a hitherto unnoticed regulatory tissue mechanism.

References:
[1] Smolen JS, Aletaha D, McInnes IB. Rheumatoid Arthritis. Lancet Volume 388, Issue 10055, 22–28 October 2016, Pages 2023–2038.
[2] Misharin AV et al. Non-classical Ly6C(-) monocytes drive the development of inflammatory arthritis in mice. Cell Rep. 2014;9:591.
[3] Kurowska-Stolarska M, Alivernini S et al. MicroRNA-155 as a pro-inflammatory regulator in clinical and experimental arthritis. PNAS 2011;108:11193.
[4] Elmesmari A, McInnes IB, Kurowska-Stolarska M. MicroRNA-155 regulates monocyte chemokine and chemokine receptor expression in Rheumatoid Arthritis. Rheumatology (Oxford). 2016 Nov;55(11):2056–2065. Epub 2016 Jul. 13.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5910

THURSDAY, 15 JUNE 2017

What to do about comorbidity?

OP0209-HPR INCIDENCE OF FIRST CARDIOVASCULAR EVENT IN SPANISH PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: PROSPECTIVE DATA FROM THE CARMA PROJECT

M.A. Martin Martinez[1], S. Castañeda[2], C. Gonzalez-Juanatey[3], F. Sanchez-Alonso[1], S. Marsal Barril[4], M. Romera-Baures[5], J. Santos-Rey[6], J.A. Pinto-Tasende[7], J. Tornero-Molina[8], R. Lopez-Gonzalez[9], M.D. Sanchez-Gonzalez[10], J. Llorca[11], M.A. Gonzalez-Gay[12]. *[1]Research of Unit of Spanish Society of Rheumatology; [2]Division of Rheumatology. Hospital Universitario la Princesa, Iis-Princesa, Madrid; [3]Division of Cardiology. Hospital Lucus Augusti, LUGO; [4]Division of Rheumatology. Hospital Universitario Vall D Hebron; [5]Division of Rheumatology. Hospital Universitario Bellvitge, Barcelona; [6]Division of Rheumatology. Hospital Virgen de la Salud, TOLEDO; [7]Division of Rheumatology. Complejo Hospitalario a Coruña, la Coruña; [8]Division of Rheumatology. Hospital Universitario de Guadalajara, Guadalajara; [9]Division of Rheumatology. Hospital Virgen de la Concha, ZAMORA; [10]Division of Rheumatolgy. Hospital Universitario de Salamanca, Salamanca; [11]Division of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, Ciber Epidemiologia y Salud Publica (Ciberesp); [12]Division of Rheumatology, Hospital Universitario Marques de Valdecilla, and Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Rheumatology Division, IDIVAL, Santander, Spain*

Objectives: To determine the incidence and risk factors implicated in the development of first cardiovascular event (CVE) in patients with chronic inflammatory rheumatic diseases (CIRD) attending rheumatology clinics after 2.5 years of follow-up.
Methods: Analysis of data after 2.5 years of follow-up in an observational prospective study [CARdiovascular in rheuMAtology (CARMA) project] that includes a cohort of patients with CIRD [rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA)] and another cohort of matched individuals without CIRD attending outpatient rheumatology clinics from 67 hospitals in Spain. The cumulative incidence per 1000 patients and the incidence density per 1000 patient-months of non-fatal CVE were estimated in both cohorts at 2.5 years from the start of the project. Weibull proportional hazard model was used to calculate the Hazard Ratio (HR) and 95% confidence interval (95% CI) of the risk factors involved in the development of CVD events. Losses to follow-up and their causes were also analyzed.
Results: The total number patient who completed the follow-up visit at 2.5 years was 2,598 (89.2% of those who started the study). Seven patients had died due to CVE and 23 because of non-CVE. The higher number of losses to follow-up was found in the control group (15.81%), because many of them were not periodically follow-up at the outpatient clinics. Cardiovascular cumulative incidence in patients with CIRD 15.30 cases per 1000 patients (95% CI: 12.93–17.67), being higher in AS patients 22.03 (95% CI: 11.01–33.04). The higher risk of developing a first CVE during the 2.5 years of follow-up was in patients with AS (HR: 4.11, 95% CI: 1.07–15.79; p: 0.04), those with older age (HR:1.09; 95% CI: 1.05–1.13, $p<0.001$), higher systolic blood pressure (HR: 1.02; 95% CI: 1.00–1.04, p=0, 01) and longer duration of the rheumatic disease (HR: 1.07; 95% CI: 1.03–1.12), $p<0.01$). In contrast, woman gender was a protective factor (HR: 0.43; 95% CI: 0.18–1.00, p=0.05).
Conclusions: Patients with AS prospectively followed-up at rheumatology outpatients clinics show higher risk of developing a first CVE than those with RA or PsA. Besides traditional CVD risk factors a longer time course of the disease is a risk factor for the development of CVD in patients with CIRD.
Acknowledgements: This project has been supported by an unrestricted grant from Abbvie, Spain. The design, analysis, interpretation of results and preparation of the manuscript has been done independently of Abbvie.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3838

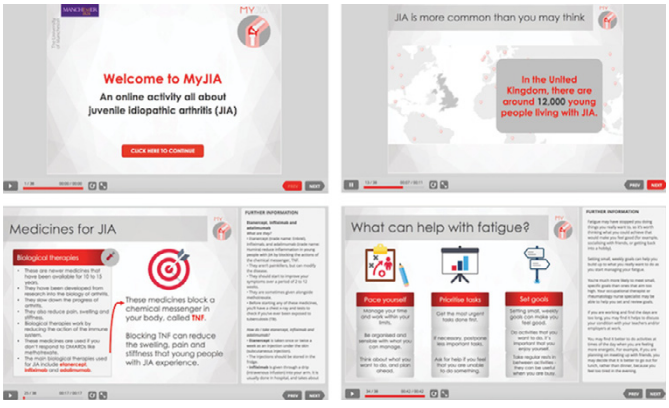
THURSDAY, 15 JUNE 2017

Difficult to reach patient groups

OP0210-PARE THE DEVELOPMENT AND EVALUATION OF AN INTERACTIVE HEALTH COMMUNICATION APPLICATION TO EDUCATE AND EMPOWER YOUNG PEOPLE LIVING WITH JUVENILE IDIOPATHIC ARTHRITIS: A PILOT STUDY

S.R. Stones[1,2], S.M. Cruickshank[3], S.M.M. Verstappen[4] on behalf of MyJIA Expert Advisory Group. *[1]School of Healthcare, University of Leeds, Leeds; [2]Faculty of Life Sciences; [3]School of Biological Sciences; [4]Arthritis Research UK Centre for Epidemiology, The University of Manchester, Manchester, United Kingdom*

Background: In parallel with clinical care, it is equally important to empower young people with juvenile idiopathic arthritis (JIA) to develop self-efficacy skills, so that they can competently self-manage their health, particularly as they transition into adult health services.[1] Capitalising on the popularity of technology, web-enabled tools represent a novel and effective way of engaging young people with JIA. A Cochrane review of Internet Health Communication Applications (IHCAs) found that IHCAs have a positive effect on self-efficacy, empowering individuals to become more knowledgeable.[2]
Objectives: The aim of this study was to: i) develop and evaluate an IHCA in young people with JIA, aged 16 to 25 years; and ii) investigate whether an IHCA enhanced young people's condition-specific knowledge, and their self-efficacy to manage their health.
Methods: Young people aged 16 to 25 with a self-reported diagnosis of JIA were recruited to take part via social media. The IHCA was built using Microsoft PowerPoint and iSpring Suite (Figure 1). A virtual advisory group of patients, parents and healthcare professionals were involved throughout the design and development of the IHCA. The contents of the IHCA was obtained for existing published sources. Matching anonymous pre- and post-participation questionnaires were used to assess differences in knowledge of JIA and self-efficacy skills.
Results: In total, 23 (79%) young people with JIA completed both pre- and post-participation questionnaires. Most young people reported that their preferred source of condition-related information was obtained via an internet search engine (83%). Prior to completing the IHCA, only 22% of young people reported that they had an excellent understanding of JIA. After completing the IHCA, there was a significant improvement in young people's condition-specific understanding. Similarly, after completing the IHCA, there was a significant improvement in young people's confidence to better self-manage their health. Interestingly, only 30% of young people reported that the information which health professionals provided to them about JIA was adequate, in terms of comprehension and usefulness. Qualitative findings identified three core themes: resource content, practical support and accessibility/functionality. Young people liked the way that information was presented, as well as practical steps they could take to improve their health.

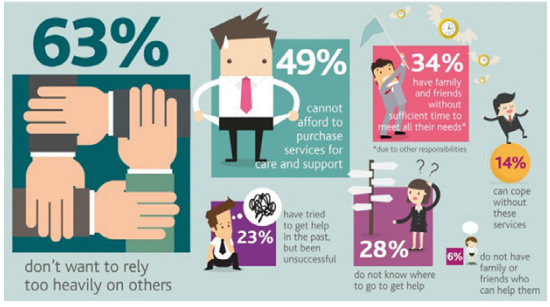


Conclusions: Quantitative results correspond with qualitative findings, indicating that the IHCA was well-received by young people with JIA. Condition-specific understanding was enhanced after completing the IHCA, as was participants' confidence in their self-efficacy and disease self-management capabilities. These results indicate that with ongoing development and larger scale evaluation, implementation of this IHCA is feasible.
References:
[1] Lindsay, S., Kingsnorth, S. et al. (2014). A systematic review of self-management interventions for children and youth with physical disabilities. Disability and Rehabilitation 36(4): 276–288.
[2] Murray, E., Burns, J. et al. (2005). Interactive health communication applications for people with chronic disease. Cochrane Database of Systematic Reviews (4).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1025

OP0211-PARE **WHO CARES? AN INVESTIGATION OF THE HEALTH AND PERCEIVED SOCIAL CARE NEEDS OF PEOPLE WITH RHEUMATOID ARTHRITIS LIVING IN SCOTLAND**

C. O'Neill[1], A. Bosworth[2], K.R. Martin[3]. *[1]Policy & Public Affairs; [2]CEO, National Rheumatoid Arthritis Society, Maidenhead; [3]Epidemiology, University of Aberdeen, Aberdeen, United Kingdom*

Background: Effective and sufficient levels of care and support for individuals newly diagnosed and those with established Rheumatoid Arthritis (RA) are needed to ensure optimal physical and mental health, as well as health-related quality of life. The aim of this study was to explore the extent of care needs among individuals with RA living in Scotland, UK and the factors that contribute to them, such as co-morbidities, perceived caregiver burden and complex care needs.
Objectives: To establish whether the health and social care needs of people with RA in Scotland were being met, if there was regional variation and what other factors impacted such as wealth and age.
Methods: A cross-sectional study of individuals with RA who responded to an online survey (available 11 Nov 2015 to 22 Jan 2016) who were aged ≥16 years, lived in Scotland and reported they had received a clinical diagnosis of RA. Respondents were allowed to skip questions they wished not to answer; standardised instruments were used (e.g., the Self-administered Comorbidity Questionnaire and the Self-Perceived Burden Scale). Descriptive analyses of quantitative data and thematic analyses of free text responses were conducted.
Results: Overall, 387 individuals participated. The majority were female, of White Scottish or White British background, 45–64 years, and lived in a household with ≥2 people. The majority, 83%, reported well established RA (diagnosis ≥2 years ago) and at least one other comorbidity (78%) – most commonly depression (30%). The average number of medications taken for RA was 3.2 (range 0–7) and 30% reported taking 3 medications in total. Of those receiving care, the majority (97/101) named family or friends/neighbours as caregivers and 76% (80/97) had an elevated level of self-perceived burden on their caregiver. Respondents who reported anxiety or depression had significantly higher average self-perceived burden scores when compared to those without, 33.0 versus 27.3.
89% responded that they did not know what types of circumstances might make them eligible for care and support from their local Council, and only 10% reported receiving information about care and support from their local council. Very few (n=40) had an assessment, with half being deemed eligible for support from their local council.



Conclusions: Survey responses suggest individuals with RA lack fundamental information about qualifying for and accessing formal resources and services provided by their local council. This is especially crucial for two reasons: 1) respondents indicated they do not want to rely heavily on others, like family or friends who are often the primary caregivers; 2) depression and anxiety are highly prevalent in this population. It is important to ensure those with RA do not have unmet needs at any stage, from being newly diagnosed to having established RA, so that they can flourish at home, at work and in their leisure time. Local councils should make access to information about help with formal social care easily accessible and ensure that health professionals know how best to sign-post people.
Acknowledgements: A partnership between the National Rheumatoid Arthritis Society (UK) and the University of Aberdeen
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1858

THURSDAY, 15 JUNE 2017

Macrophage M2 polarization: implications in fibrotizing diseases

OP0212 **ENDOTHELIN-1 INDUCES A PROFIBROTIC PHENOTYPE IN CULTURED HUMAN MICROVASCULAR ENDOTHELIAL AND CIRCULATING MONOCYTE/MACROPHAGE CELLS**

S. Soldano[1], P. Montagna[1], R. Brizzolara[1], A.C. Trombetta[1], A. Sulli[1], C. Pizzorni[1], M. Ghio[1], S. Paolino[1], V. Smith[2], M. Cutolo[1]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa, Italy; [2]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium*

Background: The alteration of microvascular endothelial cell (EC) functions and the presence of macrophages in the immune inflammatory infiltrate, followed by the transition of these cell types into a profibrotic phenotype, represent early and crucial pathological features of the fibrotic process in systemic sclerosis (SSc) (1). The alternatively activated macrophage subset M2a was found in several diseases characterized by extensive fibrosis (1). M2a macrophages express specific phenotype markers, CD206 (mannose receptor), CD204 and CD163 (scavenger receptors) as well as profibrotic molecules, primarily transforming growth factor-β1 (TGFβ1) (1). Endothelin-1 (ET1) and/or TGFβ1 are known to induce the transition of fibroblasts into profibrotic myofibroblasts, which are key mediators of fibrosis in SSc.
Objectives: To investigate the effects of ET1 in inducing a profibrotic phenotype in cultured human microvascular ECs (HMVECs) and macrophages.
Methods: HMVECs, at 3rd culture passage, were grown in endothelial cell medium (EGM2MV) and treated for 6 days with ET1 (100nM) or treated for 1 hr with ET1 receptor antagonist ($ET_{A/B}$RA, bosentan 10μM) before stimulation with ET1.
Human monocytes were isolated from peripheral blood mononuclear cells of healthy subjects using a monocyte isolation kit. The cells were maintained in RPMI growth medium for 24 hrs and then treated for 6 days with ET1 or treated for 1 hr with bosentan before stimulation with ET1.
Cultured HMVECs and monocytes maintained in EGM2MV and RPMI growth medium, respectively, were used as untreated cells. Gene and protein expression of profibrotic myofibroblast markers –α-smooth muscle actin (α-SMA), fibroblast specific protein-1 (S100A4), type 1 collagen (COL1) and fibronectin (FN) – were evaluated by quantitative real time polymerase chain reaction (qRT-PCR), Western blotting (WB) and immunocytochemistry (ICC) in cultured HMVECs. Gene and protein expression of M2a phenotype markers (CD206, CD204, CD163) and TGFβ1 were investigated by qRT-PCR and WB in cultured human macrophages. Statistical analysis was carried out by Mann-Whitney non-parametric test.
Results: In cultured HMVECs, ET1 induced the significant upregulation of the gene expression of α-SMA, S100A4 (myofibroblast markers), COL1 and FN, compared to untreated cells ($p<0.001$;$p<0.001$;$p<0.05$;$p<0.01$). $ET_{A/B}$RA significantly contrasted the ET1 mediated transition of HMVECs into a profibrotic phenotype ($p<0.05$ for α-SMA, COL1 and FN; $p<0.01$ for S100A4 vs. ET1-treated cells).
In cultured human macrophages, ET1 induced the significant overexpression of M2a markers ($p<0.05$ for CD204 and CD163;$p<0.01$ for CD206) and TGFβ1 ($p<0.01$) compared to untreated cells. $ET_{A/B}$RA significantly contrasted the ET1-mediated transition of cultured macrophages into profibrotic M2a ($p<0.05$ vs. ET1-treated cells, for all investigated proteins). Data were confirmed by WB and ICC on both cultured cell types.
Conclusions: ET1 seems to be involved in the early phases of the fibrotic process by inducing the transition of both cultured HMVECs and macrophages into a profibrotic phenotype, myofibroblast and M2a respectively (observed in SSc), a process which is apparently contrasted by $ET_{A/B}$RA treatment.
References:
[1] Wynn TA et al. Immunity. 2016;44:450–62.
Disclosure of Interest: S. Soldano: None declared, P. Montagna: None declared, R. Brizzolara: None declared, A. Trombetta: None declared, A. Sulli: None declared, C. Pizzorni: None declared, M. Ghio: None declared, S. Paolino: None declared, V. Smith: None declared, M. Cutolo Grant/research support from: Actelion
DOI: 10.1136/annrheumdis-2017-eular.4317

OP0213 **MACROPHAGES FROM A SCLERODERMA SUBGROUP WITH HIGHER SKIN SCORES EXPRESS ACTIVATION MARKERS AND INDUCE FIBROBLASTS IN CO-CULTURE**

J. King, D. Sleep, Y. Sohrabi, A. Tam, B.A. Abdi, D. Abraham, C. Denton, R. Stratton. *Centre for Rheumatology and Connective Tissue Diseases, Royal Free Hospital, London, United Kingdom*

Background: Scleroderma (SSc) is characterized by pathological fibrosis. The mechanisms by which fibrosis occurs in SSc are not fully understood.
Alternatively activated M2-like macrophages are associated with fibrosis and have been found to have an important role in pathological fibrosis in humans. Therefore, there is interest in elucidating their role in SSc. M2 macrophages express mannose receptor CD206 and are known to secrete a number of soluble factors to establish a pro-fibrotic milieu when present in damaged tissues.
Furthermore, we have shown adenosine tri-phosphate (ATP) concentration is increased in the skin of patients with SSc. Within the extra-cellular environment, ATP is a Damage-Associated Molecular Pattern (DAMP), binding the P2X class of purinergic receptors. Such mechanisms may contribute to SSc pathology.
Objectives: In this study, we explore the relationship of macrophage CD206 and $P2X_7$ expression to Rodnan Skin Score. The role of these cells in establishing fibrosis was also examined *in vitro*.
Methods: 17 SSc patients and 9 controls were consented and their skin score recorded. Macrophages were derived from peripheral blood mononuclear cells (PBMCs) and identified through CD14 expression by FACS. CD206 and $P2X_7$

co-expression was quantified. CD206 immunofluorescence of skin biopsies was also performed.
Macrophages were co-cultured with $8x10^4$ and $2x10^4$ fibroblasts in a collagen matrix and within a monolayer respectively.
Collagen gel contraction was quantified as a measure of fibrotic activity. CTGF and Collagen mRNA expression from gel matrices and cellular monolayers was quantified by qPCR.
Results: CD206 and $P2X_7$ expression is higher on SSc PBMC-derived macrophages (mean fluorescence 776.1 SD=409.1, 724.4 SD=455.3) compared to healthy controls (mean fluorescence 632.2 SD=73.7, 472.9 SD=25.4). There is significant correlation of CD206 expression to $P2X_7$ expression ($p<0.001$, r2=0.76) and CD206 expression is significantly correlated to Rodnan skin score ($p<0.05$, r2=0.26). $P2X_7$ expression is positively correlated to skin score. Double positive P2X7 and CD206 cells were seen in a subgroup with higher skin scores. Healthy fibroblasts co-cultured with scleroderma macrophages showed increased collagen mRNA by qPCR compared to co-culture with healthy macrophages ($p<0.01$). CTGF mRNA was positively correlated with macrophage P2X7 (r2=0.23) and CD206 (r2=0.81) expression. Preliminary work suggests contraction of collagen discs in fibroblast and macrophage co-culture is increased with SSc macrophages compared to healthy controls.
Conclusions: Data indicates a correlation between disease severity and CD206 expression by macrophages. Upregulation of CTGF and collagen expression in fibroblasts co-cultured with macrophages expressing high CD206 suggests a role for these cells in pathogenic fibrosis. The co-expression of high levels of $P2X_7$ with CD206 also indicates a possible role for the purinergic pathway in SSc fibrosis.
Future work will examine the mechanism of macrophage-fibroblast cross-talk and investigate the effect of inhibitors of CD206.
Acknowledgements: Rosetrees Trust
Arthritis Research UK
Scleroderma and Raynaud's UK
Royal Free Charity
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2743

FRIDAY, 16 JUNE 2017

Mucosal B cells: gatekeepers of immune function

OP0214 ACTIVATION STATUS OF MUCOSAL-ASSOCIATED INVARIANT T CELLS REFLECTS PATHOLOGY OF SYSTEMIC LUPUS ERYTHEMATOSUS

A. Chiba[1], G. Murayama[1,2], N. Tamura[2], K. Yamaji[2], Y. Takasaki[2], S. Miyake[1]. *[1]Immunology; [2]Internal Medicine and Rheumatology, Juntendo University School of Medicine, Tokyo, Japan*

Background: Mucosal-associated invariant T (MAIT) cells are innate-like lymphocytes that express a semi-invariant TCRα chain (Vα7.2-Jα33 in humans). MAIT cells are restricted by the MHC-related molecule-1 (MR1) and uniquely recognize vitamin B metabolites presented by MR1. Like other innate-like lymphocytes, MAIT cells are also activated by cytokines in the absence of exogenous antigens. Human MAIT cells are abundant and constitute approximately 5% of peripheral blood T cells, suggesting possible roles of MAIT cells in various types of immune responses.
Objectives: We aimed to investigate whether MAIT cells are involved in systemic lupus erythematous (SLE).
Methods: Peripheral blood was collected from SLE patients and healthy volunteers. Informed consent was obtained from all individuals according to institutional ethical guidelines. Disease activity was measured based on the SLE disease activity index (SLEDAI) and a SLEDAI score $\geq$5 was defined as active disease. Peripheral blood mononuclear cells (PBMC) were stained with anti-human monoclonal antibodies against CD3, γδTCR, Vα7.2TCR, CD161, CD95 (Fas) and CD69, and then analyzed by FACS. $CD19^+$B cells or $CD14^+$monocytes were isolated from PBMC of healthy controls (HC) or SLE patients by using magnetic cell sorting. MAIT cells from healthy controls were co-cultured with B cells or monocytes in the presence of MR1 ligand (MR1L), and the expression of CD69 on MAIT cells was evaluated by FACS. Cytokine levels in plasma samples and culture supernatants were measured by ELISA and Bioplex assay. PBMC were cultured in the presence of various cytokines, and CD69 expression on MAIT cells was analyzed by FACS.
Results: The frequency of MAIT cells was markedly reduced in SLE. Reduced numbers of MAIT cells were not attributable to the downregulation of surface markers, but were partially due to the enhanced cell death of MAIT cells, possibly by activation-induced cell death. The CD69 expression levels on MAIT cells in SLE correlated with disease activity. Monocytes from patients with SLE exhibited increased ability to induce MAIT cell activation, and the profound MAIT cell activating capacity of lupus monocytes was associated with enhanced IL-12 production in the culture supernatants. The plasma concentration of IL-6, IL-18 and IFNα positively correlated with the expression levels of CD69 on MAIT cells in SLE. MAIT cells were activated by cytokines including IFNα, IL-15, and IL-12 plus IL-18 in the absence of exogenous antigens.
Conclusions: These results suggest that MAIT cells reflect the pathological condition of SLE and their activated status correlates with disease activity.

References:
[1] Miyazaki Y, et al. Mucosal-associated invariant T cells regulate Th1 response in multiple sclerosis. Int. Immunol. 2011;23:529–35.
[2] Chiba A, et al. Mucosal-associated invariant T cells promote inflammation and exacerbate disease in murine models of arthritis. Arthritis Rheum. 2012; 64:153–61.
[3] Hayashi E, et al. Involvement of Mucosal-associated Invariant T cells in Ankylosing Spondylitis. J Rheumatol. 2016; 43: 1695–703.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2805

OP0215 ROLE OF INHIBITORY IGG FC RECEPTOR IIB ON B CELLS AND MONOCYTES IN YAA-RELATED MURINE LUPUS

S. Hirose[1], L. Qingshun[1], M. Ohtsuji[1], H. Nishimura[1], H. Amano[2], S.J. Verbeek[3]. *[1]Biomedical Engineering, Toin University of Yokohama, Yokohama; [2]Rheumatology and Internal Medicine, Juntendo University School of Medicine, Tokyo, Japan; [3]Human Genetics, Leiden University Medical Center, Leiden, Netherlands*

Background: FcγRIIB-deficient C57BL/6 (B6) mice spontaneously develop severe lupus nephritis in combination with *Yaa* locus (TLR7-duplication).
Objectives: The aim of this study is to clarify the cell type-specific roles of FcγRIIB for the pathogenesis of *Yaa*-related lupus.
Methods: We established B cell-specific ($CD19^{Cre}$.*Yaa*), myeloid-derived cell-specific ($C/EBP\alpha^{Cre}$.*Yaa*), and dendritic cell (DC)-specific ($CD11c^{Cre}$.*Yaa*) FcγRIIB-deficient mice on B6.*Yaa* background, and compared the disease features of these mice with full FcγRIIB-deficient B6.$Fc\gamma RIIB^{-/-}$.*Yaa* mice.
Results: $CD19^{Cre}$.*Yaa* mice developed milder lupus nephritis compared to B6.$Fc\gamma RIIb^{-/-}$.*Yaa* mice, indicating that FcγRIIB deficiency on only B cells is not sufficient for the development of severe disease. Surprisingly, $C/EBP\alpha^{Cre}$.*Yaa* mice developed similar mild disease as $CD19^{Cre}$.*Yaa* mice whereas $CD11c^{Cre}$.*Yaa* stayed disease free. These observations indicate that, in B6. $Fc\gamma RIIB^{-/-}$.*Yaa* mice, FcγRIIB deficiency on both B cells and myeloid cells, but not on DCs, contribute to the development of severe lupus with high autoantibody titers. Flow cytometric analysis showed that the frequency of peripheral $Gr\text{-}1^-$, but not $Gr\text{-}1^+$, monocytes was increased and correlated positively with the frequency of splenic PNA^+ activated B cells in B6.$Fc\gamma RIIB^{-/-}$.*Yaa* and C/EBPa^{Cre}.*Yaa*, but not $CD19^{Cre}$.*Yaa*, mice. This suggests a link between FcγRIIB deficiency on monocytes, the high frequency of $Gr\text{-}1^-$ monocytes and B cell activation. Transcriptome analysis of $Gr\text{-}1^+$ and $Gr\text{-}1^-$ monocytes revealed that B cell-stimulating factor-3 (BSF-3), IL-10, and IL-1β were all up-regulated in $Gr\text{-}1^-$ monocytes.
Conclusions: FcγRIIB on B cells and monocytes controls B cell activation and autoimmune responses via different but synergistic pathways in *Yaa*-related lupus nephritis.
References:
[1] Boross P, et al. J. Immunol. 187:1304–1313, 2011.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1315

FRIDAY, 16 JUNE 2017

PsA: the options grow!

OP0216 EFFICACY AND SAFETY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, OR ADALIMUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AN INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (CSDMARDS): A RANDOMISED, PLACEBO-CONTROLLED, PHASE 3 TRIAL

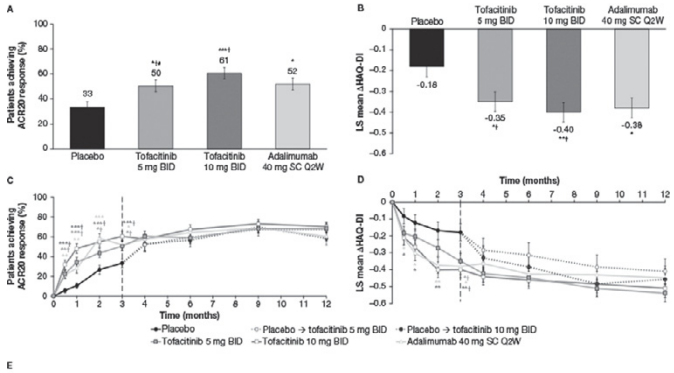
P.J. Mease[1], S. Hall[2], O. FitzGerald[3], D. van der Heijde[4], J.F. Merola[5], F. Avila-Zapata[6], D. Cieślak[7], D. Graham[8], C. Wang[8], S. Menon[8], T. Hendrikx[9], K.S. Kanik[8]. *[1]Swedish Medical Center and University of Washington, Seattle, WA, United States; [2]Cabrini Health and Monash University, Melbourne, Australia; [3]Department of Rheumatology, St Vincent's University Hospital, Dublin, Ireland; [4]Leiden University Medical Center, Leiden, Netherlands; [5]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States; [6]Centro Multidisciplinario para el Desarrollo Especializado de la Investigacion Clinica en Yucatán S.C.P, Yucatán, Mexico; [7]Poznan University, Poznan, Poland; [8]Pfizer Inc, Groton, CT; [9]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for treatment of psoriatic arthritis (PsA).
Objectives: To assess the efficacy and safety of tofacitinib vs placebo (PBO) in patients (pts) with active PsA.
Methods: Eligible pts in this randomised, PBO- and active-controlled, 12-month Phase 3 trial had $\geq$6-months' PsA diagnosis, fulfilled CASPAR criteria, had active arthritis ($\geq$3 tender/painful and $\geq$3 swollen joints) and active plaque psoriasis at screening, inadequate response to $\geq$1 csDMARD, and were tumour necrosis factor-inhibitor (TNFi)-naïve. 422 pts were randomised 2:2:2:1:1 to tofacitinib 5 or 10 mg twice daily (BID), adalimumab 40 mg subcutaneous injection every 2 weeks, or PBO (advancing to tofacitinib 5 or 10 mg BID at Month [M]3).

Stable treatment with 1 csDMARD was required. Primary endpoints comparing tofacitinib vs PBO were ACR20 response rate and change from baseline in Health Assessment Questionnaire Disability Index (ΔHAQ-DI) at M3. Secondary endpoints included: ACR20 response rates and ΔHAQ-DI through M12; pts achieving ACR50, ACR70, ≥75% improvement of PASI and PsARC at all time points; and changes from baseline in LEI, Dactylitis Severity Score and SPARCC Enthesitis Index. Radiographic progression was assessed by van der Heijde-modified Total Sharp Score (mTSS).

Results: 96.9% of pts were white and 53.3% were female; mean age was 47.9 years. 96.2% and 88.4% of pts completed M3 and M12, respectively. At M3, tofacitinib 5 and 10 mg BID significantly improved ACR20 response rates (50.5% [p≤0.05] and 60.6% [p<0.0001] vs 33.3%; Fig 1A) and ΔHAQ-DI (-0.35 [p≤0.05] and -0.40 [p<0.001] vs -0.18; Fig 1B) vs PBO, with responses maintained to M12 (Fig 1C&D). Greater efficacy was also seen for adalimumab vs PBO. Tofacitinib 5 and 10 mg BID were superior to PBO for ACR20 response rates at Week 2 (22.4% [p<0.001] and 31.7% [p<0.0001] vs 5.7%; Fig 1C). Secondary endpoints supported primary findings (data not shown). >91% of pts were radiographic non-progressors at M12 (defined as an increase from baseline in mTSS ≤0.5). M12 safety findings were similar between groups (Fig 1E). The most common adverse events were upper respiratory tract infection (7.5–10.6%), nasopharyngitis (7.5–11.5%) and headache (3.8–10.6%).

Figure 1. A. ACR20 response rates with tofacitinib vs placebo at M3, B. ΔHAQ-DI with tofacitinib vs placebo at M3, C. ACR20 response rates up to M12, D. ΔHAQ-DI up to M12, E. Safety summary (safety analysis set; all causality)



E

	Up to M3	Up to M12				
	Placebo (N=105)	Placebo → tofacitinib 5 mg BID‡ (N=52)	Placebo → tofacitinib 10 mg BID‡ (N=53)	Tofacitinib 5 mg BID (N=107)	Tofacitinib 10 mg BID (N=104)	Adalimumab 40 mg SC Q2W (N=106)
AEs, n (%)	37 (35.2)	36 (69.2)	34 (64.2)	71 (66.4)	74 (71.2)	76 (71.7)
SAEs, n (%)	1 (1.0)	3 (5.8)	4 (7.5)	8 (7.5)	4 (3.8)	9 (8.5)
Discontinuation due to AEs, n (%)	1 (1.0)	2 (3.8)	2 (3.8)	6 (5.6)	3 (2.9)	4 (3.8)
Deaths, n (%)	0	1 (1.9)*	0	0	0	0
AEs of special interest, n (%) [day of onset]						
Serious infection	0	2 (3.8) [102, 331]	0	0	1 (1.0) [132]	1 (0.9) [170]
Herpes zoster (all non serious)	0	0	0	2 (1.9) [61, 173]	2 (1.9) [221, 317]	0
Malignancy	0	0	0	3 (2.8) [1, 11, 232]	1 (1.0) [103]	0
MACE	0	1 (1.9) [139]	0	0	0	2 (1.9) [263, 345]

Nominal *p≤0.05, **p<0.001, ***p<0.0001 vs placebo; †Achieved statistical significance at p≤0.05 per the pre-specified step-down testing procedure; dashed line indicates the end of the placebo-controlled period; ‡All patients who received ≥1 dose of study medication; §Cardiac arrest; ¶Placebo groups progressed to tofacitinib 5 mg or tofacitinib 10 mg at M3
AE, adverse event; BID, twice daily; M, month; MACE, major adverse cardiovascular event; n, number of patients with event; Q2W, every 2 weeks; SAE, serious adverse event; SC, subcutaneous

Conclusions: In TNFi-naïve pts with active PsA, tofacitinib was superior to PBO in ACR20 response rates and ΔHAQ-DI at M3, with superiority vs PBO as early as Week 2 for ACR20, which was maintained to M12. No new safety risks were identified vs previous studies in other indications.

Acknowledgements: Previously presented at ACR 2016, to be presented at AAD 2017 and reproduced with permissions. This study was sponsored by Pfizer Inc. Editorial support was provided by AG McCluskey of CMC and was funded by Pfizer Inc.

Disclosure of Interest: P. Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Sun, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, CORRONA, Dermira, Janssen, Eli Lilly, Merck, Novartis, Pfizer Inc, Sun, UCB, Zynerba, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Novartis, Pfizer Inc, UCB, S. Hall Consultant for: AbbVie, Celgene, Eli Lilly, Janssen, Pfizer Inc, Roche, O. FitzGerald Grant/research support from: AbbVie, Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer Inc, Speakers bureau: Celgene, Janssen, Novartis, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer Inc, Roche, Sanofi-Aventis, UCB, Employee of: Imaging Rheumatology BV, J. Merola Grant/research support from: Biogen Idec, Consultant for: AbbVie, Amgen, Biogen Idec, Eli Lilly, Janssen, Momenta, Mallinckrodt, Novartis, Pfizer Inc, Speakers bureau: AbbVie, Eli Lilly, F. Avila-Zapata: None declared, D. Cieślak: None declared, D. Graham Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Menon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Hendrikx Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.1416

OP0217 USTEKINUMAB IS SUPERIOR TO TNF INHIBITOR TREATMENT IN RESOLVING ENTHESITIS IN PSA PATIENTS WITH ACTIVE ENTHESITIS- RESULTS FROM THE ENTHESIAL CLEARANCE IN PSORIATIC ARTHRITIS (ECLIPSA) STUDY

E.G. Araujo, M. Englbrecht, S. Hoepken, S. Finzel, A. Hueber, J. Rech, G. Schett. *Internal Medicine 3 Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany*

Background: IL-23 is considered to play an important role in the development of enthesitis. Ustekinumab (UST), a combined inhibitor of IL-12/IL-23 shows efficacy in psoriatic arthritis (PsA), which is driven by enthesial and synovial disease, while it has no therapeutic role in diseases driven by synovitis alone, such as rheumatoid arthritis. We therefore speculated that inhibition of IL-23 is particularly effective in enthesitis-driven PsA patients.

Objectives: To compare the efficacy of UST with tumor necrosis factor inhibitor (TNFi) treatment in clearing enthesitis in PsA patients.

Methods: ECLIPSA is a prospective randomized-controlled open study. Patients with PsA with active enthesitis were randomized 1:1, receiving either standard doses of UST (arm 1) or TNFi (arm 2). At baseline the following parameters were assessed: age, gender, BMI, disease duration, previous DMARDs, use of corticosteroids, use of NSAIDs, swollen and tender joint count, VAS-pain, VAS-global, NAPSI, PASI, MASES, SPARCC, LDI, BASDAI, BASFI, HAQ-DI, SF-36, FACIT-F, ESR and CRP. Primary endpoint was a SPARCC of 0 after 6 months. Patients were seen every 3 months and followed for a total of 6 months. In order to investigate the effects of study treatment over time we used 2x3 mixed design ANOVA models for both physician's and patient's reported outcomes. Furthermore, exploratory logistic regression was used to predict a SPARCC of 0 at month 6 from baseline SPARCC, PASI, NAPSI, FACIT-F and BASDAI while additionally accounting for age, gender, PsA duration and study treatment.

Results: 51 patients (UST=25; TNFi=26) were screened and 47 patients (UST=23; TNFi=24) were enrolled with 4 patients not presenting signs of active enthesitis at baseline. Mean ± SD age was 59.11±12.16 years and mean ± SD disease duration was 6.4±7.79 years. Mean± SD SPARCC at baseline was 4.87±2.69 in the UST group and 3.88±2.52 in the TNFi group. Other baseline characteristics were similar between both groups with exception of HAQ-DI, BASFI and SF-36 mental scale. In regards to the effect of study treatment (TNFi vs. UST) and time, the corresponding ANOVAs suggested an important interaction of both factors for measures of enthesitis (MASES and SPARCC), patient-reported disease activity (BASDAI and BASFI), physical well-being (SF-36 physical component summary scale), and PASI all p≤0.044 with superiority of UST. However, TNFi was superior to UST with respect to improvement of fatigue (FACIT-F), p<0.001. After 6 months, 17 out of 24 UST patients (70.8%) and 10 out of 26 TNFi patients (38.4%) reached the primary endpoint (SPARCC=0). Logistic regression predicting enthesitis-free state of disease was significantly related to study treatment only, with patients receiving UST being more likely to show no signs of enthesitis at month 6 (OR=0.037; p=0.005).

Conclusions: These results show that UST is superior to TNFi in resolving the enthesitis component of disease in PsA patients with active enthesial disease. Based on these data more stratified treatment approaches can be designed in PsA patients, where enthesitis-driven patients are targeted by IL-23/IL-17 pathway inhibitors, while more systemic disease manifestations of PsA, such as patients with polyarticular disease or those with high-level fatigue are targeted by TNFi.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5398

OP0218 EFFICACY AND SAFETY RESULTS OF GUSELKUMAB, AN ANTI-IL23 MONOCLONAL ANTIBODY, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS OVER 24 WEEKS: A PHASE 2A, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

A. Deodhar[1], A. Gottlieb[2], W.-H. Boehncke[3,4], B. Dong[5], Y. Wang[5], W. Barchuk[6], X.L. Xu[6], E. Hsia[5,7]. *[1]Oregon Health & Science University, Portland; [2]Department of Dermatology, New York Medical College, Valhalla, United States; [3]Division of Dermatology and Venereology, Geneva University Hospital; [4]Dept of Pathology and Immunology, University of Geneva, Geneva, Switzerland; [5]Janssen Research & Development, LLC, Spring House; [6]Janssen Research & Development, LLC, San Diego; [7]University of Pennsylvania School of Medicine, Philadelphia, United States*

Objectives: To evaluate the efficacy, safety, and tolerability of guselkumab (GUS), a fully human monoclonal antibody against the p19 subunit of IL-23, in patients (pts) with active psoriatic arthritis (PsA).

Methods: In this double-blind, placebo-controlled, multicenter study, pts with active PsA and ≥3% body surface area (BSA) of plaque psoriasis despite current or previous treatment with standard-of-care therapies, including those previously exposed to anti-TNFα agents, were randomized 2:1 to receive GUS 100 mg subcutaneously (SC) or placebo (PBO) at wks 0, 4, and every 8 wks (q8w) thereafter through wk44. At wk16, pts from either group with <5% improvement from baseline in both swollen and tender joint counts were eligible for early escape to open-label ustekinumab. At wk24, all remaining PBO pts crossed-over to receive GUS 100 mg, and then received GUS at wk28, and q8w thereafter through wk44. The primary endpoint was ACR 20 response at wk24. Major

secondary endpoints were PASI 75 and ACR 50 responses, change from baseline in HAQ-DI, and improvement in enthesitis (Leeds enthesitis index) and dactylitis score (by a 0–3 scoring system) at wk24; and ACR 20 response at wk16. Other secondary endpoints included change from baseline in SF-36 and proportion of pts achieving Minimal Disease Activity (MDA). Through wk24, efficacy analyses were performed in a modified Intent-to-Treat (mITT) population. Pts who met treatment failure criteria, early escaped or had missing data at wk24, were considered non-responders for ACR and MDA endpoints at wk24.

Results: 149 pts were randomized to receive study agent (PBO: 49, GUS: 100). Baseline demographics and ACR component measures were generally similar between the two groups. Four [8.2%] pts in PBO and 9 [9.0%] pts in GUS were previously exposed to TNFα agents. The study met its primary and all secondary endpoints. Significantly more GUS pts achieved ACR 20/50/70 responses and PASI 75/90/100 responses at wk24 (Table 1). Significant treatment effect on ACR20 response was observed as early as wk4 (21% vs 0, $p<0.001$), and the effect increased over time reaching the maximum by wk16 (60.0% vs. 16.3%, $p<0.001$) vs. PBO. Results for other secondary efficacy endpoints are summarized in Table 1.

Through wk24, proportions of pts with ≥1 AE were comparable between the two groups (PBO: 32.7%; GUS: 36.0%, respectively). Infections were the most common AEs (PBO: 20.4%; GUS: 17.0%, respectively). Two pts had SAEs (knee injury, n=1; myocardial infarction, n=1). There were no serious infections, malignancies, or deaths through wk24.

Table 1 Summary of Efficacy Results at Week 24 in mITT Population[a]

Efficacy Endpoints	PBO	GUS	p-value
ACR 20	18.4%	58.0%	p<0.001
ACR 50	10.2%	34.0%	P=0.002
ACR 70	2.0%	14.0%	P=0.023 (post hoc)
PASI 75	12.5%	78.6%	p<0.001
PASI 90	6.3%	66.3%	P<0.001
PASI 100	6.3%	39.8%	P<0.001
Mean (SD) change from BL in HAQ-DI score	-0.06 (0.53)	-0.42 (0.51)	p<0.001
Median % change from BL in LEI[b]	-33.33%	-100.00%	p=0.009
% of pts with unresolved enthesitis[b]	71.0%	43.4%	P=0.012
Median % change from BL in dactylitis[c]	-33.33%	-100.00%	p<0.001
% of pts with unresolved dactylitis[c]	82.6%	44.8%	P=0.001
Mean (SD) change from BL in SF-36 PCS score	0.46 (6.51)	6.59 (7.47)	P<0.001
Mean (SD) change from BL in SF-36 MCS score	0.42 (6.74)	4.95 (9.06)	p=0.002
% of pts achieving Minimal Disease Activity	2.0%	23.0%	p=0.001
Mean (SD) change from BL in PASDAS	-0.49 (1.33)	-2.50 (1.59)	p<0.001
Mean (SD) change from BL in GRACE Index	-0.35 (1.39)	-2.73 (1.76)	P<0.001
Mean (SD) change from BL in mCPDAI	-0.8 (2.26)	-3.9 (2.79)	P<0.001
Mean (SD) change from BL in DAPSA	-4.97 (20.11)	-23.08 (20.21)	P<0.001

[a]All pts randomized into the study, received at least 1 administration of study treatment (GUS or PBO), and were analyzed according to their assigned treatment group regardless of their actual treatment received; [b]Among the pts with enthesitis at baseline (PBO: N=31; GUS: N=76); [c]Among the pts with dactylitis at baseline (PBO: N=23; GUS: N=58); LEI: Leeds Enthesitis Index, PCS: Physical Component Score, MCS: Mental Component Score, PASDAS: Psoriatic ArthritiS Disease Activity Score, GRACE: GRAppa Composite score, mCPDAI: modified Composite Psoriatic Disease Activity Index, DAPSA: Disease Activity Index for Psoriatic Arthritis, BL: Baseline

Conclusions: In pts with active PsA and ≥3% BSA of psoriasis, GUS demonstrated significant improvement on joint symptoms, physical function, psoriasis, enthesitis, dactylitis and quality of life. GUS was well tolerated with no unexpected safety findings in this population.

Disclosure of Interest: A. Deodhar Grant/research support from: Janssen, Abbvie, Pfizer, Novartis, UCB, Eli Lilly, Glaxo, Consultant for: Janssen, Eli Lilly, Pfizer, Novartis, UCB, A. Gottlieb Grant/research support from: Janssen, Amgen, Abbott, Novartis, Celgene, Pfizer, Lilly, Levia, Merck, Xenoport, Dermira, Baxalta, Consultant for: Amgen Inc.; Astellas, Akros, Centocor (Janssen), Inc.; Celgene Corp., Bristol Myers Squibb Co., Beiersdorf, Inc., Abbott Labs. (Abbvie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dermipsor Ltd., Incyte, Pfizer, Canfite, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, Glaxo Smith Kline, Xenoport, Catabasis, Meiji Seika Pharma Co., Ltd, Takeda, Mitsubishi,Tanabe Pharma Development America, Inc, Genentech, Baxalta, Kineta One, KPI Therapeutics, W.-H. Boehncke Grant/research support from: Janssen, Consultant for: Abbvie, Biogen, Celgene, Novartis, Pfizer, Lilly, Speakers bureau: Abbvie, Novartis, B. Dong Employee of: Janssen Research & Development, LLC, Y. Wang Employee of: Janssen Research & Development, LLC, W. Barchuk Employee of: Janssen Research & Development, LLC, X. Xu Employee of: Janssen Research & Development, LLC, E. Hsia Employee of: Janssen Research & Development, LLC,

DOI: 10.1136/annrheumdis-2017-eular.1164

OP0219 EARLY ONSET OF EFFICACY WITH APREMILAST MONOTHERAPY IN BIOLOGIC-NAÏVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: A PHASE 3B, RANDOMIZED, CONTROLLED TRIAL

P. Nash[1], K. Ohson[2], J. Walsh[3], N. Delev[4], D. Nguyen[4], L. Teng[4], J.J. Gomez-Reino[5], J.A. Aelion[6]. *[1]University of Queensland, Brisbane, Australia; [2]Memorial University of Newfoundland, St. John's, Canada; [3]University of Utah School of Medicine, Salt Lake City; [4]Celgene Corporation, Summit, United States; [5]Hospital Clínico Universitario, Santiago, Spain; [6]West Tennessee Research Institute, Jackson, United States*

Background: ACTIVE is the first apremilast (APR) trial to evaluate time to onset of efficacy beginning at Wk 2 in biologic-naïve psoriatic arthritis (PsA) patients (pts) who may have had exposure to 1 prior conventional DMARD.

Objectives: Report the study results through Wk 52.

Methods: Pts were randomized (1:1) to APR 30 mg BID or placebo (PBO). Pts were eligible for early escape (investigator discretion) at Wk 16. At Wk 24, all pts entered active treatment with APR. The primary endpoint was ACR20 response at Wk 16. Other assessments included changes in DAS-28 (CRP), SJC, TJC, HAQ-DI, morning stiffness duration/severity, and enthesitis, as measured by the Gladman Enthesitis Index (GEI; 0=no enthesitis, 6=all 6 sites active). Along with collection of safety data, tolerability adverse events (AEs) of diarrhea were further characterized.

Results: 219 pts were randomized (APR: n=110; PBO: n=109); overall, 160/180 (88.9%) pts receiving APR completed Wk 52. Separation in the proportion of ACR20 responders to APR vs PBO was noted at Wk 2 (16.4% vs 6.4%; P=0.0252), the first post-baseline (BL) visit. Early onset of response to APR was observed across clinical assessments, with improvements in DAS-28 (CRP), SJC, HAQ-DI, enthesitis, and morning stiffness severity (Table). At Wk 16, significant ACR20 response rates were observed with APR vs PBO (38.2% vs 20.2%; $P<0.005$), with similar rates for the subset of pts with use of 1 prior non-biologic DMARD (39.2% vs 20.5%; $P<0.05$), which comprises 69% of study pts. Significant reductions in PsA disease activity/manifestations vs PBO were also demonstrated by changes in DAS-28 (CRP) ($P<0.0001$), SJC, and HAQ-DI (P=0.0229), and improvements in morning stiffness severity and GEI score (P=0.0014). With continued APR exposure, the Wk 52 ACR20/ACR50/ACR70 response rates were 63.3%/32.4%/14.0%, and percent change in SJC was –74.5%. Among APR pts with BL enthesitis, 62.8% reached a GEI score of 0. Overall incidence of AEs in the PBO-controlled period was generally similar between APR and PBO. The most commonly reported AEs (≥5% of pts) with APR vs PBO were nasopharyngitis (8.3% vs 6.4%), nausea (8.3% vs 1.8%), headache (7.3% vs 3.7%), hypertension (6.4% vs 6.4%), and diarrhea (pt or investigator reported) (14.7% vs 11.0%); using a protocol-defined characterization of diarrhea (≥2 watery/liquid stools/day), overall incidence was lower for APR and PBO (11.0% and 8.3%). Serious AEs were lower with APR vs PBO (2.8% vs 4.6%). No opportunistic infections, reactivations of TB, or cases of marked depression were seen. In general, no increase was seen in AE incidence/severity with longer-term exposure to APR.

	Wk 2		Wk 16		Wk 52
	APR n=110	PBO n=109	APR n=110	PBO n=109	APR n=171
ACR20, n/m (%)	18/110 (16.4)*	7/109 (6.4)	42/110 (38.2)§	22/109 (20.2)	107/169 (63.3)
DAS-28 (CRP), mean change	−0.59*	−0.31	−1.07‡	−0.39	−1.58
SJC, mean % change	−27.7	−17.5	−46.4‡	4.2	−74.5
HAQ-DI score (0-3), mean change	−0.13*	−0.05	−0.21*	−0.06	−0.36
HAQ-DI MCID ≥0.30, n/m (%)	24/110 (21.8)	13/109 (11.9)	39/110 (35.5)	30/109 (27.5)	78/171 (45.6)
SF-36v2 PF score, mean change	NA	NA	2.43§	−1.04	5.5
Improvement in morning stiffness severity, n/m (%)	47/110 (42.7)§	23/109 (21.1)	51/110 (46.4)§	28/109 (25.7)	98/171 (57.3)
GEI score (0-6), mean change#	−1.1*	−0.4	−1.5§	−0.4	−1.5

Full analysis set was used for Wk 2 and Wk 16; for response parameters, pts without sufficient data (observed and imputed) for the determination of response status were categorized as non-responders. Wk 52 analyses were data as observed among all pts who received apremilast, regardless of when apremilast treatment started (BL, Wk 16 or Wk 24); actual number of pts may vary for each end point depending on availability of data.
#Evaluated in pts with enthesitis at BL (GEI >0).
*$P<0.05$; §$P<0.005$; ‡$P<0.0001$ vs PBO; based on a mixed-effects model for repeated measures for continuous parameters and a Cochran-Mantel-Haenszel test for binary parameters.
APR=apremilast 30 mg BID; PBO=placebo; ACR20=20% improvement in American College of Rheumatology response criteria; n/m=number of responders/number of pts with sufficient data for evaluation; DAS-28 (CRP)=28-joint count Disease Activity Score (C-reactive protein); SJC=swollen joint count; HAQ-DI=Health Assessment Questionnaire-Disability Index; MCID=minimal clinically important differences; SF-36v2 PF=36-item Short-Form Health Survey version 2 Physical Functioning domain; NA=not assessed at time point; GEI=Gladman Enthesitis Index; pts=patients; BL=baseline.

Conclusions: In biologic-naïve pts treated with APR, onset of effect was observed starting at Wk 2 across PsA manifestations, including morning stiffness severity and enthesitis, with sustained improvements through Wk 52. AEs were consistent with those reported for other APR phase 3 PsA and psoriasis studies.

Disclosure of Interest: P. Nash Grant/research support from: Celgene Corporation, K. Ohson Grant/research support from: Celgene Corporation, J. Walsh Consultant for: Celgene Corporation and Novartis, N. Delev Employee of: Celgene Corporation, D. Nguyen Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, J. Gomez-Reino Grant/research support from: Roche and Schering-Plough, Consultant for: BMS, Pfizer, Roche, Schering-Plough, UCB, J. Aelion Grant/research support from: AbbVie, Ardea Biosciences, AstraZeneca, BMS, Celgene Corporation, Centocor, Galápagos, Genentech, GlaxoSmithKline, Human Genome Sciences, Janssen, Eli Lilly, Merck, Mesoblast, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda Pharmaceuticals, UCB, Vertex Pharmaceuticals

DOI: 10.1136/annrheumdis-2017-eular.3021

OP0220 RANDOMIZED, DOUBLE-BLIND, GLOBAL CLINICAL TRIAL TO EVALUATE EQUIVALENCE OF CHS-1420 TO ADALIMUMAB IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS

J. O'Dell[1], A. Kivitz[2], K. Papp[3], C. Leonardi[4], K. Jensen[5], H. Tang[5], B. Finck[5] on behalf of The PsOsim Study Group. *[1]University of Nebraska Medical Center, Omaha, NE; [2]Altoona Center for Clinical Research, Duncansville, PA, United States; [3]K. Papp Clinical Research, Waterloo, Ontario, Canada; [4]Central Dermatology, St. Louis, MO; [5]Coherus BioSciences, Redwood City, CA, United States*

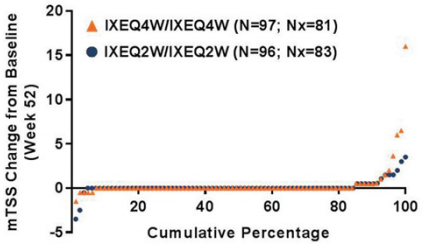
Background: CHS-1420 is being developed as a proposed biosimilar to adalimumab for the treatment of rheumatoid arthritis, plaque psoriasis (PsO), and other auto-immune diseases.
Objectives: This phase 3, randomized, double-blind, active-controlled, multicenter study evaluated the equivalence of CHS-1420 to adalimumab in patients with active, moderate-severe, chronic plaque PsO, including patients with psoriatic arthritis (PsA).
Methods: Male and female patients (aged ≥18 years) were randomized to CHS-1420 or adalimumab. Patients received 40 mg x 2 on Day 0 and then 40 mg every other week (QOW) by subcutaneous injection. To establish the equivalence of CHS-1420 to adalimumab, the 95% CI of the treatment difference for the primary endpoint, PASI75 at Week 12, had to be within pre-specified equivalence margins of ±15%. The 55-week study is ongoing, and blinded efficacy data at Week 12 and safety data through Week 16 are available. The study was not powered for statistical analysis of the PsA subgroup. Patients with PsA were evaluated based on change in the Health Assessment Questionnaire – Disability Index (HAQ-DI) and highly sensitive C-reactive protein (hs-CRP).
Results: The full analysis population for the primary efficacy endpoint consisted of 545 patients (mean age 43.9 years), with 274 and 271 in Group A and Group B, respectively. The mean BMI was 29.6 kg/m^2, and 72.3% were male. At Week 12, the proportion of patients achieving a PASI75 from Baseline was 77.7% in Group A and 74.5% in Group B. The 95% CI of the treatment difference [-3.63, 10.28] was within the pre-specified equivalence margin [-15.0, 15.0]. Sensitivity analyses supported equivalence of the two treatments.
PsA was present in 65 (23.7%) and 61 (22.5%) patients in Group A and Group B, respectively. A PASI75 was achieved by 81.5% and 77.0% of patients with PsA in Group A and Group B, respectively, at Week 12. Mean HAQ-DI scores decreased from Baseline by 0.6 and 0.7 (95% CI: -0.3, 0.3) at Week 12 in Group A and Group B, respectively. Mean hs-CRP (mg/L) decreased from Baseline by 8.9 and 6.3 at Week 12 in Group A and Group B, respectively.
In the safety population (n=545), adverse events were reported in 48.5% and 45.0% of patients, in Group A and Group B, respectively, through Week 16. Serious adverse events were reported in 1.1% and 2.2% of patients in Group A and Group B, respectively, through Week 16, and none were judged by the investigator to be related to treatment. The most common (≥5% of patients) adverse events were nasopharyngitis and upper respiratory tract infection.
Conclusions: This randomized, double-blind, global clinical trial demonstrated the equivalence of CHS-1420 to adalimumab in the treatment of chronic PsO. Both study drugs were well tolerated. Patients with PsA showed improvement with both study drugs.
Disclosure of Interest: J. O'Dell Consultant for: Coherus BioSciences, A. Kivitz: None declared, K. Papp Consultant for: 3M, Abbott/AbbVie, Akesis, Akros, Allergan, Amgen, Alza, Anacor, Applied Molecular Evolution, Astellas, Baxter, Bayer, Boehringer Ingelheim, Celgene, Celtic, Centocor, Cipher, Coherus, Dermira, Dow Pharma, Eli Lilly, Forward Pharma, Funxional Therapeutics, Galderma, Genentech, Genet, GSK, Isotechnika, Janssen, Janssen Biotech (Centocor), Kyowa Hakko Kirin, Merck, Merck-Serono, Novartis, Pfizer, C. Leonardi: None declared, K. Jensen Shareholder of: Coherus BioSciences, Employee of: Coherus BioSciences, H. Tang Shareholder of: Coherus BioSciences, Employee of: Coherus BioSciences, B. Finck Shareholder of: Coherus BioSciences, Employee of: Coherus BioSciences
DOI: 10.1136/annrheumdis-2017-eular.2490

OP0221 RADIOGRAPHIC PROGRESSION OF STRUCTURAL JOINT DAMAGE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS TREATED WITH IXEKIZUMAB OVER 52 WEEKS

D. van der Heijde[1], M. Okada[2], C. Lee[3], C.L. Shuler[3], S. Rathmann[3], C.-Y. Lin[3], P. Mease[4]. *[1]Leiden University Medical Centre, Leiden, Netherlands; [2]St. Luke's international Hospital, Tokyo, Japan; [3]Eli Lilly and Company, Indianapolis; [4]Swedish Medical Center and University of Washington, Seattle, United States*

Background: Ixekizumab (IXE), an anti-interleukin-17A monoclonal antibody, was shown to be superior to placebo (PBO) in clinical responses and inhibiting the progression of structural joint damage in patients (pts) with psoriatic arthritis (PsA) treated for 24 weeks (wks).[1]
Objectives: To assess progression of structural joint damage in PsA pts with IXE for up to 52 wks.
Methods: Biologic DMARD-naïve pts with active PsA (N=417) entered into SPIRIT-P1 (NCT01695239), a double-blind phase 3 trial. Pts must have had ≥1 joint erosion on the hand and foot x-rays confirmed by central reading *or* had a C-reactive protein level >6 mg/L at screening. 417 pts were randomized to IXE 80 mg every 2 wks (Q2W; N=103) or 4 wks (Q4W; N=107) following a 160 mg initial dose, PBO (N=106), or adalimumab 40 mg every 2 wks (ADA; active reference arm; N=101) for 24 wks. In the Extension Period (EXT: Wks 24–52), PBO and ADA pts were re-randomized (1:1) to IXEQ2W or IXEQ4W at Wk 16 (inadequate responders) or Wk 24; ADA pts underwent a washout prior to IXE treatment. All pts were assessed for structural joint damage using the van der Heijde modified PsA Total Sharp Score (mTSS, 0–528 scale). X-rays at Wks 0, 24 and 52 were scored independently by 2 readers blinded to timepoint and clinical data (average of readers). mTSS was excluded from the pre-specified analysis if the radiograph was taken after the scheduled visit date. In a post-hoc analysis, mTSS from a radiograph taken after the scheduled visit date was interpolated and considered as observed data. Any missing data at Wk 52, in either presentation, were imputed using a linear extrapolation if they had at least 1 post-baseline value.
Results: Pts had active PsA at Week 0 (Table). 381 pts (91.3%) entered the EXT, with 374 (98.2%) having radiographs collected during the EXT. Wk 52 mean (SD) mTSS change from baseline were 0.54 (2.11) and 0.09 (1.0) for pts randomized to IXEQ4W and IXEQ2W at baseline, respectively. Similar changes at Wk 52 were obtained with the post-hoc analysis (Table). The majority of IXEQ2W or IXEQ4W pts exhibited no structural progression through 1 year of IXE treatment (Figure). In pts who switched from PBO or ADA to IXE, Wk 52 mean change from baseline mTSS values scores ranged from -0.03 to 0.41 (Table).

Observed mTSS Change from Baseline Values at Week 52, Cumulative Distribution Plot



N=EXT patients; Nx= Pts with baseline and Wk 52 radiograph assessments. mTSS values from radiographs taken after the Wk 52 scheduled visit date were interpolated and considered as observed data.

Conclusions: Over a 52 wk period, minimal changes in mTSS were observed in PsA pts entering the EXT and treated with IXEQ2W or IXEQ4W.
References:
[1] Mease P et al. 2017 ARD 76(1):79.
Disclosure of Interest: D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boeringer Ingelheim, Celgene, Daiichi, Eli Lilly and Company, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, M. Okada Grant/research support from: Eli Lilly and Company, Consultant for: Eli Lilly and Company, Speakers bureau: Santen Pharmaceutical, Mitsubishi Tanabe Pharma, Pfizer, Abbott Japan, C. Lee Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, C. Shuler Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Rathmann Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, C.-Y. Lin Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Mease Grant/research support from: AbbVie, Amgen, Bristol Myers

Abstract OP0221 – Table 1. Radiographic Progression of Structural Joint Damage for EXT Pts

	PBO/IXEQ4W (N=45)	PBO/IXEQ2W (N=46)	ADA/IXEQ4W (N=49)	ADA/IXEQ2W (N=48)	IXEQ4W/IXEQ4W (N=97)	IXEQ2W/IXEQ2W (N=96)
Baseline (Week 0) Disease Characteristics, Mean (SD)						
mTSS	11.5 (15.5)	24.5 (37.3)	15.6 (24.3)	15.4 (30.2)	19.6 (33.3)	15.2 (29.1)
Tender Joint Count	18.5 (11.6)	19.2 (14.0)	18.8 (11.9)	18.8 (12.8)	20.8 (13.6)	21.3 (13.8)
Swollen Joint Count	9.6 (6.2)	10.7 (7.1)	10.1 (7.4)	9.6 (5.5)	11.0 (7.3)	12.2 (7.3)
mTSS, Pre-Specified, Mean (SD)						
Week 52 Change from Baseline	n=31	n=37	n=36	n=34	n=80	n=80
	0.27 (0.8)	0.41 (0.8)	0.32 (1.0)	-0.03 (0.4)	0.54 (2.1)	0.09 (1.0)
mTSS, Post-Hoc, Mean (SD)						
Week 52 Change from Baseline	n=44	n=45	n=47	n=45	n=97	n=96
	0.25 (0.8)	0.51 (1.1)	0.24 (0.9)	0.06 (0.5)	0.47 (1.9)	0.09 (0.9)

N = EXT pts; n = pts with baseline and ≥1 post baseline radiograph assessments.

Squibb, Celgene, Crescendo, Genentech, Janssen, Eli Lilly and Company, Merck, Novartis, Pfizer, UCB Pharma, Sun, Consultant for: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Eli Lilly and Company, Merck, Novartis, Pfizer, UCB Pharma, Sun, Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Pfizer, UCB Pharma
DOI: 10.1136/annrheumdis-2017-eular.2221

OP0222 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE PSORIATIC ARTHRITIS: 104 WEEKS RESULTS FROM A PHASE 3 TRIAL, FUTURE 2

I.B. McInnes[1], P.J. Mease[2], C. Ritchlin[3], P. Rahman[4], A. Gottlieb[5], B. Kirkham[6], R. Kajekar[7], E.M. Delicha[8], L. Pricop[7], S. Mpofu[8] on behalf of the FUTURE 2 study group. *[1]University of Glasgow, Glasgow, United Kingdom; [2]Swedish Medical Centre and University of Washington, Seattle; [3]University of Rochester, Rochester, United States; [4]Memorial University, St. John's, Canada; [5]New York Medical College, New York, United States; [6]Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom; [7]Novartis Pharmaceuticals Corporation, East Hanover, United States; [8]Novartis Pharma AG, Basel, Switzerland*

Background: Secukinumab significantly improved the signs and symptoms of psoriatic arthritis (PsA) over 52 weeks (wks) in FUTURE 2 study (NCT01752634).[1,2]
Objectives: To present longer-term (104 wks) efficacy and safety data of secukinumab from FUTURE 2 study.
Methods: Overall, 397 patients (pts) with active PsA were randomised to secukinumab (300, 150, or 75 mg) or placebo at baseline, Wks 1, 2, 3, and 4, and every 4 wks thereafter. Assessments at Wk 104 are from pts originally randomised to secukinumab and included ACR20/50/70, PASI 75/90, DAS28-CRP, SF-36 PCS, HAQ-DI, dactylitis, and enthesitis. Multiple imputation was used for analysis of binary variables and mixed-model repeated measures for continuous variables. Analyses stratified by anti-TNFα status (naïve/inadequate response or intolerance to these agents) were prespecified and are reported as observed. Safety analysis included all pts who received ≥1 dose of secukinumab.
Results: In total, 86/100 (86.0%), 76/100 (76.0%) and 65/99 (65.7%) pts in the secukinumab 300, 150, and 75 mg groups respectively completed 104 wks. Sustained clinical improvements were observed through Wk 104 with secukinumab across all clinically important domains of PsA (Table). Responses were sustained through Wk 104 regardless of anti-TNFα status. Over the entire treatment period (mean [±SD] exposure to secukinumab of 709±210.99 days), the exposure adjusted incidence rates for serious infections/infestations, candida infections, inflammatory bowel disease and malignant/unspecified tumors with secukinumab were 1.6, 2.3, 0.5 and 1.3, respectively.

Table 1. Summary of Efficacy Results at Wk 104

Variable*	Secukinumab		
	300 mg s.c. (N=100)	150 mg s.c. (N=100)	75 mg s.c. (N=99)
ACR20	69.4	64.4	50.3
ACR50	50.6	36.0	28.2
ACR70	33.1	23.1	14.9
[a]PASI 75	79.5	73.3	58.4
[a]PASI 90	69.6	52.5	33.7
SF-36 PCS, LS mean change from BL (SE)	6.8 (0.85)	5.0 (0.87)	4.1 (0.91)
DAS28-CRP, LS mean change from BL (SE)	?1.9 (0.12)	?1.7 (0.12)	?1.5 (0.13)
HAQ-DI, LS mean change from BL (SE)	?0.58 (0.05)	?0.48 (0.06)	?0.27 (0.06)
[b]Resolution of enthesitis	71.5	61.8	68.4
[c]Resolution of dactylitis	79.9	78.0	88.6

*% responders unless otherwise specified. [a]Assessed in pts with psoriasis affecting ≥3% body surface area at BL (300 mg: n=41; 150 mg: n=58; 75 mg: n=50). [b]Assessed in pts (n=56 [300 mg], 64 [150 mg] and 68 [75 mg]) with this symptom at BL. [c]Assessed in pts (n=46 [300 mg], 32 [150 mg] and 33 [75 mg]) with this symptom at BL. BL, baseline; DAS28-CRP, 28-joint disease activity score using C-reactive protein; HAQ-DI, health assessment questionnaire-disability index; LS, least squares; N, number of pts randomised; PASI, psoriasis area and severity index; SE, standard error; SF-36 PCS, short form-36 physical component summary.

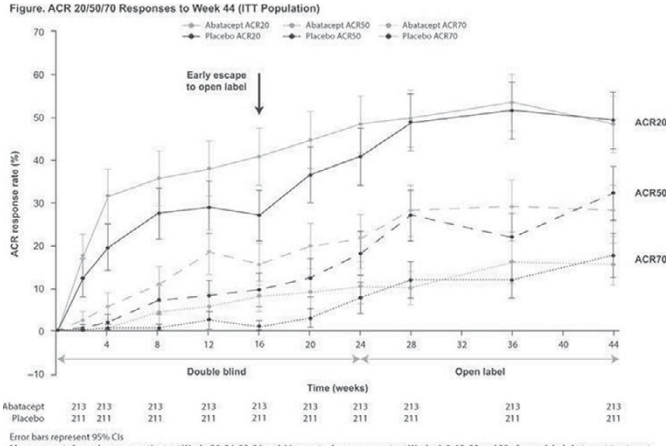
Conclusions: Secukinumab 300 and 150 mg provided sustained improvements in signs and symptoms and multiple clinical domains of active PsA through 2 years of therapy. Secukinumab was well tolerated, with a safety profile consistent with that reported previously.
References:
[1] McInnes IB, et al. Lancet 2015;386:1137–46.
[2] McInnes IB, et al. Ann Rheum Dis. 2015;74:352–3.
Disclosure of Interest: I. McInnes Grant/research support from: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB, Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB, P. Mease Grant/research support from: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Consultant for: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, C. Ritchlin Grant/research support from: Amgen, UCB, Abbvie, Novartis, and Janssen, Consultant for: Amgen, UCB, Abbvie, Novartis, and Janssen, Speakers bureau: Amgen, UCB, Abbvie, Novartis, and Janssen, P. Rahman Consultant for: Abbott, Abbvie, Amgen, BMS, Celgene, Janssen, Novartis, Pfizer and Roche. Consultant for pharmaceutical companies dealing with biologic agents in rheumatology, A. Gottlieb Grant/research support from: (paid to Tufts Medical Center until 5/11/16 thereafter: None): Centocor (Janssen) Inc., Amgen, Abbott (AbbVie), Novartis, Celgene, Pfizer, Lilly, Levia, Merck, Xenoport, Dermira, Baxalta, Consultant for: Amgen Inc., Astellas, Akros, Centocor (Janssen) Inc., Celgene Corp., Bristol Myers Squibb Co., Beiersdorf Inc., Abbott Labs. (AbbVie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dermipsor Ltd., Incyte, Pfizer, Canfite, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, Glaxo SmithKline, Xenoport, Catabasis, Meiji Seika Pharma Co. Ltd, Takeda, Mitsubishi, Tanabe Pharma Development America Inc., Genentech, Baxalta, Kineta One, KPI Therapeutics, Crescendo Bioscience, Aclaris, Amicus and Reddy Labs, B. Kirkham Grant/research support from: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Roche, and UCB, Consultant for: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Roche, and UCB, Speakers bureau: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Roche, and UCB, R. Kajekar Shareholder of: Novartis, Employee of: Novartis, E. M. Delicha Employee of: Novartis, L. Pricop Shareholder of: Novartis, Employee of: Novartis, S. Mpofu Shareholder of: Novartis, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1274

OP0223 ABATACEPT IN THE TREATMENT OF ACTIVE PSORIATIC ARTHRITIS: 1-YEAR RESULTS FROM A PHASE III STUDY

P. Mease[1], A. Gottlieb[2], D. van der Heijde[3], O. FitzGerald[4], A. Johnsen[5], M. Nys[6], S. Banerjee[5], D. Gladman[7]. *[1]Swedish Medical Center and University of Washington, Seattle; [2]New York Medical College, Valhalla, United States; [3]Leiden University Medical Center, Leiden, Netherlands; [4]St Vincent's University Hospital and University College Dublin, Dublin, Ireland; [5]Bristol-Myers Squibb, Princeton, United States; [6]Bristol-Myers Squibb, Braine-l'Alleud, Belgium; [7]University of Toronto and Toronto Western Hospital, Toronto, Canada*

Background: In the Phase III ASTRAEA trial (NCT01860976), abatacept (ABA), a selective T-cell co-stimulation modulator, significantly increased ACR20 response (primary endpoint; PE) and had an overall beneficial effect vs placebo (PBO) on musculoskeletal symptoms in patients (pts) with active psoriatic arthritis (PsA) at 24 weeks (W).[1]
Objectives: To analyse 1-year results from ASTRAEA.
Methods: Pts with active disease (≥3 swollen and ≥3 tender joints), ≥2 cm target lesion of plaque psoriasis and inadequate response/intolerance to ≥1 non-biologic DMARD were randomized (1:1) to SC ABA 125 mg weekly or PBO for 24W, followed by open-label (OL) SC ABA up to 52W. Randomization was stratified by MTX use, prior TNF inhibitor (TNFi) use and skin involvement ≥3% of body surface area. Pts without ≥20% improvement in joint counts at W16 were switched to OL ABA (early escape; EE) for 28W (total study time: 44W). Pre-specified exploratory endpoints included: ACR20/50/70 responses at W44; adjusted mean changes from baseline (BL) in DAS28 (CRP; *post hoc* analysis) and HAQ-DI at W44 and PsA-modified total Sharp/van der Heijde score (SHS) at W44 (EE pts)/W52 (non-EE pts); complete resolution of BL enthesitis and dactylitis at W44 (EE pts)/W52 (non-EE pts); and Psoriasis Area and Severity Index (PASI) 50/75 responses at W44. Analyses used the ITT population with non-responder imputation for missing values and actual data at each time point for all pts (denominator at each time point equal to number of pts in ITT population). All missing responses were imputed as non-responders, except if the missing value was between 2 visits for which the pt was a responder. In that case the missing value was imputed as a responder.
Results: Of 424 pts enrolled, 213 received ABA and 211 PBO. Most (>60%) pts had received prior TNFis. Of pts in the ABA and PBO groups, 76 (36%) and 89 (42%) were EE, 12 (6%) and 24 (11%) discontinued by PE of W24;

Figure. ACR 20/50/70 Responses to Week 44 (ITT Population)



Error bars represent 95% CIs
Measurements for early escape patients at Weeks 20, 24, 28, 36 and 44 are actual measurements at Weeks 4, 8, 12, 20 and 28 of open-label abatacept treatment
At all time points, if there were missing data, patients were imputed as non-responders, unless data were missing between two time points at which the patient had a response, in which case response was imputed

197 (92%) and 185 (88%) entered the OL period, of whom 165 (84%) and 162 (88%) completed. At W44, ACR responses at W24 were maintained for pts who continued ABA, and improved for those who switched from PBO to ABA (Figure). Continued improvements in DAS28 (CRP) and HAQ-DI after W24 were seen for ABA and PBO/ABA groups, with mean (SE) changes from BL to W44 of –1.81 (0.09) and –1.84 (0.10) in DAS28 (CRP) (changes to W24 were –1.35 [0.10] and –0.94 [0.11]) and –0.37 (0.04) and –0.38 (0.04) in HAQ-DI (changes to W24 were –0.33 [0.04] and –0.20 [0.05]), respectively. There was minimal progression based on mean (SE) change from BL in PsA-modified total SHS at W44/52 in the ABA and PBO/ABA groups: 0.18 (0.12) vs 0.30 (0.12). Complete resolution of BL enthesitis occurred in 48.6% and 43.9% and BL dactylitis in 68.9% and 60.0% of pts with ABA and ABA/PBO, respectively, at W44/52. At W44, for ABA and PBO/ABA, PASI 50 responses were 30.1% and 34.5%; PASI 75 responses were 19.9% and 16.9%. There were no new safety signals.

Conclusions: Responses were maintained across musculoskeletal endpoints up to 1 year in a relatively refractory population of pts continuing on SC abatacept. Abatacept was well tolerated.

References:

[1] Mease P, et al. Arthritis Rheumatol 2016;68(Suppl 10):Abstract 1041.

Disclosure of Interest: P. Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, Corrona, Demira, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Zynerba, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, Genentech, Janssen, Novartis, Pfizer, UCB, A. Gottlieb Grant/research support from: Centocor (Janssen), Amgen, Abbott (AbbVie), Novartis, Celgene, Pfizer, Lilly, Coronado, Levia, Merck, Xenoport, Dermira, Baxalta, Consultant for: Amgen Inc.; Astellas, Akros, Centocor (Janssen), Inc.; Celgene Corp., Bristol-Myers Squibb Co., Beiersdorf, Inc., Abbott Labs. (AbbVie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dermipsor Ltd., Incyte, Pfizer, Canfite, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, GlaxoSmithKline, Xenoport, Catabasis, Meiji Seika Pharma Co., Ltd, Takeda, Mitsubishi Tanabe Pharma Development America, Inc, Genentech, Baxalta, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boeringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, O. FitzGerald: None declared, A. Johnsen Employee of: Bristol-Myers Squibb, M. Nys Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Banerjee Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, D. Gladman Grant/research support from: AbbVie, Amgen, Celgene, Janssen, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, UCB

DOI: 10.1136/annrheumdis-2017-eular.2865

FRIDAY, 16 JUNE 2017

From classics to new: synthetic DMARDs in RA

OP0224 SIMILAR SHORT TERM CLINICAL RESPONSE TO INITIAL TREATMENT WITH HIGH VERSUS LOW DOSE METHOTREXATE IN MONO- AND COMBINATION THERAPY IN EARLY RHEUMATOID ARTHRITIS PATIENTS

S.A. Bergstra[1], C.F. Allaart[1], R. van den Berg[1,2], A. Chopra[3], N. Govind[4], T.W. Huizinga[1], R.B. Landewé[5,6] on behalf of METEOR working group.
[1]Rheumatology, LUMC, Leiden; [2]Rheumatology, Erasmus University Medical Center, Rotterdam, Netherlands; [3]Center for Rheumatic Diseases, Pune, India; [4]University of the Witwatersrand, Johannesburg, South Africa; [5]Amsterdam Rheumatology & Immunology Center, Amsterdam; [6]Zuyderland Medical Center, Heerlen, Netherlands

Background: Aiming at rapid decrease of disease activity, there has been a trend to start with higher doses of methotrexate (MTX) in newly diagnosed rheumatoid arthritis (RA) patients, both as monotherapy and in combination with other antirheumatic drugs (DMARDs). We hypothesized that in combination with other very effective medication, there might be no additional benefit of high over low doses of MTX.

Objectives: To compare early clinical response to high versus low doses of MTX in mono- and combination therapy in DMARD naive early RA patients.

Methods: RA patients included in the observational international METEOR cohort with symptom duration ≤5 years, time between diagnosis and first visit ≤2 months, MTX prescribed as (part of) first treatment, no medication change within 3 to 6 months after treatment start and available outcome data on disease activity, were selected. Patients were divided into 4 medication groups: MTX monotherapy, MTX + synthetic (cs)DMARDs, MTX + oral glucocorticoid (+ possibly csDMARDs) or MTX + biologic (b)DMARDs (+ possibly csDMARDs). Missing data were imputed using multivariate normal imputation. MTX dose was dichotomized: low dose ≤10 mg/week; high dose ≥15 mg/week. A propensity score (PS) was calculated to adjust the relationship between MTX dose and outcome for potential confounding by indication. Linear mixed model analyses for DAS, DAS28, and HAQ were performed for each medication group, with MTX-dose and time (days between assessment visit and baseline assessment) as co-variates. Associations were adjusted for the PS. Random intercept and slope were used to account for irregular time intervals between visits.

Results: Patients who started on MTX monotherapy had lower baseline disease activity and fewer were erosive and autoantibody positive; other baseline characteristics were comparable between medication groups. The number of patients on combination therapy with bDMARDs was too small to perform analyses (26 visits in 11 patients). For patients starting on MTX monotherapy, MTX+csDMARDs or MTX+glucocorticoids, the PS-adjusted effects of MTX-dose (high vs low) on DAS, DAS28 and HAQ were small and not clinically meaningful. The unadjusted main associations between MTX-dose and outcomes were often in opposite direction and/or much larger than the PS adjusted associations, suggesting that confounding by indication indeed plays a role and that (at least some) correction was achieved by adjusting for the PS (table 1).

Table 1: Unadjusted and propensity score adjusted results of the linear mixed model analyses to investigate the effectiveness of high versus low methotrexate dose on disease activity (DAS and DAS28) and physical functioning (HAQ), stratified per medication group.

	DAS		DAS28		HAQ	
Methotrexate monotherapy (n patients=449, n visits=975)						
	β	95% CI	β	95% CI	β	95% CI
MTX-dose group PS adjusted	0.052	-0.17; 0.28	0.085	-0.24; 0.41	0.043	-0.11; 0.20
MTX-dose group unadjusted	-0.55	-0.71; -0.39	-0.19	-0.45; 0.071	0.17	0.059; 0.28
Methotrexate + csDMARDs (n patients=265, n visits=574)						
	DAS		DAS28		HAQ	
	β	95% CI	β	95% CI	β	95% CI
MTX-dose group PS adjusted	0.036	-0.26; 0.33	0.0066	-0.39; 0.41	-0.014	-0.21; 0.18
MTX-dose group unadjusted	-0.19	-0.45; 0.071	-0.29	-0.65; 0.065	0.080	-0.094; 0.25
Methotrexate + oral glucocorticoid (+/-csDMARDs) (n patients=485, n visits=1075)						
	DAS		DAS28		HAQ	
	β	95% CI	β	95% CI	β	95% CI
MTX-dose group PS adjusted	-0.017	-0.26; 0.22	-0.14	-0.45; 0.17	-0.023	-0.17; 0.12
MTX-dose group unadjusted	-0.33	-0.50; -0.15	-0.64	-0.86; -0.41	0.14	0.040; 0.25

DAS=disease activity score, HAQ=health assessment questionnaire, PS=propensity score, 95% CI=95% confidence interval, MTX=methotrexate. MTX-dose group is a binary variable with low dose =10 mg/week and high dose =15 mg/week. Low dose is the reference category.

Conclusions: In a daily practice derived database in DMARD-naive early RA patients, we found no early clinical benefit of high over low initial MTX doses, neither for MTX monotherapy nor for combination therapy with MTX and csDMARDs or glucocorticoids. This seems to contradict a general trend over time to start higher MTX-doses.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1601

OP0225 THE EFFECT OF A LOW VERSUS HIGH FIRST PRESCRIBED DOSE OF METHOTREXATE ON EULAR RESPONSE AT SIX MONTHS USING DATA FROM THE RAMS STUDY

R. Davies, M. Lunt, A. Barton, K.L. Hyrich, S.M.M. Verstappen on behalf of RAMS co-investigators. *Division of Musculoskeletal & Dermatological Sciences, Centre for Musculoskeletal Research, University of Manchester, Manchester, United Kingdom*

Background: Methotrexate (MTX) is one of the most commonly used drugs for the treatment of rheumatoid arthritis (RA). Recommendations by an international panel state that oral MTX should be started at 10–15mg/week, with escalation of 5mg every 2–4 weeks up to 20–30mg/week (1). In the UK, practice varies in terms of the starting dose prescribed for MTX, likely because of a lack of published evidence on the importance of MTX dose on its efficacy and safety.

Objectives: To compare 6 month response to MTX in RA patients starting 7.5mg/wk versus those starting a 15mg/wk.

Methods: Patients were recruited to the national, UK, multi-centre (n=35) longitudinal observational Rheumatoid Arthritis Medication Study (RAMS), including patients starting MTX for the first time with complete DAS28 at baseline and six months were included in this analysis. Patients were categorized into EULAR non-responders, moderate responders or good responders. Patients were categorised into those starting a low dose of MTX (≤7.5mg/wk) (LM-group) or a high

Table 1

	LM-group (n=171)	HM-group (n=639)	P
Age, years	58 (47–69)	61 (51–69)	0.13
Gender, % female	70	60	0.03
Disease duration, months	6 (3–11)	6 (3–11)	0.65
Tender joint count	7 (3–13)	5 (2–11)	0.05
Swollen joint count	5 (2–9)	5 (2–10)	0.62
Physician VAS, mm	47 (27–67)	33 (18–50)	0.0001
Patient VAS, mm	50 (26–70)	35 (20–55)	0.0001
DAS28 score at baseline	4.2 (3.4–5.2)	4.1 (3.2–5.1)	0.24
DAS28 score at 6 months	3.5 (2.7, 4.1)	3.0 (2.2, 4.1)	0.004
HAQ score	1.3 (0.6–1.8)	0.9 (0.4–1.5)	0.001
Other nbDMARD use, n (%)	30 (17)	61 (10)	0.003
EULAR response at 6 months, n (%)			0.09
Non-responders	50 (45)	184 (42)	
Moderate responders	36 (32)	108 (25)	
Good responders	26 (23)	145 (33)	
Fully adjusted RRR (95% CI)*			
Non-responders	–	ref	
Moderate responders	–	1.01 (0.56, 1.82)	0.97
Good responders	–	2.65 (1.37, 5.14)	0.004

Scores are median [IQR].

dose of MTX (≥15mg/wk) (HM-group). A multinomial logistic regression model was used to test the association between MTX start dose and EULAR response at 6 months,with adjustments (see table) (relative risk ratio (RRR), 95% CI). The model was clustered by centre to account for the prescribing preferences of individual centres.
Results: 810 patients were included in this study: 171/810 (21%) starting low dose MTX and 639/810 (79%) starting high dose MTX. Patients in the HM-group had significantly lower physician and patient VAS scores and less functional disability compared to those in the LM-group (table). These patients were also less likely to be prescribed concomitant (nbDMARDs) (17% vs. 10%). DAS28 score at 6 months was significantly lower for patients in the HM-group.
A fully adjusted multinomial logistic regression model, clustered by centre, showed that being in the high dose MTX group does not affect the odds of having a moderate response rather than no response, but does increase the odds of having a good response (RRR: 2.65 (95% CI 1.37, 5.14)).
Conclusions: Patients with RA starting MTX on a higher dose have increased odds of having a good EULAR response compared to non-response at 6 months.
References:
[1] Visser, K. et al (2009). Multinational evidence-based recommendations for the use of methotrexate in rheumatic disorders with a focus on rheumatoid arthritis: integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3E Initiative. Ann Rheum Dis, 68: 1086–1093.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6047

OP0226 SUSTAINED EFFECTIVENESS OF METHOTREXATE WITH STEP-DOWN GLUCOCORTICOID REMISSION INDUCTION (COBRA SLIM) FOR EARLY RHEUMATOID ARTHRITIS IN A TREAT-TO- TARGET SETTING: 2-YEAR RESULTS OF THE CARERA TRIAL

V. Stouten [1], J. Joly [2], D. De Cock [1], S. Pazmino [1], K. Van der Elst [2,3], R. Westhovens [1,2], P. Verschueren [1,2] on behalf of CareRA study group. *[1]Skeletal Biology and Engineering Research Center, KU Leuven Department of Development and Regeneration; [2]Rheumatology, University Hospitals Leuven; [3]Skeletal Biology and Engineering Research Center, KU Leuven Department of Public Health and Primary Care, Leuven, Belgium*

Background: The CareRA trial showed that remission induction with MTX and a moderate-dose of Glucocorticoids (GC) (COBRA Slim) in a treat-to-target setting is effective and safe in early Rheumatoid Arthritis (eRA) patients. This strategy showed equally high remission rates at 52 weeks (W), a favourable safety profile compared to DMARD combinations and GC and very few patients had to start biologicals.
Objectives: To compare the outcome of different intensive combination treatment strategies in high-risk patients of the CareRA trial at W104, focussing on persistent disease control.
Methods: CareRA is a two-year prospective investigator-initiated pragmatic multicentre RCT; csDMARD naïve eRA patients were stratified into a high- or low-risk group based on classical prognostic markers (presence of erosions, RF, anti-CCP and DAS28-CRP). High-risk patients (n=289) were randomized to 1/3 arms: 1) COBRA Classic (n=98): Methotrexate (MTX)+Sulphasalazine+60mg prednisone tapered weekly to 7.5mg daily from W7; 2) COBRA Slim (n=98): MTX+30mg prednisone tapered to 5 mg daily from W6; 3) COBRA Avant-Garde (n=93): MTX+Leflunomide+30mg prednisone tapered to 5 mg daily from W6. From W28, GCs were tapered in all patients and stopped at W34. A predefined treat-to-target approach was applied until W52 and afterwards treatment was at the discretion of the rheumatologist. From W40, DMARD monotherapy was aimed for. From W28 onwards patients were evaluated every 3 months till W104. Efficacy measures were proportions of DAS28-CRP remission, good EULAR response, clinically meaningful HAQ response, HAQ=0 (ITT analysis). Adverse events related to therapy (AEs) were registered. Missing data were imputed by last observation carried forward.
Results: Remission rates at W104 in high-risk patients were 65.3%, 73.5% and 73.1% in the Classic, Slim and Avant-Garde group respectively (p=0.369). Also, other efficacy outcomes did not differ between groups (see table). From the high-risk patients that were in remission at year 1, 54.7%, 67.8% and 70.2% in the Classic, Slim and Avant-Garde group respectively, stayed in remission at every three-monthly evaluation until w104. Also DAS28-CRP scores remained relatively stable during the second year in these groups. In high-risk patients, the total numbers of AEs reported as related to study therapy, were 209 in 72 Classic patients, 164 in 69 Slim patients and 208 in 74 Avant-Garde patients (p=0.029). Serious AEs were reported in 3 Classic, 4 Slim and 3 Avant-Garde patients. Biologicals were started in 44 high-risk patients (15.2%), of which 7 receiving 2 different biologicals and 2 receiving 3 different ones. Biologicals were administered in 18 Classic, 11 Slim and 15 Avant-Garde patients.

	COBRA classic N=98	COBRA slim (high-risk) N=98	COBRA Avant-Garde N=93	p-value
DAS28-CRP change BL-w104	2.6±1.4	2.6±1.3	2.6±1.6	0.966
DAS28-CRP change w52-w104	0.0±1.0	0.2±1.0	0.3±1.1	0.112
DAS28 Remission w52	65.3%	60.2%	61.3%	0.741
DAS28 Remission w104	65.3%	73.5%	73.1%	0.369
Good EULAR response	78.6%	81.6%	78.5%	0.826
Clinically meaningful HAQ change	70.4%	62.2%	70.7%	0.363
HAQ = 0	39.8%	37.8%	38.7%	0.958

DAS28-CRP= 28 Joint disease activity score calculated with C-reactive protein; remission = DAS28-CRP <2.6; low disease activity = DAS-CRP ≤3.2; good EULAR response = low disease activity with a DAS28-CRP change >1.2; HAQ= health assessment questionnaire; clinically meaningful HAQ change = HAQ change >0.22.

Conclusions: All groups showed persistently high remission rates 2 years after remission induction with csDMARDs and GCs in a treat to target setting. COBRA Slim showed comparable efficacy with less adverse events compared to DMARD combinations with moderate or high GC induction dosages. In almost 70% of COBRA Slim patients achieving remission at year 1, this was maintained throughout the second year.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6472

OP0227 REMISSION INDUCTION WITH METHOTREXATE STEP-UP THERAPY VERSUS COMBINATION OF HYDROXYCHLOROQUINE, METHOTREXATE AND TRIAMCINOLONE: 3 YEAR RESULTS

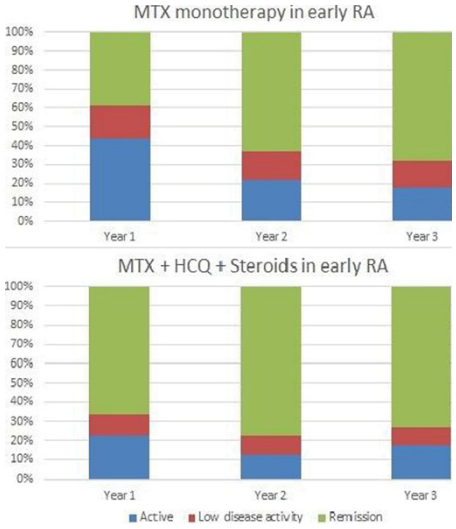
T. Brunekreef, H. Bernelot Moens. *Rheumatology & Clinical Immunology, Ziekenhuisgroep Twente, Almelo, Netherlands*

Background: The effectiveness of treat to target (T2T) in RA is widely acccepted, but there is no consensus regarding the best initial treatment in early rheumatoid arthritis[1]. Therefore, it is important to evaluate the results of such strategies in real life cohorts[2,3].
Objectives: Compare the effectiveness of step-up methotrexate (MTX) monotherapy and combination of hydroxychloroquine (HCQ), methotrexate and intramuscular injection of triamcinolone 80–120mg as initial treatment in early RA.
Methods: Historical cohorts of patients treated with MTX monotherapy (disease onset 2006–2011, N=297) and combination therapy (2012–2016, N=156) were compared. In both cohorts a b-DMARD was advised when no remission was reached within 6 months or in case of sustained activity thereafter. Baseline characteristics and disease activity (DAS28) measurements (N=4956, average 4.1/year) in the first 3 years of follow-up were available. The primary outcome measure was the proportion of patients having reached at least one DAS28 <2.6 (remission) during follow-up. Secondary outcomes were sustained remission over 36 months and time to first b-DMARD.
Results: Three patients did not start MTX, and 11 and 2 patients in the step-up and combination cohorts respectively did not have complete follow-up (Table). Within 12 months, more patients on combination treatment reached remission (88,2% vs 72.2%). In the second year these changed to 86.5% and 82.0% respectively. Combination treatment resulted in a higher percentage of DAS measurements below 2.6 over 3 years, reflecting sustained remission (Figure). A b-DMARD was started within 24 months in 20.6% of patients on monotherapy versus 14.1% on combination treatment, with an equal mean time to first b-DMARD of 12 vs 11 months after start of initial treatment.

Table 1

Table	MTX monotherapy (N=297)	MTX with HCQ and steroids (N=156)
Female, N (%)	180 (60.6)	101 (64.7)
Age (y), mean (SD, range)	59.5 (14.3, 18–89)	58.8 (12.9, 19–86)
Rheumatoid factor (N, %)	183 (61.6)	112 (71.8)
ACPA (N, %)	157 (65.3)	111 (71.2)
Follow-up (months) (range)	81 (8–132)	42 (11–62)
End of follow-up <3 yrs		
Death	4 (1.3%)	1 (0.6%)
Remission	4 (1.3%)	1 (0.6%)
Did not start MTX/Other	5 (1.7%)	1 (0.6%)
Any remission (DAS28 <2.6)		
First year	72.2%	88.2%
Second year	82.0%	86.5%
Third year	85.9%	87.0%
Start b-DMARD therapy		
First year	32 (10.8%)	17 (10.9%)
Second year	29 (9.8%)	5 (3.2%)
Third year	8 (2.7%)	5/104 (4.8%)

Conclusions: Combination treatment results in more remissions in the first year of treatment. In the second and third year the remission percentage on monotherapy comes close to combination treatment, at the cost of a 6% higher proportion of patients stepping up to biologicals. Overall, the combination of MTX with HCQ and triamcinolone results in more sustained remissions.
References:
[1] Stoffer M, Schoels M, Smolen J et al. Evidence for treating rheumatoid arthritis to target: results from a systematic literature search update. Ann Rheum Dis 2016; 75:16–22.
[2] de Jong P, Hazes J, Barendregt P et al. Induction therapy with a combination of DMARDs is better than methotrexate monotherapy: first results of the tREACH trial. Ann Rheum Dis 2013; 72:72–8.
[3] Steunebrink L, Versteeg G, Vonkeman H et al. Initial combination therapy versus step-up therapy in treatment to the target of remission in daily clinical



practice in early rheumatoid arthritis patients: results from the DREAM registry. Art Res & Ther 2016: 10.1186/s13075–016–0962–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3892

OP0228

WITHDRAWN

OP0229

EFFECT OF BASELINE SERUM CRP LEVELS ON CLINICAL EFFICACY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH FILGOTINIB: POST-HOC ANALYSIS FROM TWO PHASE 2B STUDIES

R. Westhovens[1], A. Kavanaugh[2], C. Jamoul[3], C. Tasset[3], P. Harrison[3], A. Van der Aa[3]. *[1]Rheumatology, KU Leuven, University Hospitals, Leuven, Belgium; [2]University of California, la Jolla, United States; [3]Galapagos NV, Mechelen, Belgium*

Background: Filgotinib (GLPG0634, GS-6034) is an oral, selective JAK1 inhibitor that has shown a favorable safety and efficacy profile both as add-on to methotrexate (MTX) and as monotherapy in two 24-week placebo-controlled phase 2B studies in active rheumatoid arthritis (RA) patients with inadequate response to MTX (MTX-IR)[1,2].

Objectives: To assess effect of baseline serum CRP levels on clinical efficacy in MTX-IR RA patients treated with filgotinib.

Methods: Patients were randomized in a double blind manner to placebo (PBO) or one of 3 daily doses of filgotinib (50mg, 100mg or 200mg) for 24 weeks. In the DARWIN 1 study, filgotinib on the background of MTX was evaluated as once (QD) or twice daily treatment. In the DARWIN 2 study once-daily filgotinib was assessed as monotherapy. The inclusion criterion for CRP was amended during the studies and decreased over time from 13.5 mg/L to 6.3 mg/L. This post hoc analysis included patients treated with the selected Phase 3 filgotinib doses, 100mg and 200mg QD, and PBO. Efficacy outcomes were analyzed by baseline CRP level (low: ≤9 mg/L and high: >9 mg/L, with 9mg/L as ULN).

Results: Baseline disease activity was high, with mean DAS28(CRP) scores of 5.6 and 5.7 in the low CRP subgroups for DARWIN 1 and DARWIN 2, respectively, and 6.3 in the high CRP subgroups for both studies. Mean CRP levels at baseline were elevated (16.3 - 35.3 mg/L). In both low and high CRP subgroups, patients on filgotinib 100mg or 200mg QD for 12 weeks showed efficacy over PBO, as measured by change from baseline in DAS28(CRP), CDAI and HAQ-DI, and ACR20 (Table 1). Despite slight numerical differences, baseline CRP level had no consistent effect on filgotinib efficacy, neither for endpoints including CRP (DAS28(CRP) or ACR20) nor for endpoints not including CRP (CDAI). Results were similar across both studies.

Table 1. Change from baseline in key efficacy parameters at Week 12 by CRP subgroup (mean (SE))

	DARWIN 1			DARWIN 2		
	PBO	Filgotinib 100mg QD	Filgotinib 200mg QD	PBO	Filgotinib 100mg QD	Filgotinib 200mg QD
Low CRP subgroup (≤9 mg/L)						
N	33	25	15	11	20	20
DAS28 (CRP)	-1.2 (0.30)	-2.2 (0.24)	-2.2 (0.32)	-0.9 (0.55)	-2.1 (0.33)	-2.3 (0.25)
CDAI	-18.3 (3.52)	-23.7 (2.66)	-25.1 (3.45)	-11.5 (6.19)	-25.8 (3.53)	-27.4 (3.05)
HAQ-DI	-0.21 (0.121)	-0.76 (0.133)	-0.64 (0.100)	-0.12 (0.163)	-0.74 (0.172)	-0.74 (0.158)
High CRP subgroup (>9 mg/L)						
N	53	60	71	61	50	49
DAS28	-1.2 (0.15)	-2.3 (0.19)	-2.5 (0.15)	-1.0 (0.17)	-2.0 (0.19)	-2.3 (0.19)
CDAI	-15.6 (2.04)	-23.8 (2.08)	-25.5 (1.67)	-11.7 (1.94)	-23.3 (2.38)	-24.1 (2.12)
HAQ-DI	-0.49 (0.080)	-0.61 (0.087)	-0.78 (0.076)	-0.25 (0.074)	0.65 (0.081)	-0.74 (0.086)
ACR20 by subgroup, n (%)						
Low CRP	15 (45%)	19 (76%)	10 (67%)	2 (18%)	13 (65%)	16 (80%)
High CRP	23 (43%)	35 (58%)	49 (69%)	19 (31%)	33 (66%)	34 (69%)

Conclusions: Post hoc analysis of two Phase 2B studies in MTX-IR RA patients suggests that filgotinib treatment once daily at 100mg and 200mg both on the background of MTX and as monotherapy is consistently associated with improved clinical outcomes compared to placebo, regardless of baseline CRP levels.

References:

[1] Westhovens R et al. Ann Rheum Dis 2016;0:1–11.
[2] Kavanaugh A et al. Ann Rheum Dis 2016;0:1–11.

Disclosure of Interest: R. Westhovens Grant/research support from: Roche, Consultant for: Galapagos, Speakers bureau: BMS, A. Kavanaugh Consultant for: Galapagos, Pfizer, AbbVie, Amgen, Celgene, Janssen, Novartis, Eli Lilly, UCB, C. Jamoul Employee of: Galapagos NV, C. Tasset Employee of: Galapagos NV, P. Harrison Employee of: Galapagos NV, A. Van der Aa Employee of: Galapagos NV

DOI: 10.1136/annrheumdis-2017-eular.5428

OP0230

THE EFFECTIVENESS OF ZOSTER VACCINE IN RA PATIENTS SUBSEQUENTLY TREATED WITH TOFACITINIB

K.L. Winthrop[1], A. Wouters[2], E.H. Choy[3], C. Nduaka[4], P. Biswas[2], L. Wang[5], J. Hodge[2], I. Lazariciu[6], K. Soma[5], C.F. Mojcik[2], W.F.C. Rigby[7]. *[1]Oregon Health and Science University, Portland, OR; [2]Pfizer Inc, New York, NY, United States; [3]CREATE Center, Division of Infection and Immunity, Cardiff University School of Medicine, Cardiff, United Kingdom; [4]Pfizer Inc, Collegeville, PA; [5]Pfizer Inc, Groton, CT, United States; [6]Quintiles, Saint-Laurent, QC, Canada; [7]Giesel School of Medicine at Dartmouth, Lebanon, NH, United States*

Background: Rheumatoid arthritis (RA) patients (pts) are at increased risk of herpes zoster (HZ). The most recent ACR guidelines of 2015 recommend vaccination in pts aged ≥50 years prior to starting biologic DMARDs or tofacitinib,[1]

an oral Janus kinase inhibitor for the treatment of RA. Live zoster vaccine (LZV) has shown 70% efficacy in immunocompetent adults aged 50–59 years and 51% efficacy in those aged ≥60 years.[2] We previously reported that pts with RA on background methotrexate who started 3 months of treatment with tofacitinib after LZV had similar varicella zoster virus (VZV)-specific immunity to placebo (PBO) pts, and their VZV immunity at Week 6 post-vaccination was comparable with healthy individuals aged ≥50 years.[3]

Objectives: To evaluate the long-term effectiveness of LZV in pts with RA via the incidence of HZ after treatment with tofacitinib for up to 27 months.

Methods: Data were analysed from a prior cohort of pts (n=100) given LZV and then randomised 2–3 weeks later to tofacitinib 5 mg twice daily (BID) or PBO for 12 weeks (A3921237 [NCT02147587]). At 14 weeks post-vaccination, pts joining the long-term extension (LTE) study ORAL Sequel (NCT00413699; study ongoing; database not locked) initiated open-label treatment with tofacitinib 5 or 10 mg BID. The incidence of HZ post-vaccination after tofacitinib exposure up to 27 months (based on an extended follow-up beyond January 2016 data snapshot) was evaluated. Among HZ cases, we analysed measures of VZV-specific immunity with average immunity after LZV.

Results: 112 pts were randomised to PBO (n=57) or tofacitinib 5 mg BID (n=55). 100 pts continued to receive tofacitinib in ORAL Sequel. Five cases (not adjudicated) of HZ occurred (#1: 202 days [219 days post-LZV], #2: 267 days [281 days post-LZV], #3: 702 days [748 days post-LZV], #4: 699 days [741 days post-LZV], #5: 446 days [544 days post-LZV] after initiation of tofacitinib. Cases #1, #2, #3 and #4 were monodermatomal; #5 involved 5 dermatomes. All cases resolved with treatment. Cases #1, #4 and #5 had undetectable ELISPOT measures at baseline and Week 6 post-vaccination, indicating a lack of VZV-specific immunity. Cases #2 and #3 responded adequately to vaccination by both immunoglobulin G (IgG) and ELISPOT measures, but had lower than average VZV IgG levels, both at baseline and at Week 6. (Table).

Table. VZV ELISPOT and IgG levels

	Case #1 (HZ 219 days after zoster vaccine)	Case #2 (HZ 281 days after zoster vaccine)	Case #3 (HZ 748 days after zoster vaccine)	Case #4 (HZ 741 days after zoster vaccine)	Case #5 (HZ 544 days after zoster vaccine)	Study A3921237 Tofacitinib 5 mg BID (N=54)
VZV IFNγ ELISPOT at baseline (SFCs/10^6 PBMCs)	25 (LOD)	41	25 (LOD)	25 (LOD)	25 (LOD)	48
VZV IFNγ ELISPOT at Week 6 (SFCs/10^6 PBMCs)	25 (LOD)	76	51	25 (LOD)	25 (LOD)	70
Change from baseline in VZV ELISPOT at Week 6 (SFC fold-rise; SFCs/10^6 PBMCs)	1.00	1.85	2.04	1.00	1.00	1.50
VZV IgG titer at baseline (gpELISA units/mL)	224	37	97	237	208	201
VZV IgG titer at Week 6 (gpELISA units/mL)	444	71	187	232	223	403
Change from baseline in VZV IgG titer at Week 6 (fold-rise; gpELISA units/mL)	1.98	1.92	1.93	0.98	1.07	2.11

Individual values shown for Cases #1–#5, mean values shown for Study A3921237.

One patient who lacked pre-existing varicella immunity developed disseminated primary varicella from the vaccine strain 16 days post-vaccination (reported previously[2]). This case was excluded from calculations for HZ.

BID, twice daily; HZ, herpes zoster; IFNγ, interferon gamma; IgG, immunoglobulin G; LOD, limit of detection; PBMC, peripheral blood mononuclear cell; SFCs, spot-forming cells; VZV, varicella zoster virus

Conclusions: LZV prior to treatment with tofacitinib is effective at boosting IgG levels and cell-mediated immunity towards VZV. No pts who developed both strong cell-mediated and humoral immunity against VZV developed HZ. Of the 5 pts who developed HZ, 3 did not have any cell-mediated response and 2 had a low humoral response.

References:

[1] Singh JA et al. Arthritis Care Res (Hoboken) 2016; 68: 1–25.
[2] Hales CM et al. MMWR Morb Mortal Wkly Rep 2014; 63: 729–731.
[3] Winthrop K et al. Arthritis Rheumatol 2015; 67: Abstract 12L.

Acknowledgements: This study was sponsored by Pfizer Inc. The authors would like to acknowledge Lisa McNeil. Editorial support was provided by K Haines and C Evans of CMC and was funded by Pfizer Inc.

Disclosure of Interest: K. Winthrop Grant/research support from: Bristol-Myers Squibb, Pfizer Inc, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Galapagos, Pfizer Inc, UCB, A. Wouters Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, E. Choy Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, C. Nduaka Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, P. Biswas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Hodge Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, I. Lazariciu Consultant for: Pfizer Inc, Employee of: Quintiles, K. Soma Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Mojcik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, W. F. Rigby Grant/research support from: Amgen, Pfizer Inc, Roche, Consultant for: Bristol-Myers Squibb, Eli Lilly, Pfizer Inc, Roche

DOI: 10.1136/annrheumdis-2017-eular.2437

LB0003 TOFACITINIB WITH AND WITHOUT METHOTREXATE VERSUS ADALIMUMAB WITH METHOTREXATE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS: RESULTS FROM ORAL STRATEGY, A PHASE 3B/4 RANDOMISED TRIAL

R. Fleischmann[1], E. Mysler[2], S. Hall[3], A. Kivitz[4], R. Moots[5], Z. Luo[6], S. Tatulych[7], R. DeMasi[8], K. Soma[7], R. Zhang[9], L. Takiya[8], C. Mojcik[9], S. Krishnaswami[7], S. Menon[7], J. Smolen[10]. *[1]Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX, United States; [2]Organización Médica de Investigación, Buenos Aires, Argentina; [3]Department of Medicine, Monash University, Cabrini Health, Melbourne, Australia; [4]Altoona Center for Clinical Research, Duncansville, PA, United States; [5]Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, United Kingdom; [6]Pfizer Inc, Shanghai, China; [7]Pfizer Inc, Groton, CT; [8]Pfizer Inc, Collegeville, PA; [9]Pfizer Inc, New York, NY, United States; [10]Medical University of Vienna, Vienna, Austria*

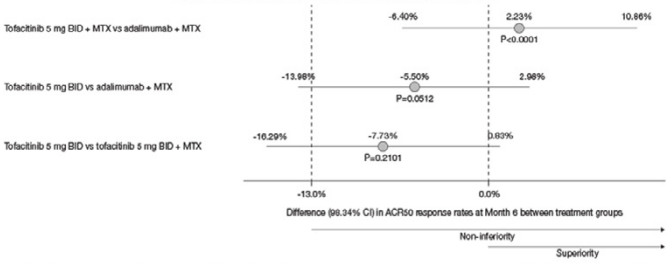
Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. There is no direct comparison of tofacitinib monotherapy vs tofacitinib +MTX in MTX inadequate responders (IR) and limited data comparing tofacitinib (±MTX) vs adalimumab (ADA) +MTX in patients (pts) with RA.

Objectives: To compare efficacy and safety of tofacitinib monotherapy, tofacitinib+MTX, and ADA+MTX in a head-to-head, non-inferiority trial in MTX-IR pts.

Methods: In this randomised, triple-dummy, active-controlled, 1-year, Phase 3b/4 trial (ORAL Strategy; NCT02187055), pts had active RA (≥4 tender/painful joints on motion and ≥4 swollen joints [28-joint count] at baseline [BL]) inadequately controlled with MTX. Pts were randomised 1:1:1 to receive tofacitinib 5 mg twice daily (5 mg mono BID), tofacitinib 5 mg BID +MTX (5 mg BID+MTX) or subcutaneous ADA 40 mg every other week +MTX (ADA+MTX); MTX dose: 15–25 mg/wk. The primary endpoint was ACR50 at Month (Mo) 6. Non-inferiority between treatments was declared if the lower bound of 98.34% two-sided confidence intervals of the difference of ACR50 response at Mo 6 was larger than -13% (based on meta analysis of ADA trials[1]), and superiority if it was larger than 0%. Other endpoints included: ACR20/50/70 and least-squares mean changes from BL in SDAI, DAS28-4(ESR) and HAQ-DI at Mos 6 and 12. Safety was assessed throughout the trial.

Results: 1146 pts were randomised and treated (5 mg mono BID: n=384; 5 mg BID+MTX: n=376; ADA+MTX: n=386). Demographics and BL disease characteristics were similar across groups. Most pts were female (82.7–83.1%), white (75.9–77.1%), with a mean age of 49.7–50.7 years, median disease duration of 5.4–6.1 years and mean HAQ-DI score of 1.6. Across groups, 80.2–81.6% of pts completed the study. ACR50 response rate at Mo 6 was 38.3% for 5 mg mono BID, 46.0% for 5 mg BID+MTX and 43.8% for ADA+MTX. Non-inferiority was demonstrated for 5 mg BID+MTX vs ADA+MTX (P<0.0001) but not for 5 mg mono BID vs ADA+MTX (P=0.0512) or 5 mg mono BID vs 5 mg BID+MTX (P=0.2101) which, although numerically different, were not statistically different (Figure). Tofacitinib monotherapy achieved the efficacy expected of an effective immunomodulator in this pt population. Secondary efficacy analyses were generally consistent with the primary analysis (Table). Adverse event (AE), serious AE and discontinuation due to AE rates were generally clinically similar across groups, though numerically fewer pts had increased alanine aminotransferase with 5 mg mono BID vs 5 mg BID+MTX or ADA+MTX.

Figure. Difference in ACR50 response rates between treatment groups at Month 6



Non-inferiority was demonstrated if the lower bound of the confidence interval was larger than -13.0%; superiority was demonstrated if the lower bound of the confidence interval was larger than 0.0%. P-values presented are from non-inferiority hypothesis testing. P-values are multiplicity-adjusted and should be compared with 0.025.

Table. Efficacy analyses and summary of safety by treatment group

	Tofacitinib 5 mg BID monotherapy (N=384)		Tofacitinib 5 mg BID + MTX (N=376)		ADA 40 mg EOW + MTX (N=386)	
EFFICACY	**Mo 6**	**Mo 12**	**Mo 6**	**Mo 12**	**Mo 6**	**Mo 12**
ACR50, n (%) – primary endpoint at Mo 6	147 (38.3)	151 (39.3)	173 (46.0)	179 (47.6)	169 (43.8)	177 (45.9)
ACR20, n (%)	249 (64.8)	237 (61.7)	275 (73.1)	264 (70.2)	274 (71.0)	261 (67.6)
ACR70, n (%)	70 (18.2)	81 (21.1)	94 (25.0)	109 (29.0)	80 (20.7)	100 (25.9)
SDAI, LSM (SE) change from BL	-23.7 (0.6)	-25.1 (0.7)	-26.6 (0.6)	-28.7 (0.7)	-25.6 (0.6)	-28.1 (0.7)
DAS28-4(ESR), LSM (SE) change from BL	-2.1 (0.1)	-2.3 (0.1)	-2.4 (0.1)	-2.7 (0.1)	-2.4 (0.1)	-2.6 (0.1)
HAQ-DI, LSM (SE) change from BL	-0.5 (0.03)	-0.6 (0.03)	-0.6 (0.03)	-0.6 (0.03)	-0.5 (0.03)	-0.6 (0.03)
SAFETY						
AEs, n (%)	226 (58.9)		231 (61.4)		253 (65.5)	
SAEs, n (%)	35 (9.1)		27 (7.2)		24 (6.2)	
Discontinuations due to AEs, n (%)	23 (6.0)		26 (6.9)		37 (9.6)	
Herpes zoster, n (%)	4 (1.0)		8 (2.1)		5 (1.3)	
Nasopharyngitis, n (%)	22 (5.7)		16 (4.3)		18 (4.7)	
Upper respiratory tract infection, n (%)	25 (6.5)		37 (9.8)		29 (7.5)	
Alanine aminotransferase increased, n (%)	8 (2.1)		23 (6.1)		26 (6.7)	
Deaths, n (%)	2 (0.5)		0 (0.0)		0 (0.0)	

Efficacy data are for the full analysis set. ACR20/50/70 used component-wise LOCF before dropout and NRI after dropout; continuous endpoint data are from a Mixed-effect Model of Repeated Measurements
Safety analysis set was identical to the full analysis set
ACR, American College of Rheumatology; ADA, adalimumab; AE, adverse event; BID, twice daily; BL, baseline; DAS; Disease Activity Score; ESR, erythrocyte sedimentation rate; EOW, every other week; HAQ-DI, Health Assessment Questionnaire–Disability Index; LOCF, last observation carried forward; LSM, least-squares mean; Mo, month; MTX, methotrexate; NRI, non-responder imputation; SAE, serious AE; SDAI, Simplified Disease Activity Index; SE, standard error

Conclusions: Tofacitinib 5 mg BID+MTX was as effective as ADA+MTX in

MTX-IR pts with RA. However, clinical outcomes of all 3 regimens, including tofacitinib 5 mg BID monotherapy, were comparable. There were no new or unexpected safety issues.

References:
[1] Machado et al. Rev Bras Reumatol 2013;53:419–430.

Acknowledgements: This study was funded by Pfizer Inc. Editorial support provided by D Binks of CMC.

Disclosure of Interest: R. Fleischmann Grant/research support from: Abbott, Amgen, Astellas, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Genentech, Eli Lilly, Janssen, Novartis, Pfizer Inc, Regeneron Pharmaceuticals Inc., Sanofi Aventis, Roche, UCB, Consultant for: Abbott, Akros, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Eli Lilly, Janssen, Novartis, Pfizer Inc, Sanofi Aventis, UCB, E. Mysler Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc and Roche, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc and Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc and Roche, S. Hall Consultant for: Pfizer Inc, Celgene, Roche, AbbVie, Eli Lilly, Janssen, A. Kivitz Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Genentech and Pfizer Inc, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Genentech and Pfizer Inc, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Genentech, and Pfizer Inc, R. Moots Grant/research support from: Biogen, Bristol-Myers Squibb, Chugai, Novartis, Pfizer, Roche, Sandoz, UCB Pharma, Consultant for: Biogen, Bristol-Myers Squibb, Chugai, Novartis, Pfizer, Roche, Sandoz, UCB Pharma, Speakers bureau: Biogen, Bristol-Myers Squibb, Chugai, Novartis, Pfizer, Roche, Sandoz, UCB Pharma, Z. Luo Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Tatulych Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. DeMasi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Soma Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Zhang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Takiya Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Mojcik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Krishnaswami Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Menon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Smolen Grant/research support from: AbbVie, Janssen, Lilly, MSD, Pfizer Inc, and Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Glaxo, ILTOO, Janssen, Lilly, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, and UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Glaxo, ILTOO, Janssen, Lilly, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, and UCB

DOI: 10.1136/annrheumdis-2017-eular.7113

FRIDAY, 16 JUNE 2017

New treatments in SLE, Sjögren's and APS

OP0231 THE EFFECT OF "TRIPLE THERAPY" WITH ANTICOAGULATION PLUS CORTICOSTEROIDS PLUS PLASMA EXCHANGE AND/OR INTRAVENOUS IMMUNOGLOBULINS ON THE MORTALITY OF CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME (CAPS) PATIENTS

I. Rodríguez-Pintó[1], G. Espinosa[1], D. Erkan[2], Y. Shoenfeld[3], R. Cervera[1] on behalf of CAPS Registry Project Group (European Forum on Antiphospholipid Antibodies). *[1]Department of Autoinmune Disease, Hospital Clínic, Barcelona, Spain; [2]Barbara Volcker Center for Women and Rheumatic Disease, Hospital for Special Surgery, New York, United States; [3]Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Aviv, Israel*

Background: Triple therapy (anticoagulation plus corticosteroids plus plasma exchange and/or intravenous immunoglobulins) is empirically prescribed for the management of catastrophic antiphospholipid syndrome (CAPS). However, previous analyses have been inconsistent regarding the beneficial effect of triple therapy on patients' survival.

Objectives: The objective of this study was to assess the effect that triple therapy has on the mortality risk of CAPS patients.

Methods: In a cohort including 525 episodes of CAPS (CAPS Registry), we evaluated the relationship between triple therapy and mortality. Patients were grouped in three based on their treatments: a) triple therapy (anticoagulation plus corticosteroids plus plasma exchange and/or intravenous immunoglobulins); b) drugs included in the triple therapy but in different combinations; c) none of the treatments included in the triple therapy. The primary endpoint was all-cause mortality. Multivariate logistic regression models were used to compare mortality risk between groups taking into account a set of possible confounding variables.

Results: The "CAPS registry" cohort included 525 episodes of CAPS accounting for 502 patients. After excluding 38 episodes (7.2%), a total of 487 episodes of CAPS accounting for 471 patients (mean age 38 years; 67.9% female; primary APS patients 68.8%) were analyzed. Overall, 177 (36.3%) patients died. Triple therapy was prescribed in 197 episodes (40.5%), other combinations in 278 (57.1%), and none of those treatments in 12 episodes (2.5%). According to these three groups, mortality rate increased up to 27.9%, 40.6%, and 75%, respectively. Triple therapy was positively associated with a higher chance of survival when compared to non-treatment (adjusted odds ratio [OR]: 7.7 95%; confidence interval [95CI] 2.0–29.7) or to treatment with other combinations of drugs included in the triple therapy (adjusted OR 6.8; 95CI 1.7–26.9). Triple therapy accounted for a 64% decrease of the risk of death in patients with CAPS that received this combination of drugs.

Conclusions: Triple therapy is independently associated to a higher survival rate among CAPS.

Acknowledgements: To the CAPS Registry Project Group (European Forum on Antiphospholipid Antibodies).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3412

OP0232 SUSTAINED SAFETY AND EFFICACY OVER 10 YEARS WITH BELIMUMAB (BEL) PLUS STANDARD SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) THERAPY (SOC) IN PATIENTS WITH SLE

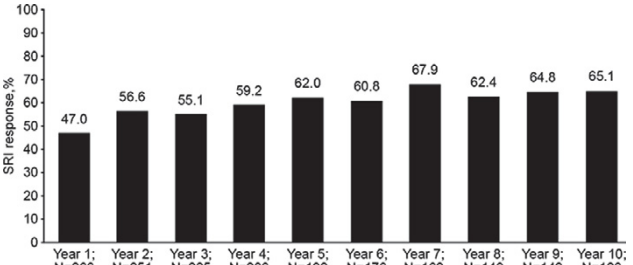
D.J. Wallace[1], E.M. Ginzler[2], J.T. Merrill[3], R.A. Furie[4], W. Stohl[5], W. Chatham[6], A. Weinstein[7], J. McKay[8], W.J. McCune[9], M. Petri[10], J. Fettiplace[11], D. Roth[12], B. Ji[13], A. Heath[14]. *[1]Cedars-Sinai Medical Center, Los Angeles; [2]SUNY Downstate Medical Center, Brooklyn; [3]Oklahoma Medical Research Foundation, Oklahoma City; [4]Northwell Health, Great Neck; [5]University of Southern California Keck School of Medicine, Los Angeles; [6]University of Alabama at Birmingham, Birmingham; [7]Washington Hospital Center, Washington DC; [8]Oklahoma State University Center for Health Sciences, Tulsa; [9]University of Michigan, Ann Arbor; [10]Johns Hopkins University School of Medicine, Baltimore, United States; [11]GSK (at the time of study), Uxbridge, United Kingdom; [12]GSK, Philadelphia, United States; [13]GSK, Uxbridge, United Kingdom; [14]GSK, Raleigh-Durham, United States*

Background: Preliminary safety and efficacy data from the Phase II BEL open-label extension study (LBSL02; NCT00071487) have been reported.

Objectives: Here we present the final 10-year data.

Methods: This was a multicentre, open-label, continuation trial (BEL112626; NCT00583362) of BEL + SoC in patients with a satisfactory response in the parent study. Patients received intravenous BEL 10 mg/kg every 4 weeks. Baseline was prior to the first ever dose of BEL.

Results: Of 298 patients in the continuation trial, 131 (44%) remained at Year 10. Total BEL exposure was 2154 patient-years. Adverse events (AEs) remained stable or decreased (Table). Two deaths (pseudomonal lung infection; cytomegaloviral pneumonia) were possibly related to BEL. SLE Responder Index (SRI) response increased (Figure). A British Isles Lupus Assessment Group (BILAG) flare (1 new A/2 new B scores) occurred in 72.6% of patients and 41.9% had a severe flare (SLE Flare Index). Prednisone dose decreased from baseline to Year 10 (Table). Of patients receiving >7.5 mg/day baseline prednisone, 32.6%



Abstract OP0232 – Table 1

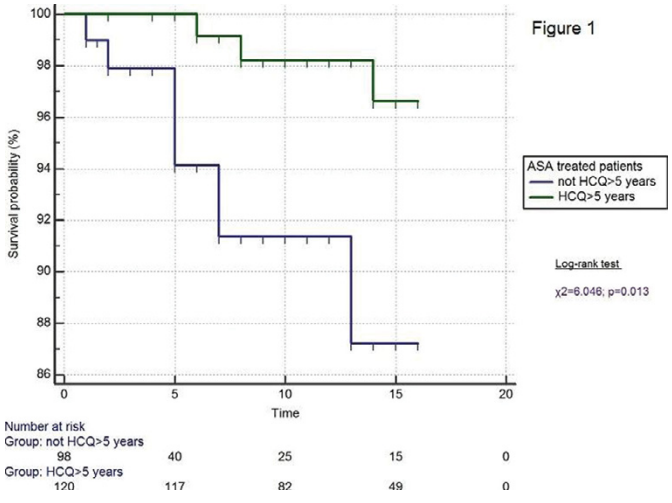
	0–1y (N=296)	1–2y (N=294)	2–3y (N=276)	3–4y (N=250)	4–5y (N=223)	5–6y (N=209)	6–7y (N=192)	7–8y (N=178)	8–9y (N=169)	9–10y (N=152)	10–11y (N=131)
Incidence of ≥1 AE, n (%)											
Overall	291 (98.3)	283 (96.3)	260 (94.2)	239 (95.6)	203 (91.0)	190 (90.9)	182 (94.8)	162 (91.0)	157 (92.9)	137 (90.1)	105 (80.2)
Resulting in discontinuation	2 (0.7)	3 (1.0)	3 (1.1)	7 (2.8)	5 (2.2)	6 (2.9)	6 (3.1)	1 (0.6)	3 (1.8)	5 (3.3)	2 (1.5)
Serious AE	41 (13.9)	43 (14.6)	50 (18.1)	30 (12.0)	40 (17.9)	33 (15.8)	35 (18.2)	34 (19.1)	28 (16.6)	25 (16.4)	14 (10.7)
Serious infections/infestations	11 (3.7)	13 (4.4)	9 (3.3)	9 (3.6)	6 (2.7)	6 (2.9)	12 (6.3)	10 (5.6)	8 (4.7)	5 (3.3)	5 (3.8)
Death	1 (0.3)	0	1 (0.4)	1 (0.4)	0	1 (0.5)	2 (1.0)	0	0	1 (0.7)	0
		Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10
Prednisone											
median % change from baseline;		-0.4;	-25.0;	-36.9;	-50.0;	-48.3;	-60.0;	-62.5;	-70.0;	-66.7;	-65.8;
25th, 75th percentile (n)		-50.0, 0 (186)	-74.2, 0 (172)	-80.0, 0 (153)	100.0, 0 (140)	-100.0, 0 (128)	0 (115)	-100.0, -10.7 (105)	-100.0, -1.6 (94)	-100.0, -0 (91)	-100.0, 0 (84)

(14/43) decreased their dose to ≤7.5 mg/day by Year 10; 9.5% (9/95) of patients receiving baseline prednisone ≤7.5 mg/day had a dose increase to >7.5 mg/day.
Conclusions: Over 10 years BEL + SoC was well tolerated and the rates and nature of AEs were consistent with the known profile of BEL. Efficacy was maintained and prednisone use decreased in those receiving >7.5 mg/day at baseline.
Acknowledgements: Study funded by GSK. Editorial assistance provided by Katie White, PhD, Fishawack Indicia Ltd, UK; funded by GSK.
Disclosure of Interest: D. Wallace Grant/research support from: GSK, Consultant for: GSK, E. Ginzler Grant/research support from: GSK, J. Merrill Grant/research support from: GSK, Bristol-Myers Squibb, Consultant for: Anthera Pharmaceuticals, Inc., GSK, EMD Serono, Inc., Lilly, AstraZeneca, Bristol-Myers Squibb, UCB, Celgene, Biogen, R. Furie Grant/research support from: GSK, Consultant for: GSK, W. Stohl Grant/research support from: GSK, Pfizer, Consultant for: Johnson & Johnson, W. Chatham Grant/research support from: GSK, A. Weinstein Grant/research support from: GSK, HGS, Consultant for: GSK, HGS, J. McKay Grant/research support from: GSK, MedImmune, Anthera Pharmaceuticals, Inc., Johnson & Johnson, Lilly, Xencor, Inc., W. McCune Grant/research support from: GSK, Lilly, M. Petri Grant/research support from: GSK, Consultant for: GSK, J. Fettiplace Shareholder of: GSK, Employee of: GSK, D. Roth Shareholder of: GSK, Employee of: GSK, B. Ji Shareholder of: GSK, Employee of: GSK, A. Heath Shareholder of: GSK, Employee of: GSK
DOI: 10.1136/annrheumdis-2017-eular.6430

OP0233 PRIMARY PROPHYLAXIS OF CARDIOVASCULAR EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE ANALYSIS OF 291 PATIENTS FROM TWO ITALIAN CENTERS

S. Fasano[1], D. Margiotta[2], L. Navarini[2], L. Pierro[1], A. Riccardi[1], I. Pantano[1], A. Afeltra[2], G. Valentini[1]. [1]*Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples;* [2]*Unit of Allergology, Immunology, Rheumatology, Campus Bio-Medico University, Rome, Italy*

Background: Systemic lupus erythematosus (SLE) is associated with an increased cardiovascular (CV) risk (1). By retrospectively investigating a one centre cohort, we have recently reported that low-dose aspirin (ASA) use is associated with a reduced CV risk in SLE (2) and long-term hydroxychloroquine (HCQ) exposure may have an additive effect (3).
Objectives: This study was conducted on 2 Italian SLE cohorts to confirm these results and assess the role, if any, of statins.
Methods: Clinical charts of SLE patients consecutively admitted to 2 University Rheumatology Units from November 2000 to December 2014 who, at admission, had not experienced any CV event, were investigated. ASA, HCQ and statins use and the occurrence of any CV event, were recorded at each visit. Kaplan-Meier analysis was performed to determine the HCQ exposure status associated with a higher CV-free survival. Cox regression analysis was carried out to identify factors independently associated with a first CV event.
Results: A total of 291 SLE patients were included in the study and followed for a median of 8 years. During follow-up, 16 CV events occurred. Kaplan Meier analysis revealed a greater CV event-free rate in the 120 ASA-treated patients taking HCQ at standard dose for more than 5 years than in the 98 patients treated with ASA alone or with HCQ for less than 5 years (Figure 1). At univariate analysis, patients with a first CV event compared with those without any thrombotic events were antiphospholipid antibody (aPL) positive (P=0.017 HR 2.91) and had significantly higher blood pressure (P=0.017 HR 3.58), hypercholesterolemia (P=0,015 HR 3.40) and higher disease damage at last visit (P=0,032 HR 1.56). Moreover, ASA treatment (P=0,012 HR 0.27) and HCQ use (P=0,012 HR 0.26) for more than 5 years were negative predictors, while statins use did not show any association (P=0.619). All other variables examined, including smoking, obesity, hypertriglyceridaemia, diabetes mellitus, disease activity, severe SLE, other medications (immunosuppressive agents, steroids) were not associated, either positively or negatively, with the occurrence of CV events. At multivariate analysis, taking ASA and HCQ for more than 5 years were protective against thrombosis (HR 0.24 and HR 0.27, respectively), while aPL positivity (HR 4.32) increased the risk of a first CV event.



Conclusions: Use of antimalarials for more than 5 years is associated with a reduced risk of a first thrombosis in SLE patients and the HCQ-ASA combination seems to synergistically reduce further the CV risk. Larger, prospective studies are needed to provide a better definition of the role of these drugs in CV primary prevention in SLE.
References:
[1] Cervera R, et al. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: a comparison of early and late manifestations in a cohort of 1,000 patients.Medicine (Baltimore). 2003.
[2] Iudici M, et al. Low-dose aspirin as primary prophylaxis for cardiovascular events in systemic lupus erythematosus: a long-term retrospective cohort study. RheumatolOxfEngl 2016.
[3] Fasano S, et al. Long-Term Hydroxychloroquine Therapy and Low-Dose Aspirin May Have an Additive Effectiveness in the Primary Prevention of Cardiovascular Events in Patients with Systemic Lupus Erythematosus [abstract]. Arthritis Rheumatol 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2517

OP0234 CLINICAL AND BIOLOGIC EFFECTS OF ICOSL BLOCKADE BY AMG 557 IN SUBJECTS WITH LUPUS ARTHRITIS

L.E. Cheng[1], Z. Amoura[2], B. Cheah[3], F. Hiepe[4], B.A. Sullivan[1], L. Zhou[1], G.E. Arnold[1], W.H. Tsuji[1], J.T. Merrill[5], J.B. Chung[1]. [1]*Amgen Inc., Thousand Oaks, United States;* [2]*Hôpital Pitié-Salpêtrière, Paris, France;* [3]*International Medical University, Kuala Lumpur, Malaysia;* [4]*Charité Universitätsmedizin Berlin, Berlin, Germany;* [5]*Oklahoma Medical Research Foundation, Oklahoma City, United States*

Background: Blockade of inducible costimulatory ligand (ICOSL) might be a promising approach for autoimmune diseases such as systemic lupus erythematosus (SLE). We evaluated AMG 557, an anti-ICOSL monoclonal antibody, in an exploratory phase 1b study of SLE subjects with inflammatory arthritis, by withdrawing background therapies to improve interpretability of a small study.
Objectives: To investigate potential efficacy, safety, and tolerability of AMG 557 in subjects with lupus arthritis.
Methods: This double-blind, randomized, placebo-controlled trial enrolled subjects with SLE and active lupus arthritis (≥4 tender and 4 swollen joints) and Systemic Lupus Erythematosus Disease Activity Index [SLEDAI] score ≥6 despite stable background immunosuppressants. Upon enrollment, investigators were permitted to use up to 20 mg/day of prednisone, which was tapered by day 85 to 7.5 mg/day or 50% of baseline, whichever was lower. Subjects received AMG 557 210 mg or placebo once weekly for 3 weeks followed by 10 additional doses every other week until day 155. At day 29, background immunosuppressants were withdrawn. The primary clinical endpoint was a composite Lupus Arthritis Responder Index at day 169; response was defined as achieving: (1) 50% decrease in combined tender and swollen joint counts, and (2) ≥1 letter improvement in the musculoskeletal subsystem of the British Isles Lupus Assessment Group (BILAG) index and (3) prespecified immunosuppressant medication withdrawal and/or prednisone taper. Safety was a co-primary endpoint. Exploratory endpoints included safety, 4-point reduction of SLEDAI, clinical indices (SLEDAI, BILAG), complement components, autoantibodies, and lymphocyte populations.
Results: Twenty subjects (19 females) were randomized (10 AMG 557, 10 placebo) at 8 sites in North America, Asia, and Europe. The primary endpoint was met by 3/10 subjects receiving AMG 557 and 1/10 subjects receiving placebo (*P*=ns). A 4-point decrease in SLEDAI score was achieved by 7/10 subjects on AMG 557 and 2/10 subjects on placebo. At day 169, subjects receiving AMG 557 had decreases from baseline in mean global BILAG and SLEDAI scores of 36% and 48% respectively, compared to 25% and 11% in subjects receiving placebo. Lupus-associated biomarkers, including serum complement indices (C3, C4, and CH50), and autoantibodies, including anti-dsDNA, demonstrated trends towards improvement relative to placebo. Treatment-emergent adverse events (AEs) were similar between placebo and AMG 557 arms; most commonly headache and upper respiratory tract infection.
Conclusions: Results from this exploratory placebo-controlled trial in lupus arthritis suggest potential clinical benefit of ICOSL blockade by AMG 557. These data support further clinical trials intervening in this costimulatory pathway in SLE and other autoimmune diseases.
Disclosure of Interest: L. Cheng Shareholder of: Amgen Inc., Employee of: Amgen Inc., Z. Amoura Consultant for: GlaxoSmithKline, AstaZeneca, BristolMyerSquibb, Amgen Inc., B. Cheah Grant/research support from: Merck, F. Hiepe Grant/research support from: Sanofi, Amgen Inc., GlaxoSmithKline, AstaZeneca, Ablynx, Consultant for: Baxalta, AstaZeneca, BristolMyerSquibb, GlaxoSmithKline, Novartix, Miltenyi, Neovacs, Hexal, Neovi, Speakers bureau: Pfizer Inc., Roche, UCB, B. Sullivan Shareholder of: Amgen Inc., Employee of: Amgen Inc., L. Zhou Shareholder of: Amgen Inc., Employee of: Amgen Inc., G. Arnold Shareholder of: Amgen Inc., Employee of: Amgen Inc., W. Tsuji Shareholder of: Amgen Inc., Johnson&Johnson, Consultant for: Celimmune, Seattle Genetics, Resolve

Therapeutics, Employee of: Formerly Amgen Inc.; Partner in the Cascadia Drug Development Group, J. Merrill Consultant for: EMD Serono, BristolMyerSquibb, Human Genome Sciences, UCB, AstraZeneca, Celgene, J. Chung Shareholder of: Amgen Inc., Employee of: Amgen Inc.
DOI: 10.1136/annrheumdis-2017-eular.1127

OP0235 A NOVEL B CELL SPECIFIC IFN-I BIOMARKER IS ASSOCIATED WITH PLASMABLAST NUMBERS FOLLOWING B CELL DEPLETION THERAPY IN SLE

Y.M. El-Sherbiny[1,2], M.Y. Md Yusof[1,2], E. Hensor[1,2], A. Rawstron[3], M. Wittmann[1,2], P. Emery[1,2], E.M. Vital[1,2]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]National Institute of Health Research Leeds Musculoskeletal Biomedical Research Unit; [3]Haematological Malignancy Diagnostic Service, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: SLE is a Type I interferon (IFN-I) mediated disease with autoreactive B cells. Plasmablasts, the immediate progeny of B cells, are expanded in SLE and correlate with disease activity. We showed that their rate of regeneration after therapeutic B cell depletion with rituximab is variable and predicts relapse[1]. IFN-I has been shown *in vitro* to induce the differentiation of B cells into plasmablasts. We previously showed that therapeutic B cell depletion with anti-CD20 mAb leads to a transient reduction in CD20-negative plasmablasts, following which plasmablasts repopulate and their numbers predict clinical relapse. We developed tetherin as a flow cytometric, cell-specific marker for IFN-I response.
Objectives: To test the hypothesis that memory B cell tetherin determines the rate of plasmablast repopulation after rituximab.
Methods: 117 rituximab-treated SLE patients were studied prosectively using BILAG-2004 and flow cytometry. In 97 responders we tested plasmablasts at 6 months as a predictor of clinical relapse before 12 months to validate our previous finding. In 50 patients pre-rituximab and 28 patients post-rituximab we performed additional flow cytometry to measure tetherin on each cell subset. Expression of 18 ISGs was measured using Taqman on PBMCs and an ISG score calculated.
Results: We divided clinical responders to rituximab into earlier relapse (12 months) or later relapse (>12 months). As in our published discovery cohort, plasmablasts were strongly predictive of clinical relapse. ROC analysis indicated that a plasmablast count of >0.0008 x 10^9/L at 6 months yielded 73% (95% CI 45–92%) sensitivity and 90% (95% CI 56–99%) specificity in predicting earlier relapse; area under the curve of 0.86.
Plasmablast numbers after rituximab were associated with Memory B cell tetherin (R=0.38, p=0.047) but not ISG score (R=0.24, p=0.219) (Table 1).
In Pre-rituximab there was no relationship between any IFN assay and plasmablast count. After rituximab treatment there was no correlation between plasmablast count and ISG expression, nor with monocyte or NK cell surface tetherin. However, memory B cell tetherin MFI was positively correlated with plasmablast count (Table 1).

Table 1

Interferon assay	Plasmablast Count (cells x10^9/L)	
	Pre-rituximab (*n* =50)	Post-rituximab (*n* =28)
ISG expression Score:	-0.11, *P*=0.448	0.24, *P*=0.219
Tetherin protein level: Monocytes	-0.08, *P*=0.592	0.20, *P*=0.296
T-cells	-0.16, *P*=0.269	0.32, *P*=0.096
NK cells	-0.14, *P*=0.324	0.05, *P*=0.795
Naïve B-cells	-0.04, *P*=0.801	0.30, *P*=0.121
Memory B-cells	0.07, *P*=0.618	0.38, *P*=0.047

Values are Spearman's Rank Correlation Coefficient and *P* values.

Conclusions: Although interferon stimulated gene expression is commonly used to measure IFN-I activity, tetherin provides a cell-specific assay. We demonstrate that by measuring IFN-I response in B cells specifically, we could explain plasmablast differentiation, and thereby clinical outcome. Memory B cell tetherin is valuable to immunophetype SLE.
References:
[1] Vital et al. Arthritis Rheum. 2011 Oct;63(10):3038–47.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6423

OP0236 BENEFIT AND SAFETY OF ANTITHROMBOTIC TREATMENT IN 264 PREGNANCIES IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

C.M. Yelnik[1], M. Lambert[1], E. Drumez[2], V. Le Guern[3], J.-L. Bacri[4], M. Guerra[5], C.A. Laskin[6], W. Branch[7], L.R. Sammaritano[5], N. Morel[3], G. Guettrot-Imbert[3], D. Launay[1], E. Hachulla[1], P.-Y. Hatron[1], J.E. Salmon[5], N. Costedoat-Chalumeau[3]. *[1]Internal Medicine Department, University of Lille, UFR Medicine, Universitary Hospital Center of Lille; [2]Biostatistics Department, University of Lille, EA 2694, Universitary Hospital Center of Lille, lille; [3]Internal Medicine Department, Paris Descartes-Sorbonne Paris Cité University, INSERM U1153, Cochin Hospital, Paris; [4]Internal Medicine Department, Hospital Center of Valenciennes, Valenciennes, France;[5]Rheumatology, Hospital for Special Surgery, New York City, United States; [6]University of Toronto and LifeQuest Center for Reproductive Medicine, Toronto, Canada; [7]University of Utah and Intermountain Healthcare, Salt Lake City, United States*

Background: The management of pregnancy in patients with antiphospholipid syndrome (APS) with aspirin and heparin is based on empiric recommendations.
Objectives: Our study aimed to evaluate the outcomes of treated patients with thrombotic and obstetric APS and the safety of antithrombotic treatments prescribed during pregnancy.
Methods: Inclusion criteria were (1) APS (Sydney criteria), (2) live pregnancy at 12 weeks of gestation (WG) with (3) follow up data until 6 weeks post-partum. Data were collected prospectively (PROMISSE study) and retrospectively (four French centers). Adverse pregnancy outcomes (APOs) were defined by fetal death or neonatal death; pre-term delivery before 36 WG due to preeclampsia or placental insufficiency; or small for gestational-age (SGA; <5th percentile). Major bleeding was defined as blood loss greater than 500mL and/or requiring surgery or transfusion.
Results: 264 pregnancies (87 collected prospectively) in 204 patients were included (46% with a history of thrombosis, and 23% with associated systemic lupus erythematosus). During pregnancy, treatment included heparin (n=253; 96%) and low-dose aspirin (n=223; 84%).
The live birth rate was 86%. APOs occurred in 32%, mostly during the 2nd trimester: fetal deaths 11%, SGA 11%, pre-term delivery before 36 WG due to preeclampsia or placental insufficiency 17%. Thirteen maternal thrombotic events occurred in 12 (4.5%) pregnancies. Forty-six maternal hemorrhagic events occurred in 40 (15%) pregnancies (30 events in the post-partum period). Major bleeding was reported in only 6 pregnancies (2.3%) and occurred only after delivery. Except for two events, post-partum hemorrhage occurred in the early post-partum before hospital discharge. No maternal death was observed.
Aspirin therapy during pregnancy was the only independent factor associated with a lower risk of APOs (odds ratio: 0.34; 95% CI: 0.15 – 0.78; p=0.01) in multivariate analysis.
Neither heparin or aspirin alone, nor combined therapy increased the risk of hemorrhage. In the retrospective cohort, emergency caesarian section was the only factor associated with hemorrhagic events during the study period (53% hemorrhages in patients who underwent emergency caesarian compared to 18%, p=0.005). Independent risk factors for APOs were elevated body mass index and the presence of lupus anticoagulant.
Conclusions: We report a high level of obstetrical complications in conventionally-treated APS pregnancies, and a beneficial effect of addition of aspirin to prevent obstetrical morbidity. Moreover, heparin and aspirin were well tolerated and did not increase risk of hemorrhage.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1926

OP0237 LIFITEGRAST OPHTHALMIC SOLUTION 5.0% FOR TREATMENT OF DRY EYE DISEASE: COMBINED EVIDENCE FROM 5 RANDOMIZED CONTROLLED TRIALS

C. Baudouin[1], M. Darvish-Zargar[2], E.J. Holland[3], C.C. Chan[4], K.K. Nichols[5], J. Tauber[6], A. Raychaudhuri[7], M. Roy[7], A. Shojaei[7]. *[1]Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, France; [2]McGill University, Montreal, Canada; [3]Cincinnati Eye Institute, Edgewood, United States; [4]University of Toronto, Toronto, Canada; [5]University of Alabama School of Optometry, Birmingham; [6]Tauber Eye Center, Kansas City; [7]Shire, Lexington, United States*

Background: Dry eye disease (DED) is a multifactorial disease of the tear film and ocular surface, characterized by ocular discomfort and visual disturbance.[1] DED is associated with a number of systemic autoimmune diseases, particularly rheumatoid arthritis and Sjögren's syndrome.[2,3] Lifitegrast is a lymphocyte function-associated antigen-1 (LFA-1) antagonist that inhibits T-cell–mediated inflammation (an underlying factor in DED) and is approved in the US for the treatment of signs and symptoms of DED (lifitegrast ophthalmic solution 5.0%, Xiidra®).
Objectives: To evaluate the combined evidence from 5 clinical trials of lifitegrast ophthalmic solution 5.0% (LIF) in subjects with dry eye disease (DED).
Methods: Adults with DED were randomized to LIF or placebo (PBO) in 5 randomized, double-masked, placebo-controlled trials: 4 12-week efficacy/safety studies (phase 2, LIF n=58, PBO n=58; phase 3 trials: OPUS-1, LIF n=293, PBO n=295; OPUS-2, LIF n=358, PBO n=360; OPUS-3, LIF n=355, PBO n=356), and a 1-year safety study (SONATA, LIF n=220, PBO n=111). Individuals with secondary Sjögren's syndrome associated with autoimmune disease (eg, rheumatoid arthritis, systemic lupus erythematosus) were eligible to participate if they were not immunodeficient/immunosuppressed, not taking steroids, and met all other inclusion and exclusion criteria. Change from baseline to day 84 in DED signs and symptoms was evaluated across the 12-week studies. Key measures were inferior corneal staining score (ICSS; 0–4 scale), eye dryness score (EDS; visual analogue scale [VAS], 0–100 scale), and visual-related function subscale of a symptom scale (0–4 scale). Pooled safety data (LIF n=1287, PBO n=1177) from all 5 trials were also analyzed.
Results: LIF improved ICSS versus PBO in the phase 2 study (secondary endpoint; treatment effect 0.35, nominal *P*=0.0209), OPUS-1 (co-primary; 0.24,

Key efficacy results of lifitegrast ophthalmic solution 5.0% across 12-week multicenter randomized controlled trials (ITT population with LOCF)

Study	Symptom endpoint	Sign endpoint
Phase 2	• Visual-related function subscale (secondary, change from baseline to day 84): TE 0.37, nominal *P*=0.0394.	• Primary endpoint of ICSS at day 84 not met. • ICSS (secondary, change from baseline to day 84): TE 0.35, nominal *P*=0.0209.
OPUS-1	• Coprimary endpoint of change from baseline to day 84 on visual-related function subscale not met.	• ICSS (co-primary, change from baseline to day 84): TE 0.24, *P*=0.0007.
OPUS-2	• EDS (VAS; co-primary, change from baseline to day 84): TE 12.61, *P*<0.0001.	• Coprimary endpoint of change from baseline to day 84 in ICSS not met.
OPUS-3	• EDS (VAS; primary, change from baseline to day 84): TE 7.16, *P*=0.0007.	• ICSS (ad hoc, change from baseline to day 84): TE 0.17, nominal *P*=0.0144.

Eye dryness score (EDS; visual analogue scale [VAS]); ICSS, inferior corneal staining score; ITT, intention-to-treat; LOCF, last observation carried forward; TE, treatment effect.

P=0.0007), and OPUS-3 (ad hoc; 0.17, nominal *P*=0.0144). LIF reduced EDS (VAS) versus PBO in OPUS-2 (co-primary; 12.61, *P*<0.0001) and OPUS-3 (primary; 7.16, *P*=0.0007). The OPUS-1 co-primary symptom endpoint of visual-related function subscale, and the OPUS-2 co-primary sign endpoint of ICSS, did not achieve statistical significance. In the pooled safety analysis, total exposure was 415.65 person-years for LIF, and 332.15 person-years for PBO. Adverse events were mostly mild or moderate in severity. There were no serious ocular treatment-emergent adverse events (TEAEs) and withdrawals due to TEAEs were infrequent (LIF, 7.0%; PBO, 2.6%).

Conclusions: LIF improved signs and symptoms of DED in adults with DED and appeared to be well tolerated with no serious ocular TEAEs reported.

References:

[1] DEWS. Ocul Surf. 2007;5:75–92.
[2] Fujita M et al. Am J Ophthalmol. 2005;140:808–13.
[3] Patel SJ, Lundy DC. Am Fam Physician. 2002;66:991–8.

Acknowledgements: This study was sponsored by SARcode Bioscience (now a wholly owned subsidiary of Shire PLC) and Shire Development LLC.

Disclosure of Interest: C. Baudouin Consultant for: Alcon Laboratories, Inc., Allergan, Dompé, Horus Pharma, Santen Inc., Thea Pharmaceuticals, M. Darvish-Zargar Consultant for: Allergan, Novartis, Abbott Medical Optics, E. Holland Grant/research support from: Alcon Laboratories Inc., Allergan, Mati Therapeutics, Omeros, PRN, Senju Pharaceuticals, Consultant for: Alcon Laboratories Inc., Allergan, Bausch & Lomb, Kala Pharmaceuticals, Mati Therapeutics, Omeros, PRN, RPS, Senju Pharaceuticals, Shire/SARcode, TearLab, TearScience, Speakers bureau: Alcon Laboratories Inc., Allergan, Bausch & Lomb, Omeros, Senju Pharaceuticals, Shire/SARcode, TearScience, C. Chan Grant/research support from: Allergan, Bausch and Lomb, TearLab, Consultant for: Allergan, Bausch & Lomb, Alcon Labs Inc., TearScience, K. Nichols Grant/research support from: Kala Pharmaceuticals, Shire PLC, TearScience, Vistakon, Consultant for: Allergan, In-Site Vision Inc., Kala Pharmaceuticals, Parion Sciences, Santen, ScienceBased Health, Shire PLC/SARcode, J. Tauber Consultant for: Allergan, Bausch & Lomb, Shire PLC, Senju Pharaceuticals, Speakers bureau: Shire/SARcode, A. Raychaudhuri Employee of: Shire PLC (at the time of the study), M. Roy Employee of: Shire PLC, A. Shojaei Employee of: Shire PLC

DOI: 10.1136/annrheumdis-2017-eular.5890

LB0002 48 WEEK COMPLETE REMISSION OF ACTIVE LUPUS NEPHRITIS WITH VOCLOSPORIN

V. Dobronravov [1], M.A. Dooley [2], S.A. Haq [3], I. Adzerikho [4], O. Bugrova [5], D. Isenberg [6], F. Houssiau [7], N. Solomons [8], R. Huizinga [8] on behalf of AURA-LV Study Group. *[1]Pavlov First St. Petersburg State Medical University, St. Petersberg, Russian Federation; [2]UNC, Chapel Hill, United States; [3]Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh; [4]Minsk Regional Clinical Hospital, Minsk, Belarus; [5]Orenburg Regional Clinical Hospital, Orenburg, Russian Federation; [6]University College Hospital, London, United Kingdom; [7]Université catholique de Louvain, Brussels, Belgium; [8]Aurinia Pharmaceuticals, Victoria, Canada*

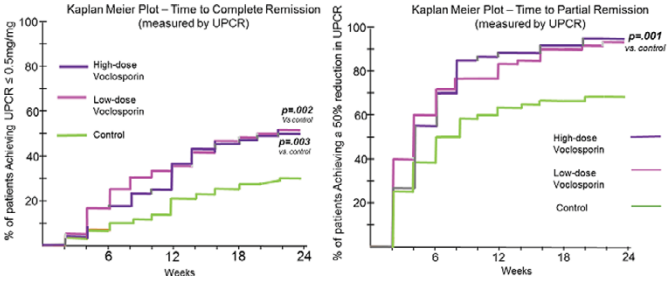
Background: Voclosporin (VCS) is a novel CNI intended for use in the treatment of autoimmune diseases such as lupus nephritis (LN). VCS's unique structure allows for less pharmacokinetic-pharmacodynamic variability and a potentially improved safety profile compared to other CNIs.

Objectives: Achievement of complete remission (CR) as assessed at week 24 (primary objective) and assessment of the efficacy over 48 weeks (secondary objective), with 2 doses of VCS (low dose VCS: 23.7mg BID and high dose VCS: 39.5mg BID) vs. placebo in subjects with active LN.

Methods: The double blind placebo controlled AURA study enrolled 265 subjects with active LN in 20 countries. Patients were randomized into 3 arms (placebo, low dose VCS or high dose VCS) in addition to MMF 2g/day and steroids (with rapid tapering). CR was defined as a confirmed urine protein/creatinine ratio (UPCR) of ≤0.5 mg/mg using first morning void and confirmed estimated glomerular filtration rate (eGFR, CKD-EPI equation) ≥60 mL/min/1.73 m^2 or no decrease from baseline in eGFR of ≥20% in the presence of low dose steroids. Partial remission (PR) was defined as a 50% reduction in UPCR. UPCR assessments were made at each visit, together with biomarker data at regular intervals.

Results: We now present the 48 week data showing improved CR rates over the 24 week data. The rate of CR was significantly higher in the low dose VCS compared to the control group (32.6% vs. 19.3%; OR: 2.03, p=0.045) at 24 weeks. It was 27.3% in the high dose VCS group (p=NS). Both doses of voclosporin demonstrated superiority to control using time to CR, PR (50% reduction in proteinuria) and time to PR.

At 48 weeks, 23.9% of patients on the control arm achieved CR comparted to 49.4% low dose (OR: 3.21, p<0.001) and 39.8% high dose (OR: 2.10, p<0.026). Over 92% of subjects experienced at least one adverse event (AE) with the most common two being infections (58% low, 66% high and 55% placebo) and GI disorders (43% low, 52% high and 38% placebo). The overall rate of serious adverse events (SAEs) was numerically higher in both voclosporin groups (28% low, 25% high, 19% placebo) with the nature of SAEs consistent with those observed in patients with highly active LN. Most deaths occurred in the first 2 months and were: low dose (infection3, ARDS2, thrombotic3, cardiac tamponade, pulmonary hemorrhage), high dose (infection, PE) and control (CVA). All were considered unrelated to drug exposure by the investigators. 3 additional deaths occurred in placebo patients after the conclusion of the 48 weeks of treatment.



Conclusions: The AURA-LV study is the first global study demonstrating the beneficial effect of VCS, in combination with MMF and steroids, in the treatment of LN. Remission rate was rapid. VCS treatment resulted in increasing CR and PR seen by week 6 despite rigorous steroid taper (mean steroid dose 4 mg at week 16). Adverse events were higher in the treated patient group with the nature in keeping with immunosuppression. These promising data will be used to plan subsequent studies of voclosporin in LN.

Acknowledgements: This data was submitted on behalf of the AURA-LV study investigators.

Disclosure of Interest: V. Dobronravov Grant/research support from: Aurinia Pharmaceuticals Inc., M. A. Dooley Grant/research support from: Aurinia Pharmaceuticals Inc., S. A. Haq Grant/research support from: Aurinia Pharmaceuticals Inc., I. Adzerikho Grant/research support from: Aurinia Pharmaceuticals Inc., O. Bugrova Grant/research support from: Aurinia Pharmaceuticals Inc., D. Isenberg: None declared, F. Houssiau: None declared, N. Solomons Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc., R. Huizinga Shareholder of: Aurinia Pharmaceuticals Inc., Employee of: Aurinia Pharmaceuticals Inc.

DOI: 10.1136/annrheumdis-2017-eular.7079

FRIDAY, 16 JUNE 2017

Axial spondyloarthritis from risk factor to clinical outcomes

OP0238 MEASUREMENT OF SPINAL MOBILITY IN AXIAL SPONDYLOARTHRITIS USING INERTIAL SENSORS: RELIABILITY AND VALIDATION PRELIMINARY RESULTS

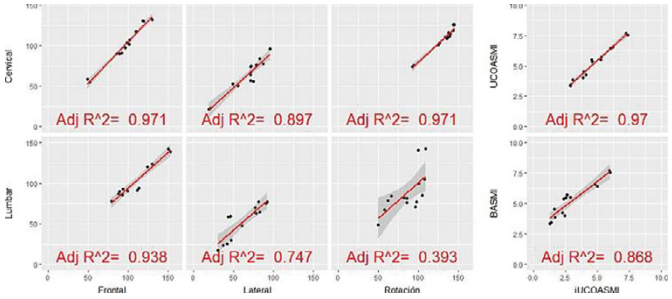
F.J. Mata-Perdigon [1], I.R. Martínez Sanchez [2], J.L. Garrido-Castro [1], C. González-Navas [1], L.M. Fernandez-Ahumada [2], D.A. Gomez [1], V.C. Perez-Guijo [1], P. Font-Ugalde [1], E. Collantes-Estevez [1]. *[1]Maimonides Institute for Biomedical Research of Cordoba; [2]University of Cordoba, Cordoba, Spain*

Background: Axial spondyloarthritis (axSpA) is a chronic rheumatic disease that causes reduction of mobility in the patients' spine. There are several indices to analyze this mobility: BASMI, which lacks precision and sensitivity to change according to different authors, and UCOASMI (1) based on motion capture, which needs extensive resources that limit its practical applicability. Inertial measurement unit sensors (IMU) give, in real time, the 3D orientation of any anatomical place

Abstract OP0238 – Table 1

	Cervical			Lumbar			Indexes		
	Frontal	Lateral	Rotation	Frontal	Lateral	Rotation	iUCOASMI	UCOASMI	BASMI
Test	104.7 (19.7)	60.9 (17.0)	111.3 (19.0)	112.5 (25.6)	62.5 (18.3)	89.2 (26.3)	4.9 (1.2)	4.7 (1.6)	2.6 (1.4)
Retest	108.1 (20.9) β	63.5 (18.7) α	110.2 (19.0) β	113.5 (25.3) β	64.3 (18.5) β	88.3 (23.0) β	5.0 (1.3) α	–	–
2 Days	104.6 (18.9) γ	62.0 (18.3) α	111.9 (16.1) γ	112.5 (25.6) β	61.7 (18.8) β	88.9 (23.8) γ	5.0 (1.2) β	4.9 (1.5) α	2.7 (1.4) β

of the patient. It could be a sensitive, flexible and cheap technology, useful for assessing mobility in AxSpa, but validation studies are needed.
Objectives: To assess reliability and validity of inertial sensors for measuring spinal mobility in patients with axSpA.
Methods: 14 subjects: 7 patients with axSpA (5 male and 2 female, age 51.4±6.7 years, evolution time 25.4±11.3 years, 85.7% B27 positive) and a control group of 7 healthy individuals matched in gender and age were recruited. Cervical and lumbar movements were evaluated using 3 IMU sensors (located at forehead, D3 and L4) and a 3D motion capture system synchronously. A test/retest was performed at 5 minutes in the same day with the IMUs and in two days with both systems. Measurements of metrology, BASMI and UCOASMI indices were obtained. An index, iUCOASMI, was calculated using the same measurements used for UCOASMI, but obtained by inertial sensors.
Results: Table shows mean values (SD) for each range of movement expressed in degrees. BASMI, UCOASMI and iUCOASMI indexes are also included. Intraclass correlation coefficient (ICC) is indicated as α: >0.98 – Excellent, β: 0.95–0.98 – Very good and γ: 0.7–0.95 – Good, δ: <0.7 – Bad. RMSE error was less than 10° for all measures. There was good correlation ($p<0.01$) between iUCOASMI with BASFI, BASG, UCOASMI and BASMI. Graph shows results of linear regression between measures obtained with both system (for example: cervical frontal flexion obtained by motion capture and IMUs have a R^2 of 0.97) and between iUCOASMI with UCOASMI and BASMI.



Conclusions: The IMU system measured range of movement, showing good ICC both in the same day and in the two days test/retest. The iUCOASMI, has also shown an excellent correlation with UCOASMI, and with BASMI. Therefore, these kind of systems, based on IMU, may be useful for analyzing spinal mobility in patients with axSpA in a more accurate and reliable way compared with conventional metrology, and more flexible and cheap than other advanced systems, improving their practical applicability.
References:
[1] Validation of a new objective index to measure spinal mobility: the University of Cordoba Ankylosing Spondylitis Metrology Index (UCOASMI). Garrido-Castro JL, et al. Rheumatol Int. 2014 Mar;34(3):401–6.
Acknowledgements: This study was supported by PIN-0079–2016 research project (Consejería de Salud de la Junta de Andalucía, SPAIN).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2965

OP0239 HISTOLOGICAL FEATURES OF JOINT AND COLONIC INFLAMMATION IN INFLAMMATORY BOWEL DISEASE PATIENTS TREATED WITH ANTI-TNF

S. Alivernini[1], D. Pugliese[2], B. Tolusso[1], L. Petricca[1], L. Bui[3], L. Guidi[2], G.L. Rapaccini[2], F. Federico[3], G. Ferraccioli[1], A. Armuzzi[2], E. Gremese[1].
[1]Institute of Rheumatology; [2]Ibd Unit; [3]Institute of Pathology, Catholic University of the Sacred Heart, Rome, Italy

Background: New onset of joint inflammation in patients under anti-TNF-alpha for inflammatory bowel disease (IBD) has been previously described. However, histological characterization of synovial and bowel compartments has not been reported so far.
Objectives: Aim of the study was to evaluate the histological characteristics of paired synovial (ST) and colonic tissues in IBD patients under TNF-alpha blockers.
Methods: Consecutive IBD patients without history of co-existing joint involvement who developed peripheral arthritis under TNF-alpha blockers, were prospectively enrolled. Each patient underwent rheumatological evaluation and ultrasound (US) assessment (using Gray scale for synovial hyperthrophy and Power Doppler Signal) of the affected joints. Each patient underwent US guided ST biopsy of the knee, following a standardized procedure[1] and colonoscopy with mucosal biopsies. Each ST and colonic paired sample was stained through immunohistochemistry (IHC) for CD68, CD21, CD20, CD3 and CD117[2]. H&E staining was performed for Paneth cells identification. Clinical and immunological parameters [Anti-citrullinated peptides antibodies (ACPA), IgM-Rheumatoid Factor (RF) and IgA-RF respectively] were collected for each patient.
Results: 10 patients with IBD [46.0±9.7 years old, 13.2±9.9 years of disease duration, 2.5±1.6 years of TNF-alpha blockers exposure, 6 with Crohn's Disease and 4 with Ulcerative Colitis respectively] were studied. All patients were negative for ACPA, IgM-RF or IgA-RF and 4 patients were under Methorexate therapy. 5 (50.0%) patients showed endoscopic and histologically proven inflammation of colonic mucosa. Moreover, IHC revealed that 6 (60.0%) patients had diffuse and 4 (40.0%) had follicular synovitis, respectively. In particular, there was a direct correlation between $CD68^+$, $CD21^+$, $CD3^+$, $CD20^+$ and $CD117^+$ cells distribution in paired ST and gut tissues in the whole cohort ($p<0.05$). No significant differences in terms of disease duration (p=0.48), TNF-alpha blockers exposure time (p=0.29), ESR (p=0.26) and CRP (p=0.91) values were found comparing patients with follicular and diffuse synovitis respectively.
Conclusions: Our findings suggest that patients with IBD may develop histologically proven synovitis during TNF-alpha treatment, showing similar histological features in terms of $CD68^+$, $CD21^+$, $CD20^+$, $CD3^+$ and $CD117^+$ cells between synovial and colonic compartments. Molecular mechanisms triggered by TNF-alpha blockers leading to joint inflammation have to be clarified.
References:
[1] van de Sande MJT et al. Ann Rheum Dis 2011.
[2] Alivernini S. et al. Nat Communications 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4301

OP0240 HOW STRONG ARE THE ASSOCIATIONS OF SPONDYLOARTHRITIS-RELATED COMORBIDITIES WITH ANKYLOSING SPONDYLITIS, PSORIATIC ARTHRITIS AND UNDIFFERENTIATED SPONDYLOARTHRITIS? A REGISTER-BASED STUDY FROM SWEDEN

K. Bengtsson[1], H. Forsblad-d'Elia[1,2], E. Lie[1], E. Klingberg[1], M. Dehlin[1], S. Exarchou[3], U. Lindström[1], J. Askling[4], L.T. Jacobsson[1]. *[1]Department of Rheumatology and Inflammation Research, Institute of Medicine, Sahlgrenska Academy at University of Gothenburg, Göteborg; [2]Departments of Public Health and Clinical Medicine, Rheumatology, Umeå; [3]Section of Rheumatology, Department of Clinical Sciences, Malmö, Lund University, Malmö; [4]Clinical Epidemiology Unit and Rheumatology Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden*

Background: Spondyloarthritis (SpA), including ankylosing spondylitis (AS), psoriatic arthritis (PsA) and undifferentiated SpA (uSpA), is a cluster of rheumatic diseases with some common genetic risk factors. These genetic risk factors are likely to result in associations of varying degree with SpA-related comorbidities such as inflammatory bowel disease (IBD), psoriasis and anterior uveitis. There

Abstract OP0240 – Table 1. Prevalence (%) and corresponding Prevalence Ratio (PR) of SpA-related comorbidities in AS, PsA and uSpA

	AS cases n (%)	PR (95% CI) (AS: GP)	PsA cases n (%)	PR (95% CI) (PsA: GP)	uSpA cases n (%)	PR (95% CI) (uSpA: GP)
Females, n (%)	*1217 (31.3)*		*4772 (54.8)*		*1503 (56.4)*	
Age, mean ±SD	*51.1±12.7*		*53.9±13.5*		*46.1±12.8*	
IBD	350 (9.0)	9.3 (7.7–11.2)	180 (2.1)	1.9 (1.6–2.3)	139 (5.2)	5.2 (4.1–6.6)
– Crohn's disease	170 (4.4)	11.6 (8.7–15.4)	78 (0.9)	2.2 (1.7–2.9)	62 (2.3)	6.5 (4.4–9.6)
– Ulcerative colitis	180 (4.6)	7.8 (6.2–10.0)	102 (1.2)	1.8 (1.4–2.3)	77 (2.9)	4.4 (3.3–6.1)
Anterior uveitis	819 (21.1)	44.8 (35.7–56.3)	145 (1.7)	3.8 (3.1–4.8)	351 (13.2)	32.4 (24.1–43.6)
Psoriasis	85 (2.2)	2.7 (2.0–3.5)	NA	NA	78 (2.9)	3.2 (2.4–4.3)
AV block	39 (1.0)	5.8 (3.6–9.4)	30 (0.3)	1.6 (1.0–2.4)	13 (0.5)	4.6 (2.1–10.0)
Aortic regurgitation*	55 (1.4)	4.7 (3.2–6.9)	41 (0.5)	1.7 (1.2–2.4)	11 (0.4)	3.0 (1.4–6.4)

AV, atrioventricular; NA, not applicable. *Aortic regurgitation includes both ICD codes for aortic regurgitation and procedure codes for aortic valve surgery.

is also a known association between AS and conduction disturbances and aortic regurgitation. Comparative analyses in the same setting of the strengths of these associations with AS, PsA and uSpA are scarce.
Objectives: To assess the strengths of the associations of different SpA-related comorbidities with a diagnosis of AS, PsA and uSpA.
Methods: All patients, aged ≥18 years, with AS (n=3884), PsA (n=8706) and uSpA (n=2665) were identified 2001 through 2005, according to specified ICD codes from the Swedish Patient Register. The register contains diagnoses from all visits in inpatient and non-primary outpatient care. Each patient was matched by year of birth, sex and county to five general population (GP) controls identified in the Population Register. Occurrence of SpA-related comorbidities prior to 1 January 2006 were also retrieved from the Swedish Patient Register. Number and proportion of cases (n (%)) with a recorded SpA-related comorbidity prior to 1 January 2006 and corresponding prevalence ratio (PR) with 95% confidence interval (CI) were calculated, overall and stratified for sex.
Results: PRs for SpA-related comorbidities were significantly elevated in all SpA subtypes compared to their matched GP controls (Table). PRs were substantially elevated in AS, intermediately elevated in uSpA, whereas only moderately increased in PsA. The results were similar in the sex-stratified analyses (not shown).
Conclusions: The strongest associations of SpA-related comorbidities were seen with AS, closely followed by uSpA, compatible with a substantial shared etiology and phenotypical expression for patients given these two diagnoses, whereas the associations between PsA and the SpA-related comorbidities were considerably weaker.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1255

OP0241 ERAP1 IS A SUSCEPTIBILITY FACTOR FOR EARLY AXIAL SPONDYLOARTHRITIS MEETING THE ASAS CLASSIFICATION CRITERIA: RESULTS FROM THE DESIR AND SPACE COHORTS

A. de Koning[1], M. Hameetman[1], C. Micelli[2], M. Dougados[3], D. van der Heijde[1], F. Kurreeman[1], F.A. van Gaalen[1]. *[1]LUMC, Leiden, Netherlands; [2]Hôpital Bicêtre; [3]Hôpital Cochin, Paris, France*

Background: Genetic research in axSpA is performed in patients with longstanding ankylosing spondylitis (AS). Early axial spondyloarthritis (axSpA) is a diverse patient group in which a minority of the patients have AS. Therefore, it is not known if recently identified genetic risk factors for AS are also risk factors for early axSpA.
Objectives: To evaluate if ERAP1 and HLA-B*4001 are susceptibility factors for early axSpA.
Methods: Patients with early axSpA meeting the ASAS classification criteria from the SPACE cohort (inclusion criteria: back pain for ≥3 months, ≤2 years, onset <45 years) and the DESIR cohort (inclusion criteria: inflammatory back pain for ≥3 months, ≤3 years, age <50) were typed for two well established AS genetic risk factors: ERAP1 SNPs rs30187 (susceptibility), rs17482078 (protective) and rs10050860 (neutral) and HLA-B*4001. Analysis of weaker AS risk factors was limited by sample size. For ERAP1, genotyped Dutch healthy controls (n=1085) and published French controls[1] were used as controls. For HLA-B*4001 healthy blood bank donors from the Netherlands (n=5584) and France (n=10177) were used as controls.
Results: In 486 DESIR patients (mean age 32.5 (SD 8.6); 50% male; 84% HLA-B27+; 18% X-SI+) and 144 SPACE patients (mean age 29.5 (SD 8); 51% male; 88% HLA-B27+; 24% X-SI+) ERAP1 SNP rs30187 was more common than in controls (OR 1.2, p=0.01 in meta-analysis; table 1). rs17482078 and rs10050860 were negatively associated with early axSpA (both 0.7 (0.6–0.9) p<0.01 in meta-analysis). Although both cohorts were sufficiently powered, HLA-B*4001 was not positively associated with early axSpA (OR 0.6 (0.4–0.9) in meta-analysis).

Table 1. Minor allele frequency and odds ratio of ERAP1 SNPs in SPACE and DESIR compared with Dutch and French controls respectively.

		SPACE n=144	Dutch controls n=1085		DESIR n=486	French controls* n=384		Meta-analysis
SNP	Risk allele	MAF	MAF	OR (95% CI)	MAF	MAF	OR (95% CI)	OR (95% CI)
rs30187	T	0.38	0.32	1.2 (1.0-1.6)	0.41	0.37	1.2 (0.9-1.5)	1.2 (1.0-1.4) p=0.01
rs17482078	T	0.14	0.21	0.6 (0.5-0.9)	0.18	0.22	0.8 (0.6-1.0)	0.7 (0.6-0.9) p<0.001
rs10050860	T	0.15	0.22	0.6 (0.5-0.9)	0.18	0.23	0.8 (0.6-1.0)	0.7 (0.6-0.9) p<0.001

* Calculated from published data (1)
ERAP1: endoplasmic reticulum aminopeptidase 1

Conclusions: ERAP1 rs30187 is a genetic risk factor for early axSpA. To our knowledge this is the first report of genetic risk factor research in early axSpA patients meeting the ASAS criteria. Larger cohorts are needed to study additional AS risk factors.
References:
[1] Kadi A, Izac B, Said-Nahal R, Leboime A, Van Praet L, de Vlam K, et al. Investigating the genetic association between ERAP1 and spondyloarthritis. Ann Rheum Dis. 2013;72(4):608–13.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5955

OP0242 HEALTH-RELATED QUALITY OF LIFE IMPROVED ONLY SLIGHTLY ALTHOUGH DISEASE ACTIVITY DECREASED OVER 3 YEARS IN EARLY AXIAL SPONDYLOARTHRITIS: 442 PATIENTS FROM THE DESIR COHORT

D. Puyraimond-Zemmour[1,2], C. Desthieux[1,2], A. Ruyssen-Witrand[3], B. Fautrel[1,2], L. Gossec[1,2]. *[1]Paris 06 university, Pierre and Marie Curie; [2]Pitie Salpetriere Hospital, Paris; [3]CHU de Toulouse, Hôpital Pierre-Paul Riquet, Toulouse, France*

Background: Current guidelines emphasize Health-related Quality of life (HRQoL) as a priority in health care but the link with disease activity is incomplete.
Objectives: The objective was to describe in patients with early axial spondyloarthritis (axSpA) the evolution of SF36 and of ASDAS-CRP over a 3 years follow up.
Methods: DESIR is an ongoing prospective, multicenter, longitudinal, observational French cohort (1). Patients had inflammatory back pain of more than 3 months and less than 3 years suggestive of axSpA. For our analysis, only patients with no missing data for MCS and PCS SF36 values during the first 3 years were included. HRQoL was assessed by the SF36 questionnaire and its 2 subscales (scored 0–100 with higher scores indicating better status): the physical composite score (PCS) including physical function, physical role, bodily pain and general health (GH) and the mental composite score (MCS) including mental health (MH), emotional role, social function and vitality. Disease activity was assessed by the ASDAS-CRP. Each outcome was assessed at baseline, 6 months, 12 months, 24 months and 36 months. The mean and median outcomes were calculated at each time-point and comparisons used ANOVA on repeated data. Baseline predictive factors associated with worse SF36 scores (lower half of mean values over 3 years) were identified by univariate then multivariate logistic regression, among the baseline variables age, gender, educational level, work status, smoking, HLAB27, radiological sacroiliitis, extra-articular manifestations (uveitis, psoriasis, inflammatory bowel disease) and ASDAS-CRP.
Results: In all, 442 patients were analyzed: at baseline, mean age was 34.2±8.6 years; mean disease duration was 18.6±10.7 months; 239 (54%) were females, 274 (62%) had HLAB27 and 124 (28%) had radiological sacroiliitis. At baseline, mean PCS, MCS and ASDAS-CRP were respectively 40.5±9.2, 40.4±11.0 and 2.6±1.0. Over 3 years, although mean ASDAS-CRP improved, HRQoL improved only slightly (Figure). All the SF36 subdomains improved (all p<0.001), though GH and MH improved less (data not shown). In univariate analysis, lower educational level, not being in a white collar job, younger age and higher ASDAS-CRP were significantly associated to lower HRQoL over 3 years. In multivariate analysis, only higher baseline ASDAS-CRP (odds ratio=0.49 [95% confidence interval 0.29; 0.79]) was associated to lower HRQoL.

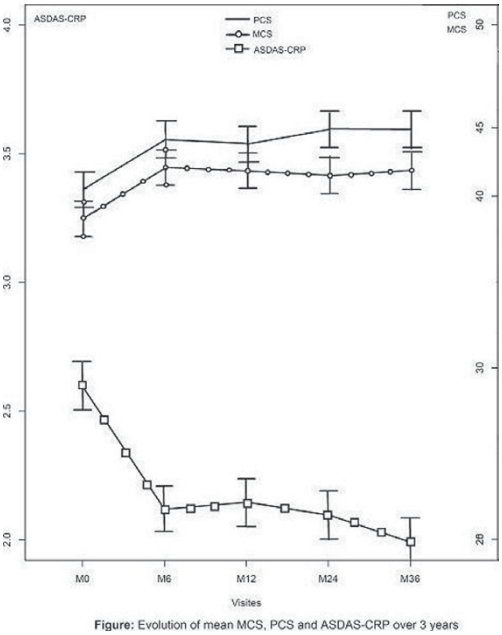


Figure: Evolution of mean MCS, PCS and ASDAS-CRP over 3 years

Conclusions: In early axSpA, HRQoL was affected similarly for the physical and mental components and only slightly improved over 3 years. In contrast, ASDAS-CRP improved substantially. However, ASDAS-CRP was a stronger driver of HRQoL than demographic characteristics. The drivers of HRQoL in inflammatory rheumatic disorders should be further explored.
References:
[1] Dougados M. et al. Clinical presentation of patients suffering from recent onset chronic inflammatory back pain suggestive of spondyloarthritis: The DESIR cohort.Joint Bone Spine, 2015;82(5):345–51.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4806

OP0243 PREDICTORS OF REMISSION AT WEEK 12 IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS RECEIVING OPEN-LABEL ADALIMUMAB TREATMENT IN THE ABILITY-3 STUDY

J. Sieper[1], R. Landewé[2], M. Magrey[3], J.K. Anderson[4], S. Zhong[4], X. Wang[4], A. Lertratanakul[4]. *[1]Charité Universitätsmedizin Berlin, Berlin, Germany; [2]University of Amsterdam, Amsterdam, Netherlands; [3]Case Western Reserve University School of Medicine at MetroHealth Medical Center, Cleveland; [4]AbbVie, North Chicago, United States*

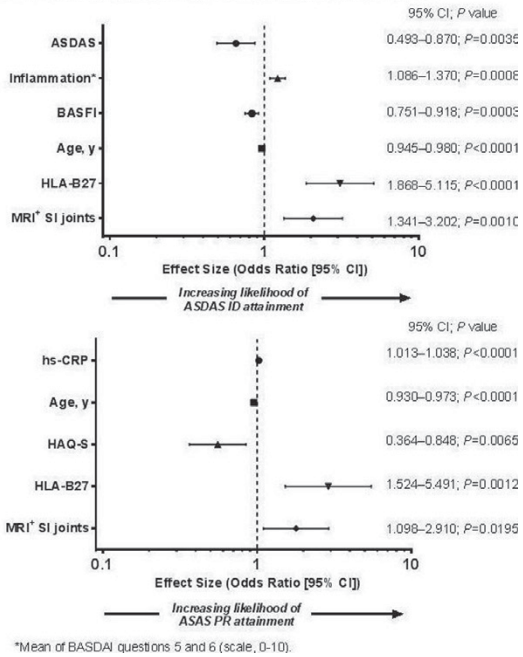
Background: Patients (pts) with non-radiographic axial spondyloarthritis (nr-axSpA) who fail nonsteroidal anti-inflammatory drug (NSAID) therapy are candidates for tumor necrosis factor inhibitor (TNFi) therapy if they have objective signs of inflammation. Baseline predictors of response to TNFi therapy, including remission, may aid clinical management.
Objectives: Describe baseline predictors of remission in nr-axSpA at wk 12 of open-label adalimumab (ADA) therapy in the ABILITY-3 study.
Methods: ABILITY-3 enrolled adult pts with nr-axSpA (fulfilling Assessment of SpondyloArthritis international Society [ASAS] criteria but not modified New York criteria) with moderately to severely active disease at screening and baseline, objective evidence of inflammation in the sacroiliac (SI) joints or spine on magnetic resonance imaging (MRI) or elevated high-sensitivity C-reactive protein (hs-CRP; defined as > upper limit of normal for the lab) at screening, and an inadequate response to ≥2 NSAIDs. Eligible pts received ADA 40 mg every other week during a 28-wk open-label lead-in period. Clinical remission was defined as Ankylosing Spondylitis Disease Activity Score inactive disease (ASDAS ID; score <1.3) or ASAS partial remission (score <2/10 in each of the 4 ASAS domains). Stepwise logistic regression was used to identify potential baseline predictors of remission at wk 12.
Results: 673 pts were enrolled (Table). Lower disease activity, increased inflammation (morning stiffness), less functional limitation (BASFI), younger age, presence of human leukocyte antigen-B27 (HLA-B27), and positive MRI of the SI joints were the strongest predictors of ASDAS ID; higher hs-CRP levels, younger age, lower functional status (HAQ-S), presence of HLA-B27, and positive MRI of the SI joints were the strongest predictors of ASAS PR (Figure).
Conclusions: In ABILITY-3, younger age, better functional status, presence of HLA-B27, and positive MRI of the SI joints consistently predicted clinical remission at wk 12 of open-label ADA treatment in pts with nr-axSpA.
Acknowledgements: AbbVie funded the study and approved the abstract for submission. Medical writing support was provided by Maria Hovenden, PhD, of Complete Publication Solutions, LLC (North Wales, PA) and was funded by AbbVie.
Disclosure of Interest: J. Sieper Grant/research support from: AbbVie, Merck, Pfizer, and UCB, Consultant for: AbbVie, Merck, Pfizer, and UCB, Speakers bureau: AbbVie, Merck, Pfizer, and UCB, R. Landewé Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, Consultant for: Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, Speakers bureau: Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, Wyeth; he is director of Rheumatology Consultancy BV, a registered Dutch company., M. Magrey Grant/research support from: Amgen, AbbVie, and UCB Pharma, Consultant for: UCB and Janssen, J. Anderson Employee of: AbbVie, S. Zhong Employee of: AbbVie, X. Wang Employee of: AbbVie, A. Lertratanakul Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.6467

Table 1. Baseline Characteristics

Mean ± SD or n (%)	ASDAS ID		ASAS PR	
	Responders (n=211)	Non-responders (n=389)	Responders (n=133)	Non-responders (n=470)
Age, y	33.6±9.7	38.9±11.4	31.8±8.7	38.5±11.2
Diagnosis duration, y	1.7±2.9	1.8±3.6	1.7±2.9	1.7±3.2
Symptom duration, y	6.1±6.2	8.2±8.1	5.3±5.7	8.0±7.8
HLA-B27 positive	183 (87)	274 (70)	119 (89)	340 (72)
ASDAS	3.4±0.8	3.7±0.8	3.7±0.9	3.6±0.8
Inflammation*	6.9±1.8	7.0±2.0	6.9±1.9	7.0±1.9
Patient global assessment of pain	7.0±1.7	7.7±1.5	7.1±1.9	7.5±1.6
hs-CRP	9.0±13.1	10.9±16.8	15.5±21.3	8.8±13.1
BASFI	4.6±2.2	5.7±2.2	4.9±2.4	5.4±2.2
HAQ-S	1.9±0.5	2.2±0.5	1.9±0.6	2.1±0.5
MRI SI joints positive	165 (78)	262 (67)	102 (77)	328 (70)
MRI spine positive	59 (28)	114 (29)	47 (35)	126 (27)

BASFI, Bath Ankylosing Spondylitis Functional Index; HAQ-S, Health Assessment Questionnaire modified for the Spondyloarthropathies. *Mean of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6 (scale, 0–10).

Figure. Results From Final Stepwise Multivariate Regression Model



*Mean of BASDAI questions 5 and 6 (scale, 0-10).

OP0244 FAMILY MATTERS: VALUE OF FAMILY HISTORY OF SPONDYLOARTHRITIS IN THE DIAGNOSTIC WORK-UP OF PATIENTS WITH CHRONIC BACK PAIN: RESULTS FROM THE SPACE AND DESIR COHORTS

Z. Ez-Zaitouni[1], A. Hilkens[1], L. Gossec[2], I.J. Berg[3], R. Landewé[4], R. Ramonda[5], M. Dougados[6], D. van der Heijde[1], F. van Gaalen[1]. *[1]Rheumatology, Leiden University Medical Center, Leiden, Netherlands; [2]UPMC University Paris 06, Paris, France; [3]Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; [4]Rheumatology, Academic Medical Center, Amsterdam, Netherlands; [5]Rheumatology Unit, DIMED, University of Padova, Padova, Italy; [6]Rheumatology, Université Paris Descartes, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, INSERM (U1153): Epidémiologie Clinique et Biostatistiques, PRES Sorbonne Paris-Cité, Paris, France*

Background: A positive family history (PFH) of spondyloarthritis (SpA) is considered a risk indicator for the presence of axial spondyloarthritis (axSpA) in patients with chronic back pain (CBP). In the ASAS classification criteria, a PFH of SpA is defined as the presence of any of the following diseases in first- or second-degree relatives: ankylosing spondylitis (AS), acute anterior uveitis (AAU), reactive arthritis (ReA), inflammatory bowel disease (IBD), and psoriasis. It is however not known if a PFH for each of these diseases contributes equally well to making a diagnosis of axSpA in patients presenting with CBP.
Objectives: To assess which SpA diseases in family members are associated with HLA-B27 and axSpA in patients with CBP.
Methods: The SPACE cohort includes patients with CBP (≥3 months, ≤2 years, onset <45 years) from various European rheumatology centers. DESIR is a French prospective multicenter cohort of patients with inflammatory back pain (IBP; ≥3 months, <3 years, onset <50 years), suggestive of axSpA. Patients underwent a full diagnostic work-up at baseline including MRI and radiographs of sacroiliac joints (local reading), laboratory assessments (e.g. HLA-B27), and assessment of all other SpA features. Patients were asked about the presence of SpA diseases in first- or second-degree relatives (AS, AAU, ReA, IBD, and psoriasis). The associations between a PFH and HLA-B27, sacroiliitis, axSpA diagnosis by the rheumatologist, and fulfilment of the ASAS classification criteria in CBP patients were assessed.
Results: In 438 patients from the SPACE cohort and 647 patients from the DESIR cohort, a PFH of AS (odds ratio (OR) 5.9 (3.5–9.9) and OR 3.3 (2.1–5.2), respectively for SPACE and DESIR) and a PFH of AAU (OR 9.8 (3.3–28.9) and OR 21.6 (2.9–160.1)) were significantly associated with presence of HLA-B27 (Table 1).Furthermore, in both cohorts a PFH of AS and a PFH of AAU were positively associated with fulfilment of the ASAS-criteria, but not with sacroiliitis on imaging (data not shown). In SPACE, but not in DESIR, a PFH of AS or AAU was associated with axSpA diagnosis (data not shown). In both cohorts, a PFH of ReA, IBD, or psoriasis was not positively associated with HLA-B27 positivity, sacroiliitis on imaging, axSpA diagnosis or meeting the ASAS criteria for axSpA.
Conclusions: In two recent CBP cohorts, a PFH of ReA, IBD, or psoriasis did not

Table 1 Association of family history manifestations with HLA-B27 in patients with chronic back pain in the SPACE cohort (n=438) and in patients with recent inflammatory back pain in the DESIR cohort (n=647).

	SPACE*				DESIR**			
	HLA-B27+ n= 174	HLA-B27- n= 262	OR (95% CI)	*P*- value	HLA-B27+ n= 376	HLA-B27- n= 270	OR (95% CI)	*P*- value
Any PFH	97	87	2.5 (1.7-3.8)	<0.001	158	91	1.4 (1.0-2.0)	0.032
AS	65	24	5.9 (3.5-9.9)	<0.001	100	27	3.3 (2.1-5.2)	<0.001
AAU	23	4	9.8 (3.3-28.9)	<0.001	28	1	21.6 (2.9-160.1)	0.003
ReA	5	9	0.8 (0.3-2.5)	0.745	1	5	0.1 (0.01-1.2)	0.075
IBD	12	21	0.9 (0.4-1.8)	0.666	17	15	0.8 (0.4-1.6)	0.551
Psoriasis	34	48	1.1 (0.6-1.8)	0.750	69	60	0.8 (0.5-1.2)	0.225

HLA-B27, human leukocyte antigen B27; Any FH, any family history manifestation in first- or second-degree relatives; AS, ankylosing spondylitis; AAU, acute anterior uveitis; ReA, reactive arthritis; IBD, inflammatory bowel disease; OR, odds ratio; 95% CI, 95% confidence interval. * 2 patients with unknown HLA-B27 status; **1 with patient unknown HLA-B27 status.

contribute to identifying axSpA in CBP patients indicating these family elements may not be very useful for diagnosis. A PFH of AS or AAU however may be useful in finding cases in low prevalence settings as these were correlated with HLA-B27 carriership.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4671

OP0245 EMPLOYMENT PERSPECTIVES OF PATIENTS WITH ANKYLOSING SPONDYLITIS IN THE BIOLOGICS ERA

C. Webers[1,2], L. Vanhoof[1], S. van Genderen[1,2], G. Plasqui[3], L. Heuft[4], M. van de Laar[5], J. Luime[6], D. van der Heijde[7], A. Spoorenberg[8], A. Boonen[1,2].
[1]MUMC; [2]CAPHRI; [3]Human Biology, UM, Maastricht; [4]Laurentius, Roermond; [5]MST, Enschede; [6]Erasmus MC, Rotterdam; [7]LUMC, Leiden; [8]UMCG, Groningen, Netherlands

Background: In the pre-biologics era, employment of patients with ankylosing spondylitis (AS) was decreased when compared to the general population. However, information on standardized employment since the introduction of biologicals is lacking. Also, while mastery (control over disease) has been identified as strong predictor of work outcome within patients with AS, it is not known whether such personality trait plays a similar role in patients compared to population subjects.

Objectives: To update the knowledge on employment and contributing factors, in particular personal factors, among Dutch patients with AS compared to general population subjects.

Methods: Data from patients and population controls participating in the Dutch cross-sectional multicenter survey-based Social Participation in AS Study (SPASS) and ≤65 years were used. Standardized employment ratios (SERs) were calculated using indirect standardization after adjusting for age, gender and education and were stratified by disease duration tertiles. Adjusted absolute employment rate (%) was calculated as "SER[AS]*employment rate [controls]". Modified Poisson regressions were performed to understand the role of mastery as a personal factor (Pearlin's Mastery scale) in patients opposed to controls, independent of socio-demographics (age, gender, education) and health-related factors (comorbidities, Physical Component Summary (PCS) of the SF-36).

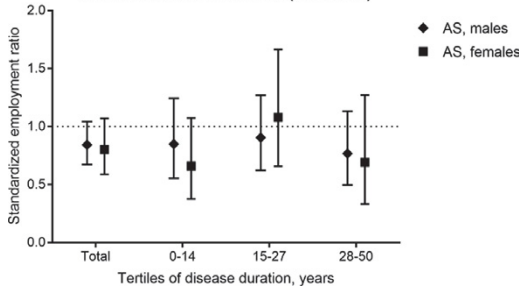
Results: 214 patients and 470 controls (127 [59.3%] and 323 [68.7%] males; mean age of 48.3 [SD 10.4] and 39.3 [SD 12.7] years, respectively) completed the online questionnaire in 2011. SERs (95% CI) of patients with AS with controls set as reference (1.00) were 0.83 (0.69–0.98) for the total group, 0.84 [0.67–1.04] for males and 0.83 [0.59–1.07] for females. There was no significant difference in SER between those with short or long disease duration (Figure 1). Adjusted absolute employment rate (%) of patients with AS was 14% lower compared to controls (69% vs. 84%). In both patients and controls, higher PCS (SF-36) was associated with being employed. While AS patients with higher (better) mastery were more likely to be employed, such association was not seen in controls ($p<0.01$ for interaction group*mastery) (Table).

Table 1. Multivariate Poisson regression exploring determinants of work participation, stratified by group (AS vs. controls)

Variable	AS (n=213)			Controls (n=465)		
	IRR	95% CI	p	IRR	95% CI	p
Age, years	0.99	0.98–1.00	<0.01	1.00	0.99–1.00	0.07
Gender, male	1.13	0.91–1.39	0.26	1.08	0.99–1.19	0.09
Education, high	–		ns†	1.09	1.01–1.18	0.02
Comorbidity (SCQ, 0–39)	0.97	0.94–1.01	0.12	0.97	0.94–1.01	0.14
SF-36 PCS (0–100)	1.02	1.00–1.03	<0.01	1.01	1.00–1.02	0.02
Mastery (7–28)	1.03	1.00–1.05	0.03	–		ns†

†Value not significant and no confounder.

Figure 1. Standardized employment ratios of patients with AS with controls set as reference (dotted line)



Conclusions: In the biologics era, employment among Dutch patients with AS remains reduced when compared to the general population, also in those with less than 15 years disease duration. As mastery in patients is independently associated with work outcome, it is worthwhile exploring whether improving personal self-management skills supports future worker participation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3472

FRIDAY, 16 JUNE 2017

RA - causes and courses

OP0246 IMPACT OF DISEASE ACTIVITY MEASURES ON SICK LEAVE IN BIOLOGICS-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS: OBSERVATIONAL DATA FROM SOUTHERN SWEDEN

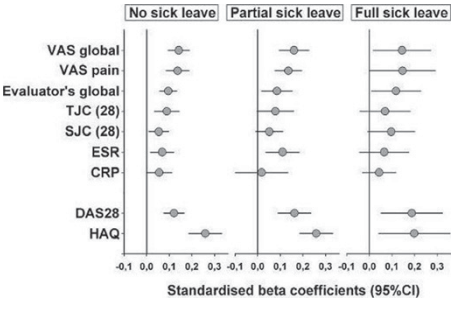
J.K. Wallman[1], J.K. Söderling[2], A. Gülfe[1], L.-E. Kristensen[3], M. Neovius[2], T. Olofsson[1]. *[1]Lund University, Department of Clinical Sciences Lund, Rheumatology, Lund; [2]Karolinska Institutet, Department of Medicine, Clinical Epidemiology Unit, Stockholm, Sweden; [3]The Parker Institute, Department of Rheumatology, Copenhagen University Hospital, Frederiksberg and Bispebjerg, Denmark*

Background: Sick leave generally represents the earliest phase of work-loss in rheumatoid arthritis (RA) patients, often on the trajectory towards more permanent disability pension. Sick leave may still change with disease activity fluctuations and is thus potentially reversible and accessible for interventions. However, data remain scarce on the importance of modifiable, non-composite disease activity measures for subsequent sick leave in RA patients treated with biologics.

Objectives: To study the impact of common, non-composite disease activity measures on sick leave in biologics-treated RA patients.

Methods: Study visits of biologics-treated RA patients of working-age (<65y) without disability pension, monitored in the population-based, observational South Swedish Arthritis Treatment Group register 2005–2011, were included (5151 visits; 957 patients). We performed association analyses between various non-composite disease activity measures at each visit and number of objectively assessed sick leave days during the month thereafter, retrieved from the Social Insurance Agency. Separate generalised estimating equation regression models were used, adjusting for age, sex, educational level, disease duration, number of previous biologics, time from start of the present biologic, and calendar year of study visit. Analyses were furthermore stratified on sick leave status the month preceding each visit (no sick leave=0 days out of 30; partial sick leave=1–29 days and full sick leave=30 days) and results are presented as standardised beta coefficients for comparability, with bootstrap-generated 95% confidence intervals. The composite 28-joint disease activity score (DAS28) and the health assessment questionnaire (HAQ) disability score were included as contrast.

Results: Out of common, non-composite disease activity measures, visual analogue scale (VAS) global and VAS pain were most strongly associated with sick leave days the month after the study visit, irrespective of baseline sick leave status (Figure). Generally, the more objective measures (erythrocyte sedimentation rate, C-reactive protein and swollen joint count (SJC)) had less impact on subsequent sick leave than the more subjective variables (VAS global, VAS pain, evaluator's global and tender joint count (TJC)). As expected, HAQ showed the strongest association.



Conclusions: More subjective disease activity measures have greater impact on sick leave in biologics-treated RA patients than do more objective variables, suggesting a stronger focus on the former ones when targeting work-loss or intervening to reduce it.

Disclosure of Interest: J. Wallman Consultant for: Novartis, Celgene and UCB, J. Söderling Grant/research support from: Participated in previous research projects fully or partly funded by Novo Nordisk and Combine Sweden, Consultant for: Served as an external consultant to AbbVie, Merck and Novartis, A. Gülfe: None declared, L.-E. Kristensen Grant/research support from: Oak Foundation, Consultant for: AbbVie, Celgene, BMS, MSD, Novartis, Pfizer, UCB, M. Neovius Grant/research support from: Participated in research projects fully or partly funded by Schering-Plough, AstraZeneca, Novo Nordisk, Pfizer and Roche (unrelated to the current work), Consultant for: Participated in advisory boards for Pfizer (rheumatology) and Abbott (non-rheumatology), T. Olofsson: None declared

DOI: 10.1136/annrheumdis-2017-eular.2883

OP0247 AN IMPROVED MATRIX TO PREDICT RAPID RADIOGRAPHIC PROGRESSION OF EARLY RHEUMATOID ARTHRITIS PATIENTS: POOLED ANALYSES FROM SEVERAL DATABASES

A. Vanier[1], J. Smolen[2], C. Allaart[3], R. Van Vollenhoven[4], P. Verschueren[5], N. Vastesaeger[6], S. Saevarsdottir[4], K. Visser[3], D. Aletaha[2], B. Combe[7], B. Fautrel[1]. *[1]UPMC Univ Paris 6 and AP-HP Pitié-Salpêtrière Hospital, Paris, France; [2]University of Vienna, Vienna, Austria; [3]Leiden University Medical Centre, Leiden, Netherlands; [4]Karolinska Institute, Stockholm, Sweden; [5]Leuven University, Leuven, Belgium; [6]Merck Sharp and Dohme, Lucerne, Switzerland; [7]Université de Montpellier 1, Montpellier, France*

Background: In early rheumatoid arthritis (RA), some patients exhibit rapid radiographic progression (RRP) after one year, associated with poor functional prognosis. Identifying at the time of diagnosis the characteristics predictive of RRP is of importance. Several matrices predicting this risk have been proposed over the last years. They were limited somewhat in terms of precision or were built using specific populations.
Objectives: To develop a matrix to predict RRP with better precision and generalizability by pooling databases from various studies.
Methods: The study is based on the pooling of individual data from cohorts (ESPOIR and Leuven) and clinical trials (BeSt, SWEFOT and ASPIRE). Included patients were adult DMARD-naïve patients with recent suspected or confirmed diagnosis of active RA for which the first therapeutic strategy after inclusion was to prescribe MTX or leflunomide in monotherapy for at least 3 months. The main outcome was the presence after one year of RRP defined as an increase in modified Sharp score (vSHS) of at least 5 points between baseline and year one. Baseline characteristics were compared by the presence of RRP to search for predictors. A logistic regression model to predict RRP was built. The best model was selected by 10-fold stratified cross-validation by maximizing the Area Under the Curve (AUC). Calibration and discriminatory power of the model were assessed. Model parameters were extracted to estimate the probability of a RRP for each combination of level of baseline characteristics.
Results: The data of 1306 patients were pooled. After one year, 236 exhibited RRP (20.6%, $CI_{95\%}$ [18.2–22.9], mean probability of RRP of 0.21). Model of prediction of RRP included as baseline characteristics Rheumatoid Factor (RF) positivity (OR=2.1 $CI_{95\%}$ [1.5–3.0]; p<0.001), erosive disease on X-rays (OR=2.3 $CI_{95\%}$ [1.7–3.2]; p<0.001), CRP>30mg/l (OR=2.1 $CI_{95\%}$ [1.5–3.0]; p<0.001), number of swollen joints>10 (OR=1.5 $CI_{95\%}$ [1.01–2.2]; p=0.048). Model calibration was good (Hosmer and Lemeshow test: p=0.79). AUC was 0.68. The matrix proposes estimated RRP probability for 36 combinations of level of baseline characteristics. Its range goes from patients with a 4.1 fold lower risk of RRP compared to average risk (probability of 0.05 $CI_{95\%}$ [0.03–0.08], patient with CRP <10mg/l, without RF, without erosive disease on X-ray, with <6 swollen joints), to patients with a 2.3 fold higher risk than average (probability of 0.47 $CI_{95\%}$ [0.39–0.55], patient with CRP >30, with RF, with erosive disease on X-ray, with >10 swollen joints).

		Absence of typical RA erosion on radiographs			Presence of typical RA erosions on radiographs		
		SJC < 6	6 ≤ SJC < 10	SJC ≥ 10	SJC < 6	6 ≤ SJC < 10	SJC ≥ 10
RF positivity	CRP ≥ 30	0.21 [0.14 ; 0.29]	0.21 [0.15 ; 0.29]	0.28 [0.21 ; 0.36]	0.37 [0.28 ; 0.47]	0.38 [0.29 ; 0.48]	0.47 [0.39 ; 0.55]
	10 ≤ CRP < 30	0.13 [0.08 ; 0.18]	0.13 [0.08 ; 0.19]	0.18 [0.12 ; 0.24]	0.25 [0.17 ; 0.33]	0.25 [0.18 ; 0.33]	0.33 [0.25 ; 0.41]
	CRP < 10	0.11 [0.07 ; 0.15]	0.11 [0.08 ; 0.15]	0.15 [0.11 ; 0.20]	0.22 [0.16 ; 0.28]	0.22 [0.17 ; 0.28]	0.29 [0.22 ; 0.36]
RF negativity	CRP ≥ 30	0.11 [0.07 ; 0.17]	0.11 [0.07 ; 0.17]	0.15 [0.10 ; 0.21]	0.22 [0.14 ; 0.31]	0.22 [0.15 ; 0.31]	0.29 [0.22 ; 0.37]
	10 ≤ CRP < 30	0.06 [0.04 ; 0.10]	0.07 [0.04 ; 0.10]	0.09 [0.06 ; 0.13]	0.13 [0.08 ; 0.19]	0.14 [0.09 ; 0.20]	0.18 [0.13 ; 0.25]
	CRP < 10	0.05 [0.03 ; 0.08]	0.06 [0.03 ; 0.08]	0.08 [0.05 ; 0.11]	0.11 [0.07 ; 0.16]	0.12 [0.08 ; 0.17]	0.16 [0.11 ; 0.22]

Conclusions: A matrix proposing RRP probability at one year with better precision (i.e. narrower $CI_{95\%}$than those previously published) in early RA for various combinations of levels of a few common baseline characteristics has been built using several databases. However, discriminating power is not ideal. Further investigations will be needed to fully explore the potential complexity of predicting RRP in early RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4752

OP0248 SERIOUS INFECTION AND ASSOCIATED RISK FACTORS IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB

K.L. Winthrop[1], M.C. Genovese[2], M. Harigai[3], L. Chen[4], C.L. Dickson[4], D.L. Hyslop[4], A. Nishikawa[5], J.D. Bradley[4], M. Dougados[6]. *[1]Oregon Health and Science Univ., Portland; [2]Stanford Univ., Palo Alto, United States; [3]Tokyo Women's Medical Univ., Tokyo, Japan; [4]Eli Lilly and Company, Indianapolis, United States; [5]Lilly Japan, K.K., Kobe, Japan; [6]Paris-Descartes Univ., Paris, France*

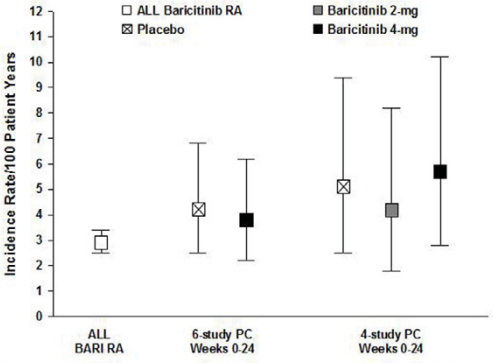
Background: Baricitinib (BARI) is an oral Janus Kinase (JAK)1/JAK2 inhibitor in development for patients (pts) with active rheumatoid arthritis (RA). Compared to the general population, RA pts have an increased rate of serious infection events (SIE) due to disease state and concomitant therapies.[1]
Objectives: To evaluate the incidence rate (IR) of SIE and associated risk factors in BARI-treated pts with active RA across 8 completed studies (4 Ph3, 3 Ph2, 1 Ph1) and 1 ongoing long-term extension (LTE) study.
Methods: The ALL BARI RA analysis set included pts exposed to any BARI dose, with exposure up to 5 years (yrs) (Phase [Ph] 1–3 and LTE studies); the comparison with placebo (PBO) was based on 6 studies (Ph 2–3) with BARI 4 mg once daily (QD) and PBO arms up to Week (Wk) 24; dose response assessment was based on 4 studies (Ph 2–3) with both BARI 2 and 4 mg QD arms up to Wk 24. An extensive list of potential risk factors for SIE was investigated in the ALL BARI RA set using Cox models; SIE risk factors among BARI-treated pts are reported (Table).
Results:
The most frequent SIE observed in the ALL BARI RA set (N=3492; 5133 pt-yrs (PY) of exposure [PYE] were pneumonia, herpes zoster, urinary tract infection, and cellulitis (all <1%), and 2 patients with SIE died (IR=0.04/100 PY). In the ALL BARI RA set, SIE were reported in 150 pts (IR=2.9/100 PY). During 0–24 Wks, similar SIE rates were observed in BARI 4 mg (N=997; 417 PYE) and PBO (N=1070; 403 PYE) groups in the 6-study set, and between BARI 2 mg (N=479; 192 PYE) and 4 mg (N=479; 194 PYE) dose groups in the 4-study set (Figure). Prior biologic use, advancing age, region of Asia (excluding Japan), non-normal body mass index (BMI), and corticosteroid use were identified as independent factors for SIE in the ALL BARI RA set (Table). Among these SIE risk factors, none significantly differed between BARI 4 mg and PBO in the 6-study dataset (data not shown).

Table 1. Hazard Ratio and 95% CI for Serious Infection in the ALL BARI RA Analysis Set

Clinical Factor	Univariate HR [95% CI]	Multivariate HR [95% CI]
Line of therapy (bDMARD-IR vs. csDMARD-IR)	1.6 [1.1, 2.3]	1.5 [1.0, 2.3]
Age (65+ vs. 18–64 yrs)[a]	2.2 [1.6, 3.2]	2.5 [1.8, 3.6]
Region (Asia [excluding Japan] vs. US/Canada)	2.4 [1.3, 4.4]	2.7 [1.4, 5.2]
BMI (kg/m^2) (vs. normal [18–24])[a]		
Underweight (<18)	3.4 [1.7, 7.0]	3.1 [1.5, 6.4]
Overweight (25–29)	1.6 [1.0, 2.4]	1.8 [1.1, 2.7]
Obese (≥30)	1.4 [0.9, 2.2]	1.8 [1.1, 2.9]
RA duration (10+ vs. 0–4 yrs)[a]	1.7 [1.1, 2.6]	–
DAS28-hsCRP (for every one unit increase)[a]	1.1 [1.0, 1.3]	–
HAQ-DI (≥1.5 vs. <1.5)[a]	1.5 [1.1, 2.1]	–
Corticosteroid dose (mg/day)[a]		
0.1–4.9 vs. none	2.2 [1.3, 3.7]	2.3 [1.4, 3.9]
5+ vs. none	1.7 [1.2, 2.5]	1.9 [1.3, 2.7]

[a]Data at baseline. Abbreviations: CI, confidence interval; HR, hazard ratio.

Figure. Serious Infection Incidence Rate and 95% CI by Analysis Set



	ALL BARI RA	6-study PC Weeks 0-24		4-study PC Weeks 0-24		
IR/100 Patient Years	2.9	4.2	3.8	5.1	4.2	5.7
All Patients	3492	1070	997	551	479	479
With Events	150	17	16	10	8	11
Patient Years	5133	403	417	195	192	194

Abbreviations: CI=confidence interval; IR=incidence rate; PC=placebo controlled; RA=rheumatoid arthritis

Conclusions: SIE incidence was similar between BARI- and PBO-treated RA pts. SIE risk factors include concomitant corticosteroids, prior biologics, non-normal BMI, Asian region of enrollment, and advancing age.
References:
[1] Listing J et al. Rheumatology. 2013;52:53–61.
Disclosure of Interest: K. Winthrop Grant/research support from: Pfizer, BMS, Consultant for: Pfizer, UCB, Abbvie, Eli Lilly and Company, Amgen, BMS, M. Genovese Grant/research support from: Eli Lilly and Company, Abbvie, Astellas, Galapagos, Pfizer, Vertex, Crescendo Bioscience, Consultant for: Eli Lilly and Company, Abbvie, Astellas, Galapagos, Pfizer, Vertex, Crescendo Bioscience, M. Harigai Grant/research support from: Bristol-Myers Squibb KK, Eisai Co Ltd, Ono Pharma, Takeda Pharma Ltd, Consultant for: Eli Lilly and Company, L. Chen Employee of: Eli Lilly and Company, C. Dickson Employee of: Eli Lilly and Company, D. Hyslop Employee of: Eli Lilly and Company, A. Nishikawa Employee of: Eli Lilly Japan K.K., J. Bradley Employee of: Eli Lilly and Company, M. Dougados Grant/research support from: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, Consultant for: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS
DOI: 10.1136/annrheumdis-2017-eular.1312

OP0249 MULTI-BIOMARKER DISEASE ACTIVITY AND AUTOANTIBODY STATUS LEAD TO COST EFFECTIVE TAPERING ALGORITHMS IN RHEUMATOID ARTHRITIS PATIENTS IN SUSTAINED REMISSION

M. Hagen[1], M. Englbrecht[1], J. Haschka[2], M. Reiser[1], A. Kleyer[1], A. Hueber[1], B. Manger[1], C. Figuereido[3], J. Fogagnolo Cobra[3], H.-P. Tony[4], S. Finzel[5], S. Kleinert[6], J. Wendler[6], F. Schuch[6], M. Ronneberger[6], M. Feuchtenberger[7], M. Fleck[8], K. Manger[9], W. Ochs[10], M. Schmitt-Haendle[10], H.-M. Lorenz[11], H. Nuesslein[12], R. Alten[13], J. Henes[14], K. Krueger[15], G. Schett[1], J. Rech[1].
[1]University of Erlangen-Nuremberg, Erlangen, Germany; [2]St.Vincent Hospital, Vinforce Study Group, Medical University of Vienna, Vienna, Austria; [3]Institutio de Rheumatologia, Sao Paolo, Brazil; [4]University of Wuerzburg, Internal Medicine 2, Wuerzburg; [5]University Medical Center Freiburg, Rheumatology and Clinical Immunology, Freiburg; [6]Rheumatology Clinical Practice Erlangen, Erlangen; [7]Rheumatology Practice and Department of Internal medicine 2, Clinic Burghausen, Burghausen; [8]Asklepios Medical Center, Department of Rheumatology and clinical Immunology, Bad Abbach; [9]Rheumatology Practice Bamberg, Bamberg; [10]Rheumatology Practice Bayreuth, Bayreuth; [11]University of Heidelberg, Medicine 5, Heidelberg; [12]Rheumatology Practice Nuremberg, Nuremberg; [13]Schlosspark Klinik, Internal Medicine/Rheumatology, Berlin; [14]University of Tuebingen, Centre for Interdisciplinary Clinical Immunolog, Tuebingen; [15]Praxiszentrum St.Bonifatius, Munich, Germany

Background: Achieving remission is the ultimate treatment goal in patients with rheumatoid arthritis (RA). With the development and wider use of highly effective disease modifying anti-rheumatic drugs (DMARD) about half of RA patients reach the disease remission state (1), raising the question about tapering or stopping anti-rheumatic treatment and appropriate predictors (2).
Objectives: To analyse the effect of a risk-stratified DMARD tapering algorithm based on multiple-biomarker disease activity (MBDA) score and anti-citrullinated protein (ACPA) status for successful DMARD tapering and treatment cost reduction in RA patients in sustained remission enrolled in the prospective randomized controlled RETRO study (3,4).
Methods: MBDA scores and ACPA status were determined in the baseline samples of 146 patients in sustained remission. Patients either continued DMARDs (arm1), tapered dose by 50% (arm 2) or stopped DMARDs after tapering (arm 3) for one year according to the RETRO study protocol. Direct treatment costs (including testing costs at baseline) were evaluated every three months. MBDA and ACPA status were used as predictors creating a risk-stratified tapering algorithm based on relapse rates.
Results: RA patients with a low MBDA score (<30) and negative ACPA showed lowest relapse risk (19%). With either single positivity for ACPA or moderate/high MBDA scores (≥30) relapse risk increased and was high in double-positive patients (61%). In MBDA negative (<30) and MBDA single-positive (≥30) groups, DMARD tapering appears feasible. Considering only patients that did not flare, costs for synthetic and biologic DMARDs in the MBDA-negative and single-positive groups (n=41) would have been 123.751,29€ for full-dose treatment over one year. Tapering and stopping DMARDs in this low-risk relapse groups allowed a reduction of 92.821,50€ (-75%) of DMARD costs. Average reduction of DMARD costs per patient were 2.350,08€ in the double negative (MBDA-/ACPA-) and single negative (MBDA- /ACPA+) group and 1.761,43€ in the MBDA single positive (MBDA+ /ACPA-) group.



Conclusions: Combining MBDA score and ACPA status allows risk stratification for successful DMARD tapering and cost-effective use of biologic DMARD. Given that previous data of the RETRO have shown that patients relapsing after tapering their DMARDs respond well to their reintroduction, a stratified tapering and stopping of DMARDs is not only a cost economic but also clinically feasible strategy.
References:
[1] Aga AB et al. Ann Rheum Dis. 2013;74:381–8.
[2] Schett G et al. Ann Rheum Dis. 2016 Aug;75(8):1428–373.
[3] Haschka J et al, Ann Rheum Dis. 2016;75:45–51.
[4] Rech J et al, Ann Rheum Dis. 2015; Oct. 19.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2988

OP0250 CAN RANKL SERUM LEVELS PREDICT FUTURE PROGRESSION TO RHEUMATOID ARTHRITIS IN ACPA NEGATIVE PATIENTS?

A. Burska[1], J. El-Jawhari[1], A.L. Tan[1], R. Wakefield[1], H. Marzo-Ortega[2], P. Conaghan[1], P. Emery[1], F. Ponchel[1], J. Freeston[1,2,3]. *[1]LIRMM, University of Leeds; [2]NIHR Leeds Musculoskeletal Biomedical Research Centre; [3]Rheumatology, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Making the earliest diagnosis of rheumatoid arthritis (RA) is crucial to initiate treatment and prevent further disease progression and joint damage. Despite recent advances with the discovery and integration of anti–cyclic citrullinated protein antibody (ACPA) in classification criteria, there is still an unmet need for new diagnostic biomarkers, notably for ACPA-negative disease. Power Doppler ultrasound has been shown to identify poor prognosis disease in ACPA negative patients.
Objectives: The receptor-activator-nuclear-factor-κB axis (RANK/RANKL) is known to regulate bone homeostasis. The aim of this pilot study is to establish whether serum RANKL levels in people with early inflammatory arthritis are associated with RA diagnosis at follow-up and to evaluate the added value of RANKL with ultrasound for early RA diagnosis.
Methods: Serum from 298 subjects (95/204 Male/Female) was collected at the baseline participant visit to the Leeds Early Arthritis clinic. Demographic (age, gender symptom duration) and clinical data (swollen and tender joint counts (SJC, TJC), CRP, DAS28, rheumatoid factor (RF) and ACPA, shared epitope (SE)) were collected.
A commercial ELISA (BioVENDOR) was used to measure RANKL. Ultrasound of 26 joints (bilateral elbows, wrists, MCP 2–3, PIP 2–3, knees, ankles and MTP 1–5) was performed at baseline recording summative scores for power Doppler (PD), grey scale hypertrophy (GS) and erosions (ERO).
Results: At 1 year follow-up, 151 patients had a confirmed diagnosis of RA (EULAR 2010 criteria) and 147 were classified as non-RA (undifferentiated arthritis, other inflammatory diagnoses or non-persistent inflammation). All routinely used biomarkers were associated with RA diagnosis (ACPA, RF, SE, TJC, SJC, CRP, DAS28, $p<0.0001$), as were imaging biomarkers (PD, GS, ERO, $p<0.001$). RANKL levels were significantly higher in RA (RA 1002.4±1053.2pmol/L, non-RA 339.2±451.5pmol/L, $p<0.0001$). A regression analysis suggested that four parameters were sufficient to account for all associations with RA: RANKL, age, SJC, and PD with 75.3% accurate prediction. An AUROC analysis suggested a cut-off for each parameter and a score was calculated, adding 1 point for each of the factors (RANKL>700, age>62, TPD>3, SJC>4). This score predicted RA with an AUROC of 0.782 ((0.23–0.840), $p<0.0001$). The same analysis repeated for ACPA negative patients only (n=193) showed similar results, providing accurate diagnosis of RA (77.6% correct by regression) and with an AUROC of 0.774 ((0.690–0.858), $p<0.0001$).
Conclusions: A score incorporating RANKL, age, SJC and PD showed good predictive value for non-RA when low and for RA when high. Furthermore, the analysis redone in ACPA-negative patients performed particularly well for predicting RA with a good AUROC value.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3226

OP0251 INCIDENCE OF KNEE AND HIP REPLACEMENTS IN RHEUMATOID ARTHRITIS PATIENTS FOLLOWING INTRODUCTION OF BIOLOGICAL DMARDS: AN INTERRUPTED TIME SERIES ANALYSIS USING NATIONWIDE HEALTH CARE REGISTERS

R. Cordtz[1,2], S. Hawley[3], D. Prieto-Alhambra[3], L.E. Kristensen[2], S. Overgaard[4], A. Odgaard[5], L. Dreyer[1,2]. *[1]Center for Rheumatology and Spine Diseases, Gentofte, Rigshospitalet; [2]The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark; [3]Musculoskeletal Pharmaco- and Device Epidemiology, NDORMS, University of Oxford, Oxford, United Kingdom; [4]Department of Orthopaedic Surgery and Traumatology, Odense University Hospital, Odense; [5]Depepartment of Orthopaedics, Herlev and Gentofte Hospital, Copenhagen, Denmark*

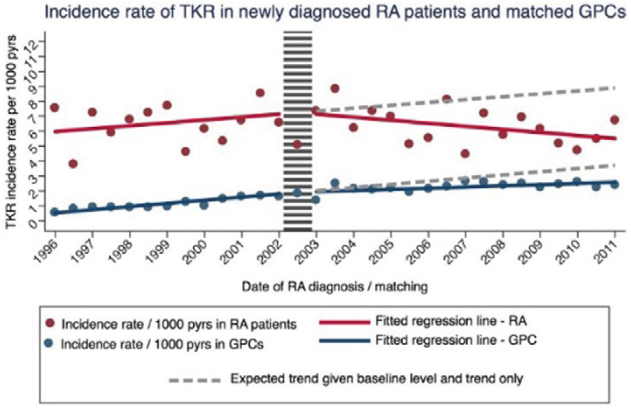
Background: Previous data have been conflicting regarding a possible impact of treatment with biological DMARDs (bDMARDs) on the need for total knee replacement (TKR) and total hip replacement (THR) in patients with rheumatoid arthritis (RA)[1].
Objectives: To investigate impact of national guidelines recommending bDMARD treatment for RA on the secular trends of TKR and THR among incident RA patients compared with matched general population controls (GPC) in Denmark.
Methods: Nationwide register-based interrupted time-series analysis using the National Patient Register and Civil Registration System.
RA: incident patients diagnosed at a rheumatology department from 1996–2011.
GPC: 10 individuals matched to each RA patient on age, sex and municipality.
Outcome: First TKR and THR, respectively.

Intervention: introduction of bDMARDs and associated publication of bDMARD recommendations in Denmark in 2002.
Statistical analyses: 5-year age- and sex-standardised incidence rates of THR and TKR calculated for incident RA patients diagnosed biannually in 1996–2011, and GPCs. Secular trends in the pre-bDMARD guideline era (1996–2002) were compared with those in the bDMARD period (2003–2016) using segmented linear regression and a 1-year lag period (2002–03). Absolute changes in TKR and THR at the midpoint (February 2007) between guideline implementation and end of study period were estimated.
Results: In total, during 1996 to 2011, 30 868 incident RA patients were identified (mean age at diagnosis 58.3 years, 70% women) and compared with 301 527 GPCs. See Table for results.

Table 1. Changes in 5-year incidence rate of total hip (THR) or total knee replacement (TKR) in incident rheumatoid arthritis (RA) patients following introduction of biological DMARDs compared with secular trends in age, sex and municipality-matched general population controls (GPC)

Cohort		n THR/TKR	Baseline incidence rate/1000 person years	Δ per year* pre-2002	Δ in level 2003	Δ per year post-2003
TKR	RA	865	5.87	+0.19	–	-0.20
	GPC	2438	0.42	+0.21	–	+0.08
THR	RA	935	8.72	-0.38	+2.23	-0.38
	GPC	4744	2.89	+0.11	–	+0.02

Stepwise backward elimination to produce most parsimonious model: p-entry <0.05 and p-exit >0.2. *Δ per year based on biannual data.



Conclusions: Prior to 2002, the incidence of TKR increased among RA patients, but started to decrease after introduction of bDMARDs and their associated guidelines in 2003 (absolute change -1.8 TKRs/1000 person years in Feb. 2007). In contrast, the incidence of TKR increased among GPCs throughout the entire study period. The incidence of THR increased in GPCs for the entire duration of the study period, whereas there was a downward going trend among RA patients, but with a surprising level increase in 2003. The overall patterns of our findings are in line with those recently reported from England and Wales[1].
References:
[1] Hawley S, Cordtz R, Dreyer L, et al. The Impact of Biologic Therapy Introduction on Hip and Knee Replacement Among Rheumatoid Arthritis Patients: An Interrupted Time Series Analysis Using the Clinical Practice Research Datalink. Arthritis Rheumatol 2016;68.
Disclosure of Interest: R. Cordtz: None declared, S. Hawley: None declared, D. Prieto-Alhambra Grant/research support from: DPA's group has received unrelated research grants from Amgen and Servier, L. E. Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, MSD, Novartis, Eli Lilly, Janssen Pharmaceuticals, S. Overgaard: None declared, A. Odgaard: None declared, L. Dreyer: None declared
DOI: 10.1136/annrheumdis-2017-eular.1227

OP0252 RHEUMATOID ARTHRITIS PATIENTS WITH CONTINUED LOW DISEASE ACTIVITY HAVE SIMILAR OUTCOMES OVER 10 YEARS, REGARDLESS OF INITIAL THERAPY

S.A. Bergstra[1], R.B. Landewé[2,3], T.W. Huizinga[1], C.F. Allaart[1]. *[1]Rheumatology, LUMC, Leiden; [2]Amsterdam Rheumatology & Immunology Center, Amsterdam; [3]Zuyderland Medical Center, Heerlen, Netherlands*

Background: Low disease activity and remission in rheumatoid arthritis (RA) patients is achieved earlier and in higher frequency when the initial treatment includes a combination of methotrexate (MTX) with corticosteroids or a biologic disease modifying anti-rheumatic drug than MTX alone. However, it is unknown whether in patients with early and persistently good response the initial treatment still has an impact on long term outcomes.
Objectives: To compare 10 years disease outcomes of RA patients with persistent low disease activity on MTX monotherapy or on initial combination therapy with infliximab or prednisone and sulfasalazine.
Methods: RA patients with 10 years follow-up from the BeSt study were analyzed. RA patients fulfilling the American College of Rheumatology 1987 criteria with <2 years symptom duration were "treated to target" aiming at disease activity score (DAS) ≤2.4, assessed with 3-monthly intervals. Patients in arms 1 and 2 started MTX monotherapy, patients in arm 3 started MTX, sulfasalazine and prednisone and patients in arm 4 started MTX and infliximab. All had DAS≤2.4 from t=6 months until t=10 years and therefore stayed on initial treatment, with patients in arms 3 and 4 tapering to monotherapy within 10 months. Patients in arms 1 and 2 were compared with patients in arms 3 and 4. Between-group differences over time were compared using (generalized) linear mixed model analyses, for the outcomes DAS, Health Assessment Questionnaire (HAQ), erythrocyte sedimentation rate (ESR), visual analogue scale (VAS) patient global health (range 0–100), percentage patients in remission and drug free remission and percentage patients with Sharp/van der Heijde score progression ≥5.
Results: At t=10 years 28/247 (11%) patients in arms 1 and 2 had sustained DAS≤2.4 compared to 68/261 (26%) patients in arms 3 and 4. Patients in arms 1 and 2 were less often ACPA positive (46% versus 54%, p=0.477), had shorter symptom duration at baseline [median (range) 14 (1–191) versus 18 (4–263) weeks, p=0.004] and less radiologic damage progression after 10 years [0 (0–16) versus 2.5 (0–26), p=0.014] than patients in arms 3 and 4. No between-group differences were found over time, except for the percentage of patients in drug free remission. Significant group-time interactions were found for DAS, ESR and VAS patient's global health, but not HAQ, percentage remission and percentage drug free remission, with slightly worse results over time for arms 3 and 4 compared to arms 1 and 2 (table 1).

Table 2: (Generalized) linear mixed model analyses to assess differences over time between MTX monotherapy responders (n=28) and combination therapy responders (n=68).

	Linear Mixed Model Analyses	β	95% CI
HAQ	Treatment group*	0.076	-0.066; 0.22
	Time	-0.0034	-0.0044; -0.0025
DAS	Treatment group*	0.031	-0.24; 0.18
	Time	-0.029	-0.037; -0.021
	Treatment group*Time	0.0056	0.0012; 0.010
ESR	Treatment group*	-3.30	-7.54; 0.93
	Time	-0.19	-0.31; -0.072
	Treatment group*Time	0.11	0.041; 0.17
VAS patient global health	Treatment group*	-4.07	-9.50; 1.37
	Time	-0.42	-0.57; -0.27
	Treatment group*Time	0.090	0.0048; 0.17
	Generalized linear mixed model analyses	**OR**	**95% CI**
SvdH score progression =5	Treatment group*	0.83	0.17; 4.01
	Time	0.94	0.83; 1.07
Remission	Treatment group*	0.58	0.32; 1.08
	Time	1.04	1.03; 1.04
Drug free remission	Treatment group*	0.14	0.033; 0.61
	Time	1.06	1.03; 1.08

*Difference between treatment groups, MTX monotherapy responders as reference group , SE = standard error, 95% CI = 95% confidence interval

Conclusions: More patients achieved continuous low disease activity on prednisone or infliximab combination therapy tapered to MTX monotherapy than on MTX monotherapy, but there appear no additional benefits of combination treatment strategies for patients who have sustained DAS≤2.4. Regardless of initial induction therapy, those who remain in low disease activity have similar long term outcomes, with only the proportion of patients in drug free remission being higher in the MTX monotherapy group. These results strongly suggest that rapid achievement of remission/LDA itself, rather than how you achieve it, is crucial for determining long-term outcome in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1707

OP0253 PASSIVE SMOKING IN CHILDHOOD AND HISTORY OF CHRONIC DIARRHEA INCREASES THE RISK OF DEVELOPING RHEUMATOID ARTHRITIS (RA)

R. Seror[1,2], G. Gusto[3], M.C. Boutron-Ruault[3], X. Mariette[1,2]. *[1]Rheumatology, Hopitaux Universitaires Paris Sud; [2]INSERM U1184, Université Paris-sud, le Kremlin-Bicetre; [3]Centre de recherche en epidemiologie et santé des populations, Inserm U1018, Villejuif, France*

Objectives: To analyse the impact of active and passive smoking and intestinal transit disorders on the risk of incident RA
Methods: This study is based on the French E3N cohort ("Etude Epidémiologique auprès de femmes de l'Education Nationale"), which included 98,995 women volunteers born between 1925 and 1950 and prospectively followed since 1990. Eleven self-administered questionnaires were sent to the participants between 1990 and 2014 to collect medical, demographic, environmental and hormonal data and dietary habits. The diagnosis of RA was collected on 2 successive questionnaires. Cases were considered certain if having declared RA and had taken a RA specific medication (methotrexate, leflunomide or biologic) since 2004 (period from which drug reimbursement data was available). Only incident and certain cases were included. Women were excluded if they had an inflammatory bowel disease and/or no information on their smoking status. Passive smoking was assessed by the following question: "When you were children, did you stay in a smoky room?". Patients were considered exposed if the answer was "yes, a few hours, or yes, several hours a day". The usual intestinal transit, reported by women prior to RA diagnosis (on average 10 years), were classified as normal

transit, chronic diarrhoea, chronic constipation, and alternation between diarrhoea and constipation.
The risk of incident RA was estimated using an age-adjusted Cox model that considers smoking status as a time-dependent variable.
Results: 70598 women from the E3N study were included in the study. A total of 1239 patients reported an incidental RA, of which 350 cases were included in the study (and 280 in the analysis of intestinal transit disorders). Non-ascertained cases were excluded form the analyses. The age at inclusion in the study was 49.0 years (± 6.4). The mean duration of follow-up was 21.2 (± 1.3) years.
Passive smoking exposure during childhood increased the association between the RA risk active and adult active smoking. In ever smokers who had childhood passive exposure to smoke, the HR was 1.73 [1.20; 2.50] as compared with non-smokers who were not exposed during childhood, while it was 1.37 [1.08; 1.73] in active smokers who were not exposed during childhood.
A history of chronic diarrhea was associated with increased RA risk (HR =2.32 [1.41, 3.81]), while chronic constipation or alternation between diarrhoea and constipation did not.

Smoking status	Controls (%) N=70248	RA (%) N=350	HR [95% CI]
Non smoker No passive smoking in childhood	32440 (46,18)	137 (39,14)	Reference
Non smoker + Passive smoking in childhood	5010 (7,13)	30 (8,57)	1,43 [0,97; 2,13]
Ever smoker No passive smoking in childhood	27394 (39,00)	147 (42,00)	1,37 [1,08; 1,73]
Ever smoker + Passive smoking in childhood	5404 (7,69)	36 (10,29)	1,73 [1,20; 2,50]
Normal transit	44254 (71.48)	187 (66.79)	Reference
Chronic diarrhea	1707 (2.76)	17 (6.07)	2.32 [1.41; 3.81]
Constipation	8661 (13.99)	43 (15.36)	1.16 [0.84; 1.62]
Alternating diarrhea - constipation	7291 (11.78)	33 (11.79)	1.07 [0.74; 1.55]

Conclusions: This study confirms the link between active smoking and the risk of RA. It suggests for the first time that in smokers, exposure to tobacco early in life, through passive smoking in childhood significantly increases this risk. Our study highlights the importance of avoiding any tobacco environment in children, especially in those with a family history of RA. Also, it shows for the first time an association between a history of chronic diarrhoea and the risk of developing RA. The association supports the hypothesis of dysbiosis (microbiota abnormality) as a risk factor for the emergence of autoimmunity. These data perfectly fit with the preclinical scheme of RA where an external event occurs at an early stage to promote emergence of auto-immunity, followed years after by clinical RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3853

FRIDAY, 16 JUNE 2017

HPR move to improve

OP0254-HPR HAND EXERCISE FOR WOMEN WITH RHEUMATOID ARTHRITIS AND DECREASED ADL ABILITY: AN EXPLORATORY RANDOMISED CONTROLLED TRIAL

K. Ellegaard, C. von Bülow, A. Røpke, C. Bartholdy, I.S. Hansen, S. Rifbjerg, R. Christensen, M. Henriksen, E. Waehrens. *The Parker Institute, Frederiksberg, Denmark*

Background: Decreased strength and range of motion in the hand are often seen in rheumatoid arthritis (RA). Positive effects on hand function in RA patients after hand exercise and individual education in joint projection including coping strategies (ADL education) is shown (1;2). However, it is unknown if a combination of both will further improve hand performance.
Objectives: To investigate the effect on ADL ability of a hand exercise program as add on to an ADL education program in women with RA.
Methods: Women with RA involving the hand on stable medication for at least three months were recruited.
At baseline participants were examined by a rheumatologist who assessed joints of the hand and ruled out contraindications for participation e.g. massive malalignment of the joints. Inflammatory markers of the blood, hand pain and grip strength were also measured. The ADL motor ability was assessed using the observation-based Assessment of Motor and Process Skills (AMPS). After baseline examination randomized to ADL education + hand exercises (intervention; IG) or only ADL education (control; CG) was made.
All participants received three to four sessions with an occupational therapist learning how to perform ADL tasks overcome their specific hand problems. The intervention group also received a hand exercise program, to be conducted four times a week, for eight weeks, containing exercises for improving range of motion and strength; once a week the exercise program was supervised by a physiotherapist, to correct and prevent overload and to increase load if possible.
Primary outcome measure was change in observed ability to perform ADL tasks (AMPS) at week 8. Secondary outcomes include grip strength, pain, joint count, inflammatory markers and self-reported function.
After eight weeks, all baseline measures were repeated and changes from baseline were calculated based on the Intention To Treat (ITT) population.
Clinicaltrials.gov Identifier: (NCT02140866)
Results: Fifty five patients were randomised to IG (n=28) or CG (n=27); 22 and 25 patients, respectively, completed the trial. The ITT-populations mean age was 63.8 (12.8) years, mean disease duration was 12.4 (11.0) years. Baseline tender and swollen joint count was 5.07 (4.85) and 1.37 (1.72) respectively, the hand pain was 41.95mm (right) and 35.78mm (left) (VAS) and hand grip strength was 18.25 kg (right) and 17.46 kg (left). Baseline AMPS ADL motor measure was 1.36 (0.46). As judged by the 95% confidence intervals, no difference in change from baseline was seen between the groups (see table).

Change from baseline in and between groups (ITT analysis)

	Intervention group (n=28)	Control group (n=27)	Difference between groups	p-value
AMPS motor	0.24 (0.09-0.39)	0.20 (0.05-0.35)	0.04 (-0.17-0.25)	0.70
Tender joint count (28 joints)	-0.57 (-1.86-0.73)	0.35 (-0.95-1.64)	-0.92 (-2.77-0.93)	0.32
Swollen joint count (28 joints)	0.25 (-0.23-0.73)	0.16 (-0.32-0.64)	0.10 (-0.59-0.77)	0.78
CRP	-0.70 (-2.41-1.02)	1.77 (-0.09-3.63)	-2.45 (-5.0-0.06)	0.06
HAQ	-0.07 (-0.17-0.03)	0.01 (-0.09-0.12)	-0.08 (-0.23-0.06)	0.24
Hand pain activity (VASmm) Right/left	-1.17 (-7.82-5.48) -3.43 (-11.07-4.20)	0.55 (-6.23-7.31) -0.81 (-8.59-6.97)	-1.71 (-11.20-7.79) -2.62 (-13.62-8.38)	0.72 0.64
Hand strength (kg) Right/left	1.43 (0.40-2.45) 1.00 (-0.47-2.47)	0.18 (-0.86-1.23) -0.36 (-1.83-1.11)	1.24 (-0.23-2.71) 1.36 (-0.71-3.44)	0.10 0.19

Conclusions: A hand exercise program as add on to an ADL education did not improve ADL ability more than ADL education alone in women with RA experiencing decreased ADL ability involving the hands.
References:
[1] Masiero S et al. Effects of an educational-behavioral joint protection program on people with moderate to severe rheumatoid arthritis: a randomized controlled trial. Clin Rheumatol 2007 Dec;26:2043–50.
[2] Lamb SE et al. Exercises to improve function of the rheumatoid hand (SARAH): a randomised controlled trial. Lancet 2015 Jan 31;385(9966):421–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2911

OP0255-HPR AN ADD-ON PROGRAMME IMPROVED THE SHORT-TERM, BUT NOT THE LONG-TERM EFFECT OF REHABILITATION IN PATIENTS WITH RHEUMATIC DISEASES: RESULTS FROM A PRAGMATIC MULTI-CENTRE STEPPED-WEDGE CLUSTER RANDOMIZED CONTROLLED TRIAL

G. Berdal[1], K. Hagen[1], H. Dagfinrud[1], P. Mowinckel[1], I. Bø[2], T.N. Dager[1], A. Dingsør[3], S. Eppeland[4], J. Hagfors[5], B. Hamnes[2], M. Nielsen[5], A.-L. Sand-Svartrud[1], B. Slungaard[6], S. Wigers[7], I. Kjeken[1]. *[1]National advisory unit on rehabilitation in rheumatology, Diakonhjemmet Hospital, Oslo; [2]Hospital for Rheumatic Diseases, Lillehammer; [3]Betanien Hospital, Skien; [4]Sørlandet Hospital, Arendal; [5]The Norwegian Rheumatism Association, Oslo; [6]Martina Hansen's Hospital, Bærum; [7]Jeløy Kurbad Rehabilitation Center, Moss, Norway*

Background: Multidisciplinary rehabilitation is widely used alongside medical treatment of patients with rheumatic diseases. Although beneficial effects of such rehabilitation have been demonstrated, patients are mostly back to their initial health status 6 to 12 months after discharge.
Objectives: To evaluate an add-on rehabilitation programme designed to enhance and prolong the effect of rehabilitation in adult patients with rheumatic diseases.
Methods: We conducted a pragmatic multi-centre stepped-wedge cluster randomized controlled trial in six rehabilitation centres in Norway. All centres started simultaneously to include patients in the control phase (traditional rehabilitation),

whereupon they switched to the intervention phase (add-on programme) sequentially and in randomised order. The add-on programme comprised structured individualized goal planning, motivational interviewing, a self-help booklet and four supportive follow-up phone calls the first five months after discharge. Data were collected on admission, discharge, 6 and 12 months after discharge. Primary outcome was health related quality of life (HR-QoL) measured by the individualized Patient Generated Index (PGI). The main statistical analysis was a linear repeated measures mixed model performed on the intention to treat population (all available data).

Results: 389 patients with various rheumatic diseases (SpA, RA, OA, and SLE) were included (table 1). A significant treatment effect of the add-on intervention on HR-QoL was found on discharge (mean difference =3.32 [95% CI: 0.27, 6.37], p=0.03). There were no significant differences between the groups at 6 and 12 months. Treatment compliance was 94%, and response rate >80% at all time points. Both groups showed a positive effect of rehabilitation in terms of increased HR-QoL at discharge, which subsequently declined, although the values remained at higher levels after 6 and 12 months compared with baseline values (figure 1).

Table 1. Baseline characteristics of included patients (n=389)

	Control group (n=195)	Intervention group (n=194)
Age, yrs, mean (min, max)	56.9 (24, 89)	57.5 (23, 89)
Gender, ♀ , n (%)	127 (65.1)	147 (75.8)
Disease duration, yrs, mean (SD)	21.0 (13.3)	19.1 (13.1)
Paid work, n (%)	69 (35.8)	76 (39.4)
Using TNF-inhibitors, n (%)	44 (22.6)	39 (20.1)

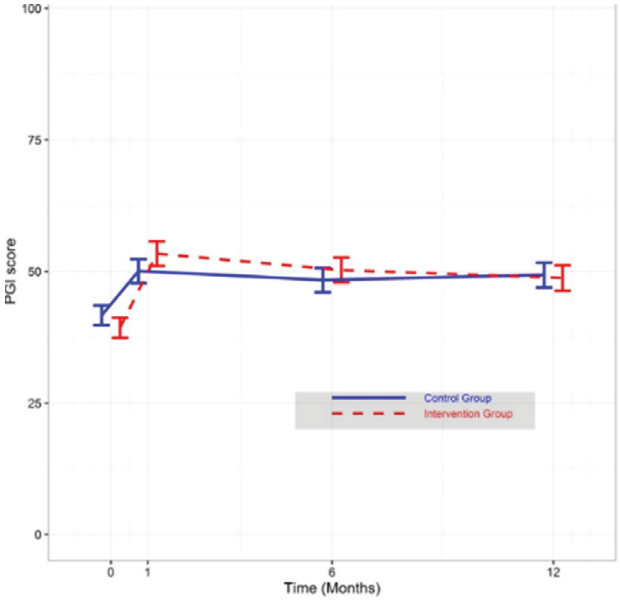


Figure 1. Health related quality of life in patients with rheumatic diseases measured by the Patient Generated Index (PGI, 0-100, 0 low HR-QoL). Vertical lines indicate the mean values (centre) with 95% confidence intervals at the four measurement time points: on admission to rehabilitation stay (baseline), at discharge, and six and twelve months after discharge. Horizontal lines show the fluctuating mean PGI values from baseline to 12 months after discharge.

Conclusions: The add-on intervention enhanced the short-term effect of rehabilitation with respect to HR-QoL, but did not prolong the effect as intended. The findings suggest that individualized structured goal planning should be considered important and relevant in rehabilitation of patients with rheumatic diseases. Although this study evaluated the effect of a complex intervention, and not the effect of single components, the results indicate that supportive telephone follow-up after discharge do not prolong the effect of rehabilitation. However, this study showed a longer lasting effect of rehabilitation in both the control- and intervention group, compared to previous reports.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3383

OP0256-HPR PHYSICAL ACTIVITY AND INACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C. Boström[1,2], F. Russ[1], F. Eriksson[1], S. Pettersson[2], I. Gunnarsson[1,2], E. Svenungsson[1,2]. *[1]Karolinska Institutet; [2]Karolinska Universitetssjukhuset, Stockholm, Sweden*

Background: Previous studies indicate that patients with systemic lupus erythematosus (SLE) have a reduced physical activity compared to controls and public health recommendations. However, most studies have used questionnaires without expressing the energy requirements for the activities.

Objectives: We investigated if self-reported physical activity, expressed in Metabolic Equivalent of Task (METs)-minutes/week, in patients with SLE is reduced. The aim was also to investigate if they fulfil the public health recommendations for physical activity.

Methods: 103 patients (93 women/10 men, mean age 51.5 (SD 15.9) years) with SLE according to the 1982 revised ACR criteria for SLE were involved. Physical activity was assessed with the short version of the International Physical Activity Questionnaire (IPAQ), which measure physical activity the last seven days. The IPAQ scientific group classify physical activity into the following categories: “inactive”, “minimally active”(equal to public health recommendations) and “health enhancing physical activity”. Those individuals who do not meet the criteria for the two latter categories are considered inactive.

Results: The patients reported that they were physically active in median 1666 (interquartile range 693; 3759) METs-minutes/week (n=84). The patients answered that they were sitting in median 6 (interquartile range 4; 8) hours/day the last week (n=98). 59.6% of the patients achieved a minimum of at least 600 METs-minutes/week, i.e. they were active 5 or more days with any combination of walking, moderate-intensity or vigorous intensity activities (“minimally active”). 17.9% achieved a minimum of at least 1500 METs-minutes/week, i.e. they were active on vigorous-intensity on at least 3 days or; achieved a minimum of at least 3000 METs-minutes/week, i.e. they were active 7 or more days on any combination of walking, moderate-intensity or vigorous intensity activities (” health enhancing physical activity”). 22.6% of the patients were “inactive”.

Conclusions: In the investigated patients with SLE, the majority were “minimally active” according to IPAQ-categories, which is sufficiently physically active according to the minimum level of public health recommendations. However, only 1/5 reached “health enhancing physical activity” category and 1/5 were considered physically “inactive”. Health professionals could use the short version of IPAQ to find out which patients with SLE need support in physical activity programmes.

References:

[1] Eriksson K et al. Physical activity in patients with systemic lupus erythematosus and matched controls. Scand J Rheumatol 2012; 41: 290–297.
[2] Ahn GE et al. Self-reported and objectively measured physical activity in adults with systemic lupus erythematosus. Arthritis Care & Research 2015; 67:701–707.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5359

OP0257-HPR RELATIONSHIP BETWEEN SLEEP DISORDERS AND DISEASE ACTIVITY IN PATIENS WITH RHEUMATOID ARTHRITIS

L. Villarreal[1], S. Henao[2], D. Buitrago-Garcia[3], P. Santos-Moreno[4]. *[1]Psychology and processes; [2]Patient service; [3]Epidemiology; [4]Rheumatology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: Rheumatoid arthritis (RA) is the prevalent autoimmune inflammatory arthritis found in adults, with the worldwide prevalence ranging from 0.4% to 1.3% (1). Patients with this condition have permanent changes with different severity of arthritis deformities as well as functional disturbances; Studies had shown that every painful condition disturbs sleep, which can lead to mood and abilities disturbances (2).

Objectives: The aim of this study was to describe the socio-demographic profile and sleep disorders in RA patients from a specialized RA clinic in Colombia and relationship with disease activity.

Methods: A descriptive cross-sectional study was performed in a specialized clinic dedicated to care patients with rheumatoid arthritis (RA). Data was collected during our psychology consultation, through semi-structured interviews and non-probability sampling. Descriptive epidemiology was applied for continuous variables, using measures of central tendency and dispersion for categorical and qualitative variables by averages and percentages. We analyzed bivariate association with Pearson’s X^2.

Results: We included 1398 patients attending to our psychology consultation. Mean age was 55±8. 80% were female and 20% male. Mean DAS28 was 2.6±1.3, mean HAQ was 1.6±1. 6; Patients had the disease for an average of 12 years ± 8; 41% of patients had comorbidities associated with non-autoimmune disease, 14% comorbidities related to autoimmune disease; 35% of our patients did not report other comorbidities. Most of patients were married 60%, followed by divorced 19%, single 14% and widowed 7%. Regarding occupation 33% were employees, 25% were housekeepers or retired due to age, 12% were retired due to disabilities, and 3% unemployed. Of the total population 45% had elementary school, 32% high school, 8% college education, 7% graduate education and 7% were illiterate. 17% of patients lived alone. When the psychologist asked about sleep disorders 69% reported no to have any, 25% primary insomnia, 1% hypersomnia, 3% OSAS and 2% alterations on the circadian rhythm. Disease activity was statically associated with sleep disorders ($p<0.00$).

Conclusions: Sleep problems are an important aspect to consider in a patient with RA and are correlated to disease activity; it is important to have a multidisciplinary care team for the patient with RA, including a psychologist that can manage this kind of illness in order to improve the life quality of patients.

References:

[1] Bautista-Molano W, Fernández-Avila D, Jiménez R, Cardozo R, Marín A, Soler MdP, et al. Epidemiological Profile of Colombian Patients With Rheumatoid

Arthritis in a Specialized Care Clinic. Reumatología Clínica (English Edition). 2016;12(6):313–8.
[2] Purabdollah M, Lakdizaji S, Rahmani A, Hajalilu M, Ansarin K. Relationship between Sleep Disorders, Pain and Quality of Life in Patients with Rheumatoid Arthritis. Journal of caring sciences. 2015;4(3):233–41.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5639

OP0258-HPR INTENSIVE PHYSICAL EXERCISE FOR ELDERLY PERSONS WITH RHEUMATOID ARTHRITIS IMPROVES PHYSICAL CAPACITY

E. Lange[1,2], D. Kucharski[3], K. Svensson[4], S. Svedlund[3], I. Gjertsson[2,3], K. Mannerkorpi[1,2]. *[1]Department of Health and Rehabilitation, Institute of neuroscience and physiology, Sahlgrenska academy, University of Gothenburg; [2]University of Gothenburg Centre for Person-centred Care; [3]Rheumatology and inflammation research, Institute of medicine, Sahlgrenska academy, Göteborg; [4]Skaraborg hospital, Skövde, Sweden*

Background: Today, more than 50% of persons with Rheumatoid Arthritis (RA) are over 65 years of age (1). Little is known about the effects of physical exercise in this age group (>65 years).
Objectives: The aim of this randomized controlled study is to investigate the effects of a person-centred progressive aerobic and resistance exercise program, led by a physiotherapist.
Methods: Seventy-four with persons with RA (24% men), mean age 70 years (SD 2.5), were recruited and randomized to an exercise interventions group or an active control group. The intervention consisted of a 20-week individual person-centered exercise program, performed three times a week with guidance from a physiotherapist. Both aerobic and resistance exercise was performed on a high intensity level. The control group followed a home exercise program twice a week. Muscle strength and endurance were assessed by the Chair Stands test, the Timed up and Go and a Bicycle endurance test. Maximal aerobic capacity (VO_2 max) was assessed with ergo spirometry. Activity limitations were assessed by SF36 Physical subscale and the Health Assessment Questionnaire (HAQ).
Results: All participants in the intervention group completed the intervention. The participants had a low disease activity with a mean Clinical Disease Activity Index of 5.4 (SD 3.9). Significant improvements were found for VO_2 max, the Chair Stands test, the Timed up and Go, the Bicycle endurance test on bicycle ($p<0{,}001$) and the SF36 physical (p=0.018) in the intervention group, when compared to the controls. No significant differences between groups were seen on HAQ.
Conclusions: Intensive progressive aerobic and resistance exercise is a feasible intervention for elderly persons with RA. Despite old age and RA the participants gained significant improvements in physical capacity.
References:
[1] Eriksson JK, Neovius M, Ernestam S, Lindblad S, Simard JF, Askling J. Incidence of rheumatoid arthritis in Sweden: a nationwide population-based assessment of incidence, its determinants, and treatment penetration. Arthritis Care Res (Hoboken). 2013;65(6):870–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2721

OP0259-HPR SUPERVISED WALKING IMPROVES AEROBIC CAPACITY, EXERCISE TOLERANCE, FATIGUE AND PERCEIVED IMPROVEMENT IN WOMEN WITH PRIMARY SJÖGREN'S SYNDROME: A RANDOMIZED CONTROLLED TRIAL

S.T. Miyamoto[1,2], V. Valim[3,4], L. Carletti[5], W.-F. Ng[6], R. Altoé[3], A.J. Perez[5], L.H. Dias[3], É.V. Serrano[3], A.M. Subtil[5], V.B. Cândido[5], M. Trenell[7], D. Lendrem[6], J. Natour[2]. *[1]Departamento de Educação Integrada em Saúde, Universidade Federal do Espírito Santo, Vitória; [2]Disciplina de Reumatologia, Universidade Federal de São Paulo, São Paulo; [3]Serviço de Reumatologia do HUCAM; [4]Departamento de Clínica Médica; [5]Laboratório de Fisiologia do Exercício (LAFEX), Universidade Federal do Espírito Santo, Vitória, Brazil; [6]Musculoskeletal Research Group, Institute of Cellular Medicine; [7]MoveLab, Physical Activity & Exercise Research, Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom*

Background: Fatigue is a very common symptom of primary Sjögren's syndrome (pSS), being reported by up to 70% of patients [1]. It is more pronounced when compared to healthy individuals [2] and patients often report that it is their greatest problem and the most difficult to cope with [3]. There is only one non-randomized controlled study on aerobic exercise in pSS with a small sample size suggesting improvement in fatigue, aerobic capacity, depression and physical function [4].
Objectives: To evaluate the safety and effectiveness of a supervised walking program in women with pSS.
Methods: Forty five sedentary women fulfilling the American European Consensus Criteria for pSS were randomized to a Training Group (TG, n=23) or Control Group (CG, n=22). Patients in the TG were submitted to supervised walking, 3 times a week, for 16 weeks. The patients of the CG were instructed to not perform any kind of regular physical exercise. Outcomes measured were aerobic capacity, fatigue, disease activity, depression, perception of pSS's symptoms and quality of life. An intent-to-treat analysis was performed.
Results: The mean change after 16 weeks of VO_{2max} ($ml.kg^{-1}.min^{-1}$), distance and FACIT-fatigue were higher in the TG than in the CG (p=0.016, p=0.043 and p=0.030, respectively) (Figure 1). Improved aerobic capacity was associated with improvements in fatigue scores and physical components of quality of life measured using SF-36. Furthermore, improved fatigue scores were associated with reduced depression and improvements in the physical and mental components of the quality of life measures. Overall, 95.4% of patients in the TG rated themselves as clinically improved versus 62% of the patients in the CG (p=0.049). There was no flare in disease activity and no serious adverse events with exercise.

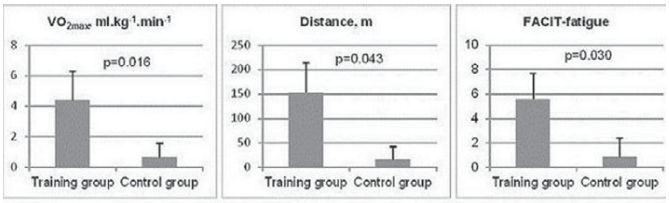


Figure 1. The exercise training group showed improved aerobic capacity, improved exercise tolerance and improved fatigue compared to controls.

Conclusions: This supervised walking program was demonstrated to be feasible and safe with improvements in the aerobic capacity, exercise tolerance, fatigue and patient perception of improvement in pSS patients.
References:
[1] Ng W-F, Bowman SJ. Primary Sjogren's syndrome: too dry and too tired. Rheumatology 2010;49(5):844–53.
[2] Strömbeck B, Ekdahl C, Manthorpe R, et al. Physical capacity in women with primary Sjögren's syndrome: a controlled study. Arthritis Rheum 2003;49(5):681–8.
[3] Meijer JM, Meiners PM, Huddleston Slater JJR, et al. Health-related quality of life, employment and disability in patients with Sjogren's syndrome. Rheumatology 2009;48(9):1077–82.
[4] Strömbeck BE, Theander E, Jacobsson LTH. Effects of exercise on aerobic capacity and fatigue in women with primary Sjogren's syndrome. Rheumatology 2007;46(5):868–71.
Acknowledgements: This work was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES Foundation [BEX 8831/14–9 to S.T.M].
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3854

OP0260-HPR HIGHER SATISFACTION WITH ACTIVITY-RELATED SYMPTOMS AFTER 15-WEEK RESISTANCE EXERCISE IN WOMEN WITH FIBROMYALGIA

K. Mannerkorpi[1,2], A. Larsson[2], A. Palstam[1], M. Ernberg[3], B. Gerdle[4], E. Kosek[5]. *[1]Inst of Neuroscience and physiology; [2]Gothenburg Center of Person-centred Care (GPCC), University of Gothenburg, Göteborg; [3]Department of Dental Medicine, Karolinska Institute, Stockholm; [4]Department of Medical and Health Sciences, Linköping University, Linköping; [5]Department of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden*

Background: Physical exercise is troublesome for most patients with fibromyalgia (FM) due to activity-induced pain. A reason for activity-induced pain is a low pain threshold. In the present study we investigated if experience of physical activity changed after 15-week progressive person-centred resistance exercise. The control group participated in 15-week relaxation program.
Objectives: To investigate how experience of physical activity changed after 15-week resistance exercise in women with FM, and if experiences correlated with pain threshold.
Methods: 130 women (age 22–64 years, symptom duration 0–35 years) with FM were randomized to 15-week resistance exercise or to a parallel relaxation program. The participants completed Experience of physical activity scale (EPA) comprising five subscales (0–7), assessing how exercise was perceived in terms of Physical relaxation (PR), Well-being (WB), Activity beliefs (AB), Activity-related symptoms (ARS), and Activity Habits (AH) (1). A lower score indicates a higher satisfaction. Pain threshold was investigated with algometer. Within-group and between-group analyses were conducted by non-parametric statistics. Correlations between algometry and ratings on EPA were investigated by Spearman correlation coefficient.
Results:
The resistance exercise group scored significantly higher satisfaction at posttest than before the intervention in their ratings on how they experienced exercise in terms of PR, WB, ARS and AH ($p<0.05$), Table 1.
Between-group analyses showed that the resistance exercise group scored significantly higher satisfaction in ARS subscale ($p<0.006$) after the intervention when compared to the relaxation group.
Significant correlations were found between algometry and PR (rs -0.32, p=0.017) as well as ARS (-0.33, p=0.015) at post-test in the resistance exercise group.

Table 1. Baseline and post-test ratings of EPA in the two groups

EPA subscales	Resistance exercise		Relaxation	
	Baseline (n=67)	15 weeks (n=56)	Baseline (n=63)	15 weeks (n=49)
PR	3.9±1.1	3.6±1.0*	4.1±1.3	3.9±1.2
WB	2.9±1.5	2.5±1.2*	2.7±1.3	2.7±1.4
AB	2.0±1.0	1.9±1.2	2.1±1.3	2.0±1.2
ARS	4.7±1.2	4.1±1.1*	4.9±1.1	4.8±1.1
AH	4.1±1.3	3.1±1.5*	3.7±1.3	3.6±1.4

Within-group changes ($p<0.05$) are marked with *.

Conclusions: Women with FM experienced a higher satisfaction with activity-related symptoms after having participated in a person-centered resistance exercise program, which is an important knowledge for health care professionals when motivating patients for exercise. Correlations between algometry and ratings on PR and ARS indicate that activity-related symptoms are partly associated with the pain threshold.

References:

[1] Mannerkorpi K, Rivano-Fischer M, Ericsson A, Nordeman L, Gard G. Experience of physical activity in patients with fibromyalgia and chronic widespread pain. Disabil Rehabil 2008;30 (3):213–21.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4997

OP0261-HPR PHYSICAL ACTIVITY LEVEL MEASURED BY ACCELEROMETER IS COMPARABLE BETWEEN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS AND CONTROLS, BUT PATIENTS SPEND LESS TIME IN VIGOROUS PHYSICAL ACTIVITY

K. Risum[1], A.M. Selvaag[1], Ø. Molberg[1], H. Dagfinrud[2], H. Sanner[1]. *[1]Oslo University Hospital; [2]Diakonhjemmet Hospital, Oslo, Norway*

Background: Previous studies indicate that juvenile idiopathic arthritis (JIA) patients have lower levels of physical activity (PA), spend more time in sedentary PA and less time in moderate and vigorous PA than controls. Associations between PA and disease variables in JIA patients are inconclusive. To our knowledge, this study is the first to compare objectively measured PA in JIA patients treated in the era of biologics with healthy controls whose data collection were conducted at the same time as the patients.

Objectives: To compare objectively measured levels and intensity of PA in JIA patients who have had access to biological treatment from disease onset with age- and sex-matched controls from the general population. Furthermore, to compare PA between JIA patients with persistent oligo- and poly-articular disease, and to examine associations between PA and disease variables in patients.

Methods: Patients, 10–16 years, with persistent oligo- or poly-articular disease (extended oligoarthritis and polyarticular RF +/-), were recruited consecutively at Oslo University Hospital in 2015. Age- and sex-matched controls were selected randomly from the Norwegian Population Registry. PA was measured with accelerometers during 7 consecutive days. The general level of PA was determined by counts per minute (cpm) and steps daily. Cut-off points for different PA categories of intensity were used as described by Evenson[1]. Present pain, and pain and fatigue during the previous week were assessed in all participants. Disease activity, functional ability, diasease duration, use of medication and lower extremity joints with active arthritis were registered in patients. Differences between study groups were analyzed with paired or unpaired analyses as appropriate.

Results: Acceptable data from the accelerometers were retrieved in 53 matched pairs, of which 45 (85%) were female. Mean age was 13.3±2.2 years in patients and 13.2±2.6 years in controls, p=0.55. 26 (49%) patients had polyarticular disease. No significant differences were found in cpm or steps daily, or in time spent in sedentary PA, light PA or moderate PA in patients vs controls (Table 1). However, patients spent significantly less time in vigorous PA than controls. No significant differences in PA variables were found between JIA subgroups. The use of biologic medication correlated weakly with cpm, r=0.30, p=0.03, while no other disease variables correlated significantly with cpm or with vigorous PA (all $r<0.30$, p=NS).

Conclusions: General level of physical activity and time spent in sedentary PA, light PA and moderate PA in JIA patients treated in the biological era are comparable with controls. However, patients spend less time in vigorous PA.

Table 1. Physical activity

	JIA (n=53)	Controls (n=53)	p-value
Counts per minute	457±194	483±135	0.45
Steps daily	9219±2679	9772±2575	0.27
Sedentary daily (min)	575±69	571±58	0.66
Light PA daily (min)	189±48	183±42	0.39
Moderate PA daily (min)	33±11	37±12	0.08
Vigorous PA daily (min)	21±12	26±14	0.04
Achieves 60 min MVPA daily n (%)	17 (32)	26 (49)	0.09

Numbers are mean ± SD or N (%).

Even though these results are promising regarding PA in JIA patients, the results indicate that patients still need to be encouraged to be physically active, with emphasis on increasing vigorous PA.

References:

[1] Evenson et al 2008.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6908

FRIDAY, 16 JUNE 2017

Gout: advances in diagnosis and management

OP0262 TRENDS AND COSTS FOR GOUT HOSPITALIZATION IN SWEDEN

M.I. Dehlin[1], V. Sigurdardottir[1], P. Drivelegka[1], A. Svärd[2], L.T. Jacobsson[1]. *[1]Dept of rheumatology and inflammation research, Institution of medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg; [2]Rheumatology Clinic, Falun Hospital, Falun, Sweden*

Background: Gout is the most common arthritic disease in the world with increasing incidence and prevalence. There are differences in gout prevalence and course of disease due to cultural, ethnical and genetic factors stressing the need for data from different parts of the world. An increase in hospitalization for gout has been shown for the last two decades in North America.

Objectives: We evaluated the trend for hospitalization of gout in western Sweden 2000 – 2012 and the health care costs for this 2009 – 2012.

Methods: Hospitalization trends for gout were studied using data from the health care consumption register in the Western Swedish Health Care Region (WSHCR) from 2000–01–01 through 2012–12–31. This area is considered to be representative for the country as a whole. Patients aged 18 years and older who were hospitalized during the study period with a principal ICD-10 diagnosis of gout (M10) at discharge were included. We calculated annual population rates for hospitalization for gout. Inflation-adjusted health care costs for the gout hospitalizations were calculated using the Cost-Per-Patient register (CPP). Dispensation of urate lowering therapy (ULT), allopurinol (M04AA01) and probenecid (M04AB01), within 6 months prior to hospitalization was identified using The Swedish Prescribed Drug Register.

Results: There were 1873 hospitalizations for gout (mean age 75.0–77.6 years, 61–74% men) between 2000 and 2012. Demographic characteristics were similar

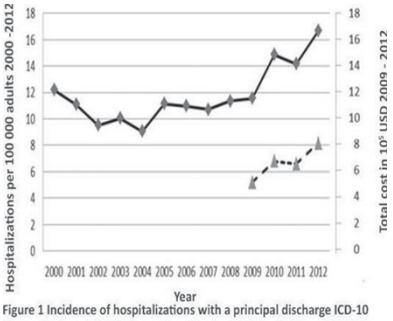


Figure 1 Incidence of hospitalizations with a principal discharge ICD-10 diagnosis of gout (M10) in western Sweden 2000 to 2012 per 100 000 adults (≥18 year) (full line,left side) and total cost for the hospitalizations in 105 USD 2009 to 2012 (dashed line, right side)

Abstract OP0262 – Table 1

	2000	2002	2004	2006	2008	2009	2010	2011	2012
Discharges, no	142	112	108	133	140	144	187	180	213
Incidence per 100 000 adults	12.2	9.5	9. 1	11.0	11.3	11.5	14.9	14.2	16.7
Men, incidence per 100 000 adults	16.1	12.3	12.9	14.4	15.7	16.0	22.0	21.1	24.3
Women, incidence per 100 000 adults	8.4	6.8	5.3	7.7	7.0	7.1	7.9	7.3	9.1
Duration, days, median (range)	3 (1–71)	3 (1–44)	5 (1–75)	5 (1–65)	5 (1–40)	5 (1–39)	5 (1–34)	5 (1–52)	5 (1–41)
Age, years, mean, SD	76.2 (12.1)	74.3 (14.9)	76.3 (11.7)	77.2 (10.2)	77.4 (11.4)	76.7 (11.6)	77.6 (12.7)	75.6 (14.1)	75.0 (13.8)
18–44	3	6	1	0	5	4	8	8	4
45–64	23	16	17	19	12	11	19	28	41
65–84	83	63	67	80	85	89	100	92	108
≥85	33	27	23	34	38	40	60	52	60
ULT, (%), 6 months before hospitalization				28 (21)	38 (27)	27 (19)	38 (20)	47 (26)	45 (21)
Total cost*, 10^5 USD						5.21	6.8	6.6	8.15

over the study period. From 2000 to 2012, the annual hospitalization rate for gout increased from 12.2 to 16.7 per 100 000 adults (p=0.0038). The increase was most pronounced in males aged 65 and above and over the last three years of the study. From 2009 to 2012 the inflation-adjusted health care costs for gout hospitalizations increased from 5.21 to 8.15 10^5 USD. The duration of hospitalizations also increased from 3 to 5 days median 2000 and 2012 respectively (p=0.021). Only a minority of patients, 19 to 27%, received ULT the 6 months preceding their hospitalization, without any obvious secular trend.

Conclusions: Incidence of hospitalization for primary gout is increasing substantially in Sweden over the last decade and this is reflected in the health care costs. The main part of this increase consists of males aged 65 and above. Only a fourth of the patients were on ULT preceding the hospitalization. These findings are further emphasized by the fact that the total amount of days for somatic inpatient care in WSHCR decreased by 9% from 2002 (1 267 900 days, mean duration 5,7 days) to 2012 (1 151 630 days, mean duration 4,9 days). The findings in this study reflects increasing incidence of the gout disease and an ageing population but also a considerable lack of treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1825

OP0263 TRANS-ANCESTRAL META-ANALYSIS IDENTIFIES 13 NEW LOCI ASSOCIATED WITH SERUM URATE LEVELS

T.R. Merriman[1], M. Cadzow[1], R. Topless[1], D. Mount[2], H. Choi[3], Y. Okada[4], J. Boocock[5], E. Stahl[6]. *[1]University of Otago, Dunedin, New Zealand; [2]Brigham and Women's Hospital; [3]Harvard Medical School, Boston, United States; [4]Osaka University, Osaka, Japan; [5]University of California Los Angeles, Los Angeles; [6]Mt Sinai School of Medicine, New York, United States*

Background: Serum urate is an important biomarker for gout disease and kidney function. Genome-wide association study (GWAS) meta-analyses have identified 28 loci in European and East Asian population samples. Combined analysis of these summary data across populations offers the opportunity to discover new serum urate associations through greater sample size and power, and trans-ancestral analyses provide the opportunity for fine-mapping associations with greater resolution given differing linkage disequilibrium patterns between populations.

Objectives: To conduct a meta-analysis of European and East Asian serum urate GWAS.

Methods: Summary statistics from European (N=110,238) (Kottgen et al. 2013) and east Asian (N=21,268) (Okada et al. 2012) meta-analyses were obtained. We used ImpG v1.0 to impute the results into 1000 Genomes phase 3 variants, and performed sample-size weighted z-score meta-analysis. Linkage-disequilibrium (LD)-independent variants with $P_{META} < 5x10–8$, not in LD ($r2<0.1$) with previously identified regions, were considered novel serum urate loci. We used functional partitioned LD score regression on all associated loci in the European GWAS to identify SNP-heritability enriched tissue-specific regulatory regions, for use as functional priors in PAINTOR fine mapping analyses to identify putative causal variants.

Results: The trans-ancestral meta-analysis of European and East Asian GWAS revealed nine new serum urate-associated loci ($P_{META}<5x10^{-8}$). Three of the new loci are located in the 11q12.3–13.2 region near the established SLC22A11/12 locus. Additional novel loci are located near the FGF5, LNC00603, HLA-DQB1, B4GALT1, BICC1 and USP2 genes. Tissue-focused functional partitioning of SNP-heritability indicated the strongest enrichments of kidney, GI and liver tissues ($P<10^{-7}$), among other significant tissues. Trans-ancestral meta-analysis and functional fine-mapping decreases the numbers of SNPs in causal variant credible sets, and for example pinpoints the rs17632159 SNP as likely causal (posterior $P>0.9$) at the TMEM171/174 locus.

Conclusions: Meta-analysis of existing GWAS increases power and leads to the identification of nine new loci associated with serum uric acid levels. Increased resolution in trans-ancestral GWAS, with functional annotation enrichments, improves fine-mapping of serum urate GWAS loci.

References:

[1] Köttgen A, et al. Genome-wide association analyses identify 18 new locis associated with serum urate concentrations. Nature Genet. 2013;45:145–54.
[2] Okada Y, et al. Meta-analysis identifies multiple loci associated with kidney function-related traits in east Asian populations. Nature Genet. 2012;44:904–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4611

OP0264 CAN MODERATE ALCOHOL INTAKE LOWER THE RISK OF MYOCARDIAL INFARCTION AND MORTALITY EVEN AMONG GOUT PATIENTS?

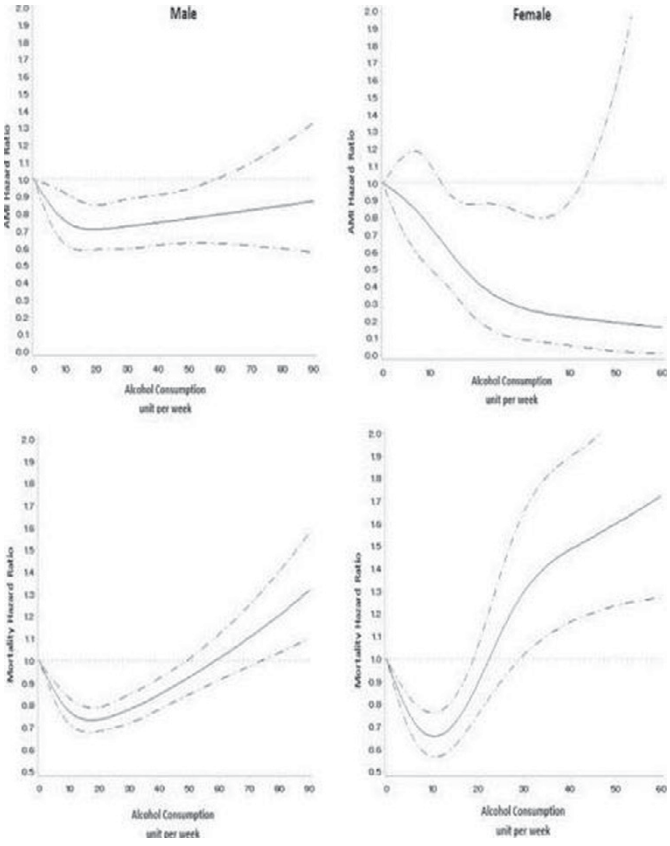
H.K. Choi[1], N. Lu[1,2], S.K. Rai[1], S.F. Keller[1], A.M. Jorge[1], Y. Zhang[1,2]. *[1]Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital; [2]Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, United States*

Background: While alcohol is a well-established risk factor for gout, many prospective studies have consistently found that moderate alcoholic consumption is associated with a 25–40% reduced risk for coronary heart disease (CHD) and death. As such, the American Heart Association (AHA) suggests that "if you drink alcohol, do so in moderation". As gout is associated with an increased risk of CHD and premature mortality, the potential benefits of drinking in moderation may also be applicable to gout patients provided that their gout is under control with other measures.

Objectives: To examine the relation between alcohol intake and the risk of acute myocardial infarction (AMI) and all-cause mortality among incident gout patients in a general population context.

Methods: We conducted a cohort study using data from an electronic medical record database representative of the UK general population, collected between 1995 and 2015. The exposure of interest was the first alcohol intake measured after gout diagnosis, and our endpoints were incident cases of AMI as well as all-cause mortality. Stratifying by sex, we calculated the hazard ratios (HR) of these endpoints according to alcohol intake categories (i.e., 0, 1–9, 10–24, 25–42, and >42 UK alcohol units/week [1 unit=8gm]), adjusting for age, smoking status, body mass index, duration of gout, comorbidities, and medication use. We performed a spline model analysis using 4 knots of the alcohol intake categories, hypothesizing a J-shaped relation as observed in general population studies.

Results: Among 55,584 gout patients (78% male, mean age of 63 years), 1,332 developed AMI and 8,362 died over a mean follow-up of 5.6 years. Compared with men who did not drink alcohol after gout onset, men who drank alcohol had a lower risk of AMI as well as mortality in a J-shaped manner (Figure 1, left panel). The multivariable HRs for developing AMI were 1.0, 0.76 (95% confidence interval [CI], 0.63–0.93), 0.68 (0.55–0.83), 0.69 (0.53–0.89), and 0.71 (0.52–0.95) for alcohol use categories of 0, 1–9, 10–24, 25–42, and >42 units/week, respectively, and the corresponding HRs for mortality were 1.0, 0.77 (95% CI, 0.71–0.82), 0.71 (0.66–0.77), 0.74 (0.66–0.82), and 0.89 (0.78–1.01) (Figure 1, left panel). While alcohol consumption levels and sample sizes were smaller among women, the J-shaped relation was more obvious and showed a significantly increased risk of mortality in the top consumption category (HR=1.68; 95% CI, 1.09–2.61) (Figure 1, right panel).



Conclusions: This general population-based study indicates that moderate alcohol intake is associated with a lower risk of AMI as well as all-cause mortality among gout patients, similar to many general population studies. These findings suggest that the AHA recommendation about moderate alcohol use may also be applicable to gout patients for their cardiac health and improved survival, provided that their gout is under control with other measures.

Acknowledgements: This project was supported in part by NIH grant P60-AR-047785 and NIH grant R01-AR-065944.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6906

OP0265 VALIDATION OF A DEFINITION FOR ATTACK (FLARE) IN PATIENTS WITH ESTABLISHED GOUT

A. Gaffo[1,2], N. Dalbeth[3], J. Singh[1,2], K. Saag[1], W. Taylor[4]. *[1]University of Alabama at Birmingham; [2]Birmingham VA Medical Center, Birmingham, United States; [3]University of Auckland, Auckland; [4]University of Otago, Otago, New Zealand*

Background: A standardized validated definition for gout attacks (flares) is not available. Two provisional definitions published in 2012 were based on patient-reported elements (patient-defined attack, pain at rest greater than 3 in a 0–10 numeric rating scale, presence of at least one swollen joint, presence of at least one warm joint) (1). These definitions had acceptable sensitivity and specificity but lacked external validation which is necessary before they can be adopted in gout clinical studies.
Objectives: To perform external validation of previously published preliminary gout attack (flare) definitions in patients with gout.
Methods: We enrolled 509 participants with gout from 17 international sites in a cross-sectional study performed during routine clinical care. All patients met the 2015 ACR/EULAR classification criteria for gout (2). Criteria for the previously published gout attack definitions were collected by a site investigator and the final adjudication of a gout attack status was done by a local expert rheumatologist, through an evaluation independent from that of the site investigator. Logistic regression, Bayesian statistics, and receiver-operator curves were used to calculate the final diagnostic performance of the gout attack definitions.
Results: The mean age of participants was 57.5 years (standard deviation [SD] 13.9) and 89% were men. Mean disease duration was 12.3 (SD 10.3) years, 35% had tophi, and 75% were taking urate-lowering therapies. The previously published and favored definition requiring the presence of 3 or more out of 4 criteria ("number of criteria") was found, using the current study data, to be 85% sensitive and 95% specific in confirming the presence of an attack in patients with gout (Table). The concurrent logistic regression model had an area under the curve of 0.97. The previously published definition based on a classification and regression tree algorithm (entry point pain at rest >3 followed by patient-defined attack "yes") was 73% sensitive and 96% specific using the current study data (Table). The "number of criteria" approach with a cut-point at 3 or more out of 4 criteria had higher diagnostic accuracy using the current study data than in its initial 2012 description (92% versus 84%, table). (1) Finally, using current study data the "number of criteria" approach at 3 or more out of 4 criteria had higher accuracy to the classification and regression tree algorithm based approach (92% versus 89%) but with a much better sensitivity (85% versus 73%).

Table. Diagnostic performance of gout attack (flare) definitions: "number of criteria"* and classification and regression tree (CART)

	Sensitivity% (95% CI)	Specificity% (95% CI)	PPV% (95% CI)	NPV% (95% CI)	Accuracy% (95% CI)
Number of criteria (current study)					
1 or more	100 (100)	66 (61-715)	57 (51-63)	100 (100)	77
2 or more	97 (94-100)	88 (84-91)	78 (72-84)	98 (97-100)	91
3 or more	85 (80-91)	95 (93-97)	88 (83-93)	94 (91-96)	92
All 4	61 (54-69)	98 (97-100)	94 (90-99)	85 (82-88)	87
3 or more (2012 provisional definition)†	91 (80-97)	82 (75-88)	64 (52-74)	96 (91-99)	84
CART‡ (current study)	73 (66-80)	96 (94-98)	90 (84-95)	89 (86-92)	89
CART (2012 provisional definition)	83	90	85	91	

CI = confidence interval, PPV = positive predictive value, NPV = negative predictive value
CART = classification and regression tree
*Criteria include: patient-defined gout attack, pain at rest greater than 3 in an 0-10 numeric rating scale, Presence of at least one swollen joint, presence of at least one warm joint
†3 or more criteria was found to have the best performance in a receiver-operator curve analysis
‡CART rule: Pain at rest > 3 followed by patient-defined gout attack positive

Conclusions: The definition requiring the presence of 3 or more out of 4 patient-reported criteria is validated to be sensitive, specific, and accurate in identifying attacks (flares) in patients with gout using an independent large international sample. Having a validated gout attack definition will improve ascertainment of outcomes in gout clinical studies.
References:
[1] Gaffo AL et al. Arthritis Rheum. 2012;65:1508.
[2] Neogi T et al. Ann Rheum Dis 2016;75:473.
Acknowledgements: Funding provided by AstraZeneca, Ardea Biosciences, Inc., and Ironwood Pharmaceuticals.
Disclosure of Interest: A. Gaffo Consultant for: SOBI, N. Dalbeth Grant/research support from: AstraZeneca, Consultant for: Takeda, Pfizer, AstraZeneca, Cymabay, and Crealta, Paid instructor for: Takeda, AstraZeneca, J. Singh Grant/research support from: Takeda, Savient, Consultant for: Savient, Takeda, Regenron, Merz, Bioiberica, Crealta, Allergan, WebMD, UBM LLC, American College of Rheumatology, K. Saag Consultant for: Takeda, Horizon, SOBI, W. Taylor Consultant for: Pfizer, AstraZeneca, Abbvie, Roche
DOI: 10.1136/annrheumdis-2017-eular.3219

OP0266 PRESENCE OF MONOSODIUM URATE CRYSTALS BY DUAL-ENERGY COMPUTED TOMOGRAPHY IN GOUT PATIENTS TREATED WITH ALLOPURINOL

N. Dalbeth[1], S. Nicolaou[2], S. Baumgartner[3], J. Hu[3], M. Fung[3], H.K. Choi[4]. *[1]University of Auckland, Auckland, New Zealand; [2]Vancouver General Hospital and University of British Columbia, Vancouver, Canada; [3]Formerly Ardea Biosciences, Inc, San Diego; [4]Harvard Medical School and Massachusetts General Hospital, Boston, United States*

Background: Chronic hyperuricemia predisposes to deposition of monosodium urate (MSU) crystals in musculoskeletal and other tissues, causing chronic inflammation, acute gout flares, joint damage, and disfiguring tophi. Dual-energy computed tomography (DECT) is a useful imaging tool to detect and quantify MSU crystal deposits.
Objectives: This study assessed the evidence of MSU crystal deposition using DECT scanning among gout patients treated with allopurinol and the potential determinants associated with the observed deposits.
Methods: The multicenter DECT study recruited patients with gout from the USA and New Zealand who were taking allopurinol at ≥300 mg daily for at least 3 months. MSU crystal deposition was measured using DECT in hands/wrists, knees, and feet/ankles bilaterally. The presence of MSU crystals as well as the total volume of crystals were assessed according to gout characteristics and serum uric acid (sUA) levels.
Results: Patients (N=153) were predominately male (92.2%), with mean (SD) age 58.5 (11.4) years, and gout duration 14.9 (10.3) years. sUA was ≥6.0 mg/dL in 49.0% of patients. 81.7% of patients took allopurinol at a stable dose of 300 mg/day and the remainder at >300 mg/day. 69.1% of patients had MSU crystal deposits with a total median crystal volume of 0.16 cm^3 (range, 0.01 to 19.53 cm^3). Those with sUA ≥6.0 mg/dL and palpable tophi showed the highest prevalence of urate deposits (90%), and those with sUA <6.0 mg/dL and no palpable tophi showed the lowest prevalence (47%). Those who reported a gout flare within the prior 3 months (versus none), were prescribed allopurinol doses >300 mg (versus 300 mg), and had palpable tophi (versus none) had greater deposit volume.

Table. Summary of Urate Deposits on DECT Scan According to Palpable Tophus Status and sUA Level.

	Tophi		No tophi		Total
	sUA ≥6.0 mg/dL (n=20)	sUA <6.0 mg/dL (n=28)	sUA ≥6.0 mg/dL (n=55)	sUA <6.0 mg/dL (n=50)[a]	(N=153)[a]
Median volume (range) for nonmissing urate deposits	0.26 (0.00, 19.53)	0.16 (0.00, 4.63)	0. 09 (0.00, 1.23)	0.00 (0.00, 0.89)	0. 07 (0.00, 19.53)
Presence of urate deposits, n (%)	18/20 (90.0)	20/28 (71.4)	44/55 (80.0)	23/49 (46.9)	105/152 (69.1)
	P=0.16[b]		P<0.001[b]		
	P<0.001[c]				
Median volume (range) for positive scans	0.37 (0.01, 19.53)	0.29 (0.05, 4.63)	0.12 (0.01, 1.23)	0.14 (0.01, 0.89)	0.16 (0.01, 19.53)

[a] MSU crystal deposition data missing in 1 patient.
[b] Fisher's Exact test and Pearson's Chi-square test for pairwise comparisons.
[c] Pearson's Chi-square test across the 4 groups.

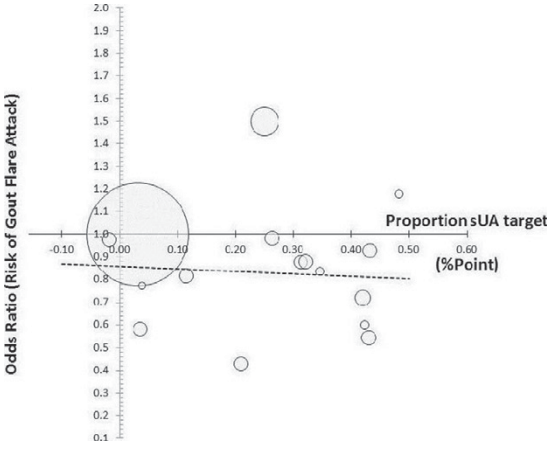
Conclusions: Despite a stable dose of allopurinol for more than 3 months, and even with sUA at the target level, a substantial proportion of patients with gout continue to have evidence of MSU crystal deposition by DECT scan. Patients with palpable tophi, sUA levels ≥6.0 mg/dL, and gout flares within the prior 3 months have a greater volume of MSU crystal deposition. These patients may need continuation and/or intensification of their urate-lowering therapy regimen.
Acknowledgements: This study was sponsored by Ardea Biosciences/AstraZeneca.
Disclosure of Interest: N. Dalbeth Grant/research support from: AstraZeneca, Consultant for: AstraZeneca, Fonterra, Takeda, Pfizer, Cymabay, Crealta, Speakers bureau: Menarini, AstraZeneca, Takeda, S. Nicolaou Grant/research support from: Siemens Healthcare, S. Baumgartner Employee of: Ardea Biosciences, Inc, J. Hu Employee of: Ardea Biosciences, Inc, M. Fung Employee of: Ardea Biosciences, Inc, H. Choi: None declared
DOI: 10.1136/annrheumdis-2017-eular.3666

OP0267 SERUM URATE AS A SURROGATE ENDPOINT FOR GOUT FLARES: RESULTS OF A SYSTEMATIC REVIEW AND META-REGRESSION ANALYSIS OF RANDOMIZED TRIALS

L. Stamp[1], M. Morillon[2], W. Taylor[3], N. Dalbeth[4], J. Singh[5], R. Christensen[6]. *[1]Medicine, University of Otago, CHRistchurch, Christchurch, New Zealand; [2]Odense University Hospital, Odense, Denmark; [3]University of Otago, Wellington; [4]University of Auckland, Auckland, New Zealand; [5]University of Alabama, Birmingham, United States; [6]Musculoskeletal Statistics Unit, The Parker Institute, Odense, Denmark*

Background: The primary outcome measure for efficacy in clinical trials of urate lowering therapy (ULT) is frequently serum urate (SU), effectively acting as a surrogate for patient-centred outcomes (e.g. gout flares). It has not been clearly demonstrated that the strength of the relationship between SU and patient-centred outcomes is strong enough for SU to be considered a surrogate.

Objectives: To determine the strength of the relationship between SU and the incidence of gout flares and thereby to determine whether SU is a valid surrogate endpoint according to the BSES3 framework.
Methods: A systematic search of Medline via PubMed, the Cochrane Central Register of Controlled Trials, EMBase via OVID, the Institute for Scientific Information Web of Science, and other sources identified relevant studies. Standardised data elements were extracted by 2 independent reviewers (LS, MBM) and disagreements resolved by discussion (RC). Eligible trials were parallel-group, randomised trials of ULT of at least 3 months duration in people with gout. For the meta-regression analysis, a mixed linear model was used to combine the ratio of flare rates between groups (SAS software, v9.4 for Windows). Trials with multiple arms were treated as individual trials, referred to as "randomised comparisons" (i.e., 3-arm trials with 2 active interventions was handled as 2 randomised comparisons). Data was analysed by meta-regression using the between-arm difference in proportion of individuals who achieved target SU (<0.36mmol/L) as independent variable from at 3 months (or 6 and 12 months if 3 month values not available) against flare rate (dependent variable).
Results: After screening 234 abstracts, 82 trials were scrutinized, of which 9 trials (with 16 comparisons) met inclusion criteria. A total of 5,696 people with gout entered into the meta-regression model. The longest RCT included was only 12 months duration. The pooled Odds Ratio (OR) suggested a small but statistically significant favourable association between the active and comparator urate lowering therapies and flare frequency (OR, 0.83; 95% CI 0.70 to 0.99]). Substantial heterogeneity was present (between trial variance: 0.07; 0.03 to 0.30). Meta-regression analysis did not reveal any statistically significant association between the proportion of individuals who achieved target SU and the observed flare rate (P=0.82); the model fit did not improve after inclusion of the covariate into the model (between trial variance: 0.08; 0.03 to 0.33) (Figure).



Conclusions: Substituting surrogate endpoints (proportion achieving target SU) for the important clinical outcome (gout flares) allows conduct of shorter smaller trials. However, based on aggregate trial-level data (meta-regression) an anticipated association between SU and gout flare could not be confirmed. Trial duration may have been too short to observe a reduction in flares and further work using data from long-term extension studies is underway.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1544

OP0268 NURSE-LED CARE VERSUS GENERAL PRACTITIONER CARE OF PEOPLE WITH GOUT: A UK COMMUNITY-BASED RANDOMISED CONTROLLED TRIAL

M. Doherty[1], W. Jenkins[1], H. Richardson[1], A. Abhishek[1], D. Ashton[1], C. Barclay[1], L. Duley[2], H. Jones[1], M. Santarelli[1], A. Sarmanova[1], M. Stevenson[3], W. Zhang[1]. *[1]Division of Rheumatology, Orthopedics and Dermatology; [2]Clinical Trials Unit, University of Nottingham, Nottingham; [3]Health Economics and Decision Science, University of Sheffield, Sheffield, United Kingdom*

Background: Despite increasing prevalence of gout in the UK (1), a variety of barriers result in suboptimal care (1,2) with only 40% of gout patients receiving urate-lowering therapy (ULT), usually at fixed dose without titration to a serum uric acid (SUA) target (1,2). Nurses successfully manage many chronic diseases in the community, and we have shown that when people with gout are fully informed and involved in management decisions uptake of ULT is high and subsequent adherence under nurse-led care is excellent (3).
Objectives: To directly compare nurse-led care to general practitioner (GP) care of people with gout in a 2 year randomised controlled trial (NIHR CRN Portfolio No.12943)
Methods: 517 participants with acute gout in the previous year were identified from 56 local GP practices and randomised to nurse-led or continuing GP care. The nurses were trained about gout and its management according to recommended best practice (EULAR and BSR guidelines) involving full information, addressing illness perceptions, and involving patients in management decisions. Assessments were undertaken at 1 and 2 years. Analysis was intention to treat (last observation carried forward).
Results: Nurse (n=255) and GP (n=262) groups were well matched at baseline for mean age (62 v 64yrs), sex (90% v 89% men), mean disease duration (11.6 v 12.7yrs), mean gout attack frequency in prior year (4.2 v. 3.8), tophi (13.7% v. 8.8%), mean SUA (443 v. 439 μmol/L), mean eGFR (71.5 v. 70.2) and ULT use (40% v. 39%) (all p>0.05). By 2yrs, 22 (8.6%) and 54 (20.6%) participants had discontinued the nurse and GP groups (p<0.001), including 2 v. 8 deaths respectively. Comparing nurse and GP groups at 2yrs: 95% v. 29% had SUA <360 μmol/L (primary outcome); 88% v. 16% had SUA <300 μmol/L; mean (SD) SUA was 252±73 v. 418±106; 97% v. 54% were on ULT; and mean (SD) dose of allopurinol was 470 (140) v. 240 (107) mg/day (all p<0.001). Mean (SD) attack frequency during the 2nd year was 0.33 (0.93) in the nurse v. 0.94 (2.03) in the GP group (p<0.001), and at 2yrs tophi were present in 2.6% (reduced) v. 9.6% respectively (p<002). Although equivalent at baseline, mean (SD) SF-36 norm-based physical component scores were better at 2yrs in the nurse group (41.31 (16.76) v. 37.87 (14.31); p<0.05).
Conclusions: Nurse-led care of people with gout in the UK community can result in high uptake and excellent adherence to ULT over a 2yr period, achievement of target SUA in >9/10 cases and consequent improvements in patient-centred outcomes and quality of life. This study reinforces the benefits of "treat-to-target". Compared to standard GP care this model is likely to be cost effective long-term and merits further consideration.
References:
[1] Doherty M. et al. Ann Rheum Dis 2012;71:1765–70.
[2] Kuo C-F. et al. Ann Rheum Dis 2015;74:661–7.
[3] Rees F. et al. Ann Rheum Dis 2013:72:826–30.
Acknowledgements: Arthritis Research UK (Award No.19703) funded this study.
Disclosure of Interest: M. Doherty Grant/research support from: AstraZeneca, Consultant for: AstraZeneca, Grunenthal, Mallinckrodt and Roche, W. Jenkins: None declared, H. Richardson: None declared, A. Abhishek Grant/research support from: AstraZeneca, D. Ashton: None declared, C. Barclay: None declared, L. Duley: None declared, H. Jones: None declared, M. Santarelli: None declared, A. Sarmanova: None declared, M. Stevenson: None declared, W. Zhang Consultant for: AstraZeneca and Grunenthal
DOI: 10.1136/annrheumdis-2017-eular.5006

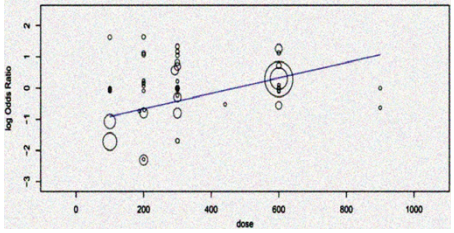
OP0269 EFFECT OF XANTHINE OXIDASE INHIBITORS ON THE INCIDENCE OF CARDIOVASCULAR EVENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

M. Bredemeier, L.M. Lopes, M.A. Eisenreich, G.K. Bongiorno, S. Hickmann. *Rheumatology Division, Hospital Nossa Senhora da Conceição - Grupo Hospitalar Conceição, Porto Alegre - RS, Brazil*

Background: There is evidence that xanthine oxidase inhibitors (XOI) may reduce the risk of major adverse cardiovascular events (MACE) (1,2) and lower blood pressure (3). To date, this evidence is based mainly on observational studies (2).
Objectives: To compare the incidence of MACE, mortality, and total and specific cardiovascular (CV) events in patients enrolled in randomized controlled trials (RCTs) comparing XOI with placebo or no treatment.
Methods: A systematic review (CRD42015016073) searching for RCTs using PubMed, EMBASE, Cochrane Library, Web of Science, and Lilacs databases, and hand searching, was ended in Dec 2016. All RCTs comparing XOIs with placebo or no treatment lasting ≥4 weeks and including only adult individuals were eligible. The primary outcomes were the incidence of MACE (CV death, non-fatal myocardial infarction, unstable angina requiring urgent revascularization, or non-fatal stroke) and mortality; total CV events (TCE), specific CV outcomes, and serious adverse events (SAE) served as secondary outcomes. Associations were tested using the Peto odds ratio (OR) without zero-cell continuity correction.
Results: In total, 81 studies including approx. 11,000 individuals reported extractable data on CV events. The use of XOI tended to be associated with lower incidence of MACE (OR=0.64, 95% CI 0.41–1.01, P=0.056), but not with mortality (0.95, 0.63–1.44). However, there was a significantly reduced incidence of TCE (0.66, 0.54–0.80, P<0.001), especially new/worsening hypertension (0.57, 0.37–0.87, P=0.009), and a trend for reduction in the incidence of new/worsening heart failure (0.74, 0.53–1.04, P=0.086). The incidence of SAE (0.86, 0.71–1.05) did not differ significantly. Subgroup analysis suggested a protective effect for MACE in studies with high prevalence (>50%) of cardiac diseases (0.52, 0.30–0.91, P=0.021). Sensitivity analysis excluding studies at high or unknown risk of bias produced no significant change in results, but reinforced the association with reduced incidence of hypertension (0.26, 0.11–0.60, P=0.001) and heart failure (0.55, 0.32–0.94, P=0.030). Separate analysis of data on purine-like XOI (allopurinol and oxypurinol) confirmed the results of the primary analysis. Exploratory metaregression analysis showed association of dose of allopurinol with higher incidence of TCE (P=0.023, random effects) and SAE (P<0.001, see Figure 1). Accordingly, in the subgroup with doses ≤300 mg/day of allopurinol, a reduction of incidence of MACE (0.36, 0.18–0.68, P=0.002), TCE (0.38, 0.26–0.54, P<0.001), and SAE (0.49, 0.34–0.71, P<0.001) was observed, while the SAE risk increased in doses >300 mg/day (1.39, 1.04–1.91, P=0.047). There was

no association of dose of non-purine-like XOI with incidence of TCE and SAE. Significant statistical heterogeneity was not observed in any test reported here.

Figure 1. Meta-regression analysis of dose of allopurinol versus logarithm of odds ratio (OR) of serious adverse events.



Conclusions: Our data from a meta-analysis of RCTs suggest that XOI reduce the incidence of CV events, an effect possibly related (at least partly) to control of hypertension. However, higher doses of allopurinol (>300 mg/day) may possibly be associated with higher risk of serious adverse events and loss of cardiovascular protection.

References:
[1] Richette et al. Nat Rev Rheumatol 2014;10:654–61.
[2] Singh et al. Arthritis Res Ther 2016;18:209.
[3] Agarval et al. J Clin Hypertens (Greenwich) 2013;15:435–42.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2674

FRIDAY, 16 JUNE 2017

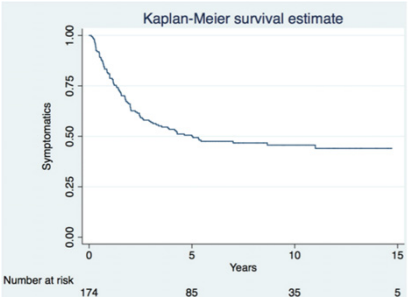
Low back pain and fibromyalgia

OP0270 LONG-TERM PROGNOSIS IN CHRONIC PLANTAR FASCIITIS BASED ON DISEASE DURATION AND ULTRASONIC CHANGES

L. Hansen[1], U. Fredberg[1], T.P. Krogh[1], T. Ellingsen[1,2], L.B. Hansen[3].
[1]Diagnostic Centre, Regional Hospital Silkeborg, Silkeborg; [2]Department of Rheumathology, Odense University Hospital, Odense; [3]Radiologic Department, University Hospital Aarhus, Aarhus, Denmark

Background: Plantar fasciitis (PF) affects 7–10% of the population over a lifetime but the long-term prognosis is unknown. This study is the greatest within the long-term prognosis of PF and have the longest follow-up time.
Objectives: The aim was to assess the long-term prognosis of chronic PF based on duration of symptoms and ultrasonic changes (tendon thickness, heel spur, echogenecity and heel fat pad) and assess if any baseline cohort characteristics had an impact on the prognosis (sex, BMI, age, smoker status, physical work/sport and bilateral pain).
Methods: At baseline (2001–11) 269 patients were diagnosed with PF based on symptoms and ultrasound findings.
At follow-up (2016) all the participants were invited to participate in the project. Everyone was interviewed and offered a new ultrasound examination of their plantar fascia at both feet.
Results: 174 (65%) participated in the study, 52% women and 48% men and 137 had an additional US examination. 54% of the participants were asymptomatic at follow-up (asymptomatic group) and the mean duration of symptoms were 725 days (range 41–4018). 46% still had symptoms (symptomatic group). The follow-up period was 9.7 years (range 4.7–27.3). The risk of having chronic PF were 45.6% (95% CI 37.9–53.0) 10 years after debut of symptoms (figure 1). A multiple cox regression analysis found that women ($p<0.01$) and participants with bilateral heel pain ($p<0.01$) had a worse prognosis. The hazard rate ratio was 0.49 (95% CI 0.30–0.80) for women (every time 100 men were getting cured pr. year only 49 women were cured pr. year) and 0.33 (95% CI 0.15–0.72) for participants with bilateral heel pain (every time 100 with unilateral pain were cured pr. year only 33 with bilateral pain were cured pr. year). The remaining baseline cohort characteristics (all p's>0.05), tendon thickness (p=0.49) and heel spur (p=0.88) did not have an impact on the prognosis (table 2).
The mean tendon thickness was at baseline 6.9 mm in the asymptomatic group and 6.7 mm in the symptomatic group. The tendon thickness was reduced significantly to 4.3 mm at follow-up in both groups (both p's<0.01). Only 24% in the asymptomatic group had a normal tendon thickness and echogenicity at follow-up (6% in the symptomatic group).
The participants had in average tried 3.8 (range 1–9) different treatment modalities and 93% received an ultrasound guided steroid injection at baseline. 11% of them were permanently cured 1 month after the injection despite symptoms for an average of 334 days' prior the injection. No atrophy of the heel fat pad was found in the sick foot who got the steroid injections compared to the contralateral foot that did not get the injection (p=0.66).
Conclusions: 45.6% had PF 10 years after debut of symptoms.
The asymptomatic participants had in average plantar fasciitis for 725 days.
The prognosis was significantly worse for women and participants with bilateral pain.

Figure 1:
Kaplan Meier survival function for all the participants. The y-axis shows the part who is symptomatic (1.00=100% is symptomatic). And the x-axis is the time in year since debut of symptoms (year 0 = debut of symptoms).



The tendon thickness decreased over time no matter of symptoms and had no impact on the prognosis, neither did heel spur.
Only 24% of the asymptomatic participants had a normal tendon on ultrasound at long-term follow-up.
Ultrasound guided steroid injection did not give atrophy of the heel fat pad in long-term follow-up.
Acknowledgements: The project was financed by The Danish Rheumatism Association and The Research Funds of Hospital Unit Central Jutland
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3152

OP0271 CORTICOSTEROID INJECTIONS FOR GREATER TROCHANTERIC PAIN SYNDROME: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

M.J. Nissen[1], L. Brulhart[2], A. Faundez[3], A. Finckh[1], D. Courvoisier[1], S. Genevey[1]. *[1]Rheumatology, Geneva University Hospital, Geneva; [2]Rheumatology, Neuchatel Hospital, Neuchatel; [3]Orthopaedics and Traumatology, Geneva University Hospital, Geneva, Switzerland*

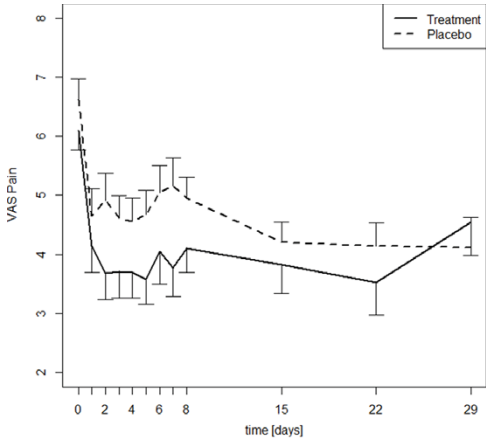
Background: Although small observational studies have suggested that local corticosteroid (CS) injection may be effective in the management of the greater trochanteric pain syndrome (GTPS), no prospective placebo controlled study has been carried out to establish the efficacy of this common intervention.
Objectives: To perform a randomized double-blind placebo controlled trial to investigate the efficacy of local CS injection in the management of GTPS.
Methods: The trial was conducted in the Rheumatology unit of a University teaching hospital in Geneva, Switzerland. Inclusion criteria were lateral hip pain (LHP) for greater than 1 month, a LHP score of ≥4 in the preceding week, failure of another standard treatment (physiotherapy, analgesics, etc.) and typical LHP reproduced by palpation of the greater trochanter (GT). Participants were randomised in a 1:1 ratio to: 1) injection with a combination of local anaesthetic and CS (Treatment group), or 2) injection with normal saline solution (Placebo group). The Treatment group received 4ml of 1% Lidocaine (Rapidocain®) and 1ml of Bethametasone (Diprophos®). The Placebo group received 5ml of sterile saline solution. Injections were performed under ultrasound guidance. The study's predefined primary outcome of interest was the difference in pain intensity at 4 weeks post-injection between the 2 groups. Secondary outcomes included the number of "responders" (pain score improvement of ≥1.5) and the number of patients with low disease activity (LDA) (pain score ≤2.0). Patients were followed up for 6 months.
Results: A total of 46 patients were included and there were no significant differences between the 2 groups at baseline (Table 1). There were no significant differences between the 2 groups in terms of the reduction in pain at one month post-injection, with scores of -1.5 and -2.5 (p=0.23) in the Treatment and Placebo groups respectively. When including all measures in the first 3 weeks and using multilevel regression, there was a marginally significant improvement

Table 1. Baseline patient characteristics

	Active treatment (n=21)	Placebo (n=25)	p-value
Age (years) [SD]	56.6 [14.6]	59.6 [13.1]	0.46
Sex (%, female)	81.0	88.0	0.51
Weight (kg) [SD]	74.4 [15.1]	74.7 [15.8]	0.95
Height (cm) [SD]	163.6 [7.7]	153.6 [32.5]	0.18
BMI [SD]	27.9 [6.1]	28.8 [4.9]	0.59
Pain over past 24 hours	6.1 [1.5]	6.6 [1.8]	0.29
Pain on palpation of GT	6.6 [2.0]	7.1 [1.9]	0.40
Past injection of GT (% yes)	38.1	40.0	0.92
Ostwestry total score [SD]	39.9 [13.1]	39.9 [14.9]	0.99
Womac pain score [SD]	251.4 [80.5]	247.2 [87.2]	0.87
Womac function score [SD]	414.6 [154.9]	366.1 [175.7]	0.33

Except where indicated otherwise, values are the mean (± standard deviation). GT = greater trochanter region.

in pain scores in favour of the Treatment group (p=0.08) (Figure 1). There were no significant differences in terms of the percentage of responders (p=0.32), or patients with LDA (p=0.50) between the 2 groups at follow up. There were no significant differences in pain scores between groups at 3 and 6 months post-injection.



Conclusions: Local corticosteroid injection in the management of GTPS is only marginally effective for a few weeks. Given the lack of long-term improvement and the potential for cortisone-related side-effects, this intervention is of limited benefit.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3458

OP0272 CHRONIC LOW BACK PAIN AND ANXIETY: SIGNIFICANT DECREASE WITH GLUCOSAMINE-CHONDROITIN SULFATE TREATMENT IN A LARGE, COMMUNITY-BASED, PILOT, OPEN PROSPECTIVE INTERVENTIONAL STUDY

G. Singh[1], L. Alekseeva[2], D. Goriachev[3], A. Barinov[3], E. Nasonov[2], A. Mithal[4]. *[1]Gastroenterology and Hepatology, Stanford University, Woodside, United States; [2]State NII of Rheumatology of Russian Academy of Sciences; [3]First Moscow State University, Moscow, Russian Federation; [4]ICORE, Woodside, United States*

Background: Low back pain (LBP) is associated with 2.3, 2.2, and 1.6 times greater odds for mood disorders, anxiety disorders and alcohol abuse respectively (1). Continued anxiety may lead to a state of "learned helplessness", and both can propagate in a vicious cycle. Glucosamine-chondroitin sulfate (GCS) combination is widely used in the treatment of OA; however there are few prospective studies of its therapeutic merits in LBP.
Objectives: To study the efficacy of GCS in the decreasing anxiety in patients with chronic LBP in a large open pilot prospective study.
Methods: We enrolled patients 40 - 65 years of age who had LBP for >12 weeks with pain intensity >3 on a 0–10 point VAS in a single-arm, open-label prospective interventional study. Major exclusion criteria were the presence of fibromyalgia, spondylolisthesis, and alcohol and/or drug abuse. All patients were treated with ARTRA (combination glucosamine hydrochloride 500 mg - chondroitin sulfate 500 mg in tablet form; Unipharm Inc.) at a dose of 1 tab bid for the first month and then 1 tab daily for the next two months. The primary endpoint was pain intensity as measured on a 0–10 point VAS. Secondary endpoints included anxiety levels measured by Spielberger's State Trait Anxiety Inventory (STAI) adapted for Russia by Khanin (2). STAI evaluates the current "state" of anxiety, asking how respondents feel "right now," using items that measure subjective feelings of apprehension, tension, nervousness, worry, and activation/arousal of the autonomic nervous system as well as aspects of "anxiety proneness," including general states of calmness, confidence, and security ("trait"). Scores for each scale range from 20 to 80, with higher scores indicating greater anxiety.
Results: A total of 8,598 subjects (mean age 52.1 years, 67.3% women, mean BMI 27.4) were enrolled in the study, and formed the intent-to-treat (ITT) population. All but 95 subjects (1.1%) completed the study. Previously-reported ITT analysis with worst observation carried forward showed an improvement in pain at rest from mean (± SD) of 5.2±1.9 at study entry to 1.4±1.6 at 3 months (p<0.0001). Pain at movement decreased from 6.8±1.6 to 2.2±1.8 (p<0.0001). There was a strong correlation between increasing baseline STAI scores and baseline pain at rest and movement (both p<0.0001). After 12 weeks of GCS treatment, STAI "state" anxiety scores dropped from 49.3 (95% CI 49.1 to 49.6) to 35.8 (95% CI 35.6 -36.0) (p<0.0001). A similar reduction was seen in "trait" anxiety scores from 48.3 (95% CI 48.0–48.5) to 39.6 (95% CI 39.3–39.8) (p<0.001).
Conclusions: Although open and uncontrolled, this large pilot community-based study shows dramatic reductions in pain and anxiety (both "state" and "trait") in patients with LBP treated with GCS. With its benign safety profile, GCS therapy deserves serious evaluation in the management of LBP in a prospective randomized double-blinded clinical trial.

References:
[1] Demyttenaere, K., et al., Mental disorders among persons with chronic back or neck pain. Pain, 2007. 129:332–42.
[2] Spielberger, C. D. (1989). State–Trait Anxiety Inventory: A comprehensive bibliography. Palo Alto, CA: Consulting Psychologists Press.
Disclosure of Interest: G. Singh Grant/research support from: Unipharm Inc., L. Alekseeva: None declared, D. Goriachev Consultant for: Unipharm Inc., A. Barinov: None declared, E. Nasonov: None declared, A. Mithal: None declared
DOI: 10.1136/annrheumdis-2017-eular.2642

OP0273 A RETROSPECTIVE DATABASE STUDY OF ONE-YEAR ADEHERNCE AND PERSISTENCE WITH PHARMACOLOGICAL THERAPY AMONG FIBROMYALGIA PATIENTS IN ISRAEL

D. Weitzman[1,2], D. Ben-Ami Shor[2,3], S. Dahan[2,4], Y. Bar-On[5], V. Shalev[1,2], G. Chodick[1,2], H. Amital[2,4]. *[1]Epidemiology and Database Resaerch, Maccabitech, Maccabi Healthcare Services; [2]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; [3]Department of Gastroenterology; [4]Department of Medicine B, Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Hashomer; [5]Department of Medicine E, Tel-Aviv Sourasky Medical Center, Tel Aviv, Israel*

Background: Fibromyalgia (FM) is a chronic debilitating disorder characterized by widespread musculoskeletal pain often accompanied by fatigue, allodynia and hyperalgesia. Literature is scarce regarding adherence to pharmacologic treatments available for FM patients.
Objectives: To assess one-year persistence and adherence with therapy among patients with FM and to identify factors associated with therapy discontinuation.
Methods: Using the comprehensive computerized database of Maccabi Healthcare Services, a large healthcare services provider in Israel, all adults (≥21 yrs) diagnosed with FM between 2008 and 2011 were identified. FM medications included the anti-convulsant pregabalin, SSRI/SNRI and tricyclic antidepressants. Time to treatment discontinuation, defined as a gap of ≥120 days in medication supply days, and proportion of days covered (PDC) with FM-specific therapies during one year from the first dispense were analyzed. Multivariable logistic regression models were constructed to analyze factors associated with low (PDC <20%) and high (PDC ≥80%) adherence.
Results: Overall 3932 eligible FM patients were identified, 88.7% females, mean) SD (age =49.2 (12.7). Pre-diagnosis use of medications of interest was documented in 41% of the patients. Of the remaining 2312, 56.1% were issued a prescription in the year following diagnosis and 45.0% dispensed at least on medication. One-year discontinuation reached 79.3% overall, and was highest for tricyclic antidepressants and lowest for SSRI/SNRI antidepressants (Table 1). Over one half of the patients (60.5%) were poorly adherent (PDC<20%) during the year and only 9.3% were highly adherent (PDC≥80%). Low adherence was less prevalent among patients diagnosed with migraines (OR=0.62, 95% CI: 0.48–0.80) or with both depression and anxiety (OR=0.55; 0.40–0.76). High adherence was positively associated with socio-economic status (p-for-trend=0.022).

Table 1. Medications prescribed and dispensed in the first year from diagnosis, proportion discontinuing and time to discontinuation in the year following first dispense (N=1296)

Drug group	Prescribed N (%)	≥1 dispense N (%)*	Discontinued	
			N (%)**	Days to discontinuation Median (IQR)
Anti-Convulsants	313 (24.1%)	228 (72.8%)	186 (81.6%)	30 (30–106)
SSRI/SNRI antidepressants	606 (46.7%)	471 (77.7%)	347 (73.7%)	41 (30–171)
Tricyclic antidepressants	767 (59.1%)	601 (78.4%)	547 (91.0%)	30 (30–90)
Any drug	1296 (100%)	1041 (80.3%)	825 (79.3%)	40.5 (30–146)

*Percent of patients with at least one dispense out of those prescribed, e.g. 228/313x100=72.8% for anti-epileptic drugs. **% of those with ≥1 dispense.

Conclusions: Persistence and adherence with FM therapy in the year following diagnosis is remarkably low. Further research is needed to assess ways to improve continuation with therapy among FM patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4578

OP0274 FIBROMYALGIA IN REAL LIFE: A NATIONAL FRENCH WEB-BASED SURVEY IN 4516 PATIENTS

F. Laroche[1], J. Guérin[1], D. Azoulay[1], J. Coste[2], S. Perrot[3]. *[1]Pain Department, Hospital university Saint Antoine; [2]Biostatistics, Hospital University Hotel Dieu; [3]Pain Department, Hospital University Cochin, Paris, France*

Background: Fibromyalgia (FM) is the most frequent widespread chronic pain disorder (1,6% of the French population) (1). The medical and socioeconomic burden is high and severity depends on medical status and symptoms as defined by the OMERACT criteria (2). Most of the studies are performed in specialized centers, recruiting the most severe patients, but very few data exist on its real impact on daily life.
Objectives: The aims were to collect demographic data, symptoms, function, diagnosis, management strategies and health care utilization in real life, in a large population, and to determine clusters of patients.

Methods: A large internet-based national survey of people suffering from FM was developed by a national patient association (Fibromyalgie-SOS Association) on their website, in France in 2014. The survey included 103 qualitative and quantitative questions that were developed by 3 medical experts (including rheumatologists) and patients.
Results: The questionnaire was completed by 4516 people. Respondents were predominantly middleaged (48 yrs) females (93%), most of whom had FM symptoms duration for 12 years and a diagnosis for 5 years. Diagnosis was made by a rheumatologist in 54% of the cases. The symptoms were concordant with the OMERACT domains (chronic pain, fatigue stiffness and other FM-associated symptoms) as previously published by Bennett in 2007 (3). The mean FIQ (Fibromyalgia Impact Questionnaire) score was 51 (0–100). 55% were currently working but 65% of them have been on sick leave in the 12 previous months. FIQ was mostly impacted by injustice feeling (+4.5), part time job (+2.4) and low income - less than 1000 euros monthly (+2.3) (linear regression).
Somatic comorbidities were mostly osteoarthritis (49%). Psychological comorbidities were injustice feeling (77%), cognitive symptoms (62%), anxiety (52%) and depression (48%). Initiating factors were reported by 73% of them: physical (50%) and/or psychological (76%). Aggravating factors included excess of activities, conflicts, traumatism and displacement. Treatments were provided by general practitioner (85%), physiotherapist (63%), rheumatologist (54%) and osteopathic manual practitioner (41%). Treatment was prescribed in 76.6% of the patients, including paracetamol alone (51.4%), paracetamol and weak opioids (64%), strong opioids (20.1%), antidepressants (81.5%), antiepileptic agents (54.5%), nonsteroidals NSAIDs (53.8%), anxiolytics (52.4%) and steroids (12.8%).
Conclusions: This unique descriptive survey in a large population provides data on symptoms, emotional distress, prescribing habits and impact of FM on daily life and work. Results show that FM is altered by emotional (including injustice feeling) and socio-economic factors.
References:
[1] Perrot S, Vicaut E, Servant D, Ravaud P. Prevalence of fibromyalgia in France: a multi-step study research combining national screening and clinical confirmation: The DEFI study (Determination of Epidemiology of Fibromyalgia). BMC Musculoskeletal Disorders 2011; 12:224.
[2] Mease P, Clauw D, Arnold L. and the OMERACT Fibromyalgia Working Group. The Journal of Rheumatology, 2011; 38: 1487–95.
[3] Bennett R. Jones J, Turk D, Russell I, Matallana L. An internet survey of 2,596 people with fibromyalgia. BMC Musculoskeletal Disorders 2007, 8:27: 1–11.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3390

OP0275 FIBROMYALGIA PREVALENCE AND IMPACT ON DISEASE ACTIVITY SCORES IN RHEUMATOID ARTHRITIS PATIENTS WHO ARE UNRESPONSIVE TO BIOLOGICAL TREATMENT

L.J. Ghib[1], M.M. Tamas[1], I. Felea[2], L. Damian[2], I. Filipescu[1], A. Mociran[2], S.-P. Simon[1], L. Muntean[1], S. Rednic[1]. *[1]Rheumatology, "Iuliu Hatieganu" University of Medicine and Pharmacy; [2]Rheumatology, Emergency County Clinical Hospital, Cluj Napoca, Romania*

Background: Rheumatoid arthritis (RA) treatment uses a treat-to-target strategy and disease assessment is based on disease activity scores (DAS) such as the DAS28 [1]. Biological drugs have proven highly effective for RA treatment in clinical studies[2], however, in real life settings, comorbidities such as fibromyalgia (FM) might influence treatment response assessed by DAS28.
Objectives: In this study we determined FM prevalence and the impact on disease activity scores in patients with RA undergoing biological treatment and if higher tender joint (TJC) correlates with lower pain threshold in patients with active RA who did not satisfy FM criteria.
Methods: We performed a cross sectional study on RA patients undergoing biological treatment who presented in our department for a 6 month period. DAS28 was calculated for all patients. FM diagnosis was considered positive if patients satisfied both the ACR 1990 and ACR 2010 FM Criteria. Pain pressure thresholds (PPT) were measured at the level of the medial knee joint line, mid sternum and middle of the tibia with a manual dolorimeter. Depression, Anxiety, Stress 21 scale (DASS21) and Health Assessment Questionnaire (HAQ) were applied to all patients.
Results: 112 patients were included, 84.8% women, mean age 55.6 (SD 11.6) with a mean disease duration of 14.5 (SD 8.5) years. Acording to DAS28ESR scores 54 (48.2%) had moderate disease activity and 26 (23.2%) had high disease activity. 17 (21.5%) of patients with DAS28ESR scores over 3.2 satisfied FM criteria. FRA and RA groups did not differ significantly concerning age, disease and biological treatment duration, seropositivity, BMI or DASS21 scores. FRA patients had significantly higher values for DAS28 ESR, DAS28 CRP, PGH and HAQ, but similar values for SJC, ESR and CRP compared to RA patients (Table 1). In RA patients without FM, TJC correlated significantly with number of trigger points (r=-0.3), PPT at knee (r=-0.4), sternum (r=-0.3) and tibial level (r=-0.2).
Conclusions: Fibromyalgia is present in a significant percent of patients who are unresponsive to biological treatment as assessed by DAS28 score. Subjective components of DAS28 are significantly higher in FRA compared to RA patients, suggesting that disease assessment should be performed using objective measures in these patients. In patients with active disease despite biological treatment whitout FM, lower pain thresholds are correlated with TJC, suggesting a possible involvement of central pain mechanisms.

Table 1. DAS28 components for RA and FRA patients

	RA (n=63), mean (SD)	FRA (n=17), mean (SD)	P value
PGH	49.9 (19.8)	68.8 (17.2)	<0.001
TJC	5 (3,9)	10 (8.5,17.5)	<0.001
SJC	2 (1,4)	2 (1,5)	0.8
ESR	27.5 (19)	32.8 (23)	0.4
CRP	8.8 (14.4)	12.8 (15.6)	0.2
DAS28 ESR	4.6 (1.08)	5.5 (1.05)	0.003
DAS28CRP	3.99 (1)	4.94 (1.09)	0.002
HAQ	1.2 (0.5)	1.7 (0.6)	0.002

PGH - patient global health, TJC -tender joint count, SJC - swollen joint count, ESR - erythrocyte sedimentation rate, CRP - C reactive protein.

References:
[1] Smolen JS, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis. 2010;69(4):631–637.
[2] Tvete IF, et al. Comparing Effects of Biologic Agents in Treating Patients with Rheumatoid Arthritis: A Multiple Treatment Comparison Regression Analysis. PLoS One. 2015;10(9):e0137258.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5430

LB0001 INTRADISCAL GLUCOCORTICOID INJECTION FOR PATIENTS WITH CHRONIC LOW BACK PAIN ASSOCIATED WITH ACTIVE DISCOPATHY: A RANDOMIZED TRIAL

C. Nguyen[1], I. Boutron[1], G. Baron[1], K. Sanchez[2], C. Palazzo[1], R. Benchimol[2], G. Paris[1], E. James-Belin[2], M.-M. Lefèvre-Colau[1], J. Beaudreuil[3], J.-D. Laredo[3], A. Béra-Louville[4], A. Cotten[4], J.-L. Drapé[1], A. Feydy[1], P. Ravaud[1], F. Rannou[1], S. Poiraudeau[1]. *[1]Université Paris Descartes; [2]Assistance Publique - Hôpitaux de Paris; [3]Université Paris Diderot, Paris; [4]Université Lille 2, Lille, France*

Background: Active discopathy is associated with a specific phenotype of chronic low back pain (cLBP). Local inflammation has a role in active discopathy-associated symptoms (1).
Objectives: To assess the efficacy of a single glucocorticoid intradiscal injection (GC IDI) in cLBP patients with active discopathy.
Methods: We conducted a prospective, parallel-group, double-blind, randomized controlled study in 3 tertiary care centers in France. 135 cLBP patients with active discopathy on MRI were enrolled. They received a single GC IDI (25 mg prednisolone acetate) during discography (n=67) or discography alone (n=68). The primary outcome was the percentage of patients with LBP intensity in the previous 48 hr <40 on an 11-point numeric rating scale (NRS, 0 no pain - 100 maximal pain) at 1 month. The main secondary outcomes were LBP intensity and persisting active discopathy on MRI at 12 months post-intervention, and spine-specific limitations in activities, health-related quality of life, anxiety and depression, employment status and analgesics and non-steroidal anti-inflammatory drugs consumption at 1 and 12 months.
Results: All randomized patients were included in the primary efficacy analysis. At 1 month, the percentage of responders (LBP intensity <40) was higher in the GC IDI than control group (36/65 [55.4%] *vs* 21/63 [33.3%]; absolute risk difference [95% confidence interval] 22.1 [5.5;38.7]); p=0.009. In the sensitivity analysis, mean reduction [95% CI] in LBP intensity from baseline to 1 month was greater in the GC IDI group compared to the control group (-32.5 [-38.2;-26.8] *vs* -17.5 [-23.3;-11.7], respectively; absolute difference [95% CI] -15.0 [-22.9;-7.1], p<0.001).
At 1 month, the percentage of patients reporting an improvement in spine-specific limitations in activities was higher in the GC IDI than control group (55/65 [84.6%] *vs* 34/63 [54.0%]; absolute risk difference [95% CI] 30.5 [15.7; 45.2], p<0.001). The 2 groups did not differ in LBP intensity at 12 months and in most of the secondary outcomes at 1 and 12 months. 102/119 (85.7%) patients would agree to a second intervention. We found no cases of rapidly destructive disc disease or intervertebral disc calcifications.
Conclusions: In active discopathy-associated cLBP, a single GC IDI reduces LBP at 1 month post-intervention but not at 12 months.
Registration: ClinicalTrials.gov number NCT00804531 (First received: December 8, 2008. Last updated: June 23, 2016).
References:
[1] Nguyen C, Poiraudeau S, Rannou F. From Modic 1 vertebral-endplate subchondral bone signal changes detected by MRI to the concept of 'active discopathy'. Ann Rheum Dis. 2015 Aug;74(8):1488–94.
Acknowledgements: The study was funded by a research grant from the French Ministry of Health (Programme Hospitalier de Recherche Clinique, project no. P070157). The authors thank URC-CIC Paris Descartes Necker/Cochin (Christelle Auger and Nellie Moulopo) for implementation, monitoring and data management of the study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7062

FRIDAY, 16 JUNE 2017

PARE abstract session

OP0276-PARE MORE PARTICIPATION, BETTER HEALTH – PROMOTING PUBLIC INVOLVEMENT IN HEALTH

S. Crisostomo[1], M. Santos[1], M. Serapioni[2], A.R. Matos[2], E.F. Mateus[3] on behalf of MAIS PARTICIPAÇÃO, melhor saúde. *[1]GAT - Grupo de Ativistas em Tratamentos, Lisboa; [2]Centro de Estudos Sociais da Universidade de Coimbra, Coimbra; [3]Liga Portuguesa Contra as Doenças Reumáticas, Lisboa, Portugal*

Background: In Portugal, the National Health Plan for 2012–2016 (1) and its extension to 2020 (2) consider citizenship-based strategies, including the involvement of patients/citizens and their representatives, as a key strategic axis to maximize health gains. However, actual policy initiatives and concrete actions have been limited to a couple initiatives without significant patient or public involvement. On the other side, several patient and citizen organizations (3–6) have been advocating for increased and meaningful involvement in health decision-making.
Objectives: To develop a Charter for Public Involvement in Health that is widely accepted and recognized by health stakeholders.
Methods: A working group was established with representatives from 13 patient organizations, 1 consumer organization and a research centre. A participatory action research methodology was used. The draft Charter was circulated for review and signature amongst more than 200 non-for-profit health-related organizations and over 50 key individuals publicly renowned for their work in health or public participation. The final version of the Charter was discussed with political and health stakeholders in a Forum held at the Portuguese parliament.
Results: A Charter for Public Involvement in Health, including the principles, scope, guidelines and means of participation was developed. In January 2017, 30 individuals (former and current political decision-makers, health care professionals, researchers and patients) and more than 82 non-for-profit health-related organizations (the majority being Portuguese disease-specific patient organizations) had signed the Charter. The conclusions of the Forum show that the Charter was recognized as a very important initiative to promote public involvement in health in Portugal. Challenges and barriers to further advancing patient and public engagement were also identified (e.g. political will, recognitions of patients as partners, patient empowerment, capacity-building, etc.). The Charter and the Forum were covered in the media and follow-up initiatives with health care professionals and hospital administrators are ongoing.
Conclusions: A patient-led Charter, developed by patient and consumer representatives, in collaboration with academia, and the public discussion with other health care stakeholders have proven successful to put public participation in the political and health care agenda.
References:
[1] Direção-Geral da Saúde – Ministério da Saúde. Plano Nacional de Saúde 2012–2016. Lisboa, Portugal; 2012.
[2] Direção-Geral da Saúde – Ministério da Saúde. Plano Nacional de Saúde – Revisão e Extensão a 2020. Lisboa, Portugal; 2015.
[3] European Patients Forum. The Value+ Policy Recommendations: Patient Involvement in Health Programmes and Policy [Internet]. Available from: http://www.eu-patient.eu/globalassets/projects/valueplus/doc_epf_policyrec.pdf.
[4] European Patients Forum. Patient Empowerment Campaign [Internet]. Available from: http://www.eu-patient.eu/campaign/PatientsprescribE/.
[5] International Alliance of Patients' Organisations. Policy statement. Patient Involvement [Internet]. 2005. Available from: http://iapo.org.uk/sites/default/filesfiles/IAPO Policy Statement on Patient Involvement.pdf.
[6] Terzi A. The patients' involvement in health policies in Europe. Roma; 2013.
Disclosure of Interest: S. Crisostomo Grant/research support from: Abbvie, Brustol-Meyers Squibb, Janssen, GSK, Pfizer, Roche and ViiV, M. Santos Grant/research support from: Abbvie, Brustol-Meyers Squibb, Janssen, GSK, Pfizer, Roche and ViiV, M. Serapioni: None declared, A. Matos: None declared, E. Mateus: None declared
DOI: 10.1136/annrheumdis-2017-eular.5980

OP0277-PARE INITIAL INFORMATION PACKAGE FOR CHILDREN DIAGNOSED WITH JIA

T. Pakkala, M. Ekroth. *Finnish Rheumatism Association, Helsinki, Finland*

Background: Both parents of children with JIA and rheumatology nurses have informed FRA from time to time that there is a need for an initial information package. There was a demand for information that catered to children's needs and provided support for them and their closest relatives at the stage when the diagnosis is shared with the family.
Objectives: The aim of the project was to make an information package for children aged 0 to 12. A child with JIA needed to be provided with information that took into consideration the child's age and developmental stage so that any fears that the child might have as a result of him or her learning of the disease were allayed. Not only information is provided through the information package; the content can also be used to encourage discussions between a parent and a child. We also wanted to include items that give pleasure, such as a stuffed toy in the form of a bunny. A further aim was to increase awareness of FRA among families with children so that as many as possible would find the services offered by FRA and its local member associations.
Methods: *The first stage* of the project involved conducting a survey in order to find out what the package should contain. The survey was directed to parents to children with JIA, rheumatology nurses and rheumatologists. The content of the information package:
1) An initial information binder with the following information: about JIA, food, physical activities & play, sitting & writing, eyes & dental care. There is also a separate section directed to parents. 2) A so-called gym tail and easy-to-do gymnastic instructions. 3) Bunny 4) Coloured pencils and a pen thickener. 5) A picture book about visiting a rheumatology clinic for the child. 6) Brochures: e.g. information about JIA for the closest relatives of a child diagnosed with JIA and health care professionals, information about FRA for families with children. 7) Gymnastics bag *The second stage* involved planning the content and the look of the material. The information package and its content needed be positive and functional – the package as a whole had to be suitable for children. The pictures and text for the picture bookwere also produced in cooperation with the healthcare professionals. Multiple channels were used to spread the information that the package had been completed, e.g. social media, the FRA website and emails to the target group.In addition, the rheumatology careunits were given instructions and informed of what to expect.
Results: The packages were very well received. We have received positive feedback from both rheumatology clinics and families with children suffering from JIA.



Conclusions: There was a real need for the information packages,and the information that they provide help both the families and the healthcare staff. When a child suffers from an illness, it affects the whole family, and hence it is crucial that comprehensive – and comprehensible – information and support are available so that everyday life runs smoothly and is meaningful, and so that a child with an illness does not feel like he or she is a burden to the family but considers him- or herself an equal member of the family.
References:
[1] We have received positive feedback from both rheumatology professionals and the families of children with JIA.
Acknowledgements: Abbvie, Pfizer, BMS, Roche,The Finnish Society for Rheumatology and the Finnish Society of Rheumatology Nurses,Åberg Express,TNT Finland,Handitec,Paintek,Anglo-Nordic and of course all the individual persons, who helped with the project.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2185

OP0278-PARE THE FRENCH PATIENT'S ASSOCIATION (AFLAR: FRENCH LEAGUE AGAINST RHEUMATISM) HAS GENERATED THE FRENCH NATIONAL ALLIANCE AGAINST OSTEOARTHRITIS AND THE FIRST GENERAL CONVENTION OF OSTEOARTHRITIS IN FRANCE: A CAMPAIGN TO CREATE A NATIONAL LOBBYING TOOL TO IMPROVE THE MANAGEMENT OF OSTEOARTHRITIS

L. Grange[1,2], F. Rannou[3], F. Berenbaum[4], C. Roques[5], F. Srour[6], C. Delaunay[7], P. Niemczynsky[8], C. Dreux[9], P. Richette[10], P.-A. Joseph[11], C. Cochet[12], J. Giraud[13], F. Alliot Launois[14], C. Gérard[15] on behalf of the French National league Against Osteoarthritis. *[1]President, AFLAR, Paris; [2]Rheumatology, CHU Grenoble Alpes, Echirolles Cedex; [3]SOFMER, SOFMER French society of physical medicine and rehabilitation; [4]President, Sfr French Society of Rheumatology; [5]AFRETH French Association for Thermal Res; [6]CNOMK French Natl. order Council of the physio Therapists; [7]SOFCOT French Society of Orthopedic Surgery and Traumatology; [8]11ONPP Natl. French Order Council of the Pedicure Podiatrist; [9]Cespharm, CONP Natl. Council of the Coll. of Pharmacists; [10]SFR french society of Rheumatology, Paris; [11]Division of Physical Medicine and Rehabilitation, University Hospital Pellegrin, Bordeaux; [12]ONPP Natl. French Order Council of the Pedicure Podiatrist; [13]Empatient; [14]Vice Presidente; [15]Treasurer, AFLAR, Paris, France*

Background: OA suffers from a lack of interest and not considered serious

enough by Health authorities taking into account the burden of the disease. AFLAR has fostered dynamics by creating a structure called the National Alliance against OA, includes national experts, patients and health professionals (HP). A initiative of this group has been to organize the first General Convention for OA.
Objectives: Its main challenge was to provide a list of actions that could potentially change the face of the disease and improve the visibility of OA along with the needs and demands from French patients.
Methods: 10 regional roundtables (with HP, patients and health institutions, around five topics) has been launched with discussions and debates and enabled the production of patient-related proposals in order to improve their care and information.
Results: 79 proposals have been selected and submitted to an online vote in order to be prioritized. Among the 5 topics addressed by the regional roundtables, cross-cutting issues were identified and 9 fields of action emerged. The final proposals were synthesized in a White Paper document and presented to the national Senate assembly. After it was broadcast to the health and public authorities in a prospect of lobbying. see in the image.

Table of the first 21 proposals from the OA French white Paper for the improvement of his management

	Proposal (keywords + listing number)	% of voting	Average /10	
1	Positioning osteoarthritis as a chronic and functional disabling disease (1.1)	50,1%	9,02	
2	Promote retention in employment for OA patient (3.1)	48%	8,97	
3	Involve supplemental health insurances in the healthcare of OA (3.6)	46,4%	8,88	
4	Develop research programs to improve the management and treatment of OA pain (4.1)	46,3%	8,91	
5	Promote recognition of disability (1.2)	45,7%	8,83	
6	Inform health professionals about the total social coverage of the disease through the national health insurance / ALD 31 or ALD 32 in France (3.7)	45,5%	8,88	
7	Promote an early diagnosis of OA (2.1)	45%	8,68	
8	Promote the training of health professionals in the field of prevention and management of osteoarthritis (2.7)	44,8%	8,86	
9	Promote the training of general practitioners on OA non-pharmacological management (2.16)	44,6%	8,77	
10	Monitor the medico-economic impact of the stoppage of one part of the OA healthcare repayment in France (3.8)	44,5%	8,80	
11	Promote the OA healthcare after surgery by physiotherapists (2.17)	43,4%	8,68	
12	Raise awareness of occupational medicine on OA management (1.3)	43,3%	8,71	
13	Promote access to physiotherapist for OA healthcare (2.18)	42,2%	8,57	
14	Improve the refund of chiropody care for OA patient (3.9)	42%	8,69	
15	Create a national registry of protheses (2.8)	42%	8,69	
16	Find additional means of refunding for OA healthcare (3.10)	41,3%	8,64	
17	Develop research programs to improve the management and treatment of OA with non pharmacological pathway (4.2)	41,2%	8,78	
18	Favour the creation of conditions of contract for the accomodation of the OA patients(3.2)	40,9%	8,62	
19	Promote Patient Therapeutic Education for OA (FTE) (3.16)	40,6%	8,65	
20	Favour the practice of adapted physical activity (2.19)	40,6%	8,48	
21	Create and generalise an "no pain kit " (2.20)	40%	8,51	

Conclusions: Although the impact of this initiative is not yet measurable, we think that it should improve the awareness of the decision-makers on the burden of the disease and provide concrete ideas to governmental and non-governmental policy makers in order to improve the quality of life of OA patients.
Acknowledgements: L. Euller-Ziegler F. Blanchet F. Beroud CE Bouvier D.Romain Bertholon, SANOIA,SNMR,CFMR. With support of Genévrier, Pierre Fabre, Expanscience Rottapharm Meda laboratory, SOFMER, CONMK & AFLAR
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1464

OP0279-PARE NRAS KNOW YOUR DAS APP SELF ASSESSMENT TOOL EMPOWERING PATIENTS

C.B. Jacklin[1], S. Arora[2]. *[1]External Affairs; [2]Media & Communications, National Rheumatoid Arthritis Society, Maidenhead, United Kingdom*

Background: NRAS has worked with Roche/Chugai for many years on the Know Your DAS resources. As the DAS28 is the most utilised disease measuring tool available and is used in many countries as part of the access criteria
Objectives: In 2015 the charity was approached about developing an app for mobile phone and tablet use to encourage DAS patient self-assessment. As well as developing the app we worked with the pharmaceutical company to develop printed updated booklets for both patients and health professionals with the addition of information on DAS self-assessment contained within. With increasing pressures on rheumatology clinic time and the emphasis on improving patient education and empowerment this additional NRAS resource is timely and much in demand.
Methods: The Know Your Das app was designed with clear step by step guides and how to video clips to demonstrate how to use the app and show how patients should examine their own joints.
NRAS hosted two user testing focus group meetings and after the launch of version one real time use was analysed. In Jan 2017 version two was released with improvements to the usability and additions including sections on adherence and stock management to aid with prescription refills.
The information entered is held securely by the individual but the DAS results can be printed off or emailed to their clinicians as appropriate. It is not envisaged that the patients' self-assessment should entirely replace the clinicians' DAS measurements but that it will facilitate a better dialogue at clinic appointments as it will give a clearer picture of how the disease has been active or not in the intervening time between appointments.
Results: As of January 2017, 2217 people have downloaded the Know your DAS app and much interest has been shown by users from outside the UK who would like to be able to use the app. Clinicians are keen to utilise the app with their patients
Conclusions: Further research needs to be carried out to compare patients adherence, engagement with their clinicians and ownership of their disease managment as a direct result of using the Know Your DAS app.
Acknowledgements: Roche/Chugai Pharmaceuticals for their funding and development of this resource
Disclosure of Interest: C. Jacklin Grant/research support from: Roche/Chugai Pharmaceuticals, S. Arora: None declared
DOI: 10.1136/annrheumdis-2017-eular.1931

OP0280-PARE PATIENT PANELS ON ACCESS AND ADHERENCE TO TREATMENT FOR SLE PATIENTS

S. Badreh, J. Andersen, A. Charlet, K. Lerstrøm, K.H. Wheeler. *Lupus Europe, Essex, United Kingdom*

Background: At the LUPUS EUROPE [forward abbreviated with LE] 2013 Convention in Paris, Professor N. Costedoat-Chalumet illustrated to the participants the critical issue of adherence to treatment (or more precisely, the lack of it). For many reasons, adhering to the prescribed treatment is a challenge for people living with Lupus, yet, "medicine only works if you take it". Understanding this area is critically important to helping people with lupus improve their quality of life.
Objectives: In LE, we wanted to know the reason(s) for this lack of adherence and how to improve it. Is lack of access also a reason for not adhering to treatment?
Methods: Two patient panels were formed to conduct in depth discussion about treatment. For each panel we invited people from our European community through our member groups. The panels were organised to represent different aspects like gender, age, time of diagnosis, main disease area and representing different countries. It was important to LE, that both patient panels were conducted by and for people living with lupus, which gives the participants a feeling of security and being understood: this is very important if you want them to share their experiences openly.
LE organised the first patient panel on November 2nd-4th 2015, bringing together 10 people living with lupus, from 7 countries, to share their experience about "treatment", with a view to help improving the quality of life of people living with lupus. The second patient panel took place on March 11–13, 2016 bringing together 9 lupus affected people from all over Europe to further explore the burden of living with lupus, and to dive into the burden of daily treatment.
The panels were conducted through a series of interactive presentations, team discussions and working groups.
Results: The key findings of both patient panels were:
1. Because "Treatment" is broad; it is both medicine based and non-drug based, and can be categorised in three ways – core, medical, and well-being; there needs to be a more holistic approach to the patient.
2. Access includes ease of contact with Health Care Practitioners, support services such as orthotics and quality information as well as availability of medicines.
3. Patients will take new medicine, provided they understand the reasons why and the side effects.
4. Each patient is responsible for their own treatment and must realise that a positive mind-set can be decisive for the treatment of the disease.
5. Patient Organisations have a critical role to play, creating a community, sharing reliable information, providing hope, raising awareness and advocating for lupus.
Conclusions: Organising a patient panel with a small closed group of patients on neutral ground in a "safe" environment has proven to be a good way of getting the patients to speak openly about a difficult subject and to reveal things, that they might not tell the health professionals. Through this initiative LE has gathered important information about access and adherence to treatment that we can now use to make suggestions about treatment and implement into our strategic plan for the years to come.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2541

OP0281-PARE EDUCATING PATIENT EXPERTS/PATIENT PARTNERS – A NEW WAY

A. Phoka Charalambous[1], I. Cederlund[2], M. Neylander[2]. *[1]Cyprus League Against Rheumatism, Nicosia, Cyprus; [2]The Swedish Rheumatism Organisation, Stockholm, Sweden*

Background: Patients general well-being is largely dependent on health care professionals. The education of these is therefore very important. It is more and more common using patients in the education of health care professionals. The Universities in Cyprus together with other health professional groups have shown interest in involving patients with RheumatoMusculoSceletalDiseases (RMDs) in the education of medical school students regarding RMDs. Besides discussing the disease, they will also learn about the obstacles faced by the patients as well as the impact on their daily life. Through this initiative, the hope is that early recognition and diagnosis is promoted as well as enhancing the knowledge and skills of future doctors.
Objectives: The aim of this project was to implement a Patient Expert project in Cyprus League Against Rheumatism (CYPLAR), and through it train RMD patients to educate medical students and other healthcare professionals regarding

RMDs. A learning partnership should be created between undergraduate medical students/healthcare professionals and the patient experts.
Methods: CYPLAR approached the Swedish Rheumatism Association for collaboration in order to implement the Patient Expert Project in CYPLAR.Funding was received from the EULAR Knowledge Transfer Programme. The collaboration was planned to consist of two meetings, one in Sweden and one in Cyprus.
1. Sweden: Two patients, members of CYPLAR, with RMDs, together with a Rheumatologist from CYPRUS visited the Swedish Rheumatism Association in Stockholm to learn about the Patient Partner Project, and receive Patient Expert training.
2. Cyprus: Two Patient Partner Instructors from the Swedish Rheumatism Association went to Cyprus 6 months after to oversee the progress of the Patient Expert programme and to make an examination of the two Patient Partners educated in Stockholm.
Results: The training session in Stockholm took place on May 2016, for two patients. They received training following the Swedish Patient Expert programme. This training was conducted by two Patient Expert Instructors, one rheumatologist and one Patient Expert. A visit to the Karolinska University Hospital with a tour of the Rheumatology Clinic and a Patient Expert demonstration was also included. The visit ended with a detailed plan formed for the implementation of the Patient Expert programme in CYPLAR.
The visit of the Swedish delegation took place in October 2016. Eight patients participated in the training. The training was made through workshops by the delegates from both organizations together with a Professor of rheumatology and a communication lecturer at the St George's University of London in Nicosia's establishments. Medical students were also involved in discussing their experience in being educated by patients. The programme also involved practice of joint examinations. The workshop was evaluated by the participants on the final day. After the workshop was concluded delegates spent a day discussing the event together. The programme was evaluated, and a future plan of action decided upon.
Conclusions: The implementation of the patient expert programme was successful.10 new Patient Experts are now available in CYPLAR.The next generation of health professionals will benefit and get a larger understanding of RMD's and in the end, the patients will benefit because the health care staff has a greater knowledge.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3705

OP0282-PARE #DOESNTSHOWDOESNTEXIST / #SYNSINTEFINNSINTE – A PHOTO CAMPAIGN BY UNGA REUMATIKER

K. Nordlund, M. Beermann. *Unga Reumatiker, Stockholm, Sweden*

Background: "Rheumatism amongst young people, is that really a thing?" "Isn't rheumatism something that only old people have?" "You seem so happy and so active, surely you can't be in pain?" These are all questions that young people with rheumatism have to listen to, and answer every day.
Yes, it's possible to have rheumatism even as a young person, and to be in pain, even though we're not letting it show. We know adjustment is possible, and that we can live our life to the fullest and follow our dreams, despite rheumatism. But sometimes it demands some extra understanding from the people around us. That's what we wanted to recognize, and created a campaign together with AbbVie.
Objectives: It can be hard to understand and fully grasp something you can't see, something that is invisible. But as young people with rheumatism, we have to live and deal with our swollen joints, with the pain and the fatigue, and with the side effects of our medication. None of which should be questioned.
We recognized that this was an issue for most people with rheumatism, and especially young people. Therefore, we wanted to start a conversation about how it is to go through life with an invisible disability.
The main purpose with our campaign was to acknowledge the fact that you can't always tell whether or not a person has a diagnosis, or is in pain. We also wanted to show young people with rheumatism that they are not alone in their situation.
Methods: We searched for young people with rheumatism in different ages and with different diagnoses. Each person in the campaign is presented in two different photos. One standard full-portrait photo in front of a white background, just showing who they are. One person held a basketball to show off her love for the sport, another one was wearing her dancing shoes and so on. The other photo is instead set in a complete dark room, with the person posing in the same way but this time with their rheumatism-affected areas lit up. We used glow in the dark-body paint and a UV-light to create this effect.
Each pair of photos is put together with the person's story about their passion in life and what it's like to live and deal with an invisible disability.
The campaign was released on October 12th 2016, on World Arthritis Day, with an event at Astrid Lindgren's children's hospital in Stockholm. The photos were printed and presented on large boards together with the personal stories.
The first photo of the campaign, a group photo of everyone participating, was also posted on our social media on October 12th and then one pair of photos was posted every day during the following week. People were also told to share their own stories under the hashtag #synsintefinnsinte
Results: The campaign ended up being our organization's most successful campaign to this date. The spread was especially great on Facebook, with the first post reaching nearly 50'000 people and the other posts reaching between 3'500 and 25'000 people every day. The campaign had more likes and shares on both Facebook and Instagram than any of our other campaigns has had so far.
The opportunity to show the photos at Astrid Lindgren's children's hospital also brought health care into the campaign and attracted great attention on site.
The photos combined with the personal stories make a powerful statement. We managed to show young people with rheumatism that they are not alone in their situation, and we look forward to the conversation continuing on at #synsintefinnsinte



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4893

FRIDAY, 16 JUNE 2017

Imaging and treamtent response in rheumatology

OP0283 ULTRASONOGRAPHIC EVALUATION IN RHEUMATOID ARTHRITIS USING THE GLOBAL OMERACT/EULAR ULTRASOUND SYNOVITIS SCORE (GLOESS)

M.S. Stoenoiu[1], A. Pesonen[1], N. Bello[2], R. Christensen[3], M. Østergaard[4], E. Naredo[2], L. Terslev[4]. *[1]Rheumatology, Cliniques Universitaires Saint-Luc, Brussels, Belgium; [2]Rheumatology, University Hospital Gregorio Marañon, Madrid, Spain; [3]Musculoskeletal Statistics Unit, Bispebjerg and Frederiksberg Hospital; [4]Center for Rheumatology and Spine Diseases, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark*

Background: Recently, a global OMERACT/EULAR ultrasound (US) synovitis score (GLOESS) combining grey-scale (GS) and power-Doppler (PD) scores has been proposed as a novel measurement tool to assess disease activity and response to therapy in patients with rheumatoid arthritis (RA)[1,2]. However, the ability of GLOESS to differentiate patients with different states of disease activity *vs.* remission in standard clinical care is not known.
Objectives: To assess the ability of GLOESS to discriminate between different clinical states of activity *vs.* remission in RA patients, and to compare clinical, GLOESS and PD US remission criteria and scores in a cross-sectional study.
Methods: Eighty RA patients from 3 centres were recruited at consecutive clinical visits: 50% were in remission and 50% had active RA according to Simple Disease Activity Index (SDAI). SDAI, Clinical Disease Activity Index (CDAI), 28-joint Disease Activity Score (DAS 28CRP), Health Assessment Questionnaire (HAQ), ACR/EULAR remission criteria were assessed. An independent investigator unaware of clinical results performed all US joint examinations of 26 joints. GLOESS, PD, and GS US sum scores per patient were assessed using OMERACT definitions. PD US remission was defined as the PD sum score =0. GLOESS remission was defined as GLOESS score $\leq$1 thereby also including possible GS grade 1.
Results: PD US remission was observed in 38 (48%) patients and GLOESS remission in 16 (20%) patients. SDAI (r=0.24; p=0.03) and CDAI (r=0.23; p=0.04) but not DAS28CRP (r=0.21; p>0.05) were weakly correlated with GLOESS scores in the whole joint set. SDAI (r=0.41; p<0.001), CDAI (r=0.40; p<0.001), and DAS28CRP (r=0.40; p<0.001) were moderately correlated with PD activity in the whole joint set. A minority of patients were classified both in GLOESS remission and in clinical remission according to SDAI (n=10), to CDAI (n=10), to DAS28CRP (n=10) and to ACR/EULAR 2011 (n=7). Less than one third of patients were classified both in PD US remission and in clinical remission according to SDAI (n=22), to CDAI (n=26), to DAS28CRP (n=27) and to ACR/EULAR 2011 (n=21). The proportion of patients in clinical remission was significantly different according to the definition considered: while 50% of the patients (n=40) were classified in remission according to SDAI, 58% (n=46) were classified in remission according to DAS28CRP, and 43% (n=34) according to CDAI and 43% (n=34) according to ACR/EULAR 2011 remission criteria.
Conclusions: We document major discrepancies between US and clinical findings and between clinical scores classifying patients in active disease *vs.* remission. Patients reaching GLOESS or PD US definitions of remission are partly different from those reaching clinical definitions of remission.
References:
[1] Naredo E, et al. The OMERACT ultrasound task force–status and perspectives. J Rheumatol. 2011;38(9):2063–2067.
[2] D'Agostino MA, et al. Exploring a new ultrasound score as a clinical predictive tool in patients with rheumatoid arthritis starting abatacept: results from the APPRAISE study. RMD Open. 2016 5;2(1):e000237. doi: 10.1136/rmdopen-2015–000237.
Acknowledgements: We acknowledge P. Durez, B. Lauwerys, A. Durnez, A.

Nzeusseu Toukap, F.A. Houssiau for fruitful discussions and/or contribution to recruitment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2387

OP0284 EVALUATION OF THE IMPACT OF BASELINE LEVELS OF MRI-DETECTED INFLAMMATION ON TREATMENT RESPONSE IN EARLY, SEROPOSITIVE, MTX-NAÏVE RA: DATA FROM THE AVERT TRIAL

H. Ahmad[1], J. Baker[2], M. Østergaard[3], P. Emery[4], P. Durez[5], J. Ye[1], S. Banerjee[1], P. Conaghan[6]. *[1]Bristol-Myers Squibb, Princeton; [2]University of Pennsylvania, Philadelphia, United States; [3]Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [4]University of Leeds and Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom; [5]Université Catholique de Louvain, Brussels, Belgium; [6]University of Leeds, Leeds, United Kingdom*

Background: AVERT (Assessing Very Early Rheumatoid arthritis Treatment) was a Phase IIIb, randomized, 24-month (M) trial with a 12M, double-blind treatment period, and included contrast-enhanced MRI of the dominant hand and wrist. MRI can provide direct evidence of joint inflammation, enabling stratification of patient (pt) data according to MRI inflammation level, e.g. low vs high.[1] This stratification is hypothesized to predict clinical treatment response.
Objectives: To evaluate the proportion of pts achieving remission at M12 by baseline (BL) MRI-detected inflammation status and treatment group.
Methods: In AVERT, pts with early RA received abatacept (ABA) + MTX, ABA monotherapy or MTX. MRI inflammation was scored by two central readers at BL and M12. In this *post hoc* analysis, pts were stratified into "low" and "high" BL MRI inflammation groups. Low: ≤3 for synovitis, ≤3 for osteitis and ≤9 when combined (osteitis double weighted);[2] high: >3, >3 or >9, respectively. The proportion of pts achieving CDAI (≤2.8), DAS28 (CRP; <2.6), SDAI (≤3.3) and Boolean (TJC ≤1, SJC ≤1, CRP ≤1 mg/dL and pt global assessment of disease activity ≤1 [0–10 cm scale]) remission at M12 was compared by BL MRI inflammation and treatment group.
Results: Of 351 pts randomized and treated, 337 (96.0%) had MRI data at BL (ABA + MTX, n=114; ABA monotherapy, n=112; MTX, n=111). Mean (SD) BL synovitis, osteitis and total scores, respectively, for pts with low MRI inflammation receiving ABA + MTX vs MTX alone were: 2.6 (2.0) vs 3.1 (2.4), 0.3 (0.6) vs 0.2 (0.5) and 3.1 (2.4) vs 3.5 (2.7); high MRI inflammation: 9.2 (3.6) vs 9.3 (3.6), 10.0 (9.7) vs 10.7 (9.8) and 29.3 (21.3) vs 30.7 (21.3). BL DAS28 (CRP), CDAI and SDAI scores, respectively, for pts with low MRI inflammation receiving ABA + MTX vs MTX alone were: 5.1 (1.1) vs 5.0 (1.3), 34.0 (14.7) vs 32.1 (15.0) and 39.9 (17.4) vs 43.5 (24.6); high MRI inflammation: 6.2 (1.2) vs 5.6 (1.4), 43.4 (16.2) vs 37.7 (18.1) and 76.9 (44.9) vs 61.1 (35.2). The proportion of pts with low BL MRI inflammation attaining remission at M12 was similar regardless of treatment. In pts with high MRI inflammation, remission rates were significantly greater in pts treated with ABA + MTX vs MTX alone (Table).

Table 1. Proportion of Patients in Remission at Month 12 by Treatment and Baseline MRI Inflammation Status*

Remission criteria	Low MRI inflammation		High MRI inflammation	
	ABA+MTX (n=63)	MTX (n=62)	ABA+MTX (n=51)	MTX (n=49)
DAS28 (CRP)	39 (61.9)	31 (50.0)	31 (60.8)†	20 (40.8)
CDAI	24 (38.1)	20 (32.3)	24 (47.1)†	10 (20.4)
SDAI	25 (39.7)	20 (32.3)	23 (45.1)†	8 (16.3)
Boolean	22 (34.9)	18 (29.0)	20 (39.2)†	8 (16.3)

Data are n (%); *low: ≤3 synovitis, ≤3 osteitis and ≤9 combined (osteitis double weighted); high: >3, >3 or >9; †p<0.05 vs MTX alone.

Conclusions: Pts with higher MRI inflammation may derive greater benefit from abatacept + MTX vs MTX alone. BL MRI inflammation is a predictor of subsequent clinical treatment response to abatacept in RA. MRI may have clinical utility in treatment decisions beyond information obtained from clinical assessments alone.
References:
[1] Gandjbakhch F, et al. J Rheumatol 2014;41:398–406.
[2] Ahmad HA, et al. Ann Rheum Dis 2016;75:624.
Disclosure of Interest: H. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, J. Baker: None declared, M. Østergaard Grant/research support from: AbbVie, Bristol-Myers Squibb, Janssen, Merck, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, Wyeth, P. Emery Grant/research support from: AbbVie, Merck, Pfizer, Roche, Consultant for: AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, Lilly, Novartis, Samsung Bioepis, P. Durez Speakers bureau: Bristol-Myers Squibb, Lilly, Janssen, Sanofi, Roche, Pfizer, J. Ye Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Banerjee Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, P. Conaghan Grant/research support from: Bristol-Myers Squibb, Consultant for: AbbVie, Lilly, Novartis, Pfizer, Speakers bureau: AbbVie, Bristol-Myers Squibb, Roche
DOI: 10.1136/annrheumdis-2017-eular.1723

OP0285 ATTENUATION OF FLUORINE-18-FLUORODEOXYGLUCOSE UPTAKE IN LARGE VESSEL GIANT CELL ARTERITIS AFTER SHORT-TERM HIGH-DOSE STEROID TREATMENT – A DIAGNOSTIC WINDOW OF OPPORTUNITY

B.D. Nielsen[1], L.C. Gormsen[2], I.T. Hansen[1], K.K. Keller[1], P. Therkildsen[1], E.-M. Hauge[1]. *[1]Department of Rheumatology; [2]Department of Nuclear Medicine and PET centre, Aarhus University Hospital, Århus, Denmark*

Background: Fluorine-18-fluorodeoxyglucose (FDG) PET/CT is increasingly used to diagnose large vessel GCA (LV-GCA) due to its excellent diagnostic accuracy[1]. However, PET/CT is not always readily available, which may compel the clinician to 1) either delay steroid treatment at the risk of GCA related complications, or 2) initiate treatment at the expense of diagnostic sensitivity of the FDG PET/CT study.
Objectives: To evaluate if FDG PET/CT can accurately diagnose LV-GCA after 3 or 10 days of high-dose steroid treatment.
Methods: Twenty-four treatment-naïve patients (16 women) with a mean age of 69 (range 57–84) years with FDG PET/CT (PET0) proven LV-GCA repeated FDG PET/CT after either 3 (PET3, n=10) or 10 days (PET10, n=14) of treatment with oral prednisolone 60 mg daily. Prior to treatment, clinical examination and laboratory tests were performed to confirm GCA and exclude differential diagnoses. A temporal artery biopsy (TAB) was performed in all patients.
Two experienced nuclear medicine physicians blinded to clinical data reviewed the FDG PET/CT images. LV-GCA was suspected if increased FDG uptake in the wall of the aorta and/or supra-aortic branches was observed. A semi-quantitative approach was applied (a.m. Meller) in which FDG uptake was graded on a 5-point scale (0; no uptake, 1; ≤ blood pool, 2; > blood pool, ≤ liver, 3; ≥ liver, 4; ≥2xliver). A score ≥3 was considered consistent with vasculitis[2]. Vascular composite scores (CS) was calculated summarizing grades from assessed vascular regions; *Aortic:* Aorta ascendens, aorta descendens and aortic arch; *aortic branches:* Vertebral, carotic and subclavian/axillary artery.
Results: Mean CRP and ESR were 72 (95% CI: 55; 94) mg/l and 81 (95% CI: 72; 90) mm/h, respectively. ACR criteria for GCA was fulfilled by 18/24 patients and 17/21 had a positive TAB. Mean number of prednisolone doses before the post-treatment FDG PET/CT were 3.1 (SD 0.3) (PET3) and 10.3 (SD 0.7) (PET10).
Vascular CS in aorta did not decrease at PET3 (9 (IQR 9–9) vs. 9 (IQR 6–9)) whereas a significant decrease was observed in aortic branches at PET3 (6.5 (IQR 6–8) vs 5.5 (IQR 5–7), p<0.01) and both vascular domains at PET10 (Aortic; 9 (IQR 9–9) vs. 5.5 (IQR 3–6), aortic branches; 7 (IQR 7–8) vs 5 (IQR 4–6)). Although, FDG uptake decreased in aortic branches after 3 days, LV-GCA could still be accurately diagnosed in 10/10 patients. By contrast, LV-GCA could only be diagnosed in 5/14 patients after 10 days (PET0 vs. PET10, p<0.01).
At day 10, VAS global was significantly higher in patients with positive PET10 compared to patients with negative PET10 (5.2 (95% CI 3.6; 7.0) vs. 2.7 (95% CI 1.2; 4.2), p<0.05). No clinically significant differences in baseline phenotypical presentation, CRP or PET CS were found between patients with positive and negative PET10, respectively.
Interrater reliability of visual FDG-uptake-grading was substantial (agreement 90%, Cohens weighted kappa 0.67).
Conclusions: In LV-GCA, high-dose steroid treatment for three or ten days differentially attenuates the regional uptake of FDG but diagnostic accuracy remains within the first three days.
References:
[1] Puppo et al. BioMed research international 2014.
[2] Stellingwerff MD et al. Medicine 2015.
Acknowledgements: Assesment of PET scans by Stine Kramer and Tronds Bogsrud is mostly appreciated.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5788

OP0286 THE UTILITY OF THE OMERACT ULTRASOUND TENOSYNOVITIS SCORING SYSTEM IN MULTICENTER CLINICAL TRIALS

M. Ammitzbøll-Danielsen[1,2], M. Østergaard[1,2], N. Esperanza[3,4], A. Iagnocco[5], I. Möller[6], M.-A. D'Agostino[7], F. Gandjbakhch[8], L. Terslev[1]. *[1]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup; [2]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark; [3]Department of Rheumatology, Joint and Bone Research Unit. Hospital Universitario Fundación Jiménez Díaz; [4]Department of Rheumatology, Hospital General Universitario Gregorio Marañón and Universidad Complutense, Madrid, Spain; [5]Dipartimento Scienze Cliniche e Biologiche, Università degli Studi di Torino, Turin, Italy; [6]Department of Rheumatology, Instituto Poal de Reumatología, Barcelona, Spain; [7]Department of Rheumatology, Assistance publique-Hôpitaux de Paris Ambroise Paré Hospital, Boulogne-Billancourt, Université Versailles Saint Quentin en Yvelines; [8]Department of Rheumatology, Praticien Hospitalier, Paris, France*

Background: Tenosynovitis is very common in patients with rheumatoid arthritis (RA) and is associated with lower physical function. Several studies have confirmed the limitations of clinical examination for detection of tenosynovitis in comparison with ultrasound (US) and a highly validated and reliable US scoring

system is therefore needed if implementing US-tenosynovitis as an outcome measure in clinical trials. The Outcome Measures in Rheumatology (OMERACT) US group's tenosynovitis scoring system has a good single and multicenter intra- and inter-observer agreement, whereas the sensitivity to change in a multicenter design has never been tested.
Furthermore, it is unknown whether low grade synovial hypertrophy without Doppler Signal represents true inflammation, i.e. can be eliminated by anti-inflammatory therapy and is sensitive to change.
Objectives: The aim of this study was to test the sensitivity to change of the OMERACT US scoring system for tenosynovitis, including minimal signs of tenosynovitis, in a multicenter design in order to validate it as an outcome measure in RA multicenter clinical trials. Furthermore, to assess the association between US and health assessment questionnaire (HAQ) and Disease Activity Score 28 for joints (DAS28).
Methods: Forty-nine patients with established RA (duration ≥1 year) and 18 early RA patients (<1 year) with US-verified tenosynovitis were recruited from six rheumatology outpatient clinics in four different countries, if they were scheduled for treatment intensification with synthetic and/or biological Disease Modifying Anti-Rheumatic Drug. Tenosynovitis was assessed at baseline, and at three and six months' follow-up, by GS and Doppler, using the semi-quantitative OMERACT scoring system. Furthermore, HAQ and DAS28 were assessed.
Results: At baseline tenosynovitis was most frequently found at the extensor carpi ulnaris and tibialis posterior tendons (70.7% and 44.4%, respectively). The overall GS score showed a statistically significant decrease from baseline median 5 (25th;75th percentile: 2;7) to 6 months 0 (0;3) and the overall Doppler score decreased statistically significant from baseline 3 (2;6) to 6 months 0 (0;1), both with a p<0.01. Both GS and Doppler showed high responsiveness (SRM>0.9), as did HAQ and DAS28 (table 1). Among tendons with grey scale (GS)=1/Doppler=0, 36 of 39 (92.3%) showed therapy-induced improvements. A change of 2.1 (95% confidence interval: 1.2;14.9) and 2.1 (CI: 1.1;13.2) in DAS28 corresponded to a change in GS and Doppler of 1 (both p=0.02) respectively, using a mixed-model for repeated measurement. However, no association between US and HAQ was found.

Table 1. Change in tenosynovitis ultrasound scores, DAS28, HAQ, and their standardized response mean, during 6 month of follow-up, for all patients

All Sites - Imaging modality (n=67)		Baseline	Δ 0-3 month	p	SRM	Δ 3-6 month	p	SRM	Δ 0-6 month	p	SRM
Grey scale	Median [25p;75p]	4 [2;7]	-2 [-3;-0]	<0.01	0.8	-1.0 [-2.0]	<0.01	0.4	-2 [-5;-1]	<0.01	0.9
	Mean ±SD	5.0 ±3.4	-2.4 ±2.9			-0.9 ±2.4			-3.3 ±3.8		
Doppler	Median [25p;75p]	3 [2;6]	-2 [-4;-1]	<0.01	0.8	0 [-2;0]	<0.01	0.3	-3 [-5;-2]	<0.01	0.9
	Mean ±SD	3.2 ±0.66	-0.8 ±0.6			0 ±0.2			-0.7 ±0.6		
DAS28	Median [25p;75p]	4.6 [3.7;5.4]	-1.4 [-1.8;-0.2]	<0.01	0.9	-0.4 [-1.3;0.1]	<0.01	0.3	-1.6 [-3.2;-0.7]	<0.01	1.1
	Mean ±SD	4.4 ±1.3	-1.4 ±1.5			-0.5 ±1.3			-1.8 ±1.7		
HAQ	Median [25p;75p]	1.0 [0.5;1.5]	-0.25 [-0.75;0]	<0.01	0.8	0 [-0.25;0]	0.02	0.5	-0.375 [-0.875;0]	<0.01	0.9
	Mean ±SD	1.0 ±0.6	-0.4 ±0.4			-0.1 ±0.3			-0.5 ±0.5		

P, p-value for Wilcoxon's test for change of paired data between 2 time points; N, number of patients; SRM, standardized response mean; DAS28, Disease Activity Score for 28 joints, using C-reactive protein; HAQ, health assessment questionnaire;. Values in brackets are values at 25th and 75th percentiles

Conclusions: In conclusion, this RA multicenter study documented a high sensitivity to change of both GS and Doppler US tenosynovitis scores, indicating utility of the OMERACT US scoring system for diagnosing and monitoring tenosynovitis in multicenter trials. Secondly, synovial hypertrophy without Doppler signal, do respond to therapy, suggesting it reflects true inflammation. Finally, changes in US tenosynovitis scores are associated with changes in DAS28.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1651

OP0287 ULTRASONOGRAPHY-DETECTED PERIPHERAL ENTHESITIS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS – ANATOMICAL DISTRIBUTION, MORPHOLOGY AND RESPONSE TO ANTI-TNF THERAPY

S. Seven, S.J. Pedersen, M. Østergaard, I.J. Sørensen, U.M. Døhn, S. Krabbe, L. Terslev. *Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine diseases, Rigshospitalet, Glostrup, Denmark*

Background: Peripheral enthesitis (PE) is a characteristic feature of spondyloarthritis (SpA) that may be asymptomatic and only detectable by imaging. Ultrasonography (US) has greater sensitivity than clinical examination for the detection of PE.[1]
Objectives: The aim of the study was to investigate the anatomical distribution, morphological abnormalities and response to anti-tumor necrosis factor (anti-TNF) therapy of US-detected PE in patients with axial SpA (axSpA) initiating adalimumab (ADA).
Methods: In a randomized, placebo-controlled, double-blinded investigator-initiated trial (NCT01029847), patients with axSpA according to the Assessment of SpA International Society (ASAS) criteria were randomized to subcutaneous ADA 40 mg every other week (eow) or placebo from baseline to week 6. From week 6 to 24, all patients received ADA 40 mg eow. Of 49 patients enrolled, 21 participated in the US sub-study. US assessment applying the OMERACT US definitions for enthesitis[2] of 10 peripheral entheseal regions (Tables 1 & 2) and clinical examination were performed at baseline, weeks 6 and 24. US was performed by an experienced investigator. Hypo-echogenicity, increased thickness and Doppler activity of the enthesis were considered signs of active inflammation, whereas insertional bone erosions, intratendinous calcifications and enthesophytes were regarded as signs of chronic lesions.[2]
Results: See tables.
Conclusions: In this axSpA cohort, US assessment primarily identified PE in the lower extremities, and predominantly chronic lesions. No change in chronic PE lesions were found during treatment indicating a low sensitivity to change of these lesions. The number of entheses with inflammatory activity was too low to detect any changes on US during ADA therapy.

Table 1. Distribution of US findings at baseline (n=21)

Entheseal regions	Enthesitis* N (%)	Chronic lesions N (%)	Inflammation N (%)
Supraspinatus tendon	6 (29)	6 (29)	0
Triceps tendon	2 (10)	1 (5)	1 (5)
Common extensor, elbow	5 (24)	5 (24)	1 (5)
Common flexor, elbow	0	0	0
Greater femoral trochanter	11 (52)	11 (52)	0
Quadriceps tendon	13 (62)	13 (62)	3 (14)
Proximal insertion of the patellar tendon	3 (14)	2 (10)	1 (5)
Distal insertion of the patellar tendon	3 (14)	2 (10)	2 (10)
Achilles tendon	17 (81)	16 (76)	4 (19)
Plantar fascia	4 (19)	0	4 (19)

*inflammation and/or chronic lesions.

Table 2: US and clinical findings during study period

	Placebo			ADA		
	Week 0 (N=10)	Week 6 (N=9)	Week 24 (N=10)	Week 0 (N=11)	Week 6 (N=11)	Week 24 (N=10)
US findings						
Supraspinatus tendon	3 (30)	2 (22)	1 (10)	3 (27)	2 (18)	1 (10)
Triceps tendon, elbow	1 (10)	0	1 (10)	1 (9)	0	2 (20)
Common extensor, elbow	0	0	0	5 (46) *	0	1 (10) ‡
Common flexor, elbow	0	0	0	0	0	0
Greater femoral trochanter	6 (60)	6 (67)	6 (60)	5 (46)	6 (55)	6 (60)
Quadriceps tendon	4 (40)	1 (11)	4 (40)	9 (82)	8 (73)	6 (60)
Proximal patellar tendon	1 (10)	0	0	2 (18)	1 (9)	1 (10)
Distal patellar tendon	2 (20)	1 (11)	1 (10)	1 (9)	1 (9)	0
Achilles tendon	7 (70)	7 (78)	8 (80)	10 (91)	7 (64)	7 (70)
Plantar fascia	1 (10)	0	0	3 (27)	3 (27)	2 (20)
Clinical findings						
MASES	4.6 (4.0)	4.0 (3.3)	2.2 (3.7)	3.0 (3.7)	2.1 (2.5)	2.0 (3.0)
LEI	0.7 (0.9)	0.9 (1.0)	0.6 (0.9)	1.1 (1.1)	0.7 (0.9)	0.3 (0.7)
SPARCC Enthesitis Index	3.2 (3.8)	3.6 (2.6)	2.2 (2.8)	2.6 (2.9)	1.6 (1.9) †	0.8 (1.1) ‡
BASDAI	7.0 (1.9)	6.4 (2.5)	4.3 (2.7) ‡	6.3 (1.3) *	4.2 (2.3) †	2.9 (2.5) ‡

N (%), Mean (SD) for LEI, SPARCC and BASDAI. Wilcoxon Rank test was applied. P<0.05 is considered significant.
* P<0.05 week 0-6; † P<0.05 week 6-24; ‡ P<0.05 week 0-24.
MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; LEI, Leeds Enthesitis Index; SPARCC, Spondyloarthritis Research Consortium of Canada; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index.

References:
[1] D'Agostino MA, et al. Ann Rheum Dis 2011, 70(8):1433–1440.
[2] Terslev L, et al. Arthritis Care Res (Hoboken) 2014, 66(5):741–748.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2781

OP0288 RELIABILITY OF A EULAR-OMERACT SEMIQUANTITATIVE SCORING SYSTEM FOR THE ASSESSMENT OF CARTILAGE IN RHEUMATOID ARTHRITIS

P. Mandl[1], E. Filippucci[2], P. Studenic[1], A. Bachta[3], D. Bong[4], G.A. Bruyn[5], C. Dejaco[6], A. Delle Sedie[7], C. Duftner[8], I. Gessl[1], H.B. Hammer[9], C. Hernandez Diaz[10], A. Iagnocco[11], K. Ikeda[12], D. Kane[13], H. Keen[14], E. Kővári[15], U. Moeller-Doehn[16], E. Naredo[17], J.-C. Nieto[18], C. Pineda[10], A. Rodriguez[19], W.A. Schmidt[20], G. Supp[1], L. Terslev[16], R. Thiele[21], D. Windschall[22], M.-A. D'Agostino[23], P.V. Balint[24]. *[1]Medical University of Vienna, Vienna, Austria; [2]Università Politecnica delle Marche, Jesi, Italy; [3]Military Institute of Medicine, Warsaw, Poland; [4]Instituto Poal de Reumatologia, Barcelona, Spain; [5]MC Groep, Lelystad, Netherlands; [6]Medical University of Graz, Graz, Austria; [7]University of Pisa, Pisa, Italy; [8]Medical University of Innsbruck, Innsbruck, Austria; [9]Diakonhjemmet Hospital, Oslo, Norway; [10]Instituto Nacional de Rehabilitación, Mexico City, Mexico; [11]Universitá degli Studi di Torino, Turin, Italy; [12]Chiba University Hospital, Chiba, Japan; [13]Trinity College Dublin, Dublin, Ireland; [14]University of Western Australia, Perth, Australia; [15]Semmelweis University, Budapest, Hungary; [16]Copenhagen University Hospital Glostrup, Copenhagen, Denmark; [17]Hospital Universitario Fundación Jiménez Díaz and Autónoma University; [18]Hospital General Universitario Gregorio Marañón and Complutense University; [19]Hospital Ramón y Cajal, Madrid, Spain; [20]Immanuel Krankenhaus, Berlin, Germany; [21]University of Rochester, Rochester, United States; [22]Asklepios Hospital, Weissenfels, Germany; [23]Université VSQY, Inserm U1173, APHP Ambroise Paré, Boulogne-Billancourt, France; [24]National Institute of Rheumatology and Physiotherapy, Budapest, Hungary*

Background: Joint destruction in rheumatoid arthritis (RA) is comprised of hyaline cartilage and bone damage, with the former more clearly associated with irreversible physical disability than bony damage.
Objectives: To test the reliability of a semiquantitative scoring system for the assessment of cartilage by musculoskeletal ultrasound (US) in a web-based exercise as well as a patient-based reliability study of patients with RA.
Methods: Static images of metacarpophalangeal (MCP) joints 2–5 in RA patients and healthy controls were acquired and a dataset of 123 anonymized images including 25 duplicate images was circulated among an international EULAR-OMERACT taskforce of 25 rheumatologist experts in US who independently scored the images using a semiquantitative scoring system. Subsequently 12 taskforce members participated in a patient-based reliability study. During this

meeting MCP joints 2–5 of 6 patients with RA were assessed twice on the same day by all experts using US machines (GE) equipped with high-frequency transducers (18–22MHz) with presets calibrated for the appropriate assessment of cartilage. Participants assessed metacarpal cartilage both in the standardized longitudinal midline scan as well as by freehand technique utilizing multiple planes and scored by the semiquantitative scoring system. Intraobserver reliability was assessed by Cohen's kappa and interobserver reliability by Fleiss' kappa.

Results: The three-grade semiquantitative (Grade 0, normal cartilage; Grade 1, minimal change; Grade 2, severe change) scoring system demonstrated excellent (kappa: 0.87) to good (kappa: 0.73) intraobserver reliability in the web-based exercise and the patient-based reliability study respectively. Interobserver reliability was good in the web-based exercise (kappa: 0.64) and moderate (kappa: 0.49) in the patient-based reliability study. The dynamic technique performed slightly better than the longitudinal midline scan alone.

Conclusions: A semiquantitative scoring system demonstrated good intra- and moderate to good inter-observer reliability in a web-based exercise and patient-based reliability study. Our study demonstrates that US is a reliable tool for evaluating cartilage and supports the use of a new semiquantitative US scoring system for evaluating cartilage change in RA.

Acknowledgements: The patient-based reliability study was supported by a research grant from UCB.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4314

OP0289 TREAT-TO-TARGET IN EARLY RHEUMATOID ARTHRITIS: ASSOCIATION BETWEEN SUSTAINED REMISSION AND JOINT DAMAGE

N.P. Sundlisater[1], A.-B. Aga[1], I.C. Olsen[1], H.B. Hammer[1], T. Uhlig[1], D. van der Heijde[2], T.K. Kvien[1], S. Lillegraven[1], E.A. Haavardsholm[1] on behalf of The Arctic study group. [1]*Diakonhjemmet Hospital, Oslo, Oslo, Norway;* [2]*Leiden University Medical Center, Leiden, Netherlands*

Background: Modern treatment of early RA is targeted towards remission. Sustained remission is viewed as more beneficial to the patient than remission at one time point, also with regards to inhibition of joint damage,(1, 2) but data are limited. Treat-to-target studies yielding high rates of sustained remission have improved the ability to assess the relationship between sustained remission and joint damage.

Objectives: To assess the frequency of no radiographic progression among early RA patients in sustained remission defined by established criteria and in patients with sustained absence of inflammation assessed by ultrasound.

Methods: RA patients with <2 years from first swollen joint who were DMARD naive with indication for DMARD treatment were included in the ARCTIC trial.(3) Patients in the ultrasound arm aiming for DAS <1.6, no swollen joints and no ultrasound power Doppler (PD) signal were included in the current analyses. Several definitions of sustained remission (12–24 months) were compared; DAS-ESR, DAS28-ESR, SDAI, CDAI, ACR/EULAR Boolean remission (based on 44 joints), no swollen joints (44SJC), no ultrasound PD signal in any joint (0–96) and minimal total ultrasound greyscale (GS) score (defined as GS ≤2, 0–96). No radiographic progression (12–24 months) was defined as <1 unit change in the van der Heijde modified Sharp score (vdHSS). Positive and negative likelihood ratios of no radiographic progression were estimated for patients in sustained remission per definition.

Results: Of 103 patients, 76 (74%) were female, mean [SD] age was 51.4 [12.9] years, disease duration 6.7 [5.3] months and DAS 3.5 [1.1]. The median [25th, 75th percentile] change in vdHSS 12–24 months was 0.49 [0.0, 1.03], and 73 (71%) patients had no radiographic progression. Sustained remission was reached by 23–61% according to the different criteria. Among patients in sustained remission, comparable proportions of patients did not progress radiographically across the different criteria (74–89%), with the most favorable result for minimal GS score (Table). Patients with sustained no PD or minimal GS score had an increased likelihood of no radiographic progression during the concurrent year (Table), but still rather weak to be useful in an individual patient. Based on the low LR+ none of the criteria identifies patients without radiographic progression very well; likewise, as the LR- is relatively high for all definitions, not being in remission does not change the probability of ongoing radiographic progression substantially.

Table The performance of sustained remission 12-24 months for identifying patients without radiographic progression in the same time period. Significant likelihood ratios in bold.

	Patients in sustained remission 12-24 months, n(%)	Patients in sustained remission and no radiographic progression 12-24 months, n(%)	Likelihood ratios of no radiographic progression 12-24 months	
			LR+ (95% CI)	LR- (95% CI)
Clinical outcomes				
DAS<1.6	46 (45)	37 (80)	1.69 (0.94, 3.05)	**0.70 (0.51, 0.98)**
DAS28<2.6	54 (52)	40 (74)	1.17 (0.76, 1.82)	0.85 (0.56, 1.29)
SDAI≤3.3	33 (32)	26 (79)	1.53 (0.74, 3.13)	0.84 (0.65, 1.09)
CDAI≤2.8	31 (30)	26 (84)	2.14 (0.91, 5.04)	**0.77 (0.61, 0.98)**
ACR/EULAR Boolean (based on 44 joints)	24 (23)	18 (75)	1.23 (0.54, 2.80)	0.94 (0.75, 1.18)
SJC44=0, (range 0-44)	50 (49)	39 (78)	1.46 (0.87, 2.44)	0.74 (0.51, 1.06)
Ultrasound				
PD=0, (range 0-96)	63 (61)	51 (81)	**1.75 (1.10, 2.78)**	**0.50 (0.32, 0.79)**
GS≤2 (range 0-96)	27 (26)	24 (89)	**3.29 (1.07, 10.10)**	**0.75 (0.61, 0.91)**

Conclusions: In this treat-to-target early RA study, sustained remission rates were generally high and radiographic progression limited. None of the sustained remission criteria were able to exclude concurrent radiographic progression. Absence of ultrasound inflammation performed best of the definitions assessed.

References:

[1] Aletaha D, et al. A&R. 2009;60(5).
[2] Lillegraven S, et al. ARD. 2012;71(5).
[3] Haavardsholm EA, et al. BMJ. 2016;354.

Disclosure of Interest: N. Sundlisater: None declared, A.-B. Aga: None declared, I. Olsen: None declared, H. Hammer Consultant for: AbbVie, Pfizer, BMS, Roche, UCB, T. Uhlig: None declared, D. van der Heijde: None declared, T. Kvien: None declared, S. Lillegraven: None declared, E. Haavardsholm Grant/research support from: AbbVie, Pfizer, MSD, Roche, UCB

DOI: 10.1136/annrheumdis-2017-eular.2366

OP0290 CORRELATION OF CXCL13 AND ULTRASSONOGRAPHIC FINDINGS OF JACCOUD ARTHROPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS

D.S. Ribeiro[1], C. Lins[1], E. Pimenta[1], V. Galvão[1], W. Santos[1], V. Machicado[1], C. Baleeiro[1], A. Pedreira[1], A.P. Duque[1], G. Rosa[1], A. Atta[2], I. Oliveira[2], M. Santiago[1]. [1]*Escola Bahiana de Medicina e Saúde Pública;* [2]*Faculdade de Farmácia, Universidade Federal da Bahia, Salvador, Brazil*

Background: Joint involvement in systemic lupus erythematosus (SLE) is one of the earliest manifestation of the disease (1).Only 2–5% of the cases develop a deforming and non-erosive type of arthritis, known as Jaccoud Arthropathy (JA). Until now, there is no serum autoantibodies marker for it (2).The chemokine CXC ligand 13 protein (CXCL13) is one of the most potent B-cell chemo attractants and is constitutively expressed in the B-cell follicles of secondary lymphoid organs (3). Its seric level has been associated to the degree of synovitis in patients with rheumatoid arthritis as studied by ultrasonography (US).

Objectives: To perform the first detailed US analysis of hands and wrists of SLE patients, with and without JA, and to correlate those findings with the levels of CXCL13,other clinical and laboratory features and disease activity

Methods: 64 patients with SLE were included, being 32 with JA and 32 without JA paired by age and disease duration. The definition of JA was based on clinical criteria recently described by Santiago (4).Patients and controls underwent a high-resolution US exam of wrists and hands. Synovial hypertrophy,tenosynovitis and erosions were evaluated according a semi-quantitative grading system according definitions provided by OMERACT (5). Serum concentrations of CXCL13 were quantified in both groups utilizing a commercially available kit. Autoantibodies such as antinuclear antibody (ANA), anti-dsDNA,anti-Sm,anti-SSA, anti-SSB were also tested. US findings were correlated with seric levels of CXCL13, other serological parameters and SLEDAI score.

Results: In the JA group, the mean age was 46.2 years and the mean duration of the disease was 17.3 years. Synovitis on US was found in 25 patients and tenosynovitis in 14. All of these findings were more frequent in SLE with JA, particularly tenosynovitis with difference statistically significant (p=0.002). In JA patients the median levels of CXCL13 was 23.21 pg/ml as compared to 11.48 pg/ml in SLE without JA group (p=0.08). There was an association between tenosynovitis and higher levels of CXCL13 in the JA group (p=0.026). Patients with active disease were more common in the JA group (p=0.004) and had increased serum levels of CXCL13 compared to patients with disease inactive (p=0.008).

Conclusions: In conclusion, the present study is one of a few to describe US findings in SLE patients with JA and it confirms that synovitis and tenosynovitis are common features in the majority of these patients. In addition, CXCL13 may be regarded as a biomarker for tendon inflammation in JA.

References:

[1] Messuti LZ, A. Joint Involvement in SLE: Controversy of RHUPUS. INTERNATIONAL TRENDS IN IMMUNITY. 2014;2(4):155–61.
[2] Galvao V, Atta AM, et al. Profile of autoantibodies in Jaccoud's arthropathy. Joint Bone Spine. 2009 Jul;76(4):356–60.
[3] Zheng B, Ozen Z, et al. CXCL13 neutralization reduces the severity of collagen-induced arthritis. Arthritis Rheum. 2005 Feb;52(2):620–6.
[4] Santiago MB. Jaccoud's arthropathy: proper classification criteria and treatment are still needed. Rheumatology intern. 2013 Nov;33(11):2953–4.
[5] Wakefield RJ. The OMERACT Ultrasound Group: status of current activities and research directions. The Journal of rheumatology. 2007 Apr;34(4):848–51.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2998

FRIDAY, 16 JUNE 2017

From genetics through epigenetics to proteomics: understanding disease mechanisms

OP0291 IDENTIFICATION OF NOVEL SUSCEPTIBILITY LOCI IN A LARGE UK COHORT OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) CASES

S.L. Smith[1,2], J. Bowes[1], J. Cobb[1,2], A. Hinks[1], S. Sampath[1], A. Yarwood[1], L. Wedderburn[3], K. Hyrich[2,4], W. Thomson[1,2] on behalf of Childhood Arthritis Prospective Study (CAPS), UK Juvenile Idiopathic Arthritis Genetics Consortium (UKJIAGC), Childhood Arthritis Response to Medication Study (CHARMS), Biologics for Children with Rheumatic Diseases (BCRD) and BSPAR-Etanercept. *[1]Arthritis Research UK CoGG, Centre for Musculoskeletal Research, The University of Manchester; [2]NIHR Manchester Musculoskeletal BRU, Manchester; [3]Arthritis Research UK Centre for Adolescent Rheumatology, UCL GOS Institute of Child Health, UCL, London; [4]Arthritis Research UK CoE, Centre for Musculoskeletal Research, The University of Manchester, Manchester, United Kingdom*

Background: Juvenile idiopathic arthritis (JIA) is a group of chronic arthropathies of unknown cause affecting children under 16yrs, and is the most common childhood inflammatory rheumatic diagnosis. In recent years great advances in dissecting the genetic basis of JIA have been made. In a landmark study, conducted on the two most common subtypes (oligoarthritis and RF-negative polyarthritis), 17 susceptibility loci were identified at genome-wide significance (p-value $<5x10^{-08}$) and a further 11 reaching suggestive significance (p-value $<1x10^{-06}$). These findings were the results of a large international collaboration using the ImmunoChip array, targetting 186 known loci in 12 autoimmune diseases. However, a limitation to the afore-mentioned study was that the analysis is limited to the selected loci; large genome-wide studies are now needed.
Objectives: The aim of this work is to identify novel genetic loci associated with disease susceptibility using a large cohort of UK JIA cases
Methods: Whole-genome genotyping data was generated using four platforms (Illumina). Following stringent quality control common variants to all four platforms were extracted from the individual datasets before merging together. Imputation was performed using the Haplotype Reference Consortium panel on the Michigan Imputation Server using Minimac3 software. SNPs with imputation accuracy ($r^2>0.5$), minor allele frequency >1% and Hardy-Weinberg p-value$>1x10^{-03}$ were retained for analysis. Association was conducted using logistic regression; using the top three principal components as covariates. Bioinformatics analysis was performed using in-house Capture Hi-C data, to study long-range interactions, to elucidate the potential function of the associated SNPs
Results: Post-QC, 2,585 cases and 5,181 controls were available for analysis with ~7.4 million SNPs. Analysis conducted within oligoarthritis and RF-negative polyarthritis cases, (n=1,617) confirmed 13 previously identified JIA risk loci and identified more than 20 potentially novel regions above suggestive significance ($2.25x10^{-05}$). Of these, rs7874896, an intergenic SNP located between *TNFSF15* and *TNFSF8* on chromosome 9 was one of the most strongly associated (p-value $3.67x10^{-07}$). *TNFSF15* is particularly interesting as by homology and function, is very similar to TNFα. Furthermore, in Crohns disease, it has been found that *TNFSF15* drives expression of pro-inflammatory cytokines (IFNγ) and TNFα from CD4+CD161+ T-cells, yet these cells were found to be resistant to anti-TNF treatment; suggesting that blockade of *TNFSF15* may possess therapeutic benefit. Further investigation of SNPs within the *TNFSF15/TNFSF8* gene region using Capture Hi-C data yielded potentially interesting interactions both within this region and with nearby genes within T- and B-cell lines
Conclusions: This study represents the largest GWAS conducted in JIA to date and our preliminary results have identified novel associations with the most common subtypes of the disease and may have highlighted a potentially novel therapeutic target
Acknowledgements: We thank Arthritis Research UK for their support: grants 20380 and 20385. CAPS was funded by Arthritis Research UK: grant 20542
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2471

OP0292 GENETIC VARIATION ASSOCIATED WITH CARDIOVASCULAR RISK IN AUTOIMMUNE DISEASES

A. Ateridо[1], J.D. Cañete[2], A. Fernández-Nebro[3], C. Ferrándiz[4], J. Tornero[5], J. Pérez-Gisbert[6], E. Domènech[4], B. Fernández-Guitiérrez[7], F. Gomollón[8], E. García-Planella[9], E. Fernández[10], R. Sanmartí[2], J. Gratacós[11], V.M. Martínez-Taboada[12], L. Rodríguez-Rodríguez[7], P.P. Perrotti[1], N. Palau[1], R. Tortosa[1], M. López-Lasanta[1], S. Marsal[1], A. Julià[1] on behalf of IMID Consortium (Spain). *[1]Vall Hebron Research Institute; [2]Hosp. Clínic de Barcelona and IDIBAPS, Barcelona; [3]Hosp. Reg. Univ. de Málaga, Málaga; [4]Hosp. Univ. Germans Trias i Pujol, Badalona; [5]Hosp. Univ. Guadalajara, Guadalajara; [6]Hosp. Univ. de la Princesa and IIS-IP; [7]Hosp. Clínico San Carlos, IDISSC, Madrid; [8]Hosp. Clínico Univ. de Zaragoza, Zaragoza; [9]Hosp. de la Santa Creu i Sant Pau, Barcelona; [10]Hosp. Univ. de Salamanca, Salamanca; [11]Hosp. Parc Taulí, Sabadell; [12]Hosp. Univ. Marqués de Valdecilla, Santander, Spain*

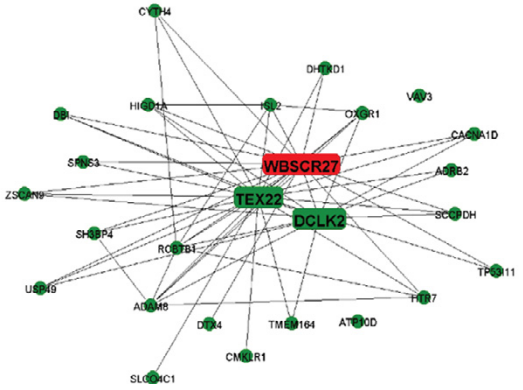
Background: Autoimmune diseases are highly disabling chronic disorders characterized by the activation of multiple immune and inflammatory pathways against self-components. Clinical studies have demonstrated that autoimmune diseases have a higher prevalence of cardiovascular events compared to the general population. Understanding the genetic and biological mechanisms underlying cardiovascular disease (CVD) risk in autoimmunity could therefore be fundamental to develop more efficient preventive and therapeutic strategies.
Objectives: The objective of this study was to characterize the genetic basis of CVD risk in autoimmune diseases.
Methods: A total of 6,485 patients from the six autoimmune diseases RA, PA, SLE, PS, CD and UC were recruited by the Spanish biomedical consortium IMID Consortium. All patients were Caucasian European from the Spain. CVD patients were defined as having ≥1 out of the 3 most frequent cardiovascular phenotypes: (i) ischemic heart disease (ii) cerebrovascular accident and (iii) peripheral arterial disease. In order to characterize the genetic basis of CVD risk in autoimmune diseases, we used genome-wide genotyping data from all autoimmune disease patients included in the study. First, we tested the association of established CVD risk variants within each autoimmune disease. Second, we analyzed the association of autoimmune disease risk variants with an increase in CVD risk. Finally, we used the cross-phenotype meta-analysis approach (CPMA) to perform a genome-wide meta-analysis and identify global genetic patterns associated with CVD risk in autoimmune diseases.
Results: A total of 17 loci previously associated with CVD risk in the general population were significantly associated with CVD risk in the autoimmune patient cohorts ($P<0.05$). From these, 4 loci were found to have significantly different genetic effects across autoimmune diseases ($P<0.05$). We also found that 6 risk loci for autoimmune diseases were associated with an increase in CVD risk, like the RA risk gene *CFLAR-CASP8*. The CPMA identified a total of 10 genetic patterns significantly associated with CVD risk across all autoimmune diseases. Two of these patterns showed a highly significant association with CVD risk in RA, PsA and SLE. The functional analysis of these two genetic patterns revealed a significant enrichment in key pathways related to the etiology of rheumatic diseases like TNFα ($FDR<0.05$) and IFNγ ($FDR<0.05$) cytokine pathways.
Conclusions: The results of the present study represent an important step towards the characterization of the genetic basis of CVD in autoimmune diseases. These findings contribute to explain the higher prevalence of cardiovascular events observed in patients with autoimmune diseases compared to the general population.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3673

OP0293 WEIGHTED GENE CO-EXPRESSION NETWORK ANALYSIS OF DMARD-NAÏVE EARLY RA PATIENTS ACHIEVING SUSTAINED DRUG-FREE REMISSION AFTER INITIATING TOCILIZUMAB THERAPY

X.M. Teitsma[1], J.W. Jacobs[1], M. Mokry[2,3], A. Pethö-Schramm[4], M.E. Borm[5], J.M. van Laar[1], J.W. Bijlsma[1], F.P. Lafeber[1]. *[1]Rheumatology and Clinical Immunology, UMC Utrecht; [2]Division of Pediatrics, Wilhelmina Children's Hospital; [3]Epigenomics Facility, UMC Utrecht, Utrecht, Netherlands; [4]F. Hoffmann-La Roche, Basel, Switzerland; [5]Roche Nederland B.V., Woerden, Netherlands*

Background: Rapidly reducing disease activity is of major importance in the management of newly diagnosed rheumatoid arthritis (RA) patients as early response strongly correlates with long-term clinical outcomes. To select patients for whom it would be favourable to initiate a biological drug from start of therapy, it is crucial to study biological pathways and biomarkers involved in treatment response.
Objectives: To identify biological networks and signature genes among disease modifying anti-rheumatic drug (DMARD)-naïve early RA patients achieving sustained drug-free remission (sDFR) after initiating treatment with tocilizumab (TCZ).
Methods: Data was used from DMARD-naïve early RA patients in the U-Act-Early trial who had been randomized to initiate TCZ therapy. The study design and details have previously been described.[1] Briefly, TCZ (8 mg/kg) was given every 4 weeks and if remission was not achieved, methotrexate (oral) was added. When the target was achieved, therapy was tapered and subsequently discontinued provided remission persisted. sDFR was reached when patients remained ≥3 months in remission while being drug-free until the end of the two-year study period. Before the first dose of medication, whole blood samples were collected and RNA was isolated from CD4 cells and analyzed using RNA sequencing. The DESeq2 package was used to identify differentially expressed genes (DEGs) between responders (achieving sDFR, n=13) and non-responders (not able to taper medication, n=11). Subsequently, weighted gene co-expression network analysis (WGCNA) was used to study clusters (modules) within the 1000 most relevant DEGs.
Results: In total, eight modules with varying sizes (10–470 genes) were identified. The module best correlated (Pearson correlation coefficient 0.52, p=0.009) with achieving sDFR included 26 genes and was used for further functional analysis. Within this module, we found three significantly enriched pathways in the Kyoto Encyclopaedia of Genes and Genomes (KEGG) database. These were calcium signalling pathway ($p=5.81E^{-04}$), carbohydrate digestion & absorption ($p=4.46E^{-02}$), and neuroactive ligand-receptor interaction ($p=2.61E^{-02}$).

Fig. 1: Network visualization of the interaction of gene co-expression in the module best correlated with achieving sustained drug-free remission. Upregulated genes are expressed as green nodes and the down-regulate gene as red node. The three rounded rectangular nodes display the highest co-expressed genes within the module (>10 connections) when applying a weight cut-off of 0.01. The average number of nodes connected at this cut-off was 4.6 (correlation coefficient 0.82).



In addition, we identified 83 overrepresented Gene Ontology (GO) terms of which granulocyte migration (p=2.70E^{-04}), myeloid leukocyte migration (p=8.95E^{-04}) and G-protein coupled amine receptor activity (p=1.25E^{-03}) were most significant. The genes in the module of interest showing the highest connectivity were the upregulated testis expressed 22 (TEX22), doublecortin lie kinase 2 (DCLK2), and the downregulated Williams Beuren syndrome chromosome region 27 (WBSCR27) gene (Fig. 1).

Conclusions: When performing network analyses of the DEGs between responders and non-responders, TEX22 and DCLK2 were identified as signature genes for treatment response to TCZ therapy. WBSCR27 was found to be associated with less chance of achieving sDFR.

References:

[1] Bijlsma JW, Welsing PM, Woodworth TG, et al. Early rheumatoid arthritis treated with tocilizumab, methotrexate, or their combination (U-Act-Early): a multicentre, randomised, double-blind, double-dummy, strategy trial. Lancet 2016; 388:343–55.

Disclosure of Interest: X. Teitsma: None declared, J. Jacobs: None declared, M. Mokry: None declared, A. Pethö-Schramm Employee of: F. Hoffmann-La Roche, M. Borm Employee of: Roche Nederland B.V., J. van Laar Consultant for: Received fees from MSD, Pfizer, Roche, Eli Lilly and BMS, J. Bijlsma Grant/research support from: Received research grants (to his department) and consultancy fees from AbbVie, BMS, Crescendo, MSD, Mundipharma, Pfizer, Roche, Sun and UCB, F. Lafeber: None declared

DOI: 10.1136/annrheumdis-2017-eular.2197

OP0294 FRACTURE PREDICTION USING A GENETIC MARKERS ALGORITHM COMPARED TO FRAX IN THREE EUROPEAN COHORTS

S. Ferrari[1], R. Rizzoli[1], R. Chapurlat[2], M.L. Brandi[3], H. Martínez[4], M. Herrero[4], J. Vergés[5], M. Artieda[6], D. Tejedor[6], A. Martínez[6], J. Blanch[7], S. Palacios[8]. *[1]Geneva University Hospital and Faculty of Medicine, Geneve, Switzerland; [2]Division of Rheumatology, INSERM U1033, Université de Lyon, Hôpital e Herriot, Lyon, France; [3]University of Florence, Florence, Italy; [4]Clinical R&D, Bioiberica; [5]Osteoarthritis Foundation International (OAFI), Barcelona; [6]R&D Department, Progenika Biopharma, A Grifols Company, Derio; [7]Hospital del Mar of Barcelona, Barcelona; [8]Palacios Institute of Health and Woman Medicine, Madrid, Spain*

Background: Numerous genome-wide association studies (GWAS) and large meta-analyses have started to unravel the multiple gene polymorphisms associated with BMD and/or fragility fractures. However the clinical utility of these genetic markers for fracture prediction remains to be established.

Objectives: To develop a DNA genotyping tool for predicting osteoporotic fractures in postmenopausal women.

Methods: 768 SNPs previously associated with osteoporosis phenotypes were identified in silico through the NHGRI GWAS catalog and BoneKey Genetics website. They were genotyped on an Illumina GoldenGate assay in 1649 postmenopausal women aged 45+ yrs belonging to three osteoporotic fractures cohorts from Switzerland, Italy and France. SNPs potentially associated (p<0.10) with prevalent and incident clinical fragility fractures in one or more of the cohorts, or in the cohorts together, were then combined in a genetic risk score (GRS). GRS association with fragility fractures was tested by forward logistic regressions adjusting for age and FN BMD. The ability of GRS for fracture prediction was evaluated by the area under the ROC curve (AUC) in the three cohorts combined, as well separately (for internal replication). For comparison, fracture probabilities were computed using FRAX clinical risk factors (without BMD) without and with the addition of GRS.

Results: The average prevalence of fragility fractures in the three cohorts was 25% (range 22 to 28%), of which half were major fractures (FRAX definition). After QC filtering, 632 SNPs in 1625 individuals were correctly genotyped, of which 73 were potentially associated with fractures in one or more cohorts. In single and multiple regression models, GRS was significantly associated with fractures (OR 1.09, CI 1.07–1.12, p<0.0001). The GRS AUC for fracture prediction was significant (0.65) and highly consistent among the three cohorts. GRS predicted major fractures as well as FRAX clinical risk factors without BMD (AUC 0.63 vs 0.58, p=0.08), and when combined with clinical FRAX, the AUC was significantly improved (0.67, p=0.0106).

Conclusions: SNPs previously associated with osteoporosis phenotypes through large GWAS and meta-analyses can be replicated for association with fragility fractures in post-menopausal women from three European countries. Our results provide a proof-of-principle that a genetic risk score (GRS) based on these SNPs represents an independent risk factor for fractures and could be developed into a genetic algorithm to improve the prediction of fragility fractures, either alone or together with FRAX.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6316

OP0295 UNIQUE WHOLE BLOOD MICRORNA BIOSIGNATURE FOR RHEUMATOID ARTHRITIS

V. Anaparti[1,2,3], I. Smolik[1,3], X. Meng[1,2,3], N. Mookherjee[2,3], H. El-Gabalawy[1,2,3]. *[1]Rheumatic Diseases Unit; [2]Manitoba Center for Proteomics and Systems Biology; [3]Internal Medicine, University of Manitoba, Winnipeg, Canada*

Background: RA susceptibility risk is disproportionately high (~2–3fold) in Indigenous North American (INA) tribes compared to other populations[1,2]. Environmental, lifestyle & genetic factors account for <20% of observed disease variance suggesting contribution of additional risk determinants[3]. Emerging evidence suggests small non-coding microRNAs (miRs) e.g. miR-155, miR-146a, miR-26b are key contributors to RA pathogenesis[4]. In this project, we examined the role of miRs on RA incidence, and association with anti-citrullinated protein antibodies (ACPA), whose appearance precedes disease symptoms. We hypothesized that differential expression of specific miRs associated with disease symptoms will facilitate RA transition in genetically susceptible first-degree relatives (FDRs).

Methods: Whole blood and peripheral blood mononuclear cells (PBMCs) were obtained from age-matched ACPA+ RA patients (n=18), non-symptomatic ACPA+ FDRs (n=12) and ACPA- healthy controls (n=12), who belonged exclusively to INA Cree-Ojibway communities of Northern Manitoba, Canada. Total RNA was isolated using miRVANA kit (Ambion). Expression of selected 32 miRs based on the published literature, and associated downstream mRNA targets, were monitored by quantitative real-time PCR, RNU48 and 18sRNA were used for input normalization for miRNA and mRNA expression respectively.

Results: Whole blood expression profiling identified 10 differentially expressed miRs in RA patients compared to control subjects. Expression of miR-103a-3p was significantly up-regulated (~2.3-fold; p=0.0062), whereas that of imiR-16, miR-24, miR-29a, miR-125a-3p, miR-203, miR-222, miR-223, miR-150 and miR-346 were down-regulated in RA patients compared to controls. Increased miR-103a-3p expression was also confirmed in PBMCs from ACPA+ RA patients (~2 fold; p=0.0040) compared to controls. Further, miR-103a-3p expression was increased in ACPA+ FDRs (>4 fold) compared to controls (p=0.0005), and ACPA+ RA patients (p=0.0149). miR-103a-3p expression was consistently elevated in ACPA+ FDRs, when we analyzed samples obtained at two independent time points (1year apart). Consistent with this, expression of AGO1 and DAPK1 mRNA, downstream targets of miR-103a-3p, was decreased significantly (p<0.05) in ACPA+ FDRs compared to controls.

Conclusions: This study defines a unique signature of dysregulated miRs amongst RA patients and their related FDRs within the INA cohort. Our results suggest a potential role of miR-103a-3p as a prognostic biomarker for pre-clinical RA.

References:

[1] Barnabe et al J Rheumatol. 2008;35(6):1145–50.
[2] Smolik et al J Rheumatol. 2013;40(6):818–24.
[3] Viatte et al Nat Rev Rheumatol. 2013;9(3):141–53.
[4] Vicente et al Nat Rev Rheumatol. 2016 Apr;12(4):211–20.

Acknowledgements: Canadian Institute of Health & Research (CIHR). *Research Manitoba*

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1480

OP0296 AUTOIMMUNE ASSOCIATED GENE PTPN22 NEGATIVELY REGULATES DECTIN-1 SIGNALLING IN DENDRITIC CELLS

H. Purvis[1], F. Clarke[1], C. Jordan[1], C. Sanchez-Blanco[1], G.H. Cornish[1], D. Rawlings[2], R. Zamoyska[3], A.P. Cope[1]. *[1]Academic Department of Rheumatology, King's College London, London, United Kingdom; [2]Seattle Children's Research Institute and Departments of Pediatrics and Immunology, University of Washington School of Medicine, Seattle, United States; [3]Institute of Immunology and Infection Research, Edinburgh University, Edinburgh, United Kingdom*

Background: A single nucleotide polymorphism within the phosphatase *PTPN22*

increases the risk of developing multiple autoimmune and connective tissue diseases.[1] Ptpn22 is a negative regulator of Syk and Src family kinases downstream of immuno-receptor signalling cascades.[2] Fungal β-glucan receptor dectin-1, signals via Syk kinase, and induces dendritic cells to secrete pro-inflammatory cytokines IL-1β, IL-6, IL-12/23p40 and TNFα, in turn allowing the induction of IL-17 secreting T-cell responses, which are critical to the clearance of fungal infections.[3] IL-17 has been implicated as a key cytokine in inflammatory responses associated with RA, JIA, and psoriasis.[4]

Objectives: To investigate if Ptpn22 regulates dectin-1 signalling and controls the capability of dectin-1 matured BMDC to promote adaptive immune responses.

Methods: GM-CSF bone marrow derived dendritic cells (BMDC) were generated from C57BL/6 WT, *Ptpn22*$^{-/-}$ or *Ptpn22*^{R619W} (human *PTPN22*^{R620W} orthologue) mice, and pulsed with $OVA_{323-339}$ in the presence or absence of the dectin-1 agonist curdlan. Activated BMDC were co-cultured *in vitro* with OT-II T-cells or adoptively transferred into OT-II mice and the resulting T-cell response assessed. Cytokine secretion from curdlan activated Ptpn22 variant mouse BMDC was determined by immunoassay and the kinetics of Syk and Erk phosphorylation were determined by immunoblot.

Results: We observed that Dectin-1 activated *Ptpn22*$^{-/-}$ BMDC had an enhanced capability to induce T-cell IL-17 secretion both *in vitro* and *in vivo* compared to WT BMDC. Following dectin-1 priming Ptpn22$^{-/-}$ BMDC secreted increased IL-1β compared to WT BMDC, and the increase in IL-1β was found to be sufficient to cause the enhanced IL-17 response induced by Ptpn22$^{-/-}$ BMDC. Dectin-1 induced IL-1β secretion was found to be Syk and Erk dependent and assessment of Syk and Erk kinetics of phosphorylation revealed that dectin-1 activated *Ptpn22*$^{-/-}$ BMDC displayed enhanced Syk and Erk phosphorylation compared to WT BMDC. Furthermore, *Ptpn22*^{R619W} BMDC (orthologue of human *Ptpn22*^{R620W}) exhibited a similar enhancement in IL-1β secretion and induced enhanced T-cell dependent IL-17 responses in vivo, indicating that the PTPN22 polymorphism behaves as a loss-of-function allele in the context of dectin-1 signals.

Conclusions: Data highlight Ptpn22 as a novel regulator of dectin-1 signals and provide a link between genetically conferred perturbation to innate receptor signalling pathways and autoimmunity.

References:

[1] Burn, G. L., Svensson, L., Sanchez-Blanco, C., Saini, M. & Cope, A. P. Why is PTPN22 a good candidate susceptibility gene for autoimmune disease? FEBS Lett. 585, 3689–98 (2011).
[2] Cloutier, J. F. & Veillette, A. Cooperative inhibition of T-cell antigen receptor signaling by a complex between a kinase and a phosphatase. J. Exp. Med. 189, 111–21 (1999).
[3] Dambuza, I. M. & Brown, G. D. C-type lectins in immunity: recent developments. Curr. Opin. Immunol. 32, 21–27 (2015).
[4] Tabarkiewicz, J., Pogoda, K., Karczmarczyk, A., Pozarowski, P. & Giannopoulos, K. The Role of IL-17 and Th17 Lymphocytes in Autoimmune Diseases. Arch. Immunol. Ther. Exp. (Warsz). 63, 435–49 (2015).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4717

OP0297 FUNCTIONAL POLYMORPHISMS OF THE ABCG2 GENE IN PRIMARY GOUT

B. Stiburkova[1,2], K. Pavelcova[3,4], L. Petru[3,4], P. Cepek[3], J. Zavada[3], K. Pavelka[3]. *[1]Institute of Rheumatology, Prague 2; [2]Institute of Inherited Metabolic Disorders, First Faculty of Medicine, Charles University; [3]Institute of Rheumatology; [4]Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic*

Background: The urate transporters are one of the genetic determinants of serum uric acid concentrations. Common dysfunctional variants of *ABCG2* are revealed to be a major cause of gout and hyperuricemia by decreasing urate excretion. In this study we describe the analysis of allelic variants in the *ABCG2* in a cohort with primary gout.

Objectives: The cohort was recruited in the Institute of Rheumatology, Prague. Gouty arthritis was diagnosed in 146 subjects (132 men, 14 women) according to the American college of rheumatology criteria 1977. Patients suffering from secondary gout and other purine metabolic disorders associated with pathological concentrations of serum uric acid were excluded.

Methods: In each patient, the family history of gout, number of gouty attacks, the presence of tophi, the occurrence of associated diseases and therapy have been assessed. All 16 exons of *ABCG2* were amplified using PCR, and sequenced directly.

Results: In the *ABCG2* gene, 19 intronic sequence variants were detected. In the case of c.689+1G>A, related to an individual with severe gouty phenotype, two abnormal splicing variants were identified: a) r.[532_689del]; b) r.[532_689del], r.[944_949del]. Identified deletions lead to frameshift and premature stop codon introduction[1]. From the 12 exon variants detected, there were nine non-synonymous: p.V12M, p.Q141K, p.R147W, p.T153M, p.F373C, p.T421A, p.T434M, p.S476P and p.D620N. Heterozygous p.V12M was detected in seven individuals. Heterozygous variants p.R147W, p.T153M, p.F373C, p.T421A, p.T434M and p.S476P were detected once, variant p.D620N twice. All these allelic variants were *in silico* predicted as a probably damaging. The p.Q141K, previously functionally characterized allelic variant with a strong effect on uric acid secretion impairment, was in cohort of gout patients presented with significantly higher minor allele frequency 0.24 (MAF), 57 heterozygotes/6 homozygotes, than in population of European origin (MAF=0.09) and world-wide population (MAF=0.12). In our cohort, the age of onset of gout had a normal distribution. Remarkably, in 75% of all individuals with early onset of gout between age 10–20 years, we detected allelic variant p.Q141K (in 6 out of 8 patients). In the age group 21–30 years, this allelic variant was detected in 42% of patients (8/19), and in the age group 61–70 years, just in 29% (13/29).

Conclusions: Our results show that genetic factor *ABCG2* should be considered as one of the strong common risks for gout. In summary, we revealed that allelic variants of *ABCG2*, especially dysfunctional variant p.Q141K, have a significant effect on earlier onset of gout.

References:

[1] Stiburkova B et al. Novel dysfunctional variant in ABCG2 as a cause of severe tophaceous gout: biochemical, molecular genetics and functional analysis. Rheumatology (Oxford). 2016 Jan;55(1):191–4.

Acknowledgements: This study was supported by the grants from the Czech Republic Ministry of Health AZV 15–26693A.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4901

OP0298 CHROMATIN INTERACTIONS REVEAL NOVEL GENE TARGETS FOR DRUG REPOSITIONING IN RHEUMATIC DISEASES

P. Martin[1], K. Duffus[1], A. McGovern[1], A. Yarwood[1], A. Barton[1,2], J. Worthington[1,2], S. Eyre[1], G. Orozco[1]. *[1]Arthritis Research UK Centre for Genetics and Genomics, University of Manchester; [2]NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom*

Background: The treatment of rheumatic diseases can be both expensive and ineffective with up to 1/3 of patient's failing to respond to current treatments. There is therefore a need to identify new treatments and to target these to individual patients. Although genetic studies have been successful in identifying common variation associated with disease susceptibility, a large proportion of these lie outside protein-coding regions. Many show enhancer activity but it is often unclear which gene(s) they regulate and how they contribute to disease. Chromatin folding brings linearly distant areas of the genome, such as promoters and enhancers, into close proximity, driving gene expression. Capture Hi-C (CHi-C) interrogates these interactions in a high-throughput, high-resolution manner, linking implicated enhancers to causal genes.

Objectives: Utilising our existing CHi-C data on 3 rheumatic diseases, RA, JIA and PsA, targeting all known genetic associations, we explored the potential to identify candidate causal genes that are targets for existing drugs, which could be repositioned for use in these diseases.

Methods: Chromatin interaction data for T- and B-cells in the 3 diseases was analysed using CHiCAGO v2 using a score cut-off of ≥5. Interactions between disease regions and promoters were identified using BEDTOOLS v2.21.0 and intersected with drug targets from DrugBank v4.5.0. Existing treatments for each disease were identified by the presence of the relevant name in the "indication" field.

Results: Overall 850 genes were identified as interacting with a disease associated region. Of these, 61 are existing drug targets (303 drugs) (Table 1) and 9 are existing therapies used in the treatment of disease, primarily RA.

Table 1. Summary of drug targets identified by CHi-C

Disease	Number of identified by CHi-C	Number of genes which are existing drug targets	Number of drugs identified	Number of drugs withdrawn	Number of drugs currently used	Number of drugs for potential repositioning
RA	510	41	106	4	9	93
JIA	324	16	74	0	1	73
PSA	196	13	147	0	0	147
All	850	61	303	4	9	290

Conclusions: Our study identifies genes which are implicated in disease, are the target of existing drugs and offer the potential for drug repositioning. Of the potential drugs identified for RA, 14 are used in the treatment of various cancers and 11 are used in the treatment of diabetes and multiple sclerosis. Interestingly, 17 potential drugs identified for PsA are used in the treatment of schizophrenia and 11 in the treatment of hypertension. This data shows a novel insight into how functional annotation of genetic associations in rheumatic diseases can provide gene targets for re-positioned therapies.

Acknowledgements: This work was funded by Wellcome Trust Research Career Development Fellowship (095684); Arthritis Research UK (grant numbers 20385, 20571); Wellcome Trust (097820/Z/11/B); European Union's FP7 Health Programme (FP7-HEALTH-F2–2012–305549, Euro-TEAM, FP7/2007–2013); Innovative Medicines Initiative (BeTheCure project 115142); Medical Research Council (MR/K015346/1); National Institute for Health Research Manchester Musculoskeletal Biomedical Research Unit; Biotechnology and Biological Sciences Research Council UK (BBS/E/B/000C0405).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2685

FRIDAY, 16 JUNE 2017

Innovative insights into mechanism of SLE, Sjögren's and APS

OP0299 SERUM AND GLOMERULAR EXPRESSION OF IL32 IN LUPUS NEPHRITIS

S. Truglia[1], C. Alessandri[1], F. Ciccia[2], A. Rizzo[2], T. Colasanti[3], F. Miranda[3], F.R. Spinelli[3], F. Ceccarelli[3], G. Triolo[2], A. Capozzi[4], M. Sorice[4], G. Valesini[3], F. Conti[3]. [1]*Medicina Interna e Specilità Mediche, Reumatologia, Sapienza Università di Roma, Roma;* [2]*Dipartimento Biomedico di Medicina Interna e Specialistica, Sezione di Reumatologia, Università di Palermo, Palermo;* [3]*Dipartimento di Medicina Interna e Specialità Mediche, Reumatologia;* [4]*Dipartimento di Medicina Sperimentale, Sapienza Università di Roma, Roma, Italy*

Background: Lupus nephritis (LN) is one of the most severe features of systemic lupus erythematosus (SLE). Several cytokines and chemokines are secreted locally in case of glomerular inflammation. Interleukin 32 (IL32) is a newly described cytokine that exhibits several properties typical of proinflammatory cytokines. *Ex vivo* and *in vitro* studies supported the role of Toll like receptors (TLRs) in LN pathogenesis and recent investigations demonstrated that Poly I:C, a ligand for (TLR) 3, strongly induced IL32 production from several cell populations.
Objectives: To investigate serum and urinary levels of IL32 in a cohort of LN patients compared to SLE patients without renal involvement and healthy controls (HC). In addition, we investigated kidney expression of IL32 and *in vitro* ability of LN patients' serum IgG to stimulate IL32 production by TLR3 activation in human embryonic kidney 293 cells line stably transfected with a TLR3 plasmid (Hek293/T3).
Methods: Serum and urinary IL32 concentrations were measured using ELISA; a polyclonal rabbit anti-human IL32 was used to evaluate the expression of IL32 in renal biopsies. To assess the production of IL32 induced by patients' IgG and the transduction pathway of TLR3 we performed Western Blot analysis for IL32, TBK1 and NFkB.
Results: We recruited 60 LN patients, 50 SLE patients without renal involvement and 30 HC; 40 LN patients had an active disease (a-LN) and the remaining 20 were in remission (r-LN). IL32 serum levels were significantly higher in patients with r-LN (median 1368, IQR 3910) and HC (median 721, IQR 2271) compared to SLE patients without renal involvement (median 203, IQR 662.8 pg/ml) (p=0.03 and p=0.018, respectively). There were no significant differences in urinary IL32 levels among LN patients, SLE patients without renal involvement and HC. In LN patients a direct association between IL32 serum levels and disease duration (p=0.02; r 0.2978) was observed. Immuno-histochemical analysis performed on renal biopsies of 20 a-LN and 8 HC showed that IL32 was strongly expressed in renal samples of LN patients, especially in patients with class IV, compared to controls. Western Blot analysis showed that antibodies isolated from LN patients induced *in vitro* production of IL32 in Hek293/T3 cells as well as the phosphorylation of NFkB and TBK1.
Conclusions: The results of the present study show increased IL32 serum levels in r-LN patients as well as increased expression of such cytokine in renal tissues of a-LN patients. IL32 renal expression and its production by Hek293/T3 cells after patients' IgG stimulation, probably mediated by TLR3, may suggest the production of IL32 directly at renal level in course of LN.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5277

OP0300 ENRICHMENT OF T FOLLICULAR-HELPER CELLS (TFH) AND EXCLUSION OF T FOLLICULAR-REGULATORY CELLS (TFR) FROM ECTOPIC GERMINAL CENTERS IN SALIVARY GLANDS OF SJOGREN'S SYNDROME PATIENTS

E. Pontarini[1], W. Murray-Brown[1], C. Croia[1], E. Astorri[1], D. Lucchesi[1], N. Lepse[1], N. Sutcliffe[2], A. Tappuni[3], C. Pitzalis[1], M. Bombardieri[1]. [1]*Centre for Experimental Medicine & Rheumatology, William Harvey Research Institute;* [2]*Barts Health;* [3]*Institute of Dentistry, Queen Mary University of London, London, United Kingdom*

Background: B/T cell aggregates in the salivary glands (SG) of Sjögren's syndrome (SS) can give rise to ectopic lymphoid structures (ELS) forming ectopic germinal centers (GCs), which has been linked to the development of MALT lymphoma (MALT-L). T follicular-helper cells (Tfh) and T follicular-regulatory cells (Tfr) are specialized CD4+ T-cells that positively and negatively regulate, respectively, the magnitude of the GCs response and the onset of autoimmunity.
Objectives: To characterize the infiltration of Tfh and Tfr in the SG infiltrates of patients with SS in the context of the presence/absence of ectopic GCs and in subjects with MALT-L.
Methods: SG biopsies with matching histology and RNA from 37 SS and 38 non-specific chronic sialadenitis (NSCS) patients were stratified as ELS-/ELS+ based on CD3/CD20/CD21/CD138 immunostaining (IHC). Histological samples and mRNA from 12 parotid MALT-L were also studied. Gene expression was measured by Taqman rt-PCR. Multicolor immunofluorescence/confocal microscopy for CD3, CD4, CD45RO, ICOS, PD1, BCL6 and FoxP3 was used to identify Tfh and Tfr.
Results: Tfh ($CD4^+CD45RO^+PD1^+ICOS^+FoxP3^-$) cells and Tfr ($CD4^+CD45RO^+PD1^+ICOS^+FoxP3^+$) cells were strongly enriched in ELS+ vs ELS- SS samples. The Tfh:Tfr ratio in ELS+ SG was approximately 2:1. Interestingly, while in tonsils Tfr were routinely detected within GCs, in ELS+ SG Tfr were predominantly excluded from the B cell follicles and accumulated in the T cell rich areas at the periphery of the lymphoid aggregates. Conversely, Tfh densely infiltrated the B cell rich areas and, within ectopic GCs, acquired BCL6. Furthermore, Tfh infiltration closely correlated with SG IL-21 mRNA expression, which in turn was strongly correlated with CD3, CD20 and CD138 IHC scores and with CXCL13, LTb, BAFF, AID and Pax5 gene expression. Finally, MALT-L samples displayed 10-fold higher IL-21 mRNA and twice as much $PD1^+ICOS^+BCL6^+$ Tfh-cells/field compared to ELS+ SS samples.
Conclusions: Within the SG of SS patients Tfh cells closely segregate with lesional IL-21 expression, localize within ELS and are strongly enriched during MALT-L development. Conversely, although Tfr cells are also recruited to ELS+ SG in SS patients, we consistently demonstrated follicular exclusion of this subset from ectopic GCs. This suggests that Tfr in SS SG fail to exert their physiological immunoregulatory properties in controlling the magnitude of the GCs response and B cell autoreactivity, as observed in tonsils.
Acknowledgements: This work was supported by project grants from the Medical Research Council (MR/N003063/1 to MB) and Arthritis Research UK (grant 20089 to MB).
Disclosure of Interest: E. Pontarini: None declared, W. Murray-Brown: None declared, C. Croia: None declared, E. Astorri: None declared, D. Lucchesi: None declared, N. Lepse: None declared, N. Sutcliffe: None declared, A. Tappuni: None declared, C. Pitzalis: None declared, M. Bombardieri Consultant for: Amgen/Medimmune, GSK and UCB
DOI: 10.1136/annrheumdis-2017-eular.6121

OP0301 TYPE I IFN GENE SIGNATURE TEST–HIGH AND –LOW PATIENTS WITH MODERATE TO SEVERE SLE DISEASE ACTIVITY HAVE DISTINCT GENE EXPRESSION SIGNATURES OF IMMUNOLOGIC PATHWAYS AND CELL TYPES

H. Liu[1], B. Higgs[1], W. Rees[1], C. Morehouse[1], K. Streicher[1], P. Brohawn[2], G. Illei[1], K. Ranade[1]. [1]*MedImmune LLC;* [2]*MedImmune, Gaithersburg, United States*

Background: Type I interferon (IFN) has been implicated in systemic lupus erythematosus (SLE) pathogenesis, and the majority of patients with SLE have elevated expression of type I IFN-inducible genes in their blood. Anifrolumab, a fully human, $IgG_1\kappa$ monoclonal antibody against the type I IFN receptor, is in Phase III development for the treatment of moderate to severe SLE (NCT02446912 and NCT02446899).
Objectives: We sought to understand other molecular pathways (either dependent on or independent of type I IFN signaling), to elucidate heterogeneous mechanisms in SLE, and to identify patient subsets for personalized disease management.
Methods: Baseline blood samples from adult patients with moderate to severe SLE from two Phase IIb clinical studies (NCT01438489, N=265; NCT01283139, N=416) were profiled with whole genome array analyses. Type I IFN gene signature (IFNGS) test status was determined by a central laboratory utilizing an analytically validated four gene (*IFI27, IFI44, IFI44L, RSAD2)* quantitative polymerase chain reaction-based test from patients' whole blood. A predetermined, delta Ct-based cut-off point, in the trough of the bimodal distribution, was utilized to segregate type I IFNGS test–high from –low patients at baseline. Blood from healthy controls was stimulated *ex vivo* with IFN-β, IFN-γ, IFN-λ, IFN-ω, or a pool of all IFN-α subtypes, with or without blocking antibodies for each IFN type, to develop IFN-type-specific signatures. Cell type- and cytokine pathway-specific gene signatures derived from the literature were also evaluated with the Phase IIb sample data. A Fisher's exact test was used for enrichment calculations (signatures cut at median), and comparisons were adjusted for multiplicity through false discovery rate.
Results: A total of 79% of SLE patients in the combined study population had a type I IFNGS test–high status. From the type I IFNGS test–high patients, 29/95 signatures evaluated had significant enrichment, including those for B cells (q=1.17E-17, odds ratio [OR]=6.4), plasma cells (q=6.96E-11, OR=3.9), and CD40L signaling (q=1.07E-08, OR=3.3), relative to type I IFNGS test–low patients. In contrast, type I IFNGS test–low patients had enrichment for eosinophils (q=5.4E-6, OR=0.39) and type II IFN (IFN-γ) specifically inducible gene signatures (q=4.6E-3, OR=0.47). These findings were significant for the combined study population, as well as for the NCT01438489 study population, and were either significant or trending for the NCT01283139 population ($q<0.05$).
Conclusions: SLE patients who are type I IFNGS test–high had elevated concentrations of B cells, plasma cells, and other inflammatory cytokine pathways. Type I IFNGS test–low patients, by contrast, were enriched for eosinophil and type II IFN pathways. These observations provide new insights into the molecular heterogeneity underlying SLE and suggest new therapeutic approaches, particularly for type I IFNGS test–low patients.
Acknowledgements: Funded by MedImmune. Medical writing support was provided by R. Plant, QXV Comms, an Ashfield business, UK.
Disclosure of Interest: H. Liu Employee of: MedImmune LLC, B. Higgs Shareholder of: AstraZeneca, Employee of: MedImmune LLC, W. Rees Employee of: MedImmune LLC, C. Morehouse Shareholder of: AstraZeneca, Employee of: MedImmune LLC, K. Streicher Employee of: MedImmune LLC, P. Brohawn

Shareholder of: AstraZeneca, Employee of: MedImmune, G. Illei Shareholder of: AstraZeneca, Employee of: MedImmune LLC, K. Ranade Employee of: MedImmune LLC
DOI: 10.1136/annrheumdis-2017-eular.3719

OP0302 SIGNIFICANT REDUCTIONS OF PATHOGENIC AUTOANTIBODIES BY SYNERGETIC RITUXIMAB AND BELIMUMAB TREATMENT EFFECTIVELY INHIBITS NEUTROPHIL EXTRACELLULAR TRAPS IN SEVERE, REFRACTORY SLE - THE SYNBIOSE STUDY

T. Kraaij[1], S.W. Kamerling[1], J.A. Bakker[2], T.W. Huizinga[3], T.J. Rabelink[1], C. van Kooten[1], Y.K. Teng[1]. *[1]Nephrology; [2]Clinical Chemistry; [3]Rheumatology, LUMC, Leiden, Netherlands*

Background: Neutrophil extracellular traps (NETs) are extracellular, decondensed DNA strands covered with antimicrobial proteins that are part of the first-line defence against pathogens. However, in SLE, overall release of NETs is increased and degradation of NETs is impaired leading to a high amount of extracellular nuclear material, potentially leading to formation of SLE-specific antibodies. These pathogenic autoantibodies deposit in glomeruli in lupus nephritis (LN) and perpetuate autoimmunity by inducing more NETs. The present study hypothesized that combining anti-CD20 mediated B-cell depletion with BAFF (B-cell activating factor) inhibition can target autoreactive plasma cells and thereby effectively reduce pathogenic autoantibodies and NET induction in severe SLE.
Objectives: The present study aimed to investigate whether Rituximab (RTX) + Belimumab (BLM) affected pathogenic antibodies in relation to NET induction in severe refractory SLE.
Methods: As part of a phase 2 proof-of-concept study, the SynBioSe study, serum levels of anti-DNA autoantibodies were measured in severe, refractory SLE patients before and after treatment with RTX following BLM. Additionally, ex vivo NET induction was assessed before and after treatment with a novel highly sensitive method based on 3D confocal laser scanning microscopy. In this assay, healthy neutrophils are incubated with 10% serum of patients and healthy controls. Furthermore, we investigated whether NET induction was mediated by immune complexes.
Results: The study included 10 severe, refractory SLE patients with lupus nephritis and 1 patient with neuropsychiatric lupus. NET induction was found to be high at baseline with a median fold induction of 4.5 [range 2.6–11.7]. After 24 weeks, NET induction was significantly decreased (median fold NET induction of 1.6 [0.4–6.1], p=0.01). In addition, treatment with RTX+BLM led to significant reduction of anti-dsDNA antibodies at week 24 with a median of 35 IU/ml [range 10–374] compared to 120 [18–505] at baseline (p=0.012). Total immunoglobulin levels temporarily declined but returned to screening levels at week 24. NET induction correlated significantly with anti-dsDNA antibody levels (r=0.42, p=0.03) and with SLEDAI scores (r=0.53, p=0.003). Therefore, we examined whether the observed NET induction could be explained by circulating immune complexes (ICx). ICx were degraded by pre-incubating anti-dsDNA positive SLE sera with nuclease, resulting in a significant decrease in NET induction (median % decrease of 91.7 [range 67.6–98.1]). In addition, depletion of IgG from anti-dsDNA positive SLE sera resulted in significantly lower NET induction. Finally, immobilized IgG isolated from anti-dsDNA positive SLE sera, but not of control serum, resulted in significant NET induction.
Conclusions: Within refractory SLE patients, RTX + BLM resulted in concordant reductions in pathogenic anti-dsDNA antibodies and NET-inducing capacity. This study strongly suggests that NET induction in SLE is mediated by immune complexes, providing a possible explanation underpinning the clinical benefits of RTX+BLM in SLE. Trial registration:ClinicalTrials.gov NCT02284984
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5706

OP0303 THE SALIVARY GLAND SECRETOME AS A POTENTIAL NEW TOOL TO IDENTIFY BIOMARKERS OF DRYNESS AND IMMUNOPATHOLOGY IN PRIMARY SJÖGREN'S SYNDROME AND NON-AUTOIMMUNE SICCA PATIENTS

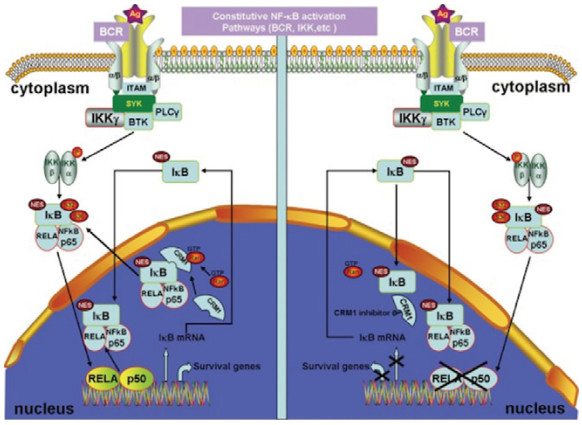
S.L. Blokland[1,2], M.R. Hillen[1,2], A.A. Kruize[2], W. de Jager[1], A. Pandit[1], J.A. van Roon[1,2], T.R. Radstake[1,2]. *[1]Laboratory of Translational Immunology; [2]Rheumatology & Clinical Immunology, UMC Utrecht, Utrecht, Netherlands*

Background: Salivary gland biopsy is essential in primary Sjögren's syndrome (pSS) diagnostics. However, tissue analysis using traditional methodology has several limitations including inaccurate quantification of lymphocytic infiltration and poor correlation with dryness. To perform biomarker identification in the target organ, tissue would have to be sacrificed. By performing saliva proteomics the biopsy tissue can be saved, but hitherto, this technique has not yielded consistent biomarkers and is limited by the absence of saliva production by many sicca patients.
Objectives: We aimed to explore whether Luminex analysis of a broad panel of cytokines in salivary gland biopsy supernatants (secretome) could provide biomarkers to stratify sicca patients and could give insights into pathogenesis.
Methods: Labial salivary gland (LSG) tissues were rinsed after biopsy and incubated in 200μL of saline for 1h at room temperature. Tissue supernatants were rendered cell-free, frozen in liquid nitrogen and stored at -80°C. In supernatants from pSS and non-Sjögren's sicca (nSS) patients 104 targets were measured by Luminex. Eight pSS and 8 nSS patients were selected for analysis based on matched biopsy weights. Results from this discovery cohort were validated in an additional cohort (n=18 nSS, n=16 incomplete SS: iSS, n=26 pSS) and correlations with clinical parameters were assessed. Non-SS were defined as sicca patients without lymphocytic infiltration in the salivary gland biopsy or anti-SSA/SSB autoantibodies. Incomplete SS patients were defined as sicca patients having lymphocytic infiltration (lymphocytic focus score (LFS)>0) and/or anti-SSA/SSB autoantibodies but do not fulfill the AECG classification criteria and are not diagnosed as pSS.
Results: Levels of 20 cytokines were significantly different between the nSS and pSS patients in the discovery cohort ($p \leq 0.05$). These 20 and 13 additionally selected cytokines based on a trend towards statistical significance and/or literature, were measured in a validation cohort. Weights of the biopsies did not significantly differ: 59.8±48.1mg in nSS vs 72.7±45.2mg in iSS vs 67.4±28.6mg in pSS. Fifteen out of these 20 cytokines were validated. From the 13 cytokines 7 were significantly elevated in pSS vs nSS. In iSS CXCL10 (IP-10) and CCL19 (MIP-3β) were significantly elevated. Cytokines correlating with LFS, ESSDAI, ESSPRI, % IgG and IgM+ plasma cells in LSG, Schirmer and/or serum IgG with Spearman $r \geq 0.4$ and $p \leq 0.05$ in pSS were selected for classification tree analysis, these were IL-2, IL-3, IFN-β, IL-21, CXCL13 (BLC), CXCL10 and CCL19. Using CXCL13 and IL-21 levels, 87.5% of pSS patients could be classified correctly. Based on the used cut off levels, 5 nSS and 9 iSS patients would be classified as pSS. Follow up of these patients may reveal development of pSS.
Conclusions: Elevated levels of numerous cytokines were found in LSG biopsy secretomes from pSS patients versus non-autoimmune sicca patients correlating with clinical parameters. This method represents a novel tool to provide insights in pSS immunopathology and to identify therapeutic targets and biomarkers for diagnosis, prognosis and treatment response.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1608

OP0304 SELECTIVE INHIBITORS OF NUCLEAR EXPORT PREVENT LUPUS PROGRESSION BY TARGETING GERMINAL CENTER FORMATION AND AUTOREACTIVE ANTIBODY SECRETING CELLS

J. Rangel-Moreno[1], S. Cochran[2], S. Tamir[2], M. Lee[2], S. Shacham[2], J. Anolik[1]. *[1]Department of Medicine, Division of Allergy, Immunology and Rheumatology, University of Rochester Medical Center, Rochester; [2]Karyopharm Therapeutics, Newton, United States*

Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by simultaneous activation of the innate and adaptive arms of the immune system. The progression of the disease is unpredictable, making its treatment a challenge. Recently the nuclear export protein Exportin 1 (XPO1, also known as CRM1) has surfaced as an attractive target for the treatment of SLE and other inflammatory disorders. Selective Inhibitor of Nuclear Export (SINE) compounds are potent, orally available and well-tolerated XPO1 inhibitors. SINE compounds exert apoptotic and anti-inflammatory effects by mediating nuclear retention of important XPO1 cargos like the NFκB pathway regulatory protein, IκB.
Objectives: Based on the central role of NFκB signaling in the activation of immune cells in SLE, we decided to evaluate the therapeutic ability of SINE compounds to modulate experimental lupus progression.
Methods: To evaluate the efficacy of SINE compounds in a preclinical model of SLE, cohorts of lupus-prone mice with established disease (elevated anti-dsDNA antibody titer and proteinuria) were dosed with SINE compound or vehicle. We used flow cytometry to enumerate immune cells and immunofluorescence to visualize germinal centers (GC) in spleen. Quantitative PCR was used to measure changes in mRNA expression for molecules key in plasma cell attraction and survival, and histology was used to evaluate inflammation, antibody deposition and pathology in kidneys of lupus-prone mice.
Results: We found that treatment with SINE compounds significantly prevented increases in proteinuria (proteinuria scores: Control: 2.12±1.12; SINE (5 mg/kg): 1.06±0.49; SINE (7.5 mg/kg): 0.85±0.55) and drastically decreased IgG deposition and kidney pathology (glomerulonephritis, tubule damage and perivascular cuffing). Prevention of kidney damage was associated with a remarkable disruption of splenic GC, a significant reduction in the number of auto-reactive antibody secreting cells (ASC), and a decrease in the accumulation of auto-reactive ASC in the inflamed kidney. Reduced numbers of plasma cells in the inflamed kidney are likely due to the drastic decrease in the expression of molecules critical for PC attraction (CCL2, CXCL9, CXCL10, CXCL11) and survival (BAFF, APRIL). The potent effect of SINE compounds on GC and auto-reactive ASC is noticeable as early as 1 week after starting therapy. However, kinetics studies showed that a more pronounced elimination of GC and auto-reactive ASC is achieved after 8 weeks. Although SINE therapy has a drastic impact on spleen architecture, recovery experiments showed that complete recovery of immune cells in spleen occurred by 4 weeks. The reversible impact of SINE compounds on SLE provides a potential window of time for immunization of lupus patients.
Conclusions: SINE compounds have demonstrated efficacy in a murine model of SLE by reducing generation, survival and function of auto-reactive immune



cells. It is likely that inhibition of the canonical NFκB pathway underlies KPT-350's inhibitory effect. Together, our findings suggest the potential of SINE compounds to have a significant impact on disease progression in SLE.

References:

[1] Figure - Zhang KJ and Wang M. Chin J Cancer Res 24(4): 380–393:2012.

Disclosure of Interest: J. Rangel-Moreno Grant/research support from: NIH Small Business Innovation Research grant, S. Cochran Employee of: Karyopharm Therapeutics, S. Tamir Shareholder of: Karyopharm Therapeutics, Employee of: Karyopharm Therapeutics, M. Lee Shareholder of: Karyopharm Therapeutics, Employee of: Karyopharm Therapeutics, S. Shacham Shareholder of: Karyopharm Therapeutics, Employee of: Karyopharm Therapeutics, J. Anolik Grant/research support from: NIH Small Business Innovation Research grant

DOI: 10.1136/annrheumdis-2017-eular.6054

OP0305 TYPE I IFN SYSTEM ACTIVATION IN NEWBORNS EXPOSED TO ANTI-RO/SSA AUTOANTIBODIES IN UTERO

M. Wahren[1], M. Hedlund[1], G.E. Thorlacius[1], M. Ivanchenko[1], N. Kyriakidis[1], L. Rönnblom[2], M.-L. Eloranta[2], A. Espinosa[1], S.-E. Sonesson[1]. *[1]Karolinska Institutet, Stockholm; [2]Uppsala university, Uppsala, Sweden*

Background: Overexpression of type I IFN-stimulated genes has been demonstrated in both SLE and SS, and induction of IFNα production in plasmacytoid dendritic cells by immune complexes containing RNA and autoantibodies, including Ro/SSA and La/SSB autoantibodies, has also been shown. During pregnancy, these autoantibodies pass over the placenta to the fetus, but it is not know if an IFN-activation takes place also in the fetus.

Objectives: In the present study, we investigated if the type I IFN system is activated in newborns exposed to anti-Ro/SSA autoantibodies *in utero*.

Methods: Anti-Ro/SSA positive mothers and their babies as well as healthy controls were included in the study. Maternal and cord blood drawn at birth was immediately separated into plasma and PBMC. mRNA expression was analyzed by microarrays, cell surface markers were assessed by flow cytometry and circulating IFNα levels by DELFIA.

Results: We observed increased expression of IFN-regulated genes and elevated plasma IFNα levels not only in anti-Ro/SSA positive women but also in their newborns, with maternal and fetal IFN scores showing a significant positive correlation (r=0.74, p=0.005). Increased expression of MHC class II was observed on $CD14^+$ monocytes of anti-Ro/SSA antibody-exposed babies, suggesting cellular activation. Notably, the IFN score of babies born to mothers receiving immunomodulatory treatment was similar to that of controls.

Conclusions: We demonstrate for the first time that anti-Ro/SSA antibody-exposed babies at risk for neonatal lupus have a pre-activated immune system with an IFN signature, elevated plasma IFNα, and increased MHC class II expression on circulating monocytes. Our data also suggest that maternal immunomodulatory treatment may modulate the IFN activity in the baby.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6581

OP0306 DOWNREGULATION OF MICRORNAS IN PLASMACYTOID DENDRITIC CELLS IS ASSOCIATED WITH A TYPE I INTERFERON SIGNATURE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

L.L. Van Den Hoogen[1,2], J.A. van Roon[1,2], R.D. Fritsch-Stork[2], C.P. Bekker[1,2], A. Pandit[1,2], M. Rossato[1,2], T.R. Radstake[1,2]. *[1]Laboratory of Translational Immunology; [2]Rheumatology and Clinical Immunology, UMC Utrecht, Utrecht, Netherlands*

Background: The most prominent alteration in the immune system of patients with SLE is a type I interferon (IFN) signature, which we recently also reported in patients with primary APS (PAPS). In SLE and APS, this signature is related to disease activity and vascular disease. Plasmacytoid dendritic cells (pDC) are considered key players in the pathogenesis of SLE and APS as they are major producers of type I IFNs. MicroRNAs (miRNAs) are short non-coding RNAs that modulate gene expression through RNA interference mechanisms and have been implicated in the dysregulation of immune cells in patients with autoimmune diseases. Here we investigated miRNA expression in pDC of patients with SLE and APS in relation to the type I IFN signature.

Objectives: To identify if pDC dysregulation in patients with SLE and APS is associated with alterations of their miRNA expression profile.

Methods: The frequency of circulating pDC was determined by flow cytometry in patients with SLE (n=49), SLE+APS (n=34) and PAPS (n=27) and healthy controls (HC, n=22). RNA was extracted from pDCs isolated from the peripheral blood of patients with SLE (n=20), SLE+APS (n=10), PAPS (n=10) and HC (n=12). pDC miRNA and transcriptome profiles were assessed by RT-qPCR by OpenArray and RNA-sequencing (RNAseq) respectively. Patients were stratified by the presence (IFN-high) or absence (IFN-low) of an IFN signature on the basis of RNAseq. pDC stimulated with TLR7 agonists were analyzed for changes in miRNA expression.

Results: The numbers of circulating pDC were reduced in peripheral blood of patients with SLE, SLE+APS and PAPS (all $p<0.001$) and did not differ among the patient groups. Among 131 expressed miRNAs, 36, 17 and 21 miRNAs were differentially expressed ($p<0.05$) in patients with SLE, SLE+APS and PAPS, respectively, as compared with HC. All but one of these miRNAs were downregulated in the patients versus HC. Only 1 miRNA was differentially expressed when comparing between SLE and SLE+APS patients and between SLE+APS and PAPS patients. No changes in expression of genes related to the biogenesis of miRNAs were observed in the pDC of the patient groups. RNAseq data revealed an IFN signature in pDC, which was strongest in SLE and SLE+APS patients. IFN-high (n=23) patients showed a stronger downregulation of miRNAs as compared with IFN-low (n=17) patients. A total of 9 miRNAs were differentially expressed between IFN-high and IFN-low patients. Pathway enrichment on targets of the top three miRNA ($p<0.001$) distinguishing between IFN-high and –low patients indicated that these miRNAs are potentially regulating pathways relevant for pDC function such as TLR signaling and endocytosis. Activation of pDCs by TLR7 agonists induced a downregulation of miRNAs in pDC, resembling the miRNA expression pattern seen in patients, in particular those with a high type I IFN signature.

Conclusions: Reduced numbers of circulating pDC and downregulation of miRNAs in pDC is shared between SLE, SLE+APS and PAPS patients. Altered miRNA expression in pDC is associated with the presence of a type I IFN signature in SLE and APS. Our data suggest that the reduced expression of a subset of miRNA underlies pDC dysregulation in SLE, SLE+APS and PAPS patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2372

FRIDAY, 16 JUNE 2017

Comorbidities in rheumatoid arthritis

OP0307 TREATMENT OF BAFF TRANSGENIC MICE WITH ANTI-TNF: MONOCLONAL ANTI-TNF ARE ASSOCIATED WITH A HIGHER RISK OF LYMPHOMA THAN ETANERCEPT

G. Nocturne[1], L. Bineta[2], S. Boudaoud[2], J. Pascaud[2], R. Seror[1], C. Nicco[3], C. Chereau[3], F. Mackay[4], F. Vincent[4], T. Lazure[5], S. Ferlicot[5], L. Stimmer[6], S. Roulland[7], R. Krzysiek[8], S. Hacein-Bey[8], F. Batteux[3], X. Mariette[1]. *[1]Rheumatology; [2]INSERM U1184, le Kremlin Bicêtre; [3]U1016, Paris, France; [4]Melbourne University, Melbourne, Australia; [5]Pathology, le Kremlin Bicêtre; [6]CEA, Fontenay aux roses; [7]Marseille Luminy, Marseille; [8]Immunology, le Kremlin Bicêtre, France*

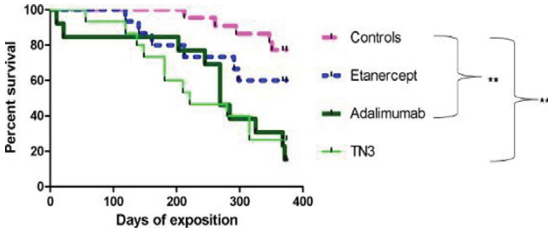
Background: Risk of lymhoma in patients with rheumatoid arthritis (RA) and disease activity is the main risk factor. The impact of treatment, notably of anti-TNF, is unclear: decreasing the risk of lymphoma by controlling activity or alterring anti-tumor immunosurveillance. Anti-TNF are not associated with an increased risk of lymphoma in large epidemiologic studies. However, the risk might vary according to the type or to the dose of anti-TNF.

Objectives: To assess if the risk of lymphoma might differ according to the type of anti-TNF, comparing monoclonal anti-TNF to the soluble receptor. For that, we used BAFF transgenic (Tg) mice as a model of autoimmunity-associated lymphomas. They develop lupus and Sjögren and 3% of them spontaneously developed lymphoma at 12–18 months

Methods: Six months aged BAFF-Tg mice were treated with anti-TNF for 12 months: etanercept (ETA) (n=15, 8 mg/kgx3/week), monoclonal anti-mouse TNF: TN3 19.12 (n=15, 20 mg/kg/week), adalimumab (ADA) (n=12, 20 mg/kg/week) or controls (n=22). Sera were assessed monthly. Crude mortality was compared among the different groups. Histological examination of the spleen was performed. The Fisher's exact test was used to compare the incidence of lymphoma among the groups.

Results: Adjunction of low dose of methotrexate during the 3 first days of treatment prevented immunization in the 3 groups for life. Using L929 cells, a cell line sensitive to TNF induced death, we confirmed that ADA was 8 to 12 times less efficient than ETA to inhibit soluble murine TNF. As expected, the mean level of ETA, TN3 and ADA were 7 μg/ml, 69 μ g/ml and 105 μg/ml, respectively. The

level of auto-antibodies and serum Ig did not significantly differ among the groups. However, crude mortality was significantly higher in mice treated with monoclonal anti-TNF compared to controls (p=0.0001 for ADA and p=0.0003 for TN3) but not for mice treated with ETA (Figure). Incidence of lymphoma was higher in mice treated with monoclonal anti-TNF: *5/15 (33%)* with TN3 (p=0.03/controls), *4/12 (33%)* with ADA (p=0.054/controls), *0/15* with ETA and *1/22 (5%)* in controls.



Conclusions: Higher mortality and increased risk of lymphoma were observed in BAFF Tg mice treated with monoclonal anti-TNF compared to etanercept. This result may be linked either to the different mechanism of action between the soluble receptor and the monoclonals or to a difference of trough level observed in the different groups even if higher levels of ADA was mandatory given the difference of effect on mouse TNF. This study demonstrates the negative impact of a prolonged anti-TNF treatment on the risk of lymphoma in the context of BAFF increase.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5651

OP0308 TNF INHIBITOR TREATMENT AND RISK OF CANCER RECURRENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE COHORT STUDY FROM SWEDEN

P. Raaschou, J. Söderling, J. Askling on behalf of the ARTIS study group. *Dept of Medicine, Karolinska Institute, Stockholm, Sweden*

Background: Clinical guidelines caution against the use of TNFi in individuals with a recent (5–10 years) history of cancer, but evidence of an increased risk of cancer recurrence is limited (1–2).

Objectives: We investigated the risk of recurrent solid non-skin cancer in patients with rheumatoid arthritis and TNFi-treatment, and if time between index-cancer and TNFi-start influence this risk.

Methods: 61.950 individuals with RA were identified in the Swedish national outpatient-care register Jan 2001-Dec 2014. Among these, 446 Individuals with at least one diagnosis of cancer (index cancer) prior to the start of TNFi-treatment were identified through linkage to the national cancer register and the ARTIS register of biologic treatment. Individuals (n=1.278) with a history of equally recent cancer of the same type and stage (invasive/in situ) were matched 3:1 to each patient starting TNFi against a background of solid cancer. Study participants were required to be in cancer remission during a period of 6 months prior to start of follow-up. The primary outcome was first recurrence or second primary of the same cancer type, identified through register-linkages until Dec 2014. Hazard ratios (HR) for recurrence or second primary were calculated using a Cox regression model with TNFi-treatment start (and a corresponding date among the matched biologics-naïve individuals) as start of follow-up. The final models were stratified for the matching variables sex, birth year, year of diagnosis of the index cancer and index cancer type and stage (invasive vs in situ), and adjusted for education level and comorbidities.

Results: The mean time from index cancer diagnosis until TNFi-treatment/start of follow-up was 9.9 and 9.5 years among the TNFi treated and their matched biologics-naïve controls, respectively. The mean follow-up (SD) from TNFi start was 4.9 (3.5) and 4.1 (3.1) years, respectively. The cancer stage distribution was similar between the two groups, apart from stage IV (0.6% among the TNFi-treated and 1.6% among the biologics-naïve). Thirty individuals (7%) among the 446 TNFi-treated developed a cancer recurrence (crude incidence rate 14/1000 person-years), compared with 89 (7%) among the 1.278 matched biologics-naive (crude incidence rate 17/1000 person-years). This corresponded to an adjusted HR for recurrent cancer of 0.69 (95% CI 0.42–1.12) in the matched analysis (table 1) comparing the TNFi treated to the biologics-naïve individuals. Stratified analyses indicated no increased risk associated with any specific cancer type with the possible exception of uterine cancer where HR for recurrence was 14.8 (95% CI 1.17–187.5), based on only 1 event among the TNFi-treated. HR for recurrence among individuals starting TNFi treatment within 5 year from index cancer was 0.67 (0.31–1.44).

Table 1 Number of patients, recurrent or second primary cancer, incidence rate per 1000 person-years (PY) and hazard ratios (HR) among TNFi treated patients with RA and their matched biologics-naïve comparators

Cancer	TNFi			Matched comparators			Adjusted* HR (95 % CI)
	N	Events (%)	IR per 1000 PY	N	Events (%)	IR per 1000 PY	
Overall	446	30 (6.7%)	13.8	1 278	89 (7.%)	17.0	0.69 (0.42-1.12)
Anorectal	29	0	0	69	4 (5.8%)	15.5	-
Breast	212	22 (10.4%)	19.9	633	46 (7.3%)	16.1	1.04 (0.57-1.89)
CNS	30	1 (3.3%)	7.0	81	3 (3.7%)	7.5	-
Colon	34	0	0	91	3 (3.3%)	11.3	-
Kidney	6	0	0	14	1 (7.1%)	16.4	-
Lung	3	1 (33.3%)	86.1	9	(.%)	0	-
Ovarial	29	1 (3.4%)	6.2	75	4 (5.3%)	12.8	-
Prostate	59	2 (3.4%)	8.7	175	17 (9.7%)	31.0	0.16 (0.03-1.00)
Urinary	16	2 (12.5%)	33.7	47	10 (21.3%)	65.5	0.80 (0.16-4.07)
Uterine	28	1 (3.6%)	6.2	84	1 (1.2%)	2.8	-

Cox regression stratified for the matching variables sex, birth year (±10 years), year of diagnosis (±5 years) of the index cancer, cancer type and stage at diagnosis (invasive vs in situ) of the index cancer, and adjusted for education and comorbidities. Within each matched strata, HRs could therefore be calculated only when events occurred among both TNFi-treated and biologics-naive.

Conclusions: Among patients with RA and a history of cancer, those selected to receive TNFi-treatment in clinical practice did not experience more cancer recurrences than patients with RA treated otherwise. We detected no differential risk depending on the timing of TNFi-start in relation to the index cancer. The generalizability of our findings to individuals with a very recent cancer, or a poor prognosis, remains unknown.

References:
[1] Raaschou P, et al. Ann Rheum Dis 2015;74:2137–2143.
[2] Mamtani R, et al. Arthritis Rheumatol 2016; 68: 2403–2411.

Disclosure of Interest: P. Raaschou: None declared, J. Söderling Grant/research support from: previous research projects fully or partly funded by Novo Nordisk and Combine Sweden, and has served as an external consultant to AbbVie, Merck and Novartis., J. Askling Grant/research support from: Abbvie, Pfizer, UCB, MSD, Roche, Lilly.

DOI: 10.1136/annrheumdis-2017-eular.5148

FRIDAY, 16 JUNE 2017

AxSpA: from bug to gut and to disease phenotype

OP0309 INTESTINAL SCLEROSTIN/SEROTONIN AXIS IS MODULATED BY DYSBIOSIS AND REGULATES ILC3 EXPANSION IN AS PATIENTS

F. Ciccia[1], G. Guggino[1], A. Rizzo[1], S. Milling[2], M. Luchetti[3], D. Baeten[4], R. Alessandro[1], G. Triolo[1]. *[1]University of Palermo, Palermo, Italy; [2]University of Glasgow, Glasgow, United Kingdom; [3]University Politecnica delle Marche, Ancona, Italy; [4]University of Amsterdam, Amsterdam, Netherlands*

Background: Sclerostin is an osteocyte-specific factor that binds to low-density lipoprotein receptor-related protein 5 (LRP5) inhibiting the Wnt signaling pathway and possibly contributing to the pathogenesis of Ankylosing spondylitis (AS). Subclinical gut inflammation observed in AS patients is characterized by the presence of dysbiosis and innate immune alterations. In the gut, LRP5 activation by unknown ligands inhibits serotonin production. Serotonin, by inducing glial derived neurotrophic factor (GDNF), controls ILC3 expansion, in the context of glial–ILC3–epithelial cell unit (GIECU). Sclerostin/serotonin axis has been never studied in AS.

Objectives: Aim of this study was to evaluate whether sclerostin is produced in the gut; to study the sclerostin/serotonin axis in AS and the effect of sclerostin on enterochromaffin cells (EC); to evaluate the presence of intestinal GIECU in AS and the role of serotonin in modulating the production of GDNF on isolated intestinal glial derived cells. We finally studied the effect of GDNF on ILC3.

Methods: Ileal, synovial and bone marrow (BM) expression of sclerostin, serotonin and GDNF were investigated by rt-PCR, immunohistochemistry and WB in 30 AS patients and 20 controls. Platelet and plasma unconjugated concentrations of serotonin were assessed by high-performance liquid chromatography (HPLC). Isolated bacteria from AS ileal biopsies were cultured with EC and serotonin expression evaluated by RT-PCR. Sclerostin and serotonin gut expression were evaluated in HLA-B27 TG rats before and after antibiotics treatment. EC were stimulated with sclerostin and the expression of THP1 assessed by RT-PCR. The presence of GIECU was studied by confocal microscopy analysis of GFAP/Tbet/Thy1. Isolated intestinal glial cells were stimulated with serotonin and the modulation of GDNF assessed by RT-PCR. The effect of GDNF on ILC3 was evaluated by flow cytometry.

Results: Sclerostin was produced in the gut and down-regulated in AS. Up-regulation of serotonin was observed in the gut, in the synovia and plasma, but not in BM of AS. Isolated intestinal bacteria from AS reduced EC serotonin production. Sclerostin down-regulation and serotonin over-expression were observed in the gut of HLA-B27 TG rats where Antibiotics increased intestinal sclerostin production and reduced serotonin expression. Treatment of isolated gut EC with sclerostin down-regulated the expression of THP1. GDNF was over-expressed in AS gut and confocal microscopy analysis demonstrated the existence of glial-ILC3-epithelial cells unit in AS patients. Finally, serotonin induces the release of GDNF by isolated intestinal glial cells and recombinant GDNF expanded RET^{+}ILC3.

Conclusions: here we demonstrate for the first time that intestinal sclerostin is the ligand of LRP5 and modulates the release of serotonin. Sclerostin/serotin axis is dysregulated in AS patients and HLA-B27 TG rats. In HLA-B27 TG rats, antibiotics restored sclerostin production and serotonin expression indicating a role of dysbiosis in modulating sclerostin/serotonin axis. Serotonin seems to be an important regulator of ILC3 expansion by inducing the production of GDNF by enteric glial cells, in the context of glial-ILC3-epithelial cells unit.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3995

FRIDAY, 16 JUNE 2017

Pregnancy meets rheumatic patients

OP0310 PREGNANCY OUTCOME IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS, A MULTICENTER COHORT-STUDY

B. Blomjous[1,2], C. Abheiden[2], S. Kroese[3], J. van Laar[3], R. Derksen[3], I. Bultink[1], A. Voskuyl[1], A. Lely[4], M. de Boer[2], J. de Vries[2], R. Fritsch-Stork[5]. *[1]Rheumatology, Amsterdam Rheumatology and Immunology Center, location VU University Medical Center, Amsterdam, Netherlands; [2]Obstetrics and Gynaecology, VU University Medical Center, Amsterdam; [3]Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands; [4]Obstetrics and Gynaecology, University Medical Center Utrecht, Utrecht, Netherlands; [5]1st Medical Department and Ludwig Boltzmann Institute, Hanusch Krankenhaus and Sigmund Freud University, Vienna, Austria*

Background: Systemic lupus erythematosus (SLE) predominantly affects women during their fertile period. During pregnancy SLE patients are prone to pregnancy complications and may experience increased disease activity.
Objectives: To investigate disease activity around/during pregnancy and pregnancy complications in a European cohort according to antiphospholipid antibody (aPL) status. Additionally data on lifetime pregnancy outcomes and comparison of first and consecutive pregnancies were analyzed.
Methods: All ongoing pregnancies of >16 weeks gestation of SLE patients (according to the ACR revised criteria) receiving joint care from rheumatologists and gynecologists in two tertiary centers in the Netherlands between 2000–2015 were included. Disease activity (using SELENA-SLE(P)DAI around and during pregnancy), flare rate according to the SELENA- SLEDAI definitions and pregnancy complications were assessed by medical chart review.
Results: From 96 women (84% Caucasian) 144 pregnancies were included. Before (<6 months), during and after pregnancy (<6 months) the median SELENA-SLE(P)DAI score was 2 and mild/moderate flare rates were 6.3%, 18.8% and 13.9% respectively. Three patients developed a severe flare during pregnancy, 2 patients postpartum; all were aPL negative. Severe maternal complications (preeclampsia, eclampsia or HELLP-syndrome) occurred in 16.2% of aPL negative, 21.4% of aPL positive SLE patients, and in 30.8% of SLE patients with antiphospholipid syndrome (APS) (GEE; no significant differences between groups). HELLP-syndrome occurred in 23.1% of SLE patients with APS and in 3.1% of SLE patients without APS (Chi-Square; p<0.01). The perinatal complications intrauterine fetal death, preterm birth, small-for-gestational age and neonatal lupus occurred in 4.1%, 32.7%, 14.8%, 1.4%, respectively (GEE; no significant differences between groups). Maternal and perinatal complication rates were similar in first (18.5% and 41.4%) and consecutive (17.6% and 35.1%) pregnancies (Chi-Square; p=0.88 and p=0.44). Of all patients, 42.7% developed a complication during all of their pregnancies (obstetrical history included).
Conclusions: This is the first study in patients with SLE demonstrating that incidence rates of pregnancy complications do not decrease in consecutive pregnancies compared to first pregnancies, in contrast to findings in the general population. Except for HELLP-syndrome, pregnancy complications were not significant different between aPL groups. Despite overall low disease activity and the absence of aPL in the majority of patients, almost half of the patients developed a complication during their pregnancies.
Disclosure of Interest: B. Blomjous: None declared, C. Abheiden: None declared, S. Kroese: None declared, J. van Laar Grant/research support from: MSD, Pfizer, Roche, Eli Lilly, BMS and Crescendo, R. Derksen: None declared, I. Bultink: None declared, A. Voskuyl: None declared, A. Lely: None declared, M. de Boer: None declared, J. de Vries Grant/research support from: Pfizer, R. Fritsch-Stork: None declared
DOI: 10.1136/annrheumdis-2017-eular.2831

OP0311 HIGH MATERNAL EXPRESSION OF SIGLEC1 ON CD14+ MONOCYTES AS A SURROGATE MARKER OF A TYPE I INTERFERON SIGNATURE IS A RISK FACTOR FOR THE DEVELOPMENT OF AUTOIMMUNE CONGENITAL HEART BLOCK

A.R. Lisney[1,2], F. Szelinski[1], K. Reiter[1], G. Burmester[1], C. Scholz[3], T. Rose[1,2], T. Dörner[1,2]. *[1]Department of Rheumatology and Clinical Immunology, Charité, Universitätsmedizin Berlin; [2]German Rheumatism Research Center (DRFZ); [3]Department of Obstetrics and Gynaecology, Charité, Universitätsmedizin Berlin, Berlin, Germany*

Background: Autoimmune congenital heart block (CHB) is a severe manifestation of neonatal lupus syndrome that is associated with placental transcytosis of maternal autoantibodies directed against the ribonucleoproteins Ro/SS-A and, to a lesser extent, La/SS-B.(1) Around 2/3 of affected mothers are diagnosed with either systemic lupus erythematosus (SLE) or primary Sjögren's syndrome (pSS),(2) which are both pathogenically driven by an upregulation of type I interferons (IFN).(3)
Objectives: Although the pleiotropic effects of type I IFN on the immune system are well documented, a potential role of type I IFN in the development of CHB has not yet been investigated. This study therefore aimed to compare maternal levels of type I IFN activation in affected and unaffected mothers, in order to provide first insights into a potential role of type I IFN in CHB development.
Methods: Blood samples, clinical data and serological parameters from 9 women with CHB pregnancies, 15 pregnant women with antibodies against Ro/SS-A but without a CHB complication ("Disease Controls", DC), and another 30 healthy pregnant women without the respective autoantibodies as controls were studied. Plasma levels of IFN-α (ELISA), interferon-gamma induced protein 10 (IP-10) (Bioplex®) and the expression of SIGLEC1 on CD14+ monocytes (flow cytometry) were analysed.
Results: Pregnant females with a CHB complication had a significantly higher expression of SIGLEC1 (p=0.0034) and IFN-α (p=0.014), but not of IP-10 (p=0.14, all MWU), compared to the DC group. Receiver operating curve (ROC) analysis between the CHB group and the DC group showed that a SIGLEC1 median fluorescence intensity (MFI) of >904 could distinguish between the groups with a sensitivity of 100% and a specificity of 64%, and a concentration of IFN-α >0.70 pg/ml with a sensitivity of 67% and a specificity of 86%. Healthy pregnant females without the respective autoantibodies had the lowest levels for all three parameters. In a cohort of 5 females, both the expression of SIGLEC1 and plasma levels of IFN-α were reduced by hydroxychloroquine and oral glucocorticoids.

Table 1. Antibody profiles

	CHB pregnancies (n=9)	Disease controls (n=14)	Healthy controls (n=30)
Anti-Ro (SS-A), n (%)	9 (100%)	14 (100%)	0
– anti-Ro52, n (%)	7 (78%)	12 (86%)	0
– anti-Ro60, n (%)	9 (100%)	8 (57%)	0
Anti-La (SS-B), n (%)	2 (22%)	4 (29%)	0

Conclusions: This is the first study to report increased type I IFN activation in pregnant females with a CHB complication. Also, we show here that IFN-α directed therapy, e.g. with hydroxychloroquine, may be especially beneficial in these females.
References:
[1] Brito-Zeron P, Izmirly PM, Ramos-Casals M, Buyon JP, Khamashta MA. Autoimmune congenital heart block: complex and unusual situations. Lupus. 2016; 25(2):116–28.
[2] Brito-Zeron P, Izmirly PM, Ramos-Casals M, Buyon JP, Khamashta MA. The clinical spectrum of autoimmune congenital heart block. Nat Rev Rheumatol. 2015;11(5):301–12.
[3] Lopez de Padilla CM, Niewold TB. The type I interferons: Basic concepts and clinical relevance in immune-mediated inflammatory diseases. Gene. 2016;576(1 Pt 1):14–21.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2618

FRIDAY, 16 JUNE 2017

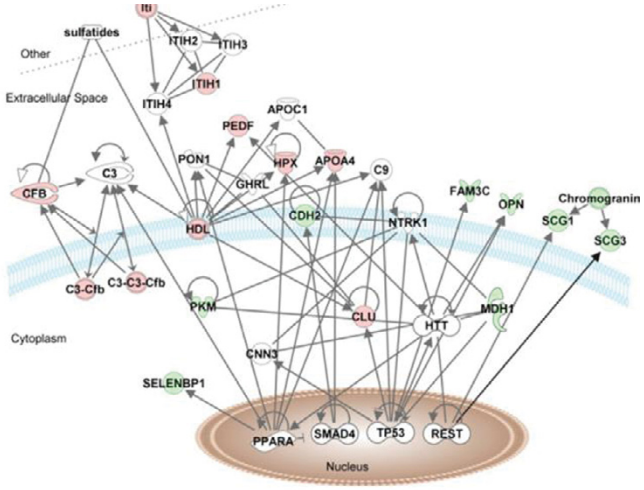
Neuronal and hormonal alterations in arthritis

OP0312 A PROTEOMIC SIGNATURE OF FATIGUE IN PRIMARY SJÖGREN'S SYNDROME

R. Omdal[1,2], E. Larssen[3,4], C. Brede[5], A. Hjelle[4], A.B. Tjensvoll[6], K.B. Norheim[1], K. Bårdsen[4], K. Jonsdottir[7], P. Ruoff[8], M.M. Nilsen[3,4]. *[1]Clinical Immunology Unit, Stavanger University Hospital, Stavanger; [2]Department of Medical Science, Faculty of Medicine and Science, University of Bergen, Bergen; [3]International Research Institute of Stavanger – IRIS; [4]Research Department; [5]Department of Medical Biochemistry; [6]Department of Neurology; [7]Department of Pathology, Stavanger University Hospital; [8]Centre for Organelle Research (CORE), University of Stavanger, Stavanger, Norway*

Background: Fatigue is a frequent and often disabling phenomenon in patients with chronic inflammatory and immunological diseases, neurodegenerative diseases, and cancer. The underlying biological mechanisms of fatigue are largely unknown and hypotheses are conflicting. It is important to uncover the pathophysiology and identify signalling pathways that generate and regulate this substantial phenomenon.
Objectives: Based on the hypothesis that fatigue originates from cerebral processes, we investigated whether relevant proteins and/or signaling pathways for fatigue could be revealed in the cerebrospinal fluid (CSF) of patients with primary Sjögren's syndrome.
Methods: Label-free shotgun mass spectrometry was performed to analyze the CSF proteome of 20 patients with primary Sjögren's syndrome. Fatigue was measured with the fatigue Visual Analogue Scale (fVAS).
Results: After depletion of high-abundance proteins, more than 800 proteins were identified and quantitated. Multivariate analyses showed that patients with low and high fatigue could be separated based on their CSF protein profiles, and 15 proteins were selected as top discriminatory proteins. Among these were apolipoprotein A4, hemopexin, pigment epithelium derived factor, secretogranin-1, secretogranin-3, selenium-binding protein 1, and complement factor B.
The figure shows the top network from Ingenuity Pathway Analysis (IPA) with 14 of

the differentially expressed proteins (red = upregulated, green = downregulated) and proteins that are directly associated to them (white molecules).



© 2000-2017 QIAGEN. All rights reserved.

Conclusions: Most of the discriminatory proteins have important roles in regulation of innate immunity, cellular stress defense, and/or functions in the central nervous system. Some have been associated with severe depression and loss of appetite, which are important features of chronic fatigue. These proteins and their interacting protein networks may therefore have central roles in the generation and regulation of fatigue, and the findings add new, relevant, and important evidence to the concept of fatigue as a biological phenomenon signaled through specific molecular pathways.

References:

[1] Norheim KB, Jonsson G, Omdal R. Biological mechanisms of chronic fatigue. Rheumatology (Oxford). 2011;50:1009–18.
[2] Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: when the immune system subjugates the brain. Nature reviews Neuroscience. 2008;9:46–56.
[3] Schutzer SE, Angel TE, Liu T, Schepmoes AA, Clauss TR, Adkins JN, et al. Distinct cerebrospinal fluid proteomes differentiate post-treatment lyme disease from chronic fatigue syndrome. PloS one. 2011;6:e17287.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3973

OP0313 P75 LOW AFFINITY RECEPTOR OF NERVE GROWTH FACTOR ON PERIPHERAL LEUKOCYTES AND CD11C-POSITIVE DENDRITIC CELLS ARE UPREGULATED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

S. Welle, A.M. Wolf, M.F. Seidel. *Medizinische Klinik III, Hematology, Oncology and Rheumatology, University Hospital of Bonn, Bonn, Germany*

Background: The nervous system regulates rheumatic diseases in neurogenic inflammation (NI). Nerve growth factor (NGF) plays a pivotal role in NI and chronic nociceptive pain of degenerative musculoskeletal diseases [1]. Clinical trials using NGF antagonists have shown impressive analgesic efficacy in these disorders [2]. However, the role of NGF in autoimmune inflammatory diseases is not completely understood although NI perhaps induces and/or mediates disease activity. NGF-receptor expression on peripheral lymphocytes may reflect NI activity.

Objectives: The aim of this study was to identify the expression levels of the NGF receptor with high affinity (TrkA) and low affinity (p75) on leukocyte subsets of SLE patients, as compared to healthy controls (HC).

Methods: The number of TrkA- and p75-positive cells was quantified in 13 SLE patients (diagnosed according to the 1997 ACR revised criteria). CD4, CD8, CD11b, CD11c, CD14, CD16, CD19, CD56 and CD66b antibodies, and isotype controls were used. Cells were quantified by multicolour flow cytometry and compared to gender and age-matched HC (n=13) using the Mann-Whitney-U-Test. Values <0.05 were considered statistically significant. Patients were further subgrouped for high or low disease activity as determined by SLEDAI, ANA, anti-dsDNA, CRP, complement C3/C4 and ESR, and compared to HC using the Kruskal-Wallis test and Mann-Whitney-U-test. NGF serum concentrations were determined by ELISA.

Results: In SLE, *TrkA* expression on peripheral leukocytes (%±SD) was not different from HC and was highest on CD14+ cells (15.5±20.6). In contrast, *p75* was significantly increased on CD16+ (2.4±3.0 vs. 0.9±0.6, p=0.044) and CD56+ leukocytes (1.5±1.7 vs. 0.4±0.3, p=0.022) in SLE vs. HC. Further subgroup analyses showed that *TrkA* (0.6±0.3 vs. 1.8±1.3, p=0.035) and *p75* (0.4±0.3 vs. 2.3±1.8, p=0.014) were decreased on CD56+ cells in patients with high SLEDAI vs. patients with low SLEDAI scores. Similarly, a reduction of *p75* on CD19+ B cells was associated with high SLEDAI (0.8±0.7 vs. 10.8±16.5, p=0.018) whereas *p75* expression was significantly higher on CD56+ cells in SLE with low SLEDAI as compared to HC (2.3±1.8 vs. 0.2±0.2, p=0.007). CD11c+ dendritic cells (DC) did not show differential expression for TrkA or p75, however, they were increased in SLE as compared to HC (5.4±2.5 vs. 2.5±0.6, p=0.0001). Interestingly, DC were also significantly elevated in SLE with high SLEDAI, anti-dsDNA, ANA and ESR. NGF serum concentrations did not differ between SLE and HC.

Conclusions: Our data for the first time demonstrate differential NGF receptor expression on an extensive panel of peripheral blood leukocytes in SLE and HC. p75 appears to be the major differentially regulated receptor for NGF. The decrease of TrkA and p75 on CD56+ and p75 on CD19+ cells in patients with high SLEDAI activity is unclear and may reflect a negative feedback mechanism. The increased CD11c+ DC might indicate additional inflammatory activation in SLE. Further studies are needed to analyse these findings.

References:

[1] Seidel MF, Herguijuela M, Forkert R, Otten U. Nerve growth factor in rheumatic diseases. Sem. Arthr. Rheum. 2010; 40(2):109–26.
[2] Seidel MF, Wise BL, Lane NE. Nerve growth factor: an update on the science and therapy. Osteoarthritis Cartilage 2013; 21(9):1223–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2493

FRIDAY, 16 JUNE 2017

Fighting osteoporosis fragilities

OP0314-HPR A HOME-BASED FALL PREVENTION PROGRAMME REDUCES FEAR OF FALLING IN SENIORS

B. Zindel [1], A. Meichtry [2], V. Krafft [1], K. Niedermann [2]. *[1]Swiss League against Rheumatisme, Zurich; [2]Zurich University of Applied Sciences, Winterthur, Switzerland*

Background: Every year, over 80,000 elderly persons in Switzerland have accidents caused by tripping and falling, and half of these falls happen at home or in the direct vicinity (1). Falls, due to its often severe medical consequences and persistent mobility impairments, together with the demographic development, are one of the most important musculo-sceletal problems and public health issue. Falls are often due to a combination of internal risk factors (such as vertigo, osteoporosis, cognitive impairments, decreased ability for dual tasking) and external risk factors (such as medication and environmental risk factors) (2). The Swiss League Against Rheumatism (SLAR) has developed a multidimensional home-based fall prevention programme, which is supported by health insurances. Trained physiotherapists (PTs) and occupational therapists (OTs) visit the seniors at home in order to perform a detailed assessment of the senior's individual risk of falling. Subsequently the PT or OT eliminates identified environmental risk factors and provide tailored exercises. After 4 weeks, a telephone call was made by the PT/OT to discuss unclear instructions and after 16 weeks, follow up data were collected by telephone.

Objectives: The objective was to evaluate the effects of the fall prevention programme.

Methods: A retrospective analysis was carried out on the data of 671 participants in 2015. Available data were participant's characteristics, fall risk factors, determined by the Timed "Up&Go" with additional motor and cognitive task) (4). Fall Efficacy Scale (5), the recommendations made by the PTs/OTs and satisfaction of the seniors.

Results: The participants were mainly female (62.6%) and had a mean age of 81.7 years (SD=5.5, range 66.1–100 years). Several risk factors were present: 64.1% fell at least once in the last year and 45% were not able to perform a dual task (TUG + additional cognitive task).

Main recommendations made by PTs/OTs were "fixing down of carpets" (56.6%) and instruction of an exercise programme (strength, balance and multi-task capability) (82.6%). After four months, fear of falling had decreased (change in FES-I: -1.24 points 95% CI: (-1.44, -1.04), p-value<0.001). 92% of the participants self-reported to follow the recommendations and 98.4% were satisfied with the programme and would recommend it to others.

Conclusions: The low-threshold, multidimensional home-based fall prevention developed by the SLAR was feasible and effective. Participants implemented the recommendations and the fear of falling' decreased. Reduced fear of falling is considered a strong predictor of falling, however a prospective study is needed to determine if the reduced fear of falling leads to a decreased number of falls.

References:

[1] Bfu, Schweiz 2014.
[2] Gschwind, Y.J., Bridenbaugh St. A. & Kressig, R. W. (2013). Sturz im Alter. In Pinter, G. Likar et al. Geriatrische Notfallversorgung Strategien und Konzepte.
[3] Shumway-Cook, A., Brauer, S. & Woollacott, M. (2000). Predicting the probability for falls in community-dwelling older adults using the Timed Up & Go Test. Physical Therapy, 80(9).
[1] Kempen, G. I. J. M., Yardley, L., van Haastregt, J. C. M., Zijlstra, G. A. R., Beyer, N., Hauer, K. & Todd, Chris (2008). The Short FES-I: a shortened version of the falls efficacy scale-international to assess fear of falling. Age and Ageing, 37(1).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3774

FRIDAY, 16 JUNE 2017

Biological agents in juvenile idiopathic arthritis: open issues

OP0315 REASONS FOR DISCONTINUATION OF BIOLOGICAL AGENTS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: DATA FROM THE PORTUGUESE REGISTER, REUMA.PT

A.F. Mourão[1], M. Eusébio[2], J. Melo-Gomes[3], F. Oliveira-Ramos[4], F. Martins[2], P. Estanqueiro[5], M. Salgado[5], M. Guedes[6], M. Conde[7], S. Carvalho[8], J. Tavares-Costa[9], C. Duarte[10], I. Brito[11], C. Furtado[12], A. Rodrigues[13], G. Sequeira[14], R. Campanilho-Marques[4], J. Branco[15], M.J. Santos[16], J. Eurico-Fonseca[17], H. Canhão[18]. *[1]Rheumatology, CHLO, EPE; [2]SPR; [3]Rheumatology, Portuguese Institute of Rheumatology; [4]Rheumatology, Pediatric Reumatology Unit, CHLN, EPE, Lisbon; [5]Pediatrics, CHUC, Coimbra; [6]Pediatrics, Centro Hospitalar do Porto - Hospital de Santo Antonio, Porto; [7]Pediatrics, Hospital Dona Estefânia, Lisbon; [8]Pediatrics, Centro Hospitalar do Médio-Ave, Famalicão; [9]Rheumatology, ULSAM - Hospital Conde de Bertiandos, Ponte de Lima, Viana do Castelo; [10]Rheumatology, Centro Hospitalar Universitário de Coimbra, Coimbra; [11]Rheumatology, Centro Hospitalar São João, Porto; [12]Rheumatology, Hospital do Divino Espírito Santo, São Miguel, Ponta Delgada; [13]Rheumatology, Hospital de Santo Espírito, Angra do Heroísmo, Angra do Heroísmo; [14]Rheumatology, Centro Hospitalar de Faro, Faro; [15]CEDOC, Nova Medical School, Lisbon; [16]Rheumatology, Hospital Garcia de Orta, Almada, Almada; [17]Rheumatology research Unit, Faculdade de Medicina de Lisboa; [18]CEDOC, EpiDoC Unit, Nova Medical School, Lisbon, Portugal*

Background: Persistence on medication mainly reflects both effectiveness and safety of a drug. Understanding the reasons to stop bDMARD in routine clinical practice can help to better define the efficacy and safety of biologic medications in children with juvenile idiopathic arthritis (JIA).
Objectives: To investigate persistence on treatment and the reasons for discontinuation of the first biological in patients with JIA.
Methods: Portuguese patients with JIA registered in Reuma.pt who started a bDMARD were analyzed. Persistence was defined as the time between treatment initiation and discontinuation of the first bDMARD. The mean time until discontinuation was calculated using Cox regression survival estimates and the reasons for discontinuation of the first bDMARD were registered.
Results: Of the 1724 JIA patients registered in Reuma.pt, 319 received biological therapy, 62% (198) female. The mean age at disease onset was 7.7±4.8 years and the mean time between the beginning of JIA and the first bDMARD was 8.2±9.4 years. The mean disease duration was 13.7±10.7 years and the mean age at the beginning of biological therapy was 15.8±9.4 years. The distribution of JIA subtypes was: 19.1% polyarticular RF-negative, 17.2% enthesitis-related arthritis, 16.6% polyarticular RF-positive, 16% extended oligoarticular, 13.5% persistent oligoarticular, 12% systemic JIA and 0.9% had undifferentiated arthritis. Considering the whole group, 53.2% have had extra-articular manifestations and 18.4% have or had had uveitis since the beginning of the disease. Persistence on treatment, before discontinuation (due to any cause) was 34.7 months (range: 0.03–182 months) adjusted for gender, biological therapy, JIA subtype, age at the beginning of biological therapy, and disease duration until initiating first bDMARD. The major reasons for drug discontinuation was inefficacy (49.6%), remission (14.2%), adverse events (10.6%), patient decision (1.6%) and pregnancy planning (1.4%). In 22.7% the reason was not specified.
Conclusions: Almost half of the JIA patients stop the first biological agent, due to lack of response, reinforcing the need for the existence of several treatment options fully studied in JIA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2959

OP0316 DURATION OF CLINICAL REMISSION AND FLARE RATES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AFTER WITHDRAWAL OF BIOLOGICAL TREATMENT (PRELIMINARY DATA)

E. Kashchenko[1], E. Alexeeva[1,2], T. Bzarova[1,2], S. Valieva[1], K. Isaeva[1], R. Denisova[1], O. Lomakina[1], T. Sleptsova[1], M. Soloshenko[1], A. Karaseva[1]. *[1]Federal State Autonomous Institution "National Scientific and Practical Center of Children's Health" of the Ministry of Healthcare of the Russian Federation; [2]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Background: Prolonged therapy with biological agents (BAs) may cause adverse events, which leads to the necessity of discontinuation of BAs in patients with juvenile idiopathic arthritis (JIA), once complete disease quiescence has been achieved.
Objectives: To estimate the length of time in clinical remission and time to disease flare after discontinuation of treatment with BAs.
Methods: 83 patients with JIA (33 – with systemic onset, 50 – with oligo- or polyarticular arthritis) were included in the survey. The cohort was 34,9% (29 patients) male and 65,1% (54 patients) female with a mean age of 11±3,69 years (range 5–17 years). All patients with systemic JIA (sJIA) were treated with tocilizumab, 35 (70%) patients with other types of JIA received etanercept, 15 (30%) – adalimumab. 14 (42,4%) patients with sJIA additionally got methotrexate, 5 (15,1%) – cyclosporine, 5 (15,1%) – glucocorticoids, 1 (3,0%) – leflunomide; 9 (25,7%) and 7 (46,6%) patients took combination therapy of etanercept or adalimumab and methotrexate. Patients were randomized into 2 main groups using envelope method: in a first group a BA was discontinued abruptly, while in the second it was tapered gradually by increasing injection/infusion interval.
Results: Duration of inactive disease/clinical remission during tocilizumab treatment was 43±12,16/37±12,16 months, etanercept – 40±13,13/34±13,17 months, adalimumab – 48±11,9/40±12,06 months. Tocilizumab, etanercept, adalimumab were discontinued in 22 (66,6%), 28 (80,0%), 11 (73,3%) patients and were tapered by increasing injection/infusion interval in 11 (33,4%), 7 (20,0%), 4 (26,7%) cases, respectively. After withdrawal of tocilizumab, etanercept and adalimumab 29 (87,9%), 24 (68,6%), 6 (40,0%) patients remained in remission of JIA for 6±10,23 (1–48) months, 6±5,07 (1–20) months and 6±13,33 (4–38) months, respectively. 4 (12,1%), 11 (31,4%), 9 (60,0%) patients flared within 8±5,65 (6–18) months, 5,5±3,49 (1,5–12) months and 4±4,64 (1–13) months after discontinuation of tocilizumab, etanercept and adalimumab, respectively.
Conclusions: Withdrawal of BAs after clinical remission for more than 1,5 years was not associated with a disease exacerbation in more than 70% of patients with JIA. A mean duration of clinical remission after withdrawal of BAs was 6 months.
Disclosure of Interest: E. Kashchenko Grant/research support from: Novartis, E. Alexeeva Grant/research support from: Roche, Abbott, Pfizer, Bristol-Myers Squibb, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Bristol-Myers Squibb, Medac, Novartis, Pfizer, T. Bzarova Grant/research support from: Roche, Pfizer, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Pfizer, S. Valieva Grant/research support from: Roche, Bristol-Myers Squibb, Speakers bureau: Roche, Merck Sharp & Dohme, Bristol-Myers Squibb, Medac, Novartis, K. Isaeva Grant/research support from: Roche, Novartis, R. Denisova Grant/research support from: Roche, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Medac, O. Lomakina: None declared, T. Sleptsova Grant/research support from: Centocor, Speakers bureau: Merck Sharp & Dohme, Bristol-Myers Squibb, M. Soloshenko: None declared, A. Karaseva: None declared
DOI: 10.1136/annrheumdis-2017-eular.5756

FRIDAY, 16 JUNE 2017

Health equity and economy - a vital relationship

OP0317-PARE AN INDEPENDENT REVIEW OF PEOPLE WITH RHEUMATOID ARTHRITIS (RA) AND THEIR CAREGIVER'S LOST WORK TIME

A. Bosworth[1], C. Jacklin[1], T. Burke[2], A. Rose[2], I. Jacob[2], S. Verstappen[3]. *[1]National Rheumatoid Arthritis Society (NRAS), Maidenhead; [2]HCD Economics, Warrington; [3]Arthritis Research UK Centre for Epidemiology Division of Musculoskeletal and Dermatological Sciences, University of Manchester, Manchester, United Kingdom*

Background: The National Rheumatoid Arthritis Society (NRAS) is the only patient-led charity in the UK focussing specifically on rheumatoid arthritis (RA) with the key responsibility of raising awareness of the impact and burden of RA. There is a lack of information about the costs and impact of RA on work in the European community; in particular the wider societal costs such as people with RA not being able to perform their job to their best ability, losing days of work due to their RA condition, and the domino effect on caregiver employment.
Objectives: To quantify the burden of RA not only on the healthcare system, but also the wider societal costs associated with RA.
Methods: In 2016 NRAS undertook a partnership with the University of Chester's commercial economics partner HCD Economics who conducted the multinational Burden of Rheumatoid Arthritis: Socioeconomic Survey (BRASS). The study used a bottom-up approach to quantify the burden of disease for people living with RA across 10 European countries including France, Germany, Italy, Spain, Denmark, Sweden, Hungary, Poland, Romania and the UK. The study collected information from patients and physicians on factors associated with managing RA, plus RA sufferers' views on life and workplace impact. It collected information on the resource use and cost of patient care including treatment costs, hospitalisation, tests, and examinations. The wider societal costs included; cost of travel to appointments, requirements for aids/equipment, informal care (non-professional), ability in employment, early retirement due to RA. Work time missed, work and activity impairment were measured using the Work Productivity and Activity Impairment (WPAI) questionnaire.
Results: Voluntary data were collected from 1782 patient forms, of which the average age was 55 years, 1274 (71%) were female and 833 (48%) were currently in work. This study found, on average, persons with RA lose one day of every 4 working days due to not being able to perform their job to their best ability, and completely miss 7% of work time over a 7 day period due to their RA (sample n of 646). In addition to not being able to perform their job to their best ability, almost a third of working persons with RA also had impairment in daily living activities such as shopping and work around the house (sample n of 735). This study also found family/friends have to care for 16% of RA sufferers. This care resulted in reduced employment or inability to work for 25% of family/friend caregivers (sample n of 121).

Conclusions: This study highlights the impact RA has on working life amongst both those with the condition and those providing support. It is hoped these metrics will allow the conversation to open and develop with employers and government on how adapting the workplace can increase productivity. Further research should also be undertaken on the economic impact both to the individuals, their carers and society.
Acknowledgements: The BRASS study was supported by unrestricted research grants from Eli Lilly and Pfizer. The study was approved by the University of Chester Ethics Committee.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5948

OP0318-PARE **CONSULTING SERVICES TO EMPLOYERS OF PEOPLE WITH RMDS**

F.J. Carreira Roca[1,2], A.I. Vázquez Lojo[3], V. Romero Pazos[4,5] on behalf of LIRE-LRG. *[1]Accesibility Dept. and Volunteer, Liga Reumatolóxica Galega (LRG), A Coruña; [2]Accesibility Consultant and Volunteer, Liga Reumatológica Española (LIRE), Madrid; [3]Board of Directors and Occupational Therapy Dept., Liga Reumatolóxica Galega; [4]International Dept., Liga Reumatolóxica Galega (LRG), A Coruña; [5]Board of Directors, Liga Reumatológica Española (LIRE), Madrid, Spain*

Background: The Eurobarometer[1] states that RMDs affect 22% of the general population which means that 10 million people are affected in Spain and more than 600.000 people in the autonomous region of Galicia where our organization, LRG, works.
Knowing that 50% of people with RMDs are currently unemployed because of their condition[2], only part of them have the legal work incapacity recognized and receive a pension. This means that RMDs not only affect the health but also the socio-economic status. Most of this people could stay at work and are willing to do so if some arrangements are made like cutting down hours, work place adaptations, flexible schedule, etc.[3]
Most employers are lacking information on how these conditions affect the employee's hability, desire and need to work and how to make the necessary adaptations for not loosing this person from the work force.
Objectives: Making the employer more aware of the positive aspects of keeping all the employees including people with RMDs not just at the work place but at full capacity, avoiding both absenteeism and presenteeism.
Helping the employer knowing about the needs of people with RMDs and the necessary adaptations for each of them.
Keep people with RMDs at work at the best possible conditions both for the employee and the employer, as efficiently and healthy as possible.
Methods: The employee with RMD has 1 session with the psychologist and 1 session with the occupational therapist (OT) to identify the difficulties in continuing to be active into their work place.
LRG HP give personalized advise to the employer about the RMDs, the needs of the employees and how to facilitate them to stay at work and minimize the work incapacity due to their chronic condition. This kind of advise is given by the OT who has treaten the employees and knows all about their needs, goes to their work place to see what are the actual conditions, identifies manageable obstacles and talks to the employers during a pre-scheduled meeting. After, an architect specialized in accesibility offers specific architectural and ergonomic solutions for adapting the work place.
Also peer support is provided by LRG in group meetings and activities of the organization.
Results: The results of this project are shown in the increase of the employees' self-confidence in their capacity to stay at work and also they are more aware of their solvable and non solvable limitations.
During 2016 we advised 14 associates of LRG, 5 of those 14 employees (1/3) stayed at work or returned to work after the consultancy.
Conclusions: This kind of actions are neccesary to make the work places more adaptable and increasing the number of people with RMDs to start a work live, to stay or go back to work.
Peer support within a patient's association is key to create a secure environment for the employees who find relief in seeing other people with RMDs having a sustainable work life.
References:
[1] European Commission. Health in the European Union. Special Eurobarometer 272e. 2007.
[2] Anna Klak, Filip Raciborski and Piotr Samel-Kowalik. Social implications of rheumatic diseases. Reumatologia 2016; 54(2): 73–78.
[3] Bevan, S., Passmore, E., Mahdon, M. (2007). Fit for Work? Musculoskeletal Disorders and Labour Market Participation. UK: The Work Foundation.
Acknowledgements: Employers: SERGAS, Correos, Inditex Group, Estrella Galicia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6342

FRIDAY, 16 JUNE 2017

Biomarkers in cardiovascular rheumatology - state-of-the-art 2017

OP0319 **HIGH SENSITIVITY CARDIAC TROPONIN T IS A BIOMARKER FOR ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS: A CROSS-SECTIONAL CONTROLLED STUDY**

G. Divard[1], R. Abbas[1], C. Chenevier-Gobeaux[2], B. Escoubet[1], M.-P. Chauveheid[1], A. Dossier[1], M. Dehoux[1], T. Papo[1], K. Sacre[1]. *[1]Paris-7 University, APHP, Bichat Hospital; [2]Paris-5 University, APHP, Cochin Hospital, Paris, France*

Background: Cardiovascular disease (CVD) is the main cause of death in systemic lupus erythematous (SLE) patients. Framingham score underestimates the risk for CVD in this population.
Objectives: Our study aimed to determine whether serum High Sensitivity Cardiac Troponin T (HS-cTnT) helps to identify SLE patients at risk for CVD.
Methods: Presence of carotid plaques was prospectively assessed by ultrasound in 63 consecutive SLE patients asymptomatic for CVD and 18 controls. Serum HS-cTnT concentration was measured using the electrochemiluminescence method. Factors associated with carotid plaques were identified and multivariate analysis was performed
Results: Framingham score was low in both SLE patients (2.1±3.8%) and controls (2.1±2.9%). Nevertheless, 23 (36.5%) SLE patients, but only 2 (11.1%) controls (p=0.039), had carotid plaque detected by vascular ultrasound. In the multivariate analysis, only age (p=0.006) and SLE status (p=0.017) were independently associated with carotid plaques. Serum HS-cTnT concentration was detectable (i.e. >3 ng/L) in 37 (58.7%) SLE patients and 6 (33.3%) controls (p=0.057). Interestingly, 87% of SLE patients with carotid plaques, but only 42.5% in SLE patients without plaques ($p<0.001$), had a detectable HS-cTnT. Conversely, 54.5% SLE patients with a detectable HS-cTnT, but only 11.5% with an undetectable HS-cTnT ($p<0.001$), had a carotid plaque. In the multivariate analysis, only BMI (p=0.006) and HS-cTnT (p=0.033) were statistically associated with carotid plaques in SLE patients. Overall, the risk of having a carotid plaque was increased by 8 (OR [95% CI]: 8.03 [1.41–74.73]) in SLE patients in whom HS-cTnT was detectable in serum.
Conclusions: Detectable HS-cTnT concentration is independently associated with subclinical atherosclerosis in asymptomatic SLE patients at apparent low risk for CVD according to traditional risk factors. These results raise the possibility that this easily obtained biomarker is useful for more rigorous risk stratification and primary prevention of CVD in SLE patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1015

FRIDAY, 16 JUNE 2017

What is behind vasculitis?

OP0320 **DETERMINANTS OF RITUXIMAB PHARMACOKINETICS AND CLINICAL OUTCOMES IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS**

D. Cornec[1,2], B. Kabat[1], J. Mills[1], M. Cheu[3], A. Hummel[1], D. Schroeder[1], M. Cascino[3], P. Brunetta[3], D. Murray[1], M. Snyder[1], F. Fervenza[1], G. Hoffman[4], C. Kallenberg[5], C. Langford[4], P. Merkel[6], P. Monach[7], P. Seo[8], R. Spiera[9], W.St. Clair[10], S. Ytterberg[1], J. Stone[11], D. Barnidge[1], U. Specks[1]. *[1]Mayo Clinic, Rochester MN, United States; [2]Rhumatologie, CHRU Brest, Brest, France; [3]Genentech Inc., San Francisco, CA; [4]Cleveland Clinic, Cleveland OH, United States; [5]Univeristy, Groningen, Netherlands; [6]University of Pennsylvania, Philadelphia PA; [7]Boston University, Boston MA; [8]Johns Hopkins, Baltimore MD; [9]Hospital for Special Surgery, New York; [10]Duke University, Durham NC; [11]Massachusetts General Hospital, Boston MA, United States*

Background: Response to rituximab (RTX) is variable in patients with ANCA-associated vasculitis (AAV), and predictors of treatment efficacy/relapse risk would be useful. Previous studies have shown that RTX pharmacokinetics (PK) is associated with treatment efficacy in patients with lymphoma.
Objectives: To study the determinants of RTX PK in patients treated for AAV and its association with clinical outcomes.
Methods: This study included 88 patients from the RTX in ANCA-Associated Vasculitis (RAVE) trial who received the full dose of RTX (4 weekly 375 mg/m^2 infusions) and had available serum samples. RTX was quantified using two different assays: a traditional ELISA and a recently developed mass spectrometry-based assay (referred to as miRAMM). We analyzed week (W)2, W4, W8, W16 and W24 serum levels and the trapezoidal area under the curve (AUC) integrating baseline, W2, W4, and W8 levels. We explored potential determinants of RTX PK using univariate and multivariate analysis, and analyzed the association of RTX PK with clinical outcomes: achievement of complete remission at 6 months (defined by a BVAS/WG score of 0 with no prednisone), time to relapse in patients who achieved complete remission, and B-cell depletion duration.

Results: RTX quantifications using ELISA and miRAMM were highly correlated, but miRAMM measured consistently higher serum levels, suggesting its ability to detect total serum RTX (including free and complexed rituximab). RTX PK was highly variable between patients, with W2 levels ranging between 43 and 259 μg/mL and AUC ranging between 2,668 and 17,513 μg/mL by miRAMM. W2 RTX levels and AUC were significantly lower in males and in newly-diagnosed patients, and were negatively correlated with body surface area, baseline B-cell count, and BVAS/WG. In multivariate analyses, the main determinants of RTX PK were sex and new diagnosis. Patients with a new diagnosis had higher baseline B-cell counts and BVAS/WG. Patients reaching complete remission at month 6 had similar mean RTX levels compared to patients who did not reach complete remission (W2 level by miRAMM: 136±44 vs 139±46, p=0.76; AUC: 8420±2875 vs 8558±3452, p=0.85). Patients with higher RTX levels generally experienced longer B-cell depletion durations, but RTX levels at the different time-points and AUC were not associated with time to any relapse or time to severe relapse. Similar results were observed when using rituximab quantification by miRAMM and by ELISA.
Conclusions: Despite a dosing protocol adjusted for body surface area, rituximab PK is highly variable between patients, its main determinants being sex and newly diagnosed disease. We did not observe an association between rituximab PK and clinical outcomes. Serum rituximab level monitoring does not seem clinically useful in this context.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3527

OP0321 RISK OF CORONARY ARTERY DISEASE AND ISCHEMIC STROKE IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS. A FRENCH POPULATION-BASED STUDY

M. Mourguet[1], D. Chauveau[2], A. Huart[3], D. Ribes[4], S. Faguer[5], L. Sailler[1], G. Pugnet[1]. *[1]Service de Médecine Interne, CHU Toulouse Purpan; [2]Département de Néphrologie et transplantation d'organes; [3]Departement de Néphrologie et Transplantation d'organes; [4]Département de Néphrologie et transplantation d'organe; [5]Département de Néphrologie et transplantation d'organertement de Néphrologie et transplantation d'organe, CHU Toulouse Rangueil, Toulouse, France*

Background: ANCA-associated vasculitis (AAVs), including granulomatosis with polyangiitis and microscopic polyangiitis, are small vessel vasculitides. Modern treatments have greatly improved survival in AAV patients, but significant long-term morbidity and mortality such as cardiovascular disease (CVD) are still associated with this disease.
Objectives: The aim of our study was to assess the incidence, mortality and predictors of CVD in patients with AAVs
Methods: We conducted a retrospective study of AAV diagnosed in Toulouse France teaching hospital between 1981 and 2015. Patients with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) were included and classified, after thorough medical chart review, according to the criteria proposed by the Chapel Hill Consensus Conference. Eosinophilic granulomatosis with polyangiitis were excuded. A survival analysis was performed. Hazard ratios and the comparative morbidity and mortality figure (CMF) was calculated as the ratio of expected number of deaths in the standard population to those observed as well as predictors of CVD in patients with AAV were also assessed.
Results: We identified 361 subjects, only 125 met the inclusion criteria, 99 GPA and 26 MPA, 65 (42%) were men and mean age was 61.3±15.7 years at CVD occurrence with a mean follow-up of 88.4±78.3 months since diagnosis.Coronary artery disease (CAD) developed in 10 patients, and ischemic stroke developed in 9 patients (incidence rates of 8.5 per 1,000 person-years and 10.2 per 1,000 person-years, respectively). CAD incidence for AAV patients is two times more than in the general population, independent of age differences between the two populations using the Midi-Pyrénées county CAD registry as a reference (CMF of 1.96; 95CI 0.88 to 4.36). Ischemic stroke incidence for AAV patients is three times more than in the general population, independent of age differences between the two populations (CMF of 3.36; 95CI 1.75 to 6.46).
Smoking habits and history of CAD at AAV diagnosis was strongly associated with CAD occurrence (adjusted HR 8.8; 95CI 2.12 to 36.56, p=0.003 and adjusted HR 10.3; 95CI 1.02 to 104.5, p=0.003, respectively). An ENT flare (adjusted HR 0.12) was a independent protective factor for CAD occurrence. We did not find any statistically significant associated factor with ischemic stroke occurrence in our cohort.
Using direct standardisation, the age adjusted mortality rate for the AAV cohort was 22.5 per 1,000 person-years and for the general population 10.2 per 1,000 person-years. This indicates that mortality for AAV patients is one and a half times more than in the general population, independent of age differences between the two populations (CMF of 1.56; 95CI 1.02 to 2.39).
Conclusions: Patients with AAV have a significantly increased risk of mortality and ischemic stroke and a non–statistically significant trend toward an increased risk of CAD. Monitoring for this complication and vigilance in modifying risk factors are particularly warranted in this patient population.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6143

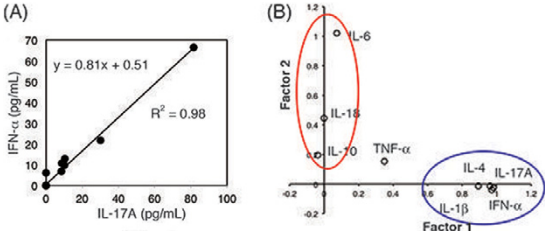
FRIDAY, 16 JUNE 2017

Cytokine taxonomy: reflection in the therapy of arthritides and other IMIDs

OP0322 A NOVEL HIERARCHICAL RELATIONSHIP BETWEEN INTERLEUKIN-17A AND INTERFERON-ALPHA IS INDICATED BY ANALYSIS OF MULTIPLE CYTOKINES IN THE SERUM OF ADULT-ONSET STILL'S DISEASE AND BEHÇET'S DISEASE

K. Sato, Y. Aizaki, Y. Araki, T. Mimura. *Department of Rheumatology and Applied Immunology, Saitama Medical University, Saitama, Japan*

Background: Adult-onset Still's disease (AOSD) and Behçet's disease (BD) are both systemic inflammatory diseases, the causes of which are largely unknown. They have been recently classified as autoinflammatory diseases, a group of diseases in which innate rather than acquired immunity plays important roles in their pathogenesis. As AOSD and BD are clinically distinct diseases, their cytokine networks should also be different.
Objectives: In this study, we attempted to quantify the levels of multiple cytokines in the serum of patients by utilizing a beads-array technique and ELISA, and then compared the serum cytokine profiles of the two diseases by factor analysis. We then sought to clarify the hierarchical relationship between interleukin (IL-) 17A and interferon (IFN-) α using peripheral blood mononuclear cells (PBMCs).
Methods: We quantified the serum levels of 10 cytokines (IFN-α, IFN-γ, IL-1β, IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-17A and tumor necrosis factor α) in 16 AOSD patients and 28 BD patients using multiplex bead array assays and IL-18 along with ELISA. The data were then subjected to factor analysis. We next stimulated PBMCs from three healthy volunteers *in vitro* with class A CpG oligodeoxynucleotides (ODNs) in the presence or absence of IL-17A for 15 hours. We performed flowcytometric analysis to examine the expression of intracellular IFN-α in plasmacytoid dendritic cells (pDCs).
Results: Two factors were extracted from the factor analysis using the data on 8 cytokines that were detectable in the serum of the patients. IL-17A and IFN-α, the levels of which showed a strong positive correlation in the serum of BD patients (Fig. A), were the main components of Factor 1, while Factor 2 consisted of IL-6, IL-10 and IL-18 (Fig. B). Patients were also plotted on a plane determined by Factors 1 and 2 according to each patient's factor scores. Those who were high in Factor 1 but low in Factor 2 were likely to be BD patients and vice versa, many of those who were high in Factor 2 but low in Factor 1 were AOSD patients. In terms of flowcytometric analysis, IL-17A alone did not induce IFN-α expression in pDCs, but it did substantially increase IFN-α-positive pDCs induced by CpG ODNs.



Conclusions: The cytokines examined were clearly separated into distinct groups by the factor analysis. Similarly, the AOSD and BD patients could be separated, although roughly. High levels of serum IL-6, -10 and -18 suggest AOSD while high levels of IFN-α and IL-17A indicate BD. To establish patterns of correlation among cytokines, it is important to focus on the cytokine concentrations in each patient, rather than the average cytokine concentrations in each of the diseases. In terms of the hierarchical relationship between IFN-α and IL-17A, a previous report suggested that IFN-α blocks IL-17A production in PBMCs from BD patients. Thus, we examined the effect of IL-17A on IFN-α production. It should be noted that the real stimulus for IFN-α release in BD is unknown. In addition, cells other than pDCs may be involved in the production of IFN-α. Nevertheless, understanding the hierarchical relationship among cytokines should prove to be helpful in clarifying the pathogenesis of various inflammatory diseases.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1678

FRIDAY, 16 JUNE 2017

Personalised care for back pain

OP0323 DISCOPATHY ASSOCIATED WITH MODIC CHANGES IS NOT RELATED TO ANY INFECTIOUS PROCESS: A PROSPECTIVE MONOCENTRIC STUDY

S. Ahmed Yahia[1], J.-W. Decousser[2], C.H. Flouzat-Lachaniette[3], F. Robineau[3], E. Audureau[4], A. Hourdille[1], F. Eymard[1], X.-J. Chevalier[1]. *[1]Rheumatology; [2]Microbiology; [3]Orthopaedic; [4]Public health, Henri Mondor hospital, Creteil, France*

Background: Low back pain (LBP) is strongly associated with Modic changes. The

hypothesis of local infectious origin was raised, especially with Proprionibacterium acnes (PA).The possibility of contamination with saprophyte germs coming from the skin during surgery by posterior approach or by epidural infiltration preceding the surgery was also discussed, but not proved.

Objectives: The main objective of this study was to evaluate the prevalence of slow growing bacterias (SGB) in the intervertebral disc (IVD) obtained during a lumbar spine surgery by anterior approach in Modic 1 and 2 changes. A secondary objective was to compare the prevalence of SGB in IVD in lumbar spine surgery obtained by anterior approach to that obtained by posterior approach in herniated disc.

Methods: 45 patients with chronic LBP or sciatica were included in the study, representing 48 IVD. When patients underwent lumbar spine surgery by an anterior approach, 2 samples of the disc were collected for bacteriological analysis: one sample from the anterior part of the disc distant from epidural space and one sample from the posterior part of the disc. 77 discs samples were obtained, 32 discs samples in Modic 1 or 2 changes by anterior approach, 26 discs samples in no Modic IVD by anterior approach, 19 disc samples obtained by posterior approach. The method to collect disc material was strictly aseptic. Samples were analysed by conventional microbial *cultures* with specialised enrichmen, molecular detection by universal rRNA gene PCR *plus* sequencing assay. Additionally, all clinical specimens were specifically tested for PA detection using a highly sensitive specific PCR

Results: Regarding bacterial cultures, 12 out 77 disc samples were positive (16%), including 10 (13%) for PA. The PA specific PCR was positive for one (1%) specimen obtained by posterior approach. The 16s RNA detection was positive for 6 specimen (8%), including one for PA (1%).Modic 1–2: Cultures were positive in 5 cases (16%) with 3 for PA (10%). No specific PA PCR was positive. Only one sample was positive for PA in both culture and 16s PCR. Comparison between anterior and posterior approach: Among the PA positive cultures, 5 were identified from anterior specimens (8.62%) and 5 from posterior specimens (26.32%). Regarding PA cultures,the posterior fragments were more frequently positive than the anterior fragments (p=0.046). The number of epidural infiltrations of the lumbar spine does not seem to influence the bacterial contamination prevalence p=0.746. The time between the epidural infiltration of the lumbar spine and the surgery does not seem to influence the bacterial contamination prevalence (more or less 6 month) p=0.23.

Conclusions: SGB has been identified in culture in 16% of the samples obtained in Modic 1 and 2 changes. The prevalence of PA in culture was significantly higher in samples of IVD collected by a posterior approach compared to anterior approach in spine surgery suggesting a contamination. The results of the specific PCR PAs with a single weakly positive sample reinforce the hypothesis of contamination.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6873

OP0324 MANAGEMENT OF MUSCULOSKELETAL PAIN USING AN ALGORITHM FOR SELECTION OF ANALGESICS

A. Karateev, A. Tsurgan, N. Gontarenko. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Musculoskeletal pain is the most common manifestation of osteoarthritis (OA) and non-specific back pain (BP). Treatment of pain includes medications with a different mechanism of action such as paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), opioid analgesics, muscle relaxants, antidepressants or local glucocorticoid (GC) injections. However, a uniform approach to sequential and complex therapy with these medications is not so far available.

Objectives: The study aims at evaluating the efficacy of combined therapy of musculoskeletal pain in real clinical practice.

Methods: In the open-label study were included 3304 patients (54.3% women and 45.7% men with average age of 48.9±14.6 years) with acute/subacute pain due to OA or BP. The exclusion criteria were the presence of severe co-morbidities and BP in association with neurological disorders. Treatment was carried out in accordance with the following algorithm: for a moderate/severe pain (>4 scores according to an 11-point numeric rating scale, NRS) use of NSAID (aceclofenac), when NSAIDs are contraindicated – tramadol with/without paracetamol, in case of mild pain – topical NSAID with/without paracetamol, and muscle relaxants as indicated. Control of treatment efficacy was carried out on day 7 (a total of 4 visits). Change of therapy could be done at each visit and include switching to the other NSAID if the prescribed drug proved to be ineffective or intolerant, local glucocorticoid (GC) injection, addition of tramadol with/without paracetamol or administration of antidepressants or anticonvulsants. The results of treatment were assessed based on the dynamics of pain using NRS, a number of patients in whom pain was relieved completely and treatment satisfaction (a 0 to 5 rating scale where 0 is the absence of the effect or pain aggravation and 5 is an excellent effect).

Results: The first prescribed medication in 97.5% of patients was oral NSAID (aceclofenac 200 mg per day) and in 67.6% of patients it was aceclofenac in combination with muscle relaxant. By visit 4, pain decreased from 6.9±1.5 to 2.2±1.3 points. Pain was completely relieved in 77.0% of patients. 227 patients (6.9%) dropped out of observation, and 16.1% of patients continued the use of analgesics after four weeks of treatment. The vast majority of patients (88.4%) evaluated treatment results as “good” or “excellent”. Switching to the other NSAID was required in 8.1% of patients, local injection of GC in 1.9%, administration of antidepressant or anticonvulsant in 1.5%, and hospitalization in 0.25% of patients. Adverse reactions (mostly dyspepsia) were noted in 2.2% of patients.

Conclusions: The use of treatment algorithm based on a complex pathogenetic approach ensures that patients receive an effective and relatively safe pain relief. Oral NSAIDs are the most expedient as first-line treatment in patients with moderate and severe musculoskeletal pain.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4447

FRIDAY, 16 JUNE 2017

Regulatory molecules in connective tissue

OP0325 TGF-BETA-INDUCED ED-A FIBRONECTIN PRODUCTION BY FIBROBLAST-LIKE SYNOVIAL CELLS CONTRIBUTES TO INFLAMMATION IN OSTEOARTHRITIS

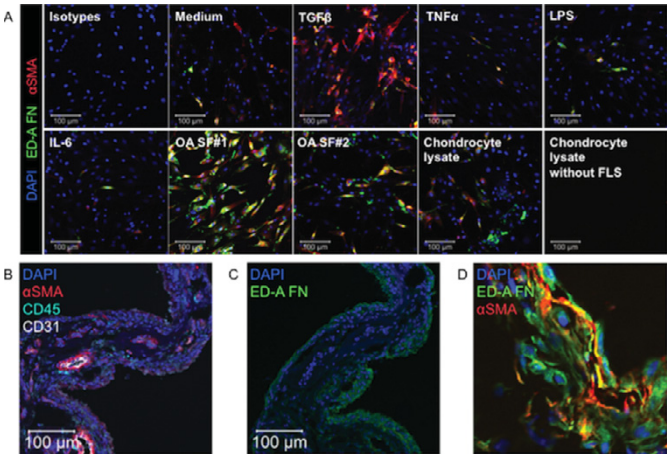
T.W. Kragstrup[1,2,3], D.H. Sohn[1,4], C.M. Lepus[1], K. Onuma[1], Q. Wang[1], W.H. Robinson[1], J. Sokolove[1]. *[1]Department of Immunology and Rheumatology, Stanford University, Stanford, United States; [2]Department of Rheumatology, Aarhus University Hospital; [3]Department of Biomedicine, Aarhus University, Aarhus C, Denmark; [4]Department of Microbiology and Immunology, Pusan National University, Pusan, Korea, Republic Of*

Background: The pathophysiology of osteoarthritis (OA) involves wear and tear, and a state of low-grade inflammation. Wear and tear leads to tissue degradation followed by tissue repair responses including TGFβ-induced myofibroblast production of extracellular matrix (ECM). Fibronectins are an essential part of the ECM, and injection of fibronectin fragments into rabbit joints is an established animal model of OA. Recently, alternatively spliced fibronectin containing the ED-A domain (ED-A FN) has been shown to activate Toll-like receptor 4.

Objectives: In this study, we hypothesize that FN fragments containing the ED-A domain could be one mechanism transducing mechanical events into inflammatory signals in OA.

Methods: Samples of synovial membrane and cartilage were obtained from patients with knee OA undergoing joint replacement surgery. Immunostaining was performed on synovial membranes. Fibroblast-like synovial cells (FLS) isolated by enzymatic digestion of remnant synovial membrane were stimulated with TGFβ, TNFα, lipopolysaccharide, IL-6, OA synovial fluid from two different donors, or chondrocyte lysate, and culture supernatants were analyzed for ED-A FN by immunofluorescence staining. ED-A FN fragments were obtained by plasmin digestion of cellular FN. Synovial cells isolated by enzymatic digestion and human monocyte-derived macrophages (MDM) were incubated with recombinant ED-A FN, plasmin, cellular FN, or cellular FN digested with plasmin; and culture supernatants were analyzed for MCP-1 and TNFα.

Results: We hypothesized that ED-A FN is produced by OA FLS in response to products reflecting tear and wear in OA. Indeed, the production of ED-A FN by OA FLS was increased by TGFβ, OA synovial fluid, and lysed chondrocytes in all experiments (n=3, see figure). ED-A FN co-localized with the myofibroblast marker αSMA in both the OA FLS (n=3) and in the OA synovial membranes (n=8). We further hypothesized that ED-A FN expression is associated with inflammation in OA. ED-A FN staining was associated with both number of lining layer cells (rho=0.85 and p=0.011) and infiltrating sublining cells (rho=0.88 and p=0.007) in the OA synovium (n=8), and co-localized with both MCP-1 and TNFα (n=5). Recombinant ED-A FN increased the production of both MCP-1 and TNFα by MDM (n=3) and OA FLS (n=3). Finally, we demonstrated that the FN fragments containing the ED-A domain generated the same production of both MCP-1 and TNFα as recombinant ED-A FN.



Conclusions: The disease process in OA shares features with the chronic

wound healing response including myofibroblast differentiation and that humeral mediators found in the joint can promote myofibroblast production of ED-A FN. We additionally show that recombinant and plasmin-derived ED-A fragments can induce generation of pro-inflammatory mediators from FLS and MDM. This study supports targeting the formation of ED-A FN or the enzymatic fragmentation of FN to reduce pro-inflammatory responses in OA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2239

OP0326 EPIGENETICALLY-DRIVEN DISTAL EXPRESSION OF THE LNCRNA HOTTIP SHAPES INFLAMMATORY, ADHESIVE AND PROLIFERATIVE CHARACTERISTICS OF HAND SYNOVIAL FIBROBLASTS IN ARTHRITIS

M. Frank Bertoncelj[1], E. Karouzakis[1], K. Klein[1], A. Bratus[2], C. Kolling[3], O. Distler[1], A. Filer[4], R.E. Gay[1], C.D. Buckley[4], S. Gay[1], C. Ospelt[1].
[1]University Hospital Zurich, Schlieren; [2]Functional Genomics Center Zurich; [3]Schulthess Klinik, Zurich, Switzerland; [4]University of Birmingham, Birmingham, United Kingdom

Background: Rheumatoid arthritis (RA) and other types of inflammatory arthritis show a characteristic pattern of joint involvement. E.g. in RA there is a predilection for the small joints of hands and feet, whereas in spondyloarthropathy, single large joints are characteristically involved. We have recently shown that synovial fibroblasts (SF), which drive joint destruction in RA, display site-specific transcriptomes and functions, shaping unique microenvironments in different joints.

Objectives: To analyze the role of transcripts expressed in SF at specific joint locations in defining location-specific functions of SF, relevant to the pathogenesis of RA.

Methods: SF were isolated from hand, elbow, shoulder, feet, knee and hip joints of RA and OA patients undergoing joint replacement surgery and from knees of nonarthritic subjects with arthralgia. Transcriptomes and epigenomes of SF were determined by RNA-seq (Illumina HiSeq 2000, n=21), qPCR, ChIP-seq (H3K4me3, H3K27me3, H3K27ac, Illumina HiSeq 2500, n=7) and Infinium HumanMethylation450 BeadChip (n=12). Proliferative, adhesive and chemotactic properties of SF were studied by xCELLigence real time cell analysis and leukocyte chemotaxis towards supernatants of SF. The lncRNA HOTTIP was silenced in hand SF using LNA GapmeR oligos, followed by RNA-seq (n=2), pathway enrichment analysis (MetaCore, Thomson Reuters, FDR$<$0.05) and qPCR (n=5).

Results: HOTTIP was the most differentially expressed transcript in distal (hand) vs. proximal (shoulder) SF. HOTTIP was specifically transcribed in SF from hand and feet SF, but absent from other joints, inferring distal-specific function to this lncRNA. Hand-specific HOTTIP expression coincided with the enrichment of activating histone marks H3K4me3 and H3K27ac, absence of repressive H3K27me3 and decreased DNA methylation at the HOTTIP promoter in hand SF. In contrast, the HOTTIP promoter displayed abundant DNA methylation and H3K27me3 in knee and shoulder SF. Silencing of HOTTIP led to downregulation of 3275 genes and upregulation of 4326 genes (log ratio $>|0.5|$, $p<0.01$, FDR$<$0.05). Distal-specific homeobox A13, a known HOTTIP target, was repressed in HOTTIP-silenced SF. Pathway enrichment analysis of genes repressed by HOTTIP silencing showed enrichment for pathways regulating cell adhesion, cell cycle, angiogenesis and inflammation, including NF-kB activation and IL-6 signalling. Meanwhile, upregulated genes were enriched in fewer pathways, e.g. IL17 and Notch signalling. 110 genes that were differentially expressed in hand vs. shoulder SF were also altered by HOTTIP silencing, e.g. TNFRSF1B and MAP3K14. Hand SF showed enhanced proliferative and chemotactic, but decreased adhesive properties compared to shoulder SF.

Conclusions: The lncRNA HOTTIP, which is exclusively expressed in small, distal joints, via epigenetic mechanisms, is a regulator of inflammatory, proliferative and adhesive properties of SF. Such a functional specialization of arthritis relevant pathways in SF might represent an imprinted site-specific "risk" signature in SF, predisposing thereby to location-specific joint pathology, e.g. enhanced severity of hand arthritis in RA.

Disclosure of Interest: M. Frank Bertoncelj Grant/research support from: euroTEAM, BTCure, IAR, Promedica, Georg und Berta Schwyzer Winiker Grant, E. Karouzakis Grant/research support from: BTCure, GSK, K. Klein Grant/research support from: BTCure, A. Bratus: None declared, C. Kolling: None declared, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha, A. Filer: None declared, R. Gay Grant/research support from: euroTEAM, BTCure, GSK, IAR, C. Buckley: None declared, S. Gay Grant/research support from: euroTEAM, BTCure, GSK, IAR, C. Ospelt Grant/research support from: euroTEAM, BTCure, CABMM, IAR, Promedica

DOI: 10.1136/annrheumdis-2017-eular.2689

FRIDAY, 16 JUNE 2017

Patient engagement in research: best practices, benefits and challenges

OP0327-PARE YOUR RHEUM – GIVING YOUNG PEOPLE A VOICE IN RHEUMATOLOGY RESEARCH

K. Cresswell[1,2], S. Parsons[1,2], S. Stones[3], J.E. McDonagh[4,5,6], W. Thomson[4,5,6], L. Lunt[7]. *[1]Public Programmes Team, Central Manchester NHS Foundation Trust, University of Manchester; [2]Manchester Academic Health Science Centre; [3]Public Contributor; [4]Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, University of Manchester; [5]NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, University of Manchester; [6]Barbara Ansell National Network for Adolescent Rheumatology; [7]Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, University of Manchester, Manchester, United Kingdom*

Background: Between 2014 and 2016, the Barbara Ansell National Network for Adolescent Rheumatology (BANNAR) commissioned research to explore young people's rheumatology research priorities and beliefs about research involvement. The next phase of this work has been to establish a UK-wide research advisory group, Your Rheum, to involve 11–24 year olds with rheumatic and musculoskeletal diseases (RMDs) more effectively in shaping research.

Objectives: To describe our experiences of developing a UK-wide research advisory group, for young people with RMDs, using both face-to-face meetings and online involvement approaches.

Methods: From September 2016, we recruited young people to the group using several approaches: including the previous research study database, through BANNAR members, through UK charities, such as Arthritis Care and via social media. To tailor options for involvement, young people were recruited to contribute to both face-to-face meetings and via online channels.

Results: Eight young people attended Your Rheum's first meeting in October 2016, where they discussed how they would like the group to work. Thirteen young people have been engaged online via a closed Facebook group, monitored by the Your Rheum facilitator. Key challenges in establishing the group have included developing age-appropriate communication approaches to appeal to the range of ages involved, devising ways of ensuring online members remain engaged with the group, and finding appropriate tasks for the group to be involved with, that are both suitable and aligned with research project timings. This involves working closely with young people, health professionals and researchers.

Conclusions: There is both a need for young people's involvement in research and a desire from young people themselves to do so. Expansion of the online network and involvement activities will allow young people across the UK to have a valuable input into research, regardless of location.

References:

[1] What do young people with rheumatic conditions think about being involved in research? 2017, S.Parsons, W.Thomson, K.Cresswell, B.Starling, J.E.McDonagh (unpublished).

Acknowledgements: This abstract presents independent work funded by Arthritis Research UK BANNAR grant 20164 via the Centre for Adolescent Rheumatology at UCL.

Supported by the National Institute for Health Research Biomedical Research Unit.

We would like to thank all of the young people who took part in the YOURR study and are currently part of Your Rheum, the clinicians, PPI coordinators and other individuals who facilitated their involvement, members of the Barbara Ansell National Network for Adolescent Rheumatology and Arthritis Care.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5807

FRIDAY, 16 JUNE 2017

Latest advances in the treatment and management of psoriatic arthritis and the latest news on the use of biosimilars in RMDs

OP0328-PARE PATIENT SAFETY IN RELATION TO BIOSIMILARS – HOW CAN WE ACT AS A PATIENT ORGANIZATION?

L.M. Thomsen. *Danish Rheumatism Association, Gentofte, Denmark*

Background: During the last years two biosimilars has been approved by the national authorities in Denmark, and implemented in the treatment of patients with arthritis. When the first biosimilars were approved in 2015, the hospitals in Denmark decided to shift native patients from the original drug to the new biosimilar. This decision caused considerable insecurity among the patients, who were afraid of biosimilars and their effectiveness and safety profile. Therefore the Danish Rheumatism Association decided to implement an effort to create better patient information and safety for patients, who had to start with a biological drug or shift from one biological drug to another or to a biosimilar.

Objectives: The purpose of the effort was to increase patient safety and to ensure that patients received independent patient information within biological drugs.
Methods: First the Association conducted a small study of how the shift of drug had taken place in the different regions. Most patients experienced that they were told by the doctors to shift to biosimilars, and furthermore they experienced a lack of information about the new biosimilars. On a national level, nearly all patients on a biological drug are registered in a national database. It is registered in the database and hospital records which drug the patient are prescribed, but it is not registered on a batch-level.
In order to change these conditions the Association started a dialog with the politicians and the authorities on a national level and the hospital-administrations on a regional level. The purpose was to improve the registration of the drugs on batch-level, to improve more independent patient information and to improve the involvement of the patient in the decision making process. The dialog was on a general level, but with several patient-stories from each region.
Results: A new national plan for better monitoring and information about biologic and biosimilars was launched in august 2015 and carried out in 2016. The plan consists of four parts: 1) Monitoring biological drugs and biosimilars on batch level, 2) Information campaign to health professionals and patients, 3) Digital solutions and easy reporting of side effects from health professionals and patients, 4) Focus on monitoring patient safety by the authorities. The Danish Rheumatism Association has participated in the work to implement the plan. In addition to the national plan the hospitals on a regional level, has invited the Rheumatism Association to participate with a representative in the working group, where national recommendations for the use of biological drugs are being made in an attempt to involve the patient perspective more. The content of the national plan and the involvement in the work with national recommendations, will be elaborated and discussed from the patients perspective throughout the presentation.
Conclusions: The implementation of biosimilars created great insecurity among patients. Therefore, the Danish Rheumatism Ass. decided to make an effort to create better patient information and safety for the patients. Through dialog with politicians, national authorities and hospital-administrations, we managed to get a national plan for better monitoring and information about biologic and biosimilars, and to be involved in the work with national recommendations for these drugs. The national plan and work with national recommendations will be elaborated in the presentation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3716

FRIDAY, 16 JUNE 2017

Switching T on and off: how T cells drive and regulate chronic inflammation

OP0329 INVOLVEMENT OF T HELPER 17 CELLS IN INFLAMMATORY ARTHRITIS DEPENDS ON THE HOST INTESTINAL MICROBIOTA

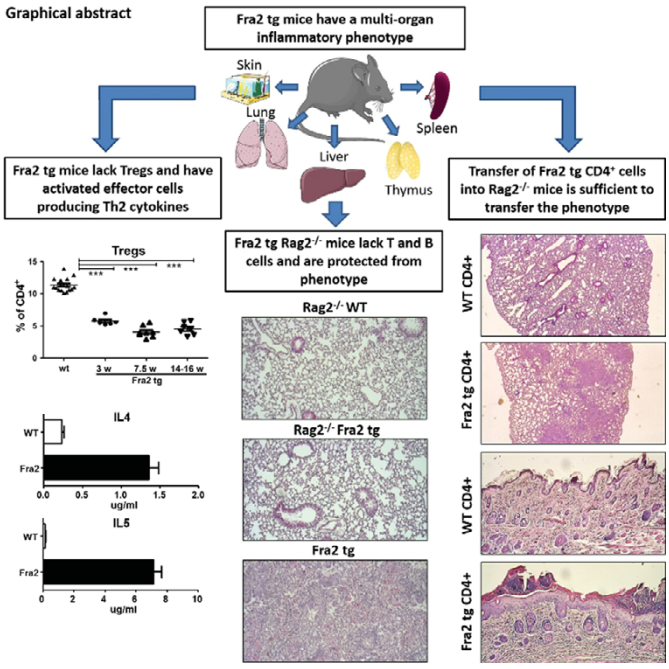
H. Evans-Marin[1], R. Rogier[2], J. Scher[1], D. Roeleveld[2], M. Koenders[2], S. Abdollahi-Roodsaz[1,2]. *[1]Medicine, New York University School of Medicine, New York, United States; [2]Rheumatology, Radboud university medical center, Nijmegen, Netherlands*

Background: Intestinal microbiota have been associated with psoriatic and rheumatoid arthritis. One of the major effects of microbiota is the induction of mucosal T helper 17 (Th17) cells. We therefore reasoned that the efficiacy of Th17-targeted therapies in arthritis may depend on the host microbiota. Previous studies focused on the role of the cytokine interleukin-17A (IL-17), rather than Th17 cells, by using IL-17 inhibitors or IL-17-deficient mice. Therefore, the role of Th17 cells, which produce multiple pro-inflammatory mediators in addition to IL-17, is not yet fully understood.
Objectives: The aim of this study was to determine the role of Th17 cells, beyond the cytokine IL-17, in arthritis, and to investigate whether Th17 cells are differentially involved in arthritis depending on the microbiota present.
Methods: We established conditional Th17-deficient mice, which exhibit a CD4-Cre-induced floxing of a part of the Rorc allele that encodes the Th17 master regulator RORγt. We compared the development of collagen-induced arthritis in Th17-deficient (CD4-Cre$^+$ Rorc$^{flox/flox}$) and -sufficient (CD4-Cre$^-$ Rorc$^{flox/flox}$) littermate mice, either colonized with known Th17 cell inducers segmented filamentous bacteria (SFB) or harboring the SFB-free Jackson microbiota. The abundance of Th1 and Th17 cells and the production of IL-17, IFNγ and GM-CSF were quantified by flow cytometry and multiplex cytokine assay.
Results: CD4-Cre$^+$ Rorc$^{flox/flox}$ mice had significantly lower Th17, but similar Th1 cell abundance, in intestinal lamina propria compared with Cre$^-$ littermate controls. Surprisingly, the total amount of IL-17A production by all lamina propria cells during arthritis was rather increased in Th17-deficient mice, with CD8$^+$ T cells and Gr1$^+$ neutrophils being the main alternative sources of IL-17. Despite this increased total IL-17 levels, conditional Th17-deficient mice developed a less severe arthritis compared with Th17-sufficient mice when intestinal microbiota comprised SFB. This suggests a role for Th17 cells in inflammatory arthritis distinct from IL-17. Accordingly, synovial inflammation, cartilage destruction and proteoglycan depletion were reduced in SFB-colonized Th17-deficient mice. While the production of IL-17 by joint-draining lymph node cells stimulated with PMA and ionomycin was similar between Th17-sufficient and –deficient mice, cells from the latter group produced significantly less IL-17 upon antigen-specific stimulation with type II collagen. Furthermore, the production of GM-CSF, another Th17 cell-derived cytokine, was significantly lower in the lymph nodes of Th17-deficient mice, an effect associated with the protection against arthritis. Importantly, substitution of the intestinal microbiota with SFB-free Jackson microbiota resulted in the loss of Th17 cell dependency of arthritis as Th17-sufficient and –deficient mice showed similar disease progression under this condition.
Conclusions: These data suggest that Th17 cells may mediate inflammatory arthritis partly through IL-17-independent mechanisms. Our observations also suggest that the involvement of Th17 cells in arthritis depends on the microbiota subset present in the host. Therefore, a microbiome-guided stratification of rheumatoid or psoriatic arthritis patients might improve the efficacy of Th17 (or IL-17)-targeted therapies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5522

OP0330 FRA2 OVEREXPRESSION LEADS TO SYSTEMIC AUTOIMMUNITY BY DECREASING IL-2 RESPONSIVENESS AND THYMIC TREG DEVELOPMENT

F. Renoux[1], M. Stellato[1], D. Impellizzieri[2], A. Vogetseder[3], R. Huang[4], A. Subramaniam[4], C. Dees[5], J.H.W. Distler[5], G. Kania[1], O. Boyman[2], O. Distler[1]. *[1]Department of Rheumatology; [2]Department of Immunology, University Hospital Zurich, Zurich; [3]Pathology, Luzerner Kantonspital, Lucerne, Switzerland; [4]Immune Mediated Diseases, Sanofi-Genzyme, Framingham, United States; [5]Department of Internal Medicine 3, University of Erlangen-Nuremberg, Erlangen, Germany*

Background: Fos-related antigen 2 (Fra2) is a transcription factor belonging to the Fos family proteins which is part of the AP-1 transcription complex. We recently described a Fra2 transgenic (tg) mouse model which develops a multi-organ inflammatory phenotype affecting skin, lungs, thymus, liver and salivary glands. We have observed abnormalities in the T cell compartment, particularly in regulatory T (Treg) cells, which led us to hypothesize that Fra2 tg mice develop a T cell driven autoimmune phenotype.
Objectives: To demonstrate the autoimmune phenotype of Fra2 tg mice and to characterize the mechanisms leading to Treg cell abnormality.
Methods: We used previously generated Fra2 tg overexpressing mice. T lymphocyte populations were analyzed by flow cytometry for expression of activation markers and secretion of cytokines. We transferred purified CD4+ T cells into Rag2-/- mice lacking T and B cells, and we generated Rag2-/-Fra2 tg mice. Bone marrow cells were transferred into lethally irradiated recipients to create Fra2-WT bone marrow chimeric mice.
Results: Fra2 tg mice backcrossed onto a Rag2$^{-/-}$ background did not develop inflammatory manifestations (n=6), demonstrating the dependence on T and/or B cells of the autoimmune phenotype. In line with this, the transfer of purified CD4$^+$ cells from 16 week-old Fra2 tg mice into Rag2$^{-/-}$ recipients was sufficient to transfer the disease phenotype (n=3). Analysis of T cell populations from Fra2 tg mice showed the presence of activated CD4$^+$ and CD8$^+$ cells in the spleen



and lungs. After *in vitro* stimulation, we found that $CD4^+$ T cells from Fra2 tg mice produced the Th2 cytokines IL-4, IL-5 and IL-13. Thus, these data strongly suggest a T cell-driven autoimmune disease in these mice.
We previously reported a striking decrease of Treg cells in Fra2 tg mice, which might explain the autoimmune phenotype observed. Supporting this idea, we found that 3 week-old mice were devoid of organ manifestations and of T cell activation, but presented the same defect in the Treg cell population (n=6, $p<0.001$). Analysis of thymuses from these young tg mice showed an abnormal development of thymic Treg (tTreg) cells. In particular, we could observe a normal population of tTreg precursors ($CD4^+CD8^-CD25^+FoxP3^-$), but a strong decrease in mature tTreg cells ($CD4^+CD8^-CD25^+FoxP3^+$, n=4), suggesting a perturbation in the transition from tTreg precursors to mature tTreg cells in Fra2 tg mice. We also found that *in vivo* stimulation with IL-2 failed to induce the proliferation of Treg cells in Fra2 tg mice compared to WT mice, suggesting that Fra2 overexpression affects IL-2 sensitivity of T cells. Finally, Fra2-WT bone marrow chimera mice also displayed a decreased percentage of Tregs confirming a cell-intrinsic and hematopoietic role of Fra2 in Treg cell development.
Conclusions: Our data suggest that Fra2 controls tTreg cell development, possibly by modulating IL-2 signaling in T cells, which leads to autoimmunity in this mouse model. This new pathway could be targeted in a translational approach to modulate the capacity of T cells to differentiate in Tregs during autoimmune disease.
Disclosure of Interest: F. Renoux Grant/research support from: Swisslife, M. Stellato: None declared, D. Impellizzieri: None declared, A. Vogetseder: None declared, R. Huang Employee of: Sanofi-Genzyme, A. Subramaniam Employee of: Sanofi-Genzyme, C. Dees: None declared, J. Distler Shareholder of: 4D Science, Grant/research support from: Anamar, Active Biotech, Array Biopharma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, Consultant for: Actelion, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi and UCB, G. Kania: None declared, O. Boyman: None declared, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha
DOI: 10.1136/annrheumdis-2017-eular.1850

SATURDAY, 17 JUNE 2017

Reverse translation - learning from clinical trials in SLE, Sjögren's and APS

OP0331 A NOVEL HUMANIZED EFFECTOR-DEFICIENT FCYRIIA ANTIBODY INHIBITS IMMUNE COMPLEX MEDIATED PROINFLAMMATORY RESPONSES

B. Chen[1], K. Vousden[2], S. Turman[1], H. Sun[1], S. Wang[1], L. Vinall[2], B. Kemp[2], S. Kasturiangan[1], E. Grant[1], M.J. Hinrichs[1], S. Eck[1], A. DiGiandomenico[1], X. Xiong[1], J. Griffiths[1], R. Herbst[1], D. Close[2], R. Kolbeck[1], G. Sims[1].
[1]MedImmune Inc, Gaithersburg, United States; [2]MedImmune Inc, Granta Park, United Kingdom

Background: Collectively, the cell surface Fc region of IgG receptors (FcγRs) engage soluble IgG and IgG containing immune complexes and trigger activation or inhibtory signals that play a critical role in the regulation of immune responses. The low affinity FcγRIIA (CD32A) is the most widely expressed activating FcγR in humans and appears to drive autoantibody and immune complex mediated autoimmune disorders. So far a therapeutic targeting this receptor has not been developed.
Objectives: To generate and characterize a novel humanized effector-deficient FcγRIIA antibody (MEDI9600) for clinical development.
Methods: The mode of action of MEDI9600 was assessed by confocal microscopy, whole blood internalization, and binding competition assays. Multiple cell based assays were used to measure autoantibody and immune complex mediated responses.
The safety of MEDI9600 was assessed in *in vitro* by neutrophil migration, activation and opsonophagocytic killing assays. Safety and pharmacokinetics were examined *in vivo* in a single-dose PK/PD study in cynomolgus monkey.
Results: We generated a humanized effector-deficient FcγRIIA antibody (MEDI9600) that potently blocks both autoantibody and immuno complex-mediated proinflammatory responses from a variety of cell types. This includes the inhibition of Toll-like receptor stimulatory immune complexes that induce type I Interferons from pDC, and the inhibition of anti-neutrophil cytoplasmic antibody (ANCA) induced production of reactive oxygen species from neutrophils, which are associated with the pathogenesis of systemic lupus and ANCA vasculitis respectively. MEDI9600 specifically binds FcγRIIA and its suppressive activity is attributed to its capacity to block ligand engagement and to internalize the receptor from the cell surface. Moreover, *in vivo* studies indicate that MEDI9600 has a favorable pharmacokinetic and safety profile.
Conclusions: We have generated MEDI9600, a specific humanized antibody antagonist of FcγRIIA with null effector function that may provide a novel therapeutic approach in the treatment of immune complex mediated diseases.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1994

SATURDAY, 17 JUNE 2017

Genomic imprinting and post-translational modifications

OP0332 THE GENOMIC ARCHITECTURE OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) BY RNA-SEQ: DISTINCT DISEASE SUSCEPTIBILITY, ACTIVITY AND SEVERITY SIGNATURES AND EXTENSIVE GENETIC EFFECTS ON WHOLE BLOOD GENE EXPRESSION

G. Bertsias[1,1,2,2], N. Panousis[3], I. Gergianaki[1,2], M. Tektonidou[4], M. Trachana[5], C. Pamfil[6], A. Fanouriakis[7], E. Dermitzakis[3], D. Boumpas[2,7,8,9,10].
[1]Rheumatology, Clinical Immunology and Allergy, University of Crete School of Medicine; [2]Laboratory of Autoimmunity and Inflammation, Institute of Molecular Biology-Biotechnology, FORTH, Iraklio, Greece; [3]Institute for Genetics and Genomics in Geneva, University of Geneva Medical School, Geneva, Switzerland; [4]Medical School, National and Kapodistrian University of Athens, Athens; [5]1st Department of Pediatrics, Aristotle University, Thessaloniki, Greece; [6]Iuliu Haţieganu University of Medicine and Pharmacy, Cluj, Romania; [7]4th Department of Medicine; [8]Joint Rheumatology Program, Attikon University Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece; [9]Medical School, University of Cyprus, Nicosia, Cyprus; [10]Laboratory of Autoimmunity and Inflammation, Biomedical Research Foundation of the Academy of Athens, Athens, Greece

Background: SLE displays significant immunological and clinical heterogeneity. Understanding the molecular basis of this variability may facilitate early diagnosis, risk stratification and personalized therapy.
Objectives: To perform full transcriptome analysis in SLE patients in order to identify molecular sub-phenotypes and explore the genomic basis for the disease susceptibility and severity.
Methods: Whole blood mRNA and genomic DNA were extracted from 142 SLE patients with varying levels of disease activity/severity and 48 matched healthy volunteers. Paired-end RNA sequencing was performed using the Illumina HiSeq 2000 platform and genotyping with the Infinium CoreExome followed by imputation from the 1000 Genomes. To integrate blood transcriptome with genotype data we used the enrichment analysis of expression-quantitative trail loci (eQTLs). The CIBERSORT tool was used to provide an estimation of the abundancies of different circulating immune cell types.
Results: We found a large number (6730, 5% False Detection Rate [FDR]) of differentially expressed genes (DEGs) between SLE patients and controls. Interferon signaling was significantly upregulated in SLE with most of the DEGs (146 out of 281) being regulated by both type I and type II interferon. Analysis of the blood composition in different immune cell types revealed global upregulation of type I interferon and antiviral response genes as well as immune cell-specific alterations in gene expression in SLE patients. Comparison of the transcriptome in active/inactive SLE and healthy individuals identified distinct "disease susceptibility" and "disease activity" gene signatures encompassing 2738 and 377 DEGs, respectively. Analysis according to individual organ involvement revealed more widespread aberrancies in gene expression in SLE patients with active nephritis as compared to activity from other organs, corresponding to oxidative phosphorylation, granulocyte activation and antimicrobial humoral response pathways. By integration of genotyping data, we mapped a total 3142 (5% FDR) *cis*-eQTLs in SLE patients suggesting extensive genetic effects on whole blood gene expression. Importantly, linear discriminant analysis enabled the definition of a set of DEGs which discriminated SLE versus healthy state with median sensitivity 83% and specificity 100%. Design of gene expression panels and expression profile/clinical trait correlation matrices for improved diagnostics, stratification and personalized therapy is in progress.
Conclusions: Specific gene networks confer susceptibility to SLE as well as to severe forms of the disease. These results may facilitate the early diagnosis, monitoring and prognosis, and the molecular taxonomy of SLE patients into pathophysiologically and prognostically distinct subsets for personalized therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6802

OP0333 DISCOVERY AND VALIDATION OF NOVEL AUTOANTIGENS IN SJÖGREN'S SYNDROME WITH POTENTIAL FOR SUBGROUPING OF DISEASE

P.K. Schulz-Knappe[1], P. Budde[1], H.-D. Zucht[1], D. Wirtz[1], K. Marquardt[1], R. Thomas[1], T. Witte[2], M. Schneider[3], K. Sivils[4], A. Rasmussen[5]. *[1]Protagen, Dortmund; [2]Dept. of Clinical Immunology and Rheumatology, Hannover Medical School, Hannover; [3]Dept. of Rheumatology, Heinrich Heine University, Düsseldorf, Germany; [4]Oklahoma Sjogren's Syndrome Center of Research Translation; [5]Oklahoma Medical Research Foundation, Oklahoma, United States*

Background: Primary Sjögren's syndrome (pSS) is a common autoimmune disease with exocrine gland dysfunction and multi-organ involvement. With the growing interest in conducting clinical trials in pSS, there is a need for new biomarkers that can be used to diagnose pSS, identify clinical subsets of pSS, predict treatment outcome and assessment of disease activity. Activation of B-cells and dysregulation of the cytokine network plays a critical role in the pathophysiology of pSS. In the exocrine glands, elevated levels of cytokines, such as type I interferon (IFN), tumor necrosis factor alpha (TNF), interleukin 12 (IL-12) and B cell activating factor (BAFF) can be found. Dysregulated pathways of the innate and adaptive immune system lead to loss of tolerance and the production of organ-specific and non-specific autoantibodies. Current diagnostic criteria for pSS utilize autoantibodies directed to nuclear antigens (ANA), especially to SS-A/Ro (TRIM21, TROVE2) and La (SSB), but those are not specific, and can be identified as well in SLE and even in healthy volunteers. Several studies have shown that not all patients with pSS are tested positive for Ro and La autoantibodies, but suggested the existence of additional autoantibodies in pSS. This autoantibody burden is not well understood for the importance of disease progression, for its role in patient segmentation, or for response to treatments.
Objectives: The discovery of novel autoantigens may provide a deeper understanding of mechanisms of actions for pSS drugs, and may be useful to stratify patients.
Methods: The autoantibody reactivity pattern of pSS serum patients was analyzed using a Luminex bead-based antigen array (SeroTag) and 1,600 selected human protein antigens from our hPEX protein library of 8,000 recombinant proteins (1). We screened over 2,000 serum samples from patients with autoimmune diseases as active controls targeting Sjögren's Syndrome (n=70), SLE (n=>500), SSc (n=>250), RA (n=>500), and over 1,000 healthy individuals to confirm known and to discover novel autoantibodies. In a validation study, novel biomarker candidate antigens were evaluated using a cohort of 350 Patients with Sjögren's Syndrome.
Results: Apart from clear confirmation the known benchmark autoantigens known for many years we have discovered a small set of additional, novel autoantibodies, which were detected in frequencies of 8 to >20% in pSS. Accumulation of autoantibody reactivities allows for a first subgroup definition of Sjögren's, and for clear segregation of SjS/SLE overlap syndrome patients.
Conclusions: A set of novel autoantigens for diagnosis and subgroup definition in Sjögren's syndrome was discovered by high content screening using a Luminex bead-based array platform. Validation in additional, large patient cohorts is ongoing.
References:
[1] Budde P et al. (2016). Lupus. (8):812–22.
Disclosure of Interest: P. Schulz-Knappe Shareholder of: Protagen AG, P. Budde Employee of: Protagen AG, H.-D. Zucht: None declared, D. Wirtz Employee of: Protagen AG, K. Marquardt Employee of: Protagen AG, R. Thomas: None declared, T. Witte: None declared, M. Schneider Consultant for: Protagen AG, K. Sivils: None declared, A. Rasmussen: None declared
DOI: 10.1136/annrheumdis-2017-eular.5725

SATURDAY, 17 JUNE 2017

Optimizing treatment for osteoarthritis: take the phenotype in account "one size does not fit all"

OP0334 PREDICTORS AND MRI-DETECTED STRUCTURAL PATHOLOGY WITH TRAJECTORIES OF KNEE PAIN SEVERITY: A 10.7-YEAR PROSPECTIVE STUDY

F. Pan[1], J. Tian[2], D. Aitken[1], F. Cicuttini[3], C. Ding[1], G. Jones[1]. *[1]Musculoskeletal Unit; [2]Public Health, Menzies Institute for Medical Research, University of Tasmania; [3]Department of Epidemiology and Preventive Medicine, Monash University Medical School, Hobart, Australia*

Background: Knee pain is the most common manifestation of knee osteoarthritis (OA) and is generally thought to get worse with time. Risk factors for knee pain have been extensively investigated; however, whether the risk factors are associated with a specific pain trajectory has not yet been comprehensively explored. Furthermore, knee structural pathology on MRI, such as bone marrow lesions (BMLs), effusion-synovitis and cartilage defects, are thought to be the origin of knee pain. However, its underlying mechanisms remain to be elucidated and hampered by a large individual variation of pain course.
Objectives: To identify distinct trajectories of knee pain over 10.7 years in an older population, to describe risk factors with identified trajectories, and to explore MRI-detected structural pathology with the trajectories.
Methods: 1,099 participants (mean age 63 years) from a population-based cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Demographic, psychological, lifestyle and comorbidities data were obtained at baseline. Knee pain was assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at each time-point. T1-weighted or T2-weighted MRI of the right knee was performed to measure knee structural pathology. Knee radiographic OA was assessed by X-ray at baseline. Group-based trajectory modelling was applied to identify pain trajectories. Multi-nominal logistic regression was used for the analyses with adjustment for potential confounders.
Results: 1,099 participants were included for the identification of pain trajectories and three distinct pain trajectories were defined. Participants in Group 1 ("Mild pain" n=568, 51.7%) had relatively stable mild pain over time. Participants in Group 2 ("Moderate pain", n=366, 33.2%) had moderate pain over time. Participants in Group 3 ("Severe pain", n=165, 15.1%) developed or displayed fluctuating severe pain over time. Compared with the "Mild pain", higher BMI, emotional problems, and musculoskeletal diseases were significantly associated with both "Moderate pain" and "Severe pain" trajectories. Also, younger age, lower education level and unemployment status were associated with "Severe pain" trajectory. The presence of cartilage defects and BMLs were associated with increased risk of "Moderate pain" and "Severe pain" trajectories before or after adjustment for potential confounders. Effusion-synovitis was not statistically associated with "Moderate pain" (P=0.082), but associated with "Severe pain" trajectory. Furthermore, a dose-response relationship was observed between number of knee structural abnormalities, and "Moderate pain" and "Severe pain" trajectories (both P for trend<0.001).
Conclusions: This is the first long-term study to identify pain trajectories and their risk factors, and explore the associations between structural pathology and pain trajectories. Three distinct pain trajectory groups were identified, suggesting that homogeneous subgroups exist and follow a specific trajectory over time despite large individual variation of pain course. Significant associations between structural pathology and pain trajectories suggest that peripheral stimuli may play a role in the development and maintenance of pain severity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1412

OP0335 EXPLORING ASSOCIATIONS BETWEEN HISTOLOGICALLY ASSESSED INFLAMMATION AND PAIN AND FATIGUE IN KNEE OSTEOARTHRITIS

M.J. Minten[1], A. Blom[2], G.F. Snijders[2], F.H. van den Hoogen[2,3], A.A. den Broeder[2,3], P. van der Kraan[2], C.H. van den Ende[1,2]. *[1]Dept. of Research, Sint Maartenskliniek; [2]Dept. of Rheumatology, Radboud University medical center; [3]Dept. of Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands*

Background: Pain and fatigue are frequent symptoms of osteoarthritis (OA). However, the exact mechanism causing these symptoms remains unclear. Inflammation is important in OA pathophysiology. Associations between inflammatory aspects and clinical outcomes have been found. However, mainly (contrast-enhanced) MRI was used to assess synovial inflammation in these studies. Using this method, inflammation is assessed in an indirect way (e.g. infrapatellar fat pad signal enhancement, synovial fluid effusion and thickening of synovial tissue). Conversely, histological assessment of synovial inflammation is regarded as the gold standard. Using this method, specific aspects of inflammation can be distinguished and rated for severity.
Objectives: To evaluate the associations of inflammation-related histological parameters of the synovium with pain and fatigue in knee OA patients.
Methods: Fifty-nine patients fulfilling ACR criteria for knee OA were recruited from two prospective studies[1,2] and gave consent for synovial biopsy using a mini knee arthroscopy. Biopsies were taken from visually inflamed areas of the synovium. Tissue sections were histologically assessed for 1) number of synovial lining cells (absolute); 2) sub-synovial infiltration; 3) fibrin deposition; 4) vascularization; 5) fibrosis; and 6) perivascular edema (scores 0–3).[3] Average scores across sections were calculated for each parameter and for all parameters together. These data were combined with longitudinal clinical data from the prospective studies (WOMAC pain, SF36 vitality; 0=worst – 100=best). Associations between individual inflammatory features and clinical outcomes over time were assessed with mixed model analyses.
Results: Patient characteristics are shown in Table 1. Relatively mild levels of inflammation were found, in line with previous research (median 1.1 [95% CI 0.9–1.6]).[3,4] Longitudinal data was available for 56 patients. Age, gender, BMI and time since symptom onset were no confounders. No significant associations were found between any histological parameter and pain or fatigue over time (Table 2).

Table 1. Patient characteristics

	Mean (Sd)
Male/Female	28/31
Age (years)	56.4 (9.8)
Symptom duration (years)	10.1 (10.3)
BMI (kg/m^2)	29.7 (5.9)
Follow-up (years)	1.2 (0.8)

Conclusions: This is the first study to examine different parameters of histologi-

Table 2. Longitudinal associations

	Median [25–75%]	Pain ß [95% CI]	Fatigue ß [95% CI]
Synovial lining cells	2.4 [1.5–3.2]]	0.5 [-2.9–3.9]	-2.3 [-5.6–1.0]
Infiltrate	1.2 [0.5–1.8]	2.9 [-4.3–10.1]	-4.7 [-11.6–2.3]
Fibrin	0.0 [0.0–0.4]	-7.1 [-17.7–3.4]	-0.1 [-10.1–10.0]
Vascularization	1.6 [1.0–2.0]	-1.2 [-8.3–5.9]	-0.5 [-7.2–6.3]
Fibrosis	0.8 [0.2–1.3]	-3.3 [-10.4–3.8]	0.8 [-6.3–7.9]
Edema	0.6 [0.2–1.3]	1.5 [-4.8–7.8]	0.2 [-6.0–6.4]
Average inflammation	1.1 [0.9–1.6]	-0.3 [-11.0–10.5]	-5.3 [-15.6–5.0]

cally assessed synovial inflammation in knee OA patients and their associations with clinical outcomes over time. We were unable to identify individual inflammatory aspects which associate with pain or fatigue. Additional research is required to identify the underlying mechanism for pain and fatigue in OA.

References:
[1] Ann Rheum Dis 2011 70:1191–6.
[2] Scand J Rheum 2011 40:225–31.
[3] Clin Rheum 2010 29:1185–90.
[4] Arthritis Rheum 2005 52:3492–501.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1776

SATURDAY, 17 JUNE 2017

Targeting adipose tissue inflammation

OP0336 ROLE OF SYSTEMIC INFLAMMATION ASSOCIATED WITH RHEUMATOID ARTHRITIS IN THE GLUCOSE AND LIPID METABOLISM: HUMANS, CIA MOUSE MODEL AND IN VITRO STUDIES

I. Arias de la Rosa[1], S. Rodriguez-Cuenca[2], Y. Jimenez-Gomez[1], P. Ruiz-Limon[1], C. Perez-Sanchez[1], M.C. Abalos[1], I. Cecchi[1], J. Calvo[1], R. Guzman[3], M. Malagon[3], E. Collantes[1], A. Vidal-Puig[2], C. Lopez-Pedrera[1], A. Escudero-Contreras[1], N. Barbarroja[1]. *[1]Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain; [2]Metabolic Research Laboratories, Wellcome Trust-MRC Institute of Metabolic Science, Addenbroke's Hospital, University of Cambridge, Cambridge, United Kingdom; [3]Department of Cell Biology, Physiology, and Immunology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain*

Background: Rheumatoid arthritis (RA) patients are at higher risk for insulin resistance (IR). The association between RA and IR, and its role on the different characteristics of the disease, such as duration and activity have not been well defined. In addition, there is a gap of knowledge regarding the link between systemic/local inflammation and insulin sensitivity and lipid metabolism in RA patients.
Objectives: To explore the effects of the inflammation on the glucose and lipid metabolism in the RA context, following three strategies: RA patients, collagen induced arthritis (CIA) mouse model and in vitro treatment of 3T3L1 adipocytes.
Methods: *Human study:* 150 RA patients and 40 healthy donors were included. IR was quantified using the homeostatic model assessment of IR (HOMA-IR). *Mouse model:* 20 CB57J/BL mice were used; 5 mice were used as non-diseased group, and 15 were used in CIA modelling: sorted in low and high activity of the disease based on the number of inflamed digits depending on the duration of the disease. Plasma, leukocytes, skeletal muscle, liver and adipose tissue were collected. *Treatment of adipocytes with serum from RA patients:* 3T3L1 adipocytes were treated with serum 10% of RA patients and healthy donors for 24h. The expression of genes and proteins involved in inflammation, lipid metabolism and insulin signalling was analysed in all the tissues and cells.
Results: Percentages of obesity, hypertension, atherogenic risk, metabolic syndrome and insulin resistance were significantly increased in the RA group. Although mean time of evolution was 7 years, no association between IR and the duration of the disease was found. Levels of HOMA-IR significantly correlated with DAS28 and C-reactive protein levels, suggesting that systemic inflammation might lead to the development of insulin resistance. In mice, the induction of arthritis promoted an alteration of the expression of genes involved in inflammation as well as lipid metabolism and insulin signalling in all the metabolic tissues and leukocytes, pointing out to an increase in lipolysis, decrease in adipogenesis and lipid accumulation and induction of IR. These results were recapitulated after treatment of adipocytes with serum from RA patients with high disease activity.
Conclusions: 1) IR was closely associated with an increase in disease activity and systemic inflammation in RA patients. 2) Induction of arthritis in mice promoted an increase in inflammation markers in skeletal muscle, adipose tissue and leukocytes, and a reduction of genes involved in lipid uptake and storage, generating an insulin resistance state in those tissues. 3) The inflammatory components in RA serum induced lypolisis, reduced adipogenesis, and increase inflammation and insulin resistance in adipocytes 3T3L1.
In sum, our results suggest that chronic inflammation associated with RA might directly impact relevant metabolic tissues, altering glucose and lipid homeostasis and favouring the development of insulin resistance.

Acknowledgements: Funded by ISCIII-FIS (CP15/00158), PI2013/0191, RD16/0012/0015 and Roche Pharma S.A.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4725

SATURDAY, 17 JUNE 2017

Trials and tribulations of medication adherence

OP0337-HPR PREDICTORS OF PATIENT REPORTED DECISION TO DISCONTINUE ANTI-RHEUMATIC MEDICATION IN RHEUMATOID ARTHRITIS PATIENTS: DATA FROM A RHEUMATOID ARTHRITIS COHORT

V. Ahluwalia[1], M. Movahedi[2,3], E. Rampakakis[3], A. Cesta[2], X. Li[2], S. Couto[2], J. Sampalis[3], C. Bombardier[2,4,5] on behalf of OBRI investigators. *[1]Department of Rheumatology, Brampton Civic Hospital, William Osler Health System, Brampton; [2]Ontario Best Practices Research Initiative, Toronto General Hospital, University Health Network, Toronto; [3]JSS Medical Research, Montreal; [4]Department of Medicine (DOM) and Institute of Health Policy, Management, and Evaluation (IHPME), University of Toronto; [5]Division of Rheumatology, Mount Sinai Hospital, Toronto, Canada*

Background: Despite the availability of safe and effective treatments and the establishment of treatment guidelines, real-world effectiveness remains suboptimal largely due to low patient adherence with prescribed treatment.
Objectives: The purpose of this study was to systematically evaluate sociodemographic, health insurance, and disease-related factors associated with patient reported decision for discontinuation of anti-rheumatic medications (ARM) in a large observational cohort of RA patients followed in Canadian routine clinical care.
Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) clinical registry and had at least two years of follow-up were included in the analysis. Treatment discontinuation due to patient reported decision was defined as ARM discontinuation. Independent predictors of ARM discontinuation were evaluated with multivariate cox-regression using both time-fixed and time-dependent variables. Factors considered included patient sociodemographics (age, gender, race, education status, annual income, smoking history), health insurance information (private vs. non-private, % coverage), disease parameters (RA duration, presence of erosion, RF positivity, DAS28, physician global, HAQ-DI, number of comorbidities), types of medications used, and physician characteristics (gender, academic position, urban vs. rural, distance from patient's residence).
Results: A total of 1,762 patients were included in the analysis with a mean (SD) age of 57.4 (13.0) years and disease duration of 8.5 (9.3) at the time of enrolment to the registry (baseline). The majorities of patients were female (77.7%), had post-secondary education (55.3%), and had private insurance (67.2%). In terms of disease severity, 54.5% had prior erosion, 69.5% were RF positive, and mean (SD) DAS28 was 4.5 (1.5).
In a multivariate analysis, married status (HR, 0.73; 95% CI 0.56–0.96), RF positivity (HR, 0.73; 95% CI 0.56–0.96), and higher number of comorbidities (HR, 0.92; 95% CI 0.85–0.99) were identified as significant predictors of ARM continuation while higher physician global score (HR, 1.10; 95% CI 1.04–1.15), NSAID use (HR, 1.75; 95% CI 1.29–2.38), and polypharmacy (HR, 1.23; 95% CI 1.07–1.40) were associated with ARM discontinuation due to patient reported decision.
Conclusions: In this systematic approach a variety of factors encompassing sociodemographics, disease, and medication characteristics, were identified as significant independent predictors of ARM discontinuation due to patient reported decision. These results should be taken into consideration when developing patient adherence support programs and in the choice of treatment regimens.

Disclosure of Interest: V. Ahluwalia Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Bristol Myers Squibb, Celgene, Hospira, Janssen, Pfizer, Roche, Sanofi, & UCB, M. Movahedi Employee of: OBRI/JSS, E. Rampakakis Employee of: JSS Medical Research, A. Cesta Employee of: OBRI, X. Li Employee of: OBRI, S. Couto Employee of: OBRI, J. Sampalis Employee of: Head of JSS, C. Bombardier Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Bristol Myers Squibb, Celgene, Hospira, Janssen, Pfizer, Roche, Sanofi, & UCB
DOI: 10.1136/annrheumdis-2017-eular.1522

SATURDAY, 17 JUNE 2017

Outcome in juvenile idiopathic arthritis

OP0338 FREQUENCY OF COMORBIDITIES IN JIA PATIENTS – RESULTS OF AN OBSERVATIONAL COHORT STUDY

K. Minden[1], N. Betenstehl[2], J. Klotsche[1], E. Seipelt[3], S. Tatsis[4], I. Foeldvari[5], G. Ganser[6], G. Horneff[7]. *[1]Epidemiology Unit, German Rheumatism Research Centre, Berlin; [2]Oberhavelkliniken, Hennigsdorf; [3]Immanuel Krankenhaus Berlin-Buch, Berlin; [4]Kath. Marienkrankenhaus; [5]Zentrum für Kinder- und Jugendrheumatologie, Hamburg; [6]St. Josef-Stift, Sendenhorst; [7]Asklepios Kinderklinik, Sankt Augustin, Germany*

Background: Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease that often persists into adulthood. In addition to disability and poorer quality of life, JIA is associated with increased long-term morbidity and mortality. The long-term risk of comorbidities in JIA patients is uncertain and guidance on risk assessment is not currently available.
Objectives: To determine the frequency of comorbid conditions in adult JIA patients.
Methods: Patients with JIA transferred from the biologic registry BIKER to the follow-up (FU) registry JuMBO were included in this analysis. All comorbidities, except for serious infections, prospectively recorded by physicians to BiKeR or JuMBO were considered. Comorbidity rates among the various JIA categories were assessed. The Medical Dictionary for Regulatory Activities (MedDRA) was used for disorder coding. Differences in the occurence of comorbidities between JIA categories were analyzed by multinomial logistic regression.
Results: A total of 1,022 young adults (67% female) with JIA and a mean FU of 7.8 (SD=3.5) years (ys) were included in this analysis. The patients' mean age was 22.5 ys (SD=3.7), and disease duration was 12.9 ys (SD=5.9) at the last FU. The majority were classified as polyarticular JIA (36.4%) at BiKeR enrollment. Patients had received a mean of 2.9 (SD=1.3) DMARDs, 77% were ever treated with biologics.
Comorbidities were reported for more than half of the patients (54%), 24.5% of the conditions were stated for the first time in adult age. Eye disorders were the most common comorbid condition group (15.1%), followed by skin and subcutaneous tissue disorders (9.3%), and psychiatric disorders (5.5%). The most frequently reported single diseases were uveitis in 14.4%, chronic secondary pain syndrome in 4.4%, hypertension in 3.6%, and psoriasis in 3.3%. In addition, inflammatory bowel diseases were reported in 2.5% of cases, other immune-mediated disorders, namely autoimmune thyroiditis in 2.5%, type1 diabetes in 0.7% and celiac disease in 0.3%, depression in 2.3%, anxiety in 0.3%, osteoporosis in 1.6%, and amyloidosis in 0.4%. Among the reported comorbidities, there was one case with a cerebrovascular accident, but none with ischemic heart disease, heart failure or diverticulitis. The rate of comorbid condition accrued in the various JIA categories (table 1) differed significantly, with the highest rate in patients with extended oligoarthritis.

Table 1: Frequency of major comorbidities (in %) in the various JIA categories in young adult age

Comorbid condition	Sys JIA	OA, persist.	OA, ext.	PA, RF-	PA, RF+	ERA	PsA	P value
	N= 48	N=97	N=169	N=278	N=94	N=205	N=97	
Any comorbid condition	58.3	47.2	64.1	45.7	47.9	51.7	62.9	0.007
Uveitis	4.2	14.4	34.9	7.9	0	16.6	10.3	<0.001
Psoriasis	2.1	1.0	0.6	1.1	0	3.4	19.6	<0.001
IBD	4.2	0	3.6	1.4	1.1	3.4	5.2	0.233
Hypertension	10.4	2.1	4.1	2.5	2.1	3.4	3.1	0.032
Osteoporosis	10.4	0	1.8	1.8	1.1	0	1.0	<0.001
Amyloidosis	4.2	0	0	0.4	0	0	0	0.001
Chronic secondary pain syndrome	2.1	5.2	4.7	6.1	3.2	4.9	1.0	0.394
Depression	4.2	1.0	2.4	2.2	1.1	2.4	3.1	0.927
Autoimmune thyroiditis	2.1	1.0	1.8	2.2	5.3	1.5	6.2	0.156
Type 1 diabetes	0	0	0	1.1	2.1	1.0	0	0.445
Celiac disease	0	0	0.6	0	1.1	0	0	0.202

Sys JIA - Systemic JIA; OA persist. – Oligoarthritis persistent; OA, ext. – Oligoarthritis extended; PA - Polyarthritis; RF- - Rheumatoid factor negative; RF+ - Rheumatoid factor positive; ERA - Enthesitis-related arthritis; PsA - Psoriatic arthritis; IBD – inflammatory bowel disease

Conclusions: Young adults with JIA have a high rate of comorbidity overall, with extraarticular JIA manifestations being the most frequently reported comorbid conditions. Comorbidity rates vary among the various JIA categories. Patients with systemic JIA have the highest rate of cardiovascular risk factors and osteoporosis, while patients with extended OA have the highest rate of uveitis. An underreporting or unawareness of comorbidities by rheumatologists is possible, guidance on risk assessment in adults with JIA is needed.
Acknowledgements: The authors thank all rheumatologists for contributing patients to the JuMBO registry. BiKeR is funded by unconditional grants from Abbvie, Germany, Novartis, Germany, and Roche, Germany, JuMBO by unconditional grants from Abbvie, Pfizer, and Roche.
Disclosure of Interest: K. Minden Speakers bureau: Pfizer, Roche, Pharm-Allergan, N. Betenstehl: None declared, J. Klotsche: None declared, E. Seipelt: None declared, S. Tatsis: None declared, I. Foeldvari: None declared, G. Ganser: None declared, G. Horneff Speakers bureau: Abbvie, Pfizer, Roche, Novartis, MSD
DOI: 10.1136/annrheumdis-2017-eular.5858

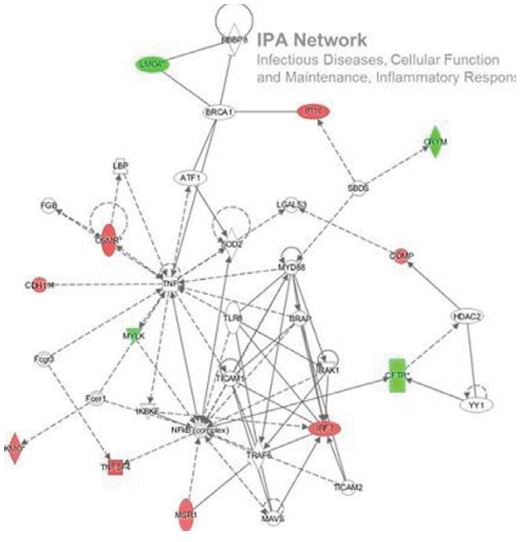
SATURDAY, 17 JUNE 2017

Systemic sclerosis

OP0339 IDENTIFICATION OF A TRANSCRIPTOMIC SIGNATURE CORRELATED WITH MODIFIED RODNAN SKIN SCORE (MRSS) IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

I. Agueusop[1], S. Illiano[2], C. Rocher[2], E. Boitier[3], J. Murphy[4], Y. Allanore[5], C.P. Denton[6], O. Distler[7], D. Khanna[8], F. Benderitter[2]. *[1]Sanofi-Aventis Deutschland GmbH, Frankfurt am Main, Germany; [2]Sanofi R&D, Chilly-Mazarin; [3]Sanofi R&D, Alfortville, France; [4]sanofi, Bridgewater, United States; [5]Paris Descartes University, Paris, France; [6]Centre for Rheumatology, Royal Free Hospital, London, United Kingdom; [7]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [8]Scleroderma program, University of Michigan, Ann Arbor, United States*

Background: To support internal compound development in systemic sclerosis, a study was performed to identify an mRSS signature in a longitudinal approach by analyzing skin biopsies.
Objectives: Identification of a gene signature that could be used as a quantitative surrogate marker for the mRSS independent of any treatment.
Methods: 77 forearm skin biopsies from 32 patients at baseline, and from the same patients after 8 weeks of treatment with SAR100842 (a LPA1 antagonist) or placebo (N=30) and after an additional 16 weeks of treatment with SAR100842 (N=15) in a phase 2 trial, were collected. Total RNA was extracted with the RNeasy® Fibrous Tissue Mini kit according to the manufacturer's instructions. Total RNA was quantified by spectrofluormetry and qualified by capillary electrophoresis using Agilent Bioanalyzer 2100. Whole transcriptome analysis was performed using Affymetrix chips. Genes highly correlated (Pearson's correlation) with the mRSS were identified at each treatment visit. A signature was identified as a set of genes whose expression levels correlated consistently either positively or negatively with the mRSS at all study visits regardless of treatment group. The correlation value between the genes and the mRSS at baseline had to be >0.5 or $<$ -0.5.The association between mRSS and the single composite marker obtained was investigated. A multivariate analysis of the correlation between the identified genes was performed using the median polish algorithm and PCA. The gene signature underwent pathway analysis using QIAGEN's Ingenuity Pathway Analysis (IPA).
Results: This methodology led to the identification of 64 genes considered for the signature and viewed as a single composite marker that was highly correlated to the mRSS. A principal component analysis was computed and the first component explaining the maximum variance in the signature was highly correlated to the mRSS at baseline and week 8. This correlation was confirmed with the median polish algorithm (Pearson's correlation coefficient of -0.75 and -0.73 respectively). The most significant disease and disorder biological functions associated with the mRSS signature genes were related to immunological diseases. A significant enrichment was also detected for genes associated with inflammatory response and connective tissue disorders with p-values from 2.98E-05 to 2.47E-02.



Conclusions: An mRSS signature was identified using skin biopsies in SSc patients. Some of these genes (i.e. IRF7, THBS1, COMP or BANK1) have been published using similar approaches in other sets of SSc patients (1), which supports our results. The functional categories of this signature are characteristic

for scleroderma pathology reflecting autoimmunity, vasculopathy, inflammation and fibrosis. This mRSS signature needs to be validated in a larger set of SSc patients including assessment of change over time.

References:
[1] Mahoney et al. PLOS Computational Biology 2015: Vol 11; 1–20.

Disclosure of Interest: I. Agueusop: None declared, S. Illiano: None declared, C. Rocher: None declared, E. Boitier: None declared, J. Murphy: None declared, Y. Allanore Grant/research support from: BMS, Genentech-Roche, Inventiva, Pfizer, sanofi, Consultant for: Actelion, Bayer, Biogen, Genetech-Roche, Galapagos, Medac, Pfizer, Sanofi, Servier, UCB, C. Denton Consultant for: Actelion, Bayer, GSK, CSL Behring, Merck-Serono, Genentech-Roche, Inventiva, Sanofi-Aventis, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, AbbVie, iQone Healthcare, Mepha, D. Khanna Grant/research support from: Bayer, BMS, Genentech/Roche, Sanofi-Aventis, NIH K24AR063120, Consultant for: Actelion, Bayer, Covis, Cytori, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis, F. Benderitter: None declared
DOI: 10.1136/annrheumdis-2017-eular.5827

SATURDAY, 17 JUNE 2017

How diet influences musculoskeletal diseases

OP0340 WEIGHT LOSS FOR OVERWEIGHT AND OBESE INDIVIDUALS WITH GOUT: A SYSTEMATIC REVIEW OF LONGITUDINAL OBSERVATIONAL STUDIES

S.M. Nielsen[1], E.M. Bartels[1], M. Henriksen[1,2], H. Gudbergsen[1], H. Bliddal[1], A. Astrup[3], F.K. Knop[4,5,6], L. Carmona[7], W. Taylor[8], J.A. Singh[9], F. Perez-Ruiz[10], L.E. Kristensen[1], R. Christensen[1]. *[1]The Parker Institute, Bispebjerg and Frederiksberg Hospital; [2]Department of physical and occupational therapy, Bispebjerg and Frederiksberg Hospital; [3]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen; [4]NNF Center for Basic Metabolic Research; [5]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen; [6]Center for Diabetes Research, Gentofte Hospital, University of Copenhagen, Hellerup, Denmark; [7]Instituto de Salud Musculoesquelética, Madrid, Spain; [8]Department of Medicine, University of Otago, Wellington, New Zealand; [9]Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, United States; [10]Rheumatology Division, Hospital de Cruces, Baracaldo, Vizcaya, Spain*

Background: Weight loss is a commonly recommended treatment for gout, but the magnitude of effect to expect has to our knowledge not previously been evaluated in a systematic review.
Objectives: The aim of this systematic review was to determine the benefits and harms associated with weight loss in overweight patients with gout.
Methods: Based on a pre-defined protocol (CRD42016037937), we searched six databases for longitudinal studies, quantitatively reporting the effect of weight loss in overweight gout patients. Risk of bias was assessed using the ROBINS-I tool. The quality of the evidence was assessed using GRADE.
Results: From 3,991 potentially eligible studies, 10 were included (incl. one RCT). Interventions included diet with/without physical activity, bariatric surgery, diuretics, metformin, or no intervention. Due to clinical heterogeneity of the included studies, data are presented for each study and synthesised separately. The effect on serum uric acid (sUA) ranged from -168 to 30 μmol/L, and 0% to 60% patients achieved sUA normalisation (i.e. sUA <360 μmol/L). Six out of eight studies (75%) showed beneficial effects on gout attacks. A dose-response relationship was indicated in two studies for sUA, sUA normalisation and gout attacks. At short term (<3 months) after bariatric surgery, one study showed temporary increase in sUA, and another showed temporary increased number of gout attacks. Other possible harmful effects, measured by proxies such as withdrawals due to adverse events and serious adverse events, were poorly reported.
Conclusions: The available evidence is in favour of weight loss for overweight gout patients, with low, moderate and low quality of evidence for an effect on sUA, sUA normalisation, and gout attacks, respectively. At short term, temporary increased sUA and gout attacks may occur after bariatric surgery. There is an urgent need to initiate rigorous prospective studies (preferably RCTs) to provide more trustworthy estimates of benefits and harms of weight loss in overweight gout patients.

References:
[1] Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis 2016:1–14, doi: 10.1136/annrheumdis-2016-209707.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2651

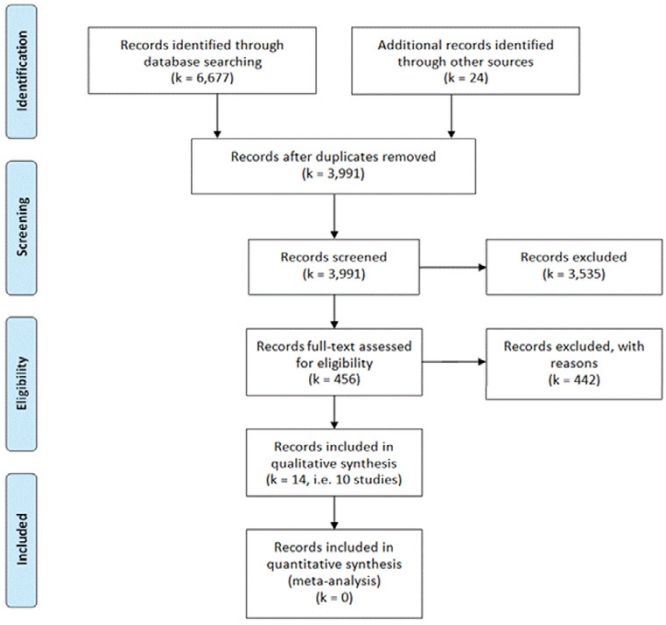


Figure 1: PRISMA flow diagram
ACR, American College of Rheumatology; CENTRAL, Cochrane Central Register of Controlled Trials; EULAR, The European League Against Rheumatism; ICTRP, the World Health Organization International Clinical Trial Registry Platform portal; pts, patients.

SATURDAY, 17 JUNE 2017

Can targeting disease activity in hand osteoarthritis improve our treatment in the 21st century

OP0341 CAN PAIN IN HAND OSTEOARTHRITIS BE ASSOCIATED WITH MRI COLLATERAL LIGAMENT ABNORMALITIES?

A.L. Tan[1,2], M.-A. D'Agostino[1,3], E. Hensor[1,2], A. Grainger[2], P. Emery[1,2], D. McGonagle[1,2]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]NIHR Leeds Musculoskeletal Biomedical Research Centre, Chapel Allerton Hospital, Leeds, United Kingdom; [3]Rheumatology Department, Hôpital Ambroise Paré, Paris, France*

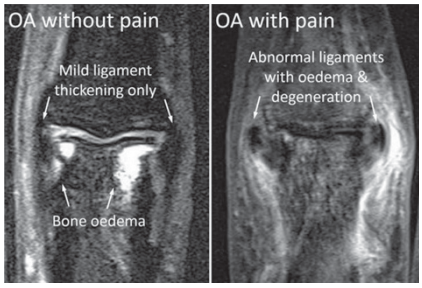
Background: Many patients with hand osteoarthritis (OA) have little symptoms. Bone oedema and synovitis have been associated to pain in OA, but inflammation involving ligaments has not been studied, likely limited by inadequate MRI resolution. We have previously found significant ligament pathology in early and established hand OA (HOA) [1].
Objectives: We hypothesise that the well innervated ligaments are key to a better understanding of the relationship between joint structure and pain in HOA. This

Abstract OP0341 – Table 1

Abnormality	Joints % (n)			Median score (IQR)		Difference* (90% CI)
	HC (n=10)	OA no pain (n=11)	OA pain (n=15)	OA no pain (n=11)	OA pain (n=15)	
Fluid	30 (3)	73 (8)	67 (10)	2 (0, 4)	1 (0, 2)	0 (-2, 1)
Capsulitis/synovitis	– (0)	36 (4)	60 (9)	0 (0, 1)	1 (0, 2)	0 (0, 2)
Extracapsular oedema	– (0)	45 (5)	73 (11)	0 (0, 2)	2 (0, 3)	1 (0, 2)
CL thickening	50 (5)	100 (11)	100 (15)	2 (2, 4)	2 (2, 4)	1 (-1, 2)
CL oedema	40 (4)	91 (10)	87 (13)	2 (1, 3)	3 (2, 4)	1 (0, 3)
CL degeneration	40 (4)	91 (10)	100 (15)	3 (1, 5)	4 (2, 6)	1 (-1, 3)
Proximal joint bone oedema	– (0)	9 (1)	20 (3)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Distal joint bone oedema	– (0)	27 (3)	20 (3)	0 (0, 1)	0 (0, 0)	0 (0, 0)
Proximal joint bone cyst	– (0)	27 (3)	47 (7)	0 (0, 2)	0 (0, 2)	0 (0, 1)
Distal joint bone cyst	10 (1)	27 (3)	7 (1)	0 (0, 1)	0 (0, 0)	0 (0, 0)

*Accounting for clustering of joints within patients. CI = confidence interval; HC = healthy controls; IQR = inter-quartile range; CL = collateral ligaments.

research aims to see if small joint collateral ligament abnormalities are worth exploring further in relationship to pain in HOA.
Methods: High-resolution contrast enhanced MRI of 26 joints in 15 patients (mean (SD) age 58.3 (8.2), 13F:2M) and 10 in 5 healthy controls (age 38 (5.6); 4F:1M) were scanned using a microscopy MRI coil. 15 joints in 8 patients were painful [median (IQR) pain VAS 4 (3, 7)). Joints were scored blinded to clinical data for joint fluid, capsule/synovitis, extracapsular oedema, collateral ligament thickening/oedema/degeneration, extensor and flexor tendons, bone oedema and cysts. All structures were graded 0–3 for normal, mild, moderate, severe, as defined in OMERACT HOAMRIS where available [2]. Proportions of joints with any level of abnormality (score>0) were calculated according to pain status (present/absent).
Results: All OA patients with and without pain had ligament abnormalities. Substantive differences in proportion of joints between healthy controls and OA patients were seen for all pathologies except tendons (no tendon abnormalities were found in all groups). Proportions of joints with capsular/synovium, extra capsular changes and proximal cysts differed between OA joints with and without pain but no substantive differences in pathology score were found. Of painful joints, 93% (14) had both ligament and capsular/synovium or extracapsular abnormality present, compared to 45% (5) of non-painful joints.

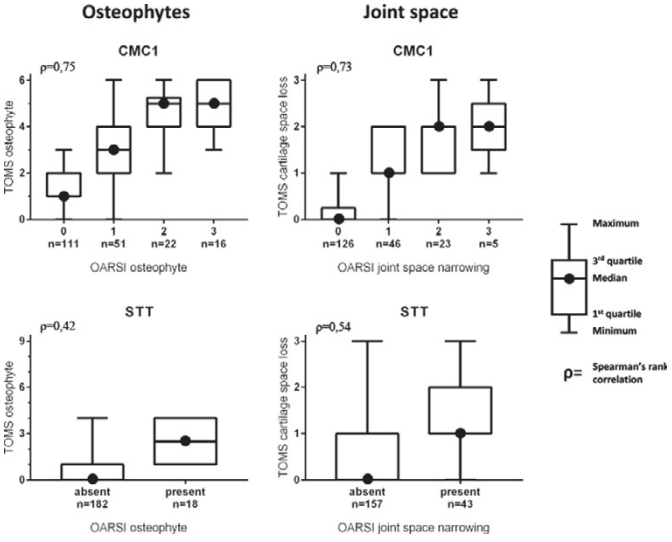


Conclusions: Modifiable abnormalities involving capsular/synovium and extra-capsular areas may be more frequently seen in painful OA joints. The presence of collateral ligament abnormalities in HOA joints, whether painful or not, suggest that the severity of ligament abnormalities in small joint OA and the degree of pain may be an important area to investigate further.
References:
[1] Tan AL, et al. Ann Rheum Dis. 2006 Oct;65(10):1267–72.
[2] Haugen IK, et al. J Rheumatol. 2014 Feb;41(2):386–91.
Acknowledgements: Funded by NIHR.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3532

OP0342 ASSESSMENT OF STRUCTURAL DAMAGE OF THE THUMB BASE IN PATIENTS WITH HAND OSTEOARTHRITIS: COMPARING THE NEWLY DEVELOPED OMERACT MAGNETIC RESONANCE IMAGING SCORING SYSTEM WITH STANDARD RADIOGRAPHY

S. van Beest[1], F.P. Kroon[1], W. Damman[1], R. Liu[1], M. Kloppenburg[1,2].
[1]Rheumatology; [2]Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands

Background: The thumb base is frequently involved in patients with hand osteoarthritis (OA), resulting in osteophytes and cartilage loss. Radiography is the most commonly used imaging modality to evaluate structural OA signs, however it is insensitive especially due to overprojection. Magnetic resonance imaging (MRI) could be a valuable alternative, however a standardized scoring method for thumb base MR images did not exist until recently OMERACT developed the thumb base OA MRI scoring system (TOMS)[1].
Objectives: Our aim was to investigate the validity of the new TOMS by comparing TOMS scores with radiographic scores.
Methods: Two hundred consecutively included patients (83.5% women, median age 60.5 years) diagnosed with primary hand OA in secondary care, who had both a dorsopalmar radiograph of the right hand and a MRI scan of the right thumb base taken at baseline, were studied. T1- and fat suppressed T2-turbo spin weighted sequences were performed in axial and coronal planes on a 1.5 Tesla extremity MRI unit. Radiographs of the first carpometacarpal (CMC1) and scaphotrapeziotrapezoid (STT) joints were scored using the OARSI atlas (osteophytes and joint space narrowing [JSN] in CMC1: 0–3 and STT: absent/present) by one reader with good intra-reader reliability, blinded for clinical and MRI data. MR images were scored using TOMS (osteophytes in CMC1: 0–6 and STT: 0–9; cartilage space loss [CSL] for both joints: 0–3) by two readers, blinded for clinical and radiographic data, with good intra- and inter-reader reliability. For further analysis we used the average of both readers, rounded down to the nearest integer. To study validity, the distribution of the TOMS scores for osteophytes and CSL were compared for the different radiographic stages for osteophytes and JSN, respectively.
Results: On MR images osteophytes were detected in the vast majority of thumb bases (CMC1 n=172; STT n=102). The score of TOMS increased with more severe radiographic stages (see figures). However, the number of patients without any osteophytes in both CMC1 and STT was considerably lower for TOMS (n=19) than for the OARSI (n=106) scoring. A similar difference was apparent for absence of CSL (n=82) versus JSN (n=108) in both CMC1 and STT. Patients with isolated STT osteophytes were quite rare for both TOMS (n=9) and the OARSI (n=5) scoring. The most prominent discrepancy between TOMS and OARSI sensitivity was found for osteophytes: an additional 168 joints (CMC1 n=84; STT n=84) were found positive with TOMS, while only 1 OARSI-positive CMC1 scored negative with TOMS.



Conclusions: Scores of osteophytes and cartilage loss assessed on MR images by TOMS were correlated with radiographic scores, indicating good validity of the TOMS. Furthermore, the frequencies of joints with osteophytes and cartilage loss assessed on MR images were higher compared to those on radiographs, suggesting high sensitivity for the TOMS.
References:
[1] Kroon FPB, Conaghan P, Foltz V, et al. Development and reliability of the OMERACT thumb base osteoarthritis MRI scoring system. J Rheumatol. 2017; in press.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2765

SATURDAY, 17 JUNE 2017

Why we do develop autoimmunity

OP0343 THE INTESTINAL INVOLVEMENT IN SYSTEMIC SCLEROSIS IS CHARACTERIZED BY A PECULIAR GUT MICROBIOTA

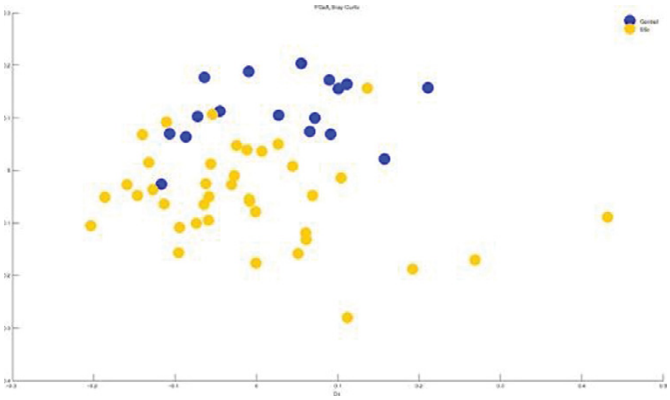
G. Natalello[1], S.L. Bosello[1], F. Paroni Sterbini[2], A. Palladini[3,4], G.B. Canestrari[1], F. Parisi[1], E. De Lorenzis[1], G. Berardi[1], B. Posteraro[5], M. Sanguinetti[2], G. Ferraccioli[1]. *[1]Institute of Rheumatology and Affine Sciences; [2]Institute of Microbiology, Università Cattolica del Sacro Cuore, Rome, Italy; [3]Paul Langerhans Institut Dresden of the Helmholtz Centre Munich at the University Clinic Carl Gustav Carus, TU Dresden, Dresden; [4]German Center for Diabetes Research (DZD e.V.), Neuherberg, Germany; [5]Institute of Public Health, Università Cattolica del Sacro Cuore, Rome, Italy*

Background: Gastrointestinal involvement is recognized as a major cause of morbidity and mortality in Systemic Sclerosis (SSc) and its pathophysiology is still unclear. Few data on composition and function of gut microenvironment in SSc are reported in the literature but there is a growing body of evidences supporting the hypothesis of a relation between gut microbiota and the host immune system.
Objectives: The goal of this study was to characterize fecal microbiota in SSc patients compared to healthy subjects to investigate whether specific microbial species may be responsible of dysbiosis in SSc. Furthermore, we investigated the composition of microbiota in the different clinical subsets of SSc.
Methods: Faecal samples were obtained from 17 healthy controls and 39 SSc patients including subjects with different skin involvement (Diffuse and Limited) and disease duration. The BMI was normal and the mean age was similar both in SSc and controls groups. The composition of microbiota was determined through 16S rRNA pyrosequencing performed using the GS Titanium technology. Rarefaction was used to uniform abudance data. α-diversity was defined by the main indexes while β-diversity was determined according to Bray-Curtis and UniFrac, represented trough Principal Coordinate Analysis (PCoA) and compared using PERMANOVA test on distance matrices. Linear Discriminant Analysis Effect Size was used to identify taxa that showed differential expression between the groups.
Results: At genus level SSc patients showed a differential expression in 12 taxa compared to controls with higher levels of *Ruminococcus*, *Streptococcus*,

Lactobacillus, *Blautia*, *Coprococcus* and *Phascolarctobacterium* and a depletion of *Bacteroides*, *Butyciromonas*, *Odoribacter*, *Succinivibrio*, *Sutterella* and *Prevotella*. The differences in microbiota composition between SSc patients and controls were supported also by PCoA of the values representing phylogenetic distance of microbial communities between specimens ($p<0.001$) (see figure). Among scleroderma patients, those with diffuse skin involvement showed a greater abundance of bacteria of Bacteroidetes phylum with significantly lower values of alpha diversity by Chao1 and species richness (p=0.01). Differences were confirmed by PERMANOVA on Bray-Curtis distance matrix (p=0.016).

PERMANOVA analysis of distance matrices (p-values adjusted according to FDR)

	Weighted UniFrac	Bray-Curtis
Control vs SSc	<0.001*	<0.001*
Control vs Diffuse	0,012*	0,0015*
Control vs Limited	0,003*	0,0015*
Control vs Early	0,003*	0,0015*
Control vs Long	0,017*	0,0015*
Diffuse vs Limited	0,259	0,016*
Early vs Long	0,49	0,156



Conclusions: Our analysis demonstrated an altered and distinct composition of gut microbiota in SSc patients compared to healthy controls. Furthermore, scleroderma patients show some differences in microbiota characteristics according to the extent of skin involvement, suggesting that microbiota may influence the severity of the disease. If validated and related to GI symptomathology and nutritional status our findings open up the opportunity of a rational intervention on microbiota to restore the gut equilibrium in SSc patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5258

SATURDAY, 17 JUNE 2017

Closing the gap between objective measures and self-report in fibromyalgia

OP0344-HPR **DEVELOPMENT OF RESPONDER CRITERIA FOR MULTICOMPONENT NON-PHARMACOLOGICAL TREATMENT IN FIBROMYALGIA**

V. Vervoort, J. Vriezekolk, C. van den Ende. *Department of Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands*

Background: Despite positive non-pharmacological treatment effects in fibromyalgia (FM) (1,2) these effects are often modest and show large individual variability. In clinical practice it is very important to assess the effectiveness of treatment for the individual patient in order to tailor further treatment. Responder criteria can assess the effectiveness of treatment and define clinically meaningful change in health outcomes on patient level. However, no specific responder criteria for non-pharmacological treatment in FM currently exist. This warrants further exploration in this field.
Objectives: 1) To define responder criteria for multicomponent non-pharmacological treatment in FM; and 2) To estimate and compare their sensitivity and specificity.
Methods: Candidate responder sets were 1) identified in literature (3–5); and 2) formulated by expert group consensus. All candidate responder sets were tested for sensitivity and specificity in a cohort of 144 patients with FM receiving multicomponent non-pharmacological treatment. Therapist's judgement about patient's goal attainment and patients' perspective on health status change, assessed at 6 months after the start of treatment, were used as gold standard.
Results: Seven responder sets were defined (three identified in literature and four formulated by expert group consensus), and comprised combinations of domains of 1) pain; 2) fatigue; 3) patient global assessment (PGA); 4) illness perceptions; 5) limitations in activities of daily living (ADL); 6) sleep. The sensitivity and specificity of literature-based responder sets (n=3) ranged between 17%>99% and 15%>95% respectively, whereas the expert-based responder sets (n=4) performed slightly better with regard to sensitivity (range 41%>81%) and specificity (range 50%>96%). Of the literature-based responder sets the OMERACT-OARSI responder set with patient's gold standard performed best (sensitivity 63%, specificity 75% and ROC area = 0.69). Overall, the expert-based responder set comprising the domains illness perceptions and limitations in ADL with patient's gold standard performed best (sensitivity 47%, specificity 96% and ROC area = 0.71).
Conclusions: We defined sets of responder criteria for multicomponent non-pharmacological treatment in fibromyalgia. Further research should focus on the validation of those sets with acceptable performance.
References:
[1] Busch AJ, et al. Exercise for treating fibromyalgia syndrome. Cochrane Database Syst Rev 2008; (4).
[2] Bernardy K, et al. Efficacy of Cognitive-Behavioral Therapies in Fibromyalgia. A systematic review and Metaanalysis of Randomized Controlled Trials. J Rheumatol. 2010; 37: 1991–2005.
[3] Arnold LM, et al. Development of responder defintions for fibromyalgia clinical trials. Arthritis Rheum. 2012;64(3):885–94.
[4] Norman GR, et al. Interpretation of changes in health-related quality of life; the remarkable universality of half a standard deviation. Med Care. 2003;41(5):582–92.
[5] Pham T, et al. OMERACT-OARSI initiative: Osteoarthritis Research Society International set of responder criteria for osteoarthritis clinical trials revisited. Osteoarthritis Cartilage. 2004; 12(5):389–99.
s **Disclosure of Interest:** None declared
DOI: 10.1136/annrheumdis-2017-eular.3629

SATURDAY, 17 JUNE 2017

Suffering in silence. Optimizing the management of psychological well-being for people with RMDs

OP0345-PARE **GROWING UP WITH ARTHRITIS – YES WE CAN! A PROJECT OF DEUTSCHE RHEUMA-LIGA IN CO-OPERATION WITH THE GERMAN ARTHRITIS RESEARCH CENTER. WITH FINANCIAL SUPPORT BY THE GERMAN FEDERAL MINISTRY OF HEALTH**

K. Cattelaens. *Deutsche Rheuma-Liga Bundesverband E.V., Bonn, Germany*

Background: Every third young person with arthritis in Germany stops therapy when he or she enters adult care! Young people with arthritis have to travel long distances to care facilities, which are specialized in transition (about 30 throughout Germany). Because there are too few rheumatologists adults with arthritis often have to wait long for a consultation. Too few doctors have experience with treating young persons with arthritis. The situation of young persons with arthritis results in little knowledge about the condition – only every second young person knows their correct diagnosis. Parents manage everything – only every 5th young person up to 17 years has been alone with their doctor without their parents. Timely and comprehensive support is lacking.
Objectives: Supported by the health ministry and in cooperation with the German Arthritis Research Center the project started in 2014. As a first step the need for support for young person with arthritis was explored. It took two years to develop a pilot project with transition peers, a homepage, camps and information material for parents and doctors. The main goal of the project is to reduce the number of young persons who discontinue care because of the necessary change from children's care to adult care.
Methods: Ten transition peers have been trained for providing support (telephone, online, personal). An online information platform www.mein-rheuma-wird-erwachsen.de (my arthritis is growing up!) was created, filled with the experiences of the peers, information and quizzes and contact offerings. Camps especially for young persons growing up with arthritis took place. For the parents information material were developed and a seminar: learn to let go! is offered to them. The transition peers are going to doctors congresses to spread information material and to present the homepage.
Results: An evaluation of the project is carried out by the German Arthritis Research Center. The online information platform is accepted, it had more than 10.000 visitors during the first year. The young users like the content of the homepage, the transition peers are accepted by the young people as well as by the doctors.
Conclusions: The model project is running for three years – from 2014 until the end of 2017. A subsequent project will focus on the communication between doctors and young patients and should continue the new activities for the young persons with arthritis, their parents and the doctors.
References:
[1] In 2016, the German rheumatology newspaper – "Zeitschrift für Rheumatologie" Nr. 6 /2016, Page 635f reported on the project with the title "Transition from pediatric to adult rheumatological care" and about the special offers from Deutsche Rheuma-Liga by Prof. Kirsten Minden and Martina Niewerth.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4956

OP0346-PARE **"LISTENING TO PAIN - UN DOLORE DA ASCOLTARE" MULTIDISCIPLINARY SUPPORT FOR WOMEN WITH FIBROMYALGIA**

S. Mingolla, S. Mingolla on behalf of Serena Mingolla Direttore Morfologie author - Francesco Riondino Vice President APMAR Onlus, Ilaria Cinieri Psychologist - Cinzia Assalve fibromyalgia Group APMAR Onlus. *APMAR, Lecce, Italy*

Background: The project "*Listening* to *Pain*- un dolore da ascoltare" is a multidisciplinary and multifactorial project addressed to women with Fibromyalgia. Fibromyalgia pain has no boundaries. People describe the pain as deep muscular aching, throbbing, shooting, stabbing, or intense burning. Quite often, the pain and stiffness are worse in the morning, and muscle groups that are used repetitively may hurt more. Pain in every muscle and the profound exhaustion are not symptoms that people can see, but they are real and may be devastating for the person with Fibromyalgia. Although the invisible nature of the condition causes credibility dilemmas for patients.
Objectives: The project aims at improve the quality of life of women with Fibromyalgia. It has the main following objectives: provide information about Fibromyalgia, raise public awareness, collect useful data for research development, give support to the person, reinforcing social networks, provide mediation of the recognition process and bio-energy structured exercise activities and classes tailored to symptoms (stiffness and fatigue) useful in boosting endurance times.
Methods: The project was launched in 2015 with a communication campaign and supervised by a group of psychologists promoting the use of humanistic bioenergetics therapy for individual consultations and collective supporting group of discussions. Participants were 50 women with a confirmed diagnosis of FMS.
In June 2015, APMAR founded its first "Group for Pathology" and launched new tools as the info point and the toll-free number.
The project includes: psychological support to women suffering from Fibromyalgia, self-help groups where women talk, meet, discuss the pain and jointly organize events and other projects; information, through the creation of brochures and different kind of materials; an info-point managed by APMAR and a toll-free number that provides information and immediate help for women feeling lonely.
Results: The psychological and physical well being of women with Fibromyalgia syndrome were enhanced by social support. Chronic Pain, depression, self-efficacy, helplessness, mood disturbance, health status, impact of FMS, were improved. Psychologists involved in the project observe a decrease of depression, greater security and openness in relations. Women started processing and overcoming the sense of loneliness and isolation, increasing knowledge and therefore awareness, acceptance of the disease.
Analyses indicated that the created social support networks were associated with greater levels of self-efficacy for pain and symptom management, higher levels of self-efficacy for function and symptom management, as well as overall psychological well being.



Conclusions: This multilateral approach was very empowering and consented women to work in the same direction to improve healthcare outcomes for people in their same conditions.
Furthermore, it helped women with Fibromyalgia get more control over their life, and promote understanding of patient empowerment. The project was also a call for action not only among patients and health professionals, but among several kinds of social groups of students, press, local policy makers and other civil society organizations.
References:
[1] APMAR National Association of People with Rheumatic and Rare Diseases - www.apmar.it info@apmar.it.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2549

SATURDAY, 17 JUNE 2017

Showcasing the EULAR Online Course for Health Professionals

OP0347-HPR **TRAINING RHEUMATOLOGY NURSE SPECIALISTS: WHAT DOES THE FUTURE HOLD?**

M.K. Nisar[1], J. Begum[2]. [1]*Rheumatology, Luton & Dunstable University Hospital;* [2]*Rheumatology, Luton, Luton, United Kingdom*

Background: Since the introduction of the Rheumatology nursing in the UK in 1980s, there has been gradual development of the "specialty". Despite the proven benefits, both clinical and economical, of a well-trained rheumatology nurse specialist and the evolution of the role, there is a lack of a clear career path for the profession.
Objectives: We undertook a pilot survey to understand the present climate of rheumatology practitioner training in the region.
Methods: Following a focus group discussion of an "ideal" development route for rheumatology practitioners, ten items were unanimously identified as areas for job progression. These included appropriate induction, prescribing skills, involvement in research and education, opportunities for combined working and scope for clinical development. A questionnaire was created based on these items and mailed to all the rheumatology units in the East of England. Replies were compiled to ascertain the current picture of regional training.
Results: There are 19 centres providing rheumatology services in the region with 51 rheumatology practitioners. All of them (100%) replied to the questionnaire. Only four units (21%) provide formal induction programme for training. 11/19 (57%) have nurse prescribers. All providers replied positive to the question pertaining nurses' participation in research and audit; 12 (63%) have presented locally or nationally and eight (42%) have submitted posters to conferences. 12 centres have partly nurse delivered early arthritis pathway and 13 have access to departmental ultrasound. Ten units provide patient educational events.
Conclusions: This is a pioneering survey outlining access of rheumatology practitioners and nurse specialists to developmental opportunities. This initiative highlights a wide variation in the provision of clear career pathway regionally. Though most centres are delivering contemporary services, these are not being used effectively for developing key team members. There is lack of formal induction programme. Though most nurses are involved in audit, less than a quarter are presenting at any level and even fewer are publishing research endeavours. Prescribing is limited to 15/51 (29%) members. Less than 20% are training to do intra-articular injections or learning musculoskeletal ultrasound. Despite patient education being a core skill for this group, only 10 units deliver these as a formal event.
In conculsion, there is wide variation in the provision of career advancing opportunities to rheumatology nurse specialists. This can potentially have a negative impact on staff recruitment and retention. There is a need for improving standards and delivery of rheumatology professionals' career development.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2786

Poster Presentations

THURSDAY, 15 JUNE 2017

Genomics, genetic basis of disease and HLA / T cell recognition

THU0001 DIFFERENTIAL METHYLATION AS A POTENTIAL BIOMARKER OF METHOTREXATE RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

N. Nair[1], D. Plant[1,2], S.M. Verstappen[1], J.D. Isaacs[3,4], A.W. Morgan[5], K.L. Hyrich[1], A. Barton[1], A.G. Wilson[6] on behalf of MATURA. *[1]Arthritis Research UK Centre for Genetics and Genomics and Centre of Epidemiology, University of Manchester; [2]NIHR Manchester Musculoskeletal BRU, CMFT, Manchester; [3]NIHR Newcastle BRU, Newcastle upon Tyne Hospitals NHS Foundation Trust; [4]Newcastle University, Newcastle; [5]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom; [6]University College Dublin School of Medicine and Medical Science, University College Dublin, Dublin, Ireland*

Background: Methotrexate (MTX) is the first-line disease modifying anti-rheumatic drug for the treatment of rheumatoid arthritis (RA). However, many patients do not respond adequately or experience adverse effects[1,2]; therefore, identifying blood-based biomarkers that predict treatment response is a research priority. DNA methylation is an epigenetic marker that modifies but does not alter DNA sequence, and it is thought that MTX may act, at least in part, by inhibiting intracellular methyl donor transfer leading to DNA hypomethylation[2].
Objectives: We aimed to identify differential DNA methylation signatures in whole blood, which may act as biomarkers predictive of response to MTX in patients with RA.
Methods: DNA methylation was measured using the HumanMethylation450 BeadChip in DNA samples from individuals recruited to the Rheumatoid Arthritis Medication Study (RAMS), a one year observational study in the UK including patients with RA starting MTX for the first time. In RAMS, demographic and clinical data are collected prior MTX start (baseline) and at 6 months after commencing MTX. DNA was extracted from whole blood samples collected baseline and at 4 weeks from patients who, at 6 months, had a EULAR good response (n=36) or EULAR poor response (n=36) to MTX. Differentially methylated positions (DMPs) between the baseline and 4 weeks, and between good and poor response were identified using linear regression, adjusting for gender, age, cell composition, baseline disease activity score (DAS28), and smoking status. Analyses also compared methylation with changes in DAS28 and the individual DAS28 components over 6 months. DMPs that showed significant differences in the test cohort were selected for replication by pyrosequencing in an independent group of 100 patients with both baseline and 4 week samples.
Results: Based on percentage change in methylation between pre-treatment and following 4 weeks of therapy, two DMPs were significantly associated with response status in samples taken at 4 weeks (p-value $<10^{-5}$). Three additional DMPs were associated with change in tender joint count, whilst three other DMPs were associated with change in swollen joint count, and a further four DMPs associated with change in C-reactive protein. Of the four DMPs tested to date, hypermethylation at cg23700278 at baseline suggests replicated association with improvement in swollen joint count by 6 months. The nearest gene to the cg23700278 locus is adrenoceptor alpha 2C (*ADRA2C*), involved in neurotransmission.
Conclusions: These preliminary results suggest DNA methylation may provide a biomarker of MTX response but requires replication in other data sets.
References:
[1] Verstappen SMM et al. (2012) Int. J. Clin. Rheu. 7(5):559–567.
[2] Kim Y, et al. (1996) J. Lab.Clin.Med. 128:165–172.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6330

THU0002 ETANERCEPT AND ADALIMUMAB EXHIBIT HETEROGENEOUS EARLY SIGNATURES OF RESPONSE IN RHEUMATOID ARTHRITIS THERAPY

J. Oliver[1], D. Plant[2], G. Orozco[1], K. Hyrich[3], A. Morgan[4], J. Isaacs[5], A.G. Wilson[6], A. Barton[1,2]. *[1]Arthritis Research UK, Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Manchester Academic Health Sciences Centre, The University of Manchester; [2]NIHR Manchester Musculoskeletal BRU, Central Manchester Foundation Trust; [3]Arthritis Research UK, Centre for Epidemiology, Centre for Musculoskeletal Research, Manchester Academic Health Sciences Centre, The University of Manchester, Manchester; [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds; [5]Institute of Cellular Medicine, Newcastle University and National Institute for Health Research Newcastle Biomedical Research Centre at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University, Newcastle; [6]UCD School of Medicine and Medical Science, Conway Institute, University College Dublin, Dublin, United Kingdom*

Background: Up to 40% of rheumatoid arthritis (RA) patients exhibit insufficient response to TNF inhibitor (TNFi) therapy, which has an adverse effect on long term outcomes. Without reliable biomarkers to direct treatment decisions, many non-responder (NR) patients experience a delay in switching to an alternative therapy. Ideally, blood-based biomarkers would be measured before treatment (baseline) and throughout treatment in order to select and monitor therapeutic response to maximise the chances of responding to the first biologic therapy.
Objectives: To compare transcriptomic changes between patients administered etanercept and adalimumab therapy, and to identify biomarkers to predict or monitor response.
Methods: From the Biologics in RA Genetics and Genomics Study Syndicate (BRAGGSS) cohort, 37 EULAR good-responders in clinical remission (GR) and 18 NR to etanercept, and 50 GR and 20 NR to adalimumab were selected. Total RNA was isolated from Tempus™-stabilised whole blood samples collected at baseline and following 3-months (3M) of therapy using the MagMAX™ RNA extraction kit. RNA was amplified and converted into biotinylated sense-strand DNA using the Affymetrix WT PLUS kit for hybridisation onto Affymetrix GeneChip® Human Transcriptome arrays. Quality control and differential expression/splice analysis were assessed using the Affymetrix Expression and Transcriptome Analysis Console™ and appropriate Bioconductor packages. Differential transcript expression was adjusted for baseline DAS, age, gender and concurrent DMARD therapy. Pathway analysis was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID) and Ingenuity Pathway Analysis (IPA) tools.
Results: In adalimumab GR, 636 genes were downregulated and 253 upregulated at 3M (FDR $p<0.05$, fold-change >1.2). There was significant upregulation of immune cell components, most notably HLA genes including *HLA-DRB1*, other RA susceptibility genes (*SLC2A4*, *PADI4* and *CD28*) and many B and T cell signalling genes. Etanercept GR exhibited a milder transcriptomic change overall, showing little overlap with adalimumab GR; 395 genes were downregulated and 27 upregulated at 3M (FDR $p<0.05$, fold-change >1.2). Downregulated genes included downstream TNF components such as mitogen activated protein (MAP) kinases, as well as genes involved in NOD-like receptor, Toll-like receptor and NF-κB signalling. Such significant changes were absent in NR to adalimumab and etanercept. Furthermore, alternative splice changes in RA-relevant genes such as *MMP9* were apparent in adalimumab GR at 3M but not etanercept GR.
Conclusions: The heterogeneity in the blood-based transcriptomic profiles of etanercept and adalimumab response observed herein suggests that different TNFi therapies function by alternative mechanisms that impact patient outcomes. It also calls into question the reliability of response studies that consider TNFi therapies as a homogenous group. The candidate biomarkers identified require replication in independent datasets but may provide early and objective response biomarkers to inform timely therapeutic switching in patients who are not responding to their current TNFi drug.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1739

THU0003 CD4+ AND B LYMPHOCYTE EXPRESSION QUANTITATIVE TRAITS AT RHEUMATOID ARTHRITIS RISK LOCI IN UNTREATED EARLY ARTHRITIS: IMPLICATIONS FOR CAUSAL GENE IDENTIFICATION?

N. Thalayasingam[1], J. Massey[2,3], A.E. Anderson[4], N. Nair[2,3], A. Skelton[4], D.W. Lendrem[4], L. Reynard[4], H.J. Cordell[5], S. Eyre[2,3], A. Barton[2,3], J.D. Isaacs[4], A.G. Pratt[4]. *[1]National Institute for Health Research Newcastle Biomedical Research Centre, Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University, Newcastle Upn Tyne; [2]Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Institute of Inflammation and Repair, University of Manchester; [3]NIHR Manchester Musculoskeletal Biomedical Research Centre, Central Manchester NHS Foundation Trust, Manchester; [4]National Institute for Health Research Newcastle Biomedical Research Centre, Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University; [5]Institute for Genetic Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom*

Background: Rheumatoid arthritis (RA) is a genetically complex disease of immune dysregulation. Genome-wide association scans (GWAS) have confirmed its association with variants at >100 genetic loci. Outside of the HLA region,

accumulating data now highlight an overlap between these risk loci and cell-specific enhancer elements that is maximal in CD4+ lymphocytes, followed by B lymphocytes

Objectives: Seeking insight into genetic risk mechanisms, we conducted and compared expression quantitative trait locus (eQTL) analyses of risk loci in CD4+ T cells and B cells from carefully phenotyped early arthritis patients naïve to therapeutic immunomodulation.

Methods: 254 patients donated RNA and DNA from purified B and/or CD4+ T-cells within 4 hours of blood draw. Genotyping and global gene expression measurement were carried out using the Illumina Human CoreExome array and either HT12v4 or WG6v3 BeadChip arrays respectively. Variants in linkage disequilibrium (LD) with 101 confirmed non-HLA RA- SNPs ($r^2>0.8$) were analysed, seeking evidence of *cis*- or *trans*- eQTLs according to whether associated probes were or were not within 4MB of these LD blocks.

Results: Genes subject to *cis* eQTL effects common to both CD4+ and B-lymphocytes at RA risk loci were *FADS1*, *FADS2*, *BLK*, *FCRL3*, *ORMDL3* and *GSDMB*. At the 8p23 *BLK-FAM167A* locus, we found adjacent genes subject to eQTLs whose activity differed markedly between cell types, the *FAM167A* effect displaying striking B-lymphocyte specificity. By contrast, *cis* eQTLs acting on *METTL21B*, *IKZF3,* and *PADI4* were unique to CD4+ lymphocytes, the latter two of these being identified for the first time in this cell subset. No *trans* eQTLs approached experiment-wide significance, and linear modelling did not identify a significant influence of biological co-variates (diagnosis, systemic inflammation, age) upon eQTL effect sizes.

Conclusions: Our findings refine understanding of candidate causal genes in RA pathogenesis, providing an important platform from which downstream functional studies may be prioritised and directed towards particular cell types.

References:

[1] Okada Y, Wu D, Trynka G, Raj T, Terao C, Ikari K, et al. Genetics of rheumatoid arthritis contributes to biology and drug discovery. Nature. 2014 Feb 20; 506(7488):376–381.

Acknowledgements: Wellcome Trust, Academy of Medical Sciences, JGW Patterson Foundation, National Institute of Health Research, Pfizer. Newcastle researchers received infrastructural support via the Arthritis Research UK Centre of Excellence for the RA pathogenesis (RACE). JM and NN are funded by an MRC/Arthritis Research UK stratified medicine award (MR/K015346/1).

Disclosure of Interest: N. Thalayasingam: None declared, J. Massey: None declared, A. Anderson: None declared, N. Nair: None declared, A. Skelton: None declared, D. Lendrem: None declared, L. Reynard: None declared, H. Cordell: None declared, S. Eyre: None declared, A. Barton: None declared, J. Isaacs: None declared, A. Pratt Grant/research support from: Pfizer

DOI: 10.1136/annrheumdis-2017-eular.4028

THU0004 CROSS PHENOTYPE ASSOCIATION MAPPING OF THE MHC IDENTIFIES GENETIC VARIANTS THAT DIFFERENTIATE PSORIATIC ARTHRITIS FROM PSORIASIS

J. Bowes[1], J. Ashcroft[1], N. Dand[2], P. Ho[1,3], C.H. Smith[4], J.N. Barker[4], N. McHugh[5], R.B. Warren[6], A. Barton[1,3] on behalf of BSTOP and BADBIR.
[1]Arthritis Research UK Centre for Genetics and Genomics, The University of Manchester, Manchester; [2]Division of Genetics and Molecular Medicine, King's College London, London; [3]NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, Manchester; [4]St John's Institute of Dermatology, Guys and St Thomas' Foundation Trust, London; [5]Royal National Hospital for Rheumatic Diseases and Dept Pharmacy and Pharmacology, University of Bath, Bath; [6]The Dermatology Centre, Salford Royal NHS Foundation Trust, Manchester, United Kingdom

Background: The identification of genetic variants that differentiate PsA from psoriasis has the potential to help us understand the underlying biological pathways that lead to the development of PsA. Associations to genetic variants within the major histocompatibility complex (MHC), in particular to *HLA-C*0602*, increase risk of both PsA and psoriasis when compared to control populations. However direct comparisons of PsA to psoriasis have led to paradoxical associations where *HLA-C*0602* has been reported to be protective of PsA. In addition *HLA-C*0602* has been reported to be associated with age of onset of psoriasis. A more recent study has reported the amino acid at position 45 of the HLA-B protein as the most important factor for differentiating PsA from psoriasis.

Objectives: Here we perform a cross phenotype association analysis in an attempt to identify genetic variants in the MHC that differentiate PsA from psoriasis in a large collection of PsA patients and psoriasis patients screened for the absence of PsA.

Methods: A total of 1069 patients with psoriasis and 981 patients with PsA from the UK were genotyped using either the Illumina Immunochip or the Illumina OmniExpress genotyping arrays. SNPs, amino acids and classical HLA alleles were imputed using SNP2HLA. Logistic regression was used to compare the imputed dosage of MHC markers between PsA and psoriasis. All analyses were repeated using age of psoriasis onset as an additional covariate.

Results: The most significant association when comparing PsA to psoriasis was to *HLA-C*0602* ($p=4.17x10^{-15}$) with a protective effect for PsA (OR 0.52, CI 0.44:0.61). *HLA-C*0602* was found to be significantly associated with a younger age of psoriasis onset ($p=1.51x10^{-60}$) where the median age of onset in years for carriage is 22 compared to 33 for non-carriage. We observed a difference in the median age of psoriasis onset in years between the PsA and psoriasis study subgroups (34 vs. 21), highlighting the potential for bias at markers associated with age of psoriasis onset. When controlling for the age of psoriasis onset in the analyses we observed no association of PsA to *HLA-C*0602* (p=0.07) and the most significant association was to the amino acid at position 97 of HLA-B ($p=1.54x10^{-9}$) where the presence of asparagine or serine residue increased risk of PsA. Asparagine at position 97 of HLA-B defines the HLA-B*2705 allele.

Conclusions: Comparing PsA to psoriasis we show *HLA-C*0602* confers no effect, either risk or protective, for PsA after correction for age of psoriasis onset. The results suggest that the previously observed protective effect of *HLA-C*0602* could be due to confounding due to a younger age of psoriasis onset in the psoriasis subgroup. When accounting for age of psoriasis onset, the primary association conferring risk for PsA in patients with psoriasis is to HLA-B amino-acid 97 where an asparagine residue defines the *HLA-B*2705* allele. In addition, this amino acid has been reported as the largest genetic effect for ankylosing spondylitis thereby refining the genetic overlap between these two spondyloarthropathies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3403

THU0005 ERAP POLYMORPHISMS AND ITS ASSOCIATION WITH HLA-B15 AND HLA-B27 POSITIVE SPONDYLARTHRITIS PATIENTS

J. Londono[1], A.M. Santos[2], J.C. Rueda[2], P. Peña[2], I. Briceño[3], E.-L. Saldarriaga[2], J.-I. Angarita[2], E. Calvo[4], M. Avila[2], N. Martinez-Rodriguez[5], H. Cubides[2], V. Parra[2], J.F. Medina[6]. *[1]Reumatología, Universidad de la Sabana-Hospital Militar Central, Bogotá; [2]Reumatología; [3]Facultad de Medicina, Grupo Genética Humana, Universidad de la Sabana, Chia; [4]Departamento de Imágenes diagnósticas, Universidad Nacional, Bogotá, Colombia; [5]Departamento de Investigación de Salúd Comunitaria, Hospital Infantil de México Federico Gomez, Ciudad de México, Mexico; [6]Departamento de Medicina Interna, Escuela de Medicina, Universidad de Navarra, Pamplona, Spain*

Background: Since 1973, the association of HLA-B27 and spondyloarthritis (SpA) is well known, however in Colombian population it is present in only 40% of patients and HLA-B15 is present almost in 25%. A mechanism of polygenic mechanism has been proposed as an explanation for the development of SpA. Endoplasmic reticulum aminopeptidase (ERAP) genes 1 and 2 have been implicated. ERAP1 is strongly associated with HLA-B27 positive patients and ankylosing spondylitis, but not with ERAP2

Objectives: To determine the association between ERAP polymorphisms and HLA-B27 or HLA-B15 positive SpA patients

Methods: 178 patients with SpA according to ASAS criteria were included in the study. HLA typing was performed by the PCR technique using the Biorad® HLA-SSP plates. The polymorphisms were determined by the RT-PCR technique using Roche® probes for ERAP1 rs27044, rs17482078, rs10050860, and rs30187. For ERAP2 the probes used were rs2910686, rs2248374 and rs2549782. The

Table 1. ERAP2 Haplotypes in HLA-B15 and B27 Patients

Haplotypes	HLA B15 n (AF)	HLA B27 n (AF)	OR (CI 95%)	*p*
TGT	**0.201**	0.078	2.943 (1.264–6.585)	0.009*
TGC	0.055	**0.227**	4.483 (1.524–13.187)	0.003*
CAT	0.021	**0.119**	9.014 (1.181–68.807)	0.009*
CAC	0.643	0.499	1.750 (0.968–3.162)	0.077
CGC	0.016	0.035	0.465 (0.053–4.056)	0.672
CGT	0.031	0.013	2.406 (0.332–17.45)	0.584
TAT	0.019	0.013	1.185 (0.106–13.29)	1.00
TAC	0.013	0.015	1.185 (0.106–13.29)	1.00

ERAP: endoplasmic reticulum aminopeptidase; AF: allelic frequency; OR: odds ratio.

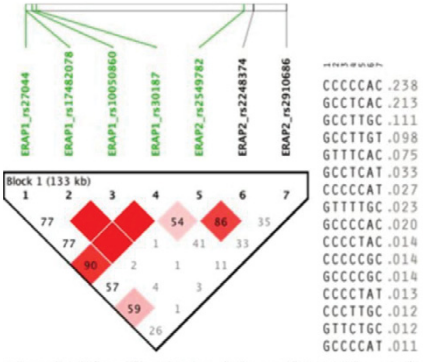


Figure 1. Linkage disequilibrium (LD) map of the ERAP gene. The value of the LD coefficient in each cell D'[(values close to 1.0) x 100] is shown. The colour map of the haplogroups represents the LD relationships, the bright red squares represent evidence of LD (log odds [LOD] score <2 and D'= 1], the light red squares indicate a slight evidence of LD (log odds [LOD] score≥2 and D'<1], and white squares mean that there is no LD and independent segregation [log odds [LOD] score<2 and D'<1]

allele and genotype frequencies polymorphisms were obtained by direct counting. In each group the Hardy-Weinberg equilibrium was evaluated using the ^{2} test. Associations were assessed using odds ratio (OR). Stata v.12.0 program was used to analyse data. The construction and analysis of haplotypes was performed using Haploview v.4.2

Results: In total 70 patients were HLA-B27 positive and 34 were HLA-B15 positive. 78 were women and 100 were men. Linkage disequilibrium map of the ERAP gene is depicted in figure 1. When analysed by ERAP2 haplotype it is observed that there is a statistically significant association with the combinations described in table 1. No associations were observed between ERAP1 haplotypes and HLA-B15 or B27

Conclusions: In the group of patients analysed, a statistically significant association was found between patients with SpA HLA-B15 positive and the haplotype TGT of ERAP2. Also HLA-B27 positive SpA patients were associated with haplotype TGC and CAT of ERAP2 with statistical significance

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5659

THU0006 TRANS-ETHNIC META-ANALYSIS OF GENOME-WIDE ASSOCIATION STUDIES IDENTIFIES GSDMA AND PRDM1 AS SUSCEPTIBILITY GENES TO SYSTEMIC SCLEROSIS

C. Terao[1], T. Kawaguchi[2], P. Dieude[3], J. Varga[4], M. Kuwana[5], M. Hudson[6], Y. Kawaguchi[7], M. Matucci-Cerinic[8], K. Ohmura[2], G. Riemekasten[9], A. Kawasaki[10], P. Airo[11], T. Horita[12], A. Oka[13], E. Hachulla[14], H. Yoshifuji[2], P. Caramaschi[15], N. Hunzelmann[16], M. Baron[6], T. Atsumi[12], P. Hassouns[17], A. Tochimoto[18], N. Ayuzawa[19], H. Yanagida[19], H. Furukawa[10], S. Tohma[20], M. Hasegawa[21], M. Fujimoto[22], O. Ishikawa[23], T. Yamamoto[24], D. Goto[10], Y. Asano[25], M. Jinnin[26], H. Endo[27], H. Takahashi[28], K. Takehara[29], S. Sato[25], H. Ihn[26], S. Raychaudhuri[1], K. Liao[1], P. Gregersen[30], N. Tsuchiya[10], V. Riccieri[31], I. Melchers[32], G. Valentini[33], A. Cauvet[34], M. Martinez[35], T. Mimori[2], F. Matsuda[2], Y. Allanore[36]. *[1]Brigham and Women's Hospital, Boston, United States; [2]Kyoto University Graduate School of Medicine, Kyoto, Japan; [3]Rheumatology Bichat Hospital, Paris, France; [4]Northwestern University Feinberg School of Medicine, Chicago, United States; [5]Keio University School of Medicine, Tokyo, Japan; [6]Jewish General Hospital and Lady Davis Research Institute, Montreal, Canada; [7]Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan; [8]University of Florence, Firenze, Italy; [9]University of Lübeck, Lübeck, Germany; [10]University of Tsukuba, Tsukuba, Japan; [11]Spedali Civili, Brescia, Italy; [12]Hokkaido University Graduate School of Medicine, Sapporo; [13]Tokai University, Isehara, Japan; [14]Lille University, Lille, France; [15]Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [16]University of Koln, Koln, Germany; [17]Johns Hopkins University, Baltimore, United States; [18]Tokyo Women's Medical University, Tokyo; [19]Utano National Hospital, Kyoto; [20]Sagamihara Hospital, National Hospital Organization, Sagamihara; [21]University of Fukui, Fukui; [22]Tsukuba, University of Tsukuba; [23]Gunma University Graduate School of Medicine, Gunma; [24]Fukushima Medical University, Fukushima; [25]University of Tokyo Graduate School of Medicine, Tokyo; [26]Kumamoto University, Kumamoto; [27]Toho University, Tokyo; [28]Sapporo Medical University School of Medicine, Sapporo; [29]Kanazawa University, Kanazawa, Japan; [30]The Feinstein Institute for Medical Research, Manhasset, United States; [31]Sapienza University of Rome, Rome, Italy; [32]University Medical Center, Freiburg, Germany; [33]Second University of Naples, Naples, Italy; [34]Paris Descartes University, Paris; [35]Batiment B Purpan Hospital, Toulouse; [36]Paris Descartes University, Paris, France*

Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis and composed of two subtypes, limited and diffuse cutaneous forms. Previous genetic studies including genome-wide association studies (GWAS) have identified 12 susceptibility loci satisfying genome-wide significance.

Objectives: To expand the list of susceptibility genes and deepen biological insights for SSc.

Methods: We performed trans-ethnic meta-analysis of GWAS in the Japanese and European populations, followed by a two-staged replication study comprising a total of 4,436 cases and 14,751 controls. Associations between significant single nuclear polymorphisms (SNPs) and neighboring genes were evaluated. Enrichment analysis of H3K4Me3, a representative histone mark for active promoter was conducted with an expanded list of SSc susceptibility genes.

Results: We identified two significant SNP in two loci, *GSDMA* and *PRDM1*, both of which are related with immune functions and associated with other autoimmune diseases ($p=1.4x10^{-10}$ and $6.6x10^{-10}$, respectively). *GSDMA* also showed a significant association with limited cutaneous SSc. We also replicated the associations of previously reported loci including a non-GWAS locus, *TNFAIP3*. *PRDM1* encodes BLIMP1, a transcription factor regulating T cell proliferation and plasma cell differentiation. The top SNP in *GSDMA* was a missense variant and correlated with gene expression of neighboring genes, and this could explain the association in this locus. We found different HLA association patterns between the two populations or two subtypes. Enrichment analysis suggested the importance of CD4 naïve primary T cell.

Conclusions: *GSDMA* and *PRDM1* are associated with SSc. These findings provide enhanced insight into the genetic and biological basis of SSc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2165

THU0007 DEEP SEQUENCING TRANSCRIPTOME ANALYSIS OF THE EFFECT OF TRAUMEEL VERSUS DICLOFENAC THERAPEUTIC ACTION IN WOUND HEALING

G.St. Laurent III[1], B. Seilheimer[2], M. Tackett[1], J. Zhou[1], D. Shtokalo[1], Y. Vyatkin[1], P. Kapranov[1], I. Toma[3], T. Mccaffrey[3]. *[1]The St. Laurent Institute, Vancouver, WA, United States; [2]Biologische Heilmittel Heel, GmbH, Baden-Baden, Germany; [3]Department of Medicine/Division of Genomic Medicine, The George Washington University, Washington, DC, United States*

Background: Anti-inflammatory agents are used widely in treating numerous inflammatory conditions. The effect of Tr14, a multitargeted natural product, was compared to diclofenac, a non-selective cyclooxygenase inhibitor, on cutaneous wound repair in mice.

Objectives: To compare the effect of diclofenac with Tr14 on the transcriptome after cutaneous wounding in the mouse.

Methods: After abrasive wounding, the wounds were treated with topical Tr14 or diclofenac at clinically relevant doses. An additional group received subcutaneous Tr14 injections. The healing wounds were analyzed for RNA transcript profiling by RNAseq at specific times (12h, 24h, 36h, 72h, 96h, 120h, 196h) after injury. Differentially expressed genes (DEGs) were computed at each time point between diclofenac vs control or Tr14 vs control using EdgeR.

Results: Across time points, Tr14 treatment modulated a number of transcripts related to key wound repair pathways such as cellular differentiation, wound contraction, and cell mobility. Diclofenac, in contrast, changed gene expression mainly in two areas: Prominent effects were observed with regard to DNA chromatin regulation and ribosomal function, further effects were observed on the prostaglandin pathway and wound repair factors. In many of the key pathways modulated by Tr14, such as the defense response and cell motility, diclofenac tended to have an opposite effect on gene expression. At 12 hours post-injury, there were 521 transcripts significantly elevated and 1027 transcripts that were decreased by diclofenac treatment. By comparison, using a similar number of transcripts altered by Tr14 treatment, only 4 transcripts were increased in common, and 5 transcripts were decreased in common, suggesting that the therapies have different effects on the transcriptome.

Conclusions: The overall patterns of the Tr14 and diclofenac responses in the transcriptome during wound repair are very different. The Tr14 effect is most pronounced on the defense response, cell motility, and anti-apoptotic pathways. In contrast, diclofenac mainly affected histones and chromatin remodeling systems, as well as ribosomal systems that would be expected to alter the translational pattern of diclofenac-treated cells.

Disclosure of Interest: G. St. Laurent, III: None declared, B. Seilheimer: None declared, M. Tackett: None declared, J. Zhou: None declared, D. Shtokalo: None declared, Y. Vyatkin: None declared, P. Kapranov: None declared, I. Toma: None declared, T. Mccaffrey Speakers bureau: TM has received speaker's honorarium from HEEL, GmbH

DOI: 10.1136/annrheumdis-2017-eular.4964

THU0008 MAST CELLS SHOW A REPROGRAMMED TRANSCRIPTIONAL SIGNATURE FOLLOWING REPEATED IGG STIMULATIONS

T. Messemaker, J. Suurmond, K. Habets, M. Heijink, J. Schonkeren, A. Dorjee, M. Giera, T. Huizinga, R. Toes, F. Kurreeman. *LUMC, Leiden, Netherlands*

Background: Mast cell numbers are increased in the rheumatoid arthritis joint. We have previously shown that mast cells can be activated by IgG-ACPA leading to the production of proinflammatory cytokines. However, not much is known about the resulting function when mast cells would repeatedly engage IgG, a likely scenario given the long life span of mast cells (up to a year) and the perpetual presence of IgG-ACPA in the joints. We have recently shown that mast cells triggered repeatedly through their Ig Fc epsilon receptor undergo a reprogramming of their responses (*Suurmond et al. JACI, 2016* by expressing de-novo transcribed genes in the antigen presentation and pathogen defence response pathways.

Objectives: The aim of the current work was to determine whether mast cells show similar changes in their response mode following repeated interactions with IgG.

Methods: Human cord blood-derived mast cells were treated for 2 weeks with plate-bound IgG. The expression profile of naive or treated mast cells was measured through RNA sequencing, quantitative RT-PCR, flow cytometry. Protein secretion was measured with ELISA and Luminex assays. Metabolic changes were measured using HPLC mass-spectrometry.

Results: Similar to our previous work on Fc Epsilon receptor, we observe a dampening of the normal IgG responses with a set of novel genes upregulated. Interestingly, de-novo expressed genes consisted of *DHCR7* and *DHCR24*, key enzymes in the cholesterol pathway. Pathway analysis confirms an enrichment of genes in this pathway following repeated IgG triggering. Preliminary data on metabolic profiling reveals a decrease in phospholipid levels in repeatedly activated mast cells.

Conclusions: Our study provides evidence that mast cells are reprogrammed upon repeated IgG triggering. In contrast to repeated Fc Epsilon Receptor triggering, different pathways are affected, implying stimulus-specific effects. Our work has important implications for the understanding the role of mast cells in rheumatoid arthritis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6326

THU0009 IN VITRO STUDIES USING CYBRIDS, SHOW THAT MTDNA FROM HEALTHY AND OA PATIENTS HAVE DIFFERENT MITOCHONDRIAL ACTIVITY

M. Fernández-Moreno[1,2], A. Dalmao-Fernandez[2], T. Hermida-Gomez[2], M.J. Sanchez-Dopico[2], M.E. Vazquez-Mosquera[2], E. Cortes-Pereira[2], S. Relaño-Fernandez[2], I. Rego-Perez[2], F.J. Blanco[2]. *[1]Centro de Investigación Biomédica en Red, Ciber-Bbm, Madrid; [2]Servicio de Reumatología. Complexo Hospitalario Universitario (CHUAC), Instituto de Investigación Biomédica de A Coruña (INIBIC), A Coruña, Spain*

Background: Mitochondrial dysfunction is well documented in OA and has the capacity to promote abnormalities in chondrocyte function and viability contributing to cartilage degeneration. Previous studies have showed the mtDNA haplogroup J are associated with incidence and progression of OA. Cybrids are optimal cellular models to study the real mitochondrial biology and function implications in the cellular behaviour, since they carry different mitochondrial variants with the same nuclear background, therefore, excluding the variations because of nuclear genome.
Objectives: The aim of this work is to test the real role of mtDNA in cellular activity, using cybrids with mtDNA from healthy donors (without OA) and from patients with knee OA.
Methods: Cybrids were developed using 143B.TK$^-$ Rho-0 cell line (nuclear donor) and platelets (mitochondrial donors) from healthy (without AO-N-) and knee OA donors. The OXPHOS function was evaluated by SeaHorse XFp after addition of oligomycin, FCCP and Rotenone/Antimycin A. The metabolic status was evaluated by glucose consumption and lactic acid production. The glycolytic activity was measure after addition of glucose, oligomycin and 2-dioxyglucose using Seahorse XFp. Appropriate statistical analyses were performed with GraphPad Prism v6.
Results: OA cybrids had lower basal respiration (92.07±39.9 and 155.5±54.08, $p<0.0005$), and maximal respiratory capacity (114.7±50.1 and 160.6±44.7, $p<0.05$) than N. The analysis of ATP production was lower in OA than in N cybrids (66.69±28.69 versus 101.5±42.04 $p\leq0.05$). The % spare respiratory capacity value for the N was significantly lower than in OA cybrids (107±16.21 versus 124.7±5.97, $p\leq0.0005$). Cybrids carrying the mtDNA from OA patients showed higher glucose consumption than N cybrids (43.77±8.87 mg/ml and 31.91±13.69 mg/ml; $p<0.05$) however in the lactic acid production did not exit differences. The glycolytic activity was evaluated and showed that OA cybrids had lower glycolysis (71.05±4.83 versus 85.43±11.18, $p<0.05$) but higher glycolytic reserve than N cybrids (56.60±7.5 versus 39.73±19.13, $p\leq0.05$).
Conclusions: Cybrids have different metabolic behaviour, being N more efficient using glucose via glycolysis. We found differences statistical significate in the parameters that describe the mitochondrial respiration capacity, in this line OA cybrids had lower mitochondrial respiration and produce less ATP than the cybrids obtained from healthy patients. These results showed that the mitochondria obtained from healthy and OA donors had a different behaviour. These data also offer a real rationale for why mitochondria alterations play an important role in the incidence of OA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5930

THU0010 ALTERED MIRNAS PROFILES IN PLASMA-DERIVED EXOSOME OF PATIENTS WITH ANKYLOSING SPONDYLITIS BY SMALL RNA-SEQ ANALYSIS

Y. Huang, T. Li, Z. Huang, W. Deng, S. Zheng, X. Guo, Z. Huang. *Guangdong No. 2 Provincial People's Hospital, Guangzhou, China*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease, which is difficult to diagnose in the early stages. Increasing evidences have shown that MicroRNAs (miRNAs) may serve as novel biomarkers for AS. Exosome can function as vehicles to deliver miRNAs in body fluids including saliva and plasma. However, the relationship between exosome-delivered miRNAs and AS has yet to be determined.
Objectives: The aim of this study is to detect the altered miRNAs profiles of plasma-derived exosome in AS patients by small RNA-Seq Analysis.
Methods: Ribo^{TM} kit was used to isolate exosome. Small RNA Sample Pre Kit was used to build libraries in 3 AS patients and 3 healthy volunteers (HV), following by IlluminaHiSeq platform sequencing and bioinformatics analysis. Quantitative reverse-transcription PCR (qRT-PCR) was used to confirm the expression of the highly-expressed miRNA in another 10 AS patients and 10 HV, and receiver-operator characteristic (ROC) curve was used to evaluate the diagnostic value of miRNAs.
Results: Small RNA-Seq analysis showed that the Q30 value of HV and AS patients were higher than 95% (Fig.1-A). The amount of miRNA in HV and AS patients were (509.667±77.501) and (632.000±43.555). 80 up-regulated and 19 down-regulated exosomal miRNAs were identified in AS patients, compared with HV ($|\log2Ratio|>1$, $P<0.05$) (Fig.1-B-C). The target genes of the 34 highly-expressed miRNAs from the 99 differently-expressed miRNAs were 7869, and the main function of these target genes are involved in the regulation of endocytosis and protein modification process analyzed by GO and KEGG. The qRT-PCR results indicated that the expression level of miRNA21–5P and miRNA423–5P in AS patients were (2.940±1.572) and (2.520±1.401) times higher than that of HV (Fig.1-D-E). ROC curve analysis showed that miRNA21–5P and miRNA423–5P had significant diagnostic value for AS with the AUC of 0.890 (CI95%: 0.723–1.057) and 0.835 (CI95%: 0.621–1.039) respectively (Fig.1-F).

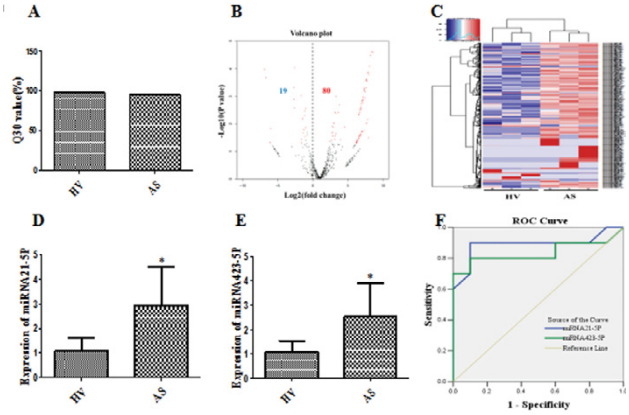


Fig.1 Altered miRNAs profiles in plasma-derived exosome of AS by small RNA-Seq Analysis
A: The Q30 value of each group. B-C: The differentially-expressed miRNAs. D-E: qRT-PCR was used to confirm the level of miRNA21-5P and miRNA423-5P. F: ROC cure was used to evaluate the diagnostic value of miRNA21-5P and miRNA423-5P. *$P<0.05$ vs HV.

Conclusions: The miRNAs profiles in plasma-derived exosome of AS patients are significant different from HV. miRNA21–5P and miRNA423–5P are higher expressed in AS patients. Thus, plasma-derived exosomal miRNAs might be reliable biomarkers to identify AS.
References:
[1] El MA. Extra-articular manifestations of ankylosing spondylitis: prevalence, characteristics and therapeutic implications. Eur J Intern Med, 2011, 22(6):554–60.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5637

THU0011 IMMUNE SIGNAL 2 CHECKPOINT MOLECULE EXPRESSION IN RHEUMATOID ARTHRITIS DISEASE PROGRESSION

A.M. Walsh[1], M. Canavan[2], Y. Guo[1], T. McGarry[2], X. Yin[1], M.D. Wechalekar[3], M.D. Smith[3], S.M. Proudman[4], C. Orr[5], S. Kelly[6], C. Pitzalis[6], D.J. Veale[5], U. Fearon[2], S. Nagpal[1]. *[1]Janssen R&d, Spring House, United States; [2]Molecular Rheumatology, Trinity Biomedical Sciences Institute, Trinity College Dublin, Dublin, Ireland; [3]Flinders University; [4]Royal Adelaide Hospital and Discipline of Medicine, University of Adelaide, Adelaide, Australia; [5]St. Vincent's University Hospital, Dublin, Ireland; [6]Queen Mary University of London, London, United Kingdom*

Background: Deep profiling of synovial tissue samples from rheumatoid arthritis (RA) patients may reveal the molecular underpinnings of phases of RA progression and provide new therapeutic targets to intervene earlier in disease pathogenesis.
Objectives: We sought to identify the molecular pathways expressed in different stages of disease (from seropositive subjects without clinically apparent synovitis to those with established disease) in synovial tissue compared to non-RA controls.
Methods: Transcriptomics profiling was performed on RNA isolated from synovial tissue biopsies. Normal synovium was collected from subjects with knee pain and without diagnosis of OA or RA (n=28). Arthralgia tissue was collected from ACPA-positive subjects without synovitis (n=10). Early RA tissue was collected from patients recently diagnosed (<1 year) with RA (n=57). Established RA tissue was collected from ACPA-positive subjects with >1 year of disease duration (n=95). Protein expression was confirmed on infiltrating immune cells from synovial biopsy cell suspensions by flow cytometry in separate RA subjects.
Results: Several pathways previously identified as important for RA pathogenesis (e.g., lymphocyte activation, osteoclast differentiation, NF-kappa B signaling) were enriched in differentially expressed genes in disease synovial biopsies compared to normal tissue samples. Interestingly, several genes known to function in T cell activation as signal 2 co-stimulatory or co-inhibitory molecules were differentially expressed, even in arthralgia and early RA subjects. 66 of 81 known co-stimulatory or co-inhibitory genes profiled were differentially expressed (FDR <5% and absolute fold-change >2) in disease samples from at least one cohort. The genes encoding co-stimulatory proteins that were increased compared to normal included *CD28*, *CD40LG*, *CD40* and *ICOS*. Interestingly, some of the genes encoding co-inhibitory proteins were increased (*PDCD1*/PD-1, *CD274*/PD-L1, *HAVCR2*/TIM3, *TIGIT, BTLA*), whereas others showed decreased expression (*C10orf54*/VISTA and *LAG3*) compared to normal controls. We focused on *CD28* expression, which is elevated in "pre-RA" arthralgia samples, proposing that anti-CD28 therapeutics could be candidates for RA disease prevention. By flow cytometry we demonstrated that a majority of CD4+ (>90%) and CD8+ (>60%) T

cells from RA synovial biopsy cell suspensions (n=4) showed surface expression of CD28.
Conclusions: We have generated a unique dataset from different phases of RA progression. Our results provide guidance for the selection of co-signaling molecules as therapeutic targets as well as for preventing the progression to RA. In particular, *CD28* expression was elevated in synovial tissue biopsies before the development of RA and it was also expressed on the majority of synovial tissue infiltrating CD4+ and CD8+ T cells from RA patients. These observations provide rationale to target CD28 for both RA treatment and disease interception.
Disclosure of Interest: A. Walsh Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson, M. Canavan: None declared, Y. Guo Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson, T. McGarry: None declared, X. Yin Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson, M. Wechalekar Grant/research support from: Johnson & Johnson, M. Smith Consultant for: Johnson & Johnson, S. Proudman: None declared, C. Orr: None declared, S. Kelly: None declared, C. Pitzalis Grant/research support from: Johnson & Johnson, Consultant for: Abbott, Astellas, MedImmune, BMS, Celgene, Grunenthal, GSK, MSD, Pfizer, Sanofi, Roche, UCB, D. Veale: None declared, U. Fearon: None declared, S. Nagpal Shareholder of: Johnson & Johnson, Employee of: Johnson & Johnson
DOI: 10.1136/annrheumdis-2017-eular.1343

THU0012 HLA-DBR1 ALLELES PROFILE IN PATIENTS WITH RHEUMATOID ARTHRITIS: RELATION TO DISEASE SUSCEPTIBILITY AND SEVERITY

A. Paradowska-Gorycka[1], B. Stypinska[1], E. Haladyj[2], K. Romanowska-Prochnicka[2], A. Pawlik[3], M. Olesinska[2]. *[1]Department of Molecular Biology; [2]Department of Connective Tissue Diseases, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw; [3]Department of Physiology, Pomeranian Medical University, Szczecin, Poland*

Background: Rheumatoid arthritis (RA) is a complex, chronic autoimmune disease (AID) that affects approximately 0.5%–1% of the population worldwide. RA is considered to be complex diseases of unknown etiology, where the environmental, immunological and genetic factors contributed to susceptibility and severity of the disease. Since the first evidence suggesting the involvement of human leukocyte antigens (HLAs) in RA was reported in 1969, the HLA region have been at the center of genetic studies of RA.
Objectives: We undertook this study to elucidate the association between HLA-DRB1 alleles profile and susceptibility to and severity of RA in a Polish population.
Methods: We analyzed the data on a total of 472 RA patients in whom HLA-DRB1 allele genotyping had been performed. DNA sequences for exon 2 of the DRB1 locus were typed using polymerase chain reaction-sequence-based typing (PCR-SBT).
Results: Identification of the variants potentially associated with risk and protection was carried out by comparison to the DKMS Polish Bone Marrow Donor Registry (41306 alleles). A significant increase in the frequency of the HLA-DRB1*15:01 ($p=0.001$), DRB1*04 ($p<0.0001$), DRB1*01:01 ($p<0.0001$),DRB1*10:01 ($p=0.003$) and *09:01 ($p<0.0001$) were identified in patients with RA and showed strong association with the disease susceptibility. Furthermore, the HLA-DRB1*07:01 allele was found to be protective ($p<0.0001$) in our RA patients. In the RA patients with HLA-DRB1*52:01 allele the mean value of PLT ($p=0.03$) and organ symptoms ($p=0.02$) were more frequent than in RA patients without this allele. In RA patients with DRB1*01:01, DRB*04 as well as DRB1*15:01 alleles the number of tender joints ($p=0.03$), diabetes ($p=0.03$) and renal failure) $p=0.03$) were observed less frequently compared with RA patients without these alleles. We also observed that in RA patients with DRB1*10:01 the VAS score was higher than in RA patients without this allele.
No association was detect between the HLA-DRB1*07:01 and DRB1*09:01 and disease activity and laboratory parameters among RA patients.
Conclusions: Current finding indicated that HLA-DRB1*15:01 DRB1*04, DRB1*01:01 and DRB1*10:01 alleles may be associated with susceptibility to as well as severity of RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5794

THU0013 TOWARDS THE DEFINITION OF A RISK MODEL PROFILE OF PERICARDITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A GENETIC STUDY

C. Perricone[1], F. Ceccarelli[1], C. Ciccacci[2], S. Rufini[2], C. Alessandri[1], F.R. Spinelli[1], E. Cipriano[1], C. Politi[2], A. Latini[2], G. Novelli[2], G. Valesini[2], P. Borgiani[2], F. Conti[1]. *[1]Lupus Clinic, Rheumatology, Department of Internal Medicine, Sapienza University of Rome; [2]Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy*

Background: We have recently demonstrated that polymorphisms (SNPs) in TRAF3IP2 gene are associated with susceptibility for systemic lupus erythematosus (SLE) and can predispose to the development of pericarditis (1). Moreover, we found that other genes previously associated with susceptibility to SLE (MIR1279, STAT4, PTPN2) seem to be involved in the development of pericarditis (2). At this purpose, we built a genetic risk model for the development of pericarditis in SLE (3).
Objectives: We aimed to expand the knowledge on the genetic risk of pericarditis in SLE by studying the role of rs2205960 (TNFSF4) and rs2233945 (ATG16L1) SNPs, previously associated with SLE susceptibility, improving our genetic risk model.
Methods: We recruited SLE patients (diagnosed according to 1997 revised ACR criteria) and healthy subjects served as controls. Study protocol included complete physical examination and blood drawing. The clinical and laboratory data were collected in a standardized, computerized, electronically-filled form (3). Clinical and laboratory features were assessed with a dichotomous score (present=1; absent=0). SNPs genotyping was performed by allelic discrimination assay. A case/control association study and a genotype/phenotype correlation analysis were performed and a risk profile model for pericarditis in SLE was built.
Results: Three-hundred fifteen SLE patients [285 F (90.5%), 30 M (9.5%), mean age 43.11±11.28 years, mean age at onset 32.19±11.84 years] and 278 healthy controls were enrolled. Pericarditis was present in 56 (17.8%) SLE patients. Deviations from Hardy–Weinberg equilibrium for the studied SNPs were not observed. The variant alleles of the rs2205960 (TNFSF4, P=0.013, OR=2.14) and of the rs2233945 (ATG16L1 P=0.009, OR=2.32) were significantly associated with susceptibility to pericarditis. A risk profile model for pericarditis considering the risk alleles of TRAF3IP2, MIR1279, STAT4, PTPN2, TNFSF4 and ATG16L1 showed that patients with more than 5 risk alleles have a significantly higher risk to develop pericarditis ($P<0.001$, OR=8.01). Anti-Sm antibodies were the only laboratory parameter associated with the development of pericarditis. Thus, a multivariate analysis by binary regression analysis, considering as dependent variable the presence or absence of pericarditis and as independent variables all the studied SNPs associated with pericarditis, was performed. In a stepwise approach including anti-Sm, TRAF3IP2, MIR1279, STAT4, PTPN2, TNFSF4 and ATG16L1 SNPs, the model explains about 25% (R^2 Cox &Snell) of the variability involved in the susceptibility to pericarditis.
Conclusions: We describe for the first time the contribution of TNFSF4 and ATG16L1 SNPs in pericarditis development in SLE patients. We improved our genetic risk profile model to better and earlier identify SLE patients more susceptible to develop this complication.
References:
[1] Perricone C, Ciccacci C, et al. Immunogenetics. 2013 Oct;65(10):703–9.
[2] Ciccacci C, Perricone C, et al. PLoS One. 2014 Nov 4;9(11):e111991.
[3] Ciccacci C, Perricone C, et al. Lupus. 2016. doi: 10.1177/0961203316679528.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6028

THU0014 NO ASSOCIATION OF SNP RS3761847 WITH THE EXPRESSION OF THE TRAF1-C5 LOCUS AND INVASION OF RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

D. Ferry[1,2], M. Trenkmann[2], K. Creevey[2], A.G. Wilson[2]. *[1]School of Medicine; [2]The Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Dublin, Ireland*

Background: Polymorphisms in the *TRAF1-C5* locus have been associated with susceptibility to rheumatoid arthritis (RA). A single nucleotide polymorphism (SNP) rs3761847, located in the first intron of the *TRAF1* gene, has been identified as an RA risk locus in a genome-wide association study (GWAS); the relationship of rs3761847 with joint damage are unclear. One of the key mechanisms of joint destruction is the degradation of and invasion of cartilage by RA synovial fibroblasts (RASF).
Objectives: To determine whether the expression of *TRAF1-C5* genes and the invasion of RASF are associated with the genotype at rs3761847.
Methods: The genotype at rs3761847 was determined using TaqMan Allelic Discrimination Assay. Invasion assays were performed using Matrigel-coated invasion chambers. Peripheral blood mononuclear cells (PBMC) were obtained by density gradient centrifugation. Neutrophils were isolated from the red blood cell layer by erythrocyte lysis; $CD14^+$ cells were separated using magnetic cell sorting. Macrophages were differentiated from plastic-adhered monocytes in M-CSF (50ng/ml) for 8 days. Cells were stimulated with lipopolysaccharide (LPS, 100ng/ml) plus interferon γ (IFNγ, 20ng/ml), interleukin 4 (IL-4, 20ng/ml) or tumour necrosis factor α (TNF-α, 10ng/ml). Gene expression was measured by SYBR Green real-time PCR using HPRT1 as a housekeeping gene.
Results: rs3761847 was in Harvey-Weinberg equilibrium in RASF (n=54, p=0.98) with genotype frequencies of 0.42 AA, 0.45 AG and 0.13 GG. When grouped by genotype, the expression of TRAF1 (total), TRAF1 transcript variant 2 and complement C5 mRNA showed no significant difference (p=0.929, p=0.583, p=0.980 respectively). This was also the case for invasion of RASF (n=43, p=0.548; mean cell count 10.4 AA, 8.3 AG and 11.1 GG). There was no correlation of genotype with common RA disease markers (CRP p=0.718, ESR p=0.179, RF titre p=0.466, ACPA titre p=0.712). In contrast, analyzing TRAF1 expression in different types of blood cells, significantly higher levels of TRAF1 mRNA were detected in monocytes carrying the AA genotype compared with the GG genotype at rs3761847, both in unstimulated (2.26-fold) as well as LPS+IFNγ-activated cells (2.04-fold; $p<0.05$, n=3 each). No significant association of TRAF1 expression or transcript variant utilization with rs3761847 was observed in the other blood-derived cell types studied, i.e. PBMC, macrophages and neutrophils,

or using other stimuli, i.e. IL-4 and TNF-α, indicating a specific function for the rs3761847 polymorphism in unstimulated and LPS+IFNγ-activated monocytes.
Conclusions: Our findings suggest that there is no relationship between invasive capacity of RASF or expression of TRAF1-C5 genes and genotype at rs3761847. In contrast, we report an association of the rs3761847 genotype and TRAF1 expression in monocytes. These data underline the importance of studying genotype-phenotype associations in the different cell types relevant for RA pathogenesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6066

THU0015 INVESTIGATION OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) IN GREECE: NEW SUSCEPTIBILITY LOCI

M.I. Zervou[1], D.G. Dimopoulou[2], E. Eliopoulos[3], M. Trachana[4], P. Pratsidou-Gkertsi[4], A. Andreou[3], A. Garyfallos[2], G.N. Goulielmos[1]. *[1]Medical School, University of Crete, Heraklion, Crete; [2]4th Department of Internal Medicine, Hippocratio Hospital, Aristotle University of Thessaloniki, Thessaloniki; [3]Biotechnology, Agricultural University of Crete, Athens; [4]1st Department of Pediatrics, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Background: Juvenile idiopathic arthritis (JIA) is an autoimmune disease characterized by persistent chronic arthritis, in which both genetic and environmental components are involved [1]. Different genetic variations have been reported as risk factors for JIA, but a difficulty of the replication of results in different ethnic backgrounds indicates the existence of an ethnic heterogeneity of genetic factors for JIA.
Objectives: We sought to validate three single nucleotide polymorphisms (SNPs), namely *PTPRC* (rs10919563), *TYK2* (rs34536443) and *PRKCQ* (rs4750316), previously found to be associated with JIA [2–4], and to investigate whether the 27-bp VNTR polymorphism on intron 4 of *eNOS,* which is associated with various autoimmune diseases so far [5], is associated with risk for JIA in Greece.
Methods: The sample set consisted of 125 JIA patients and 221 healthy controls from Northern Greece. Genotyping of the three SNPs was performed with Taqman primer-probe sets, using a Real-Time PCR platform (Applied Biosystems, ViiA™ 7 Real-Time PCR System), while *eNOS* VNTR polymorphism was genotyped by PCR. Odds ratios (OR) and 95% confidence intervals (CI) were calculated and the statistical difference in allele distribution was assessed by means of x^2 test or Fisher's exact test. Bioinformatic analysis was performed using BlastP, Pymol and Maestro and Desmond (Schrodinger Inc.).
Results: A case–control association study was conducted enrolling 4 successfully genotyped markers. *eNOS* only was found to be associated with JIA. Genotype a/a and allele "a" were more common in individuals with JIA than in controls ($p<0.0001$, OR=0.15, 95% CI 0.065–0.37 and $p<0.0001$, OR=0.34, 95% CI 0.23–0.49, respectively). No associations with JIA were detected for *TYK2, PTPRC* or *PRKCQ*. Aiming to investigate the structural consequences and the structure/function relationships accompanying the Pro1104 to Ala (rs34536443) mutation on TYK2 protein, bioinformatics analysis was performed. Combining 3D-modeling and Molecular Dynamics simulations we have noted changes in structural flexibility, affecting the functionality of the kinase domain of TYK2.
Conclusions: This study demonstrated for the first time that *eNOS* VNTR polymorphism is associated with susceptibility to JIA, thus suggesting that the risk allele "a" may confer susceptibility to clinically distinct disorders. Apart from the previously reported evidence for the role of *PTPRC* rs10919563, *PRKCQ* rs4750316 and *TYK2* rs34536443 in an increased risk for JIA, our results demonstrate no association of these genes with JIA in the Greek population. However, the lack of association of *PTPRC* SNP with JIA is in line with previous data reported from cohorts in US and Australia. Taken together, the results highlight the importance of comparative studies in different populations, considering that replication of previously identified markers is paramount to determine which SNPs represent true risk loci, thus pointing towards key disease pathways which warrant further study.
References:
[1] Ravelli and Martini (2007). Lancet 369:767–78.
[2] Hinks et al (2010). Ann Rheum Dis 69:1049–53.
[3] Hinks et al. (2012). Ann Rheum Dis 71:1117–21.
[4] Hinks et al (2013). Nat Genet 45: 664–9.
[5] Vazgiourakis et al (2007). Lupus 16:867–74.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2258

THU0016 A COMPREHENSIVE CONTRIBUTION OF GENES OF THE HYPOXIA INDUCIBLE FACTOR-1 ALPHA SIGNALING PATHWAY TO KNEE OSTEOARTHRITIS SUSCEPTIBILITY

J. Fernandez-Torres[1,2], G.A. Martínez-Nava[1], A. López-Reyes[1], Y. Zamudio-Cuevas[1], D. Clavijo-Cornejo[1], K. Martínez-Flores[1], M.C. Gutiérrez-Ruíz[2], L.E. Gómez-Quiroz[2], C. Pineda[1]. *[1]Laboratorio de Líquido Sinovial, Instituto Nacional de Rehabilitacion; [2]Cellular Physiology Laboratory, Universidad Autónoma Metropolitana-Iztapalapa, Mexico City, Mexico*

Background: The hallmark of osteoarthritis (OA) is the breakdown of articular cartilage. Articular cartilage is an avascular tissue, and this generates a hypoxic microenvironment. Hypoxia inducible factor-1α (HIF-1α) is the main transcriptional regulator of cellular and developmental response to hypoxia.
Objectives: The present study was designed to investigate whether genetic polymorphisms of the HIF-1α signaling pathway are involved in the development of knee OA.
Methods: A total of 243 unrelated Mexican-mestizo individuals comprising 93 knee OA patients and 150 healthy controls were recruited into the study. 42 genetic polymorphisms from 22 genes involved in the HIF-1α signaling pathway (*PIK3R1*, *AKT2*, *GSK3B*, *IL6*, *AGER*, *HIF1A*, *EGLN1, VHL*, *HIF1AN*, *VEGFA*, *EPO*, *NOS2*, *NOS3*, *IGF1*, *EGF*, *EDN1*, *MMP1*, *MMP3*, *MMP13*, *CA*, *COL2A1*, *COL3A1*) were genotyped in cases and controls using TaqMan-based allelic discrimination assays.
Results: After adjusting for age, sex and admixture, significant associations with knee OA were found for 7 SNPs in the case-control study. The following genotypes and alleles were associated with protection against OA: the CT genotype of the *HIF1AN* rs11190613 polymorphism (OR=0.44, 95% CI=0.19–1.0, *P*=0.05); the AA genotype of the *VEGFA* rs1570360 polymorphism (OR=0.14, 95% CI=0.02–0.69, *P*=0.016); the GT genotype and T allele of the *VEGFA* rs729761 polymorphism (OR=0.47, 95% CI=0.22–1.0, *P*=0.05; and OR=0.51, 95% CI=0.27–0.97, *P*=0.041, respectively); the GA genotype of the *COL2A1* rs1793953 polymorphism (OR=0.40, 95% CI=0.20–0.79, *P*=0.008); and the GG genotype and G allele of the *CKM* rs4884 polymorphism (OR=0.34, 95% CI=0.14–0.84, *P*=0.019; and OR=0.51, 95% CI=0.32–0.82, respectively). Otherwise, the CT genotype of the *COL3A1* rs2138533 polymorphism (OR=2.89, 95% CI=1.28–6.5, *P*=0.01); and the GA genotype of the *IGF1* rs35767 polymorphism (OR=2.22, 95% CI=1.11–4.43, *P*=0.024) were associated with an increased risk of OA. However, by using of epistatic interactions between HIF-1α pathway polymorphisms, we found that the gene-gene interaction had a synergistic effect over the estimated OR-values (see table).

a	b	OR_i	OR_c*	P_{int}
VEGFA rs1570360	*COL3A1* rs2138533			
GG	CC	1		0.027
	CT	2.89	4.51	
	TT	1.24	11.1	
COL3A1 rs2138533	*IGF1 rs35767*			
T	G	1		0.037
	A	1.49	3.26	
CKM rs4884	*COL3A1 rs2138533*			
A	C	1		0.036
	T	1.27	4.08	
COL2A1 rs1793953	*HIF1AN* rs11190613			
A	T	1		0.05
	C	0.71	0.35	

OR_i = initial OR-value; OR_c* = combined OR-value obtained by "b" column interaction with "a" column; P_{int} = *P*-value of the intreraction.

Conclusions: In this study we could observe that the gene-gene interaction of the HIF-1α signaling pathway highly increases the risk of developing OA, with the exception of *COL2A1* and *HIF1AN* interaction which had a protective role against OA. Further studies are needed to validate this results.
References:
[1] Fernández-Torres J, et al. Polymorphic variation of hypoxia inducible factor-1 A (HIF1A) gene might contribute to the development of knee osteoarthritis: a pilot study. BMC Musculoskelet Disord 2015; 16:218.
[2] Rodríguez-Fontanela C, et al. Assessment of osteoarthritis candidate genes in a meta-analysis of nine genome-wide association studies. Arthritis Rheumatol 2014; 66:940–949.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2131

THU0017 COMBINATION OF EGFR AND BLYS GENE EXPRESSION IN LUPUS NEPHRITIS

L.A. Mas[1,2], S. Retamozo[2,3], F. Bonisconti[1,2], E.V. Palomino[1,2], J.P. Pirola[2,3], V. Saurit[2,3], A. Alvarellos[2,3], T. Alvarellos[1,2]. *[1]Immunogenetics, Hospital Privado. Universitario de Córdoba; [2]Instituto Universitario de Ciencias Biomédicas de Córdoba; [3]Rheumatology, Hospital Privado. Universitario de Córdoba, Cordoba, Argentina*

Background: Lupus nephritis (LN) is a severe complication of Systemic Lupus Erythematosus (SLE). Non-invasive biomarkers are needed for diagnosis of LN and to identify patients at risk of a renal flare (1). Thus the presence of biomarkers associated with inflammation, tissue damage or cell activation in the urine of patients with LN may be a useful tool in the evaluation of LN patients.
The glomerular filtration rate (GFR) is considered the best overall index of renal function in health and disease. Because GFR is difficult to measure in clinical practice, most clinicians estimate the GFR (eGFR) from the serum creatinine concentration (2).
B Lymphocyte Stimulator (BLyS) is a cytokine that fosters B cell activation, antibody production, B cell - T cell interaction and plasma cell survival. These events have been demonstrated to play a role in patients with LN (3).
Objectives: We evaluated urinary levels of BLyS as biomarker for LN and their relationship with eGFR.

Methods: Urine samples (n=86) were obtained from LN patients and classified in two groups: patients with eGFR >60 (GFRhigh, n=68, 62F/6M, age: 34.07±13.24) and patients with eGFR ≤60 (GFRlow, n=18, 14F/4M, age: 35.22±13.76). RNA from urine samples was isolated using TRIzol-Chloroform technique and then reverse-transcribed using random primers. Levels of BLyS expression were evaluated using Quantitative Real Time PCR (QPCR). All amplifications were carried out in duplicate and threshold cycle (C_t) scores were averaged for calculations of relative expression values. The C_t scores were normalized against C_t scores by subtracting the corresponding β2Microglobuline (β2M) control, or $DCt=C_{t,gene}- C_{t,B2M}$.To test for differential gene expression between groups, a two sample t-test was performed to compare the DCt in the two groups.
Results: DCt is inversely proportional to BLyS's expression. We evaluated data from ΔCt analysis observing that mRNA levels of BLyS in eGFRlow (6.193±1.787) were higher than those from eGFRhigh (7.564±2.326), with a statistically significant difference between groups (p=0.0288).

	eGFRlow	eGFRhigh	
BLyS (ΔCt)	6.193±1.787	7.564±2.326	p=0.0288

Conclusions: In the present cross-sectional study, increased levels of BLyS were observed in patients with eGFR ≤60. These gene expression results might be linked to B cell activation and proliferation in kidney and thus in urine samples. Combination of eGFR and BLyS appears to be a good biomarker.
References:
[1] Rahman A. Can measuring urinary biomarkers improve the management of lupus nephritis? Arthritis Research & Therapy 2012, 14:127.
[2] Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999 Mar 16; 130 (6):461–70.
[3] Phatak S, Chaurasia S, Mishra SK, Gupta R, Agrawal V, Aggarwal A, Misra R. Urinary B cell activating factor (BAFF) and a proliferation inducing ligand (APRIL): potential biomarkers of active lupus nephritis. Clin Exp Immunol. 2016. Epub ahead of print.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4793

THU0018 ANGIOTENSINOGEN AS A MARKER OF INJURY IN LUPUS NEPHRITIS

L.A. Mas[1,2], S. Retamozo[2,3], M.J. Haye Salinas[3], V. Saurit[2,3], E.V. Palomino[1,2], J.L. De la Fuente[2,4], M. Angelina[2,5], J.P. Pirola[2,3], A. Alvarellos[2,3], T. Alvarellos[1]. *[1]Immunogenetics, Hospital Privado. Universitario de Córdoba; [2]Instituto Universitario de Ciencias Biomédicas de Córdoba; [3]Rheumatology; [4]Nephrology, Hospital Privado. Universitario de Córdoba; [5]Nephrology, Hospital Raúl Ferreyra, Cordoba, Argentina*

Background: Lupus Nephritis (LN) is one of the most severe forms of systemic lupus erythematosus (SLE) (1). Angiotensinogen (AGT) gene encodes the only glycoprotein known to be a precursor of the vasopresor angiotensin II (Ang II). Ang II is also a growth factor and a profibrogenic cytokine (2). In kidney transplantation AGT has been founded down expressed in biopsies with chronic allograft dysfunction (3). In LN, AGT deserves evaluation.
Objectives: To investigate AGT expression in biopsies and urines from LN patients.
Methods: 32 biopsies/urines paired from 32 LN patients was included. Kidney biopsies were evaluated according to the ISN/RPS classification system. Levels of AGT were evaluated using Quantitative Real Time PCR. Threshold cycle (C_t) scores were averaged for calculations of relative expression values. The C_t scores were normalized against C_t scores by subtracting β2Microglobuline control, or $\Delta Ct=C_{t,gene}- C_{t,B2M}$. Data expressed as ΔCt are inversely proportional to gene expression level. Nonparametric Mann Whitney test analysis and Anova with Bonferroni test were performed.
Results: 26 (81.3%) patients were female with a mean age at biopsy time of 31.9±29 years. The SLEDAI at the time of biopsy was 10.5 (IQR 0–15.7) and SLICC ≥1 in 13 (32.5%), hypocomplementemia 13/31 (41.9%) and positive DNA in 11/29 (37.9%) patients. Biopsies from patients with proteinuria ≥0.5 and renal failure (n=23), proteinuria isolated (n=14), LN remission (n=9), renal failure (n=7) and nephrotic syndrome (n=2) were performed. The mean value of ΔCt AGT gene expression in renal biopsy was 4.50 (IQR 3.51 – 5.67) and AGT in urine samples was 13.94 (IQR 11.66 – 17.89).
Conclusions: In the present study we found a potential utility of AGT mRNA levels in samples of active vs remission LN patients. Prospective studies are needed for confirming these results.

Table 1. AGT gene expression in biopsies and urines samples

	Class I/ Normal Biopsies n=3	Class II Biopsies n=6	Class IV Biopsies n=12	Class V/VI Biopsies n=10	p p
ΔCt AGT Biopsies*	5,57 (3,60–5,57)	3,67 (2,19–5,37)	5,34 (4,75–10,93)	4,35 (3,45–4,57)	0,02
ΔCt AGT Urines**	14,11 (12,44–14,11)	11,19 (9,53–11,59)	16,77 (12,88–18,25)	15,06 (12,16–17,62)	0,01

*p<0,05 class IV *vs* II; **p<0,05 Class IV *vs* II.

Table 2. AGT gene expression in biopsies according proteinuria levels

	Proteinuria ≤0,5	Proteinuria >0,5	p
ΔCt AGT Biopsies	3,60 (3,34–4,41)	4,79 (3,73–6,39)	0,04

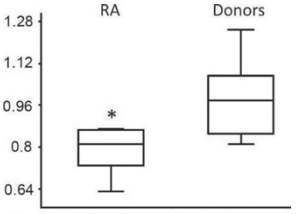
References:
[1] Yajuan Li et al. Biomarkers Profiling for Lupus Nephritis. Genomics Proteomics Bioinformatics 11; 158–165, 2013.
[2] Eriguchi M et al. Assessment of urinary angiotensinogen as a marker of podocyte injury in proteinuric nephropathies. Am J Physiol Renal Physiol 310: F322–F333, 2016.
[3] Mas V et al. Establishing the molecular pathways involved in chronic allograft nephropathy for testing new non-invasive diagnostic markers. Transplantation. 83:448–57, 2007.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6760

THU0019 FEATURES OF TELOMERE LENGTH DISTRIBUTION ON INDIVIDUAL CHROMOSOMES IN RHEUMATOID ARTHRITIS

M. Barkovskaya[1], A. Bogomolov[2], N. Knauer[1], E. Blinova[1], A. Sizikov[3], N. Rubtsov[2], V. Kozlov[1]. *[1]Laboratory of the Clinical Immunopathology, Research Institute of Fundamental and Clinical Immunology; [2]Laboratory of the Morphology and Function of Subcellular Components, Institute of Cytology and Genetics SB RAS; [3]Department of Clinical Rheumatology, Clinic of Immunopathology, Novosibirsk, Russian Federation*

Background: Telomeres are nucleoprotein structures,that protect the ends of chromosomes during cell divisions [1,2,3]. Previously it was found, that average telomere length in immune cells is reduced in atopic and autoimmunity disorders.This fact indicates an early immune aging in immune-mediated diseases [4,5]. The distribution of telomere repeats on different chromosomes has an individual telomere profile in humans [6] and may be a congenital feature, that accelerates immunosenescence.
Objectives: The purpose of this study was to evaluate the length of telomeres in the arms of individual chromosomes in patients with RA and healthy donors.
Methods: The study included 6 patients with RA and 6 healthy donors (the median age 51.5 (50–54) and 51.5 (49–53) years respectively). Metaphase spreads obtained from PBMCs were used in this study. Written informed consent was obtained from each person enrolled in the study. At the time of sampling, RA inpatients characterized with acute exacerbation of the disease received treatment at the Clinic of Immunopathology,Novosibirsk. RA was diagnosed by clinicians according to ACR/EULAR 2010. For measurement of the telomere length on individual chromosome arms we used Q-FISH with $(C_3TA_2)_3$ PNA-probe. Inverted DAPI banding was used for chromosome identification according to ISCN 2013. The new MeTeLen software was developed to estimate the telomere repeats relative quantity (http://www.bionet.nsc.ru/en/development/application-development/development-of-a-computer/metelen.html) in metaphase images.
Results: When comparing the telomere length, it was found, that telomere on chromosome 16 p are shorter in patients with RA than in donors. Since each person has an individual telomere profile, we also analyzed the presence of shortened telomere sequences on individual chromosome arms relative to the average length of telomeres for each subject separately. As a result, patients with RA have a larger number of significantly shortened telomeres than donors (see Table).

Comparison group	Chromosome arms with shortened telomere repeats
Healthy volunteers	12p, 19p, 2q, 20q
Patients with RA	7p, 12p,16p, 17p, 19p, 2q, 20q, 21q



Telomere length on chromosome 16 p (expressed in relative units) in patients with RA and healthy donors. Data are presented as median and interquartile range, *-significant difference (p< 0.05, Mann-Whitney U test).

Conclusions: The revealed features of telomeric profiles of patients with RA may be an indication of a proliferative stress, that occurs as a result of the mass immune cell proliferation in the immunopathology. It can be assumed, that the presence of a great number of shortened telomeres can promote cell death through apoptosis. The observed shortening of the telomere length on chromosome 16 p in RA may be relevant in its pathogenesis. It is known, that telomere shortening can lead to increased gene expression near the telomere DNA region. Thus, in 16 p 13 a number of genes is localized, that are associated with RA or may be involved in its development.

References:
[1] Olovnikov A.M, J. Theor. Biol. 41(1):181–190, 1973.
[2] Blackburn E.H., Gall J.G., J. Mol. Biol. 120:33–53, 1978.
[3] Hayflick L, Exp. Cell. Res. 37:614–636, 1965.
[4] Andrews N.P. et al., Gerontology 56(4):390–403, 2010.
[5] Dehbi A. ZA. Et al., Clin. Immunol. 9(12):1193–1204, 2013.
[6] Graakjaer J. et al., Mech. ageing dev., 124(5): 629–640, 2003.
Acknowledgements: The study was funded by RSF (research project No 14–15–00346).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3649

THU0020 INCREASED EXPRESSION OF CCN4/WISP1 IN OSTEOARTHRITIC ARTICULAR CARTILAGE IS EPIGENETICALLY REGULATED AND DISRUPTS CARTILAGE HOMEOSTASIS

M. van den Bosch[1], Y.F. Ramos[2], W. den Hollander[2], N. Bömer[2], R.G. Nelissen[3], J.B. Bovée[4], A.B. Blom[1], I. Meulenbelt[2]. *[1]Experimental Rheumatology, Radboud university medical center, Nijmegen; [2]Department of Molecular Epidemiology; [3]Department of Orthopedics; [4]Department of Pathology, Leiden University Medical Center, Leiden, Netherlands*

Background: Previously, we described increased expression of Wnt-1-induced signaling protein 1 (*Wisp1*) in murine synovium and cartilage after induction of two experimental osteoarthritis (OA) models. *Wisp1* is a downstream target of the canonical Wnt signaling pathway that has been shown to play a pivotal role in the etiopathology of OA. In line with this, we have observed increased breakdown of the articular cartilage after overexpression of *Wisp1* in naïve mouse knee joints, whereas *Wisp1*$^{-/-}$ mice revealed decreased cartilage degeneration in three independent experimental OA models compared to wild type controls. Together, these data indicate a direct correlation between *Wisp1* and OA in mice.
Objectives: In the current study we set out to characterize the relation between expression of *WISP1* and human OA.
Methods: Articular cartilage from preserved and degenerated OA areas was collected from 39 Caucasian end-stage OA patients. Cartilage from non-OA-diagnosed individuals was collected after femoral neck fractures. Cartilage degeneration was classified according to the Mankin scoring system. DNA was isolated to determine correlation between *WISP1* expression and methylation profiles using Generalized Linear Mixed Model (GLMM). RNA expression levels were determined with microarray analysis and RNA sequencing. Immunohistochemical staining was used to determine WISP1 protein expression. Recombinant WISP1 was added to human chondrocyte microparticles, and cartilage extracellular matrix deposition was determined by measuring cartilage microparticle size and Safranin O/Fast Green staining.
Results: We observed increased WISP1 expression in cartilage of OA patients compared to non-OA-diagnosed controls. Moreover, within OA patients, both WISP1 mRNA and protein expression were significantly increased in OA-affected cartilage compared to preserved regions of the same joint, and WISP1 expression significantly correlated with Mankin score. Interestingly, we found that positional CpG dinucleotides were hypomethylated in cartilage of OA-affected areas as compared to unaffected areas from the same joint, which correlated with increased RNA expression as determined with both microarray analysis and RNA sequencing analysis. Of note, methylation levels of a CpG affecting *WISP1* transcription were found to highly significantly correlate to a single nucleotide polymorphism (SNP) at the *WISP1* locus. Next, to investigate effects of increased WISP1 levels on chondrocyte microparticles, we added human recombinant WISP1. This resulted in a significantly decreased deposition of cartilage extracellular matrix as reflected by decreased microparticle circumference, and a strongly decreased proteoglycan content, suggesting that increased WISP1 levels are detrimental to cartilage.
Conclusions: The expression of WISP1, both RNA and protein, is increased in OA-affected as compared to preserved articular cartilage. This increased expression is inversely correlated with methylation levels of a positional CpG for WISP1, which was found to be under the influence of a SNP at the *WISP1* locus. Together, our results suggest that tight regulation of *WISP1* expression via methylation is essential to maintain cartilage homeostasis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4010

THU0021 THE ANALYSIS OF PRF1, STX11, UNC13D AND STXBP2 GENE IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS WITH MACROPHAGE ACTIVATION SYNDROME

P. Wei[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: We investigated the clinical characteristics of 34 cases with systemic juvenile idiopathic arthritis (SJIA) and macrophage activation syndrome (MAS) and analyzed PRF1, UNC13D, STX11 and STXBP2 gene so as to figure out the genetic pathogenic mechanism.
Methods: The clinical characteristics of 34 cases with sJIA and MAS were retrospectively analyzed, and the coding sequences of PRF1, UNC13D, STX11 were amplified. DNAMAN software and NCBI BLAST were used to compare sequences. The chi-square test was employed to compare the distribution of allele and genotype frequencies between SLE patients and healthy controls.
Results: Among the 34 cases, 69% were males, and the average age was 6 years. 85% (29/34 cases) of the cases underwent genetic testing and four SNPS loci were detected: PRF1 c. 1061 c > T (rs885822); UNC13D c. 659 c > T (rs3744007); STXBP2 c. 1483 T > c (rs10001) and STXBP2 c. 1616 A > G (rs6791). Compared with control group, genotype and allele frequencies of PRF1 rs885822 and STXBP2 rs10001 among the MAS cases were of significant difference (rs885822: allele frequency 2 =4.52, p=0.03; genotype frequency: 2 =5.52, p=0.02. rs10001: allele frequency 2 =21.33, p=0.00; genotype frequency: 2 =19.58, p=0.00). There were no significant differences in genotype and allele frequencies of UNC13D rs3744007 and STXBP2 rs6791 between MAS group and control group (rs3744007: allele frequency 2 =1.89, p=0.17; genotype frequency: 2 =1.59, p=0.45. rs6791: allele frequency 2 =1.69, p=0.19; genotype frequency: 2 =2.09, p=0.35). The main characteristics of the cases were persistent fever, progressive hepatosplenomegaly, a sharp decline in blood cells, effusion, significantly increased serum liver enzymes, hyperlipidemia, etc. Some children had mucosal bleeding, neurological dysfunction, etc. More than 82% children had upper respiratory tract infection before MAS onset. 90% of children had remission, while three cases developed multiple organ failure and died.
Conclusions: Macrophage activation syndrome is fatal complication caused by immune imbalance. Early detection and treatment is the key to improve the prognosis. The SNP PRF1 rs885822 and STXBP2 rs1001 may be concurrent with the pathogenesis of SJIA-MAS. The SNP UNC13D rs3744007 and STXBP2 rs6791 may not play a role in SJIA-MAS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2138

THU0022 REPLICATION ANALYSIS OF GENE-GENE INTERACTION BETWEEN HLA-DQA2 AND HLA-DQB2 VARIANTS IN ITALIAN RHEUMATOID ARTHRITIS PATIENTS

R. Bassi Andreasi[1], M.F.J. Khan[1], E. Galuppi[2], M. Govoni[2], M. Rubini[1]. *[1]Biomedical and Specialty Surgical Sciences; [2]Medical Sciences, University of Ferrara, FERRARA, Italy*

Background: Rheumatoid Arthritis (RA) is a complex and multifactorial disease, caused by multiple interactions between genetics and environmental factors. In the context of RA genetics, the Human Leukocyte Antigen (HLA) exerts a primary role. Approximately 90% of RA patients show alleles at the HLA-DRB1 locus, codifying for 5 Amino Acids, known as "*shared epitope*" (SE). SE is associated with increased risk to develop RA and more severe phenotype, but it does not entirely explain HLA contribution to disease risk.
Moreover, it is generally accepted that occurrence risk could be determined by specific gene-gene interactions. A study carried out in USA (NARAC) reported a particular interaction between SNPs in the HLA class II region: HLA-DQA2 (rs9275595) and HLA-DQB2 (rs10807113). Results showed 11 fold increased risk to develop RA in patients carrying both variants (Liu *et al.*, 2011), while single variants did not significant contribute to the RA risk (Odds ratio, OR, respectively, 1.6 and 1.0).
Gene-gene interaction between HLA-DQA2 and HLA-DQB2 SNPs is remarkable, considering that glycoproteins codified by these genes combined each other and create a quaternary structure.
Objectives: To replicate NARAC study evidence in Italian population, we genotyped rs9275595 (HLA-DQA2) and rs10807113 (HLA-DQB2) variants using a case/control model.
Methods: The study included a cohort of 316 Italian RA patients and a matched group of 443 healthy control individuals. All subjects were genotyped for HLA-DQA2 T>C (rs9275595) and HLA-DQB2 A>C (rs10807113) using TaqMan technology and Real-Time PCR.
Results: Replication test performed in our Italian RA cohort did not identify significant interaction between two variants analyzed.
However, considering the single variant rs9275595, the results showed a significantly increased risk to develop RA. Taking T/T genotype as the reference, C/C homozygotes showed significant association with a 3.82 fold increased risk of RA (OR=3.821 95% CI (2.017–8.351) p-value=0.00063). The SNP acted under an additive model: T/C heterozygotes showed significant OR=1.988 (95% CI 1.458–2.711, p-value=0.00002).
Conclusions: The results of this study do not confirm the gene-gene interaction previous reported in the NARAC cohort (Liu *et al.*, 2011). However, outcomes suggest that HLA-DQA2 rs9275595 could contribute to RA pathogenesis in the Italian population.
References:
[1] Liu C, Ackerman HH, Carulli JP. A genome-wide screen gene-gene interactions for rheumatoid arthritis susceptibility. Hum Genet. 2011 May;129(5):473–85.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6252

THU0023 SYNOVIAL FLUID MIRNAS MULTIMARKER ANALYSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

R. Shumnalieva[1], D. Kachakova[2], S. Monov[1], R. Kaneva[2], Z. Kolarov[1], R. Rashkov[1]. *[1]Department of Internal Medicine, Clinic of rheumatology, Medical University - Sofia; [2]Department of Medical Chemistry and Biochemistry, Molecular Medicine Center, Medical University - Sofia, Sofia, Bulgaria*

Background: Recent epigenetic studies reveal the pathogenic role of micro-ribonucleic acids (microRNAs) and their targets in the inflammatory process in rheumatoid arthritis (RA). miRNAs play crucial role in controlling and modulating immunity and their abnormal expression has been linked to the deregulated function of regulatory T cells, to the chronic synovial inflammation and bone destruction[1–3].
Objectives: To perform a multimarker analysis of synovial fluid (SF) expression levels of miR-146a, miR-155 and miR-223 in RA patients in regard to their role as diagnostic biomarkers.
Methods: Total RNA was isolated from the SF of 48 RA patients and 11 healthy controls (HCs) and expression levels of miR-146a, miR-155 and miR-223 were determined by quantitative real-time polymerase chain reaction (qPCR), SybrGreen technology. Relative changes of gene expression levels of the miRNAs were calculated by $2^{-\Delta\Delta Ct}$method and SPSS were used for statistical analysis. RNU6B gene was used as a reference control for normalization. Receiver operating characteristic (ROC) curve analysis using RQ values was constructed in order to evaluate the diagnostic accuracy of these miRNAs in SF for distinguishing RA patients from HCs.
Results: miR-146a, miR-155 and miR-223 showed overexpression in RA SF compared to HCs (in 70.83%, 79.17% and 79.17% of the patients, respectively) and could be used to differentiate RA patients from HCs ($p=4.8x10^{-4}$, $p=8x10^{-5}$ and $p=2.8x10^{-4}$, respectively). The ROC curve analysis showed diagnostic accuracy for miR-146a with area under the curve (AUC)=0.769, 95% CI=0.600÷0.938, p=0.006, with sensitivity of 75% and specificity of 72.3%; AUC for miR-155 was 0.858 (95% CI=0.757÷0.959, $p=2.3x10^{-4}$) with sensitivity of 81.3% and specificity of 81.8%; AUC for miR-223=0.841 (95% CI=0.724÷0.958, $p=4.6x10^{-4}$), with sensitivity of 87.5% and specificity of 72.7%. The diagnostic accuracy improved when performing a multimarker analysis with AUC for the combination of miR-146a and miR-155=0.871 (0.776–0.967, $p=1.4x10^{-4}$), AUC for miR-146a and miR-223=0.867 (0.753–0.982, $p=1.6x10^{-4}$), AUC for miR-155 and miR-223=0.907 (0.823–0.991, $p=2.6x10^{-5}$). AUC for the combination of all three miRNAs was 0.915 (0.840–0.990, $p=2.02x10^{-5}$) with 89.6% sensitivity and 81.8% specificity.
Conclusions: Local miRNA expression levels could serve as diagnostic biomarkers in RA patients. The multimarker analysis of the expression levels of miR-146a, miR-155 and miR-223 in SF has better diagnostic accuracy than their single use in the clinical practice.
References:
[1] Chen XM, Huang QC, Yang SL, Chu YL, Yan YH, Han L et al. Role of Micro RNAs in the Pathogenesis of Rheumatoid Arthritis. Medicine (Baltimore). 2015; 94(31):e1326.
[2] Churov AV, Oleinik EK, Knip M. MicroRNAs in rheumatoid arthritis: altered expression and diagnostic 2. potential. Autoimmun Rev. 2015; 14(11):1029–37.
[3] Murata K, Yoshitomi H, Tanida S, Ishikawa M, Nishitani K, Ito H, Nakamura T. Plasma and synovial fluid microRNAs as potential biomarkers of rheumatoid arthritis and osteoarthritis. Arthritis Res Ther. 2010;12(3):R86.
Acknowledgements: The study was supported by Grant 14-D/2012 and 55/2013 funded by MU-Sofia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6406

THU0024 WHOLE GENOME LINKAGE AND EXOME SEQUENCING ANALYSES IN AN AUTOSOMAL RECESSIVE TAKAYASU ARTERITIS FAMILY

I. Karacan[1], S.N. Esatoglu[2], E. Tahir Turanlı[1,3], A. Tolun[4], E. Seyahi[2]. *[1]Istanbul Technical University, Dr. Orhan Ocalgiray Molecular Biology-Biotechnology and Genetics Research Centre, Institute of Science, Engineering and Technology, Molecular Biology, Biotechnology and Genetics Program; [2]Istanbul University, Cerrahpasa Medical School, Department of Internal Medicine, Division of Rheumatology; [3]Istanbul Technical University, Department of Molecular Biology and Genetics; [4]Boğaziçi University, Department of Molecular Biology and Genetics, Istanbul, Turkey*

Background: Takayasu arteritis (TA) is a rare chronic inflammatory disease of the aorta and its major branches, seen predominantly in females. Its etiology is unknown, however, there is a growing body of evidence to suggest genetic contribution to the pathogenesis of the disease: a) The disease is relatively frequent in Asia, b) Several familial cases of TA have been published (1) and even, autosomal recessive inheritance pattern has been suggested (2), c) Genetic association with HLA-B*52 across multiple ethnicities has been confirmed (3), and d) A multi-ethnic genome-wide association studies (GWAS) study in TA established additional genetic susceptibility loci (4–5).
Objectives: We studied a consanguineous family consisting of two affected and one unaffected sibs and their healthy parents in order to identify the causative mutation or linked loci.
Methods: Whole genome single nucleotide polymorphism (SNP) genotyping was performed for five family members using Illumina OmniExpress-24 BeadChip targeting ~700,000 SNP markers. Using genotyping data, we performed multi-point parametric linkage analysis assuming recessive inheritance and complete penetrance. Also, exome sequencing was performed for index patient to search for a rare, homozygous deleterious variant in the possibly linking regions.
Results: Whole-genome linkage analysis resulted in 25 genomic regions with LOD score above 1.50. Within the family members, all candidate regions shared homozygosity by only affected individuals. Causative variant search in linkage regions identified seven homozygous candidate variants in which five of them were located in 19q13.33. Candidate non-synonymous variants were found in *ANXA8L*, *EHBP1L1*, *MYH14*, *KCNJ14*, *SYNGR4*, *TULP2* and *SHANK1* genes.
Conclusions: This is the first whole genome linkage analysis in a TA family with recessive inheritance. Linkage and following exome sequencing analyses revealed seven possible variants that may be causative to disease. Further variant and candidate gene investigations are still in process.
References:
[1] Morishita KA, et al. Familial Takayasu arteritis – a pediatric case and a review of the literature. Pediatr Rheumatol Online J. 2011 Feb 2;9:6.
[2] Jeeva I, et al. Atypical Takayasu arteritis: a family with five affected siblings. Med Sci Monit. 2007 Aug;13(8):CS101–5.
[3] Sahin Z et al. Takayasu's arteritis is associated with HLA-B*52, but not with HLA-B*51, in Turkey. Arthritis Res Ther. 2012 Feb 6;14(1):R27.
[4] Renauer PA et al. Identification of Susceptibility Loci in IL6, RPS9/LILRB3, and an Intergenic Locus on Chromosome 21q22 in Takayasu Arteritis in a Genome-Wide Association Study. Arthritis Rheumatol. 2015 May;67(5):1361–8.
[5] Saruhan-Direskeneli G,. Identification of multiple genetic susceptibility loci in Takayasu arteritis. Am J Hum Genet. 2013 Aug 8;93(2):298–305.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6370

THURSDAY, 15 JUNE 2017

Cytokines and inflammatory mediators

THU0025 IL-6 TRANS-SIGNALING CAUSES ACCELERATED ATHEROSCLEROSIS IN DISEASE PRONE ANIMALS

R. Davies[1], H.S. Jin[1], K. Sime[1], J.O. Williams[2], C.R. Thompson[1], G.W. Jones[1], K. Allen-Redpath[1], S.A. Jones[1], T.R. Hughes[1], S. Rose-John[3], A.S. Williams[1], E.H.S. Choy[1]. *[1]Institute of Infection and Immunity; [2]Cardiff School of Biosciences, Cardiff University, Cardiff, United Kingdom; [3]Institüt of Biochemistry, Christian-Albrecht Universität, Kiel, Germany*

Background: Cardiovascular (CV) disease is a major cause of mortality in patients with rheumatoid arthritis (RA). CV risk is increased early in the disease course. Subclinical inflammation and dyslipidaemia are often seen in RA before patients become symptomatic, suggesting the presence of subclinical CV disease. Inflammation, as measured by acute phase reactants, is associated with CV disease in RA. Interleukin (IL)-6 is a major driver of the acute phase response in RA. Notably, systemic elevations in inflammatory cytokines including IL-6 correlate with CV risk. Importantly, IL-6 regulates both immune homeostasis and inflammatory processes linked with chronic disease progression. Control of these processes is regulated by two modes of IL-6 signaling; classical IL-6 receptor signaling and IL-6 trans-signaling. Cellular responses controlled by IL-6 trans-signaling are mediated via soluble IL-6 receptor (sIL-6R) and is widely considered to promote deleterious pro-inflammatory outcomes [1]. We hypothesize that atherosclerosis may predate diagnosis of RA, and is accelerated by IL-6 trans-signaling during active arthritis. Here, we investigate this hypothesis using the established ApoE-deficient (*apoE*$^{-/-}$) mouse model of atherosclerosis.
Objectives: To examine the effect of IL-6 classical and trans-signaling on atherosclerosis by administering IL-6 or Hyper-IL-6 (a IL-6: sIL-6R fusion protein) to *apoE*$^{-/-}$ mice.
Methods: Male *apoE*$^{-/-}$ mice were fed a high-fat diet for 8 weeks starting at 8 weeks of age. Mice were divided into 4 groups. Group 1 received IL-6 (160 ng twice weekly, delivered i.p.), and Group 2 and 3 received Hyper-IL-6 (500 ng and 1 μg delivered i.p. twice weekly) for 8 weeks. Group 4 received PBS twice weekly for 8 weeks. Serial transverse 7 um brachiocephalic artery cross-sections were cut and stained with haematoxylin and oil red-O. Lesion size was determined by computer-assisted morphometry, using Image J on stained sections. Brachiocephalic plaque size in mice treated with PBS, IL-6 and Hyper-IL6 were compared using ANOVA and post-hoc Tukey t test.
Results: Mice treated with Hyper-IL-6 1μg had significantly larger brachiocephalic plaques (mean plaque area 0.73±0.04 mm^2) than those administered PBS (0.018±0.01 mm^2, p <0.001), and IL-6 (0.033±0.017 mm^2, p =0.015; Fig.1A). Similarly, mice administered Hyper-IL-6 [1μg] had a significantly higher percentage of the brachiocephalic artery occupied by plaques (45.3±18.1%) compared to those administered PBS (10.38±6.7%, p <0.001) or IL-6 (20.1±10.2%, p =0.002) (Fig.1B). Mice administered Hyper-IL-6 [0.5μg] had significantly higher percentage plaque (27.7±16.2%) than PBS administered mice, p=0.015. There was no significant difference in total cholesterol, HDL, LDL, triglycerides, free fatty acids or cholesterol:HDL ratio between the groups.

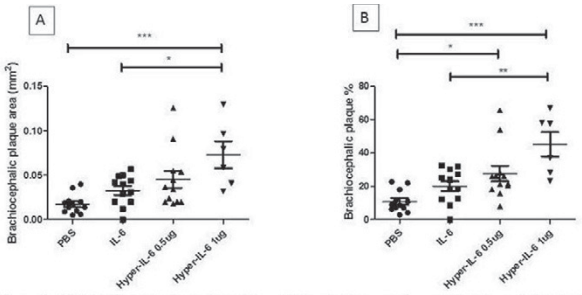


Figure1. (A) Significantly larger brachiocephalic plaque area in *apoE*$^{-/-}$ mice administered Hyper-IL-6 1μg compared to mice administered IL-6 or PBS. B) Significantly higher brachiocephalic plaque percentage in *apoE*$^{-/-}$ mice administered Hyper-IL-6 compared to PBS, and significantly higher brachiocephalic plaque percentage in *apoE*$^{-/-}$ mice administered hyper-IL-6 1μg compared to IL-6.

Conclusions: IL-6 trans-signaling leads to accelerated atherosclerosis in disease susceptible animals. This effect is independent of changes in serum lipid profiles.

References:

[1] Rose-John S. IL-6 Trans-Signaling via the Soluble IL-6 Receptor: Importance for the Pro-Inflammatory Activities of IL-6. Int. J. Biol. Sci. 2012;8(9):1237–1247.

Acknowledgements: This work was funded by Arthritis Research UK, grant number 20760.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2871

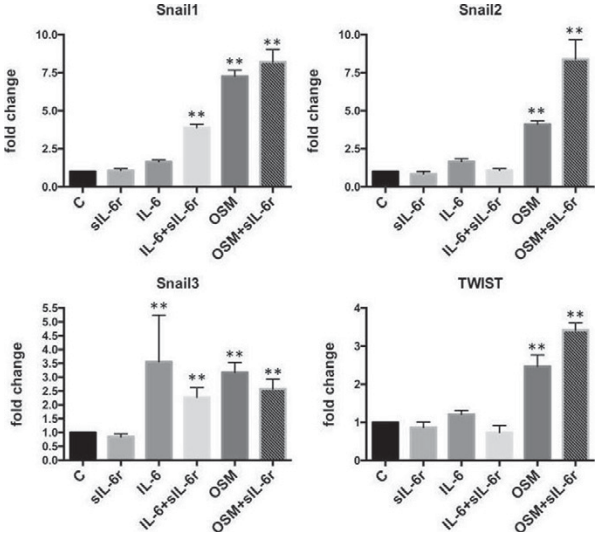
THU0026 OSM IS MORE EFFECTIVE THAN IL-6 AT INDUCING ENDOMT OF HUMAN DERMAL MICROVASCULAR CELLS

K. Nevin[1], L. Stawski[2], M. Feeney[1], N. Wisniacki[1], M. Trojanowska[2].
[1]*Immuno-Inflammation Therapeutic Area Unit, GlaxoSmithKline, Stevenage, United Kingdom;* [2]*Arthritis Centre, Boston University, Boston, United States*

Background: Oncostatin-M (OSM) and interleukin-6 (IL-6) are members of the IL-6 superfamily and signal via glycoprotein 130 (gp130). OSM signals with either the type I receptor complex, gp130/ Leukemia Inhibitory Factor Receptor (LIFR), or the type II receptor complex, gp130/OSM receptor (OSMR), whilst IL-6 signals via gp130 with the IL-6 receptor (IL-6R) or by trans signalling with soluble IL-6R (sIL6-R). Endothelial cells (ECs) express both gp130 and OSMR [Brown TJ et al 1991], however it is unclear whether ECs express IL-6R [Romano M et al 1997; Nilsson MB et al 2005]. Endothelial to mesenchymal transition (EndoMT) is the phenotypic transition of ECs into mesenchymal cells where ECs lose their specific EC markers, detach from the endothelial layer and initiate the expression of mesenchymal cell products. EndoMT is associated with vascular dysfunction, one of the early manifestations of systemic sclerosis. The role of OSM and IL-6 in EndoMT has not yet been fully elucidated.

Objectives: To determine the effect of OSM and IL-6/sIL-6R on microvascular EC migration, proliferation and EndoMT.

Methods: Human dermal microvascular ECs (HDMECs) were treated with human recombinant proteins OSM (1–100 ng/mL), IL-6 (10–100 ng/mL) and sIL-6R (10–100 ng/mL). Cell migration and proliferation were measured with Live-Cell imaging system over 50 hours and analysed using a two-way ANOVA. Secretion of Collagen type I protein was measured at 48 hours by western blot analysis of media supernatant from HDMEC cultures. Changes in VE-Cadherin and F-actin expression were examined by immunofluorescence over 72 hours.



Gene expression was measured at 3 hours using quantitative RT-PCR analysis and analysed by Student's paired T-Test.

Results: OSM and IL-6, with or without IL-6R, significantly increased ($P<0.001$, n=3 donors) HDMEC migration and proliferation and secretion of extracellular matrix (ECM) protein Collagen I compared to the control group. OSM, but not IL-6 with or without sIL-6R, reduced expression of EC marker VE-Cadherin and increased expression of elongated F-actin stress fibres (n=2 donors). OSM significantly affected ($P<0.05$, n=3 donors) expression of EndoMT genes *SNAIL1*, *SNAIL2*, *SNAIL3* and *TWIST* [Figure 1] and ECM genes *MMP1*, *MMP2 TIMP1* and *TIMP2* compared to the control. Many of the gene changes in response to OSM were further augmented by co-stimulation with sIL-6R. IL-6 with or without sIL-6R only significantly affected ($P<0.05$, n=3 donors) EndoMT genes *SNAIL1* and *SNAIL3* and ECM gene *TIMP1*.

Conclusions: OSM induced a stronger EndoMT phenotype in HDMECs in comparison to IL-6, suggesting that OSM is capable of initiating EndoMT activity in microvascular cells. The augmented effects observed for OSM with sIL-6R also suggests that OSM is capable of binding the sIL-6R and initiating signalling in HDMECs *in vitro*.

References:

[1] Brown TJ, Rowe JM, Liu JW and Shoyab M. Regulation of IL-6 expression by oncostatin M. J Immunol 1991:147:2175–2180.

[2] Nilsson MB, Langley RR and Fidler IJ. Interleukin-6, secreted by human ovarian carcinoma cells, is a potent proangiogenic cytokine. Cancer Res 2005:65:10794–10800.

[3] Romano M, Sironi M, Toniatti C, Polentarutti N, Fruscella P, Ghezzi P, Faggioni R, Luini W, van Hinsbergh V, Sozzani S, Bussolino F, Poli V, Ciliberto G, and Mantovani A. Role of IL-6 and its soluble receptor in induction of chemokines and leukocyte recruitment. Immunity 1997:6:315–325.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1271

THU0027 CLUSTERIN IS ELEVATED IN SERUM AND MUSCLE TISSUE IN IDIOPATHIC INFLAMMATORY MYOPATHIES AND IS ASSOCIATED WITH DISEASE ACTIVITY

T. Lennerová, L. Vernerová, M. Klein, M. Tomčík, H. Mann, V. Hrušková, K. Pavelka, J. Vencovský, L. Šenolt. *Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic*

Background: Clusterin (also known as apolipoprotein J) is a molecular chaperone that participates in inflammatory and apoptotic processes. Recent data indicate its possible protective role in the development of chronic autoimmune disorders.

Objectives: The aim of this study was to analyse the skeletal muscle expression of clusterin and its serum levels in patients with idiopathic inflammatory myopathies (IIM) and in healthy donors, and to examine the association of clusterin with disease activity.

Methods: Clusterin mRNA expression in skeletal muscle specimens, obtained by muscle biopsy (mini-invasive Bergstrom technique), was determined using qPCR in 10 patients with IIM and 10 healthy subjects. Serum concentrations of clusterin were measured by ELISA (Biovendor) in 65 patients with IIM (27 dermatomyositis (DM), 28 polymyositis (PM), 10 immune-mediated necrotizing myopathy (IMNM)) and in 54 healthy individuals. Disease activity was assessed using myositis intention to treat index (MITAX), myositis disease activity assessment visual analogue scales (MYOACT), health assessment questionnaire (HAQ) and global disease assessment evaluated by doctor and patient. Data are presented as mean ± SD.

Results: Clusterin mRNA expression in skeletal muscles was increased in patients with IIM compared to healthy donors (p=0.029). In addition, serum clusterin levels were significantly higher in all IIM patients than in healthy subjects (87.1±22.8 vs 68.4±12.4, $p<0.0001$) and also in individual subsets of patients in comparison to the control group (DM: 87.7±24.7, PM: 86.1±23.2, IMNM: 88.15±18.0, $p<0.0001$ for all). Clusterin levels in all patients with IIM positively correlated with MYOACT (r=0.337, p=0.008), MITAX (r=0.357, p=0.004) and global disease assessment evaluated by doctor (r=0.309, p=0.015). In patients with DM, positive correlations with MYOACT (r=0.499, p=0.009), MITAX (r=0.491, p=0.009), HAQ (r=0.470, p=0.014), global disease assessment evaluated by doctor (r=0.559, p=0.004), γ-glutamyl transpeptidase and asparate aminotransferase were found (r=0.504, p=0.007; r=0.429, p=0.025, respectively). PM and IMNM subsets showed no significant association.

Conclusions: We demonstrate increased local and systemic expression of clusterin in IIM patients compared to healthy individuals and its association with disease activity, especially in dermatomyositis.

Acknowledgements: Supported by the project of MHCR for conceptual development of research organization 00023728 and project NV16–33746A.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5792

THU0028 TYPE I INTERFERON SIGNATURE IN THE PERIPHERAL BLOOD AND CXCL4 PLASMA LEVELS IN PATIENTS WITH SYSTEMIC SCLEROSIS

N.I. Vlachogiannis, V.-K. Bournia, A. Nezos, P.F. Christopoulos, M. Patsouras, P.G. Vlachoyiannopoulos, C.P. Mavragani, P.P. Sfikakis. *Joint Academic Rheumatology Program, National and Kapodistrian University of Athens Medical School, Athens, Greece*

Background: Type I Interferon (IFN) pathway is activated in Systemic Sclerosis (SSc) and represents a therapeutic target currently being tested in clinical trials, while higher IFNα levels have been also associated with pulmonary fibrosis in these patients. On the other hand, *in vitro* experiments using plasmacytoid dendritic cells from patients with SSc suggest an interplay between the chemokine (C-X-C motif) ligand 4 (CXCL4), a potential biomarker in SSc, and type I IFN. [1]
Objectives: To test the hypothesis that type I IFN-induced gene expression in the peripheral blood associates with particular clinical and laboratory features, including plasma CXCL4 levels, in patients with SSc.
Methods: Forty six patients with limited and 19 with diffuse SSc (60/65 women, aged 54±14 years, disease duration ranging between 0.5–27 years) and 20 healthy controls were examined. Peripheral whole blood samples (3ml) were subjected to cDNA synthesis and the expression of 3 genes (IFIT1, MX1, IFI44) that are preferentially induced by type I IFN was quantified by real time PCR. Type I IFN individual scores were calculated as described [2]; scores were arbitrarily considered as high when exceeding the mean value plus 3SD of the corresponding healthy control scores. Plasma CXCL4 levels were determined by ELISA.
Results: A high type I IFN score (i.e.>8) ranging from 8.4 to 145 was found in 21/65 (32.3%) patients with SSc, compared with none of 20 healthy controls (p:0.002). SSc patients with high type I IFN scores demonstrated higher erythrocyte sedimentation rate and lower diffusing lung capacity for carbon monoxide (DLCO) levels than the remaining patients (p:0.002 and p:0.02, respectively, by Mann-Whitney U test). Other disease variables, including extent of skin involvement and autoantibodies, were not associated with high type I IFN score. Individual type I IFN scores positively correlated with the corresponding CXCL4 plasma levels (Spearman's r: 0.53, p-value: 0.02).
Conclusions: A prominent type I IFN signature was observed in the peripheral blood of one third of patients with SSc in association with upregulated inflammatory response, reduced DLCO levels and higher CXCL4 plasma levels. Further prospective data are required to establish the role of type I IFN as an additional novel biomarker in SSc.
References:
[1] van Bon L, Affandi AJ, Broen J, et al. Proteome-wide analysis and CXCL4 as a biomarker in systemic sclerosis. N Engl J Med 2014;370:433–43. doi:10.1056/NEJMoa1114576.
[2] Nezos A, Gravani F, Tassidou A, et al. Type I and II interferon signatures in Sjogren's syndrome pathogenesis: Contributions in distinct clinical phenotypes and Sjogren's related lymphomagenesis. J Autoimmun 2015;63:47–58. doi:10.1016/j.jaut.2015.07.002.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4066

THU0029 BACTERICIDAL/PERMEABILITY-INCREASING PROTEIN DOWNREGULATES THE INFLAMMATORY RESPONSE TO PATHOGENIC CRYSTALS IN VITRO AND IN VIVO

A. Scanu[1], R. Luisetto[2], F. Oliviero[1], P. Galozzi[1], R. Ramonda[1], L. Punzi[1]. *[1]Rheumatology Unit, Dept. of Medicine, University of Padova; [2]Dept. of Surgical Oncological and Gastroenterological Sciences, Padova, Italy*

Background: Bactericidal/permeability-increasing protein (BPI) is a cationic protein mainly produced by polymorphonuclear cells (PMN) which exerts an antimicrobial activity by damaging bacterial membranes and interacts with specific cell surface receptors, such as toll-like receptors (TLRs). BPI has been detected in synovial fluid of patients with different arthritis, including crystal-induced arthritis.
Objectives: To evaluate the effects and mechanisms of action of BPI in *in vitro* and *in vivo* models of crystal-induced inflammation.
Methods: The human monocytic cell line THP-1 was primed for 3 h with phorbole myristate acetate (300 ng/ml), reincubated overnight, and treated with sterile synthetic monosodium urate (MSU) (0.5 mg/ml) or calcium pyrophosphate (CPP) (0.1 mg/ml) crystals for 24 h in presence or absence of BPI (5 μ g/ml). In some experiments, cells or crystals were pretreated with BPI for 2 h before stimulation. BPI inhibition experiments were carried out with antibody against TLR2 or TLR4. Cell supernatants were tested by ELISA for interleukin (IL)-1β and IL-8 production. Chemotactic effect of culture supernatants was evaluated in chemotaxis chamber by the migration of freshly isolated peripheral blood PMN.
As regard the study in vivo, air pouches were raised on the backs of CD1 mice (n=7 per condition). 2 mg of MSU crystals in 1 ml of PBS were injected into the pouch in the presence or absence of 0.1 mg of BPI for 3 h. Controls received 1 ml of PBS. After the sacrifice, pouch fluids were recovered by washing with 2 ml of PBS. Leukocyte count in lavage fluids was obtained using a hemocytometer and the percentage of PMN was determined by May-Grünwald-Giemsa staining. IL-1β, chemokine (C-X-C motif) ligand 1 (CXCL1) and IL-6 levels were measured in exudates by ELISA.
Results: Exposure of THP-1 cells to different types of crystals increased the production of IL-1β (MSU: 406.62±12.00 pg/ml; CPP: 357.07±25.17 pg/ml) and IL-8 (MSU: 3798.56±24.64 pg/ml; CPP: 3427.74±22.33 pg/ml). The release of both cytokines induced by crystals was significantly diminished in the presence of BPI (76% IL-1β, 58% IL-8), and tended to be more pronounced when cells, but not crystals, were pretreated with the protein (90% IL-1β, 65% IL-8). The presence of antibody anti-TLR2 or anti-TLR4 did not affect the BPI inhibitory effect. Supernatants of crystal-stimulated cells increased the migration of PMN cells which was reduced in the presence of BPI.
The injection of MSU crystals into the subcutaneous pouches of mice induced leukocyte infiltration (10.2±3.39 x 10^5 cells/ml) comprising 68.6±8.75% of PMN. IL-1β (32.33±6.35 pg/ml), CXCL1 (467.07±27.47 pg/ml) and IL-6 (624.61±29.41 pg/ml) were measured in lavage fluids. The co-injection of MSU crystals and BPI inhibited leukocyte influx by 60% and PMN infiltration by 87% and, in turn, the levels of all assessed cytokines were reduced (81% IL-1β, 70% CXCL1, 35% IL-6).
Conclusions: This study shows that BPI reduces the crystal-induced inflammatory process *in vitro* and *in vivo* by inhibiting pro-inflammatory cytokine release and PMN recruitment. The mechanism of action of BPI may include the direct interaction with activated cells in a TLR-independent manner.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4865

THU0030 IL-2IC SUPPRESSES CIA IN MICE BY THE TH1/TH17 IMMUNE RESPONSES DUE TO ENHANCEMENT OF BOTH TREG NUMBERS AND TREG FUNCTIONS

Y. Yokoyama[1], T. Iwasaki[2], S. Kitano[1], T. Furukawa[1], A. Satake[3], K. Matsui[1], H. Sano[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, Hyogo; [2]Department of Pharmacy, Hyogo University of Health Sciences, Kobe; [3]1st Department of Internal Medicine, Kansai Medical University, Hirakata, Japan*

Background: Interleukin-2 (IL-2) induces regulatory T cells (Tregs) and reduces disease activity such as graft versus-host disease and systemic lupus erythematosus. IL-2/anti-IL-2 monoclonal antibody immune complex (IL-2IC) increases the half-life of IL-2 *in vivo* and specifically induces Tregs. We previously demonstrated that administration of IL-2IC suppressed collagen-induced arthritis (CIA) in mice (EULAR 2015).
Objectives: To clarify complex regulatory network of IL-2IC in autoimmune arthritis, we examined the suppression mechanism of IL-2IC induced Tregs to Th1 and Th17.
Methods: Male DBA/1 mice were immunized by injection of 200μg of Type II collagen emulsified with an equal volume of complete Freud adjuvant intradermally at the base of the tail of mice (first immunization). Second immunization was given 21 days after first immunization. IL-2ICs were prepared by mixing 5μg of anti-IL-2 antibody (clone JES6–1D) with 1μg of mouse IL-2 for 15 minutes. The mice were injected with either PBS as a control or IL-2IC (5μg /mouse) intraperitoneally for 3 days. Mouse paws were scored for arthritis using a macroscopic scoring system ranging from 0 to 4 (0, no swelling or redness; 1, swelling/redness of paw or one joint; 2, two joints involved; 3, more than two joints involved; and 4, severe arthritis of the entire paw and joints). The arthritic score for each mouse is the sum of the scores of all four paws. Peripheral blood cells were stained with anti-CD25 (PC61), anti–CD4 (RM4–5), anti-Foxp3 (FJK-16s) and CD4+CD25+Foxp3+ Tregs were analyzed by flow cytometry. Th1 and Th17 cells infiltrating in the synovium were examine by immunohistochemistry stained with anti-IFN-g and IL-17 mAb. CD4+CD25+ Treg cells were analyzed for suppressive activity against proliferation of effector CD4+ T cells. For intracellular cytokine staining, spleen cells which were removed in day 28, were stimulated with PMA, ionomycin, and breferdin for 6 hours and intracellular cytokine staining were performed by using anti-IFN-γ, anti-IL-10, anti-IL-17, and analyzed by flow cytometry.
Results: To define the effects of IL-2IC on established CIA, IL-2IC was administered for 3 days from day 21 to day 23 after the first immunization (day 0 to day 2 after the second immunization) of CIA. To define the effect of IL-2IC on early stages of disease induction we administered IL-2IC from day 0 to day 2 after first immunization. We observed a significant decrease in both the incidence and severity of arthritis in these CIA mice. Injection of IL-2IC effectively elicited more than 2-fold expansion of CD4+CD25+Foxp3+ Tregs in peripheral blood cells than control mice. Th1 and Th17 cells infiltrations in the synovium were significantly inhibited by IL-2IC treatment. *In vitro* suppression assay demonstrated significant augmentation of the suppressive capacity of CD4+CD25+Treg cells in IL-2IC treated mice. Intracellular cytokine staining revealed that IL-10 production by CD4+ cells in IL-2IC treated spleen increased four folds than in controls, and IFN-γ-producing helper T cells (Th1) and IL-17-producing helper T cells (TH17) were significantly decreased.
Conclusions: These observations indicate that IL-2IC not only induce Tregs, but also augments Treg function by enhancing IL-10 production. Thereby Tregs suppress Th1 and Th17 cells.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4644

THU0031 THERAPEUTIC TREATMENT OF ANTI-FRACTALKINE MONOCLONAL ANTIBODY INHIBITS JOINT DESTRUCTION IN COLLAGEN-INDUCED ARTHRITIS MODEL

K. Hoshino-Negishi[1], M. Ohkuro[2], T. Nakatani[1], W. Ikeda[1], Y. Kuboi[1], N. Ishii[1], T. Yamauchi[1], N. Yasuda[1], T. Imai[1]. *[1]Research & Development, KAN Research Institute. Inc., Kobe-Shi; [2]Research Project Promotion Group, EA Pharma Co., Ltd., Kawasaki-ku, Japan*

Background: In the Phase 1/2 clinical study, E6011, a novel humanized anti-fractalkine (FKN) monoclonal antibody (mAb) demonstrated a promising efficacy in active rheumatoid arthritis (RA) patients who were inadequately controlled by MTX and/or TNF-a inhibitors. However, the effect of anti-FKN mAb on joint destruction remains to be elucidated. In RA, synovium-infiltrated monocytes/macrophages cause synovitis and cartilage damage. Osteoclasts are generated from osteoclast precursor cells (OCPs) and cause bone erosion. FKN is expressed on endothelial cells and fibroblast-like synoviocytes in synovium in both experimental arthritis model and RA patients. FKN is also expressed on osteoblasts in neonatal mouse calvariae. CX3CR1, the receptor for FKN, is expressed on monocytes/macrophages and OCPs. Therefore, the interaction of FKN and CX3CR1 might play important roles in migration, differentiation and activation of these cells, leading to cartilage damage and bone erosion.
Objectives: We examined the efficacy of an anti-FKN mAb on collagen-induced arthritis (CIA) in mice, especially on joint destruction.
Methods: For the induction of CIA, DBA/1J mice were immunized with bovine type II collagen. Anti-FKN mAb or control IgG was injected twice a week from the day of the 1st immunization (for the prophylactic treatment) or after the onset of CIA (for the therapeutic treatment). The clinical arthritis score was defined as the sum of the scores of four paws. Plasma concentrations of IL-6, TNF-a, serum amyloid A (SAA), Tartrate-Resistant Acid Phosphatase type 5b (TRAP-5b), Cartilage Oligomeric Matrix Protein (COMP) and Matrix Metalloproteinase 3 (MMP-3) were measured using ELISA. Radiological score was measured by the soft x-ray images of limb bones. Alcian blue/Alizarin red and Tartrate-Resistant Acid Phosphatase (TRAP) staining were performed for histopathological analysis of ankle joints.
Results: In the prophylactic treatment, anti-FKN mAb markedly reduced the clinical arthritis score, soft x-ray score, and plasma levels of TRAP-5b, COMP and MMP-3, whereas plasma levels of IL-6, TNF-a and SAA were not significantly reduced compared with control IgG-treated mice. Histopathological analysis demonstrated almost complete suppression of joint destruction and dramatic reduction in the number of TRAP-positive cells by the treatment of anti-FKN mAb. Importantly, therapeutic treatment of anti-FKN mAb also significantly ameliorated clinical arthritis score and soft x-ray score. Synovitis, pannus formation, cartilage degradation and bone erosion were also strongly suppressed and the number of TRAP-positive cells in joint was also decreased by the therapeutic treated of anti-FKN mAb.
Conclusions: Anti-FKN mAb demonstrated a remarkable efficacy in the arthritis score without affecting systemic inflammatory parameters and inhibited the joint destruction with the marked reduction of osteoclasts in CIA model. These results suggest that inhibition of FKN/CX3CR1 axis by a humanized anti-FKN mAb, E6011, is an attractive therapeutic strategy for the treatment of both inflammatory synovitis and joint destruction of RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3599

THU0032 THE ROLE OF S100A9 IN PAIN RESPONSE DURING EXPERIMENTALLY INDUCED ACUTE SYNOVITIS

E.J.W. Geven, E.N. Blaney-Davidson, E.L. Vitters, A.W. Sloetjes, B. Walgreen, A.B. Blom, P.L.E.M. van Lent. *Experimental Rheumatology, Radboud university medical center, Nijmegen, Netherlands*

Background: Synovitis-associated pain is an important aspect of arthritis pathology. Several inflammatory mediators released by the synovium have been implicated in the regulation of pain, including S100A8 and S100A9 which may regulate pain either via direct stimulation of TLR4 on the nerve endings in the synovium or via stimulation of the dorsal root ganglia (DRG), thereby enabling an increased phagocyte infiltration.
Objectives: To investigate the role of S100A9 in the pain response after induction of an acute synovitis using streptococcal cell walls (SCW) as a trigger, comparing $S100A9^{-/-}$ mice and their WT controls.
Methods: Acute synovitis was induced by a single i.a. injection of SCW in the knee joint of C57Bl6 (WT) mice and $S100A9^{-/-}$ mice, control mice received an i.a. saline injection. Serum S100A8/A9 levels were investigated by ELISA and expression of S100A8 and S100A9 in synovium and DRG by immunohistochemistry. Joint swelling and cell influx was assessed by ^{99m}Tc accumulaiton and histology, respectively. Pain response were investigated Incapacitance Tester (weight bearing), Catwalk (gait analysis) and von Frey's filaments (mechanical allodynia). Gene expression of inflammatory mediators and neuron activation markers in DRG were determined by q-PCR.
Results: A single i.a. injection of SCW resulted in increased synovial expression of S100A8 and S100A9 and subsequent increased serum S100A8/A9 levels (2.6-fold, $P<0.001$) 1 day p.i., which returned to basal levels at 7 days p.i. The increased expression of S100A9 did not contribute to the development of inflammation since joint swelling and cell influx were similar in WT and $S100A9^{-/-}$ mice 1 day p.i. Using the Incapacitance Tester, WT mice showed a marked and significant decrease in percentage of weight bearing on the SCW injected hindpaw (28%) compared to saline injection (47%, $P<0.001$) 1 day p.i., whereas $S100A9^{-/-}$ mice did not. In addition, gait analysis showed that the stand-phase of the unaffected paws were significantly increased in WT mice 1 day p.i., which will reduce the load on the inflamed paw, while in $S100A9^{-/-}$ mice these parameters were not altered. No difference in mechanical allodynia was observed, both mouse strains showed a similar reduction of paw withdrawal threshold (4.2 and 4.5 fold decrease respectively). Analysis of DRG showed no increased phagocyte infiltration after SCW injection as determined by S100A8 and S100A9 immunohistochemistry and no change in gene expression of MCP-1, KC, IL-1β or TNF was measured. However, expression of neuron activation markers NAV1.7, ATF3 and GAP43 were significantly increased at 1 day after SCW injection in WT mice as compared to saline injected mice (P =0.022, 0.004 and 0.030, respectively) while SCW injection in $S100A9^{-/-}$ mice did not show increased expression, which is in line in with the reduced pain response observed earlier in $S100A9^{-/-}$ mice.
Conclusions: These findings show that S100A9, which is released from the synovium upon inflammation, is an important mediator of inflammatory pain response in the knee, and that during the acute phase of inflammation is likely regulated via direct activation of TLR4 on nerve endings in the synovium and not via increased infiltration of phagocytes in the DRG.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5800

THU0033 LOCAL INJECTION OF ADIPOSE-DERIVED MESENCHYMAL STROMAL CELLS IN EXPERIMENTAL INFLAMMATORY OA RESULTS IN INTERLEUKIN-1β-MEDIATED ATTRACTION OF PMNS AND REDUCED S100A8/A9 RELEASE

S. van Dalen, A. Sloetjes, M. Helsen, B. Walgreen, E. Geven, P. van Lent. *Experimental Reumatology, Radboud university medical center, Nijmegen, Netherlands*

Background: Recent studies have shown that mild synovitis in early phases of osteoarthritis (OA) is conducive to development of joint damage. OA synovitis is characterized by elevated levels of pro-inflammatory factors like S100A8, S100A9, interleukin-6 (IL-6), and interleukin-1 beta (IL-1β). S100A8/A9 was found to be crucial in mediating joint destruction in inflammatory experimental OA. Previously we found that adipose-derived mesenchymal stromal cells (ASCs) exhibit immunosuppressive characteristics and reduce joint pathology after local application into mouse knee joints with experimental inflammatory OA. This protective effect is only perceived after intra-articular injection in early but not late stage OA, suggesting that the effect may be mediated by an inflammatory milieu.
Objectives: To examine the working mechanism of ASCs after early injection in experimental OA.
Methods: Experimental OA was induced by injection of collagenase into murine knee joints (CiOA). Total knee joints were stained with haematoxylin/eosin and the PMN-specific antibody NIMP-R14. ASCs were isolated from murine adipose tissue and stimulated for 24h with IL-1β or S100A8/A9. Gene expression in stimulated cells was analyzed using qPCR. Protein levels of chemokines and cytokines were measured in culture supernatant using Luminex. Migration of MACS isolated bone marrow (BM-) PMNs towards ASC-conditioned medium (CM) was examined using Transwell inserts. ASCs were co-cultured with BM-PMNs and analyzed using histology and Luminex.
Results: ASC injection into day 7 CiOA knee joints (when synovitis and IL-1β and S100A8/A9 levels are highest) caused a strong attraction of mainly PMN-like cells and their clustering around ASCs in the synovium shortly after injection (6h), which was confirmed by immunohistochemistry. IL-1β stimulation of ASCs in vitro strongly increased gene expression of PMN-attracting chemokines KC, CXCL5, and CXCL7 as well as protein levels of KC, whereas S100A8/A9 did not. The migration of BM-PMNs through Transwell inserts towards CM of IL-1β-stimulated ASCs was significantly increased (from 5% to 10%) when compared to CM of non-stimulated ASCs. Next, ASCs were co-cultured with BM-PMNs in the presence or absence of IL-1β. After 6h, a clear clustering of neutrophils around ASCs was observed, with a significant increase in the number of ASCs clustering with PMNs, as well as a significantly elevated number of clustering PMNs per ASC after IL-1β stimulation. Interestingly, association of PMNs with ASCs lead to a significantly lowered release of KC protein by ASCs (69% and 76% lower after 24h and 48h respectively), as well as a significantly reduced release of S100A8/A9 protein by the PMNs. This coincided with lowering of S100A8/A9 levels in washouts of inflamed synovium 6h and 48h after injection of ASCs in day 7 CiOA knee joints.
Conclusions: Local application of ASCs in inflamed CiOA knee joints results in attraction and clustering of PMNs with ASCs in the synovium. This presumably runs via IL-1β-mediated up-regulation of chemokine release by ASCs, and ultimately results in significantly lowered S100A8/A9 levels.
Acknowledgements: This research was supported by the Dutch Arthritis Association.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5841

THU0034 THE INFLAMMATORY POTENTIAL OF CALCIUM PYROPHOSPHATE CRYSTALS DEPENDS ON THEIR CAPACITY TO INDUCE NF-κB AND MAPK PATHWAYS

F. Renaudin[1,2], L. Campillo-Gimenez[1], P. Gras[3], C. Combes[3], M. Cohen-Solal[1,4], F. Lioté[1,4], H.-K. Ea[1,4]. *[1]UMR1132, Bioscar, Inserm; [2]University Paris Diderot, Paris; [3]Ensiacet, CIRIMAT, Inpt-Ups-CNRS, Toulouse; [4]Pôle locomoteur, Service de Rhumatologie, centre Viggo Petersen, AP-HP, Hôpital Lariboisière, Paris, France*

Background: Calcium pyrophosphate (CPP) crystal-induced inflammation is mainly driven by interleukin (IL)-1β. IL-1β production involves a two-step process including the formation of pro-IL-1β through NF-κB activation and its maturation inti active IL-1β through NLRP3 inflammasome activation. Two CPP crystal phases, namely monoclinic and triclinic CPP dehydrated (m- and t-CPPD) crystals are identified in synovial fluids. We have recently demonstrated that m- and t-CPPD display different inflammatory potentials marked by a differential level of IL-1β production and other pro-inflammatory mediator expression.
Objectives: We aimed to assess the intracellular pathways upstream CPP crystal-induced IL-1β production, according to the different inflammatory properties of CPP crystal phases.
Methods: Four synthesized and pyrogen-free CPP crystals [a-CPP (amorphous), m-CPPD or tetrahydrated (m-CPPT) and t-CPPD] (Gras P et al. 2014) and monosodium urate (MSU) crystals were used, *in vitro*, to stimulate THP-1 cell line or mouse bone marrow-derived macrophages (BMDM) in the presence or not of pharmacological inhibitors: Bay-117085 (Bay, NF-κB inhibitor); SB203580 (SB, MAPK p38 inhibitor); SP600125 (SP, JNK inhibitor) and PD98059 (PD, p42/44 MAPK inhibitor). The expression of pro- and anti-inflammatory cytokine genes was assessed by qRT-PCR, and IL-1β or IL-8 production by ELISA; MAPK phosphorylation by immunoblot. NF-κB activation was quantified in THP-1 cells containing a gene reporter plasmid under control of NF-κB transcriptional factor. *In vivo*, we used murine air pouch model to assess the effects of NF-κB inhibition in CPP crystal-mediated inflammation.
Results: We previously demonstrated that *in vitro* m-CPPD crystals were the most inflammatory CPP crystals and induced a higher production of mature IL-1b associated to a higher expression of NLRP3 protein, and a higher IL-8 production and expression of inflammatory cytokine genes (IL-1β, IL-6, IL-8, IL-33, TNF, COX-2) than t-CPPD, m-CPPT and MSU crystals. a-CPP crystals did not have inflammatory property. m-CPPD crystals induced a higher NF-kB activation and a higher phosphorylation p38, p42/44 and JNK MAPKs than t-CPPD and MSU crystals. In parallel, we showed that inhibition of NF-κB completely abrogated mature IL-1b and IL-8 secretion and pro-IL-1β synthesis induced by all CPP crystals. Inhibition of JNK and p42/44 MAPK with SP and PD respectively, decreased both IL-1β secretion and NF-κB activation induced by CPP crystals. *In vivo* IL-1β and IL-8 production and neutrophil infiltration induced by m-CPPD crystals were dramatically decreased by NF-κB inhibitor.
Conclusions: Our results showed that IL-1β and IL-8 production induced by CPP crystals is completely dependent of NF-κB signaling. They suggested that the inflammatory potential of different CPP crystals relied on their capacity to activate both MAPK and NF-κB pathways. Differential level of NF-κB activation is partially dependent of MAPK phosphorylation. Additional studies are ongoing to investigate the underlying mechanisms.
References:
[1] Gras P et al Structure of the calcium pyrophosphate monohydrate phase (Ca2P2O7.H2O): towards understanding the dehydration process in calcium pyrophosphate hydrates. Acta Crystallogr C Struct Chem. 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4741

THU0035 CYTOKINE PROFILING OF AQUEOUS HUMOR IN BEHÇET'S DISEASE PATIENTS WITH ACTIVE OCULAR INVOLVEMENT

A. Soriano[1,2], S. Croci[3], L. Cimino[4], M. Bonacini[3], E. Calò[3], A. Zerbini[3], M. Parmeggiani[3], L. Fontana[4], C. Salvarani[5]. *[1]Department of Internal Medicine, Rheumatology Unit, Arcispedale Santa Maria Nuova - IRCCS, Reggio Emilia, Italy, Reggio Emilia; [2]Campus Bio-Medico University of Rome, Rome; [3]Clinical Immunology, Allergy and Advanced Biotechnologies Unit; [4]Ocular Immunology Unit; [5]Department of Internal Medicine, Rheumatology Unit, Arcispedale Santa Maria Nuova – IRCCS, Reggio Emilia, Italy*

Background: Behçet's disease (BD) is a systemic inflammatory disorder with unknown etiology. Uveitis and retinal vasculitis occur in 60–80% of patients during the disease course. Previous data on cytokine profiling in aqueous humor (AH) of patients with active BD-related uveitis suggested that both T helper (Th) 1 and Th17 cells are involved in immunopathogenesis [1]. Furthermore, higher levels of Natural Killer T (NKT) cells (CD3+ CD56+) have previously been found in AH of patients with BD-related uveitis as compared to other types of uveitis [2]. However, data on magnitude and patterns of cytokines in BD-related uveitis remain scarce.
Objectives: To examine cytokine production as well as frequency of NK and NKT cells in AH from BD patients with active uveitis as compared to patients with active Vogt-Koyanagi-Harada (VKH) disease-related uveitis.
Methods: AH from 8 adult patients with BD (1990 ISGB criteria [3]) and active uveitis, and from 7 patients with active VKH were analyzed. Definition of "active" uveitis included ≥2 cells in the anterior chamber (Hogan scale, 1950) and/or 2+ vitritis (Nussenblatt scale, 1990), papillitis, macular edema and retinal vasculitis with active "photo fundus". AH from 5 subjects undergoing cataract surgery were included as controls. Cytokines' concentrations were determined with Bio-Plex Pro-Human cytokine 27-plex assay. Frequency of NK and NKT cells was determined by flow cytometry using anti-CD3, -CD56, -CD16 antibodies.
Results: Higher levels of IL-1b, IL-1RA, IL-5, IL-7, IL-6, G-CSF, IFN-g, IP-10, TNF-a IL-8 and MIP1a were found in AH from patients with BD and VKH compared to controls. G-CSF and IFN-g were detected in AH from BD and VKH patients, but not in the control group. Lower levels of GM-CSF were found in BD and VKH patients, while IL-6 levels were 3000-fold increased, as compared to controls. No differences were detected between BD and VKH patients in terms of cytokine levels. However, AH from 4 BD patients showed a peculiar distinct cytokine pattern, when analyzed by unsupervised cluster analysis. Intriguingly, a higher amount of neutrophils/mL was found in AH from these 4 BD cases. Frequency of NKT (CD3+ CD56+) cells was higher in BD patients as compared to VKH, while that of NK (CD56+ $CD3^{neg}$) cells was similar and that of T cells ($CD56^{neg}$CD3+) was lower. Finally, no difference was found between NK subsets in terms of proportion of CD16+ cells in both BD and VKH groups.
Conclusions: AH of both BD and VKH groups showed increased levels of IL-6, G-CSF and IFN-g, which might suggest their potential role in the immunopathogenesis of these types of endogenous uveitis. However, a distinct cytokine profile able to distinguish the two conditions remains to be identified. Additionally, our preliminary results confirm the previous observation of increased NKT cells levels in BD uveitis as compared to VKH.
References:
[1] El Asrar A.M., et al. Clin Immunol 2011;139:177–84.
[2] Yu H.G., et al. Clin Exp Immunol 2004;137:437–443.
[3] International Study Group for Behçet's Disease. Lancet 1990;335:1078–80.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6635

THU0036 ROLES OF IL-8 IN RANK-L- AND ACPA-MEDIATED OSTEOCLASTOGENESIS

A. Cîrciumaru, Y. Liu, A. Krishnamurthy, S.M. Mia, V. Joshua, M. Engström, V. Malmström, M. Sun, H. Wähämaa, B. Rethi, A. Catrina. *Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Sweden*

Background: We have shown previously in various experimental models that anti-citrullinated protein antibodies (ACPAs) can contribute to bone erosion and arthralgia through IL-8 dependent mechanisms.
Objectives: In cell cultures osteoclasts (OCs) played a prominent role in the ACPA-induced IL-8 secretion and therefore we decided to characterize in detail the autocrine regulation of OC differentiation by IL-8 in the presence or absence of ACPAs.
Methods: Peripheral blood CD14-positive monocytes were used to generate OCs in the presence of M-CSF and RANKL. Expression levels of IL-8 and CXCR1/2 were monitored during OCs maturation using intracellular flow cytometry, cytometric bead array, immunohistochemistry and RT-PCR. Inhibition of IL-8 and its receptors were performed in OC cultures using IL-8 neutralizing antibodies and small molecule CXCR1 and CXCR2 antagonists (Reparixin, SB-332235), in the presence or absence of polyclonal ACPAs. OC numbers were counted using light microscope after TRAP staining.
Results: Macrophages and developing OCs secreted high levels of IL-8 in response to the cytokine M-CSF. IL-8 expression kinetic was characterized by transient peaks when new cytokine was added, followed by very low level of steady-state production. In the presence of ACPAs IL-8 production increased 3–4 fold during late phases of OC differentiation. With the help of IL-8 neutralizing antibodies or inhibitors acting on the IL-8 binding chemokine receptors CXCR1 and CXCR2 we showed that the M-CSF induced IL-8 plays a crucial role in OC differentiation in the presence of exogenous RANK-L. In the presence of ACPAs OC differentiation was further enhanced in response to the ACPA-mediated increase in IL-8 production. The CXCR1 and CXCR2 inhibitors Reparixin and SB-332235 significantly inhibited the RANKL-mediated osteoclastogenesis at 100μM and 10μM respectively, both in the presence or absence of ACPAs. By using the inhibitors at low concentrations we could counteract the ACPA-mediated increase in OC development without interfering with steady state OC differentiation.
Conclusions: Our findings further support an important role for IL-8 in bone biology and in the ACPA-mediated OC differentiation both under physiological conditions and in the presence of ACPAs. Together with previous data showing in vivo, our data indicated that small molecule CXCR1 and CXCR2 antagonists could provide novel therapeutic tools for targeting OCs in ACPA+ individuals.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6886

THU0037 IMMUNOGENICITY IN A TERTIARY CARE HOSPITAL: OUR EXPERIENCE

A.G. Valle[1], M. Garijo Buffort[2], M. Retuerto Guerrero[2], C. Iñiguez[2], E. Díez[2], C. Moriano[2], A. López[2], M. Martín[2], C. Álvarez[2], T. Pérez Sandoval[2].
[1]Rheumathology, Hospital Can Misses, Ibiza; [2]Rheumathology, Complejo Asistencial Universitario, León, Spain

Background: The drugs called Anti-TNF inhibitors are capable of inducing an immune response (immunogenicity) Its effectiveness may be affected by the development of Anti-Drug Antibodies (Ab)
Objectives:
- To assess the frequency of appearance of Anti-Drug Antibodies: Infliximab (IFX), Adalimumab (ADA), etanercept (ETN)
- To classify the failures of response
- To analyse the relationship between anti-TNFα antibodies and concomitant treatment with DMARDs
- To observe whether there is a link between risk factors and drug levels

Methods: This is a retrospective, descriptive, observational study of patients with Rheumatoid Arthritis (RA), Spondyloarthritis (SpA), Psoriatic arthritis (PsA), Seronegative arthritis (SA) and Enteropathic arthritis (EA) with active disease and that were treated in the "University Health Care Hospital of León" between Jan-2015 and Jan-2016. Using ELISA Technology and the kits Promonitor®, it was possible to detect serum levels of IFX ADA, ETN (reference values>2.5μg/mL, 5–8μg/mL and 0.8–1.2μg/mL respectively) and of anti-drug antibodies. The samples were collected the same day of the administration, prior to it, always in a trough level. The gathered data was: demographic data, activity, time-to-disease progression, prior treatment with biologics, concomitant DMARDs, duration of the biologic treatment and dosage, quantization levels, anti-TNF antibodies, cardiovascular risk factors (CVRF) and smoking habits.
Results: Variables to study:
N=40: IFX 50%, ADA 30%, ETN 20%.
Age 53.6±3.7 years old [95% CI], Women: 55%, time-disease progression: 12.3±2.7 years old.
Type of disease: RA 47.5%, SpA 15%, PsA 20%, SA 7.5%, EA 10%.
DAS28: 3.5±0.4, BASDAI 4.7±0.5, BASFI 4.3±1.4.
Prior treatment with biologics (30%): IFX 15%, ADA 66%, ETN 12.5%.
Frequency of administration: IFX 8.6±0.36 weeks, ADA 2.25±0.36 weeks, ETN 1.1±1.0 weeks.
Reasons for requesting the levels:
- Secondary failure (82%): IFX 90%, ADA 66.7%, ETN 75%
- Primary failure (17%): IFX 5%, ADA 33%, ETN 25%
- Infusion reactions (2.5%)

Drug levels within the therapeutic range: IFX 10%, ADA 41%, ETN 50%.
Formation of anti-TNF Ab of the sample: IFX 30%, ADA 16%, ETN 0%.
DMARDs: presence of 62.5% (MTXsc 64%, MTXvo 20%, Leflunomide, Sulfasalazine e Hydroxychloroquine 16%).
Conclusions: We found the following conclusions:
- In the data collected, we observe that the IFX (30%) is the most immunogenic drug, followed by the ADA (16%) and being the ETN (0%) the one that so far has not presented anti-drug Ab, outcomes in agreement with the medical literature
- The main reason for requesting has been the secondary failure (90%)
- The suboptimal levels of the drug and the presence of specific ab are correlated with the loss of clinical response. In our case, the proper range of drug is only objective in 10% of the patients treated with IFX, 41% with ADA and 50% with ETN
- The concomitant use of DMARDs in our study has not been shown to decrease levels of Ab, being the MTX the most used in our patients (84%). We observed no correlation between the occurrence of Ab, the use of DMARDs or the type of disease
- The monitoring of the levels of anti-TNF drug may be useful to individualize the treatment, to avoid possible side effects and to make decisions regarding the continuation or change of therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2800

THU0038 BIMEKIZUMAB DUAL INHIBITION OF IL-17A AND IL-17F PROVIDES EVIDENCE OF IL-17F CONTRIBUTION TO CHRONIC INFLAMMATION IN DISEASE-RELEVANT CELLS

A. Maroof[1], R. Okoye[1], T. Smallie[1], D. Baeten[2], S. Archer[1], C. Simpson[1], M. Griffiths[1], S. Shaw[1]. *[1]UCB Pharma, Slough, United Kingdom; [2]UCB Pharma, Brussels, Belgium*

Background: IL-17A and IL-17F share structural homology and have similar biological function[1]. Although the contribution of IL-17A to immune-mediated inflammatory diseases has been widely reported[1–3], the role of IL-17F is less well characterised in human tissue inflammation. Bimekizumab, a humanised monoclonal IgG1 antibody, was developed to neutralise both IL-17A and IL-17F potently and selectively, and is under clinical development as a treatment for psoriatic arthritis (PsA) and other immune-mediated conditions such as psoriasis.
Objectives: To assess the involvement of IL-17F in chronic inflammation in tissue from patients with PsA and disease-relevant cells, and to determine the effect of dual neutralisation of IL-17A and IL-17F in suppressing inflammation, compared with blockade of IL-17A.
Methods: Synovial and lesional skin tissue from patients with PsA was probed by immunostaining for expression of IL-17F protein. Normal dermal fibroblasts and synoviocytes, in the presence of TNFα, were stimulated with recombinant IL-17A and IL-17F to assess the inflammatory response. Using cytokine-specific blocking antibodies, the individual and combined effects of IL-17A and IL-17F were explored with: pro-inflammatory cytokine expression in a complex *in vitro* model (synoviocytes from patients with PsA and normal dermal fibroblasts were treated with pro-inflammatory mediators from supernatant [SN] of sorted Th17 cells), microarray and cell migration studies.
Results: IL-17F expression was observed in tissue biopsies from patients with PsA. In normal dermal fibroblasts, normal synoviocytes and synoviocytes from patients with PsA, stimulation with recombinant IL-17F promoted production of pro-inflammatory mediators, such as IL-6 and IL-8, though to a lesser extent than with recombinant IL-17A. Treatment of Th17 SN-stimulated synoviocytes from patients with PsA with bimekizumab (neutralising IL-17A and IL-17F) led to greater reductions of IL-6 (42% lower $p<0.05$) and IL-8 (35% lower $p<0.05$) production than IL-17A inhibition. Bimekizumab treatment of Th17 SN-stimulated normal dermal fibroblasts also reduced production of IL-6 (35% lower $p<0.0001$) and IL-8 (57% lower $p<0.0001$) more than IL-17A alone. Combining IL-17A + IL-17F monoclonal antibodies produced similar results to bimekizumab. Levels of expression of 27 inflammation-linked genes, including *CXCL1*, *CXCL2*, *CXCL3* and *IL-15RA*, were lower with dual neutralisation of IL-17A and IL-17F by bimekizumab versus inhibition of IL-17A. Suppression of migration of neutrophils (Fig.) and monocytes, both involved in tissue destruction in immune-mediated diseases, was substantially greater with bimekizumab treatment than with single blockade of IL-17A.

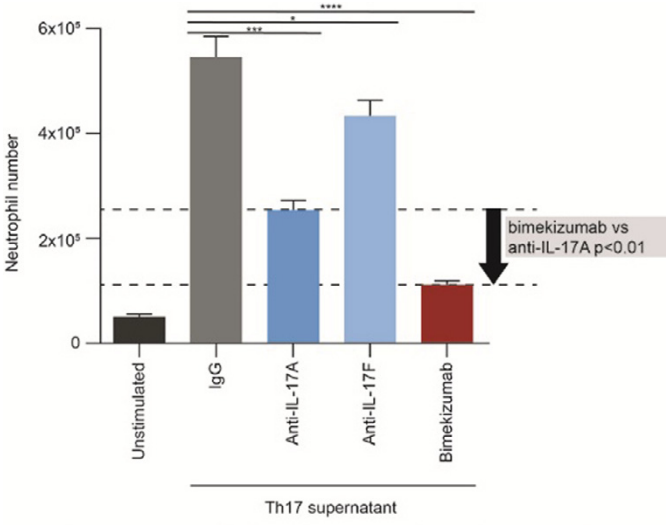


Fig. Quantification of neutrophil migration following treatment with cytokine-specific antibodies and bimekizumab. * represents a significant reduction of cell migration vs IgG control, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

Conclusions: Dual neutralisation of IL-17A and IL-17F provides evidence for the contribution of IL-17F to inflammation in joints and skin beyond IL-17A alone. As a result, dual inhibition of IL-17A and IL-17F by bimekizumab may provide an effective treatment for immune-mediated inflammatory diseases such as PsA.
References:
[1] C Johansen et al. Br J Dermatol 2009:160:319–24.
[2] AL Lima et al. Br J Dermatol 2016:174:514–21.
[3] C Doe et al. Chest 2010:138:1140–7.
Disclosure of Interest: A. Maroof Employee of: UCB Pharma, R. Okoye Employee of: UCB Pharma, T. Smallie Employee of: UCB Pharma, D. Baeten Grant/research support from: UCB Pharma, Consultant for: AbbVie, Pfizer, MSD, Roche, BMS, Novartis, Eli Lilly, Boehringer Ingelhaim and Glenmark, S. Archer Employee of: UCB Pharma, C. Simpson Employee of: UCB Pharma, M. Griffiths Consultant for: UCB Pharma, Employee of: UCB Pharma, S. Shaw Employee of: UCB Pharma
DOI: 10.1136/annrheumdis-2017-eular.4966

THU0039 LIPIDOMICS ANALYSIS OF HDL PARTICLE IN INFLAMMATORY RHEUMATIC DISEASES: ALTERATION OF PHOSPHOLIPID COMPOSITION AND ROLE OF INFLAMMATION

C. Giraud[1], F. Capel[2], F. Dutheil[3], B. Pereira[4], M. Soubrier[1], A. Kontush[5], M. Lhomme[6], J.L. Sebedio[2], A. Tournadre[1]. *[1]Rheumatology, CHU Gabriel Montpied; [2]Unité nutrition humaine, UMR 1019/Inra; [3]AME2P, Blaise Pascal University; [4]Biostatistic/ "Delegation Recherche Clinique et Innovation", CHU Gabriel Montpied, Clermont Ferrand; [5]INSERM UMR_s 1166 – Ican, Université Pierre et Marie Curie – Paris 6; [6]ICANalytics, ICAN, Paris, France*

Background: Rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylsosing

spondylitis (SA) are associated with an increased cardiovascular (CV) mortality. Quantitative abnormalities in lipid profiles are insufficient to explain this excess of CV risk and a qualitative approach of HDL composition is required to identify loss of atheroprotective functions and to correctly identify patients at risk. Atheroprotective functions of HDL are directly linked to the structure of HDL mainly composed of phospholipids (PL).

Objectives: The main objective of this study is to analyze the PL composition of HDL in patients with chronic inflammatory rheumatic diseases and to compare to matched healthy controls.

Methods: HDL structure was assessed in patients with active RA (ACR criteria), PsA (CASPAR criteria) and SA (ASAS criteria) patients before initiating first biologic and in healthy controls matched for age, sex and body mass index. Dyslipidemia treatment or pathology which could interfere with lipid profile were excluded. Demographics data, disease activity, cardiometabolic profile and plasma samples were collected. HDL particle were isolated from plasma after two step ultracentrifugation using gradient of density. Lipidomics analysis were performed using liquid chromatography coupled with mass spectrometry. Phospholipid composition between patients and controls was compared using multivariate analyses to take into account possible confounding variables determined according to univariate results and clinical relevance (age, tobacco consumption, steroids use). Multidimensional analyses as factorial mixed data analysis (FMDA) were performed to complete these analyses.

Results: 19 RA, 19 PsA and 12 SA were analyzed (table 1). 220 phospholipids species were identified among which 2 major classes were modified in rheumatic diseases. Phosphatidylcholine (PC) decreased in RA and PsA ($p<0.01$ and <0.05 respectively) while lysophosphatidylcholine (LPC) increased significantly ($p<0.01$, and <0.05 respectively). Some phospholipids species as PC 40: 8 ($p<0.001$), LPC 16:0 ($p<0.001$), LPC 18:0 ($p<0.001$) were identified as discriminant marker of HDL composition in rheumatic disease as compared to controls.

	RA (mean±SD)	Controls (mean±sd)	PsA (mean± sd)	Controls (mean±sd)	SA (mean±sd)	Controls (mean±sd)
Number of patients	19	18	19	17	12	12
Age	55.32 ±10,91	58.78 ±4,61	49.63± 8.04 **	57.65±4.77 **	45.33±6.56 ***	57.17±5.69***
Sexe (W/M) (%M)	1/18 (5,3%)	1/17 (5,5%)	10/9 (53%)	10/7 (58%)	8/4 (67%)	8/4 (67%)
BMI (kg/m²)	24.22 ±4,81	22.13 ±2,92	27.78± 7.60	24.55±3.63	25.49±4.16	23.69±2.92
ApoB/ApoA1	0.67 ±0,15	0.63 ±0,15	0.77± 0.21	0.75±0.14	0.74±0.12	0.75±0.17
CRP (mg/L)	31.16 ±43,98 ***	0.80 ±0,72 ***	19.74±17.33 ***	1.40±1.83 ***	2.88±1.97 *	1.91±2.17 *
CV family history Y/N (%)	1/18 (5,3%)	0/18 (0%)	1/18 (5,2%)	0/17 (0%)	0/12 (0%)	0/12 (0%)
CV personal history Y/N (%)	0/19 (0%)	0/18 (0%)	0/19 (0%)	0/17 (0%)	0/12 (0%)	0/12 (0%)
High blood pressure Y/N (%)	4/15 (21%) *	0/18 (0%) *	2/17 (11%)	0/17 (0%)	4/8 (33%) *	0/12 (0%) *
Diabetes mellitus Y/N (%)	1/18 (5,3%)	0/18 (0%)	1/18 (5,2%)	0/17 (0%)	0/12 (0%)	0/12 (0%)
Current tabacco use Y/N (%)	5/14 (26%) *	0/18 (0%) *	5/14 (26%)	0/17 (0%)	6/6 (50%) **	0/12 (0%) **
Disease duration (years)	6,68±6,33					
DAS 28 CRP score	4.56 ±1,45		4.00± 0.99			
BASDAI			55.67±18.58		61.14±14.09	
Corticosteroid treatment Y/N (%)	10/9 (53%)		2/17 (11%)		1/11 (8,3%)	
NSAI treatment Y/N (%)	9/10 (47%)		6/13 (32%)		6/6 (50%)	
Methotrexate treatment Y/N (%)	15/4 (79%)		9/10 (47%)		1/11 (8,3%)	

Table 1 : Demographics data, cardiometabolic profile and diseases caracteristics

* p<0.05, **p<0.01, ***p<0.0001 using T test or Chi-squared

Conclusions: Phospholipids composition of HDL is altered in RA and PsA. These alterations could explain a loss of atheroprotective functions and the excess of CV risk observed in RA and PsA patients. Chronic inflammation, through the activation of phospholipase A2 type II which hydrolyze PC into LPC, could modify the structure of HDL phospholipids and thus could impact HDL functionality such as cholesterol efflux, LDL oxidation modulation, anti-inflammatory and vasculoprotective properties. These preliminary data suggest the major role of inflammation in these alterations.

References:

[1] Tselepis AD et al. Atheroscler Suppl. 2002;3(4):57–68.
[2] Kontush A, et al. J Lipid Res. 2013;54(11):2950–63.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5491

THU0040 NOVEL AKT ACTIVATOR SC-79 IS A POTENTIAL TREATMENT FOR ALCOHOL-INDUCED OSTEONECROSIS OF THE FEMORAL HEAD

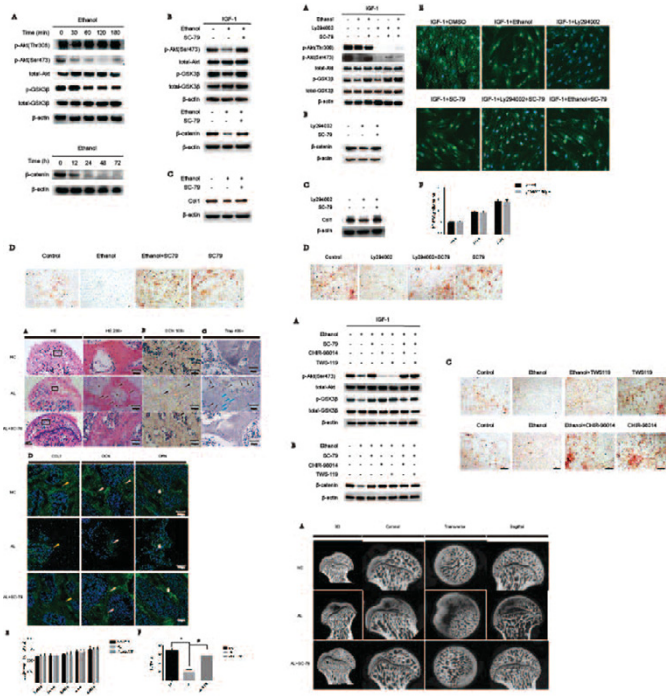
C. Yixuan. *Orthopedics, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China*

Background: Alcohol is known to be one ofthe leading risk factors for osteonecrosis of the femoral head. However, the underlying etiology and protective strategiesof alcohol-induced osteonecrosis of the femoral headhavenot been clarified.

Objectives: The aim of this study was to explore the molecular mechanism of alcohol-induced osteonecrosis of the femoral head, and to investigate the protective effect of SC-79 on the disease.

Methods: In vitro, we employed RT-PCR, alizarin red staining, alkaline phosphatase activity testing, western blot, immunofluorescence staining to investigate the effect of ethanol on hBMSCs. In vivo experiments, immunofluorescence staining, TRAP, TUNEL and micro-CT were performed to investigate the development of ONFH.

Results: In vitro, we found that ethanol could significantly impair the expression of osteogenic genes of RUNX2 and OCN, downregulate osteogenic differentiation, impair IGF-1 induced membrane recruitment of the Akt, suppress the Akt-Ser473 phosphorylationand the subsequent activation of Akt/GSK3β/β-catenin signaling in bone mesenchymal stem cells. Functional studies further confirmed this signaling was the critical mediator during the ethanol-induced inhibitory effects on osteogenesis of BMSCs.Thus, the dephosphorylation of Akt-Ser473 in Akt/GSK3β/β-catenin signaling pathway might be a potential mechanism in the pathogenesis of alcohol-induced osteonecrosis of the femoral head.SC-79, a novel Akt activator was introduced in this study to block the dephosphorylation effect of ethanol on Akt-Ser473 both in vitro and in vivo. In the rat model of alcohol-induced osteonecrosis of the femoral head, micro-CT and histopathological analyses revealed obvious osteonecrosis changes in alcohol-administrated rats while significantly less developed in SC-79 injected rats. OPN, OCN and COL1 immunofluorescence staining revealed that osteogenic response of femoral heads was markedly reduced after alcohol administration, but significantly reversed by SC-79 treatment.



Conclusions: Hence, we discovered alcohol-induced osteonecrosis of the femoral headwas associated with the suppression of the Akt-Ser473 in Akt/GSK3β/β-catenin pathway in BMSCs. The administration of SC-79, to elevate Akt activation, might be a clinical strategy to prevent the development of alcohol-inducedosteonecrosis of the femoral head.

Acknowledgements: The current study was supported by National Natural Science Foundation of China (81272003, 81301572) and SMC-Chen Xing Plan for Splendid Young Investigators of Shanghai Jiao Tong University.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1927

THU0041 PROGRANULIN AND DERIVATIVES CAN BE EMPLOYED AS LATENT DUAL-FUNCTION CHONDROGENIC AND ANTI-INFLAMMATORY THERAPEUTICS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

C.M.A. Schultz, Y. Chernajovsky. *Bone & Joint Research Unit, Queen Mary, University of London, London, United Kingdom*

Background: Rheumatoid Arthritis (RA) is a debilitating inflammatory disease of the joints afflicting around 1% of Western populations. Some of the best treatments are anti-TNF agents, but these only achieve remission in 60% of patients and cause deleterious side effects. Progranulin (PGRN), a cysteine-rich, multi-domain growth factor was reported to bind TNF-receptors (TNFR) blocking pro-inflammatory signalling[2], as well as stimulating chondrogenesis[3]. PGRN is cleavable and its peptides have pleiotropic effects, some of which may be beneficial and others refractory to ameliorating RA. Granulin A (GRN A) was shown to interact with cartilage ECM protein COMP[4]. Atsttrin – comprising 3 fused PGRN regions, was shown to ameliorate arthritic disease[2]. The latency associated peptide (LAP) of TGFβ1 can be fused to short peptides and cytokines via a MMP cleavage site to facilitate targeting to inflamed sites such as RA joints, reducing side effects and enhancing *in vivo* half-life[1]. We hypothesised that a peptide based on PGRN could be fused to LAP and used to both block TNF and stimulate cartilage regeneration in RA joints in a targeted way.

Objectives: To produce a panel of PGRN derivatives fused to LAP. To determine the chondrogenic and anti-TNF capacities of the fragments in the presence and absence of MMP activation. To evaluate their efficacy in the CIA model of RA.

Methods: Micromass cultures of C28/I2 chondrocytes and C3H10T1/2 mesenchymal cells were employed to determine the ability of PGRN fragments to stimulate chondrogenesis. HT-29 and WEHI-164 TNF sensitive cells were used to evaluate the anti-TNF capacity of LAP-PGRN fragments. Co-immunoprecipitation was used to characterise interactions between PGRN fragments and TNFRII. DBA/1 fibroblasts transduced with lentivirus encoding LAP-PGRN fusions were delivered to DBA/1 mice with CIA to assess anti-arthritic effects.
Results: PGRN, LAP-PGRN, LAP-GRN A and LAP-Atsttrin were cloned and expressed in mammalian expression systems. PGRN elevated sulphated proteoglycan production in micromass cultures of C28/I2 human chondrocytes, and also stimulated proliferation of C3H10T1/2 cells. Furthermore, PGRN reduced TNF-mediated catabolism of extracellular matrix in established chondrogenic C3H10T1/2 micromass cultures. LAP-PGRN, LAP-GRN A and LAP-Atsttrin potentiated BMP2 mediated chondrogenesis in C3H10T1/2 micromasses. PGRN failed to protect WEHI-164 fibroblasts or HT-29 colorectal carcinoma cells from TNF-mediated cytotoxicity despite interacting with TNF receptor *in vitro* by co-immunoprecipitation. LAP-PGRN, LAP-GRN A and LAP-Atsttrin all failed to protect WEHI-164 cells from TNF-mediated cytotoxicity, even after MMP1 cleavage and release. CIA disease progression was reduced in DBA/1 mice treated with autologous fibroblasts overexpressing murine Etanercept or PGRN relative to control treatment. LAP-Atsttrin was more effective than LAP-PGRN and LAP-GRN A at reducing arthritic symptoms relative to LAP-Empty controls.
Conclusions: These findings suggest that PGRN could be used as a targeted dual-function chondrogenic and anti-inflammatory treatment for RA, but these effects are not elicited directly through the TNF pathway.
References:
[1] Adams et al., Nat Biotechnol. 2003 Nov;21(11):1314–20.
[2] Tang et al., Science. 2011 Apr 22;332(6028):478–84.
[3] Feng et al., FASEB J. 2010 Jun;24(6):1879–92.
[4] Xu et al., J Biol Chem. 2007 Apr 13;282(15):11347–55.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5170

THU0042 LONGITUDINAL IP-10 SERUM LEVELS ASSOCIATE WITH THE COURSE OF DISEASE ACTIVITY AND ACHIEVING DMARD-FREE SUSTAINED REMISSION IN RHEUMATOID ARTHRITIS

A. van Hooij[1], D. Boeters[2], E. Tjon Kon Fat[3], S. van den Eeden[1], P. Corstjens[3], A. van der Helm-van Mil[2], A. Geluk[1]. *[1]Department of Infectious diseases; [2]Department of Rheumatology; [3]Department of Molecular Cell Biology, Leiden University Medical Center, Leiden, Netherlands*

Background: Although rheumatoid arthritis (RA) is a chronic autoimmune disease that is persistent in the majority of patients, 10–15% of the RA patients achieve disease modifying anti-rheumatic drugs (DMARD)-free sustained remission over time. Biological mechanisms underlying the persistence of inflammation in RA are yet unidentified. It is well established that increased serum levels of IFN-γ-induced protein 10 (IP-10) are associated with (acute) increased inflammatory responses against mycobacterial pathogens causing leprosy and tuberculosis, thereby providing useful diagnostic tools in these infectious diseases. Based on previous genetic susceptibility studies, we hypothesize that there is an overlap between inflammatory responses observed in these mycobacterial diseases and those observed in RA. Therefore, we determined the association between serial IP-10 serum levels and achieving DMARD-free sustained remission as well as disease activity scores (DAS)-remission.
Objectives: To 1) assess the association between IP-10 levels over time in patients that have persistent RA versus patients that achieve DMARD-free sustained remission, and 2) determine the association between IP-10 levels and DAS.
Methods: 139 serum samples of 34 RA-patients (1987-criteria), obtained at the time of diagnoses and at yearly intervals thereafter, were studied. 15 patients had persistent RA and 19 patients achieved DMARD-free sustained remission after a median follow up of 2.7 years. IP-10 serum levels were measured using a previously developed, user-friendly lateral flow assay. Baseline and change in IP-10 levels over time were compared between patients with persistent RA and those achieving DMARD-free sustained remission. The association between the change in IP-10 level and the change in DAS was studied; in addition the course of the absolute IP-10 levels and the DAS over time was plotted for individual patients.
Results: IP-10 serum levels varied from 316 – 53,685 pg/ml between RA-patients. Patients that had persistent arthritis or achieved DMARD-free sustained remission over time did not differ in baseline IP-10 levels (median persistent RA 1991 pg/ml and median DMARD-free sustained remission 3292 pg/ml, p=0.19). However, a significant decrease in IP-10 levels over time was observed in patients achieving DMARD-free sustained remission (p=0.003), whereas IP-10 levels remained stable in patients with persistent RA. Changes in IP-10 levels correlated well with changes in DAS scores (p=0.05). Also at the level of individual patients, a strong correlation between IP-10 levels and DAS over time was observed.
Conclusions: These longitudinal data indicate that IP-10 levels are associated with perseverance of RA as well as with disease activity. Rapid diagnostic tests measuring IP-10 levels can therefore be helpful in monitoring of RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4019

THU0043 TARGETED MEDICINE: THERAPEUTIC USE OF FUNCTIONAL CYTOKINE ASSAYS IN COMPLEX INFLAMMATORY ARTHRITIS

E.E.P. Htut[1], L. Ceron-Gutierrez[2], R. Doffinger[2,3], J. Rees[1]. *[1]Rheumatology; [2]Immunology, Addenbrooke's Hospital; [3]National Institute of Health Research, Cambridge Biomedical Research Centre, Cambridge, United Kingdom*

Background: Functional cytokine assays have been limited to experimental models of inflammatory arthritis without translation into clinical therapy.
Objectives: To illustrate the successful use of functional cytokine assays in providing targeted treatment for complex inflammatory arthritis.
Methods: A 24 year old male presented in 2014 with a florid asymmetrical polyarthritis associated with an elevated acute phase response (ESR 50, CRP 42, ALP 132). He had no history of psoriasis, inflammatory bowel or eye disease and no family history.
Vasculitis and viral arthritis screen, ACE, ANA, Anti dsDNA, RF and CCP were negative. He was positive for HLA B27 without evidence of spondyloarthropathy on imaging. He was noted to have a monoclonal gammopathy of uncertain significance with normal bone profile, unremarkable urinary BJP and whole body CT scan. His joint symptoms responded to corticosteroid therapy with the addition of hydroxychloroquine and methotrexate. In 2015, his clinical condition had significantly deteriorated with worsening joint inflammation, 3 kg weight loss with a sudden rise in acute phase response, without proven infection. His functionality declined with long term sickness from work.
Biochemical tests revealed: Hb 123, MCV 87.2, Plt 393, Neutrophil 7.76, ESR 86, Alb 31, Calcium 2.68, ALP 387 (noted to be of bony origin), CRP 286, Ferritin 1161, PT 13, and APTT 39. Renal function, protein electrophoresis, blood film, haemolytic screen, viral and autoimmune liver screens were unremarkable. Hydroxychloroquine and methotrexate were temporarily with-held at this stage, although he was maintained on prednisolone 20 mg, with a partial response in his joint symptoms. An infiltrative pathology was a concern and was subsequently excluded.
The next therapeutic step would have been an anti-TNF agent. Nevertheless, due to his atypical and complex disease course, cytokine assays were performed to further characterise his disease profile and provide targeted treatment. Results showed an elevated IL6 production; IV Tocilizumab was selected for the treatment of his inflammatory arthritis. He has had a remarkable response in terms of his systemic and joint symptoms as well as considerable biochemical improvement. He was able to de-escalate his corticosteroid regime and return to work.
Results: TNF alpha, IL1 beta, and IL-6 are important inflammatory mediators and targets of intervention in the treatment of Rheumatoid arthritis. They may be induced *in vivo* and *in vitro* using Toll like receptor mediated innate activation. Active Whole Blood Cytokine Profiling was performed for the patient and compared to healthy controls. Innate activation of whole blood with various TLR agonists including LPS (TLR4), PAM3 (TLR1/2), Imiquimod (TLR7) revealed low induction of TNF alpha and IL1 beta in the patient when compared to controls. In contrast, the patient showed an elevated IL-6 production. Patient's cytokine levels in serum and in non-activated whole blood were normal.
Conclusions: Our case highlights the potential progression to personalised medicine in achieving optimal patient outcome delivered in a cost-effective way. Functional cytokine assays in the appropriate context and within selected patient groups can help to achieve disease remission by allowing targeted treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5497

THU0044 CHONDROITIN SULPHATE INHIBITS MONOCYTE CHEMOATTRACTANT PROTEIN-1 RELEASE FROM 3T3L1 ADIPOCYTES: A NEW TREATMENT OPPORTUNITY FOR OBESITY-RELATED METABOLIC SYNDROMES?

E. Montell[1], T.V. Stabler[2], V.B. Kraus[3]. *[1]Pre-Clinical R&D Area, Bioiberica, Barcelona, Spain; [2]Duke Molecular Physiology Institute; [3]Duke Molecular Physiology Institute. Division of Rheumatology, Duke University School of Medicine, Durham, United States*

Background: Monocyte chemoattractant protein-1 (MCP-1) overproduction from inflamed adipose tissue is a major contributor to obesity-related metabolic syndromes. We have recently published that chondroitin sulphate (CS) can attenuate the monosodium urate (MSU) crystal mediated THP-1 macrophage inflammatory response reflected by reduced release of pro-inflammatory cytokines IL-1β and TNFα. We have also recently determined that the CS inhibitory effect is not acting at the inflammasome but upstream, most likely by inhibiting activation of NF-κB.
Objectives: We sought to determine whether CS had a similar inhibitory effect on MCP-1 release from lipopolysaccharide (LPS) stimulated adipocytes.
Methods: We cultured 3T3-L1 embryonic fibroblasts and induced their differentiation into adipocytes using an established protocol. We then treated the adipocytes with LPS to induce inflammation and thus MCP-1 release. At the same time we added varying concentrations of CS (Bioibérica, Spain) in a physiologically relevant range (10–200 μg/ml) and 24h after we measured MCP-1 release (R&D Systems, Minneapolis, MN, USA). We also cultured THP-1 monocytes and tested whether CS (200 μg/ml) could inhibit cell migration induced by human recombinant MCP-1. Monocyte chemotaxis in response to 24h exposure to

varying concentrations (0, 3.125–100 ng/ml) of recombinant human MCP-1 (R&D Systems) was tested using the CytoSelect 96-well cell migration assay (Cell Biolabs, San Diego, CA, USA). All experiments were run a single time with each treatment group run in triplicate. After normalization for cell viability, cell culture results were expressed as fold change from the media only negative control (no CS, no LPS). One-way ANOVA with Bonferroni's post-hoc test and post-hoc linear trend were performed on cell culture results using Graphpad Prism software (La Jolla, CA, USA).

Results: We found that LPS (1μg/ml) caused a significant rise in MCP-1 release ($p<0.0001$) from 3T3-L1 adipocytes. CS in physiologically achievable concentrations (100–200 μg/ml) produced a dose dependent reduction ($p<0.01$ at 100 μg/ml and $p<0.001$ at 200 μg/ml) of MCP-1 release from 3T3-L1 adipocytes in response to LPS. Recombinant MCP-1 (25–100 ng/ml) caused a dose dependent increase ($p<0.001$ at 25ng/ml and $P<0.0001$ at 100ng/ml) in cell migration of THP-1 monocytes. CS at the highest test concentration (200 μg/ml) had no effect on MCP-1 mediated THP-1 migration.

Conclusions: Our data demonstrate that CS inhibits the release of MCP-1 from 3T3-L1 adipocytes that have been stimulated with LPS, but has no effect on the chemotactic action of MCP-1 on THP-1 monocytes. Furthermore, our work data strongly suggests that it is the inhibition of MCP-1 release by CS that underlies this effect and not a direct inhibition of the chemotactic action of MCP-1 by CS. Given the importance of MCP-1 over-production in obesity-related metabolic syndromes, inhibiting the release of MCP-1 from adipocytes by CS, and thus blocking the recruitment of macrophages to adipose tissue, could provide a new treatment opportunity for these syndromes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2140

THU0045 IL-21 AND IL-22 ARE INVOLVED IN BONE DESTRUCTION IN RHEUMATOID ARTHRITIS PATIENTS

E. Kuca-Warnawin[1], W. Kurowska[1], A. Radzikowska[1], G. Pracon[2], T. Burakowski[1], M. Olszewska[3], I. Slowinska[4], I. Sudol-Szopinska[2], W. Maslinski[1]. *[1]Department of Pathophysiology and Immunology; [2]Department of Radiology; [3]Department of Anesthesiology and Intensive Care; [4]Department of Rheumoorthopaedic Surgery, National Institute of Geriatrics, Rheumatology, and Rehabilitation, Warsaw, Poland*

Background: Inflammatory process in bone marrow (BM) observed on MRI scans of rheumatoid arthritis (RA) patients (called bone marrow oedema) was shown to proceed joint destruction in RA. Our previous studies supported the concept that BM actively participate in the pathogenesis of RA by TLR triggered B cell activity (1), increased number of activated T cells and increased level of proinflammatory cytokines (2,3). Cytokines play a key role in the bone destruction of rheumatoid arthritis.

Objectives: To investigate the levels of IL-21 and IL-22 in RA BM plasma and their association with bone destruction.

Methods: BM samples were obtained from RA and osteoarthritis (OA) patients during total hip replacement surgery. Levels of IL-17AF, IL-21, IL-22, RANKL and cathepsin K in BM plasma were determined by specific ELISA tests. We analyzed pelvic radiographs of 22 patients with RA admitted to the NIGRR and subjected to total hip replacement. Radiographs were taken a day or two before surgery. In our study we assessed hip joint changes semi-quantitatively with the use of the proposed scoring system including primary RA (juxta-articular osteoporosis, axial joint space narrowing, inflammatory cyst presence, bony erosion) and late RA changes (axial migration of the femoral head, femoral head deformation, avascular necrosis of femoral head, femoral head subluxation).

Results: We found increased levels of activated T cell associated cytokines IL-21 (924.8 pg/ml vs 688.6 pg/ml, $p<0.05$) and IL-22 (94.5 pg/ml vs 65.8 pg/ml, $p<0.05$) in BM plasma of RA patients in comparison to osteoarthritis (OA) patients. Interestingly levels of both of these cytokines strongly correlated positively with concentration of osteoclastogenesis/osteoclast activity marker RANKL and cathepsin K. Surprisingly level of IL-17AF did not correlate with RANKL or cathepsin K. Furthermore, concentration of IL-21 was statistically significantly higher in patients with more severe radiologically assessed bone destruction. Median value of concentration of IL-21 in RA patients with small bone destruction was 797.4 pg/ml, with mild bone destruction was 1037.8 pg/ml, with severe bone destruction (1079.0 pg/ml).

Conclusions: Our results show an association between BM plasma levels of IL-21 and IL-22 and bone destruction, supporting the hypothesis that IL-21 and IL-22 are important pathogenic factors of this disease. Therapy targeting IL-21 and IL-22 may be of value in preventing bone erosions in patients with RA.

References:

[1] W Rudnicka et al.: Eur J Immunol 2009; 12.
[2] E Kuca-Warnawin et al.: Ann Rheum Dis Jan;70(1):227–33.
[3] E Kuca-Warnawin et al.: Reumatologia 2016;54(2):51–3.

Acknowledgements: This work was sponsored by grant No UMO-2011/03/B/NZ6/05035 from National Science Centre, Poland.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5701

THU0046 CALCIUM PYROPHOSPHATE AND MONOSODIUM URATE CRYSTAL-INDUCED PROSTAGLANDIN E2 PRODUCTION INVOLVES NF-κB ACTIVATION AND ROS PRODUCTION, INDEPENDENTLY OF INTERLEUKIN-1BETA AXIS

F. Renaudin[1,2], L. Campillo-Gimenez[1], C. Combes[3], M. Gosset[4], M. Cohen-Solal[1,5], F. Lioté[1,5], H.-K. Ea[1,5]. *[1]UMR1132, Bioscar, Inserm; [2]University Paris Diderot, Paris; [3]CIRIMAT, Université de Toulouse, INPT, UPS, CNRS, Ensiacet, Toulouse; [4]EA 2496, UFR Odontologie, Paris Descartes, Montrouge; [5]Service de Rhumatologie, centre Viggo Petersen, AP-HP, hôpital Lariboisière, Paris, France*

Background: Monoclinic and triclinic calcium pyrophosphate dihydrated (mCPPD and tCPPD) and monosodium urate (MSU) crystals are responsible in human for relapsing acute arthritis. CPP and MSU crystal-triggered inflammation depends on several inflammatory mediators including interleukin (IL)-1β and prostaglandin (Pg) E2. IL-1β production is governed by NF-κB, NLRP3 inflammasome and caspase-1 activation. PgE_2 derives from arachidonic acid (AA) synthesis, which is regulated by cytosolic phospholipase A2 ($cPLA_2$), and cyclooxygenase-(COX) 2 activation. CPP crystal-induced IL-1β production is well documented, but CPP crystal-induced PgE2 production remains unclear.

Objectives: To evaluate how CPP crystals induce PgE_2 production and the role of IL-1β in this process.

Methods: Synthetic and pyrogen-free m-CPPD, t-CPPD and MSU crystals were used to stimulate human monocyte cell line (THP-1 cells) and primary bone marrow-derived macrophages (BMDM) of wild type (wt) and NLRP3 inflammasome deficient ($nlrp3^{-/-}$) mice. Pharmacological inhibitors were used to assess the role of oxidative stress (N-acetyl-L-cysteine, NAC) and NF-κB pathway (Bay-117085). PgE_2 and IL-1β production were quantified by ELISA, gene expression by qRT-PCR, $cPLA_2$ by immunoblot. NF-κB activation was assessed in THP-1 cells containing a reporter gene under control of NF-κB p65 promotor. *In vivo*, CPP crystal-induced PgE2 production was evaluated in the air pouch model in the presence or not of NF-κB inhibitor or NAC.

Results: *In vitro*, m- and t-CPPD and MSU crystals rapidly induced the production of PgE_2 and IL-1β by THP-1 cells and BMDM. PgE_2 production was associated with $cPLA_2$and NF-κB activation along with increased expression of COX-2 (20 fold) and its receptor EP2 and EP4 genes. While CPP crystal-induced IL-1β production was abolished in THP-1 cells by treatment with caspase-1 inhibitor and in $nlrp3^{-/-}$ BMDM, CPP crystal-induced PgE_2 was not modified suggesting IL-1β- and NLRP3-independent pathways. Interestingly, CPP crystal-induced PgE_2 production was completely abrogated by NF-κB inhibitor treatment and significantly decreased by the antioxidant NAC; in both case, COX-2 gene expression was dramatically inhibited. *In vivo*, treatment with NAC or Bay strongly inhibited IL-1β and PgE_2 production and cellular infiltrate induced by CPP crystals.

Conclusions: PgE_2 production mediated by CPP and MSU crystals is activated by NF-κB signaling, independently of NLRP3/IL-1β production axis. Moreover, ROS production, known as a NLRP3 activator in response to CPPD or MSU crystals, is also involved in the regulation of PgE_2 production. The relations between these different pathways are under investigation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5505

THU0047 RESVERATROL AND ITS PRECURSOR POLYDATIN INHIBIT CRYSTAL-INDUCED INFLAMMATION IN VITRO BY DECREASING OXIDATIVE STRESS AND IL-1BETA ACTIVATION PATHWAY

Y. Zamudio-Cuevas[1], F. Oliviero[2], E. Belluzzi[2], A. Scanu[2], L. Andretto[2], P. Galozzi[2], M. Favero[2], R. Ramonda[2], P. Spinella[3], G. Ravagnan[4], A. Lopez-Reyes[5], L. Punzi[2]. *[1]Instituto Nacional de Rehabilitación, Mexico City, Mexico; [2]Rheumatology Unit, University of Padova; [3]Clinica Nutrition Unit, University of Padova, Padova; [4]Istituto di Farmacologia Traslazionale (IFT) – CNR, Roma, Italy; [5]Instituto Nacional de Rehabilitación, Mexico City, Mexico*

Background: Resveratol (RES) and its natural precursor polydatin (PD) are polyphenol compounds that display a broad variety of beneficial effects including anti-apoptotic and anti-inflammatory properties.

Objectives: This study aimed to investigate the role of RES and PD in the inflammatory process induced by monosodium urate (MSU) and calcium pyrophosphate (CPP) crystals in vitro. Their effect was evaluated though IL-1β, NLRP3 inflammasome, reactive oxygen species (ROS), nitric oxide (NO) and the phagocytosis index assessment.

Methods: A monocytic cell line (THP-1) was primed for 3 hours with phorbol myristate acetate (PMA) (100ng/ml) and stimulated with synthetic MSU (0.05mg/ml) and CPP (0.025mg/ml) crystals. RES and PD were added to cultures at, respectively, 100μM and 200μM. Experiments were carried out either adding RES and PD along with crystals, or pretreating cells (2 hs) with polyphenols and removing them before crystal stimulation. IL-1β were evaluated in cell supernatants and at intracellular level by ELISA assay. IL-1β and NLRP3 expression was assessed by RT-PCR. Reactive oxygen species (ROS) and NO were measured by cytometric analysis using fluorogenic probes (CellROX Deep Red Reagent and DAF-FM, respectively). Crystal phagocytosis index was calculated at different time points using polarized light microscopy.

Results: RES and PD inhibited IL-1b induced by crystals both at extracellular

and intracellular level. This inhibition was more pronounced after polyphenol cell pretreatment. In this case cytokine production was completely suppressed both in control and in stimulated cells. Cell pretreatment was extremely effective also in reducing mRNA expression of IL-1 after crystal stimulation while NLRP3 expression was to some extent affected by RES. RES and PD had a slight inhibitory effect on crystal phagocytosis when added along with the stimulus, while pretreated cells did not show any difference in the phagocytosis index. ROS production induced by MSU crystals was more pronounced (4 fold increase) with respect to CPP crystals (2 fold increase). RES was more effective than PD in inhibiting ROS production ($p<0.05$ crystals vs crystals+RES). The pretreatment showed a more marked decrease of ROS than the simultaneous treatment and the effect reached significance for both PD and RES. Similar inhibitory effects have been obtained when NO production was considered.

Conclusions: Our results demonstrated that RES and PD are effective in inhibiting crystal-induced inflammation affecting IL-1 production and NLRP3 expression and activation. Data obtained after cell pretreatment allow us to hypothesize that these polyphenols act on specific signaling pathway preventing inflammation, and that this action is independent from crystal phagocytosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6830

THU0048 SOLUBLE URIC ACID INCREASED THE EXPRESSION OF ABCG2 AND PDZK1 IN HUMAN INTESTINAL CELL LINES THROUGH THE TLR4/NLRP3/CASPASE-1 AND PI3K/AKT SIGNALING PATHWAYS

M. Chen, X. Lu, H. Wu. *Department of Rheumatology, the Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China*

Background: Hyperuricemia is the key pathophysiological basis of gout[1]. The most common reason generating hyperuricemia is verified the obstacle of urate excretion by current researches[2]. The intestine is known as the most important organ involved the excretion of uric acid besides the kidney[1]. ABCG2 has an outsized genetic contribution to extra-renal underexcretion and causes a compensatory increase in urinary urate output[3]. PDZK1 is a kind of an important structural protein regulated ABCG2 function, by potential molecular interaction with ABCG2[4].

Objectives: The present study was undertaken to explore the effect and its related mechanisms of soluble uric acid on the urate excretion PDZK1 and ABCG2 in HT-29 and Caco-2 cell lines

Methods: HT-29 and Caco-2 cell lines were used as a well-established model of human intestinal epithelial cells. Cells were pretreated with or without inhibitors and then stimulated with soluble uric acid. siRNA transfection was used to assess the interaction between ABCG2 and PDZK1. qRT-PCR and western blotting were used to measure mRNA and protein levels, respectively. Subcellular fractionation methods and immunofluorescence were used to examine the proteins in different subcellular compartments. Flow cytometry experiments examined the function of ABCG2.

Results: Soluble uric acid significantly up regulated the expression of PDZK1 and ABCG2 in human intestinal cell lines. It also activated TLR4/NLRP3/caspase-1 inflammasome and PI3K/AKT signalling pathway through the phosphorylation of the ser473 pAkt. The increased expression of PDZK1 and ABCG2 was suppressed by a block of TLR4 (TAK-242) and caspase-1 inhibitor (acetyl–YVAD–chloromethylketone) and partly reduced by wortmanning, a specific inhibitior of PI3K. Additionally, lipopolysaccharide (LPS), the potent inducer of inflammatory responses mediated through TLR4, activated TLR4/NLRP3/caspase-1 inflammasome and up regulated the expression of ABCG2 and PDZK1. Besides, the stimulation of soluble uric acid facilitated the translocation of ABCG2 from intracellular compartment to plasma membrane and increased the transport activity. Furthermore, PDZK1 knockdown via siRNA significantly inhibited the expression and transport activity of ABCG2 regardless of the activation by soluble uric acid.

Conclusions: The PI3K/AKT and TLR4/NLRP3/caspase-1 signaling pathways modulate ABCG2 and PDZK1 expression stimulated by soluble uric acid in human intestinal cells. PDZK1 plays a pivotal role in the regulation of ABCG2.

References:

[1] Dalbeth N, Merriman TR, Stamp LK. Gout. Lancet. 2016;388(10055):2039–52.
[2] Perez-Ruiz F, Calabozo M, Erauskin GG, Ruibal A, Herrero-Beites AM. Renal underexcretion of uric acid is present in patients with apparent high urinary uric acid output. Arthritis and rheumatism. 2002;47(6):610–3.
[3] Matsuo H, Tsunoda T, Ooyama K, Sakiyama M, Sogo T, Takada T, et al. Hyperuricemia in acute gastroenteritis is caused by decreased urate excretion via ABCG2. Scientific reports. 2016;6:31003.
[4] Takada Y, Matsuo H, Nakayama A, Sakiyama M, Hishida A, Okada R, et al. Common variant of PDZK1, adaptor protein gene of urate transporters, is not associated with gout. The Journal of rheumatology. 2014;41(11):2330–1.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5673

THU0049 29-KDA FIBRONECTIN FRAGMENT SUPPRESSED HMGB1-DEPENDENT AUTOPHAGY PATHWAY IN HUMAN ARTICULAR CHONDROCYTES

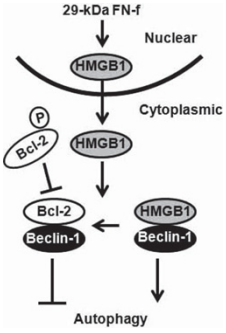
M. Choi[1], I.Y. Park[1], K.M. Son[2], H.S. Hwang[1], H.A. Kim[1]. *[1]Hallym University Sacred Heart Hospital; [2]Hallym University Dongtan Sacred Heart, Gyeonggi-do, Korea, Republic Of*

Background: Fibronectin fragments found in synovial fluid induce the catabolic responses in cartilage. High mobility group protein Box 1 (HMGB1), a damage-associated molecular pattern (DAMP), resides in the nucleus, translocates into the cytosol in response to various stimuli, and is subsequently released into the extracellular space.

Objectives: In this study, we investigated the effect of 29-kDa fibronectin fragment (29-kDa FN-f) on HMGB1-mediated autophagy pathway in primary human chondrocytes.

Methods: Human articular chondrocytes were enzymatically isolated from articular cartilage. The mRNA and protein levels of HMGB1 were measured by quantitative real-time PCR (qRT PCR) and Western blot analysis. The translocation of nuclear HMGB1 into cytoplasm was determined by western blot and immunofluorescence microscopy. Activation of mammalian target of rapamycin (mTOR), protein kinase B (Akt) and 1A/1B-light chain 3 (LC3) was measured by western blot analysis. Interaction of HMGB1 and Beclin-1 were evaluated by immunoprecipitation (IP). Release of HMGB1 into extracellular medium was measured by ELISA.

Results: HMGB1 was significantly reduced in human osteoarthritis (OA) cartilage compared to normal cartilage. qRT PCR and Immunoblotting assay revealed that 29-kDa FN-f significantly reduced expression of HMGB1 at the mRNA and protein levels and also led to the translocation of the nuclear HMGB1 into the cytoplasm, together with decreased levels of Beclin-1 and phosphorylated Bcl-2. Using IP analysis, we demonstrated that in the presence of 29-kDa FN-f the association of HMGB1 and Beclin-1, which led to HMGB1-dependent autophagy pathway, was decreased, whereas the association of Bcl-2 and Beclin-1 was increased. In addition, prolonged treatment with 29-kDa FN-f significantly increased the release of HMGB1 into the culture medium. A variety of evidence, including down-regulated LC3-II, an autophagy marker, and increased phosphorylated 4EBP1 and p70S6K, substrates of mTOR, revealed that 29-kDa FN-f subsequently suppressed autophagy in primary chondrocytes by activating Akt/mTOR signaling pathway.



Conclusions: These results demonstrated that 29-kDa FN-f has a harmful impact on chondrocytes through suppressing HMGB1-dependent autophagy pathway and releasing HMGB1, DAMP, to extracellular space.

References:

[1] Kwak et al. Current Understanding of HMGB1-mediated Autophagy. J. Bacteriol. Virol. 43 (2013) 148–154.
[2] Heinola et al. High mobility group box-1 (HMGB-1) in osteoarthritic cartilage. Clinical. Exp. Rheumatol. 28 (2010) 511–518.
[3] Hwang et al. Fibronectin fragment-induced expression of matrix metalloproteinases is mediated by MyD88-dependent TLR-2 signaling pathway in human chondrocytes. Arthritis. Res. Therapy. 17 (2015) 320.

Acknowledgements: This study was supported by a grant (HI14C2248 and HI15C2699) from the Korean Health Technology R&D Project, Ministry of Health & Welfare, Republic of Korea and the Basic Science Research Program through the National Research Foundation (NRF) of Korea funded by the Ministry of Education (2014R1A1A2059823).

Disclosure of Interest: None declared

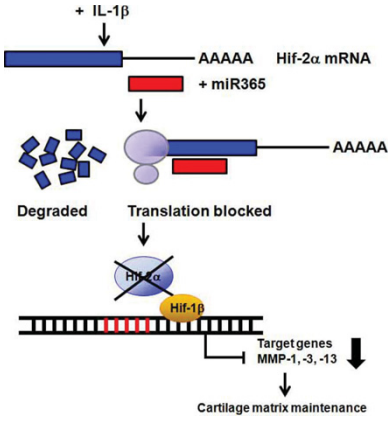
DOI: 10.1136/annrheumdis-2017-eular.2812

THU0050 MICRORNA-365 INHIBITS IL-1β-INDUCED CATABOLIC FACTOR EXPRESSION BY TARGETING HIF-2α IN HUMAN PRIMARY CHONDROCYTES

M.H. Lee[1], J.-I. Hong[1], H.S. Hwang[1], K.M. Son[2], H.A. Kim[1]. *[1]Hallym University Sacred Heart Hospital, Kyunggi; [2]Hallym University Dongtan Sacred Heart Hospital, Gyeonggi, Korea, Republic Of*

Background: MicroRNAs, small noncoding RNA molecules, are involved in the pathogenesis of various diseases such as cancer and arthritis. Endothelial PAS

domain protein-1/hypoxia-inducible factor-2α (EPAS-1/ HIF-2α) is a catabolic transcription factor that regulates osteoarthritis (OA) cartilage destruction.
Objectives: In this study, we examined whether microRNA-365 (miR-365) affects interleukin (IL)-1β-induced expression of catabolic factors in chondrocytes via regulation of HIF-2α.
Methods: Total RNA was isolated from normal and OA cartilage tissues and human chondrocytes. miR-365 expression was quantified by TaqMan assay. The effects of miR-365 on HIF-2α and HIF-2α-modulated genes were assessed by quantitative real-time reverse polymerase chain reaction (qRT-PCR), Western blot analysis, and enzyme-linked immunosorbent assay (ELISA). Direct interaction of miR-365 with the 3' untranslated region (UTR) of HIF-2α mRNA was examined using a luciferase reporter assay. Nitrite concentration was measured in culture medium using a Griess assay.
Results: miR-365 levels were significantly decreased in human OA cartilage relative to normal cartilage. Overexpression of miR-365 significantly suppressed IL-1β-induced expression of HIF-2α in human articular chondrocytes. Pharmacological inhibition of various IL-1β-associated signaling pathways revealed mitogen-activated protein kinase and nuclear factor-κB as the primary pathways driving IL-1β-mediated decreases in miR-365 and subsequent increase in HIF-2α expression. Using a luciferase reporter assay encoding the 3'UTR of human HIF-2α mRNA, we showed that overexpression of miR-365 significantly suppressed IL-1β-induced up-regulation of HIF-2α. Furthermore, miR-365 overexpression significantly suppressed IL-1β-induced expression of catabolic factors, including cyclooxygenase-2, inducible nitric oxide synthase, and matrix metalloproteinase-1, -3 and -13, and nitric oxide (NO) production in chondrocytes.



Conclusions: MiR-365 regulates IL-1β-stimulated catabolic effects in human chondrocytes by modulating HIF-2α expression.
References:
[1] Yang et al. Hypoxia-inducible factor-2alpha is a catabolic regulator of osteoarthritic cartilage destruction, Nat. Med. 16 (2010) 687–693.
[2] Akhtar et al. Haqqi, MicroRNA-27b regulates the expression of matrix metalloproteinase 13 in human osteoarthritis chondrocytes, Arthritis Rheum. 62 (2010) 1361–1371.
[3] Park et al. MicroRNA-558 regulates the expression of cyclooxygenase-2 and IL-1beta-induced catabolic effects in human articular chondrocytes, Osteoarthritis Cartilage 21 (2013) 981–989.
Acknowledgements: This study was supported by the Basic Science Research Program through the National Research Foundation (NRF) of Korea funded by the Ministry of Education (2014R1A1A2059823 and 2016R1D1A1B03932259).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2818

THU0051 ASSOCIATION BETWEEN BIOACTIVE TNF AND EULAR RESPONSE TO TNF INHIBITORS IN RHEUMATOID ARTHRITIS

J. Poudroux[1], H. Marotte[1], J.-E. Gottenberg[2], S. Paul[3]. *[1]Rheumatology, CHU Saint Etienne, Saint Priest en Jarez; [2]Rheumatology, CHU Strasbourg, Strasbourg; [3]Immunology, CHU Saint Etienne, Saint Priest en Jarez, France*

Background: ROC study provided data to manage rheumatoid arthritis (RA) treatment after a failure to a first TNF blocker (1). We previously reported that high circulating TNF bioactivity was associated with good clinical response (2).
Objectives: To explore ability of TNF bioactivity to predict response to second TNF blocker.
Methods: Here, we assessed TNF bioactivity in 130 RA patients from the group rotation to a second TNF blocker at the time of randomisation and after 6 months. Clinical and biological data were recorded at baseline and 6 month with Eular response assessed at 6 month.
TNF bioactivity was assessed with HEK-Dual TNF cells adapted from our previous work (2). Due to non-normalised distribution, non parametrical analysis were performed.
Results: Baseline circulating TNF bioactivity was similar according to Eular response. However, circulating TNF bioactivity at 6 month was associated with clinical response with low TNF bioactivity in responders. A ROC analysis suggested a cut-off at 0.320 with a sensitivity at 92% and a specificity at 41%.
Conclusions: After a failure of a first TNF blocker, circulating TNF bioactivity is not able to predict response to a second TNF blocker despite a lower level in responders compared to non-responders.
References:
[1] Gottenberg J-E, Brocq O, Perdriger A, Lassoued S, Berthelot J-M, Wendling D, et al. Non-TNF-Targeted Biologic vs a Second Anti-TNF Drug to Treat Rheumatoid Arthritis in Patients With Insufficient Response to a First Anti-TNF Drug: A Randomized Clinical Trial. JAMA. 2016 Sep 20;316(11):1172–80.
[2] Marotte H, Maslinski W, Miossec P. Circulating tumour necrosis factor-alpha bioactivity in rheumatoid arthritis patients treated with infliximab: link to clinical response. Arthritis Res Ther. 2005;7(1):R149–155.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4227

THU0052 LEVELS OF INFLAMMATORY SEROLOGIC BIOMARKERS IN HLA-B27 AND HLA-B15 POSITIVE PATIENTS WITH SPONDYLOARTHRITIS

J. Londono[1], A.M. Santos[2], J.C. Rueda[2], P. Peña[2], I. Briceño[3], E.-L. Saldarriaga[2], J.-I. Angarita[2], E. Calvo[4], M. Avila[2], N. Martinez-Rodriguez[5], H. Cubides[2], V. Parra[2], J.F. Medina[6]. *[1]Reumatología, Universidad de la Sabana-Hospital Militar Central, Bogotá; [2]Reumatología; [3]Faculltad de Medicina, Grupo Genética Humana, Universidad de la Sabana, Chia; [4]Departamento de Imágenes diagnósticas, Universidad Nacional, Bogotá, Colombia; [5]Departamento de Investigación de Salúd Comunitaria, Hospital Infantil de México Federico Gomez, Ciudad de Mexico, Mexico; [6]Unidad de Entrenamiento Clínico, Facultad de Medicina, Universidad de Navarra, Pamplona, Spain*

Background: A main challenge in spondyloartritis (SpA) management was the availability of reliable biomarkers related with disease activity, or predicting joint damage and the response to treatment. Although erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are currently used as biomarkers for disease activity, they lack sensitivity, specificity and reproducibility. With the understanding of SpA pathogenesis, additional biomarkers like metalloproteinase 3 (MMP-3), interleukin (IL)-1a, IL-6, lipopolysaccharide-binding protein (LBP), tumour necrosis factor a (TNFa), macrophage colony stimulating factor (M-CSF), interferon gamma (INF-g), IL-17 and IL-23, had been proposed
Objectives: We aimed to evaluate the associations of MMP-3, IL-1a, IL-6, M-CSF, LPB, IL-17 and IL-23 levels in SpA patients positive for HLA-B27 or HLA-B15
Methods: 178 patients (100 men and 78 women) with SpA according to ASAS criteria were included in the study. HLA typing was performed by PCR using the Biorad® HLA-SSP ABDR plates. The levels of TNFa, IL-1a, IL-6, INF-g and IL-17 were measured by a cytometric bead-array (CBA Flex Set) using a FACS Canto II Flow CytometerÔ. Enzyme-linked immunosorbent assay (ELISA) was used to determine serum levels of IL-23, M-CSFand MMP-3. CRP and LBP levels were measured by chemiluminescence. Statistical analysis was made with SPSS v19. For comparison of quantitative variables with a normal distribution we used the Student's *t*-test. Categorical variables were presented in frequency charts and percentages, and the Chi-squared test and Fisher's exact test were used when necessary, for comparing groups. Two-tailed P-value <0.05 was considered statistically significant
Results: Of the 178 patients, 70 were positive for HLA-B27, 34 for HLA-B15 and 74 had other HLA-B. According to ASAS classification criteria, 152 patients had axial SpA (axSpA) manifestations, 161 had peripheral SpA (pSpA) manifestations, and 148 patients had mixed axial and peripheral manifestations. Figure 1 shows the mean levels of inflammatory serologic biomarkers in these subgroups of patients

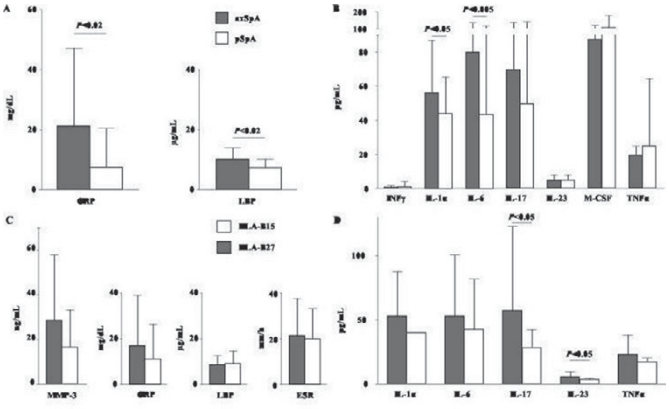


Figure 1. A. Disease activity biomarkers (CRP: C-reactive protein; LBP: lipopolysaccharide-binding protein) in axial spondyloarthritis (axSpA) and peripheral spondyloarthritis (pSpA); B. Cytokines (INFγ: interferon gamma; IL: interleukin; M-CSF: macrophage colony stimulating factor; TNFα: tumour necrosis factor alpha) in axSpA and pSpA; C. Disease activity biomarkers (MMP-3: metalloproteinase 3; ESR: erythrocyte sedimentation rate) in HLA-B27 and HLA-B15 positive SpA patients, D. Cytokines in HLA-B27 and HLA-B15 positive SpA patients

Conclusions: High levels of IL-17 and IL-23 were associated with the presence of HLA-B27, which mainly correlates with an axial presentation of the disease as

compared to HLA-B15 patients. Accordingly, the genotype (presence of HLA-B27 or HLA-B15) and phenotype (axial or peripheral involvement) may help physicians when considering a targeted therapy of SpA patients with IL-17 inhibition in a context of personalized medicine

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5628

THU0053 SELECTIVE ACTIVATION OF AN AMPK-CREB-NRF2-DEPENDENT PATHWAY BY CELECOXIB INDUCES VASCULOPROTECTIVE GENES AND MITIGATES AGAINST CARDIOVASCULAR RISK

F. Alrashed, D. Calay, C.C. Thornton, A. Bauer, A. Kiprianos, D.O. Haskard, A. Seneviratne, J.J. Boyle, J.C. Mason. *Rheumatology and Vascular Sciences, Imperial College London, London, United Kingdom*

Background: Although concern remains about the athero-thrombotic risk posed by COX-2-selective inhibitors (COXIBs), the recent PRECISION trial demonstrated non-inferiority of moderate dose celecoxib when compared to naproxen and ibuprofen with respect to cardiovascular safety, with fewer actual CV events recorded for celecoxib. Moreover, celecoxib proved significantly safer than either comparator in regard to gastrointestinal events[1]. Given the markedly different cardiovascular risk associated with celecoxib and rofecoxib, we investigated the hypothesis that, in addition to cyclo-oxygenase inhibition, celecoxib specifically activates COX-2-independent AMP kinase (AMPK) signalling to exert protective effects in the vascular endothelium.

Objectives: To investigate COX-2-independent vasculoprotective signalling pathways activated by celecoxib in human endothelium.

Methods: *In vitro* studies of celecoxib, rofecoxib, ibuprofen and naproxen were performed on human umbilical vein and human aortic endothelial cells (HUVEC and HAEC). Inhibition of signalling pathways was achieved using siRNA. The vascular effects of celecoxib *in vivo* were studied in C57Bl/6 mice fed celecoxib (1000 ppm) or control chow (48 hrs). Aortic tissue was snap-frozen and sections studied by immunofluorescence confocal microscopy.

Results: At therapeutically relevant concentrations celecoxib (1–10μ M) induced the vasculoprotective protein heme oxygenase-1 (HO-1) in HUVEC and HAEC (EC) ($p<0.01$). In contrast, rofecoxib and the commonly used non-selective NSAIDs ibuprofen and naproxen failed to induce HO-1. Celecoxib derivative 2,5-dimethyl-celecoxib (DMC), which lacks COX-2 inhibition, also upregulated HO-1, implicating a COX-2-independent mechanism. Immunoblotting demonstrated that celecoxib and DMC induce AMPK$\alpha^{(Thr172)}$ and CREB-1$^{(Ser133)}$ phosphorylation leading to Nrf2 nuclear translocation ($p<0.05$). These responses were not seen with ibuprofen or naproxen, while siRNA depletion of AMPKα abrogated celecoxib-mediated CREB and Nrf2 activation ($p<0.05$). Acting via the same pathway, celecoxib induced additional cytoprotective genes including H-ferritin. *In vivo*, celecoxib similarly increased HO-1 and H-ferritin in murine aortic endothelium when compared to control-fed mice ($p<0.05$). Functionally, celecoxib treatment inhibited TNF-α-induced NF-κB p65$^{(Ser536)}$ phosphorylation by increasing AMPK activity. This attenuated VCAM-1 upregulation via induction of HO-1, as revealed by HO-1 siRNA ($p<0.05$). Similarly, celecoxib prevented the IL-1-mediated increase of IL-6 mRNA ($p<0.01$). These responses were not seen with ibuprofen or naproxen.

Conclusions: Celecoxib induces anti-inflammatory, anti-oxidant proteins HO-1 and H-ferritin in human vascular endothelium via a novel AMPK-CREB-Nrf2-dependent pathway. This mechanism may contribute to the important and marked differences in cardiovascular risk between celecoxib and rofecoxib. Understanding mechanisms underlying NSAID heterogeneity may ultimately lead to the development of safer anti-inflammatory drugs.

References:

[1] Nissen SE et al. Cardiovascular Safety of Celecoxib, Naproxen, or Ibuprofen for Arthritis. N Engl J Med. 2016;375:2519–29.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2841

THU0054 UTILITY OF SEROLOGICAL PARAMETERS IN GIANT CELL ARTERITIS FOR PREDICTING DISEASE COMPLICATIONS

K. Lakota[1,2], J. Feichtinger[3,4], B. Burja[1], T. Kuret[1], P. Žigon[1], Ž. Rotar[1], R. Ješe[1], S. Sodin-Šemrl[1,2], S. Čučnik[1,5], G. Thallinger[3,4], M. Tomšič[1,6], A. Hočevar[1]. *[1]Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana; [2]FAMNIT, University of Primorska, Koper, Slovenia; [3]Institute of Molecular Biotechnology, Graz, Austria, Graz University of Technology; [4]OMICS Center Graz, BioTechMed Graz, Graz, Austria; [5]Faculty of Pharmacy; [6]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia*

Background: Giant Cell Arteritis (GCA) is a systemic vasculitis affecting primarily large and medium sized arteries. Immediate high dose steroid treatment may prevent urgent complications, such as vision loss and cerebrovascular insults[1–3]. However, there is a clear lack of data on predicting serological markers and their association to clinical complications.

Objectives: To investigate serological parameters that support clinicians in predicting complications in a large, clinically well-characterized set of untreated GCA patients at time of diagnosis.

Methods: The study included 98 GCA patients (67% female) with a median (IQR) age 74.1 (67.3–78.8) years and a median (IQR) symptome duration time of 30 (20–90) days). Healthy blood donors (HDs, n=52, 61.5% female, median (IQR) age of 41.95 (20.4–63.1) years) served as controls. GCA complications studied were visual disturbances (including permanent loss of vision), relapses, peripheral artery involvement and claudication. Levels of 27 serum analytes were measured using Luminex xMAP Technology. Interleukin-6 (IL-6) and serum amyloid A (SAA) levels were tested using ELISA and nephelometry, respectively.

Results: The highest, significantly elevated analytes in GCA vs. HDs were SAA (85-fold > HDs mean values), IL-23 (63-fold) and IL-6 (11-fold). IL-13, α-fetoprotein and MMP-2 were significantly decreased in GCA, while levels of IL-2, IL-17A and TNF-α were unchanged. PCA analysis revealed a signature analyte profile positioning towards the HD cluster. SAA, CRP, haptoglobin, ESR, thrombocyte # and matrix metalloproteinase-1 (MMP-1) all negatively associated with visual disturbances, confirming our previous data. Age showed significant association to permanent visual loss, with older patients being more affected[3]. SAA, CRP and ESR at presentation were found to be predictive of relapsing disease, while MMP-2 negatively associated with relapse. VCAM-1, α-fetoprotein, MARCO and IL-27 were all negatively associated with peripheral artery involvement. MMP-2 and MARCO showed positive association with claudication, while IL-18 was negatively associated.

Conclusions: In our large study of untreated GCA patients we highlight the importance of using serological acute phase parameters, MMPs and other analytes for predicting complications.

References:

[1] Weyand CM, Goronzy JJ. Medium- and large-vessel vasculitis. N Engl J Med 2003, 349:160–169.
[2] Nesher G: The diagnosis and classification of giant cell arteritis. J Autoimmun 2014, 48–49:73–75.
[3] Hocevar A et al. Do Early Diagnosis and Glucocorticoid Treatment Decrease the Risk of Permanent Visual Loss and Early Relapses in Giant Cell Arteritis: A Prospective Longitudinal Study. Medicine (Baltimore) 2016, 95:e3210.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3467

THU0055 LOW MOLECULAR WEIGHT BAFF SIGNALING INHIBITORS AMELIORATE IL-6, IL-10 AND IGG PRODUCTION IN VITRO AND IN VIVO MODELS OF AUTOIMMUNE DISEASES

K. Yoshimoto[1], K. Suzuki[1], K. Sugahara[2], T. Takeuchi[1]. *[1]Keio University School of Medicine, Tokyo; [2]Mitsubishi Tanabe Pharma Corporation, Yokohama, Japan*

Background: In our previous study, we reported that soluble BAFF (sBAFF) robustly enhanced IL-6 production by peripheral monocytes of patients with primary Sjogren's syndrome (pSS) and that the expression level of a BAFF receptor (BR3) was significantly elevated in pSS monocytes. We also found that the proportion of BR3-positive monocytes to total monocytes was positively and significantly correlated with the serum IgG level of pSS patients. Investigation of the interaction of monocytes and B cells showed that IgG production by B cells was enhanced by sBAFF-stimulated monocytes. These data collectively suggest that the elevated expression of BR3 on monocytes is involved in IgG overproduction by B cells which is often observed in pSS, and that BAFF signaling via BR3 is a possible therapeutic target to treat pSS. A high throughput screening of a low molecular weight compound library successfully discovered two pyrrolopryimidine derivatives, BIK12 and BIK13, which inhibit sBAFF binding to BR3. We found that these compounds inhibited not only IL-6 production by BAFF-stimulated monocytes, but also IgG production by B cells co-cultured with the monocytes.

Objectives: To elucidate the mechanism of inhibitory activities of these compounds on BAFF signaling pathways, we measured production of IL-10 as well as IL-6 by monocytes *in vitro*, both of which work for B cell activation. In addition, we analyzed *in vivo* effects of the compounds on production of autoantibody and cytokines in autoimmune disease model mice.

Methods: Peripheral monocytes and B cells were prepared from healthy individuals. The monocytes were stimulated with sBAFF and cultured *in vitro* with or without peripheral B cells in the presence of BIK-12 or BIK-13. The amounts of IL-6, IL-10 and IgG were measured by ELISA. BIK-13 was administered intraperitoneally to MRL/lpr mice, an animal model of autoimmune diseases, three times a week for 6 months. Serum levels of an anti-ds DNA antibody, IL-6 and IL-10 were measured by ELISA.

Results: sBAFF enhanced the production of not only IL-6, but also IL-10 by peripheral monocytes *in vitro*. As expected, BIK12 and BIK-13 significantly suppressed production of IL-6 and IL-10 by BAFF-stimulated monocytes *in vitro* in a dose dependent manner. Notably, IgG production by B cells co-cultured *in vitro* with sBAFF-stimulated monocytes was significantly suppressed by these compounds. The compounds did not exhibit toxicities to the cells in the dose range. These data suggest that BAFF signaling via BR3 lead to production of IL-6 and IL-10 in monocytes, and the cytokines in turn mediates the signal to B cells resulting in IgG overproduction. Interestingly, serum levels of an anti-dsDNA antibody, IL-6 and IL-10 in MRL/lpr mice received BIK13 simultaneously declined as compared to control mice. These data collectively suggest that the compound was also efficacious *in vivo*.

Conclusions: BIK-13, a pyrrolopyrimidine derivative, suppressed IgG production

by B cells through affecting monocytes. IL-6 and/or IL-10 may intermediate the effect. Our findings strongly suggest that BAFF signaling via BR3 is a possible therapeutic target for drug discovery to treat pSS or other intractable autoimmune diseases which accompany hypergammaglobulinemia. Moreover, these compounds may provide novel tools to explore the pathological mechanism of the development of these autoimmune diseases.

Disclosure of Interest: K. Yoshimoto: None declared, K. Suzuki: None declared, K. Sugahara Employee of: Mitsubishi Tanabe Pharma Corporation, T. Takeuchi Grant/research support from: Mitsubishi Tanabe Pharma Corporation

DOI: 10.1136/annrheumdis-2017-eular.4176

THU0056 FREE FATTY ACIDS PROMOTE INFLAMMATION VIA OSTEOBLASTS AND OSTEOCLASTS FROM PATIENTS WITH RHEUMATOID ARTHRITIS OR OSTEOARTHRITIS

K. Frommer[1], A. Schäffler[2], U. Lange[1], S. Rehart[3], J. Steinmeyer[4], M. Rickert[4], U. Müller-Ladner[1], E. Neumann[1]. *[1]Dept. of Internal Medicine and Rheumatology, Kerckhoff-Klinik, Justus-Liebig-University of Giessen, Bad Nauheim; [2]Dept. of Internal Medicine III, Endocrinology, Diabetes, Metabolism, Justus-Liebig-University of Giessen, Giessen; [3]Dept. of Orthopaedics and Trauma Surgery, Agaplesion Markus Hospital, Frankfurt; [4]Dept. of Orthopaedics and Orthopaedic Surgery, University Hospital Giessen and Marburg, Giessen, Germany*

Background: Various inflammatory cardiovascular and metabolic diseases such as atherosclerosis, coronary heart diseases and type 2 diabetes are associated with chronically elevated free fatty acid (FFA) levels. With inflammation being a factor in pathological bone loss, FFA may also be contributors to bone loss in osteoarthritis (OA) and/or rheumatoid arthritis (RA).

Objectives: To investigate whether FFA have an influence on osteoblasts and osteoclasts from patients with RA or OA, in a way that may alter bone degradation in these diseases.

Methods: Primary osteoblasts (OB) were isolated from cancellous bone of OA and RA patients undergoing knee joint surgery. Osteoclasts (OC) were differentiated from peripheral blood mononuclear cells (PBMC). OB and OC were stimulated with the saturated FFA palmitic acid (PA) and the unsaturated FFA linoleic acid (LA) (100 μM each). Immunoassays were used to quantify protein secretion. mRNA expression levels were quantified by real-time PCR. Mineralization activity was quantified using Alizarin Red S staining, differentiated OC were quantified by counting TRAP-positive multinuclear cells (>2 nuclei). Toll-like receptor (TLR) 4 and TLR2 were blocked by neutralizing antibodies.

Results: When stimulated with FFA, OB from RA and OA patients secreted higher amounts of the proinflammatory cytokine IL-6 (up to 9-fold) and the chemokines IL-8 (up to 221-fold), GRO-a (from below detection level to detectable levels) and MCP-1 (up to 16-fold). Differences in the degree of response were more dependent on the patient than the disease. RANKL as well as OPG, OB-secreted modulators of OC differentiation, as well as OB differentiation markers (e.g. osterix, osteocalcin) were not influenced by FFA on mRNA or protein level. The effect of FFA on mineralization activity of OB varied between patients, yet overall there was no significant difference between FFA-treated and untreated OB. Expression of the two Wnt signaling molecules, axin-2 and b-catenin, was not changed by PA or LA, suggesting no involvement of the Wnt signaling pathway in the effects observed by FFA in OB. On the other hand, TLR4 blockade significantly reduced PA-induced IL-8 secretion by OB (by 93%), while blocking TLR2 had no effect. In both RA and OA OC, IL-8 secretion was significantly enhanced by PA and LA, with a clear time-dependency within the differentiation process for RA OC but not for OA OC. The number of TRAP positive multinuclear cells decreased for RA OC by approx. 50%, which was in agreement with the reduced TRAP secretion by a factor of 2–3 at d14. mRNA expression of various osteoclast activity markers (CLCN7, CTSK, TCIRG) was not altered.

Conclusions: Inflammation is promoted by FFA via both OB and OC from patients with RA or OA, thus possibly indirectly contributing to bone loss while no direct effect on OB/OC activity could be observed. In OB, these effects are probably mainly mediated by TLR4, while TLR2 and Wnt pathways do not play a role.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3488

THU0057 LIPID PROFILING OF PLASMA IN RHEUMATOID ARTHRITIS PATIENTS BY LIQUID CHROMATOGRAPHY–TANDEM MASS SPECTROMETRY

K. Murakami[1], I. Murakami[1], A. Ioan-Facsinay[2], M. Giera[3], M. Hashimoto[4], A. Yoshida[1], T. Usui[1], N. Kuramoto[1], R. Nakashima[1], Y. Imura[1], H. Yoshifuji[1], K. Ohmura[1], T. Mimori[1]. *[1]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto, Japan; [2]Department of Rheumatology; [3]Center for Proteomics and Metabolomics, Leiden University Medical Center, Leiden, Netherlands; [4]Department of the Control for Rheumatic Diseases, Graduate School of Medicine, Kyoto University, Kyoto, Japan*

Background: Previously it has been described that lipid and lipid mediators are present in synovial fluid from patients with rheumatoid arthritis (RA). It is, however, currently unknown to what extent these lipid mediators are involved in disease pathophysiology.

Objectives: The aim of this study is to clarify which lipid mediators in plasma correlate with disease activity of RA.

Methods: We obtained blood from RA patients registered in the KURAMA (Kyoto University Rheumatoid Arthritis Management Alliance) cohort. None of the patients was treated with glucocorticoids or NSAIDs, both of which could affect lipid metabolism. Targeted lipidomics, using a LC–MS/MS (liquid chromatography–tandem mass spectrometry) platform was used for the identification of lipids present in the patients' plasma. SDAI (simplified disease activity index) was examined in this cohort and lipidomics profiling and disease status were combined. Data were statistically analyzed by Spearman's rank correlation coefficient test or multivariate regression analysis.

Results: Twenty-six RA patients were enrolled; female ratio: 84%, mean age: 63.0 years old, mean disease duration: 18.7 years and mean SDAI 5.26. In this group, patients age was significantly correlated with SDAI (p value =0.005, Spearman's rho =0.552). By LC-MS/MS analyses, 23 lipid components were identified and quantified. Multivariative regression analysis (Standard Least Squares) revealed that 19,20-diHDPA (Dihydroxydocosapentaenoic acid) and 14,15-diHETE (Dihydroxyeicosatetraenoic acid) significantly explained SDAI score independently of sex and age.

Among the composite measure for SDAI, the best correlated component with TJC (tender joint count) was LA (Linoleic acid, p=0.002, rho = -0.611), that with patient VAS (visual analogue scale) was 19,20-diHDPA (p=0.032, rho =0.440), and that with CRP was DHA (Docosahexaenoic acid, p=0.021, rho = -0.452).

Additionally, principal component analysis was carried out. In the first primary component (PC1), absolute eigenvecotor values of AdA (Adrenic acid), ALA (Alpha-linolenic acid), DHA, DPA (Docosapentaenoic acid) and LA are more than 0.25, among which DHA was strongly correlated with PC1 (p<0.0001, rho =0.902). PC1 positively and significantly explained TJC count independent of sex and age.

Table. Parameter Estimates by Standard Least Squares (Role variant = SDAI)

	Lower 95%	Upper 95%	Std. Beta	p value
Intercept	-39.2	-6.63	0	0.008
19,20-diHDPA	4.54	16.55	0.707	0.003
14,15-diHDPE	-26.4	-6.24	-0.62	0.003
Age	0.08	0.56	0.455	0.013
Sex				0.475

Conclusions: Since 19, 20-diHDPA (metabolized from DHA) and 14,15-diHETE (from EPA, eicosapentaenoic acid) are both generated by cytochrome P450-catalyzed epoxidation followed by conversion to the vicinal diols by epoxide hydrolase, such kind of enzymes might be key molecules connecting lipid metabolism and RA. Although a replication study is inevitable, a certain kinds of lipid and lipid mediator profiles may be associated with disease activity, especially analgesic descriptors such as tender joint count.

References:

[1] Giera M, et al. Lipid and lipid mediator profiling of human synovial fluid in rheumatoid arthritis patients by means of LC-MS/MS. Biochim Biophys Acta. 2012, 1821(11):1415–24.

Acknowledgements: None.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4052

THU0058 S100A11 PROTEIN IS UP-REGULATED IN PATIENTS WITH IDIOPATIC INFLAMMATORY MYOPATHIES AND IS ASSOCIATED WITH DISEASE ACTIVITY

L. Andres Cerezo[1], H. Hulejová[1], B. Šumová[1], T. Lennerova[1], M. Klein[1], H.F. Mann[1], J. Zámečník[2], K. Pavelka[1], J. Vencovský[1], L. Šenolt[1]. *[1]Department of Rheumatology, 1st Faculty of Medicine, Charles University Prague, Institute of Rheumatology; [2]Department of Pathology and Molecular Medicine, 2nd Faculty of Medicine, Charles University Prague, University Hospital Motol, Prague, Czech Republic*

Background: S100A11 (calgizzarin) is a member of the S100 protein family that participates in regulating number of biologic functions and is associated with oncogenesis and inflammation. Recent data suggest involvement of S100A11 in myocardial damage.

Objectives: The aim of our study was to analyze the expression of S100A11 in patients with idiopathic inflammatory myopathies (IIMs) and its potential association with disease activity parameters and IIMs-related clinical features.

Methods: immunohistochemistry in patients with polymyositis/dermatomyositis (PM/DM, n=5/6) and control individuals with myasthenia gravis (MG, n=5). S100A11 in plasma was measured by ELISA (Biovendor) in 112 patients with IIMs (PM, n=41; DM, n=41; and cancer associated myositis (CAM), n=30) and in 42 healthy controls (HC). Patients with PM/DM fulfilled Bohan and Peter diagnostic criteria and CAM was defined as cancer occurring within 3 years of the diagnosis of myositis. Clinical disease activity was assessed by myositis disease activity assessment (MYOACT), physician and patient's global activity using visual analogue scales (VAS), manual muscle testing (MMT) and health assessment questionnaire (HAQ). Muscle enzymes CK, LD, ALT, AST and CRP were measured by routine laboratory techniques. Autoantibodies were detected by immunoprecipitation.

Results: S100A11 protein was up-regulated in the muscle from patients with IIMs compared to MG. In PM/DM patients, S100A11 was accumulated in the cytoplasm of regenerating and necrotizing muscle fibers and on the sarcolemma of most fibers. Only some mononuclear infiltrate cells showed S100A11 positivity. In patients with MG, S100A11 was detected on the sarcolemma only. Moreover, S100A11 was increased in plasma of patients with IIMs compared to HC (3.82 [1.47–72.9] vs. 2.84 [1.67–11.18] ng/ml; p=0.0076). When divided into groups, patients with DM and CAM showed significant elevation of plasma S100A11 compared to HC (4.10 [2.22–50.81] and 4.52 [1.53–9.11] vs. 2.84 [1.67–11.18] ng/ml; p=0.004 and p=0.02, respectively). Levels of S100A11 did not differ between PM and HC. In all patients, S100A11 correlated with LD (r=0.300, p=0.001), CK (r=0.217, p=0.025) and AST (r=0.343, p<0.001), with MYOACT (r=0.279, p=0.005) and with muscle, pulmonary and skin disease activity (r=0.199, p=0.040; r=0.224, p=0.025 and r=0.307, p=0.001). S100A11 levels were elevated in autoantibody-positive group compared to autoantibody-negative group of patients with IIMs (5.22 [1.45–69.29] vs 3.44 [1.58–12.12], p=0.010).
Conclusions: S100A11 is up-regulated in the circulation of patients with IIMs and correlates with disease activity. Accumulation of S100A11 in the muscle of patients with myositis may indicate its potential role in the process of cell necrosis and fiber regeneration.
Acknowledgements: Supported by grant 15–34065A of the Agency for Healthcare Research of the Czech Republic and MHCR 023728.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4758

THU0059 ONCOSTATIN M INDUCES INFLAMMATION AND DIFFERENTIALLY REGULATES TNF ALPHA-INDUCED PRO-INFLAMMATORY MECHANISMS AND NOTCH SIGNALLING IN THE RA JOINT

M.M. Hanlon[1], D. Veale[2], S. Wade[1], M. Biniecka[2], U. Fearon[1], T. McGarry[1]. *[1]Molecular Rheumatology, Trinity Biomedical Sciences Institute, Trinity College Dublin; [2]Centre for Arthritis and Rheumatic Diseases, St Vincents University Hospital, University College Dublin, Dublin, Ireland*

Background: Oncostatin M (OSM) is a pleiotropic cytokine, highly expressed in the RA joint that displays both agonistic and antagonistic effects depending on the inflammatory microenvironment. This study examines the effect of OSM on inflammation, the Notch-1 signalling pathway which plays a critical role in vascular development and angiogenesis and finally on TNFα-induced pro-inflammatory mechanisms in Rheumatoid Arthritis.
Objectives: To examine the effect of OSM on cytokine/chemokine production, angiogenesis and the Notch-1 signalling pathway in synovial fibroblasts and endothelial cells and whether OSM potentiates the effects of TNFα-induced pro-inflammatory effects.
Methods: Primary RA synovial fibroblasts (RASFC) isolated from RA synovial biopsies obtained at time of knee arthroscopy and human dermal microvascular endothelial cells (HMVEC) were grown to confluence. RASFC and HMVEC were cultured with OSM (10ngml) alone or in combination with increasing concentrations of TNFα (0.01–1ng/ml). IL-6, IL-8, RANTES, GROα and MCP-1 cytokines/chemokines were quantified in culture supernatants by ELISA. Functionally, angiogenesis and invasion were assessed by matrigel tube formation and Transwell invasions assays respectively, and VEGF in cell lysates quantified by Real-time PCR. Finally, Notch-1, its ligands Delta-like-ligand 4 (DLL-4) and Jagged-1 (Jag-1) and downstream transcriptional repressors – Hey-1 and Hey-2 were quantified by Real-time PCR.
Results: OSM alone significantly induced IL-6 and MCP-1 while inhibiting IL-8 and GROα in RASFC and HMVEC culture supernatants, compared to basal control. OSM alone induced RANTES expression in HMVEC with little effect observed for RASFC. OSM potentiated the effect of increasing concentrations of TNFα on IL-6 and MCP-1 secretion from RASFC and HMVEC. Conversely OSM significantly inhibited TNFα-induced IL-8 and GROα secretion from both RASFC and HMVEC. Interestingly, OSM significantly inhibited TNFa-induced RANTES expression in HMVEC yet conversely potentiated this effect in RASFC. At a functional level, OSM induced both RASFC and HMVEC invasion and induced network formation and VEGF expression in HMVEC. OSM significantly induced Notch-1 in RASFC and HMVEC in a time dependent manner, but interestingly differentially regulated the Notch-1 ligands, with induction of Jag-1 only observed in RASFC, and induction of DLL-4 only observed in HMVEC. Finally OSM differentially regulated Notch-1 downstream transcriptional repressors in HMVEC, significantly inducing Hey-2 while simultaneously inhibiting Hey-1.
Conclusions: OSM is a pleiotropic cytokine that displays divergent effects with both pro- and anti-inflammatory mechanisms within the inflamed joint, effects that appear to be dependent on cell type and the inflammatory microenvironment. Targeting OSM or downstream signalling pathways may lead to new potential therapeutic strategies or adjuvant therapies, particularly for those patients who have sub-optimal responses.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6334

THU0060 T CELL-DERIVED IL-17A AND IL-17F DRIVE BONE FORMATION FROM HUMAN PERIOSTEAL STEM CELLS: IMPLICATIONS FOR ENTHESOPHYTE FORMATION

M. Shah[1,2], A. Maroof[1], R. Al-Hosni[3], P. Gikas[4], N. Gozzard[1], S. Shaw[1], S. Roberts[1,2]. *[1]UCB Pharma, Slough; [2]University College London; [3]Institute of Orthopaedics and Musculoskeletal Science; [4]The Royal Orthopaedic Hospital, London, United Kingdom*

Background: Pathological bone formation associated with spondyloarthropathies (SpA) is a major cause of structural tissue damage causing permanent disability. A paucity of *in vitro* models that faithfully replicate human skeletal biology has impeded research into the cellular and molecular triggers for this osteoimmunological phenomenon. Nevertheless, clinical and animal studies have defined IL-17 signalling as a key regulator of SpA disease; however, the role of IL-17 in bone pathology is unclear. IL-17-producing γδ-T cells have a critical function in periosteal bone formation for fracture repair[1]. The periosteum has also been implicated in pathological bone formation during SpA disease progression[2].
Objectives: To investigate IL-17 signalling in the context of pathological bone formation using a biomimetic human periosteum derived stem cell (hPDSC) model of osteogenic differentiation.
Methods: hPDSCs were obtained through enzymatic digestion of periosteal biopsies from patients undergoing orthopaedic surgery. Expanded cultures were then treated with recombinant human IL-17A, IL-17F, or both over 96h. The expression of gene markers was then evaluated. Alternatively, hPDSCs were stimulated using a biomimetic protocol in combination with IL-17A and IL-17F, or human T-cell supernatants (SNs) (as a surrogate disease-like inflammatory milieu). Antibodies with strong-affinity to IL-17A, IL-17F, or bimekizumab (a humanised monoclonal IgG1 antibody with strong affinity for both IL-17A and IL-17F) were used to define the role of these cytokines in the SNs. Expression of osteogenic markers and matrix mineralisation was assessed to define *in vitro* bone formation.
Results: Under basal conditions IL-17A and IL-17F significantly up-regulated *IL-6* expression. Additionally, IL-17A and IL-17F transiently enhanced the expression of the osteogenic transcription factor *RUNX-2*. When IL-17 cytokines were combined in a biomimetic differentiation protocol, both IL-17A and IL-17F promoted osteogenic differentiation. Importantly, IL-17F enhanced the expression of most osteogenic markers to a greater extent than IL-17A alone following 9 days' exposure. Conversely, IL-17A treatment resulted in elevated *in vitro* mineralisation vs IL-17F. Th17 and γδ-T cell SNs potently enhanced hPDSC osteogenic differentiation and mineralisation. Whilst *IL-6* expression and *in vitro* bone formation were blocked by neutralisation of IL-17A or IL-17F, dual neutralisation of IL-17A and IL-17F in the inflammatory milieu exhibited the greatest effect on most of the tested parameters.
Conclusions: These data show that both IL-17A and IL-17F enhance *in vitro* osteogenic differentiation and bone formation from hPDSCs. The source of these cytokines has not been established but is likely to involve entheseal resident γδ-T cells. We propose that following their release, IL-17A and IL-17F drive pathological bone formation resulting in enthesophytes at the enthesis/periosteum interface. Current therapeutics display limited efficacy in blocking enthesophyte formation, hence inhibition of both IL-17A and IL-17F offers an attractive therapeutic strategy to prevent this debilitating feature of SpA.
References:
[1] Ono, et al. Nat Commun 2016;7:10928.
[2] Lories, et al. Arthritis Res Ther 2009;11:221.
Disclosure of Interest: M. Shah Grant/research support from: UCB Pharma, Employee of: UCB Pharma, A. Maroof Employee of: UCB Pharma, R. Al-Hosni: None declared, P. Gikas: None declared, N. Gozzard Employee of: UCB Pharma, S. Shaw Employee of: UCB Pharma, S. Roberts Employee of: UCB Pharma
DOI: 10.1136/annrheumdis-2017-eular.3826

THU0061 REGULATION OF OSTEOCLAST RECRUITMENT AND ACTIVATION BY RESOLVIN D1

H.A. Benabdoune, P. Rondon, Q. Shi, J.C. Fernandes, H. Fahmi, M. Benderdour. *Research Centre, Sacré-Coeur Hospital of Montreal, Room K-3045, Montreal, Canada*

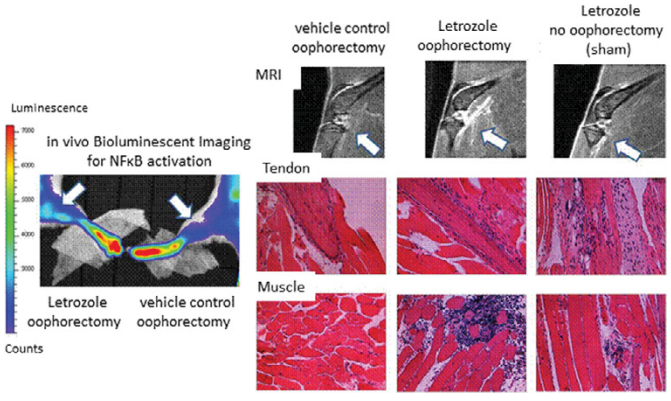
Background: Resolvin-D1 (RvD1) is a derivative of omega-3 fatty acids and a potent anti-inflammatory agent synthesized during the resolution phase of inflammation. In human cartilage, we recently reported that RvD1 strongly inhibited a number of factors involved in inflammation, catabolism, oxidative stress, and apoptosis.
Objectives: The overall objective of this study is to further investigate RvD1 effects on bone metabolism in vitro.
Methods: First, murine macrophages RAW267.4 were used to assess osteoclasts (OC) recruitment and bone resorption. RAW264.7 cells were incubated with 50 ng/ml LPS with or without RvD1 (0 - 10 μM) for 48 hours. Cell viability was verified with the MTS test. OC phenotype *markers, namely* TRAP and cathepsin-K, were assessed by western blot, enzymatic staining and immunocytochemistry. Levels of TNF-α, IL-1β, IL-6, IL-10, were measured by ELISA, and PGE_2 levels by EIA. NO release was measured by Greiss reaction.
To investigate bone resorption, RAW264.7 cells were seeded in hydroxyapatite plates, then treated with 50 ng/ml LPS with or without RvD1 (0.5 and 1 μ M) for 48 hours. Plot formation was assessed by Von Kossa staining.

Second, human osteoblasts (Ob) were obtained from post-surgery discarded trabecular bone of osteoarthritic (OA) patients who underwent total knee arthroplasty. First passage human OA Ob were treated either with RvD1 (0.1 - 1 μM) alone, or with 20 nM VitD3 with or without RvD1 (0.1 - 1 μ M), for 48 hours. Cell viability was evaluated with the MTS test. Alkaline phosphatase (PAL) activity and osteocalcin (OCN) release was determined by colorimetric reaction and ELISA, respectively.
Results: In RAW264.7 cells, our results clearly show that RvD1 strongly reduces OC recruitment and activation as indicated by the inhibition of TRAP and cathepsin K expression as well as TNF-α, IL-1β, IL-6, PGE_2 and NO release, as well as the concurrent enhancement of IL-10 levels. Besides, RvD1 decreases bone resorption through the inhibition of plots formation in hydroxyapatite matrix. In human OA Ob, RvD1 partially decreases VitD3-induced PAL activity, while it maintains OCN expression at control levels.
Conclusions: Our in vitro results clearly show that RvD1 may play an important role in the regulation of bone metabolism. Additionally to our previous data, our findings suggest that RvD1 may offer a novel and original perspective to make a real contribution to musculoskeletal and bone diseases therapy.
Acknowledgements: This study was supported by Canadian Institute of Health Research (CIHR) grant (#IMH 131570) and by the Center of Excellence for Arthroplasty Research.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2934

THU0062 NOVEL ANIMAL MODEL OF AROMATASE INHIBITOR-INDUCED ARTHRALGIA SUGGESTS AN ESTROGEN-INDEPENDENT INFLAMMATORY MECHANISM

N.A. Young[1], E. Thomas[1], B. Snoad[1], J. Sharma[1], M. Mobeen[1], A.C. DeVries[2], A. Bratasz[3], M. Lustberg[4], W. Jarjour[1], R. Reinbolt[4].
[1]Rheumatology and Immunology; [2]Department of Neuroscience; [3]Small Animal Imaging Core; [4]Medical Oncology, The Ohio State University Wexner Medical Center, Columbus, United States

Background: Aromatase Inhibitors (AIs) block physiological estrogen production in peripheral tissues and significantly improve overall survival rates of post-menopausal, hormone receptor-positive breast cancer patients by reducing tumor recurrences. However, half of patients taking these drugs develop aromatase inhibitor induced arthralgia (AIIA), which is characterized by severe pain and inflammation in various joints. Since AIIA leads to suspension of therapy in 20% of patients, reducing incidence may provide sustained AI treatment and enhanced long-term survival.
Objectives: In order to establish a better understanding of the inflammatory mechanism and to create a platform that can be used to explore interventional strategies, our objective in this study was to design a novel animal model of AIIA.
Methods: Female BALB/C-Tg (NFκB-RE-luc)-Xen mice, which have a firefly luciferase cDNA reporter gene under the regulation of 3 κB responsive binding sites, were oophorectomized and treated with AI (letrozole) by daily subcutaneous injections. Control groups included oophorectomized mice receiving vehicle control injections and non-oophorectomized mice treated with AI. Bioluminescent imaging of hind limbs was performed after 3 weeks on the in vivo imaging system (IVIS) to measure NFκB activation. At 5 weeks, knee joints and surrounding tissue were imaged on the BioSpec 94/30 micro-MRI. Legs were collected for histopathological analysis and serum cytokine levels were measured at experimental endpoint.
Results: Bioluminescent imaging showed significantly enhanced NFκB activation in the hind limbs compared to oophorectomized controls receiving vehicle treatment. Analysis of knee joints and legs by MRI imaging showed enhanced signal detection in the joint space and surrounding tissue following AI treatment. Surprisingly, enhanced MRI detection was also demonstrated in non-oophorectomized mice that were treated with AI. Histopathological analysis further demonstrated mild inflammation in the synovial tissue and joint damage in mice treated receiving AI both with and without oophorectomy. Moreover, tenosynovitis and inflammatory muscle tissue infiltrates were detected in AI-treated mice and serum cytokine levels of IL-2, IL-4, IL-6, and CXCL1 were significantly elevated.



Conclusions: Collectively, these data establish a novel mouse model of AIIA and suggest that the pathogenesis of AI-induced inflammation is estrogen-independent. Future studies will be directed into the characterization of this inflammatory mechanism to provide insight into potential therapeutic strategies directed at mitigating this adverse inflammatory burden.
References:
[1] Henry NL, Giles JT, Ang D, et al. Prospective characterization of musculoskeletal symptoms in early stage breast cancer patients treated with aromatase inhibitors. Breast cancer research and treatment. 2008;111(2):365–372.
[2] Mao JJ, Stricker C, Bruner D, et al. Patterns and risk factors associated with aromatase inhibitor-related arthralgia among breast cancer survivors. Cancer. 2009;115(16):3631–3639.
Acknowledgements: Stefanie Spielman Fund for Breast Cancer Research and The Wexner Medical Center.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5424

THU0063 IL-1 FAMILY CYTOKINES AND RECEPTORS IN IGG4-RELATED DISEASE

R. Capecchi[1], P. Italiani[2], I. Puxeddu[1], F. Pratesi[1], A. Tavoni[3], D. Boraschi[2], P. Migliorini[1]. *[1]Clinical and Experimental Medicine, Clinical Immunology Unit, university of Pisa, pisa; [2]Institute of Protein Biochemistry, National Research Council, Naples; [3]Clinical and Experimental Medicine, University of Pisa, Clinical Immunology Unit, university of Pisa, pisa, Italy*

Background: IgG4-related disease (IgG4-RD) is a fibroinflammatory condition that can affect almost any organ, characterized by lymphoplasmocytoid infiltrate, obliterative phlebitis and storiform fibrosis often associated with eosinophilia and increased levels of IgG4. Cytotoxic CD4 T cells producing IL-1b [D1], TGFb1 and IFN-gare detectable in peripheral blood of patients and high IL-18 expression has been found in affected organs.
Objectives: To evaluate the role of IL-1 family cytokines in IgG4-RD, by analyzing cytokines and receptors in sera.
Methods: Nine patients fulfilling the proposed criteria (Umehara, 2012) for the diagnosis of IgG4-RD were recruited. Cytokines of the IL-1 family (IL-1a, IL-1b, IL-33, IL-18), soluble receptors (sIL-1R1, sIL-1R2, sIL-1R3, sIL-1R4) and antagonists (IL-1Ra, IL-18BP) were measured in sera by multiarray ELISA assay. Free IL-18 was calculated using the law of mass action.
Results: Most patients had a multiorgan disease; retroperitoneum, salivary glands, pancreas and lymph nodes were most frequently affected. IL-18 ($p=0.007$) and free IL-18 ($p<0.0001$), sIL-1R1 ($p=0.0005$), sIL-1R2 ($p=0.0013$), and sIL-1R4 ($p=0.0006$) were significantly increased in IgG4-RD sera compared with healthy controls.
Conclusions: In IgG4-RD patients, at variance with other autoimmune or autoinflammatory conditions, the increase in IL-18 levels is not counterbalanced by IL-18BP, leading to high levels of free IL-18.The free cytokine may affect T cell subset balance and induce IFN-g production. The parallel increase of sIL-1R1 and sIL-1R2 suggests an efficient dampening of inflammatory IL-1bsignaling at the tissue level, while high levels of sIL-1R4 may be associated with vascular remodeling and fibrosis, as observed in animal models of obesity and in human cardiovascular disorders.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5816

THU0064 ADAM-10 AS A TOCILIZUMAB TREATMENT PREDICTIVE FACTOR IN RHEUMATOID ARTHRITIS

T. Isozaki, S. Nishimi, A. Nishimi, S. Ishii, T. Tokunaga, H. Furuya, K. Wakabayashi, T. Kasama. *Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan*

Background: A disintegrin and metalloproteinases (ADAMs) are a family of transmembrane and secreted proteins. ADAM-10 has been reported to be the enzyme responsible for the release of a number of chemokines and cytokine receptors. We have shown that ADAM-10 is overexpressed on rheumatoid arthritis (RA) synovial tissue endothelial cells (ECs) and lining cells compared with osteoarthritis and normal tissues. We also demonstrated that ADAM-10 mediates EC migration and tube formed.
Objectives: In order to demonstrate for ADAM-10 in clinical side, we focused on ADAM-10 as predictive factor for treatment with biologics in RA.
Methods: The serum was collected from patients before the initial treatment with biological therapies. Fifteen patients were treated with adalimumab (ADA), and 20 patents were treated with tocilizumab (TCZ). ADAM-10 and fractalkine/CX3CL1 were measured by enzyme-linked immunosorbent assay at 0, 12, 24 and 54 weeks. Clinical disease activity was evaluated by clinical disease activity index (CDAI). Following biological therapies, we defined biologic-responders as patients whose DAS28 scores decreased by more than 1.2 at 24 weeks. ADAM-10 baseline was also compared between responders and nonresponders at 24 weeks.
Results: There were no significant differences were observed in the mean age, gender ratio, dosages of predonisolone and methotraxate between ADA and TCZ groups. In ADA group, baseline DAS28 for the 15 patients was 4.8±0.3 (2.5–7.2).

On the other hands, baseline DAS28 for the 20 patients was 4.8±0.3 (2.5–6.8) in TCZ group. There were no differences between ADA and TCZ groups. RA patients with an insufficient response to ADA or TCZ showed highly significant improvement of DAS28 after 12 weeks (2.9±0.3 and 2.2±0.4, respectively), and 24 weeks (2.5±0.4 to 2.2±0.2, respectively). ADAM-10 highly correlates with CDAI, and fractalkine/CX3CL1. Serum ADAM-10 levels were no remarkable change after treatment with ADA despite decrease of disease activity of RA. On the other hand, serum ADAM-10 levels in patients who were treated with TCZ were significantly diminished following successful treatment and clinical improvement (baseline 408±88 pg/ml and 54 weeks 138±51 pg/ml, $p<0.05$). Univariate logistic regression analysis, baseline of DAS28 (ESR), baseline of CDAI, and ADAM-10 were selected as significant variables for improvement of DAS28 (ESR) at 24 weeks. Multiple regression analysis showed that ADAM-10 was only identified as independent predictive variable for improvement of DAS28 (ESR) at 24 weeks. ADAM-10 baseline in TCZ responder was significantly higher than TCZ nonresponders at 24 weeks (620±134 pg/ml and 109±25 pg/ml, respectively, $p<0.05$).

Conclusions: This study indicates that ADAM-10 is correlated with RA disease activity, and is higher in TCZ responders. These results suggest that ADAM-10 may be a predictor of treatment effectiveness for RA with TCZ.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4594

THU0065 CYTOKINES AND LIPOCALIN-2 IN PREGNANT WOMEN WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

T.T. Pedersen[1], M.H. Fenstad[2], T.S. Moksnes[1], M. Wallenius[1], T.H. Flo[3], M. Haug[3]. *[1]Norwegian National Advisory Unit on Pregnancy and Rheumatic diseases; [2]Dep. of Immunology and Transfusion Medicine, St. Olavs Hospital; [3]Centre of Molecular Inflammation Research and Dep. of Cancer Research and Molecular Medicine, NTNU, Trondheim, Norway*

Background: Rheumatoid arthritis (RA), and especially seronegative RA, is often ameliorated by pregnancy, while systemic lupus erythematosus (SLE) is prone to flare and associated with pregnancy complications. Cytokines and chemokines are of great importance for immune processes during pregnancy. The inflammatory marker Lipocalin-2 (LCN2) has become increasingly relevant as a potential clinical biomarker of rheumatic diseases (1). LCN2 is produced in the maternal-fetal interface during normal pregnancies and correlates with the presence and severity of preeclampsia (2).

Objectives: To obtain a better understanding of immune regulation and the disparate immune responses in pregnant women with RA and SLE. In this pilot study, we analyzed levels of multiple cytokines, chemokines and LCN2 in women with seropositive RA, seronegative RA, SLE and healthy controls during pregnancy and postpartum.

Methods: The Norwegian National Advisory Unit on Pregnancy and Rheumatic Diseases collect serum samples in a biobank from women with inflammatory rheumatic diseases before pregnancy, during pregnancy week 10–12, week 23–25, week 30–32 and 6 weeks, 6 months and 12 months postpartum. Control serum samples were collected from healthy pregnant women at matching time-points. We analyzed serum cytokine and chemokine levels using a multiplex assay. A sandwich ELISA was used to measure LCN2. In this pilot study we included pregnant women with SLE (n=4), seropositive RA (n=4), seronegative RA (n=2) and healthy pregnant controls (n=4). The total cohort consists so far of 18 pregnant women with SLE and 23 pregnant women with RA.

Results: We observed lower LCN2 levels during pregnancy in SLE patients, compared to controls and RA patients. LCN2 levels in seropositive RA patients and controls were found to be comparable during pregnancy, whereas pregnant women with seronegative RA showed higher LCN2 levels. Levels of IFNγ, IL-6 and IP-10 were higher in SLE than in RA patients during the course of pregnancy. IL-17 was slightly higher only in seropositive RA patients compared to controls. TNFα was slightly higher in both SLE and RA patients compared to controls, levels of anti-inflammatory IL-10 were very low or undetectable in all groups.

2. Trimester	Controls	SLE	Seropos RA	Seroneg RA
LCN2 (ng/ml)	285,5 (±74,7)	126,5 (±44,6)	232,6 (±67,4)	330,2 (±3,2)
IFNγ (pg/ml)	15,0 (±22,4)	40,4 (±65,1)	6,9 (±5,2)	26,1 (±9,9)
IL-6 (pg/ml)	3,4 (±1,9)	5,9 (±2,0)	3,8 (±1,5)	5,3 (±1,0)
IP-10 (pg/ml)	60,3 (±14,5)	138,3 (±92,1)	61,7 (±8,9)	64,9 (±7,3)
IL-17 (pg/ml)	1,3 (±1,3)	2,3 (±2,2)	4,8 (±9,0)	0,6 (±0,2)
TNFα (pg/ml)	2,2 (±2,5)	4,2 (±5,4)	3,3 (±3,5)	3,2 (±0,7)

Conclusions: We found interesting differences in cytokine, chemokine and LCN2 levels during pregnancy in women with SLE, seropositive RA and seronegative RA. The results need confirmation in the total cohort and will be further explored for a better understanding of the disparate immune modulation of RA and SLE during pregnancy.

References:

[1] Abella V et al. Biomarkers. 2015;20(8):565–71.
[2] Kim SM et al. Reproductive sciences. 2013;20(9):1083–9.

Acknowledgements: This study is supported by grants from St. Olavs Hospital and Norsk Revmatikerforbund.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1916

THU0066 OSTEOCLAST DIFFERENTIATION GENE EXPRESSION PROFILING REVEALS CCL4 MEDIATES RANKL-INDUCED OSTEOCLAST MIGRATION

W. Xuan[1], X. Feng[2], Y. Shi[1], F. Wang[3], M. Zhang[1], W. Tan[1]. *[1]Rheumatology; [2]Traditional Chinese Medicine; [3]Department of Cardiology, the First Affiliated Hospital of Nanjing Medical University, China, nanjing, China*

Background: The migration of osteoclast from circulation and bone marrow into bone surface has suggested as a novel therapeutic point for bone erosion in RA.

Objectives: We explored the mechanisms involved in osteoclast migration.

Methods: Gene expression profiling was identified by microarray analysis and validated by Real-time PCR during differentiation of bone marrow-derived macrophages (BMMs) into osteoclast (OCs). RANKL induced osteoclast precursor cell line RAW264.7 migration and invasion in the presence and absence of anti-CCL4 antibody was measured in vitro. Intracellular signaling pathway was assessed by Western blotting. Osteoclast formation was identified by TRAP staining.

Results: A panel of 11 chemokines signal was significant increase in osteoclastic differentiation of BMMs by Microarray. High expression of CCL4 was validated in primary BMMs and RAW264.7 cell line during differentiated into OCs. RANKL induced osteoclast precursor cell migration and invasion was decreased upon addition of anti-CCL4 antibody. OCs formation and OCs related genes expression were not affected by CCL4 inhibition. Neutralization of CCL4 promoted the PI13K phosphorylation at 45 to 60min after RANKL stimulation in RAW264.7.

Conclusions: CCL4 regulates RANKL-induced OCs migration, suggesting that CCL4 inhibition could be bone protective in RA

References:

[1] Boyce BF: Advances in the regulation of osteoclasts and osteoclast functions. Journal of dental research 2013, 92(10):860–867.
[2] Crotti TN, Dharmapatni AA, Alias E, Haynes DR: Osteoimmunology: Major and Costimulatory Pathway Expression Associated with Chronic Inflammatory Induced Bone Loss. Journal of immunology research 2015, 2015:281287.
[3] Boyle WJ, Simonet WS, Lacey DL: Osteoclast differentiation and activation. Nature 2003, 423(6937):337–342.

Acknowledgements: Support for this work was obtained from the National Natural Science Foundation of China (NSFC): 30701129 (WT), 30901332 (FW), 81172845 (WT), 81273294 (MZ), National Natural Science Foundation of Jiangsu province: BK2011851 (WT), BK2012875 (MZ), the special project of clinical medicine from Jiangsu province: BL2013034 (MZ), A Project Funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD), and scholarship from Asia Pacific League of Associations for Rheumatology (APLAR) and International League of Associations for Rheumatology (ILAR) (WT).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4255

THU0067 NLRP3 INFLAMMASOME ACTIVITY IN MONOCYTES IS REGULATED BY 12/15-LIPOXYGENASE

Y. Kusche, K. Barczyk-Kahlert, J. Roth. *Institut Der Immunologie, Münster, Germany*

Background: Activation of the NLRP3 inflammasome is a major inflammatory pathway in monocytes in response to various exogenous and endogenous stimuli. However, negative regulation of inflammasome activity is not well understood. Glucocorticoids (GC) are drugs of choice for the treatment of many inflammatory diseases. Recently, we could show that treatment of monocytes with GC leads to re-programming towards a specific population involved in resolution of inflammation. Gene analysis has shown up-regulated expression of 12/15-lipoxygenase (12/15-LOX) in GC-and LPS/GC-treated monocytes. 12/15-LOX reacts with polyunsaturated-fatty-acids to generate anti-inflammatory lipid-mediators, which contribute to resolution of inflammation.

Objectives: The aim of our study was to determine the contribution of 12/15-LOX on the inflammatory response on murine monocytes.

Methods: Bone marrow-derived monocytes were isolated from wild-type (wt) C57BL/6 and 12/15-LOX$^{-/-}$ mice and stimulated with GC and/or LPS as well as various inhibitors or stimulants. Gene expression was analyzed using qRT-PCR. Protein expression was examined by Western-Blot, Flow-Cytometry and ELISA. T-cell response was analyzed by co-culture of stimulated monocytes with allogenic T-cells.

Results: 12/15-LOX$^{-/-}$ monocytes showed slightly higher secretion of IL-1β as compared to wt cells after LPS stimulation. The differences between wt and 12/15-LOX$^{-/-}$ were much more pronounced when monocytes were additionally exposed to ATP. LPS treatment markedly enhanced expression of pro-IL-1β in 12/15-LOX$^{-/-}$ monocytes. No differences could be observed between wt and 12/15-LOX$^{-/-}$ monocytes in secretion of other proinflammatory mediators as well as the expression of inflammasome components. However, expression of cleaved caspase-11 was up-regulated in 12/15-LOX$^{-/-}$ monocytes exposed to LPS. Additionally, inhibition of caspase-11, caspase-1 and 5-LOX significantly reduced the high secretion of IL-1β in 12/15 LOX$^{-/-}$ monocytes. Interestingly, 12/15-LOX$^{-/-}$ rather than wt monocytes stimulated with LPS led to enhanced T-cell proliferation.

Conclusions: Our results demonstrate that 12/15-LOX plays a regulatory role during inflammatory immune response by counteracting the NLRP3 inflammasome activity through down-regulation of caspase-11 and 5-LOX activity. Thus, we identified a novel negative regulatory pathway of inflammasome activity.

References:
[1] Barczyk, K. et al. Glucocorticoids promote survival of anti-inflammatory macrophages via stimulation of adenosine receptor A3. Cancer 116, 1–3 (2010).
[2] Conrad, D.J. The arachidonate 12/15 lipoxygenases. A review of tissue expression and biologic function. Clinical reviews in allergy&immunology17, 71–89 (1999).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4897

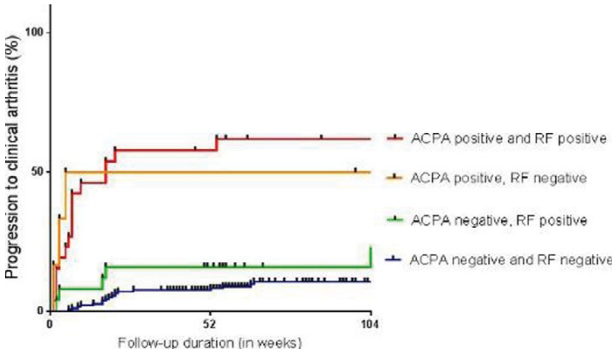
THURSDAY, 15 JUNE 2017

Rheumatoid arthritis - prognosis, predictors and outcome

THU0068 THE RISK OF INDIVIDUAL AUTOANTIBODIES, AUTOANTIBODY COMBINATIONS AND AUTOANTIBODY LEVELS FOR ARTHRITIS DEVELOPMENT IN CLINICALLY SUSPECT ARTHRALGIA

R.M. Ten Brinck, H.W. van Steenbergen, M.A. van Delft, M.K. Verheul, R.E. Toes, L.A. Trouw, A.H. van der Helm-van Mil. *Rheumatology, Leiden University Medical Centre, Leiden, Netherlands*

Background: Autoantibody testing is helpful to predict progression to arthritis in subjects at risk. Previous longitudinal studies mainly focussed on autoantibody-positive arthralgia patients. Consequently predictive values of autoantibodies were evaluated relative to each other. This study assessed risks of having anticitrullinated protein antibodies (ACPA), rheumatoid factor (RF) and/or anti-carbamylated protein antibodies (anti-CarP) for arthritis development in arthralgia patients considered at risk for RA by rheumatologists based on clinical characteristics (Clinically Suspect Arthralgia, CSA).
Objectives: To assess risks of having anticitrullinated protein antibodies (ACPA), rheumatoid factor (RF) and/or anti-carbamylated protein antibodies (anti-CarP) for arthritis development in arthralgia patients considered at risk for RA by rheumatologists based on clinical characteristics (CSA).
Methods: Baseline ACPA, RF and anti-CarP antibodies of 241 patients, consecutively included in the CSA-cohort, were studied in relation to development of clinical arthritis during a median follow-up of 103 (IQR 81–114) weeks.
Results: ACPA, RF and anti-CarP antibodies were all univariably associated with arthritis development, hazard ratios (95% CI) were 8.5 (4.7–15.5), 5.1 (2.8–9.3) and 3.9 (1.9–7.7). Only ACPA, and not RF or anti-CarP, was independently associated (HR 5.1, 2.0–13.2). Relative to autoantibody-negative CSA-patients, ACPA-negative/RF-positive patients had HRs of 2.6 (1.04–6.6), ACPA-positive/RF-negative patients 8.0 (2.4–27.4), and ACPA-positive/RF-positive patients 10.5 (5.4–20.6, Figure). PPVs for development of clinical arthritis within two years were: 38% for ACPA-negative/RF-positive, 50% for ACPA-positive/RF-negative, and 67% for ACPA-positive/RF-positive patients. Higher ACPA-levels were not significantly associated with increased progression to clinical arthritis, in contrast to higher RF-levels. Autoantibody levels were stable during follow-up.



Conclusions: ACPA conferred the highest risk for arthritis development and had an additive value to RF. However, >30% of ACPA-positive/RF-positive CSA-patients did not develop arthritis during two-year follow-up. Thus CSA and information on autoantibodies is insufficient to accurately identify imminent autoantibody-positive RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4721

THU0069 HOW MANY RHEUMATOID ARTHRITIS PATIENTS IN REMISSION EXPERIENCE PAIN? WHAT TYPES AND WITH WHAT FREQUENCY WERE PAINKILLERS RECEIVED? IS REACHING REMISSION A REALISTIC GOAL?

E. Torikai, M. Suzuki, Y. Matsuyama. *Orthopaedic Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan*

Background: The primary treatment goal in rheumatoid arthritis (RA) patients is to reach remission. Earlier diagnosis, advancements in disease-modifying antirheumatic drugs, and improved treatment strategies have enabled increasing numbers of RA patients to achieve remission. However, the definition of remission involves the fulfillment of specific criteria, which include a number of swollen and tender joints, the erythrocyte sedimentation rate (ESR), and the visual analog scale of pain (VAS pain). Some patients with RA in remission wished to take painkillers because they experienced pain and physical limitations in their daily life or at work. Is reaching remission a realistic goal?
Objectives: To evaluate VAS pain and patient's global assessment (PGA) in those with RA in remission, and to determine the types and frequency of which painkillers were received.
Methods: In a study of 554 RA patients with a definite RA diagnosis according to 1987 ACR criteria, we enrolled 235 patients (82% females). All patients had DAS28-ESR <2.6, defined as clinical remission, and had no acute pain as a result of operation or trauma. The mean age and disease activity were 53.6 years and 2.67, respectively. Seventy-one percent of patients were treated with MTX, 30.2% with glucocorticoids, and 38.4% with a biological agent. We evaluated VAS pain and PGA and investigated why patients experienced dissatisfaction with VAS pain and PGA. Moreover, we elucidated how many patients used painkillers and what types of painkillers were used.
Results: The mean values of clinical and laboratory data were described as follows: 28 swollen joints, 0.69; 28 tender joints, 1.56; RF, 157 IU/mL; C-reactive protein, 0.14 mg/dL; ESR, 19 mm/h; and health assessment questionnaire disability index score, 0.618. Steinblocker stages (I/II/III/IV) were (166/51/18/0), respectively and Steinblocker classes (I/II/III/IV) were (155/68/12/0), respectively. The mean VAS pain was 1.81. Thirty-five (14.9%) of 235 patients had VAS pain >3 (Fig. 1). The mean PGA was 1.54. Seventeen patients (7.2%) reported PGA >3 (Fig. 2). Reasons for VAS pain or PGA of >3 were musculoskeletal pain (48.6%), neuropathic pain (23.1%), psychological reasons (9.3%), and other (19%). Thirty-one patients (13.2%) were treated with painkillers such as NSAIDs (46.2%), acetaminophen (22.5%), pregabalin (18.6%), tramadol (4.1%), and other (8.6%). The mean values for VAS pain and PGA were improved after using painkillers by 0.73 and 0.36, respectively. There was a significant difference in the improvement rate of VAS pain and PGA between pre-use and post-use of pain-killer (Fig. 3).

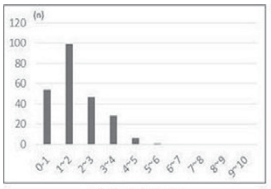


Fig.1 VAS pain

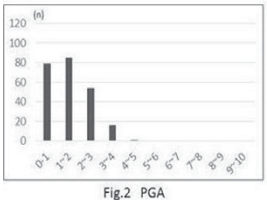


Fig.2 PGA

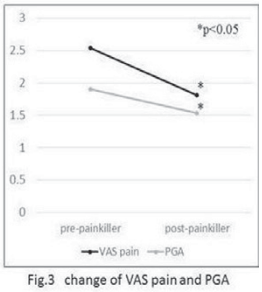


Fig.3 change of VAS pain and PGA

Conclusions: VAS pain and PGA are important for understanding the patients' functional disabilities and problems. We should attend to patients' demands and make an informed decision to form a realistic goal for RA treatment. Given that VAS pain and PGA were improved because of the use of painkillers in the current study, we suggest that the ability to appropriately prescribe painkillers is an important method with which to satisfy RA patients in remission.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1760

THU0070 TREAT-TO-TARGET IN RA: WHAT LEVEL OF TREATMENT RESPONSE IS NECESSARY BY 3 MONTHS IN ORDER TO ACHIEVE THE TREATMENT TARGET BY 6 MONTHS? RESULTS FROM A REAL LIFE STUDY

V. Norvang[1], I.C. Olsen[1], E.K. Kristianslund[1], T. Uhlig[1], T.K. Kvien[1], D. Aletaha[2], J. Smolen[2], E.A. Haavardsholm[1]. *[1]Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; [2]Division of Rheumatology, Department of Internal Medicine 3, Medical Universitiy of Vienna, Vienna, Austria*

Background: When initiating therapy with disease-modifying anti-rheumatic drugs

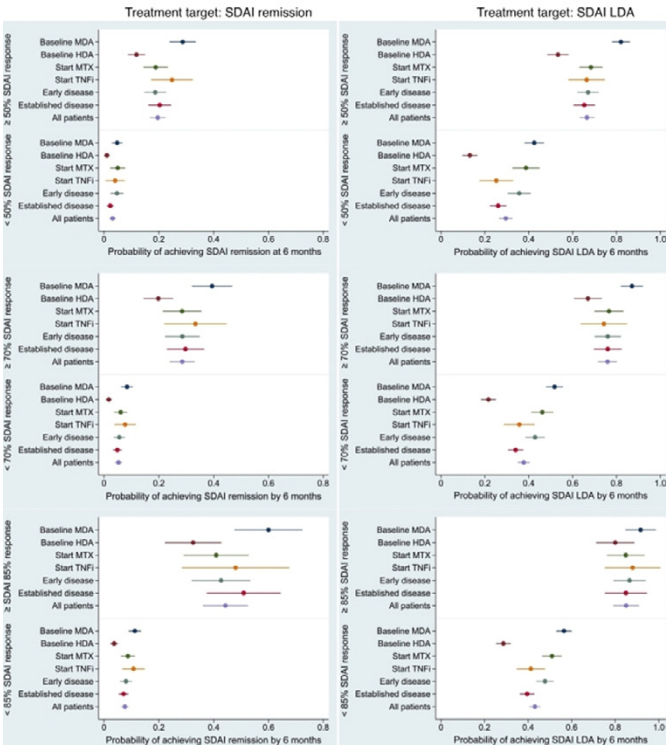
(DMARDs) in patients with rheumatoid arthritis (RA), treatment adoptions are recommended if no improvement in disease activity is seen within 3 months, or if the treatment target has not been reached by 6 months.[1] A pooled analyses from several pivotal RCTs showed that RA patients who did not achieve a minor treatment response by 3 months were unlikely to reach the treatment target by 6 months.[2]

Objectives: To examine what level of treatment response is needed after 3 months of therapy in order to achieve the treatment target of remission (REM) or low disease activity (LDA) by 6 months in a routine clinical setting.

Methods: Data were provided by NOR-DMARD, a prospective, multicentre, observational study. We selected RA-patients enrolled between December 2000 and November 2012, who were biological DMARD-naïve and had a moderate or high disease activity (MDA or HDA, respectively) according to the Simplified Disease Activity Index (SDAI) when initiating therapy. All analyses were performed for the total group of included patients (n=1610), as well as for the following sub-groups: disease duration over (n=895) or under (n=681) 12 months, baseline SDAI MDA (n=825) or HDA (n=785), DMARD-naive patients starting methotrexate (MTX) (n=537) and patients starting tumour necrosis factor inhibitor (TNFi) (n=248). We used a diagnostic test approach, created receiver operating characteristic curves and generated sensitivities, specificities and likelihood ratios (LRs) for all improvement cut-points (0–100%) at the 3-month visit. Furthermore, we tested the ability of established response criteria (SDAI 50/70/85 response) at 3 months to predict the desired target of SDAI remission or SDAI LDA at 6 months.

Results: At inclusion median (IQR) disease duration was 2 (0.2–8.8) years and mean (SD) SDAI was 28.3 (12.8). At 6 months 46.8% of all patients had achieved LDA and 10.8% had reached remission. Not achieving a minor treatment response (SDAI 50% response) by 3 months was associated with decreased probability of reaching remission at 6 months (LR- 0.27), but gave little prognostic information regarding the probability of reaching LDA (LR- 0.49). Patients with HDA at baseline who did not achieve at least 50% improvement in disease activity by 3 months had very low probability of reaching the treatment target by 6 months (LR- 0.15 for remission and LR- 0.30 for LDA). SDAI 85% response at 3 months was predictive of reaching the treatment target at 6 months (LR+ 6.56 for remission and LR+ of 6.45 for LDA). For the total group of patients, a reduction in SDAI of 60.2% was needed at 3 months to predict LDA at 6 months with 80% specificity, while 69.2% improvement was necessary to predict remission.

SDAI response at 3 months and probability of achieving the treatment target by 6 months



Conclusions: These results from a routine clinical setting confirm results from RCTs demonstrating a predictive association between treatment response at 3 months and achievement of the treatment target by 6 months in RA-patients. Assessments at 3 months can inform clinicians to continue or adjust ongoing DMARD-therapy in a treat-to-target strategy aiming for remission or LDA by 6 months.

References:

[1] Smolen JS, et al. Ann Rheum Dis 2014;73(3):492–509.
[2] Aletaha D, et al. Ann Rheum Dis 2016;75(8):1479–85.

Disclosure of Interest: V. Norvang: None declared, I. Olsen: None declared, E. Kristianslund: None declared, T. Uhlig: None declared, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer, Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Norvartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, D. Aletaha Consultant for: Abbvie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, UCB, Speakers bureau: Abbvie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, UCB, J. Smolen Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celltrion, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, BMS, Celltrion, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, UCB, E. Haavardsholm Grant/research support from: AbbVie, Pfizer, Roche, MSD, UCB, Consultant for: AbbVie, Pfizer, Roche, Eli Lilly, Celgene, UCB
DOI: 10.1136/annrheumdis-2017-eular.2900

THU0071 RADIOGRAPHIC PROGRESSION IN EARLY RHEUMATOID ARTHRITIS PATIENTS FOLLOWING INITIAL COMBINATION VERSUS STEP-UP TREAT TO TARGET THERAPY IN DAILY CLINICAL PRACTICE: RESULTS FROM THE DREAM REGISTRY

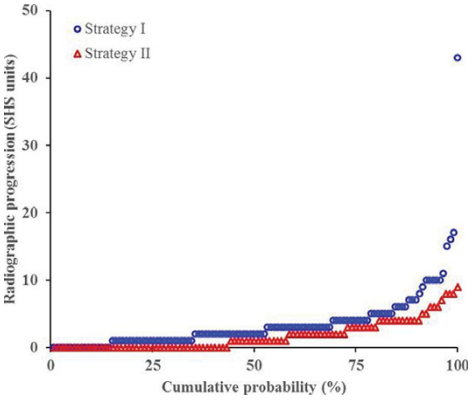
L.M. Steunebrink[1], G.A. Versteeg[2], H.E. Vonkeman[1], P.M. ten Klooster[3], M. Hoekstra[4], M.A. van de Laar[1]. *[1]Arthritis Center Twente, Department of Rheumatology, Department Psychology, Health & Technology, Medisch Spectrum Twente, University of Twente; [2]Arthritis Center Twente, Department of Rheumatology, Department Psychology, Health & Technology, Medisch Spectrum Twente, University of Twente; [3]Department Psychology, Health & Technology, University of Twente, Enschede; [4]Department of Rheumatology, Isala, Zwolle, Netherlands*

Background: Early and aggressive targeted treatment with disease modifying anti-rheumatic drugs (DMARDs) has been shown to lead to substantial reductions in disease activity (1,2) and radiologic damage in patients with early rheumatoid arthritis (RA) (3,4).

Objectives: The aim of this study was to compare the first-year radiographic progression rates between a treat-to-target (T2T) strategy with initial combination therapy (strategy II) versus an initial step-up monotherapy (strategy I).

Methods: A total of 128 patients from strategy II was individually matched with 128 patients from strategy I on sex, age (± 5 yrs.) and baseline disease activity (± 0.5 on the DAS28). Differences in radiographic progression scores and the number of patients experiencing a minimal clinically important difference (≥5 SHS points; MCID) between both strategies were tested with Mann Whitney U test and chi-square test. Next, linear and logistic regression analyses were performed to examine which baseline variables were associated with radiographic progression scores and the probability of experiencing an MCID within 1 year.

Results: Patients with initial combination therapy had slightly higher baseline disease activity scores and pain scores, but better mental health scores. Patients with initial monotherapy had significantly more, and more frequently clinically relevant, radiographic progression after one year. Experiencing a MCID was associated with fewer tender joints (p=0.05) and higher ESR (p=0.02) at baseline.



Conclusions: Excellent radiographic outcome was achieved for patients treated according to a protocolled T2T strategy in daily clinical practice. Patients treated with initial monotherapy had significantly more short-term radiographic progression than patients treated with initial combination therapy.

References:

[1] Steunebrink LMM, Vonkeman HE, ten Klooster PM, et al. (2016) Recently diagnosed rheumatoid arthritis patients benefit from a treat-to-target strategy: results from the DREAM registry. Clin Rheumatol 35:609–615. doi: 10.1007/s10067–016–3191–3.
[2] Steunebrink LMM, Versteeg GA, Vonkeman HE, et al. (2015) Initial combination therapy versus step-up therapy in treatment to the target of remission in daily clinical practice in early rheumatoid arthritis patients: results from the DREAM registry. Arthritis Res Ther 18:60. doi: 10.1186/s13075–016–0962–9.
[3] Stenger AA, Van Leeuwen MA, Houtman PM, et al. (1998) Early effective suppression of inflammation in rheumatoid arthritis reduces radiographic progression. Br J Rheumatol 37:1157–63.

[4] Goekoop-Ruiterman YPM, de Vries-Bouwstra JK, Allaart CF, et al. (2008) Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis (the BeSt study): A randomized, controlled trial. Arthritis Rheum 58:S126–35. doi: 10.1002/art.23364.

Acknowledgements: We would like to thank all the patients, rheumatology nurses, and rheumatologists who participated in our study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1638

THU0072 RISK OF REVISION, PROSTHETIC JOINT INFECTION AND DEATH FOLLOWING TOTAL HIP OR KNEE ARTHROPLASTY IN PATIENTS WITH RHEUMATOID ARTHRITIS – A NATIONWIDE COHORT STUDY FROM DENMARK

R.L. Cordtz[1,2], L.E. Kristensen[2], S. Overgaard[3], A. Odgaard[4], H. Lindegaard[5], L. Dreyer[1,2]. *[1]Center for Rheumatology and Spine Diseases, Gentofte, Rigshospitalet; [2]The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen; [3]Dept. of Orthopaedic Surgery and Traumatology, Odense University Hospital, Odense; [4]Dept. of Orthopaedics, Herlev and Gentofte Hospital, Copenhagen; [5]Dept. of Rheumatology, Odense University Hospital, Odense, Denmark*

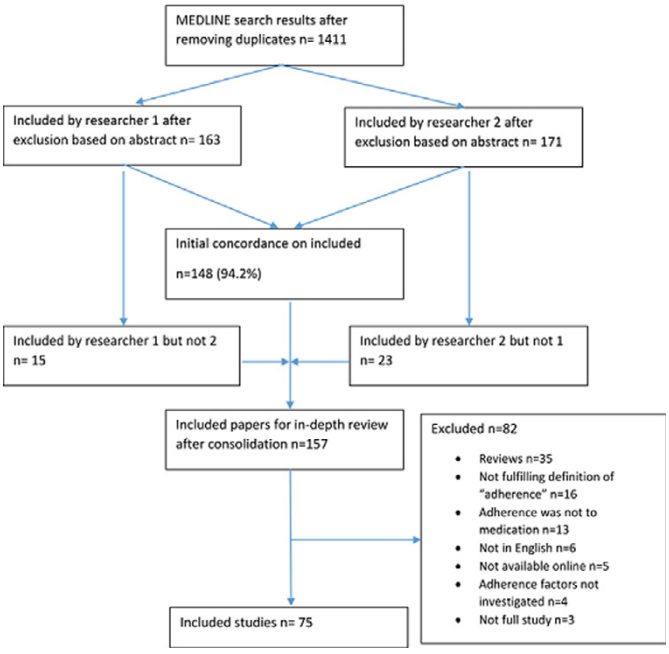
Background: Studies have shown that rheumatoid arthritis (RA) patients are at increased risk of prosthetic joint infection (PJI) but with non-uniform results for mortality risk, following total hip and knee arthroplasty (THA and TKA, respectively). The impact of biological DMARD (bDMARD) treatment on the risk of these outcomes is unknown.
Objectives: To investigate the risk of revision, PJI and death following THA and TKA in 1) RA compared with osteoarthritis (OA) patients and 2) RA patients treated with bDMARDs compared with those not.
Methods: Register-based cohort study linking the National Patient Register, DANBIO, Danish Hip Arthroplasty Register and Danish Knee Arthroplasty Register.
Follow-up: from date of THA/TKA to date of any of the outcomes, to 10 years of follow-up or end of 2014, whichever came first.
Statistics: Fine-Gray competing risks analyses to calculate confounder adjusted sub-Hazard Ratios (aSHR) with 95% confidence intervals (95% CI) for revision and PJI; Cox proportional hazard models to calculate aHR for risk of death.
Results: We identified 3913 RA and 120 499 OA patients. In DANBIO, 360 bDMARD and 1586 not-bDMARD treated RA patients were eligible for analysis. See Table for results.
Conclusions: We report an increased risk of death and PJI but a lower risk of revision in patients with RA compared with OA following THA and TKA. In RA patients, prednisolone, but not bDMARD treatment within the year prior and/or following THA and TKA was associated with an increased risk of death.
Disclosure of Interest: R. Cordtz: None declared, L. E. Kristensen: None declared, S. Overgaard Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, MSD, Novartis, Eli Lilly, Janssen Pharmaceuticals, A. Odgaard: None declared, H. Lindegaard: None declared, L. Dreyer Consultant for: LD has received fees for speaking and consultancy by MSD, UCB and Janssen pharmaceuticals.
DOI: 10.1136/annrheumdis-2017-eular.1742

THU0073 FACTORS ASSOCIATED WITH TREATMENT ADHERENCE IN RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

E.T. Goh[1], A.J.X. Soo[1], J. Galloway[2], S. Norton[2], E. Nikiphorou[2]. *[1]University College London; [2]King's College London, London, United Kingdom*

Background: Nonadherence to treatment in rheumatoid arthritis (RA) has been shown to negatively impact on treat to target goals and disease outcomes. Identifying and targeting potential factors influencing nonadherence is therefore crucial in optimising patient management.
Objectives: To determine factors associated with nonadherence in patients with RA.
Methods: An electronic search was performed by two independent reviewers using MEDLINE and focusing on articles published from inception to January 2017. The search strategy combined the thesaurus (MeSH) and expanded keyword searches of two concepts: RA and treatment adherence. Inclusion criteria included observational studies and clinical trials examining potential factors associated with nonadherence. Exclusion criteria included articles not in English or without online access and those with a focus on forms of therapy other than medication. Agreement between raters at the screening stage was high (97%, kappa=.87).
Results: The primary search yielded 1411 papers, from which 75 were eventually identified as suitable for full review (Figure). Of the 75 papers, 65 were based on observational studies and 10 on clinical trials. Factors associated with nonadherence were broadly categorized into patient-related factors (socio-demographic factors, patient perceptions [beliefs/knowledge/attitudes]), disease-related factors (disease duration/severity, comorbidities, functional disability) and treatment-related factors (drug type/ method of administration/duration/regimen complexity, combination therapy). The majority (70% of all included studies) of studies reported significant associations between patient-driven factors and nonadherence. Adherence was found to be negatively associated with socioeconomic status, health literacy, and beliefs/perceptions/knowledge of the disease and treatment. Studies reported poorer mental health state (n=6) and greater disability/pain (n=7) to be implicated in nonadherence. Disease duration was largely non-significant in treatment adherence, although a few studies reported a negative correlation (n=3). Combining biologics with DMARDs was associated with improved adherence. However, considering non-biologic DMARDs only, adherence rates were higher amongst monotherapy users. One study identified polypharmacy to be negatively associated with adherence. Drug side effects were associated with nonadherence (n=7).

Figure. Study selection process & outcomes.



Conclusions: Patient-related factors including personal perceptions were among key contributors to nonadherence to medication in RA patients. This highlights the need for addressing patient-driven perceptions, along with disease and treatment

Acknowledgements: Many thanks to Simon Coates and Julia Garthwaite of Library Services at University College London for their advice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5137

Abstract THU0072 – Table 1. aSHRs and aHRs for risk of revision, PJI or death following THA/TKA in patients with RA compared with OA; and bDMARD treated RA patients compared with not-bDMARD treated, respectively

	RA (n=3913) vs OA (n=120 499)			bDMARD (n=360) vs no bDMARD (n=1586)		
	Revision aSHR (95% CI)	PJI aSHR (95% CI)	Death aSHR (95% CI)	Revision aSHR (95% CI)	PJI aSHR (95% CI)	Death aSHR (95% CI)
RA vs OA	0.71 (0.57–0.89)†	1.84 (1.55–2.18)†	1.58 (1.48–1.70)†	–	–	–
bDMARD treated§	–	–	–	0.99 (0.40–2.42)	0.94 (0.42–2.12)	0.97 (0.62–1.51)
Age at surgery	0.98 (0.98–0.98)†	1.00 (0.99–1.00)	1.09 (1.09–1.09)†	1.01 (0.98–1.03)	1.00 (0.97–1.02)	1.10 (1.08–1.12)†
Previous infection w/ hospitalization	1.48 (1.34–1.64)†	1.70 (1.53–1.90)	1.50 (1.45–1.56)†	0.94 (0.38–2.36)	1.56 (0.83–2.94)	2.14 (1.51–3.02)†
Chronic obstructive pulmonary disease	1.17 (0.99–1.37)	1.32 (1.11–1.56)	1.96 (1.86–2.06)†	2.26 (0.77–6.64)	1.19 (0.41–3.45)	1.08 (0.63–1.86)
Seropositive RA (seronegative as ref.)	–	–	–	1.33 (0.31–5.67)	4.54 (0.65–31.67)	1.92 (0.92–3.97)
csDMARD treated§	–	–	–	0.77 (0.33–1.81)	1.04 (0.53–2.02)	0.65 (0.44–0.96)†
Prednisolone treated§	–	–	–	1.72 (0.80–3.70)	1.18 (0.54–2.58)	1.88 (1.28–2.76)†

*Multivariate models were further adjusted for sex, calendar period (2000–02; 2003–05; 2006–08; 2009–11; 2012–14), DAS-28-CRP (remission, low; moderate or high DAS according to EULAR Remission Criteria), HAQ-DI and history of diabetes mellitus or ischaemic heart disease. †$p<0.05$. §Exposure defined as treatment in year prior and/or following surgery. Abbreviations: csDMARD, conventional synthetic DMARD; DAS28-CRP, Disease activity score using 28-joint count and C-reactive protein.

THU0074 BODY MASS INDEX IN EARLY RHEUMATOID ARTHRITIS IN UNDERWEIGHT PATIENTS IS ASSOCIATED WITH MORE PROGRESSION OF EROSIONS OVER 15 YEARS AND IN OBESE PATIENTS WITH LESS PROGRESSION OF JOINT SPACE NARROWING

S. Ajeganova[1], K. Forslind[2], B. Svensson[2], I. Hafström[1]. [1]*Department of Medicine Huddinge, Karolinska Instiutet, Stockholm;* [2]*Department of Clinical Sciences, Lund University, Lund, Sweden*

Background: Previous short-term follow-up studies and subanalyses of clinical trials in rheumatoid arthritis (RA) have suggested that low body mass index (BMI) is associated with more radiographic joint progression and high BMI with less. The effect of BMI on progression of erosion score (ES) and joint space narrowing (JSN) could be different in underweight and obese patients.
Objectives: To investigate the association between BMI in early RA with radiographic damage during 15 years; to examine if known predictors of a worse radiographic outcome could explain differential radiographic outcome in low and high BMI groups.
Methods: Four hundred and seventy-three patients from the BARFOT study included from 1992 to 1999 who performed their 15-year assessment were studied. The patients were assessed at inclusion and after 1, 2, 5, 8 and 15 years. The groups were defined by BMI (kg/m^2) at inclusion: BMI $\leq$20, (n=27), BMI 20$<$25 (n=210), BMI 25$<$30 (n=179), and BMI$\geq$30 (n=57). X-rays of hands and feet were scored by the Sharp-van der Heijde scoring method (SHS). Linear mixed models with SHS, ESR, CRP, SJC and TJC as outcome, and BMI at inclusion as predictor was used, adjusted for age, sex, initial treatment, ACPA and smoking.
Results: At baseline, total score of SHS, ES and JSN did not differ between BMI groups. There were more women and smokers in BMI$\leq$20 group and older patients in BMI$\geq$30 group. The baseline disease characteristics were similar in the BMI groups.
For the patients with BMI$\leq$20 at inclusion, BMI was associated with a higher predicted SHS progression during follow-up, effect size 5.11 (95% CI 1.72 to 15.15) p=0.005, while for the patients with BMI$\geq$30 at inclusion, BMI was associated with lower SHS, effect size 0.92 (0.86 to 0.99) p=0.028. The directions of association between BMI at inclusion and ES and JSN were similar to that for the total SHS. The effect size of the association with erosion progression was however significant only in the BMI$\leq$20 group, 1.15 (2.72 to 6.42) p=0.025 (in the BMI$\geq$30 group 0.95 (0.90–1.00) p=0.074). On the other hand, association between BMI and JSN progression was significant only in the BMI$\geq$30 group, 0.93 (0.87 to 0.99) p=0.033 (in the BMI$\leq$20 group 2.53 (0.83–7.67) p=0.096).
There were no associations between BMI and radiographic damage in BMI 20$<$25 and BMI 25$<$30 groups.
We found no significant association between BMI and ESR, CRP, SJC, TJC over time in the BMI$\leq$20 group. In the BMI$\geq$30 group, BMI was associated with a higher predicted CRP during follow-up, effect size 1.06 (1.01 to 1.12) p=0.028, but not with ESR and SJC. Compared to the patients with BMI 20–25, patients with BMI$\geq$30 had higher TJC over 15 years, 3.17 (1.06 to 9.27) p=0.038.
Conclusions: Underweight at onset of RA is associated with more radiographic damage up to 15 years and obesity with less joint damage, independent of sex, ACPA and smoking status. The effect of BMI is not explained by measures of disease activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4141

THU0075 THE RELATIONSHIP BETWEEN DISEASE ACTIVITY AND DISABILITY IS MEDIATED BY PAIN AND FATIGUE IN EARLY RHEUMATOID ARTHRITIS

S. Twigg[1,2], E.M.A. Hensor[1], P. Emery[1], A.W. Morgan[1], A. Tennant[3] on behalf of Yorkshire Early Arthritis Register. [1]*Leeds Institute Rheumatic and Musculoskeletal Medicine, University of Leeds;* [2]*National Institute for Health Research- Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom;* [3]*Swiss Paraplegic Research, Nottwil, Switzerland*

Background: Disability in early rheumatoid arthritis (RA) is correlated with disease activity. However, the relationship between these two clinical outcomes is relatively under-investigated. Understanding how disability is driven by disease activity will allow targeted interventions to improve function in early RA, alongside the suppression of inflammation.
Objectives: To identify mediators in the relationship between disease activity and disability in early RA.
Methods: Cases with new consultant-made diagnoses of RA were recruited to Yorkshire Early Arthritis Register within 24 months of symptom onset. At the baseline assessment, clinical variables were collected including the 3 variable disease activity score from counts of 28 tender and swollen joints and C-reactive protein (DAS28), Health Assessment Questionnaire (HAQ) and visual analogue scores (VAS) of pain and fatigue. Structural equation models (SEM) were constructed to evaluate the relationship between DAS28, HAQ, pain, symptom duration (SD), age and fatigue.
Results: Of 721 cases included, 482 were female and 239 male. Median age was 58 for both genders and median HAQ was 1.25 and 1.00 for women and men, respectively. A path model within a SEM framework (Figure 1) was a good fit to the data (Chi square 7.528, df=6, p=0.2748; CFI 0.997; RMSEA 0.027). However, the model could not be applied simultaneously to both genders; although estimates of regression coefficients did not vary between males and females (metric invariance), model intercepts were different. In earlier models, age was not a significant predictor and regressions of fatigue on DAS28 were not significant: the effect of DAS28 upon fatigue was fully mediated by pain. Standardised coefficients of direct and indirect effects of DAS28 on HAQ are shown in Table 1, together with Sobel tests for significance of mediator variables. The greatest effect upon HAQ was the direct effect from DAS28, but some of the effect of DAS28 on HAQ was partially mediated by pain. Furthermore, the effect of pain upon HAQ was also partially mediated through fatigue. According to the Sobel test, pain and fatigue were significant mediators in both females and males.

Table 1 Total, Direct and Indirect effects upon HAQ

Standardised effect upon HAQ	Females			Males		
	Estimate	SE	p	Estimate	SE	p
DAS28 total	0.412	0.040	<0.001	0.508	0.053	<0.001
DAS28 indirect	0.139	0.024	<0.001	0.163	0.033	<0.001
DAS28- direct	0.282	0.046	<0.001	0.344	0.060	<0.001
DAS28 via pain and fatigue	0.038	0.010	<0.001	0.032	0.014	0.025
DAS28 via pain	0.101	0.024	<0.001	0.131	0.033	<0.001
Sobel test statistic (fatigue via pain)	3.280	0.002	0.001	2.279	0.002	0.022
Sobel test statistic (Pain)	3.920	0.085	<0.001	3.253	0.122	0.001

SE, standard error.

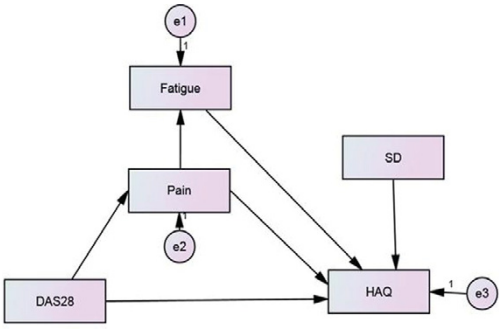


Figure 1. Path diagram to show the relationship between disease activity and disability mediated by pain and fatigue.
SD, symptom duration; e1-3, error terms (representing the unexplained variance in outcomes)

Conclusions: DAS28 dominates the impact upon HAQ in early RA; pain is shown to be an important mediator of the effects of DAS28 on HAQ, while fatigue is important as a mediator of the effect of pain on HAQ. This adds to previous evidence that pain is a driver of fatigue in RA (1) and suggests that interventions to manage pain could be important adjuncts to supression of inflammation in early RA, in order to optimise function.
References:
[1] Druce KL, Jones GT, Macfarlane GJ, Basu N. (2015) Arthritis & Rheumatology, 67: 2303.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6152

THU0076 DISEASE-MODIFYING TREATMENT REGIMENS HAVE BEEN INSUFFICIENT TO REDUCE THE INCIDENCE OF SYSTEMIC AA AMYLOIDOSIS ASSOCIATED WITH RHEUMATOID ARTHRITIS IN CONTRAST TO A SIGNIFICANT REDUCTION IN THOSE WITH JUVENILE IDIOPATHIC ARTHRITIS

T.A.-B. Youngstein[1], T. Lane[1], J. Gilbertson[1], J. Pinney[1], T. Rezk[1], R. Manwani[1], C.C. Quarta[1], A. Wechalekar[1], S. Mahmood[1], S. Sachchithanantham[2], M. Fontana[1], C. Whelan[1], J.D. Gillmore[3], P.N. Hawkins[1], H.J. Lachmann[1]. [1]*National Amyloidosis Centre, UCL Division of Medicine;* [2]*National Amyloidosis Centre, UCL Division of Medicine, London;* [3]*National Amyloidosis Centre, National Amyloidosis Centre, UCL Division of Medicine, London, London, United Kingdom*

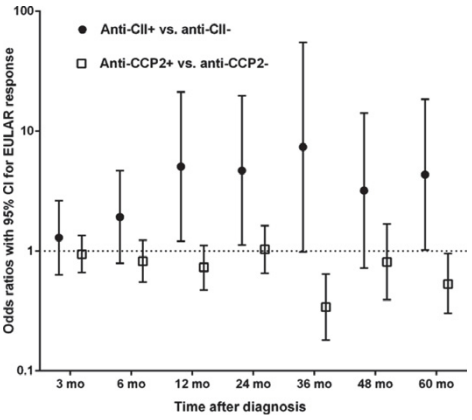
Background: The UK National Amyloidosis Centre has the largest known cohort of individuals with AA amyloidosis, with 660 cases since 1990. A third present in end stage renal failure (33%), with a median survival of 133 months from diagnosis[1]. Over 27 years the rate of new cases has remained remarkably constant with a median of 24 diagnoses per annum (IQR 18.5–30.5) but responsible for a decreasing proportion of new cases of systemic amyloidosis from 35% in the first 5 years to 6% in the last 5 years of the cohort.
Objectives: We sought to determine to what extent advances in treatment of the inflammatory arthritides have influenced the aetiology of AA Amyloidosis over time.
Methods: Retrospective analysis of the UK National Amyloidosis Centre AA

Amyloidosis database containing baseline demographic and clinical data. Data was analysed using a Chi-squared test (GraphPad Prism 7.0).
Results: Between 1990–2000 there were 188 new cases of AA Amyloidosis of which 51 (27.1%) had an underlying diagnosis of rheumatoid arthritis (RA), median age at diagnosis of amyloid was 60 years. 37 (19.7%) had a diagnosis of Juvenile Idiopathic Arthritis (JIA), median age 29 years. Between 2007 and 2017 there were 270 new diagnoses of AA Amyloidosis, of whom 57 had RA (21.1%), median age 66 years, and 5 (1.9%) had JIA, median age 37 years. Since the widespread use of combination disease-modifying and biologic therapy there has been a significant reduction in the incidence of JIA-associated AA Amyloidosis ($p<0.0001$). In contrast, the incidence of RA-associated AA Amyloidosis is unchanged ($p<0.1357$).
Conclusions: Advances in the treatment of JIA have significantly reduced the incidence of AA Amyloidosis in this cohort. In contrast, despite largely the same medication and similar treatment targets, RA continues to be responsible for a substantial proportion of new cases of AA Amyloidosis. One possible explanation for this may be that current assessment of disease activity in RA is sufficient to identify those at risk of joint damage or radiological progression of disease but insufficient for identifying peristent subclinical biochemical inflammation. One approach for reducing this risk may be the routine measure of the AA Amyloid precursor protein, serum Amyloid A protein (SAA) in those with RA, as it is well established that levels of SAA of below 10mg/L prevents the accumulation of AA Amyloid in those with inflammatory disease.
References:
[1] Lachmann, H. J., Goodman HJ, Gilbertson JA, Gallimore JR, Sabin CA, Gillmore JD, Hawkins PN (2007). Natural history and outcome in systemic AA amyloidosis. N Engl J Med 356(23): 2361–2371.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5005

THU0077 ANTI-COLLAGEN TYPE II ANTIBODIES ARE ASSOCIATED WITH AN ACUTE ONSET RHEUMATOID ARTHRITIS PHENOTYPE AND PROGNOSTICATE LOWER DEGREE OF INFLAMMATION

V.A. Manivel[1], M. Mullazehi[1], L. Padyukov[2], H. Westerlind[3], L. Klareskog[2], L. Alfredsson[3], S. Saevarsdottir[2], J. Rönnelid[1]. *[1]Immunology genetics and Pathology, Uppsala University, Uppsala; [2]Rheumatology Unit, Department of Medicine, Karolinska University Hospital and Karolinska Institutet; [3]Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden*

Background: Anti-collagen II antibody (anti-CII) positive RA patients present with early but not persistent signs of inflammation and joint erosions. This early anti-CII-dependent phenotype coincides with high anti-CII levels around the time of RA diagnosis, whereafter anti-CII levels drop. Our previous studies showed that this phenotype is associated with *in vitro* cytokine production by monocytes, activation of granulocytes, and enhanced chemokine production by monocyte/granulocyte cocultures, stimulated with anti-CII containing immune complexes. These *in vitro* findings argue that elevated anti-CII levels at time of RA diagnosis are functionally related to the corresponding acute onset RA phenotype.
Objectives: Our previous comparison done in a small RA cohort (n=274) describe that anti-cyclic citrullinated peptide 2 (anti-CCP2) positive patients have a severe long-term prognosis but anti-CII positive patients have transient inflammation. In the present study we wanted to extend this in a large RA cohort with clinical follow-up data, and to relate to HLA-DRB1* alleles.
Methods: Anti-CII and anti-CCP2 were measured at baseline in 773 patients from the Swedish Epidemiological Investigations in Rheumatoid Arthritis (EIRA) study with clinical follow-up data from the Swedish Rheumatology Quality (SRQ) registry, and 1476 patients with HLA-DRB1* information. Comparisons were done concerning CRP, ESR, TJC, SJC, DAS28, DAS28CRP, pain-VAS, global-VAS and HAQ at 8 occasions during 5 years, and association to HLA-DRB1* alleles.
Results: Anti-CII was detected in 6.6% (97/1476), and anti-CCP2 in 57.9% (855/1476) of the patients. There was no significant difference in treatment strategy at diagnosis for patients with and without those antibodies. Anti-CII associated with elevated CRP, ESR, SJC, DAS28 and DAS28CRP at diagnosis and up to six months, whereas anti-CCP2 associated with SJC and DAS28 from 6 months to 5 years, but not earlier. The anti-CII-associated phenotype was strong, and predominated also in anti-CII/anti-CCP2 double positive patients. Compared to baseline levels, anti-CII was asscociated with improvements in CRP, ESR, SJC, TJC and DAS28 over time, whereas anti-CCP2 was associated with deteriorations in SJC and DAS28 over time, compared to antibody negative patients. Anti-CII positive patients achieved EULAR good or moderate response more often than negative patients whereas the opposite was found for anti-CCP2 positive patients (figure). Anti-CII was positively associated with HLADRB1*01 and HLADRB1*03, with significant interaction, and double positive individuals had >14 times higher mean anti-CII levels than HLA double negatives. Whereas smoking associated with elevated anti-CCP2 levels, smokers has lower anti-CII levels.



Conclusions: Anti-CII seropositive RA represents a distinct phenotype, in many respects representing the converse to the clinical, genetic and smoking associations described for ACPA. Although not diagnostically useful, early anti-CII determinations predict favourable inflammatory outcome in RA. The combined analysis of anti-CII and ACPA/anti-CCP2 may be a new two-dimensional tool for predicting the prognosis and chosing therapy in newly diagnosed RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2776

THU0078 CONCOMITANT USE OF CONVENTIONAL SYNTHETIC DMARDS AND RESPONSE TO BARICITINIB

A. Kavanaugh[1], C. Helt[2], D. Muram[2], J. Alam[2], V. Arora[2], A.L. Pinto Correia[2], I. de la Torre[2], R. van Vollenhoven[3]. *[1]UC San Diego School of Medicine, la Jolla; [2]Eli Lilly and Company, Indianapolis, United States; [3]Amsterdam Rheumatology & Immunol Center, Amsterdam, Netherlands*

Background: Baricitinib (BARI), an oral JAK1/JAK2 inhibitor, is in development for patients (pts) with moderate to severe rheumatoid arthritis (RA).[1,2]
Objectives: This post-hoc analysis of two phase 3 studies assessed whether concomitant use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) altered the response or safety outcomes to BARI in RA pts and evaluated the effect of concomitant corticosteroid use on the efficacy of BARI.
Methods: Pts with ≥6 swollen and tender joints and no prior biologic DMARD use were enrolled. In RA-BEAM (NCT01710358), methotrexate (MTX)-inadequate responder (IR) pts were randomised to PBO once daily (QD), BARI 4 mg QD, or adalimumab 40 mg biweekly.[1] In RA-BUILD (NCT01710358), csDMARD-IR pts were randomised to placebo (PBO) or BARI (2 or 4 mg) QD.[2] Pts continued background csDMARD (including MTX) therapy. This post-hoc analysis included the PBO (N=716) and BARI 4 mg (N=714) pts and assessed the number and type of concomitant csDMARDS and concurrent corticosteroid use.
Results: 71%, 21%, and 6% of PBO pts were taking MTX alone, MTX + ≥1 other csDMARD, and non-MTX csDMARDs, respectively; in BARI 4 mg pts, the

Abstract THU0078 – Table 1. Efficacy and Safety Through 12 Weeks Based on Concomitant csDMARD Usage

	Placebo (N=716)			Baricitinib 4 mg (N=714)		
	MTX Alone (n=506)	MTX + ≥1 csDMARDs (n=147)	Non-MTX csDMARDs (n=43)	MTX Alone (n=527)	MTX + ≥1 csDMARDs (n=131)	Non-MTX csDMARDs (n=42)
Efficacy measures						
ACR20	210 (42)	57 (39)	17 (40)	361 (69)	85 (65)	25 (60)
ACR50	84 (17)	18 (12)	7 (16)	227 (43)	52 (40)	13 (31)
ACR70	20 (4)	7 (5)	3 (7)	106 (20)	19 (15)	5 (12)
SDAI ≤11	92 (18)	18 (12)	10 (23)	221 (42)	45 (34)	14 (33)
SDAI ≤3.3	8 (2)	3 (2)	0	52 (10)	4 (3)	2 (5)
DAS28-ESR ≤3.2	11 (2)	3 (2)	1 (2)	58 (11)	11 (8)	2 (5)
DAS28-ESR <2.6	35 (7)	10 (7)	4 (9)	129 (24)	27 (21)	7 (17)
Safety measures						
≥1 adverse event	442 (87)	132 (90)	39 (91)	465 (88)	116 (89)	40 (95)
≥1 serious adverse event	14 (3)	4 (3)	3 (7)	14 (3)	1 (1)	1 (2)
Discontinuation due to adverse event	16 (3)	2 (1)	0	11 (2)	5 (4)	3 (7)
Death	1 (0.2)	1 (0.7)	0	0	0	0

Data are n (%).

rates were 74%, 18%, and 6%, respectively. Oral corticosteroids were used in 56% of PBO and 55% of BARI pts at baseline; pts continued use throughout the studies. The differences in clinical efficacy between BARI 4 mg and PBO at 12 weeks was similar regardless of the number or type of csDMARDs concomitantly used (Table) or the concomitant use of corticosteroids (data not shown). The rates of serious adverse events and discontinuation due to adverse events were comparable regardless of the number or type of csDMARDs used (Table) or corticosteroid use.

ACR20/50/70=20%, 50%, and 70% improvement in American College of Rheumatology criteria; csDMARDs=conventional synthetic disease-modifying antirheumatic drugs; DAS28-ESR=Disease Activity Score 28-erythrocyte sedimentation rate; MTX=methotrexate; SDAI=Simple Disease Activity Index.

Conclusions: BARI has demonstrated clinical safety and efficacy in a wide range of pts, regardless of the number of concomitant csDMARDs or concomitant use of corticosteroids.

References:

[1] Taylor PC et al. Arthritis Rheumatol 2015;67(S10):3927–3928.
[2] Dougados M et al. Ann Rheum Dis 2017;76:88–95.

Disclosure of Interest: A. Kavanaugh Consultant for: Eli Lilly and Company, C. Helt Employee of: Eli Lilly and Company, D. Muram Employee of: Eli Lilly and Company, J. Alam Employee of: Eli Lilly and Company, V. Arora Employee of: Eli Lilly and Company, A. L. Pinto Correia Employee of: Eli Lilly and Company, I. de la Torre Employee of: Eli Lilly and Company, R. van Vollenhoven Grant/research support from: Abbvie, Amgen, BMS, GSK, Pfizer, Roche, UCB, Consultant for: Abbvie, Biotest, BMS, Celgene, Crescendo, GSK, Janssen, Eli Lilly and Company, Merck, Novartis, Pfizer, Roche, UCB, Vertex

DOI: 10.1136/annrheumdis-2017-eular.1342

THU0079 EVALUATION OF SYNOVITIS IN THE FOOT AND THE ANKLE NOT INCLUDED IN THE 28-JOINT DISEASE ACTIVITY SCORE USING ULTRASONOGRAPHY AND HISTOLOGICAL FINDINGS IN THE PATIENTS WITH RHEUMATOID ARTHRITIS

A. Abe, H. Ishikawa. *Rheumatology, Niigata Rheumatic Center, Shibata, Japan*

Background: In the treatment of rheumatoid arthritis (RA), the early diagnosis and early medical treatment via tight control have become increasingly important with the advent of biological therapy. Ultrasonography (US) for the affected joints enables the evaluation of synovial hypertrophy, effusion and bone erosion in real time. US is a reliable method that can detect more erosive sites than radiography. US is now utilized widely and is a reliable tool of rheumatologists for diagnosing RA and evaluating the disease activity.

Objectives: This study was conducted to clarify the relationship between the systemic disease activity, local disease activity using US and a synovial histopathological evaluation.

Methods: Between March 2011 and September 2015, 668 joints were surgically treated on the whole, and synovial biopsies were performed at the time of surgery. Among them, a total of 118 toes and 21 ankles, which are not included in the 28-joint disease activity score (DAS28), were investigated. Just before surgery, the US probe was placed on the dorsal aspect of the ankle and/or the toes to evaluate the activity of local synovitis. The maximum grade of power Doppler (PD) signal was determined, ranging from 0 to 3. The serum C reactive protein (CRP), matrix metalloproteinase-3 (MMP-3) and DAS28 values were also examined just before surgery. A histopathological examination of the gathered synovium at the surgical site was performed using the Rooney score (RS). Biological disease-modifying antirheumatic drugs were used in 45 cases, namely infliximab in 7 cases, etanercept in 16, adalimumab in 7, tocilizumab in 6, abatacept in 4, certolizumab pegol in 1, and golimumab in 4.

	DAS28	CRP (mg/dL)	MMP-3 (ng/mL)	RS
PD0 (n=82)	3.07 (1.07)	0.40 (0.67)	106.96 (193.69)	18.38 (3.35)
PD1 (n=32)	3.43 (1.19)	0.67 (1.08)	117.11 (92.83)	22.38 (6.58)
PD2 (n=20)	3.41 (0.89)	0.61 (0.71)	124.81 (52.61)	32.85 (6.96)
PD3 (n=5)	3.13 (0.52)	0.78 (0.76)	150.46 (123.87)	29.40 (4.51)

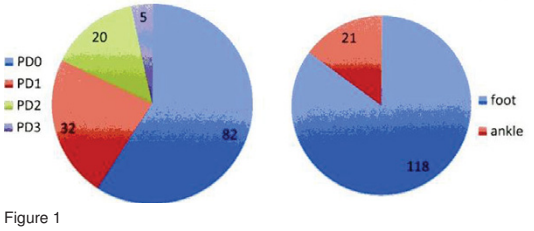


Figure 1

Results: The PD score was grade 0 in 82 cases, 1 in 32 cases, 2 in 20 cases and 3 in 5 cases. The total RS and its item scores except for "proliferating blood vessels" correlated well with the PD signal intensity. The systemic disease activity, as indicated by DAS28, CRP and MMP-3, had no significant correlation with the local PD signal intensity. However, the DAS28, CRP and MMP-3 values and each RS item score, except for "proliferating blood vessels", were significantly lower in the PD grade 0 group than in the PD grades 1, 2 and 3 groups.

Conclusions: No PD signal intensity in the ankle and foot indicates systemically well-controlled disease activity. US is an excellent tool for determining local synovitis as well as the systemic disease activity in patients with RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2011

THU0080 DEPRESSION AND ANXIETY REDUCE THE LIKELIHOOD OF ACHIEVING REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS: REAL LIFE DATA FROM THE NOR-DMARD STUDY

B. Michelsen[1,2], E.K. Kristianslund[2], K.M. Fageli[2], E. Lie[2], H.B. Hammer[2], G. Haugeberg[1,3], T.K. Kvien[2]. *[1]Dept. of Rheumatology, Hospital of Southern Norway Trust, Kristiansand; [2]Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo; [3]Dept. of Rheumatology, Martina Hansens Hospital, Bærum, Norway*

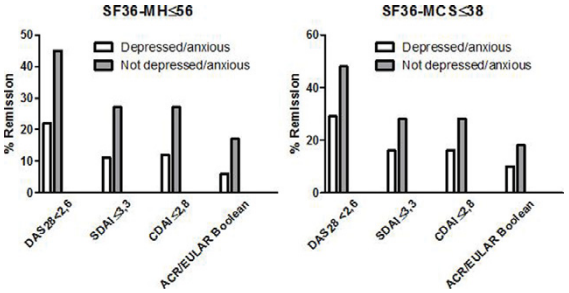
Background: Depression and anxiety are reported to predict poorer treatment outcomes in rheumatoid arthritis (RA).[1] Whether this can be confirmed in larger prospective observational studies using various remission criteria remains to be explored.

Objectives: To investigate the predictive value of baseline depression/anxiety on the likelihood of achieving remission in RA as well as the associations between baseline depression/anxiety and the components of the remission criteria at follow-up.

Methods: From the prospective, multi-center NOR-DMARD study we included RA patients starting first-time tumour necrosis factor inhibitors (TNFi) and DMARD naïve RA patients starting methotrexate (MTX) between year 2006 and 2012. The following two criteria for depression/anxiety were assessed: 1) the Medical Outcomes Survey Short Form-36 (SF-36) Mental Health subscale (MH)≤56 and 2) the SF-36 Mental Component Summary score (MCS)≤38.[2] The predictive value of baseline depression/anxiety on remission after 3 and 6 months treatment was explored in prespecified logistic regression models adjusted for age, sex, disease duration and smoking and the associations between baseline depression/anxiety and the different components of the remission criteria at follow-up in prespecified multiple linear regression models adjusted for age, sex, disease duration and smoking.

Results: A total of 1450 RA patients were included (mean (SD) age 54.4 (13.5) years, median (25th-75th percentile) disease duration 0.4 (0.0–5.0) years, 68.7% females and 28.6% current smokers). According to the SF-36MH≤56/SF-36MCS≤38 criteria 18.1/29.9% of the patients were depressed/anxious at baseline, respectively. Lower percentages of patients with versus without baseline depression/anxiety achieved remission at 3 and 6 months treatment (unadjusted analyses, figure). Baseline depression/anxiety negatively predicted remission after 3 and 6 months (adjusted analyses, table 1 and 2).

The findings were confirmed in separate subgroup analyses of TNFi/MTX treated patients. Baseline depression/anxiety were associated with increased patient's and evaluator's global assessment and 28 tender joint count at 3 and 6 months, but not with level of acute phase reactants or 28 swollen joint count.



Abstract THU0080 – Table 1. Odds ratio (95% CI) for remission in patients with versus without baseline depression/anxiety according to the SF36-MH ≤56 criterion

Months	DAS28<2.6	SDAI≤3.3	CDAI≤2.8	ACR/EULAR Boolean
3	0.48 (0.32–0.73), p<0.001	0.43 (0.25–0.74), p=0.003	0.38 (0.22–0.65), p<0.001	0.27 (0.13–0.57), p=0.001
6	0.36 (0.24–0.56), p<0.001	0.35 (0.20–0.60), p<0.001	0.38 (0.23–0.63), p<0.001	0.31 (0.16–0.61), p=0.001

Abstract THU0080 – Table 2. Odds ratio (95% CI) for remission in patients with versus without baseline depression/anxiety according to the SF36MCS ≤38 criterion

Months	DAS28ESR <2.6	SDAI ≤3.3	CDAI ≤2.8	ACR/EULAR Boolean
3	0.67 (0.49–0.93), p=0.02	0.51 (0.34–0.78), p=0.002	0.47 (0.32–0.70), p<0.001	0.35 (0.21–0.59), p<0.001
6	0.45 (0.32–0.63), p<0.001	0.46 (0.31–0.69), p<0.001	0.48 (0.33–0.69), p<0.001	0.46 (0.29–0.72), p=0.001

Conclusions: Depression and anxiety may reduce likelihood of remission based on composite scores in RA and should be taken into account in individual patients when making a shared decision on a treatment target.

References:
[1] Matcham et al.Rheumatology. 2016;55(2):268–78
[2] Matcham et al.BMC musculoskel disorders. 2016;17:224.

Disclosure of Interest: B. Michelsen: None declared, E. Kristianslund: None declared, K. Fageli: None declared, E. Lie Consultant for: Hospira, Pfizer, UCB, Speakers bureau: AbbVie, Celgene, H. Hammer Consultant for: AbbVie, Pfizer, UCB, Roche, MSD, BMS and Novartis., Speakers bureau: AbbVie, Pfizer, UCB, Roche, MSD, BMS and Novartis., G. Haugeberg: None declared, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB

DOI: 10.1136/annrheumdis-2017-eular.1787

THU0081 DIFFERENCES IN PATIENT-REPORTED OUTCOMES BETWEEN BARICITINIB AND COMPARATORS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVED LOW DISEASE ACTIVITY OR REMISSION

B. Fautrel[1], M. van de Laar[2], B. Kirkham[3], R. Alten[4], R. Cseuz[5], S. Van der Geest[6], B. Zhu[7], F. De Leonardis[8], P. Taylor[9]. *[1]University Pierre et Marie Curie, Paris, France; [2]Arthritis Centre Twente, Medisch Spectrum Twente, Enschede, Netherlands; [3]Guys Hospital, London, United Kingdom; [4]Schlosspark Klinik, Berlin, Germany; [5]Revita Private Clinic for Rheumatology, Budapest, Hungary; [6]Eli Lilly & Company, Utrecht, Netherlands; [7]Eli Lilly and Company, Indianapolis, United States; [8]Eli Lilly & Company, Geneva, Switzerland; [9]University of Oxford, Headington, United Kingdom*

Background: Achieving remission is the ideal goal in treating rheumatoid arthritis (RA). In a randomised phase 3 trial, high remission and low disease activity (LDA) rates were achieved with baricitinib (BARI). However, little is known about the differences in patient reported outcomes (PROs) among patients (pts) who have already achieved these targets.

Objectives: To compare PROs between BARI, adalimumab (ADA), and placebo (PBO) in pts with RA who achieved LDA or remission in the Phase 3 RA-BEAM study.

Methods: 1305 pts with RA and background treatment with methotrexate were randomised to receive PBO (n=488), ADA (n=330), or BARI 4 mg (n=487) for 52 wks (24 wks for PBO). In each treatment group, pts in remission (DAS28-ESR$<$2.6) and with LDA (DAS28-ESR$\leq$3.2) at wk 24 were assessed from baseline for the following PROs: Pain VAS, HAQ-DI, WPAI, Morning Joint Stiffness (MJS), and FACIT-F. Sensitivity analyses were conducted for pts in remission or LDA by DAS28-CRP, SDAI, or CDAI. The assessment of response at wk 24 was determined by using the observed data, and the missing values for PRO measures were imputed by using mLOCF.

Results: Among pts in LDA, significantly greater improvements in Pain VAS and HAQ-DI scores were observed with BARI than ADA and PBO, and significantly greater improvements in MJS were observed with BARI and ADA than PBO. Significantly greater residual pain and HAQ-DI scores were observed with PBO. Among pts in remission, significantly greater improvements in pain and HAQ-DI scores were also observed with BARI than PBO. Patients in remission or LDA showed greater numerical improvement and less residual impairment in other PROs with BARI and ADA than PBO (Table 1). Consistent results were observed using other composite measures to define LDA and remission.

PRO Measures	Baseline	Residual Mean Value at Wk 24	Observed Change at Wk 24	Baseline	Residual Mean Value at Wk 24	Observed Change at Wk 24	Baseline	Residual Mean Value at Wk 24	Observed Change at Wk 24
	For Patients in Remission from BARI 4 mg (n=87)			For Patients in Remission from ADA (n=57)			For Patients in Remission from PBO (n=24)		
Pain VAS (mm)	56.5	10.1	-46.4**	48.2	11.5	-36.7	43.8	16.5	-27.3
HAQ-DI	1.3	0.3†	-0.9**	1.1	0.3	-0.7*	1.1	0.5	-0.5
FACIT-F	32.5	43.3	10.9	35.7	44.6†	8.9	32.8	41.1	8.3
MJS Duration (min)	125.2	24.8	-100.4	118.0	18.3	-99.6	51.5	73.4	21.9
Activity Impairment (%)	52.1	14.4	-37.7	41.2	14.6	-26.7	37.5	17.5	-20.0
	For Patients in LDA from BARI 4 mg (n=154)			For Patients in LDA from ADA (n=110)			For Patients in LDA from PBO (n=46)		
Pain VAS	57.8	11.9†	-45.9***†	52.5	14.3	-38.2	45.2	18.5	-26.8
HAQ-DI	1.4	0.4†	-1.0**†	1.2	0.4	-0.8	1.1	0.5	-0.6
FACIT-F	30.3	43.1	12.8	33.3	43.7	10.4	33.6	42.6	9.0
MJS Duration (min)	116.9	25.4	-91.6*	116.0	20.9	-95.0*	77.1	53.7	-23.4
Activity Impairment (%)	52.7	15.9	-36.8*	47.3	17.0	-30.3	43.5	20.0	-23.5

†= significant at .05 level vs PBO using *t*-test. ***, **, * = significant at .001, .01, .05 levels, respectively, vs PBO. ‡ = significant at .05 level vs ADA using ANCOVA model with change value as dependent variable and treatment, region, baseline joint erosion status (1-2 erosions plus seropositivity; 3 erosions), and baseline value as factors. For MJS duration for remission, PBO, n=17; BARI 4 mg, n=57; ADA, n=37; and for LDA, PBO, n=30; BARI 4 mg, n=96; ADA, n=62.

Conclusions: The preliminary findings from this study suggest that BARI showed greater improvements in pain and HAQ-DI compared to ADA for pts in LDA, and greater improvements in pain and HAQ-DI scores as well as less physical impairment compared to PBO for pts in LDA and remission.

Acknowledgements: The authors acknowledge the contribution of Inmaculada de la Torre MD, PhD, Senior Medical Advisor.

Disclosure of Interest: B. Fautrel: None declared, M. van de Laar: None declared, B. Kirkham: None declared, R. Alten Consultant for: Eli Lilly and Company, R. Cseuz Consultant for: Eli Lilly and Company, S. Van der Geest Employee of: Eli Lilly and Company, B. Zhu Employee of: Eli Lilly and Company, F. De Leonardis Employee of: Eli Lilly and Company, P. Taylor Consultant for: Eli Lilly and Company; Abvie

DOI: 10.1136/annrheumdis-2017-eular.2213

THU0082 LUNG INVOLVEMENT IN ACPA POSITIVE SUBJECTS: A PILOT STUDY ON THE ROLE OF LABORATORY, FUNCTIONAL AND IMAGING MARKERS

B. Lucchino[1], M.C. Gerardi[1], C. Iannuccelli[1], M.P. Guzzo[1], M. Di Paolo[2], M. Bonini[2], F. Vaccaro[2], P. Palange[2], F. Vullo[3], D. Diacinti[3], G. Valesini[1], M. Di Franco[1]. *[1]Department of Internal Medicine and Medical Specialities; [2]Department of Public Health and Infectious Diseases; [3]Department of Radiology, Sapienza university of Rome, Roma, Italy*

Background: The ACPA-positive Rheumatoid Arthritis (RA) is a complex disease. Signs of immune activity against citrullinated proteins may be present years before the onset of clinical manifestations. Recent findings suggest that the lung may represent an early site of autoimmune-related injury in ACPA-positive patients without signs of arthritis.

Objectives: The purpose of the present study was to evaluate the presence of subclinical pulmonary abnormalities in ACPA-positive subjects without arthritis and in RA-patients through laboratory, functional and imaging markers.

Methods: Eleven ACPA-positive subjects without arthritis, 10 patients naïve to therapy with early ACPA-positive RA ($<$6 months duration) and 9 with established ACPA-positive RA ($<$36 months duration) were consecutively enrolled. Subjects underwent baseline pulmonary function tests (PFTs), DLCO measurement and CPET. The evaluation of Surfactant protein D (SP-D) serum levels was performed in all the patients and in 9 healthy controls matched for age and sex with an ELISA test. Twenty-four subjects underwent chest high-resolution computer tomography (HRCT), in order to evaluate parenchymal or airways abnormalities.

Results: The cohort consisted of 7 men and 23 women, mean age 48,93 (DS+/-12.1). PFTs resulted abnormal only in 2 patients. A DLCO reduction was observed in 54.5% of ACPA-positive subjects without RA, in 60% and in 55.6% of patients with early and established RA, respectively. In RA patients, an inverse correlation between disease duration and DLCO/Va (r=-0.50; p=0.03) was observed. The exercise tolerance at CPET was reduced in 54.5% of ACPA-positive subjects without RA, in 20% of patients with early RA and in 55.6% of those with established RA. Serum SP-D levels were higher in established RA (p=0.079), in ACPA-positive subjects and early RA than in healthy controls. ACPA levels positively correlated (r=0.45;p=0.01) with CPET parameters of ventilation inefficiency, suggesting a ventilation/perfusion mismatch. A negative correlation between ACPA and SP-D levels and CPET metabolic parameters was also observed. The presence of pulmonary nodules was the most common alteration founded at HRCT, equal to 28% in ACPA-positive subjects without arthritis, in 66% and 87% of patients with early and established RA, respectively. In the last group, all patients showed parenchymal abnormalities. There was also a significant (p=0.022) higher frequency of lung abnormalities in patients with established disease compared with the other two groups.

Conclusions: The early lung involvement in RA is often subclinical and baseline PFT's are scarcely informative. Although preliminary, these findings suggest that DLCO, CPET parameters and SP-D can represent early markers of the subclinical lung injury. Furthermore, lung abnormalities detectable at HRCT seem to develop early in the course of the disease. However, additional studies are needed to clarify lung abnormalities in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6216

THU0083 THE RELEVANCE OF ELEVATED CRP AS AN INCLUSION CRITERION IN CLINICAL TRIALS IN PATIENTS WITH RHEUMATOID ARTHRITIS

C. Scoville[1], J. Subotícki[2], S. Zhong[2], E. Keystone[3]. *[1]Idaho Falls Arthritis Clinic, Idaho Falls; [2]AbbVie, N Chicago, United States; [3]Mount Sinai Hospital, Univ of Toronto, Toronto, Canada*

Background: Elevated C-reactive protein (CRP) is often used as an entry criterion in clinical trials (CT) of patients (pts) with rheumatoid arthritis (RA), resulting in the potential exclusion of pts with active disease and high screen failure rates[1].

Objectives: To assess the relevance of requiring an elevated CRP ($\geq$1 mg/dL) as an inclusion criterion for clinical, functional, and radiographic outcomes.

Methods: This *post hoc* analysis used data from 2 randomized CTs in RA pts with an inadequate response to methotrexate (MTX). In DE019, pts on background MTX received adalimumab (ADA) or placebo (PBO)[2]; in MUSICA, pts received either 7.5 or 20 mg MTX, along with ADA[3]. Data from MUSICA were used

to confirm observations from DE019. Pts were subgrouped by CRP level at entry (CRP <1 mg/dL, ≥1 mg/dL). Baseline (BL) demographics and disease characteristics were summarized for each group. Clinical efficacy was assessed through swollen/tender joint count (S/TJC) at 66/68 joints, pain, patient global assessment (PtGA), physician global assessment (PhGA), CRP, clinical disease activity index (CDAI), 28-joint disease activity score based on CRP (DAS28-CRP), and proportions of pts achieving ACR20/50/70. Functional outcomes were assessed by the disability index of the health assessment questionnaire (HAQ-DI), and radiographic outcomes by the modified total Sharp score (mTSS). Outcomes were assessed in pts with CRP <0.8 mg/dL in DE019, which included pts with CRP levels as low as 0.75 mg/dL Observed data are reported at week 24.

Results: In DE019, 183 pts (89 and 94 in the ADA and PBO arms, respectively) had CRP <1 mg/dL and 224 pts (118 and 106, respectively) had CRP ≥1mg/dL. Pts with elevated CRP had higher BL disease activity compared with those with CRP <1 mg/dL at entry (not shown). After 24 wks of treatment with ADA, pts in both CRP subgroups experienced significant improvements in most clinical and functional outcomes vs PBO (Table). In pts with CRP <0.8 mg/dL, the ACR20 response rate difference (30.4, p<.001) and the difference in ΔmTSS (-1.3, p<.05) for ADA vs PBO treatment were still significant. Compared to pts with CRP <1 mg/dL, pts with elevated CRP experienced greater clinical and functional improvements. However, within the ADA subgroups, pts with elevated CRP had smaller differences vs PBO in mTSS, perhaps reflecting higher joint damage at BL. In general, similar trends were observed in MUSICA (not shown).

Disease characteristics at Week 24 in patients with CRP <1 or ≥1 mg/dL at entry in DE019

	CRP <1			CRP ≥1		
	PBO n=79	ADA n=74	Difference	PBO n=75	ADA n=101	Difference
TJC68	-13.2	-17.2	-3.2	-11.7	-16.5[e]	-6.0***
SJC66	-7.1	-11.3	-4.3**	-6.7	-12.5[e]	-5.0***
Pain	-13.0	-24.5	-11.7***	-20.3[c]	-35.8	-14.4***
PtGA	-11.0	-24.2	-13.2***	-20.7[c]	-35.5	-16.1***
PhGA	-24.4	-35.0	-10.2**	-28.0[c]	-43.2	-14.2***
HAQ-DI	-0.26[f]	-0.49	-0.24**	-0.38	-0.68	-0.31***
CRP	0.1	0.02	-0.08[g]	-0.54	-2.05	-1.08**
DAS28-CRP	-1.19	-1.92	-0.75***	-1.26[c]	-2.33[e]	-1.10***
CDAI	-15.9	-22.7	-7.6***	-15.7[c]	-26.5[e]	-11.1***
ACR20, n/N (%)	32/79 (41)	50/74 (68)	27***	30/72 (42)	82/99 (83)	41***
ACR50, n/N (%)	9/79 (11)	34/74 (46)	35***	11/72 (15)	46/99 (46)	31***
ACR70, n/N (%)	6/79 (8)	19/74 (26)	18**	0/72 (0)	19/99 (19)	19***
mTSS	0.93[a]	-0.32[b]	-1.30**	1.63[g]	0.79[d]	-0.84

Change from baseline values and least square mean differences (using ANCOVA) are reported for continuous endpoints. p-values for binary endpoints are calculated based on chi-square test or Fisher's exact test. ***, **, *: p < .001, .01 and .05, respectively for differences between treatment groups for change from BL. Missing values are not imputed.
[a]n=82, [b]n=76, [c]n=72, [d]n=102, [e]n=99, [f]n=78, [g]n=84 .
TJC68, tender joint count at 68 joints; SJC66, swollen joint count at 66 joints; PtGA, patients global assessment of disease activity; PhGA, physician's global assessment of disease activity; HAQ-DI, disability index of health assessment questionnaire; CRP, C-reactive protein; DAS28-CRP, 28-joint disease activity score based on CRP; CDAI, clinical disease activity index; mTSS, modified total Sharp score; ACR20/50/70, 20, 50 and 70% improvement in the American College of Rheumatology criteria

Conclusions: While pts with elevated CRP at entry experienced larger improvements from BL in clinical and functional outcomes upon treatment, significant improvements in most outcomes were also observed in those without elevated CRP at entry (as low as 0.75 mg/dL), suggesting that an elevated CRP may not be required to see differences between active and inactive treatment.

References:

[1] Von Vollenhoven et al. 2015, Arthritis Rheum 67: 2855–2860.
[2] Keystone et al. 2004. Arthritis Rheum;5:1400–11.
[3] Kaeley et al. 2016. J Rheum;8:1480–9.

Acknowledgements: AbbVie: study sponsor, contributed to study design, data collection, analysis and interpretation; writing, reviewing, and approval of the final version. Medical writing assistance: Naina Barretto, of AbbVie.

Disclosure of Interest: C. Scoville Speakers bureau: AbbVie, J. Subotocki Employee of: AbbVie, S. Zhong Employee of: AbbVie, E. Keystone Grant/research support from: AbbVie, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Centocor, F Hoffmann-LaRoche, Genentech, Genzyme, Merck, Novartis, Nycomed, Pfizer, and UCB., Consultant for: AbbVie, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Centocor, F Hoffmann-LaRoche, Genentech, Genzyme, Merck, Novartis, Nycomed, Pfizer, and UCB., Speakers bureau: AbbVie, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Centocor, F Hoffmann-LaRoche, Genentech, Genzyme, Merck, Novartis, Nycomed, Pfizer, and UCB.

DOI: 10.1136/annrheumdis-2017-eular.2316

THU0084 AGREEMENT BETWEEN THE DAS28-ESR AND THE DAS28-CRP AND FACTORS RELATED TO THE DISCREPANCIES BETWEEN DISEASE ACTIVITY LEVELS ACCORDING TO THESE 2 SCORES IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE ESPOIR COHORT

C. Gaujoux-Viala[1,2], M. Belkacemi[3], A. Cantagrel[4], B. Fautrel[5], B. Combe[6].
[1]Rheumatology, Nîmes University Hospital; [2]EA2415, Montpellier University, Nîmes; [3]IURC, EA2415, Montpellier; [4]Rheumatology, Toulouse University Hospital, Toulouse; [5]Rheumatology, Pitié-Salpêtrière Hospital, APHP, Paris; [6]Rheumatology, Lapeyronie Hospital, Montpellier, France

Background: DAS28 is often used as a treatment decision tool in patients with rheumatoid arthritis (RA) in the daily clinic. Although different versions of DAS28 have previously been validated, and although disease activity thresholds are the same, it is not clear whether DAS28-ESR and DAS28-CRP can be used interchangeably in individual patients.

Objectives: The aims of our study were to examine the agreement between these two DAS28 versions in individual early RA patients in the daily clinic and to idenditify factors related to the discrepancies between disease activity levels according to these 2 scores.

Methods: Baseline and 6 months data from 677 patients with early RA (ACR EULAR 2010) were extracted from the French cohort of early arthritis ESPOIR (at least 2 swollen joints for less than 6 months, DMARD naïve) and were used to calculate DAS28-ESR and DAS28-CRP. Disease activity levels according to the DAS thresholds and EULAR responses were assessed. Intraclass correlation coefficient [ICC] and weighted kappa (k) were calculated. The Bland-Altman method was used to examine the bias between the DAS scores and the 95% limits of agreement (LoA). Multivariate logistic regression was used to determine the patient and RA features independently associated with discrepancies between disease activity levels according to DAS28-ESR and DAS28-CRP.

Results: The mean value of DAS28-CRP (5.04±1.16 at M0 and 3.38±1.33 at M6) was smaller than that of mean DAS28-ESR (5.33±1.24 at M0 and 3.51±1.42 at M6). Agreement between the scores was excellent: ICC=0.93 at M0 and M6. Agreement between disease activity levels according to the 2 scores was good: k=0.70 at M0 and 0.75 at M6. Agreement between EULAR responses at M6 according to the 2 scores was good: k=0.78. At M0, the bias of DAS28-CRP was -0.28 (LoA -1.16, 0.59) and -0.14 (LoA -1.17, 0.89) at M6.There were discrepancies between disease activity levels according to the 2 scores in 122 (18.6%) patients at M0 with clear difference in moderate (88 patients for DAS28-CRP vs 29 for DAS28-ESR) and high disease activity (18 patients for DAS28-CRP vs 80 for DAS28-ESR), and in 171 (28.1%) patients at M6 with clear difference in remission (42 patients for DAS28-CRP vs 29 for DAS28-ESR) and high disease activity (9 patients for DAS28-CRP vs 32 for DAS28-ESR). At M0, presence of erosion (OR 95% CI=1.76 [1.07–2.90]), better mental component of the SF36 (OR 95% CI=2.14 [1.38–3.31]), fewer tender joint counts (TJC) and better physical component of the SF36 (PCS) (with significant interaction between TJC and PCS) were associated with discrepancies between disease activity levels according to the 2 scores. At M6, only being male (OR 95% CI=1.62 [1.09–2.41]) was associated with discrepancies.

Conclusions: DAS28-CRP significantly underestimated disease activity compared to DAS28-ESR. Agreement was high between the 2 scores, good for disease activity levels and EULAR responses. In the individual patient, however, the two scores may differ considerably. The scores should not be used interchangeably in the daily clinic without caution.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6492

THU0085 TIME TO REMISSION AND THE ACHIEVEMENT OF SUSTAINED REMISSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: SITE VARIATION ANALYSIS IN THERAPEUTIC STRATEGY FROM THE CANADIAN EARLY ARTHRITIS COHORT (CATCH)

C. Barnabe[1], O. Schieir[2], G. Hazlewood[3], J. Pope[4], C. Hitchon[5], S. Bartlett[6], G. Boire[7], E. Keystone[2], D. Tin[8], B. Haraoui[9], V. Bykerk[10], C. Thorne[8] on behalf of Canadian Early Arthritis Cohort (CATCH) Investigators. *[1]University of Calgary, Calgary; [2]University of Toronto, Toronto; [3]Medicine, University of Calgary, Calgary; [4]Western University, London; [5]University of Manitoba, Winnipeg; [6]McGill University, Montreal; [7]University of Sherbrooke, Sherbrooke; [8]South lake Regional Health Centre, Newmarket; [9]Universite de Montreal, Montreal, Canada; [10]Hospital for Special Surgery, New York, United States*

Background: Treatment response in ERA reflects individual prognostic factors and therapeutic selection which may be influenced by provider experience and beliefs. This may lead to variations in rates of and time to remission across centres involved in multi-site cohorts.

Objectives: We compared therapeutic strategies across Canadian ERA clinics in relation time to CDAI and DAS28 remission, and frequency of attaining sustained remission.

Methods: Data were analyzed for patients with >1 year of follow-up, enrolled at sites with >40 patients at baseline and >30 patients with 2 years of follow-up data. We determined time to remission and frequency of sustained remission (2 consecutive visits at least 6 months apart), using DAS28 and CDAI scores. Treatment strategy was determined as initial and ever use of oral methotrexate monotherapy, subcutaneous methotrexate monotherapy, methotrexate-based combinations, non-methotrexate DMARDs, triple therapy, or biologic therapy.

Results: 1,749 participants from 13 centers with mean age 54 years, 73% female, mean DAS28 4.9 (SD 1.4) and mean CDAI 25.6 (SD 14.6) were included. There were significant differences between centers in participant characteristics (gender, age, symptom duration, body mass index, comorbidities, smoking status, education, ethnicity, marital status, seropositive status, erosions). The

initial therapeutic strategies were oral methotrexate monotherapy 16% (site range 0%>55%), subcutaneous methotrexate monotherapy 15% (0%>45%), methotrexate-based combination therapy 30% (10%>47%), non-methotrexate DMARDs 19% (4%>44%), triple therapy 11% (0%>60%), and biologics 2% (0%>18%). At 60 months of follow-up, the frequency of use of these strategies was relatively stable except for biologics which increased to 21% (0%>80%). The mean and median time to DAS28 remission was 12.4 months (SD 12.1, range 8.6 to 17.2) and 9 (IQR 3, 18) months respectively. The mean and median time to CDAI remission was 14.8 (SD 13.5, range 10.3 to 21.2) and 9 (IQR 6, 18) months respectively. The frequency of sustained DAS28 remission was 50% (site range 20–70%), and CDAI 35% (12–58%). At the two sites with the highest rates of sustained remission and shortest time to remission, patients had fewer comorbidities and the initial treatment strategy was preferentially methotrexate-based combination therapies, and with eventual advancement to biologics in 7 and 39% in patients. In contrast, the patients at the site with the lowest rates of sustained remission and longest time to remission had long symptom duration at treatment initiation, highest body mass index and proportion with ≥2 comorbidities, worse socioeconomic status and higher baseline DAS28. This site also had the highest proportion of patients treated with biologics at the baseline visit, escalating to 80% by 60 months.

Conclusions: Treatment strategy and patient characteristics vary across CATCH sites and contribute to variable rate and frequency of achieving sustained remission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5695

THU0086 THE USE OF A BLINDED TRUNCATED ULTRASOUND POWER DOPPLER JOINT COUNT VALIDATES EFFICACY DATA FROM AN EARLY PHASE OPEN LABEL DRUG STUDY TREATING RHEUMATOID ARTHRITIS

C. Wiesenhutter[1,2], *[1]Department of Family Medicine, University of Washington, Seattle; [2]Coeur d'Alene Arthritis Clinic, Coeur d'Alene, United States*

Background: Small open label pilot trials generate important information on tolerability, toxicity, pharmacokinetics, and antigenicity in the early phase investigation of new compounds in the treatment of rheumatoid arthritis (RA). However, because the standard disease activity measures (DAMs), such as the disease activity score in 28 joints (DAS28) have a major subjective component, the efficacy data acquired in such trials is generally felt to be much less reliable than that obtained in blinded trials. Incorporating more objective DAMs, and performing them in a blinded fashion, might enhance the validity of efficacy data in such an early clinical setting.

One possible disease activity measure to fulfill this role would be an ultrasound power Doppler joint count (UPD) which has been shown to correlate with conventional clinical measures[1].

Objectives: To determine whether the blinded use of a truncated (low joint count) UPD in an early phase RA trial correlates with other DAMs in the trial and contributes to validation of efficacy of the drug.

Methods: The results of an open label trial in which Staph Protein A (PRTX-100, Protalex Inc.) was given to patients with active RA has been previously reported[2]. Standard disease activity measurements were obtained. In addition, an UPD was performed utilizing a truncated methodology in which three sites at the dorsal wrist and three dorsal metacarpal sites were analyzed bilaterally for a total of twelve sites studied. There were a total of 117 UPDs performed on eleven patients. UPD were acquired in less than five minutes per study. These UPDs were stored digitally and subsequently read in duplicate in a blinded fashion after completion of the study by the investigator (CW). Each joint site was subjectively scored from 0 (normal) to 3 (severe) with a possible total score of 0 -36 Intra-observer reliability was determined by two-way random intra-class correlations (ICC). Significant changes of UPD and clinical DAMs from baseline to single time points were assessed by the Wilcoxon signed rank test and correlations were performed by the Spearman's rho test (p). Effect size was determined by standardized mean difference (SMD).

Clinical assessments and UPDs were obtained weekly for the first month, then monthly for five more months.

Results: Intra-observer UPD score reproducibility was high (ICC =0.886). Significant reductions ($p<0.05$) in UPD and the DAS28 were found at day 22 and on all subsequent visits. Correlations between UPD and DAMs total scores were moderate to strong. However, the total differences from baseline and visits did not correlate, except for CRP (n=67 p=0.471, $p<0.001$). Also, some individual time points showed differences such as baseline vs day 196 (see table). SRMs for both UPD and DAMs were high, but higher for the DAS28 (1.00–2.16) than for the UPD (0.83–1.10).

Absolute Numbers UPD vs Disease Activity Measures / Differeces UPD vs Disease Activity Measures on Visit Day 196

	N	USP vs	Prob	N	USP vs	
DAS28CRP	71	p=.555	***	11	p=.639	*
DAS28ESR	98	p=.521	***	11	p=.542	*
ESR	97	p=.440	***	11	p=.043	NS
CRP	63	p=.540	***	11	p=588	*
Jt Pain	111	p=.466	***	11	p=.152	NS
Jt. Swelling	113	p=.468	***	11	p=.509	*
Pt. Global	113	p=.313	***	11	p=.422	NS
Dr Global	113	p=.634	***	11	p=.342	NS
CDAI	113	p=.502	***	11	p=.365	NS
Vectra	33	p=.525	***	11	p=.093	NS
	prob <0.05 *		prob <0.01 **		prob <0.001 ***	

References:

[1] D'Agostino, M. Ann Rheum Dis doi:10.1136/annrheumdis-2015–207709.

[2] Wiesenhutter, C Ann Rheum Dis 2016;75:1019 doi:10.1136/annrheumdis-2016-eular.2540.

Acknowledgements: C. Wiesenhutter Grant/research support from Protalex Inc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2537

THU0087 DAILY AND DIURNAL VARIATION AND DETERMINATION OF THE MINIMALLY IMPORTANT DIFFERENCE IN RHEUMATOID ARTHRITIS PATIENTS WITH MODERATE TO HIGH MULTI-BIOMARKER DISEASE ACTIVITY SCORES

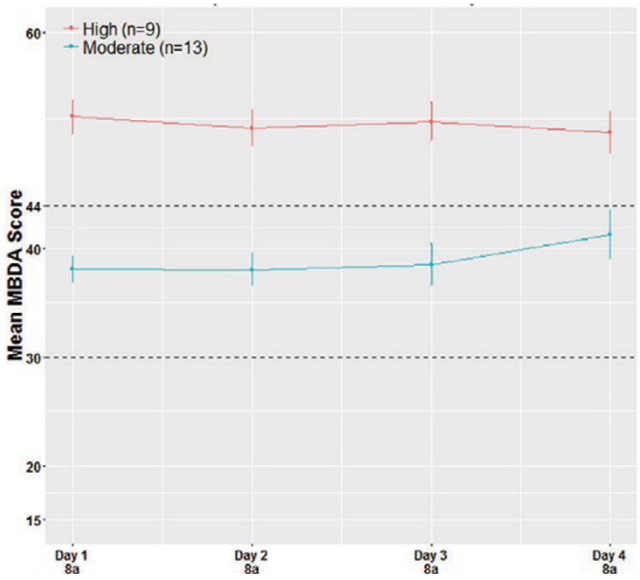
D. Chernoff[1], R.J. Bolce[1], C.C. Hwang[1], X. Wang[1], A. Kivitz[2], J.R. Curtis[3]. *[1]Crescendo Bioscience Inc., South San Francisco; [2]Altoona Center for Clinical Research, Duncansville; [3]The University of Alabama at Birmingham, Birmingham, United States*

Background: The Multi-Biomarker Disease Activity (MBDA) score has been validated as a disease activity metric in rheumatoid arthritis (RA) patients. Patients initiating new therapy or changing therapy frequently have moderate to high MBDA scores. Understanding short term biological variation of MBDA scores in these patients is important in order to determine a minimally important difference (MID).

Objectives: To evaluate biological variation in MBDA scores over a 24-hour period and from day to day in patients with clinically stable RA with moderate to high MBDA scores at baseline and to determine the MID in these patients.

Methods: We performed an analysis of 22 RA patients with moderate or high baseline MBDA scores. Adults with clinically stable seropositive RA (>8 weeks without DMARD and/or biologic medication changes and ≤10 mg prednisone per day) who had MBDA scores of moderate (MBDA 30–44) or high (MBDA >44) were eligible. Serum samples were obtained 5 times over the first 24-hour period (8 AM, 12 PM, 4 PM, 8 PM, and 8 AM); at 12 PM in the next 24-hour period; and at 8 AM the next 2 consecutive days, for a total of 8 timepoints. An additional midnight sample was excluded from the analysis because this timepoint is not relevant to normal clinical practice hours. Diurnal variation was calculated using 5 timepoints over the first 24 hours. Daily variation was determined using 4 timepoints taken at 8 AM on successive days. Combined diurnal and daily variation was calculated using 8 timepoints over 4 days. For each patient, absolute changes in MBDA scores were calculated for all possible pairs of timepoints for: a) diurnal variation (total 220 pairs), b) daily variation (total 132 pairs) and c) diurnal and daily variation (total 616 pairs). MID was calculated as the 90th percentile of absolute

Figure 1. Mean (SE) MBDA Scores over Four Days for Patients with Moderate (n=13) or High (n=9) MBDA Scores at Baseline

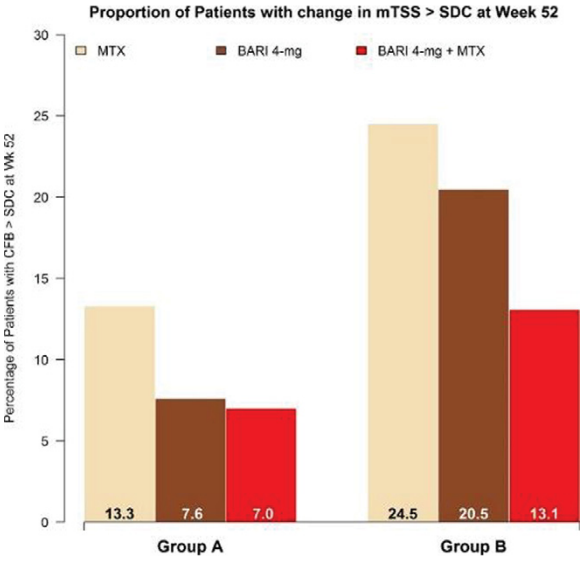


changes using all diurnal and daily variation data. Bootstrapping was used to validate the result.
Results: Of patients included in the analysis, 13 had moderate MBDA scores and 9 had high MBDA scores at baseline. Baseline demographics were: 73% women, mean age 61.8 (SD: 12.1) years, mean MBDA score 43.9 (SD: 8.3), and mean CDAI 20.2 (SD: 17.1). No patients were on glucocorticoids. Based on the analysis of the absolute change of MBDA score in the data with daily and diurnal variation combined, the mean was 3.4 (SD: 3.8), the median (Q1, Q3) was 2 (1, 5), and the MID was calculated as 7. Similar results were obtained using a bootstrap method. Minimal variability in mean MBDA scores was observed over 4 days for patients with moderate and high baseline MBDA scores (Figure 1).
Conclusions: Based upon the short term biologic variability of moderate and high MBDA scores, the MID was 7 units. An absolute change exceeding this threshold is unlikely due to diurnal and daily biological variation of the MBDA scores.
Disclosure of Interest: D. Chernoff Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., R. Bolce Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., C. Hwang Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., X. Wang Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., A. Kivitz Consultant for: Genentech, Pfizer, UCB, Janssen, J. Curtis Grant/research support from: Crescendo Bioscience Inc., Consultant for: Crescendo Bioscience Inc.
DOI: 10.1136/annrheumdis-2017-eular.5517

THU0088 STRUCTURAL DAMAGE PROGRESSION IN PATIENTS TREATED WITH METHOTREXATE, BARICITINIB MONOTHERAPY OR BARICITINIB + METHOTREXATE BASED ON THEIR LEVEL OF CLINICAL RESPONSE IN THE PHASE 3 RA-BEGIN STUDY

D. van der Heijde[1], P. Durez[2], G. Schett[3], E. Naredo[4], M. Østergaard[5], G. Meszaros[6], N. Bello[6], I. De la Torre[6], P. Lopez-Romero[6], D. Schlichting[7], E. Nantz[7], R. Fleischmann[8]. *[1]Leiden University Medical Centre, Leiden, Netherlands; [2]UCL-Saint Luc, Bruxelles, Belgium; [3]Universitätsklinikum Erlangen, Erlangen, Germany; [4]Hospital Universitario Fundación Jimenez Diaz, Madrid, Spain; [5]Copenhagen Centre for Arthritis Researc, Copenhagen, Denmark; [6]Eli Lilly & Company, Madrid, Spain; [7]Eli Lilly & Company, Indianapolis; [8]U Texas SW Medical Center, Dallas, United States*

Background: Baricitinib (BARI), an oral inhibitor of Janus kinase (JAK) 1 and JAK 2, is being developed for the treatment of rheumatoid arthritis (RA). RA-BEGIN was a phase 3 double-blind, three-arm multicentre study of BARI administered as monotherapy or in combination with methotrexate (MTX) to patients (pts) with early active RA who had no or limited treatment with DMARDs. Methotrexate (MTX) monotherapy was the active comparator.
Objectives: To evaluate the proportion of pts with structural damage progression, defined as change from baseline (CFB) greater than the smallest detectable change (SDC) in mTSS at week (wk) 52, depending on their disease state as measured by DAS28-CRP.
Methods: Pts were classified into two groups based on DAS28-CRP. Group A included pts who achieved sustained DAS28-CRP $\leq$3.2 at weeks 16, 20 and 24. Pts who did not achieve DAS28-CRP $\leq$3.2 consecutively at weeks 16, 20 and 24 and pts with missing DAS28-CRP at any of those 3 visits were included in Group B. The proportion of pts with CFB mTSS > SDC at wk 52 was estimated for each treatment arm for the two defined groups of response. The SDC in mTSS in the RA-BEGIN population at wk 52 was 1.4. Missing mTSS at wk 52 were imputed using linear extrapolation based on baseline data and the most recent radiographic data prior to the missed radiograph. No formal statistical tests were performed and comparisons are merely descriptive. All analyses were post-hoc.
Results: Out of the 584 pts of the modified-ITT population (all randomised pts who received at least 1 dose of study drug) in the RA-BEGIN study, 212 were classified in Group A: 21.4% (45/210), 42.1% (67/159), and 46.5% (100/215) for MTX, BARI and BARI+MTX, respectively. The odds ratios for sustained DAS28-CRP $\leq$3.2 response (weeks 16, 20 and 24) to BARI and BARI+MTX vs. MTX, were respectively 2.8 (95% CI 1.7–4.4) and 3.3 (95% CI 2.1–5.1). Pts classified in Group A maintained an adequate level of response up to wk 52. Further, pts in Group A (sustained DAS28-CRP $\leq$3.2) on either BARI + MTX or BARI, were less likely to show structural progression than patients who achieved sustained DAS28-CRP $\leq$3.2 on MTX. Pts in Group B on MTX or BARI monotherapy were more likely to show structural progression than patients who did not achieve a sustained DAS28-CRP $\leq$3.2 response on BARI + MTX (Figure 1).
Footnote: Group A: Patients who achieved sustained DAS28-CRP $\leq$3.2 (NRI) at weeks 16, 20 and 24 (N=212); Group B: Complement group
Conclusions: In patients who achieved sustained low DAS28-CRP scores, progression rates compared to MTX were reduced to a similar degree with BARI as monotherapy or in combination with MTX. Compared to MTX in patients who did not achieve sustained low DAS28-CRP scores, progression rates were reduced most markedly with combination therapy.
Disclosure of Interest: D. van der Heijde Consultant for: Abbvie, Amgen, Astellas, AstraZeneca, BMS, Boeringer Ingelheim, Celgene, Daiichi Sankyo, Eli Lilly and Company, Galapagos, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, P. Durez: None declared, G. Schett: None declared, E. Naredo: None declared, M. Østergaard Consultant for: Abbvie, BMS, Boehringer-Ingelheim,



Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, and Wyeth, G. Meszaros Employee of: Eli Lilly & Company, N. Bello Employee of: Eli Lilly & Company, I. De la Torre Employee of: Eli Lilly and Company, P. Lopez-Romero Employee of: Eli Lilly & Company, D. Schlichting Employee of: Eli Lilly and Company, E. Nantz Employee of: Eli Lilly and Company, R. Fleischmann Consultant for: Abbvie, Amgen, Astra Zeneca, BMS, Celgene, Janssen, Eli Lilly and Company, Novartis, Roche, Sanofi-Aventis, Pfizer, UCB
DOI: 10.1136/annrheumdis-2017-eular.2223

THU0089 M-DAS28, DAS28 (CRP) AND RAPID3 SCORES AT BASELINE ARE GOOD PREDICTORS OF RADIOGRAPHIC DISEASE PROGRESSION AT 1 AND 2 YEARS: DATA FROM THE AMPLE TRIAL

E. Keystone[1], H. Ahmad[2], Y. Yazici[3], E. Muratti[4], J. Ye[2], M. Bergman[5]. *[1]University of Toronto, Toronto, Canada; [2]Bristol-Myers Squibb, Princeton; [3]New York University School of Medicine, New York, United States; [4]Bristol-Myers Squibb, Montreal, Canada; [5]Drexel University College of Medicine, Philadelphia, United States*

Background: Clinicians rely on time-efficient, validated disease activity assessments to help predict disease progression accurately in patients (pts) with RA. The utility in predicting structural damage progression for the Routine Assessment of Patient Index Data 3 (RAPID3)[1] is largely unknown, while that of DAS28 (CRP)[2] and modified (M-)DAS28 have been previously reported.[3]
Objectives: This *post hoc* analysis examined the relationship between baseline disease activity measures and their ability to predict structural damage progression in the Phase III AMPLE (NCT00929864) trial.[4]
Methods: AMPLE was a randomized, investigator-blinded study in which MTX-experienced pts with active RA $\leq$5 years received SC abatacept 125 mg weekly or adalimumab 40 mg every 2 weeks in combination with stable-dose MTX. Logistic regression analysis was used to correlate the effect of disease activity at baseline on radiographic (X-ray) progression at Months (M) 12 and 24. Disease activity was assessed using M-DAS28,[3] DAS28 (CRP), RAPID3, CDAI and SDAI. Radiographs were scored using the modified Sharp/van der Heijde scoring system; progression was defined as change from baseline in total score greater than the smallest detectable change, which was calculated as SD/square root (2) x 1.96 (where SD is standard deviation of paired differences of change from baseline in total score between two readers).
Results: Logistic regression analysis was carried out for all randomized and treated pts (abatacept, n=318; adalimumab, n=328). For these patients, M-DAS28, DAS28 (CRP) and RAPID3 at baseline were significant predictors of radiographic progression at M12 and M24, baseline SDAI was a significant predictor at M12 but not M24 and baseline CDAI was not a significant predictor at either time point

Logistic regression model and area under ROC curves for the impact of disease activity at baseline on radiographic progression at M12 and M24 (all randomized and treated patients)

Disease activity measure	M12			M24		
	OR (95% CI)	p value	AUC	OR (95% CI)	p value	AUC
CDAI	1.02 (1.00, 1.04)	NS	0.5762	1.01 (0.99, 1.03)	NS	0.5416
SDAI	1.02 (1.00, 1.04)	<0.05	0.5963	1.02 (1.00, 1.03)	NS	0.5634
DAS28 (CRP)	1.47 (1.15, 1.90)	<0.01	0.6271	1.31 (1.03, 1.67)	<0.05	0.5911
RAPID3	1.26 (1.08, 1.47)	<0.01	0.6270	1.16 (1.01, 1.34)	<0.05	0.5871
M-DAS28	1.51 (1.25, 1.83)	<0.001	0.6624	1.36 (1.13, 1.63)	<0.01	0.6208

AUC = area under the curve; M = month; NS = not statistically significant; OR = odds ratio; ROC = receiver operating characteristic.

(Table). Receiver operating characteristic curves showed that M-DAS28, DAS28 (CRP) and RAPID3 had higher predictive value (area under the curve) than CDAI or SDAI for radiographic progression at M12 and M24 (Table). There was no impact of treatment arm on predictors of radiographic outcomes.

Conclusions: In this *post hoc* analysis, disease activity scores at baseline according to M-DAS28, DAS28 (CRP) and RAPID3 were good predictors of radiographic progression at M12 and M24 and were more predictive than other measures of disease activity tested, with M-DAS28 demonstrating the greatest degree of prediction.

References:
[1] Yazici Y, et al. J Rheumatol 2008;35:603–9.
[2] Salaffi F, et al. BMC Musculoskelet Disord 2011;12:120.
[3] Baker JF, et al. Arthritis Rheumatol 2014;66:794–802.
[4] Schiff M, et al. Ann Rheum Dis 2014;73:86–94.

Disclosure of Interest: E. Keystone Grant/research support from: Abbott, Amgen, AstraZeneca, Bristol-Myers Squibb, F. Hoffmann-La Roche, Janssen, Lilly, Novartis, Pfizer, sanofi-aventis, UCB, Consultant for: Abbott, AstraZeneca, Biotest, Bristol-Myers Squibb, Crescendo, F. Hoffmann-La Roche, Genentech, Janssen, Lilly, Merck, Pfizer, UCB, Speakers bureau: Amgen, Abbott, AstraZeneca, Bristol-Myers Squibb, F. Hoffmann-La Roche, Janssen, Pfizer, Sanofi, Genzyme, UCB, H. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Y. Yazici Grant/research support from: Genentech, Celgene, Bristol-Myers Squibb, Consultant for: Genentech, Celgene, Bristol-Myers Squibb, E. Muratti Employee of: Bristol-Myers Squibb, J. Ye Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Bergman Shareholder of: Pfizer, Johnson & Johnson, Consultant for: AbbVie, Bristol-Myers Squibb, Amgen, Celgene, Genentech, Pfizer, Janssen, Speakers bureau: Norvatis, Abbvie, Celegene

DOI: 10.1136/annrheumdis-2017-eular.1930

THU0090 INFLUENCE OF AGE AT DISEASE ONSET ON CLINICAL, FUNCTIONAL, AND ULTRASONOGRAPHIC OUTCOMES IN A MONOCENTRIC EARLY RHEUMATOID ARTHRITIS COHORT

E. Galuppi, I. Farina, C. De Giorgio, C.A. Scirè, M. Govoni. *Department of Medical Sciences, UOC Rheumatology, University of Ferrara and Azienda Ospedaliero-Universitaria Sant'Anna, Ferrara, Italy*

Background: Rheumatoid Arthritis (RA) onset may occur at any age and peaks in the fifth decade. Because the mean age of general population is continually increasing and since older age could impact on outcomes, late-onset RA (LORA) will probably become a relevant issue for health care system in the next future. A better characterization of LORA could help rheumatologist in the therapeutic decision-making process tailored on the individual patient.

Objectives: To investigate the relationship between age at disease onset and clinical, ultrasonographic and functional outcomes.

Methods: Early RA (ERA) patients fulfilling 2010 ACR/EULAR, with available clinical ad ultrasonographic follow-up of at least 1 year, who consecutively attended our Early Arthritis Clinic between 2009–2014, were retrospectively analyzed. Patients were pooled into 3 groups by age at RA onset: <45 years (young-onset RA [YORA] group 1), 45 to 60 years (intermediate-onset RA [IORA] group 2), and >60 years (late-onset RA [LORA] group 3). At baseline biological, functional and ultrasonographic data were recorded. The following items were compared at baseline and after 12 months from diagnosis: $DAS28_{CRP}$ remission rate, functional disability using the Health Assessment Questionnaire (HAQ), power doppler (PWD) score, Methotrexate (MTX) treatment, use of glucocorticoids (GCs).

Table 1 Baseline demographic and disease characteristics of 3 groups.

	Whole sample (n=223)	YORA (n=46)	IORA (n=81)	LORA (n=96)	P-value (overall)	P-value LORA vs YORA	P-value LORA Vs IORA
Female, n (%)	164 (73.5)	40 (86.9)	59 (72.8)	65 (67.7)	0.051	0.014	0.4
Lag time onset to diagnosis (months), median (IQR)	4 (2-7)	5 (3-8)	4 (2-6)	3 (2-6)	0.03	0.0001	0.03
RF, n (%)	112 (50.2)	26 (56.5)	42 (51.8)	44 (45.8)	0.45	0.42	0.23
ACPA, n (%)	127 (56.9)	28 (60.8)	50 (61.7)	49 (51)	0.30	0.15	0.27
TJC, median (IQR)	6 (2-12)	2 (1-8)	6 (4-11)	7 (3.5-12)	0.0005	0.0001	0.50
SJC, median (IQR)	3 (1-7)	2 (0-4)	3 (1-7)	4 (2-8)	0.0054	0.0013	0.34
CRP (mg/dl), median (IQR)	0.9 (0.4-2.1)	0.58 (0.24-1.3)	0.7 (0.4-1.59)	1.3(0.5-2.91)	0.0014	0.001	0.0091
$DAS28_{CRP}$, median (IQR)	4.44(3.61-5.33)	3.71 (3.24-4.61)	4.40 (3.74-5.32)	4.75 (3.8-5.6)	0.0013	0.0003	0.13
SDAI, median (IQR)	24.45(15.7-33.7)	18.57 (10.8-28)	23.5 (15.5-32.9)	26.1 (18-38.5)	0.0032	0.0011	0.06
PWD MSUS, median (IQR)	5 (1-9)	1 (0-7.5)	5 (2-8)	8 (3-10.5)	0.002	0.0001	0.03
HAQ-DI, median (IQR)	0.87 (0-5-1.4)	0.65 (0.25-1.25)	0.87 (0.5-1.25)	1 (0.62-1.75)	0.0091	0.0033	0.05
MTX (%)	70.85	65.22	75.31	69.79	0.46	0.58	0.41
MTX dose mg/week, median (IQR)	10 (10-10)	10 (10-10)	10 (10-15)	10 (10-10)	0.02	0.42	0.01
GCs (%)	86.55	86.96	83.95	88.54	0.66	0.78	0.37
GCs dose (mg/daily), median (IQR)	5 (5-10)	5 (5-9)	5 (5-10)	5 (5-10)	0.59	0.42	0.76

P global comparison for 3 groups by Kruskal-Wallis test. Comparison for 2 group by Mann Whitney test.

Table 2 Adjusted odds ratios (aORs) for $DAS28_{CRP}$ remission, PWD MSUS remission and HAQ score <0.5 at 1 year follow up

Outcome 1 year	IORA	YORA		LORA	
		aOR [95%CI]	P-value vs IORA	aOR [95%CI]	P-value vs IORA
$DAS28_{CRP}$ REM	reference	1.42 (0.63-3.18)	0.38	2.95 (1.48-5.86)	0.002
PWD MSUS REM	reference	1.21 (0.40-3.69)	0.72	1.18 (0.51-2.73)	0.69
HAQ score <0.5	reference	0.75 (0.33-1.73)	0.51	1.24(0.61-2.53)	0.53

aOR: odds ratio adjusted for gender, baseline $DAS28_{CRP}$, MTX use, glucorticoid use, serology.

Results: The main baseline demographic and disease characteristics of the whole sample of ERA (n=223) and the 3 age groups- YORA (46), IORA (81) and LORA (96)- are summarised in Table 1. Age at RA-onset was independently associated with $DAS28_{CRP}$ remission at 1 year (Table 2).

Conclusions: In a cohort of ERA, older age at disease onset is associated with a more active pattern disease at the beginning but with a greater probability of $DAS28_{CRP}$ remission at 1 year.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5011

THU0091 HIGH MULTI-BIOMARKER DISEASE ACTIVITY SCORE IS ASSOCIATED WITH HIGH RISK OF RADIOGRAPHIC PROGRESSION IN SIX STUDIES

J.R. Curtis[1], C.H. Brahe[2], M. Ostergaard[2], M.L. Hetland[2], K. Hambardzumyan[3], S. Saevarsdottir[3], X. Wang[4], E.H. Sasso[4], T.W. Huizinga[5]. *[1]Univ. of Alabama at Birmingham, Birmingham, United States; [2]Copenhagen Center for Arthritis Research, Copenhagen, Denmark; [3]Karolinska Univ. Hospital and Karolinska Institutet, Stockholm, Sweden; [4]Crescendo Bioscience Inc., South San Francisco, United States; [5]Leiden Univ. Medical Center, Leiden, Netherlands*

Background: The multi-biomarker disease activity (MBDA) test uses a validated algorithm with 12 serum protein biomarkers to assess disease activity in patients with RA. The MBDA score has previously been found to be a predictor of risk for radiographic progression (RP).

Objectives: To evaluate data from six cohorts to collectively establish the relationship between the MBDA score and risk for RP.

Methods: Clinical, MBDA score and radiographic data were analyzed for 6 cohorts with N>100: Leiden, SWEFOT Year 1, SWEFOT Year 2, OPERA Year 1, and AMPLE Year 1 (abatacept and adalimumab arms) (see Figure). Analyses used published results when available or patient-level data when not (i.e., for Leiden; and for OPERA CRP analyses). Frequency of RP over one year was determined by category of MBDA score (low, moderate [30–44], high on a scale of 1–100) at the start of the year for four cohorts and by category of MBDA score at the end of the year for AMPLE cohorts (as published). RP was defined using the threshold for change in total modified Sharp score (ΔmTSS) specific to each study (2 to >5 TSS units). Positive and negative predictive values (PPV and NPV) were determined for each study by comparing patients with high MBDA score (>44), DAS28-(ESR/CRP) (>5.1 or >4.09) or CRP (>3 mg/dL) vs. those in a not-high category. Relative risk (RR) for RP was determined for each study, and in a meta-analysis of the non-overlapping patient groups with MBDA scores available at the start of the year (Leiden, SWEFOT Year 1 and OPERA Year 1). Results of multivariate analyses and analyses that combined MBDA score with other risk factors for RP were summarized.

Results: The 6 study cohorts included patients receiving csDMARDs alone or with adalimumab, infliximab or abatacept. Overall rates of RP were 10–26%. In each study, RP was most frequent among patients with a high vs. not-high MBDA score (>44 vs. ≤44). For high MBDA scores, NPVs were 93–97% and PPVs were 18–32%, with RR values of 3.6–9.5 (P=0.002 to <0.0001) (Figure). In a meta-analysis of the Leiden, SWEFOT Year 1 and OPERA Year 1 cohorts, RR was 5.1 (P<0.0001) for MBDA categories, and 1.4 (P=0.23) and 1.6 (P=0.01) for categories of DAS28-CRP or CRP, respectively. Previously published multivariate analyses in the Leiden and SWEFOT Year 1 cohorts showed that MBDA score was an independent predictor of RP compared with other predictors. In the Leiden cohort, MBDA score was the strongest predictor and high MBDA score

Association between radiographic progression (RP) and high MBDA score (>44)

Cohort	N	RP cutoff	Overall % RP	PPV for MBDA >44	NPV for MBDA >44	Relative Risk[1] (95% CI)	P-value
Leiden	163	>5.0	17%	31%	93%	4.3 (1.9, 9.5)	<0.0001
OPERA Year 1	164	≥2.0	26%	31%	97%	9.5 (1.4, 66.3)	0.0009
SWEFOT Year 1	235	>5.0	18%	21%	97%	7.1 (1.0, 49.9)	0.008
Meta-analysis (LEIDEN + OPERA Year 1 + SWEFOT Year 1)						5.1[3] (2.5, 10.1)	<0.0001
SWEFOT Year 2	133	>5.0	13%	32%	95%	6.2 (2.4,16.5)	0.0001
AMPLE Year 1 (Aba)	181	>2.2[4]	10%	18%	96%	4.5 (1.6,13.1)	0.003
AMPLE Year 1 (Ada)	186	>2.2[4]	11%	24%	93%	3.6 (1.6,8.1)	0.002

PPV, positive predictive value; NPV, negative predictive value. 1. Relative risk = PPV/(1-NPV). 2. Random-effect model used for meta-analysis. 3.Aggregated relative risk. 4. ΔTSS cutoff for RP was defined in Fleischmann et al (*Arthritis Rheumatol* 2016;68:2083–9) as >smallest detectable change (SDC), however no value was specified; SDC for AMPLE was specified as 2.8 and 2.2 in prior AMPLE publications (Weinblatt 2013; Schiff 2014).

Treatments; reference; data source:
LEIDEN (csDMARDs); Li et al. *Rheumatology (Oxford)*. 2013;55:357–66; Unpublished patient-level data only.
OPERA (MTX+placebo-adalimumab+IA corticosteroids/MTX+adalimumab+IA corticosteroids); Brahe et al. *Arthritis Rheumatol*. ACR 2016 Abstract 2520; Published data and unpublished patient-level data for analysis of CRP categories.
SWEFOT Year 1 (MTX/ triple therapy/MTX+infliximab); Hambardzumyan K, et al. *Ann Rheum Dis*. 2015;74:1102–9; Published data only.
SWEFOT Year 2 (triple therapy/MTX+infliximab); Hambardzumyan K et al, *RMD Open*. 2016 Mar 1;2(1):e000197; Published data only.
AMPLE Year 1 (abatacept and adalimumab arms, analyzed separately); Fleischmann et al. *Arthritis Rheumatol* 2016;68:2083–9, Curtis et al. *Arthritis Rheumatol*. 2016 Nov 3. doi: 10.1002/art.39981 and *Fleischmann et al. *Arthritis Rheumatol*. 2016 Dec 19. DOI: 10.1002/art.40021; Published data only, from Fleischmann et al(*).

discriminated between high and low risk for RP among patients with high SJC (>5) or high DAS28-CRP, with PPV as high as 57%.
Conclusions: High MBDA scores were associated with increased risk for RP in 6 study cohorts, including patients treated with csDMARDs, TNFi and abatacept. Based on high NPVs (≥93%), the MBDA score used alone had clinical value for identifying patients with little or no risk of RP. Combining the MBDA score with clinical measures yielded PPVs approaching 60%, suggesting that biomarkers can help stratify patients by their risk for RP.
Disclosure of Interest: J. Curtis Grant/research support from: Crescendo Bioscience Inc., Consultant for: Crescendo Bioscience Inc., C. Brahe: None declared, M. Ostergaard Grant/research support from: AbbVie, BMS, Boehringer-Ingelheim, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Celgene, Sanofi, Regeneron, Novartis, T Jensen, M. Hetland Grant/research support from: AbbVie, BMS, MSD, Pfizer, Crescendo Bioscience Inc., UCB, Eli Lilly, Speakers bureau: Orion, K. Hambardzumyan: None declared, S. Saevarsdottir: None declared, X. Wang Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., E. Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., T. Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringher, Takeda, Zydus, Epirus, Eli Lilly
DOI: 10.1136/annrheumdis-2017-eular.5557

THU0092 CHORONIC PAIN INCREASES INDEPENDENT OF THE DISEASE ACTIVITY AND DEPRESSION IN FEMALES WİTH RHEUMATOİD ARTHRITIS

F.G. Yurdakul, A. Kılıçarslan, H. Bodur. *Department of Physical Medicine and Rehabilitation, Ankara Numune Training and Research Hospital, Ankara, Turkey*

Background: Chronic pain is a key component of rheumatoid arthritis (RA). Although pain is reduced with the control of inflammation at the first years of the disease, pain increases over time with different pathways just as central sensitization. Fatigue, sleep problems and depressive symptoms with chronic pain are common problems in patients with RA (1,2).
Objectives: We aimed to investigate the frequency of widespread pain, sleep disorders, fatigue, and depressive symptoms in RA patients. Furthermore discrepancy of these symptoms and disorders were analyzed between female and male RA patients.
Methods: One hundred and sixty one RA patients (female: 119, male: 42) and 68 healthy controls (female: 52, male: 16) were enrolled in the study. Widespread pain index (WPI) with nineteen body parts that was identified by 2010 fibromyalgia diagnostic criteria was interrogated. Pain visual analog scale (VAS), Health Assessment Questionnaire (HAQ), Physician global assessment (PhGA), Fatigue severity scale (FSS), Pittsburgh sleep quality index (PSQI), Beck depression inventory (BDI) were evaluated in both RA patients and healthy controls. Morning stiffness (MS), Rheumatoid arthritis quality of life (RAQOL) and disease activity score 28 (DAS28) were assessed in RA patients. Data were analyzed in female and male RA patients.
Results: The mean PhGA, HAQ, BDI, FSS, WPI values of RA patients were worse than healthy controls (p=0.012, 0.000, 0.008, 0.033, 0.044 respectively). There was no difference between RA and healthy controls in terms of sleep disorders. The mean age, disease duration, MS, swollen joint count, C-reactive protein, PhGA and BDI were similar in female and male RA patients. WPI, VAS pain, tender joint count, HAQ, RAQOL, FSS, PSQI, and DAS 28 were higher in females (Table 1).

Table 1. Clinical features in female and male RA patients

	Female RA patients (n=119)	Male RA patients (n=42)	p
Widespread pain index	4.70±4.97	2.65±3.99	0.04*
PhGA	2.87±2.16	2.09±1.63	0.08
DAS28	3.39±1.39	2.68±1.11	0.01*
CRP	10.77±13.62	12.59±14.20	0.24
Tender Joint Count	10.92±13.47	6.78±13.09	0.03*
Swollen Joint Count	0.88±2.67	0.31±0.69	0.690
HAQ	1.06±0.83	0.68±0.66	0.04*
RAQOL	14.34±10.06	7.59±8.83	0.00*
FSS	35.57±19.24	22.21±14.41	0.00*
PSQI	8.02±5.58	5.00±4.20	0.00*
BDI	15.71±13.34	11.28±12.56	0.06

PhGA: Physician global assessment, DAS: Disease activity score, CRP: C Reactive protein, HAQ: Health Assessment Questionnaire, RAQOL: Rheumatoid arthritis quality of life, FSS: Fatigue severity scale, PSQI: Pittsburgh sleep quality index, BDI: Beck depression inventory.

Conclusions: RA is a disease that increases fatigue, depressive symptoms and widespread pain.DAS 28 scores were higher due to the increased pain scores and tender joint count that are subjective parameters in female RA patients. Pain scores in females are significantly higher than in males, and pain exacerbated by central sensitization pathway in women may lead to sleep disorders and fatigue, but not increase depressive symptoms.
References:
[1] The role of central nervous system in the generation and main tance of chronic pain in rheumatoid arthritis, osteoarthritis and fibromyalgia. Lee YC, Nassikas NJ, Clauw DJ. Arthritis Research and Therapy (2011) 13:211–221.
[2] Fatigue in patients with rheumatic diseases. Dupond JL. Joint Bone Spine (2011). 78:156–160.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5846

THU0093 PERSISTENCE OF POWER DOPPLER ULTRASOUND-DETECTED RESIDUAL SYNOVITIS IN CONSECUTIVE ULTRASOUND EXAMINATIONS IN RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION PREDICTS UNFAVORABLE OUTCOME OVER ONE YEAR

G. Mouterde[1], C. Lukas[1], N. Filippi[1], G. Marin[2], N. Molinari[2], J. Morel[1], B. Combe[1]. *[1]Rheumatology department; [2]Department of Statistics, Lapeyronie hospital, Montpellier, France*

Background: Some studies revealed an association of Power Doppler (PD) ultrasound (US)-detected residual synovitis (PDUSS) and risk of relapse and radiographic progression (RP), in individual patients in rheumatoid arthritis (RA). However, the longitudinal relationship between clinical remission and repeated US residual lesions during follow-up is not so well-known.
Objectives: The aim of this study was to evaluate the ability of PDUSS in consecutive examinations to predict unfavorable outcome (i.e. clinical relapse or RP) at 1 year.
Methods: RA patients ≥18 years fulfilling 2010 ACR-EULAR criteria, treated with synthetic or biologic (b) DMARDs and in clinical remission (DAS28-ESR<2.6 and no clinically active synovitis) for less than 6 months, were included in the longitudinal prospective SONORE study (ClinicalTrials.gov identifier: NCT02618954). Clinical and biological characteristics of patients were collected at baseline, and every 3 months during 1 year. RA treatment had to be stable during follow-up. A standard US examination on 40 joints for the presence of synovial hypertrophy and PD signal was performed by an independent investigator blinded to clinical and radiographic data at each visit during 1 year. Presence of US synovitis was defined by a PD signal≥1 in at least one joint. Radiographs of hands, wrists and feet were scored at baseline and 1 year. Outcome measures: RP was defined by an increase ≥1 point of the modified total Sharp score. A relapse was defined by a DAS28>3.2 at ≥1 follow-up visits AND a change of DMARDs, excluding change due to safety issues; or an increase in the DMARD or Corticosteroid (CS) dosage (≥5mg/d). Baseline variables, including PDUSS and its persistence during the follow-up, were assessed for their association with time to progression to unfavorable outcome using univariate then stepwise multivariate Cox regression analyses to obtain adjusted HRs.
Results: The 115 included patients had a mean (SD) age of 58.9 (±12.8) years, mean disease duration of 9.3 (±9.3) years, a mean duration of remission of 2.1 (±2.3) months. 74.8% were female, 79.1% of the patients were anti-CCP positive, 51.4% had erosive disease. The mean DAS28-ESR was 2.03 (±0.63). 59.2% received methotrexate, 59.9% bDMARD and 11.7% CS. PDUSS was detected in ≥1 joint in 75 patients (72.1%) at baseline. 41/75 (54.7%) had persistence of at least one PDUSS during the follow-up. 26 (23.2%) had a relapse (after a mean duration of 9.1 (±2.6) months) or a RP at 1 year. In multivariate analysis, persistence of at least one PDUSS during the follow-up (HR=5.24 [1.74–22.5], p=0.009) and baseline number of tender joints (HR=1.32 [0.95–1.68], p=0.052) were predictors of relapse or RP at 1 year. Duration of remission, other baseline US findings including baseline PDUSS, autoantibodies, and erosive disease had no additional predictive value.
Conclusions: Persistence of a PDUSS during the follow-up, rather than baseline PDUSS, predicts unfavorable outcome at 1 year in RA patients in clinical remission. This suggests that initial US findings are not sufficient to justify therapeutic change, but that the persistence of a residual PDUSS requires careful follow-up, and might even potentially merit strategy adaptation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5479

THU0094 FACTORS ASSOCIATED WITH RADIOGRAPHIC REMISSION (RR) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) WHILE NON-BIOLOGICALDISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS) USING

O. Iaremenko, G. Mykytenko. *Internal Diseases at Stomatological Faculty, O.O. Bogomolets National Medical University, Kyiv, Ukraine*

Objectives: To assess the factors associated with RR achievement in patients (pts) with RA while non-biological DMARDs using.
Methods: A cohort of 174 pts with RA (50.6% with early RA) was prospectively assessed at baseline and 2 years by the Disease Activity Score (DAS28) and the Sharp–van der Heijde Score (SHS). Mean age at inclusion was 52.0±0.91 yrs, disease duration – 51.3±4.82 month. 82.7% of the pts were women; 62.6% were positive for rheumatoid factor (RF) and 75.9% - for antibodies against cyclic citrullinated peptides (aCCP). Pts were treated with methotrexate (MTX) (mean dose – 11.6±0.29 mg/w, n=157), leflunomide (LF) (19.2±0.28 mg/d, n=95), sulfasalazine (SS) (2 g/d, n=76) or combination of DMARDs (CD) (n=74). After 2 yrs of DMARDs therapy 41 pts (23.5%) reached RR (ΔSHS≤0.5). No one pts using low dose of MTX (7.5 mg/week) achieved remission so they were excluded from further analysis. According to RR achievement in 2 yrs pts were divided into

2 groups (41and 92 pts who achieved RR and didn't respectively). After 2 yrs the factors associated with RR achievement in pts with RA while non-biological DMARDs using were assessed.

Results: Before study, pts in both groups were comparable by all demographic, clinical and X-ray characteristics, frequency of DMARDs prescribed. They differed only in frequency of RF-positivity (39.0 and 57.6% respectively in pts achieved RR and didn't, $p<0.05$), aCCP-positivity (21.7 and 73.3% respectively, $p<0.001$) and aCCP level (6.06±0.88 and 105.3±22.7 U/ml respectively, $p<0.001$).

There was strong and moderate positive correlation between RR achivement and aCCP-negativity ($r=0.57$, $p<0.05$), low aCCP level ($r=0.45$, $p<0.05$) and ΔDAS28 ($r=0.35$, $p<0.05$).

Results of multinomial logistic regression analyses (SPSS, V.22, IBM) showed that RF-negativity was the only independent predictor of RR achievement ($B=3.14$, $p<0.05$).

41.7% pts in RR achieved clinical remission by DAS28 as well. Only 19.7% pts achieved clinical remission without RR ($p<0.05$ vs pts achieved clinical and RR) and 12.5% pts achieved RR without clinical response (DAS28>5.1, ΔDAS28≤1.2 or any value of DAS28 with ΔDAS28≤0.6; $p<0.01$).

After 2 years of treatment the mean value of ΔDAS28 in comparison groups (with and without RR) did not differ (2.79±0.28 vs 2.33±0.17 respectively) so there was a discrepancy between clinical and radiological outcome.

Conclusions: Baseline predictors associated with achieving of radiographic remission in pts with RA are RF- and aCCP-negativity, low level of aCCP, but independent predictor of radiographic remission achievement is the only RF-negativity.

The discrepancy between the frequency of clinical and radiographic remission achievement in RA patients is observed.

After 2 yrs of non-biological DMARDs treatment 41.7% pts with RA achieves radiographic and clinical remission at the same time.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2682

THU0095 IMPACT OF ULTRASOUND-DETECTED TENOSYNOVITIS AND SYNOVITIS ON DISEASE FLARE, DISABILITY AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RA IN CLINICAL REMISSION: RESULTS OF THE STARTER STUDY

G. Sakellariou[1], G. Filippou[2], E. Bellis[3], C.A. Scirè[4], G. Carrara[5], A. Iagnocco[6] on behalf of STARTER study group and US Study Group of the Italian Society for Rheumatology. *[1]IRCCS Policlinico San Matteo Foundation, Pavia; [2]University of Siena, Siena; [3]Ospedale Mauriziano, Torino; [4]Italian Society for Rheumatology, Milan; [5]Italian Society for Rheumatology, Milano; [6]Università degli Studi di Torino, Torino, Italy*

Background: In patients with RA in remission subclinical ultrasonographic (US) synovitis (-S) relates to flare and radiographic progression. The impact of tenosynovitis (-T) on flare, disability and radiographic progression is not known.

Objectives: To evaluate the predictive role of US-detected tenosynovitis and synovitis in RA patients in remission on flare, disability and radiographic progression over 12-months.

Methods: STARTER is a multicentre cohort study of the US Study Group of the Italian Society for Rheumatology. Participants were selected on the basis of a reliability exercise and the availability of high-end equipment with high frequencies probes. Patients with RA in remission underwent clinical and US evaluation. US -T and -S were assessed categorically by Grey Scale (GS) and power Doppler (PD) at 11 joints, extensor and flexor tendons in both hands. Patients were assesed at baseline, 6 and 12 months. The primary outcome was flare within 12 months (defined as increase in DAS28>1.2 or >0.6 if final DAS28>3.2). The secondary outcomes were progression of disability (increase ≥2.3 in the Health Assessment Questionnaire (HAQ)) and radiographic progression (increase in the total Sharp van Der Hejide score (SHS) ≥4.3) at 12 months. Logistic models were used to measure the relationship between GS-T/-S, PD-T/-S and outcomes, results were presented as odds ratios (OR) and 95% confidence interval (CI), adjusted for pre-specified confounders.

Table 1

	OR (95% CI)	Adj OR (95% CI)
ΔDAS28 >1.2 or >0.6 if final DAS28 >3.2		
PD-T	0.59 (0.16,2.15)	0.47 (0.12,1.82)
PD-S	1.64 (0.93,2.90)	1.59 (0.86,2.92)
PD-T + PD-S	*2.75 (1.45,5.20)*	*2.09 (1.06,4.13)*
GS-T	1.59 (0.53,4.72)	1.37 (0.42,4.41)
GS-S	2.18 (0.97,4.92)	1.88 (0.79,4.46)
GS-T + GS-S	*2.88 (1.34,6.14)*	*2.25 (1.00,4.06)*
ΔHAQ ≥0.23		
PD-T	0.64 (0.13,3.03)	0.81 (0.16,4.01)
PD-S	0.79 (0.37,1.68)	0.71 (0.32,1.54)
PD-T + PD-S	1.49 (0.68,3.26)	1.33 (0.57,3.11)
GS-T	0.77 (0.22,2.73)	0.64 (0.17,2.45)
GS-S	0.83 (0.34,1.97)	0.61 (0.24,1.54)
GS-T + GS-S	0.93 (0.42,2.02)	0.64 (0.27,1.53)
ΔTotal SHS ≥4.3		
PD-T	0.82 (0.09,7.37)	0.54 (0.05,5.76)
PD-S	1.61 (0.71,3.64)	1.60 (0.68,3.79)
PD-T + PD-S	1.53 (0.60,3.93)	1.09 (0.38,3.11)
GS-T	0.78 (0.08,7.88)	0.67 (0.06,7.50)
GS-S	2.38 (0.72,7.84)	1.78 (0.49,6.48)
GS-T + GS-S	1.91 (0.59,6.15)	1.24 (0.34,4.49)

Results: 361 patients (72.3% f, mean age (sd) 56.1 (13.3), median disease duration (IQR) 7.1 years (3.6–13.5)) were included, complete radiographs were available for 189/361 (52.3%) patients. 98/326 (30.6%) patients had a flare within 12 months, 70/340 (20.59%) had an increase in HAQ and 39/189 (20.6%) radiographic progression. Results are presented in Table 1. Flare was predicted only if –T and –S, assessed by both GS and PD, were concurrently present, while both –T and-S and their combination did not predict HAQ or SHS progression.

Conclusions: In patients with RA in clinical remission, US-detected synovial and tenosynovial inflammation relates to the risk of flare, while in a short term follow-up the effect on disability and radiographic progression is limited. These results might have been influenced by the short follow-up and limited power for secondary outcomes. US might integrate the clinical management of RA patients in clinical remission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4774

THU0096 MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) IS ASSOCIATED WITH THE PROGRESSION OF STRUCTURAL BONE DAMAGE IN RHEUMATOID ARTHRITIS PATIENTS IN REMISSION

G. Schett[1], S. Finzel[2], M. Hagen[1], M. Englbrecht[1], J. Haschka[3], C. Figuereido[4], J. Fogagnolo Cobra[4], J. Rech[1]. *[1]University of Erlangen-Nuremberg, Erlangen; [2]University Medical Center Freiburg, Rheumatology and Clinical Immunology, Freiburg, Germany; [3]St.Vincent Hospital, Vinforce Study Group, Medical University of Vienna, Vienna, Austria; [4]Institutio de Rheumatologia, Sao Paolo, Brazil*

Background: Due to an increasing number and an earlier use of effective disease modifying anti-rheumatic drug (DMARD) therapy a growing number of rheumatoid arthritis (RA) patients reaches a state of clinical remission of disease. Whether clinical remission completely protects from structural bone damage, however, is still a matter of debate as conventional radiographic methods have their limitation in the sensitivity to characterize bone damage. Furthermore, residual activity of inflammation associated with the generation of inflammatory markers may characterize a subset of RA patients in remission, associated with higher prevalence and/or progression of bone damage.

Objectives: To test whether residual systemic inflammation is associated with structural bone damage and the progression of structural bone damage in RA patients in sustained remission.

Methods: RA patients (i) fulfilling the 2010 EULAR/ACR classification criteria of RA, (ii) having a positive anti-citrullinated protein antibody (ACPA) status and (iii) being in DAS28-ESR remission for 6 months were included. High-resolution peripheral quantitative computed tomography (HR-pQCT) of the right hand was done at baseline and after 1year. Erosion numbers and erosion volumes were assessed in the metacarpophalangeal joints. Vectra-DA tests measuring the serum levels of twelve different inflammation markers (CRP, SAA, IL-6, TNFR1, MMP-1, MMP-3, EGF, VEGF-A, VCAM-1, YKL-40, leptin and resistin) were performed in the baseline samples. MBDA score was calculated according to previously defined algorithms with low MDBA score defined as <30 units and moderate to high scores as ≥30 units (1).

Results: 100 ACPA+ RA patients in sustained remission were investigate (mean±SD age: 57±14 ys; disease duration: 4.8±4.9 ys; DAS28: 1.7±0.5;63% females; 100% MTX treatment, 38% MTX+TNFi treatment). 65 patients had low (<30), 25 patients has moderate (≥30–44 and 10 patients had high (>44) MBDA scores. Patients in the different MBDA categories had similar age, sex, disease duration, DAS28 scores and DMARD treatment. Baseline HR-pQCT analysis showed that erosion numbers and volumes were significantly ($p<0.001$) higher in patients with high MBDA scores. Higher erosion numbers (>10) and larger erosions (>10 mm^3) were exclusively found in patients with moderate to high MBDA scores. MBDA scores were correlated to erosion numbers ($p<0.001$) and volumes ($p=0.0018$). Longitudinal analysis showed significant progression of erosions only in patients with high MBDA scores. Furthermore, progression (>5mm^3 increase in volume) over 1 year was confined to methotrexate treated patients, while tumor necrosis factor inhibitor treated patients were protected from progression even in case of moderate to high MBDA scores. However there were only 4 patients treated with TNFi that had a high MBDA score.

Conclusions: These data show that residual disease activity assessed by MBDA score is associated with structural damage and progression of structural damage in RA patients in sustained remission.

References:

[1] Curtis JR, van der Helm-van Mil AH, Knevel R, et al.Validation of a novel multi-biomarker test to assess rheumatoid arthritis disease activity. Arthritis Care Res 2012;64:1794–803.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6227

THU0097 CHANGE IN SELF-REPORTED PAIN REFLECTS PSYCHOLOGICAL AND FUNCTIONAL STATE RATHER THAN INFLAMMATORY BURDEN IN UNITED STATES LATINOS WITH ESTABLISHED RHEUMATOID ARTHRITIS

G. Karpouzas, E. Hernandez, C. Cost, S. Ormseth. *Rheumatology, Harbor-UCLA Medical Center, Torrance, United States*

Background: Pain represents the cardinal complaint in patients with rheumatoid arthritis (RA). It may reflect inflammation, structural damage, or aberrant processing and regulatory mechanisms.
Objectives: We evaluated whether changes in pain reflect inflammatory burden variation or non-inflammatory factors in Latinos with established RA in the United States (US).
Methods: We evaluated 271 patients from a single academic center with complete data in parameters of interest on 2 visits, 12 months apart. Demographics, serologies, swollen and tender joint assessments, sedimentation rate, fatigue-VAS (visual analogue scale), pain-VAS, depression assessment (Patient Health Questionnaire-PHQ9), functional disability (Health Assessment Questionnaire, HAQ-DI), presence of erosions and irreversible articular damage (IAD, including subluxation, fusion, arthrodesis, or prosthesis) were recorded. Principal components factor analysis with varimax rotation determined latent variables of symptom change. Multinomial logistic regression modeling with forward stepwise entry determined parameters associated with clinically meaningful change in pain compared to no change
Results: Two factors met acceptance criteria (Eigenvalues $\geq$1) with values of 2.57 and 1.31 respectively (Table 1). Following rotation, factor 1 loadings comprised change in fatigue, pain, depression scores, and functional disability, representing non-inflammatory factors. Conversely, factor 2 encompassed changes in tender and swollen joints and ESR, representing inflammation. Clinically relevant improvement in pain significantly correlated with respective improvements in fatigue, depression, functional disability and tender joints (Table 2); worsening pain was negatively associated with change in disability or fatigue.

Table 1: Principal Component factor analysis with change variable loadings

	Factor 1*	Factor 2*
Fatigue change	0.814	-0.019
Pain change	0.757	0.216
PHQ9 change	0.716	0.024
HAQ-DI change	0.569	0.328
Swollen joint count change	0.095	0.828
Tender joint count change	0.238	0.696
Sedimentation Rate change	0.003	0.642
* Factor 1 explains 30.6% of variance and factor 2 explains 24.8%		

Table 2: Factors associated with clinically meaningful change in self-reported pain

	parameters	B	Std Error	p-value	OR	95% CI
Worsening	Intercept	-1.437	0.213	0.000		
	PHQ9 change	-0.011	0.034	0.752	0.989	0.925-1.058
	TJC change	-0.026	0.025	0.314	0.975	0.927-1.025
	HAQ-DI change	-1.254	0.358	0.000	0.285	0.142-0.575
	Fatigue change	-0.223	0.073	0.002	0.800	0.693-0.923
Improving	Intercept	-1.186	0.192	0.000		
	PHQ9 change	0.088	0.035	0.012	1.092	1.020-1.169
	TJC change	0.066	0.028	0.016	1.069	1.012-1.128
	HAQ-DI change	0.627	0.317	0.048	1.871	1.005-3.483
	Fatigue change	0.204	0.067	0.002	1.226	1.075-1.339
Reference category is no change						

Conclusions: In Latinos with established RA, change in pain reporting reflects alterations in non-inflammatory parameters such as fatigue, depression and functional disability rather than inflammation. Active screening and consideration of those factors may inform therapeutic interventions, balance patient and physician expectations, and optimize patient satisfaction and clinical outcomes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6813

THU0098 THE NAILFOLD CAPILLAROSCOPY IN RHEUMATOID ARTHRITIS: QUANTITATIVE ANALYSIS AND CLINICAL AND SEROLOGICAL CORRELATION

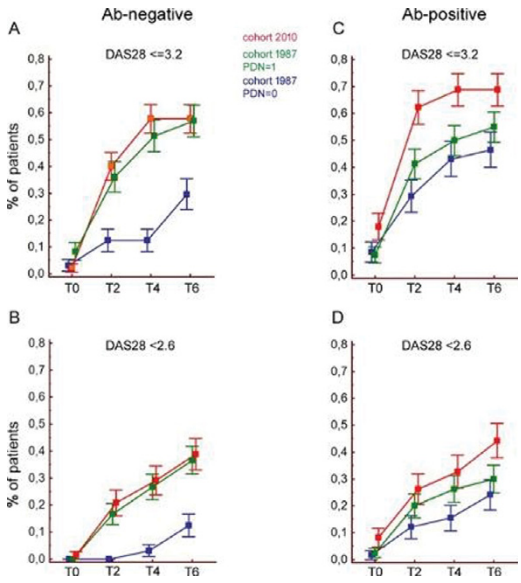
G. Cuomo, E. Frongillo, L. Pirro, A. Del Mastro, C. Romano. *Dipartimento Assistenziale Integrato di Medicina Interna, UOC Medicina Interna - Università degli Studi della Campania - Luigi Vanvitelli, Napoli, Italy*

Background: Nailfold videocapillaroscopy (NVC) abnormalities have been reported in patients with Rheumatoid Arthritis (RA). Nevertheless only few studies evaluated the grades of the detected alterations (1,2). In 1994, Hachulla et al., showed microvascular permeability alterations in RA, to confirming the existence of a microangiopathy (3). In addition, Meyer et al. showed modifications of the normal blood flow velocity and microvascular dysfunction in RA (4).
Objectives: The aim of this study was to evaluate, in RA patients and healthy controls (HC), the microcirculatory abnormalities through NVC, applying a qualitative and quantitative method. We also correlated abnormalities with clinical and immunological features
Methods: Thirty-five HC (35 females, 7 males, median age 55, range 32–70) and 70 RA patients (61 females, median age 58 years, range 30–75; median disease duration 12 years, range 1–20) consecutively admitted to our outpatient clinic, were examined. All patients underwent a full clinical-serological characterization. Both patients and controls underwent NVC, with optical probes of 200X (VideoCap 2.5). We excluded patients who showed conditions known to compromise microcirculation, such as diabetes, hypertension, overlap with other connective tissue diseases or certain pharmacological treatments. The following NVC parameters were evaluated with a semiquantitative method: capillary enlargement (ectasias), microhemorrhages, mean capillary density, capillary tortuosity (5).
Results: NVC alterations were detected in 55 of 70 (68.6%) RA patients: 40 (57%) patient showed ectasic capillaries; 21 (30%) decrease of the mean capillary density; 12 (17%) microhemorrhages; 46 (65.7%) capillary tortuosity. No patient had megacapillaries and/or neoangiogenic abnormalities.
A statistically significant difference between HC and RA patients was found for the detection of ectasias ($p<0,0001$) and for the decrease of the mean capillary density ($p<0,001$).
No differences emerged in RA patients between NVC pattern and/or immunological (ANA, ACPA, Rheumatoid Factor) and/or serological profile (ESR, CRP, lipid profile).
Nevertheless we found a correlation between NVC abnormalities (microhrmorrhages) and activity disease evaluated by DAS28 (p=0.0037)
Conclusions: Our study confirms the presence of a sub-clinical microvascular involvement in RA patients either with or without microvascular clinical manifestations.
In our opinion capillaroscopy can be considered a valid technique in inflammatory joint diseases to analyze microvascular circulation. Moreover, the correlation of NVC specific alteration with disease activity suggests the importance of these features in the assessment of RA patients.
References:
[1] Granier F, et al. Arthristi Rheum 1996.
[2] Nagy and Czirjiak. J Eur Acad Derm Venerol 2004.
[3] Hachulla et al, J Rheumatol 1994.
[4] Meyer. Rheumato Int 2007.
[5] Ingegnoli et al,Seminar Arthitis Rheum 2009.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6829

THU0099 THE 2010 CLASSIFICATION CRITERIA AND A MORE AGGRESSIVE TREATMENT STRATEGY IMPROVE CLINICAL OUTCOMES IN SEROPOSITIVE BUT NOT SERONEGATIVE RHEUMATOID ARTHRITIS

G. Crepaldi, S. Bugatti, F. Benaglio, G. Sakellariou, A. Manzo, C. Montecucco, R. Caporali. *Department of Rheumatology, IRCCS Policlinico San Matteo Foundation, Pavia, Italy*

Background: Current guidelines recommend an early and intensive treatment in patients diagnosed with rheumatoid arthritis (RA), and the 2010 ACR/EULAR Classification Criteria were developed with the aim of allowing earlier diagnosis and treatment (1,2). Recent studies highlighted some differences in disease activity between seropositive and seronegative RA patients at disease onset (3).
Objectives: To investigate whether the application of the 2010 ACR/EULAR Classification Criteria and a more aggressive treatment strategy improve clinical outcomes in patients with early RA irrespective of the autoantibody status.
Methods: 584 early, treatment-naïve RA patients were recruited in the years 2005–2014. RA diagnosis was made according to the ACR 1987 criteria in 2005–2010 (n=360, cohort 1987), and to the 2010 ACR/EULAR criteria in 2011–2014 (n=224, cohort 2010). Patients were classified in autoantibody (Ab)-negative (negative rheumatoid factor (RF) and/or anticitrullinated peptide antibody (ACPA) and Ab-positive (RF and/or ACPA positive). Methotrexate (MTX) was used at the initial dosage of 10 mg/week in cohort 1987, and 15 mg/week in cohort 2010, and progressively increased if low disease activity (LDA) (DAS28$\leq$3.2) was not met. The frequency and predictors of LDA and clinical remission (DAS28$<$2.6) over 6 months were assessed by Cox regression.
Results: In Ab-negative patients, LDA and clinical remission were achieved in 62.8% and 37.2% of the cases, and the 2010 cohort did not show significantly improved outcomes (HR [95% CI] 0.86 [0.611.23] for LDA; 1.04 [0.651.69] for remission) (Figure 1A,B). In contrast, in Ab-positive patients, the application of the 2010 classification criteria and higher dosages of MTX were associated with increased frequency of LDA after adjustment for confounders (age, sex, prednisone, baseline DAS28; HR [95% CI] 1.39 [1.012]) (Figure 1C). Clinical remission was achieved in 41.3% of the cases, compared to 29.6% in the 1987 cohort (p=0.17) (Figure 1D).
Conclusions: Early diagnosis and a more aggressive treatment strategy with MTX lead to significantly improved outcomes in autoantibody positive RA. The management of seronegative patients remains suboptimal.
References:
[1] Smolen JS et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. Ann Rheum Dis 2016.
[2] Aletaha D et al. 2010 rheumatoid arthritis classification criteria: an ACR/EULAR collaborative initiative. Ann Rheum Dis 2010.
[3] Nordberg LB et al. Patients with seronegative RA have more inflammatory activity compared with patients with seropositive RA in an inception cohort of DMARD naive patients classified according to 2010 ACR/EULAR criteria. Ann Rheum Dis 2017.



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5101

THU0100 IN EARLY INFLAMMATORY ARTHRITIS A LYMPHOID PATHOTYPE SIGNFICANTLY ASSOCIATES WITH REQUIREMENT FOR BIOLOGIC THERAPY AT 12 MONTHS FOLLOW UP: RESULTS FROM THE PATHOBIOLOGY OF EARLY ARTHRITIS COHORT (PEAC)

G. Lliso-Ribera[1], F. Humby[1], S. Kelly[1], M. Bombardieri[1], M. Lewis[1], R. Hands[1], V. Rocher[1], F. Bene[1], A. Nerviani[1], C. Buckely[2], P. Taylor[3], I. McInnes[4], C. Pitzalis[1]. *[1]Experimental Medicine and Rheumatology, Queen Mary University London, London; [2]Centre for Translational Inflammation Research, University of Birmingham, Birmingham; [3]Kennedy Institute of Rheumatology, University of Oxford, Oxford; [4]Experimental Medicine and Rheumatology, University of Glasgow, Glasgow, United Kingdom*

Background: Early aggressive treatment in RA equates to better long term outcomes, however targeting aggressive therapies including biologics to patients with the worse prognosis is critical to deliver acceptable risk/benefit ratios and health economic improvements. Such an approach requires prognostic biomarkers, whether the well recognised heterogeneity in synovial pathobiology in early RA translates to specific disease outcomes is currently unknown.
Objectives: The aim of this study was to investigate whether in a treatment naïve early inflammatory arthritis cohort, baseline synovial pathotype significantly associates with disease outcome at 12 months.
Methods: 166 consecutive DMARD naïve patients recruited as part of PEAC at Barts Health NHS Trust with synovial tissue suitable for analysis were included. At baseline patients were classified as RA (2010 ACR/EULAR criteria) or undifferentiated (UA). All patients underwent a baseline synovial biopsy of a clinically active joint along with collection of demographic data. Patients were subsequently treated with DMARD +/- steroid therapy with aim for low disease activity (DAS <3.3). At 6 month follow up patients were escalated to biologic therapy if fulfilling UK NICE guidelines. At 12 months patients were classified as: (i) no treatment, (ii) DMARDs, and (iii) Biologic +/- DMARDs. Sequentially cut sections of baseline synovial biopsies underwent immunohistochemical staining and semi-quantitative scoring (0–4) to determine the degree of CD20+Bcells, CD3+T cells, CD68+ lining (l) and sublining (sl) macrophage and CD138+ plasma cell infiltration. Sections were categorised into 3 pathotypes, (i) Fibroid: (CD68 SL<2 and or CD3, CD20, CD138<1), (ii) Myeloid: (CD68SL>2, CD20<1 and or CD3>1) and (iii) Lymphoid: (grade 2–3 CD20+ aggregates, CD20>2).
Results: 79% were classified as RA and 21% as UA. Mean disease duration was 9.27 months. 92% (153/166) patients had follow-up at 12months. 29% (44/153) of patients were classified as fibroid, 34% (52/166) as myeloid and 37% (57/166) as lymphoid. At baseline patients with a lymphoid pathotype had a significantly higher CRP and DAS28 and were significantly more likely to be sero positive for for RF and ACPA ($p<0.05$), suggesting that a lymphoid pathotype is associated with higher levels of disease activity. At 12 months follow up a significantly higher proportion of patients classified as lymphoid vs myeloid or fibroid (58% vs 21% vs 21%) required biologic therapy.
Conclusions: Results demonstrate that in an early inflammatory arthritis cohort a lymphoid pathotype significantly associates with higher disease activity at baseline, sero positivity for RF and ACPA and a requirement for more aggressive therapy at 12 month. This supports a direct role for synovial lymphoid structures in disease pathogenesis and suggests a role as a prognostic biomarker facilitating early stratification of aggressive therapeutic intervention.

N=153	Fibroid (44)	Myeloid (52)	Lymphoid (57)	p-value
No treatment (14) n (%)	6 (42%)	6 (42%)	2 (14%)	<0.05*
DMARD (101) n (%)	30 (29%)	38 (37%)	33 (32%)	
Biologic +/– DMARD (38) n (%)	8 (21%)	8 (21%)	22 (58%)	

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6042

THU0101 CARDIOVASCULAR MAGNETIC RESONANCE IMAGING CHARACTERISATION OF CARDIOVASCULAR ABNORMALITIES IN INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS

G.J. Fent[1], L. Hunt[2,3], K.S. Mankia[4,5], B. Erhayiem[1], J.R. Foley[1], P. Garg[1], P.P. Swoboda[1], J. Andrews[4,5], J.P. Greenwood[1], P. Emery[4,5], S. Plein[1], M.H. Buch[1,5]. *[1]Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, UK; [2]NIHR Leeds Musculoskeletal Medicine, University of Leeds, United Kingdom; [3]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, United Kingdom; [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine; [5]NIHR Leeds Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*

Background: Inflammation is the primary contributor to excess cardiovascular (CV) disease in rheumatoid arthritis (RA), with evidence of subclinical abnormalities observed even in treatment-naïve, early RA [1]. Preliminary reports suggest citrullinated proteins are present in atherosclerotic plaque [2]. It is unclear whether immunological changes of anti-citrullinated protein antibody (anti-CCP+) positive individuals "at risk" of developing RA are associated with CV abnormality.
Objectives: To perform a pilot study to explore whether subclinical CV abnormalities are present in anti-CCP+ individuals at risk of developing RA.
Methods: Sixteen consecutive patients with non specific MSK symptoms but no synovitis, detectable anti-CCP antibody and 30 age-matched healthy controls (HC) underwent a multi-parametric 3.0T (Philips Achieva) cardiovascular magnetic resonance (CMR) study. Neither group had any history of CV disease. At-risk individuals were categorised as low and high absolute risk for RA development (<50% and ≥50% respectively) according to a published risk model [3]. CMR post-processing was performed using CVI [42] (Circle Cardiovascular Imaging, Canada).
Results: HC and at risk individuals were well matched for baseline characteristics (table 1). Aortic strain values (distensibility, strain and stiffness index β) were lower, indicating increased aortic stiffness, in at-risk individuals than HC, numerically most pronounced those classified high risk (table 2). There were no differences in LV mass and function, late gadolinium enhancement, myocardial T1 (measure of myocardial composition) or LV S prime (longitudinal LV systolic function) (table 2).

Table 1. Baseline characteristics

	All 'at risk' RA patients (n= 16)	Healthy controls (n=30)	p value
Age (years)	53±11	50 ± 15	0.59
Males	4/16 (25%)	10/30 (33%)	0.57
Systolic BP (mmHg)	121±17	120±13	0.82
Diastolic BP (mmHg)	64±11	64±11	0.81
BMI (kg/m^2)	28±5	27±6	0.47
Diabetes	2/16	0/30	0.05
Active smoker	1/16 (6%)	3/30 (10%)	0.68
Ex-smoker	11/16 (69%)	5/30 (17%)	0.001
Mean absolute pre-	45%	-	-

Table 2. Results table

	All 'at risk' RA individuals (n= 16)	Low 'at risk' RA individuals (n=10)	High 'at risk' RA individuals (n=6)	Healthy controls (n=30)	p value
Aortic Distensibility (10^{-3}mmHg)	3.6±1.4	4.1±1.5	2.8±0.5	4.7 ± 2.0	0.05
Aortic strain	0.20±0.06	0.21±0.07	0.18±0.03	0.25 ± 0.09	0.03
Aortic stiffness index, β	3.5±1.0	3.2±1.0	4.0±0.8	2.7 ± 0.8	0.007
Myocardial native T1	1215±35	1213±36	1218±37	1202 ± 36	0.25
Late Gadolinium enhancement	1/16	0/6	1/10	1/30	-
LV ejection fraction (%)	62±4	62±5	63±3	62±5	0.94
RV ejection fraction (%)	55±6	54±4	58±7	54±6	0.47
Indexed LV mass (g/m^2)	46±10	45±8	49±14	49±8	0.29
Indexed LV volume (ml/m^2)	83±12	81±13	87±12	80±11	0.34
LV S prime (s-1)	1.1±0.1	1.2±0.1	1.0±0.1	1.1±0.1	0.37

Conclusions: Anti-CCP+ individuals with non-specific MSK symptoms (in particular, a high risk group), exhibit increased aortic stiffness. This suggests presence of CV abnormalities prior to development of RA and implies a role of autoantibody-mediated development of atherosclerosis. These findings warrant further investigation in larger scale studies.

References:

[1] Erhayiem B et al. Newly diagnosed, treatment-naive patients with rheumatoid arthritis have early abnormalities of vascular and myocardial function. J Cardiovasc Magn Reson 2015;17:P285.
[2] Sokolove J et al. Brief report: citrullination within the atherosclerotic plaque: a potential target for the anti-citrullinated protein antibody response in rheumatoid arthritis. Arthritis Rheum 2013;65:1719–24.
[3] Rakieh C et al. Predicting the development of clinical arthritis in anti-CCP positive individuals with non-specific musculoskeletal symptoms?: a prospective observational cohort study. Ann Rheum Dis 2015;74:1659–1656.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4969

THU0102 CLINICAL DISEASE ACTIVITY MEASURES ARE IMPORTANT DRIVERS OF MAJOR CHANGE IN MEDICAL TREATMENT IN US VETERANS ENROLLED IN THE VETERANS AFFAIRS RHEUMATOID ARTHRITIS (VARA) REGISTRY

G.W. Cannon[1,1], C.-C. Teng[2], N.A. Accortt[3], D. Collier[3], S. Mehrotra[2], B.C. Sauer[2]. *[1]Rheumatology; [2]Salt Lake City Va Medical Center, Salt Lake City; [3]Amgen, Thousand Oaks, United States*

Background: Current guidelines encourage the measurement of rheumatoid arthritis (RA) disease activity and directing therapy to achieve a low disease state or remission (treat-to-target). Many RA patients with documented moderate to severe disease activity remain on their current therapy without change.

Objectives: This study investigated Veterans Affairs (VA) clinical data to identify patient factors associated with a major change in RA therapy and to determine the relative importance of these different factors.

Methods: US Veterans enrolled in the VARA registry were included if they had: 1) high/moderate disease activity (DAS28≥3.2) at index date, 2) 18 months of VA data prior to the index date and 3) two or more other DAS28 measured during the preceding 18 months separated by at least three months. A major change was report if within 7 days before to 90 days after the index date there was either: 1) initiation or escalation of DMARDs, 2) initiation or increase dose of prednisone and/or 3) ≥2 joint injections.

Baseline DAS28 was estimated during the observation period prior to the index date using an area under the curve calculation and compared to the DAS28 at the index date. Patients were categorized as have a worsening or improvement of disease if the DAS28 at index date was 0.6 higher or lower than the average DAS28 during the observation period respectively. Other patients were categorized as no change in DAS28.

Analyses of clinical variables including components of the DAS28 and patient and physician reported measures were compared in patients with and patients without a major change in therapy.

Results: Of 941 patients who met study criteria, only 388/941 (41.2%) had a major change of therapy. Patients with worsening DAS28 were more likely to have a major change 183/369 (49.5%) than no DAS28 change 170/454 (37.4%) and improved DAS28 35/118 (29.6%) (P<0.001). Clinical variables were strongly associated with changes in therapy among patients with worsening disease activity and not as strongly associated with change in therapy in those with no change disease activity. Clinical variables were not significantly associated with major change in patients with disease improvement, though that group had the smallest sample size. Ten representative clinical variables with the highest association with major change are included below.

	Comparison of Patients with Major Change to Patients without Major Change					
Demographic elements	DAS28 worsening (n=369)		DAS 28 no change (n=454)		DAS 28 improved (n=118)	
Major Change at Index Date - Number (%)	183/369 (49.5%)		170/454 (37.4%)		35/118 (29.6%)	
Age at RA Disease Onset - Mean (SD)	52.4±13.7		51.4±13.7		50.9±12.9	
Age at Index Date - Mean (SD)	65.3±10.6		65.6±11.0		64.0±10.8	
Male - Number (%)	328 (88.9%)		410 (90.3%)		99 (84.0%)	
Clinical Variables from VARA registry	RR (CI 95)	p-value	RR (CI 95)	p-value	RR (CI 95)	p-value
DAS28 Score At Index Date	1.25 (1.11 - 1.42)	<0.001	1.30 (1.12 - 1.51)	0.001	1.23(0.82 - 1.82)	0.318
Baseline DAS28 Score during 18 months observation period	1.20 (1.05 - 1.37)	0.009	1.27 (1.09 - 1.47)	0.002	1.27 (0.86 - 1.87)	0.219
Swollen Joint Count	1.03 (1.00 - 1.04)	0.031	1.05 (1.01 - 1.08)	0.006	1.06 (0.99 - 1.12)	0.070
Tender Joint Count	1.02 (1.00 - 1.04)	0.027	1.01 (0.98 - 1.03)	0.530	0.98 (0.91 - 1.07)	0.671
Modified Health Assessment Questionnaire (MD HAQ)	1.08 (0.87 - 1.37)	0.051	1.03 (0.81 - 1.31)	0.743	0.90 (0.50 - 1.61)	0.722
Pain Score	1.07 (1.01 - 1.13)	0.028	1.04 (0.99 - 1.10)	0.145	0.93 (0.83 - 1.05)	0.257
Patient Global Assessment	1.01 (1.00 - 1.01)	0.093	1.01 (1.00 - 1.02)	0.014	1.00 (0.98 - 1.01)	0.560
Physician Global Assessment	1.00 (0.99 - 1.01)	0.474	1.01 (1.00 - 1.02)	0.002	1.01 (0.99 - 1.02)	0.402
Erythrocyte Sedimentation Rate	1.01 (1.00 - 1.01)	0.073	1.00 (1.00 - 1.01)	0.582	1.00 (0.99 - 1.02)	0.630
C-reactive Protein	1.04 (1.00 - 1.08)	0.056	1.08 (1.00 - 1.17)	0.990	1.08 (0.92 - 1.28)	0.344

Conclusions: More than half of the patients with moderate disease activity did not have a major change in therapy. The likelihood of a major change in therapy increased with worsening disease activity. The clinical variables assessed were more strongly associated with change in therapy in patients with worsening of disease. Clinical disease activity measures are highly associated with the decision to initiate major changes. Future work will investigate the potential added value of administrative variables. This work emphasizes the need for methods to systematically collect and utilize clinical disease activity measurements, particularly longitudinally, to improve the treat-to-target strategy.

Acknowledgements: Work Sponsored by VA Specialty Care Centers of Innovation, VA Health Service Research and Development, and Amgen.

Disclosure of Interest: G. Cannon Grant/research support from: Amgen, C.-C. Teng Grant/research support from: Amgen, N. Accortt Shareholder of: Amgen, Employee of: Amgen, D. Collier Shareholder of: Amgen, Employee of: Amgen, S. Mehrotra Grant/research support from: Amgen, B. Sauer Grant/research support from: Amgen

DOI: 10.1136/annrheumdis-2017-eular.1413

THU0103 ANTI-RA33 AUTOANTIBODIES ARE ASSOCIATED WITH THERAPEUTIC RESPONSES TO METHOTREXATE AND ANTI-TNF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

G. Steiner[1], D. Sieghart[1], P. Studenic[1], T. Horn[2], D. Aletaha[1], J. Smolen[1]. *[1]Internal Medicine III-Rheumatology, Medical University Vienna; [2]Phadia Austria GmbH, Thermo Fisher Scientific, Vienna, Austria*

Background: Besides the determination of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), anti-RA33 antibodies (which are directed to the nuclear antigen hnRNP-A2) could be of additional diagnostic and/or prognostic value in patients with rheumatoid arthritis (RA) because they are also found in RF/ACPA negative patients (1, 2).

Objectives: So far, published data on anti-RA33 antibodies refer only to the IgG isotype. It was therefore the aim of this study to measure the prevalence of anti-RA33 IgG, IgM and IgA antibodies in patients with RA and to determine their potential prognostic value regarding prediction of response to treatment.

Methods: A total of 255 patients were tested for the presence of IgG, IgM and IgA anti-RA33 antibodies by a newly developed EliA® (Thermo Fisher Scientific). All patients had initially been treated with conventional synthetic drugs (mostly methotrexate) and were subsequently treated with at least one TNF inhibitor. Therapeutic responses to MTX and TNF blocking biologicals were calculated in an inception cohort (n=104) who had started their DMARD therapy at our clinic. To define therapeutic responses the simplified disease activity index (SDAI)50 and American College of Rheumatology (ACR)20 responses were calculated.

Results: Among the 255 patients, 11% tested positive for anti-RA33 IgG antibodies, 15% for IgM antibodies and 6% for IgA antibodies. Altogether, 62 patients (24%) had at least one type of anti-RA33 antibody: 24 patients were RF-negative, 26 were ACPA-negative and 18 were RF/ACPA double negative. Thus, in 32 patients (13%), anti-RA33 was the only antibody specificity. Regarding response to anti-TNF therapy (Figure 1A), in the group of patients testing positive for anti-RA33 antibodies of any isotype (with or without concomitant RF and/or ACPA) the percentage of SDAI50 responders (24%) was significantly lower (p=0.0117) than in anti-RA33 negative (but RF/ACPA positive) patients (42% responders) and similar to the group of completely seronegative patients (21% responders). In contrast, regarding responses to MTX (Figure 1B) the percentage of SDAI50 responders was significantly higher (p<0.0001) among anti-RA33 positive patients (with or without RF and/or ACPA) (59% responders) compared to anti-RA33 negative (but RF/ACPA positive) patients (37% responders) and seronegative patients (24% responders).

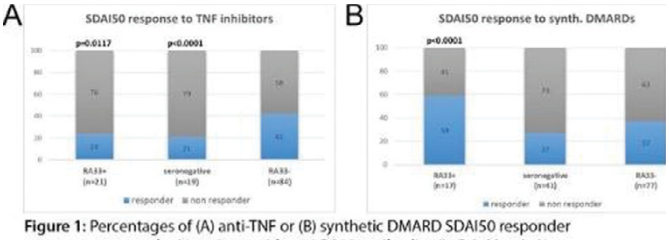


Figure 1: Percentages of (A) anti-TNF or (B) synthetic DMARD SDAI50 responder versus non responder in patients with anti-RA33 antibodies (IgG, IgM or IgA), seronegative patients (RA33-RF-ACPA-) compared to RA33 negative patients.

Conclusions: In agreement with previous findings (1,2) anti-RA33 antibodies reduced the diagnostic gap left by ACPA and RF and thus the percentage of seronegative patients by 13%. Importantly, the presence of anti-RA33 antibodies was associated with a favourable response to MTX on the one hand and with a diminished response to TNF inhibitors on the other hand. Therefore, these antibodies appear to have some prognostic value for prediction of therapeutic responses and could become helpful tools in therapeutic decision making.

References:

[1] Nell VPK, Machold KM, Stamm TA, et al. Autoantibody profiling as early diagnostic and prognostic tool for rheumatoid arthritis. Ann Rheum Dis 2005, 64:1731–6.
[2] Yand X, Wang M, Zhang X et al. Diagnostic accuracy of anti-RA33 antibody for rheumatoid arthritis: systematic review and meta-analysis. Clin Exp Rheumatol. 2016; 34:539–47.

Disclosure of Interest: G. Steiner Consultant for: Phadia Austria GmbH, Thermo Fisher Scientific, D. Sieghart: None declared, P. Studenic: None declared, T. Horn Employee of: Phadia Austria GmbH, Thermo Fisher Scientific, D. Aletaha: None declared, J. Smolen: None declared

DOI: 10.1136/annrheumdis-2017-eular.6116

THU0104 BOTH MRI AND HAQ-DI CAN PREDICT RELAPSES FOLLOWING ALL TREATMENT WITHDRAWAL IN MTX-NAÏVE PATIENTS WITH RA IN REMISSION AFTER 12 MONTHS OF ABATACEPT THERAPY IN THE AVERT TRIAL

H. Ahmad[1], J. Baker[2], M. Østergaard[3], P. Emery[4], T. Huizinga[5], J. Ye[1], S. Banerjee[1], P. Conaghan[4]. *[1]Bristol-Myers Squibb, Princeton; [2]Philadelphia VA Medical Center & the University of Pennsylvania, Philadelphia, United States; [3]Copenhagen Center for Arthritis Research, Rigshospitalet and University of Copenhagen, Copenhagen, Denmark; [4]University of Leeds and Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom; [5]Leiden University Medical Center, Leiden, Netherlands*

Background: Factors predictive of relapse need to be identified to aid therapy withdrawal decisions for patients with RA achieving remission with treatment. AVERT (NCT01142726) was a Phase IIIb, randomized, active-controlled trial in patients with early RA.[1] After a 12-month, double-blind treatment period with abatacept + MTX, or abatacept or MTX monotherapy, patients with DAS28 [CRP] <3.2 could enter a 12-month withdrawal period (all treatment stopped).
Objectives: To evaluate *post hoc* whether MRI scores, patient characteristics and disease activity at Month 12 were predictors of clinical relapse at Month 18 and Month 24 after treatment withdrawal in AVERT.
Methods: Synovitis, erosion and bone oedema in the dominant hand and wrist MRI were scored at Month 12 using the RA MRI scoring system (RAMRIS). Patient characteristics (pain, age, weight, HAQ-DI) and disease measures (CRP, SJC28, TJC28, DAS28 [CRP], CDAI, SDAI) were recorded at Month 12. The influence of these factors on the proportion of patients who relapsed (doubling of TJC28 and SJC28, and DAS28 [CRP] ≥1.2 increase relative to Month 12) by Month 18 and Month 24 was assessed.
Results: A total of 172 patients achieving DAS28 remission (DAS28 [CRP] <2.6) at Month 12 in any treatment group were included in the analysis. Numbers of patients who relapsed at Month 18 and Month 24 were 100 and 113, respectively. Of the patient characteristics, disease activity and imaging factors analysed at Month 12, only MRI synovitis, erosion and oedema scores, as well as HAQ-DI scores, were significantly associated ($p<0.05$) with relapse status at both Month 18 and Month 24 (Table).
Conclusions: MRI and HAQ-DI scores in patients in DAS28 remission predicted clinical relapses 6 and 12 months after complete drug withdrawal in the AVERT trial. The clinical decision on whether to withdraw therapy in MTX-naïve patients with RA in remission may benefit from an assessment of imaging and physical function prior to drug withdrawal.
References:
[1] Emery P, et al. Ann Rheum Dis 2015;74:19–26.
Disclosure of Interest: H. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, J. Baker: None declared, M. Østergaard Grant/research support from: AbbVie, Bristol-Myers Squibb, Janssen, Merck, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, Wyeth, P. Emery Grant/research support from: AbbVie, Merck, Pfizer, Roche, Consultant for: AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, Lilly, Novartis, Samsung Bioepis, T. Huizinga Grant/research support from: EU & Dutch Arthritis Foundation, Consultant for: Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Crescendo Biosciences, Inc, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, UCB, Inc., Eli Lilly, Speakers bureau: Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, J. Ye Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Banerjee Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, P. Conaghan Grant/research support from: Bristol-Myers Squibb, Consultant for: AbbVie, Lilly, Novartis, Pfizer, Speakers bureau: AbbVie, Bristol-Myers Squibb, Roche
DOI: 10.1136/annrheumdis-2017-eular.1649

THU0105 PREDICTION OF RESPONSE TO CERTOLIZUMAB-PEGOL IN RHEUMATOID ARTHRITIS (PRECEPRA) BY FUNCTIONAL MRI OF THE BRAIN – AN INTERIM ANALYSIS OF AN ONGOING INVESTIGATOR INITIATED PHASE III TRIAL

H. Schenker[1], A. Hess[2], L. Konerth[2], M. Sergeeva[2], J. Prade[2], A. Kleyer[1], M. Reiser[1], A. Hueber[1], M. Englbrecht[1], E. Feist[3], R.E. Voll[4], B. Bannert[4], C. Baerwald[5], J. Rösch[6], A. Doerfler[6], G. Schett[1], J. Rech[1]. *[1]Department of Internal Medicine 3, University of Erlangen-Nuremberg; [2]Institute of Pharmacology and Toxicology, University of Erlangen, Erlangen; [3]Department of Rheumatology and Immunology, Charité, Berlin; [4]Clinic for Rheumatology and Clinical Immunology, University of Freiburg, Freiburg; [5]Department of Rheumatology, University of Leipzig, Leipzig; [6]Department of Neuroradiology, University of Erlangen-Nuremberg, Erlangen, Germany*

Background: Tumor necrosis factor inhibitors (TNFi) signify a major advance in the treatment of rheumatoid arthritis (RA). However, treatment success initially remains uncertain as one third of patients do not respond adequately to TNFi.
Objectives: We investigated whether brain activity associated to arthritis measured by functional magnetic resonance imaging (fMRI) can function as a predictor of response to TNFiin RA patients.
Methods: This is an interim analysis of the first 50 patients of the PreCePRA trial, a multi-center, double-blind, placebo-controlled fMRI trial on patients with RA. [1] [2] Active RA patients failing csDMARDs with a DAS28-ESR >3.2 and at least three tender and/or swollen joints received a baseline brain BOLD fMRI scan upon joint compression at screening. Patients werethen randomized into a 12-week double-blinded treatment phase with placebo (arm 1) or 200mg certolizumab-pegol eow (arm 2; fMRI Bold signal>2000 voxel i.e. $2cm^3$, arm 3; fMRI Bold signal <2000 voxel). LDA 3mo. Primary end point was DAS28-ESR low disease activity at 12 weeks. A 12 weeks follow-up phase in which patients were switched from the placebo to the treatment arm folowed the blinded phase. fMRIwas carried out at baseline as well as after 12 and 24 weeks of or placebo.
Results: In 31 patients (responders) baseline signal volume i.e. sum of significantly coupled voxels after the FDR thresholding was significatly higher compared to 19 patients (non-responders) ($p<0.001$) allowing discrimination between the two groups prior to treatment. In responders we detected an persitent decrease of the BOLD volume from baseline to week 12 and week 24 ($r^2=0.561$) whereas the BOLD volume in non-responders persitently increased ($r^2=0.589$).

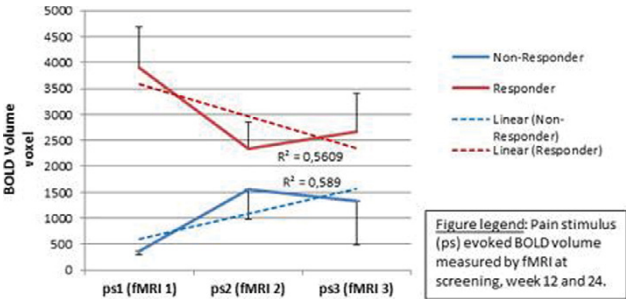


Figure legend: Pain stimulus (ps) evoked BOLD volume measured by fMRI at screening, week 12 and 24.

Conclusions: Based on this interim analysis we conclude that high BOLD volumes in fMRI, indicating high-level brain representation of pain in arthritis. These data represent the first encouring signal of the PreCePRA brain fMRI study supporting the concept that increased RA-related brain activity is related to response to TNFi.
References:
[1] Rech, J., et al., Association of brain functional magnetic resonance activity with response to tumor necrosis factor inhibition in rheumatoid arthritis. Arthritis Rheum, 2013.65(2): p. 325–33.
[2] Hess, A., et al., Blockade of TNF-alpha rapidly inhibits pain responses in the central nervous system. Proc Natl Acad Sci U S A, 2011.108(9): p. 3731–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5067

THU0106 ROUTINE CLINICAL ASSESSMENT OF JOINT DAMAGE TO EVALUATE OUTCOME IN RHEUMATOID ARTHRITIS

H. Bernelot Moens, A. terAvest, D. Berendsen, C. Haagsma. *Rheumatology & Clinical Immunology, Ziekenhuisgroep Twente, Almelo, Netherlands*

Background: Early treatment of rheumatoid arthritis (RA) with treat-to-target strategies aims to reduce disease activity and to prevent joint damage. Assessment of the quality of care is commonly based on measurements of disease activity, functioning and well being. In clinical trials, radiographic scores are widely used to assess structural joint damage, but these are not applicable in routine care and limited to hands and feet. Only a few studies evaluated clinical assessment of irreversible joint damage (e.g. surgery) as outcome. The RA articular damage (RAAD) score counts structural damage in all joints that that are affected by RA[1]. It correlates with radiographic damage[2]. We have applied this score since 2014 in routine care.

Abstract THU0104 – Table 1. MRI and HAQ-DI Scores at Month 12 in Patients With vs Without Relapse by Month 18 and Month 24*

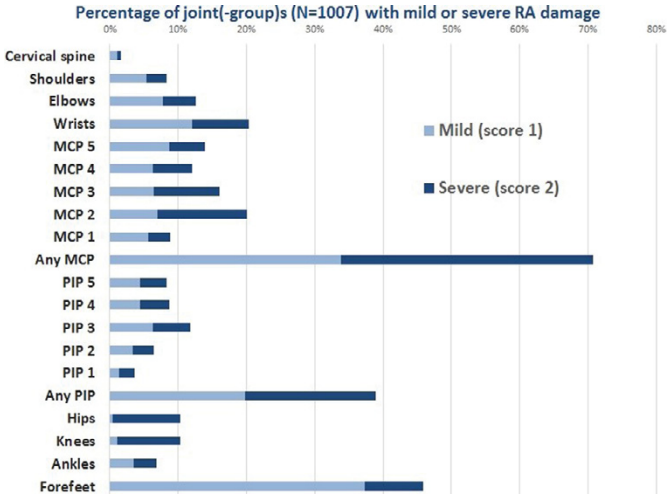
	Patients with vs without relapse at Month 18		Patients with vs without relapse at Month 24	
Score	Estimated difference in scores at Month 12 (95% CI)	p value	Estimated difference in scores at Month 12 (95% CI)	p value
MRI synovitis	1.051 (0.291, 1.810)	0.0070	1.088 (0.256, 1.920)	0.0107
MRI erosion	3.244 (1.694, 4.795)	<0.0001	3.076 (1.550, 4.601)	0.0001
MRI oedema	1.503 (0.650, 2.356)	0.0007	1.423 (0.644, 2.202)	0.0004
HAQ-DI	0.194 (0.050, 0.338)	0.0088	0.201 (0.050, 0.353)	0.0095

*Month 18: 92 with relapse, 63 without relapse; Month 24: 103 with relapse, 52 without relapse.

Objectives: Evaluate the feasibility of a simple clinical joint damage score and describe the increment over time in RA patients with varying disease duration.
Methods: Cross-sectional study in all patients with a clinical diagnosis of RA visiting the outpatient clinic in 2015 and 2016. Rheumatologists and nurses from the outpatient department of a large regional hospital received a single training to perform the RAAD score. Scores of 0 (no damage), 1 (mild) or 2 (severe: ankylosis, luxation or joint surgery) were assigned to 35 joints (maximum score: 70) with a disease activity score, and stored in the electronic patient record system. Baseline data including ACR 2010 criteria were also registered.
Results: In 1007 (67.3%) of 1496 RA patients seen over 2 years RAAD-scores were performed. 652 (64.7%) were female, average age (SD, range) was 62.6 (13.1, 19–95), disease duration 9.9 (9.6, 0–65) years. Rheumatoid factor and ACPA were positive in 70.6% and 70.3% respectively.
RAAD scores related to disease duration illustrate that at disease onset 86%, and after 20 years 37% of the patients has no joint damage (Table). Distribution over joints shows the classical predominance of damage in MCP, PIP and MTP joints (Image). Structural damage in shoulders or elbows was present in 8.3% and 12.5%, in knees and hips in 10,3% each. Despite current treatment strategies, irreversible joint damage of more than 5 joints is present in 6.3% within 10 years.

Table 1. Accumulation of irreversible joint damage score with disease duration, number (%)

RAAD-score	1st year (N=69)	2–4 yrs (N=228	5–9 yrs (N=253)	10–19 yrs) (N=239)	≥20 yrs (N=218)
0 (no joint damage)	59 (86)	158 (69.3)	145 (57.3)	81 (33.9)	80 (36.7)
1–5	8 (12)	65 (28.5)	92 (36.4)	103 (43.1)	42 (19.3)
6–10	2 (3)	4 (1.8)	11 (4.3)	34 (14.2)	28 (12.8)
11–20			4 (1.6)	13 (5.4)	36 (16.5)
>20		1 (0.4)	1 (0.4)	8 (3.3)	32 (14.7)
Average (range)	0,4 (0–6)	0,9 (0–23)	1,6 (0–37)	2,2 (0–18)	9,0 (0–59)



Conclusions: Clinical assessment of joint damage is a feasible parameter of long term outcome in RA. Reflecting overall joint damage, the RAAD-score provides a broader view than radiographic scoring of hands and feet and is easy to apply in routine care. Given the slow increment a single assessment per 5 years may suffice to compare structural joint damage across cohorts of patients.
References:
[1] Zijlstra T, Bernelot Moens H, Bukhari M. The rheumatoid arthritis articular damage score: first steps in developing a clinical index of long term damage in RA. Ann Rheum Dis. 2002;61:20–3.
[2] Hammer H, Odegard S, Fagerhol M, et al. Calprotectin is strongly and independently correlated with joint inflammation and damage in rheumatoid arthritis. Ann Rheum Dis 2007;66:1093–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4437

THU0107 ASSOCIATION OF GLOBAL DNA METHYLATION WITH MTX RESPONSE AND ADVERSE EVENTS IN EARLY RHEUMATOID ARTHRITIS

H. Gosselt[1], M.D. Rotte[1], M. Chisholm[1], M. Hazes[2], R.D. Jonge[3], S. Heil[1].
[1]Clinical Chemistry; [2]Rheumatology, Erasmus Medical Center, Rotterdam; [3]Clinical Chemistry, VUMC, Amsterdam, Netherlands

Background: Methotrexate (MTX) is a first-line therapy in early Rheumatoid Arthritis (RA). However, ~30% of treated patients do not respond to the medicine or need to abrogate treatment because of severe adverse events. Since MTX interferes with the folate cycle and thereby influences the methylation cycle, we hypothesize that methylation status at start therapy is associated with response and adverse events after three months of MTX treatment enabling personalized medicine.
Objectives: Examine global methylation status of early Rheumatoid Arhtritis patients before and after 3 months of MTX use between responders and non-responders and patients that do or do not experience adverse events.
Methods: To assess global methylation status, DNA was isolated at baseline from whole blood of 120 patients from the Treatment in the Rotterdam Early Arthritis Cohort (tREACH), a multicenter, stratified single-blind clinical trial of patients with early RA. Methylation status of 7 CpG sites within Long-interspersed nuclear elements (LINE-1) were analyzed and quantified by Matrix Assisted Laser Desorption Ionization time of flight Mass Spectrometry (MALDI-TOF MS). Results were compared between MTX responders and non-responders based on a low disease activity (DAS28 <3.2) at three months of treatment and patients experiencing ≤2 or ≥3 adverse events. Gastrointestinal adverse events were assessed separately.
Results: No statistical differences in the mean of 7 LINE-1 CpGs were observed between responders and non-responders, nor in patients experiencing ≤2 or ≥3 adverse events. However, methylation status of specific CpG sites within LINE-1 did show significant changes. Baseline CpG_2 methylation levels were positively correlated with the DAS28 score at t3 (p=0.018) and baseline methylation levels in CpG_5 and CpG_8.9 were significantly higher in patients experiencing ≥3 adverse events (p=0.018 and p=0.034, respectively). Besides, CpG_5 methylation levels were particularly increased in patients experiencing gastrointestinal adverse events (p=0.038).
Conclusions: Global methylation status is associated with non-response and adverse events to MTX in early RA patients and can therefore be implemented in future prediction models.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4686

THU0108 SUBCLINICAL CENTRAL NERVOUS SYSTEM DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS: DISEASE ACTIVITY AND CYTOKINES

I. Tekeoğlu, S. Sağ, A. Kamanlı, M.S. Sağ, K. Nas. *Department of Physical Medicine and Rehabilitation, Rheumatology, Faculty of Medicine, Sakarya University, Sakarya, Turkey, sakarya, Turkey*

Background: We aimed in this study to investigate blood-brain barrier (BBB) dysfunction in RA patients who had no neurological symptoms, and were receiving synthetic DMARD treatment.
Objectives: We investigated correlations between cranial MRI images and brain specific proteins (S100 Beta, GFAP), cytokines (IL-1 beta, IL-17) in plasma which had important roles in disease activity.
Methods: In our study, 57 patients (46 females and 11 males) were included included in RA group, and 34 patients (24 females and 10 males) in the control group. All of RA patients were receiving synthetic DMARD treatment. Demographic characteristics of all patients were recorded. Disease activity was evaluated by using DAS-28. Mini-mental test (MMT) was used for evaluation of cognitive functions, and Fazekas scale was used to evaluate cranial MR lesions. S100 beta, GFAP, claudin, IL-17, and IL-1 beta levels were measured in peripheral blood of both groups.
Results: Demographic characteristics were similar between the groups, and there was no statistically significant difference in gender, age, and body mass index (BMI) between patient and control groups (p>0.05). S100 beta, and GFAP levels were significantly higher in RA group (p<0.05). No difference was determined in hyperintense lesions diagnosed in cranial MR between patient and control groups (p>0.05). There were positive correlations between IL-17 S100 beta and GFAP, and IL-1 beta and S100 beta.
Conclusions: In our study, we have shown that blood-brain barrier may be damaged subclinically in RA patients, brain specific proteins related to BBB dysfunction may be increased in the peripheral blood, and BBB dysfunction may be related to cytokines which play an important role in disease pathogenesis. In conclusion, cytokines which circulate in the peripheral blood in RA may cause subclinical BBB damage. Further large scale studies with long-term follow-up are required which will support this hypothesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2313

THU0109 UPDATED ESTIMATION OF THE EQ5D QUALITY OF LIFE QUESTIONNAIRE UTILITY VALUES THROUGH HAQ-DI MAPPING FOR SPAIN

I. Gorostiza[1], L. Ansola[2], E. Galindez[3]. *[1]Research Unit; [2]Research Unit; [3]Rheumatology, H. Universitario Basurto, Vizcaya, Spain*

Background: Rheumatoid arthritis (RA) deeply affects the quality of life (QoL) of patients. The preferred approach to evaluate treatment efficiency is to value health as patient preferences known as utilities, and subsequently, calculate Quality-Adjusted Life Years gained. A new 5-level of severity EQ5D has recently released and a new tariff proposed for Spain (Ramos-Goñi,2016). Although QoL questionnaires are not of routine use in clinical practice, it is possible to estimate it using the Health Assessment Questionnaire Disability Index (HAQ-DI)
Objectives: To develop a function that allows the estimation of EQ5D-5L utility values from HAQ-DI updated to the newest proposed tariff for Spain

Methods: Patients with RA from two teaching hospitals, participating in a prospective observational study completed the HAQ-DI and EQ5D-5L at 0–6-12 month follow-up visits. Inclusion criteria: ACR RA diagnosed patients, on biologic treatment and whose disease activity remained stable at least for 3 months EQ5D-5L is a standardized, generic instrument for describing and valuing health and QoL, consisting in a five-dimensional descriptive system (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and a visual analogue scale. A country-specific tariff converts patient's answer to a 0–1 (full health) utility index. HAQ-DI is a self-completed questionnaire used to assess the functional ability using 20 items, distributed across 8 dimensions and resulting in a four-level disability scale (0–3). In addition, socio-demographic and clinical data where recorded.To estimate the EQ5D-5L utility index OLS models were built. As this index is bounded to the [-0.416, 1] interval, Tobit models were also considered. Hereafter, the index was transformed to the open interval (0,1) and estimated through beta regression with a logit link. To determine the relationship grade between the index and the HAQ-DI scale and obtain residuals without trend, GAM models were used. Best fitting models were determined by AIC, MAE and RMSE. All analyses were performed using R software

Results: 217 questionnaires fulfilled by 77 patients. Mean (SD) age was 57.0 (12.9), 87% women, AR duration 13.7 (7.1), mean DAS28 2.72 (1.00) and HAQ-DI 0.77 (0.60). Baseline EQ5D index: 0.768 (0.182). All the OLS estimation models resulted in the interval limits defined by the index, so Tobit models were not considered. When considering the linear model we obtained the best results with the HAQ-DI term and its third power: EQ5D5L = 0.9232 – 0.1760×HAQ – 0.0172×HAQ^3 (AIC=–221.62; MAE=0.0974; RMSE=0.1363); for beta regression, we obtained the best model with the HAQ-DI to the first power alone: logit (EQ_01) = 2.5821 – 1.1165×HAQ (AIC=–444.4; MAE=0.0691; RMSE=0.0958). Considering the AIC and the residuals together, we obtained the best fitting model with the beta regression approach, with neither age nor sex

Conclusions: So far, only a utility function using HAQ-DI and an older EQ5D-3L version was available for Spain (Carreño,2011). This updated utility function can be used as a practical approach to predict RA patients' QoL and EQ5D utility score for Spain when clinicians/researchers need them for clinical practice or cost-effectiveness analyses and generic QoL measurements are not available

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4836

THU0110 THE IMPORTANCE OF SUSTAINED REMISSION FOR LONGTERM OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS

J. Smolen[1], C. Gabay[2], D. Aletaha[1], P. Emery[3], I. Sainsbury[4], Y. Zhang[4], A. Kavanaugh[5]. *[1]Medical Univ of Vienna, Vienna, Austria; [2]Univ of Geneva, Geneva, Switzerland; [3]Leeds Inst of Rheumatic & Musculoskeletal Medicine, Leeds, United Kingdom; [4]AbbVie, N Chicago, IL; [5]Univ of California, San Diego, CA, United States*

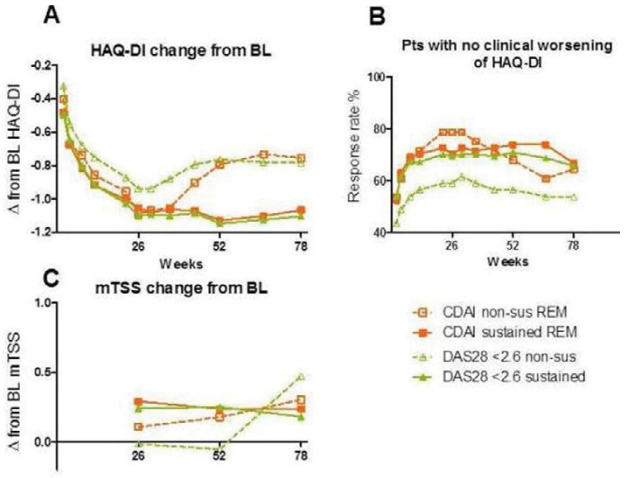
Background: In patients (pts) with rheumatoid arthritis (RA), the long-term impact of sustained versus (vs) transient clinical remission (REM) has not been assessed thoroughly, although REM duration has been shown to affect structural outcomes[1]. The relationship of different definitions of clinical remission (REM) with function and structural integrity has not been assessed.

Objectives: To explore the importance of sustained REM or disease control for long-term outcomes, and assess various definitions of REM in adalimumab (ADA) long-term trials.

Methods: Data are from 2 trials of ADA in early RA pts; In PREMIER, pts received ADA, methotrexate (MTX) or ADA+MTX for 2 years (yrs), after which they could enter an open label (OL) period for upto 8 yrs[2]. In OPTIMA, pts received ADA+MTX, or placebo (PBO) +MTX for 26 weeks (wks). Based on whether or not pts achieved DAS28-CRP <3.2 at wks 22 and 26, pts withdrew ADA, continued on PBO+MTX, ADA+MTX or OL ADA+MTX until Wk 78[3]. For this analysis, non-sustained REM/disease control was defined as meeting one of the following at 6 months but not 1 yr: DAS28-CRP <2.6; simplified disease activity index (SDAI) ≤3.3; clinical disease activity index (CDAI) ≤2.8. Sustained REM/disease control was defined as meeting these criteria at both 6 months and 1 yr. The mean change from baseline in health assessment questionnaire-disability index (ΔHAQ-DI), or modified total Sharp score (ΔmTSS), and the number of pts without clinical worsening of HAQ-DI (Δ≤0.22) were assessed over 78 wks for OPTIMA, or 5 yrs for PREMIER. NRI and LOCF were used for binary and continuous variables, respectively.

Results: In OPTIMA, by any of the REM criteria, pts in sustained REM had larger mean ΔHAQ-DI over time (Fig 1A) vs pts in non-sustained REM. Pts with non-sustained DAS28-CRP <2.6 vs non-sustained CDAI REM had numerically smaller ΔHAQ-DI up to Wk 52. Over time, more pts in sustained vs non-sustained REM using DAS28-CRP<2.6 (but not CDAI or SDAI criteria) did not have clinical worsening of HAQ-DI, possibly due to more suppression of inflammatory components upon achieving CDAI REM but not DAS28-CRP <2.6 in these early RA pts (Fig 1B). At Wk 78, ΔmTSS at Wk 78 was smaller for pts in sustained vs non-sustained DAS28-CRP <2.6, and similar for sustained and non-sustained CDAI REM (Fig 1C). Somewhat fewer pts at Wk 78 may have contributed to some variability. Trends were similar in PREMIER (not shown).

Conclusions: Pts who were in sustained disease control/REM had better clinical, functional and radiographic outcomes over the long- term, vs pts in a more transient state, regardless of the REM criteria used, although for CDAI REM, functional and radiographic outcomes were similar for sustained and non-sustained REM, in line with its higher stringency.



For LOCF: CDAI non-sustained REM N=28, CDAI sustained REM N=84, DAS28 <2.6 non-sustained, N=39, DAS28 <2.6 sustained, N=137; For NRI: CDAI non-sustained REM at Wk 26, N=22, at Wk 78, N=18; CDAI sustained REM at Wk 26, N=59, at Wk 78, N=56 DAS28 <2.6 non-sustained, at Wk 26, N=23, at Wk 78, N=21; DAS28 <2.6 sustained, at Wk 26, N=95, at Wk 78, N=90

References:
[1] Aletaha et al, Arthritis & Rheum. 2009;5:1242.
[2] Breedveld et al. 2006. Arthritis & Rheum;54:26.
[3] Smolen et al. 2014. Lancet;383:321.

Acknowledgements: AbbVie: study sponsor, contributed to design, data collection, analysis, interpretation; and writing, reviewing, approval of final version. Medical writing: Naina Barretto, of AbbVie.

Disclosure of Interest: J. Smolen: None declared, C. Gabay Grant/research support from: AbbVie Inc, Amgen, BMS, MSD, Pfizer, Roche, Celgene, Sanofi, and Regeneron., Consultant for: AbbVie Inc, Amgen, BMS, MSD, Pfizer, Roche, Celgene, Sanofi, and Regeneron., D. Aletaha Grant/research support from: AbbVie Inc., Pfizer, Grünenthal, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche., Consultant for: AbbVie Inc., Pfizer, Grünenthal, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche., P. Emery Grant/research support from: research grants and consulting fees from Pfizer, MSD, AbbVie Inc., Bristol-Myers Squibb, UCB, Roche, Novartis, Samsung, Sandoz and Lilly., Consultant for: research grants and consulting fees from Pfizer, MSD, AbbVie Inc., Bristol-Myers Squibb, UCB, Roche, Novartis, Samsung, Sandoz and Lilly., I. Sainsbury Employee of: AbbVie, Y. Zhang Employee of: AbbVie, A. Kavanaugh Grant/research support from: AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB., Consultant for: AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB.

DOI: 10.1136/annrheumdis-2017-eular.2779

THU0111 NOVEL AUTOANTIBODY PROFILES IN RHEUMATOID ARTHRITIS AND THEIR ASSOCIATION WITH RADIOGRAPHIC PROGRESSION IN THE SCOTTISH EARLY RHEUMATOID ARTHRITIS INCEPTION COHORT AND BIOBANK (SERA)

J. Nijjar[1], F. Morton[1], A. Gilmour[1], C. Paterson[1], H. Bang[2], D. van der Heijde[3], K. Raza[4], C. Buckley[4], D. Porter[5], I. McInnes[1]. *[1]University of Glasgow, Glasgow, United Kingdom; [2]Orgentec Diagnostika GmbH, Mainz, Germany; [3]LUMC, Leiden, Netherlands; [4]University of Birmingham, Birmingham; [5]NHS GGC, Glasgow, United Kingdom*

Background: Antibodies against citrullinated peptides are useful in the diagnosis of rheumatoid arthritis (RA) and are associated with poorer prognosis and greater radiographic progression. Novel autoantibodies recognising several post-translational modifications (PTM) are now emerging including anti-carbamyl, and anti-acetyl antibody classes. Less is known of their prognostic significance.

Objectives: To determine the prevalence of autoantibodies to modified vimentin and/or CCP2 (anti citrullinated (CCP), anti carbamylated (Carb), anti acetylated (Acet)) in a subset of the Scottish Early RA (SERA) inception cohort (n=212) and to correlate them with baseline and radiographic progression over 12 months.

Methods: Baseline and 12m hand and foot radiographs were scored by two readers independently, blinded to patient information and time order according to the Sharp van der Heijde score (SvH). Serum samples from the SERA biobank were analysed with recently published anti-modified protein assays. Patients with citrullinated antibodies (CCP) had antibodies to modified vimentin and/or antibodies to CCP2. Clinical, radiographic and autoantibody data were analysed in R.

Results: See Table 1.

In patients with early RA four main antibody profiles were detected: patients

Table 1

	Negative n=35	CCP n=65	CCP_Carb n=36	CCP_Carb_Acet n=76
Female (%)	74.1	72.3	66.75	52.6
Age, mean	64.1	54.9	60.5	56.7
Disease duration, mean, months	6.6	14.7	11.7	13.2
Smoked (%)	54.3	67.7	77.8	67.1
DAS28-ESR, mean (complete data)	5.5 (30)	4.7 (56)	5.1 (30)	5.2 (64)
Radiographic Scores				
Baseline Erosion score, mean	2.9	2.8	7.2	3.3
Baseline JSN score, mean	3.3	3.4	6.6	3.5
Baseline Total SvH Score, mean	6.2	6.2	13.8	6.8
Mean change in Total SvH score over 12 months	0.5	0.5	1	1.8

with anti CCP antibodies (n=65), antibodies to anti CCP and anti Carb (n=36), antibodies to all three PTM (n=76) and antibody negative patients (n=35). Overall there was low radiographic progression in this sample of the SERA cohort. EULAR non-responders had greater progression compared to good responders (Least square mean difference in SvH over 12 m of 1.6, p=0.019).
Baseline SvH erosion scores are 4.4 points higher in the CCP_Carb group compared to CCP alone (p=0.009) (Table 2 + Fig 1).

Table 2

Comparison	LS mean difference in baseline erosion score	P value
CCP_Carb vs CCP	4.4	0.009
CCP_Carb vs CCP_Carb_Acet	3.9	0.017
CCP_Carb vs Negative	4.3	0.026
Comparison	**LS mean difference in SvH change over 12 months**	**P value**
CCP_Carb_Acet vs CCP	1.3	0.016
CCP_Carb_Acet vs Negative	1.3	0.046

Total SvH 12m progression is 1.3 points higher in the triple positive group compared to the CCP group alone (p=0.016) (Table 2 + Fig 2). Total SvH progression is also higher when comparing the triple positive to the negative group (p=0.046).

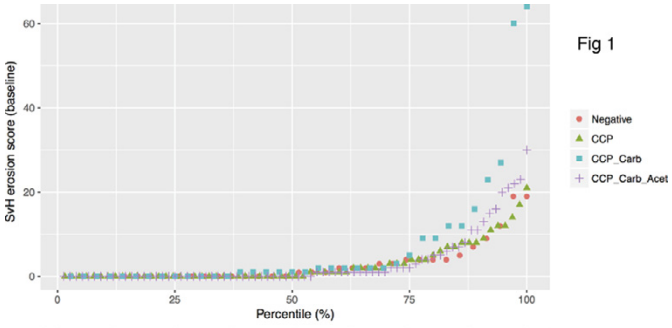


Fig 1

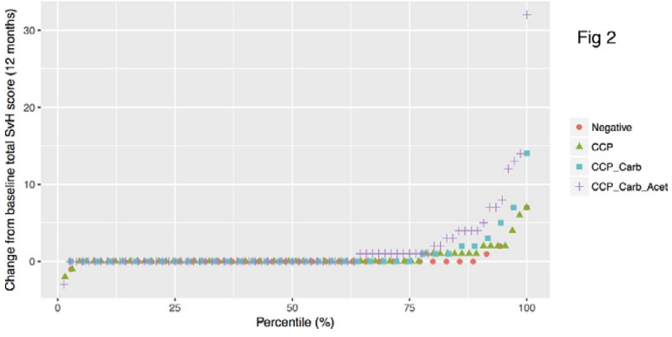


Fig 2

Conclusions: RA patients with antibodies to citrullinated peptides only have lower baseline erosions and less radiographic progression over 12m compared to those with a wider autoantibody repertoire. Baseline differences in erosion suggest that these antibodies may be pathogenic during the pre-RA disease process. Radiographic progression increases with autoantibody repertoire suggesting ongoing immune activation.
Disclosure of Interest: J. Nijjar: None declared, F. Morton: None declared, A. Gilmour: None declared, C. Paterson: None declared, H. Bang Employee of: Orgentec Diagnostike GmbH and holds patent for mutated citrullinated vimentin as diagnostic tool, D. van der Heijde Employee of: Director of Imaging Rheumatology, K. Raza: None declared, C. Buckley: None declared, D. Porter Grant/research support from: Pfizer co-funded the SERA cohort, I. McInnes: None declared
DOI: 10.1136/annrheumdis-2017-eular.2844

THU0112 STRESS AND DEPRESSION IN PATIENTS WITH EARLY INFLAMMATORY POLYARTHRITIS: NATURAL HISTORY AND ASSOCIATIONS WITH DISEASE ACTIVITY, DISABILITY AND PAIN OVER FIVE YEARS

J.M. Gwinnutt[1], D.P.M. Symmons[1,2], A.J. MacGregor[3,4], J.R. Chipping[3,4], T. Marshall[3,4], M. Lunt[1], S.M.M. Verstappen[1]. *[1]Arthritis Research UK Centre for Epidemiology, University of Manchester; [2]NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester University Hospitals NHS Foundation Trust, Manchester; [3]Norwich Medical School, University of East Anglia; [4]Rheumatology Department, Norfolk and Norwich University Hospitals NHS Trust, Norwich, United Kingdom*

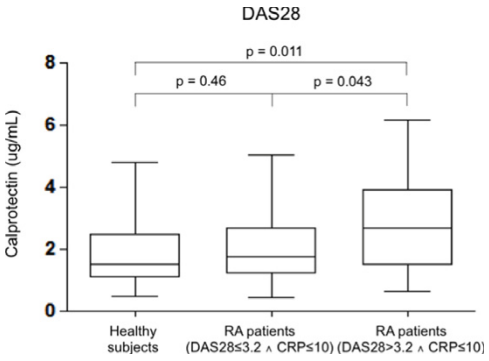
Background: Stress and depression are common in patients with inflammatory polyarthritis (IP). There is little research on long term patterns of depression and stress or how these variables relate to disease activity, disability and pain.
Objectives: To describe the natural history of stress and depression over five years and to assess the association of baseline, one year prior and current disease activity, disability and pain with longitudinal stress and depression.
Methods: Patients recruited to the Norfolk Arthritis Register (NOAR) (inclusion criteria: ≥2 swollen joints for ≥4 weeks) from 2005–2008 were included in this analysis. Demographics, medication use, 51 swollen/tender joint counts (SJC51/TJC51), pain visual analogue scale, HAQ, comorbidities and the Arthritis Impact Measurement Scales 2 (AIMS2) depression and stress subscales (range 0–10; high score = worse health status) were collected at baseline and years 1, 2, 3 and 5. Rheumatoid factor (RF), anti-cyclic citrullinated peptide antibodies (anti-CCP2) and C-reactive protein (CRP) were measured in baseline blood samples. ACR/EULAR 2010 RA criteria were applied to baseline characteristics. Depression and stress over five years were described using descriptive statistics. Multivariate random effects models were applied to assess the association of baseline disease activity (SJC51/TJC51), pain and disability with depression and stress over time adjusting for baseline age, gender, RF, anti-CCP2, CRP, sDMARD use, comorbidities, depression and stress. Similar methods were used to assess one year prior and current disease activity, pain and disability's association with stress and depression. Missing data were imputed using multiple imputation.
Results: 509 patients were included (median (IQR) age: 57 (45, 68) years; 321 (63.1%) female; 305 (59.9%) ACR/EULAR RA). Baseline median (IQR) depression and stress were 2.5 (1.5, 4.5) and 4.0 (2.5, 5.5) respectively and remained constant over five years. Baseline SJC51, TJC51, pain and HAQ were not independently associated with depression or stress over five years. Current HAQ and pain, but not SJC51/TJC51, were independently associated with depression and stress (per unit increase in HAQ: depression β 0.83, 95% CI 0.69, 0.97; stress β 0.76, 95% CI 0.61, 0.90; per 1cm increase in pain: depression β 0.09, 95% CI 0.06, 0.12; stress β 0.09, 95% CI 0.05, 0.12). Higher HAQ was independently associated with increased depression and stress one assessment later (per unit increase in HAQ: depression β 0.21, 95% CI 0.09, 0.32; stress β 0.21, 95% CI 0.10, 0.33) but not pain, SJC51 or TJC51.
Conclusions: There were no associations between measures of disease activity and depression or stress. Prospectively higher HAQ scores were associated with worse psychological health a year later. This may have implications for holistic management of IP.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3432

THU0113 SERUM CALPROTECTIN MAY REFLECT INFLAMMATORY ACTIVITY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS DESPITE NORMAL C-REACTIVE PROTEIN

J. Hurnakova[1], H. Hulejova[1], J. Zavada[1], M. Komarc[2], L. Andres Cerezo[1], H. Mann[1], J. Vencovsky[1], K. Pavelka[1], L. Senolt[1]. *[1]Institute of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic; [2]Department of Methodology, Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic*

Background: About a half of patients with rheumatoid arthritis (RA) have normal or low C-reactive protein (CRP) levels[1–3]. Calprotectin is a promising and probably more specific biomarker of disease activity than conventionally used acute phase reactants.
Objectives: The aim of this study was to analyse levels of serum calprotectin in RA patients with clinically active disease and with low CRP (<10 mg/L).
Methods: A total of 160 RA patients and 32 healthy subjects were enrolled in this study. All patients underwent clinical examination (DAS28). The levels of calprotectin were analyzed in patients with moderate to high disease activity with low CRP levels and in healthy subjects. The discriminatory capacity of calprotectin to identify clinically active patients in spite of normal CRP was assessed using ROC curves.
Results: Out of all RA patients, 74/160 (46.3%) had low CRP and were in remission or had low activity at the same time. However, 51/160 (32%) had low CRP levels despite moderate to high disease activity according to DAS28. In these patients, calprotectin levels were significantly higher than in patients with low CRP in remission or with low disease activity at the same time (mean 2.7±1.5 vs. 2.1±1.2 μg/mL, p=0.043) and differed from that in healthy subjects (mean 2.7±1.5 vs. ± 1.9±1.2 μg/mL, p=0.011) (Figure 1). The discriminatory capacity for calprotectin to distinguish clinically active vs. inactive patients in spite of low CRP

using AUC of the DAS28 was 0.607 (95% CI 0.503 to 0.711, p=0.043) with an optimal cut-off 2.5 μg/mL.



Conclusions: The present study demonstrates that calprotectin may reflect inflammatory activity in RA patients where CRP fails to do so.

References:

[1] Pincus T, Sokka T. Laboratory tests to assess patients with rheumatoid arthritis: advantages and limitations. Rheum Dis Clin North Am 2009;35(4):731–4.
[2] Sokka T, Pincus T. Erythrocyte sedimentation rate, C-reactive protein, or rheumatoid factor are normal at presentation in 35%>45% of patients with rheumatoid arthritis seen between 1980 and 2004: analyses from Finland and the United States. J Rheumatol 2009;36(7):1387–90.
[3] Pincus T, Gibson KA, Shmerling RH. An evidence-based approach to laboratory tests in usual care of patients with rheumatoid arthritis. Clin Exp Rheumatol 2014;32(5 Suppl 85):S-23–8.

Acknowledgements: This work was supported by a project of the Ministry of Health of the Czech Republic for conceptual research development by organization [023728], Charles University Grant Agency (GAUK grant), Czech Republic [880217] and Specific Academy Research Projects (SVV) [260 031].

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3340

THU0114 EFFECTS OF SMOKING ON BARICITINIB EFFICACY IN PATIENTS WITH RHEUMATOID ARTHRITIS: POOLED ANALYSIS FROM TWO PHASE 3 CLINICAL TRIALS

J. Curtis[1], P. Emery[2], G. Burmester[3], V. Arora[4], J. Alam[4], D. Muram[4], L. Klareskog[5]. *[1]University of Alabama at Birmingham, Birmingham, United States; [2]Leeds MSK Biomed/Chapel Allerton Hospital, Leeds, United Kingdom; [3]Universitatsklinikum Charite, Berlin, Germany; [4]Eli Lilly and Company, Indianapolis, United States; [5]Karolinska Institutet, Stockholm, Sweden*

Background: The efficacy of some rheumatoid arthritis (RA) therapies is reduced among patients who are smokers.

Objectives: This post-hoc analysis of two phase 3 studies assessed the effects of patient smoking status on the response to baricitinib treatment in patients with RA.

Methods: In RA-BEAM (NCT01710358), patients with inadequate response to methotrexate were randomized to placebo once-daily (QD) (N=488), baricitinib 4 mg QD (N=487), or adalimumab 40 mg biweekly (N=330).[1] In RA-BUILD (NCT01721057), patients with inadequate response to conventional synthetic disease modifying antirheumatic drugs (csDMARDs) were randomized to placebo (N=228) or baricitinib (2 mg, N=229; or 4 mg, N=227) QD.[2] Patients continued background csDMARD therapy in both studies. This post-hoc analysis was conducted in the placebo (N=716) and baricitinib 4 mg (N=714) patients. Patient-reported smoking status was categorized as current (smokers) or not current (non-smokers).

Results: Among 1,430 evaluable patients who received placebo or baricitinib 4 mg, 290 (20.3%) were smokers. Smoking status at baseline did not affect the clinical results of treatment with baricitinib for 24 weeks; smokers who received placebo were numerically less likely than non-smokers receiving placebo to achieve most clinical outcomes (Table). Baricitinib's effect on modified total Sharp score was more pronounced among nonsmokers (interaction p-value =0.07).

Table 1. Efficacy outcomes at week 24 with data up to rescue

	Placebo (N=716)		Baricitinib 4 mg (N=714)	
	Smoker (n=139)	Non-Smoker (n=577)	Smoker (n=151)	Non-Smoker) (n=562)
ACR20	44 (31.7)	231 (40.0)	108 (71.5)	399 (71.0)
ACR50	24 (17.3)	119 (20.6)	76 (50.3)	270 (48.0)
ACR70	8 (5.8)	49 (8.5)	49 (32.5)	151 (26.9)
SDAI ≤3.3	5 (3.6)	19 (3.3)	24 (15.9)	88 (15.7)
SDAI ≤11	24 (17.3)	137 (23.7)	72 (47.7)	294 (52.3)
CDAI ≤2.8	4 (2.9)	24 (4.2)	24 (15.9)	89 (15.8)
CDAI ≤10	22 (15.8)	137 (23.7)	71 (47.0)	289 (51.4)
DAS28-hsCRP ≤3.2	24 (17.3)	123 (21.3)	75 (49.7)	296 (52.7)
DAS28-hsCRP <2.6	9 (6.5)	53 (9.2)	51 (33.8)	192 (34.2)
HAQ-DI ≥0.3	47 (33.8)	219 (38.0)	103 (68.2)	346 (61.6)
HAQ-DI ≥0.22	61 (43.9)	254 (44.0)	108 (71.5)	381 (67.8)
mTSS change ≤0*	68/96 (70.8)	250/356 (70.2)	78/107 (72.9)	304/363 (83.7)

Data are n (%). *mTTS data are from RA-BEAM only.

Conclusions: This analysis of smokers and non-smokers in two RA trials demonstrated that the beneficial effect of baricitinib treatment versus placebo was similar on all clinical endpoints, but may differ for structural damage progression.

References:

[1] Taylor PC et al. Arthritis Rheumatol 2015;67(suppl 10) abst 2L.
[2] Dougados M et al. Ann Rheum Dis 2017;76:88–95.

Disclosure of Interest: J. Curtis Grant/research support from: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche/Genentech, Corrona, UCB, Myriad, Eli Lilly and Company, Consultant for: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche/Genentech, Corrona, UCB, Myriad, Eli Lilly and Company, Employee of: University of Alabama at Birmingham, P. Emery Consultant for: Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company, G. Burmester Consultant for: Eli Lilly and Company, V. Arora Employee of: Eli Lilly and Company, J. Alam Employee of: Eli Lilly and Company, D. Muram Employee of: Eli Lilly and Company, L. Klareskog Grant/research support from: Janssen, Pfizer, BMS, GSK, AbbVie, Roche.

DOI: 10.1136/annrheumdis-2017-eular.1341

THU0115 DISABILITY (HAQ) AND QUALITY OF LIFE (SF-12) AS RELATED TO ADHERENCE AND HEALTH LITERACY IN PATIENTS WITH RHEUMATOID ARTHRITIS

J.G. Kuipers[1], M. Koller[2], F. Zeman[2], K. Mueller[2], J.U. Rueffer[3]. *[1]Rheumatology, Red Cross Hospital Bremen, Bremen; [2]Center for Clinical Studies, University Hospital Regensburg, Regensburg; [3]German Fatigue Society, Cologne, Germany*

Background: Disabilities in daily living and quality of life are key endpoints to evaluate the outcome of treatment for rheumatoid arthritis (RA). Among factors that may contribute to good outcome are adherence (i.e., the extent to which patients' behaviors corresponds with agreed recommendations from their doctor) and health literacy (patients' understanding and use of health information).

Objectives: The survey included a representative, nationwide sample of German physicians specialized in RA and patients with RA. The physician questionnaire included the disease activity score (DAS28) and medical prescriptions. The patient questionnaire included fatigue (EORTC QLQ-FA13), health assessment questionnaire (HAQ), quality of life (SF-12), health education literacy (HELP), and patients' listings of their medications.

Methods: Adherence was operationalized in various ways: patient-reported (CQR5), behavioral (correspondence between physicians and patients listings of medications), physician-assessed (five-point rating scale ranging from 1=very adherent to 5=not at all adherent) and a combined measure of physician rating (1= very adherent, 0 = less adherent) and the match between physicians' prescriptions and patients' accounts of their medications (1 = perfect match, 0 = no perfect match), leading to three categories of adherence: high, medium and low. Linear regressions were calculated using HAQ and SF-12 (physical and psychological) as dependent variables and adherence, health literacy and the set of demographic and clinical variables as predictor variables.

Results: A total of 708 pairs of patient and physician questionnaires were analyzed. The mean age of the patients, of whom 73% were women, was 60 years (SD=12).

Multiple regression analyses show, that health literacy is an independent predictor for HAQ and both SF-12 scales. Adherence by doctor is an independent predictor for both SF-12 scales while the adherence composite score is an independent predictor for HAQ and SF-12 psychological. Taking all 4 rheumatoid medications as prescribed is an independent predictor for HAQ and SF-12 physical. All models

Table 3: Multiple linear regression models

		HAQ*			SF-12 Physical			SF-12 Psychological		
MLR model*	Predictor	B (95%-CI)	p-value	R^2	B (95%-CI)	p-value	R^2	B (95%-CI)	p-value	R^2
Model 1	All 4 rheumatism agents taken as prescribed	4.41 (.45, 8.38)	.029	20 %	2.39 (.51, 4.28)	.013	16 %	.34 (-1.67, 2.35)	.741	15 %
	Adherence by doctor (ref. medium or less adherence)									
	adherent	1.79 (-3.89, 7.45)	.534		3.14 (.43, 5.86)	.023		.74 (-2.15, 3.64)	.615	
	Very adherent	3.01 (-2.56, 8.58)	.289		3.28 (.61, 5.95)	.016		3.10 (.254, 5.95)	.033	
	Health education literacy*	.330 (.229, .431)	<.001		.141 (.093, .189)	<.001		.220 (.169, .272)	<.001	
Model 2	All 4 rheumatism agents taken as prescribed	3.22 (-.87, 7.32)	.123	20 %	2.00 (.04, 3.96)	.046	15 %	-.11 (-2.20, 1.98)	.919	15 %
	Adherence composite score (ref. low adherence)									
	medium adherence	2.22 (-1.16, 6.06)	.256		.67 (-1.17, 2.51)	.476		.12 (-1.84, 2.08)	.905	
	high adherence	5.06 (.62, 9.50)	.026		1.48 (-.65, 3.61)	.172		2.74 (.47, 5.01)	.018	
	Health education literacy*	.323 (.222, .423)	<.001		.141 (.093, .190)	<.001		.223 (.171, .274)	<.001	

All models are adjusted for sex, age, drinking alcohol (y/n), smoking status (y/n) and sport activities (y/n);
B, regression coefficient; 95%-CI, 95%- confidence interval; *linearly transformed on a scale from 0 (negative/low) to 100 (positive/high)

are additionally controlled for age, sex, smoking (y/n), drinking alcohol (y/n), sport (y/n).
Conclusions: This study showed that HAQ and SF-12 were related to adherence and health literacy. This finding highlights the importance of patient education and counseling in order to increase both, medical understanding and adherence to therapy.
Acknowledgements: The TRACE-Study was sponsored by an unrestricted grant from Chugai.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5415

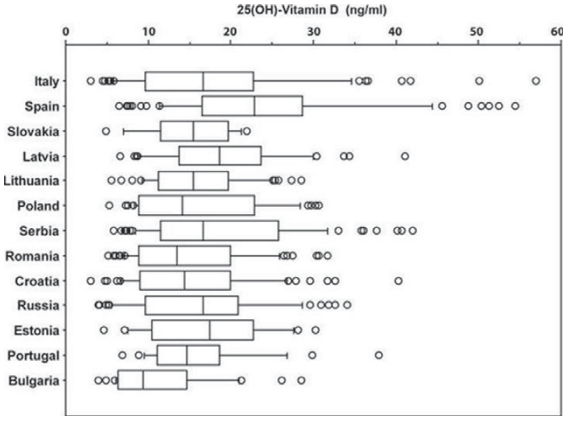
THURSDAY, 15 JUNE 2017

Rheumatoid arthritis - comorbidity and clinical aspects

THU0116 EUROPEAN MULTICENTRE PILOT SURVEY TO ASSESS VITAMIN D AND CLINICAL STATUS IN RHEUMATOID ARTHRITIS PATIENTS

M. Cutolo[1], J. Vojinovic[2], A. Tincani[3], S. Soldano[1], L. Andreoli[3], F. Dall'Ara[3], F. Salaffi[4], R. Ionescu[5], K. Simic Pasalic[6], I. Balcune[7], I. Ferraz-Amaro[8], M. Tlustochowicz[9], I. Butrimiene[10], E. Punceviciene[10], N. Toroptsova[11], S. Grazio[12], J. Morovic-Vergles[13], P. Masaryk[14], K. Otsa[15], M. Bernardes[16], V. Boyadzhieva[17], A. Sulli[1]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genoa, Italy; [2]Clinical Centre, Medical Faculty, University of Nis, Nis, Serbia; [3]Rheumatology and Clinical Immunology Unit, University of Brescia, Brescia; [4]Clinical Rheumatology, Università Politecnica delle Marche, Ancona, Italy; [5]Division of Rheumatology, University of Medicine and Pharmacy, Bucharest, Romania; [6]Institute of Rheumatology, University of Belgrade, Belgrade, Serbia; [7]Division of Rheumatology, Paula Stradina Clinical Hospital, Riga, Latvia; [8]Division of Rheumatology, Hospital Universitario de Canarias, Tenerife, Spain; [9]Department of Internal Medicine and Rheumatology, Military Institute of Medicine, Warszawa, Poland; [10]Centre of Rheumatology, Vilnius University Hospital, Vilnius, Lithuania; [11]Department of Epidemiology and Genetics of Rheumatic Diseases, Institute of Rheumatology, Moscow, Russian Federation; [12]University Department for Rheumatology, Physical and Rehabilitation Medicine, Clinical Hospital Centre Sisters of Mercy; [13]Division of Clinical Immunology and Rheumatology, University of Zagreb, Zagreb, Croatia; [14]National Institute of Rheumatic Diseases, Piestany, Slovakia; [15]Department of Rheumatology, Tallinn Central Hospital, Tallin, Estonia; [16]Rheumatology Department of São João Hospital Center, University of Porto, Porto, Portugal; [17]Clinic of Rheumatology, University Hospital St. Iv. Rilski, Sofia, Bulgaria*

Background: Vitamin D (25(OH)D) deficiency seems a distinct risk factor influencing prevalence and severity of several autoimmune diseases. Several studies suggest that low serum concentrations of vitamin D are frequent in rheumatoid arthritis (RA) patients, and an inverse relationships have been reported between 25(OH)D serum concentrations and disease activity or disability.
Objectives: European multicentre cross-sectional study to collect data on vitamin D serum concentrations in RA patients from different countries, and to investigate the relationship with disease activity, disability and quality of life in a large population.
Methods: The survey involved 625 RA patients (mean age 55±11 years, mean disease duration 11±9 years) and 276 age and sex-matched healthy subjects from 13 European countries. Serum samples for 25(OH)D measurement were collected during winter time (December-March) and analyzed in a central laboratory using chemiluminescence immunoassay (DiaSorin). Thirty-six percent of RA patients were treated with vitamin D analogues. Patient past medical history, Rheumatoid Arthritis Impact Diseases (RAID) score, Health Assessment Questionnaire (HAQ) and DAS28-CRP were also collected. Statistical analysis was performed by non parametric tests.



Results: Mean serum concentration of 25(OH)D was found significantly lower in RA patients (17.6±9.7 ng/ml) when compared to matched controls (18.9±9.4 ng/ml) (p=0.01), Several statistically significant differences between European countries were observed (possibly linked to different latitude, sun exsposure and dietary habits) (see figure). Vitamin D deficiency (<20 ng/ml) was found in almost 66% of RA patients, and severe deficiency (<10 ng/ml) was detected in almost 25% of them; insufficiency (between 20 and 30 ng/ml) was found in 27% of RA patients. Only 6% of the RA patients were found within the normal concentrations (>30 ng/ml). Male and female RA patients showed similar 25(OH)D values. Negative statistically significant correlations were found between 25(OH)D serum concentrations and RAID (p=0.05) HAQ (p=0.04) and DAS28-CRP (p<0.001) scores in the RA patients group.
Conclusions: This European survey add new evidences that vitamin D insufficiency/deficiency is frequent in RA patients with statistically significant differences between several countries. Vitamin D serum concentrations negatively correlate with the clinimetric indexes for disease activity, disability and quality of life in the present cohort of RA European patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5977

THU0117 INDEPENDENT ASSOCIATIONS OF DISEASE CHARACTERISTICS AND CARDIOVASCULAR RISK FACTORS WITH LEFT VENTRICULAR DIASTOLIC FUNCTION IN RHEUMATOID ARTHRITIS

A.M. Millen[1], L. Mokotedi[1], S. Gunter[1], C. Robinson[1], G.R. Norton[1], A.J. Woodiwiss[1], L. Tsang[1], P.H. Dessein[1,2]. *[1]Cardiovascular Pathophysiology and Genomic Research Unit, School of Physiology, University of the Witwatersrand, Parktown, Johannesburg, South Africa; [2]Rheumatology Division, Universitair Hospital Brussel, Brussels, Belgium*

Background: Heart failure contributes to the excess mortality experienced by patients with rheumatoid arthritis (RA) (1). Impaired diastolic function represents a pre-clinical cardiac alteration which is highly predictive of cardiac events and often progresses to heart failure. Diastolic dysfunction is the most common cause of heart failure in patients with a preserved ejection fraction. Whereas RA is associated with an increased prevalence of impaired diastolic function (2,3), the pathophysiological mechanisms that mediate this comorbidity await further elucidation.
Objectives: This study aimed to identify potential determinants of ventricular (LV) diastolic function in patients with RA.
Methods: LV diastolic function was determined in 176 patients with RA; 9 patients had established cardiovascular disease. LV diastolic function was determined by echocardiography from the ratio of early-to-late transmitral blood flow velocity (E/A), the ratio of E to the mean of the lateral and septal wall myocardial tissue lengthening at the mitral annulus (e') (E/e'), and the lateral e'. Relationships of comprehensively evaluated traditional cardiovascular risk factors and RA characteristics with markers of LV diastolic function were determined in confounder adjusted multivariate regression models.
Results: Disease duration (partial r=-0.23, p=0.00), rheumatoid factor status (partial r=-0.16, p=0.04) and erythrocyte sedimentation rate (partial r=-0.16, p=0.04) were associated with lower logarithmically transformed (log) E/A. Upon further adjustment for left ventricular mass index or relative wall thickness, these relationships remained significant (p≤0.05). Diastolic blood pressure was related to log E/e' (partial r=-0.16, p=0.04); this association was no longer significant after additional adjustment for left ventricular mass index (p=0.06) or relative wall thickness (p=0.06). Disease duration (partial r=-0.32, p=0.00), waist-to-hip ratio (partial r=-0.29, p=0.00) and triglycerides (partial r=-0.17, p=0.03) were related to log lateral e'. These relationships remained significant upon further adjustment for left ventricular mass index (for all p=0.00) or relative wall thickness (for all p=0.00). In sensitivity analysis among RA patients without established cardiovascular disease (n=167), the results were not materially altered.
Conclusions: Modifiable traditional cardiovascular disease risk factor and disease characteristics are consistently associated left ventricular diastolic function in RA.
References:
[1] Nicola PJ, Crowson CS, Maradit-Kremers H et al. Contribution of congestive heart failure and ischemic heart disease to excess mortality in rheumatoid arthritis. Arthritis Rheum 2006;54:60–7.
[2] Gonzalez-Juanatey C, Testa A, Garcia-Castelo A et al. Echocardiographic findings in long-term treated rheumatoid arthritis patients without clinically evident cardiovascular disease. Semin Arthritis Rheum 2004;33:231–8.
[3] Liang KP, Myasoedova E, Crowson CS et al. Increased prevalence of diastolic dysfunction in rheumatoid arthritis. Ann Rheum Dis 2010;69:1665–70.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4205

THU0118 WHAT IS THE ROLE OF STEROIDS IN INDUCING DIABETES MELLITUS IN PATIENTS WITH RHEUMATOID ARTHRITIS? AN OBSERVATIONAL COHORT STUDY

A. Emamifar[1], R. Hviid Larsen[2], R. Asmussen Andreasen[1], I.M. Jensen Hansen[1,3]. [1]*Rheumatology;* [2]*Medicine, Svendborg Hospital, Odense University Hospital, Svendborg;* [3]*DANBIO, Copenhagen, Denmark*

Background: Patients with Rheumatoid Arthritis (RA) are at increased risk of Diabetes Mellitus (DM) probably due to immune system activation or RA treatment with steroids.[1] However the pathology of DM in RA is not fully understood.
Objectives: To define the prevalence of DM in our RA patients population. Furthermore, to clarify the role of steroid treatment to induce DM in the RA patients.
Methods: All patients with diagnosis of RA who were registered in Danish Danbio Registry at time of study, Nov 2016, were included. To find the concurrent DM, patients' medical records including past medical history and lab tests (Hemoglobin A1c and Blood Sugar) were reviewed. In addition, year of DM as well as RA diagnoses were extracted from Fyns Diabetes Database and Danbio respectively to the extent that data were available. Patients' drug histories were searched for information about steroid treatment if diagnosis of RA was made prior to diagnosis of DM.
Results: Of 1035 patients with diagnosis of RA, 104 (10%) patients had DM. Of 104 RA patients with DM, data regarding the year of diagnosis for both RA and DM was found in 55 patients which of them 15 patients were diagnosed with RA before DM, one patient was diagnosed with both DM and RA at the same year and 39 patients were diagnosed with RA after DM. However, only one patient, of those who were firstly diagnosed with RA, was prescribed prednisolone during the time period between diagnoses of RA and thereafter DM. Of 15 patients with prior diagnosis of RA to DM, 13 patients were diagnosed according to 1987 classification criteria (Old) for RA and 2 patients were diagnosed according to 2010 classification criteria (New). Out of 39 patients where DM was diagnosed before RA, 10 patients was diagnosed based on the old criteria and 29 patients was diagnosed based on the new RA criteria [Fig 1A and 1B]. Patients with firstly diagnosed DM were more often diagnosed according to the new RA criteria and, on the contrary, patients with latterly diagnosed DM were more often diagnosed with old RA criteria ($p<0.001$).

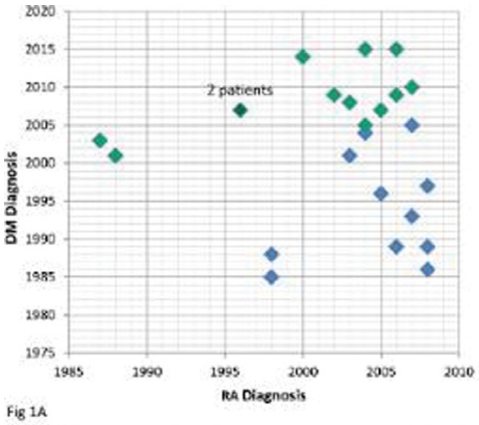


Fig 1A

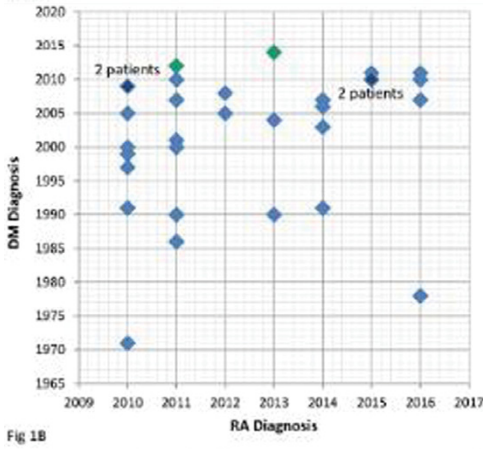


Fig 1B

Figure 1A: In 13 Rheumatoid Arthritis (RA) patients who were diagnosed according to 1987 classification criteria for RA, diagnosis of RA was made earlier than Diabetes Mellitus and **Figure 1B:** In 2 Rheumatoid Arthritis (RA) patients who were diagnosed according to 2010 classification criteria for RA, diagnosis of RA was made earlier than Diabetes Mellitus.

Conclusions: The prevalence of DM in this RA population (10%) was about twice of Danish population (5.7%). The role of steroid treatment in which to what extent increases the risk of DM is not clear, however in this study it was negligible, why we propose that the pathology of DM in RA patients most importantly deals with the role of immune system activation namely Tumor Necrosis Factor alpha and not the treatment modality i.e. steroids.

References:

[1] Jiang P, Li H, Li X. Diabetes mellitus risk factors in rheumatoid arthritis: a systematic review and meta-analysis. Clin Exp Rheumatol 2015;33:115–21.

Acknowledgements: We thank Mrs. Maryam Mousavi for her contribution to data collection.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3167

THU0119 ASSESSMENT OF RHEUMATOID CACHEXIA AND ITS ASSOCIATION WITH CLINICAL, FUNCTIONAL AND THERAPEUTIC OUTCOMES

A.L.D. Moro[1], V. Hax[1], R.C.E. Santo[2], T. Fighera[3], W. Kisaki[2], C.V. Brenol[1], R.M. Xavier[1]. [1]*Rheumatology Service, Hospital de Clínicas de Porto Alegre;* [2]*Universidade Federal do Rio Grande do Sul;* [3]*Endocrinology Service, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil*

Background: Rheumatoid arthritis (RA) is a chronic and inflammatory disease that besides articular symptoms leads to loss of muscle mass in presence of stable or increased fat mass (FM), condition defined as rheumatoid cachexia (RC). RC is associated with a worse prognosis, but it is still overlooked in clinical practice.
Objectives: To evaluate the prevalence of rheumatoid cachexia (RC) in patients with rheumatoid arthritis (RA) and determine its correlation with the features of RA, the level of physical activity and with the current therapy.
Methods: Ninety one RA patients in a cross-sectional study underwent total body dual-energy x-ray absorptiometry (DXA) for measurement of total and regional fat mass index (FMI; Kg/m^2), lean mass index (LMI; Kg/m^2), bone mineral content (BMC; Kg/m^2) and fat free mass index (FFMI; Kg/m^2) to assess the prevalence of RC. The associations of measures of body composition with RA features - age, diagnosis time, Health Assessment Questionnaire (HAQ), Disease Activity Score in 28 joints (DAS 28), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) -, level of physical activity (measured by International Physical Activity Questionnaire – IPAQ) and current therapy were explored.
Results: Mean age was 56.8±7.3, disease duration 9 years (3 – 18), DAS28 3.65±1.32, HAQ 1.12 (0.25 – 1.87) and use duration of biological agents was 25 months (17.8 – 52.5). 17% of the patients had FFMI below the 10th percentile and FMI above the 25th percentile of a reference population and 33% of the patients had FFMI below the 25th percentile and FMI above the 50th percentile, condition known as RC, according to the more recently used definitions. FFMI correlated negatively only with age ($r=-0.219$; $p=0.037$) and disease duration ($r_s=-0.214$; $p=0.042$). FMI correlated positively with CRP ($r_s=0.229$; $p=0.029$), ESR ($r_s=0.235$; $p=0.025$), DAS 28 ($r_s=0.273$; $p=0.009$) and HAQ ($r_s=0.297$; $p=0.004$). Among patients under biologics, 3.8% (n=1) had RC versus 23% (n=15) of those not taking biologics ($p=0.033$), according to the stricter definition.
Conclusions: The prevalence of RC was considerable and deserves additional research. Besides that, patients under biological therapy had lower prevalence of RC, suggesting a protective effect of biological agents.

References:

[1] Hugo M, Mehsen-Cetre N, Pierreisnard A, Schaeverbeke T, Gin H, Rigalleau V. Energy expenditure and nutritional complications of metabolic syndrome and rheumatoid cachexia in rheumatoid arthritis: an observational study using calorimetry and actimetry. Rheumatology. 2016; 55(7): 1202–09.
[2] Masuko K. Rheumatoid cachexia revisited: a metabolic co-morbidity in rheumatoid arthritis. Front Nutr 2014; 24: 1–20.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1894

THU0120 PREVALENCE OF CHRONIC KIDNEY DISIASE IN REUMATOID ARTHRITIS PATIENTS AND IT'S ASSOCIATIN WITH MULTIMORBIDITY

A.Y. Zakharova[1], E. Galushko[1], Y. Uskova[2], A. Gordeev[1]. [1]*Nasonova Reserch Institute of Rheumatology, MOSCOW, RUSSIA;* [2]*Central Clinical Hospital of Russian President Administration, Moscow, Russian Federation*

Background: RA pts commonly present with multiple concurrent chronic disease. The great importance is attached to cardiovascular diseases due to their proven association with high frequency of morbidity and death. Much attention has been paid to the potential role of high-grade systemic inflammation and classical modifiable CVD risk factors – such as hypertension, dyslipidaemia, insulin resistance/metabolic syndrome, obesity, physical inactivity and smoking. A recent meta-analysis has shown that renal impairment is a strong independent cardiovascular risk factor in the general population [1].
Objectives: To assess the prevalence and associations of CKD in RA pts (ACR/EULAR 2010y.) and relate with pts multimorbid background, RA activity and duration.
Methods: 209 RA pts (F-70,6%, mean age 67,0±11,3y), admitted to rheumatology division from 1999 to 2015, were included into analysis. RA duration was 19

[6;93] mo, average disease activity (DAS28) 5,2±1,7. CKD was defined as the presence of markers of renal impairment (proteinuria≥1+, hematuria≥2+ or leucocyturia≥2+) and/or eGFR<60 ml/min/1,73m^2 (using CKD-EPI formula) persistent beyond 3 months. The extent of multi-morbid environment was rated using Cumulative Illness Rating Score (CIRS) [2]. CIRS was calculated using the 5 score scale (0–4) to assess 14 major organ systems of the body (0–56).

Results: The prevalence of CKD was 82,3% (172), and 30,1% (63) had eGFR<60 ml/min/1,73m, and 50,2% pts had CKD stage 2. The range of proteinuria was 12,4%. In group of pts with CKD 3–5 stage the prevalence of arterial hypertension (AH) was 84%, ischemic heart disease (IHD) - 63,5%, diabetes militants 2 22%, oncology 12,7%. Mean CIRS value in RA pts was 15 [10;19] scores. The eGFR was independent of the RA duration (r=-0,01, *p*=0,86) and RA activity (r=0,09, *p*=0,17). There was found the strongest correlation of eGFR with CIRS (r=-0,61, p<0,01), age (r=0,58; *p*<0,05), AH (r=-0,34, p<0,01), IHD (r=-0,28, p<0,05), BMI (r=-0,17; r=0,35), uric acid levels (r=-0,37), as well as with hemoglobin level (r=0,19) and HAQ scores (r=0,31; r=0,32). No correlation was found between eGFR and oncology, gender, VAS score, and ESR, CRP, cholesterol (*p*>0,05).

Conclusions: CKD is a serious condition associated with premature mortality, decreased quality of life, and increased health-care expenditures, but it doesn't consider as comorbid disorder of RA. The CKD prevalence is greater among aged RA pts than in general population and it has a stronger correlation with multimorbid burden than traditional factors. Compromised renal function, apart from the age, is of dominant importance in pts management issues, limiting the range of available effective therapies, thus, aggravating RA natural course on one side, and inducing and catalyzing the severity of dysmetabolic syndrome, AH and anemia – on the other.

References:

[1] Hudon C, Fortin M, Vanasse A. Cumulative illness rating scale was a reliable and valid index in a family practice context. J Clin Epidemiol 2005;58:603–8.
[2] Matsushita K, van der Velde M, Astor BC et al. Lancet 2010;375:2073–81.

Acknowledgements: None.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6839

THU0121 ULTRASOUND IN THE ASSESSMENT OF CARPAL TUNNEL SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Di Matteo, E. Filippucci, G. Smerilli, A. Draghessi, S. Gasparini, A. Incorvaia, M. Di Carlo, W. Grassi. *Clinica Reumatologica, Università Politecnica delle Marche, Jesi (AN), Italy*

Background: Carpal tunnel syndrome (CTS) is one of the most frequent extra-articular manifestations of rheumatoid arthritis (RA). Ultrasound (US) has proven to represent a reliable tool for the diagnosis of CTS [1]. However, its role in the diagnosis of CTS in patients with RA has been poorly investigated.

Objectives: The aim of this study is to evaluate the US findings at carpal tunnel level in a cohort of patients with RA, focusing on those with a clinical diagnosis of CTS.

Methods: Patients with RA fulfilling the ACR/EULAR 2010 classification criteria were consecutively enrolled. The diagnosis of CTS was made according to the American Academy of Neurology practice parameter for CTS [2]. The MSUS assessment was carried out using a MyLab Twice (Esaote SPA) US system working with a 18–22 MHz linear probe. The power Doppler (PD) frequency was set between 7.5 and 11.3 MHz. The following grey scale (GS) US parameters were assessed at the carpal tunnel level: cross-sectional area (CSA) of the median nerve at the carpal tunnel inlet (at the level of the pisiform and scaphoid bones), presence of flexor tenosynovitis and palmar radio-carpal synovitis (both in GS and PD), presence of crystal macro-aggregates and marked bone profile irregularities. The median nerve was considered enlarged if its CSA was more than 12 mm^2. We evaluated the presence of intra-neural PD signals at the carpal inlet and scored its entity (0=no PD signal, 1=one single vessel within median nerve, 2=two or three single or two confluent vessels and 3=more than three single or more than two confluent vessels). PD was considered "positive" if grade 1 or more was found.

Results: We included 40 RA patients. CTS was diagnosed in 19 out of 80 wrists (23.8%) and in 13 out of 40 RA patients (32.5%). Enlarged median nerve was found in 3 out of 19 wrists with CTS (15.8%) and in 6 out of 61 wrists without CTS (9.8%). Flexor tenosynovitis was found in 7 out of 19 wrists with CTS (36.8%) and in 5 out of 61 wrists without CTS (8.2%). Palmar radio-carpal synovitis was found in 2 out of 19 wrists with CTS (10.5%) and in 3 out of 61 wrists without CTS (4.9%). Crystal macro-aggregates were not detected in any of the scanned wrists. Marked bone profile irregularities were found in 2 out of 19 wrists with CTS (10.5%) and in 14 out of 61 wrists without CTS (23%). Positive intra-neural PD was found in 9 out of 19 wrists with CTS (47.4%) and in 9 out of 61 wrists without CTS (14.7%).

Conclusions: These preliminary results suggest that MSUS could be a useful tool in the diagnosis of CTS also in patients with RA. Intra-neural PD and flexor tenosynovitis were the most frequently MSUS abnormalities detected in RA patients with CTS. The inflammatory involvement of the tendinous and joint structures which are part of the carpal tunnel could lead to median nerve compression and CTS symptoms and should be considered in the MSUS assessment of CTS.

References:

[1] McDonagh C, Alexander M, Kane D. The role of ultrasound in the diagnosis and managment of carpal tunnel sindrome: a new paradigme. Rheumatology (Oxford). 2015 Jan;54(1):9–19.doi: 10.1093/rheumatology/keu275.
[2] Practice parameters for carpal tunnel syndrome (summary statement). Report of the quality standards subcommittee of the American Academy of Neurology. Neurology 1993;43:2406–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4448

THU0122 QUANTITATIVE ASSESSMENT AND ANALYSIS OF HAND MUSCLE VOLUME

A. Friedberger[1], C. Figueiredo[2], O. Museyko[1], A. Grimm[1], I. D'Oliveira[2], T. Bäuerle[3], J. Rech[2], O. Chaudry[1], M. Uder[3], G. Schett[2], K. Engelke[1]. *[1]Institute of Medical Physics, University Erlangen-Nuremberg; [2]Department of Medicine 3, University Erlangen-Nuremberg; [3]Radiological Institute, University Hospital Erlangen-Nuremberg, Erlangen, Germany*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by bone, cartilage and muscle loss. While bone and cartilage damage have been extensively studied in the past, the effects of RA on volume and composition of hand muscles have not yet been studied. This situation is surprising, since visible hand muscle atrophy is a hallmark of RA and quantification of muscle composition is of growing interest.

Objectives: Quantitative assessment of hand muscle volume and fat using MRI.

Methods: A random forest based method was used to segment hand muscle in T1 weighted MR scans of 76 RA patients (37 males, 26–87 years, mean 61 years). The segmentation procedure is fully automated but allows for manual corrections of wrongly segmented areas. Multimodal registration of the muscle segmentation masks to MR Dixon Fat Fraction images was used for fat quantification.

Outcome parameters were absolute hand and muscle volume (V_H^{abs} resp. V_M^{abs}), relative muscle volume $V_M^{rel} = V_M^{abs}/V_H^{abs}$ and absolute and relative fat content (V_F^{abs} resp. V_F^{rel}).

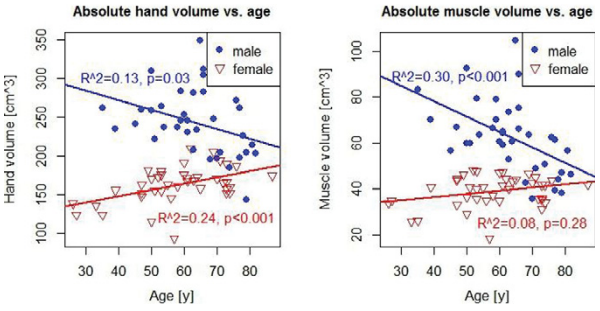
Student's t-tests were performed for gender discrimination. Linear regression was used to model age dependency. Further a multivariate regression was used to model dependence on predictors BMI, RA disease duration, DMARD treatment duration, HAQ, DAS28, RF, ESR and CRP after age adjustment. Dixon sequences were not available for all patients, therefore fat analysis could only be done in 17 females.

Results: V_M^{abs} in males was significantly higher than in females (p<0.001, means: 63 cm^3 vs. 29 cm^3). Similar results were observed for V_H^{abs} (p<0.001, means: 243 cm^3 vs. 163 cm^3) and V_M^{rel} (p=0.02, means: 0.256 vs. 0.239).

The table show the results of the linear regression analysis for significant predictors of males and females, respectively. The figure shows age dependence of V_M^{abs} and V_H^{abs}.

	Age	BMI (age adj.)	Disease duration (age adj.)
Males			
V_M^{abs}	p<0.001, R^2=0.25	p<0.001, R^2=0.61	ns.
V_H^{abs}	p=0.03, R^2=0.13	p<0.001, R^2=0.50	ns.
V_M^{rel}	p<0.001, R^2=0.30	p=0.04, R^2=0.35	p=0.02, R^2=0.36
Females			
V_M^{abs}	ns.	ns.	p=0.07, R^2=0.16
V_H^{abs}	p<0.001, R^2=0.24	ns.	ns.
V_M^{rel}	ns.	ns.	p=0.06, R2=0.12

V_F^{abs} and V_F^{rel} showed no dependence on age or disease duration. V_F^{abs} but not V_F^{rel} was highly correlated with V_M^{abs} and V_H^{abs} (both: p<0.001, R^2=0.75). V_F^{rel} was positively correlated with BMI (p=0.03, R^2=0.32), a weaker but not significant effect was observed for V_F^{abs}.



Conclusions: Results for muscle volume were highly sex specific. Males showed higher V_M^{abs}, V_H^{abs} and V_M^{rel}. Nevertheless V_M^{abs} and V_H^{abs} in males showed significant decrease with age while the opposite but weaker effects were observed in females. Relative fat volume depends on BMI but is independent of muscle volume.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6084

THU0123 NEW PERSPECTIVES IN DIAGNOSIS OF INTERSTITIAL LUNG DISEASE RELATED TO RHEUMATOID ARTHRITIS. VALIDATION STUDY OF AN ELECTRONIC STETHOSCOPE AND AD HOC SOFTWARE FOR DETECTION OF PULMONARY CRACKLES

A. Manfredi[1], M. Sebastiani[1], G. Cassone[1], A.L. Fedele[2], V. Venerito[3], M. Trevisani[4], F. Furini[5], O. Addimanda[6], E. Gremese[2], F. Iannone[3], G. Della Casa[1], S. Cerri[1], G. Sandri[1], F. Pancaldi[7], F. Luppi[1], C. Ferri[1] on behalf of InsPiRAtE study group. *[1]Policlinico di Modena, University of Modena and Reggio Emilia, Modena; [2]Catholic University of Rome, Rome; [3]University of Bari, Bari; [4]Sant'Orsola-Malpighi Hospital, Bologna; [5]University of Ferrara, Ferrara; [6]University of Bologna, Bologna; [7]Department of Sciences and Methods for Engineering, University of Modena and Reggio Emilia, Modena, Italy*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by synovial joint swelling and tenderness, secondary to the immune-system dysfunction, often complicated by extra-articular manifestations. Among them, lung involvement is very frequent and interstitial lung disease (ILD) represents one of the deleterious complications of RA with impact on both therapeutic approach and overall prognosis. Nevertheless, diagnosis of ILD often remains missing or delayed.
Objectives: To preliminarily evaluate the predictive value of pulmonary sound recorded by an electronic stethoscope (ES) and elaborated by an ad hoc software in identification of RA-ILD diagnosed by mean of high resolution computed tomography (HRCT) in a multicenter study.
Methods: RA patients who underwent HRCT in the last 12 months were enrolled. They were all auscultated with the ES (Littmann 3200^{TM} 3M, USA), bilaterally, at dorsal level, in at least 3 pulmonary fields (medium and basal). All tracks recorded were analyzed by a suitably developed software capable of recognizing pathological crackles in lung sounds. Results were compared with radiologic findings detected in a blind manner by an expert radiologist.
Results: One hundred and six RA patients were enrolled (M/F: 1/2.5, mean age 68.7±10.3); among them 45 (42.5%) showed ILD at HRCT. Three patients were excluded because of a low quality of the sound recorded. The algorithm showed a sensitivity and specificity of 72.1% and 84.4%, respectively and a positive/negative predictive value of 69.1% and 86.3%, respectively.
Conclusions: Despite preliminary, these data suggest an important role of ES in clinical practice for an early diagnosis of ILD in RA patients and a significant reduction of inappropriate prescription of HRCT. Since very different types of ILD can occur in course of RA, with different radiologic features and localization, proper development of the measurement setup (ES and ad hoc software for the detection of PC) could further increase its predictive value, in particular to avoid incorrect records and misdiagnosis. The routinely employment of ES and proper software, combined to clinical findings (cough, dyspnea) and respiratory lung function, could increase our ability to early identify ILD in RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5419

THU0124 OCCUPATIONAL EXPOSURE TO ASBESTOS AND RISK OF RHEUMATOID ARTHRITIS

A. Ilar[1], P. Gustavsson[1], P. Wiebert[1], C. Bengtsson[1], L. Klareskog[2], L. Alfredsson[1]. *[1]The Institute of Environmental Medicine; [2]Department of Medicine, Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden*

Background: Airborne agents are considered important environmental triggers of rheumatoid arthritis (RA) among genetically susceptible individuals. Due to the known association between silica dust and RA, we wanted to study the association between RA and another silicate mineral; asbestos.
Objectives: The aim of this study was to estimate the risk of RA from ever occupational asbestos exposure as well as years with exposure among men and women.
Methods: The study base consisted of men and women living in Sweden from 1968 until 2012. RA patients were identified from the National Patient Register, the Swedish Rheumatology Register (SRQ), the Swedish population-based case-control study EIRA or the Swedish Prescribed Drug Register. We matched ten controls from the national population register per case on age, county and sex. Data on occupational histories were collected from the national population and housing censuses carried out in 1960, 1970, 1975, 1980 and 1990. A job-exposure matrix (JEM) containing historical exposure estimates from 1955–1995 to asbestos was applied to the study participants' occupational histories.
We used unconditional logistic regression to assess the odds ratios (ORs) and 95% confidence intervals (CIs) of RA associated with ever exposure and years of exposure to asbestos. ORs were adjusted for ever exposure to silica dust, which was also generated from a JEM. One of the data sources (EIRA) contained self-reported information on potential confounders. Analyses on this data source were carried out to estimate the confounding effect from pack-years of cigarette smoking and alcohol use.
Results: 167 143 cases and 1 701 200 controls were included in the analysis. The proportion of participants who had ever worked with asbestos was 38% among male cases, 35% among male controls, 3% among female cases and 3% among female controls.
Ever vs. never asbestos exposure resulted in an OR of 1.15 (95% CI: 1.13–1.17) among men and 1.00 (95% CI: 0.96–1.04) among women. The ORs decreased to 1.09 (95% CI: 1.07–1.12) and 1.00 (95% CI: 0.96–1.04) for men and women respectively after adjusting for silica exposure. Asbestos exposed men were more likely than women to have worked with asbestos for a longer period of time, but the risk of RA did not appear to increase with years with the exposure. Male participants with 30 or more years of asbestos exposure at work had an OR of 1.10 (1.02–1.19) after adjustment for silica exposure.
1,882 male and 4,107 female study participants belonged to the EIRA study and had complete information on potential confounding factors. The OR among men went from 1.61 (95% CI: 1.32–1.97) to 1.35 (95% CI: 1.08–1.70) when we additionally adjusted for silica exposure, pack-years of smoking and alcohol use. Among women the OR went from 1.34 (95% CI: 0.93–1.93) to 1.07 (95% CI: 0.73–1.57). Risks were higher for the ACPA- RA subtype, with adjusted ORs of 1.63 (95% CI: 1.18–2.24) for men and 1.14 (95% CI: 0.66–1.98) for women.
Conclusions: Asbestos exposure is associated with RA among men, and mainly the ACPA- RA subtype. The increased risk remained after adjustments for potential confounders.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5084

THU0125 PROGRESSION OF SUBCLINICAL ATHEROSCLEROSIS OVER ELEVEN YEARS IS INCREASED IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

A. Södergren[1], K. Karp[2], E. Lundström[3], T. Smedby[4], B. Möller[5], S. Rantapää-Dahlqvist[1], S. Wållberg-Jonsson[1]. *[1]Rheumatology, Dept of Public Health and Clinical Medicine; [2]Dept of Surgical and Perioperative Sciences; [3]Dept of Public Health and Clinical Medicine, Umeå; [4]Rheumatology, Östersund; [5]Rheumatology, Luleå, Sweden*

Background: Patients with rheumatoid arthritis (RA) have an increased mortality and morbidity due to cardiovascular disease (CVD).
Objectives: In this prospective follow up over eleven years, we investigated the progression of atherosclerosis measured by intima media thickness (IMT), in relation to traditional CVD risk factors and inflammation, in patients with early RA compared to controls.
Methods: Patients from northern Sweden diagnosed with early RA are consecutively recruited into an ongoing prospective study. A subgroup aged $\leq$60 years (n=54) was consecutively included for ultrasound measurements of IMT of a. Carotis communis at inclusion (T0), and after 11 years (T11). 31 age-sex-matched controls were included. The patients were clinically assessed, SCORE, Reynolds Risk Score and Larsen score were calculated and blood samples drawn from all individuals at T0 and T11. Data and results presented in this abstract are preliminary.
Results: Patients with RA as well as controls had a significant aggravation in IMT over 11 years (0.52 at T0 and 0.68 at T11 in RA: $p<0.001$; 0.54 at T0 and 0.63 at T11 in controls: $p<0.05$; IMT in RA vs controls at T0 and at T11: $p>0.05$). The patients with RA had a significantly higher progression in IMT from T0 until T11 (0.16 vs 0.08, $p<0.001$). In simple linear regression analyses among RA-patients, the IMT at T11 was significantly associated with several variables at T0: age, systolic blood pressure, SCORE, Reynolds Risk Score, tPA, L-selectin (inversely), MCP-1 and Larsen score. The progression in IMT over 11 years was associated with age and Larsen score at T0.
Conclusions: In this prospective study, the progression of sub-clinical atherosclerosis over 11 years was significantly higher in patients with RA than in controls. The IMT at T11 was associated with several traditional cardiovascular risk factors, as well as disease severity, at time of diagnosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1965

THU0126 THE EFFECT OF GLUCOCORTICOIDS ON BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

A.-B.G. Blavnsfeldt[1], M.D. Thomsen[2], S. Tarp[3], B. Langdahl[4], E. Hauge[1], A. de Thurah[1]. *[1]Department of Rheumatology, Aarhus University Hospital, Aarhus; [2]Diagnostic Centre, Silkeborg Regional Hospital, Silkeborg; [3]The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen; [4]Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Aarhus, Denmark*

Background: The role of glucocorticoids (GCs) in the treatment of rheumatoid arthritis (RA) is widely debated. GCs stimulate bone resorption and impair bone formation (1). Inflammatory cytokines also stimulate bone resorption, and patients with RA have a high risk of osteoporosis (OP) and fragility fractures (2). However, in patients with RA, impairment of bone formation by GCs may be counter-balanced by reduced systemic inflammation and increased physical activity.
Objectives: This systematic review aims to assess the effect of oral prednisolone and prednisone on bone mineral density (BMD) in patients with RA analyzed in randomized, controlled trials (RCT).
Methods: We performed a systematic literature search and identified double-blinded RCTs comparing prednisolone or prednisone with placebo and measuring

BMD dual-energy absorptiometry at baseline and at least once thereafter. Two authors independently reviewed references, extracted data and assessed risk of bias. We assessed quality of evidence using the GRADE methodology. Primary outcomes were mean change in BMD at the hip and lumbar spine. Secondary endpoints included RA disease activity and radiographic progression.
Results: We identified 7 studies. Studies were comparable regarding study population and intervention. Risk of bias was considered low for BMD outcomes. Data completeness was low in some studies. We found no statistically significant difference in change in BMD from 0 to 24 months neither at the lumbar spine (Standard Mean Difference (SMD) 0.02 (95% CI -0.16, 0.12)) nor at the hip (SMD -0.11 (95% CI -0.25, 0.02)). Disease activity was significantly lower in the GC groups (mean difference in DAS28 -0.32 (95% CI -0.52, -0.11). Concomitant treatment of RA differed between studies, as did OP prophylaxis. However, sensitivity analyses excluding a study with different distribution of OP prophylaxis between groups receiving GCs or placebo did not alter the estimates. Quality of evidence was rated moderate for BMD outcomes.
Conclusions: In this group of double-blinded RCT studies we found no difference in change in BMD in patients with RA who received GCs compared to those who received placebo. The interpretation of this is difficult as it challenges the well-established fact that GCs negatively impact BMD. However, our findings suggest that in a population with early RA, followed for two years, the dampening of inflammation as well as increased physical activity may outweigh the inherent effects of GCs. This concurs with our finding of lower disease activity in the groups receiving GCs.
References:
[1] Libanati CR, Baylink DJ. Prevention and treatment of glucocorticoid-induced osteoporosis. A pathogenetic perspective. Chest 1992 Nov;102(5):1426–1435.
[2] van Staa TP, Geusens P, Bijlsma JW, Leufkens HG, Cooper C. Clinical assessment of the long-term risk of fracture in patients with rheumatoid arthritis. Arthritis Rheum 2006 Oct;54(10):3104–3112.
Disclosure of Interest: A.-B. Blavnsfeldt: None declared, M. Thomsen: None declared, S. Tarp: None declared, B. Langdahl Grant/research support from: Novo Nordisk, Eli Lilly and Orkla Health, Speakers bureau: Merck, Amgen, Eli Lilly and UCB, E. Hauge Grant/research support from: AbbVie and Roche, Consultant for: MSD and AbbVie, A. de Thurah: None declared
DOI: 10.1136/annrheumdis-2017-eular.5750

THU0127 THE DYNAMICS OF MENTAL DISORDERS FREQUENCY IN COMPLEX DMARDS, BIOLOGICS AND ANTIDEPRESSANTS TREATMENT OF RHEUMATOID ARTHRITIS PATIENTS

A. Abramkin[1], T. Lisitsyna[1], D. Veltishchev[2], O. Seravina[2], O. Kovalevskaya[2], E. Nasonov[1]. *[1]Nasonova Research Institute of Rheumatology; [2]Moscow Research Institute of Psychiatry MoH, Moscow, Russian Federation*

Background: mental disorders (MD) (anxiety/depressive (ADD) and cognitive (CD)) occur in rheumatoid arthritis (RA) patients (pts) very often, they are usually stress-related and, probably, have common pathogenesis chains with RA. In this connection the disease-modifying anti-rheumatic drugs (DMARDs) and biologics drugs treatment may be effective in ADD in RA-pts.
Objectives: to determine the frequency of MD dynamics during DMARDs, biologics and antidepressants treatment of RA-pts in prospective 5yrs study.
Methods: 128 RA-pts were enrolled in this study. All of them met the full ACR criteria. 86% RA-pts were women with a mean age of 47,4±1,0 (M±m) yrs. RA activity was assessed by DAS28 and was high (5,25±0,17 (M±m)) in the beginning of the study. 67% RA-pts were taking prednisone (5±2,7 mg/day),80% RA-pts - DMARDs, 26% - biologics (rituximab – 11%, anti-TNF-α – 10%, anti-IL6 – 5%). MD were diagnosed by psychiatrist in accordance with the ICD-10 in semi-structured interview. The severity of depression and anxiety was evaluated by Montgomery–Asberg Depression Rating Scale (MADRS) and Hamilton Anxiety Rating Scale (HAM-A). CD were diagnosed with psychology and neuropsychology methods. ADD were diagnosed in 121 (94,5%) and CD – in 87 (67,9%) of RA-pts. Major depressive disorder (MDD) was found in 41 (32%), minor depressive disorder (MinDD) – in 50 (39%) and anxiety disorders (AD) – in 30 (23,4%) of RA-pts. The occurrences of MD were evaluated in one and five yrs in 105 from 121 (87%) RA-pts divided into the following treatment groups: 1 – DMARDS (n=32), 2 - DMARDs + antidepressants (sertraline or mianserine) (n=37), 3 – DMARDs + biologics (n=27), 4 - DMARDs + biologics + antidepressants (sertraline or mianserine) (n=9).
Results: *Group 1:* the frequency of MDD was increased from 24,6% to 34,8% in a year and to 42,8% in 5 yrs (p=0,09); MinDD – from 47,8% to 60,8% (p=0,19) and 50% in 5 yrs; the number of pts with AD decreased from 27,5% to 4,3% (p=0,014) and 4,8% (p=0,021) accordingly. The frequency of CD was increased from 64,3% to 78,3% (p=0,16) in 5 yrs. *Group 2:* the frequency of MDD was decreased from 47,4% to 15,7% (p=0,049) in a year and to disappearance of depressive symptoms (p<0,001) in 5 yrs; MinDD – from 26,3% to 15,8% and to disappearance (p<0,001) in 5 yrs; AD – from 26,3% to 10,5% and to disappearance (p<0,001) in 5 yrs. The frequency of CD was decreased from 78,9% to 60% (p=0,25). *Group 3:* the frequency of MDD was unchanged (40,7%, 45,4% and 42,8% accordingly); the frequency of MinDD was increased not significantly – 40,7%, 40,9% and 52,4%; but AD – was significantly decreased (from 18,5% - to disappearance in a year (p=0,042) and 5 yrs (p=0,047)). The frequency of CD was increased from 77,8% to 85%. *Group 4:* the frequency of MDD was decreased significantly from 66,7% to 16,7% in a year and to disappearance in 5 yrs (p=0,03); MinDD and AD were decreased from 16,7% both to disappearance. The occurrence of CD was decreased from 71,4% to 57,1%.
Conclusions: the results demonstrated the best positive dynamics of MD (ADD and CD) frequency in the groups of RA-pts receiving antidepressants treatment in combination with DMARDs and biologics. There was no positive dynamics of MD in patients group receiving DMARDs and mild positive dynamics of AD in the group receiving biologics.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3759

THU0128 FEATURES OF ULTRASOUND DOPPLEROGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SUBCLINICAL HYPOTHYROID DYSFUNCTION

A. Knyazeva[1], O. Rebrova[1], N. Bludova[1], T. Meshcheryakova[2]. *[1]Internal Medcine, SI "Lugansk State Medical University"; [2]Ultrasound Department, Lugansk Clinical Regional Hospital, Lugansk, Ukraine*

Background: Now it is proved that the leading reason for the decline in life expectancy in patients with rheumatoid arthritis (RA) are cardiovascular (CV) disease. The increase in CV risk in patients with RA is associated with increased progression of atherosclerotic vascular lesions. Autoimmune inflammatory process in RA affects the vascular endothelium contributes to the appearance of CV events and increased mortality of patients with RA. It is known that when SHTD increased levels of proinflammatory cytokines. Also, when there is an increase SHTD thickness complex intima-media (CIM)
Objectives: To study the characteristics of ultrasound dopplerography in patients with RA with SHTD
Methods: The observation 139 patients with RA. The I group consisted of 91 patients with RA and SHTD, the II - 48 patients with RA without SHTD. Patients in group I and II did not differ significantly by age and duration of RA. Detection of endothelial dysfunction was performed using ultrasound dopplerography vessels in accordance with international guidelines
Results: In the study of endothelial regulation of vascular tone in both groups of patients revealed the presence of disturbances, as determined signs of reduced endothelium-dependent vasodilation (EDVD) and endothelium-independent vasodilation (EIVD) compared with regulatory measures, which EDVD brachial artery (BA) is greater than or equal to 10% and EIVD BA - 15%. Defined EDVD significant decrease in group II, in contrast to the I (T=4.5, p<0.001), which amounted to 8.3±3.0% and, respectively 10.6±2.1%. EIVD figure was in group II 12.9±3.8%, and in the I – 15.4±1.5%, which also had significant differences (T=4.5, p<0.001) (Table 1).

Table 1

Indicators	I group (n=48)	II group (n=91)	p
D_0, cm	3.8 (3.7; 3.9)	3.9 (3.7; 4.2)	0.16
D_1, cm	4.3 (4.1; 4.5)	4.3 (4.0; 4.5)	0.83
D_2, cm	4.5 (4.3; 4.7)	4.5 (4.2; 4.7)	0.09
V_0, cm/s	55.6 (52.6; 61.1)	52.6 (44.2; 58.2)*	0.002
V_1, cm/s	76.1 (71.6; 79.6)	70.8 (62.6; 76.6)*	<0.001
EDVD, %	10.6±2.1	8.3±3.0*	<0.001
EIVD, %	15.4±1.5	12.9±3.8*	<0.001
CIM, mm	0.73 (0.71; 0.79)	0.97 (0.95; 1.0)*	<0.001
C	0.45 (0.34; 0.71)	0.26 (0.18; 0.46)*	0.002

Note: * p<0.05.

It is also a distinction between the two groups in terms of the thickness of the CIM (Z=9.7, p<0.001), exceeding in group II. Determined a significant decrease in the coefficient of sensitivity to endothelial shear stress (C) in patients with RA, who was in I group of 0.45 (0.34; 0.71), and in II - 0,26 (0.18; 0.46) that there was a statistical difference in this index between the groups of patients (Z=3.6, p<0.001) due to a significant reduction in patients of group II.
The performed analysis of variance indicated that there SHTD influence on the development of disorders of vascular endothelial function in motor RA patients. The SHTD presence in group II patients significantly affected the reduction EDVD, EIVD, C (H=13.8, p<0.001; H=14.5, p<0.001; H=10.2, p=0.001).
Conclusions: The analysis indicated the presence of influence SHTD on the development of disorders of vascular-motor endothelial function in RA patients. These data show that the presence SHTD patients with RA leads to a significant increase in the risk of developing CVD. This requires a more careful study of RA patients for early detection and correction of comorbidities that worsen the clinical course of RA
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3238

THU0129 CD8+CD28- T-LYMPHOCYTES ARE ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

B. Wahlin[1], A.E. Fasth[2], K. Karp[3], K. Lejon[4], A. Södergren[1], S. Wållberg-Jonsson[1]. *[1]Public health and clinical medicine/Rheumatology, Umeå university, Umeå, Umeå; [2]Rheumatology Unit, Department of Medicine at Solna, Karolinska institutet, Stockholm; [3]Surgical and Perioperative Sciences; [4]Clinical Microbiology, Immunology, Umeå university, Umeå, Umeå, Sweden*

Background: Patients with rheumatoid arthritis (RA) have an increased mortality and morbidity due to cardiovascular disease and accelerated progression of atherosclerosis. Altered populations of T-lymphocytes are associated with atherosclerosis, and chronic infection with cytomegalovirus (CMV) affects the T-cell-population.
Objectives: To study the association between subsets of T-lymphocytes, subclinical atherosclerosis assessed by intima-media thickness (IMT) and antibodies against CMV in patients with RA.
Methods: Patients with new-onset RA (n=71), aged ≤60 years at diagnosis, were consecutively included in a study of development of atherosclerosis. Ultrasound measurement of IMT of a. carotis communis was undertaken at inclusion (T0), after five years (T5) and after 11 years (T11) (n=54). At T11, flow-cytometry was undertaken to investigate subsets of T-lymphocytes (CD45+CD3+), where CD4, CD8, CD28, CD56 and CX3CR1 was studied. CX3CR1 is the ligand of fractalkine, an adhesion molecule expressed on activated endothelial cells to attract leukocytes. Serological analysis for CMV was undertaken from samples collected at T0, T5 and T11.
Results: The percentage of CD8+T-lymphocytes lacking the co-stimulatory molecule CD28 (CD8+CD28-) was significantly (standardized beta coefficient 0.39, p-value 0.01) associated with IMT at T11 in a linear regression model including T0 variables smoking, systolic blood pressure and cholesterol. No association with IMT was seen for CD4+CD28- T-lymphocytes. CX3CR1 was expressed in 71% of CD8+CD28- T-lymphocytes, compared with 8.2% of CD8+CD28+. The prevalence of immunoglobulin G seropositivity for CMV was 47/70 (67%), 42/66 (57%) and 34/56 (52%) at T0, T5 and T11 respectively. Patients with constantly positive CMV serologies (T0, T5 and T11) had a significantly higher percentage of CD8+CD28- and CD4+CD28- T-lymphocytes. Also the proportion of cells expressing CX3CR1 was in both CD4+ and CD8+ T-lymphocytes associated with constantly positive serologies for CMV.
Conclusions:
Subclinical atherosclerosis in patients with RA was associated with CD8+CD28- T-lymphocytes in a regression model adjusted for traditional cardiovascular risk factors. Positive serologies for CMV were associated with an increased proportion of CD8+CD28- T-lymphocytes and T-lymphocytes expressing CX3CR1.
Disclosure of Interest: B. Wahlin: None declared, A. Fasth Employee of: Novartis Sweden AB, K. Karp: None declared, K. Lejon: None declared, A. Södergren: None declared, S. Wållberg-Jonsson: None declared
DOI: 10.1136/annrheumdis-2017-eular.4364

THU0130 IMPROVEMENT IN MEASURES OF DEPRESSED MOOD AND ANHEDONIA IN TWO RANDOMIZED, PLACEBO-CONTROLLED PHASE III STUDIES OF SIRUKUMAB, A HUMAN ANTI-INTERLEUKIN-6 ANTIBODY, IN PATIENTS WITH RHEUMATOID ARTHRITIS

Y. Sun[1], B. Hsu[2], D. Wang[3], M. Curran[2], W.C. Drevets[1], G. Chen[4], G.M. Wittenberg[1]. *[1]Janssen Research & Development, LLC, Titusville; [2]Janssen Research & Development, LLC, Spring House, Pa; [3]Janssen Research & Development, LLC, Raritan; [4]Janssen Research & Development, LLC, la Jolla, United States*

Background: Interleukin-6 (IL-6) is one of the known neuroactive-cytokines involved in neuronal plasticity and stress coping and is associated with depression. Depressive symptoms are common in patients with rheumatoid arthritis (RA), a disease characterized by high peripheral IL-6. Previous analysis of a Phase II study[1] showed that sirukumab, a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, can help reduce depressive symptoms in RA patients.
Objectives: To further assess and validate the effects of sirukumab on relieving depressive symptoms in RA patients.
Methods: We conducted a post-hoc analysis of 2 Phase III, randomized, double-blind, placebo-controlled trials evaluating efficacy and safety of sirukumab in the treatment of RA. SIRROUND-D enrolled patients with active RA despite disease-modifying anti-rheumatic drugs and having serum C-reactive protein (CRP)≥8mg/L at baseline. SIRROUND-T enrolled patients with active RA despite anti-TNF therapy and having serum CRP≥8mg/L or erythrocyte sedimentation rate≥28mm/h at baseline. Patients using antidepressants were excluded from the analysis. Patients were grouped by presence/absence of prevalent depressed mood and anhedonia (PDMA), based on the self-reported frequencies of these 2 core depressive symptoms in the SF-36, requiring one present at least "most of the time" and the other "some of the time" in the past 4 weeks. A depression score was derived based on the 2 core depressive symptoms of SF-36. Relief of depressive symptoms in patients with PDMA was evaluated by comparing changes in the depression score from baseline to week 8 between the placebo and combined sirukumab groups directly and with adjustment for RA activity as measured by the Disease Activity Score-28 with CRP. Changes in depression score were also analyzed in RA patients who did not have an ACR50 response to sirukumab. The combined effect of anti-IL-6 treatment was estimated using meta-analysis of 2 Phase III, 1 Phase II studies of sirukumab and 1 Phase II study of the anti-IL-6 cytokine antibody siltuximab.
Results: At baseline, 19% and 22% of patients were classified as PDMA in the 2 studies, respectively. Sirukumab treatment, compared to placebo, significantly improved depressive symptoms by week 8 among PDMA patients (p=0.022 and 0.046 for the 2 studies, respectively) before adjusting for changes in RA activity. Within the sirukumab group, the reduction in depressive symptoms remained significant after adjusting for changes in RA activity ($p<0.0001$) and in ACR50 non-responders at week 8 ($p<0.0001$), while differences in improvements between the sirukumab and placebo group reduced to trends. Meta-analysis of 4 anti-IL-6 studies (1 siltuximab, 3 sirukumab) revealed that anti-IL-6 treatment helps alleviate depressive symptoms even after adjusting for changes in disease activity (Standardized Mean Difference =0.25, p=0.03).
Conclusions: Our findings are consistent with previous results from a phase II RA study. Peripheral anti-IL-6 cytokine treatment is associated with improvement in depressive symptoms in RA patients, possibly supporting a role for IL-6 dysfunction in depression.
References:
[1] Ann Rheum Dis2015;74(Suppl2): 720.
Disclosure of Interest: Y. Sun Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Develoment, LLC, B. Hsu Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Develoment, LLC, D. Wang Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Develoment, LLC, M. Curran Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Develoment, LLC, W. Drevets: None declared, G. Chen: None declared, G. Wittenberg: None declared
DOI: 10.1136/annrheumdis-2017-eular.3263

THU0131 PREMATURE CORONARY HEART DISEASE FREQUENCY IN RHEUMATOID ARTHRITIS WHO ARE RECEIVING BIOLOGIC AGENTS: HUR-BIO REAL LIFE RESULTS

B. Armagan[1], A. Sari[1], A. Erden[1], L. Kilic[1], E.C. Erdat[2], O. Karadag[1], A. Akdogan[1], S. Apras Bilgen[1], U. Kalyoncu[1], S. Kiraz[1], I. Ertenli[1]. *[1]Hacettepe University, Department of Internal Medicine, Division of Rheumatology; [2]Hacettepe University, Department of Internal Medicine, Hacettepe University, Ankara, Turkey*

Background: Patients with rheumatoid arthritis (RA) are at increased risk of coronary heart disease (CHD) overall, as well as death from CHD. A direct impact of chronic inflamation on the vascular system, secondary effects of physical inactivity and some drugs used in the management of RA are shown as the reasons for the increase in this comorbidity (1).
Objectives: We aim to determine the frequency of CHD in the RA patients who receive biological agents.
Methods: Hacettepe University Biologic Registry (HUR-BIO) includes demographic and clinical data of patients treated with biological agent since 2005. By August 2016, 1235 RA patients were recorded in the database. Age, smoking status, comorbidities, current and previous treatments were analysed in 1000 patients. Disease activity was estimated by the 28-joint activity calculator (DAS28-ESR) and DAS28-CRP. Functional assesment was evaluated by the Health Assessment Questionnaire (HAQ). Premature CHD should be defined if clinical CHD or sudden death is documented in male younger than 55 years of age and in female younger than 65 years of age.
Results: Overall 1000 patients (79,8% female) were enrolled in this study. Mean age was 53,1±12,6 years old, mean disease duration was 12,3±9,3 years. CHD was detected 57 (5,7%) patients and female/male was 38/19. Premature CHD was observed in 38 (66,7%) patients. CHD patients had more frequently male, older, higher classical risk factors, higher baseline ESR level and higher functional disability (Table). HAQ score also remained high in CHD group at last visit. Classical cardiovascular risk factors, sex, seropositivity, disease activity score and HAQ score were similar in the premature and other CHD group. Coronary artery stenting, coronary artery bypass surgery and medical treatment was applied in 12 (21%), 20 (35,1%) and 25 (43,9%) CHD patients, respectively. There was no statistical difference in treatment of premature and other CHD.

Table 1. Characteristic of patients who have CHD or not

	CHD (n=57)	No CHD (n=943)	p
Female n (%)	38 (66,6)	19 (80,6)	0,011
Hypertansion n (%)	38 (66,6)	271 (28,7)	<0.001
Diabetes Mellitus n (%)	11 (19,3)	97 (10,3)	0.033
Smoking (current/past) n (%)	30 (52,6)	370 (39,2)	0.003
Age mean (SD)	64,7 (9,9)	52,4 (12,4)	<0.001
Baseline Erythrocyte sedimentation rate (SD)	45,7 (30,3)	36,1 (24,6)	0.009
Baseline HAQ mean (SD)	1,27 (0,64)	1,02 (0,62)	0.025
Last HAQ mean (SD)	0,84 (0,64)	0,66 (0,58)	0.024

CHD: Coronary heart disease, HAQ: Health Assessment Questionnaire.

Conclusions: As a results CHD were detected in 5,7 percents of RA patients who are receiving biological agents. Importantly, two third of these patients have

premature CHD. Classical risk factors are observed more frequently in CHD patients as expected but interestingly, no additional risk factors other than age were detected between premature and other CHD patients. This suggests that the primary factor triggers premature CHD is the underlying inflammatory rheumatic disease. The presence of CHD was determined by patient history which the limitation of our study. We did not assess to subclinical CHD in this study.

References:
[1] Comorbidity in rheumatoid arthritis, Carl Turesson, Swiss Medical Weekly, 2016.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4269

THU0132 IMMUNOGENICITY AND SAFETY OF 23-VALENT PNEUMOCOCCAL VACCINE FOR PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM 2-YEAR FOLLOW UP

M.S. Sergeeva, B.S. Belov, G.M. Tarasova, E.N. Alexandrova, A.A. Novikov, M.V. Cherkasova, D.E. Karateev, E.L. Luchikhina, Y.V. Muravyev, D.V. Buhanova. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Comorbid infections have significant impact on morbidity and mortality, especially in autoimmune diseases. Prevention of infection is an integral part of supervision of these patients.
Objectives: To investigateimmunogenicity and safety of 23-valent polysaccharide pneumococcal vaccine in patients with rheumatoid arthritis (RA) treated with diseases modifying anti rheumatic drugs (DMARDs) and biologic diseases modifying anti rheumatic drugs (bDMARDs) during the 2-year follow-up.
Methods: Out of 110 subjects (81 females (73,6%), 29 males (26,4%) aged 23–76 years) included into the study, 79 were RA patients and 31 were controls with a history of ≥2 episodes of lower respiratory tract infections (bronchitis, pneumonia). 52 patients with RA were on methotrexate (MTX), 14 were on leflunomide (LEF), 13 were ontumor necrosis factor alpha inhibitors (iTNF-α)+MTX. One dose (0,5 ml) of 23-valent polysaccharide pneumococcal vaccine was administered subcutaneously without discontinuation of MTX/LEF or 28–30 days prior to initiation of iTNF-α. Totally four study visits were preplanned: initial vaccination visit and 3 control visits in 1, 3 and 12 months after vaccinationfor 110 patients. 39 RA patients were followed up for 2 years (24 months). Routine evaluation during each visit included physical exams and laboratory tests. Levels of antibodies to pneumococcal capsular polysaccharide were measured using VaccZymeTM PCPIgG 2 kit (The Binding Site Group Ltd, Birmingham, UK). Post-immunization response coefficient was calculated for each participant as the ratio of AB levels during visits II, III, IV and V to baseline AB level at Visit I.
Results: Not a single caseof clinicallyor radiographically confirmed pneumonia was documented during the follow up period. Pronounced positive immune reaction after administration of the vaccine under investigation was documented in RA patients during different therapies, i.e., significant post-immunization response coefficient increase. There were 61% responders among RA patients and 70% responders among the controls during one-year follow-up. Dynamics of post-immunization response coefficient in RA patients during 2-year follow up are presented in the Table. RA patients and the control group are marked more than 2-foldsignificant increase in the content of antibodies in 3 monthsafter the vaccination. Despite the decline in their concentrationsto 12 months, it remained at the proper level and was increased to 24 month follow-up.Good tolerability of the vaccine was documented in 65% of cases, satisfactory (injection site pain, swelling and hyperemia of the skin up to 2 cm in diameter and subfebrilefever) in 35% of cases. As these reactions had no causal relationship with current RA therapy, and fully resolved within 24 hours without additional treatment, no RA therapy modification was required.Pronounced DAS28 positive dynamics in RA patients (4,27 and 2,68 at Visit I and Visit V, respectively, $p<0,001$) indicates the absence of any negative impact of vaccination on disease activity.

Table. Post-immunization response coefficient dynamics in RA patients during 2 year follow up. Me [25,75 percentile]. (n=39).

	Visit II (1 month)	Visit III (3 Month)	Visit IV (12 month)	Visit V (24 month)
RA patients	2,33* [1,6;3,8]	3,55* [2,32;6,23]	2,64* [2,03;6,39]	3,07* [1,56;6,18]

*$p<0,05$

Conclusions: Thus, all given prove the sufficient immunogenicity and safety of 23-valent pneumococcal vaccine in RA patients, getting different therapeutic regimens,during the 2-year follow-up.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2070

THU0133 SERUM PENTRAXIN-3 IN THE ASSESSMENT OF CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

B. Targonska-Stepniak, M. Piotrowski, R. Zwolak, M. Majdan. *Department of Rheumatology and Connective Tissue Diseases, Medical University of Lublin, POLAND, Lublin, Poland*

Background: Rheumatoid arthritis (RA) is associated with the increased cardiovascular (CV) morbidity and mortality due to accelerating, progressive atherosclerosis. The chronic, systemic inflammatory process is responsible for both joint damage and increased CV risk in RA patients. Pentraxin 3 (PTX3) is an inflammatory marker, a member of long pentraxin superfamily, supposed to be involved in inflammatory process as well as in atherosclerosis.
Objectives: The goal of the study was to assess the role of PTX3 as an inflammatory marker in patients with RA and to evaluate the relationship between PTX3 and CV risk markers [carotid intima-media thickness (cIMT), QTc distance (dQTc), lipid profile].
Methods: The study group consisted of 72 consecutive RA patients, 60 (83,3%) female and 12 male (16,7%), with the mean (SD) age 53,4 (10,29) (range 21–71) and disease duration 16,8 (10,3) years (range 2–49). The activity of RA was estimated by clinical examination with the disease activity score in 28 joints (DAS28). Remission or low disease activity was observed in 35 (48,6%) patients; moderate or high disease activity (DAS28 >3,2) in 37 (51,4%) patients. Disease modifying antirheumatic drugs (DMARDs) used in the treatment included: methotrexate 61 (84,7%) patients, chlorochine or hydroxychlorochine 9 (12,5%), leflunomide 4 (5,6%), cyclosporine 1 (1,4%) patient. The majority of patients 54 (75%) were treated with biological DMARDs, currently or in the past.
Results: The mean (SD) PTX3 concentration in RA patients was 4,57 (2,83) ng/ml (range 1,43- 16,07). The mean (SD) cIMT value was 0,86 (0,2) mm (range 0,43–1,77). There were 19 (26,4%) RA patients with advanced atherosclerosis (presence of atherosclerotic plaques).
The positive, significant correlations were found between PTX3 concentration and other inflammatory markers: C-reactive protein (CRP) (R=0,5), ESR (R=0,46) and white blood cell count (WBC) (R=0,41). PTX3 concentration was also correlated with clinical disease activity markers: DAS28 value (R=0,41), as well as with tender joint count (TJC) (R=0,01), swollen joint count (SJC) (R=0,009), patient's global assessment of the disease activity (R=0,02).
The mean (SD) PTX3 concentration was significantly higher in patients with moderate/high RA activity in comparison with remission/low disease activity [5,56 (3,29) vs 3,48 (1,71) ng/ml, p=0,001] and in patients anti-CCP positive compared with anti-CCP negative [4,57 (2,58) vs 3,02 (0,85) ng/ml, p=0,04].
The mean (SD) PTX3 concentration was significantly higher in patients with definite atherosclerosis (cIMT >0,9 mm) than in patients with subclinical or no atherosclerosis [5,77 (3,02) vs 3,99 (2,58) ng/ml, p=0,04], as well as in patients with atherosclerotic plaques in comparison with no plaques (6,18 (2,83) vs 4,02 (2,64) ng/ml, p=0,0006).
There was a negative correlation between PTX3 and dQTc (R= -0,33, p=0,007).
Conclusions: The results of the study suggest a twofold role of PTX3:
1. an inflammatory marker of the joint disease activity
2. a biomarker indicating intensity of atherosclerosis, estimated by greater cIMT value and the presence of atherosclerotic plaques. The negative correlation between PTX3 and dQTc suggests the increased risk of sudden cardiac death due to shortening of dQTc.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3303

THU0134 INTERSTITIAL LUNG DISEASE AND RHEUMATOID ARTHRITIS. MULTICENTER STUDY WITH TOCILIZUMAB

C. Fernández-Díaz [1], J. Narvaez-García [2], M. Martín-López [3], P. Rubio-Muñoz [4], S. Castañeda-Sanz [5], N. Vegas-Revenga [1], L. Dominguez-Casas [1], V. Calvo-Rio [1], M. Gonzalez-Gay [1], R. Blanco [1]. *[1]Rheumatology, Hospital Universitario Marques de Valdecilla, Santander; [2]Rheumatology, Hospital Universitario Belvitge, Barcelona; [3]Rheumatology, Hospital 12 de Octubre, Madrid; [4]Rheumatology, Hospital Universitario Germans Trias i Pujol, Barcelona; [5]Rheumatology, Hospital la Princesa, Madrid, Spain*

Background: Interstitial Lung Disease (ILD) is a severe extraarticular manifestation of rheumatoid arthritis (RA). AntiTNFα drugs and conventional disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate (MTX) have been involved in the development of ILD. IL6 has been implicated in the pathogenesis of ILD (Kobayashi J et al). However, a fatal case of exacerbation of ILD has been described with tocilizumab (TCZ) (Kawashiri SY el at).
Objectives: Our aim was to assess the efficacy and safety of TCZ in ILD associated with AR.
Methods: Multicenter study of RA patients with ILD treated with TCZ. ILD was diagnosed by high-resolution computed tomography (HRCT). TCZ was used at standard dose (8 mg/k/iv/4 weeks). We have analyzed the following variables: a) 1-point change in the degree of dyspnea according to the Modified Medical Research Council (MMRC); b) Forced Vital Capacity (FVC) improvement ≥10%; and improvement ≥10% in DLCO; c) HRCT, and d) joint assessment (DAS28 score).
Results: We studied 12 patients (9 women/3 men) with ILD related to RA.

The mean age±SD was 57.1±16.1 years. The mean evolution of RA was 9±5.8 years. The patients had previously received the following DMARDs; MTX (n=12), leflunomide (LFN) (8) sulfasalazine (SSZ) (3) hydroxichloroquine (HCQ) (1) azathioprine (AZA) (2), gold salts (2). In addition, 11 patients had previously received biological drugs: adalimumab (4) anakinra: (1), etarnecept (4), rituximab (4), infliximab (1), certolizumab (1), abatacept (1). RA was seropositive in 11 cases (92%). Besides HRCT, the diagnosis of ILD was confirmed by biopsy in 4 patients. In 2 patients ILD was drug-related: MTX (n=2). TCZ was prescribed in monotherapy (n=8) or combined with other DMARDs (4). These DMARDs were: LFN (2), MTX (1), AZA (1). In many patients the dyspnea and DLCO remain stable (Table). After a follow-up of 12 months, 2 patients withdrew TCZ, 1 patient for ILD worsening and 1 patient for joint inefficacy.

Table 1

	Baseline	3th month	6th month	12th month
MRC, n (%)		11	8	11
– No change		11 (100)	7 (87)	8 (73)
– Improvement		0	0	2 (18)
– Worsening		0	1 (13)	1 (9)
FCV, n (%)		2	5	9
– No change		2 (100)	5 (100)	6 (67)
– Improvement		0	0	2 (23)
– Worsening		0	0	1 (12)
DLCO, n (%)		2	4	9
– No change		1 (50)	3 (75)	9 (100)
– Improvement		0	0	0
– Worsening		1 (50)	1 (25)	0
HRTC, n (%)		0	2	10
– No change			1 (50)	7 (70)
– Improvement			0	0
– Worsening			1 (50)	3 (30)
DAS28 – *mean*	4.46±1.40	3.35±1.19	3.23±1.04	2.98±0.95
CRP (mg/dl) – *mean*	3.23±2.96	1.11±0.98	1.48±0.95	1.15±0.84
ESR (mm/1st h) – *mean*	45.17±28.84	16.16±10	16.16±11.41	17.47±25.45

Conclusions: In our knowledge, this is the largest series that assess the EPID associated with RA treated with TCZ. We observed that in many cases pulmonary involvement remains stable.

References:
[1] Kobayashi J et al. Chest 1995; 108: 311.
[2] Kawashiri SY el at. Rheumatol Int 2012; 32: 4023–6.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3580

THU0135 THE COURSE OF LOWER EXTREMITY FUNCTION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS OVER THE FIRST FIVE YEARS

M. Mellblom Bengtsson[1], C. Book[1,2], S. Hagel[3,4], L.T. Jacobsson[5], C. Turesson[1,2]. *[1]Department of Rheumatology, Skåne University Hospital; [2]Rheumatology, Department of Clinical Sciences, Malmö, Lund University, Malmö; [3]Rheumatology, Department of Clinical Sciences, Lund, Lund University; [4]Department of Rheumatology, Skåne University Hospital, Lund; [5]Department of Rheumatology and Inflammation Research, Sahlgrenska Academy at Gothenburg University, Gothenburg, Sweden*

Background: Rheumatoid arthritis (RA) frequently involves joints of the feet and the knees. Disability related to arthritis in the lower extremities has a major impact in many patients, but has not been extensively studied.

Objectives: To investigate lower extremity function in early RA, using validated tests, and to assess its relation to other disease parameters.

Methods: Consecutive patients with early RA (symptom duration ≤12 months) in an inception cohort from a well-defined area were followed according to a structured protocol, with visits at inclusion and after 1, 2 and 5 years. Lower extremity function was investigated using the Index of Muscle Function (IMF) (1), a validated battery of tests by which the patient's general ability, muscle strength, muscular endurance and balance/coordination are assessed by a physiotherapist. The scores on the subscales are added for a total IMF score (IMF total) of 0–40. A subscore of the Health Assessment Questionnaire Disability Index (HAQ-DI), based on the 10 questions that are mainly dependent on function of the lower extremities (the HAQ-DI-LE (2)) was calculated, as well as a modified HAQ-DI-LE (mHAQ-DI-LE) that included only the three HAQ-DI domains in which all questions relate mainly to the lower extremities. Changes in the IMF total score and subtest scores between visits were analyzed using the Wilcoxon signed rank test. Correlations between disease parameters were assessed using Spearman's rank test.

Results: A total of 106 patients (67% women, mean age 61 years, mean baseline DAS28 4.4, median baseline HAQ-DI 0.75) were included. Data on IMF total were available for 100, 89 and 67 patients at the 1, 2 and 5-year visits. Lower extremity function improved from baseline to the 1-year visit (IMF total median 10; interquartile range (IQR) 4–16 vs. 7; IQR 3–12) (p=0.01). This was followed by a decline in lower extremity function, in particular between the 2-year and 5-year visits (IMF total median 8 (IQR 3–13) vs 9.5 (IQR 3.75–18.25); p=0.001). This was mainly due to worsening in test results for muscle strength (median 4 (IQR 1–6) vs 5 (IQR 2–9); p=0.001) and for balance/coordination (median 2 (IQR 0–4) vs 3 (IQR 2–6); p=0.001). At baseline, IMF total correlated with HAQ-DI-LE (r=0.46), mHAQ-DI-LE (r=0.49) and HAQ-DI (r=0.40) (all p<0.001), whereas there were weaker correlations with CRP (r=0.24; p=0.02) and DAS28 (r=0.28; p=0.004). There were consistent correlations between IMF total and HAQ-DI-LE, mHAQ-DI-LE and HAQ-DI at all time points, but no significant correlations for IMF total with CRP and DAS28 at the 2-year visit.

Conclusions: In early RA, there was improvement in lower extremity function during the first year, followed by a gradual decline, possibly explained by lack of complete disease control and aging. Tests of muscular function in the lower extremities may reveal aspects of RA disease severity that are not fully captured by standard disease activity measures, and may add important information regarding functional loss.

References:
[1] Ekdahl et al. Advances in Physiotherapy 1999; 1: 45–55.
[2] Ekdahl et al. J Clin Epidemiol 1989; 42: 947–54.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4223

THU0136 NESFATIN-1 EXPRESSION IS ASSOCIATED WITH REDUCED ATHEROSCLEROTIC DISEASE RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

C. Robinson[1], L. Tsang[1], A. Solomon[1], A. Woodiwiss[1], S. Gunter[1], H.-C. Hsu[1], G. Norton[1], A. Millen[1], P. Dessein[1,2]. *[1]Cardiovascular Pathophysiology and Genomic Research Unit, School of Physiology, University of the Witwatersrand, Johannesburg, South Africa, Johannesburg, South Africa; [2]Rheumatology Division, Universitair Hospital Brussel, Brussels, Belgium*

Background: Nesfatin-1 comprises a peptide that is involved in appetite suppression, energy homeostasis and fluid regulation, and was recently documented to participate in a range of cardiometabolic pathways (1,2). There is currently a need for the identification of novel biomarkers in the elucidation of CVD risk and its stratification in persons with rheumatoid arthritis (RA). The role of nesfatin-1 in cardiovascular disease risk among RA patients is uncertain.

Objectives: We investigated the potential impact of nesfatin-1 on subclinical cardiovascular disease manifestations in patients with RA by determining the associations of nesfatin-1 concentrations with atherosclerosis and circulating levels of matrix metalloproteinase (MMP)-2 that mediates plaque stability and those of MMP-3 and MMP-9 that cause plaque vulnerability.

Methods: Nesfatin-1 concentrations were measured in 236 (114 black; 122 white) RA patients. Relationships of nesfatin-1 concentrations with ultrasound determined carotid intima-media thickness (cIMT) and plaque and MMP levels were identified in confounder adjusted multivariate regression models.

Results: Nesfatin-1 concentrations were inversely associated with c-IMT (β (SE) = -0.022 (0.008), p=0.00) and directly with MMP-2 levels (β (SE) =0.117 (0.031), p=0.00). After adjustment for conventional risk factors and RA characteristics, these associations persisted (c-IMT: β (SE) = -0.017 (0.008), p=0.04; MMP-2: β (SE) =0.116 (0.033), p=0.00). Patient characteristics did not influence the nesfatin-1-to-cIMT relation (interaction p≥0.7). By contrast, the Disease Activity Score in 28 joints (DAS28) and Clinical Disease Activity Index impacted the nesfatin-1-to-cIMT association (interaction p=0.04 and 0.02, respectively). Nevertheless, in stratified analysis, nesfatin-1 concentrations were related to those of MMP-2 in patients with no or mild (β (SE) =0.148 (0.054), p=0.00) and moderate or high disease activity (β (SE) =0.086 (0.041), p=0.04) as determined by DAS28 (cut-off value 3.6) as well as by CDAI (cut-off value =10) (β (SE) =0.130 (0.048), p=0.00 and 0.107 (0.046), p=0.02), respectively).

Conclusions: Nesfatin-1 concentrations are consistently associated with a reduced atherosclerosis burden and increased MMP-2 levels in patients with RA.

References:
[1] Oh-I S, Shimizu H. Identification of nesfatin-1 as a satiety molecule in the hypothalamus. Nature. 2006;443:709–712.
[2] Dore R, Levata L, Lehnert H, Schulz C. Nesfatin-1: functions and physiology of a novel regulatory peptide. Journal of Endocrinology. 2016; e-pub ahead of print: doi: 10.1530/JOE-16–0361.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4595

THU0137 IMPACT OF PERIODONTAL AND RHEUMATIC DISEASE MARKERS ON FIRST-DEGREE RELATIVES OF PATIENTS WITH RHEUMATOID ARTHRITIS ACCORDING TO AGE GROUP

C. Romero-Sanchez[1,2], S. Giraldo[3], J. De-Avila[1], M.A. Cano-Bermuedez[1], L. Chila-M.[1], J. Bello-Gualtero[2], P. Chalem[4], W. Bautista[3], J. Londono[5], C. Pacheco-Tena[6], G. Lafaurie[1], R. Valle-Oñate[7]. *[1]Unit of Oral Basic Investigation/School of Dentistry, Universidad El Bosque; [2]Department of Rheumatology and Inmunology, Hospital Militar Central, Bogotá, Colombia; [3]School of Medicine, Universidad Militar Nueva Granada; [4]Departamento de Reumatologia, Fundacion Instituto de Reumatologia Fernando Chalem, Bogotá D.C; [5]Spondyloarthropaty Group, Rheumatology Universidad de la Sabana, Chia, Colombia; [6]Departamento de Reumatologia, Investigacion y Biomedicina S.C., Chihuahua, Mexico; [7]Departamento de Reumatologia, Hospital Militar Central, Bogotá, Colombia, Bogotá D.C., Colombia*

Background: Rheumatoid arthritis (RA) and periodontal disease (PD) have

similar underlying pathologic processes and share a general deregulation of the inflammatory response.
Objectives: To evaluate PD markers in first-degree relatives (FDR) of consanguinity individuals of patients with rheumatoid arthritis to compared with controls and to establish an association to rheumatic activity according to age groups
Methods: 201 FDR individuals and 201 matched controls were included. Clinical evaluation of rheumatologic and periodontal condition was performed. *P. gingivalis, P. gingivalis* IgG1 and IgG2, ESR, CRP, RF, ACPAs, painful and swollen joints were assessed. A frequencies analysis, comparisons and a logistic regression model were made. The study was approved by local ethics committee.
Results: 37.3% of patients with overweight and 10.1% obsesses. Subjects with more than one swelling joint were 21 subjects <30 years, 5 between 31–40, 5 between 41 to 50 subjects and 9 subjects over 50, for more one painful joint were 73. The RF was present in 8.0%, APCA in 13%, RA33 in 1%. 67.3% had a diagnosis of PD, 81.6% had a moderate-severe p=0.003.*P. gingivalis* was in 47,9%, and *P. gingivalis* IgG1 were in 54.7%. It was evidenced that 25.3% patients presented BMI>30, where 81.8% had periodontitis p=0.006. Regression analysis on the whole group shows a risk to present BMI>25 (OR 1.67 IC-95% 1.02 – 2.74 p=0.042), ACPAs (OR 3.7 IC-95% 1.34–10.22 p=0.012), at least one pain join (OR2.51 IC-95% 1.42–4.44 p=0.001) and gingival index (OR4.57 IC-95% 1.76–11.80 p=0.002) in FDR individuals. Based on age the risk to develop PD was increasing: individuals among 30 to 40 years shows OR 2.76 (IC-95% 1.24–6.18, p=0.013); among 41 to 50 years, OR 4.72 (IC-95% 1.81–12.32, p=0.001); and for >50 years individuals an OR 6.22 (IC-95% 2.55–15.1, p=0.0001). The discriminating analysis by age rank shows that FDR individuals <30 years (n=67) exhibited high risk to have at least one pain join (OR 3.84 IC-95% 1.28–11.47 p=0.016). In subjects among 30 to 40 years (n=46), the risk was associated with periodontal pocket (OR1.44 IC-95% 1.05–4.98 p=0.021), one or more pain join (OR 3.56 IC-95% 1.22–10.40 p=0.020) which it was maintained until 50 years individuals (n=35) (OR4.32 IC-95% 1.11–16.78 p=0.0034), individuals >50 years (n=53) show high risk to present BMI>25 (OR 4.00 IC-95% 1.46–10.45 p=0.007).
Conclusions: Obesity, ACPA and periodontitis can be considered as relevant conditions associated with the development of RA in FDRs. However, the analysis based on age group shows that periodontal markers do not appear early in FDR individuals; however, clinical rheumatologic variables are manifested and maintained over time.
References:
[1] Bello-Gualtero JM et al. J Periodontol 2016;87:346–356.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5500

THU0138 DAS 28 CORRELATED POORLY WITH THE OBJECTIVE EVIDENCE OF INFLAMMATION AS DETECTED BY ULTRASOUND (US) EXAMINATION OF HANDS AND FEET IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS (RA)

C. Ciurtin, G. Brown, A. Cotton, J. Guinto, A. Jones, V. Morris. *Department of Rheumatology, University College London NHS Trust, London, United Kingdom*

Background: The Disease Activity Score including 28 joint count (DAS-28) is the most widely used outcome measure in RA. However, despite evidence that metatarsophalangeal (MTP) joints are often the first joints affected in RA, DAS-28 score does not incorporate them.
Objectives: Our study aimed to investigate the correlation between DAS-28 assessment and objective evidence of active joint inflammation using the US examination of both hands and feet, including wrists, metacarpophalangeal (MCP), proximal interphalangeal (PIP), and MTP joints.
Methods: A retrospective study was conducted, including 87 patients who were referred to the US clinic for an examination of their hands and feet in the last 6 months (46 patients with RA and 43 controls - patients with other inflammatory or degenerative arthropathies). Information about demographics, disease duration, current treatment, inflammatory markers, and DAS-28 scores was captured. The US OMERACT criteria were used for grading synovial hypertrophy, and assessing for the presence of Power Doppler (PD) signal, erosions and osteophytes. Statistical analysis methods included T-test, Mann-Whitney U test, Z score for proportions and Spearman's correlation coefficients.
Results: In the RA group, DAS-28 had a weakly positive correlation with the cumulative PD scores of their hands and feet joints (R=0.14, P=0.02), but did not correlate with PD score of MTP joints (R=0.03, P=0.09). In the control group, DAS-28 did not correlate significantly with either the total PD scores of feet (R=0.42, P=0.26) or hands and feet joints (R=0.5, P=0.25). Sensitivity of US examination of hands alone compared to hands and feet was 74.3% for the RA group, while the sensitivity of US feet to detect the presence of PD was 59.2% when compared to the US of both hands and feet.
Conclusions: We found that DAS-28 correlated poorly with objective evidence of inflammation as detected by US of the hands and feet, and this correlation was lost when only the presence of inflammation in the feet was taken into consideration. Further validation of our results in a larger study including patients stratified based on the disease duration might help understand which patient subgroups are more likely to have their disease activity significantly under-evaluated using DAS-28 outcome measure.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3308

THU0139 DEPRESSIVE SYMPTOMS AND VITAMIN D IN PATIENTS WITH EARLY ARTHRITIS

D. Freier[1], M. Biersack[1], J. Detert[1], G.-R. Burmester[1], R. Uebelhack[2], T. Braun[1], V. Hoehne-Zimmer[1]. *[1]Rheumatology; [2]Psychiatry, Charité-University Medicine, Berlin, Germany*

Background: There is a high prevalence of depression in patients with rheumatic disorders. Especially, in rheumatoid arthritis, it is one of the most prevalent co-morbidities with 16% to 38%. Vitamin D (VD) deficiency is one of the known risk factors for depressive disorders. On the other hand, a VD deficiency has often been detected in rheumatic diseases. A possible correlation between these two co-morbidities has not been investigated so far in patients with early arthritis (EA).
Objectives: The aim of this study was to examine the association between VD deficiency and depression and/or anxiety disorders in patients who have presented themselves for the first time in the EA clinic.
Methods: Patients with a suspected EA (at least one swollen joint without previous trauma or joint infection with a symptom duration of 6 weeks to 12 months) received a screening date within five work days. The VD status (25-hydroxy-VD_3) was obtained during the first EA clinic consultation. In addition, each patient completed questionnaires on the disease history, as well as evaluated self-assessment questionnaires including the health assessment questionnaire (HAQ) and the Hospital Anxiety and Depression Scale (HADS). The hereby-obtained results of disease activity, VD-status and HADS-scores were investigated. In the observation period from June 2012 to March 2015, 75 patients fulfilled the inclusion criteria of completed results and questionnaires as well as a disease duration of less than 12 months.
Results: The mean age of this EA cohort was 51.7±16.9 years (♀ 65.3%, mean disease duration: 4.0±3.0 months). The prevalence of VD deficiency (<75 nmol/l) was 73.3%. 48.0% of EA patients showed a positive global distress score (≥13). The mean HADS global distress score in VD sufficient patients was 10.2±8.6 vs 13.3±6.9 in deficient patients. The observed difference was not statistically significant. There was neither an association between gender, age and VD status nor was there any difference in the laboratory parameters (e.g. C-reactive protein, rheumatic factor, anti citrullinated peptide, hemoglobine) or assessment of functional status (e.g. HAQ, disease activity score by 28 joints).
Conclusions: The prevalence of VD deficiency is higher in EA patients with 73% than in the general German population (vs. 60%). The prevalence of positive distress with 50% is also higher. Interestingly, no association of deficient VD levels and positive distress in the HADS was detected in our examined EA cohort. This might be explained by the early stage of disease, but further studies are necessary to evaluate this new insight.
References:
[1] Dougados, M., et al., Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis, 2014. 73(1): p. 62–8.
[2] Linseisen J, Bechthold A, Bischoff-Ferrari HA et al. Vitamin D und Prävention ausgewählter chronischer Krankheiten – Stellungnahme. In: V. DGfEe, ed. Bonn 2011.
[3] Merlino LA, Curtis J, Mikuls TR, Cerhan JR, Criswell LA, Saag KG, et al. Vitamin D intake is inversely associated with rheumatoid arthritis: results from the Iowa Women's Health Study. Arthritis Rheum. 2004;50(1):72–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4351

THU0140 SPECKLE TRACKING ECHOCARDIOGRAPHY EVALUATION OF CORONARY TERRITORIES IN MEXICAN MESTIZO PATIENTS WITH RHEUMATOID ARTHRITIS

D.Á. Galarza-Delgado[1], J.R. Azpiri-López[2], I.J. Colunga-Pedraza[1], F.J. Torres-Quintanilla[2], R.E. Ramos-Cázares[1], A. Valdovinos-Bañuelos[1], A. Martínez-Moreno[3], R.I. Arvizu-Rivera[3], R. Vera-Pineda[3], J.A. Cárdenas-de la Garza[3], M.A. Garza-Elizondo[1], M.A. Benavides-González[2], F. Hervert-Cavazos[2]. *[1]Rheumatology; [2]Cardiology; [3]Internal Medicine, Hospital Universitario "Dr. José Eleuterio González", UANL, Monterrey, Mexico*

Background: The main cause of death in patients with rheumatoid arthritis (RA) is atherosclerotic cardiovascular disease. Speckle Tracking Echocardiography (STE) is an imaging technique that analyses the local and global myocardial function by assessing the myocardial deformation (strain). This technique is useful in addressing early alterations in ischemic pathologies (1,3).
Objectives: The aim of this study was to analyze if longitudinal strain abnormalities correspond with vascular territories, and compare the results between RA-patients and matched controls.
Methods: An observational cross-section case-control study was designed. Patients that fulfilled the 1987 ACR and/or 2010 ACR/EULAR classification criteria for RA, were 40–75 years old, with no overlap syndromes and no history of atherosclerotic cardiovascular disease were included. The control group was integrated by age- and sex-matched subjects, with no rheumatologic or cardiovascular diseases. A standard transthoracic echocardiogram was performed by a

board-certified echocardiographer. Affection of coronary territories was compared between groups using longitudinal strain by speckle tracking according to the European Society of Cardiology and the American Society of Echocardiography recommendations.

Results: A total of 53 RA-patients and 24 control subjects were included. Demographic characteristics for each group are shown in table 1. There was no statistical difference in global longitudinal strain between RA-patients and controls (-20.86±2.82 vs -21.19±2.46, p=0.62). Comparison of longitudinal strain values of the three vascular territories evaluated between RA-patients and controls did not reach statistical difference (Table 2).

Table 1. Demographic characteristics

	RA group (n=53)	Control group (n=24)	*p*
Age, mean ± SD	55.54±9.11	52.81±6.61	0.172
Women, n (%)	51 (96.2)	26 (96.3)	0.988
Body Mass Index, mean ± SD	27.53±5.85	28.05±4.66	0.956
Hypertension, n (%)	18 (33.96)	5 (18.5)	0.149
Type 2 Diabetes mellitus, n (%)	7 (13.2)	4 (14.8)	0.844

Table 2 – Variable comparison

	RA group (n=53)	Control group (n=24)	*p*
Global Longitudinal Strain, mean ± SD	-20.86 ± 2.82	-21.19 ± 2.46	0.620
Anterior descendent territory, mean ± SD	-21.16 ± 3.13	-21.64 ± 2.91	0.510
Circumflex territory, mean ± SD	-20.12 ± 3.28	-21.09 ± 3.1	0.207
Right coronary territory, mean ± SD	-18.98 ± 2.38	-18.79 ± 2.37	0.735

Conclusions: Contrary to previous published evidence (1, 2), there was no statistical difference in global longitudinal strain between RA patients and controls. Coronary territories are not affected in RA patients in comparison with controls. Further studies with a larger cohort are necessary to determine the usefulness of strain in the evaluation of subclinical cardiovascular disease.

References:

[1] Fine et al. Evaluation of myocardial function in patients with rheumatoid arthritis using strain imaging by speckle-tracking echocardiography, Ann Rheum Dis. 2014 Oct;73(10):1833–9.
[2] Sitia S, Tomasoni L, Cicala S, et al. Detection of preclinical impairment of myocardial function in rheumatoid arthritis patients with short disease duration by speckle tracking echocardiography. Int J Cardiol 2012;160:8–14.
[3] Batir et al, Herz. 2015 Jun;40(4):669–74. Preclinical impairment of myocardial function in rheumatoid arthritis patients. Detection of myocardial strain by speckle tracking echocardiography.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5669

THU0141 CAN WE PREDICT THROMBOTIC TENDENCY IN RHEUMATOID ARTHRITIS: A THROMBOELASTOGRAPHIC ANALYSIS

S. Türk[1], D. Üsküdar Cansu[1], H. Üsküdar Teke[2], T. Kaşifoğlu[1], M. Akay[2], M. Bilgin[3], C. Korkmaz[1]. *[1]Eskişehir Osmangazi University School of Medicine, Rheumatology; [2]Eskişehir Osmangazi University School of Medicine, Hematology; [3]Eskişehir Osmangazi University School of Medicine, Bioistatistics, Eskişehir, Turkey*

Background: Arterial and venous thromboembolism were proven to be increased in cases with rheumatoid arthritis (RA) (1). It would be interesting to predict thrombosis in these patients by a laboratory test. Rotational thromboelastography (ROTEM) is a viscoelastometric clotting test to evaluate the kinetics of clot formation and fibrinolysis which provides global information on cellular and soluble procoagulant/anticoagulant protein interactions.

Objectives: Our aim was to determine the thrombosis predisposition in RA patients by thromboelastography and to identify the possible clinical and laboratory risk factors for thrombotic tendency in RA patients.

Methods: 85 RA patients (mean age: 54.12±13 yrs; female: 66 (77.6%) diagnosed based on 2010 ACR/EULAR classification criteria were sequentially recruited. Patients were receiving either conventional synthetic disease modifying antirheumatic drugs (csDMARD) or were receiving biological treatments. Age- and gender matched 35 healthy individuals were enrolled as a control group. Complete blood count (CBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels were measured and DAS-28 scores were calculated. ROTEM was applied at the same time and clotting time (CT, seconds), clot formation time (CFT, seconds), and maximum clot firmness (MCF, mm) were determined. A shorter CT and/or CFT values and/or a higher MCF levels imply tendency towards hypercoagulability.

Results: RA patients with a higher disease activity were found to have a shorter I-CFT and a higher I-MCF (p values p=0.020, p=0.033, respectively). Correlation analysis revealed shorter I-CFT and E-CFT and higher I-MCF and E-MCF in those with more active disease, hence indicating a higher tendency to thrombosis. DAS-28 score, high level of CRP, and increased platelet count were identified as variants affecting thromboelastography in favor of thrombosis susceptibility.

Conclusions: Disease activation in RA patients may lead to hypercoagulability, independent of the ongoing medication of patients. Considering the fact that the predictive value of ROTEM parameters for further thrombosis, additional studies are needed whether pro-thrombotic state in RA may herald thrombosis in the presence of inflammation.

References:

[1] Mameli A, Barcellona D, Marongiu F. Rheumatoid arthritis and thrombosis. Clin Exp Rheumatol. 2009;27:846–55.

Acknowledgements: None.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3807

THU0142 MATRIX METALLOPROTEINASE-3 AND ANTIBODIES (IGG) AGAINST OXIDIZED LOW-DENSITY LIPOPROTEIN LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Gerasimova, T. Popkova, M. Cherkasova, E. Alexandrova, A. Novokov. *V.A.NASONOVA Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Rheumatoid arthritis (RA) is associated with an unexplained increased cardiovascular risk. Matrix metalloproteinase-3 (MMP-3) is the most important protease involved in RA inflammation which may play a role in the development of cardiovascular events. Antibodies against oxidized low-density lipoprotein (oxLDL) are known to be involved in the development of inflammation and atherosclerosis. Specific role of MMP-3 and antibodies against oxLDL in cardiac pathology in RA patients (pts) is not well investigated.

Objectives: To compare MMP-3 and oxLDL-IgG antibody levels, as well as lipid profiles in pts with active RA and healthy controls.

Methods: Thirty nine RA pts (33 women and 6 men, median age 56,5 [49; 65] years), with active arthritis (mean disease duration 96 [48; 190] months; DAS28 5,8 [5,3;6,3]; HAQ 1,8 [1,3; 2,2]) were enrolled in the study. Twenty three pts (59%) received methotrexate, 5 (13%) – the combination of methotrexate with oral glucocorticoids, 10 (26%) - oral glucocorticoids monotherapy.

The control group consisted of 29 volunteers (21 women and 8 men, median age 58,5 [53; 62] years). Serum MMP-3 and oxLDL-IgG levels were measured by enzyme-linked immunosorbent assay (ELISA).

Results: Elevated MMP-3 levels were detected more frequently in RA pts (31/39 (79%)) vs healthy controls (2/29 (7%), $p<0,0001$). MMP-3 concentrations were higher in RA pts (57,0 [36,6; 114,3ng/ml), than in the control group subjects (13,4 [9,9; 20,4]mg/ml, $p<0,0001$). MMP-3 levels demonstrated significant correlation with ESR ($r=0,64$, $p<0,05$) and CRP ($r=0,52$, $p<0,05$) values.

OxLDL-IgG levels in RA pts and healthy controls did not differ significantly (290,3 [111,3; 608,6] mU/ml, and 228,1 [125,1; 338,8] mU/ml, respectively $p>0,05$). Rates of dyslipidemia were similar in RA pts (23/39 (59%) and control group subjects (15/29 (52%). Concentrations of lipids were also similar in both groups and were as follows: total cholesterol was 5,2 [4,9; 6,2] mmol/l in RA pts and 6,3 [5,1; 6,6] mmol/l in the control group; HDL cholesterol - 1,7 [1,4; 2,0] mmol/l and 1,7 [1,5; 2,1] mmol/l, LDL cholesterol - 3,3 [2,8; 4,0] mmol/l and 3,6 [3,0; 4,0] mmol/l, triglycerides - 1,3 [1,0; 1,6] mmol/l and 1,4[1,1; 1,8] mmol/l, the atherogenic index of plasma - 2,4 [1,8; 2,8] and 2,4 [1,9; 3,0], respectively. Showed no correlation between the levels of oxLDL-IgG and lipids in both groups. In the RA group, concentrations of HDL cholesterol were negatively correlated with MMP-3 ($r=-0,5$, $p<0,05$), C-reactive protein ($r=-0,53$, $p<0,05$), and DAS28 ($r=-0,4$, $p<0,05$).

Conclusions: RA pts exhibited higher serum MMP-3 levels than healthy individuals. OxLDL-IgG levels were similar in RA pts and healthy subjects. Obtained results suggest that MMP-3 and CRP may produce a negative impact on HDL-cholesterol levels in patients with active RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5217

THU0143 CHOLESTEROL EFFLUX CAPACITY OF HDL IS OTHERWISE IMPROVED BY DIFFERENT BIOLOGIC-DMARDS IN RHEUMATOID ARTHRITIS

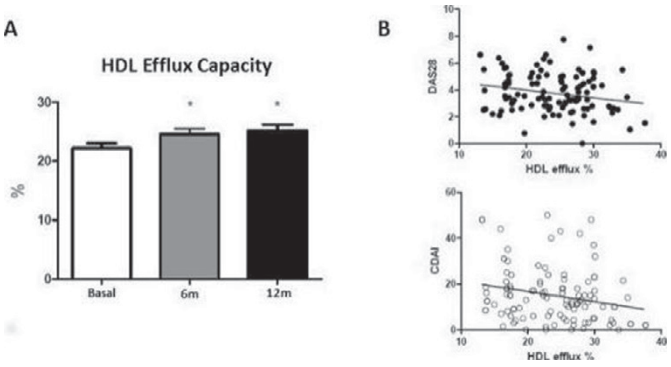
F. Cacciapaglia[1], S. Perniola[1], J. Härdfeldt[2], M. Nivuori[1], O. Magazzino[1], M.G. Giannotta[1], M. Giannini[1], M.G. Anelli[1], A. Moschetta[2], F. Iannone[1]. *[1]DETO - Unit of Rheumatology; [2]DIM - Clinica Medica "Cesare Frugoni", University of Bari, Bari, Italy*

Background: Rheumatoid arthritis (RA) patients have an increased mortality for cardiovascular (CV) events, not completely explained by impaired cholesterol levels or other traditional CV risk factor (1). Target therapy with effective control of systemic inflammation have been demonstrated to improve articular outcomes, but the effect on CV risk is still under investigation (2). The ability of high-density lipoprotein (HDL) to accept cholesterol from macrophages (HDL cholesterol efflux capacity; HDLc-EC) is a key step in reverse cholesterol transport, with significant consequences on incident atherosclerotic CV disease (3), but this marker in RA have still alternate evidence (4,5).

Objectives: To assess the effects of different biological DMARDs on HDLc-EC in RA

Methods: Disease activity data and blood samples from 40 patients with RA before and up to 12 months after starting a biologic therapy were collected. The study included patients starting intravenously administered Abatacept (ABA;n=10), Infliximab (INF;n=10), Tocilizumab (TCZ;n=10), and Rituximab (RTX;n=10), at approved dose regimens for RA treatment. HDLc-EC was measured on paired serum samples using THP-1 macrophages and a fluorometric assay for cholesterol measurement. ANOVA was used to compare paired continuous data, and Pearson' r value was calculated for correlations.

Results: Disease activity assessed by DAS28-CRP and CDAI significantly dropped during all treatments. No significant changes in total and high or light density cholesterol fractions were detected. HDLc-EC at baseline was 22±3% with a statistically significant increase up to 25±3% and 27±4% after 6 and 12 months of treatment, respectively ($P<0.001$) [Figure A]. Patients treated with INF and RTX demonstrated the higher rise in HDLc-EC, already after 6 months and lasting up to 12 months of treatment. ABA and TCZ treated patients after 6 months had a slight HDLc-EC rising, with a subsequent plateau. We observed an opposite correlation between HDLc-EC and disease activity by DAS28-CRP and CDAI (r=-0.2;P=0.01) [Figure B]. Finally, no CV events were detected during the study follow-up.



Conclusions: Biologic treatment can influence the HDLc-EC of RA patients, already after 6 months of therapy, and is associated with changes in disease activity and inflammatory status. Infliximab and Rituximab seem to have an enhanced impact on HDLc-EC. Future studies need to address the mechanisms beyond these intriguing findings.

References:

[1] Arts EE et al. Ann Rheum Dis. 2015;74:998–1003.
[2] Woodworth TG, den Broeder AA. Best Pract Res Clin Rheumatol. 2015;29:543–9.
[3] Rohatgi A. et al. N Engl J Med 2014;371:2383–93.
[4] Liao KP et al. J Am Heart Assoc. 2015;4(2).
[5] Ormseth MJ. et al. Arthritis Rheumatol. 2016;68:2099–105.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2680

THU0144 COGNITIVE FUNCTION OF PATIENTS WITH RHEUMATOID ARTHRITIS IS ASSOCIATED WITH DISEASE ACTIVITY BUT NOT CAROTID ATHEROSCLEROTIC CHANGES

G.-T. Kim[1], H.-S. Tag[1], Y.-K. Kim[1], S.-G. Lee[2], E.-K. Park[2], J.-H. Park[2], J.-W. Lee[3], S.-H. Kim[4], J.-H. Lee[5]. *[1]Department of Internal Medicine, Kosin University College of Medicine; [2]Department of Internal Medicine, Pusan National University Hospital; [3]Department of Internal Medicine, Busan St. Mary's Hospital; [4]Department of Internal Medicine, Inje University College of Medicine; [5]Department of Internal Medicine, Maryknoll Medical Center, Busan, Korea, Republic Of*

Background: Rheumatoid arthritis (RA) is a complex inflammatory disease that has features of atherosclerosis and cognitive decline. Although the relationship between atherosclerosis and cognitive impairment has been studied and replicated, whether cognitive deficits in RA can be attributed to their atherosclerotic changes is not well understood.

Objectives: This study investigated the cognitive function in patients with RA using the Korean version of the Consortium to Establish a Registry for Alzheimer's disease (CERAD-K) neuropsychological battery and evaluated whether cognitive function was affected by the carotid arterial atherosclerosis.

Methods: We examined seventy RA patients and forty healthy controls. RA activity was assessed by disease activity score with 28 joints-*erythrocyte sedimentation rate* (DAS28-ESR) and objective memory impairment was defined as a performance score of 1.5 standard deviations below the respective age-specific, education-specific, and sex-specific normative means for at least one of the four episodic memory tests in CERAD-K; the Word List Memory, Word List Recall, Word List Recognition, and Constructional Recall tests [1]. Carotid arteries were scanned for the presence of plaque and intima-media thickness (IMT). We assessed potential risk factors of cognitive impairment in RA patients using regression analyses.

Results: Of the CERAD-K subtests, there were a significant difference between the RA patients and healthy controls in verbal fluency (12.97±3.73 vs 15.48±4.57, respectively; p=0.004) and Boston Naming Test (11.50±2.08 vs 12.30±1.77, respectively; p=0.035). Carotid ultrasound revealed significantly more plaques in the RA patients than in the healthy controls (39% vs 15%, respectively; p=0.017). RA patients with memory impairment have significantly higher score of DAS28-ESR (4.14±0.99 vs 2.60±0.88, respectively; $p<0.001$), age (65.71±7.71 vs 58.50±11.33, respectively; p=0.009), and mean cIMT (0.56±0.10 vs 0.50±0.08, respectively; p=0.027) compared to RA patients without memory impairment. In multivariable regression analysis, CERAD-K total score showed a significant negative correlation with age (β=-0.415, $p<0.001$) or DAS28-ESR (β=-4.685, $p<0.001$), but no correlation was found between CERAD-K total score and presence of plaque or cIMT (Table 1).

Table 1. Regression analysis of mean CERAD-K total scores and clinical parameters

	Univariable analysis				Multivariable analysis		
Total (n=70)	Coefficient (β)	95% CI	P	R^2	Coefficient (β)	95% CI	P
Age (years)	-0.494	(-0.711, -0.277)	<0.001	0.232	-0.415	(-0.607, -0.224)	<0.001
Male (%)	2.121	(-5.079, 9.320)	0.559	0.005			
RF (IU/MI)	0.003	(-0.014, 0.020)	0.733	0.002			
hsCRP (mmol/L)	-0.074	(-0.284, 0.135)	0.482	0.007			
DAS28	-5.402	(-7.552, -3.252)	<0.001	0.270	-4.685	(-6.629, -2.742)	<0.001
TC	0.020	(-0.038, 0.078)	0.484	0.007			
Mean cIMT	-26.082	(-56.267, 4.103)	0.089	0.042			
Presence of plaque	-1.209	(-6.79, 4.371)	0.667	0.003			

RF: rheumatoid factor, hsCRP: high sensitivity C-reactive protein, DAS28: disease activity score 28, TC: total cholesterol, cIMT: carotid intima-media thickness

Conclusions: Our results indicate that disease activity of RA and aging contribute to cognitive impairment, but there was no association between cognitive function and clinical or subclinical carotid atherosclerotic changes in RA patients.

References:

[1] Lee JH, Lee KU, Lee DY, Kim KW, Jhoo JH, Kim JH, et al. Development of the Korean version of the consortium to Establish a Registry for Alzheimer's disease Assessment Packet (CERAD-K): clinical and neuropsychological assessment batteries. J Gerontol B Psychol Sci Soc Sci 2002;57:47–53.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3942

THU0145 IMPACT OF DIFFERENT FORMULATIONS OF "PATIENT GLOBAL ASSESSMENT" ON REMISSION CLASSIFICATION BY DISEASE ACTIVITY INDICES IN RHEUMATOID ARTHRITIS

G. Eugénio[1], R. Ferreira[1,2], C. Silva[3], C. Medeiros[1], J.A.P. Silva[1,3], C. Duarte[1,3]. *[1]CHUc-Huc; [2]UICiSA:E; [3]FMUC, Coimbra, Portugal*

Background: Patient global assessment (PGA) of disease activity is included in a large number of composite indices of disease activity and definitions of remission in Rheumatoid Arthritis (RA). However, the actual question is formulated in a variety of different ways according to the instrument considered.

Objectives: To evaluate how 6 different formulations of PGA affect patient estimates and impact upon disease activity and remission rates as assessed by 4 Disease Activity Indices.

Methods: Consecutive RA patients followed in a Rheumatology outpatient department were included in this cross-sectional study. Data collection comprised: 28 joint counts (tender and swollen), C-reactive protein (CRP) and 6 different PGA formulations. The chosen formulations were the ones stated in the: v1) Portuguese National Registry Reuma.pt, the locally used formulation; v2) ACR/EULAR provisional definition of remission (considered in this study as the "standard"); v3) CDAI and SDAI; v4) Disease Activity Score (DAS28) assessment of general health; v5) DAS28 assessment of disease activity (the currently used); v6) one, exploratory, developed by the investigators, including idiomatic cultural expressions. ACR/EULAR Boolean criteria, CDAI, SDAI, and DAS28-CRP (4v) were used to test how these 6 PGA formulations change the rates of remission. PGA differences were assessed by descriptive analyses (including patients with PGA $\leq$10 and $\leq$20mm) and Bland-Altman test.

Results: In total, 193 patients were included (82% female, mean (SD) age of 59 (13) years, mean disease duration of 12 (9) years and 31% under biologics). The average PGA ranged from 42.3 (25.3) to 48.1 (26.7)mm as measured in different formulations. The ACR/EULAR (v2) formulation yielded the largest proportion of

Table 1. Descriptive statistics of the 6 PGA's formulations (n=193)

PGA Formulation	Mean (SD)	PGA below cut-off n (%)	
		$\leq$10 mm	$\leq$20mm
v1 Reuma.pt	47.5 (28.0)	26 (13.5)	43 (22.3)
v2 ACR/EULAR	43.5 (27.9)	31 (16.1)	48 (24.9)
v3 CDAI/SDAI	47.2 (25.9)	23 (11.9)	34 (17.6)
v4 DAS28-GH	42.9 (25.3)	27 (14.0)	42 (21.8)
v5 DAS28-DA	42.3 (25.3)	28 (14.5)	44 (22.8)
v6 Investigators	48.1 (26.7)	22 (11.4)	35 (18.1)

patients scoring ≤10mm (16.1%), corresponding to a difference of up to 4.7% versus other PGAs. Similar results were found for the ≤20 cut-off (Table 1).
By using different PGA's formulations the rates of remission calculated with different indices can vary between 4.7% and 6.7% (Table 2).
Bland-Altman chart confirmed the low agreement between ACR/EULAR formulation and the other PGA formulations (p<.05), except for the DAS "general health" (p=.054).

Table 2. Remission rates according to four composite indexes with the 6 PGA's formulations (n=193)

PGA Formulation	Definition – n (%)			
	ACR/EULAR Boolean	SDAI	CDAI	DAS28 4vCRP
v1 Reuma.pt	19 (9.8)	32 (16.8)	33 (17.1)	97 (50.5)
v2 ACR/EULAR	25 (13.0)	36 (19.1)	39 (20.0)	100 (51.7)
v3 CDAI/SDAI	16 (8.3)	27 (14.1)	26 (13.5)	91 (47.3)
v4 DAS28-GH	20 (10.4)	29 (15.2)	33 (17.1)	99 (51.4)
v5 DAS28-DA	19 (9.8)	29 (15.2)	30 (15.5)	100 (51.7)
v6 Investigators	17 (8.8)	27 (14.1)	27 (14.0)	97 (50.0)
Max. dif. within definition	9 (4.7)	9 (4.7)	13 (6.7)	9 (4.7)

Conclusions: The use of different PGA formulations has clinical implications in disease activity, which, in turn, can influence therapeutic decisions. The establishment of a single standardised formulation seems warranted.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5518

THU0146 QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS - DEMOGRAPHIC AND SOCIO-ECONOMIC ASSOCIATIONS

H. Baharuddin[1], N. Zainudin[2], H. Mohd Yusoof[2], I.S. Lau[2]. *[1]Rheumatology, Universiti Teknologi MARA; [2]Rheumatology, Hospital Selayang, Selangor, Malaysia*

Background: The primary goal of treating patients with rheumatoid arthritis (RA) is to maximise long-term HRQol.[1]Quality of life (Qol) in patients with RA may be substantially impacted by their inability to perform daily activities, a shift in family roles, more restricted employment opportunities, increased financial burden and social dependency and reduced recreational activities.[2]
Objectives: To investigate the Qol among RA patients and its association with demographic and socioeconomic details.
Methods: This is a cross-sectional study conducted in a rheumatology outpatient clinic in Malaysia. Patients who fulfilled 2010 ACR/ EULAR classification criteria for RA were asked to answer WHOQOL-BREF questionnaire and specific questions on demographics and socio-economic details, during their attendance to rheumatology clinics. WHOQOL-BREF is a self-report quality of life questionnaire on individual's perception of quality of life and health, physical health, psychological, social relationships and environment domains.
Data was analysed using SPSS 20. Student's t-test was used to analyse the mean difference between two groups and chi-square test was used to analyse between 2 categorical data. Pearson correlation was used to analyse correlation between two groups of continuous data. p<0.05 was considered significant.
Results: The mean age of patients in this study was 53.10 (±14.3) years, with majority being females (80.4%) and married (70.6%). Half of the patients were Malays (49.0%). 51.0% rated overall quality of life as good and 41.2% rated overall health as satisfied. The mean transformed scores were 55.2 (±15.9) in physical health, 57.3 (±15.9) in psychological, 59.2 (±18.1) in social relationships and 58.2 (±15.2) in environment domains.
There were significant differences in the transformed scores for Malay (65.5±15.9) and non-Malay (53.1±18.2) in the social relationship domain; t (49) =2.58, p=0.01, and for education at secondary level and above (65.9±14.9) and primary level (48.0±16.6), t(49)=-3.87, p<0.01. We found no significant association between race and education level; 17 (53.1%) Malays and 15 (46.9%) non-Malays had education level of secondary and higher, X^2(1, N=51) =0.58, p=0.48. Patients with household income of less than RM 3, 000 had significantly lower scores compared to those with higher household income, in overall perception of quality of life (3.3±0.9 vs 4.0±0.6; t(49)=-2.8, p<0.01), overall perception of health (2.9±0.9 vs 3.6±0.7, t(49)=-2.97, p<0.01), physical health domain (51.2±16.2 vs 63.8±11.6, t(49)=-2.78, p=0.01) and psychological domain (53.3±16.3 vs 66.1±10.9, t(49)=-2.85, p=0.01).
Conclusions: Patients with RA perceived their Qol to be moderate in all domains. Social relationship was perceived to be better in Malays and patients with higher educational level. Low income was significantly associated lower overall quality of life and health, physical and psychological health.
References:
[1] Smolen JS, Breedveld FC, Burmester GR et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. Ann Rheum 2015; 0, 1–13.
[2] Matcham F, Scott IC, Rayner L et al (2014). The impact of rheumatoid arthritis on quality-of-life assessed using the SF-36: A systemic review and meta-analysis. Seminars in Arthritis and Rheumatism 2014; 44: 123–130.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7026

THU0147 THORAX CT FINDINGS IN A LARGE COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS: HUR-BIO REAL LIFE RESULTS

A. Sari, B. Armagan, A. Erden, L. Kilic, O. Karadag, A. Akdogan, S. Apras Bilgen, I. Ertenli, U. Kalyoncu, S. Kiraz. *Rheumatology, Hacettepe University School of Medicine, Ankara, Turkey*

Background: Lungs are one of the target organs in rheumatoid arthritis (RA) patients. Interstitial lung disease (ILD), rheumatoid nodules, pleural effusion, bronchiectasia and small airway disease are common manifestations of lung involvement.
Objectives: Objective of this study was to evaluate distribution of Thorax CT findings and treatment features in RA patients registered in a biologic registry.
Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a prospective, single center database of biological treatments including 1229 RA patients by August 2016. Demographics, clinical and serological features of patients and thorax CT results performed in Hacettepe University between 2000 and 2016 were retrospectively evaluated. Patients whose CT was reported as small airway disease or ILD by radiologists, were evaluated as a subgroup. Data included type of biological treatments before diagnose of ILD and at last control as well.
Results: Among 1229 patients (78.8% female), mean age was 53.3±12.9 and disease duration was 11.4±7.9. Thorax CT had been performed in 203 (16.5%) patients. Distribution of pathologic findings in thorax CT was represented in Table 1. 29 patients (%2.4) were diagnosed as ILD with regard to CT findings. Patients with ILD were older (64.5±6.7 vs 60.6±10.1, p=0.039) and more frequently positive for rheumatoid factor (RF) (25/27 (%92.6) vs 77/121 (%63.3), p=0.003) than patients without ILD. ILD was detected before beginning of biologics in 11 (37.9%) patients and during biologic treatment in 18 (62.1%) patients. Honeycombing was seen in 10 (34.5%) patients. First choice of biologic agent was RTX in 10 (34.5%) and TNFi in 19 (65.5%) patients. In ILD patients, mean follow-up duration was 51±31 months and first biologic was switched to another in 16 (55.2%) of patients. At the last follow-up visit 19 (65.5%) patients were on rituximab, 3 (10.3%) patients were on abatacept and 7 (24.1%) were on TNFi. Small airway disease was detected in 19 (9.3%) patients. History of smoking was present in only 4 (21.0%) of patients with small airway disease.

Table 1. Distribution of thorax CT findings

Thorax CT finding	N (%)
Interstitial thickening	13 (6.4)
Reticular densities	31 (15.3)
Ground glass opacities	33 (16.3)
Nodules	35 (17.3)
Effusion	18 (8.9)
Bronchiectasia	46 (22.7)
Traction bronchiectasia	17 (8.4)

Conclusions: Broncіectasia, rheumatoid nodules, small airway disease and ILD were the most frequent CT findings of RA patients. Rituximab was the choice of first biologic treatment in one third of patients, however two-thirds of patients were on rituximab therapy at the last follow-up visit. Lung involvement stands out as an important factor in selection of biologics.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4076

THU0148 INCREASE OF NIGHT QT-INTERVAL DURATION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB DURING 12-MONTH FOLLOW-UP

I.G. Kirillova, D. Novikova, E. Luchikhina, E. Markelova, H. Udachkina, N. Demidova, A. Misiyuk, T. Popkova, A. Volkov, L. Denisov, D. Karateev. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Objectives: to evaluate dynamic of ECG parameters in RA pts treated with tofacitinib (TOFA) during 12-month follow-up.
Methods: After 12-m follow-up the ECG parameters by 12 lead ECG and 24h ECG was assessed in 28 RA pts treated with TOFA (22 women, median age 54 [40;62] years, disease duration 39,5 [16,5;60,0] m, moderate to high activity (DAS28–5.1 [4.6;6.0], SDAI–26 (21;34)), positive for ACCP (75%)/RF (79%), who were non-responders to MTX at least 15 mg/week and/or other synthetic DMARDs and bDMARDs. TOFA therapy was started in all pts with dose 5 mg BID per os followed by the dose escalation to 10 mg BID in 8 (29%) pts. TOFA used in combination with MTX in 27 (96%) pts, leflunomide in 1 (4%). Low-dose oral corticosteroids (<10 mg/day prednisone or equivalent) were received by 9 (35%) pts. Remission or LDA was achieved in 55% pts (DAS28), 77% (SDAI). At baseline the most of pts had multiple CVRF and subclinical organ damage (arterial hypertension-67%, overweight-57%, abdominal obesity-61%, physical inactivity-64%, smokers/ex-smokers-25%/21%, menopausal status-59%, DM type 2–7%, mSCORE≥5%>21%, subclinical carotid atherosclerosis-64%, cardiac heart failure with preserved ejection fraction-7%. Cardioprotective therapy received 16 (57%) pts (beta-blockers–7, angiotensin II receptor type 2/ACE inhibitors–11, statins–11, dihydropyridine calcium channel blockers-7).
Results: There was no difference in heart rate (HR), QTc interval duration,

QRS duration measured by 12-lead ECG in RA pts treated with TOFA (table 1). However, an increase in PQ interval duration was observed (p=0,04). There were significantly decrease of mean HR (p<0,003), increase of QRS duration (p<0,03), QTc (p<0.03), night QTc (p<0,02) in 24 h ECG ambulatory recording. HR, PQ, QTc duration were changed independently of beta-blockers therapy. The number of pts with QTc≥440 ms increased from 11% to 21% (p>0.05). A change in QTc duration correlated negatively with dynamics of DAS 28, SDAI (r=-0,4, p<0,05), DM (r=0,5, p<0,02), dBP (r=-0,4, p<0,04). There were also significantly increase number of ventricular premature beats (p<0,03).

Table 1. ECG characteristics of pts with RA treated with TOFA

	Baseline	After 12 months
12-lead ECG		
Heart rate, bpm	71 [64;81]	69 [61;78]
PQ, ms	133 [126;131]	150 [130;160]*
QRS, ms	83 [79;89]	84 [80;91]
QTc, ms	421 [406;434]	410 [398;420]
24 h ECG		
Heart rate, bpm	78 [70;84]	74 [65;80]*
QRS, ms	82 [73;91]	85 [73;92]*
QTc, ms	409 [402;425]	415 [406;427]*
QTc night, ms	414 [400;434]	420 [408;437]*
VPB pts, n (%)	18 (66)	22 (78)
Ventricular premature beats, n	14 [7;50]	280 [15;3423]*

Data are presented in median values and IR (unless otherwise noted), *p<0,05 before and after TOFA treatment (nonparametric paired Wilcoxon test).

Conclusions: A significant decrease in HR and an increase in QRS, night QTc interval duration, number of ventricular premature beats by 24h ECG were observed in RA pts treated with tofacitinib (TOFA) during 12-month follow-up. QTc duration correlated with dynamic of disease activity, DM type 2 and diastolic BP.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5119

THU0149 A CLINICAL AND PATHOLOGICAL CHARACTERIZATION OF METHOTREXATE-ASSOCIATED LYMPHOPROLIFERATIVE DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Nakano [1], A. Nawata [1,2], S. Nakayamada [1], S. Iwata [1], K. Hanami [1], S. Kubo [1], I. Miyagawa [1], M. Yoshikawa [1], K. Saito [1], Y. Tanaka [1]. *[1] The First Department of Internal Medicine; [2] Department of Pathology, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan*

Background: Methotrexate (MTX) is used as an anchor drug for the treatment of rheumatoid arthritis (RA). Patients with RA have a modestly increased risk of developing lymphoproliferative disorders (LPD). Furthermore, although sometimes spontaneous regression occurs after withdrawal of MTX, LPD developed during the treatment with MTX is broadly defined as MTX-associated LPD (MTX-LPD).
Objectives: To characterize the risk factors concerning MTX-LPD and to consider optimal treatment after occurrence of LPD in patients with RA.
Methods: We retrospectively evaluated 51 RA patients with LPD from 2006 to 2015 in our institution. MTX-LPD patients were divided into two groups; regressive LPD after MTX cessation (N=27) and persistent LPD though MTX was tapered (N=24), and the clinical characteristics, pathology and treatment outcomes were compared. EBV infection and IL-6 receptor (IL-6R) expression were analyzed by in situ hybridization and immunohistochemistry.
Results: There was no significant difference in disease duration, stage, disease activity of RA, the positive rate of Epstein–Barr virus-encoded small RNAs, EBERs (42.7 vs 50.0%) and treatment with TNF-inhibitors (40.7 vs 45.8%) between regressive LPD and persistent LPD. Age of LPD onset (59.1 vs 68.3), CRP (2 vs 5 mg/dl) and the weekly MTX dose (10.9 vs 8.4 mg/w) significantly differed between the groups. Of note, IL-6R was highly expressed in both group (75.0 vs 66.7%). Among regressive LPD, 3 patients developed DLBCL later. persistent LPD showed poorer prognosis and worse mortality than regressive LPD. An older age and anemia were poor prognostic factors. Of 51 patients, 41% achieved sustained low disease activity (LDA) with other DMARDs except MTX. Nine of 10 patients refractory to DMARDs were controlled by tocilizumab (TCZ) and kept LDA.
Conclusions: Taken together, it seems unreasonable to be lump the persistent-group into the same category as MTX-LPD. The high expression rate of IL-6R and the high responsiveness to TCZ suggest that IL-6/IL-6R is likely to play a role in the development of LPD in patients with RA.
Disclosure of Interest: K. Nakano: None declared, A. Nawata: None declared, S. Nakayamada: None declared, S. Iwata: None declared, K. Hanami: None declared, S. Kubo Speakers bureau: Bristol-Myers, I. Miyagawa: None declared, M. Yoshikawa: None declared, K. Saito: None declared, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, Consultant for: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, GlaxoSmithKline, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, GlaxoSmithKline
DOI: 10.1136/annrheumdis-2017-eular.4660

THU0150 OPTIMIZING COMORBIDITY RISK MANAGEMENT IN RA BY TRANSLATING A NURSE-LED INTERVIEW INTO AN EASILY INTERPRETABLE TRAFFIC LIGHT SYSTEM

K. Krüger [1], R. Eder [2], C. Müller [3], R. Hecker [3]. *[1] Rheumatologisches Praxiszentrum St. Bonifatius, München; [2] Rheumapraxis am Spitaltor, Deggendorf; [3] Abbvie Deutschland Gmbh & Co. Kg, Wiesbaden, Germany*

Background: Due to its inflammatory nature, rheumatoid arthritis (RA) is associated with a variety of comorbidities and individual risk factors [1]. The benefit of a nurse-led programme on RA comorbidity management has been reported recently [2].
Objectives: To describe a new assessment tool for patient risk management and report the difference between structured versus expert guided assessment following standard of care in a construct-validation cohort.
Methods: The ongoing cluster randomized multicentre study ERIKO is longitudinally assessing individual risk profiles of patients with RA in Germany. The aim of this study is to test the benefit of applying a nurse-led scoring algorithm for individual risk profiles followed by a structured patient consultation (active arm) as compared to local standard of care.
The ERIKO-Score was calculated by rating validated assessment tools and treatment guidelines and translating their outcome into a three-level ordinal score defined by the categories low, intermediate or high risk, including nominal weights for risk management (e.g. condition is being treated with goals achieved or not). Scores were interpreted numerically by rating categories with 0, 1 and 2 points, respectively.
We included cardiovascular (CV) risk (ESC-guideline), infection risk (RABBIT risk calculator), vaccination status (guideline), fracture risk (FRAX), tooth status (PSI), depression- (PHQ-9) and health-related quality of life (hrQoL, RAID). The same risk categorization was prompted in all centres at the screening visit without providing the rating tools.
This analysis compares SOC ratings from the screening visit (month zero) with the baseline ERIKO-scores at month three in the active arm. No statistical hypothesis testing was performed in this analysis.
Results: This analysis included 283 patients from 31 centres specialized in rheumatology care randomized to the active study arm. 82.3% were female with a mean age of 57.8 years (sd 12.1) and a mean DAS28 of 2.6 (sd 1.1). The mean total ERIKO-Score was slightly higher at baseline as compared to applying the scoring algorithm on SOC ratings at the screening visit (5.33 +- 1.95 vs. 4.32 +- 2.61, respectively, table 1). The discrepancy was mainly driven by CV risk, vaccination status, tooth status and depression risk, that were more often rated worse by applying the ERIKO score than by SOC, while infection- and fracture risk were more frequently rated lower by the ERIKO-Score (table 2). The strongest discrepancy between SOC ratings and ERIKO-Score (Δ =2 points) were observed for tooth status (N=54), CV risk (N=25) and vaccination status (N=25) (table 2). SOC ratings were strongly based on expert opinion with the most frequently cited tools being vaccination guidelines (38.9%), bone mineral density measurement (BMD) (39.6%) and RABBIT-infection risk-score (23.1%).

Table 1 ERIKO Score at baseline visit (3 months)

N = 283 [5]	Ordinal Risk Rating				Numeric interpretation	
Dimension	missing [%(N)]	Low [%(N)]	Intermediate [%(N)]	High [%(N)]	Median (IQR)	Mean (sd)
CV risk	9.2 (26)	27.9 (79)	26.5 (75)	36.4 (103)	1 (2)	1.1 (0.80)
Vaccination status	9.2 (26)	15.9 (45)	50.5 (143)	24.4 (69)	1 (1)	1.1 (0.66)
Infection risk	9.2 (26)	79.9 (226)	10.2 (29)	0.7 (2)	0 (0)	0.1 (0.36)
Risk of major osteoporotic fracture	9.9 (28)	52.7 (149)	32.9 (93)	4.6 (13)	0 (1)	0.5 (0.59)
Tooth status	11.3 (32)	5.3 (15)	55.1 (156)	28.3 (80)	1 (1)	1.3 (0.56)
Depression risk	9.2 (26)	46.3 (131)	39.6 (112)	4.9 (14)	0 (1)	0.5 (0.60)
hrQoL	9.2 (26)	33.9 (96)	47.3 (134)	9.5 (27)	1 (1)	0.7 (0.64)

[5] n = 26 without data at baseline.

Table 2 Discrepancy between ERIKO-Score and ratings following SOC (baseline vs. screening)

	Δ = 1 or 2 points (total)			Δ = 2 points (low vs. high)	
Dimension	No difference [%(N)]	SOC risk lower [%(N)]	SOC risk higher [%(N)]	SOC risk lower [%(N)]	SOC risk higher [%(N)]
CV risk[a]	35.0 (99)	44.2 (125)	10.2 (29)	8.5 (24)	0.4 (1)
Vaccination status[b]	34.6 (98)	38.5 (109)	17.7 (50)	7.4 (21)	1.4 (4)
Infection risk[b]	63.6 (180)	6.0 (17)	21.2 (60)	0	3.2 (9)
Risk of major osteoporotic fracture[b]	36.8 (104)	15.2 (43)	38.9 (110)	1.4 (4)	3.5 (10)
Tooth status[a]	18.4 (52)	47.7 (135)	23.3 (66)	15.5 (44)	3.5 (10)
Depression risk[b]	48.4 (137)	30.7 (87)	11.7 (33)	3.2 (9)	3.2 (9)
hrQoL[b]	64.6 (166)	18.0 (51)	14.1 (40)	2.1 (6)	0.4 (1)

[a] n = 30 without data at screening or baseline; [b] n = 26 without data at baseline

Conclusions: A nurse-led comorbidity risk assessment in rheumatology practices seems feasible. Applying the ERIKO-Score based on validated tools led to a

higher risk grading than the predominantly expert-opinion based SOC. Construct validation of the ERIKO-Score is ongoing.

References:
[1] Dougados M, et al. Ann Rheum Dis 2014;73:62–8.
[2] Dougados M, et al. Ann Rheum Dis 2015;74:1725–33.

Acknowledgements: We are grateful to Dr. Imma Fischer (Tübingen) for statistical support.

Disclosure of Interest: K. Krüger Consultant for: AbbVie Deutschland GmbH & Co. KG, Speakers bureau: AbbVie Deutschland GmbH & Co. KG, R. Eder Consultant for: AbbVie Deutschland GmbH & Co. KG, C. Müller Shareholder of: Abbvie Inc., Employee of: AbbVie Deutschland GmbH & Co. KG, R. Hecker Shareholder of: Abbvie Inc., Employee of: AbbVie Deutschland GmbH & Co. KG

DOI: 10.1136/annrheumdis-2017-eular.3395

THU0151 ACPA ARE ASSOCIATED WITH LOW BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS

L. Bautista Aguilar, A. Salmoral Chamizo, R. Jimenez Gasco, I. Gomez Gracia, P. Font Ugalde, M.L. Ladehesa Pineda, E.C. Lopez Medina, L. Perez Sanchez, A. Escudero Contreras, E. Collantes Estevez. *Rheumatology, Reina Sofia University Hospital/IMIBIC/ University of Cordoba, Cordoba, Spain*

Background: Several studies have related ACPA with the presence of bone erosion in rheumatoid arthtitis patients as they induce the differentiation and activation of osteoclasts

Objectives: Our main aim is to evaluate the association of ACPA with bone mineral density (BMD) in RA

Methods: Case-control study of 73 RA patients (2010 EULAR criteria) and a long standing disease of 5 years. Demographic and clinical variables were collected. BMD values using densitometry at the lumbar (CL), hip (CT) and femoral neck (CF) were collected. The presence of low bone mineral density (osteopenia: tscore$\leq$-1) and ACPA levels were compared using logistic regression analysis, adjusting variables related to BMD: age, sex, menopause, body mass index (BMI), habit Smoking, disease duration, daily corticoid doses, methotrexate treatment and inflammatory disease activity (DAS28)

Results: A group of 73 patients were included (14 men) with a mean age of 66,45±10,41 years, mean body mass index 28,48±5,22 kg/m^2, mean long standing disease of 2,28±1,75 years and mean DAS 28 of 3,17±1,18. A total of 29 patients were negative for ACPA compared to 44 patients that were positive for ACPA. Osteopenia in lumbar spine was found in 82.2% of patients 65.8% hip and 75.3% in femoral neck. Logistic regression was performed without finding statistically significant association between osteopenia and inflammatory activity (DAS 28), vitamin D levels and positive rheumatoid factor, adjusted for variables that can modify BMD. ACPA Positive (any titer) were associated with the presence of lumbar spine osteopenia (OR 7.19, 95% CI 1.77–29.17) (p=0.006), hip (OR 15.17, 95% CI 3.96–58.18) (p=0.001) and femoral neck (OR 3.76; 95% CI 1.20–11.82) (p=0.023). In addition, a simple variance analysis (ANOVA) was performed to compare T scores and ACPA levels divided into three categories: $\leq$25U/mL, 25–300U/mL and$>$300U/mL. ACPA group $\leq$25U/mL differed in mean T score values in lumbar spine, hip and femoral neck. No differences were found between ACPA positive patients with low and high levels for T score values.

Conclusions: ACPA positivity in RA is associated with an increased risk of osteopenia in lumbar spine, hip and femoral neck independently of other variables that may modify bone mineral density. These data suggest that ACPA may play a role in bone remodeling

References:
[1] Referencias: Harre et al.J Clin Invest (2012), 122(5):1791–1802.
[2] Bugatti et al. Arthritis Research & Therapy (2016), 18:226.
[3] Geusens and Lem. Arthritis Research & Therapy (2011), 13:242.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4422

THU0152 WHO ARE THE PATIENTS WITH RHEUMATOID ARTHRITIS (RA) WHO ARE GETTING COMORBIDITY SCREENING PROCEDURES IN ACCORDANCE WITH GUIDELINES? A STUDY OF 769 ESTABLISHED RA PATIENTS

L. Gossec, F. Foissac, M. Soubrier, F. Fayet, T. Bardin, C. Beauvais, G. Chales, I. Chary-Valckenaere, E. Dernis, L. Euller-Ziegler, R.-M. Flipo, P. Gaudin, S. Guis, T. Marhadour, X. Mariette, G. Mouterde, S. Pouplin, P. Richette, A. Ruyssen-Witrand, T. Schaeverbeke, J. Sibilia, M. Dougados. *COMEDRA working group, Paris, France*

Background: Patients with RA are either more at risk of, or less well screened for, several comorbidities including cardiovascular (CV) risk, cancer, infections and osteoporosis.[1] Recommendations have been developed on how and at what frequency to screen for comorbidities in RA patients.[2]

Objectives: to characterise patients who are being screened correctly (i.e., in accordance with recommendations).

Methods: *Study design:* This was an open long-term (3 years) extension of the COMEDRA 6 month randomized controlled trial in which patients with definite, stable RA were visiting a nurse for comorbidity assessment and screening counselling.[3] For this analysis, only the final visit data were used cross-sectionally. *Assessment of comorbidity screening:* A score was developed to quantify comorbidity screening procedures in accordance with guidelines:[4] this score gives 50 points to CV risk screening, 20 points to cancer screening, 20 points to pneumococcus and influenza vaccination and 10 points to osteoporosis screening. The score ranges 0–100 and 0 indicates optimal screening. *Factors associated with optimal screening:* demographic and disease characteristics were compared between patients considered well-screened (lowest tertile for screening score) versus other patients. *Statistical analysis:* Variables with p$<$0.20 in univariate analysis were entered into the multivariate analysis using a backward stepwise logistic regression.

Results: 769 patients were assessed: mean (±SD) age 62 (±11) years, mean disease duration 17 (±10) years; 614 (80%) were women and 535 (70%) were receiving a biologic. Disease was well-controlled (mean DAS28 2.8±1.3). The mean comorbidity screening score was 24.3 (±17.8) (range, 0–100). The 316 patients (41% of all patients) in the lowest tertile for this score (i.e., with a score $\leq$15) were less often smokers: odds ratio [95% confidence interval] 0.45 [0.28 – 0.72], were more often treated for hyperlipidemia (2.58 [1.85 – 3.61]), and were more often treated with a biologic (1.97 [1.4 – 2.76]).

Conclusions: Comorbidity screening is suboptimal in RA. Patients who were better screened were more frequently already followed-up for hyperlipidemia and were more frequently receiving biologics but more less frequently smokers. Thus it seems getting optimal screening may reflect both patient characteristics but also physician attention to comorbidity in certain situations. Empowering patients to be responsible for the comorbidity screening reminders should be explored.

References:
[1] Ref 1. Baillet A, Gossec L et al. Ann Rheum Dis. 2016;75(6):965–73.
[2] Ref 2. Gossec L et al. Joint Bone Spine. 2016;83(5):501–9.
[3] Ref 3. Dougados M, Soubrier M et al. Ann Rheum Dis. 2015;74(9):1725–33.
[4] Ref 4. Gossec L et al. Arthritis Rheumatol. 2016; 68 (suppl 10): abstract. http://acrabstracts.org/abstract/screening-for-and-management-of-comorbidities-after-a-nurse-led-program-results-of-a-3-year-longitudinal-study-in-776-established-ra-patients/.

Acknowledgements: grant from Roche France and from the French National Research Program (PHRC AOM 12072).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2991

THU0153 VASCULAR MORBIMORTALITY IN RHEUMATOID ARTHRITIS (RA) PATIENTS AND ITS RELATION WITH VASCULAR STUDY

L. Montolio-Chiva, M. Robustillo-Villarino, C. Vergara-Dangond, M. Aguilar-Zamora, E. Valls-Pascual, D. Ybáñez-García, A. Martínez-Ferrer, V. Núñez-Monje, J.J. Alegre-Sancho. *Rheumatology, Hospital Universitario Dr. Peset, Valencia, Spain*

Background: RA patients have a higher risk of vascular events, especially cardiac ones. Besides, mortality in these patients is 54% higher than the general population. Nowadays, we have non-invasive techniques that allow us to detect subclinical vascular damage.

Objectives: To describe subclinical vascular affection in a sample of RA patients and to explore its relationship with mortality and with the development of vascular events.

Methods: Ambispective observational study with analytical components. We included, consecutively, RA patients controlled in a tertiary hospital. We gathered demographic (sex, age, body mass index [BMI]), clinical (traditional vascular risk factors, previous vascular events), and analytical variables (atherogenic index, glomerular filtration [GF] [MDRD], CRP, ESR). Other variables were collected retrospectively from the electronic medical record. We estimated the modified SCORE. We explored the extracranial branches of the carotid artery with an Esaote MyLab70XVG ultrasound device with a linear probe (7–12mHz) and an automated program measuring intima media thickness (IMT) by radiofrequency ("Quality intima media thickness in real-time, QIMT"), and the presence of atheroma plaques, as per the Mannheim consensus, was registered. We also determined pulse wave velocity (PWV) by a validated MobilOGraph® device. We considered an IMT$>$900 $\mu$and a PWV$\geq$10m/s as pathologic values. We prospectively collected mortality and the development of new vascular events over three years. Statistical analysis was performed using SPSS 17.0 software.

Results: We included 198 patients, excluding 13 because of previous vascular events. The mean age was 65,8 years (DE 13,3) and most of them were women (76,2%). The mean BMI was 27,29 (DE 4,84). 27% were smokers, 42,7% hypertensive, 46,7% dyslipemic and 10,8% were diabetic. The mean duration of RA was 17,37 years. 74,6% of patients were seropositive (RF and/or ACPA) and 75, 5% had erosions. 74,6% received glucocorticoids, 58,4% NSAIDs, 98,9% DMARDs and 35,7% biologic therapies. The mean CRP and ESR were 9,45mg/L (DE: 32,2) and 14,04mm/h (DE:14,46), respectively. The mean modified SCORE was 1,81 (DE: 1,79).

Regarding the vascular study, 48,6% of the patients had atheroma plaques, 31,7% had a pathologic PWV with a mean value of 9,13 (DE 2,12), and 16,7% had a pathologic IMT with a mean value of 754 μ(DE 168,52).

During 3 years of follow up, we registered 26 (14,1%) vascular events: 9,7% cardiac, 2,1% cerebral and 2,2% peripheral. There were 5 deaths: 3 vascular, 1 infectious and 1 respiratory. The development of vascular events was related with the presence of atheroma plaques (p 0,008) and with pathologic PWV (p

0,028), as well as with the presence of erosions, GF, HTA and dyslipidemia. The appearance of cardiac events was related, also, with the use of NSAID (p 0,041). The presence of a pathologic IMT (p 0,032) and HTA (p 0,044) were the only variables related with death from any cause.

Conclusions: A combination of carotid ultrasonography and arterial stiffness study can help us to best identify patients with RA who have an increased risk of dying or developing a vascular event.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3469

THU0154 ASSOCIATION BETWEEN PLASMA LIPIDS, DISEASE ACTIVITY AND PCSK9 LEVELS IN RA PATIENTS

M. Heslinga[1], G. Lambert[2], A. Thedrez[3], J. Kastelein[4], M. Nurmohamed[1,5]. *[1]Amsterdam Rheumatology and immunology Center | Reade, Amsterdam, Netherlands; [2]University of la Reúnion, Saint-Denis; [3]University of Nantes, Nantes, France; [4]Academic Medical Center; [5]Amsterdam Rheumatology and Immunology Center | VU University Medical Center, Amsterdam, Netherlands*

Background: Patients with rheumatoid arthritis (RA) are at increased cardiovascular risk with contribution of both inflammation and traditional risk factors. Dyslipidemia is an important risk factor and lipid-lowering therapy plays a key role in cardio-preventive treatment. A new class of low density lipoprotein cholesterol (LDL-C) lowering drugs, proprotein convertase subtilisin/kexin type 9 (PCSK9)-inhibitors are now emerging. In view of a lower rate of musculoskeletal side effects these drugs might be preferred over statins in patients with RA. Active inflammation in RA leads to a decline in lipid levels, but the relation between inflammation and PCSK9 levels is unknown.

Objectives: To assess PSCK9 levels in RA patients, and the relationship with lipid levels and disease activity.

Methods: PSCK9 levels were assessed using ELISA in 97 randomly selected patients. Lipid profile assessment comprised TC, HDL-C, LDL-C and triglycerides. Disease activity was assessed using disease activity score of 28 joints (DAS28).

Results: The mean age of RA patients was 54.5 years (± 10.8) and they were predominantly female (74.2%). The mean PCSK9 value in RA patients was 214.75 (± 73.3), which is similar to that in the general population [1]. PCSK9 values were associated with TC (corrected B 22.34, 95% CI 6.80–37.88, p0.005) and triglycerides (corrected B 21.02, 95% CI -0.84–42.89, p0.044) (table 2). 77 patients had low disease activity (DAS28 ≤3.2), 11 patients had medium disease activity (DAS28 >3.2 and ≤5.1) and 20 patients had highly active disease (DAS28 >5.1). Mean PCSK9 values were 213.01, 246.96 and 258.30 ng/mL, respectively. Patients with active disease had a higher PCSK9 level (corrected B 42.555 95% CI 0.769–84.341, p 0.046) compared to patients with low disease activity (table 1).

Table 1. Relation between plasma lipids, disease activity and PCSK9 levels

	B	95% CI	P-value
TC	21.86	7.03–36.69	0.004
*	21.88	6.52–37.24	0.006
**	22.34	6.80–37.88	0.005
Triglycerides	21.02	-0.84–42.89	0.059
*	19.81	-2.91–42.53	0.087
**	24.81	0.68–48.94	0.044
HDL-C	13.03	-14.97–41.03	0.358
*	14.57	-14.61–43.79	0.324
**	11.04	-20.15–42.23	0.484
LDL-C	14.23	-1.93–30.38	0.084
*	13.59	-2.81–29.99	0.103
**	15.22	-1.51–31.95	0.074
TC/HDL ratio	6.28	-4.4–16.9	0.245
*	5.95	-5.12–17.03	0.289
**	8.64	-3.36–20.64	0.156
DAS28 (low vs. high disease activity)†	45.284	4.865–85.884	0.029
*	42.028	0.652–83.405	0.047
**	42.555	0.769–84.341	0.046

*Corrected for age and gender, **Corrected for age, gender and BMI. †Low disease activity: DAS28 >3.2, and high disease activity: DAS28 ≤5.1. BMI = Body Mass Index, DAS28 = Disease activity score of 28 joints, HDL = high density lipoprotein, LDL = low density lipoprotein, TC=Total cholesterol.

Conclusions: PCSK9 levels in RA are similar to the general population. RA patients with active disease had higher PCSK9 levels compared to patients with low disease activity. Altogether, PCSK9 inhibitors could be an alternative treatment for dyslipidemia in RA patients who experience side effects of statins, albeit that a formal trial still has to be conducted in this category of patients.

References:

[1] Lambert G, Petrides F, Chatelais M et al. J Am Coll Cardiol. 2014 Jun 10;63(22):2365–73.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2121

THU0155 IMPACT OF BASELINE MODIFIED RHEUMATIC DISEASE COMORBIDITY INDEX (MRDCI) ON DRUG SURVIVAL AND EFFECTIVENESS OF BIOLOGICAL DRUGS IN PATIENTS AFFECTED WITH RHEUMATOID ARTHRITIS (RA), SPONDYLOARTHRITIS (SPA), AND PSORIATIC ARTHRITIS (PSA) IN REAL-WORLD SETTINGS

M. Fornaro[1], M. Di Carlo[2], S. Gentileschi[3], M.G. Giannotta[1], L. Cantarini[3], F. Salaffi[2], G. Lapadula[1], F. Iannone[1]. *[1]Department of Rheumatology, University of Bari, Bari; [2]Rheumatology Department, Polytechnic University of Marche, Jesi; [3]Research Center of Systemic Autoinflammatory Diseases and Behçet's Disease Clinic, Department of Medical Sciences, Surgery and Neurosciences, University of Siena, Siena, Italy*

Background: The overall assessment of patients with systemic arthritis can not exclude comorbidities, which may impact therapeutic outcomes.

Objectives: To assess the impact of baseline modified rheumatic disease comorbidity index[1] (mRDCI) on drug survival and effectiveness of biological drugs in patients affected with Rheumatoid arthritis (RA), Spondyloarthritis (SpA), and Psoriatic Arthritis (PsA) in real-world settings.

Methods: Patients (nr. 635) with RA (nr. 214), SpA (nr. 213), and PsA (nr. 208) starting a biological drug were retrospectively analysed. mRDCI was scored at baseline, and disease characteristics were recorded at entry and at last observation. Drug retention was analysed using Kaplan–Meier curves. Cox-regression models were used to estimate the association of mRDCI with drug discontinuation and clinical outcomes, the achievement of clinical remission based on 28 joint-Disease Activity Score (DAS28) <2.6 for RA and PsA, and on Ankylosing Spondylitis-C-reactive protein Disease Activity Score (ASDAS-CRP) <1.3 for SpA.

Results: Baseline mRDCI significantly correlated with the number of biological drug switches (rho 0.47). Drug persistence was significantly higher in patients with mRDCI=0 (96.4%), than in those with mRDCI ≥2 (83.9%). Compared to mRDCI ≥2 patients, those without comorbidities showed significantly higher drug survival rate in PsA (p=0.0001) or SpA (p=0.02), but not in RA (Figure 1). mRDCI was also found to be a predictor of definitive drug discontinuation (HR 1.53) and of failure to achieve DAS28 based remission in RA (HR 0.66) or PsA (HR 0.77), and ASDAS-CRP driven remission in SpA (HR 0.43).

Table 1. Baseline demographics of patients with Psoriatic Arthritis (PsA), Rheumatoid arthritis (RA), and Spondyloarthritis (SpA)

	All (n=635)	PsA (n=208)	RA (n=214)	SpA (n=213)
Age (mean ± SD)	51.1±13	51.3±12	54.2±12	47.8±13
Female, n (%)	407 (64)	136 (65)	172 (80)	99 (46)
Normal weight (BMI ≤25), n (%)	278 (44)	84 (40)	111 (52)	83 (39)
Overweight (BMI >25 ≤30), n (%)	242 (28)	78 (37)	64 (30)	100 (47)
Obese (BMI >30), n (%)	115 (18)	46 (22)	39 (18)	30 (14)
Disease duration (months)	79.8±92	69.9±123	72.8±75	74.9±80
mRDCI, n (%)				
0	302 (48)	87 (42)	92 (43)	123 (58)
1	128 (21)	51 (25)	44 (21)	33 (15)
2	88 (14)	24 (12)	34 (16)	30 (14)
3	53 (8.3)	24 (11)	15 (7.0)	14 (6.6)
4	30 (4.7)	12 (5.8)	12 (5.6)	6 (2.8)
5	13 (2.0)	5 (2.4)	7 (3.3)	1 (0.5)
6	9 (1.4)	2 (1.0)	6 (2.8)	1 (0.5)
7	9 (1.4)	2 (1.0)	3 (1.4)	4 (1.9)
8	3 (0.5)	1 (0.5)	1 (0.5)	1 (0.5)

Values are the mean 1 SD unless otherwise indicated. BMI = Body Mass Index; mRDCI = modified Rheumatic Diseases Comorbidity Index.

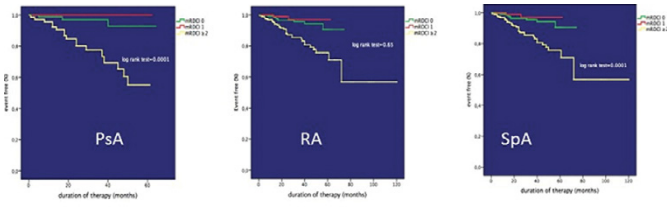


Figure 1. Kaplan-Meier curves for patients affected with Rheumatoid arthritis (RA), Spondyloarthritis (SpA), and Psoriatic Arthritis (PsA)

Conclusions: This study provided evidence that baseline mRDCI negatively impacts the persistence on biologic treatments and the clinical outcomes in patients with RA, SpA, and PsA in real-life settings.

References:

[1] Staetgens et al. Content and construct validity of the Rheumatic Diseases Comorbidity Index in patients with gout. Rheumatology (2015)Sep;54(9):1659–1663.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1502

THU0156 CLINICAL ASSESSMENT VERSUS ULTRASONOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICAL AGENTS - THE IMPACT OF CONCOMITANT FIBROMYALGIA

M.M. Tamas[1], L.-J. Ghib[1], C.I. Bondor[2], I. Felea[3], L. Damian[3], I. Filipescu[1], A. Mociran[3], S.-P. Simon[1], L. Muntean[1], S. Rednic[1]. *[1]Rheumatology; [2]Department of Medical Informatics and Biostatistics, "Iuliu Hatieganu" University of Medicine and Pharmacy; [3]Rheumatology, Emergency County Clinical Hospital, Cluj Napoca, Romania*

Background: Concomitant fibromyalgia (FM) may increase subjective components of the disease activity scores (DAS) in rheumatoid arthritis (RA), thus leading to an improper assessment of treatment response. Ultrasonography (US) is currently used in clinical practice as an objective measure of the disease activity. The US7 German score was demonstrated to be sensitive to change, reflecting the therapeutic response in RA patients [1].
Objectives: To evaluate clinical and US parameters in RA patients with or without concomitant FM, undergoing biological therapy.
Methods: RA patients treated with various biological agents who presented in our Department of Rheumatology were consecutively enrolled. Patients underwent clinical and laboratory examinations. US was performed by an experienced sonographer, blinded to clinical evaluation. Synovitis and synovial/tenosynovial vascularity were scored semiquantitatively (grade 0–3) by gray-scale (GS) and power Doppler (PD) US. Tenosynovitis (TS) and erosions were scored for presence [1].
Patients were divided in two groups according to the difference between tender joint count (TJC) and swollen joint count (SJC): ≥7 RA-FM group, <7 RA-nonFM group, representing the "joint count" criteria for FM, after the study of Pollard *et al.* [2].
Results: Thirty-nine patients were included, 77% women, mean age 55.2±11.3 years, mean disease duration 15.25±9.4 years. Nine out of 39 (23%) patients were classified as having associated FM. Disease duration and treatment were comparable between groups.
Significantly higher values for TJC, patient global assessment (PGA), DAS 28 were found in the RA-FM group, with no differences for SJC or inflammatory markers (ESR, CRP). GS and PD-US7 scores were similar between groups (Table 1).

Table 1. Clinical and US findings in RA-nonFM and RA-FM groups

	RA-nonFM (n=30)	RA-FM (n=9)	*P* value
PGA (mm)	41.33 (18.28)	58.88 (17.63)	<0.001
TJC	3 (0–10)	12 (9–17)	<0.001
SJC	2 (0–7)	1 (0–6)	0.54
ESR (mm/h)	22.26 (18.42)	27.33 (16.87)	0.21
CRP (mg/l)	8.46 (17.84)	8.67 (9.11)	0.66
DAS28 CRP	3.33 (0.98)	5.13 (1.18)	0.015
GS Synovitis US7 score	3.80 (4.37)	2.67 (1.66)	0.96
PD Synovitis US7 score	1.67 (2.90)	1.22 (1.20)	0.59
Erosions US7 score	3.77 (2.75)	4.89 (2.85)	0.29
GS TS US7 score	0.30 (0.84)	0.44 (0.73)	0.31
PD TS US7 score	0.20 (1.10)	0.33 (0.71)	0.08

In the RA non-FM, but not in the RA-FM group, GS and PD-US7 correlated with SJC (r=0.44, *p*=0.015 – GS synovitis, r=0.47, *p*=0.008 – PD synovitis; r=0.57, *p*=0.001 – GS TS; r=0.46, *p*=0.011 – PD TS) and PD synovitis negatively correlated with the "joint count" criteria (r=-0.44, *p*=0.015).
Conclusions: Concomitant FM in RA patients undergoing biological therapy lead to higher DAS28 scores, but not to synovial inflammation on US. US-PD correlates with clinically detected synovitis in the non-FM group. US is expected to modify treatment decision and to prevent RA mistreatment especially in RA-FM patients.
References:
[1] Backhaus M, et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. Arthritis Rheum. 2009;61(9):1194–201.
[2] Pollard LC, et al. Fibromyalgic rheumatoid arthritis and disease assessment. Rheumatology (Oxford). 2010;49(5):924–928.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3971

THU0157 RELATIONSHIP OF MATRIX METALLOPROTEASE 3 TITER AND SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM THE CHIKARA STUDY

M. Tada, Y. Yamada, K. Mandai, N. Hidaka. *Orthopaedic Surgery, Osaka City General Hospital, Osaka, Japan*

Background: Patients with rheumatoid arthritis (RA) show a lower muscle mass[1] and higher prevalence of sarcopenia than healthy individuals. A prospective observational study (CHIKARA study, registration number: UMIN000023744) was started to clarify the influence of changes in disease activity for sarcopenia.
Objectives: We investigated the relationship between sarcopenia and disease activity at baseline in patients with RA.
Methods: We analyzed baseline data from the CHIKARA study (Correlation research of sarcopenia, skeletal muscle and disease activity in rheumatoid arthritis). Sarcopenia was diagnosed using the criteria of the Asia Working Group on Sarcopenia[2]. Muscle mass, body fat mass, total body water, bone mass, and basal metabolic rate were measured using a body composition analyzer (MC-780A; TANITA, Tokyo, Japan). We investigated correlations between sarcopenia and disease activity (DAS28-ESR, SDAI, physical function (HAQ), and laboratory data using uni- and multivariate analyses.
Results: Participants comprised 100 patients with RA (females, 78%; mean age, 66.1 years). Mean disease duration was 5.5 years, DAS28-ESR was 3.55, and the percentage of subjects with sarcopenia was 28%. Table 1 shows risk factors for sarcopenia. Sarcopenia correlated with weight, body mass index (BMI), body fat mass, muscle mass, basal metabolic rate, Steinbrocker stage, CRP bone mass, and matrix metalloprotease (MMP)-3 on univariate analysis. Glucocorticoid dosage, rheumatoid factor, and anti-CCP antibody showed no correlation with sarcopenia. BMI, body fat mass, and MMP-3 were identified as independent risk factors on multivariate analysis. MMP-3 over 90.7 ng/ml was a risk factor for sarcopenia by ROC curve analysis (odds ratio, 3.09; p=0.023).

Table 1. Risk factors for sarcopenia in patients with RA

	Univariate		Multivariate		
	R	*P*	Odds ratio	95% CI	*P*
Weight	-0.421	<0.001	–	–	–
BMI	-0.490	<0.001	0.307	0.185–0.509	<0.001
Body fat mass	-0.219	0.002	1.318	1.124–1.546	0.001
Muscle mass	-0.325	0.001	–	–	–
Basal metabolic rate	-0.419	<0.001	–	–	–
Steinbrocker stage	0.206	0.039	–	–	–
CRP	0.201	0.045	–	–	–
Bone mass	-0.374	<0.001	–	–	–
MMP-3	0.238	0.017	1.012	1.003–0.021	0.01

Conclusions: The percentage of sarcopenia was 28% in patients with RA. Low BMI, high body fat mass, and high MMP-3 represented independent risk factors for sarcopenia. A relationship between MMP-3 and sarcopenia was indicated by this study.
References:
[1] Inui K., Koike T., Tada M., et al. Sarcopenia is apparent in patients with rheumatoid arthritis, especially those with biologics -TOMORROW study-. EULAR 2015 abstract (AB0359).
[2] Chen Lk., Liu LK., Assantachai P., et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2014; 15: 95–101.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2334

THU0158 IMMUNE RESPONSE EFFICIENCY AFTER VACCINATION IN RA AND SPA PATIENTS TREATED WITH BIOLOGICS AND IMMUNOSUPPRESSIVE AGENTS: A SYSTEMATIC LITERATURE REVIEW

M. Tissier[1], A. Molto[1], S. Kolta[1], O. Fogel[1], M. Dougados[1], J. Morel[2], C. Miceli-Richard[1]. *[1]Hopital Cochin Paris, Paris; [2]CHU Montpellier, Montpellier, France*

Background: One of the most effective strategies to prevent infections is vaccination, especially in patients treated with biologics and immunosuppressive (IS) agents. Nevertheless, the effectiveness of the resulting immune response in these patients has been questioned.
Objectives: To perform a systematic literature review aiming to assess evidence available regarding immune response efficiency (IRE) and the ideal schedule for vaccination in RA and SpA patients treated with Methotrexate (MTX), TNF inhibitors (TNFi), anti-CD20 (rituximab, RTX), anti-CTLA4 (abatacept, ABA) or anti-IL6 (tocilizumab, TCZ).
Methods: A systematic literature review was conducted by searching in PubMed all studies with the MeSH terms "[Rheumatoïd Arthritis" OR "Spondyloarthritis"] AND ["vaccination" OR "vaccines"] AND ["Methotrexate" OR "Abatacept" OR "Tocilizumab" OR "Rituximab" OR "Adalimumab" OR "Certolizumab" OR "Etanercept" OR "Golimumab" OR "Infliximab"], with no limitation regarding time of publication. Only studies evaluating the IRE were included. Case reports, general reviews and meta-analysis were excluded.
Results: After exclusion criteria, 35 studies (out of 60 studies retrieved) assessing IRE in RA or SpA patients were selected, under MTX (n=35), TNFi (n=18), RTX (n=8), ABA (n=4) or TCZ (n=5). The studied vaccines were mostly the trivalent seasonal Influenza (n=20), the anti-pneumococcal vaccine (n=16), and few studies regarding the tetanus toxoid vaccine (TTV) (n=2), Hepatitis A vaccine (n=1) and accidental revaccination against yellow fever (n=2). Most studies (32/35) evaluated the IRE using the antibody (Ab) titer. When studying the anti-pneumococcal and influenza vaccination, the primary outcome was mainly the seroresponse 3 to 6 weeks after vaccination (i.e. Ab ratio post/pre-vaccine) but some studies (15/35) also assessed the seroprotection rate (i.e. patients with an effective titer of protective Ab), and some (3/35) the effectiveness of seroresponse using the opsonization index rate.
Regarding the anti-pneumococcal and influenza vaccination, MTX, RTX, and ABA were reported to impair the immune response; neither TNFi nor TCZ were shown to decrease seroresponse.

Regarding TTV, one study showed persistent seroresponse in patients treated with TNFi; a second study showed no difference between MTX and RTX in response to T-cell dependant protein Ag TTV.
Two studies reported no significant difference in efficiency or tolerance in patients accidentally revaccinated against yellow fever under TNFi.
Conclusions: These observations highly suggest that an effective vaccination for patients treated with MTX, RTX, and ABA should necessitate a therapeutic window or a scheduled treatment spacing, in order to offer the best protection against Influenza and Pneumococcal infection. This might not be necessary in patients under TNFi or TCZ; nevertheless, further studies are necessary to optimize the vaccination modalities.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1396

THU0159 RHEUMATOID ARTHRITIS MAY NOT INFLUENCE EATING BEHAVIOURS CHARACTERISTICS

N. Bulut[1], M.E. Tezcan[2]. *[1]Family Medicine; [2]Rheumatology, Kartal Research and Education Hospital, Istanbul, Turkey*

Background: Patients with rheumatoid arthritis (RA) have an increased risk of obesity and cardiovascular disease compared with the general population (1). Eating behaviours may play an important role in obesity and cardiovascular disease.
Objectives: We hypothesised that RA patients have impaired eating behaviours that may have a role in obesity. For evaluating this hypothesis, we compared eating behaviours of patients with RA, osteoarthritis (OA) and healthy controls.
Methods: One hundred and fifty-seven RA patients (M/F: 23/134) who fulfilled the 2010 American College of Rheumatology (ACR) RA classification criteria, 31 hand OA patients (M/F: 1/30) who fulfilled 1990 ACR hand OA criteria and 60 healthy controls (M/F: 9/51) were enrolled to the study who applied to Kartal Dr. Lutfi Kirdar Training and Research Hospital Rheumatology outpatient clinic. Eating behaviours was assessed by the Three-Factor Eating Questionnaire (TFEQ).Demographic data, smoking status, co-morbidities, anthropometric measurements, VAS pain score were analyzed.
Results: There were no differences between three groups in demographic features and anthropometric measurements (table1). Moreover, there were no differences between three groups in cognitive restraint and emotional eating scores.Although,healthy controls had significantly higher uncontrolled eating scores than the RA group ($p<0.05$), uncontrolled eating scores of all three groups were lower than Turkish people average scores (2) (table2).

Table 1. Demographic and Anthropometric features of study groups

	RA (n=157)	OA (n=31)	Healthy Controls (n=60)	*p*
Age	51.00 (40.00–57.50)	50.00 (46.75–62.00)	48.00 (39.25–53.75)	0.06
Gender (M/F)	23/134 (14.6/85.4)	1/30 (3.2/96.8)	9/51 (15.0/85.0)	0.21
Education (year)	5.00 (5.00–10.00)	5..00 (5.00–11.00)	5.00 (5.00–11.00)	0.42
Smoking ((%)	24.2	23.3	20.7	0.86
Co-morbid disease	55.8	64.5	49.2	0.37
Lenght (cm)	160.00 (155.00–165.00)	157.00 (155.00–160.00)	160.50 (157.00–166.75)	0.06
Weight (kg)	75.00 (67.00–85.00)	77.00 (66.00–85.00)	74.00 (64.00–84.50)	0.73
BMI (kg/m^2)	29.150 (25.50–33.20)	31.100 (27.12–35.07)	27.550 (23.87–32.77)	0.15
VAS pain (0–100)	10.00 (0.00–30.00)	10.00 (10.00–30.00)	N/A	0.07

RA, Rheumatoid Arthritis; OA, Osteoarthritis; BMI, Body mass index; VAS, Visual analog score.

Table 2. Eating behaviours of study groups

	RA (n=157)	OA (n=31)	Healthy Controls (n=60)	*p*
Uncontrolled eating scores	10.00 (8.00–12.00)	10.00 (8.00–13.00)	11.00 (9.00–14.00)	0.047
Cognitive restraint scores	16.00 (13.00–18.00)	16.00 (14.00–19.00)	14.00 (11.25–18.00)	0.075
Emotional eating scores	5.00 (3.00–8.00)	5.00 (3.75–11.00)	4.00 (3.00–7.00)	0.066

Conclusions: This was the first study using the TFEQ in patients with RA. In our study, we found that disease features of RA may had no effect on eating behaviors.
References:
[1] Kitas GD, Erb N. Tackling ischemic heart disease in rheumatoid arthritis. Rheumatology (Oxford). 2003;42(5):607–13.
[2] Kıraç D, Kaspar EÇ, Avcılar T, Çakır ÖK, Ulucan K, Kurtel H, ve ark. Obeziteyle ilişkili beslenme alışkanlıklarının araştırılmasında yeni bir yöntem "Üç Faktörlü Beslenme Anketi". MÜSBED. 2015;5(3):162–9.
Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6596

THU0160 DISEASE MODIFYING ANTIRHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE: A PROSPECTIVE STUDY

N. Mena-Vazquez[1], C. Gómez-Cano[2], C. Aguilar-Hurtado[3], M. Rojas-Giménez[1], S. Manrique-Arija[1], C. Domic[1], C. Fuego-Valera[1], I. Ureña-Garnica[1], F.G. Jiménez-Núñez[1], G. Diaz-Cordoves[1], M.V. Irigoyen-Oyarzábal[1], M. Padín-Martín[3], A. Fernández-Nebro[1]. *[1]Department of Rheumatology at the University Regional Hospital of Malaga (HRUM). Institute for Biomedical Research in Malaga (IBIMA). Malaga University., Malaga; [2]Department of Rheumatology Hospital Valme, Sevilla; [3]Department of Radiology, Malaga, Spain*

Objectives: To describe the evolution of interstitial lung disease (ILD) in RA patients treated with disease modifying antirheumatic drugs (DMARDs) for 1 year in real clinical practice conditions.
Methods: *Design:* Prospective observational case-series. *Patients:* Patients with RA (ACR/EULAR 2010 criteria) and ILD (American Thoracic Society/European Respiratory criteria) from two centres (Regional Hospital of Málaga and Valme Hospital of Sevilla) were included. *Protocol:* All patients with RA and ILD who visited outpatient clinic from January to December 2015. They were reviewed according to a predetermined protocol for systematic data collection. Resolution Computed Tomography (HRCT),Pulmonary function test (PFT) and echocardiogram were requested for all patients.This visit was marked as v0 (index date). At 12 months (v12) the joint assessment (DAS28), echocardiogram, PTF and HRCT were again evaluated. HRCT's were assessed by the same radiologist with expertise in chest radiology. *Outcomes:* At v12:(1)improvement (ie improvement in FVC$\geq$10% or DLCO$\geq$15% and no radiological progression),(2)non-progression (stabilization or improvement in FVC$\leq$10% or DLCO$<$15% and no radiological progression),(3)progression (worsening of FVC$>$10% or DLCO$>$15% and radiological progression), or (4) death due to ILD. *Variables:* Description of ILD type (Nonspecific interstitial pneumonia/Usual interstitial pneumonia) and lung function by PTF, HRCT.Presence of PTH by echocardiogram and dyspnoea.Collection of adverse events. *Statistical analysis:* Descriptive analysis and Wilcoxon or T test between the v0 and v12. One factor ANOVA between sDMARD,bDMARD and combination therapy groups.
Results: The main characteristics at V0 of the patients (n=22) are shown in the table. Seven patients (31.8%) received a sDMARDs with a bDMARDs; 12 patients (54.5%) in monotherapy with sDMARD, with MTX being the most frequent (34.7%); 3 (13.6%) in monotherapy with bDMARDs (Table 1). Three patients (13.6%) had improvement (1 with MTX, 1 with RTX and 1 with HCX + RTX), 15 patients (68.2%) remained stable (4 with MTX, 3 with LFN, 1 with HCQ, 1 AZA, 1 ABT, 1ABT + SSZ, 2 MTX + ETN, 1 HCQ + RTX, and 1 HCQ + ADA);and 3 (13.0%) got worse of ILD (1 with MTX developed unknown lung mass, 1 with LFN and 1 with LFN + IFX). One patient died during follow-up due to respiratory infection (under treatment with RTX). No patient developed PPH. We did not find significant differences between v0 DAS28 and at 12 months (2.55 [0.75] vs 2.42 [1.22], p=0.567) or in HAQ 1.15 [0.93] vs 1.25 [0.78], p=0.450). There were no significant differences in PTF, HRCT or DAS28 at v12 between sDMARD, bDMARD and combination therapy groups. Four patients (18.2%) had adverse effects: 2 respiratory infections, 1 oral herpes simplex and 1 tooth infection.

VARIABLES	Patients
Sex (Female), n (%)	12 (54.5)
Age (years), mean (DE)	69.4 (7.0)
Smoker, n (%)	4 (18.2)
Body mass index (BMI), mean (SD	28.9 (6.0)
Disease duration (months), mean (SD)	211.9 (131.5)
ILD duration (months), mean (SD)	64.5 (47.1)
Rheumatoid factor, n (%)	21 (95.5)
Anti–cyclic citrullinated peptide, n (%)	21 (95.5)
Erosions, n (%)	16 (72.7)
DAS28, mean (DE)	2.55 (0.7)
HAQ, mean (DE)	1.15 (0.9)
Treatment	
sDMARD, n (%)	19 (86.4)
Methotrexate, n (%)	8 (36.4)
Leflunomide, n (%)	5 (22.7)
Sulfasalazine, n (%)	1 (4.5)
Hydroxychloroquine, n (%)	4 (18.2)
Azathioprine	1 (4.5)
bDMARDs, n (%)	10 (45.5)
Rituximab, n (%)	4 (18.2)
Abatacept, n (%)	2 (9.1)
Etanercept, n (%)	2 (9.1)
Infliximab, n (%)	1 (4.5)
Adalimumab, n (%)	1 (4.5)

Conclusions: Most patients with RA and ILD who are receiving treatment with DMARD (82%)remained stable or improved after at least 1 year of both synthetic and biological DMARD treatment. However, a significant percentage of patients had an adverse outcome. More prospective studies with a greater number of patients are necessary to identify the influence of DMARDs in this evolution.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5824

THU0161 SYNDECANS ARE CORRELATED WITH HIGH TITRES OF ANTIBODIES AGAINST CITRULLINATED PROTEINS ANTIGENS (ACPAS) IN SERA FROM ACTIVE RHEUMATOID ARTHRITIS

N.A. Rodriguez-Jimenez[1], E.G. Cardona-Muñoz[2], J.I. Gamez-Nava[1], E.E. Perez-Guerrero[3], M. Ponce-Guarneros[4], E.Y. Vera-Navarrete[3], A. Nava-Zavala[1], T.A. Garcia-Cobian[2], M. Salazar-Paramo[1], L. Gonzalez-Lopez[5]. *[1]UMAE, Hospital de Especialidades Centro Medico de Occidente, Instituto Mexicano del Seguro Social; [2]Universidad de Guadalajara, Guadalajara, Mexico; [3]Doctorado en Farmacologia, Universidad de Guadalajara, Guadalajara; [4]Unidad de Medicina Familiar No. 97, IMSS, Magdalena, Jalisco; [5]Hospital General Regional No. 110, IMSS, Guadalajara, Mexico*

Background: Syndecans includes a group of proteins from the cell-surface heparan-sulfate proteoglycan family, with a relevant role in chronic inflammation of synovial tissue in patients with rheumatoid arthritis (RA) participating in the cell-matrix and cell-cell interactions. Syndecans are differentially expressed in the synovial tissue: syndecan-1 (SDC-1) is expressed mainly in mononuclear cells, syndecan-3 (SDC-3) is mainly expressed by synovial endothelial cells and syndecan-4 (SDC-4) is expressed by B lymphocytes regulating B cell development and survival. Currently, there is strong evidence that antibodies directed to citrullinated protein antigens (ACPAs) are associated with a more severe disease in RA. Nevertheless, to date, there is a lack of information about the relation between serum syndecan levels and serum concentrations of rheumatoid factor (RF) and ACPAs.
Objectives: To evaluate the association between serum SDC-1, SDC-3 and SDC-4 levels with serum concentrations of RF and ACPAs.
Methods: Eighty-one, patients with RA were included. We assessed clinical characteristics including disease activity by DAS-28, functioning by HAQ-Di. Serum concentrations of RF were measured by nephelometry, two ACPAs were measured: anti-CCP2 and anti-mutated citrullinated vimentin (anti-MCV) antibodies using ELISA. Serum levels of SDC-1, SDC-3 (ng/mL) and SDC-4 (pg/mL) were measured by ELISA. We compared the serum levels of these syndecans in the ACPA+ group (group 1) versus ACPA- group (group 2) with Student t-test. A correlation analysis (Pearson tests) was performed to identify the strength of association between concentrations of syndecans with concentrations of ACPAs and other variables.
Results: Patients with RA had a mean age of 50±11 yrs, 75% were RF+ and 64% were ACPA+. In patients with ACPAs+ were observed higher serum concentrations of SDC-3 ($p=0.003$) and SDC-4 ($p<0.001$). SDC-1 correlated significantly with anti-MCV ($r=0.53$, $p<0.001$). Serum concentrations of SDC-3 correlated significantly with anti-CCP titres ($r=0.53$, $p=0.003$) and anti-MCV ($r=0.46$, $p=0.02$); whereas SDC-4 levels correlated significantly with anti-CCP titres ($r=0.61$, $p<0.001$) and RF ($r=0.53$, $p=0.003$). Additionally, serum SDC-1 levels correlated with decrement in response to treatment with synthetic DMARDs ($r=-0.25$, $p=0.026$). SDC-1 did not correlate with serum SDC-3 ($p=0.8$) and SDC-4 ($p=0.8$); whereas serum SDC-3 and SDC-4 had a strong correlation ($r=0.8$, $p<0.001$).
Conclusions: Serum SDC-3 and SDC-4 are increased in ACPA-positive RA patients. These data suggest that syndecans might be useful as serum biomarkers for discriminate a group of patients with RA and more severe disease.
References:
[1] Patterson AM, et al. Ann Rheum Dis. 2008 May;67(5):592–601.
[2] Endo T, et al. Arthritis Rheumatol. 2015 Sep;67(9):2512–22.
Acknowledgements: This project was supported by a grant from the Fondo de Investigacion en Salud del Instituto Mexicano del Seguro Social: FIS/IMSS/PROT/G15/1448.
Disclosure of Interest: N. Rodriguez-Jimenez: None declared, E. Cardona-Muñoz: None declared, J. Gamez-Nava: None declared, E. Perez-Guerrero: None declared, M. Ponce-Guarneros: None declared, E. Vera-Navarrete: None declared, A. Nava-Zavala: None declared, T. Garcia-Cobian: None declared, M. Salazar-Paramo: None declared, L. Gonzalez-Lopez Grant/research support from: Dr. L Gonzalez-Lopez is a recipient of a Fundacion IMSS Scholarship, Mexico.
DOI: 10.1136/annrheumdis-2017-eular.4965

THU0162 RELATIONSHIP BETWEEN LEVELS OF HUMAN PEPTIDYL ARGININE DEIMINASE-4 WITH CHRONIC PERIODONTITIS SEVERE IN RHEUMATOID ARTHRITIS

O. Vega[1], T. Rubin de Celis[1], D. Tamayo[2], R. Flores[2], A. Madariaga[3], Y. Laura[4], R. Gamboa[5]. *[1]Rheumatology, Reumacenter; [2]Medicine; [3]Dentistry, Hospital III, EsSalud; [4]Immunology, Reumacenter, Juliaca; [5]National Hospital Guillermo Almenara, Essalud, Lima, Peru*

Background: Both Peptydil arginine deiminase of *P. gingivalis* (pPAD), and the human enzyme (hPAD), could citrullinarize peptides from the bacteria and human host in Rheumatoid Arthritis patients (RA). Chronic periodontitis (CP) could be associated with a constant generation of citrullinated proteins, and it lead to a proportional hPAD enzymatic production.
Objectives: The aim was to demonstrate the association between serum levels of hPAD4 and severe Periodontitis in patients with rheumatoid arthritis.
Methods: Patients with RA (n=127) matched with healthy controls (n=120) were studied in a cross-sectional study. Levels of human recombinant antigens for hPAD4; cyclic citrullinated peptide antibody (CCP3, IgG), Rheumatoid factor (IgM) and C-reactive protein (CRP); determined by ELISA test.
The CP was classified according to the recommendations of the International Workshop for Classification of Periodontal Diseases and Conditions. Bivariate analysis to demonstrate the associations, and non-parametric analyzes were used according to the case.
Results: There were no significant demographic diffrences between the two groups. The median hPAD4 level was 1.21 (95% CI 1.4–1.7) in RA and 0.75 (95% CI 0.94–1.26) ng/ml in controls, ($p<0.004$). The median hPAD4 level in patients with RA and CP was 1.32 (95% CI 1.39–1.9) Vs control with CP 0.7 (95% CI 0.94–1.5) ng/ml, $p<0.04$.
The frequency of CP was higher in patients with RA than in controls (66.9 vs 43%, $p<0.000$; OR: 2.65 (95% CI: 1.58–4.44); these values showed a low correlation (0.24). The median level of hPAD4 was associated with CP extension, $p<0.000$ and severity, $p<0.000$.
A significant correlation was found between levels of hPAD4 with the DAS28 ESR score ($p<0.002$). The high score of HAQ-DI (>2.0) correlated with hPAD4 levels ($P<0.001$). The group of people with higher HAQ-DI score and at the same time with greater severity of CP (n=12) showed increased levels PAD4 ($p<0.025$).
Conclusions: hPAD4 levels correlate with the severity of CP independent of the RA presence and in RA subjects with high score of disability and activity disease. The hPAD4 could be proposed as a serological marker of clinical severity in chronic diseases such as CP and RA.
References:
[1] Rose, H.M., C. Ragan, and et al., Differential agglutination of normal and sensitized sheep erythrocytes by sera of patients with rheumatoid arthritis. Proc Soc Exp Biol Med, 1948. 68(1): p. 1–6.
[2] Girbal-Neuhauser, E., et al., The epitopes targeted by the rheumatoid arthritis-associated antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues. J Immunol, 1999. 162(1): p. 585–94.
[3] Lundberg, K., et al., Antibodies to citrullinated alpha-enolase peptide 1 are specific for rheumatoid arthritis and cross-react with bacterial enolase. Arthritis Rheum, 2008. 58(10): p. 3009–19.
[4] Mikuls, T.R., et al., Periodontitis and Porphyromonas gingivalis in patients with rheumatoid arthritis. Arthritis Rheumatol, 2014. 66(5): p. 1090–100.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3358

THU0163 THE ASSOCIATION BETWEEN INFLAMMATORY JOINT DISORDERS AND CORONARY HEART DISEASE: NATIONWIDE REGISTER STUDY IN 50 444 PATIENTS

P. Muilu[1], V. Rantalaiho[2,3], H. Kautiainen[4,5], L. Virta[6], K. Puolakka[7]. *[1]Department of Medicine, Tampere University Hospital; [2]Centre for Rheumatic Diseases, Tampere University Hospital; [3]Faculty of Medicine and life sciences, University of Tampere, Tampere; [4]Department of General Practice and Primary Health Care, University of Helsinki and Helsinki University Hospital, Helsinki; [5]Unit of Primary Health Care, Turku University Hospital; [6]Social Insurance Institution of Finland, Turku; [7]Department of Medicine, South-Karelia Central Hospital, Lappeenranta, Finland*

Background: Inflammatory joint disorders (IJD) are associated with cardiovascular (CV) problems, including coronary heart disease (CHD). This association is best known for rheumatoid arthritis (RA); but also for ankylosing spondylitis and

Table 1. A) The prevalence of coronary heart disease (CHD) at the index date among patients with inflammatory joint diseases (IJD's) compared to their controls. B) The incidence of CHD among IJD patients compared to the controls during follow up.

		A) Index date[a]			B) Follow up[b]		
		CHD %		OR (95% CI)	Incidence of CHD per 1000 patient years		IRR
Men	N	Case	Control[c]		Case	Control	
RA+	6004	11.5	9.9	1.20 (1.09 to 1.33)	8.3	5.8	1.46 (1.27 to 1.67)
RA-	3071	10.3	9.2	1.14 (0.98 to 1.31)	6.1	5.4	1.12 (0.92 to 1.37)
UA	2503	5.9	5.8	1.03 (0.84 to 1.26)	5.8	3.8	1.51 (1.19 to 1.93)
SpA	4349	1.6	1.3	1.21 (0.90 to 1.64)	2.3	1.6	1.44 (1.09 to 1.89)
PsA	3424	3.9	3.9	1.04 (0.84 to 1.28)	4.5	3.3	1.36 (1.09 to 1.70)
Women							
RA+	12159	5.1	4.8	1.05 (0.95 to 1.16)	2.6	2.3	1.14 (0.98 to 1.32)
RA-	6713	5.7	4.7	1.26 (1.11 to 1.44)	2.6	2.0	1.32 (1.08 to 1.61)
UA	4896	3.0	2.7	1.11 (0.90 to 1.36)	2.5	1.5	1.67 (1.28 to 2.18)
SpA	4047	0.8	0.6	1.37 (0.89 to 2.11)	0.8	0.6	1.42 (0.87 to 2.31)
PsA	3278	2.0	1.6	1.23 (0.91 to 1.67)	2.2	1.5	1.53 (1.10 to 2.13)

[a] The date when the special reimbursement for IJD came effective
[b] The time period after the index date until Dec 31st 2014
[c] Three control subjects were matched for each patient with IJD

psoriatic arthritis (PsA). However, these findings are mainly based on materials from an era of less active treatment of the IJD's and thus progress in this theory may have happened. Further, many cases fail to fulfil any classification criteria. We found no published data on CV risk in unspecified arthritis (UA).
Objectives: To investigate the association between the five most common IJDs and CHD based on a nationwide large register data in Finland during 2000–14.
Methods: From the register maintained by the Social Insurance Institution (SII), we collected data on all Finnish patients granted a new special reimbursement (SR) on medications for the following IJDs during 2000–14: seropositive RA (ICD10 code M05), seronegative RA (M06), UA (M13), spondyloarthritis (SpA) (M45–46), and PsA (L40). For these patients, Population Register Centre matched three controls, standardized for age, sex, and place of residence. The index date was determined to be the date when the SR for IJD came effective. From the case and control groups we analysed the frequency of individuals that had SR also for CHD (ICD10 codes I20–25) at the index date, or to whom it was granted by SII during the observation period.
Results: Altogether 201 776 individuals (50 444 cases and 151 332 controls) were identified. The frequencies of the individuals having CHD by the index date and the incidences of CHD during follow-up are presented in table 1.
Conclusions: Compared to general population, CHD was overrepresented at RA diagnosis, especially in seropositive men and seronegative women, while other patients had comparable rates of CHD with the population. After the index day, the incidence of CHD was increased in all patient groups except for men with seronegative RA and women with seropositive RA or SpA. Thus, the CV risk associated to IJDs remains in this millennium, and also pertains to UA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2027

THU0164 SUBCLINICAL ATHEROSCLEROSIS AND CARDIOVASCULAR EVENTS IN ITALIAN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM MULTICENTER GIRRCS (GRUPPO ITALIANO DI RICERCA IN REUMATOLOGIA CLINICA E SPERIMENTALE) STUDY

P. Ruscitti[1], D.P.E. Margiotta[2], L. Navarini[2], F. Macaluso[3], D. Iacono[4], F. D'Onofrio[5], G. Emmi[6], F. Atzeni[7], M. Prete[8], F. Perosa[8], P. Sarzi-Puttini[7], L. Emmi[6], F.P. Cantatore[5], G. Triolo[3], R. Giacomelli[1], G. Valentini[4].
[1]Rheumatology Section, Department of Biotechnological and Applied Clinical Science, University of L'Aquila, L'Aquila; [2]Clinical Medicine and Rheumatology Department, Campus Bio-Medico University of Rome, Rome; [3]Rheumatology Section, Department of Internal Medicine, University of Palermo, Palermo; [4]Rheumatology Section, Department of Clinical and Experimental Medicine, Second University of Naples, Naples; [5]Rheumatology Section, Department of Medical and Surgical Sciences, University of Foggia Medical School, Foggia; [6]Department of Experimental and Clinical Medicine, University of Florence, Florence; [7]Rheumatology Section, L. Sacco University Hospital, Milan; [8]Systemic Rheumatic and Autoimmune Diseases Unit, Department of Biomedical Sciences and Human Oncology, University of Bari Medical School, Bari, Italy

Background: Several studies showed a close relationship between Rheumatoid Arthritis (RA) and accelerated atherosclerosis [1,2]. At the best of our knowledge, no such study has been carried out in a large Italian series.
Objectives: To investigate the prevalence of presence of subclinical atherosclerosis and history of cardio-cerebrovascular events (CVEs), in 1266 patients consecutively admitted to Rheumatology Units throughout the whole Italy.
Methods: From 01/01/2015 to 31/12/2015, 1266 consecutive patients admitted to GIRRCS centres, satisfying ACR/EULAR criteria for RA were investigated for: i. traditional cardiovascular risk factors: gender, age, smoking habit, cholesterol, triglycerides, glycemia, systemic arterial hypertension (SAH), metabolic syndrome (MS), type 2 diabetes (T2D); ii. RA aspects: disease duration as assessed from the first symptom, disease activity as evaluated by DAS28, radiographic damage by joint X-ray, and joint surgery; iii. subclinical atherosclerosis, as assessed by ultrasound technique and/or atherosclerotic peripheral lesions; iv. history of CVEs.
Results: We evaluated 1176 patients out of 1266, that were investigated for both CVEs and subclinical atherosclerosis. They were mostly females (80.52%), with a median age of 60 years (range 18–91 years), a median disease duration of 12 years (range 0.8–25 years), seropositive in 69.21%. Nineteen percent were in remission; 17.51% presented low disease activity; 39.45% moderate disease activity, 22.61% high disease activity.
Out of 1176 patients, 217 (18%) showed evidence of subclinical atherosclerosis: a figure lower than that reported worldwide (32.7%) [2]. Eighty-two patients (6.9%) had a history for CVEs (58 myocardial infarction, 38 heart failure, 10 ischemic transitory attack, 7 Stroke), too this figure is lower than that reported worldwide (8.5%) [3,4]. In multivariate analysis, older age (p=0.0001, OR:1.069, CI95%:1.05–1.09), MS (p=0.0001, OR:3.417, CI95%:2.16–5.40) and SAH (p=0.0001, OR:3.714, CI95%:2.23–6.17) and high disease activity (p=0.001, OR:2.117, CI95%:1.35–3.32) were significantly associated with the presence of subclinical atherosclerosis. Male gender (p=0.0001, OR:3.465, CI95%:1.94–6.185), MS (p=0.005, OR:2.542, CI95%:1.29–4.52), T2D (p=0.007, OR:2.324, CI95%:1.29–4.29) and SAH (p=0.001, OR:4.921, CI95%:2.14–11.45) and higher disease activity (p=0.003, OR:1.316, CI95%:1.15–1.68) were significantly associated with a history of CVEs.
Conclusions: This is the first Italian multicenter study on subclinical and clinical atherosclerosis in patients with RA. We pointed out a low prevalence of both subclinical atherosclerosis and history of CV events. Nonetheless, a high disease activity and presence of cardiovascular risk factors were found to play a role, similarly to other countries.
References:
[1] Ruscitti P, et al. PLoS One. 2017;12:e0170108.
[2] Ambrosino P, et al. Thromb Haemost. 2015;113:916–30.
[3] Solomon D et al. Ann Rheum Dis. 2010;69:1920–5.
[4] Avina-Zubieta JA, et al. Ann Rheum Dis. 2012;71:1524–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4733

THU0165 RISK OF HERPES ZOSTER IN PATIENTS WITH RHEUMATOID ARTHRITIS IN THE BIOLOGICS ERA BASED ON THE IORRA COHORT

R. Yamaguchi[1], A. Nakajima[1], E. Inoue[2], M. Ochiai[1], Y. Shimizu[1], N. Sugimoto[1], E. Tanaka[1], K. Ikari[1], A. Taniguchi[1], H. Yamanaka[1]. *[1]Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan; [2]National Center for Child Health and Development, Center for Clinical Research for Development, Tokyo, Japan*

Background: A high incidence of herpes zoster (HZ) in patients with rheumatoid arthritis (RA) has been reported (1). According to our previous report on the incidence of HZ in Japanese patients with RA enrolled in the IORRA (Institute of Rheumatology, Rheumatoid Arthritis) cohort from 2005 to 2010, the standardized incidence rate (SIR) of HZ per 1,000 patient-years was 9.1 (95% confidence intervals [95% CIs]: 6.2–12.9) (2). In that study, 3.0% of patients used biologics at baseline. Subsequently, the use of biologics has increased, and many new potent disease-modifying antirheumatic drugs (DMARDs) have been introduced. The treatment strategy for RA has progressed in recent years; thus, it is important to investigate whether there is a change in the HZ incidence rate and the risk factors for HZ with the expanded use of biologics.
Objectives: To elucidate the incidence of HZ and risk factors for HZ in RA patients in the IORRA cohort.
Methods: The IORRA cohort is a large, single institute-based, observational cohort of RA patients established at the Institute of Rheumatology, Tokyo Women's Medical University, in 2000. Among patients with RA enrolled in the IORRA surveys from 2010 to 2015, the incidence of HZ was extracted based on patients' self-report and confirmed by the medical records. The SIR with 95% CIs was calculated and risk factors for HZ were analyzed using a Cox regression analysis.
Results: For 7,815 patients with RA (female, 84.7%) who were analyzed, the median [interquartile range (IQR)] age was 61.0 [49.7–68.9] years, and disease duration was 10 [4–18] years. Baseline drugs (median dose [IQR]) included prednisolone (PSL, 4 [2–5] mg/day) in 36.8%, methotrexate (MTX, 8 [6–10] mg/week) in 70.4%, and biologics in 14.7% of patients. Among 7,815 patients with 25,863 patient-years of observation (male, 3,828; female, 22,035), 340 HZ events were confirmed in 309 patients (21 patients had multiple events). The SIR per 1,000 patient-years was 8.5 (95% CI: 6.9–10.5) in total, 6.0 (95% CI: 3.7–9.2) in males, and 11.0 (95% CI: 8.7–13.7) in females. The following hazard ratios (HR) were found: unit increase of age, 1.14 (95% CI: 1.03–1.26, $p<0.05$); J-HAQ score 0.5–1.5 (reference J-HAQ score =0), 1.51 (95% CI: 1.09–2.10, $p<0.05$); MTX use, 1.58 (95% CI: 1.06–2.36, $p<0.05$); and biologics use, 1.88 (95% CI: 1.44–2.47, $p<0.01$). PSL use was not a risk factor (PSL dose <5 mg/day: HR 1.17 [95% CI: 0.91–1.51, p=0.22]; PSL dose $\geqq$ 5 mg/day: HR 1.17 [95% CI: 0.72–1.91, p=0.52]; the reference PSL dose =0 mg/day).
Conclusions: The drugs that were a risk factor for HZ were PSL and MTX in our previous study when the use of biologics was not prevalent. In this study, the drugs that were a risk factor for HZ were MTX and biologics, but not PSL in the era when the use of biologics became frequent.
References:
[1] Wolfe F et al. Rheumatology (Oxford). 2006;45:1370.
[2] Nakajima A et al. Mod Rheumatol 2015;25:558.
Disclosure of Interest: R. Yamaguchi: None declared, A. Nakajima Consultant for: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., Speakers bureau: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., E. Inoue: None declared, M. Ochiai: None declared, Y. Shimizu: None declared, N. Sugimoto Speakers bureau: Takeda Pharmaceutical and Bristol Myers Squibb., E. Tanaka Consultant for: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical., K. Ikari Grant/research support from: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., Speakers bureau: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., A. Taniguchi Grant/research support from: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., Speakers bureau: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., H. Yamanaka Grant/research support from: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-

Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Consultant for: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Speakers bureau: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers.
DOI: 10.1136/annrheumdis-2017-eular.3046

THU0166 COMPARISON OF THE RISK OF COMORBIDITIES BETWEEN PATIENTS WITH RHEUMATOID ARTHRITIS AND DIABETES MELLITUS USING JAPANESE HEALTH INSURANCE DATABASE

R. Sakai[1], S. Kasai[2], M. Tsutsumino[1], H. Yamanaka[1], N. Miyasaka[3], M. Harigai[1]. *[1]Division of Epidemiology and Pharmacoepidemiology in Rheumatic Diseases, Institute of Rheumatology, Tokyo Women's Medical University; [2]Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University; [3]Tokyo Medical and Dental University, Tokyo, Japan*

Background: Patients with rheumatoid arthritis (RA) have a higher risk of comorbidities such as infections[1], cardiovascular diseases[2], and fractures[3] than general population. To understand the risk of these comorbidities in RA more precisely, it is needed to compare the risk between RA and other chronic diseases. A Dutch study[4] showed that patients with RA had comparable risk of cardiovascular diseases to diabetes mellitus (DM). Because of possible racial or ethnic difference of risks of comorbidities, it is warranted to compare the risk between RA and DM in Asian countries.
Objectives: To compare risk of hospitalized infections (HIs), cardiovascular diseases and stroke (CVDs), and fractures between RA and DM cases using Japanese health insurance database.
Methods: This retrospective longitudinal population-based study was conducted using claims data provided by the Japan Medical Data Center Co., Ltd. We defined individuals as RA cases if they met all of the following: 1) had at least 6 months of continuous enrollment in the health insurance database; 2) had at least one RA diagnostic code and at least one prescription of disease-modifying antirheumatic drugs between January 2005 and December 2013; and 3) were ≥50 years old (RA group, n=3,607). Among individuals who met above criteria 1) and had at least DM diagnostic code and at least one prescription of drugs for DM, but did not meet 2), we selected age- (±5 years), gender-, calendar year of the observation start, and observation length-matched DM cases at 1:3 ratio (RA: DM) (DM group, n=10,821). Each comorbidity was defined as follows: HIs, at least one ICD10 code and one prescription of drugs for infections with hospitalization; CVDs, at least one ICD10 code and one prescription of drugs or medical procedures for CVDs with hospitalization; fractures, at least one ICD10 code for fractures. We calculated incidence rates (IR) with 95% confidence interval (CI) of each comorbidity in the two groups up to 10 years and adjusted odds ratio (OR) of RA compared with DM for each comorbidity using generalized estimating equation.
Results: The median age was 58, and 75.1% were female in the both groups. The IR [95% CI] of HIs, CVDs, and fractures was 2.8 [2.5–3.2]/100 patient years (PY), 9.2 [7.4–11.4]/1,000 PY, 16.7 [14.2–19.6]/1,000 PY in the RA group, 2.8 [2.6–3.0]/100PY, 26.3 [24.4–28.3]/1,000PY, 10.3 [9.1–11.6]/1,000PY in the DM group respectively. The OR [95% CI] of RA (vs. DM) for HIs, CVDs, fractures was 0.9 [0.8–1.1], 0.4 [0.3–0.6], 1.3 [1.0–1.7] after adjusting for baseline characteristics.
Conclusions: This study revealed that patients with RA had significantly lower risk of CVDs than and similar risk of HIs and fractures to those with DM using health insurance database for the first time in Asia.
References:
[1] Arthritis Rheum, 2002;46:2287–93.
[2] Ann Rheum Dis, 2012:71:1524–29.
[3] Arthritis Res Ther, 2010;12:R154.
[4] Arthritis Rheum, 2009;61:1571–9.
Acknowledgements: This work was supported by the research grant from the Ministry of Health, Labour, and Welfare, Japan.
Disclosure of Interest: R. Sakai Grant/research support from: Ayumi Pharmaceutical Co., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Nippon Kayaku Co., Ltd., Taisho Toyama Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., and Teijin Pharma Ltd.,Bristol-Meyers Squibb, S. Kasai: None declared, M. Tsutsumino Grant/research support from: Ayumi Pharmaceutical Co., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Nippon Kayaku Co., Ltd., Taisho Toyama Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., and Teijin Pharma Ltd., H. Yamanaka Grant/research support from: Chugai Pharmaceutical Co. Ltd., Astellas Pharma Inc., Bristol-Meyers Squibb, AbbVie Japan Co. Ltd., Daiichi-Sankyo, Mitsubishi-Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., UCB Japan., Consultant for: Chugai Pharmaceutical Co. Ltd., Astellas, Bristol-Meyers Squibb, AbbVie Japan Co. Ltd., Daiichi-Sankyo, Mitsubishi-Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., UCB Japan., Speakers bureau: Chugai Pharmaceutical Co. Ltd., Astellas, Bristol-Meyers Squibb, AbbVie Japan Co. Ltd., Daiichi-Sankyo, Mitsubishi-Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., UCB Japan., N. Miyasaka: None declared, M. Harigai Grant/research support from: Ayumi Pharmaceutical Co., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Nippon Kayaku Co., Ltd., Taisho Toyama Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., and Teijin Pharma Ltd.,Eisai,
DOI: 10.1136/annrheumdis-2017-eular.4558

THU0167 ASSOCIATION OF BIOLOGIC ANTIRHEUMATIC THERAPY WITH THE RISK OF DEVELOPING TYPE 2 DIABETES IN ADULTS WITH RHEUMATOID ARTHRITIS: NEW EVIDENCE FROM REAL WORLD DATA

S.K. Paul[1], O. Montvida[2], J.H. Best[3], S. Gale[3], A. Pethoe-Schramm[4], K. Sarsour[3]. *[1]University of Melbourne, Melbourne; [2]QIMR Berghofer Medical Research Institute, Brisbane, Australia; [3]Genentech, South San Francisco, CA, United States; [4]F. Hoffmann-La Roche, Basel, Switzerland*

Background: While rheumatoid arthritis (RA) has been associated with the increased risk of developing type 2 diabetes mellitus (T2DM), few basic science studies have indicated the possible beneficial role of some biologic disease-modifying antirheumatic drugs (bDMARDs), including the interleukin-6 (IL-6) based DMARDs, on insulin resistance in patients with RA.
Objectives: To evaluate the impact of treatment with bDMARDs, including the IL-6 inhibitors, on the probability of developing T2DM in a real world setting.
Methods: From the Centricity Electronic Medical Records of GE Healthcare, a longitudinal cohort of 192,509 US adults (age≥18 years) with diagnosis of RA from January 2000 to April 2016 was selected. Patients were excluded if they had a prior history of diabetes, cancer and micro- or macro-vascular diseases at diagnosis of RA. Four mutually exclusive antirheumatic treatment groups (TGs) were identified by diagnosis date (Dx) and treatment initiation date (ID): tocilizumab (TCZ, n=843), TCZ+Other bDMARDs (TCZ+obDMARD, n=2489), non-TCZ other bDMARDs (obDMARD, n=45,262) and no bDMARD (n=143,915). Within the treatment groups, 142,225 patients had a minimum 6 months of exposure before development of T2DM or end of follow-up. Treatment-effects regression models were used to estimate the probabilities (95% CI) of developing T2DM during follow-up in the 4 TGs after adjusting and balancing with inverse-probability-weighted regression for various factors including age, sex, smoking status, body mass index, use of non-biologic DMARDs, use of statins, anaemia status and follow-up time post ID.
Results: At diagnosis, the 142,225 patients were on average 55 years old, 22% male, 71% white Caucasian, 13% with anaemia, and 32% obese with mean BMI of 29 kg/m^2. About 28%/42% were using statins/MTX at diagnosis or during follow-up before development of T2DM. During mean 4.6 years of follow-up from Dx, 2.6%/2.6%/5.3%/5.8% developed T2DM in the TCZ/TCZ+obDMARD/obDMARD/no bDMARD TGs. The adjusted probability of developing T2DM was 0.05 (95% CI: 0.04, 0.05) in no bDMARD group; with significantly lower probability of developing T2DM in TCZ [0.02 (95% CI: 0.01, 0.04)], TCZ+obDMARD [0.03 (95% CI: 0.02, 0.04)] and obDMARD [0.01 (95% CI: 0.01, 0.02)] groups (Table). Hypertension, higher BMI and Statin use were associated with significantly higher probability of developing T2DM by 0.25 (95% CI: 0.16, 0.35), 0.08 (95% CI: 0.07, 0.08) and 0.36 (95% CI: 0.27, 0.47) respectively. Patients with anaemia had 8% higher likelihood of developing T2DM (p=0.13). Among those who received any bDMARD, those who ever received TCZ had significantly lower probability of developing T2DM (0.024, 95% CI: 0.02, 0.03), compared to those who were never exposed to TCZ therapy.

Table: The probability of developing T2DM, adjusted by age, sex, BMI, anaemia; balanced on hypertension, follow-up, obDMARDs and statin usage.

	Probability (95% CI)	Difference (95% CI)
No bDMARD	0.046 (0.045, 0.048)	–
obDMARD Only	0.041 (0.039, 0.044)	-0.005 (-0.008, -0.002)
TCZ Only	0.025 (0.006, 0.043)	-0.022 (-0.04, -0.003)
TCZ+obDMARD	0.018 (0.01, 0.026)	-0.029 (-0.037, -0.02)
Among those who received any bDMARDs		
No TCZ	0.046 (0.044, 0.049)	–
TCZ	0.023 (0.017, 0.029)	-0.024 (-0.03, -0.017)

Conclusions: This study indicates the possible beneficial role of IL-6 inhibitors (TCZ) in reducing the likelihood of developing T2DM among adults without major co-morbidities at diagnosis of RA.
Acknowledgements: Funding by F. Hoffmann-La Roche/Genentech.
Disclosure of Interest: S. Paul Grant/research support from: Therapeutic Innovations Australia, O. Montvida: None declared, J. Best Employee of: Genentech, S. Gale Employee of: Genentech, A. Pethoe-Schramm Employee of: F. Hoffmann-La Roche, K. Sarsour Employee of: Genentech
DOI: 10.1136/annrheumdis-2017-eular.5222

THURSDAY, 15 JUNE 2017

Rheumatoid arthritis - non biologic treatment

THU0168 PATIENTS' POSITIVE BELIEFS AND CERTAINTY PREDICT METHOTREXATE ADHERENCE IN A RHEUMATOID ARTHRITIS COHORT: THE RAMS STUDY

H.F. Hope[1], K. Hyrich[2], F. Varney[3], S. Wilkes[3], S.M. Verstappen[2], L. Cordingley[4]. *[1]NIHR Manchester Musculoskeletal Biomedical Research Unit, Centre for Musculoskeletal Research; [2]Arthritis Research UK Centre for Epidemiology; [3]Division of Psychology and Mental Health; [4]Centre for Musculoskeletal Research and Dermatological Science, University of Manchester, Manchester, United Kingdom*

Background: Living with RA confers substantial uncertainty about the long-term outcomes of the disease and the occurrence of possible medication associated adverse events (ADEs). This latter uncertainty may be particularly apparent when new therapies are initiated and reduce patient adherence.
Objectives: The aim of this study was to evaluate whether patients' negative and/or uncertain illness beliefs during methotrexate (MTX) therapy are associated with adherence.
Methods: This was a sequential mixed-methods design study using data from the Rheumatoid Arthritis Medications Study (RAMS). RAMS is a 12 month observational study in the UK recruiting patients with RA commencing MTX for the first time. Clinical and demographic data were collected at baseline and patients were asked to complete a weekly diary recording MTX intake (adherence) and reasons for not taking MTX. In addition there was a free text section in the diary where patients could comment about any aspect of their disease or care. Six month diary data were used for the purpose of this study.Patients were categorised as non-adherent if the proportion of adherent weeks was <90%.
Phase 1:Using a random sample (n=50/417) of patient diaries with free text comments a coding system was developed to categorise illness events and beliefs contained in these data. Inter-rater reliabilities for codes rated by three judges were calculated using intraclass correlation coefficients (ICC) and unreliable codes (ICC<0.6) dropped.
Phase 2:179 of 200 diaries from adherent and non-adherent individuals were randomly selected, coded and categorised into illness belief profiles (IBPs) by three researchers blind to adherence data.Univariate logistic regression analyses adjusted for age and gender were used to investigate the association between IBPs and MTX non-adherence behaviour (<90% adherence).
Results: Phase 1: ten codes with ICCs ranging from 0.6–1.0 were used to create three IBPs (Table):"Positive & Certain" (PC), "Negative & Certain" (NC) and "Negative and Uncertain" (NU) (Fig.).
Phase II, the median age of the sample was 62 [51.8–65.6] years, 67% were women and the median disease activity score was 4.3 [3.4–5.2]. Being PC lowered the odds of non-adherence (OR 0.32, 95% CI 0.12–0.85), being NU increased the odds of non-adherence (OR 2.7, 95% CI 1.0–7.0), but being NC didn't associate with non-adherence during the first six months of therapy (OR 0.98, 95% CI 0.31–3.2).

Table 1. The reliability (ICC) of codes that contribute to the IBPs

IBP	Codes	ICC (95% CI)
Positive	Treatment response	0.73 (0.60–0.83)
	ADE cessation	0.79 (0.68–0.87)
	Positive emotion	0.77 (0.65–0.85)
	Positive attribution	0.60 (0.44–0.74)
Negative	Disease flare	0.93 (0.89–0.96)
	ADE	0.81 (0.71–0.88)
	Severity attribution	0.62 (0.46–0.75)
	Negative emotion	0.81 (0.71–0.89)
	Negative attribution	0.81 (0.71–0.88)
Certainty/Uncertainty	Certainty/Uncertainty	1.0 (1.0–1.0)

Positive & Certain (N=89)	Negative & Certain (n=148)	Negative & Uncertain (n=35)
"Pain has reduced in my joints this week"	"Methotrexate too strong, however in lot of pain in knees"	"I think the cramp may be the HCQ not the MTX"
"Can write with right hand"	"Pain is still unbearable and (MTX) not working"	"It may be the flu injection what has give me side effect"\
"Wrists much less painful"	"Ankle and wrist still painful and inflamed"	"Fingers and wrist quite painful & lots of pins and needles. Due to heat?"
"Not feeling any side effects"	"Methotrexate had no effect at all at this stage"	"Upset stomach, ate out, so could have been that?"
"Feeling better this week"	"Same as last week seems to be worse"	"Swelling of wrist-knee don't know if tabs caused it"
"Almost all pain gone - whoopee!"	"Stomach ache and nausea much worse after every meal"	"Difficult to tell if MTX side effects, still ill"

Figure. Examples of patient comments that contributed to each IBP

Conclusions: People who are uncertain about how to attribute illness events are less likely to adhere within the first six months of starting MTX therapy. Encouraging patients to actively monitor their progress with therapy and providing them with support to understand likely effects of MTX may help optimise DMARD use.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2463

THU0169 ONE-THIRD OF PATIENTS WITH RHEUMATOID ARTHRITIS ELIGIBLE FOR A FIRST BIOLOGIC ARE NOT ADHERENT TO METHOTREXATE: RESULTS OF FORGET, A CROSS-SECTIONAL SURVEY OF 244 PATIENTS

C. Beauvais[1], V. Hautin-Monteil[2], M.-C. Ducrot[3], R.-M. Flipo[4]. *[1]Rheumatology Department, Saint Antoine Hospital, APHP, Paris; [2]Roche; [3]Agence A+A, Boulogne-Billancourt; [4]Rheumatology department, Roger Salengro Hospital, Lille, France*

Background: Adherence to Methotrexate (MTX) is not optimal in patients with rheumatoid arthritis (RA)[1]. Low adherence may lead to insufficient response and unjustified initiation of biologics.
Objectives: The objectives were 1-assess the self-reported adherence rate to MTX of RA patients insufficient responders to MTX (MTX-IR) when an initiation of biologics was being considered 2- Investigate the factors of low adherence among these patients 3- collect the physicians' estimation of their patients' adherence level.
Methods: Patient recruitment was done through rheumatologists: RA patients, MTX-IR, biologic-naive, eligible for a biologic according to the rheumatologist's opinion. The rheumatologist completed a questionnaire on his practice and estimation on the patient's level of adherence and provided the patient with a self-administered questionnaire on his disease and treatments, to be sent directly to the data center. The patient's questionnaire contained the CQR19 (Compliance Questionnaire for Rheumatology [2]. The purpose of assessing adherence was not specified to the patient.
Results: From May to July 2016, 78 rheumatologists recruited 269 patients who referred 244 self-administered questionnaires, 214 assessed for CQR 19 score; 200 questionnaires were completed by both patients and their rheumatologist. Patients were 72% women, mean age 54 years, 58% had at least 1 comorbidity, mean DAS28 score 4.07, mean RAID score 5.7/10. The percentage of non-adherent patients was 34%: adherence rate <80% according to the CQR.
Non-adherent patients had a higher RAID score (5.7 vs 5.0; p<0.01) whereas DAS 28 was not significantly different (4.14 vs 4.04). They more often presented osteoporosis (18% vs 4%, p<0.01), reported reluctance to take treatment (40% vs 24%, p<0.01), had more negative beliefs (40% vs 24%; p<0.01), and poor support from relatives (67% vs 84%, p<0.011). Good-adherent patients were more often followed in a private practice (31% vs 10%, p<0.01) and reported more information received from their rheumatologist (94% vs 85%, p<0.05). No correlation was found between adherence and age, subcutaneous versus oral route of administration or perceived tolerance.
88% of rheumatologists reported they detect adherence at every consultation, asking direct (76%) or open (46%) questions. Adherence was underestimated by rheumatologists: a 67% concordance was found between the rheumatologist's rating and the patient's reported adherence. Non-adherent patients to MTX were more often proposed biologic treatment in combination with MTX than patients with good compliance (91% vs 68%, p<0.01).
Conclusions: This survey showed for the first time that 34% of MTX-IR patients show poor adherence to MTX at the time of the initiation of a first biologic. Negative beliefs and poor support from relatives are factors of non-adherence. Studies will be needed to understand physicians' attitudes toward non-adherence and what strategy of biologics prescription they are likely to consider.
References:
[1] DiBenedetti D Rheumatol Ther 2015.
[2] de Klerk E et al, J Rheumatol 1999.
Acknowledgements: This study was funded by Chugai Pharma France.
Disclosure of Interest: C. Beauvais: None declared, V. Hautin-Monteil Employee of: Roche France, M.-C. Ducrot: None declared, R.-M. Flipo: None declared
DOI: 10.1136/annrheumdis-2017-eular.5445

THU0170 OUTCOMES OF THE RAPID DOSE ESCALATION OF METHOTREXATE IN JAPANESE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS; RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

M. Tsutsumino[1], R. Sakai[1], M. Kihara[2], K. Amano[3], R. Yoshimi[4], M. Inoo[5], H. Dobashi[6], T. Sugihara[7], T. Hidaka[8], H. Kohsaka[2], N. Miyasaka[2], M. Harigai[1]. *[1]Tokyo Women's Medical University; [2]Tokyo Medical and Dental University, Tokyo; [3]Saitama Medical Center, Saitama; [4]Yokohama City University School of Medicine, Yokohama; [5]Utazu Hospital; [6]Kagawa University, Kagawa; [7]Tokyo Metropolitan Geriatric Hospital, Tokyo; [8]Shiminnomori Hospital, Miyazaki, Japan*

Background: Methotrexate (MTX) is the anchor drug for treatment of rheumatoid arthritis (RA), but tolerance to MTX is substantially different across ethnics and few studies have assessed efficacy and safety of rapid dose escalation regimen of MTX in Japanese patients with early RA.

Objectives: To evaluate outcomes of rapid dose escalation regimen of MTX compared with conventional treatment.
Methods: We implemented a randomized, controlled trial that enrolled patients with RA who fulfilled all of the following criteria: 20 to 70 years-old, disease duration ≤2 years, SDAI ≥11, and without prior use of MTX, tacrolimus (TAC) or biologics. Patients were randomized into rapid escalation (RE) group or conventional treatment (CT) group at 1:1 ratio. In RE group, doses of MTX were escalated up to 0.25 mg/kg/wk within 8 wks after start of MTX and increased maximum tolerable dose or 16 mg/wk until wk 12. If a patient achieved SDAI remission at wk 12, MTX was continued at the same dose. If a patient did not achieve SDAI remission at wk 12 or showed intolerance to MTX, use of TAC or TNF inhibitor (TNFi) were allowed. In CT group, patients were treated with either MTX, TAC, salazosulfapyridine, or bucillamine by the discretion of physicians until wk 12. If a patient achieved SDAI remission at wk 12, same treatment was continued. If a patient did not achieve remission at wk 12, use of TNFi was allowed. Patients were treated by the discretion of physicians at wk 24 and onward. We set two primary endpoints; the percentage of patients achieving SDAI remission and Boolean remission at wk 24. We planned to enroll 120 patients per arm based on expected SDAI remission rates at wk 24, alpha and beta errors and dropout rates.
Results: Enrollment was terminated prematurely and all patients were followed for 48 wks. Of 115 enrolled patients, 57 were randomly assigned to RE group and 58 to CT group. Baseline demographics were similar between the two groups. The median baseline values (RE vs. CT) were 24.9 and 25.9 for SDAI, 0.88 and 0.69 for HAQ, and 0.64 and 0.61 for EQ-5D, respectively. At wk 24, the percentages of patients achieving remission in RE and CT groups were 42% and 28% by SDAI criteria (p=0.1, χ^2 test), and 35% and 17% (p=0.03, χ^2 test) by Boolean criteria, respectively. Median values of HAQ at wk 24 in RE and CT groups were 0 and 0.13 (p=0.096, M-W U test), and those of EQ-5D were 0.78 and 0.77 (p=0.12, M-W U test), respectively. At wk 48, these values were not statistically different between the two groups. There were no significant differences between the two groups with incidence of severe adverse events.
Conclusions: The rapid dose escalation regimen of MTX provided significantly superior Boolean remission rate and tended to provide superior SDAI remission than conventional treatment in patients with early RA in the short term.
Disclosure of Interest: M. Tsutsumino Grant/research support from: Ayumi Pharmaceutical Co., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Nippon Kayaku Co., Ltd., Taisho Toyama Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., and Teijin Pharma Ltd., R. Sakai Grant/research support from: Ayumi Pharmaceutical Co., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Nippon Kayaku Co., Ltd., Taisho Toyama Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Teijin Pharma Ltd., and Bristol-Meyers Squibb., M. Kihara: None declared, K. Amano Grant/research support from: Pfizer Japan Inc., R. Yoshimi Grant/research support from: Bristol-Myers K.K., M. Inoo: None declared, H. Dobashi: None declared, T. Sugihara Grant/research support from: Takeda Pharmaceutical Co. Ltd., Mitsubishi-Tanabe Pharma Co., Chugai Pharmaceutical Co., Ltd., Janssen Pharmaceutical K.K, Santen Pharmaceutical Co., Ltd., Astellas Pharma Inc., Bristol Myers Squibb K.K., Abbvie Japan Co., Ltd., Takeda Pharmaceutical Co., Ltd, and Astellas Pharma Inc., T. Hidaka: None declared, H. Kohsaka Grant/research support from: Ayumi Pharmaceutical Co., Pfizer Japan Inc., Mitsubishi-Tanabe Pharma Corp., Takeda Pharmaceutical Co. Ltd., AbbVie Japan Co. Ltd., Eisai Co., Ltd., Chugai Pharmaceutical Co. Ltd., Bristol-Meyers Squibb, Astellas Pharma Inc., UCB Japan, N. Miyasaka: None declared, M. Harigai Grant/research support from: Ayumi Pharmaceutical Co., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Nippon Kayaku Co., Ltd., Taisho Toyama Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Teijin Pharma Ltd., Eisai, Pfizer Japan Inc., Sanofi-Aventis KK., Santen Pharmaceutical Co., Ltd and Sekisui Medical Co., Ltd.
DOI: 10.1136/annrheumdis-2017-eular.3335

THU0171 INCREASED FUNCTIONAL ACTIVITY OF FOXP3+REGULATORY T CELLS IN THE PERIPHERAL BLOOD OF DMARDS-NAÏVE METHOTREXATE-TREATED PATIENTS WITH EARLY RA USING

A. Avdeeva[1], Y.P. Rubtsov[2], T.V. Popkova[1], D.T. Diykanov[2], E.L. Nasonov[1]. *[1]Nasonova Research Institute of Rheumatology; [2]Lomonosov Moscow State University, Moscow, Russian Federation*

Objectives: To analyze the effect of methotrexate (MT) therapy on the percentage and absolute number of FoxP3+ regulatory T (Treg) cells in the peripheral blood of MT-naïve patients (pts) with early RA we used Treg immunostainingwith antibodies to surface markers and Foxp3 with subsequent flow cytometric analysis
Methods: 45 MT-naïve pts with early RA (39 females, Me;IQR age 52.0 (32.5–57.5) years, RA duration 5 (4–6) months, DAS 28 5.01 (4.18–5.8), RF positive -71.1%, ACPA - positive-88.9%) were included into the study. All pts were administered subcutaneous MT as the first-line DMARD at 10 mg/week with rapid dose escalation up to 20–25 mg/week. Human blood mononuclear cells were isolated from whole venous blood by Ficoll–Hypaque centrifugation and subjected to multicolor flow cytometry analysis. Tregs were stained for different surface markers, and proportions of marker-positive subsets (FoxP3+CD25+; CD152+surface; CD152+intracellular; FoxP3+CD127-; CD25+CD127-; FoxP3+ICOS+; FoxP3+CD154+; FoxP3+CD274+) were determined; 20 healthy donors made the control group
Results: After 24 weeks of MT therapy value DAS 28 was 3.1 (2.7–3.62); SDAI 7.4 (4.2–11.4); DAS 28 remission/low disease activity was achieved in 22 (56.4%) pts, based on SDAI – in 25 (64.1%) pts; while MT failure based on EULAR response was documented in 4 (10.3%) pts. Lower percentages of FoxP3+CD25+ cells ((5.53 (4.09–6.48 vs 6.92 (5.84–7.96)), percentages and absolute number of FoxP3+ICOS+ cells ((6.91 (2.14–11.47) vs 10.83 (9.27–13.7); 0.0035 (0.0013–0.0067) vs 0.0068 (0.0039–0.009)), and percentages and absolute number of FoxP3+CD154+ cells ((0.47 (0.19–0.83) vs 1.51 (1.12–2.08); 0.0002 (0.00009–0.0005) vs 0.00087 (0.00047–0.0014)), and FoxP3+CD274+ T-cells (0.63 (0.34–1.49) vs 1.94 (1.16–2.25); 0.0003 (0.0002–0.00065) vs 0.001 (0.0006–0.0016), $p<0,05$ in all cases) were documented in early RA pts versus healthy donors.
An increase in the percentage of CD4+cells (from 45.0 (38.0–49.2) to 46.8 (39.9–53.2)); an increase in the relative and absolute number of CD152+surface 0.65 (0.22–1.67) vs 2.07 (1.11–3.81); 0.0002 (0.0001–0.0008) vs 0.0007 (0.0004–0.002); and moderate decrease in the relative and absolute number of FoxP3+ICOS+ cells 5.3 (2.1–11.3) vs 4.1 (1.6–6.6); 0.002 (0.001–0.006) vs 0.0015 (0.0006–0.003), $p<0.05$ in all cases, was registered after 24 weeks of MT therapy. After 24 weeks of MT therapy the level of CD152+surface in the RA pts group was higher compared with healthy donors 2.1 (1.11–3.81) and 0.51 (0.34–1.2); 0.0007 (0.0004–0.002) and 0.0003 (0.00014–0.0008), respectively, $p<0.05$
Treg levels and phenotype were analyzed in pts groups based on MT efficacy by 24th week of treatment. Higher percentages and absolute number of FoxP3+CD274+ cells (1.25 (0.43–2.3) 0.0004 (0.0002–0.001) were detected in patients achieving SDAI remission (n=25), compared to pts with moderate disease activity (SDAI>11 n=14) (0.44 (0.2–0.69) 0.00016 (0.0001–0.0004), $p<0.05$)
Conclusions: MT therapy in early RA pts results in increased Treg suppressor activity according to growing percentages and absolute number of CD152+surface and FoxP3+CD274+ cells, more pronounced among pts, achieving remission/low disease activity following treatment. Increased levels of these markers are indicative of improved Tregs functional activity after successful MT therapy
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3668

THU0172 IMPROVEMENT OF DISEASE ACTIVITY IN A 5-YEAR COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED UNDER TREAT TO TARGET RECOMMENDATIONS AND A MULTISPECIALITY CARE MODEL RECEIVING CONVENTIONAL DMARD THERAPY

P. Santos-Moreno[1], D. Gomez[1], E. Castillo[1], R. Giraldo[1], G. Ballesteros[1], L. Villarreal[2], J. Bello[3], D. Buitrago-Garcia[3]. *[1]Rheumatology; [2]Psychology and processes; [3]Epidemiology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: Treat to Target (T2T) strategy becomes from the need to develop therapeutic targets and tools to achieve defined outcomes in rheumatoid arthritis (RA), this strategy has become recognized as a standard of good practice embodying the principle that rapid attainment of remission, or low disease activity, can halt joint damage and maintain good quality of life.
Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy for a 5 year period in patients with conventional DMARD therapy in a large cohort of patients from a Colombian specialized in RA center with multidisciplinary care model (MCM).
Methods: A descriptive dynamic cohort study was performed. Records of patients using conventional DMARD treatment from specialized in RA center were reviewed; those patients were followed-up under T2T standards. Clinical follow-up was according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1). Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it. MCM model means that every patient is seen by the other specialties involved in care as a minimum three times a year. We divided patients in three groups: low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients. Descriptive epidemiology was done, percentages and averages were calculated; the median of each variable was analyzed using t-Student assuming normality for DAS28 distribution and the level activity disease was analyzed using Pearson's statistics.
Results: We included 1443 patients, 84% were women and 16% were men. Mean age was 62±11 years; mean DAS28 at beginning was 4.0±1; regarding disease activity 57% were in moderate disease activity and 17% in severe disease activity. While at 5 year follow up mean DAS was 2.92±0.65, 48% achieved remission, 30% low disease activity, with decrease to 20% in moderate disease activity and 2% in severe disease activity.

ACTIVITY LEVEL	TIME 0 n(%)	2012-2013 n(%)	2013-2014 n (%)	2014-2016 n (%)
REM	-	380(26%)	530(37%)	698(48%)
LDA	380 (26%)	495(34%)	487(34%)	437(30%)
MDA	782 (54%)	439(30%)	401(28%)	284(20%)
SDA	281 (19%)	129(9%)	25(2%)	24 (2%)

Conclusions: There is a significant improvement of DAS28 in a cohort of RA

patients receiving only conventional DMARDs therapy, treated and followed under T2T strategy recommendations and a MCM model.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5592

THU0173 LONG TERM SAFETY AND EFFICACY OF FILGOTINIB IN A PHASE 2B OPEN LABEL EXTENSION STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS UP TO 144 WEEKS

R. Alten[1], R. Westhovens[2], A. Kavanaugh[3], M. Genovese[4], K. Winthrop[5], M. Greenwald[6], L. Ponce[7], F. Enriquez[8], M. Stanislavchuk[9], M. Mazur[10], A. Spindler[11], R. Cseuz[12], N. Nikulenkova[13], M. Glowacka-Kulesz[14], I. Szombati[15], A. Dudek[16], L. Meuleners[17], C. Tasset[17], P. Harrison[17], A. Van der Aa[17]. *[1]Schlosspark-Klinik, Berlin, Germany; [2]University Hospitals, Leuven, Belgium; [3]University of California, la Jolla; [4]Stanford University School of Medicine, Palo Alto; [5]Oregon Health and Science University, Portland; [6]Desert Medical Advances, Palm Springs, United States; [7]Cons. Priv., Temuco, Chile; [8]Clinstile SA de CV, Col.Roma, Mexico; [9]Vinnitsya Reg Clin Hosp, Vinnitsya, Ukraine; [10]IMSP Inst. de Cardiologie, Chisinau, Moldova, Republic of; [11]Centro Méd. Priv. Reum., Tucumau, Argentina; [12]Revita Reumatológiai Kft, Budapest, Hungary; [13]Vladimir Reg Clin Hosp, Shosse, Russian Federation; [14]Silesiana Centrum Medyczne, Wroclawska, Poland; [15]Qualiclinic Kft, Budapest, Hungary; [16]AMED Medical Center, Warsaw, Poland; [17]Galapagos NV, Mechelen, Belgium*

Background: Filgotinib (GLPG0634, GS-6034) is an oral JAK1 selective inhibitor with a favorable safety and efficacy profile in two 24-week Phase 2b studies as add-on to methotrexate (DARWIN 1) or as monotherapy (DARWIN 2) in patients with active rheumatoid arthritis (RA). Three daily doses were tested (50mg, 100mg or 200mg) in comparison to placebo.
Objectives: To assess long term safety and efficacy of filgotinib 200mg daily in patients from the DARWIN 3 Phase 2 open-label extension study.
Methods: Patients who completed DARWIN 1 or 2 and enrolled in DARWIN 3 received filgotinib 200mg once daily or 100mg twice daily, depending on prior treatment assignment. The DARWIN 3 data cut off was when the last patient reached extension Week 60. For safety, all data from the first intake of filgotinib in DARWIN 1/2/3 were analysed (up to 144 weeks).
Results: 877 patients participated in DARWIN 1 or 2, 790 completed and 739 entered DARWIN 3 from 22 countries (82% females, mean age 53y). 559 patients (75.6%) completed Week 60, 9.3% discontinued due to positive Quantiferon, 7.8% due to other adverse events, 6.8% for other reasons and 0.3% due to insufficient response. Overall exposure to filgotinib was 1314 patient-years (PYE). Treatment-emergent adverse events (157.7/100PYE), serious adverse events (5.3/100PYE) and serious infections (1.9/100PYE) occurred at similar rates compared to the core studies, however infections decreased on a percentage basis from 15% (109/739, W0–12) to 5% (25/549, W85–96). 16 cases of Herpes zoster were reported (1.2/100PYE), 6 cases of malignancy (excl. NMSC) (0.5/100PYE) and 1 case of MACE (0.1/100PYE). There was no active case of tuberculosis. Three fatalities were reported (0.2/100PYE). Mean change from baseline (CFB) at Week 96 and CTCAE toxicity grading in lab parameters of special interest are shown in table 1.

Table 1. Mean CFB at Week 96 and CTCAE toxicity grading of selected lab parameters

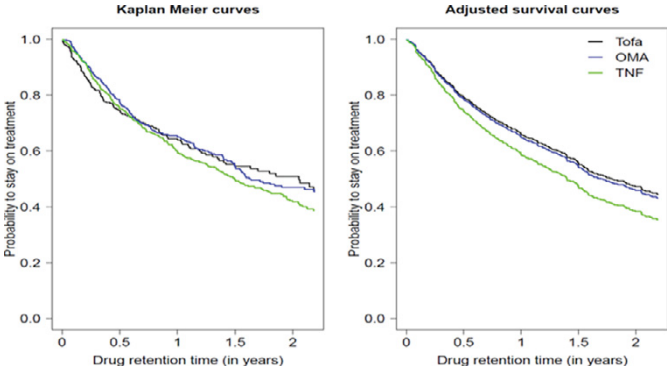
	Mean CFB	CTCAE Grade 3–4 (%)
Hb	+6.5 g/L	0.4
Neutrophils	–1.73 giga/L	1
Lymphocytes	–0.19 giga/L	2
Creatinine	+8.2 μmol/L	0
ALT	+6.1 U/L	0.4
LDL	+13%	–
HDL	+23%	–
Tot chol/HDL	–4%	–
NK cells	–0.02 giga/L	–

Based on an observed case analysis 84% (505/601), 65% (389/601), 44% (267/601) and 51% (299/587) of patients reached ACR20, ACR50, ACR70 and DAS28(CRP) remission at Week 60 respectively.
Conclusions: With 1314 patient-years of exposure, the safety profile of filgotinib appears consistent with that of previously reported double-blind studies and the clinical response appears durable.
References:
[1] Westhovens R et al. Ann Rheum Dis 2016;0:1–11.
[2] Kavanaugh A et al. Ann Rheum Dis 2016;0:1–11.
Disclosure of Interest: R. Alten Grant/research support from: Galapagos, R. Westhovens Grant/research support from: Roche, Consultant for: Galapagos, Speakers bureau: BMS, A. Kavanaugh Consultant for: Galapagos, Pfizer, AbbVie, Amgen, Celgene, Janssen, Novartis, Eli Lilly, UCB, M. Genovese Grant/research support from: Abbvie, Eli Lilly, Pfizer, Astellas, Vertex, Consultant for: Galapagos, Gilead, Abbvie, Eli Lilly, Pfizer, Astellas, Vertex, K. Winthrop Grant/research support from: BMS, Pfizer, Consultant for: pfizer, BMS, lilly, Abbvie, Roche, UCB, Galapagos, Amgen, M. Greenwald Grant/research support from: Abbvie,Amgen, Bristol Myers Squibb, Celgene, Galapagos, Gilead, Lilly, Merck, Pfizer, UCB, Consultant for: Lilly, Pfizer, L. Ponce: None declared, F. Enriquez: None declared, M. Stanislavchuk: None declared, M. Mazur: None declared, A. Spindler: None declared, R. Cseuz: None declared, N. Nikulenkova: None declared, M. Glowacka-Kulesz: None declared, I. Szombati: None declared, A. Dudek: None declared, L. Meuleners Employee of: Galapagos NV, C. Tasset Employee of: Galapagos NV, P. Harrison Employee of: Galapagos NV, A. Van der Aa Employee of: Galapagos NV
DOI: 10.1136/annrheumdis-2017-eular.5460

THU0174 DRUG RETENTION OF TOFACITINIB VERSUS BIOLOGIC ANTIRHEUMATIC AGENTS IN RHEUMATOID ARTHRITIS: OBSERVATIONAL DATA FROM THE SWISS SCQM REGISTRY

A. Finckh[1], L. Herzog[2], A. Scherer[2], J. Dudler[3], B. Moeller[4], A. Ciurea[5], R. Mueller[6], P. Hasler[7], P. Exer[8], I. von Muehlenen[8], D. Kyburz[9], C. Gabay[1], P. Zufferey[10] on behalf of the Physicians of the SCQM. *[1]HUG, Geneva; [2]SCQM Foundation, Zurich; [3]HFR, Fribourg; [4]Inselspital, Bern; [5]USZ, Zurich; [6]KSSG, St Gallen; [7]KSA, Aarau; [8]Rheuma-Basel Practice; [9]USB, Basel; [10]CHUV, Lausanne, Switzerland*

Background: The oral Janus kinase inhibitor tofacitinib (Tofa) was licensed in Switzerland in 2013 for the treatment of moderate to severe rheumatoid arthritis (RA) patients having failed methotrexate. Besides Tofa, rheumatologists in Switzerland have the choice between 7 alternative bDMARDs licensed with similar indications, including 5 TNF inhibitors (TNFi) and 2 bDMARDs with other modes of action (OMA-bDMARDs).
Objectives: To compare the drug retention rate of three alternative treatment options licensed with a similar indications, namely Tofa, TNFi and OMA-bDMARDs, using data from the Swiss registry.
Methods: This is an observational cohort study within the Swiss Clinical Quality Management registry (SCQM). All therapies with Tofa, TNFi, and OMA-bDMARDs initiated in adult RA patients between August 1, 2013 and Dec 1, 2016 were considered. The exposure of interest was treatment with Tofa vs TNFi and vs OMA-bDMARDs (Abatacept or Tocilizumab). The primary outcome was drug retention defined as the time from initiation to discontinuation of treatment. We used Kaplan Meier curves to display drug retention and Cox proportional hazard models stratified by seropositivity to analyze the hazard for treatment discontinuation. We adjusted for potential confounders, including gender, age, disease duration, seropositivity, BMI, smoking status, DAS28-CRP and the total number of previous bDMARDs. We applied multiple imputation to account for missing baseline covariate data.
Results: A total of 1996 therapies were initiated during the study period (376 Tofa, 928 TNFi, 692 OMA-bDMARDs). Some differences in disease and treatment characteristics existed between the 3 groups, in particular TNFi tended to be used in patients with fewer previous bDMARDs experience, younger age and shorter disease duration. The crude overall drug retention was similar between the 3 three drug groups (p=0.24) (Figure 1A). The adjusted analysis demonstrated a slightly higher hazard of drug discontinuation with TNFi compared to Tofa [HR 1.27 (95% CI: 1.02 – 1.57, p=0.03)], while no difference was observed for OMA-bDMARDs and Tofa [HR 1.03 (95% CI: 0.83 – 1.28, p=0.76)] (Figure 1B). Complete case results were consistent with results using multiple imputation of baseline covariates. Other variables significantly associated with drug discontinuation were a higher number of previous bDMARDs (p <0.001) and increasing BMI values (p=0.03), while combination therapy with sDMARDs tended to decrease discontinuation (p=0.08)



Conclusions: The results of this observational study suggest that Tofa is a valuable alternative to treatment options in RA, with Tofa drug retention at least comparable to other available bDMARDs.
Acknowledgements: Disclosure. Investigator Initiated Research grant supported by Pfizer.
Disclosure of Interest: A. Finckh Grant/research support from: BMS, Speakers bureau: Abbvie, BMS, Pfizer, Roche, UCB, L. Herzog: None declared, A. Scherer: None declared, J. Dudler: None declared, B. Moeller: None declared, A. Ciurea: None declared, R. Mueller: None declared, P. Hasler: None declared, P. Exer: None declared, I. von Muehlenen: None declared, D. Kyburz: None declared, C. Gabay: None declared, P. Zufferey: None declared
DOI: 10.1136/annrheumdis-2017-eular.6804

THU0175 INFLAMMATION DETECTED WITH MODERN SENSITIVE MRI ANALYSIS DEMONSTRATES THAT THERAPEUTIC RESPONSE AS EARLY AS ONE MONTH PREDICTS 12-MONTH RADIOGRAPHIC PROGRESSION: DATA FROM A STUDY USING TOFACITINIB AND METHOTREXATE IN METHOTREXATE-NAÏVE PATIENTS WITH EARLY RA

P.G. Conaghan[1,2], M.A. Bowes[3], M. Østergaard[4], G. Guillard[3], D. Chapman[5], A. Stein[6], J. Andrews[5], Z. Xie[7], A. Koenig[8], K. Soma[7], B. Wilkinson[7]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]NIHR Leeds Musculoskeletal Biomedical Research Unit, Chapel Allerton Hospital, Leeds; [3]Imorphics Ltd, Manchester, United Kingdom; [4]Copenhagen Center for Arthritis Research, Copenhagen, Denmark; [5]Pfizer Inc, New York, NY; [6]Quintiles, Morrisville, NC; [7]Pfizer Inc, Groton, CT; [8]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. A novel automated quantification method for RA MRI-detected pathology using statistical shape modelling technology (RAMRIQ) provides a tool that may be even more responsive than the sensitive RAMRIS semi-quantitative standard.[1]
Objectives: To determine if early changes in RAMRIQ were predictive of subsequent MRI and radiographic damage progression in a study of tofacitinib for the treatment of early RA in methotrexate-naïve patients with minimal radiographic progression.
Methods: We used data from an exploratory, Phase 2 randomised controlled trial comparing tofacitinib, methotrexate and the combination (n=109) in methotrexate-naïve patients with early active RA.[1] All patients met ACR classification criteria for active RA. MRI was performed at baseline and at 1, 3, 6 and 12 months. A single centralised reader read all MRI data; data for each patient were randomised by time point and read in the same sitting. We examined changes in synovitis, osteitis and erosions for RAMRIQ and RAMRIS at 1 and 3 months and performed univariate analyses on their relationship to RAMRIS, RAMRIQ and radiographic progression (modified Total Sharp Score [mTSS]) at 12 months.
Results: Reduction in RAMRIQ synovitis and osteitis at 1 and 3 months were significantly associated with reduction in RAMRIS erosion progression at 12 months (Table). Improvement in RAMRIQ synovitis and osteitis at 1 and 3 months were also associated with reduction in radiographic progression at 12 months, while RAMRIQ erosions at 1 and 3 months were not significantly associated with radiographic progression (Table). Early changes in RAMRIS erosion at 1 and 3 months were associated with radiographic progression at 12 months (Table). Treatment with tofacitinib alone or in combination with methotrexate was also associated with reduced progression in RAMRIS erosions (p=0.017 and p=0.007, respectively).

Table. Univariate analyses of the relationship between RAMRIQ and RAMRIS measurements at Month 1 and 3 and RAMRIS erosion and radiographic progression at Month 12.

p value	RAMRIS erosion progression (Month 12)	Radiographic progression (mTSS; Month 12)
Change in RAMRIQ synovitis		
Month 1	0.004	<0.001
Month 3	0.008	0.008
Change in RAMRIQ osteitis		
Month 1	0.001	<0.001
Month 3	<0.001	<0.001
Change in RAMRIQ erosions		
Month 1	-	0.075
Month 3	-	0.530
Change in RAMRIS erosions		
Month 1	-	0.001
Month 3	-	0.005

mTSS, modified Total Sharp Score; RAMRIQ, quantitative RAMRIS; RAMRIS, Rheumatoid Arthritis MRI Scoring System

Conclusions: In this study, sensitive automated detection demonstrated that change in synovitis and osteitis predict subsequent RAMRIS erosion and radiographic progression. Treatment with tofacitinib as monotherapy or in combination with methotrexate was also highly predictive of no progression of erosive damage. Because of its enhanced sensitivity, novel quantitative imaging analysis has the potential to change RA clinical trial design where assessing structural damage is an objective.
References:
[1] Conaghan PG et al. Ann Rheum Dis 2016; 75: 1024–1033.
Acknowledgements: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by S Morgan of CMC and was funded by Pfizer Inc.
Disclosure of Interest: P. G. Conaghan Consultant for: AbbVie, Eli Lilly, Flexion, Novartis, Pfizer Inc, Roche, Speakers bureau: AbbVie, Novartis, Roche, M. A. Bowes Employee of: Imorphics Ltd, M. Østergaard Grant/research support from: AbbVie, Centocor, Merck, Consultant for: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Eli Lilly, GSK; Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer Inc, Regeneron, Roche, Schering-Plough, Takeda, UCB, Wyeth, Speakers bureau: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Eli Lilly, GSK; Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer Inc, Regeneron, Roche, Schering-Plough, Takeda, UCB, Wyeth, G. Guillard Employee of: Stryker Co, D. Chapman Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, A. Stein Employee of: Quintiles, J. Andrews Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Z. Xie Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, A. Koenig Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Soma Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, B. Wilkinson Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
DOI: 10.1136/annrheumdis-2017-eular.2435

THU0176 EFFICIENCY AND SAFETY OF RAPAMYCIN COMBINED WITH LOW-DOSE IL-2 TREATMENT COMPARED WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Z. Li[1], H. Niu[1], M. Chen[1], H. Yao[1], J. Luo[1], C. Gao[2], X. Li[1], C. Wang[1]. *[1]Rheumatology, the Second Hospital of Shanxi Medical University, Taiyuan, Shanxi, China; [2]Pathology, Brigham and Women's Hospital, Harvard Medical School, Brigham and Women's Hospital, Harvard Medical School, United States*

Background: The molecular target rapamycin (mTOR) signaling can regulate between effector and regulatory T cell lineage commitment [1]. Rapamycin, the inhibitor of mTOR, has appeared to be a new therapy for several autoimmune diseases, such as systemic lupus erythematosus [2].
Objectives: To evaluate whether rapamycin is beneficial in patients with Rheumatoid Arthritis (RA), and compared with Methotrexate in efficiency and safety.
Methods: Fifty-eight DMARDs-naive RA patients were enrolled, thirty-eight were treated with Rapamycin (0.5 mg every 2 days, combined with IL-2 50WIU per day for 5 days), the others with Methotrexate (10mg per week) taken as control. Clinical improvement and immunological assessments were performed at baseline, 1 and 12 weeks. Treatment group assessed CD4+ T cell subsets by flow cytometry at baseline, 1 and 12 weeks.
Results: We enrolled 58 patients. At baseline, patients had a mean DAS28 of 3.34 (0.81). Rapamycin group and Methotrexate group included 38 and 20 patients, respectively, with no significant differences in baseline characteristics. At 1 week, the mean DAS28 after Rapamycin treatment (2.43 [0.77]) and Methotrexate (2.25 [0.86]) was not significantly different (P=0.43). Same as ESR (24.74 [24.53], 21.76 [24.27], P=0.66). The dose of glucocorticoid during hospitalization of rapamycin treatment group (720.8 [554.3]) was lower than Methotrexate (1202.3 [943.1], P=0.042). The length of hospital stay of Rapamycin (14.5 [3.9]) was lower than Methotrexate (21.0 [3.8], P<0.001). Rapamycin administration resulted in an increase in the absolute counts of Treg cells from a median of 36.82 cell/ul (at week 0) to 99.80 cell/ul (at week 1) (P<0.001). The ratios of Th17/Treg cells showed a reduction from a median of 0.16 to 0.09, and the difference was significant (P=0.047). At 12 week, 5 patients treated with Rapamycin dropped out because of non-compliance. the mean DAS28 was not significantly different (2.36 [0.97], 2.16 [0.86], P=0.51). The same as the daily dose of glucocorticoid (10.21 [32.3], 9.16 [40.1], P=0.804). The absolute counts of Treg cells increased from a median of 36.82 cell/ul (at baseline) to 43.26 cell/ul after Rapamycin administration (P=0.028). The ratios of Th17/Treg had no significant difference from a median of 0.16 at baseline to 0.12 at week 12 (P=0.937). Liver enzyme elevations occurred on 2 patients after Methotrexate therapy for 1 week. However, there were no serious adverse events observed during the 12-week period of rapamycin treatment.
Conclusions: Rapamycin combined with the low-dose IL-2 appears to be a safe and effective therapy for RA, by a rapid increase of circulating Treg cells and a correction of the ratio of Th17/Treg cells, which has gotten a same response compared with Methotrexate.
References:
[1] Zheng Y. The mTOR kinase differentially regulates effector and regulatory T cell lineage commitment.[J]. Immunity, 2009, 30(6):832–844.
[2] Fernandez D, Bonilla E, Mirza N, et al. Rapamycin Reduces Disease Activity and Normalizes T Cell Activation–Induced Calcium Fluxing in Patients With Systemic Lupus Erythematosus[J]. Arthritis & Rheumatology, 2006, 54(9):2983–2988.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4575

THU0177 ABT-494 PHARMACOKINETICS FOLLOWING ADMINISTRATION OF THE ONCE-DAILY EXTENDED-RELEASE TABLET FORMULATION BEING UTILIZED IN THE ONGOING RHEUMATOID ARTHRITIS PHASE 3 TRIALS

M.-E.F. Mohamed[1], J. Zeng[1], I.-H. Song[2], A.A. Othman[1]. *[1]Clinical Pharmacology and Pharmacometrics; [2]Immunology Clinical Development, AbbVie, North Chicago, United States*

Background: ABT-494 is a selective Janus Kinase 1 inhibitor. In two Phase 2b studies in subjects with rheumatoid arthritis, 6 mg and 12 mg twice-daily (BID) doses of ABT-494 immediate-release formulation achieved optimal benefit-risk profiles. To enhance patients' compliance, an extended-release formulation was developed targeting to achieve comparable exposures with the 6 mg and 12 mg BID of the immediate-release formulation with once-daily (QD) administration.

Objectives: The objective of this work was to characterize the pharmacokinetics of ABT-494 with the extended-release formulation that is currently being utilized in Phase 3.
Methods: Comparison of ABT-494 pharmacokinetics from the immediate-release and extended-release formulations was conducted following multiple-dose administration in healthy subjects. Two cohorts of subjects were evaluated. In the first cohort, healthy subjects (N=12) received multiple 15 mg QD doses of the extended-release tablet formulation and multiple 6 mg BID doses of the immediate-release capsule formulation for 7 days. In the second cohort, healthy subjects (N=12) received multiple 30 mg QD doses of the extended-release tablet formulation and multiple 12 mg BID doses of the immediate-release capsule formulation for 7 days. Both evaluations were conducted following an open-label, randomized, 2-period, 2-sequence, crossover design under fasting conditions. ABT-494 plasma concentrations were measured and pharmacokinetic parameters were calculated using non-compartmental analyses.
Results: At steady-state, ABT-494 AUC0–24 ratio [and 90% confidence interval] was 0.94 [0.84 – 1.05], C_{max} ratio was 0.91 [0.74 – 1.12] and C_{min} ratio was 1.09 [0.85 – 1.40] for the 15 mg QD regimen of the extended-release formulation relative to the 6 mg BID regimen of the immediate-release formulation. Similarly, ABT-494 mean $AUC_{0–24}$ ratio was 0.97 [0.87 – 1.09], C_{max} ratio was 0.90 [0.73 – 1.11] and C_{min} ratio was 0.87 [0.75 – 1.02] for the 30 mg QD regimen of the extended-release formulation relative to the 12 mg BID regimen. All evaluated regimens were well-tolerated by healthy subjects.
Conclusions: ABT-494 regimens of 15 mg QD and 30 mg QD of the extended-release formulation, currently being utilized in Phase 3 RA studies, provide similar exposures to 6 mg BID and 12 mg BID, respectively of the immediate-release capsule formulation previously shown to provide optimal benefit-risk profiles in RA Phase 2 trials.
Disclosure of Interest: M.-E. Mohamed Shareholder of: AbbVie, Employee of: AbbVie, J. Zeng Shareholder of: AbbVie, Employee of: AbbVie, I.-H. Song Shareholder of: AbbVie, Employee of: AbbVie, A. Othman Shareholder of: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.3224

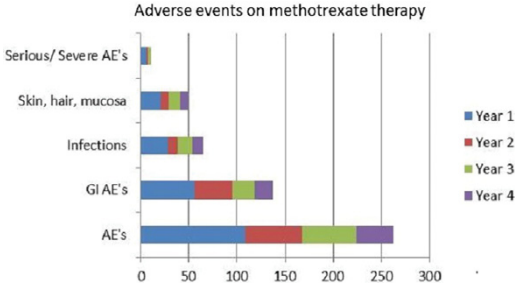
THU0178 LONG TERM SAFETY PROFILE OF METHOTREXATE IN PATIENTS WITH RA IN ROUTINE CARE

A.B. Nalawade[1], S.M. Akerkar[2], B.D. Pandey[3]. *[1]Rheumatology, Sancheti Institute, Pune; [2]Mumbai arthritis clinic, Mumbai; [3]Rheumatology, Fortis Hospital, Delhi, India*

Background: Methotrexate is the anchor drug used most widely as monotherapy or combination therapy with other DMARDS & biologics in treatment of RA. It is widely perceived by clinicians to have potentially dangerous adverse effects (AE). The present study was designed to assess safety of long term methotrexate in patients with RA on standard care in clinical practice.
Objectives: To evaluate the safety of long term methorexate therapy in patients with RA
Methods: RA patients on methotrexate therapy at recommended doses (15–25 mg per week) as monotherapy or in combination with other conventional dmards or biologics for over 4 years were enrolled between Jan 2016 to Dec 2016. Since the objective was to assess safety, those patients initiated on methotrexate 4 years ago but had discontinued due to adverse effects were also included. Patients were analysed with a questionnaire and review of past records from the clinic. The questionnaire included questions about duration and compliance of methotrexate therapy, any untoward effects that patient felt were due to methotrexate and direct questions related to known methotrexate side effects. Investigations were reviewed from past records.Data were presented by 1- year intervals starting from the time patient received first dose of methotrexate. Adverse events (AE), rate of discontinuation and abnormal laboratory results were analysed per 100 patient (pt.) years in 1 year intervals.
Results:

Females, no. (%)	205 (89.9%)
Age, mean ± SD (years)	48.6 (±10.8)
Disease duration, mean ± SD (years)	8.4 (±5)
Seropositive (RF and/ or ACPA)	207 (91%)
Methotrexate monotherapy (%)	55 (24%)

The cumulative exposure to methotrexate was 926 patient years. Of 228 patients, 218 continued methotrexate through 4 years. Overall 10 patients discontinued methotrexate over 4 years, 5 due to GI intolerance and 1 due skin allergy in the first year. In subsequent years 2 patients were withdrawn due to chronic cough, 1 due to raised transaminases and 1 patient after severe infection and pancytopenia. Incidence of AEs, severe AEs, infections, laboratory abnormalities and discontinuations due to AE's declined during 4 years exposure. The most common AEs included nausea and dyspepsia (24.6/ 100 pt. years in first year with declining incidence through 4 years). The second most common AE reported was infections (7/100 pt. years). Most common infections were mild UTI & respiratory tract infections.14 patients initially asymptomatic or having mild nausea reported significantly increased nausea in year 4 and beyond, all responding to reduction of methotrexate dose. The incidence of severe AE that needed hospitalisation &/ or discontinuation of methotrexate was 2.6/100 pt. years in year 1 with declining events over time. The cumulative risk of serious AE over 4 years was 1.2/ 100 pt. years.



Conclusions: Methotexate therapy was well tolerated over 4 years treatment period with a good safety profile. Most of the AE's were mild to moderate severity not needing discontinuation of methotrexate. Study has limitations since it is retrospective observational study with small patient number from two outpatient rheumatology clinics. Some AE's may have been underestimated as patient compliance not ascertained and patients with AE's may have lost to follow up. Some effects may have been overestimated as precise causality is not proven. During the 4 years methotrexate treatment, no new safety concerns emerged.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4055

THU0179 INCIDENCE OF DEEP VEIN THROMBOSIS AFTER TOTAL HIP REPLACEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Rybnikov, E. Byalik, S. Makarov, T. Reshetnyak, A. Khramov, E. Naryshkin, D. Ivanov, V. Pavlov. *Orthopaedic, V.A.Nasonova research institute of rheumatology, Moscow, Russian Federation*

Background: The purpose of this study was to compare incidences of VTE in patients with rheumatoid arthritis (RA) and osteoarthritis (OA) after total hip arthroplasty, different strategies for prevention of VTE and evaluate their efficiency.
Objectives: To evaluate the efficiency of prevention of VTE in patients with rheumatoid arthritis and osteoarthritis after total hip replacement under comparable conditions.
Methods: A one-year prospective cohort study was performed on 173 primary THA patients operated in V.A. Nasonova Research Institute of Rheumatology for the period 2016. Of these, 91 patients with RA (52.6%) and 82 patients with OA (47.4%). For a comparative analysis of the efficiency of anticoagulant therapy, each patient group was divided into 2 subgroups by type of drug therapy. The first - nadroparin calcium (the drug therapy was started for 12 hours after the operation at a dose of 0.1 ml per 10 kg of body weight one time per day), the second - nadroparin calcium with transfer to dabigatran etexilate (the first stage of 4 hours after the operation was started therapy by nadroparin calcium, and then after the removal of the epidural catheter moved to the dabigatran etexilate).Doppler ultrasonography (DUS) was routinely performed preoperatively and on postoperative day 7, 14, then 1 time a month for diagnosing a deep venous thrombosis (DVT). Time of observation was 6 months.
Results: DVT were reported in 8 (4.8%) patients, 2 of them (1.2%) with RA and 6 (3.4%) with OA. Distal DVT developed on 8 and 17 days after total hip replacement in RA patient's group. They received nadroparin calcium only. 5 patients with VTE after surgery from OA group used nadroparin calcium and 1 patient was on combined drug therapy. Of the 8 cases of VTE - 6 (75%) were asymptomatic and 2 (25%) with development of clinical and laboratory picture. All cases of thrombosis in a group of RA was asymptomatic. In a perioperative period of clinically significant bleeding was not seen.
Conclusions: Cases of VTE in patients with RA, despite the large number of risk factors, under comparable conditions is significantly lower than patients with OA. The number of asymptomatic DVT dominates symptomatic both comparison groups. In patients with RA and OA who were from the first group have reported 6 cases of VTE and only 1 case of VTE have reported in patients who were from second group. Prevention of VTE by combination of LMWH and NOACs was more effective and safety in RA and OA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6422

THU0180 SYSTEMS BASED INVESTIGATION OF THE ANTI-IMMUNOGENIC POTENTIAL OF DMARDS FOR RHEUMATOID ARTHRITIS USING HUMAN PRIMARY CELL-BASED BIOMAP® PHENOTYPIC PROFILING

A. O'Mahony[1], E. Choy[2]. *[1]BioMAP Division, DiscoverX Corporation, South San Francisco, United States; [2]Division of Infection and Immunity, Cardiff University School of Medicine, Cardiff, United Kingdom*

Background: Biologics represent a rapidly growing class of approved and investigational drugs routinely used to treat multiple diseases, including inflammatory and rheumatic diseases[1]. Unfortunately, the success of such therapeutics is

undermined by their immunogenicity and the development of anti-drug antibodies (ADA) associated with treatment failure and hypersensitivity reactions[2]. Methotrexate (MTX) has been shown to reduce the generation of an ADA response[3]. The ability of other conventional synthetic Disease Modifying Anti-Rheumatic Drugs (csDMARDs) to mitigate unwanted immunogenicity, and prolong efficacy in patients who cannot tolerate methotrexate, is less clear.

Objectives: We previously reported that MTX markedly inhibited the production and release of soluble immunoglobulin (sIgG) by human primary B cells co-cultured with PBMC (BT system) in the *in vitro* BioMAP® phenotypic screening panel[4,5]. MTX also had anti-proliferative effects on human primary tissue and immune cell types[6]. We evaluated other csDMARDs to determine if they were broadly active or, were more similar to MTX in selectively blocking sIgG production and therefore would be more likely to reduce ADA associated with biologics.

Methods: A series of csDMARDS (sulfasalazine, hydroxychloroquine, cyclosporine, leflunomide and azathioprine) were profiled at 4 concentrations across the BioMAP Diversity PLUS™ panel to generate phenotypic activity profiles. In addition to assessing sIgG production, effects on a broad scope of disease-relevant readouts related to primary cell activation and proliferation, inflammation, wound healing, tissue/matrix remodeling, and fibrosis were also evaluated.

Results: Similar to MTX, cyclosporine, leflunomide and azathioprine strongly inhibited sIgG production at all tested concentrations. In contrast, treatment with sulfasalazine or hydroxychloroquine did not decrease sIgG indicating these compounds may not mitigate the immunogenicicty of biologics. In contrast to MTX, several csDMARDS were broadly active in many BioMAP systems. Bioinformatics analysis was used to identify distinct mechanistic signatures for these agents in the BioMAP Panel.

Conclusions: These results support application of the BioMAP *in vitro* assay systems, widely utilized for preclinical drug discovery, to determine the suitability of csDMARDS as anti-immunogenic co-treatments to extend the clinical efficacy of biologics. Clinical studies are needed to confirm these results, however, in inflammatory bowel diseases and to a less extent in rheumatoid arthritis, azathioprine has been shown to reduce immunogenicity of biologics[7].

References:

[1] Rosman, Z, et al., (2013) BMC Medicine. April;11:882.
[2] Mok CC., (2013) Clin Rheumatol. Oct;32(10):1429–35.
[3] Jani M, (2014) Rheumatology. Feb;53(2):213–22.
[4] Berg EL, et al., (2015) Int J Mol Sci. Jan 5;16(1):1008–295.
[5] Tan, T, et al., (2013) Arthritis & Rheumatism. 65 Supplement 10:18666.
[6] O'Mahony et al., (2014) Annals of the Rheumatic Diseases. June. 73(Suppl 2):365–365.
[7] Krieckaert CLM et al. (2010) Arthritis Res Ther. May; 12(5): 217.

Acknowledgements: We acknowledge the contributions of BioMAP operations, bio-analytics and support staff to this data. Thanks to the BioMAP Research Biology team for their analysis and interpretation of BioMAP profiling data.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1942

THU0181 CLINICAL CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS ONGOING METHOTREXATE THERAPY NOT ACHIEVING DAS28 "LOW DISEASES ACTIVITY": A MATCHED CASE-CONTROL ANALYSIS FROM THE MARI STUDY

A. Giusti[1], M. Manara[2], E. Bruschi[3], V. Azzolini[4], N. Belai Beyene[5], S. Corbanese[6], F. De Gennaro[7], L.S. Martin-Martin[8], A.B. Molica Colella[9], M.R. Pozzi[10], N. Romeo[11], T. Rossini[12], A. Severino[13], L. Sinigaglia[2], G. Bianchi[1]. *[1]Rheumatology, "La Colletta" Hospital, Arenzano, Genoa; [2]Rheumatology, A.O. Istituto Ortopedico G. Pini; [3]Rheumatology Unit, ASST Grande Ospedale Metropolitano Niguarda, Milano; [4]Department of Rheumatology, ASL-TO4, Ospedale Ivrea, Ivrea; [5]Department of Internal Medicine, Azienda ICP Milano, P.O. E. Bassini, Milano; [6]Department of Internal Medicine, O.C. di Vittorio Veneto, Vittorio Veneto; [7]Department of Internal Medicine, A.O. Istituti Ospitalieri, Cremona; [8]Department of Internal Medicine, Ospedale Regina Apostolorum, Albano Laziale; [9]Department of Rheumatology, A.O. Ospedali Riuniti Papardo-Piemonte, Messina; [10]Department of Internal Medicine, A.O. San Gerardo, Università Milano-Bicocca, Monza; [11]Rheumatology Unit, ASO Santa Croce e Carle, Cuneo; [12]Department of Internal Medicine, Ospedale Valduce, Como; [13]Department of Allergology and Clinical Immunology, IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy*

Background: Methotrexate (MTX) is the DMARD of first choice in the treatment of rheumatoid arthritis (RA).

Objectives: To investigate the clinical characteristics and describe therapeutic approaches in RA patients ongoing MTX not achieving a DAS28 "low disease activity" score.

Methods: This is a case-control analysis including 186 patients (mean age±SD, 61±12 years, 16% males) who did not achieve a DAS28 "low disease activity" score (defined by a value ≤3.2) and 558 age- and gender-frequency-matched (1:3), randomly selected controls (mean age age±SD, 61±13 years) who achieved a DAS28 "low disease activity" from the original cohort investigated in the MARI study. The MARI study enrolled RA patients on treatment for at least 12-month with MTX. Demographic, clinical, laboratory and pharmacological characteristics of patients recorded at baseline visit were considered for the current analysis. We first compared the characteristics of patients who reached the endpoint with those of subjects who did not by univariate analyses, thereafter, we performed a multivariate model to identify predictors of not achieving the endpoint. We further investigated the therapeutic approaches in patients not achieving the endpoint.

Results: Compared to patients with a DAS28 ≤3.2, subjects not achieving the endpoint presented with a significant higher (mean±SD) weight and BMI (DAS28 ≤3.2: 25±4 versus DAS28 >3.2: 26±5, P=.022), and longer duration of symptoms (months±SD) before the RA diagnosis (11±15 versus 15±20, P=.009). A higher proportion of subjects within the group not achieving the endpoint presented with polyarticular disease (DAS28 ≤3.2: 57% versus DAS28 >3.2: 96%, P<.001), erosive arthritis (49% versus 73%, P<.001), extra-articular symptoms (3% versus 10%, P<.001), positive RF test (63% versus 73%, P=.013), and increased CRP (13% versus 53%, P<.001). The proportion of patients treated with oral MTX was 25% in the subgroup with DAS28 ≤3.2 and 15% in the subgroup with DAS28 >3.2 (P=.004). In the logistic regression analysis, the variables predictive of a DAS28 >3.2 were polyarticular disease (OR 4.0, 95% CI 2.4–6.7, P<.001), erosive arthritis (OR 2.2, 95% CI 1.4–3.4, P<.001), and increased CRP (OR 7.4, 95% CI 4.9–11.4, P<.001). In patients who did not reach the endpoint, the main therapeutic strategies were: a change in the route of administration of MTX (DAS28 >3.2: 13% versus DAS28 ≤3.2: 4%, P<.001) in favor of subcutaneous MTX, an increase of the dose of MTX (13% versus 2%, P<.001), and the prescription of a new biologic (12% versus 1%, P<.001).

Conclusions: Our results identified a number of variables potentially associated the risk of not achieving a DAS28 "low disease activity" score in RA patients ongoing MTX treatment. Longitudinal studies are warranted.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4619

THU0182 MONOTHERAPY WITH THE JAK1-SELECTIVE INHIBITOR FILGOTINIB DISPLAYS AN ANTI-INFLAMMATORY BIOMARKER PROFILE IN RHEUMATOID ARTHRITIS PATIENTS

A. Kavanaugh[1], A. Van der Aa[2], C. Jamoul[2], W. Li[3], L. Goyal[3], Y. Pan[3], P. Harrison[2], C. Tasset[2], J. Tarrant[3], R. Galien[4]. *[1]University of California, la Jolla, United States; [2]Galapagos NV, Mechelen, Belgium; [3]Gilead Sciences, Foster City, United States; [4]Galapagos SASU, Romainville, France*

Background: Janus kinases (JAKs) are key proteins in the signal transduction of many cytokines and growth factors. The selective JAK1 inhibitor filgotinib (GLPG0634, GS-6034) has been evaluated in a 24-week phase 2B study (DARWIN 2) as monotherapy in active rheumatoid arthritis (RA) patients with inadequate response to methotrexate and has shown a good safety and efficacy profile[1].

Objectives: To gain insight into filgotinib mode of action as monotherapy in RA patients by analysing the impact of filgotinib on a broad panel of immune modulators in the serum.

Methods: RA patients received either placebo (PBO), or filgotinib monotherapy at 50mg, 100mg or 200mg once daily (QD). Serum samples were collected at baseline, week 4 and week 12 and analysed using the 18-plex bead-based immunoassay (HSTCMAG-28SK Merck-Millipore) on BioPLEX-200 instrument to measure cytokine concentration. Median % change from baseline for biomarkers are reported for week 4 and 12. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups and PBO.

Results: Following treatment with filgotinib at 100 mg QD and 200mg QD, there were significant reductions in cytokines important in expansion and activity of multiple T cell subsets and innate immunity compared to PBO (see Table). These changes include decreases in proinflammatory cytokines (IL-6, IL-1β, and TNFα), T_H1-related (IL-2, IFN-γ and IL-12), T_H2-related (IL-4, IL-5, and IL-13) and T_H17-related cytokines (IL-1β, IL-6, IL-17A, IL-21 and IL-23). All doses of

Table 1. Median percent change of biomarkers from baseline

	Week 4			Week 12		
	PBO (N=61)	Filgotinib 100mg QD (N=62)	Filgotinib 200mg QD (N=65)	PBO (N=61)	Filgotinib 100mg QD (N=63)	Filgotinib 200mg QD (N=65)
GM-CSF	0	-11***	-9***	6	-11***	-21***
IFN-γ	13	-15***	-13***	6	-21***	-23***
IL-1β	6	-10**	-13***	8	-24***	-16***
IL-2	4	-9**	-13***	10	-22***	-21***
IL-4	10	-8***	-8***	21	-17***	-22***
IL-5	2	-10**	-3*	3	-20***	-14***
IL-6	17	-20**	-35***	-13	-34*	-52***
IL-7	2	-10***	-1^{NS}	0	-22***	-21**
IL-8	1	-1^{NS}	-1^{NS}	-7	-4^{NS}	-8^{NS}
IL-10	6	-12***	-17***	13	-18***	-26***
IL-12	8	-7***	-14***	6	-20***	-23***
IL-13	1	-10**	-13**	13	-8***	-20***
IL-17A	7	-9***	-12***	1	-21***	-16**
IL-21	11	-14***	-10***	4	-26***	-23***
IL-23	3	-12***	-12***	-4	-24***	-31***
MIP-1α	5	-5***	-8***	3	-7***	-6**
MIP-1β	3	-6**	-6*	3	-5^{NS}	3^{NS}
TNF-α	5	-7***	-12***	5	-11**	-14**

P values comparing % changes between filgotinib and PBO groups: NS p>0.05; *p<0.05; **p<0.01; ***p<0.001.

filgotinib also reduced the B- and T-cell development cytokine IL-7. In contrast, IL-8 was not affected by filgotinib. Reductions in MIP1α, MIP1β and GM-CSF are in line with a down modulation of innate immune activity.
Conclusions: Treatment of RA patients with filgotinib monotherapy resulted in significant reduction in the levels of a broad range of cytokines related to T_H1, T_H2, T_H17 and potentially B cells, as well as innate immunity. This observed anti-inflammatory activity of filgotinib is consistent with its efficacy in RA patients.
References:
[1] Kavanaugh A et al. Ann Rheum Dis 2016;0:1–11.doi:10.1136/annrheumdis-2016–210105.
Disclosure of Interest: A. Kavanaugh Consultant for: Galapagos, Pfizer, Abbvie, Amgen, Celgene, Janssen, Novartis, Eli Lilly, UCB, A. Van der Aa Employee of: Galapagos NV, C. Jamoul Employee of: Galapagos NV, W. Li Employee of: Gilead Sciences, L. Goyal Employee of: Gilead Sciences, Y. Pan Employee of: Gilead Sciences, P. Harrison Employee of: Galapagos NV, C. Tasset Employee of: Galapagos NV, J. Tarrant Employee of: Gilead Sciences, R. Galien Employee of: Galapagos SASU
DOI: 10.1136/annrheumdis-2017-eular.5814

THU0183 IMPROVED ADHERENCE TO NEWLY PRESCRIBED DMARDS WITH CO-PRESCRIPTION WITH LOW DOSE STEROIDS IN RHEUMATOID ARTHRITIS PATIENTS ATTENDING CLINIC AT A DISTRICT GENERAL HOSPITAL IN THE UK

A. Nugaliyadde[1,2], K. Culfear[2], A. Nandagudi[2], A. Bharadwaj[2]. *[1]Department of Rheumatology, Teaching Hospital Kandy, Kandy, Sri Lanka; [2]Department of Rheumatology, Basildon and Thurrock University Hospital, Basildon, United Kingdom*

Background: Non-adherence to DMARDs is associated with disease flares and increased disability. Adherence rates to prescribed medicine regimes in people with Rheumatoid Arthritis vary from 30–80% in different studies. Improving adherence to therapy leads to better disease outcome and reduced costs associated with management of RA.
Objectives: This study was carried out as a pilot study to look at the effect of co-prescription of steroids on the adherence and side effects to newly prescribed DMARDS in patients with rheumatoid arthritis.
Methods: This is a prospective, observational cohort study, for the duration of three months per participant. Patients were selected sequentially from those attending outpatient clinic at Basildon Hospitals with a confirmed diagnosis of rheumatoid arthritis (ACR/EULAR criteria), and had been planned to start on a new DMARD by the treating physician. Baseline data included demographics, disease characteristics and data regarding steroid co- prescription including route, dose and duration. Patients were reviewed at three months to look at DMARD adherence defined by continuation of the DMARD. We looked at the side effect profile as possible contributing factor to non-adherence. The effect of co-prescription with steroids and other demographic data on treatment duration was investigated using Kaplan-Meier survival plots. Logistic regression analysis was used to investigate the effect of co- prescription of steroids on continuation of medication.
Results: Fifty one patients were recruited to the study. Median age at the time of enrolment was 61 years (IQR 46–71), 73% were females and 92% were caucasians. seventy percent of the patients were seropositive and DMARD naïve with a mean DAS CRP at recruitment of 4.13 (1.21). Seventeen (33%) patients were co-prescribed with steroids at the initiation of DMARDs. Out of these 59% (n=10) were DMARD naïve. Thirteen patients received a tapering dose of oral prednisolone with a mean starting dose of 13.8mg daily (range 3mg - 20 mg) for a mean duration of 10.8 weeks. Two patients received oral prednisolone 5mg daily for 12 week. The mean cumulative dose of oral prednisolone prescribed was 632.2mg. The two remaining patients received 120 mg of depomedrone IM.
The non adherence rate for our cohort was 35%, 6% for patients co-prescribed with steroids versus 50% for patients who were not co-prescribed with steroids. The odds ratio for likelihood of discontinuation for patients who were not co-prescribed with steroids versus patients who were, was 16 (1.94–134.5, p=0.011).
At the end of three months 25% of the whole cohort, 12% of the patients who were co-prescribed with steroids versus 32% of the patients who were not co-prescribed with steroids reported side effects to the DMARD initiated. the odds ratio for reporting side effects with steroid co-prescription was 0.28 (0.054–1.438, p=0.12).
Conclusions: Co-prescription of low dose steroids with initiation of DMARDs increases the chances of adherence and possibly reduces the side-effect profile
References:
[1] van den Bemt BJ, Zwikker HE, van den Ende CH. Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature. Expert Rev Clin Immunol. 2012;8(4):337–351.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2182

THU0184 ADHERENCE PROFILES TO METHOTREXATE OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) ELIGIBLE FOR BIOLOGICS: TYPOLOGIES FROM FORGET, A CROSS-SECTIONAL SURVEY OF 244 PATIENTS

C. Beauvais[1], V. Hautin-Monteil[2], M.-C. Ducrot[3], R.-M. Flipo[4]. *[1]Rheumatology Department, Saint Antoine Hospital, APHP, Paris; [2]Roche France; [3]Agence A+A, Boulogne-Billancourt; [4]Rheumatology department, Roger Salengro Hospital, Lille, France*

Background: Adherence to Methotrexate (MTX) is not optimal in RA patients [1]. Conflicting determinants of adherence have been identified in literature. Our hypothesis was that the discordant results were related to different typologies of patients.
Objectives: Determine the Methotrexate adherence profiles of patients with RA eligible for biologics.
Methods: The FORGET survey carried out in 2016 was aimed to assess the MTX adherence rate of RA patients, insufficient responders to MTX, biologic-naive, when an initiation of biologics was being considered. Non-adherence was defined as a compliance rate <80% according to the CQR19 (Compliance Questionnaire for Rheumatology) [2]. The factors tested were socio-demographic characteristics, DAS 28, RAID, CQR responses, beliefs, voluntary or involuntary dose skipping, social and medical support.
Results: Of the 244 patients analyzed, the non-adherence rate was 34%. The rather weak correlation between adherence (CQR) and the disease impact (RAID) tended to confirm the hypothesis of different profiles. Four typologies of patients were determined. Groups G1 and G2 were non-adherent patients with high (G1) or lower (G2) impact. Groups G3 and G4 were patients with good adherence with high (G3) or lower impact (G4. Significant adherence factors were found for these 4 groups (p<0.01) (table).

	Non-adherent patients		Adherent patients	
	G1	G2	G3	G4
%	14	19	33	34
CQR 19 (%)	21	40	78	88
RAID (0–10) mean	6,7	4,6	6,3	3,7
Skipped doses (%)	66	55	15	11
Skipped does without doctor's recommendation (%)	38	41	3	3
I comorbidity or more (%)	62	68	57	45
Depression (%)	31	14	12	3
Anxiety	16	9	9	1
Good information received (%)	69	83	81	93
I find constrains to take may treatment (% yes)	59	61	21	6
I tolerate my treatment badly (% yes)	47	18	16	18
I think every day about may arthritis (% yes)	83	63	88	53
I find it hard to keep may professional obligations because of my arthritis (% yes)	79	38	65	32
I feel well informed about my arthritis (% yes)	69	83	81	93
I had support from my relatives (% yes)	55	55	82	96
My treatment is doing me more harm than good (% no agreement at all)	0	22,7	36,8	71
The most important reason to take my treatment is that I can still do what I want to do (% complete agreement)	6,3	11,4	17,2	60,5
I do not expect miracles from my treatment (% no agrement at all)	0	0	10,3	23

Conclusions: Four adherence profiles to Methotrexate have been identified. Among the non-adherent patients, 2 topologies are opposed: 1- patients in state of suffering, with low support from relatives, negative beliefs and significant professional impact. 2-patients with less disease impact, who perceived their treatment with constraints although well tolerated. Detection of patients' profiles may allow targeted strategies to improve or maintain adherence.
References:
[1] DiBenedetti D Rheumatol Ther 2015.
[2] de Klerk E et al, J Rheumatol 1999.
Acknowledgements: This study was funded by Chugai Pharma France.
Disclosure of Interest: C. Beauvais: None declared, V. Hautin-Monteil Employee of: Roche France, M.-C. Ducrot: None declared, R.-M. Flipo: None declared
DOI: 10.1136/annrheumdis-2017-eular.5523

THU0185 COMPARISON OF TOFACITINIB SAFETY AND EFFICACY IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO CONVENTIONAL SYNTHETIC DMARDS, OR TO ONE OR MORE BIOLOGICAL DMARDS

C. Charles-Schoeman[1], J. Kremer[2], S. Krishnaswami[3], K. Soma[4], J. Geier[4], R. Zhang[4], S. Strengholt[4], G. Burmester[5]. *[1]University of California, Los Angeles, CA; [2]Albany Medical College and the Center for Rheumatology, Albany, NY; [3]Pfizer Inc, Groton, CT; [4]Pfizer Inc, New York, NY, United States; [5]Charité – University Medicine Berlin, Berlin, Germany*

Background: Tofacitinib is an oral JAK inhibitor for the treatment (tx) of rheumatoid arthritis (RA). Studies have shown diminishing response to tx in RA patients (pts) when cycling through TNF inhibitors. Prior analyses assessed tofacitinib in csDMARD-inadequate response (IR) pts vs overall bDMARD-IR pts.

Objectives: To compare tofacitinib safety and efficacy in RA pts who have previously failed tx (lack of efficacy and/or safety reasons) with csDMARDs, with pts who failed tx with either 1 or ≥2 prior bDMARDs.
Methods: Data from pts who received ≥1 dose of tofacitinib in 19 RA studies up to 96 months (2 Phase [P] 1; 9 P2; 6 P3; 2 LTE studies [1 LTE ongoing; data as of March 2015]) were used in this analysis. Data were pooled across all 19 studies for safety assessments in the All RA population: csDMARD-IR, n=4377; bDMARD-IR, n=838 (1 bDMARD-IR, n=533; ≥2 bDMARD-IR n=305). Safety was also assessed up to 24 months in pts randomised to tofacitinib 5 or 10 mg BID or placebo (PBO) in a pooled P2/P3 randomised controlled trial (RCT) population (8 P2, 6 P3 studies; csDMARD-IR, n=3328; bDMARD-IR, n=782). Incidence rates (pts with events/100 pt-years) were calculated for serious AEs (SAEs), serious infections (SIs) and herpes zoster (HZ). Efficacy was assessed by pts achieving ACR20 response and DAS28-4(ESR) ≤3.2 at Month 3 in a pooled P3 RCT population (csDMARD-IR, n=2375; bDMARD-IR, n=664).
Results: Prior to tofacitinib tx, bDMARD-IR pts had longer RA duration, greater disease burden and more corticosteroid use vs csDMARD-IR pts. SAEs were more common among bDMARD-IR vs csDMARD-IR pts in both the P2/P3 RCT and the All RA populations; SAE rates were not higher in pts failing ≥2 bDMARDs vs 1 bDMARD (Table). Incidence rates for SIs were generally greater in pts with IR to bDMARDs vs csDMARDs in the All RA population, but generally lower in pts with IR to 1 or ≥2 bDMARDs vs csDMARDs in the P2/P3 RCT population; incidence with 5 mg BID was lower for 1 vs ≥2 bDMARDs in the P2/P3 RCT population. Incidence rates for HZ were similar between pts with IR to csDMARDs or 1 bDMARD, but appeared numerically greater in pts with IR to ≥2 bDMARDs in both the P2/P3 RCT and the All RA populations. A similar pattern was observed across tofacitinib and PBO groups. Efficacy at Month 3 in the P3 RCT population was greater with both tofacitinib doses vs PBO. Although absolute response was smaller in pts with IR to bDMARDs vs csDMARDs, generally similar efficacy was observed in pts with IR to 1 or ≥2 bDMARDs (Table).

Table. Selected safety and efficacy outcomes by prior failed treatment.

		csDMARD-IR-only	Overall bDMARD-IR	1 bDMARD-IR	≥2 bDMARD-IRs
P2/P3 RCT population (0–24 months);* incidence rate (pts with event/100 pt-years) (95% CI)					
SAEs	Tofacitinib 5 mg BID	12.4 (10.3, 14.8)	12.6 (7.8, 19.3)	12.7 (6.8, 21.7)	12.6 (5.4, 24.7)
	Tofacitinib 10 mg BID	9.7 (7.9, 11.8)	12.5 (7.6, 19.3)	12.1 (6.3, 21.1)	13.1 (5.6, 25.7)
	Placebo	11.5 (7.6, 16.8)	20.5 (9.8, 37.7)	19.8 (7.3, 43.1)	21.6 (5.9, 55.4)
SIs	Tofacitinib 5 mg BID	3.4 (2.4, 4.7)	1.7 (0.4, 5.0)	0.9 (0.0, 5.2)	2.9 (0.4, 10.6)
	Tofacitinib 10 mg BID	3.4 (2.4, 4.7)	3.0 (1.0, 7.1)	3.0 (0.6, 8.7)	3.2 (0.4, 11.4)
	Placebo	1.7 (0.5, 4.3)	4.1 (0.5, 14.7)	3.3 (0.1, 18.3)	5.4 (0.1, 30.1)
HZ	Tofacitinib 5 mg BID	3.9 (2.8, 5.3)	5.3 (2.4, 10.0)	2.8 (0.6, 8.3)	9.1 (3.4, 19.9)
	Tofacitinib 10 mg BID	4.8 (3.5, 6.3)	6.3 (3.0, 11.6)	6.2 (2.3, 13.4)	6.6 (1.8, 16.8)
	Placebo	2.6 (0.9, 5.5)	0.0 (0.0, 7.5)	0.0 (0.0, 12.1)	0.0 (0.0, 19.8)
All RA population (up to 96 months); incidence rate (pts with event/100 pt-years) (95% CI)					
SAEs	Tofacitinib 5 mg BID	9.7 (8.9, 10.6)	14.8 (11.4, 18.9)	15.9 (11.5, 21.3)	12.8 (7.7, 20.0)
	Tofacitinib 10 mg BID	9.7 (9.0, 10.4)	11.6 (10.0, 13.3)	11.8 (9.8, 14.0)	11.3 (8.8, 14.3)
	All tofacitinib doses	9.7 (9.2, 10.2)	12.2 (10.8, 13.8)	12.6 (10.8, 14.7)	11.6 (9.3, 14.3)
SIs	Tofacitinib 5 mg BID	2.9 (2.5, 3.4)	4.5 (2.8, 6.8)	4.7 (2.7, 7.8)	4.1 (1.6, 8.4)
	Tofacitinib 10 mg BID	2.7 (2.3, 3.1)	3.5 (2.7, 4.4)	4.0 (2.9, 5.3)	2.6 (1.5, 4.1)
	All tofacitinib doses	2.8 (2.5, 3.1)	3.7 (2.9, 4.5)	4.1 (3.2, 5.3)	2.9 (1.9, 4.2)
HZ	Tofacitinib 5 mg BID	3.7 (3.2, 4.3)	4.8 (3.0, 7.2)	3.6 (1.8, 6.4)	7.1 (3.5, 12.7)
	Tofacitinib 10 mg BID	4.2 (3.8, 4.7)	4.4 (3.5, 5.5)	4.1 (3.0, 5.5)	4.9 (3.3, 7.0)
	All tofacitinib doses	4.0 (3.7, 4.4)	4.5 (3.6, 5.5)	4.0 (3.0, 5.2)	5.4 (3.9, 7.2)
Efficacy endpoints in the P3 RCT population at Month 3; % of pts					
ACR20	Tofacitinib 5 mg BID	59.4***	43.5***	45.3*	40.6*
	Tofacitinib 10 mg BID	65.4***	50.6***	50.6***	50.6***
	Placebo	27.1	24.6	27.2	20.0
DAS28-4(ESR) ≤3.2	Tofacitinib 5 mg BID	15.9***	12.7*	11.9	14.0*
	Tofacitinib 10 mg BID	21.1***	15.8**	15.7*	16.5*
	Placebo	3.9	4.9	5.8	3.4

*p<0.05; **p<0.001; ***p<0.0001 vs placebo
[a]Placebo data up to 6 months only
Δ, change from baseline, BID, twice daily; bDMARD, biological disease-modifying antirheumatic drug; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-4(ESR), Disease Activity Score in 28 joints with erythrocyte sedimentation rate, HZ, herpes zoster; IR, inadequate response, P, Phase, pts, patients, pt-years, patient-years; RA, rheumatoid arthritis; RCT, randomised controlled trial; SAE, serious adverse event; SI, serious infection

Conclusions: SAEs and SIEs were more common in tofacitinib- and PBO-treated pts with IR to bDMARDs vs csDMARDs; increased risk was generally not observed with increasing number of prior bDMARDs. HZ risk appeared greater with ≥2 bDMARDs vs 1 bDMARD. Efficacy was greater with tofacitinib vs PBO for csDMARD-IR and bDMARD-IR pts, with similar response observed in pts with IR to ≥2 or 1 bDMARD. These data support the use of tofacitinib in different lines of therapy, although the analysis is limited by smaller sample size in some groups.
Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by N Jones of CMC and was funded by Pfizer Inc.
Disclosure of Interest: C. Charles-Schoeman Grant/research support from: AbbVie, Bristol-Myers Squibb, Pfizer Inc, Consultant for: Amgen, Pfizer Inc, Regeneron-Sanofi, J. Kremer Shareholder of: Corrona, LLC, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Genentech, Eli Lilly, Pfizer Inc, Employee of: Corrona, LLC, S. Krishnaswami Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Soma Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Geier Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Zhang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Strengholt Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, G. Burmester Grant/research support from: UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Hexal, Janssen, Medimmune, MSD, Novartis, Pfizer Inc, Roche, Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Hexal, MSD, Novartis, Pfizer Inc, Roche
DOI: 10.1136/annrheumdis-2017-eular.2346

THU0186 MAGNITUDE AND DURATION OF EARLY RESPONSE WITH TOFACITINIB: POST-HOC ANALYSIS OF TWO PHASE 3, PLACEBO-CONTROLLED STUDIES

D. Aletaha[1], A. Kivitz[2], G. Valenzuela[3], J. Tesser[4], S. Hays[5], H. Li[5], C.A. Connell[6], E. Bananis[5], A. Soonasra[5], J.S. Smolen[7]. *[1]Department of Internal Medicine 3, Medical University of Vienna, Vienna, Austria; [2]Altoona Center for Clinical Research, Duncansville, PA; [3]Integral Rheumatology & Immunology Specialists, Fort Lauderdale, FL; [4]Arizona Arthritis & Rheumatology Associates, Glendale, AZ; [5]Pfizer Inc, Collegeville, PA; [6]Pfizer Inc, Groton, CT, United States; [7]Division of Rheumatology, Medical University of Vienna and Hietzing Hospital, Vienna, Austria*

Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. ORAL Solo (NCT00814307) and ORAL Sync (NCT00856544) were two Phase 3 index studies that demonstrated the efficacy of tofacitinib in adult patients (pts) with RA who were DMARD inadequate responders (DMARD-IR). Early onset of effect is a clinically meaningful endpoint.
Objectives: This post hoc analysis examined the magnitude and durability of early response to tofacitinib in ORAL Solo and ORAL Sync.
Methods: ORAL Solo and ORAL Sync were double-blind, placebo (PBO)-controlled, parallel-group studies in pts with active RA and an inadequate response to ≥1 conventional synthetic (cs) or biologic (b) DMARDs. Pts were randomised to tofacitinib 5 mg BID, tofacitinib 10 mg BID, PBO advanced to tofacitinib 5 mg BID, or PBO advanced to tofacitinib 10 mg BID, either as monotherapy in ORAL Solo or with background csDMARDs in ORAL Sync. In ORAL Solo, pts randomised to PBO were advanced to tofacitinib at Month (M) 3; in ORAL Sync, pts randomised to PBO were advanced to tofacitinib at M3 (non-responders) or M6 (all other pts). In this post hoc analysis, the following clinical efficacy data for pts on tofacitinib or PBO (prior to advancement to tofacitinib) ± csDMARDs, were evaluated at Week 2, M3 and M6 (ORAL Sync only; no M6 PBO comparison in ORAL Solo): change from baseline (CFB) in Clinical Disease Activity Index (CDAI) >12,[1] HAQ-DI CFB ≥0.22, CDAI ≥50% improvement from baseline, CDAI ≥70% improvement from baseline, CDAI ≥85% improvement from baseline, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score improvement from baseline ≥4, Pain visual analogue scale (VAS) score CFB ≥10. This analysis was post hoc and multiplicity adjustment was done.
Results: Clinical efficacy endpoint data are summarised in the Table. At Week 2, more patients receiving tofacitinib 5 or 10 mg BID ± csDMARDs (compared with PBO ± csDMARDs) achieved a CDAI CFB >12, HAQ-DI CFB ≥0.22, CDAI ≥50% improvement from baseline and pain VAS CFB ≥10. By M3, more pts receiving tofacitinib 5 or 10 mg BID ± csDMARDs (compared with PBO ± csDMARDs) achieved the efficacy outcomes measured including improvements from baseline in FACIT-F scores ≥4, CDAI ≥50%, CDAI ≥70% and CDAI ≥85%. Responses attained at M3 were maintained or increased at M6.

Table. Clinical efficacy endpoints from Week 2 to Month 6 in ORAL Sync and ORAL Solo (FAS[a]; NRI[b])

		ORAL Solo			ORAL Sync		
Improvement from baseline, % pts (95% CI)		Tofacitinib 5 mg BID (N=241)	Tofacitinib 10 mg BID (N=243)	PBO (N=122)	Tofacitinib 5 mg BID + csDMARDs (N=312)	Tofacitinib 10 mg BID + csDMARDs (N=315)	PBO + csDMARDs (N=158)
CDAI >12	Week 2	37.1 (31.0, 43.6)*	43.9 (37.5, 50.5)*	18.5 (12.0, 26.6)	30.4 (25.3, 35.9)*	36.8 (31.3, 42.5)*	17.4 (11.8, 24.3)
	Month 3	71.6 (65.4, 77.2)*	75.5 (69.6, 80.8)*	42.5 (33.5, 51.9)	56.0 (50.3,61.6)*	64.7 (59.1, 70.1)*	32.5 (25.2, 40.4)
	Month 6	79.5 (74.4, 84.6)	78.8 (73.7, 84.0)	NA	53.7 (48.0, 59.4)*	62.1 (56.4, 67.6)*	34.4 (27.0, 42.4)
HAQ-DI ≥0.22	Week 2	49.0 (42.5, 55.5)*	50.6 (44.1, 57.2)*	37.8 (29.1, 47.2)	45.6 (40.0, 51.4)*	53.1 (47.3, 58.8)*	34.2 (26.8, 42.2)
	Month 3	59.6 (53.1, 65.9)*	65.3 (58.9, 71.3)*	39.2 (30.4, 48.5)	49.0 (43.3, 54.7)*	57.1 (51.4, 62.7)*	23.7 (17.3, 31.2)
	Month 6	67.5 (61.6, 73.4)	66.1 (60.1, 72.1)	NA	49.7 (44.0, 55.4)*	55.5 (49.8, 61.2)*	23.7 (17.3, 31.2)
CDAI ≥ 50%	Week 2	19.8 (15.0, 25.5)*	25.1 (19.7, 31.1)*	8.4 (4.1, 14.9)	18.0 (13.8, 22.7)*	20.5 (16.1, 25.5)*	9.0 (5.0, 14.7)
	Month 3	57.3 (50.8, 63.7)*	58.1 (51.6, 64.4)*	25.8 (18.3, 34.6)	45.3 (39.7, 51.0)*	56.5 (50.8, 62.2)*	22.3 (16.1, 29.6)
	Month 6	68.6 (62.7, 74.5)	66.4 (60.4, 72.4)	NA	48.5 (42.9, 54.3)*	58.8 (53.1, 64.4)*	29.3 (22.3, 37.1)
CDAI ≥70%	Week 2	5.1 (2.6, 8.7)	11.3 (7.6, 16.0)*	2.5 (0.5, 7.2)	4.9 (2.8, 8.0)	8.6 (5.7, 12.4)*	3.2 (1.1, 7.4)
	Month 3	33.1 (27.1, 39.4)*	40.7 (34.4, 47.2)*	14.2 (8.5, 21.7)	24.3 (19.6, 29.5)*	31.4 (26.2, 36.9)*	7.6 (4.0, 13.0)
	Month 6	41.8 (35.6, 48.1)	49.0 (42.7, 55.3)	NA	31.4 (26.3, 36.9)*	37.9 (32.5, 43.6)*	16.6 (11.1, 23.3)
CDAI ≥ 85%	Week 2	2.1 (0.7, 4.9)	5.0 (2.6, 8.6)	2.5 (0.5, 7.2)	1.0 (0.2, 2.8)	3.3 (1.6, 6.0)*	0.7 (0.0, 3.5)
	Month 3	14.6 (10.4, 19.8)*	17.8 (13.2, 23.3)*	5.8 (2.4, 11.7)	9.4 (6.4, 13.2)*	11.4 (8.1, 15.6)*	1.3 (0.2, 4.5)
	Month 6	22.2 (16.9, 27.4)	27.0 (21.4, 32.6)	NA	10.7 (7.5, 14.7)	18.3 (14.1, 23.1)*	5.7 (2.7, 10.6)
FACIT-F ≥4	Month 1	NA	NA	NA	46.2 (40.4, 52.0)	58.1 (52.3, 63.7)*	39.0 (31.2, 47.1)
	Month 3	61.2 (54.7, 67.4)*	63.4 (56.8, 69.6)*	42.2 (33.1, 51.8)	38.6 (33.1, 44.3)*	51.2 (45.4, 56.9)*	21.8 (15.6, 29.1)
	Month 6	59.2 (53.0, 65.5)	62.4 (56.2, 68.6)	NA	40.9 (35.3, 46.6)*	47.2 (41.5, 53.0)*	21.2 (15.0, 28.4)
Pain VAS ≥10	Week 2	57.3 (50.8, 63.7)*	61.1 (54.6, 67.3)*	41.2 (32.2, 50.6)	46.3 (40.6, 52.0)*	52.9 (47.2, 58.6)*	36.5 (29.0, 44.6)
	Month 3	69.3 (63.1, 75.1)*	73.9 (67.8, 79.3)*	42.5 (33.5, 51.9)	50.0 (44.3, 55.7)*	57.5 (51.7, 63.1)*	28.7 (21.7, 36.4)
	Month 6	71.0 (65.2, 76.7)	71.0 (65.2, 76.7)	NA	48.4 (42.7, 54.1)*	56.2 (50.4, 61.8)*	30.6 (23.5, 38.4)

*p<0.05 vs PBO; the normal approximation for the difference in binomial proportions was used to test the superiority of each dose of tofacitinib to PBO. [a]Included all randomised patients who took ≥1 dose of study medication. [b]Patients who withdrew for any reason before Month 6, or patients who were advanced to tofacitinib after Month 3 (only for ORAL Sync) had their values on or after withdrawing or advancing set to Non-Response in this analysis. N = total number in each treatment group, number of patients available for the analysis may vary for individual endpoints. PBO group included only those patients who had not yet advanced to tofacitinib.
Comparisons for tofacitinib vs PBO at Month 6 not available for ORAL Solo as all PBO patients advanced to tofacitinib at this time point.
BID, twice daily; CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic DMARD; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FAS, full analysis set; NA, not available; NRI, non-responder imputation; PBO, placebo; Pts, patients; VAS, visual analogue scale.

Conclusions: DMARD-IR pts with active RA receiving tofacitinib ± csDMARDs appeared to show greater improvements compared with PBO in clinical disease

activity, HAQ-DI, and pain as early as Week 2 (first post-baseline assessment), and improvements in fatigue by M3. Responses were maintained or improved through M3 (monotherapy) or M6 (with background csDMARDs).

References:
[1] Curtis JR et al. Arthritis Care Res (Hoboken) 2015; 67:1345–1353.

Acknowledgements: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by AG McCluskey of CMC and was funded by Pfizer Inc.

Disclosure of Interest: D. Aletaha Consultant for: AbbVie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, BMS, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, and UCB, A. Kivitz Grant/research support from: AbbVie, Amgen, Bristol Myers Squibb, Genentech, Pfizer Inc, Consultant for: AbbVie, Amgen, Bristol Myers Squibb, Genentech, Pfizer Inc, Speakers bureau: AbbVie, Amgen, Bristol Myers Squibb, Genentech, Pfizer Inc, G. Valenzuela Speakers bureau: AbbVie, Janssen, Eli-Lilly, Merck, Novartis and Pfizer Inc, J. Tesser Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, S. Hays Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, H. Li Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. A. Connell Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, E. Bananis Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, A. Soonasra Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. S. Smolen Grant/research support from: AbbVie, Janssen, Lilly, MSD, Pfizer Inc, and Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Glaxo, ILTOO, Janssen, Lilly, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, and UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Glaxo, ILTOO, Janssen, Lilly, MedImmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, and UCB

DOI: 10.1136/annrheumdis-2017-eular.1556

THU0187 DO WE TODAY ALTERNATIVE THERAPIES RHEUMATOID ARTHRITIS TWO OR MORE DISEASE-MODIFYING DRUGS? THE STORY OF HOW A SIMPLE DRUG PENTOXIFYLLINE MAY ENHANCE THE ACTION OF METHOTREXATE IN RHEUMATOID ARTHRITIS

D.S. Bublikov, D.A. Anchugina, I.E. Babushkin. *Altay State Medical University, Barnaul, Russian Federation*

Background: The treatment of patients with RA (rheumatoid arthritis) is a complicated task, because the achievement of remission and low level of activity often requires administration of 2–3 disease-modifying drugs. In such conditions we often face with the rise of treatment costs and with the increase of therapy side effects. That is why relevant is the search of the drugs increasing the effect of the "gold standard" of RA – therapy - methotrexate, and also frequently used sulphasalazine and leflunomid. Treatment of prior to "Treat to target" is difficult enough, forcing researchers around the world to look for the ways to improve the effectiveness of RA treatment.

Objectives: To explore the possibilities of reducing RA activity on the disease activity score DAS28 CRP by adding pentoxifylline to the methotrexate, sulfasalazine and leflunomide treatment.

Methods: This study included women (n=131) with RA longer than 1 year in duration, having a seropositive rheumatoid factor, and DAS28 CRP activity score of 3.2–5.1. Middle aged – 46.44±3.24 years old. All patients received a 15.50±2.50 mg oral dose of methotrexate per week, 2000±500 mg oral dose of sulfasalazine per day, 20±5 mg oral dose of leflunomide per day. Patients were divided into two groups - those who only had disease-modifying drugs (DMARDs) (n=80) and those who were treated with an oral dose of methotrexate and 1200 mg of pentoxifylline per day (n=51).

Results: The baseline for both groups of RA patients did not differ significantly in terms of the level on the DAS28 CRP (p=0.812). On 14th day of the group who were taking pentoxifylline, the DAS28 CRP disease activity score was significantly lower by 12.5% ($p<0.001$). After 28 days, the users had a DAS28 CRP disease activity score index difference. The difference between two groups is statistically significant. In the group that were treated with pentoxifylline in addition to DMARDs (p=0.001) the index was found to be 8.3% lower. For 28 days, the methotrexate group's disease activity according to the DAS28 CRP activity score significantly decreased by 14.3% from the baseline ($p<0.001$). For 28 days, the pentoxifylline + DMARDs group also achieved a statistically significant reduction in the index according to the DAS28 CRP activity score by 20.5% ($p<0.001$)

The disease activity index for the two groups for 14 and 28 days is shown in the table.

The DAS28 CRP Index in the two groups of RA patients

Groups of patients Observation time	Group DMARDs (n=80)	Group DMARDs +) Pentoxifylline (n=51)	Statistical significant differences between the two groups
Baseline	3.11±0.05	3.13±0.05	p=0.812
For 14 days	3.06±0.05	2.69±0.06	p<0.001
For 28 days	2.71±0.04	2.48±0.06	p=0.001

Conclusions: Thus, converting the monotherapy DMARDs to pentoxifylline will significantly reduce the activity of RA, while avoiding many of the adverse effects of the other combination therapies. This data requires further long-term research.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7019

THU0188 EFFICACY AND SAFETY OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO DID NOT RESPOND TO SYNTHETIC AND BIOLOGICAL DMARDS IN CLINICAL PRACTICE

E.L. Luchikhina[1], D. Karateev[2], A. Misiyuk[1], N. Demidova[1], G. Loukina[1], D. Abdulganieva[3], A. Baranov[4], A. Babaeva[5], L. Evstigneeva[6], O. Ivanova[7], V. Mazurov[8], O. Semagina[9], A. Sizikov[10], V. Sorotskaya[11], E. Nasonov[2]. *[1]Early arthritis department; [2]Nasonova Research Institute of rheumatology, Moscow; [3]Kazan State Medical University, Kazan; [4]Yaroslavl State Medical University, Yaroslavl; [5]Volgograd State Medical University, Volgograd; [6]Ekaterinburg 1st Regional Clinic Hospital, Ekaterinburg; [7]4 Voronezh Regional Clinical Hospital, Voronezh; [8]North-western State Medical University named after I.I.Mechnikov, Saint-Petersburg; [9]Samara Regional Clinical Hospital, Samara; [10]Scientific Research Institute of Clinical immunology, Novosibirsk; [11]2nd Sity Hospital, Tula, Russian Federation*

Background: Tofacitinib (TOFA) is so far the only representative of a new class of Jak-kinase inhibitors in rheumatology. Despite extensive data on TOFA obtained from 3rd phase studies, for use in clinical practice, the information is limited.

Objectives: To study the efficacy and safety of TOFA in RA in clinical practice.

Methods: We represent the combined data from two parallel IV Phase open-label observational clinical trials, modelling clinical practice, conducted by very similar protocols in 11 rheumatology centers in Russia. Inclusion criteria were active RA, methotrexate (MTX) failure, and/or other synthetic or biologic DMARDs failure. In total, 142 pts (26 males, 116 females, age 51,5±12,2 years, disease duration 88,6±78,1 months, 86,6% RF(+), 76,6% ACPA(+), 81,7% with erosive disease, DAS28-ESR 5,89±1,03, SDAI 35,7±13,4, HAQ 1,59±0,64) were included. 32 (22,5%) pts had biologics in history. TOFA used in the dose of 5 mg BID for 6 months, with possibility to increase to 10 mg BID (carried out in 27 pts after 11,3±2,7 weeks). 115 (81%) pts received TOFA in combination with MTX (18±4,5 mg per week), 18 with leflunomide or sulfasalazine, 9 pts used TOFA in monotherapy.

Results: 129 (90,8%) pts successfully completed the six-month period of treatment. TOFA was withdrawn due to lack of response in 6 cases, adverse events (AEs) in 4 (pneumonia, arterial hypertension, skin vasculitis, mouth ulcers), withdrawal of informed consent – 2, protocol violation – 1. At month 3 SDAI score decreased to 14,6±10,9 ($p<0,01$), 55 (42,6%) pts achieved SDAI LDA and 22 (17,1%) SDAI remission; HAQ decreased to 0,95±0,61, HAQ≤0,5 observed in 36 (27,9%) pts. After 6 months, SDAI and HAQ scores decreased to 10,5±8,6 and 0,83±0,64 resp. ($p<0,01$); 81 (62,8%) pts achieved SDAI LDA and 29 (22,5%) SDAI remission; HAQ≤0,5 observed in 48 (37,2%) pts. Results of treatment in patients with and without biological DMARDs in history were similar. Pts who needed dose escalation of TOFA had worse results at month 3 compared to others (SDAI 21±10,2 and to 13,2±10,7 resp., p=0,02), but after increase of the dose to 10 mg BID at month 6 they showed a slightly better result (SDAI 9,5±7,1 and to 10,7±8,9 resp., p=0,54). Only 2 serious AEs (pneumonia and skin vasculitis) observed. We didn't see any case of Herpes zoster in our group.

Conclusions: TOFA was effective in patients with severe RA who did not respond to both synthetic and biological DMARDs (achievement of SDAI LDA in 42,6% of pts at month 3 and in 62,8% at month 6). Dose escalation to 10 mg BID can be useful in ¼ of patients who do not respond to standard dose of TOFA. TOFA has shown a good safety profile.

Acknowledgements: This scientific study was supported by grant by Pfizer.

Disclosure of Interest: E. Luchikhina Grant/research support from: Pfizer, Biocad, Speakers bureau: Abbvie, Pfizer, Tirupharm, D. Karateev Grant/research support from: Pfizer, Consultant for: Pfizer, Tirupharm, Biocad, Egis, R-Pharm, Novartis, Speakers bureau: Abbvie, Bristol Myers Squibb, Pfizer, Roche, Tirupharm, Biocad, R-Pharm, Novartis, Egis, MSD, UCB, A. Misiyuk: None declared, N. Demidova: None declared, G. Loukina: None declared, D. Abdulganieva: None declared, A. Baranov: None declared, A. Babaeva: None declared, L. Evstigneeva: None declared, O. Ivanova: None declared, V. Mazurov: None declared, O. Semagina: None declared, A. Sizikov: None declared, V. Sorotskaya: None declared, E. Nasonov: None declared

DOI: 10.1136/annrheumdis-2017-eular.5475

THU0189 SAFETY OF FOUR TREATMENT REGIMENS IN EARLY RHEUMATOID ARTHRITIS

E. Fedorenko[1], G. Lukina[2], Y. Sigidin[3], D. Karateev[3]. *[1]Moscow Clinical Scientific Center; [2]Moscow Clinical Scientific Center, V.A.Nasonova Research Institute of Rheumatology; [3]V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Objectives: To compare safety data in patients (pts) with early (<2 years duration) RA who were randomised to receive 4 different regimens of treatment.

Methods: One hundred forty-one pts with RA of less than 2 years duration (122 women, mean age 51 years, mean disease duration 24 weeks, mean DAS 28 5,9; 64% RF-positive,59% ACCP-positive) were randomly allocated to receive one of the following treatment regimens: methotrexate (MTX, up to 20 mg/week,

35 pts); MTX plus prednisolone (P) 10 mg daily (MTX-P, 34 pts); MTX-P plus methylprednisolone (MP) 1000 mg intravenously on the first day of treatment (MTX-P-MP, 35 pts); leflunomide 20 mg daily (LEF, 37 pts). Duration of treatment was one year. Control points were 3, 6 and 12 months from the initiation of therapy. Safety data was assessed at the main control points.

Results: One hundred twenty-seven pts completed the study. Side effects were registered in the same number of patients in each group (9 patients; 24,3%>26%). Therapy had to be stopped in six patients due to side effects: MTX - 1 (depigmentation of the skin), MTX-P - none, MTX-P-MP - 1 (stomatitis) and LEF - 4 (dermatitis-2; pancytopenia with platelet count 43 $\times 10^9$/L, erythrocyte $2{,}9\times 10^{12}$/L, WBC 2×10^9/L-1; angioedema, periorbital edema and dermatitis with itching-1). Other side effects were mild: MTX - 8 pts (dyspepsia-1, elevation of transaminases-6, hair loss-1), MTX-P - 9 pts (Cushing's syndrome - 1, hair loss - 1, anemia - 1, elevation of transaminases - 4, arterial hypertension - 2), MTX-P-MP - 8 pts (hair loss-1,dermatitis-1, elevation of transaminases-5, Cushing's syndrome - 1) and LEF - 5 pts (elevation of transaminases-5). At baseline all groups were comparable in their demographic, clinical and radiographic characteristics.

Conclusions: In most cases side effects were moderate or minimal. The most serious side effects, leading to the discontinuation of the therapy, were registered in LEF group. There was no withdrawal of treatment in MTX-P group. Safety profile was the same in all groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6717

THU0190 DERMATOLOGICAL GUIDELINES FOR MONITORING METHOTREXATE TREATMENT REDUCE DRUG-SURVIVAL COMPARED TO RHEUMATOLOGICAL GUIDELINES

H. Bernelot Moens[1], F. Busger op Vollenbroek[1], R. Janssens[2], C. Doggen[3].
[1]Rheumatology & Clinical Immunology; [2]Dermatology, Ziekenhuisgroep Twente, Almelo; [3]Health Technology and Services Research, University of Twente, Enschede, Netherlands

Background: Methotrexate (MTX) is widely used in the treatment of psoriasis and psoriatic arthritis (PsA). To prevent MTX-induced adverse events dermatological MTX guidelines advise a higher number and frequency of blood tests than rheumatological guidelines (1,2). These differences are not based on evidence indicating a higher risk for patients with psoriasis compared to PsA.

Objectives: Compare the effects of MTX monitoring strategies by rheumatologists and dermatologists.

Methods: Patients with psoriasis or PsA in a Dutch teaching hospital. Inclusion criteria: start methotrexate (MTX) between 2006 and 2012 and scheduled follow-up by dermatologist or rheumatologist. Exclusions: incomplete availability of lab data. Start and stop dates and dosing of MTX and folic acid, reasons for withdrawal of MTX, numbers and results of laboratory tests performed for MTX safety, occurrence of any serious adverse event (SAE) were retrieved from electronic records.

Results: PsA patients used higher initial and maximum doses of MTX and folic acid, but psoriasis patients had a higher frequency of abnormal liver function tests, resulting in a striking difference in withdrawal of MTX (Table). In PsA MTX was more often withdrawn for remission, and less frequently for ineffectiveness leading to longer drug survival in the first course of treatment. There were no differences in the occurrence of SAE or death between these groups. Hospital admissions related to infection were recorded in 6 (3.1%) PsA vs 4 (2.1%) psoriasis patients.

Table 1. MTX dose, lab results, and reasons for withdrawal

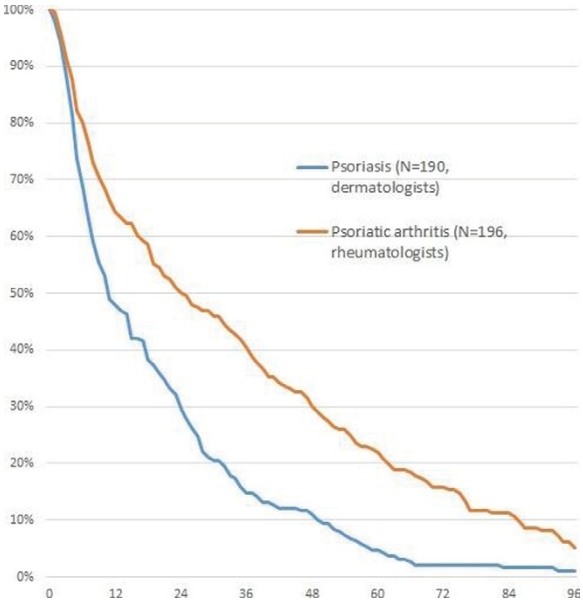
	Psoriasis (N=190)	Psoriatic arthritis (N=196)
Men, N (%)	86 (45.3)	95 (48.5)
Age (y), mean (SD)	52.3 (16.2)	51.8 (13.8)
Prior treatment with MTX	8 (4.2)	39 (19.9)**
MTX starting dose (mg/week)	12.2 (3.7)	15.2 (3.0)**
Folic acid starting dose (mg/week)	4.9 (0.7)	8.4 (5.6)**
Duration of first treatment course (months)	19.0 (19.5)	34.3 (30.5)**
Laboratory visits per treatment month	0.62 (0.81)	0.50 (0.34)*
Abnormal lab results per treatment month	0.14 (0.26)	0.03 (0.07)**
Abnormal lab results per laboratory visit	0.26 (0.39)	0.06 (0.11)**
Reasons for withdrawal of MTX		
Ineffectiveness	46 (24.1%)	31 (15.8%)*
Remission	14 (7.3%)	21 (10.7%)
Abnormal laboratory result	29 (15.2%)	8 (4.1%)**
Drug toxicity (mild, including infection)	47 (24.6%)	52 (26.5%)
Serious Adverse Event	2 (1.0%)	2 (1.0%)
Death (not related to MTX)	2 (1.0%)	4 (2.0%)
Other	22 (11.6%)	15 (7.6%)

Numbers: mean (SD), *P value ≤0.05; **P-value <0.001 (Fisher's exact test),

Conclusions: Monitoring by dermatologists resulted in more abnormal liver function tests and shorter drug survival of MTX. The monitoring strategy by rheumatologists was not associated with increased SAEs. This supports the safety of current rheumatological guidelines and suggests reconsideration of a higher number of liver function tests in dermatological guidelines.

References:

[1] Menter A, Korman NJ, Elmets C et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. J Am Acad Dermatol. http://dx.doi.org/10.1016/j.jaad.2009.03.027.



[2] Barker J, Horn EJ, Lebwohl M et al. Assessment and management of methotrexate hepatotoxicity in psoriasis patients: Report from a consensus conference to evaluate current practice and identify key questions toward optimizing methotrexate use in the clinic. J Eur Acad Dermatol Venereol 2011;25:758–64.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2524

THU0191 EFFECTS OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, ON PATIENT-REPORTED OUTCOMES IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS

H. Yamanaka[1], Y. Tanaka[2], T. Takeuchi[3], N. Sugiyama[4], T. Hirose[4], N. Yoshii[4], Y. Morishima[4], S. Toyoizumi[4]. *[1]Tokyo Women's Medical University, Tokyo; [2]University of Occupational and Environmental Health, Kitakyushu; [3]Keio University; [4]Pfizer Japan Inc, Tokyo, Japan*

Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Improvements in patient-reported outcomes (PROs) have been reported in the global population of the Phase (P)2, P3 and long-term extension (LTE) tofacitinib studies.

Objectives: To explore the effect of tofacitinib on PROs in Japanese patients (pts) with RA.

Methods: In this post hoc analysis, data from Japanese pts with RA were obtained from two 12-week randomised dose-finding P2 studies in methotrexate (MTX) inadequate responder (IR) and DMARD-IR pts (NCT00603512/A3921039 and NCT00687193/A3921040), one 24-month P3 study in MTX-IR pts (ORAL Scan; NCT00847613/A3921044) and an open-label, LTE study in pts who completed a qualifying P2 or P3 study (NCT00661661/A3921041; completed April 2014). Pts received tofacitinib 5 or 10 mg twice daily (BID) or placebo (PBO) (P2 and ORAL Scan; no PBO in LTE). In ORAL Scan, non-responder PBO pts advanced to tofacitinib at Month 3; all remaining pts were advanced at Month 6. PROs included: mean change from baseline in Pt's Global Assessment of Arthritis (PtGA; visual analogue scale [VAS]), Physician's Global Assessment of Arthritis (PGA; VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI), Pain (VAS), Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F), Medical Outcomes Study (MOS) Sleep Scale and Short-Form Health Survey (SF-36) domain scores. Significance was declared for $p\leq 0.05$ for the P2 and P3 studies reported here.

Results: The analysis included 238 pts from P2 studies, 118 pts from ORAL Scan and 486 pts from the LTE study. Demographics and baseline characteristics were similar between treatment groups for all studies. In P2 studies at Week 12, tofacitinib 5 and 10 mg BID demonstrated significantly greater improvements from baseline vs PBO in PtGA, PGA, HAQ-DI, Pain, FACIT-F, MOS Sleep Scale and in 4 (Physical Function [PF], Role-Physical [RP], Bodily Pain [BP] and General Health [GH]) of the 8 SF-36 domain scores (Table). Significant improvements in PtGA, PGA, HAQ-DI, Pain and FACIT-F vs PBO were seen as early as Week 2. In ORAL Scan at Month 3, statistically significant improvements from baseline in PtGA, PGA, HAQ-DI and Pain were seen for both tofacitinib 5 and 10 mg BID vs PBO (Table) and these were maintained to Month 24. Significant improvements vs PBO as early as Month 1 were seen for PGA (tofacitinib 10 mg BID) and Pain (both doses). In the LTE study, mean changes from LTE study baseline in PtGA, PGA, HAQ-DI and Pain were -32.5, -40.8, -0.5 and -32.9, respectively, for all tofacitinib doses at Week 2, and -40.7, -50.2, -0.7 and -42.4, respectively, at Week 168. Mean changes from baseline in SF-36 domain scores at Week 12 and

Week 168, respectively, were: 7.5 and 8.6 (PF); 6.9 and 6.9 (RP); 10.4 and 11.6 (BP); 5.7 and 5.4 (GH); 7.2 and 6.1 (Vitality [VT]); 5.0 and 4.5 (Social Function [SF]); 6.3 and 5.5 (Role-Emotional [RE]); and 6.1 and 4.8 (Mental Health [MH]).

Table. PROs in Japanese patients with active RA treated with tofacitinib (full analysis set*)

	Phase 2						Phase 3		
	Study A3921039 (NCT00603512) (Week 12)			Study A3921040 (NCT00687193) (Week 12)			ORAL Scan (Month 3) (A3921044; NCT00847613)		
	Placebo (N=24)[a]	Tofacitinib 5 mg BID (N=24)[a]	Tofacitinib 10 mg BID (N=21)[a]	Placebo (N=48)[a]	Tofacitinib 5 mg BID (N=50)[a]	Tofacitinib 10 mg BID (N=49)[a]	Placebo (N=21)[b]	Tofacitinib 5 mg BID (N=44)[b]	Tofacitinib 10 mg BID (N=44)[b]
LS mean (SE) change from baseline									
PtGA (VAS)[c]	-8.8 (3.8)	-38.9 (3.8)***	-37.6 (4.0)***	-1.0 (3.1)	-34.6 (3.1)***	-43.6 (3.0)***	-5.9 (4.3)	-25.9 (3.0)**	-27.9 (3.0)***
PGA (VAS)[c]	-16.1 (3.4)	-45.9 (3.4)***	-43.7 (3.6)***	-8.4 (2.7)	-36.9 (2.7)***	-49.4 (2.7)***	-9.0 (3.6)	-34.0 (2.5)***	-37.3 (2.5)***
HAQ-DI[c]	-0.1 (0.1)	-0.5 (0.1)***	-0.5 (0.1)***	0.2 (0.1)	-0.6 (-0.1)***	-0.7 (0.1)***	-0.1 (0.1)	-0.5 (0.1)***	-0.6 (0.1)***
Pain (VAS)[c]	-6.1 (3.8)	-34.3 (3.8)***	-36.8 (4.0)***	-1.1 (3.0)	-34.4 (3.0)***	-42.9 (3.0)***	-4.5 (4.2)	-36.6 (2.9)***	-29.2 (2.9)***
FACIT-F[d]	-1.6 (1.4)[e]	6.8 (1.3)****[e]	3.8 (1.4)**[e]	-1.4 (1.0)[e]	7.5 (1.0)****[e]	8.5 (1.0)****[e]	-	-	-
MOS Sleep Scale – overall sleep problems[f]	3.6 (2.0)[e]	-6.7 (2.0)***[e]	-3.6 (2.1)**[e]	2.0 (1.9)[e]	-7.1 (1.9)***[e]	-8.0 (1.9)***[e]	-	-	-
SF-36 domain scores,[f,e] LS mean (SE) change from baseline									
Physical Function	1.3 (1.2)	6.3 (1.2)**	7.3 (1.3)**	-2.5 (1.1)	5.8 (1.1)***	9.6 (1.1)***	-	-	-
Role-Physical	1.3 (1.7)	7.3 (1.7)*	6.4 (1.8)*	-0.7 (1.2)	6.2 (1.2)***	8.9 (1.2)***	-	-	-
Bodily Pain	1.6 (1.4)	9.8 (1.4)***	10.7 (1.5)***	0.3 (1.1)	9.7 (1.1)***	12.6 (1.1)***	-	-	-
General Health	-0.2 (1.2)	6.3 (1.2)**	6.5 (1.3)**	0.2 (0.9)	5.4 (0.9)***	7.6 (0.9)***	-	-	-
Vitality	1.2 (1.7)	6.5 (1.7)*	4.8 (1.8)	3.4 (0.8)	6.6 (0.8)*	12.0 (0.8)***	-	-	-
Social Function	1.4 (1.7)	5.3 (1.7)	5.7 (1.9)	-0.7 (1.3)	4.7 (1.3)*	4.6 (1.2)*	-	-	-
Role-Emotional	0.5 (1.9)	3.6 (1.9)	4.4 (2.0)	-1.5 (1.5)	5.6 (1.4)**	8.0 (1.4)***	-	-	-
Mental Health	0.7 (1.7)	6.9 (1.7)*	2.2 (1.9)	0.6 (1.3)	8.6 (1.3)***	7.6 (1.3)**	-	-	-

Nominal *p≤0.05; **p<0.001; ***p<0.0001 vs placebo
[a]All randomised patients who received ≥1 dose of study medication; [b]PROs were not captured for all randomised and treated patients; [c]Data are FAS longitudinal model; [d]Data not available for Study A3921044; [e]Data are FAS mixed-effects model

BID twice daily; FACIT-F, Functional Assessment of Chronic Illness Therapy - Fatigue; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire-Disability Index; LS, least squares; MOS, Medical Outcomes Study; PtGA, Patient's Global Assessment of Arthritis; PGA, Physician's Global Assessment of Arthritis; PRO, patient-reported outcome; RA, rheumatoid arthritis; SE, standard error; SF-36, Short-Form Health Survey; VAS visual analogue scale

Conclusions: Tofacitinib 5 and 10 mg BID significantly improved PROs in Japanese pts with RA enrolled in the P2, P3 and LTE studies.
Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Haines of CMC and was funded by Pfizer Inc.
Disclosure of Interest: H. Yamanaka Grant/research support from: AbbVie, Astellas, Ayumi, Bayer, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Nippon Kayaku, Nippon Shinyaku, Ono, Pfizer Inc, Taisyo-Toyama, Takeda, Teijin Pharma, Torii, UCB, YL Biologics, Consultant for: AbbVie, Astellas, Ayumi, Bayer, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Nippon Kayaku, Nippon Shinyaku, Ono, Pfizer Inc, Taisyo-Toyama, Takeda, Teijin Pharma, Torii, UCB, YL Biologics, Speakers bureau: AbbVie, Astellas, Ayumi, Bayer, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Nippon Kayaku, Nippon Shinyaku, Ono, Pfizer Inc, Taisyo-Toyama, Takeda, Teijin Pharma, Torii, UCB, YL Biologics, Y. Tanaka Grant/research support from: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Takeda, Consultant for: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, GSK, Janssen, Mitsubishi-Tanabe, Pfizer Inc, Sanofi, Takeda, Teijin, YL Biologics, Speakers bureau: AbbVie, Asahi Kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, GSK, Janssen, Mitsubishi-Tanabe, Pfizer Inc, Sanofi, Takeda, Teijin, YL Biologics, T. Takeuchi Grant/research support from: AbbVie, Asahi Kasei, Astellas, Ayumi, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Taisyo-Toyama, Takeda and Teijin Pharma, Consultant for: AbbVie, Astellas, Bristol-Myers Squibb, Celtrion, Chugai, Daiichi-Sankyo, Eisai, Janssen, Mitsubishi-Tanabe, Nippon Kayaku, Pfizer Japan Inc, Takeda, Speakers bureau: AbbVie, Asahi Kasei, Astellas, AstraZeneca, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly Japan, Janssen, Merck Serono, Mitsubishi-Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Takeda, N. Sugiyama Shareholder of: Pfizer Inc, Employee of: Pfizer Japan Inc, T. Hirose Shareholder of: Pfizer Inc, Employee of: Pfizer Japan Inc, N. Yoshii Shareholder of: Pfizer Inc, Employee of: Pfizer Japan Inc, Y. Morishima Shareholder of: Pfizer Inc, Employee of: Pfizer Japan Inc, S. Toyoizumi Employee of: Pfizer Japan Inc
DOI: 10.1136/annrheumdis-2017-eular.1402

THU0192 INFORMING PATIENTS ABOUT METHOTREXATE FOR THE TREATMENT OF RHEUMATOID ARTHRITIS WITH PATIENTS IN THE UNITED KINGDOM – A SURVEY OF RHEUMATOLOGISTS' STRATEGIES

H.F. Hope[1], S.M. Verstappen[2], L. Cordingley[3], K. Hyrich[2]. *[1]NIHR Manchester Musculoskeletal Biomedical Research Unit; [2]Arthritis Research UK Centre for Epidemiology; [3]Division for Musculoskeletal Research and Dermatological Science, University of Manchester, Manchester, United Kingdom*

Background: Rheumatologists are the primary prescribers of methotrexate (MTX) for the treatment of rheumatoid arthritis (RA) in the United Kingdom (UK), however rheumatologists' views on their clinical practices are largely unknown. The authors conducted a qualitative study that highlighted a number of factors that contributed to their ability to discuss and commence MTX, which included how emotionally and cognitively prepared patients were to discuss treatments. The aim of this study was to further explore these themes with an online survey.
Objectives: The aims of this study were:1)To establish the views of rheumatologists about MTX for the treatment of rheumatoid arthritis (RA), 2)To examine if rheumatologists' views influenced discussing or commencing MTX during the initial consultation.
Methods: An online survey was designed and subsequently refined based on interviews with rheumatologists in the UK. The survey asked rheumatologists about their clinical setting, and their views and practices with respect to treating RA with MTX. Rheumatologists were asked how often specific pieces of MTX information were discussed during a consultation to commence MTX (5=Always to 1=never). They were also asked to identify the barriers to discussing these issues. The questionnaire included a factorial survey ie. two patient vignettes where we manipulated the following factors; male/female, emotionally prepared/unprepared and no/negative prior knowledge. Rheumatologists could select "information overload" as a barrier to communication with the patient. Random mixed effects models tested if these patient factors and information overload associated with 1) commencing and 2) discussing MTX.
Results: Ninety-six rheumatologists seeing approximately eight (IQR:5–12) new patients a week with 15±7 years of experience completed the survey. Rheumatologists reported they often/always discussed ten (IQR 8–11) pieces of information during a consultation (Fig 1A), and information overload was identified as a communication barrier (48%); 52% of rheumatologists expected the nurse to discuss MTX therapy (Fig 1B). Sixty rheumatologists completed one, and 56 rheumatologists two vignettes (n=116). The vignette conditions and information overload significantly associated with "Commencing MTX" (X^2=53.85, p <.0001, R^2=.21) and discussing MTX (X^2=30.9, p =.002, R^2=.19). Gender* emotional preparedness (β=-4.27, 95% CI:-7.33,-1.21), and information overload*emotional preparedness (β=-3.03, 95% CI:-5.24, -.82) associated with MTX commencement, whilst only gender*emotional preparedness with discussing MTX (β=-3.86, 95% CI:-6.82, -.90).

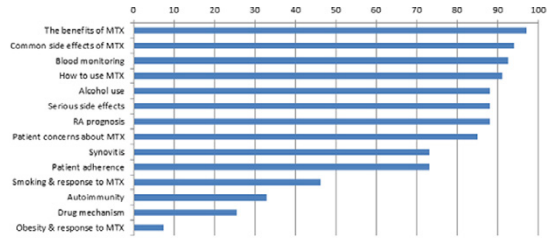


Fig.1A. The specific pieces of MTX-related information rheumatologists in the UK report they often/always discuss in clinic (%)

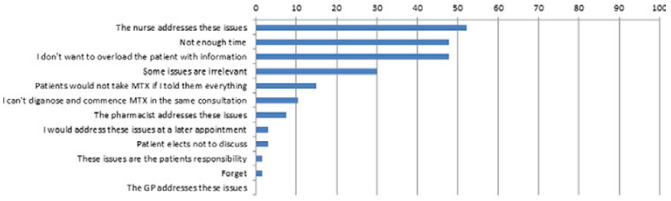


Fig.1B. The reasons rheumatologists in the UK give for not always discussing MTX-related information in clinic (%)

Conclusions: Currently UK rheumatologists convey a large amount of information to patients during early consultations. Almost half of rheumatologists identified the need to communicate large amounts of information in clinical consultations as a barrier to discussing MTX therapy. These data reflect the challenge clinicians face in trying to execute effective shared decision-making practices. Strategies to address patients' emotional responses to their diagnosis and being overloaded with MTX information are needed. Staggering presentation of information during clinical consultations may benefit some patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2429

THU0193 REESTABLISHMENT OF EFFICACY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN RHEUMATOID ARTHRITIS PATIENTS AFTER TEMPORARY DISCONTINUATION

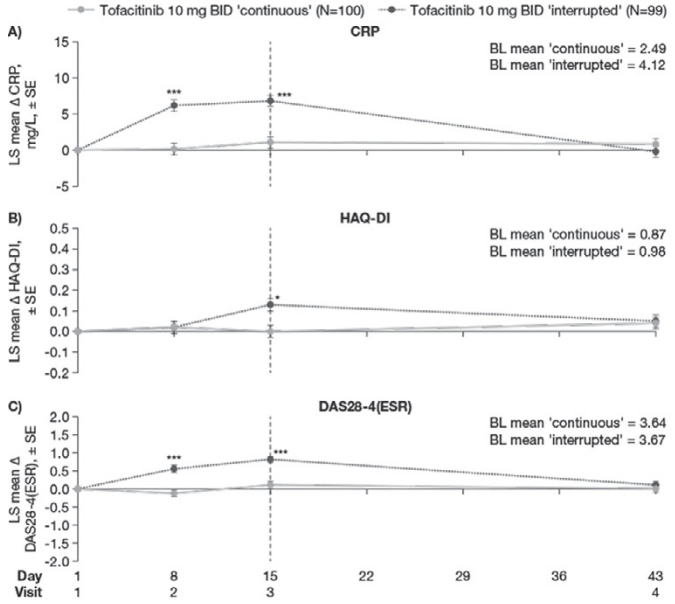
J. Kaine[1], J. Tesser[2], R. DeMasi[3], L. Takiya[3], L. Wang[4], M. Snyder[3], H. Fan[4], J. Wollenhaupt[5]. *[1]Sarasota Arthritis Research Center, Sarasota, FL; [2]Arizona Arthritis & Rheumatology Associates, Glendale, AZ; [3]Pfizer Inc, Collegeville, PA; [4]Pfizer Inc, Groton, CT, United States; [5]Schön-Klinik Hamburg-Eilbek Teaching Hospital of the University of Hamburg, Hamburg, Germany*

Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).
Objectives: To assess the efficacy and safety of tofacitinib after temporary discontinuation and reinitiation of therapy in RA patients (pts).
Methods: Data were collected from a randomised, parallel-group (grp), controlled, open label, vaccine sub-study in RA pts participating in a long-term extension (LTE) study (NCT00413699). Pts were ≥18 years of age with active RA and had received tofacitinib 10 mg BID for ≥3 months. The sub-study included 2 treatment (tx) grps: "continuous tx" (tofacitinib 10 mg twice daily [BID] as monotherapy or with methotrexate [MTX]) and "interrupted tx" (tofacitinib withdrawn for 2

weeks post-randomisation [Day 1–Day 15; Visits 1–3], then tofacitinib 10 mg BID reinitiated as monotherapy or with MTX at Visit 3); randomisation was stratified by MTX use. Pneumococcal and influenza vaccines were administered to all pts on Day 8 (Visit 2; vaccine titers reported previously[1]). Blood samples were taken on Days 8, 15 (Visit 3) and 43 (Visit 4). Efficacy endpoints included change from baseline in C-reactive protein (CRP), Health Assessment Questionnaire Disability Index (HAQ-DI) and Disease Activity Score in 28 joints, erythrocyte sedimentation rate (DAS28-4[ESR]) at each visit. A mixed-effects model with repeated measures was used to evaluate treatment effect at each visit. Analyses for efficacy were exploratory, with no multiplicity adjustment for comparisons.

Results: Of the 199 pts in this analysis (continuous, n=100; interrupted, n=99), 117 received concomitant MTX. At LTE study baseline (BL) in the continuous and interrupted grps, respectively: 81.8/83.8% of pts were white, 84.8/86.9% were female and mean age was 55.0/53.9 years. BL (Day 1) values for CRP, HAQ-DI and DAS28-4(ESR) were generally similar between groups. At Day 8, mean CRP and DAS28-4(ESR) significantly increased from BL for interrupted vs continuous tx; HAQ-DI values were similar between grps (Figure). As expected at Day 15, mean CRP, HAQ-DI and DAS28-4(ESR) significantly increased from BL for interrupted vs continuous tx. After tofacitinib reinitiation for 28 days (Day 43), changes in CRP, HAQ-DI and DAS28-4(ESR) were similar between grps and approached BL levels. Adverse events (AEs) were experienced by 35.4% and 49.5% of pts receiving interrupted and continuous tx, respectively. The most frequent treatment-emergent AEs were bronchitis and upper respiratory tract infection (each AE: 6 pts) and vaccination-related immunisation reaction, myalgia and rash (each AE: 5 pts). Serious AEs occurred in 3 pts (3%) in each grp. In total, 1 pt (1%), in the interrupted tx grp, discontinued due to a study-drug related AE; no pts discontinued due to disease flare.

Figure. LS mean change from BL in RA efficacy endpoints over time from a vaccine sub-study with temporary tofacitinib dose interruption



*p<0.05, ***p<0.0001 for 'interrupted' vs 'continuous' tx
Dashed line indicates the end of the dose interruption period which began at BL
Δ, change from BL; BID twice daily; BL, baseline; CRP, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire Disability Index; LS, least squares; RA, rheumatoid arthritis; SE, standard error; tx, treatment

Conclusions: Efficacy of tofacitinib 10 mg BID can be reestablished following loss of efficacy during temporary (2 weeks) tx discontinuation in pts with RA. Pts receiving continuous tx maintained efficacy throughout the study. Further investigations are required.

References:

[1] Winthrop KL et al. Ann Rheum Dis 2016; 75: 687–695.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Haines of CMC and was funded by Pfizer Inc.

Disclosure of Interest: J. Kaine Speakers bureau: Bristol-Myers Squibb, Pfizer Inc, J. Tesser Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, R. DeMasi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Takiya Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Snyder Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, H. Fan Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Wollenhaupt Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.2375

THU0194 THE ROLE OF ENHANCED LIVER FIBROSIS (ELF) SCORE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH METHOTREXATE

J. Swierkot[1], M. Frankowski[2], M. Skoczynska[2], A. Starba[2], M.S. Gomulkiewicz[3], P. Wojtala[2], M. Bujak[3]. *[1]Department of Rheumatology and Internal Medicine, Medical University Wroclaw; [2]Department of Rheumatology and Internal Medicine; [3]Department of Radiology, Wroclaw University Hospital, Wroclaw, Poland*

Background: MTX is still a basic medicament used in treatment of patients with RA. One of its adverse reaction is its hepatoxicity. Previous studies have established high diagnostic accuracy of the ELF score to assess hepatic fibrosis in chronic viral hepatitis and fatty liver disease.

Objectives: The aim of the research was the evaluation of the usefulness of ELF markings, by patients treated with MTX, as an indicator which shows potential liver damage.

Methods: In the research were analyzed results of 96 patients with RA treated with MTX. Average age of patients was 60 (19–85 years old), median of body mass was 70 kg (46–140), median of BMI was 26 (16–46). Average time of taking MTX were 4 years and median of the accumulated dose was 3140 mg (12,5–27400mg). Disease activity in the moment of evaluation, evaluated by DAS 28, was 4,3 (0,98–8,42).

Achieved results ELF, PIIINP were correlated with body mass, BMI, dose of MTX, other illnesses (e.g. diabetes), taken nonsteroidal anti-inflammatory drugs and statins. In statistical analysis were used Pearson correlation and U Mann-Whitney test.

Results: The ELF values correlated with age, accumulated dose and DAS 28. Along with the increase of accumulated dose of MTX, disease activity and by older patients, were observed higher ELF values (the differences were statistically significant). The PIIINP values correlated with patients' body mass, accumulated dose of MTX and disease activity, evaluated by DAS 28. The differences were statistically significant. Along with the increase of body mass, accumulated dose and DAS 28, were observed higher values of PIIINP. Patients with diabetes had statistically higher values of PIINP (average: 11.13, median: 11,38), than patients without diabetes (average: 8.06, median: 7.15). There was observed no relationship between ELF and PIIINP results with taken nonsteroidal anti-inflammatory drugs and statins.

Conclusions: The ELF test, and one of its elements, PIIINP, may be useful in the evaluation of patients with higher probability of hepatotoxic effect of MTX. Special attention should be paid to older, obese patients, with diabetes, patients who take higher accumulated dose of MTX and with higher disease activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6865

THU0195 CONSISTENT EFFICACY AND SAFETY OF TOFACITINIB IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE OR INTOLERANCE TO NON-MTX CSDMARDS

J. Tesser[1], A. Gül[2], E. Olech[3], K. Oelke[4], T. Lukic[5], C.W. Murray[6], C. Zhang[6], L. Takiya[6]. *[1]Arizona Arthritis & Rheumatology Associates, Glendale, AZ, United States; [2]Istanbul University, Istanbul, Turkey; [3]UNLV School of Medicine, Las Legas, NV; [4]Rheumatic Disease Center, Glendale, WI; [5]Pfizer Inc, New York, NY; [6]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. In clinical practice, a proportion of patients (pts) with RA may not be candidates for treatment with the conventional synthetic DMARD (csDMARD) methotrexate (MTX).[1]

Objectives: To evaluate tofacitinib 5 or 10 mg BID efficacy and safety using pooled data from 8 Phase (P) 2 and 6 P3 trials in RA pts who were (1) inadequate responders (IR)/intolerant to csDMARDs, but did not have an IR or intolerance to MTX or biologic DMARDs (ie, non-MTX csDMARD-IR population) or (2) pts with an IR/intolerance to any csDMARD including MTX but not bDMARD-IR (ie, 2nd-line population).

Methods: Month 3 efficacy outcomes included proportions of pts achieving ACR20/50/70 responses, and Disease Activity Score 28-4(ESR) (DAS28-4[ESR])<2.6 (remission), as well as change from baseline in DAS28-4(ESR) and Health Assessment Questionnaire-Disability Index (HAQ-DI) scores. No multiplicity adjustments were made. Crude incidence rates (CIR; unique pts with events/100 pt-years) based on adverse event (AE) reporting through Month 24 were calculated for treatment-emergent AEs (TEAEs), serious AEs (SAEs), discontinuations (DCs) due to AEs and AEs of special interest.

Results: In the P2/3 tofacitinib RA trials, prior csDMARDs received by the non-MTX csDMARD-IR and 2nd-line populations, respectively were: chloroquine (17.7% and 37.2%), hydroxychloroquine (13.7% and 22.7%), leflunomide (19.4% and 20.9%), MTX (7.3% and 93.3%), sulfasalazine (31.1% and 27.1%) and others (8.0% and 11.1%); pts may have received >1 prior csDMARD. The non-MTX csDMARD-IR population included 208, 247 and 82 pts receiving tofacitinib 5 and 10 mg BID or placebo (PBO), respectively; the 2nd-line population comprised 1206, 1266 and 856 pts, respectively. Baseline characteristics were generally similar between populations except for mean RA duration (5.2–7.2 years, non-MTX csDMARD-IR pts; 8.2–8.5 years, 2nd-line pts). Most pts were female (80.3–85.4%), mean age range was 49.7–52.5 years and mean DAS28-4(ESR)

score ranged from 6.2–6.5. Tofacitinib 5 and 10 mg BID achieved higher ACR responses and greater changes from baseline in DAS28-4(ESR) and HAQ-DI scores vs PBO at Month 3 in both populations (Table). Numerically higher proportions of non-MTX csDMARD-IR pts achieved efficacy outcomes vs 2nd-line population. CIRs for SAEs, DCs due to AEs and AEs of special interest were similar across groups; CIRs for TEAEs were higher with PBO vs tofacitinib. AE frequency was generally lower in the non-MTX csDMARD-IR population vs 2nd-line population.

Table. Efficacy outcomes at Month 3 and safety outcomes to Month 24

	Tofacitinib 5 mg BID		Tofacitinib 10 mg BID		PBO	
	Non-MTX csDMARD-IR	Second-line	Non-MTX csDMARD-IR	Second-line	Non-MTX csDMARD-IR	Second-line
% pts (95% CI) achieving efficacy outcome, FAS, NRI						
ACR20 response	69.3 (62.5–75.6)[a]	59.4 (56.1–62.5)[a]	74.0 (67.6–79.7)[a]	65.4 (62.3–68.4)[a]	25.0 (14.0–39.0)	27.1 (23.2–31.3)
ACR50 response	35.6 (29.1–42.7)[a]	30.7 (27.8–33.8)[a]	44.8 (38.1–51.6)[a]	35.0 (32.0–38.2)[a]	11.5 (4.4–23.4)	8.8 (6.5–11.7)
ACR70 response	16.3 (11.5–22.2)[b]	12.1 (10.1–14.4)[a]	23.3 (17.9–29.5)[a]	17.2 (14.8–19.8)[a]	5.8 (1.2–16.0)	2.7 (1.4–4.5)
DAS28-4(ESR)<2.6	9.2 (5.5–14.4)	6.5 (4.9–8.4)	16.9 (12.1–22.7)[a]	10.2 (8.2–12.5)	4.0 (0.5–13.7)	1.6 (0.7–3.3)
LSM (SE) change in score from baseline in efficacy outcome, FAS						
DAS28-4(ESR)	-2.1 (0.1)[a]	-1.9 (0.1)[a]	-2.5 (0.1)[a]	-2.1 (0.1)[a]	-1.0 (0.2)	-0.9 (0.1)
HAQ-DI	-0.5 (0.0)[a]	-0.5 (0.0)[a]	-0.6 (0)[a]	-0.5 (0.0)[a]	-0.2 (0.1)	-0.2 (0.0)
Safety outcomes, CIR (95% CI)						
TEAE	118.4 (99.9–139.2)	192.4 (179.8–205.8)	136.3 (116.8–158.1)	193.7 (181.3–206.9)	264.1 (183.9–367.3)	292.2 (265.8–320.5)
SAE	8.5 (5.2–12.9)	12.4 (10.3–14.8)	7.4 (4.6–11.3)	9.7 (7.9–11.8)	10.8 (1.3–39.1)	11.5 (7.6–16.8)
DC due to AE	7.1 (4.2–11.2)	9.7 (7.8–11.8)	7.2 (4.5–11.0)	10.4 (8.6–12.6)	10.8 (1.3–39.1)	11.9 (7.9–17.2)
SIE	2.8 (1.1–5.7)	3.4 (2.4–4.7)	1.4 (0.4–3.5)	3.4 (2.4–4.7)	5.4 (0.1–30.1)	1.7 (0.5–4.3)
OI, excluding TB	0.4 (0.0–2.2)	0.2 (0.0–0.7)	0.0 (0.0–1.3)	0.5 (0.2–1.1)	0.0 (0.0–19.9)	0.0 (0.0–1.6)
TB	0.0 (0.0–1.4)	0.0 (0.0–0.4)	0.3 (0.0–1.9)	0.7 (0.3–1.3)	0.0 (0.0–19.9)	0.0 (0.0–1.6)
Herpes zoster	1.2 (0.2–3.5)	3.9 (2.8–5.3)	3.5 (1.7–6.4)	4.8 (3.5–6.3)	0.0 (0.0–19.9)	2.6 (0.9–5.5)
MACE	0.8 (0.1–2.9)	0.4 (0.1–1.1)	0.7 (0.1–2.6)	0.6 (0.2–1.3)	0.0 (0.0–41.1)	0.6 (0.0–3.5)
Malignancies[#]	0.4 (0.0–2.2)	0.7 (0.3–1.4)	0.3 (0.0–1.9)	0.7 (0.3–1.5)	0.0 (0.0–19.9)	0.0 (0.0–1.6)

[a]p<0.001; [b]p<0.05 vs PBO; [#]excluding non-melanoma skin cancer; AE, adverse event; CI, confidence interval; CIR, crude incidence rate; csDMARD, conventional synthetic disease modifying antirheumatic drug; DAS28-4(ESR), disease activity score 28-4(ESR); DC, discontinuation; FAS, full analysis set; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, inadequate response; LSM, least squares mean; MACE, major adverse cardiovascular events; MTX, methotrexate; NRI, non-responder imputation; OI, opportunistic infection; PBO, placebo; SAE, serious AE; SE, standard error; SIE, serious infection event; TB, tuberculosis; TEAE, treatment emergent adverse event

Conclusions: This analysis indicates that tofacitinib is associated with similar efficacy and safety outcomes between csDMARD-IR (including MTX-IR) pts and those who are csDMARD-IR but not MTX-IR. This suggests a favourable tofacitinib benefit/risk profile for RA pts who have a contraindication to or refuse treatment with MTX and failed other csDMARDs.

References:

[1] Lopez-Olivo MA et al. Cochrane Database Syst Rev 2014; CD000957.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Nicholson of CMC and was funded by Pfizer Inc.

Disclosure of Interest: J. Tesser Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, A. Gül Consultant for: AbbVie, Bristol-Myers Squibb, MSD, Novartis, Pfizer Inc, Roche, Servier, UCB, Xoma, E. Olech Grant/research support from: AbbVie, Amgen, Celgene, Genentech, Janssen, Regeneron, Sanofi-Aventis, UCB, Vertex Pharmaceuticals, Consultant for: AbbVie, Amgen, Celgene, Genentech, Janssen, Regeneron, Sanofi-Aventis, UCB, Vertex Pharmaceuticals, K. Oelke Grant/research support from: Novartis, Consultant for: Novartis, Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb, Pfizer Inc, Crescendo Biosciences, UCB, T. Lukic Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Murray Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Zhang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Takiya Shareholder of: Pfizer Inc, Consultant for: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.1828

THU0196 SYSTEMATIC REVIEW AND META-ANALYSIS OF MALIGNANCIES, EXCLUDING NON-MELANOMA SKIN CANCER, IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB OR BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

J.J. Gomez-Reino[1], T. Checchio[2], J. Geier[3], M. Boy[2], S. Ahadieh[2], S. Menon[2], S. Krishnaswami[2]. *[1]Fundacion Ramon Dominguez, Hospital Clinico Universitario, Santiago de Compostela, Spain; [2]Pfizer Inc, Groton, CT; [3]Pfizer Inc, New York, NY, United States*

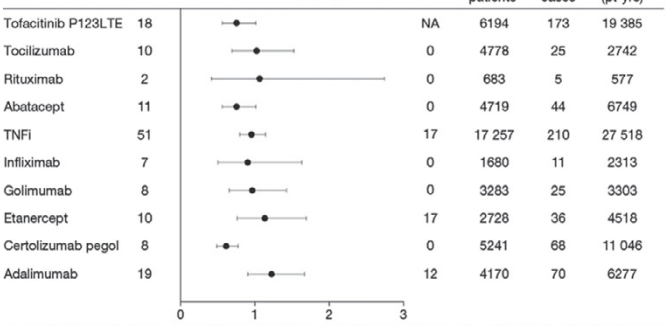
Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). The limited size of the control groups (placebo and active comparator) and limited duration of treatment within the tofacitinib RA clinical trial programme do not permit precise direct comparative assessments for adverse events of long latency, including malignancies, therefore a meta-analytic approach was taken.

Objectives: To compare the rate of malignancies in patients (pts) with moderately to severely active RA within the tofacitinib RA clinical trial programme with estimates from published trial data of approved biologic (b)DMARDS using meta-analytic methods.

Methods: Incidence rates (IR; pts with events per 100 pt-years [yrs] exposure) for tofacitinib were calculated using pooled data from randomised controlled trials (RCT) and long-term extension (LTE) studies. Two Phase (P) 1 studies, 9 P2 studies, 6 P3 studies and 2 LTE studies (one study ongoing; database unlocked at March 2015 data cut off) constituted the P123LTE dataset; pts received 1, 3, 5, 10, 15, 30 mg BID or 20 mg QD of tofacitinib. A systematic literature review of published RCT and LTE studies (through August 2014) of approved bDMARDs (abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab) was conducted. IRs for the endpoint of interest (all malignancies [excluding non-melanoma skin cancers (NMSC)]) were calculated for each bDMARD utilising a random-effects meta-analytic model with a restricted Maximum Likelihood Estimator for between-study variances. Estimates of Q statistic and I^2 were generated to determine the existence and degree of heterogeneity related to the study pool.

Results: The tofacitinib P123LTE dataset included 6194 pts with a total exposure of 19 385 pt-yrs. A total of 64 bDMARD articles were extracted for analysis, representing 58 unique studies and approximately 27 000 pts. Study populations were generally consistent across studies and treatments: mean pt age ranged from 51–54 yrs; mean percentage of pts who were female was 74–84%; and mean baseline C-reactive protein level was 20–31 mg/L. The IR (95% confidence interval [CI]) of malignancy for tofacitinib in the P123LTE dataset was 0.89 (0.76, 1.04) (Figure). Estimated IRs (95% CI) of malignancy were 0.75 (0.56, 1.01) for abatacept, 1.06 (0.41, 2.74) for rituximab, 1.02 (0.69, 1.52) for tocilizumab and 0.95 (0.79, 1.14) for tumour necrosis factor inhibitors (adalimumab, certolizumab, etanercept, golimumab and infliximab) (Figure).

Figure. Incidence rates for all malignancies (excluding NMSC) with biologic DMARDs and tofacitinib across RCTs and LTE studies



The results displayed include a continuity factor (r=0.05) to account for zero incidence rates. Tofacitinib data included through March 2015. Clinical trials for non-tofacitinib studies were conducted between 1997 and 2014.
CI, confidence interval; DMARD, disease-modifying antirheumatic drug; I^2, percent of total variability due to heterogeneity; LTE, long-term extension; NA, not applicable; NMSC, non-melanoma skin cancer; pt-yr, patient-year; RCT, randomised controlled trial; TNFi, tumour necrosis factor inhibitor

Conclusions: The results of this meta-analysis indicate that the tofacitinib IR for all malignancies (excluding NMSC) in pts with moderately to severely active RA is within a similar range to those reported in published interventional studies of similar RA populations treated with approved bDMARDs.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by N Jones and C Viegelmann of CMC and was funded by Pfizer Inc.

Disclosure of Interest: J. Gomez-Reino Grant/research support from: AbbVie, Novartis, Pfizer Inc, Roche, UCB, Consultant for: Pfizer Inc, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, MSD, Pfizer Inc, Roche, UCB, T. Checchio Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Geier Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Boy Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Ahadieh Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Menon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Krishnaswami Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.1960

THU0197 TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF RHEUMATOID ARTHRITIS: SAFETY AND EFFICACY IN OPEN-LABEL, LONG-TERM EXTENSION STUDIES OVER 8 YEARS

J. Wollenhaupt[1], J. Silverfield[2], E.B. Lee[3], K. Terry[4], K. Kwok[5], S. Abramsky[5], M. Wang[5], C. Nduaka[6], R. DeMasi[6], L. Wang[4]. *[1]Schön-Klinik Hamburg-Eilbek Teaching Hospital of the University of Hamburg, Hamburg, Germany; [2]Healthpoint Medical Group, Tampa, FL, United States; [3]Seoul National University, Seoul, Korea, Republic Of; [4]Pfizer Inc, Groton, CT; [5]Pfizer Inc, New York, NY; [6]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: The objective of this analysis was to report tofacitinib safety, tolerability and clinical efficacy in long-term extension (LTE) studies with up to 105 months of observation.

Methods: Data were pooled from two open-label studies (NCT00413699 [ongoing; database not locked at January 2016 data-cut] and NCT00661661) of patients with RA who had participated in Phase 1/2/3 tofacitinib studies. Patients received tofacitinib 5 or 10 mg twice daily (BID) as monotherapy or with background disease-

modifying antirheumatic drugs (DMARDs). Primary endpoints were adverse events (AEs) and confirmed laboratory safety data. Secondary endpoints included clinical efficacy measures (American College of Rheumatology [ACR] 20/50/70 response rates, Disease Activity Score using 28 joint counts and erythrocyte sedimentation rate [DAS28-4(ESR)], Health Assessment Questionnaire-Disability Index [HAQ-DI] and clinical disease activity index [CDAI]). Safety data were included up to Month 105 and efficacy data up to Month 90 (n≤100 at Month 96).

Results: A total of 4967 patients were treated (mean [max] duration: 1215 [3182] days). Total tofacitinib exposure was 16,711 patient-years; 77.4% of patients maintained their initial dose. In total, 2370 patients (47.7%) discontinued (AEs: 1131 [22.8%]; insufficient clinical response: 175 [3.5%]). The most common AE classes were infections and infestations (68.9%) and musculoskeletal/connective tissue disorders (39.0%). The most common AEs were nasopharyngitis (18.7%), upper respiratory tract infection (17.2%), bronchitis and urinary tract infection (12.2% each). Serious AEs occurred in 28.6% of patients and serious infection events (SIEs) in 8.8% of patients. Malignancies, excluding non-melanoma skin cancer, were reported in 3.0% of patients. Incidence rates (IR; patients with events per 100 patient-years) for AEs of interest (with 95% confidence intervals [CIs]) and laboratory observations are provided in Table 1. IRs for SIEs and malignancies through Month 105 did not increase compared with reported data through Month 96.1 No new safety risks were identified. Clinical responses were sustained from Month 1 to Month 90 (Table 2).

Table 1. Safety outcomes and laboratory observations in LTE studies (up to 105 months) of tofacitinib in patients with RA

	Tofacitinib (5 and 10 mg BID) ± background DMARDs N=4967
Incidence rates (patients with events per 100 patient-years) for AEs of interest (95% CI)	
SAEs	9.5 (9.0, 10.0)
SIEs	2.6 (2.4, 2.9)
Malignancies (excluding NMSC)	0.9 (0.8, 1.0)
Confirmed laboratory abnormalities, n (%)	
Haemoglobin ≤7 g/dL or decrease in haemoglobin of ≥3 g/dL from BL	97 (2.0)
Neutrophil <0.5 x 10^3/mm^3	0 (0.0)
Lymphocyte <0.5 x 10^3/mm^3	64 (1.3)
ALT ≥3 x ULN	292 (5.9)
AST ≥3 x ULN	167 (3.4)
Increase in serum creatinine of ≥50% from BL	147 (3.0)

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; BL, baseline; CI, confidence interval; DMARDs, disease-modifying antirheumatic drugs; LTE, long-term extension; NMSC, non-melanoma skin cancer; RA, rheumatoid arthritis; SAEs, serious adverse events; SIEs, serious infection events; ULN, upper limit of normal.

Table 2. Clinical outcomes in LTE studies (up to 90 months) of tofacitinib in patients with RA

	Tofacitinib (5 and 10 mg BID) ± background DMARDs		
	BL	Month 1	Month 90
		N=4907	N=171
ACR20 response rates, %	–	73.0	83.0
ACR50 response rates, %	–	49.2	56.1
ACR70 response rates, %	–	28.9	32.7
	N=4782	N=4776	N=168
DAS28-4(ESR), mean (SE)	6.29 (0.01)	3.75 (0.02)	3.38 (0.09)
	N=4924	N=4880	N=170
HAQ-DI, mean (SE)	1.42 (0.01)	0.82 (0.01)	0.76 (0.05)
		N=4802	N=169
CDAI, mean change from BL (SE)	–	-24.0 (0.20)	-28.5 (1.02)

ACR, American College of Rheumatology criteria; BID, twice daily; BL, baseline; CDAI, clinical disease activity index; DAS28-4(ESR), Disease Activity Score using 28 joint counts and erythrocyte sedimentation rate; DMARDs, disease-modifying antirheumatic drugs; HAQ-DI, Health Assessment Questionnaire-Disability Index; LTE, long-term extension; RA, rheumatoid arthritis; SE, standard error.

Conclusions: In patients with RA who remained in the LTE studies, tofacitinib (5 or 10 mg BID) with or without background DMARDs was associated with consistent safety through Month 105 and sustained clinical efficacy through Month 90.

References:

[1] Wollenhaupt J et al. Arthritis Rheumatol 2015; 67 (suppl 10): Abstract 1645.

Acknowledgements: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by M Bell of CMC and was funded by Pfizer Inc.

Disclosure of Interest: J. Wollenhaupt Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, J. Silverfield Grant/research support from: Pfizer Inc, Speakers bureau: Pfizer Inc, E. B. Lee Consultant for: Pfizer Inc, K. Terry Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Kwok Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Abramsky Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Nduaka Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. DeMasi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.1166

THU0198 COMPARISON OF EFFICACY BETWEEN COMBINATION THERAPY WITH IGURATIMOD AND SULFASALAZINE WITH METHOTREXATE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: PROPENSITY SCORE ANALYSIS

K. Tokunaga[1], A. Shiraishi[2], H. Oshikawa[1], N. Hagino[3], J. Nishino[4], S. Tohma[5]. *[1]Department of Rheumatology, Japanese Red Cross Kumamoto Hospital, Kumamoto; [2]Emergency Department, Kameda Medical Center; [3]Department of Rheumatology, Teikyo University Chiba Medical Center, Chiba; [4]Department of Orthopedic Surgery, Faculty of Medicine, The University of Tokyo, Tokyo; [5]Department of Rheumatology, Clinical Research Center for Allergy and Rheumatology, Sagamihara National Hospital, Sagamihara, Japan*

Background: Iguratimod (IGU) is a small-molecule disease-modifying antirheumatic drug (DMARD) that has been shown to suppress inflammation via the inhibition of nuclear factor-kappa B activation in vitro. The efficacy of combination therapy with IGU and methotrexate (MTX) has been demonstrated in comparison with that of placebo in rheumatoid arthritis (RA). However, its efficacy in comparison with other DMARDs such as sulfasalazine (SSZ) has not been elucidated.

Objectives: To clarify the efficacy of combination therapy with IGU in comparison with that of SSZ with MTX in typical clinical practice.

Methods: We analyzed data from 16,825 RA patients registered in a large database (NinJa: National Database of Rheumatic Diseases by iR-net in Japan) from April 2011 to March 2015 (1). In this study, we compared the two groups who received IGU or SSZ in addition to methotrexate in the earlier year. We excluded patients who started receiving biologic DMARDs, and IGU or SSZ the year prior to the study period, and those whose regimens were changed to other DMARDs such as tacrolimus and bucillamine. Baseline characteristics were compared using the *t* test, Wilcoxon test, or chi-square test. Fisher analysis was conducted for both outcomes. The predicted probability of IGU treatment was calculated by fitting a logistic regression model using all clinically relevant variables as presented in Table 1. Moreover, to reduce the effect of treatment-selection bias and potential confounding in this observational study, we performed rigorous adjustment for significant differences in the baseline characteristics of patients with propensity-score matching using the following algorithm: 1:1 optimal match with a ±0.15 caliper and no replacement. We used the standardized difference to measure covariate balance, whereby a standardized mean difference of >0.1 represents meaningful imbalance. The outcome was remission rate with disease activity score 28 CRP (DAS28-CRP) in the year after initiation of IGU or SSZ therapy.

Results: The group that received IGU in addition to MTX included 66 patients; the other group that received SSZ in addition to MTX included 163 patients. Table 1 shows the results of the pre- and post-propensity score matching of patients' characteristics. Sixty-five patients were compared in each group after score matching. The remission rates of DAS28-CRP in the following year was 77.2% (44/57 patients) and 71.7% (38/53 patients; P=0.52) in the IGU and SSZ groups, respectively.

Table 1. Patients' Characteristics in Full and Propensity Score-Matched Cohorts according to Initiation of Iguratimod or Sulfasalazine

Characteristic	Full Cohort			Propensity Score-Matched Cohort		
	IGU (n = 66)	SSZ (n = 163)	SMD	IGU (n = 65)	SSZ (n = 65)	SMD
Sex, male (%)	32 (19.6)	11 (16.7)	0.077	13 (20.0)	11 (16.9)	0.079
Age per decade (mean [SD])	5.57 (1.44)	5.70 (1.15)	0.097	5.78 (1.36)	5.66 (3.24)	0.099
MTX (mg/week) (mean [SD])	9.38 (3.38)	9.34 (3.28)	0.01	9.26 (3.51)	9.42 (3.24)	0.048
PSL (mg/day) (mean [SD])	1.72 (2.53)	1.71 (2.53)	0.002	1.51 (2.32)	1.74 (2.54)	0.093
SJC 66 (mean [SD])	2.38 (3.57)	3.03 (3.68)	0.207	3.15 (4.10)	2.97 (3.67)	0.047
TJC 68 (mean [SD])	2.70 (4.61)	2.85 (4.52)	0.033	2.57 (4.91)	2.86 (4.55)	0.062

IGU: iguratimod; MTX: methotrexate; PSL: prednisolone; SD: standard deviation; SJC: swollen joint count; SMD: standardized mean difference; SSZ: sulfasalazine; TJC: tender joint count

Conclusions: Combination therapy with IGU or SSZ and methotrexate for rheumatoid arthritis did not show a significant difference in disease activity. Further studies are needed.

References:

[1] Matsui T, Kuga Y, Kaneko A, et al. Disease Activity Score 28 (DAS28) using C-reactive protein underestimates disease activity and overestimates EULAR response criteria compared with DAS28 using erythrocyte sedimentation rate in a large observational cohort of rheumatoid arthritis patients in Japan. Ann Rheum Dis. 2007;66(9):1221–6.

Acknowledgements: NinJa has been supported in part by a research grant from the Health and Labor Sciences, funded by the Ministry of Health, Labor, and Welfare of Japan.

Disclosure of Interest: K. Tokunaga Paid instructor for: AbbVie, Eisai Co. Ltd., and Mitsubishi Tanabe Pharma, A. Shiraishi Paid instructor for: Chugai Pharmaceutical Co., Ltd., H. Oshikawa: None declared, N. Hagino Grant/research support from: Mitsubishi Tanabe Pharma, Chugai Pharmaceutical Co. Ltd., and Bristol Meyers Squibb, Paid instructor for: Santen Pharmaceutical Co. Ltd. and Takeda Pharmaceutical Co. Ltd., J. Nishino: None declared, S. Tohma Grant/research support from: Pfizer Japan Inc., Eisai Co., Ltd., and Chugai Pharmaceutical Co. Ltd.

DOI: 10.1136/annrheumdis-2017-eular.6157

THU0199 TOFACITINIB IMPROVES LEFT VENTRICULAR MASS AND CARDIAC OUTPUT IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Kume, K. Amano, S. Yamada, T. Kanazawa, K. Hatta. *Rheumatology, Hiroshima Clinic, Hiroshima, Japan*

Background: Rheumatologists need to develop primary prevention strategies for cardiovascular disease (CVD) in rheumatoid arthritis (RA) patients. We reported tofacitinib (Tofa) improved arterial stiffness in RA patients. RA is associated with an increased *left* ventricular mass index (LVMI), a strong marker of cardiovascular mortality.There is no evidence that Tofa effects on left ventricular (LV) morphology and function.

Objectives: To study the effect of Tofa plus methotrexate (MTX) on LV morphology and function in MTX resistant active RA patients, in a cohort study design.

Methods: RA patients were eligible if they had active disease despite treatment with MTX. All patients have no steroids, and no previous history of CVD. Consecutive 28 patients with moderate to severe active RA patients (DAS28>3.2) despite MTX were received Tofa plus MTX. LV morphology and function was assessed with cardio-MRI at baseline and 24 weeks follow-up. Cardiovascular risk factors and clinical data were collected at regular visits.

Results: 24 patients completed 24 weeks. Left ventricular mass index (LVMI) was attenuated significantly by Tofa (week 0-week24, –12.4±5.4 g/m^2; p=0.0002). Cardiac output (CO) was attenuated significantly by Tofa (week 0-week24,-0.87±1.2l/min). DAS28 and CRP improved significantly by Tofa (week 0-week24; DAS28: -2.26±0.91; CRP: 14.1±8.7 mg/l) ($p<0.05$). Surprisingly, the change of disease activity (DAS 28 and CRP) is no correlation with the change of LVMI or CO in this study. Observationally, 4 cases significantly improved right ventricular mass as well as left ventricular mass (20% improved right ventricular mass index from baseline).

Conclusions: Tofa improved LVMI and CO in active RA despite MTX. TCZ improves LVMI and CO independently of its effects on disease activity. Tofa might be improved right ventricular mass. JAK-STAT pathway might be an important role of LV hypertrophy. Tofa, JAK-STAT pathway blocking, may prevent cardiovascular morbidity and mortality in RA.

References:

[1] Tocilizumab monotherapy reduces arterial stiffness as effectively as etanercept or adalimumab monotherapy in rheumatoid arthritis: an open-label randomized controlled trial. Kume K, et al.J Rheumatol. 2011 Oct;38(10):2169–71. doi: 10.3899/jrheum.110340. Epub 2011 Aug 1.PMID: 21807781.

[2] Etanercept normalises left ventricular mass in patients with rheumatoid arthritis. Claire Immediato Daïen et al. Annals of the rheumatic diseases. 2013 Jun; 72(6); 881–7. doi: 10.1136/annrheumdis-2012–201489.

Acknowledgements: Thanks for Noriko Kuwaba to calculate data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1098

THU0200 RISK FOR DEVELOPING ADVERSE EFFECTS CAUSED BY SALAZOSULFAPYRIDINE IN RHEUMATIC DISEASES

K. Nakanishi[1], M. Kinjo[2]. [1]*Okinawa Hokubu Hospital, Nago;* [2]*Okinawa CHUBU Hospital, Uruma, Japan*

Background: Salazosulfapyridine is non-antimicrobial sulfonamides, which is used as a synthetic disease modified anti-rheumatic-drug (DMARD) for rheumatoid arthritis and psoriatic arthritis. Prior study suggested sulfa allergy may be more commonly seen in patients with positive anti- Ro/SS-A antibody (anti-Ro).

Objectives: To identify the risk factor for adverse effects (AEs) caused by salazosulfapyridine in patients with rheumatic diseases.

Methods: We retrospectively identified patients ≥18 years old who received salazosulfapyridine at a tertiary medical center in Japan between 2010–2015. Data were collected on the incidence of AEs, clinical features and autoantibodies.

Results: We identified 313 patients with rheumatic diseases who received salazosulfapyridine. Median age was 61 (range, 20–95); 215 of 313 (67%) were female (Table). The incidence of AEs was 15% (48/313); Median duration until developing AEs was 14 days (range, 2–50). AEs included rash (28), fever (19), elevated liver function tests (13), gastrointestinal symptoms (9), lymphadenitis (3), neutropenia and eosinophilia (1). Factors associated with AEs are female gender, positive anti-Ro or psoriatic arthritis. Multivariate logistic controlling for age, gender and anti-Ro showed that positive anti-Ro has 2.33 odds (P=0.03; 95% CI: 1.07–5.08) of having AE of salazosulfapyridine. Among patients without anti-Ro, subjects with psoriasis showed 9.95 odds (P<0.001; 95% CI: 3.51–28.2) of developing AEs than non-psoriatic patients.

Conclusions: AEs caused by salazosulfapyridine are common in patients with rheumatic diseases. Presence of anti- Ro or psoriasis may be a risk factor for AEs caused by salazosulfapyridine.

Table

	With AEs (n=48)	Without AEs (n=265)	P value
Age over 60 years — no. (%)	22 (46)	26 (56)	0.21
Female sex — no. (%)	42 (88)	173 (65)	0.002
Clinical diagnosis			
Rheumatoid arthritis — no. (%)	26 (54)	214 (81)	0.002
Sjogren's syndrome — no. (%)	15 (31)	31 (12)	0.001
Psoriatic arthritis — no. (%)	19 (40)	11 (4)	<0.001
Anti-Ro/SS-A antibody — no. (%)	14 (29)	28 (11)	0.006

References:

[1] Suyama Y, Okada M, Rokutanda R, et al: Safety and efficacy of upfront graded administration of trimethoprim-sulfamethoxazole in systemic lupus erythematosus: A retrospective cohort study. Mod Rheumatol. 2016;26:557–61.

[2] Maezawa R, Kurasawa K, Arai S, et al: Positivity for anti-RNP antibody is a risk factor for adverse effectscaused by trimethoprim-sulfamethoxazole, a prophylactic agent for P. jiroveci pneumonia, in patients with connective tissue diseases. Mod Rheumatol. 2013;23:62–70.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2409

THU0201 OLDER AGE, HYPOALBUMINAEMIA AND RENAL FAILURE MIGHT BE POOR PROGNOSIS FACTORS FOR LOW DOSE METHOTREXATE-INDUCED MYELOSUPPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

X.-N. Wei, D.-H. Zheng, Y.-Q. Mo, J.-D. Ma, Y.-L. Chen, L. Dai. *Rheumatology, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China*

Background: Methotrexate (MTX) serves as an anchor drug in rheumatoid arthritis (RA) and the maximal dose of MTX from EULAR recommendation is 25–30 mg/w. Small cases retrospective cohort studies reported that the mortality rate of RA patients with low dose (5–25 mg/w) MTX-induced myelosuppression was about 17–25%. However, studies of low dose MTX-induced myelosuppression are rare in Chinese RA patients.

Objectives: To perform a retrospective case series analysis of the characteristics and outcomes of RA patients with low dose MTX-induced myelosuppression in China.

Methods: RA patients hospitalized at Sun Yat-Sen Memorial Hospital from January 2001 to December 2016 were recruited. Clinical data were collected and adverse effects were recorded simultaneously. Low dose MTX-induce myelosuppression was diagnosed as white blood cell $<4\times10^9$/L together with hemoglobin <130 g/L and platelet count $<130\times10^9$/L after treatment of MTX without an alternative cause for pancytopenia. Data were showed as mean ± standard deviation.

Results: (1) There were 1137 RA patients recruited and 17 patients (1.5%) of them were hospitalized for low dose MTX-induce myelosuppression. Among these 17 patients, 53% were females, age was 68±5 years, disease duration was 12±11 years.

(2) Four (23.5%) patients had dose errors, taking MTX 5–10mg daily for 24 days (range: 5–80), MTX accumulated dose was 25–200mg before myelosuppression. Mean MTX dose in the other patients (n=13, 76.5%) was 11.0±1.7 mg/w (range: 7.5 –15), course of MTX was 10±11 months (range: 0.5–48). Four (30.8%) patients manifested myelosuppression within the first month after taking MTX, and 4 (30.8%) patients had been well on a stable drug dose (7.5–12.5) for more than one year before myelosuppression, 2 patients manifested myelosuppression after adding MTX dose to 15mg/w for 2 months.

(3) Fifteen (88.2%) patients had oral mucositis, eight of them had involvement of both oral mucosa and skin. Fever was noticed in 10 (58.8%) patients. Infections were recorded in 6 (35.3%) patients, manifested as pneumonia (n=4), sepsis (n=1), urinary tract infection (n=1) and skin soft tissue abscesses (n=1). Two patients experienced abdominal pain and melena.

(4) Among the patients with neutropenia [n=17, mean neutrophil count: $(0.74\pm0.76)\times10^9$/L, range: 0–1.83], 9 (52.9%) developed severe neutropenia with neutrophil counts below 0.5×10^9/L. Five patients developed severe thrombocytopenia (platelet count $<20\times10^9$/L), and severe anemia occurred in 4 patients (hemoglobin <65g/L). Hypoalbuminemia (30.0±2.8 g/L) was noted in all patients. Glomerular filtration rate (GFR)≤30 ml/min/1.73 m^2 was noted in 4 (23.5%) patients and GFR≤50 ml/min/1.73 m^2 in 12 (70.6%) patients.

(5) Pancytopenia recovered (n=17) after discontinuation of MTX and supplementation of folic acid (10–30mg/d). Only 3 (17.6%) patients were treated with rescue intravenous leucovorin. Thirteen (76.5%) were treated with granulocyte colony stimulating factor (G-CSF) and 7 (41.2%) required blood products. Fifteen (88.2%) required antibiotic therapy. Sixteen (94.1%) patients was recovered and discharged, only one patient die from acute brainstem infarction but not from myelosuppression.

Table 1 Characteristics of 17 RA patients with low dose MTX-induce myelosuppression

Case	Age (y)	Sex	Dose (mg/w)	Dose errors	Fever	Mucositis	Neutrophil count (×10^9/L)	Platelet count (×10^9/L)	Hemoglobin (g/L)	GFR (ml/min/1.73 m^2)	Albumin (g/L)	Outcome
1	74	F	10	+	-	+	0.32	107	87	50.0	34.2	Recovered
2	65	M	10	+	+	+	0.25	2	65	49.8	27.1	Recovered
3	69	M	15	+	+	+	2.43	11	53	46.9	32.2	Recovered
4	60	M	15	+	+	+	0.12	61	77	57.4	32.4	Recovered
5	71	M	10	-	+	-	0	18	78	21.3	27.3	Recovered
6	68	F	10	-	-	+	1.64	112	84	39.1	35	Recovered
7	57	F	10	-	+	+	0.13	11	109	52.2	30.3	Recovered
8	76	M	10	-	+	+	0.62	39	88	48.3	18.9	Recovered
9	75	F	10	-	-	+	1.12	106	106	28.4	32.3	Recovered
10	63	F	10	-	+	+	0.67	37	65	33.0	32.9	Recovered
11	64	F	10	-	+	+	0	69	72	32.7	30.2	Recovered
12	70	M	10	-	-	+	0.34	93	73	55.1	28.7	Recovered
13	69	M	7.5	-	+	+	1.83	112	83	47.0	34.8	Recovered
14	62	F	15	-	-	+	0.28	124	53	23.3	31.2	Recovered
15	80	M	12.5	-	-	+	1.05	49	70	42.4	28.8	Recovered
16	74	F	12.5	-	-	-	1.75	106	74	61.8	28.6	Recovered
17	57	F	10	-	+	+	0.02	11	67	17.6	26	Died

Conclusions: Older age, hypoalbuminaemia and renal failure might be poor prognosis factors for low dose MTX-induce myelosuppression in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3723

THU0202 UNAFFORDABLE CONVENTIONAL AND ABSENT BIOLOGIC DMARDS: INCREASING THE BURDEN OF RHEUMATOID ARTHRITIS IN FYROM

O. Gjeorgjieva, N. Memeti, L. Damjanovska-Krstikj. *University Rheumatology Clinic, University Sts Cyril and Methodius, Skopje, Macedonia, The Former Yugoslav Republic Of*

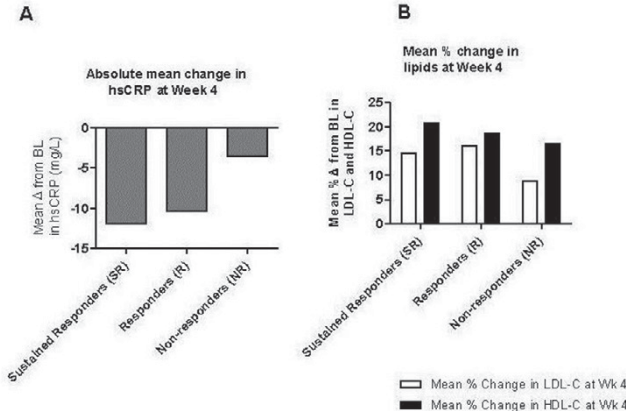
Background: In the developing world rheumatologists and their patients are struggling to implement treat to target therapy in established Rheumatoid Arthritis (RA)which means they can hardly establish remission and low disease activity which is the mainstay of the RA treatment. The main reason is the lack of conventional synthetic and biological (c and b) DMARDs in the therapeutic armamentarium as well as their high cost which increases already difficult burden of RA.
Objectives: The aim of the study is to evaluate the RA treatment and treatment expenses in a group of patients with established RA in FYR of Macedonia including the availability of DMARDs.
Methods: We have conducted a cross-sectional study at the University Rheumatology Clinic in Skopje, including 100 patients with established RA, who fulfilled RA classification criteria from 2010. Physical examination, laboratory analyses and DAS28 were performed and all patients filled a questionnaire with 13 questions about treatment expenses and availability.
Results: There were 82 females and 18 males, with mean age of 59 and disease duration of 8.3 (SD 7,3) years and moderate disease activity DAS28 3,9+/-1,47 and 75% of seropositive RA (double positive 30%, Ant-CCP positive 30%, RF positive 15%) with mean CRP of 21,5 mg/L They spend from 10 to 100 Euros monthly (on average 27+/-17,6) for the cs DMARDs therapy. Almost 80% think that the cs DMARDs therapy is too expensive for them and 100% of them could not afford to pay or co-pay for b DMARDs. Most of the patients (49%) are using single cs DMARDs. Double and triple c DMARD therapy is used by 32% vs 17%, respectively. Even though it is highly effective, patients consider triple cs DMARD therapy expensive and with very low compliance because of the high costs and low tolerability. Only 2% of the patiens are using b DMARDS using rituximab, the only available biologic DMARD therapy in FYROM. Around 70% are taking low dose prednisolone. Almost 50% of the patients cannot take the cs DMARD therapy with a prescription and have to buy their DMARDS without any coverage from the insurance fund and the same percent have problems to find the c DMARDs with prescription because it is not available. Almost half of the patients have heard about the b DMARDs, most of them from their rheumatologist and 54% of them would like to receive it. The patient's reasons for taking b DMARDs are presented in Graph 1.
Conclusions: High expenses and low availability of c DMARDs on prescription and the urgent need for b DMARDs are adding the burden of RA in developing countries including FYROM with the increased need for full coverage for conventional DMARDs and at least partial coverage of biologic DMARDs, especially anti-TNF agents by the insurance companies. The use of biosimilars might be highly appreciated in the future.
References:
[1] Aletaha D, Neogi T, Silman AJ et al. 2010 Rheumatoid arthritis classification criteria: An ACR/EULAR collaborative initiative. Arthritis Rheum 2010; 9 (62):2569–2581.
[2] O'Dell JR. Therapies for active rheumatoid arthritis after methotrexate failure N Engl J Med 2013; 369:307–318.
[3] Avci AB, Feist E, Burmester GR. Biologicals in rheumatoid arthritis current and future RMD Open 2015.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6485

THU0203 CHANGES IN C-REACTIVE PROTEIN AND LIPID LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ABT-494, A SELECTIVE JAK-1 INHIBITOR

M. Nurmohamed[1], Y. Zhang[2], J. Lin[2], H. Camp[2]. *[1]Amsterdam Rheumatology Immunology Ctr, VU Univ Medical Ctr, Amsterdam, Netherlands; [2]AbbVie, N Chicago, United States*

Background: In patients (pts) with rheumatoid arthritis (RA) treated with ABT-494, dose-dependent increases in levels of low and high density lipoprotein cholesterol (LDL-C and HDL-C) were observed, along with decreases in levels of C-reactive Protein (CRP). Whether these changes are due to the control of inflammation or a direct effect on CRP production in the liver is not known.
Objectives: To explore the relationship between changes in HDL-C or LDL-C and CRP with ABT-494 treatment, and to assess whether the effect on lipids is dependent on improvement of RA signs and symptoms.
Methods: Data were from two phase 2b controlled trials of ABT-494 in RA pts with inadequate response or intolerance to TNF inhibitors (TNF-IR, BALANCE-1)[1], or with inadequate response to methotrexate (MTX-IR, BALANCE-2)[2]. Pts treated with placebo or 3,6,12,18 mg ABT-494 twice daily for 12 weeks (wks) are included. Levels of high sensitivity (hs) CRP, total cholesterol (TC), LDL-C and HDL-C were measured at baseline (BL) and Wk 2,4,6, 8 and 12. Atherogenic burden at BL and Wk 12 was assessed by ratio of ApoB:ApoA1 and TC:HDL-C in 6 mg and 12 mg dose groups in both studies. Pearson's coefficients were calculated *post hoc* to assess possible correlations between HDL-C or LDL-C levels (or changes from BL) with other variables including (high sensitivity) hsCRP, at BL and Wk 12. Pts were subgrouped by response: Sustained responders (SR), pts who achieved an ACR20 response at every visit from Wk 2–12; Responders (R), pts who achieved ACR20 at least once, but not at every visit; Non-responders (NR), pts who did not achieve ACR20 at any visit.
Results: The ratios of LDL-C:HDL-C[1,2] and TC:HDL-C remained unchanged after 12 wks of treatment with ABT-494. The ratio of ApoB:ApoA1 also remained unchanged from BL to Wk 12: in BALANCE-1, 0.61 to 0.58 for the 6 mg (n=19), and 0.62 to 0.60 for 12 mg (n=11) groups, and in BALANCE-2, 0.62 to 0.64 for the 6 mg (n=18) and 0.69 to 0.66 for 12 mg (n=16) groups. An inverse relationship between LDL-C or HDL-C and hsCRP was observed throughout the treatment period. At Wk 4, among the variables tested, the strongest correlation was observed between changes from BL in hsCRP and LDL-C (-0.29, $p<0.001$) or HDL-C (-0.26, $p<0.001$). Out of 420 pts, 104 pts (25%) were ACR20 SR, 251 pts (60%) were R and 65 pts (15%) were NR. Compared to NR, SR and R had a greater absolute reduction in hsCRP (Fig. 1A). A robust percentage increase in HDL-C was observed in all 3 groups (20.8%, 18.5% and 16.4% in SR, R and NR, respectively). Compared to the SR and R (14.6% and 16%, respectively), a smaller percentage increase in LDL-C was observed in the NR (8.9%) (Fig. 1B).

Figure 1



Conclusions: Atherogenic burden did not increase in pts treated with ABT-494 for 12 wks. Compared to non-responders, pts with a clinical response experienced a larger increase in lipids and a larger decrease in hsCRP. Limited data from these phase 2 studies suggest that there might not be an increased risk of cardiovascular events. Results from the larger phase 3 trials can provide more information.
References:
[1] Kremer et al. 2016, Arthritis & Rheum;68:2867.
[2] Genovese et al. 2016, Arthritis & Rheum;68:2857.
Acknowledgements: AbbVie: study sponsor, contributed to study design, data collection, analysis and interpretation; writing, reviewing, and approval of the final version. Medical writing: Naina Barretto, of AbbVie.
Disclosure of Interest: M. Nurmohamed Grant/research support from: Abbvie, Bristol–Myers Squibb, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Janssen, UCB and Sanofi., Consultant for: Abbvie, Bristol–Myers Squibb, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Janssen, UCB and Sanofi., Y. Zhang Employee of: AbbVie, J. Lin Employee of: AbbVie, H. Camp Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.2807

THU0204 RELATIONSHIPS BETWEEN METHOTREXATE DOSAGES AND CLINICAL VARIABLES IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ACHIEVED REMISSION WITH METHOTREXATE MONOTHERAPY: A STUDY USING THE IORRA OBSERVATIONAL COHORT STUDY

M. Tochihara[1], Y. Katsumata[1], E. Inoue[1,2], Y. Kawaguchi[1], E. Tanaka[1], A. Nakajima[1], K. Ikari[1], A. Taniguchi[1], H. Yamanaka[1]. *[1]Institute of Rheumatology, Tokyo Women's Medical University; [2]National Center for Child Health and Development, Tokyo, Japan*

Background: Considerable variability exists in the way rheumatologists prescribe methotrexate (MTX) therapy in patients with rheumatoid arthritis (RA), including the dosage [ref.1]. Start higher doses or fast dose escalation are associated with higher efficacy, but also with more toxicity. In addition, factors such as renal function, body size, and age of the patient can affect the optimal dosage of MTX.
Objectives: We aimed to study the relationships between MTX dosages and clinical variables in patients with RA who achieved remission with MTX monotherapy.

Methods: The "Institute of Rheumatology, Rheumatoid Arthritis (IORRA)" is a single-center prospective observational cohort study established at our institute in 2000. Data (physicians' and patients' disease assessments, laboratory data, and many other patient information) were collected from approximately 5,000 RA patients biannually. More than 99% of RA patients treated at our institute were enrolled in this cohort, and >98% of patients answered and mailed their questionnaires back to us every time. Among the RA patients who were registered in the IORRA cohort study from 2011 through 2015, 603 patients fulfilled the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Boolean-based definition of remission in RA, at least once and used only MTX as disease-modifying antirheumatic drugs (DMARDs) including biological DMARDs for 5 years. Relationships between MTX dosages and gender, disease duration, height, body weight, body mass index, body surface area, serum creatinine (SCr), estimated glomerular filtration rate (eGFR), creatinine clearance (by Cockcroft-Gault Equation), rheumatoid factor, and anti-cyclic citrullinated peptide antibody when remission was first reached by each patient were analyzed by univariate analyses using Pearson correlation coefficient and Welch's *t* test. Subsequently, a multiple regression analysis was performed.
Results: Univariate analyses detected several candidate clinical variables associated with MTX monotherapy dosages in RA patients who achieved remission: height, body weight, body surface area, SCr, eGFR, and CCr (p =0.004, 0.050, 0.241, <0.001, <0.001, and <0.001, respectively). Subsequently, a multiple regression model developed a best-fit model with the following variables; age, height, body weight, and SCr (standardized partial regression coefficient = -0.20, 0.10, 0.07, and -0.22, respectively), while its adjusted coefficient of determination was 0.114.
Conclusions: There were significant relationships between MTX monotherapy dosages and age, height, body weight, and renal function in RA patients who achieved remission. However, the low coefficient of determination indicated the model accounted for limited variability with the specified variables.
References:
[1] Visser K and van der Heijde D. Optimal dosage and route of administration of methotrexate in rheumatoid arthritis: a systematic review of the literature. Ann Rheum Dis. 2009;68:1094.
Disclosure of Interest: M. Tochihara: None declared, Y. Katsumata: None declared, E. Inoue: None declared, Y. Kawaguchi: None declared, E. Tanaka Consultant for: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical, Speakers bureau: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical, A. Nakajima Consultant for: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., Speakers bureau: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., K. Ikari Grant/research support from: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., Speakers bureau: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., A. Taniguchi Grant/research support from: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., Speakers bureau: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., H. Yamanaka Grant/research support from: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Consultant for: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Speakers bureau: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers.
DOI: 10.1136/annrheumdis-2017-eular.3333

THU0205 EFFECTS OF THE JAK1-SELECTIVE INHIBITOR FILGOTINIB ON MULTIBIOMARKER DISEASE ACTIVITY SCORES IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO METHOTREXATE

M.C. Genovese[1], W. Li[2], L. Goyal[2], Y. Pan[2], A. Van der Aa[3], C. Jamoul[3], P. Harrison[3], C. Tasset[3], R. Galien[4], J. Tarrant[2]. *[1]Division of Immunology & Rheumatology, Stanford University School of Medicine, Palo Alto; [2]Gilead Sciences, Foster City, United States; [3]Galapagos NV, Mechelen, Belgium; [4]Galapagos SASU, Romainville, France*

Background: Filgotinib (GLPG0634, GS-6034) is an oral selective JAK1 inhibitor that has been evaluated in a 24-week phase 2B study (DARWIN 1) on the background of methotrexate (MTX) treatment in active rheumatoid arthritis (RA) patients who were MTX inadequate responders[1].
Objectives: To evaluate the effect of filgotinib compared to placebo on a multi-biomarker disease activity (MBDA) score that measures 12 disease-related biomarkers of inflammation and joint injury in RA patients taking background MTX.
Methods: Serum samples of RA patients who were on a stable dose of MTX and received either placebo (PBO) or filgotinib 100mg or 200mg once daily (QD), were tested for MBDA components (Crescendo Biosciences, CA, US) at baseline, week 4 and week 12. Median % change from baseline for MBDA score and individual components are reported for week 4 and week 12. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups *vs.* PBO.
Results: Baseline MBDA scores and component values (median; interquartile range) were similar in PBO (55; 45–64), 100mg QD (58; 42–66), and 200mg QD (59; 50–67.5) treatment groups. Filgotinib treated patients had reductions in the MBDA score from baseline at both the 100mg and 200mg QD dose levels, but not in the PBO group. At both weeks 4 and 12, these reductions in the filgotinib treated groups were significantly different from the PBO group. Most of the individual components contributed to the decrease in MBDA score, but the largest reductions were observed for serum amyloid A (SAA), C-reactive protein (CRP), and IL-6, and the biomarkers of joint-damage, matrix metalloproteinase 3 (MMP3), MMP1, vascular endothelial growth factor (VEGF), and YKL40 (human cartilage glycoprotein 39). There was an increase in leptin and no change in epidermal growth factor (EGF) concentrations.

Table 1. Median percent change from baseline of MBDA score and component concentrations

	Week 4			Week 12		
	PBO (N=62)	Filgotinib 100mg QD (N=63)	Filgotinib) 200mg QD (N=68)	PBO (N=65)	Filgotinib 100mg QD (N=62)	Filgotinib par 200mg QD (N=68)
MBDA SCORE	-1	-20***	-24***	-5	-19***	-24***
CRP	15	-57***	-71***	-8	-66***	-78***
EGF	14	-18^{NS}	-8^{NS}	0	-10^{NS}	0^{NS}
IL-6	-15	-34**	-60***	-20	-41**	-63***
LEPTIN	0	8^{NS}	18^{NS}	6	14^{NS}	23*
MMP-1	10	-16***	-24***	-6	-18**	-26***
MMP-3	0	-24**	-33***	-9	-25***	-43***
RESISTIN	1	-12**	-22***	-1	-15*	-16***
SAA	8	-45***	-65***	7	-49***	-67***
TNF-RI	0	-11***	-26***	0	-11***	-15***
VCAM-1	5	-10***	-15***	0	-8**	-16***
VEGF	3	-16***	-25***	-2	-16***	-26***
YKL-40	2	-12*	-32***	-7	-17^{NS}	-33***

p-values comparing % changes between filgotinib and PBO groups NS, p>0.05; *p<0.05; **p<0.01; ***p<0.001.

Conclusions: RA patients treated with filgotinib in combination with MTX had significant reductions in the MBDA score that was driven by key RA biomarkers encompassing both inflammation and joint injury. These findings are consistent with the filgotinib efficacy observed in RA patients over 12 weeks.
References:
[1] Westhovens R, et al. Ann Rheum Dis 2016;0:1–11. doi:10.1136/annrheumdis-2016–210104.
Disclosure of Interest: M. Genovese Grant/research support from: Abbvie, Eli Lilly, Pfizer, Astellas, Vertex, Consultant for: Galapagos, Gilead, Abbvie, Eli Lilly, Pfizer, Astellas, Vertex, W. Li Employee of: Gilead Sciences, L. Goyal Employee of: Gilead Sciences, Y. Pan Employee of: Gilead Sciences, A. Van der Aa Employee of: Galapagos NV, C. Jamoul Employee of: Galapagos NV, P. Harrison Employee of: Galapagos NV, C. Tasset Employee of: Galapagos NV, R. Galien Employee of: Galapagos SASU, J. Tarrant Employee of: Gilead Sciences
DOI: 10.1136/annrheumdis-2017-eular.5738

THU0206 THE JAK1-SELECTIVE INHIBITOR FILGOTINIB REDUCES MULTIPLE MARKERS OF INFLAMMATION LINKED TO VARIOUS PATHOLOGIC CELL TYPES AND PROCESSES IN RHEUMATOID ARTHRITIS PATIENTS

P. Taylor[1], R. Westhovens[2], A. Van der Aa[3], C. Jamoul[3], W. Li[4], L. Goyal[4], Y. Pan[4], P. Harrison[3], C. Tasset[3], J. Tarrant[4], R. Galien[5]. *[1]University of Oxford, Oxford, United Kingdom; [2]University Hospitals, Leuven; [3]Galapagos NV, Mechelen, Belgium; [4]Gilead Sciences, Foster City, United States; [5]Galapagos SASU, Romainville, France*

Background: JAK1, 2, 3 and TYK2 are cytoplasmic tyrosine kinases that mediate intracellular signaling of many cytokines and growth factors. Filgotinib (GLPG0634, GS-6034) is a JAK inhibitor with high selectivity for JAK1 over other JAK family members. Filgotinib has a favorable safety and efficacy profile in two Phase 2B studies in active rheumatoid arthritis (RA) patients who were methotrexate (MTX) inadequate responders.
Objectives: To assess the effect of filgotinib on a background of MTX treatment on markers of inflammation in RA patients.
Methods: Serum samples from RA patients who were on a stable dose of MTX and received either placebo (PBO), filgotinib 100mg or 200mg once daily (QD), were collected at baseline, week 4 and week 12 and analyzed for 35 soluble serum biomarkers by validated single-plex or multiplex immunoassays. Median % changes from baseline for biomarkers are reported. Wilcoxon rank-sum test assessed the significance of difference between filgotinib treated groups and PBO.
Results: Filgotinib treatment induced a dose-dependent and significant decrease

in a variety of biomarkers implicated in RA pathogenesis including inflammation (IL-1β, IL-6, TNFα and SAA), matrix degradation and cartilage destruction (MMP1 and MMP3), immune cell trafficking (CXCL10, ICAM-1 and VCAM-1) and angiogenesis (VEGF). Cytokines involved in T_H1 (IFN-γ, IL-2, IL-12) and T_H17 (IL-1β, IL-6, IL-21, IL-23) cell subset differentiation and activity were significantly decreased. Additionally, decrease in the B-cell chemoattractant CXCL13 and the myeloid growth factor GM-CSF supports the anti-inflammatory effects of filgotinib treatment.

Table 1. Median percent change of biomarkers at week 12 from baseline for PBO and 200mg QD dose

	PBO (N=78)	Filgotinib 200mg QD (N=75)		PBO (N=78)	Filgotinib 200mg QD (N=75)		PBO (N=78)	Filgotinib 200mg QD (N=75)
BAFF	-2	-6^{NS}	IL-2	-7	-20**	MIP-1β	0	-7*
CRP	-8	-78***	IL-21	0	-28**	MMP-1	-6	-26***
CXCL-13	3	-40***	IL-23	-6	-25***	MMP-3	-9	-43***
EGF	0	0^{NS}	IL-4	0	0^{NS}	RESISTIN	-1	-16***
GM-CSF	0	-26***	IL-5	2	-14**	SAA	7	-67***
ICAM-1	0	-14***	IL-6	-20	-63***	sgp130	0	4^{NS}
IFN-γ	-2	-21*	IL-7	1	-17***	TNF-α	1	-15***
IL-10	-3	-17**	IL-8	-2	-12^{NS}	TNF-RI	0	-15***
IL-12	0	-24***	IP-10	-2	-31**	VCAM-1	0	-16***
IL-13	-1	-8**	LEPTIN	6	23*	VEGF	-2	-26***
IL-17A	2	-18*	MCP-1	4	-8^{NS}	YKL-40	-7	-33***
IL-1β	-2	-26***	MIP-1α	1	-8**			

p-values comparing % changes between filgotinib and PBO groups: NS, $p>0.05$; *$p<0.05$; **$p<0.01$; ***$p<0.001$.

Conclusions: Treatment with filgotinib decreased several factors that have key roles in RA for matrix degradation, cartilage destruction, angiogenesis, leukocyte adhesion and recruitment. The changes were accompanied by decreases in cytokines that promote and activate T_H1, T_H17, B-cells and myeloid cells that are important in RA. These findings provide insights into filgotinib mechanism of action and are consistent with its efficacy observed in RA patients.

Disclosure of Interest: P. Taylor Consultant for: Galapagos NV, Pfizer, Eli Lilly, UCB, GSK, R. Westhovens: None declared, A. Van der Aa Employee of: Galapagos NV, C. Jamoul Employee of: Galapagos NV, W. Li Employee of: Gilead Sciences, L. Goyal Employee of: Gilead Sciences, Y. Pan Employee of: Gilead Sciences, P. Harrison Employee of: Galapagos NV, C. Tasset Employee of: Galapagos NV, J. Tarrant Employee of: Gilead Sciences, R. Galien Employee of: Galapagos SASU

DOI: 10.1136/annrheumdis-2017-eular.5799

THU0207 THE EFFECT OF THE USE OF GLUCOCORTICOIDS ON HEALTH ASSESSMENT QUESTIONNAIRE IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL REMISSION –DATA FROM KANSAI CONSORTIUM FOR WELL-BEING OF RHEUMATIC DISEASE PATIENTS (ANSWER COHORT)-

R. Hara[1], T. Fujimura[1], M. Hashimoto[2], M. Furu[2], W. Yamamoto[2], T. Hirano[3], K. Ebina[4], S. Yoshida[5], K. Nagai[5], H. Amuro[6], Y. Son[6], T. Onishi[7], K. Akashi[7], M. Katayama[8], T. Kira[9], N. Shimmyo[1], A. Kido[1], Y. Akai[1], T. Fujimoto[1], Y. Tanaka[1]. *[1]The Center for Rheumatic Diseases, Nara Medical University, Nara; [2]Department of the Control for Rheumatic diseases, Graduate School of Medicine, Kyoto University, Kyoto; [3]Department of Respiratory Medicine, Allergy and Rheumatic Disease, Graduate School of Medicine, Osaka University; [4]Department of Orthopaedic Surgery, Osaka University, Graduate School of Medicine; [5]Department of Internal Medicine (I), Osaka Medical College; [6]First Department of Internal Medicine, Kansai Medical University, Osaka; [7]Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe; [8]Department of Rheumatology and Clinical Immunology, Osaka Red Cross Hospital, Osaka; [9]Department of the Control for Rheumatic diseases, Nara Medical University, Nara, Japan*

Background: In the treatment of patients with rheumatoid arthritis (RA), glucocorticoids (GCs) with csDMARDs remain an important treatment option given their capacity to increase clinical, structural and functional efficacy. On the other hand, it is reported that GCs usage even at low dosage significantly deteriorated functional capacity in patients with low disease activity state. In these previous study, disease activity and subsequent joint destruction have no small influence on functional disability.

Objectives: To investigate the effect of the use of glucocorticoids (GCs) in patients with RA who had maintained clinical remission on functional ability.

Methods: Among 2,649 patients with RA who achieved DAS-ESR<2.6 after 2013 in the multi-center cohort, 1,171 patients who had maintained DAS-ESR<2.6 were eligible. Clinical and demographic characteristics were collected at baseline. We calculated odds ratio (OR) (95% confidence interval) of the use and dose of GCs to predict the yearly progression of HAQ-DI score adjusted for age, sex, BMI, disease duration, RF titer, ACPA titer, CRP, MMP-3, DAS28-ESR, HAQ-DI, use of MTX and use of biologic DMARDs as covariates in multiple logistic regression model.

Results: Characteristics of patients at baseline were as follows (median (IQR), proportion). The age was 61 (48–68) years, female was 70.6%, disease duration was 4.5 (1.7–10.7) years, RF-positive was 64.4%, ACPA-positive was 70%, DAS28-ESR was 2.0 (1.6–2.6), HAQ-DI score was 0.125 (0–0.5). Of the 1,171 patients, 235 (20.1%) patients had been treated with oral GCs when achieving clinical remission. CRP (0.06 (0–0.2) vs 0.03 (0–0.1), p=0.03), MMP-3 (106.1 (73.2–172.8) vs 49.5 (36.5–77.2), p<0.001), SDAI (2.9 (1.5–5.9) vs 2.6 (1.0–4.8), p=0.003), DAS28-CRP (1.6 (1.3–2.0) vs 1.5 (1.2–1.9), p=0.008), patients' global assessment (mm) (15 (5–31) vs 11 (3–25), p=0.006), physicians' global assessment (mm) (6 (3–12) vs 5 (0–10), p=0.001) and HAQ-DI (0.38 (0–0.88) vs 0.13 (0–0.38), p<0.001) were significantly higher and disease duration was significantly longer (year) (8.9 (3.2–19.6) vs 4.1 (1.6–9.3), p<0.01) in the GCs group compared to the non-GCs group. One hundred and fifty-eight (67.2%) patients had been treated with GCs during follow up, and median dose was 4.5 (2.5–5.5) mg/day. Two hundred and eighty-seven (24.5%) patients' yearly change of HAQ-DI score incresed. The adjusted OR of the use of GCs at baseline was 2.06 (1.21–3.51). The adjusted OR of the daily dose of GCs <5mg was 1.61 (0.73–3.56), whereas that of GCs≧5mg was 2.65 (1.11–6.34) in patients with keeping GCs use.

Conclusions: The use of GCs in RA patients with sustained remission was the risk factor of progression of HAQ-DI score dose-dependently.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6924

THU0208 METHOTREXATE POLYGLUTAMATES LEVELS IN ERYTHROCYTES WERE GENETICALLY AFFECTED IN RA PATIENTS WITH LOW DISEASE ACTIVITY FOR LONG PERIOD

S. Kumagai[1,2], M. Nishida[2], Y. Uemura[1], M. Izumi[2], K. Abe[2], K. Yoneda[2], Y. Noda[2], S. Sendo[3], A. Ohishi[3], M. Shinohara[3], G. Tsuji[2]. *[1]Shinko Institute for Medical Research; [2]Center for Rheumatic DIseases, Shinko Hospital; [3]Graduate School of Medicine, Kobe University, Kobe, Japan*

Background: Detection of the intracellular levels of polyglutamated MTX (MTX-PGn) can predict response of MTX or possibly its adverse effects. As efficacy and toxicity of MTX differs among individual patients, we had proposed a predictive model for MTX efficacy consisting of 9 SNPs (2015 EULAR). In the present study, we measured erythrocyte MTX-PGn in RA patients with low disease activity for long time receiving a stable dose of MTX, investigated their associations with genetic polymorphisms, and speculated MTX dose required to reach possible effective MTX-PG levels.

Objectives: To investigate if erythrocytes MTX-PGn concentration is associated with the 9 SNPs in 7 genes reportedly related to MTX-efficacy in RA patients with low disease activity.

Methods: The study was cross-sectional using 121 adult patients with RA in Shinko Hospital. All patients enrolled had received a stable dose of MTX (mean 8.9±0.3 mg/week), and kept lower disease activity (DAS28-CRP <2.7, mean 1.9±0.4) for at least 3 months. Concentrations of MTX-PG with 1 - 5 glutamate residues (PG1- PG5) in erythrocytes were quantitated by LC-ESI-MS/MS as described by den Boer et al. Nine SNPs in 7 genes previously found to associate with efficacy of MTX by us were genotyped by RT-PCR (Applied Biosystems, Inc.). First, association of the 9 SNPs with concentrations on MTX-PGn was analyzed by one-way layout (Wilcoxon signed-rank test). Secondly, multivariate logistic regression analyses were performed to estimate roles of MTX dose and polymorphisms in concentrations of MTX-PGn.

Results: Total PGn concentrations were 82.1±31.7 nmol/L (m±SD) and positively correlated with MTX dose (Rs =0.4104, p<0.001), but range of concentration was rather wide even if the dose was same. By one-way layout, GGH c.452C>T was associated with PG1, PG2, and total PG, SLC19A1 c.80G>A with total PG, and SLC28A3_c.267G>A with PG3. Three SNPs (FPGS c. 192T>C, EPHX1_c.357G>A, SLC28A3_c.267G>A) were related to MTX doses. Next, we investigated roles of MTX dose and 9 SNPs in maintenance of MTX-PGn concentrations as by multiple regression analyses. As PG1 levels were related to GGH c.452C>T but not to MTX dose, PG1 levels were 38.2±19.6 and 54.8±21.5 nmol/L in CC and CT genotypes, respectively (P=0.0291). MTX dose was strongly associated with PG3 levels as well as with those of PG4. MTX-PG3 levels were regressed as follows; MTX-PG3 (nmol/L) = -0.035 +[2.04 * MTX dose] + [2.34 * SLC19A1 c.80G>A] + [-2.01 * FPGS c.*192T>C]. When upper and lower limits of them were defined, we can speculate MTX dose to reach the effective levels for individual patients. However, the ranges of effective levels were rather wide, suggesting that effectiveness of MTX may depend on not only concentrations of MTX-PG but also responsiveness to MTX-PG.

Conclusions: We measured erythrocyte MTX-PGn in RA patients with low disease activity and investigated for their associations with MTX dose and genetic polymorphisms. We could speculate MTX dose required to reach possible effective MTX-PG levels in individual patient.

References:

[1] Den Boer E, et al: Measuring methotrexate polyglutamates in red blood cells: A new LC-MS/MS-based method. Anal Bioanal Chem, 405:1673–1681, 2013.

Disclosure of Interest: S. Kumagai Consultant for: Sysmex CO, M. Nishida: None declared, Y. Uemura: None declared, M. Izumi: None declared, K. Abe: None declared, K. Yoneda: None declared, Y. Noda: None declared, S. Sendo: None declared, A. Ohishi: None declared, M. Shinohara: None declared, G. Tsuji: None declared

DOI: 10.1136/annrheumdis-2017-eular.2585

THU0209 LYMPHOCYTE SUBSETS IN BIOPSY SPECIMEN ARE ASSOCIATED WITH SPONTANEOUS REGRESSION OF LYMPHOPROLIFERATIVE DISORDERS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH METHOTREXATE

T. Kameda[1], M. Izumikawa[1], M. Inoo[2], I. Onishi[2], N. Kurata[2], S. Nakashima[1], H. Shimada[1], H. Ozaki[1], R. Wakiya[1], A. Kondo[1], N. Kadowaki[1], H. Dobashi[1].
[1]Department of internal medicine division of endocrinology and metabolism, Hematology, Rheumatology and Respiratory Medicine, Kagawa University; [2]Internal medicine, Utazu hospital, Kagawa, Japan

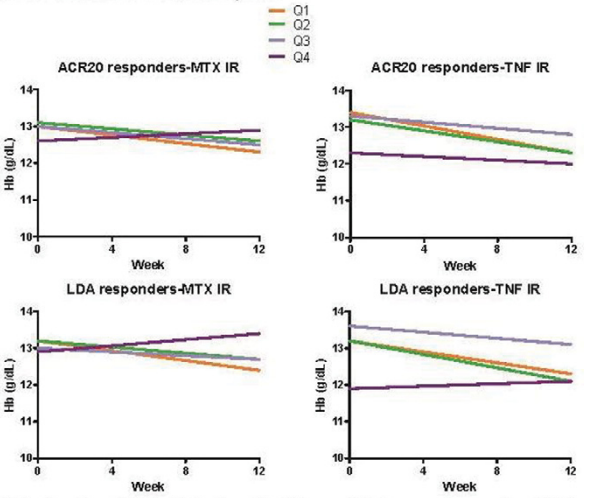
Background: Patients with rheumatoid arthritis (RA) have a high risk for lymphoproliferative disorders (LPDs). An LPD in a patient treated with methotrexate (MTX) is known as MTX-associated LPD (MTX-LPD), which is classified among immunodeficiency-associated lymphoproliferative disorders (ID-LPD) as "other iatrogenic ID-LPD" in the 2008 World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues (1). We previously reported that MTX is an independent risk factor for LPD onset in Japanese patients with RA (2). In MTX-LPD, MTX withdrawal can result in spontaneous regression of LPD. In addition, limited evidence indicates that Epstein–Barr virus infection is related to spontaneous regression of MTX-LPD. No biomarker has been identified that predicts spontaneous regression of MTX-LPD.
Objectives: To identify a biomarker that predicts spontaneous regression of MTX-LPD in RA patients.
Methods: We enrolled RA patients from Kagawa Prefecture, Japan, who developed MTX-LPD during the period from June 2010 through December 2016. RA was diagnosed in accordance with the American College of Rheumatology 1987 classification criteria and was treated with disease-modifying antirheumatic drugs, including MTX. The patients were divided into two groups: those followed-up after discontinuation of MTX alone (MTX withdrawal group) and those who received chemotherapy at 1 month or later after MTX discontinuation (chemotherapy group). The following variables were compared between groups: change in peripheral lymphocyte subsets after MTX discontinuation, serum soluble interleukin-2 receptor, and lymphocyte subsets and Epstein–Barr virus–encoded RNAs in a biopsy specimen from a lesion.
Results: We enrolled 43 MTX-LPD patients (29 in the withdrawal group and 14 in the chemotherapy group). From among these groups, we selected 32 patients for analysis of changes in peripheral lymphocyte subsets (23 in the withdrawal group and 9 in the chemotherapy group) and 22 for analysis of lymphocyte subsets in a lesion specimen (11 each in the withdrawal group and chemotherapy group). Peripheral lymphocyte counts were significantly higher after MTX discontinuation in the withdrawal group. Analysis of lymphocyte subsets from lesion specimens revealed significantly higher CD8-positive lymphocyte counts in the chemotherapy group than in the withdrawal group.
Conclusions: Lymphocyte count differed before and after MTX discontinuation, and a higher CD8-positive lymphocyte count in a lesion specimen was associated with spontaneous regression of MTX-LPD. These findings may help identify a predictive marker for MTX-LPD treatment and management.
References:
[1] Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al., WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. IARC Press, Lyon, 2008.
[2] Association of higher methotrexate dose with lymphoproliferative disorders onset in rheumatoid arthritis patients. Kameda T, Dobashi H, Miyatake N, Inoo M, Onishi I, Kurata N, Mitsunaka H, Kawakami K, Fukumoto T, Susaki K, Izumikawa M, Nakashima S, Shimada H, Takeuchi Y, Haba R, Mano S, Onishi H, Imataki O, Matsunaga T. Arthritis Care Res (Hoboken). 2014 Sep;66(9):1302–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4683

THU0210 CHANGES IN HEMOGLOBIN LEVELS UPON TREATMENT WITH ABT-494, A SELECTIVE JAK-1 INHIBITOR, AND RELATION TO BASELINE LEVELS OF C-REACTIVE PROTEIN

V. Strand[1], M. Genovese[1], J. Kremer[2], M. Schiff[3], Y. Li[4], J. Sokolove[4].
[1]Stanford Univ, Palo Alto; [2]Albany Medical College, Albany, NY; [3]Univ of Colorado, Denver, CO; [4]AbbVie, N Chicago, IL, United States

Background: Patients (pts) with rheumatoid arthritis (RA) often have inflammation-related anemia of chronic disease, partially due to IL-6 and its induction of hepcidin. High levels of the inflammatory marker C-reactive protein (CRP) are largely induced by IL-6. Treatment with JAK inhibitors has been associated with both rise and fall in hemoglobin (Hb) levels, possibly due to inflammation control and inhibition of JAK2 (which is involved in erythropoiesis), respectively [1,2].
Objectives: To examine the association of changes in Hb upon treatment with ABT-494 with baseline (BL) CRP levels.
Methods: This *post hoc* analysis used data from two phase 2b randomized controlled trials (RCT) of ABT-494: in RA pts with inadequate responses or intolerance to TNF inhibitors (TNF-IR, BALANCE-1)[3], and in pts with inadequate responses to methotrexate (MTX-IR, BALANCE-2)[4]. The analyses included pts receiving ABT-494 at 6 or 12 mg. Pts were subgrouped by quartiles of BL CRP. For each RCT, and for the pooled data from both, changes from BL in Hb (g/dL) were determined after 12 weeks (wk) of treatment with ABT-494, for the overall population and for pts who achieved ACR20 or DAS28-CRP $\leq$3.2 responses at Wk 12. For ACR20 and DAS28-CRP $\leq$3.2, non-responder imputation was used. For changes in Hb, data are as observed. Significance was determined by ANCOVA.
Results: In pooled data from 110 and 100 pts from BALANCE-1 and -2 respectively, higher BL CRP was associated with smaller mean decreases in Hb at Wk 12 (p=.074). In the MTX-IR trial, pts in the highest CRP quartile had a mean increase from BL in Hb (+0.28 g/dL) vs pts in the lower quartiles who had mean decreases in Hb ($p<.01$). In both RCTs, ACR20 or DAS28-CRP $\leq$3.2 responders had smaller decreases in Hb vs non-responders at Wk 12. Among DAS28-CRP $\leq$3.2 responders, pts in the higher CRP quartiles had significantly smaller mean decreases in Hb vs pts in the lower quartiles ($p<.01$ for MTX-IR and $p<.05$ for TNF-IR pts). Responders in the highest BL CRP quartile also had a mean increase in Hb (+0.31 and + 0.54 g/dL for MTX-IR ACR20 and DAS28-CRP $\leq$3.2 responders respectively, + 0.15 g/dL for TNF-IR DAS28-CRP $\leq$3.2 responders) (Fig. 1A–D). While similar trends between BL CRP levels and changes in Hb at Wk 12 were observed among ACR20 or DAS28-CRP $\leq$3.2 non-responders, the differences in Hb levels between the quartiles were not significant. Despite the small mean changes, the mean Hb values remained within the normal range for females (lower limit of normal 11.5 g/dL)

Figure 1. Hb levels at BL and Week 12 in patients by baseline CRP quartile in patients who achieved an ACR20 or LDA response.



Q1 is the lowest, and Q4 the highest quartile. Q1 was within the normal range, for which the upper limit is 5 mg/L. CRP quartile cutoffs are as follows: In MTX-IR, Q1: ≤2.5 mg/L, Q2: >2.5 and ≤5.9 mg/L, Q3: >5.9 and ≤18.3 mg/L, Q4: >18.3 mg/L; in TNF-IR, Q1: ≤3.1 mg/L, Q2: >3.1 and ≤7.0 mg/L, Q3: >7.0 and ≤16.7 mg/L, Q4: >16.7 mg/L.

Conclusions: Upon treatment with ABT-494, pts with the highest CRP (a potential surrogate for IL-6) at BL had a mean increase in Hb compared to decreases in those with lower CRP. This effect was more apparent in pts with clinical responses. This suggests that effective treatment of RA-associated inflammation with ABT-494 may counterbalance the small Hb reduction associated with JAK inhibition.
References:
[1] Schulze-Koops et al 2017, Rheumatology;56:46.
[2] Genovese et al 2016, NEJM; 374:13.
[3] Kremer et al 2016, Arthritis & Rheum;68:2867.
[4] Genovese et al 2016, Arthritis & Rheum;68:2857.
Acknowledgements: AbbVie: Study sponsor, involved in study design, data collection, analysis, and interpretation, and in publication writing, review, and final approval. Medical writing: Naina Barretto, of AbbVie.
Disclosure of Interest: V. Strand Consultant for: AbbVie, Afferent, Amgen, Biogen Idec, Bioventus, BMS, Carbylan, Celgene, Celltrion, CORRONA, Crescendo, Genentech/Roche, GSK, Hospira, Iroko, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi, SKK, Takeda, UCB, Vertex, M. Genovese Grant/research support from: AbbVie, Lilly, Astellas, Vertex, Pfizer, Galapagos, Gilead, Consultant for: AbbVie, Lilly, Astellas, Vertex, Pfizer, Galapagos, Gilead, J. Kremer Grant/research support from: AbbVie, Lilly, Novartis, Pfizer, MedImmune, Sanofi, and Regeneron, Consultant for: AbbVie, Lilly, Novartis, Pfizer, MedImmune, Sanofi, and Regeneron, Employee of: CORONA, M. Schiff Consultant for: AbbVie, Speakers bureau: AbbVie, Y. Li Employee of: AbbVie, J. Sokolove Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.3216

THU0211 META-ANALYSIS OF SERIOUS INFECTIONS WITH BARICITINIB, TOFACITINIB AND BIOLOGIC DMARDS IN RHEUMATOID ARTHRITIS

V. Strand[1], S. Ahadieh[2], R. DeMasi[3], S. Krishnaswami[2], J. Geier[4], S. Menon[2], J.J. Gomez-Reino[5]. *[1]Division of Immunology/ Rheumatology, Standford University, Palo Alto, CA; [2]Pfizer Inc, Groton, CT; [3]Pfizer Inc, Collegeville, PA; [4]Pfizer Inc, New York, NY, United States; [5]Fundacion Ramon Dominguez, Hospital Clinico Universitario, Santiago de Compostela, Spain*

Background: Tofacitinib is an oral Janus kinase (JAK) inhibitor for the treatment of rheumatoid arthritis (RA). Baricitinib is a JAK inhibitor being investigated for RA. Serious infection events (SIEs) have been reported in RA randomised controlled trials (RCTs) but limited head-to-head data are available to directly compare rates of these events for tofacitinib vs biologic (b)DMARDs and baricitinib.
Objectives: We present an updated meta-analysis of published RCTs and corresponding long-term extension (LTE) studies to contextualise the risk of SIEs[1] with tofacitinib and extend this work to include the JAK inhibitor baricitinib.
Methods: An initial systematic literature search (Medline, Embase, PubMed and regulatory submission documents) was conducted for SIEs with tofacitinib and bDMARDs (abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab).[1] A subsequent systematic literature review of RCTs was conducted using Medline, BIOSIS, Embase and conference abstracts to evaluate SIEs with baricitinib. Incidence rates (IRs; patients with events per 100 patient-years) were calculated for each agent, utilising a random effects meta-analytic model using R (version 2.15.2 for tofacitinib and bDMARDs; version 3.2.2 for baricitinib) with a Restricted Maximum Likelihood Estimator for between-study variances. Risk ratios and risk differences were calculated for each agent vs control across RCTs up to rescue of patients randomised to receive placebo using the random effects Mantel-Haenszel method.
Results: Six RCTs with baricitinib were included in this updated analysis. In the original analysis, 70 RCTs and 18 LTE studies met inclusion criteria for tofacitinib and bDMARDs. The table provides a summary of the meta-analyses conducted for SIE IRs (with and without LTE), risk ratios and risk differences relative to control. The IRs (95% confidence interval [CI]; heterogeneity [I^2]) for baricitinib were 4.75 (2.32, 9.74; I^2=19%) for 2 mg and 3.67 (2.33, 5.78; I^2=36%) for 4 mg. The analysis of risk ratios (p values 0.22 for 2 mg; 0.95 for 4 mg) and risk differences (p values 0.41 for 2 mg; 1.00 for 4 mg) did not reveal a significant difference from control for both doses of baricitinib, which is consistent with analyses of tofacitinib and bDMARDs. There were limited data to assess SIE incidence for baricitinib (4 mg) monotherapy vs in combination with methotrexate (MTX); the RA-BEGIN study showed IRs of 3.77 (1.7, 8.4) and 2.33 (0.97, 5.59), respectively. Pooled IR estimates for tofacitinib from the development programme were 1.70 (0.91, 2.92) and 1.79 (1.00, 2.95) for 5 and 10 mg BID monotherapy, respectively; when administered in combination with MTX, the IRs were 3.44 (2.41, 4.76) and 3.42 (2.42, 4.70) for 5 and 10 mg BID, respectively.

Table: Serious infection incidence rates, risk ratios and risk differences for tofacitinib vs biologic DMARDs and baricitinib[1]

Drug	Incidence rate (95% CI), per 100 pt-yr		Risk ratio (95% CI)	Risk difference (95% CI), %
	RCT+LTE	RCT	RCT	RCT
Abatacept	3.04 (2.49, 3.72)	2.97 (2.17, 4.07)	1.18 (0.45, 3.09)	0.4 (-0.72, 1.51)
Rituximab	3.72 (2.99, 4.62)	3.45 (2.73, 4.36)	1.01 (0.46, 2.22)	-0.42 (-1.63, 0.79)
Tocilizumab	5.45 (4.26, 6.96)	5.39 (4.05, 7.18)	1.82 (1.22, 2.73)	1.51 (0.68, 2.33)
Infliximab	6.11 (5.24, 7.12)	6.42 (5.50, 7.50)	0.83 (0.33, 2.06)	-0.52 (-3.56, 2.53)
Etanercept	4.06 (3.26, 5.08)	3.90 (2.76, 5.52)	1.00 (0.07, 15.24)	0.00 (-9.39, 9.39)
Certolizumab	7.59 (5.80, 9.94)	7.59 (5.80, 9.94)	2.18 (1.06, 4.50)	1.96 (0.8, 3.12)
Golimumab	5.31 (4.09, 6.89)	5.31 (4.09, 6.89)	1.3 (0.43, 3.90)	0.68 (-0.31, 1.67)
Adalimumab	5.04 (3.80, 6.69)	5.47 (3.92, 7.64)	2.27 (0.84, 6.13)	1.16 (-0.34, 2.67)
TNF inhibitors	4.90 (4.41, 5.44)	5.50 (4.86, 6.23)	1.50 (1, 2.25)	0.94 (0.25, 1.63)
Tofacitinib 5 mg, P2/P3	NA	2.71 (2.00, 3.58)[a] 2.35 (1.36, 4.06)[b]	1.34 (0.43, 4.15)	0.27 (-0.36, 0.9)
Tofacitinib 10 mg, P2/P3	NA	2.72 (2.04, 3.56)[a] 2.80 (1.95, 4.01)[b]	1.67 (0.60, 4.65)	0.42 (-0.22, 1.05)
Tofacitinib P123LTE (All doses)	2.74 (2.51, 2.99)[a]	NA	NA	NA
Baricitinib 2 mg	NA	4.75 (2.32, 9.74)	1.13 (0.24, 5.35)	-0.35 (-1.72, 1.02)
Baricitinib 4 mg	NA	3.67 (2.33, 5.78)	0.82 (0.34, 1.97)	-0.21 (-1.11, 0.69)

[a] Estimate from pooled patient-level data
[b] Estimate from random effects meta-analytic model

CI, confidence interval; DMARDs, disease-modifying antirheumatic drugs; JAK, Janus kinase; LTE, long-term extension; NA, not applicable; P2/P3, Phase 2 and Phase 3 studies; P123LTE, Phase 1, 2, 3 and LTE studies; pt-yr, patient year; RCT, randomised controlled trial; risk ratio, relative risk compared with placebo; risk difference, risk difference compared with placebo; TNF, tumour necrosis factor

Conclusions: The results from these meta-analyses suggest that the risk of SIEs (IRs, risk ratios and risk differences) with tofacitinib is comparable with published rates for bDMARDs and baricitinib in patients with moderate to severe RA.
References:
[1] Strand V et al. Arthritis Res Ther 2015; 17: 362.
Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Nicholson and C Viegelmann of CMC and funded by Pfizer Inc.
Disclosure of Interest: V. Strand Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, CORRONA, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, S. Ahadieh Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. DeMasi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Krishnaswami Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Geier Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Menon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Gomez-Reino Grant/research support from: AbbVie, MSD, Novartis, Pfizer Inc, Roche, UCB, Speakers bureau: AbbVie, Biogen, Bristol-Myers Squibb, Janssen, MSD, Pfizer Inc, Roche, UCB
DOI: 10.1136/annrheumdis-2017-eular.2439

THU0212 THE IMPROVEMENT OF ULTRASONOGRAPHIC FINDINGS FOR 24 WEEKS MAY PREDICT REMISSION AT 52 WEEKS IN JAPANESE RHEUMATOID ARTHRITIS PATIENTS TREATED WITH IGURATIMOD THERAPY

Y. Kanayama[1], H. Nagasaka[2], M. Shimotake[2], F. Miyachi[2], K. Fujita[2], A. Nagata[2]. *[1]Orthopedic Surgery and Rheumatology; [2]Clinical technology, Toyota Kosei Hospital, Toyota, Japan*

Background: Iguratimod (IGU) suppressed tumor necrosis factor-alpha-induced production of interleukin (IL)-6, IL-8, and monocyte chemoattractant protein 1 via inhibition of nuclear factor kappa B activation in cultured human synovial cells and human acute monocytic leukemia cells. We reported the clinical efficacy of IGU at ACR2014 and EULAR2015. However there is still few studies of improvement of ultrasonographic findings in rheumatoid arthritis (RA) treated with IGU.
Objectives: To evaluate the efficacy of IGU therapy in patients with RA using ultrasonography (US).
Methods: Participants comprised 54 Japanese RA patients who had recently received IGU. All patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria. Patients underwent clinical and laboratory assessments from baseline to 52 weeks, and US assessments at baseline, 12 and 24 weeks. Gray scale (GS) and power doppler (PD) signals were scored using a semi-quantitative scale from 0 to 3 at 26 (0–78) synovial sites (22 joints) in the following joints: bilateral first to fifth metacarpopharangeal (MCP) joints (dorsal recess); first interphalangeal (IP) and second to fifth proximal interphalangeal (PIP) (dorsal recess) joints; and the wrists (dorsal radial, median and ulnar).
Results: The patients included 16 males and 38 females. The mean age was 65.4±11.6 years; the mean disease duration was 9.3±10.8 years; and the number of MTX combination, other DMARD excluded combination, IGU monotherapy and Biologics combination were each 32, 10, 8 and 4 cases.
Clinical findings related to RA were as follows: tender and swollen joint count, 4.2±2.9 and 3.2±2.1; patient's and physician's global assessment of disease activity, 40.2±24.0 and 40.2±19.9mm; CRP, 1.0±1.2 mg/dL; ESR, 31.2±18.2 mm/h; DAS28-ESR, 4.37±0.88 and SDAI, 16.4±7.0. The mean DAS28-ESR improved to 3.43±0.94 and 2.98±0.88 at Week 12 and 24 ($p<0.001$, $p<0.001$) and the mean SDAI improved to 8.8±6.1 and 6.3±5.2 at Week 12 and 24 ($p<0.001$, $p<0.001$) significantly. The mean GS score changed from 16.8±12.5 at baseline to 15.8±11.2 (p=0.458) and 14.8±10.3 (p=0.103) at week12 and 24. The mean PD score changed from 7.6±6.8 at baseline to 5.8±6.0 (p=0.053) and 5.3±5.4 (p=0.05) at week12 and 24. In the achieved remission for DAS28-ESR at Week52 (n=16) and not achieved or discontinued IGU patients (n=38), the respective changes in GS and PD scores from baseline to 12 or 24 weeks were as follows: ΔGS score: -3.7±0.8 vs 0.1±6.8 (p=0.068) at 12 weeks and -5.8±5.7 vs -0.4±9.8 (p=0.008) at 24 weeks; and ΔPD score: -3.4±5.6 vs -1.1±5.2 (p=0.065) at 12 weeks and -4.9±6.3 vs -1.2±6.1 (p=0.013) at 24 weeks (Fig.1). Areas under the receiver operating characteristic curves for the ΔGS and ΔPD score at each time point for remision achievement at 52 weeks were each 0.643 and 0.648 from week0 to 24 and 0.725 (cut-off index -3, odds ratio 5.60, sensitivity 0.74, specificity, 0.67) and 0.706 (cut-off index -1, odds ratio 4.71, sensitivity 0.63, specificity, 0.73) from week0 to 24 (Fig.2).

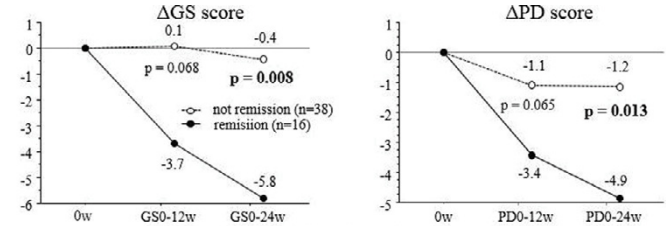


Figure 1 : Respective changes in ΔGS and ΔPD score from baseline to Week 24 in the achieved remission for DAS28-ESR at Week52 and not achieved or discontinued IGU patients

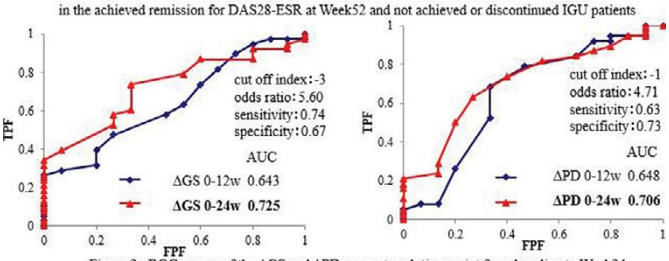


Figure 2 : ROC curves of the ΔGS and ΔPD score at each time point from baseline to Week24 for predicting the achieved remission at Week 52 after starting IGU therapy

Conclusions: The IGU therapy improved not only the disease activity not also the inflammatory synovitis. The present study provides evidence supporting t the improvement of GS and PD score from baseline to week24 may predict whether the achieved remission or not at Week 52.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6948

THU0213 COMPARATIVE EFFICACY AND SAFETY OF BARICITINIB 2 MG AND 4 MG IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Y.H. Lee, Y.H. Seo, G.G. Song. *Rheumatology, Korea University Medicial Center, Seoul, Korea, Republic Of*

Background: Baricitinib is a potent, selective JAK1 and JAK2 inhibitor. Baricitinib has been investigated in phase II and phase III studies of active patients with rheumatoid arthritis (RA). who showed an inadequate response to disease-modifying antirheumatic drugs (DMARDs), including methotrexate (MTX) and biologics. However, due to the lack of adequate multiple comparisons, the comparative efficacy and safety of baricitinib in various treatment regimens with different dosages or in combination with DMARDs or MTX remains unclear.
Objectives: This study aimed to assess the relative efficacy and safety of once-daily baricitinib 2 mg and 4 mg administration in patients with active RA.
Methods: We performed a literature search using MEDLINE, EMBASE, the Cochrane Controlled Trials Register, and the EULAR and ACR conference proceedings. In this network meta-analysis, randomized controlled trials (RCTs) examining the efficacy and safety of baricitinib in patients with active RA were included. A Bayesian network meta-analysis was conducted to combine the direct and indirect evidence from the RCTs.
Results: Seven RCTs involving 3,461 patients met the inclusion criteria. There were 10 pairwise comparisons, including 7 direct comparisons and 5 interventions. The ACR20 response rate was significantly higher in the baricitinib 4 mg in combination with disease-modifying antirheumatic drugs (DMARD) group than in the placebo+DMARD group (OR 3.13, 95% CrI 2.32–4.33). Compared with the placebo+DMARD group, the baricitinib 4 mg, baricitinib 2 mg+DMARD, and adalimumab 40 mg+MTX groups showed a significantly higher ACR20 response rate. The ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that baricitinib 4 mg+DMARD was likely to elicit the best ACR20 response rate (SUCRA =0.7930), followed by baricitinib 4 mg (SUCRA =0.7034), baricitinib 2 mg+DMARD (SUCRA =0.6304), adalimumab 40 mg+MTX (SUCRA =0.3687), and placebo+DMARD (SUCRA =0.0045). By contrast, the safety based on the number of treatment-emergent adverse events (TEAEs) did not differ significantly among the 5 interventions.
Conclusions: Baricitinib 2 mg and 4 mg administered once daily was an efficacious intervention for active RA that had no significant risk of TEAE development.
Acknowledgements: None
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1245

THU0214 LONG-TERM OUTCOME OF IGURATIMOD, CONVENTIONAL SYNTHETIC DISEASE-MODIFYNG ANTI-RHEUMATIC DRUD DEVELOPED IN JAPAN, IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-WORLD CLINICAL SETTING

Y. Hirano, M. Isono, Y. Okada, Y. Oishi. *Rheumatology, Toyohashi Municipal Hospital, Toyohashi, Japan*

Background: Iguratimod (IGU) is csDMARDs developed in Japan and used in Japanese daily practice since 2012. Although IGU was developed as an anti-inflammatory drug at first, anti-rheumatic effect was found in experiments using type II collagen-induced arthritis model mice[1)]. Main mode of action of IGU was thought to be inhibition of NF-kB resulted in decreased production of IL-6, IL-8 and TNF-alpha[2)]. Clinical trials performed in Japan showed that efficacy of IGU was equal to sulfasalazine when used as monotherapy in patients with rheumatoid arthritis (RA)[3)]. Additive efficacy to MTX was also shown in double-blind randomised trial in RA patients [4)]. Although several short-term results were published[5)], long-term results in daily clinical setting is lacking.
Objectives: To investigate long-term outcome of IGU in patients with RA.
Methods: 120 RA patients treated with IGU in our institute from April 2013 to June 2016 were included. Patients' characteristics, factors influencing to prescribing of IGU (why was IGU chosen as treating csDMARDs?), drug continuation rates (Kaplan-Meier) were investigated. Time course of disease activity (DAS28-CRP & SDAI) was also investigated using 65 cases who passed 2 years after starting of IGU.
Results: Baseline characteristics was as below. Mean age was 64.9 years old, %female was 74.2%, mean RA duration was 10.0 years and MTX was concomitant in 50.0% of cases. 82% of patients had factors influencing to prescribing IGU and intolerance of dose escalation of MTX was 1st reason (23.3%), old age over 80 years old was 2nd reason (16.7%) and economical reason was 3rd (14.2%) (Table1). Drug continuation rates were 71.1% at 1 year, 48.9% at 2 years and 43.1% at 3 years (Fig1). Time course of disease activity (baseline-6 months-1 year-2 year) was 3.6–3.0–3.0–3.0 in DAS28-CRP. In 15 cases in remission of DAS28-CRP at 2 years, 2 were classified with high disease activity and 9 were moderate disease activity at baseline (Fig2).

Table 1. Factors Influencing to Prescribing of Iguratimod (120 RA patients)

	Number of Cases	%
Intolerance of MTX doze escalation	28	23.3
Old age (over 80 years old)	20	16.7
Economical difficulties	17	14.2
Chronic Infection	13	10.8
Interstitial Pneumonia	13	10.8
Chronic Kidney Disease	12	10.0
Severe Lung Disease Except for Interstitial Pneumonia	10	8.3
Past History of Malignant Lymphoma or Lymphoproliferative Disease	9	7.5
Strong Anxiety for Side Effect of Biologics by Patients	7	5.8
Past History of Severe Adverse Event of Biologics	6	5.0
Treating Malignant Tumor	4	3.3
Others	1	0.8
Total	140*	

* There were RA patients who have 2 or more factors.

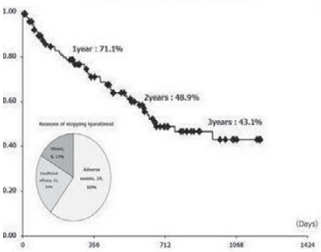


Fig1. Drug Continuation Rate of Iguratimod in 120 RA Patients (Kaplan-Meier method)

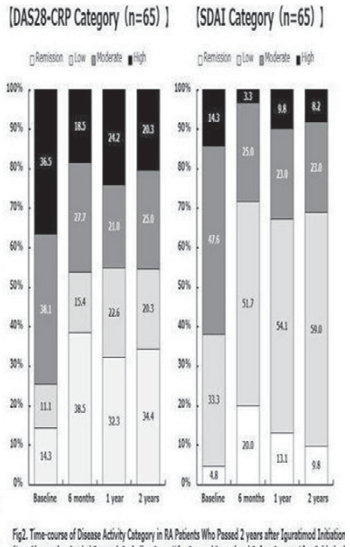


Fig2. Time-course of Disease Activity Category in RA Patients Who Passed 2 years after Iguratimod Initiation (Last Observation Carried Forward, Including Cases Who Stopped Iguratimod Before 2 years After Initiation)

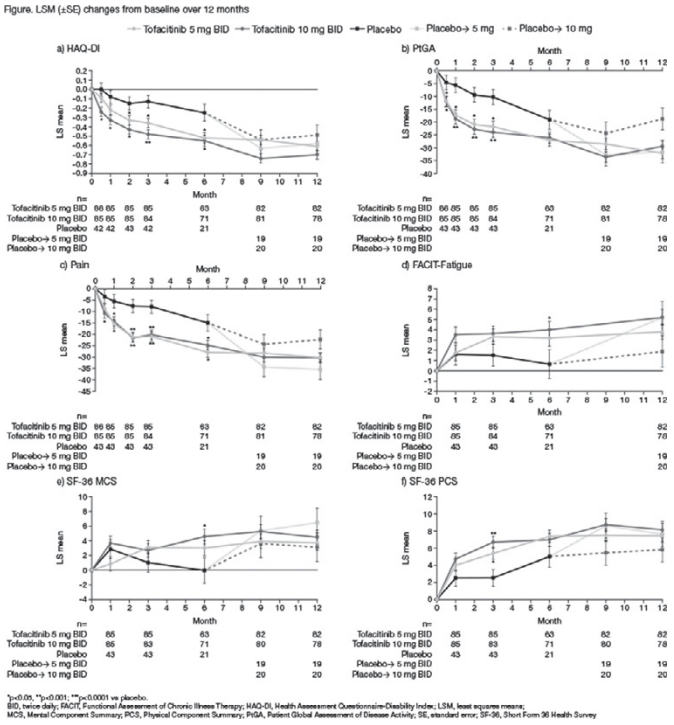
Conclusions: Efficacy of IGU in RA patients who had intolerance of MTX dose escalation or usage of biologics was observed. Although biological DMARDs is effective in RA patients, the cost is very expensive. IGU is comparative cheap (¥9,200/month) and suitable for RA patients with economical difficulties. As IGU decreased TNF-alpha production via inhibition of NF-kB, MTX+IGU may have similar mode of action with MTX+TNF inhibitor. Drug continuation rates were decreased over time and escape of efficacy may occur in some patients. Otherwise, IGU was very effective in some cases. Some of RA patients with high disease activity decreased disease activity greatly to remission state at 2 years after initiation of IGU.
References:
[1] Aikawa et al. Inflamm res. 51; 188–194 2002.
[2] Kohno et al. J Rheumatol. 28; 2591–2596 2001.
[3] Hara et al. Mod Rheumatol. 17; 1–9 2007.
[4] Ishiguro et al. Mod Rheumatol. 23; 430–439 2013.
[5] Yoshioka et al. Mod Rheumatol. 26; 169–174 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4852

THU0215 EFFECTS OF TOFACITINIB ON PATIENT-REPORTED OUTCOMES IN A PHASE 3 STUDY OF CHINESE PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND AN INADEQUATE RESPONSE TO DMARDS

Z. Li[1], Y. An[1], G. Li[2], L. Wang[3], K. Kwok[4], Q. Wu[2] on behalf of China ORAL group. *[1]Peking University People's Hospital; [2]Pfizer Inc, Beijing, China; [3]Pfizer Inc, Groton, CT; [4]Pfizer Inc, New York, NY, United States*

Background: Rheumatoid arthritis (RA) worsens patients' health-related quality of life.[1] Tofacitinib is an oral Janus kinase (JAK) inhibitor for the treatment of RA. Improvements in patient-reported outcomes (PROs) have been reported in the global population of Phase 3 tofacitinib trials.[2]
Objectives: To explore the effect of tofacitinib administered with conventional synthetic DMARDs (csDMARDs) on PROs in Chinese patients with RA and an inadequate response to DMARDs.
Methods: This was a post-hoc analysis of data from Chinese patients in the 12 month, double-blind Phase 3 study ORAL Sync (NCT00856544), with patients randomised 4:4:1:1 to tofacitinib 5 mg BID, tofacitinib 10 mg BID, placebo (PBO)→tofacitinib 5 mg BID or PBO→tofacitinib 10 mg BID, with csDMARDs. Non-responders (defined as those who did not achieve a 20% improvement in both of the swollen or tender joint counts) receiving PBO advanced blindly to tofacitinib at Month 3; all remaining PBO patients advanced to tofacitinib at Month 6. Least squares mean changes from baseline were reported for Health Assessment Questionnaire-Disability Index (HAQ-DI), patient assessment of arthritis pain (VAS), patient global assessment of disease activity (PtGA), Functional Assessment of Chronic Illness Therapy (FACIT) Fatigue scale, Short Form-36 Health Survey (SF-36), EuroQol five dimensions questionnaire (EQ-5D), and Work Limitations Questionnaire (WLQ), using a mixed-effects model for repeated measures. All patients receiving ≥1 dose of study treatment with ≥1 post-baseline assessment were included.
Results: Overall 216 patients were included (n=86, tofacitinib 5 mg BID; n=86, tofacitinib 10 mg BID; n=22, PBO→tofacitinib 5 mg BID; n=22, PBO→tofacitinib

10 mg BID). There were no major differences in demographics or baseline characteristics between treatment groups. At Month 3, tofacitinib resulted in significantly greater changes in HAQ-DI (5 mg BID, $p<0.05$; 10 mg BID, $p<0.001$), PtGA (5 mg BID, $p<0.05$; 10 mg BID, $p<0.001$), Pain (5 mg BID, $p<0.001$; 10 mg BID, $p<0.001$) and SF-36 Physical Component Summary (PCS) scores (5 mg BID, $p<0.05$; 10 mg BID, $p<0.001$) vs PBO (Figure). Numeric improvements in FACIT-Fatigue, SF-36 Mental Component Summary (MCS) [Figure] and EQ-5D health state profile (utility scores) were observed at Month 3 with tofacitinib vs PBO. There were no improvements in WLQ observed at Month 3 with tofacitinib vs PBO. Improvements were generally maintained at 6 and 12 months (Figure). The proportion of patients achieving HAQ-DI improvement $\geq$0.22 from baseline at Month 3 was significantly higher with tofacitinib vs PBO (5 mg BID, $p<0.05$; 10 mg BID, $p<0.05$).



*p<0.05, **p<0.001, ***p<0.0001 vs placebo.
BID, twice daily; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire-Disability Index; LSM, least squares means; MCS, Mental Component Summary; PCS, Physical Component Summary; PtGA, Patient Global Assessment of Disease Activity; SE, standard error; SF-36, Short Form 36 Health Survey

Conclusions: Tofacitinib 5 and 10 mg BID administered with csDMARDs significantly improved PROs including SF-36 PCS, PtGA, physical function and pain vs PBO. These improvements were maintained for up to 12 months in Chinese patients with RA.

References:

[1] Strand V, Khanna D. Clin Exp Rheumatol 2010; 28: S32-S40.
[2] Strand V et al. Arthritis Care Res (Hoboken) 2016. doi:10.1002/acr.23004.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by C Evans of CMC and was funded by Pfizer Inc.

Disclosure of Interest: Z. Li Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Y. An Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, G. Li Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Kwok Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Q. Wu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.2273

THURSDAY, 15 JUNE 2017

SLE, Sjögren's and APS - etiology, pathogenesis and animal models

THU0216 URINARY NEUROPILIN-1: A NEW BIOMARKER APPROACH IN THE PROGNOSIS OF LUPUS NEPHRITIS

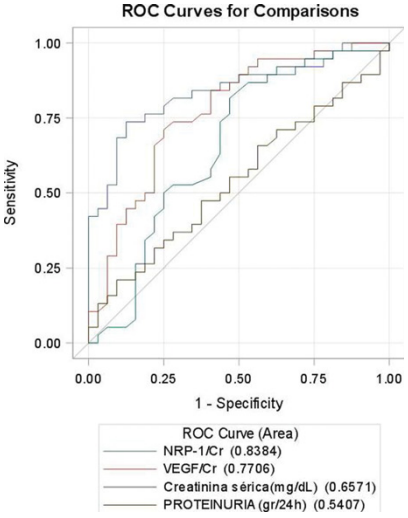
M. Torres-Salido[1], C. Solé-Marcé[1], M. Vidal[2], J. Cortés-Hernández[1], J. Ordi-Ros[1]. *[1]Vall Hebron Institute Research (Vhir); [2]Renal Pathology, Vall d'HEBRON Hospital, Barcelona, Spain*

Background: Lupus nephritis (LN) affects up to 50% of patients with SLE and is a major cause of morbidity, despite modern therapeutic approaches [1,2]. To date, renal biopsy is still the gold standard for diagnosing and classifying the degree of renal inflammation and scarring, but its invasiveness makes it unsuitable for serial monitoring. A novel biomarker to predict the evolution of renal inflammatory injury is still needed. Neuropilin-1 (NRP-1) has important functions in adult tissues, being involved in axonal guidance, vascular endothelial sprouting, regeneration and organ repair and immunosupression [3].

Objectives: Evaluate the protein and expression levels of NRP-1 at the time of the renal flare in patients with lupus nephritis and determine whether they could predict the disease progression.

Methods: Urine and serum of 70 patients with LN with nephrotic proteinuria, 25 patients with chronic non-lupus related nephopathy, and 25 healthy controls were analyzed by qPCR-RT and ELISA to determinate the levels of mRNA/protein of NRP-1. Immunohistochemistry of protein levels were done in renal biopsy (N=5). Urine and serum from 39 other patients with LN with nephrotic proteinuria were collected prospectively during two years.

Results: Increases in mRNA expression and protein concentration of NRP-1 were identified in urine samples of LN patients in flare compared with the different control groups. However, significant NRP-1 levels were found in LN patients that gone into remission compared with patients in non-remission after one year of treatment ($p<0.0001$). Urinary VEGFA, VEGFR1, VEGFR2 and SEMA3A mRNA and protein levels were also determinate. Results were confirmed with immunohistochemistry in renal biopsies (N=5). We observed a strong correlation with NRP-1 protein levels and VEGFA protein levels ($r=0.466$, $p<0.0001$). Areas under the receiver operating characteristic curve of urinary NRP-1 and VEGFA protein levels to distinguish between remission and non-remission patients were 0.8384 and 0.7706, respectively (Figure 1). In a prospective study (N=39), urinary protein NRP-1 and VEGFA levels decreased in LN patients going to complete remission; but no those with non-response that maintain their low levels during all the follow-up.



Conclusions: For first time, we demonstrate that urinary levels of NRP-1 might reflect the evolution of renal inflammatory injury and could be used as novel biomarker to predict the recovery of LN.

References:

[1] Cervera R, Khamashta MA, Font J, et al. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: a comparison of early and late manifestations in a cohort of 1,000 patients. Medicine (Baltimore) 2003;82:299–308.
[2] Baker KP, Edwards BM, Main SH, et al. Generation and characterization of LymphoStat-B, a human monoclonal antibody that antagonizes the bioactivities of B lymphocyte stimulator. Arthritis Rheum.2003;48:3253–65.
[3] Gagnon ML, Bielenberg DR, Grechtman Z, et al. Identification of a natural soluble neuropilin-1 that binds vascular endothelial growth factor: in vivo expression and antitumor activity. Proc Natl Acad Sci USA2000;97:2573–2578.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5729

THU0217 DNA METHYLATION ANALYSIS IN MULTIPLE CELLULAR COMPARTMENTS DEMONSTRATES A UNIVERSAL DNA METHYLATION INTERFERON SIGNATURE IN MULTIPLE CELLULAR COMPARTMENTS AND PREDOMINANT B-CELL HYPERMETHYLATION IN TWINS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C.J. Ulff-Møller[1,2], F. Asmar[3], Y. Liu[2], A.J. Svendsen[4], F. Busato[2], K. Grønbæk[3], J. Tost[2], S. Jacobsen[1]. *[1]Copenhagen Lupus and Vasculitis Clinic, Rigshospitalet, Copenhagen, Denmark; [2]Laboratory for Epigenetics and Environment, Centre National de Génotypage, CEA – Institut de Génomique, Evry, France; [3]Department of Haematology, Rigshospitalet, Copenhagen; [4]Epidemiology, Biostatistics and Biodemography, University of Southern Denmark, Odense, Denmark*

Background: Systemic lupus erythematosus (SLE) is a complex autoimmune

disease. High monozygotic twin discordance implies a role for non-genetic effects in disease pathogenesis. Previous epigenome-wide association studies (EWAS) have demonstrated a role for DNA methylation in SLE, but different immune cell subsets have so far been insufficiently characterised. The disease discordant twin model is a powerful design for detecting SLE-associated DNA methylation variation.

Objectives: To investigate genome-wide DNA methylation changes in sorted CD4+ T-cells, monocytes, granulocytes and B-cells from twin pairs with at least one SLE-affected twin.

Methods: Altogether 15 SLE twin pairs participated in the study, of which 6 pairs were monozygotic (MZ) and 9 were dizygotic (DZ), including 2 concordant pairs (1 MZ, 1 DZ). Disease activity was evaluated using the SLE disease activity index (SLEDAI). Peripheral blood was processed using gradient density centrifugation for the granulocyte fraction and the mononuclear cell fraction was sorted serially for CD14+ monocytes, CD4+ T-cells and B-cell enrichment using a RoboSep device (Stemcell Technologies). DNA was extracted using the DNA/RNA/miRNA Universal kit (Qiagen). Genome-wide DNA methylation was evaluated using the Infinium HumanMethylation450K BeadChip (Illumina). Paired analyses were performed using a Wilcoxon test with $p<0.01$ and median differential methylation $>7\%$ considered as statistically significant. Top differentially methylated genes were validated using pyrosequencing.

Results: In paired analyses of discordant SLE twins without restriction to probe category, we found 176, 510, 393 and 2882 differentially methylated CpGs in CD4+ T-cells, monocytes, granulocytes and B-cells, respectively. Restricted to the promoter and transcription start sites, there were 55, 327, 247 and 1628 genes in CD4+ T-cells, monocytes, granulocytes and B-cells with differentially methylated CpGs, respectively. In all cell types, there was a profound hypomethylation of interferon-regulated genes, including *IFI44L, DTX3L, PARP9* and *IFITM1*, which was more pronounced in twins with recent flare within the past 2 years. In contrast to the other cell types, hypermethylation was predominantly observed in B-cells. Using Ingenuity Pathway Analysis, the top upstream regulators of hypermethylated genes in B-cells were *TNF, miR-146a-5p* and *EP300*. Hypomethylation of CpGs was validated in all cell types at the genes *IFI44L, PARP9, IFITM1, LGALS3BP, LOXL1, MIR10A, PLSCR1* and *RSAD1*, in B-cells and granulocytes at *TACSTD2* and at *MIR146B* in B-cells. Hypermethylation of CpGs was validated in B-cells alone for *CXCR5, DDR1* and *TRAF5*.

Conclusions: Robust hypomethylation of interferon-regulated genes is common to all major cellular compartments in SLE twins. The finding of hypermethylated CpGs in B-cells is novel and might be of interest to SLE pathogenesis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6090

THU0218 CIRCULATING MICRORNAS AS BIOMARKERS FOR DIAGNOSIS AND TYPIFYING THE ATHEROTHROMBOTIC STATUS IN ANTIPHOSPHOLIPID SYNDROME

C. Perez-Sanchez[1], I. Arias-de la Rosa[1], M.A. Aguirre[1], P. Ruiz-Limon[1], N. Barbarroja[1], Y. Jimenez-Gomez[1], M.C. Abalos-aguilera[1], E. Collantes-Estevez[1], M. Teresa-Herranz[2], J. Lozano-Herrero[2], C. Martinez[2], R. Gonzalez-Conejero[2], M.J. Cuadrado[3], C. Lopez-Pedrera[1]. *[1]IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba; [2]IMIB-Arrixaca /University of Murcia/ Internal Medicine Service, Morales Meseguer Hospital, Murcia, Spain; [3]Lupus Research Unit and St. Thomas Hospital, London, United Kingdom*

Background: The course of antiphospholipid syndrome (APS) may rapidly progress from asymptomatic to severe manifestations. Thus, timely diagnosis is essential to improve accuracy of therapy. The role of circulating microRNAs (miRNAs) as potential biomarkers of disease has not yet been analysed in APS.

Objectives: To investigate the contribution of circulating miRNAs to the pathogenesis of APS and their potential role as non-invasive biomarkers of the disease.

Methods: Ninety APS patients and 42 healthy donors (HD) were included in the study. Clinical and inflammatory parameters were analysed. As a complement to standard clinical follow-up, the ankle-brachial index (ABI) and carotid intima-media thickness (CIMT) were determined. miRNA expression profiling was performed in plasma by PCR-Array, and the Ingenuity Pathways analysis software (IPA) was used to identify specific miRNAs and target proteins associated to the pathogenesis of APS. RT-PCR and ELISA/Bioplex of selected genes and proteins were used to validate microarray data. The diagnostic value of specific miRNAs signatures (ratios) as disease biomarkers was evaluated by ROC curves analysis. To assess the specificity of these signatures in APS, the expression of the selected miRNAs was analysed in plasma from 23 thrombotic patients without associated autoimmune disease. Monocytes isolated from HD and endothelial cells (ECs) were treated in vitro with antiphospholipid antibodies (aPL-IgGs) purified from the serum of APS patients, and the changes promoted on the levels of selected miRNAs and their potential targets were analysed.

Results: The PCR-Array identified 39 circulating miRNAs differentially expressed, including 19 up-regulated and 20 down-regulated in APS. IPA analysis recognized 11 miRNAs as potential modulators of target genes involved in the physiopathology of APS. Logistic Regression and ROC curve analyses identified a signature of 10 miRNA ratios as biomarkers for diagnosis of APS with great accuracy (AUC:0.81), along with 2 miRNA ratios as biomarkers for typifying the atherothrombotic status (pathologic CIMT) of APS (AUC:0.76). Patients with thrombosis but without associated autoimmune disease displayed a specific miRNA profile, distinct from that of APS patients. The miRNA signature was related to clinical features of APS such as the occurrence of foetal loss and the type of thrombosis suffered, and correlated with parameters linked to autoimmunity (aPL-IgG titers), inflammation, and thrombosis (ABI, ESR, TF, PAI-1, MCP-1, VEGF-A and VEGF-R1). In vitro treatment of monocytes and endothelial cells with aPL-IgG antibodies promoted a significant deregulation in the secreted levels of the selected miRNAs and atherothrombotic target proteins.

Conclusions: miRNA levels in the serum of APS patients -modulated by aPL-IgG antibodies- are potential novel biomarkers for diagnosis and typifying of their atherothrombotic status, thus constituting a useful tool in the prevention and management of the disease.

Acknowledgements: Supported by CTS794 and ISCIII (FIS15/1333 and RIER RD16/0012/0015).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4699

THU0219 AUTOANTIBODY PROFILE OF CHILDREN WITH JUVENILE DERMATOMYOSITIS FROM A TERTIARY CARE CENTRE IN NORTH INDIA

S. Guleria[1,1], A. Sharma, A. Gupta, A. Rawat, D. Suri, S. Singh. *Pediatric allergy and immunology, Pgimer Chandigarh, Chandigarh, India*

Background: Juvenile dermatomyositis (JDM) is a rare childhood autoimmune inflammatory muscle disorder that can result in severe disability or death. Children with JDM can have autoantibodies in their sera like other autoimmune diseases [1]. Over the last few years, few novel Myositis Specific Antibodies (MSA) have been identified. Some phenotypical associations have been described with these autoantibodies like anti p-140 (anti NXP2) has been shown to have correlation with calcinosis in children with JDM [1–2].

Objectives: To study autoantibody profile and to look for phenotypical associations of autoantibodies in JDMS.

Methods: Cross-sectional retrospective study. All children diagnosed to have JDM, registered from 1995 to 2015 in Pediatric Rheumatology Clinic at Post Graduate Institute of Medical Education and Research Chandigarh, India and who were tested for autoantibodies were included in the study. Clinical findings, antinuclear antibodies (ANA), autoantibody for MSA and myositis associated autoantibodies (MAA) were noted from the careful scrutiny of case records. Immunoglobulin G (IgG) antibodies against Jo1, threonyl-tRNA synthetase (PL7), alanyl-tRNA synthetase (PL12), glycyl-tRNA synthetase (EJ), Signal Recognition Particle (SRP), Mi-2, MDA-5, Transcriptional intermediary factor 1-γ (TIF-1γ), Ku, PMScl 100, Scl 70 and SSA/Ro 52 have been done by Immunodot. Evaluation for anti p-140 or Nuclear Matrix Protein (NXP2) and anti 200/100 or 3-Hydroxy-3-Methyglutaryl-Coenzyme (HMG CoA reductase) was done using ELISA.

Results: Antinuclear antibody (ANA) testing was done in 97 patients. Forty six (47.4%) tested positive. In addition, MSA and MAA were assessed. Anti-SRP antibodies were present in 4 (11.4%) children, anti-MDA5 in 3 (8.6%), anti-Mi2 in 1 (2.9%) and 1 patient tested positive for anti-SSA/Ro52 antibodies. All 4 children with anti-SRP were girls, had polycyclic course and 2 of them developed calcinosis. Patients with anti-MDA5 had predominant skin involvement, less severe muscle disease and followed a monocyclic course. Two of them had arthritis/arthralgia at the time of presentation. The only patient with anti-Mi2 had normal muscle strength/endurance at the time of follow up. None of the patients had anti synthetase antibodies (anti-Jo1, anti-PL-7, anti-PL-12, anti-EJ), anti-ku or anti-Scl-70. None of the subjects tested positive for anti-NXP2 or anti- HMG CoA.

Conclusions: Prevalence of autoantibodies in children with JDM in our study is similar to what has been described previously. Type of autoantibodies, though, is not similar. This may be due to ethnic differences of the population. Autoantibodies were tested in children while they were on treatment. This may have resulted in lower positivity. Evaluation of autoantibody profile at the time of diagnosis may assist in predicting the course of disease and response to treatment.

References:

[1] Targoff IN, Mamyrova G, Trieu EP, Perurena O, Koneru B, O'Hanlon TP, et al. A novel autoantibody to a 155-kd protein is associated with dermatomyositis. Arthritis Rheum 2006; 54: 3682–9.

[2] Gunawardena H, Wedderburn LR, Chinoy H, Betteridge ZE, North J, Ollier WER, et al. Autoantibodies to a 140-kd protein in juvenile dermatomyositis are associated with calcinosis. Arthritis Rheum 2009;60: 1807–14.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2954

THU0220 SELETALISIB, A NOVEL SELECTIVE PI3KΔ INHIBITOR WITH THERAPEUTIC POTENTIAL IN INFLAMMATION AND AUTOIMMUNITY

A. Payne, M. Juarez, G.I. Johnston, E. Helmer, M. Thomson. *UCB Pharma, Slough, United Kingdom*

Background: PI3Kδ is predominantly expressed in lymphocytes; the role it plays in immune disease has encouraged the development of inhibitors targeting

its kinase activity. Inhibitors of PI3Kδ have been approved or are in clinical development for the treatment of B cell malignancies; their therapeutic potential in inflammatory and autoimmune disease is being explored. Seletalisib is a selective and potent PI3Kδ inhibitor that has been profiled in preclinical and early clinical studies.
Objectives: To assess the therapeutic potential of seletalisib in inflammatory and autoimmune disease.
Methods: *In vitro* cell-based studies were performed on blood samples taken from healthy volunteers (HV) or from patients with primary Sjogren's Syndrome (pSS) and/or psoriasis. In addition, samples were analysed from a single ascending dose study in HV (NCT02207595) and a multiple ascending dose study in HV and psoriasis patients (NCT02303509). T and B cell responses in the presence and absence of seletalisib were assessed by flow cytometry or a Meso-Scale discovery assay (Meso-Scale Diagnostics, MD, USA), following activation of the T cell- or B cell-receptor by receptor cross-linking or via stimulation with specific antigens. The functional selectivity of seletalisib was assessed in the BioMap system (DiscoverX, CA, USA). Translational studies used flow cytometry and/or immunofluorescence to demonstrate the presence of active PI3K signalling in diseased tissue, through expression of phosphorylated-AKT (pAKT) or -ribosomal protein S6 (pS6). The effect of seletalisib on PI3K signalling was determined by phospho-flow cytometry. Target engagement was determined through measurement of basophil degranulation in healthy subjects, and assessment of lesion severity score in skin biopsies from patients with psoriasis that were treated with seletalisib.
Results: Preclinical studies showed seletalisib potently inhibited T cell differentiation and function (IC_{50} range: 2–31 nM). Further, it blocked activation and proliferation of B cells (IC_{50} range: 16–49 nM). When profiled in a wide range of primary cell assay systems, including fibroblasts, epithelial, endothelial and vascular smooth muscle cells, seletalisib showed significant activity only in those systems containing lymphocytes, demonstrating its functional selectivity towards PI3Kδ-expressing cells. Expression of the PI3K pathway in lymphocytes was shown at the site of disease in clinical samples both from patients with psoriasis and pSS. Seletalisib inhibited PI3K signalling, measured by a reduction in pAKT and pS6 expression, in T cells derived from patients with psoriasis.
In first-in-man studies, mean seletalisib plasma concentration-time profiles increased with increasing dose after single and multiple dosing, with no major deviations from dose proportionality. There was no unexpected accumulation or loss of exposure after multiple dosing (time-independent pharmacokinetic (PK) profile) and apparent $t_{1/2}$ values (approx. 20h) were supportive of once-daily dosing. Inhibition of basophil degranulation in healthy subjects and effects on the cellular composition in lesional skin biopsies from patients with psoriasis, provided indications of target engagement, following treatment with seletalisib.
Conclusions: Seletalisib is a potent, selective PI3Kδ inhibitor with an attractive preclinical and human PK profile; clinical studies are ongoing.
Disclosure of Interest: A. Payne Shareholder of: UCB Pharma, Employee of: UCB Pharma, M. Juarez Shareholder of: UCB Pharma, Employee of: UCB Pharma, G. Johnston Shareholder of: UCB Pharma, Employee of: UCB Pharma, E. Helmer Shareholder of: UCB Pharma, Employee of: UCB Pharma, M. Thomson Shareholder of: UCB Pharma, Employee of: UCB Pharma
DOI: 10.1136/annrheumdis-2017-eular.5132

THU0221 DOWNREGULATED EXPRESSION OF MIR200B-5P IN MINOR SALIVARY GLANDS (MSG) OF PATIENTS WITH SJÖGREN'S SYNDROME (SS) ASSOCIATED LYMPHOMA

E.K. Kapsogeorgou, A. Papageorgiou, M. Voulgarelis, A.G. Tzioufas.
Pathophysiology, School of Medicine, National and Kapodistrian University of Athens, ATHENS, Greece

Background: The miRNAs of the miR-200 family are critical regulators of oncogene and tumor suppressor genes. Preliminary data from a limited number of patients with SS-associated lymphoma suggested that the expression of miR200b-5p in MSGs may be downregulated in lymphoma.
Objectives: To validate whether low miR200b-5p MSG-levels are associated with SS-related lymphomas and if they are deregulated before lymphoma development, suggesting a possible prognostic value.
Methods: miR200b-5p expression was analyzed by quantitative real-time PCR in total RNA from MSG tissues obtained from 77 SS patients and 9 patients with non-SS sialadenitis associated with sarcoidosis, HCV infection (4 each) or HBV (1 that was also diagnosed with MALT lymphoma). with chronic sialadenitis associated with sarcoidosis, HCV (4-each) or HBV infection (1 who was also diagnosed with MALT-lymphoma). SS-patients included 28 that did not develop lymphoma during follow-up (without lymphoma; median follow-up time since biopsy performance, range: 6yrs, 1–12.75yrs), 18 that developed lymphoma in the future (prelymphoma; median follow-up time till lymphoma diagnosis, range: 3.59yrs, 0.42–8.5yrs, 15-MALT, 2-NMZL, 1-DLCBL) and 32 with SS-associated lymphoma at the time of biopsy (lymphoma; 25-MALT, 2-NMZL, 2-DLCBL, 1-BALT, 1-LP and 1-SLL). In 15 cases, we had sequential MSG-samples from prelymphoma patients who transitioned to lymphoma (12-MALT, 2-NMZL, 1-DLCBL).
Results: Tukey's multiple comparison revealed that miR200b-5p levels were significantly down-regulated in MSG tissues of prelymphoma and lymphoma SS-patients (mean relative expression±SE: 0.37±0.10 and 0.26±0.06, respectively) compared to SS-patients without lymphoma (0.67±0.07; $p \leq 0.05$ and $p \leq 0.0001$ for pre- and lymphoma, respectively) or non-SS sialadenitis (0.85±0.28, $p \leq 0.05$ and $p \leq 0.01$, respectively). Interestingly, low miR200b-5p levels were detected in HBV patient that had MALT lymphoma (0.17). The expression of miR200b-5p was not found to differ between patients with SS without lymphoma and non-SS sialadenitis, or SS-associated pre-lymphoma and lymphoma. The analysis of the 15 cases of SS patients that had sequential samples before and on lymphoma diagnosis revealed that miR200b-5p levels do not significantly change over transition to lymphoma. The miR200b-5p expression levels were negatively correlated with the biopsy focus score (r:-0.6550, $p < 0.0001$), whereas they were not associated with the site or the number of involved sites, the type or the stage of lymphoma.
Conclusions: The significantly low levels of miR200b-5p in MSG tissues of patients with SS-associated prelymphomas and lymphomas suggest that miR200b-5p deregulation is implicated in SS-lymphomagenesis. The downregulation of miR200b-5p in prelymphoma samples and the lack of change over transition to lymphoma suggest that it can serve as a prognostic marker for future lymphoma development. The prognostic value of miR200b-5p in SS-associated lymphomas, the expressing cell types and affected molecular pathways are under investigation.
Acknowledgements: Funded by the Hellenic College of Rheumatology
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6708

THU0222 PROPHYLACTIC AND THERAPEUTIC ADMINISTRATION OF AN ANTI-CD40 ANTAGONIST ANTIBODY BLOCKS AND REVERSES PROTEINURIA AND NEPHRITIS IN NZB/W-F1 MICE

S. Perper, S. Westmoreland, Z. Liu, M. Duval, J. Seagal, B. McRae, S. Clarke.
Abbvie, Worcester, United States

Background: The CD40-CD40L pathway is a potential target for the treatment of autoimmune diseases, as CD40 is a costimulatory receptor on antigen presenting cells (APCs) critical for the induction and maintenance of an immune response through binding CD40L on T cells. In the absence of CD40, both humoral and cellular responses to foreign antigens are severely impaired. In particular, disruption of this pathway prevents the development of disease in lupus-prone mice.
Objectives: The objective of this work is to evaluate whether prophylactic and therapeutic treatment with an antagonistic anti-CD40 antibody prevents and reverses nephritis and other manifestations of lupus in lupus-prone mice.
Methods: NZB/W-F_1 mice were i.p. administered anti-CD40 prophylactically or therapeutically at various doses once or twice per week. Prophylactic treatment of NZB/W-F_1 mice began at 26 weeks of age and continued for 9 weeks, while therapeutic treatment was initiated in NZB/W-F_1 mice after they developed severe proteinuria (urine protein $\geq$300 mg/dL). Proteinuria was monitored weekly by urinalysis, and at study termination blood and spleen cells were analyzed by flow cytometry. Additionally, histological analysis of kidney, spleen, and salivary glands were performed, as well as gene transcription analysis of the kidney by microarray.
Results: As expected, prophylactic and therapeutic administration reduced the number of splenic germinal center (GC) B cells and T follicular helper cells (Tfh). Prophylactic treatment blocked development of proteinuria and extended survival in NZB/W-F_1 mice. Significantly, therapeutic anti-CD40 treatment reversed established, severe proteinuria in NZB/W-F_1 mice and extended their survival. In agreement, the kidneys and salivary glands of treated mice exhibited reduced inflammation compared to control mice, and the kidneys exhibited lower CD40, IFN-I and chemokine gene signatures compared to controls. Interestingly, anti-CD40 decreased expression of genes in kidney belonging to the "hepatic fibrosis" pathway, possibly explaining the improvement of kidney function.
Conclusions: Anti-CD40 treatment prevents the onset and reverses ongoing nephritis and sialadenitis in NZB/W-F_1 mice. Resolution of ongoing nephritis results in restoration of low or normal urine protein levels. Thus, treatment with an antagonistic anti-CD40 is a strong candidate for clinical study in SLE.
Disclosure of Interest: S. Perper Employee of: Abbvie, S. Westmoreland Employee of: Abbvie, Z. Liu Employee of: Abbvie, M. Duval Employee of: Abbvie, J. Seagal Employee of: Abbvie, B. McRae Employee of: Abbvie, S. Clarke Employee of: Abbvie
DOI: 10.1136/annrheumdis-2017-eular.1583

THU0223 ELEVATED MTORC1 SIGNATURE IN B CELLS FROM SJÖGREN'S SYNDROME PATIENTS CORRELATES WITH B CELL HYPERACTIVITY THAT IS ABROGATED BY MTOR INHIBITION: A NOVEL THERAPEUTIC STRATEGY TO HALT B CELL HYPERACTIVITY IN PSS?

S.L. Blokland[1,2], M.R. Hillen[1,2], C.G. Kommer-Wichers[1,2], A.A. Kruize[1], J.C. Broen[1,2], J.A. van Roon[1,2], T.R. Radstake[1,2]. *[1]Rheumatology & Clinical Immunology; [2]Laboratory of Translational Immunology, UMC Utrecht, Utrecht, Netherlands*

Background: A hallmark feature of primary Sjögren's syndrome (pSS) is B cell hyperactivity, including presence of autoantibodies, aberrant presence of B cells and plasma cells in the salivary glands, elevated serum IgG levels and increased risk of lymphoma development. The mTOR pathway is essential for cell growth,

survival and proliferation of B cells and mTOR inhibition has been shown to be effective in immune B cell suppression in transplant patients and in treatment of B cell lymphomas. Interestingly, in a pSS mouse model mTOR targeting inhibited lymphocytic infiltration in the lacrimal gland. However, mTOR activation in B cells has not been studied in pSS patients.
Objectives: To study the mTOR pathway in B cells of pSS patients as a potential therapeutic target to inhibit B cell hyperactivity.
Methods: Expression of mTOR pathway genes (MTOR, RPTOR, RICTOR, DEPTOR, AKT1, IGF1R, IGF1, PTEN) were assessed on an OpenArray platform in purified peripheral blood B cells and monocytes from pSS patients (n=12), non-Sjögren's sicca patients (n=17) and healthy controls (HC, n=9). Correlations with clinical parameters including lymphocytic focus score, ESSDAI and serum IgG levels were assessed. Flow cytometry analysis for B cell subset distribution was performed to assess potential effects of B cell subset distribution on gene expression differences. Culture experiments were performed to study inhibition of the mTORC1 pathway (phosphorylated S6, kinase activity downstream of mTORC1) in association with inhibition of B cell proliferation and IgG production by mTOR inhibition.
Results: RPTOR and IGF1R expression were significantly increased in B cells from pSS patients (p=0.019 and p=0.018, respectively) and correlated with serum IgG levels (r=0.429, p=0.020, and r=0.462, p=0.012). Differences in expression of mTOR pathway genes were not found in monocytes. To indicate the mTOR signature a cumulative mTORC1 score was calculated consisting of Z scores (AKT1 + IGF1R + IGF1 + RPTOR + MTOR – PTEN – DEPTOR) which was significantly elevated in pSS (p=0.027), correlating with serum IgG levels (r=0.463, p=0.011). Frequencies of memory and naïve B cells did not differ between pSS patients and HC in this cohort (p=0.415). Activation of B cells in culture resulted in phosphorylation of S6, which indicates increased mTORC1 activity, in accordance with B cell proliferation and IgG production in both HC and pSS patients. Inhibition of mTOR by rapamycin decreased pS6 (n=4, n=2 HC, n=2 pSS, MFI 1400±335 vs 935±306, p=0.060), strongly reduced B cell proliferation (n=6, n=3 HC, n=3 pSS, 80.8±9.9 vs 19.1±15.8%, $p<0.001$), reduced IgG+ B cells (n=6, n=3 HC, n=3 pSS 39.5±15.5 vs 11.1±5.7%, p=0.001) and decreased IgG production (n=4, n=2 HC, n=2 pSS, 160±180 pg/mL vs 25.3±13.0 pg/mL p=0.060).
Conclusions: Presence of an mTORC1 signature in B cells from pSS patients correlating with B cell hyperactivity indicates a role for mTORC1 in B cell activation in this disease. The fact that B cell proliferation and IgG production is effectively inhibited by rapamycin suggests that mTOR inhibition represents a potential therapeutic strategy for pSS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1616

THU0224 ASSOCIATION OF IRAK-M WITH NEUROPSYCHIATRIC SYMPTOMS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

S. Sacre, R. Thwaites, K. Davies. *Brighton and Sussex Medical School, University of Sussex, Brighton, United Kingdom*

Background: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease, where a breakdown in immune tolerance leads to sustained inflammation and tissue damage. Patients exhibit multi-organ involvement with a diverse range of symptoms that include arthritis, nephritis, neuropsychiatric events and dermatological complaints. Interleukin-1 receptor-associated kinase M (IRAK-M), a negative regulator of toll-like receptor (TLR) signalling has previously been associated with SLE in a murine study [1]. Deficiency of IRAK-M was observed to exacerbated disease in a SLE model in C57BL/6-lpr/lpr mice [2].
Objectives: This study aimed to investigate the expression of IRAK-M in monocytes from SLE patients compared with healthy control donors and measure downstream cytokine production upon TLR stimulation.
Methods: The study was approved by the Brighton East Research Ethics Committee and the *National Research Ethics Service* Committee North West – Lancaster. Whole venous blood was collected from 39 SLE patients and 19 healthy donors. Peripheral blood mononuclear cells were purified from whole blood after which monocytes were isolated using $CD14^+$ selection beads. Expression of IRAK-M was determined relative to the geometric mean of the housekeeping genes glyceraldehyde 3-phosphate dehydrogenase and hypoxanthine phosphoribosyltransferase 1 by quantitative polymerase chain reaction. Cultured monocytes were stimulated with TLR ligands. Cytokine production was measured by enzyme-linked immunosorbent assay.
Results: IRAK-M expression was increased in the SLE patient group, however many of the patients did not show elevated expression compared to healthy donors. When stratified by disease symptoms, a clear correlation was observed between low expression of IRAK-M and neuropsychiatric symptoms which was not evident when evaluating other SLE symptoms. Interestingly, TLR activation led to elevated cytokine production in SLE patient monocytes that correlated with the basal level of IRAK-M expression in individual donors. Further investigation revealed that SLE monocytes demonstrated a reduced upregulation of IRAK-M after TLR activation compared to healthy donors.
Conclusions: Increased expression of IRAK-M was not unexpected in the SLE group due to the systemic inflammatory nature of the disease. However, not all patients presented with increased levels of IRAK-M and upon activation were less able to upregulate IRAK-M compared to healthy donors, suggesting a reduced capacity to resolve inflammation. This was reflected in the elevated cytokine production observed from SLE monocytes. Thus, low expression of IRAK-M in SLE monocytes is linked to elevated inflammatory cytokine production and may be a biomarker for neuropsychiatric symptoms in SLE patients.
References:
[1] Kobayashi, K., et al. Cell, 2002. 110(2): p. 191–202.
[2] Lech, M., et al. Ann Rheum Dis, 2011. 70(12): p. 2207–17.
Acknowledgements: Study funded by Brighton and Sussex Medical School.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6201

THU0225 ROLE OF THE IL-12/IL-35 BALANCE IN SJÖGREN'S SYNDROME

O. Fogel[1], E. Rivière[2], R. Seror[2], G. Nocturne[2], S. Boudaoud[3], B. Ly[3], J.-E. Gottenberg[4], V. Le Guern[1], J.-J. Dubost[5], J. Nititham[6], K. Taylor[6], P. Chanson[2], P. Dieudé[7], L. Criswell[6], C. Miceli[1], X. Mariette[2]. *[1]Hopital Cochin; [2]Hopital Bicêtre; [3]Inserm UMR1184, Paris; [4]Hopital de Hautepierre, Strasbourg; [5]Hopital Montpied, Clermont-Ferrand, France; [6]UCSF, San Francisco, United States; [7]Hopital Bichat, Paris, France*

Background: An interferon (IFN) signature is involved in the pathogenesis of primary Sjögren's syndrome (pSS), but whether the signature is type 1 or 2 remains controversial. Mouse models and genetic studies suggested the involvement of T helper 1 and type 2 IFN pathways. Likewise, polymorphisms of interleukin 12A gene (*IL-12A*), which encodes for IL-12p35, have been associated with pSS. IL-12p35 subunit is shared by 2 heterodimers, IL-12 and IL-35.
Objectives: To confirm the genetic association of *IL-12A* polymorphism and pSS and elucidate the involvement of the IL-12/IL-35 balance in pSS by functional studies.
Methods: The genetic study involved 673 patients with pSS from 2 French pSS cohorts and 585 healthy French controls. Functional studies were performed on sorted monocytes, stimulated or not. IL-12A mRNA and IL-12 and IL-35 protein levels were assessed by qRT-PCR and by ELISA and a multiplex kit for IL-35 and IL-12, respectively.
Results: We confirmed the association of the *IL-12A* rs485497 polymorphism and pSS and found an increased serum protein level of IL-12p70 in pSS patients carrying the risk allele (p=0.016). Serum level of IL-12p70 was greater in patients than controls (p=0.0001), especially patients with more active disease (p=0.05); conversely IL-35 level was decreased in patients (p=0.0001) especially in patients with a more active disease (p=0.05).
Conclusions: Our findings emphasize the involvement of the IL-12/IL-35 balance in the pathogenesis of pSS. Serum IL-35 level was associated with low disease activity, in contrast to serum IL-12p70 level, which was rather associated with a more active disease.
Acknowledgements: We thank Dr Odile Devergne (Université Paris Descartes, AP-HP, Hôpital Necker, Paris) for her expertise on the IL-35 ELISA kit to ensure the quality and reproducibility of this test.
The authors thank the following investigators of the ASSESS cohort prospective cohort of patients with Sjögren's syndrome (all in France) who recruited the patients and conducted follow-up: A. L. Fauchais (Limoges), S. Rist (Orleans), V. Le Guern (Paris), G. Hayem (Paris), J. Sibilia (Strasbourg), J. Morel (Montpellier), A. Saraux (Brest), A. Perdriger (Rennes), X. Puechal (Le Mans), E Hachulla (Lille) and V. Goeb (Rouen).
The authors thank Dr J. Benessiano, S Tubiana and all staff members of the Bichat Hospital Biological Resource Center (Paris) for their help in centralizing and managing biologic data collection from the French ASSESS,
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3586

THU0226 DIFFERENTIAL SUSCEPTIBILITY OF TH17 AND T REGULATORY CELLS TO APOPTOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS – THE MODULATORY EFFECTS OF STATIN

J. Sun, J. Frostegard, A. Liu. *Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden*

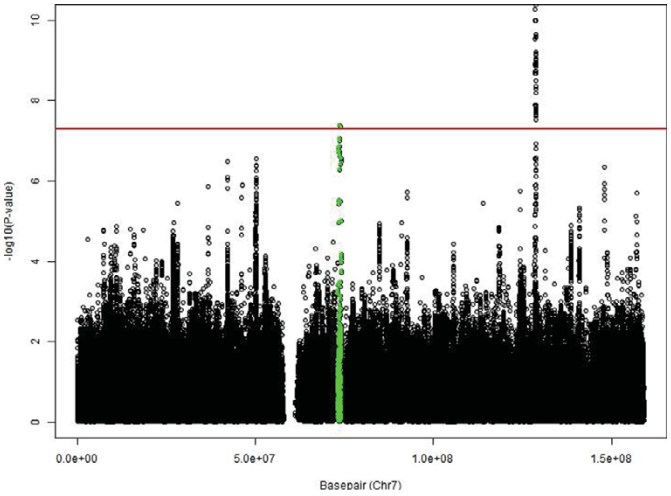
Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder. Patients with SLE have accelerated cardiovascular disease. Recent studies show there are more Th17 while less T regulatory (Treg) cells in the SLE patients. Th17/Treg imbalance may contribute to the pathogenesis of SLE.
Objectives: To investigate the underlying mechanisms of Th17/Treg imbalance, we test the proportion and susceptibility of Th17 and Treg to apoptosis, and the modulatory effects of statin in the SLE patients.
Methods: Totally 17 SLE patients and 20 gender- and age-matched control subjects were enrolled for this study. Peripheral blood mononuclear cells were isolated, either analyzed ex vivo, or cultured in the conditions to induce Th17 and/or Treg polarization. The proportion of Th17/Treg cells and frequency responding to apoptosis were analyzed by multiple color flow cytometry. Cytokines in cell culture supernatants and plasma were tested by ELISA. T cell polarization-related transcription factors were detected by quantitative real time PCR.
Results: The proportion of Th17 ($CD4^+IL17^+$) cells were higher in SLE patients,

both in ex vivo and in the Th17-polarizing cultures. While the frequencies of Treg ($CD4^+CD25^+CD127^{dim/-}$) cells were lower in the corresponding populations. Higher levels of IL17 and IL6 were detected in plasma of SLE patients. Responding to CD95-induced apoptosis the frequency of $CD4^+IL17^+$ cells from SLE patients was substantially lower, but that of $CD4^+CD25^+CD127^{dim/-}$ cells from Treg-polarizing cultures was considerably higher. With treatment of atorvastatin, $CD4^+IL17^+$ cell population in cultures derived from SLE patients showed an increased susceptibility to CD95-induced apoptosis. However, the $CD4^+CD25^+CD127^{dim/-}$ cell population had reduced response to apoptosis. Accordingly, the ratio of transcription factor RORC/FoxP3 decreased in T cell cultures of SLE patients.
Conclusions: Th17 cells were more resistant than Treg cells to CD95-induced apoptosis in SLE as compared to control subjects. Statins counteracted the dysregulated susceptibility of SLE T cells to apoptosis. Our findings reveal a novel mechanism underlying the imbalance of Th17/Treg and show a potential interest to the treatment of the patients with SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6193

THU0227 GENOME-WIDE ASSOCIATION META-ANALYSIS IDENTIFIES FIVE NEW LOCI FOR SYSTEMIC LUPUS ERYTHEMATOSUS

A. Julià[1], P. Carreira[2], R. Blanco[3], F.J. López-Longo[4], J.J. Pérez-Venegas[5], A. Olivé[6], J.L. Andreu[7], M.A. Aguirre-Zamorano[8], P. Vela[9], J.M. Nolla[10], J.L. Marenco de la Fuente[11], A. Zea[12], J.M. Pego[13], M. Freire[14], E. Díez[15], M. López-Lasanta[1], M. López-Corbeto[1], N. Palau[1], R. Tortosa[1], E. Trallero[1], A. Aterido[1], D. Absher[16], R.M. Myers[17], A. Fernandez-Nebro[18], S. Marsal[1].
[1]Grup de Recerca de Reumatologia, Vall Hebron Research Institute, Barcelona; [2]Rheumatology Department, Hospital Universitario 12 de Octubre, Madrid; [3]Rheumatology Department, Hospital Universitario Marqués de Valdecilla, Santander; [4]Rheumatology Department, Hospital Universitario Gregorio Marañón, Madrid; [5]Rheumatology Department, Hospital del SAS de Jerez de la Frontera, Cádiz; [6]Rheumatology Department, Hospital Universitari Germans Trias i Pujol, Badalona; [7]Rheumatology Department, Hospital Universitario Puerta de Hierro, Madrid; [8]Rheumatology Department, Hospital Universitario Reina Sofía, Córdoba; [9]Rheumatology Department, Hospital General Universitario de Alicante, Alicante; [10]Rheumatology Department, Hospital Universitari de Bellvitge, Barcelona; [11]Rheumatology Department, Hospital de Valme, Sevilla; [12]Rheumatology Department, Hospital Universitario Ramón y Cajal, Madrid; [13]Rheumatology Department, Hospital do Meixoeiro, Vigo; [14]Rheumatology Department, Hospital Universitario A Coruña, A Coruña; [15]Rheumatology Department, Hospital Complejo Asistencial Universitario de León, León, Spain; [16]Absher Lab; [17]Myers Lab, HudsonAlpha Institute for Biotechnology, Huntsville, United States; [18]Rheumatology Department, Hospital Regional Universitario de Málaga, Málaga, Spain

Background: Recent genome-wide association studies (GWAS) have identified more than 50 loci associated with systemic lupus erythematosus but they explain less than 30% of the heritability of the disease. Meta-analysis including new populations can contribute to identify additional genetic risk factors.
Objectives: The aim of the presents study was to identify additional genetic risk loci for SLE.
Methods: We performed a meta-analysis using data from a recent large scale GWAS from 4,036 cases and 6,959 controls from Caucasian European ancestry [1] and a newly genotyped cohort of 907 SLE patients and 1,524healthy controls from Spain. Genetic association was tested at the single-marker level using linear regression and at the pathway-level using Fisher's modified method.
Results: Combining the two cohorts we identified genome-wide significant association ($P<5E-8$) at five new loci: three SNPs at intragenic regions and two intergenic loci at chromosomes *7q11.23* (Manhattan plot for chromosome 7 is shown in Figure; new SLE risk region SNPs highlighted in green) and *17q21.31*.



Several of the new associated genes are functionally associated with B cell regulation. After multiple test correction, *B Cell Receptor signaling*, *Biopeptides* and *Cell surface interactions at the vascular wall* pathways were also significantly associated with SLE risk.
Conclusions: In conclusion, we have identified five new risk loci for SLE through a meta-analysis including a new GWAS.
References:
[1] Bentham J, Morris DL et al. Nature Genetics 2015.
Acknowledgements: We would like to thank the clinical researchers and patients participating in the IMID Consortium for their collaboration. We would also like to thank the international SLE consortium for access to the data.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2854

THU0228 INTRA-RENAL ACTIVATION OF ADAPTIVE IMMUNE EFFECTORS IS ASSOCIATED WITH HIGHER DISEASE SEVERITY IN LUPUS NEPHRITIS

C. Pamfil[1], N. Demoulin[2], M. Jadoul[2], S. Aydin[3], F.A. Houssiau[1,4], B. Lauwerys[1,4]. *[1]Pôle de pathologies rhumatismales systémiques et inflammatoires, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain; [2]Department of Nephrology; [3]Department of Pathology; [4]Department of Rheumatology, Cliniques universitaires Saint-Luc, Brussels, Belgium*

Background: Chronic renal impairment remains a feared complication of lupus nephritis (LN). Yet, little is known about mechanisms and markers of disease severity in the lupus kidney.
Methods: We performed high-throughput transcriptomic studies (Illumina HumanHT12 v4 Expression Beadchips) on archived (- 80 degrees) kidney biopsies from 32 SLE patients and 8 controls (pre-transplant donors). Unsupervized clustering and differential gene expression studies were performed using GeneSpring software. Pathway analyses were carried on using DAVID and GSEA. Clinical and biological data were retrieved from the patients' medical records. Immunohistochemistry experiments (CD3, CD20, CD21) were performed on the same samples, and on an additional cohort of 37 SLE kidney biopsies. Syndecan-1 (SDC1) was used as a marker of renal tubular cell response to stress.
Results: Compared to controls, LN samples overexpressed transcripts involved in interferon signature, apoptosis, chemokines, antigen presentation, T and B cell activation.
Unsupervized clustering studies isolated 14 SLE samples based on their gene expression features. These samples were characterized by a significantly lower estimated GFR at the time of biopsy (T0) (50.7 versus 97.4 ml/min/1.72m^2), but also at follow-up (49.1 versus 85.8 ml/min/1.72m^2) compared to the other SLE samples. Yet, apparent renal disease duration at T0, disease duration at last follow-up (median 91.5 versus 86 months), double-stranded DNA antibody titers at T0 and other relevant characteristics (histological scores, proteinuria, numbers of subsequent flares) were not different between both groups.
From a transcriptomic point of view, these 14 samples were characterized by the overexpression of transcripts and pathways involved in adaptive immune responses: antigen presentation, T cell differentiation and B cell activation.
Immunohistochemistry studies confirmed a significant association between the presence of CD3 and CD20 positive cells in the interstitial space and lower estimated GFR at baseline in the same, but also in an independent set of samples. The presence of CD3 and CD20 positive cells was also associated with lower SDC1 expression on renal tubular cells. Low SDC1 expression on renal tubular cells was strongly associated with impaired kidney function at baseline.
Conclusions: LN kidney biopsy samples from patients with lower estimated GFR are characterized by the overexpression of transcripts pointing to the activation of a local antigen-dependent immune response. Activation of "second wave" immune effectors in the LN kidney is a known feature of the disease, and impacts kidney function through alterations in the function of renal tubular cells.
Acknowledgements: *The research leading to these results has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n°115565, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007–2013) and EFPIA companies' in kind contribution*
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3427

THU0229 DNA HYPOMETHYLATION AND DECREASED HYDROXYMETHYLATION IS ASSOCIATED WITH DECREASED ANTIOXIDANT RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS

E. Grau Garcia[1], C.M. Feced Olmos[1], M. Fernandez Matilla[2], E. Labrador Sánchez[1], F.M. Ortiz-Sanjuan[1], N. Fernández-Llanio[2], K. Arévalo Ruales[1], R. Negueroles Albuixech[1], J. Ivorra Cortes[1], J.J. Fragio Gil[1], I. Martínez Cordellat[1], R. González Mazarío[1], I. Chalmeta Verdejo[1], L. Gonzalez Puig[1], C. Alcañiz Escandell[1], C. Nájera Herranz[1], I. Cánovas Olmos[1], E. Vicens Bernabeu[1], J.E. Oller Rodriguez[1], J.A. Castellano Cuesta[2], V. Fornés Ferrer[3], D. Hervás Marín[3], L. Olivares González[4], R. Rodrigo Nicolás[4], J.A. Román Ivorra[1]. *[1]Rheumatology Department, HUP la Fe; [2]Rheumatology Section, Hospital Arnau de Vilanova; [3]Biostatistics Unit; [4]Molecular, Cellular and Genomic Biomedicine, IIS la Fe, Valencia, Spain*

Background: Systemic lupus erythematous (SLE) shows increased DNA demethylation. An intermediate step to DNA demethylation is the DNA hydroxymethylation, where 5-mC is oxidized into 5-hmC. Hydroxymethylation is not completely understood and it may be related to oxidative stress in SLE patient.
Objectives: To analyze the association between the hydroxymethylation and demethylation, with the antioxidant response and SLE pathophysiology.
Methods: We analyzed in 142 SLE patients and 34 healthy controls the serum concentration of glutathione (GSH) and glutathione disulphide (GSSG) by UPLC-MS/MS, superoxide dismutase (SOD) and total antioxidant capacity (TAC) by colorimetric methods. 5-mC and 5-hmC levels were measured by colorimetric methods. Complete blood-test was made and clinical data by personal interview was collected. Biostatistical analysis with R (3.3.2.) was performed.
Results: There is a correlation between the methylation and hydroxymethylation rate ($P<0.001$), and both were lower in patients than in controls (P=0.024; $P<0.001$). GSH and GSSG values were lower in patients (P=0.033 y P=0.003), but GSH/GSSG ratio was not statistically different in both groups. SOD levels were higher in patients (P=0.001), but TAC did not show significant differences. Higher demethylation is associated to lower TAC values in patients and healthy controls (P=0.005; P=0.01). In patients, decreased SOD values are associated with higher demethylation and lower hydroxymethylation rates ($P<0.001$; P=0.007). SOD and TAC levels are increased in SLE patients with higher demethylation and lower hydroxymethylation (P=0.001; $P<0.001$). We did not observe any association between 5-mC or 5-hmC levels and GSH, GSSG or GSH/GSSG ratio. Higher demethylation is associated to vascular symptoms (defined by RELESSER study) and lupus anticoagulant (AL) positivity (P=0.041; P=0.015), and lower hydroxymethylation to mucocutaneous damage (defined by RELESSER study) and AL positivity (P=0.015; P=0.009). Lower levels of GSH and GSSG were associated to increased accumulated damage assessed by SLICC (P=0.01; P=0.005), and lower SOD values with longer disease duration (P=0.001).
Conclusions: We observed higher demethylation and lower hydroxymethylation in SLE patients than in controls, related to increased SOD activity. Moreover higher demethylation leads to lower TAC levels. These epigenetic disorders are related to antioxidant response disruptions in SLE patients, probably because of the chronic inflammatory condition. Our results suggest that epigenetic processes are involved in SLE physiopathology.
Acknowledgements: Financial support by GVA (GV15/83) is acknowledged.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2905

THU0230 HIF1A (RS11549465) AND AKNA (RS10817595) GENE POLYMORPHISMS ARE ASSOCIATED WITH PRIMARY SJÖGREN'S SYNDROME

G. Hernandez-Molina[1], J.M. Rodríguez-Pérez[2], J. Fernández-Torres[3], G. Lima[1], N. Pérez-Hernández[2], A. López-Reyes[3], G.A. Martínez-Nava[3]. *[1]Immunology and Rheumatology, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran; [2]Department of Molecular Biology, Instituto Nacional de Cardiologia; [3]Synovial Fluid Laboratory, Instituto de Rehabilitacion, Mexico City, Mexico*

Background: HIF-1α is the main transcriptional regulator of cellular and developmental response to hypoxia, and also participates in the integration of the T cell receptor and cytokine receptor-mediated signals of CD4+ helper cells. Another transcription factor also involved in the immune responses is the AT-hook transcription factor (AKNA).
Objectives: To evaluate the allele and genotype frequencies of polymorphic sites of *HIF1A* and *ANKA* genes in primary Sjögren's syndrome (pSS).
Methods: We included 110 patients with pSS and 141 ethnically matched healthy controls. Three *HIF1A* gene polymorphisms *(Pro582Ser, Ala588Thr, and C191T) and two AKNA genes polymorphism (-1372C>A, and Pro624Leu*) were genotyped using TaqMan probes in a Real-Time PCR instrument. Associations between pSS and genotypes, alleles and inheritance models of the SNPs of interest were evaluated by logistic regression adjusted by age and gender.
Results: Most of the patients were females (95.4%), median age 55 years and median disease duration of 7.8 years. The *C/T* genotype and the *T* allele of the *HIF1A Pro582Ser* polymorphism protected against pSS (OR=0.22; 95% CI=0.09–0.52; $P<0.01$; and OR=0.26; 95% CI=0.12–0.58; $P<0.01$; respectively). Whereas under a recessive model adjusted by age and gender, the *AKNA -1372C>A* polymorphism A/A genotype was associated with an increased risk of pSS (OR=2.60; 95% CI=1.11–6.12; *P*=0.03). Parotid enlargement was associated with the *HIF1A* gene polymorphism (rs11549465), conferring protection for the C/T genotype vs. C/C (OR=0.22; 95% CI 0.05–0.90, *P*=0.03). The allele T of the same polymorphism was also associated with parotid enlargement (OR=0.24, 95% CI=0.65–0.95; *P*=0.04). We did not find any association with any other clinical or serological feature.
Conclusions: We identified *HIF1A Pro582Ser T* allele and *C/T* genotype as well as *AKNA -1372C>A* polymorphism A/A genotype as genetic factors associated with pSS. Further studies in other populations are needed to validate our findings and to shed some light on their functional implications.
References:
[1] Palazon A, Goldrath A, Nizet V, Johnson R. HIF transcription factors, inflammation and immunity. Immunity 2014; 41:518–28.
[2] Sims-Mourtada JC, Bruce S, McKeller MR, et al. The human AKNA gene expresses multiple transcripts and protein isoforms as a result of alternative promoter usage, splicing, and polyadenylation. DNA Cell Biol 2005;24:325–38.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2406

THU0231 IL-17 POLARIZATION OF MAIT CELLS DERIVE FROM THE ACTIVATION OF TWO DIFFERENT PATHWAYS

G. Guggino[1], F. Ciccia[2], M. Lo Pizzo[2], D. Di Liberto[2], L. Saieva[2], P. Ruscitti[2], P. Cipriani[3], G. Sireci[2], R. Alessandro[2], F. Dieli[2], R. Giacomelli[3], G. Triolo[2]. *[1]DIBIMIS; [2]University of Palermo, palermo; [3]University of L'Aquila, L'Aquila, Italy*

Background: Primary Sjogren Syndrome (pSS) is a chronic inflammatory disorder affecting exocrine glands. Both IL-23 and the downstream cytokines IL-17 and IL-22 are recognised as key players in the disease. Therefore, the identification of the cellular sources and inducers of IL-17 is crucial in the understanding of the drivers of inflammation in pSS. Mucosal-associated invariant T (MAIT) cells recognize riboflavin derivatives presented by the MHC class I-like molecule MR1.
Objectives: Recently, MAIT cells have been implicated in the pathogenesis of autoimmune disorders and found expanded in salivary glands of pSS patients. Their expression of IL7R and IL23R, makes them potential contributors to the pathogenesis of pSS.
Methods: Mononuclear cells from 16 patients with pSS and 14 subjects with non Sjogren Syndrome secca syndrome (nSS) were isolated from blood and salivary glands. We assessed the phenotype and cytokine expression of MAIT cells by surface and intracellular flow cytometry analysis. The function of MAIT cells was assessed upon *in vitro* stimulation with recombinant IL-7, IL-23 or their specific ligand lumazine (a Vitamin B2 precursor previously reported to be recognized by and specifically activate MAIT cells).
Results: MAIT cells were reduced in frequency in peripheral blood but not in minor salivary glands of patients with pSS, compared with nSS. *In vitro* stimulation of MAIT cells from pSS patients induced cytokine production which was dependent on priming with IL-7, IL-23 or specific antigen (lumazine) stimulation. Particularly, IL-7 and IL-23 guarantee IL-17 polarization of MAIT cells by two different pathways via the activation of STAT3 or RORc respectively.
Conclusions: This study confirms a potential role for MAIT cells in pSS and, for the first time, links IL-7 and IL-23 to the IL-17 polarization of MAIT cells in these patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5885

THU0232 INHIBITING THE ACTIVATION OF COMPLEMENT C5 BY MESENCHYMAL STEM CELLS IN THE TREATMENT OF LUPUS NEPHRITIS

H.-J. Ma[1,2], C. Liu[1], Z.-Y. Zhang[1], R.-H. Feng[1], W.-C. Li[1], L.-Y. Sun[1]. *[1]Department of Rheumatology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing; [2]Department of Rheumatology, The First Affiliated Hospital of Xinxiang Medical University, Weihui, China*

Background: Excess activation of the complement system is involved in the development and progression of systemic lupus erythematosus (SLE). Allogeneic umbilical cord mesenchymal stem cells (UC-MSC) transplantation has achieved good clinical efficacy for refractory SLE, however, the exact mechanism is unclear. Our previous work found that deposits of C5a and C5b-9 were significantly enhanced in severe lupus nephritis (LN), which suggested that antagonists of C5 might contribute to the treatment of LN, in other words, effective therapy for LN may be involved in inhibiting the activation of C5.
Objectives: To observe the clinical effect of UC-MSC on SLE model mice (B6.lpr), and explore the mechanism of MSC inhibiting the activation of complement C5 in lupus mice.
Methods: 26-week-old female B6.lpr mice were randomly allocated in four groups, which were given the following treatments, CTX (200mg/kg), UC-MSC ($1x10^6$), C5aRa (W-54011, 1mg/kg), and an equal volume of 0.5%DMSO. 24 hours urine and peripheral blood were collected periodically. All mice were sacrificed at 40 weeks of age.Urine protein to creatinine ratio was used to estimate daily urine protein excretion. Plasma creatinine was measured by a biochemical analyzer. Plasma levels of C3, C5a, soluble C5b-9, and anti-dsDNA

antibody were determined by ELISA. Histopathological evaluation of renal lesions was undertaken by HE, PAS, PASM and Masson staining under light microscopy. Podocyte foot processes were assayed by the transmission electron microscopy. Depositions of C5a, C5b-9, and MBL were detected by immunohistochemistry assay. Immunofluorescence was utilized to detect the expression of C5aR1, IgG, IgM, IgA, C3, C1q, and properdin in the glomeruli.

Results: At the end point, proteinuria of mice in the former three groups was significantly reduced when compared with the control mice, and renal function was also improved in both MSCT and CTX groups. Plasma level of C3 was significantly elevated in mice of MSCT and C5aRA groups. Furthermore, mice in MSCT group appeared a remarkably decreased C5a in the circulation. Compared to control mice, no significant difference was found in plasma levels of anti-dsDNA and SC5b-9, although there were decline trends in other three groups. Pathological analysis showed that the proliferation of glomerular cells and foot process fusion were significantly inhibited in MSCT treated mice. Immunohistochemistry showed that deposits of C5a and C5b-9 were significantly decreased in the MSCT group. Immunofluorescence examination showed that the expression of IgG, C3, C1q, and properdin was significantly decreased in MSCT treated mice, meanwhile, the expression of MBL was also significantly reduced in these mice.

Conclusions: The activation of the complement system was obviously involved in the glomerulonephritis in lupus mice. Allogeneic UC-MSC transplantation can effectively improve the clinical outcome of lupus mice. Possible mechanism of MSCT might be related to inhibit the activation of complement C5 in the circulation and local kidney via interrupting the classical, alternative, and lectin pathways. The potential involved contributors of UC-MSC are currently under study.

References:

[1] Vignesh P, et al. Clin Chim Acta. 2016.

Disclosure of Interest: None declared

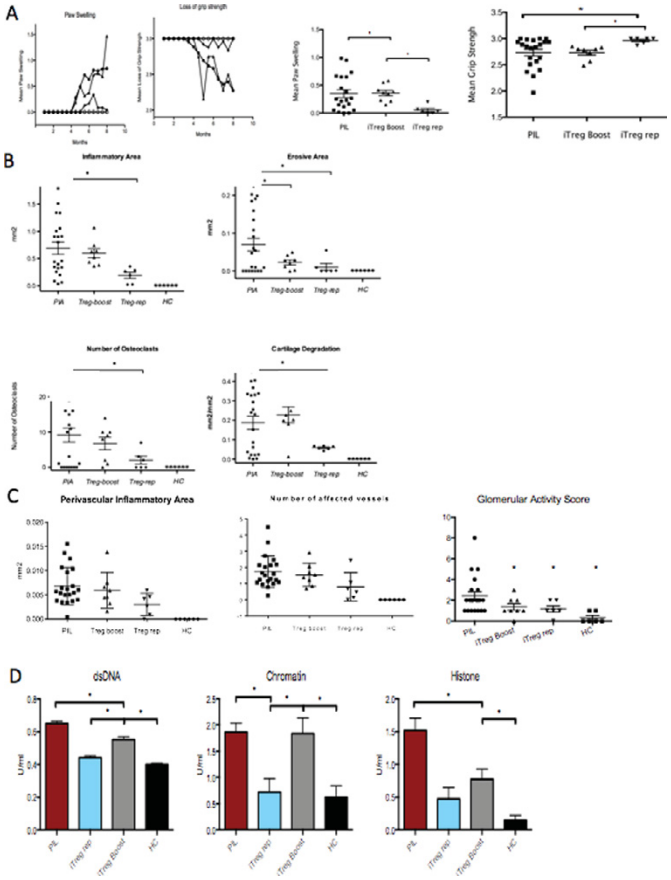
DOI: 10.1136/annrheumdis-2017-eular.2559

THU0233 IN VITRO INDUCED REGULATORY T-CELLS CAN AMELIORATE SEVERITY OF PRISTANE INDUCED LUPUS (PIL)

H. Leiss, B. Jacobs, I. Gessl, A. Puchner, J. Smolen, G. Stummvoll.
Rheumatology, Medical University Vienna, Vienna, Austria

Background: Pristane induced lupus (PIL) is a well-established murine model for environmentally induced systemic lupus erythematosus (SLE). Mice develop specific autoantibodies and show symptoms of SLE including arthritis, diffuse proliferative immune complex glomerulonephritis and haemorrhagic pulmonary capillaritis.

Objectives: To investigate the therapeutic effects of in vitro -induced regulatory T cells (iTreg) in the murine model of PIL.



Methods: BALB/c mice were injected i.p. with either 0.5ml of pristane (PIL) or PBS (controls). Naive $CD4^+$ thymocytes were sorted and cultured and cell suspensions with >80% of $CD4^+FoxP3^+$ cells (iTreg) were injected intravenously (i) once when PIL was induced ($5x10^6$ iTreg (iTreg-single)) or (ii) every 4 weeks ($1x10^6$ iTreg, iTreg-rep). Animals were monitored for paw swelling and grip strength. After 8 months histological analysis evaluated for cartilage degradation, number of osteoclasts and the extent of inflammation and bone erosion. Glomerulonephritis and pneumonitis were quantified using the kidney biopsy score and a newly adapted histomorphometric image analysis system; inflammatory tissue was further analyzed by tissue cytometry. Serum levels of anti-dsDNA, anti-histone and anti-chromatin antibodies were measured by ELISA.

Results: Monthly injections of $1x10^6$ iTreg reduced the clinical as well as the histological severity of PIL-arthritis, seen by a higher mean grip strength (2.96±0.02 vs. 2.73±0.06, $p<0.01$), less mean paw swelling (0.04±0.02 vs. 0.36±0.07, $p<0.01$) and retardation of the symptom onset (Figure A). 62% of PIL-mice and 33% of iTreg-rep mice had erosive arthritis. There was a significant reduction of arthritis severity in all histological parameters (inflammatory area in mm^2 0.19±0.06 vs. 0.69±0.11; erosive area in mm^2 0.01±0.01 vs. 0.07±0.02; number of osteoclasts 2±1.13 vs. 9.14±2; cartilage degradation in mm^2 0.06±0.01 vs. 0.19±0.03, all $p<0.01$, Figure B). The single boost of $5x10^6$ iTreg could not prevent joint manifestations. However, a slight retardation in "loss of grip strength" and a significantly less erosive area was observed. In regards to the cellular composition of the inflammatory tissue in paws, a significantly increased relative amount of CD4+Foxp3+ cells was seen in the iTreg-rep group compared to the PIL group (in % 5.2±2.3 vs. 0.6±0.2, $p<0.01$).

Repeatedly injected mice (iTreg-rep) had significant less pulmonary involvement (perivascular inflammatory area in mm^2/mm^2 lung area 0,003±0,001 vs. 0,007±0,001, $p<0.01$) and renal disease (glomerular activity score 1,17±0,31 vs. 2,43±0,39, $p<0.05$) compared to PIL (Figure C). Corresponding, iTreg-rep mice had significantly lower serum levels of disease-associated auto-antibodies (Figure D).

Conclusions: Repeated injections of iTreg ameliorate the clinical and histological severity of PIL- manifestations. A single boost of iTreg at the time of disease induction does not prevent manifestations, but retards the onset of symptoms. Thus iTreg have significant positive effects on PIL, which may have consequences for future approaches in treating SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3020

THU0234 EPIGENETIC CELL COUNTING: A NOVEL TOOL TO QUANTIFY IMMUNE CELLS IN SALIVARY GLANDS DETECTS ROBUST CORRELATIONS OF TFH CELLS WITH IMMUNOPATHOLOGY

J.A. van Roon[1,2], F.M. Moret[1,2], S.L. Blokland[1,2], A.A. Kruize[2], G. Bouma[3], A. van Maurik[3], S. Olek[4], U. Hoffmueller[4], T.R. Radstake[1,2]. *[1]Laboratory of Translational Immunology; [2]Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands; [3]Immunoinflammation TAU, GlaxoSmithKline, Stevenage, United Kingdom; [4]Epiontis GmbH, Berlin, Germany*

Background: Histological analysis of salivary glands for decades has been a valuable tool in the characterization of patients with primary Sjögren's syndrome (pSS) and non-Sjögren's sicca (nSS) patients. Importantly, it has helped in understanding the immunopathology of sicca patients. Nonetheless, standardization of histological assessments, e.g. to quantify lymphocytic foci or germinal centers is lacking, contributing to improper classification of disease and assessment of risk of lymphoma for example. Also, detailed and reproducible quantification of the heterogeneity of inflammatory cells and their contribution to immunopathology is lacking. Recent progress in epigenetics has revealed that cell-specific DNA methylation profiles can be applied to reliably quantify numbers of cells in blood and tissues.

Objectives: To investigate whether epigenetic cell counting can serve as a novel reliable tool to quantify immune cells in salivary glands of sicca patients.

Methods: DNA was isolated from frozen tissue sections of 13 nSS, 12 probable SS, 29 pSS and 7 overlap SS patients. Bisulfite conversion of demethylated DNA sites was followed by cell specific qPCR that was used to calculate the percentage of cell subsets related to the total number of cells quantified by housekeeping gene expression. Percentages of epigenetically counted cells were correlated to gene expression generated by RNA-Seq analysis of matched salivary gland tissue and histological and clinical parameters (LFS, %IgA+ plasma cells, serum IgG, SSA positivity).

Results: Strongly increased percentages of epigenetically quantified percentages of CD3, CD4, CD8, B cells, T follicular helper (Tfh) cells and Treg cells in pSS vs nSS patients were observed (all $p<0.001$, CD8 $p<0.01$). These inflammatory cell types all strongly correlated with LFS (all at least $p<0.001$, CD8 $p=0.014$), local B cell hyperactivity (% IgA+ cells, all $p<0.001$, except CD8 $p=0.06$ and B cells, $p=0.127$) and systemic B cell hyperactivity (all at least $p<0.01$, except CD8 $p=0.051$). Th17 cells were not significantly different between nSS and pSS patients. Only CD8 T cells were significantly increased in probable SS patients as compared to nSS patients ($p<0.05$). Percentages of CD3 and B cells positively correlated with CD3 and CD19 RNA expression ($r=0.608$, $p<0.0001$; $r=0.597$, $p<0.0001$, resp.). Interestingly, percentages of Tfh cells correlated with CXCL13 ($r=0.789$, $p<0.0001$), IL7R, CXCR5 and ICOS RNA expression (all $p\leq0.001$) and were strongly associated with autoimmunity (SSA positivity, $p<0.001$).

Conclusions: Epigenetic cell counting is a promising novel tool to reproducibly and easily quantify immune cells in the (inflamed) labial salivary gland of sicca patients with relatively low amount of tissue needed (<1 mm^3). Considering the potential of this technique to include a huge number of (cell-specific) biomarkers we believe this opens up new standardized ways for salivary gland analysis with high relevance for patient classification, understanding of immunopathology and clinical trials.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4933

THU0235 EXOSOME-DELIVERED MIR-146A REGULATES SENESCENCE OF BONE MARROW- MESENCHYMAL STEM CELLS FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS THROUGH TARGETING IRAK1 AND TRAF6

J. Ji, Y. Wu, X. Kong, Z. Zhang, Z. Gu[1,1]. *Department of Rheumatology, Affiliated Hospital of Nantong University, Nantong, China*

Background: Exosomes are membrane nano-vesicles secreted by a multitude of cells that harbor biological constituents such as proteins, lipids, mRNA and microRNA. Recent study suggests that microRNAs can be transferred between cells and mediate target gene repression. Our research group revealed the senescence of bone marrow-mesenchymal stem cells from systemic lupus erythematosus patients,which participated in the development of SLE. However, the relationship between senescence of MSCs and miRNAs remains unclear.
Objectives: In this study, we investigated whether exosomes act as intercellular messengers delivering microRNA that modulate the senescence of BM-MSCs from SLE patients and its possible mechanism.
Methods: Tewelve female SLE patients and healthy subjects were enrolled in the study. All patients were females, and their age distribution was similar to that of the cases. Serum were collected from these persons. All BM-MSCs were Isolated by density gradient centrifugation. Serum-derived exosomes were extracted by Total Exosome Isolation reagent and confirmed by transmission electron microscope and western blot. The internalization of exosomes was detected by immunofluorescence. QRT-PCR was used to distinguish the difference of expression of miR-146a in exosomes between normal group and SLE group. Different exosomes stimulated normal BM-MSCs, then detecting expression of miR146a by qRT-PCR, detecting expression of IRAK1 and TRAF6 by WB, observing the activity of β-gal of cells, the changes of cytoskeletal structure by F-actin staining and the distribution of cell cycle by flow cytometry. We used miRNA mimics and miRNA inhibitor to interfere the expression of miR-146a.
Results: Serum-derived exosomes could be taken up by BM-MSCs through the plasma membrane due to treatment of BM-MSCs with exosomes. After stimulation of exosomes in normal MSCs, miR146a was decreased, but, IRAK1 and TRAF6 was activated. And, the cell volume and the number of SA-β-gal positive in SLE BM-MSCs was increased. The organization of cytoskeleton was neatly disordered. The rate of cell proliferation was decreased. The miR-146a mimics in SLE BM-MSCs can significantly reverse the senescence.
Conclusions: Exosomes-delivered miR-146a in the serum of SLE patients can promote the senescence of BM-MSCs through targeting IRAK1 and TRAF6. Exosomes play an important role in the pathogenesis of SLE.
Acknowledgements: This research was supported by grants from the National Natural Science Foundation of China (81471603).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6033

THU0236 ANTIBODIES TOWARDS ATP-BINDING CASSETTE TRANSPORTER ABCA1: A NEW MECHANISM FOR ATHEROSCLEROSIS IN SLE?

M. Fernandes Das Neves[1,2], J.R. Batuca[3], F. Batista[2], C. Favas[2], H. Célia[2], J. Delgado Alves[2]. *[1]CEDOC - Chronic Disease Research Center, NOVA Medical School/Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon; [2]Medicine IV, Professor Doutor Fernando Fonseca Hospital, Amadora; [3]CEDOC - Chronic Disease Research Center, NOVA Medical School/Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon, Portugal*

Background: Systemic Lupus Erythematosus (SLE) is considered an independent risk factor for cardiovascular disease and patients with SLE have an increased burden of atherosclerotic vascular disease[1]. High-density lipoproteins (HDL) are the plasma lipoproteins responsible for reverse cholesterol transport[2]. HDL protective effect on cardiovascular disease is attributed to the cholesterol efflux capacity as well as to its anti-oxidant and anti-inflammatory properties[3]. Dyslipidemia is frequent amongst patients with SLE, characteristically with low HDL levels.
ATP-binding cassette transporter ABCA1, also known as the cholesterol efflux regulator protein, is a ubiquitous cholesterol transporter that is highly expressed in macrophages. Its main function is to donate cholesterol to apolipoprotein A-I (ApoA-I) in lipid-poor HDL particles. As such, ABCA1 closely influences HDL levels and its role in atherosclerosis has been increasingly studied[4].
Objectives: This study was undertaken to determine if antibodies against ABCA1 can be detected in patients with SLE through enzyme-linked immunosorbent assay (ELISA).
Methods: Patients with SLE were divided in two groups: group A, with low damage (based on less than 4 SLICC criteria), and group B, with high damage (based on the presence of at least 4 SLICC criteria). Groups A and B were compared with a control group. 48 patients were enrolled (13 in group A and 35 in group B), and 18 age and gender-matched healthy controls were included in the control group. IgG anti-ABCA1 and anti-HDL antibodies were assessed by home-made ELISAs, using commercially available ABCA1 synthetic peptide and HDL from healthy donors.
Results: There were no differences between group A and the control group. Group B had higher titers of anti-ABCA1 antibodies when compared with group A (p=0.016) and the control group (p=0.022). For positivity we considered values superior to 3 standard deviations above the mean of healthy controls. Four patients showed positive anti-ABCA1 titers (11.4%).
Conclusions: This is the first time that naturally occurring antibodies against ABCA1 are detected by ELISA. These antibodies are increased in patients with SLE that have higher damage, measured by SLICC classification criteria. Future studies will determine their pathogenic role and the potential use of a standardized ELISA to detect anti-ABCA1 antibodies in clinical practice.
References:
[1] Stojan G, Petri M. Atherosclerosis in systemic lupus erythematosus. J Cardiovasc Pharmacol. 2013; 62(3):255–262.
[2] Lewis GF, Rader DJ. New insights into the regulation of HDL metabolism and reverse cholesterol transport. Circ Res. 2005;96:1221–1232.
[3] Navab M, Yu R, Gharavi N, et al. High-density lipoprotein: antioxidant and anti-inflammatory properties. Curr Atheroscler Rep. 2007;9(3):244–8.
[4] Soumian S, Albrecht C, Davies AH, Gibbs RGJ. ABCA1 and atherosclerosis. Vasc Med. 2005; 10:109–119.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7013

THU0237 WHOLE TRANSCRIPTOME ANALYSIS OF APL TREATED HUVECS MAPS PROINFLAMMATORY AND PROCOAGULANT PATHWAYS

M.D. Patsouras[1], S. Foutadakis[2], E. Alexopoulou[2], M. Agelopoulos[2], D. Thanos[2], A.G. Tzioufas[1], P.G. Vlachoyiannopoulos[1]. *[1]Department of Pathophysiology, Medical School National Kapodistrian University; [2]Biomedical Research Foundation Academy, Athens, Greece*

Background: Antiphospholipid syndrome is an autoimmune thrombophillia characterized by recurrent thromboembolism and or pregrancy morbidity in the presence of antiphospholipid antibodies (aPL). β2GPI which is the major autoantigen in the syndrome forms complexes with anti-B2GPI autoantibodies that activate platelets, monocytes and endothelial cells. Previous studies have shown that anti-β2GPI-β2GPI complexes activate TLR4 and TLR6 on endothelial cells leading to NFκB, MAPK activation and Tissue Factor and proinflammatory cytokine expression.[1,2]
Objectives: To evaluate the whole transcriptome of endothelial cells that have been stimulated with aPL-B2GPI complexes.
Methods: Human umbilical Vein Endothelial cells (HUVECs) were isolated from 2 APS patients and 4 Healthy control women upon delivery. Healthy donor HUVEC were stimulated with IgG isolated from APS patients with high aPL titers and healthy individuals in the presence of B2GPI. Consequently total mRNA was isolated, cDNA libraries were created and whole transcriptome sequencing (RNASeq) was performed. Gene expression data were validated in protein levels with immunohistochemistry in placenta tissues from APS patients and healthy individuals.
Results: Whole transcriptome analysis of HUVECs stimulated with aPL-β2GPI complexes and IgG from healthy individuals revealed 680 differentially expressed genes, among which 377 were upregulated and 303 downregulated in the aPL stimulated endothelial cells. Characteristic examples of the upregulated genes are IL-6, IL-8, VCAM1, SELE and TGFB2 and TGFBR1. Bioinformatics analysis revealed that the upregulated genes belong mainly to the cytokine-cytokine receptor interaction (hsa053323), MAPK signaling pathway (hsa04010), TNF signaling pathway (hsa04668) and NOD-like receptor pathway (hsa04621). Characteristic examples of the downregulated genes include the CBX4, CBX8, BCOR and HDAC7 genes. Interestingly some of the proteins encoded by these genes play role in the epigenetic modification of DNA. Immunohistochemical staining on placenta biopsies from APS patients and healthy individuals for IL-6, IL-8, IL-18, NFkB, TF, TNF-a, E-SELECTIN, MAPK8, TGFB2 and TGFBR1 showed increased intensity in the signal of endothelial cells on APS specimens validating thus the RNASeq results in the tissues.
Conclusions: RNASeq of endothelial cells treated with aPL and B2GPI reveals a thoroughly analysed proinflamatory and procoagulant phenotype. Moreover differential expression of DNA modifying proteins suggests the possible epigenetic regulation of gene expression on endothelial cells in APS syndrome. Ongoing experiments aim to analyze histone acetylation and methylation status of the promoters of the selected genes that were shown to be differentially expressed.
References:
[1] Pierangeli SS, Vega-Ostertag ME, Gonzalez EB. New targeted therapies for treatment of thrombosis in antiphospholipid syndrome. Expert reviews in molecular medicine. 2007;9(30):1–15.
[2] Vega-Ostertag M, Casper K, Swerlick R, Ferrara D, Harris EN, Pierangeli

SS. Involvement of p38 MAPK in the up-regulation of tissue factor on endothelial cells by antiphospholipid antibodies. Arthritis and rheumatism. 2005;52(5):1545–54.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5880

THU0238 P-GLYCOPROTEIN MONOCLONAL ANTIBODY IMPROVES LUPUS-LIKE SYNDROME IN MRL/LPR MICE

M. Wang, P. Zeng, G. Zhou, J. Lv, Q. Wang. *Department of Rheumatology and Immunology, Peking University Shenzhen Hospital, Shenzhen, Guangdong 518036, CHINA., Shenzhen, China*

Background: Preventing steroid resistance and maintaining disease control are significant challenges to overcome in treating SLE patients[1]. P-glycoprotein (P-gp) of membrane transporters, a product of the multiple drug resistance (MDR)-1 gene, is known to play a pivotal role in the acquisition of drug resistance to chemotherapy in autoimmune diseases[2].Inhibition of P-gp could overcome such drug resistance[3,4]. So we observed the effect of P-gp monoclonal antibody on MRL/lpr lupus mice.

Objectives: To investigate the efficacy of P-glycoprotein monoclonal antibody in the treatment of the MRL/lpr mice.

Methods: Twenty four 14- week- old MRL/lpr female mice were divided into 3groups:group 1 (G1)were treated with P-glycoprotein monoclonal through caudal vein, group 2 (G2)were treated with P-glycoprotein monoclonal three times and group 0 (G0)were treated with 0.5ml normal saline as controls. Twenty-four hours proteinuria and body weight were assessed every two weeks.Enzyme linked immunosorbent assay (ELISA)was used to measure the levels of serum anti-dsDNA antibodies. The histopathology changes of the kidneys were observed.

Results: From the 22th week,the body weight of groups Gl and G2 increased significantly than that of the group G0 ($p<0.05$). At the 22th weeks,the 24 hours proteinuria in group Gl (1.9±1.1)mg and G2 (1.4±0.9)mg was decreased than that in group G0 (3.1+1.9)mg ($p<0.05$), and at the 26th weeks,that of groups G1 (2.4±1.4)mg and G2 (1.8±1.1)mg was also significantly decreased than in group G0 (5.3±2.2)mg ($p<0.01$). At week 26,serum creatinine decreased significantly in both groups G1 (7.0±2.9)umol/L and G2 (6.1±2.5)umol/L than in group G0 (12.7±1.3)umol/L ($p<0.05$). One week after treatment, the levels of anti-dsDNA antibodies in group Gl (43±19)x10^2 U/ml and G2 (45±32)x10^2 U/ml were both significantly decreased than those of the group G0 (87±39)x10^2 U/ml ($p<0.05$),and at the 26th weeks the difference between group G2 (35±11)xl0^2 U/ml and G0 (59±35)x10^2 U/ml was statistically significant. The nephron crescent formation in group G1 (0.11±0.05)and G2 (0.09±0.01)was significandy lower that of the group G0 (0.23±0.07) ($p<0.05$), and that of group G2 was significantly less that of group Gl ($p<0.05$).

Conclusions: P-glycoprotein monoclonal antibody is very effective in treating MRL/lpr mice.It is safe and free of rejection reactions.

Table 1. Effects of P-gp monoclonal antibody on the levels of anti-dsDNA antibodies, serum creatinine and the routine blood test of MRL/lpr mice ('X±s)

Group	Number	ds-DNA ($\times10^2$U/ml)	Scr (μmol/ml)	WBC ($\times10^9$/L)	HB (g/L)	PLT ($\times10^9$/L)
G1	8	48±19	8.3±2.4*	7.8±3.6*	124±8	118±97*
G2	8	35±11#	6.1±3.5#	5.9±4.2#	138±13	132±85#
G0	8	59±35	13.2±.8	3.1±2.9	110±11	76±61

Notes: *G1 vs G0 $p<0.05$, #G2 vs G0 $p<0.05$.

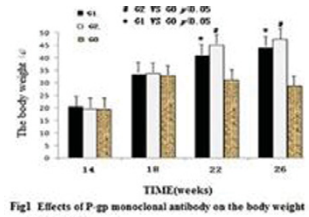


Fig1 Effects of P-gp monoclonal antibody on the body weight of MRL/lpr mice

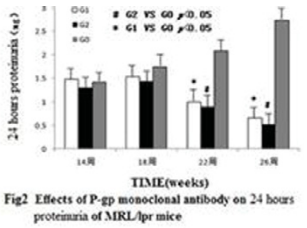


Fig2 Effects of P-gp monoclonal antibody on 24 hours proteinuria of MRL/lpr mice

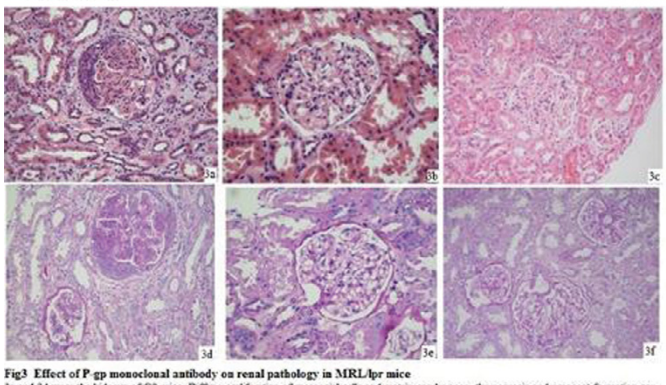


Fig3 Effect of P-gp monoclonal antibody on renal pathology in MRL/lpr mice
3a and 3d were the kidneys of G0 mice. Diffuse proliferation of mesangial cells and matrix can be seen, the necrosis and crescent formation can be seen in a few capillarie. Tubular lumen dilated and renal tubular epithelial cells shedding. Renal interstitial inflammatory cell infiltration, Arteriolar wall thickening and lumen stenosis. 3b and 3e were the kidneys of G1 mice. The mesangial cells and stroma were mildly proliferated, the basement membrane was thickened,but no crescent and no thickening of the epithelium. There was no inflammatory cell infiltration and fibrosis in the renal interstitium. 3c and 3f were the kidneys of G2 mice. There was no obvious inflammatory cell infiltration in the renal interstitium

References:

[1] Barnes PJ.Mechanisms and resistance in glucocorticoid control of inflammation. J Steroid Biochem Mol Biol. 2010,120(2–3):76–85.
[2] García-Carrasco M, Mendoza-Pinto C, Macias Díaz S, et al. P-glycoprotein in autoimmune rheumatic diseases.See comment in PubMed Commons belowAutoimmun Rev.2015,14(7):594–600.
[3] Advani R, Visani G, Milligan D, Saba H, Tallman M, Rowe JM,et al. Treatment of poor prognosis AML patients using PSC833 (valspodar) plus mitoxantrone, etoposide, and cytarabine (PSC-MEC). Adv Exp Med Biol. 1999,457:47–56.
[4] Fisher GA, Lum BL, Hausdorff J, Sikic BI. Pharmacological considerations in the modulation of multidrug resistance. Eur J Cancer. 1996,32A(6):1082–1088.

Acknowledgements: We thank prof. Guofeng GAO's assistance in editing the manuscript.

Disclosure of Interest: M. Wang Grant/research support from: NO, P. ZENG Consultant for: NO, G. ZHOU Employee of: NO, J. LV Paid instructor for: NO, Q. WANG Grant/research support from: NO, Speakers bureau: NO

DOI: 10.1136/annrheumdis-2017-eular.1730

THU0239 SERUM HMGB1 AND TLR4 LEVELS AS NOVEL BIOLOGICAL MARKERS FOR THE ACTIVITIES OF NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

Q. Huang[1], C. Yuan[2], H. Ren[1], M. Yang[1]. *[1]Department of Rheumatology; [2]Department of Neurology, Nanfang Hospital, Southern Medical University, Guangzhou, China*

Background: Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) is a severe complication of SLE, including a variety of neurological and psychiatric features. Previous studies have demonstrated the close relationship between NPSLE and inflammation. HMGB1-TLR4 signaling pathway is the up-stream pathway of NF-κB, which could upregulate the expression of various cytokines and other inflammatory mediators.

Objectives: The objective of the study was to explore the potential mechanism of HMGB1-TLR4 axis in SLE.

Methods: The study population consisted of 107 SLE patients and 43 age- and sex-matched healthy controls. 73 SLE patients had active disease. 36 of these had NPSLE. The serum anti-NR2A antibodies levels were measured by ELISA. Clinical and serological parameters were assessed according to routine procedures. HMGB1 and TLR4 levels were measured by ELISA.Statistical analyses were performed by using the chi-square test and the t-test.

Results: CNS manifestations accounted for 94% (34/36 patients), while involvement of the PNS was 6% (2/36patients). The majority of the manifestations were Seizure disorders (n=17; 47.2%),Headache (n=12; 33.3%), Cognitive dysfunction (n=10; 27.8%), Psychoses (n=8; 22.2%).Within the group of active patients those with NP manifestations had higher HMGB1 levels (0.451 (0.292 to 0.583)) compared to active patients with non-NP manifestations (0.356 (0.098 to 0.436)). In patients with NP (0.429 (0.313 to 0.526)) and non-NP (0.375 (0.196 to 0.478)) manifestations during active periods of the disease, TLR4 levels significant increased in comparison to the controls. TLR4 levels were significantly higher in active patients (0.401 (0.196 to 0.526)) compared to quiescent patients. There was a significant positive correlation between levels of HMGB1 and TLR4 in the total patients group ($P<0.0001$, r=0.939).We observed a correlation between HMGB1 levels and SLEDAI ($P<0.0001$, r=0.804). Also, TLR4 levels showed a significant correlation with SLEDAI ($P<0.0001$, r=0.809). HMGB1 levels correlated with anti-dsDNA levels ($P<0.0001$, r=0.558). Similarly, TLR4 showed a correlation with anti-dsDNA levels ($P<0.0001$, r=0.522).We observed a negative correlation in the total SLE group between C3, C4 and HMGB1 levels ($P<0.0001$, r=-0.545 and $P<0.0001$, r=-0.270 respective. Also, TLR4 showed a significant negative correlation with C3 and C4 ($P<0.0001$, r=-0.559 and $P<0.0001$, r=-0.285 respectively).

Conclusions: Our data suggest that HMGB1-TLR4 axis plays an important role in the pathogenesis of SLE as well as NPSLE.

Acknowledgements: This work was supported by The President Foundation of Nanfang Hospital, Southern Medical University (NO. 2014C009, NO.2015C021).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6410

THU0240 DEFECTIVE REGULATION BY ATP-GATED IONOTROPIC P2X7 RECEPTOR DRIVES T FOLLICULAR HELPER CELL EXPANSION IN SYSTEMIC LUPUS ERYTHEMATOSUS

R. Gualtierotti[1], C.E. Faliti[2,3], M. Gerosa[1,4], F. Grassi[3,5], P.L. Meroni[1,4,6]. *[1]Lupus Clinic, Division of Rheumatology, ASST G. Pini; [2]Istituto Nazionale Genetica Molecolare "Romeo ed Enrica Invernizzi", Milan, Italy; [3]Institute for Research in Biomedicine, Università della Svizzera Italiana, Bellinzona, Switzerland; [4]DISCCO, Department of Clinical Science and Community Health; [5]Department of Medical Biotechnology and Translational Medicine (BIOMETRA), University of Milan; [6]IRCCS Istituto Auxologico Italiano, Milan, Italy*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune

disease of unknown aetiology. The deregulated activation of T follicular helper (Tfh) cells in secondary lymphoid organs may play a pivotal role in the activation of B cells and production of autoantibodies. Both murine and human Tfh cells were shown to be sensitive to extracellular ATP via purinergic P2X7 receptor. P2X7 is a non-selective ionic channel that in the presence of high concentrations of ATP or prolonged stimulation opens to a pore permeable to molecules up to 900 Da and causes cell death. Mice deleted for P2rx7 show a significantly worsened outcome of pristane-induced SLE. Expansion of circulating Tfh (cTfh) cells has been correlated with increased levels of autoantibodies and more severe clinical manifestations in SLE.

Objectives: Our aim was to investigate the possible role of P2X7 receptor activity in driving cTfh expansion in a cohort of SLE patients. Patients with primary antiphospholipid syndrome (PAPS) and healthy donors (HD) served as normal controls.

Methods: Forty-two adult patients with SLE (SLEDAI >4), 14 patients with primary antiphospholipid syndrome (PAPS) and 34 sex- and age-matched healthy donors (HD) were included. Circulating Tfh cells were isolated as a CCR7loPD1+ cells. In 32 patients with SLE, we investigated permeability of Tfh cells to Yo-Pro-1 staining over time at FACS upon stimulation with the P2X7 selective agonist BzATP and the presence of a correlation (Spearman's rho) between Tfh cells expansion and Yo-Pro uptake. We analysed *in vitro* differentiation of CXCR5+PD1+ Tfh cells and sensitivity of this pathway to BzATP in CD4 naïve cells isolated from 4 SLE and 4 healthy donors in the presence of a mixture of Activin A and IL-12, with or without BzATP.

Results: As previously reported, SLE patients had a significant expansion of the CCR7loPD-1+ cTfh cells [SLE (n=42): 38.3±12.8% versus HD (n=34]): 21.6±4.5%, ****$p<0.0001$]. There was no significant difference in the representation of cTfh cells between PAPS patients ([n=14] 22.6±6.6%) and HD (p=0.6714). The analysis of BzATP induced Yo-Pro-1 permeability revealed a significantly increased resistance to P2X7-mediated cell death in SLE patients as compared to HD and PAPS patients (fold increase of Yo-Pro-1-positive cells at 450 sec, HD [n=28]: 5±2.3%; SLE [n=32]: 3±1.7%, ****p=0.003; PAPS [n=14]: 5±2.9%, **p=0.0042). Furthermore, Spearman's rho showed a significant correlation between the percentage of cTfh cells and the degree of Yo-Pro uptake (r -0.37). *In vitro* generation of Tfh cells from HD naïve cells revealed a significant response to inhibition by BzATP, which was not present when SLE naïve cells were used.

Conclusions: The CCR7loPD-1+ cTfh cells are significantly expanded in SLE but not PAPS patients compared to HD. The degree of expansion correlates with diminished sensitivity to P2X7-mediated cell death. This defective regulation is present also within *in vitro* differentiation of Tfh from naïve cells isolated from SLE patients. Our data suggest a selective defect of P2X7-mediated control of Tfh cell generation and expansion in SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3914

THU0241 DECREASED CIRCULATING CXCR3+CCR9+ TH CELLS ARE ASSOCIATED WITH ELEVATED LEVELS OF THEIR LIGANDS CXCL10 AND CCL25 IN THE SALIVARY GLAND OF PATIENTS WITH SJÖGREN'S SYNDROME TO POTENTIALLY FACILITATE CONCERTED MIGRATION

S.L. Blokland[1,2], M.R. Hillen[1,2], S. Meller[3], B. Homey[3], G.M. Smithson[4], A.A. Kruize[1], T.R. Radstake[1,2], J.A. van Roon[1,2]. *[1]Department of Rheumatology & Clinical Immunology; [2]Laboratory for Translational Immunology, UMC Utrecht, Utrecht, Netherlands; [3]Department of Dermatology, University of Düsseldorf, Düsseldorf, Germany; [4]Takeda Pharmaceuticals International, Takeda Pharmaceuticals International, CA, United States*

Background: Primary Sjögren's syndrome (pSS) is characterized by dryness and lymphocytic infiltration in the salivary glands. Both CXCR5+ T follicular helper (Tfh) cells and CCR9+ Tfh-like cells and their specific chemotactic ligands CXCL13 and CCL25 are present at increased levels in the salivary glands of pSS patients. Recently, we and others found that CCR9+ Th cells are elevated in pSS peripheral blood and co-express CXCR3 and other chemokine receptors, known to be differentially expressed by Th cell subsets. CCR9+ Th cells play an important role in mucosal immunity and have been shown to produce high levels of IFN-γ, like CXCR3+ Th1 cells. Since ligands of CXCR3 (CXCL9/10/11) are abundantly expressed in the salivary glands of pSS patients the potential role of this receptor in conjunction with CCL25 was studied in comparison with other chemokine receptors.

Objectives: To study potential chemokine interactions causing enhanced migration of CCR9+ T cells into the salivary glands in pSS.

Methods: CXCL10, CCL25, CXCL13, CCL17 and CCL20 mRNA and protein expression in the salivary gland of pSS and non-Sjögren's sicca (nSS) patients was assessed (mRNA: n=9 vs n=9 and protein: n=26 vs n=34, respectively). Frequencies of CXCR3, CCR9, CXCR5, CCR4 and CCR6 expressing Th cells in blood of pSS patients and healthy controls were assessed by flow cytometry (n=11 vs n=11). Chemotaxis assays (n=3 HC, n=5 pSS) were performed to study migration induced by CXCL10 and CCL25.

Results: CCL25, CXCL10 and CXCL13 expression were increased in pSS compared to nSS patients, both at mRNA and protein level (all $p\leq0.02$). CCL17 and CCL20 expression were low and detectable in only few patients. Protein levels of CXCL10 and CXCL13 correlated with lymphocytic focus scores and all 3 chemokines correlated with serum IgG levels in pSS (all $p<0.05$). CCL25 protein levels strongly correlated with CXCL10 (r=0.545, p=0.004) but not with CXCL13. A relative decrease of CXCR3+ cells was found in the CCR9+ Th subset in the peripheral blood of pSS patients (p=0.04), which was most pronounced in the effector and effector memory subsets (64% vs 26%, p=0.03 and 51% vs 27% p=0.01, respectively). CCR4 or CCR6-expressing CCR9+ Th cells and CXCR3 or CCR6-expressing CXCR5+ Th cells were not decreased. To test the hypothesis that CXCR3 ligands and CCL25 facilitate migration, co-migration of lymphocytes in response to CXCL10 and CCL25 was studied. CXCL10 and CCL25 induced synergistic Th cell chemotaxis in vitro (p=0.02 and $p<0.01$ as compared to CCL25 or CXCL10 only, respectively).

Conclusions: The decreased frequency of CXCR3+CCR9+ Th cells in blood of pSS patients may be due to a concerted action of overexpressed ligands at the site of inflammation. Elevated expression of ligands CXCL10 and CCL25 in the salivary gland and the synergistic effect on chemotaxis in vitro indicate a potential role for these chemokines in formation of lymphocytic infiltrates in exocrine glands of pSS patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2830

THU0242 BIOLOGICAL PATHWAY ANALYSIS IN PRIMARY SJÖGREN'S SYNDROME ASSOCIATED LYMPHOMA

S. Al-Ali[1,2], A. Skelton[3], S. Cockell[3], J. Tarn[1], K. James[4], S. Bowman[5], B. Griffiths[6], D. Young[1], U. Registry[1], W.-F. Ng[1]. *[1]Institute of Cellular Medicine, Newcastle University, Newcastle Upon Tyne, United Kingdom; [2]Department of Biology, College of Science/University of Basrah, Basrah, Iraq; [3]Bioinformatics Support Unit; [4]School of Computing Science, Newcastle University, Newcastle Upon Tyne; [5]University Hospital Birmingham, Birmingham; [6]Freeman Hospital, Newcastle Upon Tyne, United Kingdom*

Background: Lymphoma development is a serious complication of Primary Sjögren's syndrome (pSS). To date, the biological processes that may be involved in pSS-associated lymphoma are not fully understood.

Objectives: The aim of our study is to use microarray gene expression data from a well-defined cohort of pSS patients to identify biological processes that may be relevant to pSS-associated lymphoma.

Methods: pSS patients and healthy controls from the UK primary Sjögren's syndrome registry (UKPSSR) were used in this study. All patients fulfilled the AECG criteria. Whole genome gene expression data from whole blood RNA samples (n=144) stratified into five clinical subsets (pSS=61, pSS with lymphoma=16, pSS with other cancers=21, pSS with paraproteinemia=23 and healthy controls=23) were used for the pathway analysis. A list of 68 differentially expressed genes in pSS-associated lymphoma compared with pSS (non lymphoma) were uploaded into the Ingenuity Pathway Analysis (IPA) analytic tool. Similar approach was also used for comparison between the lymphoma and other pSS subject groups. Finally, we also examined the regulators and pathways involved in the genes from the gene expression signature in pSS-associated lymphoma we have previously described (*BMS1*, *NUDT14* and *MGST3*) [1].

Results: In pSS-associated lymphoma the top canonical pathway was "Aryl Hydrocarbon Receptor (AHR) signaling," which includes *MGST3*. Several other canonical pathways also included the genes of the 3-gene biosignature of pSS-associated lymphoma. The downstream effects and gene-gene interactions were explored through molecular networks analysis. Furthermore, important upstream regulators of the 3 biosignature genes include *NFE2L2*, *PPARA* and *TOCF1* were identified.

The pathway analyses of the other pSS subgroups showed 67 common canonical pathways showed among all the pSS subgroups. Focusing on pSS-associated lymphoma versus healthy controls, 94.9% of the canonical pathways in this comparison were in common with the canonical pathways identified when comparing pSS-associated lymphoma with pSS. The "Interferon Signaling pathway" was the top pathway for all pSS subgroups comparing with healthy controls. In addition, all the non-lymphoma pSS subgroups showed similar patterns in the downstream analysis which differ from the pSS-associated lymphoma group.

Conclusions: The pathway analysis revealed different possible pathways that might be involved in lymphoma development in pSS and indicates a unique gene expression signature exist in pSS-associated lymphoma. These results might provide a deeper understanding and a direction for future studies to investigate lymphoma development in pSS patients.

References:

[1] Al-Ali S, et al. Whole blood transcriptomic signature of primary Sjögren's syndrome associated lymphoma. Biomarkers and Targeted Therapeutics in Sjögren's (BATTS) Conference, 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4820

THU0243 CAN THE INCREASE OF LOBULES / FOCI RATIO BE HISTOPATHOLOGICAL EVIDENCE OF PRIMARY SJÖGREN'S SYNDROME

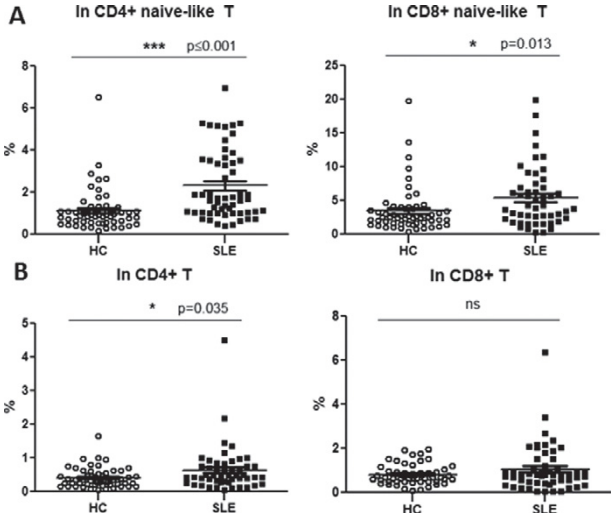
B. Ünal[1], V. Yazısız[2], G.Ö. Elpek[1], M. Göçer[3], M.E. Terzioğlu[2]. *[1]Pathology; [2]Rheumatology; [3]Internal Medicine, Akdeniz University, ANTALYA, Turkey*

Background: Minor salivary gland biopsy from the lip region is commonly used for primary Sjögren's syndrome (SS) diagnosis. It is accepted that changes of histopathology is the most important component of diagnostic criteria. In this study, we analyzed the relationship between histopathological changes and laboratory findings/clinical features in SS patients and control group.
Objectives: The aim of this study was to determine the histopathological changes in minor salivary tissue for SS diagnosis
Methods: A total of 69 minor salivary gland biopsies (29 Sjögren's syndrome and 40 controls) were included in the study. Biopsies were evaluated by a blind pathologist unaware of the diagnosis. Histopathological findings were noted as ductal dilatation, fat tissue percentage ($<$10% or $>$10%), acinar atrophy, ductal/ acinar ratio and lobules/foci ratio. It was evaluated whether there was a relationship between histological changes and age, gender, ANA, anti-SSA, anti-SSB, RF and Chisholm scores.
Results: The lobules/foci ratio of patients with Sjögren's syndrome was significantly higher than the control group ($p<0.001$). The cutoff value of the lobules/foci ratio for SS diagnosis was 0.8. Furthermore, there was a significant correlations between the lobules/foci ratio greater than 0.8 and antibodies (ANA, RF, anti-Ro) positivity and Chisholm score ($p<0.01$). Other histopathological findings such as ductal dilatation, fat tissue percentage, acinar atrophy, and ductal/atherine ratio do not distinguish SS from non-SS.
Conclusions: The results of this study revealed that only the lobules/foci ratio from histopathological changes has a strong relation with SS diagnosis. It can be important for pathologists to distinguish SS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4014

THU0244 THE ROLE OF STEM CELL-LIKE MEMORY T CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Y.J. Lee, H. Kwon, E.B. Lee. *Seoul National University, Seoul, Korea, Republic Of*

Background: The stem cell-like memory T (Tscm) cell, a special subset of memory T cell, has a potential to self-renew and differentiate into wide spectrum of T cells[1]. However, the role of Tscm in autoimmune disease such as systemic lupus erythematosus (SLE) remains to be unknown.
Objectives: To investigate the levels of Tscm cells in SLE patients compared with healthy controls and to understand the functional characteristics of the Tscm cells from SLE patients.
Methods: Fifty two SLE patients and 57 healthy controls (HCs) were enrolled. To detect Tscm cells which are designated as $CD3^+$ $CD4^+$/$CD8^+$ $CD45RO^-$ $CCR7^+$ $CD62L^+$ $CD45RA^+$ $CD27^+$ $CD28^+$ $CD127^+$ $CD122^+$ $CD95^{hi}$, flow cytometry was performed after staining peripheral blood mononuclear cells (PBMCs, $1x10^7$ cells/mL) with fluorescence-conjugated antibodies. To ascertain the differentiation ability of Tscm cells, different subsets of T cells including naïve-like T, central memory T, effector memory T and follicular helper T cells (Tfh) were evaluated after stimulating the isolated Tscm cells with anti-CD3/CD28 antibodies for 6 days. To investigate the function of the Tfh cells derived from Tscm cells, secreted IgG antibodies were measured from the supernatants by ELISA after incubating Tfh –containing differentiated Tscm cells with autologous B cells and SEB for 6 days.
Results: Among the naive-like T ($CD3^+$ $CD4^+$ $CCR7^+$ $CD45RO^-$ $CD45RA^+$ $CD62L^+$) cells, the proportion of $CD4^+$ and $CD8^+$ Tscm cells was significantly higher in SLE patients than HCs (for $CD4^+$ T cells, 2.29±0.22 (SLE) vs 1.11±0.13 (HC), p-value$\leq$0.001; for $CD8^+$ T cells, 5.36±0.63 (SLE) vs 3.41±0.44 (HC), p-value=0.013). Among the total $CD4^+$ T cells, the ratio of Tscm to $CD4^+$ T cells was higher in SLE patients than in healthy controls (0.63±0.10 (SLE) vs 0.40±0.04 (HC), p-value=0.035) (Fig 1). SLE and HC Tscm cells could differentiate into naive-like T, central memory T, effector memory T cells and renewed themselves in response to α-CD3/CD28 stimuli. In addition, in response to the same stimuli, SLE Tscm cells could differentiate into more Tfh cells than HC Tscm cells could (for $CXCR5^+$ $ICOS^+$ $PD\text{-}1^+$ cells in $CD4^+$ T cells, 9.30% (SLE) vs 5.41% (HC) and for $Bcl\text{-}6^+$ cells in $CD4^+$ T cells, 34.29% (SLE) vs 19.20% (HC)). Tscm-derived Tfh cells could help B cells produce antibodies *in vitro* (12007.81±4457.54 (SLE) vs 2082.18±517.82 (HC)).
Conclusions: Proportions of Tscm cells among T cells is increased in SLE patients compared with HCs and the Tscm cells may help maintain SLE by its ability to differentiate into Tfh cells.
References:
[1] Luca Gattinoni et al, A human memory T cell subset with stem cell-like properties. Nature Medicine, 2011, 17: 1290-U325.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2116



THU0245 MAMMALIAN TARGET OF RAPAMYCIN PATHWAY MIGHT CONTRIBUTE THE MINOR SALIVARY GLAND CHANGES IN BOTH SJOGREN'S SYNDROME AND SYSTEMIC SCLEROSIS PATIENTS

Z.Z. Gumus[1], F. Cakalagaoglu[2], Z. Soypacaci[3], M. Ozmen[4], D. Solmaz[4], S. Gucenmez[4], O. Gercik[4], S. Akar[4]. *[1]Internal Medicine; [2]Pathology; [3]Nephrology; [4]Rheumatology, Izmir Katip Celebi University Ataturk Education and Research Hospital, Izmir, Turkey*

Background: The *Mammalian Target of Rapamycin* (mTOR), a multiprotein complex, controls cell growth, proliferation, survival and plays an important role in immunity and inflammation. *Transforming Growth Factor-β1* (TGF-β1) leads to an increase in mTOR levels by protein kinase B (PKB or Akt) pathway. *Phosphatase and tensin homolog* (PTEN) affects mTOR pathway by inhibiting Akt. Recently, increased activities of TGF-β1 and mTOR were established in a mouse model of SSc. However the role of mTOR pathway, which might be a potential treatment target, in the human salivary gland inflammation is not evaluated systematically before.
Objectives: Therefore, we aimed to examine the activity of mTOR pathway and TGF-β1 in human minor salivary gland biopsies of Sjogren's Syndrome (SjS) and systemic sclerosis (SSc) patients.
Methods: Immunohistochemical technique was used to analyze the expression of mTOR, PTEN and TGF-β1 in human minor salivary gland biopsies of SjS, SSc and SjS-SSc overlap patients. Immunohistochemical staining was evaluated by light microscopy and staining intensity was scored semi-quantitatively (Figure 1). The biopsy specimens were also examined for the degree of fibrosis.
Results: Formalin fixed sections of minor salivary gland biopsies of 58 SjS (57 female [98.3%]), 14 SSc (13 female [92.8%]) and 23 SjS-SSc overlap patients (all female) were included in the study. All biopsy specimens of SjS and overlap patients had a focus score of $\geq$1. There is no significant difference regarding mTOR expression between groups (P=0.622). mTOR expression was found in 94.4% in SjS group, 100% in overlap and 90% in SSc patients. PTEN protein was expressed in 87.2% of patients with SjS, 57.9% of overlap and 100% of SSC patients and the difference was statistically different (P=0.023). Although ductal epithelial TGF-β1 expression was similar between groups (P=0.345), acinar

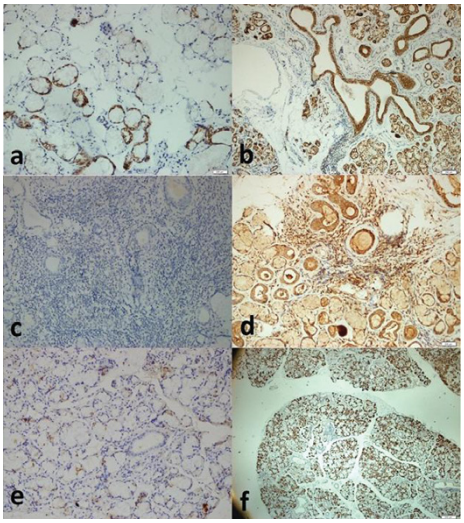


Figure 1. Minor salivary gland biopsy pictures with different stainings of mTOR [1 positive (a) and 3 positive staining (b)], PTEN [negative staining (c) and score 2 (d)] and TGF-β1 [negative staining (e) and score 3 (f)].

cell expression is more frequent in SSc (72.7%) and overlap patients (85.7%) in comparison with SjS (58.2% and *P*=0.004). Additionally, most of the acinar TGF-β1 staining was strong positive in SSC patients (45.5% vs 19.0% and 3.6%).
Conclusions: The results of our study showed that mTOR may be one of the common pathways for the pathology/inflammation observed in both SjS and SSc. Thus, there may be a room for mTOR inhibitors for the treatment of both diseases. Additionally PTEN and TGF-β1 expression, in particular acinar TGF-β1 might be a distinctive feature of SSc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5191

THURSDAY, 15 JUNE 2017

SLE, Sjögren's and APS - clinical aspects (other than treatment)

THU0246 THE IMPACT OF CLASSIFYING SLE PATIENTS WITH THE SLICC-2012 VERSUS THE ACR-1997 CLASSIFICATION CRITERIA ON EARLY DIAGNOSIS, SEVERITY, AND DAMAGE: DATA FROM THE COMMUNITY-BASED CRETAN LUPUS REGISTRY

I. Gergianaki[1,2], A. Fanouriakis[3], C. Adamichou[2], G. Spyrou[4], P. Sidiropoulos[2], D. Boumpas[1,3,5,6,7], G. Bertsias[1,2]. *[1]Laboratory of Autoimmunity and Inflammation, Institute of Molecular Biology-Biotechnology, FORTH; [2]Rheumatology, Clinical Immunology and Allergy, University of Crete School of Medicine, Iraklio; [3]4th Department of Medicine, Attikon University Hospital, National and Kapodistrian University of Athens Medical School, Athens; [4]Laboratory of Autoimmunity and Inflammation, University of Crete School of Medicine, Iraklio; [5]Laboratory of Autoimmunity and Inflammation, Biomedical Research Foundation of the Academy of Athens, Athens, Greece; [6]Medical School, University of Cyprus, Nicosia, Cyprus; [7]Joint Rheumatology Program, Attikon University Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece*

Background: Systemic Lupus Erythematosus (SLE) often poses challenges to diagnosis in clinical practice and classification in research. The 2012 SLICC criteria have been recently introduced, with validation studies suggesting greater sensitivity yet equal or lower specificity compared to the 1997 ACR criteria. However, the prognostic significance of classifying SLE patients with the $SLICC^{2012}$ versus the ACR^{1997} criteria is not known.
Objectives: To evaluate the impact of $SLICC^{2012}$ versus ACR^{1997} SLE classification in terms of clinical characteristics and outcome.
Methods: Both the $SLICC^{2012}$ and the ACR^{1997} classification criteria were applied to adult SLE patients enrolled in the community-based Cretan Lupus Registry over the period 1999–2013. Classified cases were assessed at the end of 2013 in terms of disease severity (determined by the severity of manifestations and the use of lupus treatments) and organ damage (assessed by the SLICC/ACR damage index). Cases who fulfilled both criteria during the observation period were categorized according to which set of criteria was satisfied first and then compared for the frequency of individual criteria.
Results: At the end of the observation period (year 2013), fewer SLE patients had been classified with the $SLICC^{2012}$ (n=602) as compared with the ACR^{1997} (n=750) criteria. The female-to-male ratio (12.6:1 versus 13:1) and the mean (±SD) age at the time of diagnosis (42±15 versus 43±15 years) were comparable between $SLICC^{2012}$ and ACR^{1997}-classified cases, respectively. Lupus was classified as mild, moderate and severe in 50%, 33% and 17% of the ACR^{1997}- as compared to 42%, 34% and 23% of the $SLICC^{2012}$-classified patients ($p<0.001$). Damage occurred in 30.5% of the ACR^{1997} versus 36% of the $SLICC^{2012}$ cohort (p=0.01) despite comparable disease duration. Patients who fulfilled both sets of criteria (n=512) were categorized into three groups based on which criteria were fulfilled first, i.e. group 0 (concurrently: 87% of cases), group 1 ($SLICC^{2012}$ after ACR^{1997}: 5%), and group 2 ($SLICC^{2012}$ before ACR^{1997}: 8%). We found that malar rash and neurologic disorder were significantly more prevalent in group 1 (malar rash: 54.3%, 80.8% and 48.8% in groups 0, 1 and 2, respectively, p=0.02; neurologic disorder: 3.7%, 15.4% and 0%, respectively, p=0.05). Conversely, group 1 patients had significantly lower frequency of non-scarring alopecia (51.3%, 23.1% and 68.3%, respectively, p=0.02) and synovitis (23.9%, 0% and 29.3%, respectively, p=0.012).
Conclusions: Application of the $SLICC^{2012}$ criteria may result in classification of SLE patients with more severe disease compared to those who fulfill the ACR^{1997} criteria, which may have important implications in terms of trial design; however, these data need to be validated. Lack of inclusion of malar rash in the $SLICC^{2012}$ criteria and of non-scarring alopecia in the ACR^{1997} criteria may delay the classification of SLE patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6734

THU0247 THE PRESENCE OF ANTI-RO AND ANTI-LA ANTIBODIES IS ASSOCIATED WITH TUBULOINTERSTITIAL DAMAGE IN LUPUS NEPHRITIS

A. Londono Jimenez[1], W.B. Mowrey[2], A. Broder[3]. *[1]Department of Medicine, Montefiore Medical Center/Albert Einstein College of Medicine; [2]Epidemiology and Population Health, Albert Einstein College of Medicine; [3]Division of Rheumatology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, United States*

Background: Moderate-to-severe tubulointerstitial damage (TID) is associated with poor renal outcomes in lupus nephritis (LN) independent of glomerular pathology[1]. Specific antibody profiles associated with TID in LN have not been identified. Unlike glomerular damage, TID is not associated with anti-dsDNA or complement levels[1]. An association between TID and the presence of anti-Ro/La antibodies has been proposed in Sjögren's syndrome[2]. Whether these antibodies are associated with TID in LN is not known.
Objectives: To study an association between anti-Ro/La antibodies and moderate-to-severe TID in LN.
Methods: We identified all patients who fulfilled ACR and/or SLICC criteria for SLE. Patients were included if they had an index renal biopsy consistent with LN between January 2005 and July 2015 and had complete data on TID and anti-Ro/La. Medical history, demographic and laboratory data were ascertained from chart review. TID was defined as the presence of moderate or severe tubular atrophy and/or interstitial fibrosis from the renal biopsy reports.
Results: of the 157 LN patients, 39 (25%) had moderate/severe TID (Table). As expected, moderate/severe TID was associated with older age, class III/IV±V LN and lower estimated glomerular filtration rate (eGFR) at biopsy. Anti-Ro antibodies were present in 55 (47%) of patients with none/mild TID and 17 (44%) of patients with moderate/severe TID (p=0.74). Both anti-Ro and anti-La antibodies were present in 11 (9%) of patients with none/mild TID vs 11 (28%) of patients with moderate/severe TID (p=0.003). In the logistic regression model adjusted for age, eGFR and LN class, the presence of both anti-Ro and anti-La antibodies was associated with a 3-fold increase in the odds of TID, OR 3.1, 95% CI (1.1–9.1), p=0.04.

Baseline characteristics by TID (none/mild vs. moderate/severe)

	None/Mild TID (n=118)	Moderate/Severe TID (n=39)	p-value
Age, median (IQR), years	26 (17, 37)	41 (25, 53)	<0.001
Men, n (%)	21 (18)	10 (26)	0.29
Black Race, n (%)	55 (47)	22 (56)	0.29
Hispanic ethnicity, n (%)	41 (40)	12 (38)	0.79
Charlson comorbidity index, median (IQR)	3 (1, 4)	3 (1, 4)	0.09
Creatinine (mg/dL), median (IQR)	0.8 (0.6, 1.2)	1.6 (1, 2.6)	<0.001
eGFR mL/min/1.73m^2, median (IQR)	91 (61, 127)	42 (26, 75)	<0.001
Protein/Creatinine ratio (mg/mg), median (IQR)	2.2 (1.0, 4.9)	2.1 (1.5, 5.5)	0.68
LN class n (%)			0.008
I/II	10 (9)	0	
III/IV ± V	71 (61)	34 (87)	
V	35 (30)	5 (13)	
Low C3, n (%)	83 (75)	23 (70)	0.51
Low C4, n (%)	76 (70)	22 (67)	0.69
Elevated dsDNA, n (%)	70 (68)	21 (66)	0.81
Anti-Ro, n (%)	55 (47)	17 (44)	0.74
Anti-Ro and anti-La, n (%)	11 (9)	11 (28)	0.003

Conclusions: The presence of anti-Ro and anti-La antibodies is associated with moderate/severe TID, independent of age, LN class and eGFR. Understanding the role of anti-Ro/La in the mechanisms underlying TID in LN may lead to novel preventive and therapeutic strategies.
References:
[1] Yu F, et al. Kidney Int 2010;77:820–9.
[2] Francois H, et al. Nat Rev Nephrol, 2016;12(2):82–93.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2237

THU0248 THE ASSOCIATION BETWEEN SYSTEMIC LUPUS ERYTHEMATOSUS TO BIPOLAR DISORDER – A REAL-LIFE STUDY

S. Tiosano[1,2], O. Gendelman[1,2], D. Comaneshter[3], H. Amital[1,2], A. Cohen[3,4], D. Amital[5]. *[1]Sackler School of Medicine, Tel-Aviv University, Tel-Aviv; [2]Internal Medicine 'B', Sheba Medical Center, Ramat-Gan; [3]Chief physician's office, Clalit Health Services, Tel-Aviv; [4]Siaal Research Center for Family Medicine and Primary Care, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva; [5]Ness Ziona Beer Yaacov Mental Health Center, Beer Yaacov, Israel*

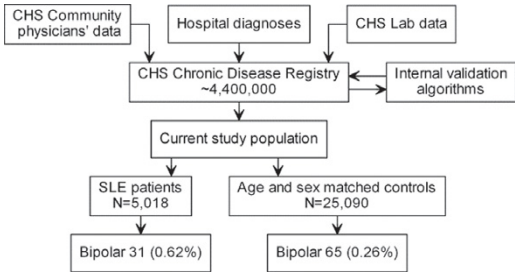
Background: Systemic Lupus Erythematosus (SLE) is a chronic, autoimmune disease that has a wide variety of physical manifestations, including neuropsychiatric features. Bipolar Disorder (BD) is a chronic, phasic affective disorder that may present as depression or as mania. Neuropsychiatric symptoms in SLE develop in 20%>70% of SLE patients during the course of the disease and in half of these patients they precede the diagnosis of SLE[1–4]. In half of the patients, neuropsychiatric manifestations occur prior to the diagnosis of SLE[5].

Objectives: The objective of this study was to investigate the association between SLE and Bipolar Disorder (BD) using big data analysis methods.
Methods: Patients with SLE were compared with age- and sex-matched controls regarding the proportion of BD in a cross-sectional study. Chi-square and t-tests were used for univariate analysis and a logistic regression model was used for multivariate analysis, adjusting for confounders. The study was performed utilizing the chronic disease registry of Clalit Health Services medical database.
Results: The study included 5,018 SLE patients and 25,090 matched controls. BD was found in a higher proportion among SLE patients compared to controls (0.62% vs. 0.26%, respectively, $p<0.001$). BD patients had a greater proportion of smokers compared to non-BD patients (62.5% vs 23.5%, respectively, $p<0.001$). In a multivariate analysis, smoking and SLE were both found to be significantly associated with BD.

Multivariate logistic regression model of covariates associated with Bipolar disorder

	OR	CI	p
Age	1.01	1.00, 1.02	0.137
Gender: Female	1.63	0.96, 2.97	0.087
SES:			
Medium vs. Low	1.06	0.66, 1.69	0.816
High vs. Low	1.17	0.67, 1.98	0.575
Smoking	4.80	3.16, 7.39	<0.001
SLE	**1.74**	**1.11, 2.66**	**0.012**

SES: Socioeconomic status, SLE: Systemic lupus erythematosus.



Conclusions: SLE was found to be independently associated with BD. These findings may imply that an autoimmune process affecting the central nervous system among lupus patients facilitates the expression of concomitant BD.
References:
[1] Kivity S, Shoenfeld Y. Association between autoantibodies and neuropsychiatric manifestations of autoimmune disease: comment on the article by Lauvsnes et al. Arthritis Rheumatol 2015; 67(6):1683.
[2] Meszaros ZS, Perl A, Faraone SV. Psychiatric symptoms in systemic lupus erythematosus: a systematic review. J Clin Psychiatry 2012; 73(7):993–1001.
[3] Unterman A, Nolte JE, Boaz M, Abady M, Shoenfeld Y, Zandman-Goddard G. Neuropsychiatric syndromes in systemic lupus erythematosus: a meta-analysis. Semin Arthritis Rheum 2011; 41(1):1–11.
[4] Zandman-Goddard G, Chapman J, Shoenfeld Y. Autoantibodies involved in neuropsychiatric SLE and antiphospholipid syndrome. Semin Arthritis Rheum 2007; 36(5):297–315.
[5] Kivity S, Agmon-Levin N, Zandman-Goddard G, Chapman J, Shoenfeld Y. Neuropsychiatric lupus: a mosaic of clinical presentations. BMC Med 2015; 13:43.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3667

THU0249 SUBCLINICAL HAND ARTHROPATHY IN PATIENTS WITH SYSTEMIC LUPUS ERITHEMATOSUS

C.A. Guillen-Astete, M. Revenga-Martinez, A. Zea-Mendoza. *Rheumatology Department, Ramon y Cajal University Hospital, Madrid, Spain*

Background: As well as other systemic inflammatory diseases with joint compromise, there is an interest to identify the presence of synovitis in systemic lupus erythematosus (SLE) patients, in every follow up consultation. In SLE, the research about subclinical synovitis (that, which is clinically unnoticed but demonstrable by means of image studies) is quiet limited. The majority of studies focused on the use of ultrasound (US) assessment of patients with SLE included non selected patients so many of them counted with patients with chronic synovitis or even deformities. Due to that their results are difficult to compare and the real prevalence of subclinical synovitis is still unknown.
Objectives: To determine the prevalence of synovitis in a selected cohort of patients without clinical evidence of arthritis or synovitis.
Methods: We performed a prospective study on 96 SLE patients grouped as follows: Group 0 (20) without no historical or present joint symptoms, Group 1 (34) with intermittent joint pain and Group 2 (42) with intermittent arthritis without deformities or erosions. A systematic US study of the carpal, 2nd and 3rd MCP joint of the non dominant hand were performed to all patients. US findings were expressed according to the nomenclature EULAR recommendations for synovitis, power Doppler signal and composite synovitis index.
Results: Six patients from group 0 showed any grade of synovitis (30%), 13 from group I (38.2%) and 18 from group II (42.8%). From the whole group of subjects, those with at least a synovitis finding was 37 (38.5%).
Into the 2nd MCP joint, 4 patients (20%) from group 0 showed any grade of synovitis, one of them (5%) with power Doppler (PD) signal. The composite index of synovitis and PD signal (CSI) was 0.3 DE 0.36. In group 1, 9 patients (26.5%) showed any grade of synovitis, 4 of them also showed PD signal (11.8%). The CSI for this group was 0.44 DE 0.48. In group 2, 15 patients (14.3%) showed any grade of synovitis and 6 of them also showed PD signal (14.3%). The CSI for this group was 0.59 DE 0.55. Globally, we detected synovitis in 28/96 patients (29.2%) and PD signal in 11 (11.5%).
Into the 3rd MCP joint, 5 patients (25%) from group 0 showed any grade of synovitis, one of them (5%) also had PD signal. The CSI for this group was 0.3 DE 0.36. In group 1, 8 patients had synovitis (23.5%), 3 of them also showed PD signal (8.8%). The CSI for this group was 0.38 De 0.46. In group 2, 15 patients showed any kind of synovitis (35.7%), 4 of them with PD signal (9.5%). CSI index for this group was 0.57 DE 0.61. Globally there where 27/96 patients with synovitis (28.1%) and 8 with PD signal.
Into the carpal dorsal aspect, 5 patients of group 0 has synovitis (25%) and 3 PD signal (15%). CSI was 0.5 DE 0.54. In group 1, 12 patients had synovitis (35.3%) and 5 PD signal (14.7%) CSI was 0.58 DE 0.54 In group 2, 16 patients has synovitis (38.1%) and 8 PD signal. CSI was 0.61 DE 0.51. Globally, 33/96 has synovitis (34.4%) and 16 PD signal (16.7%).
Conclusions: As far as our knowledge goes, this is the first US prevalence study in SLE patients where all deforming and erosive arthritis have been excluded. We have demonstrated that approximately one third of patients without joint symptoms had any grade of synovitis detectable by ultrasonography. The prognosis meaning of our findings will require further prospective initiatives.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1298

THU0250 EFFECT OF FETAL UMBILICAL ARTERY DOPPLER ON PREDICTION OF ADVERSE PREGNANCY OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Z. Zhan, D. Chen, Q. Qiu, Y. Yang. *Department of Rheumatology, the First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China*

Background: Pregnancies in women with SLE resulted in an increase of adverse pregnancy outcomes (APOs). The predictive value of fetal umbilical artery Doppler examinations for APOs has been reported, while not widely be assessed in SLE pregnant women.
Objectives: To ascertain the predictive value of fetal umbilical artery Doppler for fetal APOs in SLE pregnancies.
Methods: A fetal Doppler ultrasound examination was performed on all fetuses during the third trimester (28～36 weeks of gestation) and the term pregnancy (37～42 weeks of gestation). The Doppler flow parameters of umbilical arteries were recorded, including pulsatility parameter (PI), resistance index (RI), the peak value of umbilical arteries at end-systole (Vmax, also abbreviate as S) and the peak value of umbilical arteries at end-diastole (Vmin, also abbreviate as D). The value of S/D was automatically calculated. Clinical data and pregnancy outcomes were also analyzed retrospectively.
Results: In total, 109 cases of pregnant SLE women performed fetal umbilical artery Doppler at the third trimester and 82 at the term pregnancy. Among the 109 cases, 65 resulted in one or more APOs, including 45 with premature delivery, 23 with intrauterine growth restriction (IUGR), 16 with fetal distress, 8 with neonatal lupus (NLE) and 3 with congenital malformation. Fetus with APOs had higher S/D values compared with fetus without APOs (2.9±0.9 VS. 2.4±0.5, P=0.001). In addition, other Doppler indexes did not differ significantly across groups. The area under the receiver operating characteristic curve was 0.7 (P=0.003) for S/D values, with the optimal cutoff of 2.8. At this cutoff, sensitivity (46.2%) and specificity (90.9%) had the best combination, whereas the positive and negative predictive values were 83.3% and 52.1%, respectively. Among the 82 cases with term pregnancy, 23 resulted in APOs, including 11 with IUGR, 15 with fetal distress, 4 with NLE and 1 with congenital malformation. All of the Doppler indexes (S/D, PI, RI, Vmax and Vmin) in fetus with APOs were higher than those without APOs, but no statistical significance were found between the 2 groups.
Conclusions: Umbilical artery Doppler was a good monitor method for APOs in the third trimester. S/D values were sensitive and specific predictors for APOs in pregnancies complicated by SLE. Women with more than 2.8 S/D could start strict monitoring to rapidly identify and treat obstetric complications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2210

THU0251 DIFFERENT RESPONSES TO INDUCTION THERAPY IN TWO ONSET CATEGORIES OF LUPUS NEPHRITIS

M. Nakano[1], A. Mimori[2], R. Kamei[1], K. Suga[1], A. Yashima[1], S. Yamada[1], Y. Takahashi[1], H. Yamashita[1], H. Kaneko[1]. *[1]Division of Rheumatic Diseases, National Center for Global Health and Medicine, Tokyo; [2]Division of Nephrology and Rheumatology, Iwate Prefectural Central Hospital, Morioka, Japan*

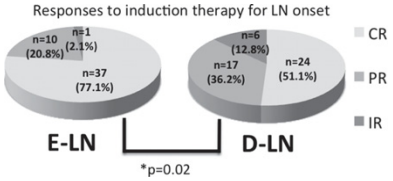
Background: We previously reported different clinical features, serological profiles and activities in two onset categories of lupus nephritis (LN): LN that

developed as a flare of systemic lupus erythematosus (SLE) after treating the prior non-renal SLE conditions successfully (delayed, D-LN) and LN manifesting at the time of SLE onset (early, E-LN).[1)] More frequent flares and higher serum titers of anti-dsDNA antibody during the LN flares were observed in D-LN than E-LN groups, suggesting that D-LN may reflect intractable SLE conditions. However, we had not analyzed whether there is a difference in the response to treatment between the two groups.

Objectives: This study investigated possible differences in the response to induction therapy between E-LN and D-LN.

Methods: We retrospectively examined 95 LN (48 E-LN, 47 D-LN) patients who attended our hospital between January 1991 and May 2016. All of them were diagnosed with SLE according to the American College of Rheumatology criteria and were shown to have LN on renal biopsy. First, we compared the clinical features of E-LN and D-LN, such as sex, age at SLE and LN onset, urinary protein, serum creatinine, serum anti-dsDNA titer, serum C3, prevalence of serum anti-Sm, renal biopsy histological types and induction therapy options at LN onset. Then we compared the response to therapy at 24 weeks for LN onset and flares between the two groups. The response to treatment was classified into complete response [CR; urine protein to creatinine ratio $<$50 mg/mmol and normal or near-normal (within 10%)GFR], partial response [PR; $\geq$50% reduction in proteinuria to sub-nephrotic levels and (near-) normal GFR], and insufficient response [IR; anything else]. We analyzed the data using chi-square test, Fisher's exact test and the Mann–Whitney *U*-test. We further evaluated predictors of treatment response at LN onset using univariate and forward stepwise multivariate Cox regression analysis.

Results: Higher serum C3 (56.4±22.4 *vs.* 46.3±22.7 mg/dl, p=0.03) were observed in D-LN groups. The proportion of histological types (I or II/III or III+V/IV or IV+V/V: 6/7/26/9 *vs.* 4/5/26/12, p=0.77) and induction therapy options at LN onset were similar between the two groups. However, the response to the therapy for LN onset was better in E-LN than D-LN (CR/PR/IR: 37/10/1 *vs.* 24/17/6, p=0.02) (Fig). Univariate Cox regression analysis indicated that severe proteinuria, elevated serum creatinine, class IV or IV+V on renal biopsy and D-LN were associated with non-CR (PR+IR) to induction therapy for LN onset ($p<0.05$). Multivariate Cox regression analysis including variables identified as significant in univariate analyses showed that severe proteinuria [hazard ratio (HR) 1.35, p=0.007] and D-LN [HR 4.96, p=0.003] were independent predictors of non-CR to the induction therapy. LN flares were observed in 13/48 E-LN and 20/47 D-LN patients, and IR was observed in 15.4% (2/13) of E-LN and 40.0% (8/20) of D-LN patients.



Conclusions: In this study, the relatively poorer treatment response was observed in D-LN compared with E-LN patients and D-LN was a predictor of poorer treatment response independent of renal histology and the severity of nephritis at LN onset.

References:

[1] Nakano M, et al. Different clinical features, serological profiles and activities in two onset categories of lupus nephritis. EULAR 2016 congress London, SAT 0313.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2694

THU0252 NAILFOLD CAPILLAROSCOPY IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW AND CRITICAL APPRAISAL

S. Wijnant[1], F. Ingegnoli[2], K. Melsens[1], K. Thevissen[3], F. De Keyser[1,3], S. Decuman[1], E. Deschepper[4], O. Distler[5], U. Müller-Ladner[6], Y. Piette[3], V. Riccieri[7], N. Ughi[2], E. Vandecasteele[8], M. Cutolo[9], V. Smith[1,3]. *[1]Department of Internal Medicine, Ghent University, Ghent, Belgium; [2]Department of Clinical Sciences and Community Health, ASST Gaetano Pini, Division of Rheumatology, University of Milan, Milan, Italy; [3]Department of Rheumatology, Ghent University Hospital; [4]Department of Public Health, Biostatistics Unit, Ghent University, Ghent, Belgium; [5]University Hospital Zurich, Zurich, Switzerland; [6]Rheumatology and Clinical Immunology, University of Giessen/Kerckhoff-Klinik, Bad Nauheim, Germany; [7]Department of Internal Medicine and Clinical Specialities, Sapienza University, Rome, Italy; [8]Department of Cardiology, Ghent University Hospital, Ghent, Belgium; [9]Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genova, Italy*

Background: Systemic lupus erythematosus (SLE) is a rheumatic disease with common vascular involvement. Nailfold capillaroscopic changes have been described in SLE. Although, until today there is no clear role yet for capillaroscopy in classifying or staging the disease.

Objectives: To systematically review and critically appraise the literature on capillaroscopic changes described in SLE.

Methods: A sensitive search, on behalf of the EULAR study group on microcirculation in Rheumatic Diseases, was developed in Web Of Science, PubMed and Embase to identify all original research studies in which SLE patients had capillaroscopy. Two reviewers identified titles, abstracts and full texts. Exclusion criteria were: ACR criteria for SLE were not met, less than 5 patients were included in the study, there was no information on capillaroscopy in SLE, no original research or non-English language. All included articles underwent quality appraisal. Results were summarised according to density, dimensions, morphology, haemorrhages, semi quantitative assessment, qualitative assessment (see table) and correlation of capillaroscopic changes with clinical and laboratory parameters.

Results: From 172 articles captured, 36 articles were included in this review. The following capillaroscopic parameters were significantly more prevalent in SLE patients compared to healthy controls (see table): tortuous capillaries, abnormal morphology, haemorrhages, nailfold capillaroscopic score, "non-specific patterns" and "scleroderma like pattern". Hairpin shaped capillaries were significantly more prevalent in healthy controls compared to SLE patients. For clinical and laboratory parameters, Raynaud's phenomenon (RP), gangrene and 24 hours proteinuria were significantly correlated with capillaroscopic changes.

				Significant	Non-significant	Conclusion
Quantitative evaluation	Density	Mean density		4 studies	4 studies	Non-conclusive
		Avascularity		2 studies	0 studies	
	Dimensions	Diameter	Mean limb diameter	4 studies	2 studies	Non-conclusive
			Mean width	2 studies	2 studies	
			Enlarged width	4 studies	0 studies	
			Giant	1 study	0 studies	
		Length		3 studies	2 studies	Non-conclusive
	Morphology	Normal morphology		3 studies	0 studies	Significant more hairpin morphology in healthy controls compared to SLE patients and more tortuous capillaries in SLE patients compared to healthy controls
		Abnormal morphology		5 studies	0 studies	Significant more abnormal morphology in SLE patients compared to controls
	Haemorrhages			2 studies	0 studies	Significant more haemorrhages in SLE patients compared to controls
	NFC score			2 studies	0 studies	Significant higher NFC score in SLE patients compared to controls
Qualitative evaluation	Other patterns			1 study	0 studies	Significant more nonspecific and scleroderma-like pattern in SLE patients compared to controls

Conclusions: This first systematic review on capillaroscopy in SLE attests conclusive significant differences in morphology, haemorrhages, semi quantitative assessment, qualitative assessment and some clinical and laboratory parameters. Further large scale research is ongoing through the EULAR study group on microcirculation in Rheumatic Diseases to further define its role.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2920

THU0253 TRIPLE POSITIVITY TO ANTIPHOSPHOLIPID ANTIBODIES IN PRIMARY ANTIPHOSPHOLIPID SYNDROME: INCREASED RISK OF ARTERIAL THROMBOSES AND ABORTIONS

F. Signorelli, G. Balbi, R.A. Levy. *Rheumatology, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil*

Background: Triple positivity (TP) to antiphospholipid antibodies (aPL) has been associated with increased risk of thrombotic and gestational events in different populations of antiphospholipid syndrome (APS) patients. Nonetheless, the majority of the studies evolved APS secondary to systemic lupus erythematosus (SLE).

Objectives: To investigate whether TP increases the risk of criteria and non-criteria manifestations in primary APS (pAPS) patients.

Methods: A cross-sectional study was performed in a group of 74 outpatients who fulfilled APS classification criteria (Sydney; N=67) or with thrombocytopenia and persistent circulating aPL, but no criteria manifestations of APS (N=7), seen in our department. Clinical and serological features collected during medical

Table 1. Demographic and clinical characteristics

Variable	Triple positivity (N=19)	No triple positivity (N=55)	P value
Age	41.7±10.3	44±13.5	NS
Female gender	17 (89.5)	44 (80.0)	NS
Caucasian	14 (73.7)	37 (67.3)	NS
Time first manifestation (mo)	143 (97–240)	124.7 (67–176)	NS
Time diagnosis (mo)	55 (26–134)	64 (43–103)	NS
Criteria manifestations*			
Thrombotic	17 (89.5)	45 (81.8)	NS
Arterial	10 (52.6)	17 (30.3)	NS
Venous	10 (52.6)	35 (63.6)	NS
Abortion 3+	3 (20.0)†	1 (2.8)††	p=0.043
Thrombotic + obstetric	10 (58.8)‡	10 (23.8)‡‡	p=0.008
Non criteria			
Livedo	9 (47.4)	11 (20.0)	p=0.023
Thrombocytopenia	7 (36.8)	10 (18.2)	NS
Valvulopathy**	2 (10.5)	6 (10.9)	NS
Raynaud phenomenon	7 (36.8)	12 (21.8)	NS
Leg ulcers	1 (5.3)	4 (7.3)	NS
Nephropathy	0	1 (1.8)	NS
Migraine	8 (42.1)	25 (45.5)	NS

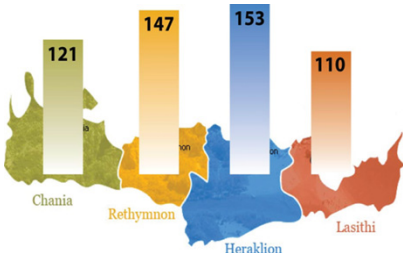
*N=67; **N=49; †N=15; ††N=36; ‡N=17; ‡‡N=42. Mo = months. NS = not significant, NA = not applicable. Values showed as N (%) for categorical variables, Mean ± SD for normal distribution and Median (interquartil range) for asymmetrical distribution.

examination and by chart review were correlated to the presence or not of aPL TP.
Results: Nineteen out of 74 pAPS patients had aPL TP (25.7%). Demographic and clinical characteristics are shown in Table 1. In a bivariate analysis, TP was associated with the presence of combined thrombotic and obstetric manifestations (p=0.008), three or more abortions (abortion 3+; p=0.043), and livedo (p=0.023). In a multivariate regression analysis, the model was adjusted to age, sex, race and variables with p<0.10 in the bivariate analysis (arterial thrombosis, abortion 3+, livedo, thrombocytopenia, and thrombotic+obstetric). After the analysis, arterial thrombosis (OR 5.74; CI95% 1.31–25.05; p=0.02) and abortion 3+ (OR 12.55; CI95% 1.01–156.54; p=0.049) were associated with TP.
Conclusions: In our cohort of primary APS patients, triple positivity was associated with arterial thromboses and the occurrence of 3 or more abortions, with increased risk over 5 and 12 folds, respectively.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6774

THU0254 COMPARISON OF URBAN VERSUS RURAL ENVIRONMENT ASSOCIATED SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): RISK AND CLINICAL FEATURES

I. Gergianaki[1,2], A. Fanouriakis[3], C. Adamichou[2], G. Spyrou[4], P. Sidiropoulos[2], D. Boumpas[1,3,5,6,7], G. Bertsias[1,1,2,2]. *[1]Laboratory of Autoimmunity and Inflammation, Institute of Molecular Biology-Biotechnology, FORTH; [2]Rheumatology, Clinical Immunology and Allergy, University of Crete School of Medicine, Iraklio; [3]4th Department of Medicine, Attikon University Hospital, National and Kapodistrian University of Athens Medical School, Athens; [4]Laboratory of Autoimmunity and Inflammation, University of Crete School of Medicine, Iraklio; [5]Laboratory of Autoimmunity and Inflammation, Biomedical Research Foundation of the Academy of Athens, Athens, Greece; [6]Medical School, University of Cyprus, Nicosia, Cyprus; [7]Joint Rheumatology Program, Attikon University Hospital, National and Kapodistrian University of Athens Medical School, Athens, Greece*

Background: SLE originates from the complex interplay between genetic, epigenetic and environmental factors but the effects of the latter remain elusive. Very few studies have examined the impact of the place of residence (urban/rural) on SLE clinical profile and outcomes.
Objectives: To evaluate the effect of rural versus urban place of residency with regards to: i) SLE occurrence; ii) delay in diagnosis; iii) clinical manifestations, severity and non-reversible organ damage; iv) comorbidities and hospitalizations.
Methods: We employed data from the Lupus Epidemiology & Surveillance project in Crete (750 adult SLE patients with ≥4 ACR-1997 classification criteria). Crete is a Mediterranean island with genetically stable and homogenous population in ethnicity and sociodemographic characteristics, with no significant inequalities regarding access to healthcare facilities; 61% of the inhabitants live in rural (<10,000 people) and 47% in urban areas (>10,000 people). Demographics and residency history were retrieved from face interviews. In 200 patients with exclusively urban or rural residence, a subanalysis was performed in relation to disease risk, diagnosis age, disease severity, renal and neuropsychiatric involvement, and organ damage (SLICC damage Index [SDI]).
Results: SLE prevalence (December 2013) varied across the four geographical prefectures of Crete (Figure 1) and was significantly higher in urban ($165/10^5$) than rural ($123/10^5$) areas (p<0.001). The relative risk of SLE in urban versus rural regions was 2.0 (95% Confidence Interval 1.5–2.9). Notably, patients in urban regions had lower age of diagnosis (38.0±13.4 *vs.* 44.5±14.8 years, p=0.005) and female-to-male ratio (6.5:1 *vs.* 11:1) than those in rural regions. Delay >2 years between symptoms onset and SLE diagnosis occurred in 42% of patients from rural areas as compared to 32% of those from urban areas (p=0.01). Acute cutaneous lupus was more prevalent in the rural environment (83.9% vs. 72.6%, p=0.05) whereas the opposite trend was noted for discoid rash (2.3% vs. 16.8%, p=0.001). Nephritis occurred less frequently (10.3% *vs.* 12.4%) and neuropsychiatric disease was more prevalent (14.9% *vs.* 10.6%) in rural than urban patients albeit non-significantly. Prevalence of mild, moderate, and severe disease was 42%, 40%, and 18% in patients from rural areas, the respective figures being 55%, 28% and 18% in those from urban areas (p=0.12). Hospitalization due to active lupus did not differ between the two groups. At last follow-up, 45.3% of the patients living in urban and 51.9% of patients in rural areas had no organ damage (p=0.89). Concurrent allergic diseases were more frequent in urban patients (30.9% *vs.* 14.3%, p=0.045), particularly allergic rhinitis (8.8% *vs.* 2.3%, p=0.05).



Conclusions: SLE may be more prevalent in urban than rural regions and urbanization is associated with increased risk of SLE and earlier age of disease onset.
Our results suggest an important effect of the environment on SLE occurrence and characteristics, which warrants further investigation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6779

THU0255 COMPARISON OF REMISSION AND LUPUS LOW ACTIVITY STATE AS PREDICTORS OF ORGAN DAMAGE

M. Petri[1], L.S. Magder[2]. *[1]Johns Hopkins University School of Medicine; [2]University of Maryland, Baltimore, United States*

Background: Outcome measures that combine control of SLE activity and prednisone reduction are clinically relevant. A clinical goal in SLE is to reduce risk of long-term organ damage.
Objectives: We assessed whether two recently proposed disease activity outcomes were predictive of future damage.
Methods: For each month of follow-up in a large SLE cohort, we determined whether the patient was in Clinical Remission (as defined by the DORIS work group) or low lupus disease activity state (LLDAS) (as defined by Franklyn et al.). Clinical Remission was defined as a PGA<0.5, clinical SLEDAI=0 and no prednisone or immunosuppressants. Clinical Remission on Treatment allowed for prednisone≤5mg/day and immunosuppressant use. LLDAS was defined as a SLEDAI ≤4, PGA ≤1.0, no major organ activity, and no new activity. LLDAS on treatment allowed for prednisone use ≤7.5 mg/d and immunosuppressants. Damage was defined using the SLICC/ACR index.
Results: There were 81,118 person-months observed among 2,026 patients (92% female, 53% Caucasian, 39% African-American). Table 1 shows the rates of damage, per person month, in subgroups defined by Remission or LLDAS.

Table 1. Rates of new damage, in subgroups defined by past levels of disease activity

Percentage of prior months in:	Number of person-months observed	Number of months with an increase in SLICC/ACR damage	Rate of damage per 100 person-months	Rate ratios	P-values
Clinical Remission					
None	35,772	406	1.13	1.0 (Ref)	
Not none, but <25%	14,358	102	0.71	0.60 (0.48, 0.75)	<0.0001
25% to 50%	6573	50	0.76	0.66 (0.46, 0.94)	0.023
50% to 75%	3845	27	0.70	0.63 (0.42, 0.97)	0.035
75%+	1,641	10	0.61	0.58 (0.30, 1.15)	0.12
Clinical Remission on Treatment					
None	16,491	250	1.52	1.0 (Ref)	
Not none, but <25%	20,169	170	0.84	0.54 (0.44, 0.67)	<0.0001
25% to 50%	14,344	103	0.72	0.46 (0.36, 0.60)	<0.0001
50% to 75%	8396	54	0.64	0.43 (0.30, 0.60)	<0.0001
75%+	2,789	18	0.65	0.45 (0.27, 0.75)	0.0019
LLDAS					
None	30,366	343	1.13	1.0 (Ref)	
Not none, but <25%	10,880	106	0.97	0.86 (0.69, 1.07)	0.18
25% to 50%	5012	40	0.80	0.70 (0.51, 0.98)	0.037
50% to 75%	8494	60	0.71	0.63 (0.48, 0.83)	
75%+	7,527	46	0.61	0.54 (0.40, 0.73)	<0.0001
LLDAS on Treatment					
None	7,656	117	1.53	1.0 (Ref)	
Not none, but <25%	10,555	134	1.27	0.83 (0.65, 1.06)	0.14
25% to 50%	12,686	129	1.02	0.66 (0.51, 0.85)	0.0013
50% to 75%	18,151	133	0.73	0.48 (0.37, 0.61)	0.0010
75%+	13,141	82	0.62	0.40 (0.30, 0.54)	<0.0001

Damage rates were relatively low when LLDA was achieved at least 50% of the time. These rates were similar to those experienced by patients who met a more stringent treatment restriction with Remission on Treatment at least 50% of the time.
Conclusions: The equivalence of LLDAS and DORIS remission on treatment is welcome news, as LLDAS on treatment >50% of the time is an easier goal to achieve (3 times more person-months observed in our cohort) and more realistic as a clinical trial outcome.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1646

THU0256 DEVELOPMENT AND VALIDATION OF A SCORE TO PREDICT THE RISK OF SEVERE INFECTION IN SLE

B. Tejera Segura[1], I. Rúa-Figueroa[2], J. Pego-Reigosa[3], V. del Campo Pérez[3], D. Isenberg[1], A. Rahman[1]. *[1]University College London Hospital, London, United Kingdom; [2]Hospital Universitario Dr.Negrín, Las Palmas de Gran Canaria; [3]Complejo Hospitalario Universitario de Vigo, Vigo, Spain*

Background: Infection is a major cause of morbidity and mortality in SLE patients. It would be helpful to have a tool to predict the risk that an individual patient with SLE will develop serious infection.
Objectives: To develop a predictive risk calculator algorithm (SCORE) that

assesses the probability of serious infection (i.e. leading to hospitalization) in SLE patients and to test it in an independent cohort.
Methods: The SCORE was developed using data from the RELESSER (Spanish Society of Rheumatology Lupus Registry) cohort of 3658 SLE patients. A Cox regression model for repeated events (Andersen-Gill) was applied to assess which demographic and clinical factors were independently associated with increased risk of developing serious infection (Table 1). The SCORE was then validated using retrospective data from the UCLH (University College London Hospital) cohort including 699 SLE patients. Median SCORE values were compared between sub-groups of patients using the U-Mann-Whitney test.
Results: Among 699 SLE UCLH patients, 98 (14%) developed serious infection. We compared these patients with 111 SLE controls who have never suffered serious infection. The characteristics of both groups are summarized in table 2. The infection group were more likely to have suffered previous infection (P=0.001) and/or hospitalized for SLE (P<0.001) and had renal and joint disease (P=0.005). Over a quarter of the infection group died from their infection. Median (Md) SCORE at diagnosis in SLE patients with infection was 4.27 (IQR 3.18) which was significantly higher than in the control group (Md 2.55, IQR 3.79) (z=3.341; P=0.0008). Md SCORE before infection in patients was 5.3 (IQR 3.68) which was significantly higher than SCORE at diagnosis (z=-5.733; P≤0.001) in those patients. By ROC analysis, we defined three possible cut-offs to distinguish patients with and without infection. The area under the ROC curve was 0.66 (CI 95% 0.56 to 0.71). A cut-off for SCORE at diagnosis >3.18 identified patients who would develop serious infection with sensitivity (S)76.5% and specificity (SPC) 50.5%. For SCORE >3.79, S was 64.3% and SPC 57.7%. For SCORE >4.24, S was 64.3% and SPC 60.4%.

TABLE 1 – FACTORS INCLUDED IN THE "SCORE"

Risk factor	B	P-value	HR
Age at diagnosis (>46 years old)	0.1163	0.001	1.12
Latin American ethnicity	0.427	0.001	2.40
Corticosteroids (>10 mg/day) at time of calculating SCORE	0.2878	0.001	1.33
Sex=male	0.3692	0.0001	1.49
Previous hospitalization (for SLE)	1.0049	<0.00001	2.73
Katz index	0,062	0.002	1.06
Prior infection at any time	0.8739	<0.0001	2.40

Table 2

	SLE-infection (n=98)	SLE-non infection (n=111)	P value
Gender	Females: 90 (91.8) Males: 8 (8.2%)	Females: 103 (92.8%) Males: 8 (7.2%)	ns
Mean age (diagnosis of SLE)	30.5 (27)	31 (18)	ns
Ethnicity	Caucasian 48 (49%) Latin American 3 (3.06%) African/Caribbean 28 (28.6%) Asian 7 (7.1%) Other 12 (12.2%)	Caucasian 72 (64.9%) Latin American 2 (1.8%) African/Caribbean 20 (18.02%) Asian 6 (5.4%) Other 12 (10.8%)	ns
Median length of follow-up (IQR)	9.5 (14) yrs	14 (9) yrs	**0.001**
Previous treatment	Steroids (at any time) 89 (90.8%)	Steroids (at any time) 61 (55%)	**<0.001**
	MMF 25 (25.5%)	MMF 23 (20.7%)	ns
	AZA 46 (47%)	AZA 29 (26.1%)	**<0.001**
	Cyclophosphamide 20 (20.4%)	Cyclophosphamide 13 (11.7%)	**0.01**
	Biological treatment 24 (24.5%)	Biological treatment 22 (19.8%)	ns
Patients with >1 Infection	18 (18.4%)		

Conclusions: We have developed a SCORE for predicting risk of serious infection in SLE and validated it in an independent cohort. Given the potential mortality from such infections, this SCORE could be clinically useful though the moderate sensitivity and specificity necessitate caution and further prospective studies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4130

THU0257 ENHANCED ACTIVATION OF NLRP3 INFLAMMASOMES IN PATIENTS WITH SJÖGREN'S SYNDROME

J.N. Kim, S.-K. Kim, J.-Y. Choe. *Division of Rheumatology, Department of Internal Medicine, Catholic University of Daegu School of Medicine, Daegu, Korea, Republic Of*

Background: There has been data about pathogenic role of NLRP3 inflammasome in Sjögren's syndrome. However, linkage between their clinical features and NLRP3 inflammasome has not been clearly defined.
Objectives: The aim of this study is to identify the association of NLRP3 inflammasome with clinical features in patients with primary Sjögren's syndrome.
Methods: A total 25 female patients with Sjögren's syndrome and gender-matched 25 healthy controls were consecutively enrolled. The mRNA expression for target genes including NLRP3, ASC, caspase-1, IL-1b, and IL-18 in peripheral blood mononuclear cells (PBMCs) were measured using real-time polymerase chain reaction. Serum IL-1b and IL-18 expression were also measured by ELISA method. Clinical information and disease activity and damage for Sjogren's syndrome such as EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and Sjögren's Syndrome Disease Damage Index (SSDDI) were collected at the time of enrollment. Statistical analysis were applied including Spearman's correlation coefficient and Mann-Whitney t-test.
Results: Patients with Sjögren's syndrome was found to be highly expressed in mRNA IL-1b and its protein, compared to controls (p<0.001 and p=0.001, respectively). The mRNA levels of caspase-1 and ASC were significantly higher than those in controls (p=0.021 and p=0.008, respectively), but not mRNA level of NLRP3. The mRNA level of IL-1b is closely related with mRNA level of NLRP3 and ESR (r =0.549, p<0.001 and r =0.577, p=0.003, respectively). Serum IL-1b protein expression in Sjögren's syndrome was found to be associated with mRNA level of caspase-1. Based on SSDDI, patients with SSDDI ≥1 was older and higher IL-1b and NLRP3 mRNA expression, compared to those with SSDDI =0 (p=0.035, p=0.005, and p=0.016, respectively).
Conclusions: This study confirmed that activation of NLRP3 inflammasome might implicated the pathogenesis of Sjögren's syndrome.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3068

THU0258 SERUM PARAOXONASE 3 LEVELS ARE DECREASED AND PARAOXONASE 3 ACTIVITY IS REDUCED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AS COMPARED TO HEALTHY CONTROLS

A. Dhooria[1], K. Priyanka[2], A. Sharma[1], I. Verma[2], A. Lal[3], S. Singh[1]. *[1]Internal Medicine; [2]Biochemistry; [3]Radiodiagnosis, PGIMER, Chandigarh, India*

Background: Premature atherosclerosis is a well recognised comorbidity in patients with SLE (1). Elevated levels of circulating Oxidised Low Density Lipoprotein (OxLDL) have been described in SLE patients, especially in those with a history of cardiovascular disease (2). Paraoxonase 3 (PON 3) is believed to play a role in prevention of atherosclerosis by contributing towards the anti oxidant actions of high density lipoprotein (HDL).
Objectives: To determine serum PON3 levels and PON 3 activity in patients with SLE and compare them with healthy controls.
Methods: Serum PON 3 levels and PON3 activity were determined in 100 patients of SLE with no prior history of coronary artery disease and they were compared with those of 50 healthy controls who did not have diabetes, hypertension or coronary artery disease. Serum PON3 concentration was determined by enzyme-linked immunosorbent assay (ELISA) using anti-PON3 antibody specific for human PON3. PON 3 activity was estimated using Spectrophotometric assay which quantified the hydrolysis of dihydrocoumarin at 270 nm (3).
Results: PON 3 levels were lower in SLE patients (P<0.001) and PON 3 activity was reduced (p<0.001) as compared to healthy controls. In subgroup analysis of SLE patients, PON 3 activity and levels did not correlate with disease activity. On Univariate analysis, serum creatinine (r^2=0.06, p<0.002), age (r^2=0.03, p=0.035), and SLE status (r^2=0.27, p<0.001) contributed to PON3 levels. On Univariate analysis, serum creatinine (r^2=0.15, p<0.001), AST (r^2=0.04, p=0.01), ALT (r^2=0.16, p<0.001) and SLE status (r^2=0.77, p<0.001) contributed to PON3 levels. On multivariate analysis, only SLE status predicted PON 3 levels (P<0.001) and PON 3 activity (p<0.001).

Parameter	SLE patients	Healthy controls	P value
Serum Creatinine (mg/dl)	0.55 (0.19)	0.58 (0.19)	<0.001
Aspartate aminotransferase (U/L)	22 (11)	21 (18)	0.02
Alanine aminotransferase (U/L)	12.45 (13)	26.5 (15)	<0.001
Alkaline Phosphatase (U/L)	70 (34)	63.5 (49)	0.408
Total cholesterol (mg/dl)	155 (67)	168.5 (25)	0.076
Low density lipoprotein (mg/dl)	84.5 (44)	102 (28)	0.023
High density lipoprotein (mg/dl)	41 (21)	43 (11)	0.329
Triglyceride (mg/dl)	136 (96)	129 (64)	0.359
Very low density lipoprotein (mg/dl)	27 (19)	26 (12)	0.344
Paraoxonase 3 activity*	38.43 (37.64)	69.54 (27.80)	<0.001
Paraoxonase 3 levels**	0.54 (0.32)	2.41 (1.06)	<0.001

All values are in Median (Interquartile Range). *μmol ml^{-1} min^{-1}, **μg ml^{-1}.

Conclusions: PON3 levels are reduced and PON 3 activity is decreased in patients with SLE as compared to healthy controls, the difference was attributable to the disease itself. This may contribute to premature atherosclerosis in these patients.
References:
[1] Nikpour M, Urowitz MB, Gladman DD. Premature atherosclerosis in systemic lupus erythematosus. Rheum Dis Clin North Am. 2005;31:329–54.
[2] Frostegard J, Svenungsson E, Wu R et al. Lipid peroxidation is enhanced in patients with systemic lupus erythematosus and is associated with arterial and renal disease manifestations. Arthritis Rheum. 2005;52:192–200.

[3] Draganov DI, Teiber JF, Speelman A et al. Human paraoxonases (PON1, PON2, and PON3) are lactonases with overlapping and distinct substrate specificities. J Lipid Res. 2005;46:1239–47.

Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3459

THU0259 RESPIRATORY SYMPTOMS IN PRIMARY SJÖGREN'S SYNDROME, A CROSS-SECTIONAL STUDY OF THE OASIS COHORT

A. Dumusc[1], B. Fisher[2], F. Barone[2], A. Richards[3], A. Poveda[3], J. Higham[3], S. Rauz[2], S. Bowman[1]. *[1]University Hospitals Birmingham NHS Foundation Trust; [2]Institute of Inflammation and Ageing, University of Birmingham; [3]Birmingham Dental Hospital, Birmingham, United Kingdom*

Background: In previous studies, 5 to 35% of patients with primary Sjögren's syndrome (pSS) are reported to have respiratory symptoms (RS). Pulmonary involvement varies from a dry cough due to airway dryness to life-threatening interstitial lung disease.
Objectives: To evaluate RS prevalence in patients with pSS and compare characteristics of pSS patients with and without RS to those in patients without pSS suffering from ocular or oral dryness.
Methods: Cross-sectional study of patients at the time of their inclusion in the OASIS cohort between 2014 and September 2016. This UK prospective research cohort includes patients with suspected pSS or known pSS and aims to collect long-term high quality data with regular clinical, dental and ophthalmological assessments. We asked systematically all the patients if they had any RS. In case of clinically significant RS, pulmonary function tests (PFTs) were requested, and if needed, a high-resolution chest tomography (HRCT) was performed. We included in the analysis only patients fulfilling the AECG (2002) criteria for pSS and excluded patients with secondary Sjögren's syndrome. Characteristics of pSS patients with and without RS and non-pSS patients with sicca symptoms were compared. For statistical analysis, we used unpaired t test, Mann-Whitney test, Fisher's exact test and Chi-square test when appropriate. $P \leq 0.05$ was considered statistically significant.
Results: Among the 157 patients included in the cohort, 70 fulfil the AECG criteria for pSS and 63 have sicca symptoms without pSS. In the pSS/sicca non-pSS groups, 25.7%/15.9% had RS (cough 10.0%/7.9% and breathlessness 15.7%/6.3%) and 5.7%/1.6% an abnormal chest clinical examination respectively. PSS patients with pre-existing lung disease (n=11) had significantly more RS than pSS patients without it (n=59): 54.5% versus 20.3% (p=0.03).
PSS patients with RS or abnormal chest clinical examination (n=21) had a higher ESSDAI index value (mean ±SD) than patients without them (n=49) (7.8±5.7 versus 5.0±4.9, p=0.04), essentially due to a higher constitutional domain score (1.7±2.1 versus 0.6±1.5, p=0.01) and a higher respiratory domain score (1.3±2.8 versus 0, $p<0.01$). They also had a higher ESSPRI index value (mean ±SD), which is a patient reported outcome: 7.4±1.7 versus 6.0±2.1 (p=0.05). There were no differences between pSS patients with and without RS in terms of demographic characteristics, objective measurements of tear and saliva production, histological focus scores and auto-immunity profiles.
In this same group of pSS patients, 10 PFTs and 9 HRCTs were requested and showed abnormal results in 60.0% and 55.6% respectively. A reduced gas transfer was the most common finding in PFTs (DLCO mM/min/kPa, % predicted value, mean ±SD: 66.7±11.7). Among these patients, 2 patients were diagnosed with interstitial lung disease. Both had abnormal PFTs and HRCT.
Conclusions: One third of pSS patients presented with respiratory symptoms or abnormal chest clinical examination at inclusion in our cohort. These patients had higher ESSDAI and ESSPRI index values but did not differ in terms of objective saliva and tear production measurements and auto-antibody profile. Reduced gas transfer was the most common abnormal finding in PFTs.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4759

THU0260 LOW PLASMA CONCENTRATIONS OF APOLIPOPROTEIN M CORRELATE TO DISEASE ACTIVITY AND ENDOTHELIAL DYSFUNCTION IN SLE

A. Bengtsson[1], H. Tydén[1], C. Lood[1], B. Gullstrand[1], B. Dahlbäck[2], A. Jönsen[1]. *[1]Rheumatology, Institution of Clinical Sciences, Lund University, Lund; [2]Clinical Chemistry, Institution of Translational Medicine, Malmö, Sweden*

Background: ApoM is an antiatherogenic and vasculoprotective 25kDa apolipoprotein suggested to play a role in keeping endothelial barrier integrity.
Objectives: The aims of the current study were to determine the impact of SLE disease activity on apoM levels and investigate if apoM levels reflect endothelial function in SLE.
Methods: Plasma concentrations of apoM were measured with ELISA in two SLE cohorts, all patients fulfilling ≥4 American College of Rheumatology (ACR) classification criteria for SLE, and 100 healthy controls (HC). Patients in cohort I had active disease as evaluated with SLEDAI scores. In cohort II endothelial function was measured by EndoPAT 2000 and correlated to apoM levels. A low Reactive Hyperemia Index (RHI) value indicated endothelial dysfunction (ED).
Results: In cohort I, the plasma levels of apoM were found to be significantly decreased in SLE ($p<0.0001$), and the apoM concentrations correlated inversely to disease activity (SLEDAI, r= -0.29, p=0.0063. ApoM was also significantly lower in patients with active nephritis, leukopenia, anti-DNA antibodies or rash compared to patients without these manifestations.
In cohort II, using linear regression analysis, there was a positive correlation between apoM levels and the RHI value, indicating endothelial dysfunction, in the younger SLE patients: β=0.94 CI 95% 0.22,1.65 r=0.32 p=0.011.
Conclusions: SLE related inflammation may have an impact on lower plasma apoM, which may affect the endothelium and the process towards cardiovascular disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5757

THU0261 PREGNANCY COURSE AND OUTCOME IN SLE PATIENTS COMPARED TO PATIENTS WITH OTHER CONNECTIVE TISSUE AND INFLAMMATORY RHEUMATIC DISEASES - DATA FROM A PROSPECTIVE COHORT STUDY

A. Strangfeld[1], C. Bungartz[1], A. Weiß[1], M. Schneider[2], J. Richter[2], A. Zink[1,3], R. Fischer-Betz[2]. *[1]German Rheumatism Research Centre, Berlin; [2]Department of Rheumatology & Hiller Research Unit, University Hospital, Düsseldorf; [3]Charité University Medicine, Berlin, Germany*

Background: Patients with systemic lupus erythematosus (SLE) are at increased risk for pregnancy complications and adverse pregnancy outcomes. During the past decades, advances in drug treatment and management during pregnancy made successful pregnancy in patients with SLE possible. Less is known about pregnancy course in other connective tissue diseases (OCTD).
Objectives: To compare pregnancy courses and outcomes in SLE patients with those in OCTD patients and patients with other inflammatory rheumatic diseases.
Methods: The German Rhekiss register is designed as nationwide, web-based longitudinal observational cohort study. Pregnant patients with confirmed diagnose of inflammatory rheumatic disease are eligible to be enrolled until the 20th week of pregnancy regardless of drug treatment. At baseline, sociodemographic parameters, prior pregnancies, comorbidities and antibody status are reported. During pregnancy, rheumatologists and patients report drug treatments, course of the maternal disease, development of fetus and complications once per trimester. After delivery, the pregnancy outcome and child development during the first two years of life are collected.
Results: Until October 2016, data of 392 patients were available and grouped according to their disease in SLE patients, those with other connective tissue disease (OCTD) and patients with all other diagnoses (allO). 121 women had already completed their pregnancy with known outcome. Of them, most patients in the OCTD group were diagnosed with undifferentiated connective tissue disease

	SLE	Other connective tissue diseases	All other diagnoses
Patient characteristics at enrolment			
Pregnancies, n	**85**	**71**	**236**
Maternal age [years]	31.8 (4.4)	32.9 (3.9)	32.4 (4.3)
Disease duration [years]	7.3 (5.9)	5.8 (6.05)	8.3 (7.6)
BMI > 30, n (%)	4 (8.7)	1 (2.6)	10 (8)
Disease activity (physician global) [0-10] in the first trimester	1.5 (1.3)	1.7 (1.5)	2.6 (2.2)
Rheumatoid factor positive, n (%)	9 (14.8)	12 (25.5)	48 (34.5)
Lupus anticoagulant positive, n	6	1	1
Anticardiolipin antibody positive, n	13	3	1
Anti-β2-GP-1 positive, n	10	3	2
Antiphospholipidsyndrome, n	10	1	1
SLEDAI	1.7 (2.3)	-	-
RAID [0-10]	1.8 (1.6)	1.9 (2.0)	2.1 (2.0)
Outcomes of pregnancies			
Completed pregnancies, n	**32**	**25**	**64**
Miscarriages, n (wk of gestation)	2 (wk 9/12), 1 elective (wk21)	2 (wk 14 & 21)	2 (wk 5 & 10)
No. of patients with flares during pregnancy			
1 – 2 flares	2	5	37
3 – 4 flares	0	0	10
5 – 6 flares	0	0	4
Life births, n: **preterm** (< 37th wk)	5 + 2x twins	2 + 1x twins	7 + 1x twins
at term (≥ 37th wk)	19 + 3x twins	20	53 + 1x twins
Mean birth weight [gramm] of singletons born at term	3123	3234	3477
Serious complications during pregnancy (n patients)	HELLP Syndrome (1) severe preeclampsia (1) serious bleedings (2) preterm labour (1) serious infection (2) thrombotic embolism (1)	HELLP Syndrome (2) preeclampsia (2) preterm rupture of membranes (1) serious infection (1)	*none*
Non-serious complications (n patients)	gestational diabetes (2) infections (1)	gest. diabetes (1) infections (1)	gest. diabetes (3) infections (4)
Congenital malformation / complication	multiple anomalies → elective termination palatine cleft (suspected Pierre-Robin-Syndrome) hämangioma at leg congenital megaureter	sacral agenesis hexadactylus (both sides)	hip dysplasia sacral hämangioma
Postpartal maternal complications	cerebral insult serious pyelonephritis hypertensive crisis	*none*	*none*
Neonatal complications (n children)	serious infections (3) lethal sepsis (1) serious icterus (1)	serious infection (3) serious respiratory distress (3) hypoglycaemia (1)	non-serious infection (1) serious respiratory distress (1)

If not otherwise indicated values are mean (SD). wk= week of gestation.

(9), Sjögren Syndrome (5) and mixed connective tissue disease (5). The allO group included rheumatoid arthritis (28), psoriatic arthritis (10), spondyloarthritis (11), and JIA (8). The proportion of children born at term was lowest in patients with SLE (79%), compared to OCTD (91%) and allO patients (88%). The table shows selected baseline and outcome parameters.

In early pregnancy, more patients with SLE reported low disease activity and a higher proportion was diagnosed by the rheumatologist as having mild disease than in the other diagnoses groups. During pregnancy, flares occurred rarely in SLE and OCTD patients, whereas a substantial proportion of patients in the allO group had multiple flares. However, serious complications during and after pregnancy occurred more often in SLE and OCTD patients, as well as congenital anomalies and complications. Due to the low number of events and completed pregnancies, associations to suspected risk factors couldn't be analyzed yet.

Conclusions: Although most patients with SLE or OCTD had a favorable course and outcome of pregnancy, compared to patients with other inflammatory rheumatic diseases substantially more complications and adverse pregnancy outcomes occurred. The association to specific risk factors predicting adverse pregnancy outcomes could not yet be analyzed. At the time of the EULAR congress we expect at least twice as much completed pregnancies.

All patients with SLE and OCTD should be tightly screened during pregnancy with timely and adequate adjustment of drug treatments.

Acknowledgements: Rhekiss is a collaborative project of the DRFZ Berlin and the Rheumazentrum Rhein-Ruhr e.V. Düsseldorf, jointly funded by both institutions.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6714

THU0262 CHANGES IN SONOELASTOGRAPHIC CHARACTERISTICS IN SJÖGREN'S SYNDROME – A FIVE-YEAR FOLLOW UP

B. Hofauer, M. Bas, N. Mansour, A. Knopf. *Otorhinolaryngology/Head and Neck Surgery, Klinikum Rechts Der Isar, Technical Universitiy Munich, Munich, Germany*

Background: The role of sonography in the evaluation of salivary gland alterations in patients with suspected Sjögren's Syndrome (SS) and its benefit with regard to the diagnosis is part of continuing investigation. Studies on sonoelastographic alterations in the salivary glands of patients with SS have been published during the last years and were able to prove significant differences compared to patients with sicca-symptoms without fulfilling the AECG classification criteria [1, 2]. The available knowledge on longitudinal changes in sonoelastographic characteristics is still limited.

Objectives: Which variations of sonoelastographic salivary gland alterations can be observed during the five-year follow up of patients with primary Sjögren's Syndrome?

Methods: Patients with primary Sjögren's Syndrome (pSS) diagnosed according to the AECG classification criteria were included in this study. The EULAR SS Patient Reported Index (ESSPRI) was applied for the evaluation of patient's symptoms and the EULAR SS Disease Activity Index (ESSDAI) for systemic features. During 2011 and 2016 the sonoelastographic alterations of the salivary glands in patients with primary Sjögren's Syndrome were evaluated. Acoustic Radiation Force Impulse (ARFI) imaging (=shear wave velocity), Real Time Tissue Elastography (RTTE) and Virtual Touch Tissue Imaging (VTTI) were applied for the sonoelastographic evaluation in addition to B-Mode sonography (BMUS). Results of BMUS, RTTE and VTTI were graded with appropriate scoring systems.

Results: Fifty patients diagnosed with pSS were included (45 female, age: 56 years SD =16). In 2011 the mean ESSPRI score was 8.3 (SD =4.6) and the mean ESSDAI score was 5.6 (SD =7.5). Initially, the mean ARFI value of parotid glands was 2.99m/s (SD =0.93) and the mean ARFI value of the submandibular glands was 2.15m/s (SD =0.57). Clinical examination and sonoelastographic evaluation was repeated after five years in 2016, revealing a mean ESSPRI score of 6.1 (SD =3.2, p=0.002) and a mean ESSDAI score of 4.6 (SD =7.0, $p<0.001$). After five years a significant decline of ARFI values could be observed in the parotid gland (2.33m/s, SD =0.70, $p<0.001$) while no significant changes of the ARFI of the submandibular gland could be observed. Results of RTTE and VTTI did not change significantly. The mean time interval between onset of first symptoms and first sonographic examination in 2011 was 57.3 months (SD =60.8).

Conclusions: The five-year sonoelastographic follow up of salivary gland alterations in patients with pSS revealed a decline in the severity of sonoelastographic alterations of the parotid gland in ARFI imaging, indicating a certain capability for modulation of salivary gland affection in pSS.

References:

[1] Hofauer B et al. Sonoelastographic Modalities in the Evaluation of Salivary Gland Characteristics in Sjögren's Syndrome. Ultrasound Med Biol 2016; 2) Knopf A et al. Diagnostic utility of Acoustic Radiation Force Impulse (ARFI) imaging in primary Sjoegren's syndrome. Eur Radiol 2015.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6436

THU0263 PREVALENCE OF REMISSION AND ITS EFFECTS ON ORGAN DAMAGE AND QUALITY OF LIFE IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C.C. Mok, L.Y. Ho, S.M. Tse, K. Chan. *Medicine, Tuen Mun Hospital, HK, Hong Kong*

Background:

Objectives: To study the effect of disease remission on organ damage and quality of life in Chinese patients with systemic lupus erythematosus (SLE).

Methods: Patients who fulfilled the ACR classification for SLE were studied. Their remission status at last visit was determined by the European consensus (DORIS definition): (1) Complete remission (clinical SLEDAI=0, serology inactive); and (2) Clinical remission (clinical SLEDAI=0, serology active). These two categories were further divided into those who required ongoing immunosuppressive treatment (prednisone $\leq$5mg/d or other immunosuppressive agents) and who did not. The increase in SLE organ damage (SDI) score since 5 years prior to recruitment was compared between patients who were and were not in remission for $\geq$5 years. Participants were randomly selected for assessment of quality of life by using both the validated version of SF36 and the LupusPRO (version 1.8) and comparison was made between those who did and did not achieve remission for $\geq$5 years by the independent Students' t-test.

Results: 769 SLE patients were studied (92% women; age 46.4±14.6 years, SLE duration 12.6±8.1 years). At last visit, clinical remission was present in 259 (33.7%) patients (median 43 months) and complete remission (clinically and serologically inactive) was present in 280 (36.4%) patients (median 51 months). Clinical/complete remission for $\geq$5years was achieved in 64 (8.3%) and 129 (16.8%) of the patients, respectively. 53 (6.9%) patients in remission $\geq$5 years were taken off all medications including HCQ (drug-free). Compared with patients who did not remit, those remitted $\geq$5 years were older (49.9±13.2 vs 45.7±15.8; p=0.004), and had significantly lower prevalence of renal involvement, leukopenia or thrombocytopenia. Significantly fewer patients who remitted for $\geq$5 years were maintained on prednisolone compared to others (31% vs 68%; $p<0.001$). The increase in SDI scores over the preceding 5 years was 0.17±0.53 in patients who had complete/clinical remission off-therapy (except HCQ) for $\geq$5 years (N=88), 0.25±0.51 in those remitted for $\geq$5 years but maintained on immunosuppressive medications (N=105), 0.41±0.84 in those remitted for $<$5 years (N=346) and 0.67±1.10 in those who did not remit (N=230), respectively. The increase in SDI was statistically higher in those remitted for $\geq$5 years than $<$5 years (p=0.007) or those who did not remit ($p<0.001$). Logistic regression showed that patients with remission for $<$5 years or who did not remit had an increase in the risk of new damage accrual as compared to those with remission for $\geq$5 years (OR 2.42 [1.50–3.89]; $p<0.001$), adjusted for age, sex, SLE duration, SDI scores 5 years prior and the daily maintenance prednisolone dose at last visit. Among 453 patients who had QOL assessment, remission for $\geq$5 years was associated with significantly higher higher physical component and mental component scores of the SF36 than those who did not remit. Patients with remission for $\geq$5 years had significantly higher scores in the individual health-related domains (except cognition) of the LupusPRO than those who did not remit.

Conclusions: Durable remission can be achieved in a quarter of patients with SLE. Patients with remission for $\geq$5 years have significantly less damage accrual and better QOL. Prolonged remission is an appropriate parameter for outcome assessment in SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3947

THU0264 RESPONSIVENESS OF LUPUSPRO V1.8 AMONG CHINESE PATIENTS WITH LUPUS

C.C. Mok[1], J. Block[2], M. Jolly[2]. [1]*Medicine, Tuen Mun Hospital, HK, Hong Kong;* [2]*Medicine and Behavorial Sciences, Rush University Medical Center, Chicago, United States*

Background: LupusPRO v1.7 is a patient reported outcome tool for patients with systemic lupus erythematosus (SLE) that has undergone psychometric validation and responsiveness studies in the US.

Objectives: To report results on responsiveness of LupusPRO among Chinese patients with SLE.

Methods: 430 patients with SLE meeting the ACR classification criteria were recruited in Hong Kong, China at a single center for this observational study. LupusPRO scores from two visits one year apart were analyzed for responsiveness and Minimal Clinically Important Difference (MCID) against patient report and physician assessed anchors of changes in health. Two patient reported anchors were used (Global change in health and item 2 of Short Form 36 form). Physician assessed anchors of change in health were disease activity (Physician global assessment-PGA, SELENA-SLEDAI) and damage (SLICC-SDI/ACR). Change in PGA of $\geq$0.3 and SELENA-SLEDAI of $\geq$4 in either direction was used to define worsening in disease activity. Our primary outcomes of interest were was summary HRQOL and HRQOL domains, as non HRQOL domains tend not to change over short time periods. Analysis of variance was used to compare changes in LupusPRO summary and domain scores against the anchors.

Results: Mean (SD) age of participants was 42 (14) years. Ninety five percent were women. Mean (SD) PGA, SELENA-SLEDAI and SDI at baseline were 0.5 (0.5), 2.9 (3.0) and 0.7 (1.2) respectively. Summary HRQOL, and HRQOL

domains (Lupus Symptoms, Physical Health, Pain-Vitality, Emotional Health and Body Image) were responsive to changes in patient reported and physician assessed health status (disease activity and damage) (Table 1). Procreation and Cognition domains showed responsive trends with patient reported change in health status, while Lupus Medications domain was responsive additionally to changes in Damage.

Table 1: Responsiveness of LupusPRO to change in Health

		Patient-reported Change						Physician Assessed Change									
	Anchor Used →	PGC			Global Change in Health			PGA			SELENA-SLEDAI			SDI			
	Category	N	Mean Change	P Value	N	Mean Change	P Value	N	Mean Change	P Value	N	Mean Change	P Value	N	Mean Change	P Value	
LupusPRO HRQOL	Worse	138	-3.84	<0.001	137	-3.79	<0.001	72	-3.39	0.000	48	-2.73	0.002	33	-7.68	0.000	
	Same	139	0.17		138	0.25		253	-0.12		343	-0.13		405	0.31		
	Better	138	2.88		138	2.98		305	2.08		43	3.8					
Lupus Symptoms	Worse	137	-2.85	0.034	137	-2.73	0.015	72	-6.22	<0.001	48	-5.78	0.005	33	-5.36	0.142	
	Same	139	-1.02		138	-1.18		254	0.78		343	0.32		405	0.27		
	Better	138	3.11		138	3.11		305	3.77		43	6.25					
Cognition	Worse	138	-4.42	0.101	137	-4.77	0.07	72	-2.48	0.808	48	-1.79	0.555	33	-5.36	0.822	
	Same	139	-0.56		138	-0.83		253	-0.55		343	-0.55		405	-0.65		
	Better	138	1.08		138	1.03		305	-0.65		43	-4.77					
Procreation	Worse	138	-2.75	0.06	137	-2.75	0.08	72	-2.48	0.855	48	-1.56	0.546	33	-4.17	0.512	
	Same	139	0.42		138	0.4		253	0.15		343	0.26		405	0.09		
	Better	138	1.27		138	1.27		305	0.88		43	-1.63					
Physical Health	Worse	138	-5.85	<0.001	137	-6.16	<0.001	72	-4.45	0.048	48	-4.89	<0.001	33	-5.95	0.139	
	Same	139	-0.78		138	-0.89		254	-0.54		343	-1.58		405	-0.36		
	Better	138	3.23		138	3.23		305	1.85		43	9.02					
Lupus Medications	Worse	138	-2.44	0.183	137	-2.44	0.183	72	0.88	0.358	48	1.01	0.658	33	-9.52	0.002	
	Same	139	1.84		138	2.1		253	1.84		343	2.12		405	1.89		
	Better	138	2.47		138	2.47		305	2.82		43	12.47					
Pain-Vitality	Worse	138	-5.38	0.001	137	-5.83	0.001	72	-3.72	0.008	48	-5.42	<0.001	33	-16.08	0.005	
	Same	139	-0.84		138	-0.84		253	-2.41		343	-1.38		405	-0.88		
	Better	138	2.78		138	2.78		305	4.00		43	9.88					
Emotional Health	Worse	138	-0.81	0.136	137	-1.03	0.347	72	-1.74	0.377	48	-2.47	0.028	33	-10.52	0.009	
	Same	139	-0.69		138	-0.93		253	-0.15		343	0.52		405	1.15		
	Better	138	2.98		138	2.98		305	3.21		43	7.88					
Body Image	Worse	138	-4.41	0.002	137	-4.41	0.002	72	-8.38	0.06	48	-0.30	0.838	33	-8.18	0.088	
	Same	139	2.29		138	2.29		253	0.12		343	0.98		405	0.73		
	Better	138	2.94		138	2.94		305	5.29		43	7.07					
LupusPRO non HRQOL	Worse	138	-1.61	0.137	137	-1.59	0.139	72	0.34	0.575	48	-0.75	0.932	33	-1.96	0.603	
	Same	139	-1.29		138	-1.49		254	0.48		343	-0.45		405	-0.46		
	Better	138	1.67		138	1.67		305	1.98		43	-0.95					
Desires-Goals	Worse	138	-1.81	0.144	137	-1.81	0.144	72	-4.26	0.308	48	0.34	0.886	33	-8.68	0.125	
	Same	139	-0.24		138	-0.61		254	0.49		343	-1.42		405	-0.68		
	Better	138	1.86		138	1.9		305	2.98		43	-1.81					
Social Support	Worse	138	-1.33	0.982	137	-1.88	0.778	72	1.18	0.43	48	0.28	0.403	33	-1.49	0.898	
	Same	139	-1.88		138	-2.18		254	0.28		343	-1.22		405	1.18		
	Better	138	-0.34		138	-0.54		305	-0.18		43	-7.51					
Coping	Worse	138	-1.18	0.428	137	-0.92	0.475	72	0.36	0.271	48	-4.42	0.188	33	-1.36	0.936	
	Same	139	1.84		138	1.18		254	1.45		343	2.05		405	1.27		
	Better	138	3.38		138	3.58		305	4.98		43	0.00					
Satisfaction with Treatment	Worse	138	0.8	0.448	137	1.43	0.159	72	1.74	0.357	48	0.58	0.547	33	1.00	0.825	
	Same	139	-0.85		138	-0.66		254	-0.54		343	0.04		405	0.42		
	Better	138	2.45		138	2.45		305	4.28		43	3.65					

Conclusions: LupusPRO summary HRQOL and HRQOL domains show responsiveness to changes in patient-reported and physician assessed changes in health status in this observational study among Chinese SLE patients. Results support inclusion of LupusPRO into larger clinical trials to allow for robust estimates of responsiveness.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3943

THU0265 IDENTIFYING THE LINKS BETWEEN IRON DEFICIENCY AND FATIGUE IN ADOLESCENTS AND YOUNG ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

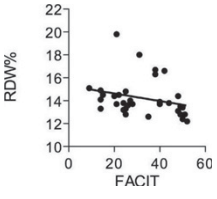
C. Wincup[1], Y. Ioannou[1], T. Richards[2], F. Josephs[1], L. Suffield[1], A. Rahman[1]. *[1]Department of Rheumatology; [2]Division of Surgery & Interventional Science, University College London, London, United Kingdom*

Background: Between 80–90% of patients with systemic lupus erythematosus (SLE) report fatigue to be the single most troublesome and debilitating symptom of their illness.[1] Recent studies have found that functional iron deficiency and iron deficiency anaemia have been linked with fatigue and decreased cognitive performance.[2] Increased red blood cell distribution width (RDW) is an early indicator of iron deficiency that can be useful in assessing iron stores in patients with SLE who may have an elevated serum ferritin due to underlying inflammation.

Objectives: To investigate the relationship between early iron deficiency (measured by RDW) and fatigue in adolescents and young adults with SLE.

Methods: Adolescent and young adult patients with SLE were recruited prospectively between November 2016 and January 2017. All patients were asked to complete the Functional Assessment of Chronic Fatigue Illness Therapy (FACIT) Fatigue Scale v4, in which a numerical score between 0–52 is generated. Lower scores indicate more fatigue. Standard measures of lupus disease activity including Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), Complement C3 levels, anti-double stranded DNA binding (anti-dsDNA) and SLEDAI were recorded. Haemoglobin (Hb) and RDW were also measured. Anaemia was defined by World Health Organisation criteria (male Hb $<$130g/L and female Hb $<$120g/L). Non-parametric analysis was performed using Spearman's rank with a p-value $<$0.05 felt to be significant.

Results: 33 patients aged between 16.7 and 27.5 years (median age 20) were included. 85% of the patients were female. Their FACIT scores were lower than those published for healthy individuals of the same age group - median 24, IQR 22–44 for SLE vs median 43, IQR 35–48 for healthy. There was no statistically significant correlation between FACIT Fatigue score and SLEDAI (p=0.92), anti-dsDNA (p=0.36), C3 levels (p=0.37), ESR (p=0.30) or CRP (p=0.85). Interestingly a statistically significant negative correlation between FACIT Fatigue score and RDW was observed (p=0.012; r=-0.43). A correlation between FACIT Fatigue score and Hb was noted although this was not statistically significant (p=0.079). 12 of the 33 patients were found to be anaemic (11 female, 1 male). Analysis of the sub-group of 21 non-anaemic patients found FACIT Fatigue Score and RDW continue to show a statistically significant association (p=0.026; r=-0.49).



Conclusions: Fatigue is a common and debilitating symptom described by young patients with SLE. Standard serological and clinical markers of disease activity did not correlate with the burden of fatigue. Increased RDW has been shown for the first time to correlate with increased fatigue in patients with lupus, suggesting that iron deficiency may play a significant role in the manifestation of this troublesome symptom. A trial of therapeutic iron infusions in the treatment of fatigue in SLE is planned.

References:

[1] Tench CM, McCurdie I, White PD, D'Cruz DP. The prevalence and associations of fatigue in systemic lupus erythematosus. Rheumatology 2000;39:1249–1254.

[2] Greig AJ, Patterson AJ, Collins CE, Chalmers KA. Iron deficiency, cognition, mental health and fatigue in women of childbearing age: a systematic review. J Nutr Sci 2013;29;2:e14.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2440

THU0266 DAMAGE INDEXES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SECONDARY ANTIPHOSPHOLIPID SYNDROME: DIAPS VS SLICC/ACR DAMAGE INDEX

D. Potarniche[1], D. Mazilu[2], I. Saulescu[2], A. Borangiu[2], L. Groseanu[2], C. Constantinescu[2], V. Vlad[1], F. Berghea[2], V. Bojinca[2], D. Opris-Belinski[2], A. Balanescu[2], D. Predeteanu[2], R. Ionescu[2]. *[1]"Sfanta Maria" Clinical Hospital; [2]"Sfanta Maria" Clinical Hospital, "Carol Davila" University of Medicine, Bucharest, Romania, Bucharest, Romania*

Background: Systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are systemic autoimmune diseases that have overlaping irreversible organ damages. Since SLICC/ACR Damage Index (SDI) misses key features of APS, the Damage Index in patients with Thrombotic Antiphospholipid Syndrome (DIAPS) was proposed.

Objectives: To assess the differences in indexes available for measuring organ damage in a cohort of patients with SLE and secondary APS.

Methods: Clinical records of patients with SLE and secondary APS were reviewed. Data on medical history and clinical manifestations were collected. The two damage indexes, SDI and DIAPS, were applied. Comparison between the two indexes was done for each organ system affected.

Results: Sixty five clinical charts were reviewed, 5 had been excluded for incomplete information. SDI and DIAPS was recorded in 60 patients. Patient's mean age was 45.05±14.61 years, with mean disease duration of 9.47±6.96 years. Mean SDI in our cohort was 4,15±2.58 and mean DIAPS – 4.08±3.41. SDI correlated significant to DIAPS (R=0.826, p$<$0.000). Neuropsyhiatric manifestations were found in 25 patients (41.7%). Their mean SDI value was 4.92±2.73 and DIAPS value of 5.52±3.47. DIAPS value was higher in the subgroup of patients with neuropsyhiatric (p=0.006) and respiratory system damage (p=0.037). This difference was not observed regarding SDI value. DIAPS value correlated significantly to neurological (R=0.397, p=0.002) and pulmonary damage (R=0.364, p=0.004), but not to SDI value. No diferrences were observed between the two scores regarding perypheral vascular manifestation (DIAPS p=0.221, SDI p=0.136) and renal involvement (DIAPS p=0.062, SDI p=0.078).

Conclusions: SDI may underestimate APS related damage in patients with SLE and secondary regarding neurological and pulmonary organ involvement. Given the implications for high morbidity and mortality, DIAPS may be the appropriate damage score to be used.

References:

[1] P. Alba et al. Organ Damage and Quality of Life in Antiphospholipid Syndrome. Current Rheumatology Reports. February 2016, 18:7.

[2] Barbhaiya et al. Utility of the Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) Damage Index for Antiphospholipid Antibody (aPL) Positive Patients. [abstract]. Arthritis Rheum 2011;63 Suppl 10:7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4384

THU0267 METABOLIC SYNDROME AND HEALTH-RELATED QUALITY OF LIFE IN SYSTEMIC LUPUS ERYTHEMATOSUS

D.P.E. Margiotta, F. Basta, M. Vadacca, G. Dolcini, F. Pignataro, A. Vernuccio, C. Mazzuca, L. Navarini, A. Afeltra. *Unit of Allergology, Immunology and Rheumatology, Università Campus Bio-Medico di Roma, Rome, Italy, Rome, Italy*

Background: Systemic Lupus Erythematosus (SLE) is associated to a huge prevalence and incidence of cardiovascular diseases (CVDs) due to accelerated atherosclerosis. Several evidences demonstrated that metabolic syndrome (MeS) could contribute to CVDs burden in SLE. In general population, MeS components and, according to some reports, MeS itself are associated to worsened Health related Quality of Life (HR-QoL). In SLE patients, a severe decline of HR-QoL has been widely demonstrated.

Objectives: In the study, we evaluated the association between MeS, HR-QoL and QoL-related factors, such as depression, fatigue and physical activity.
Methods: We conducted a cross-sectional study with retrospective evaluation of disease activity, damage and therapies cumulative dosage. MeS was defined according to International Federation of Diabetes (IFD) criteria. All patients were evaluated to explore MeS IFD criteria and other CVD risk factors (familiar history, lifestyle, smoking). SLE disease activity and damage were evaluated using SELENA-SLEDAI and SDI indices, respectively. Disease flares were retrospectively assessed by SFI index. HR-QoL was quantified by SF-36 instrument. We used Beck Depression Inventory (BDI) to assess depression and Facit-Fatigue to evaluate fatigue. Physical activity was quantified using International Physical Activity Questionnaire (IPAQ) and expressed according to categorical IPAQ total score. Patients also completed Pittsburgh Sleep Quality Index (PSQI) exploring sleep pathology.
Results: We enrolled 55 SLE patients (2 male and 53 female). Mean age was 45±12.5. MeS prevalence was 23.6% and obesity (according to IFD definition) was recorded in 36.4% of patients. SLE patients with MeS presented reduced scores in SF-36 summary components MCS and PCS compared to patients without MeS (p 0.002 and p 0.04, respectively). The SF-36 individual components significantly decreased in MeS were the Mental Health, the Physical Rose and the Social Role (p 0.003, p 0.03, p 0.05, respectively). In multiple linear regression the values of MCS was significantly associated only to obesity (p 0.01), while neither MeS it self nor any MeS components were associated to PCS values. BDI score was significantly higher and Facit-Fatigue score was reduced in SLE patients meeting MeS criteria compared to subjects without MeS ($p<0.0001$, p 0.005, respectively). A greater proportion of SLE patients with MeS presented almost mild depression (p 0.03). We found to be physically inactive, according to IPAQ score, the majority of SLE patients with MeS compared to patients without MeS ($p<0.0001$). In multiple logistic regression, factors related to MeS were the Number of flares in the previous one year [OR (95% CI) 13.7 (1.7–107.8)], to have a BDI>13 (to have almost mild depression) [OR 0.05 (0.004–0.87)] and to be physically inactive (IPAQ=1) [OR 33.5 (2.3–496.4)].
Conclusions: HR-QoL seems to be compromised in SLE patients with MeS, especially in mental components. Moreover, SLE patients with MeS often presented depression, are burdened by more severe fatigue and frequently are physically inactive. The presence of MeS in SLE was associated to the number of flare and, above all, to the physical inactivity, while not having depression seems exert a protective effect on MeS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6712

THU0268 PREVALENCE AND FEATURES OF CELIAC DISEASE IN PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES: RESULTS OF A LARGE MULTICENTER STUDY

E. Bartoloni[1], A. Alunno[1], O. Bistoni[1], L. Cavagna[2], L. Nalotto[3], C. Baldini[4], R. Priori[5], G. Picarelli[5], C. Fischetti[6], F. Franceschini[7], L. Quartuccio[8], F. Carubbi[9], M. Fredi[7], C. Montecucco[2], A. Doria[3], M. Mosca[4], G. Valesini[10], A. Gabrielli[6], S. De Vita[11], R. Giacomelli[9], R. Gerli[1]. *[1]Rheumatology Unit. University of Perugia, Perugia; [2]Department of Rheumatology. University of Pavia, Pavia; [3]Rheumatology Unit. University of Padova, Padova; [4]Rheumatology Unit. University of Pisa, Pisa; [5]Rheumatology Unity. Sapienza University, Roma; [6]University 'Politecnica delle Marche', Ancona; [7]Rheumatology and Clinical Immunology. Spedali Civili of Brescia, Brescia; [8]Rheumatology Clinic. University of Udine, Udine; [9]Division of Rheumatology. University of L'Aquila, L'Aquila; [10]Rheumatology Unit. Sapienza University, Roma; [11]Rheumatology Clinic. University of Udine, Udine, Italy*

Background: Celiac disease (CD) is an inflammatory and immune-mediated gluten-dependent enteropathy occurring in genetically susceptible individuals. CD is recognized to affect between 0.6% and 1% of worldwide population, with wide regional differences. Disease clinical features are protean and highlight the systemic nature of the disease. In recent years, an increased prevalence of CD has been also reported in patients with connective tissue diseases (CTDs). This association may be due to a shared genetic predisposition, to immunological mechanisms and/or exposure to a common triggering event. However, this observation remains controversial since data are usually based on descriptive case reports. Different methods of antibody detection and enrolled population sample size may contribute to result discordance. Moreover, CD diagnosis is often delayed because disease clinical spectrum may be atypical mimicking rheumatologic conditions and autoimmune disease itself may display typical symptoms of CD. Undoubtedly, awareness of CD occurrence in CTDs is important to prevent potential long-term systemic complications related to an unrecognized CD in these patients.
Objectives: To evaluate the prevalence of overt and subclinical CD and features of the disease in a large cohort of patients with systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and primary Sjögren's syndrome (pSS) with a multicenter prospective study involving 9 Italian Rheumatology Units.
Methods: Data from consecutive 580 SLE, 354 pSS and 524 SSc patients were collected. Disease-specific features were registered in patients with known CD. Remaining patients were tested for IgA transglutaminase (Eu-tTG® human IgA new, Eurospital S.p.A., Trieste). Anti-endomysium (EMA) IgA and IgG were tested in IgA tTG positive and borderline patients. Esophagogastroduodenoscopy with duodenal biopsy was proposed in IgA tTG+/EMA+, IgA tTG-/EMA+ and IgA tTG±/EMA+ patients.
Results: CD prevalence was 1,7% in SLE, 7% in pSS and 1,3% in SSc patients. Higher frequency of elevated liver enzymes was detected in SLE-CD and of herpetiform dermatitis in SSc-CD patients in comparison to the other groups ($p<0.05$ for both). Interestingly, pSS-CD and SSc-CD patients were younger and had a lower age at diagnosis in comparison to pSS and SSc without CD ($p<0.05$ for all). Of interest, higher prevalence of CD was detected in SSc patients with diffuse form in comparison to limited SSc (86% vs 14%, p=0.002).
Conclusions: The results of the present large multicenter study confirm higher prevalence of CD in CTD patients, especially in pSS. Screening of CD may be considered in younger patients with CTD and lower age at diagnosis. The strong association of CD with the diffuse type of SSc is of note and suggests that different, still unexplored, pathogenic mechanisms may characterize the two subsets of the disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4388

THU0269 ELECTROCARDIOGRAPHIC NONSPECIFIC ST-T ABNORMALITIES ARE ASSOCIATED WITH HIGHER MODIFIED FRAMINGHAM RISK SCORE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITHOUT CLINICAL CARDIOVASCULAR DISEASE

E. George, T. Perez-Recio, L. Geraldino-Pardilla. *Department of Rheumatology, Columbia University College of Physicians & Surgeons, New York, United States*

Background: Cardiovascular disease (CVD) is a leading cause of mortality in systemic lupus erythematosus (SLE). Traditional CVD risk scores underperform in SLE. Interestingly, a high prevalence of nonspecific ST-T changes (NST-T) has been recently reported in lupus patients[1,2]. These electrocardiographic findings are known to increase the risk for myocardial infarction, coronary artery disease, CVD, and all-cause mortality[3] in the general population, but in SLE this association remains unknown. Therefore, we sought to define the association of NST-T with the modified Framingham Risk Score (mFRS) as a surrogate outcome for CVD[4].
Objectives: To evaluate if NST-T are associated with higher mFRS in SLE patients without clinical cardiovascular disease.
Methods: Adult SLE patients without clinical CVD continuously seen at the Columbia University Lupus Center between April 2016 and January 2017, meeting 1997 American College of Rheumatology classification criteria for SLE were studied. Twelve-lead electrocardiogram (EKG), high sensitivity C-reactive Protein (hsCRP), demographics, disease-specific characteristics, medication use, and CVD risk factors were ascertained. Univariable and multivariable linear regression models were constructed to test the association of NST-T with the mFRS.
Results: Seventy-four lupus patients were studied (baseline characteristics in table 1). In univariable analysis, patients with NST-T had a significantly higher mFRS (0.44, p=0.018). There were no confounders identified in the analysis. However after adjusting for variables associated with the mFRS: smoking, diabetes, hsCRP, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index [SDI], aspirin use, this association remained statistically significant (0.38, p=0.05). Image 1 shows the association of mFRS with NST-T vs no NST-T.

Age, years ± SD	39±13
Female, n (%)	67 (90%)
Hispanic, n (%)	56 (77%)
African American, n (%)	14 (19%)
Body mass index	30±8.3
Median Disease Duration, years (IQR)	6.5 (4–12)
Median SLEDAI (IQR)	4 (2–8)
Moderate-Severe Disease activity (SLEDAI ≥6), n (%)	23 (31%)
Median SDI, n (%)	0 (0–1)
hsCRP median (IQR)	2.4 (1–6.5)
ESR , Median (IQR)	37 (23–51)
Anti-DNA, n (%)	44 (60%)
Anti-SSA, n (%)	42 (59%)
Anti-Smith, n (%)	21 (30%)
Ever smoker, n (%)	16 (22%)
Hypertension, n (%)	22 (30%)
Diabetes, n (%)	6 (8%)
mFRS, median (IQR)	0.5 (0–1.8)
NST-T abnormalities, n (%)	27 (38%)

Conclusions: Non Specific ST-T changes are independently associated with a higher mFRS in SLE patients without clinical CVD.
References:
[1] Bourré-Tessier J, Urowitz MB, Pineau CA. et al. Electrocardiographic findings in systemic lupus erythematosus: data from an international inception cohort.Arthritis Care Res (Hoboken). 2015 Jan;67(1):128–35.
[2] Geraldino-Pardilla L,Gartshteyn Y, Piña P, et al.ECG non-specific ST-T and QTc abnormalities in patients with systemic lupus erythematosus compared with rheumatoid arthritis. Lupus Sci Med. 2016 Dec 16;3(1):e000168.
[3] Daviglus ML, Liao Y, Stamler J, et al. Association of Nonspecific Minor ST-T

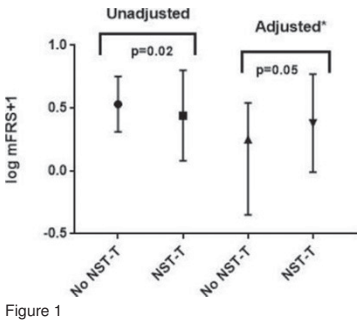


Figure 1

Abnormalities With Cardiovascular Mortality The Chicago Western Electric Study. JAMA. 1999;281(6):530–536.
[4] Urowitz MB, Ibañez D, Gladman DD,et al. Modified Framingham Risk Factor Score for Systemic Lupus Erythematosus. J Rheumatol. 2016 May;43(5):875–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4655

THU0270 HOMOCYSTEINE, ANTIPHOSPHOLIPID ANTIBODIES AND RISK OF VASCULAR EVENTS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

G. Stojan, W. Fu, M. Petri. *Rheumatology, Johns Hopkins University, Baltimore, United States*

Background: SLE patients have higher plasma total homocysteine concentrations compared to healthy controls. Hyperhomocysteinemia in SLE is a potentially modifiable, independent risk factor for stroke and thrombotic events, hypertension, and coronary artery calcification.
Objectives: We investigated the association of homocysteine levels with the presence of antiphospholipid antibodies as well as the potentially additive thrombotic risk in patients with antiphospholipid antibodies who have hyperhomocysteinemia.
Methods: To analyze the association between hyperhomocysteinemia and the presence of antiphospholipid antibodies in SLE, 844 patients with homocysteine measurements were included in the analysis. 237 patients had at least one measurement over 15 umol/L. Patients were followed quarterly after cohort entry. The association of hyperhomocysteinemia with antiphospholipid antibodies is detailed in Table 1.

Table 1. Homocysteine and antiphospholipid antibody positivity

	Homocysteine (umol/L)		Odd ratios (95% CI)	P value	Adj. Odd ratios (95% CI)	Adj. P value
	≥15 (%)	<15 (%)				
Anti-cardiolipin	43.24	57.62	0.56 (0.37,0.84)	0.0049	0.54 (0.36,0.81)	0.0033
Anti-B2 Glycoprotein	16.98	29.69	0.48 (0.28,0.82)	0.0076	0.46 (0.27,0.8)	0.0054
Lupus anticoagulant	19.82	29.29	0.6 (0.36,0.98)	0.0404	0.54 (0.33,0.91)	0.0190

To analyze the prevalence of vascular events among SLE patients with antiphospholipid antibodies based on homocysteine levels, 571 patients with positive antiphospholipid antibodies and at least one homocysteine measurement were included in the analysis. There were 166 patients with at least one homocysteine measurement over 15 umol/L.
The lupus anticoagulant was assessed by dRVVT with mixing studies and confirmatory tests. Anticardiolipin and anti-beta2 glycoprotein 1 were measured by ELISA (INOVA). Vascular events were defined as stroke, myocardial infarction, digital gangrene, and deep vein thrombosis.
Results:

Table 2. Prevalence of vascular events among SLE patients with antiphospholipid antibodies based on homocysteine levels

	Abnormal Homocysteine >15 umol/L N (%)	Normal Homocysteine N (%)	P value
Superficial Thrombosis	4 (2.41)	12 (2.96)	0.7176
Deep vein thrombosis	37 (22.29)	58 (14.36)	0.0257
Stroke	17 (10.24)	30 (7.41)	0.3139
Myocardial infarction	13 (7.83)	11 (2.72)	0.0099
Digital Gangrene	4 (2.41)	8 (1.98)	0.7523

Conclusions: SLE patients with elevated homocysteine were less likely ($p<0.05$) to have any of the antiphospholipid antibodies. Among patients with SLE who have antiphospholipid antibodies, elevated homocysteine is associated with a significantly higher prevalence of myocardial infarction and deep vein thrombosis ($p<0.05$).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6705

THU0271 THE PERFORMANCE OF DIFFERENT CLASSIFICATION CRITERIA IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME AND ANALYSIS OF THEIR CONTRIBUTION FOR DEFINITIVE DIAGNOSIS, WHEN EITHER CRITERIA USED ALONE OR IN COMBINATION

Z. Kosuva Ozturk[1], G. Kenar[2], H. Yarkan Tugsal[2], B. Zengin[2], G. Can[2], F. Onen[2], M. Birlik[2]. [1]*Internal Medicine;* [2]*Rheumatology, Dokuz Eylul University School of Medicine, Izmir, Turkey*

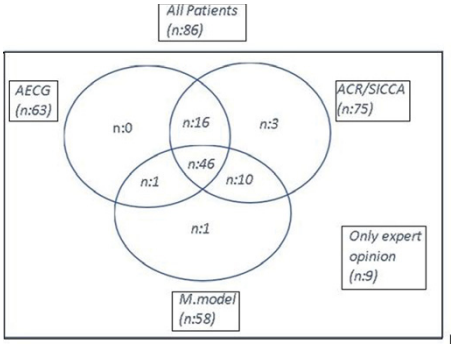
Background: Many classification criteria sets have been proposed for primary Sjögren's Syndrome (pSS),consisting of variable features of the disease.Despite increasing number of criteria sets, expert opinion is still keeping its importance for the diagnosis of pSS.
Objectives: We aimed to compare the performance of 3 classification criteria sets for pSS, to determine the agreement between each other and expert opinion and to investigate diagnostic contribution with any combined use of these criteria.For those assessments, American-European Consensus Criteria (AECG), American Collage of Rheum (ACR)/Sjögren Int. Clinical Alliance (SICCA) criteria and *L.S. Martin et al.* criteria named Mathematical model (M.model) had chosen.The M.model is a criteria set known to be noninvasive and proposed as highly specific.
Methods: 86 patients (F: 96%, mean age: 51.7±11.8) following up in our clinic with the diagnosis of pSS were enrolled to the study.Expert opinion had been taken as gold standard for pSS diagnosis. Patients were questioned for eye/mouth dryness. Antinuclear antibody (ANA), complement (C3, C4), anti-Ro and anti-La, serum protein electrophoresis, rheumatoid factor (RF), break-up time (BUT) and Schirmer, minor salivary gland biopsy results were analysed cautiously. The aforementioned criteria sets, were implemented to assess the classification. The percentage of exact agreement and Kappa test was calculated.
Results: Number of patients classified as pSS according to ACR/SICCA, AECG and M.model criteria were 75 (87%), 63 (73%) and 58 (67%) respectively. 9 patients (10%) did not fulfill any of these 3 criteria but they were diagnosed as pSS according to expert opinion (Image 1). The Kappa test was moderate between the ACR/SICCA and AECG criteria and slightly low between the M.model with the AECG and ACR/SICCA criteria (Table 1). According to our proposed combination model, number of patients classified as pSS, either AECG or M.model was 74(86%); either AECG or ACR/SICCA model was 76(88%); either ACR/SICCA or M.model was 77 (89.5%) (Table 2). In the triple combination of our model, if all 3 criteria used concomitantly, only 46 (51%) of patients fulfill the criteria simultaneously; however if any of 3 criteria sets used 77 (89.5%) patients fulfill as pSS.

Table 1

	AECG	ACR/SICCA	M.MODEL
AECG		%83 K: 0.50	%68 K: 0.25
ACR/SICCA	%83 K: 0.50		%75 K: 0.34
M.MODEL	%68 K: 0.25	%75 K: 0.34	

Table 2

	Classsification criteria	(n)	(%)
According to 1 criteria	ACR/SICCA	75	87,2
	AECG	63	73,2
	M. model	58	67,4
According to either of 2 criteria	ACR/SICCA or M.model	77	89,5
	AECG or ACR/SICCA	76	88,3
	AECG or M. model	74	86
According to either of 3 criteria	AECG or ACR/SICCA or M.model	77	89,5
According to concomitant use of 3 criteria	AECG + ACR/SICCA + M.model	46	51.6



Conclusions: In this study, ACR/SICCA classification criteria for pSS was found the most compatible criteria set with expert opinion, when it used alone. The combination of either ACR/SICCA or M.model was found to be the most sensitive binary combination for classification with similar results as triple combination.This study showed that a small group of patients could not be classified as pSS even if the criteria sets were used with concomitant combinations. It was determined that experienced specialists were largely need to recognize and distinguish these patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6074

THU0272 VISFATIN IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: AN IMMUNE METABOLIC INTERPLAY

H.E.S. Mansour[1], H.M. Farouk[1], M.A. Abdulrahman[1], N.O. El-Azizi[1], N.M. Lotfy[2], A.S.M. Farouk[1]. *[1]Internal Medicine & Rheumatology; [2]Clinical patholgy & Immunology, Facilty of Medicine- Ain Shams University, Cairo, Egypt*

Background: Visfatin is a proinflammatory cytokine (adipocytokine) that is secreted in excess from adipose tissue in obese individuals, and it has numerous metabolic and autoimmune implications: it stimulates the secretion of IL-6, IL-8, IL-10, IL-18 and TNF-α. In SLE patients these may influence disease activity and delays remission (1).
Objectives: To assess the possible effects of obesity & serum visfatin levels on SLE patients and its clinical relevance on disease process, activity and occurrence of insulin resistance.
Methods: This study was performed on 60 SLE patients satisfying the 1997 American College of Rheumatology revised criteria (ACR) and 60 apparently normal individuals with matched age and sex as control groups. All subjects were classified according to BMI into 4 groups (non-obese and obese SLE patients, non-obese and obese control persons). All patients were subjected to full history & clinical examination, assessment of SLE disease activity was done using BILAG-2004 index, laboratory investigations were done (CBC, ESR, fasting blood glucose, renal and liver function tests, lipids profile, fasting plasma insulin, calculation of insulin resistance by HOMA score, measurement of serum visfatin level by ELISA kit) and diagnosis of metabolic syndrome according to WHO definition.
Results: There were statistically significant higher grades of cardiorespiratory manifestations of BILAG score in obese compared to non-obese SLE patients. 40% of obese lupus patients were hypertensive, while only 16.6% of non-obese SLE patients A statistically significant higher prevalence of metabolic syndrome in obese compared to non-obese SLE patients. There were statistically significant higher levels of total serum cholesterol; serum triglyceride, fasting blood sugar, fasting insulin, insulin resistance and serum visfatin; but lower level of HDL in obese SLE patients compared to non- obese SLE. The same observations were recorded on comparing non-obese SLE patients to non-obese controls & obese SLE to obese controls. A statistically significant higher level of insulin resistance and prevalence of metabolic syndrome were found among obese SLE patients when compared to obese controls and non-obese SLE patients compared to non-obese controls. Regarding serum visfatin levels obese SLE patients have significantly higher serum visfatin levels than non-obese SLE patients than obese controls than non-obese controls.In all SLE patients there were statistically significant positive correlations between serum visfatin levels and each of: BMI, waist circumference, haematological manifestations, total BILAG score of disease activity, serum triglycerides, liver functions (ALT, AST, alkaline phosphatase and total serum proteins). While a significant negative with HDL level.
Conclusions: Obesity (BMI) is an independent risk factor in SLE patients that increases the SLE disease activity and complications. Visfatin is an adipocytokine its level significantly increased in obese SLE patients & it is positively correlated with disease activity.
References:
[1] Ouchi N, Parker JL, Lugus JJ and Walsh K.Nat Rev Immunol 2011; 11: 85–97.
Acknowledgements: We thanks all the participating patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2079

THU0273 PREVALENCE AND FACTORS ASSOCIATED WITH FATIGUE IN FEMALE SLE PATIENTS AT THE HOSPITAL DEL MAR / PARC DE SALUT MAR

I. Carrión-Barberà, T. Salman-Monte, S. Castell, F. Castro, P. Corzo, F. Ojeda, L. Polino, E. Beltrán, C. Pérez, J. Carbonell. *Rheumatology, Hospital del Mar, Barcelona, Spain*

Background: In patients with SLE, subjective parameters are very important as they have a great impact on the quality of life. Among them, fatigue is the most prevalent symptom in SLE, as it occurs in more than 90% of patients (1). Likewise, approximately 50% of patients consider fatigue the most disabling symptom of the disease (2). Despite its high prevalence and impact on quality of life, fatigue has not been extensively studied in patients with SLE.
Objectives: To determine the prevalence of fatigue in our cohort as well as the factors with which it is associated, its relationship with demographic variables, vitamin D levels, treatments, SLE symptoms and disease activity.
Methods: A cross-sectional study was carried out including female patients with SLE (ACR 1997 criteria) who regularly attended the Parc de Salut Mar-IMAS in Barcelona between January 2012 and May 2014. We collected sociodemographic data, vitamin D supplementation, the VAS fatigue, pharmacological treatment, main serological markers of SLE, and plasma levels of 25-hydroxy vitamin D. The association between fatigue and the different variables was evaluated by the Spearman's rho correlation coefficient for the continuous and the Mann-Whitney U test for the categorical variables.
Results: One hundred and two consecutive female patients were included. The fatigue variable was evaluated through a fatigue VAS with a mean score of 52.84 (range 0–100), a median of 59.00 and a standard deviation of 29.86. A statistically significant relationship was found between fatigue and age, MHAQ, SLICC and photosensitivity in the entirety of the 102 patients. As for the relationship between fatigue and vitamin D insufficiency (25-OH vit. D≤30 levels), the sample was divided into patients receiving vitamin D supplementation (N=60) and without supplementation (N=40), finding a significant relationship between fatigue and vitamin D insufficiency in the group without supplementation.

Table 1. Correlation between fatigue and the different SLE variables studied

Age**	Correlation coefficient	0.289
	p-value	0.003
	N	102
MHAQ**	Correlation coefficient	0.484
	p-value	0.000
	N	102
SLICC**	Correlation coefficient	0.256
	p-value	0.009
	N	102
25-0H-VitD**	Correlation coefficient)	-0.356
	p-value	0.024
	N (not supplemented)	40
Photosensitivity*	55.32 [30–80]	p-value = 0.043
	N	102

Significant value $p<0.05$. Med [P25–P75]. *Mann-Whitney U test; **Spearman's rho test.

Conclusions: Fatigue is highly prevalent among female patients with SLE. A statistically significant association was found between the presence of fatigue, on the one hand, and age, MHAQ, SLICC, photosensitivity, and vitamin D insufficiency in the group of patients without supplementation on the other. It is necessary to carry out further studies with a larger sample and with validated fatigue measurement scales to confirm our findings.
References:
[1] Zonana-Nacach, A., Roseman, J. M., McGwin, G., Friedman, A. W., Baethge, B. A., Reveille, J. D., et al., and the LUMINA Study Group. Systemic lupus erythematosus in three ethnic groups. VI. Factors associated with fatigue within 5 years of criteria diagnosis. Lupus 2000; 9: 101–9.
[2] Krupp, L. B., LaRocca, N. G., Muir-Nash, J., Steinberg, A. D. The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. Arch. Neurol. 1989; 46: 1121–3.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4674

THU0274 FOOTPRINTS OF NEUTROPHIL EXTRACELLULAR TRAPS ARE ELEVATED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

I. Jeremic[1], O. Djuric[2], B. Bonaci Nikolic[3]. *[1]Institute of Rheumatology, Belgrade; [2]Insttute of Epdemiology; [3]Institute of Allergy and Clinical Immunology, Belgrade, Serbia*

Background: Impaired removal of apoptotic waste in patients with systemic lupus erythematosus-SLE has been long known as important factor that trigger autoimmune response. Neutrophil extracellular traps could be another source of autoantigens in patients with SLE.
Objectives: The aim of this study was to compare NETs markers (free DNA, myeloperoxidase) and dnase I in SEL patients and healthy controls, as well to assess their relationship with serological markers of SLE disease activity (C3 and C4 complement components, anti-dsDNA antibodies) and SLEDAI score (clinical disease activity index).
Methods: We analysed 111 sera obtained from 84 SEL patients (60 patients had 1 sample and 24 patients had 2 or 3 samples) and 50 healthy blood donors. Serum levels of myeloperoxidase, B-cell activating factor-BAFF, cell free DNA, complement components C3 and C3, antibody to dsDNA by CLIFT end ELISA assays, netolitic activity and DNAse I were measured. The group of 35 patients was selected (11 with *de novo* disease) for which clinical data were recorded.
Results: SLE patients had significantly higher concentration of free serum DNA (1.69±0.23 vs. 1.42±031 ng/mL, p=0.0003), dnase I (10.4±6.9 vs. 5.8±5.7 U/mL, $p<0.05$), anti-MPO antibodies (13.8±43.4 vs. 0.9±0.3 U/mL, $p<0.001$) and myeloperoxidase activity (1607±2353 vs. 560.3±182.5 RU, $p<0.05$) in comparison to healthy controls. The ability of sera to degrade NETs was similar in both groups. Free DNA, dnase I, BAFF and anti-MPO levels as well myeloperoxidase activity showed significant correlation with anti-dsDNA antibodies measured by ELISA test. None of studied parameters showed correlation with C3 and C4 complement components. C3 and anti-dsDNA antibodies measured by indirect immune fluorescence were independent predictors of SLEDAI score in multivariate analysis, while BAFF and dnase I were significant in univariate analysis. Free cDNA was predictor of SLEDAI score higher than 7 in univariate analysis.
Conclusions: Increased amount of NETs markers found in lupus sera confirms their role in SLE pathogenesis. Determination of NETs markers could be useful serological parameter to follow disease activity in SLE patients.
References:
[1] Skiljevic D, Jeremic I, Nikolic M, Andrejevic S, Sefik-Bukilica M, Stojimirovic B, et al. Serum DNase I activity in systemic lupus erythematosus: correlation with immunoserological markers, the disease activity and organ involvement. Clin Chem Lab Med. 2013;51(5):1083–91.
[2] Garcia-Romo GS, Caielli S, Vega B, Connolly J, Allantaz F, Xu Z, et al. Netting Neutrophils Are Major Inducers of Type I IFN Production in Pediatric Systemic Lupus Erythematosus. Sci Transl Med.2011;3(73):7.

[3] Hakkim A, Fürnrohr BG, Amann K, Laube B, Abed UA, Brinkmann V, et al. Impairment of neutrophil extracellular trap degradation is associated with lupus nephritis. Proc Natl Acad Sci U S A. 2010;107(21):9813–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4879

THU0275 IMPORTANCE OF SERUM TITERS OF ANTIBODIES AGAINST DOMAIN 1 OF B2 GLYCOPROTEIN 1

J.A. Gómez-Puerta[1,2], T. Urrego[2], A. Hernández[3], S. Ruiz Giraldo[3], C. Rua[4], J. Duque Botero[3], M. Velázquez[5], A.P. Cadavid[5], A.L. Vanegas-García[1,6], C.H. Muñoz[1,6], L.A. González[1], G. Vásquez[1,2]. *[1]Grupo de Reumatología; [2]Grupo de Inmunología Celular e Inmunogenética; [3]Departamento de Medicina Interna; [4]Grupo de Investigación en Trombosis; [5]Grupo de Reproducción, Universidad de Antioquia; [6]Grupo de Reumatología, Hospital San Vicente Fundación, Medellín, Colombia*

Background: There is an increasing interest in the study of domain reactivity of antibodies against β2 glycoprotein I (anti-B2GPI) in patients with antiphospholipid syndrome (APS). Antibodies targeting domain 1 of the molecule (anti-D1) as the most relevant autoantibody subpopulation. Previous information of anti-D1 B2GPI comes from APS cohorts with Caucasian, Asian, and African-American patients. However, there are no studies in Mestizo and Afro-Latin American patients.
Objectives: Our aim was to evaluate the prevalence of Anti-D1 B2GPI antibodies in a cohort of Colombian patients with systemic lupus erythematosus (SLE) with and without thrombosis, primary APS and patients with previous history of recurrent miscarriages (RM) without APS criteria.
Methods: In this cross-sectional study we measured Anti-D1 B2GPI antibodies in a group of patients from Rheumatology Department, Coagulation clinic and Recurrent Pregnancy Loss Program at the Reproduction Group at Hospital San Vicente Fundación and Universidad de Antioquia, respectively, at Medellín, Colombia. Anti-D1 B2GP1 antibodies were tested using a chemiluminescent immunoassay (QUANTA Flash B2GPI IgG, Inova Diagnostics). Mann-Whitney tests were used to compare data.
Results: One hundred and seventy seven (median age 33.5±12.1 years; 89% women) patients were included. One hundred thirty eight patients had SLE (78%), 27 primary APS (15%) and 13 RM (7%). Fifty five (31%) out of 177 patients had history of thrombosis and 41 (23%) of pregnancy losses. Overall, Anti-D1 B2GPI antibodies were positive (>20 CU) in 35 (20%) of patients. Anti-D1 B2GPI were positive in 23%, 17% and 0% of patients with primary APS, SLE and RM, respectively. Overall, serum Anti-D1 B2GPI were significantly higher in patients with than without previous thrombosis (149.1±336.1 vs 16.3±61.8 CU, p<0.0001) and in patients (SLE or primary APS) with previous history of pregnancy losses (40.2±123.1 vs 21.0±74.5 CU, p=0.04). Anti-D1 B2GPI were significantly higher in patients with primary APS vs SLE with thrombosis, and in patients with SLE with thrombosis vs SLE without thrombosis (Figure). No clinical associations were found among Anti-D1 B2GPI antibodies and other APS features.

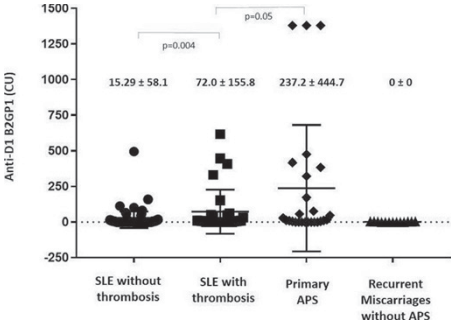


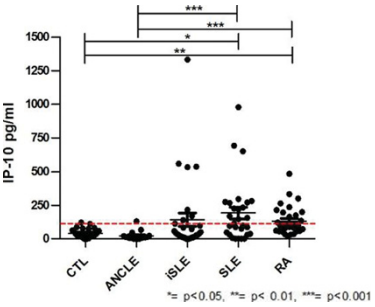
Figure 1. Mean serum levels of Anti-D1 B2GPI in a cohort of 177 patients.

Conclusions: Serum titers of Anti-D1 B2GPI antibodies were more than 9 times and 2 times higher in patients with thrombosis and pregnancy losses, respectively. In addition, serum titers were significantly higher in patients with primary APS than in SLE patients with thrombosis. Whether Anti D1- B2GPI antibodies titers are useful to differentiate patient with primary and secondary APS requires further analysis.
Acknowledgements: JA Gómez-Puerta was supported by Colciencias (conv. 656 de 2014). Anti-D1 B2GPI antibodies were provided by Inova, Werfen, Colombia
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2767

THU0276 INTERFERON-RELATED CHEMOKINE IP-10 IS A POTENTIAL BIOMARKER IN INCOMPLETE SYSTEMIC LUPUS ERYTHEMATOSUS

W. Lambers[1], K. De Leeuw[1], M. Jonkman[2], H. Bootsma[1], J. Westra[1]. *[1]Rheumatology and Clinical Immunology; [2]Dermatology, UMCG, Groningen, Netherlands*

Background: Incomplete SLE (iSLE) is the designation of patients who display symptoms that are typical for SLE, but with insufficient criteria to fulfil the diagnosis. Unfortunately, predictive biomarkers for SLE development are lacking. Increased IFN-type I production is an important factor in the pathogenesis of SLE. Interferon-regulated chemokines therefore could possibly be useful as biomarkers for disease progression to SLE. Candidate biomarkers IFN-γ induced protein 10 (IP-10) and monocyte chemo attractant protein (MCP-1) have shown to be increased in SLE and to correlate with disease activity.
Objectives: To determine possible candidate biomarkers IFN-γ induced protein 10 (IP-10) and monocyte chemo attractant protein (MCP-1) in patients with iSLE.
Methods: Serum samples were collected of 30 iSLE patients, 29 SLE patients, and 17 ANA-negative patients with histologically proven cutaneous lupus erythematosus (ANCLE). Outcomes were compared with 25 age- and gender-matched controls (CTL) and 31 rheumatoid arthritis (RA) patients as disease control group. Levels of IP-10 and MCP-1 were measured using ELISA.
Results: IP-10 was significantly increased in SLE and RA patients compared with CTL and ANCLE. IP-10 levels were increased in 23% of iSLE patients. These patients had higher SLE disease activity index (SLEDAI) and more frequently decreased C3 level and joint involvement compared to those with normal IP-10 levels. Regarding MCP-1 levels, no significant differences were found between any of the groups and no correlations with clinical markers was found.



Conclusions: Levels of IP-10, but not MCP-1, might be useful as a predictive biomarker for progression to SLE in patients with iSLE, although future prospective longitudinal analyses are needed to confirm this hypothesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4016

THU0277 REASONS FOR DEFICIENCY OF PHYSICAL INACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

L. Lipovskiy, C. Baerwald, O. Seifert. *Rheumatology Unit, Department of Internal Medicine, University Hospital Leipzig, Leipzig, Germany*

Background: Systemic lupus erythematosus (SLE) is associated with musculoskeletal complaints, fatigue and reduced quality of life. Physical exercise can play a crucial role in the treatment of rheumatic diseases, optimizing both physical and mental health.
Objectives: To characterize physical activity (PA) and its impact on SLE patients.
Methods: 85 SLE outpatients (92% female; age 44.2±12.5; 57.5% with SLEDAI score ≤5, 42.5% with SLEDAI score ≥6) were included in this study. The following questionnaires were utilized: painDETECT, visual analog scale for pain (VAS 0 - 100 mm), short-form health survey (SF - 36, quality of life), the FACIT-Fatigue Scale and the Health Assessment Questionnaire (HAQ - DI). PA was assessed for every patient using the long form of International Physical Activity Questionnaire (IPAQ - LF) and the Metabolic Equivalent of Task (MET) minutes per week (min/wk) (physiological measurement expressing calories of physical activities). The participants were classified in 3 groups according to the PA levels conferring to the guidelines of IPAQ. Physical inactivity was defined as fewer than 150 min/week spent in moderate or vigorous physical activities. Furthermore, the patient reasons "to be not physical active" and their opinion regarding the influence of PA on disease-related symptoms (on a scale of 0–10) were obtained.
Results: 10.6% of SLE patients were physically inactive (525.2±277.3 MET-Min/wk), 31.8% had a moderate physical activity, and 57.6% were physically active. Physical inactivity was associated with higher fatigue (FACIT-F, p<0.04) and lower "vitality" (SF-36, p<0.03) scores. Moreover, the subjective impact of fatigue on PA was significantly higher in physically inactive patients compared to physically active patients (the patient's score: 7.75±1.25 vs. 5.5±0.94, p<0.04). Moderate and severe pain (more than 40 mm VAS) was also associated with physical inactivity (OR 12.38, 95% CI 1.69 to 144.3, p=0.0056). In contrast, HAQ-DI was not related to levels of PA. Although physical inactivity correlated

with a higher total disease activity score (SLEDAI ≥6) (OR 9.9, 95% CI 2.1 to 49.9, p=0.0056), neither of the single SLEDAI items and organ manifestations including musculoskeletal manifestations was associated with physical inactivity. Interestingly, the study could not detect any statistical difference in organ manifestations and SLEDAI scores between patients with moderate and high PA. According to the patient's report, the main SLE-related reasons "not to be physically active" for all three groups were "lupus flare" (35.6%), "fatigue" (26.9%) as well as "joint complaints" (15.7%). The main general barriers for PA were "comorbidity" (35,6%) and "lack of motivation" (26,9%). Furthermore, the subjective impact of "bad weather conditions" on physical activity was significantly greater in physically inactive patients compared with the two other groups (the patient's report: 6.58±2.3 vs. 3.49±0.7, p<0.03).

Conclusions: The main reason for the patients not to be physically active was fatigue and pain. The study also indicates that not only somatic symptoms could decrease the levels of PA in SLE patients. Further research on psychological factors is needed. The study underlines the need for management strategies that specifically target physical activity as a part of an overall SLE management program.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6024

THU0278 COMPARISON OF THE 2016 ACR/EULAR AND THE 2002 AECG CLASSIFICATION CRITERIA IN A COHORT OF PATIENTS WITH SUSPECTED PRIMARY SJÖGREN'S SYNDROME

M. Le Goff[1], D. Cornec[2], S. Jousse-Joulin[2], D. Guellec[2], S. Costa[2], T. Marhadour[2], R. Le Berre[2], S. Genestet[2], B. Cochener[2], S. Boisrame-Gastrin[2], Y. Renaudineau[2], J.-O. Pers[2], A. Saraux[2], V. Devauchelle-Pensec[2]. *[1]Rheumatology; [2]CHRU Brest, Brest, France*

Background: New consensual classification criteria for primary Sjögren's syndrome (pSS) have been recently developed and endorsed by ACR and EULAR. They differ substantially from previously used AECG criteria in that they consider systemic involvement (defined as ESSDAI score ≥1) as well as sicca symptoms as entry criteria before applying a weighted score. Evaluation of the concordance and differences between the two sets of criteria in independent patient populations is mandatory to establish how future clinical studies using the new criteria will be comparable to previously published studies. Major salivary gland ultrasonography (SGUS) has demonstrated promising diagnostic performance in previous studies, but was not included in these new classification criteria.

Methods: This cross-sectional study was conducted in the monocentric Brittany cohort (DIApSS cohort) of patients with suspected pSS (sicca symptoms, parotidomegaly or extraglandular manifestations suggestive of pSS). All patients had standardized clinical examination, basic biology, immunological tests and minor labial salivary gland biopsy. SGUS in mode B was performed by the same experienced operator, who was blinded to the diagnosis. Agreement between the two sets of criteria was assessed using Cohen's κ coefficient and the characteristics of discordant patients were detailed.

Results: 290 patients were prospectively included between 2006 and 2016. Mean age was 55.6±13.2 years, 92.1% were female and mean duration of the symptoms 6.0±6.6 years. More patients fulfilled ACR/EULAR criteria (n=125, 43.1%) than AECG criteria (n=114, 39.3%). 114 patients (39.3%) fulfilled both criteria, 11 (3.8%) fulfilled ACR/EULAR only, 0 AECG only and 165 (56.9%) none of the criteria. Concordance between both criteria was good (kappa=0.9). Compared to patients fulfilling both criteria, patients fulfilling ACR/EULAR but not AECG criteria (n=11) had similar age, similar symptom duration, but less frequent sicca symptoms (eye dryness 18.2% versus 96.5%; mouth dryness 54.5% versus 97.4%, p<0.01 for both), and less frequent salivary gland dysfunction (salivary flow ≤0.1 ml/min: 20% versus 70.9%, p<0.01).They had characteristic features of pSS, with frequent systemic involvement at diagnosis (90.9%), positive salivary gland biopsy (90.9%), abnormal SGUS (44.4%) and presence of anti-SSA/SSB autoantibodies (45.4%). 46.5% of them had a diagnosis of pSS according to the physician. Among patients negative for the two sets of criteria, 12% had an abnormal SGUS and 10.3% received a clinical diagnosis of pSS based on physician opinion.

Conclusions: Agreement between AECG criteria and new ACR/EULAR criteria is good suggesting that they select quite similar patients. ACR/EULAR criteria display a slightly higher sensitivity and are able to detect more patients with systemic involvement, but some of these patients did not have pSS according to the physician diagnosis. As previously demonstrated for AECG criteria, SGUS inclusion into ACR/EULAR criteria may further enhance their sensitivity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5446

THU0279 ARE THE PULMONARY INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS ASSOCIATED WITH A HIGHER PREVALENCE OF COMORBIDITIES?

M. Cebanu[1], V. Salaru[2], V. Sadovici[3], M. Pasali[3], N. Loghin-Oprea[3], M. Mazur[3], L. Mazur[4], G. Ciobanu[1]. *[1]Emergency Medicine; [2]Family Medicine; [3]Rheumatology; [4]Cardiology, State University of Medicine and Pharmacy "Nicolae Testemitanu", Chisinau, Moldova, Republic of*

Background: Patients with systemic lupus erythematosus have a very high burden of comorbidities. Identification and management of these comorbidities are critical for optimal medical care to this population.

Objectives: To assess the prevalence of comorbidities in SLE patients with pulmonary involvement.

Methods: In a cross-sectional study, patients who fulfiled the SLICC (2012) classification criteria for SLE, were recruited from Rheumatology Departement. Data collection included demographics, disease duration, physician-rated indices of disease activity (by SLAM), damage (by SLICC/ACR DI) and Charlson comorbidity Index. The pulmonary involvement was assessed by chest X-ray, EcoCG Doppler and pulmonary functional tests.

Results: The study included 106 patients (97 women, 9 males) with a mean age (±SD) of 41,1±12,6 yrs, mean disease duration of 90,3±87,3 months. The disease activity by SLAM was 11±5,17 points and mean SLICC/ACR DI 1,9±2,4 points (66% of patients had at least 1 point). Pulmonary assessment revealed that 45 (42,5%) patients had different types of pulmonary involvement due to lupus: pleuritis - 24 patients, pneumonitis – 1 patient, pulmonary embolism – 4 patients, interstitial lung disease – 15, shrinking lung syndrome – 1 and pulmonary arterial hypertension – 9 patients. The most frequent comorbidities in study group were: arterial hypertension - in 57 (53,7%) cases, from which 33 (57,9%) patients had pulmonary involvement and 24 (42,1%) without, obesity (BMI>30 kg/m^2) had 29 (27,4%) patients, from which 17 (58,6%) with lung involvement and 12 (41,4%) without, anemia (Hb<110g/l) had 24 (22,6%) patients, from them 14 (58,3%) with lung disease and 10 (41,7%) patients - without, heart failure (I-II NYHA) had 23 (21,7%) patients, from them 20 (86,9%) were with lung implication, thyroiditis had 22 (20,8%) and 15 (68,2%) of them were with pulmonary involvement, diabetes mellitus type II had only 6 (5,7%) patients and half of them had lung disease. Assessing the impact of associated diseases through Charlson comorbidity index, we found that the score for patients diagnosed with damage to the respiratory system was twice as big vs. patients without respiratory impairment from SLE (6,3±2,4 vs. 3,4±1,4 points). Also, Charlson comorbidity score ≥1 was identified as a risk factor for lung involvement (OR 5,5294, 95% CI 2,367 – 12,91, p<0,01). Evaluation of disease activity by SLAM showed that patients with lung involvement have a higher disease activity vs. patients without (13,9±6,0 vs. 8,9±4,0, p<0,05).

Conclusions: On the one hand, according to our results patients with SLE and pulmonary involvement have a higher prevalence of comorbidities comparative with patients without them. Hypertension was found to be the most common comorbidity and it was determined in 73,3% of patients with impaired respiratory system (p<0,01). On the other hand, association of comorbidities (Charlson comorbidity score ≥1) was identified as a risk factor for lung lesions.

References:

[1] Rees F., Doherty M., Grainge M. et al. The Burden of Comorbidity in Systemic Lupus Erythematosus. Rheumatology (2015), 54 (suppl_1): i166.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6776

THU0280 COMPARISON OF CLASSIFICATION CRITERIA FOR SJÖGREN'S SYNDROME FROM 2002 AND 2016 IN AN INCIDENT COHORT DIAGNOSED 2007 TO 2011 FROM STOCKHOLM COUNTY SWEDEN

M. Kvarnström, M. Wahren-Herlenius. *Dep. of Medicine, Unit of Experimental Rheumatology, Karolinska Institutet, Karolinska Uniververity Hospital, Stockholm, Sweden*

Background: The current American-European Consensus Criteria (AECC) from 2002 has been the most widely used and applied all over the world. New classification criteria for Sjögren's syndrome was published in 2016, designed in a collaboration between ACR and EULAR. They are made up of a scoring system in which 4 points are required for classification. The weight/score is as follows:

- Labial salivary gland biopsy with focal lymphocytic sialadenitis and focus score of ≥1 foci/4 mm^2 – 3
- Anti-SSA/Ro positive – 3
- Ocular Staining Score ≥5 (or van Bijsterveld score ≥4) in at least 1 eye – 1
- Schirmer's test ≤5 mm/5 minutes in at least 1 eye – 1
- Unstimulated whole saliva flow rate ≤0.1 ml/minute – 1.

Objectives: Comparison of classification criteria for Sjögren's syndrome from 2002 and 2016 in a 5 year cohort of incident patients diagnosed 2007 to 2011 from Karolinska University Hospital, Stockholm County, Sweden.

We wanted to examine the consistency between the different classification criteria.

Methods: We compared a cohort of all diagnosed patients with primary Sjögren's syndrome during the years 2007 to 2011 at the Dep. of Rheumatology at Karolinska University Hospital in Stockholm Sweden. Data on the item Ocular Staining Score ≥5 was not available since it is not included in AECC. The cohort consisted of 199 patients all fulfilling the 2002 AECC. Another eight patients did

not fulfill the criteria but were regarded as possible Sjögren's syndrome under development by the rheumatologist who investigated them.
Results: 196 of the 199 pSS patients also fulfilled the new criteria from 2016. The three patients who did not only had SSB autoantibodies and no positive biopsy. Of eight patients with suspicion of Sjögren's syndrome under development, three fulfilled the new criteria.
Conclusions: The classification criteria for Sjögren's syndrome from 2002 and 2016 are consistent. This study indicates a possibility that the new criteria may be more sensitive early in the disease development, as long as the classification is not based on autoantibody positivity against SSB.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5377

THU0281 LONG-TERM PROGNOSIS AND PREDICTINGFACTORS OF CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A MULTI-CENTER COHORT STUDY FROM CSTAR REGISTRY

M. Li[1], Z. Wang[1], Y. Wang[2], X. Zeng[1] on behalf of CSTAR. [1]*Peking Union Medical College Hospital;* [2]*Chinese Academy of Medical Science, Beijing, China*

Objectives: To investigate the long-term outcomes, both mortality and damage, and related prognostic factors of patients with systemic lupus erythematosus (SLE) in the CSTAR (Chinese SLE Treatment and Research group) registry cohort.
Methods: All of the patients were enrolled from April 2009 to February 2010. They were followed up at clinic and were telephone interviewed at the endpoint. Demographic data, clinical manifestations, activity (SLEDAI-2K), damage scores (SLLIC/Damage Index), and medications were collected. Data were censored at the last clinic visit or telephone interview. Survival rates were studied by Kaplan-Meier method, and COX proportional hazard model was adopted to perform the analysis of predicting factors for mortality.
Results: A total of 2104 patients were recruited at baseline, and 1494 patients were successfully followed up. The cumulative 1, 3 and 5-year survival ratesfrom diagnosis were 99.0%, 98.1% and 97.1%. 78 patients died during follow-up, and the main death causes were infection (34.6%), active disease (26.9%), cardiovascular and cerebrovascular events (6.41%) and malignancy (5.13%). At entry, 247 patients presented with irreversible organ damage and it increased to 398 patients at the endpoint. The major accumulated organ damages were renal (25.9%), musculoskeletal (20.2%), neuropsychiatric (12.4%), and pulmonary (10.8%) damage. Cox regressionshowed that male, late onset age (≥50y), onset to diagnosis time ≥1 year, previous organ damage, renal involvement, pulmonary arterial hypertension, neuropsychiatric involvement, serositis and the number of involved organ systems ≥3predict for higher mortality.

Table 1: Independent predictors of mortality obtained by univariate analysis

Univariate analysis	HR	95%CI	*p*
Age at onset ≥ 50 years	3.935	2.111-7.334	<0.001
Onset to diagnosis ≥ 1 year	1.996	1.251-3.186	0.004
Gender	2.082	1.119-3.873	0.021
Baseline organ damage*	2.846	1.757-4.610	<0.001
Renal involvement*	2.434	1.425-4.156	0.001
Hematologic involvement*	1.605	0.978-2.635	0.061
Interstitial lung disease*	2.167	0.973-4.823	0.058
Pulmonary arterial hypertension*	4.126	2.107-8.081	<0.001
Neuropsychiatric involvement*	2.290	1.169-4.486	0.016
Serositis*	2.580	1.605-4.148	<0.001
No. of involved organ systems (1) *	1.793	0.719-4.466	0.210
No. of involved organ systems (2) *	2.045	0.805-5.195	0.133
No. of involved organ systems (≥3) *	5.638	2.339-13.589	<0.001

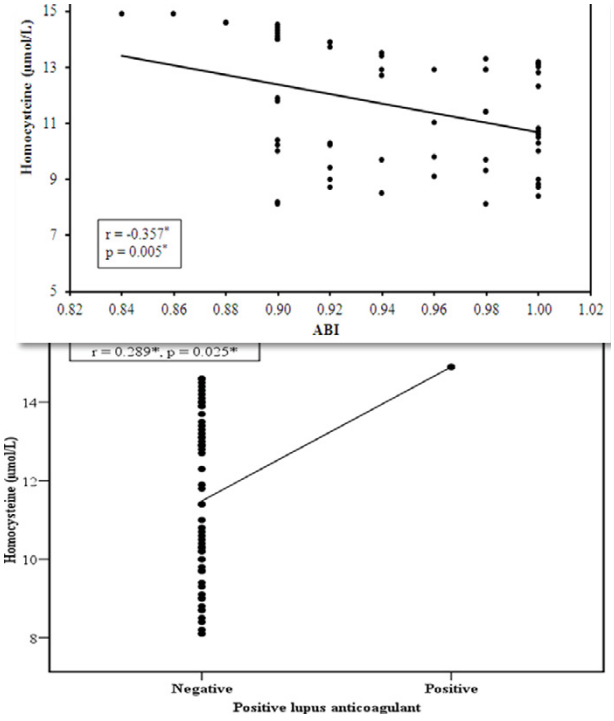
* Performed after controlling of gender, onset age and time from onset to diagnosis

Conclusions: Long-term survival rates have improved for Chinese SLE patients. Early diagnosis, preventing fromthe emerging systemic organ involvements and organ damagecould be the treating target for the management of SLE patients in China.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5791

THU0282 HOMOCYSTEINE: ANY ROLE IN PERIPHERAL VASCULAR DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS?

N. Mohannad[1], M. Tayel[2], M.H. Megallaa[3]. [1]*Internal Medicine, Rheumatology Unit, Alexandria University Hospitals, Alexandria University;* [2]*Internal Medicine, Rheumatology Unit;* [3]*Internal Medicine, Alexandria University, Alexandria, Egypt*

Background: Many are the independent risk factors for premature atherosclerosis in general & peripheral vascular disease (PVD) in particular in SLE patients. Plasma homocysteine (HCY) is a known risk factor for atherosclerosis. Atherosclerosis can lead to many cardiovascular diseases as myocardial infarction, stroke and claudication
Objectives: To compare the occurrence PVD of the lower extremity of SLE patients (pts) with age and sex matched controls and evaluate the role of HCY level in its occurrence
Methods: Body mass index (BMI), blood pressure, lipid profile, titers of autoantibodies [ANA, anticardiolipin antibodies ACL (IgM, IgG)], C3, C4, plasma HCY level were assessed, SLEDAI and (SLICC/ACRDI)were calculated. PVD evaluation was done by measuring Ankle Brachial Index (ABI) with values <0.9 considered diagnostic of PVD; in 60 SLE pts and 30 age-matched controls. Patients with previous hypertension, diabetes, other collagenic diseases & smokers were excluded
Results: Eighty-eight percent of the pts were women. The mean age (SD) was 30.40 (11.46) years & mean disease duration 3.61 (4.92)years. 50 pts were asymptomatic, 5 had mild & 5 had moderate claudications.SLE pts had significant higher total cholesterol (TC), LDL than controls 224.1±57.8 vs 181.1±41.1 mg/dl & 162.7±57.0 vs 119.5±13.4 (<0.001*) respectively, higher HCY 11.6±2.1 & 6.4±0.1 μmol/L (p<0.001*) & lower HDL 47.2±13.1 &52.6±3.7 mg/dl (p=0.004*). Low ABI was found in 30% of SLE pts but none of the controls (p=0.001*) & was correlated with higher HCY level (p=0.005*), TC & LDL (p<0.001* & p<0.001*), but not TG (p=0.748) or asymptomatic pts, presence of mild or moderate claudications (p=0.468,1.000, 0.154), still its value negatively correlated with lupus anticoagulant (LA) (p=0.002), ACL IgM (p<0.001*), the presence of lupus nephritis (LN) (p<0.001*) & SLICC/ACRDI (p=0.017*) but not with disease duration (dd) (p=0.535), Anti ds DNA (p=0.364), ACL IgG (p=0.8940), C4 (p=0.168) or SLEDAI (p=0.074).No correlation was found between HCY level and pts' age, dd, age at diagnosis, BMI, Anti ds DNA, ACL IgG, C4 & SLEDAI (p=0.521, 0.098, 0.946, 0.502, 0.346, 0.335, 0.325, 0.787). A positive correlation was found between HCY level and LA, ACL IgM, TC, LDL, the presence of LN & SLICC/ACRDI with a p value of 0.025*, <0.001*, <0.001*, 0.003*, 0.001*, 0.001* & negative one with HDL p=0.023*



Conclusions: 83.3% of SLE pts were asymptomatic or had atypical symptoms of PVD still 30% of the patients had low ABI. ABI can be a more reliable, non-invasive test to assess PVD than the conventional methods of pulse palpation or history of claudication in SLE pts.Both traditional & nontraditional risk factors of atherosclerosis are important but HCY can play a role, among other factors, as independent risk factor of PVD in SLE
References:
[1] Rayford R et al. PVD in SLE Patients. J Clin Rheum. 2013; 7:367–70.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4615

THU0283 RESILIENCE AND ASSOCIATED FACTORS AMONG WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

P. Munguía-Realpozo[1], M. García-Carrasco[2,3], J. León-Vázquez[4], M.F. Balcazar-Vargas[2], E.A. Jiménez-Herrera[4], I. Etchegaray-Morales[4], C. Mendoza Pinto[2,4]. *[1]Rheumatology, Hospital de Especialidades Centro Médico Nacional "La Raza" IMSS, Cd. México; [2]Immunology and Rheumatology, Medicine School, BUAP; [3]Systemic Autoimmune Diseases Research Unit, Hgr 36-Cibior, IMSS; [4]Systemic Autoimmune Diseases Research Unit, Hgr-36-Cibior Imss, Puebla, Mexico*

Background: Resilience is the human capacity to respond positively to adverse situations, enabling individuals to achieve, maintain, or recover physical or emotional health after devastating illness, losses, or other stressful situations. Resilience may be an important factor in health promotion.
Objectives: The aim of this study was to evaluate resilience and possible associated factors in patients with systemic lupus erythematosus (SLE).
Methods: In a cross-sectional study, 123 SLE women and 133 age-matched controls were evaluated using the Spanish version of Wagnild and Young's Resilience Scale (WYRS, 1993). SLE patients underwent a structured interview to collect sociodemographic data, including socioeconomic status measured by the Graffar method. The Center for Epidemiologic Studies Depression Scale (CES-D) was used to measure depressive symptoms.
Results: The median age and duration disease of SLE women was 45 (IQR: 34–54) years and 11 (IQR: 8–15) years, respectively. Thirty-three percent had depressive symptoms (CESD score $\geq$16). Resilience scores did not differ between patients and controls (median 80 IQR: 75–87 vs.80 IQR: 74–85;p=0.38). However, patients with SLE had a higher personal competence factor than controls. Personal competence factor correlated negatively with age and socioeconomic status (R= -0.220, p: 0.05 and R= -0.357, $p<0.001$) and positively with educational level (R=0.324, $p<0.001$). Less resilience (lower WYRS scores) correlated with depressed mood (higher CESD scores) (R= -0.537, $p<0.001$).
Conclusions: Resilience in patients with SLE did not differ from that of controls. Age, socioeconomic status and depressive symptoms correlated with low resilience. Educational level correlated with higher resilience.
References:
[1] Windle G, Bennett K, Noyes J. A methodological review of resilience measurement scales. Health Qual Life Outcomes. 2011; 9(8): 1–18.
[2] Pousa DA, Revoredo LS, Vilar MJ and Chavez EM. Resilience and Treatment Adhesion in Patients with Systemic Lupus Erythematosus. Open Rheumatol J. 2014; 8: 1–8.
Acknowledgements: We would like to thank David Buss for his valuable guidance and advice during this project.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2481

THU0284 PREDICTING SURVIVAL IN 6240 PATIENTS WITH PRIMARY SJÖGREN' SYNDROME (BIG DATA SJÖGREN PROJECT)

P. Brito-Zerón[1,2], N. Acar-Denizli[3], M. Zeher[4], A. Rasmussen[5], X. Li[6], C. Baldini[7], J.-E. Gottenberg[8], D. Danda[9], L. Quartuccio[10], G. Hernandez-Molina[11], A.A. Kruize[12], S.-H. Park[13], M. Kvarnström[14], S. Praprotnik[15], D. Sene[16], E. Bartoloni[17], R. Solans[18], T. Mandl[19], Y. Suzuki[20], M. Rischmueller[21], G. Nordmark[22], G. Fraile[23], A. Sebastian[24], H. Bootsma[25], T. Nakamura[26], V. Valim[27], R. Giacomelli[28], R. Seror[29], V. Devauchelle-Pensec[30], B. Hofauer[31], M. Bombardieri[32], V. Trevisani[33], D. Hammenfors[34], R. Priori[35], S.G. Pasoto[36], J. Morel[37], S. Retamozo[38], T.A. Gheita[39], F. Atzeni[40], C. Vollenveider[41], X. Mariette[29], M. Ramos-Casals[2] on behalf of the EULAR-SS Task Force Big Data Consortium. *[1]Hosp CIMA-Sanitas; [2]Hosp Clínic, Barcelona, Spain; [3]Msgsü, Istanbul, Turkey; [4]Univ, Debrecen, Hungary; [5]OMRF, Oklahoma, United States; [6]Anhui Hosp, Hefei, China; [7]Univ, Pisa, Italy; [8]Univ, Strasbourg, France; [9]CMC, Vellore, India; [10]Santa Maria, Udine, Italy; [11]INCMNSZ, México, Mexico; [12]UMC, Utrecht, Netherlands; [13]Catholic Univ, Seoul, Korea, Republic Of; [14]Karolinska Instit, Stockholm, Sweden; [15]UMCL, Ljubljana, Slovenia; [16]Lariboisière Hosp, Paris, France; [17]Univ, Perugia, Italy; [18]Hosp Vall Hebron, Barcelona, Spain; [19]Lund Univ, Malmö, Sweden; [20]Univ, Kanazawa, Japan; [21]TQEH, Adelaide, Australia; [22]Univ, Uppsala, Sweden; [23]Hosp Ramón Cajal, Madrid, Spain; [24]Med Hosp, Wroclaw, Poland; [25]Univ, Groningen, Netherlands; [26]Univ, Nagasaki, Japan; [27]UFES, Vitória, Brazil; [28]Univ, L'Aquila, Italy; [29]Univ Paris Sud, Paris; [30]Univ, Brest, France; [31]TUM, München, Germany; [32]QMUL, London, United Kingdom; [33]UNIFESP, Sao Paulo, Brazil; [34]Haukeland Hosp, Bergen, Norway; [35]Sapienza Univ, Rome, Italy; [36]USP, Sao Paulo, Brazil; [37]Univ, Montpellier, France; [38]INICSA, Cordoba, Argentina; [39]Univ, Cairo, Egypt; [40]L.Sacco Univ Hosp, Milan, Italy; [41]German Hosp, Buenos Aires, Argentina*

Objectives: To correlate the main features at diagnosis with survival in a multicenter international cohort of patients with primary Sjögren syndrome (SS).
Methods: The Big Data Sjögren Project was formed in 2014 to take a "high-definition" picture of the main features of primary SS by merging international SS databases (9302 consecutive patients recruited from 21 countries of the 5 continents)
Results: Data about survival at the last visit was available in 6240 patients (5831 women, mean age at diagnosis of 53yrs, 82% White). After a mean follow-up of 7.1yrs, 407 (6%) patients died. Patients who died were more frequently men (10% vs 6%, p=0.004) and White (96% vs 81%, $p<0.001$), had a higher mean age at diagnosis (64 vs 52yrs. $p<0.001$) and a higher frequency of abnormal ocular (95% vs 87%, $p<0.001$) and oral (90% vs 79%, $p<0.001$) tests in comparison with survivors; sicca symptoms and salivary gland biopsy were unrelated to survival. Immunologically, patients who died showed a higher frequency of RF (52% vs 46%, p=0.039) and cryoglobulins (18% vs 7%, $p<0.001$). Logistic regression identified as independent variables the age at diagnosis (OR 1.07), male gender (OR 1.77), abnormal ocular (OR 5.79) and oral (OR 2.10) tests, and cryoglobulins (OR 3.10). Time-adjusted multivariate Cox proportional-hazards regression analysis confirmed age at diagnosis (OR 1.12, CI95% 1.10–1.14), male gender (OR 2.12, CI95% 1.36–3.29) and cryoglobulins (OR 2.43, CI95% 1.72–3.42) as independent variables related to death.
Conclusions: An older age at diagnosis, male gender and serum cryoglobulins were the principal risk factors associated with death in this large multiethnic cohort of patients with primary SS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4446

THU0285 USE OF CONTRACEPTIVE METHODS IN A SINGLE CENTER COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS FROM ARGENTINA

R.A. Gomez, F.M. Paniego, M. Garcia Carrasco, D. Dubinsky, G. Nasswetter. *Rheumatology, Hospital de Clinicas Jose de San Martin, Ciudad Autónoma de Buenos Aires, Argentina*

Background: Systemic Lupus Erythematosus (SLE) may associate with flares, an unfavorable course and the need of teratogenic treatment during pregnancy. Not every contraceptive method (CM) may be used in this patients. There are guidelines for their use according to existing morbidity and SLE activity[1].
Objectives: Describe the use of CM in a cohort of outpatients with SLE
Methods: Descriptive, observational, cross-sectional study. Patients $\geq$16 years old with SLE (SLICC 2012) and $\geq$1 visit during the last year of our database were included. Those with menopause were excluded. We analyzed demographic data; disease duration; antiphospholipid antibodies (aPL) and antiphospholipid syndrome (APS) (Sapporo 2006); socioeconomic status (Graffar scale); disease activity (SELENA-SLEDAI) and accrual damage (SLICC); use of teratogens: Methotrexate (MTX), Mycophenolate (MYC), Cyclophosphamide (CYC), biologic drugs (BD), self-reported sexual status (active/non active) and CM: intrauterine device (IUD), condom (Cdm) and hormonal contraceptive pill (CP).
Results: 132/219 were included. Female 91.6%, age: 30.1 (16–49) years, disease duration: 38.5 (1–324) months, SELENA-SLEDAI: 3.5 (0–29), SLICC: 0.5 (0–5).
Sexual status and use of CM: were available for 120 patients. Sexually active (SA) 73%, female 77%. CM in SA patients: 74%: 5% CP, 77% Cdm and 18% IUD.
CM in female patients stratified by Graffar (GF): GF I (n=1): none SA; GF II: (n=19): 84% SA, 75% of them used CM (75% Cdm, 25% IUD); GF III (n=33): 82% sexually active, 81% used CM (86% Cdm, 14% IUD), GF IV (n=41) 75% SA, 68% used CM (9% CP, 71% Cdm, 19% IUD), GF V (n=4) 100% SA, 50% used CM (50% CP, 50% Cdm); GF NA (n=11) 55% SA, 83% used CM (80% Cdm, 20% IUD).
CM in female patients stratified by SLE activity: SLEDAI $<$3 (n=62): 76% SA, 77% of them used CM (3% CP, 83% Cdm, 14% IUD); SLEDAI 3–12 (n=42): 81% SA, 76% used CM (8% CP, 69% Cdm, 23% IUD); SLEDAI $>$12 (n=60): 60% SA, 67% used CM (100% Cdm).
CM in female patients using teratogenic drugs: MTX (n=8): 100% SA, 75% of them used CM (17% CP, 66% Cdm, 17% IUD); MYC (n=20): 80% SA, 88% used CM (71% Cdm, 29% IUD); CYC (n=3): 33% SA, 100% used CM (100% Cdm); Belimumab (n=1): 100% SA, 100% surgical CM (tubectomy).
aPL was evaluated in 96/132 patients. 17/96 had positive aPL and 5/17 fulfilled APS criteria. 2/17 patients had no CM data available, none with APS. 9/17 patients with aPL were female, 55% SA and all of them used Cdm. 3/5 patients with APS were female, all SA, 66% used Cdm.
Conclusions: Condom was the most reported CM. Use of CM was more frequent in the upper social stratus (GF I-III) respect to the lower (GF IV-V).
The proportion of sexually active female patients was similar in those using teratogenic drugs compared with who had not used them.
The self-reported sexual status was similar despite of SLEDAI stratification, being similar in patients with low or high disease activity.
We deem necessary education, counseling and evaluation of use of the CM in every visit of patients with SLE.
References:
[1] Andreoli L, Bertsias GK, Agmon-Levin N, et al. Ann Rheum Dis, doi:10.1136/annrheumdis-2016–209770.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3922

THU0286 RECURRENCE OF ARTERIAL AND VENOUS THROMBOSES IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

G. Balbi, F. Signorelli, R.A. Levy. *Rheumatology, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil*

Background: Antiphospholipid syndrome (APS) is the thrombophilia associated with the highest risk of recurrence of both arterial and venous thromboses. (1,2) In addition to the standard of care (lifelong oral anticoagulation), identification of other risk factors is important to provide better care and to reduce the incidence of rethrombosis.
Objectives: To investigate the risk factors associated with recurrence of arterial and venous thromboses in primary APS patients.
Methods: A cross-sectional study was performed in a group of 80 outpatients who fulfilled APS classification criteria (Sydney). The patients were regularly seen in our department, and clinical and serological features were collected during visits and by chart review. They were classified as recurrent or not, and these groups were compared. Recurrence was defined as the presence of 2 or more thrombotic events during lifetime. Patients with 1 thrombotic event were classified as "no recurrent". No history of thrombosis was the only exclusion criteria.
Results: Of 80 pAPS patients, thirty-five had arterial thrombosis and 54 had venous thrombosis. Of them, thirty-six had recurrent thromboses (11 arterial and 25 venous). Demographic and clinical characteristics of the arterial group are shown in Table 1. In a bivariate analysis, recurrent arterial thromboses were associated with hypertension (p=0.016) and positivity to lupus anticoagulant (LA; p=0.033), and recurrent venous thrombosis correlated to obesity (BMI$\geq$30 kg/m^2; p=0.003). In a multivariate regression analysis, the model of recurrent arterial thromboses was adjusted to age, sex, and variables with p$<$0.10 in the bivariate analysis (age, hypertension, dyslipidemia, and positivity to lupus anticoagulant). Hypertension (OR 9.02; CI95% 1.05–77.5; p=0.045) and age (OR 1.16; CI95% 1.01–1.33; p=0.035) increased the risk of relapse of arterial thrombosis.

Table 1. Demographic and clinical characteristics of patients with recurrent and non-recurrent arterial thromboses (N=35)

Variable	Arterial recurrence (N=11)	No arterial recurrence (N=24)
Age	53.5±7.7	41.9±11.7
Female gender	10 (90.9)	18 (75)
Caucasian	8 (72.7)	14 (58.3)
Time first manifestation (mo)	185 (120–300)	150 (59,3–204)
Risk factors		
Hypertension	8 (72.7)	7 (29.2)
Diabetes	1 (9.1)	1 (4.2)
Dyslipidemia	8 (72.7)	9 (37.5)
Obesity (BMI$\geq$30 kg/m^2)	4 (36.4)	7 (29.2)
Premature CVD	3 (27.3)	2 (8.3)
Smoking	5 (45.5)	9 (37.5)
Non criteria		
Livedo	4 (36.4)	9 (37.5)
Thrombocytopenia	1 (9.1)	4 (16.7)
Valvulopathy	1 (11.1)*	2 (13.3)**
Raynaud phenomenon	4 (36.4)	6 (25.0)
Migraine	6 (54.5)	12 (50.0)

*N=9; **N=15. Mo = months. CVD = cardiovascular disease. Values showed as N (%) for categorical variables, Mean ± SD for normal distribution and Median (interquartil range) for asymmetric distribution.

Conclusions: This data suggests that hypertension, a traditional cardiovascular risk factor, is associated with increased risk of recurrent thrombosis and, therefore, should be controlled in pAPS patients. Besides, each additional year of age is associated with the risk of 16% of a new arterial thrombotic event.
References:
[1] R. Cervera, M.A. Khamashta, Y. Shoenfeld, et al., Morbidity and mortality in the antiphospholipid syndrome during a 5-year period: a multicentre prospective study of 1000 patients, Ann. Rheum. Dis. 68 (2009) 1428–1432.
[2] M. Turiel, P. Sarzi-Puttini, R. Peretti, et al., Thrombotic risk factors in primary antiphospholipid syndrome: a 5-year prospective study, Stroke 36 (2005) 1490–1494.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6981

THU0287 CENTRAL ARTERIAL STIFFNESS MEASURED BY THE AUGMENTATION INDEX IS INCREASED IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AND IS DETERMINED BY THE LEVELS OF IGM-β2-GLYCOPROTEIN AND THE SMALL-DENSE HDL PARTICLES

S. Parra[1,2], N. Amigo[3], M. Heras[4], D. Ibarreche[5], M. Benavent[6], A. Navarro[6], E. Garcés[6], A. Castro[1,2]. *[1]Autoimmune diseases unit, Sant Joan's university Hospital; [2]Institut investigacions Sanitaries Pere i Virgili, Reus, Spain; [3]Centre for Omic Sciences, Institut Investigacions Sanitaries Pere i Virgili; [4]Lipid resarch unit (URLA), Rovira i Virgili university; [5]Unitat de medicina vascular i del metabolisme (UVASMET), Sant Joan University Hospital; [6]Internal medicine, Sant Joan's university Hospital, Reus, Spain*

Background: Patients affected by Systemic Lupus Erythematosus (SLE) show an increase in cardiovascular mortality and morbidity. The accelerated atherosclerosis observed in patients with SLE cannot be entirely explained by the traditional cardiovascular risk factors. Patients with SLE show increased subclinical atherosclerosis determined by an increased carotid arterial thickness, endothelial dysfunction and central arterial stiffness. Analysis of lipoproteins by magnetic nuclear resonance (MNR) provide information of those lipoproteins associated with subcinial atherosclerosis in SLE.
Objectives: To investigate the metabolic and immunological factors associated with the presence of central arterial stiffness determined by the Augmentation Index (AIx) as well as the detailed analysis of the lipid profile performed by magnetic nuclear resonance (MNR)
Methods: Descriptive cross-sectional study of 69 women with SLE compared with a control group of 34 age matched healthy women. On the same day of the study, blood extraction, physical examination and augmentation index (AIx) obtained by Peripheral Arterial Tonometry were performed. The carotid intima-media thickness (IMTc) was also performed on the same day of the study to correlate the arterial stiffness with another subclinical atherosclerosis marker. Analysis of lipoprotein populations by NMR (Liposcale,Biosfer Teslab) were performed.
Results: Patients with SLE showed significant increased arterial stiffness respect the control group (20.30 (21.54)% vs 10.84 (11.51)%, *P*=0.0021)The values of AIx were well correlated with Framingham risk score (r=0.486, P <0.001) as well as the IMTc (r=0.456, P<0.001). The classic cardiovascular risk factors associated with the AIx were the SBP levels (r=0.456, P<0.001) and age (r=0.456, P <0.001). Patients under antimalarial drugs showed significant decreased AIx (11.74 (11.28) vs 24.97 (20.63); *P*=0.024. Immunological variables associated with AIx were levels of C4 (r=0.259; *P*=0.046) and the IgM-β2-glycoprotein levels (r=0.284, P=0.284).As for the lipoprotein populations, AI values correlated with ApoB plasma levels, remnant particles, the number of large, medium and small VLDL particles, the number of small LDL particles and the number of small-dense HDL particles. In the multivariate analysis we found that age (β=0.377 (0.117–0.636), *P*=0.005) IgM-B2-GLP levels (β=0.303 (0.026–0.580),*P*=0.033) and the small-dense HDL particles (β=1,463 (0.605–2.322), *P*=0.001).
Conclusions: SLE patients show increased central arterial stiffness respect healthy population. Patients treated with antamalarial drugs show lower arterial stifness. In multivariate analyses variables that predicted levels of AIx were age, levels of IgM-β2-glycoprotein and the number of small-dense HDL particles.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3974

THU0288 COMPARISON OF THE CLINICAL, SEROLOGICAL, AND PROGNOSTIC DIFFERENCES AMONG JUVENILE-, ADULT-, AND LATE-ONSET LUPUS NEPHRITIS IN KOREAN PATIENTS: A CASE-CONTROL STUDY

S.-S. Lee[1,1], J.-H. Kang, J.-E. Kim, K.-E. Lee, D.-J. Park. *Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic Of*

Objectives: SLE patients present with different clinical and serological manifestations according to the age at disease onset. However, it is not known whether there is an association between disease onset age and the clinical presentation of lupus nephritis (LN). Therefore, we investigated whether LN patients could be distinguished based on the time of disease onset and, if so, whether the groups differed in their clinical, laboratory features and long-term prognosis in ethnically homogeneous Korean patients.
Methods: We enrolled 117 SLE patients with available clinical data at the time of renal biopsy for LN from the lupus cohort at Chonnam National University Hospital. We divided the LN patients according to the age at LN diagnosis into three groups [juvenile-onset LN (JLN), diagnosed at $\leq$18 years; adult-onset LN (ALN), diagnosed at 18–50 years; and late-onset LN (LLN), diagnosed at $>$50 years] and compared the baseline demographic, clinical, histological, and relevant laboratory findings. We also compared the treatment and long-term prognosis of LN according to those three groups.
Results: Of the 114 LN patients, 20 (17.5%), 84 (71.8%), and 13 (11.1%) had JLN, ALN, and LLN, respectively. LLN patients were less educated than ALN and JLN patients (p <0.001). Hypertension and diabetes mellitus at the onset of LN were more common in LLN patients than ALN or JLN patients (p<0.001 and?p=0.037, respectively). Regarding the laboratory findings, LLN patients had a higher white blood cell count and lower eGFR than ALN or JLN patients (p<0.011 and 0.002, respectively). Histologically, LLN patients had more chronicity indices and a higher chronic score (p =0.006, p =0.019, p<0.001 and p<0.001, respectively). Anti-Ro antibodies were found more frequently in ALN patients and less frequently in JLN patients (p =0.024) and lower complement levels were more common in JLN patients and less common in LLN patients (p<0.011 and 0.002, respectively). During a mean follow-up of 76.5 months, the development of chronic kidney disease and death from any cause were higher in LLN patients than in JLN and ALN patients (p =0.028 and p =0.038, respectively).
Conclusions: LN patients present with different clinical and serological manifestations according to age at disease onset. Interestingly, LLN patients had more chronicity at the time of renal biopsy, and more deterioration of kidney function and death on long-term follow-up, than JLN and ALN patients. Therefore, LLN patients should be monitored and managed carefully to avoid poor outcomes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2365

THU0289 B-CELL ACTIVATING FACTOR GENE EXPRESSION IN URINARY SAMPLE AND RENAL BIOPSY FOR MONITORING DISEASE ACTIVITY IN LUPUS NEPHRITIS

S. Retamozo[1,2], L. Mas[3], M.J. Haye Salinas[4], V. Saurit[4], F. Caeiro[4], A. Diller[5], J. De La Fuente[6], M. Angelina[7], N.R. Benzaquen[4], J.P. Pirola[4], A. Alvarellos[4], T. Alvarellos[3]. *[1]Rheumatology, Hospital Privado Universitario de Córdoba; [2]INICSA, CONICET; [3]Molecular Biology; [4]Rheumatology; [5]Pathology; [6]Nephrology, Hospital Privado Universitario de Córdoba; [7]Nephrology, Hospital Raul A Ferreyra, Cordoba, Argentina*

Objectives: To evaluate BLyS as biomarker in disease activity in urinary sample and renal biopsy from patients with LN.
Methods: Retrospective study. Between June 2009 and October 2013, 32 patients with SLE and LN fullfilling SLE classification criteria of ACR 1997 were included. The renal biopsies were evaluated according to the ISN/RPS classification system. The gene expression levels of BLyS were quantified using Quantitative Real Time PCR (QPCR). The relative quantification method was used for analysis, where Ct was normalized to an endogenous control β2Microglobulina (β2M) (ΔCt BLyS). The data expressed as ΔCt are inversely proportional to gene expression level. The value of BLyS is expressed as median (M) and interquartile range (IQR) for filing a non-normal distribution.
Results: 26 (81.3%) patients were female with a mean age at diagnosis of 26.9±13 years and 31.9±29 years at the time of renal biopsy. The SLEDAI at the time of biopsy was 10.5 (IQR 0–15.7) and SLICC ≥1 in 13 (32.5%), hypocomplementemia 13/31 (41.9%) and positive DNA in 11/29 (37.9%) patients. Biopsies from patients with proteinuria ≥0.5 and renal failure (RF) (n=23, 71.9%), proteinuria isolated (n=14, 43.8%), LN remission. The value of the BLyS gene expression in renal biopsy was 8.09 (IQR 7.37–9.16) and BLyS in urinary sample was 6.45 (IQR 5.62–7.76).
Conclusions: BLyS detection in urinary samples could be a potential biomarker for predicting lupus nephritis activity. Our data confirm that the BLyS as urinary biomarker is present in patients with active renal disease especially in patients with proliferative glomerulonephritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4523

THU0290 CLINICAL BACKGROUND FACTORS RELATED TO SILENT OSTEONECROSIS OF THE FEMORAL HEAD UPON INITIATION OF STEROID THERAPY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

T. Kuroda[1], N. Tanabe[2], H. Sato[1], T. Nakatsue[1], Y. Wada[1], M. Nakano[3], I. Narita[1]. *[1]Division of Clinical Nephrology and Rheumatology, Niigata University Graduate School of Medical and Dental Sciences; [2]Department of Health and Nutrition, Faculty of Human Life Studies, University of Niigata Prefecture; [3]Department of Medical Technology, School of Health Sciences, Faculty of Medicine, Niigata University, Niigata, Japan*

Background: Osteonecrosis of the femoral head (ONF) occurs frequently (3–40%) in patients who receive corticosteroid therapy for SLE. MRI can accurately visualize pathological abnormalities of the femoral head, being much more sensitive than plain radiography. To analyze the risk factors associated with steroid-induced ONF, the best approach would be to examine early changes in the femoral head using MRI and any early clinical events attributable to steroid therapy. For treatment of SLE, a number of strategies may be selected according to the clinical conditions of patients, and treatments may differ slightly among hospitals. Therefore, for better clarification of the background factors associated with ONF, the optimum approach would be to analyze the treatment strategy, selection of steroid, initial dose of steroid and drugs used together with steroid in a cohort of patients treated at a single hospital.
Objectives: To clarify the factors related to silent ONF in patients with SLE treated at a single institution.
Methods: One hundred six patients (12 males and 94 females) with SLE were selected on the basis of having been newly diagnosed and requiring high-dose prednisolone, including pulse therapy with methylprednisolone, as the initial treatment. All the patients initially underwent plain radiography and MRI at the start of corticosteroid treatment to detect any early changes in the femoral head, and subsequent examinations were performed three months later. Laboratory parameters were evaluated at the start of steroid treatment and one month thereafter. All statistical analyses were performed with SPSS v. 13 (SPSS Inc., Chicago, IL, USA). Differences demonstrated by 2-tailed tests were considered statistically significant at *P* (two-sided) <0.05, and marginally significant at *P*=0.05–0.10.
Results: By three months after the start of corticosteroid treatment, asymptomatic ONF was diagnosed by MRI in 30 patients (28.3%), being bilateral in 17 and unilateral in 13. Serological activity (C3, C4, CH50 and anti-ds DNA antibody), renal function (eGFR, serum creatinine and urinary protein), anti-phospholipid antibodies, and SLEDAI were not correlated with asymptomatic ONF. BMI, BSA, and the initial dose of prednisolone per unit body weight, BMI and BSA were also not correlated with asymptpmatic ONF. No preventive effect of ONF was observed by pretreatment with statins. However, patients with angiitis and a elevated total cholesterol level at 4 weeks after the start of steroid treatment tended to show a higher incidence of ONF. Patients with a higher triglyceride level both before and 4 weeks after the start of steroid treatment showed a significantly higher frequency of asymptomatic ONF (P<0.001).
Conclusions: Asymptomatic ONF is common in patients with SLE. A high triglyceride level is a significant risk factor for ONF, and large epidemiologic surveys would help to shed light on early events such as silent ONF in patients receiving steroid therapy.
Acknowledgements: This study was supported by a research grant from the Research Committee on Idiopathic Osteonecrosis of the Femoral Head of the Ministry of Health, Labour, and Welfare of Japan.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2249

THU0291 GENDER INFLUENCE ON CLINICAL, BIOLOGICAL AND IMMUNOLOGICAL ASPECTS OF SYSTEMIC LUPUS ERYTHEMATOSUS

T. Ben Salem, M. Tougorti, I. Naceur, I. Ben Ghorbel, M. Lamloum, M.H. Houman. *Internal Medicine, Rabta university hospital, Tunis, Tunisia*

Background: Systemic lupus erythematosus (SLE) is more frequent in women but seems to be more severe in men.
Objectives: The aim was to study gender influence on clinical, biological and immunological features of SLE
Methods: It's a retrospective study conducted in an internal medicine department. Patients with systemic lupus erythematosus (ACR revised criteria) were included. Data were recorded and compared using SPSS. Variables with a p≤0.05 were considered to be statistically significant.
Results: A total of 246 SLE patients were included; 224 female and 19 male (sex ratio F/M was 11.78). Mean ages at disease onset and at SLE diagnosis were comparable for men and women respectively 35.63±14.31 vs 32.7±13.36 years and 35.8±14.3 vs 34.5±13.6 years.
SLE diagnosis was made earlier in men with an average delay (from first sign of the disease to diagnosis) of 6.1 months vs 21.4 months (p=0.02). Clinically, photosensitivity was significantly more frequent in women (81.4% vs 58.8%; p=0.03). Women complained from alopecia more frequently than men but the difference was not statistically significant (35.1% vs 14.3%; p=0.09). Arthritis were two times more frequent in women (50.7% vs 25%; p=0.04). Lupus nephritis us well us lupus pancreatitis were significantly more frequent in men, respectively 66.7% vs 41.6% (p=0.039) and 11.1% vs 1.4% (p=0.047). There were no differences according to gender in neurological involvement and seritis. No significant differences were observed between men and women concerning hematological disorders. Anti-DNA, anti-Sm, anti-RNP, anti-SSA, anti-SSB, anti-cardiolipin and anti-B2GP1 antibodies frequencies were similar in both genders.
Conclusions: SLE diagnosis was made earlier in men than women, this could be explained by more severe disease in men [1]. However this hypothesis has been highly controversial [2]. Cutaneous and joints manifestations seem to be more frequent in women whereas serious manifestations like lupus nephritis and neurological involvements were more frequent in men [3–4]. In our study, only lupus nephritis and pancreatitis were more frequent in men.
References:
[1] Andrade RM, Alarcon GS, Fernandez M, Apte M, Vila LM, Reveille JD. Accelerated damage accrual among men with systemic lupus erythematosus: XLIV. Results from a multiethnic US cohort. Arthritis Rheum. 2007;56:622–30.
[2] Murphy G, Isenberg D. Effect of gender on clinical presentation in systemic lupus erythematosus. Rheumatology (Oxford). 2013;52:2108–15.

Abstract THU0289 – Table 1. BLyS gene expression in urinary sample and renal biopsy according to clinical and histological findings

Variables	ΔCt BLyS Urinary	p	ΔCt BLyS Biopsy	p
SLEDAI =0/ SLEDAI ≥6	**7.52 (6.59–11.19)/5.94 (5.52–7.08)**	**0.04**	8.03 (6.90–10.20)/8.15 (7.35–9.10)	0.82
Bx LN in remission/LN active	**7.52 (6.59–11.19)/5.94 (5.52–7.08)**	**0.04**	8.03 (6.90–10.20)/8.15 (7.35–9.10)	0.82
MDRD ≥60/ MDRD <60	**6.76 (6.018.12)/5.60 (5.16–7.19)**	**0.04**	8.03 (6.95–8.95)/8.41 (7.45–13.40)	0.42
Proteinuria <0.5/Proteinuria ≥0.5	**7.52 (6.59–11.19)/5.94 (5.52–7.08)**	**0.04**	8.03 (6.90–10.20)/8.15 (7.35–9.10)	0.82
Without tubular atrophy in Bx /Tubular atrophy in Bx	**7.83 (6.43–11.67)/6.14 (5.51–7.24)**	**0.03**	8.16 (6.44–8.52)/8.09 (7.42–10.55)	0.53

Abstract THU0289 – Table 2. BLyS gene expression in urinary sample and renal biopsy according to the classification of LN

	Class I/Normal Bx	Class II Bx	Class IV Bx	Class V/VI Bx	P
ΔCt BLyS Renal Biopsy	7.56 (6.50–7.56)	8.41 (7.36–10.37)	7.95 (7.37–10.04)	8.28 (7.37–11.80)	0.88
ΔCt BLyS Urinary***	**7.28 (9.95–7.28)**	**8.41 (7.36–10.37)**	**5.65 (5.45–6.40)**	**6.34 (5.74–7.32)**	**0.003**

***p<0.05 Class I/normal with class IV, Class II with IV, class II with V/VI.

[3] Tan TC, Fang H, Magder LS, Petri MA. Differences between male and female systemic lupus erythematosus in a multiethnic population. J Rheumatol. 2012;39:759–69.
[4] Boodhoo KD, Liu S, Zuo X. Impact of sex disparities on the clinical manifestations in patients with systemic lupus erythematosus: A systematic review and meta-analysis. Medicine. 2016;95(29):e4272.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2323

THU0292 DIAGNOSTIC ACCURACY OF ULTRASOUND AND ULTRASONOGRAPHIC FEATURES OF SALIVARY GLANDS IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

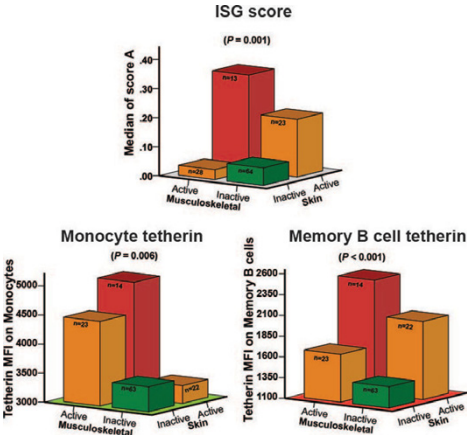
V. Milic, G. Radunovic, N. Damjanov. *Institute of Rheumatology, Belgrade, Serbia*

Objectives: To analysis ultrasonography (US) changes of salivary glands (SG) in patients with primary Sjogren's syndrome (pSS) and assessment of their accuracy for diagnosis pSS.
Methods: This study included 205 pSS patients (mean age 53.9±11.5, disease duration 5.6 years) and 87 healthy controls (mean age 52.3±14.7). All pSS patients fulfilled the AECG diagnostic criteria. The disease activity was measured by EULAR SS disease activity index (ESSDAI). Parotid and submandibular glands on both sides were assessed for size, parenchymal echogenicity and inhomogeneity, posterior glandular border and presence of intraglandular lymph nodes. Inhomogeneity of the salivary glands were graded according to the De Vita scoring system [0) homogenous glands; 1) mild inhomogeneous - isolated hypoechogenic areas; 2) evident inhomogeneous - scattered hypoechogenic areas, and/or multiple punctate or linear densities; 3) grossly inhomogeneous – large or confluents hypoechogenic areas, and/or to linear densities, and/or multiple cysts. The global SGUS score (0–6) was the sum of the scores of each pair of salivary glands. Statistical analysis was performed by SPSS v16. Data were compared using *t*-test, χ^2 test and Mann-Whitney U test. The optimal cut-off value for SGUS score was calculated as the area under the receiver operating characteristic curve (AUC-ROC).
Results: Xerophtalmia and xerostomia were presented in 185/205 (90.2%) and 186/205 (91.2%), respectively. According to ESSDAI, the majority of pSS patients 88/205 (43%) had moderate disease activity. Seventy-eight per cent of pSS patients were anti-SSA antibody positive, 44% anti-SSB/La antibody positive. Biopsy of LSG was positive in 140/172 (81.4%) pSS patients. US abnormalities were established in 197 (96%) pSS patients and in 16 (18%) controls ($p<0.0001$). Pathological sizes of salivary glands were more frequently in pSS patients than controls, 111 (54.2%) vs. 3 (3.4%) patients, respectively ($p<0.0001$). The echogenicity of the salivary glands was pathological changes in 142 (69.3%) pSS patients and in only 5 (5.7%) control group ($p<0.0001$). The pathological glandular border was frequently in pSS patients than control group, 48 (23.4%) vs. 2 (2.3%), $p<0.0001$. No differences were detected between the two groups of patients for enlarged intraglandular lymph nodes. Most of pSS patients had pathological inhomogeneity, 197/205 (96.1%) vs. 16/85 (18.4%) in control group ($p<0.0001$). The median SGUS was significantly higher in pSS patients in comparison with control group [median (range) 4 (0–6) vs. 0 (0–2), $p<0.0001$]. Forty-five percent of pSS patients had SGUS score 4. The SGUS cut-off ≥ 2 showed specificity of 89.5% and sensitivity 89.3%. Diagnostic accuracy of the parenchymal inhomogeneity was very good (AUC-ROC 0.89), followed by the glandular echogenicity (AUC-ROC 0.81), the glandular size (AUC ROC 0.75), the posterior border (AUC ROC 0.60), and the presence of intraglandular lymph nodules (AUC ROC 0.49), respectively.
Conclusions: Our findings confirm that most of established pSS patients had pathological SGUS features. Among US parameters, parenchymal inhomogeneity was the most discriminant feature for diagnosis of SS. There is the growing evidence that ultrasound should be considered as the useful method for evaluation of salivary glands in pSS patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5046

THU0293 B-CELL RESPONSES TO TYPE I INTERFERON DEFINE DISEASE ACTIVITY IN SLE AND CAN BE MEASURED BY CELL SURFACE TETHERIN (CD317)

Y.M. El-Sherbiny[1,2], M.Y. Md Yusof[1,2], A. Psarras[2], E. Hensor[1,2], R. Tooze[3], G. Doody[3], M. Wittmann[1,2], P. Emery[1,2], E.M. Vital[1,2]. [1]*National Institute of Health Research Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust;* [2]*Leeds Institute of Rheumatic and Musculoskeletal Medicine;* [3]*Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, United Kingdom*

Background: SLE is a Type I interferon (IFN-I) mediated disease with autoreactive B cells. Whole blood interferon-stimulated gene (ISG) expression is used to measure IFN-I status but does not consistently correlate with clinical features and therapy response. ISG expression may be influenced by differing response in individual cell subsets as well as IFN-g. Tetherin is a cell surface protein encoded by the interferon-stimulated gene *BST2*.
Objectives: To evaluate tetherin expression as a novel cell-specific flow cytometric biomarker for IFN-I response.
Methods: *In vitro,* we tested response of expression of *BST2* and 30 other ISGs to stimulation with IFN-a and IFN-g, as well as dose response of *BST2* and tetherin protein in B cells. Sorted cells (Monocyte, T, NK, naïve and memory B, plasmablast) from 8 controls and 10 SLE patients were used to test variation in expression of 31 ISGs between cell subsets and whether tetherin measured by flow cytometry is a cell specific marker for IFN-I response. Samples from 156 SLE patients, 30 ACPA+ANA- RA (DAS28>3.2) patients and 22 healthy controls (HC) were used in 3 clinical validation studies of tetherin vs. ISG score against diagnosis, disease activity (BILAG-2004) and plasmablast repopulation after rituximab.
Results: Some ISGs' expression in B cells increased in response to both IFN-a and IFN-g. Others, which included *BST2*, were selective for IFN-a. An 18-gene ISG score derived from this latter group was calculated for comparison with tetherin.
Results from cell sorting showed that ISG Score was highest in monocytes; other subsets were 75–85% lower ($p<0.001$). SLE-associated increase in expression (SLE:HC ratio) varied between 2.56 (T cells) to 4.93 (plasmablasts).
Diagnosis: ISG score differentiated HC from SLE with ratio 3.58 (1.94 – 6.61) and large effect size 0.14 (partial eta squared). Using tetherin for cell specific IFN response revealed marked differences between subsets. Monocytes did not differentiate HC and SLE at all with ratio 1.19 (0.87 – 1.61) and effect size 0.03. Memory B cells had medium-large effect size of 0.11 with ratio 1.59 (1.21 – 2.09). Comparing SLE and RA the largest effect size was for plasmablast Tetherin at plasmablasts at 0.23, with ratio 2.20 (1.66 – 2.93).
Disease activity: ISG score was associated with cutaneous disease activity (BILAG A/B) but not musculoskeletal (Fig 1). Monocyte tetherin was associated with musculoskeletal disease activity but not cutaneous. Memory B cell tetherin was associated with disease activity in both these organs. Memory B cell tetherin was increased with renal (p=0.005) or haematological (p=0.005) activity with no differences in ISG score for these domains (p=0.152, p=0.989 respectively).
Plasmablast numbers after rituximab were associated with Memory B cell tetherin (R=0.38, p=0.047) but not ISG score (R=0.24, p=0.219).



Conclusions: ISG expression in unsorted blood is influenced by IFN-g and cellular composition of the sample as well as IFN-I. Flow cytometric measurement of surface tetherin is a cell-specific assay for IFN-I that avoids these problems. Memory B cell tetherin was better associated with plasmablast numbers and clinical features of disease than monocyte tetherin or ISG score.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6002

THURSDAY, 15 JUNE 2017

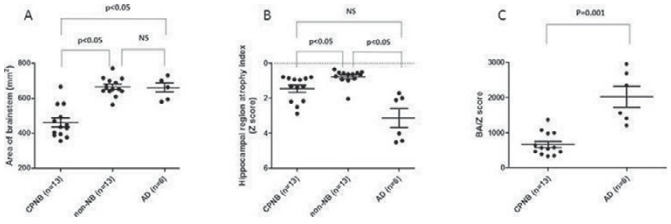
Vasculitis

THU0294 DIFFERENTIAL PATTERNS OF ATROPHY IN HIPPOCAMPUS AND BRAINSTEM BETWEEN CHRONIC PROGRESSIVE NEURO-BEHCET'S DISEASE AND ALZHEIMER'S DISEASE

H. Kikuchi[1], K. Asako[1], T. Yanagida[1], H. Kono[1], S. Hirohata[2]. [1]*Department of Internal Medicine, Teikyo University School of Medicine, Tokyo;* [2]*Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Kanagawa, Japan*

Background: Central nervous system involvement is one of the most serious complications in Behçet's disease (BD). This condition is referred to as neuro-Behçet's disease (NB) and can be classified into acute type (ANB) and chronic progressive type (CPNB) based upon differences in the clinical course and responses to corticosteroid treatment. Cerebellar ataxia, such as gait disturbances and dysarthria, is one of the representative manifestations in CPNB. Accordingly, brainstem atrophy is frequently observed in CPNB, but not in ANB. Notably, progressive neurobehavioral changes mimicking those in Alzheimer's disease (AD) are also frequently observed in CPNB, but these changes cannot be accounted for by brainstem atrophy.

Objectives: In the present study, volumes of the hippocampus were examined to identify the responsible lesions for neurobehavioral changes in CPNB, and patterns of atrophy in the hippocampus and brainstem were compared between patients with CPNB and AD.
Methods: The subjects were 32 patients, including 13 with CPNB (11 males and 2 females, age 51.2±12.1 years old [mean ± SD]), 13 with Behçet's disease without NB (non-NB) (10 males and 3 females, age 54.4±11.4 years old), and 6 with AD (5 males and 1 female, age 78.8±7.5 years old). All patients with BD satisfied the international classification criteria for BD. CPNB was defined as intractable, slowly progressive neurobehavioral changes and/or cerebellar ataxia accompanied by persistent elevation of interleukin-6 of >20 pg/mL in cerebrospinal fluid on two different occasions at an interval of at least 2 weeks. All patients with AD satisfied Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV criteria. Brain magnetic resonance imaging (MRI) was obtained from each subject. The areas of the midbrain tegmentum and pons were measured on mid-sagittal sections of T1-weighted images using image analysis software (Image J ver.1.45: NIH, USA). Severity of gray matter loss in the hippocampal region and whole brain were investigated using Voxel-Based Specific Regional Analysis System for Alzheimer's Disease (VSRAD) software (Eisai Co., Ltd) to determine the degrees of hippocampal region atrophy (Z score) and whole-brain atrophy (WBAI). Thus, the 1/Z score is positively correlated with the hippocampus volume. The ratio of the degree of brainstem atrophy to that of hippocampal atrophy was evaluated by the brainstem area value divided by the 1/Z score (BA/H score) in each patient.
Results: The brainstem area was significantly decreased in CPNB (461.8±87.3 [mean ± SD]) compared with that in AD (661.9±56.1) and non-NB (666.1±50.6) (Figure A). VSRAD analysis showed that Z score was significantly increased in CPNB (1.46±0.70) and AD (3.13±1.21) compared with that in non-NB (0.77±0.40) (Figure B). Of note, the BA/H score, reflecting the brainstem/hippocampus volume ratio, was much lower in CPNB than in AD [663.5±311.8 vs 2018±667.6, p=0.001] (Figure C).



Conclusions: These results indicate that the hippocampus, in addition to the brainstem, is a common target lesion in CPNB, and this accounts for the progressive neurobehavioral dysfunction in this disease. Moreover, the data emphasize that brainstem atrophy is disproportionately greater than hippocampal atrophy in CPNB, in contrast to AD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1207

THU0295 CLINICAL FEATURES OF TAKAYASU'S ARTERITIS FROM AN INCEPTION COHORT: EARLY DISEASE IS CHARACTERIZED BY "SYSTEMIC INFLAMMATION"

F. Alibaz-Oner on behalf of Turkish Takayasu Arteritis Study Group.
Rheumatology, Marmara University, School of Medicine, Istanbul, Turkey

Background: There is only retrospective and very limited data for the long term prognosis of Takayasu's Arteritis (TAK), a rare large-vessel vasculitis. In this study, we aimed to present the preliminary results of a Takayasu Inception Cohort settled for long term, prospective follow-up of only newly-diagnosed patients with TAK.
Methods: Patients fullfilling the American College of Rheumatology 1990 criteria for TAK and diagnosed in the last 12 months were included to the study. Patients' data were recorded in an electronic database of an international "Takayasu's Arteritis Registry" requiring baseline and at least annual visits. Data is compared with an historical Turkish cohort previously published (Bıçakçıgil, et al, 2009).
Results: The study included 128 patients (age: 38.9±13.1 years, F/M: 112/16) with TAK from 15 tertiary Rheumatology centers in Turkey. The mean symptom duration of patients was 5.2 years at diagnosis. According to the angiographic classification, 59.2% of the study group had type I and only 17.2% had type V disease. When we compared our results to our retrospective cohort (previously published by Turkish Takayasu Arteritis Study Group), constitutional symptoms (72.2% vs 66%) and limb claudication (62.3% vs 48%) were observed to be more frequent, whereas pulselessness (35.6% vs 88%) was less in the inception cohort.(Table 1) Carotidynia was present only in the inception cohort. Similarly, mucocutaneous symptoms also seem to be a feature of newly-diagnosed disease (26.4% vs 8.8%). Regarding comorbidities at diagnosis, the rate of dyslipidemia was 22%, diabetes mellitus 6%, smoking 28.5% and obesity (BMI>30) 15.8% among TAK patients. All patients were given oral corticosteroid (CS) therapy (0.5–1 mg/kg) at diagnosis, 10 patients (7.8%) also having CS pulses. In addition to CSs, 55 patients (43%) were given methotrexate, 14 patients (11%) azathioprine and 5 (4%) cyclophosphomide at disease-onset.

Table 1. Clinical characteristics of Inception and Retrospective Cohorts from Turkey

	Inception Cohort (n=128)	Retrospective Cohort (Bıçakçıgil et al.) (n=248)
Constitutional symptoms	91/126 (72.2%)	163/248/ (66%)
Limb claudication	66/106 (62.3%)	119/248 (48%)
Carotidynia	26/104 (25%)	–
Pulseless	37/104 (35.6%)	218/248 (88%)
Musculoskeletal manifestations	66/124 (53.2%)	104/248 (42%)
Mucocutaneous manifestations	32/121 (26.4)	22/248 (8.8%)
Respiratory manifestations	40/122 (32.8%)	22/184 (12%)
Neurologic manifestations	58/124 (46.8%)	156/248 (63%)
Cardiac involvement	23/106 (21.7%)	141/248 (57%)
Ophthalmologic involvement	29/125 (23.2%)	57/248 (36%)

Conclusions: Our results suggest that, in an inception cohort, signs and symptoms of "systemic inflammation" is more prominent in newly-diagnosed TAK patients, whereas vascular extent and damage accumulates during the disease course. The long term follow-up of our inception cohort will better show the actual course and predictors of prognosis in TAK.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3856

THU0296 THE ROLE OF ULTRASOUND IN THE MANAGEMENT OF GIANT CELL ARTERITIS (GCA) IN ROUTINE CLINICAL PRACTICE

S. Monti[1,2], A. Floris[3], C. Ponte[4], S. Vaggers[2], W.A. Schmidt[5], A.P. Diamantopoulos[6], C. Pereira[2], R. Luqmani[2]. *[1]Rheumatology, University of Pavia, IRCCS Policlinico San Matteo Foundation, Pavia, Italy, Pavia, Italy; [2]NDORMS, Rheumatology Department, Nuffield Orthopaedic Centre, University of Oxford, Oxford, United Kingdom; [3]Rheumatology, University Clinic and AOU of Cagliari, Cagliari, Italy; [4]Rheumatology, Hospital de Santa Maria, Rheumatology research Unit Instituto de Medicina Molecular, Lisbon Academic Medical Centre, Lisbon, Portugal; [5]Rheumatology, Immanuel Krankenhaus Berlin, Medical Centre for Rheumatology Berlin-Bu, Berlin, Germany; [6]Rheumatology, Hospital of Southern Norway Trust, Kristiansand, Norway*

Background: Colour Doppler sonography (CDS) is an emerging diagnostic tool for giant cell arteritis (GCA), however, its use in routine practice is still not widespread.
Objectives: To develop a protocol using CDS and explore its value in the routine care of patients with GCA.
Methods: We developed a structured scanning protocol for CDS of temporal and axillary arteries (total of 8 anatomical sites scanned per patient) based on previously published methods. We tested the protocol on consecutive patients referred to a single rheumatology centre, with suspected or established GCA, between July 2014 and September 2016. We defined a positive scan by the presence of halo in at least one branch of a temporal artery (TA) or one axillary artery (AX). We report data from the first 293 consecutively scanned cases.
Results: We assessed 293 patients (mean age 72±10, female/male 196/97), of whom 118 had clinically confirmed GCA. Amongst new referrals with confirmed diagnosis of GCA, 44% had a positive scan; two patients with a positive scan did not have GCA. 82% of new referrals patients showed exclusive TA involvement, 25% concomitant AX, and 4% exclusive AX involvement. High-dose glucocorticoid therapy had already been started in 78% of these patients for an average of 17±33 days. Amongst this group, the sensitivity of CDS was 46% (95% IC 37%>55%), specificity 98% (95% CI 93%>99.8%), positive predictive value 96% (88%>99.6%), and negative predictive value 60% (95% IC 52%>68%). During the period of observation, the rate of temporal artery biopsies (TAB) decreased significantly from 42% to 25% (p=0.002). During follow up, CDS was positive in 21% of 89 routine scans in asymptomatic individuals, compared to 58% in patients with confirmed clinical flares (45% of whom had negative inflammatory markers). Over time, the number of halos per patient reduced; only new or flaring patients showed a halo in >4 sites. Halo size at the TA did not change significantly (average thickness 0.6±0.1 mm), however, the size of AX artery halos significantly reduced from first referral (1.6±0.4 mm) to follow up (1.4±0.2, p=0.01) or during subsequent flares (1.4±0.2, p=0.02).
Conclusions: We have developed and tested a standardised methodology for CDS evaluation of GCA. CDS provides a high positive predictive value for a diagnosis of GCA in unselected patients from routine clinical practice, although prior high dose glucocorticoid therapy is likely to reduce its sensitivity. CDS allows for a significant reduction of TAB. We explored the role of CDS to detect disease flares and demonstrated a significant reduction in the extent of abnormalities, and of the size of halo of the AX arteries during follow up or flares. These findings could have a significant impact on the management of patients with suspected and confirmed GCA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4063

THU0297 A NOVEL ULTRASOUND SCORING SYSTEM FOR GIANT CELL ARTERITIS

S. Monti[1,2], C. Ponte[3], G. Carrara[4], F. Rumi[4], A. Hutchings[5], B. Dasgupta[6], R. Luqmani[1]. *[1]NDORMS, Rheumatology Department, University of Oxford, Oxford, United Kingdom; [2]Rheumatology, University of Pavia, IRCCS Policlinico San Matteo Foundation, Pavia, Italy, Pavia, Italy; [3]Rheumatology, Hospital de Santa Maria, CHLN, Lisbon, Portugal; [4]Epidemiology Unit, Italian Society of Rheumatology, Milan, Italy; [5]Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, London; [6]Rheumatology, Southend University Hospital, NHS Foundation Trust, Westcliff-on-Sea, United Kingdom*

Background: Colour duplex sonography (CDS) can be used for giant cell arteritis (GCA) to detect inflammatory oedema of the vascular wall, known as "halo". A standardized, quantitative score to grade the severity and extension of vascular involvement detected by CDS has not yet been developed.
Objectives: To develop and test different scoring models of CDS findings in patients with new onset GCA, and to correlate the models with final diagnosis, histologic findings, and outcome.
Methods: We selected patients with a positive CDS and a confirmed diagnosis of GCA from the Temporal Artery Biopsy vs Ultrasound in Diagnosis of GCA (TABUL) study (1). We designed CDS models combining different ultrasonographic information based on available evidence, or hypothesized clinical relevance of size, anatomical distribution, and extent of halos, summing up to a final numeric score.
Results: We included 135 GCA patients (male/female: 43/92), age 73.3±8. Fourty four patients (24%) had a positive CDS, but not a final diagnosis of GCA. We designed 8 different CDS models (Figure 1). Models 1, 4, 6, and 7 were significantly associated with a confirmed diagnosis of GCA (Table 2). Model 7 better discriminated patients with GCA from non-GCA: area under the curve (AUC): 0.844 (0.766–0.923). All, except models 5 and 8, correlated with a temporal artery biopsy (TAB) result diagnostic for GCA. Most models correlated with histologic findings involving the media or transmural infiltrate, but not with small vessel or adventitial involvement. None of the models correlated with permanent ischaemic sequelae, however, the low number of events might have affected the results.

Figure 1. Ultrasound scoring models

Model	Scoring formula
Model 1	Sum of sites with halos in TA and AX
Model 2	Defined as either bilateral halo on any TA branches OR bilateral halo on AX
Model 3	(Number of sites with halo on TA * average halo thickness among TA branches) + (number of sites with halo on AX * average halo thickness on AX)
Model 4	(Number of sites with halo on TA * maximum halo thickness among TA branches) + (number of sites with halo on AX * maximum halo thickness among AX)
Model 5	(Average halo thickness among TA + add "1" if bilateral halo on TA) + (average halo thickness among TA + add "1" if bilateral halo on AX)
Model 6	(Maximum halo thickness among TA + add "1" if bilateral halo on TA) + (maximum halo thickness among AX + add "1" if bilateral halo on AX)
Model 7	(Maximum thickness among TA * 2 if bilateral) + (maximum halo thickness among AX * 2 if bilateral)
Model 8	(Average thickness among TA * 2 if bilateral) + (average halo thickness among AX * 2 if bilateral)

TA: temporal artery; AX: axillary artery; * multiply by.

Conclusions: The CDS findings that better correlate with a diagnosis of GCA, and TAB findings are: the number of positive sites, the size of the halo (maximum, rather than average thickness), and the presence of bilateral halos, variably combined into a unique score. We plan to test these models in a new cohort of patients with suspected GCA, to determine their validity.
References:
[1] Luqmani R, Lee E, Singh S, et al. The Role of Ultrasound Compared to Biopsy of Temporal Arteries in the Diagnosis and Treatment of Giant Cell Arteritis (TABUL): a diagnostic accuracy and cost-effectiveness study.Health Technol Assess 2016;20:1–238.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4069

THU0298 LONG TERM OUTCOME OF PATIENTS WITH TAKAYASU ARTERITIS- A SINGLE CENTRE STUDY

R. Goel[1], D. Danda[1], G. Joseph[2], A. Nair[1], V. Jayseelan[3], L. Jayaseelan[3], S. Kumar[4], P. Bacon[5]. *[1]Clinical Immunology and Rheumatology; [2]Cardiology; [3]Biostatistics; [4]Child Health, Christian Medical College, Vellore, Tamil Nadu, Vellore, India; [5]School of Immunity and Infection, University of Birmigham, Birmigham, United Kingdom*

Background: Takayasu Arteritis (TA), a large vessel vasculitis is characterised by a variable clinical course and outcome that differs across populations. Most studies are limited by small sample size.
Objectives: (i) To study treatment outcome in our TA patients with a follow up of ≥12 months (ii) Construct a prediction model for subset of patients with sustained inactive disease.
Methods: Consecutive patients with TA attending our clinics between 1998 and April 2016 were recruited. Details of baseline demography, clinical profile, angiography, disease extent using DEI.Tak, laboratory parameters and TADS (Takayasu arteritis damage score) were recorded. At each follow up visit, disease activity was assessed by Indian Takayasu Activity score (ITAS-2010 (CRP) and imaging, while damage was assessed by TADS for patients who followed up for ≥12 months (retrospectively for 179 and prospectively for 72 patients). Treatment response was classified as complete response (CR), partial response and no-response. Sustained inactive disease was defined as maintenance of CR throughout the follow up with steroid dose reduced to ≤5mg/day. Relapse was defined as return of active disease after CR. Statistical analysis was performed using SPSS-16. Intergroup comparisons were performed by nonparametric test. Logistic regression was used for determining independent associations. Optimal cut off values were determined using receiver operating curve and prediction model was constructed. Efficacy of medications was compared by Cox proportional hazards model.
Results: Baseline details were noted for 503 patients: mean age at onset of 25.6±11.1 years, disease duration 12 (6–48) months, diagnostic delay 6 (3–24) months) and 77.9% were females.
Among 251 patients with follow up of at least 12 months, 95.2% received steroids along with II line immunosuppressant in 93.6% (mycophenolate in 63.7%). Tocilizumab was given induction or rescue therapy to 44 patients. Revascularisation procedures were performed in 71.7%. Complete (ITAS 2010 = 0, CRP <6mg/L, angiowise non-progression) and partial response was achieved in 176 patients (70.1%) and 42 (16.7%) respectively within 6 months.
During a median follow up of 42 (IQR: 24–81) months, 116 (46.2%) maintained complete response till their last follow up with cumulative relapse free survival of 83%, 70% and 55% at 1, 2 and 3 years respectively. A model including baseline CRP≤6.1mg/L, type 4 disease and DEI.Tak <9 predicted sustained inactive disease with an AUC of 70.2 (63.3–77.2, p=0.000). Initial steroid dosage of 0.5mg/kgday was similar to 1mg/kg/day in terms of response or relapse. Overall, there were only 15 (5.9%) patients who never responded to treatment. There were 2 fatalities. At the last visit, 176 (70.5%) had stable disease. Damage progression (delta TADS) was lower in patients with sustained inactive disease than the rest, p=0.000.
Conclusions: Medical management arrested disease activity, damage progression and mortality in our cohort. Low baseline CRP and DEI.Tak scores and type 4 disease independently predicted sustained inactive disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4258

THU0299 UNDERSTANDING THE HETEROGENEITY OF LARGE-VESSEL VASCULITIDES

E. Tombetti[1], A. Ambrosi[2], C. Godi[2], B. Ariff[1], A.A. Manfredi[2], J. Mason[1]. *[1]Imperial College London and Imperial College NHS Trust, London, United Kingdom; [2]San Raffaele Hospital and Vita-Salute University, Milan, Italy*

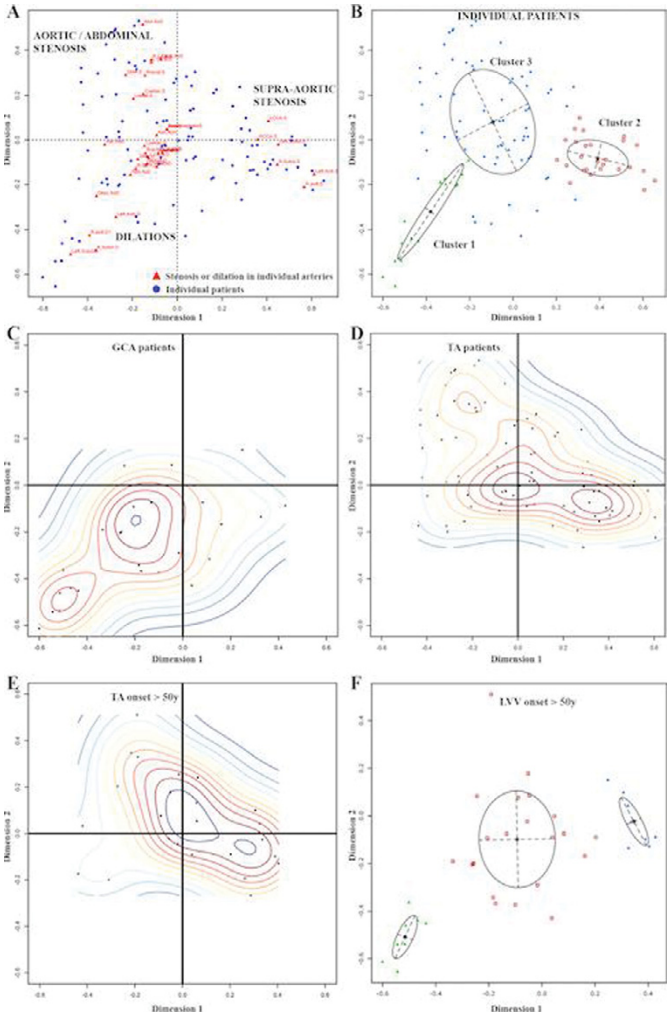
Background: Adult large-vessel vasculitides (LVV) are rare conditions, currently classified as two different diseases, Takayasu arteritis (TA) and giant cell arteritis (GCA), on an empirical basis. Insight into phenotypic and pathogenic differences between the two is scarce at best. Arterial involvement, despite being the central disease feature, has been poorly addressed by research. We have developed two novel, imaging-based scores (the arteritis stenosis score [ASS] and arteritis dilation score [ADS]). ASS and ADS define stenotic and aneurysmal disease in a

Abstract THU0297 – Table 2. Correlation of the different models with clinical and histologic variables

Median (IQR)		Model 1	Model 2		Model 3	Model 4	Model 5	Model 6	Model 7	Model 8
			0	1						
Predicting a diagnosis of GCA	0	2 (1–3)	25 (57%)	19 (43%)	3 (2–4.2)	1 (0.4–2.3)	2.7 (1.9–3.4)	1 (0.4–1.8)	0 (0–1.4)	1.3 (0.6–2.7)
	1	3 (1–5)	60 (44%)	75 (56%)	3.3 (1.8–6.2)	2.1 (0.8–4.4)	3.2 (2.1–3.7)	1.6 (0.7–2.3)	2 (1.2–2.8)	1 (0–1.8)
	p	**0.028**	0.21		0.52	**<0.001**	0.47	**0.003**	**<0.001**	0.35
TAB diagnostic for GCA	0	2 (1–3.5)	31 (61%)	20 (39%)	2.5 (1.2–3.4)	1 (0.6–2.4)	2.1 (1.2–3.5)	1.2 (0.4–1.7)	1.4 (1–2)	0.3 (0–2.2)
	1	3 (2–5)	24 (32%)	52 (68%)	5 (2.9–7.5)	2.8 (1.8–6)	3.5 (2.7–4)	1.9 (1.4–2.5)	2.2 (1.4–3)	1.1 (0.2–1.6)
	p	**<0.001**	**0.002**		**0.007**	**<0.001**	0.064	**<0.001**	**0.008**	0.90
Transmural infiltrate	0	2 (1–3.3)	34 (61%)	22 (39%)	2 (1.3–3.4)	1.1 (0.6–2.4)	1.9 (1.1–3.3)	1.1 (0.4–1.7)	1.4 (1.1–2)	0.2 (0–2.2)
	1	3 (2–4)	6 (23%)	20 (77%)	2.8 (1.6–3.2)	2.6 (1.5–3.6)	2.8 (2.2–3.1)	1.9 (1.5–2.3)	1.7 (1.2–2.5)	0.8 (0.2–1.2)
	p	**0.011**	**0.003**		0.96	**0.003**	0.51	**0.002**	0.29	0.96

Comparison between satisfying (1) or not satisfying (0) the considered variable.

core-set of 17 arteries and respectively represent the sum of stenosis and dilation scores in individual arteries[1].
Objectives: To use ASS, ADS and the stenosis and dilation scores of individual arteries to describe a cohort of LVV patients and identify heterogeneity between patients.
Methods: The ASS, ADS and individual artery scores have been derived from 110 LVV (81 TA, 29 GCA) patients. Model-based clustering optimising the Bayesian Information Criterion and principal component analysis were performed.
Results: Arterial involvement was shown to be differed in GCA and TA: TA has higher ASS than GCA (median, IQR: 20, 11–29 Vs 5, 0–11; $p<0.001$) and lower ADS (0, 0–5 Vs 6, 0–13; $p=0.019$). The scatterplot of ASS and ADS revealed incomplete overlap of arterial involvement in GCA and TA. No differences were seen in TA with disease onset before or after 40 yrs. Age at onset, ASS and ADS did not correlate in TA, suggesting stenotic and aneurysmal arterial remodelling are independent. In GCA, ASS and ADS were negatively correlated ($\rho=-0.401$; $p=0.031$) and ADS correlated with age at onset ($\rho=0.383$; $p=0.040$), suggesting the existence of a biologic "switch" between arterial stenosis and dilation, regulated by age at onset.
We accounted for geographical distribution of lesions by evaluating the scores of individual arteries with correspondence analysis. Arterial involvement was symmetric with tripolar segregation: stenosis in the supra-aortic branches, stenosis in the aorto-abdominal district and arterial dilation (Fig 1A). When patients exhibited the first two components, three different clusters were recognised (Fig 1B), with different ASS, ADS and damage as assessed by the TA damage score ($p<0.001$ for all tests). 27/29 (93%) of GCA patients were included in cluster 1 and 3, while 77/81 (95%) of TA clustered in 2 and 3. Of interest, density graphs showed (i) a different distribution of arterial involvement in GCA and TA (Fig 1C-D), and (ii) potential for identification of novel disease subsets (2 in GCA and 3 in TA). A comparable distribution was seen in TA with onset before or after 40 yrs (Fig 1E). Lastly, when patients with disease onset after 50 yrs (11 TA, 28 GCA) were studied, a trimodal distribution was observed, suggesting discrete phenotypes of arterial involvement exist, rather than a continuum (Fig 1F).



Conclusions: Arterial involvement differs in TA and GCA, although some overlap exists. Elderly TA is similar to juvenile TA, while a potential biologic "switch", yet to be identified, regulating the final outcome of arterial remodelling and influenced by ageing, is present in GCA. Three main patterns of arterial involvement appear to exist. LVVs represent the composition of different discrete subsets rather than a phenotypic continuum.
References:
[1] : Tombetti et al. EULAR 2015 Poster FRI0258.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6386

THU0300 CENTRAL NERVOUS SYSTEM INVOLVEMENT IN GRANULOMATOSIS WITH POLYANGIITIS (WEGENER) IN A LARGE SERIES OF PATIENTS WITH ANCA-ASSOCIATED VASCULITIDES (AAV).REVAS STUDY-GEAS-SEMI

R. Solans-Laqué[1], M. Rodriguez-Carballeira[2], M. Castillo[3], G. Fraile[4], J. Rios[5], X. Solanich[6], F. Martinez-Valle[1], L. Saez[7], F. Pasquau[8], E. Fonseca[9] on behalf of REVAS Study group. *[1]Internal Medicine, Vall Hebron University Hospital, Barcelona; [2]Internal Medicine, Mutua Hospital, Terrassa; [3]Internal Medicine, Virgen Rocio Hospital, Sevilla; [4]Internal Medicine, Ramon y Cajal Hospital; [5]Internal Medicine, la Paz University Hospital, Madrid; [6]Internal Medicine, Bellvitge University Hospital, Hospitalet; [7]Internal Medicine, Miguel Servet University Hospital, Zaragoza; [8]Internal Medicine, Marina Baixa Hospital, Alicante; [9]Internal Medicine, Cabueñes Hospital, Gijon, Spain*

Background: GPA is a necrotizing systemic vasculitis that usually involves ENT, lung and kidneys. Neurological manifestations appear in 25–50% of patients, usually involving peripheral nervous system. CNS involvement, has been reported in only 7–11% of cases
Objectives: to describe the clinical features and outcome of patients with GPA and CNS involvement in a large series of patients with AAV
Methods: multicenter retrospective-longitudinal study that encompassed patients diagnosed with AAV between Jan 1995 and Nov 2014 in 21 Centres from Spain (REVAS Study). Statistical anlysis was performed using SSPS vs20 package
Results: 455 patients (188 GPA, 167 MPA and 100 EGPA) were included. Mean age at diagnosis was 55.7±17.2y. ANCA were positive in 86.8% of cases (35.8% C-ANCA, 51% P-ANCA). Median time to diagnosis was 4 weeks (IQR 10). Median follow-up time was 80 months (IQR 105). Neurological involvement was documented in 156 (34.5%) patients, but only 33 (7.3%) presented CNS involvement at disease onset. From those patients, 20 (60.6%) had GPA. Mean age at diagnosis of patients with GPA and CNS involvement was 51.1±16.7y. ANCA were positive in all cases (15 C-ANCA-PR3, 5 P-ANCA-MPO). Headache was the main neurological symptom (60%) followed by sensory (45%) and motor impairment (35%). MRI and/or angio-CT scan were performed in all cases. Cerebral ischaemic lesions were observed in 10 patients, and granulomatous lesions in 9, including pachymeningitis (n=6), spinal cord pachymeningitis (n=2) and isolated granulomatous lesions (n=1). Lumbar puncture was performed in 8 (40%) patients and revealed CSF abnormalities in 70. Diagnosis was confirmed by meningeal biopsy (n=2), ENT biopsies (n=5) and renal biopsy (n=2) in patients with CNS granulomatous lesions, and by renal, pulmonary or peripheral nerve biopsy in patients with CNS ischemic lesions. Headache was predominant in patients with granulomatous lesions, while sensory and motor impairment were predominant in patients with ischemic lesions. Mean BVAS at disease onset was 29.2±9.7, significantly higher than in GPA total cohort (18.2±9.2). Renal involvement was more common in patients with ischaemic lesions than in those with granulomatous (80% vs. 40%, $p<0.001$), and ENT involvement in patients with granulomatous forms (70% vs. 50%, $p<0.005$). Most patients (70%) received oral CF for induction therapy. Two patients received rituximab. For maintenance therapy, 25% of patients received AZA, 20% MMF and the remaining CF. 70% of patients received TM-SX. During follow-up, 58.8% and 40% of patients developed bacterial and opportunistic infections, respectively. Infections were related to oral CF therapy ($p=0.029$). Long-term neurological sequelae were noted in patients with ischaemic lesions (40%) and spinal cord pachymeningitis (100%)
Conclusions: Patients with GPA and CNS involvement have more severe disease at presentation and more treatment-related side effects than patients without CNS involvement. Long-term neurological sequelae are more frequent in patients with ischaemic lesions and spinal cord pachymeningitis
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2520

THU0301 SAFETY FOLLOWING INITIATION OF RITUXIMAB IN GRANULOMATOSIS WITH POLYANGIITIS (GPA) OR MICROSCOPIC POLYANGIITIS (MPA): INTERIM ANALYSIS OF THE RITUXIMAB IN ANCA-ASSOCIATED VASCULITIS REGISTRY (RAVER)

J. Niles[1], N. Allen[2], J.A. Block[3], C.L. Koening[4], C.A. Langford[5], A. Abril[6], A.S. Lee[6], P.A. Merkel[7], L.E. Mertz[8], P.A. Monach[9], L.W. Moreland[10], P.H. Nachman[11], T. Peikert[8], R.F. Spiera[12], D. Wallace[13], F. Erblang[14], M.D. Cascino[15], P. Duncombe[16], V. Malik[14], P. Brunetta[15]. *[1]Massachusetts General Hospital, Boston, MA; [2]Duke University Medical Center, Durham, NC; [3]Rush University Medical Center, Chicago, IL; [4]University of Utah, Salt Lake City, UT; [5]Cleveland Clinic Foundation, Cleveland, OH; [6]Mayo Clinic, Jacksonville, FL; [7]University of Pennsylvania, Philadelphia, PA; [8]Mayo Clinic, Rochester, MN; [9]Boston Medical Center, Boston, MA; [10]University of Pittsburgh School of Medicine, Pittsburgh, PA; [11]University of North Carolina, Chapel Hill, NC; [12]Hospital for Special Surgery, New York, NY; [13]Wallace Rheumatic Disease Research Center, Los Angeles, CA, United States; [14]F. Hoffmann La-Roche, Ltd., Basel, Switzerland; [15]Genentech, Inc., South San Francisco, CA, United States; [16]prn Statistical Consulting Services, Ltd., Ely, United Kingdom*

Background: Therapy-related serious adverse events (SAEs) are important causes of morbidity in patients with GPA or MPA. Long-term safety data of rituximab in GPA/MPA are limited.
Objectives: To characterize safety events in an observational registry of patients with GPA/MPA initiating rituximab.
Methods: This interim analysis of RaVeR, an ongoing open-label real-world study of adult patients with GPA or MPA initiating rituximab (dose/frequency determined by investigator), was conducted when 50% of patient-years (PY) were collected (July 2015). Safety events included serious infections (SI), infusion-related reactions (IRR), serious cardiac events, malignancies, and other serious events. Crude incidence rates (IR) and 95% CI were calculated. Trial registration number: NCT01613599
Results: 97 patients (291 PY) received rituximab, of whom 70% received rituximab retreatment. Median follow-up was 2.4 years. Overall, 91% of patients were ANCA-positive and 78% had GPA. 17 patients (17.5%) had a history of plasmapheresis or dialysis; 20 (20.6%) were receiving rituximab plus cyclophosphamide at baseline. 33 patients had 71 SAEs (32.4/100 PYs [95% CI: 25.32–40.89]). 11 patients had 20 SIs (9.13/100 PYs [95% CI: 5.58–14.10]). 9 patients (9.3%) experienced 13 serious cardiovascular (CV) events (5.93/100 PYs [95% CI: 3.16–10.15]), 12 of which were reported as unrelated to rituximab. Of the 13 CV events, 9 were atrial arrhythmias and most patients had associated renal or CV disease history. There were no serious IRRs or SAEs within 24 hours of rituximab infusion. There were 6 deaths (2.74/100 PYs [95% CI: 1.01–5.96]); causes of death included septic shock, interstitial lung disease, congestive heart failure, cardio-respiratory arrest and 2 deaths of unknown etiology. The severe disease flare rate was 5.94/100 PYs (95% CI: 3.16–10.15). Among patients who received rituximab retreatment, the IRs of SAEs (26.1/100 PYs) and SIs (7.29/100 PYs) were not increased compared with the overall cohort.

Table. Observed safety events of interest

	Number of events	IR per 100 PY (95% CI)
All SAEs	71 in 33 pts (34%)	32.42 (25.3 to 40.9)
Serious infections	20 in 11 pts (11%)	9.13 (5.58 to 14.1)
Serious cardiac events	13 in 9 pts (9%)	5.93 (3.16 to 10.15)
Serious vascular events	6 in 5 pts (5%)	2.74 (1.01 to 5.96)
Malignancies	2 in 2 pts (2%)	0.91 (0.11 to 3.30)

IR, incidence rate; PY, patient-year; SAE, serious adverse event.

Conclusions: In this interim analysis of patients with GPA/MPA treated with rituximab, SAEs were not increased compared with comparable cohorts of patients with renal involvement. Safety events did not increase with rituximab retreatment. These results are consistent with the known safety profile of rituximab and provide preliminary long-term, practice-level safety data for rituximab in GPA/MPA.
Acknowledgements: This study was funded by F. Hoffmann-La Roche, Ltd.
Disclosure of Interest: J. Niles: None declared, N. Allen Grant/research support from: Genentech, Inc., J. Block: None declared, C. Koening Grant/research support from: VA Merit, C. Langford: None declared, A. Abril: None declared, A. Lee: None declared, P. Merkel: None declared, L. Mertz: None declared, P. Monach Grant/research support from: Genentech, Inc.; Bristol-Meyers Squibb; GlaxoSmithCline, Speakers bureau: Medscape, L. Moreland Grant/research support from: Genentech, Inc.; Pfizer; Bristol-Meyers Squibb, Consultant for: Pfizer; Boehringer Ingeheim, P. Nachman: None declared, T. Peikert: None declared, R. Spiera: None declared, D. Wallace: None declared, F. Erblang Employee of: F. Hoffmann-La Roche, Ltd., M. Cascino Employee of: Genentech, Inc., P. Duncombe Shareholder of: prn Statistical Consulting Services, Ltd., V. Malik Employee of: F. Hoffmann-La Roche, Ltd., P. Brunetta Employee of: Genentech, Inc.
DOI: 10.1136/annrheumdis-2017-eular.1177

THU0302 HISTOLOGY FINDINGS IN GIANT CELL ARTERITIS (GCA) AND THEIR RELATIONSHIP WITH THE ULTRASOUND RESULTS: ANALYSIS OF DATA FROM THE TABUL STUDY (TEMPORAL ARTERY BIOPSY VS ULTRASOUND IN DIAGNOSIS OF GIANT CELL ARTERITIS)

C.B. Ponte[1,2], S. Monti[3], S. Singh[4], A. Hutchings[5], A. Diamantopoulos[6], B. Dasgupta[7], W.A. Schmidt[8], R.A. Luqmani[9]. *[1]Department of Rheumatology, Hospital de Santa Maria; [2]Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal; [3]Department of Rheumatology, IRCCS Policlinico S. Matteo Foundation, University of Pavia, Pavia, Italy; [4]Nuffield Department of Surgical Sciences, University of Oxford, Oxford; [5]Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, London, United Kingdom; [6]Department of Rheumatology, Hospital of Southern Norway Trust, Kristiansand, Norway; [7]Department of Rheumatology, Southend University Hospital, NHS Foundation Trust, Southend-on-Sea, United Kingdom; [8]Department of Rheumatology, Immanuel Krankenhaus Berlin, Medical Centre for Rheumatology Berlin-Buch, Berlin, Germany; [9]Nuffield Department of Orthopaedics Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom*

Background: Although temporal artery biopsy (TAB) has been the gold standard for diagnosis of GCA, ultrasound has superior sensitivity but lower specificity. Occasionally, histological evidence of inflammation is restricted to the *vasa vasorum*, the periadventitial small vessels, or both, which could limit the diagnostic sensitivity of ultrasound for GCA. Moreover, false positive ultrasound results have been described in patients with arteriosclerosis on histology.
Objectives: To compare histologic findings with ultrasound results from patients with suspected GCA included in the TABUL study (a multinational study to assess the relative performance of ultrasound and TAB for diagnosing GCA).
Methods: All patients with newly suspected GCA underwent an ultrasound of both temporal and axillary arteries, followed by a TAB, within 7 days of commencing glucocorticoid therapy. TAB pathological diagnoses were analysed and the different histologic features were compared with the ultrasound results using Chi-square or Fisher exact tests.
Results: Results for TAB and ultrasound were available in 388 patients (69% with a final clinician's diagnosis of GCA). An artery was definitely obtained in 363 (94%) TABs; the pathological diagnosis was GCA in 104 (29%) cases, arteriosclerosis in 35 (10%), normal in 203 (56%) and other conditions in 21 (6%). All TABs compatible with GCA also had a final clinician's diagnosis of GCA (73% with positive ultrasound). Table 1 shows that ultrasound positivity occurred more frequently in patients where the media was the predominant site of inflammation (p=0.01). The ultrasound result was positive in 9 (26%) cases where TAB was consistent with arteriosclerosis, 8 (89%) of whom had a final clinician's diagnosis of GCA. The ultrasound was positive in 64 (32%) cases where TAB was normal, 52 (81%) of whom had a final clinician's diagnosis of GCA.

Table 1: Relationship between the histologic features of patients with a TAB diagnosis of GCA and ultrasound results

Histologic features (n patients)	Ultrasound positive (n=76)	Ultrasound negative (n=28)	*p value*
Predominant site of inflammatory cellular infiltrate			
Predominant intima infiltrate (n=8)	7 (87.5%)	1 (12.5%)	*0.679*
Predominant IEL infiltrate (n=13)	10 (76.9%)	3 (23.1%)	*1.000*
Predominant media infiltrate (n=21)	20 (95.2%)	1 (4.8%)	*0.010*
Predominant adventitia infiltrate (n=19)	11 (57.9%)	8 (42.1%)	*0.099*
Predominant *vasa vasorum* infiltrate (n=4)	2 (50%)	2 (50%)	*0.293*
Predominant transmural infiltrate (n=39)	26 (66.7%)	13 (33.3%)	*0.254*
Histologic specific findings			
Presence of giant cells (n=74)	58 (78.4%)	16 (21.6%)	*0.056*
Presence of vessel complete occlusion (n=24)	17 (70.8%)	7 (29.2%)	*0.778*
Presence of IEL fragmentation (n=86)	61 (70.9%)	25 (30.1%)	*0.386*
Presence of intimal hyperplasia (n=91)	65 (71.4%)	26 (28.6%)	*0.506*

TAB = temporal artery biopsy; IEL= internal elastic lamina

Conclusions: Amongst patients with suspected GCA, ultrasound is more likely to be positive when histological inflammation is predominantly present in the intima-media. No significant correlation between histologic findings and negative ultrasound results was found, but the small number of cases with predominant *vasa vasorum* infiltrates in our cohort limited this analysis. There was only one false positive ultrasound in patients with arteriosclerosis on TAB.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3544

THU0303 CLINICAL FEATURES AND PROGNOSIS OF ANCA-ASSOCIATED VASCULITIS WITH RENAL INVOLVEMENT AT DIAGNOSIS

S. Fukui, N. Iwamoto, T. Shimizu, M. Umeda, A. Nishino, T. Koga, S.-Y. Kawashiri, Y. Hirai, K. Ichinose, M. Tamai, H. Nakamura, T. Origuchi, A. Kawakami. *Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan*

Background: Kidneys are major organs targeted by antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Clinical manifestations, laboratory data, and prognosis of AAV with renal involvement at diagnosis are not elucidated.

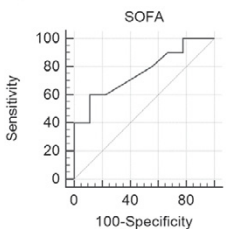
Objectives: We compared clinical features of AAV with renal involvement with patients without renal involvement.
Methods: We conducted an observational study of 104 patients with AAV (12 eosinophilic granulomatosis with polyangiitis, 23 granulomatosis with polyangiitis (GPA), 66 microscopic polyangiitis, 3 renal limited vasculitis) between in 2008 to 2016 in Nagasaki University Hospital. Using medical records, we analyzed the patients' baseline variables, laboratory data, clinical symptoms, and therapeutic outcomes after treatments including episodes of relapses, initiations of dialysis, and death. Renal involvement was defined as the state with estimated glomerular filtration rate <60 mL/min/1.73 m^2 or microscopic hematuria (2+ or greater) which were not caused by renal diseases except for AAV.
Results: Sixty-nine patients had renal involvement. Patients with renal involvement group had higher median age at diagnosis than patients without renal involvement group (75 years vs. 66 years, $p<0.001$). Patients with renal involvement included fewer GPA patients compared to other AAV types. Patients with renal involvement had lower hemoglobin levels (10.3 g/dL vs. 12.3 g/dL) and lower platelet levels ($23.7x10^4/\mu L$ vs. $28.7x10^4/\mu L$). Patients with renal involvement had higher erythrocyte sedimentation rate (78mm/h vs. 20mm/h), MPO-ANCA titers (116 U/mL vs. 58 U/mL) and urine protein levels (0.81 g/gCr vs. 0.15 g/gCr). Patients with renal involvement had lower C3 levels, but CH50 and C4 levels did not differ between in two groups. There were no differences in treatments including doses of prednisolone and use of methylprednisolone pulse and cyclophosphamide between in two groups. Multivariable regression analysis revealed that age at diagnosis is the most significant explanatory variable to renal involvement. Nineteen percent of patients with renal involvement had initiations of dialysis. Multivariable analysis demonstrated estimated glomerular filtration rate at diagnosis is the most significant explanatory variable to initiations of dialysis (p=0.010). Receiver operating characteristic curve showed the cutoff level of estimated glomerular filtration rate to distinguish initiations of dialysis was 37mL/min/1.73 m^2 (sensitivity=79%, specificity=70%, area under the curve=0.80). Assessed by a log-rank test, overall survival rate did not differ between in two groups (p=0.29).
Conclusions: Patients with renal involvement had higher age at diagnosis. Patients with renal involvement included fewer GPA patients. Patients with renal involvement had lower C3 levels. Estimated glomerular filtration rate at diagnosis is the most significant explanatory variable to initiations of dialysis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2859

THU0304 VASCULITIS PATIENTS ADMITTED TO INTENSIVE CARE UNIT: IMPLICATIONS FROM A SINGLE-CENTER RETROSPECTIVE STUDY

A. Watad[1], O. Shovman[2], N.L. Bragazzi[3], Y. Shoenfeld[4], H. Amital[5], Y. Haviv[6]. *[1]Internal Medicine B; [2]Department B, Sheba Medical Center, Tel Aviv, Israel; [3]Department of Health Sciences, Genova university, Genoa, Italy; [4]Zabludowicz center for Autoimmune Diseases; [5]Sheba Medical Center, Tel Aviv, Israel; [6]Department of General Intensive Care, Sheba Medical Center, Tel Aviv, Israel*

Background: Vasculitides are a heterogeneous group of disorders that are characterized by the inflammation of the vasculature vessels. Vasculitides may present as a life-threatening condition and cause higher rates of morbidity and mortality. There are few studies assessing the outcome and prognosis of patients with vasculitides admitted to the intensive care (ICU).
Objectives: To assess the outcome of vasculitides patients required admission to ICU and to identify factors associated with mortality
Methods: A retrospective study was carried out, including all patients who were diagnosed with vasculitides and admitted to the ICU of the Sheba Medical Center, Tel-Hashomer, throughout the years 2000–2014. Continuous variables were computed as mean±standard deviation, whilst categorical variables were recorded as percentages, where appropriate. Student's t-test and chi-squared analyses were performed for investigating the impact of the clinical variables on mortality.
Results: Twenty-five vasculitides patients admitted to the ICU were included in the present study (mean age 52±14y, sex ratio M/F: 12/13). The mortality rate among these patients was 48%. Leading causes for ICU admission were: infection (64%), vasculitides exacerbation (34%), and hemorrhage (16%). Variables significantly associated with mortality were: the use of Rituximab prior to admission ICU (p=0.039), involvement of the hemodynamic system (p=0.024), the SOFA score (p=0.041), blood infections during the first week at ICU (p=0.018) and persisting after the first week (p=0.007).

Figure 1. Receiver Operating Characteristic (ROC) analysis of the predictive power of the Sequential Organ Failure Assessment (SOFA) score, in predicting the mortality of vasculitis patients admitted at intensity care unit (ICU), in terms of sensitivity and specificity.



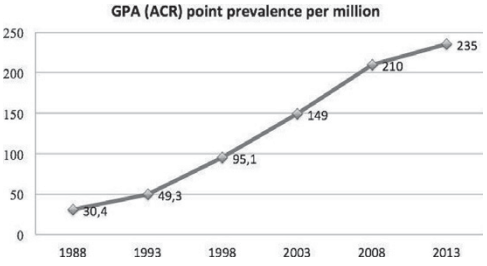
Conclusions: Our study confirms the high mortality rate among vasculitides patients and mainly among those requiring admission to ICU. SOFA score and pre-admission treatment with rituximab have been found to be predictive of mortality.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4431

THU0305 EPIDEMIOLOGY OF ANCA-ASSOCIATED VASCULITIS IN NORTHERN NORWAY

A.T. Nilsen[1], R.A. Watts[2], W. Koldingsnes[1]. *[1]Department of Rheumatology, University Hospital of North Norway, Tromsø, Norway; [2]Norwich Medical School, University of East Anglia, Norwich, United Kingdom*

Background: The ANCA-associated vasculitides (AAV) have increased in prevalence since the 1980s, with granulomatosis with polyangiitis (GPA) being most prevalent in Caucasian population in circumpolar areas. This was also shown in a study on GPA in northern Norway between 1984 and 1998, which further showed an increasing incidence [1].
Objectives: The present study aimed to investigate the subsequent 15-year period in the same region, now including all the AAVs.
Methods: The study area has 11 hospitals, no private specialist in rheumatology or nephrology, and an adult population of 371 928. We retrospectively searched all hospital databases, using ICD-10 codes potentially compatible with AAV. Patients diagnosed with AAV from 1999 through 2013 according to the European Medicines Agency (EMEA) algorithm, and for GPA also the subgroup fulfilling the American College of Rheumatology (ACR) 1990 criteria, were included. For prevalence data, patients residing in the area, but with AAV diagnosis prior to 1999, were included too.
Results: Using the EMEA algorithm, 90 incident cases were classified as GPA, 39 as microscopic polyangiitis (MPA) and 14 as eosinophilic granulomatosis with polyangiitis (EGPA). Within the GPA group, 78 patients also met the ACR criteria. The results for incidence and prevalence are given in Table 1:

		Annual incidence/million				Point prevalence at 31. Dec		
		1999–2003	2004–2008	2009–2013	Total period	2003	2008	2013
ACR	GPA	11,4	16,7	12,5	13,6	149	210	235
EMEA	GPA	11,4	19,9	15,7	15,8	149	226	261
EMEA	MPA	2,7	6,5	11,0	6,8	10,8	31,9	63,3
EMEA	EGPA	2,7	2,7	1,6	2,3	13,5	18,6	30,4
EMEA	All AAV	16,8	29,0	28,2	24,9	173	276	354



Conclusions: The GPA incidence and prevalence in this study are the highest reported. Though the incidence has stabilized, prevalence is still increasing, albeit at a decelerating rate (Graph 1). Moreover, the total AAV prevalence doubled in the last 10 years, exceeding previous estimates. Incidence of MPA and EGPA are both within the range found elsewhere. But the MPA incidence appears to be rising reminiscent of GPA before the turn of the century.
References:
[1] Koldingsnes W, Nossent H. Epidemiology of Wegener's granulomatosis in northern Norway. Arthritis Rheum. 2000;43(11):2481–2487.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4158

THU0306 PREVALENCE AND CHARACTERISTICS OF NEUROPATHY IN PATIENTS WITH ANCA ASSOCIATED VASCULITIDES: DATA FROM THE DCVAS STUDY

A. Bischof[1,2,3], V.K. Jaeger[4], M.P. Collins[5], R.D.M. Hadden[6], R. Luqmani[7], R. Suppiah[8], A. Craven[7], T. Daikeler[9]. *[1]Neurology, University of California San Francisco, San Francisco, United States; [2]Neurology, University Hospital Basel, Switzerland; [3]Immunology Clinic; [4]Rheumatology, University Hospital Basel, Basel, Switzerland; [5]Neurology, Medical College of Wisconsin, Milwaukee, United States; [6]Neurology, King's College Hospital, London; [7]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom; [8]Rheumatology, Auckland District Health Board, Auckland, New Zealand; [9]Rheumatology, University Hospital Basel, Switzerland, Basel, Switzerland*

Background: Epidemiological data on vasculitic neuropathy (VN) in ANCA associated vasculitides (AAV) are scarce and controversial. The Diagnostic and

Classification Criteria for Primary Systemic Vasculitis (DCVAS) study is a large multinational, observational case control study collecting detailed data from patients with primary vasculitides at inclusion.
Objectives: To describe the prevalence, associations with other disease characteristics and patterns of VN in patients with AAV at initial presentation.
Methods: Patients included in the DCVAS study and having completed 6 months follow-up until December 2016 were screened. All patients with a diagnosis of AAV confirmed by an independent expert team were included. VN was diagnosed by clinical features, neurophysiology and/or nerve biopsy. AAV organ manifestations were identified by described symptoms or by the items from the vasculitis damage index. Laboratory parameters and histology were retrieved from the database. Data were analysed descriptively.
Results: By Dec 2016, 1268 patients with a physician submitted diagnosis of AAV had their case summaries reviewed by an expert panel and the diagnosis of AAV confirmed in 839. 484 (58%) had GPA, 195 (24%) MPA, 150 (18%) EGPA and 10 (1.2%) an unclassified AAV. Of these patients, 247 (29.4%) had findings compatible with VN. Mean age in patients with and without VN was 58.7 (SD 15) and 55.4 (SD 17) years, respectively. 133 (53.9%) of patients with VN and 289 (48.8%) without VN were female. VN was diagnosed by biopsy in 5.7%, by the presence of mononeuritis multiplex in 10.1% and by the description of new onset peripheral neuropathy in the context of AAV in 84.2%. Frequency of VN was 19.4% in GPA, 24.1% in MPA and 68.0% in EGPA. 5.6% of patients had motor, 27.9% sensory, 36.4% had sensorimotor neuropathy, and 7.4% had neuropathy exclusively documented on VDI. VN was associated with older age (p=0.008), the presence of MPO-ANCA (p=0.005), skin ($p \leq 0.001$), musculoskeletal ($p \leq 0.001$), cardiac (p=0.001) and multiorgan (>5 organs) involvement (p=0.05) and with the absence of renal (p=0.002), gastrointestinal (p=0.03) and eye involvement ($p \leq 0.001$).
Conclusions: VN has a high prevalence in patients with AAV. In EGPA, more than half of the patients suffered from peripheral nerve involvement. A typical clinical scenario (e.g. older age, MPO positivity, skin and joint/muscle involvement) may help to identify patients at risk of neuropathy. DCVAS was not primarily designed to assess VN, therefore these data should be interpreted with caution.
References:
[1] Collins MP, Arnold WD, Kissel JT. The neuropathies of vasculitis. Neurol Clin. 2013;31(2):557–595.
[2] Craven A, Robson J, Ponte C, et al. ACR/EULAR-endorsed study to develop Diagnostic and Classification Criteria for Vasculitis (DCVAS). Clin Exp Nephrol. 2013;17(5):619–621.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4151

THU0307 NMR-BASED SERUM METABOLOMICS OF PATIENTS WITH TAKAYASU ARTERITIS (TA): RELATIONSHIP WITH DISEASE ACTIVITY

A. Jain[1], D. Kumar[2], R. Misra[1], P.A. Bacon[3], A. Guleria[4], D.P. Misra[4], S. Singh[4], D. Dubey[4], S. Chaurasia[4], S. Kumar[4], U. Kumar[4], S.K. Mishra[4], A. Zanwar[4], A. Rawat[4]. *[1]Clinical Immunology, SGPGIMS; [2]CBMR, Lucknow, India; [3]Department of Rheumatology, Birmingham, United Kingdom; [4]Affiliation not provided*

Background: Takayasu arteritis (TA) is a chronic large vessel vasculitis of unknown etiopathogenesis. The serological and radiological parameters currently used to assess the disease activity are not highly specific and there is a pertinent need for a biomarker discovery. In our previous study [1], NMR based serum metabolomics had revealed distinctive metabolic signatures in patients with TA compared to age/sex matched healthy controls. In this study we sought to investigate whether these distinctive metabolites correlate with disease activity.
Objectives: To identify the discriminatory serum metabolic profiles and their correlation with disease activity.
Methods: Patients with TA fulfilling ACR criteria were assessed for disease activity by ITAS 2010, with a score of 4 or more, considered as active. The serum metabolic profiles of active and inactive TA patients were obtained at 800 MHZ NMR spectrometer and were compared using multivariate orthogonal partial least-squares discriminant analysis (OPLS-DA) to identify metabolites that changed in response to disease activity [based on PLS-DA VIP (variable importance on projection) score >2.0 and permutation test, p-value <0.01].
Results: 88 patients were categorized into active (34) and inactive (54) groups. Median age in active and inactive groups was 25 years and 27 years respectively. Female to male ratio was 3.4:1 in the active group and 5:1 in the inactive group. Majority had class V disease. Mean duration of illness was 4.0±3.5 years in active TA and 6.5±5.5 years in inactive TA group. An exquisite separation in OPLS-DA score plot showed metabolic differences between active and inactive TA patients (Fig. 1A). The key metabolite entities identified with highest discriminatory potential (VIP score >2) were glucose, glutamine, glycine, N-acetyl glycoprotein (NAG), choline, and low/very-low density lipoproteins (LDL/VLDL). Of them glucose, glycine, and NAGs were elevated in the sera of active TA patients, whereas glutamine, choline and LDL levels were decreased in these patients. Receiver operating characteristic (ROC) curve analysis revealed NAG has the highest potential to discriminate active from inactive TA patients (area under the ROC curve was 0.75 (p-value <0.0001) (Fig. 1B, 1C).
Conclusions: The study revealed discriminatory metabolites between active and inactive TA patients and evaluated the possibility of NAG as a clinical biomarker for activity judgment in this disease. However, more work needs to be done to validate the results in a large cohort of patients in a longitudinal manner.

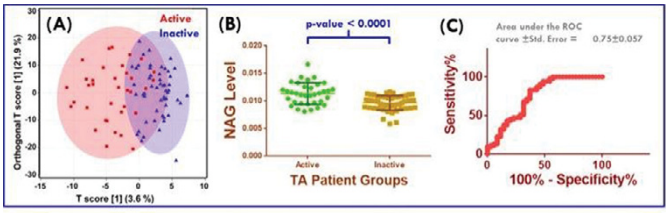


Figure 1: **(A)** 2D score plot obtained from OPLS-DA analysis of 1D ^{1}H NMR spectra. **(B)** Scatter plot showing the serum levels of NAG in active and inactive Takayasu arteritis (TA) patients. The center line refers to the median; whereas the dark lines above and below the center line indicate the 25th and 75th percentiles. **(C)** The receiver operating characteristic (ROC) curve analysis performed to evaluate the specificity, sensitivity, and area under ROC curve (AUC) of NAG peak, showing discriminatory potential of NAG metabolite, based on univariate (box plot) and ROC curve analysis.

References:
[1] Guleria A, Misra DP, Rawat A, Dubey D, Khetrapal CL, Bacon PA, Misra R, and Kumar D, NMR based serum metabolomics discriminates Takayasu Arteritis from Healthy Individuals: A proof of principle study" Journal of Proteome Research (2015), 14 (8), 3372–3381.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6057

THU0308 EXTENSIVE ANALYSIS OF T CELL RECEPTOR GAMMA (TCRG) GENE REARRANGEMENTS REVEALS A SIMILAR REPERTOIRE IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA) AND IN HYPEREOSINOPHILIC SYNDROME (HES)

C. Baldini[1], S. Galimberti[2], E. Ciabatti[2], I. Petrini[3], G. Tarrini[2], M. Latorre[4], E. Elefante[1], F. Ferro[1], R. Grossi[2], N. Pisanti[2], M. Petrini[2], M. Mosca[1]. *[1]Clinical and Experimental Medicine, Rheumatology Unit; [2]Clinical and Experimental Medicine, Hematology Unit; [3]Translational Research and New Technology in Medicine, General Pathology; [4]Cardio-Thoracic and Vascular Department, University of Pisa, Pisa, Italy*

Background: Hypereosinophilia-associated syndromes are a heterogeneous group of diseases characterized by sustained and elevated blood eosinophilia with evidence of eosinophil-induced organ damage. Classically, Eosinophilic granulomatosis with polyangiitis (EGPA) and Hypereosinophilic syndrome (HES) present several overlapping clinical and laboratory features, making it challenging to correctly insert patients in restricted and well-defined categories with specific and more effective therapeutic approaches. Therefore, great efforts are ongoing searching for novel biomarkers able to differentiate these two disorders in daily practice.
Objectives: To detect T cell receptor gamma (TCRG) clonal rearrangements in EGPA and HES, comparing the frequency distribution of V region and J region segment utilization in the study population.
Methods: In this single center study, we included consecutive patients with a diagnosis of EGPA and HES. Inclusion criteria were: documentation of a persistent peripheral eosinophilic count of ≥1.5 x109/L and signs or symptoms of organ involvement. Clinical and laboratory data of the patients were collected. Sequence-based determination of the frequency distribution of TCRG Gene Rearrangements was performed using next-generation sequencing with the Illumina MiSeq (LymphoTrack TRG assay, Invivoscribe).
Results: We included 21 patients (9 with EGPA and 12 with HES). Four EGPA patients were MPO-ANCA positive. We detected TCRG clonal rearrangements in 44% (4/9) patients with EGPA and in 42% (5/12) patients with HES (p-value = n.s). No association was observed between TCRG clonal rearrangements and ANCA status in EGPA patients. Recurrent TCRG gene rearrangements were observed; in particular, Vg10JgP1 (5 cases) and Vg4Jg1/2 (4 cases) were detected in both EGPA and HES, whereas Vg9Jg1/2 (2 cases) and Vg10Jg1/2 (2 cases) were found only in patients with HES.
Conclusions: Even if preliminary, this study reveals a similar T cell receptor gamma repertoire in EGPA and HES, thus suggesting a possible antigen-driven inflammatory response underlying hypereosinophilia in both EGPA and HES. Moreover, our results would suggest that the TCR clonality cannot be used as a tool for the differential diagnosis between EGPA and HES.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4340

THU0309 TREATMENT WITH METHOTREXATE AND RISK OF RELAPSES IN PATIENTS WITH GIANT CELL ARTERITIS IN CLINICAL PRACTICE

D. Freites Núñez, J. Font, C. León, I. Morado, L. Rodríguez-Rodríguez, L. León, Z. Rosales, B. Fernández, J. Jover, L. Abásolo. *Reumatologia, Hospital Clinico San Carlos, Madrid, Spain*

Objectives: To assess the incidence rate of relapses and to analyze the risk of relapses in patients with *Giant Cell Arteritis* (GCA) treated with and without

Methotrexate (MTX), in clinical practice. Other factors associated were also investigated.
Methods: An inception cohort of GCA was assembled in the out-patient clinic at Hospital Clinico San Carlos, including patients from the date of diagnosis (Jan-1991 until Sept-2013), and followed-up until Sept-2014. Main outcome: relapses defined as after an objective improvement, patient has again symptoms or signs of GCA with high ESR and the need to increase corticosteroids at least 10mg. The independent variable was exposure to MTX over time. Covariables: Sociodemographic, clinical, and treatment. Incidence rates of relapses (IR) per 100 patient-years with their 95% confidence intervals [CI] were estimated using survival techniques. Time of exposure comprised the period from diagnosis until: lost of follow-up, main outcome, exposure to MTX or the end of the study. MTX influence on IR was analyzed by multivariable Cox models.
Results: 168 patients were included (675 patient-years). 80% of them were female, with a mean age of 76±7 years. 65% of the patients were on MTX, with mean dose of 10 mg/week. 31% of patients had relapses with an IR of 12 [9.6–14.9]. The median number of relapses was 1 [1–2], with a median lag time of 1.6 [0.6–6.3] years. In the multivariate analysis, exposure to MTX had less risk of flaring compared to those never on MTX ($p<0.05$). Other variables included in the final model were: visual alterations, constitutional symptoms or malaise at clinical presentation of GCA.
Conclusions: The use of MTX seems to decrease the risk of recurrences. We also found other factors influencing on flares.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6118

THU0310 FREQUENCY OF RELAPSES AND TREATMENT DISCONTINUATION DURING LONG-TERM FOLLOW-UP OF PATIENTS WITH GIANT CELL ARTERITIS

C. Tsalapaki, A. Lazarini, K. Antonatou, K. Thomas, K. Klavdianou, C. Koutsianas, D. Vassilopoulos. *Joint Rheumatology Program, Clinical Immunology-Rheumatology Unit, 2nd Department of Medicine and Laboratory, National and Kapodistrian University of Athens School of Medicine, Hippokration General Hospital, Athens, Greece*

Background: There are limited data regarding the long term outcomes of patients with giant cell arteritis (GCA) in the modern therapeutic era.
Objectives: To evaluate relapse, treatment discontinuation and complication rates in GCA patients during long term follow-up.
Methods: A retrospective systematic chart review of GCA patients who were followed in an Academic Rheumatology Unit between 2002 to 2016 was performed. Demographic, clinical, laboratory and treatment data were collected and analyzed.
Results: 53 GCA patients were included in the study. 62% (n=33) were women with a mean age at diagnosis of 73±8.8 years and median duration of symptoms of 1.3 months. 41 patients (77%) had biopsy proven GCA while in 5 patients (9%) there was evidence of large vessel involvement. At presentation, the most common symptoms were headache (60%), fever (51%), scalp tenderness (47%), jaw claudication (39%), visual disturbances (23%), polymyalgia rheumatica symptoms (9%) and vision loss (6%). Regarding laboratory data at baseline, the median ESR and CRP were 101 mm/h and 50 mg/dl respectively while the mean hemoglobin (Hb) and platelet (PLT) count was 11.3±1.2 g/dl and 381.000±134.000, respectively. All patients were initially treated with tapering doses of pos steroids (mean start prednisolone dose: 42±12 mg/day) while 2 patients (4%) were given IV steroid pulses. During follow-up (3.1±2.7 years), for patients with did not adequately respond or could not tolerate steroids, non-biologic (n=12, 23%) or biologic DMARDs (n=4, 7%) were added. Relapses requiring change in immunosuppressive therapy occurred in more than half of patients (n=28, 53%); among these 67% were laboratory and 56% clinical relapses. Osteoporosis (17%), cataracts (7%), fractures (4%) and avascular necrosis (2%) developed during chronic steroid treatment. At the last follow-up visit, 39% (n=21) of patients had discontinued steroids and 31% (n=17) all treatments. Comparing the group of patients who had discontinued treatment (D/C group) to those who were unable to stop therapy (continued therapy group), there were no statistically significant differences (age, duration of symptoms at diagnosis, initial steroid dose, baseline and follow-up ESR, CRP, Hb and platelet values, relapses, co-administration of DMARDs, comorbidities), except from gender (females: D/C group=41%, continued therapy group=72%, p=0.03). Kaplan-Meier analysis also showed that the median time to discontinuation of treatment was longer in females compared to males (log rank p=0.018).
Conclusions: In this long-term follow-up study, relapses occurred in more than half of GCA patients while only one out of three patients were able to discontinue all therapies. Among different variables, only male sex was associated with earlier treatment discontinuation.
Acknowledgements: Supported by research grants from the Special Account for Research Grants (S.A.R.G.), National and Kapodistrian University of Athens, Athens, Greece.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6115

THU0311 FECAL MICROBIOTA IN BEHÇET'S SYNDROME PATIENTS WITH MUCOCUTANOUS AND UVEITIS INVOLVEMENT

D. Tecer[1], F. Gogus[1], A. Kalkancı[2], M. Erdogan[2], S. Coban[3], M. Hasanreisoglu[4], T. Karakan[5]. *[1]Department of Physical Medicine and Rehabilitation, Division of Rheumatology; [2]Department of Medical Microbiology; [3]School of Medicine phase 3 student; [4]Department of Ophthalmology; [5]Department of Gastroenterology, Gazi University, Faculty of Medicine, Ankara, Turkey*

Background: Innate immunity has a major role in the pathogenesis of Behçet's syndrome. The gut microbiota is an active component of the immune system. It plays an important role in the formation of the immune system in the early life and in the continuation of immune homeostasis through the life. Dysbiosis, imbalance in the gut microbiota, can lead to many serious metabolic and inflammatory pathologies
Objectives: We aimed to investigate the gut microbiota structure in Behçet's syndrome patients with mucocutanous and uveitis involvement only.
Methods: 6 patients with Behçet's syndrome with uveitis, 12 patients with familial Mediterranean fever (FMF) and 9 patients with Crohn's disease (CD) and 10 healthy controls were included. Patients, positive and healthy controls were excluded if they had one of the following combined diseases/situations: a) gastrointestinal surgical history (e.g. bariatric surgery, gastrectomy or colectomy), b) antibiotic or probiotics use in the last 3 months, c) specific dietary restriction, d) malignancy, e) additional autoimmune disease or inflammatory bowel disease. Total DNA was extracted from fecal samples using the QIAamp DNA stool Mini Kit following the manufacturer's instructions (Qiagen). Next generation sequencing of 16SrRNA gene was performed using Ion Torrent Technology. Partial 16S rRNA ene sequences were amplified from extracted DNA using the 16S Metagenomics Kit (Life Technologies). The integrity of the PCR amplicons was analyzed by gel electrophoresis. PCR products were purified using AMPure XP DNA purification beads and Invitrogen DynaMaq magnet apparatus. DNA concentration of the amplified sequence was equalized through the Qubit System (Life Technologies). The libraries was created by using the Ion Plus Fragment Library Kit. Barcodes were also added to each sample using the Ion Express Barcode Adapters Kit. Emulsion PCR was carried out using the Ion One Touch 2 machine. Sequenciing of the amplicon libraries was carried out on a 318 chip the Ion Torrent Personal Genome Machne System and Ion PGM Hi-Q kit. 16S rRNA sequences were analyzed by Ion Reporter Software.
Results: In healthy subjects, fecal microbiota consisted predominatly of Bacteroidetes (53.2%) including Bacteroides and Prevotella genuses. Firmicutes such as Bacilli, Clostridia, followed, consisting 31.2% of the bacterial community. Fecal bacterial flora of patients with Behçet's syndrome consisted of Firmicutes (45%), Proteobacteria (23%) such as Enterobacteriaceae and Prevotellaceae, and Bacteriodetes (10%). FMF cases were found to be colonized by Firmicutes (39.3%), Bacteriodetes (32.2%) and Proteobacteria (13.6%) predominantly. CD cases were colonized by Enterobacteriacea (43%), and other Proteobacteria groups, followed by Bacteriodetes (15.4%) and Firmicutes (8.8%).
Conclusions: Fecal flora of patients with Behçet's syndrome and of positive control groups (FMF and CD) differed significantly from that of healthy controls. In a subgroup of patients with Behçet's disease with uveitis and muscucutaneaous involvement only, firmicutes species seem to be the dominant bacterial fecal flora.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6541

THU0312 PERFORMANCE CHARACTERISTICS AND PREDICTORS OF TEMPORAL ARTERY ULTRASOUND AND BIOPSY FOR THE DIAGNOSIS OF GIANT CELL ARTERITIS IN A REAL WORLD POPULATION; A PROSPECTIVE COHORT STUDY

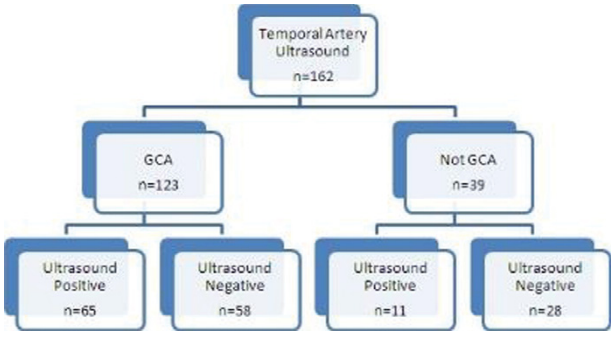
R. Conway[1], S. Di Bello[1], L. O'Neill[1], G.M. McCarthy[2], C.C. Murphy[3], D.J. Veale[1], U. Fearon[4], R.P. Killeen[5], E.J. Heffernan[5], E.S. Molloy[1]. *[1]Rheumatology, St Vincents University Hospital; [2]Rheumatology, Mater Misericordiae University Hospital; [3]Ophthalmology, Royal College of Surgeons in Ireland; [4]Molecular Rheumatology, Trinity College Dublin; [5]Radiology, St Vincents University Hospital, Dublin, Ireland*

Background: The diagnosis of giant cell arteritis (GCA) remains a clinical one. Temporal artery (TA) ultrasound (US) has been proposed as a new diagnostic tool in GCA.
Objectives: To assess the performance characteristics of TA US and biopsy in routine clinical practice.
Methods: All patients presenting with suspected GCA to our institutions are recruited to a prospective registry. Patients who had both a TA US and biopsy performed at the time of presentation were included in the current study. US was performed by 2 radiologists. The performance characteristics of both tests were compared to physician diagnosis at six months following presentation. Predictive factors for positive US and biopsy were explored in univariate and multivariable logistic regression analyses.
Results: 162 patients were included, 123 (76%) with GCA. Mean (SD) duration of glucocorticoids was 6.6 days (19.4) at the time of TA US and 6.2 days (8.4) at the time of TA biopsy. US had a sensitivity of 52.8% (95% CI 43.7, 61.9) and specificity of 71.8% (95% CI 54.9, 84.5). There were 11 false positive US results; 5 with migraine, 2 other vasculitides, 2 local infections, 2 malignancies. Biopsy

had a sensitivity of 48.8% (95% CI 39.7, 57.9) and specificity of 97.4% (95% CI 84.9, 99.9). A hypothetical sequential strategy of US followed by biopsy in the case of negative US had a sensitivity of 78.9% (95% CI 70.1, 85.5) and specificity of 71.8% (95% CI 54.9, 84.5), equivalent to a simultaneous testing strategy. Time on glucocorticoids did not significantly impact the results of US or biopsy. The only factor independently predictive of a positive US was male sex (OR 5.53, 95% CI 2.72 to 11.22, p<0.001). The only factor independently predictive of a positive biopsy was jaw claudication (OR 2.40, 95% CI 1.11, 5.21, p=0.027).

Table 1. Performance Characteristics of Ultrasound, Biopsy, and Combination Strategies

Strategy	Sensitivity	Specificity	PPV	NPV	PLR	NLR
Ultrasound alone	52.8	71.8	85.6	32.6	1.87	0.66
Biopsy alone	48.8	97.4	98.0	37.6	19.02	0.53
Sequential (Biopsy only if US positive)	22.8	97.4	96.6	28.6	8.88	0.79
Sequential (Biopsy only if ultrasound negative)	78.9	71.8	89.8	51.9	2.80	0.29
Simultaneous	78.9	71.8	89.8	51.9	2.80	0.29
Procedure, glucocorticoid duration						
Ultrasound, all, n=162	52.8	71.8	85.6	32.6	1.87	0.66
Ultrasound, 0 days, n=80	51.9	76.9	82.4	43.5	2.25	0.63
Ultrasound, >0 ≤3 days, n=27	46.2	100	100	6.0	Infinity	0.54
Ultrasound, >3 ≤7 days, n=25	60.0	40.0	80.0	20.0	1.00	1.00
Ultrasound, >7 ≤14 days, n=18	64.3	50.0	81.8	28.6	1.29	0.71
Ultrasound, >14 days, n=12	44.4	100	100	37.5	Infinity	0.56
Biopsy, all, n=162	48.8	97.4	98.0	37.6	19.02	0.53
Biopsy, 0 days, n=53	46.9	100	100	55.3	Infinity	0.53
Biopsy, >0 ≤3 days, n=24	66.7	83.3	92.3	45.5	4.00	0.40
Biopsy, >3 ≤7 days, n=38	47.1	100	100	18.2	Infinity	0.53
Biopsy, >7 ≤14 days, n=29	47.8	100	100	33.3	Infinity	0.52
Biopsy, >14 days, n=18	37.5	100	100	17.0	Infinity	0.63



Conclusions: TA US is a useful tool in the diagnosis of GCA; however false positive tests occur in 7% and thorough clinical assessment remains crucial. Prior glucocorticoid treatment has no clear impact on results.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4629

THU0313 INFERIOR AND SUPERIOR VENA CAVA THROMBOSIS IN BEHCET S DISEASE. MOROCCAN EXPERIENCE

F.Z. Alaoui[1], M. Moudatir[2]. *[1]Internal medicine; [2]12 rue la saone, Polo, University hospital ibn rochd, Casablanca, Morocco*

Background: Behcet's disease (BD) is a systemic disorder with a vascular tropism where the vessels might be affected. Venous thrombosis is the most common vascular complication. Among its locations, vena cava thrombosis (VCT) are rare but can be life-threatening.
The purpose of this work is to specify the frequency of VCT in the course of Behcet's disease in morocco and to analyse epidemiological, clinical and therapeutic modalities.
Objectives: This retrospective study was conduced in the internal medicine department of the University Hospital IbnRochd of Casablanca, over a period of thirty-five years between 1980 and 2016.
Methods: Where included 1618 cases of Behcet's disease, all diagnosed in our service and meeting the diagnosis criteria as defined by the international study group (ISG) for Behcet's disease.
Results: 52 patients with VCT – 47 men and 4 women - were gathered during this period, representing a rate of 3.30% of 1572 cases, with a mean age of 35 years (ranges 17–54).
The diagnosis of VCT and BD was concomitant in 10 cases and occurred during the course of the disease in 42 cases after an average of 6 years of evolution.
Among the localization. Inferior VCT is the most frequent localization (32 patients, including 15 cases of Budd- Chiari syndrome). The superior VCT was reported in 24 patients, whereas 5 patients had both a superior and inferior VCT.Vena cava thrombosis was associated with deep venous thrombosis (DVT) of the lower limbs in 24 cases and with an aneurysm in 7 cases (pulmonary artery: 4 cases, femoral artery: 2 cases, abdominal aorta; 1 case).
Regarding the therapeutic modalities, 41 patients were under anti-coagulant treatment, 45 patients received corticosteroids and 51 of the patients were under immunosuppressive agents (cyclophosphamide,azathioprine).
The evolution was significantly improved after the introduction of the immunosuppressive therapy, which were firstly initiated in 2006.
Conclusions: Vena cava thrombosis in the context of Behcet's disease is a very serious pathology threatening the patient's vital and functional prognosis.
Preventive measures, early diagnosis and effective treatment are the keys to a successful management of such complications' risks.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6965

THU0314 RADIOLOGIC ACTIVITY IS THE MAJOR DETERMINANT FOR PHYSICIANS WHILE DECIDING ACTIVE DISEASE IN TAKAYASU ARTERITIS

G. Kenar[1], P. Cetin[2], H. Yarkan[1], B. Zengin[1], G. Can[1], M. Birlik[1], F. Onen[1]. *[1]Rheumatology, Dokuz Eylul University School of Medicine, Izmir; [2]Rheumatology, Dumlupınar University, Kutahya, Turkey*

Background: There are no valid follow-up parameters in the assessment of disease activity in Takayasu arteritis (TA).
Objectives: We investigated the impact of incorporation of vascular imaging into ITAS in the assessment of disease activity in TA.
Methods: 52 patients who fulfilled the ACR criteria were included in the study. PGA, Kerr et al.'s criteria and ITAS2010/ITAS-A scores were evaluated in all patients in serial visits. All the patients were followed using 3–6 monthly B-mode/Doppler ultrasonography (USG) and 6–12 monthly magnetic resonance angiography (MRA).
Radiological activity (Rad) was defined based on the presence of any of the 3 parameters including new vessel involvement by any technique (5 points),increase in vessel wall thickness on USG (3 points) and vessel wall edema on MRA (3 points).Then we incorporated these scores with ITAS-A to obtain a composite disease activity index (ITAS2010-A-Rad) (Table 1). Active disease was defined as ITAS-A-Rad >4 points.
Results: Total 410 visits of 52 TA patients (mean age 50.7 yrs, F: 92.3%, mean follow-up duration:6.4±2.9 yrs) were evaluated. Radiological assessment was done in 359 visits (by USG in 271 and by MRA in 190). Patients were categorized as having active disease in 194 visits (47.4%) according to PGA and 72 visits (17.5%) according to Kerr et al. criteria.The agreement between them was fair (66%, κ: 0.29). Radiological activity was determined in 105 out of 359 visits (29.2%). The total agreement between radiological activity and Kerr at al. criteria was 83% (κ: 0.58). It was found to be 76% (κ: 0.52) between radiological activity and PGA.
Mean ITAS-A-Rad scores were found to be significantly higher in visits with active disease compared to visits with inactive disease according to both PGA and Kerr et al. criteria (Table 2). The ITAS-A-Rad was significantly correlated with all the other activity parameters including ITAS2010, ITAS-A, and APRs.
There were 43 visits with new vessel involvement by any radiologic technique; all visits included patients with active disease based on both PGA and Kerr et al. criteria. Whereas in 50% of these visits, patients had normal CRP, and %49 had normal ESR.
The agreement between ITAS2010 and PGA was fair (69%, κ: 0.38).When APR was added (ITAS-A), it did not improve (68%, κ: 0.34). But the agreement between

Table 1. The definition of ITAS-A-Rad Score

Clinical	ITAS2010			0–
Laboratory	APR	ESR	0 for ESR<20 1 for 21–39 2 for 40–59 3 for >60 mm/h	0–3
		CRP	0 for CRP≤5 1 for 6–10 2 for 11–20 3 for >20mg/l	
Radiology	Radiological activity	New vessel involvement with any radiological method		5
		B-mode Doppler USG	Progression on vessel wall thickness	3
		MRA	Presence of vessel wall edema	3
Total	ITAS-A-RAD Score			

ITAS-A-Rad Score >4 –> Activity.

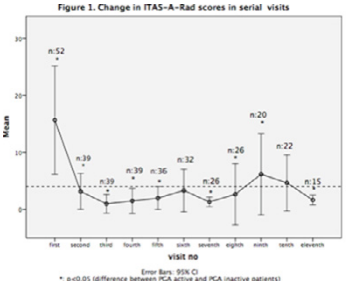


Table 2. Response to change: The mean ITAS-A-Rad scores in serial visits

	ITAS-A-Rad score (mean±SD)		
Visit no	PGA: active	PGA: inactive	P
1	16.72±6.3	5.25±4.9	<0.001*
2	6.23±4.6	1.92±3.8	<0.001*
3	5.11±3.3	1.40±1.63	<0.001*
4	4.11±2.47	1.60±1.72	<0.001*
5	6.36±5.6	1.36±1.7	<0.001*
6	3.20±2	2.95±39	0.29
7	4±2.3	1.76±2.7	<0.001*
8	5.3±3.8	1.3±1.77	<0.001*
9	4.33±6.02	1.21±2.3	0.02*
10	6.67±4.5	1.5±2.3	0.06
11	4±2.7	1.10±0.99	0.028*

ITAS-A-Rad and PGA (72%, κ: 0.50) and also Kerr et al. criteria (82%, κ: 0.56)was found to be moderate. Interestingly, when only USG (ITAS-A-USG) or only MRA (ITAS-A-MRA) was used, the agreement with PGA was remained unchanged (73%, κ: 0.45 and 76%, κ: 0.52, respectively).
When responsiveness to change of ITAS-A-Rad score was evaluated by serial visits of patients, it was found that the mean value of the score was discriminative for activity according to PGA in 9 of 11 visits (Figure 1).
Conclusions: The results of this study suggest that ITAS-A-Rad may be used to be a valuable follow-up parameter in the assessment of disease activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6271

THU0315 CENTRAL NERVOUS SYSTEM INVOLVEMENT IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS: A SINGLE CENTER EXPERIENCE

G.E. Fragoulis[1], S. Lionaki[2], A. Venetsanopoulou[1], P.G. Vlachoyiannopoulos[1], H.M. Moutsopoulos[1], A.G. Tzioufas[1]. *[1]Pathophysiology Department; [2]Nephrology Department, University of Athens, School of Medicine, Athens, Greece*

Background: Peripheral nerve involvement is relatively frequently encountered in patients with granulomatosis with polyangiitis (GPA). Central nervous system (CNS) manifestations are reported to occur in about 10% of GPA patients.
Objectives: We aimed to estimate the prevalence of CNS involvement in Greek patients with GPA, describe the related clinical characteristics, and identify possible predicting factors for its occurrence. We also compared the clinical picture and long term outcomes of GPA patients with and without CNS involvement.
Methods: The medical charts of all patients with ANCA-associated and biopsy proven small vessel vasculitis (AAV), diagnosed in our hospital between 1995–2015, were retrospectively reviewed and GPA patients with CNS involvement were identified. Demographics, serological and clinical features, at the time of AAV diagnosis, of CNS involvement and during the follow-up time, were recorded. Comparisons of disease characteristics and outcomes, including patient survival, relapse rate and treatment-related adverse events, were performed between GPA patients with and without CNS involvement.
Results: 77 patients with GPA were identified in our AAV registry. Of these, nine (11.7%) developed CNS manifestations, either at clinical presentation (33.3%) or during the follow-up (66.7%). At the time of CNS involvement, all patients were characterized by increased acute phase reactants and all but one patients had vasculitic manifestations in several other organs/systems and increased titers of ANCA. CNS symptomatology included: sensor and/or sensorimotor symptomatology (33.3%), severe headache and hearing loss (33.3%), delirium and seizures (22.2%), diplopia (11.1%) and cerebellar symptoms (11.1%). Findings from MRI were: cerebral ischemic lesions (55.6%), focal dural thickening with enhancement (22.2%), orbital mass formation (11.1%) and mastoiditis causing facial nerve palsy bilaterally (11.1%). Patients with CNS involvement, compared to those without, at initial AAV diagnosis, experienced vasculitic manifestations of the ENT system more frequently (77.8% *versus* 25.4%, p=0.004) and they had a lower disease activity, as assessed by the BVAS score, while during the overall course of the disease experienced lung vasculitis less frequently (44.4% vs. 79.4%, p=0.02). Comparisons between GPA patients with and without CNS manifestations did not reveal any differences in long-term outcomes including relapse rate rate/100 person-months, (95% CI) [1.812 (0.920–3.229) Vs 1.033, (0.757–1.378), respectively] (p=0.171), survival (Mantel-Cox test, p=0.244) and treatment-related adverse events
Conclusions: CNS involvement was recorded in 11.7% of our GPA patients, either during the initial phase or as a late disease sequela. ENT involvement and low BVAS score at disease onset were more common in GPA patients with CNS manifestations. Based on our results, CNS involvement did not affect the long term outcomes of GPA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6574

THU0316 EPIDEMIOLOGY OF TAKAYASU ARTERITIS IN NORTHERN ITALY

G. Restuccia[1], L. Boiardi[1], P. Macchioni[1], M. Catanoso[1], P. Mancuso[2], C. Salvarani[1]. *[1]Rheumatology, Arcispedale S Maria Nuova; [2]Servizio interaziendale di epidemiologia, Azienda unità sanitaria locale, Reggio Emilia e Arcispedale S Maria Nuova, Reggio Emilia, Italy*

Background: Takayasu arteritis (TAK) is a large vessel vasculitis of unknown etiology, predominantly affecting the aorta and/or its major branches and occurring before the age of 40 years.TAK has been described worldwide with an annual incidence in Europe ranging from 0.4 to 1.3 /1.000.000. TAK is more common in female. In the largest study from Japan, the female to male ratio was eight to one. In a recent Swedish epidemiologic study no male were identified. There are no epidemiological studies regarding Takayasu arteritis in Italian population.
Objectives: To investigate the epidemiology of Takayasu arteritis in a Northern Italy area.
Methods: All patients with incident TAK diagnosed between 1997 and 2015 living in the Reggio Emilia area were identified by capture and re-capture checking at computerized discharge diagnosis codes (ICD10) and at outpatients databases from rheumatology, internal medicine, surgery, pathology, imaging departments of Reggio Emilia Hospital and by examining the Reggio Emilia district database for rare diseases.The Reggio Emilia population is predominantly of Caucasian origin (92.5%) with a yearly increase in general population of 0.5% (from 438.588 inhabitants in 1997 to 533.827 in 2015).
Results: There were 5 women satisfyng ACR 1990 criteria for TAK diagnosis during the 18 years study period. The overall age and sex-adjusted 18 years incidence per 100.000 persons aged <40 years was 2.2. (95% CI:0.71 to 5.09). The overall age-and sex-adjusted 20 years incidence per 100,000 women aged <40 years was 4.5. (95% CI:1.46 to 10.48). Median age at disease onset was 36y and at diagnosis was 39 years. The prevalence of TAK in the general population on December 31 2015 was 0.9 (95% CI: 0.31 to 2.19) while in female population aged <40 years was 4.4 (95% CI 1.47 to 10.54). All patients are still alive on December 31 2015.
Conclusions: As observed in other epidemiological studies, TAK is a rare disease also in Northern Italy with a large prevalence of female.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5477

THU0317 CARDIOVASCULAR RISK FACTORS AND COMORBID DISEASES IN TAKAYASU ARTERITIS

H. Masyan[1], N.S. Esatoglu[2], A.M. Celik[1], V. Hamuryudan[2], H. Yazıcı[2], E. Seyahi[2]. *[1]Department of internal medicine; [2]Department of internal medicine, Division of Rheumatology, Cerrahpasa medical faculty, Istanbul, Turkey*

Objectives: Cardiovascular complications are the main causes of morbidity and mortality in the course of Takayasu arteritis (TA).In addition to the occlusive vasculitis,hypertension and accelerated atherosclerosis are possibly other factors playing role in the ethiopathogenesis of these complications.Although,strict management of traditional cardiovascular risk factors is advocated to diminish the effect of cardiovascular complications,we still do not know whether traditional risk factors and other comorbid conditions are increased or operative.In this study we looked at the frequency of traditional atherosclerotic risk factors and comorbid conditions among patients with TA and suitable diseased and healthy controls.
Methods: We studied 88 (77F,11M) consecutive TA patients and 71 (66F,5M) SLE patients,between May and November 2016.In addition,age and gender matched, 96 (80F, 16M) healthy controls were included.Study participants were interviewed with the help of a standardized questionnaire that assess the presence or absence of traditional atherosclerotic risk factors and several comorbid conditions according to the Charlson comorbidity index.Additionally,Framingham coronary heart disease risk score was calculated.
Results: Smoking was more frequent among the healthy controls,whereas hypertension and family history of cardiovascular diseases were more common among TA patients.Patients with SLE were found to have less hyperlipidemia.The Framingham risk scores did not differ among the groups.Pericardial/pleural and renal diseases were more frequently observed in SLE patients,whereas cardiovascular diseases and chronic lung diseases were more common in TA patients.Inflammatory bowel diseases were only observed in TA patients.

	Takayasu arteritis (n=88; 77F/11 M)	SLE (n=71; 66 F/5 M)	Healthy controls (n=96; 80 F/16 M)	P value
Age, mean ± SD	44±12	42±12	45±11	NS
Age at disease onset, mean ± SD	31±12	29±11	–	NS
Smoking (current and past), n (%)	27 (31)	30 (42)	47 (49)	<0.05
Hyperlipidemia, n (%)	32 (44)	15 (25)	41 (48)	0.018
Hypertension, n (%)	47 (53)	23 (32)	22 (23)	<0.01
Diabetes mellitus, n (%)	8 (9)	6 (7)	15 (16)	NS
Median [IQR] Framingham risk score	3 [1–9]	3 [1–5]	3 [2–7]	NS
Familial history of cardiovascular diseases, n (%)	41 (47)	15 (21)	22 (23)	<0.01
Cardiovascular diseases, n (%)	47 (53)	13 (18)	1 (1)	<0.01
Valvular heart disease, n (%)	34 (39)	12 (17)	7 (7)	<0.01
Chronic pulmonary diseases, n (%)	11 (13)	1 (2)	5 (6)	<0.05
Pleural/pericardial diseases, n (%)	7 (8)	14 (20)	0	<0.01
Renal diseases, n (%)	10 (11)	19 (27)	8 (8)	<0.05
Other accompanying rheumatologic diseases and amyloidosis, n (%)	10 (11)	15 (21)	1 (1)	<0.01
Inflammatory bowel diseases, n (%)	9 (11)	0	0	<0.01
Inflammatory upper/lower back pain, n (%)	21 (24)	23 (32)	6 (6)	<0.01
Family history of rheumatologic diseases, n (%)	26 (30)	25 (35)	4 (4)	<0.01

Conclusions: Traditional atherosclerotic risk factors are not increased in TA.Comorbidities in these patients are mainly due to the complications of vascular involvement.The frequency of inflammatory bowel diseases and inflammatory upper/lower back pain is substantially high and deserves further research. Moreover, the increased incidence of cardiovascular and rheumatologic diseases among the first-degree relatives of TA patients suggest that genetic mechanisms may play role in TA
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6280

THU0318 CORONARY ARTERY DISEASE IN PATIENTS WITH BEHÇET'S DISEASE: A RETROSPECTIVE, SINGLE CENTER STUDY

H. Chen[1], Y. Zhang[2], W. Chen[3], J. Liu[1], L. Wang[1], F. Zhang[1], W. Zheng[1]. *[1]Rheumatology, Peking Union Medical College Hospital, BEIJING; [2]Oncology and immunology, The fourth hospital of Hebei Medical University, Hebei; [3]Cardiology, Peking Union Medical College Hospital, BEIJING, China*

Background: Behçet's disease (BD) is a chronic inflammatory disease affecting various size of arteries and veins. Coronary artery disease (CAD), a life-threatening condition, is rarely reported in patients BD.
Objectives: To investigate the clinical characteristics of BD patients complicated with CAD, and to elucidate the potential risk factors of CAD in BD patients.
Methods: We retrospectively reviewed all the medical records of BD patients who were admitted to our institute from 2001 to 2016. CAD was defined as aneurysm, stenosis and (or) occlusion of coronary arteries confirmed by angiography or contrast-enhanced computer tomography. BD patients with CAD and age- and gender-matched BD patients without CAD (at 1:3 ratio) were enrolled. Demographic, clinical and laboratory data were systemically collected, analyzed and compared between two groups.
Results: In total, 19 patients, including 17 male and 2 female, were complicated with CAD. The mean onset age of BD was 34 and the mean duration from the onset of BD to the diagnosis of CAD was 4.1 year. Angina pectoris (8/19) and acute myocardial infarction (8/19) were the most common cardiac symptoms, arrhythmia was presented in one patient, and three patient remained asymptomatic. Coronary artery aneurysm, stenosis and occlusion were presented in 9, 13 and 3 patients, respectively. Smoking (7/19) was frequently observed, while hypertension (3/16), diabetes mellitus (2/19), obesity (1/19) and alcohol consumption (1/19) were rarely present. Additionally, seven arterial and two venous extra-cardiac vasculopathies were presented. Oral ulceration (19/19) and skin lesions (16/19) were the most common BD-associated symptoms. Comparing with BD patients without CAD, patients with BD presented with higher ESR (mean, 34.4 vs 16.3 mm/hr, p=0.0018) and CRP (mean, 36.4 vs 12.2 mg/L, p=0.002), more frequency of skin lesions (84% vs 55%, p=0.0334) and pathergy reactions (37% vs 26%, p=0.0103). Furthermore, multivariate analysis confirmed that elevated CRP was a independent risk factor of CAD (OR 1.032, 95% CI 1.011–1.053, p=0.003).
Conclusions: CAD, a rare complication of BD, predominately affect male patients. BD patients with CAD presented with active BD disease symptoms and elevated inflammatory markers, which implicated aberrant vascular inflammation was the key mechanism of CAD in BD patients. CRP, but not traditional CAD risk factors, was the risk factor of CAD in BD patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5991

THU0319 MR ANGIOGRAPHY FOR EVALUATION OF VASCULAR INFLAMMATION IN ELDER PATIENTS WITH LARGE VESSEL VASCULITIS

I. Smitienko[1], P. Novikov[2], E. Atyasova[1]. *[1]Medical Center "Petrovskie Vorota"; [2]Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Objectives: The aim of the study was to evaluate the feasibility of MR angiography (MRA) for evaluation of vascular inflammation in elder patients with large vessel vasculitis.
Methods: 16 patients with established on PET with 18F-FDG large vessel vasculitis (14 female and 2 male; average age 66 years) were enrolled in our study. 14 patients had got giant cell arteritis (just only 3 biopsy-proven cases), 2 patients with isolated aortitis of thorax aorta and 2 cases of PMR-associated arteritis. The average duration of any disease was 8 months. All patients underwent MRA with or without contrast enhancement of aorta and its branches at 1.5 Tesla (Siemens Magnetom Essenza). All patients had repeated MRA at 6 and 12 months. All images were studied by one specialist. We evaluated the role of mural oedema as a sign of activity of vasculitis. The results of MR-angiography were compared with clinical and laboratory data, ultrasound and PET with 18F-FDG.
Results: A total of 42 MRA were obtained in 16 patients. Significant mural oedema of thorax aorta or large arteries was shown by imaging in 20 of 42 cases (48.0%) and correlated with clinical and laboratory signs of vasculitis activity, progressive arterial stenosis detected by ultrasound and increased uptake of 18F-FDG on PET. 12 patients with high degree of inflammation on MRA were streroid-naïve. In 22 cases (52%), MRA had showed mild or moderate oedema of the arteries' wall. Low-moderate activity of vascular inflammation in our patients was associated with moderate or high of immunosuppressive therapy (prednisolone 40–60 mg/day). However, gradual reduction in the intensity of immunosuppression in 4 patients with mild mural oedema was associated with development of relapse of large vessel vasculitis. Notably, contrast enhancement did not improve significantly edema imaging.
Conclusions: Visualisation of artery wall oedema by MRA may be a usefull approach to detect persisting inflammation in elder patients with large vessel vasculitis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3616

THU0320 DIFFERENT PATTERNS OF VASCULAR INVOLVEMENT IN PET/CT ACCORDING TO CRANIAL SYMPTOMS IN BIOPSY PROVEN GIANT CELL ARTERITIS, A PRELIMINARY STUDY

J. Mestre Torres[1], I. Navales[2], F. Martínez[1], J. Loureiro[1], S. Bujan[1], C. Pérez[1], M. Simó[2], R. Solans[1]. *[1]Internal Medicine; [2]Nuclear Medicine, Hospital Vall d'Hebron, Barcelona, Spain*

Background: GCA is the most frequent vasculitis in patients over 50 years old. It involves large vessels (LV) such as aorta, carotid, vertebral and subclavian arteries. After the development of new imaging techniques, extracranial LV involvement has been increasingly described. Past studies showed a trend in worse prognosis in those patients with aortitis at diagnosis but larger studies are needed to determine the clinical implications of these results. Correlation between symptoms at diagnosis and PET evaluation has not been done.
Objectives: To evaluate aortic and supraaortic involvement in a new onset GCA cohort through PET/CT. To compare aortic and supraaortic involvement in patients with and without cranial ischemic symptoms.
Methods: Prospective study including all newly diagnosed biopsy-proven GCA patients in 2016 according to ACR criteria. PET/CT was performed during initial evaluation. Clinical data, blood tests and PET/CT results were recorded. Ischemic symptoms included jaw claudication (JC) and visual symptoms. Analysis was made using Stata IC/14. Patients were compared according to clinical presentation (presence vs absence of ischemic symptoms) with Fisher exact test.
Results: 18 patients were included (63.6% were women). At diagnosis age was 77.4±8.7 years (mean ± SD). Patients presented headache (78.6%), polymyalgia rheumatica (14.3%), constitutional syndrome (42.8%), JC (42.9%) and visual symptoms (35.7%). On physical examination pulse was decreased in 78.6% of patients. Blood tests showed anemia in 71.4% with an ESR 90.41±33mm/h (mean ± SD). PET/CT was performed after (median, intercuartilic range) 6.5 days (2 - 10 days). Analysis of vascular uptake was semiquantitative. Aortic involvement was present in 42.9% of patients. Supraaortic and vertebral arteries were involved in 42.8%. Baseline characteristics were similar to other cohorts. At the time of diagnosis, proportion of aortitis was significantly lower (p=0.049) in patients with ischemic symptoms when compared to those without. We could not find any differences between these two groups when analyzing the presence of increased vascular uptake in carotid and vertebral arteries. Limitations of the study are the small size of the cohort and the variability of the PET/CT protocols among literature. However, we think this study is important because it shows the differences between these two subgroups of GCA.
Conclusions: In this study, patients with cranial ischemic symptoms showed less involvement of large vessels when compared to those GCA patients that presented with systemic symptoms. These results suggest that there may be different physiopathological subsets leading to GCA. Further studies are needed to better understand these mechanisms.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3528

THU0321 ALTERATIONS IN THE PERIPHERAL B CELL COMPARTMENT IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (CHURG-STRAUSS SYNDROME)

M. Rizzi, M. Engesser, R.E. Voll, A. Troilo, I. Janowska, N. Venhoff, J. Thiel. *Rheumatology/Clinical Immunology, University Hospital Freiburg, Freiburg, Germany*

Background: Eosinophilic granulomatosis with polyangiitis (EGPA) belongs to the group of ANCA associated vasculitides. While the combination of asthmatic symptoms and vasculitis characterize the disease clinically, eosinophilia and increased serum IgE concentrations are serologic hallmarks. The role of B lymphocytes in EGPA has not been defined so far, but therapeutic response to rituximab in EGPA points towards a role of B-cells in the pathogenesis of EGPA.
Objectives: To characterize the peripheral B cell compartment in patients with EGPA, to analyze the in vivo potential of B lymphocytes to class-switch to IgE, and to assess in vitro the differentiation of naïve B cells to IgE-secreting plasmablasts.
Methods: Laboratory work-up included ANCA-status, eosinophils, IgE, IgG, IgA, IgM, and peripheral $CD19^+$ B-cell count. B cell subpopulations (naïve, marginal zone, class-switched B cells and plasmablasts) were analyzed by staining PBMCs with fluorescent-labeled monoclonal antibodies against: CD27, CD20, CD38, IgD, IgG, IgA, IgE, CD21, and BAFF-R. For in vitro differentiation assays magnetically isolated B lymphocytes from EGPA patients and aged matched healthy controls were stimulated with CD40L and IL-21 and IL-4 in enriched Iscoves' medium supplemented with 10% FCS, 1 μg/mL insulin, 2.5 μg/mL apo-transferrin, 1% nonessential amino acids, 2 mmol/L glutamine, and 1 μg/mL reduced glutathione. Starting the culture with equal number of B cells, the absolute number of plasmablasts, and IgE class switched cells after 9 days was determined by counting the events in the $CD27^{high}CD38^{high}$ gate or the $IgG/A/D^-IgE^+$ gate by flow cytometry. IgE secretion in the supernatant was measured by ELISA.
Results: 18 patients (8 females, median age 59 years) with EGPA diagnosed according to ACR and CHC-criteria were included into the study. 22% of patients were ANCA-positive. Immunosuppressive therapy was azathioprine in 11 patients, methotrexate in 3 patients, and leflunomid or mycophenolate in one patient each and two patients received no immunosuppressive treatment. 7 patients had a history of a prior cyclophosphamide therapy. Median lymphocyte count was

normal ($1.2x10^3/\mu l$; normal range 1.1 to $3.2x10^3/\mu$ l) but peripheral B cell numbers were markedly diminished ($37/\mu l$, normal range: 100 – $500/\mu l$). While the percentage of naïve B cells (53%) and marginal zone like B cells (10.5%) were within normal range, the percentage of class-switched memory B cells was high (28.2%). To assess the in vitro class switch capacity to IgE the number of IgE class-switched cells after 9 days of culture was determined by counting the events in the IgG/A/D-IgE+ gate. The percentage of IgE-switched cells was 6.8% (range: 0.3%>34%) and not statistically different from healthy controls.

Conclusions: In the EGPA-patients we report we observed markedly diminished B-cells despite of normal lymphocyte counts. Within the B cell compartment, there was a shift towards later B cell maturation stages. The in vitro B-cell development to IgE class-switched cells was not increased in EGPA-patients pointing towards a non-B cell intrinsic mechanism.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6507

THU0322 DESCRIPTIVE STUDY OF ASIAN INDIAN PATIENTS WITH RHEUMATOID VASCULITIS IN RETROSPECT: A SINGLE, TERTIARY CARE CENTRE EXPERIENCE

J. Mathew[1], A. Ganapati[1], R. Goel[1], S. Pulikool[1], A.J. Mathew[1], R. Janardhana[1], M. Gowri[2], D. Danda[1]. *[1]Rheumatology; [2]Biostatistics, Christian Medical College, Vellore India, Vellore, India*

Background: Rheumatoid vasculitis (RV) is a severe extra-articular manifestation of rheumatoid arthritis (RA), with high morbidity and mortality reported in literature

Objectives: To describe the Asian Indian perspective on RV patients, their clinico-laboratory features and their outcome along with the factors affecting them

Methods: A retrospective review of electronic medical records of 8984 RA patients from January 2007 to August 2016, was done for those satisfying Scott & Bacon criteria for RV[1]. Probable RV was defined as patients not satisfying Scott & Bacon Criteria, but were managed like RV after exclusion of alternate diagnosis. Birmingham Vasculitis activity score (BVAS) version 3[2] was used for monitoring activity of RV

Results: 63 patients of RV were identified, with a study period prevalence of 0.7%, in our RA cohort. 33 (52.4%) patients were female. Mean age of patients was 50.7±11.5 years with median duration of RA being 6 years. Involvement of Peripheral Nervous System (PNS) was the commonest manifestation of RV in 52/63 (82.5%) patients followed by skin in 34/63 (53.9%) patients. Rheumatoid Nodule was seen in 14/ 63 (22.2%) patients. Percentage of current and ex-smokers combined,was same as rheumatoid nodule prevalence. 52 (82.5%) patients had biopsy evidence of vasculitis.26/51 (50.9%)patients were started on mycophenolate mofetil, 13/51 (25.5%)patients on cyclophosphamide, 8/51 (15.7%) patients on azathioprine, 4/51 (7.8%) patients on Methotrexate as immunosuppressive (IS) agent along with mean dose of 46.6±13.7 (0.86±0.23mg/kg/day) prednisolone. Additionally, Rituximab & IVIg were used in 2 patients each respectively. 3 months after initiation of immunosuppression 26/50 (52%) patients on follow-up were in remission and 39/47 (82.9%) patients attained remission at 6 months. Mean time to achieve remission was 151.1±86.3 days. All IS agents were equally effective in inducing remission at 3 and 6 months and showed statistically similar BVAS reduction at 3 and 6 months from baseline (t test & chi-square test). 7 (11.2%) deaths noted in the cohort at their respective last visit during 195.3 patient years cumulative follow up. Multiple regression analysis showed that at baseline, presence of PNS involvement, eosinophilia, thrombocytosis, higher BVAS score and higher steroid requirement were predictors of persistently active vasculitis and absence of eye involvement and higher hemoglobin % at baseline were predictors for remission, at 3 months ($p<0.05$). 4/50 (8%) patients had relapse of vasculitic symptoms. 2 and 5 year survival rates were 96.2% and 83.9% respectively

Conclusions: Our cohort of Asian Indian RV was compartively younger with lesser RA duration, less percentage of ever-smokers, lesser rheumatoid nodule prevalence, higher PNS involvement with better survival/mortality rates compared to published literature. All IS agents showed equal rates of BVAS remission & BVAS reduction at 3 and 6 months of treatment

References:

[1] Scott DG, Bacon PA. Intravenous cyclophosphamide plus methylprednisolone in treatment of systemic rheumatoid vasculitis. Am J Med. 1984 Mar;76(3):377–84.

[2] Mukhtyar C, Lee R, Brown D, Carruthers D, Dasgupta B, Dubey S, et al. Modification and validation of the Birmingham Vasculitis Activity Score (version 3). Ann Rheum Dis. 2009 Dec;68(12):1827–32.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5993

THU0323 THE INCIDENCE RATES OF ANCA-ASSOCIATED VASCULITIDES IN NORTHERN GERMANY (SCHLESWIG-HOLSTEIN) REMAIN STABLE BETWEEN 1998 TO 2014

K. Herlyn[1], W.L. Gross[2], E. Reinhold-Keller[2]. *[1]Rheumatology, Private Practice, Lübeck; [2]Rheumatology, Klinikum Bad Bramstedt, Bad Bramstedt, Germany*

Objectives: To assess the incidence of ANCA-associated vasculitides (AAV) in a stable population by registering all newly diagnosed patients in a large region in Northern Germany. To investigate the epidemiology and pattern of AAV over seventeen years in a prospective study.

Methods: Between 1/1/98 and 31/12/14 all newly diagnosed cases of AAV (Granulomatosis with polyangiitis (GPA), microscopic polyangitis (MPA), eosinophilic granulomatosis with polyangitis (EGPA)) as defined by the Chapel Hill Consensus Conference 1992 were identified in a large mixed rural/urban northern German region consisting of 2,83 million habitants in a population-based prospective study. The following sources were explored on a regular basis: (a) departments of all hospitals, including their outpatient clinics; (b) all departments of pathology, and (c) the reference immunological laboratories serving the catchment area. All cases were re-evaluated by the authors.

Results: Within the observation period of seventeen years 551 patients were identified as having a new diagnosis of AAV in the catchment area, the incidence rate was 12 (range 8 -16)/million/year. GPA represents 70% of the AAV with an incidence rate of 7.9 (range 6–12)/million/year (95% CI 1;11 - 5*;19*), MPA with an incidence rate of 2.4 (range 1–5)/million/year (CI 0;3 – 1;9) and EGPA 1.1 (range 0–2)/million/year (CI 0;4).

Incidence rates of GPA were on average three times higher than those of MPA and seven times higher than CSS. The incidence rates were stable between 1998 and 2014, our observations did not reveal significant differences. Gender differences were not observed. People diagnosed with MPA were on average 66.4 years old.

Conclusions: Results of our unique population based vasculitis register over seventeen years assessing the incidence of AAV in a region of 2.83 million habitants in northern Germany demonstrate stable incidence rates for AAV. Variances between years have been observed, but no pattern or periodicity. Compared to other studies investigating small regions or referral centers the incidence rates for AAV were comparable to the incidence rates observed in Norway, Sweden and the United States, lower than those in United Kingdom, but higher than in Spain and Vilnius. The incidence rates of MPA are significantly higher in Japan, whereas GPA and CSS have rarely been diagnosed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3283

THU0324 NEUTROPHILS IN GIANT CELL ARTERITIS: MONITORING DISEASE PROGRESSION DURING THERAPY TAPERING

T. Kuret[1], K. Lakota[1,2], P. Žigon[1], M. Ogrič[1], Ž. Rotar[1], R. Ješe[1], S. Sodin-Šemrl[1,2], S. Čučnik[1,3], M. Tomšič[1,4], A. Hočevar[1]. *[1]Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana; [2]FAMNIT, University of Primorska, Koper; [3]Faculty of Pharmacy; [4]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia*

Background: Giant Cell Arteritis (GCA) represents a medical emergency due to risk of permanent vision loss and/or cerebrovascular insults. Polymyalgia rheumatic (PMR) frequently coexists with GCA[1]. No diagnostic or prognostic markers are yet known for GCA and predicting relapses during steroid therapy tapering is difficult. Biomarkers, such as serum amyloid A (SAA) and interleukin-6 (IL-6) provide added value for monitoring inflammation and a recent investigational study indicated the potential use of neutrophils and their surface markers in GCA pathogenesis[2].

Objectives: To determine the percentage of neutrophils, T and B cells, and the mean fluorescence intensity (MFI) of L-selectin (CD62L) and integrin αM (CD11b) on $CD16^+$ neutrophils in peripheral blood of newly diagnosed, untreated GCA and PMR patients vs. healthy controls (time 0) and at GCA follow-up (7, 30 and 90 days after therapy).

Methods: Flow cytometry of stained, lysed and fixed whole blood[2] was performed in 10 GCA patients (6 followed longitudinally), 7 PMR patients and 5 healthy controls (7-colour immunophenotyping kit, Miltenyi). Levels of SAA and IL-6 were measured in sera of GCA patients (n=6) using nephelometry and ELISA, respectively.

Results: Percentage of neutrophils was significantly higher at time 0 in GCA and PMR patients compared to healthy controls. Expression of both CD62L and CD11b on $CD16^+$ neutrophils was also higher in GCA and PMR patients, as compared to healthy controls. Longitudinally, GCA patients showed an initial decrease in percentage of neutrophils at day 7 in comparison with time 0, increasing on days 30 and 90, while both T ($CD4^+$) and B cells exhibited a significant elevation in % at day 7, with a decline at days 30 and 90. The MFI of neutrophil CD62L steadily decreased from day 0 (85.80±45.45) to day 7 (71.99±29.93) and day 30 (57.61±42.17), while showing a substantial increase on day 90 (88.54±60.35). CD11b expression diminished initially and remained reduced on day 90. Levels of SAA and IL-6 declined sharply from day 0 to 7 (>10-fold drop) and day 30, with gradual elevation of both on day 90.

Conclusions: Neutrophil CD62L may represent a good surface marker for monitoring disease progression following glucocorticoid tapering. SAA and IL-6 exhibit a sharp decrease at early time points, increasing at day 90. In the future, a larger, longer study of neutrophils and their CD62L expression could support clinicians in their decision when and how to re-evaluate therapy in GCA patients.

References:

[1] Schmidt J, Warrington KJ. Polymyalgia rheumatica and giant cell arteritis in older patients: diagnosis and pharmacological management. Drugs & aging. 2011;28651–66.

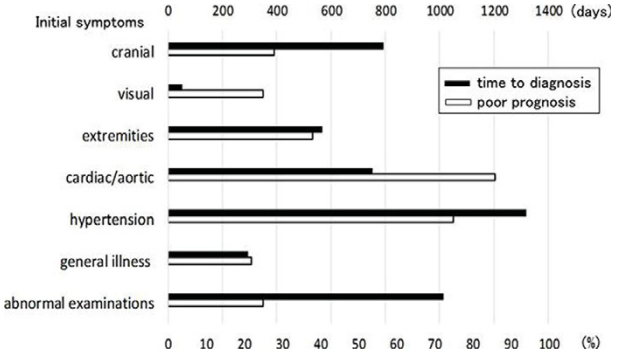
[2] Nadkarni S et al. Investigational analysis reveals a potential role for neutrophils in GCA disease progression. Circ.Res. 2014;114:242–48.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3652

THU0325 RELATIONSHIP OF THE INITIAL SYMPTOMS TO THE DIAGNOSIS DELAY AND POOR PROGNOSIS IN PATIENTS WITH TAKAYASU ARTERITIS

K. Matsumoto, Y. Kaneko, K. Izumi, K. Yamaoka, T. Takeuchi. *Internal Medicine, Division of Rheumatology, Keio University School of Medicine, Tokyo, Japan*

Background: Clinical courses of Takayasu arteritis are of great variety. Its non-specific initial symptoms can cause the delay in diagnosis and lead to poor prognosis. However, the symptoms of very early phase of Takayasu arteritis and their effects on diagnosis delay and prognosis are unclear.
Objectives: To clarify the characteristics of initial symptoms of Takayasu arteritis, the delay in diagnosis, and its relationship with prognosis.
Methods: The consecutive patients with Takayasu arteritis with analysable information in our hospital were enrolled. Initial symptoms, laboratory findings before diagnosis, the duration from symptom onset to diagnosis, and prognosis were investigated. Initial symptoms were divided into 7 groups; cranial symptoms (dizziness, syncope, headache, neck pain, hemi-paralysis, and jaw claudication), visual symptoms (vision loss and visual field loss), extremities symptoms (claudication of extremities, coldness of limbs, bilateral difference in blood pressure, and limb numbness), cardiac/aortic symptoms (dyspnea on exertion, palpitation, and chest compression), hypertension, general illness (fever, fatigue, body weight loss, and arthralgia), and abnormal medical examinations (heart murmur, bruit on any extremities, and abnormal chest X-ray). Poor outcome was defined as a cardiovascular surgery or death.
Results: A total of 98 patients were enrolled with the median observation period of 12.1 years (range, 1 month to 59 years). Eighty-seven (88.7%) were female and the mean age at diagnosis was 37 years. The mean duration from the initial symptoms to diagnosis was 600 days. Thirty-four (34.7%) patients had poor outcomes. The initial symptoms before diagnosis were cranial symptoms in 25%, visual symptoms in 5%, extremities symptoms in 20%, cardiac/aortic symptoms in 7%, hypertension in 9%, general illness in 26%, and abnormal medical examinations in 8%. The duration from symptom onset to diagnosis was 792, 52, 567, 752, 1318, 293 and 1014 days (p=0.10), respectively; the rate of poor outcome was 28, 25, 38, 86, 75, 22, and 25% (p=0.010), respectively. The duration from symptom onset to diagnosis was longer in the patients with poor prognosis than those without (837 vs 493 days, p=0.06). The patients with extremities symptoms were younger (29.6 vs 38.9 years, p=0.026) than those with the other symptoms, and patients with cardiac/aortic symptoms were older (49.7 vs 36.3 years, p=0.044). The patients without general illness showed lower levels of C-reactive protein (3.26 vs 5.86 mg/dl, p=0.048), erythrocyte sedimentation rate (38.3 vs 66.6 mm/h, p=0.01), and platelet counts ($29.4*10^4$ vs $34.0*10^4/\mu l$, p=0.09), and resulted in poor outcome more frequently than those with (42.6 vs 22.6%, p=0.058).



Conclusions: The initial symptoms of Takayasu arteritis before diagnosis varied widely, and majority of them were non-specific. Lacking inflammatory signs were related with delayed diagnosis and poor prognosis.
References:
[1] Takayasu M, et al. Acta Soc Ophtalmol Jpn 1908; 12:554–561.
[2] Ishikawa K, et al. Circulation 1994; 90:1855–1860.
[3] Nakaoka Y, et al. Int Heart J 2013; 54:405–411.
[4] Vanoli M, et al. Arthritis Rheum 2005 15; 53(1):100–107.
Acknowledgements: We thank all the members of the Division of Rheumatology.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4181

THU0326 SHORT AND LONG-TERM FOLLOW-UP WITH ADALIMUMAD IN REFRACTORY UVEITIS ASSOCIATED TO BEHÇET'S DISEASE. MULTICENTER STUDY OF 74 PATIENTS

L. Domínguez-Casas[1], V. Calvo-Río[1], E. Beltrán[2], J. S-Bursón[3], M. Mesquida[4], A. Adán[4], M. Hernandez[4], M. H-Grafella[5], E. V-Pascual[6], L. M-Costa[7], A. Sellas[8], M. Cordero-Coma[9], M. Díaz-Llopis[10], R. Gallego[10], D. Salom[10], J. G-Serrano[11], N. Ortego[12], J. Herreras[13], A. G-Aparicio[14], O. Maíz[15], A. Blanco[15], I. Torre[16], D. Díaz-Valle[17], E. Pato[17], E. Aurrecoechea[18], M. Caracuel[19], F. Gamero[20], E. Minguez[21], C. Carrasco[22], A. Olive[23], J. Vázquez[24], O. R-Moreno[25], J. Manero[25], S. Muñoz[26], M. Gandia[27], E. Rubio-Romero[28], F. Toyos-SMiera[29], F. López-Longo[30], J. Nolla[31], M. Revenga[32], N. Vegas-Revenga[1], C. Fernández-Díaz[1], R. Demetrio-Pablo[1], M. González-Gay[1], R. Blanco[1]. *[1]HUMV, Santander; [2]H Mar, Barcelona; [3]H Valme, Sevilla; [4]H Clinic, Barcelona; [5]H General; [6]H, Valencia; [7]H Peset, Zaragoza; [8]H Vall d'Hebron, Barcelona; [9]H, León; [10]H FE, Valencia; [11]H Cecilio; [12]H Cecilio, Granada; [13]IOBA, Valladolid; [14]H, Toledo; [15]H, Donostia; [16]H Basurto, Bilbao; [17]HS Carlos, Madrid; [18]H, Torrelavega; [19]H, Córdoba; [20]H, Cáceres; [21]H Clínico, Zaragoza; [22]H, Mérida; [23]H G Trias, Badalona; [24]H, Ferrol; [25]H Servet, Zaragoza; [26]HU Infanta Sofía, San Sebastian de los Reyes; [27]H P Mar, Cádiz; [28]H V Rocío; [29]H V Macarena, Sevilla; [30]H G Marañon, Madrid; [31]H Bellvitge, Barcelona; [32]H R Cajal, Madrid, Spain*

Objectives: To evaluate the efficacy of adalimumab (ADA) in short and long term follow-up in refractory uveitis of Behçet's disease (BD)
Methods: Multicenter study. Ocular inflammation was evaluated according to "SUN working Group" (Am J Ophthalmol 2005;140:509–516), and the macular thickening with OCT. A comparison was carried out between baseline, and follow-up visits. Results are expressed as mean±SD or median [IQR]. Continuous variables were compared with Wilcoxon test.
Results: We studied 74 patients/132 affected eyes (39M/35W); mean age 38.7±11.3. The ocular pattern was panuveitis (n=45), posterior uveitis (n=14), anterior uveitis (n=14) and intermediate uveitis (n=1). Before ADA, systemic treatment with corticosteroids, iv metilprednisolone (n=23), Cyclosporin A (58), azathioprine (33), metotrexate (31) and other drugs (28) was used. The dose of ADA was 40 mg/2 weeks/ sc in monotherapy (n=22) or combined (n=52). Most patients showed a rapid and progressive improvement (TABLE). The 24 patients (37 affected eyes) with CME showed a significant improvement.
ADA was optimized in 23 (31.1%) that were in remission for 15.3±9 months. Interval of administration was increased to 3 (n=6), 4 (13), 5 (1), 6 (1) and 8 weeks. After a mean follow-up of 13.0±9.7 months after optimization, 21 patients were stable and 2 had a severe flare. In 4 patients ADA was stopped after 35.2±9.3 months in remission. The main adverse effects observed were lymphoma (n=1), pneumonia (1), and 2° bacteriemia by E. Coli (1)

TABLE. EVOLUTION OF OCULAR PARAMETERS

	Basal	2nd week	1st month	6th month	1st year	2nd year	3rd year
VA (mean±SD)	0.5±03 n=146	0.6±0.3* n=144	0.6±0.2* n=143	0.7±0.2* n=120	0.8±0.2* n=112	0.8±0.2* n=89	0.8±0.2* n=41
Cells in the anterior chamber (median [IQR])	1 [0-2] n = 144	0 [0-2]* n= 142	0 [0-1]* n=142	0 [0-0]* n= 120	0 [0-0]* n = 116	0 [0-0]* n = 92	0 [0-0]* n = 42
Vitritis (median [IQR])	1 [0-2] n= 145	1 [0-1]* n= 143	0 [0-1]* n= 143	0 [0-0]* n= 124	0 [0-0]* n= 116	0 [0-0]* n= 92	0 [0-0]* n= 42
Retinal vasculitis (% affected eyes)	53.3% n= 144	43.2%** n= 141	36.4%* n= 142	11.4%* n= 123	4.1%* n= 116	0.6%* n= 92	0.6%* n= 42
OCT (μ) (mean±SD)	345.5±134.5 n= 82	341.1±108.6* n= 65	309.8±8* n= 64	268.1±38.4* n= 52	254.4±38.5* n= 55	259.5±41.2* n= 42	254.5±48.9* n= 20

*p<0.05
Abbrev: VA= visual acuity

Conclusions: ADA was effective in short and long-term follow-up in refractory uveitis associated to BD. Optimization or even suspension of ADA is possible.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3577

THU0327 ASSOCIATION BETWEEN THE TC/HDL RATIO AND DISEASE ACTIVITY IN PATIENTS WITH TAKAYASU ARTERITIS

L. Pan[1], J. Du[2], H. Liao[1]. *[1]Rheumatology and Immunology; [2]Beijing An Zhen Hospital, Capital Medical University., Beijing, China*

Background: Accelerated atherosclerosis has become the main cause of morbidity in patients with autoimmune diseases such as RA and SLE [1]. The Cholesterol/High-density Lipoprotein Cholesterol (TC/HDL-C) ratio is a high discriminatory power index for coronary heart disease. A high TC/HDL-C ratio has been intensively used as a predictor of CVDs [2]. EULAR Task Force recommended that the TC/HDL-C ratio should be regarded as an important prognostic indicator for future cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) [3]. However, the relationship between the TC/HDL-C ratio and disease activity of Takayasu arteritis (TAK) is unclear.
Objectives: To investigate changes in the TC/HDL-C ratio and to evaluate the relationship between the TC/HDL-C ratio and disease activity of TAK.
Methods: A retrospective study of 103 patients with TAK and 73 healthy controls was performed. We compared the triglyceride (TG), TC, low-density lipoprotein cholesterol (LDL-C), HDL-C and TC/HDL-C ratio between patients and healthy controls, and we analyzed correlations between the lipid parameters and indexes

of TAK activity. A ROC curve was used to determine the predictive value of TC/HDL-C ratio in patients group.

Results: The TG level was higher in patients with TAK than in the controls (p=0.000). The TC, LDL-C, and HDL-C levels were significantly lower in patients with TAK than in the controls (p=0.000, p=0.000, and p=0.000, respectively). The HDL-C level was significantly lower in the active TAK group than in the inactive TAK group (p=0.005). The TC/HDL-C ratio was significantly increased in patients with disease activity (p=0.001), and it exhibited a positive relationship with the high-sensitivity C-reactive protein level (r=0.234, p=0.003) and Kerr score (r=0.219, p=0.031). In addition, the TC/HDL-C ratio of 3.698 was determined as a predictive cut-off value of TAK (sensitivity 61.0%, specificity 78.6%, area under the curve=0.743) (Figure 1).

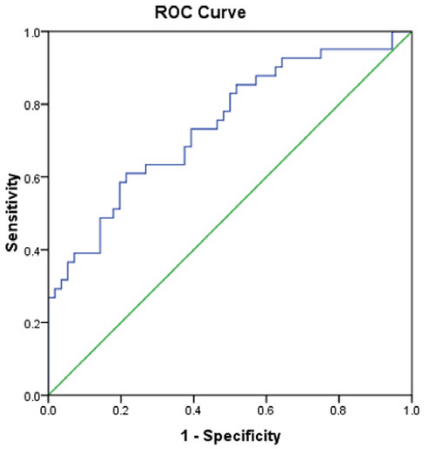


Figure 1.Receiver-operating characteristic curve for the TC/HDL-C ratio.
The area under the curve was 0.743, with sensitivity and specificity of 61.0%and 78.6%

Conclusions: For the first time, we showed that serum levels of TC, LDL-C, and HDL-C were significantly lower in patients with TAK, and the TC/HDL-C ratio has a positive relationship with the disease activity of TAK, suggesting that the TC/HDL-C ratio may be a potential indicator for monitoring the disease activity of patients with TAK.

References:

[1] Symmons DP, Gabriel SE: Epidemiology of CVD in rheumatic disease, with a focus on RA and SLE. Nat Rev Rheumatol 2011, 7(7):399–408.
[2] Zhou Q, Wu J, Tang J, Wang JJ, Lu CH, Wang PX: Beneficial Effect of Higher Dietary Fiber Intake on Plasma HDL-C and TC/HDL-C Ratio among Chinese Rural-to-Urban Migrant Workers. Int J Environ Res Public Health 2015, 12(5):4726–4738.
[3] Peters MJ, Symmons DP, McCarey D, Dijkmans BA, Nicola P, Kvien TK, McInnes IB, Haentzschel H, Gonzalez-Gay MA, Provan S et al: EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis 2010, 69(2):325–331.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1564

THU0328 PREDICTORS OF SEVERE DAMAGE IN ANCA-ASSOCIATED VASCULITIS: DATA FROM A MONOCENTRIC INCEPTION COHORT

M. Felicetti, R. Padoan, M. Cerchiaro, M. Zen, L. Punzi, F. Schiavon. *Department of Medicine DIMED, Operative Unit of Rheumatology, University of Padova, Padova, Italy*

Background: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are multi-systemic diseases associated with anti-neutrophil cytoplasmic antibodies (ANCA). Patients develop severe and irreversible damage, even in early stages of the disease, but data about prognostic factors are limited.

Objectives: To assess items and predictors of severe damage in a monocentric cohort of ANCA-associated vasculitis (AAV) patients, classified as GPA or MPA.

Methods: Clinical and serological data of patients, followed-up in a daily practice setting, were retrospectively revised. Severe damage, defined as a Vasculitis Damage Index (VDI) ^{3} 5, was assessed after 12 months and at last examination (LE). The five most important items, predictors of severe damage and their increase rate were analysed at the beginning and at the last examination.

Results: 69 patients were included, 53 (76.8%) classified as GPA and 16 (23.2%) as MPA. According to EUVAS classification 7 (10.1%) were affected by limited disease, 14 (20.3%) by early systemic disease, 35 (50.7%) by generalized disease and 13 (18.9%) by severe disease. Patients were middle aged at diagnosis (54.6±15 years) with a diagnostic latency of 9.6±16.4 months, mostly caucasian (98.6%) and equally represented in sex (female 53.6%). Mean follow-up was 54.5±41.9 months. The number of flare/year at LE was significantly higher in anti-PR3 patients if compared to anti-MPO (1.0±1.1 vs 0.3±0.5, p=0.028).

The VDI items most frequently observed are listed in Figure 1.

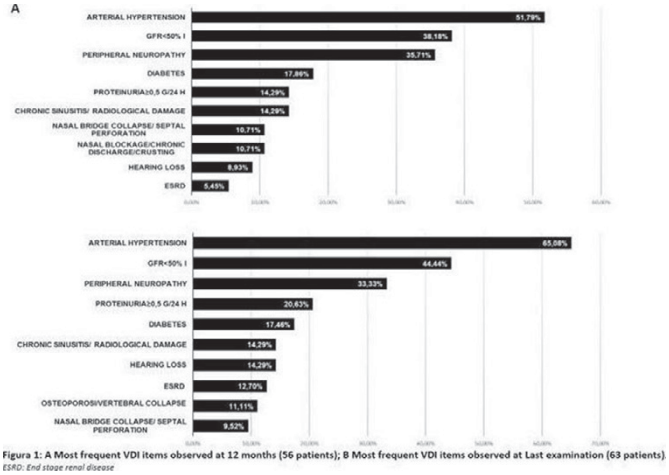


Figura 1: A Most frequent VDI items observed at 12 months (56 patients); B Most frequent VDI items observed at Last examination (63 patients).
ESRD: End stage renal disease

We measured their frequencies and increase rate from diagnosis to the LE: arterial hypertension increased from 3 (4.7%) to 41 (65.1%) (+60.3% (IC 95% 48–71%), p<0.0001), GFR<50% from 1 patient (1.6%) to 28 (44.4%) (+42.8 (IC 95: 31–55), p<0.0001), neuropathy from 4 (6.3%) to 22 (34.9%) (+28.6% (IC 18–41), p<0.0001), diabetes from 0 (0%) to 11 (17.5%) (+17.5% (IC 10–29); p=0.0011) and proteinuria>0.5 g 24 h from 1 (1.6%) to 13 (20.6%) (+19% (IC 11–31); p=0.0006).

Severe damage, defined as VDI≥5, increased over time, being present in none patient at diagnosis and in 14 (25.9%) at last examination.

At univariate analysis, number of flares/year (p=0.012), BVASv3 at diagnosis (p=0.03), steroid pulses therapy (p=0.04) and steroid cumulative dose (p=0.03) were identified as predictive factors of severe damage in the first year. Conversely, creatinine at LE (p=0.04), numbers of hospitalizations (p=0.009) and steroid cumulative dose at LE (p=0.47) were found to be predictors of long-term severe damage. Interestingly, ANCA pattern did not influence damage severity and only slightly differences in VDI items was noted between anti-PR3 and anti-MPO positive patients.

Conclusions: Our results highlights that knowing severe damage predictors is key in short and long term treat to target patient's management.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5633

THU0329 BUDD-CHIARI SYNDROME IN BEHÇET'S DISEASE: A RETROSPECTIVE MULTICENTER STUDY

L. Akyol [1], B. Toz [2], Ö. Bayındır [3], O. Zengin [4], D. Üsküdar Cansu [5], M. Yiğit [6], G. Yıldırım Çetin [7], A. Omma [8], A. Erden [9], O. Küçükşahin [10], M.S. Altuner [1], B.S. Çorba [11], A.U. Ünal [12], H. Küçük [13], A. Küçük [14], A. Balkarlı [15], E. Gönüllü [16], A.N. Tufan [17], S. Bakırcı Üreyen [18], S. Yılmaz Öner [19], S. Kobak [20], A. Yazıcı [21], M. Özgen [1], A. Şahin [22], S.S. Koca [23], B. Erer [2], A. Gül [2], K. Aksu [3], G. Keser [3], A.M. Onat [4], B. Kısacık [4], T. Kaşifoğlu [5], A. Çefle [21], U. Kalyoncu [9], M. Sayarlıoğlu [1]. *[1]Internal Medicine, Div. of Rheumatology, Ondokuz Mayıs University School of Medicine, Samsun; [2]Internal Medicine, Div. of Rheumatology, Istanbil University School of Medicine, Istanbil; [3]Internal Medicine, Div. of Rheumatology, Ege University School of Medicine, Izmir; [4]Internal Medicine, Div. of Rheumatology, Gaziantep University School of Medicine, Gaziantep; [5]Internal Medicine, Div. of Rheumatology, Osmangazi University School of Medicine, Eskişehir; [6]Internal Medicine, Div. of Rheumatology, Pamukkale University School of Medicine, Denizli; [7]Internal Medicine, Div. of Rheumatology, Sütçü İmam University School of Medicine, Kahramanmaraş; [8]Internal Medicine, Div. of Rheumatology, Numune Hospital; [9]Internal Medicine, Div. of Rheumatology, Hacettepe University School of Medicine; [10]Internal Medicine, Div. of Rheumatology, Yıldırım Beyazıt University School of Medicine, Ankara; [11]Statistics, Ondokuz Mayıs University School of Medicine, Samsun; [12]Internal Medicine, Div. of Rheumatology, Marmara University School of Medicine, Istanbil; [13]Internal Medicine, Div. of Rheumatology, Gazi University School of Medicine, Ankara; [14]Internal Medicine, Div. of Rheumatology, Necmettin Erbakan University School of Medicine, Konya; [15]Internal Medicine, Div. of Rheumatology, Antalya Training and research hospital, Antalya; [16]Internal Medicine, Div. of Rheumatology, State hospital, Eskişehir; [17]Internal Medicine, Div. of Rheumatology, Uludağ University School of Medicine, Bursa; [18]Internal Medicine, Div. of Rheumatology, Training and Research hospital, Sakarya; [19]Internal Medicine, Div. of Rheumatology, Bakırköy Dr. Sadi Konuk Training and Research Hospital; [20]Internal Medicine, Div. of Rheumatology, Liv Hospital, Istanbil; [21]Internal Medicine, Div. of Rheumatology, Kocaeli University School of Medicine, Kocaeli; [22]Internal Medicine, Div. of Rheumatology, Cumhuriyet University School of Medicine, Sivas; [23]Internal Medicine, Div. of Rheumatology, Fırat University School of Medicine, Elazığ, Turkey*

Background: The aim of this study was to determine the demographic, clinical,

laboratory and management characteristics along with the clinical course of Budd-Chiari syndrome (BCS) associated with Behçet's disease (BD).
Methods: Sixty patients with BD with BCS (40 male, 20 female) were identified in 23 rheumatology centers (Group I). A total of 169 consecutive patients (100 male, 69 female) with BD who did not have clinically apparent BCS during the follow-up were evaluated as the control group (Group II).
Results: Comparison of the demographic and clinical findings between the Group I and the Group II were as follows: The mean age of disease onset was 23.1 +/- 6.7 years vs. 26.8±0.6 years (p=0.013), mean age at diagnosis was 27.2±0.9 vs. 30.4±0.6 years (p=0.008), arthritis was 10% vs. 28.4% (p=0.002), papulopustular skin lesion was 48.3% vs 69.2% (p=0.003), central nervous system (CNS) involvement 10% vs. 3% (p=0.03), cardiac involvement was 16.7% vs. 2.4% ($p<0.001$), superficial thrombophlebitis was 23.3% vs. 4.7% ($p<0.001$), and deep vein thrombosis was 58.3% vs. 15.4% ($p<0.01$). On diagnosis 50% of BD patients with BCS were classified as Child-Pugh A. Inferior vena cava obstruction was observed in 38.3% and portal vein thrombosis was seen in 3.3% of the patients with BCS. Mortality in BCS patients with BD was 18.3%. BCS related treatment after diagnosis in patients with BD were as follows: 71.7% of patients were treated with monthly cyclophosphamide intravenous pulses, 53.3% received intravenous pulse corticosteroids, 55.9% used azathioprine, 54.2% had warfarine treatment, and 50.8% were treated with low molecular weight heparin.
Conclusions: This study shows a higher frequency of cardiac and CNS involvement, superficial thrombophlebitis, papulopustular skin lesion, deep vein thrombosis in BD patients with BCS. Arthritis was observed less common in BD patients with BCS. The mean age onset was lower in patients with BCS. Medical treatment with immunosuppressive agents and anticoagulation appears to be the treatment of choice in BD patients with BCS. The majority of the patients with BCS were Child–Pugh class A on diagnosis. The inferior vena cava is frequently involved and, often associated with deep vein thrombosis and cardiac involvement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3559

THU0330 MYCOBACTERIAL CORD FACTOR ANALOG INDUCES HIGH IL-6 SECRETION AND MINCLE RECEPTOR EXPRESSION IN PATIENTS WITH TAKAYASU ARTERITIS

N. Gupta[1], J. Kabeer Doss[2], H. Mohan[2], R. Goel[2], D. Danda[2]. *[1]CHRistian Medical College, VELLORE, Vellore, India; [2]Clinical Immunology & Rheumatology, CHRistian Medical College, VELLORE, Vellore, India*

Background: Association between Takayasu Arteritis (TA) and Tubcerculosis (TB) has been in vogue for years. Scientific evidence for this association is limited.
Objectives: To study pro-inflammatory cytokine responses and mRNA expression in patients with TA on exposure to Trehalose-6,6-dibehenate (TDB), a synthetic analogue of mycobacterial cord factor in comparison with healthy controls.
Methods: Patients with type V TA satisfying 1990 ACR criteria and age and sex matched healthy controls were recruited. 10 ml blood was collected in heparin coated tube. PBMCs were separated by density gradient centrifugation. PBMCs were cultured with and without 5μg/ml and/or 50 μg/ml of TDB for 48 hours in RPMI medium at 5% co2 incubator. IL-6, TNF-αand IL-17 were measured in cell culture supernatant. RNA was extracted from the cells and quantification of gene expression was performed using sequence specific primers with SYBR green in Step One Plus™ Real-Time PCR Systems (Applied Biosystems).
Results: Twenty two TA patients and 21 age and sex matched healthy controls were recruited. Baseline characteristic of cases included median (range) age:26.5 years (15–49), male:femaleratio of 5:17, ITAS-CRP2010: 7 (1–26) and DEITAK: 7.5 (1–21). Both patients and controls showed response by secreting IL-6 and TNF-α upon stimulation withTDB. Relative induction of IL-6 was significantly higher in TA [31.88 (0.74–168)] as compared to healthy controls [1.931 (0.644–8.21); $p<0.002$]. IL-17 was undetectable even upon TDB stimulation. Relative mincle expression was significantly upregulated by TDB in TA1.03 (0.623–1.346) fold, as compared to healthy controls 0.43 (0.36–0.57) fold ($p<0.05$). Relative gene expressions of IL-6, IL-8, TNFα, IFN-gand BCL-10 were not significantly different between TA and healthy controls.
Conclusions: Stimulation with TDB led to higher secretion of IL-6 and increased mincle expression in PBMCs of TA patients as compared to healthy controls.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6068

THU0331 MYELOPEROXIDASE DEPLETION IS A SELECTIVE FEATURE OF TAKAYASU ARTERITIS AND PREDICTS THE CLINICAL OUTCOME

A.A. Manfredi, G.A. Ramirez, V. Canti, E. Tombetti, M. Baldini, E. Baldisera, P. Rovere-Querini, N. Maugeri. *San Raffaele Scientific Institute, Milano, Italy*

Background: Takayasu's arteritis (TA) is a rare large-vessel vasculitis characterized by persistent remodelling of the vessel walls. The role of innate immune cells in TA is poorly understood. Biomarkers to be used for assessment of TA activity and clinical outcome are missing. A trimodal pattern of myeloperoxidase (MPO) distribution (simultaneous occurrence of neutrophils with complete depletion, reduced and normal content of the enzyme) is detectable in the very early phase of acute myocardial infarction and has been associated with a burst of neutrophil interaction with activated platelets[1]
Objectives: Here, we aimed at characterizing the phenotype of neutrophils and platelets in patients TA and correlating these biological findings with clinical data.
Methods: neutrophil MPO expression has been studies in 93 subjects, including 21 TA patients, 20 age- and sex-matched healthy donors that served as controls, 25 patients with chronic stable atherosclerosis (CSA), eight patients with giant cell arteritis (GCA), five patients with gramulomatosis with polyangitis (GPA), four patients with eosinophilic GPA (EGPA) and ten patients with polymyalgia rheumatica (PMR). Blood samples were collected and processed as described[1–3]. Neutrophil MPO content, platelet P-selectin and High-Mobility Group B1 (HMGB1) in platelet derived microparticles (PDμP) release were assessed by flow cytometry. TA patients were then followed up for a median time of 3.43 years.
Results: The trimodal distribution of neutrophils MPO content was identified in 17/21 TA, 1/8 GCA, 0/10 PMR, 0/25 CSA, 0/5 GPA and 0/4 EGPA patients; moreover in 0/20 healthy controls (ANOVA, F=15.22, $p<0.0001$). Neutrophil MPO content and the presence of neutrophils with complete MPO depletion in TA patients correlated inversely with i) platelet P-selectin expression ($p<0.01$), ii) the fraction of $HMGB1^{+}$-PDμP ($p<0.01$) and iii) disease duration, implicating an association of platelet and neutrophil activation with the disease natural history. In fact, the Kaplan Mayer analysis reveals that TA patients that had neutrophils with complete MPO depletion are at a significantly increased risk of ischemic complications during the follow up (long-rank=4.864, p=0.027, HR=36.15 abd CI-95%=0.15–7.51).
Conclusions: Neutrophils and platelets are significantly activated in TA. Paroxysmal neutrophils activation, leading to complete MPO depletion, is a common feature and predict ischemic events and as such the clinical disease outcome.
References:
[1] Maugeri N, Rovere-Querini P, Evangelista V, et al. An intense and short-lasting burst of neutrophil activation differentiates early acute myocardial infarction from systemic inflammatory syndromes. PLoS One 2012;7:e39484.
[2] Manfredi AA, Baldini M, Camera M, et al. Anti-TNFalpha agents curb platelet activation in patients with rheumatoid arthritis. Annals of the rheumatic diseases 2016;75:1511–20.
[3] Maugeri N, Campana L, Gavina M, et al. Activated platelets present high mobility group box 1 to neutrophils, inducing autophagy and promoting the extrusion of neutrophil extracellular traps. Journal of thrombosis and haemostasis: JTH 2014;12:2074–88.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4940

THU0332 CARDIAC INVOLVEMENT IN POLYARTERITIS NODOSA: A RETROSPECTIVE PATHOLOGICAL STUDY OF 37 AUTOPSY CASES

O. Zimba[1], M. Bagriy[2]. *[1]the Department of Internal Medicine, Danylo Halytsky Lviv National Medical University, Lviv; [2]Department of Pathological Anatomy, Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine*

Background: Cardiac involvement is a significant cause of the death and disability in systemic vasculitis. The comprehensive analysis of histopathologic findings in polyarteritis nodosa (PN) can help better understand mechanisms of excessive cardiovascular risk in patients with systemic vasculitis.
Objectives: To investigate the variation of cardiac pathological findings in autopsy cases of PN.
Methods: A retrospective analysis of cardiac pathological changes was performed in 37 autopsy cases of PN over period of 15 years. There were 28 males and 9 females, ranging from 23 to 85 years. The median age at disease onset was 35, 7 years; the median duration of disease was 2.1 years with a range of 2 month to 7 years.
Results: The destructive-productive vasculitis of the coronary arteries have been found in 30 cases (81.1%) of PN. The vessels most affected were myocardial, and epicardial medium and small-sized arteries. Histologically, the remodelling of coronary artery tree in PN had a wide range of acute and chronic changes that likely were depended on the duration of the disease. There were three types of pathological findings: (1) arteritis with predominantly destructive changes; (2) arteritis with predominantly proliferative changes; (3) destructive-productive arteritis. The early phase of PN has been characterized by abnormalities of vessels wall from mucoid swelling to fibrinoid necrosis. The most common was panarteritis with involvement of all layers of the arterial wall, and inflammatory responses with intramural, and perivascular infiltrates, mainly composed of lymphocytes, and neutrophils. However, endo-, meso-, and periarteritis also were observed in some cases. The most remarkable lesions in coronary arteries were the nodules visible to the naked eye along coronary arteries. They were present in 9 cases (30%), and can be described as well-demarcated nodular thickening of the artery walls with size from 0.1 to 0.4 cm. The pathological basis of nodules are areas of focal inflammation, destruction and aneurysmal dilatations of artery wall. In cases of chronic course of PN, the intimal hyperplasia due to proliferation of endothelial cells have been observed. Interestingly, that this productive endarteritis with luminal narrowing of coronary arteries was common in patients who were exposed to different types of occupational xenobiotic (silica dust, pesticides, insecticides, solvents, heavy metals). In 5 (16.7%) cases, luminal occlusion due to intimal proliferation, fibrosis and thrombus formation

led to the myocardial infarction, and death. Pathological manifestation of cardiac involvement in PN included the left ventricular hypertrophy due to renovascular arterial hypertension in 26 cases (70.3%). In addition, interstitial myocarditis was observed in 4 cases (10.8%).

Conclusions: Our date suggest that cardiac involvement is common in polyarteritis nodosa (81.1%), and coronary vasculitis affecting medium and small-sized arteries with wide range of acute and chronic changes can be the life-threatening condition.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6950

THU0333 ARE THE DEMOGRAPHIC AND CLINICAL FEATURES OF POLYARTERITIS NODOSA SIMILAR BETWEEN THE UK AND TURKEY?

O. Karadag[1,2], A. Erden[1], E.D. Batu[1], S. Gopaluni[2], A. Sari[1], B. Armagan[1], I. Ertenli[1], S. Ozen[1], D. Jayne[2]. *[1]Hacettepe University Vasculitis Centre, Ankara, Turkey; [2]Vasculitis and Lupus Clinic Addenbrooke's Hospital, University of Cambridge, Cambridge, United Kingdom*

Background: Polyarteritis Nodosa (PAN) is the first described but the least frequent primary systemic vasculitis. Various subgroups of necrotizing vasculitis have separated out from PAN, and are now defined such as HBV-related, cutaneous PAN or monogenic forms of vasculitis. There is a paucity of information on the current phenotypes and, ethnic and geographic differences of PAN.

Objectives: This study compares the demographic and clinical features between two PAN cohorts.

Methods: A retrospective survey of databases from two vasculitis centres between 1990–2016 for PAN patients fulfilling the EMEA Vasculitis Classification algorithm. All paediatric patients met the Ankara 2008 (EULAR/PReS endorsed) criteria for childhood PAN. Patients with typical angiographic and/or histopathologic findings consistent with PAN were included. Demographics, and clinical characteristics, Disease Extent Index (DEI) and Vasculitis Damage Index were recorded. A subgroup analysis based on disease extent between the UK patients with Turkish (TR) patients was performed.

Results: 93 (M/F: 51/42) patients (UK: 47, TR: 46) were recruited into the study. The mean age was 46.7 (20.7) years. Three were HBV-related, 20 (21.5%) had paediatric onset, 16 (16.5%) were cutaneous PAN.

Turkish patients had younger disease of onset (28.7 (17.8) vs. 43.0 (18.0), $p<0.001$). Twelve (26%) of Turkish patients had a monogenic disease (FMF association in 7, DADA2 in 5).

Cutaneous PAN was more frequent in the UK group (12 pts vs. 4pts, p=0.031) whereas renal involvement was increased in the TR group (Table). In contrast to systemic involvement, female predominance was seen in cutaneous PAN (40.3% vs. 68.8%, p=0.037). DEI was similar in both systemic involved groups (6.1 (2.4) vs. 6.5 (2.3), p=0.428). No difference was found between paediatric and adult onset patients except for frequency of cutaneous lesions (100% vs. 64.3%, p=0.002).

During a median 67.5 (32–126) months follow up, 13 patients deceased. No difference was found between the groups regarding relapse rate, death and vasculitis damage index (Table).

Table: Demographic and clinical characteristics of PAN patients

	All patients n: 93	UK cohort (n:47)	Turkish cohort (n: 46)	p
Age at time of study	46.7 (20.7)	52.5 (19.6)	33.6 (17.1)	**<0.001**
Age at diagnosis, years	35.8 (19.2)	43.0 (18.0)	28.7 (17.8)	**<0.001**
Time to diagnosis, months	2 (1-6)	2 (1-5)	3 (2-8)	**0.041**
Sex, male, %	54.8	44.7	65.2	**0.047**
Any constitutional symptoms, %	87.7	87.1	88.1	0.898
Any cutaneous manifestations, %	71.7	68.1	75.6	0.426
Musculoskeletal manifestations, %	78.0	76.7	82.6	0.278
Neurologic manifestations, %	38.8	32.5	54.3	0.089
Testicular pain/tenderness (men only), %	20.3	28.5	16.7	0.310
Renal involvement, %	58.0	40.4	76.1	**<0.001**
Gastrointestinal manifestations, %	47.1	48.8	45.0	0.733
Follow up, months	67.5 (32-126)	79.0 (35.0-143.0)	65 (29.5-108)	0.669
Response to treatment, % • Complete • Partial • No response	 58.5 30.8 10.8	 60.4 30.2 9.4	 54.5 31.8 13.7	0.838
Any relapse,%	57.1	58.9	52.9	0.675
Death, %	14.0	12.7	15.2	0.733
VDI	1 (0-1)	1 (0-1)	1 (0-2)	0.632

Values are labeled as mean (SD or median (IQR 25%-75%), VDI: Vasculitis Damage Index

Conclusions: Even though, the Turkish group had a younger disease onset and higher additional monogenic disease; disease extent, relapse rate, death, and damage index were similar in both groups. Among the cutaneous PAN group there was a female predominance. A multi-centre GWAS study could highlight the impact of genetic background on disease presentation and severity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5074

THU0334 EVALUATION OF SUBCLINICAL VASCULAR DAMAGE IN PATIENTS WITH POLYMYALGIA RHEUMATICA: A CROSS-SECTIONAL STUDY USING AN INTEGRATED, NON-INVASIVE APPROACH OF COLOR DOPPLER ULTRASOUND AND CARDIO-ANKLE VASCULAR INDEX (CAVI) MEASUREMENT OF ARTERIAL STIFFNESS

P. Sessa[1], I.M. Rutigliano[1], R. Scrivo[1], V. Silvestri[2], F. Ciciarello[3], G. La Torre[4], F. Conti[1], R. Priori[1], C. Alessandri[1], V. Riccieri[1], M. Di Franco[1], B. Gossetti[2], G. Valesini[1]. *[1]1) Department of Internal Medicine and Medical Specialties; [2]2) P. Stefanini General and Specialist Surgery Department; [3]3) Department of Cardiovascular Science; [4]4) Department of Public Health and Infectious Diseases, University of Rome la Sapienza, Roma, Italy*

Background: The association of chronic inflammatory rheumatic disorders with an increased risk of vascular disease, especially cardiovascular and cerebrovascular disease, is a consolidated matter, but data on polymyalgia rheumatica (PMR) are still inconsistent.

Objectives: The aim of our cross-sectional study was to investigate the presence of vascular damage in patients with PMR by analyzing subclinical vascular disease through validated, non-invasive cardiovascular disease markers.

Methods: We enrolled patients with PMR diagnosed according to the EULAR classification criteria and, as controls, patients with major cardiovascular risk factors (MCVRF) including hypertension, diabetes, hypercholesterolemia, cigarette smoking, and obesity. In all of them we performed color Doppler ultrasound to evaluate the common carotid intima-media thickness (IMT), the prevalence of carotid artery stenosis and of anterior-posterior abdominal aortic diameter (APAD); we also assessed the cardio-ankle vascular index (CAVI) to measure arterial stiffness and contextually the ankle-brachial index (ABI) to investigate the presence of lower-extremity peripheral arterial disease.

Results: Forty-eight patients with PMR and 56 with MCVRF were included. Demographic parameters were balanced between groups. A significant increase of IMT (1.03±0.23 *vs* 0.89±0.20; p=0.02), CAVI (8.59±1.23 vs 7.59±0.93; p=0.01) and APAD values (22.03±4.86 *vs* 19.14±4.65; p=0.03) was found in PMR patients with respect to MCVRF controls. No differences were reported with regards to the prevalence of carotid artery stenosis or ABI values between the two groups. No significant correlation between disease duration or duration of glucocorticoid treatment and IMT or CAVI values was found in PMR patients. Results of bivariate analysis showed a significant correlation between IMT and CAVI in both PMR and MCVRF patients (r^2=0.845 and 0.556, respectively; $p<0.001$).

Conclusions: Our study adds new information on cardiovascular risk in PMR patients, showing an increase in subclinical cardiovascular lesions and paving the way for further studies to define the utility and modality of cardiovascular screening for primary prevention in these patients.

References:

[1] Hancock AT et al. Risk of vascular events in patients with polymyalgia rheumatica. CMAJ 2014; 186: E495–501.

[2] Shirai K et al. A novel blood pressure–independent arterial wall stiffness parameter; cardio-ankle vascular index (CAVI). J Atheroscler Thromb 2006; 13101–7.

[3] Masugata H et al. Cardio-ankle vascular index for evaluating immunosuppressive therapy in a patient with aortitis syndrome. Tohoku J Exp Med 2010; 222:77–81.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4831

THU0335 ACETYLCHOLINESTERASE IS HIGHLY EXPRESSED IN THE INFLAMED VESSEL WALL OF PATIENTS WITH GIANT CELL ARTERITIS

P. Therkildsen[1], B.D. Nielsen[1], K.K. Keller[1], T. Steiniche[2], L.C. Gormsen[3], I.T. Hansen[1], E.-M. Hauge[1]. *[1]Department of Rheumatology; [2]Department of Histopathology; [3]Department of Nuclear Medicine and PET Centre, Aarhus University Hospital, Aarhus, Denmark*

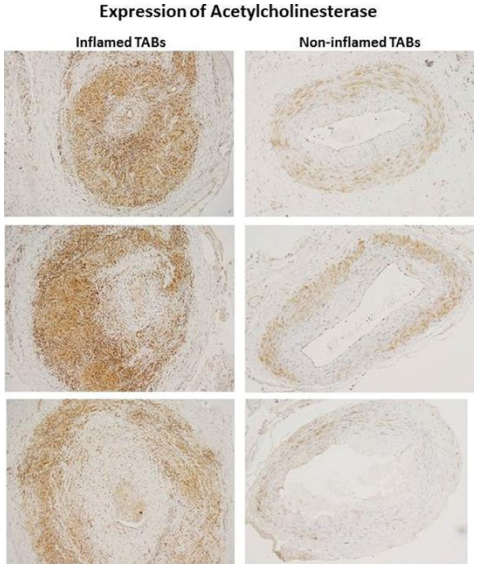
Background: The temporal artery biopsy (TAB) remains the gold standard in the diagnosis of giant cell arteritis (GCA) and is part of the ACR Classification criteria for GCA. However, TABs are false-negative in 10–60% of cases [1]. Cellular studies have shown that activated immune cells upregulate the acetylcholinesterase (AChE) expression [2]. If AChE is upregulated in the active GCA vessel wall, it may potentially improve the TAB as a diagnostic tool.

Objectives: To investigate the *in-situ* expression of acetylcholinesterase (AChE) in the vessel wall of patients with biopsy-positive GCA and compare to non-GCA patients.

Methods: In this histological case-control study, TABs from a total of 24 TAB-positive GCA and 44 TAB-negative non-GCA patients (21 patients with a final diagnosis of PMR, 23 patients with other diagnosis) were retrospectively selected from TABs performed between January 2012 and December 2015. A total of 295 TABs were assed for inclusion. Only positive TABs showing clear transmural inflammation were included. Patients treated with >7 days of prednisolone prior to the TAB were excluded. Clinical data were obtained from electronic patient records to confirm or dismiss clinical diagnosis. *TAB-HE-stains* were reviewed by a pathologist with expertise in vasculitis. Immunohistochemical methods were used to determine the AChE expression. The histological inflammation and AChE

expression were assessed and graded on 0–1-2 scale, blinded to histological and clinical data. Solitary AChE staining of the media was not included in the assessment.

Results: 24 positive and 44 negative TABs, with corresponding clinical positive and negative GCA diagnosis, were included in this study. We found that 10/24 positive TABs showed high AChE expression (grade 2) and 14/24 showed moderate AChE expression (grade 1). No AChE expression was observed outside the media in negative TABs from non-GCA patients (i.e. grade 0). The AChE expression was in 79% agreement with the degree of histological inflammation with a kappa value of 0.58. Prednisolone treatment for up to 7 days did not suppress the AChE expression. Neither the AChE expression, nor the histological inflammation showed correlation to any clinical or biochemical findings.



Conclusions: Our study shows that high to moderate AChE expression was observed in all 24 biopsies from TAB-positive GCA patients and that the AChE expression was in good agreement with the histological inflammation. No non-specific AChE expression was observed outside the media in any of the 44 TABs from TAB-negative non-GCA patients. This indicates that AChE could play a significant role in the inflammatory process in GCA and may be a potential biomarker in inflammatory diseases such as GCA.

References:

[1] Luqmani, R., et al., The Role of Ultrasound Compared to Biopsy of Temporal Arteries in the Diagnosis and Treatment of Giant Cell Arteritis (TABUL): a diagnostic accuracy and cost-effectiveness study. Health Technol Assess, 2016. 20(90): p. 1–238.

[2] Fujii, T., et al., Expression of acetylcholine in lymphocytes and modulation of an independent lymphocytic cholinergic activity by immunological stimulation. Biogenic Amines, 2003. 17(4–6): p. 373–386.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4935

THU0336 GIANT CELL ARTERITIS (GCA) IN OCTOGENARIAN PATIENTS

R. Solans-Laqué[1], E. Fonseca[2], B. Escalante[3], A. Martinez-Zapico[4], G. Fraile[5], M. Conesa[6], M. Abdilla[7], M. Monteagudo[8], J. Lasso[9], E. Calvo[10], B. Gracia[3], M. Castillo[11], J. Mestre[1] on behalf of REVAS Study Group (GEAS-SEMI).
[1]Internal Medicine, Vall Hebron University Hospital, Barcelona; [2]Internal Medicine, Cabueñes Hospital, Gijon; [3]Internal Medicine, Lozano Blesa Hospital, Zaragoza; [4]Internal Medicine, Central Hospital (HUCA), Asturias; [5]Internal Medicine, Ramon y Cajal Hospital, Madrid; [6]Internal Medicine, Miguel Servet Hospital, Zaragoza; [7]Internal Medicine, Alzira Hospital, Valencia; [8]Parc Taule Hospital, Sabadell; [9]Internal Medicine, Alcañiz Hospital, Teruel; [10]Internal Medicine, San Jorge Hospital, Huesca; [11]Internal Medicine, Virgen Rocio Hospital, Sevilla, Spain

Background: GCA is the most common systemic vasculitis in elderly people. It is characterized by granulomatous involvement of the major branches of the aorta with predilection for the temporal arteries. Headache is the most frequent initial complaint, and permanent visual loss the most feared complication.

Objectives: to describe the initial manifestations and outcome of CGA in octogenarian patients, and to investigate if there are some differences compared to younger patients

Methods: demographic, clinical and histological features, treatment and outcome of all patients with biopsy-proven GCA recruited at 11 different Hospitals from Spain (REVAS Study) were analysed. Statistical analysis was performed using SPSS vs. 20

Results: among the 418 patients included in the study, 180 (27.5%) were older than 80 y at disease onset (mean age 83.77±3.1, range 80–92y). Cardiovascular risk factors (hypertension, hypercholesterolemia, diabetes) were more prevalent in octogenarian patients than in younger (73% vs. 50%, p=0.018). Headache was the most frequent initial complaint (78.5%), followed by polymyalgia rheumatica (49.6%), jaw claudication (48.7%) and toxic syndrome (43.5%). A total of 28 (24.35%) patients suffered permanent visual loss, due to anterior ischemic optic ischemic neuropathy (n=26) or central retina vein thrombosis (n=4). When compared with younger patients, neither headache, nor jaw claudication, nor scalp tenderness and polymyalgia, were more common in octogenarian patients. Only fever was less common in patients >80 y at diagnosis than in younger (27.7% vs. 72.3%, p=0.006), and permanent visual loss was most prevalent among octogenarian patients (24.3% vs. 15.7%, OR 1.73, 95CI 1.1–2.9, p=0.04). We found an inverse correlation between fever and permanent visual loss (p=0.001). Blindness was significantly correlated with jaw claudication (p=0.006) and amaurosis fugax (p=0.001). We did not found any significant correlation between blindness and vascular risk factors. Regarding to LAB, ESR was higher in octogenarian patients (p=0.006) as well as thrombocytosis >400.000 platelets/mm (p=0.026). No differences were found related to anaemia prevalence. Inflammatory infiltrate with lumen occlusion and giant cells were significantly more prevalent in temporal artery biopsies from patients with permanent bilateral visual loss (p=0.007 and p=0.01, respectively). No differences were found related to treatment. All patients received oral prednisone at tapering dosage, 85.9% calcium and vitamin D supplementation, and 60% bifosfonates. We did not found differences related to treatment-side effects (osteoporotic fracture, diabetes, infections) between octogenarian patients and the younger.

Conclusions: octogenarian patients with GCA have an increased risk of developing permanent visual compared to younger patients. The presence of jaw claudication and amaurosis fugax must prompt to initiate corticosteroid treatment quickly. No differences were found related to treatment side effects in octogenarian patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5247

THU0337 CLASSIFICATION OF ANTINEUTROPHILIC CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS AND CLINICAL IMPACT AND OUTCOME

S. Deshayes[1], A. Aouba[1], K. Kathy[2], D. Mariotte[2], T. Lobbedez[3], N. Martin Silva[1]. *[1]Department of Internal Medicine; [2]Department of Immunology; [3]Department of Nephrology, CHU Côte de Nacre, Caen, France*

Background: Antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitis (AAV) have overlapping manifestations. Classifications based on clinical criteria or ANCA specificity have emerged to individualize homogenized group of patients in terms of clinical forms and outcomes.

Objectives: The aim of our study was to retrospectively re-evaluate the clinical impact and outcome of our monocentric AAV patients' cohort, according to classifications based on clinical criteria and/or ANCA specificity.

Methods: A retrospective monocentric study carried out in Caen university hospital led to identify proteinase-3 (PR3) or myeloperoxidase (MPO)-ANCA AAV patients (via an ELISA technique), respectively from March 1997 to June 2016, and from September 2011 to June 2016. Patients with eosinophilic granulomatosis with polyangiitis were excluded. AAV were classified between granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA), and limited or severe forms according to respectively European Medicines Agency vasculitis algorithm and WGET group. Categorical variables were reported as percentages and compared using Chi^2 or Fisher's tests according to expected frequencies. Continuous variables were expressed as means and analyzed using Student's t-test. Associations between survival, or relapse free survival, and AAV classifications were evaluated by the log-rank test. A p-value <0.05 was considered to be statistically significant.

Results: A total of 150 GPA/MPA were included.

Table 1

	anti-MPO GPA (n=20)	anti-PR3 GPA (n=74)	anti-MPO MPA (n=43)	anti-PR3 MPA MPA (n=13)
Male %	35	54	67	54
Renal involvement %	75	61	88	92
Ear-nose-throat involvement %	65	77	12	0
Lung involvement %	70	80	70	31
Skin involvement %	25	30	21	38
Neurological involvement %	45	24	23	31
Rheumatologic involvement %	55	62	37	54
Limited vasculitis, %	40	23	12	23
Relapse %	50	50	21	8
Death %	0	23	19	31
Initial BVAS, median ± SD	20±7.2	18.5±7.4	17±5.1	15±7.5
Age at diagnosis (years), median ± SD	66.5±11	60±17	62±13	70±21
Follow-up (months), median ± SD	49±47	55±65	50±37	33±108

As expected, ear-nose throat involvement were significantly higher in PR3-ANCA vs MPO-ANCA, and GPA vs MPA (p<0.001). Survival was significantly higher in

Abstract THU0337 – Table 2

p (significant higher parameter)	Male	Renal involvement	Lung involvement	Rheumatologic involvement	Limited vasculitis	Initial BVAS
PR3 vs MPO	0.71	**0.011** (MPO)	0.74	**0.03** (PR3)	0.74	0.38
GPA vs MPA	0.09	**<0.001** (MPA)	**0.03** (GPA)	**0.02** (GPA)	0.08	**0.035** (GPA)
MPO GPA vs PR3 GPA	0.14	0.25	0.38	0.57	0.13	0.64
MPO GPA vs MPO MPA	**0.02** (MPA)	0.27	0.99	0.19	**0.018** (GPA)	**0.048** (GPA)
MPO MPA vs PR3 MPA	0.52	1	**0.005** (MPO)	0.35	0.38	0.88

anti-MPO GPA but relapse-free survival was lower, compared to anti-MPO MPA (p=0.038 and p=0.015, respectively), without difference in treatments. Relapse-free survival was lower in GPA, compared to MPA (p<0.001). Among GPA patients, there was significantly more deaths in PR3 than MPO patients (p=0.02), but without significant difference between ANCA types for all other considered criteria, including survival (p=0.06).

Conclusions: The clinicopathological classification appeared as the strongest criteria for distinguish homogeneous forms and prognosis of AAV. Besides their diagnostic value, ANCA may not exhibited further great interest, especially in GPA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2274

THU0338 CLINICAL PRESENTATION AND OUTCOMES OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS: ANCA-NEGATIVE VERSUS ANCA-POSITIVE

E. Zagvozdkina, P. Novikov, S. Moiseev. *Sechenov First Moscow State Medical University, Moscow, Russia, Moscow, Russian Federation*

Objectives: The aim of the prospective study was to compare clinical presentation at diagnosis and long-term outcomes of eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA) patients according to antineutrophil cytoplasmic antibody (ANCA) status.

Methods: EGPA was classified according to the Revised CHCC Nomenclature and ACR1990 criteria. Activity of vasculitis was evaluated using BVAS. A minor relapse was defined as an increase in at least one new or worse minor item and no major BVAS items. A major relapse was an increase in at least one major BVAS item.

Results: We followed 93 patients with EGPA for a mean±SD of 6.3±6.5 years. Their mean±SD age was 46.6±13.8 years, and 96.8% patients had a history of asthma. The most common EGPA manifestations at diagnosis included ENT manifestations (88.2%), fever (78.5%), peripheral neuropathy (73.1%), lung involvement (59.1%) and skin lesions (49.5%). Thirty seven of 93 patients (39.8%) were ANCA-positive. These patients had significantly more frequent myalgia and mononeuritis multiplex, than the ANCA-negative patients. The difference in occurrence of kidney disease between the two groups did not reach statistical significance. However, all three patients with rapidly progressive kidney failure were ANCA-positive. BVAS at diagnosis and VDI at the end of the follow-up were significantly higher for ANCA-positive patients. The follow up duration was 587.7 patient-years. The incidence of all vasculitis relapses was 14 per 100 patient-years, including major and minor vasculitis relapses (5.3 and 8.7 per 100 patient-years, respectively). The 3- and 5-year relapse-free survival rate was 65.4% (95% CI 54.6–76.2) and 43.1% (95% CI 30.4–55.7), respectively. The frequency of vasculitis relapses was 21.0 per 100 patient-years in the ANCA-positive group versus 19.6 per 100 patient-years in the ANCA-negative group (P=0.4).

Table 1. Main clinical characteristics at diagnosis of the 71 patients with EGPA, according to ANCA status

Manifestations	ANCA+ (n=37)	ANCA- (n=34)	P
Fever	30 (81.1)	25 (73.5)	0.57
Myalgia	22 (59.5)	10 (29.4)	**0.02**
ENT	33 (89.2)	30 (88.2)	1.00
Lung	24 (64.9)	19 (55.9)	0.47
Cutaneous	24 (64.9)	15 (44.1)	0.10
Peripheral neuropathy	30 (81.1)	21 (61.8)	0.11
Mononeuritis multiplex	17 (45.9)	6 (17.6)	**0.01**
Cardiovascular	13 (35.1)	10 (29.4)	0.62
Gastrointestinal	4 (10.8)	4 (11.8)	1.00
Renal	11 (29.7)	5 (14.7)	0.16
BVAS at diagnosis, mean ± SD	16.86±6.44	12.62±5.52	**<0.01**
VDI at the end of the follow-up	2.43±1.57	1.76±1.16	**<0.01**

Conclusions: The characteristics of EGPA patients differ according to their ANCA status, although long-term outcomes were similar in both groups. EGPA is characterized by relapsing course of disease. The minor vasculitis relapses predominated in the structure of relapses.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5259

THU0339 FECAL CALPROTECTIN LEVELS AS AN INDICATOR OF ACTIVE DISEASE IN BEHÇET'S SYNDROME PATIENTS WITH GASTROINTESTINAL INVOLVEMENT: A CONTROLLED STUDY

S.N. Esatoglu[1], I. Hatemi[2], Y. Ozguler[1], G. Hatemi[1], H. Uzun[3], A.F. Celik[2], H. Yazici[1]. *[1]Istanbul University, Cerrahpasa Medical School, Department of Internal Medicine, Division of Rheumatology; [2]Istanbul University, Cerrahpasa Medical School, Department of Internal Medicine, Division of Gastroenterology; [3]Istanbul University, Cerrahpasa Medical School, Department of Biochemistry, Istanbul, Turkey*

Background: Elevated fecal calprotectin (FC) levels indicate activity in Crohn's disease (CD) and ulcerative colitis and are used as non-invasive biomarkers in these diseases. Gastrointestinal involvement of Behçet's syndrome (GIBS) shows clinical and endoscopic similarities to CD. A previous study suggested that FC may help to diagnose GIBS patients (1), but we are not aware of any studies addressing its role in identifying disease activity in such patients.

Objectives: To determine whether FC helps to distinguish active GIBS patients from those in remission.

Methods: We collected fecal and serum specimens before colonoscopy from 39 GIBS patients who agreed to participate (Table). Twenty-six patients were asymptomatic whereas 13 had abdominal pain and/or diarrhea. We also filled disease activity index for intestinal Behçet's disease (DAIBD) and Crohn's disease activity index (CDAI) in each patient. Active gastrointestinal (GI) involvement was defined as having ulcers on colonoscopy. We included 22 active and 25 inactive CD patients as controls. We used 150 μg/g as the cut-off for a positive FC level. None of the patients were receiving NSAIDs that could increase FC levels.

Results: Among the 39 GIBS patients, 14 had active ulcers on colonoscopy (8/13 symptomatic and 6/26 of asymptomatic). FC level was >150 μg/g in 12/14 active GIBS patients and in 6/25 patients in GI remission (OR: 19, 95% CI: 3 to 110). The median FC and CRP levels were higher among active GIBS patients whereas serum calprotectin levels were not different (Table). Among CD patients, 16/25 active patients and 3/22 patients in remission had a FC level >150 μg/g (OR: 11, 95% CI: 11 to 49). There was a high correlation between FC and CDAI scores (r=0.64, p<0.001) and a very high correlation between FC and DAIBD scores (r=0.71, p<0.001), while FC was not correlated with serum calprotectin and CRP levels. Among the 6 GIBS patients who had high FC levels despite being in remission for GI involvement, 2 had active mucocutaneous lesions, 1 had concomitant macrophage activation syndrome (MAS), 1 had polycythemia vera with trisomy 8 and 2 were started high dose corticosteroids. Repeat FC levels could be obtained in 3 of these patients, after the resolution of MAS and mucocutaneous lesions, and were <150 in all 3.

Table 1. Demographic, clinical and laboratory features of active GIBS patients and in GIBS patients who are in remission

	Active GIBS (n=14)	GIBS in remission (n=25)	*P* value
Gender, M/F	5/9	10/15	0.15
Mean±SD age, years	47.5±7.2	40±11	0.03
Median (IQR) FC, μg/g	301 (176–957)	30 (30–134)	*<0.001*
FC ≥150 μg/g, n (%)	12 (86)	6 (24)	*<0.001*
Median (IQR) serum calprotectin, ng/mL	98 (39–128)	69 (54–101)	0.5
Median (IQR) serum CRP, mg/dL	2 (1–5)	3 (2–15)	0.07
Median (IQR) CDAI scores	52 (4–189)	30 (0–92)	0.2
Median (IQR) DAIBD scores	40 (4–81)	20 (0–37)	0.1

Conclusions: FC seems to be a useful non-invasive tool for identifying active GI involvement in GIBS patients. Whether the presence of other BS manifestations can cause false positive results in GIBS patients in remission remains to be studied. On the other hand, serum calprotectin levels do not seem to be useful in identifying active disease in GIBS patients.

References:

[1] Kim DH et al. J Gastroenterol Hepatol. 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6124

THU0340 ADRENAL INSUFFICIENCY DURING GLUCOCORTICOID TREATMENT IN PATIENTS WITH POLYMYALGIA REUMATICA OR GIANT CELL ARTERITIS

T. Laursen[1], H. Locht[1], B. Jensen[1], S. Borresen[2], U. Feldt-Rasmussen[2], L. Hilsted[3], E.M. Bartels[4]. *[1]Center for Rheumatology and Spine Diseases, Rigshospitalet; [2]Department of Endocrinology, Rigshospitalet; [3]Department of Clinical Biochemistry, Rigshospitalet; [4]The Parker Institute, Department of Rheumatology, Copenhagen, Denmark*

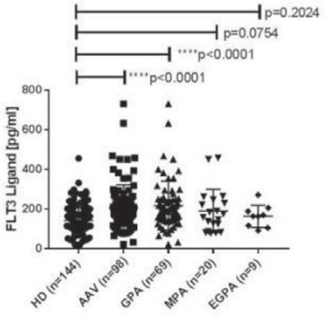
Background: Adrenal insufficiency secondary to long-term systemic glucocorticoid treatment is a well-recognized problem. However, the extent and prevalence of this phenomenon has not been thoroughly explored.
Objectives: To investigate the prevalence of adrenal insufficiency in patients with polymyalgia reumatica (PMR) and giant cell arteritis (GCA) during treatment with low doses of prednisolone (<10mg/day) assessed by the adrenal response to a 250 microgram Synachten® test. To explore whether potential adrenal insuffiency was associated with duration of steroid treatment.
Methods: Outpatients were examined when prednisolone doses were between 2.5 and 10 mg/day for >6 months. Adrenal function was evaluated after a 48-hour pause of prednisolone, using a 250 μg Synachten® (ACTH) test where plasma cortisol levels were measured at baseline and 30 minutes after Synacthen injection. Adrenal insufficiency was defined as plasma cortisol <420 nmol/l after 30 minutes according to the validated Roche Elecsys®Cortisol II assay. Accummulated doses of prednisolone for the individual patients were calculated. A multiple regression analysis was used to test for an association between the plasma cortisol after 30 minutes and the accumulated dose of prednisolone.
Results: Forty-eight patients (35 women) completed the Synachten® test. Seven (14.6%) patients exhibited adrenal insufficiency. Median age was 74 years (Range: 57–89 years). Median accumulated dose was 3.402 mg (Range: 820–21.200mg). Median plasma cortisol after 30 minutes was 562 nmol/l (Range: 92–989 nmol/l). In patients with adrenal insufficiency, median plasma cortisol was 122 nmol/l (Range: 56–275 nmol/l) at baseline and 207 (Range: 92–420 nmol/l) after 30 minutes. In patients without adrenal insufficiency, median plasma cortisol was 359 (Range: 9–710 nmol/l) at baseline and 584 nmol/l (Range: 429–989 nmol/l) after 30 minutes. Accumulated doses of prednisolone did not differ in patients with and without adrenal insufficiency (p=0.49). Plasma cortisol after 30 minutes was not associated with accumulated dose of prednisolone (estimate –0.01, 95% CI: –0.02 to 5.39, p=0.06), when adjusting for sex and age.
Conclusions: Iatrogenic adrenal insufficiency was prevalent among patients with PMR or GCA treated with low dose prednisolone. Adrenal function was not associated with the accumulated dose of prednisolone, or the duration of steroid treatment. A Synacthen® test is a valuable tool to evaluate the adrenal function, when steroid treatment is tapered in these patients. Latent symptoms of adrenal insufficiency may explain why some patients are reluctant to discontinue steroid treatment even after the inflammatory condition has gone into remission.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6623

THU0341 FLT3 LIGAND CONCENTRATIONS ARE ELEVATED IN ANCA-ASSOCIATED VASCULITIDES (AAV) AND ARE INFLUENCED BY IMMUNOSUPPRESSIVE THERAPY

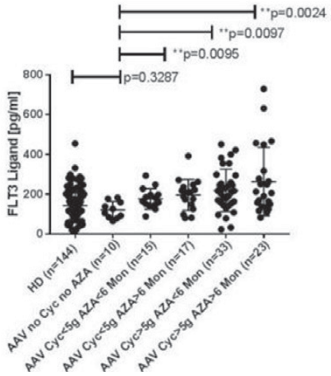
N. Venhoff, J. Thiel, R.E. Voll, A.C. Venhoff, U. Salzer. *Department of Rheumatology and Clinical Immunology, University Medical Center Freiburg, Medical Faculty, University of Freiburg, Freiburg, Germany*

Background: The cytokine Flt3 ligand is an important cofactor for early hematopoiesis by mainly driving the development of lymphoid and early B-cell precursors. In the periphery functions of Flt3 are more pleiotropic involving the differentiation of regulatory T-cells, dendritic cells as well as peripheral B-cells. Besides its well-known roles in hematological disorders and as an indicator of bone marrow (BM) output capacity, the possible involvement of FLT3 ligand in autoimmune disorders was only discovered recently.
Objectives: Our primary aim was to analyze if FLT3 ligand serum concentrations are affected in AAV patients. Secondary aims were to correlate the FLT3 ligand serum concentrations with clinical and laboratory parameters. And, since FLT3 ligand concentrations are elevated in different states of bone marrow failure, we also wanted to evaluate FLT 3ligand as a marker for treatment related BM toxicity in AAV patients.
Methods: We performed a cross sectional study using a sandwich ELISA to determine FLT3 ligand concentrations in the serum of 98 well characterized AAV patients (69 GPA, 20 MPA and 9 EGPA) and 144 healthy controls (HC). Statistical evaluation was done using Mann-Whitney or unpaired, two-tailed Student's t-test.
Results: In patients with AAV, FLT3 ligand concentrations were significantly elevated (207 pg/ml +/- 116.2 in AAV versus 142.5 pg/ml +/- 65.98 in HC; p<0.0001). Disease specific analysis revealed significantly elevated FLT3 ligand concentrations in GPA (217.6 pg/ml +/- 123; p<0.0001), but no significant differences for MPA and EGPA when compared to HC. FLT3 ligand concentrations did not correlate to serological or clinical markers of disease activity, however, overall disease activity was low in the studied cohort. To assess the influences of treatment regimen on FLT3 ligand concentrations, we focused our analysis on treatment histories of cyclophosphamide (CYC) and azathioprine (AZA) and grouped the patient cohort according to the cumulative CYC dose (< or >5g) and/or duration of AZA therapy (< or >6 months). AZA and CYC naïve patients (n=10) showed FLT3 concentrations comparable to HC (121 pg/ml +/- 42.3), but in patients with low dose CYC and short term AZA therapy FLT3 concentrations were significantly higher (176.6 pg/ml +/- 51.6), both compared to treatment naïve patients and HC (p=0.0095 vs. AZA/CYC naïve, p=0.0105 vs HC). Intensified treatment was associated with even further increased concentrations of FLT 3 ligand with highest concentrations found in patients treated with >5g CYC cumulative dose or AZA treatment for >6 months (263.4 pg/ml +/- 172.6; p=0.0024 vs. AZA/CYC naïve, p<0.0001 vs HC).

Elevated FLT3 serum concentrations in ANCA-associated vasculitides



FLT3 ligand serum concentrations are influenced by therapy



Conclusions: Flt3 ligand concentrations are elevated in patients with AAV, especially in patients with GPA. The elevation more likely reflects the therapeutic regimen and history than disease activity as we could show that patients with more intensive treatment including both CYC and AZA show higher FLT3 ligand serum levels when compared to patients with less intense therapy.
References:
[1] Ramos MI et al. FMS-related tyrosine kinase 3 ligand (Flt3L)/CD135 axis in rheumatoid arthritis. Arthritis Res Ther. 2013; 15:R209.
[2] Giri N et al. Immune status of patients with inherited bone marrow failure syndromes.Am J Hematol. 2015; 90:702–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6349

THU0342 UTILIZING "REAL LIFE" DATA IN ORDER TO EVALUATE THE ASSOCIATION BETWEEN GIANT CELL ARTERITIS AND AUTOIMMUNE THYROID DISEASE

Y. Yavne[1], S. Tiosano[2], A. Watad[2], D. Comaneshter[3], Y. Shoenfeld[2], A.D. Cohen[3,4], H. Amital[5]. *[1]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; [2]Department of Medicine 'B', Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Hashomer; [3]Chief Physician's Office, Clalit Health Services, Tel Aviv; [4]Siaal Research Center for Family Medicine and Primary Care, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva; [5]Department of Medicine 'B', Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Aviv, Israel*

Background: In 1977, How et al.[1] described the case of a simultaneous presentation of giant cell arteritis (GCA) and hypothyroidism. In the following decades, numerous studies have attempted to determine whether a significant interaction exists between GCA and autoimmune thyroid dysfunction, with conflicting results[2–5].
Objectives: To evaluate whether a genuine association exists between GCA and autoimmune thyroid disease.
Methods: Utilizing the medical database of Clalit Health Services, we compared the proportion of autoimmune thyroid disease between patients with GCA and age- and gender-matched controls in a cross-sectional study. Univariate analysis was performed using Chi-square and student *t-test* and a multivariate analysis was performed using a logistic regression model.
Results: 5,663 GCA patients and 23,308 age- and gender-matched controls were

included in the study. The proportion of hypothyroidism amongst GCA patients was increased in comparison with controls (18.2% vs. 6.91%, respectively, *p-value* <0.001), as was hyperthyroidism (2.56% and 1.19% respectively, *p-value* <0.001). After controlling for confounders, GCA demonstrated a robust independent association with hypothyroidism on multivariate logistic regression (OR 1.297, 95% CI 1.187–1.418, Table 1). In contrast, when a similar model was performed in order to assess the nature of the association between GCA and hyperthyroidism, it was found to be non-significant, with an OR of 1.097.

Table 1. Multivariate logistic regression of covariates associated with hypothyroidism

Characteristic	OR	CI	P
Age	1.03	1.02–1.03	<0.001
Gender (Female)	3.32	2.93–3.79	<0.001
BMI	1.02	1.01–1.03	<0.001
SES:			
Medium vs. Low	1.42	1.28–1.58	<0.001
High vs. Low	1.63	1.45–1.83	<0.001
GCA	1.30	1.12–1.42	<0.001

BMI: Body Mass Index, kg/m^2, SES: Socioeconomic status, GCA: Giant Cell Arteritis.

Conclusions: GCA patients have a higher proportion of hypothyroidism in comparison with matched controls. A significant association between GCA and hyperthyroidism was not found. Physicians treating GCA patients should consider screening for thyroid dysfunction on a regular basis.

References:

[1] How J, Bewsher PD, Walker W. Giant-cell arteritis and hypothyroidism. Br Med J. 1977;2(6079):99.
[2] Wiseman P, Stewart K, Rai GS. Hypothyroidism in polymyalgia rheumatica and giant cell arteritis. BMJ. 1989;298(6674):647.
[3] Bowness P, Shotliff K, Middlemiss A, Myles AB. Prevalence of hypothyroidism in patients with polymyalgia rheumatica and giant cell arteritis. Rheumatology. 1991;30(5):349–351.
[4] Duhaut P, Bornet H, Pinède L, et al. Giant cell arteritis and thyroid dysfunction: multicentre case-control study. BMJ. 1999;318(7181):434–435.
[5] Myklebust G, Gran JT. A prospective study of 287 patients with polymyalgia rheumatica and temporal arteritis: clinical and laboratory manifestations at onset of disease and at the time of diagnosis. Rheumatology. 1996;35(11):1161–1168.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2555

THU0343 THE EFFECT OF ADALIMUMAB ON CLINICAL MANIFESTATIONS AND PRO-INFLAMMATORY CYTOKINES MILIEU IN PATIENTS WITH BEHCET'S DISEASE

Y. Braun-Moscovici, Y. Tavor, D. Markovits, K. Toledano, A. Rozin, M.A. Nahir, A. Balbir-Gurman. *Rheumatology Department, Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion, Haifa, Israel*

Background: Behcet's disease is a multisystemic chronic relapsing inflammatory disease, classified among the vasculitides. The aetiology of Behcet's disease is unknown. Several cytokines, among them TNF-α, are involved in the pathogenesis of the disease.

Objectives: We aimed to assess efficacy and safety of Adalimumab (ADA) in patients with active Behcet's arthritis not responding to one or more DMARDS and to assess the impact of treatment on the cytokine milieu.

Methods: Eligible patients (pts) with active arthritis were enrolled in a 24 weeks single center prospective open-label study. Pts who relapsed within 12 weeks following ADA discontinuation could enter a 3 year extension study. The efficacy was assessed by 68 tender and 66 swollen joint count, patient visual analogue scale (VAS) for pain, physician overall disease activity VAS, health assessment questionnaire (HAQ), Behçet's Disease Current Activity Form (BDCAF), C reactive protein (CRP) and erythrocyte sedimentation rate (ESR). TNF-α,IL-1β, IL-6, INF-γ, IL-10 and IL-17a were evaluated at baseline, after 24 and 48 weeks of treatment, by ProcartaPlex Human High Sensitivity – Immunoassay kit. Trough ADA serum levels and anti-drug antibodies were measured at baseline, week 24 and 48.

Results: Ten pts (6 females),age (mean, standard deviation –SD) 45 (8.4) years, with a disease duration of 11.6 (10) years, were enrolled and treated with subcutaneous ADA 40mg every 2 weeks for 24 weeks. The results are described in Table1. A statistically significant improvement was observed in swollen joint count, physician VAS and BDCAF and in IL-6 levels, but not in tender joint count or HAQ. Resolution of oral and urogenital ulcers was achieved in all pts. Significant reduction of pain was reported by 40% of pts. No relapse of uveitis or other disease manifestations occurred during the study. The reduction in IL-6 levels correlated with the physician VAS and BDCAF but not with HAQ. No correlation was found between change in IL-10 level and VAS pain. The levels of INF-γ, IL-17A, TNF-α were undetectable in all pts. IL-1β was elevated in 1 patient only. ADA serum trough levels were in the therapeutic range in 7/10 pts. One patient developed high antidrug antibodies titer and ADA serum trough level of 0 with a concomitant increase in VAS pain and IL-6 concentration. Another patient with low ADA trough levels and no antibodies improved after providing ADA weekly. The disease relapsed in 9/10 pts, within 4–6 weeks following ADA interruption, 7 pts enrolled into the extension study.

	Baseline mean (SD)	24 weeks mean (SD)	P
Swollen joints	4.6 (4.2)	0.6 (0.4)	0.006
Tender joints	19 (18.7)	12.6 (10.9)	Non significant (NS)
Physician VAS	51.5 (18.5)	24.5 (16)	0.002
Patient pain VAS	72 (19)	56 (33)	NS
BDCAF	5.4 (1.6)	2.1 (1.4)	0.001
HAQ	1.76 (0.8)	1.6 (0.9)	NS
IL-6 pg/ml	10.06 (13.4)	2.02 (0.8)	0.042

Conclusions: ADA treatment was well tolerated and achieved a significant improvement in arthritis and mucocutaneous manifestations and lowered IL-6 serum concentration in all study pts but only 40% reported significant pain reduction. A subset of pts with insufficient improvement in joint tenderness and generalized pain may require comprehensive pain management besides anti-inflammatory therapy.

Acknowledgements: ABBVIE donated the study medication and supported the lab work
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4939

THU0344 A RHEUMATOLOGY LED PATHWAY FOR THE INITIAL MANAGEMENT OF GCA IMPROVES DIAGNOSTIC OUTCOMES COMPARED TO THE GENERALIST

Z. Farah, M. Gulati, M. Matheou, H. Alam, S. Hamdulay. *Rheumatology, Northwick Park Hospital, London, United Kingdom*

Background: Giant Cell Arteritis (GCA) is a medical emergency requiring prompt and appropriate management to prevent complications. The British Society of Rheumatology (BSR) has set out guidelines on the appropriate management of suspected GCA targeting both primary and secondary-care physicians. Hospitals increasingly use care-pathways to facilitate appropriate initial management of GCA by non-rheumatologists. Evidence is limited, however, on the impact of such interventions on patient care.

Objectives: To evaluate the impact of designing a GCA care-pathway for non-rheumatologists (acute and general physicians) on patient care in terms of: (i) duration from referral to temporal artery biopsy (TAB) and rheumatology review; (ii) glucocorticoid therapy burden; and (iii) proportion of referrals with a final diagnosis of GCA

Methods: We performed a retrospective study of all patients diagnosed with GCA between 3 periods: prior to introducing a GCA pathway (2007–2009), rheumatology led GCA pathway (2010–2012), and non-rheumatology led GCA pathway (2012–2016). We identified patients from a TAB database and collected general demographic data, initiation of glucocorticoid therapy, referral for TAB and rheumatology clinic, date of TAB and clinic review, biopsy findings, and final diagnosis.

Results: Table 1 summarises the main findings. After introducing the rheumatology-led pathway (2010–2012), rate of referrals for TAB per month declined to 0.78, the proportion of patients having a TAB within 14 days of referral reached 100%, and the proportion of patients with a positive biopsy increased to 30% suggesting appropriate use of the pathway and an improvement in care. However introducing a non-rheumatology led GCA pathway (2012–2016), led to increased referral numbers. The proportion of TAB within 14 days decreased, and the proportion with a positive biopsy declined (17%).

Abstract THU0344 – Table 1

	Before GCA Pathway	Rheumatology Led GCA Pathway (1st Cycle)	Non-Rheumatology Led GCA Pathway (2nd Cycle)
Dates	Pre-2010 (Jan 07–Sep 09)	2010 to 2012 (Jan 10–Mar 12)	2016 (Nov 12–June 16)
Study Design	Retrospective	Retrospective	Retrospective
Source of Data	Histology database, electronic records	Histology database, electronic records	Histology database, electronic records
Number of Patients Biopsied	54	21	129
Number of Months	33	27	44
Rate of Biopsies (pts/month)	1.64	0.78	2.93
Days from referral to TAB; Median (min-max)	5 (0–56)	5 (0–13)	9 (0- 45)
Proportion with TAB within 14 days	87%	100%	66.2%
Proportion with a positive biopsy for GCA	26%	30%	17%
Mean Age (years)	73	73	71
Gender Ratio (M:F)	18:36 (F 66.7%)	4:17 (F 80.9%)	48:81 (F 62.7%)
OUTCOME	GCA Pathway introduced	Pathway continued	Pathway review

The non-rheumatology led GCA pathway was associated with higher glucocorticoid burden. In this cohort, 23/55 (41.8%) patients who were found not to have GCA received more than 21 days of high dose steroids (40–60mg Prednisolone) whilst awaiting rheumatology review. 4 patients whose final diagnosis was not GCA received high dose steroids for more than 30 days (max 109 days).

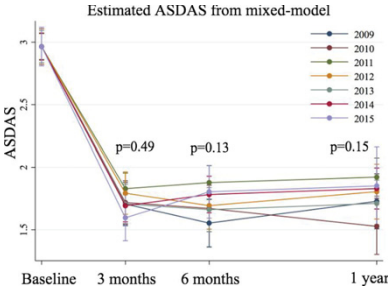
Conclusions: 1. Availability of a rheumatology-led GCA pathway leads to improved care for patients with suspected GCA

2. Easy access for referral of patients with headache as assessed by the non-specialist can lead to over-use of the pathway and inappropriate referrals

3. Non-rheumatology-led GCA pathway can lead to a high glucocorticoid burden, especially in an elderly demographic with other comorbidities

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1248



DOI: 10.1136/annrheumdis-2017-eular.2161

THURSDAY, 15 JUNE 2017

Spondyloarthritis - treatment

THU0345 REAL-LIFE EFFECTIVENESS OF TNF INHIBITORS IN AXIAL SPONDYLARTHRITIS: ARE CHANGING NATIONAL POLICIES ON CHOICE OF TNF INHIBITOR REFLECTED IN RESPONSE TO TREATMENT?

E.K. Kristianslund[1], K.M. Fagerli[1], E. Lie[1], A. Wierød[2], S. Kalstad[3], E. Rødevand[4], F. Krøll[5], P. Mielnik[6], T.K. Kvien[1], I.C. Olsen[1]. *[1]Department of Rheumatology, Diakonhjemmet Hospital, Oslo; [2]Department of Rheumatology, Drammen Hospital, Drammen; [3]Department of Rheumatology, University Hospital of North Norway, Tromsø; [4]Department of Rheumatology, St. Olavs Hospital, Trondheim; [5]Revmatismesykehuset, Lillehammer; [6]Department of Rheumatology, Førde Central Hospital, Førde, Norway*

Background: Tumour necrosis factor inhibitors (TNFi) have revolutionized treatment of axial spondylarthritis (axSpa). The five different available TNFi have not been compared directly, and whether effectiveness differs between agents is unknown. In Norway national authorities consider the different TNFi equivalent, and since 2009 the least expensive drug following an annual national tender has been the drug-of-choice in the publicly funded healthcare system. This has lead to variations across different years in drug use where choice of TNFi has been predominantly based on national price policy and not clinical characteristics.

Objectives: Comparing response to TNFi during the first year of treatment of axSpA in biologics-naïve patients over years with highly varying uptake of different TNFi.

Methods: We included the 981 biologics-naïve patients with axSpA from the NOR-DMARD register who started their first TNFi from 2009 through 2015. The preferred drugs in national recommendations were: 2009 adalimumab, 2010 golimumab, 2011 etanercept, 2012 etanercept, 2013 golimumab, 2014 certolizumab, 2015 certolizumab/biosimilar infliximab (CT-P13). We compared the estimated change in Ankylosing Spondylitis Disease Activity Score (ASDAS) between treatment years at 3, 6 and 12 months after treatment start using a mixed model with subject-specific random intercept, adjusting for baseline disease activity, age, sex and treatment centre.

Results: Demographics, drug uptake and baseline characteristics for each year 2009–2015 are listed in table 1. The preferred drug was started in 57–91% of patients. There was a trend towards lower ASDAS and disease duration over time. There were no differences in treatment effectiveness between the years, regardless of the substantial differences in type of TNFi used (figure).

Conclusions: Real-life data do not show differences in response to TNFi despite large annual variation in type of TNFi prescribed, indicating similar effectiveness of the available TNFi in patients with axSpA. This supports the practice of selecting drug based on cost and feasibility of use, as is the current practice in Norway. Further adoption of this principle can provide access to TNFi treatment to more patients, as it reduces costs and healthcare resources are limited.

Disclosure of Interest: E. K. Kristianslund: None declared, K. M. Fagerli: None declared, E. Lie Consultant for: AbbVie, Celgene, Hospira, Pfizer, UCB., A. Wierød: None declared, S. Kalstad: None declared, E. Rødevand: None declared, F. Krøll: None declared, P. Mielnik: None declared, T. K. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, I. C. Olsen: None declared

Abstract THU0345 – Table 1. Demographics and baseline characteristics

	2009	2010	2011	2012	2013	2014	2015	p-value
N	110	104	200	124	148	192	103	
Age (years), mean (SD)	42.3 (11.2)	40.3 (11.5)	41.7 (13.0)	40.0 (12.0)	40.9 (12.7)	41.6 (11.8)	41.6 (12.3)	0.76
Proportion male	66.1%	61.2%	50.8%	55.6%	52.7%	54.7%	57.3%	0.19
Years since diagnosis, median (IQR)	4.51 (0.77, 14.69)	3.79 (0.61, 12.74)	2.63 (0.47, 12.88)	1.70 (0.56, 11.08)	0.76 (0.22, 6.78)	0.60 (0.19, 3.44)	1.41 (0.18, 10.76)	<0.001
ASDAS, mean (SD)	3.26 (0.84)	3.20 (0.92)	3.10 (0.94)	2.96 (1.01)	3.02 (0.87)	2.87 (0.89)	2.71 (1.01)	<0.001
Adalimumab	90.9%	29.8%	22.0%	14.5%	24.3%	12.0%	0.0%	<0.001
Certolizumab	0.0%	1.9%	0.0%	0.8%	12.8%	77.1%	49.5%	
Etanercept	7.3%	8.7%	63.5%	69.4%	4.7%	2.6%	1.9%	
Golimumab	0.0%	58.7%	11.0%	11.3%	57.4%	2.6%	4.9%	
Infliximab	1.8%	1.0%	3.5%	4.0%	0.7%	0.5%	0.0%	
Biosimilar infliximab	0.0%	0.0%	0.0%	0.0%	0.0%	5.2%	43.7%	

p-values for between-year differences.

THU0346 CONCOMITANT FIBROMYALGIA IN AXIAL SPONDYLOARTHRITIS HAS A NEGATIVE IMPACT ON TNF ALPHA BLOCKERS TREATMENT EFFECT IN REAL LIFE

A. Moltó, A. Etcheto, L. Gossec, S. Perrot, N. Boudersa, P. Claudepierre, N. Roux, F. Berenbaum, A. Martin, L. Sparsa, P. Coquerelle, M. Soubrier, M. Dougados. *Predict-SpA Study Group, Paris, France*

Background: Coexisting fibromyalgia (FM) in axial spondyloarthritis (axSpA) can represent therapeutic challenges, particularly when evaluating the treatment effect of biologics (i.e. TNF alpha blockers (TNFb)). Indeed, since FM patients often report high levels of pain and disability there is the risk of classifying such patients as refractory to TNFb (ie, as not reaching a significant improvement in disease activity).

Objectives: To evaluate the impact of concomitant FM on the TNFb treatment effect in axSpA.

Methods: *Design:* Prospective observational national study with 2 visits 3 months apart (baseline and 12 weeks after TNFb initiation) (Predict-SpA study ClinicalTrials.gov: NCT03039088). *Patients:* axSpA patients (diagnosis according to treating rheumatologist) initiating a TNFb. *Data collection:* the FiRST questionnaire (Fibromyalgia Rapid Screen Test) which screens for FM, patients and disease characteristics and effectiveness measures (e.g. ASAS response components). *Statistical analysis:* FM positive screening was defined by a FIRST score ≥5/6; the primary efficacy outcome was the ASAS 40. Non-responder imputation and baseline observation carried forward imputation (for binary and continuous outcome variables, respectively) was performed. Impact of FM on the TNFb treatment effect was evaluated by multivariable logistic regression, with ASAS 40 as the dependent variable and FM as the independent variable; were also included in the model other factors previously reported in the literature as associated with treatment efficacy (i.e. X-ray and MRI sacroiliitis, abnormal CRP (>6mg/L), HLA B-27, smoking status, previous TNFb exposure, age<40 and male gender).

Results: Among the 527 patients enrolled in the study, 508 patients were analysed. Mean age was 41.4 (±11.6), 237 (46.7%) were women, with a 6.1±8.5 mean disease duration. Among them, 192 (37.8%) were screened as FM by the FiRST questionnaire. Overall efficacy of the TNFb was good (ASAS40, 201/508 (39.6%)) though 50 patients (9.8%) patients discontinued the TNFb before the follow-up visit and were considered as non-responders.

Patients with FM presented less frequently an ASAS 40 response (87/192 (45.3%) vs 171/316 (54.1%), for the FM vs non-FM groups according to the FIRST definition. Presence of FM was independently associated with poorer ASAS40 response (adjusted odds ratio, OR =0.5 [95% CI 0.3 – 0.8]) while X-ray sacroiliitis (1.8 [1.2 – 2.8]), abnormal CRP (1.6 [1.0 - 2.4]) and absence of previous exposure to TNFb (1.7 [1.1 – 2.6]) were found to be associated with an ASAS40 response.

Conclusions: This study 1) confirms the "conventional" predisposing factors of TNFb treatment response such as X-ray sacroiliitis, abnormal CRP and absence of previous exposure to TNFb; and 2) suggests that concomitant FM influences treatment response. FM deserves to be screened in axSpA, in particular in case of a decision to initiate a TNFb therapy.

References:

[1] Perrot S, Bouhassira D, Fermanian J; Cercle d'Etude de la Douleur en Rhumatologie. Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain. 2010;150:250–6.

Acknowledgements: The PredicSpA study was supported by MSD thanks to an unrestricted grant.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2509

THU0347 IMPACT OF OBESITY ON THE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS IN AXIAL SPONDYLOARTHRITIS

R. Micheroli[1], M. Hebeisen[2], A. Scherrer[2], L. Wildi[1], P. Exer[3], G. Tamborrini[4], J. Bernhard[5], B. Möller[6], P. Zufferey[7], M.J. Nissen[8], A. Ciurea[1]. *[1]University Hospital Zurich; [2]SCQM, Zurich; [3]Rheuma-Basel; [4]UZR, Basel; [5]Bürgerspital, Solothurn; [6]Inselspital, Bern; [7]CHUV, Lausanne; [8]University Hospital Geneva, Geneva, Switzerland*

Background: Few studies have investigated the impact of obesity on response to tumour necrosis factor inhibitors (TNFi) in patients with axial spondyloarthritis (axSpA).
Objectives: To investigate the impact of different Body Mass Index (BMI) categories on TNFi response in a large cohort of patients with axSpA.
Methods: Patients within the Swiss Clinical Quality Management cohort were included if they fulfilled the ASAS criteria for axSpA, started a first TNFi after recruitement and had available BMI data as well as a baseline and follow-up visit at 1 year (±6mo) (N=632). Patients were categorized according to BMI: normal (BMI 18.5 to <25), overweight (BMI 25 to 30) and obese (BMI >30). We evaluated the proportion of patients achieving the 40% improvement ASAS criteria (ASAS40) as well as Ankylosing Spondylitis Disease Activity Score (ASDAS) improvement and status scores at 1 year. Patients having discontinued the TNFi were considered non-responders. We controlled for age, sex, HLA-B27, axSpA-type, BASDAI, BASMI, elevated CRP, current smoking and physical exercise in multiple adjusted logistic regression analyses.
Results: In comparison to normal weight and overweight patients, obese individuals were significantly older, had a longer symptom duration and higher BASFI and BASMI levels, while ASDAS levels were comparable between the 3 groups (Table 1). Data to calculate the ASAS40 response was available in 496 patients (78%). It was reached by 44%, 35% and 28% of patients with normal weight, overweight and obesity, respectively, (p=0.02; Table 2). A significantly lower odds ratio (OR) for achieving ASAS40 response was found in adjusted analyses in obese patients vs patients with normal BMI (OR 0.30, 95% confidence interval (CI) 0.11–0.73, p=0.01). Comparable results were found for the other outcomes assessed. The respective adjusted ASAS40 OR in overweight vs. normal weight patients was 0.69, 95% CI 0.38–1.24, p=0.22.

Table 1. Baseline characteristics at start TNFi

Parameter	N	BMI category		
	632	Normal (N=331)	Overweight (N=202)	Obese (N=99)
Male sex, %	632	54	74*	64
Age, years	632	37.0 (11.2)	40.6 (11.5)*	44.2 (10.9)*#
Symptom duration, years	627	11.8 (10.1)	13.0 (11.4)	15.8 (11.7)*#
HLA-B27 positive, %	579	81	77	72
BASDAI	552	5.3 (2.0)	5.7 (1.9)*	5.8 (1.8)*
ASDAS-CRP	520	3.4 (0.9)	3.5 (0.9)	3.6 (0.9)
Elevated CRP, %	587	55	49	59
BASFI	558	3.6 (2.4)	4.2 (2.4)*	4.9 (2.6)*
BASMI	541	2.0 (2.0)	2.2 (1.9)	3.0 (2.3)*

*P values <0.015 compared with patients with normal weight. #P values <0.015 compared with patients with overweight. Values are the mean (SD).

Table 2. Unadjusted response rates after 1 year of treatment with a first TNF inhibitor

Outcome	N	BMI category			P*
	496	Normal (N=258)	Overweight (N=162)	Obese (N=76)	
ASAS40	496	44	35	28	0.02
ASDAS improvement ≥1.1	425	60	46	38	0.002
ASDAS <2.1	472	56	39	31	<0.001
ASDAS improvement ≥2	425	26	24	14	0.14
ASDAS <1.3	472	30	15	10	<0.001

Values are the %. *Overall P value.

Conclusions: Obesity is associated with significantly lower response rates to TNFi in patients with axSpA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2703

THU0348 SAFETY AND EFFICACY OF INTRAVENOUS GOLIMUMAB IN ADULT PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS THROUGH WEEK 28

A. Deodhar[1], J.D. Reveille[2], D.D. Harrison[3], L. Kim[3], K.H. Lo[3], E. Hsia[3,4]. *[1]Oregon Health & Science University, Portland; [2]University of Texas Health Sciences Center, Houston; [3]Janssen Research & Development, LLC, Spring House; [4]University of Pennsylvania School of Medicine, Philadelphia, United States*

Objectives: Subcutaneous (SC) golimumab (GLM) is currently approved for adult patients (pts) with RA, PsA, and AS. The GO-ALIVE study was designed to evaluate the safety and efficacy of IV GLM in adult pts with active AS.
Methods: GO-ALIVE is a Phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled trial. Pts (aged ≥18 yrs) had a diagnosis of definite AS (per modified New York criteria) and BASDAI ≥4, total back pain visual analogue scale ≥4, and CRP ≥0.3mg/dL. Pts were randomized (1:1) to IV GLM 2mg/kg at weeks (wks) 0, 4, and every 8 wks or PBO at wks 0, 4, and 12, with crossover to GLM at wk16. Up to 20% of pts could have had a prior anti-TNF agent (other than GLM), and up to 10% of pts could have complete ankylosis of the spine. The primary endpoint was ASAS20 at wk16. Major secondary endpoints were ASAS40, BASDAI50, and change in BASFI score at wk16. Some of the other statistically-controlled assessments were BASMI, and ASAS partial remission. Pts were monitored for adverse events (AEs). Data through wk28 are reported here.
Results: 208 pts were randomized and received study agent (PBO: 103; GLM: 105). Baseline demographic and disease characteristics were similar between treatment groups. 78% of pts were male, mean age was 39 yrs; mean disease duration was 5.5 yrs, 89.9% were HLA-B27 positive, 5.8% had complete ankylosis of the spine, 14.4% used a prior anti-TNF. At wk16, significantly greater proportions of GLM pts vs PBO had ASAS20 (73.3% vs. 26.2%), ASAS40 (47.6% vs. 8.7%), and BASDAI 50 (41.0% vs. 14.6%) responses (all p<0.001; Table). Reductions in BASFI were also significantly greater with GLM. ASAS20 was significantly higher with GLM than PBO as early as wk2 (37.1% vs 19.4%; p=0.005). Responses in the GLM group were maintained through wk28. PBO pts who crossed over to GLM at wk16 had improvements in clinical response at wk20 that were maintained through wk28. Through wk16, 23.3% of PBO pts and 32.4% of GLM pts had ≥1 AE. Infections were the most common type of AE (PBO, 7.8%; GLM, 11.4%). Through wk28, 34.8% of all GLM-treated pts had ≥1 AE; nasopharyngitis (5.4%) was the most common. Two pts (1.0%) had SAEs (pancreatitis, n=1; pneumonia, n=1). Both were randomized to GLM. There were no opportunistic infections, malignancies, or deaths through wk28. The rate of infusion reactions was low (1.5%). 3 pts treated with GLM had 4 reactions; none was serious or severe.

Table. Efficacy at week 16.

	Placebo	Golimumab 2 mg/kg
Patients randomized, n	103	105
Clinical efficacy		
ASAS20, n (%)	27 (26.2%)	77 (73.3%)**
ASAS40, n (%)	9 (8.7%)	50 (47.6%)**
BASDAI 50, n (%)	15 (14.6%)	43 (41.0%)**
Change from baseline in BASFI, n	98	105
mean (SD)	-0.5 (2.0)	-2.4 (2.1)**
ASAS partial remission, n (%)	4 (3.9%)	17 (16.2%)*
Change from baseline in BASMI (linear), n	96	100
mean (SD)	-0.1 (0.5)	-0.4 (0.6)**

*p < 0.01; **p ≤ 0.001
ASAS20/40, ≥20%/40% improvement in ASsessment in Ankylosing Spondylitis (ASAS) International Working Group criteria; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; SD, standard deviation

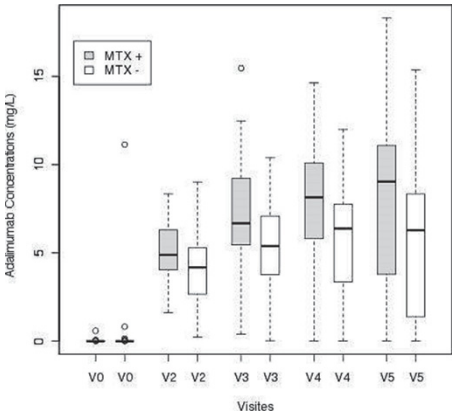
Conclusions: IV GLM 2mg/kg was efficacious in reducing the signs and symptoms of AS compared with PBO. GLM was well-tolerated through wk28; the safety profile was consistent with other anti-TNFs, including SC GLM.
Disclosure of Interest: A. Deodhar Grant/research support from: Janssen, Amgen, Abbvie, GSK, Elli Lilly, Novartis, Pfizer, UCB, Consultant for: Janssen, Elli Lilly, Novartis, Pfizer, UCB, J. Reveille Grant/research support from: Janssen Scientific Affairs, LLC., D. Harrison Employee of: Janssen Research & Development, LLC, L. Kim Employee of: Janssen Research & Development, LLC, K. H. Lo Employee of: Janssen Research & Development, LLC, E. Hsia Employee of: Janssen Research & Development, LLC
DOI: 10.1136/annrheumdis-2017-eular.1020

THU0349 METHOTREXATE REDUCES ADALIMUMAB IMMUNOGENICITY IN PATIENTS WITH SPONDYLOARTHRITIS: A RANDOMIZED CLINICAL TRIAL

E. Ducourau[1,2,3], T. Rispens[4], E. Dernis[5], F. Le Guilchard[6], L. Andras[6], A. Perdriger[7], E. Lespessailles[3], A. Martin[8], G. Cormier[9], T. Armingeat[10], V. Devauchelle-Pensec[11], E. Solau-Gervais[12], B. Le Goff[13], A. de Vries[14], E. Piver[15,16], D. Ternant[17,18], P. Goupille[1,2], D. Mulleman[1,2]. *[1]Rheumatology, Université François Rabelais de Tours, CNRS 7292; [2]Rheumatology, CHRU de Tours, Tours; [3]Rheumatology, CHR d'Orléans, Orléans, France; [4]Landsteiner laboratories, Sanquin Research, Amsterdam, Netherlands; [5]Rheumatology, CH du Mans, le Mans; [6]Rheumatology, CH de Blois, Blois; [7]Rheumatology, CHRU de Rennes, Rennes; [8]Rheumatology, CH de Saint-Brieuc, Saint-Brieuc; [9]Rheumatology, CH de la Roche-sur-Yon, la Roche-sur-Yon; [10]Rheumatology, CH de Saint-Nazaire, Saint-Nazaire; [11]Rheumatology, CHRU de Brest, Brest; [12]Rheumatology, CHRU de Poitiers, Poitiers; [13]Rheumatology, CHRU de Nantes, Nantes, France; [14]Biologicals Lab, Sanquin Diagnostic Services, Amsterdam, Netherlands; [15]Biochemistry, Université François Rabelais de Tours, Inserm U 966; [16]Biochemistry, CHRU de Tours; [17]Pharmacology-Toxicology, Université François-Rabelais de Tours, CNRS 7292; [18]Pharmacology-Toxicoloy, CHRU de Tours, Tours, France*

Background: TNF inhibitors are effective in treating spondyloarthritis (SpA).

However, anti-drug antibodies (ADA) may be responsible for decreased efficacy. Methotrexate reduces adalimumab immunogenicity in rheumatoid arthritis (1).
Objectives: The aim of the study was to evaluate the effect of methotrexate on ADA detection in SpA patients receiving adalimumab.
Methods: One hundred and ten SpA patients eligible for adalimumab 40 mg S/C eow were randomized on a 1:1 ratio to receive MTX 10 mg s/c every week, 2 weeks prior (V0) adalimumab (MTX+), or adalimumab alone (MTX-). ADA detection and adalimumab concentration were assessed 4 weeks (V2), 8 weeks (V3), 12 weeks (V4) and 26 weeks (V5) after starting adalimumab (V1). The main outcome was the percentage of positive patients for ADA detection at V5 or last available visit.
Results: Patients' characteristics (sex, previous TNF inhibitors, disease duration, HLA B27 +/-, BMI) were comparable between the two groups. One hundred and seven patients were analyzed, 55 in the MTX+ group versus 52 in the MTX- group. ADA were detected at V5, in 39/107 (36.4%) patients; 13/52 (25%) in the MTX+ group versus 26/55 (47.3%) in the MTX- group (p=0.03). Adalimumab concentrations were statistically higher in the MTX+ group as compared with the MTX- group at V2, V3, V4 and V5 (Figure 1). There was no difference in terms of adverse events and efficacy between the two groups.



Conclusions: MTX reduces immunogenicity and ameliorates pharmacokinetics of adalimumab in SpA patients. The clinical impact of this combination requires longer period studies.
References:
[1] Krieckaert CL, Nurmohamed MT, Wolbink GJ. Ann Rheum Dis 2012.
Acknowledgements: The authors thank Bruno Giraudeau for his methodological advice in the study design; Yoann Desvignes for technical support with the study protocol; Elody Marnat for data management; Coraline Gadras and Céline Vignault for blood sample management; Anne-Claire Duveau for technical assistance. This work was promoted by the Regional University Hospital Center of Tours and supported by grants from the French Ministry for Health and Sport within the framework of the "Programme Hospitalier de Recherche Clinique 2011" and received fundings from the "Lions Club, Tours Val de France" and from Nordic Pharma who provided subcutaneous methotrexate. This work was a collaborative venture by HUGO (Hôpitaux Universitaires du Grand Ouest – Western France University Hospitals Network).
Disclosure of Interest: E. Ducourau: None declared, T. Rispens: None declared, E. Dernis: None declared, F. Le Guilchard: None declared, L. Andras: None declared, A. Perdriger: None declared, E. Lespessailles Grant/research support from: MSD, Novartis, UCB, Pfizer, Consultant for: MSD, Novartis, UCB, Pfizer, A. Martin: None declared, G. Cormier: None declared, T. Armingeat: None declared, V. Devauchelle-Pensec: None declared, E. Solau-Gervais: None declared, B. Le Goff: None declared, A. de Vries: None declared, E. Piver: None declared, D. Ternant Consultant for: Sanofi, Amgen, P. Goupille Consultant for: Abbvie, Biogaran, BMS, Hospira, Janssen, MSD, Pfizer, Sanofi-Genzyme, UCB, D. Mulleman Grant/research support from: Nordic Pharma, Abbvie, Consultant for: MSD, Novartis, UCB, Pfizer
DOI: 10.1136/annrheumdis-2017-eular.1527

THU0350 EFFECT OF NSAID CONSUMPTION ON CARDIOVASCULAR EVENTS IN SPONDYLOARTHRITIS

E. Rivière[1,2], A. Etcheto[3], F. Van den Bosch[4], D. Van der Heijde[5], R. Landewé[6], M. Dougados[3], A. Molto[3] on behalf of ASAS-COMOSPA taskforce.
[1]Rheumatology, Bicêtre Hospital, INSERM U1184, le Kremlin Bicêtre; [2]Rheumatology B, Cochin Hospital; [3]Rheumatology B, Cochin Hospital, INSERM U1153, Paris, France; [4]Rheumatology, Ghent Universituy Hospital, Ghent, Belgium; [5]Rheumatology, Leiden University Medical Center, Leiden; [6]Rheumatology and Immunology Center, ARC, Amsterdam and Zuyderland Hospital Heerlen, Amsterdam, Netherlands

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) have been reported to increase cardiovascular (CV) risk. Studies on NSAIDs safety in patients with spondyloarthritis (SpA) are rare and contradictory. However, this question is highly relevant for these patients with chronic NSAIDs use and increased CV risk (1).
Objectives: The objective of this study was to determine the relationship between NSAIDs use and the occurrence of CV events, including myocardial infarction (MI) and stroke, in patients with SpA.
Methods: This is an ancillary study of the observational, cross-sectional, multicenter, international ASAS-COMOSPA study. The inclusion criteria were: age >18 years and SpA diagnosis. In order to overcome prescription bias when comparing patients who ever received/did not receive NSAIDs, a propensity score (PS) to predict NSAIDs intake was calculated. Patients who had never received NSAIDs were matched to patients who ever received an NSAID according to the PS. In this matched population, the probability for a patient to present a CV event was estimated by logistic regression. Furthermore, in the global population of the study, factors associated with the occurrence of CV event were explored by logistic multivariate analysis, here including the NSAIDs score (2) of the last three months, age and gender, and using the PS as an adjustment variable.
Results: Of the 3984 patients enrolled in the study, data on CV event occurrence were available for 3961 patients. Among them, 3548 patients received NSAIDs (89.6%) and 378 had never received NSAIDs (10.4%). Patients who had never received NSAIDs had more often inflammatory bowel disease (9.9% vs 5.3%), and a less severe disease (% of bamboo patients: 2.0% vs 7.6%). Among the 756 matched patients, 29 (3.8%) patients reported a CV event (21 MI, 13 strokes and 5 MI + stroke). The number of patients with CV event was not significantly different between the two groups, ever and never NSAIDs exposure respectively (16 (2,1%) vs 13 (1,7%), OR =1.86 [0.496–6.989]). No difference was observed between the two groups for MI and stroke compared separately (12 (1,6%) vs 9 (1,2%), OR =2.96 [0.417–21.013] and 8 (1,1%) vs 5 (0,7%), OR =0.926 [0.288–22.108] respectively). In the second model, where PS was used as a covariate, the occurrence of overall CV event was independently associated with age (OR =2.7 [2.3–3.2]) and male sex (OR =1.9 [1.2–3.0]), but not with the NSAIDs score (OR =1.0 [0.9–1.1]).
Conclusions: The use of NSAIDs does not seem to be associated with the occurence of CV event in patients with SpA, however it cannot be excluded that the study is underpowered. Further prospective studies are needed to confirm these results.
References:
[1] Haroon NN, et al. Ann Intern Med. 2015;163(6):409–16.
[2] Dougados M, et al. Ann Rheum Dis. 2011;70(2):249–51.
[3] Moltó A, et al. Ann Rheum Dis. 2016;75(6):1016–23.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2665

THU0351 ADALIMUMAB TAPERING WITH COMBINED METHOTREXATE CAN BE EFFECTIVE AS MAINTENANCE THERAPY IN SPA-RELATED UVEITIS

F. Lian, J. Zhou, Y. Wang, H. Xu, L. Liang, X. Yang. *Dept. of Rheumatology, 1St Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China*

Background: Anti-TNF agents have deeply improved the therapeutic efficacy of spondyloarthritis (SpA)-related uveitis [1]. Despite the benefits of anti-TNF drugs, patients need to stay on this treatment for a long time. There has been a clear medical need to consider the long-term safety and increased drug costs. Unanswered question for physicians is whether TNF blockers can be reduced or even stopped in SpA-related uveitis, or how can it be reduced in patients have achieved remission or LDA. The current study aimed to investigate the effectiveness and safety of adalimumab tapering strategy in SpA-related uveitis. We tried to find a way in balancing the quality of the patients' lives, the side effects and the cost-effectiveness.
Objectives: The aim of this study was to evaluate the effectiveness of tapering of adalimumab combined with MTX in patients with spondyloarthritis (SpA)-related uveitis.
Methods: We performed a retrospective analysis. SpA patients with uveitis admitted to a south China hospital were enrolled. Demographic information, clinical characteristics, laboratory findings, intraocular inflammation, visual acuity, and macular thickness were documented every 3 to 6 months.
Results: In 32 cases of SpA-related uveitis who achieved clinical remission for at least 6 months after receiving a standard dose of adalimumab in combination of MTX, adalimumab was tapered and MTX was continued. Dosing interval of adalimumab were spaced by 30% every 3 months up to complete stop. Twenty-six cases without MTX were analyzed for comparison. No significant difference of demographic characteristics and BASDAI, CRP, ESR was found between the two groups at the baseline. During the first 12 months of adalimumab tapering, the mean BASDAI remained stable in both groups. No recurrent uveitis was found in the group with combined MTX. In the group without combined MTX, 2 patients (2/26, 7.7%) presented increased anterior chamber inflammation and visual acuity. At the end of 24 months, mean BASDAI, CRP and ESR remained low in both groups. Two cases (2/32, 6.3%) in the group of combined MTX were documented increased BASDAI higher than 4, but no recurrent uveitis was observed. Altogether 5 cases (5/32, 15.6%) in the group of combined MTX had recurrent uveitis, in which 4 cases (4/5, 80%) initiated adalimumab tapering at 6 months' remission. In comparison, 8 cases (8/26, 30.8%, $p<0.001$) in the group without combined MTX had recurrent uveitis, in which 6 cases initiated

adalimumab tapering at 6 months' remission and 2 cases initiated adalimumab tapering at 9–12 months' remission. No patients had recurrent uveitis at 12 months' remission or longer in both groups. Adalimumab plus MTX were well tolerated in all patients.

Conclusions: For maintaining remission of SpA-related uveitis, adalimumab tapering can be effective when combined with MTX. Initiation of the tapering after 12 months' remission largely lower the rate of recurrence.

References:

[1] Jaffe GJ, Dick AD, Brézin AP, et al. Adalimumab in Patients with Active Noninfectious Uveitis. N Engl J Med. 2016 Sep 8; 375(10):932–43.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2507

THU0352 TOFACITINIB TREATMENT IS ASSOCIATED WITH ATTAINMENT OF THE MINIMALLY IMPORTANT REDUCTION IN AXIAL MRI INFLAMMATION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

W.P. Maksymowych[1], D. van der Heijde[2], X. Baraliakos[3], A. Deodhar[4], M. Brown[5], S.P. Sherlock[6], D. Li[7], D. Fleishaker[8], T. Hendrikx[7], K.S. Kanik[8].
[1]University of Alberta, Edmonton, AB, Canada; [2]Leiden University Medical Center, Leiden, Netherlands; [3]Rheumazentrum Ruhrgebiet, Herne, Germany; [4]Oregon Health & Science University, Portland, OR, United States; [5]Queensland University of Technology, Brisbane, Australia; [6]Pfizer Inc, Cambridge, MA; [7]Pfizer Inc, Collegeville, PA; [8]Pfizer Inc, Groton, CT, United States

Background: Tofacitinib is an oral Janus kinase inhibitor. The minimally important changes (MICs) for the SPondyloArthritis Research Consortium of Canada (SPARCC) MRI sacroiliac joint (SIJ) and spine scores based on agreement with global change scores by readers are ≥2.5 and ≥5, respectively.[1]

Objectives: To assess whether MIC in SIJ and spine can discriminate between tofacitinib and placebo (PBO) in patients (pts) with ankylosing spondylitis (AS) and if this is concordant with clinical responses.

Methods: In this 16-week (wk), Phase 2, double-blind, dose-ranging study (NCT01786668),[2] 207 adult pts meeting modified New York AS criteria were randomised 1:1:1:1 to PBO or tofacitinib 2, 5 or 10 mg twice daily (BID) for 12 wks. Clinical endpoints included in this post-hoc analysis were: Assessment of SpondyloArthritis International Society 20% improvement (ASAS20) and ASAS 40% improvement (ASAS40) response rates, AS disease activity score major improvement (ASDAS MI; change ≥2.0 from baseline), ASDAS inactive disease (ASDAS ID; <1.3), Bath AS disease activity index (BASDAI), Bath AS functional index (BASFI) and back pain. Pts (%) achieving MIC in SIJ, spine and both SIJ and spine, in tofacitinib and PBO groups, were summarised based on observed data, and pooled tofacitinib (5 and 10 mg BID) vs PBO data were compared using Fisher's exact test. Concordance between achieving MIC and Wk 12 clinical responses was assessed. Wk 12 clinical responses were compared between pts achieving/not achieving MIC.

Results: MRI data for 164 pts were evaluated. Baseline demographics were generally balanced between treatment groups and typical of AS populations.[2] Tofacitinib 2, 5 and 10 mg BID improved mean (range) SPARCC scores vs PBO (SIJ: -2.2 [-22.0, 10.5], -3.5 [-34.5, 11.0], -3.6 [-29.0, 0.5] vs -0.7 [-9.5, 6.5]; spine: -3.2 [-34.5, 20.5], -5.5 [-36.5, 8.0], -6.7 [-32.5, 7.5] vs -0.8 [-8.0, 14.0]). Approximately 3 times more pts achieved MIC in SIJ or spine in the pooled tofacitinib group vs PBO (SIJ: 34.1% vs 11.8%, $p<0.05$; spine: 38.6% vs 11.8%, $p<0.01$). Achieving MIC in SIJ and spine correlated with clinical response. In pts on tofacitinib, ASAS20, ASAS40 and ASDAS MI responses were more likely in pts achieving MIC in SIJ or spine (Table) vs not achieving MIC. Compared with not achieving MIC, pts on tofacitinib achieving MIC in SIJ had larger improvements in BASDAI, BASFI and back pain.

Conclusions: Pts who received tofacitinib who had AS experienced clinically meaningful reductions in axial MRI inflammation. Pts achieving MIC for MRI inflammation had increased clinical response rates.

References:

[1] Maksymowych WP et al. J Rheumatol 2012; 39: 1666–1674.
[2] van der Heijde D et al. Ann Rheum Dis 2016; In press.

Acknowledgements: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by A Pedder of CMC and funded by Pfizer Inc.

Disclosure of Interest: W. Maksymowych Grant/research support from: AbbVie, Pfizer Inc, Sanofi, UCB, Consultant for: AbbVie, Amgen, Eli Lilly, Janssen, Merck, Novartis, Pfizer Inc, Sanofi, UCB, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Meyers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer Inc, Roche, Sanofi-Aventis, UCB, Employee of: Imaging Rheumatology BV, X. Baraliakos Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Novartis, Pfizer Inc, Roche, MSD, UCB, A. Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Speakers bureau: AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer Inc, UCB, M. Brown Grant/research support from: AbbVie, Janssen, Leo Pharma, UCB, Consultant for: AbbVie, Janssen, Novartis, Pfizer Inc, UCB, Speakers bureau: AbbVie, Janssen, Novartis, Pfizer Inc, UCB, S. Sherlock Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, D. Li Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, D. Fleishaker Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Hendrikx Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

Table. Relationship between Wk 12 clinical response rates and achievement of MIC

	ASAS20 n/N (%)	ASAS40 n/N (%)	ASDAS MI n/N (%)	ASDAS ID n/N (%)
Placebo				
SIJ ≥MIC (2.5)	3/4 (75.0)	1/4 (25.0)	0/4	0/4
SIJ <MIC (2.5)	14/29 (48.3)	6/29 (20.7)	3/28 (10.7)	3/28 (10.7)
Spine ≥MIC (5)	3/4 (75.0)	2/4 (50.0)	2/4 (50.0)	1/4 (25.0)
Spine <MIC (5)	14/29 (48.3)	5/29 (17.2)	1/28 (3.6)	2/28 (7.1)
Tofacitinib 2 mg BID				
SIJ ≥MIC (2.5)	9/12 (75.0)	7/12 (58.3)	5/12 (41.7)	2/12 (16.7)
SIJ <MIC (2.5)	15/29 (51.7)	12/29 (41.4)	3/30 (10.0)	4/30 (13.3)
Spine ≥MIC (5)	11/12 (91.7)	8/12 (66.7)	4/12 (33.3)	3/12 (25.0)
Spine <MIC (5)	13/28 (46.4)	11/28 (39.3)	4/29 (13.8)	3/29 (10.3)
Tofacitinib 5 mg BID				
SIJ ≥MIC (2.5)	15/17 (88.2)	10/17 (58.8)	6/17 (35.3)	2/17 (11.8)
SIJ <MIC (2.5)	21/25 (84.0)	12/25 (48.0)	5/26 (19.2)	5/26 (19.2)
Spine ≥MIC (5)	12/14 (85.7)	8/14 (57.1)	5/15 (33.3)	3/15 (20.0)
Spine <MIC (5)	24/28 (85.7)	14/28 (50.0)	6/28 (21.4)	4/28 (14.3)
Tofacitinib 10 mg BID				
SIJ ≥MIC (2.5)	9/13 (69.2)	8/13 (61.5)	4/13 (30.8)	4/13 (30.8)
SIJ <MIC (2.5)	18/31 (58.1)	12/31 (38.7)	9/31 (29.0)	4/31 (12.9)
Spine ≥MIC (5)	13/18 (72.2)	10/18 (55.6)	7/18 (38.9)	2/18 (11.1)
Spine <MIC (5)	14/26 (53.9)	10/26 (38.5)	6/26 (23.1)	6/26 (23.1)
Pooled tofacitinib 5 and 10 mg BID				
SIJ ≥MIC (2.5)	24/30 (80.0)	18/30 (60.0)	10/30 (33.3)	6/30 (20.0)
SIJ <MIC (2.5)	39/56 (69.6)	24/56 (42.9)	14/57 (24.6)	9/57 (15.8)
Spine ≥MIC (5)	25/32 (78.1)	18/32 (56.3)	12/33 (36.4)	5/33 (15.2)
Spine <MIC (5)	38/54 (70.4)	24/54 (44.4)	12/54 (22.2)	10/54 (18.5)

ASAS, Assessment of SpondyloArthritis International Society; ASDAS, ankylosing spondylitis disease activity score; BID, twice daily; ID, inactive disease; MI, major improvement; MIC, minimally important change; SIJ, sacroiliac joints; Wk, week

DOI: 10.1136/annrheumdis-2017-eular.2447

THU0353 CHANGE IN MRI STRUCTURAL LESIONS IN THE SACROILIAC JOINT AFTER TWO YEARS OF ETANERCEPT THERAPY IN COMPARISON TO A CONTEMPORARY CONTROL COHORT IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

W.P. Maksymowych[1], M. Dougados[2], R.G. Lambert[1], R. Landewe[3], A. Molto[2], P. Claudepierre[4], M. de Hooge[5], R. Bonin[6], J.F. Bukowski[6], H. Jones[6], I. Logeart[7], R. Pedersen[6], A. Szumski[8], B. Vlahos[6], D. van der Heijde[5].
[1]University of Alberta, Edmonton, Canada; [2]Paris Descartes University, Hôpital Cochin, Paris, France; [3]Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands; [4]Universite Paris Est Creteil, Creteil, France; [5]Leiden University Medical Center, Leiden, Netherlands; [6]Pfizer, Collegeville, United States; [7]Pfizer, Paris, France; [8]InVentiv Health, Princeton, United States

Background: Demonstrating a structural effect of TNF inhibitors in axial SpA (axSpA) is challenging.

Objectives: To compare 2 yrs of structural lesion changes on T1W MRI in the sacroiliac joints (SIJ) of pts receiving etanercept (ETN) in a clinical trial to similar pts not receiving biologics in a cohort study.

Methods: Pts had recent onset non-radiographic (nr)-axSpA fulfilling ASAS criteria. Study group: pts receiving ETN 50 mg once weekly for 2 yrs in EMBARK (NCT01258738). Control group: pts in a longitudinal cohort study not receiving biologics for 2 yrs (DESIR, NCT01648907). Outcome measure: change in structural lesions of erosion, backfill, fat metaplasia, and ankylosis. MRI images were read by 3 experienced readers unaware of image chronology and pt group, using the SpondyloArthritis Research Consortium of Canada SIJ Structural Score (SSS).[1] For each group, differences were calculated between percentages of patients experiencing increases and decreases in structural lesion scores over 2

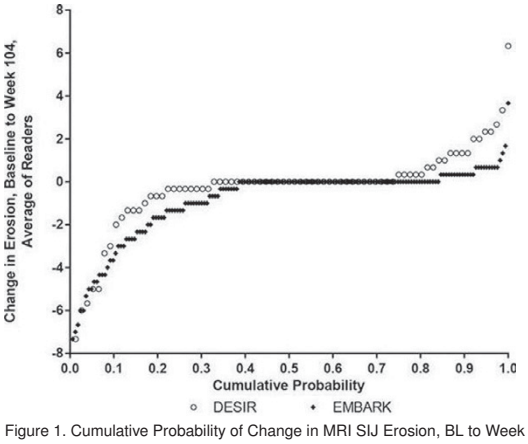


Figure 1. Cumulative Probability of Change in MRI SIJ Erosion, BL to Week 104.

Abstract THU0353 – Table 1. Observed Change in MRI SIJ Structural Lesions, BL to Week 104

Structural lesion	Cohort	Decreased n/N (%)	Increased n/N (%)	Mean Difference* (95% CI)†	Mean differences (Control – ETN) (95% CI)
Erosion	Control	14/76 (18.4)	10/76 (13.2)	-5.3% (-18.1, 7.6)	18.8% (3.5, 34.1)†§
	ETN	46/162 (28.4)	7/162 (4.3)	-24.1 (-32.1, -16.0)	17.8% (2.1, 33.6)‡§
Backfill	Control	2/76 (2.6)	10/76 (13.2)	10.5% (1.7, 19.3)	-5.5% (-16.6, 5.5)†
	ETN	1/162 (0.6)	27/162 (16.7)	16.0% (10.1, 22.0)	-3.7% (-15.2, 7.8)‡
Fat metaplasia	Control	0/76 (0)	7/76 (9.2)	9.2% (2.6, 15.9)	1.8% (-6.6, 10.2)†
	ETN	2/162 (1.2)	14/162 (8.6)	7.4% (2.7, 12.2)	-2.4% (-11.2, 6.4)‡
Ankylosis	Control	0/76 (0)	1/76 (1.3)	1.3% (-1.3, 3.9)	1.3% (-2.2, 4.9)†
	ETN	2/162 (1.2)	2/162 (1.2)	0% (-2.4, 2.4)	1.5% (-3.1, 6.2)‡

Based on 2 of 3 readers assigning same category; otherwise considered no change. Some pts started with the lowest possible score and could not decrease. *Percent pts with increase – percent pts with decrease. †One-way ANOVA. ‡Adjusted for covariates listed in Methods. § $P<0.05$.

yrs. Treatment effect was analyzed without and with adjustment for the baseline (BL) covariates of sex, symptom duration, smoking status, HLA-B27 status, ASDAS-CRP, SPARCC MRI SIJ score, and SIJ radiography score.

Results: At BL, pts with MRI images in the control (DESIR, N=76) and ETN (EMBARK, N=162) cohorts differed significantly in symptom duration, smoking status, ASDAS-CRP and SPARCC MRI SIJ score. The table presents structural lesion changes on MRI. The mean difference between control and ETN was significant for erosion (table). Figure shows cumulative probability plot.

Conclusions: This analysis confirms the slow rate of structural lesion progression in the SIJ over 2 yrs in nr-axSpA and suggests a lower rate of progression with ETN than without a TNF inhibitor.

References:

[1] Maksymowych WP, et al. J Rheumatol. 2015;42:79–86.

Disclosure of Interest: W. P. Maksymowych Grant/research support from: AbbVie, Pfizer, Sanofi, Consultant for: AbbVie, Amgen, Eli Lilly, Janssen Pharmaceutica, L.P, Novartis, Pfizer, Sanofi, UCB, M. Dougados Grant/research support from: Pfizer, Abbvie, UCB, Merck, Lilly, Sanofi, Consultant for: Pfizer, Abbvie, UCB, Merck, Lilly, Sanofi, R. G. Lambert Consultant for: Bioclinica, R. Landewe Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, Consultant for: Abbott/Abbvie, Ablynx, Amgen, Astra-Zeneca, BMS, Celgene, Janssen (formerly Centocor), Galapagos, GSK, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-plough, TiGenix, UCB, Wyeth, Employee of: Is a director of Rheumatology Consultancy BV, which is registered company under Dutch law, A. Molto Grant/research support from: Pfizer, UCB, Consultant for: Abbvie, BMS, MSD France- Merck, Pfizer, UCB, P. Claudepierre Grant/research support from: Pfizer, Roche-Chugai, MSD, Consultant for: Abbvie, BMS, Celgene, Janssen, Novartis, Merck, Pfizer, Roche, UCB, M. de Hooge: None declared, R. Bonin Shareholder of: Pfizer, Employee of: Pfizer, J. Bukowski Shareholder of: Pfizer, Employee of: Pfizer, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, I. Logeart Shareholder of: Pfizer, Employee of: Pfizer, R. Pedersen Shareholder of: Pfizer, Employee of: Pfizer, A. Szumski Employee of: InVentiv Health, B. Vlahos Shareholder of: Pfizer, Employee of: Pfizer, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boeringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, Employee of: Director of Imaging Rheumatology bv.

DOI: 10.1136/annrheumdis-2017-eular.1864

THU0354 DISEASE WORSENING AND SAFETY IN PATIENTS SWITCHING FROM ORIGINATOR INFLIXIMAB TO BIOSIMILAR INFLIXIMAB (CT-P13) IN THE RANDOMIZED NOR-SWITCH-STUDY: EXPLORATIVE ANALYSIS IN SPA PATIENTS

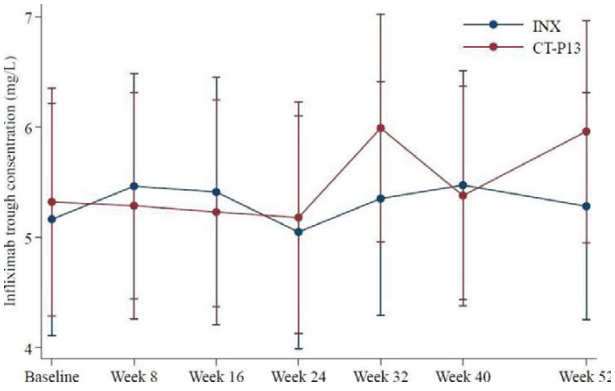
G.L. Goll[1], I.C. Olsen[1], N. Bolstad[2], K.K. Jørgensen[3], M. Lorentzen[4], C. Mørk[5], J. Jahnsen[3], E.A. Haavardsholm[1], T.K. Kvien[1] on behalf of the NOR-SWITCH study group. *[1]Dept of Rheumatology, Diakonhjemmet Hospital; [2]Biochemistry DNR, Oslo University Hospital, Oslo;[3]Gastroenterology, Akershus University Hospital, Lørenskog; [4]Dermatology, Oslo University Hospital, Oslo; [5]Dermatology, St Olav University Hospital, Trondheim, Norway*

Background: The NOR-SWITCH study is a 52-week randomized, double-blind, non-inferiority, phase IV switch trial in patients with Crohn's disease (CD), ulcerative colitis (UC), spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA) and plaque psoriasis (Ps) on stable treatment with originator infliximab (Remicade®, INX), funded by the Norwegian government. Previously, primary analyses of the pooled indications have been published[1].

Objectives: To investigate efficacy, safety and immunogenicity in SpA patients treated with continuous INX vs patients switched to CT-P13 (biosimilar infliximab, Remsima®) in the NOR-SWITCH study (explorative analyses).

Methods: Patients were randomized 1:1 to continued INX or switch to CT-P13. Serum drug levels were analyzed by automated in-house assay. The primary endpoint was disease worsening according to disease-specific composite measures and/or consensus between investigator/patient. Exploratory subgroup analyses examined disease worsening and safety in SpA. The primary endpoint was analysed by logistic regression, adjusted for diagnosis and disease duration.

Results: Demographics, occurrence of disease worsening, change in disease measures and treatment-emergent adverse events (TEAE) were similar (Table), as were serum drug levels for INX and CT-P13 (Figure).



Conclusions: Explorative analyses in the NOR-SWITCH study showed similar efficacy, drug levels and safety in SpA patients switched to CT-P13 as those on continuous INX. The study was not powered to show non-inferiority within each diagnosis.

References:

[1] Jørgensen KK et al. Switching from originator infliximab to biosimilar CT-P13 compared to maintained treatment with originator infliximab (NOR-SWITCH): a 52-week randomised double-blind non-inferiority trial. The Lancet, in press.

Disclosure of Interest: G. Goll Consultant for: AbbVie, Boehringer Ingelheim,

Abstract THU0354 – Table 1. Demographics, baseline characteristics (FAS), percentage of patients with disease worsening, change in disease measures during 52 weeks follow-up (PPS)

Demographics, baseline characteristics	INX	CT-P13	
Total number of SpA patients PPS/FAS	43/45	42/46	
Age (years) mean (SD)	50.0 (10.3)	52.8 (10.8)	
Females	7 (16%)	8 (17%)	
Duration of ongoing INX treatment (years) mean (SD)	8.6 (3.1)	8.7 (3.2)	
Immunosuppressive co-medication	15 (33%)	10 (22%)	
HLA B27 pos	31 (94%)	33 (87%)	
Disease worsening			95% CI of group difference after 52 weeks
All study patients	53 (26.2%)	61 (29.6%)	-12.7–3.9%
SpA	17 (39.5%)	14 (33.3%)	-14.5–27.2%
Change in disease measures from baseline			
Physician Global Assessment of Disease Activity (0–10)	-0.1 (1.4)	-0.5 (1.3)	0.53–0.53
Patient Global Assessment of Disease Activity (0–10)	0.1 (2.2)	-0.4 (1.8)	-0.08–0.62
Log_{10} erythrocyte sedimentation rate (mm/h)	0.0 (0.3)	-0.0 (0.3)	-0.14–0.06
Log_{10} C-reactive protein (mg/L)	-0.0 (0.4)	-0.1 (0.4)	-0.11–0.15
ASDAS	0.1 (0.6)	-0.2 (0.7)	-0.27–0.24
BASDAI	0.3 (1.0)	-0.2 (1.4)	-0.50–0.47
TEAE (FAS)	116	102	

Data are n (%), mean (SD) or median (25–75 percentiles). 95% CI, 95% confidence interval of the adjusted treatment difference. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index. ASDAS, Ankylosing Spondylitis Disease Activity Score. FAS, Full Analysis Set. PPS, Per Protocol Set. TEAE, treatment emergent adverse events.

Orion Pharma, Novartis, Pfizer, I. Olsen: None declared, N. Bolstad: None declared, K. Jørgensen Consultant for: Celltrion, Intercept, AbbVie, Tillott, M. Lorentzen: None declared, C. Mørk Consultant for: Cellgene, AbbVie, Galderma Nordic, ACOhud, Novartis, LEOPharma, J. Jahnsen Consultant for: Celltrion, Orion Pharma, Pfizer, MSD, AbbVie, Takeda, Napp Pharma, AstroPharma, E. Haavardsholm Consultant for: AbbVie, UCB, Pfizer, MSD, Roche, T. Kvien Consultant for: Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lily, Epirus, Hospira, Merck-Serono, Novartis, Orion Pharma, Pfizer, Sandoz, UCB
DOI: 10.1136/annrheumdis-2017-eular.4438

THU0355 INFLUENCE OF ADALIMUMAB AND SULFASALAZINE ON STRUCTURE OF HYALINE CARTILAGE OF HIP JOINTS IN PATIENTS WITH ANKYLOSING SPONDILITIS

A. Petrov, H. Zayaeva, A. Petrov. *Medical Academy named after Georgievsky, Crimean Federal university named after V.I. Vernadsky, Simferopol, Russian Federation*

Background: The impairment of hip joints has significant prognostic value on functional status of patients with Ankylosing spondylitis (AS) [1]. One of possible yearly marker of hip joints structure damage in patients with AS may be changing in volume of hyaline cartilage [2]. But clinical significance of this marker in monitoring of hip joint structure changes during treatment is underinvestigated.
Objectives: To investigate changes in width of hyaline cartilage of hip joints in patients with AS under treatment with sulfasalazine and adalimumab during 12 month.
Methods: The 53 patients with AS (42 male, 9 female, average age is 37.6 years old, duration of disease is 14–152 month) were included into study. All patients were treated by NSAIDs and sulfasalazine (2 g per day) at least 3 month before study. In treatment of 27 patients (1st group) was added adalimumab (40 mg subcutaneously every 2 weeks), other 26 patients (2nd group) were left on previous treatment regime. Patients were observed during 12 months of treatment including measurements of pain visual analog scale (VAS) in hip movements, maximal distance between ankles, pelvic X-ray and sonography of hip joints by 10–18 MHz probe. BASRI-Hips index was applied for radiographic estimation of structural damage of hip joints [3]. During sonography width of hip joint capsule and hyaline cartilage were measured. The Mann-Whitney-U test was used for comparison of changes in clinical and sonographic data between two groups of patients.
Results: After 12 month treatment period in patients of 1st group in comparison with patients of 2nd group more significant decrease of pain VAS during hip movements (on 27.3 [18.8; 32.5] mm vs 4.7 [0.5; 9.6] mm, $p<0,01$), increase of maximal distance between ankles (on 124.3 [92.3;145.6] mm vs 3.5 [1.2; 6.5] mm, $p<0,05$) and decrease of joint capsule width (on 2.4 [1.0; 3.6] mm vs 0.4 [0.0;1.1] mm, $p<0,05$) had been determined. In patients of 1st group width of hyalinic cartilage had been increased on 0.15 [0.4; 0.22] mm, while in patients of 2nd group width of hyalinic cartilage had been decreased on 0.8 [0.0; 1.4] mm ($p<0,05$). These cartilage changes were accompanied by decrease of mean BASRI-Hips index on 1 point in 2nd group and absence of changes of BASRI-Hips index in 1st group. The correlation between changes in width of hip hyalinic cartilage and pain VAS during movement in hip joints (r=-0.52 [0.38; 061]) and maximal distance between ankles (r=+0.47 [0.32; 0.60]) had been revealed.
Conclusions: Treatment with adalimumab leads to decrease of clinical and sonographic signs of coxitis and improvement of hyaline cartilage structure. The increase of width of hip hyalinic cartilage correlates with clinical effect of treatment of coxitis in patients with AS. More prolonged observation is needed for analysis of correlation between changes in hyaline cartilage structure and radiographic progression of hip joints damage in AS.
References:
[1] Baraliakos X., Braun J. Hip involvement in ankylosing spondylitis: what is the verdict? Rheumatology 2009;49(1):3–4.
[2] Maksymowych W.P. Ankylosing spondylitis – at the interface of bone and cartilage. J Rheumatol 2000;27(10):2295–301.
[3] MacKay K, Brophy S, Mack C, et al. The development and validation of a radiographic grading system for the hip in ankylosing spondylitis: the bath ankylosing spondylitis radiology hip index. J Rheumatol. 2000;27:2866–72.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1672

THU0356 THE RANK OF ADMINISTRATION AND NOT THE MOLECULE HAS AN IMPACT ON THE ANTI TNF TREATMENT RESPONSE IN AXIAL SPA

A. Moltó, A. Etcheto, L. Gossec, S. Perrot, N. Boudersa, P. Claudepierre, N. Roux, F. Berenbaum, A. Martin, L. Sparsa, P. Coquerelle, M. Soubrier, M. Dougados. *Predict-SpA Study Group, Paris, France*

Background: Five different sub-cutaneous TNF alpha blockers (TNFb) are available for the treatment of NSAID-refractory and active axial spondyloarthritis (axSpA). The efficacy of these drugs in axSpA has been well reported in several RCT and real-life studies separately or as a group, but only very few head-to-head studies have compared each molecule's treatment effect in axSpA. Also, some data suggest that TNFb treatment effect in patients failing to a first TNFb is poorer than in TNFb-naïve patients, but some other suggest that response to a second TNFb might be comparable.
Objectives: to describe TNFb prescription and treatment response of each TNFb, and to compare treatment response in TNFb- naïve/not naïve axSpA patients in a real-life setting.
Methods: Prospective, multicenter, usual care study with 2 visits (baseline and 12 weeks after TNFb initiation, Predict-SpA study, ClinicalTrials.gov: NCT03039088)). *Patients:* axSpA patients (diagnosis according to treating rheumatologist) initiating a TNFb. *Data collection:* Patients and disease characteristics at baseline. Previous exposure to TNFb was collected. Disease activity and function measures were collected at both visits. The choice of the TNFb to be started during the trial was at the treating rheumatologist's discretion. *Statistical analysis:* effectiveness was defined by the BASDAI50 response. Non-responder imputation and baseline observation carried forward imputation (for binary and continuous outcome variables, respectively) were performed for patients who discontinued the TNFb treatment between baseline and the follow-up visit.
Results: Among the 527 patients enrolled in the study, 508 patients were included in the analysis (1 patients was excluded due to missing data on all disease activity measures at baseline, and 18 patients were excluded due loss of follow-up between baseline and the follow-up visit). Mean age was 41.4 (±11.6), 237 (47%) were women, with a 6.1±8.5 mean disease duration. 377/508 (74%) were TNFb-naïve while 66 (13%), 35 (7%),19 (3.7%),8 (2%) and 3 (1%) had previously received, 1,2, 3, 4 and >4 TNFb, respectively.
In the whole study population the most frequently prescribed TNFb was etanercept (197 (39%)), followed by adalimumab (131 (26%)), golimumab (88 (17%)), infliximab 53 (10%) and certolizumab (39 (8%)); the same order was observed in TNFb naïve patients; however, in patients previously exposed to TNFb, the most frequently prescribed TNFb was infliximab (31 (24%)) followed by golimumab (29 (22%)), adalimumab (29 (22%)), certolizumab (22 (17%)) and etanercept (20 (15%)).
BASDAI50 responses were comparable for all TNFb molecules: 52%, 52%, 48%, 53% and 49% for etanercept, adalimumab, golimumab, infliximab and certolizumab, respectively.
BASDAI 50 response was comparable in patients TNFb-naïve and patients previously exposed to only 1 previous TNFb (53% vs. 52%, for naïve vs. non-naïve patients) but significantly decreased after (i.e. 37% and 36.% for patients previously exposed to 2 and to 3 or more TNFb)
Conclusions: this study suggests that the TNFb treatment response is similar across the different available molecules but this treatment response decreased in case of a previous use of two TNFb.
Acknowledgements: This study was conducted thanks to an unrestricted grant from MSD
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2678

THU0357 NO SPECIFIC IMPACT OF CONCOMITANT FIBROMYALGIA ON THE ANTI TNF TREATMENT EFFECT IN AXIAL SPONDYLOARTHRITIS PATIENTS WITHOUT RADIOGRAPHIC STRUCTURAL DAMAGE OR OBJECTIVE SIGNS OF INFLAMMATION

A. Moltó, A. Etcheto, L. Gossec, S. Perrot, N. Boudersa, P. Claudepierre, N. Roux, F. Berenbaum, A. Martin, L. Sparsa, P. Coquerelle, M. Soubrier, M. Dougados. *Predict-SpA Study Group, Paris, France*

Background: Currently, the European Medicine Agency (EMA) is recommending the use of anti-TNF in case of active NSAID refractory axial (ax) spondyloarthritis (SpA) only in the presence of either structural radiographic damage of the sacroiliac Joints (SIJ) or objective signs of inflammation (either elevated CRP or inflammation at MRI-SIJ) probably mainly because of the fear of a concomitant fibromyalgia (FM).
Objectives: To evaluate the interaction of a concomitant FM on the anti-TNF response with regard to the application of the EMA recommendation
Methods: *Study design:* Prospective, multicenter, longitudinal (12 weeks) open trial (Predict-SpA, ClinicalTrials.gov: NCT03039088). *Patients (pts):* axSpA requiring an anti-TNF. *Data collected:* At baseline, 1/Radiographic SIJ damage 2/ MRI-SIJ inflammation 3/ Elevated CRP 4/ FM according to the FiRST (Fibromyalgia Rapid Screen Test) questionnaire. At baseline and after 12 weeks of therapy: BASDAI. *Statistical analysis:* Non Responder Imputation (NRI), Baseline Carried Forward Technic (BOCF) in case of missing data. Interaction test between the presence of FM and the fulfillment of the EMA recommendation (defined by the presence of either structural radiographic damage of the SIJ or objective signs of inflammation (either elevated CRP or inflammation at MRI-SIJ)) on the anti TNF treatment response (BASDAI50)
Results: Of the 508 enrolled pts (females: 46.7%, age: 41.4+11.6 years old, HLA B27 positive: 57.5%, X-Ray sacroiliitis: 53.2%, inflammation at MRI-SIJ: 52.0%), only 59 had no structural damage at SIJ-X-Rays and no inflammation at MRI-SIJ (12%). A concomitant FM was noticed in 42% *vs* 37% of pts treated in accordance *vs* not with the EMA recommendation, respectively (p=0.44). The anti-TNF treatment effect was higher in the groups of pts treated in accordance (vs not) with the EMA recommendation (BASDAI 50: 52% *vs* 39%, respectively; p=0.054). There was a trend (but not statistically significant) suggesting an interaction of the concomitant FM on the anti TNF treatment response with regard

to the application of the EMA recommendation (interaction p value=0.140). In the 59 pts not treated in accordance with the EMA recommendation, the treatment effect in the sub-groups of pts without (*vs* with) concomitant FM was 38% vs 40% respectively, p=0.891. In the 449 pts treated in accordance with the EMA recommendation, the treatment effect in the sub-groups of pts without (*vs* with) concomitant FM was 56% vs 46%, p=0.042).

Conclusions: This study suggests that 1/ French rheumatologists are applying the EMA recommendation in daily practice 2/ these recommendations result in a better outcome in terms of short term symptomatic treatment effect. In this study, concomitant FM was not more frequently observed in patients without (*vs* with) objective sign of structural damage or inflammation and the impact of a concomitant FM was not more pronounced (or even lower) in pts without (vs with) objective sign of structural damage or inflammation.

References:

[1] Perrot S, et al. Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain.2010;150:250–6.

Acknowledgements: This study was conducted thanks to an unrestricted grant from MSD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4718

THU0358 ROSUVASTATIN IMPROVES NITRIC OXIDE AND ENDOTHELIAL FUNCTION AND SUPPRESSES INFLAMMATORY DISEASE ACTIVITY IN ANKYLOSING SPONDYLITIS

A. Syngle[1], N. Garg[2], P. Krishan[2]. *[1]Cardio Rheuma, Healing Touch City Clinic, Chandigarh and Fortis Multi Speciality Hospital, Mohali, India, Chandigarh; [2]Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, India*

Background: Nitric oxide (NO) regulates the synthesis of several inflammatory mediators, functions of inflammatory cells in the inflamed joint and plays a central role in the regulation of blood vessel tone[1]. Therefore, NO inhibitors represent important therapeutic advancement in the management of inflammatory diseases. Rosuvastatin improves NO and endothelial dysfunction in patients with heart failure[2] but its effect on NO has not yet been tested in Ankylosing Spondylitis (AS) patients.

Objectives: To investigate the effect of rosuvastatin on nitrite levels (NO surrogate) and its relationship with endothelial function and inflammatory measures in AS.

Methods: 40 consecutive patients (20 in Rosuvastatin (10 mg/day) and 20 in placebo arm) meeting the modified New York criteria for AS, with active disease despite treatment with conventional synthetic DMARDs were recruited. Serum nitrite estimation was carried out by Griess reaction. Flow-mediated dilatation (FMD) was assessed using AngioDefender. Inflammatory measures included– BASDAI, BASFI, ESR and CRP. Pro-inflammatory cytokines (TNF-α, IL-6 and IL-1) were measured at baseline and after 24 weeks.

Results: After 24 weeks, significant improvement in serum nitrite was observed in rosuvastatin group (5.27±0.26 to 4.11±0.19, p<0.01) compared with placebo (5.47±0.26 to 5.36±0.23, p=0.33). At 24weeks; FMD, TNF-α, and IL-6 improved significantly in rosuvastatin group compared with placebo. At 24 weeks; ESR, CRP, BASDAI and BASFI significantly improved in rosuvastatin group compared with placebo. After treatment with rosuvastatin, nitrite correlated inversely with FMD (r=-0.47, p=0.03) (Fig.1A) and positively with TNF-α (r=0.64, p=0.01) (Fig.1B), CRP (r=0.52, p=0.01) (Fig.1C) and LDL (r=0.54, p=0.01) (Fig.1D).

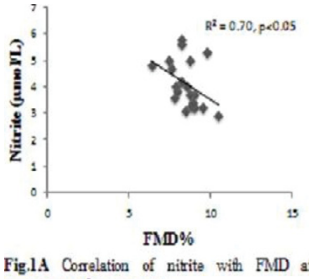


Fig.1A Correlation of nitrite with FMD after treatment with rosuvastatin

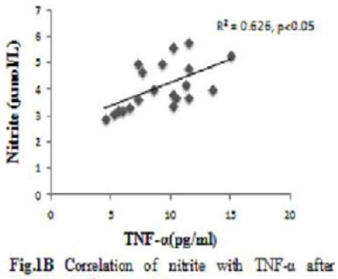


Fig.1B Correlation of nitrite with TNF-α after treatment with rosuvastatin

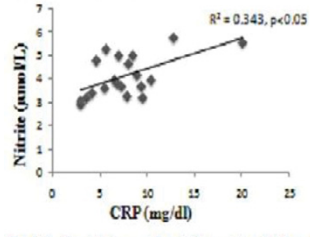


Fig.1C Correlation of nitrite with CRP after treatment with rosuvastatin

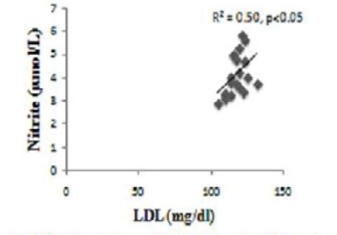


Fig.1D Correlation of nitrite with LDL after treatment with rosuvastatin

Conclusions: Rosuvastatin reduced serum nitrite concentration and improved endothelial dysfunction in AS patients. Rosuvastatin lowers the proinflammatory cytokines, especially IL-6 and TNF-α, which downregulates CRP production and thus the production of NO. Rosuvastatin also favorably improved the lipid levels in AS patients. Rosuvastatin exerts anti-inflammatory, immunomodulatory and vasculoprotective effect in ankylosing spondylitis through both cholesterol dependent and cholesterol independent pathways

References:

[1] Sharma et al. Inflammopharmacology 2007;15:252–9.
[2] Schäfer et al. Arterioscler Thromb Vasc Biol 2005;25:1071–1077.

Acknowledgements: None.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5062

THU0359 SECUKINUMAB DEMONSTRATES CONSISTENT SAFETY OVER LONG-TERM EXPOSURE (UP TO 3 YEARS) IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: POOLED ANALYSIS OF THREE PHASE 3 TRIALS

A. Deodhar[1], X. Baraliakos[2], H. Marzo-Ortega[3], J. Sieper[4], M. Andersson[5], B. Porter[6], T. Fox[5]. *[1]Oregon Health & Science University, Portland, United States; [2]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Herne, Germany; [3]Nihr Lmbru, Ltht&lirmm, UoL, Leeds, United Kingdom; [4]Charité University Medicine Berlin, Berlin, Germany; [5]Novartis Pharma AG, Basel, Switzerland; [6]Novartis Pharmaceuticals Corp., East Hanover, United States*

Background: Safety data for secukinumab in the treatment of ankylosing spondylitis (AS) have been reported from three Phase 3 studies: MEASURE 1 (NCT01358175)[1], MEASURE 2 (NCT01649375)[1] and MEASURE 3 (NCT02008916).[2]

Objectives: To report long-term (up to 3 years) pooled safety and tolerability data for secukinumab in AS (data cut-off: 25 June 2016).

Methods: Overall, 371, 219 and 226 patients with active AS were randomised in MEASURE 1, MEASURE 2 and MEASURE 3, respectively. Study design, efficacy and safety results of these studies have been published earlier.[1,2] Secukinumab doses differed in the studies and included intravenous 10 mg/kg or subcutaneous (75–300mg) multi-dose loading, followed by subcutaneous (s.c.) maintenance dosing (75, 150, or 300mg). Data collected up to the last patient performing the Wk 156 visit in MEASURE 1, the Wk 104 visit in MEASURE 2, and the Wk 52 visit in MEASURE 3 were pooled at the patient level. Exposure-adjusted incidence rates were calculated to account for differences in treatment exposure and analyses included all patients who received ≥1 dose of secukinumab 150 or 300mg.

Results: A total of 510 patients were included in the analysis (968.9 patient-years of exposure). The exposure-adjusted AE and SAE rates with secukinumab across the entire safety period were 159.2 and 5.4 per 100 patient-years, respectively. Nasopharyngitis, diarrhoea and headache were the most frequently reported AEs. The incidences of *Candida* infections, serious infections, inflammatory bowel disease, major adverse cardiac events, neutropenia and uveitis were low and consistent with previous reports over shorter exposure periods[1] (Table). No cases of suicidal ideation or depression were reported.

Table 1. Summary of pooled safety across 3 AS studies (Entire safety period)

	Any secukinumab dose (N=510)
Total exposure, patient-years	968.9
Minimum–maximum exposure (days)	1–1530
Death, n (%)	0
AEs by EAIR: AE per 100 Patient-years (95% CI)	
Any AE	159.2 (144.4, 175.1)
Any SAE	5.4 (4.0, 7.1)
Frequent AEs[1]	
Nasopharyngitis	13.6 (11.2, 16.5)
Diarrhoea	6.4 (4.9, 8.3)
Headache	6.7 (5.1, 8.7)
Upper respiratory tract infection	4.3 (3.1, 5.9)
AEs of special interest	
Candida infections	0.8 (0.4, 1.6)
Serious infections	0.7 (0.3, 1.5)
Inflammatory Bowel Disease	0.4 (0.1, 1.1)
Crohn's disease	0.2 (0.0, 0.7)
Ulcerative colitis	0.2 (0.0, 0.7)
MACE	0.4 (0.1, 1.1)
Neutropenia	1.2 (0.6, 2.1)
Uveitis	1.6 (0.9, 2.6)

[1]AEs that occurred in Any secukinumab group with an IR >4.0 during the entire safety period. AE, adverse event; CI, confidence interval; EAIR, exposure adjusted incidence rate per 100 patient-years; MACE, major adverse cardiac events; N, number of patients in the analysis; n, number of patients with event; SAE, serious adverse event.

Conclusions: This longer-term safety assessment of secukinumab in the treatment of AS was consistent with previous reports and did not identify any new safety signals.

References:

[1] Baeten D, et al. N Engl J Med 2015;373:2534–48.
[2] Kivitz A, et al. XIX PANLAR 2016, Panamá City, Panama. Poster No. P-081.

Disclosure of Interest: A. Deodhar Grant/research support from: AbbVie, Amgen,

Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB; advisory board member: Eli Lilly, Janssen, Novartis, Pfizer, and UCB., X. Baraliakos Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, and Werfen, Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, and Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, and Werfen, H. Marzo-Ortega Grant/research support from: Janssen and Pfizer, Consultant for: AbbVie, Celgene, Janssen, Novartis and UCB, Speakers bureau: Abbvie, Celgene, Janssen and UCB, J. Sieper Grant/research support from: for AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, Consultant for: for AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer, and UCB, M. Andersson Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis, T. Fox Shareholder of: Novartis, Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.4894

THU0360 IMPROVEMENTS IN SLEEP PROBLEMS AND PAIN IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS TREATED WITH INTRAVENOUS GOLIMUMAB: 28-WEEK RESULTS OF THE PHASE III GO-ALIVE TRIAL

A. Deodhar[1], J.D. Reveille[2], E.K. Chan[3], S. Peterson[4], N. Li[4], E. Hsia[4,5], L. Kim[4], K.H. Lo[4], D.D. Harrison[4], C. Han[6]. *[1]Oregon Health & Science University, Portland; [2]University of Texas Health Sciences Center, Houston; [3]Janssen Global Services, LLC, Raritan; [4]Janssen Research & Development, LLC, Spring House; [5]University of Pennsylvania School of Medicine, Philadelphia; [6]Janssen Global Services, LLC, Malvern, United States*

Objectives: To investigate the effect of intravenously administered (IV) Golimumab (2 mg/kg), an anti-TNFα monoclonal antibody, on sleep problems, total back pain, and night back pain in adult patients (pts) with active Ankylosing Spondylitis (AS).
Methods: GO-ALIVE is a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial. Pts (aged ≥18 years) had a diagnosis of definite AS (per modified New York criteria) and BASDAI ≥4, total back pain visual analogue scale (VAS) ≥4, and CRP ≥0.3mg/dL. At baseline, 208 pts were randomized to IV golimumab 2mg/kg (N=105) at Wks 0, 4, and every 8 wks or placebo (N=103) at Wks 0, 4, and 12, with crossover to IV golimumab at Wk 16 and through Wk 52. Sleep problems were assessed using the Medical Outcomes Study Sleep Scale (MOS-SS, range 0–100), a generic instrument designed to assess six dimensions of sleep, including 1) Sleep disturbance, 2) Somnolence, 3) Sleep adequacy, 4) Snoring, 5) Awaken short of breath or headache, and 6) Quantity of sleep/optimal sleep during the past 4 wks. The six dimensions are also used to generate the composite Sleep Problems Index. An increase in score from baseline represents improvement. Total back pain and night back pain over the past wk were assessed using VAS (0–10 cm; 0=no pain, 10=most severe pain). Wk 28 results are presented here. Unadjusted p-values of least square mean differences (LSMD) between treatment groups were based on analysis of covariance (ANCOVA) controlling for prior anti-TNF therapy.
Results: Mean changes in MOS-SS Sleep Index and 6 subscales are presented in Table 1. Improvement ($p<0.05$) in the MOS-SS sleep index and 4 subscales at Wk 8 was observed in golimumab compared to placebo, and in the sleep index and 4 subscales at Wk 16. Improvements from baseline to Wks 8 and 16 in pts' assessment of total back pain (cm) were greater ($p<0.001$) in golimumab than placebo (-2.70 vs -0.86 and -3.15 vs -1.15, respectively), and after placebo crossed over to golimumab, the differences diminished at Wk 28 (-3.14 vs -3.34, respectively). Improvements at Wks 8 and 16 from baseline in pts' assessment of night back pain (cm) were also greater ($p<0.001$) in golimumab than placebo (-3.03 vs -0.87 and -3.44 vs -0.85, respectively), and differences diminished at Wk 28 (-3.47 vs -3.42, respectively). Changes from baseline in all subscales of MOS-SS were correlated (Spearman correlations ranging between -0.10 and -0.45) with total back pain (TBP) and night back pain (NBP) at Wks 8, 16, and 28 (p values <0.05), with the exception of Snoring and both TBP and NBP at Wk 16. Change in NBP was associated with change in Sleep Problem Index at all 3 time points (p=0.002, p=0.001, and p=0.031, respectively). In the general linear model, most of the association between change in TBP and change in Sleep Problem Index was explained by the association between change in NBP and change in Sleep Problem Index.

Table 1. Summary of mean (standard deviation) changes in MOS-SS and its subscales.

	GLM	PBO	GLM	PBO	GLM	PBO*
MOS-SS	N=104	N=102	N=104	N=102	N=104	N=102
	Week 8		Week 16		Week 28	
Mean (SD) change from baseline in:						
Sleep problems index:	5.10 (7.86) p<0.001	1.72 (7.36)	6.63 (7.18) p<0.001	2.49 (8.16)	6.58 (8.05)	5.88 (8.29)
Sleep disturbance:	4.44 (8.81) p=0.001	1.32 (7.09)	6.08 (7.76) p<0.001	2.37 (7.88)	6.32 (8.42)	5.07 (8.17)
Somnolence:	3.37 (7.34) p=0.016	1.21 (8.58)	5.27 (7.05) p<0.001	1.47 (8.18)	4.82 (7.87)	4.54 (7.81)
Sleep adequacy:	3.12 (8.24) p=0.037	1.80 (8.59)	4.14 (8.36) p=0.012	2.09 (8.93)	3.73 (7.88)	5.75 (10.15)
Snoring:	1.97 (7.71) p=0.30	0.82 (6.58)	1.24 (7.72) p=0.98	1.04 (6.24)	1.90 (7.39)	0.89 (7.28)
Awaken short of breath or headache:	4.64 (12.44) p=0.043	1.15 (10.02)	4.08 (12.26) p=0.20	1.50 (11.20)	4.19 (12.50)	3.00 (11.21)
Quantity of sleep/optimal sleep:	0.13 (0.57) p=0.43	0.10 (0.52)	0.13 (0.59) p=0.019	0.01 (0.57)	0.16 (0.56)	0.19 (0.56)

*At Wk28. PBO has crossed over to GLM

Conclusions: Adult pts with active AS treated with IV golimumab showed improvements in sleep problems, total back pain, and night back pain. Night back pain improvement was associated with improvement in sleep problems.
Disclosure of Interest: A. Deodhar Grant/research support from: Janssen, Amgen, Abbvie, GSK, Eli Lilly, Novartis, Pfizer, UCB, Consultant for: Janssen, Eli Lilly, Novartis, Pfizer, UCB, J. Reveille Grant/research support from: Janssen Scientific Affairs, LLC., E. Chan Employee of: Janssen Global Services, LLC, S. Peterson Employee of: Janssen Research & Development, LLC, N. Li Employee of: Janssen Research & Development, LLC, E. Hsia Employee of: Janssen Research & Development, LLC, L. Kim Employee of: Janssen Research & Development, LLC, K. H. Lo Employee of: Janssen Research & Development, LLC, D. Harrison Employee of: Janssen Research & Development, LLC, C. Han Employee of: Janssen Global Services, LLC

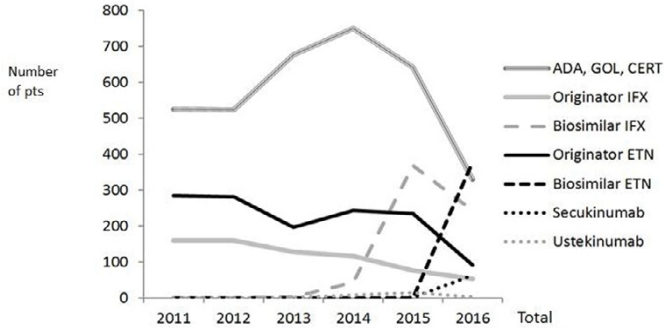
DOI: 10.1136/annrheumdis-2017-eular.5325

THU0361 PRESCRIPTION PATTERNS OF BIOLOGICAL DISEASE MODIFYING DRUGS AND BIOSIMILARS IN ANKYLOSING SPONDYLITIS – A COLLABORATION BETWEEN BIOLOGICAL REGISTERS IN THE FIVE NORDIC COUNTRIES

B. Glintborg[1], K. Chatzidionysiou[2], J. Askling[2], K. Aaltonen[3], E. Kristianslund[4], B. Gudbjornsson[5], D. Nordström[3], M.L. Hetland[1], L. Dreyer[1], L.E. Kristensen[1], T.S. Jørgensen[1], K. Eklund[3], G. Grondal[5], S. Ernestam[2], J. Joensuu[3], T. Kvien[4], E. Lie[4], K. Fagerli[4], A.J. Geirsson[5], H. Jonsson[5], L. Jacobsson[2]. *[1]On behalf of the DANBIO registry, Copenhagen, Denmark; [2]On behalf of the SRQ/ARTIS registry, Stockholm, Sweden; [3]On behalf of the ROB-FIN registry, Helsinki, Finland; [4]On behalf of the NOR-DMARD registry, Oslo, Norway; [5]On behalf of the ICEBIO registry, Reykjavik, Iceland*

Background: Large-scale real life observational cohorts are needed to study effectiveness and early signals of rare safety issues of new biological disease modifying drugs (bDMARDs) and biosimilars (bsDMARDs) in ankylosing spondylitis (AS). Combining data from biological registries would facilitate this. The Nordic countries have several similarities that would justify such aggregated analyses including similar health care systems with universal access to population based health care, availability of b/bsDMARDs through a tax-paid system and the registration of use and effectiveness of bDMARDs in inflammatory diseases in a prospective manner in drug registries.
Objectives: To explore the prescription patterns of old (TNF-inhibitors) and newer bDMARDs (secukinumab, ustekinumab) including bsDMARDs (SB4, CT-P13) over time in AS in the Nordic countries in order to illustrate the potential of a common Nordic collaboration.
Methods: Data regarding the numbers of AS patients (pts) (ICD10 code M45) who initiated bDMARD treatment (irrespective of treatment course number) during the period 2011–2016 were collected from the Nordic rheumatologic biological registries SRQ (Sweden), NOR-DMARD (6 Norwegian treatment centres), DANBIO (Denmark), ROB-FIN (Finland, 2011–2015) and ICEBIO (Iceland).
Results: In total, 6,610 bDMARD treatment initiations were identified (Sweden 3654, Norway 1078, Denmark 782, Finland 789, Iceland 307).
The prescription patterns of bDMARDs changed substantially over time. In 2016, the number of pts initiating a bsDMARDs exceeded those starting an originator bDMARD (figure). Few patients were treated with ustekinumab (Denmark <10 pts, Finland <10, Sweden 26) and secukinumab (Denmark <10 pts, Sweden 57).

Figure. The 5 Nordic countries, total number of AS patients initiating bDMARD per year



	2011	2012	2013	2014	2015	2016	Total
ADA, GOL, CERT	526	523	677	751	642	330	3449
Originator IFX	160	160	128	116	76	54	694
Biosimilar IFX	0	0	4	44	369	244	661
Originator ETN	285	282	197	244	235	91	1334
Biosimilar ETN	0	0	0	0	0	378	378
Secukinumab	0	0	0	0	1	64	65
Ustekinumab	0	0	1	9	15	4	29
Total	971	965	1007	1164	1338	1165	6610

ADA: Adalimumab, GOL: Golimumab, CERT: Certolizumab Pegol , IFX: Infliximab, ETN: Etanercept

Conclusions: The use of bsDMARDs in AS is rapidly increasing. The use of drugs with new modes of action is still low, which illustrates the need for collaboration across countries to provide real life data with sufficient power for new innovative therapies in the future. The Nordic rheumatologic registries represent a unique

opportunity to study effectiveness and safety of bDMARDs, including bsDMARDs in AS.

Acknowledgements: Partly funded by a grant from NordForsk

Disclosure of Interest: B. Glintborg Grant/research support from: abbvie, K. Chatzidionysiou: None declared, J. Askling Grant/research support from: AbbVie, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Samsung, K. Aaltonen Speakers bureau: AbbVie, BMS, Janssen, MSD, Pfizer, Roche, UCB, E. Kristianslund: None declared, B. Gudbjornsson Grant/research support from: Actavis, Celgene, MSD, Pfizer, D. Nordström Speakers bureau: AbbVie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, UCB, M. Hetland Grant/research support from: Orion, BMS, AbbVie, Biogen, Pfizer, MSD, L. Dreyer Speakers bureau: MSD, UCB, Janssen Pharmaceuticals, L. E. Kristensen Speakers bureau: Pfizer, AbbVie, Biogen, Amgen, UCB, Celegene, BMS, MSD, Novartis, Eli Lilly, Janssen pharmaceuticals, T. Jørgensen Speakers bureau: AbbVie, Roche, Novartis, UCB, Biogen, K. Eklund: None declared, G. Grondal: None declared, S. Ernestam: None declared, J. Joensuu Grant/research support from: Pfizer, T. Kvien Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, E. Lie Speakers bureau: AbbVie, Celgene, Hospira, Pfizer, K. Fagerli: None declared, A. J. Geirsson: None declared, H. Jonsson: None declared, L. Jacobsson Consultant for: Abbvie, Celegen, MSD, Novartis, UCB

DOI: 10.1136/annrheumdis-2017-eular.1891

THU0362 EFFECT OF BIOTECHNOLOGICAL DRUGS ON EXTRA-ARTICULAR MANIFESTATIONS OF ANKYLOSING SPONDYLITIS: SYSTEMATIC REVIEW

A.L.R. Pinto [1], C.V. Pessoa [1,2], L.S. Inês [1,3]. *[1]Faculty of Health Sciences, University of Beira Interior, Covilhã; [2]Rheumatology, Local Health Unit of Guarda, Guarda; [3]Rheumatology, Coimbra Hospital and Universitary Centre, Coimbra, Portugal*

Background: Treatment with biotechnological agents (infliximab, etanercept, adalimumab, golimumab and certolizumab pegol) in ankylosing spondylitis (AS) is effective. However, evidence regarding the potential efficacy of these anti-TNF drugs in the extra-articular manifestations of ankylosing spondylitis, namely in uveitis (UV), inflammatory bowel disease (IBD) and dactylitis is scarce.

Objectives: To analyze evidence on efficacy of anti-TNF drugs approved for AS treatment in UV, IBD and dactylitis associated with AS.

Methods: A systematic literature review was performed using the PubMed and Cochrane Library databases. Randomized controlled trials (RCT), meta-analyzes and observational studies (OS) reporting efficacy of anti-TNF agents in extra-articular manifestations of AS were included.

Results: Fifty studies were included (seventeen RCTs, six meta-analyses and twenty seven observational studies). From the RCT we extracted the results presented in Table 1 for uveitis and in Table 2 for IBD. None reported results for dactylitis. Of the meta-analyzes included, only one presents results. These one shows that the incidence of uveitis is lower in patients taking etanercept than placebo (incidence of 8.6 and 19.3 per 100 patients per year, respectively; p value =0.03). In OS comparing different drugs, in one the risk of developing uveitis was 1.9 times higher in patients under etanercept compared to those under adalimumab (p value =0.0223) and a risk similar to those under infliximab and those under adalimumab. In another we have a percentage of patients with uveitis, during the course of the study, under etanercept of 8.0% and under infliximab of 4.0%. In the OS, the percentage of patients with UV events with infliximab was in a range of 0.0%>3.1% with a follow-up interval between 2 years and 5 years; with etanercept was 0.9%>29.6% and a follow-up time interval between 12 weeks to 7 years; with adalimumab there is only one study with duration of 2 years reporting 3.9% UV events. Regarding IBD reported in OS, there was 3.7%>7.7% patients with events under treatment with etanercept over a follow-up time of 3.2–7 years; with adalimumab only a 2-year study reported IBD in 0.6% of cases. We did not find results regarding for other extra-articular manifestations or anti-TNF drugs.

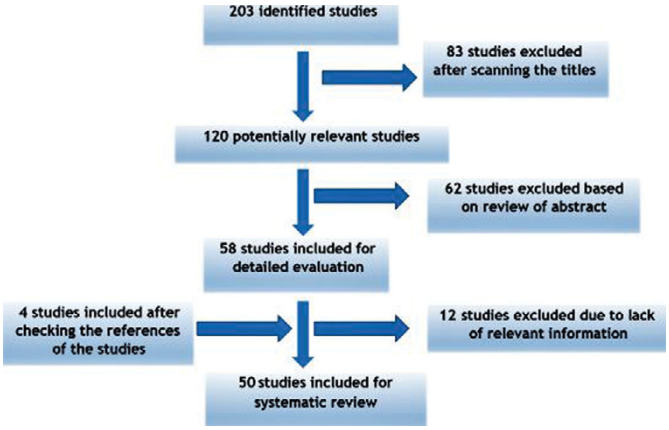
Table 1. Percentage of patients with events of uveitis on Randomized Controlled Trials

Uveitis	Randomized Controlled Trials	
	% patients with events under therapy	% patients with events under placebo
Infliximab	2,9	8,6
Etanercept	1,1	3,5
Adalimumab	No results	No results
Golimumab	No results	No results
Certolizumab pegol	0,9	2,8

Table 2. Percentage of patients with events of inflammatory bowel disease on Randomized Controlled Trials

Inflammatory Bowel Disease	Randomized Controlled Trials	
	% patients with events under therapy	% patients with events under placebo
Infliximab	No results	No results
Etanercept	1,1	0,7
Adalimumab	1,0	0,0
Golimumab	No results	No results
Certolizumab pegol	0,0	0,9

Conclusions: Efficacy of anti-TNF drugs on extra-articular manifestations of AS is under-reported in RCTs. Available data suggests possible efficacy of infliximab, adalimumab and certolizumab in UV, and of certolizumab in IBD. No evidence is available about anti-TNF efficacy in AS-associated dactylitis. Future studies with anti-TNF drugs should better report on extra-articular manifestations in AS.



Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5138

THU0363 IMPACT OF ADALIMUMAB ON CLINICAL OUTCOMES, HEALTHCARE RESOURCE UTILIZATION AND SICK LEAVES IN ANKYLOSING SPONDYLITIS PATIENTS IN CENTRAL AND EASTERN EUROPE

D. Opris-Belinski [1], S. Erdes [2], S. Grazio [3], L. Šenolt [4], M. Hojnik [5], O. Nagy [6], L. Iosub [7], S. Szántó [8]. *[1]Rheumatology, Sf. Maria Clinical Hospital, Carol Davila University of Medicine, Bucharest, Romania; [2]V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; [3]Univ. Dpt. of Rheumatology, Clinical Hospital Centre Sisters of Mercy, Croatia, Zagreb, Croatia; [4]Dpt. of Rheumatology, 1st Faculty of Medicine, Charles Univ, Institute of Rheumatology, Prague, Czech Republic; [5]AbbVie, Global Medical Affairs, Ljubliana, Slovenia; [6]AbbVie, Global Medical Affairs, Budapest, Hungary; [7]AbbVie, Global Medical Affairs, Bucharest, Romania; [8]Rheumatology, Faculty of Medicine, Univ. of Debrecen, Debrecen, Hungary*

Background: Ankylosing spondylitis (AS) represents a considerable socioeconomic burden due to early disease onset, development of functional disability and life-time costs. The impact of originator adalimumab on the extent of outpatient attendance, hospitalizations and sick leave in relation to clinical outcomes is not known in Central and Eastern Europe (CEE).

Objectives: To evaluate disease activity, physical function, selected health care resource utilization and sick leaves in patients treated with adalimumab in clinical practice in CEE countries.

Methods: This was a 52-week multi-center post-marketing observational study conducted in 5 countries in CEE. Eligible AS patients were prescribed originator adalimumab according to the local practice; 5 study visits (V) were performed approx. 3 months apart. Disease activity was measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Index ($ASDAS_{CRP}$), treatment response as BASDAI50 and $\triangle ASDAS \geq -2$ (at study end), physical function by Bath Ankylosing Spondylitis Functional Index (BASFI). Data on AS related healthcare resource utilization and sick leave during the study was recorded prospectively through a systematic interview with the patient at each study visit. For pre-and post-treatment comparison, the same sort of data were recorded retrospectively at baseline visit for the 3-month period preceding adalimumab therapy, verified against chart review, then multiplied by 4 to match the prospective follow-up duration. Descriptive statistics were used; last observation carried forward data are presented herein.

Results: 452 patients were enrolled, 360 completed the study. Mean age was 42.9 (±12.1) yrs; 68.7% were male and 62.7% were employed at baseline. Average disease duration was 7.7 (±8.7) yrs. Mean BASDAI and ASDAS decreased from 6.3 (±2.1) and 4.0 (±1.1) at baseline to 2.3 (±2.0) and 1.9 (±1.1) at study end, respectively; mean BASFI from 6.2 (±2.3) to 2.6 (±2.3). BASDAI and ASDAS based treatment response was seen at study end in 72.3% and 58.9% of patients, respectively. The mean number of hospital admissions and inpatient days decreased from 2.8 (±3.9) to 0.9 (±2.8) and from 23.0 (±40.8) to 3.9 (±17.7), respectively (pre- and post-treatment). The mean number of sick leaves and sick leave days decreased from 3.2 (±8.8) to 1.1 (±5.6) and from 32.2 (±69.2) to 5.1 (±24.5), respectively (employed patients only, n=282). The reduction of hospital admissions/days, sick leaves and sick leave days were higher in treatment responders compared to non-responders. No new safety signal was detected.

Conclusions: Treatment with adalimumab in routine clinical practice in 5 CEE countries resulted in clinically meaningful improvements in disease activity and physical function as well as reduced healthcare resource utilization and sick leaves.

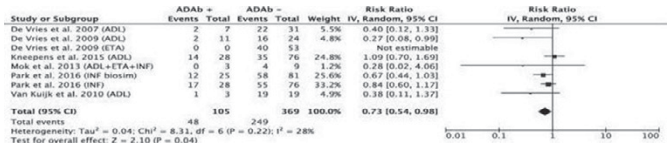
Acknowledgements: The design, study conduct, and financial support for the

clinical trial were provided by AbbVie. AbbVie participated in the interpretation of data, drafting, review, and approval of the abstract.
Disclosure of Interest: D. Opris-Belinski Consultant for: Abbvie, BMS, Pfizer, Roche, Teva and consulting fees from Abbvie, BMS, Pfizer, Roche, Teva., S. Erdes Consultant for: Abbvie, MSD, Pfizer, USB, BIOCARD, Gedeon Richter, Dr. Reddy's, Novartis., S. Grazio Consultant for: Abbvie/Abbott Lab, Roche, MSD, Eli Lilly, Pfizer, Boehringer Ingelheim, Grünenthal, Stada, Sanofi-Aventis, PharmaSwiss, Berlin-Chemie, Pliva/Teva, Belupo, Krka, consulting fees from: Abbvie/Abbott Lab, Roche, MSD, Eli Lilly, Pfizer, Grünenthal, L. Šenolt Consultant for: AbbVie, Bristol-Myers Squibb, Celgene Corporation, Eli Lilly, Merck Sharp and Dohme, Novartis, Pfizer, Samsung, Takeda, UCB., M. Hojnik Employee of: AbbVie, O. Nagy Employee of: AbbVie, L. Iosub Employee of: AbbVie, S. Szántó Consultant for: Abbvie, Bristol Myers-Squibb, Novartis, Pfizer, Roche, Teva
DOI: 10.1136/annrheumdis-2017-eular.5244

THU0364 IMMUNOGENICITY OF ANTI-TNF DRUGS AND CLINICAL RESPONSE IN PATIENTS WITH SPONDYLOARTHRITIS

D. Geiger[1], Y. Degboe[1], T. Barnetche[2], A. Cantagrel[1], A. Ruyssen-Witrand[1], A. Constantin[1]. *[1]Rheumatology, Centre de Rhumatologie, CHU Purpan, Place du Dr Baylac, Toulouse Cedex 9; [2]Rheumatology, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France*

Background: Antidrug antibodies (ADAb) seem to be associated with a loss of response in immune-mediated inflammatory diseases (1) and in psoriatic arthritis (2).
Objectives: To assess the effect of ADAb on clinical response in patients with spondyloarthritis (SpA) treated with anti-TNF drugs.
Methods: We conducted a systematic literature review of controlled trials and observational studies assessing the effect of ADAb on response to anti-TNF drugs (Adalimumab (ADL), Certolizumab (CTZ), Etanercept (ETA), Golimumab (GOL) and Infliximab (INF)) in patients with axial or peripheral SpA. Databases analysed were PubMed, the Cochrane library, and ACR/EULAR meeting abstracts, until January 2017. A meta-analysis was performed using the inverse variance approach and statistical heterogeneity was assessed with the Cochran Q-test and I^2 values. A statistical threshold of 5% was considered as significant.
Results: Over 1,387 publications screened, 7 studies were selected for meta-analysis (3–9). These studies were observational studies (n=6) or controlled trial (n=1); involved patients with axial or peripheral SpA (n=6) or psoriatic arthritis (n=1); included treatments with ADL (n=4), ETA (n=1), INF and INF biosimilar (n=2), or various anti-TNF drugs (n=1). ADAb rates varied between anti-TNF drugs: 0% for ETA, 13.6–31.4% for ADL, 0–28.9% for INF. Patients with ADAb were less often responders than patients without ADAb in 6 studies, more often responders in one study, while the risk ratio (RR) for response was not assessable in one study due to the absence of ADAb. The weighted pooled RR (95% CI) for response to anti-TNF drugs was 0.73 (0.54–0.98) in ADAb+ in comparison with ADAb- patients (p=0.04) (see figure). There were trends towards more infusion reactions and lower serum drug levels in patients with ADAb (data not shown).



Conclusions: According to the results of this meta-analysis, ADAb positivity is associated with a lower rate of response to anti-TNF agents in patients with SpA.
References:
[1] The immunogenicity of anti-TNF therapy in immune-mediated inflammatory diseases: a systematic review of the literature with a meta-analysis, Garcês.S and al, ARD 2014; 72:1947–1955.
[2] The comparative immunogenicity of biologic therapy and it's clinical releavance in psoriatic arthritis: a systematic review of the literature, Balsa.A and al, ACR 2016, Abstract number 1691.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5726

THU0365 DO EXTRA-ARTICULAR MANIFESTATIONS AFFECT THE CHOICE OF BIOLOGIC THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS? A MULTICENTRE REAL-LIFE ANALYSIS

E.G. Favalli[1], S. D'Angelo[2], A. Carletto[3], A. Becciolini[1], F. Martinis[3], G. Tramontano[2], M.G. Raimondo[4], M. Biggioggero[4], A. Marchesoni[1], M. Rossini[3], I. Olivieri[2]. *[1]Department of Rheumatology, Gaetano Pini Institute, Milano; [2]Rheumatology Institute of Lucania (IRel) - Rheumatology Department of Lucania, San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, Potenza; [3]UOC Reumatologia, Dipartimento di Medicina, AOUI, Verona; [4]Department of Clinical Sciences and Community Health, Division of Rheumatology, University of Milan and Gaetano Pini Institute, Milano, Italy*

Background: Extra-articular manifestations (EAMs), such as uveitis, inflammatory bowel diseases (IBD) and psoriasis (PsO), frequently complicate the disease course of patients with axial spondyloarthritis (axSpA), although prevalence data on this regard are still controversial. The occurrence of EAMs might also contribute to the decision of introducing a biologic therapy and even influence the choice between the available TNF inhibitors (TNFis).
Objectives: The aim of this study is to retrospectively evaluate the prevalence of EAMs in a multicentre cohort of axSpA patients treated with TNFi, investigating how these influenced the choice of treatment.
Methods: Clinical data from axSpA patients treated with a TNFi between May 2003 and May 2016 where obtained from a multicentre registry. Prevalence of EAMs (uveitis, IBD and PsO) was calculated at the time of TNFi prescription, evaluating their distribution according to drug subgroup.
Results: The study included 503 patients with axSpA (172 [34.2%] women, mean age [±SD] 40.5 [±13.2] years, mean disease duration 9.7 [±14.7] years), receiving a total of 675 lines of treatment (I-line n=503, II-line n=118, ≥ III-line n=54) with a TNFi (272 infliximab [IFX], 173 adalimumab [ADA], 89 golimumab [GOL], 141 etanercept [ETN]). At the time of TNFi introduction, 28.6% patients claimed at least one EAM (IBD 11.3%, uveitis 10.9%, and PsO 8.8%). The baseline presence of at least one EAM was associated with a more frequent prescription of an anti-TNF monoclonal antibody rather than etanercept (34.1% versus 21.9%, respectively; p=0.005). In detail, EAMs were found in 41.6, 36.9, 29.8, and 21.9% patients treated with GOL, ADA, IFX, or ETN, respectively. The prevalence of IBD was significantly higher (p=0.004) in patients treated with ADA (12.7%), IFX (14.3%), or GOL (11.2%) compared with ETN (4.9%). Uveitis was numerically more frequent in GOL (20.2%) and ADA (13.3%) rather than IFX (9.5%) and ETN (9.9%) groups. Finally, PsO prevalence was similar in patients treated with ADA (10.9%) and GOL (10.1%), and numerically lower in the ETN (7.1%) and IFX (5.9%) groups.
Conclusions: In our cohort of axSpA patients treated with TNFis, EAMs were highly represented. The presence of extra-articular involvement has been carefully taken into account when a TNFi was required to better control the disease. In particular, IBD and uveitis drove more frequently the choice toward an anti-TNF monoclonal antibody instead of the receptor.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3779

THU0366 GASTROINTESTINAL INFECTIONS IN PATIENTS WITH SPONDYLOARTHRITIS TREATED WITH ANTI-TNF DRUGS: RESULTS OF GISEA REGISTER

F. Atzeni[1], V. Panetta[2], M. Sebastiani[3], F. Salaffi[4], A. Carletto[5], R. Foti[6], F. Iannone[7], G. Elisa[8], M. Govoni[9], A. Marchesoni[10], E.G. Favalli[10], R. Gorla[11], R. Ramonda[12], P. Sarzi-Puttini[13], G. Ferraccioli[8], G. Lapadula[7] on behalf of GISEA group. *[1]Rheumatology Unit, University Hospital L. Sacco, Milan, Italy, Milan; [2]L'altrastatistica Consultancy & Training, Biostatistics Office, Rome; [3]University Hospital of Modena, Modena; [4]Polytechnic University of Marche, C. Urbani Hospital, Jesi; [5]Rheumatology Unit, University of Verona, Verona; [6]Rheumatology Unit, Vittorio-Emanuele University Hospital of Catania, Catania; [7]University of Bari, Bari; [8]Division of Rheumatology, Institute of Rheumatology, Catholic University of the Sacred Heart, Rome; [9]Department of Medical Sciences, UOC of Rheumatology, Santa Anna University Hospital, Ferrara; [10]G. Pini Orthopedic Institute, Milan, Milan; [11]Rheumatology and Immunology Unit, Spedali Civili, Brescia; [12]University of Padua, Padua; [13]Rheumatology Unit, University Hospital L.Sacco, Milan, Italy*

Background: Tumour necrosis factor (TNF) plays a pivotal role in controlling intracellular of bacterial infection. The BSR Biologics Register (BSRBR) has reported an increase in the occurrence of listeria and salmonella infections in anti-TNF-treated rheumatoid arthritis patients in comparison with those patients treated with non-biological DMARDs.
Objectives: The aim of this study was to determine the incidence of gastrointestinal infection in the anti-TNF-treated spondyloarthritis (SpA) patients in the GISEA registry, and identify the factors associated with its development.
Methods: The prospective GISEA registry was designed to collect real-world clinical data concerning patients with RA or SpA treated with biological drugs. The baseline information includes demographics, disease duration, HAQ-DI, DAS-28, BASDAI, BASFI and BASMI scores, steroid use, smoking history and comorbidities.
Results: Of the 3321 anti-TNF-treated SpA patients in the registry (1731 males, 52.2%; mean age 47±13 years; median disease duration three years, interquartile range [IQR] 0–8), 1065 (32%) were treated with infliximab (IFN), 1052 (32%) with adalimumab (ADA), and 1204 (36%) with etanercept (ETN). Two thousand, one hundred and five patients (63.4%) had a median of one comorbidity (IQR 0–2], the most frequent being hypertension (701), thyroid diseases (281), diabetes mellitus (207), cardiopathy (189), and osteoporosis (145). In combination with the biological drug, 919 patients (27.7%) received steroids and 2451 (79.9%) at least one DMARD. The median follow-up was three months (IQR 1–2 years). Twenty-two patients 0.7% experienced bacterial gastrointestinal infections, the most frequent being due to listeria, klebsilla and salmonella. The crude incidence rate was 2.5 per 1000 patient-years (95% CI 1.6–3.7). Univariate analysis showed that female gender (OR 3.9, 95% CI 1.5–10.0; p=0.004) and comorbidities (OR 3.4, 95% CI 1.0–3.5; p=0.049) were associated with a high risk of gastrointestinal infections, and that the use of IFN rather than ETN and ADA (p=0.712 and p=0.238) was not associated with a higher risk of gastrointestinal infections.

Furthermore, univariate models showed that age (p=0.738), disease duration p=0.090, previous DMARDs (p=0.616), and HAQ (p=0.674) and BASFI (scores p=0.850) were not statistically significant predictors of gastrointestinal infections.
Conclusions: The incidence rate of gastrointestinal infections in SpA patients treated with anti-TNF drugs is not increased. Being female and having comorbidities are predictive factors of gastrointestinal infections.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5936

THU0367 THE INFLUENCES OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON SERUM VEGF AND BMP-2 LEVELS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

G. Gao, L. Lu, Z. Li, Y. Li. *Rheumatology, the First Affiliated Hospital of Zhengzhou Unversity, Zhengzhou, China*

Background: VEGF has been found abnormal in patients with SpA and related to disease activity [1,2]. BMP-2 has a function of promoting the osteophyte formation, and may be involved in the integration process of AS spine [3,4]. VEGF and BMP-2 interact with each other, participating in the formation of osteoblast [5]. COX-2 works together with the expressions of BMP2 and VEGF is an important factor of heterotopic ossification [6].
Objectives: To investigate the serum levels of VEGF and BMP-2 in axSPA treated with NSAIDs and their possible relationship with disease activity.
Methods: 120 patients with axSPA were randomized administered with imrecoxib or celecoxib respectively for 3 months. Serum VEGF and BMP-2 were detected. ESR, CRP, BASDAI, BASFI and SPARCC were measured.
Results: A statistically significant change was found in ESR, BASDAI, patients global assessment of disease activity, Schober test and SPARCC following treatment with imrecoxib or celecoxib (P <0.05). There were no statistically significant differences between the two groups. (P >0.05). There was statistically significant difference in serum VEGF levels before and after treatment (240.89±17.68 pg/ml vs 187.00±11.42 pg/ml, P<0.05), but no difference in BMP-2 (231.74±104.44 vs 226.80±116.26 pg/ml, P>0.05). A significant correlation was found between VEGF level and ESR, CRP, BASFI, tragus-up-wall distance and finger to floor distance, lumbar side flexion,Schober test and intermalleoar distance (r=0.628, 0.542, 0.238, 0.299, 0.353, -0.369, -0.373, -0.359, -0.274, P<0.05).And the BMP-2 levels were correlated with CRP and lumbar side flexion (r =0.213, -0.190, P<0.05). Serum VEGF levels were significantly increased in HLA-B27-positive patients than in HLA-B27-negative ones (P<0.05).
Conclusions: NSAIDs can not only improve symptoms and function, but also reduce sacroiliitis possibly by affecting the levels of VEGF and BMP. Imrecoxib and celecoxib have the same efficacy.The response to treatment was correlated with the expression of HLA-B27.
References:
[1] Appel H,Janssen L,Listing J,Heydrich R,Rudwaleit M,Sieper J.Serum levels of biomarkers of bone and cartilage destruction and new bone formation in different cohorts of patients with axial spondyloarthritis with and without tumor necrosis factor-alpha blocker treatment.Arthritis Res Ther;2008:10:R125.
[2] Liu KG,He QH,Tan JW,Liao GJ.Expression of TNF-alpha, VEGF, and MMP-3 mRNAs in synovial tissues and their roles in fibroblast-mediated osteogenesis in ankylosing spondylitis.Genet Mol Res;2015:14:6852–6858.
[3] Poddubnyy D,Conrad K,Haibel H,Syrbe U,Appel H,Braun J,et al. Elevated serum level of the vascular endothelial growth factor predicts radiographic spinal progression in patients with axial spondyloarthritis.Ann Rheum Dis;2014:73:2137–2143.
[4] Chen MH,Chen HA,Chen WS,Chen MH,Tsai CY,Chou CT.Upregulation of BMP-2 expression in peripheral blood mononuclear cells by proinflammatory cytokines and radiographic progression in ankylosing spondylitis.Mod Rheumatol;2015:25:913–918.
[5] Minamizaki T,Yoshiko Y,Kozai K,Aubin JE,Maeda N.EP2 and EP4 receptors differentially mediate MAPK pathways underlying anabolic actions of prostaglandin E2 on bone formation in rat calvaria cell cultures.Bone;2009:44:1177–1185.
[6] Pape HC,Marcucio R,Humphrey C,Colnot C,Knobe M,Harvey EJ.Trauma-induced inflammation and fracture healing. J Orthop Trauma. 2010 2010–09–01;24:522–5.
Acknowledgements: no.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5582

THU0368 CLINICAL AND IMAGING CHARACTERISTICS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS REPORTING FLARE SYMPTOMS IMMEDIATELY PRIOR TO NEXT DOSE IN ROUTINE TNFI THERAPY

R. Ansell, H. Mathieson, M. Merashli, N. Busquets-Pérez, D. McGonagle, H. Marzo-Ortega. *Nihr Lmbru, Leeds Teaching Hospitals Trust and LIRMM, University of Leeds, Leeds, United Kingdom*

Background: Tumour necrosis factor inhibitors (TNFi) are highly efficacious in axial spondyloarthritis (axSpA) with significant clinical responses mirrored in resolution of MRI determined bone marrow oedema (BMO) lesions representative of active inflammation in the sacroiliac joints (SIJ) and spine. However, symptom flare suggesting loss of response is common with many patients reporting deterioration days or weeks prior to the next dose. We hypothesised that intermittent suppression of inflammation with longer acting TNFis such as adalimumab or infliximab may be associated with a greater likelihood of recurrence of MRI determined BMO lesions than shorter acting agents such as etanercept.
Objectives: To explore the relationship between symptom flare immediately prior to next treatment dose and recurrence of MRI determined BMO lesions with different TNFi in axSpA.
Methods: Proof-of-concept, single centre study. Eligible participants were adults with axSpA established on adalimumab, etanercept or infliximab describing loss of response immediately prior to next treatment dose. Loss of response was defined as subjective “flare” or “wearing off” of drug effect before the expected duration of treatment effect. Participants attended at three points: Baseline: first day of treatment cycle (day of drug dose); Endpoint 1: 3–4 days after dose; and Endpoint 2: within 48 hours of next dose. ASDAS-CRP and whole spine and SIJ MR imaging utilising 3T MRI scanner were performed at each visit. Images were scored according to the semi-quantitative Leeds MRI scoring system by two observers blinded to participant identity and date of scan.
Results: 38 participants (16 adalimumab; 12 etanercept; 10 infliximab) with a total 113 MRI scans were analysed. 71% (n=27) male; 60% (n=23) HLA-B27+ with no differences between the groups; 73.7% (n=28) fulfilled mNYC for AS; the remainder were classified as nr-axSpA. 58% (n=22) had at least 1 Grade 1 BMO lesion at baseline with lesions more commonly seen with longer acting drugs (5/12 in etanercept group; 9/16 in adalimumab group; 8/10 in infliximab group) and 11 (50%) had at least 1 Grade ≥2 lesion (Table 2). There was a trend towards number and severity of BMO lesions fluctuating through the treatment cycle (Figure 1) mimicking subjective loss of response, also reflected on the ASDAS-CRP (Table 1) but this did not reach statistical significance.

Table 1. Median (range) ASDAS-CRP by drug and visit

	Baseline	Endpoint 1	Endpoint 2
Etanercept	2.94 (1.5–4.4)	2.46 (1.8–4.0)	3.18 (1.1–4.2)
Adalimumab	2.97 (1.7–5.5)	2.17 (1.0–7.9)	2.79 (1.4–5.3)
Infliximab	3.3 (3.0–4.7)	2.93 (1.0–4.5)	3.31 (2.8–4.8)

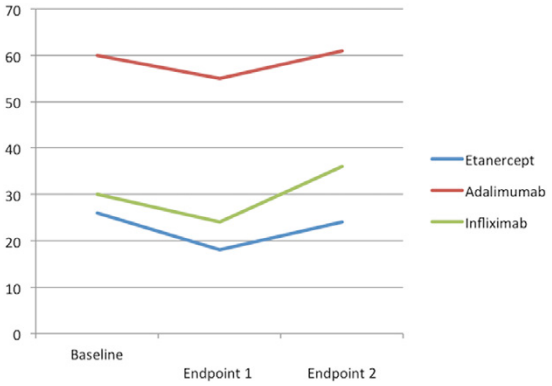


Figure 1. Total number of BMO lesions (grade 1 and ≥2).

Conclusions: This small proof-of-concept study shows subtle fluctuations on MRI changes of BMO and ASDAS-CRP corresponding to time of subjective “flare” before next scheduled TNFi dose in subjects with axSpA. Although these changes may be more common with the longer acting TNFi our data are not confirmatory. Larger studies are required to explore this concept further as these observations are potentially relevant for disease progression since cycles of inflammation and its subsequent suppression could theoretically increase the risk of new bone formation.
Acknowledgements: This study was sponsored by Pfizer.
Disclosure of Interest: R. Ansell Grant/research support from: Pfizer, H. Mathieson: None declared, M. Merashli: None declared, N. Busquets-Pérez: None declared, D. McGonagle Grant/research support from: Celgene, Janssen & Pfizer, Consultant for: AbbVie, Celgene, Janssen, Novartis, UCB, Speakers bureau: Abbvie, Celgene, Janssen, UCB., H. Marzo-Ortega Grant/research support from: Janssen & Pfizer., Consultant for: AbbVie, Celgene, Janssen, Novartis, UCB. S, Speakers bureau: Abbvie, Celgene, Janssen, UCB.
DOI: 10.1136/annrheumdis-2017-eular.6653

THU0369 SECUKINUMAB 150MG PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE ANKYLOSING SPONDYLITIS WITH HIGH RETENTION RATE: 3-YEAR RESULTS FROM PHASE III TRIAL, MEASURE 2

H. Marzo-Ortega[1], C.W. Legerton[2], J. Sieper[3], A.J. Kivitz[4], R. Blanco[5], M. Cohen[6], E.M. Delicha[7], S. Rohrer[7], H. Richards[7] on behalf of the MEASURE 2 study group. *[1]Nihr Lmbru, LTHT and LIRMM, UoL, Leeds, United Kingdom; [2]Low Country Rheumatology, Articularis Healthcare, Charleston, United States; [3]University Clinic Benjamin Franklin, Berlin, Germany; [4]Altoona Center for Clinical Research, Duncansville, United States; [5]Hospital Universitario Marqués de Valdecilla, Santander, Spain; [6]McGill University, Montreal, Canada; [7]Novartis Pharma AG, Basel, Switzerland*

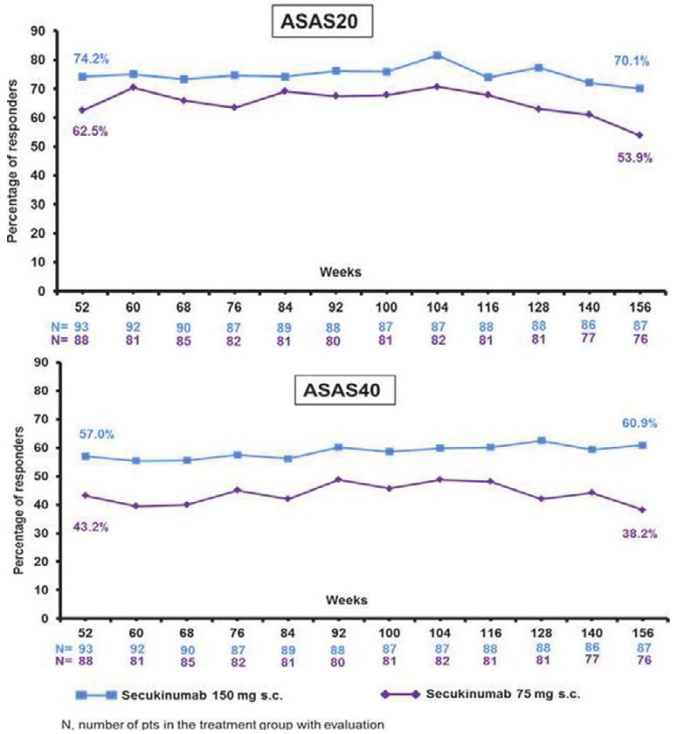
Background: Secukinumab improved signs and symptoms of ankylosing spondylitis (AS) over 2 years in the MEASURE 2 study (NCT01649375).[1,2]
Objectives: To report the efficacy and safety of secukinumab over 3 years from the MEASURE 2 study.
Methods: 219 patients (pts) with active AS were randomised to subcutaneous secukinumab 150mg (72 pts), 75mg (73 pts) or placebo (PBO, 74 pts). At Week (Wk) 16, PBO treated pts were re-randomised 1:1 to secukinumab 150mg or 75mg, irrespective of clinical response. Pts initially randomised to secukinumab and those who switched from PBO to secukinumab at Wk 16 were included in the analysis (secukinumab 150mg, N=106 and secukinumab 75mg, N=105). Outcome measures at Wk 156 included ASAS20 and 40, ASDAS-CRP inactive disease, ASAS5/6, BASDAI, SF-36 PCS and ASAS partial remission. Data are reported as observed. Safety analyses included all pts who received ≥1 dose of secukinumab.
Results: At 156 wks, the completion rates for secukinumab 150mg was 81.1% (86/106) and 72.4% (76/105) for 75mg. Higher discontinuation rates for 75mg were in part due to lack of efficacy or patient/guardian decision. Efficacy observed across endpoints from Wks 52 to 156 are summarised in the Table. Higher responses were observed in the 150mg group (Table and Figure). Over the entire study period, the mean exposure [±SD] to secukinumab was 914.3±315.5 days. The exposure-adjusted incidence rates with Any secukinumab for infections/infestations, Crohn's disease, malignant/unspecified tumours and major adverse cardiovascular events were 1.5, 0.6, 0.6 and 0.6 per 100 pt-years, respectively.
Conclusions: Secukinumab 150mg provided sustained improvement in the signs & symptoms along with physical functions with over 80% retention rate through 3 years in pts with AS. Safety profile remained favourable and was consistent with previous reports.[1,2]
References:
[1] Baeten et al. N Engl J Med. 2015;373:2534–48.
[2] Marzo-Ortega et al. Ann Rheum Dis. 2016;75:812–3.
Disclosure of Interest: H. Marzo-Ortega Grant/research support from: Janssen and Pfizer, Consultant for: Abbvie, Celgene, Janssen, Novartis and UCB, Speakers bureau: Abbvie, Celgene, Janssen and UCB, C. Legerton Grant/research support from: AbbVie, Ablynx, Acerta, Amgen, AstraZeneca, Celgene, GSK, Janssen, E. Lilly, BMS, Pfizer, Novartis, Sandoz, UCB, Daiichi Sankyo, ChemoCentryx, Boehringer Ingelheim, Speakers bureau: Novartis, Celgene and Amgen, J. Sieper Grant/research support from: AbbVie, Pfizer and Merck, Consultant for: AbbVie, Pfizer, Merck, UCB and Novartis, Speakers bureau: AbbVie, Pfizer, Merck and UCB, A. Kivitz Consultant for: AbbVie, Pfizer, Genentech, UCB and Celgene, Speakers bureau: AbbVie, Pfizer, Genentech, UCB and Celgene, R. Blanco: None declared, M. Cohen Consultant for: Abbvie, Amgen, BMS, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi and UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi and UCB, E. M. Delicha Employee of: Novartis, S. Rohrer Shareholder of: Novartis, Employee of: Novartis, H. Richards Shareholder of: Novartis, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1295

Table 1. Summary of Efficacy Results at Wks 52 and 156

Variable	Wk	Secukinumab	
		150mg	75mg
ASAS20, % responders (n/N)	52	74.2 (69/93)	62.5 (55/88)
	156	70.1 (61/87)	53.9 (41/76)
ASAS40, % responders (n/N)	52	57.0 (53/93)	43.2 (38/88)
	156	60.9 (53/87)	38.2 (29/76)
ASDAS-CRP Inactive Disease, % pts (n/N)	52	19.4 (18/93)	17.2 (15/87)
	156	25.6 (22/86)	12.0 (9/75)
ASAS 5/6, % responders (n/N)	52	61.3 (57/93)	49.4 (44/89)
	156	58.6 (51/87)	40.8 (31/76)
±SD (N)	52	-3.2±2.3 (93)	-2.5±2.2 (89)
	156	-3.3±2.5 (87)	-2.5±2.3 (76)
±SD (N)	52	7.6±7.7 (94)	6.4±7.3 (85)
	156	6.3±9.8 (84)	4.5±9.7 (72)
ASAS partial remission, % pts (n/N)	52	24.7 (23/93)	18.0 (16/89)
	156	32.2 (28/87)	11.8 (9/76)

ASAS, Assessment of Spondyloarthritis International Society criteria; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high sensitivity C-reactive protein; n, number of responders; N, number of pts in the treatment group with evaluation SD, standard deviation; SF-36 PCS, Short Form-36 physical component summary.

Figure: ASAS20/40 response rate through Week 156



N, number of pts in the treatment group with evaluation

THU0370 INCREASED INTERLEUKIN-17A CONCENTRATION REMAINS HIGH IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TUMOR NECROSIS α INHIBITORS WITHIN THE YEAR

I.Z. Gaydukova, A. Rebrov. *Hospital Therapy, Saratov State Medical University, Saratov, Russian Federation*

Background: Ankylosing spondylitis (AS) is associated with changes in the serum cytokines concentrations. During the treatment cytokines profile could change in different manner.
Objectives: The aim of the study was to evaluate the changes in concentration of interleukin-17A (IL-17A) in patients with AS, treated with tumor necrosis factor α inhibitors (anti-TNFα) during the year.
Methods: 30 patients with AS, fulfilled m. New-York criteria, with BASDAI ≥4.0 and NSAIDs non-responders were involved in the study. Mean age of AS patients at baseline was 38.35±9.19 years (M ± SD), the duration of AS was 11.4±9.6 years, 22 (73.3%) of patients – male. 20 healthy volunteers were involved as controls (mean age 40.1±7.7 years, male - 12 (60%). All AS patients were treated during the year with Remicade (infliximab, MSD®)) - 5 mg/kg at the recommended scheme. BASDAI, $ASDAS_{CRP}$ indices were calculated, C-RP, TNFα and IL-17A levels were measured before the treatment with anti-TNFα (baseline) and 52±2 weeks after the baseline. Number of patients achieved ASAS 20, ASAS 40 responses, and ASAS partial remission was evaluated. The statistics was performed with SPSS17.
Results: Baseline concentrations of TNFα and IL-17A in AS patients were higher than in healthy subjects (28.4±14.4 and 2.4±2.1, respectively, p<0.000). Significant reduction of AS activity, but not of IL-17A serum concentration was marked at week 52, Table 1.
24 (80%) achieved ASAS 20, 18 (60%) – ASAS 40, 12 (40%) of patients with

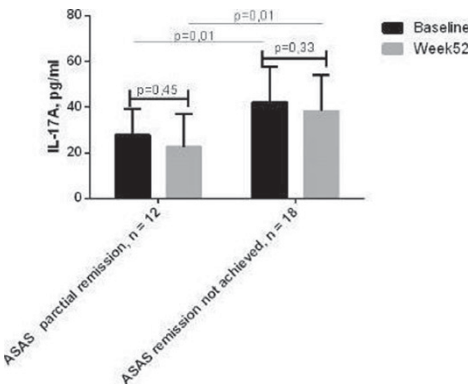


Table 1. Clinical and laboratory characteristics of AS activity at baseline and week 52, n=30

	Baseline	Week 52	p
Pain, Me [Q25;Q75]	6.0 [7.0; 9.0]	3.4 [1.0; 5.0]	<0.000
BASDAI, Me [Q25;Q75]	6.6 [4.4; 8.85]	3.2 [2.1; 7.6]	<0.000
ASDAS, Me [Q25;Q75]	3.8 [3.5; 4.4]	2.1 [1.26; 4.26]	<0.000
C-RP, mg/l, M±SD	12.3±3.9	4.3±1.7	<0.000
TNF α, pg/ml, M±SD	17.8±7.6	7.3±3.2	<0.000
IL-17A, pg/ml, M±SD	28.4±14.4	32.1±12.2	0.29

AS achieved ASAS partial remission. IL-17A was lower in patients who achieved remission compared to patients who did not achieve remission (figure).
Conclusions: Serum concentration of IL-17A remains stable in patients treated with anti-TNFα during the year. The baseline and final concentrations of serum IL-17A are higher in patients with AS who do not achieved ASAS partial remission compared to those who achieved the remission.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5305

THU0371 THERAPY MODIFICATIONS IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH A BIOLOGIC IN THE UNITED STATES – DESCRIPTIVE ANALYSES FROM AN ADMINISTRATIVE CLAIMS DATABASE

J.A. Walsh[1], O. Adejoro[2], B. Chastek[2], G. Chun[3], Y. Park[3]. *[1]University of Utah School of Medicine, Salt Lake City, UT; [2]Optum, Eden Prairie, MN; [3]Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States*

Background: For patients with active ankylosing spondylitis (AS), biologic therapy has been shown to be an effective treatment option. Physicians treating patients with biologic therapy may modify the treatment by adding non-biologic medications and/or escalating the dose of the biologic; however, limited data exist on how these therapy modifications are used in patients with AS receiving biologic treatment in real-world settings.
Objectives: To describe therapy modifications (adding non-biologic medications or dose escalation of the biologic therapy) in patients with active AS who newly initiated treatment with biologic therapy in the United States.
Methods: This study used US administrative pharmacy and medical claims data from the Optum Research Database. Adult patients with AS who newly initiated (no evidence of use in the 12 months prior) a biologic between January 1, 2013 and January 31, 2015, and were continuously enrolled in a commercial or Medicare Advantage health plan 12 months before (baseline period) and 15 months following the index date, defined as the date of first pharmacy fill or medical infusion, were included. To reduce confounding by patients with an early switch/discontinuation, therapy modifications were identified only in those who persisted on the index biologic for >90 days. Therapy modifications identified included initiation of add-on medications (disease-modifying antirheumatic drugs, nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, corticosteroids, antidepressants, anxiolytics, sleeping aids and topical analgesics) after the first 90 days of persistence, and dose escalation of the index biologic. Dose escalation was defined as a patient receiving a dose >10% above the reference dose from the product label for ≥90 days.
Results: Of the 333 patients with AS included who persisted on their index biologic for >90 days, 88.3% initiated a subcutaneous tumor necrosis factor inhibitor (TNFi-SC; adalimumab, certolizumab pegol, etanercept or golimumab) as their index biologic and 11.7% initiated an intravenous TNFi (TNFi-IV; infliximab). During the 12-month baseline period, patients had a mean (standard deviation) number of claims of 3.9 (6.6) for opioids, followed by 2.5 (3.1) for NSAIDs, 1.9 (2.8) for corticosteroids and 1.8 (3.7) for antidepressants. Overall, 44.7% of patients received ≥1 additional medication during the period from 90 days after the index date to the end of persistence with the index biologic or 12-month post-index period. The most commonly added medications were corticosteroids (16.8%), opioids (12.9%), NSAIDs (10.2%) and antidepressants (7.2%) (Table 1). Overall, 7.2% of patients had a dose escalation of the index biologic (38.5% for TNFi-IV and 2.7% for TNFi-SC) in the immediate 12-month post-index period.

Table 1. Add-on medications initiated from 90 days after the index date to the end of persistence or 12 months among patients with AS

Additional Medication, n (%)	Total (N = 333)	TNFi-SC (n = 294)	TNFi-IV (n = 39)
Any medication	149 (44.7)	129 (43.9)	20 (51.3)
Corticosteroid	56 (16.8)	46 (15.6)	10 (25.6)
Opioid	43 (12.9)	39 (15.5)	4 (10.3)
NSAID	34 (10.2)	30 (10.2)	4 (10.3)
Antidepressant	24 (7.2)	22 (7.5)	2 (5.1)
Anxiolytic	23 (6.9)	18 (6.1)	5 (12.8)
csDMARD	15 (4.5)	13 (4.4)	2 (5.1)
Topical analgesic	13 (3.9)	9 (3.1)	4 (10.3)
Sleeping aid	9 (2.7)	8 (2.7)	1 (2.6)
tsDMARD	0 (0.0)	0 (0.0)	0 (0.0)

AS, ankylosing spondylitis; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IV, intravenous; SC, subcutaneous; TNFi, tumor necrosis factor inhibitor; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.
* TNFi-SC includes adalimumab, certolizumab, etanercept and golimumab.
† TNFi-IV includes infliximab.

Conclusions: In this descriptive, administrative claims-based study from the US, approximately 45% of patients with AS initiated an add-on medication while receiving biologic therapy. Further research is needed to better understand optimal therapy strategies for patients with AS.
Acknowledgements: This study was sponsored by Novartis Pharmaceuticals Corporation, East Hanover, NJ.
Disclosure of Interest: J. Walsh Consultant for: Novartis, O. Adejoro Employee of: Optum, B. Chastek Employee of: Optum, G. Chun Employee of: Novartis, Y. Park Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.3035

THU0372 EFFECT OF TNFI VERSUS NSAID ON SPINAL RADIOGRAPHIC PROGRESSION OVER 4 YEARS IN EARLY ANKYLOSING SPONDYLITIS: RESULTS FROM TWO OBSERVATIONAL COHORTS IN SOUTH KOREA

J.W. Park[1], M.J. Kim[1], J.K. Park[1], Y.J. Lee[2], E.B. Lee[1], Y.W. Song[1], E.Y. Lee[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul; [2]Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Gyeonggi-do, Korea, Republic Of*

Background: It is uncertain whether early suppression of inflammation by tumor necrosis factor inhibitor (TNFi) leads to a decreased radiographic progression in axial spondyloarthritis (axSpA).
Objectives: To compare the radiographic progression over 4 years in patients with early ankylosing spondylitis (AS) using TNFi versus nonsteroidal antiinflammatory drug (NSAID)
Methods: A total of 215 patients with early AS (symptom duration<10 years) were included based on the availability of radiographs at baseline and 2- and/or 4-years of follow up. Among them, 135 patients with TNFi were from SNUH-biologics cohort (TNFi group) and other 80 patients with NSAID were from control cohort in Seoul National University Bundang Hospital (NSAID group). Radiographic progression was assessed by two blinded readers using modified Stokes AS Spinal Score (mSASSS). Linear mixed model was applied to compare the radiographic progression between the two groups after adjustment for clinical factors. We also performed a sensitivity analysis after the propensity score matching in which age, smoking status, baseline CRP and baseline mSASSS were included as covariates.
Results: Patients in the TNFi group showed higher baseline BASDAI (6.7 vs. 3.1) and CRP (2.2 vs. 1.1mg/dL) as compared with those in the NSAID group. There were no differences between the two groups regarding age, gender, HLA-B27, smoking status and baseline radiographic damage. Overall, radiographic progression rate (95% CI) during the observation was 0.72 (0.57–0.87) unit/year. TNFi group showed significantly slower progression than NSAID group (β=-0.33 unit/year, p=0.042). This result was consistent after adjusting for age, smoking status, baseline CRP and presence of baseline syndesmophytes (β=-0.50 unit/year, p=0.001) (Table). In the subgroup analysis of patients without baseline syndesmophytes, TNFi group showed no radiographic progression over time whereas NSAID group did not (0.03 [-0.22–0.27] vs. 0.45 [0.20–0.71] unit/year). These results were not changed when the same analysis was performed in the post-matched population (78 TNFi group vs. 78 NSAID group).

Table 1. Radiographic progression over time in early AS patients using NSAID vs. TNFi

	Univariable analysis		Multivariable analysis[b]	
	Regression coefficient (95% CI)[a]	*p* value	Regression coefficient (95% CI)	*p* value
Age>40	0.82 (0.48–1.16)	<0.001	0.27 (-0.07–0.61)	0.124
Ever-smoker	0.31 (-0.01–0.62)	0.056	0.08 (-0.20–0.37)	0.568
Baseline CRP (mg/dL)	0.12 (0.05–0.18)	0.001	0.10 (0.04–0.16)	0.002
Baseline syndesmophytes	1.30 (1.00–1.62)	<0.001	1.14 (0.80–1.48)	<0.001
Group	-0.33 (-0.65–0.01)	0.042	-0.50 (-0.79–0.22)	0.001
NSAID group	0.93 (0.68–1.18)	<0.001	0.45 (0.18–0.71)	0.001
TNFi group	0.60 (0.40–0.79)	<0.001	-0.06 (-0.31–0.19)	0.648

[a]Regression coefficient indicates the progression of mSASSS over one year. [b] Gender, HLA-B27, baseline BASDAI and time-averaged NSAID index were not included because they did not show a significant ($p<0.1$) interaction with time in the univariable analysis.

Conclusions: In patients with early AS, TNFi led to a decreased radiographic progression as compared with NSAID treatment. This result suggests that early and durable suppression of inflammation using TNFi can have beneficial effect on the radiographic outcome of AS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3321

THU0373 USE OF CORTICOSTEROID HIP JOINT INJECTIONS IN SPONDYLOARTHRITIS PATIENTS UNDER TNF ALPHA INHIBITORS

K. Maatallah[1], A. Ben Ouhiba[1], I. Mahmoud[2], S. Belghali[3], W. Hamdi[1], M. Kchir[1], R. Tekaya[2], L. Abdelmoula[2]. *[1]Department of Rheumatology, M.T Kassab Institute; [2]Department of Rheumatology, Charles Nicolle Hospital; [3]Department of Rheumatology, Farhat Hached Hospital, Tunis, Tunisia*

Background: The hip disease is a serious complication of spondyloarthritis (SpA), engaging the functional prognosis of patients. TNF alpha inhibitors are a breakthrough for the treatment of SpA and the management of this complication.
Objectives: To assess the efficacy of TNF alpha inhibitors on hip involvement in SpA by evaluating the use of intra-articular corticosteroid infiltrations.
Methods: Observational cohort study that included 94 SpA patients with hip disease (ASAS2009). Two groups were studied. Group 1 (G1): patients under anti-TNF alpha therapy and Group 2 (G2): TNF alpha inhibitors naive patients. Clinical (BASDAI, BASFI, hip (pain/mobility), index of severity for osteoarthritis for the hip (ISH)), biological (CRP) data were assessed and the use of corticosteroid hip joint infiltration was compared. Evaluations were performed and compared between the 2 groups at baseline (T0), two years (T2) and Tn (greater than or equal to 3 years). The correlation study was made by Pearson test. A correlation was considered statistically significant if $p<0.05$.
Results: Group 1 and 2 included 48 and 46 patients respectively. The socio demographic and clinical characteristics of the disease were comparable between the two groups. Biological and radiological assessments of the two groups were comparable at T0. Group 1 had however a more active disease and a greater functional impairment. NSAIDs were prescribed in 40% of patients in G1 and 86% in G2 ($p<0.0001$). DMARDS were prescribed in 20 patients in G1 and in 22 patients in G2 ($p=0.6$). In G1 patients received infliximab, adalimumab and etanercept in 48%, 15% and 37% of cases respectively. Four patients of G1 and three of G2 patients received intra-articular corticosteroid infiltration in the year prior to the initial assessment ($p=0.7$). Assessment at T2 showed a greater improvement in clinical and biological parameters of the disease in group 1 than in group 2 with Δ (T2-T0) significantly lower in group 1 for the BASDAI ($p<0.0001$), the BASFI ($p<0.0001$) and the ISH ($p=0.017$). The number of painful hip was significantly lower in group 1 ($p<0.0001$). The evaluation at Tn showed a sustained clinical and biological efficacy of TNF alpha inhibitors in Group 1. The use of corticosteroid injections was significantly higher in group 2. Table 1 summarizes the assessment of different parameters at T2 and Tn.
Conclusions: Hip involvement is a marker of severity of spondyloarthritis. Anti-TNF alpha treatment is effective on hip disease. It reduces the use of intra articular injections of corticosteroids.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6177

THU0374 LONG-TERM EFFECTS OF TNF-ALPHA INHIBITORS ON BONE MINERAL DENSITY AND THE INCIDENCE OF VERTEBRAL FRACTURES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

K. Beek[1], M. van der Weijden[1], W. Lems[1], C. van Denderen[2], M. Nurmohamed[1], I. van der Horst-Bruinsma[1]. *[1]Rheumatology, Amsterdam Rheumatology immunology Centre/VUmc and Reade; [2]Rheumatology, Amsterdam Rheumatology immunology Centre/Reade, Amsterdam, Netherlands*

Background: Ankylosing Spondylitis (AS) is not only characterized by pathological bone formation leading to ankylosis, but also by bone loss which may lead to vertebral fractures (VFx). TNF-alpha inhibitors (TNFi) have proven to be effective in blocking the inflammation process. A few studies also showed an increase of Bone Mineral Density (BMD) in AS patients treated with TNFi [1–3] but the incidence of VFx after two years of treatment was increased.[3–4]
Objectives: To evaluate the long-term effect of TNFi on BMD and the incidence of VFx in patients with AS.
Methods: Consecutive TNFi naive patients diagnosed with AS according to the Modified New York criteria were included. Patients were recruited from the VUmc and the Amsterdam Outpatient clinic Reade and were treated with TNFi for 4 years. BMD at hip and lumbar spine (LS) were measured at baseline, after 2 and 4 years. T-scores were categorized as "normal BMD", "osteopenia" and "osteoporosis", based on the WHO osteoporosis criteria.[5] The incidence of VFx was determined by two observers using the Genant method.[6]
Results: In total, 70 AS patients with complete datasets (67.1% male) were included. The mean age was 41.6 years and the disease duration (time since diagnosis) was 9.8 years. At baseline 42% of the patients had a decreased BMD of the hip and 34% of the spine, of whom 19 patients (27%) had both a decreased hip BMD as well as a decreased lumbar BMD. The BMD of spine and hip improved after 2 and 4 years of TNFi treatment (Table 1). In 7 patients (10%), 8 VFx were observed both at baseline and after 2 years. After 4 years of TNFi-treatment 11 VFx were observed in 9 patients.
After 4 years, 2 out of 9 patients with ≥1 VFx had a decreased BMD at hip and lumbar spine whereas the other 7 patients had a normal BMD. The majority of VFx was localized in the mid or lower thoracic spine.

Table 1, BMD measurement in spine and hip of 70 AS patients treated with TNFi

	Baseline	After 2 years of TNFi	After 4 years of TNFi
Osteopenia LS*	23 (32.9)	19 (27.1)	21 (30.0)
Osteoporosis LS	6 (8.6)	3 (4.3)	2 (2.9)
Abnormal BMD LS	29 (41.5)	21 (31.4)	23 (32.9)
Osteopenia total hip	22 (31.4)	19 (27.1)	16 (22.9)
Osteoporosis total hip	2 (2.9)	2 (2.9)	3 (4.3)
Abnormal BMD total hip**	24 (34.3)	21 (30.0)	19 (27.2)
Patients with VFx	7 (10.0)	7 (10.0)	9 (12.9)
Total number of VFx	8	8	11

*Lumbar Spine; **N=68, because 2 patients had a total hip replacement. Abnormal BMD = osteopenia and/or osteoporosis according to WHO guideline[6]. Vertebral fractures (VFx) are presented in number of patients with a VFx and the actual prevalence of VFx. Outcomes are presented in n (%).

Conclusions: The percentage of relatively young AS patients with a decreased BMD at baseline of the hip and lumbar spine was high (34–41%). After 4 years of TNFi-treatment the BMD of the lumbar spine improved in 8.6% of the patients and of the hip in 7.2% of the patients. At baseline, several vertebral fractures were found and a few additional vertebral fractures were observed after 4 years of treatment.
References:
[1] Visvanathan S et al. Ann Rheum Dis 2009.
[2] Arends S et al. Arthritis Res Ther 2012.
[3] van der Weijden et al. J Reumatol 2016.
[4] Maas F et al. ClinExpRheumatol 2016.
[5] Kanis JA et al. J Bone MinerRes 1994.
[6] Genant HK et al. J Bone MinerRes 1993.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3398

THU0375 CHARACTERISTICS ASSOCIATED WITH IMPROVEMENTS IN SPARCC SIJ AND ASDAS SCORES IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS TREATED WITH ETANERCEPT

K. de Vlam[1], A. Burden[2], M.A. Dilleen[3], C. Boone[4]. *[1]Katholieke Universiteit, Leuven, Belgium; [2]Quanticate, Hitchin; [3]Pfizer, Sandwich, United Kingdom; [4]Pfizer, SA/NV, Medical Department, Brussels, Belgium*

Background: The EMBARK trial of etanercept (ETN) (NCT01258738)[1] has demonstrated the long-term efficacy of ETN in patients with non-radiographic axial spondyloarthritis (nr-axSpA) and shown correlations between decreased inflammation and clinical outcomes.[2]
Objectives: To determine which baseline (BL) characteristics are associated with clinical improvements after 48 weeks of treatment with ETN in patients with nr-axSpA.
Methods: This post hoc analysis was performed on data from patients with nr-axSpA enrolled in the 92-week open-label phase of the EMBARK trial. The primary analysis population was the EMBARK modified intent-to-treat (mITT) population (patients who had ≥1 dose of ETN, had ≥1 on-therapy evaluation, and met the Assessment in Ankylosing Spondylitis classification criteria for axSpA). Patients' SpondyloArthritis Research Consortium of Canada (SPARCC) sacroiliac joint (SIJ) scores and Ankylosing Spondylitis Disease Activity Scores (ASDAS) were recorded, and patients were divided into 4 quadrants (Q1–4) based on the minimally important change (MIC) for each instrument (SPARCC SIJ score, change from BL [cfb] of ≥2.5; ASDAS, cfb ≥1.1). Patients in Q1 achieved MIC in SPARCC SIJ but did not achieve MIC in ASDAS. Q2 did not achieve MIC in SPARCC SIJ and did not achieve MIC in ASDAS. Q3 did not achieve MIC in SPARCC SIJ but achieved MIC in ASDAS. Q4 achieved MIC in SPARCC SIJ and achieved MIC in ASDAS. Missing data were imputed using last observation carried forward. *P*-values were obtained using the Chi-squared test (categorical variables) and the Kruskal-Wallis test (continuous variables) in order to compare BL characteristics across improvement status. Multivariable

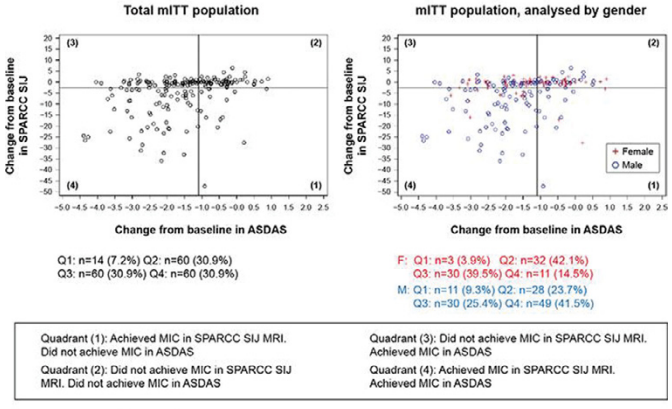
Abstract THU0373 – Table 1. Comparison of Clinical and biological variations between the 2groups at T2 and Tn

	T2/T0			Tn/T0		
	G1	G2	p	G1	G2	p
ΔISH	-7,7 [-19, 2]	-1,6 [-19, 8]	**0,01**	-9,3 [-20, 2]	0,1 [-4, 4]	**0,005**
ΔBASFI	-2,7 [-9, 7]	1,1 [-1, 4]	**<0,0001**	-3,2 [-9, 1]	0,2 [-3, 6]	**<0,0001**
ΔBASDAI	-3 [-8, 3]	0,4 [-3, 5]	**<0,0001**	-3,4 [-9, 2]	-0,9 [-6, 4]	**0,001**
Hip pain (%)	35	75	**<0,0001**	20	67	**<0,0001**
Limitation of hip mobility (%)	71	83	0,2	50	86	**<0,0001**
ΔCRP (mg/l)	-33,6 [-132,69]	-6,1 [-72,18]	0,3	-25,5 [-89, 6]	-1 [-99,58]	**0,04**
Corticosteroids hip joint injections (n)	1	3	0,2	0	4	**0,04**

multinomial logistic regression modelling was used to calculate which BL characteristics were associated with clinical improvements when adjusted for all other BL characteristics.

Results: At screening, male patients had significantly higher median SPARCC SIJ scores compared with female patients (4.83 [range 0.0–48.0] vs 1.5 [0.0–32.0], $P<0.0001$). At wk48, 69.1% of 194 patients achieved MIC in either SPARCC SIJ scores, ASDAS or both (Q1/3/4, Figure). There was a statistically significant difference in the number of male versus female patients who achieved MIC in both scores (Q4), compared with patients who achieved MIC in only one or neither (Q1–3, Figure) ($P<0.0001$). However, multinomial logistic regression modelling showed that age ($P=0.0358$), BL ASDAS ($P<0.0001$), and screening SPARCC Spine ($P=0.0358$) and SPARCC SIJ ($P<0.0001$) scores, not gender, were significantly associated with achievement of MIC in both SPARCC SIJ and ASDAS at wk48 for the total population (after adjustment for the effects of other variables).

Figure: Numbers of Patients who Did or Did Not Achieve MIC in SPARCC SIJ Score (≥2.5 cfb) or ASDAS (≥1.1 cfb)



ASDAS, Ankylosing Spondylitis Disease Activity Scores; cfb, change from baseline; MIC, minimally important change; mITT, modified intent-to-treat; SIJ, sacroiliac joint; SPARCC, SpondyloArthritis Research Consortium of Canada.

Conclusions: Although BL summaries showed a significant difference in gender across quadrants, the BL SPARCC SIJ score was strongly correlated with gender (male patients had more inflammation). When both were included in a multivariable model, gender was non-significant. Only age, BL ASDAS, and screening SPARCC SIJ and Spine scores were associated with MIC after 48 weeks of etanercept treatment.

References:

[1] Dougados M, et al. Arthritis Rheumatol. 2014;66:2091–102.
[2] Maksymowych WP, et al. Ann Rheum Dis. 2016;75:1328–35.

Disclosure of Interest: K. de Vlam Consultant for: Abbott, Celgene, Janssen, Pfizer, and UCB, Speakers bureau: Abbott, Celgene, Janssen, Pfizer, and UCB, A. Burden Employee of: Quanticate, M. A. Dilleen Shareholder of: Pfizer, Employee of: Pfizer, C. Boone Shareholder of: Pfizer, Employee of: Pfizer

DOI: 10.1136/annrheumdis-2017-eular.1873

THU0376 REAL-WORLD USE OF SECUKINUMAB WITH AND WITHOUT A LOADING REGIMEN AMONG PATIENTS WITH ANKYLOSING SPONDYLITIS IN THE UNITED STATES: PATIENT PROFILE AND DOSING

K. Oelke[1], G. Chun[2], Y. Li[2], X. Liu[3], Y. Park[2]. *[1]Rheumatic Disease Center, Glendale; [2]Novartis Pharmaceuticals Corporation, East Hanover; [3]KMK Consulting, Inc, Morristown, United States*

Background: Secukinumab is a fully human anti–interleukin-17 monoclonal antibody approved for the treatment of patients with moderate to severe plaque psoriasis, psoriatic arthritis and ankylosing spondylitis (AS), and may be administered with or without a loading regimen of 150 mg at weeks 0, 1, 2, 3 and 4 followed by maintenance dosing every 4 weeks. The dosing pattern of secukinumab in a real-world setting of patients with AS has not been evaluated since its approval in the United States on January 15, 2016.

Objectives: To describe the demographic, clinical and treatment characteristics (loading, dose) of patients with AS who were treated with secukinumab in routine clinical practice in the United States.

Methods: Retrospective data from the Symphony Health Solutions Lx commercial claims database were used to identify AS patients who had ≥1 secukinumab treatment between January 15, 2016 and June 30, 2016. Patients eligible for inclusion were ≥18 years of age who had the diagnosis of AS and ≥1 pharmacy or medical claim in the 12 months prior to their first secukinumab treatment (index date). Patient demographics and secukinumab dosage were examined at the index date. Clinical characteristics, comorbidities and treatment history in the 12 months prior to the index date were identified and presented by use versus no use of a loading regimen of secukinumab.

Results: A total of 152 patients who initiated secukinumab were included in this study; the mean (SD) age of included patients was 45.3 (11.1) years and 53.9% were female. Of the 152 patients, 119 patients (78.3%) received a loading regimen and 33 (21.7%) did not. Patient demographics, clinical characteristics and treatment history were not significantly different between the two cohorts (Table 1). The majority of patients (65.5%) with loading initiated secukinumab with the 150-mg dose, whereas the majority of patients (60.6%) without loading initiated with the 300-mg dose. More than half of the patients in each cohort received a biologic therapy during the 12-month baseline period (loading, 65.5%; no loading, 51.5%). Other prior treatments included oral corticosteroids (30.3% for both), conventional synthetic disease-modifying antirheumatic drugs (DMARDs) (loading, 31.9%; no loading, 21.2%) and targeted synthetic DMARDs (loading, 4.2%; no loading, 12.1%). The prevalence of comorbidities was similar between the two cohorts, with the most prevalent comorbidities being hypertension (19.1%), rheumatoid arthritis (19.1%) and other skin diseases (18.4%).

Table 1. Demographics, clinical characteristics and treatment history of patients with AS treated with secukinumab with or without a loading dose of 150 mg

	Overall (n = 152)	Loading (n = 119)	No Loading (n = 33)
Age, mean (SD), years	45.3 (11.1)	46.0 (10.8)	42.6 (11.9)
Female, n (%)	82 (53.9)	67 (56.3)	15 (45.5)
Region, n (%)			
South	46 (30.3)	37 (31.1)	9 (27.3)
Northeast	37 (24.3)	29 (24.4)	8 (24.2)
Midwest	36 (23.7)	25 (21.0)	11 (33.3)
West	33 (21.7)	28 (23.5)	5 (15.2)
Index dose, n (%)			
150 mg	91 (59.9)	78 (65.5)	13 (39.4)
300 mg	61 (40.1)	41 (34.5)	20 (60.6)
Physician specialty, n (%)			
Rheumatology	121 (79.6)	94 (79.0)	27 (81.8)
Internal medicine	8 (5.3)	5 (4.2)	3 (9.1)
Treatment history, n (%)			
NSAID	38 (25.0)	27 (22.7)	11 (33.3)
Oral corticosteroid	46 (30.3)	36 (30.3)	10 (30.3)
csDMARD	45 (29.6)	38 (31.9)	7 (21.2)
tsDMARD	9 (5.9)	5 (4.2)	4 (12.1)
Biologic	95 (62.5)	78 (65.5)	17 (51.5)
Etanercept	31 (20.4)	23 (19.3)	8 (24.2)
Adalimumab	30 (19.7)	27 (22.7)	3 (9.1)
Certolizumab	22 (14.5)	19 (16.0)	3 (9.1)
Golimumab	17 (11.2)	13 (10.9)	4 (12.1)
Infliximab	15 (9.9)	12 (10.1)	3 (9.1)
Ustekinumab	3 (2.0)	3 (2.0)	0 (0.0)
Comorbidities, n (%)			
Rheumatoid arthritis	29 (19.1)	21 (17.6)	8 (24.2)
Hypertension	29 (19.1)	24 (20.2)	5 (15.2)
Other skin diseases	28 (18.4)	23 (19.3)	5 (15.2)
Hyperlipidemia	25 (16.4)	19 (16.0)	6 (18.2)
Fatigue	19 (12.5)	13 (10.9)	6 (18.2)
Depression	18 (11.8)	13 (10.9)	5 (15.2)
Cancer	17 (11.2)	12 (10.1)	5 (15.2)
Psoriatic arthritis	17 (11.2)	13 (10.9)	4 (12.1)
Diabetes	10 (6.6)	9 (7.6)	1 (3.0)
Anxiety	8 (5.3)	6 (5.0)	2 (6.1)
Obesity	6 (3.9)	4 (3.4)	2 (6.1)

AS, ankylosing spondylitis; csDMARD, conventional synthetic disease-modifying antirheumatic drug; NSAID, nonsteroidal anti-inflammatory drug; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.

Conclusions: In this retrospective, administrative claims-based study, the majority of patients with AS initiated secukinumab treatment with a loading regimen. Although only the 150-mg dose of secukinumab is approved for the treatment of AS, almost 40% of patients received the 300-mg dose, indicating a need to better understand patient and treatment characteristics for secukinumab in patients with AS. The results of this study provide early insights into real-world use of secukinumab with and without a loading regimen in patients with AS in the United States.

Acknowledgements: This study was sponsored by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

Disclosure of Interest: K. Oelke Consultant for: Novartis, Speakers bureau: Amgen, AbbVie, Bristol-Meyers Squibb, Pfizer, G. Chun Employee of: Novartis, Y. Li Employee of: Novartis, X. Liu Consultant for: Novartis, Employee of: KMK Consulting, Inc, Y. Park Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.1543

THU0377 LOW DOSE IL-2 THERAPY CAN RECOVERY TH17/TREG CELL BALANCE IN PATIENTS WITH SPONDYLOARTHROPATHY THROUGH INCREASING REGULATORY T CELLS NUMBERS

F. Jinnan[1], X. Dan[1], C. Qianqian[1], Q. Kaili[1], G. Chong[2], L. Xiaofeng[1]. *[1]Department of Rheumatology, The Second Hospital of Shanxi medical University, Taiyuan, China; [2]Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, Boston, American Samoa*

Background: The imbalance in the number of Th17 and Treg cells is suggested to be associated with the pathogenesis of SpA. Recent studies have shown that interleukin-23 (IL-23) and Th17 play a crucial role in the pathogenesis of SpA. However the status of CD4+CD25+Foxp3+Treg cells which exert immunoregulatory functions are remains to investigate.

Objectives: To explore the status of the immunologic balance between Th17 cells and Treg cells in patients with SPA, and to assess the effect of low dose IL-2 on the peripheral CD4+ T cells.
Methods: Two hundred and two patients, who met the Assessment of Spondyloarthritis International Society (ASAS) criteria were enrolled and given conventional therapy, including Nonsteroidal Anti-inflammatory Drugs (NSAIDs), biological agents, Sulfasalazine, glucocorticoid. Eighty seven patients were not only given conventional therapy, but also injected subcutaneously low-dose IL-2 (50 WIU/day for 5 days). Clinical and laboratory indicators were compared before and after IL-2 treatment. The $CD4^+$ T cells in peripheral blood were measured by multicolor flow cytometry. The side effects were observed in the course of therapy.
Results: The absolute number and ratio of CD4 + CD25 + FOXp3 + regulatory T cells in peripheral blood of patients with SPA was significantly decreased compared with the healthy control group, (25.13 (18.76,37.37) vs. 33.06 (22.87,42.33), $P<0.001$); Th17/Treg (0.29 (0.18, 0.49) vs. 0.20 (0.15, 0.34), P=0.001). The absolute number of Treg cells increased more than 3-times (22.70 (14.47, 30.10) vs.67.87 (48.21, 105.82), $p<0.001$) after 5 days of low-dose IL-2 treatment. Th17/Treg was significantly higher (0.32 (0.18, 0.57) vs. 0.20 (0.15, 0.34), $P<0.001$) before treatment compared with healthy controls.
Conclusions: The decrease of CD4 + CD25 + FOXp3 + Treg cells might play a key role in the pathogenesis of SpA. Low dose IL-2 therapy can restore and maintain the balance of Th17 and Treg cells by increasing Treg cells numbers selectivity. The therapy is safe. More attention should be paid on the long term benefits of low-dose IL-2 therapy in the further research.
References:
[1] Wu Y, Ren M, Yang R, Liang X, Ma Y, Tang Y, et al. Reduced immunomodulation potential of bone marrow-derived mesenchymal stem cells induced CCR4 + CCR6 + Th/Treg cell subset imbalance in ankylosing spondylitis. Arthritis Res Ther. 2011;13:R29.
[2] Jandus C, Bioley G, Rivals JP, Dudler J, Speiser D, Romero P. Increased numbers of circulating polyfunctional Th17 memory cells in patients with seronegative spondylarthritides. Arthritis Rheum. 2008;58:2307–17.
[3] Wendling D, Guillot X, Prati C. The IL-23/Th 17 pathway in spondyloarthritis: the royal road. Joint Bone Spine 82(1), 1–4 (2015).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2648

THU0378 IMPACT OF THE ADALIMUMAB PATIENT SUPPORT PROGRAM ON CLINICAL OUTCOMES IN ANKYLOSING SPONDYLITIS: RESULTS FROM THE COMPANION STUDY

L. Bessette[1], C. Thorne[2], B. Millson[3], K. Charland[3], K. Donepudi[3], T. Gaetano[4], V. Remple[4], M. Latour[4], M.-C. Laliberté[4]. *[1]Department of Medicine, Laval University, Quebec City; [2]Southlake Regional Health Centre, Newmarket; [3]QuintilesIMS, Kirkland; [4]AbbVie Corporation, St. Laurent, Canada*

Background: Adalimumab (ADL) is a TNF-alpha inhibitor indicated for various inflammatory autoimmune diseases including ankylosing spondylitis (AS). Patients receiving ADL in Canada are eligible to enroll in the AbbVie Care patient support program (PSP) which provides them with personalized services including ongoing care coach calls (CCC). In a previous study, rheumatology patients enrolled in Abbvie Care receiving CCC demonstrated significantly greater persistence and adherence to ADL than patients that did not receive CCC (no-CCC).
Objectives: The objective of this study was to examine if ADL patients receiving CCC through the ADL PSP had an increased likelihood of achieving controlled disease state as determined by a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score <4 compared to those not receiving CCC.
Methods: A longitudinal analysis using de-identified aggregate-level data collected through the AbbVie Care PSP was performed. Probabilistic matching was used to link patient-level records from the ADL PSP database to records from the QuintilesIMS longitudinal prescription transactions database (LRx). Patients were indexed on the date of their first ADL transaction between January 2010 and October 2015. The ADL PSP database included patient measurements of the BASDAI, a measure of disease activity. To be eligible, patients had to have a baseline BASDAI measurement between 90 days before and 30 days after their index date and have had a follow-up BASDAI measurement 6 to 18 months later. Only patients that were confirmed to be persistent on ADL as confirmed through the LRx records were included in the comparison. Controlled disease (BASDAI <4) at the time of the follow-up BASDAI assessment was compared in patients having received CCC and patients without CCC. Robust Poisson regression was used to estimate the adjusted relative risk (RR) of controlled disease. Analyses were adjusted for patient age group, sex, region, prior biologic use, days lapsed between BASDAI assessments, and baseline disease control status category.
Results: A total of 249 AS patients met eligibility criteria and 123 (49%) of these had received CCC. Of the 249 patients, 184 (74%) had controlled disease (BASDAI <4) at the follow-up assessment, 98 (80%) in the CCC group and 86 (68%) in the no CCC group. In the multivariable regression analysis, there was a 23% increased likelihood of achieving controlled disease in the CCC group relative to the group without CCC (RR=1.23, 95% confidence interval: 1.06–1.42; p-value =0.0055).
Conclusions: AS patients receiving tailored services through the ADL PSP in the form of care coach calls have an increased likelihood of achieving controlled disease within 6 to 18 months. These results may help refine interventions aiming at improving clinical outcomes in AS patients.
Acknowledgements: Project management support for this study was provided by Jennifer Glass from QuintilesIMS. Analytical support was provided by Marc Duclos from QuintilesIMS. This support was funded by AbbVie.
Disclosure of Interest: L. Bessette Grant/research support from: Abbvie, Amgen, BMS, Janssen, Roche, UCB, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant for: AbbVie, Amgen, BMS, Janssen, Roche, UCB, Pfizer, Celgene, Lilly, Novartis, Speakers bureau: AbbVie, Amgen, BMS, Janssen, Roche, UCB, Pfizer, Merck, Celgene, Lilly, Novartis, C. Thorne Grant/research support from: Abbvie, Amgen, Celgene, CaREBiodam, Lilly, Novartis, Pfizer, Consultant for: AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, Speakers bureau: Medexus/Medac, B. Millson Consultant for: AbbVie, Employee of: QuintilesIMS, K. Charland Consultant for: AbbVie, Employee of: QuintilesIMS, K. Donepudi Consultant for: AbbVie, Employee of: QuintilesIMS, T. Gaetano Shareholder of: AbbVie, Employee of: AbbVie, V. Remple Shareholder of: AbbVie, Employee of: AbbVie, M. Latour Shareholder of: AbbVie, Employee of: AbbVie, M.-C. Laliberté Shareholder of: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.6529

THU0379 IMPACT OF TIME SINCE DIAGNOSIS, AGE, AND NUMBER OF PRIOR NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON 52-WEEK CLINICAL RESPONSE TO ADALIMUMAB IN PATIENTS WITH ANKYLOSING SPONDYLITIS

J. Sieper[1], A. Deodhar[2], M. Hojnik[3], Y. Zhang[4], M. Dougados[5]. *[1]Charité Universitätsmedizin Berlin, Berlin, Germany; [2]Oregon Health & Science University, Portland, United States; [3]AbbVie, Ljubljana, Slovenia; [4]AbbVie Inc., N Chicago, United States; [5]René Descartes University and Hôpital Cochin, Paris, France*

Background: Ankylosing spondylitis (AS) patients (pts) were found to respond better to TNF inhibitors (TNFi) if treated early in the disease course.[1] The actual disease onset and hence disease duration is not always known. Previously, younger age was found to have the largest positive impact on clinical outcomes following 12 weeks (wks) of adalimumab (ADA) treatment.[2]
Objectives: The objective of this analysis was to examine the impact of time since diagnosis, age, and number of prior NSAIDs as surrogates for disease duration on clinical outcomes in AS pts from ATLAS trial treated with ADA for 52 wks.
Methods: ATLAS[3,4] was a phase 3 randomized double-blind placebo (PBO)-controlled trial evaluating the safety and efficacy of originator ADA in pts with active AS who failed NSAID therapy. In this post hoc analysis, pts who received at least one dose of ADA during the PBO-controlled period or open label extension and received prior NSAID(s) at baseline (BL) were categorized by BL: (1) time since diagnosis (<2 vs ≥ 2; <5 vs ≥ 5; <10 vs ≥ 10 years [y]), (2) age (<35, 35–45, and >45 y), and (3) number of prior NSAIDs (≤ 2 vs >2). The effect of time since diagnosis, age, and number of prior NSAIDs on AS outcome measures following 52 wks of ADA treatment was examined.
Results: At wk 52, 274 pts had received at least one dose of ADA and had at least one prior NSAID at BL. A majority of pts were ≥ 5 y since AS diagnosis (188 [68.6%]), ≤ 45 y of age (163 [59.5%]), HLA-B27+ (213 [77.7%]), and had ≤ 2 prior NSAIDs (158 [57.7%]). Pts with shorter time since diagnosis were generally younger (late thirties). Across all subcategories, $>70\%$ of pts were male. The BL disease activity measures were numerically similar across most categories. Following 52 wks of ADA treatment, the proportions of pts achieving ASAS20 and ASAS40 responses were numerically higher and mean decreases in BASDAI and BASFI scores from BL larger in subcategories with shorter time since diagnosis, younger age, and fewer prior NSAIDs (Table). There were significant differences in ASAS40, BASDAI, and BASFI scores between time since diagnosis (<2 vs ≥ 2 and <5 vs ≥ 5 y) and age (<35 vs >45 y) subcategories.

Table. Clinical Responses Following 52 Weeks of ADA Exposure in Patients Categorized by Time Since Diagnosis, Age, and Prior NSAID(s).

Outcome measure	Time since diagnosis (years)						Age (years)			Prior NSAID(s)	
	<2 (n=53)	≥2 (n=221)	<5 (n=86)	≥5 (n=188)	<10 (n=150)	≥10 (n=124)	<35 (n=76)	35–45† (n=87)	>45† (n=111)	≤2 (n=158)	>2 (n=116)
ASAS20, n (%)	39 (73.6)	153 (69.2)	64 (74.4)	128 (68.1)	105 (70.0)	87 (70.2)	58 (76.3)	63 (72.4)	71 (64.0)	115 (72.8)	77 (66.4)
ASAS40, n (%)	35 (66.0)	104 (47.1)*	53 (61.6)	86 (45.7)*	83 (55.3)	56 (45.2)	47 (61.8)	46 (52.9)	48 (41.4)**	86 (54.4)	53 (45.7)
ΔBASDAI, mean (SD)‡	-4.1 (2.6)	-3.0 (2.5)*	-3.9 (2.5)	-2.9 (2.5)*	-3.5 (2.7)	-2.9 (2.4)	-3.7 (2.7)	-3.2 (2.6)*	-2.8 (2.4)***	-3.3 (2.5)	-3.0 (2.6)
ΔBASFI, mean (SD)‡	-2.8 (2.4)	-2.2 (2.0)*	-2.7 (2.2)	-2.1 (2.0)**	-2.4 (2.3)	-2.1 (1.9)*	-2.7 (2.4)	-2.3 (1.9)*	-2.0 (2.0)***	-2.5 (2.1)	-2.0 (2.1)

P-values are based on Pearson's Chi-square test for comparison: ***, $P<.001$; **, $P<.01$; *, $P<.05$.
†P-values based on comparison with <35 years.
‡Change from baseline to week 52.
NSAID = Non-Steroidal Antiinflammatory drug; ASAS = Assessment of SpondyloArthritis international Society classification criteria; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; SD = Standard Deviation; BASFI = Bath Ankylosing Spondylitis Functional Index.

Conclusions: Following 52 wks of ADA treatment, shorter time since diagnosis and younger age were associated with greater clinical responses and improvements in disease activity and functionality. Although younger age (<35 vs >45 y) had significant positive impact on the clinical outcomes similar to wk 12 results, shorter time since diagnosis (<2 vs ≥ 2 and <5 vs ≥ 5 y) was also associated with better 52-wk clinical outcomes. These results suggest that early effective treatment intervention may improve long-term clinical outcomes in AS pts.
References:
[1] Rudwaleit, M. et al. Ann Rheum Dis, 2004; 63:665–70.
[2] Sieper, J. et al., Arthritis Rheumatol. 2016; 68 (suppl 10).
[3] Van der Heijde, D. et al., Ann Rheum Dis, 2007; 67:1218–21.

[4] Sieper, J. et al., Ann Rheum Dis, 2012; 71:700–6.
Acknowledgements: AbbVie funded the study (NCT00085644), contributed to its design, and participated in data collection, analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.
Disclosure of Interest: J. Sieper Grant/research support from: AbbVie, Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sun Pharma, and UCB, Consultant for: AbbVie, Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sun Pharma, and UCB, Speakers bureau: AbbVie, Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sun Pharma, and UCB, A. Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, Glaxo-Smith-Kline, Merck-Sharp-Dohme, Novartis, Pfizer, Sun Pharma, and UCB, Consultant for: AbbVie, Amgen, Eli Lilly, Glaxo-Smith-Kline, Merck-Sharp-Dohme, Novartis, Pfizer, Sun Pharma, and UCB, Speakers bureau: AbbVie, Amgen, Eli Lilly, Glaxo-Smith-Kline, Merck-Sharp-Dohme, Novartis, Pfizer, Sun Pharma, and UCB, M. Hojnik Shareholder of: AbbVie, Employee of: AbbVie, Y. Zhang Shareholder of: AbbVie, Employee of: AbbVie, M. Dougados Grant/research support from: AbbVie, Lilly, Merck, Novartis, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Lilly, Merck, Novartis, Pfizer, Sanofi, and UCB, Speakers bureau: AbbVie, Lilly, Merck, Novartis, Pfizer, Sanofi, and UCB
DOI: 10.1136/annrheumdis-2017-eular.1302

THU0380 RESULTS OF A REAL LIFE DOSE-REDUCTION STRATEGY FOR ANTI-TNFALPHA INHIBITORS IN A COHORT OF PATIENTS WITH SPONDYLOARTHRITIS

M.C. Castro-Villegas[1,2], P. Font-Ugalde[1,2,3], M. Romero-Gomez[1,2], M. Arredondo-López[3], E.C. López-Medina[1], R. Ortega-Castro[1,2], J. Calvo-Gutierrez[1,2,3], A. Escudero-Contreras[1], E. Collantes-Estévez[1,2,3].
[1]Reina Sofía University Hospital; [2]IMIBIC; [3]Universidad de Córdoba, Cordoba, Spain

Background: Published reports suggest that patients with Spondyloartrhitis (SpA) in remission under treatment with TNFalpha inhibitors (TNFi) could obtain the same benefit at lower dose of the drug.
Objectives: To evaluate effectiveness of a strategy of dose reduction of TNFi in SpA patients in clinical remission and to explore baseline characteristics predictive of maintenance of the response.
Methods: Retrospective observational study, including patients with SpA meeting ASAS criteria treated with TNFi following a dose optimization protocol (lower doses or longer intervals than aproved), from 2008 to 2015. Criteria for optimization was patients with BASDAI≤2 and/or C reactive protein level (CRP)≤5 mg/L for at least 6 months. Patients who relapsed (BASDAI>2 and/or CRP>5mg/L) returned to standard dose. Clinical/analytical parameters and drug's survival time until relapse were recorded. SPSSv.17 software was used for contrast means. Survival Kaplan-Meyer curves was analysed.
Results: 149 SpA patients treated with TNFi, 32/149 patients (21.5%) included in optimization protocol. 27 patients (84.37%) with increased interval between doses, remaining with reduced dosification. Table 1 shows baseline characteristics of patients on optimization group (mean±SD or proportion). 18/32 patients (56.2%,IC:39.01–73.4) maintained clinical remission with optimized dose at 36.5 months (median). Table 2 shows activity parametres of both relapsed and maintained response patients. There were either baseline differences or at optimization time between patients who maintained remission and not, but relapsed patients showed higher CRP at optimization time, without statistically significant differences. 72.2% (13/18) of patients on sutained remission were naive for TNFi, although no significant difference compared to switcher patients on the median survival (31.9 vs 20.9 months, P=0.9). No baseline predictor of sustained response at optimized dose were found. CRP<5 mg/L at optimization time showed a trend towards longer survival (43.4 vs 13.3 months), without differences statistically significant (p=0.09).
Conclusions: Optimization of TNFi in SpA is possible and allows up to half of patients to maintain clinical remission, but no baseline factors predictors of sustained response after optimization was found.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2633

Table 1

	Optimized patients (n=32)	
Age (years)	47.2±10.6	
Gender (%) Male/Female	84.4/15.6	
Disease duration (years)	12.2±10.4	
	Baseline	Optimization time
BASDAI (0–10)	4.2±2,6	2.1±2.2
BASFI (0-10)	4±2.7	2.8±2.9
ESR (mm/1°h)	19±20.1	8.5±8.5
CRP (mg/L)	13.1±18.7	6.4±9.7
Number of previous TNFi	0.3±0.6	
Current TNFi (%)		
Infliximab	31.3%	
Adalimumab	21.9%	
Etanercept	25%	
Golimumab	21.9%	

Table 2

	Not-sustained remission (n=14)			Sustained Remission (n=18)		
	Basaline	Optimization time	Flare time	Baseline	Optimization time	Last visit
BASDAI (0–10)	3.8±2.4	2±1.8*	2.4±1.9*#	4.4±2.8*	2.1±2.5*	1.7±1.4*
BASFI (0–10)	4.3±2.8	2.8±2.8*	2.9±3*	3.7±2.6	2.8±3.1	2.1±1.6*
ESR (mm/1°h)	17.1±22.5	9.3±11.1	10.2±8.3	20.4±18.8	7.8±6.1*	8±6.4*
CRP (mg/L)	10.9±12.2	9.7±12.4	3.4±5.7*#	14.6±22.5	3.7±6.1*	2.5±5*

Statistical significant differences: *compare to baseline; #compared to optimization time.

THU0381 CERTOLIZUMAB PEGOL IS EFFECTIVE IN UVEITIS ASSOCIATED TO SPONDYLOARTHRITIS REFRACTORY TO OTHER TUMOUR NECROSIS FACTOR INHIBITORS

M.V. Hernández[1], M. Mesquida[2], V. Llorens[2], M. Sainz de la Maza[2], R. Blanco[3], V. Calvo[3], O. Maiz[4], A. Blanco[5], A. Urruticoechea[6], J.R.D.D. Jiménez de Aberásturi[7], P. Ahijado[8], E. Judez[9], P. Tejón[10], S. Peña[11], A. Adan[2], R. Sanmartí[1]. *[1]Rheumatology; [2]Ophtalmology, Hospital Clínic, Barcelona; [3]Rheumatology, Hospital Marqués de Valdecilla, Santander; [4]Rheumatology; [5]Ophtalmology, Hospital Universitario Donostia, San Sebastián; [6]Rheumatology, Hospital Can Misses, Ibiza; [7]Rheumatology, Txagorritxu Hospital, Vitoria; [8]Rheumatology, Hospital Universitario Infanta Elena, Madrid; [9]Rheumatology, Complejo Hospitalario Universitario de Albacete, Albacete; [10]Rheumatology; [11]Ophtalmology, Hospital Universitario General de Castellón, Castellón, Spain*

Background: Uveitis is one of the most common extra-articular manifestations of patients with spondyloarthritis (SpA). In severe cases, uveitis may require the use of biological therapy, primarily tumor necrosis factors inhibitors (TNFi), being the most currently used infliximab and adalimumab. However, another TNFi such as certolizumab pegol (CZP), with indication for SpA patients, could be an effective option in cases of inefficacy or adverse events to other TNFi, as we have previously reported (1).
Objectives: Our objective is to analyze the effectiveness and the safety profile of CZP in patients with refractory SpA-associated-uveitis
Methods: Observational, multicentric, retrospective study. We selected all patients with a diagnosis of SpA (including ankylosing spondylitis (AS), psoriatic arthritis (PsA), non-radiographic axial SpA (nr-axSpA) and SpA associated to inflammatory bowel disease (IBD-SpA)) who had refractory uveitis (confirmed by an Ophthalmologist) as main extra-articular manifestation, and who received CZP for at least 6 months. Variables analyzed: age, sex, diagnosis, type of uveitis, duration since the first uveitis episode and number of eyes affected; previous treatment (NSAID, disease-modifying anti-rheumatic drugs (DMARDs), immunossuppressive or biological therapy); outcome, and time to follow-up.
Results: Twenty-four eyes of 13 patients (10 men); age 49.5±11.7 (range 29–71 years) were included in the study. Diagnosis were: seven AS, four PsA, one nr-axSpA, and one IBD-SpA. Type of uveitis: 9 anterior, 3 panuveitis, and 1 intermediate uveitis. Mean disease duration was 151±117.1 months (range 5–420). 84.6% patients had previously received biological therapy (46.1% ≥2 biological agents). 61.5% received CZP in monotherapy and 5 patients received concomitant treatment: 4 methotrexate and 1 azathioprine. In all cases CZP was started due to inefficay to previous treatment except for 2 cases whose primary reason was the occurrence of adverse events (one injection site reaction and one development of relapsing polychondritis). After a follow-up of 13.1±6.6 months (range 6–27), 9 patients are still on CZP treatment. Ten eyes showed improvement of visual acuity (41.7%), 10 remained stable and 2 worsened. During the follow-up no serious adverse events were reported. Four cases withdrew CZP treatment: 2 due to worsening of articular symptoms but with no uveitis activity; 1 due to macular edema and 1 due to uveitis activity. One patient switch to infliximab, one to golimumab, and 2 required switch to tocilizumab. In all 13 patients except 2, CZP achieved a good control of SpA activity.
Conclusions: CZP demonstrated effectiveness in patients with uveitis-associated to SpA refractory to previous TNFi treatment.
References:
[1] Llorenç V et al. Ocul Immunol Inflamm. 2016; 24: 167–72.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4425

THU0382 CHANGE IN SACROILIAC JOINT STRUCTURAL RADIOGRAPHIC DAMAGE AFTER TWO YEARS OF ETANERCEPT THERAPY IN COMPARISON TO A CONTEMPORARY CONTROL COHORT IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

M. Dougados[1], W.P. Maksymowych[2], R. Landewe[3], A. Molto[1], P. Claudepierre[4], M. de Hooge[5], R.G. Lambert[2], R. Bonin[6], J.F. Bukowski[6], H. Jones[6], I. Logeart[7], R. Pedersen[6], A. Szumski[8], B. Vlahos[6], D. van der Heijde[5]. *[1]Paris Descartes University, Hôpital Cochin, Paris, France; [2]University of Alberta, Edmonton, Canada; [3]Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands; [4]Universite Paris Est Creteil, Creteil, France; [5]Leiden University Medical Center, Leiden, Netherlands; [6]Pfizer, Collegeville, United States; [7]Pfizer, Paris, France; [8]InVentiv Health, Princeton, United States*

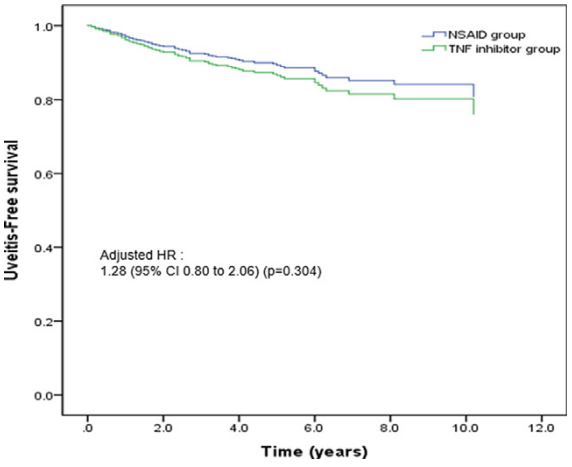
Background: Despite the well-known symptomatic and anti-inflammatory effect

of TNF inhibitors in axial SpA (axSpA), demonstrating a structural effect is challenging.
Objectives: To compare 2 yrs of radiographic sacroiliac joint (SIJ) changes in pts receiving etanercept (ETN) in a clinical trial to similar pts not receiving biologics in a cohort study.
Methods: Pts had recent onset non-radiographic (nr)-axSpA fulfilling ASAS criteria. Study group: pts receiving ETN 50 mg once weekly for 2 yrs in EMBARK (NCT01258738). Control group: pts in an ongoing longitudinal cohort study not receiving biologics for 2 yrs (DESIR, NCT01648907). Outcome measure: change in x-ray SIJ score per mNY criteria (0–4 per SIJ). X-rays were read by 3 experienced readers unaware of image chronology and pt group. Primary endpoint: change (mean of 3 readers) in total SIJ score (-8 to +8). Binary endpoints: (1) shift from baseline (BL) mNY+ to wk-104 mNY- and vice versa; (2) change in SIJ score $\geq$1 (left or right SIJ); (3) change in SIJ score $\geq$1 in $\geq$1 SIJ, with change from 0 to 1 and from 1 to 0 considered no change. Treatment effect was analyzed without and with adjustment for the baseline (BL) covariates of sex, symptom duration, smoking status, HLA-B27 status, ASDAS-CRP, SPARCC MRI SIJ score, and SIJ radiography score.
Results: At BL, the control (DESIR, N=197) and ETN (EMBARK, N=164) cohorts differed significantly in all covariates listed above. The difference in change in total SIJ score for control vs ETN, adjusted for covariates, was small but significant: least-squares mean (95% CI): 0.08 (-0.03, 0.20) vs -0.14 (-0.26, -0.01); p=0.008. The table presents x-ray changes. When adjusted for covariates, the mean difference between control and ETN was significant for 2 of the 3 binary endpoints (table).
Conclusions: This analysis confirms the slow rate of radiographic SIJ progression over 2 yrs in nr-axSpA. The observed data suggest a lower rate of progression with ETN than without a TNF inhibitor.
Disclosure of Interest: M. Dougados Grant/research support from: Pfizer, Abbvie, UCB, Merck, Lilly, Sanofi, Consultant for: Pfizer, Abbvie, UCB, Merck, Lilly, Sanofi, W. P. Maksymowych Grant/research support from: AbbVie, Pfizer, Sanofi, Consultant for: AbbVie, Amgen, Eli Lilly, Janssen Pharmaceutica, L.P, Novartis, Pfizer, Sanofi, UCB, R. Landewe Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, Wyeth, Consultant for: Abbott/Abbvie, Ablynx, Amgen, Astra-Zeneca, BMS, Celgene, Janssen (formerly Centocor), Galapagos, GSK, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-plough, TiGenix, UCB, Wyeth, Employee of: Is a director of Rheumatology Consultancy BV, A. Molto Grant/research support from: Pfizer, UCB, Consultant for: Abbvie, BMS, MSD France- Merck, Pfizer, UCB, P. Claudepierre Grant/research support from: Pfizer, Roche-Chugai, MSD, Consultant for: Abbvie, BMS, Celgene, Janssen, Novartis, Merck, Pfizer, Roche, UCB, M. de Hooge: None declared, R. G. Lambert Consultant for: Bioclinica, R. Bonin Shareholder of: Pfizer, Employee of: Pfizer, J. Bukowski Shareholder of: Pfizer, Employee of: Pfizer, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, I. Logeart Shareholder of: Pfizer, Employee of: Pfizer, R. Pedersen Shareholder of: Pfizer, Employee of: Pfizer, A. Szumski Employee of: InVentiv Health, B. Vlahos Shareholder of: Pfizer, Employee of: Pfizer, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boeringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB, Employee of: Director of Imaging Rheumatology bv.
DOI: 10.1136/annrheumdis-2017-eular.1860

THU0383 INCIDENCE OF UVEITIS IN NON-STEROIDAL ANTI-INFLAMMATORY DRUGS VERSUS TUMOR NECROSIS FACTOR INHIBITORS USERS AMONG PATIENTS WITH ANKYLOSING SPONDYLITIS: A RETROSPECTIVE COHORT STUDY

M.J. Kim, E.E. Lee, E.Y. Lee, Y.W. Song, E.B. Lee. *Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic Of*

Background: Uveitis associated with ankylosing spondylitis (AS) often recurs and may lead to ocular complications. It remains to be known whether non-steroidal anti-inflammatory drugs (NSAIDs) or TNF inhibitors (TNFi) is more effective in reducing the recurrence of uveitis in patients with AS.
Objectives: To evaluate the effect of NSAIDs and TNFi on preventing recurrence of uveitis in patients with AS.
Methods: This retrospective cohort study included 1061 patients diagnosed with AS at Seoul National University Hospital between January 2004 and December 2015. Patients' clinical factors and laboratory findings were collected from the patients' electric medical records. Patients were divided into those who were treated with NSAIDs (n=623) or TNFi (n=438) which included etanercept, adalimumab, infliximab and golimumab. The incidence rates of new-onset uveitis during each treatment was compared using Cox proportional hazard model after adjusting age, sex, disease duration, history of uveitis, smoking status, ESR, CRP, and HLA-B27. Propensity-score matched comparison was also performed as sensitivity analysis (n=168 in the TNFi group and n=168 in the NSAID group).
Results: Among the 1061 patients, those in the TNFi group had longer disease duration (11.75±7.14 vs 6.22±4.42 years), higher ESR, CRP level (40.97±33.87 vs 23.32±22.09 mm/h, 2.69±3.41 vs 1.12±1.93 mg/L, respectively) and higher proportion of patients who had previous history of uveitis before the treatment (22.4 vs 15.4%). The incidence rates of uveitis were 3.60 (95% CI 2.97 to 4.42) per 100 person-year in the NSAID group and 6.03 (95% CI 5.15 to 7.04) per 100 person-year in the TNFi group. The adjusted hazard ratio for the new-onset uveitis during the treatment in the TNFi group versus the NSAID group was 1.28 (95% CI 0.80 to 2.06) (p=0.304). When compared with NSAID group, etanercept group showed higher incidence of uveitis than the other TNFi: etanercept (HR 1.96 [1.41 to 2.74]), adalimumab (HR 0.65 [0.40 to 1.05]), infliximab (HR 0.50 [0.22 to 1.14]) and golimumab (HR 0.79 [0.25 to 2.50]). The propensity score-matched population was also consistent with the crude comparison between NSAID group and TNFi group (HR 1.29 [0.73 to 2.28]) (p=0.388).



Conclusions: The effect of TNFi on reducing the incidence of uveitis is comparable to NSAIDs in patients with AS. Uveitis occurred more commonly with treatment with etanercept compared with the other treatments.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3424

THU0384 THE EFFECT AND SAFETY OF YISAIPU (YISAIPU) IN THE TREATMENT OF PATIENTS WITH NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN CHINA

M. Zhao[1], G. Shi[2], Y. Tao[3], X. Wang[4], S. Cao[1], Z. Lin[1], Z. Liao[1], Q. Kong[4], J. Gu[1]. *[1]Rheumatology department, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou; [2]Rheumatology department, The First Affiliated Hospital of Xiamen University, Xiamen; [3]Rheumatology department, The Second Affiliated Hospital of Guangzhou Medical University; [4]Radiology department, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease, which includes AS and nr-axSpA. Anti-TNF-α agents, such as Yisaipu (Yisaipu) are frequently used in nr-axSpA patients in China, but the related data is limited.
Objectives: The aim of this research is to assess the efficacy and safety of Yisaipu in the treatment of patients with nr-axSpA in China.
Methods: The inclusion of study population consisted of 150 patients who met the ASAS criteria for axial SpA but not the modified New York radiographic criteria for AS, had a score of $\geq$4 on the BASDAI or a score of $\geq$2.1 on the ASDAS-CRP and had been treated unsuccessfully with $\geq$1 NSAIDs for 4-week. Patients were assigned to receive Yisaipu (made in China) 50 mg/week and continued background NSAID treatment for 24 weeks (open-label study). At week 24, the

Abstract THU0382 – Table 1. Observed Radiographic Changes from BL to Week 104

Endpoint	Cohort	Improved n/N (%)	Worsened n/N (%)	Mean Difference* (95% CI)†	Mean differences (Control – ETN) (95% CI)
mNY criteria	Control	3/193 (1.6)	6/193 (3.1)	1.6% (-1.5, 4.6)	3.4% (-0.7, 7.5)†
	ETN	4/161 (2.5)	1/161 (0.6)	-1.9% (-4.6, 0.9)	4.7% (-0.5, 9.9)‡
Δ $\geq$1 grade in $\geq$1 SIJ	Control	21/193 (10.9)	36/193 (18.7)	7.8% (0.1, 15.4)	9.6% (-0.9, 20.2)†
	ETN	19/161 (11.8)	16/161 (9.9)	-1.9% (-9.1, 5.4)	18.2% (5.6, 30.9)‡§
Δ $\geq$1 grade in $\geq$1 SIJ; Δ from 0 to 1 and 1 to 0 considered no Δ	Control	16/193 (8.3)	29/193 (15.0)	6.7% (-0.1, 13.5)	7.4% (-2.1, 16.8)†
	ETN	15/161 (9.3)	14/161 (8.7)	-0.6% (-7.2, 6.0)	16.4% (5.1, 27.8)‡§

Based on 2 of 3 readers assigning same category; otherwise considered no change. Some patients started with lowest possible score and could not improve. Δ, change. *Percent pts with worsening – percent pts with improvement. †One-way ANOVA. ‡Adjusted for covariates listed in Methods. § P=0.005.

primary efficacy end point was the improvement of ASDAS-CRP. Secondary end points included ASAS 20, ASAS 40, ASAS 5/6, ASAS partial remission and BASDAI. Safety was evaluated during scheduled visits.

Results: 123 patients with active nr-axSpA were enrolled between April 19, 2014, and July 10, 2015. The mean age of the 123 nr-SpA patients was (25.3±5.9) years. The ASDAS-CRP and BASDAI decrease from 2.7±0.9 to 0.7±0.4, from 4.5±1.5 to 0.9±0.8, respectively between weeks 0 and 24. The patients achieved the ASDAS-CRP<2.1 was 96.7%. ASDAS-CRP major and important improvement were achieved by 41.4%, 79.8%, respectively at weeks 24. ASAS 20, ASAS 40, ASAS5/6 and ASAS partial remission were achieved by 75.0%, 54.8%, 64.5%, 89.3%, respectively at weeks 24. Yisaipu-treatment was associated with statistically significant improvements in all parameters, including BASFI, BASMI, PGA, PhGA, ESR and CRP concentrations. Most adverse events in the open-label phase were mild or moderate in severity.

Conclusions: Yisaipu was effective and well-tolerated during the 24-week study period and was associated with a significant improvement in the signs and symptoms of active nr-axSpA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3846

THU0385 ASSESSMENT OF RELATIONSHIP BETWEEN BELIEFS' ABOUT MEDICINES AND TREATMENT ADHERENCE IN ANKYLOSING SPONDYLITIS PATIENTS

M. Cinar[1], F.I. Cinar[2], E. Tekgoz[1], R. Horne[3], S. Yilmaz[1]. *[1]Department of Internal Medicine, Division of Rheumatology, University of Health Sciences, Gulhane Medical Faculty; [2]Gulhane School of Nursing, University of Health Sciences, Ankara, Turkey; [3]UCL School of Pharmacy, Centre for Behavioural Medicine, University College, London, United Kingdom*

Background: Ankylosing spondylitis (AS) is a chronic disease requiring long-term treatment. Patients' beliefs about medicines and treatment may affect their treatment adherence and treatment success.

Objectives: In this study, we aimed to investigate the relationship between beliefs about medicines and treatment adherence in AS patients.

Methods: This cross-sectional study was conducted in a single tertiary rheumatology clinic. One hundred and fifty three AS patients were enrolled to the study. Socio-demographic and medical characteristics of the patients were recorded to a patient interview form. In order to evaluate the general and personal views of the patients about drugs, the Turkish Translation of the Beliefs about Medicines Questionnaire (BMQ-T) (Cinar et al in 2016) was used. According to this survey, the beliefs about medicines are composed of the following sections: Specific Necessity, Specific Concerns, General Overuse and General Harm. Medication adherence was assessed by using the Morisky Green Levine Medication Adherence Scale (MGLS) (1986). Adherence was measured on a scale of 0 to 4, in which higher scores represent lower medication adherence and vice versa. Patients who reported a score of 0 on the MGLS were classified as adherent. All other patients were classified as nonadherent. Categorical variables were compared with Chi-square test, while continuous variables were compared with independent samples t test. To evaluate potential risk factors for non adherence, logistic regression method was used.

Results: The mean age of the patients was 35.15±8.19 years. The mean time from first symptom (disease duration) was 10.0±6.1 years. The vast majority of the patients (n=145; 94.8%) were male. One hundred patients (65.4%) were using NSAIDs and 83 patients (54.2%) were using anti-TNF. According to the MGLS scores, 56 (36.6%) patients were compatible with treatment, and 97 patients (63.4%) were found to be incompatible with the treatment. As the BMQ-T-Specific Necessity scores increased, drug compliance was also increased (p=0.006), on the other hand, as the BMQ-T-Specific Concerns, BMQ-T-General Overuse and BMQ-T-General Harm scores increased, drug compliance was decreased (p=0.023, 0.002, <0.001, respectively). There were significant positive correlations between Specific Concerns (p=0.002), General Overuse (p=0.031) and General Harm (p=0.024) score levels with the increase in patients' BASDAI score. While there was significant correlation between the disease duration and the General Overuse scores in the negative direction (p=0.016), there was significant correlation between the disease duration and the Specific Necessity scores in the positive direction (p=0.002). As 1 unit increase in the BMQ-T-Specific Necessity score decreased the risk of treatment nonadherence by 0.38 fold, on the other hand, 1 unit increase in the BMQ-T-General Harm score raised the risk to 3.21.

Conclusions: In our study, the belief of AS patients about the necessity of treatment they were using, found to increase treatment adherence, while harm potential of the treatment was decreasing the adherence. In other words, to enhance the treatment adherence of AS patients, it is essential to convince the patients about the necessity of treatment and relieve the anxiety they carry about potential adverse effects.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4091

THU0386 USE OF BIOLOGICS AND NSAIDS IN TREATING PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN THE US-BASED CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

P.J. Mease[1], D. van der Heijde[2], C. Karki[3], M. Liu[3], R. Pandurengan[3], Y. Park[4], J.D. Greenberg[3,5]. *[1]Seattle Rheumatology Associates, Seattle, WA, United States; [2]Leiden University Medical Center, Leiden, Netherlands; [3]Corrona, LLC, Southborough, MA; [4]Novartis, East Hanover, NJ; [5]New York University School of Medicine, New York, NY, United States*

Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease affecting the sacroiliac joints and spine. Treatment primarily consists of first-line nonsteroidal anti-inflammatory drugs (NSAIDs) and/or biologic therapy when disease activity persists despite NSAID therapy. Although many studies have evaluated the efficacy of these treatments, there are few studies that have characterized NSAIDs and/or biologic therapy among patients with axSpA in the United States.

Objectives: To characterize patients with axSpA treated with NSAIDs only, biologics only, or both NSAIDs and biologics at the time of enrollment in the US-based Corrona PsA/SpA Registry.

Methods: This study included all patients with axSpA diagnosed by the rheumatologist aged ≥18 years enrolled in the Corrona Registry between March 2013 and September 2016 who were treated with NSAIDs only, biologics only, or both NSAIDs and biologics at the time of enrollment (baseline). Patients fulfilled the Assessment of SpondyloArthritis international Society classification criteria.[1] Demographics, clinical characteristics, disease activity measures and treatment history were collected at enrollment and described for each group.

Results: As of September 2016, 359 patients with axSpA met the study inclusion criteria; at baseline, 224 patients (62.4%) were receiving NSAIDs (92 [25.6%] with NSAIDs only and 132 [36.8%] with both NSAIDs and biologics) and 135 patients (37.6%) were receiving biologics only. Baseline characteristics were similar across all treatment subgroups with regards to age, race and body mass index. Fewer females were treated with biologics (with/without NSAIDs) compared to the NSAIDs only group. At baseline, patients treated with NSAIDs or both NSAIDs and biologics were older, had longer duration of disease with worse disease activity (measured by ASDAS and BASDAI), functional impairment (BASFI and HAQ-DI) and had worse pain and fatigue compared to those treated with biologics only (Table 1). 88–96% of patients receiving biologics (with or without NSAIDs) had prior biologic use compared to only 25% of NSAIDs only group. Patients treated with biologics only reported decreased percentage of impairment while working, overall work impairment and activity impairment at baseline compared with patients treated with NSAIDs only and both NSAIDs and biologics.

Table 1. Baseline clinical and patient-reported characteristics of patients with axSpA in the Corrona PsA/SpA Registry stratified by NSAID and biologic use

Characteristics*	NSAIDs Only (n = 92)	Biologics Only (n = 135)	NSAIDs and Biologics (n = 132)
Age, years	48.6 (15.0)	46.1 (13.6)	48.1 (13.2)
White, n (%)	81 (91.0)	120 (93.0)	118 (92.9)
Male, n (%)	53 (58.9)	88 (65.7)	91 (70.5)
BMI, kg/m^2	29.4 (6.1)	29.7 (7.1)	28.7 (6.1)
Disease duration, years	18.3 (13.0)	16.1 (12.7)	19.2 (11.5)
History of prior csDMARD use, n (%)	23 (25.0)	55 (40.7)	47 (35.6)
History of prior biologic use, n (%)	24 (26.1)	130 (96.3)	117 (88.6)
ASDAS-CRP	2.1 (0.7)	1.9 (0.8)	2.1 (0.9)
BASDAI (0-10)	4.4 (2.5)	3.7 (2.5)	4.4 (2.6)
BASFI (0-10)	3.7 (2.9)	3.1 (2.8)	3.5 (2.9)
Patient pain (VAS 0-100)	49.9 (29.5)	37.3 (28.7)	44.4 (30.5)
Patient-reported fatigue (VAS 0-100)	47.1 (29.4)	45.7 (28.6)	49.9 (30.7)
Morning stiffness, n (%)	88 (95.7)	114 (84.4)	117 (88.6)
HAQ-DI (0-3)	0.7 (0.6)	0.5 (0.6)	0.6 (0.7)
WPAI-GH			
Absenteeism (% Work time missed)	5.3 (17.8)	5.5 (15.5)	7.5 (18.6)
Presenteeism (% Impairment while working)	28.7 (28.0)	21.7 (24.3)	29.4 (26.2)
Work Productivity (% Overall work impairment)	26.1 (26.4)	22.8 (25.7)	32.5 (37.7)
Activity Impairment (% Activity impairment)	41.0 (29.9)	31.4 (30.7)	39.8 (31.6)

ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score using C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BMI, body mass index; HAQ, Health Assessment Questionnaire; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment questionnaire: general health.

* All values are presented as "mean (SD)" unless otherwise stated. Current NSAID use included acetylsalicylic acid, celecoxib, diclofenac, ibuprofen, meloxicam, naproxen and others. Current biologic use included abatacept, adalimumab, anakinra, apremilast, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, secukinumab, tocilizumab and ustekinumab.

Conclusions: About two-thirds of patients with axSpA were treated with NSAIDs (with or without biologics) and about three-fourths of patients were treated with biologics (with or without NSAIDs) at enrollment. Patients that were already treated with biologics without NSAIDs at enrollment showed better measures of disease activity and PROs compared with the other treatment groups. Future research will assess changes in clinical and disease characteristics over time by treatment subgroup.

References:

[1] Rudwaleit M, et al. Ann Rheum Dis. 2009;68(6):777–783.

Acknowledgements: Corrona, LLC, has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly and Company, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.

Disclosure of Interest: P. Mease Grant/research support from: Celgene, Novartis, AbbVie, Amgen, BMS, Lilly, Pfizer, UCB, Consultant for: Celgene, Corrona,

Novartis, AbbVie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Merck, Pfizer, UCB, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi Aventis and UCB, Employee of: Imaging Rheumatology BV, C. Karki Employee of: Corrona, LLC, M. Liu Employee of: Corrona, LLC, R. Pandurengan Employee of: Corrona, LLC, Y. Park Employee of: Novartis, J. Greenberg Shareholder of: Corrona, LLC, Consultant for: Lilly, Genentech, Janssen, Novartis, Pfizer, Employee of: Corrona, LLC

DOI: 10.1136/annrheumdis-2017-eular.1530

THU0387 THE CLINICAL IMPORTANCE OF THE THYROID NODULES DURING TUMOR NECROSIS FACTOR-ALPHA INHIBITOR THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

R. Terlemez[1], K. Akgün[2], D. Palamar[2], H. Sarı[2]. *[1]Physical medicine and rehabilitation, Şişli Hamidiye Etfal Research and Training Hospital; [2]Physical medicine and rehabilitation, Istanbul University Cerrahpasa Faculty of Medicine, Istanbul, Turkey*

Background: TNF is a pivotal regulator of inflammation and the cytokine system. Besides this, there is no doubt that TNF has a major role in cancer biology. TNF has a dual defensive and offensive role in carcinogenesis (1). TNF-blocking treatment has led to improvements in the management of inflammatory diseases.Even though their efficacy as anti-inflammatory drugs is well-proven, there are some concerns about the adverse effects of anti-TNF therapy (2). Basic research suggests that the evaluation of infections and malignancy as major adverse effects should be performed effectively (3). However, some studies conducted so far have dubious notions that anti-TNF therapy increases the risk of cancer (3,4).
Objectives: Objective: The clinical importance of the thyroid nodules in patients with axial spondyloarthritis (ax-SpA) rests with the need to exclude thyroid malignancy. The aim of this study is to assess the risk of thyroid malignancy in ax-SpA patients receiving anti-TNF therapy.
Methods: From September 2015 until December 2015, 70 patients diagnosed with ax-SpA according to ASAS criteria, were included in the research. Forty of the patients had received anti-TNF therapy, and 30 of the patients were anti-TNF naive. A clinician from the Physical Medicine and Rehabilitation clinic performed ultrasonography on all patients to screen for thyroid nodule(s). If thyroid ultrasonography revealed an abnormal finding, the patient was referred to a radiologist.
Results: The mean (SD) age was 38±9.87 years; % 75.7 of the patients were male. None of the demographic differences between the groups were statistically significant. Fifteen of the forty patients that received anti-TNF therapy and eleven of the thirty anti-TNF naive patients had thyroid nodule(s). Four patients from the anti-TNF group underwent fine needle aspiration biopsy, and two of them were diagnosed with papillary thyroid carcinoma. None of the nodules in anti-TNF naive patients required biopsy. When compared to the normal population, the standardized incidence ratio (SIR) was found to be increased in both male (SIR: 2.03% 95 CI: 1.9 to 18) and female (SIR: 2.7% 95 CI: 2.6 to 24) cases.
Conclusions: We see a mild increase in thyroid malignancies in ax-SpA patients that received anti-TNF therapy. Consequently, the thyroid gland should also be taken into consideration while screening for malignancy before anti-TNF therapy.
References:

[1] Wajant, Harald. The role of TNF in cancer. Death Receptors and Cognate Ligands in Cancer. Springer Berlin Heidelberg, 2009. 1–15.
[2] Dixon, W. G., et al. Influence of anti-tumor necrosis factor therapy on cancer incidence in patients with rheumatoid arthritis who have had a prior malignancy: results from the British Society for Rheumatology Biologics Register. Arthritis care & research 62.6 (2010): 755–63.
[3] Bongartz, Tim, et al. Anti-TNF antibody therapy in rheumatoid arthritis and the risk of serious infections and malignancies: systematic review and meta-analysis of rare harmful effects in randomized controlled trials. Jama 295.19 (2006): 2275–85.
[4] Askling, Johan, et al. Risks of solid cancers in patients with rheumatoid arthritis and after treatment with tumour necrosis factor antagonists. Annals of the rheumatic diseases 2005;64:1421–6.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1013

THU0388 EFFICACY AND SAFETY OF ADALIMUMAB IN PATIENTS WITH NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE 28-WEEK OPEN-LABEL PERIOD OF THE ABILITY-3 STUDY

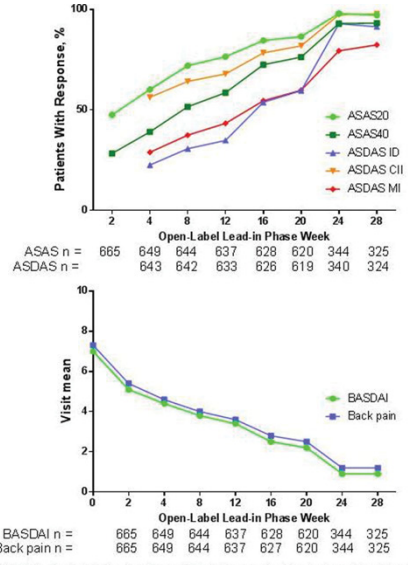
R. Landewé[1], J. Sieper[2], R. Inman[3], A.L. Pangan[4], X. Wang[4], J.K. Anderson[4]. *[1]University of Amsterdam, Amsterdam, Netherlands; [2]Charité Universitätsmedizin Berlin, Berlin, Germany; [3]Toronto Western Hospital, Toronto, Canada; [4]AbbVie, North Chicago, United States*

Background: Adalimumab (ADA) significantly improved clinical response at wk 12 vs placebo in patients (pts) with non-radiographic axial spondyloarthritis (nr-axSpA) in the ABILITY-1 study. The subsequent, ongoing ABILITY-3 study is assessing continuation vs withdrawal of ADA in nr-axSpA pts who respond to ADA.
Objectives: Evaluate the efficacy and safety of ADA during the open-label lead-in period of ABILITY-3.
Methods: ABILITY-3 has a 28-wk lead-in open-label ADA (40 mg every other wk) period; pts who achieve sustained remission (Ankylosing Spondylitis Disease Activity Score inactive disease [ASDAS ID] at wks 16, 20, 24 and 28) are randomized to double-blind placebo (withdrawal) or ADA (continuation) for 40 wks (ongoing). From wk 20–28, pts who did not achieve ASDAS ID were discontinued. Adult pts with nr-axSpA (fulfilling Assessment of SpondyloArthritis international Society [ASAS] criteria but not modified New York criteria) with objective evidence of inflammation in the sacroiliac joints or spine on MRI or elevated hs-CRP at screening; active disease at baseline (defined by ASDAS ≥2.1, BASDAI ≥4, and total back pain score ≥4); and inadequate response to ≥2 NSAIDs were eligible.
Results: Of 673 pts enrolled, 51% were women and mean BASDAI was 7.0±1.4 (Table). At wk 28, 305 (45%) pts were randomized (ASDAS ID: 33% at wk 12, 44% sustained at wk 28; nonresponder imputation) and 368 (55%) pts discontinued (not achieving sustained remission, n=300 [45%]; other reasons, n=68 [10%]). In observed analysis, 59%, 35%, and 22% of pts achieved ASAS40, ASDAS ID, and ASAS partial remission, respectively, at wk 12, similar to wk 12 data from ABILITY-1 pts with objective inflammation at baseline. The proportions of pts achieving ASAS20, ASAS40, ASDAS ID, ASDAS CII, and ASDAS MI increased, and mean BASDAI and back pain scores decreased over time (observed analysis; Figure). Adverse events (AEs) were reported by 468 pts (70%), most commonly nasopharyngitis (n=121 [18%]), upper respiratory tract infection (n=81 [12%]), and headache (n=56 [8%]); serious AEs occurred in 19 (3%) pts.

Table 1. Baseline Characteristics

Mean ± SD	(n=673)
Age	37.3±11.1
White, n (%)	651 (97)
Female, n (%)	343 (51)
Symptom duration, y	7.7±7.7
HLA-B27 positive, n (%)	515 (77)
TJC	6.5±10.4
SJC	1.9±4.0
MASES	3.4±3.5
PGA-disease activity	6.5±1.5 n=671
Patient-pain	7.4±1.7
BASDAI	7.0±1.4
ASDAS	3.6±0.8
hs-CRP	9.6±15.0
BASFI	5.3±2.2
HAQ-S	2.1±0.6

BASFI, Bath Ankylosing Spondylitis Functional Index; HAQ-S, Health Assessment Questionnaire for the Spondyloarthropathies; hs-CRP, high-sensitivity C-reactive protein; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; PGA, physician global assessment; SJC, swollen joint count; TJC, tender joint count.



BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CII, clinically important improvement; MI, major improvement.
Patients who did not achieve ASDAS ID were discontinued at week 20–28 visits.

Conclusions: Baseline disease activity was higher in ABILITY-3 pts than reported in prior trials. After 28 wks of open-label ADA therapy, disease activity improved and sustained remission was achieved in 44% of pts. Efficacy and safety in this nr-axSpA population were consistent with findings from ABILITY-1.

Acknowledgements: AbbVie funded the study and approved the abstract for submission. Medical writing support was provided by Maria Hovenden, PhD, of Complete Publication Solutions, LLC (North Wales, PA) and was funded by AbbVie.

Disclosure of Interest: R. Landewé Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, Consultant

for: Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, GlaxoSmithKline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB, and Wyeth, Speakers bureau: Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB, and Wyeth, J. Sieper Grant/research support from: AbbVie, Merck, Pfizer, and UCB, Consultant for: AbbVie, Merck, Pfizer, and UCB, Speakers bureau: AbbVie, Merck, Pfizer, and UCB, R. Inman Grant/research support from: AbbVie, Amgen, Janssen, Lilly, and Novartis, A. Pangan Employee of: AbbVie, X. Wang Employee of: AbbVie, J. Anderson Employee of: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.6119

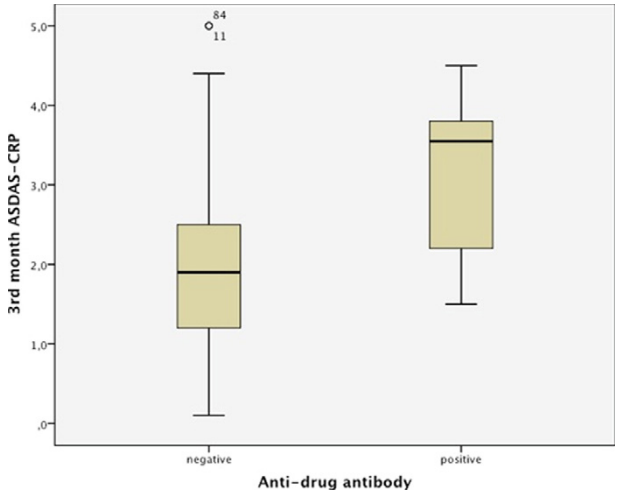
THU0389 IS THERE ANY ROLE OF IMMUNOGENICITY ON THE RESPONSE TO THE ANTI-TUMOR NECROSIS FACTOR ALPHA THERAPY IN PATIENTS WITH ANKYLOSING SPONDYLITIS: THE FIRST RESULTS OF A PROSPECTIVE COHORT STUDY

S. Akar[1], M. Cinar[2], G. Sargin[3], O. Karadag[4], G. Kinikli[5], M. Ozmen[1], O. Gercik[1], U. Kalyoncu[4], S. Yilmaz[2], T. Senturk[3], G. Keser[6], G. Hatemi[7], F. Yargucu[6], Y. Ozguler[7], A. Cefle[8], D. Kozaci[9], D. Solmaz[1], B. Kisacik[10]. *[1]Rheumatology, Katip Celebi University Faculty of Medicine, Izmir; [2]Rheumatology, Gulhane Military Hospital, Ankara; [3]Rheumatology, Adnan Menderes University Faculty of Medicine, Aydın; [4]Rheumatology, Hacettepe University Faculty of Medicine; [5]Rheumatology, Ankara University Faculty of Medicine, Ankara; [6]Rheumatology, Ege University Faculty of Medicine, Izmir; [7]Rheumatology, Istanbul University Cerrahpasa Faculty of Medicine, Istanbul; [8]Rheumatology, Kocaeli University Faculty of Medicine, Kocaeli; [9]Biochemistry, Ankara Yildirim Beyazid University Faculty of Medicine, Ankara; [10]Rheumatology, Gaziantep University Faculty of Medicine, Gaziantep, Turkey*

Background: Although anti-tumour necrosis factor agents (anti-TNFs) are very effective in most patients with ankylosing spondylitis (AS) significant proportion of patients quit the treatment due to non-response or adverse events. The development of anti-drug antibodies (ADAs) and low serum drug levels might have a mechanistic role in loss of efficacy of or the development of adverse events in patients treated with anti-TNFs. There is limited data regarding the immunogenicity of anti-TNFs in patients with AS.
Objectives: Therefore the aim of this study was to evaluatethe relationship between the formation of ADAs, serum through drug levels and clinical response to anti-TNFs in patients with AS.
Methods: In total 350 AS patients with a new anti-TNF agent prescription in the last two weeks period were planned to include this multi-center prospective observational cohort study. Herein we are presenting the data of first 102 patients who had >3months follow-up. Clinical data and serum samples were collected at baseline and at every three months of treatment. Serum drug levels and ADAs were measured by ELISA in one center to avoid inter-assay variability.
Results: 102 biologic naïve AS patients (75 [74%] male, mean (±SD) age; 37.2±10.7 years) who started anti-TNF agents (14 infliximab [13.7%], 27 adalimumab [26.5%], 33 etanercept [32.4%] and 28 golimumab [27.5%]) were included in the present analysis. In comparison to baseline values BASDAI, ASDAS-CRP and CRP values were significantly decreased in third months of follow-up ($P<0.001$) (table). At 12 weeks of follow-up 9 patients (9%; 2 on infliximab and 7 adalimumab) had ADAs and 20 (20%; 10 on adalimumab, 4 infliximab, 4 golimumab and 2 etanercept) had no detectable drug levels.The presence of ADAs were significantly correlated with serum drug levels ($P<0.001$). Up to 12 months of follow-up none of patients treated etanercept developed ADAs. Third month BASDAI and ASDAS-CRP values were significantly higher in patients with ADAs (BASDAI values were 5.2±1.4 vs 3.0±1.8; $P<0.001$ and ASDAS-CRP values were 3.1±1.0 vs 1.9±1.1; $P<0.001$) (figure) and patients with no detectable drug levels BASDAI values were 4.1±1.8 vs 2.9±1.8; $P=0.012$ and ASDAS-CRP values were 2.7±1.3 vs 1.9±1.0; $P=0.015$).
Conclusions: ADAs against anti-TNF agents might develop as early as 12 weeks of treatment. Our results confirm that ADA development may hinder the anticipated response to anti-TNF agents in patients with AS.

Table 1. Baseline and third month's follow-up indicators of activity and response in AS patients treated with anti-TNF agents

	Baseline	Third month
BASDAI	6.8±5.2	3.2±1.9
ASDAS-CRP	4.1±2.5	2.0±1.1
CRP	23.8±32.8	7.9±13.9



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3729

THU0390 EFFECT OF REHABILITATION ON THE CHEST EXPANSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS

S.D. Jandric. *Department for FRM, Faculty of Medicine, University of Banjaluka, Banja Luka, Republic of Srpska, Bosnia and Herzegovina*

Background: Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis that leads to pain, stiffness, progressive spinal deformity, and spinal fusion, limitation of the spine, rib cage motion and severe functional impairment. Pulmonary function is altered in AS owing mainly to the limited chest expansion.
Objectives: The purpose of this study was to investigate the effect of rehabilitation on the limited chest expansion measured by respiratory index and relationship between duration of the rehabilitation and age, disease onset, disease duration and respiratory index in patients with AS during physical treatment and rehabilitation.
Methods: The study was designed as a retrospective study that included 47 consecutive AS patients (33 male and 14 female), average age of 52.53±11.58 years that were hospitalized and treated in rehabilitation center. Average duration of the rehabilitation was 17.77±5.92 days. Respiratory index was measured for all AS patients at the beginning and at the end of rehabilitation with a centimeter ribbon. Student's t-test and Pearson's test of correlation were used for statistically analysis.
Results: Average disease duration was 13.35±8.74 years, disease onset was at 39.64±12.87 years. Respiratory index was 1.98±1.34 cm at beginning of rehabilitation and 3.01±1.75 cm at the end of rehabilitation. The difference was statistically significant (t=8.025, $p<0.001$). Pearson's test of correlation was shown statistically significant correlation between value of respiratory index at beginning and at the end of rehabilitation (r=0.872, $p<0.001$). Duration of the rehabilitation (hospital days) statistically significant correlate with value of respiratory index at beginning rehabilitation (r=-0.289, $p<0.05$), but not with age, disease duration and disease onset ($p>0.05$).
Conclusions: The physical therapy and rehabilitation has led to the improvement the respiratory index in patients with AS, which confirms its effectiveness. The value of respiratory index at beginning rehabilitation is associated with duration of the rehabilitation. Significant limitation in respiratory index indicates longer hospital stay. These results could be having importance in planning of rehabilitation of patients with AS.

References:
[1] Reveille JD, Ximenes A, Ward MM. Economic considerations of the treatment of ankylosing spondylitis. Am J Med Sci. 2012;343(5):371–4.
[2] Berdal G, Halvorsen S, van der Heijde D, Mowe M, Dagfinrud H. Restrictive pulmonary function is more prevalent in patients with ankylosing spondylitisthan in matched population controls and is associated with impaired spinal mobility: a comparative study. Arthritis Res Ther. 2012;14(1):R19.

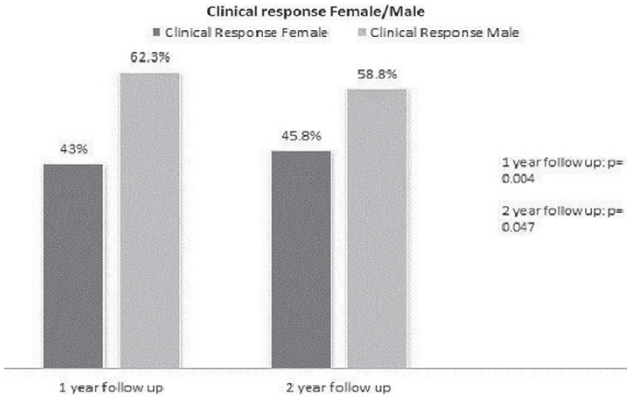
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2669

THU0391 FEMALE GENDER IS ASSOCIATED WITH A POORER RESPONSE TO TNF INHIBITORS IN ANKYLOSING SPONDYLITIS

T. Rusman, M.T. Nurmohamed, J.C. van Denderen, I. Visman, I.E. van der Horst-Bruinsma. *Amsterdam Rheumatology immunology Center |Departments of Rheumatology VU University Medical Center & Reade, Amsterdam, Netherlands*

Background: Limited data are available on the influence of gender and lifestyle factors, such as smoking, alcohol consumption and Body Mass Index (BMI) on disease activity and response to TNF inhibitors (TNFi) in ankylosing spondylitis (AS).
Objectives: This study aimed to determine whether these factors influence age at diagnosis, disease activity and response to TNFi.
Methods: In a prospective study, clinical data (age, gender, C-reactive protein, Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Score (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Metrology Index (BASMI), smoking, alcohol consumption and BMI) were collected in AS patients from a observational cohort, who started or switched treatment with TNFi. Data were collected at baseline and after 6, 12 and 24 months. Independent T-tests and linear regression analyses were performed to assess the influence of gender and lifestyle factors on age at diagnosis and disease activity.

Results: In total, 312 consecutive AS patients, 34% female, were included with a mean follow-up of 18.9 months. Most patients (172, 55%) showed significant improvement after start of TNFi of whom 86 patients (28%) had a clinically important (ASDAS decrease >1.1) and 86 (26.9%) a major clinical improvement (ASDAS decrease >2.2). BMI was significantly correlated with age at diagnosis (p=0.016; 95% CI: 0.07 – 0.65): an increase of BMI with three points delayed the AS diagnosis with one year. At baseline, smoking and gender were not correlated with the ASDAS, but BASDAI and BASMI were both inversely related to BMI. Male gender was significantly associated with a higher chance at clinical response (improvement of the BASDAI with 50% or a 2 point decrease) to TNFi (p=0.041). At one year follow-up the clinical improvement of males versus females was respectively 62% vs. 43% and at two year follow-up 59% vs. 46%. Males also showed a significantly higher ASDAS improvement after one year of follow-up compared to females (p=0.015).



Conclusions: Significantly less females had a clinical response compared to males after one and two years of TNFi treatment. A higher BMI not only prolonged the time to AS diagnosis up to one year, but also negatively influenced the BASDAI and BASMI scores. Female gender and high body weight should be taken into consideration when the efficacy of TNFi is assessed, by stratifying for these factors in the analysis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1290

THU0392 DO WE REALLY NEED DMARDS ADDITION TO ANKYLOSISNG SPONDYLITIS PATIENTS TREATED WITH TUMOR NECROSIS FACTOR ALPHA INHIBITORS?

T. Reitblat[1], O. Cohen[1], D. Aharoni[2], E. Hadrian[2], G. Reifman[1], Y. Braun-Moscovici[3], A. Balbir-Gurman[3]. *[1]Department of Rheumatology; [2]Laboratory Service, Barzilai Mc, Ashkelon; [3]B. Shine Rheumatology Unit, Rambam Health Care Campus and Rappaport Faculty of Medicine, Technion, Heifa, Israel*

Background: The management of systemic inflammatory diseases, such as Rheumatoid arthritis (RA) and Ankylosing spondylitis (AS) has been revolutionized with the introduction of tumor necrosis factor alpha inhibitors (TNF-I). Significant reduction in disease activity and achievment of remission resulted in halting of joint damage and improved quality of life. Unfortunately, approximatly 15–30% of patients fail to reach desirable improvement or lose drug effectiveness with time. It may be explained by immunogenicity and production of human anti chimeric antibodies (HACA). Presence of HACA against TNF-I have been associated with low levels of the drug and lose of therapeutic response. The prevalence of HACA in RA is estimated between 20–40%, and in AS between 25–64%. The difference in the pathogenesis of RA and AS as well as diverce approach in using disease modifying anti-rheumatic drugs (DMARDs) may influence HACA production and TNF-I levels in these conditions.

Objectives: To compare the incidence of HACA and Infliximab, Etanercept, Adalimumab levels in patients with RA and AS with respect to concomitant DMARDs.

Methods: Patients' with RA and AS data treated with TNF-I for at least 3 months in whom tests for HACA and Infliximab, Etanercept, Adalimumab levels were available were extracted from patients' files. Data included: demographics, concomitant treatment, and disease activity scores (BASDAI for AS and DAS-28 for RA). Serum for assessment of drugs level (ELISA) and HACA (ADAb;Promonitor, Bridging, ELISA) was obtained before the next drug administration. Univariate comparison was done using Student t test for the continuous variables and Chi square test for the categorical variables (P <.05 was considered significant).

Results: Data on 53 patients with AS (mean age 47.9±11.9 years, 41.5. % female) and 29 patients with RA (mean age 54.8±8.1 years, 75, 9% female) were available: 22 RA patients were treated with Methotrexate and 7 with other DMARDs; no one AS patient was treated with concomitant DMARDs. High level of HACA was found in 22.6% AS patients and in 34.5% RA patients (p>0.05); 86.8% patients with AS reached theurapethic level of drug compared to 69% RA patients (p=0.027). Drugs levels were similar in AS and RA patients (Table). Low disease activity (DAS28-CRP<3.2) was registered in 62.1% RA patients and in 81.4% AS patients (BASDAI <4).

Conclusions: Despite significant difference in the use of concomitant DMARDs, patients with AS and RA had similar prevalence of HACA. Moreover, higher proportion of patients in AS group reached therapeutic level of TNF-I. The data supports the hypothesis, that immune responce to TNF-I may be different in AS and RA and, therefore, the addition of DMARDs to prevent development of HACA in patients with AS may be unnecessary.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2584

THU0393 SECUKINUMAB PROVIDES SUSTAINED REDUCTION IN FATIGUE IN PATIENTS WITH ANKYLOSING SPONDYLITIS THROUGH 3 YEARS: LONG-TERM RESULTS OF TWO RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED PHASE 3 STUDIES

T.K. Kvien[1], A. Deodhar[2], L. Gossec[3], P.G. Conaghan[4], V. Strand[5], M. Østergaard[6], N. Williams[7], B. Porter[8], K. Gandhi[8], S. Jugl[9]. *[1]Diakonhjemmet Hospital, Oslo, Norway; [2]Oregon Health & Science University, Portland, Oregon, United States; [3]UPMC University Paris 06, Paris, France; [4]University of Leeds, Leeds, United Kingdom; [5]Stanford University School of Medicine, Palo Alto, CA, United States; [6]Copenhagen Center for Arthritis Research (COPECARE), Glostrup, Denmark; [7]RTI Health Solutions, Durham, NC; [8]Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States; [9]Novartis Pharma AG, Basel, Switzerland*

Background: In patients (pts) with ankylosing spondylitis (AS), fatigue is a common symptom negatively affecting health-related quality of life (HRQoL) and social functioning. Secukinumab (SEC), a fully human anti–IL-17A mAb, rapidly improved signs and symptoms, physical functioning, and HRQoL in pts with AS.[1,2]

Objectives: To assess the long-term effects of SEC on fatigue in TNF inhibitor (TNF)-naïve and TNF inhibitor inadequate responder/intolerant (TNF-IR) AS pts in MEASURE 1 and MEASURE 2.

Methods: 371 and 219 pts were randomized to SEC or placebo (PBO) in MEASURE 1 (10 mg/kg IV followed by 150 or 75 mg SC) and MEASURE 2 (150 or 75 mg SC), respectively. At Week (Wk) 16, non-responder PBO pts were re-randomized to SEC 150 or 75 mg SC (in MEASURE 1, PBO pts achieving ASAS20 response at Wk 16 were switched to SEC at Wk 24). Fatigue was measured at baseline (BL) and Wks 4, 8, 12, 16, 24, 52, 104 and 156 using FACIT-F, which assesses fatigue in the previous 7 days using 13 questions graded on a 0–4 scale (higher scores=less fatigue). An increase from BL in FACIT-F score of ≥4 points (based on MCID) was used to define "response". Approximately 69% of pts were TNF-naïve and 31% were TNF-IR across both trials. Analyses were based on the full analysis set and subgroups stratified by prior TNF therapy. Correlations between BL characteristics and improvements in fatigue were investigated using a logistical regression model. Only data from the approved dose (SEC 150 mg) are presented.

Results: FACIT-F was 24.5–25.6 and 22.6–24.3 at BL across groups in MEASURE 1 and 2, respectively. Improvements in FACIT-F with SEC at Wk 16 were sustained through Wk 156 in MEASURE 1 and Wk 104 in MEASURE 2 (Table). Rapid and sustained fatigue responses were also seen in subgroups stratified by prior TNF use. In the overall population, LS mean changes (±SEM) from BL in FACIT-F scores were significantly greater with SEC vs PBO at Wk 16 in both MEASURE 1 (7.60±0.99 vs 3.34±1.00, *P*=0.002) and MEASURE 2 (8.10±1.09 vs 3.27±1.09, *P*=0.018); reductions in fatigue were sustained throughout the entire follow up in both trials (MEASURE 1 Wk 156: 9.81±0.95; MEASURE 2 Wk 104: 9.27±1.13). Similar results were reported in both TNF-naïve and TNF-IR pts. Correlational analyses based on pooled data from both trials did not identify any BL factors that

Table: FACIT-F responders in MEASURE 1 and MEASURE 2 with secukinumab 150 mg[a]

	Proportion of Patients with FACIT-F Response[b], % (n/m)			
	Week 16	Week 52	Week 104	Week 156
MEASURE 1[c]				
Overall (N=87)	66.7 (58/87)	73.6 (64/87)	72.2 (57/79)	75.6 (65/86)
TNF-naïve (N=70)	70.0 (49/70)	75.7 (53/70)	70.3 (45/64)	74.3 (52/70)
TNF-IR (N=17)	52.9 (9/17)	64.7 (11/17)	80.0 (12/15)	81.3 (13/16)
MEASURE 2				
Overall (N=72)	77.6 (52/67)	80.6 (50/62)	81.4 (48/59)	–
TNF-naïve (N=44)	86.0 (37/43)	90.0 (36/40)	84.6 (33/39)	–
TNF-IR (N=28)	62.5 (15/24)	63.6 (14/22)	75.0 (15/20)	–

[a]Observed data are shown; [b]Defined as improvement (increase in FACIT-F score) by ≥4.0 points from BL; [c]Data shown are from patients who entered the MEASURE 1 long-term extension study at Week 104 (NCT01863732)
m, number of patients with sufficient data for evaluation; N, number of patients randomized to SEC 150 mg
n, number of responders

consistently predicted improvement in fatigue response at Wks 16, 52, and 104. A one-unit increase in BL BASDAI score (i.e. worsening) was a significant factor for achieving FACIT-F response at Wk 104 (P=0.02).

Conclusions: SEC provided sustained improvements in fatigue for up to 156 wks in both TNF-naïve and TNF-IR pts with AS. Fatigue response was generally higher in TNF-naïve pts.

References:

[1] Baeten. NEJM 2015;373:2534–48.
[2] Kvien. ARD 2016;75(Suppl2):823.

Disclosure of Interest: T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, A. Deodhar Grant/research support from: Eli Lilly, Janssen, Novartis, Pfizer, UCB, Abbvie, Amgen, GSK, L. Gossec Grant/research support from: BMS, Lippy, Pfizer, Consultant for: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, P. Conaghan Consultant for: Abbvie, BMS, Lilly, Novartis, Pfizer, Roche, Speakers bureau: Abbvie, BMS, Lilly, Novartis, Pfizer, Roche, V. Strand Consultant for: AbbVie, Amgen, BMS, Celgene, Celltrion, CORRONA, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi, and UCB, M. Østergaard Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Janssen, Merck, Novartis, Orion, Pfizer, Regeneron, Roche, UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Janssen, Merck, Novartis, Orion, Pfizer, Regeneron, Roche, UCB, N. Williams Employee of: RTI Health Solutions, B. Porter Shareholder of: Novartis, Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.1839

THU0394 RHEUMATOLOGISTS USE DIFFERENT CUT OFFS FOR DISEASE ACTIVITY IN REAL LIFE – THE EXPERIENCE WITH GOLIMUMAB IN ANKYLOSING SPONDYLITIS – A SUBANALYSIS FROM THE NON-INTERVENTIONAL GO-NICE TRIAL

J. Braun[1], X. Baraliakos[1], U. Kiltz[1], K. Krüger[2], G.R. Burmester[3], S. Wassenberg[4], M.H. Thomas[5]. *[1]Rheumazentrum Ruhrgebiet, Herne; [2]Rheumatologisches Praxiszentrum, München; [3]Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin, Berlin; [4]Rheumazentrum Ratingen, Ratingen; [5]Medical Affairs, MSD Sharp & Dohme GmbH, Haar, Germany*

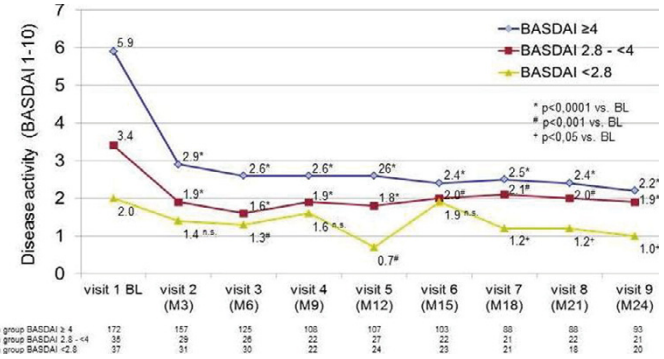
Background: International recommendations for the management of axial spondyloarthritis including ankylosing spondylitis (AS) suggest a BASDAI level of disease activity of ≥4 to indicate treatment with biologics. Other cut-offs have rarely been studied so far.

Objectives: Therefore, we were interested to learn about the level of disease activity used in daily routine to start anti-TNF therapy.

Methods: In a posthoc subanalysis of the non-interventional, prospective, study GO-NICE that has been performed in a real life setting in Germany we used data from biologic naïve patients with established AS to study the initial BASDAI values before the start of therapy with Golimumab 50mg SC once monthly. Established standardized outcome measures were used.

Results: Out of a total of 543 AS-patients (pts.) documented in 126 German centers, 244 biologic-naïve pts. were eligible. A total of 134 pts. (54.9%) completed the 24 month observational period. The majority of pts. (70.5%), had a BASDAI ≥4 (group (gr.).1), while 14.3% had a BASDAI of ≥2.8 - <4 (gr.2) and 15.1% even had a BASDAI <2.8 (gr.3, Table). The patient demographics did not differ much between these 3 groups, the proportion of males was numerically somewhat lower in gr.1. The proportion of pts. with an elevated CRP was highest in gr.2 at BL. The BASDAI in gr.1,2 and 3 was initially 5.9±1.3, 3.4±0.4 and 2.0±0.8, dropped significantly to 2.2*±2.0, 1.9*±1.2 and 1.0±1.2 within 3 months (*p<0.0001 vs. BL), and decreased significantly (p<0.005) to 2.2±1.7, 1.9±1.7 and 1.4±1.0 at month 24, respectively (fig.).The BASDAI 50% improvement was 68.8%, 44.8%, and 45.2% at month 3, and increased to 84.9%, 61.9%, and 55.0% at month 24, respectively.

Conclusions: The most interesting observation of this real life study and posthoc analysis is certainly that almost a third of the pts. were included in the study who did not reach the recommended BASDAI cut-off of ≥4. Furthermore the data show that the patients with a BASDAI 2.8 - <4 seem to have significant benefit of anti-TNF treatment, while this was not really the case with in pts. with a BASDAI <2.8. This finding should lead to a reevaluation of the established BASDAI cut-off of ≥4. Future studies should also evaluate the performance of an ASDAS cut-off.



It seems likely that especially pts. with elevated CRP levels and a BASDAI <4 will benefit from this new strategy. We think that in light of the rather weak correlation of pain and "objective" parameters of inflammation such as CRP and MRI the here reported observation does make some sense. Regarding the treatment with golimumab no new safety signals were detected.

Disclosure of Interest: J. Braun Consultant for: AbbVie (Abbott), Amgen, Biogen, Boehringer Ingelheim, BMS, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Epirus, Hospira, Janssen, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, X. Baraliakos Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Novartis, Pfizer, Roche, MSD and UCB, U. Kiltz Consultant for: AbbVie, Chugai, Janssen, MSD, Novartis, Pfizer, Roche and UCB, K. Krüger Consultant for: AbbVie, BMS, Celgene, Janssen Biologics, MSD, Pfizer, Roche, and Sanofi-Aventis, G. Burmester Consultant for: AbbVie, BMS, MSD, Pfizer, Roche, and UCB, S. Wassenberg Consultant for: AbbVie, Chugai, Janssen Biologics, MSD, Novartis, Pfizer, Roche, and USB, M. Thomas Employee of: MSD Sharp & Dohme GmbH

DOI: 10.1136/annrheumdis-2017-eular.5759

THU0395 HIGH NUMBER OF PREVIOUS BIOLOGIC USE AND COMORBIDITIES IN FIRST REAL WORLD SECUKINUMAB STUDY IN PSA AND AS – NON-INTERVENTIONAL, AQUILA STUDY IN GERMANY

U. Kiltz[1], C. Legeler[2], M. Maier-Peuschel[2], J.A. Veit[2], C. Mann[2], H.-P. Tony[3]. *[1]Rheumazentrum Ruhrgebiet, Rheumazentrum Ruhrgebiet, Herne; [2]Novartis, Nürnberg; [3]Medizinische Klinik und Poliklinik II, Universität Würzburg, Würzburg, Germany*

Background: Secukinumab has been shown to significantly improve symptoms of psoriatic arthritis (PsA)[1] and ankylosing spondylitis (AS)[2] in numerous phase III studies. Still, as randomized, controlled, clinical trials often limit their patients to a very strict and selected group, further data on real world evidence is necessary to assess efficacy in a broader patient group.

Objectives: To evaluate baseline characteristics regarding demographics, disease activity and comorbidities in patients with active PsA or AS in daily practice treated with secukinumab in Germany.

Methods: AQUILA, a non-interventional, multi-center, 52-week study enrolling 2000 patients with active PsA or AS. Patients are documented as treated in clinical practice. Here, we will report the baseline characteristics of a subgroup of 347 patients who have been enrolled in the study. At baseline patient's health status, selected comorbidities and disease history was assessed using routine parameters (among others: CRP, joint count, BASDAI). Furthermore, overall disease activity and quality of life has been documented using ASAS-HI (AS) and PsAID-12 item (PsA).

Results: 108 AS- and 239 PsA-patients were included, majority of AS patients were male, in PsA the majority was female. Previous bDMARD exposure was high in both groups, percentage of NSAID and cDMARD exposure varied (Tab). For PsA patients elevated CRP (Tab) and a high number of tender (8.4) and swollen joints (4.4) was reported. Assessed comorbidities included coronary heart disease (9.7%), stroke (2.5%), heart failure (2.9%) and depression (13.4%). Effect of PsA on patient's life at baseline was reported via PsAID-12 item with a mean score of 5.0 (±2.2). AS patients enrolled in this trial had a high disease activity with a mean BASDAI of 5.5 (±2.0) and elevated CRP (Table). Considered comorbidities were coronary heart disease (4.6%), stroke (0%), heart failure (0.9%) and depression (12%). Patient's impairments due to AS were assessed at baseline with the ASAS-HI, reporting a mean score of 8.1 (±3.6).

Conclusions: The baseline characteristics of the population are comparable with

Abstract THU0394 – Table 1. Demographics and baseline characteristics

	BASDAI ≥4 (n=172)	BASDAI 2.8–<4 (n=35)	BASDAI <2.8 (n=37)	Total AS patients (n=244)
Mean age [years] ± SD (range)	41.9±12.5 (18–72)	44.7±11.6 (20–69)	39.1±12.5 (23–69)	41.9±12.4 (18–72)
Proportion males n (%)	117 (68.0%)	29 (82.9%)	27 (73.0%)	173 (70.9%)
Mean time since first diagnosis [years] ± SD	8.8±9.5	10.1±10.2	8.7±9.0	9.0±9.5
Mean C-reactive protein (CRP) [mg/l] ± SD (range)	18.4±52.8 (0.3–660.0)	27.7±74.1 (0.3–426.0)	18.3±17.8 (1.0–60.6)	19.7±52.7 (0.3–660.0)
Above normal range yes, no, n (%)	75 (45.2%), 91 (54.8%)	21 (65.6%), 11 (34.4%)	18 (51.4%), 17 (48.6%)	114 (48.9%), 119 (51.1%)

Characteristics	AS; n=108	PsA; n=239
Age (Mean±SD)	46.9±12.7	53.4±11.9
Male (%)	62.0	42.7
CRP (mg/L) (Mean±SD)	14.8±22.5	11.8±18.0
Previous NSAID exposure (%)	61.1	24.7
Previous cDMARD exposure (%)	39.8	72.8
Previous bDMARD exposure (%)	68.5	72.8
Lack of efficacy of prev. bDMARD (%)	82.4	85.1

other studies in the phase III program of secukinumab[1,2]. Major difference is represented by the high number of biological-experienced patients and comorbidities. Potential differences between these real world results and previously obtained phase III results will have to be discussed to assess their impact on patients.

References:
[1] McInnes IB et al. Lancet. 2015;386(9999):1137–46.
[2] Baeten D et al. Lancet. 2013;382(9906):1705–13.

Disclosure of Interest: U. Kiltz Grant/research support from: AbbVie, Chugai, MSD, Novartis, Pfizer, Roche, UCB, Consultant for: AbbVie, Chugai, MSD, Novartis, Pfizer, Roche, UCB, C. Legeler: None declared, M. Maier-Peuschel Employee of: Novartis, J. Veit Employee of: Novartis, C. Mann Employee of: Novartis, H.-P. Tony Grant/research support from: AbbVie, Astra-Zeneca, BMS, Chugai, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi, Consultant for: AbbVie, Astra-Zeneca, BMS, Chugai, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi

DOI: 10.1136/annrheumdis-2017-eular.6164

THU0396 EFFICACY OF SWITCHING BDMARDS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM A SYSTEMATIC LITERATURE REVIEW

V. Navarro-Compán[1], E. de Miguel[1], A. Balsa[1], P. Diaz del Campo[2], J. Gratacós[3]. *[1]Hospital la Paz, IdiPaz; [2]Spanish Society of Rheumatology, Madrid; [3]Hospital Parc Taulí, Sabadell, Spain*

Background: bDMARDs (TNF or IL-17 inhibitors) have been shown to be efficacious in patients with axial spondyloarhritis (axSpA). However, approximately 30–50% of patients who receive a first bDMARD do not respond well. Current practice in these patients is switching to another bDMARD but the scientific evidence for this attitude is sparse.

Objectives: To evaluate the efficacy of switching bDMARDs in patients with axSpA.

Methods: A systematic literature review until February 2016 was performed using Medline, EMBASE and Cochrane databases. Furthermore, abstracts from the previous EULAR and ACR meetings were reviewed. The research question was formulated according to the PICOS method: Population (axSpA patients); Intervention (bDMARD); Outcome (clinical response); and Setting (longitudinal studies with follow-up ≥12 weeks of follow up including data from ≥50 patients). Data was extracted using a form developed for this specific purpose. The quality of the studies was assessed based on CEBM Oxford. Clinical response in patients who switched to a second bDMARD was determined and compared with the one achieved after receiving the first bDMARD (a TNFi in all cases). Results are shown as median (range) and relative frequencies (%).

Results: In total, 7 studies out of 1506 retrieved citations were included. All studies included patients with ankylosing spondylitis (AS). The study design was prospective observational (n=3), retrospective observational (n=2), open-label trial (n=1) and post-hoc analysis from two RCTs (n=1). The level of evidence for all the studies was 4. In these studies, a total of in 4678 patients received a first bDMARD and 1198 patients switched to a second bDMARD (a TNFi in all cases except in 51 patients that switched to secukinumab). Baseline characteristics of patients included in the studies were: 41 (38–44) years old, 67% (64–74) males, 78% (74–89) HLA-B27+ and BASDAI before switching 6.2 (5.3–6.5). The most frequent reason to switch bDMARD was inefficacy, followed by intolerance/adverse events. Median (range) time to assess response after switching was 6 (3–12) months. The criteria to define clinical response were heterogeneous. BASDAI50 was employed in four studies and the percentage of patients who achieved this response after the first and the second bDMARD for each study was: (63% vs 41%), (50% vs 28%), (54% vs 37%), (72% vs 56%), respectively. The response for the other three studies was based on different definitions, being as follows: BASDAI <4 (83% vs 78%), ASAS20 response (67% vs 48%) and retention rate after one year (65% vs 60%). The reason to switch bDMARD (intolerance or inefficacy) was not found as a significant predictor of treatment response in most of the studies. In addition, two studies reported data (n=137 and 11 patients) to evaluate the efficacy of switching to a third bDMARD (TNFi in both cases). The percentage of patients who responded (BASDAI50) to the third TNFi was 30% and 52%, respectively.

Conclusions: In patients with AS who do not respond to a first TNFi, switching to another bDMARD (either a TNFi or secukinumab) is efficacious in a considerable number of patients (30–50%). However, the clinical response after receiving a second bDMARD is lower to the one experienced after the first TNFi. Published data for switching to a third bDMARD is very limited.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5717

THU0397 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE ANKYLOSING SPONDYLITIS: 3-YEAR RESULTS FROM A PHASE 3 EXTENSION TRIAL (MEASURE 1)

X. Baraliakos[1], A.J. Kivitz[2], A. Deodhar[3], J. Braun[1], J.C. Wei[4], E.M. Delicha[5], Z. Talloczy[6], B. Porter[6] on behalf of the MEASURE 1 study group.
[1]Ruhr-University Bochum, Herne, Germany; [2]Altoona Center for Clinical Research, Duncansville; [3]Oregon Health & Science University, Portland, United States; [4]Chung Shan Medical University Hospital, Taichung, Taiwan, Province of China; [5]Novartis Pharma AG, Basel, Switzerland; [6]Novartis Pharmaceuticals Corporation, East Hanover, United States

Background: Rapid and sustained improvements in the signs and symptoms of ankylosing spondylitis (AS) have been reported with secukinumab, a fully human anti–IL-17A mAb, over the first 2 years (yrs) in the Phase 3 MEASURE 1 trial.[1,2]

Objectives: To report efficacy and safety of secukinumab through 3 yrs in an extension trial (NCT01863732) to the core MEASURE 1 trial.

Methods: After the 2-yr core trial, patients (pts) receiving secukinumab 150 or 75mg s.c. were invited to enter a 3-yr extension trial. Efficacy results at Week (Wk) 156 are reported for pts who were originally randomised to secukinumab. Assessments at Wk 156 included ASAS20/40, BASDAI, BASDAI50, SF-36 PCS, ASAS partial remission (ASAS PR) and ASDAS-CRP. Binary and continuous variables used multiple imputation and MMRM estimates, respectively. Analyses by anti-TNF use (naïve/intolerant to or inadequate response [IR]) was pre-specified and reported as observed. Safety analyses included all pts who received ≥1 dose of secukinumab.

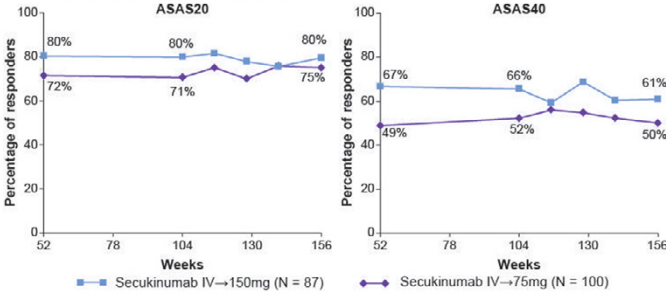
Results: A total of 290/371 pts (78%) completed the 2-yr core trial. Of these, 274 pts entered the extension trial, with 260 completing 156 wks (83/87 pts [95%] in IV→150mg; 95/100 pts [95%] in IV→75mg; 82/87 [94%] pts in placebo→secukinumab). At Wk 156, clinical improvements were sustained across all endpoints (Table, Figure). Similar trends were observed regardless of prior anti-TNF use (Table). Across the treatment period (secukinumab exposure [mean±SD]: 964.3±372.1 days), exposure-adjusted incidence rate with secukinumab for serious infections, Crohn's disease and malignant/unspecified tumours was 1.1, 0.5 and 0.5 per 100 pt-yrs, respectively.

Table 1. Summary of 156-wk efficacy results

	Observed data		Missing data considered[a]	
	Secukinumab IV→150mg (N=87)	Secukinumab IV→75mg (N=100)	Secukinumab IV→150mg (N=87)	Secukinumab IV→75mg (N=100)
ASAS, % response				
ASAS20/40	80/62[b]	76/50[b]	80/61	75/50
ASAS PR	27[b]	14[b]	27	14
BASDAI				
Baseline, mean±SD	6.1±1.5	6.0±1.5	6.1±1.5[#]	6.0±1.5[#]
Mean change from baseline[c]	–3.3±2.4[b]	–3.0±1.7[b]	–3.1±0.2	–2.9±0.2
	Secukinumab IV→150mg		Secukinumab IV→75mg	
Analysis by anti-TNF status[d]				
Anti-TNF-naïve[e]	N=70		N=76	
ASAS20/40, % response	80/61		76/48	
Anti-TNF-IR[e]	N=17		N=24	
ASAS20/40, % response	81/63		74/57	

[a]Missing data of binary variables were imputed and for continuous variables MMRM estimates are shown. [b]Evaluable data available in n=86 and n=98 pts in the secukinumab IV→150mg and IV→75mg groups, respectively. [c]Least squares mean±SE for MMRM estimates and mean±SD for observed data. [d]Observed data. [e]Evaluable data available in n=70 and 75 pts (naïve) and n=16 and 23 pts (IR) in the secukinumab IV→150mg and IV→75mg groups, respectively. [#]Observed data provided for reference. IV, pts received secukinumab 10mg/kg i.v. loading at baseline, Wks 2 and 4; N, number of pts in the extension trial.

Figure. ASAS20 and ASAS40 responses through Week 156



Data presented after multiple imputation through Week 156. ASAS20 and ASAS40 responses through Week 104 have been reported previously.[2] N, number of patients in the extension trial

Conclusions: Secukinumab provided sustained efficacy in signs/symptoms and physical function in pts with active AS over 3 yrs. Secukinumab was well tolerated with a favorable safety profile consistent with that reported previously.[1,2]

References:
[1] Baeten D, et al. N Engl J Med 2015;373:2534–48.
[2] Braun J, et al. Ann Rheum Dis 2016;doi: 10.1136/annrheumdis-2016-209730.

Disclosure of Interest: X. Baraliakos Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, A. Kivitz Consultant for: AbbVie, Pfizer, Genentech, UCB, Celgene, Speakers bureau: Celgene, Pfizer, Genentech, A. Deodhar Grant/research support from: Eli Lilly, Janssen, Novartis, Pfizer, UCB, Consultant for: Eli Lilly, Janssen, Novartis, Pfizer, UCB, J. Braun Grant/research support from: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, UCB, Consultant for: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, UCB, Speakers bureau: Abbvie (Abbott), Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, EBEWE Pharma, Medac, MSD (Schering-Plough), Mundipharma, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis, UCB, J. Wei Grant/research support from: BMS, Janssen, Pfizer, Sanofi-Aventis, Novartis, Consultant for: Pfizer, Celgene, Chugai, UCB Pharma, TSH Taiwan, Speakers bureau: AbbVie, BMS, Chugai, Janssen, Pfizer, E. Delicha Employee of: Novartis, Z. Talloczy Shareholder of: Novartis, Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis

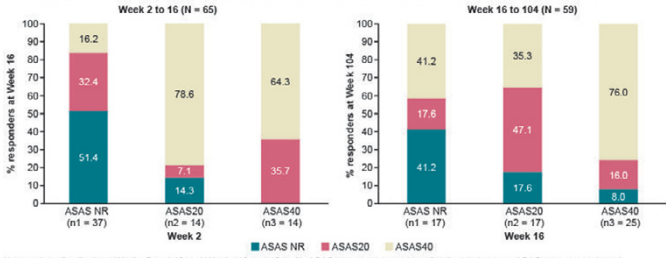
DOI: 10.1136/annrheumdis-2017-eular.1195

THU0398 SECUKINUMAB SUSTAINS INDIVIDUAL CLINICAL RESPONSES OVER TIME IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 2-YEAR RESULTS FROM A PHASE 3 TRIAL, MEASURE 2

X. Baraliakos[1], M. Schiff[2], K. Pavelka[3], A. Widmer[4], B. Porter[5], C. Gaillez[4] on behalf of the MEASURE 2 study group. *[1]Ruhr-University Bochum, Herne, Germany; [2]University of Colorado, Denver, United States; [3]Charles University, Prague, Czech Republic; [4]Novartis Pharma AG, Basel, Switzerland; [5]Novartis Pharmaceuticals Corporation, East Hanover, United States*

Background: The assessment of achieving, maintaining or improving clinical response to biologics in ankylosing spondylitis (AS) is a part of treat-to-target recommendations aimed at optimising treatment goals.[1]
Objectives: To evaluate patient (pt)-level secukinumab data and assess the likelihood of achieving, maintaining or improving an Assessment of SpondyloArthritis international Society (ASAS) response from Week (Wk) 2 (early response) to Wk 16 (primary endpoint) and from Wk 16 to Wk 52 or 104 (sustained effect) in pts with active AS from the MEASURE 2 trial.[2,3]
Methods: This is a *post-hoc* analysis of AS pts originally randomised to secukinumab 150mg (approved dose) who completed the 16-wk double-blind treatment period, followed by long-term uncontrolled treatment. Shift analyses on ASAS response between Wks 2 and 16 and Wks 16 and 52 or 104 were performed on subgroups of secukinumab 150mg treated pts categorised by their highest ASAS criteria response at the earlier time point (ASAS non-responder [ASAS NR], ASAS20 responder, ASAS40 responder) and evaluating whether this response was improved, sustained, or worsened at the later time point, based on observed analysis.
Results: Overall, 65, 61 and 59 pts treated with secukinumab 150mg had available data to determine ASAS responses for shift analyses from Wk 2 to 16 and Wk 16 to 52 or 104, respectively. At baseline, mean age was 41.9±12.5 years, mean time since diagnosis was 7.0±8.2 years and mean Bath Ankylosing Spondylitis Disease Activity Index score was 6.6±1.5. Approximately half of the ASAS NR pts at Wk 2 or 16 subsequently developed an ASAS 20 or 40 response at the later time point of Wk 16 or 52, respectively. A total of 79% pts improved their response from ASAS20 to ASAS40 at Wk 16 (Wk 2 to 16) and another 44% pts improved their response from ASAS20 to ASAS40 from Wk 16 to 52. A majority (64% and 84%) of ASAS40 responders at Wk 2 or 16 maintained this response at Wk 16 or 52, respectively. Similar trends were observed in responses from Wk 16 to 104 (Figure).
Conclusions: In this *post-hoc* pt-level analysis, the majority of secukinumab 150mg treated pts maintained or improved their ASAS responses over time, consistent with the sustainability of group-level ASAS responses reported previously.[2,3] In particular, the majority of pts who achieved either an ASAS20 or ASAS40 response at Wk 2 or 16 maintained or improved their response at Wks 16, 52 or 104, respectively.
References:
[1] Smolen JS, et al. Ann Rheum Dis 2014;73:6–16.
[2] Baeten D, et al. N Engl J Med 2015;373:2534–48.
[3] Marzo-Ortega H, et al. Ann Rheum Dis 2016;75:812–3.

Figure. Shift analyses on ASAS responses in secukinumab 150mg from Week 2 to 16 and 16 to 104



N = number of patients at Weeks 2 and 16 and Weeks 16 and 104 with ASAS status; n1 = number of patients who were ASAS non-responders at Week 2 or 16; n2 or n3 = number of patients who achieved ASAS20 or ASAS40 at Week 2 or 16; Percentages were calculated by considering n1 to n3 as denominator at Weeks 16 and 104. Patients with multiple responses are counted once at Week 2 and counted once in best response at Week 16 or 104.

Disclosure of Interest: X. Baraliakos Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, Consultant for: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Werfen, M. Schiff Consultant for: Abbvie, BMS, Lilly, J&J, Speakers bureau: Abbvie, K. Pavelka Speakers bureau: MSD, AbbVie, Roche, UCB, Amgen, Hospira, Egis, Pfizer, Medac, BMS, A. Widmer Shareholder of: Novartis, Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis, C. Gaillez Shareholder of: Novartis, BMS, Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.1196

THU0399 TAPERING THERAPY OF TNF-INHIBITOR FOR MRI CHANGES IN SPONDYLOARTHRITIS

Y. Song, Y. Cui, X. Zhang, H. Zeng, Y. Zeng. *Goungdong General Hospital, Goungzhou, China*

Background: TNF-inhibitors could significantly improve disease activity of SpA patients, however, there is still no answer to the effect of prolonged the interval of TNF-inhibitors on MRI changes.
Objectives: The aim of the study was to investigate whether prolonged the interval of TNF-inhibitor injection could maintain SpA at low disease activity and improve imaging changes of sacroiliac joint.
Methods: A total of 98 SpA patients were included and 67 of them received TNF-i with or without conventional DMARDs. TNF-i included Etanercept, Infliximab and Adalimumab. The full dosage treatment was defined as patients received Etanercept 50 mg per week, Infliximab 4 mg/kg at 0, 2, 6 week and Adalimumab 40 mg every two weeks. The dose of Etanercept was gradually reduced to 50 mg every two weeks, 50 mg every three weeks and then 50 mg per month. The infusion of Infliximab was reduced to every 8 weeks, every 12 weeks and then every 16 weeks. The interval of Adalimumub injection was changed from 3 weeks to 4 weeks and then to two months. After full dose treatment in the first 3 months, patients who administrated TNF-i were evaluated every 3–6 months. According to laboratory tests including ESR, CRP and IgA levels, BASDAI, BASFI, ASDAS results and sacroiliac joint SPARCC scores, the interval of TNF-i treatment was prolonged gradually. Fat metaplasia, bone erosion, sclerosis and ankylosis changes on MRI were compared between baseline, 4–6 months and 1–2 years.
Results: After 3 months of treatment, inflammatory indexes, BASDI, BASFI, ASDAS and SPARCC scores were significantly lower than baseline ($P<0.05$). After 4–6 months of treatment, ESR, CRP and IgA levels were greatly lower than before (8 (3,25) *vs.* 2 (1,3) mm/h, 4.97 (1.83,14.5) *vs.* 1.71 (1.24,2.82) mg/l, 2.96±1.34 *vs.* 2.20±1.01mg/l, Table 1, $P<0.01$). Compared to baseline, significant reduction of BASDAI and BASFI score was observed in TNF-inhibitor

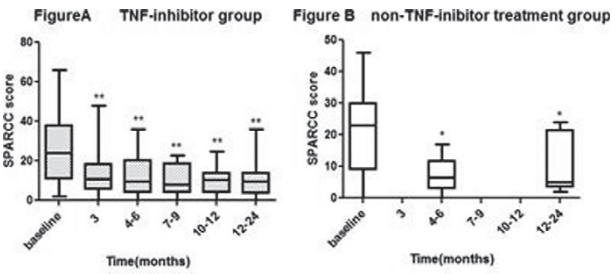


Figure 1 SPARCC score changes in TNF-inhibitor(A) and non-TNF-inhibitor(B) treatment group

Abstract THU0399 – Table 1. ESR, CRP and IgA changes before and after treatment

		Baseline	3 months	4–6 months	7–9 months	9–12 months	12–24 months
ESR (mm/h)	TNF-inhibitor	8 (3,25)	2 (1,3.75)**	2 (1,3)**	7 (2,9)	2.93 (2,6)	5.05 (2,17.75)
	non-TNF-inhibitor	10 (5,36)	–	2 (2,8)	–	–	4 (0.5,10.5)
CRP (mg/L)	TNF-inhibitor	4.97 (1.83,14.5)	1.54 (1.03,3.02)*	1.71 (1.24,2.82)**	4.89 (1.95,8.75)	2.01 (1.25,4.37)	4.21 (1.0,10.83)
	non-TNF-inhibitor	6.85 (3.11,16.05)	–	1.95 (1.59,5.34)	–	–	4.72 (1.8,7.43)
IgA (mg/L)	TNF-inhibitor	2.96±1.34	1.88±1.38	2.20±1.01**	1.92±1.63	1.78±1.32	2.45±1.63
	non-TNF-inhibitor	3.47±1.63	–	1.95±1.35	–	1.79±2.53	1.47±1.48

*P<0.05, **P<0.01.

group. The SPARCC scores in TNF-i group also decreased significantly (Figure1, $P<0.01$). There was no significant progress in fat metaplaisa, bone erosions, sclerosis and ankylosis during the follow-up period ($P>0.05$). Even though the inflammatory indexes and clinical evaluation of non-TNF-i group did not improved remarkably, SPARCC score were significantly reduced at 4–6 months and 1–2 years ($P<0.05$).
Conclusions: TNF-i could reduce clinical and imaging inflammatory degree. Prolonged the interval of TNF-i treatment could maintain low disease activity and improve bone marrow edema, whereas fat metaplasia, bone erosion, sclerosis and ankylosis were not exacerbated.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4775

THU0400 RISK FACTORS OF SAGITTAL TRANSLATION AFTER PEDICLE SUBTRACTION OSTEOTOMY ON ANKYLOSING SPONDYLITIS

Y.-S. Park, J. Kim, J.-S. Park. *Department of Orthopaedic Surgery, Hanyang University Guri Hospital, Guri city, Korea, Republic Of*

Background: Few studies on sagittal translation and its risk factors after pedicle subtraction osteotomy (PSO) in ankylosing spondylitis (AS) patients have been conducted. There is also no study on overall evaluation of radiologic parameters as the candidate of its risk factor.
Objectives: The aim of this study was to report the cases of sagittal translation which developed after PSO in AS patients with kyphotic deformity and to analyze its risk factors
Methods: The subjects of this study were 53 AS patients (58 cases) who underwent PSO to correct their kyphotic deformity between March 2006 and August 2016. The 53 subjects consisted of 45 males and 8 females. Their mean age was 39.3 12 Tit'>7.9 (range: 29–67). After osteotomy, the patient was examined for the presence of sagittal translation in the correction site through intraoperative radiograph. The low modified Stoke AS spine score (mSASSS) was measured before the surgery. The vertebral parameters such as lumbar lordosis angle, thoracic kyphotic angle, and sagittal vertical axis, and the pelvic parameters such as pelvic incidence, pelvic tilt, and sacral slope were also measured before and after the surgery.
The subjects were grouped according to the presence and absence of sagittal translation, and their radiologic parameters were compared. In addition, the correlation between sagittal translation and each parameter was analyzed. Complications that developed during and after the surgery were also analyzed.
Results: Sagittal translation developed in 16 subjects (30%) or 17 cases (29.3%). The mean lumbar lordosis angle and the mean sagittal vertical axis of both the sagittal translation (ST) group and the non-sagittal translation (Non-ST) group were successfully corrected (p=0.000, respectively). A significant difference in preoperative mean sacral slope was observed between the groups (p=0.045). The ST group showed a significantly higher mSASSS (48.1±20.7) than the Non-ST group (36.8±16.2) (p=0.002). In the multivariate regression analysis, sagittal translation was positively correlated with mSASSS (odds ratio 1.34, P=0.002) and the preoperative sacral slope (odds ratio 1.46, P=0.009), and negatively correlated with the difference between preoperative and postoperative thoracic kyphotic angle (odds ratio 0.68, P=0.01). Both groups showed no finding of permanent neurologic complication after the surgery.
Conclusions: The incidence of sagittal translation after pedicle subtraction osteotomy was closely related with the severity of ankyloses in AS patients. Therefore, when pedicle subtraction osteotomy is performed for AS patients with severe ankyloses and high sacral slope, it is required that surgeon consider sagittal translation which could induce neurologic complication.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4239

THURSDAY, 15 JUNE 2017

Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis

THU0401 ULTRASOUND EVALUATION IN FOLLOW-UP OF URATE-LOWERING THERAPY IN GOUTY PATIENTS: THE USEFUL STUDY

M. Forien[1], E. Norkuviene[2], P. Richette[3], G. Mouterde[4], H.-K. Ea[3], F. Lioté[3], M. Petraitis[2], T. Bardin[3], J. Ora[3], P. Dieudé[1], S. Ottaviani[1]. *[1]Rheumatology, Hôpital Bichat, Paris, France; [2]Rheumatology, Lithuanian University of Health Sciences, Kaunas, Lithuania; [3]Rheumatology, Lariboisière Hospital, Paris; [4]Rheumatology, Lapeyronie Hospital, Montpellier, France*

Background: Ultrasonography (US) has demonstrated its ability to detect urate deposition in gouty patients. Some US features have been suggested to be specific such as tophus and the double contour (DC) sign. In contrast to the usefulness of US for diagnosis, data are lacking on its role in follow-up of gout deposition after initiation of urate-lowering therapy (ULT).
Objectives: We aimed to determine the ability of US to show disappearance of urate deposits in gouty patients requiring ULT.
Methods: We performed a 6-month multicentre prospective study. To be included in the study, patients needed to have: i) a proven gout (identification of monosodic urate crystal in synovial fluid analysis or tophus aspiration), ii) presence of US features of gout (tophus and/or DC sign) at knee and/or first metatarsophalangeal joints (MTP1s). Serum uric-acid (SUA) level was assessed at baseline, M3 and M6. US evaluations were performed at baseline, M3 and M6 after starting ULT, by one local rheumatologist, blinded to SUA levels and clinical data. The primary outcome was the decrease (absolute value and percentage of decrease) of US tophus after 6 months of ULT, according to the final SUA levels. The secondary outcome was the mean percentage of joint sites with DC sign disappearance. Three stages of SUA levels were defined (high SUA levels: >360 μmol/l, low SUA: 300 -360 μmol/l, very low SUA: <300 μmol/l.
Results: A total of 79 gouty patients (mean ± SD age 61.8±14 years, 91% of males) were included. The mean disease duration was 6.3±6.1 years. Tophi were found at clinical exam in 29% of patients. Baseline SUA levels were 530±97 μmol/l. At least one US tophus and DC sign were found in 74 (93.7%) and 68 (86.1%) of patients, respectively. Allopurinol and febuxostat was started in 26 (33%) and 53 (67%) patients, respectively. A total of 67 patients were completers at 6 months. Among those M6 completers, 39 and 18 patients achieved a very low and low SUA levels, respectively. The 10 remaining patients maintained high SUA levels. Comparison of US features of gout modifications between the 3 groups of final SUA levels revealed a higher decrease of US tophus size and higher proportion of DC sign dissolution among patients with lowest SUA levels (Table 1). Additionally, final M6 SUA levels was associated with: decrease size of tophus (r=0.5093 [0.3012; 0.6711], P<0.0001), percentage of decrease of the tophus size (r=0.5352 [0.3332; 0.6902], P<0.0001) and inversely correlated with the proportion of DC sign dissolution (r=-0.624 [-0.763; -0.4298]).

Table 1. Modifications of US features of gout after 6 months of ULT

M6 SUA levels, mmol/l	SUA <300 N=39	SUA 300–360 N=18	SUA >360 N=10	P*
Delta size tophus, mean ± SD mm	-6.5±4.1	-4.4±3.0	-0.0±1.5	P=0.00046
% of decrease of tophus	-56.6±32.9	-31.5±24.3	-10.3±17.2	P=0.00028
% of joint site with DC sign dissolution	80.8	59.9	1.1	P<0.0001

*Kruskal-Wallis test. DC: double contour; SD: standard deviation; SUA: serum uric acid levels.

Conclusions: US is able to detect decrease or disappearance of US urate deposits after ULT. Additionally, the decrease of US deposits is strongly correlated with lowest SUA levels. These data suggest that US could be useful for ULT management in gouty patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4941

THU0402 ULTRASONOGRAPHY AND DUAL-ENERGY CT (DECT) DO NOT PROVIDE THE SAME QUANTIFICATION OF URATE DEPOSITION IN GOUT: RESULTS FROM A CROSS-SECTIONAL STUDY

T. Pascart[1], A. Grandjean[2], L. Norberciak[3], V. Ducoulombier[2], M. Motte[2], H. Luraschi[2], M. Vandecandelaere[2], C. Godart[2], E. Houvenagel[2], N. Namane[2], J.-F. Budzik[4]. *[1]Rheumatology; [2]Hopital Saint Philibert, LOMME, France; [3]Biostatistics; [4]Radiology, Hopital Saint Philibert, LOMME, France*

Background: Gout is due to monosodium urate (MSU) deposition in joints and soft tissues. Ultrasonography (US) and dual-energy CT (DECT) have been shown to be effective in detecting MSU deposits. Both techniques can examine tophi size. DECT is effective to identify soft-tissue MSU deposits and US can show joint deposition with the double contour (DC) sign. It is unknown if these two techniques provide the same quantification of the extent of urate deposition on a given patient.
Objectives: The main objective of this study is to compare the tophus size measured by US and by DECT. The secondary objective is to evaluate the correlation between the prevalence of the US DC sign and the global volume of urate deposits measured by DECT.
Methods: This prospective cross-sectional study included patients fulfilling the 2015 ACR/EUALR criteria for gout. Patients underwent US and DECT examinations of their knees and feet. The largest US tophi was selected as the index tophus. US examination of the DC sign was performed on the femoro-patellar joints, talo-crural joints and 1st metatarsophalangeal joints. Total volume of urate deposits of knees and feet was measured by DECT. The primary endpoint was the intra-class correlation coefficient (ICC) of the volume of the index tophus measured by US and DECT [CI 95%].
Results: A total of 64 patients were included in the study, of which 35 patients presented with at least one US tophus. Patients were in average 64.5±16.3 years old, 84.4% were male, had an average ACR/EULAR score of 13.6±2.5, and disease duration was 12±14.7 years. Overall, 44 patients (68.8%) were currently taking urate lowering therapy and 22 patients (34.4%) had clinical tophi. Out of the 35 US selected largest tophi, 6 tophi were not seen in DECT. Of the tophi identified with both techniques, 21 were localized in the feet and 8 in the knees. The ICC of the tophus volume assessment by US and DECT was 0.45 [0.12–0.69]. The average volume of the largest US tophi was 2.7±6.5 cm^3 and 1.5±3.3cm^3 when measured by DECT. If the index tophus was localized in the knee, the ICC was 0.36 [0–0.82] and was 0.68 [0.37–0.86] if the tophus was in

the foot. The Spearman correlation coefficient between the DECT urate volume and the number of joints with a positive DC sign was 0.15.
Conclusions: US and DECT do not provide the same assessment of tophus size. The correlation is improved when considering tophi localized in the feet. The number of joints with positive DC sign does not correlate to the volume of urate deposition in the soft tissues measured by DECT.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4118

THU0403 URATE-LOWERING TREATMENT AND RISK OF INCIDENT UROLITHIASIS IN PEOPLE WITH GOUT: A NESTED CASE-CONTROL STUDY

C.-F. Kuo, J.-S. Chen. *Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan, Province of China*

Background: A higher risk of urolithiasis has been reported in gout patients. However, whether urate-lowering treatments, including both xanthine oxidase inhibotors and uricosuric agents, are beneficial to reduce the risk or urolithiasis in gout patients has not been examined.
Objectives: To investigate the independent associations between urate-lowering treatment (ULT) and the risk of urolithiasis in incident gout patients.
Methods: We conducted a nested case-control study based on the Taiwan National Health Insurance Research Database (NHIRD), which was used to identify 473,858 newly diagnosis gout patients during the period from January 1, 2000 through December 31, 2004. All these patients were followed until December 31, 2013. We considered patients who first diagnose incident urolithiasis after the date of entry cohort (gout onset) as cases and the diagnostic date was defined as index date. Each case was matched up to five eligible controls whose follow-up period included the case's index date by sex, birth of year and gout diagnosis year. And the index date of case was assigned to the matched controls. Odds ratios (ORs) and 95% confidence interval (CI) of urolithiasis associated with cumulative defined daily dose (cDDD) of xanthine oxidase inhibitor and uricosuric agents were main ourcome measures.
Results: Gout patients with incident urolithiasis (n=32,654) occurring after the initial diagnosis of gout aged 20–79 were age- and sex-matched 1:5 to 163,270 gout patients without urolithiasis. After adjusting for age, sex, urbanization status, income, occupation, and pertinent drugs and comorbidities, the OR of urolithiasis associated with use of ULT among gout patients were 1.04 (95% CI 1.00 to 1.07) for those with 28–90 cDDD, 0.95 (95% confidence interval 0.91–0.99) for 91–365 cDDD and 0.77 (95% confidence interval 0.73–0.82) for >365 cDDD, compared with those with a cDDD <28. The OR (95% CI) for urolithiasis associated with xanthine oxidase inhibitor use was 0.94 (0.89–0.99) for 28–90 cDDD, 0.90 (0.84–0.97) for 91–365 cDDD and 0.73 (0.63–0.83) for >365 cDDD. For uriscouric agents, the OR (95% CI) for urolithiasis among those with 28–91, 91–365 and <365 cDDD were 1.04 (1.01, 1.08), 0.94 (0.90–0.98) and 0.78 (0.73–0.84), respectively.
Conclusions: Higher ULT consumption was associated with a lower risk of urolithiasis. Xanthine oxidase inhibitors associated with reduced urolithiasis risk consistently across the range of consumption studied but for uricosuric agents inadequate cumulative dose results in a higher risk despite the risk reduced gradually with a higher cumulative dose.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2913

THU0404 SELF-REPORTED SEVERITY OF GOUT IN A PRIMARY CARE SETTING AND ASSOCIATED FACTORS – RESULTS FROM A GOUT SURVEY IN PRIMARY CARE

A.J. Landgren, M. Dehlin, U. Bergsten, V. Sigurdardottir, P. Drivelegka, T. Zverkova Sandström, L. Jacobsson. *Department of Rheumatology and Inflammation Research, Institution of Medicine, Sahlgrenska Academy. University of Gothenburg., Gothenburg, Sweden*

Background: Patients with gout are usually seen in primary care. There are numerous reports regarding severity of gout in cohort studies and patients seen in more specialized care, less is known about the spectrum of severity of the disease in primary care.
Objectives: To describe the pattern of self-reported disease severity of gout and predictors thereof in a primary care setting.
Methods: All patients above 18 with an ICD10-diagnosis of gout at a health care visit in primary care (Jan 2015 through Aug 2016) were identified from primary care within the Western Sweden Health Care Region (WSHCR). 941 patients were identified and included in the study. They were sent a questionnaire with questions regarding comorbidities, demographics, gout characteristics and Health Assessment questionnaire (HAQ) reflecting disability. Self-reported disease severity was assessed by a three-level Likert scale (mild, moderate, severe). Possibly associated factors were analyzed by bivariate logistic regression (binary outcome: mild vs. moderate/severe) models and factors that were statistically significant were further analyzed by multivariate analysis.
Results: The response rate was 54%. Response rates were significantly lower in women overall and in men under the age of 50. Covariates that were significantly associated with more severe self-reported severity of gout in the bivariate logistic regression models (Table 1) were: female sex, hyperlipidemia, higher number of previous attacks, attack during last month, HAQ. In the multivariate analysis objective measures of gout severity such as more than ten previous attacks and attack during last month were strongly associated with the patients grading of severity, in addition to presence of hyperlipidemia (Table 1).

Table 1. Characteristics of gout patients stratified by disease severity and logistic regression models

Covariates	Mild* n=272	Moderate* n=130	Severe* n=62	Univariate analyses** OR (95% CI)#	Multivariate analyses (OR (95% CI)#
Age in years (mean)	70.8	71.9	71.8	1.01 (0.99–1.02)	N/A
Female sex (%)	12.9	18.5	22.6	1.67 (1.01–2.76)	1.54 (0.85–2.80)
Education ≤9 years (%)	24.8	27.6	46.6	1.46 (0.97–2.21)	N/A
Diabetes (%)	22.8	27.1	27.4	1.29 (0.84–1.98)	N/A
Kidney disease (%)	6.6	9.3	11.3	1.59 (0.81–3.12)	N/A
BMI (mean)	27.9	28.2	27.8	1.02 (0.97–1.06)	N/A
Hyperlipidemia (%)	29.4	44.2	46.8	2.00 (1.36–2.95)	2.13 (1.39–3.28)
Duration of gout in years (mean)	10.4	11.2	8.5	1.00 (0.98–1.01)	N/A
Total number of attacks (%):					
1	19.5	6.4	12.1	ref	ref
2–5	50.0	40.8	39.7	1.93 (1.01–3.67)	1.51 (0.77–2.96)
6–10	14.8	20.8	13.8	2.98 (1.42–6.25)	2.12 (0.97–4.62)
>10	15.6	32.0	34.5	5.00 (2.48–10.09)	3.15 (1.49–6.65)
Attack during the last month (%)	11.5	30.4	30.6	3.43 (2.10–5.61)	1.81 (1.36–2.41)
ULT¶ (%)	46.3	50.8	50.0	0.85 (0.46–1.55)	N/A
HAQ§ (mean)	0.24	0.29	0.51	1.56 (1.09–2.24)	1.20 (0.80–1.81)
Tophus (%)	14.3	21.3	4.8	1.17 (0.69–1.98)	N/A

*Self-reported disease severity. **ORs reflects yes vs no for dichotomous covariates, per year for age and duration and per unit for HAQ. #Moderate/severe vs mild, ¶Urate-lowering therapy. § Health assessment questionnaire.

Conclusions: Over 40% of patients with gout in a primary care setting rated their disease as moderate or severe. The validity of the patients rating was supported by other covariates reflecting disease severity. The observations that women and those with hyperlipidemia reported a more severe disease needs to be further explored.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3452

THU0405 KILLING TWO BIRDS WITH ONE STONE? THE DASH DIET AND THE RISK OF GOUT: 26-YEAR FOLLOW-UP OF A PROSPECTIVE COHORT

S.K. Rai[1], T.T. Fung[2,3], N. Lu[1], S.F. Keller[1], G.C. Curhan[4,5], H.K. Choi[1,4]. *[1]Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital; [2]Department of Nutrition, Harvard T.H. Chan School of Public Health; [3]Department of Nutrition, Simmons College; [4]Channing Division of Network Medicine, Department of Medicine; [5]Renal Division, Department of Medicine, Brigham and Women's Hospital, Boston, United States*

Background: The Dietary Approaches to Stop Hypertension (DASH) diet, which reduces blood pressure and is recommended in cardiovascular disease (CVD) (1,2), has also been found to lower serum uric acid (SUA) levels, particularly among those with hyperuricemia (3). Thus, the DASH diet may be particularly useful in gout care by reducing both SUA and CVD risk, especially among patients with hypertension which affects 74% of gout patients (4), thereby "killing two birds with one stone". However, corresponding data for the risk of gout are not available. In contrast, a Western dietary pattern may increase the risk of gout.
Objectives: To prospectively examine the relation between the DASH and Western dietary patterns and the risk of gout among men.
Methods: Using the Health Professionals Follow-up Study, we prospectively examined the relation between the DASH and Western diets and incident gout in 44,444 male participants with no history of gout at baseline. Using validated food frequency questionnaires, each participant was assigned a DASH score (reflecting high intake of fruits, vegetables, nuts and legumes, low-fat dairy products, and whole grains, and low intake of sodium, sweetened beverages, and red and processed meats) and a Western pattern score (reflecting higher intake of red and processed meats, French fries, refined grains, sweets, and desserts). We identified incident cases of gout meeting the preliminary ACR survey criteria for gout, adjusting for potential confounders including age, total energy intake, body mass index (BMI), diuretic use, history of hypertension, history of renal failure, and intake of alcohol and coffee. We conducted stratified analyses to evaluate whether the association between the DASH and Western pattern scores and the risk of gout varied according to BMI, alcohol use, and hypertension status.
Results: During 26 years of follow-up, we documented 1,731 confirmed cases of incident gout. A higher DASH score was associated with a lower risk for gout (multivariable relative risk [RR] for extreme quintiles, 0.68 [95% confidence interval, 0.57 to 0.80]; P for trend <0.001) (Table 1). In contrast, a higher Western pattern score was associated with an increased risk for gout (multivariable RR for extreme quintiles, 1.42 [95% confidence interval, 1.16 to 1.74]; P for trend=0.005) (Table 1). These associations persisted regardless of BMI, alcohol use, and hypertension status, and there was no significant interaction with these variables (all P for interaction >0.17).

Table 1. Relative Risk of Incident Gout According to Quintiles of DASH and Western Dietary Pattern Scores

Variable	Frequency of Intake (serving/d)					P for trend
	Q1	Q2	Q3	Q4	Q5	
DASH Diet						
Cases/PY	396/192891	391/195970	366/196511	332/192697	246/193455	
Age-adjusted RR (95% CI)	1.0	0.96 (0.83,1.10)	0.88 (0.77,1.02)	0.81 (0.70,0.94)	0.60 (0.51,0.70)	<0.001
Multivariable RR (95% CI)	1.0	0.90 (0.79,1.04)	0.87 (0.76,1.01)	0.82 (0.70,0.95)	0.68 (0.57,0.80)	<0.001
Western Diet						
Cases/PY	287/190572	347/194533	365/196671	346/197114	386/193182	
Age-adjusted RR (95% CI)	1.0	1.19 (1.02,1.39)	1.25 (1.07,1.46)	1.18 (1.01,1.38)	1.35 (1.16, 1.57)	<0.001
Multivariable RR (95% CI)	1.0	1.09 (0.93,1.28)	1.15 (0.98,1.36)	1.12 (0.94, 1.33)	1.42 (1.16, 1.74)	0.005

Abbreviations: RR, relative risk; CI, confidence interval; PY, person-years.
Age-adjusted models adjusted for age and total energy intake.

Conclusions: The DASH dietary pattern is associated with a lower risk of gout, suggesting that its urate-lowering effect among hyperuricemic individuals translates to a lower risk of gout. Conversely, the Western dietary pattern is associated with a higher risk of gout. The DASH diet may provide an attractive preventive dietary approach for the risk of gout, particularly given the high level of cardiovascular comorbidities among this patient population.

References:

[1] N Engl J Med. 1997;336(16):1117–24.
[2] N Engl J Med. 2010;362(22):2102–12.
[3] Arthritis Rheumatol. 2016;68(12):3002–3009.
[4] Am J Med. 2012;125(7):679–687.

Acknowledgements: This research was supported by NIH grant R01AR065944.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3925

THU0406 SERUM URIC ACID LOWERING TREATMENT APPEARS UNNECESSARY DURING HEMODIALYSIS

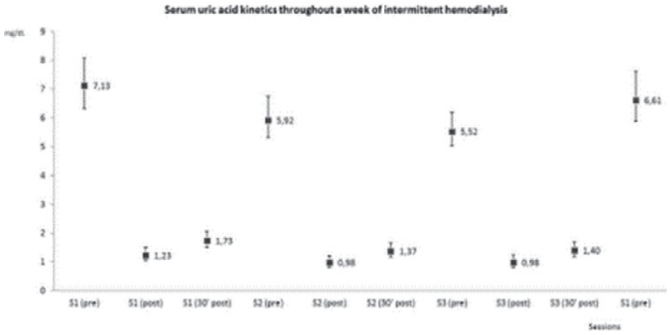
M. Andrés[1,2], R. Soriano[1], E. Oliveira[3], C. Trigo[3], M.D. Arenas[4], E. Pascual[2,5].
[1]Departamento de Medicina Clínica, Universidad Miguel Hernández; [2]Seccion de Reumatologia; [3]Servicio de Análisis Clínicos, Hospital General Universitario de Alicante; [4]Unidad de Nefrología, Hospital Vithas Perpetuo Socorro; [5]Emeritus Professor, Universidad Miguel Hernández, Alicante, Spain

Background: Gout patients often suffer from renal disease, some ultimately developing end-stage renal disease (ESRD) and requiring hemodialysis (HD) replacement therapy. Though some reports suggested that tophi disappear after HD, urate-lowering agents are frequently continued, often based on persistent high SUA levels before HD. Also, the impact of SUA levels in the survival of patients on hemodialysis (HD) is under discussion.

Objectives: To assess the SUA reduction achieved under HD and analyze the kinetics of SUA in a week of intermittent HD.

Methods: SUA levels were determined before and after HD sessions in consecutives 96 patients with end-stage renal disease (ESRD), and compared through paired samples Student's t test. Variables related to HD were analyzed whether associated with SUA reductions ≥80% using Student's t test or ANOVA. Also, a kinetics study on selected 10 patients with hyperuricemia (SUA before HD>6.8 mg/dL) throughout intermittent HD sessions in a week period was performed; differences in SUA levels were analyzed by repeated measures ANOVA.

Results: Patients were mean aged 66.5 years (SD±13.8), 62 males (64.6%). Mean time on HD replacement was 7.1 years (±7.2). Before starting HD, 43.0% had hyperuricemia and 21.6% reported gout. Sixteen (16.4%) continued on urate-lowering agents after HD. Mean SUA levels before and after HD session was 5.2mg/dL (± 1.0) and 1.0mg/dL (±0.4), respectively. Mean SUA reduction following HD was 80.2% (95% CI 78.4–82.0); 51 patients (56.7%) showed SUA reduction ≥80%. HD-related variables Kt/v<1.3 (p=0.006) and blood efflux<400mL/min (p=0.004) significantly associated with achieving SUA reduction ≥80%. Figure shows the SUA kinetics study: SUA significantly reduced all over the period and persisted below hyperuricemia threshold (p=0.015).



Conclusions: Under HD replacement therapy SUA levels effectively reduced and persisted below saturation point, suggesting that urate-lowering therapy appears unnecessary for patients with gout and ESRD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2392

THU0407 HIGH GOUT CLASSIFICATION SCORE IS ASSOCIATED WITH ULTRASOUND FINDINGS IN PATIENTS WITH CRYSTAL-PROVEN GOUT

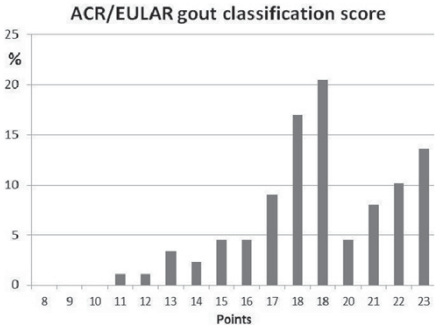
T. Uhlig, L.F. Karoliussen, E.A. Haavardsholm, T.K. Kvien, H.B. Hammer.
Rheumatology, Diakonhjemmet Hospital, Oslo, Norway

Background: The recent ACR/EULAR classification (1) classify gout in patients with at least 8 out of maximum 23 points, but presence of monosodium urate crystals in a symptomatic joint/tophus alone is sufficient for gout classification without need for further scoring. It is not known how in crystal-proven patients with increased serum urate (sUA) the whole range of classification points distribute.

Objectives: To determine the distribution along the spectrum of ACR/EULAR criteria in crystal-proven patients with insufficiently treated sUA levels, and if disease factors in gout are associated with high classification scores.

Methods: Baseline data from a prospective observational study were used from patients with crystal-proven gout who presented after a recent gout flare. Included patients had at baseline insufficiently treated sUA level (>360 μmol/L [>6 mg/dl]). Demographic, clinical data and sUA levels were collected from September 2015 to December 2016 in one rheumatology department. Ultrasound of joints was assessed with one total score for double contour sign, tophus, and aggregates in several joints and tendons/entheses. The score for ACR/EULAR criteria for gout was calculated.

Results: 89 patients were included, with baseline mean (SD) age 56.0 (14.8) years, 92% males, 88% Caucasians, disease duration 7.9 (7.3) years, presence of palpable tophi 19%, ultrasound score 19.9 (13.8), serum urate 486 (90) μmol/L, creatinine 78 (18) ml/min, creatinine clearance 78 (18) ml/min, ESR 14 (14) mm/h, body mass index 29.4 (4.9) kg/m^2, comorbidity score [SCQ] 3.5 (3.2), and physical function [HAQ] 0.34 (0.51). All patients satisfied clearly the scoring arm of the classification criteria with a median (range) 19 (11 – 23) of 23 possible points (Figure 1). Patients with a median and higher score above the median (≥19 points) vs. lower score reported more gout flares during the last 12 months (p<0.001), had longer disease duration (9.2 vs. 6.2 yrs, p=0.05), and a higher ultrasound score (23.9 vs. 14.9, p=0.001). The groups with high and low scores were similar for age, gender, ethnicity, level of education, BMI, physical function, comorbidity score, sUA level and kidney function.



Conclusions: As expected, patients seen in the clinic with crystal-proven gout and at least slightly increased sUA also satisfy the scoring arm of the new classification criteria for gout, supporting their clinical use. Patients with classification points above the median had more flares in the preceding year, and a higher urate burden assessed by ultrasound, but did not have other indicators for a more severe disease.

References:

[1] Neogi T et al. Ann Rheum Dis 2015;74:1789–98.

Disclosure of Interest: T. Uhlig: None declared, L. F. Karoliussen: None declared, E. A. Haavardsholm: None declared, T. K. Kvien Consultant for: Fees for speaking and/or consulting from AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, H. B. Hammer: None declared

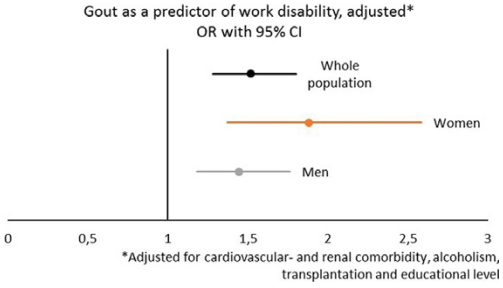
DOI: 10.1136/annrheumdis-2017-eular.2196

THU0408 GOUT IS AN IMPORTANT PREDICTOR OF WORK DISABILITY IN BOTH MEN AND WOMEN

V. Sigurdardottir[1,2], P. Drivelegka[1], A. Svärd[2], L.T. Jacobsson[1], M. Dehlin[1].
[1]Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, University of Gothenburg, Gothenburg; [2]Centre for Clinical Research Dalarna, Falun, Sweden

Background: Gout is the most common form of inflammatory arthritis with a prevalence of 1.5% in our area in the age group 50–59 years (1). Gout has a

substantial association with several comorbidities. Studies on the impact of gout on work disability on a population level are scarce.
Objectives: The primary objective of the study was to investigate if gout was a predictor of work absenteeism exceeding 90 days in a calendar year, controlling for comorbidites and socioeconomic status in men and women separately. Another aim of the study was to explore if urate lowering therapy (ULT) attenuated the risk of work disability for gout cases.
Methods: Gout cases were defined in the population based health care database (VEGA) of the Western Swedish Health Care Region (WSHCR) by having a first diagnosis of gout in the years 2003–2009 by ICD-10 codes (M10 and M14.0) in VEGA. Cases were included if their age at the time of diagnosis of gout was ≤62 years. Five controls for each case, matched for age, sex and place of residence were chosen from the census register by Statistics Sweden. Individuals with any work disability in the year before the index year were excluded from analysis. Data on predefined comorbidities registered previous to the index year was collected from VEGA by ICD-10 codes. Data on prescribed medications was collected from the national prescription database. Data on educational level, income and number of days per calendar year with sick-leave and disability pension was provided by Statistics Sweden. Conditional logistic regression taking into account the 1-to-5 matched design of the study was performed in individuals without work disability in the year before the index date for the outcome of ≥25% (≥90 days) work disability in the year after the index year. Possible predictors of work disability for gout cases were analyzed using logistic regression
Results: 3068 incident gout cases (females N=554 (18%)) of working age without prior work disability were matched to 15,077 population controls. After matching, 3258 controls with prior work disability were excluded leaving 11,819 controls for analysis. Of the women with gout, 69 (12.5%) became ≥25% work disabled in the year after the index-year as opposed to 117 (6.1%) of the female controls, p<0,0001. 163 men with gout (6,5%) became ≥25% disabled vs. 377 (3.8%) of male controls, p<0,0001. After adjusting for comorbidities and educational level gout increased the risk of work disability to a similar extent for men (OR 1.4, 95% CI 1.2–1.8) and women (OR 1.9, 95% CI 1.4–2.6). Cardiovascular and renal comorbidity as well as alcoholism, female sex and low educational level (less than 12 years) were important predictors of work disability in gout patients whereas receiving ULT during the time period being studied did not attenuate the risk (OR 0.8, 95% CI 0.5–1.1).

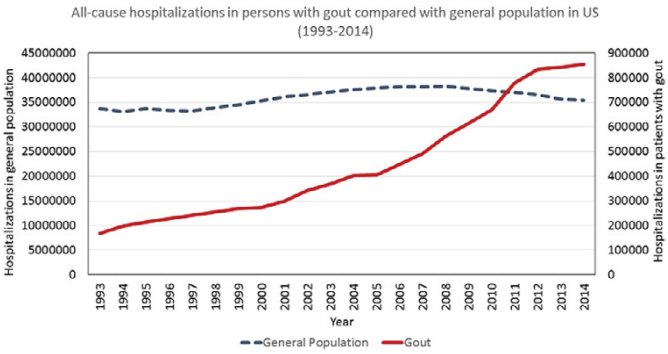


Conclusions: Gout is a significant independent predictor of work disability in both men and women. ULT did not attenuate the risk of work disability early after diagnosis for gout cases in this study, possibly explained by under-prescribing and sub-optimal dosage as previously shown in our region (1).
References:
[1] Dehlin M, Drivelegka P, Sigurdardottir V, Svard A, Jacobsson LT. Incidence and prevalence of gout in Western Sweden. Arthritis research & therapy. 2016;18:164.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4022

THU0409 NOT JUST A SWOLLEN BIG TOE: INCREASING ALL-CAUSE HOSPITALIZATIONS IN PATIENTS WITH GOUT IN THE UNITED STATES: 1993–2014

G. Singh[1], A. Mithal[2], A. Mithal[3]. [1]*Gastroenterology and Hepatology, Stanford University;* [2]*Student;* [3]*Epidemiology, ICORE, Woodside, United States*

Background: Gout is a disorder of uric acid metabolism and often presents as acute severe joint pain. However, several recent studies have highlighted systemic complications of associated hyperuricemia in patients with gout, including possible increased risk of renal and cardiovascular comorbidities.
Objectives: To study all-cause hospitalizations in patients with gout in the United States (US) from 1993 to 2014.
Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in NIS from 1993 to 2014 with a primary or secondary diagnosis of gout, and compared them to total all-cause US hospitalizations during the same period. US population estimates and projections for the resident US population were obtained from the US Census Bureau.
Results: There were 789.8 million all-cause hospitalizations in 6.4 billion person-years of observation from 1993 to 2014 (123.4 hospitalizations per 1,000 person-years). During this time-period, 9,741,598 hospitalizations occurred in patients with gout (152.2 per 100,000 person-years). All-cause US hospitalizations increased from 33.7 million in 1993 to 35.4 million in 2014, an increase of 4.8% over 22 years (Figure, dotted blue line). All-cause hospitalizations in gout patients have increased from 167,441 in 1993 (64.2 per 100,000 person-year) to 854,475 in 2014 (267.9 per 100,000 person-years, a dramatic increase of over 410% (p<0.0001, Figure solid red line). In 2014, hospitalizations in gout patients accounted for over 4.6 million hospital days at a total national cost of over US $42.6 billion.



Conclusions: All-cause hospitalizations in patients with gout in the US have significantly increased by 410% in the last 22 years, almost hundred-fold of the 4.8% increase in US population all-cause hospitalization rate in the same time-period. This calls for an increase need for identification and management of serious co-morbid conditions in patients with gout.
Disclosure of Interest: G. Singh Grant/research support from: Horizon Pharmaceuticals, A. Mithal: None declared, A. Mithal: None declared
DOI: 10.1136/annrheumdis-2017-eular.5458

THU0410 GOUT AND THE RISK OF INCIDENT ERECTILE DYSFUNCTION: A BODY MASS INDEX-MATCHED POPULATION-BASED STUDY

N. Schlesinger[1], N. Lu[2], H.K. Choi[2]. [1]*Medicine, Rutgers/ Robert Wood Johnson Medical School, New Brunswick;* [2]*Medicine, Harvard Medical School, Boston, United States*

Background: Gout is the most common inflammatory arthritis. Erectile dysfunction is common in the general population; however, evidence regarding erectile dysfunction among gout patients is limited.
Objectives: Our purpose was to study whether there was an increased risk of erectile dysfunction among gout patients, as compared with the general population.
Methods: We conducted a cohort study using The Health Improvement Network, an electronic medical record database in the United Kingdom. Up to five individuals without gout were matched to each case of incident gout by age, enrolment time, and body mass index. Multivariate Hazard Ratios for erectile dysfunction were calculated after adjusting for smoking, alcohol consumption, comorbidities and medication use.
Results: We identified 2290 new cases of erectile dysfunction among 38,438 patients with gout (mean age 63.6 years) and 8447 cases among 154,332 individuals in the comparison cohort over a 5-year median follow up (11.9 vs. 10.5 per 1000 person-years, respectively). Univariate (age, entry time and body mass index-matched) and multivariate Hazard Ratios for erectile dysfunction among patients with gout were 1.13 (95% CI, 1.08 to 1.19) and 1.15 (95% CI, 1.09 to 1.21), respectively. In our sensitivity analysis, restricting gout cases to those receiving anti-gout treatment (n=31,227) the magnitude of relative risk was stronger than the primary analysis; (multivariate Hazard Ratios =1.29; 95% CI, 1.22 to 1.37).
Conclusions: This population-based study suggests an increased risk of erectile dysfunction among gout patients, supporting a possible role for hyperuricemia and inflammation as independent risk factors for erectile dysfunction.
References:
[1] Jackson G, et al. Int J Clin Pract 2002; 56: 663.
[2] Clarson L, et al. Ann Rheum Dis 2015; 74: 4642.
[3] Schlesinger N, et al. J Rheumatol 2015; *42*: 1893.
[4] Vlachopoulos C, et al. Eur Urol 2007; *2*:1590.
Disclosure of Interest: N. Schlesinger Grant/research support from: Astra Zeneca, Consultant for: Astra Zeneca, Horizon, Celgene, ProteoThera, Pfizer, N. Lu: None declared, H. Choi Grant/research support from: Astra Zeneca, Consultant for: Takeda, Selecta
DOI: 10.1136/annrheumdis-2017-eular.2710

THU0411 TOPHUS BURDEN. CLINICAL EVALUATION DURING 3 YEARS FOLLOW-UP IN GRESGO COHORT

A. Maya Gutierrez[1], C.O. Lopez Lopez[2], E. Alvarez Hernandez[1], C. Gomez Ruiz[1], I. Peláez Ballestas[1], R. Burgos-Vargas[1], J. Vazquez Mellado[1,3].
[1]Rheumatology; [2]Medicina Física y Rehabilitación, Hospital General de México; [3]Facultad de Medicina, UNAM, Mexico, Mexico

Background: Tophus burden (TB) was proposed by OMERACT as mandatory domain for chronic gout studies. Image methods although useful, frequently are not available in daily clinical practice.
Objectives: To evaluate TB clinically in a cohort of gout patients during 3 years follow-up.
Methods: We analyzed baseline and follow-up data (6, 12, 18, 20, 24, 30 and 36 months) of patients with gout (ARA/CGD/ACR-EULAR) from the GRESGO cohort; this analysis includes the patients with ≥1 clinical nodule(s) considered as tophi in the baseline visit. Index tophi size (ITS) was considered as the longer axis of the bigger tophi. TB evaluations: 1) Tophi number (T); 2) ITSt (cm) measured with tape; 3) ITSca (cm), measured with caliper; 4) ITSco, measured with compass. 5) Index tophi hardness (ITh) or consistency, by VAS (0: very soft-10 hard as a rock). This protocol was approved by the local IRB and patients signed and informed consent for their participation.
All the patients received treatment for gout and associated diseases according to published guides and available drugs. The evaluations were done by the same group of physicians (Rheumatologists and Residents). Variables: TB measures, demographic, clinical and biochemical variables. HAQ and EUROQoL and VAS for pain and general health. Inter/intraobserver variability were evaluated. Statistical analysis: t test, X2, r, kappa, Friedman and multiple correlation.
Results: 298 patients; 97%males, 203 (68%) tophaceous gout, age, age at onset and duration of the disease were: 46.4±12.7 32.4±12.4 and 14.7±9.3 years respectively. Available ULT: Allopurinol and probenecid, colchicine as prophylaxis. Mean allopurinol dose prescribed at baseline visit was 346.9±154 mg/d and 550±205 mg/d 3 years later.TB values (see table). Index tophi size had r>0.93 among the 3 evaluations (ITSt, ITSca, ITSco) and r<0.3 with ITh. Inter and intraobserver variability was 0.8 and 0.9 respectively; there was significant improvement *(p<0.001) in ITS, sUA, painful, swollen, limited to motion joints, HAQ, EuROQoL, VAS pain, VAS health (patient and physician) also improved significantly.

	Baseline	6mo	12mo	18mo	24mo	30mo	36mo
ITSt*	6.4±3.7	5.9±3.7	5.6±3.7	5.7±3.9	5.2±4.0	5.6±3.3	4.5±3.3
ITSca	5.1±2.8	4.6±2.7	4.7±2.6	4.7±2.9	4.4±2.7	4.6±2.4	3.6±1.9
ITSco	5.1±3.0	4.6±2.8	4.7±2.7	4.9±3.0	4.3±2.8	4.6±2.5	3.8±1.8
ITh	7.3±1.7	6.8±1.9	7.1±1.6	6.7±1.9	6.5±1.8	6.6±2.0	6.3±1.6
HAQ*	0.6±0.7	0.4±0.5	0.3±0.5	0.4±0.4	0.3±0.4	0.4±0.5	0.2±0.4
AGA*	8.3±12	0.8±1.3	0.6±2.6	0.3±0.8	0.2±0.6	0.2±0.4	0.3±0.6
sUA*	8.3±2.2	7.3±2.0	6.8±1.9	6.3±1.9	6.3±2.5	5.5±1.6	5.8±1.8
Allopurinol*	347±154	445±165	477±178	491±180	534±205	504±183	556±193

Values represent mean and SD. *p<0.01 ITS in cm; ITh: VAS in cm. AGA number of acute attacks in the last 6 months. sUA: mg/dL, allopurinol dose mg/day.

Conclusions: In our cohort, ITSt was the best measure for TB evaluation, the 3 ITS measures had a good correlation between them and less with ITh or consistency. Patients with tophaceous gout, improved significantly with allopurinol and probenecid during 3 years follow-up in TB (ITSt) as well according to the other OMERACT proposed domains for chronic gout.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2142

THU0412 TREATMENT WITH NERIDRONATE IN CHILDREN AND ADULTS WITH OSTEOGENESIS IMPERFECTA: DATA FROM OPEN-LABEL, NOT CONTROLLED, THREE-YEAR ITALIAN STUDY

A. Fassio, L. Idolazzi, O. Viapiana, C. Benini, E. Vantaggiato, A. Giollo, M. Rossini, D. Gatti. *Rheumatology, Aoui Verona Reumatologia, Verona, Italy*

Background: Osteogenesis Imperfecta (OI) is a rare generalized connective tissue disease. Its main features are skeletal fragility and substantial growth deficiency [1]. Currently, bisphosphonates showed to increase bone mineral density (BMD). A positive effect on prevention of fractures both in adults and in children is reported by some studies, but generally data are still inconsistent [2].
Neridronate is an amino-bisphosphonate licensed in Italy for the treatment of OI.
Objectives: to assess the long-term efficacy and safety of the treatment in patients with OI.
Methods: the patients were divided by age into two groups and observed for 3 years: 55 patients younger than 20 years old and 114 patients older than 20 years old. Neridronate was administered by i.v. infusion at the dosage of 2 mg/kg, up to a maximum of 100 mg at three months intervals. DXA of the lumbar spine, hip and ultradistal radius were evaluated every 6 months. Blood calcium, phosphate, bone turnover markers and fasting urinary calcium/creatinine ratio, were obtained at baseline and every 3 months.
Results: the mean lumbar spine and total hip BMD and BMC significantly increased from baseline up to month 36 in both patients groups. The mean ultradistal radius BMD significantly increased from baseline to any time point in patients younger than 20 years, while, in patients older than 20 years, BMD significantly increased from baseline only at month 18, 30 and 36 respectively. The mean ultradistal radius BMC significantly increased from baseline to any time point in patients younger than 20 years, while there were no substantial or statistically significant changes from baseline to any time point in patients aged older than 20 years. The mean number of fractures observed in the 3 years of treatment was significantly lower than that observed in the 3 years before the start of treatment in both groups (table 1).
Most of AEs were symptoms of an acute phase reaction, which was reported in 47.3% of patients younger than 20 years and in 22.8% of those older than 20 years. Serious adverse events (SAEs) were reported in 19 patients (34.5%) younger than 20 years and in 26 patients (22.8%) aged older than 20 years. None of the reported SAEs in both groups was considered as treatment-related.

Table 1, Results of number of fractures per patient during treatment in the two patient populations

Number of fractures, mean ± SD (range)	Age ≤20 years	Age >20 years
Before treatment (3 years	2.7±2.37 (0–8)	0.6±1.28 (0–8)
During treatment (3 years)	0.9±1.43 (0–7)	0.3±0.56 (0–3)
– Wilcoxon signed rank test p-value	<0.001	0.003

Conclusions: long-term treatment with i.v.neridronate has positive effects on BMD, BMC, bone turnover markers and fracture risk with a good safety profile in both groups.
References:
[1] Hoyer-Kuhn H, Netzer C, Semler O. Osteogenesis imperfecta: pathophysiology and treatment. Wien Med Wochenschr 1946 2015;165:278–84. doi:10.1007/s10354–015–0361-x.
[2] Hald JD, Evangelou E, Langdahl BL, et al. Bisphosphonates for the Prevention of Fractures in Osteogenesis Imperfecta: Meta-Analysis of Placebo-Controlled Trials. J Bone Miner Res 2015;30:929–33. doi:10.1002/jbmr.2410.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2717

THU0413 SERUM URATE AND ITS ASSOCIATION WITH BLOOD PRESSURE AND ENDOTHELIAL DYSFUNCTION IN YOUNG ADULTS

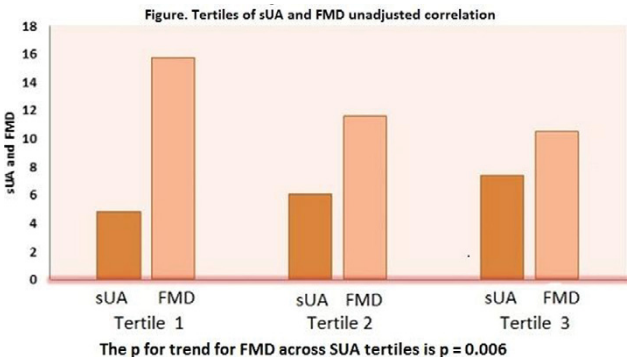
M.B. Saddekni[1], K.G. Saag[1], T. Dudenbostel[1], D.A. Calhoun[2], S. Oparil[2], D.I. Feig[3], P. Muntner[4], P.J. Foster[1], S.R. Biggers[5], E.J. Rahn[5], P. Li[6], D.T. Redden[6], A.L. Gaffo[5]. *[1]UAB School of Medicine, Division of Clinical Immunology and Rheumatology; [2]UAB School of Medicine, Division of Cardiovascular Disease; [3]UAB School of Medicine Division of Nephrology; [4]UAB School of Public Health, Department of Epidemiology; [5]Department of Medicine, Division of Rheumatology and Immunology; [6]UAB School of Public Health, Department of Biostatistics, University of Alabama at Birmingham, Bimringham, United States*

Background: Both serum urate (sUA) and endothelial dysfunction have been associated with hypertension and cardiovascular disease. Increasing sUA level has been associated with endothelial dysfunction and higher inflammatory markers. To date, however, few studies have examined the relationship between sUA, endothelial dysfunction, and blood pressure (BP) including young and largely healthy individuals.
Objectives: To determine whether there is an association between higher sUA, endothelial dysfunction as measured by flow-mediated dilation (FMD), and BP in young adults.
Methods: We conducted a cross-sectional analysis of baseline data for consecutively enrolled individuals (age 18 – 40 years). Enrollment criteria included baseline systolic BP (SBP) ≥120 and <160 mmHg or diastolic BP (DBP) ≥80 and <100 mmHg, and sUA ≥5.0 mg/dL for men or ≥4.0 mg/dL for women. Endothelial dysfunction measured by FMD, 24- hours ambulatory BP monitoring (ABPM) and sUA level were obtained. Associations between sUA, FMD, and ABPM variables were evaluated using a general linear model. Adjustments for age, gender, race, and BMI were applied after significant univariate results.
Results: 86 participants included in the analysis. Participants recruited had a mean age (±standard deviation) of 28.5±6.9 years, 36% were female, 41% African-Americans, mean BMI was 29.2±6.8 kg/m^2, and mean sUA was 5.9±1.2 mg/dL (n=77, range from 3.9 to 8.5 mg/dL). We found no significant cross-sectional associations between sUA, FMD, and BP variables assessed by ABPM (Table). Participants in the upper tertile of sUA had significantly worse FMD than those in the lower tertiles (Figure). However, this difference was no longer significant after multivariable adjustment age, gender, race, and BMI.

Table 1. Cross-sectional correlation between sUA, FMD, and Ambulatory Blood Pressure parameters

Parameters	r	p-value
sUA and FMD	-0.112	0.351
sUA and SBP	0.037	0.766
sUA and DBP	-0.012	0.924
sUA and MAP	0.056	0.657

Conclusions: In this cross-sectional analysis of young adults, there was no evidence to support an association between sUA levels and endothelial



dysfunction or BP. Endothelial dysfunction or BP might be associated with changes in sUA when measured longitudinally in individuals, but not when measured cross-sectionally in populations. Larger studies will be needed to confirm these results.

References:
[1] Ruggiero, C. Am J Cardiol, 2007. 100(1): p. 115–21.
[2] Rossi, R. J Am Coll Cardiol, 2004. 44(8): p. 1636–40.
[3] Feig, D. JAMA, 2008. 300(8): p. 924–32.

Acknowledgements: National Institute of Arthritis and Musculoskeletal and Skin Diseases P50AR060772, K24AR052361 (to KGS).

Disclosure of Interest: M. Saddekni: None declared, K. Saag Grant/research support from: AstraZeneca, Crealta, Takeda, Consultant for: Ardea/AstraZeneca, Crealta, Takeda, T. Dudenbostel: None declared, D. Calhoun: None declared, S. Oparil Grant/research support from: NHLBI Brigham and Women's Hospital, Center CVD Prev, Novartis Pharmaceutical Corporation, AstraZeneca AB (Duke University), Actelion Pharmaceuticals US,NIH/NHLBI, Merck and Co., Consultant for: Amgen, Bayer, Boehringer Ingelheim, AstraZeneca, Medtronic, GlaxoSmithKline, Forest Labs Inc., D. Feig: None declared, P. Muntner: None declared, P. Foster: None declared, S. Biggers: None declared, E. Rahn: None declared, P. Li: None declared, D. Redden: None declared, A. Gaffo Grant/research support from: Amgen, AstraZeneca, Consultant for: Cymabay, Ardea, Employee of: US Government

DOI: 10.1136/annrheumdis-2017-eular.5313

THU0414 INCIDENCE AND PREDICTORS FOR NEPHROLITHIASIS IN GOUT PATIENTS AND THE GENERAL POPULATION

A.J. Landgren[1], L. Jacobsson[1], U. Lindström[1], T.Z. Sandström[1], E. Fjellstedt[2], P. Drivelegka[1], V. Sigurdardottir[1], L. Björkman[1], M. Dehlin[1]. *[1]Department of Rheumatology and Inflammation Research, Institution of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg; [2]Department of Nephrology and Transplantation, SUS University Hospital, Malmö, Sweden*

Background: A well-known complication of gout is an increased risk for nephrolithiasis (NL). The incidence rate of NL in the general population varies in different studies between 85 and 170/100 000 person-years, with a peak incidence in the ages 40–49 years. Several medications used in gout patients could affect the risk for NL, including allopurinol, losartan, thiazide- and loop-diuretics. Effect of these medications on risk of NL in gout patients, and the general population, has only scarcely been studied.

Objectives: In this cohortstudy we investigated: 1) overall incidence of NL in gout and general population (GP) controls 2) risk for first time NL in gout patients vs general population (GP) controls, and 3) predictors for first time NL in both groups separately.

Methods: Gout patients were identified from the regional health care database in western Sweden (VEGA), containing ICD10-codes for all regional Healthcare visits from 2000. Matched (birthyear, sex, county) GP controls were selected from the population register. National registers and VEGA were used to retrieve information on comorbidities, socioeconomic factors and current medications at start of follow-up. The study population had to be above 19 years of age, without NL prior to start of follow-up, and living in the Western Swedish Health Care Region (WSHCR). Follow-up began 2006–01–01, or at the first gout-diagnosis if this occurred later, and ended at death, emigration or 2012–12–31, whichever occurred first. Incidence rates (IR) per 1000 person-years and hazardratios (HR) were calculated. Possible predictors for NL were based on risk factors presented in the literature.

Results: 29,968 gout patients and 138,678 matched GP controls were included. In gout patients there were 678 NL-events (IR: 6.2 per 1000 pyrs at risk (95% CI: 5.7–6.6)) and in GP controls 2125 (IR 3.9 per 1000 pyrs at risk (95% CI 3.7–4.0)). Risk for NL was increased in gout (HR=1.49, 95% CI: 1.35–1.64), and was higher in men compared to women (P<0.0001) in all age groups for gout cases and controls. All comorbidities and medications were more frequent in cases compared to controls (p<0.0001) at start of follow-up. Risk-factors for NL such as kidney disease (KD), obesity, diabetes were 2–4 times more common in gout patients compared to GP controls. Predictor point estimates for NL were similar in gout cases and GP controls (Figure 1), except for losartan which increased the risk of NL in GP controls (HR=1,47, 95% CI: 1.01–2.13) but not in gout patients. Loop-diuretics appeared to decrease the risk for NL in both cohorts (P<0.0001), whereas other cardiovascular (CVD) drugs had no effect.

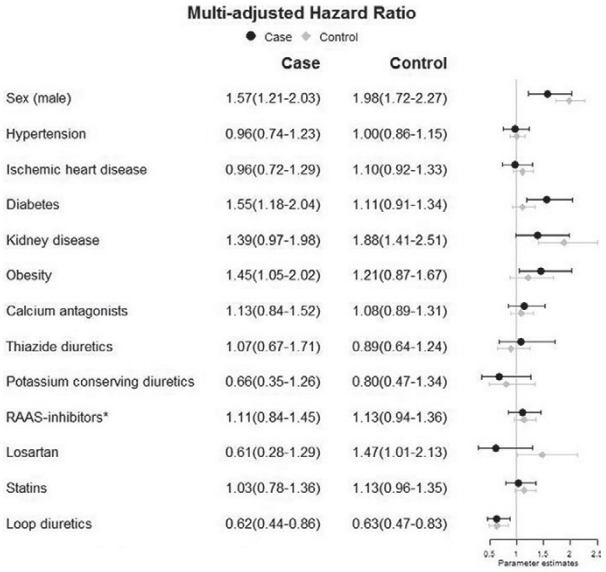


*Figure 1 Predictors for first time nephrolithiasis (NL) in patients with gout and GP controls without gout, analyzed by multivariate proportional hazards analyses, adjusting for age and other covariates in the figure, *Renin-angiotensin-aldosterone-System-Inhibitors excluding losartan*

Conclusions: The risk for NL was increased by 50% in gout patients, compared to controls. Overall pattern of predictors was similar in gout patients and population controls. In patients with gout, male sex, diabetes mellitus (DM), obesity predicted NL, whereas use of loop diuretics was protective. Overall, the most commonly used CVD drugs did not increase the risk for NL in patients with gout.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2836

THU0415 A STRUCTURED MONITORING PROGRAM FOR DRUG ALLERGY IN PATIENTS NEWLY INITIATED ON ALLOPURINOL

B.Y. Thong[1], K.-Y. Gan[2], B.-H. Ang[2]. *[1]Rheumatology, Allergy and Immunology; [2]Pharmacy, Tan Tock Seng Hospital, Singapore, Singapore*

Background: Allopurinol allergy (drug eruption, severe cutaneous adverse reactions [SCAR] and drug induced hypersensitivity syndrome [DiHS]) develops during the first 2–12 weeks after initiation. SCAR risk factors include Chinese ethnicity, HLA-B*5801 positivity and chronic kidney disease. HLA-B*5801 testing to prevent SCAR has not been shown to be cost-effective in Singapore.

Objectives: To retrospectively study whether a structured monitoring program (SMP) can lead to early diagnosis of allopurinol allergy and prevent development of SCAR/DiHS.

Methods: SMP patients (cases) managed by rheumatologists were compared with controls managed by non-rheumatologists during the study period 1 Jan 2015 to 30 Jun 2016. Cases upon initiation of allopurinol had baseline full blood count (FBC), serum creatinine (Cr), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) measured. If drug eruptions/abnormal laboratory tests developed during monitoring, allopurinol was stopped. The electronic dispensing system and computerized medical records were used for collection of patient demographics, indication for allopurinol use, initiation dose, monitoring intervals, laboratory results and clinical features of drug allergy. This was compared with the control group without an SMP. Chi square tests were used to compare differences in proportions and Mann-Whitney U test for differences in medians. P value ≤0.05 was considered statistically significant.

Results: There were 61 cases and 30 controls with comparable age (p=0.81), ethnicity (>80% Chinese) (p=0.63) and estimated glomerular filtration rate, eGFR (p=0.72). There were significantly more cases with tophaceous gout (41% vs 10%, p=0.003), while more controls tumour lysis syndrome prophylaxis (30% vs 0%, p<0.001). Median (interquartile range, IQR) starting dose of 50 (50) mg was lower among cases versus controls of 100 (200) mg (p<0.001); all cases had baseline and follow-up laboratory tests compared to controls (p<0.001). Cases were followed up at a median (IQR) of 2 (1.1) weeks after initiation then 5 (2.0) weeks after the first visit, whereas controls were reviewed 8 (8.9) weeks after initiation, then 11 (4.6) weeks after the first visit. Two patients in the SMP group with normal eGFR developed maculopapular eruption (MPE), 1 elevated ALT/AST, and 1 both MPE and elevated ALT/AST within the first 14 days of initiation. One control with lymphoma and baseline eGFR 31 ml/min/1.73m^2 developed DiHS (fever, MPE, elevated ALT/AST less than twice upper limit of normal) 43 days after initiation for tumour lysis prophylaxis. This occurred while on 2-weekly monitoring of FBC, ALT, AST. There were no cases of SCAR in both groups.

Conclusions: SMP facilitates early diagnosis of allopurinol allergy/DiHS which occurred during the first 2–6 weeks after initiation. Whether early cessation of allopurinol prevents development of SCAR, and reduces the need for HLA-B*5801 testing will require a larger prospective study.

References:
[1] Wang CW, Dao RL, Chung WH. Immunopathogenesis and risk factors for allopurinol severe cutaneous adverse reactions. Curr Opin Allergy Clin Immunol 2016;16:339–45.
[2] Dong D, Tan-Koi WC, Teng GG, Finkelstein E, Sung C. Cost-effectiveness analysis of genotyping for HLA-B*5801 and an enhanced safety program in gout patients starting allopurinol in Singapore. Pharmacogenomics 2015;16:1781–93.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2531

THU0416 RAPID TOPHUS RESOLUTION IN CHRONIC REFRACTORY GOUT PATIENTS TREATED WITH PEGLOTICASE

B. Mandell[1], A. Yeo[2], P. Lipsky[3]. *[1]Department of Medicine, Cleveland Clinic, Cleveland, OH; [2]Horizon Pharma, Lake Forest, IL; [3]AMPEL BioSolutions, LLC, Charlottesville, VA, United States*

Background: It has been suggested that the velocity of resolution of tophi in persons with chronic tophaceous gout is related to the serum urate levels.[1] However, few subjects with a persistent serum urate less than 4.0 mg/dL were studied. Pegloticase is a recombinant uricase conjugated to polyethylene glycol approved in the US for treatment of patients with chronic refractory gout. It profoundly decreases serum uric acid in responders to <1 mg/dL. The results from the pegloticase clinical trials provided the opportunity to determine the impact of persistent and markedly low levels of serum urate on the velocity of tophus resolution.

Objectives: To assess the velocity of tophus resolution in subjects treated with pegloticase for chronic refractory gout.

Methods: This analysis used results from two randomized controlled trials (RCTs) of 6 months duration.[2,3] For tophus measurements, serial standardized digital photographs were analyzed by a blinded reader using computer-assisted quantitative measurement software. Subjects were defined as responders and nonresponders based upon maintenance of a serum urate <6 mg/dL during intensive monitoring periods after 3 and 6 months of treatment.

Results: During the 6 months of the RCTs, a total of 952 tophus measurements were analyzed in 87 subjects, including 341 in 30 responders; 361 in 36 nonresponders receiving pegloticase infusions; and 250 in 21 subjects receiving placebo infusions. Mean serum urate levels in these subjects were 10.1, 0.3 and 0.3 mg/dL at baseline, 3 months and 6 months in responders; 10.7, 8.9 and 9.6 mg/dL in nonresponders; and 10.2, 9.8 and 9.7 mg/dL in placebo treated patients, respectively. At baseline, the mean tophus area in responders was 581.6 +/- 742.7 mm^2 (mean ± SD; n=90 tophi); in nonresponders it was 676.5+/-1416.6 mm^2 (n=93 tophi); and in placebo treated subjects it was 672.9+/-1039.5 mm^2 (n=66 tophi). By regression analysis, the velocity of tophus resolution over the 6 months of treatment was 50.1 mm^2/month in responders; 14.0 mm^2/month in nonresponders; and 13.9 mm^2/month in placebo treated patients (responders versus nonresponders or responders vs placebo treated subjects (p=0.001)). In responders, the mean time to total tophus resolution was estimated to be 347 days (11.5 months, with a range of 5.6–36.4 months). During the 6 month treatment period, the area under the curve (AUC) of multiple serum urate measurements in responders was 6,067.9+/-6,781.6 mg/dL hr compared with 34,647.4+/-8,586.7 and 42,451.1+/-6,396.1 mg/dL·hr in nonresponders and placebo treated subjects, respectively (p<0.001). In responders, there was a significant correlation between the velocity of tophus resolution and serum urate AUC (p=0.009).

Conclusions: Pegloticase treatment causes a rapid resolution of tophi in responders as predicted from the profound and persistent serum urate lowering associated with this therapy.

References:
[1] Perez-Ruiz F et al, Arthritis Rheum 2002; 47:356–60.
[2] Sundy JS, et al. JAMA. 2011;306:711–720.
[3] Becker MA, et al. Ann Rheum Dis. 2013;72:1469–1474.

Disclosure of Interest: B. Mandell Grant/research support from: Horizon, Consultant for: Horizon, Ironwood, A. Yeo Consultant for: Horizon Pharma, P. Lipsky Consultant for: AstraZeneca, Celgene, EMD Serono, GSK, Horizon Pharma, Janssen, Medimmune, Pfizer, Roche, Sanofi, UCB

DOI: 10.1136/annrheumdis-2017-eular.5417

THU0417 PERIPHERAL NEUROPATHY IN PATIENTS WITH GOUT. ALTERATIONS BEYOND LOCAL DAMAGE

C.O. Lopez Lopez[1], E. Corzo Dominguez[1], M.D.L.L. Montes-Castillo[1], H. Llinas[2], E. Alvarez Hernandez[2], I. Peláez Ballestas[2], R. Burgos Vargas[2], J. Vazquez-Mellado[2]. *[1]Rehabilitation; [2]Rheumatology, Hospital General de Mexico, Mexico city, Mexico*

Background: Peripheral neuropathies (PN), are peripheral nervous system disorders associated to several causes. According to distribution are classified as: Local (mononeuropathy [MNP]) or Systemic (Multiple mononeuropathy [MNPM] and polyneuropathy [PNP]). PN in gout has been scarcely described. Previous reports only consider MNP of median nerve at the wrist and MNP of the ulnar nerve at the elbow, due to tophus compression.

Objectives: To describe the frequency and characteristics of PN in patients with gout and its association to gout related variables, co-morbidity and treatment.

Methods: Consecutive patients from GRESGO, a cohort of 450 gout (ARA/CGD/ACR-EULAR) patients seen for the first time at Rheumatology department and treated according to published guidelines for gout. Variables included: demographic, clinical, biochemical data, HAQ and 3 questionnaires for PN (DN4, LANSS and MNSI) previously translated and validated in our country. We performed Nerve Conduction Studies (NCS) following AAME guidelines (Include:Sensory action potential [sural, ulnar and median nerves], Compound muscle action potential [peroneal, tibial, median and ulnar nerves] and late F-wave [tibial and ulnar nerves]). This protocol was approved by the local IRB and the patients signed an informed consent. *Statistical analysis:* Student's t test, Mann–Whitney U test and X2.

Results: We included 162 gout patients, 98% males, 72% tophaceous gout, 48% severe tophaceous gout (STG), mean age 49.4±12 years, 14±10 years of disease duration, educational level 8±4 years, BMI 27.9±4.6kg/m^2.

According to questionnaires: 56% DN4, 45% MNSI and 36% LANSS could be classified as PN. Sixty five percent had abnormal NCS: MNP: 52%, most of them (58%) neuropraxia. PNP 35% and 13% MNPM in them, axonal damage was reported in 88%. MNP localization: Median nerve/carpal tunnel (89%); peroneal nerve/fibula head (7.4%); ulnar nerve/elbow (1.8%) and tibial nerve/ankle (1.8%). For associated factors, Gout+Local PN (L-PN) patients were compared with Gout without PN as well as Gout+Systemic PN (S-PN) (see table). Hypertriglyceridemia and dyslipidemia were significantly more frequent among L-PN patients; in other hand, frequency of tophi, STG and mean HAQ values were significantly more frequent in S-PN patients, there were no significant differences among other clinical data associated with gout itself.

Table 1. Factors associated to Gout+PN. Values represent % unless specified

Variable	Gout+L-PN n=55	Gout+S-PN n=51	Gout Without PN n=56	p
Alcoholism/Smoking	85/69	82/68	85/73	NS
Chronic renal failure	18	17	16	NS
Hyperglycemia/Diabetes	25	31	21	NS
Obesity	27	23	29	NS
Hypertriglyceridemia/Dyslipidemia	**58/69**	27/41	35/40	**0.02**
Hypertension	40	28	34	NS
Tophus	70	**81**	65	**0.05**
STG	55	**60**	41	**0.04**
Index tophi size (cm)*	5.3±3.5	6.5±4.1	6.2±4.7	NS
HAQ*	0.38±0.49	**0.59±0.58**	0.37±0.50	**0.01**
Serum uric acid*	8.1±2.7	7.9±2.3	7.9±2.3	NS
Previous treatment:			NS	
Glucocorticoids	52	68	52 70	
Colchicine	51	46	50	
Allopurinol	71	69	70	

*Mean±SD.

Conclusions: PN is common among gout patients, PN could be diagnosed by questionnaires (particularly DN4) and NCS in 65%. L-PN (median nerve most of them) explain 52% of the cases, in 48% S-PN was found, in these group PNP is more frequent. Hypertriglyceridemia is associated with L-PN and STG to S-PN. The role of uric acid and/or crystals needs to be evaluated.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5060

THU0418 A PROOF-OF-CONCEPT STUDY: TREATING TO THE TARGET WITH URATE LOWERING THERAPY IN REAL-WORLD GOUT PATIENTS

C.A. Janssen[1], T.L. Jansen[2], M.A. Oude Voshaar[1], H.E. Vonkeman[1], M.A. van de Laar[1]. *[1]Arthritis Center Twente, Department of Psychology, Health and Technology, University of Twente, Enschede; [2]Department of Rheumatology, Viecuri Medical Center, Venlo, Netherlands*

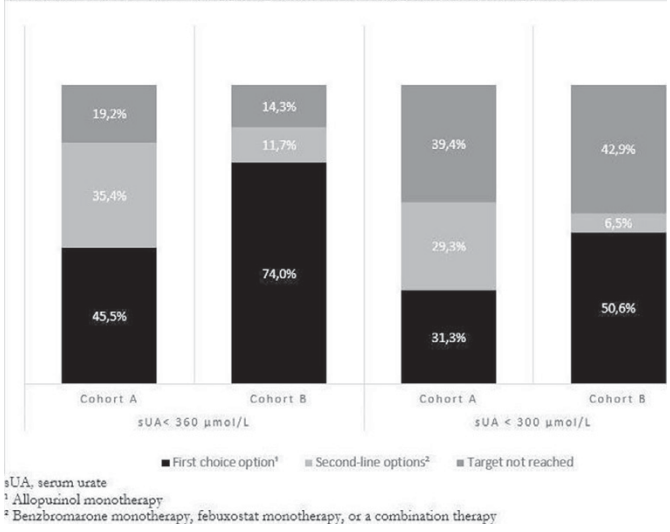
Background: Gouty arthritis is a common, potentially disabling and increasingly prevalent disease [1]. Last year, the European League Against Rheumatism (EULAR) task force gout updated the 2006 recommendations for the management of gout [2,3]. The guideline stresses the application of a targeted approach when initiating urate lowering therapy (ULT) in gout patients for reaching the recommended serum urate (sUA) target values. However, data on clinical outcomes of real-world gout patients treated according to this approach are limited.

Objectives: To examine the clinical outcomes achieved in two patient cohorts in which differing targeted ULT treatment approaches were employed, both aiming to reach the EULAR recommended sUA targets.

Methods: We conducted a retrospective chart review study. Gout patients were included that had been treated at the rheumatology departments of two clinical centers in the Netherlands, applying different targeted ULT treatment approaches. Patients in cohort A followed an approach combining two modes of action once allopurinol monotherapy failed to reach the predefined target, whereas patients in cohort B were treated with sequential monotherapy following allopurinol

monotherapy failure. Outcome parameters were defined to reflect the EULAR recommendations concerning ULT [3].
Results: A total of 177 patients were included in the study; 99 in cohort A and 78 in cohort B. The majority (N=146, 82.5%) of the included patients from both cohorts were able to meet the predefined sUA target of <360 μmol/L. In addition, more than half (N=104, 58.8%) of the patients reached the stringent sUA target of <300 μmol/L. The proportion of patients reaching sUA targets did not differ significantly (p=0.51) between the cohorts, with 80.8% (n=80) of the patients in cohort A reaching the primary sUA target, compared to 85.7% (n=66) in cohort B (Figure 1). In total, patients following treatment with first-line allopurinol, second-line monotherapy options or second-line combination therapy, 102/124 (82.3%), 25/31 (80.6%) and 19/21 (90.5%) respectively, reached the primary sUA target.

Figure 1: Proportion of patients reaching the EULAR recommended sUA targets in cohort A (n=99) and cohort B (n=77), applying different ULT targeted treatment approaches



sUA, serum urate
¹ Allopurinol monotherapy
² Benzbromarone monotherapy, febuxostat monotherapy, or a combination therapy

Conclusions: This chart review provides a proof-of-concept of the treat-to-target approach in gout patients when a targeted approach with ULT is applied. However, our study also shows that not all patients may reach targets using currently available treatment options. Prospective, pragmatic randomized studies to investigate differences between specific treatment regimes in gout patients, together with costs, safety and patient-reported outcome measures are needed.
References:
[1] Kuo C-F, Grainge MJ, Zhang W, et al. Global epidemiology of gout: prevalence, incidence and risk factors. Nat Rev Rheumatol 2015;11:649–62. doi:10.1038/nrrheum.2015.91.
[2] Zhang W, Doherty M, Bardin T, et al. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis 2006;65:1312–24. doi:10.1136/ard.2006.055269.
[3] Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis 2017;76:29–42. doi:10.1136/annrheumdis-2016–209707.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2377

THU0419 RISK OF TOTAL HIP AND KNEE REPLACEMENT IN GOUT PATIENTS PRIOR TO AND FOLLOWING DIAGNOSIS: A NATIONAL POPULATION STUDY IN TAIWAN

C.-F. Kuo, J.-S. Chen, K.-H. Yu, S.-F. Luo. *Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Taoyuan, Taiwan, Province of China*

Background: Total joint replacement (TJR) is a major surgical procedure aiming to replace damaged natural joints with artificial prosthesis to restore function and alleviate pain. Total knee replacement (TKR) and total hip replacement (THR) are two common replacement procedures, mainly as a result of osteoarthritis, rheumatoid arthritis, trauma, fracture and infection. Whether gout associates with a greater risk of TJR independent of these primary risk factors is controversial, despite tophaceous or chronic deforming gouty arthritis may lead to joint destruction and subsequent TJR
Objectives: We carried out a case control study using the National Health Insurance (NHI) database with full coverage of the general population of Taiwan to investigate the burden of TJR in gout patients at diagnosis compared to matched controls. We further followed incident gout patients and their matched controls after diagnosis to compare their subsequent risk for TJR.
Methods: The Taiwan National Health Insurance database was used to identify 74,729 new diagnosis gout patients in 2005. These were matched 1:1 to 74,729 controls by birth year and sex with people who did not have gout diagnosis or urate-lowering treatment prescription. Odds ratios (ORs) of total hip or knee replacement (THR or TJR) at diagnosis and hazards ratios (HRs) after diagnosis were estimated adjusted for gender, age at diagnosis, comorbidities, co-medications, place of residence, income and occupation.
Results: Gout was associated with adjusted ORs (95% CIs) of 0.87 (0.54 to 1.40), 1.01 (0.57 to 1.79), 0.93 (0.64 to 1.35) for the THR, TKR and TJR at diagnosis, respectively. The incidence rate of THR or TKR in the patients with gout was 1.60 and 1.76 (per 1,000 person-years) which was higher than matched controls (0.99 and 0.98, respectively). Gout was also associated with an adjusted HR (95% CI) of 1.41 (1.19 to 1.68), 1.37 (1.16 to 1.61) and 1.37 (1.22 to 1.56) for developing THR, TKR and TJR.
Conclusions: Compared to matched controls people with gout did not have an increased risk of TJR at diagnosis but the risk increased substantially after diagnosis. Whether adequate urate-lowering treatment reduces the risk requires further study.
References:
[1] Kuo CF, Grainge MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. Nature reviews. Rheumatology 2015;11:649–62.
[2] Roddy E, Zhang W, Doherty M. Are joints affected by gout also affected by osteoarthritis? Ann Rheum Dis 2007;66:1374–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2885

THU0420 IMPROVED SURVIVAL OF POST-MYOCARDIAL INFARCTION PATIENTS TREATED WITH ZOFENOPRIL COMBINED WITH XANTINE OXIDASE INHIBITORS AS COMPARED TO PLACEBO OR OTHER ACE-I

C. Bentivenga [1], E.R. Cosentino [1], F. Ventura [1], G. Magri [1], I. Ricci Iamino [1], S. Bacchelli [1], E. Ambrosioni [1], D. Degli Esposti [1], N. Malavolta [1], S. Corvaglia [1], G. Vukatana [1], C. Borghi [2] on behalf of SMILE. [1] *Cardiac-Thoracic-Vascular Department, Azienda Ospedaliera Universitaria Sant'Orsola-Malpighi;* [2] *Cardiac-Thoracic-Vascular Department, University of Bologna, Bologna, Italy*

Background: Oxidative stress is increased in hyperuricemic patients with acute myocardial infarction (AMI). In these patients, use of sulfhydrylACE-inhibitors (ACEIs), such as zofenopril or captopril, and xanthine oxidase inhibitors (XOIs), may potentially result in an enhanced antioxidant effect and improved survival. However, the benefit of such combination in post-myocardial infarction has never been verified.
Objectives: To test the usefulness of the combination therapy Zofenopril + XOI in improving survival free from MACE in post-AMI patients
Methods: We re-analyzed the data of the four SMILE (Survival of Myocardial Infarction Long-term Evaluation) studies by grouping patients according to the type of ACEIs and the use of XOIs. 165 (31.4%) of the 525 patients were treated with XOIs (79 under zofenopril and 86 under placebo, lisinopril or ramipril), whereas 360 were not (192 zofenopril and 168 placebo or other ACEIs). In these four groups, we separately estimated the 1-year combined risk of major cardiovascular events (MACE, death or hospitalization for cardiovascular causes).
Results: MACE occurred in 10.1% of patients receiving zofenopril + XOIs, in 18.6% receiving placebo or other ACEIs + XOIs, in 13.5% receiving zofenopril without XOIs and in 22.0% receiving placebo or other ACEIs, but no XOIs (p=0.034 across groups). Rate of survival free from MACE was significantly larger in patients treated with zofenopril and XOIs than with other ACEIs with no XOIs [hazard ratio: 2.29 (1.06, 4.91), p=0.034]. A non-significant trend for superiority of zofenopril + XOIs combination was observed vs. zofenopril alone [1.19 (0.54, 2.64), p=0.669] or vs. placebo or other ACEIs combined with XOIs [1.82 (0.78, 4.26), p=0.169].
Conclusions: Our retrospective analysis suggests an improved survival free from MACE in post-AMI patients treated with a combination of an ACEI and urate lowering drug with antioxidant activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5012

THU0421 FEMALE PRIMARY GOUT HAD ITS UNIQUE ULTRASOUND FEATURES

D.F. Lin [1], X. Guo [1], J. Cao [1], Y. Wu [2], J. Gu [1]. [1] *Rheumatology department;* [2] *Ultrasound department, the 3rd Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China*

Background: Primary gout is a metabolic disease occurred in male and post-menopause female in most cases. Though the ultrasound features of gout had been discovered for several years, no reports illuminated whether there would be difference presentations between different genders in the joints.
Objectives: We employed ultrasound instead of dual-energy CT to explore more refined pathological manifestations of primary gout in different genders.
Methods: All cases were confirmed as gout fulfilling 1997 ACR classification criteria. All cases excluded secondary gout induced by drug, tumor, hypertension, diabetes mellitus, renal failure. Ultrasound was performed during chronic stage of gout but not at acute attack. The process was done by 2 observers blinded to

each other, blood tests. Final diagnosis was determined by the third US expert if the 2 observers got the different conclusion. Bilateral toes, dorsal feet, ankle, knee, wrist, fingers, elbow, and shoulder were detected to find 6 features of gout suggested by OMERCT: tophus, "snow storm"-like effusion, cloudy synovium in grey scale, double-contour sign, bone erosion and Power Doppler (PD) signal. Each above positive presentations in each above range would get 1 point and the sum scores would be ranged from 0 to 84. Serum uric acid (UA) was recorded too.

Results: 1) 23 female and 139 male were recruited in the program. The female-male ratio was 1:6. Mean age and disease duration of the female subjects were elder than male ones (female:male=57.2±14.1: 44.7±14.7 years old) with longer disease duration to confim the diagnosis (female:male = 10.9:1.2 months). The average serum UA level in female was lower than male group (female:male = 413.8±162.1umol/L, 515.5±156.9umol/L, sig$<$0.05).

2) The intra-observer reliability from 20% samples random seclection showed an overall agreement of 80%, 92%, 96%, 87%, 80%, 73% for tophus, "snow storm"-like effusion, cloudy synovium in grey scale, positive double-contour sign, bone erosion and PD signal with kappa value of 0.78, 0. 92, 0.95, 0.86, 0.79, 0.72, respectively.

3) The difference showed female gout had higher frequency of tophus, bone erosion and lower frequency of effusion while the other indexes were equal:topus scores (female:male=87%:,74.1%), cloudy synovium grey scale scores (female:male=65.2%:62.6%), effusion scores (female:male=17.4%,31.7%), bone erosion scores (female:male=30.4%,16.5%), power dopplar scores (female:male=34.8%,41%), positive double-contour signs (60.9%:59.9%. The top 2 affected ranges were ankle (female:male=69.6%:55.3%), knee (female:mlae=60.9%:54.0%). Furthermore, female gout had more frequently occurred not in the less typical ranges such as fingers (female:male=34.7%:19.4%), elbow (8.7%:2.7%), which might be the cause for delayed diagnosis.

Conclusions: Though the level of serum UA was lower, Female gout had its unique ultrasound features with more tophus, bone erosion and less effusion compared to male gout. The less typical ranges were recommended for US examinations.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2636

THU0422 SEL-212: ENHANCED SERUM URIC ACID CONTROL IN HYPERURICEMIC PATIENTS THROUGH SELECTIVE MITIGATION OF ANTI-DRUG ANTIBODIES AGAINST PEGSITICASE

E. Sands[1], A. Kivitz[2], L. Johnston[1], T.K. Kishimoto[1]. [1]*Selecta Biosciences, Watertown;* [2]*Altoona Center for Clinical Research, Duncansville, United States*

Background: Recent EULAR recommendations for refractory gout treatment with pegylated uricase (pegloticase) acknowledge the risk of allergic reactions related to the development of anti-drug antibodies (ADAs) [1]. ADAs also affect the efficacy of treatment [2]. As a novel approach to treatment, we demonstrated that co-administration of pegsiticase (another pegylated uricase) and a synthetic vaccine particle encapsulating rapamycin (SVP-R) showed improved control of serum uric acid (sUA) in uricase-deficient mice by inducing antigen-specific immune tolerance to pegsiticase [3]. Here we describe the impact of SEL-212, a combination product of SVP-R and pegsiticase, on ADA formation and sUA levels in hyperuricemic patients in a Phase 1 open-label multicenter clinical trial.

Objectives: To assess the initial safety and impact on sUA levels and ADA formation of SEL-212, which is designed to be the first non-immunogenic uricase therapy for refractory gout.

Methods: Cohorts of hyperuricemic (sUA $\geq$6 mg/dL) patients consented to a single dose of 0.4 mg/kg pegsiticase alone, SVP-R alone (0.03–0.5-mg/kg), or 0.4 mg/kg pegsiticase co-administered with SVP-R (0.03–0.3-mg/kg; SEL-212). ADAs and sUA were assessed at baseline and 7, 14, 21, and 30 days after dosing.

Results: Sixty-three patients were enrolled with a median age of 49.4 years. Mean baseline sUA was 7.4±1.3 mg/dL. Patients dosed with pegsiticase alone showed an immediate drop in sUA, which returned to baseline levels by 14–21 days in 4 of 5 subjects, correlating with the induction of ADA titers $>$1000. Patients treated with SVP-R alone showed no meaningful change in sUA.

In contrast, patients treated with SEL-212 showed a dose-dependent inhibition of anti-uricase ADAs and corresponding decrease in sUA levels through at least day 30 after a single injection. Seven of 10 patients treated with SEL-212 at a SVP-R dose of 0.1 mg/kg showed no detectable sUA at day 30, and all 10 subjects dosed with SEL-212 at SVP-R doses of 0.15 or 0.3 mg/kg showed sustained control of sUA through at least day 30. There was a strong correlation between maintenance of low uric acid levels at day 30 and with low or no ADA titers.

SEL-212 was generally well tolerated at effective dose levels. One SAE (grade 2 rash) was observed in the lowest of the three effective dose levels (0.1 mg/kg SVP-R). A second SAE was determined by the investigator to be not related to study drug. All SAEs fully resolved. No SAEs were observed with SEL-212 at the higher effective dose levels of SVP-R (0.15 or 0.3 mg/kg). The maximum tolerated dose was defined at 0.3 mg/kg.

Conclusions: Data suggest that a single dose of SEL-212 in hyperuricemic patients can tolerably, therapeutically and durably control sUA for $\geq$30 days, correlating with inhibition of ADAs. These results supported monthly dosing in an ongoing Phase 2 multi-dose study in symptomatic gout patients and the potential use of SVP-R to mitigate ADAs for other immunogenic biologics.

References:

[1] Richette P, et al., 2017, 76:29–42.
[2] Lipsky PE, et al., Arthritis Res Ther. 2014, 16:R60.
[3] Kishimoto, TK, et al., Nat Nanotechnol. 2016, 11:890–899.

Disclosure of Interest: E. Sands Employee of: CMO for Selecta Biosciences, A. Kivitz: None declared, L. Johnston Employee of: COO for Selecta Biosciences, T. K. Kishimoto Employee of: CSO for Selecta Biosciences

DOI: 10.1136/annrheumdis-2017-eular.3548

THU0423 THE RELATIONSHIP BETWEEN CLINICAL DISEASE ACTIVITY, SYMPTOM DURATION AND ULTRASONOGRAPHIC CHANGES IN GOUT

E. Norkuviene[1], M. Petraitis[1], I. Apanaviciene[1], D. Virviciute[2], A. Baranauskaite[1]. [1]*Rheumatology;* [2]*Institute of Cardiology, Lithuanian University of Health Sciences, Kaunas, Lithuania*

Background: Ultrasonography (US) has recently been validated and used as an objective diagnostic tool for urate deposition also joint damage and was proposed as an outcome measure in gout [1–2].

Objectives: Our aim was to investigate the relationship between clinical gout activity and load of US changes.

Methods: Sixty monosodium-urate-crystal-confirmed gout patients (52 men) and 36 healthy normouricemic controls were prospectively included in one centre. The relationship between clinical symptoms and US gout-related changes investigating 36 joints and 4 tendons (m. triceps and patellar) was evaluated using Spearman's correlation.

Results: The total number of intraarticular T, periarticular T, total T, total DC, and total E found per patient on ultrasound ranged from 0–26, 0–4, 0–30, 0–29, and 0–18, accordingly.The number of acute attacks per year/per life had a significant positive correlation with the total number of intraarticular T (rs=0.518/0.652; p$<$0.0001), total number of intraarticular and periarticular T (rs=0.552/0.699; p$<$0.0001), the total number of DC (rs=0.374/0.551; p$<$0.01), the total number of erosions (rs=0.374/0.542; p$<$0.01), and the total tophus area (rs=0.420/0.549; p$<$0.01) measured on US per patient. Strong, positive correlation was observed between the number of subcutaneous tophi and total US tophus area (rs=0.628), total number of DC (rs=0.612) and erosions (rs=0.526), found per patient on US, all p$<$0.0001. Disease duration significantly positively correlated with the load of US T, E and DC (p$<$0.0001) in the investigated sites. There was no correlation between CRP and US, also no correlation between the uric acid concentration and US changes: total number of T (rs=0.193, p=0.139), DC (rs=0.179, p=0.170) or E (rs=0.063, p=0.634) found per patient. The tophus area measured in two first metatarsophalangeal joints (MTP) positively correlated with subcutaneous tophus count (rs=0,404; p=0,001), the US intraarticular T count (rs =0,732; p$<$0,0001) total US DC count (rs =0,477; p$<$0,0001) total intraarticular tophus area (rs =0,829; p$<$0,0001)and total tophus area other than first MTP joints (rs =0,603; p$<$0.0001).

Conclusions: Ultrasonographic gout -related changes strongly positively correlate between each other and with subjective also objective signs of disease activity, increasing with disease duration in gout. The size of tophi inside the first metatarsophalangeal joints could be representative of the total body urate load and could be chosen as an outcome measure for the longitudinal gout studies.

References:

[1] Neogi T, Jansen TLTA, Dalbeth N, Fransen J, Schumacher HR, Berendsen D, et al. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2015 Sep 9; 74(10):1789–98.
[2] Ottaviani S, Gill G, Aubrun A, Palazzo E, Meyer O, Dieudé P. Ultrasound in gout: a useful tool for following urate-lowering therapy. Jt Bone Spine 2015 Jan; 82(1):42–4.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6466

THU0424 GOUT AT THE SPINE: A RETROSPECTIVE STUDY WITH DUAL-ENERGY COMPUTED TOMOGRAPHY

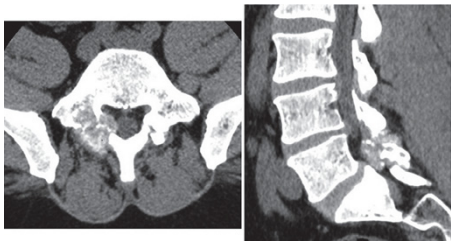
E. Chotard[1], J.M. Sverzut[2], F. Lioté[1,3], T. Bardin[1,3], H.-K. Ea[1,3]. [1]*AP-HP, hôpital Lariboisière, Service de Rhumatologie, centre Viggo Petersen, Paris;* [2]*Centre cardiologique du Nord, Service de Radiologie, St Ouen;* [3]*INSERM UMR1132, Bioscar, University Paris Diderot, Paris, France*

Background: Gout is due to monosodium urate (MSU) crystal deposition after chronic hyperuricemia. Although MSU crystal deposition can occur in every joint and peri-articular structure, spine involvement is scarcely reported. Dual energy computed tomography (DECT) is a performant tool to assess urate deposits, especially in deep structures such as intervertebral discs and apophyseal joints.

Objectives: to describe spinal DECT features of urate monosodium deposits compared to peripheral joint DECT.

Methods: Patient with gout diagnosis (MSU crystal identification by polarized microscopy or fulfilling "Nijmegen's criteria" (1)) who had undergone DECT were included from November 2012 to June 2016. Images were analyzed by

a trained musculoskeletal radiologist. For each DECT, clinical and biochemical characteristics of each patient were collected retrospectively.
Results: 22 patients (men 77%), mean age 62.5 years and mean BMI 28.4 kg/m^2 were included. Mean gout duration was 108.0±114.4 months, mean of last available serum uric acid level was 520±193 μmol/l, and 15 patients had at least one clinical tophus. Mean estimated glomerular filtration rate (MDRD formula) was 47±27 ml/min/1.73 m^2. One patient was on hemodialysis and one had received kidney transplant.
A total of 39 DECT has been performed: 28 of peripheral joints and 11 of the spine (9 lumbar, 1 sacroiliac and 1 cervical). Spinal DECT were done in 10 patients to explore recurrent inflammatory pain (n=3 lumbar, 1 cervical and 1 buttock) or mechanical back pain (n=2 lumbar). 4 spinal DECT were performed in asymptomatic patients with extended peripheral tophi. Spinal MSU crystal deposits were disclosed by DECT in 83% (5/6) and 25% (1/4) of symptomatic and asymptomatic patients, respectively. In all painful patients, MSU crystal deposition was considered as a likely explanation of spinal symptoms. MSU crystal depositions was identified in apophyseal joints (n=5), cervical intervertebral disc (n=1) and yellow or interspinous ligaments (n=4). All involved apophyseal joints were eroded (figure 1). No vertebral bone erosion was observed. Calcification of spinal tophus was observed in 4 patients. DECT identified peripheral deposits in 15/18 (83.3%) patients. In peripheral DECT, bone erosions were observed in 71.4% and joint effusion in 32.1% of DECT positive peripheral joints. MSU crystal depositions were observed in tendons, cartilages or synovial membranes in 82.1% of positive DECT joints and in soft tissues in 64.3% of positive patients. MSU crystal deposits were calcified in 7 cases.



Conclusions: MSU crystal depositions at the spine are present in 60% of patients in this retrospective DECT study. DECT can represent a performing imaging procedure for their detection in symptomatic patients. Further studies are needed to assess the clinical utility of DECT of the spine in gout.
References:
[1] Janssens HJ, Fransen J, van de Lisdonk EH, et al. A diagnostic rule for acute gouty arthritis in primary care without joint fluid analysis. Arch Intern Med 2010;170:1120–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6835

THU0425 THE FIRST METATARSOPHALANGEAL JOINT (MTP1) IS NOT THE MAIN LOCALIZATION OF GOUT AT DIAGNOSIS IN SUB-SAHARAN AFRICA

F. Kemta Lekpa, M.S. Doualla, H. Namme Luma. *Service de Médecine Interne, Douala General Hospital, Douala, Cameroon*

Background: Numerous data in sub-Saharan Africa suggest that MTP1 is not the hallmark of gout (1–5).
Objectives: We carried out this study with the aim to determine the joint most involved at the time of diagnosis of gout in Cameroon.
Methods: We performed a cross-sectional study in all outpatients seen at the Rheumatology unit of the Douala General Hospital, Cameroon, between 2004 and 2014. We included patients with diagnosis of gout according to ACR criteria 1977.
The main characteristics of gout at diagnosis were collected, particularly the joints involved.
A $p<0.05$ was significant.
Results: At the end of this study, 511 patients (415 men and 96 women) with the diagnosis of gout were included. The mean age was 55.9±10.8 years.
Joint pain (n=508, 99.4%) was the leading reason for consultation at the time of diagnosis. The knees (n=300, 62.6%)), ankles (n=187, 39.0%) and MTP1 (n=128, 26.7%) were the most affected joints. Table 1 presents the frequency of the joints affected, comparing our results with those of the other African series.
There was no difference between MTP1 and others joints location (particularly knees and ankles) according to age, sex, place of residence, duration of disease, uric acid level, and associated comorbidities ($p>0.05$).
Conclusions: MTP1 is not the joint most involved at the time of diagnosis of gout in sub-Saharan Africa. Diagnosis of gout should be considered before any inflammatory knee and ankle pain in patients from sub-Saharan Africa. Genetic studies would provide a better understanding of this feature.
References:
[1] Kodio B, et al. Afr J Rheumatol. 2015 3(1): 22–26.
[2] Adelewo OO, et al. Afr J Rheumatol. 2014 1(2): 23–28.
[3] Singwé-Ngandeu M, et al. Mali Medical. 2009 24:17–20.

Table 1. Comparison of the most affected joints of the different African series*

	Our study (Cameroon), 2017	Kodio (Mali), 2015	Adelowo (Nigeria), 2014	Singwé-Ngandeu (Cameroon), 2009	Mijiyawa (Togo), 2000	Cassim (South Africa), 1994
Number of patients	511	100	146	139	160	107
Sex (M/F)	415/96	45/55	108/38	131/8	159/1	93/14
Mean age	55.9±11	57	53.4±11	55.7±10	44	50.5±11.5
Joints involved (tender and/or stiffness), n (%)						
Knees	**300 (62.6)**	**92 (92%)**	**81 (55.5)**	60 (43.2)	82 (51.2)	**91 (85)**
Ankles	187 (39.0)	45 (45%)	50 (34.2)	**67 (48.2)**	90 (56.2)	66 (61.7)
1st MTP joint	128 (26.7)	22 (22%)	21 (14.4)	65 (46.8)	**100 (62.5)**	80 (74.8)
Wrists	93 (19.4)	20 (20%)	14 (9.6)	30 (21.6)	30 (18.7)	–
Elbows	81 (16.9)	14 (14%)	12 (8.2)	20 (10.7)	35 (21.9)	–
PIP joints	56 (11.7)	–	13 (8.9)‡	–	15 (9.4)†	–
MCP joints	53 (11.1)	–	–	–	–	–
Tarsal region	50 (10.4)	–	–	–	50 (31.2)	–
Shoulders	49 (10.2)	6 (6%)	–	–	–	–
Others MTP joints	24 (5.0)	–	–	–	15 (9.4)	–
DIP joints	15 (3.1)	–	–	–	–	–
Others	30 (6.3)	1 (1%)	–	13 (9.6)	9 (5.6)	–

*In bold, the joint most involved; †Unspecified fingers on joints; ‡PIP & MCP joints.

[4] Mijiyawa M, et al. Joint Bone Spine. 2000;67(5):441–5.
[5] Cassim B, et al. Ann Rheum Dis. 1994 Nov;53(11):759–62.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6799

THU0426 LONG-TERM ADHERENCE TO URATE-LOWERING THERAPY IN GOUT: DO NOT BLAME ON THE PATIENTS

F. Perez-Ruiz, I. Urionagüena, S.P. Chinchilla. *Rheumatology Division, Hospital Universitario Cruces and Biocruces Health Research Institute, Baracaldo, Spain*

Background: adherence to urate-lowering treatment (ULT) in patients with gout is reported to be lower than 50% in the first year, below 20% at 2-year, and worse than in other chronic conditions such as hypertension, diabetes, or hyperlipidemia.
Objectives: to evaluate adherence to ULT both overall and during follow-up, to compare it to the adherence to medications for associated comorbidities, and to explore potential causes for non-adherence to ULT.
Methods: transversal study of a nested cohort of patients in a gout clinic in the hospital setting who were scheduled for a follow-up visit during 6 consecutive months in 2016. General data of patients, along with variables related to gout and to comorbid conditions are systematically retrieved at first visit; prescribed ULT, doses, adherence, and serum urate levels were obtained during the follow-up visits. Adherence was retrieved as medication possession rate (MPR) according to pharmacy offices from government electronic databases (including >98% of the general population). Also, MPRs of drugs prescribed for hypertension, diabetes (only oral), and hyperlipidemia were obtained; if more than one drug prescribed for any of the previous, the best adherence per comorbidity treatment was entered. Good adherence was considered as MPR>80 percent of that prescribed, target serum urate (sUA) as <0.36 mmol/L. Patients are educated at first visit and encouraged to be adherent from baseline through follow-up visits.
Results: adherence data were available from 209 patients who were scheduled for a follow-up visit during the observation period; 14 (6.7%) patients did not atend the visit. This sample was formed by 90% male, only 55% had received ULT previous to first visit, median age was 65 years at follow-up visit, 47% and 44% showed poliarticular and tophaceous disease at baseline, respectively. MPR overall showed a median of 89% (IQR 79–94, N=209) for ULT (72% had MPR>80), and 89% (IQR 81–94, N=119), 88% (IQR 79–94, N=65), and 82% (IQR 77–93, N=28) for hypertension, hyperlipidemia, and diabetes respectively ($p<0.05$ only for diabetes).
Adherence was lower for patients who did not attend the scheduled visit (median MPR 58% vs. 86%, MPR >80, 21% vs. 75%, $p<0.01$). Adherence was lower during the first year (80%, N=67) compared to 2nd and 3rd year period (86%, N=67) or 4 year or over (89%, N=75). MPR>80 was 57%, 76% y 81% for the same periods of follow-up, respectively. Good adherence was associated to a rate of target serum urate of 90%, compared to 72% for patients showing MPR<80.
Male gender and un-attendance to scheduled visit were statistically associated to MPR<80 in multivariate analysis, and numerically to increasing age and overall comorbidity.
Conclusions: adherence to ULT measured as MPRs in a cohort of educated patients is good, sustained during follow-up, and similarly good to that for comorbid conditions (hypertension, hyperlipidemia, and diabetes); therefore, we cannot blame poor adherence on the patients anymore. Targeting absenteeism could be an opportunity for further improvement.
Disclosure of Interest: F. Perez-Ruiz Consultant for: Amgen, Ardea, AstraZeneca, Gruenenthal, Menarini, Speakers bureau: AstraZeneca, Gruenenthal, Menarini, I. Urionagüena: None declared, S. Chinchilla: None declared
DOI: 10.1136/annrheumdis-2017-eular.2994

THU0427 AMBIENT AIR POLLUTION AND RISK OF ACUTE GOUT FLARES; A TIME-SERIES STUDY

H.J. Ryu[1], M.R. Seo[1], H.J. Choi[1], J. Cho[2], H.J. Baek[1]. [1]*Rheumatology;* [2]*Occupational and Environmental Medicine, Gachon University Gil Medical Center, Incheon, Korea, Republic Of*

Background: Air pollution is caused by substances that consists of solid particles, liquid droplets, or gases including carbon monoxide (CO), nitrate (NO), sulfur dioxide (SO_2), ozone (O_3), lead, toxic product from tobacco smoke and particulate matter (PM). Inhaled air pollutants can induce oxidative stress and this can contribute to trigger or exacerbate systemic inflammation and autoimmunity. The relations of air pollution with rheumatic diseases have been reported, especially in rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis and juvenile idiopathic arthritis. Gout is an inflammatory disease caused by deposition of monosodium urate (MSU) crystals. Acute gout flares is initiated with activation of the NLRP3 inflammasome and release of IL-1β by MSU crystals. PM $<10\mu m$ in diameter (PM_{10}) exposure has been reported to activate NLRP3 inflammasome in airway epithelial cells. The influence of air pollutants including PM_{10} to acute gout flares has not yet been known.
Objectives: To investigate the association between air pollution and acute gout flares
Methods: We obtained data from the National Health Insurance Database between 2007 and 2015 in Incheon, Republic of Korea by Health Insurance Review and Assessment (HIRA) service. The HIRA data included age, gender, national health insurance type, diagnosis code based on the International Classification of Diseases version 10 (ICD–10), visit date, procedure code, and prescription code. We studied the subjects of age $\geq$19 years who visited emergency department (ED) due to acute gout flare between 2008 and 2015. Acute gout flare was defined as an ED visit due to gout (ICD-10, M10) with any prescription of non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, steroids, or colchicine. Comorbidities and prescription history were collected. The data of ambient PM_{10}, O_3, NO_2, CO, and SO_2 levels were obtained from the Ministry of Environment data sources. We performed time-series study. The generalized additive models with Poisson distribution were used to investigate the association between single air pollutant level and acute gout flares. To examine the delayed effect of air pollutant exposure before the ED visit day on acute gout flare, we established cumulative lag models (averaging levels of consecutive days).
Results: The total number of ED visits for acute gout flare from 2008 to 2015 in Incheon was 139,665, including 48.8% of 40–59 year-old men. The ED visits for acute gout attack were most likely to occur in summer (29.1%). Among the ED cases of acute gout flares, 11.0% had a prescription history of allopurinol or febuxostat for the six months before the visit. The relative risks (RRs) of PM_{10} and O_3 at lag0–7 were 1.02 (1.01–1.03) and 1.07 (1.06–1.08), respectively. NO_2, CO, and SO_2 did not show significant association with acute gout flares. Acute gout flares showed more significant association with O_3 in the cases with hypertension and use of NSAIDs, colchicine, or statins. PM_{10} was more significantly associated with acute gout flares in the cases with congestive heart failure.
Conclusions: Ambient air pollution can induce acute gout flares and its influence on acute gout flares may increase according to the comorbidities or medications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6188

THU0428 ON THE INCIDENCE OF GOUT FLARES IN PRIMARY CARE: A RETROSPECTIVE COHORT STUDY

H. Janssens[1], M. Janssen[2], J. Fransen[3], M. Flendrie[4]. [1]*Department of Primary and Community Care, Radboud University Medical Centre, Nijmegen;* [2]*Rheumatology, Rijnstate Hospital, Arnhem;* [3]*Radboud University Medical Centre;* [4]*Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands*

Background: From rheumatologist point of view (secondary care) there is a serious concern about suboptimal treatment of gout patients in primary care with warnings for worse prognostic consequences.(1) Some refer even to a "state of suboptimal gout care" promoted by "substantial gaps between rheumatologists and primary care providers" in their approaches to gout care:(2) the strategy of "treating-to-target" (to lower serum uric acid (SUA) levels $<$0.36mmol/L) versus "treating-to-avoid-symptoms" (often without addressing hyperuricemia).(3) Most studies on gout care in the primary care setting checked patients for prescribed urate lowering treatment (ULT), SUA assessments or reached SUA target levels, omitting the major patient related clinical end point of gout, flare frequency.(4)
Objectives: To quantify the occurrence of flares and the use of ULT, in primary care patients with gout, and to analyze patient characteristics related to low or high flare frequency.
Methods: A retrospective cohort study (setting one Dutch primary care center with an integrated medical praxis and pharmacy). Electronic medical records of ca. 5800 enlisted patients were used to select all patients with gout, to analyze their ULT use, and to assess flare frequency in a 2-year time window (2014–2015). Flare was defined as each pharmacy delivery of an anti-inflammatory drug or pain killer linked to a morbidity code for gout. Associations were studied between high or low flare frequency and patient characteristics by univariate logistic regression.
Results: Of 173 included patients (prevalence 3%; mean age 66.4 yr; 75.7% men) 38.7% used ULT persistently during the 2-year time-window. Median time after initial diagnosis was 8.0 yr (IQR 3.0–14.5). Mean total numbers of flares in two years was 2.7 (SD: 4.7), median 1.0 (IQR: 0.0–4.0). Of the patients not receiving ULT (n=106, 61.3%) 41.5% had never, 25.5% one or two, and 6.6% more than six flares during two years. No associations were found between patient characteristics (e.g. age, time after initial diagnosis, crystal diagnosis, ULT use, cardiovascular co-morbidity, diuretic use) to differentiate patients with "no-or-1-flare" and "2-or-more-flares" per two years.
Conclusions: Occurrence of flares in this stringently observed primary care cohort of patients with gout was very low, even if most patients did not use prophylactic ULT. Only 6.6% of patients experienced $>$6 flares in two years. Patients, in particular those not using ULT and with a low flare frequency (the majority), may reflect individuals with a distinctive (moderate) disease activity. They probably do not fulfill the general accepted advancing course of gout with ongoing and increasing flare frequency, MSU deposition, tophus formation, and joint damage. Immediate lifelong ULT for them may not be automatically indicated. Our study shows that suboptimal gout management in the perception of rheumatologists (secondary care) does not lead to an abundant number of gout flares in primary care patients. This urges to caution when recommendations based upon secondary care guide lines are advised for primary care patients with gout.
References:
[1] Doherty M, et al. Ann Rheum Dis 2012;71:1765–70.
[2] Dalbeth N, et al. Arthritis Rheumatol 2017;69:22–34.
[3] McLean RM, et al. Ann Intern Med 2017;166:73–4.
[4] Morillon MB, et al. BMJ Open 2016;6:e012026.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6295

THU0429 CLINICAL SIGNIFICANCE OF INCREASED SERUM LEVELS OF FGF23 IN FIBROUS DYSPLASIA

H. Florez[1], S. Mandelikova[1], X. Filella[2], A. Monegal[1], N. Guañabens[1], P. Peris[1]. [1]*Rheumatology Department;* [2]*Clinical Biochemistry Department, Hospital Clinic, Barcelona, Spain*

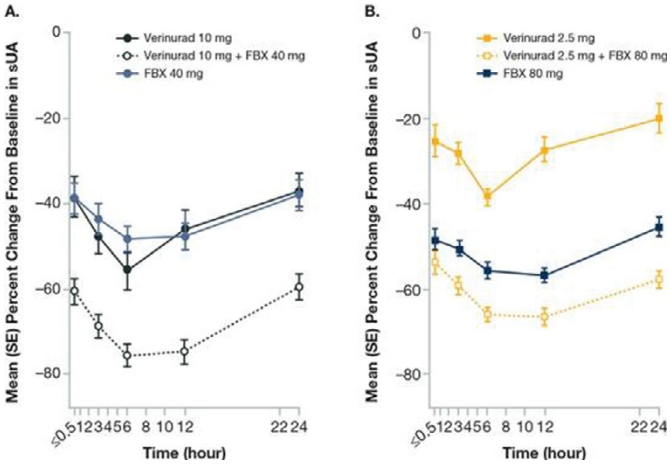
Background: Fibrous dysplasia of bone (FD) is an uncommon skeletal disorder, caused by missense mutations of the *GNAS1* gene and is characterized by the development of fibro-osseous lesions that replace normal bone. FD can present with a broad spectrum of clinical manifestations, including the development of hypophosphatemic osteomalacia which is due to the production of the phosphaturic hormone fibroblast growth factor 23 (FGF-23) by the dysplastic bone tissue. Nevertheless, the prevalence of this clinical complication is not well known.
Objectives: To analyse the serum levels of FGF-23 in patients with FD and determine their relationship with the extension and activity of the disease, as well as with serum phosphate levels.
Methods: Twelve patients (7F:5M) with FD with a mean age of 50.67±16.4 years (24–79) were included. The clinical reports of the patients were reviewed, with special attention to the extension and activity of the disease, number and location of the affected bones, clinical complications and treatments received. Serum FGF-23 values were recorded in all subjects (determined by Immunotopics, CA, USA [measuring FGF23 C- terminal], normal value $<$130 RU/ml), as well as serum phosphate and calcium values, bone turnover markers and their evolution with treatment.
Results: Serum levels of FGF-23 were increased ($>$130 RU/ml) in 6/12 patients (50%). In patients with and without high FGF-23 levels the number of affected bones (2.2±2 *vs.* 1.9±1, respectively) and the skeletal locations of FD were similar as was the age in both groups of patients (48.2±14 *vs.* 53.2±19 years). In addition, FD disease activity and extension were similar in the two groups as were the bone turnover marker values (FAO, PINP and CTx). Strikingly, differences between serum phosphate values were not observed between the two groups (FGF23 $>$130: 3.9±0.9 mg/dl *vs.* FGF23 $<$130: 3.5±0.6 mg/dl). Indeed, none of the patients with high FGF-23 levels had low serum phosphate values. Following bisphosphonate (zoledronate) treatment, there were no significant changes in FGF-23 values. Nevertheless, an increase of 123% was found in one patient receiving denosumab, although hypophosphatemia was not associated.
Conclusions: Patients with FD frequently present elevated FGF-23 values with no effects on serum phosphate levels, thereby suggesting the presence of an alteration in processing this protein in the dysplastic bone tissue in this disease. The role of denosumab treatment in FD and its repercussion on FGF-23 levels need further study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5261

THU0430 PHARMACOKINETICS, PHARMACODYNAMICS, AND TOLERABILITY OF CONCOMITANT MULTIPLE DOSE ADMINISTRATION OF VERINURAD (RDEA3170) AND FEBUXOSTAT IN HEALTHY ADULT MALE SUBJECTS

J.T. VanderLugt[1], M. Gillen[2], X. Yang[3], J. Hall[3]. *[1]Jasper Clinical Research & Development, Kalamazoo, MI; [2]AstraZencea, Gaithersburg, MD; [3]Ardea Biosciences, Inc., San Diego, CA, United States*

Background: Verinurad (RDEA3170) is a novel selective uric acid reabsorption inhibitor in clinical development for the treatment of gout and asymptomatic hyperuricemia.
Objectives: This Phase 1, single-blind, multiple dose, drug-drug interaction (DDI) study evaluated the pharmacokinetics (PK), pharmacodynamics, and tolerability of verinurad in combination with febuxostat (FBX) in healthy male volunteers.
Methods: Subjects were randomized to receive once-daily doses of FBX or verinurad or placebo alone for 7 days, FBX + verinurad or FBX + placebo on days 8–14, and the alternative single agent (FBX or verinurad or placebo) on days 15–21. Subjects received either the combination of verinurad 10 mg + FBX 40 mg or verinurad 2.5 mg + FBX 80 mg. Serial plasma/serum and urine samples were drawn at predetermined time points on Days 7, 14 and 21, and assayed for verinurad, FBX, and uric acid. Baseline samples were drawn on Day –1. Safety was assessed by adverse event (AE) reports, laboratory tests, vital signs, and electrocardiograms (ECGs).
Results: Of 23 randomized subjects, 20 completed the study. FBX 40 mg had no apparent effect on the plasma C_{max} and AUC for verinurad 10 mg, whereas FBX 80 mg increased the plasma C_{max} and AUC for verinurad 2.5 mg by 25% and 33%, respectively. Verinurad had no effect on FBX PK. Renal clearance of verinurad was unchanged by FBX.
The mean maximal reduction in serum uric acid (sUA) was 76% with verinurad 10 mg + FBX 40 mg compared with verinurad 10 mg (56%) or FBX 40 mg (49%) alone (Figure 1A) and was 67% with verinurad 2.5 mg + FBX 80 mg compared with verinurad 2.5 mg (38%) or FBX 80 mg (57%) alone (Figure 1B). Consistent with the mechanism of action (MOA) of verinurad, 24-hr fractional excretion of uric acid (FEUA) increased (2.5 mg: 7.6%; 10 mg: 12.8%) vs baseline (6.5% and 6.0%, respectively). Renal clearance of uric acid (CL_{UR}) increased similarly (2.5 mg: 9.0 mL/min; 10 mg: 12.3 mL/min) vs baseline (8.3 and 7.3 mL/min, respectively). The increases were maintained for 24 hours with verinurad 10 mg + FBX 40 mg (FEUA: 11.8%; CL_{UR}: 13.6mL/min). Consistent with its MOA, FBX 40 mg and 80 mg decreased the amount of uric acid excreted in urine (246 and 221 mg, respectively, vs baseline: 695 and 818 mg), FEUA (4.79 and 4.18%, respectively, vs baseline: 6.31 and 6.54%), and CL_{UR} (4.91 and 4.96 mL/min, respectively, vs baseline: 7.71 and 8.73 mL/min). No serious AEs, discontinuations due to AEs, or clinically significant laboratory or ECG abnormalities were noted during the study.

Figure 1: Mean (SE) percent change from baseline in sUA at steady state following verinurad 10 mg or FBX 40 mg or the combination (A) or verinurad 2.5 mg or FBX 80 mg or the combination (B)



Conclusions: No DDI was found with the verinurad 10 mg + FBX 40 mg combination and only a modest one with verinurad 2.5 mg + FBX 80 mg. Both combinations were safe and well tolerated and resulted in greater reduction of sUA than either verinurad or FBX alone. These results support the continued development of this novel approach for the treatment of gout and hyperuricemia.
Disclosure of Interest: J. VanderLugt: None declared, M. Gillen Employee of: AstraZeneca, X. Yang Employee of: Ardea Biosciences, Inc., J. Hall Employee of: Ardea Biosciences, Inc.
DOI: 10.1136/annrheumdis-2017-eular.5264

THU0431 COMPARATIVE EFFECTIVENESS OF ALLOPURINOL VERSUS FEBUXOSTAT FOR PREVENTING INCIDENT RENAL DISEASE IN OLDER ADULTS: AN ANALYSIS OF MEDICARE CLAIMS DATA

J. Singh, J. Cleveland. *University of Alabama at Birmingham, Birmingham, United States*

Background: Large scale randomized studies are underway to assess whether compared to placebo, each XO-inhibitor, allopurinol or febuxostat, can prevent renal function loss. This evidence is needed and will confirm their nephroprotective potential. However, neither study will answer a key question: Does the renal protective effect of allopurinol differ from that of febuxostat?
Objectives: To assess the comparative effectiveness of allopurinol vs. febuxostat for preventing incident renal disease in elderly.
Methods: In a retrospective cohort study using Medicare claims data, we included patients newly treated with allopurinol or febuxostat (baseline period of 183 days without either medication). We used 1:5 propensity-matched Cox regression analyses to compare the hazard ratio (HR) of incident renal disease with allopurinol use and allopurinol dose vs. febuxostat (reference category). Sensitivity analyses included multivariable-adjusted regression models.
Results: There were 31,465 new allopurinol or febuxostat treatment episodes in 26,443 patients; 8,570 ended in incident renal disease. Crude rates of incident renal disease per 100,000 person-days were 53 with allopurinol vs. 93 with febuxostat. Crude rates of incident renal disease per 100,000 person-days were lower with higher daily dose: allopurinol $<$200, 200–299 and $\geq$300 mg/day with 65, 48 and 43; and febuxostat 40 mg and 80 mg/day with 93 and 89, respectively. In propensity-matched analyses, compared to febuxostat use, allopurinol use was associated with lower HR of incident renal disease, 0.61 (95% confidence interval (CI): 0.49, 0.77). Compared to febuxostat 40 mg/day, allopurinol doses $<$200, 200–299 and $\geq$300 mg/day were associated with lower HR of incident renal disease, 0.75 (95% CI: 0.65, 0.86), 0.61 (95% CI: 0.52, 0.73) and 0.48 (95% CI: 0.41, 0.55), respectively. Sensitivity analyses using multivariable-adjusted regression confirmed these findings.
Conclusions: Allopurinol was more effective than febuxostat in preventing incident renal disease in elderly patients. Future studies need to examine the mechanism of this renal benefit of allopurinol.
Disclosure of Interest: J. Singh Grant/research support from: Savient, Takeda, Consultant for: Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology, J. Cleveland: None declared
DOI: 10.1136/annrheumdis-2017-eular.6837

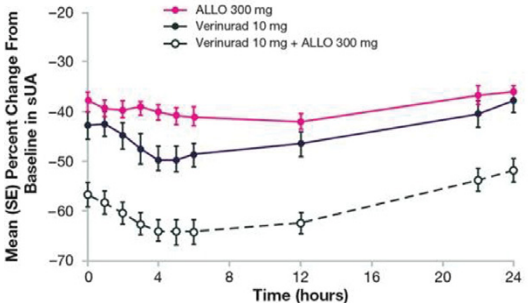
THU0432 PHARMACOKINETICS, PHARMACODYNAMICS, AND TOLERABILITY OF CONCOMITANT MULTIPLE DOSE ADMINISTRATION OF VERINURAD (RDEA3170) AND ALLOPURINOL IN ADULT MALE SUBJECTS WITH GOUT

J. Hall[1], M. Gillen[2], X. Yang[1], S. Liu[1], S. Walker[2], V. Clauson[1], M. Kankam[3]. *[1]Ardea Biosciences, Inc., San Diego, CA; [2]AstraZeneca, Gaithersburg, MD; [3]Vince and Associates Clinical Research, Inc., Overland Park, KS, United States*

Background: Verinurad (RDEA3170) is a novel selective uric acid reabsorption inhibitor in clinical development for the treatment of hyperuricemia and gout.
Objectives: This Phase 1, single-blind, multiple dose, drug-drug interaction study evaluated the pharmacokinetics (PK), pharmacodynamics, and tolerability of verinurad in combination with allopurinol (ALLO) in adult male subjects with gout.
Methods: Adult males with gout, aged 18–75 years, with serum uric acid (sUA) $\geq$8 mg/dL were randomized to receive once-daily oral doses of ALLO 300 mg or verinurad 10 mg alone for 7 days, ALLO 300 mg + verinurad 10 mg on Days 8–14, and the alternative single agent (verinurad 10 mg or ALLO 300 mg) on Days 15–21. Colchicine 0.6 mg was taken once daily from day –14. Serial plasma/serum and urine samples were drawn at predetermined time points on Days 7, 14 and 21 and assayed for verinurad, ALLO, oxypurinol (OXY), colchicine, and uric acid. Baseline samples were drawn on Day –1. Safety was assessed by adverse event (AE) reports, laboratory tests, vital signs, and electrocardiograms (ECGs).
Results: Subjects (N=12) were mostly white (58.3%) with mean (SD) age of 51 (10) years. Following multiple doses, ALLO had no effect on C_{max} and AUC of verinurad. ALLO C_{max} was increased 33% but AUC was unaltered by verinurad. The C_{max} and AUC for OXY, the active metabolite of ALLO, were reduced 32% and 38%, respectively, by verinurad. Colchicine plasma exposures were unaltered by verinurad. ALLO had no effect on urinary excretion of verinurad, whereas urinary excretion of OXY was increased 19% by verinurad.
The mean maximal decrease in sUA was 65% with verinurad + ALLO compared with verinurad (51%) or ALLO (43%) alone (Figure). Consistent with the mechanism of action (MOA) of verinurad, 24-h fractional excretion of uric acid (FEUA) and clearance of uric acid (CL_{UR}) were increased in the absence (9.2% and 11.5 mL/min, respectively) or presence of ALLO (7.9% and 11.8 mL/min) vs baseline (4.5% and 5.7 mL/min) or ALLO alone (3.7% and 5.0 mL/min). Consistent with its MOA, ALLO decreased the amount of uric acid excreted in 24-h urine (363 mg) compared with baseline (683 mg), verinurad alone (739 mg) or verinurad + ALLO (522 mg) but had no effect on FEUA or CL_{UR}. No

serious AEs, discontinuations due to AEs, or clinically significant laboratory or ECG abnormalities were noted.

Figure: Mean (SE) percent change from baseline in sUA at steady state following verinurad 10 mg or ALLO 300 mg or in combination



Conclusions: Although a modest drug–drug interaction was found between verinurad and ALLO, the combination was safe and well tolerated at the studied doses and resulted in greater reduction of sUA than either alone. These results support the evaluation of verinurad + ALLO as an alternative once-daily treatment option for hyperuricemia and gout.
Disclosure of Interest: J. Hall Employee of: Ardea Biosciences, Inc., M. Gillen Employee of: AstraZeneca, X. Yang Employee of: Ardea Biosciences, Inc., S. Liu Employee of: Ardea Biosciences, Inc., S. Walker Employee of: AstraZeneca, V. Clauson Employee of: Ardea Biosciences, Inc., M. Kankam: None declared
DOI: 10.1136/annrheumdis-2017-eular.5308

THU0433 PHARMACODYNAMIC AND PHARMACOKINETIC STUDY OF VERINURAD (RDEA3170) IN ADULT MALE SUBJECTS WITH MILD, MODERATE, AND SEVERE RENAL IMPAIRMENT: A PHASE 1, OPEN-LABEL STUDY

W.B. Smith[1], J. Hall[2], J.K. Berg[3], M. Kazimir[3], A. Yamamoto[2], S. Walker[4], C. Lee[2], T.C. Marbury[5]. *[1]Volunteer Research Group, Knoxville, TN; [2]Ardea Biosciences, Inc., San Diego, CA; [3]DaVita Clinical Research, Minneapolis, MN; [4]Astrazeneca, Gaithersburg, MD; [5]Orlando Clinical Research Center, Orlando, FL, United States*

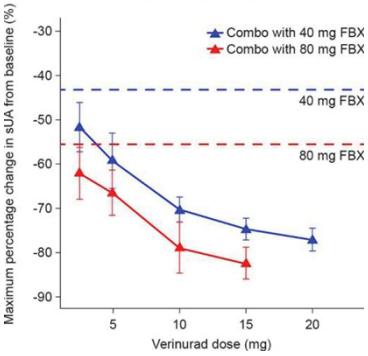
Background: Verinurad (RDEA3170) is a high-affinity, selective URAT1 inhibitor in development for the treatment of gout and asymptomatic hyperuricemia.
Objectives: This Phase 1, single-dose, open-label study investigated the pharmacodynamics (PD), pharmacokinetics (PK), and safety of oral verinurad in adult subjects with mild, moderate, or severe renal impairment and matched controls with normal renal function (NCT02219516).
Methods: Adult males aged 18–85 years were enrolled with a screening serum uric acid (sUA) 4.5–10 mg/dL and creatinine clearance calculated by Cockcroft-Gault formula of 60 to <90 mL/min (mild renal impairment), 30 to <60 mL/min (moderate impairment), 15 to <30 mL/min (severe impairment), or ≥90 mL/min (matched controls). Oral verinurad 15 mg was administered once under fasted conditions. Serial blood and urine samples were taken 30 min before and up to 72 hours postdose. Safety assessments included laboratory, ECG, and vital sign parameters as well as adverse event (AEs) reporting.
Results: PD data were based on 7–8 subjects per group. Verinurad decreased sUA in all groups, with greatest changes in the normal function and mild renal impairment groups. Mean (SD) maximal % change in sUA from baseline (Emax) was -38.3 (14.8)%, -36.9 (13.6)%, -20.5 (6.64)%, and -12.6 (6.94)%, respectively, in the normal function and mild, moderate, and severe renal impairment groups. Increase in the amount of excretion of uric acid due to verinurad treatment decreased in subjects with moderate and severe renal impairment. Plasma Cmax and AUC of verinurad increased with decreasing renal function. Verinurad at the 15 mg dose was well tolerated, with no serious AEs, no subject withdrawals due to AEs, and no Renal Events Adjudication Committee (REAC)-adjudicated renal events during treatment. One patient in each renal impairment group had treatment-emergent AEs considered possibly related to verinurad, which were categorized as gastrointestinal in nature. There were no clinically meaningful changes noted in laboratory values or vital signs.
Conclusions: The sUA lowering effect of verinurad was observed across the spectrum of renal function. Consistent with the verinurad renal-dependent mechanism of action, decreasing sUA lowering was demonstrated with increasing renal impairment. Verinurad safety and tolerability were similar across all stages of renal impairment.
Disclosure of Interest: W. Smith Employee of: Volunteer Research Goup, J. Hall Employee of: Ardea Biosciences, Inc., J. Berg Employee of: DaVita Clinical Research, M. Kazimir Employee of: DaVita Clinical Research, A. Yamamoto Employee of: Ardea Biosciences, Inc., S. Walker Employee of: AstraZeneca, C. Lee Employee of: Ardea Biosciences, Inc., T. Marbury Employee of: Orlando Clinical Research Center
DOI: 10.1136/annrheumdis-2017-eular.5327

THU0434 PHARMACODYNAMIC EFFECTS AND SAFETY OF VERINURAD (RDEA3170) IN COMBINATION WITH FEBUXOSTAT VERSUS FEBUXOSTAT ALONE IN ADULTS WITH GOUT: A PHASE 2A, OPEN-LABEL STUDY

R. Fleischmann[1], P. Winkle[2], J. Hall[3], S. Valdez[3], S. Liu[3], X. Yan[3], L. Hicks[3], M. Hernandez-Illas[4]. *[1]University of Texas, Southwestern Medical Center, Metroplex Clinical Research Center, Dallas, TX; [2]Anaheim Clinical Trials, Anaheim, CA; [3]Ardea Biosciences, Inc., San Diego, CA; [4]4QPS MRA (Miami Clinical Research), Miami, FL, United States*

Background: Verinurad (RDEA3170) is a high-affinity, selective URAT1 inhibitor in development for the treatment of gout and asymptomatic hyperuricemia.
Objectives: This Phase 2a, randomized, open-label, multicenter study investigated the multiple-dose pharmacodynamics (PD), pharmacokinetics (PK), and safety of oral verinurad in combination with febuxostat versus febuxostat alone in adults with gout (NCT02246673).
Methods: Patients aged ≥18 and ≤75 years with gout and serum uric acid (sUA) ≥8 mg/dL were randomized to 1 of 5 cohorts to receive febuxostat (40 mg and 80 mg) alone and in combination with verinurad (dose range 2.5 mg to 20 mg; 4 treatment periods per cohort, each treatment period 7 days). Medications were administered once daily ~30 min after breakfast. Colchicine 0.6 mg for gout flare prophylaxis was initiated at approximately Day -14 (start of urate-lowering therapy [ULT]) washout) or Day -7 if not on ULT. Serial blood and urine samples were measured at preset intervals on Days -1, 1, 7, 14, 21, and 28 for PD and PK endpoints. Safety assessments included adverse events (AEs) and laboratory, electrocardiograms, and vital sign parameters.
Results: Sixty-four patients were randomized (n=12–14 per cohort). Serum PD data pooled across cohorts demonstrated maximal % decrease in sUA from baseline (Emax) at 8–12 h after dosing. Addition of verinurad to febuxostat decreased sUA in dose-dependent manner (Figure 1). Greater sUA reductions were observed for dose combinations of verinurad ≥5 mg with febuxostat 40 mg versus febuxostat 80 mg alone. The rate of urinary uric acid excretion was reduced by febuxostat alone, but comparable to baseline levels with verinurad combined with febuxostat. Verinurad plasma exposures increased with verinurad dose and were comparable for febuxostat 40 mg and 80 mg doses. No drug-drug interaction on verinurad and febuxostat plasma PK parameters was observed. Verinurad at doses from 2.5 mg to 20 mg was well tolerated, with no serious AEs, withdrawals due to AEs, or renal-related events. The most frequent treatment-emergent AE possibly related to study medication was pain in extremity, in 2 patients receiving verinurad. Laboratory values and vital signs showed no clinically meaningful changes. There were no cases of serum creatinine elevation ≥1.5x baseline.

Figure 1. Maximum sUA percentage change



Conclusions: Verinurad coadministered with febuxostat dose-dependently decreased sUA while maintaining urine uric acid levels comparable to baseline. All dose combinations of verinurad and febuxostat in this study were generally well tolerated with no serious AEs or renal-related events during combination treatment.
Disclosure of Interest: R. Fleischmann Grant/research support from: Ardea Biosiences, Inc, P. Winkle Employee of: Anaheim Clinical Trials, J. Hall Employee of: Ardea Biosiences, Inc., S. Valdez Employee of: Ardea Biosiences, Inc., S. Liu Employee of: Ardea Biosiences, Inc., X. Yan Employee of: Ardea Biosiences, Inc., L. Hicks Employee of: Ardea Biosiences, Inc., M. Hernandez-Illas: None declared
DOI: 10.1136/annrheumdis-2017-eular.5367

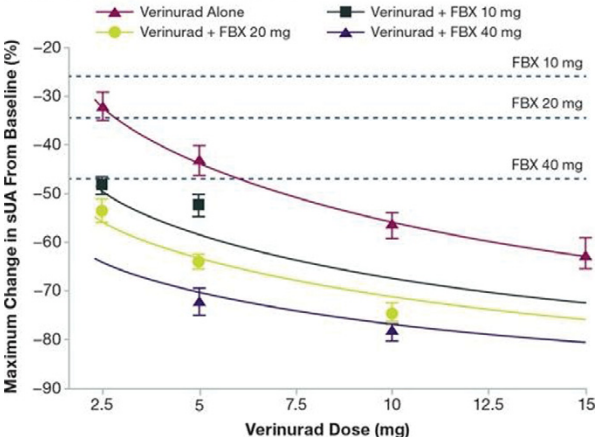
THU0435 PHARMACODYNAMICS, PHARMACOKINETICS, AND SAFETY OF VERINURAD (RDEA3170) IN COMBINATION WITH FEBUXOSTAT VERSUS FEBUXOSTAT ALONE AND VERINURAD ALONE IN JAPANESE ADULTS WITH GOUT OR ASYMPTOMATIC HYPERURICEMIA: A PHASE 2A, OPEN-LABEL STUDY

M. Shiramoto[1], S. Liu[2], Z. Shen[2], J. Hall[2]. *[1]SOUSEIKAI PS Clinic, Fukuoka, Japan; [2]Ardea Biosciences, Inc., San Diego, CA, United States*

Background: Verinurad (RDEA3170) is a high-affinity URAT1 inhibitor in development for the treatment of gout and asymptomatic hyperuricemia.

Objectives: This Phase 2a, randomized, open-label, single-site study investigated the multiple-dose pharmacodynamics (PD), pharmacokinetics (PK), and safety of oral verinurad in combination with febuxostat versus febuxostat alone and verinurad alone in Japanese male adults with gout or asymptomatic hyperuricemia (NCT02317861).
Methods: Japanese male patients aged ≥20 and ≤70 years with gout or asymptomatic hyperuricemia and serum uric acid (sUA) ≥8 mg/dL were randomized to 1 of 6 cohorts to receive febuxostat (10 mg, 20 mg, and 40 mg) alone, febuxostat in combination with verinurad (dose range 2.5 mg to 10 mg); verinurad (2.5 mg to 15 mg) alone; or benzbromarone (50 mg) alone (4 treatment periods per cohort, each treatment period 7 days). The study drugs were administered once daily in the morning after breakfast. Serial blood and urine samples were measured at preset intervals on Days -1, 1, 2, 7, 8, 14, 15, 21, 22, 28 and 29 for PD and PK endpoints. Safety assessments included adverse events (AEs) and laboratory, electrocardiograms, and vital sign parameters.
Results: Seventy-two patients with gout (n=37) or hyperuricemia (n=35) were randomized in this study. Addition of verinurad (2.5 mg to 10 mg) to febuxostat (10 mg, 20 mg, or 40 mg) decreased sUA in dose-dependent manner (Figure). Verinurad coadministered with febuxostat increased the amount of uric acid recovered in urine (Aeur), compared with baseline and the same dose of febuxostat administered alone, yet comparable with benzbromarone. Plasma Cmax and AUC exposures of verinurad and febuxostat exhibited dose proportional increases within the investigated dose range. No clear PK drug-drug interaction of verinurad and febuxostat with each other was observed. Verinurad at doses from 2.5 mg to 15 mg was well tolerated, with no serious AEs or withdrawals due to AEs. One treatment-emergent AE (diarrhea) was considered possibly related to both verinurad and febuxostat. Laboratory values and vital signs indicated no clinically meaningful changes.

Figure: Maximum percent change from baseline in sUA following varying verinurad doses in combination with FBX versus FBX 10, 20, or 40 mg alone



Conclusions: Verinurad coadministered with febuxostat dose-dependently decreased sUA while maintaining Aeur comparable to benzbromarone. All dose combinations of verinurad and febuxostat in this study were generally well tolerated.
Disclosure of Interest: M. Shiramoto Employee of: SOUSEIKAI PS Clinic, S. Liu Employee of: Ardea Biosciences, Inc., Z. Shen Employee of: Ardea Biosciences, Inc., J. Hall Employee of: Ardea Biosciences, Inc.
DOI: 10.1136/annrheumdis-2017-eular.5391

THU0436 CLINICAL SIGNIFICANCE OF DELTA NEUTROPHIL INDEX IN THE DIFFERENTIAL DIAGNOSIS BETWEEN SEPTIC ARTHRITIS AND ACUTE GOUT ATTACK WITHIN 24 HOURS AFTER HOSPITALISATION

J.Y. Pyo, S.M. Jung, J.J. Song, Y.-B. Park, S.-W. Lee. *Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea, Republic Of*

Background: The most important differential diagnoses of acute monoarticular arthritis are septic arthritis and acute gout attack. Identifying infection is crucial in preventing the devastating outcome of septic arthritis.
Objectives: The delta neutrophil index (DNI) is a value that corresponds to the fraction of circulating immature granulocytes. As DNI reflects the burden of infection, we evaluated this index as a differentiating marker between septic arthritis and acute gout attack.
Methods: The medical records of 149 patients with septic arthritis and 194 patients with acute gout attack were reviewed. A specific cell analyser, ADVIA 2120, was used to measure DNI. Clinical and laboratory markers associated with predicting septic arthritis were assessed by using logistic regression.
Results: Patients with septic arthritis showed higher levels of DNI than those with acute gout attack (3.3 vs. 0.6%, $P<0.001$). Similar results were observed in patients without monosodium urate (MSU) crystal confirmation or those with normouricemia (3.3 vs. 0.5 and 3.1 vs. 0.7%, respectively; $P<0.001$ for both). A DNI level of 1.9% was determined as the cut-off value for predicting septic arthritis. In the multivariate analysis, DNI was the most powerful independent value for predicting septic arthritis (odds ratio 14.003).

Table 1. Comparison of variables between patients with acute gout attack and those with septic arthritis

Variables	Patients with acute gout attack (n=194)	Patients with septic arthritis (n=149)	Total (n=343)	p-value
Age, years	65.0±15.0	60.9±16.4	63.2±15.8	0.016
MSU crystals confirmed, n (%)	81 (41.8%)	N/A	81 (23.6%)	N/A
Positive culture, n (%)	N/A	98 (65.8%)	97 (28.3%)	N/A
WBC count, /mm^3	9600.0±3000.0	11,200.0±4700.0	10,300.0±3900.0	<0.001
DNI, %	0.6±0.9	3.3±4.0	1.8±3.0	<0.001
ESR, mm/h	61.7±33.8	78.2±32.5	69.3±34.2	<0.001
CRP, mg/L	76.5±68.7	126.6±104.0	98.7±89.6	<0.001
BUN, mg/dL	29.5±21.9	22.7±14.7	26.6±19.4	0.001
Creatinine, mg/dL	1.9±1.9	1.2±1.7	1.6±1.8	<0.001
Uric acid, mg/dL	7.6±2.5	4.4±1.6	6.3±2.7	<0.001

Table 2. Multivariate analysis of the predictive values for septic arthritis in patients with acute gout attack and those with septic arthritis*

Variables	Odds ratio	95% Confidence interval	p-value
WBC count ≥14,000.0/mm^3	1.888	0.563, 6.337	0.303
DNI ≥1.9%	14.003	5.683, 34.508	<0.001
ESR ≥70.0 mm/h	2.505	1.109, 5.657	0.027
CRP ≥106.0 mg/L	3.032	1.276, 7.209	0.012
Uric acid ≥7.0 mg/dL	0.031	0.011, 0.086	<0.001

Conclusions: This study showed the possibility of using DNI as a differentiating marker between septic arthritis and acute gout attack at the crucial early phase. DNI showed its relevance regardless of confirmation of MSU crystal deposition or serum level of uric acid.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2084

THU0437 IMPACT OF DIURETICS ON THE URATE LOWERING THERAPY IN PATIENTS WITH GOUT: ANALYSIS OF AN INCEPTION COHORT

L. Ranieri[1], C. Contero[2], M. Andrés[1,2]. *[1]Seccion de Reumatologia, Hospital General Universitario de Alicante; [2]Departamento de Medicina Clínica, Universidad Miguel Hernández, Alicante, Spain*

Background: Use of diuretics is a common bystander in patients with gout, and it has been reported to impair response to allopurinol [1,2] and likely lead to treatment failure and refractoriness. However, after the introduction of new urate-lowering therapies (ULT) and treat-to-target strategies, whether this inconvenient effect of diuretics persists has not received critical attention to date.
Objectives: To analyze the impact of the diuretic therapy on the response to ULT in patients with gout.
Methods: Retrospective analysis of an inception cohort in patients with crystal-proven gout (Jan2014-Nov2016). Patients were classified according to the use of diuretics (loop and/or thiazide) at baseline. The primary outcome variables were the reduction of serum uric acid (SUA) levels and the achievement of different objectives of SUA (6, 5, and 4mg/dL); as secondary outcome variable the maximum dose of ULT was registered, as well as other clinical, analytical, and ULT-related data. A comparative analysis was performed according to the use of diuretics, using Student's t and chi-2 tests. Also, the analysis was stratified according to the ULT used.
Results: The inception cohort included 225 patients with an average age of 65 years (SD 14.1), being 86.2% of them men. The median duration of gout at inclusion was 4 years (p25–75 1–10) and 21.3% presented tophi. At baseline, the median (p25–75) SUA and estimated glomerular filtration rate were 8.2 mg/dL (7.2–9.2) and 75.9 mL/min (27.2–88.3), respectively. A total of 98 patients

Outcome variable	Diuretic therapy		p
	No	Yes	
Whole sample (N=209)	N=117	n=92	
– SUA reduction (mg/dL), mean (SD)	3.2 (2.1)	3.7 (2.5)	0.196
– SUA<6 (%)	80.0%	75.9%	0.458
– SUA<5 (%)	61.0%	50.6%	0.126
– SUA<4 (%)	31.4%	28.9%	0.575
Allopurinol (n=158)	N=92	N=66	
– SUA reduction (mg/dL), mean (SD)	3.1 (1.9)	3.2 (2.0)	0.813
– SUA<6 (%)	80.6%	74.2%	0.337
– SUA<5 (%)	60.2%	43.9%	0.043
– SUA<4 (%)	28.0%	21.2%	0.334
– Maximum dose (mg/day), mean (SD)	316.5 (126.9)	278.6 (121.8)	0.053
Febuxostat (n=33)	N=14	N=19	
– SUA reduction (mg/dL), mean (SD)	3.7 (3.4)	5.6 (3.1)	0.147
– SUA<6 (%)	70.0%	82.4%	0.456
– SUA<5 (%)	70.0%	76.5%	0.711
– SUA<4 (%)	60.0%	58.8%	0.952
– Maximum dose (mg/day), mean (SD)	80.0 (16.3)	80.0 (25.3)	0.348

(43.6%) were on diuretics mainly for hypertension (64.7%), heart failure (9.4%), and renal failure (5.9%). Follow-up data was available from 209 patients (92.9%), with a median 9 months of follow-up (4–14). ULT used was allopurinol in 172 patients (82.6%), febuxostat in 34 (16.5%), and benzbromarone in only 2 cases (0.9%). Regarding the baseline characteristics, patients on diuretics were older, had higher rates of females, hypertension, diabetes, and cardiovascular disease, and showed higher SUA and lower glomerular filtration rate. The table shows the outcomes comparison according to diuretic treatment, globally and stratified by type of ULT (excluding the two cases of benzbromarone). Except for a lower achievement of SUA<5 in the allopurinol subgroup, no significant differences were found either globally or by type of ULT.

Conclusions: Despite its high rate, diuretics currently seem to not have a significant impact on the achievement of the different objectives of treatment of patients with gout.

References:
[1] Rheumatology; 55:1172.
[2] Br J Clin Pharmacol; 81:277.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3905

THU0438 LACK OF PREDICTIVE VALUE OF THE NIAID/FAAN CRITERIA TO IDENTIFY SUBJECTS WITH EVIDENCE OF IMMUNE ACTIVATION AFTER RECEIVING PEGLOTICASE FOR CHRONIC REFRACTORY GOUT

L. Calabrese[1], A. Kavanaugh[2], A. Yeo[3], P. Lipsky[4]. *[1]Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, OH; [2]Division of Rheumatology, Allergy, & Immunology, UCSD, la Jolla, CA; [3]Horizon Pharma, Lake Forest, IL; [4]AMPEL BioSolutions, LLC, Charlottesville, VA, United States*

Background: The NIAID/FAAN criteria have been widely applied to identify anaphylaxis despite having only modest specificity.1,2

Objectives: To evaluate the predictive value of the NIAID/FAAN criteria to identify evidence of immune activation in subjects with chronic refractory gout treated with pegloticase in randomized clinical trials (RCTS) who experienced infusion reactions (IRs), by assessing the capacity of biochemical testing for immunologic activation to confirm the likelihood of anaphylaxis.

Methods: During the RCTs supporting the approval of pegloticase for treatment of chronic refractory gout, subjects remained on therapy despite becoming nonresponders, which reflected the development of anti-drug antibodies (ADA); ~60% of subjects continued to receive pegloticase despite elevated ADA titers and many had IRs. In subjects receiving pegloticase every 2 weeks (q2w), 22/85 (25.9%) had a total of 43 IRs and 34/84 (40.5%) receiving pegloticase every 4 weeks (q4w) had a total of 70 IRs. 21/22 (95.5%) and 29/34 (85.3%) subjects with IRs in the q2w and q4w groups, respectively, were nonresponders. The 113 total IRs were categorized post hoc as to whether they met NIAID/FAAN criteria for anaphylaxis. Six IRs in 6 subjects met criteria, 53 IRs in 33 subjects had only one feature and were designated as "hypersensitivity", and 54 IRs in 29 subjects had no features and were designated "other". The clinical courses of these IRs and whether they were associated with elevated tryptase levels as a measure of mast cell degranulation or complement consumption as a measure of immune complex activity were assessed.

Results: Of a total of 852 infusions in subjects receiving q2w pegloticase, 43 (5.0%) were associated with IRs as were 70 of 830 infusions (9.5%) in subjects receiving q4w pegloticase. Of the 70 IRs associated with q4w administration, 3 (4.3%) met the criteria for anaphylaxis, 31 (44.3%) for hypersensitivity and 36 (51.4%) were other. The respective values for subjects receiving pegloticase q2w were 3/43 (7.0%),22/43 (51.1%), and 18/43 (41.9%). A total of 14 IRs (12.4%) were associated with elevated tryptase and 31 (27.4%) with decreased complement CH50 levels. Immunologic abnormalities were not significantly different in the 3 groups, with 16.7%, 17.0% and 7.4% of anaphylaxis, hypersensitivity and other IRs, respectively, having increased tryptase; and 0%, 30.2%%, and 27.8%, respectively, having decreased complement. No subjects were classified as experiencing anaphylaxis by investigators, none required hospitalization, and 60.7%, continued to receive pegloticase.

Conclusions: Post-hoc designation of pegloticase-treated subjects as meeting NIAID/FAAN criteria for anaphylaxis was not associated with a higher frequency of biochemical evidence of immune activation or a more severe clinical course. In pegloticase-treated subjects, the NIAID/FAAN anaphylaxis criteria did not identify subjects with IRs associated with elevated tryptase and decreased complement CH50 levels.

References:
[1] Sampson HA, et al. J Allergy Clin Immunol. 2006;117:391–397.
[2] Campbell RL, et al. J Allergy Clin Immunol. 2012;129:748–752.

Disclosure of Interest: L. Calabrese Consultant for: BMS, Genentech, Horizon, Crescendo, Pfizer, GSK, Regeneron, UCB, Abbvie, Janssen, A. Kavanaugh Consultant for: Abbvie, Amgen, Janssen, BMS, UCB, Pfizer, A. Yeo Consultant for: Horizon Pharma, P. Lipsky Consultant for: AstraZeneca, Celgene, EMD Serono, GSK, Horizon Pharma, Janssen, Medimmune, Pfizer, Roche, Sanofi, UCB

DOI: 10.1136/annrheumdis-2017-eular.3906

THU0439 MORE OBESITY AND HIGHER SERUM URIC ACID IN EARLY-ONSET GOUT PATIENTS IN SOUTH CHINA

Q.-H. Li[1], L.-X. Chen[2], Y.-H. Li[1], D.-H. Zheng[1], Y.-Q. Mo[1], L. Dai[1], J.-J. Liang[1], X.-N. Wei[1]. *[1]Department of Rheumatology; [2]Department of Internal Medecine, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China*

Background: Gout incidence increases in a linear fashion with age until 70 years. It was reported that there was a trend of earlier gout onset. Few studies about clinical features of early-onset gout in China are reported.

Objectives: To investigate the characteristics of early-onset gout in south China.

Methods: Patients with primary gout were recruited between June 2012 and December 2016. Face to face interview was carried out to collect demographic information, clinical characteristics of gout and comorbid diseases. The patients with gout onset before age 30 were defined as early-onset group. The other gout patients were enrolled as control group.

Results: (1) Five hundred and one gout patients were recruited, including 99 (19.8%) in the early-onset group and 402 (80.2%) in the control group. The onset age of the early-onset group was 24.2±5.8 (range 14–30) and the control group was 51.7±13.9 (range 31–84). There was no significant difference of gout duration between early-onset group and control group (P<0.05, Table 1). (2) Compared with the control group, the early-onset group presented lower frequency of flare in last year, higher serum uric acid and higher proportion of sUA>10mg/dl (P<0.05, Table 1). Body mass index (BMI) and prevalence of obesity were higher in the early-onset group (P<0.05, Table 1). The early-onset group exhibited lower prevalence of hypertension, diabetic mellitus, urolithiasis and chronic kidney disease (CKD) (P<0.05, Table 1). (3) There were 20 patients (20.2%) with tophi in the early-onset group. Compared with the 79 early-onset gout patients without tophi, the patients with tophi presented higher age (39.6±8.9 VS 29.1±6.2, P<0.001), duration of gout (12.6±4.8 VS 4.5±4.8, P<0.001), number of involved joints (12.5±9.3 VS 4.3±3.7, P<0.001) and prevalence of CKD (30.0% VS 10.1%, P=0.034), and lower BMI (23.7±3.7 VS 26.6±4.1 kg/m^2, P=0.004). Logistic regression demonstrated that higher disease duration [OR 1.30, 95% CI (1.15, 1.46), P<0.001] and lower BMI [OR 0.80, 95% CI (0.67, 0.96), P=0.015] were associated with tophi in the early-onset gout patients.

Table 1. Comparison of variables between early-onset group and control group

	Early-onset group (N=99)	Control group (N=402)	P
Age, years	30.4±8.2	57.9±13.5	<0.001
Female, %	1.0%	12.7%	<0.001
Age of onset, years	24.2±5.8	51.7±13.9	<0.001
Duration of gout, years	6.2±5.8	6.2±5.6	0.953
Frequency of flare in last year	6.4±7.5	9.3±10.9	0.022
sUA, mg/dl	10.6±2.4	8.9±2.5	<0.001
>10mg/dl, %	59.6%	32.8%	<0.001
No. of involved joints	5.9±6.0	5.9±5.5	0.981
Tophi, %	20.2%	26.1%	0.397
Alcohol overuse, %	35.4%	34.1%	0.811
BMI, kg/m^2	26.1±4.2	24.8±3.9	0.004
Obesity, %	27.3%	15.5%	0.005
Dyslipidemia, %	51.5%	54.0%	0.666
Hypertension, %	14.1%	44.0%	<0.001
DM, %	6.1%	24.6%	<0.001
Urolithiasis, %	19.2%	33.6%	0.007
eGFR, ml/min/1.73m^2	84.8±51.0	62.9±19.7	<0.001
CKD, %	14.1%	45.6%	<0.001

sUA: serum uric acid; BMI: body mass index; DM: diabetic mellitus; eGFR: estimated glomerular filtration rate; CKD: chronic kidney disease.

Conclusions: Early-onset gout exhibited higher sUA and was associated with obesity but not with hypertension, diabetic mellitus and renal insufficiency. Longer disease duration and lower BMI were associated with tophi in the early-onset gout patients.

Acknowledgements: The present study was supported by Guangdong Natural Science Foundation, China (Grant no. 2014A030310086) to Qian-Hua Li.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6307

THU0440 TEMPORAL TRENDS OF VENOUS THROMBOEMBOLISM RISK BEFORE AND AFTER DIAGNOSIS OF GOUT. A GENERAL POPULATION-BASED STUDY

L. Li[1,2], N. McCormick[1,2], E.C. Sayre[1], J. Esdaile[1,2], D. Lacaille[1,2], H. Xie[1,3], H.K. Choi[1,4], J.A. Avina-Zubieta[1,2]. *[1]Arthritis Research Canada, Richmond; [2]The University of British Columbia, Vancouver; [3]Simon Fraser University, Burnaby, Canada; [4]Harvard Medical School, Boston, United States*

Background: Data on the risk of venous thromboembolism (VTE, including deep venous thrombosis and pulmonary embolism) in patients with gout are scarce.

Objectives: 1) To estimate the overall risk of VTE in an incident gout cohort; 2) To estimate the temporal trends of VTE before and after gout diagnosis compared with the general population.

Methods: We conducted a matched cohort study using a population based administrative health database that includes all outpatient visits, hospital admissions, vital statistics, and dispensed medications for all residents in British Columbia, Canada. Gout cases were defined using one ICD-9/10 code (274/M10) from a

physician or hospital visit. To ensure incident gout, we required that all cases have ≥10 years of prior registration without a gout diagnosis. Gout cases were matched 1:1 with controls on age, sex, and cohort entry time. Prior VTE events were excluded after matching. VTE was defined using ICD-9/ICD-10 codes plus use of oral anti-coagulant. We calculated incidence rate ratios (IRRs) and age, sex, and entry time matched multivariable hazard ratios (HRs) for the risk of VTE. Sensitivity analyses were conducted to assess for unmeasured confounders (e.g., obesity).

Results: Among 105,307 individuals with newly diagnosed gout (61% male, mean age of 58 yrs), we observed 1,212 VTE events (mean follow-up time of 5.3 yrs). The fully adjusted HR was 1.27 (95% CI, 1.16–1.39) (Table 1). Our results remained significant in the sensitivity analyses (OR of 2.0 between gout and unmeasured confounder and a 50% prevalence for obesity). There were 437 incident VTE events within 3 yrs prior to the gout diagnosis. Compared to controls, during the 3rd, 2nd, and 1st yrs before gout diagnosis, the fully adjusted HRs for VTE in patients with imminent gout were 1.51, 1.58 and 1.73. The corresponding HRs in the 1st, 2nd, 3rd, 4th, and 5th yrs after gout diagnosis were 1.54, 1.39, 1.38, 1.37, and 1.32, respectively.

Table 1

	Gout (N)	Control (N)	No. of VTE events		IRRs (95% CI)	Age-, sex-adjusted (95% CI)	Fully adjusted* (95% CI)
			Gout	Control			
Before gout diagnosis							
-3yrs	105,744	106,219	437	254	1.73 (1.48,2.03)	1.68 (1.44,1.96)	1.51 (1.29,1.77)
-2yrs	105,638	106,146	331	181	1.84 (1.53,2.22)	1.78 (1.49,2.14)	1.58 (1.31,1.90)
-1yr	105,493	106,055	186	90	2.08 (1.61,2.70)	2.01 (1.56,2.58)	1.73 (1.34,2.24)
After gout diagnosis							
1yr	105,307	105,965	229	116	1.99 (1.58,2.51)	1.92 (1.54,2.40)	1.54 (1.22,1.94)
2yrs	105,307	105,965	390	234	1.68 (1.43,1.99)	1.63 (1.39,1.92)	1.39 (1.18,1.64)
3yrs	105,307	105,965	540	331	1.65 (1.43,1.89)	1.60 (1.39,1.83)	1.38 (1.20,1.59)
4yrs	105,307	105,965	667	414	1.63 (1.44,1.85)	1.58 (1.40,1.79)	1.37 (1.21,1.56)
5yrs	105,307	105,965	775	506	1.55 (1.38,1.74)	1.51 (1.35,1.68)	1.32 (1.18,1.49)
Overall	105,307	105,965	1,212	858	1.44 (1.32,1.57)	1.40 (1.29,1.53)	1.27 (1.16,1.39)

*Adjusted for Charlson comorbidity index, cancer, alcoholism, hypertension, sepsis, trauma, healthcare utilization, NSAIDs, HRT, glucocorticoid and fractures, surgery within 1 year before entry cohort.

Conclusions: Patients with gout have an increased risk of VTE. The risk increases gradually before gout diagnosis, peaks in the year prior to gout diagnosis, and then progressively declines. Our findings suggest that hyperuricemia or gout associated inflammation may be a contributing factor for VTE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4146

THU0441 SYNOVIAL FLUID LEUKOCYTE COUNT AND ITS ASSOCIATION WITH CRYSTAL DEPOSITION IN ASYMPTOMATIC HYPERURICEMIA: A PRELIMINARY REPORT

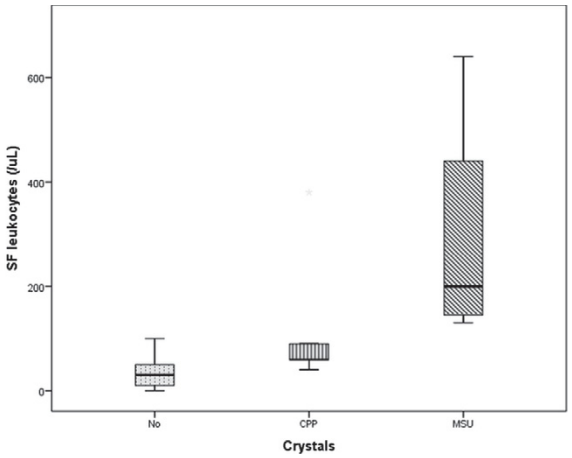
M. Andrés[1,2], J.A. Bernal[2], M.D. Arenas[3], E. Pascual[2,4]. *[1]Departamento de Medicina Clínica, Universidad Miguel Hernández; [2]Seccion de Reumatologia, Hospital General Universitario de Alicante; [3]Unidad de Nefrología, Hospital Vithas Perpetuo Socorro; [4]Emeritus Professor, Universidad Miguel Hernández, Alicante, Spain*

Background: Joint deposits of monosodium urate (MSU) crystals in asymptomatic hyperuricemia (AH) may associate with more severe forms of atherosclerosis [1]. It likely relates with crystal-driven subclinical inflammation, a phenomenon well described in gout [2] but to date not assessed in AH.

Objectives: To assess the synovial fluid (SF) leukocytes count in patients with AH depending on the presence of crystals.

Methods: Consecutive patients with AH were selected from nephrology clinics. Hyperuricemia threshold was established at serum uric acid (SUA) ≥7mg/dL; those on current urate-lowering therapy were excluded. Ultrasound (US) of knees, ankles and first metatarsophalangeal joints was performed blinded to clinical and laboratory data, in order to perform US-guided aspiration and obtain SF samples. These samples were analyzed in fresh by two observers, using a compensated polarized light microscope equipped with two viewing stations. The second observer was in addition unaware of US findings. The presence of leukocytes and crystals was established by consensus. SF leukocyte count was performed using a Neubauer counting camera. Mann-Whitney's U and Kruskal-Wallis' H were used to compare difference in leukocyte counts between groups.

Results: To end of January 2017, 30 patients have been assessed, with SF samples available from 27 (three showed no joint effusion at US). Median age was 70 years (p25–75 59.8–75.5), and 16 of them (60%) were males. Median (p25–75) SUA and estimated glomerular filtration rate were 8.1 mg/dL (7.6–8.5) and 37.0 mL/min (31.0–47.5), respectively. Seven (25%) were on diuretics. After microscopy evaluation, MSU crystals were found in four patients (14.8%), calcium pyrophosphate (CPP) crystals in five (18.5%), and no crystals in 18 (66.7%). Figure shows median leukocytes count according to crystal group: 200/mm^3 (138–540) in MSU group; 60/mm^3 (50–235) in CPP group; and 30/mm^3 (10–53) in those with no crystal at SF. A statistically significant difference was found between the three groups (p=0.001), and comparing MSU crystals and no crystals groups (p<0.001); no difference was found between MSU and CPP groups (p=0.111).



Conclusions: In a preliminary report, MSU crystal deposition in patients with AH leads to higher SF leukocyte count, indicating low-grade inflammation. Despite low numbers and being an ongoing study, this significant finding might contribute to explain the severe atherosclerosis data recently reported in AH patients with silent crystal deposits.

References:

[1] Arthritis Rheumatol 2016;68:1531.
[2] Arthritis Rheum 1991;34:141.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3258

THU0442 EHEALTH SUPPORTED COLLABORATIVE CARE MODEL FOR GOUT INVOLVING RHEUMATOLOGY, PHARMACY, AND DIETETICS: PROOF-OF-CONCEPT OBSERVATIONAL STUDY

M.A. De Vera[1,2], A. Howren[1], N. Tsao[1], H. Choi[3], A. Kydd[4], R. Friesen[5], K. Shojania[2,4]. *[1]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver; [2]Arthritis Research Canada, Richmond, Canada; [3]Department of Medicine, Massachusetts General Hospital, Boston, United States; [4]Division of Rheumatology, University of British Columbia; [5]Providence Health, Vancouver, Canada*

Background: Sub-optimal quality of care for gout, the most common inflammatory arthritis, has called for novel models to improve care and outcomes of patients.

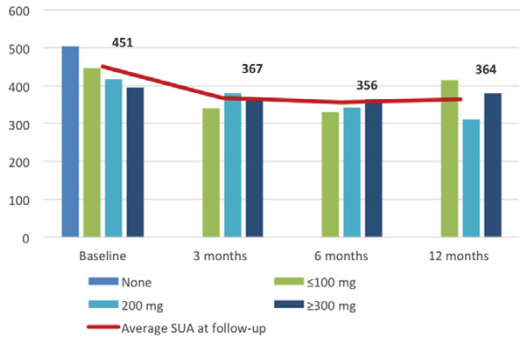
Objectives: Our objective was to evaluate the feasibility of the "Virtual Gout Clinic Study" (VGCS) a collaborative approach to gout management involving rheumatology, pharmacy, and dietetics that take advantage of eHealth, namely, shared access of electronic medical records (EMRs), to support this unique, decentralized model of care.

Methods: *Design:* We conducted a 1-year, proof-of-concept, longitudinal observational study with a target of 30 patients. *Eligibility:* Patients with gout were eligible if they were: 1) seen in 1 of 4 rheumatology practices with 8 rheumatologists participating across British Columbia, Canada; 2) experienced ≥1 flare in the past year; 3) have a serum uric acid (SUA) level ≥360 μmol/L within the previous 2 months. *Follow-up:* Within the *VGCS*, patients receive follow-up with their rheumatologist on an as needed-basis, monthly telephone consults from the study pharmacist, and 1 telephone consult with the dietician. In this decentralized model of care, health care professionals are not co-located but have access to the patient's EMR to facilitate remote communication and collaboration. *Outcomes:* Prospective data was collected at baseline, 3, 6, and 12 months. The primary outcome measure was SUA at 12-months, specifically below recommended target level of 360 μmol/L. Secondary outcomes included patient reported outcome measures including the Compliance Questionnaire Rheumatology, Health Assessment Questionnaire Disability Index, and EQ-5D, as well as information on interventions provided within the *VGCS*.

Results: Overall, 33 individuals with gout participated in the *VGCS*. There were 22 males (88%) and mean age was 60.8±15.3 years. 29, 28, and 25 patients have completed follow-up at 3, 6, and 12 months respectively. At baseline, 22 (67%) patients were prescribed urate-lowering therapy (ULT; 21 with allopurinol and 1 with febuxostat). The remaining 11 patients initiated ULT during the study period. Figure 1 shows mean SUA decreased over baseline, 3, 6, and 12 months from 451 μmol/L, 367 μmol/L, 356 μmol/L, and 364 μmol/L, respectively, with 67% of patients having SUA <360 μmol/L at 12 months. A total of 126 pharmacist and 24 dietician consults have been provided. Pharmacist interventions included: uptritration of allopurinol dosage for 15 patients, restarting of ULT for 4 non-adherent patients, discontinuation of unnecessary medications for 12 patients, and renewals of prescription medications using solely electronic communications for 4 patients.

Conclusions: These findings provide evidence for the feasibility and effectiveness of the *VGCS*. With respect to feasibility, we successfully established the shared EMR framework between rheumatologists and study pharmacist and dietitian and demonstrated utility with respect to facilitating communication and collaborative

Figure 1. SUA according to allopurinol dose (baseline to 12 months)



care between health care providers and providing outcomes data. With respect to effectiveness, findings show declining SUA over follow-up with over two-thirds of patients achieving target at the end of follow-up.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4177

THU0443 HYPERURICEMIA IS ASSOCIATED WITH INCREASED CORONARY ARTERY CALCIFICATION IN MEN BUT NOT WOMEN

M.I. Dehlin[1], P. Drivelegka[1], V. Sigurdardottir[1], O. Angerås[2], L.T. Jacobsson[1], H. Forsblad d'Elia[1,3]. *[1]Dept of rheumatology and inflammation research, Institution of medicine, Sahlgrenska Academy, University of Gothenburg; [2]Department of Cardiology, Sahlgrenska University Hospital, Gothenburg; [3]Departments of Public Health and Clinical Medicine, Rheumatology, Umeå University, Umeå, Sweden*

Background: Hyperuricemia is closely associated to cardiovascular disease although it has not been defintively established whether it is a marker or a causative agent. Serum uric acid (sUa) is strongly linked to the metabolic syndrome, hypertension (HT), dyslipidemia (DL) and higher BMI and higher levels are seen in men compared to women. Coronary artery calcification (CAC) is associated with future risk of atherosclerotic CV events in addition to these traditional cardiovascular risk factors (CVRF). CACs are present in atherosclerotic arteries and can be quantified and scored non-invasively by computed tomography. The Swedish CArdioPulmonarybioImage Study (SCAPIS) extensively characterizes a Swedish cohort of 30 000 men and women aged between 50 and 64 years. A comprehensive pilot study in 1111 individuals was completed in 2012. In this pilot study we have examined the relation between CACs and sUa

Objectives: Examine the association bewteen sUa and CAC in men and women seperately.

Methods: In the SCAPIS pilot study we identified 1106 (552 males) individuals who were screened for traditional CVDRFs, such as HT, DL, diabetes mellitus (DM), smoking, physical activity (PA), educational level (EDU), BMI, high sensitive CRP (hsCRP). CACs, reflecting calcification of coronary arteries, was determined according to Agatston[1]. We measured sUa and related quartiles to CACs with multiple logistic regression analyses adjusting for traditional CVDRFs. CAC was defined positive if ≥1.

Table 1. Baseline characteristics of the study population divided by sex

Variables	Male, n=552	Female, n=556
Age, years, mean, (SD)	57.8 (4.5)	57.6 (4.3)
BMI, mean, (SD)	27.7 (4.0)	26.9 (3.7)
hsCRP, (mean, SD)	2.3 (3.3)	2.4 (3.7)
CAC positive, (%)	305 (55%)	142 (26%)
Smoking status, never	226 (41%)	249 (45%)
Smoking status, previous	242 (44%)	222 (40%)
Smoking status, active	82 (15%)	81 (15%)
Hypertension (%)	178 (32%)	190 (34%)
Diabetetes mellitus (%)	45 (8%)	23 (4%)
Dyslipidemia (%)	160 (29%)	128 (23%)

Table 2. Quartiles of sUa and age as predictors for presence of CAC (>0 CACs score) in male and female in multivariate logistic regression analyses adjusted for age, smoking, BMI, DM, DL, HT, hsCRP, EDU and PA

sUa, μmol/L,	Male		sUa, μmol/L,	Female	
	Odds ratio, multivariate*, (CI)	p-value		Odds ratio, multivariate*, (CI)	p-value
31–305, Ref			143–229, Ref		
306–350	2.1 (1.2–3.7)	0.01	230–262	0.9 (0.5–1.7)	0.7
351–404	1.8 (1–3.3)	0.04	263–305	1 (0.5–2)	0.9
405–665	2 (1–3.8)	0.04	306–702	1.2 (0.6–2.3)	0.6
Age 50–55, Ref					
Age 56–60	2.2 (1.4–3.6)	0.001		3.6 (2–6.5)	<0.0001
Age 61–66	3.8 (2.2–6.3)	<0.0001		4.3 (2.4–7.9)	<0.0001

Results: Age, BMI, smoking status, hsCRP, HT and DL showed no differences between sex while presence of CAC and diabetes was twice as common in men (Table 1). The three upper quartiles of sUa, (>306 μmol/L), all significantly ($p<0.05$) predicted presence of CACs in men even adjusting for HT, DL, DM, smoking, PA, EDU, BMI, hsCRP and age in multivariate logistic regression, but not in women (Table 2).

Conclusions: Higher levels of sUa is associated with presence of CACs in men but not in women. This may merely reflect the earlier onset of atherosclerosis in men or possibly suggest biological differences in the effect of sUa on calcification of coronary arteries between sexes.

References:

[1] Agatston AS et al Quantification of coronary artery calcium using ultrafast computed tomography J Am Coll Cardiol 1990.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2714

THU0444 INTEGRATED SAFETY OF LESINURAD, A NOVEL URIC ACID REABSORPTION INHIBITOR FOR THE TREATMENT OF GOUT

M.A. Becker[1], R.T. Keenan[2], P.P. Khanna[3], R. Malamet[4], K. Bos[4], J. Li[4], J. Hu[5], W.B. White[6]. *[1]University of Chicago, Chicago; [2]Duke University School of Medicine, Durham; [3]University of Michigan, Ann Arbor; [4]AstraZeneca Pharmaceuticals, Wilmington; [5]Formerly Ardea Biosciences, Inc, San Diego; [6]University of Connecticut School of Medicine, Farmington, United States*

Background: Lesinurad is a selective uric acid reabsorption inhibitor recently approved at 200 mg daily in combination with a xanthine oxidase inhibitor (XOI) for treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid on an XOI (allopurinol or febuxostat) alone.

Objectives: To investigate the safety profile of lesinurad (LESU), we integrated safety data based on: (1) 3 large, pivotal, placebo-controlled, 12-month phase III (core) trials evaluating LESU 200 mg and LESU 400 mg in combination with an XOI; and (2) 2 extension studies, in which LESU-treated patients continued to receive LESU + XOI at the same dose and initially placebo-treated patients were randomized to receive LESU 200 mg or LESU 400 mg in addition to the XOI provided in the preceding core trial.

Methods: Safety data were pooled from the 3 core studies and 2 12-month extension studies using descriptive statistics for patients receiving ≥1 dose of study medication. To adjust for varying treatment durations, treatment-emergent adverse events (TEAEs) are expressed as exposure-adjusted incidence rates (number of subjects with events per 100 person-years [PY]).

Results: In the core studies, adverse event rates were comparable for XOI alone and LESU 200 mg + XOI groups for any TEAEs, serious TEAEs, and TEAEs leading to discontinuation (Table 1). Adverse event rates were higher with LESU 400 mg + XOI. Major adverse cardiovascular event (MACE) rates, which included cardiovascular death, myocardial infarction, or stroke, in the core studies were 0.71 (95% CI 0.15, 2.08), 0.96 (0.26, 2.47), and 1.94 (0.84, 3.82) per 100 PY for XOI

Table 1. Pooled Analysis of Exposure-Adjusted Adverse Event Incidence Rates in 3 Pivotal Placebo-Controlled 12-Month Phase III Studies Evaluating Lesinurad 200 mg and 400 mg in Combination with Xanthine Oxidase Inhibitors

Adverse Event Category [n (rate)]	XOI alone (N=516) (PY=408.5)	LESU 200 mg + XOI (N=511) (PY=396.3)	LESU 400 mg + XOI (N=510) (PY=390.5)
Any TEAE	363 (88.9)	386 (97.4)	407 (104.2)
Any TEAE with RCTC toxicity Grade 3 or 4	48 (11.8)	52 (13.1)	67 (17.2)
Any TEAE possibly related to randomized study medication	80 (19.6)	98 (24.7)	118 (30.2)
Any TEAE possibly related to XOI	52 (12.7)	49 (12.4)	66 (16.9)
Any TEAE possibly related to prophylaxis	52 (12.7)	56 (14.1)	61 (15.6)
Any serious TEAE	29 (7.1)	24 (6.1)	44 (11.3)
Any fatal TEAE	0 (0)	2 (0.5)	3 (0.8)
Any TEAE leading to randomized study medication discontinuation	28 (6.9)	32 (8.1)	48 (12.3)

Table 2. Pooled Analysis of Exposure-Adjusted Adverse Event Incidence Rates in 3 Pivotal Placebo-Controlled 12-Month Phase III Studies + 2 Extension Studies Evaluating Lesinurad 200 mg and 400 mg in Combination with Xanthine Oxidase Inhibitors

Adverse Event Category [n (rate)]	LESU 200 mg + XOI (N=666) (PY=926.5)	LESU 400 mg + XOI (N=666) (PY=917.9)
Any TEAE	531 (57.3)	552 (60.1)
Any TEAE with RCTC toxicity Grade 3 or 4	93 (10.0)	115 (12.5)
Any TEAE possibly related to randomized study medication	158 (17.1)	187 (20.4)
Any TEAE possibly related to XOI	77 (8.3)	101 (11.0)
Any TEAE possibly related to prophylaxis	76 (8.2)	81 (8.8)
Any serious TEAE	63 (6.8)	84 (9.2)
Any fatal TEAE	7 (0.8)	7 (0.8)
Any TEAE leading to randomized study medication discontinuation	68 (7.3)	86 (9.4)

LESU, lesinurad; PY, patient years; RCTC, Rheumatology Common Toxicity Criteria; TEAE, treatment-emergent adverse event; XOI, xanthine oxidase inhibitor. Exposure-adjusted incidence rates are expressed as subjects with events per 100 person-years.

alone, LESU 200 mg + XOI, and LESU 400 mg + XOI, respectively. Renal-related TEAE rates in the core studies were 5.6, 7.3, and 15.4 per 100 PY, respectively. Longer exposure in the core + extension studies did not result in increases in any TEAEs, serious TEAEs, or TEAEs leading to discontinuation (Table 2). MACE rates were low in the core + extension studies, at 1.05 (95% CI 0.50, 1.93) and 1.48 (0.81, 2.48) in the LESU 200 mg + XOI and LESU 400 mg + XOI groups, respectively. Renal events in the core + extension studies were lower in the LESU 200 mg + XOI than LESU 400 mg + XOI group at 8.6 and 14.6, respectively.

Conclusions: Lesinurad at the approved dose of 200 mg once daily demonstrated a consistent, acceptable safety profile. There were no new safety concerns in the extension studies.

Acknowledgements: This study was funded by Ardea Biosciences/AstraZeneca.

Disclosure of Interest: M. Becker Grant/research support from: Takeda, Savient, Ardea/AstraZeneca, Consultant for: Takeda, Savient, Horizon, Ardea/AstraZeneca, CymaBay, Pfizer, R. Keenan Consultant for: AstraZeneca, Ironwood, Horizon, P. Khanna Grant/research support from: AstraZeneca, R. Malamet Employee of: AstraZeneca, K. Bos Employee of: AstraZeneca, J. Li Employee of: AstraZeneca, J. Hu Employee of: Ardea Biosciences, W. White Consultant for: AstraZeneca

DOI: 10.1136/annrheumdis-2017-eular.3674

THU0445 GOUTY ARTHRITIS: DECISION MAKING FOLLOWING DUAL ENERGY CT SCAN IN CLINICAL PRACTICE, A RETROSPECTIVE ANALYSIS

M. Gamala[1], S. Linn-Rasker[2], M. Nix[2], B. Heggelman[2], J. van Laar[1], P. Pasker-de Jong[2], J. Jacobs[1], R. Klaasen[2]. *[1]University Medical Center, Utrecht; [2]Meander Medical Centre, Amersfoort, Netherlands*

Background: Gout is associated with joint damage, and increased cardiovascular morbidity; it is important to diagnose and treat it. However, although clinical presentation may be strongly suggestive of gout, joint aspiration and microscopy not always yield the diagnosis. The latest technique to visualize monosodium uric acid MSU depositions and thus to diagnose gout is Dual Energy CT scan (DECT).[1]

Objectives: To establish whether DECT is a diagnostic tool, i.e. associated with initiation or discontinuation of a urate lowering drug (ULD). Second, whether DECT results (gout deposition y/n) can be predicted by clinical and laboratory variables.

Methods: Digital medical records of 147 consecutive patients with clinical suspicion of gout at the outpatient clinic of the Department of Rheumatology of Meander Medical Centre, Amersfoort, the Netherlands who underwent DECT between January 1, 2013 and December 31, 2014 were analyzed retrospectively. Collected were clinical data including medication before and after DECT, lab results, and results from diagnostic joint aspiration and DECT. The relationship between DECT results and clinica, and laboratory results was evaluated by univariate regression analyses; predictors showing a $p<0.10$ were entered in a multivariate logistic regression model with the DECT result as outcome variable. A manual backward stepwise technique was applied.

Results: 87 patients were diagnosed with gout based on demonstration of MSU crystals in synovial fluid (SF) or positive DECT result. In 30 patients, DECT was the only conformation of gout; in 29 of them ULD was started and in 1 it was intensified. Following DECT, the current ULD was stopped in 3 patients. The clinical and laboratory variables associated with the DECT result are presented in table 1. In the multivariable regression model, cardiovascular disease y/n (OR 3.07, 95% CI 1.26–7.47), disease duration in years (OR 1.008, 95% CI 1.001–1.016), frequency of attack per year (OR 1.23, 95% CI 1.07–1.42), creatinine clearance in ml/min (OR 2.03, 95% CI 0.91–1.00) were independently associated with positive DECT results.

Table 1. Univariate model analyses of predictors of positive DECT results

	OR (95% CI)	p
Gender (reference: male gender)	0.48 (0.24–0.99)	0.04
Body Mass Index (per kg/m^2)	1.03 (0.96–1.11)	0.36
Cardiovascular disease yes/no	2.72 (1.36–5.42)	0.04
Diabetes mellitus yes/no	3.69 (1.26–10.71)	0.01
Urate lowering therapy use at the moment of DECT yes/no	2.6 (1.15–6.28)	0.02
Disease duration years	1.01 (1.005–1.02)	0.01
Frequency of attacks per year	1.2 (1.08–1.33)	0.01
Uric acid levels between flares (per μmol/L)	1.004 (1.001–1.007)	0.008
Creatinine clearance (per ml/min)	0.95 (0.92–0.99)	0.01
Joint involvement at the moment of DECT: MTP1 or other joints	1.69 (1.05–3.37)	0.1
Past first metatarsophalangeal (MTP1) joint involvement yes/no	3.37 (1.69–6.72)	0.01
MSU crystals at microscopy yes/no	1.62 (1.23–2.17)	0.001

Conclusions: DECT has impact on clinical decisions on ULD therapy. It may be a useful diagnostic imaging tool for patients who cannot undergo joint aspiration because of contraindications or with difficult to aspirate joints, or those who refuse joint aspiration.

References:

[1] Choi HK et al. Dual energy CT in gout: a prospectieve validation study. Ann Rheum Dis 2012; 71:1466–71.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1881

THU0446 PREVALENCE AND INCIDENCE OF NON-GOUT CRYSTAL ARTHROPATHY IN SOUTHERN SWEDEN FROM THE SOCIOECONOMIC PERSPECTIVE

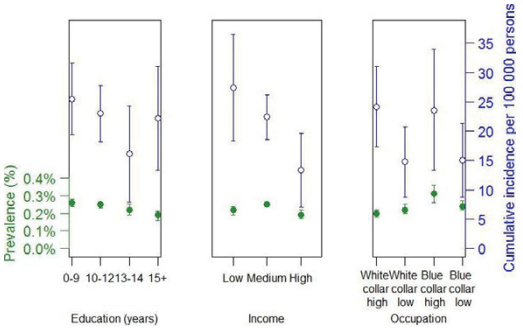
M. Hameed[1], A. Turkiewicz[2], T. Saxne[3], L. Jacobsson[4], M. Englund[5], M.C. Kapetanovic[6]. *[1]Department of Clinical Sciences, Lund, Section for Rheumatology, Lund University, Lund and Skåne University Hospital, Section for Rheumatology in Lund and Malmö, Sweden, Malmö; [2]Lund University, Faculty of Medicine, Department of Clinical Sciences Lund, Orthopedics, Clinical Epidemiology Unit, Lund, Sweden; [3]Department of Clinical Sciences, Lund, Section for Rheumatology, Lund University, Lund, Section for Rheumatology in Lund and Malmö, Lund; [4]Department of Rheumatology & Inflammation Research, Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Gothenburg; [5]Lund University, Faculty of Medicine, Department of Clinical Sciences Lund, Orthopedics, Clinical Epidemiology Unit; [6]Department of Clinical Sciences, Lund, Section for Rheumatology, Lund University, Lund and Skåne University Hospital, Section for Rheumatology in Lund and Malmö, Sweden, Lund, Sweden*

Background: Recently, we reported the prevalence of gout to be 1.7% among adults in the Skåne region in southern Sweden (1). Few epidemiological data are available on non-gout crystal arthropathy and none for this region.

Objectives: The objective of this study was to study the prevalence and incidence of non-gout crystal arthropathy (including chondocalcinosis, acute/subacute/chronic calcium pyrophosphate/hydroxyapatite or other crystal deposition disease) in southern Sweden from the socioeconomic perspective.

Methods: The Skåne Healthcare Register includes information on all health care visits with given ICD10-coded diagnoses for all citizens in the region (total population 1.3 million). SHR was searched for all adult (≥18 years) residents in Skåne region in year 2014, who between 1998 and 2014 had received at least one diagnosis of non-gout crystal arthropathy (ICD-10 code M11.0- M11.9) by any physician. The crude point prevalence at December 31st 2014 and the cumulative incidence in the calendar year 2014 were calculated. In addition, we examined the 2014 age- and sex- standardized point prevalence and cumulative incidence of non-gout crystal arthropathy according to occupation (white collar /blue collar with high or low skilled occupations), income (low/middle/high) and level of education (primary school/high school/university).

Results: The crude 2014 point prevalence and 2014 cumulative incidence (95% CI) of non-gout crystal arthropathy were 0.23% (0.22% - 0.24%) and 21.5 (18.6–24.3) cases per 100 000 persons at risk, respectively. Compared to women, men had numerically but not significantly higher prevalence (0.26% vs 0.20%) and incidence (24.6 vs 18.5 per 100 000 persons). This pattern remained regardless of age. The mean (SD) age of a person with prevalent non-gout crystal arthropathy was 71.5 (14.4) years. Both prevalence and incidence increased with increasing age and were highest in individuals ≥85 years (prevalence 1.4%), but decreased with years of education. Persons with middle income and blue collar high skilled occupation (e.g. skilled agricultural, forestry and fishery workers and craft and related trades workers) had the highest point prevalence and incidence of non-gout crystal arthroplasty (figure).



Conclusions: Although considerably less prevalent than gout in southern Sweden non-gout crystal arthropathy affects about 0.2% of the adult population, i.e. a similar prevalence as for psoriatic arthritis in the same region. The prevalence increases with age and is highest among individuals aged 85 years or higher. There is a socioeconomic gradient with more affected individuals among people with lower level of education, middle income, and more manual work.

References:

[1] Kapetanovic MC, Hameed M, Turkiewicz A, at al. Prevalence and incidence of gout in southern Sweden from the socioeconomic perspective. RMD Open. 2016 Nov 1;2(2):e000326. eCollection 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3089

THU0447 CO-MORBID GOUT IS ASSOCIATED WITH INCREASED CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH TYPE 2 DIABETES, BUT NOT CARDIOVASCULAR EVENTS OR MORTALITY

M. Mian[1], S.K. Patel[2], B. Wai[1], P.M. Srivastava[1], R.R.C. Buchanan[1,2], L.M. Burrell[1,2]. *[1]Department of Medicine, Austin Health; [2]Department of Medicine, University of Melbourne, Melbourne, Australia*

Background: Gout is an inflammatory arthropathy characterised by elevated serum uric acid levels. In Australia, gout has a prevalence of 1.7 - 4%.[1] This increased to ~10% in community based Australian patients with type 2 diabetes, although elevated serum uric acid did not predict cardiovascular (CV) or all-cause mortality.[2] To date, the long-term outcomes of patients with diabetes and comorbid gout being followed up in the hospital out-patient setting have not been studied.
Objectives: To compare cardiovascular risk factors and long-term outcomes and mortality in patients with type 2 diabetes according to the presence or absence of gout.
Methods: 1,405 patients with type 2 diabetes were prospectively recruited from the outpatient setting at Austin Hospital. Baseline cardiovascular risk factors and comorbidities were identified. Patients were classified as having gout if they gave a history of gout or were taking medication for the treatment of gout. For statistical analysis, patients with diabetes (Group 1) were compared to those with diabetes and gout (Group 2). Cardiovascular events and long-term CV mortality were assessed over a 10 year period.
Results: There were 1,329 patients with diabetes (Group 1; 95%) and 76 with diabetes and gout (Group 2; 5%). Patients with gout were older (68±11 vs. 64±12y, p=0.004), more likely to be male (80% vs. 59%, p<0.0001), with higher triglyceride levels (2.6 vs 1.9 mmol/L, p=0.002), lower HDL (1.05 vs. 1.24 mmol/L, p<0.0001), higher BMI (33 vs. 31, p=0.026), and were more likely to have nephropathy (55% (n=35) vs. 26% (n=311), p<0.0001) with increased albumin creatinine ratio (3.4 vs 1.8 g/mmol, p=0.002). Despite the worse cardiovascular risk profile in those with gout and diabetes, cardiovascular events and all-cause mortality were not significantly different between the groups (Group 1, 27% (n=333) vs. 35% (n=23) in Group 2, p=0.201).
Conclusions: Although patients with comorbid gout and type 2 diabetes have a worse cardiovascular risk factor profile compared to those with diabetes alone, this was not associated with increased cardiovascular morbidity or all-cause mortality. These results suggest that elevated uric acid and gout are markers rather than determinants of CV mortality.
References:
[1] Robinson PC, Taylor WJ, Merriman TR. Systemic review of the prevalence of gout and hyperuricaemia in Australia. Internal Med J 2012; 42(9):997–1007.
[2] Ong G, Davis WA, Davis TME. Serum uric acid does not predict cardiovascular or all-cause mortality in type 2 diabetes: the Fremantle Diabetes Study. Diabetologia 2010; 53: 1288–129.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3596

THU0448 CHARACTERIZATION OF PATIENTS WITH CHRONIC REFRACTORY GOUT WHO DO AND DO NOT HAVE CLINICALLY APPARENT TOPHI: RESPONSE TO PEGLOTICASE

N.L. Edwards[1], J. Singh[2], O. Troum[3], A. Yeo[4], P. Lipsky[5]. *[1]Department of Medicine, University of Florida, Gainesville, FL; [2]University of Alabama at Birmingham, Birmingham, AL; [3]Keck School of Medicine, University of Southern California, Los Angeles, CA; [4]Horizon Pharma, Lake Forest, IL; [5]AMPEL BioSolutions, LLC, Charlottesville, VA, United States*

Background: The term "chronic refractory gout" defines a subset of chronic gout patients who are either intolerant of or unresponsive to standard uric acid (UA) lowering therapy (ULT). Subjects (N=85) meeting this definition were enrolled in a study of pegloticase (8 mg every 2 weeks [q2w], the approved dose), a mammalian recombinant uricase conjugated to polyethylene glycol that is approved for the treatment of gout refractory to conventional oral ULT. Of this group of subjects, 73% had clinically apparent tophi, whereas 27% did not.
Objectives: To determine the clinical characteristics and response to pegloticase therapy in patients with chronic refractory gout with and without clinically apparent tophi.
Methods: This analysis used results from two pivotal randomized controlled trials[1] to assess the clinical characteristics and the efficacy of pegloticase (8 mg q2w) in patients with chronic refractory gout with or without tophi at baseline. The results for serum urate (UA), flares, Patient Global Assessment (PGA), tender and swollen joints (TJC and SJC), bodily pain, Health Assessment Questionnaire-Disability Index (HAQ-DI), and the Arthritis-Specific Health Index (ASHI) and Bodily Pain from the Medical Outcomes Study Short Form 36 item (SF-36) were determined for each group.
Results: The analysis included patients with chronic refractory gout, 62 with tophi at baseline and 23 without tophi. Chronic refractory gout patients in the two groups were similar at baseline, with the only significant differences in mean values between tophaceous and nontophaceous gout groups as follows: TJC, 14.2 vs 5.00 (P=0.01); SJC, 10.9 vs 3.4 (P=0.003); ASHI, 50.4 vs 64.7 (P=0.03); and HAQ-DI, 1.3 vs 0.6, respectively (P=0.001). Other measures of disease impact and comorbidities were not significantly different between groups. Treatment with pegloticase 8 mg q2w resulted in significant and comparable reductions in serum UA in both groups. Comparison of results from baseline and after 6 months of treatment for patients with tophi at baseline indicated significant reductions in serum UA (P<0.0001), flares (P<0.0001), PGA (P<0.0001), TJC and SJC (both P<0.0001), HAQ-DI (P=0.02), and SF-36 Bodily Pain (P<0.0001). Results for patients without clinically apparent tophi at baseline indicated significant improvements in serum UA (P<0.0001), flares (P=0.004), PGA (P=0.009), TJC (P=0.01), SJC (P=0.003), SF-36 Bodily Pain (P=0.03), and ASHI (P=0.0001).
Conclusions: These results indicate that chronic refractory gout patients may present with or without clinically apparent tophi. Tophaceous patients are distinguished by more tender and swollen joints, greater disability, and greater arthritis severity, but otherwise are similar to nontophaceous patients. Both groups had significant clinical benefit over 6 months of treatment with pegloticase.
References:
[1] Sundy JS, Baraf HS, Yood RA, et al. JAMA. 2011;306:711–720.
[2] Baraf HS, Becker MA, Gutierrez-Urena SR, et al. Arthritis Res Ther. 2013;15:R137.
Disclosure of Interest: N. L. Edwards Consultant for: AstraZeneca, Horizon Pharma, Ironwood Pharmaceuticals, SOBI International, J. Singh: None declared, O. Troum Shareholder of: Theralogix, Grant/research support from: Abbvie, Amgen, CORONA, Novartis, Pfizer, R-Pharm, Consultant for: Abbvie, Amgen, BMS, Pfizer, Roche, Genentech, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Novartis, Pfizer, Roche, Genentech, A. Yeo Consultant for: Horizon Pharma, P. Lipsky Consultant for: AstraZeneca, Celgene, EMD Serono, GSK, Horizon Pharma, Janssen, Medimmune, Pfizer, Roche, Sanofi, UCB
DOI: 10.1136/annrheumdis-2017-eular.4077

THU0449 EVIDENCE BASED DEVELOPMENT OF CRITERIA FOR COMPLETE RESPONSE IN PATIENTS WITH CHRONIC REFRACTORY GOUT

N. Schlesinger[1], P. Khanna[2], A. Yeo[3], P. Lipsky[4]. *[1]Department of Medicine, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ; [2]Rheumatology, University of Michigan, Ann Arbor, MI; [3]Horizon Pharma, Lake Forest, IL; [4]AMPEL BioSolutions, LLC, Charlottesville, VA, United States*

Background: Preliminary criteria for remission in gout patients have recently been proposed. These include serum urate, acute flares, tophus, pain and patient global assessment.[1] These preliminary criteria were based on consensus exercises and have not yet been tested in a large clinical trial database of chronic gout patients. Because of the availability of clinical results from subjects with chronic refractory gout treated with pegloticase (8 mg every 2 weeks), a mammalian recombinant uricase conjugated to polyethylene glycol that is approved in the US for treatment of adult patients with chronic gout refractory to oral urate lowering therapy[2], the utility of these proposed criteria could be assessed.
Objectives: To test the utility of the preliminary criteria to discern a complete response (CR) in subjects with chronic refractory gout treated with pegloticase (8 mg every 2 weeks).
Methods: Data from two randomized clinical trials (RCT) evaluating the impact of pegloticase therapy in subjects with chronic refractory gout were examined.[2] Of this group of subjects, 42% had persistently lowered serum urate and 58% did not meet the urate-lowering endpoint of this RCT. Initially, individual patient data was reviewed to establish the frequency with which subjects, who were responders to pegloticase, met the proposed remission criteria. Mixed modeling was then employed on data from these subjects to determine the components of the model that best correlated with time of maximum benefit.
Results: Of 34 pegloticase responders, 25 (73.5%) met the published criteria[1] of remission. However, pain assessment was often an outlier; data obtained by visual analogue scale and Medical Outcomes Study Short Form-36 questionnaire often differed. Mixed modeling was, therefore, carried out using the data obtained from the subjects meeting criteria for remission to determine the components that best correlated with time to maximum benefit. Other clinical outcome measures assessed in the clinical trial were also analyzed. Besides serum urate levels in the mixed modeling analysis, the components of response that best correlated with time of maximum benefit included assessment of tophi (analyzed photographically), number of swollen joints, number of tender joints and patient global assessment. Using these criteria, 25 of the responders (73.5%) and 29.4% of the entire pegloticase-treated population met criteria for a CR. The median time to reach a CR was 252 days (range: 126–966 days). Of interest, when a decrease in serum urate was omitted, 6 (12.2%) of the pegloticase nonresponders also met criteria for a CR. Patients receiving placebo did not achieve the composite outcome measure considered as CR.
Conclusions: These results have defined criteria for achieving CR in individuals with chronic refractory gout treated with pegloticase and suggest that most individuals who persistently lowered their serum urate levels while on pegloticase reached criteria for CR in a median of 8.4 months. This composite CR definition can serve as an evidence-based target aiding the design and endpoints of future clinical trials.
References:
[1] deLautour H, Taylor WJ, Adebajo A, et al. Arthritis Care Res. 2016;68:667–672.
[2] Sundy JS, Baraf HSB, Yood RA, et al. JAMA. 2011;306:711–720.
Disclosure of Interest: N. Schlesinger Grant/research support from: As-

traZeneca, Consultant for: Pfizer, AstraZeneca, Proteothera, Celgene, Horizon, P. Khanna Grant/research support from: AstraZeneca, Consultant for: Horizon, Ironwood, Selecta Bio, A. Yeo Consultant for: Horizon Pharma, P. Lipsky Consultant for: AstraZeneca, Celgene, EMD Serono, GSK, Horizon Pharma, Janssen, Medimmune, Pfizer, Roche, Sanofi, UCB
DOI: 10.1136/annrheumdis-2017-eular.4114

THU0450 HOSPITAL READMISSIONS FOR GOUT IN THE UNITED STATES: A NATIONAL DATABASE STUDY

N. Annapureddy[1], A. Saha[2], P. Poojary[3,4], K. Chauhan[4], G. Nadkarni[4].
[1]Division of Rheumatology and Immunology, Vanderbilt University Medical Center, Nashville; [2]Department of Public Health; [3]Department of Public Health; [4]Division of Nephrology, Icahn School of Medicine at Mount Sinai, New York, United States

Background: Gout is associated with significant burden and risk of readmission. Little is known about readmissions among Gout patients on a national level in the United States.
Objectives: The aim of this study was to describe unplanned hospital readmission rates among adult gout patients and assess predictors of readmission.
Methods: We analyzed the 2013 National Readmission Database (NRD) to quantify readmission rates among Gout patients. The NRD includes weighted discharge data from 21 geographically diverse states accounting for 49.3% of the U.S. population. It includes approximately 14 million un-weighted discharges (49.1% of all U.S. discharges) corresponding to 36 million annual discharges nationwide. NRD data is from patients with non-Medicare payers (Medicaid, private, self-pay, or other). Gout hospitalizations were identified using the International Classification of Diseases, ninth Revisions, Clinical Modification (ICD-9-CM) diagnosis code 274.0x. All hospitalizations for patients age $\geq$18 were included. In efforts to exclude routine readmissions, we excluded those admissions related to pregnancy, those for chemotherapy, admissions where the patient was readmitted the same day as they were discharged, who had deaths during the same index hospitalizations, hospitalizations for less than 24 hours, and those with missing discharge. We utilized Chi-square tests, t tests and Wilcoxon rank-sum tests as appropriate. Survey logistic regression was used to assess the relationship between potential predictors for readmissions and the odds of at least one 30-day unplanned readmission. This analysis was chosen given the NRD data, which involves nested, weighted observations that are inherently stratified in clusters to produce national estimates.
Results: A total of 10708 index hospitalizations which had Gout as the primary diagnosis were included in the analysis. Among those with a primary Gout diagnosis, there were 1212 30-days readmissions (11.3%). 14.3% percent of patients with Gout as the primary diagnosis on index hospitalization were readmitted with the same diagnosis. The next most common readmission diagnoses were congestive heart failure (CHF), septicemia, and acute and unspecified renal failure (Figure 1A). In multivariable analysis of index hospitalizations with Gout as the primary diagnosis, CHF (OR 1.25, 95% CI, 1.05–166), chronic kidney disease (CKD) (OR 1.54, 95% CI, 1.23–1.92), atrial fibrillation (AF) (OR 1.33, 95% CI, 1.10–1.78), deep venous thrombosis (DVT) (OR 1.29, 95% CI, 1.03–1.88), APR-DRG severity level 3 and 4 (OR 1.51, 95% CI, 1.01–2.38 and OR 2.10, 95% CI, 1.06–4.58), discharge to specialized care (OR 1.47, 95% CI, 1.07–2.02), discharge to home health care (OR 1.35, 95% CI, 1.03–1.77), and discharge against medical advice (OR 3.85, 95% CI, 1.50–9.91), were significantly associated with 30-days readmission after adjusting for demographics, comorbidities, hospital characteristics, payer type, and the APR-DRG severity scale (Figure 1B).
Conclusions: In a national readmissions database, 11.3% of patients admitted with a primary diagnosis of Gout were readmitted within 30 days. Significant predictors of readmission included CHF, CKD, AF, APR-DRG severity level 3 or 4 and any discharge other than routine.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6468

Figure 1A: Primary causes of Readmission

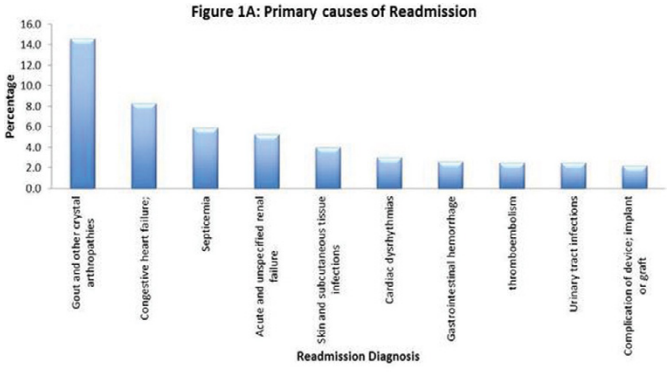
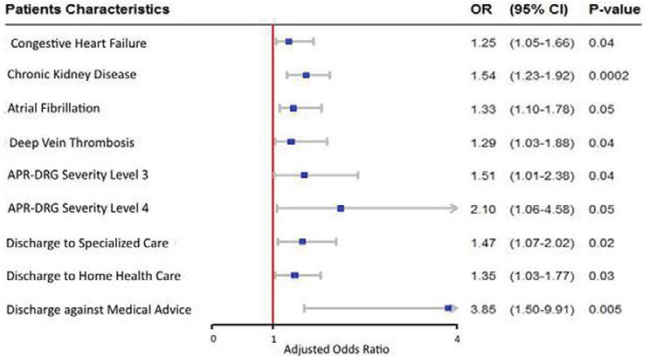


Figure 1B: Predictors for Primary Gout Readmissions



THU0451 A METHOD FOR COUNTING CALCIUM PYROPHOSPHATE CRYSTALS IN THE SYNOVIAL FLUID

P. Montagna, R. Brizzolara, S. Soldano, M. Cutolo, M.A. Cimmino. *Department of Internal Medicine, University of Genova, Genova, Italy*

Background: Identification of calcium pyrophosphate dihydrate (CPP) crystals in the synovial fluid (SF) from inflamed joints provides a definitive diagnosis of CPP deposition disease (CPPD) (1). CPP crystals may also be found in non-inflamed joints, allowing diagnosis also during asymptomatic periods (2). SF analysis and CPP crystals count could be used to evaluate disease activity during follow-up. It is more difficult than the count of monosodium urate (MSU) crystals, already tested in a previous work (3), for CPP crystals show different shapes, are often very minute and non-birefringent.
Objectives: To study an objective method for counting CPP crystals in the SF.
Methods: The SFs aspirated from the knees of 15 consecutive patients (8 men) affected by CPPD diagnosed according to the EULAR definition were analysed. Cytological evaluation included SF leukocyte and differential count. For crystal detection, a small drop of fresh SF was placed on a glass slide and examined by compensated polarized microscopy (400x). To facilitate crystal count, the slide was divided into 4 equal parts drawing a cross with a pencil. The count was performed by continuous viewing and for each field both the number of birefringent and non-birefringent crystals was noted. Two observers evaluated separately 6 SFs and repeated the count after 24 hours. SFs were divided into 4 groups: SFs with $<$50, from 50 to 400, from 401 to 1200, and $>$1200 crystals.
Results: Mean time needed for the count was 60 minutes. Inter-reader agreement was 0.68 (0.47–0.88) for CPP crystals, 0.68 (0.50–0.85) for the birefringent ones and 0.60 (0.38–0.81) for the non-birefringent. Intra-reader agreement was 0.48 (0.17–0.78) for the first examiner and 0.30 (0.14–0.74) for the second. In 7 patient the SF was aspirated from an inflamed knee. Crystal number did not correlate with the presence of knee inflammation (r=0.41; p=0.19), the SF volume (r=0.14; p=0.61), the number of leukocytes (r=0.36; p=0.19), the % of PMN (r=0.25; p=0.37), and the presence of intracellular crystals (r=0.31, p=0.27). Actively inflamed joints had a higher SF volume [11 ml (10–20 ml) vs. 2 ml (1–10 ml), p=0.03] and a higher percentage of PMN [72% (0–94%) vs. 12% (0–68%), p=0.028]. SF with intracellular crystals showed also a higher percentage of PMN (57.1%±34.3% vs. 3%±6% p=0.006).
Conclusions: Our preliminary results indicate that CPP crystal count is less reliable and more time-consuming that that of MSU crystals. Non-birefringent crystals show lower inter-reader agreement than birefringent ones.
References:
[1] Pascual E. J Rheumatol 1996; 35:306–8.
[2] Martinez A. Arthritis Rheum 1995; 38:S 246.
[3] Montagna P. Reumatismo 2015; 67(1):29–32.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5045

THU0452 IMMEDIATE AND LONG TERM EFFICACY OF ANAKINRA IN ACUTE FLARES DUE TO HYDROXYAPATITE CALCIFICATIONS: A REAL-LIFE EXPERIENCE OF 13 CASES

P. Zufferey, R. Valcov, A. So. *DAL, CHUV, Lausanne, Switzerland*

Background: Calcifications composed of hydroxyapatite (HA) crystals can induce acute and severe pain accompanied by signs of acute inflammation. In a previous pilot study, we have shown that anakinra was effective in acute flare of calcific periarthritis of the shoulder in the short term
Objectives: The goal of this retrospective observational study was to confirm these results in a larger set of patients, extending the observation to other localizations and to report on the long-term follow-up.
Methods: All consecutive patients with an acute flare due to HA deposition and treated with anakinra between March 2011 and November 2016 were included. Flare was defined as symptoms of acute pain at rest present for $<$10 days. None of the patients had corticosteroid therapy in the last 2 weeks, none had responded to at least 48 hours of high doses of NSAIDs or other rheumatologic diseases explaining the symptoms. Clinical evaluation consisted of patient assessment of pain by VAS (10mm scale) at days 0, 1, 3, 21 and joint mobility. CRP and ESR measurements, ultrasound and x-ray examinations were performed before the

treatment and at least once again after the treatment. Anakinra 100mg daily was administered for 1 to 3 consecutive days. Other baseline demographic data and long-term follow up data were collected from the patients' charts and after phone call to the patients

Results: 13 patients fulfilled the inclusion criteria. 12 had a flare at the shoulder, 1 at the first MCP of the hand. The acute inclusion flare was the first episode in 9/13 subjects. At baseline, mean pain VAS:8.8/10 Active and passive motion was severely restricted in all patients. Local inflammation was sufficiently severe to induce an elevation of the CRP and ESR in 10/12 patients. By ultrasound, the mean size of calcifications was 17 mm. Only one had an arc-shaped aspect with shadowing, the others were fragmented. *Short term follow-up:* Pain diminished drastically and rapidly, typically within hours, in most patients after the first injection and was almost absent at day three (mean VAS 1.7/10), stable at 3 weeks (mean VAS: 2.1). At follow-up ultrasound, the calcification disappeared in none of the patients but, in most cases, a reduction (50% mean size reduction) and a fragmentation was observed.*Long term follow-up:* The median duration was 24 months, (range 4 to 74 months). Only 2/ 12 patients experienced an acute relapse. These two patients already suffered from chronic shoulder pain and had prior flares before the treatment with anakinra. Mild chronic pain, essentially related to movement (mean VAS: 2.7), was still present in 5 patients. Two patients regularly took NSAIDs; the others did not use any painkiller

Conclusions: This study suggests that IL-1β inhibition may be an interesting therapeutic approach in acute flares in relation with hydroxyapatite calcification. Moreover this treatment does not seem to be associated with rebound or recurrence of flares in the long term.

References:

[1] Zufferey P, So AK.A pilot study of IL-1 inhibition in acute calcific periarthritis of the shoulder Ann Rheum Dis. 2013 Mar;72(3):465–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2730

THU0453 HEART AND CAROTID CHANGES IN FIFTY-THREE GOUT PATIENTS TREATED WITH XANTHINE OXIDASE INHIBITORS: A FOLLOW-UP STUDY

R.N. Gancheva[1,2], A. Kundurdjiev[1,2], M. Ivanova[1,2], T. Kundurzhiev[2,3], Z. Kolarov[1,2]. *[1]Medical Faculty; [2]Medical University; [3]Faculty of Public Health, Sofia, Bulgaria*

Background: Gout connects to cardiovascular (CV) morbidity and higher risk of death due to CV events. A few ultrasound studies assess the way in which heart and vessels change over time in gout patients (pts). It is still unclear whether treatment with allopurinol or febuxostat reduces to some extent target organ damage.

Objectives: We aimed to establish heart and vessels alterations developing over time in gout pts and to find out whether treatment with allopurinol or febuxostat is associated with a change in these structures.

Methods: A total of 53 gout pts were examined and divided into two groups: 31 gouty arthritis without tophi, 24 males and 7 females aged 55.8±12.3 years and 22 gouty tophi, 20 males and 2 females aged 59±9 years. Pts underwent multimodal ultrasound examination at study entry and one year and six months thereafter. Aortic root diameter (Ao), left atrium (LA) size, thickness of the interventricular septum (IVS) and of posterior wall (PW) of the left ventricle, end-diastolic volume index (EDVi), end-systolic volume index (ESVi), stroke volume index (SVi), fractional shortening (FS), and ejection fraction (EF) were recorded with 2.5 MHz transducer. Intima-media thickness (IMT) and rigidity of the common carotid arteries, judged by the values of the common carotid artery resistive index (CCARI), were examined with 10 MHz transducer. Statistical analyzes were done by chi-square or Fisher's exact test, One-Sample Kolmogorov-Smirnov, Shapiro-Wilk and Paired-Samples T-test. Within-subjects effects and between-subjects effects were assessed by the Repeated Measures ANOVA.

Results: At the two time points of pts' examination there was no deviation in Hb (p=0.412), Ht (p=0.866), serum uric acid (p=0.877), serum albumin (p=0.515), eGFR (p=0.793), EDVi (p=0.248), ESVi (p=0.345), SVi (p=0.357), FS (p=0.516) and CCARI (p=0.244), but PW tended to be thicker (p=0.067). Ao (p=0.008), LA (p=0.001), IVS (p=0.007) increased, and EF (p=0.026) decreased between the two examinations. In gouty arthritis without tophi and in gouty tophi Ao (mean±SD; 39.42±5.00 vs 39.14±3.77, p=0.471), LA (mean±SD; 39.10±5.11 vs 43.86±5.95, p=0.088), IVS (mean±SD; 12.77±1.58 vs 13.47±1.54, p=0.910) and IMT (mean±SD; 0.93±0.17 vs 1.05±0.17, p=0.237) changed similarly over time, but the reduction in EF was more pronounced in gouty tophi (p=0.031). In pts not taking allopurinol an increase in LA (p=0.012), IVS (p=0.006) and IMT ($p<0.001$) was registered. In those treated with allopurinol Ao (p=0.011), LA (p=0.022) increased, EF (p=0.016) decreased and no change in IVS (p=0.523) and IMT (p=0.165) was found. Pts who had not received febuxostat tended to have greater Ao (p=0.063), larger LA (p=0.003), thicker IVS (p=0.046), thicker IMT ($p<0.001$) and lower EF (p=0.034). In contrast, no change was registered in Ao (p=0.559), LA (p=0.332), IVS (p=0.125), EF (p=0.689) and IMT (p=0.163) in treated with febuxostat.

Conclusions: Over time in gouty arthritis without tophi and gouty tophi similar changes in the heart and carotids develop, but heart pumping function is more affected in the later stage of the disease. Heart and carotids morphology and function are preserved in pts treated with febuxostat. In the allopurinol group cardiac morphological and functional alterations occur with no change in IMT.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2516

THU0454 ROLE OF PHYSICAL EXERCISE IN PATIENTS WITH HIP ARTHROPLASTY FOR ASEPTIC NECROSIS OF THE FEMORAL HEAD

R.I. Marcu, S. Patru, A.C. Bighea, D. Matei. *Medical Rehabilitation, University of Medicine and Pharmacy, Craiova, Romania*

Background: Necrosis of the femoral head has a slow but progressive evolution, increasing degradation of the joint, worsening instability, with permanent pain and reduced walk perimeter. In the advanced stages of the disease, the only effective treatment is replacement of the joint (hip arthroplasty).

Objectives: The objective of our study was to examine the effects of a two weeks kinetic program on pain and functional status in patients with hip arthroplasty for aseptic necrosis of the femoral head.

Methods: We conducted an observational, prospective, randomized study on a sample of 47 patients with hip arthroplasty for aseptic necrosis of the femoral head. Patients were randomly assigned to a control group (23 patients) who received only analgesics and NSAID's when needed (group 1) and a study group (24 patients) whose therapeutic program included daily physical exercise (group 2). Patients were initially evaluated and after two weeks of rehabilitation treatment. The clinical and functional parameters assessed were: pain on a visual analogue scale (100 mmVAS), physical impairments (muscular strength and mobility of hip joint) and disabilities (Tinetti Gait Scale, D'Aubigné Scale and movement capacity).

Results: The scores for functional parameters improved: pain- 42.6% (group 2) and 33.4% (group 1) (p=0.000054); physical impairments: muscular strength- 8.3% (group 2), without improving by group 1, mobility: 41.8% (group2) and 21.4% (group 1); disabilities: Tinetti Gait Scale- 33.6% (group 2) and 22.1% (group 1), D'Aubigné Scale- 35.8% (group 2) and 22.4% (group 1), movement capacity- 55.8% (group2) and 31.9% (group 1). The results were statistic significant ($p<0.05$).

Conclusions: Improvement of pain, physical impairments and disabilities for the study group certifies the efficacy of the rehabilitation program including physical exercise in patients with hip arthroplasty for aseptic necrosis of the femoral head and motivates the continuation of the study on a longer period of time and on a larger number of patients. Rehabilitation program must begin right after patients underwent surgery for hip replacement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5130

THU0455 RENAL SAFETY OF LESINURAD: A POOLED ANALYSIS OF PHASE III AND EXTENSION STUDIES

R. Terkeltaub[1], R. Malamet[2], K. Bos[2], J. Li[2], D.S. Goldfarb[3], M. Pillinger[4], D. Jalal[5], J. Hu[6], K. Saag[7]. *[1]University of California, San Diego; [2]AstraZeneca Pharmaceuticals, Wilmington; [3]New York University School of Medicine; [4]New York University Langone Medical Center, New York; [5]University of Colorado Anschutz Medical Center, Aurora; [6]Formerly Ardea Biosciences, Inc, San Diego; [7]University of Alabama at Birmingham, Birmingham, United States*

Background: Lesinurad (LESU) is a selective uric acid reabsorption inhibitor approved in the United States and European Union at a 200 mg daily dose in combination with a xanthine oxidase inhibitor (XOI) for treatment of hyperuricemia associated with gout in patients unable to achieve target serum uric acid on an XOI (allopurinol or febuxostat) alone.

Objectives: To investigate the renal safety of LESU, data were pooled from 3 pivotal, placebo-controlled, 12-month phase III (core) studies evaluating lesinurad 200 mg (LESU200) and 400 mg (LESU400) in combination with an XOI and from 2 extension studies, where patients continued LESU+XOI at the same dose or were randomized from placebo to LESU200 or LESU400 plus an XOI.

Methods: Renal-related and kidney stone safety data were pooled from core studies to compare LESU200+XOI and LESU400+XOI with an XOI alone and from core studies + extension studies to evaluate the impact on renal safety of extended LESU+XOI treatment. Renal-related treatment-emergent adverse events (TEAEs) were a customized list of 36 preferred terms selected from the Medical Dictionary for Regulatory Activities (MedDRA) Renal and Urinary Disorders System Organ Class (SOC), the Investigations SOC, and the Acute Renal Failure MedDRA Standardized MedDRA Query (SMQ). Descriptive statistics are provided for patients receiving $\geq$1 dose of study medication. To adjust for varying treatment duration, TEAEs are expressed as exposure-adjusted incidence rates (EAIRs; number of subjects with events per 100 person-years).

Results: In the core studies, EAIRs for any renal-related TEAE, serious renal-related TEAEs, and renal-related TEAEs leading to discontinuation were similar with an XOI alone and LESU200+XOI and lower than with LESU400+XOI (Table 1). Similar results were found for kidney stone and serious kidney stone TEAEs. The most common renal-related TEAE was increased serum creatinine (sCr). EAIRs for sCr elevations $\geq$1.5x baseline were higher with LESU+XOI than XOI alone (Table 1). Overall, 75% and 84% of sCr elevations in the XOI alone and LESU+XOI groups, respectively, were resolved at last study assessment; 75% and 66% resolved without interruption of medication. Exposure to extended

LESU+XOI treatment in the core+extension studies did not show an increase from core studies in EAIRs for any renal-related or kidney stone adverse event category (Table 2).

Table 1. Exposure-Adjusted Renal-Related and Kidney Stone Adverse Event Incidence Rates in Core Studies

	XOI alone (N=516) (PY=408.5)	LESU200+XOI (N=511) (PY=396.3)	LESU400+XOI (N=510) (PY=390.5)
Renal-Related Adverse Event Category [n (rate)]			
Any TEAE	23 (5.6)	29 (7.3)	60 (15.4)
Serious TEAE	2 (0.5)	0	5 (1.3)
Any TEAE leading to randomized study medication discontinuation	5 (1.2)	6 (1.5)	17 (4.4)
sCr elevations ≥1.5 x baseline	12 (2.9)	29 (7.3)	73 (18.7)
Kidney Stone Adverse Event Category [n (rate)]			
Kidney stone TEAEs	9 (2.2)	3 (0.8)	13 (3.3)
Serious kidney stone TEAEs	1 (0.2)	0	3 (0.8)

LESU, lesinurad; XOI, xanthine oxidase inhibitor; sCr, serum creatinine; PY, patient years. Exposure-adjusted incidence rates are expressed as subjects with events per 100 person-years.

Table 2. Exposure-Adjusted Renal-Related and Kidney Stone Adverse Event Incidence Rates in Core+Extension Studies

	LESU200+XOI (N=666) (PY=926.5)	LESU400+XOI (N=666) (PY=917.9)
Renal-Related Adverse Event Category [n (rate)]		
Any TEAE	80 (8.6)	134 (14.6)
Serious TEAE	4 (0.4)	13 (1.4)
Any TEAE leading to randomized study medication discontinuation	17 (1.8)	32 (3.5)
sCr elevations ≥1.5 x baseline	75 (8.1)	156 (17.0)
Kidney Stone Adverse Event Category [n (rate)]		
Kidney stone TEAEs	10 (1.1)	18 (2.0)
Serious kidney stone TEAEs	1 (0.1)	5 (0.5)

LESU, lesinurad; XOI, xanthine oxidase inhibitor; sCr, serum creatinine; PY, patient years. Exposure-adjusted incidence rates are expressed as subjects with events per 100 person-years.

Conclusions: Lesinurad at the approved dose of 200 mg once daily combined with XOI demonstrated comparable rate of adverse events to XOI alone. There was no clinically relevant increase in these adverse events with the extension of treatment beyond 1 year.

Acknowledgements: This study was funded by Ardea Biosciences/AstraZeneca.

Disclosure of Interest: R. Terkeltaub Consultant for: Ardea Biosciences/AstraZeneca, SOBI, Horizon, Revive, Aequus, Relburn, Selecta, ProteoThera, R. Malamet Employee of: AstraZeneca, K. Bos Employee of: AstraZeneca, J. Li Employee of: AstraZeneca, D. Goldfarb Consultant for: AstraZeneca, Revive, Cymabay, Retrophin, M. Pillinger Grant/research support from: Takeda, Consultant for: AstraZeneca, Crealta/Horizon, D. Jalal: None declared, J. Hu Employee of: Ardea Biosciences, K. Saag Consultant for: Ardea/AstraZeneca, Horizon, Takeda

DOI: 10.1136/annrheumdis-2017-eular.4632

THU0456 RATE OF HOSPITALIZATION FOR HEART FAILURE IS LOWER IN PATIENTS WITH CONTROLLED GOUT VERSUS UNCONTROLLED GOUT

R. Morlock[1], P. Chevalier[2], A.B. Klein[3]. *[1]YourCareChoice, Ann Arbor, United States; [2]QuintilesIMS, Zaventem, Belgium; [3]AstraZeneca Pharmaceuticals, Gaithersburg, United States*

Background: Hyperuricemia is associated with worsened outcomes in patients with heart failure (HF). However, little is known about the association between gout and HF.

Objectives: To assess the impact of gout control on the rate of hospitalization for acute HF in a prevalent gout population.

Methods: This retrospective database analysis used data from the Clinical Practice Research Datalink-Hospital Episode Statistics (UK) from Jan 1, 2009 to Dec 31, 2011. Patients were required to have evidence of "prevalent established gout" (ie, treated with urate-lowering therapy [ULT] or eligible for ULT based on ACR guidelines) between Jan 1, 2009 and Dec 31, 2009 and be aged ≥18 on index date (Jan 1, 2010). Follow-up extended from Jan 1, 2010 to Dec 31, 2011. HF rate was calculated as the percentage of eligible patients having ≥1 HF-related hospitalization over the course of the calendar year. In each calendar year, patients were considered to have controlled gout if they had no elevated serum uric acid (sUA; ≥6 mg/dL), no diagnosis of tophus, and no flare documented. Uncontrolled gout was defined as ≥1 elevated sUA or 1 tophus diagnosis during the year. In this analysis patients with no documented sUA were considered not evaluable. To mitigate the limited availability of sUA data, a sensitivity analysis was conducted using an alternate definition of control status: if sUA was available, controlled was defined as no elevated sUA, no flare, and no tophi and uncontrolled was defined as ≥1 elevated sUA, tophus, or flare; if sUA was unavailable, controlled was defined as medication possession ratio (MPR)>80% and uncontrolled defined as 0%<MPR≤80%. Here, patients with no documented sUA and MPR=0% were not evaluable. The odds ratio of HF was modeled in each post-index year using logistic regression models, with adjustment for control status (in previous or current year), gender, age, and Charlson Comorbidity index as covariates.

Results: A total of 29,758 eligible gout patients were identified. Within the subset of patients with available sUA (4762 in 2010 and 4385 in 2011), the HF rate was consistently lower in patients whose gout was controlled in the ongoing year (adjusted OR: 0.253 in 2010 [P=0.032]; 0.268 in 2011 [P=0.019]). The sensitivity analysis conducted using MPR as a proxy for control in a larger population (26,999 patients in 2010 and 26,176 patients in 2011) yielded similar results (OR: 0.387 in 2010 [P<0.001]; 0.462 in 2011 [P<0.001]).

Conclusions: This study suggests that patients with controlled gout have a lower risk of being hospitalized for HF. Further studies would be required to validate this finding on larger samples.

Acknowledgements: This study was sponsored by Ardea Biosciences/AstraZeneca.

Disclosure of Interest: R. Morlock Consultant for: AstraZeneca, Ironwood, Ardea Biosciences, P. Chevalier Employee of: QuintilesIMS, A. Klein Employee of: AstraZeneca

DOI: 10.1136/annrheumdis-2017-eular.5008

THU0457 LESS THAN HALF OF PATIENTS TREATED WITH HIGH-DOSE ALLOPURINOL REACH SUA TARGET

R. Morlock[1], D.C. Taylor[2], S. Baumgartner[3]. *[1]YourCareChoice, Ann Arbor; [2]Ironwood Pharmaceuticals, Inc., Cambridge; [3]drB Consulting, Spokane, United States*

Background: Although allopurinol is FDA approved for up to 800 mg per day and EMEA authorized for up to 900 mg per day, most patients receive 300 mg per day or less.

Objectives: To describe physician, patient, and treatment characteristics in gout patients treated with allopurinol and to assess the proportion of patients reaching serum uric acid (sUA) target by allopurinol dose.

Methods: Patient data from a quantitative survey of physicians were utilized and results confirmed through chart review. Initial and current dose of allopurinol, presence of co-morbid conditions, sUA lab results, physician specialty, and patient characteristics were assessed. Data on number of patients achieving target sUA≤6mg/dL were also collected. Descriptive characteristics are presented as proportions or means and standard deviations (SD). Multivariate and descriptive statistics are used to describe patients with sUA≤6 mg/dL.

Results: A total of 251 rheumatologists and 250 primary care physicians were interviewed. Of 2505 patients with gout, 1437 (57%) were treated with allopurinol. Use of high-dose allopurinol significantly differed by country with less than 6.5% of patients in France, Germany, and Spain given >300mg, whereas 10.2%, 19.5%, and 33.6% of patients in Italy, the US, and the UK, respectively, received a daily dose >300mg ($p<0.01$). Over 12 months the percentage of patients achieving sUA ≤6.0 mg/dL differed across the 6 countries. Looking across all countries, only 43.8% and 44.7% of patients achieved sUA <6.0mg/dL with 301–599mg and ≥600mg of allopurinol QD, respectively. A multivariable-adjusted model found patients with tophi (OR 3.42; $p<0.01$), co-existing alcoholism (OR 1.73; $p<0.05$), COPD (OR 2.01; $p<0.05$), smoking cessation treatment (3.49; $p<0.05$), and from the UK (OR 3.98; $p<0.01$) were more likely to be using >600mg of allopurinol. Regardless of allopurinol dose, the co-variates UK vs. other countries (OR 3.51; $p<0.01$), time on therapy >24 months (OR 1.39; $p<0.01$), and chart-documented co-existing hypertension (OR 1.36; $p<0.05$) were predictive of achieving sUA <6 mg/dL. Whereas physician sub-specialty [general practitioners vs. rheumatologists (OR 0.56; $p<0.01$)], having tophi (OR 0.72; $p<0.05$), and chart-documented co-existing alcoholism (OR 0.67; $p<0.05$), hyperlipidemia (OR 0.74; $p<0.05$), and kidney stones (OR 0.49; $p<0.05$) were found to be associated with not achieving sUA <6 mg/dL. After adjusting for confounding factors, over a 12-month period, there was no difference in achieving sUA <6 mg/dL for those treated with high- vs. low-dose allopurinol.

Conclusions: Allopurinol is approved for up to 800mg in the US and 900mg in the EU but the majority of patients are treated with ≤300mg per day. Less than 50% of patients achieve sUA <6mg/dL at any dose of allopurinol. These data suggest a need for consideration of new treatment options on top of allopurinol for uncontrolled gout patients.

Acknowledgements: This study was funded by Ironwood Pharmaceuticals.

Disclosure of Interest: R. Morlock Consultant for: Received consulting fees from AstraZeneca and Ironwood Pharmaceuticals, and was a consultant of Ardea Biosciences, Inc, a member of the AstraZeneca Group, at the time of the research, D. Taylor Employee of: Employee of Ironwood Pharmaceuticals, S. Baumgartner Employee of: Formerly full-time employees of Ardea Biosciences, Inc., a member of the AstraZeneca Group

DOI: 10.1136/annrheumdis-2017-eular.6234

THU0458 READY OR NOT? CHANGES IN THE CLINICAL PROFILE OF GOUT PATIENTS OVER THE LAST 25 YEARS

S.P. Chinchilla[1,2], I. Urionagüena[3], F. Perez-Ruiz[1,2,3]. *[1]University of the Basque Country, Bilbao; [2]Arthritis Research Group, BioCruces Health Research Institute; [3]Rheumatology Division, Hospital Universitario Cruces, Barakaldo, Spain*

Background: The number of publications associated to gout, as well as the prevalence of the disease, has increased in recent years. Gout is a rising cause of hospital admissions and emergency consults. More so in patients with comorbidities, it has even replaced rheumatoid arthritis as the principal rheumatological condition causing admissions (1). Some questions arise in this setting: What are the characteristics of our patients? How have they changed over the past years?
Objectives: To analyze possible changes in the epidemiologic, clinical and biochemical profiles of gout patients during a period of 25 years.
Methods: Data was collected from a prospective cohort of gout patients, from a crystal arthritis clinic in a tertiary hospital, with a reference population of half a million inhabitants. A period of 25 years was reviewed, between 1992 and 2016 (n =1137), with further division into five quinquennia (Q) for comparison purposes. When entering the cohort, epidemiologic, clinic, laboratory and imaging data are systematically collected. Variables susceptible to change in time were considered: age, gender, gout specific clinical data (articular pattern, presence of tophi), previous admissions due to gout, comorbidities and association with other conditions. Quantitative variables were analyzed with ANOVA and Bonferroni correction; qualitative variables with chi-square test. Inclusion of patients to the cohort was approved by the hospital ethics committee. Results from extreme quinquennia are reported (1stQ: 1992–1996/5thQ 2011–2016 or 2ndQ: 1997–2001/4th: 2006–2010). All results are statistically significant unless stated otherwise.
Results: Differences were observed amongst the periods of five years and age at first visit (1stQ: 54.1±10.9/5thQ: 64.6±13.8 years); gender (1stQ: 2.6%/5thQ: 12.2% of women, respectively). There were no differences when comparing with years of disease evolution before the first visit.
Initial comorbidities: important differences pertaining the prevalence of cardiovascular disease were observed (2ndQ: 26.3%/5thQ: 43.2%), as well as renal disease (1stQ: 16.7%/5thQ: 45.2%), hypertension (1stQ: 27.3%/5thQ: 75.1%) and hyperlipidaemia (1stQ: 50.6%/5thQ: 61.2%) –although this was not the case for Diabetes Mellitus. There was difference amongst periods and association with acute episodes of calcium pyrophosphate arthritis (1stQ: 3.8%/5thQ: 5.9%).
Initial clinical characteristics: differences were found in presentation with tophi (2ndQ: 23.6%/4thQ: 40.1%); polyarticular disease (1stQ: 32.9%/5thQ: 41.3%); hospital admission on the year prior to inclusion (1stQ: 14.5%/5thQ: 24.4%); use of diuretics (1stQ: 6.4%/5thQ: 45.9%); and uricaemia, the latter with no relevant clinical significance.
Conclusions: The profile of gout patients has notably changed in the past 25 years: we have elder, more complex patients, with higher rates of hospital admissions, with severe forms of disease and important comorbidities. When considering these results, we believe that a substantial proportion of gout patients will require specialized attention in the coming years.
References:
[1] Lim SY, Lu N, Oza A, et al. Trends in Gout and Rheumatoid Arthritis Hospitalizations in the United States, 1993–2011. JAMA. 2016 Jun 7;315(21):2345–7.
Disclosure of Interest: S. Chinchilla Grant/research support from: BBK-BioCruces Post Fellowship Research Grant 2016–2017, I. Urionagüena: None declared, F. Perez-Ruiz Consultant for: Amgen, Ardea, AstraZeneca, Grünenthal, Menarini, Speakers bureau: AstraZeneca, Grünenthal, Menarini
DOI: 10.1136/annrheumdis-2017-eular.5459

THU0459 EXPLORING DUAL MODULATION OF GLUT9 AND OAT3, AN APICAL AND BASOLATERAL TRANSPORTERS IN PROXIMAL TUBULES AND EXPERIMENTAL MICE

S.H. Lee, S.B. Kim, D.-S. Oh. *The K-herb Research Centre, Korea Institute of Oriental Medicine, Daejeon, Korea, Republic Of*

Background: Uric acid homeostasis is a set of the balance in glomerular filtration, tubular secretion, reabsorption, and excretion. In the course of cascade, two kinds play a pivotal role; efflux transporters in apical at renal proximal tubular membrane, uptake ones in basolateral at membrane. The former has been of interest in the targets for uricosuric effects, however, dual modulation of the two could keep uric acid balance in stable ways.
Objectives: The aim of this study was to assess the uptake of seven test articles in the course of the expressions of apical/basolateral transporters in potassium oxonate (PO)-treated kidney epithelial cell lines (Caco-2, MDCK, LLC-PK1) and ICR mice.
Methods: The selected cell lines were treated with potassium oxonate (0.25 mM) and then modulated by seven test articles, the commercial herbal products (SITK01 through SITK06 and SITT01) at dose range of 0.015–1 mg/mL. To determine efficacious dose range by each test article, three cell lines, Caco-2, MDCK and LLC-PK1 cells were assessed with MTT assay. Forty eight ICR mice were injected intraperitoneally with PO at a dose of 200 and 400 mg/kg and then blood draws were conducted 0, 6, 12, 24, 72 hours after PO administration. The levels of uric acid and transporters were also measured by ELISA assay and Western blotting analysis in those cell lines.
Results: Treatment of SITK01 through SITK03 and SITT01 at concentration (250 mg/mL) decreased the cell viability. The PO-stimulated kidney epithelial cells with SITK01 through SITK03 treatment increased GLUT9 by 2.5 folds and decreased OAT3 by 1.5 folds (versus controls, p=0.012, and p=0.017, respectively). In PO-treated mice, uric acid levels were increased through GLUT9 and OAT3 transporters. The results indicated that SITK01, SITK02, and SITK03 showed the potential on uricosuric effects in a dual modulation of apical/basolateral sides of kidney epithelial tubular membranes.

Table 1. Protein expression of transporters in apical and basolateral membranes of proximal tubular epithelial cells and potassium oxonate-treated experimental mice

Membrane domain	Functions	Transporters	Caco-2	MDCK	LLC-PK1	Potassium Oxonate-treated mice
Apical	Palpation of excretion	SLC22A12 (URAT1)				++
		SLC2A9 (GLUT9)	+	++	++	++
		ABCG2 (BCRP)				
Basolateral	Inhibition of reabsorption	SLC22A6 (OAT1)		+	++	
		SLC22A8 (OAT3)	+++	+++	+	++

Conclusions: The present findings demonstrated that three commercial herbal products showed potentials to reduce hyperuricaemia-induced condition by changing protein expression levels in a transporter-uptake assay. The OAT3 and GLUT9 could be further investigated as the uricosuric group-targets on the bilateral sides at kidney epithelial tubular membranes.
References:
[1] Fromm MF, König J. Transporters and drug-drug interactions: important determinants of drug disposition and effects. 2015 Nature Reviews Drug Discovery 14, 543–560.
[2] Giacomini KM, Lawrence Lin, Sook Wah Yee, Richard B. Kim & Kathleen. SLC transporters as therapeutic targets: emerging opportunities. 2015 Nature Reviews Drug Discovery 14, 543–560.
Acknowledgements: This study was supported by the Traditional Korean Medicine R&D program funded by the Ministry of Health & Welfare through the Korea Health Industry Development Institute (KHIDI, Grant # HI16C0864). The commercial products were donated by the virtue of Kracie Pharma, Ltd. and Tsumura & Co.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2816

THU0460 BARRIERS TO GOUT CARE: A SYSTEMATIC REVIEW AND THEMATIC SYNTHESIS OF 120 PROVIDERS AND 480 GOUT PATIENTS FROM QUALITATIVE STUDIES

S.K. Rai[1,2], H.K. Choi[1,2], S. Choi[3], A. Townsend[1,4], M.A. De Vera[1,5]. *[1]Arthritis Research Canada, Vancouver, Canada; [2]Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Boston, United States; [3]Faculty of Medicine, University of British Columbia, Vancouver, Canada; [4]Exeter Medical School, University of Exeter, Exeter, United Kingdom; [5]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, Canada*

Background: Despite gout's well-known pathogenesis and the availability of effective urate-lowering therapy (ULT), management remains poor. However, limited research has sought to improve care among this patient population. An in-depth understanding of provider and patient perspectives on barriers to the delivery of optimal gout care is critical to informing the development of evidence-based interventions to effectively improve disease management and patient outcomes.
Objectives: To systematically review and thematically synthesize qualitative studies to date reporting provider and patient barriers to gout management.
Methods: We conducted a mapped search of MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature, and Social Sciences Citation Index databases and selected qualitative studies reporting provider and patient perspectives on gout management. Thematic synthesis was used to combine the source studies and identify key themes across studies. Two authors independently read and annotated the data and after discussion agreed on an initial coding framework. Concepts were organized into descriptive themes, and the relationships between these descriptive themes were further explored to develop higher-order analytical themes.
Results: Our search strategy retrieved 2,750 articles after the removal of duplicates. After full-text review, 20 studies spanning several geographic settings worldwide (i.e., the US, the UK, New Zealand, Australia, and the Netherlands) met all inclusion criteria and were included in our systematic review. Of these, 16 studies reported gout patient perspectives (n=480 patients), while only 7 studies reported provider perspectives (n=120 providers, including general practitioners, rheumatologists and other specialists, and allied health professionals). Thematic synthesis identified three predominant interlocking analytical themes among providers: (a) knowledge gaps and management approaches, (b) perceptions and beliefs about gout patients, and (c) system barriers to optimal gout care (Table 1). We further identified four predominant themes among gout patients: (a) limited gout knowledge (e.g., the "curable" nature of gout), (b) attitudes toward taking medication, (c) interactions with healthcare providers, and (d) practical barriers to chronic medication use (Table 1).

Table 1. Illustrative Provider and Patient Quotations from Source Studies

Analytical Theme	Quotation	Reference
Provider Barriers		
Knowledge gaps and management approaches	"I think that there is lack of knowledge by both patients and health professionals. I just thought you just had gout flare ups and then it just went away, so there is definitely a need for education and better training."	Spencer *et al.*
Perceptions and beliefs about gout patients	"Adherence to uric acid-lowering therapy is not a problem in patients with gout, since they are well aware of the fact they will get new gout attacks if they do not take their medication."	Spaetgens *et al.*
System barriers to optimal gout care	"It's another thing, too, the time issue. Cause if you're really, really busy, you don't spend time to talk to the patient, you don't have time, if we're busy."	Humphrey *et al.*
Patient Barriers		
Limited gout knowledge	"I think I have accepted the fact that there is no cure. It is up to me just to minimize it, I think. I don't think there is any cure because I haven't talked to anybody who has had it and say they don't get it anymore. Is that possible?"	Lindsay *et al.*
Attitudes toward taking medication	"So I know gout's never going to kill me, right. So I don't want to be taking – I don't want to be rattling around full of tablets all the time".	Richardson *et al.*
Interactions with healthcare providers	"I don't think they gave you enough. It kind of wasn't even the basics. There were no follow-ups or anything and I was going regularly. There must have been time in there. I didn't know about uric acid levels or what I should aim for. In my mind, I never had it explained."	Te Karu *et al.*
Practical barriers to chronic medication use	"I'm frequently too busy with school pressures to worry about taking medication regularly."	Katz *et al.*

Conclusions: Our thematic synthesis identified several barriers to gout care, particularly knowledge gaps among both providers and patients as well as implementation barriers to the provision of optimal care. Knowledge translation initiatives emphasizing the "curable" nature of gout targeting both providers and patients as well as strategies to reduce system barriers and support regular medication use are urgently needed to improve gout care.

Acknowledgements: This study was supported in part by a grant from the Canadian Institutes of Health Research (PCS 146388). We wish to thank the Arthritis Patient Advisory Board of Arthritis Research Canada for providing their consumer input into this project.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4298

THU0461 ACCURACY OF HUMASENS-PLUS POINT-OF-CARE URIC ACID METER USING CAPILLARY BLOOD OBTAINED BY FINGERTIP PUNCTURE

S. Fabre[1], P. Clerson[2], J.-M. Launay[3], J.-F. Gautier[4], T. Vidal-Trecan[4], J.-P. Riveline[4], A. Platt[5], A. Abrahamsson[6], J.N. Miner[7], G. Hughes[5], P. Richette[1], T. Bardin[1]. *[1]Rheumatology department, Hôpital Lariboisière, Paris; [2]Soladis Clinical Studies, Roubaix; [3]Biochemistry department; [4]Diabetology department, Hôpital Lariboisière, Paris, France; [5]Personalised Healthcare Unit, AstraZeneca, Cambridge, United Kingdom; [6]Personalised Healthcare Unit, AstraZeneca, Mölndal, Sweden; [7]Research and development, Ardea Biosciences Inc., San Diego, CA, United States*

Background: A key factor in the success of gout management is the long-term lowering of uricemia below predetermined targets (300 or 360µ mol/l). Monitoring of uricemia in gout patients is therefore important, and is presently done in the laboratory on plasma samples obtained after venous puncture. An accurate uric acid (UA) meter allowing rapid testing by the health care professionals and self-measurement by the patient should improve management of gout.

Objectives: This study aimed to assess the reliability of immediate UA measurement in capillary blood samples obtained from fingertip puncture using the HumaSens^{Plus} point-of-care meter (meter) compared with that of a standard laboratory assay (lab).

Methods: Capillary UA levels were measured from 236 consenting diabetic patients using the commercially available HumaSens^{Plus} UA meter (European Conformity marked and approved for EU market use). Each patient also had a plasma UA measurement in the biochemistry laboratory using an uricase automated colorimetric assay. Since the UA meter has a dynamic range of 180–1190µ mol/l, when the values were out-ranged (meter reading LO or HI), they were individually compared to corresponding plasma measurements. Agreement between capillary and plasma UA levels was assessed by Intraclass Correlation Coefficient (ICC) and Bland-Altman graphic representation. Best capillary UA threshold for detection of hyperuricemia (plasma UA>360µmol/l) was determined from a ROC curve, relationship between methods were identified by regression. Impact of potential confounding factors (biological parameters/treatments) was searched. A total of 206 paired measurements were required for estimation of an ICC of 0.80 with a precision of 0.10 at alpha risk of 0.05%. To better understand discrepancies between meter and lab, results were compared to reference plasma UA measurements by liquid chromatography-mass spectrometry (LC-MS) in a subgroup of 77 patients who gave complementary consent.

Results: Fourteen capillary samples were read LO by the meter: 11 were confirmed by lab to be below 180µmol/l and 3 were above (189, 206 and 428µmol/l). Two capillary samples were read HI and were measured at 303 and 213µmol/l by lab. In the remaining 222 samples with meter and lab values, ICC was 0.90 [0.87–0.92] and Bland-Altman curve showed acceptable agreement over all the tested values. Best meter threshold for detection of hyperuricemia by the HumaSens^{Plus} meter was 330µmol/l (sensitivity 0.89, specificity 0.89, area under the ROC curve 0.95). Based on regression, plasma uricase of 360µmol/l corresponded to 343µmol/l. Among the biological parameters tested, only hematocrit impacted capillary uric acid measurements, however negligibly. No medication appeared to significantly affect test results. Plasma uricase measurements were better correlated to LC-MS measurements (r=0.98 [0.96–0.99]) than capillary measurements (r=0.84 [0.75–0.90]).

Conclusions: Results of the HumaSens^{Plus} meter were reasonably comparable to those of the laboratory assay. It is easy to use and may be useful in clinic and in epidemiologic studies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2787

THU0462 MORTALITY IN PATIENTS WITH GOUT: A SYSTEMATIC REVIEW

S. Mitchell[1], H. Liedgens[2], E. Johannes[3]. *[1]Decision Resources Group, Bicester, United Kingdom; [2]Head Health Economics and Outcomes Research Market Access, SBU Europe; [3]Head Market Access Europe, Grünenthal GmbH, Aachen, Germany*

Background: Gout is a chronic, progressive, inflammatory disease characterised by elevated serum uric acid (sUA) levels (1). In Europe the prevalence of gout ranges from 0.9–2.5%, and is increasing (2). Published data indicate that gout is an independent risk factor for both all-cause and cardiovascular (CV)-related mortality (3, 4).

Objectives: To conduct a systematic review to identify studies reporting the association between gout and mortality (all-cause and CV-related).

Methods: Relevant publications were identified by interrogating electronic databases; Medline & MEDLINE In-Process, EMBASE and the Cochrane Library (accessed 3 May 2016). Eligibility criteria included adult patients with a definitive diagnosis of acute/chronic gout (self-reported/physician diagnosed), with no restriction on publication date, study design or geography.

Results: Nineteen studies met the pre-defined inclusion criteria and were reviewed. The studies were conducted in: the US (n=8); Taiwan (n=5); Canada (n=3); Spain (n=1); Singapore (n=1); and the UK (n=1). In addition to patients having a diagnosis of acute/chronic gout, 6 of the 19 studies were conducted in the following patient subgroups: renal transplant (n=1); chronic kidney disease (n=2); patients with a recent acute myocardial infraction (n=2); and patients with heart failure (n=1). There were several consistent finding across the 19 studies: (i) gout was associated with an increase in both all-cause mortality (reported hazard ratios [HR] ranged from 1.13 to 2.37) and CV-related mortality (reported HR ranged from 1.10 to 3.88) compared with patients without gout; (ii) the increased risk in all-cause mortality was primarily driven by an increase in CV-related mortality; (iii) the increased mortality risk was higher in females than males. One study reported that the presence of tophi was independently associated with a higher risk of all-cause mortality. Notably one study reported that patients who received urate-lowering therapy (ULT) have a statistically significant lower all-cause mortality and CV-related mortality risk relative to patients who do not receive ULT.

Conclusions: This systematic review confirms that gout is associated with an increased risk of all-cause and CV-related mortality; this was consistently reported across the eligible studies. The findings highlight the risk associated with gout and emphasise the need for appropriate treatment of this curable disease.

References:

[1] Keenan R, et al. Etiology and pathogenesis of hyperuricemia and gout. Kelley's textbook of rheumatology. Elsevier Saunders. 2013;94:1533–53.
[2] Richette P, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2016:annrheumdis-2016-209707.
[3] Lottmann K, et al. Association between gout and all-cause as well as cardiovascular mortality: a systematic review. Curr Rheumatol Rep. 2012;14(2):195–203.
[4] Clarson L, et al. Increased cardiovascular mortality associated with gout: a systematic review and meta-analysis. Eur J Prev Cardiol. 2015;22(2):335–43.

Disclosure of Interest: S. Mitchell: None declared, H. Liedgens Employee of: Grünenthal GmbH, E. Johannes Employee of: Grünenthal GmbH

DOI: 10.1136/annrheumdis-2017-eular.6062

THU0463 EPIDEMIOLOGY OF GOUT AND HYPERURICEMIA IN NEW CALEDONIA

T. Bardin[1], E. Magnat[2], P. Clerson[3], P. Richette[4], B. Rouchon[2]. *[1]Rheumatology, Hôpital lariboisière, Paris, France; [2]Agence Sanitaire et Sociale, Nouméa, New Caledonia; [3]Soladis Clinical Studies, Roubaix; [4]Rheumatolofy, Hôpital Lariboisière, Paris, France*

Background: New Caledonia is a Pacific island of 270.000 inhabitants with mixed ethnicities, including Melanesians (39.1%) and Polynesians (10.2%) and people from European ancestry (27.2%).

Objectives: To determine the prevalence of gout and hyperuricemia in the various ethnicities and to characterize associated factors.

Methods: A 3-degree random sample of the population aged 18 to 60 years old was redressed according to the 2014 New Caledonia census. Face-to-face interviews were performed by trained nurses who used a predefined questionnaire along with planned physical measurements. All participants underwent capillary measurement of creatinine level (StatSensor) and all men and only women older

than 40 years underwent uricemia testing (HumaSens). Gout was defined by a validated algorithm (1). Hyperuricemia was defined by capillary level equivalent to plasma uric acid level (PUA) >6 mg/dl (2) and/or urate lowering drug (ULD) prescription.
Results: 1.144 participants (mean age 37.7 years; 50.4% men) were included. Prevalence of gout in the entire redressed sample was 3.3% (95% CI 2.2–4.9). The prevalence was 4.1% (1.8–8.9), 2.6% (1.4–4.7), 6.7% (2.5–16.8), and 1.9% (0.5–6.6) for Europeans, Melanesians, Polynesians and other ethnicities, respectively. After adjustment for age and sex, Polynesians showed higher risk for gout than Europeans (adjusted odds ratio [aOR] 4.57 [95% CI 1.3–16.7]). Prevalence of hyperuricemia, determined in 658 participants, was 67.0% (95% CI 61.9–71.6). Prevalence of hyperuricemia was greater for Polynesians (aOR 9.17 [3.2–26.4]), Melanesians (aOR 4.02 [2.2–7.2]) and other ethnicities (aOR 2.18 [1.1–4.5]) than Europeans. On univariate analysis, factors associated with gout were hyperuricemia, male gender, age, BMI, waist circumference, renal failure, hypertension, diabetes, history of major episodes of depression and cancer but not dietary factors or physical activity, despite a consistent association with BMI. Among gout and non-gout patients, 45.9% and 0.7% were receiving ULT. Overall, 29.6% of patients receiving ULD had proper control of PUA levels (≤6 mg/dl).
Conclusions: As compared with Europe, in New Caledonia, the prevalence of gout and hyperuricemia was high, including in patients with European descent, as was previously reported for New Zealand (3). The prevalence of gout and hyperuricemia differed by ethnicity. For Melanesians, the prevalence of hyperuricemia was higher but risk of gout similar to that for Europeans, so factors (e.g., genetics) other than those involved in hyperuricemia may intervene in the risk of gout.
References:
[1] Richette et al. Ann Rheum Dis 2015;74:1684–90.
[2] Fabre et al ACR meeting, Washington 2016.
[3] Winnard et al Rheumatology 2012;51:901–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3409

THU0464 A GENOME-WIDE ASSOCIATION STUDY OF GOUT IN PEOPLE OF EUROPEAN ANCESTRY

T.R. Merriman[1], M. Cadzow[1], M. Merriman[1], A. Phipps-Green[1], R. Topless[1], A. Abhishek[2], M. Andres[3], L. Bradbury[4], R. Buchanan[5], K. Cremin[6], E. de Guzman[4], J. de Zoysa[7], M. Doherty[2], C. Hill[8], T. Huizinga[9], T. Jansen[10], M. Janssen[11], L. Joosten[12], F. Kurreeman[9], S. Lester[8], F. Liote[13], D. Macartney-Coxson[14], H. Matsuo[15], G. McCarthy[16], S. McCormick[1], R. Murphy[7], K. Pavelka[17], F. Perez-Ruiz[18], J. Puig[19], T. Radstake[20], P. Riches[21], M. Rischmueller[8], E. Roddy[22], M. Smith[23], E. Stahl[24], B. Stiburkova[17], R. Stubbs[25], A.-K. Tausche[26], R. Torres[19], R. Walker[1], K. Yamamoto[27], M. Brown[4], H. Choi[28], N. Dalbeth[7], A. So[29], L. Stamp[1], T. Flynn[1]. *[1]University of Otago, Dunedin, New Zealand; [2]University of Nottingham, Nottingham, United Kingdom; [3]Universidad Miguel Hernández, Alicante, Spain; [4]Queensland University of Technology, Brisbane; [5]University of Melbourne, Melbourne; [6]University of Queensland, Brisbane, Australia; [7]University of Auckland, Auckland, New Zealand; [8]Queen Elizabeth Hospital, Adelaide, Australia; [9]Leiden University Medical Center, Leiden; [10]VieCuri Medical Centre, Venlo; [11]Rijnstate Hospital, Arnhem; [12]Radboud University Medical Center, Nijmegen, Netherlands; [13]Hospital Lariboisière, Paris, France; [14]Environmental and Scientific Research, Wellington, New Zealand; [15]National Defense Medical College, Saitama, Japan; [16]University College Dublin, Dublin, Ireland; [17]institute of Rheumatology, Prague, Czech Republic; [18]Hospital de Cruces, Vizcaya; [19]Hospital Universitario la Paz, Madrid, Spain; [20]University Medical Centre Utrecht, Utrecht, Netherlands; [21]University of Edinburgh, Edinburgh; [22]Keele University, Newcastle, United Kingdom; [23]Flinders Medical Centre and Repatriation Hospita, Adelaide, Australia; [24]Mt Sinai School of Medicine, New York, United States; [25]P3 Research Ltd, Wellington, New Zealand; [26]University of Dresden, Dresden, Germany; [27]Kurume University, Kurume, Japan; [28]Harvard Medical School, Boston, United States; [29]University of Lausanne, Lausanne, Switzerland*

Background: Gout progresses through three stages: hyperuricemia, deposition of monosodium urate (MSU) crystals, and innate immune system response to MSU crystals. Genome wide association studies (GWAS) have provided insight into the molecular control of progression to hyperuricemia. However, less is known about the progression from hyperuricemia to gout.
Objectives: To conduct a GWAS for gout (where an immune response to MSU crystals has occurred) using 5,835 cases - the largest GWAS of gout to date.
Methods: The GWAS comprised 3 data sets: NZ/Eurogout (2,365 clinically-ascertained cases; 1,485 controls), the Health Professionals Follow-Up (HPFS) and Nurses' Health Studies (NHS) (1,038 cases, self-ascertained using ACR criteria; 1,095 controls), and UK Biobank (2,432 cases, ascertained by self-report of gout, hospital records, and/or use of urate-lowering therapy; 102,989 controls). The NZ/Eurogout samples were genotyped using the Illumina CoreExome v24 bead chip array (547,644 markers), the HPFS/NHS samples using the Illumina OmniExpress v12 bead chip array (730,525 markers), and the UK Biobank samples using an Affymetrix Axiom array (820,967 markers). UK Biobank genotypes had been imputed to ~73.3M SNPs. Neither the NZ/Eurogout nor NHS/HPFS genotype sets were imputed. Markers common to all three data sets (279,939) were associated with gout (adjusted for sex, age) within each data set separately using PLINK 1.9. An inverse-variance weighted meta-analysis was done with meta v4.4 in R.
Results: There were seven loci with genome-wide significant ($P<5x10^{-8}$) evidence for association with gout: *SLC2A9* (OR=1.67), *ABCG2*(OR=1.72), *GCKR* (OR=1.24), *SLC17A1-A4* (OR=1.20), *SLC22A12* (OR=1.21), *PDZK1* (OR=1.14), *TRIM46* (OR=1.18).
Conclusions: All seven loci have been previously associated with serum urate levels in GWAS. Our data emphasise the relative importance of genetic control of serum urate, compared to the genetic control of MSU crystal formation or the innate immune response, in determining gout.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5634

THU0465 CALCIUM PYROPHOSPHATE DEPOSITION DISEASE AND OSTEOARTHRITIS: TWO FACES OF THE SAME MEDAL? AN ULTRASONOGRAPHIC AND MICROSCOPY STUDY

V. Picerno[1], A. Scanu[2], A. Adinolfi[1], C.A. Scirè[3], B. Frediani[1], L. Punzi[2], G. Filippou[1]. *[1]University of Siena, Siena; [2]University of Padua, Padua; [3]University of Ferrara, Ferrara, Italy*

Background: Calcium pyrophosphate deposition disease (CPPD) and Osteoarthritis (OA) are frequently associated and CPPD with OA is recognized as a clinical subtype [1]. However, the differences in pathogenetic, microscopic and clinical aspects between the two diseases are not clear and how CPPD and OA could affect each other is still a matter of debate.
Objectives: To assess the differences between CPPD and OA in terms of anatomic alterations of the joint, evaluated with US, and characteristics of the synovial fluid (SF) of knees affected by CPPD and/or OA.
Methods: consecutive patients reaching the outpatient clinic for the presence of knee pain and with any amount of joint effusion were eligible for the study. Patients with diagnosis or suspicion of chronic inflammatory rheumatic conditions were excluded. All enrolled patients underwent US of the knee for the assessment of joint effusion (JE), synovial hypertrophy (SH), synovial power Doppler (PD), femuro-tibial osteophytes (FTO) and alterations of the femoral hyaline cartilage (FHC), using a semiquantitative score (0: normal to 3: severe alteration) and finally a US guided aspiration of the SF. SF was examined by optical and polarized light microscopy to determine total and differential white blood cell (WBC) counts, and for crystal identification. The concentration of the main inorganic ions involved in CPP crystal formation ($P_2O_7^{4-}$, PO_4^{3-}, Ca^{2+} and Mg^{2+}) was assessed by fluorometric and colorimetric assays. CPP crystal detection was also used for the classification of patients. Further, in CPPD patients, a count of the CPP crystals detectable in a single slide was carried out. Depending on the variables, chi-square, Mann Whitney and Spearman Ro tests were used for statistical analysis.
Results: 49 patients (28 women), mean age 70.29 yo (SD±10.93) were enrolled in the study; 23 subjects presented OA and 26 CPPD (23.07% acute arthritis, 77.6% CPPD with OA). At US, a statistically significant difference between CPPD and OA was found only for the grade of effusion, being more abundant in CPPD patients. On the contrary, no differences were found regarding SH, PD, FTO, FHC. SF analysis showed that CPPD patients presented a higher volume of SF, a higher total WBC count with a higher polymorphonuclear (PMN) cells percentage and lower monocytes percentage than patients with OA. Further, both total cell count and PMN percentage were positively correlated with the number of crystals in the SF. On the other hand, no statistically significant differences were found in the content of inorganic ions between the two groups.
Conclusions: According to these results, patients with CPPD and OA present some distinct features, mainly regarding the characteristics of the SF, compared to patients with OA alone. These differences may reflect different underlying pathogenetic pathways for the two diseases. Surprisingly, the concentration of inorganic ions in the two populations was similar.Further studies are necessary in order to better understand the link between CPPD and OA and the role of ions concentration in the SF for the formation of crystals.
References:
[1] Zhang W et al. European League Against Rheumatism reccomandations for calcium pyrophosphate deposition. Pat I: terminology and diagnosis. Ann Rheum Dis 2011; 70: 563–570.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6606

THU0467 SAFETY AND EFFICACY OF FEBUXOSTAT IN ADVANCED CKD PATIENTS WITH HYPERURICEMIA

Y.-J. Oh, E.S. Park, S.S. Ahn, K.Y. Lee, S.-J. Byun, J.Y. Pyo, S.M. Jung, S.-W. Lee, Y.-B. Park, J.J. Song. *Internal medicine, Yonsei University College of Medicine, Seoul, Korea, Republic Of*

Background: In chronic kidney disease (CKD) patients, hyperuricemia is a common finding and might be one of modifiable risk factors for renal progression. However, dosing adjustments and increased risk of serious side effects of uric acid lowering agents in patients with reduced renal function lead to undercorrection of hyperuricemia, especially in patients with advanced CKD. Febuxostat is highly

effective and well-tolerated to treat hyperuricemia in CKD patients. Although several evidences demonstrated the usefulness of febuxostat in hyperuricemic CKD patients, clinical studies aimed at the CKD patients with inappropriately controlled hyperuricemia by allopurinol have been relatively lacking.
Objectives: The study objective is to evaluate the safety and efficacy of febuxostat in patients, who had CKD with severe renal impairment and did not meet with the target uric acid levels using allopurinol.
Methods: Data were collected from 168 patients who had CKD with more than stage 3b and changed from allopurinol to febuxostat due to uncontrolled hyperuricemia between 2005 and 2014 at Yonsei University Medical Center. Uric acid and creatinine were analyzed at baseline and during the first 6 and 12 months after conversion of febuxostat. Estimated glomerular filtration rate was calculated using the formula of MDRD equation. The patients were defined as a well-controlled state when the uric acid values of the study subjects reached within 6.0 mg/dL.
Results: The mean age was 60.7±14.6 years, and 129 patients (76.8%) were male. The number of patients was 25 (14.9%) in CKD stage 3b, 75 (44.6%) in stage 4, 8 (4.8%) in stage 5, 38 (22.8%) in patients treated with maintenance dialysis, 22 (13.1%) in patients underwent kidney transplantation. The mean estimated GFR (eGFR) and uric acid levels at baseline was 23.1±17.3 ml/min/1.73m^2 and 8.3±2.4 mg/dL, respectively. Most of the patients was treated with 40 or 80mg of febuxostat during the study period. The mean uric acid levels at 6- and 12-month after febuxostat treatment were significantly reduced compared to uric acid levels at baseline (5.2±2.1 mg/dL at 6-month and 4.9±2.2 mg/dL at 12-month, $p<0.001$, respectively). More than 70% of study subjects reached to the target of uric acid levels less than 6mg/dL at 6- and 12-months after treatment of febuxostat [122 (72.6%) patients at 6-month and 133 (79.2%) patients]. The creatinine levels at baseline and 6-month were comparable (3.42±2.03 vs. 3.38±2.16 mg/dL at baseline and 6-month, p=0.61), meanwhile, the creatinine levels were significantly increased after 12-month compared to those at baseline (3.69±2.46 mg/dL, $p<0.01$). Abnormality of liver function test was observed in only one patient during the follow up period. None of the patients did not discontinue drug due to adverse events.
Conclusions: Present study demonstrated that substantial hyperuricemic CKD patients treated with febuxostat were achieved the target of uric acid levels without adverse events. Febuxostat is an effective and safe uric acid lowering drug in allopurinol-intolerant patients with advanced CKD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2925

THURSDAY, 15 JUNE 2017

Fibromyalgia

THU0468 DIAGNOSTIC EXPERIENCE OF PATIENTS WITH FIBROMYALGIA – A SYSTEMATIC SYNTHESIS OF QUALITATIVE STUDIES

A.M. Mengshoel[1], J. Sim[2], B. Ahlsen[1], S. Madden[3]. *[1]Institute of Health and Society, University of Oslo, Oslo, Norway; [2]Institute for Primary Care and Health Sciences, Keele University, Staffordshire; [3]Faculty of Medical Science, Anglia Ruskin University, Chelmsford and Cambridge, United Kingdom*

Background: In recent years, the evidence-based practice (EBP) movement has become embraced by clinicians and scientists world-wide. A guiding principle of the EBP is that the best evidence available should inform clinical practice. At the same time, patients' experiences should be taken into consideration in the clinical disicion-making. Over the years, the diagnosis of fibromyalgia (FM) has been subject to numerous debates among scientists and clinicians. Despite that a diagnosis may lead to a biographical disruption, be a starting point for patients to make sense of their illness, and shape expectations for the future, the diagnostic debates have not been appreciably informed by how patients themselves perceive the diagnosis.
Objectives: To examine how individuals experience the process and consequences of receiving a diagnosis of fibromyalgia
Methods: A systematic literature search of qualitative studies up to May 2016 was performed. A systematic search was carried out in Medline (*n*=562), PsychInfo (n=430), Cinahl, AMED (*n*=95), and Social Science Citation Index (*n*=486) up to May 2016, supplemented by items from the authors' knowledge of the literature. Duplicates, quantitative studies, studies addressing chronic pain with no specification of diagnosis or including patients with other diagnoses, editorials, reviews, conference reports and dissertations were excluded. After this reading 93 qualitative studies of patients' experience were read to identify whether they included information about patients' diagnostic experience. Twenty-six papers, one book and a book chapter were included. Information about diagnostic experiences were extracted and subjected to an interpretive analysis in accordance with principles of meta-ethnography.
Results: Years were normally spent consulting specialists in an attempt to confirm the reality of symptoms and make sense of the illness. In this process, the reality of the illness was questioned. Great relief was expressed at finally achieving the FMS diagnosis. However, relief waned when therapies proved ineffective. Health professionals and others again questioned whether individuals were genuinely ill, that the illness had a psychological nature, and whether they were doing their best to recover. For the patients, the diagnosis did not provide a meaningful explanation of their suffering and had limited power to legitimate illness. The patients felt blamed for their failure to recover which meant their personal credibility and moral identity were put at stake.
Conclusions: The FMS diagnosis has limitations in validating and making sense of patients' illness experiences and in providing social legitimation of their illness. Social relationships are strained during the diagnostic process and in the course of ineffective therapies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5035

THU0469 COMPARATIVE EFFECTIVENESS OF TAI CHI VERSUS AEROBIC EXERCISE FOR FIBROMYALGIA: A RANDOMIZED CONTROLLED TRIAL

C. Wang[1], C. Schmid[2], R. Fielding[3], W. Harvey[1], K. Reid[3], L.L. Price[1], J. Driban[1], R. Kalish[1], R. Rones[4], T. McAlindon[1]. *[1]Tufts Medical Center, Boston; [2]Brown University School of Public Health, Providence; [3]Tufts University; [4]Center for Mind-Body Therapies, Boston, United States*

Background: Fibromyalgia is a complex disorder with strong psychological and pain components. Tai Chi is an integrated mind-body approach that enhances both physical and mental health and has great potential to treat fibromyalgia (1–2).
Objectives: We aimed to investigate whether Tai Chi is more effective with longer lasting effects than aerobic exercise.
Methods: We conducted a 52-week, single-blind, randomized trial of Tai Chi vs. aerobic exercise for fibromyalgia (ACR 1990 and 2010 diagnostic criteria). Participants were randomized to 1 of 4 Tai Chi interventions: 12 or 24 weeks of Tai Chi once or twice per week, or aerobic exercise held twice per week for 24 weeks. The primary endpoint was change in the Revised Fibromyalgia Impact Questionnaire (FIQR) score at 24 weeks. Secondary endpoints included change in patient's global assessment, the Hospital Anxiety and Depression scale (HADS), Sleep Quality Index (PSQI), arthritis self-efficacy scale (ASES-8), and quality of life. The comparative efficacy of the five groups was determined using longitudinal models based on the intent-to-treat principal.
Results: The mean age of subjects was 52 years (SD 12), mean years of body pain of 9 years (SD 8), 92% were women, and 61% were white. Treatment groups did not differ in baseline outcome expectation. The average of all 4 Tai Chi groups, compared to aerobic exercise, showed significant improvements in FIQR scores, patient's global, anxiety, and self-efficacy. All other outcomes favored Tai Chi over aerobic exercise (Table 1). The Tai Chi treatment with the same dosage as the aerobic group demonstrated an even larger effect for FIQR and for most other outcomes. The benefit of Tai Chi was consistent across instructors.
Conclusions: Tai Chi is more effective than aerobic exercise and can be considered as an important therapeutic option for patients with fibromyalgia.
References:
[1] Jones KD. Recommendations for resistance training in patients with fibromyalgia. Arthritis Res Ther 2015;17:258.
[2] Wang C, Schmid CH, Rones R, et al. A randomized trial of tai chi for fibromyalgia. N Engl J Med 2010;363:743–54.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3484

Abstract THU0469 – Table 1. Between-Group Differences in Outcomes at Week 24

Variable	Aerobic Exercise vs Tai Chi groups combined		Tai Chi 12-week vs 24-week		Tai Chi 1x/week vs 2x/week		Aerobic Exercise 2x24 Weeks vs Tai Chi 2x24 Weeks	
	Mean (95% CI)	P-Value	Mean (95% CI)	P-Value	Mean (95% CI)	P-Value	Mean (95% CI)	P-value
FIQR	5.5 (0.6, 10.4)	**0.03**	9.6 (2.6, 16.6)	**0.007**	4.5 (-2.5, 11.4)	0.21	16.2 (8.7, 23.6)	**<0.0001**
Patient's Global	0.9 (0.3, 1.4)	**0.005**	0.7 (-0.2, 1.5)	0.12	0.4 (-0.4, 1.2)	0.35	1.6 (0.7, 2.5)	**0.0006**
HADS Depression	0.7 (-0.3, 1.6)	0.16	1.4 (0.1, 2.6)	**0.04**	0.7 (-0.6, 1.9)	0.31	2.1 (0.5, 3.7)	**0.01**
HADS Anxiety	1.2 (0.3, 2.1)	**0.006**	0.4 (-0.8, 1.6)	0.55	-0.2 (-1.4, 1.0)	0.74	2.1 (0.6, 3.6)	**0.008**
ASES	1.0 (0.5, 1.6)	**0.0004**	0.5 (-0.3, 1.3)	0.23	0.1 (-0.7, 0.9)	0.73	1.5 (0.6, 2.5)	**0.002**
PSQI	0.3 (-0.6. 1.3)	0.49	1.0 (-0.4, 2.3)	0.16	0.3 (-1.0, 1.7)	0.62	1.0 (-0.6, 2.5)	0.22
SF-36 MCS	2.5 (-0.1, 5.0)	0.06	4.4 (0.8, 8.1)	**0.02**	-0.4 (-4.0, 3.2)	0.83	6.2 (1.9, 10.6)	**0.006**
SF-36 PCS	0.3 (-1.7, 2.2)	0.79	2.4 (-0.3, 5.1)	0.09	1.2 (-1.5, 3.9)	0.38	2.0 (-1.3, 5.3)	0.24

Positive scores indicate improved outcome in second listed group. Boldface indicates statistically significant differences between groups.

THU0470 WORK AND PROFESSIONAL RECOGNITION IN FIBROMYALGIA PATIENTS – A NATIONAL FRENCH WEB BASED SURVEY ON SICK LEAVE IN 1870 FIBROMYALGIA FEMALE PATIENTS

F. Laroche[1], D. Azoulay[1], J. Guérin[1], J. Coste[2], S. Perrot[3]. [1]*Pain Department, Hospital University Saint Antoine;* [2]*Biostatistics, Hospital University Hotel Dieu;* [3]*Pain Department, Hospital University Cochin, Paris, France*

Background: Fibromyalgia (FM) induces work limitations with an increase of number of days of sick leave 3 to 4 fold higher (1, 2).
Objectives: Our objectives were to analyze work status, to determine risk factors for sick leave and to compare women working to women in sick leave during the past 12 months in a female population with FM.
Methods: 1870 female workers suffering from FM were selected from a large internet-based national survey of 4516 responders (Fibromyalgie-SOS Association website in France in 2014). Women having a FIRST score ≥5/6 were included.
Results: 1870 patients participated to the survey: 955 with full time job, 149 with part time job (related to FM status) and 766 on sick leave (7% 1–3 months, 27.3% 3–12 months and 62% >12 months). Fibromyalgia Impact questionnaire (FIQ) score was slightly lower in the 1104 patients currently working compared to the 766 on sick leave (56 versus 58.7), but not clinically different. 64,5% of the population have been on sick leave during the last 12 months (average duration: 37 mean days for full time job and 122 among those with part time job).
Women being in sick leave were older (p<0,0001), single (p=0,0321), had less financial income (p<0,0001), used more antidepressants (p=0,0085) and more anti epileptics (p=0,0102). Recognition of FM by occupational physicians or social security doctors were lower among the workers (p<0.0001).
In the 1104 currently working, more than 33% have never been visiting their occupational physician and 44,2% rarely. They reported no support from these doctors (p=0,0011) particularly those having not being on sick leave. Independent criteria of sick leave were transportation time (p=0.0131), work difficulties (p=0.0031), hinders career progress (p=0.0196), sedentary occupation and repetitive work (p=0.0195).
Conclusions: These data on a large fibromyalgia population shows that clinical status and also professional factors may influence work ability and sick leave.
The work factors include work difficulties, transportation time, sedentary and repetitive occupation. These results should be taken into account by the work professionals in order to facilitate work capacity in FM patients.
References:
[1] Sicras-Mainar A, Rejas J, Navarro R, Blanca M, Morcillo A, Larios R, Velasco S VillarroyaC. Treating patients with fibromyalgia in primary care settings under routine medical practice: a claim database cost and burden of illness study. Arthritis Research & Therapy 2009, 11:R54.
[2] White K. Comparing self-reported function and work disability in 100 community cases of fibromyalgia syndrome versus controls in London, Ontario: the London Fibromyalgia Epidemiology Study. Arthritis Rheum. 1999;42:76–83.
Acknowledgements: Fibromyalgia SOS french Association.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3387

THU0471 THE EFFECTS OF TAPPING THERAPY ON PAIN, SYMPTOM SEVERITY, DYSFUNCTIONS IN DAILY LIFE, DEPRESSION, AND QUALITY OF LIFE IN PATIENTS WITH FIBROMYALGIA: A RANDOMIZED CONTROLLED TRIAL

H.J. Suh[1], S.T. Choi[2], J.-S. Song[2], S.H. Shin[3]. [1]*Seoul National University Hospital;* [2]*Internal Medicine, CHUng-Ang University College of Medicine;* [3]*Kyung Hee University Nursing Science, Seoul, Korea, Republic Of*

Background: Fibromyalgia is a disorder characterized by chronic widespread musculoskeletal pain, often accompanied by fatigue, cognitive disturbance, psychiatric symptoms, and multiple somatic symptoms. Various pharmacological and non-pharmacological therapies have been tried in the management of fibromyalgia. However, unfortunately, management remains a challenge.
Objectives: Taping therapy has been shown to be effective for pain relief in various musculoskeletal diseases. However, there was no trial for the patients with fibromyalgia. In this study, we evaluated the effects of taping therapy in patients with fibromyalgia.
Methods: This study is a randomized controlled trial with 60 fibromyalgia patients. All patients were satisfied with the 2010 American College of Rheumatology diagnostic criteria for fibromyalgia. Participants were randomized to the Kinesio taping group (n=30) and to the non-elastic paper taping group (n=30) for the control. Taping experiment was performed for three weeks (twice a week) through the one-to-one meeting. Pain, symptom severity, dysfunctions in daily life, depression, and quality of life (QoL) were assessed with the widespread pain index (WPI), severity score (SS), fibromyalgia impact questionnaire (FIQ), Beck depression inventory (BDI), and the EQ-5D INDEX and EQ-5D VAS, respectively.
Results: The mean ages of taping group and the control group were 54.3±12.0 years and 53.2±12.7 years, respectively, and female patients were 25/30 (83.3%) and 27/30 (90.0%) in both groups, respectively, and there were no differences between two groups in the medication use such as anti-depressants and muscle relaxants. Patients showed significant improvements after Kinesio taping therapy in pain (10.50±3.98 vs. 5.70±2.73, $p<0.001$), symptom severity (7.93±2.24 vs. 5.27±1.98, $p<0.001$), dysfunction in daily life (65.03±18.75 vs. 43.25±18.87, $p<0.001$), depression (18.17±8.55 vs. 13.00±6.75, $p<0.001$) and QoL (EQ-5D INDEX, 9.10±1.54 vs. 7.67±1.40, $p<0.001$; EQ-5D VAS, 38.33±24.65 vs. 56.67±27.93, $p<0.001$), respectively. In the control group, however, the significant improvement was detected only in pain (10.53±3.87 vs. 9.27±3.57, $p=0.012$). The changes before and after treatment in the Kinesio taping group revealed significant differences from those in the control group: pain ($p<0.001$), symptom severity ($p<0.001$), dysfunction in daily life ($p<0.001$), depression ($p=0.001$) and QoL ($p<0.001$ and $p<0.001$), respectively. There was no serious adverse event.
Conclusions: This study shows that Kinesio taping therapy has effects on pain, symptom severity, dysfunctions in daily life, depression, and quality of life in the patient with fibromyalgia. Taping therapy could be a useful non-pharmacological management modality for the fibromyalgia patient.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4576

THU0472 FAST3 (FIBROMYALGIA ASSESSMENT SCREENING TEST): A COMPOSITE INDEX BASED ON MDHAQ PROVIDES CLUES TO THE PRESENCE OF SECONDARY FIBROMYALGIA IN PATIENTS WITH A PRIMARY DIAGNOSIS OF RHEUMATOID ARTHRITIS AT HIGHER LEVELS THAN IDENTIFIED IN THE MEDICAL RECORD: A CROSS SECTIONAL STUDY FROM ROUTINE CARE

I. Castrejon[1], K. Gibson[2], J.A. Block[1], T. Pincus[1]. [1]*Rheumatology, Rush University Medical Center, Chicago, United States;* [2]*Rheumatology, Liverpool Hospital, Sydney, Australia*

Background: Secondary fibromyalgia (FM) is reported in 17% of RA patients[1], but may be under-recognized in patients with classical RA findings. A FAST3 (fibromyalgia assessment screening test) index based on 3 MDHAQ (Multidimensional Health Assessment Questionnaire) scores gives similar results to ACR fibromyalgia criteria based on a widespread pain questionnaire,[2] to assist in recognizing patients with secondary FM[3].
Objectives: To study patients with a primary diagnosis of RA seen in routine care for the proportion identified as having secondary FM according to a physician diagnosis in the medical record versus a FAST3 Index of MDHAQ scores.
Methods: All patients complete an MDHAQ/RAPID3 at all visits in the waiting area in routine care. The MDHAQ includes 0–10 scores for physical function, pain, and patient global estimate, compiled into RAPID3, as well as a 0–48 RADAI self-report score of painful joints, and 0–60 symptom checklist. FAST3 has been developed previously as the 0–3 sum of 1 point each for 3 MDHAQ scores: pain VAS ≥6, RADAI ≥16, and symptom checklist ≥16.[3] FAST scores of ≥2/3 had >80% agreement with ACR FM criteria based on a widespread pain questionnaire[2] to identify secondary FM.[3] A random visit for each patient with a primary diagnosis of RA with complete data was studied. The number with a diagnosis of secondary FM in the medical record was compared to the number with FAST3 scores of 0, 1, 2, 3, and with each of the 3 FAST3 components. Receiver-operating characteristic (ROC) curves were generated to estimate sensitivity and specificity for each cut-point of the FAST3 score, using a diagnosis of secondary FM by the physician as the external criterion.
Results: 287 patients with RA were studied, of whom 10 (3.3%) had a diagnosis of secondary FM by the physician in the medical record and 61 (22%) had FAST3 scores of 2 or 3 (Table), including 6 of 10 identified as having FM in the medical record. Overall, FAST3 was 0 in 161 RA patients (56%), 1 in 59 (20.6%), 2 in 46 (16%), and 3 in 21 (7.3%) (Table). Overall, 55 additional RA patients were identified by FAST3 versus the medical record as having possible secondary FM. The ROC area was 0.73 (95% CI, 0.57–0.89) (data not shown).

Table 1. FAST3 (fibromyalgia assessment screening tool) Index and 3 individual components according to diagnosis of fibromyalgia by rheumatologist in medical record

	Clinical FM-No	Clinical FM-Yes	Total
Total	277	10	
FAST (fibromyalgia assessment screening tool) Index			
0	159 (57%)	2 (20%)	161
1	57 (21%)	2 (20%)	59
2	42 (15%)	4 (40%)	46
3	19 (7%)	2 (20%)	21
Individual component measures			
Pain >6	92 (33%)	7 (70%)	99
Pain <6	185 (67%)	3 (30%)	188
RADAI >16	68 (25%)	6 (60%)	74
RADAI <16	209 (75%)	4 (40%)	213
Symptom checklist >16	38 (14%)	3 (30%)	41
Symptom checklist <16	239 (86%)	7 (70%)	246

Conclusions: The same MDHAQ used to score RAPID3 may also provide a FAST3 score as a screening tool for secondary FM in RA (and other) patients (including primary FM). Secondary FM may be under-diagnosed by clinicians in routine care. Further validation of FAST3 in other settings is needed.
References:
[1] Wolfe F, et al. J Rheum 2011;31:695–700.
[2] Wolfe et al, J Rheumatol 2011;38:1113–22.
[3] Gibson K, et al. Arthritis Rheumatol. 2016; 68 (suppl. 10).

Disclosure of Interest: I. Castrejon: None declared, K. Gibson: None declared, J. Block: None declared, T. Pincus Shareholder of: Health Report Services, Inc
DOI: 10.1136/annrheumdis-2017-eular.5209

THU0473 POLYSYMPTOMATIC DISTRESS SCALE, WIDE SPREAD PAIN INDEX, AND SYMPTOM SEVERITY SCALES, AND THEIR CORRELATES IN 169 PATIENTS WITH FIBROMYALGIA SYNDROME

K. Yaseen[1], S. Kaouk[2], D. Bork[3], W.S. Wilke[3], C. Gota[3]. *[1]Internal Medicine, Cleveland Clinic; [2]Rheumatology, John Carroll University; [3]Rheumatology, Cleveland Clinic, Cleveland, United States*

Background: The polysymptomatic distress scale (PSD) is considered a measure of FM severity and ranges from 0 to 31. It is calculated by adding the two components of the American College of Rheumatology (ACR) 2010 fibromyalgia (FM) criteria, widespread pain index (WPI) and symptoms severity scale (SS).
Objectives: Determine the relationship between depression, anxiety, function disability and pain related disability, with fibromyalgia severity as measured by PSD and its subsets, WPI and SS.
Methods: All consecutive FM patients who met the ACR 2010 criteria completed the following questionnaires: PSD, patient health related questionnaire (PHQ-9), a measure of depressive symptoms, general anxiety disorder questionnaire (GAD-7), health assessment questionnaire disability index (HAQ-DI), and pain disability index (PDI).
Results: Of 169 patients, 85.7% were women, mean age 42.3 (13.3), BMI 29.3 (7.1), PHQ-9 13.7 (5.2), GAD-7 10.2 (9.1), HAQ-DI 1.6 (2.9), PDI 6 (2.1), WPI 14.3 (2.7), SS 10 (1.6). In univariate analysis PSD correlated significantly ($p<0.01$) with PHQ-9 (0.576), PDI (0.422), and GAD-7 (0.356). Widespread pain index correlated significantly with PHQ-9 (0.313), GAD-7 (0.239), HAQ-DI (0.259), and PDI (0.296). Symptom severity scale correlated significantly with PHQ-9 (0.496), GAD-7 (0.337), HAQ-DI (0.275), PDI (0.340). A linear regression analysis model, which included PHQ-9, GAD-7, PDI and HAQ-DI predicted 0.269 of PSD variance, p=0.001, and only PDI remained significantly correlated with PSD. A similar model predicted 0.348 of SS variance, ($P<0.0001$), and only PHQ-9 remained significantly correlated with SS. This model did not significantly predict WPI variability.
Conclusions: Depression, anxiety, pain disability and functional disability predict a small variance of fibromyalgia severity measured by PSD. In regression analysis, pain disability measured by PDI is the only variable that remains independently correlated with PSD. None of these variables predicted WPI, while depression measured by PHQ-9 remains independently correlated with SS, indicating that PSD subsets measure different dimensions of FM.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4343

THU0474 A CROSS-SECTIONAL STUDY INTO THE EFFECTIVENESS OF THE FIBROMYALGIA RAPID SCREENING TOOL FOR DETECTING FM IN PATIENTS WITH CHRONIC ARTHRITIS UNDERGOING FULL AND TAPERED BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUG THERAPY

L. Valor, D. Hernández Flórez, T. del Río, I. Janta, J. Martínez Barrio, J.G. Ovalles B., B. Serrano, R. González Benítez, C. Sáenz Tenorio, J.C. Nieto, C. González, I. Monteagudo, F.J. López-Longo. *Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain*

Background: The determination of fibromylagia (FM) in patients presenting diffuse, chronic arthritis is fraught. The Fibromyalgia Rapid Screening Tool (FiRST) is a validated questionnaire with high sensitivity and moderate specificity shown to be able to identify up to 89% of FM cases, even when accompanied by anxiety, depression or functional disability. Decisions to embark upon a course of full or tapered biological disease-modifying antirheumatic drugs (bDMARD) are influenced in part by patient self-assessment scores as well as concomitant pathologies.
Objectives: To evaluate the prevalence of FM using the FiRST questionnaire in bDMARD-treated chronic arthritis patients.
Methods: This cross-sectional study included 325 patients [178 (54,8%) females and 147 (45,2%) males] diagnosed with chronic arthritis and treated with bDMARD. Patients were consecutively recruited from the Biological Therapy Unit from January to March 2015 all having undergone full or tapered bDMARD for at least 1 year. Dosage tapering had been applied to patients considered to be in remission. All patients self-completed the FiRST questionnaire with a score>5/6 considered positive. Clinical assessment was carried out by one specialist only. Demographic, clinical and laboratory variables were recorded with pathology-specific indices used to assess disease status, i.e.DAS28-ESR, DAS28-CRP, SDAI, CDAI, BASDAI, BASFI, ASDAS-CRP. Patient pathologies were classified as peripheral arthritis (PerAR: RA, PsA, PerSpA) or axial spondyloarthropathy type (AxSpA).
Results: A total of 68/325 (21%) patients scored >5/6 in the FiRST. Disease duration and previous bDMARD usage were not significant regarding scores <5/6. In the PerAR vs. AxSpA group, we observed that 19% (n=43) and 35% (n=25) scored FiRST>5/6, respectively (p=NS). Fifteen per cent of patients with tapered bDMARD registered scores >5/6 against 85% of patients in full bDMARD dosage (p=0.001). There were a higher number of remission patients in the PerAR group as defined under DAS28-ESR, SDAI and CDAI [(96%, 94% and 94%) (p=0.01, p=0.04, p=0.032), respectively]. Association was found in the PerAR subgroups between tapered bDMARD and remission in RA patients only, as defined under DAS28-VSG, SDAI and CDAI (p=0.026, p=0.04, p=0.043, respectively). In the AxSpA tapered bDMARD subset, 86% of patients were considered to be in clinical remission as set out under BASDAI (p=0.019).
Conclusions: No difference was observed between the PerAR and AxSpA groups for FiRST>5/6. Fewer patients undergoing tapered bDMARD dosage recorded FiRST scores >5/6. Therefore, early identification of chronic arthritic patients presenting FiRST>5/6 may prove to be an important step in furthering understanding of clinical activity in diffuse arthritis as well as offering improved diagnostic and therapeutic outcomes to bDMARD-treated patients with possible concomitant FM.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4768

THU0475 EVALUATION OF PELVIC FLOOR STRENGTH AND URINARY INCONTINENCE IN WOMEN WITH FIBROMYALGIA

M.A.G. Pontes Filho[1], H.C.S.C. Fusco[2], E.A.G. Ferreira[2], A.P. Marques[2]. *[1]Reumatologia, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo; [2]Fisioterapia, Fonaudiologia e Terapia Ocupacional, Universidade de São Paulo, Sao Paulo, Brazil*

Background: Fibromyalgia (FM) is characterized by the *American College of Rheumatology* as chronic widespread pain referred for at least 3 months. In 2010, a new diagnostic criteria was proposed and includes symptoms such as fatigue, sleep disorder and memory. Currently, pelvic floor dysfunctions and urinary incontinence (UI) are considered public health problems with high prevalence and great impact on quality of life (QoL) and on women's self-esteem. Physiotherapists have been working to create a new treatment proposal that can cover all aspects of FM, however there are few studies that include pelvic floor evaluation and urinary continence of this population.
Objectives: To assess the strength of the pelvic floor and urinary loss in women with FM.
Methods: We evaluated 126 sexually active women, aged between 19 and 65 years, with and without medical diagnosis of FM, matched for age and menopausal status, in a single center. The exclusion criteria were sexually transmitted or neurological diseases, pregnancy and use of medications with urinary side effects (urinary loss or retention). We collected in a single interview personal and gynecological data, applied the King Health Questionnaire (KHQ) for incontinent women and accomplished the evaluation of pelvic floor muscle strength according to the Oxford Classification Modified and perineometry. The participants signed the Informed Consent Form. We used for statistical analysis t test for independent variables and Mann-Whitney Test for the others.
Results: The FM patients presented the weaker pelvic floor ($p<0.001$) and had lower values in perineometry (p=0.04) than control women. Regarding urinary loss, 64.5% reported UI against 26.6% of women without FM. In the KHQ evaluation, in General Health and Emotions domains, women with FM presented worse performance ($p<0.001$ and p=0.046, respectively).
Conclusions: Urinary incontinence is a frequent finding in FM, and it could be related to the degree of strength of the pelvic floor muscles. This condition affects negatively QoL, especially with regard to emotions and general health.
References:
[1] Wolfe, et al. The American College of Rheumatology Preliminary Diagnistic Criteria for Fibromyalgia and Measurement of Symptom Severity. Arthritis Care & Research, v.2, n.5, pg. 600–610, 2010.
[2] Jones, K. D. et al. Pelvic Floor and Urinary Distress in Women with Fibromyalgia. Pain Management Nursing, v. 16, n. 6, p. 834–840, Dec 2015.
Acknowledgements: This study received funds from CAPES (Coordination for the Improvement of Higher Education Personnel - Government Research Agency) with scholarship to one of the co-authors.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6261

THU0476 EVALUATION OF SEXUAL FUNCTION IN WOMEN WITH FIBROMYALGIA

M.A.G. Pontes Filho[1], H.C.S.D.C. Fusco[2], R.T. Cônsolo[2], E.A.G. Ferreira[2]. *[1]Reumatologia, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo; [2]Fisioterapia, Fonaudiologia e Terapia Ocupacional, Universidade de São Paulo, Sao Paulo, Brazil*

Background: Fibromyalgia (FM) is defined by the *American College of Rheumatology* as a syndrome of unknown etiology, characterized by chronic and widespread musculoskeletal pain. In 2010, a new diagnostic criteria was proposed and involves not only pain but symptoms such as depression, muscle fatigue, non-restorative sleep and urinary disorders. This may lead to a lack of interest or difficulty in the sexual act, which tends to be aggravated by depression, which is manifested by low self-esteem, decreased desire and orgasm, and pain during sexual intercourse.

Objectives: Compare the sexual function of women with and without FM.
Methods: Sexually active women aged between 19 and 65 years with and without medical diagnosis of FM in a single center, matched for age and menopausal status, were evaluated. The exclusion criteria were pregnancy and use of medications with urinary side effects (urinary loss or retention). In a single interview the participants signed the Informed Consent Form and answered questions about personal and gynecological data. The protocol The Sexual Quotient – Female Version (QS-F) was applied to assess sexual performance. We used for statistical analysis t test for independent variables and Mann-Whitney Test for the others.
Results: In this study, 126 women were evaluated with age of 43.73±10.48 years. Most of the patients were married, representing 58.7%. A total of 50% participants had 1 or 2 children, 22.2% between 3 and 4 children and 27.8% had no children. Regarding the age of menarche and manopausal status, no differences were observed between groups (p=0.70 and p=0.08, respectively). The QS-F score revealed significantly lower scores for women with FM when compared to the healthy group ($p<0.001$). We observed the same results in the domains: Desire and Sexual Interest ($p<0.001$), Excitation Phase (p=0.019) and Satisfaction and Orgasm ($p<0.001$). Regarding the Pain and Comfort domain, no differences were observed between the groups (p=0.307). However, when they were questioned about dyspareunia in the physiotherapeutic evaluation, it was observed that 51.6% of FM patients reported pain in sexual act against only 26.6% of healthy women (p=0.005).
Conclusions: Women with FM performed poorly on QS-F general score and in most domains, except for pain and comfort. When they were questioned in the physiotherapeutic evaluation about dyspareunia, we observed that women with FM had more pain in sexual intercourse, which may occurred due to the way the question was asked. As consequence, women with FM report worse sexual performance, especially with regard to desire, arousal phase and orgasm rate.
References:
[1] Wolfe, et al. The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity. Arthritis Care & Research, v.2, n.5, pg. 600–610, 2010.
[2] Rebecca G. Rogers, M.D. Sexual function in women with pelvic floor desorders. Can Urol Assoc J.; v 7, n. 9–10, p. 199–201, 2013.
Acknowledgements: This study received funds from CAPES (Coordination for the Improvement of Higher Education Personnel - Government Research Agency) with scholarship to one of the co-authors.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6293

THU0477 DOES FIBROMYALGIA AFFECT PHYSICAL ACTIVITY OF THE PATIENTS?

M. Alkan Melikoglu[1], S. Dogantekin[2]. *[1]Rheumatology, ATATURK UNIVERSITY FACULTY of MEDICINE, Rheumatology; [2]Physical medicine and Rehabilitation, ATATURK UNIVERSITY FACULTY of MEDICINE, Erzurum, Turkey*

Background: Fibromyalgia syndrome (FMS) as a chronic pain condition can cause impaired physical activity level of the patients.
Objectives: The purpose this case-control study was to evaluate the physical activity levels of patients with FMS and to assess a possible relation between physical activity and disease characteristics.
Methods: Seventy patients with FMS and 50 age-gender matched controls were included in the study. The demographic features and duration of symptoms of the participants were recorded. The level of pain was evaluated using the visual analogue scale (VAS). The Fibromyalgia Impact Questionnaire (FIQ) scoring system was used for the evaluation of the impact of FMS. Also for assessing the physical activity in our participants, we used The International Physical Activity Questionnaire (IPAQ). Mann–Whitney U and Pearson correlation tests were used for group comparisons and was used for correlation analyses.
Results: The mean age of the patients and healthy controls were 41,90±8,53 years and 41,52±9,01 years, respectively. Symptom duration of the patients was 61,0±45,8 months. The patients with FMS presented significantly less transportation-related, recreational and total physical activity levels, besides reporting significantly less time spent walking and less time spent in vigorous activities than healthy controls ($p<0,05$). Also, in patients with FMS, there was a negative correlation between pain and the scores of self-reported moderate or vigorous physical activity ($r =- 0.41$, $p<0.01$). However, we couldn't find any correlation between FIQ and IPAQ scores.
Conclusions: Patients with FMS are physically less active than healthy individuals of similar profile. This reduced activity seems to be associated with pain, but not with the impact of the disorder. In the approach to the patient with FMS, considering the patient's physical activity behavior can contribute to the management of the disorder. In future studies assessing the effect of exercise in FMS, consideration of the patients' physical activity level may contribute to a complete evaluation of the patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3092

THU0478 DETERMINATION OF COMORBIDITIES IN FIBROMYALGIA SYNDROME

U. Bilge[1], T. Kaşifoğlu[2], N.S. Yaşar Bilge[2], H. Balcıoğlu[1], Y.E. Sarı[1], M. Kayhan[1], I. Ünlüoğlu[1]. *[1]Eskişehir Osmangazi University Faculty of Medicine Department of Family Medicine, Eskişehir Osmangazi University Faculty of Medicine Department of Family Medicine; [2]Eskişehir Osmangazi University, Eskişehir Osmangazi University Faculty of Medicine Department of Internal Medicine Division of Rheumatology, Eskişehir, Turkey*

Background: Although fibromyalgia syndrome is diagnosed by excluding other possible diagnosis based on the patient's clinical features, in recent the studies, it was shown that comorbid diseases affect the course of fibromyalgia.
Objectives: The aim of this study is to evaluate the comorbid diseases of patients with fibromyalgia and to determine the rates of comorbid diseases
Methods: In this study, age, gender and comorbid diseases of patients above 18 years and diagnosed with fibromyalgia by a were evaluated in the database system of the hospital retrospectively.
Results: A total of 509 patients were examined in our study. 51 of the patients were male, 458 were female (mean age was 50.24±12.32). Of the patients, 345 (67.8%) had at least one comorbid disease while 164 (32.2%) had no comorbid disease. In the study, 187 of the patients (36.7%) had cardiovascular diseases, 157 of the patients (30.8%) had endocrine diseases, 63 of the patients (12.4%) had rheumatologic diseases, 30 of the patients (5.9%) had neurological diseases, 14 of the patients (2.8%) had other autoimmune diseases, 10 of the patients (2.0%) had cancers, 129 of the patients (25.3%) had mental disorders, 45 of the patients (8.8%) had chronic lung diseases, 37 of the patients (7.3%) had osteoporosis, 11 of the patients (2.2%) had other diseases (chronic pancreatitis, chronic renal failure, nephrotic syndrome, deep vein thrombosis, hepatitis serology positivity, pulmonary thromboembolism, organ transplantation).
Conclusions: FMS is an important disease that is increasing in frequency in recent years. FMS, which can be seen with many diseases, is in fact related to physicians from many branches, and it is useful to evaluate FMS patients with their comorbid conditions on their follow-up.
References:
[1] Choy EH & Mease PJ. Key symptom domains to be assessed in fibromyalgia (outcome measures in rheumatoid arthritis clinical trials). Rheumatic Disease Clinics of North America, 2009; 35(2):329–337.
[2] Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Arthritis & Rheumatism, 1990; 33(2):160–172.
[3] Soran N, Altındağ Ö, Demirkol A, Sallı A, Yılmaz H, Kocabaş H, et al. Depression level and relation with clinical parameters in fibromyalgia syndrome. Rheumatism, 2008; 23:1–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5877

THU0479 THE PREVALENCE OF XEROSTOMIA IN PATIENS WITH FIBROMYALGIA

N.M. Lloves Schenone, A. Secco, V. Durigan, S. Scarafia, F.E. Romanini, M. Mamani. *Servicio de Reumatología, Hospital Bernardino Rivadaiva, Buenos Aires, Argentina*

Background: Fibromyalgia (FM) is a rheumatic disease characterized by diffuse, chronic musculoskeletal pain, of non-articular origin, which is evidenced by the palpation of painful points in specific anatomical areas and is usually accompanied by non-repairing sleep, Tiredness, morning stiffness, cognitive alterations, among others.
FM affects approximately 0.5 -5% of the population, having a maximum prevalence between 40 and 50 years. No racial or socioeconomic predisposition has been determined to date.
Sicca syndrome whose term encompasses xerophthalmia, xerostomia, xeroderma and xerovagina, has been described in patients with FM. Xerostomia is the sensation of dry mouth due to lack or decrease of saliva. There are no clinical studies that determine the prevalence of xerostomia in patients with FM and on the other hand the reduction of salivary flow in these patients has not been studied with objective tests.
Objectives: The aim of this study was to determinate the frecuency of xerostomia in patients with diagnosis of Fibromyalgia and describe their clinical and epidemiologic characteristics.
Methods: Patients were included according 1990 and 2010 ACR Classification criteria. Patients taking drugs that cause xerostomia were excluded as well as the ones presenting other rheumatologic diseases. Xerostomia was assessed by interrogation and physical examination, and a sialometry was performed in order to determinate the decrease of salival flow. A sialometry was positive if the saliva flow was under 1.5 ml in 15 minutes. In case of presenting positive sialometry patients were studied to rule out Sjogren Syndrome with laboratory and minor salivary gland biopsy.
Results: 50 patients were recruited during the study. The 100% of them were women. The mean age was 47 years old (DS+-8.5), while the mean time of evolution of FM was 6 years. 29 patients reported xerostomia of which 4 presented positive sialometry. No positive sialometry was found in the group that did not referred xerostomia. Smoking was more prevalent in patients with FM who did not

report xerostomia with respect of those who reported xerostomia (31.8% vs 6.9%, p 0.02). There were not associations between xerostomia and hypothyroidism, diabetes or menopause. The presence of Sjogren Syndrome was rule out in those 4 patients whose sialometry was positive.

Conclusions: The prevalente of xerostomía was 51%. No statistically significant associations were found in patients who reported xerostomia. A decrease in objective salivary flow was not demonstrated in patients with FM.

References:

[1] The fibromyalgia impact questionnaire: development and validation" Burckhardt CS; " Validación de la versión española del Fibromyalgia Impact Questionnaire" S. Monterdea.
[2] " The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity".
[3] " The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2074

THU0480 MULTICENTER, PROSPECTIVE, CONTROLLED DOUBLE-BLIND STUDY COMPARING FIB-19-01, A PHYTOTHERAPY TREATMENT FOR FIBROMYALGIA, TO A DIETARY SUPPLEMENT AND TO CONVENTIONAL TREATMENT IN PATIENTS SUFFERING FROM FIBROMYALGIA

P. Bertin[1], D. Baron[2], M. Barmaki[3], I. Russ[4], C. Maindet-Dominici[5], P. Fardellone[6], P. Ginies[7], T. Conrozier[8], J. Nizard[9]. *[1]Rheumatology, CHU Limoges, Limoges; [2]Rheumatology, CH Lannion, Lannion; [3]Pain, Clinique MutualisteEugène André, Lyon; [4]Pain, Hopital residence du Parc, Marseille; [5]Pain, CHU Grenoble, Grenoble; [6]Rheumatology, CHU Amiens, Amiens; [7]Pain, CHU Montpellier, Montpellier; [8]Rheumatology, Nord Franche Comté Hospital, Trevenans; [9]Pain, CHU Nantes, Nantes, France*

Background: Current therapeutic modalities for fibromyalgia syndrome (FMS) do not provide satisfactory results to a high percentage of patients and new approaches have to be explored.

Objectives: This randomised, double-blind, controlled study was aimed to assess the efficacy and safety of adding a new treatment of herbal medicine, specifically developed to improve the quality of life of patients with FMS (Fib-19–01), to the current therapeutic regimen.

Methods: In this double-blind, placebo-controlled study, females with FMS, insufficiently improved by their current treatments, were randomised in one of the 3 following arms: Patients of arm 1 received Fib-19–01, 1 tablet twice a day. Those of arm 2 received a food supplement claimed to have analgesic properties (FSAP), in a double-blind way, and patients of arm 3 continued the previous treatment. without adding anything else (NoT). All continued the conventional treatment throughout the 6 months of follow-up. Inclusion criteria: women suffering from FMS (ACR criteria) with a Fibromyalgia Index Questionnaire FIQ $>$46. The primary endpoint was the change in FIQ score between baseline (Day 0) and month 6 (M6). Secondary Criteria included variation between D0 and M6 of the following scores: Pichot scale, Pittsburgh Sleep Quality Index (PSQI) index, SF-12 mental and social, SF-12 physical, HAD scales for depression and anxiety. Statistical analysis: Comparison intra-group (D0-M6) and intergroup on the ITT population.

Results: The ITT and per protocol populations were constituted of 101 and 75 patients. They were not statistically different and were in accordance with that expected (age 49, BMI 25, high percentage of antidepressant and anticonvulsant treatments). FIQ decrease throughout the follow-up was significant only in the Fib-19–01 group; ($p<0.001$). In intergroup comparison, improvement was higher for Fib-19–01 (-13.5) than in the 2 other groups (-5.4 and -5.6) but the difference did not reach statistical significance (p=0.08). Analysis of variance in repeated measurements of FIQ showed a significant difference between Fib-19–01 and FSAP (p=0.03). On the secondary criteria, only Fib-19–01 patients were improved for PICHOT scale ($p<0.001$), PQSI (p=0.02), SF12 mental and social ($p<0.001$), HAD anxiety (p=0.003) and depression (p=0.004). In intergroup comparison Fib-19–01 was superior to FSAP for Pichot scale (p=0.013), mental and social SF12 (p=0.018), HAD depression (p=0.013). No significant difference was found between FSAP and NoT groups. Therefore, in this study FSAP acts as a placebo which gives the results of this study a level of evidence I. All treatments were well and similarly tolerated.

Conclusions: A 6-month treatment with Fib-19–01 improved all FMS scores excepted the physical SF 12, as opposed to FSAP and conventional treatment alone, which did not significantly improve any. This study showed that Fib-19–01 has a therapeutic effect in the FMS chiefly on the components "fatigue", "emotion and social life" and "depression" of the disease, without safety concern.

Disclosure of Interest: P. BERTIN: None declared, D. BARON: None declared, M. BARMAKI: None declared, I. RUSS: None declared, C. MAINDET-DOMINICI: None declared, P. FARDELLONE: None declared, P. GINIES: None declared, T. CONROZIER Consultant for: LABRHA SAS, J. NIZARD: None declared

DOI: 10.1136/annrheumdis-2017-eular.3790

THU0481 VALIDATION OF THE PROPOSED 2016 REVISION TO 2010 ACR PRELIMINARY FIBROMYALGIA DIAGNOSTIC CRITERIA IN A TERTIRAY CARE SETTING

S. Ahmed, A. Aggarwal, A. Lawrence. *Clinical Immunology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India*

Background: The 2010 Fibromyalgia Diagnostic Criteria was designed for primary care[1]. The 2011 modification was a simplified version for self-reporting of fibromyalgia[2]. The 2016 revision combines both, and is supposed to be used also in tertiary setting[3]. This requires validation.

Objectives: To validate the Proposed 2016 revision with respect to (1) expert physician diagnosis and (2) 1990 ACR Classification Criteria.

Methods: Patients referred to a tertiary care centre with suspicion of Fibromyalgia were evaluated using the Proposed 2016 revision. Patients with other rheumatological diseases were excluded. Considering the expert physician opinion and American College of Rheumatology (ACR) 1990 Classification as gold standards, sensitivity, specificity, and likelihood ratios were calculated. Also, validated Hindi language versions of Brief Patient Health Questionnaire (BPHQ), Generalised Anxiety Disorder-7 (GAD7), and Toronto Alexithymia Scale-20 (TAS20) were filled up by the participants.

Results: Out of 101 patients, 77 were diagnosed as Fibromyalgia by the expert. The 2016 criteria and ACR1990 criteria were met by 79 and 67 patients respectively. The 2016 had high sensitivity but much lower specificity as compared with either the expert diagnosis or ACR1990 criteria (Table 1). Visual Analogue Scale (VAS) for pain, BHPQ, GAD7, and TAS20 scores were 7.2±2.3, 14.1±5.1, 11.3±5.5 and 58.0±14.0 (Mean±SD) respectively. Patients with or without fibromyalgia as per each of the three criteria had no significant difference in these scores.

Table 1. Sensitivity, Specificity, Likelihood ratios as compared to other criteria as gold standard, and agreement with the same

	2016 modification vs Expert opinion	2016 modification vs ACR 1990 criteria	ACR 1990 criteria versus Expert opinion
Sensitivity	87%	89.5%	79.2%
Specificity	50%	44.1%	75%
Positive likelihood ratio	1.74	1.60	3.17
Negative likelihood ratio	0.26	0.24	0.28
Kappa	0.38	0.37	0.47

Conclusions: Non-tender point based criteria have been validated in primary care. However, in tertiary care where patients are referred to as fibromyalgia, there are mimics with similar comorbidities as evident by high BPHQ, GAD7 and TAS20 scores. Even after exclusion of other rheumatological conditions, the 2016 Criteria has poor specificity. Thus, it should be used as a screening tool than a diagnostic criterion in tertiary care.

References:

[1] Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, Russell AS, Russell IJ, Winfield JB, Yunus MB. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care Res (Hoboken). 2010 May;62(5):600–10.
[2] Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RS, Mease P, Russell AS, Russell IJ, Winfield JB. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia. J Rheumatol. 2011 Jun;38(6):1113–22.
[3] Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Häuser W, Katz RL, Mease PJ, Russell AS, Russell IJ, Walitt B. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. Semin Arthritis Rheum. 2016 Dec;46(3):319–329.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2566

THU0482 EVOLUTION OF COMORBID FIBROMYALGIA FREQUENCY IN AXIAL SPONDYLOARTHRITIS PATIENTS STARTING AN ANTI-TNF AGENT, AND CORRELATION TO ANTI-TNF EFFICACY. THE PREDICT-SPA STUDY

S. Perrot, A. Moltó, A. Etcheto, N. Boudersa, P. Claudepierre, N. Roux, F. Berenbaum, A. Martin, L. Sparsa, P. Coquerelle, M. Soubrier, L. Gossec, M. Dougados. *Predict-SpA Study Group, Paris, France*

Background: Fibromyalgia (FM) is a frequent comorbid condition in axial spondyloarthritis (axSpA). It is not known how FM comorbidity may respond to the management of SpA, and especially to anti-TNF agents.

Objectives: To evaluate the change of comorbid FM status of axSpA patients starting an anti-TNF treatment.

Methods: A prospective multicenter national study involving 39 rheumatology centers in France, analyzing 519 patients with axSpA requiring anti-TNF therapy (ClinicalTrials.gov: NCT03039088). Patients were screened for FM with the FiRST questionnaire before and after 3 months of anti-TNF. Kappa coefficient was calculated to determine the agreement of the FiRST at M0 and M3. Response to anti-TNF (BASDAI50 response was compared according to positive screening for FM or not, at both time-points using chi2 tests.

Results: Of the 519 enrolled pts, 504 (with complete data on the FiRST questionnaire) were analyzed at M3. A positive screening for comorbid FM was found in 192 pts (38%) at M0 and in 127 (25%) pts at M3. Correlation between FiRST at M0 and M3 was weak with a Kappa coefficient correlation of 0.4 [0,3 - 0,5].
Four groups were identified: group [+/+] with comorbid FM at M0 and M3: N=93 (18%; group [+/-] with comorbid FM at M0 but not at M3: N=99 (20%); group [-/-] without comorbid FM at M0 and M3: N=278 (55%); group [-/+] without comorbid FM at M0 but at M3: N=34 (7%)
Changes in the status of comorbid FM (disappearance or appearance) was observed in 134 pts (26%). In the 193 pts with baseline comorbid FM, after 3 months of anti-TNF treatment, comorbid FM was no longer found in 99 (51%)%.Efficacy at M3 was significantly better, according to BASDAI 50, in patients without comorbid FM at M3 (Table).

	FM status according to the FIRST questionnaire at M0/M3 (N total=504)			
	+/+	+/–	–/–	–/+
Number of patients	93	99	278	34
Number of patients reaching BASDAI 50 at M3	26 (28%)	61 (61.6%)	162 (58.3%)	8 (25.5%)

Conclusions: There is a high frequency of comorbid FM screened by the FiRST in active axSpA, decreased by 51%f after 3 months of anti-TNF treatments. Persistence of FM after 3 months of anti-TNF treatment is associated with lower anti-TNF response. Further studies are required to analyze the impact of screening FM before starting anti-TNF therapy in axSpA.
References:
[1] Perrot S, et al. Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain. 2010;150:250–6.
Acknowledgements: This study was conducted thanks to an unrestricted grant from MSD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4688

THU0483 CHARACTERISTICS OF PATIENTS WITH ACTIVE AXIAL SPONDYLOARTHRITIS AND COMORBID FIBROMYALGIA. DIFFERENCES ACCORDING TO FIBROMYALGIA SCREENING (FIRST QUESTIONNAIRE) AND FIBROMYALGIA CLASSIFICATION (ACR1990)

S. Perrot, A. Moltó, A. Etcheto, N. Boudersa, P. Claudepierre, N. Roux, F. Berenbaum, A. Martin, L. Sparsa, P. Coquerelle, M. Soubrier, L. Gossec, M. Dougados. *Predict-SpA Study Group, Paris, France*

Background: Fibromyalgia (FM) can be a comorbid condition in axial spondyloarthritis (axSpA). FM screening questionnaires and classification criteria fulfillment may demonstrate different prevalence and patients' characteristics may differ.
Objectives: To evaluate frequency of comorbid FM, and the differences between axSpA patients with/without comorbid FM according to screening (FiRST) and classification tools (ACR1990 FM criteria).
Methods: A multicenter national study involving 39 rheumatology centers in France included 519 patients with axSpA starting an anti-TNF treatment (PredictSpA study; ClinicalTrials.gov: NCT03039088). Patients (pts) were screened for FM with the FiRST questionnaire and classified as FM by ACR 1990 criteria. Demographic characteristics, comorbidities, axSpA characteristics, CRP and imaging were recorded in all patients. Kappa coefficient (and its 95% CI) was calculated to compare FiRST and ACR1990 criteria. Baseline characteristics associated with FM were evaluated by univariable and multivariable logistic regression (including the variables with a p value$<$0.20 in the univariable analysis).
Results: In the 519 pts (females: 46%, age: 42±12 years, mean BASDAI 5.7±2.0, mean ASDAS-CRP 3.3±0.9), a comorbid FM was screened in 38% and diagnosed in 16% of pts. Agreement between FiRST and ACR1990 was poor, with a Kappa coefficient of 0.2 [0.2–0.3].
In the multivariable analysis, comorbid FM (by the FiRST questionnaire) in axSpA patients was independently associated with a lower education level, more sick leave, more heel pain, more frequent second line anti-TNF. Comorbid FM defined by the ACR1990 classification criteria was independently associated with heel pain and inversely associated with B27 haplotype. (Table)

Table 1

Number of patients	Fibromyalgia according to FiRST questionnaire		Odds-ratio [95% CI]
	yes (199)	no (320)	
Education level (> high school)	72 (37%)	163 (51%)	0,6 [0,4- 0,9]
Sick leave (yes)	108 (54%)	134 (42%)	1,5 [1,0 - 2,2]
Heel pain (yes)	127 (64%)	151 (47%)	1,6 [1,1–2,5]
Etanercept at baseline (yes)	63 (32%)	137 (43%)	0,6 [0,4–0,9]

Table 2

Number of patients	Fibromyalgia according to ACR 1990 criteria		Odds-ratio [95% CI]
	yes (84)	no (435)	
HLA B27 (positive)	27 (32%)	272 (63%)	0.39 [0.22–0.68]
Heel pain (yes)	61 (73%)	217 (50%)	2.03 [1.16–3.56]

Conclusions: FM is frequently associated with active axSpA, with poor correlation between screening (FiRST) and diagnosis (ACR1990) test. Several characteristics are associated with comorbid FM, depending on FM classification and screening tools.
References:
[1] Perrot S et al. Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain. 2010;150:250–6.
Acknowledgements: This study was conducted thanks to an unrestricted grant from MSD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4702

THURSDAY, 15 JUNE 2017

Basic science in paediatric rheumatology

THU0484 RO60 EXPRESSION DECREASES WITH AGE IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF CHILDREN AND ADOLESCENTS AND CORRELATES WITH TLR7 STIMULATION IN PDCS OF PREPUBERTAL CHILDREN

A. Radziszewska, K. Webb, H. Peckham, Y. Ioannou. *Arthritis Research UK Centre for Adolescent Rheumatology at University College London, Great Ormond Street Hospital and UCLH, University College London, London, United Kingdom*

Background: Auto-antibodies to the RNA binding protein Ro60 are present in patients with autoimmune disorders such as systemic lupus erythematosus (SLE). In addition to its established role as an auto-antigen, Ro60 has been found to bind Alu RNA retroelements whereby it may target Alu retroelement RNA for degradation suggesting a novel putative function of this auto-antigen. If Ro60 modulates the amount of cellular RNA then one may hypothesise an association with toll-like receptor (TLR) 7 stimulation threshold.
Objectives: To measure the physiological levels of intracellular Ro60 protein in healthy children and adolescents and investigate a possible link between Ro60 protein expression and interferon-α (IFN-α) production after TLR7 stimulation.
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from blood from 48 healthy children and adolescents (age range 6.7–17.9 years old). Cell lysates from thawed PBMC samples were tested for Ro60 expression by Western blot. PBMCs were also stimulated for 20 hours with TLR7/8 agonist R848, at 1ug/ml in the presence of brefeldin A, and plasmacytoid dendritic cell (pDC) IFN-α expression was measured using flow cytometry. Statistical tests to measure correlation between IFN-α expression in (pDCs) and PBMC Ro60 expression were performed using SPSS.
Results: Ro60 expression in PBMCs correlated negatively with age (Spearman's rho = -0.317, p=0.032). When participants were divided into two groups based on their self-reported puberty status, Ro60 expression was higher in the pre-pubertal group (p=0.02). There was, however, no difference in Ro60 expression between males and females (p=0.44) or when sexes were stratified according to pubertal status. pDC IFN-α production after TLR 7 stimulation, did not correlate with ex vivo PBMC Ro60 expression overall (Spearman's rho =0.159, p=0.302) however a moderate positive correlation was observed in pre-pubertal samples only (Spearman's rho =0.554, p=0.021).
Conclusions: Ro60 expression decreases with age in healthy young people. These findings need to be confirmed in a larger cohort and further studies are necessary to investigate the link between Ro60 expression and TLR7 signalling across different age groups as well as in patients with SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5073

THU0485 POLYMORPHISM OF SOME GENES INVOLVED IN IMMUNE AND INFLAMMATORY RESPONSES IN BELARUSIAN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS AND OTHER ARTICULAR PATHOLOGY

H.A. Yatskiu[1], N.V. Nikitchenko[1], N.V. Savina[1], T.D. Kuzhir[1], A.M. Tchitchko[2], A.V. Sukalo[2], R.I. Goncharova[1]. *[1]Institute of Genetics and Cytology, National Academy of Sciences of Belarus; [2]Belarusian State Medical University, Minsk, Belarus*

Background: Etiology and pathogenesis of juvenile idiopathic arthritis (JIA), which prevails among pediatric rheumatic diseases, are insufficiently clear. The study of molecular-genetic basis of JIA is of great interest for revealing genetic predisposition and early diagnosis.
Objectives: The present study aimed to analyze seven SNPs in five genes involved in immune and inflammatory responses: *TNFα* (rs1800629, rs361525), *PTPN22* (rs24766012), *MIF* (rs755622, rs5844572), *CTLA4* (rs5742909), *STAT4* (rs7574865), as well as in two DNA repair genes *XPD* (rs1799793) and *XRCC1* (rs25487) in different conditions.

Methods: 94 patients diagnosed with JIA (mean age 8.78±5.21), 95 children with articular syndrome (mean age7.90±4.81) and 164 hospital controls without any signs of autoimmune or inflammatory diseases (mean age13.99±2.68) were included in the study. The JIA patients were divided into subgroups according to IIAR classification criteria; among them 63 patients were diagnosed with oligoarthritis and 16 with RF- polyarthritis. Genomic DNA was extracted from blood samples by means of phenol-chloroform method. SNPs were genotyped using PCR-RFLP or fragmental analysis.
Results: The allele frequencies for all SNPs in the hospital control group were similar to those characteristic of other Europeans. No differences were found between the frequencies of the TNFα risk alleles across all three groups. Hence, both SNPs in the TNFα locus were not associated with JIA and other articular pathologies in our study. The same is true for -318C>T *CTLA4* polymorphism. Unlike these genes, *PTPN22* C1858T polymorphism influenced developing arthritis in children since heterozygous CT genotype was associated with articular pathology (rather than JIA) in the total group (OR=1.87, 95% CI [1.06–3.30], p=0.04), especially in males (OR=3.50, 95% CI [1.61–7.63], p=0.0016). In the latter case, it was effective even being combined with any genotypes in the -308G>A TNFα locus (OR=2.73, 95% CI [1.19–6.24], p=0.018). When analyzing *MIF* polymorphisms (rs755622 and rs5844572), the evident trend to increased carrying genotypes containing the risk allele *MIF*-173C was observed in females with JIA as compared to controls and significantly elevated frequency of this risk allele in females with RF- polyarthritis as compared to males (p =0.037). In females with JIA, increased frequency of heterozygous *MIF*-794 $CATT_{7,8}$ genotype as compared to the controls (OR =7.78, 95% CI [0.95 – 63.8], p=0,056) was also revealed. *STAT4* polymorphism (rs7574865) demonstrated subtype-related association with JIA due to increased frequency of the minor allele in patients with polyarthitic form of JIA as compared to both hospital controls (p=0.01; OR =2.45; 95% CI [1.19–5.04]) and other articular pathology (p=0.001; OR =3.37; 95% CI [1.56–7.28]). The same SNP was also associated with developing arthritis in females. As to role of DNA repair genes, carriers of *XPD* heterozygous Asp/Asn genotype had an enhanced risk of JIA in females (OR=2.14; 95% CI [1.05–4.35]; p=0.05).
Conclusions: Thus, the gender- and subtype-specific associations of some SNPs studied with developing joint pathologies including JIA are found in the Belarusian child population.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4813

THURSDAY, 15 JUNE 2017

Paediatric rheumatology

THU0486 ANGIOPOETIN-2 AS A NEW VALUABLE MARKER OF DISEASE ACTIVITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

J. Świdrowska-Jaros, E. Smolewska. *Department of Pediatric Rheumatology, Medical University of Lodz, Lodz, Poland*

Background: Angiopoetin-2 (ANG-2) is one of the main angiogenesis modulators. As synovial angiogenesis is considered to be an important early step in the course and pathogenesis of juvenile idiopathic arthritis (JIA), it may be a valuable marker of activity of the disease.
Objectives: To evaluate ANG-2 serum and synovial fluid levels in JIA patients and its possible correlation with disease activity and the degree of ultrasound-detected synovial angiogenesis.
Methods: Serum levels of vascular markers were measured in 63 patients with JIA (aged 1,5–17) and 31 age-matched healthy controls. Synovial fluid was collected from 17 JIA patients. Disease activity (low, medium and high) was assessed by JADAS-27 scale. Ultrasound examination of inflamed joints was performed in each JIA patient and synovial angiogenesis was evaluated by means of Power Doppler ultrasonography (PDUS) and the 4th grade vascularity scale (0–3).
Results: ANG-2 serum levels were higher in children with JIA comparing to the healthy controls (5,5±1,2 ng/ml vs. 1.9±1.4 ng/ml). Serum concentration of ANG-2 in JIA children increased with disease activity (1,4±0,9 ng/ml vs. 1,4±1,0 ng/ml vs. 1,8±2,2 ng/ml), whereas Ang-2 levels in the synovial fluid were the highest in the high disease activity (3,4±2,5 ng vs. 12,5±9,5 ng/ml vs. 26,4±9,0 ng/ml, $p<0,05$). Concentration of ANG-2 in serum correlate with the synovial vascularization obtained by PDUS (0–3, accordingly 1,5±0,8 ng/ml vs. 1,3±0,9 ng/ml vs. 1,5±1,0 ng/ml vs. 13,2±8,7 ng/ml, $p<0,01$) The same pattern was observed for ANG-2 levels in synovial fluid and PDUS grade (0–3, accordingly 3,8±1,0 ng/ml vs. 5,1±4,1 ng/ml vs. 13,5±2,0 ng/ml, $p<0,01$).
Conclusions: ANG-2 might be a valuable marker in JIA children with high disease activity. Together with ultrasound examination, it may add more information about disease severity, what may be helpful in introducing the correct therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1185

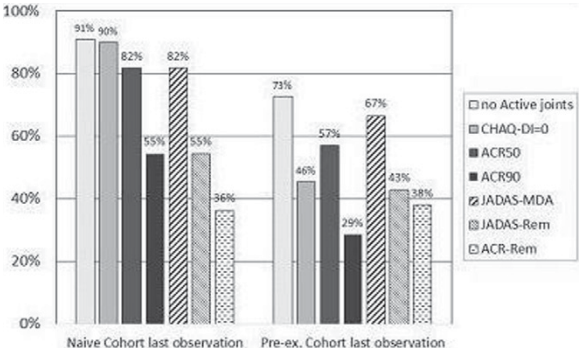
THU0487 REAL-LIFE TREATMENT WITH CANAKINUMAB IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS – FIRST EXPERIENCE FROM THE BIKER REGISTRY

G. Horneff[1], F. Dressler[2], A. Thon[3], K. Minden[4] on behalf of BIKER collaborative group. *[1]Paediatrics, Asklepios, Sankt Augustin; [2]MMH Hannover, Hannover; [3]Paediatrics, MMH Hannover; [4]Charité, Berlin, Germany*

Background: Canakinumab (CAN) had demonstrated its efficacy and safety in SJIA pts (1).
Objectives: To report on the experience with CAN treatment in SJIA in the clinical practice in Germany.
Methods: Data on patients' and disease characteristics, disease activity and safety reports from the German BIKER registry were analysed.
Results: Until Dec. 2016, 37 pts exposed to CAN were identified. In 12 pts used CAN as first biologic, 25 pts were pretreated: Tocilizumab 15, Anakinra 11, Etanercept 9, Adalimumab 9. 3 patients in the pre-exposed cohort had experienced a macrophage activation syndrome. Pts' and disease characteristics are outlined in table 1. Pts pretreated were older, had a longer disease duration and more comorbidities than naïve patients. The proportion of pts with active arthritis, active systemic features and both were comparable. Disease activity at baseline was higher in the naïve cohort suggesting some clinical benefit from pretreatment. Dosing of CAN was comparable (*3.9+/-0.4 vs. 3.5+/-0.7mg/kg)* as well as the median treatment duration (0.8vs.1year). Treatment efficacy at last follow up was better in the naïve cohort with more pts reaching a PedACR 30/50/70/90 response while JADAS- or ACR-remission rates were comparable. Treatment was discontinued by 42% in the naïve and 48% in the exposed cohort. Reasons were inefficacy (n=7;19%), intolerance (n=2;5%) and remission (n=7;19%) of the disease and other (n=2;5%).

Table 1. Baseline characteristics

	Biologics naive	Biologics pre-exposed
N (female gender)	12 (17%)	25 (52%)
Age at JIA onset (years); mean ± SD; Median (IQR)	4.4±4.0; 3.0 (2.0–4.9)	6.0±4.8; 3.7 (2.6–7.1)
Age start of Canakinumab (years); mean ± SD; Median (IQR)	7.1±4.9; 5.6 (3.1–10.2)	9.8±4.8; 10.6 (5.5–14)
Disease duration (years); mean ± SD; Median (IQR)	2.8±4.1; 0.7 (0.3–3.9)	3.8 ± 4.2; 1.9 (0.6–8.7)
Concomitant treatment at baseline: NSAIDS/Steroids/MTX	6 (50%)/6 (50%)/3 (25%)	10 (40%)/11 (44%)/4 (16%)
Patients with active joints	7 (58.3%)	10 (47.6%)
Patients with active systemic features	7 (58.3%)	10 (47.6%)
Patients with active arthritis and systemic features	4 (36.4%)	4 (19.1%)
Active joint count	1.8±1.7; 2.5 (0–3)	2.1±3.3; 0 (0–3)
Physician global VAS (0–10)	5.2±2.8; 6.2 (3.2–7.2)	3.8±3.4 ; 3.7 (0.7–6.3)
Patient Global VAS (0–10)	4.8±2.9; 4.6 (2.7–7)	3.3±2.9; 2.6 (0.6–5.1)
CHAQ-DI (0–3)	0.71±0.65	0.65±0.84
ESR (mm/h)	28.2±22.8	15.4±20.1
CRP (mg/l)	70.5±58	12±23
JADAS10	15.7±8.3	10.5±7.9



Conclusions: First experience with CAN for treatment of sJIA in clinical practice is presented. A high proportion of pts gained significant improvement. JADAS remission was reached by about 50% and ACR remission by 25–57% in both biologics pre-exposed and naïve pts while few pts discontinued treatment in remission so far. Intolerance was rare. The further long term surveillance of sJIA pts exposed CAN is intended by the registry.
References:
[1] Ruperto N, Brunner HI, Quartier P, et al. Two randomized trials of canakinumab in systemic juvenile idiopathic arthritis. N Engl J Med 2012;367(25):2396–406.
Acknowledgements: The authors thank I.Foeldvari, M.Hufnagel, J.Kuemmerle-Deschner, F.Weller-Heinemann, M.Sailer-Hoeck, A.Hospach, G.Heubner, C.Rietschel and B-U.Keck for contributing to the Canakinumab cohort. The German Registry is supported by an unrestricted grant from Abbvie, Germany Novartis, Germany, and Roche, Germany.
Disclosure of Interest: G. Horneff Speakers bureau: Abbvie, Novartis, Chugai, F. Dressler Speakers bureau: Novartis, Pfizer, A. Thon: None declared, K. Minden Speakers bureau: Abbvie, Pfizer,Roche,Genzyme,Pharm-Allergan

DOI: 10.1136/annrheumdis-2017-eular.1745

THU0488 THE IMPACT OF OLIGOARTICULAR AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS OVER THE FIRST FIVE YEARS FOLLOWING DIAGNOSIS

S.J.W. Shoop-Worrall[1,2], S.M. Verstappen[1], J.E. McDonagh[2,3,4], W. Thomson[2,5], K.L. Hyrich[1,2] on behalf of CAPS. *[1]Arthritis Research UK Centre for Epidemiology, the University of Manchester; [2]NIHR Manchester Musculoskeletal BRU, Central Manchester University Hospitals NHS Foundation Trust and University of Manchester Partnership; [3]Centre for MSK Research, the University of Manchester; [4]Manchester Academic Health Science Centre; [5]Arthritis Research UK Centre for Genetics and Genomics, the University of Manchester, Manchester, United Kingdom*

Background: Information regarding longer-term outcomes in JIA largely pre-date the introduction of biologic therapies and have been cross-sectional.
Objectives: The aim of this study was to assess outcomes over the first 5 years of disease in children diagnosed with oligoarticular and polyarticular JIA since 2001.
Methods: Children with oligoarthritis, rheumatoid-factor (RF) negative or positive polyarthritis were selected if recruited to the Childhood Arthritis Prospective Study (CAPS), a UK multicentre inception cohort, between October 2001 and January 2011. The following outcomes were assessed annually to five years and included in this analysis: functional ability (Childhood Health Assessment Questionnaire (CHAQ)), the absence of limited joints, overall psychosocial health (psychosocial scale on the Child Health Questionnaire (CHQ)) and the proportion of children with CHQ psychosocial scores two standard deviations below the population mean (CHQ psychosocial$<$30).
Outcomes were assessed descriptively over time and differences between subtypes were assessed by applying multilevel (patient-level) zero-inflated negative binomial (CHAQ), logistic (absence of limited joints, percent CHQ psychosocial$<$30) and linear (CHQ psychosocial) regression analyses, adjusting for gender, age at presentation and hospital.
Results: Of 832 children, 70% were female, 68% had oligoarticular, 28% RF-negative and 5% RF-positive polyarticular JIA. Eighty four percent had ever been treated with NSAIDs, 74% corticosteroids, 55% with DMARDs and 21% with biologics within follow-up.
Baseline CHAQ was good to moderate (median 0.8, IQR 0.1 to 1.4) and only 21% of children had no limited joints reported at this time. CHQ psychosocial scores (median 50, IQR 39 to 55) were moderate, with 11% children scoring at least two standard deviations under the population mean. Overall improvements were evident in all outcomes over the first year then remained stable with no further improvements at the cohort level evident to five years.
Patients with RF-negative polyarthritis experienced significantly poorer outcomes across all variables than those with oligoarthritis. Those with RF-positive polyarthritis recorded similar CHAQ scores to patients with RF-negative polyarthritis but had the lowest odds of no limited joints (OR: 0.4, 95% CI 0.3 to 0.7) and the poorest CHQ psychosocial scores (4.8 points worse and 4.7 times the odds of scores $<$2 standard deviations of population mean), compared with those with oligoarthritis.
Conclusions: On average, the largest improvement in functional ability, limited joints and psychosocial health occur in the first year following diagnosis, perhaps confirming the importance of early treat-to-target strategies. Patients with polyarticular JIA subtype have poorer parent and physician-reported outcomes than those with oligoarthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3785

THU0489 ADIPOSITY AND INFLAMMATORY ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS COULD THEY BE RELATED?

G. Diaz-Cordoves Rego[1], R. Galindo-Zavala[2], E. Nuñez-Cuadros[2], S. Manrique-Arija[1], N. Mena Vazquez[1], C. Domic-Bueno[1], M. Rojas-Gimenez[1], C. Fuego-Varela[1], R. Caparros-Ruiz[1], L. Cano-Garcia[1], A. Fernandez-Nebro[1]. *[1]Rheumatology, University Regional Hospital of Malaga (HRUM). Institute Biomedical Research In Malaga (IBIMA). Malaga University. Málaga, Spain; [2]Paediatric Department, Universitary Children Hospital of Malaga, Málaga, Spain*

Background: Adults with rheumatoid arthritis have been shown to have a reduction in lean mass and increased adiposity, despite presenting normal Body Mass Index (BMI). Several studies have shown increased adiposity induces a proinflammatory state which lead to a worse response to treatment. There are few publications about this subject in juvenile idiopathic arthritis (JIA)
Objectives: Describing body composition and anthropometric parameters in JIA patients, and evaluating relationship between adiposity and inflammatory in these children.
Methods: Observational cross-sectional study, in JIA patients from 4 to 15 years, monitored by a Pediatric Rheumatology Unit. Monoarticular forms were excluded. Anthropometric, clinical and treatment data were recorded. DXA (measuring bone and fat mass) were obtained. Fat Mass Index (FMI) was defined as fat mass (kg)/height (m^2) and fat-free mass index (FFMI) as lean mass (kg)/height (m^2). JADAS27 index was used to evaluate inflammatoty activity.
Results: We analyzed 80 patients, whose characteristics are shown in table 1. The most frequent JIA subtype was oligoarticular (16.3% extended,47.5% persistent) followed by polyarticular (25.1%). Twenty five percent of patients had uveitis. Fifty percent them had inactive disease with treatment, 26% had activity and 23% were inactive without treatment. Regarding the treatment, 52.5% were on methotrexate and 30% on a biological drug (22.5% antiTNFα, 5% antiIL-1, 2.5% antiIL-6). Disease duration average was 6.6 years (± 3.7SD). JADAS27 index mean score was 2 (±4SD), CRP 4.7mg/l (±9,5SD), ESR 8.7mm (±7,2SD) and CHAQ 0.17 (± 0,38SD). Anthropometric parameters are shown in table 1. Mean JADAS27 index score in patients with normal BMIwas lower (1.7±3.6 SD) than mean JADAS27 index score in overweight and obese patients (3.3±6.0SD), although this difference was not significantly (p=0.255). In multiple linear regression, an increase of 0.3 JADAS27 was observed for each unit of FMI increase (p=0.03). This relationship was maintained in the multivariate analysis (B0.015; p0.01) independently of JIA subtype and received treatment.

Variable	n=80
Age in years, median (±SD)	10,7 (3,3)
Sex,female; n (%)	56 (70)
Race caucasian,n (%)	76 (95)
BMI Median kg/m^2 (±SD)	18,2 (4,2)
BMI Percentile, median (±SD)	42,0 (29,9)
Waist perimeter, median,cm (±SD)	64,8 (11,3)
Hip perimeter cm (±SD)	77 (13,6)
Index waist/hip (±SD)	0,84 (0,06)
Obesity*, n (%)	6 (7,5)
Overweigh*, n (%)	12 (15)
Abdominal obesity,n (%)	12 (15)
Total fat (kg),median (±SE)	11,36 (8,9)
Total Lean (kg),median (±SD)	26,1 (8,9)
Total mass (kg),median (±SD)	38,8 (16,7)
Trunk fat/total fat, median (±SD)	0,42 (0,5)
Legs fat/ total fat, median (±SD)	0,42 (0,44)
FMI (%) median (±SD)	7,5 (5,3)
FFMI (%) median (±SD)	17,8 (3,8)

Conclusions: In JIA patients, there is a linear relationship between FMI and disease activity measured by JADAS27, but most patients had a normal BMI. The establishment of this relationship (fat-inflammatory activity) would be transcendental due to the need to optimize the recommendations in the JIA approach.
References:
[1] Alvarez-Nemecye J, Buenfil-Rello FA, Pacheco Pantoja EI. Association between body composition and disease activity in rheumatoid arthritis. A sistematic review. Reumatol Clin. 2016;12(4):190–5.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6014

THU0490 MULTICENTRE STUDY OF LUPUS NEPHRITIS URINARY BIOMARKERS IN ADULT AND PAEDIATRIC PATIENTS

P. Costa Reis[1,2], K. Maurer[2], L. Schanberg[3], J.M. Burnham[2], E. von Scheven[4], K. O'Neil[5], M. Klein Gitelman[6], M. Petri[7], K.E. Sullivan[2]. *[1]Hospital de Santa Maria, Lisbon, Portugal; [2]The Children's Hospital of Philadelphia, Philadelphia; [3]Duke University, Durnham; [4]University of California San Francisco, San Francisco; [5]Indiana University, Indianapolis; [6]Children's Hospital of Chicago, Chicago; [7]Johns Hopkins University, Baltimore, United States*

Background: Glomerulonephritis is an important cause of morbidity and mortality in patients with systemic lupus erythematosus, particularly in children. Presently, renal histology is used for the diagnosis of lupus nephritis (LN), but it only offers a description of a confined area of the kidney and is seldom repeated for monitoring due to its invasiveness. Urinary biomarkers that reflect LN activity and have prognostic value are much needed to guide the judicious use of immunosuppressive drugs in these patients.
We focused on three potential LN biomarkers: HER2, TWEAK and VCAM1.
HER2 (Human Epidermal Growth Factor Receptor 2) controls cell proliferation by regulating the intracellular levels of miR-26a and miR-30b, which inhibit the expression of cell-cycle related genes. HER2 was recently shown to be dramatically overexpressed in the kidneys of LN patients and in NZM2410 mice.
TWEAK (TNF-related weak inducer of apoptosis) is involved in pro-inflammatory responses, angiogenesis and fibrosis. TWEAK is increased in the kidneys of LN patients.
VCAM1 (vascular cell adhesion molecule 1) participates in the acute phase of inflammation, controlling leukocyte infiltration. Urinary VCAM1 has emerged as a reliable indicator of the LN activity index.
Objectives: To determine the clinical value of urinary HER2, TWEAK and VCAM1 as biomarkers of LN activity.
Methods: A multicentre study is being performed in an adult and paediatric cohort. All patients have biopsy-proven LN. Clinical data and urine samples are being collected in each visit. Controls are age and sex matched individuals without renal disease. Flares are identified with the SELENA-SLEDAI flare index. Urine supernatants are analysed by commercial enzyme-immunoassays for HER2, TWEAK and VCAM1.
Results: Currently, we have studied 83 LN paediatric patients and 38 controls.

The majority are female (85%). The average age is 15±2.5 years. This cohort includes Hispanic (36%), Asian (29%), African-American (21%) and Caucasian (11%) children. LN class III or IV was diagnosed in 67% of patients. Nearly all were treated with hydroxychloroquine and steroids (95%). Other drugs used include mycophenolate mofetil (85%), cyclophosphamide (43%), rituximab (27%) and tacrolimus (2%).

A significant increase in urinary HER2, TWEAK and VCAM1 levels was found in LN patients (p=0.005; p=0.006; p=0.01, respectively) when compared to controls. HER2 levels reflected disease activity, increasing during flares.

In an adult cohort of LN patients (N=126) composed mainly of females (80%) with an average age of 46±13 years, we also found a significant increase of urinary HER2 when compared to controls (p=0.002).

A strong correlation between the urinary levels of HER2, TWEAK and VCAM1 was not found.

Conclusions: Urinary HER2, TWEAK and VCAM1 were significantly increased in a paediatric cohort of LN patients. In addition, significantly higher urinary HER2 levels were also found in an adult LN cohort. This on-going study will further evaluate if these urinary markers, alone or in combination, can reflect disease activity and predict renal flares, analysing their potential value in clinical practice.

References:

[1] PMIDs: 26016809; 22727560; 22788914.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5223

THU0491 COMPARISON OF CLINICAL AND SEROLOGICAL FEATURES OF JUVENILE AND ADULT-ONSET NEUROPSYCHIATRIC LUPUS IN SPANISH PATIENTS

S. Garrote Corral, A. García Fernández, W.A. Sifuentes Giraldo, A.L. Boteanu, M.L. Gámir Gámir, A. Zea Mendoza. *Rheumatology, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Neuropsychiatric (NP) manifestations are a main cause of morbidity and mortality in juvenile-onset systemic lupus erythematosus (jSLE). Some studies suggest that they are more frequent and severe in jSLE than in adult-onset SLE (aSLE).

Objectives: To compare the clinical and serological profile of pediatric and adult patients with neuropsychiatric lupus (NPSLE) treated in a Spanish tertiary center.

Methods: A retrospective study of patients with jSLE (age of onset: 0–18y) and aSLE (age of onset: >18y) seen in our center during the period 1988–2016 was performed. Case definitions of the American College of Rheumatology were used to identify NPSLE manifestations. Demographics, clinical and serological data were obtained through a review of their medical records.

Results: A total of 69 patients with NPSLE were included, aSLE 41 (59%) and jSLE 28 (41%), the comparison of groups is presented in the table. Most of them were Caucasian (92%), mean age at diagnosis in adults was 36.4 years (range: 19–68) and 13.9 years (range: 8–18) in children. The proportion of males was higher in the latter group. The mean duration of the disease was significantly greater in adults, as well as the time from SLE diagnosis to NP manifestation onset, although without significant difference. Central NP manifestations were the most frequent in both groups (aSLE 93%, jSLE 96%) regarding to the peripheral manifestations (aSLE 12%, jSLE 11%). The most frequent manifestations in aSLE were headache (29%), cerebrovascular disease (27%), seizures (17%) and myelopathy (15%), whereas in jSLE were seizures (46%), headache (29%), mood disorder/depression (25%), psychosis (18%) and autonomic disorders (18%). A significant group of patients presented ≥2 central manifestation during their evolution (aSLE 32%, jSLE 41%), with the mean number of manifestations in adults being 1.36 (range: 1–3) and in children 1.44 Range: 1–4). Patients with jSLE developed lupus nephritis (LN) with a significantly higher frequency, as well as higher titres of anti-DNA antibodies, erythrocyte sedimentation rate (ESR) and hypocomplementemia. During the study period there was mortality in 2 cases of aSLE and 2 jSLE (5% and 7%, respectively).

	Juvenile NPSLE	Adult NPSLE	p-value
No. of patients	28 (41%)	41 (59%)	–
Women:men	20:8	39:2	0.0060*
Time of disease (months)	19.8	232.5	0.0001*
NP manifestations at onset	7 (25%)	11 (27%)	0.8651
Time from diagnosis to NP manifestation (months)	42.4	87.1	0.1268
Lupus nephritis	16 (57%)	9 (22%)	0.0028*
Antiphospholipid syndrome	5 (18%)	10 (24%)	0.5182
ANA ≥1/1280	8 (29%)	11 (27%)	0.8736
Anti-DNA ab (IU/ml)	178.9	39.4	0.0005*
Anti-Ro/SSA ab	10 (36%)	17 (41%)	0.6308
Anticardiolipin ab	4 (14%)	10 (24%)	0.3054
Anti-ß2 glycopotein I ab	5 (18%)	7 (17%)	0.9328
Lupus anticoagulant	8 (29%)	10 (24%)	0.6977
Cryoglobulins	6 (21%)	3 (7%)	0.0874
ESR (mm/h)	53.8	35.7	0.0199*
CRP mg/l	4.6	4.7	0.9687
C3 low (<80 mg/dl)	22 (79%)	16 (39%)	0.0012*
C4 low (<16 mg/dl)	22 (79%)	13 (32%)	0.0001*

Conclusions: Our results corroborate that juvenile patients with NPSLE present higher disease activity compared to adults. There was no significant diference in the time from SLE diagnosis to NP manifestation onset, but tended to be shorter in jSLE. The spectrum of NPSLE was varied both groups and an important proportion developed ≥2 manifestation. Mortality continues to be important in NPSLE in both age groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3425

THU0492 MACROPHAGE ACTIVATION SYNDROME AS THE INITIAL MANIFESTATION OF JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS

S. Sato, Y. Uejima, E. Suganuma, T. Takano, S. Fujinaga, Y. Kawano. *Saitama Children's Medical Center, Saitama, Japan*

Background: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening complication of autoimmune diseases in children. Little is known about the association between MAS and the onset of juvenile systemic lupus erythematosus (jSLE).

Objectives: The aim of this study was to determine the frequency and clinical features of MAS as the initial complication of jSLE.

Methods: During 2004 and 2016, we retrospectively reviewed the clinical and laboratory features of 46 jSLE patients diagnosed at the Saitama Children's Medical Center. Patients who were complicated with MAS at the same time as jSLE. These patients were compared with a control group composed of jSLE patients without MAS. The MAS was diagnosed according to preliminary guidelines.

Results: Fifteen patients (32.6%) developed MAS during the initial stage of jSLE. Fever, leukopenia, thrombocytopenia, hyperferritinemia hypofibrinogenemia, increased aspartate aminotransferase (AST), and increased lactate dehydrogenase (LDH) were more frequently observed in patients having jSLE with MAS than in those having jSLE without MAS. No differences were observed in serum C3 and C4 levels, or erythrocyte sedimentation rate (ESR) ($P<0.05$). Especially, Seven patients (46.7%) had *neurologic* symptoms that were significantly higher in those with MAS ($P<0.01$). All patients received corticosteroids when jSLE with MAS diagnosis was established, among whom seven received pulse methylprednisolone therapy. Two patients were treated with IVIG. Nine patients with MAS were treated with immunosuppressants, including cyclophosphamide and mycophenolate mofetil, *azathioprine*. No patient involved in this study died.

Conclusions: MAS can be the initial manifestation of jSLE. MAS may be an underrecognized complication of jSLE. MAS with jSLE should be suspected in patients with high fever, cytopenia, and a liver disorder. In addition, we found that in jSLE with MAS patients, they had more neurologic symptoms compared to jSLE without MAS. Early diagnosis and intensive therapy is essential to improve the clinical outcome.

References:

[1] Parodi A, Davì S, Pringe AB, Pistorio A, Ruperto N, et al. Macrophage activation syndrome in juvenile systemic lupus erythematosus: a multinational multicenter study of thirty-eight patients. Arthritis Rheum. 2009 Nov;60(11):3388–99.

[2] Pringe A, Trail L, Ruperto N, Buoncompagni A, Loy A, et al. Macrophage activation syndrome in juvenile systemic lupus erythematosus: an underrecognized complication? Lupus. 2007;16(8):587–92.

[3] Gormezano NW, Otsuzi CI, Barros DL, da Silva MA, Pereira RM, et al. Macrophage activation syndrome: A severe and frequent manifestation of acute pancreatitis in 362 childhood-onset compared to 1830 adult-onset systemic lupus erythematosus patients. Semin Arthritis Rheum. 2016 Jun;45(6):706–10.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5935

THU0493 STUDY OF LONG-TERM OUTCOME OF CHILDREN WITH JUVENILE DERMATOMYOSITIS FROM A SINGLE-CENTRE IN NORTH INDIA

A. Sharma, A. Gupta, A. Rawat, D. Suri, S. Singh. *Pediatrics, Post Graduate Institute of Medical Education and Research, Chandigarh, India, Chandigarh, India*

Background: Juvenile dermatomyositis (JDM) is a rare inflammatory myopathy seen in children. There have been few studies on long-term outcome in children with JDM

Objectives: To assess long-term outcome of JDM using validated measures of outcome

Methods: All children diagnosed to have JDM for more than 2 years and registered in Pediatric Rheumatology Clinic at PGIMER, Chandigarh, India, were deemed eligible for recruitment. Study period was from January 1, 2015 to June 30, 2016. Those who were not on regular follow-up were called for assessment which was done by a single observer using Childhood Myositis Assessment Scale (CMAS), Manual Muscle Testing 8 (MMT8), Myositis Disease Activity Assessment Tool (MDAAT), abbreviated cutaneous assessment tool (aCAT), Myositis Damage Index (MDI) and Childhood Health Assessment Questionnaire (CHAQ).

Results: Thirty-five children were enrolled in this study, 22 (62.9%) were on regular follow-up. Mean age was 13.9yrs (range 4–29yrs). Mean age at diagnosis was 7.51yrs with median interval between onset of symptoms and diagnosis

being 5 months. Mean duration of disease at the time of enrolment was 7.18yrs. Disease course was monocyclic in 24 (68.6%). Muscle strength was normal in 71.4%. Severe involvement defined as MMT8 score below 64 was seen in 8.6%. Cutaneous activity was determined by aCAT with 40% children having some form of cutaneous activity. Based on MYOACT, 31.4% children had evidence of disease activity at the time of cross-sectional assessment with skin being the commonest organ system involved in 28.6% followed by muscles in 22.9%. Twenty-one (60%) children had some form of cutaneous damage. Calcinosis in 12 (34.3%) and lipodystrophy in 8 (22.9%). Twenty four subjects had an MDI score of $\geq$1 suggesting damage in at least one organ system. Most commonly affected organs were skin, endocrine and muscles in 20, 12 and 9 subjects respectively. Nine (25.7%) subjects in our study had some form of a physical dysfunction suggested by a CHAQ score above 0. Previous studies on long-term outcomes in children with JDM have either not used validated outcome measures or have used fewer measures [1–3].

Conclusions: Highlight of our study is the use of validated outcome measures for evaluation of long-term outcomes. After mean disease duration of 7.18 yrs, 1/3rd subjects had evidence of disease activity with almost 1/10th having moderate to severe activity. About 2/3rd had damage in at least one organ system. Skin was the most common organ affected by activity as well as damage. About 1/4th had reduced physical functioning. Thus, JDM is not a disease where one time treatment would suffice and regular long-term follow-up is required. Counselling of the caregivers is also critical for them to adhere to follow-up. Larger long-term studies using validated outcome measures are required to confirm these findings.

References:

[1] Singh S, Bansal A. Twelve years experience of juvenile dermatomyositis in North India. Rheumatol. Int. 2006;26:510–5.
[2] Huber AM, Lang B, LeBlanc CM, Birdi N, Bolaria RK, Malleson P, et al. Medium- and long-term functional outcomes in a multicenter cohort of children with juvenile dermatomyositis. Arthritis Rheum. 2000;43:541–9.
[3] Ravelli A, Trail L, Ferrari C, Ruperto N, Pistorio A, Pilkington C, et al. Long-term outcome and prognostic factors of juvenile dermatomyositis: a multinational, multicenter study of 490 patients. Arthritis Care Res. 2010;62:63–72.

Acknowledgements: None.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1528

THU0494 CLINICAL FEATURES OF CHILDREN WITH KAWASAKI DISEASE IN DIFFERENT AGE GROUPS IN SOUTHWEST CHINA

L. Shi[1], J. Li[1], D. Qie[2], L. Qiao[2]. *[1]Peking University International Hospital, Beijing; [2]West China Second University Hospital, Chengdu, China*

Background: Kawasaki disease (KD) is a systemic vasculitis characterized by acute and prolonged fever. The prevalence of coronary artery abnormality (CAA) is as high as 11%. The young infants usually have the increased risk of CAA, but do not have the typical clinical manefestations of KD.

Objectives: To explore clinical features of children with KD in different age groups to improve the prognosis of KD.

Methods: A total of 218 children with kawasaki disease were divided into the infants group, the toddlers' group, the pre-school age group and the school age group. Retrospective analysis of clinical data were performed among the groups. Categorical data were compared with each other statistically by Chi-square analysis. Statistical significant was defined as $P < 0.05$. Due to the insufficient cases of school age group and five cases of patients with entire clinical data, the analysis was focused on the other three groups and excluded the five cases in the following statistical analysis.

Results: (1) Among the 218 KD patients, the male to female ratio was 1.5:1 and the recurrence rate was 1.8%. Seven cases (3.2%) were diagnosed as atypical KD, and 84 (38.5%) patients accepted intravenous gamma globulin (IVIG) treatment after the sixth day of KD onset. The incidence of IVIG-resistent KD was 8.7% and the rate of coronary dilation was 11.5%. (2) Fever was the most common clinical feature (100%). The bilateral bulbar conjunctiva injection and the change in mucosa of oropharynx were 85.4% and 81.2% respectively. Moreover, cough (40.5%), diarrhea (16.9%) and vomiting (8.5%) were also very common in the present KD patients. (3) Patients from the toddlers' group were more common to develop lymphadenopathy and skin rash (χ^2=7.784, P=0.02; χ^2=10.794, P=0.005), but were less frequently to be documented with cough and diarrhea (χ^2=7.334, P=0.026; χ^2=18.447, P=0.000). (4) The incidence of increased platelets was more common in the infants group (χ^2=7.552, P=0.023). Comparing with the urine test among three groups, the toddlers' group had a higher incidence of sterile pyuria (χ^2=10.653, P=0.005), and infants younger than 12 months old had a lower incidence of proteinuria and positive urine ketone (χ^2=15.507, P=0.000; χ^2=40.336, P=0.000).

Conclusions: The respiratory tract, the digestive and urinary systems are involved commonly in Kawasaki disease, and patients from different age groups showed different clinical features, which should be pay more attention to promote the prognosis.

References:

[1] Kowalczyk M,Turska-Kmiec A,Ziolkowska L,et al. [Symptoms, diagnosis and characteristic abnormalities in the coronary arteries in Kawasaki disease in children]. Med Wieku Rozwoj, 2010. 14(4):344–349.
[2] Burns JC,Shike H,Gordon JB,et al. Sequelae of Kawasaki disease in adolescents and young adults. J Am Coll Cardiol, 1996. 28(1):253–257.
[3] Newburger JW,Takahashi M,Gerber MA,et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation, 2004. 110(17):2747–2771.DOI: 10.1161/01.CIR.0000145143.19711.78.

Acknowledgements: This work was supported by grants from the Natural Science Foundation of China (81501396 to Dr. Lianjie Shi, and 81302554 to Dr. Fanlei Hu).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5864

THU0495 EFFECTIVENESS OF CHILDHOOD VACCINATIONS IN CAPS PATIENTS TREATED WITH CANAKINUMAB: RESULTS FROM AN OPEN-LABEL PHASE 3 EXTENSION STUDY

P. Brogan[1], M. Hofer[2], J. Kuemmerle-Deschner[3], B. Lauwerys[4], A. Speziale[5], X. Wei[6], R. Laxer[7]. *[1]Infection, Immunology, and Rheumatology, UCL Institute of Child Health, and Great Ormond Street Hospital NHS Foundation Trust, London, United Kingdom; [2]Unité Romande de Rhumatologie Pédiatrique, Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [3]University Hospital Tuebingen, Tuebingen, Germany; [4]Cliniques Universitaires Saint-Luc and Université Catholique de Louvain, Brussels, Belgium; [5]Novartis AG, Basel, Switzerland; [6]Novartis Pharma, Beijing, China; [7]University of Toronto, The Hospital for Sick Children, Toronto, Ontario, Canada*

Background: Canakinumab (CAN) has been shown not to impair antibody production following vaccination in children in an open-label phase 3 study (NCT01302860).[1] Here we present the results from the extension of this study.

Objectives: To evaluate the presence of protective antibody levels following immunisation with inactivated vaccines in CAPS patients during extension study.

Methods: Patients who completed the core study were allowed to continue into the extension study on the standard dosing regimen of 2 mg/kg subcutaneous CAN every 8 weeks or on last dose/dosing regimen received in the core study. Vaccination response was evaluated using post-vaccination antibody titres at 4 and 8 weeks after immunisation. Patients were considered assessable for an antibody response to a specific vaccination if they had a measurement of antibody titre 0–14 days post-vaccination (pre-vaccination assessment) and at least 1 subsequent measurement of antibody titre at 4 weeks and/or 8 weeks post-vaccination. However, for patients with adequate pre-dose antibody titres and maintained during the trial, the specific patient vaccination was deemed non-assessable.

Results: During the extension phase, of 17 patients ($\leq$6 years), 4 received 8 types of vaccinations against *Corynebacterium diphtheriae*, *Bordetella pertussis*, *Neisseria meningitidis*, *Clostridium tetani*, influenza type A and type B, *Haemophilus influenzae* B, *Streptococcus pneumoniae*, or hepatitis B. Of 20 unique patient-vaccination cases, 17 were assessable for a vaccination response, whereas for the remaining 3, pre-dose antibody titre was not available. For 16 (94.1%) assessable cases, post-vaccination antibody titres increased above protective levels. For one patient who received Tetravec formulation (diphtheria, tetanus and acellular pertussis combination), the response observed for 1 (vaccination against *Clostridium tetani*) of the 3 vaccines included in Tetravac represented optical density rather than antibody concentrations and hence considered non-evaluable. For 19/20 patient-vaccinations, including those without pre-dose antibody titres, protective levels were observed during the study, which were maintained throughout the extension study.

Conclusions: Canakinumab appeared to have no effect on post-vaccination antibody production following the administration of non-live vaccines in CAPS patients.

References:

[1] Brogan P, et al. Arthritis Rheumatol. 2015;67:(S10).

Disclosure of Interest: P. Brogan Grant/research support from: Novartis, Roche and SOBI, Consultant for: Novartis, M. Hofer Consultant for: Novartis, J. Kuemmerle-Deschner Grant/research support from: Novartis, SOBI, Baxalta, Consultant for: Novartis, B. Lauwerys: None declared, A. Speziale Employee of: Novartis, X. Wei Employee of: Novartis, R. Laxer Grant/research support from: Novartis for Database funding

DOI: 10.1136/annrheumdis-2017-eular.3349

THU0496 PULMONARY SYMPTOMS AS THE FIRST PRESENTATION OF KAWASAKI DISEASE IN CHILDREN

A. Gupta, A. Kumar, D. Suri, S. Singh. *Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India, Chandigarh, India*

Background: Kawasaki disease (KD) is a medium vessel vasculitis which predominantly affects children less than 5 years of age. Though principal clinical features are mucocutaneous, KD in children may have multiple systemic manifestations, including pulmonary, which may create diagnostic difficulties for the treating physician.

Objectives: We describe our experience of managing children with uncommon pulmonary presentation of KD.

Methods: Five hundred and sixty five (565) children were diagnosed with KD during the period from January 1993 to December 2016 in Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India. Nine children had pulmonary presentation of KD. A retrospective case review with respect to clinical presentation, radiological findings and treatment was done.
Results: Pulmonary presentation of KD was seen in 1.6% patients. Mean age at diagnosis of KD was 2.9years (range 9months – 4 years). 77.8% patients had no features suggestive of KD either on history or at presentation. First sign of KD was noted at a mean duration of 17.6 days (range 6–28 days) from the onset of symptoms. Periungual desquamation was the most common clinical sign seen in 66.6% patients followed by erythematous rash and perianal desquamation in 33.3% patients each.
Persistent fever, thrombocytosis and elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were seen in all patients. Microbiological investigations showed evidence of infection in only 2 patients – methicillin sensitive staphylococcus aureus in pus and positive mycoplasma agglutinin titre in one patient each. Parenchymal consolidation was the most common radiological finding (100%) followed by pleural effusion (55.5%), empyema (33.3%) and pneumothorax (11.1%). Coronary artery abnormalities were evident on echocardiography in 22.2% patients with dilatation of right coronary artery and left main coronary artery in 1 patient each.
All patients received intravenous antimicrobials for pneumonia. Intravenous immunoglobulin (IVIG) at 2g/kg was given after a mean duration of 24 days of onset of fever. Fever, which was unresponsive to intravenous antimicrobials, responded to IVIG therapy in all except 2 patients which required a second dose of IVIG. 55.5% patients required intercostal drainage tube (ICDT) insertion, 2 patients required streptokinase and 1 patient each required video assisted thoracoscopic surgery (VATS) and decortication. Mean follow up period was 15.9 months (range 0–62 months).
Conclusions: Pulmonary involvement in patients with KD is uncommon and is less commonly recognized. Unresolving pneumonia in a child who continues to be febrile despite adequate antimicrobials with elevated inflammatory markers can be a clue towards the diagnosis of KD. Early recognition can prevent delays in diagnosis and shorten the hospital stay.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6278

THU0497 RHEUMATOLOGICAL MANIFESTATIONS OF X-LINKED AGAMMAGLOBULINEMIA: PROFILE OF 17 CASES FROM A TERTIARY CARE CENTER IN NORTH INDIA

A. Gupta, D. Suri, A. Gupta, A. Rawat, S. Singh. *Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India, Chandigarh, India*

Background: X-linked agammaglobulinemia (XLA) is characterized by recurrent bacterial sino-pulmonary infections. Arthritis can be seen in 10–30% patients of hypogammaglobulinemia (1) and is usually a mono- or oligoarthritis of large joints, but polyarthritis has also been defined.
Objectives: We describe our experience of managing children with XLA who presented with rheumatological manifestations.
Methods: Sixty two children were diagnosed with XLA during the last 10 years in Primary Immunodeficiency Clinic, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh, India. Seventeen children had rheumatological manifestations. A retrospective case review with respect to clinical presentation, musculoskeletal findings and treatment was done.
Results: Rheumatological manifestations were seen in 27.4% patients of XLA. Thirteen out of 17 patients had a proven mutation in *Btk gene*. Mean age at symptom onset was 3.3 years (range 6 months – 13 years) and mean age at diagnosis of XLA was 5.6 years (range 1.5- 10 years). Rheumatological manifestations were seen at a mean age of 8.7 years (range 1.5- 20 years). In 2 patients, arthritis preceded the diagnosis of XLA while 10 patients developed rheumatological manifestations after the diagnosis of XLA. Arthritis as an initial presentation of XLA was seen in 5 patients.
Oligoarthritis was the most common presentation seen in 15 patients. Knee was the most commonly involved joint (11 patients) followed by ankle joint in 5 patients and shoulder, wrist and hip arthritis in 2 patients each. One patient each had arthritis involving proximal interphalangeal joints of both hands, clinical evidence of sacroiliitis and spondylodiscitis involving L4–5 and L5-S1 vertebrae. Three patients manifested as septic arthritis (fever, redness, warmth and pus in joint) involving shoulder, ankle and knee joint respectively.
Joint aspiration and/or arthrotomy had been performed in 8 patients, however cultures were sterile in all. Microbiological investigations for mycoplasma infection (viz. culture and polymerase chain reaction) in joint fluid/pus could not be performed due to unavailability. All patients received replacement intravenous immunoglobulin (IVIG - 400 mg/kg body weight) and co-trimoxazole prophylaxis. Eight patients received macrolide antimicrobials (erythromycin or azithromycin) for clinical suspicion of mycoplasma arthritis.
One patient expired during the course of his illness while four patients were lost to follow up. Arthritis showed clinical improvement after IVIG replacement therapy in remaining 12 patients with resolution of arthritis after first dose in 11 patients and after 6 months of replacement therapy in 1 patient. None of the patients had recurrence of joint symptoms on follow up, however radiological evidence of spondylodiscitis persisted in one patient.
Conclusions: Arthritis is a relatively frequent manifestation in patients with hypogammaglobulinemia. Family history and history of recurrent infections in a child with arthritis may provide a clue towards the diagnosis of primary immunodeficiency. Prompt institution of regular IVIG replacement therapy results in resolution of arthritis and prevents its recurrence.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6820

THU0498 PFAPA SYNDROME IN LARGE PEDIATRIC POPULATION: A SINGLE CENTER EXPERIENCE

E. Pehlivan, A. Adrovic, S. Sahin, K. Barut, O. Kul, O. Kasapcopur. *Pediatric Rheumatology, Istanbul University, Cerrahpasa Medical School, Istanbul, Turkey*

Background: Periodic fever, aphthosis, pharyngitis, and adenitis (PFAPA) syndrome is an auto-inflammatory condition of unknown etiology. It is the second most common auto-inflammatory disease in our country, following familial Mediterranean fever. Previous studies showed that tonsillectomy represents efficient treatment options.
Objectives: Our aim was to explore the main clinical features, response to tonsillectomy and long–term outcome of PFAPA pediatric patients in a single cohort. We assessed association of MEFV gene mutation with disease characteristics and treatment response.
Methods: We reviewed medical records of patients who were diagnosed with PFAPA syndrome between the January 2010 and June 2016. All of the recorded 562 patients were called by the telephone and 365 (65%) of them were reached. Demographic, clinical and therapeutically features were taken from the patients' medical records. Data on clinical course and the disease outcome were collected by using a structured questionnaire which was fulfilled during the phone conversation between investigator and patients parents.
Results: A total of 365 patients with PFAPA were examined: 154 (42%) of them were female. The mean age at disease onset, at diagnosis and at the investigation was 22.79±18.8, 41.7±21.7 and 77.14±31.35 months, respectively. The most common disease feature at the disease onset was: recurrent fever in 365 (100%), cryptic tonsillitis in 365 (100%) and aphtous stomatitis in 317 (88%). Sixty three (17%) patients met the criteria for both PFAPA and FMF. MEFV gene mutation analysis was performed in 93 (25%) patients and 51 of them (54%) had a heterozygous mutation in exon 10. Surgical treatment was performed in 158 (43%) patients. Complete clinical remission was achieved in 127 (80.3%) patients. Six (3%) showed no response to surgical treatment while 25 (15.8%) patients had a partial response. In patients with partial clinical response, frequency of fever attacks decreased significantly from 17.5 to 7.3 attack per year ($p<0.05$). Among patients who did not respond to tonsillectomy,11 (52.4%) were carrier of MEFV heterozygous mutation in exon 10. There was a statistically significant difference between patients with and without coexistence of FMF features, according to surgical treatment response ($p<0.05$).The mean age of resolution of PFAPA symptoms in patients who underwent tonsillectomy was 52±22.4 months and in patients without tonsillectomy 66±22.6 months.
Conclusions: Although PFAPA symptoms usually resolve before age of eight, some patients' complaints persist. FMF should be considered in tonsilloadenoidectomy unresponsive PFAPA patients, especially in endemic regions like Turkey. Tonsilloadenoidectomy seems to be an effective treatment option for pediatric PFAPA patients.
References:
[1] Vanoni F, Theodoropoulou K, Hofer M. PFAPA syndrome: a review on treatment and outcome. Pediatr Rheumatol Online J 2016;14:38.
[2] Batu ED, Kara Eroğlu F, Tsoukas P, et al. Periodic Fever, Aphthosis, Pharyngitis, and Adenitis Syndrome: Analysis of Patients From Two Geographic Areas. Arthritis Care Res (Hoboken) 2016;68:1859–1865.
[3] Celiksoy MH, Ogur G, Yaman E, et al. Could familial Mediterranean fever gene mutations be related to PFAPA syndrome? Pediatr Allergy Immunol. 2016;27:78–82.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4617

THU0499 ANTI-MULLERIAN HORMONE IN A COHORT OF YOUNG ADULT WOMEN WITH JUVENILE IDIOPATHIC ARTHRITIS

C. Di Mario[1], M.R. Gigante[1], A. Musto[1], A. Barini[2], A. Barini[2], B. Tolusso[1], G. Ferraccioli[1], E. Gremese[1]. *[1]Institute of Rheumatology; [2]Institute of Biochemistry and Clinical Biochemistry, Fondazione Policlinico Universitario A. Gemelli, Catholic University of the Sacred Heart, Rome, Italy*

Background: Juvenile Idiopathic Arthritis (JIA) represents one of more common chronic disease of the childhood, affects young people before sixteen and persists into their reproductive years. It is reported in one study that fertility was not impaired in JIA women but potentially it can be compromised by pharmacological treatments such as the prolonged immunosuppressive therapy used in young women patients (1). The Anti-Müllerian Hormone (AMH) is secreted from granulosa ovary cells and serum levels of Anti-Müllerian Hormone are used as a measure of ovarian reserve, reflecting the number of primary follicles.

Objectives: The aims of this study were to evaluate AMH serum levels in a cohort of young adult women affected from JIA, to compare these levels between patients and healthy controls and to assess whether the presence of the disease and the influence of previous exposure to disease-modifying antirheumatic drugs (DMARDs) and of other disease parameters may affect the ovarian reserve.
Methods: Forty women with a diagnosis of JIA, aged 18 to 25 years and with regular menses, and 20 healthy women age-matched were evaluated. Anti-Müllerian Hormone serum levels were measured according to a 2-stage enzyme-linked immunosorbent assay (ELISA) technique using a commercially available kit (AMH Gen II ELISA; Beckman Coulter). Clinical and demographic characteristics, disease duration, previous and current therapies disease activity score on 44 joints (DAS), health assessment questionnaire (HAQ) were performed at the time of blood sample.
Results: JIA patients had a mean age of 21.4±3.2 years, a disease duration of 11.5±6.6 years, a DAS of 1.22±0.58, and 12 (30%) were smokers. No significant differences were found in our cohort of JIA and healthy subjects in AMH serum levels (5.6±0.4 vs 6.6±0.6 ng/ml, respectively, p=0.5).
Considering the JIA cohort, 23 patients (57.4%) were treated with methotrexate (MTX) for a mean period of 2.1±3.1 years and 20 (50%) with anti-TNF drugs for 4.3±2.3 years. Twelve JIA women (30%) were treated with both MTX and anti-TNF. No correlations were found between AMH serum levels and patients age (p=0.6), disease duration (years) (p=0.67) and duration of therapy with MTX (p=0.5) or anti-TNF (p=0.11).
Dividing JIA patients according to MTX use, no differences were observed between MTX users and non users patients in AMH levels (6.0±0.5 vs 5.1±0.5 ng/ml, respectively, p=0.22), age, disease duration and other clinical characteristics. Patients expose to anti-TNF had AMH serum levels tendentially higher then non users patients (6.3±0.6 vs 4.9±0.5 ng/ml, respectively p=0.07).
Conclusions: In our JIA group of young adult JIA women, ovarian reserve seems not be changed by the presence of the disease, the long disease duration and the use of immunosuppressive drugs. These findings could be important for adult JIA patients.
References:
[1] Ostensen M et al. J Rheumatology 2000;27:1783–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4761

THU0500 PHOTOBIOSTIMULATION OF CHRONIC CERVICAL PAIN IN JUVENILE POLYARTHRITIS

C. Ailioaie, L.M. Ailioaie. *Dept. of Medical Physics, Iasi, Romania, "Al. I. Cuza" University, Iasi, Romania*

Background: Chronic pain management in juvenile arthritis constitutes a special provocation not only for the medical doctors, but also for the patients and parents. Despite the extensive use of the biological agents with high efficacy, combined with the multimodal therapies, chronic pain still remains an important issue for the public health, with implications on the activities of daily living and the scholar performances. Lasers could be used for transmitting biological messages and initiating metabolic changes within living cells: no more pain, much more energy, will contribute to muscular and joints repair.
Objectives: Aim of the present study was to evaluate the effects of photobiostimulation combined with DMARDs in patients with juvenile polyarthritis and chronic cervical pain.
Methods: 62 patients diagnosed with juvenile polyarthritis (ILAR criteria), 11.4 years mean age were randomly divided in Group I (42 patients treated with local laser biostimulation and methotrexate), comparatively with a Group II - control (20 patients) treated with methotrexate and *placebo* laser, for a period of 9 months. Group I received local laser biostimulation with a dose of 2.5 J/cm^2 in 14 latero-cervical painful points, corresponding to the 7 cervical vertebrae, 1 point on the insertion of sternocleido-mastoidian muscle on the styloid processus, and 1 point on each loco-regional submandibular lymphatic ganglions, using a GaAlAs laser probe of 670 nm, 25 mW output power and a modulation frequency of 10 Hz. 45 joules were applied daily as laser treatment, 10 sessions per month, repeated 3 times, in the 9 months. For all the patients, the main medication was methotrexate in a dose of 0.6 mg/kg (maximum 20 mg) per week, steroids and symptomatic drugs, when necessary. Tutors and the older children have signed the informed consent. Measurement of the subjective pain was on VAS (0 – 100 mm), and objective pain was assessed with an electronic device, the Algometer Commender. The range of motion for flexion/extension, and the rotation to the left/right of the cephalic extremity was measured with Dualer IQ Inclinometer.
Results: In the end of study, the level of chronic pain estimated with Commander Algometer decreased by 74.6% in Group I, compared with only 41% in the control Group, and the range of motion in the affected cervical segment assessed with Dualer Inclinometer increased by 66% in the first Group, compared with only 34% in *placebo* group.
Conclusions: Laser biostimulation proved to be an effective method for the complex management of chronic pain in juvenile polyarthritis.
References:
[1] Ravelli A, Martini A. Juvenile idiopathic arthritis. Lancet. 2007;369:767–778.
[2] Ravelli A, et al. Oral versus intramuscular methotrexate in juvenile chronic arthritis. Clin Exp Rheumatol. 1998;16:181–83.
[3] Ailioaie LM, Litscher G, Weber M, Ailioaie C, Litscher D, Chiran DA. Innovations and Challenges by Applying Sublingual Laser Blood Irradiation in Juvenile Idiopathic Arthritis. International Journal of Photoenergy 2014(2):1–8, June 2014. DOI: 10.1155/2014/130417.
[4] Ailioaie C, Lupusoru-Ailioaie LM. Beneficial effects of laser therapy in the early stages of rheumatoid arthritis onset. Laser Therapy.1999;Vol. 11–2, 79–87.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6831

THU0501 EFFICACY AND SAFETY OF METHOTREXATE AS MAINTENANCE THERAPY FOR CHILDREN WITH ANTI–N-METHYL-D-ASPARTATE RECEPTOR (NMDAR) ENCEPHALITIS: EXPERIENCE OF A SINGLE CENTER

D. Ramos-Bello, A.N. Rangel-Botello, G. Aguilera Barragan-Pickens, T.A. Luna-Zúñiga, A.J. Pedro-Martínez, G. Martínez-Flores, A. Bravo-Oro, C. Abud-Mendoza. *Unidad regional de Reumatología y Osteoporosis, Hospital Central "Dr. Ignacio Morones Prieto" y Facultad de Medicina de la Uaslp, SLP, SLP, Mexico*

Background: Autoimmune-mediated encephalitis (A-ME) in children remains as a diagnostic and therapeutic challenge (1). These patients have a 12% risk of relapse, which is usually more severe (2). We previously proposed the therapy with methotrexate (MTX) for this condition (3), and we are offering now additional data on its potential benefits.
Objectives: To describe the outcome of children with A-ME receiving MTX for at least one year after stabilization of symptoms.
Methods: In this retrospective study we recruited 11 patients (7 females) with A-ME, a mean age of 7.5 years (range 8 months - 14 years), and with a median follow up of 22 months. In all cases, anti-NMDAR antibodies (subunit NR1) were detected in the CSF. Data from these patients were collected by consulting medical records. Relapse of encephalitis was defined as new onset of symptoms occurring after at least 2 months of remission, in the absence of other CNS disease.
Results: Patients presented with seizures (n=10), behavioral changes (n=11), psychosis (n=11), speech problems (n=10), and autonomic/breathing dysregulation (n=9). Patients were initially treated with methylprednisolone pulses (n=11), rituximab (n=6), intravenous immunoglobulins (n=4), cyclophosphamide (n=3) and MTX (n=11). Complete remission was observed in all cases, and maintenance therapy with MTX (10 mg/m^2 BSA) was started in all them, with gradual tapering until it was stopped. Interestingly, no relapses have been observed in any case during the mean follow up. One patient had mild oral ulcers and other showed mild elevation of liver enzymes; both events remitted after discontinuing the treatment for a couple of weeks.
Conclusions: Since relapses in patients with A-ME are a relatively frequent, the immunosuppressive therapy to prevent them is fully justified (4). Moreover, MTX therapy in pediatric patients is safe and usually well tolerated (3,5,6). The recommended dose is less than 15 mg/m^2 BSA or 1 mg/kg, with a maximal dose of 40 mg and with folic acid supplementation. In this regard, our study suggests that MTX administration (10 mg/m^2 BSA) during at least one year is a viable and effective therapy for maintenance treatment of A-ME. Accordingly, we did not detect relapses in the 11 patients studied with a median follow up time of 22 months and with an acceptable safety profile.
References:
[1] AlHakeem AS, et al. Neurosciences (Riyadh). 2017;22:67–68.
[2] Titulaer MJ, et al. Lancet Neurol. 2013;12:157–165.
[3] Bravo-Oro A, et al. Rev Neurol. 2013;57:405–410.
[4] Lin JJ, et al. Pediatr Neurol. 2014;50:574–80.
[5] Weibel L, et al. Br J Dermatol. 2006;155:1013–20.
[6] Li SC, et al. Arthritis Care Res. 2012;64:1175–1185.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2726

THU0502 EFFICACY AND SAFETY OF CANAKINUMAB IN PATIENTS WITH STILL'S DISEASE: A POOLED ANALYSIS OF SJIA DATA BY AGE GROUPS

E. Feist[1], P. Quartier[2], B. Fautrel[3], R. Schneider[4], P. Sfriso[5], P. Efthimiou[6], L. Cantarini[7], K. Lheritier[8], K. Leon[9], C. Karyekar[9], A. Speziale[8]. *[1]Charite-Universitätsmedizin, Berlin, Germany; [2]Necker-Enfants Malades Hospital; [3]Pitie Salpetriere Hospital, Paris, France; [4]PRCSG, Cincinnati, United States; [5]University of Padova, Padova, Italy; [6]Weill Cornell Medical College, New York, United States; [7]University of Siena, Siena, Italy; [8]Novartis Pharma AG, Basel, Switzerland; [9]Novartis Pharmaceuticals Corporation, East Hanover, United States*

Background: Still's disease presents in paediatric and adult patients (pts) as a disease continuum with similar symptoms and pathophysiology.[1,2]
Objectives: To evaluate the efficacy and safety of canakinumab (CAN), a selective human anti-IL1 β monoclonal antibody, in SJIA pts from pooled data across 3 age groups (grps): children, adolescent and adults (the latter representing adult-onset Still's disease [AOSD] population).
Methods: Data of CAN treated pts were pooled from 4 SJIA studies (NCT00426218, NCT00886769, NCT00889863, NCT00891046). CAN was ad-

ministered at 4 mg/kg every 4 weeks (wk). Efficacy parameters (adapted ACR [aACR] paediatric responses, juvenile idiopathic arthritis [JIA] ACR responses, pts with inactive disease), CRP levels over 12 wk and safety were assessed by age grp. One study [NCT00426218] was excluded for efficacy outcomes.
Results: 216 children (2–<12 years [y]), 56 adolescents (12–<16 y) and 29 adults (≥16 y) were analysed for efficacy outcomes. The efficacy parameters across the 3 age grps were largely comparable (Table 1). The safety profile of CAN was similar across age grps (Table 2). One death was reported (adolescents grp). Clinical, laboratory and immunogenicity data showed no notable differences between the age grps.

Table 1. Responses by age grp and time point

Age group	%	aACR paediatric; n/N (%)		JIA ACR; n/N (%)	
		Day 15	Day 85	Day 15	Day 85
Children	≥30	158/216 (73.1)	90/133 (67.7)	169/216 (78.2	93/133 (69.9)
	≥70	109/216 (50.5)	77/133 (57.9)	111/216 (51.4)	77/133 (57.9)
	≥100	46/216 (21.3)	42/133 (31.6)	47/216 (21.8)	42/133 (31.6)
Adolescents	≥30	47/56 (83.9)	20/27 (74.1)	47/56 (83.9)	20/27 (74.1)
	≥70	33/56 (58.9)	18/27 (66.7)	33/56 (58.9)	18/27 (66.7)
	≥100	15/56 (26.8)	8/27 (29.6)	15/56 (26.8)	8/27 (29.6)
Adults	≥30	25/29 (86.2)	15/18 (83.3)	25/29 (86.2)	15/18 (83.3)
	≥70	19/29 (65.5)	13/18 (72.2)	19/29 (65.5)	12/18 (66.7)
	≥100	4/29 (13.8)	4/29 (13.8)	4/18 (22.2)	4/18 (22.2)

Age group	Inactive disease; n/N (%)		CRP, median; mg/L (n/N)	
	Day 15	Day 85	Day 15	Day 85
Children	40/216 (18.5)	32/133 (24.1)	12.00 (211/216)	9.75 (168/216)
Adolescents	18/56 (32.1)	10/27 (37.0)	10.00 (55/56)	8.40 (45/56)
Adults	6/29 (20.7)	8/18 (44.4)	4.50 (26/29)	7.80 (23/29)

Table 2. Adverse events (AEs)

	Children, n (%) N = 233	**Adolescents**, n (%) N = 60	**Adults**, n (%) N = 31
AEs (at least 1)	202 (86.7)	53 (88.3)	27 (87.1)
AEs leading to study drug discontinuation	26 (11.2)	10 (16.7)	6 (19.4)
AEs most common/special interest			
Infections and infestations	176 (75.5)	42 (70.0)	23 (74.2)
Gastrointestinal disorders	122 (52.4)	32 (53.3)	18 (58.1)
Musculoskeletal and connective tissue disorders	119 (51.1)	33 (55.0)	16 (51.6)
Opportunistic infections	3 (1.3)	4 (6.7)	1 (3.3)
Neutropenia	11 (4.7)	2 (3.3)	0
SAE (at least 1)	81 (34.8)	25 (41.7)	9 (29.0)

Conclusions: Pooled analyses indicate similar efficacy of CAN across all the age grps of children, adolescents and adult SJIA pts. There were no meaningful differences in safety profiles across the different age grp. These analyses suggest similar efficacy of CAN in AOSD pts as observed in the SJIA pts.
References:
[1] Jamilloux. Immunol Res 2015;61:53–62.
[2] Nirmala. Pediatric Rheumatol 2015;13:50.
Disclosure of Interest: E. Feist Grant/research support from: Novartis, Consultant for: Novartis, P. Quartier Grant/research support from: Abbvie, Novartis, Pfizer, Chugai-Roche, Consultant for: Abbvie, Novartis, Pfizer, Sobi, Roche, Speakers bureau: Abbvie, Novartis, Sobi, Roche, B. Fautrel Grant/research support from: AbbVIe, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgène, Hospira, Janssen, Lilly, MSD, NORDIC Pharma, Pfizer, Roche, SOBI, UCB, R. Schneider Grant/research support from: Novartis, Consultant for: Novartis, P. Sfriso Consultant for: Novartis, P. Efthimiou: None declared, L. Cantarini Consultant for: Sobi, Novartis, Abbvie, K. Lheritier Employee of: Novartis, K. Leon Employee of: Novartis, C. Karyekar Employee of: Novartis, A. Speziale Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1979

THU0503 IDENTIFICATION OF OPTIMAL SUBCUTANEOUS (SC) DOSES OF TOCILIZUMAB IN CHILDREN WITH POLYARTICULAR-COURSE JUVENILE IDIOPATHIC ARTHRITIS (PCJIA)

F. De Benedetti[1], N. Ruperto[2], D. Lovell[3], A.V. Ramanan[4], R. Cuttica[5], J.E. Weiss[6], M. Henrickson[3], H. Schmeling[7], J. Anton[8], K. Minden[9], J. Hsu[10], K. Bharucha[11], S. Wimalasundera[12], A.K. Kadva[11], R. Upmanyu[12], N.L. Mallalieu[10], A. Martini[2], H. Brunner[3]. *[1]IRCCS Ospedale Pediatrico Bambino Gesù, Rome; [2]PRINTO Coordinating Ctr, Genoa, Italy; [3]PRCSG, Cincinnati Children's Hosp Med Ctr, Cincinnati, United States; [4]Bristol Royal Hosp for Children, Bristol, United Kingdom; [5]Hosp Gral de Niños Pedro Elizalde, Buenos Aires, Argentina; [6]Hackensack U Med Ctr, Hackensack, United States; [7]Alberta Children's Hosp/U Calgary, Calgary, Canada; [8]Hosp Sant Joan de Deu, Barcelona, Spain; [9]Charité U Med Berlin, Berlin, Germany; [10]Roche Innovation Ctr, New York; [11]Genentech, S San Francisco, United States; [12]Roche Products Ltd, Welwyn Garden City, United Kingdom*

Background: Efficacy and safety of intravenous (IV) tocilizumab (TCZ) have been shown in patients (pts) with pcJIA.[1]
Objectives: Determine appropriate dosing regimens of SC TCZ in pcJIA.
Methods: Pts were aged 1–17 y with pcJIA, inadequate response/intolerance to MTX and TCZ-naive or receiving TCZ IV with adequate disease control. TCZ SC was administered open label by body weight (BW)–based dosing modeled on IV dosing in pcJIA and SC dosing in adult rheumatoid arthritis: pcJIA pts <30kg received TCZ 162mg every 3 wks (Q3W) and pts ≥30kg received TCZ 162mg Q2W for 52 wks. Safety, efficacy (exploratory) and model-computed pharmacokinetic (PK) and pharmacodynamic (PD) parameters were assessed.
Results: 52 pts were enrolled; 27 <30kg and 25 ≥30kg BW; 85% and 56% were TCZ naive. Since no notable difference in steady state PK occurred in naive vs non-naive pts, pooled data are shown. Median C_{min} was similar between BW groups and higher than with TCZ IV (TCZ IV median C_{min}: 3.2 μg/mL for 10mg/kg <30kg BW and 7.3 μg/mL for 8mg/kg ≥30kg BW) ensuring adequate exposure from SC doses. Median C_{max} was lower from SC than IV dosing. Changes in PD parameters for TCZ-naive pts were consistent with those for TCZ IV. JADAS-71 generally improved (Table), with trends consistent with those for TCZ IV. Infections were the most frequent adverse event (AE), reported in 36 pts; 2 serious infections occurred in 1 pt. Injection site reactions occurred in 15% pts in the <30kg group and 44% pts in the ≥30kg group. The most common symptoms were erythema, swelling, hematoma, pain and pruritus. No serious hypersensitivity, AE leading to withdrawal, opportunistic infection, serious hepatic AE or death occurred. Overall there were 4 serious AEs in 3 pts (7.9/100 pt-y, consistent with that for TCZ IV).

	TCZ 162mg SC Q3W, BW <30kg (n=27)	TCZ 162mg SC Q2W, BW ≥30kg (n=25)
Model-computed steady state PK parameters, median [range]		
C_{min}, μg/mL	13.4 [0.2, 52.3]	12.7 [0.2, 23.8]
C_{max}, μg/mL	62.4 [39.4, 121.1]	29.7 [7.6, 50.3]
$AUC_{12weeks}$, μg/mL×day	2998 [1465, 7708]	1933 [324, 3098]
Change from baseline to week 52[a] in PD markers and efficacy, median [range]; TCZ-naive pts		
IL-6, pg/mL	27.3 [3.5, 173.9], n=11	12.2 [–6.2, 30.9], n=9
sIL-6R, ng/mL	612.1 [399.4, 808.4], n=14	429.3 [245.5, 585.6], n=11
CRP, mg/L	–1.3 [–17.0, 0.5], n=21	–0.8 [–22.9, 0.0], n=12
ESR, mm/h	–11.0 [–40.0, 0.0], n=21	–6.0 [–35.0, 0.0], n=12
JADAS-71	–16.8 [–40.3, –4.4], n=21	–12.9 [–48.1, –2.3], n=12

[a]Week 51 for Q3W group. AUC, area under the concentration curve; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IL-6, interleukin-6; sIL-6R, soluble IL-6 receptor.

Conclusions: The BW-based TCZ SC dosing regimens for pcJIA provided adequate exposure to support efficacy comparable to that for TCZ IV, with an acceptable benefit-risk profile.
References:
[1] Brunner HI et al. Ann Rheum Dis 2014;74:1110–7.
Disclosure of Interest: F. De Benedetti Grant/research support from: Novartis, Roche, Pfizer, SOBI, AbbVie, Novimmune, BMS, Sanofi, N. Ruperto Consultant for: AbbVie, Amgen, Alter, AstraZeneca, Baxalta Biosimilars, Biogenidec, Boehringer, BMS, Celgene, CrescendoBio, EMD Serono, Hoffmann-La Roche, Italfarmaco, Janssen, MedImmune, Medac, Novartis, Novo Nordisk, Pfizer, Sanofi Aventis, Servier, Takeda, UCB Biosciences GmbH, Speakers bureau: AbbVie, Amgen, Alter, AstraZeneca, Baxalta Biosimilars, Biogenidec, Boehringer, BMS, Celgene, CrescendoBio, EMD Serono, Hoffmann-La Roche, Italfarmaco, Janssen, MedImmune, Medac, Novartis, Novo Nordisk, Pfizer, Sanofi Aventis, Servier, Takeda, UCB Biosciences GmbH, D. Lovell Grant/research support from: NIH, NIAMS, Consultant for: Astra-Zeneca, Bristol Meyers Squibb, AbbVie, Pfizer, Roche, Novartis, UBC, Forest Research Institute, Horizon, Johnson & Johnson, Biogen, Takeda, Genentech, GlaxoSmithKline, Boehringer Ingelheim, Celgene, Janssen, A. Ramanan Speakers bureau: Roche, AbbVie, R. Cuttica Consultant for: Roche, Novartis, Lilly, GlaxoSmithKline, Bristol-Myers Squibb, Janssen, Speakers bureau: Roche, Novartis, Lilly, GlaxoSmithKline, Bristol-Myers Squibb, Janssen, J. Weiss: None declared, M. Henrickson: None declared, H. Schmeling Grant/research support from: Janssen, Pfizer, UCB Biosciences GmbH, J. Anton Grant/research support from: Roche, K. Minden Grant/research support from: AbbVie, Pfizer, Roche, Speakers bureau: AbbVie, Pfizer, Roche, Genzyme, Pharm-Allergan, J. Hsu Employee of: Roche, K. Bharucha Employee of: Genentech, S. Wimalasundera Employee of: Roche Products Ltd., A. Kadva Employee of: Genentech, R. Upmanyu Employee of: Roche Products Ltd., N. Mallalieu Shareholder of: Roche, Employee of: Roche, A. Martini Consultant for: Abbvie, Boehringer, Celgene, CrescendoBio, Janssen, MedImmune, Novartis, NovoNordisk, Pfizer, Sanofi Aventis, Vertex, Servier, Speakers bureau: Abbvie, Boehringer, Celgene, CrescendoBio, Janssen, MedImmune, Novartis, NovoNordisk, Pfizer, Sanofi Aventis, Vertex, Servier, H. Brunner: None declared
DOI: 10.1136/annrheumdis-2017-eular.2483

THU0504 QUANTIFYING PHYSICAL EDUCATION ATTENDANCE AND ITS RELATIONSHIP TO PAIN SEVERITY AND FATIGUE IN ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS – RESULTS FROM THE GERMAN NATIONAL PAEDIATRIC RHEUMATOLOGICAL DATABASE

F. Milatz[1], M. Niewerth[1], N. Geisemeyer[1], J. Peitz[2], C. Rietschel[3], T. Lutz[4], A. Holl-Wieden[5], K. Minden[1,6]. *[1]Epidemiology Unit, German Rheumatism Research Center Berlin, Berlin; [2]Pediatric Rheumatology Centre, Asklepios Clinic, Sankt Augustin; [3]Pediatric Rheumatology, Clementine Children's Hospital, Frankfurt/Main; [4]Medical Centre for Children and Adolescents, University Hospital Heidelberg, Heidelberg; [5]Children's Hospital, University Hospital Würzburg, Würzburg; [6]Children's University Hospital, Charité University Hospital, Berlin, Germany*

Background: Regular physical education (PE) can help adolescents achieve the recommended amount of daily physical activity and provide immediate health benefits, by positively affecting musculo-skeletal development, mental health and social behavior. Adolescents with juvenile idiopathic arthritis (JIA) are less physically active and have lower fitness levels than their healthy peers [1]. Moreover, pain and fatigue are one of the most frequent complaints and identified as one of the causes behind impaired (social) functioning [2].
Objectives: To describe the participation rate in PE and to assess its relationship to pain and fatigue in adolescents with JIA.
Methods: Cross-sectional data of adolescents with JIA recorded in the National Paediatric Rheumatological Database (NPRD) in the year 2015 were considered for the analyses. Disease characteristics were provided by rheumatologists along with patient-reported outcomes and participation in PE. Relationship to PE was assessed by using spearman's correlation.
Results: In 2015, a total of 3,289 adolescents with JIA (females 66%, mean disease duration 5 years, persistent oligoarthritis 30%) aged 13 to 17 were recorded. About 60% of the patients reported to participate in PE "always" (56% of girls, 69% of boys), whereas about 18% stated to be fully exempt from participating in PE (20% of girls, 14% of boys). Significant differences were observed among JIA subtypes, whereby patients with enthesitis-related arthritis participated more frequently than patients with rheumatoid factor-positive polyarthritis (64% vs. 46%). The mean pain level was 2.1, the mean fatigue level 1.8. Participation in PE was negatively correlated with self-reported pain intensity ($r=-0.43$) and fatigue ($r=-0.32$). Significant associations were found between PE attendance and age, sex, disease duration, functional status as well as disease activity measured by CHAQ and JADAS3–10, respectively ($p<0.05$).
Conclusions: 6 of 10 adolescents with JIA participate in PE always, whereby higher rates of self-reported attendance are associated with less severe pain and fatigue. Since exercise programs in JIA lead to significant improvements in quality of life, it is likely that physical education attendance plays an important role in pain reduction and social functioning improvement in JIA.
References:
[1] van Brussel M et al. Aerobic and anaerobic exercise capacity in children with juvenile idiopathic arthritis. Arthritis Rheum 2007;57:891–7.
[2] Eyckmans L et al. What does it mean to grow up with juvenile idiopathic arthritis? A qualitative study on the perspectives of patients. Clin Rheumatol. 2011;30:459–65.
Acknowledgements: The National Paediatric Rheumatological Database has been funded by the German Children Arthritis Foundation (Deutsche Kinder-Rheumastiftung).
Disclosure of Interest: F. Milatz: None declared, M. Niewerth: None declared, N. Geisemeyer: None declared, J. Peitz: None declared, C. Rietschel: None declared, T. Lutz: None declared, A. Holl-Wieden: None declared, K. Minden Speakers bureau: Pfizer, Roche, Pharm-Allergan
DOI: 10.1136/annrheumdis-2017-eular.4744

THU0505 LOW LITERACY BUT NOT PARENTAL SMOKING OR BREAST FEEDING WORSENS OUTCOME IN JUVENILE IDIOPATHIC ARTHRITIS IN A LOW INCOME POPULATION

F.A.C. Rocha[1], J.I. Vasques[1], L.N. Rocha[1], M.G. Aguiar[1], J.P.E. Accioly[1], C.N. Lechiu[1], L.H.A. Costa[1], M.F.C.D. Silva[2], A.R.X. Feitosa[2], H.A.L. Rocha[3], C.N. Rabelo Jr.[2]. *[1]Internal Medicine, Universidade Federal Do Ceara; [2]Pediatric Rheumatology, Hospital Geral de Fortaleza; [3]Health Department, Universidade Federal Do Ceara, Fortaleza - CE, Brazil*

Background: JIA data from underdeveloped regions are scant. We evaluated JIA patients living in low latitude (3º43'S), highly exposed to sunlight. We have shown their mean serum vitamin D levels as the higher ever reported, being not associated to disease status. Here are data on monthly income, breastfeeding, parental smoking, and literacy in this JIA cohort.
Methods: Clinical and demographic data [n (%)] from 165 JIA patients followed between May 2015 - Dec 2016 in two reference outpatient centers in Fortaleza-CE Brazil were consecutively collected. Family income (more or less than 300 US$/month), breast feeding (more or less than 3 months), literacy [more or less than 8 school-years (SY)], and parental smoking (present/absent) were compared using Juvenile Arthritis Disease Activity Score (JADAS27), Childhood Health Assessment Questionnaire (CHAQ) and presence of deformities as prognostic outcomes.
Results: Mean age was 14±4.9 years with 94 (56.9); 63 (38), 40 (24), 37 (22.4), 19 (11.5), 5 (3), and 1 (0.6) of the polyarticular, enthesitis-related, oligoarticular, systemic, undifferentiated, and psoriatic categories, respectively. Mean total CHAQ was 0.4±0.58 with a trend to be higher in polyarticular (0.55±0.69) than oligoarticular (0.3±0.4) category as well as higher JADAS 27 and more deformities in the former. Among 97 respondents, all but one patient was ever breastfed with 71 (73) for more than 3 months; 15 (17) out of 86 mothers were smokers and 28 (33.7) out of 83 smoked among family respondents; 49 (56.3) out of 87 parents had less than 8 SY and only 3 had superior level; 32 (37.6) out of 85 respondents earned less than 300US$. Lower literacy was associated to worse CHAQ ($p=0.021$). Neither maternal/family smoking nor breastfeeding time was associated to outcome. Lower income *per se* did not affect outcome.
Conclusions: This is the largest JIA database coming from an equatorial region reporting social and environmental aspects. Low literacy predominates, meaning more than half with less than elementary school, affecting prognosis. There is a low income profile and most family constituents do not smoke. Different from other countries, polyarticular category prevails despite low mean CHAQ *vis-à-vis* data from wealthy regions. Breast feeding for more than 1 month is almost universal and having breastfed for more than 3 months did not appear to influence prognosis
Acknowledgements: Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq - Grant 459334/2014–0
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5190

THU0506 ASSOCIATION OF NEUTROPHIL-TO-LYMPHOCYTE RATIO, PLATELET-TO-LYMPHOCYTE RATIO, PLATELET INDICES AND SERUM AMYLOID A LEVELS IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

F. Dörtbaş[1], E. Comak[2], E. Isıyel[3]. *[1]Rheumatology, Emsey Hospital, Istanbul; [2]Pediatric Nephrology and Rheumatology, Akdeniz University, Antalya; [3]Pediatric Nephrology and Rheumatology, Kocaeli Derince Training and Research Hospital, Kocaeli, Turkey*

Background: Familial mediterranean fever (FMF) is an autosomal recessive, inherited, autoinflammatory disease characterized by recurrent, self-limited bouts of fever and inflammation. Persistent subclinical inflammation was related to increased risk of developing the serious complications, such as life- threatening amyloid a (AA) amyloidosis. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and platelet indices [mean platelet volume (MPV) and platelet distribution width (PDW)] are simple, inexpensive, and useful markers to determine inflammation. Although, there have been a lots of data regarding inflammatory markers in FMF, little information was available the relationship between NLR, PLR, MPV and serum amyloid A levels.
Objectives: The aim of this study was to investigate association of NLR, PLR, platelet indices and serum amyloid A levels in children with FMF
Methods: The medical records of children with FMF were reviewed retrospectively. Information including demographic features, clinical and laboratory findings, SAA and C-reactive protein (CRP) levels, type of MEFV mutation were collected from the hospital's computerized database following approval by the local ethics commitee. The NLR and PLR were calculated from a complete blood count. Children (<7 years old) was excluded from study due to age related features of neutrophil-to-lymphocyte ratio.
Results: Our study group included 127 children (60 males, 67 females) with FMF, diagnosed according to the Turkish pediatric FMF criteria. Their mean age was 11.35±3.69 years, their mean age at time of disease onset was 8.73±3.93 years, and their mean follow up period was 28.32±2.90 months. Thirty two children (25.2%) were homozygous, 56 children (44.0%) were compound heterozygous and 39 children (30.7%) were heterozygous for MEFV gene. In study population, the mean SAA levels, C-reactive protein (CRP) levels and e*rythrocyte* sedimentation rate (ESR) were 9.21±13.88 mg/L, 1.38±2.31 mg/dl and 16.64±12.59 mm/hour, respectively. Significant positive correlations were found between SAA, ESR, CRP and NLR ($r=0.2$, $p=0.02$; $r=0.28$, $p=0.001$; $r=0.32$, $p=0.001$, respectively). Hovewer, we did not find any significant correlation between SAA, ESR, CRP and platelet indices (MPV, PDW) and PLR (all $p>0.05$).
Conclusions: Our finding suggest that simply calculating NLR from complete blood count may be used as an additional indicator of inflammation in children with FMF. But, platelet indices and PLR cannot be used as a laboratory markers predicting inflammation in these children.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5149

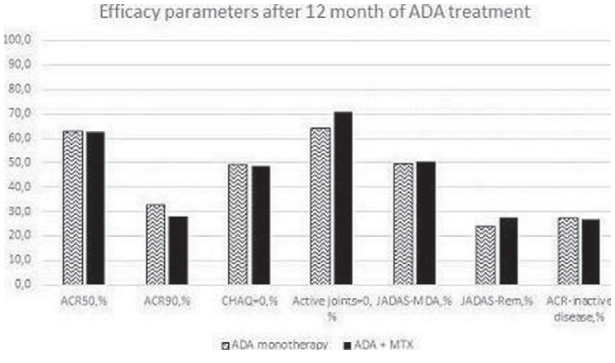
THU0507 LONG-TERM EXPERIENCE WITH ADALIMUMAB FOR THE TREATMENT OF JUVENILE IDIOPATHIC ARTHRITIS. 5- YEAR DATA FROM THE GERMAN BIKER REGISTRY

A. Klein[1], K. Minden[2], I. Foeldvari[3], G. Ganser[4], J.P. Haas[5], R. Trauzeddel[6], A. Hospach[7], F. Weller-Heinemann[8], G. Horneff[1] on behalf of BIKER collaborative group. *[1]Asklepios, Sankt Augustin; [2]Charité, Berlin; [3]Private office, Hamburg; [4]Ped Rheumatol, Sendenhorst; [5]German Ped Rheum Centre, Garmisch-Partenkirchen; [6]Chidrens Hospital, Helios Klinikum Berlin Buch, Berlin; [7]Paediatric Rheumatology, Olgahospital, Stuttgart; [8]Paediatric Rheumatology, Klinikum Bremen Mitte, Bremen, Germany*

Background: Since the approval of Adalimumab (ADA) for treatment of juvenile idiopathic arthritis (JIA), it has become a valuable option, which significantly improved the outcome of patients.
Objectives: To report efficacy (as observed) and safety of ADA in clinical practice.
Methods: Data from the German BiKeR register from 2011 to 2016 are reported. Baseline patient characteristics, treatment response and safety data were compared. Treatment response was analyzed using JIA-ACR criteria, JADAS score and improvement of functional status (Childhood Health Assessment Questionnaire disability index, CHAQ), JIA-ACR-scores, JADAS10-minimal disease activity (MDA), JADAS-remission and ACR-inactive disease criteria were analysed.
Results: 589 non-systemic JIA patients exposed to Adalimumab with at least one follow-up report were identified in the German BIKER registry, representing 1143.9 patient years (PY) of exposure to ADA and 1206.5 observation years including 90 days after discontinuation. At Baseline, 58.2% received combination with methotrexate (MTX). Patients on combination treatment had more frequently ANA, less frequently HLA-B27, had higher JADAS 10 and more often received systemic steroids (9.9% vs. 22.2%, p=0.0002). ADA dosage was 0.8mg/kg in both cohorts.
At month 12 JIA-ACR 30/50/70/90 and JADAS-MDA/-remission/ACR-inactive disease was reached by 66/63/49/33/50/24/27% on monotherapy with ADA and 68/63/45/28%/50/28/27 on combination of ADA and MTX (not significant). Response rates at month 24 were 67/66/54/35/65/32/29% on ADA monotherapy and 67/61/46/31/57/35/30% on ADA+MTX combination cohort (not significant).
The rate (/100PY) of all adverse events (AE)/serious AE/infections/serious infections/uveitis events was 52.3/2.2/16.4/4.6 upon monotherapy and 65.3/5.1/2.3/16.4/6.2 upon combination. Only rates for any AE were significantly higher upon combination (p=0.008) as well as rate of elevated transaminase (p=0.01). Rate of patients with an uveitis event was higher upon combination (9.6% vs. 5.3%, p=0.007)

Table 1

	ADA monotherapy	ADA + MTX	P
N, female (%)	223 (70)	343 (70)	n.s.
Age onset/disease duration; mean (SD)	7.1 (±4.3)/6.0 (3.7)	6.5 (4.5)/5.0 (3.7)	n.s.
RF neg. Poylarthritis, n (%)	77 (34.5)	126 (36.7)	n.s.
RF pos. Poylarthritis, n (%)	7 (3.1)	17 (5.0)	n.s.
pers. Oligoarthritis, n (%)	12 (5.4)	29 (8.5)	n.s.
ext. Oligoarthritis, n (%)	59 (26.5)	95 (27.7)	n.s.
ERA, n (%)	49 (22.0)	47 (13.7)	p=0.01
PsA, n (%)	15 (6.7)	22 (6.4)	n.s.
unclassified JIA, n (%)	4 (1.8)	7 (2.0)	n.s.
ANA/B27, n (%)	111 (49.8)/ 56 (25.1)	210 (61.2)/ 57 (16.6)	p=0.009/ p=0.02
Comorbidity Uveitis, n (%)	19 (8.5)	32 ((9.3)	n.s.
Baseline active joints mean (SD)	3.5 (5.6)	3.8 (5.5)	n.s.
Phy VAS mean (SD)	37.6 (28.6)	42.7 (28.3)	n.s.
Pat VAS mean (SD)	27.9 (24.9)	30.9 (24.9)	n.s.
CHAQ mean (SD)	0.4 (0.6)	0.4 (0.6)	n.s.
ESR mean (SD)	14.3 (15.2)	18.1 (17.7)	n.s.
CRP mean (SD)	4.3 (7.4)	8.3 (15.8)	n.s.
Baseline JADAS10 mean (SD)	9.9 (7.0)	11.3 (7.1)	p=0.02



Conclusions: Adalimumab demonstrated high response rates and an acceptable risk profile. Efficacy and safety of monotherapy was not inferior to combination therapy with MTX.
Disclosure of Interest: A. Klein: None declared, K. Minden Speakers bureau: Abbvie, Pfizer,Roche,Genzyme,Pharm-Allergan, I. Foeldvari: None declared, G. Ganser: None declared, J. Haas: None declared, R. Trauzeddel: None declared, A. Hospach: None declared, F. Weller-Heinemann: None declared, G. Horneff Grant/research support from: Abbvie, Chugai, Novartis, Pfizer,Roche
DOI: 10.1136/annrheumdis-2017-eular.3457

THU0508 PSYCHOLOGICAL FEATURES OF CHILDREN WITH RHEUMATIC DISEASES

I. Chyzheuskaya[1], L. Byelyaeva[1], R. Filonovich[2], L. Zajtseva[2]. *[1]Pediatrics, Belarusian Medical Academy of Postgraduate Education; [2]Pediatrics, 4th City Children's Clinical Hospital of Minsk, Minsk, Belarus*

Background: Rheumatic diseases (RD) in children are characterized by a wide spectrum of clinical manifestations, and variability of flow, the defeat of many body systems, including the musculoskeletal system, which often leads to early disability. The disease brings the children not only physical suffering and psychological distress as a result of the pathological process may be sufficiently stable defects in appearance, affecting the minds of the growing person.
Objectives: To study the psychological characteristics of children with rheumatic diseases.
Methods: 167 patients with RD were examined in the period from 2008 to 2015. In the I group included 115 children with juvenile idiopathic arthritis (JIA) (mean age 11,9±3,4 years), II group consisted of 34 children with juvenile scleroderma (JS) (mean age 12,4±2,8 years), III - 18 children with systemic lupus erythematosus (SLE) (mean age 13,1±1,7 years). As control group examined 30 healthy children aged 9–17 years (mean age 12,93±0,4 years). To investigate the expression of reactive anxiety (RA) and personal anxiety (PA) in children older than 9 years was used scale Ch.D.Spielberg. In order to study the intensity of anxiety was used M.Luscher color test. To identify the individual psychological characteristics of the individual patient questionnaire used G.J.Eysenck for teenagers, consisting of 60 questions, including the scale of extroversion, introversion, neuroticism and the scale of "the scale of lies". Testing patients and interpretation of the results was carried out together with a psychologist.
Results: The test Spielberg results indicate that significantly more ($P<0.001$), medium and high levels of anxiety both reactive and personal, occurred in children with RD. This suggests the presence of children with RD border states with the threat of self-assessment features, reducing the threshold of resistance to stressful situations. The average RA and PA indices were significantly higher ($P<0.001$) in children with RD in comparison with indicators of reactive and personal anxiety in children in the control group (46,09±0,88 points for the JS, 43,77±1,37 points for JIA, 45,07±1,83 points for SLE and 27,6±0,62 points for the control group, respectively, RA; 42,22±1,68 points for the JS, 37,84±1,27 points for the JIA, 44,76±0,88 points for SLE and 28,7±0,51 points, respectively, RA for the control group).
Results of the study with the help of M.Lusher's color test revealed the intensity of anxiety in children with JS, SLE and JIA. Evaluation results of the study showed that children and adolescents with RD clearly manifested trend bias pri-mary colors on the 6,7,8 positions, and more - in the first place.
In order to identify characteristics of temperament in patients aged 13–17 years were asked to complete a questionnaire G.J.Eysenck for undergrowth Cove. The majority of surveyed teens both clinical groups manifest emotional instability (73.3% of patients with JS and 70% of patients with JIA) and features typical of introversion (60% of patients with SS and 68% of patients with JIA) (verified differences were found) between the groups. According to G.J.Eysenck, high rates of introversion in conjunction with emotional instability correspond to the alarm state.
Conclusions: As a result, psychometric studies found that the characteristic of emotional tension, anxiety, isolation for children with RD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6869

THU0509 IMPROVEMENT OF DISEASE ACTIVITY IN PATIENTS WITH COLCHICINE-RESISTANT FMF, HIDS/MKD AND TRAPS ASSESSED BY AUTOINFLAMMATORY DISEASE ACTIVITY INDEX (AIDAI): RESULTS FROM THE CLUSTER TRIAL

I. Kone-Paut[1], M. Piram[1], S. Benseler[2], M. Hofer[3], H. Lachmann[4], H.M. Hoffman[5], M. Gattorno[6], J. Frenkel[7], J.B. Kuemmerle-Deschner[8], S. Ozen[9], J. Levy[10], C.S. Karyekar[11], F. De Benedetti[12]. *[1]APHP, CHU de Bicêtre, Univ Paris Sud, le Kremlin Bicêtre, France; [2]Alberta Children's Hospital, Calgary, Canada; [3]University of Lausanne, Lausanne, Switzerland; [4]UK National Amyloidosis Centre, London, United Kingdom; [5]University of California, la Jolla, United States; [6]G. Gaslini Institute, Genoa, Italy; [7]University Medical Center, Utrecht, Netherlands; [8]University Hospital Tuebingen, Tuebingen, Germany; [9]Hacettepe University, Ankara, Turkey; [10]BIOP, Reinach, Switzerland; [11]Novartis Pharmaceuticals Corporation, East Hanover, United States; [12]IRCCS Ospedale Pediatrico Bambino Gesú, Rome, Italy*

Background: AIDAI is a novel validated tool for assessment of disease activity in autoinflammatory diseases.[1] CLUSTER study (NCT02059291) demonstrated that canakinumab (CAN; an anti- IL-1β antibody) is efficacious in resolving active flare and in preventing new flare in patients (pts) with colchicine resistant familial Mediterranean fever (crFMF), hyper-IgD syndrome/mevalonate kinase deficiency (HIDS/MKD) and TNF receptor-associated periodic syndrome (TRAPS).[2]

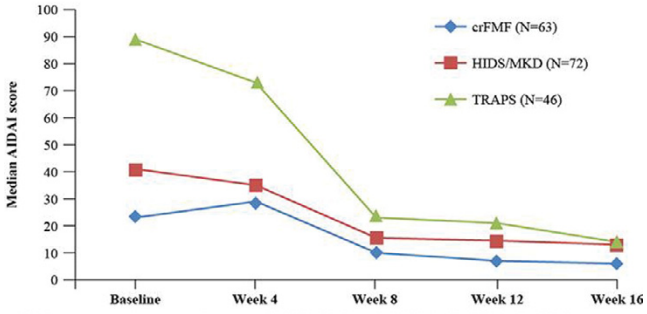
Objectives: To assess AIDAI score and evaluate correlation between AIDAI and disease/response characteristics over 16 weeks (wks) of CAN treatment in CLUSTER.
Methods: CLUSTER study design and results have been presented.[2] AIDAI was calculated as the sum of 12 items[1] for 30 consecutive days. AIDAI score was calculated if the first score was recorded ≥29 days before baseline (BL). Missing items were imputed beyond last evaluable measurement by LOCF. Proportion of pts with inactive disease (ID; AIDAI score <9) was calculated at Wk 16. Correlation analysis of AIDAI with C-reactive protein (CRP), serum amyloid A (SAA), physician global assessment (PGA) and sheehan disability score (SDS), and child health questionnaire–psychological/physical (CHQ–PsCS/PCS) and short form 12–physical/mental (SF12–PCS/MCS) component summaries were performed at BL and Wk 16, with significance set at $p<0.05$.
Results: Median AIDAI scores decreased over time (Fig 1). Proportion of pts with ID at Wk 16 was 52% in crFMF, 40% in HIDS/MKD and 46% in TRAPS cohorts. AIDAI at Wk 16 correlated significantly with: SDS in all 3 cohorts; PGA in HIDS/MKD and TRAPS; SF12–MCS in crFMF and HIDS/MKD (Table 1). CRP and SAA did not correlate with AIDAI.

Table 1. Correlation between AIDAI and disease activity/response variables at Week 16

	Correlation coefficient (95% CI)		
	crFMF (N=63)	HIDS/MKD (N=72)	TRAPS (N=46)
CRP	–0.12 (–0.36; 0.14)	0.23 (–0.01; 0.45)	0.12 (–0.19; 0.42)
SAA	–0.01 (–0.27; 0.25)	–0.05 (–0.30; 0.21)	0.06 (–0.26; 0.37)
PGA	0.23 (–0.02; 0.46)	**0.35§ (0.12; 0.55)**	**0.73* (–0.54; 0.85)**
CHQ – PsCS	–0.18 (–0.56; 0.26)	–0.25 (–0.55; 0.11)	–0.33 (–0.72; 0.22)
CHQ – PCS	–0.33 (–0.66; 0.11)	**–0.46§ (–0.70; –0.14)**	–0.48 (–0.80; 0.04)
SF12 – PCS	–0.26 (–0.57; 0.11)	–0.23 (–0.68; 0.35)	**–0.52‡ (–0.81; –0.03)**
SF12 – MCS	**–0.45‡ (–0.70; –0.10)**	**–0.55‡ (–0.84; –0.03)**	0.09 (–0.43; 0.56)
SDS	**0.47† (0.22; 0.67)**	**0.37§ (0.10; 0.59)**	**0.41‡ (0.06; 0.67)**

*$p<0.0001$; †$p<0.001$; §$p<0.01$; ‡$p<0.05$.

Fig 1. Median AIDAI scores over 16 weeks



AIDAI score was calculated as the sum of all 12 daily items (YES=1 or NO=0) during 30 days.
Missing AIDAI assessments between first and last AIDAI assessments were imputed as NO.
Missing AIDAI assessments after last AIDAI assessment were imputed as NO.
LOCF, last observation carried forward.

Conclusions: CAN demonstrated rapid and sustained disease control assessed with AIDAI over 16 wks. Approximately half of crFMF and TRAPS pts, and 40% of HIDS/MKD patients had inactive disease after 16 wks of treatment. AIDAI improvements at Wk 16 correlated with patient and physician driven evaluations (PGA, SF12–MCS and SDS). CRP and SAA are indicators of response to treatment, rather than a disease activity parameter.
References:
[1] Piram M, et al. Ann Rheum Dis. 2014;73: 2168–73.
[2] De Benedetti F, et al. Ann Rheum Dis. 2016;75:615–6.
Disclosure of Interest: I. Kone-Paut Grant/research support from: Novartis, SOBI and Roche, Consultant for: Novartis, SOBI, Pfizer, AbbVie and Roche, M. Piram Consultant for: Novartis, Pfizer, AbbVie, Speakers bureau: Novartis, S. Benseler Consultant for: Novartis, SOBI and AbbVie, M. Hofer Consultant for: Novartis and AbbVie, H. Lachmann Consultant for: Novartis, SOBI, Takeda and GSK, Speakers bureau: Novartis and SOBI, H. Hoffman Consultant for: Novartis, Speakers bureau: Novartis, M. Gattorno Grant/research support from: Novartis and SOBI, Consultant for: Novartis and SOBI, J. Frenkel Grant/research support from: Novartis and SOBI, J. Kuemmerle-Deschner Grant/research support from: Novartis, Consultant for: Novartis, SOBI and Baxalta, S. Ozen Speakers bureau: Novartis and SOBI, J. Levy Paid instructor for: Novartis, C. Karyekar Employee of: Novartis, F. De Benedetti Grant/research support from: Pfizer, AbbVie, Roche, Novartis, Novimmune and BMS
DOI: 10.1136/annrheumdis-2017-eular.5655

THU0510 UKRAINIAN REGISTRY OF JIA PATIENTS RECEIVING BIOLOGICS: IMPLEMENTATION INTO CLINICAL PRACTICE AND RECENT DATA

I.V. Biliavska[1], V.M. Kovalenko[1], O.P. Bortkevych[1], O.O. Garmish[1], Y.E. Boyko[2], L.I. Omelchenko[1], O.A. Oshlyanska[1], T.V. Marushko[1], L.F. Bogmat[3], N.S. Shevchenko[3]. [1]*Task Force, Ukrainian association of Rheumatologists, Kyiv;* [2]*Task Force, Ukrainian association of Rheumatologists, Lviv;* [3]*Task Force, Ukrainian association of Rheumatologists, Kharkiv, Ukraine*

Background: The situation with a treatment of juvenile idiopathic arthritis (JIA) is complicated in Ukraine. Mainly due to financial reason biological therapy is hardly accessible for Ukrainian patients. Nevertheless, some patients with JIA receive biologics within governmental programme. Clinical data of these patients were scattered and not systematized until 2014. The Task Force of Ukrainian Association of rheumatologists, by analogy to other European registries, has developed a registry of JIA patients receiving biologics. Ukrainian register of JIA patients is an observational, prospective, non-interventional clinical study.
Objectives: The main aim of Ukrainian register of JIA patients is an assessment of long-term safety, efficacy and cost of biological treatment of JIA. in the routine clinical practice.
Methods: 33 clinical sites from different regions of Ukraine are participating. Inclusion criteria: i) diagnosis of JIA: ii)age ≤2 years old, iii)planned start of biological therapy due to JIA; iv)negative screening for tuberculosis; v)provided informed consent. Patients have undergone standard clinical assessment every 3 months. Disease activity is measured using JADAS27 in all age groups. ANA, HLAB27, RF and anti-CCP detection are highly recommended. Uveitis and other comorbid conditions should also be fixed.
Results: 339 patients were enrolled into the study during 3 years. 64% of patients are girls. Mean age–10.98±4.41 years, with mean disease duration –5.81±3.48 years. The duration of the period between diagnosis and biologics start was 54.31±40.28 months. Comorbid conditions were found in 41.03% patients. In 14.65% of the patients uveitis was diagnosed. Most common JIA subtypes in patients receiving biologics are pJIA with negative RF (45%), sJIA (20%), enthesitis-associated JIA (11%) and persistent oligoarthritis (11%). 67.3% of enrolled patients received adalimumab (ADA); 27.9%>tocilizumab (TOZ) and 4.8%>etanercept, respectively. During observational period biologics was discontinued in 19.8% of patients due to different reasons: adverse events were observed in 6.7% (ADA) and 16.7% (TOZ), insufficient efficiency of 23.3% (ADA) and 33.3% (TOZ), remission - 6.7% (ADA); drug absence - 63.3% (ADA) and 50% (TOZ), respectively. Comparative analysis of ADA and TOZ efficacy was performed in the 144 patients with pJIA with negative RF. Administration either ADA or TOZ resulted in statistically significant reducing of disease activity according to JADAS27. In ADA group after 3 months of administration JADAS27 decreased from 16.3±10.3 to 10.0±7.8 ($p<0.00001$). In TOZ group after 3 months of administration JADAS27 reduced from 22.2±12.2 to 13.1±9.1 ($p=0.0012$). The functional disability of the patients also statistically significant decrease in both treatment group starting from 3 months of administration: 1.1±0.8 to 0.7±0.7 ($p=0.0081$) in ADA and 1.6±1.0 to 1.0±0.7 in TOZ, respectively.
Conclusions: Ukrainian national registry of JIA patients provides real-life long-term data concerning safety, efficacy, outcomes and comparative analysis of biologics in Ukrainian population of JIA patients. Data collection continues and the data received expected to be a background for clinical decision-making in future.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4681

THU0511 TOCILIZUMAB IS A PROMISING TREATMENT OPTION FOR THERAPY RESISTENT JUVENILE LOCALISED SCLERODERMA PATIENTS

I. Foeldvari[1], J. Anton[2], M. Friswell[3], B. Bica[4], J. de Inocencio[5], A. Aquilani[6], N. Helmus[1]. [1]*Hamburg Center for Pediatric and Adolescent Rheumatology, Am Schön Klinik Eilbek, Hamburg, Germany;* [2]*Sant Joan de Déu Hospital, Barcelona, Spain;* [3]*Great North Children's Hospital, Newcastle, United Kingdom;* [4]*Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil;* [5]*Pediatric Rheumatology Unit University Hospital 12 de Octubre, Madrid, Spain;* [6]*Ospedale Bambino Gesù, Rome, Italy*

Background: Juvenile localised scleroderma (jlSc) is an orphan disease. Most patient respond to treatment ot methotrexate or mycophenolate. In case of nonresponse or partial response, based on the promising tocilizumab (TOC) data of adult systemic sclerosis studies, TOC seems to be a promising option. There is no publication regarding the effectiveness of tocilizumab in jLS.
Objectives: To assess the effectivity of TOC in jlSC patients, who had nonresponse or partial response on conventional therapy.
Methods: Participants of the pediatric rheumatology email board were asked, if they follow patients with jlSc, who are treated with TOC. Clinical characteristics and the response to TOC was assessed.
Results: Six centers responded to the survey from the email board, with around 800 participatns, and reported 11 patients. The mean age of the patients at disease onset was 5.5 years. Disease duration at time of the intiation of TOC was 53.5. months (range 9 to 109). 5 patients had linear subtype, 3 of them with facial involvement, 2 of them Parry Romberg and one of them coup de sabre. Three had generalized subtype, 2 mixed subtype and 1 limited subtype/morphea. Before starting TOC patients received 10/11 Methotrexate, 7/11 Mycophenolate, 1 abatacept and 1 anti-TNF therapy. Reason to start TOC was in 9 patients increase in Localised Scleroderma Activity Index [1] (mLoSSI). In two patients increased extracutaneous activity was the indication, in one increased activity of arthritis and in the other increased activity of the central nervous system involvement.

The mean duration of tocilizumab therapy was 14.75 months. 2 patients received s.c. accoding the poly JIA dosing and all other i.v. There were diferent i.v doses applied, 5 of them 8mg/kg every 4 weeks, one of them 8 mg /kg every three weeks, 1 every two weeks and 1 pateints received 10 mg /kg every 3 weeks. 3/11 received TOC as monotherapy. 8/11 as combination therapy, 6 of them with Methotrexate and one of each with Mycophenolate or Tacrolimus. Therapy success was refelected by a decreased mLoSSI in 8/11 patients and in 6 patients by a decrease in the Localosed Scleroderma Skin Damage Index [1] (LoSDI). No new lesion occured during the treatment and in the patients with Parry Romerg subtype (n=2) no increase in the facial atrophy occured. In 8/8 patients physician global (VAS 0–100) decreased and in 8/8 the patients global disease activity (VAS 0–100) decreased. In 3/3 patients, were it was applicable, the number of acitve joints decreased, in one patients the limb discrepancy decreased. The mean modified Rodnan skin score assessed in 8 patients decreased from the mean value of 9.6 to 5.5.

Conclusions: In this small cohort of patients TOC seems to be a promising rescue medication in methotrexate/mycophenolate nonresponsive patients. A prospective controlled study would be important to prove the seen effect in a controlled way.

References:

[1] Arkachaisri T, Vilaiyuk S, Torok KS, Medsger TA, Jr.: Development and initial validation of the localized scleroderma skin damage index and physician global assessment of disease damage: a proof-of-concept study. Rheumatology (Oxford) 2010, 49(2):373–381.

Disclosure of Interest: I. Foeldvari Consultant for: add board chugai, <1000 US$, J. Anton Grant/research support from: Grants of Roche, M. Friswell: None declared, B. Bica: None declared, J. de Inocencio: None declared, A. Aquilani: None declared, N. Helmus: None declared

DOI: 10.1136/annrheumdis-2017-eular.3179

THU0512 FLUORESCENCE OPTICAL IMAGING IN JUVENILE PATIENTS WITH AND WITHOUT INFLAMMATORY PEDIATRIC RHEUMATIC JOINT DISEASES

M. Beck[1], J. Klotsche[1], A.-M. Glimm[2], S. Ohrndorf[2], S. Werner[2], G. Horneff[3], M. Backhaus[2], R. Trauzeddel[4], K. Minden[1], H. Girschick[5]. *[1]Deutsches Rheuma Forschungszentrum; [2]Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin Berlin, Berlin; [3]Asklepios Kinderklinik Sankt Augustin GmbH, Sankt Augustin; [4]Department of Pediatric Rheumatology, Helios Klinikum Berlin-Buch; [5]Children's Hospital, Vivantes Hospital im Friedrichshain, Berlin, Germany*

Background: Imaging techniques play an important role in making a diagnosis and in the evaluation of treatment effectiveness as well as in the outcome assessment of juvenile idiopathic arthritis (JIA). Fluorescence optical imaging (FOI) has been shown to visualize inflammation in arthritis of wrist and finger joints. FOI is a simple and cost-effectively imaging technique that is well tolerated by the patients.

Objectives: Firstly, to determine the association and agreement of FOI with ultrasonography (US) and physician's assessment of swollen and active joints. Secondly, to estimate the predictive power of FOI to distinguish between patients with and without inflammatory pediatric rheumatic joint diseases.

Methods: A total of 95 patients were enrolled in three pediatric rheumatology centers in Berlin, Germany. FOI and US (in greyscale (GS) and power Doppler (PD)) were performed in each patient. The FOI software automatically generated the PrimaVista mode (PVM). Furthermore, three phases (P1, P2, P3) were defined dependent on the signal intensity in the fingertips. Each joint was scored semiquantitatively (0=no signal up to 3=strong signal, more than 50% of affected joint area) in each of the three phases and PVM. US was additionally graded by a semiquantitative score of each joint for synovitis (synovial thickening and joint effusions) in GS and hyperperfusion in PD mode. The joints were defined as active if the FOI or US reached a score of at least 1, respectively. We report the results on 27 patients in this interim analysis.

Results: The mean disease duration was 3.5 years (SD=3.2), the mean cJADAS-10 was 11.0 (SD=12.3), the mean number of active joints in the hand was 3.4 (SD=5.8). Half of the patients had polyarthritis (51.8%) and one third had a non-inflammatory rheumatic disease. A total of 810 joints in 27 patients could be analyzed. Among those, 140 (17.3%) had a positive US synovitis score, 87 (10.7%) a positive US power Doppler signal, 93 (11.5%) a clinically active joint and 133 (16.4%) a positive FOI PVM. Taking the US synovitis score as reference, the FOI PVM had a sensitivity of 40%, a specificity of 86% and an overall agreement of 79%. Taking the active joint count as reference, the FOI PVM had a sensitivity of 46%, a specificity of 88% and an overall agreement of 83%. The area under curve was 0.91 for US power Doppler, 0.84 for US GS synovitis, 0.76 and 0.93 for FOI PVM and P2 for the ability to distinguish between patients with and without inflammatory rheumatic diseases. FOI and US scores correlated highly with the cJADAS-10 and the physicians global. In contrast, the patient-reported outcomes pain and fatigue did not show any correlation with FOI and US scores.

Conclusions: FOI and US had a comparable predictive power to distinguish between patients with and without inflammatory rheumatic diseases in pediatric/juvenile patients. The agreement between active joint count, US and FOI was high. FOI may provide a cost-effective method to evaluate inflammation in finger and hand joints.

Acknowledgements: The study was supported by an unrestricted educational grant by Pfizer.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6339

THU0513 NEONATAL MANIFESTATIONS OF IMMUNE-MEDIATED RHEUMATIC DISEASES: A RETROSPECTIVE LONGITUDINAL STUDY IN A TERTIARY HOSPITAL

J. Bernardo[1], I. Brito[1], H. Guimarães[2], M. Guimarães[3], R. Fonseca[1]. *[1]Rheumatology; [2]Pediatrics; [3]Gynecology and Obstetrics, Faculty of Medicine of the University of Porto, Porto, Portugal*

Background: Autoimmune rheumatic diseases such as systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome (APS) and Sjögren's syndrome (SS) are part of a clinical spectrum eligible to affect women in child-bearing ages, affecting neonatal outcomes. Cardiac, cutaneous, haematological, hepatic complications and, more rarely, pulmonary complications have been described.

Objectives: This project aims to describe the occurrence of neonatal lupus manifestations and possible associated clinical factors among women with immune-mediated rheumatic diseases.

Methods: A retrospective longitudinal study was performed including pregnant women with immune-mediated rheumatic diseases seen in a multidisciplinary group for autoimmune diseases during pregnancy between January 2010 and December 2015. Clinical and demographic data as well as and pregnancy outcomes and neonatal manifestations were collected through consultation of clinical files. Patients with and without neonatal lupus were compared using Mann-Whitney, qui-square and fisher tests (SPSS 24.0). Significance level was set as <0.05.

Results: We included 151 gestations from a total of 140 women with a mean age of 32,5±4,4 years; 4 gestations were twin pregnancies. Within these 151 gestations, 54 (35,8%) women had SLE, 17 (11,3%) had Sjögren's syndrome, 17 (11,3%) had rheumatoid arthritis, 41 had APS (27,2%), 11 (7,3%) had Behçet's disease, 4 (2,6%) had systemic sclerosis, 8 (5,3%) had mixed connective tissue disease and 16 (10,6%) had other immune-mediated diseases. 35 (23,2%) had anti-SSA/La antibodies, 18 (11,9%) had anti-SSB antibodies, 6 (4,0%) had anti-URNP antibodies and 43 (28,5%) had anti-nuclear antibodies. During follow-up, 142 (94,0%) babies were born and 7 (4,6%) abortions and 2 (1,3%) foetal losses occurred. 6 (4,2%) neonates were born with neonatal lupus and 1 (0,7%) died *in uterus* with a complete heart block. Out of the 6 babies with manifestations, 4 (66,7%) were cardiac, 2 (33,3%) were cutaneous, 1 (16,7%) was hepatic, 2 (33,3%) were haematological and 1 (16,7%) was pulmonary. Neonatal lupus manifestations occurred more frequently in mothers with SS (23.5% vs 2.2%; p=0.003), anti-SSa/Ro (20% vs 0%; $p<0.001$), and anti-SSb/La (27.7% vs 1.5%; $p<0.001$).

Conclusions: Our study proved a link between immune-mediated rheumatic diseases and specific neonatal outcomes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6136

THU0514 PREDICTIVE VALUE OF SUBCLINICAL SYNOVITIS DETECTED BY DOPPLER ULTRASOUND IN RELATION TO FLARE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH BIOLOGIC THERAPY AFTER TAPERING BIOLOGIC THERAPY

J.C. Nieto-González[1], A. Boteanu[2], J.C. López-Robledillo[3], P. Collado[4], A. Rodríguez[2], D. Clemente[3], M.L. Gámir[2], I. Monteagudo[1], E. Naredo[5]. *[1]Rheumatology, Hospital G.U. Gregorio Marañón; [2]Rheumatology, Hospital Universitario Ramón y Cajal; [3]Rheumatology, Hospital Infantil Universitario Niño Jesús; [4]Rheumatology, Hospital Universitario Severo Ochoa; [5]Rheumatology, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain*

Background: Anti-TNF therapy is effective and safe in JIA. Changes in anti-TNF doses are common when remission is achieved[1]. Subclinical synovitis on Doppler mode (PD) detected by ultrasound can predict flares in adult RA, but it is not yet clear in JIA[2]

Objectives: The aim of this study is to evaluate the predictive value of subclinical synovitis detected by PD-US in relation to flares in patients with JIA on remission under anti-TNF when therapy is tapered. The preliminary results were presented at the EULAR congress 2015 in Rome (FRI0520).

Methods: Observational, prospective and multicenter study. We included JIA patients on remission at least 6 months with anti-TNF, ETN and ADA, in whom anti-TNF was tapered due to clinical decision. ETN was tapered by increasing the injection 3 days and ADA by increasing a week. Patients were clinically assessed every 3 months and also with PD-US at baseline. Bilateral US assessment included joints and tendons. Adult synovitis definitions and semiquantitative scoring system were used, no synovitis definitions are available for JIA. We collected demographics (date of birth, JIA subcategory, previous and current treatments. Flare was defined as clinical signs and/or symptoms of arthritis that required increase of systemic therapy

Results: We included 57 patients, with 19 patients (33.33%) having a flare

during the 12 months follow-up. 38 patients (66.67%) were receiving ETN and 19 (33.3%) ADA, of which 11 patients (28.95%) had a flare with ETN and 8 patients (42.11%) with ADA. Table 1 shows demographics. Median time to flare was 5.73 months (IR 2–93–8.9). Concomitant methotrexate was lower in patients with flare (26.32% vs 71.05%). In 18 patients (31.58%), a previous tapering was done and median time of remission before being included was 22 months (IR 15.5–28.5). US does not predict flare in our cohort. Global synovitis score at baseline was 4 (IQR 1.3–10.8) and 0 in BM and PD respectively, and tenosynovitis was 0 both BM and PD

	All patients (n: 57)	Patients with flare (n: 19)
Gender; women (%)	39 (68.42)	10 (52.63)
Time of remission previous to tapering median months (IR)	22 (15.5–28.5)	35 (35)
Biologic therapy (ETN/ADA)	38/19	11/8
Concomitant DMARD, n (%)	32 (56.14)	5 (26.32)
Previous tapering, n (%)	18 (31.58)	5 (26.32)
JIA subcategories: n (%)		
Persistent oligoarticular JIA	15 (26.32)	5 (33.33)
Extended oligoarticular JIA	14 (24.56)	4 (28.57)
RF– polyarticular JIA	15 (26.32)	5 (33.33)
RF+ polyarticular JIA	2 (3.51)	1 (50)
Enthesitis related JIA	3 (5.26)	2 (66.6)
Psoriatic JIA	8 (14.04)	2 (25)

Conclusions: Anti-TNF tapering was safe in our JIA patients in more than half of patients after 1 year follow-up. US did not predict flares in our patients. Concomitant treatment with methotrexate was more frequent in patients who remained on remission

References:

[1] Cai Y. Rheumatol Int.2013.
[2] Magni-Manzoni S.Ann Rheum Dis.2013.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3561

THU0515 DISABILITY AND LOWER QUALITY OF LIFE IS ASSOCIATED WITH SOCIOECONOMIC PASSIVITY IN YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS

K. Rebane[1], L. Ristolainen[2], H. Relas[3], T. Orenius[2], H. Kautiainen[4], R. Luosujärvi[5], K. Aalto[6], H. Säilä[2]. *[1]Children's Hospital, University of Helsinki and Helsinki University Central Hospital; [2]ORTON Research Institute, ORTON Foundation; [3]Unit of Primary Health Care and Department of General Practice, Helsinki University Hospital Helsinki; [4]Helsinki University Central Hospital; [5]Unit of Primary Health Care and Department of General Practice, Helsinki University Central Hospital; [6]Children's Hospital, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland*

Background: Health related quality of life of adult patients with juvenile idiopathic arthritis (JIA) is shown to be significantly lower compared to the general population.[1,2]

Objectives: We aimed to recognize young adults with JIA who are socioeconomically passivated and to assess which areas of self-rated health are associated with the emergence of passivity symptoms.

Methods: We studied 195 young adults with JIA using questionnaires addressing demographics, health behavior, and physical activity. The HAQ questionnaire was used to assess functional ability, quality of life was assessed with RAND-36, depressive symptoms were assessed with BDI-II, and self-esteem was evaluated by using the Rosenberg scale. Patients were classified as active if they were engaged in studying, working, maternal leave or military service; and as passive, if they were unemployed or on disability pension.

Results: 80% of the patients were female, mean age was 23 years, and disease duration was approximately 15 years. Patients in the passive group participated less in leisure time non-physical activities (p =0.033), they felt more disturbed during their leisure time (p =0.010). Leisure time physical activity did not reveal statistically significant differences between the groups. The majority of the patients in the passive group (58%) had only basic education (p<0.001), they visited their doctor more frequently (p=0.019) and they used oral prednisolone more often (p<0.018). Approximately 70% of the patients received disease modifying antirheumatic drugs, and nearly half of the patients were treated with biologicals in both of the groups. Mean disability scores on HAQ were higher in the passive group (p=0.012). Depressive symptoms did not differ between the groups. Self-esteem was lower in the passive group (p=0.002). Results in health related quality of life revealed statistically significant differences between the groups: physical functioning (p=0.049), social functioning (p =0.020), and emotional well-being (p=0.047) were significantly lower in the passive group.

Conclusions: Patients being socioeconomically more passive showed higher degrees of disability, reporting lower physical functioning, self-esteem, emotional well-being, and social functioning. Those patients should be recognized earlier and activating interventions should be provided.

References:

[1] Foster HE, Marshall N, Myers A, Dunkley P, Griffiths ID. Outcome in adults with juvenile idiopathic arthritis: A quality of life study. Arthritis Rheum. 2003;48(3):767–75.
[2] Barth S, Haas JP, Schlichtiger J, Molz J, Bisdorff B, Michels H, et al. Long-Term Health-Related Quality of Life in German Patients with Juvenile Idiopathic Arthritis in Comparison to German General Population. PLoS One. 2016;11(4): e0153267.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5730

THU0516 LONGER TERM OUTCOMES OF CRMO IN A TERTIARY ADOLESCENT AND YOUNG ADULT RHEUMATOLOGY CENTRE IN THE UK

K.E.N. Clark, F. Josephs, N. Daly, Y. Ioannou, C.L. Murphy, D. Sen.
Rheumatology, University College London Hospitals, London, United Kingdom

Background: Chronic relapsing multifocal osteomyelitis (CRMO) is a rare autoinflammatory bone condition presenting primarily in children and adolescents. It characteristically affects the epiphysis and metaphysis of long bones, and presents with bony pain, local swelling and warmth.

Objectives: The aim of this study was to collate our tertiary adolescent rheumatology centre's experience of managing patients with CRMO, and establish their longer term outcomes, possible by the fact we have a cohort of patients with CRMO under long-term follow-up.

Methods: We carried out a retrospective case note review of all patients who are known to our service with a diagnosis of CRMO, presenting between age 13–20.

Results: In total 17 patients were identified as having CRMO, presenting between 1999 and 2015. 10 patients were female, and 7 patients male. The median age of initial symptoms, and age of presentation was 12 years (range1–16 years).

Median duration of follow up is 4.75 years (range 1–16.5 years). Since initial diagnosis, 3 patients evolved into a SAPHO (synovitis, acne, pustolosis, hyperostosis, osteitis) phenotype, 3 an ERA (enthesitis related arthritis) phenotype and 2 patients developed oligoarticular juvenile idiopathic arthritis (JIA).

35% of patients have a purely unifocal disease, and 65% have multifocal disease as confirmed by whole body MRI. 70.5% patients had recurrent episodes of inflammation, while 29.5% of patients had only one flare and then reached remission (either clinical or confirmed with MRI). 15 patients had their diagnosis confirmed with biopsy, while 2 did not due to site of disease. Their diagnosis is assumed based on clinic impression, and typical radiographic findings.

Sites of disease confirmed in our patients include lower limbs (70% patients), upper limbs (35% patients), clavicle (29.4%), mandible (17.6%) and spine/pelvis (23.5%).

All patients were treated with NSAIDs. In terms of treatments used since diagnosis, 76% patients have been on methotrexate (MTX), 47% had one infusion of pamidronate, and 23% required more than one infusion of pamidronate. Other medications include sulfasalazine (SSZ), azathioprine, risedronate and anti-TNFs (adalimumab, etanercept and infliximab).

On last clinic review, with or without imaging, 35% of patients continue to have active disease. Currently 29% patients are on MTX alone, 23% patients are on adalimumab and MTX, and 35% are only maintained on NSAIDS. Of those without active disease 5 patients (45%) are not on any DMARD or biologic therapy.

Conclusions: We present here our experience of managing adolescent patients with CRMO.

The perceived wisdom is that CRMO is a self-limiting disease which eventually goes into remission. However our centre's experience is that nearly 50% of our patients have a disease which evolves into another systemic autoimmune disease, mainly SAPHO, polyarticlar or enthesitis related JIA. Previous case series have suggested only 0–30% of patients' disease evolves. This may be a reflection of our older cohort of patients, who are only referred to our service with ongoing disease.

The majority of patients have a recurrent and multifocal course of disease. The most common site of disease was in the lower limbs. All patients were treated with NSAIDS, and a combination of DMARDS, bisphosphonates and biologic agents have been used, which has resulted in remission of disease in the majority of patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5188

THU0517 LARGE VESSEL VASCULITIS IN INFANTS - A CASE SERIES

L. Das[1], J.H.T. Tan[1], X.C. Gao[1], S.F. Hoh[1], T. Arkachaisri[1,2]. *[1]Rheumatology and Immunology Services, Department of Paediatric Subspecialties, KK Women's and Children's Hospital; [2]Duke-NUS Medical School, Singapore, Singapore*

Background: Large vessel involvement following recrudescent or recalcitrant Kawasaki Disease or other vasculitidies in young children have been limited to few case reports and outcomes are still unclear.

Objectives: To describe and compare the characteristics and outcomes of 6 patients with large vessel vasculitis diagnosed between 2013 to 2015 in KK Hospital, Singapore

Methods:

Demographic and disease characteristic information were collected and median, interquartile range (IQR) & percentiles were used to describe the data.

Results: 6 patients were included in the analysis. Median age was 3.75 months

(IQR 3.75, 4). Other than 1 Filipino 2 year old girl (patient C), all other infants were of Chinese Singaporean origin and were less than age 1 year at onset; 4 male and 1 female. All patients were found to have multiple areas of irregular, thickened vessel walls with enhancement, involving the aorta and additional medium sized arteries on Magnetic Resonance Angiography (MRA).
Only patients C and F presented with prolonged fever and or less than 1 clinical feature of KD. C developed a unilateral enlarged lymph node on recrudescence of fever 1 month after the initial event. She was then found to have dilated CA (dCA) and consequently abnormal MRA. Other patients had significant KD Index scores and complete KD presentations.
Of the 4 patients who received only 1 dose of IVIG; C and F had diagnosis change from atypical KD to Takayasu Arteritis and G developed rhinovirus and then rotavirus as reason for prolonged fever. Patient A received IV steroids and then Infliximab. All patients received steroids. Patients A and B both developed a psoriasiform rash post-Infliximab which resolved on follow up.
Patient F and Patient B died 3 months and 17 months after diagnosis. Patient F, presented with fever, fussiness and enteritis aged 4 months. Her symptoms recurred 2 weeks after onset. Due to differential hypertension, she received an echocardiogram and subsequently MRA and cardiac catherization. Cause of death at age 7 months was small bowel perforation with arteritis and consequent intra-abdominal sepsis.
Patient B, presented with complete features of KD at age 2 months. His course was noted for recrudescence 2 weeks and 4 weeks after initial IVIG. He developed giant coronary aneurysms with abnormal MRA findings; developed myocardial infarction at age 8 months and proceeded to require a Left Ventricular Assist Device but died age 13 months from multi-organ failure.
3/6 (50%) developed aneurysms, D and F were giant. 4 surviving patients, had improvement in all vessels but continued activity in the aorta on follow up MRA, they remain on Methotrexate with no active clinical findings.

Table 1: Patient characteristics

ID	Hg# (g/DL)	WBC count (10^9/L)	Platelet count (10^9/L)	CRP (mg/L)	Time to initial MRA (weeks)	Follow up MRA (months)	Immunosuppression
A	10.8	11.3	357	130	2	20	ifx
B	8.9	24.76	595	178.4	4	8	ifx
C	9.9	15.34	532	64.4	4	8	mtx
D	9.6	26.23	270	108.3	2	died	n
E	8.6	19.99	750	175.2	1	died	ctx
F	11.7	18.54	497	142	4	6	ifx, mtx

#Hg Hemoglobin, IFX infliximab , MTX methotrexate, CTX cyclophosphamide

Conclusions: Extensive involvement of the systemic arteries and aorta in all patient were noted on initial MRA. Follow up imaging, showed improvement in all vessels. After 1 year of follow up, complete resolution occurred only in medium vessels.
Mortality in this patient cohort was 2/7 (28.6%).
This is an observational case series and our findings will need to be reproduced in larger groups of patients.
References:
[1] Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment, and long term management of Kawasaki disease. Circulation 2004;110:2747–71.
[2] McCulloch M, Andronikou S, Goddard E, et al. Angiographic features of 26 children with Takayasu's arteritis. Pediatr Radiol (2003) 33: 230–235.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5812

THU0518 BIOLOGICAL THERAPY IN NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS FOLLOWED IN ADULT RHEUMATOLOGY DEPARTMENT: HUR-BIO REAL LIFE RESULTS

L. Kilic[1], A. Sari[1], B. Armagan[1], A. Erden[1], Ö. Karadag[1], A. Akdogan[1], S. Apras Bilgen[1], S. Kiraz[1], S. Ozen[2], U. Kalyoncu[1], A.I. Ertenli[1]. *[1]Department of Rheumatology; [2]Department of Pediatric Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey*

Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disorder in childhood and more than one-third of patients have active inflammation during adult years that can cause disability.
Objectives: To define the demographic and clinical characteristics of non-systemic JIA (ns-JIA) patients under biological therapy followed in adult rheumatology department.
Methods: Hacettepe University Biologic Registry (HUR-BIO) is a single center biological registry since 2005. HUR-BIO database includes demographic and clinical characteristics of patients, disease activity parameters, history of articular prosthesis. The use of biological agents in routine rheumatology practice has been approved by the Ministry of Health since 2003.
Results: In this study, 95 (72.6% women) ns-JIA patients were included. The demographic and clinical characteristics of the patients were shown in the table. The first biological agents were; Etanercept (63.2%), adalimumab (16.8%), infliximab (12.6%) and the others 7 (7.4%). After a mean follow-up of 60 (48) months, 42 (44.2%) patients required biologic switch. The last visit HAQ scores of 75 patients were known and 16 (21.3%) patients had HAQ score $\geq$1.0 (female 15/54 vs. male 1/21, p=0.029). The last visit DAS-28 score of 72 patients was known and 46 (63.9%) patients had remission or low disease activity. 14 patients (14.7%) had history of articular prosthesis and were all female. Patients with history of articular prosthesis were older [39.1±10.1 vs. 29.6±10.3 years, p<0.0001], had longer disease duration [25.7±6.6 vs. 17.2±11.9 years, p=0.001] and had longer time until the biological therapy [19.6±8.4 vs. 11.5±11.6 years, p=0.002]. The time until the biological therapy of 38 ns-JIA patients diagnosed after 2003 was shorter [3.2±2.9 vs. 19.4±10.6 years, p<0.001].

Table 1. The Demographic and Clinical Characteristics of the ns-JIA Patients

	All Patients (n=95)	Female (n=69)	Male (n=26)	p
Age mean (SD)	31.0 (10.8)	32.2 (10.9)	28.0 (10.0)	0.025
Age at first symptom, mean (SD)	9.9 (5.0)	9.5 (4.0)	10.9 (4.9)	0.22
Age at diagnosis, mean (SD)	12.5 (6.7)	12.3 (7.3)	13.2 (4.5)	0.62
Disease duration (year), mean (SD)	18.5 (11.6)	19.9 (11.2)	14.6 (12.1)	0.012
Time until the biological therapy (year) mean (SD)	12.7 (11.5)	14.2 (11.5)	8.7 (11.0)	0,01
History of hip or knee prosthesis, n (%)	14 (14.7)	14 (20.3)	0	0.01
RF or anti-CCP (+), n (%)	42 (44.2)	34 (49.3)	8 (30.8)	0.11
Biological switch, n (%)	42 (44.2)	32 (46.4)	10 (38.5)	0.64
Last visit HAQ mean (SD)	0.51 (0.62)	0.62 (0.67)	0.22 (0.35)	0.005
Last visit DAS-28 mean (SD)	2.85 (1.56)	3.14 (1.47)	2.18 (1.59)	0.009

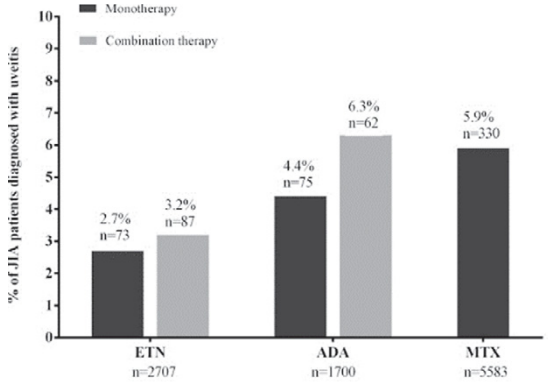
RF: romatoid factor, CCP: cyclic citrillinated peptide, ns-JIA: non-systemic JIA, HAQ: Health Assessment Questionnaire, SD: Standard deviation.

Conclusions: Structural damage and history of articular prosthesis was more common in female ns-JIA patients receiving biological therapy. Functional disability and disease activity were also higher in female patients. On the other hand, the follow-up ns-JIA patients had a good level of remission and low disease activity.The shorter duration until the time of biological treatment in patients diagnosed after 2003 indicates that both pediatric and adult rheumatologists have begun to treat these patients more effectively.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4133

THU0519 ETANERCEPT, ADALIMUMAB AND METHOTREXATE UTILIZATION BY JUVENILE IDIOPATHIC ARTHRITIS PATIENTS AND THE OCCURRENCE OF UVEITIS

K. Roshak[1], J.M. Sopczynski[2], R.M. Suehiro[3], L. Marshall[3]. *[1]Drexel University, Philadelphia; [2]R&d Bt Bi, Predictive Informatics; [3]Medical Affairs, Pfizer, Collegeville, United States*

Background: Juvenile idiopathic arthritis (JIA) is a chronic arthritis with an onset before 16 years of age, that persists for at least 6 weeks, and has an unknown etiology.[1] Uveitis is a serious and common extra-articular manifestation of JIA, affecting 12–30% of patients (most commonly female with ANA+ oligoarthritis JIA category).[2,3] JIA-associated uveitis can be treated with biologic disease modifying antirheumatic drugs (bDMARDs), including TNF inhibitors (TNFi) such as etanercept (ETN), infliximab (IFX), and adalimumab (ADA), after failure of first-line treatments, such as topical corticosteroids and/or conventional synthetic DMARDs (csDMARDs), such as methotrexate (MTX).[2] Of note, reports exist that ETN use has been associated with uveitis flares or new-onset uveitis while an observational study reported similar uveitis flare rates for both ADA and ETN.[4,5]
Objectives: To conduct an analysis on the occurrence of uveitis in patients with JIA treated with ETN, ADA, or MTX. Combination therapy of ETN, ADA, and MTX was also assessed.
Methods: International Statistical Classification of Diseases (ICD)-9 diagnosis codes in a Truven MarketScan® claims database were used to identify JIA patients diagnosed with uveitis over a 5-year interval. The analysis assessed the proportion of JIA patients (aged 0–19 years) treated with ETN, ADA, or MTX, as monotherapy or in combination. The percentage of patients diagnosed with uveitis and the time interval for uveitis diagnosis in patients with JIA was determined.
Results: A total of 22,789 patients with JIA where included in this analysis and exhibited a mean age of 11.4 years, were predominantly female (69%), and mean JIA disease duration was 3 years. This total included 19,814 patients with chronic, or not otherwise specified, polyarticular JIA. A total of 2581 (11.3%) patients, of mean age 10.2 years, of which 73% were female, were diagnosed with uveitis. The numbers of JIA patients receiving biologic and/or MTX therapy and proportions with a uveitis diagnoses are shown in the Figure.
Conclusions: This analysis showed a similar occurrence of uveitis in JIA patients treated with ETN or ADA, either as monotherapy or in combination with MTX.
References:
[1] Petty RE, et al. J Rheumatol 2004;31:390–2.
[2] Clarke SL, et al. Pediatr Rheumatol Online J 2016;14:27.
[3] Wentworth BA, et al. F1000Prime Rep 2014;6:41.
[4] Schmeling H, Horneff G. Rheumatology (Oxford) 2005;44:1008–11.
[5] Foeldvari I, et al. Arthritis Care Res 2015;67:1529–35.
Disclosure of Interest: K. Roshak: None declared, J. M. Sopczynski Shareholder of: Pfizer, Employee of: Pfizer, R. M. Suehiro Shareholder of: Pfizer, Employee of: Pfizer, L. Marshall Shareholder of: Pfizer, Employee of: Pfizer



Note: Combination refers to ETN + MTX or ADA + MTX
Abbreviations: JIA, juvenile idiopathic arthritis; ETN, etanercept; ADA, adalimumab; MTX, methotrexate

Figure 1. To show the patients with JIA receiving a monotherapy (with ETN, ADA or MTX) or a combination therapy and the number of uveitis diagnoses.

DOI: 10.1136/annrheumdis-2017-eular.1857

THU0520 PELVIC ULTRASOUND IN THE ASSESSMENT OF SEXUAL MATURITY IN GIRLS WITH JUVENILE IDIOPATHIC ARTHRITIS

L.M. Gonçalves[1], S.H. Machado[2], R.M. Xavier[3], P.J.C. Maróstica[4], C. Kopacek[5], I.R.S. Lucena[6]. *[1]Student, PUCRS; [2]Pediatrics rheumatology, HCPA; [3]Rheumatology service; [4]Pediatrics service, Hcpa/UFRGS; [5]Endocrinology service, HCSA; [6]Radiology service, HCPA, Porto Alegre, Brazil*

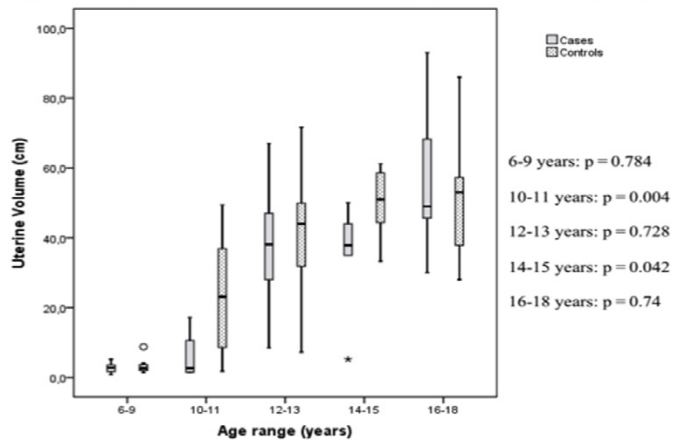
Background: Delayed puberty is common in children with chronic illnesses such as Juvenile Idiopathic Arthritis (JIA),especially in cases with an earlier age of onset.Its etiology is multifactorial and includes low weight,complications arising from the disease itself and the adverse effects of treatment.
Objectives: To compare uterine and ovarian size as well as artery pulsatility between girls with juvenile idiopathic arthritis (JIA) and healthy participants using abdominal pelvic ultrasound,and identify these findings and pubertal staging,sex hormones and disease characteristics in girls with JIA.
Methods: This study involved 44 girls with JIA and 59 healthy controls aged between six and 18 incomplete years.Pelvic ultrasound was used to determine uterine volume and length,the corpus/cervix ratio,ovarian volume and length,and the pulsatility index (PI) of uterine arteries.Hormone levels were also measured in girls with JIA.
Results: All US parameters were associated with Tanner stages in the control group ($p<0.001$).Uterine and ovarian measures were smaller in girls with JIA than in the control group.The mean PI of uterine arteries was higher in girls with JIA.Comparisons by age group revealed that uterine volumes were smaller in girls with JIA aged between 10 and 11 years (p=0.004) and 14 to 15 years (p=0.042),and the corpus/cervix ratio was smaller in girls aged 10 to 11 years (p=0.007).US measures were not associated with disease factors in the JIA group.LH and estradiol levels were found to be positively associated with ovarian and uterine size ($p<0.001$),but negatively correlated with the mean PI of uterine arteries ($p<0.01$).
Conclusions: Pelvic US is a sensitive method for the assessment of sexual maturation in girls,and can identify developmental delays in girls with JIA which may not be detected by Tanner staging.

Table 1. Comparison of abdominal pelvic US findings between control participants and patients with JIA

Variables*	Patients (n=?44)	Control participants (n=?59)	p
Uterine volume (cm^3)	10.5 (2.4–40)	36.6 (8.8–50.9)	0.009
Uterine length (cm)	4.92±1.83	5.91±1.80	0.008
Corpus to cervix ratio (cm)	1.18±0.25	1.36±0.27	0.001
Endometrium (mm)	1.4 (0–5.2)	5.4 (1.4–7.2)	0.016
Left Ovarian Length (cm)	2.60±0.69	3.04±0.84	0.006
Left Ovarian Volume (cm^3)	3.3 (1.5–5.2)	5.0 (3.0–7.1)	0.004
Right Ovarian Length (cm)	2.79±0.71	3.17±0.75	0.013
Right Ovarian Volume (cm^3)	2.9 (1.5–6.3)	5.9 (3.0–9.1)	0.006
Mean uterine PI	4.6 (2.7–6.5)	2.5 (1.9–5.1)	0.025

PI, pulsatility index. *Described as median (25th-75th percentile) or mean ± standard deviation.

Figure 1 – Comparison of uterine volume between groups across different age ranges



Conclusions: Pelvic US is a sensitive method for the assessment of sexual maturation in girls,and can identify developmental delays in girls with JIA which may not be detected by Tanner staging.

References:
[1] Pozo J,Argente J.Delayed puberty in chronic illness.Best Pract Res Clin Endocrinol Metab 2002;16:73–90.
[2] Holm K,Laursen EM,Brocks V,Muller J.Pubertal maturation of internal genitalia:authors' reply.Ultrasound Obstet Gynecol 1995;6:452–3.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4389

THU0521 ENTHESITIS-RELATED ARTHRITIS: NON-PERIPHERAL PATTERN IS ASSOCIATED WITH TH17 CELLS

M. Katsicas, C. Carrara, A. Bernasconi, J. Rossi, R. Russo. *Immunology & Rheumatology, Hospital de Pediatría Garrahan, Buenos Aires, Argentina*

Background: Enthesitis-related arthritis (ERA) is a category of juvenile idiopathic arthritis. Different proinflammatory cytokines linked to the Th1 and Th17 T- cell subsets have been implicated in its pathogenesis. Limited data are currently available about the relationship between disease activity and the clinical pattern and the percentage of Th1and Th17 T- cell subsets.
Objectives: To analyze Th1 and Th17 cell subsets in patients with ERA and to compare with age-matched healthy controls. To assess the association between disease activity and disease clinical pattern with Th1and Th17 cells subsets
Methods: Patients with ERA (according to ILAR criteria) were included in a cross sectional study. Disease activity measures were collected in random visits: active joint count (AJ), pain score (0–10), presence of active enthesitis (AE), sacroiliac pain (SIP), lumbar pain (LP),lumbar limitation (LL) by Schöber's test, wellbeing according to the patient using a visual analogue scale (VASp, 0–10), disease activity according to the physician (VASphy, 0–10), JADAS-10, JSpADA, and ESR/CRP were evaluated. Patients were classified based on the disease pattern (peripheral and non-peripheral) depending on the presence or absence of AJ and/or AE. Functional capacity was also assessed by CHAQ. Presence of radiologic sacroiliitis (MRI/X-rays) and treatment with TNF inhibitors (TNFi) were recorded. Th-17 and Th-1 cells were quantified by flow cytometry in PBMCs stimulated with PMA/IO. Age-matched healthy children without disease or medication were recruited as normal control. Comparison between groups (Mann-Whitney Utest) and correlation tests as appropiate
Results: Twenty-nine patients (90% M) fulfilled inclusion criteria. HLA-B27 was positive in 13 (45%). Median age at observation was 12 years and median disease duration was 2.1 years. Activity and functional measures were (medians): AJ 1, pain 0.25, VASp 0.5, VASphy 1, JADAS-10 7, JSpADA 1.75, ESR 15 mm/h, and CHAQ $\geq$0,5=8 patients (27%). AE was present in 1 (3%), SIP in 7 (24%), LP in 6 (21%), and LL in 12 (41%) children. Nineteen (65%) patients showed JADAS >1 and 21 (76%) JSpADA>0. Radiologic sacroilitis was recorded in 21 (72%) children. Fourteen (48%) patients were treated with TNFi. Th1cell percentage in ERA was 8.5±3.4% (range, 4–17.4) while healthy controls was 5.8±3.8% (range, 1.2–14.2), p=0.023. Th17cell% in ERA was 0.90±0.44 (range, 0.39–2.34%) while controls was 0,55±0.38 (range, 0,17–1,61%); p=0.004. There was no difference between T-cells% and active/inactive disease. Eighteen (62%) children showed peripheral pattern, while 11 (38%) exhibited non-peripheral. Peripheral and non-peripheral groups showed Th17%cells 0.90 (0.39–1.74) vs 1.14 (0.64–2.44) respectively (p=0.018).Significant correlations were Th1 with AJ (r=0.45 p=0.004) and Th17with LP (r=0.83 p=0,0001), LL (r=0.47 p=0.03).
Conclusions: Th1 and Th17 cells subsets were significantly higher in ERA compared with healthy controls. However, T-cells showed no significant difference between patients with active versus inactive disease. Interestingly, non-peripheral pattern showed higher Th17% cells respect to patients with peripheral disease.Our results suggest that Th17 evaluation could help identify different phenotypes that benefit from Th-17 blocking strategies.

References:
[1] Biologic agents in juvenile spondyloarthropathies. Katsicas MM, Russo R. Pediatr Rheumatol Online J.2016Mar 12;14 (1):17.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6726

THU0522 CORRELATION BETWEEN SERUM CALPROTECTIN (MRP8/14), CLINICAL AND ULTRASOUND ASSESSMENT IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

M. Romano, V. Gerloni, M. Gattinara, O. De Lucia, P.L. Meroni. *Rheumatology, G.Pini Istitute, Milan, Italy*

Background: MRP8/14 (also known as calprotectin) has been widely studied as

potential predictor of disease activity and response to treatment in inflammatory diseases. In Juvenile Idiopathic Arthritis (JIA), MRP8/14 levels are highly predictive of disease flares in systemic JIA. In a more heterogeneous group of JIA patients (pts), MRP8/14 levels have been shown to predict response to MTX. High levels of baseline MRP8/14 are associated with good response to anti-TNF treatment, whereas elevated MRP8/14 levels at time of discontinuation are associated with higher chance to flare. In clinical practice, ultrasound could be usefull to define the state of disease activity. Indeed, PD-US assessment of synovial vascularization has been shown to be more sensitive than serum markers of inflammation in the identification of active disease in JIA.

Objectives: To explore the association between calprotectin, clinical and US assessment in JIA pts.

Methods: A total of 30 consecutive pts (aged under 18 years) with oligo or poly JIA were assessed by US, clinical examination and MRP8/14 serum levels. Serum MRP8/14 was measured by ELISA in all pts and in 20 age matched healthy controls. Ultrasonographic B-mode and power Doppler assessment of 44 joints each pts were performed. Patients were evaluated using Wallace criteria.

Results: 30 consecutive non systemic JIA pts (F 18) were evaluated: 13 persistent and 8 extended oligoarticular, 6 polyarticular (1 RF positive), 2 ERA, 1 psoriatic JIA. Median age at disease onset was 10.6 yrs (mean 10.8, range 2–16). Mean disease duration was 5.4 yrs (range 0.1–15.9). Mean active joints was 2 (range 0–26). 14 pts were active according to Wallace criteria and 16 pts were active according to US evaluation. Ultrasonographic B-mode and power Doppler assessment was significantly correlated with clinical examination (Mcnemar test p=0.683, Cohen's K 0.602). The majority of our enrolled pts were in phase of oligoarticular involvement with minimal disease activity (median active joints=0). No statistically significant difference in serum MRP8/14 was found between all JIA pts and healthy controls (p=0.33). No statistically significant difference in serum MRP8/14 was found between active (according to clinical examination) JIA pts and healthy controls (p=0.69) and between inactive JIA pts and healthy control (p=0.23). Concentrations of MRP8/14 in active and inactive pts according to Wallace were not significantly different (p=0.75). No statistically significant difference in serum MRP8/14 was found between active and inactive pts according to US assessment (0.85). Only 6 pts (4 out of 6 with polyarticular course) showed calprotectin levels higher than normal. We found a correlation between calprotectin and CRP (Spearman r 0.4380, p=0.01) and between calprotectin and ESR (Spearman r 0.3800, p=0.05).

Conclusions: To our knowledge this is the first study to examine the correlation between MRP8/14 levels, clinical and US assessment in JIA. Serum levels of MRP8/14 (a biomarker of activation of the innate immune system) are not significatively different in oligoarticular JIA from healthy controls. Calprotectin high levels, could be related with a poliarticular disease either in clinical activity or in subclinical remission. However our study need to be extended to a larger number of pts followed prospectively.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6951

THU0523 MORTALITY AND CAUSES OF DEATH AMONG JUVENILE IDIOPATHIC ARTHRITIS PATIENTS IN FINLAND

M. Kyllonen [1,2], H. Kautiainen [3], K. Puolakka [4], P. Vahasalo [1,5]. *[1] Pedego Research Unit, Oulu University; [2] Internal Medicine, Oulu University Hospital, Oulu; [3] General practise and Primary health care, Helsinki University, Helsinki; [4] South Karelia Central Hospital, Lappeenranta; [5] Pediatrics, Oulu University Hospital, Oulu, Finland*

Background: Juvenile idiopathic arhritis (JIA) is an inflammatory arthritis that begins before 16 years of age and persists more than 6 weeks. The prevalence of JIA is approximately 1 to 2 per 1,000 children. Only 40–60% of JIA patients had inactive disease at follow-up (1).

An increase rate of mortality has been observed in JIA. A follow-up study (1960–1993) in the United States reported early deaths especially in systemic JIA (2). The same was found in an follow-up study in Scotland (3). However two follow -up studies in United States and one study in Germany showed no increased mortality (4,5,6).

Objectives: To explore mortality rates and causes of death in JIA patients in Finland compared with the general population.

Methods: All incidents patients with JIA during 2000–2014 were collected from the nationwide register of special reimbursements for disease-modifying antirheumatics drugs, maintained by the Social Insurance Institution of Finland. The National Population Registry identified three age, sex and residence matched controls for each case. Death certificate data up to 2015 were obtained from the Statistics of Finland.

Results: Altogether 4,180 JIA patients (62% girls) were identified. Mean age at diagnosis was 8.3 years. The average follow-up was 6.6 years (IQR 3.1–10.5). These patients were compared with 12,511 controls.

During 28.941 follow-up years, 11 JIA patients (6 girls, 5 boys) and 23 controls (12 girls, 11 boys) died.

Mean age at death was 20.3 years (range 11–30) in the JIA patients and 23.1 years (range 9–29) years in the control group. (p=0.17).

Cumulative mortality in the patients with JIA was 0.4% (95% CI 0.2–0.8%) compared to 0.3% (95% CI 0.2–0.5%) in the controls, hazard ratio was 1.44 (95% CI 0.70–2.95).

Accidents were the most common (54%) cause of death in the patients with JIA, but suicide (39%) in the controls. Alcohol, drug abuse and depression contributed more to deaths in the control (39%) than in JIA group (1%), p=0.053.

Conclusions: Juvenile idiopathic arthritis is not associated with a higher mortality rate in children and young adults.

References:

[1] Ravelli et al. Juvenile idiopathic arthritis. Lancet 2007;369: 767–78.
[2] French et al. Increased mortality in adults with a history of juvenile rheumatoid arthritis. ArthrRheum 2001;44: 523–527.
[3] Thomas et al. National study of cause-spesific mortality in rheumatoid arhtritis, juvenile chronic arthritis and other rheumatic conditions: a 20 year follow up. JRheumatology, 2003;30:958–965.
[4] Hashkes P et al. Mortality outcomes in pediatric rheumatology in the US. ArthrRheum 2010;62:599–608.
[5] Krause et al. Juvenile idiopathic arthritis in Olmsted County, Minnesota 1960–2013. ArthrRheum 2016; 68: 247–254.
[6] Minden et al. Long- term outcome in patients with juvenile idiopathic arthritis. ArthrRheum 2002; 46: 2392–2401.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4042

THU0524 VITAMIN D DEFICIENCY AND RISK FOR CARDIOVASCULAR DISEASE IN JUVENILE IDIOPATHIC ARTHRITIS

M.H. Abu-Zaid [1], A.M. El-Barbary [1], R.A. Gaber [2], H.H. Abdelnabi [3]. *[1] Rheumatology and Rehabilitation, Faculty of Medicine Tanta University Egypt; [2] Biochemistry; [3] Pediatric, Faculty of Medicine Tanta University, Tanta, Egypt*

Background: Vitamin D is not a classic vitamin but rather a prohormone which converted primarily in the liver into its major circulating form, 25-hydroxy-vitamin D [25(OH) D]. Serum levels of vitamin D have been found to be low in juvenile idiopathic arthritis (JIA) as in several autoimmune diseases [1]. There are some evidences of an association between serum vitamin D and cardiovascular disease risk [2].

Objectives: To assess the association between serums levels of 25-hydroxy-vitamin D and cardiovascular disease risk factors in juvenile idiopathic arthritis

Methods: A prospective cross-sectional study was done on 30 patients with JIA according to the criteria of the International League of Associations for Rheumatology (ILAR) and 30 healthy volunteers matched for age and gender. Patients with other causes of dyslipidemia or those whom receiving vitamin D supplements or lipid-lowering medications were excluded from this study.

Systolic and diastolic blood pressure was measured to all patients and controls

Also; all patients and controls underwent laboratory tests of plasma 25(OH)D, Serum High-Density Lipoprotein (HDL), Low-Density Lipoprotein cholesterol (LDL). Echocardiography, carotid intima media thickness (cIMT), flow mediated dilatation of the brachial artery (FMD) also was done to all patients and controls.

Vit D levels were then correlated in each subgroup with the other clinical, laboratory and radiological parameters. We predefined Vit D insufficiency as being $<$50 nmol/l and Vit D deficiency as being $<$25 nmol/l.

Results: The mean serum vitamin D levels of all patients were 23.8 nmol/l ±16.59. Only 7patients (23.3%) have adequate vitamin D levels (50–75 nmol/l). While Vitamin D insufficiency (serum vitamin D: 25 – 50 nmol/l) and deficiency (serum vitamin D level $<$25 nmol/l) were found in 9 (30%) and 14 patients (46.7%), respectively. JIA patients had significantly lower vitamin D levels as compared to controls ($p<0.01$). JIA patients had higher systolic and diastolic blood pressure than controls although these differences were not statistically significant ($p>0.05$) and all levels were still in normal values. Subjects with vitamin D deficiency or insufficiency had significantly lower values for HDL cholesterol and significantly elevated values for LDL cholesterol as compared to controls and patients with adequate vitamin D levels, with significant positive correlation between 25(OH)D and HDL cholesterol, and significant inverse correlation between 25(OH)D and LDL levels.

Patients with lower levels of vitamin D had significantly higher cIMT and lower FMD ($p<0.01$) With significant positive correlation between 25(OH)D and FMD, and significant inverse correlation between 25(OH)D and cIMT, while there were no significant differences in echocardiography results.

Table 1

Vit D levels	HDL	LDL	cIMT	FMD
	r=0.8493	r= -0.6032	r= -0.6616	r=0.8527

Conclusions: Vitamin D deficiency is a cardiovascular risk factor in juvenile idiopathic arthritis.

References:

[1] Çomak E, Doğan ÇS, Uslu-Gökçeoğlu A, Akbaş H, Özdem S, Koyun M, Akman S. Association between vitamin D deficiency and disease activity in juvenile idiopathic arthritis. Turk J Pediatr. 2014; 56(6):626–31.
[2] Suzanne E. Judd and Vin Tangpricha. Vitamin D Deficiency and Risk for Cardiovascular Disease. Am J Med Sci. 2009; 338(1): 40–44.

Acknowledgements: Thanks to Dr. Samar Abd Alhamed for her efforts in completing statistics in this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1214

THU0525 SAFETY OF ADALIMUMAB ± METHOTREXATE FOR THE TREATMENT OF POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS (PJIA): STRIVE REGISTRY

N. Ruperto[1], H. Brunner[2], K. Nanda[2], M. Toth[2], I. Foeldvari[1], J. Bohnsack[2], D. Milojevic[2], C. Rabinovich[2], D. Kingsbury[2], K. Marzan[2], P. Quartier[1], K. Minden[1], E. Chalom[2], G. Horneff[1], R. Kuester[1], J. Dare[2], M. Bereswill[3], J. Kalabic[3], H. Kupper[3], A. Martini[1], D. Lovell[2]. *[1]PRINTO-IRCCS Gaslini, Genova, Italy; [2]PRCSG, Cincinnati Children's Hospital Medical Center, Cincinnati, United States; [3]AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany*

Background: JIA is the most common chronic inflammatory rheumatic disease of childhood. TNF inhibitors are used for long-term control of pJIA disease.
Objectives: To evaluate the 7 year (y) safety of Adalimumab treatment with or without methotrexate (ADA±MTX) when used in current clinical practice for treatment of patients (pts) with active pJIA.
Methods: This is a 7 y interim analysis of an ongoing, multicenter, non-interventional, observational registry of pts with pJIA with up to10 y safety follow-up. Included pts were treated with ADA±MTX or MTX alone as comparison arm according to routine clinical care in PRINTO/PRCSG centres in EU, USA and Australia. MedDRA observational adverse events (AEs) were recorded from 1st day in the registry through last contact, irrespective of duration of registry treatment.
Results: In January 2014, enrollment was complete. As of June 1, 2016 cut-off date, 838 pts (301- MTX arm and 537 - ADA±MTX arm) were treated in the registry. There were 39 pts who rolled over from MTX to ADA±MTX arm. At registry entry mean pJIA disease duration was 1.3 y and 3.7 y and mean AJC71 was 5.8 and 5.2 for MTX and ADA±MTX arms, respectively. CHAQ disability index was 0.6 for both arms. Mean duration of study drug exposure in registry was 2.0 y (range: 0.0 – 7.1) and 2.5 y (range: 0.0 – 7.9) for MTX and ADA±MTX arms, respectively. Mean duration of observation in registry was 3.9 y (range: 0.0 – 7.2) and 3.5 y (range: 0.0 – 7.9) for MTX and ADA±MTX arms, respectively. Overall, 213 pts (70.8%) in MTX and 225 pts (41.9%) in ADA±MTX arms discontinued registry drug through 7 y. Main reasons (not exclusively) for registry drug discontinuation for MTX arm: pts required additional therapy (32.6%), other (13.3%), lack of efficacy (11.6%), AEs (9.3%), or pts achieved JIA remission (8.6%); for ADA±MTX arm: lack of efficacy (17.9%), other (7.3%), lost to follow-up (5.6%), AEs (5.4%), or pts achieved JIA remission (5.0%). Frequencies and rates of treatment-emergent AEs (from 1st dose date of registry drug in registry up to last dose + 70 days in registry, excluding AEs occurring during treatment interruption) were similar to those reported for observational AEs (from 1st day in registry up to last contact irrespective of drug treatment duration) (Table). Rate of serious infections was similar between MTX and ADA±MTX arms. One pt (0.2%) reported an event of opportunistic infection (fungal oesophagitis) in ADA±MTX arm. No reports of deaths, malignancies, active tuberculosis, oral candidiasis, demyelination, or congestive heart failure.

Table. Overview of the Observational Adverse events

	MTX		ADA±MTX			
			ADA only		ADA + MTX#	
	N=301 n (%)	PYs=1170.3 E (E/100 PYs)	N=160 n (%)	PYs=517.0 E (E/100 PYs)	N=377 n (%)	PYs=1338.5 E (E/100 PYs)
Any AE	157 (52.2)	505 (43.2)	66 (41.3)	216 (41.8)	178 (47.2)	553 (41.3)
AE at least "possibly drug related" per the investigator	87 (28.9)	197 (16.8)	30 (18.8)	66 (12.8)	88 (23.3)	177 (13.2)
Severe AE	17 (5.6)	23 (2.0)	14 (8.8)	22 (4.3)	25 (6.6)	41 (3.1)
Serious AE	32 (10.6)	52 (4.4)	21 (13.1)	39 (7.5)	56 (14.9)	95 (7.1)
AE leading to discontinuation of study drug or study	28 (9.3)	36 (3.1)	13 (8.1)	19 (3.7)	25 (6.6)	40 (3.0)
Infectious AE	87 (28.9)	179 (15.3)	38 (23.8)	75 (14.5)	105 (27.9)	187 (14.0)
Serious infectious AE	14 (4.7)	17 (1.5)	6 (3.8)	8 (1.5)	22 (5.8)	30 (2.2)
Injection site-related AE	6 (2.0)*	8 (0.7)	5 (3.1)	6 (1.2)	24 (6.4)	32 (2.4)

E, events; PYs, patient years (Observation time irrespectively of study drug treatment duration). *3 patients experienced injection site-related AEs with etanercept injections. During the registry, 52 (17.3%) pts in MTX arm and 45 (8.4%) pts in ADA arm started with a biologic DMARD. #MTX was used at any point of time during the course of the registry.

Conclusions: Overall, ADA±MTX was well-tolerated in these pts with pJIA with no new safety signals. The retention rate for registry drug was higher in ADA±MTX arm compared to MTX arm.
Acknowledgements: AbbVie sponsored the study & contributed with PRINTO & PRCSG to analysis, review, approval of the abstract. X. Leahy & A. Deshmukh (AbbVie) contributed to research. Medical writing: G. Patki (AbbVie).
Disclosure of Interest: N. Ruperto Grant/research support from: AbbVie Inc., AstraZeneca, Bristol-Myers Squibb, Janssen Biologics B.V., Eli Lilly and Co., "Francesco Angelini", GlaxoSmithKline, Italfarmaco, Novartis, Pfizer, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, and Wyeth Pharmaceuticals, Employee of: GASLINI Hospital, Speakers bureau: Astellas, AstraZeneca, Bristol-Myers Squibb, Italfarmaco, Janssen Biologics B.V., MedImmune, Roche, and Wyeth/Pfizer, H. Brunner Consultant for: AbbVie Inc., AstraZeneca, Centocor, Bristol-Myers Squibb, Boehringer-Ingelheim, Pfizer, Regeneron, Hoffman La-Roche, Novartis, Takeda, UCB, and Genentech, Speakers bureau: Genentech Pharmaceuticals, K. Nanda Consultant for: Medac Pharma, Inc., M. Toth: None declared, I. Foeldvari Consultant for: AbbVie and Novartis, J. Bohnsack Consultant for: Novartis, D. Milojevic Consultant for: Genentech and Novartis, C. Rabinovich Grant/research support from: UCB Pharma, Janssen, D. Kingsbury: None declared, K. Marzan Grant/research support from: AbbVie, P. Quartier Grant/research support from: AbbVie, Novartis, Pfizer, BMS, Chugai-Roche, Medimmune, Servier, and Swedish Orphan Biovitrum, Consultant for: AbbVie, Novartis, Pfizer, BMS, Chugai-Roche, Medimmune, Servier, Swedish Orphan Biovitrum, and Sanofi, K. Minden Grant/research support from: Pfizer, AbbVie and Roche/Chugai, Consultant for: Pfizer, Roche, and Pharma-Allergan, Speakers bureau: Pfizer, Roche, and Pharma-Allergan, E. Chalom Speakers bureau: AbbVie, G. Horneff Grant/research support from: AbbVie, Pfizer, Novartis, and Roche, Speakers bureau: AbbVie, Novartis, Sobi, Pfizer, and Roche, R. Kuester Grant/research support from: AbbVie Inc. and Wyeth/Pfizer, J. Dare Grant/research support from: AbbVie, AstraZeneca, Bristol-Myers Squibb, Horizon Pharma, Medac, Pfizer, Roche, and UCB, M. Bereswill Shareholder of: AbbVie, Employee of: AbbVie, J. Kalabic Shareholder of: AbbVie, Employee of: AbbVie, H. Kupper Shareholder of: AbbVie, Employee of: AbbVie, A. Martini Grant/research support from: AbbVie Inc., AstraZeneca, Bristol-Myers Squibb, Janssen Biologics B.V., Eli Lilly and Co., "Francesco Angelini", GlaxoSmithKline, Italfarmaco, Novartis, Pfizer, Roche, Sanofi Aventis, Schwarz Biosciences GmbH, Xoma, and Wyeth Pharmaceuticals, Employee of: GASLINI Hospital, Speakers bureau: Astellas, AstraZeneca, Bristol-Myers Squibb, Italfarmaco, and MedImmune, D. Lovell Consultant for: AstraZeneca, Centocor, Bristol-Myers Squibb, Pfizer, Regeneron, Hoffman La-Roche, Novartis, UBC, Xoma, Genentech, Amgen and Forest Research, Speakers bureau: Wyeth Pharmaceuticals
DOI: 10.1136/annrheumdis-2017-eular.2010

THU0526 SHORT AND LONG-TERM FOLLOW-UP OF TOCILIZUMAB FOR SEVERE JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED UVEITIS

N. Vegas-Revenga[1], V. Calvo-Río[1], M. Santos-Gómez[2], I. Calvo[3], M. González-Fernández[3], B. López-Montesinos[3], M. Mesquida[4], A. Adan[4], M. Hernández[4], O. Maíz[5], A. Atanes[6], B. Bravo[7], C. Modesto[8], G. Díaz-Cordovés[9], N. Palmou-Fontana[1], J. Loricera[1], M. González-Vela[1], R. Demetrio-Pablo[1], L. Domínguez-Casas[1], C. Fernández-Díaz[1], J. Hernández[1], M. González-Gay[1], R. Blanco[1]. *[1]HUMV, Santander; [2]H, Torrelavega; [3]H Fe, Valencia; [4]H Clinic, Barcelona; [5]H, Donostia; [6]HUAC, A Coruña; [7]H Nieves, Granada; [8]H V d'Hebron, Barcelona; [9]H, Málaga, Spain*

Objectives: To assess the efficacy of tocilizumab (TCZ) at short and long term follow-up for severe juvenile idiopathic arthritis-associated uveitis.
Methods: Multicentre study of 25 patients who had inadequate response to traditional treatment with corticosteroids and at least one conventional immunosuppressive drug including biological therapy. The outcome variables were the degree of inflammation, visual acuity and macular thickness. The results are expressed as mean±SD for normally distributed variables, or median [IQR] when are not. Comparison of continuous variables was performed using the Wilcoxon test.
Results: We studied 25 patients (21 women/4 men); mean age 18.6±8.3. Uveitis was bilateral in 22. JIA subsets were oligoarthritis (n=17), polyarthritis (5), psoriatic (2) and enthesitis-related arthritis (1). Ocular sequelae at TCZ onset were cataracts (13), glaucoma (7), synechiae (10), band keratopathy (12), maculopathy (9), and amblyopia (5). Pattern of uveitis was: anterior (17), panuveitis (4), intermediate (2) and posterior (2). Before TCZ, they had received corticosteroids, conventional immunosuppressive drugs and biologics, including adalimumab (24), etanercept (8), infliximab (7), abatacept (6), rituximab (2), anakinra (1), and golimumab (1). TCZ dosage regimen was 8 mg/kg IV/4 weeks (21), every 2 weeks (2), every 8 weeks (1), or 2.9 mg/kg sc every week (1). All outcome variables showed a rapid and maintained improvement (Table 1) after

Abstract THU0526 – Table 1

	Baseline	1st week	2nd week	1st month	3rd month	6th month	1st year	2nd year	3rd year
Visual acuity mea±SD	0.57±0.35	0.55±0.35	0.56±0.35	0.59±0.33	0.6±0.32*	0.63±0.32*	0.63±0.35*	0.59±0.32*	0.45±0.34*
Anterior chamber cells median [IQR]	1 [0–1]	0.75 [0–1]*	0.5 [0–1]*	0 [0–0.5]*	0 [0–0]*	0 [0–0]*	0 [0–0]*	0 [0–0]*	0 [0–0]*
Vitritis median [IQR]	0 [0–0]	0 [0–1]	0 [0–0]	0 [0–0]	0 [0–0]*	0 [0–0]*	0 [0–0]*	0 [0–0]*	0 [0–0]
OCT (microns) mean±SD	358.69±92.17	351.4±108.29	336.5±100.9*	313.4±91.28*	280.7±35.03*	274.9±101.33*	245.4±29.4*	239.6±33.5	ND

*p<0.05 compared with basal.

a follow up of one year (n=21), 2 years (n=11), and 3 years (n=5). A reduction in the daily median dose of prednisone from 10 mg [0–15 mg] to 0 [0–0 mg] in 3 years, ($p<0.05$) was observed. After a median follow-up of 20.5±11.7 months in 4 patients, the interval between TCZ doses was increased to 5 weeks (n=2), 6 weeks (1) and 7 weeks (1) because of remission. TCZ had to be withdrawn due to articular inefficiency (1) or articular and ocular inefficiency (1). The main adverse effects were severe autoimmune thrombocytopenia, autoimmune anemia and thrombocytopenia, pneumonia, viral conjunctivitis and bullous impetigo in 1 patient each.

Conclusions: TCZ is useful at short and long term follow-up for severe Juvenile Idiopathic Arthritis-associated uveitis. It is possible to optimize the TCZ dose.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5265

THU0527 PEDIATRICIAN AND ADULT RHEUMATOLOGIST COLLABORATING IN A MULTIDISCIPLINARY REUMA-PED CLINIC. IS THIS TRANSITIONAL CARE MODEL EFFECTIVE?

P. Collado[1], A. Rubio[1], R. Diaz-Delgado[2], C. Calvo[2], R. Mustienes[1], F. Rey[1], C. Bonilla[1], E. Cruz[1]. *[1]Rheumatology; [2]Pediatric, Hospital Universitario Severo Ochoa, Madrid, Spain*

Background: Transitional care should be a planned movement of adolescents with chronic diseases from child-centred to adult-oriented health care system. Recently a EULAR/PReS taskforce has developed the first international set of recommendations and standards for transitional care[1].

Objectives: To describe the results from a specific transitional care programme.

Methods: The current transitional care programme includes a multidisciplinary PED-REUMA clinic (MPRC) weekly and a non-defined period of rheumatologic follow-ups by the same rheumatologist of MPRC. The transitional care team is composed of two pediatricians, one adult rheumatologist -as transition coordinator-, a clinical nurse specialist and administrative support, as well as a psychologist and physiotherapists. Clinical information and therapies were collected throughout the disease course, and the HEADSS method of psychosocial interviewing has been included recently.

Population of the present study included young patients (YP) from that programme who are going to transfer to adult-oriented health care system. Descriptive study of socio-demographics and clinic features was included, as well as patients' adherence. YP confidence to be transferred and satisfaction with the current transitional process were measured using on a scale of 0 to 10. In patients suffering from juvenile idiopathic arthritis (JIA), clinical status of disease activity and clinical remission and CHAQ were tested before transfer.

Results: Twenty-seven YP with female predominance (63%) were included. The average age was 21±3 yo at time of a planned transfer and 16±3.4 yo at inclusion to the MPRC. JIA was the commonest condition whereas dermatomyositis was uncommon. Up to 63% patients required some DMARDs during the MPRC follow-up, but only a 37% needs maintained immunosuppressive therapies and three (11%) patients required changing the therapeutic target before transfer. YP adherence to rheumatologist appointments was high. Regarding HEADSS data: most YP were students and living at family home, around 50% gave up sports or other activities due to homework or exams, 29% of YP occasionally drank some alcohol but none used tobacco, and 47% of YP felt sad or down once in a while. Patient's confidence to be transferred was 7.7±2.1 (mean±SD; min-max: 2–10). YP showed high satisfaction with the current transitional process, 9.7±0.4 (min-max: 9–10).

Before transfer, 17 patients with JIA showed a mean±SD value of JADAS10 of 2±5 (min-max, 0–18), clinical remission on/off medication was 23% and 53% respectively. Mostly functional status reported by patient was low, YP-rated CHAQ (mean 0.06; min-max, 0.0–0.75).

Conclusions: To the best of our knowledge, this is the first study evaluating a Spanish transitional care programme. The study reports a positive impact across adolescence of our transitional care model in a real life situation. Implementation of recommendations depended on the local available resources.

References:

[1] Foster HE. EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases. Ann Rheum Dis Published Online First: [1, November 2016] doi:10.1136/ annrheumdis-2016–210112.

Acknowledgements: Beatriz Jimenez. Auxiliary to the clinical nurse specialist and administrative support of Rheumatology Department.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5444

THU0528 STING-ASSOCIATED VASCULOPATHY WITH ONSET IN INFANCY (SAVI): A DIFFERENTIAL DIAGNOSIS OF INFLAMMATORY INTERSTITIAL LUNG DISEASE

R. Dagher[1], R. Ghiye[1], G. Nicolas[1], H. Feghali[1], M.C. Fadous Khalife[1], L. Seabra[2], Y.J. Crow[2]. *[1]Pediatrics, Notre Dame de Secours University Hospital, Byblos, Lebanon; [2]Paris-Descartes University, Sorbonne-Paris-Cite, Institut Imagine, INSERM UMR 1163, Paris, France*

Background: STING-Associated Vasculopathy with onset in Infancy (SAVI) is an auto-inflammatory monogenic disease. SAVI is caused by an upregulation of type I interferon signaling due to sporadic or inherited gain-of-function mutations in the STimulator of INterferon Gene (STING)/Transmembrane Protein 173 (*TMEM173).* The first description of this phenotype, and the identification of the mutated gene, was in 2014. SAVI is characterized mainly by cutaneous vasculopathy leading to necrotic lesions, and progressive interstitial lung disease with secondary fibrosis.

Objectives: SAVI is a rare disease with unknown prevalence. To the best of our knowledge, 25 cases have been reported so-far. These patients variably manifest cutaneous lesions and inflammatory lung disease. Here we present a case of SAVI with onset of features at the age of 3 years.

Methods: A now 8 year old boy born to non-consanguineous parents was described to have experienced recurrent fevers, polyarthralgia and polyarthritis, livedo of the limbs, facial telangiectasia, necrotic lesions of auricles and digits and failure to thrive since the age of 3 years. He has normal cognitive development. His familial history is notable for epilepsy in 2 of his siblings and Behcet disease in a paternal cousin.

Laboratory tests at age 6.5 years revealed increased ESR (60mm/h) while CRP varied from 3 to 14 mg/L. ANA titres were positive (1/640), with normal complement level and negative anti-DNA. c-ANCA and p-ANCA were negative. ECA and lysozymes were in the normal range. Although the child had no respiratory symptoms, chest X-ray revealed diffuse interstitial parenchymal infiltrates. Chest angio-CT showed ground-glass lesions with fibrotic bands and mediastinal and para-hilar adenopathies. FVC and DLCO were reduced on pulmonary functional testing. Lung biopsy was not performed.

Empirical treatment with pulse and oral corticosteroids along with azathioprine was started. Over a period of one year, systemic inflammation and skin involvement regressed dramatically, but his lung disease showed no improvement.

Results: Genetic testing identified a previously reported V155M mutation in *TMEM173*.



Conclusions: SAVI is associated with significant morbidity and mortality. The diagnosis should be considered in children with interstitial lung disease after more common causes have been ruled out. Steroids and immunosuppressive therapies apparently show no efficacy in avoiding progression to irreversible lung damage. Promising results with treatment by Janus Kinase inhibitors as a means of blocking signaling downstream of the type I interferon receptor were recently published.

References:

[1] Y. Liu, A.A. Jesus, B. Marrero, et al. Activated STING in a vascular and pulmonary syndrome. N Engl J Med, 371 (2014), pp. 507–518.
[2] N. Jeremiah, B. Neven, M. Gentili, et al. Inherited STING-activating mutation underlies a familial inflammatory syndrome with lupus-like manifestations. J Clin Invest, 124 (2014), pp. 5516–5520.
[3] Fremond ML, Rodero MP, et al. Efficacy of the Janus Kinase 1/2 inhibitor ruxolitinib in the treatment of vasculopathy associated with TMEM173-activating mutations in 3 children. J Allergy Clin Immunol. 2016 Dec; 138(6): 1752–1755.

Acknowledgements: We thank Isabelle Melki for her valuable assistance in this case.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4489

THU0529 METHOTREXATE TREATMENT RESPONSE IN NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

R. Bakry, G. Horneff. *Asklepios, Sankt Augustin, Germany*

Background: Methotrexate is approved and recommend as first line disease modifying antirheumatic drug (DMARD) in polyarticular juvenile idiopathic arthritis (JIA). In can be used orally or via s.c. injection.

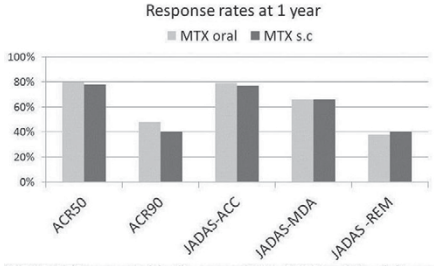
Objectives: S.c MTX is thought to be more efficious or act more rapidly than oral MTX. Thus we want to analyse the kinetic of response in JIA patients treated with oral versus s.c. MTX.

Methods: In the German BIKER registry a cohort of biologics naïve JIA patients starting treatment with MTX was built. The data bank was screened for patients treated with MTX orally vs. s.c for the first time. The JIA-ACR 90 and the JADAS10 definition of remission were used as outcome parameters.

Results: 410 JIA patients received treatment with oral MTX and 384 received s.c. MTX. RF negative polyarthritis was the most common JIA category (50%/51%)

followed by by extended oligoarthritis (27%/26%), polyarticular psoriatic arthritis (18%/16%) and RF positive polyarthritis (5%/8%). Disease duration (2.3+/-3.0 vs 1.9+/-2.7 was statistically higher in the oral cohort (p=0.04) but age at onset and baseline were similar. The baseline disease activity was higher in the s.c. cohort (JADAS10 16.5+/-7.2 compared to 14.7+/-8.2; $p<0.001$ and active joint count 9.0+/-10.1 vs. 7.4+/-7.7; p=0,011). The weekly MTX dosages were comparable with 13.6+/-5.4mg and 13.3+/-4.5 mg. Concomitant treatment with NSAIDS (95%/89%), oral steroids (24%/25%) or intraarticular steroids (6%/8%) were comparable.

After 12 months of treatment, 150 (38.3%) reached a JIA ACR90 with oral MTX and 131 (35%) with s.c MTX while 86 (21. 8%) and 72 (19.5%) reached JADAS-remission (JADAS10$\leq$1). By Kaplan-Meyer- analysis no difference in the early kinetic of response was found. Upon total observation for up to 7.5 years in the intention to treat population (patients discontinuing MTX due to inefficacy or intolerance or starting a biologic were calculated as non-responders) more patients in the oral cohort reached a JADAS-remission (162; 41%) than with s.c MTX (126; 34%) which was stastically borderline significant (p=0,05; odd's ratio 1.2 [95CI 1.0–1.8]).



JADAS-ACC= acceptable disease activity, MDA=minimal disease activity, Rem=remission

Conclusions: Data from the BIKER registry out of the clinical practice do show a high rate of JIA patients reaching a significant JIA-ACR response as well as JADAS-remission upon MTX as a sole DMARD. However, on the long term more patients with oral MTX reached JADAS remission. By Kaplan Meyer analyses we did not observe a superiority of s.c. MTX in the kinetic of response. The limitations of our analysis lie the character of a registry study, the lack of randomisation and study protocol leaving all decisions to start or to stop MTX by the responsible rheumatologist. Thus such data are preliminary and should be confirmed by randomized studies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3530

THU0530 CHARACTERIZATION OF A COHORT OF PSORIATIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS FROM A PAEDIATRIC UNIVERSITY HOSPITAL IN SPAIN

S. Hernández-Baldizón[1], A. Zacarías-Crovato[2], V. Torrente-Segarra[3], J. Calzada-Hernández[2], J. Sanchez Manubens[2], E. Iglesias[2], R. Bou Torrent[2], J. Anton[2]. *[1]Rheumatology, Juaneda Miramar Hospital, Palma de Mallorca; [2]Paediatric Rheumatology Unit, Sant Joan de Deu University Hospital, (Esplugues)Barcelona; [3]Rheumatology, Moises Broggi General Hospital, Hospitalet de Llobregat, Spain*

Background: Juvenile Psoriatic Arthritis (JPsoA) is a subtype of Juvenile Idiopathic Arthritis (JIA) present in 7% of JIA patients (1). Psoriasis is present in 0.5–1% of children. Diagnosis is often difficult, with the articular manifestations often preceding skin disease by years. Data is scarce in the Spanish population.

Objectives: Describe demographical and clinical caracteristics of our cohort of JPsoA.

Methods: Descriptive, transversal study of patients attended from 1/2012–12/2016. Included were all complyers with ILAR Criteria (2) for JPsoA (Edmonton 2001). We also included the Wallace Criteria for clinical inactive disease (3) as a variable and endpoint. Data were included and analyzed using SPSS MAC 20.

Results: 31 patients were included: 18 (59%) girls, 13 (41%) boys. All Caucasian. They comprised 5% of all our JIA patients in that period.

Mean age at diagnosis was 7.4 years. All were RF-; 9 (29%) ANA+; 4 (12.9%) HLA-B27+; articular onset 17 (55%) and cutaneous onset 14 (45%). 9 (29%) had Temporomandibular Joint (TMJ) symptoms: 5 (16%) had pain and 4 (12.9%) had a positive MRI for TMJ synovitis.

Plaque psoriasis 14 (45%), guttata 3 (9.6%) and 3 (9.6%) had both. Dactylitis 8 (26.6%); enthesitis 6 (19.35%). Joint disease was mainly oligoarticular 15 (48%), monoarticular 14 (45%) and polyarticular 1 (3.2%). Axial disease 4 (12.9%) at follow-up. 7 (22.5%) uveitis; 5 (77%) were ANA +. 3 (9.6%) onicodistrophia and 6 (19.3%) enthesitis.

All patients received NSAIDs; 30 (96%) methotrexate; 6 (19.3%) switched to leflunomide. 16 (51.6%) received biologic treatment and 9 (29%) more than one. Articular debutants 10 (32.2%) received biologic treatment more than the those with cutaneous onset 6 (19.35%). We report 3 (9.6%) anti-TNF/paradoxal psoriasis events.

Wallace Inactivity Criteria were achieved in 25 (80.6%), with no differences between the biologic and DMARDS groups in time up to Achieving Wallace Criteria (TimeWall). TMJ positive MRI did have a negative effect on TimeWall with 2 (66.6%) $\geq$8 yr (8, 11y) to TimeWall.

Conclusions: We describe the clinical features and demographics of a series of spanish JPsoA patients. We found more oligoarticular and monoarticular involvement and an important presence of enthesitis and dactylitis; higher frecuency of uveitis than published data (22.5% vs. 10–15%). Some were ANA-, reinforcing the need for screening. More than half required biologic treatment, and several cases we needed to switch drugs. Almost 60% of the patients were girls. Articular onset was associated with more active, harder to treat disease. TMJ positive RMI was associated with longer TimeWall. However, Wallace Criteria were not achieved globally.

References:

[1] T.R.Southwood, R.E. Petty, P.N. Malleson, et al. Psoriatic arthritis in children, Arthritis Rheum. 32 (1989) 1007–1013.

[2] Petty RE, Southwood TR, Manners P, et al. ILAR Classification of Juvenile Idiopathic Arthritis: second revision, Edmonton 2001, J. Rheumatol. 31 (2004) 390–392.

[3] Wallace CA, Giannini GH, Et Al. American College of Rheumatology provisional criteria for defining clinical inactive disease in select categories of juvenile idiopathic arthritis. Arthritis Care Res (Hoboken). 2011 Jul;63(7):929–36.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6645

THU0531 USE OF RITUXIMAB IN PAEDIATRIC RHEUMATOLOGY - EXPERIENCES FROM A SINGLE TERTIARY CENTRE

S. Deepak[1], R. Obrien[2], K. Warrier[1], E. Mcdermott[2], S. Rangaraj[1]. *[1]Paediatric rheumatology, Nottingham Childrens hospital; [2]Immunology, Nottingham university Hospitals NHS Trust, Nottingham, United Kingdom*

Background: Rituximab is an anti-CD20 monoclonal antibody therapy used widely in the management of paediatric rheumatological conditions. Studies suggest that Rituximab is safe and effective in rheumatic autoimmune diseases, but data on paediatric use remains limited. Although Rituximab spares plasma cells, hypogammaglobulinaemia can still develop, leading to recurrent infections. Frequency of hypogammaglobulinaemia in children receiving Rituximab for rheumatological conditions is unknown.

Objectives: To analyse the use of Rituximab in a tertiary Paediatric Rheumatology centre over the last 15 years (2001–2015). The primary aims were to identify the number of patients who received Rituximab, the underlying diagnoses and the response to treatment. Our secondary aims were to identify the incidence of hypogammaglobulinemia associated with Rituximab use and the frequency and severity of infections. Frequency of monitoring of immunoglobulin levels, lymphocyte subsets and functional antibodies to pneumococcus were noted.

Methods: Retrospective analysis of case notes, electronic records and laboratory data of patients who received Rituximab in the paediatric rheumatology department from 2001–2015.

Results: A total of 22 patients received Rituximab (total of 1500mg/m^2 per cycle over 2 – 4 divided doses) during the study period. 3 were excluded due to insufficient data. Median time of commencement of Rituximab from diagnosis was 2 years 8 months. Of these, 12 patients achieved remission within 6 to 12 months. Rituximab was discontinued in the non-responders at 12 months.

Diagnosis	No of patients		Median No of cycles	Remission achieved
Polyarticular JIA	RF +	2	3.5	2 (100%)
	RF -	4		0
JDM	6		3	5 (83%)
SLE	5		2	4 (80%)
Vasculitis (GPA)	2		2.5	1 (50%)

8 patients (42%) were noted to have hypogammaglobulinaemia at some point. The role of cyclophosphamide contributing to hypogammaglobulinaemia could not be excluded in 2 and a further patient is currently being investigated for an underlying primary immune deficiency. In the remaining 5 (26%) patients, we believe the low IgG levels are secondary to Rituximab, of which two needed long term Ig replacement. Overall 12 patients reported recurrent/severe infections of which 6 had low immunoglobulin levels.

Conclusions: RF+ JIA patients appear to have responded the best to Rituximab and RF- JIA patients the least (0/4), with good results in JDM and SLE subgroups (80–83%). The incidence of hypogammaglobulinaemia secondary to Rituximab in our cohort was 26%, which can be prolonged and worsen with increased number of cycles. Prior treatment with cyclophosphamide may be contributory. We suggest regular monitoring of immunoglobulin levels and lymphocyte markers on all patients prior to commencement of Rituximab and regular intervals subsequently, including further cycles.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3311

THU0532 PAEDIATRIC UVEITIS IN FRENCH REFERRAL OPHTHALMOLOGIC CENTERS: A DESCRIPTIVE ANALYSIS OF 74 CHILDREN

L. Moal[1], A. Rousseau[2], C. Titah[3], M. Labetoulle[4], B. Bodaghi[5], S. Guillaume Czitrom[6]. *[1]Service de Medecine des Adolescents; [2]Service d'Ophtalmologie, CHU Bicetre, le Kremlin Bicetre Cedex; [3]Service d'Ophtalmologie, Fondation Rothschild, Paris; [4]Service d'Ophtalmologie, CHU Bicetre, le Kremlin Bicetre; [5]Service d'Ophtalmologie, CHU Pitie-Salpetriere, APHP, Paris; [6]Service de Medecine des Adolescents, CHU Bicetre, APHP, le Kremlin Bicetre, France*

Background: Uveitis in children is rare. Intensive interactions between ophthalmologists and paediatric rheumatologists are needed in order to choose the best therapeutic strategies for severe uveitis attacks.
Objectives: Describe a cohort of 74 patients with paediatric uveitis.
Methods: Retrospective analysis of children followed for uveitis before 18, by one paediatric rheumatologist (SGC) for systemic treatments' management and members of 3 ophthalmologic departments specialized in uveitis care in children (AR, CT, ML and BB) in Paris, during the 2006–16 period.
Results: There were 74 paediatric uveitis, 42 anterior (57%, group1), 16 intermediate (21%, gr2), 7 posterior (9%, gr3) and 9 pan-uveitis (12%, gr4). Gender was equal in gr2–4, but there were more females in gr1. At presentation, mean ages were 8.6±4.1, 9.8±3.9, 9.1±3.6 and 10±4.2 years old. Mean follow-up was 3.7±3.7 years. JIA was the leading cause of gr1 uveitis (45%); gr2–3 uveitis were idiopathic in 81% and 86%, respectively. In gr4, etiologies were found in 7 out of 9 patients (Behçet-3, JIA-2, BBS-1, TINU-1).

Table 1

Complications	I: Anterior uveitis (42) 51%	II: Intermediate uveitis (16) 71%	III: Posterior uveitis (7) 71%	IV: Panuveitis (9) 100%
Cataracts	25%	21%		44%
Papilledema	19%	21%		56%
HTP/Glaucoma	16%			
Macular edema			29%	33%
Vitreous hemorr.		21%		33%
Retinal detach.		29%		33%
Blindness	6% (n=2Uni)	7% (n=1Uni)	29% (n=2Bi)	33% (n=2Uni+1Bi)

Conclusions: Paediatric uveitis induce a very high-level burden in children, even when anterior and sometimes despite optimal therapeutic management in tertiary care centers. Their early recognition and tight control in specialized units are absolutely required in order to decrease the level of definitive complications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6629

THU0533 DO JIA CORE OUTCOME VARIABLES AT BASELINE PREDICT CLINICALLY INACTIVE DISEASE STATES AT ONE YEAR?

S.J.W. Shoop-Worrall[1,2], S.M. Verstappen[3], J.E. McDonagh[4,5,6], W. Thomson[4,7], K.L. Hyrich[3,4] on behalf of CAPS. *[1]Arthritis Research UK Centre for Epidemiology, the University of Manchester; [2]NIHR Manchester Musculoskeletal BRU, Central Manchester University Hospitals NHS Foundation Trust and University of Manchester Partnership; [3]Arthritis Research UK Centre for Epidemiology, the University of Manchester; [4]NIHR Manchester Musculoskeletal BRU, Central Manchester University Hospitals NHS Foundation Trust and University of Manchester Partnership; [5]Centre for MSK Research, the University of Manchester; [6]Manchester Academic Health Science Centre; [7]Arthritis Research UK Centre for Genetics and Genomics, the University of Manchester, Manchester, United Kingdom*

Background: Identifying predictors for early clinically inactive disease (CID) would allow stratified treatment decisions at diagnosis, minimising the burden of unnecessary therapies. JIA core outcome variables (COVs) are routinely collected and would therefore be convenient predictors. However, different groups of children are identified by current CID definitions (Wallace's preliminary criteria vs. clinical Juvenile Arthritis Disease Activity Score in 10 joints (cJADAS10)) and predictors may differ depending on which CID outcome is applied.
Objectives: To assess whether baseline COVs predict achievement of CID according to Wallace's preliminary criteria or the cJADAS10 cut-off in patients with JIA.
Methods: Children and young people enrolled to the Childhood Arthritis Prospective Study (CAPS), a UK multicentre inception cohort, before January 2011, were selected if diagnosed with oligoarticular, RF-negative or RF-positive polyarticular JIA.
At one year following initial presentation to paediatric rheumatology, children were classified as i) CID according to Wallace's preliminary criteria and ii) CID according to cJADAS10. Baseline COVs (active joint count, limited joint count, physician's global, parental global, functional ability (Childhood Health Assessment Questionnaire (CHAQ)) and ESR) were tested for predictive ability for these outcomes using univariate and forced-entry multivariate logistic regressions, adjusting for age and symptom duration at initial presentation, gender and ILAR subtype. Multiple imputation accounted for missing data.
Results: Of 829 children included, 70% were female and the majority had oligoarticular JIA (68%). At one year, 28% had achieved CID according to Wallace's preliminary criteria and 38% according to the cJADAS10 (21% CID on both).
In univariate analyses, increased baseline CHAQ and physician's global assessment score predicted lower odds of achieving both CID states. In addition, increased active joints (OR: 0.97, 95% CI0.94, 0.99), and patient/parent global assessment scores (OR: 0.87, 95% CI 0.81, 0.93) predicted lower odds of CID on the cJADAS10 only. In multivariate analyses, one increased CHAQ point at baseline independently predicted 28% lower odds of CID on the cJADAS10 (95% CI 0.53, 0.98). However, no baseline COVs predicted CID on Wallace's preliminary criteria. No demographic variables were significantly predictive in any model.
Conclusions: There were different predictors for CID on the cJADAS10 vs. Wallace's preliminary criteria. Children with poor functional ability at initial presentation are less likely to achieve CID on the cJADAS10. These children could be targeted with more aggressive treatment strategies to better control their disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3738

THU0534 BASELINE CHARACTERISTICS AND DESCRIPTIVE SAFETY DATA OF INTRAVENOUS ABATACEPT-TREATED PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN A US HEALTHCARE CLAIMS DATABASE

T. Simon[1], S. Singhal[2], N. Ray[2], Z. Guo[1]. *[1]Bristol-Myers Squibb, Princeton, United States; [2]Mu Sigma, Bangalore, India*

Background: Abatacept (ABA), the first selective co-stimulation modulator approved and used for the treatment of moderate-to-severe polyarticular juvenile idiopathic arthritis (JIA), has a mechanism of action that is different from other biologic (b)DMARDs.
Objectives: To describe the baseline (BL) characteristics and validated safety outcomes of patients (pts) with a diagnosis of JIA in a US healthcare claims database treated with IV ABA and those with a minimum of 12 months (M) of ABA treatment.
Methods: Pts aged <18 years (yrs), diagnosed with JIA and in the Truven Health MarketScan® database between 1 Jan 2006 and 30 Sep 2014 were eligible for inclusion. Pts were required to have ≥180 days (d) of continuous health plan enrolment prior to a diagnosis of JIA based on two International Classification of Diseases, Ninth Revision, Clinical Modification codes (714.3x) within 90 d. BL characteristics and prior bDMARD use were analysed for two IV ABA-treated groups: a total cohort and a subgroup of pts with ≥12M of treatment. Three categories evaluated prior bDMARD use claims: biologic holiday (other bDMARD in history but not within 180 d of BL), biologic switcher (other bDMARD within 180 d of BL) and true initiator (no history of other bDMARD). Incidence rates (IR; number of events/person yrs [p-y] of exposure) per 100 p-y of exposure with 95% CI were calcuated for infections, malignancies and uveitis.
Results: A total of 238 IV ABA-treated pts were identified with 89 pts having ≥12M of ABA treatment. The mean (SD) follow-up duration was 1.73 (1.28) yrs for the total IV ABA cohort and 2.28 (1.03) yrs for the ≥12-M subgroup. Most pts were female, and mean age was 12.4 yrs. Overall, the total IV ABA cohort was more likely to have a claim in the BL period for asthma and cardiovascular disease versus the ≥12-M subgroup; the ≥12-M subgroup was more likely to have uveitis (Table). The most frequent other bDMARD claim for the total IV ABA-treated pts in the biologic holiday group was etanercept (41.9%), and adalimumab for

BL Characteristics	Total IV ABA cohort (n=238)	IV ABA ≥12-M subgroup (n=89)
Female, n (%)	195 (81.9)	78 (87.6)
Age, mean (SD)	12.4 (3.2)	12.4 (3.2)
Uveitis, n (%)	22 (9.2)	11 (12.4)
Asthma, n (%)	21 (8.8)	6 (6.7)
Cardiovascular disease, n (%)	18 (7.6)	6 (6.7)
bDMARDs, n (%)	84 (35.3)	30 (33.7)
Non-biologic DMARDs, n (%)	105 (44.1)	37 (41.6)
Inpatient visits, mean (SD)	0.2 (0.8)	0.1 (0.3)
Outpatient visits, mean (SD)	11.6 (10.7)	10.0 (9.8)

Abstract THU0532 – Table 2

Treatments	I: Anterior uveitis (42)	II: Intermediate uveitis (16)	III: Posterior uveitis (7)	IV: Panuveitis (9)
High dose systemic steroid	45% (19)	80% (12)	71% (5)	100% (9)
Synth DMARDs	66% (27) (MTX-26, AZA-2)	60% (9) (MTX, AZA)	71% (5) (MTX, AZA)	78% (7) (MTX, AZA, COL)
SynthDMARDs + Biologics	34% (14) (IFX-4, ADA-10)	33% (5) (IFX-1, TCZ-1, IFN-4)	43% (3) (IFX-2, IFN-1)	33% (3) (IFX-3)
Surgery	18% (7) (cataracts – 5, glaucoma – 1, keratopathy – 1)	20% (3) (cataracts – 3, vitrectomy – 1)	0	63% (5) (cataracts – 2, glaucoma – 1, vitrectomy – 1, antiangio. inj.– 1)

biologic switchers (34.5%). For the total IV ABA cohort, six hospitalized infection claims were reported with an IR (95% CI) of 2.4/100 p-y (0.9, 5.3) and an IR of 2.8/100 p-y (1.2, 5.9) for new-onset uveitis. There were no validated cases of malignancies in the follow-up period.

Conclusions: Compared with an overall JIA population[1], abatacept pts are slightly older, more likely to use additional prior biologics, and have a history of asthma or cardiovascular disease. The rates of hospitalized infection and new onset of uveitis in this study are within published ranges[2,3] and are consistent with findings in the abatacept JIA registry.[4]

References:
[1] Simon, TA et al. Paediatric Rheumatology European Society Congress 2016; Poster P344.
[2] Beukelman et al. Arthritis Res Ther 2016;18:210.
[3] Foeldvari I et al. Arthritis Care Res 2016;68:46–54.
[4] Lovell, DJ et al. Arthritis Rheumatol 2016;68(Suppl 10):495–6.

Disclosure of Interest: T. Simon Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Singhal Consultant for: Bristol-Myers Squibb, N. Ray Consultant for: Bristol-Myers Squibb, Z. Guo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.1474

THU0535 LONG-TERM FOLLOW-UP OF 12 CASES OF CORONARY GIANT ANEURYSM AFTER KAWASAKI DISEASE

T. Sato[1], J. Somura[1], S. Hoshino[1,2,3], O. Furukawa[1], N. Okamoto[2,4], Y. Maruo[1]. *[1]Department of Pediatrics, Shiga University of Medical Science; [2]Department of Pediatrics, Omihachiman Community Medical Center; [3]Department of Pediatrics, Nagahama Red Cross Hospital; [4]Department of Pediatrics, Okamoto Kids Clinic, Shiga, Japan*

Background: The incidence of Kawasaki disease has been increasing since it was first reported by Tomisaku Kawsasaki in 1967. Among complications of the condition, the formation of coronary artery aneurysms is the most important. In particular, giant aneurysms with diameters that exceed 8 mm are likely to not regress and result in serious complications, such as acute myocardial infarction.

Objectives: To understand the long-term course of patients with giant aneurysms and Kawasaki disease as well as to consider the cause of aneurysm formation and its appropriate treatment.

Methods: We retrospectively studied the long-term course of 12 cases of giant coronary artery aneurysms accompanied with Kawasaki disease, which were being followed at Shiga University of Medical Science Hospital, Omihachiman Community Medical Center, and Nagahama Red Cross Hospital. These are three major facilities in Shiga prefecture of Japan, whose population is 1.4 million, comprising 200,000 children.

Results: Ten male and two female patients were included. The average current age was 16.8 years, the median age was 14.3 (10.7–18.9) years, and 5 cases were of adults. The average age at the time of onset was 3.5 years, the median age was 3.7 years (1.8 - 4.4), and all experienced onset between 1 and 5 years of age. The mean period from onset to treatment start was 6.7 days (median 5.0 (4.3–8.3)), but the average period until fever declined was 16.0 days and only three patients' temperature was reduced in 10 days. Aneurysm formation occurred at 14.1 days on average (median 12 (10–17)). The average size of the maximum coronary artery aneurysm at onset was 11.3 mm, and the median size was 9.5 mm (8.8 mm – 13.8 mm).The average and median follow-up periods were 13.2 years and 11.7 years (5.4–13.4), respectively. The number of patients received steroid therapy was four, and all their onset was after 2006. None received infliximab or underwent plasmapheresis.

During the course of the condition, all patients underwent multiple centripetal echocardiography. Among all cases, 7 underwent coronary angiography CT, 10 underwent myocardial scintigraphy. All 12 patients underwent cardiac catheterization and the total number of underwent cardiac catheterization for them was thirty-one. Two adult patients had a history of acute myocardial infarction and had undergone cardiac bypass surgery. Through this survey, we found that 9 cases developed giant coronary artery aneurysm between 1983 and 2007, and 3 cases between 2012 and 2015 used prednisolone.

Conclusions: All patients are currently receiving anticoagulant therapy and undergoing diagnostic imaging. In our prefecture, the incidence of giant coronary artery aneurysm accompanied with Kawasaki disease has been decreasing gradually. From 2007 to 2012, in which high dose gamma globulin therapy (2g/kg) has become commonly underwent for Kawasaki disease in Japan, there were no giant aneurysm formation in our hospitals. Three patients in whom giant aneurysms developed between 2012 and 2015 were taking oral prednisolone, thereby suggesting a relationship between prednisolone and giant aneurysm formation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4886

THU0536 CHILDHOOD ONSET OF BEHÇET DISEASE (BD) SYMPTOMS IN AN ADULT COHORT OF BD PATIENTS

V. Paisal[1], E. Al-Abadi[1], S. Protheroe[2], D. Carruthers[3], D. Situnayake[3], S. Powell[4], D. Mitton[4], T. Southwood[1]. *[1]Paediatric Rheumatology; [2]Paediatric Gastroenterology, Birmingham Children's Hospital; [3]Behçet Syndrome National Centre of Excellence, Birmingham and Midland Eye Centre; [4]Behçet Syndrome National Centre of Excellence, Birmingham and Midland Eye Centre, Birmingham, United Kingdom*

Background: Behçet Disease (BD) is rarely reported in children. It a systemic inflammatory condition characterised by autoinflammatory and vasculitic clinical features including recurrent oral aphthosis, genital ulceration, skin, eye, neurological and vascular inflammation, which is most commonly diagnosed between 20–40 years of age. It is unclear how many adult patients with BD have the onset of symptoms during childhood.

Objectives: The aim of our study was to investigate the age of symptom onset in a large cohort of adult patients with BD.

Methods: Since 2012, the Behçet Syndrome National Centre of Excellence, Birmingham and Midland Eye Centre, has used a multidisciplinary approach aiming to shorten time to diagnosis of BD, reduce blindness and morbidity, improve knowledge and ensure equity in access to biological therapies. Patient demographic and disease information, including patient recalled age at symptom onset, symptom sequence, documented clinical signs, treatment and outcome data are maintained in a secure web-based clinical data archive. For this study, the database was interrogated to determine patient age at recalled onset of the first BD symptoms, the sequence in which symptoms appeared and whether the ISG classification criteria for the diagnosis of BD were fulfilled before the age of 16 years.

Results: To June 2016, 478 patients aged between 11–68 years had data recorded in the BD database. 60 patients (12.7%, 49 females) who fulfilled International Study Group criteria for the diagnosis of BD, reported that the onset of their first symptoms was before the age of 16 years (range 2–15 years). All 60 patients reported recurrent oral ulceration and 55 reported genital ulceration but with a reported time interval between the onset of these 2 features of 0–44 years. Of the 60 patients, 26 patients reported sufficient symptoms to have fulfilled ISG criteria before their 16th birthday, including the coincident onset of recurrent oral and genital ulceration in 15/26 patients. Eye disease was only reported in 1 patient and a positive family history of BD in 5/26 patients. 11/26 patients reported a delay between the onset of oral and genital ulcers of a mean of 5.45 years (range 1–11 years).

Conclusions: Many adults with BD recall the onset of their first symptoms before their 16th birthday, usually with recurrent oral and genital ulceration. We speculate that greater awareness of BD in childhood may reduce the delay in diagnosis of this chronic condition.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6077

THU0537 FAMILY AND PATIENT'S PERCEPTION OF DIETARY INTERVENTION IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

E.M. Little[1], S. Grevich[2], J.L. Huber[3], D.L. Suskind[4,5], M.C. Bradford[4], A.M. Stevens[2,6], Y. Zhao[2,4]. *[1]Department of Pediatrics, Alaska Native Medical Center, Anchorage; [2]Pediatric Rheumatology, Seattle Children's Hospital, Department of Pediatrics, University of Washington; [3]Division of Nutrition, Seattle Children's Hospital; [4]Center for Clinical and Translational Research, Seattle Children's Research Institute; [5]Gastroenterology, Seattle Children's Hospital, Department of Pediatrics, University of Washington; [6]Center for Immunity and Immunotherapies, Seattle Children's Research Institute, Seattle, United States*

Background: Juvenile idiopathic arthritis (JIA) is the most common pediatric rheumatologic illness and can lead to significant disability. Complementary and alternative treatments are commonly practiced by families of patients with JIA, and >40% of patients with chronic arthritis seek dietary changes after their diagnosis. Dietary intervention studies in adults with rheumatoid arthritis showed moderate improvement in joint symptoms. Dietary supplements of omega-3 fatty acids have been tested in children with chronic arthritis and found to be associated with less NSAID use and lower serum IL-1 and TNF levels. There is an increasing need to understand if there is a role for dietary therapy in chronic arthritis.

Objectives: We aimed to evaluate the prevalence of special diets and the perception of the effectiveness of these diets on arthritis in JIA. We also assessed the interest of dietary interventions and perceived barriers.

Methods: An online survey was designed through a REDCap database capturing demographic information, self- or parent-initiated special dietary interventions and self- or parent-observing effects on joint symptoms, willingness to participate in a dietary intervention study. The survey link was posted on social media websites and distributed by the Arthritis Foundation. Descriptive statistical analyses were performed.

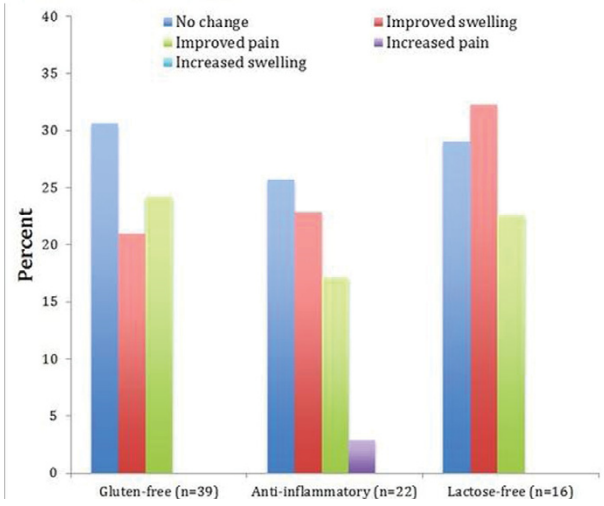
Results: A total of 265 responses were received from adult patients who had JIA and parents of children with JIA. We excluded 14 patients with inflammatory bowel disease or celiac disease-related arthritis and 24 responders with incomplete answers. Demographic and JIA characteristics of adult and pediatric patients are listed in Table 1. Ninety patients (63 children with JIA, 27 adults with history of JIA) had tried a special diet for arthritis. The top three special diets reported by parents included a gluten-free diet (62%), an anti-inflammatory diet (53%),

and a lactose-free diet (26%). There were similar clinical responses among the three diets (Figure 1). Twenty-five to thirty percent reported no change in joint symptoms whereas 20–30% reported improved pain or joint swelling. Sixty-one (34%) parents were willing to participate in a 3-month dietary intervention study and 78 (44%) parents answered "it depends".

Table 1

Population	Adult patients (n=49)	Pediatric patients (n=178)
Number of joints affected, n (%)		
≥5	43 (88)	125 (70)
<5	5 (10)	51 (29)
Treatment exposure, n, (%)		
Systemic glucocorticoid	40 (82)	108 (61)
DMARDs	44 (90)	146 (82)
Biologicals	35 (71)	114 (64)

Figure 1. Parental report of clinical responses to a gluten-free diet, an anti-inflammatory diet and a lactose-free diet in children



Conclusions: This is the first report of the family/patient perspective of the role of dietary intervention on JIA. Almost half of the affected patients attempted special diets, and many reported improvement in symptoms. Future interventional studies with objective outcome measurements are needed to validate these reports.

Acknowledgements: The authors would like to thank all the patients and families who have taken the survey. Arthritis Foundation and Facebook JA groups have helped distribute the survey.

Disclosure of Interest: E. Little: None declared, S. Grevich Grant/research support from: supported by Pfizer Medical and Academic partnership program, J. Huber: None declared, D. Suskind: None declared, M. Bradford: None declared, A. Stevens Grant/research support from: funded by Kineta Inc and Seattle Genetics. She has a license agreement with Quest Diagnostics., Y. Zhao: None declared

DOI: 10.1136/annrheumdis-2017-eular.2330

THURSDAY, 15 JUNE 2017

Other orphan diseases

THU0538 EFFECTS OF GLUCOCORTICOIDS AND METHOTREXATE-BASED THERAPEUTIC REGIMENS ON B CELL SUBPOPULATIONS IN PATIENTS WITH IGG4-RELATED DISEASE

M. Lanzillotta[1], E. Della Torre[1], R. Milani[2], E. Bozzalla[1], L. Rovati[1], E. Bozzolo[1], M. Falconi[3,4], L. Dagna[1,4]. *[1]Internal Medicine, Allergy and Clinical Immunology; [2]Unit of Immuno-hematology and Bone Marrow Transplant; [3]Pancreatic Surgery Unit, San raffaele Scientific Institute; [4]Università Vita-Salute San Raffaele, Milan, Italy*

Background: IgG4-related disease (IgG4-RD) is a systemic fibro- inflammatory disorder characterized by fibrotic lesions infiltrated by IgG4 positive plasma cells (1). The prompt clinical responses obtained after B cell depletion with rituximab in IgG4-RD patients suggest that B lymphocytes drive the pathogenesis of this condition and sustain disease activity (2). This conclusion, however, requires further confirmation because IgG4-RD responds also to non-B cell depleting therapies such as glucocorticoids and methotrexate

Objectives: To evaluate the effects of glucocorticoids and methotrexate-based therapeutic regimens on B lymphocyte subpopulations in patients with IgG4-RD.

Methods: Sixteen patients with active IgG4-RD were studied. FACS analysis was performed on peripheral blood in order to identify the following B cell subpopulations: total B cells (CD19+CD20- and CD19+CD20+ cells), circulating plasmablasts (CD19+CD20- CD27+CD38++ cells), naïve B cells (CD19+CD20+CD27-CD38+ cells), memory B cells (CD19+CD20-CD27+CD38- cells), circulating plasma cells (CD38+CD138+ cells). Disease activity was assessed by means of the IgG4-RD responder index (IgG4-RD RI). Flow cytometry was performed at baseline and after six months of immunosuppressive therapy with glucocorticoids (0.6–1mg/kg/day) and/or methotrexate (10–20mg/week). 16 sex and age matched healthy subjects were used as controls.

Results: At baseline, circulating plasmablasts were expanded in IgG4-RD patients (median 3780 cell/mL; range 330–9300) compared to controls (median 280 cell/mL; range 0–1000) ($p<0.05$); total B cells (median 133000 cell/mL; range 34000–569000) and naïve B cells (median 13080 cell/mL; range 1970–64270) were reduced in IgG4-RD patients compared to controls (median 280 cell/mL; range 194–330; and median 54020 cell/mL; range 21050–106780, respectively) ($p<0.05$). No circulating plasma cells were detected in healthy controls. No differences in memory B cells were observed ($p>0.05$). Circulating plasmablasts but not other B cell subsets positively correlated with serum IgG4 levels, number of organ involved, and IgG4-RD RI ($p<0.05$). At six months follow-up, the median IgG4-RD RI decreased from 9 to 2. Circulating plasmablasts, circulating plasma cells, and naïve B cells counts decreased in all patients together with disease improvement (p=0.0002, 0.0002 and 0.025 compared to baseline values, respectively); total B cells and memory B cells were unaffected by immunosuppressive therapy.

Pt	Age (years)	Sex	Organ involvement	Atopy	Eosinophil (cell/uL) (<400)	ESR (mm/hr) (<12)	CRP (mg/dL) (<6)	IgG4 (mg/dL) (<135)	PBL (cell/mL) (<650)	Naive B Cell (cell/mL)	Memory B Cell (cell/mL)
1	83	F	Pancreas - Biliary tree	-	100	13	46	1360	9000	8940	26940
2	73	F	Pancreas - Lymph nodes	+	300	4	Neg	534	7000	13030	15750
3	53	F	Aorta	-	500	21	21.3	185	6000	59800	107710
4	69	M	Pancreas - Lungs	-	300	21	46.3	343	5400	1970	6590
5	73	M	Pancreas – Biliary tree - Lungs	-	500	7	Neg	4900	9000	8370	9340
6	69	F	Aorta	-	300	38	14	420	1000	20830	55040
7	64	M	Pancreas	-	470	-	-	308	4000	13130	11060
8	57	M	Lacrimal glands – Salivary glands - Pancreas	+	300	<12	<6	1120	2020	30310	31210
9	60	M	Lymph nodes	-	200	15	10	313	5130	3370	48590
10	76	M	Biliary tree	-	200	-	<6	314	2150	56490	27760
11	66	M	Pancreas	-	600	59	<6	362	1760	43510	21600
12	54	M	Lymph nodes	+	1800	?	?	799	9300	18420	21880
13	70	M	Pancreas – Lymph nodes	-	300	20	<6	221	3560	11220	9980
14	79	M	Salivary glands- Aorta - Pancreas	-	200	19	<6	498	2520	64270	6860
15	67	M	Pancreas	-	200	-	-	586	940	9900	20070
16	61	M	Pancreas	-	100	<12	<6	137	330	12490	25970

Conclusions: Non-B cell depleting therapies based on glucocorticoids and/or methotrexate induce clinical improvement and deplete circulating plasmablasts, plasma cells and naïve B cells in patients with IgG4-RD; circulating total B cells and memory B cells are not affected by glucocorticoids and methotrexate. Our study, performed with non-B cell depleting agents, provides clinical evidences that circulating plasmablasts are likely linked to IgG4-RD pathogenesis and disease activity.

References:

[1] Della Torre E, Lanzillotta M, Doglioni C. Immunology of IgG4-related disease. Clin Exp Immunol. 2015.

[2] Wallace ZS, Mattoo H, Carruthers M, et al. Plasmablast as a biomarker of IgG4-related disease, independent of serum IgG4 concentrations. 2014.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3291

THU0539 SARCOIDOSIS IN SPAIN: CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS AT DIAGNOSIS IN 1082 PATIENTS

R. Pérez-Alvarez[1], B. Kostov[2], A. González García[3], R. Gómez De La Torre[4], M. Lopez Dupla[5], B. De Escalante[6], A. Alguacil[7], J. Chara[8], J. Velilla[9], J. Rascón[10], J.S. Garcia Morillo[11], C. Feijoo[12], E. Fonseca[13], M. Bonet[14], J.L. Callejas[15], G. de la Red[16], E. Calvo[17], C. Soler[18], E. Peral[19], J.F. Gómez Cerezo[20], G. Cruz-Caparrós[21], P. Perez[22], S. Rodríguez Fernández[23], B. Pinilla[24], A. Gato[25], M. Akasbi[26], A. Robles[27], I. Ojeda[28], M.J. Vives[29], C. Morcillo[30], M. Penadés[31], M. De Vicente[32], M. Ramos-Casals[33], L. Pallarés[10], P. Brito-Zerón[30,33] on behalf of the SARCOGEAS-SEMI Registry. *[1]Hosp Alvaro Cunqueiro, Vigo; [2]IDIBAPS, Barcelona; [3]Hosp Ramón y Cajal, Madrid; [4]HUCA, Oviedo; [5]Hosp Joan XXIII, Tarragona; [6]Hosp Clínico, Zaragoza; [7]Hosp Virgen de la Salud, Toledo; [8]Hosp Josep Trueta, Girona; [9]Hosp Miguel Servet, Zaragoza; [10]Hosp Son Espases, Palma de Mallorca; [11]Hosp Virgen del Rocio, Sevilla; [12]Hosp Parc Taulí, Sabadell; [13]Hosp de Cabueñes, Gijón; [14]Althaia, Manresa; [15]Hosp San Cecilio, Granada; [16]Hosp Esperit Sant, Santa Coloma; [17]Hosp General San Jorge, Huesca; [18]Hosp de Sta Caterina, Girona; [19]Hosp Virgen Macarena, Sevilla; [20]Hosp Infanta Sofía, Madrid; [21]Hosp de Poniente, Almería; [22]Hosp Puerta del Mar, Cádiz; [23]Hosp da Barbanza, A Coruña; [24]Hosp Gregorio Marañón, Madrid; [25]CH, Albacete; [26]Hosp Infanta Leonor; [27]Hosp la Paz, Madrid; [28]Hosp Valle del Guadiato, Córdoba; [29]San Joan de Déu, San Boi; [30]Hosp CIMA-Sanitas, Barcelona; [31]Hosp de Manises, Valencia; [32]Hosp Nuestra Señora del Prado, Talavera; [33]Hosp Clínic, Barcelona, Spain*

Objectives: To characterize the main features at presentation of sarcoidosis in a large multicenter cohort from Southern Europe.

Methods: In January 2016, the Autoimmune Diseases Study Group (GEAS-SEMI) created a national registry (SARCOGEAS) of patients with sarcoidosis. Sarcoidosis was diagnosed in agreement with the criteria proposed by the ATS/ERS/WASOG 1999 statement, and extrathoracic disease was classified with the 2014 WASOG instrument.
Results: The cohort consisted of 1082 patients (82% biopsy-proven), including 618 (57%) women and 464 (43%) men, with a mean age at diagnosis of 47yrs; 140 (13%) patients were born outside Spain, 965 (89%) were White, 69 (6%) Hispanic, 30 (3%) Black/African American and 18 (2%) Asian. Thoracic involvement was present at diagnosis in 979 (90%) patients, including 437 (40%) patients with stage I, 374 (35%) with stage II, 123 (11%) with stage III and 26 (2%) with stage IV. The most frequently reported extrathoracic involvements at diagnosis were cutaneous in 385 (36%) patients, extrathoracic lymph nodes in 218 (20%), liver involvement in 151 (14%) and ocular involvement in 118 (11%). Potentially life-threatening WASOG involvements were reported in frequencies less than 10%, including neurological involvement in 77 (7%) patients, kidney involvement in 59 (5%) or cardiac involvement in 21 (2%). Therapeutic approaches at diagnosis included the use of oral glucocorticosteroids in 637 (59%) patients, immunosuppressive agents in 84 (8%, mainly methotrexate in 63 patients) and biological agents in 15 (1%, mainly infliximab in 10 cases).
Conclusions: In this large series of sarcoidosis from Southern Europe, clinical presentation is dominated by adenopathies (both thoracic and extrathoracic) and cutaneous involvement (erythema nodosum), with lower frequencies in the main extrathoracic involvements than that reported in US and Japanese series.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4387

THU0540 EFFICACY AND SAFETY OF ADALIMUMAB IN BEHÇET'S DISEASE RELATED UVEITIS: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

C. Fabiani[1], A. Vitale[2], G. Emmi[3], L. Vannozzi[4], G. Lopalco[5], S. Guerriero[5], I. Orlando[2], R. Franceschini[6], D. Bacherini[4], L. Cimino[7], A. Soriano[8], B. Frediani[2], M. Galeazzi[2], F. Iannone[9], C. Salvarani[10], L. Cantarini[2].
[1]Department of Ophthalmology, Humanitas Research Hospital, Milano; [2]Unit of Rheumatology, University of Siena, Siena; [3]Department of Experimental and Clinical Medicine; [4]Department of Surgery and Translational Medicine, Eye Clinic, University of Firenze, Firenze; [5]Interdisciplinary Department of Medicine, Rheumatology Unit, University of Bari, Bari; [6]Ophthalmology and Neurosurgery Department, University of Siena, Siena; [7]Department of Ophthalmology, Arcispedale Santa Maria Nuova IRCCS; [8]Department of Rheumatology, Arcispedale Santa Maria Nuova IRCCS, Reggio Emilia, Italy, Reggio Emilia; [9]Unit of Rheumatology, University of Bari, Bari; [10]Department of Rheumatology, Arcispedale Santa Maria Nuova IRCCS, Reggio Emilia, Italy

Background: Current information on the use of adalimumab (ADA) in the treatment of ocular Behçet's disease (BD) is still based mainly on small series or case reports; nonetheless preliminary evidence is promising.
Objectives: The study aim was to evaluate the efficacy of ADA in a large series of BD-related uveitis.
Methods: We performed a multicenter retrospective observational study including 40 selected patients (66 eyes) receiving ADA. Clinical data were retrospectively analyzed at baseline, at 3 and 12 months of treatment. Primary end-point was: reduction of ocular inflammatory flares. Secondary end-points were: improvement of Best Corrected Visual Acuity (BCVA), reduction of macular thickness measured by optical coherence tomography (OCT), reduction in the occurrence of vasculitis assessed by fluorescein angiography (FA), evaluation of statistically significant differences between patients treated with ADA monotherapy and those undergoing ADA plus DMARDs and in patients firstly treated with ADA compared to patients previously administered with other biologics; ADA steroid sparing effect was also evaluated.
Results: During the first 12 months of ADA therapy the number of flares significantly decreased from 200 flares/100 patients/year to 8.5 flares/100 patients/year ($p<0.0001$). Similarly BCVA improved if compared to baseline (7.4±2.9 versus 8.5±2.1, $p=0.03$). OCT findings significantly improved showing a mean reduction of central macular thickness (CMT) of 27.27±42.8 microns at the end of follow up ($p<0.006$). FA identified retinal vasculitis in 22 cases at baseline (55%), 8 (20%) cases after 3 months and in only one (2.5%) case at 12-month follow-up. FA improvement was highly significant at 3 and 12-month follow-up if compared to baseline ($p<0.0001$ and $p=0.006$, respectively).
Conclusions: ADA is highly effective and safe for the treatment of BD-related uveitis, providing a long-term control of ocular inflammation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1026

THU0541 ROLE OF IL-1 INHIBITION IN ADULT ONSET STILL'S DISEASE (AOSD): A RETROSPECTIVE, OBSERVATIONAL MULTICENTRIC STUDY FROM THE ITALIAN SOCIETY OF RHEUMATOLOGY STUDY GROUP ON AUTOINFLAMMATORY DISEASES

S. Colafrancesco[1], R. Priori[1], P. Sfriso[2], G. Valesini[1], L. Punzi[2], M. Galeazzi[3], L. Cantarini[3] on behalf of The Study Group on Autoinflammatory diseases (Italian Society of Rheumatology). *[1]Dipartimento di medicina interna e specialità mediche, Sapienza University of Rome, Rome; [2]Department of Medicine - DIMED, University of Padova, Padova; [3]Department of Medical Sciences, Surgery and Neurosciences, University of Siena, Siena, Italy*

Background: IL-1 pathway plays a major role in the pathogenesis of Adult onset Still's disease (AOSD). IL-1 inhibitors [Anakinra (ANK) and Canakinumab (CAN)] proved their efficacy in AOSD as demonstrated in several case-reports and small case-series. However, due to the disease rarity, large randomized control trials are still lacking.
Objectives: To retrospectively evaluate the efficacy and safety of the use of IL-1 inhibitors (ANK and CAN) in patients with AOSD.
Methods: Data from patients with diagnosis of AOSD (Yamaguchi criteria) referred by 18 different Italian centres were retrospectively collected. Clinical and serological features as well as concomitant treatments, were collected on a dedicated database at the beginning of anti-IL-1 treatment (baseline) and then after 3, 6 and 12 months of follow-up. The Pouchot's score was used to evaluate disease activity.
Results: Data from 140 patients were collected (Table). All were treated with ANK and 4 were subsequently switched to CAN after ANK failure. The systemic pattern vs the chronic-articular were present in ANK and CAN groups in 104/140 (74.2%) and 3/4 (75%), respectively, vs 48/140 (25.8%) and 1/4 (25%), respectively. MTX was the most commonly used DMARD before ANK or CAN [91/140 (75.8%), 2/4 (50%) respectively]. In ANK group, the most commonly used previous biologic drug (bDMARD) was etanercept (79.3%). ANK was adopted as second-line bDMARD in 29/140 (20.7%) patients. In most of the cases it was administered at 100 mg/day in 126/140 patients (90%). CAN was employed at 150 mg every 8 weeks. ANK was effective on all AOSD clinical (fever, rash, pneumonia, pericarditis, pleuritis, sorethroat, lymphadenopathy, hepatomegaly, myalgia, arthritis, MAS) and serological (increased liver enzymes, hyperferritinemia, leucocytosis) manifestations ($p<0.0001$). The Pouchot's score was significantly reduced at all time points ($p<0.0001$). In ANK group no difference in treatment response was identified stratifying patients according to age, sex, pattern of disease, monotherapy vs combination. ANK primary and secondary inefficacy after 12 months were 15/140 (10.7%) and 11/140 (7.8%) cases, respectively. Adverse events (AEs) [mainly represented by in situ (28/47, 59.5%) or diffused (12/47, 25.5%) skin reactions and infections (12/47, 12.7%)] were the main reason for ANK discontinuation. Similarly, in CAN group Pouchot's score and clinical and serological features significantly ameliorated at all time points

Clinical features	ANK group	CAN group
Sex (M/F)	47/93	0/4
Age at onset (mean±SD, years)	35.4 ± 17	34.7 ± 13.3
Age at diagnosis (mean±SD, years)	37.4 ± 16.1	34.2 ± 15.4
Disease duration before treatment (mean±SD, months)	50.33 ± 81.67	58.33 ± 48.4
Previous therapies:	137/140 (97.8%)	4/4 (100%)
- STEROIDS	120/140 (85.7%)	2/4 (50%)
- DMARDs	29/140 (20.7%)	2/4(50%)
- bDMARDs		
Monotherapy	34/140 (24.2%)	2/4 (50%)
Combination therapy (+DMARDs)	106/140 (75.8%)	2/4 (50%)
N° Patient baseline	140 (100%)	4/4 (100%)
N° patients 3 months	118 (84.2%)	4/4 (100%)
N° patients 6 months	109 (77.8%)	4/4 (100%)
N° patients 12 months	97 (69.2%)	3/4 (75%)
N° patients at the time of this study	69 (49.2%)	2/4 (50%)
Mean duration of therapy (mean±SD, months)	35.7 ± 36.1	22.1 ± 16.5
AEs	47/140 (33.5%)	0/4 (0%)
Reasons of discontinuation:		
-AEs	24/71 (33.8%)	0/4 (0%)
-Remission	20/71 (28.1%)	1/4 (25%)
-Primary inefficacy	16/71 (22.5%)	0/4 (0%)
-Loss of efficacy	11/71 (15.4%)	1/4 (25%)
Pouchot's score at baseline	5.5 ± 1.9	4.2±2.6
Pouchot's score at 3 months	1.1 ± 1.4	1.2±1.8
Pouchot's score at 6 months	0.6 ± 1.2	1.5±1.9
Pouchot's score at 12 months	0.4 ± 0.8	1±1.4
% patients with steroids (baseline)	137/140 (97.8%)	4/4 (100%)
% patients with steroids (time of the study)	22/69 (31.8%)	2/2 (100%)
% patients with DMARDs (baseline)	120/140 (85.7%)	2/4 (50%)
% patients with DMARDs (time of the study)	35/69 (50.7%)	0/2 (0%)

($p<0.0001$). No AEs occurred with CAN, only in one case (1/4, 25%) treatment was stopped for loss of efficacy.
Conclusions: To our knowledge this is the largest retrospective observational study evaluating the efficacy and safety of ANK and CAN in AOSD. A prompt response was demonstrated already at 3 months of follow-up both in ANK and CAN groups. ANK proved to be effective in both patterns of disease, appearing also safe on the infectious risk. Nonetheless, skin reaction may represent a not negligible AEs during ANK treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6166

THU0542 ANTI-INTERLEUKIN 1 THERAPY IN FMF AMYLOIDOSIS: A SINGLE CENTER EXPERIENCE (CASE SERIES)

S. Ugurlu, B. Ergezen, A. Hacioglu, H. Ozdogan. *Division of Rheumatology, Department of Internal Medicine, Cerrahpasa Medical Faculty, University of Istanbul, Istanbul, Turkey*

Background: Recently there is increasing number of reports investigating the efficacy of anti-interleukin-1 (anti-IL1) therapy in AA-amyloidosis.
Objectives: Here we report our experience in IL-1 blockade in AA amyloidosis secondary to FMF.
Methods: Twenty nine FMF patients with secondary AA-amyloidosis with insufficient response to colchicine were treated with anti-IL-1 agents (canakinumab and anakinra). Creatinine (Cre), 24-hour urine protein (UP), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were measured before and throughout the treatment to evaluate the response and side effects.
Results: Twenty nine (16 female, 13 male) patients with FMF-related amyloidosis were administered anti-IL1 agents (12 on canakinumab, 17 on anakinra) in addition to colchicine in 27 patients, with a mean dose of 1.4±0.6 mg/day. The mean age was 40.13±11.76, while the mean duration of FMF was 28.79±10.51 years. The mean follow-up was 13.92±11.31 months for anakinra and 11.82±9.92 months for canakinumab.
Initial Cre levels were less than 1.5 mg/dl in 13 patients (range 0.37-.5). In this subgroup proteinuria decreased significantly from 3739.87±4860.41 to 1321.45±2015.62 mg/day while Cre was stable (0.91±0.30 mg/dl to 1.04±0.39 mg/dl) and acute phase response was normalized (CRP from 6.16±7.86 mg/l to 5.20±9.64 mg/l, ESR from 27.3±18.63 to 14±8.04).In the second group there were 11 patients with initial Cre levels higher than 1.5mg/dl (range 1.73–3.76). Proteinuria decreased from 6321.66±5936.43 to 4827.55±6264.43 mg/day, Cre increased from 2.53±0.76 to 3.07±1.70mg/dl, while there was a decrease in the APR in this subgorup (CRP from 40±64.65 mg/l to 26.71±26.76 mg/l, ESR from 57.37±37.65 to 39.11±27.72).
There are two patients on hemodialysis whereas two underwent renal transplantation. Global patient assessment score of the whole group was decreased from 7.44±2.54 to 3.89±3.53 with anti-IL-1.
Anakinra was stopped in 11 and canakinumab in 3 patients, due to irresponsiveness in 8 and 2 patients respectively. Among patients in whom anakinra was terminated 9 were later treated with canakinumab. Twenty four patients are still recieving anti-IL-1treatment (16 on anakinra, 8 on canakinumab).
Conclusions: Anti IL-1 treatments seems to be effective and safe in the treatment of AA amyloidosis secondary to FMF. The beneficial effect of this approach is more pronounced in patients with creatinine levels of less that 1.5 mg/dl.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5397

THU0543 A RETROSPECTIVE OVERVIEW OF THE TREATMENT MODALITY, OUTCOME AND RELAPSE RISK OF IGG4 RELATED DISEASE IN HONG KONG: A DATASET OF 108 PATIENTS FROM FOUR REGIONAL HOSPITALS

C.P. Tang[1], K.L. Lee[1], K.W. Lee[2], W.L. Ng[3], M.C. Wan[4], K.Y. Yuen[5]. *[1]Medicine, PYNEH; [2]Medicine, HKSH; [3]Medicine, UCH; [4]Medicine, RH; [5]Medicine, QMH, HK, Hong Kong*

Background: Currently most consensus suggests treating IgG4 related disease (IgG4RD) with prednisolone 0.6mg/kg/day tapering over 6 months while some experts prefer continuation of steroid up to 3 years (1–3).
Objectives: In this retrospective study, the treatment modality, response and relapse risk of IgG4RD patients over the past ten years from four regional hospitals in Hong Kong were analyzed.
Methods: Four regional hospitals participated with study period from 1/1/2006 to 30/6/2016. Patients were diagnosed IgG4RD according to the Japanese Comprehensive Diagnostic Criteria for IgG4RD. Treatment response at 6 months was recorded as complete, partial or non-remission based on the patient's and physician's perspective. Relapse was defined as disease progression either clinically or radiologically.
Statistical analysis: The association between treatment response and steroid dosage was analyzed by multivariate logistic regression. Risk factors for relapse were analyzed by multivariate cox regression and the hazard ratio was reported.
Results: 37 cases had surgical excision and disease recurred in 5 cases (relapse rate =13.5%). 87 patients (81%) received steroid treatment. The mean starting prednisolone was 33.5mg daily, with a mean duration of 95.2 weeks. At 6 months, 5 patients (6%) had no response, 34 patients (41%) had partial remission and 44 patients (53%) had complete remission.
29 patients also received other immunosuppressants, including azathioprine (n=25), mycophenolate mofetil (MMF) (n=6), cyclosporine A (n=4), mercaptopurine (n=2) and rituximab (n=1). The overall response rate for azathioprine and MMF was 64% and 67% respectively.
In the final multiple logistic regression, an initial prednisolone 30mg daily or above was associated with a higher complete remission at 6 months (OR=3.4, p=0.079) and the effect was more seen in patients with salivary and orbital involvement (OR=6.8, p=0.10)
18 patients relapsed after steroid was stopped and 6 patients relapsed while on prednisolone 2.5–7.5mg daily. The one year, two year and three year relapse rate were 13.3%, 24.1% and 26.5% respectively.
In the final multivariate cox regression, the presence of maintenance steroid was associated with a lower relapse risk (Hazard ratio=0.121, p=0.000) while serum IgG4 level above twice upper limit of normal (Hazard ratio=5.283, p=0.029) and hepatobiliary involvement (Hazard ratio=2.164, p=0.095) were associated with a higher relapse risk.
Conclusions: Most patients (94%) had good response to steroid. Patients with hepatobiliary involvement and serum IgG4 level above twice upper limit of normal were at higher relapse risk and a low dose, maintenance prednisolone for longer period is recommended.
References:
[1] Kleger A, et al. IgG4-related autoimmune diseases: Polymorphous presentation complicates diagnosis and treatment. Deutsches Arzteblatt international. 2015;112(8):128–35.
[2] Ghazale A, et al. Immunoglobulin G4-associated cholangitis: clinical profile and response to therapy. Gastroenterology. 2008;134(3):706–15.
[3] Kamisawa T, et al. Standard steroid treatment for autoimmune pancreatitis. Gut. 2009;58(11):1504–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2154

THU0544 THE IMPORTANCE OF R202Q POLYMORPHISM IN CLINICAL EXPRESSION OF FMF: A SINGLE CENTER CROSS-SECTIONAL STUDY

S. Yilmaz[1], E. Tekgoz[1], F.I. Cinar[2], M. Cinar[1]. *[1]Department of Internal Medicine, Division of Rheumatology, University of Health Sciences, Gulhane Medical Faculty; [2]Gulhane School of Nursing, University of Health Sciences, Ankara, Turkey*

Background: Familial Mediterranean fever (FMF) is an autosomal recessive inherited disease with recurrent fever and inflammatory episodes of serous membranes. The MEFV (Mediterranean fever) gene in the short arm of chromosome 16 is affected in the FMF. This gene encodes for a protein called 'Pyrin'. The erroneously synthesized Pyrin protein due to MEFV mutations is unable to control the post inflammatory process. Although there have been many efforts to find out genotype-phenotype association in FMF, no clear relationship has been clarified.
Objectives: In this study, the relationship between FMF clinical symptoms and MEFV gene mutations and polymorphism was investigated.
Methods: Total of 158 patients with FMF was included to the study that was conducted in a tertiary rheumatology outpatient clinic. The demographic and clinical features, as well as MEFV gene mutations were recorded in a "Patient Assessment Form". The clinical status of the disease was evaluated with FMF-severity score-2 (F-SS-2). The associations between clinical features and genetic alterations were calculated with Pearson Chi-square test.
Results: The mean age of patients was 24.3±5.1, mean delay in diagnosis was 5.6±6.3 years, and 155 of the patients (%98.1) were male. The percentage of patients stating they use colchicine regularly was 136 (86.1%), and mean dose was 1.4±0.3 mg/day. The most frequent mutation was M694V (76.6%), and R202Q, M680I and E148Q were found in a descending order (60.8%, 19.0% and 13.9%, respectively). The FMF severity score was found to be higher in patients carrying M694V mutation (p=0.01). In comparison with negative family history for FMF, M694V was more prevalent in patients with positive family history (82.0% vs 67.2%, p=0.035). Besides, M694V mutation found to be associated with arthritis (p=0.045). E148Q mutation was associated with the history of orchitis (p=0.029). The most significant relation between E148Q and clinical feature was family history of hemodialysis (p=0.005). The prevalence of non-periodic myalgia was %34.2, and this symptom was not present in patients carrying V726A mutation (p=0.005). M694V/R202Q was the most prevalent compound heterozygosis and found in 16 patients (10.1%). This mutation (M694V/R202Q) was associated with fewer frequencies of myalgia and peritonitis, and with good response to colchicine.
Conclusions: The presence of R202Q polymorphism is associated with FMF, and should be considered in the routine genetic analysis of the disease. In our patients, its co-existence with M694V seems to be associated with good response to colchicine, and to alleviate the severity of the disease expression of M694V, which is known to be associated with severe course.
References:
[1] Mor A, Shinar Y, Zaks N, Langevitz P, Chetrit A, Shtrasburg S, Rabinovitz E, Livneh A. Evaluation of disease severity in familial Mediterranean fever. Semin Arthritis Rheum. 2005 Aug;35(1):57–64.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4294

THU0545 COMPARISON OF THE CLINICAL AND LABORATORY FEATURES AT ONSET BETWEEN MULTICENTRIC CASTLEMAN'S DISEASE AND ADULT-ONSET STILL'S DISEASE

A. González García[1], W.A. Sifuentes Giraldo[2], J.L. Morell Hita[1], J.L. Patier de la Peña[2]. *[1]Rheumatology; [2]Internal Medicine, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Multicentric Castleman's disease (MCD) is a disorder characterized by polyclonal proliferation of B lymphocytes that is frequently associated with autoimmune manifestations and connective tissue diseases. MCD presents high levels of IL-6 and systemic symptoms such as fever, arthralgia, hepatosplenomegaly and serositis, so it is recommended to include MCD in the differential diagnosis of adult-onset Still's disease (AOSD). However, there are no studies comparing both groups of patients.
Objectives: To compare the clinical and laboratory features at onset between patients with MCD and AOSD seen in a Madrid tertiary care hospital.
Methods: We performed a retrospective observational study in patients with diagnosis MCD and AOSD attended our center between January 1989 and December 2015. The variables included demographics, clinical manifestations, laboratory tests and Yamaguchi's criteria.
Results: A total of 34 patients were included, 17 with MCD and 17 with AOSD. The comparison of the characteristics of both groups is presented in the table. There were no differences in age, uration of disease (MCD 158,6 days and AOSD 250,5 days, p=0,3919), diagnostic delay (MCD 18,4 and AOSD 52,2, p=0,2711), arthritis, myalagias, pleuritis or macrophagic activation syndrome, but persistent fever, rash, arthralgia, pharyngitis and pericarditis were significantly more frequent in ESA, whereas male gender, human immunodeficiency virus (HIV) and/or human herpes virus 8 (HHV8) infection, hepatosplenomegaly and lymphadenopathy were significantly higher in MCD. In the laboratory test results, leukocytosis and hypertransaminasemia were significantly higher in AOSD. 52.9% of patients with MCD met 5 or more Yamaguchi's criteria for AOSD.

	Multicentric Castleman's disease (n=17)	Adult-onset Still's disease (n=17)	p-value
Male:female ratio	2.4:1	0.4:1	0.0163
Age at diagnosis (mean ± SD)	46.4±13.1	37.5±13.5	0.0598
HIV infection	35.2%	0%	0.0154
HHV8 infection	35.2%	0%	0.0154
Persistent fever	47.1%	94.1%	0.0078
Rash	29.4%	64.7%	0.0392
Arthralgias	35,3%	88.2%	0.0014
Arthritis	0%	17.6%	0.0696
Pharyngitis	0%	41.2%	0.0029
Hepatosplenomegaly	47.1%	5.9%	0.0065
Pericarditis	0%	23.5%	0.0332
Pleuritis	17.6%	11.7%	0.6217
Lymphadenopathy	100%	17.6%	0.0001
Macrophage activation syndrome	11.7%	17.6%	0.6282
Leucocytes >10000/mm^3	35.2%	76.5%	0.0156
Increased transaminases	0%	58.8%	0.0002
Erythrosedimentation rate (mm/Hg)	52	77.5	0.1104
C-reactive protein (md/dl)	75.1	109.5	0.3699
Ferritin (ng/ml)	240	1926	0.1234

Conclusions: Patients with MCD may present common systemic manifestations and laboratory abnormalities at onset with AOSD and up to 50% of them may fulfill Yamaguchi's criteria for this disease, so MCD should be taken into account in its differential diagnosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6228

THU0546 IMPACT OF BONE LOCALISATION ON THE PROGNOSTIC OF LANGERHANS CELL HISTIOCYTOSIS: A MONOCENTRIC RETROSPECTIVE STUDY

J.-G. Letarouilly[1], N. Segaud[1], B. Wallaert[2], P.-Y. Hatron[3], R.-M. Flipo[1]. *[1]Rhumatologie, CHRU Lille Hôpital Roger Salengro; [2]Pneumologie, CHRU Lille Hôpital Calmette; [3]Médecine interne, CHRU Lille Hôpital Huriez, Lille, France*

Background: Langerhans cell histiocytosis (LCH) is a rare condition, and mostly affects children. Bone is the most commonly involved organ, with bone lesions in 50% of patients. In a recent work, Aricò et al. described that the probability of survival in children suffering from a multisystemic LCH with risk organ involvement was reduced if patient did not have any bony lesion [1]. There is no such a study in adult patients.
Objectives: The objective of the study was to know the bone impact on the prognosis of adult LCH.
Methods: A retrospective monocentric study was performed using data from the patients hospitalized for a LCH at Centre Hospitalier Régional Universitaire de Lille, a university hospital between 2001 and 2015. All patients with LCH and at an age of 18 years or older were included. Patients were excluded if they did not receive any osteoarticular imaging (radiography, scintigraphy, PET, MRI).
Results: Our study initially included 70 patients had LCH. After screening 54 patients met the inclusion criteria: 31 had bone localization (BLG) and 23 none (NBLG). The two groups showed differences. The lesion leading to the diagnosis was mostly osteoarticular (18 patients) in BLG and pulmonary (18 patients) in NBLG. The BLG presented more multisystemic form than the NBLG (20 vs 2, p<0.0001). Both groups were equivalent for comorbidities (p=0,206 for cancer and p=0,756 for cardiovascular disease), number of smokers and age at diagnosis (36.8+/- 14.15 years vs 36.7+/- 12.6 years, p=0.96 and 25 vs 22, p=0.06).
Treatment was required for 14 patients in BLG and for 2 in NBLG. In BLG, 8 patients were treated medically, mostly by corticosteroid therapy and chemotherapy (7), one patient underwent radiotherapy. 6 patients were treated by surgery. In NBLG, 2 patients were treated by corticosteroid therapy. There was no surgery in NBLG (table 1). 3 patients died in BLG, 2 directly related to LCH and one from postoperative infectious complications. One patient died in NBLG from hematologic pathology (chronic myelomonocytic leukemia). The time between diagnosis and death was one, six and 22 months in BLG, 36 months in NBLG. 7 patients presented relapses in BLG. 5 had been treated by medical treatment, one surgically and one had no previous treatment. The time of relapse was six, 8, 12, 14, 16, 52 and 72 months. 4 presented new bone lesions, 1 pulmonary lesions, 1 dermatologic lesions and 1 neurologic lesion (table 1). There was no relapse in NBLG. Unfortunately, there was a lack of statistical power to conclude about the bone impact on the prognosis.
Conclusions: Patients with bone location and those with no bone location are two different phenotypes of adult LCH. Patients with bone location are more proned to have a multisystemic relapsing disease. A multicentric study with a larger number patients is needed to bring more robust data to answer about bone impact on the prognosis of adult LCH.
References:
[1] Aricò M, Astigarraga I, Braier J, et al. Lack of bone lesions at diagnosis is associated with inferior outcome in multisystem langerhans cell histiocytosis of childhood. Br J Haematol 2015;169:241–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6790

THU0547 CHARACTERIZATION OF A GROUP OF 12 PATIENTS WITH MEVALONATE KINASE DEFICIENCY: SYMPTOMS AND TREATMENT WITH IL-1 INHIBITORS

A. Kozlova[1], V. Burlakov[1], N. Kuzmenko[1], S. Zimin[2], T. Varlamova[1], O. Barabanova[2], E. Raikina[1], A. Shcherbina[1]. *[1]Immunology, Federal State Budgetary Institution "National Scientific and Practical Center of Pediatric Hematology, Oncology and Immunology named after Dmitry Rogachev" of the Ministry of Healthcare of the Russian Federation; [2]Immunology, Children's Clinical Hospital N9, Moscow, Russian Federation*

Background: Mevalonate kinase deficiency (MKD) is a rare autosomal recessive autoinflammatory disease caused by mutations in MVK gene. MKD patients typically have an early onset of symptoms including recurrent episodes of high fever, abdominal pain, diarrhea and vomiting, arthralgia and lymphadenopathy (AIDAI criteria for HIDS). However not all patients have typical symptoms at the time of onset. MKD treatment remains an unsolved problem, since none of the modalities previously used for MKD treatment are fully effective in the disease control.
Methods: We conducted a retrospective analysis of clinical features of twelve patients (6 females, 6 males) with genetically confirmed MKD. Nine patients received therapy with inhibitors of IL-1 (Anakinra and/or Canakinumab). One of the patients died from amyloidosis and macrophage activation syndrome (MAS) prior to treatment initiation, her diagnosis was verified *post mortem*.
Results: Ten patients had manifested within the first 6 months of life, one – at the age of 1.5 years, one – at three years of age,. During the course of the disease all patients had periodic fever and peripheral lymphadenopathy (mainly cervical group), as well as abdominal pain, nausea/vomiting. Five patients had diarrhea, sometimes with blood, one patient suffered from severe constipation. Rash was seen in eight patients, myalgia, artralgia were observed only in six. Oral ulcers were noted in seven children. Three patients had neurological involvement, one patient had it as the main symptom. One patient had periorbital edema and hyperemia during attacks, which to our knowledge, have not been reported previously in MKD. One patient developed amyloidosis and MAS before IL1 inhibitor treatment initiation, which led to her death. In patients receiving anti-IL-1 therapy AIDAI index decreased from 58.3±11,2 before to 1,5±1,4 after 6 month of therapy (p=0.003).
Conclusions: MKD symptoms can be variable and sometimes atypical, which requires physician's awareness. In our cohort of MKD patients anti IL-1 therapy was highly effective.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2238

THU0548 PSORIASIS IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

A. Erden[1], E.D. Batu[2], E. Bilgin[3], H.E. Sonmez[2], E. Seyhoglu[3], S. Demir[2], L. Kilic[1], A. Sari[1], B. Armagan[1], O. Karadag[1], A. Akdogan[1], I. Ertenli[1], S. Kiraz[1], S.A. Bilgen[1], S. Ozen[2], U. Kalyoncu[1]. *[1]Department of Rheumatology; [2]Department of Pediatrics Rheumatology; [3]Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey*

Background: Familial Mediterranean fever (FMF) is a periodic fever syndrome caused by *MEFV* mutations. FMF may be associated with psoriasis in some cases. Previous study has shown that psoriasis was more common in the relatives of FMF patients [1].
Objectives: We aimed to investigate the prevalence of psoriasis among FMF patients and their relatives.
Methods: FMF patients followed at Hacettepe University Adult and Pediatric Rheumatology Departments between January and August 2016 were consecutively enrolled to this study. Demographic data, clinical manifestations, laboratory data and *MEFV* variant analysis were documented by medical file screening and face-to-face interview. The presence of psoriasis and psoriatic arthritis in patients and their relatives (first [Mother, father, children]-second [Brothers, grandchildren, grandfather and grandmother]-third degree [Nephew, uncle, maternal uncle, aunt, paternal aunt] relatives) and drug use history were also questioned. The patients were accepted to have psoriasis if the diagnosis was made by a dermatologist.
Results: 351 FMF patients (177 adults; 174 children) were included in this study (Table). 70.1% of adult patients were female, 29.9% were male. 53.4% of pediatric patients were female, 46.6% were male. The median age (min-max) of the adult patients was 35 (19–63), while the median age of the pediatric patient group was 10 (2–18). The onset age of symptom was 12 (0–39) in the adult group and 3 (1–14) in the pediatric group. The median age at diagnosis was 25 (2–52) in the adult group and 5 (1–18) in the pediatric group. Thirteen (3.7%) patients had psoriasis. Psoriasis was more common in adult patients than pediatric patients (p=0.02). Psoriasis was present in 22 (12.4%) of adult patients' and 9 (5.2%) of pediatric patients' relatives (p=0.023). The frequency of psoriasis in one or more relatives of all FMF patients was found to be 8.8%.

Table. Demographic and clinical characteristics of 177 adult and 174 pediatric patients with familial Mediterranean fever (FMF)

Characteristics	Adult patients (n=177)	Pediatric patients (n=174)	p value
Gender, female, n (%)	124 (70.1)	93 (53.4)	**0.001**
Abdominal pain, n (%)	159 (89.8)	166 (95.4)	**0.046**
Fever, n (%)	152 (85.9)	170 (97.7)	**<0.0001**
Arthralgia, n (%)	147 (83.1)	76 (43.7)	**<0.0001**
Arthritis, n (%)	93 (52.5)	27 (15.5)	**<0.0001**
Pleuritic chest pain, n (%)	104 (58.8)	14 (8)	**<0.0001**
Erysipelas-like erythema, n (%)	57 (32.2)	6 (3.4)	**<0.0001**
Pericarditis, n (%)	7 (4)	0 (0)	**0.007**
Amyloidosis, n (%)	5 (2.8)	1 (0.6)	0.215
Family history of FMF[a], n (%)	99 (55.9)	94 (54)	0.719
Parental consanguinity, n (%)	44 (25)	25 (14.4)	0.012
Hemodialysis history in family associated with FMF, n (%)	20 (11.3)	11 (6.3)	0.132
Psoriasis, n (%)	11 (6.2)	2 (1.1)	**0.020**
Psoriatic arthritis, n (%)	3 (1.7)	1 (0.6)	0.623
Psoriasis in any degree relatives, n (%)	22 (12.4)	9 (5.2)	**0.023**
Psoriasis in 1° relatives, n (%)	5 (2.8)	2 (1.1)	0.44
Psoriasis in 2° relatives, n (%)	5 (2.8)	6 (3.4)	0.73
Psoriasis in 3° relatives, n (%)	15 (8.5)	1 (0.6)	**<0.0001**

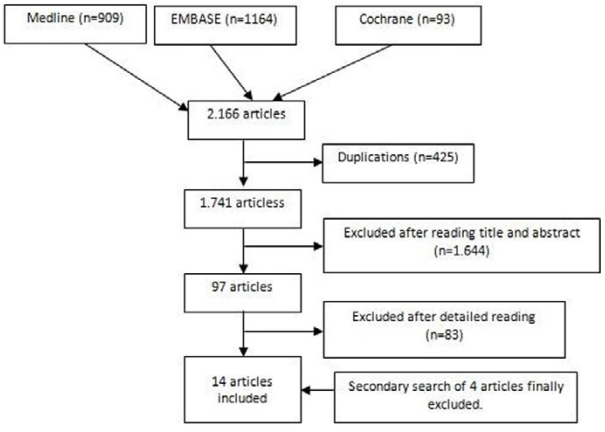
Conclusions: IL-1 has an essential role for signaling early T helper 17 (Th17) differentiation and Ashida et al have shown the presence of Th17 cells in the upper dermis of psoriasis-like lesions in a patient with FMF [2]. We may speculate that high IL-1 in FMF may cause Th17 activation and stimulation of keratinocytes; and this may be the reason for higher frequency of psoriasis in FMF patients. Thirteen (3.7%) patients had psoriasis; more common than the normal population (0.40%) (p<0.0001). FMF increases the likelihood of psoriasis in relatives of FMF patient. Thus, FMF patients should be questioned and carefully examined for psoriasis lesions and psoriasis family history.
References:
[1] Barut, K., et al., Inceased frequency of psoriasis in the families of the children with familial Mediterranean fever. Clin Exp Rheumatol, 2016. 34(6 Suppl 102): p. S137.
[2] Ashida, M., et al., Psoriasis-like lesions in a patient with familial Mediterranean fever. J Dermatol, 2016. 43(3): p. 314–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4235

THU0549 SYSTEMIC TREATMENT FOR ACUTE ANTERIOR UVEITIS (SYNTHETIC AND BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS): A SYSTEMATIC REVIEW

A. Gómez-Gómez[1,2], E. Loza[3], M.P. Rosario[3], L. Carmona[3], G. Espinosa[4], J.M. García Ruíz de Morales[5], J.M. Herrera[6], S. Muñoz-Fernández[2,7], M. Cordero[8]. *[1]Rheumatology, Hospital Universitario Madrid Sanchinarro; [2]Rheumatology, Hospital Universitario Infanta Sofía; [3]Instituto de Salud Musculoesquelética (InMUSC), Madrid; [4]Autoimmune diseases unit, Institut Clinic de Medicina i Dermatología, Hospital Clínic, Barcelona; [5]Immunology unit, Complejo Asistencial Universitario e Instituto de Biomedicina Universidad de León (IBIOMED), León; [6]Instituto Universitario de Oftalmobiología (IOBA), Universidad de Valladolid, CIBER-BBN. Hospital Clínico Universitario, Valladolid; [7]Department of Medicine, Universidad Europea de Madrid, Madrid; [8]Uveitis Unit, IBIOMED, León, Spain*

Background: Acute anterior uveitis (AAU) is the most common form of uveitis. Most of them are idiopathic, followed by those related to rheumatic conditions. One third of AAU patients may present recurrences, some requiring systemic disease-modifying antirheumatic drugs (DMARDs). The use of DMARDs in AAU is heterogeneous.
Objectives: To perform a systematic and critical review of the literature about the use of synthetic and biologic DMARDs in adult patients with AAU.
Methods: *Selection criteria:* Articles including adult patients with non-infectious AU treated with synthetic or biologic DMARDs including efficacy, and/or safety or cost-effectivity data were selected. Only meta-analysis, systematic reviews, clinical trials and observational studies (OS) were included.
Search strategies for Medline, Embase and Cochrane Library databases up to 3–2016 were designed.
Article selection: 2 independent reviewers. Selected articles were analyzed in detail.
Quality asessment of the studies: Oxford scale and Jadad scale were used.
Analysis and data presentation: evidence and results tables.
Results: 14 articles included, 2 RCTs and 12 OSs, with low or moderate quality. The mean duration/follow-up, number (n) and patients characteristics were highly variable. The definition of the anatomic classification of AUs was generally not clear. Systemic DMARDs were used, including Methotrexate (MTX), Azathioprine (AZA), Cyclosporine A (CsA) and anti-TNFα (Adalimumab (ADA), Golimumab (GLM)), at usual dosage prescription. Number of flares, disease activity and corticoid sparing (CS) effect were the most common outcomes, with big differences between studies in variables included and their definitions.
MTX showed efficacy in disease remission, n of flares, time between flares, lower activity and CS effect. *SSZ* showed lower n of flares and improvement in visual acuity (VA) in AS-associated AAU patients. *AZA* (low quality RCT) showed no differences in VA, Tyndall, flares or IOP. A prospective OS showed lower activity and CS effect. *CsA* (moderate quality OS) showed efficacy improving activity and as CS agent (mid/long term). *Anti-TNFα: ADA*, (2 OSs) with SpA-associated AU patients lowered n of flares (mid/long term), can improve VA, Tyndall and be used as CS agent. *GLM* in AU patients refractory to DMARDs (some to other biologics), showed CS effect in 2 studies. One showed improvement in VA and Tyndall, but not in OCT or n of flares. Adverse events recorded were those usually registered for all these drugs.

Figure 1. Article selection strategy.



Conclusions:
1. Evidence quality is low.
2. Great variability.
3. MTX showed efficacy in idiopathic and systemic disease-associated (SDA) AU.(EL 2c; RG B).
4. SSZ showed efficacy in idiopathic and SDA AU.(EL 3a; RG B-C).
5. AZA seems to be effective in naïve and DMARDs-refractory AU (EL 3a; RG C).
6. CsA showed efficacy in idiopathic and SDA AU (EL 2c; RG B-C).
7. ADA showed efficacy in idiopathic and SDA AU, naïve or DMARDs-refractory AU (EL 2c; RG B).

8. GLM showed efficacy in DMARD-refractory AU (2nd line and further) and other biologic therapies (EL 3a; RG B-C).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2626

THU0550 TREATMENT AND OUTCOMES IN SPANISH PATIENTS WITH IGG4-RELATED DISEASE

A. Fernández-Codina[1], I. Pinal-Fernández[2], B. Pinilla[3], C. López[4], R. Solans-Laque[1], G. Fraile-Rodríguez[5], E. Fonseca-Aizpuru[6], J.M. Cameselle-Tejeiro[7], S. Prieto-González[8], J. Pardos-Gea[1], J. Gil[9], T. Rossinyol[10], M.J. Núñez-Fernández[11], G. Salvador-Cervelló[12], F. Martínez-Valle[1] on behalf of Spanish Registry of IgG4-related disease (REERIGG4). GEAS-SEMI. *[1]Systemic Autoimmune Diseases Unit, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [2]Muscle Disease Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, United States; [3]Internal Medicine, Hospital General Universitario Gregorio Marañón; [4]Internal Medicine, Hospital General Gregorio Marañón; [5]Internal Medicine, Hospital Ramón y Cajal, Madrid; [6]Internal Medicine, Hospital de Cabueñes, Gijón; [7]Pathology, Hospital Clínico Universitario, Santiago de Compostela; [8]Vasculitis Research Unit, Hospital Clinic i Provincial, Barcelona; [9]Internal Medicine, Hospital Río Hortega, Valladolid; [10]Internal Medicine, Hospital de Manacor, Manacor; [11]Internal Medicine, Complejo Hospitalario de Pontevedra, Pontevedra; [12]Internal Medicine, Hospital la Fe, Valencia, Spain*

Background: There is a lack of strong evidence on IgG4-related disease (IgG4-RD) treatment. There is only one clinical trial published, supporting the use of rituximab in American patients.
Objectives: To describe the treatments used in a series of patients diagnosed with IgG4-RD in Spain and to review the outcomes.
Methods: Clinical data were obtained from the Spanish Registry of IgG4-RD from October 2013 to January 2016, including 14 centers. Outcomes were assessed by a self-made response scale and the IgG4 responder index (RI). We categorized the outcomes as a total response (disappearance of the pseudotumoral lesions and absence of symptoms), partial response (<50% regression of the tumefactive lesions or persistence of inflammation without symptoms) and no response if no changes were noticed. Treatment failure was considered if an increase of the activity, mass size or reappearance of symptoms were noticed among patients under treatment.
Results: Sixty-eight patients were included. Twenty-six (38%) were females, mean age 53.4 years. Thirty-six patients (52.9%) had systemic IgG4-RD involving >1 tissue. The most commonly involved tissues were: retroperitoneum (33%), orbital pseudotumor (28%), and maxillary and paranasal sinuses (24%). The main treatments used were: steroids (90%), surgery (45%) and azathioprine (19%).
All treatments were successful in achieving complete or partial response. The mean pre and post-treatment RI values were 6.7 (SD 4.6) and 1.9 (SD 2.6) respectively. There were no differences between systemic and non-systemic disease regarding the chosen treatments and the outcomes. The combination azathioprine-steroids was used in 12 patients. Fourteen percent of them relapsed (considering relapse as an increase of the inflammation, mass size or reappearance of symptoms, since the first month after the treatment withdrawal). The treatment failed in 28.6% of them. The combination steroids-rituximab was indicated in 6 patients, showing no relapses and 1 treatment failure. The majority of patients treated with azathioprine or rituximab combined with steroids had a systemic disease (6.6 and 80%, respectively). Nearby all of them had already failed other previous treatments.
Conclusions: In our series, IgG4-RD has been treated with a myriad of drugs and procedures. The outcomes have been acceptable but the disease tended to relapse (21%) and the treatment failures were common (27%), probably due to the lack of well-defined treatment schemes supported by solid studies. Steroids were still the cornerstone of the treatment. Rituximab results were promising in our study but the number of patients was limited. Azathioprine, in combination with steroids, may be an accessible alternative treatment for IgG4-RD that should be explored. The RI correlated with the treatment outcomes and will have an important role monitoring future studies on IgG4-RD therapies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1135

THU0551 ARTHRITIS IN SARCOIDOSIS - A MULTI-CENTRE STUDY FROM INDIA

A. Jain, V. Agarwal on behalf of Arthritis in Sarcoidosis Group (A.S.G.): Jain A, Agarwal Vikas, Agarwal Vinita, Aggarwal A, Aggarwal P, Chowdhury AC, Ghosh P, Lawrence A, Misra DP, Misra R, Mohapatra M, Nath A, Negi VS, Pandya SC, Reddy VV, Prasad S, Shobha V, Singh YP, Tripathy SR, Wakhlu A. *Clinical Immunology, SGPGIMS, Lucknow, India*

Background: 10–15% of sarcoid patients have associated arthropathy. Chronic arthritis is less common varying from 1–2% [1].Data on articular manifestations of the disease from India is sparse.[2]
Objectives: To study the clinical manifestations of sarcoid arthritis patients from India.
Methods: Case records of patients presenting to ten rheumatology centres from 2005 to 2016 with sarcoidosis were retrospectively reviewed. Joint involvement was assessed clinically, classified as acute or chronic depending on duration of symptoms lesser or greater than 6 months respectively.
Results: A total of 103 patients with sarcoid arthritis were reviewed. 58 patients were classified as Lofgren syndrome. Pattern of joint involvement revealed ankle as most commonly affected in both the groups (Table1). Wrist, MTP and PIP involvement was significantly more common in chronic sarcoid arthritis (table 1). Peripheral lymphadenopathy, plaques and uveitis were more frequent ($p<0.05$) in chronic sarcoid arthritis (50%, 20.8%, 25% respectively) compared to those with acute sarcoid arthritis (16.5%,6.3%,6.4% respectively). 45 of 62 patients with acute arthritis with follow up details had achieved complete remission.15/24 patients with chronic sarcoid arthritis patients with a median follow up of 2 years had achieved complete remission with 14, 11 and 5 patients on steroids, methotrexate and hydroxychloroquine respectively. One patient with concomitant interstitial lung disease had died due to lung infection.

Table 1. Clinical characteristics of patients with sarcoid arthritis from India

	Acute, n=79	Chronic, n=24
Age (years)	40† (33.5 TO 51)**	42.5† (35–55)**
Male : Female	0.9:1	1.7:1
Duration of Symptoms (years)	0.25† (0.08 to 1.5)**	0.72† (0.5 to 4)**
Oligoarthritis (≤4 joints)	58 (73.4)*#	12 (50)*
Polyarthritis (≥5 joints)	19 (24.1)*	12 (50)*
Ankle	71 (89.9)*	21 (87.5)*
Wrist	22 (27.8)*	16 (66.7)*‡
MTP	5 (6.3)*	5 (20.8)*‡
PIP	12 (15.2)*	9 (37.5)*‡
Hilar/Mediastinal Lymphadenopathy	66 (83.5)*	21 (87.5)*
ILD	23 (29.1)*	12 (50)*

*Percentage; †Median; **IQR. ‡$p<0.05$. #One patient each had dactylitis and enthesitis as the only musculoskeletal manifestation.

Conclusions: Acute oligoarthritis was the commonest presentation with ankle most commonly affected joint. Wrist, PIP, MTP involvement were more common in chronic sarcoidosis. One of the limitation was retrospective analysis.
References:
[1] Ungprasert P, Crowson CS, Matteson EL. Clinical Characteristics of Sarcoid. Arthropathy: A Population-Based Study. Arthritis Care & Research. 2016; 68(5):695–9.
[2] Govindarajan V, Agarwal V, Aggarwal A, Misra R. Arthritis in sarcoidosis. J. Assoc Physicians India. 2001;49:1145–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5978

THU0552 COMPLIANCE TO COLCHICINE TREATMENT IN FAMILIAL MEDITTERRANEAN FEVER RELATED AMYLOIDOSIS

B. Yurttas[1], S. Ugurlu[2], H. Ozdogan[2]. *[1]Department of Internal Medicine; [2]Department of Internal Medicine, Division of Rheumatology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey*

Objectives: To assess the colchicine compliance in patients diagnosed with Familial Mediterrenean Fever (FMF) related amyloidosis in our center.
Methods: Fourty one patients (18 male/23 female) were questioned with regards to colchicine compliance by using retrospective scanning of patient data.
Results: The mean age at the symptomatic onset of FMF was 7.13±5.24 years. The mean age at the time of the FMF diagnosis was 21.21±14.85 years. The mean age at the initiation of colchicine treatment was 21.42±14.75 years and the mean age at time of the diagnosis of amyloidosis was found 29.57±12.14 years. Mean duration of the disease was 31.702±11.84 years and the duration of delayed diagnosis was 14.35±13.84 years. Maximum dose of colchicine was 2,103±0,673 mg/day. Compliance of colchicine treatment was poor in FMF related amyloidosis during their follow-up (11/25, %44), rates of skipped doses were also high (17/25, %68). Compliance rates were high in patients in whom FMF and amyloidosis were diagnosed simultaneously (12/13, %93), rates of skipped doses were also low (2/13, %14). One of the patients diagnosed with FMF after the diagnosis of amyloidosis was compliant, two of them were non-compliant; with regards to skipping doses, two patients were found to be compliant and therefore never skipped doses while one was skipping doses. The compliance to colchicine was high in all FMF patients once amyloidosis was evident (31/41, %75), and rates of skipped doses were also low (12/41, %30). In five FMF patients, amyloidosis was observed despite their compliance to treatment.
Conclusions: The overall delay of diagnosis in FMF patients with amyloidosis was found to be high. Particularly the FMF patients who were diagnosed with amyloidosis during their follow up were found to have lower rates of compliance. There were also a group of patients who were diagnosed with amyloidosis despite adequate and convenient colchicine treatment. It was emphasized that not only the early diagnosis and adequate treatment, but also the close follow up is important in managing FMF patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5126

THU0553 LOW ALKALINE PHOSPHATASE LEVELS: COULD IT BE HYPOPHOSPHATASIA?

C. Tornero[1], P. Aguado[1], S. García[1], J. Tenorio[2], P. Lapunzina[2], A. Buño[3], J.M. Iturzaeta[3], C. Plasencia[1], I. Monjo[1], A. Balsa[1]. *[1]Rheumatology; [2]Genetics; [3]Clinical Laboratory, la Paz University Hospital, Madrid, Spain*

Background: Hypophosphatasia (HPP) is a rare inherited disorder of bone and mineral metabolism, caused by mutations in the ALPL (alkaline phosphatase liver type) gene, with reduction of activity of the tissue-non-specific isoenzyme of ALP (TNSALP). The clinical presentation is variable and adult forms of the disease are usually milder than those affecting infants and children, easily overlooked or misdiagnosed, which can lead to erroneous therapeutic decisions.
Objectives: The primary objectives of our study are to estimate the prevalence of patients with adult forms of HPP in a group of patients with persistent hypophosphatasemia, to analyze their clinical and functional characteristics and to compare these findings between those presenting or not these mutations.
Methods: In this Cross-sectional study, 1.536.711 ALP measurements owing to 386.356 patients were evaluated during a six-year period (2009–2015). Patients having at least two values below 35 IU/l and none above 45 IU/l constituted the study population. In total, 427 patients were included. Among them, 31 patients were excluded because of presenting causes of secondary HPP and 13 because of lost to follow-up. 108 patients were contacted by phone to fulfill a questionnaire about manifestations related to HPP and health assesment and in order to obtain blood samples to perform the genetic test.
Results: Demographic and clinical characteristics of both groups are shown in Table 1. Of the 108 patients evaluated, the genetic test results of 39 patients are available at this moment (the rest of the results are currently pending). 59% (23/39) tested positive for the genetic mutation.Despite data are still partial and although the results did not achieve statistical significance, we observed with a greater relevance a higher proportion of patients with HPP presenting with chronic bone pain (48,7% vs 25,6%,p=0,157), muscle weakness (15,4% vs 2,6%, p=0,112) and more necessity of analgesic medication (p=0,107) in patients with HPP in comparison with the control group. Furthermore, there was a non-significant trend in the HPP-group to present dental abnormalities and premature dental loss (7,6%), absent manifestations in the control group (p=0,123). In addition, orthopedic surgery was more common in the HPP group (12,8%) compared with the other group (0%), p=0,04. The prevalence of stress fractures was also higher in patients with HPP (7,69%). No significant differences were found in demographic characteristics, vertebral fractures, calcific periarthritis, condrocalcinosis, or FRAX index. In terms of biochemical tests, serum phosphate levels were higher in the HPP group (4,18 mg/dl) in relation to the control group (3,52 mg/dl), p=0,05. No differences were observed neither in pain assessment, measured with the Visual Analogue Scale nor in the Health Assessment Questionaire for disability between both groups.
Conclusions: The diagnosis of HPP can be difficult and is often missed or delayed, particularly in adults. The prevalence of HPP between patients with persistent low ALP is high and although the clinical presentation is milder in adults, it often presents with chronic bone pain, weakness, stress fractures and dental abnormalities. These data should promote a more proactive attitude towards detection of adult HPP.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5547

Pts Characteristics	HPP group N= 23	Control group N= 16	P value
Demographic characteristics			
Mean age ± DS	52,78 ±13,28	49,13 ±10,70	p=0,366
Sex - Male - Female	 10/39 (25,6%) 13/39 (33,3 %)	 4/39 (10,2%) 12/39 (30,7%)	p= 0,236
Race - Caucasic - Black	 22/39 (56,4 %) 1/39 (2,56%)	 16/39 (41 %) 0/39 (0%)	p=0,398
Clinical characteristics			
Chronic bone pain, n/N (%)	19/39 (48,7 %)	10/39 (25,6%)	P= 0,157
Muscle weakness, n/N %)	6/39 (15,4%)	1/39 (2,6%)	P=0,112
Calcific periarthritis, n/N(%)	4/39 (10,25%)	1/39 (2,56%)	p=0,282
Condrocalcinosis n/N (%)	2/39 (5,12%)	0/39 (0%)	p=0,215
Patients presentig stress fractures, n/N (%)	3/39 (7,69%)	0/39 (0%)	
Vertebral fractures (n/N) (%)	2/39 (5,12%)	0/39 (0%)	p=0,193
Dental abnormalities and teeth loss n/N (%)	3/39 (7,69%)	0/39 (0%)	P= 0,123
History of orthopedic surgery	5/39 (12,8 %)	0/39 (0 %)	P=0,048
Use of analgesic medication for pain, n/N (%)	16 /39 (41,03%)	7 /39 (17,9%)	P=0,107
History of kidney disease	5/39 (12,8%)	2/39 (5,12%)	P=0,384
Biochemical data			
Alkaline phosphatase ± DS	21,6 ± 6,76	29,69 ± 3,44	P=0,0001
Serum calcium ± DS	9,34 ± 0,4	9,34 ± 0,4	P=0,994
Urine calcium ± DS	61, 47 ± 51,3		
Serum phosphate ± DS	4,18 ± 9,91	3,52 ± 0,48	P= 0,05
Urine phosphorus ± DS	341 ± 433		
Quality of life assessment			
VAS pain ± DS	3,86 ± 2,5	2,71 ± 3,1	P= 0,221
HAQ-DI ± DS	0,23 ± 0,36	0,2 ± 0,43	P= 0,764

THU0554 IMMUNOGLOBULIN G4-RELATED DISEASE IN HONG KONG – CLINICAL FEATURES, TREATMENT PRACTICES AND ASSOCIATIONS

P.H. Li, C. Ho, C.-S. Lau. *Department of Medicine, Queen Mary Hospital, Hong Kong, Hong Kong*

Background: Immunoglobulin (Ig) G4-related disease (IgG4-RD) is a systemic immune-mediated disease unifying what were previously considered to be unrelated individual organ disorders. The diagnosis and treatment of this characteristic fibroinflammatory condition continues to evolve, but generally remains an under-recognised disease. Local data outside Japanese and Caucasian populations is lacking and few studies have examined factors to predict disease severity or disease prognostication.
Objectives: We conducted this study to review the clinical features, treatment practices and factors associated with more extensive disease involvement in Hong Kong.
Methods: We retrospectively evaluated all patients with IgG4-RD over the past 13 years in our centre and combined this with patient data extracted from previous local publications. We analysed the clinical features, treatment practices and factors associated with the number of organ systems involved.
Results: One hundred and four patients (55 from our centre and 49 from literature review) were identified. Patients were predominantly older men (mean age 61.9 years, male:female ratio 3:1). Hepatobiliary and pancreatic (40.4%), salivary gland (33.6%), lymph nodes (29.8%) and eye (19.2%) were the most common systems involved. Lymphadenopathy was associated with glucocorticoid use (OR=2.65, p=0.034). Over 90% of patients had a serum greater than 135 mg/dl and a IgG4/total IgG ratio greater than 8%. Pre-treatment serum IgG4 levels correlated with the number of organ systems involved (β=0.347, p=0.004), and specifically with salivary gland involvement (mean 1109 mg/dl vs. 599 mg/dl, p=0.012).
Conclusions: We identified pre-treatment serum IgG4-RD to be associated with multi-system disease, especially with salivary gland involvement, highlighting the potential for its use in disease prognostication and monitoring. The reason for this particular correlation remains uncertain but highlights the importance of screening for salivary gland involvement in all IgG4-RD patients, especially in the presence of higher serum IgG4 levels. We also describe the clinical features and treatment modalities of the largest cohort of IgG4-RD in Hong Kong thus far. Increased physician awareness and multidisciplinary efforts are required for optimal management of this masquerading disease. Future studies, especially focusing on treatment strategies within the contexts of different epidemiology and patient characteristics, are urgently needed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1120

THU0555 THE RELIABILITY OF TWO VASCULITIS ACTIVITY SCORES (BIRMINGHAM VASCULITIS ACTIVITY SCORE AND BEHCET'S DISEASE CURRENT ACTIVITY FORM2006) IN ANTICIPATING DAMAGE IN A GROUP OF PATIENTS DIAGNOSED WITH BEHCET'S DISEASE

C.G. Buzatu, S.E. Daia-Iliescu, I. Saulescu, A. Borangiu, T. Gudu, V. Bojinca, D. Predeteanu, A. Balanescu, R. Ionescu, D. Opris-Belinski. *Internal Medicine and Rheumatology, "Saint Mary" Clinical Hospital, Bucharest, Romania*

Background: Validated disease activity scores and damage measurements were developed over time in order to allow a better way to evaluate patients and decide treatment plans.There are scores designed for a great variety of vasculitis like Birmingham Activity Score and others that are more specific like Behcet's Disease Current Activity Form2006.
Objectives: To evaluate the ability of the activity scores (BVASv3and BDCAF)to predict damage,and the influence of immunosuppressive therapy on damage progression,as measured byVDI, in a group of patients with Behcet's Disease.
Methods: A study was performed on a cohort of patients diagnosed with Behcet's Disease under surveillance in one tertiary Rheumatology Centre, from a non-endemic area.All documented cases of Behcet's Disease have been diagnosed according to The International Criteria for Behçet's Disease.The Birmingham Activity Score (BVAS)v3, Behcet's Disease Current Activity Form2006 (BDCAF)and Vasculitis Damage index (VDI) were calculated for all patients. Spearman's correlation coefficients were calculated between BVASv3 Score, BDCAF, VDI and immunosuppressive treatment.WindowsExcel/SPSS20.0 has been used to analyse the data.
Results: 20 patients were included in the study, with ages at the time of the

diagnosis between 13and 60years, 14 (70%) under the age of 40,with a male predominance 60% (12 patients). All patients presented active disease at the time of the diagnosis. In the clinical case series, Spearman's rank correlation coefficient between BVASv3 and BDCAFwas strong r=0,862with p<0,001.The outcome analysis after remission was calculated and rank correlation coefficient betweenVDI, and both BVASv3 and BDCAF was moderate (VDI-BVASv3 r=0,747, p<0,001, VDI- BDCAF r=0,795, p<0,001).As for immunosuppression induction decision and activity scores,the correlation coefficient was moderate (r=0,734 for BVASv3,r=0,647 for BDCAF)with p<0,001. There was a moderate correlation between immunosuppressive treatment and VDI (r=0,700, p<0,001). Since the cause of damage (vasculitis vs. treatment)is not taken into consideration when we calculate VDI, we tried to observe if there are any connections between this and immunosuppression duration. There was a mild correlation and no statistical impact between cyclophosphamide treatment duration and damage calculated as VDI (r=0,474, p=0,36).In contrast, when rank correlation coefficient between cortisone therapy and VDI was calculated, a moderate statistical impact was observed (r=0,609, p<0,001).

Conclusions: Birmingham Vasculitis Activity score (BVAS) v3 and Behcet's Disease Current Activity Form2006 (BDCAF) are reliable tools for evaluating disease activity in patients with Behcet's Disease. They are able to anticipate the need for immunosuppressive therapy and the damage progression, as calculated with Vasculitis Damage Index (VDI).

References:

[1] Mukhtyar C, Lee R, et al. Modification and validation of the Birmingham vasculitis activity score, Ann Rheum Dis, 2009.

[2] Flossmann O, et al. Development of comprehensive disease assessment in systemic vasculitis. Ann Rheum Dis, 2007.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4932

THU0556 SALIVARY GLAND ENLARGEMENT IN IGG4-RELATED DISEASE IS ASSOCIATED WITH MULTIORGAN INVOLVEMENT AND HIGHER BASAL DISEASE ACTIVITY

E. Martin-Nares[1], A. Angeles-Angeles[2], G. Hernandez-Molina[1].
[1]Rheumatology; [2]Pathology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

Background: IgG4-related disease (IgG4-RD) is an immune-mediated condition which clinical spectrum encompasses single or multiple organ involvement. Enlargement of major and minor salivary glands is one of the main disease features. Whether salivary gland enlargement is associated with systemic involvement has not been previously evaluated.

Objectives: To elucidate if salivary gland enlargement is associated with systemic disease.

Methods: We included patients with an established diagnosis (definitive: organ involvement, biopsy proven and high IgG4 levels, probable: organ involvement, biopsy proven without high IgG4 levels, possible: organ involvement, high IgG4 levels without histology) of IgG4-RD according to the Comprehensive Diagnostic Criteria, who regularly attend a tertiary referral center in Mexico City (2000–2017). We retrospectively collected demographics, clinical (organ involvement, disease activity and damage assessed by the IgG4-RD Responder Index [IgG4-RD RI] at basal and at 6 months of follow-up, number of relapses, remission and treatment), basal laboratory (C3, C4, ESR, PCR, total eosinophil count, IgG4 levels) as well as imaging and histologic data.

Results: We included 32 patients, 17 (53.1%) men, mean age 50.2±14.1 years and median disease duration 20.5 months. Seven (21.9%) have a definitive diagnosis, 12 (37.5%) probable and 13 (40.6%) possible. Overall we identified 21 anatomic sites affected, mainly pancreas 56.2%, lymph nodes 56.2%, lacrimal glands 37.5% and bile duct 34.3%. Salivary gland involvement was present in 12 (37.5%) patients (2 parotid, 3 minor salivary gland and 7 both). Among these patients, only 5 (41.6%) referred dry mouth and in 7 patients (58.3%) glandular enlargement was the onset disease feature. Salivary glandular enlargement was identified only radiologically in 5 patients (41.6%) and both clinical and radiologically in 7 (58.3%) patients. When we compared patients with (n=12) vs. without (n=20) salivary gland enlargement, the first group had a higher number of affected organs (6.5 vs. 2, p=0.0001) and absolut eosinophil's count (348 vs. 137.5/mm^3, p=0.05), a higher prevalence of lacrimal glands (75% vs. 15%, p=0.002), lymph nodes (91.7% vs. 35%, p=0.002) and lung involvement (33.3% vs. 0%, p=0.01), azathioprine use (83.3% vs. 30%, p=0.003), as well as a higher basal IgG4-RD RI (12 vs. 6, p=0.001) and a longer delay in diagnosis (64 month vs. 6.5 months, p=0.001). We did not find differences regarding gender, age, IgG4 serum levels, C3, C4, ESR, PCR, antinuclear antibodies, rheumatoid factor, anti-Ro/SSA and anti-La/SSB antibodies (negative in all patients), number of relapses, remission at 6 months and damage. We performed a logistic regression analysis (only including the number of organs, the basal IgG4-RD RI and time of follow-up) and found an association of salivary glandular enlargement with the basal IgG4-RD RI (OR 1.63, 95% CI 1.12–2.35, p=0.009).

Conclusions: Our study highlights the systemic nature of IgG4-RD. Patients with salivary gland enlargement should be routinely screened for systemic involvement.

References:

[1] Carruthers M, Stone J, Deshpande V, et al. Development of an IgG4-RD Responder Index. Int J Rheumatol. 2012;2012:259408.

Acknowledgements: No acknowledgements to report.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5609

THU0557 VENOUS VESSEL WALL THICKNESS IN LOWER EXTREMITY IS INCREASED IN MALE BEHCET'S DISEASE PATIENTS WITHOUT VASCULAR INVOLVEMENT

F. Alibaz-Oner[1], A. Mutis[1], R. Ergelen[2], Z. Erturk[1], T. Ergun[3], H. Direskeneli[1].
[1]Rheumatology; [2]Radiology; [3]Dermatology, Marmara University, School of Medicine, Istanbul, Turkey

Background: Vascular involvement is seen in up to 40% of the patients with Behcet's Disease (BD), especially in young males and is one of the major causes of mortality and morbidity. Lower extremity vein thrombosis due to vascular inflammation is the most frequent form of vascular involvement in BD. Recently, assessment of vessel wall thickness (VWT) and venous dilatation by US is suggested to be valuable in patients with vascular inflammation.

Objectives: In this study, we investigated whether vessel wall thickness or dilatation is present in young male BD patients prone to venous vascular disease.

Methods: Fifteen male patients with BD without major organ involvement followed in Marmara University Behcet's Clinics, 14 healthy male controls and 14 male patients with Ankylosing Spondylitis (AS) were included the study. Bilateral lower extremity venous doppler ultrasonography (US) was performed by an experienced radiologist blinded to cases. No patient was under immunosuppressive treatment. Bilateral common femoral vein (CFV) wall thickness and great/small saphenous vein dilatations were examined. Behçet Syndrome Activity Score (BSAS) was used for the general assessment of disease activity.

Results: The mean disease duration was 9.1±6.3 years in patients with BD. BSAS score was 28.9±19. Bilateral CFV wall thickness was significantly higher in BD patients compared to healthy controls and AS (p=0.001, p=0.002, respectively for right CFV; p=0.001, p<0.001, respectively for left CFV) (Table 1). The width of great and small saphenous veins were also higher in patients with BD, but without reaching statistical significance. There were no correlations between BSAS and wall thickness of any vessel.

Table 1. Venous wall measurements of lower extremity in study groups

	Behçet's Disease (n=15)	Healthy Controls (n=14)	Ankylosing Spondylitis (n=14)	P value
Age, years	30.2±4.5	30±5.9	30.8±4.2	0.891
Body Mass Index (kg/m^2)	23.5±3.5	23.8±2.8	26.3±3.8	0.080
Right Common femoral VWT (mm)	0.69±0.4	0.26±0.08	0.28±0.27	<0.001
Left Common femoral VWT (mm)	0.74±0.4	0.31±0.13	0.23±0.13	<0.001
Right Great saphenous width (mm)	2.94±2.6	2.1±0.71	2.5±0.73	0.436
Left Great saphenous width (mm)	3.1±2.2	2.5±0.65	2.4±1.1	0.512
Right Small saphenous width (mm)	2.4±1.8	1.4±0.3	1.7±0.5	0.126
Left Small saphenous width (mm)	2.1±1.5	1.5±0.8	1.8±0.6	0.315

VWT: Venous wall thickness.

Conclusions: In preliminary results of our study, an increased venous vessel wall thickness in lower extremity was shown in male BD patients without vascular involvement. As a similar change was not observed in controls, we think, increased VWT might be an early sign of venous inflammation in patients with BD rather than a result of non-specific systemic inflammation. Further studies with a larger group of patients is planned.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4125

THU0558 THERAPEUTIC RESPONSE TO PREDNISONE ACCORDING TO THE AGE IN POLYMYALGIA RHEUMATICA: A CONTROLLED STUDY

A. Charpentier[1,2], F. Verhoeven[1], M. Sondag[1], X. Guillot[1,2], C. Prati[1,2], D. Wendling[1,3]. *[1]Rhumatologie, CHRU de Besançon; [2]Ea 4267 " Pepite "; [3]EA 4266 " Agents pathogènes et inflammation ", Université de Bourgogne Franche-Comté, Besançon, France*

Background: Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disorder which usually affect patients over 65 years old. Different poor prognostic factors are involved in prednisone response including rapid decrease of prednisone dose or female sex. To date, there is no data relating the impact of the age on therapeutic response in PMR.

Objectives: The aim of this study was to compare, in case of PMR, the response to prednisone in patients younger than 60 to patients over 65 years old.

Methods: This was a retrospective, monocentric study. We included patients suffering from PMR, meeting ACR 2012 criteria. Patients were classified into two groups, one group with patients less than 60 years, and one group with patients over 65 years. We registered demographic, clinical, biological, and imaging data as well as therapeutic response profile. The local inflammation was evaluated with PET scan, by studying each anatomical site usually affected by PMR. Then, the rate of inflammation was scored from 0 to 3, according to the intensity of uptake compared to liver. The treatment was standardized. The initial dose of prednisone was of 0.3mg/kg/j during the two first weeks, then, the dose was slowly decreased

by 10% each month. The main endpoint was a steroid dependence defined by the recurrence of PMR symptoms and/or the increase of CRP at two times during the decrease of prednisone.
Results: We included 14 patients younger than 60 years old (average age 54+/- 0.8 years) and 28 patients older than 65 years old (average age 75.8 +/- 1.5 years). The population younger than 60 years was mainly male (60% VS 27%, $p<0.05$). Both groups were similar in terms of morning stiffness (2,1±0,4 VS 1,9±0,3 hours; $p>0.05$), disease duration (4,2±0,8 VS 4,1±0,6 months; $p>0.05$), leukocytes rate (8,3±1,37 VS 8±0,7 G/L; $p>0.05$) and percentage of antinuclear antibodies rate over 1/320 (20% VS 10%; $p>0.05$). However, regarding to local inflammation, the intensity of FDG uptake highlighted by the Pet scan was lower among young patients (score of 16,9±1,7 VS 26,5±3,0; $p<0.05$). Furthermore, we observed a significant difference concerning therapeutic response according to the age: 60% of the young patients developed a steroid dependence compared to20% in group of old patients ($p<0.05$). Moreover, the introduction of methotrexate was necessary for 35% of the young patients against 6.5% ($p<0.05$).
Conclusions: Our study is the first to highlight the age as a bad prognosis factor in case of PMR. This difference is independent to the systemic inflammation and surprisingly, local inflammation (assessed by the TEP score) is more important in elderly people. Young patients suffering from PMR are mostly men and are more dependent on steroids. Thus, methotrexate could be straightaway proposed, particularly in patient younger than 60 years old.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4033

THU0559 PERSISTENT PRURITIC SKIN LESIONS WITH DYSKERATOTIC CELLS IN UPPER LAYER OF EPIDERMIS ARE SPECIFIC AND ASSOCIATED WITH HIGH LEVELS OF SERUM IL-18 IN ADULT-ONSET STILL'S DISEASE

H. Nishikawa, Y. Taniguchi, N. Aoyama, Y. Terada. *Kochi Medical school, Nankoku, Japan*

Background: Adult-onset Still's disease (AOSD) is an acute and systemic inflammatory disorder that is characterized by high spiking fever, evanescent rash, arthralgia/arthritis and hyperferritinemia. However, recent reports showed that not only typical evanescent salmon-colored rash but also atypical skin lesions, persistent pruritic papules and plaques, could be associated with AOSD.
Objectives: The aim of this study is to assess the clinical significance of dyskeratotic cells in skin lesions of Japanese patients with AOSD.
Methods: We retrospectively assessed clinical and histological findings of skin lesions including persistent pruritic skin lesions in Japanese patients with AOSD (n=12). Moreover, we compared serological and histological finding of AOSD with that of dermatomyositis (DM) (n=6), drug eruptions (DE) (n=6), and Graft versus Host disease (GVHD) (n=6).
Results: AOSD with persistent pruritic skin lesions (n=7) histologically showed dyskeratotic cells only in upper layer of epidermis and horny layer without intraepidermal infiltrations of inflammatory cells. These dyskeratotic cells were positive by TUNEL and single stranded DNA (ssDNA) stainings, suggesting apoptotic cells. AOSD with evanescent rash (n=5) histologically showed no dyskeratosis. On the other side, the pathological findings of DM (n=6), DE (n=6) and GVHD (n=6) had dyskeratotic cells in all layers of epidermis with inflammatory cells infiltrations. Notably, AOSD with dyskeratosis (n=7) had significant higher levels of serum IL-18 (74,300∼307,000 pg/ml) than AOSD without dyskeratosis (n=5).
Conclusions: AOSD with persistent pruritic skin lesions is characterized and specific by prominent epidermal apoptosis, especially involving the upper layers. Therefore, it could play a pivotal role to recognize the atypical skin lesions of AOSD for correct early diagnosis. Finally, the high levels of serum IL-18 might be related with epidermal apoptosis of keratinocyte in AOSD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1766

THU0560 DEVELOPMENT OF SYMPTOMS IN VERY EARLY PHASE IN PATIENT WITH ADULT ONSET STILL DISEASE

H. Tamai, Y. Kaneko, N. Nishina, J. Kikuchi, T. Takeuchi. *Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan*

Background: Adult onset Still Disease (AOSD) is a systemic inflammatory disease presenting various non-specific symptoms like fever, arthralgia and pharyngalgia. Those symptoms are mimicking common cold, which could lead to the delayed diagnosis. However, little is known about the profiles and development of symptoms in very early phase before diagnosis.
Objectives: To clarify the clinical course of AOSD symptom development in very early phase and its effect on the diagnosis delay.
Methods: Consecutive patients with AOSD with enough information in our hospital were enrolled. Initial symptoms before and at diagnosis were investigated in detail. The gradual course from the initial symptoms to the fulfilment of Yamaguchi criteria for AOSD was examined.
Results: A total of 51 patients were enrolled. The mean age at diagnosis was 45.0±18.9 years old and 41 (80%) were female. All patients were met with the Yamaguchi criteria. The mean duration from the first symptom to diagnosis was 50.4 days. The duration from the first symptom to the first visit to the medical facility including a general physician was 19.1 days, and that from the first medical facility visit to the first blood test was 8.0 days. While the first symptom was arthralgia in 29 (34.1%), fever in 20 (23.5%), and eruption in 20 (23.5%), pharyngalgia in 13 (15.3%), at diagnosis, fever was found in all patients, eruption in 47 (92.2%), arthralgia in 45 (88.2%), pharyngalgia in 34 (66.7%), lymphadenopathy and/or splenomegaly in 35 (68.6%), increased white blood cell (WBC) count in 44 (86.3%), ferritin elevation in 42 (82.4%), liver enzyme elevation in 41 (80.4%), negative rheumatoid factor (RF) and anti-nucleolar antibody (ANA) in 30 (58.8%). Arthralgia developed 41.9 days prior to the diagnosis, fever 40.9 days, eruption 29.5 days, pharyngalgia 24.5 days and lymphadenopathy and/or splenomegaly 14.8 days. WBC increase was detected 17.8 days prior to the diagnosis, negative RF and ANA 15.1 days, liver enzyme elevation 14.6 days, and ferritin elevation 10.9 days. At 14 days from the first symptom, 32 (62.7%) met 3 of Yamaguchi criteria, 23 (45.1%) met 4, and 19 (37.3%) met 5. At 28 days, 40 (78.4%) met 3 of Yamaguchi criteria, 32 (62.7%) met 4, and 27 (52.9%) met 5. The duration to diagnosis was significantly shorter in the patients with eruption developing within 7 days since the first symptoms than those without (35.2 vs 74.3 days, p=0.03)
Conclusions: The mean duration from the first symptom to the diagnosis of AOSD was approximately 50 days, and only a half of the patients met Yamaguchi criteria at 28 days after first symptom. The time of eruption emergence affected the early diagnosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4212

THU0561 CLINICAL PRACTICE GUIDELINE FOR DIAGNOSIS AND MANAGEMENT OF CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME

K. Legault[1], C. Hillis[1], C. Yeung[1], A. Iorio[1], M. Crowther[1], E. Akl[2], M. Carrier[3], R. Cervera[4], F. Dentali[5], D. Erkan[6], G. Espinosa[7], M. Khamashta[8], J. Meerpohl[9], K. Moffat[10], S. O'Brien[11], V. Pengo[12], J. Rand[13], I. Rodriguez Pinto[7], L. Thom[14], H. Schunemann[1]. *[1]McMaster University, Hamilton, Canada; [2]American University of Beirut, Beirut, Lebanon; [3]University of Ottawa, Ottawa, Canada; [4]University of Barcelona, Barcelona, Spain; [5]Insubria University, Insubria, Italy; [6]Weill Medical College of Cornell University, New York, United States; [7]Barcelona Hospital Clinic, Barcelona, Spain; [8]King's College London, London, United Kingdom; [9]University of Freiburg, Freiburg, Germany; [10]Hamilton Health Sciences, Hamilton, Canada; [11]Nationwide Children's, Columbus, United States; [12]University of Padova, Padua, Italy; [13]NY Presbyterian Hospital, New York, United States; [14]None, Oxford, United Kingdom*

Background: Catastrophic antiphospholipid syndrome (CAPS) is characterized by the rapid onset of widespread or multifocal large and/or small vessel thrombosis associated with multi-organ failure in patients meeting the serological criteria for antiphospholipid syndrome [1]. Mortality in CAPS approaches 50% [2].
Objectives: The RARE-BestPractices project group identified CAPS as a rare disease condition of interest in which to develop a clinical practice guideline. The project was run in partnership with McMaster University, and used the GIN-McMaster Guideline Development checklist and Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology to develop guidelines on rare diseases [3].
Methods: The CAPS guideline was coordinated by a steering committee including representatives from RARE-BP and methodologists from McMaster University. The CAPS guideline panel consisted of 19 international members, including patient representation. The panel used the GradePro software to brainstorm and prioritize potential questions and outcomes. Systematic reviews were performed for each question. To supplement the published evidence, we compiled raw data for mortality from the CAPS Registry, and systematically elicited expert opinion from the panel members using a systematic observation form. For each question an evidence profile and evidence to decision table was generated and shared.
Results: The question prioritization step generated 47 questions, which were ranked to identify the top priorities. The top 10 questions were chosen for guideline development, yielding 7 therapy and 3 diagnostic questions. The outcome generation step yielded 7 outcomes.
The questions were addressed during an in-person panel meeting, held on April 27, 2016 in Barcelona, Spain, with follow-up via webinar on June 3, 2016, and with web-based voting completed July 31, 2016.
Recommendations were developed for all questions and will be discussed in detail.
Conclusions: Ten recommendations were issued by the CAPS Guideline Panel to assist clinicians in diagnosis and management of suspected CAPS patients. Future research is needed to improve evidence quality in rare diseases such as CAPS. The GIN-McMaster Guideline Development Checklist and the GRADE methodology were effective in producing a rigorous guideline in this rare disease.
References:
[1] Asherson R. The catastrophic antiphospholipid syndrome. J Rheumatol 1992.
[2] Cervera R, Bucciarelli S, Plasín M, et al. Catastrophic antiphospholipid syndrome (CAPS): descriptive analysis of a series of 280 patients from the "CAPS Registry". J Autoimmun 2009;32:240–5.

[3] Guyatt G, Oxman A, Vist G, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2085

THU0562 INFLAMMATORY JOINT DISEASE TRIGGERED BY IMMUNE CHECKPOINT INHIBITORS

L. Tucker, S. Sacks, H. Al-Mossawi. *Rheumatology, Oxford University Hospitals NHS Foundation Trust, OXFORD, United Kingdom*

Background: Immune checkpoint modulation has changed the cancer therapy landscape in recent years [1]. Randomised controlled trials now demonstrate superiority to standard chemotherapy in squamous cell lung cancer, renal cell cancer [2], squamous cell head and neck cancer [3] and malignant melanoma [4]. However, blockade of these checkpoints results in a multitude of autoimmune sequelae including joint disease. As these therapies become first-line in oncology, they will likely place a significant burden on rheumatology services.
Objectives: To establish the prevalence of rheumatological manifestations of checkpoint blockade in a non-trial standard care setting.
Methods: All patients treated with Nivolumab or Ipilimumab (as single agent or in combination) in a standard care setting within a single centre were included and the number of suspected cases with rheumatological manifestations identified from the case records.
Results: 75 patients have been treated with Nivolumab single agent and 12 with combination Nivolumab plus Ipilimumab in Oxford over the last 15 months. Within that cohort, there were 7 suspected cases of joint disease giving a potential prevalence of 8%. Of those 7, 2 had confirmed disease requiring therapy, both had received Nivolumab/Ipilimumab combination. Both cases were rheumatoid factor and CCP negative. One case responded to prednisolone only, while the second case was refractory to steroids, methotrexate and infliximab but responded to IL-6 blockade with Tocilizumab.
Conclusions: We observed an approximate 8% prevalence of checkpoint mediated autoimmune joint disease within a relatively short follow up period of 15 months. The longer-term prevalence may be higher. Both patients requiring therapy had been exposed to Ipilimumab suggesting the inflammatory joint toxicity with this agent may be higher than that caused by Nivolumab.
Checkpoint immunotherapy is set to become the first-line standard of care in a number of cancers. This will lead to an increased demand for rheumatology services. The rheumatology community needs to develop strategies and trials in order to classify and treat these patients appropriately.
References:
[1] Mellman I, Coukos G, Dranoff G. Cancer immunotherapy comes of age. Nature. 2011; 480:480–9.
[2] Motzer RJ, Escudier B, McDermott DF, et al. Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma. NEJM. 2015; 373:1803–1813.
[3] Ferris RL, Blumenschein G, Fayette J, et al. Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. NEJM. 2016; 375:1856–1867.
[4] Larkin J, Chiaron-Sileni V, Gonzalez R et al. Combined Nivolumab and Ipilimumab or Monotherapy in Untreated Melanoma. N Engl J Med. 2015; 373:23–34.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3875

THU0563 THE IMMUNOMODULATION EFFECT OF BM-MSCS ON THE INFLAMMATORY CHEMOKINES OF RATS WITH COLLAGEN TYPE II INDUCED ARTHRITIS

J. Fan, L. Zhang, D. Ma, G. Zhang, K. Xu, J. Gao. *Rheumatology, Shanxi DaYi Hospital, Shanxi Academy of Medical Sciences, Taiyuan, China*

Background: Rheumatoid arthritis (RA) is an autoimunme disease.The DMARDs is mian treatment but side effects are very high. Bone marrow mesenchymal stem cells (MSCs) have immunoregulatory function so it can be used to treat RA. This study was designed to investigate the effect of BMSCs on chemokines in CIA rats.
Objectives: To observe the immunomodulation effects of BM-MSCs on the Inflammatory Chemokines of rats with collagen-induced arthritis (CIA).
Methods: Rats MSCs were isolated and expanded from bone marrow cells by density gradient centrifugation and adhering to the culture plastic bottle, and the phenotypes were assessed by flow cytometry. We established collagen induced arthritis rats model. A total of six groups. The MSCs treatment groups contain the early and advanced stages. Meanwhile, there are normal control and CIA control group,The latter also contains the early and advanced stages. Also,there is the positive control group of MTX, by intraperitoneal injection of a small dose of MTX (0.9mg/kg/w), for six weeks. $1x10^6$ /kg BM-MSCs were implanted through tail vein to MSCs treatment groups, model control groups with equal amounts of saline served as controls.At forty two day,stream multi-factor detection technique were used to detect the level of RANTES, MCP-1 and IP-10 in serum of CIA rats.
Results: The level of RANTES, AMCP-1, AIP-10 was higher in CIA control group than normal group ($P<0.05$); After MTX treatment, these factors level were significantly difference than the CIA control group ($P<0.05$). These factors level were lower in early BMSCs treatment groups than early CIA control groups ($P<0.05$), while the late MSCs treatment group versus the later CIA control group showed no statistically significant difference ($P>0.05$). The early and late MSCs treatment group versus the MTX treatment group showed no statistically significant difference ($P>0.05$).
Conclusions: In this study MSCs has shown significant immune modulatory effects. It down regulates the level of Inflammatory Chemokines in CIA rats. The early treatment group is more effective than the late treatment group.
References:
[1] Stuad JM,Cremer MA,Townes AS,et a1.Type II collagen induced arthritis in rats: passive transfer with serum and evidence that IgG antieollagen antibodies can cause arthritis.J Exp Med,1982,155:l-16.
[2] Brahn E, Peacock DJ, Banquerigo ML. Suppression of collagen-induced arthritis by combination cyclosporin A and methotrexate therapy. Arthritis Rheum.1998,34 (10):1282–1288.
[3] Dominici M, Le Blanc K, Mueller I, et al. Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. Cytotherapy. 2006;8(4):315–317.
[4] Park MJ, Kwok SK, Lee SH, et al.Adipose tissue-derived mesenchymal stem cells induce expansion of Interleukin-10 producing regulatory B cells and ameliorate autoimmunity in a murine model of systemic lupus erythematosus.Cho Cell Transplant. 2014 Dec 12. [Epub ahead of print].
[5] Kehoe O, Cartwright A, Askari A,et al.Intra-articular injection of mesenchymal stem cells leads to reduced inflammation and cartilage damage in murine antigen-induced arthritis. J Transl Med. 2014,12:157.
Acknowledgements: Mesenchymal stem cell;Arthritis,rheumatoid; Collagen II induced arthritis (CIA);Inflammatory chemokine.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3470

THU0564 IGG4-RELATED DISEASE IN THE MALTESE POPULATION

S. Chetcuti Zammit[1], M. Rogers[2], P. Ellul[1]. *[1]Gastroenterology; [2]Rheumatology, Mater Dei Hospital, Msida, Malta*

Background: IgG4-related disease (IgG4-RD) is an increasingly recognised immune-mediated fibro-inflammatory condition, most commonly affecting the pancreas.
Objectives: The aim of our study was to determine the incidence, organ involvement and outcome of IgG4-RD in the Maltese population.
Methods: The case notes of all patients who had their IgG4 level checked between 2008 and 2015 at Mater Dei Hospital were reviewed. Patients who had their IgG4 level checked inappropriately were excluded. Patients were then stratified according to the "Comprehensive diagnostic criteria for IgG4-related disease" [1].
Results: 25 patients were included in this retrospective, observational study. 60% (n=15) of patients were males and mean age was 70 years (SD±64.8). The mean IgG4 level was 0.7159 g/L (SD±0.851) (normal range 0.052–1.250g/L).
Organs involved included: pancreas (n=15), biliary tree (n=3), salivary glands (n=1), lymph nodes (n=8), lungs (n=4), thyroid gland (n=2), bone (n=1), heart (n=1), sinuses (n=2). 36% (9 patients) had involvement of more than one organ.
Blood tests at time of diagnosis demonstrated a raised mean ESR (65.7mm1st Hr; SD±36.1) and a raised mean CRP (143 mg/L SD± 112). White cell count was mostly normal (mean $11.7x10^9$/L SD±4.91).
92% of patients (n=23) had organ swelling on radiological testing. 32% (n=8) of patients had raised IgG4 levels. A histological diagnosis was obtained in 8% (n=2) of patients presenting with cervical lymphadenopathy and sinusitis respectively.
According to the "Comprehensive diagnostic criteria for IgG4-RD"[1], the diagnosis was definite in 4% (n=1), possible in 28% (n=7) and probable in 4% (n=1) of patients. 64% (n=16) only had organ swelling on imaging studies, satisfying 1 criterion.
One patient was diagnosed with malignancy during the course of disease. Patients with hepatobiliary and pancreatic involvement underwent ERCP and stenting. Patients who developed pancreatic pseudocyst as a complication of pancreatitis underwent drainage. One patient (4%) developed pancreatic insufficiency and 32% (n=8) experienced recurrent pancreatitis requiring hospital admission. Four patients (16%) passed away.
Conclusions: In concordance with current literature, our study has shown that IgG4-RD in the Maltese population is a rare disorder affecting mainly elderly males. The commonest organs involved were the pancreas and lymph nodes. The inflammatory markers ESR and CRP were always raised, thus acting as possible biomarkers for monitoring of disease activity.
References:
[1] Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. Mod Rheumatol. 2012 Feb;22(1):21–30.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3713

THU0565 MACROPHAGE ACTIVATION SYNDROME IN ADULTS WITH INFLAMMATORY RHEUMATIC DISEASES

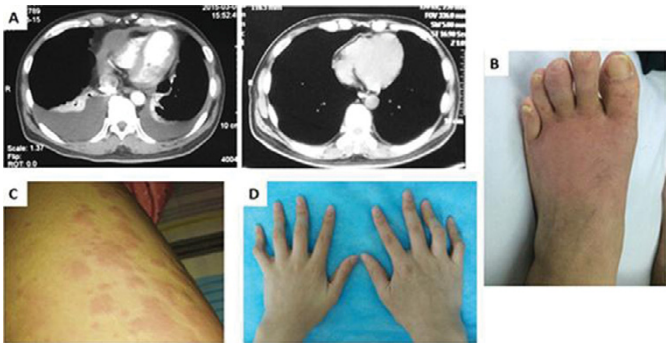
M. Olejárová[1,2], K. Jarošová[2]. *[1]Clinic of Rheumatology, 1st Medical Faculty, Charles University; [2]Institute of Rheumatology, Praha 2, Czech Republic*

Background: Macrophage activation syndrome (MAS) is a rare hyperinflammatory condition characterised by macrophage activation and infiltration resulting in a multi organ damage. MAS is considered to be a type of secondary hemophagocytic lymphohistiocytosis. It is a life threatening complication of various autoimmune or autoinflammatory rheumatic diseases, particularly systemic juvenile idiopathic arthritis (sJIA). Clinical manifestations include hepatosplenomegaly, increase of liver function tests, pancytopeny, neurolological manifestations etc. High doses of glucocorticosteroids (GC), cyclosporine A (CyA) and etoposide are a treatments of choice. In refractory cases biologicals may be an option, too.
Objectives: To point out this very rare but severe complication may occur also in adult patients with rheumatic diseases.
Methods: We report 4 successfully treated cases of adult MAS in rheumatic patients seen in our clinic during the years 2009 – 2016. A review of the literature regarding the efficacy of biologics in MAS treatment is also presented.
Results: We have observed four patients with MAS, two with adult onset Still disease (AOSD), one with rheumatoid arthritis (RA) and one with sJIA. All of the patients were young (20 -33 years, mean age 27,0±5,61 years) with the duration of the primary disease ranging from 9 months to 11 years (mean 4,18±4,01 years). Three patients were in remission of the primary diseases prior to MAS manifestation, only in the last and most severe patient (AOSD) the activity of the underlying disease was not controlled. A demographic and clinical characteristic of the patients is summarized in the table.
All 4 patients were successfully treated, one with high doses of glucocorticosteroids (GC), two with combination GC plus CyA. The last and most severe one had MAS refractory to the combination GC + CyA and must have been added biological therapy (tocilizumab). We reviewed also another cases of MAS treated with biologics which have been published.
Conclusions: Our cases illustrate that MAS may develop also in adult patient with various rheumatic diseases (JIA, AOSD, RA) despite the low activity or remission. It occurs particularly in younger subjects. As the MAS symptoms may overlap with the symptoms of the primary disease (JIA, AODS) the diagnosis may be difficult. MAS must be suspected in inflammatory rheumatic diseases patients with sudden increase of CRP, extreme increase of ferritin, liver function tests and decrease of platelets. An immediate treatment with GC, CyA and etoposide is essential; biologicals (anakinra, canakinumab or tocilizumab) may be benefitial in refractory cases.
Acknowledgements: Supported by MHCR Research project 00000023728.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5784

THU0566 CLINICAL AND GENETIC PHENOTYPES OF CHINESE PATIENTS WITH ADULT AUTOINFLAMMATORY DISEASES: REPORT FROM AN ADULT REFERENCE CENTER

M. Shen, D. Wu, X. Zeng. *Peking Union Medical College Hospital, Beijing, China*

Background: Autoinflammatory diseases (AUID) is a group of disorders characterized by dysfunction of innate immunity which caused by gene mutations leading to coded proteins changes, finally causing uncontrolled systemic inflammation. AUID are usually diagnosed during pediatric age. However, adult-onset disease or diagnosis during adulthood has been occasionally described. Moreover, AUID have been hardly reported in the Chinese population.
Objectives: We aimed to characterize the clinical and genetic phenotypes of Chinese adult patients with AUID.
Methods: We prospectively evaluated clinical and genetic features of adult patients (≥16 years) suspected monogenic AUID in the period April 2015 to May 2016, at the adult AUID center, Department of Rheumatology, Peking Union Medical College Hospital. The definite diagnosis of each disease was deemed to be present if both clinical phenotypes and genetic confirmation were met.
Results: During the study period, a total of 37 adult patients with clinical phenotypes suspicious of monogenic AUID requested for a genetic study. A final diagnosis of monogenic AUID was achieved in 16 patients (43.2% of patients tested). Two additional patients were diagnosed with periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome. Finally, a total of 18 patients with AUID were diagnosed and follow-up in our center, including 7 (38.9%) familial Mediterranean fever (FMF), 2 (11.1%) tumor necrosis factor-receptor associated periodic syndrome (TRAPS), 3 (16.7%) cryopyrin-associated periodic syndrome (CAPS), 3 (16.7%) NLRP12-autoinflammtory disease (NLRP12-AD), 1 (5.6%) Blau syndrome (BS), and 2 (11.1%) PFAPA. Disease onset during adulthood was observed in 15 (83.3%) patients, and the final diagnosis was delayed with a mean time of 10 years. Adult AUID patients usually carried low-penetrance mutations and gene variants were presented as heterozygosis or compound heterozygosis.



Conclusions: Adult AUID is not uncommon. FMF, CAPS, and NLRP12-AD are relatively common monogenic AUID in Chinese adult patients. Adult-onset AUID may be related to the presence of low-penetrance mutations, being characterized by nonspecific, incomplete or atypical disease patterns, leading to a delay of diagnosis. The interpretation of gene analysis in adult suspected AUID should be performed with caution, and if possible, should be referred to expert physicians in the field in adult AUID center.
References:
[1] Muscari I, et al. The diagnostic evaluation of patients with potential adult-onset autoinflammatory disorders: our experience and review of the literature. Autoimmun Rev 2012,12:10–13.
[2] Hernández-Rodríguez J, et al. Clinical and genetic characterization of the autoinflammatory diseases diagnosed in an adult reference center. Autoimmun Rev 2016,15:9–15.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1685

THU0567 RAPID IMPROVEMENT WITH TOCILIZUMAB IN REFRACTORY AND SEVERE UVEITIC CYSTOID MACULAR EDEMA

N. Vegas-Revenga[1], V. Calvo-Río[1], N. Palmou-Fontana[1], M. Mesquida[2], A. Adan[2], M. Hernández[2], E. Beltrán[3], E. Valls[4], D. Díaz-Valle[5], G. Díaz-Soriano[6], M. Hernández-Grafella[7], L. Martínez-Costa[7], I. Calvo[8], A. Atanes[9], L. Linares[10], C. Modesto[11], E. Aurrecoechea[12], M. Cordero[13], L. Domínguez-Casas[1], C. Fernández-Díaz[1], J. Hernández[1], M. González-Gay[1], R. Blanco[1]. *[1]HUMV, Santander; [2]H Clinic, Barcelona; [3]H Valencia; [4]H, Valencia; [5]H S Carlos, Madrid; [6]H, Málaga; [7]H Peset; [8]H Fe, Valencia; [9]HUAC, A Coruña; [10]H Arrixaca, Murcia; [11]H V d'Hebron, Barcelona; [12]H Sierrallana, Torrelavega; [13]H, León, Spain*

Background: In uveitis, remission-inducing therapy with even more vigor than does rheumatology is mandatory. Since the eye is so much less forgiving of chronic inflammation than is the joint, with profound life-altering consequences. Cystoid macular edema (CME) is the leading cause of blindness in uveitis.
Objectives: To evaluate the rapid efficacy of Tocilizumab (TCZ) in refractory CME.
Methods: Multicentre study of 25 patients with CME due to non-infectious uveitis who had inadequate response to traditional treatment with corticosteroids and at least one conventional immunosuppressive drug including in most cases biological therapy (n=22). CME was defined as OCT >300 μm.
The outcome variables were the degree of inflammation, visual acuity, macular thickness. The results are expressed as mean±SD for normally distributed variables, or as median [IQR] when are not. Comparison of continuous variables was performed using the Wilcoxon test.
Results: 25 patients (17 women/8 men), mean age 33.6±18.9 years were studied. The associated diseases were: juvenile idiopathic arthritis (9), Behçet's (7), Birdshot (4), idiopathic (4), sarcoidosis (1). The ocular pattern was: panuveitis (9), anterior uveitis (7), posterior uveitis (5) and intermediate uveitis (4). Most patients had bilateral involvement (24). Prior to TCZ they received: intraocular corticosteroids (22), iv. methylprednisolone (7), methotrexate (MTX) (19), cyclosporine A (CSA) (17), mycophenolate (4), azathioprine (2), leflunomide (2), cyclophosphamide (1), sulfasalazine (1), acetazolamide (1) and thalidomide (1). The biological used before TCZ were infliximab (8), adalimumab (19),

Abstract THU0565 – Table 1

Patient	Age (years)	Primary disease			Clinical manifestations of MAS	Treatment
		Dg.	Duration	Treatment prior to MAS		
L.H., female	23	JIA	11 years	MTX	hepatosplenomegaly, increase of ALT, AST, pancytopenia, serositis	GC high doses (i.v. pulses), cyclosporine
P.V., male	20	RA	2 years	MTX, SAS	fever, pancytopenia, hepatosplenomegaly, increase of ALT, AST, pericarditis	GC high doses (oral), cyclosporine
P.D., male	32	AODS	3 years	MTX	fever, hepatosplenomegaly, increase of ALT, AST, pancytopenia,	GC high doses (oral)
V.N., female	33	AODS	9 months	MP, AZA	fever, pancytopenia, hepatosplenomegaly, increase of ALT, AST, alveolar hemorrhage	GC high doses (i.v. pulses), cyclosporine, tocilizumab

	Baseline	1st week	2nd week	1st month
OCT (microns), mean±SD	415.7±177.15	413.3±162.9*	388.06±158.1*	330.8±104.2*
Visual acuity, mean±SD	0.39±0.31	0.4±0.31	0.45±0.3*	0.51±0.3*
Anterior chamber cells, median [IQR]	1 [0–1]*	0.5 [0–1]*	0 [0–1]*	0 [0–0]*
Vitritis, median [IQR]	1 [0–2]	1 [0–1.5]	0 [0–1]*	0 [0–0.5]*

*$p<0.05$ compared with basal data.

etanercept (2), golimumab (2), rituximab (2), abatacept (3), anakinra (1) and daclizumab (1).

TCZ administration schedule was 8 mg/kg/4 weeks iv. (n=23), every 2 weeks (1) and subcutaneously 162 mg/2 weeks (1). TCZ was used in monotherapy (13) or combined with conventional immunosuppressive drugs (12). Most of intraocular inflammation parameters showed a rapid improvement after TCZ onset (Table), with corticosteroid-sparing effect (15.9±13.6 to 8.5±5.17 mg; p=0.001). Remission was achieved in 8 patients and improvement in 17. After one month of therapy, no side effects were observed.

Conclusions: TCZ seems a rapid effective treatment in refractory uveitic CME.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5215

THU0568 PREVALENCE AND AUTOIMMUNE RHEUMATIC DISEASE IN PATIENTS WITH AUTOIMMUNE/INFLAMMATORY SYNDROME INDUCED BY ADJUVANTS ASSOCIATED TO SILICONE BREAST IMPLANT

O. Vera Lastra, N.E. Torres-Oliva, G. Medrano-Rodriguez, M.D.P. Cruz-Dominguez, J. Sepulveda Delgado, L.J. Jara, G. Medina. *Internal Medicine, Hospital Especialidades CMN la Raza. Instituto Mexicano Seguro Social, Mexico City, Mexico*

Background: Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) has been associated with previous exposure to various agents such as silicone implants, which elicit chronic stimulation of the immune system against the prosthetic material and clinical manifestation of autoimmune disease. This is particularly the case in genetically susceptible hosts.

Objectives: The aim is to describe de prevalence, family background and main autoimmune rheumatic disease (ARD) associated to silicone breast implant (SBI).

Methods:

We study a cohort of 150 patients with diagnosis of ASIA associated injection of mineral oil and silicone breast implant (SBI) in a tertiary Hospital, from 2011 to 2016. All patients were evaluated for the fulfilment of ASIA criteria. We only included patients with ASIA criteria associated with SBI plus criteria for an autoimmune rheumatic disease according to The American College of Rheumatology or EULAR. We excluded patient with ASIA and without ARD.

Results: There were 17 women patients with mean age 42.4±15.3 years, mean disease duration of disease 8±3. The clinical manifestation post SBI appeared 8±2 years later.

The ARD were systemic sclerosis (SSc) 5, systemic lupus erythematosus (SLE) 3, rheumatoid arthritis (AR) 3, overlap syndrome 2 (SSc plus SS and SLE plus SSc, Sjogren syndrome 1, Takayasu arteritis 1, Still disease 1, antiphospholipid syndrome 1, and 3 patients also had secondary fibromyalgia. Five Patients had more than 2 autoantibodies, 4 patients had relatives with an ARD. All patients are being treated according to the ARD (steroids plus immunosuppressive 8 patients, immunosuppressive 7, and only steroids 2), in 4 patients the prosthesis were withdrawn with improvement of clinical manifestations.

Conclusions: We found a prevalence of ASIA associated to SBI of 11%. The main ARD were SSc, SLE and RA. In these cases of ASIA associated with SBI some had genetic predisposition to ARD. The use of SBI is not recommended in women who have a family history of ARD.

References:

[1] Colaris MJ et al. Two hundred cases of ASIA syndrome following silicone implants: a comparative study of 30 years and rewiew of current literature. Immunol Res 2016 Jul 13.

[2] Jara LJ, et al. Severe manifestation of autoimmune syndrome induced by adjuvants (Shoenfeld's syndrome) Immunol Res Jul 13.

[3] Watad et a. Autoimmune/Inflammatory induced by adjuvants (Shoenfeld's syndrome) UN update. Lupus 2017 Jan 1.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5588

THU0569 TREATMENTS OF UVEITIS IN A REFERRAL MULTIDISCIPLINARY UNIT IN NORTHERN SPAIN

P. Fanlo[1], H. Heras[2], O. Terry[1], G. Espinosa[3], A. Adan[4]. *[1]Autoimmune Sistemic Disease Unit; [2]Ophthalmology, Complejo Hospitalario de Navarra, Pamplona; [3]Autoimmune Sistemic Disease Unit; [4]Ophthalmology, Hospital Clinic, Barcelona, Spain*

Background: Intraocular inflammation is one of the leading causes of visual impairment and blindness. Early and appropiate treatment is mandatory for avoiding complications.

Objectives: To describe the treatments prescribed in a cohort of patients with uveitis in a referral multidisciplinary unit from northern Spain.

Methods: Retrospective analysis of clinical records of patients evaluated in the Uveitis Multidisciplinary Unit of the Complejo Hospitalario of Navarra since January 2010 until March 2015. We analyzed the demographic characteristics and treatments received in the following 3 months after first visit.

Results: We identified 500 patients, 50% women with a mean age of 47.9 +/- 16.4 years. The most frequent type of uveitis was anterior uveitis (65,4%), followed by posterior uveitis (17,6%), panuveitis (15,2%), and intermediate uveitis (1,8%). Considering the etiology, 31.2% were unclassifiable, followed by non-infectious systemic disease in 29.2%.During the 3-month follow-up, 904 treatments were prescribed. The most frequent treatment was ocular topical (39%), followed by immunosuppressive treatment (27%), antimicrobial (14%), other treatments (10%) and less biological (3%), surgical (3%) and finally periocular (2%) and intravitreal (2%) treatment.Topical ocular treatment: 350 patients received topical ocular treatment, which accounts for 70% of patients. Among topical ocular treatments, 15% of the samples were treated with topical steroids, 54% were topical steroids associated with another topical treatment, 2% were topical antiglaucomatous, 2% received other topical treatments and 27% of the sample did not receive topical treatment.Immunosuppressive treatment: 249 immunosuppressive treatments were prescribed. 50% of the patients received immunosuppressive treatment. Among the immunosuppressive treatments, 25% of the patients received oral steroids, 6% salazopyrine, 4% methotrexate, 5% azathioprine, 2% mycophenolate mofetil, 5% oral steroids associated with another immunosuppressant, 15% salazopyrine associated with another immunosuppressant, 1% other immunosuppressive treatment and 49% of patients did not receive any immunosuppressive treatment.Biological Treatments: 25 patients in the cohort received biological treatment, this represents 5% of patients. The biological treatment types were distributed as follows: 3% of the patients received adalimumab treatment, 1% received infliximab, 1% received other biological treatments, and 95% of the patients did not receive biological treatments.The number of treatments received per patient was analyzed and 50 patients (10%) received no treatment, 152 patients (30%) received 1 treatment, 189 patients (38%) received 2 treatments, 75 patients (15%) Had received 3 treatments, 23 patients (5%) had received 4 treatments, 9 patients (2%) had received 5 treatments and lastly 2 patients had received 6 treatments.

Conclusions: The majority of patients received the combination of two treatments. Topical steroids and oral steroids were the most frequent treatments used.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1937

THU0570 ANAKINRA AS A SUCCESSFUL TREATMENT OF IDIOPATHIC RECURRENT PERICARDITIS: TAPER OR NOT TO TAPER? CASE SERIES AT THE UNIVERSITY OF SOUTHERN CALIFORNIA

P.S. Chhibar, G. Ehresmann. *Rheumatology, University of Southern California, Los Angeles, United States*

Background: Idiopathic Recurrent Pericarditis can be challenging to treat in patients unresponsive to NSAIDs, aspirin, colchicine and immunosuppressive drugs. Patients become steroid dependent and tapering precipitates recurrences.

Objectives: Report 2 adult cases of idiopathic recurrent pericarditis treated successfully with Anakinra.

Methods: Chart review of 2 patients with idiopathic recurrent pericarditis treated with anakinra at the Keck Medical Center of USC. Literature review on treatment of idiopathic recurrent pericarditis with anakinra.

Results: Case 1: 60-year-old Caucasian male had five episodes of idiopathic pericarditis in 2011. Serologic workup including ANA, anti-dsDNA, malignant and infectious workup was negative. Initially, patient responded to prednisone 0.4 mg/kg/day. Adding colchicine, azathioprine and methotrexate failed to prevent recurrence. Pericarditis developed whenever prednisone was tapered below 20 mg/day with bursts of CRP to 78 mg/dl. In 2012, Anakinra 100 mg sq daily resulted in immediate clinical response and normalization of CRP (1mg/dl). Prednisone and methotrexate were tapered with no recurrence. Gradually Anakinra was tapered to 3 times/week, then once a week, with no recurrence. Case 2: 37-year-old African American male had four episodes of recurrent pericarditis. He had positive ANA 1:320, but negative anti-dsDNA, anti-smith, negative infectious and malignancy workup. Initially, patient responded to prednisone 0.6 mg/kg/day and colchicine. Tapering steroids below 40 mg/day resulted in recurrent pericarditis. Sequential addition of hydroxychloroquine, methotrexate, mycophenolate mofetil, and azathioprine failed to prevent recurrence. Anakinra 100 mg sq daily resulted in prompt resolution of symptoms, normalization of acute phase reactants and allowed successful tapering of steroids. Anakinra is being slowly tapered over the past year, with no recurrence.

Conclusions: Idiopathic recurrent pericarditis, which requires chronic corticosteroids, should be treated by adding another immunosuppressive agent. European Society of Cardiology guidelines recommend azathioprine, cyclophosphamide, methotrexate, hydroxychloroquine, cyclosporine or mycophenolate mofetil. Anakinra has demonstrated success in treating autoinflammatory and autoimmune diseases including FMF, TNF receptor associated periodic syndrome, rheumatoid arthritis and in patients with TRAPS mutation TNFRSF1A. This represented the possibility to decrease inflammation by blocking interleukin-1. Using this rationale we treated our patients. Picco et al reported three pediatric cases treated with anakinra, where its discontinuation resulted in recurrence.

Vassilopoulos et al reported three adult cases, where two were not treated with immunosuppressive drugs before anakinra and one had recurrence after anakinra was tapered. The Double Blind Placebo Controlled Clinical Trial AIRTRIP, shows efficacy of anakinra in treating 11 patients with recurrent pericarditis over 14 months. It is unclear from this study if anakinra should be tapered or not. We suggest that once steroids and immunosuppressive drugs have been discontinued, anakinra should be gradually tapered over months, to avoid relapse. These experiences warrant further long term controlled trials in order to determine the efficacy and appropriate treatment regimen of anakinra for recurrent pericarditis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1141

THU0571 THE CLINICAL FEATURES OF 223 BEHCET'S DISEASE PATIENTS IN JAPAN

R. Saito[1], K. Nishimura[1], H. Mukoyama[1], Y. Nakamura[1], T. Nagamoto[1], K. Akashi[2], A. Onishi[2], Y. Kogata[2], J. Saegusa[2], A. Morinobu[2], T. Yokota[1]. *[1]Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, Kurashiki; [2]Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan*

Background: Behcet's disease is a systemic vasculitis disease with oral and genital aphthous ulcers, ocular involvements, skin manifestations, arthritis, gastrointestinal manifestations, neurogenic diseases and vascular involvements. Patients with Behcet's disease are known to distribute along the ancient Silk Road, including Japan.
Objectives: We evaluate the clinical features of Behcet's disease in Japan.
Methods: We retrospectively investigated 223 patients (108 males and 115 females) who fulfilled the International Criteria for Behcet's Disease (ICBD) from January, 2006 until May, 2015.We examined sex, onset age, disease type, clinical symptoms, laboratory data and medications.
Results:
Median age at diagnosis was 36.0±12.8 years old. Oral ulcers were the most common manifestation (98.2%), followed by genital ulcers (62.4%), ocular involvements (53.2%), erythema nodosum (53.2%), acneiform lesions (51.8%), arthritis (38.6%), gastrointestinal manifestations (25.1%), neurogenic diseases (9.0%), and vascular involvements (8.1%). The relationship of HLA and disease manifestations was studied in 123 patients (41.5% with HLA-B51 and 24.1% with HLA-A26). The frequency of acneiform lesions, ocular involvements and HLA-B51 was significantly higher in male, while genital ulcers and arthritis were significantly higher in female. Patients with ocular involvements showed a higher assosiation rate with neurogenic diseases and HLA-B51, and lower wih gastrointestinal manifestations. TNFα inhibitor (infliximab or adalimumab) were used for 66 cases (30%), and it could be continued for 1 year in 91%, and for 2 years in 83%.

Table 1

	Total (n=223)	Male (n=108)	Female (n=115)	p value
Oral ulcers	218/222 (98.2%)	105/107 (98.1%)	113/115 (98.3%)	0.94
Skin manifestations	190/220 (86.4%)	90/107 (84.1%)	100/113 (88.5%)	0.34
Erythema nodosum	116/218 (53.2%)	49/105 (46.7%)	67/113 (59.3%)	0.06
Acneiform lesions	113/218 (51.8%)	65/105 (61.9%)	48/113 (42.5%)	0.004
Thrombophlebitis	11/218 (5.0%)	5/105 (4.8%)	6/113 (5.3%)	0.85
Ocular involvements	118/222 (53.2%)	68/108 (63.0%)	50/114 (43.9%)	0.004
Genital ulcers	138/221 (62.4%)	58/107 (54.2%)	80/114 (70.2%)	0.01
Artiritis	86/223 (38.6%)	33/108 (30.6%)	53/115 (46.1%)	0.02
Gastrointestinal manifestations	56/223 (25.1%)	23/108 (21.3%)	33/115 (28.7%)	0.20
Neurogenic diseases	20/223 (9.0%)	12/108 (11.1%)	8/115 (7.0%)	0.28
Vascular involvements	18/223 (8.1%)	6/108 (5.6%)	12/115 (10.4%)	0.18
HLA-B51 positive	51/123 (41.5%)	32/62 (51.6%)	19/61 (31.1%)	0.02
HLA-A26 positive	28/116 (24.1%)	14/56 (25.0%)	14/60 (23.3%)	0.91

Table 2

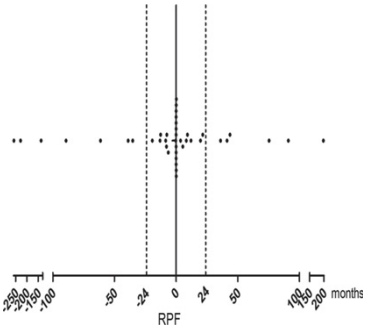
	Total (n=223)	With ocular involvements (n=118)	Without ocular involvements (n=104)	p value
Gastrointestinal manifestations	56/223 (25.1%)	17/118 (14.4%)	39/104 (37.5%)	<0.001
Neurogenic diseases	20/223 (9.0%)	19/118 (16.1%)	1/104 (1.0%)	<0.001
Vascular involvements	18/223 (8.1%)	7/118 (5.9%)	11/104 (10.6%)	0.21
HLA-B51 positive	51/123 (41.5%)	36/69 (52.2%)	15/54 (27.8%)	0.006
HLA-A26 positive	28/116 (24.1%)	19/65 (29.2%)	9/51 (17.6%)	0.15

Conclusions: A higher incidence of gastrointestinal manifestations was observed in patients with Behcet's disease in Japan. Patients with ocular involvements showed a higher assosiation rate with neurogenic diseases, and lower wih gastrointestinal manifestation. Most patients could continue TNFα inhibitor safety and effectively.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4216

THU0572 ASSOCIATION BETWEEN RETROPERITONEAL FIBROSIS AND MALIGNANCY: A POSSIBLE PARANEOPLASTIC SYNDROME

S.J. Lee[1], J.S. Eun[1], E.Y. Lee[2], G.B. Bae[1], E.J. Nam[1], Y.W. Song[2], Y.M. Kang[1]. *[1]Internal Medicine, Division of Rheumatology, Kyungpook National University Hospital, Daegu; [2]Internal Medicine, Division of Rheumatology, Seoul National University Hospital, Seoul, Korea, Republic Of*

Background: Retroperitoneal fibrosis (RPF) are associated with malignancies. However it is unclear what is the incidence of malignancies and whether particular malignancies are more prevalent in RPF.
Objectives: The objective of this study was to examine standardized incidence ratios (SIRs) of cancers in patients with retroperitoneal fibrosis (RPF) compared with age- and sex-matched general population.
Methods: Medical records of 111 patients diagnosed as having RPF by computed tomography, positron emission tomography and/or histological evaluation were reviewed. Forty one cases of cancers, which were confirmed by biopsies, were identified in 35 patients with RPF. SIRs were calculated for cancers, cancer types, and age at cancer diagnosis and stratified according to RPF-cancer intervals compared with general population in Korea.
Results: The mean ± SD age at RPF diagnosis was 59.1±14.9 years, and 69.4% of the patients were male. The cancer SIR (95% confidence intervals) in patients with RPF relative to age- and sex-matched individuals in the general population was 3.18 (2.23 - 4.41) [2.65 (1.7 - 3.94) in men; 5.34 (2.76 - 9.32) in women]. The most frequent cancer was unspecified urinary organ cancers with SIR of 733.41 (238.14 – 1711.53). SIRs of multiple myeloma [27.58 (3.34 – 99.64)], renal cell cancers [9.53, (1.15 - 34.42)] and unspecified cancers [16.92, (2.05 - 61.12)] were also significantly higher than in general population. Whereas cancers were most frequently developed in the eighth decade of life, the peak SIR was observed in the fifth decade (8.41, 2.29 – 21.53). When stratified by RPF-cancer intervals, SIR was 6.85 (4.55 - 9.90) within 2 years of RPF diagnosis, while no significant increase in SIR was found out of 2 years. Malignancies (n=28) within 2 year of RPF diagnosis included unspecified urinary organ cancer (n=4), stomach cancer (n=4), lung cancer (n=4), colon cancer (n=3), renal cell cancer (n=2), pancreatic cancer (n=2), unspecified cancer (n=2), rectal cancer (n=1), gallbladder cancer (n=1), non-Hodgkin lymphoma (n=1), multiple myeloma (n=1), prostate cancer (n=1), thyroid cancer (n=1) and gastrointestinal stromal tumor (n=1). Predominant origin of these malignancies were epithelial cell types [transitional cell carcinomas (n=4), adenocarcinoma (n=16)].



Conclusions: RPF was strongly associated with cancers, particularly within 2 years of RPF diagnosis. Our results indicate that cancer screening in patients with RPF should may be performed regularly up to 2 years after RPF diagnosis.
References:
[1] Temporal relationship between cancer and myositis identifies two distinctive subgroups of cancers: impact on cancer risk and survival in patients with myositis. Kang EH, Lee SJ et al Rheumatology (Oxford). 2016 Sep;55(9):1631–41.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6168

THU0573 CONCOMITANT AUTOIMMUNE DISEASES IN PATIENTS WITH SARCOIDOSIS

S. Kobak[1], F. Sever[2], H. Semiz[3], M. Orman[4]. *[1]Rheumatology, Istinye University Faculty of Medicine, LIV Hospital, Istanbul; [2]Chest Diseases, Medicalpark Hospital; [3]Internal Medicine; [4]Statistics, Ege University Faculty of Medicine, Izmir, Turkey*

Background: Sarcoidosis is a chronic granulomatous disease characterized by non-caseating granuloma formation. It can mimic many rheumatic diseases and/or may be coexist with them. There are limited data in the literature about the association of sarcoidosis with autoimmune diseases.
Objectives: The purpose of this study is to determine the frequency and characteristics of autoimmune diseases associated with patients with sarcoidosis.
Methods: One hundred and thirty-one sarcoidosis patients folowed-up in single rheumatology center were included in the study. Demographic, clinical, laboratory and radiological data of these cases were evaluated retrospectively. The

characteristics of autoimmune diseases associated with sarcoidosis (sarcoidosis-overlap group) patients and isolated sarcoidosis (isolated sarcoidosis group) were analyzed and compared.

Results: Autoimmune disease was detected in 15 (11.5%) of 131 patients with sarcoidosis (1Sjögren syndrome, 3rheumatoid arthritis, 1Still disease, 1scleroderma, 4ankylosing spondylitis, 1familial Mediterranean fever, 1gut arthritis, 1immune trombocytopenic purpura, 1Hashimoto thyroiditis and 1Graves disease). Most of these diseases occurred before (such as RA, AS, Still, FMF) and others after sarcoidosis diagnosis. Among 15 sarcoidosis patients with autoimmune disease 10 were female and 5 were male, the mean age was 50.8 years and mean disease duration was 3 months (1–30 months). When compared with isolated sarcoidosis patients, more hand finger joint involvement, RF positivity, higher ESR and less NSAIDs usage were found in patients with sarcoidosis-overlap group (p=0.035, p=0.049, p=0.015, p=0.018 respectively). There was no statistically significant differences between the two groups when evaluated for demographic, clinical parameters and other treatment modalities.

Conclusions: Concomitant autoimmune diseases in patients with sarcoidosis may be often seen. This patients are characterized with more hand finger joint involvement, RF positivity, higher ESR and less NSAIDs usage. Therefore, in patients with a diagnosis of sarcoidosis, it is necessary for the physician to be careful and to make a wider differential diagnosis in terms of the presence of another underlying autoimmune disease. Multicenter, prospective studies involving large numbers of patients are needed to understand whether the association of sarcoidosis-autoimmune diseases is based only on coincidence or on a common etiopathogenesis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1376

THU0574 CLASSICAL IMMUNOSUPPRESSION AND DAMAGE PROGRESSION IN A GROUP OF PATIENTS DIAGNOSED WITH BEHCET'S DISEASE

S. Daia-Iliescu, C. Buzatu, A. Borangiu, I. Saulescu, L. Groseanu, V. Bojinca, A. Balanescu, D. Predeteanu, R. Ionescu, D. Opris-Belinski. *Internal Medicine and Rheumatology, Sf. Maria Clinical Hospital, Bucharest, Romania*

Background: Behcet's Disease is a rare type of vasculitis that involves both arterial and venous blood vessels of all sizes. The type of organ involvement and overall disease activity evaluated in the clinical practice determine the course of treatment and the decision to initiate immunosuppression. Activity scores such as Birmingham Vasculitis Activity score (BVASv3), Behcet's Disease Current Activity Form2006 (BDCAF), or damage indices like Vasculitis Damage Index (VDI) have been developed in this respect.

Objectives: To evaluate the ability of classical immunosuppressant therapy to prevent damage progression. To find the correlation between disease activity scores: BVASv3, BDCAF, long term treatment, immunosuppressant use and damage after remission, as calculated by VDI.

Methods: A study on a cohort of patients diagnosed with Behcet's Disease from an Internal Medicine and Rheumatology Clinic was performed. Activity and damage scores,BVASv3,BDCAF and VDI after obtained remission, were calculated. The documented cases were diagnosed according to the International Criteria for Behçet's Disease (ICBD).Windows Excel/SPSS20.0 (Spearman's correlation)were used to analyse the data.

Results: The study included 16 patients treated with long term cortisone and immunosuppressive therapy. The mean age at the time of the diagnosis was 32.3years with a male predominance 62% (10 patients). Severe systemic involvement was present in 10 cases (Ophthalmological involvement-6cases, recurrent venous thrombosis-6cases, pulmonary vasculitis-1 case, severe cardiac involvement-1case, central nervous system involvement-3cases) and all patients received classical immunosuppression (cyclophosphamide, azathioprine).The mean scores for BVASv3 and BDCAF at the time of the diagnosis were 9 and 4.12.A strong correlation was identified between BVASv3 and BDCAF (r=0.830, p<0,001). The use of immunosuppressive therapy due to severe organ involvement and long-term immunosuppression correlated stronger with BVASv3 (r=0.718) than with BDCAF (r=0.533). Vasculitis damage index (VDI) calculated after remission was obtained. There was an important correlation between disease activity scores and damage (BVASv3-VDI r=0,687,p<0,001, BDCAF-VDI r=0,676, p<0,001). Types of treatment were evaluated, a comparison was made between long-term cortisone therapy and immunosuppression.There was a stronger correlation between long term cortisone use and VDI (r=0,600) than between immunosuppression duration and damage (r=0,472).

Conclusions: Damage progression is influenced by disease activity, as calculated by activity scores (BVASv3 and BDCAF). Classical immunosuppression is used for severe organ involvement and for limiting new organ lesions once started. There was a stronger correlation between long-term cortisone use and VDI than between immunosuppression duration and damage. The damage index increased by irreversible organ damage due to disease activity and long term cortisone use, but not due to the immunosuppressive therapy.

References:

[1] DavatchiF,et al How to deal with Behcet's disease in daily practice. Int J Rheum Dis. 2010 May.

[2] Raashid Ahmed Luqmani Disease assessment in systemic vasculitis. Nephrol Dial Transplant 2015.

Acknowledgements: The first two authors,Sinziana Daia-Iliescu and Casandra Buzatu contributed equally to this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5530

THU0575 EFFICACY OF RITUXIMAB IN RESISTANT PALINDROMIC RHEUMATISM:FIRST REPORT IN LITERATURE

S. Sreenath[1], S. Cherian[1], G. Antony[1], U. Mony[2], P. Shenoy[1]. *[1]Centre for Arthritis and Rheumatism (CARE); [2]Molecular Medicine, AIMS, Cochin, India*

Background: Palindromic rheumatism (PR) although often considered as a benign disease can be severe and resistant to DMARDs in some patients. In these patients it can result in almost daily attacks, migrating from joint to joint resulting in poor quality of life. Rituximab has been proven to be effective in treatment of seropositive RA.

Objectives: To determine the efficacy and safety of Rituximab in patients with seropositive PR who had an inadequate response to CsDMARDs

Methods: PR was diagnosed based on criteria proposed by Hannonen P et al. Seropositive (ACPA±RF positivity) PR patients who had active disease despite being treated with two Cs DMARDs for >3 months, were treated with Rituximab. Active disease was defined as >4 attacks per month requiring intake of NSAIDS. All the patients were started on 500mg of rituximab after baseline work up. If complete control of palindromic attacks was not achieved and B cells were detectable in the peripheral blood by flow cytometry another 500 mg infusion was given after 2 weeks. Patients were continued on maximum tolerable dose of DMARDS. Patients were given repeat infusion of Rituximab once the patient developed clinical relapses as evidenced by recurrence of palindromic attacks.

Results: Twenty three patients with a mean age of 44.60±13.51 yrs and mean disease duration of 5.47±3.25 yrs were included. All patients were positive for ACPA while 17 patients were positive for RF. These patients were on a background of minimum of 2 DMARDs. Despite the maximum tolerable dose of DMARDs they had mean attack rate of 5.30±2.38 attacks per month. During a mean follow up of 14.17±8.62 months seven patients required two infusions and three patients required three infusions. Of the 33 infusions 500 mg was effective in controlling the attacks majority (88%) of the times. Seven patients required another 500 mg infusion after 2 weeks as initial 500 mg dose failed to achieve complete control of disease and B cell were not depleted in the peripheral blood. At one month follow up all patients achieved complete control of disease. Remission lasted for 10.33±5.75 months. When symptoms recurred patients were treated with rituximab again and all regained complete control of the symptoms. None of the patients evolved into RA during the study period. No serious adverse events were observed. Five patients experienced minor allergic reactions during infusion which were managed according to the standard protocol.

Conclusions: This case series indicates in patients of PR resistant to Cs DMARDs rituximab not only achieves disease control but also prevents progression to RA. To best of our knowledge this is the first report regarding efficacy of rituximab in PR. Although it needs to be proved in a larger blinded RCT this early data indicates that Rituximab may be a therapeutic option to prevent development of RA in seropositive patients.

References:

[1] Hannonen P, Möttönen T, Oka M. Palindromic rheumatism. A clinical surveyof sixty patients. Scand J Rheumatol. 1987;16(6):413–420.

[2] Sanmarti R, Cañete JD, Salvador G. Palindromic rheumatism and other relapsing arthritis. Best Pract Res ClinRheumatol. 2004;18(5):647–661.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5723

THU0576 THERAPEUTIC OPTIONS FOR PATIENTS WITH RARE RHEUMATIC DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS

T.T.A. Bender[1], M. Mücke[1,2,3], J. Leyens[1], C. Stieber[1,4], D. Kravchenko[5], M.F. Seidel[6,7]. *[1]Center for Rare Diseases Bonn (ZSEB); [2]Institute of General Practice and Family Medicine; [3]Department of Palliative Medicine; [4]Institute of Human Genetics; [5]University Hospital Bonn, Bonn, Germany; [6]Department of Oncology, Hematology and Rheumatology, University Hospital Bonn, Bonn, Germany; [7]Schmerzklinik Basel, Basel, Switzerland*

Background: Rare rheumatic diseases are challenging for both patients and clinicians. This problem is further propelled by the scarce number of approved treatment regimens. Therapy is often limited to immunosuppression with corticosteroids or off-label use of drugs for common rheumatic diseases.

Objectives: We have recently described a set of 82 classified rare diseases in rheumatology [1]. In this systematic review, we analysed the evidence for therapeutic regimens from randomized clinical trials of rare rheumatic diseases.

Methods: For this systematic review and meta-analysis, we searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, PUBMED and SCOPUS, up to 20th of October 2016. To validate the search strategy, we selected sentinel references.

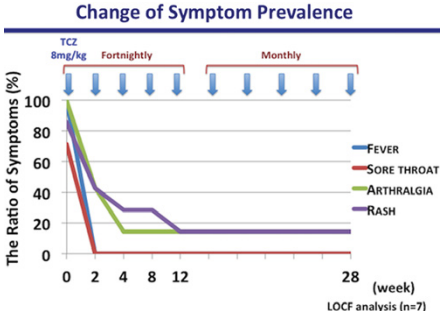
We included randomized controlled trials regarding rare rheumatic diseases and put a focus on pharmacological treatment compared with placebo, application of

two drugs, or standard therapy. The term "rare" was defined by the European Union as a condition that occurs in no more than 1 in 2,000 individuals.
Two review authors independently assessed trial quality and extracted the data. We screened the search results and included studies if they met the selection criteria. If we identified two or more trials that investigated the same rare disease and used the same assessment tools we performed a meta-analysis.
Results: 135 studies were screened, of which 34 met the inclusion criteria. In total, we analysed data on 11 different orphan diseases, encompassing 2,324 participants. There was a high degree of statistical and clinical heterogeneity in these trials. Several sources of potential bias were identified in the included studies, for example, a lack of description of the blinding methods and allocation concealment, as well as the small size of the study populations. We included studies such as rituximab against cyclophosphamide in ANCA-associated vasculitis. These studies demonstrated a non-inferiority of rituximab. The meta-analysis resulted a combined odds ratio (OR) of 1.42 in favour of rituximab (95% CI). Further meta-analyses were possible for another 22 studies involving, among others, Behçet's disease, systemic sclerosis, cryopyrin-associated periodic syndromes, and giant cell arteritis. Compounds studied were immunosuppressants like corticosteroids, methotrexate and azathioprine, or biologicals such as rilonacept, infliximab, and canakinumab.
Conclusions: A high degree of evidence is hampered by the limited number of study participants in each trial. On the other hand, diseases such as systemic sclerosis, ANCA-associated vasculitides, or Behçet's disease had more high quality trials available. The amount of data for most other rare disease remains unsatisfactory.
References:
[1] Leyens J, Stieber C, Bender TTA, Mücke M, Seidel MF. (2016) Classification of rare diseases in rheumatology demonstrates a combined prevalence double to the prevalence of ankylosing spondylitis. Ann. Rheum. Dis. 75(Suppl2): 618.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2946

THU0577 TOCILIZUMAB MONOTHERAPY FOR ADULT ONSET STILL'S DISEASE – RESULTS OF 52-WEEK TREATMENT OF A PROSPECTIVE, SINGLE-CENTER, SINGLE-ARM, OPEN TRIAL

T. Kondo, Y. Okada, A. Shibata, K. Chino, T. Kurasawa, A. Okuyama, H. Takei, K. Amano. *Department of Rheumatology and Clinical Immunology, Saitama Medical Center, Saitama Medical University, Kawagoe, Saitama, Japan*

Background: Adult-onset Still's disease (AOSD) is a systemic inflammatory disease of unknown etiology. Corticosteroids still provide mainstay AOSD therapy despite various adverse effects. Recently, AOSD patients have been successfully treated with anti-cytokine therapies such as with TNF-α blocking agents, an IL-1 receptor antagonist, and an anti-IL-6 receptor monoclonal antibody. Among these case reports, TCZ seems to be highly effective for treating patients refractory to TNF antagonists and IL-1 antagonist.
Objectives: To assess the efficacy and safety of tocilizumab (TCZ) monotherapy for the induction therapy of adult onset Still's disease (AOSD) in a prospective single-arm, single-center, cohort, pilot study.
Methods: Seven AOSD patients (male 2, female 5) who had agreed with our prospective trial since April 2010 till May 2015 were enrolled. Our study protocol is that patients received 8 mg/kg of intravenous TCZ fortnightly for the first two months (five courses), then monthly for the next 5 months and after that they stop TCZ therapy and we monitor symptoms about AOSD relapses. In this report, we evaluated the efficacy and safety in 52 week. Efficacy was evaluated by serum markers (WBC, CRP and serum ferritin), clinical symptoms and ratio of patients who required additional therapy, and safety was evaluated by adverse events for 52 week.
Results: The mean age was 41.4. The ratio of fever, arthralgia, rash and sore throat are 100% (n=7/7), 100% (n=7/7), 85.7% (n=6/7) and 71.4% (n=5/7) respectively. LOCF analysis revealed that WBC, CRP and serum ferritin level decreased significantly from 14757±4667/μl to 6985±2903/μl, from 13.4±7.1mg/dl to 0.3±0.6mg/dl and from 6927±5376ng/ml to 2416±5589ng/ml at month 7 (TCZ final infusion) respectively (each, $P<0.01$). The improvement rate of fever, arthralgia and eruption were 100% (n=7/7), 85.7% (n=6/7) and 85.7% (n=6/7) respectively at month 7. One patient couldn't continue TCZ therapies because of lack of efficacy (14.3%, n=1) and required additional therapy (prednisolone) at week 2. Another patient also abandoned this trial due to adverse event (14.3%, n=1, urinary tract infection). The other 5 patients could complete the 7-month course of the study and had no symptoms at month 7. Four of five patients had no flare-up signs until month 5 after stopping TCZ. One patient had relapse symptoms such as rash and arthralgia and increased serum level of CRP and serum ferritin at month 2 after final TCZ infusion. There were no serious adverse events during the course of the trial.



Conclusions: TCZ monotherapy can be an alternative treatment strategy for AOSD in some patients.
References:
[1] Sakai R, et al.:Clin Rheumatol. 2012 Mar;31(3):569–74.
[2] Ortiz-Sanjuán F et al.: Arthritis Rheumatol. 2014 Jun;66(6):1659–65.
Disclosure of Interest: T. Kondo: None declared, Y. Okada: None declared, A. Shibata: None declared, K. Chino: None declared, T. Kurasawa: None declared, A. Okuyama: None declared, H. Takei: None declared, K. Amano Grant/research support from: Chugai Pharmaceutical Co.Ltd.
DOI: 10.1136/annrheumdis-2017-eular.4922

THU0578 SPECTRUM OF THE DISEASES WITH ORBITAL INVOLVEMENT IN RHEUMATOLOGY: SINGLE-CENTER STUDY

V. Vasilyev [1], V. Gorodetskiy [1], T. Safonova [2], N. Probatova [3], N. Kokosadze [3], A. Pavlovskaya [3], A. Kovrigina [4], I. Gaiduk [5]. *[1] Nasonova Research Institute of Rheumatology; [2] Research Institute of Ophthalmic diseases; [3] N.N. Blochin Russian Cancer Research Center; [4] Hematology Research Center; [5] A.I. Evdokimov Moscow State Dental University, Moscow, Russian Federation*

Background: It is assumed that in ophthalmological clinical practice lymphoproliferative disorders in patients with affection of different orbital organs and tissues constitute 25–55% and 21% of patients have IgG4-related ophthalmic disease [1,2].
Objectives: To evaluate the most common conditions affecting the orbit in rheumatologic clinical practice.
Methods: During 2004 – 2016 years 138 patients (male – 33, female - 105) with eyelid edema and/or tumefactive lesions in the orbit were examined in Nasonova Research Institute of Rheumatology. In all patients full clinical, ophthalmological, serological (rheumatoid factor, C-reactive protein, IgG, IgG4, IgM, IgA, ANA, anti-Ro/La, C3/C4 complement) examination was carried. In all cases diagnosis was verified pathomorphologicaly with immunohystochemical staining (anti-CD 138, CD 68, IgG, IgG4, κ-chain, λ-chain). Diagnosis was established on the basis of pathomorphological examination of different tissues: orbit – 79 patients, parotid salivary gland – 40, submandibular salivary gland – 14, nasal – 4, lymph nodes – 3 and other – 6. In 79 cases (54%) the diagnosis was established on the results of orbital biopsy.
Results: Different non-neoplastic diseases were diagnosed in 108 patients (78.5%) and 30 had different conditions of hematological spectrum, including malignant conditions in 25 (18.2%) patients (see table 1). Some patients at baseline had simultaneous involvement of the major salivary glands (23 patients with IgG4-related disease, 35 with sarcoidosis, 12 with non-Hodgkin lymphomas and 2 with AL-amyloidosis). The most rare conditions affecting the orbit were Cogan's syndrome, relapsing polychondritis, Erdheim-Chester disease, NK/T-cell nasal lymphoma and calcifying aponeurotic fibroma.

Table 1. Spectrum of the diseases with orbital involvement in rheumatologic practice (n=138)

	N, pts	N, %		N, pts	N, %
Non-neoplastic conditions	**108**	**78.5**	**Hematologic conditions**	**30**	**21.5**
• IgG4-related disease	48	35.0	• non-Hodgkin lymphomas	20	14.5
• Granulematous lesions (sarcoidosis, granulematosis with polyangiitis, necrosing sarcoidal granulematosis)	41	29	• Erdheim-Chester disease	1	0.7
• Autoimmune dacryoadenitis (non-differentiated)	7	5	• AL-amyloidosis	3	2.1
• Idiopathic orbital inflammation	7	5	• NK/T-cell nasal lymphoma	1	0.7
• Endocrin ophthalmopathy	2	1.4	• Histiocytosis	4	2.9
• Cogan's syndrome	1	0.7	• Calcifying aponeurotic fibroma	1	0.7
• Relapsing polychondritis	1	0.7			

Conclusions: In rheumatologic practice in 78.5% of patients with orbital involvement different non-neoplastic conditions are diagnosed: IgG4-related ophthalmic disease (35.0%), granulematous lesions (29%). The most common hematological disorders in rheumatologic clinic are non-Hodgkin lymphomas (17.5%) and histiocytosis (3.5%).
References:
[1] Japanese study group of IgG4-related ophthalmic desease. A prevalence

study 0f IgG4-related ophthalmic disease in Japan.JpnJOphthalmol.2013;57: 573–579.
[2] Shields JA et al. Survey of 1264 patients with orbital tumors and simulating lesions: the 2002 Montgomery Lecture, part I. Ophthalmology.2004;111: 997–1008.
[3] Goto H et al. Diagnostic criteria for IgG4-related ophthalmic disease. JpnJOphthalmol.2015;59:1–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4309

THU0579 HYPOCOMPLEMENTEMIA IS RELATED TO ELEVATED SERUM LEVELS OF IGG SUBCLASSES OTHER THAN IGG4 IN IGG4-RELATED KIDNEY DISEASE

Y. Fujisawa, I. Mizushima, S. Tsuge, S. Hara, F. Suzuki, K. Ito, H. Fuji, K. Yamada, M. Kawano. *Division of Rheumatology, Department of Cardiovascular and Internal Medicine, Kanazawa City, Japan*

Background: IgG4-related kidney disease (IgG4-RKD) is a comprehensive term for renal lesions associated with IgG4-related disease [1]. IgG4-RKD is frequently complicated by hypocomplementemia [1, 2, 3], but its clinical significance and mechanisms have not been clarified.
Objectives: This study aimed to investigate clinical features of IgG4-RKD patients with hypocomplementemia compared with those without it, leading to clarification of the clinical significance and mechanisms of hypocomplementemia.
Methods: We extracted 25 patients with IgG4-RKD between September 2005 and December 2016 in our hospital. Based on the presence/absence of hypocomplementemia at diagnosis, we divided them into a hypocomplementemia group (n=11) and normal complement group (n=14), and retrospectively analyzed various clinical features (age, sex, serum IgG levels, serum IgG4 levels, gaps between serum IgG and IgG4 level, ratio of serum IgG to serum IgG4, serum IgG subclasses, serum IgE levels, serum creatinine levels, urinary protein and urinary occult blood, urinary β2-microglobulin, urinary N-acetyl-β-D-glucosaminidase, initial dose of prednisolone, serum IL-2R levels, multiple organ lesion) during the clinical course in the two groups.
Results: The patients comprised 18 men and 7 women with an average age of 67.5 years (range, 44 to 81 years). Serum IgG levels (3971±729 mg/dL vs. 2157±598 mg/dL; $p<0.001$), gaps between serum IgG and IgG4 level (2992±770 mg/dL vs. 1482±444 mg/dL; $p<0.001$), serum IgG1 levels (2043±1025 mg/dL vs. 891±209 mg/dL; p=0.017), and the number of involved organs (4.1±1.1 vs 2.9±1.1; p=0.018) were significantly different between the two groups, while serum IgG4 levels (979±477 mg/dL vs. 791±575 mg/dL; p=0.298) and serum creatinine levels (1.96±1.89 mg/dL vs. 1.09±0.48 mg/dL; p=0.298) were not. At relapse of renal lesions, although both groups showed serum IgG4 re-elevation, the hypocomplementemia group showed exacerbation of hypocomplementemia and re-expansion of gaps between serum IgG and IgG4 level, while the normal complement group did not.
Conclusions: Hypocomplementemia may be associated with multiple organ involvement and elevation of IgG subclasses other than IgG4 including IgG1 in IgG4-RKD. In patients who initially show hypocomplementemia, a decline in serum complement levels implies renal lesion relapse.
References:
[1] Kawano M et al. Proposal for diagnostic criteria for IgG4-related kidney disease. Clin Exp Nephrol. 2011 Oct;15(5):615–26.
[2] Saeki T et al. Clinicopathological characteristics of patients with IgG4-related tubulointerstitial nephritis. Kidney Int. 2010 Nov;78(10):1016–23.
[3] Raissian Y et al. Diagnosis of IgG4-related tubulointerstitial nephritis. J Am Soc Nephrol. 2011 Jul;22(7):1343–52.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4257

THURSDAY, 15 JUNE 2017

Education

THU0580 WHAT ARE THE PATIENTS' ISSUES AND NEEDS RELATED TO THEIR BIOLOGICS (BDMARDS) AND METHOTREXATE (MTX) TREATMENT IN DAILY LIFE: A QUANTITATIVE CROSS-SECTIONAL SURVEY AMONG 344 PATIENTS TO DEVELOP AN EDUCATIONAL SMARTPHONE APP

C. Beauvais[1], S. Tropé[2], A. Lafourcade[3], D. Carnet[4], L. Grange[5], L. Carton[6], D. Lafarge[7], G. Montagu[8], T. Pham[9], F. Tubach[10], J. Sellam[11] on behalf of Therapeutic education section of the French Society of Rheumatology and Club Rhumatismes Inflammation. *[1]Rheumatology, Saint Antoine Hospital. APHP, Paris; [2]Association ANDAR, Montpellier; [3]Biostatistics, AP-HP Hôpital Pitié-Salpétrière, Paris; [4]ANDAR, Montpellier; [5]Rheumatology, Echirolles; [6]Association AFLAR; [7]Association AFS; [8]Unknowns, Strategic and Innovation Consulting, Paris; [9]Rheumatology, Hôpital Sainte-Marguerite, AP-HM, Marseille; [10]Biostatistics, Public Health, and Medical Information, AP-HP Hôpital Pitié-Salpétrière; [11]Reumatology, AP-HP St-Antoine, Univ Paris 06, Paris, France*

Background: MTX and bDMARDs are the core treatments of chronic inflammatory arthritis (IA). We lack information on the patients' problems and needs in daily life, particularly on safety issues.
Objectives: 1-collect the most frequent issues 2-explore the patients' perceptions on a dedicated smartphone application (SP App) 3) determine the profile of the patients interested.
Methods: The survey was conducted on line. The questionnaire was designed by rheumatologists, methodologists, anthropologists, members of patients association (AP) and included 1-a non-exhaustive list of potential issues in daily life (fever, vaccines, ...) and practical aspects 2-a list of potential use of the App 3-free opinions 4- Two self-administrated questionnaire to test patients' knowledge on bDMARDs [1] and MTX [2].
Results: The survey was carried out from June to August 2016 on the websites of the PA. Non-associative patients were recruited by 3 rheumatologists who provided the Internet link. 344 patients responded, 331 analyzed, 83% female, 50% had rheumatoid arthritis, 40% had spondyloarthritis, mean age 53 years, 60% were AP; 67% were treated with MTX, 70% had bDMARDs, 34% had MTX-bDMARDs combotherapy.
66% of patients reported problems; 67% had needed help or advice. The main issues were infections (27%), vaccines (13%), surgery (10%), dental care (7%), self-administration (6%), conservation/travelling (9%) and skipped doses (5%).
Among the 76% patients who have a SP, 80% use Apps and 32% Apps for their health. Among users, 87% patients would find an App useful to manage their treatment (36% rather agree and 51% strongly agree), 82% for symptoms requiring to stop their treatment, 93% for situations related to safety, 80% as a reminder of their treatment, 80% to know what to do in case of a skipped dose, 77% to have a safety checklist before treatment administration, 66% to recall the modalities of self-injections. Patients interested in the App are younger ($p<0.05$) non-associative ($p<0.05$) and live in medium-sized cities ($p<0.01$). No correlation was found with other sociodemographic characteristics, level of education, type/duration of arthritis or knowledge.
Conclusions: Two-third of patients with arthritis face issues related to their treatment especially in case of infections, vaccination, surgery and travelling. A dedicated App is considered useful by 87% patients who already have a SP. The potential use of the App may improve safety, adherence and self-management in daily life.
References:
[1] Gossec L et coll. Joint Bone Spine. 2013; Fayet F et coll J Clin Nurs. 2016.
Acknowledgements: Grant: French Society of Rheumatology with the institutional funding by Biogen, Nordic Pharma, Roche.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5549

THU0581 WHAT WE SEE, WHAT WE LEARN, AND THE PREVALENCE OF RHEUMATIC DISEASES IN OUR POPULATION: A DIAGNOSIS CORRELATION STUDY

D. Vega-Morales[1], J.A. Esquivel-Valerio[1], R. Ortiz-Lopez[2], A.C. Arana-Guajardo[1], M.A. Garza-Elizondo[1]. *[1]Rheumatology Service; [2]Rheumatology, Hospital Universitario Dr. José Eleuterio González, Monterrey, Mexico*

Background: The postgraduate program in rheumatology aims learning of musculoskeletal and autoimmune disorders. In México, objectively-structured clinical examination (OSCE) is applied in postgraduate certification processes by the Mexican Board of Rheumatology annually [1]. Peláez-Ballestas et al. described an epidemiological study (COPCORD, Community Oriented Program for the Control of Rheumatic Diseases) of 19,213 individuals in 5 regions in our country where they found a prevalence of musculoskeletal pain in 25.5%, osteoarthritis in 10.5%, back pain in 5.8%, rheumatic regional pain syndromes in 3.8%, rheumatoid arthritis (RA) in 1.6%, and fibromyalgia in 0.7% [2].
Objectives: The aim of the study is to describe the student training in rheumatic diseases and correlate them with OSCE assessment and the prevalence of rheumatic diseases in our population.
Methods: An observational and analytical study was made between March 2014 to March 2015 in a single rheumatology training center at University Hospital. Student training was defined according to the times they evaluated patients with a determined diagnosis, this information was obtained by medical records. We categorize OSCE questions according to the rheumatic diagnosis. Finally, the two results were compared with prevalence of the rheumatic diagnosis according to COPCORD, which were registered according a score pain >4. We made descriptive statistics and a Spearman's Rho to evaluate the correlations of the diagnosis frequencies by each category.
Results: We reviewed 6279 medical records, 854 (13.6%) were of first-time evaluation. We had 5,400 (86.4%) women, with a mean age of 47.9 (SD 15.45) years.
Descriptive statistics are in Table 1 and Figure 1, which included: medical consultations, OSCE assessment and a column with rheumatologic diagnosis according to COPCORD.
The Spearman correlation coefficients of the 32 different diagnoses were: student training vs OSCE 0.492 (p=0.004), student training vs COPCORD 0.597 (p=0.01) and OSCE vs COPCORD 0.624 (p=0.01).
Conclusions: Although the most common musculoskeletal disease in our community did not obtain the frequency observed by students or evaluated in

Table 1

	Resident		MRC		COPCORD	
	n	%	n	%	n	%
RA	1776	28,28	35	15,28	307	5,93
OA	1061	16,90	9	3,93	2017	38,98
SLE	800	12,74	27	11,79	13	0,25
Soft tissue	554	8,82	10	4,37	2230	43,10
FM	476	7,58	5	2,18	0	0,00
Sjögren S	357	5,69	7	3,06	0	0,00
Osteoporosis	307	4,89	5	2,18	0	0,00
SSc	170	2,71	11	4,80	4	0,08
APS	111	1,77	10	4,37	0	0,00
Spondyloarthritis	111	1,77	5	2,18	27	0,52
Miositis	99	1,58	10	4,37	0	0,00
Juvenile Arthritis	87	1,39	3	1,31	0	0,00
PsA	86	1,37	5	2,18	0	0,00
Vasculitis ANCA	79	1,26	5	2,18	0	0,00
Raynaud	61	0,97	5	2,18	0	0,00
Crystal arthropaties	58	0,92	15	6,55	576	11,13
Connective tissue	45	0,72	0	0,00	0	0,00

the OSCE, we observed a moderate correlation. We considered it is important to enhance the knowledge and improve the OSCE according to the most prevalent diseases to prepare the future rheumatologists.

References:
[1] Pascual Ramos V, et al. Reumatol Clin 2014; doi: 10.1016/j.reuma.2014.10.007.
[2] Peláez-Ballestas I, et al. J Rheumatol Suppl 2011;86:3–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3317

THU0582 2-YEAR ADHERENCE TO THE TREATMENT OF OSTEOPOROSIS FOLLOWING A THERAPEUTIC PATIENT EDUCATION PROGRAM

D. Poivret[1], C. Wilcke[2], V. Noirez[1], C. Goetz[1,3]. *[1]Chr Metz Thionville; [2]URPS Grand Est; [3]PARC, Chr Metz Thionville, Metz, France*

Background: The management of osteoporosis requires drug treatment and changes in lifestyle. Adherence to medication does not exceed 50% at one year. Changes in lifestyle are rarely explored. Therapeutic requires a relay to continue the follow-up over several years

Objectives: To improve the follow-up of the patient, we have created cooperation between the attending physician and the pharmacy pharmacist initiated by the patient himself

Methods: We proposed a therapeutic patient education for patients treated for osteoporosis to participate in two half-day ETP sessions a year apart. Educational objectives are: The treatment of osteoporosis requires at least 5 years of treatment, and must be associated with the absorption of three dairy products per day, maintaining physical activity and preventing falls. Each patient participating in a therapeutic education session receives a follow-up notebook containing six doctor questionnaires and six pharmacist questionnaires. The patient remains the owner of the notebook. We were able to study the results of the 2-year questionnaires for 72 patients included in 2013 and 2014.

Results: 53/72 patients continue their treatment at 2 years. 4 patients died, 1 had an atypical fracture of the femoral shaft, 6 stopped treatment due to dental treatment, 3 had contraindications to any anti-osteoporotic treatment, 1 decided to discontinue treatment due to d Multiple Sclerosis, 11 decided to leave the program. 3 patients were lost to follow-up, ie 14/72 patients of whom we no longer have any news. Of the 53 patients who continued treatment, 24 sent back a doctor and pharmacist questionnaire to 2 years. 4 doctors and 2 pharmacists refused to complete the questionnaires. The study of pharmacist questionnaires received at 2 years shows that 83% of patients continue to consume 3 dairy products per day compared to 73% at 6 months, 65% maintained physical activity, 17% improved it, 9% decreased. The ground balance was satisfactory for 78% of patients compared with 71% at 6 months. 71% never forget their treatment, compared with 69% at 6 months. 8% wanted to stop their treatment, stable figure compared to questionnaires received at 6 months. All patients knew what their treatment was for at one year and 96% met the conditions for taking the medication. 69% do not forget it at two years against 86% at one year, thanks to the intervention of the pharmacist. Only 6% wanted to stop the treatment at two years due to side effects, 17% to 1 year, but did not stop after consultation with the doctor and/or pharmacist.

During the two-year follow-up, all patients were phone called at least once by a secretary, mostly several times. The notebook is driven by the patient himself, many oh them report to the nurse that it give them an active role which afoord them to continue the treatment

Conclusions: 58% of the patients enrolled continue treatment at two years, 15% have stopped the treatment as a side effect. An active role given to the patient and a collaboration between physicians and pharmacists thus promote adherence to treatment and also changes in lifestyle

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1681

THU0583 EFFECT OF AN ONLINE EDUCATIONAL INTERVENTION IN THE KNOWLEDGE OF PATIENT REGISTRIES AND PATIENT-REPORTED OUTCOMES AMONG RHEUMATOLOGISTS

E. Jackson[1], E. McCardell[1], J.R. Curtis[2]. *[1]Medscape Education, New York; [2]Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, United States*

Background: Patient-reported outcomes (PROs) have evolved into an essential element in managing rheumatoid arthritis (RA), working in concert with physician-based tools to assess disease activity and health-related quality of life [1].

Objectives: A study was conducted to determine whether an online educational intervention could effectively address a knowledge gap and an underlying educational need in applying data from patient registries including PROs in the management of patients with RA.

Methods: An online educational intervention focusing on advances in RA patient registries was developed and made available online. The intervention consisted of a 30-minute video-based roundtable discussion between 3 experts in treatment of RA. The intended audience was rheumatologists who treat patients with RA. The educational impact was assessed by comparing participants' responses to 4 identical paired pre- and post-assessment questions. Data representing a statistical sampling of the overall learner population was collected from 5/29/2015 through 8/13/2015. Statistical analysis comprised a paired (within-physician) 2-tailed t-test comparing mean pre-intervention and post-intervention scores, McNemar's $\chi 2$ statistic for measuring changes in responses to individual. Cramer's *V* determined the overall effect of the intervention.

Results: Analysis of pre- versus post-activity responses by rheumatologists (n=36) demonstrated a significant improvement ($P<0.05$) in overall knowledge with a robust effect size ($V=0.339$). This activity resulted in increased knowledge surrounding several specific areas of RA management, such as drug safety, alternative means of collecting PRO data, and issues surrounding pregnancy in women with RA. The absolute percentage increases in correct individual responses to these topics (all $P<0.05$ except where noted), included:

- 33% increase (36% vs. 69%) in rheumatologists who recognized the results from pooled registries in Europe – 11 registries from 9 countries – regarding the safety of tumor necrosis factor-alpha inhibitor therapy,
- 28% increase (36% vs 64%) in rheumatologists who recognized that biosensor-based devices can provide passive data regarding patient outcomes,
- 14% increase (47% vs 61%, $P=.237$) in rheumatologists who identified the connected CORRONA-OTIS registries that provide information on patients with RA who become pregnant,
- 62% increase (19% vs 81%) in rheumatologists who identified that patient registry data can be used to support a risk mitigation strategy for prescribing a specific DMARD in patients who may become pregnant during therapy.

Conclusions: An online educational intervention was associated with significant improvement in knowledge levels of rheumatologists in several important aspects of RA management, including interpretation of data from patient registries and adverse effect profiles of approved therapies. Future directions for education include additional reinforcement regarding the roles for PROs in patient management, and assessing the impact of improved rheumatologists' knowledge on care delivery and patient outcomes.

References:
[1] van Tuyl LH, Michaud K. Patient-Reported Outcomes in Rheumatoid Arthritis. Rheum Dis Clin North Am. 2016 May;42(2):219–37. Epub 2016 Mar 17.

Acknowledgements: The educational intervention and outcomes measurement were funded through an independent educational grant from Bristol Myers Squibb.

Disclosure of Interest: E. Jackson: None declared, E. McCardell: None declared, J. Curtis Shareholder of: CORRONA; Amgen Inc.; AbbVie Inc.; Pfizer Inc; Bristol-Myers Squibb Company; Crescendo Biologics, Grant/research support from: Roche; Genentech, Inc.; UCB Pharma, Inc.; Janssen Pharmaceuticals, Inc., Consultant for: Roche; Genentech, Inc.; UCB Pharma, Inc.; Janssen Pharmaceuticals, Inc., Speakers bureau: CORRONA; Amgen Inc.; AbbVie Inc.; Pfizer Inc; Bristol-Myers Squibb Company; Crescendo Biologics

DOI: 10.1136/annrheumdis-2017-eular.6284

THU0584 FIVE YEARS OF EXPERIENCE WITH THE LUPUS ACADEMY: AN EFFECTIVE MODEL FOR BUILDING A ROBUST COMMUNITY OF PRACTICE FOR GEOGRAPHICALLY DIVERSE LEARNERS

R. Cervera[1], R.A. Furie[2], Z. Amoura[3], A. Jacobson[4], E. Pozniak[4]. *[1]Hospital Clinic, Barcelona, Spain; [2]Hofstra North Shore-LIJ School of Medicine, New York, United States; [3]Pitie-salpetriere Hospital, Paris, France; [4]Siyemi Learning, Manchester, United Kingdom*

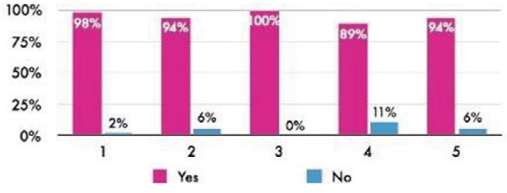
Background: Systemic lupus erythematosus (SLE) is a complex yet low prevalence disease. Without a community of lupus specialists to establish consensus and guide best practices, rheumatologists have limited opportunities to develop skills and maintain competence in SLE care.

Objectives: The objectives of this initiative were to 1) create an independent community of physicians interested in the pathogenesis, diagnosis, and management of patients with SLE and related conditions; 2) share insights and practical guidance for implementing evidence-based care; 3) develop needs-driven contin-

uing medical education (CME) relevant to different levels of clinical expertise; 4) promote collaboration models with publishers to create space for dialogue and community building; and 5) involve patient advocacy groups to steer physician education and incorporate the patient voice into educational activities.
Methods: The Lupus Academy (http://lupus-academy.org) was established in 2011 as an independent CME initiative led by a Steering Committee of international experts in SLE.[1] Educational activities are designed around unmet clinical needs identified by the Steering Committee, learner survey data, and feedback from patient advocacy groups (including Lupus Europe).
Results: As of February 2017, the Lupus Academy has grown to a global community of >2,500 committed learners with an interest in SLE. The Steering Committee has guided the development and delivery of 5 2.5-day annual meetings; 4 1-day regional meetings; a meeting toolkit for learner-advocates to host meetings in their home regions; and 3 e-learning courses, with 2 additional courses in production. The 5th Annual Meeting of the Lupus Academy (6–8 May 2016) hosted 101 attendees from Europe, North and South America, and Asia. Learners reported that the learning objectives of the meeting were met (Figure). An assessment of educational effectiveness demonstrated improvements in clinical knowledge and competence (Moore's Outcomes Levels 3/4) as a result of meeting participation: 67% of learners reported a commitment to implementing changes in clinical practice, 11% reported that the educational content reinforced their current practice, and 20% reported a willingness to modify their current practice with additional training.
The most recent regional meeting, the Lupus Academy Middle East Summit Conference (9–10 December 2016), hosted 153 attendees from 13 countries representing diverse specialities: rheumatology (53%), internal medicine (13%), nephrology (11%), clinical immunology (5%), and other (18%). The majority of learners agreed or strongly agreed that the meeting provided an effective platform for the discussion of new ideas in SLE (96%) and challenged the current thinking around lupus care (96%).

Having attended this meeting, I am better able to:

1. Apply novel developments in scientific research around SLE in their clinical practice
2. Implement optimal diagnostic methods and optimal disease management of refractory lupus nephritis patients and of those patients with both SLE and rheumatoid arthritis
3. Increase competence in identifying difficult clinical cases from the broad spectrum of lupus patients and effectively manage them - including patients displaying manifestations involving lungs, GI, liver and CNS, as well as paediatric and pregnant patients
4. Implement new therapeutic options inherited from other therapeutic specialities
5. Apply learnings from other disease areas to achieve optimal treatments outcomes in patients with SLE



Conclusions: The Lupus Academy serves as an effective model for building a consortium-led, evidence-based educational resource and community of practice for rheumatologists, other physicians with an interest in SLE, and patient advocacy groups.
References:
[1] Ball J, Cervera R, Elzebroek N, Levy RA, Pozniak E. Developing an appropriately supported CME-accredited programme in Europe. J Euro CME. 2013;2:37–44.
Acknowledgements: Lupus Academy Steering Committee (http://lupus-academy.org/home/lupus-academy-steering-committee/).
Disclosure of Interest: R. Cervera Consultant for: GSK, UCB, AstraZeneca, Pfizer, Celgene, R. Furie Grant/research support from: AstraZeneca, BiogenIdec, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, GlaxoSmithKline, Janssen, Mallinckrodt Pharmaceuticals, Medimmune, Pfizer, Sanofi, Takeda, UCB, Consultant for: Anthera, AstraZeneca, Baxalta, BiogenIdec, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Eisai, EMD Merck, Estrela (Janssen), GlaxoSmithKline, Janssen, Mallinckrodt Pharmaceuticals, Medimmune, Novartis, Pfizer, Sanofi, UCB, Z. Amoura Grant/research support from: GSK, Amgen, BMS, Actelion, Roche, Teva, Lilly, Consultant for: GSK, Amgen, BMS, Lilly, A. Jacobson: None declared, E. Pozniak: None declared
DOI: 10.1136/annrheumdis-2017-eular.2073

THU0585 THE PATIENT'S UNIVERSITY - AN INNOVATIVE CONCEPT IN THE EDUCATION OF PATIENTS WITH RHEUMATOID ARTHRITIS

F. Rodriguez[1], L. Villarreal[2], P. Santos-Moreno[3], M. Cabrera[4], D. Buitrago-Garcia[5], C. Caicedo[6]. *[1]Patient Program; [2]Psychology and processes; [3]Rheumatology; [4]Engineer and processes; [5]Epidemiology, Biomab, Center for Rheumatoid Arthritis, Bogota; [6]Public Health, Universidad Nacional de Colombia, Bogota, Colombia*

Background: Rheumatoid arthritis (RA) is a chronic, inflammatory autoimmune disease of unknown etiology, it is a long term condition that causes pain, disability and affects the quality of life (1). In another countries has been demonstrated how patient education can empower the individual giving as a result a better decision making between the practitioner and patient in order to obtain better health care outcomes compared to patients that are not involved in educational activities (1).
Objectives: The objective of this work is to show how through a progressive program of patient education we reach the concept of the "expert patient" and the "patients' university".
Methods: We performed a systematic review of the literature in global and regional databases (Pubmed, Medline, Scopus, Lilacs), in order to search for information on this research question-hypothesis. Subsequently and under a Delphi-modified methodology and consensus of experts lay the conceptual bases on this particular subject – patient's education in rheumatic disease. As a result of the above was defined a proposal for the constitution and development of the program of patient's education in a RA specialized center under the concept of the "expert patient" (EP) and the "patients' university"(PU).
Results: From conceptual point of view specific themes regarding patient's education were developed by a coordinator who, after a review of the literature, presented a specific proposal on the particular topic that was discussed with the panel members and then voted on and finally implemented within the EP y PU concepts. In a specialized RA center in Bogotá Colombia during 2016 we started a patient and caregiver oriented program to support the clinical treatment in patients with RA. The structure of the program was an educational-recreational strategy where we integrated health education (disease activity, pharmacovigilance, psychology and nutrition) and recreational activities such as crafts, yoga, aerobics and dance lessons with a periodicity of two times per week. We called the program "Gest-Art". As a result of this pilot program we obtained a positive impact and perception among patients and care takers; we had the participation of 600 people during the whole year. The next phase is to develop a step-by-step program to initially train and then specialize patient focus groups (expert patient); and later develop a model of continuous improvement (updating) that we will call the university of patients.
Conclusions: From this experience we can conclude that the implementation of this educational program opened the opportunity to empower and motivate our patients and caregivers to be actively participative with the disease management and health care, also the program has been a space for the patients to share their experiences and to propose new strategies to improve the program.
References:
[1] Prothero L, Georgopoulou S, de Souza S. Patient involvement in the development of a handbook for moderate rheumatoid arthritis. 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6170

THU0586 SAFETY OF BIOLOGICS AND CONVENTIONAL DMARDS: AN ETHNOGRAPHIC STUDY INVESTIGATING PATIENTS' DECISIONS AND PRACTICES TO DEVELOP AN EDUCATIONAL SMARTPHONE APP

G. Montagu[1], C. Beauvais[2], F. Madrisotti[1], T. Pham[3], S. Tropé[4], F. Tubach[5], J. Sellam[6] on behalf of Therapeutic education section of the French Society of Rheumatology and Club Rhumatismes Inflammation. *[1]Sociology and research, Unknowns, Strategic and Innovation Consulting; [2]Rheumatology, AP-HP St-Antoine hospital, Paris; [3]Rheumatology, Hôpital Sainte-Marguerite, AP-HM, Marseille; [4]Association Nationale de Défense contre L'Arthrite Rhumatoïde (ANDAR), ANDAR; [5]Biostatistics, Public Health, and Medical Information, AP-HP Hôpital Pitié-Salpétrière; [6]Rheumatology, AP-HP St-Antoine, Univ Paris 06, Paris, France*

Background: Safety and adherence to DMARDs are critical for patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA). Few digital tools exist to help patients on these issues.
Objectives: We aimed to decipher the mechanisms of patients' decisions and practices with their DMARDs to develop an educational smartphone application (SP App).
Methods: An ethnographic study was designed by 3 rheumatologists, 1 methodologist, patient associations and by 2 anthropologists who conducted the interviews. The study involved 21 patients (enough to reach saturation), recruited by diversity of clinical and sociological profiles. The panel included 16 women and 5 men, median age 46 years-old (extremes 26–70), 12 with RA and 9 with SpA (median disease duration 13 years, extremes 2–38). Nine patients were treated by biologic DMARDs monotherapy, 7 by conventional DMARDs monotherapy and 5 by bDMARD-cDMARD combotherapy. Interviews were conducted using in-depth semi directive and biographic methods. The interview guide was constructed around 3 fields: 1 the organization of the patients' everyday life with their disease, 2 treatment practices, 3 the impact of arthritis on their social and professional activities and relationships. Interviews were recorded and transcribed for analysis.
Results: Patients play an active role in the management of their disease. They have to learn to live with it in order to control its impact and course. This learning progressively occurs throughout a non-linear 4-stages career: 1) from 1st symptoms to diagnosis, 2) search for the right treatment and the right dosage, 3) stabilization of the disease and the treatment, 4) dealing with a complication or an unexpected event. Back and forth between stages 2, 3 and 4 are frequent.
This learning implies a partnership-based doctor-patient relationship, and the development of specific skills around safety: dealing with health care system

(i.e. knowing which healthcare professionals they need), dealing with information (i.e. knowing how to identify relevant sources). Patients do lots of experiments (changing their DMARD dosage on their own initiative, trying alternative medicine or food exclusions...) and ritualizing their DMARDs administration. Such rituals represent a reflexive moment for the patients dedicated to themselves and their disease.

During the stage of stabilized disease and treatment, rituals tend to improve observance but also increase safety problems because of habits, over-confidence, and forgetting of risky situations. Patients renew interest about safety concerns in case of an unexpected complication.

Conclusions: Starting from the patients' point of view, this ethnographic study emphasizes a tension between observance and safety. Practices by which patients appropriate their treatment create habits that improve observance but also increase safety problems. It seems necessary to support the patients in updating their safety skills. A SP App could contribute to this goal only if its use finds its place in the patients' ritual.

Acknowledgements: Grant: French Society of Rheumatology with institutional funding by Biogen, Nordic Pharma, Roche

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5368

THU0587 PUBLIC AWARENESS OF RHEUMATIC DISEASES IN CYPRUS - NEED FOR IMPROVEMENT

J. Joseph[1,2], I. Armata[1], A. Antoniadou[1], P. Maini[1]. [1]*St. George's University of London Programme, University of Nicosia Medical School;* [2]*Rheumatology, Aretaeion Hospital, Nicosia, Cyprus*

Background: Public awareness regarding rheumatic diseases is a constant aim of patient societies and health care professionals in rheumatology. A high level of awareness will help identification and early treatment, it would avoid unnecessary investigations and costs and more importantly, it would assist functioning of patients with such conditions in society, with the understanding and support they deserve.

Objectives: The aim was to study public awareness regarding rheumatic conditions. Specifically, what constitutes a rheumatic condition, which doctor deals with these, what is their frequency and what age groups are affected.

Methods: During the rheumatic diseases awareness week in May 2016, doctors, medical students and members of the Cyprus League against Rheumatism, walked the streets of major cities and invited passers-by to answer a few simple questions. This was optional and at the end of the questions, information was provided, based on the answers and on any additional queries raised by people.

Results: 400 people provided answers. There were slightly more women than men and ages ranged from 13 to 86 years. Almost 50% did not know what a rheumatologist does. Only 11% could name 3 rheumatic conditions. Although the majority stated that rheumatic diseases occur in the elderly, 2/3 were unaware that they can affect children. Most people correctly identified which specialists should deal with asthma or eczema, but a huge majority did not know who should be consulted for back pain, tendon problems or osteoporosis. Although 75% had heard of rheumatoid and osteoarthritis, 75% of people had never heard of ankylosing spondylitis or fibromyalgia and only about half had heard of psoriatic arthritis or lupus. Most people stated that rheumatic conditions in general, affect 10–20% of people.

Conclusions: There was significant lack of awareness as to what rheumatologists do, what constitutes a rheumatic disease, the fact that it affects young people and the link between rheumatology and back pain, tendon problems and osteoporosis. All these points need to be included in public education. Of the major rheumatic diseases, the next awareness campaign needs to include ankylosing spondylitis, fibromyalgia, psoriatic arthritis and lupus.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2172

THU0588 ARE RHEUMATOID ARTHRITIS PATIENTS WILLING TO USE AN E-HEALTH INTERACTIVE SELF-ASSESSMENT WEBSITE? ANALYSES OF 159 PATIENTS FROM A RANDOMISED CONTROLLED TRIAL OVER 12 MONTHS

L. Gossec[1], A. Cantagrel[1], M. Soubrier[1], J.M. Joubert[2], W. Czarlewski[2], B. Combe[1], J.M. Berthelot[1], D. Wendling[1], E. Dernis[1], L. Grange[1], C. Beauvais[1], A. Perdriger[1], H. Nataf[1], M. Dougados[1], H. Servy[1]. [1]*CarNET Study Group, Paris;* [2]*UCB Pharma, Colombes, France*

Background: Interactive, online electronic (e)-health services with patient-reported outcome measure (PROM)-based instruments may be helpful for patients (pts). Sanoïa is a secure, independent e- and mobile (m)-health platform developed to allow pt self-assessment, storage of questions to ask physicians, and self-monitoring of disease status. The platform offers a dedicated set of scores, PROMs and information about different diseases, including rheumatoid arthritis (RA).

Objectives: To characterise pts with RA who chose to access e-health services regularly over a 12-month (mo) period.

Methods: Post-hoc analysis of CarNET (NCT02200068): a French, multicentre, 12-mo randomised controlled trial. Pts with RA were randomised to: access to Sanoïa (30-min training via the telephone with no further incentive to access the platform) or usual care (normal internet use without access to Sanoïa). The Sanoïa group pts used a home-based e-Case Report Form to record frequency of Sanoïa access, satisfaction with the platform (0–10 scale; 0=completely satisfied, 10=not satisfied), and barriers to use (from a pre-specified list). Baseline pt characteristics associated with more frequent use (above the median) were analysed by univariate and multivariate logistic regression.

Results: 159 RA pts were randomised to the Sanoïa arm: mean±SD age was 56.1±13.1 years, disease duration was 15.0±11.5 years and 132 (83.0%) of pts were female. Mean DAS28 was 2.7±1.2 with 57.2% of pts in remission; 115 (72.3%) were taking a biologic; 23.3% had attended therapeutic education sessions; 15.7% were members of pt associations; and 53.5% had participated in university-level studies. Overall, 41 pts (25.7%) never accessed Sanoïa and 81 (50.9%) accessed the platform at least twice; median=2, mean±SD=4.4±11.3 connections/pt over the 12 mos. 54 pts (34.0%) used Sanoïa for $\geq$2 mos with a noticeable investigator effect (0.3±0.2, 0–1 scale). Mean satisfaction with the platform was very high (1.5±1.5), with 90% scoring satisfaction $\leq$3. One barrier was expressed in 11.8% of cases: "the platform is not useful for me since I am in remission". In multivariate analysis, the only variable associated with greater usage of Sanoïa was being a member of a pt association: odds ratio [95% CI]=1.44 [1.17–1.77].

Conclusions: A quarter of pts who participated in this trial to assess e-health did not access the platform whereas half accessed the platform at least twice. Pts expressed high satisfaction and the only barrier was lower usefulness when in remission. e-Health is a promising tool for self-management in RA. The impact of offering additional services should also be explored in a further study.

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: L. Gossec Grant/research support from: UCB Pharma, Lilly, Consultant for: AbbVie, BMS, Celgene, Janssen, Novartis, MSD, UCB, A. Cantagrel: None declared, M. Soubrier: None declared, J. M. Joubert Employee of: UCB Pharma, W. Czarlewski Employee of: UCB Pharma, B. Combe Grant/research support from: Merck Pfizer Inc, Roche-Chugai, Consultant for: Merck, Pfizer, Roche-Chugai, UCB Pharma, Bristol-Myers Squibb, Celgene, Eli Lilly, Speakers bureau: Merck, Pfizer, Roche-Chugai, UCB Pharma, Bristol-Myers Squibb, Celgene, Eli Lilly, Novartis, J. M. Berthelot: None declared, D. Wendling: None declared, E. Dernis: None declared, L. Grange: None declared, C. Beauvais Speakers bureau: UCB Pharma, A. Perdriger: None declared, H. Nataf: None declared, M. Dougados Grant/research support from: UCB Pharma, AbbVie, Pfizer, Lilly, Merck, Novartis, H. Servy Shareholder of: Sanoïa platform operating company: e-health services, Employee of: Sanoïa

DOI: 10.1136/annrheumdis-2017-eular.1972

THU0589 PATIENT-PERCEIVED COPING WAS ASSOCIATED WITH PATIENT-PERCEIVED QUALITY OF PATIENT-PHYSICIAN INTERACTIONS IN 320 PATIENTS WITH RHEUMATOID ARTHRITIS

L. Gossec[1], C. Desthieux[1], A. Cantagrel[1], M. Soubrier[1], J.M. Berthelot[1], J.M. Joubert[2], B. Combe[1], W. Czarlewski[2], D. Wendling[1], E. Dernis[1], L. Grange[1], C. Beauvais[1], A. Perdriger[1], H. Nataf[1], M. Dougados[1], H. Servy[1]. [1]*CarNET Study Group, Paris;* [2]*UCB Pharma, Colombes, France*

Background: There has been growing emphasis on the importance of shared decision-making in rheumatoid arthritis (RA).[1,2] Patient-physician (pt-phy) shared decision-making necessitates open and thorough discussions and good interactions.

Objectives: This analysis explored pt-perceived quality levels of pt-phy interactions and characteristics of pts when these interactions are described as very good by pts.

Methods: CarNET (NCT02200068) was a French, 12-month, multicentre randomised controlled trial to assess access to an e-health platform (Sanoïa) allowing self-assessment of disease.[1,2] This was a post-hoc analysis, using baseline data only. Pts had confirmed RA and were enrolled by their treating rheumatologist. Pt-perceived pt-phy interactions were assessed through the pt-reported questionnaire Perceived Efficacy in Patient-Physician Interactions (PEPPI-5)[3] which consists of 5 items, each starting with "How confident are you in your ability to ..." (eg. "... know what questions to ask a doctor?"). Pts rated each item on an 11-point scale; 0=not at all confident, 10=very confident. Total PEPPI-5 scores range from 0–50; higher scores represent higher perceived self-efficacy in pt-phy interactions. Factors associated with a higher PEPPI-5 (ie. >median) were analysed by univariate and multivariate logistic regression (factors included pt demographics, phy demographics, disease characteristics and activity including pt-perceived coping [scored 0–10 in the Rheumatoid Arthritis Impact of Disease (RAID) questionnaire; lower scores indicate better coping]).

Results: Of 320 RA pts (159 vs 161; Sanoïa vs usual care), mean±SD age was 57.0±12.7 years, disease duration was 14.6±11.1 years and 253 (79.1%) were female. Mean DAS28 was 2.7±1.2, 54.1% were in DAS28 remission (<2.6); 216 (67.5%) were taking a biologic; 21.9% had previous therapeutic education sessions; 15.3% were members of pt associations; and 51.9% had followed university-level studies. The mean±SD PEPPI-5 score was 39.2±7.8 and the

median was 40. In univariate analyses, associations with $p<0.05$ were observed between pt-perceived coping (p=0.0008), erosive disease (p=0.03) and DAS28 remission (p=0.05) and a high PEPPI-5; associations with $p<0.2$ were observed for older age (p=0.07) and HAQ-DI $\leq$0.5 (p=0.12). In multivariate analyses, the only factor associated with high PEPPI-5 was pt-perceived coping (odds ratio [95% CI]=0.85 [0.76–0.96]; p=0.007).

Conclusions: Among RA pts whose disease was well controlled, pt-perceived pt-phy interactions were good. Pt-perceived coping was associated with better pt-perceived pt-phy interactions, indicating that perhaps pts who felt in control were more at ease with their phy, or vice-versa. The data did not allow us to attribute causality. These elements are important in the shared decision-making process.

References:

[1] www.sanoia.com.
[2] Gossec L. Arthritis Rheum 2016;68:S10.
[3] ten Klooster P. Patient Educ Couns 2012;87(1):125–30.

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: L. Gossec Grant/research support from: UCB Pharma, Lilly, Consultant for: AbbVie, BMS, Celgene, Janssen, Novartis, MSD, UCB, C. Desthieux: None declared, A. Cantagrel: None declared, M. Soubrier: None declared, J. M. Berthelot: None declared, J. M. Joubert Employee of: UCB Pharma, B. Combe Grant/research support from: Merck Pfizer Inc, Roche-Chugai, Consultant for: Merck, Pfizer, Roche-Chugai, UCB Pharma, Bristol-Myers Squibb, Celgene, Eli Lilly, Speakers bureau: Merck, Pfizer, Roche-Chugai, UCB Pharma, Bristol-Myers Squibb, Celgene, Eli Lilly, Novartis, W. Czarlewski Employee of: UCB Pharma, D. Wendling: None declared, E. Dernis: None declared, L. Grange: None declared, C. Beauvais Speakers bureau: UCB Pharma, A. Perdriger: None declared, H. Nataf: None declared, M. Dougados Grant/research support from: UCB Pharma, AbbVie, Pfizer, Lilly, Merck, Novartis, H. Servy Shareholder of: Sanoïa platform operating company: e-health services, Employee of: Sanoia

DOI: 10.1136/annrheumdis-2017-eular.1973

THU0590 THE USE OF A PORTFOLIO AMONG YOUNG RHEUMATOLOGISTS: RESULTS OF AN EMEUNET SURVEY

M. Van Onna[1], F. Sivera[2], V. Navarro-Compán[3], E. Nikiphorou[4], A. Moltó[5], S. Ramiro[6] on behalf of the EMEUNET Working Group. *[1]Department of Internal Medicine, division of Rheumatology, Maastricht University Medical Center +, Maastricht, Netherlands; [2]Rheumatology, Hospital General Universitario de Elda, Alicante; [3]Rheumatology, la Paz University Hospital, Madrid, Spain; [4]Rheumatology, Whittington Hospital, London, United Kingdom; [5]Rheumatology, Cochin Hospital, René Descartes University, Paris, France; [6]Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

Background: Portfolios are increasingly used in medical education. A portfolio may stimulate deep learning, deliver summative assessment and encourage reflection on clinical practice. A portfolio is seen as the key connection between learning at the organizational and the individual level.

Objectives: To (1) explore the perceptions of young rheumatologists about the use of a portfolio and to (2) study the barriers and facilitators when implementing a portfolio at a national and international level.

Methods: A survey was sent by email to all EMEUNET (Emerging EULAR Network) members. EMEUNET is a group of young rheumatologists and researchers within EULAR-member countries. Descriptive statistics were used to analyse initial data collected (Nov-Dec 2016). Weighted averages were calculated (i.e. mean in which each item being averaged is multiplied by a number (weight) based on the item's relative importance).

Results: 132 participants responded (64% female; mean age 33.5 years (SD 4.3 years); 34 countries). In total, 56.3% of participants were working as rheumatologists; 32.8% were rheumatologists in training. 49.6% of the participants indicated that a portfolio was already used by rheumatology fellows working at their institution; in 71.9% of these cases, this portfolio was also used at a national level. 50.4% of participants did not use a portfolio during their training; of these, 86.7% (strongly) agreed that a portfolio might be a useful tool.

Several barriers for successful implementation of a portfolio were identified by the participants. The main barrier was that a portfolio was not developed at a national level, and if developed at a national level, there were often no incentives to use it (Table 1). According to participants, the top 3 competencies that should be collected and reflected upon in the portfolio were (weighted average; importance 0 (not important) – 10 (extremely important)): practical skills (e.g. ultrasound) (8.2); correct use of diagnostics and therapeutic armamentarium (7.9); clinical skills (e.g. history taking) (7.8). The skills chosen as the least important to be included in a portfolio were: information on management tasks (6.5); promoting hospital-based care (e.g. writing a protocol) (6.6); theoretical and clinical knowledge (6.7).

Table 1. Perceived barriers with regard to the implementation of a portfolio.

Barrier	Response* (n = 122)
Participants who work/ed with a portfolio (n= 58)	
No incentives to use it	50.0%
Limited time	46.6%
Lack of clarity about how and when to use it	31.0%
Lack of interest by stake holders	29.3%
Difficult to access the required forms	12.1%
Participants who did not work/ed with a portfolio (n=64)	
Portfolio not developed on national level	51.6%
No added value recognized to it	21.9%
Initiatives, but lack of clarity about how and when to use it	12.5%
Initiatives, but no incentives to use it	9.4%

*More than one answer allowed. 10 (7.6%) participants did not answer the question.

Conclusions: A portfolio is generally considered a valuable tool and half of the participants already work with it. However, several barriers may prevent optimal implementation. Developing a core set of rheumatology-oriented competencies and a template for a portfolio to be used across institutions and eventually countries could promote implementation and harmonize training.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2280

THU0591 ASSESSING THE READABILITY AND PATIENT COMPREHENSION OF MEDICINE INFORMATION SHEETS PROVIDED TO PATIENTS BY AUSTRALIAN RHEUMATOLOGISTS

M. Oliffe[1], J. Johnston[2], D. Freeman[1], H. Bagga[1], P.K. Wong[3]. *[1]Mid-North Coast Arthritis Clinic, MNCAC; [2]Faculty of Education, Southern Cross University; [3]Mid-North Coast Arthritis Clinic, UNSW Rural Clinical School, Coffs Harbour, Australia*

Background: Literacy is "the ability to read and use written information and to write appropriately in a range of contexts".[1] Low literacy is associated with poorer health outcomes, including increased mortality.[2] Those accessing the healthcare system require adequate literacy to understand written instructions regarding medication, appointments and medication doses. We have previously shown in >200 rural and urban Rheumatology patients that <15% of patients had low health literacy and <1/3 of patients incorrectly followed dosing instructions for common Rheumatology drugs.[3] Up to 24% of US Rheumatology patients had a reading level of $\leq$8th grade.[4] These findings are concerning, as Rheumatologists often use medications such as MTX or bDMARDS with severe side effects. Rheumatologists often provide written information regarding these medications to patients.

Objectives: To assess i) the readability of Patient Medicine Information Sheets (PMIS) regarding medications provided to patients by Australian Rheumatologists, and ii) patient comprehension of these documents.

Methods: Thirty-one English-language PMIS from the Australian Rheumatology Association (ARA) website were assessed for readability using Readability Studio™ (Oleander Software). This software uses the number of sentences, words, syllables and characters in a sample of writing to estimate the required grade level and reading age of the target population using several readability scales (eg Flesch scale, Gunning Fog and Simple Measure of Gobbledygook, or SMOG).

To assess comprehension, a random sample of 100 patients from MNCAC was asked to read an ARA PMIS about one of the following medications: MTX, NSAIDS, Adalimumab, Abatacept or prednisone. He/she then answered five multiple choice questions about the content. A time limit of 15 minutes for reading the PMIS and answering the questions was allowed.Approval was obtained from the local HREC as a low/negligible risk project. Results are expressed as mean ± sem.

Results: The mean Flesch scale value (range 0–100, 0=very confusing; 100=very easy) of the 31 PMIS assessed was 51.1±0.6 (fairly difficult). The mean FORCAST grade level and reader age was 11±0 and 16–17 years, respectively. The mean Gunning Fog grade level was 11.4±0.1 with a reader age of 16–17 years. The mean SMOG grade level was 11.8±0.1 with a mean reader age of 16–17 years. At time of writing, comprehension was assessed in 7 of the planned 100 patients. So far, the mean number of correct answers was 3.2±0.5 (max. score of 5).

Conclusions: The ARA PMIS are suitable for readers who have completed a grade level $\geq$11 with a reading age $\geq$16 years. A low literacy population (< grade 8) will probably struggle to understand the content. These findings need to be extended to the PMIS used in other countries and has implications for the design of better patient information material.

References:

[1] Australian Government, Department of Education Employment and Training. The Australian Language and Literacy Policy. Canberra 1991.
[2] Baker DW et al. Arch Intern Med 2007;167:1503–1509.
[3] Wong PK et al. Medicine (Baltimore) 2014 Nov;93(25):e129.
[4] Swearingen CJ et al. J Clin Rheumatol 2010;16:359–364.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4811

THU0592 DO JUNIOR DOCTORS PRESCRIBE DISEASE MODIFYING ANTI RHEUMATIC DRUGS SAFELY?

M.K. Nisar[1], H. Weller[2]. *[1]Rheumatology, Luton & Dunstable University Hospital; [2]Rheumatology, Luton, Luton, United Kingdom*

Background: Patients with rheumatic diseases occupy over 50,000 bed days annually in the National Health Service. Adverse drug events are major causes of harm to patients in hospitals and are associated with prolonged length of stay with higher costs. National Patient Safety Agency has issued several alerts regarding DMARDs and Methotrexate overdose remains a "never event". Prescribing medications, including DMARDs for rheumatology patients, is one of the chief responsibilities of junior doctors.
Objectives: We undertook a pilot survey of junior doctors and medical students to understand their level of prescribing confidence with an aim to develop a teaching program.
Methods: Following a focus group discussion based on NPSA safety alerts and BSR DMARD monitoring guidelines, ten items were unanimously identified as core knowledge required for safe prescribing. A questionnaire was created based on these elements. Junior doctors and final year medical students were surveyed at our academic institution. Replies were compiled to ascertain their understanding of safe prescribing and troubleshooting DMARD related issues.
Results: 41 junior doctors of all grades and nine medical students contributed to the survey. Only 6/50 (12%) felt confident in prescribing whereas 16/50 (32%) had borderline confidence and remaining 56% felt it was beyond their expertise. Of the 41 junior doctors, 19 (46%) had never even prescribed DMARD despite encountering such patients on the wards. Principal reasons for this included lack of confidence (40%), paucity of knowledge (15%) and no formal education (32%). Questions pertaining to safe prescribing were confidently answered by only 4/50 (8%) participants.
Conclusions: To our knowledge, this is the first survey to demonstrate that there are serious shortcomings in junior doctors' understanding of safe DMARD prescribing. Inadequate training and hence poor confidence among front line medical staff remains the main cause of this issue. Despite consistent evidence suggesting that rheumatology teaching in medical schools has historically been poor and active measures taken in recent past to identify better ways to address the issues, this study highlights major knowledge gaps among everyday and future prescribers. Focused strategy and better training of junior doctors, both during and after graduation, are pivotal to providing better care for patients prescribed DMARDs during inpatient hospital stay.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1691

THU0593 QUALITATIVE ASSESSMENT OF US-GUIDED INJECTION VIDEOS PUBLISHED ON VIDEO SHARING PLATFORMS

S.H. Bourdaim, C. Darrieutort-Laffite, Y. Maugars, B. Le Goff. *Rheumatology, University Hospital of Nantes, Nantes, France*

Background: Ultrasound (US) guided injections are becoming widespread in the treatment of rheumatic articular disorders. US allows a real time assessment of the needle progression and increase the accuracy of the injection. Video sharing platforms can be sources of information and learning material for healthcare professionals as for patients.
Objectives: We conducted this cross-sectional study to assess the quality of educational resources on US-guided articular and periarticular injections published on video sharing platforms.
Methods: YouTube, Dailymotion and Vimeo were searched using predefined keywords on US-guided shoulder, elbow, wrist, hand, hip, knee, ankle, and foot injections. The videos were classified according to their source. We determined the injection site and the explanations shown for each site. We collected information on patient positioning, equipment, needle, ultrasound settings and teaching material used by the author. When demonstration was performed live in patient, the compliance with the rules of asepsis and the accuracy of the injection were evaluated. Overall, videos were evaluated for quality on a 5-point ordinal global quality scale (GQS) (from 1 = poor quality to 5 = excellent quality). Results are given as median (min-max).
Results: We found 69979 results with the keywords. We screened 2802 videos by titles and included 153 videos (10.05 hours). Most of videos were published on Youtube (92.2%) and 82.4% included oral explanation. 53.6% videos were published by medical advertisement or profit companies and only 9.2% videos by university, professional organization or physician group. Among the 41.2% videos showing live demonstration of injection on the patient only 25.4% followed the strict rules of asepsis. When the videos included US cineloops of injection, 10.4% of them were outside the target. Very few videos gave details about information on the pathophysiology of the disease (6.5%), the risk (0.7%), the benefice (11.2%) or the products used for the injection (58.2%). Overall, 3.3% of the videos were classified as "Excellent quality" on the GQS, 24.2% as "Good quality", 23.5% as "Moderate quality", 34.6% as "Generally poor quality" and 14,4% "Poor quality". We compared the characteristics of the good quality videos (GQS score $\geq$4) versus the one rated $\leq$3. Better quality videos were longer (1.3 min ((0.07–1.05) versus 3.62 (0.32–40.43) min), had oral explanation (95% versus 77%; p=0.008). They more frequently showed the clinical and US site of injection and accurately reached their target (90% versus 68%). They were significantly more viewed (m2719 (13–80195) versus 856 (11–60174); p=0.026) and more liked (1 (0–80) versus 7 (0–58) (p=0.002)). However, some poor quality videos had more than 60000 views. Quality of the video created by medical advertisement or profit companies were not different from those coming from university but significantly better than those from individual physician or with unknown origin (p=0.011).
Conclusions: Our study reveals a generally a low quality of US guided learning videos available on the most popular video sharing platforms. We observed a lack of information on the treatment, its risks and benefits. Strict aseptic techniques are rarely followed and the injection can be outside the target. Finally, we identified characteristics associated with the quality of the video that can be used to improve their educational impact in the future.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6396

THU0594 DEVELOPING THE KOREAN LEEDS SATISFACTION QUESTIONNAIRE (KOREAN-LSQ) IN RHEUMATOID ARTHRITIS: A CROSS-CULTURAL VALIDATION USING RASCH ANALYSIS

S.-K. Cho[1], D. Kim[1], S.J. Cha[1], D. Yoo[1], S.-H. Kim[2], J. Hill[3], M. Ndosi[4], Y.-K. Sung[1]. *[1]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul; [2]Department of Measurement and Evaluation of Physical Education, Chungbuk National University, Cheongju, Korea, Republic Of; [3]Harrogate, Harrogate; [4]Centre for Health and Clinical Research, University of the West of England, Bristol, United Kingdom*

Background: The Leeds Satisfaction Questionnaire (LSQ)[1] is a patient-completed questionnaire designed to measure satisfaction among patients attending a rheumatology outpatient clinic. It was originally developed in the UK and it comprises 45 items grouped into 6 subscales: general satisfaction, information, empathy, technical competence, attitude, access and continuity.
Objectives: To undertake cross-cultural adaptation and validation of the LSQ in RA for use in Korea.
Methods: The adaptation of the LSQ from English into Korean was established according to guideline of cross-cultural adaptation of self-report measures.[2] Patients with RA were then recruited from an outpatient clinic of a university hospital in South Korea and Cross-cultural validation of the Korean-LSQ was carried out by Rasch analysis using the WINSTEPS program. Model data fit was determined by Infit and Outfit statistics ($\geq$0.50 and $\leq$1.50). If the values of the Infit and Outfit are 1.00, the observed score perfectly fit the expected model. The unidimensionality of the scale was determined by separation index (SI $\geq$2.00) and reliability (RI $\geq$0.80).
Results: An adequate conceptual equivalence was achieved following the adaptation process. The dataset for validation comprised 125 patients, 103 (82.4%) of whom were female, mean (SD) age =47.2 (12.5) and disease duration =52.8 (69.4) months. Forty-item of the 45 items had acceptable fit statistics (individual item data not shown). The individual items overall had good separation index and reliability (SI =5.98 and RI =0.97). Analysis of the 6 subscales of the Korean-LSQ resulted in good fit to the Rasch model (Table 1), high internal consistency and unidimensionality (Person SI =2.31 and RI =0.84; item SI =5.44 and RI =0.97).

Table 1. Fit statistics for testlets

LSQ subscales (testlets)	Infit		Outfit		Point-biserical correlation
	MNSQ	ZSTD	MNSQ	ZSTD	PTMEA CORR.
LSQ_general	1.12	0.90	1.12	0.70	0.80
LSQ_information	1.05	0.40	1.05	0.30	0.64
LSQ_empathy	0.64	-3.30	0.59	-2.80	0.79
LSQ_technical competence	1.06	0.40	1.05	0.30	0.77
LSQ_attitude	1.06	0.50	0.91	-0.40	0.74
LSQ_access&continuity	1.05	0.50	1.08	0.60	0.76

MNSQ = mean-square; For model fit: MNSQ lie within $\geq$0.50 and $\leq$1.50).

Conclusions: Fit to the Rasch model confirmed that the construct validity, reliability, and unidimensionality of the Korean-LSQ were preserved after the adaptation process. The Korean LSQ is a valid and reliable tool for measuring satisfaction with care among patients with RA in South Korea.
References:
[1] Hill J, et al. Survey of satisfaction with care in a rheumatology outpatient clinic. Ann Rheum Dis. 1992; 51(2): 195–7.
[2] Beaton DE, et al. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine. 2000; 25(24): 3186–91.
Acknowledgements: This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI16C0061).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4799

THU0595 THE VIEWS AND PERCEPTIONS OF NON-SPECIALIST, HOSPITAL JUNIOR DOCTORS ON JOINT ASPIRATION OF THE ACUTE HOT-SWOLLEN-JOINT, AND THEIR TRAINING IN THIS CLINICAL SKILL

Z. Farah. *Rheumatology, Imperial Healthcare Trust, London, United Kingdom*

Background: BSR guidance on managing hot-swollen-joints recommends early joint aspiration (arthrocentesis) to rule out septic arthritis and avoid morbidity and mortality. In such patients, the initial assessment is often performed by junior doctors prior to specialist review. Previous audit suggests poor adherence to recommended guidance. Our previous quantitative survey in 2 hospitals found low self-reported confidence at managing hot-swollen-joints in 72 of 140 (52%) respondents; 58 (42%) participants reported inadequate exposure, and 43 (31%) inadequate training. There is limited research exploring the reasons behind poor uptake of arthrocentesis by junior doctors.
Objectives: To determine the perceptions of junior doctors about joint aspirations, their training to perform this important skill and how training could be improved
Methods: The focus group included two foundation doctors, two senior house-officers and two registrars. Focus group questions were developed from themes that emerged from our previous quantitative survey. The session was recorded using an iPhone, then anonymously transcribed verbatim. The transcript was analysed using an emergent coding technique drawn from grounded theory approach. The data was coded over three passes.
Results: Decision to aspirate a joint appeared to be influenced by internal and external factors. Internal factors included their previous experience, which was variable with one who *"did 7 aspirations"* and another who *"[had] not had any experience at all."* Other factors like anatomical knowledge, level of seniority and prior training were presented. Negative emotions emerged with participants using words like *"weary"*, *"anxious"* and *"scary"*, particularly *"fear of serious consequences"* when describing joint aspiration.
External factors included procedure-related factors like technical difficulty, and the type of joint to be aspirated. Consensus suggested that all joints except the knee should be left to the specialist. Context-related factors included time constraints. The group emphasised the importance of recurrent exposure and opportunity to practice aspirations. Availability of supervision influenced the decision to aspirate, particularly if by the rheumatologist.
Training in arthrocentesis appeared to be inconsistent. Positive comments included succinct dedicated training experiences by an expert using simulation, immediate feedback followed by practice. Negative comments emerged such as training was inconsistent and of poor timing, or trainees lacked the opportunity to subsequently practice. Participants then proposed methods of how to improve training in arthrocentesis.
Conclusions: The decision to aspirate is a complex interaction between internal and external factors combining knowledge, attitudes and emotions with circumstances and context. The participants emphasise training in knee aspirations, but not other joints due to lack of exposure. Immediate feedback during training in arthrocentesis is key. Inability to continue regularly practicing the procedure in real patients may be a barrier to retaining the skill. A review of training in joint aspiration may be required in order to improve uptake of this skill in practice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1250

THU0596 RHEUMATOLOGY SPECIALTY TRAINING IN EUROPEAN UNION COUNTRIES

N. Cikes[1], J. Dudler[2], F. Lioté[3], D.E. Bax[4], N.D.S. Bax[4] on behalf of UEMS Rheumatology Section and Board Union Européenne des Médecins Spécialistes, Avenue de la Couronne 20, Bruxelles 1050. *[1]University of Zagreb School of Medicine, Zagreb, Croatia; [2]Department of Rheumatology, HFR Fribourg – Hôpital Cantonal, Fribourg, Switzerland; [3]Rheumatology Department, Univ Paris Diderot, Inserm UMR 1132, Hospital Lariboisière, Paris, France; [4]The Medical School, University of Sheffield, Beech Hill Road, Sheffield, United Kingdom*

Background: The Union of European Medical Specialists (UEMS) seeks through its speciality Sections and Boards (S&B) to enhance the training of its doctors and to encourage and support the movement of doctors between countries. The Rheumatology S&B has delegates from all EU countries and has developed a document (European Training Requirements (ETR) – at uemsrheumatology.eu) that provides guidance about the rheumatology curriculum.
Objectives: To determine:
1. The extent of use of the Rheumatology ETR by EU countries
2. The extent of use of logbooks in recording the progress of a trainee
3. If training centres are accredited
4. If national assessment programmes exist for trainees
5. If a country has quality assurance and enhancement processes in rheumatology training

Methods: A questionnaire was sent to all S&B members asking questions in relation to all of the objectives with one follow-up questionnaire to non-responders. Verification of responses as well as obtaining responses from continuing non-responders occurred in December 2016.
Results: Nineteen countries responded. Most (18/19) have developed and implemented their own curriculum, often with the influence of the ETR, and also are using a logbook to record the progress of trainees. Training Centres are required to undergo accreditation in 15/19 countries. Another three countries are planning to introduce this. One country does not have an accreditation programme. After accreditation only 8 countries have quality assurance (QA) and enhancement (QE) programmes. In one of these countries the QA and QE processes are variable. Two other countries are either discussing or developing such processes. In 14 countries trainees are assessed to determine their suitability to become specialists. In one of these countries the approach is variable. Two other countries are planning to introduce assessments. Three countries do not assess their trainees.
Conclusions: Most EU countries have implemented their own, and varied, curricula for rheumatology training. All countries either use or are planning to use a portfolio, again variable in nature, to record trainees' progress. Thus, it appears that at present any pan-European standardised curriculum or logbook will be of limited utility.
Most countries require training centres to undergo accreditation. However, less than half of the countries have a continuation of quality assurance or quality enhancement processes after accreditation with some countries it seems having no plans to do so.
At present, a specialist in one European country is required by European law to be recognised as such in another. This study did not determine the nature of the assessments undertaken in different countries but this is not of current relevance within Europe as regards the possible movement of a doctor from one country to another for professional reasons.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3314

THU0597 FLIPPED LEARNING: CAN RHEUMATOLOGY LEAD THE SHIFT IN MEDICAL EDUCATION?

Y. El Miedany[1,1], M. El Gaafary[2], N. El Arousi[3], S.S. Youssef[3]. *[1]Rheumatology, Darent Valley Hospital, Dartford, United Kingdom; [2]Community and Public health; [3]Rheumatology and Rehabilitation, Ain Shams University, Cairo, Egypt*

Background: Flipped Classroom is a model that is quickly gaining recognition as a novel teaching approach among health science. Flipped learning turns the usual teaching model on its head. The idea is that students learn new content outside the classroom (usually online) and then tackle assignments in lessons, giving tutors more time to help them with aspects they don't understand.
Objectives: 1. to implement a flipped classroom teaching for rheumatology topics for both under and postgraduate education. 2. to evaluate outcomes of teaching using a post-flipped classroom assessment and a student perceived effectiveness and satisfaction questionnaire.
Methods: Ten online videos on topics of how to take rheumatology history, individual joint examination, handling cases of monoarthritis and polyarthritis, and metabolic bone disease were made available for the students. 39 undergraduate 35 postgraduate trainees were included in this educational activity. The students were exposed to online lecture content prior to the class-time active learning session. The teaching session adopted an interactive learning environment and the course instructor served as a facilitator rather than a dominator for the instructional process, provided in-class applied learning opportunities and offered timely feedback/guidance to students. Evaluation of the teaching session was assessed using a scenario based learning and an evaluation check list. The students were asked to complete a questionnaire based on a 5-point Likert scale: 1 (strongly disagree) to 5 (strongly agree) to assess for their perceived effectiveness and satisfaction. The outcomes of the evaluation sheet and students' questionnaire, were compared to 40 undergraduate and 34 postgraduate trainees who were taught in the last year on the same topics in a lecture-based model using the standard teaching protocols, followed by scenario based learning sessions, student evaluation and satisfaction survey.
Results: There was no significant difference regarding socio-demographics between the 2 students' groups included in this study. Outcomes of the flipped learning revealed that 94% of the students viewed the videos prior to the class session, and 96% attended the education sessions in comparison to 86% attendance in the traditional teaching group. Students reported an increase in knowledge, a positive learning experiences and perceptions of the flipped classroom model. Students' perceived effectiveness and satisfaction scores were significantly higher among the flipped learning in contrast to the traditional teaching comparative group (4.9 vs 4.3, $p<0.05$). Similarly, analysis of the students' assessment scores after the scenario based learning sessions was higher in the flipped learning group compared to the students taught by traditional methods ($p<0.01$).
Conclusions: Implementation of the flipped learning for the rheumatology topics demonstrated a successful and promising platform for using technology to make better use of the students' time, and for increasing their satisfaction with the necessary didactic learning. Active learning increases student engagement and can lead to improved retention of knowledge.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4501

THU0598 CAN YOU HEAR THE JOINTS CRYING? MUSCULOSKELETAL EXAMINATION IN JUNIOR DOCTORS' MEDICAL ADMISSION CLERKINGS

F.Y.H. Kwok, L.H. Lee, A. Gupta. *Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom*

Background: Physical examination is an indispensable skill in the art of medicine which, together with history taking, enables physicians to achieve a clinical diagnosis. Previous studies have consistently shown wide variations in the documentation of physical examination findings on systemic review (1,2). In particular, musculoskeletal examination was found to be frequently omitted.
Objectives: The aim of this study was to evaluate the quality of junior doctors' medical admission clerking, with a focus on clinical examination.
Methods: Fifty acute medical admission clerking entries by junior doctors in a university hospital were reviewed. Case notes were assessed for clinical details and physical examination performed.
Results: Mean age was 69. The commonest presenting complaint was fall or collapse. Musculoskeletal examination was only documented in 24% of admitted patients. There was disparity in the quality of documentation, ranging from complete omission to comments such as "valgus deformity", "erythema", "limited abduction" and "unable to SLR". Overall, the documentation of cranial nerves examination, limb neurological examination, abbreviated mental test and Glasgow coma scale was less robust (40%, 52%, 48% and 66% respectively). The documentation of musculoskeletal and neurological examination contrasts markedly with other systems: respiratory system 100%, cardiovascular system 98% and abdominal system 98%.
Conclusions: The omission of musculoskeletal examination may reflect a general apathy towards musculoskeletal health. Despite fall or collapse being the most common reason for medical admission in this study, musculoskeletal examination was only documented in a minority of patients. With an aging patient population, it is vital for physicians to address musculoskeletal disorders which are likely to be more prevalent on the acute medical take. Junior doctors' lack of confidence in performing musculoskeletal examination may also be another contributing factor. It is important that junior doctors are provided feedback on their clinical assessment by senior doctors when essential components of examination are omitted. National training programmes should consider including these areas in postgraduate curriculum to ensure competency is achieved.
References:
[1]) Doherty M, Abawi J, Pattrick M. Audit of medical inpatient examination: a cry from the joint. J R Coll Physicians Lond 1990;24(2):115–8.
[2]) Myers A, McDonagh JE, Gupta K, et al. More "cries from the joints": assessment of the musculoskeletal system is poorly documented in routine paediatric clerking. Rheumatology (Oxford) 2004;43(8):1045–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2602

THURSDAY, 15 JUNE 2017

Public health, health services research and health economics

THU0599 BENEFIT RISK RATIO FOR BIOLOGICAL AGENTS IN JUVENILE IDIOPATHIC ARTHRITIS, A META-ANALYSIS OF RANDOMIZED CLINICAL TRIALS

N. Cabrera[1], P. Janiaud[1], A. Belot[2], B. Kassai[1,3], J.-C. Lega[1]. *[1]UMR 5558 CRNS Lyon; [2]University of Lyon 1; [3]Clinical Investigation Center/CIC 1407, INSERM, Lyon, France*

Background: The biological agents (BAs) have revolutionized the care and have improved the prognosis of juvenile idiopathic arthritis (JIA). Effectiveness and short-term tolerance was well established in randomized clinical trials (RCTs), initially in JIA. However, there is an insufficient evidence for the long-term tolerance[1]. The serious adverse events (SAEs) include infections, malignancies and drug induced auto-immune diseases (e.g. uveitis).
Objectives: To assess the benefit/risk balance of BAs assessed by RCTs vs placebo or vs standard treatment in JIA, using meta-analysis (MA) technique.
Methods: All RCTs in JIA comparing BAs to placebo or standard treatment (e.g. methotrexate) published between 1950 and February 2016 were eligible. Data source: Cochrane, Medline, ClinicalTrial.gov register. The ILAR classification for JIA[2] was used and the clinical efficacy of treatment was measured by the ACR pediatric score[3]. Efficacy was analyzed considering the design of study. Effectiveness (ACRpedi30) was estimated as the measure of the benefit of the BAs and SAEs as a measure of risk by random effect models. The benefit/risk balance was analyzed using the net efficacy adjusted for risk (NEAR)[4]. An OR >1 indicates that the treatment has a beneficial effect and OR <1 a deleterious effect. Subgroups analyses were made to account the heterogeneity of JIA. We explored potential heterogeneity by subgroups analysis according with BAs and JIA subtypes.
Results: We included 20 RCTs conducted in JIA encompassing 1533 children. The disease duration, at the inclusion of RCTs, varies between 2 and 6 years for most studies. The maintenance of the therapeutic effect was estimated in the studies using withdrawal design in 6 studies. The maintenance of clinical response showed a large heterogeneity. Sub-groups analyses showed that the heterogeneity is marked in the systemic JIA[5]. The global NEAR OR was in favor of BAs in parallel (OR 3.83, CI 1.49–9.82) and withdrawal (OR 2.75, CI 1.51–5.01) trials. The efficacy of BAs in JIA was superior to the placebo in parallel (OR 5.46, CI 2.26–13.21) and withdrawal (OR 3.52, CI 2.15–5.77) trials. In RCTs (parallel and withdrawal design), SAEs did not differ between BAs and control (OR 1.18, CI 0.73–1.9). No death occurred at follow-up.
Conclusions: This is the first MA assessing all BAs used in all JIA categories combined. This MA in patients with JIA shows that the benefit/risk ratio of BAs in JIA is favorable.
References:
[1] Klotsche, J. et al. Long-term safety of etanercept and adalimumab compared to methotrexate in patients with juvenile idiopathic arthritis (JIA). Ann. Rheum. Dis. 75, 855–861 (2016).
[2] Petty, R. E. et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J. Rheumatol. 31, 390–392 (2004).
[3] Consolaro, A. et al. Optimisation of disease assessments in juvenile idiopathic arthritis. Clin. Exp. Rheumatol. 32, S-126–130 (2014).
[4] Boada, J. N. et al. Net efficacy adjusted for risk (NEAR): a simple procedure for measuring risk:benefit balance. PloS One 3, e3580 (2008).
[5] Tarp, S. et al. Efficacy and safety of biological agents for systemic juvenile idiopathic arthritis: a systematic review and meta-analysis of randomized trials. Rheumatol. Oxf. Engl. 55, 669–679 (2016).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4568

THU0600 CUMULATIVE ADVERSE CHILDHOOD EXPERIENCES ARE ASSOCIATED WITH POOR OUTCOMES IN ADULTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

K. DeQuattro[1], L. Trupin[1], P.P. Katz[1], C. Lanata[1], E.H. Yelin[1], L.A. Criswell[1], C.G. Helmick[2], M. Dall'Era[1], J. Yazdany[1]. *[1]Division of Rheumatology, University of California San Francisco, San Francisco; [2]Division of Rheumatology, Centers for Disease Control and Prevention, Atlanta, United States*

Background: Adverse childhood experiences (ACE) such as abuse, neglect and household challenges are associated with poorer adult health status and onset of rheumatic diseases. There has been no research associating ACE with outcomes among adults with systemic lupus erythematosus (SLE).
Objectives: To characterize relationships of ACE and health outcomes of disease activity, damage, quality of life and depression in SLE patients.
Methods: Data were derived from the California Lupus Epidemiology Study (CLUES), a population based, multi-ethnic cohort of patients with SLE. Participants completed self-report measures of SLE activity (Systemic Lupus Activity Questionnaire; SLAQ), damage (Brief Index of Lupus Damage; BILD), quality of life (SF-36), depression (Patient Health Questionnaire; PHQ8) and sociodemographics. They completed the Adverse Childhood Experiences (ACE) survey, a validated 10-item scale covering 3 domains (abuse, neglect and household challenges prior to age 18). We compared demographics and SLE outcomes by ACE score and domains using ANOVA.
Results: The 166 CLUES participants were mostly women (89%) and were racially/ethnically diverse (31% non-Hispanic White, 22% Hispanic, 15% African American, 31% Asian American). Mean age was 44±14; mean age at diagnosis 28±12. The median ACE score was 1; 30 (18%) had a score of 4 or higher. ACE scores $\geq$4 were more common in Hispanic (27%) and African American (32%) participants (p=0.01) compared to other races/ethnic groups, and in participants with poverty level incomes (61% vs 13%, p$<$0.001); but did not differ by education or age at study entry or diagnosis. Higher overall ACE scores were associated with greater SLE activity and damage, poorer quality of life, and higher levels of depressive symptoms. For each ACE domain, increasing scores were generally associated with worse outcomes, but did not always reach statistical significance (Table).

Table 1. SLE Outcomes by Adverse Childhood Event (ACE) Scores and Domains

	Score	n	Outcomes [mean (sd)]			
			SLAQ	BILD	SF36PCS	PHQ8
Total ACE score	0	66	6.0 (6.2)	1.7 (2.0)	46.0 (10.5)	4.3 (4.1)
	1	31	6.9 (5.4)	1.4 (1.5)	44.3 (8.5)	4.8 (4.0)
	2–3	39	11.2 (7.6)	1.7 (2.1)	41.0 (10.5)	7.8 (5.6)
	4+	30	11.8 (8.0)	3.0 (2.9)	38.1 (11.1)	7.3 (4.6)
		p-value	$<$0.001	0.02	$<$0.001	0.003
Household Challenges	0*	66	6.0 (6.2)	1.7 (2.0)	46.0 (10.5)	4.3 (4.1)
	1	33	9.1 (6.6)	1.8 (2.2)	42.3 (8.8)	6.3 (5.7)
	2+	24	11.5 (8.0)	2.4 (2.2)	40.3 (10.6)	7.6 (5.1)
		p-value	0.002	0.35	0.04	0.01
Neglect	0*	66	6.0 (6.2)	1.7 (2.0)	46.0 (10.5)	4.3 (4.1)
	1	33	11.6 (7.0)	2.4 (2.7)	37.7 (9.9)	8.1 (4.8)
	2+	24	9.8 (7.4)	1.6 (0.9)	42.2 (5.2)	6.4 (2.6)
		p-value	$<$0.001	0.33	0.001	$<$0.001
Abuse	0*	66	6.0 (6.2)	1.7 (2.0)	46.0 (10.5)	4.3 (4.1)
	1	26	10.1 (6.3)	1.7 (1.9)	38.8 (10.4)	8.1 (4.5)
	2+	26	13.9 (7.6)	3.0 (3.2)	37.5 (10.6)	6.9 (4.5)
		p-value	$<$0.001	0.04	$<$0.001	$<$0.001

*Zero-level excludes respondents with scores in other ACE domains.

Conclusions: Adverse childhood experiences are reported frequently in individuals with SLE; accumulation of adverse experiences is associated with poor SLE outcomes. Higher scores in each domain, especially childhood neglect or abuse, were associated with poorer health measures in adulthood. Further research regarding ACE patterns and SLE outcomes is warranted.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5568

THU0601 CARDIOVASCULAR SCREENING AMONG PATIENTS WITH INFLAMMATORY ARTHRITIS: TO WHAT EXTENT DO PATIENTS FOLLOW RECOMMENDATIONS?

A.H. Kjeldgaard[1], K. Hørslev-Petersen[1], R.D. Christensen[2], J. Søndergaard[2], J. Primdahl[3]. *[1]King Christian X's Hospital for Rheumatic Diseases, Graasten; [2]Research Unit for General Practice, University of Southern Denmark, Odense; [3]King Christian X's Hospital for Rheumatic Disease, Graasten, Denmark*

Background: Patients with inflammatory arthritis (IA) have a substantially increased risk for cardiovascular (CV) disease and consequently regular screening is recommended (1).
Objectives: To investigate whether patients with known IA and high CV risk follow the recommendation, given in a nurse-led CV risk screening consultation, to consult General Practice in order to reduce their CV risk. Furthermore to investigate the influence of socioeconomic position and gender.
Methods: A register-based cohort study comprising outpatients at King Christian X's Hospital for Rheumatic Diseases, Graasten, Denmark, diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or spondylo arthritis (SpA), who had participated in at least one screening consultation based on the EULAR recommendations (1) between 1st of July 2012 and 1st of July 2015. The primary outcome was a consultation with their GP and at least one intervention of relevance for CV risk within 3 months after the screening consultation.
Results: 1266 patients, 18–85 years of age, were included; 72.5% with RA and 27.5% with SpA or PsA. Of the 447 (35%) with high risk of CV disease, 60% consulted GP after the screening visit compared to 55% for the 819 patients with low risk of CV disease. Of the 60% of patients with high risk who consulted their GP, 41% had at least one relevant intervention. Education $\geq$10 years increased the odds for non-compliance (Odds Ratio [Confidence interval]) (0.72 [0.56;0.92], p=0.01) and age above 65 years increased the odds for compliance (1.50 [1.15;1.95], p=0.03). Income, diagnosis, gender, Low Density Lipoprotein level and systolic blood pressure did not significantly influence the odds to consult their GP after the screening consultation. Among high risk patients, 7.4% had their blood glucose checked at a GP consultation and 6.3% had their blood-pressure measured with at-home equipment after the screening consultation as opposed to 4.8% and 1% among low risk patients.
Conclusions: After a screening consultation, 40% of the patients with high risk of CV disease did not consult their GP at all in the following 3 months. At least 33% of the patients with high risk followed the recommendations to consult their GP and 27% consulted their GP for reasons not possible to clarify in this study. Only age and higher education had a significant influence on the outcome.
References:
[1] Peters, M.J., et al., EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis, 2010. 69(2): p. 325–31.
Acknowledgements: We would like to thank The Danish Rheumatism Association and the Henrik Henriksens fund for financial support for this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1908

THU0602 WORKER PRODUCTIVITY LOSS REMAINS A MAJOR ISSUE FOR PATIENTS WITH INFLAMMATORY ARTHRITIS AND OSTEOARTHRITIS: RESULTS FROM THE INTERNATIONAL EULAR-PRO WORKER PRODUCTIVITY STUDY

S. Leggett[1], A. Bosworth[2], C. Hoffstetter[3], A. Boonen[4], D. Lacaille[5], C. Mihai[6], C. Talli[7], S. Hagel[8], G. Crepaldi[9], S. Ramiro[10], S. Dadoun[11], S. Verstappen[12,13] on behalf of EULAR-PRO at-work productivity co-investigators. *[1]Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester; [2]NRAS, Maidenhead, United Kingdom; [3]OMERACT, Ontario, Canada; [4]Division of Rheumatology, Maastricht University Medical Centre, Maastricht, Netherlands; [5]Arthritis Research Centre of Canada, University of British Columbia, Vancouver, Canada; [6]Internal Medicine and Rheumatology Clinic, Dr. Ion Cantacuzino Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [7]Rheumatology, East Tallinn Central Hospital, Tallin, Estonia; [8]Department of Clinical Sciences Lund, Section of Rheumatology, Lund University and Skane University hospital, Lund, Sweden; [9]Division of Rheumatology, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; [10]Leiden University Medical Centre, Leiden, Netherlands; [11]APHP Pitie-Salpetriere Hospital, Department of Rheumatology, Paris, France; [12]Arthritis Research UK Centre for Epidemiology, University of Manchester; [13]NIHR Manchester Musculoskeletal BRU, Central Manchester Univ. Hospitals NHS Foundation Trust, Manchester, United Kingdom*

Background: Rheumatic and Musculoskeletal Diseases such as Inflammatory arthritis (IA) and osteoarthritis (OA) are one of the biggest causes of disability and worker productivity loss which has recently been recognized by European policy makers and the World Health Organization (WHO). However, limited information is available about job characteristics and the level of both presenteeism and absenteeism in employed persons with IA or OA across countries.
Objectives: To describe job characteristics and worker productivity loss in patients with IA and OA in Europe and Canada.
Methods: Patients with IA or OA in paid employment from seven countries within Europe and from Canada were recruited to the EULAR-PRO Worker productivity study. Patients completed a questionnaire including questions about their job, job characteristics and the Work Productivity and Activity Impairment Questionnaire (WPAI) measuring percent hours absent and the percentage their disease affected productivity while working (0–100%=disease completely prevented work). Patients also completed several health-related patient reported outcome measures, including: the Health Assessment Questionnaire (HAQ), Visual Analogue Scale (VAS) general well-being, and EuroQol-5D (EQ-5D).
Results: 503 patients were included in this large international study. Mean (SD) age was 47 (10) years, median [IQR] disease duration 12 [5, 21] years and 94% had IA. 42% had a predominately mentally demanding job, 10% physically demanding job, and 48% a combination; with overall 34% reporting their job being very demanding (see table for country specific results). Respectively 12% and 5% of patients were able to often or always postpone work tasks if need be, whilst, respectively 19% and 51% never or sometimes received help from colleagues which may depend on job/employment type and company size. Twenty-one% of patients reported that they missed time off work due to ill-health in the past week (median [IQR] % time missed due to ill-health 20% [9–50]). Interestingly, a total of 11% were unsatisfied with their current job; and 23% of patients did not disclose their disease to their employer.

	United Kingdom N=76	France N=45	Netherlands N=96	Estonia N=81	Sweden N=66	Romania N=62	Italy N=31	Canada N=46
Age, years	48 (8)	46 (10)	49 (11)	46 (11)	49 (9)	42 (9)	47 (9)	51 (9)
Gender, female	53%	60%	54%	62%	73%	55%	84%	83%
VAS well-being, mm	39 [21-60]	28 [18-49]	30 [11-60]	43 [20-62]	38 [20-61]	35 [12-55]	32 [14-65]	28 [15-60]
HAQ-score	0.63 [0.25-1]	0.25 [0.13-0.63]	0.38 [0-0.5]	0.38 [0.1-0.75]	0.63 [0.38-.88]	0.13 [0-0.63]	0.25 [0-0.5]	0.5 [0.13-1]
EQ-5D	0.62 [0.57-0.69]	0.69 [0.66-0.73]	0.73 [0.62-0.73]	0.66 [0.52-0.73]	0.66 [0.62-0.73]	0.69 [0.62-0.90]	0.69 [0.62-0.88]	0.62 [0.55-0.73]
General job demands:								
Slightly demanding	12%	11%	34%	66%	12%	16%	7%	20%
Demanding	41%	40%	40%	30%	41%	54%	50%	33%
Very demanding	47%	49%	26%	4%	47%	30%	43%	47%
Job satisfaction:								
Satisfied	57%	78%	84%	81%	67%	74%	73%	71%
Neutral	19%	11%	11%	13%	17%	21%	17%	11%
Unsatisfied	24%	11%	4%	6%	17%	5%	10%	18%
% Absent in previous week due to ill-health	16%	20%	15%	26%	23%	18%	26%	33%
% Work time missed due to ill-health*	24 [9-100]	20 [13-34]	50 [19-72]	19 [10-50]	15 [9-50]	15 [9-50]	19 [5-33]	15 [3-50]
% impairment due to ill-health while working (WPAI)#	20 [0-50]	20 [0-30]	20 [0-50]	20 [0-40]	30 [5-45]	20 [10-50]	20 [0-50]	20 [10-60]

Scores are mean (SD) or median [IQR] depending on the distribution of the data.
Categorical data are presented as %.
* In those absent due to ill-health
# WPAI (0= condition no effect on work – 10=condition completely prevented work) * 100%.

Conclusions: This is one of the largest international studies investigating worker productivity loss in patients with IA and OA. It highlights the burden of the disease across countries and the importance of increasing awareness of rheumatological conditions in order to prevent presenteeism and long-term sick leave by providing the best available intervention to the individual patient in paid employment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5041

THU0603 DISEASE BURDEN OF KNEE OSTEOARTHRITIS PATIENTS UNDERGOING JOINT REPLACEMENT COMPARED TO MATCHED CONTROLS: A POPULATION-BASED ANALYSIS OF A DUTCH MEDICAL CLAIMS DATABASE

J.T.H. Nielen[1,2,3], A. Boonen[4], P.C. Dagnelie[1], B. van den Bemt[5,6], P. Emans[7], F. Lafeber[8], W.E. van Spil[8], F. de Vries[2,3], P. Welsing[8,9]. *[1]Epidemiology, Maastricht University; [2]Clinical Pharmacy & Toxicology, Maastricht University Medical Center, Maastricht; [3]Pharmacoepidemiology & Clinical Pharmacology, Utrecht University, Utrecht; [4]Rheumatology, Maastricht University Medical Center, Maastricht; [5]Pharmacy, Sint Maartenskliniek; [6]Pharmacy, Radboud University Medical Center, Nijmegen; [7]Orthopaedics, Maastricht University Medical Center, Maastricht; [8]Rheumatology & Clnical Immunology; [9]Julius Center, Utrecht University Medical Center, Utrecht, Netherlands*

Background: Knee osteoarthritis (OA) is a progressive joint disease generally associated with increasing pain. In severe symptomatic knee OA, knee prosthesis

(KP) can improve health-related quality of life. In the Netherlands, the incidence of KPs and KP revisions has increased, but health care costs related to these procedures over time and their determinants are unknown.[1]

Objectives: To provide estimates of age and sex-specific incidence of KPs, revision KPs, and prosthesis complications in patients with knee OA. To determine average annual health care costs of patients undergoing KP compared with matched controls in the Netherlands, and to understand drivers of costs.

Methods: All KPs in knee OA patients in the Achmea Health Database were identified and matched by age, sex, and region to a maximum of four controls. Incidence rates of KPs, KP revisions, and their complications (/1000 persons) from 2006–2013 were determined. Annual health care cost and excess costs compared to matched controls, preceding, during and after surgery were calculated and associated factors evaluated using longitudinal regression analysis.

Results: The incidence of KPs, KP revisions, and complications increased between 2006 and 2013. This increase was strongest in younger age categories and in men (Table 1). Annual health care costs slightly increased up to the year of surgery, with highest costs in the year of surgery. Post-surgery costs remained slightly higher than pre-surgery costs. High post-surgery costs were mainly associated with subsequent KPs. Other factors associated with high excess costs were younger age, female gender, and complications.

Table 1. Sex-specific incidence rates (per 1,000 person years) of all KPs, KP revisions, and complications associated with knee OA

	2006 IR	2007 IR	2008 IR	2009 IR	2010 IR	2011 IR	2012 IR	2013 IR
All KPs								
Male	0.81	0.86	1.04	1.04	1.11	1.19	1.26	1.26
Female	2.01	1.96	2.08	2.09	2.09	2.23	2.20	2.37
Total	2.82	2.82	3.12	3.13	3.20	3.42	3.46	3.62
KP revisions								
Male	0.04	0.06	0.08	0.07	0.07	0.07	0.12	0.10
Female	0.12	0.10	0.13	0.12	0.14	0.18	0.17	0.21
Total	0.16	0.16	0.21	0.20	0.22	0.26	0.29	0.31
Complications								
Male	0.11	0.13	0.16	0.15	0.19	0.20	0.24	0.27
Female	0.23	0.28	0.33	0.36	0.40	0.42	0.52	0.53
Total	0.34	0.41	0.49	0.52	0.59	0.62	0.76	0.80

Abbreviations: KP = Knee prosthesis, OA = Osteoarthritis, IR = Incidence rate.

Conclusions: These results underscore the increasing burden associated with severe knee OA, especially in younger age categories. Improved guidelines aimed at avoiding complications and revisions are required to counteract this trend.

References:

[1] Dutch Arthroplasty Register (LROI). Arthroplasty in the Picture, Annual Report of the Dutch Arthroplasty Register. 2014.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2101

THU0604 THE ASSESSMENT OF THE DUTCH QUALITY REGISTRY RHEUMATOID ARTHRITIS QUALITY INDICATORS IN THREE PILOT HOSPITALS

S. Mahmood[1], L. van Tuyl[1], P. van Riel[2], S. Rongen[2], D. van Schaardenburg[1], C. Allaart[3], R. van den Berg[3,4], H. Moens[5], R. Landewé[1]. *[1]Amsterdam Rheumatology and immunology Center, Amsterdam; [2]Bernhoven, Uden; [3]LUMC, Leiden; [4]Erasmus MC, Rotterdam; [5]Ziekenhuis Groep Twente, Almelo, Netherlands*

Background: While practical guidelines and recommendations play an important role in the treatment of RA, rheumatologists often tend to deviate from these guidelines (1). This may result in disparity of quality of care among individual doctors and hospitals. To establish the best possible care, quality measures are needed. These aim to quantify the quality of the delivered care and will form the foundation of quality registries. Standardization of care processes in combination with public reporting of performance (by means of a quality registry) has been suggested to improve quality of care (2).

Objectives: To develop feasible quality indicators (QIs), endorsed by the different stakeholders of the Dutch Quality registry Rheumatoid Arthritis (DQRA).

Methods: An expert group of 8 rheumatologists, 2 patient representatives and 1 healthcare insurer representative developed a minimal set of QIs via a Delphi-like procedure (3), endorsed by the Dutch Society for Rheumatology. Since October 2015, these QIs have been registered by rheumatologists and rheumatology nurses, once a year in 26 hospitals, along with a patient evaluation questionnaire regarding the received care. To determine whether it is feasible to collect these QIs in daily practice, retrospective data from three hospitals was obtained (hospital A (university), B and C (non-academic)).

Feasibility was determined by evaluation of:

1. Completeness of registered data (figure 1)
2. Possibility to calculate disease activity categories (remission, low-high disease activity)
3. Possibility to calculate changes over time in disease activity categories
4. Extraction of data regarding (b)DMARD use

Results: Selected QIs are:

1. Percentage of patients in a certain disease activity category
2. Percentage of patients using a certain (b)DMARD
3. Patient reported experience with received care

Hospital B provided only data from one year (2014) and was not able to extract data on medication from their electronic record system.

Table 1. Assessment of feasibility of the DQRA QIs

Disease activity category				
Indicator (DAS28)	Hospital A (n=791)	Hospital B (n=1395)	Hospital C (n=822)	Mean
Remission	43.6%	45.1%	63.6%	50.8%
Low disease activity	16.3%	15.2%	14.1%	15.2%
Moderate disease activity	32.8%	30.1%	19.1%	27.3%
High disease activity	7.3%	9.6%	3.2%	6.7%
Changes over time in disease activity categories (2014–2015)				
Indicator (DAS28)	Hospital A (n=415)	Hospital B	Hospital C (n=653)	Mean
Stable over time	48.7%	N.A.	58.8%	53.8%
Decreased in disease activity category	24.8%	N.A.	17.9%	21.4%
Increased in disease activity category	26.5%	N.A.	23.3%	24.9%
DMARD use				
Indicator	Hospital A (n=1081)	Hospital B	Hospital C (n=1105)	Mean
sDMARD monotherapy	41.2%	N.A.	51.6%	46.4%
sDMARD combination therapy	29.4%	N.A.	27.8%	28.6%
bDMARD	29.4%	N.A.	16.0%	22.7%
No DMARDs	0%	N.A.	4.7%	0%

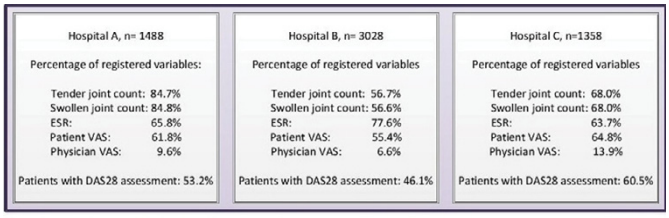


Figure 1: completeness of registered data

Conclusions: The DQRA is the first to incorporate perspectives from three stakeholders (patients, physicians and healthcare insurers) and successfully formed a limited set of QI. Collection of these indicators was feasible in two out of the three participating hospitals and offers insight in differences in provided and perceived care for RA patients.

References:

[1] Mahmood et al. Best Pract Res Clin Rheumatol 2015.
[2] Chassin et al. Health Aff 2002.
[3] Mahmood et al. ARD 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1824

THU0605 IMPACT OF NON-PERSISTENCE TO SUBCUTANEOUS TNF-ALPHA INHIBITORS ON MEDICAL RESOURCE UTILIZATION AND COSTS

M. Belhassen[1], F. Tubach[2], C. Hudry[3], M.-C. Woronoff[4], L. Levy-Bachelot[5], L. Lamezec[5], E. Van Ganse[1], B. Fautrel[6]. *[1]Hesper 7425, Health Services and Performance Research, University Claude Bernard Lyon 1, PELyon, Pharmacoepidemiologie Lyon, Lyon; [2]APHP, Hôpital Pitié-Salpêtrière, Département de Biostatistiques, Santé publique et Information médicale, APHP, Centre de Pharmacoépidémiologie (Cephepi); INSERM, UMR 1123 ECEVE; Université Pierre et Marie Curie Paris 6, Sorbonne Universités; [3]AP-HP Hôpital Cochin, Paris; [4]CHU Besançon, Université Franche-Comté, Comue Ubfc, UMR INSERM 1098, Besançon; [5]Merck Sharp & Dohme, Paris, France; [6]Sorbonne Universités, UPMC Univ Paris 06; AP-HP, Rheumatology Department, Pitié Salpétrière University Hospital, Paris, France., Paris, France*

Background: Biotherapies such as subcutaneous tumour necrosis factor-alpha inhibitors (SC-TNFis) have transformed the management of rheumatoid diseases. The assessment of SC-TNFis non-persistence and its impact on medical resource utilization and costs are needed.

Objectives: The objective was to assess the impact of non-persistence to subcutaneous TNF-alpha inhibitors on medical resource utilization and costs, for patients initiating treatment with an SC-TNFi in France.

Methods: The Système National d'Information Inter-régime [French national health insurance scheme information-sharing system] (SNIIRAM) database lists all outpatient and inpatient healthcare consumption for individuals covered by the general health insurance scheme. Using French claims data, conditions were diagnosed using Long Term Disease status and hospital admission, based on ICD-10 codes of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. Patients were then identified through first-line prescription filled for adalimumab (ADA), etanercept (ETA), certolizumab pegol (CZP) and golimumab (GLM) between 2012/07/01 and 2012/12/31. 12-months persistence status was

Abstract THU0605 – Table 1. Comparison of overall costs between persistent and non-persistent patients (n=1,575)

	Mean cost/patient (SD)			P-value
	Persistent	Non-persistent	Difference (persistent – Non persistent)	
Drugs costs	10,726.29 (6,285.74)	7,443.47 (10,199.31)	3,282.82 (-3,913.57)	<0.0001
Biotherapies	9,520.45 (3,601.16)	3,807.88 (4,887.48)	5,712.57 (-1,286.32)	<0.0001
Others	1,205.84 (5,596.59)	3,635.59 (9,818.49)	-2,429.75 (-4,221.89)	<0.0001
Non-drugs costs	3,066.42 (4,765.38)	4,658.24 (6,330.43)	-1,591.81 (-1,565.04)	<0.0001
Including sick leave compensations	525.00 (2,029.22)	1,162.55 (3,309.37)	-637.55 (-1,280.15)	<0.0001
Hospital admissions	1,234.64 (3,957.32)	3,712.15 (7,124.84)	-2,477.50 (-3,167.52)	<0.0001
Total cost	15,027.36 (10,268.24)	15,813.86 (16,976.21)	-786.50 (-6,707.97)	0.0495

estimated with Kaplan Meier analysis. A patient was considered as non-persistent in the event of a prolonged interruption of the therapy during 91 days or more. Persistent and non-persistent patients were compared, after a 1:1 propensity score matching, in term of medical resource utilization and costs (from a National Health Service perspective) in the subsequent 12-month period.

Results: Among 3,804 patients initiating treatment with an SC-TNFi in France between 2012/07/01 and 2012/12/31, 2,133 were classified as persistent at 12 months and 1,671 as non-persistent. After the 1:1 propensity score matching, 1,575 patients were studied in each group. Persistent patients had a lower overall cost than non-persistent patients (-787€): persistent patients had higher costs for drugs (+3,283€), due to the cost of biotherapies, but had lower costs associated to non-drugs (-1,592€) and hospital admissions (-2,478€).

Conclusions: The results indicate that persistence to treatment with SC-TNFi may be associated with cost offsets in terms of non-biologic costs, particularly for hospital admissions. However, as always the case with observational data, residual confounding factors could explain part of the results (e.g. disease severity).

Disclosure of Interest: M. Belhassen Employee of: PELyon, F. Tubach: None declared, C. Hudry Consultant for: ABBVIE, MSD, BMS, PFIZER, ROCHE, CELGENE, NOVARTIS, BIOGEN, UCB, SANDOZ, AMGEN., Employee of: COCHIN Hospital, M.-C. Woronoff: None declared, L. Levy-Bachelot Employee of: MSD France, L. Lamezec Employee of: MSD France, E. Van Ganse Consultant for: PELyon; ALK ABELLO; AstraZeneca; Bayer; BMS; BIF; GSK; IMS; LASER; MSD, B. Fautrel Grant/research support from: AbbVie, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgène, Hospira, Janssen, Lilly, MSD, NORDIC Pharma, Pfizer, Roche, SOBI, UCB

DOI: 10.1136/annrheumdis-2017-eular.2129

THU0606 COGNITIVE DYSFUNCTION IN CONNECTIVE TISSUE DISEASES

A. Dima [1], L. Groseanu [1,2], A. Balanescu [1,2], D. Predeteanu [1,2], D. Opris-Belinski [1,2], A. Borangiu [1,2], D. Mazilu [1,2], V. Bojinca [1,2], R. Ionescu [1,2]. *[1] Internal Medicine and Rheumatology, Sf Maria Clinical Hospital; [2] Department 5 - Internal Medicine, University of Medicine and Pharmacy Carol Davila, Bucharest, Romania*

Background: Several studies documented the presence of cognitive dysfunction in different rheumatologic autoimmune diseases, but the absence of standard criteria of diagnostic and of an index with patients in which this dysfunction occurs, makes the mentioned studies often lead to divergent conclusions.

Objectives: To evaluate the impact of four autoimmune diseases:Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Systemic Sclerosis (SSc) and Ankylosing Spondylitis (AS) on patient cognition and to identify potential factors which lead to cognitive dysfunction occurrence in this diseases.

Methods: This is a case-control study that included randomly selected patients with SLE, RA, SSc and AS from a University hospital and a matched control group. Data collected included: demographics, patients' education and specific data related to disease (duration, activity scores: DAS284v for RA patients, BASDAI in patients with AS, SLICC/SLEDAI for SLE patients and EUSTAR score/Rodnan score for SSc patients, damage indexes, organ involvement, treatment) and comorbidities. Cognition was assesed using MoCA Test (Montreal Cognitive Assessment The Test). The data were then processed using SPSS 23 version software.

Results: The study group included 255 patients: 58 RA patients, 52 SLE, 70 SSc and 25 AS patients and 50 healthy matched controls.

In all groups of patients, cognitive dysfunction prevalence was higher than control group (RA-64.98%, SLE -57.69%, SS -44.29%, AS -35.72% vs. 24% in the control group).

The differences were statistically significant for the RA group (p=0.00), the SLE group (p=0.001), and the SS group (p=0.001).

For the RA group none of the items analyzed (demographics, disease characteristic, patient' education) showed a significant correlation with cognitive dyfunction.

The same lack of correlation was also noted in AS and SSc patients. For the SLE group the only variable analyzed with a significant impact statistically was the SLEDAI score over 12 (p=0.002).

Also, this study did not find a significant statistically association between the presence of antiphospholipid syndrome.

Cognitive dysfunction seems to be more frequent and severe in RA and SLE patients compared to AS patients (p=0.014, respectively p=0.05).

Conclusions: The results obtained in this study show that, indeed, cognitive dysfunction is an issue to be watched very carefully in patients with autoimmune diseases. The appearance of cognitive dysfunction has a negative impact on life quality of these patients, the pathophysiological mechanisms that contribute to it's appearance are intricate and difficult to isolate.

References:

[1] Sabbadini MG, Manfredi AA, Bozzolo E, et al. Central nervous system involvement in systemic lupus erythematosus patients without overt neuropsychiatric manifestations. Lupus 1999; 8: 11–19.

[2] L. Groseanu, T. Gudu, R. Ionescu. Significance of cognitive impairment in systemic sclerosis. Ann Rheum Dis2016;75(Suppl2): 526.

[3] Appenzeller S, Bertolo MB, Costallat LT. Cognitive impairment in rheumatoid arthritis. Methods Find Exp Clin Pharmacol 2004;26:339–43.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5206

THU0607 RISK FACTORS FOR EARLY RETIREMENT IN SYSTEMIC SCLEROSIS

A.M. Gheorghiu [1,2], C. Vrancianu [1,2], C. Draganescu [1,2], R. Oneata [1,2], L. Macovei [1,2], M. Sasu [1,2], M. Milicescu [1,2], O. Olteanu [1,3], M. Speriatu [1,2], M. Bojincă [1,2], V. Stoica [1,2], C. Mihai [1,2]. *[1] Carol Davila University of Medicine and Pharmacy; [2] Internal Medicine and Rheumatology; [3] Cantacuzino Hospital, Bucharest, Romania*

Background: Systemic sclerosis (SSc) is a connective tissue disease characterized by skin and internal organs fibrosis, microvascular impairment and frequently by disability and early retirement.

Objectives: To assess employment status, risk factors for early retirement (ER) and the associations of ER with disease characteristics and with patients' health-related questionnaires (Scleroderma Health Assessment Questionnaire (SHAQ)) and hand function (Duruoz hand index (DHI)).

Methods: This study included patients with SSc according to the 2013 ACR/EULAR classification criteria, examined in our EUSTAR center from 11.2011 to 11.2016, who were under the legal age of retirement of in our country (62 years). Patients completed a work assessment questionnaire, the DHI and the SHAQ, as well as a full assessment as per the recommendations of EUSTAR.

Logistic regression was used to investigate the associations between employment status (outcome) and potential predictors (including socio-economic status, education, disease characteristics and health-related questionnaires).

Results: There were 66 patients (8 males, mean±SD age 49.1±9.3 years, 19 with diffuse cutaneous SSc (dcSSc), 46 with history of digital ulcers (DUs) and 23 with joint contractures) included. Forty-two patients lived in urban environments and 42 had higher education (high school or above).

Twenty patients were active professionally, whereas 46 were retired, of which 32 retired because of SSc. Of those active professionally, 8 had to do manual labor, 7 had to spend many hours at work standing and 3 had a cold or moist work environment.

Using logistic regression adjusted for age and gender, higher education was found to be highly associated with employment (OR (95% CI) 9.0 (1.5, 52.4)), whereas labor conditions (manual labor, stress) had no significant influence on employment status in our cohort. No association was found between employment status and disease characteristics or SHAQ and DHI questionnaires.

Conclusions: SSc is associated with substantial work disability and unemployment. Completing less education than high school was associated with early retirement.

Acknowledgements: ** This abstract was realized as part of the "Development of a computer-based nailfold videocapillaroscopy (NVC) system for longitudinal evaluation of patients with systemic sclerosis" (QUANTICAP) project, financed by the UEFIS-CDI PN-II-PT-PCCA-2013–4-1589 grant.*

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5892

THU0608 ASSOCIATION BETWEEN ALLOPURINOL DOSE-TITRATION AND SERUM URIC ACID LEVELS IN GOUT PATIENTS: US ELECTRONIC HEALTH RECORD DATA

A.-C. Fu [1], D.C. Taylor [2], D.S. Reasner [2]. *[1] Ironwood Pharmaceuticals, Inc., Cambridge, Ashmore and Cartier Islands; [2] Ironwood Pharmaceuticals, Inc., Cambridge, United States*

Background: Allopurinol is a first-line urate lowering therapy for patients with gout. The American College of Rheumatology guidelines recommend allopurinol dose-titration to maintain serum uric acid (sUA) levels <6 mg/dl.

Objectives: To understand allopurinol dose-titration relative to sUA levels.
Methods: This retrospective study used the de-identified Humedica electronic medical record database. The study included all sUA and allopurinol records among gout patients (ICD-9-CM: 274.xx) ≥18 years old with first gout diagnosis in 2007 – 2015. An episode was defined as an allopurinol initial dose (ID) prior to (closest) and titrated dose (TD) after (within 30 days) an sUA test. Dose-titration was categorized as an episode with a dose-change (up-titration: ID < TD; down-titration: ID > TD), or no-dose-change (ID = TD). For multiple different doses recorded on the same prescription date, the sum of doses was taken as daily dosage. Episodes were considered uncontrolled when sUA ≥6 mg/dl. Descriptive episode-level analyses were performed.
Results: Within 64,609 episodes, 57% of episodes were uncontrolled (sUA: 6 to <8 mg/dl: 38%; 8 to <10 mg/dl: 15%; ≥10mg/dl: 4%). Seventy-one percent of uncontrolled episodes were no-dose-change, 21% were up-titrated, and 7% were down-titrated. Within no-dose-change episodes, 51% were uncontrolled and lower doses corresponded to higher percentages of uncontrolled episodes (<100mg/day: 88%; 100mg/day: 70%; >100, <300 mg/day: 49%; 300mg/day: 38%; >300mg/day: 36%). Seventy-eight percent of dose-change episodes were uncontrolled, of which 100 to 300 mg/day (39%) was the most frequent dose titration. Overall, the most frequent TD was 300 mg/day (52%) followed by 100mg/day (36%), >100 – <300mg/day (8%), >300mg/day (3%), and <100mg/day (<1%).
Conclusions: Allopurinol dose is not generally titrated regardless of sUA control. This pattern suggests a need for active management of patients with gout with uncontrolled sUA including consideration of new treatment options in addition to allopurinol.
References:
[1] Juraschek SP et al. Gout, urate-lowering therapy, and uric acid levels among adults in the United States. Arthritis Care Res (Hoboken). 2015 Apr;67(4): 588–92.
[2] Khanna D et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. Arthritis Care Res (Hoboken). 2012 Oct;64(10):1431–46.
Acknowledgements: This study was funded by Ironwood Pharmaceuticals.
Disclosure of Interest: A.-C. Fu Employee of: Employee of Ironwood Pharmaceuticals, D. Taylor Employee of: Employee of Ironwood Pharmaceuticals, D. Reasner Employee of: Employee of Ironwood Pharmaceuticals
DOI: 10.1136/annrheumdis-2017-eular.6314

THU0609 REGIONAL DIFFERENCES IN HEALTH CARE UTILIZATION IN THE KHOALA COHORT, A FRENCH POPULATION BASED COHORT OF SYMPTOMATIC KNEE AND/OR HIP OA PATIENTS

A.-.-C. Rat[1,2], J.-H. Salmon[3], A. Saraux[4], C. Gard[5], F. Guillemin[1,6], B. Fautrel[7]. *[1]Ea 4360 Apemac, Lorraine Université; [2]Rheumatology, CHRU Nancy, Nancy; [3]Rheumatology, CHU Reims, Reims; [4]Rheumatology, la Cavale blanche University, hospital and université de Bretagne occidentale, Brest; [5]Pharmacy, Pitié Salpetrière hospital, Paris; [6]CIC 1433 Epidémiologie clinique, Inserm, CHRU, Université de Lorraine, Nancy; [7]Rheumatology, Université Pierre et Marie Curie (UPMC)-Paris 6 GRC-UMPC 08 (EMOIS), Paris, France*

Background: In hip and knee OA, one of the leading causes of global disability, recent population-based data of health care practices and utilization are scarce. Describing patterns of care of patients is important to adapt health care practices and guide interventions to optimize patients' use of health care services.
Objectives: The aim of the project was to describe health care utilization and associated factors of a representative sample of patients with knee or hip symptomatic OA.
Methods: The KHOALA cohort is a French population-based multicenter cohort of patients with symptomatic knee and/or hip OA, aged between 40 and 75 years old recruited between 2007 and 2009. The representativity of the cohort allows for generalizing the results
Results: Among the 878 patients, 609 (69%) were women, 222 (25%) have hip OA, 607 (69%) knee OA and 49 (6%) both hip and knee OA. Groll comorbidity index (0–18) was 3.1 (1.6). Radiographic K&L grades 2, 3 and 4 were 69.8%, 26.1% and 4.1% for hip OA respectively and 44.5%, 30.3%, and 25.2% for knee OA.
In multivariate analyses, increased pain was independently associated with increased number of patients using pain killers (non-opioids and weak opioids), symptomatic slow-acting drugs or steroid injections but not NSAIDs. Increased age or being retired was associated with increased use of non-opioid drugs or decreased prescription of NSAIDs but not with opioid drugs. Weak opioid drugs were more frequently used by patients with low than high education and by those consulting a rheumatologist. The geographical effect was important, independently of the symptoms, with OR=0.3 (95% CI 0.2–0.7) and OR=0.5 (95% CI 0.2–0.9) for south vs north/east and west vs north/east respectively for weak opioids use with the same trend for non-opioids use. On the opposite, physiotherapy was more frequently prescribed in the south than in the north OR=2.1 (95% CI 1.3–3.5). More patients consulted a rheumatologist in large (>50,000) than small cities (<2,000) OR=2.8 (95% CI 1.6–5.1) but this was not the case for orthopedic surgeons consultations. Pain was not independently associated with consultations with the different health care professionals. Instead the number of patients consulting different health care professionals increased with functional impairment. Consulting an orthopedic surgeon was less frequent for patients with more comorbidities, retired, with decreased vitality or who also did not consult a rheumatologist.
Conclusions: Even if symptoms and patients characteristics are strongly associated with treatments use and health care professional consultations, regional or rural vs cities differences are important independently of pain, function or other quality of life domains. Whether these differences are due to health care professional prescriptions or patients life style and behaviors are still to be explored.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6322

THU0610 RHEUMA SPACE: STANDARD PRACTICE AIMING CLINICAL EXCELLENCE IN RHEUMATOLOGY

C. Macieira[1], L. Cunha-Miranda[2], P. Nero[3], P. Lucas[4], J. Eurico da Fonseca[1,5], J. Canas da Silva[6] on behalf of Rheuma Space study group. *[1]Department of Rheumatology, Centro Hospitalar Lisboa Norte; [2]Department of Rheumatology, Instituto Português de Reumatologia; [3]Department of Rheumatology, Hospital CUF Descobertas, Lisbon; [4]QuintiliesIMS, Porto Salvo; [5]Faculdade de Medicina da Universidade de Lisboa, Lisbon; [6]Department of Rheumatology, Hospital Garcia de Orta, Almada, Portugal*

Background: The quality of medical care and the implementation of measures to improve it are crucial steps for the development of Rheumatology in Europe. Quality indicators were obtained through a four-step rand-modified Delphi methodology. A final set of 26 quality indicators was defined within Donabedian framework dimensions: 9 "structure", 11 "processes" and 6 "outcomes" indicators. Herein we describe the second implementation phase of a national program, Rheuma Space (RS), aiming at quality improvement in Rheumatology.
Objectives: To develop a quality improvement plan for care provided by Rheumatology Departments (RD). In this second phase we present the results of the RD evaluation.
Methods: A measurement scale on quality/excellence thresholds was developed for each of the 26 criteria. Eight RD participated in the project and each one set up an Investigation Team of 2–3 members for field criteria measurement and evaluation that required the use of different data sources and focused on the period: 2014 – 1st semester of 2015. After data analysis an individual report was delivered and discussed with each of the 8 RD. Afterwards public presentation and discussion of the results took place.
Results: "Structure" was evaluated in terms of personal, training, facilities, equipment and budgeting:
- RD lack Rheumatology specialists and need fully dedicated nurses
- Training plans exist in all RD, but physicians allocate few time to research
- Equipment is appropriate, nonetheless microscopes and computers could be updated
- Internal contracting is well established and professionals are committed to targets

"Processes" were evaluated in terms of access and medical care, clinical records, physician-patient communication and multidisciplinary patient management:
- Triage criteria for first appointments should be standardized, despite compliance for "High Priority" patients
- Follow up could be more frequent, but direct access in emergencies is guaranteed
- Reuma.pt registry is mainly used for patients under biologics and data completion could improve
- Multidisciplinary care is provided, but patient coverage and specialty diversity can increase.

"Outcomes" were evaluated in terms of clinical outcomes, patient and personal satisfaction:
- Average working absence is <15days/patient/year, but is much higher in more affected patients
- Almost 1/3 of patients requested early retirement at a median age >50years
- Patients are satisfied with provided care and physicians' attitude, but less with RD facilities
- Professionals are satisfied with working environment, however criticize career related aspects.

Conclusions: The 26 quality indicators set the basis of this quality management tool that was applied to 8 Portuguese RD. Strengths and weakness were identified and an individual Department report was elaborated and discussed. Interventions are now being planned based on these results in order to ensure quality standards of structure and process criteria for a patient oriented clinical practice, favouring desirable continuous quality improvement on health outcomes.
Acknowledgements: Investigation Teams from the eight Rheumatology Departments that participated in the Rheuma Space Project.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4122

THU0611 LONG-TERM FOLLOW-UP OF 269 CHILDREN BORN TO MOTHERS WITH SYSTEMIC AUTOIMMUNE DISEASES: A NATIONAL SURVEY FROM 24 RHEUMATOLOGY CENTERS

C. Nalli[1], L. Andreoli[1], C. Carini[1], M. Rodrigues[2], F. Dall'Ara[1], M.G. Lazzaroni[1], E. Bartoloni-Bocci[3], C.B. Chighizola[4], C. Campochiaro[4], P. Conigliaro[5], A. Corrado[6], S. D'Angelo[7], M. Favaro[8], E. Generali[4], M. Gerosa[4], M. Larosa[8], M. Meroni[9], M. Padovan[10], G. Pazzola[11], S. Peccatori[12], I. Prevete[5], V. Ramoni[13], G. Sebastiani[5], V. Signorini[14], C. Tani[14], M. Trevisani[15], M. Vadacca[5], E. Vivaldelli[16], E. Visalli[17], L. Zuliani[18], A. Afeltra[5], E. Baldissera[4], A. Brucato[19], F.P. Cantatore[6], R. Caporali[13], M. Cutolo[9], A. Doria[8], R. Foti[17], A. Gabrielli[18], R. Gerli[3], M. Govoni[10], A. Maier[16], N. Malavolta[15], P.L. Meroni[4], G. Minisola[5], C.M. Montecucco[13], M. Mosca[14], I. Olivieri[7], G. Paolazzi[12], R. Perricone[5], N. Romeo[20], A. Ruffatti[8], M.G. Sabbadini[4], C. Salvarani[11], C. Selmi[4], L. Sinigaglia[4], A. Tincani[1]. *[1]-, Brescia, Italy; [2]-, Coimbra, Portugal; [3]-, Perugia; [4]-, Milano; [5]-, Roma; [6]-, Foggia; [7]-, Matera-Potenza; [8]-, Padova; [9]-, Genova; [10]-, Ferrara; [11]-, Reggio Emilia; [12]-, Trento; [13]-, Pavia; [14]-, Pisa; [15]-, Bologna; [16]-, Bolzano; [17]-, Catania; [18]-, Ancona; [19]-, Bergamo; [20]-, Cuneo, Italy*

Background: Rheumatic diseases (RD) affect women during reproductive age. Children's outcome is a major topic for counselling on family planning, but no large studies are available.
Objectives: We aimed at assessing the long-term health conditions of children born to mothers with RD through a self-reported questionnaire.
Methods: 24 Rheumatology Centers distributed the questionnaire (65 multiple choice and 12 open-answer questions) to consecutive women with RD attending their outpatient clinic during September 2015. Data were compared according to maternal diagnosis (MD) -chronic arthritis (CA) or connective tissue disease (CTD)- and to the timing of pregnancy (before or after MD of RD).
Results: The survey yielded data about 269 children born to 184 mothers (63 CA, 121 CTD). According to MD, children had a mean age of 17.1 (±9.6 SD) and 14.4 (±9.0 SD) years at the time of interview, and male children were 52/93 (56%) and 91/176 (52%), respectively. Twenty-nine children in the CA group (31.2%) and 64 in the CTDs group (36.4%) were born after MD of RD. Pre-term delivery (before 37 weeks) was observed in 48 cases (17.8%), mostly children born to mothers with CTD (37/48, 77%).
Regarding school performance, 12 children (4.5%) repeated one year of school, in 7 cases for indolence, in 3 for learning disabilities (LD)/health problems (HP), in 2 for family problems. Eleven of these children were born before MD. Overall, 9 children (3.3%) were diagnosed with a LD and 53 children were affected by HP requiring either hospitalization or evaluation by a Specialist (Table). Three children (1%) were affected by autoimmune disease.

269 children born to mothers with RDs	Children born to women with CA (n=93)	Children born to women with CTDs (n=176)
LEARNING DISABILITIES AND NEURODEVELOPMENTAL DISORDERS n=9/269 (3.3%)		
BEFORE maternal diagnosis	1/64 (1.6%) 1 "slow learner" (1 SGA female)	4/112 (3.6%) 2 LD; 1 ADHD; 1 Autism Spectrum Disorder
AFTER maternal diagnosis *In utero* exposure: - to drugs - to maternal autoantibodies	0/29 (0%)	4/64 (6.3%) 3 LD; 1 ADHD n=3 (3 low dose prednisone; 1 azathioprine) n=4 (3 ANA, 2 anti-dsDNA, 2 anti-Ro/SSA, 2 aCL IgG)
HEALTH PROBLEMS (ACUTE AND CHRONIC DISEASES) n=53/269 (19.7%)		
BEFORE maternal diagnosis	12/64 (18.8%) 1 Juvenile Rheumatoid Arthritis; 1 Diabetes Mellitus type 1; 8 AD; 2 Pneumonitis	23/112 (20.5%) 1 Chronic Autoimmune Thyroiditis; 1 Early infantile epileptic encephalopathy; 1 perinatal death (respiratory distress); 3 CD; 5 AD; 4 acute disease*; 4 chronic disease*; 4 surgery
AFTER maternal diagnosis	3/29 (10.3%) 1 Trisomy 21; 1 Enterovirus meningitis; 1 CD+AD	15/64 (23.4%) 1 FUO; 3 CD; 5 AD; 1 acute disease*; 2 chronic disease*; 3 surgery

aCL: anti-cardiolipin antibodies; AD: Atopic Dermatitis; ADHD: Attention Deficit and Hyperactivity Disorder; ANA: anti-nuclear antibodies; anti-dsDNA: anti-double stranded DNA antibodies; CD: Celiac Disease; FUO: Fever of Unknown Origin; LD: Learning Disabilities (dyslexia, dyscalculia, dysgraphia); SGA: small for gestational age; *non-neurological, non-immunological, non-infectious conditions.

Conclusions: The long-term follow-up of children born to women with RD is reassuring of an outcome similar to that of the general pediatric population (GPP). Autoimmune diseases are not frequent. Problems seem to cluster in children born to CTD, especially after MD, with a higher frequency of LD (6.3% vs 2.5–3.5% of GPP), but no particular pattern of exposure to maternal autoantibodies nor drugs was observed.
Acknowledgements: Statistical analysis supported by an unrestricted grant by UCB Pharma
Thanks to Patients Associations and Participants to the survey
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1844

THU0612 PROVIDING HEALTHCARE FOR THE POOREST IN EAST INDIA – A REPORT FROM A CHARITY INITIATIVE, SHAKUNTALA HOSPITAL

C.H. Brahe, U. Rydholm, M. Pikwer, K. Schreiber, C. Ståhl-Hallengren, B. Bylander, R. Dash. *The Indo-Swedish Rheumatology Foundation (ISRF), Malmø, Sweden*

Background: The region of Odisha in India has a population of over 40 million people and 45% are living in poverty. Approximately one percent of the population is affected by inflammatory rheumatoid diseases. In order to provide early diagnosis and adequate treatment initiation to prevent long term disability, patients require easily accessible basic health care and rheumatologists.
Accessible and affordable health care for patients with inflammatory diseases may not only improve disease diagnosis and management, but also improve their quality of life significantly
Objectives: The aim of our abstract is:
1) To raise awareness of the need of support for common rheumatoid diseases in the developing world
2) To present Shakuntala Hospital as an example of a successful charity initiative
Methods: The Indo-Swedish Rheumatology Foundation (ISRF) is an association of physicians whose main aim is to raise awareness, fundraise and to provide health care for patients suffering from inflammatory arthropathies. In order to bridge the gap between our advanced level of knowledge and treatment options in the western world and patients suffering from rheumatologic diseases in the Indian state Odisha we have established this unique association. ISRF, including Shakuntala Hospital, was founded in 2013 and has so far not only provided health care through diagnostic and treatment support, but also ensured patient education and physiotherapy. Health camps are organized in the peripheral communities in order to screen, diagnose and initiate first line treatment and refer these patients for follow-up care to Shakuntala Hospital for further treatments with disease modifying antirheumatic drugs (DMARD), disease monitoring and physiotherapy. Shakuntala Hospital is an example of a non-profit hospital with the aim to provide health care amongst the poorest areas in India.
Results: We have so far registered over 2,000 patients under our care, which includes patients registered in Shakuntala Hospital and in our peripheral care health camps. So far we have established outpatient care for patients with inflammatory arthritis in the districts of Balasore, Maurbhanja, Bhddark, Keonjhar, Jajpur districts of Odisa and Mednapur district of West Bengal and raised more than 32.000 Euro by ISRF from fundraising initiatives.
Inspired by a Swedish model our osteoarthritis (OA) school was founded in October 2016 providing 6 week training courses with the main focusing on patients with knee OA.
Furthermore, ISRF has increased awareness of skeletal fluorosis and provide a comprehensive focus with cleaning of drink water in co-operation with the Royal Technical High School in Stockholm.



Conclusions: Shakuntala Hospital is an example of a successful charity initiative in order to provide healthcare for the poorest patients in East India. Awareness needs to be risen in order to further foster future support for Shakuntala Hospital.
References:
[1] http://www.shakuntalahospital.com/.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4424

THU0613 EXPLORING THE IMPACT OF HEALTH STATUS AND WELL-BEING OF PEOPLE WITH INFLAMMATORY ARTHRITIS ON PRESENTEEISM IN THE WORKPLACE: A QUALITATIVE STUDY

C.J. Jones[1], K. Payne[1], B. Gannon[2], S. Verstappen[3]. *[1]Manchester Centre for Health Economics, The University of Manchester, Manchester, United Kingdom; [2]Mater Research Institute Chair in Health Economics, Centre for Business and Economics of Health, Brisbane, Australia; [3]Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research, Manchester, United Kingdom*

Background: Presenteeism can be defined as the reduction in work performance due to ill-health at the workplace. Musculoskeletal conditions, including

inflammatory arthritis (IA), are one of the most common causes for presenteeism. There are no "gold standard" methods to identify, measure, or value the impact of presenteeism. Some evidence suggests the impact of presenteeism can be indirectly estimated using measures of health status and well-being.

Objectives: To explore whether selected measures of health status and well-being, commonly used in economic evaluations are conceptually useful to capture those aspects of IA that are associated with presenteeism.

Methods: A sample of individuals, aged 18 years and above, working in the UK with rheumatoid arthritis (RA), ankylosing spondylitis (AS), or psoriatic arthritis (PsA), was recruited via patient support groups. Semi-structured telephone interviews were designed to understand if, and how, RA, AS or PsA affects an individual's ability to work. Framework Analysis Methods were used and coding involved deductive and inductive approaches. A deductive approach was used to derive potential themes from measures of health status [EuroQol-5 Dimension-5 level (EQ5D-5L) and Short Form 6 Dimension (SF6D)], and well-being [(ICEpop CAPability measure for Adults (ICECAP-A)]. An inductive approach was used to generate other themes not captured by these measures.

Results: Twenty-two employed individuals with RA (n=10), AS (n=9) or PsA (n=3) were interviewed; 82% were female and, of the 22 patients, 23% had a manual job. The majority of interviewees explained that symptoms of the conditions increase levels of presenteeism, including: pain; stiffness; fatigue; emotional mental health; mental clarity. These symptoms make completing activities at work difficult, which, in turn, affects an individual's capability to maintain a successful career. The ICECAP-A was found to be a useful measure to capture the overall impact of presenteeism resulting from RA, AS or PsA. The SF6D and EQ5D were more specific measures capturing particular symptoms and activities that increase levels of presenteeism (see Table 1).

Table 1

	Measure		
Theme	ICECAP-A	SF6D	EQ5D
Achievement /Progress	x		
Decisions	x		
Energy	x	x	
Independence	x		
Mental Health	x	x	x
Mobility	x	x	x
Pain	x	x	x
Self-care	x	x	x
Settled /Secure	x		
Social Interaction	x		
Support	x		
Usual Activities	x	x	x
Vigorous Activities	x	x	

Two further themes were identified using inductive methods: mental clarity and feeling understood. The effect of mental clarity or feeling understood is not captured by any of the domains in EQ-5D-5l or SF6D. The ICECAP-A is potentially able to capture the impact of these themes in the respective domains ability to achieve and progress and ability to gain support.

Conclusions: This study suggests that three existing measures (EQ5D, SF6D, and ICECAP-A) were successful, in different degrees, to capture the impact of presenteeism that result from the aspects and symptoms of IA. Potentially, these measures may be used in economic evaluations to capture the impact of presenteeism.

Acknowledgements: This work was supported by Arthritis Research UK and the Medical Research Council [20665]

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1803

THU0614 FIDELITY OF AN INTERVENTION TO INCREASE PHYSICAL ACTIVITY IN OLDER ADULTS WITH CHRONIC PAIN: ANALYSIS OF AUDIO-RECORDED CONSULTATIONS FROM THE IPOPP PILOT TRIAL

C. Jinks [1], J. Proctor [1], E.L. Healey [1], J. McBeth [2], C.A. Chew Graham [1] on behalf of iPOPP team. *[1]Research Institute for Primary Care & Health Sciences, Keele University, Keele; [2]Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, United Kingdom*

Background: Physical activity levels are low in people >65 years and those with chronic musculoskeletal pain, yet increased physical activity can lead to reduced pain. Walking is acceptable to older people with pain, but interventions to increase walking in this population are untested. The iPOPP pilot trial investigated feasibility and acceptability of a walking intervention delivered by trained Health Care Assistants (HCAs) in 4 general practices in an individually randomised three arm trial (usual primary care, pedometer only and iPOPP, n=50 each arm). The iPOPP intervention comprised two consultations (1 week apart) and 8 weekly follow-up prompts (postcard, email or text).

Objectives: To investigate fidelity of the iPOPP intervention to inform design of a full-scale randomised controlled trial.

Methods: HCAs were asked to record 6 consultations (3 participants, first and second consultation). A fidelity checklist was developed (aligned to HCA training) and included activities expected (pedometer, user guide, walking diary, pain toolkit given; discussion of walking behaviour and barriers; action planning to develop walking goals; review of progress; positive feedback; revision of goals; relapse prevention strategies; and, preference for weekly prompts). Activities were scored as "Yes" (completed as intended), "partial" (some evidence), "No" (no evidence) or "NA" (not applicable). The checklist was applied to one recording (JP, CCG, CJ). Minor amendments clarified interpretation of checklist headings before application to 3 more recordings (JP, CCG). JP then scored remaining recordings (n=14).

Results: 3 HCAs recorded 18 consultations (9 first, 9 second). Most first consultations did not use the allocated 30 minutes (average 14 minutes). The pedometer, user guide, walking diary and pain toolkit were all given but there was a lack of explanation of the pain toolkit. Evidence of the benefits of walking on pain was well delivered (N=8), motivators to walk and goals were discussed in all 9, with goals set in 7. Barriers to walking were not always discussed (N=4) exploration of maintenance strategies lacking, especially with those patients who perceived themselves as already physically active. All HCAs arranged a second consultation within one week which were brief (average 6.5 minutes) and focused mainly on use of the pedometer. Patient goals were partially re-visited (N=7) and barriers to walking partially addressed (N=5). Maintenance strategies were not discussed (N=8).

Conclusions: Core iPOPP intervention components were well delivered. However we have identified areas to optimise ahead of a full-scale trial (how to discuss barriers to walking and maintenance strategies, development of motivational interviewing skills to support revision of goals, HCA knowledge of local activities). These findings will be triangulated with data from interviews with HCAs and participants to provide further evidence of the feasibility and acceptability of the iPOPP intervention.

Acknowledgements: Keele Clinical Trials Unit, Keele University supported the trial. ELH, CJ, and CCG are part funded by the NIHR Collaborations for Leadership in Applied Health Research and Care West Midlands. The views expressed in this paper are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3232

THU0615 PARTICIPANTS' EXPERIENCE OF THE MAKING IT WORK PROGRAM, AN ONLINE PROGRAM TO HELP PEOPLE WITH INFLAMMATORY ARTHRITIS REMAIN EMPLOYED

A. Li [1], C. Backman [1,2], B. van As [1], P. Rogers [1], M. Gignac [3,4], L. Li [1,2], J. Esdaile [1,2], D. Lacaille [1,2]. *[1]Arthritis Research Canada, Richmond; [2]University of British Columbia, Vancouver; [3]University of Toronto; [4]Institute of Work and Health, Toronto, Canada*

Objectives: Health services addressing employment needs for people with arthritis are lacking. To address this need, we developed the Making it Work (MiW) program, an online self-management program aimed at helping people with inflammatory arthritis (IA) deal with employment issues. As part of a randomized controlled trial evaluating program effectiveness, this study reports on participants' experiences with various aspects of the program.

Methods: All participants in the MiW program between Jan20 and Dec7 2016 were included. Participants were recruited from rheumatologist practices, outpatient arthritis programs, a national consumer organization (Arthritis Consumer Experts), and community advertisements in BC, Alberta and Ontario. Eligibility criteria included: having IA; being currently employed; age 18–59 yrs; concern about their ability to work; and access to a computer. The program consisted of 5 online self-learning modules, 5 online group meetings facilitated by a vocational counsellor, an individual ergonomic assessment by an occupational therapist and an online session with a vocational counsellor. Feedback questionnaires were administered online after participants completed the program. Descriptive analyses were performed.

Results: The sample included 69 participants [80% female; mean (SD) age: 45.3 (10.5) yrs; 83% Caucasian; 91% with post-secondary education; 52% with RA, AS: 19%, SLE: 17%; PsA: 12%]. Overall, participants expressed satisfaction with the program with 94.2% agreeing (69.6% strongly and 24.6% somewhat) they would recommend this program to someone they know. When asked to rate program components on a scale of 0–10 where 0=not useful at all and 10=very useful, participants rated all components favourably: median [25Q;75Q] for online modules: 8 [7;10], with highest ratings for the fatigue module (rated 10 by 42%); online group meetings: 9 [7.5;10]; ergonomic and VRC assessments: 8 [7;10] each. Although participants had 2 weeks between meetings to complete the module, 55% did the module the week of, and 42% the day before, the group meeting. Median time to complete each module was 60 min. 81% enjoyed being able to listen to the information (somewhat or strongly agreed), although 35% stated they would have preferred to read the information than listen to a narrator. 74% expect to use the online modules again in the future. Participants were also satisfied with the online group meetings: 93% were very or somewhat satisfied with the group facilitation; 87% satisfied with the group dynamic; 84% comfortable with the online format. When asked to rate their online group meeting experience on a scale of 1 to 10, median [25Q;75Q] ratings for: ability to follow group discussion was 10 [9;10]; getting to know other participants: 7 [7;10]; feeling listened to and understood 9 [8;10]; feeling that group was supportive 9 [7;10]. 20% said it was difficult for them to attend group meetings.

Conclusions: In general, participants were highly satisfied with all aspects of the

MiW program. Our study demonstrates that self-management programs, including group meetings, can be successfully delivered using an online format, which facilitates wider dissemination, with greater convenience to patients, and at lower costs.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5246

THU0616 PATIENTS' PERCEPTION ON DISEASE PROGRESSION AND ADHERENCE TO BIOLOGIC THERAPY

E. Cefai, D. Balzan, C. Mercieca, A.A. Borg. *Rheumatology, Mater Dei Hospital, Msida, Malta*

Background: Adherence to medication depends on several factors such as medication beliefs, psychosocial factors, illness beliefs and concerns. The consequences of non-adherence are not insignificant, both from the clinical and health economic aspects.
Objectives: To assess medication adherence of patients taking biologics who are in remission or who have low disease activity and patients' perception of disease progression.
Methods: Forty-four consecutive patients attending a dedicated biologic clinic and treated with TNF inhibitors were interviewed following their visit. Patients were asked about adherence to treatment, adverse effects, concerns about biologics and their perception of disease progression. Demographic and disease activity data were recorded.
Results: Forty-four patients (23 females, 21 males) participated in the survey (21 suffered from rheumatoid arthritis, 17 from ankylosing spondylitis and 6 from psoriatic arthritis). The mean age was 55.1 (SD 12.62) years. The mean DAS28 was 2.26 (SD 1.03) and the mean BASDAI was 4.21 (SD 2.1). Minimal or no pain was reported by 75%, mild or no fatigue by 78% and 77% had no restriction of activities of daily living. Medication adherence was reported as high by 68% and moderate by 32%. There were no patients who had a low level of adherence. 5% of patients admitted to be unaware of the need to omit their biologic when ill and 40% when requiring surgery.
One out of 4 patients reported to have experienced adverse events, most commonly infections. 19% claimed to be moderately or very concerned about the adverse effects. On further questioning about the severity of potential adverse effects, 45% were unsure as to what the severity might be. When asked about duration of therapy, 29% replied more than 10 years; whilst 71% were unsure on when, if ever, the biologic is going to be stopped. Patients were also asked whether they believed that the biologic had successfully stopped further joint damage and 68% replied yes, 9% replied no, whilst 23% were unsure. Of those who replied yes, this perception was based on the absence or reduction of symptoms.
Conclusions: In this cohort of patients with low disease activity or remission, a third of patients still reported sub-optimal adherence to TNF inhibitor use. The benefits of adherence to biologic therapies need to be reinforced at every visit and factors leading to non-adherence addressed. Adverse effects remain a major concern that needs to be addressed, even in patients who have been on biologics for many years and have sustained remission or low disease activity. A quarter of patients were unsure whether biologics have stopped joint damage. Patients' perception of joint damage progression needs to be explored to find ways of making it more understandable to patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3221

THU0617 INFORMATION ON DISEASE AND TREATMENT OF PATIENTS WITH RHEUMATIC DISEASES TREATED WITH SUBCUTANEOUS BIOLOGICALS: SOURCES AND SATISFACTION. RHEU-LIFE SURVEY

F. de Toro[1], E. Batlle[2], C. González[3], M. Calvo[4], M. Arteaga[4], L. Cea-Calvo[4]. *[1]INBIC, A Coruña; [2]D.Salud Sant Joan, Alicante; [3]H.G.U.Gregorio Marañón; [4]Medical Affairs, Merck Sharp & Dohme, Madrid, Spain*

Objectives: To know the sources by which patients with rheumatic diseases treated with subcutaneous (SC) biological drugs obtain information on their treatment, their satisfaction with the information received from the hospital staff and their perception of the degree of information they have.
Methods: RHEU-LIFE was a survey handed by 50 rheumatologists from Spanish outpatients hospital offices to patients on SC biological drugs. They completed the survey anonymously at home and returned it by pre-paid post-mail. They selected from a list their sources of information (being able to mark all their sources), their satisfaction with the information received from the hospital staff and whether they had sought additional information in other sources.
Results: The survey was handed to 1000 patients and 592 returned it (59.2%, mean age 51.7 years, 57.6% women). The source of information most frequently mentioned was the rheumatologist (table) and, infrequently, the nurse or the hospital pharmacist. 46.1% had received information on the SC biological only orally, 6.0% written and 45.2% in both ways. The percentages quite or very satisfied with the information received were 42.6% and 44.5% respectively, 10.6% felt "neither satisfied nor dissatisfied" and 2.1% and 0.2% dissatisfied or very dissatisfied. The % quite/very satisfied was higher when the information came from the rheumatologist (89.6% vs 59.6% when the rheumatologist was not mentioned as source of information, $p<0.001$), and also when information was given both oral and written (92.8% vs 86.1% if only oral information was given, $p=0.0125$). Some 45.2% had sought information on the SC biological in sources different to the hospital staff, the % being higher among younger patients (<43 years: 65.2%: 43–52 years: 51.4%, 53–61 years: 39.1%, >61 years: 20.6%, $p<0.001$) those with higher education level (without studies: 14.3%, primary: 31.6%, secondary: 55.6%, vocational: 59.5%, university or higher degrees: 64.9%, $p<0.001$), and in those treated with a first biological SC drug (49.9%, vs. 37.7% and 37.2% with a second or third or further, $p=0.014$).

Sources from which patients received information on the different treatments and on the biological drug (patients could mark more than one option)

	General information	Information on the SC biological
Rheumatologist	91.9%	91.0%
Nurse	10.2%	17.9%
Hospital pharmacist	3.2%	11.5%
Other	5.3%	3.6%
Do not remember	1.2%	0.8%
Did not receive any information	0.8%	1.7%

Conclusions: Patients with rheumatic diseases mention the rheumatologist as their main source of information. The % who mentioned nurses or pharmacists was low, although the latter are very frequently visited for dispensing the drug. Satisfaction with the information received was high, but clearly lower when the rheumatologist did not inform the patient. Nearly half reported having sought information in sources other than the hospital staff.
Acknowledgements: Endorsed by ConArtritis (National Coordinator of Patients with Arthritis). Funded by Merck Sharp & Dohme of Spain
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3214

THU0618 THE FACTORS AFFECTING WORKPLACE AND HOUSEHOLD LIFE IN ANKYLOSING SPONDYLITIS: A MULTI-DIMENSIONAL STUDY

B. Taser[1], F.F. Ayhan[1,2], P. Borman[1,3], A. Karagöz[1]. *[1]Physical medicine & rehabilitation, Ankara Training and Research Hospital, Ankara; [2]Physical therapy & rehabilitation, Uşak University, School of Health Sciences, Uşak; [3]Physical medicine & rehabilitation, Hacettepe Medical School, Ankara, Turkey*

Background: Work disability (WD) is the final stage of work problems and may be prevented by effective treatment and ergonomic interventions in earlier stage of work productivity loss and work instability. Contextual factors, disease related factors and local social security systems may also affect WD.
Objectives: We aimed to determine the predictive factors of work productivity and work stability in Turkish patients with ankylosing spondylitis
Methods: One-hundred patients with ankylosing spondylitis (31 females and 69 males) were included into this study. Demographics, working state, Bath scores of disease activity, functional and radiologic state, quality of life, cardiopulmonary functions (echocardiography, exercise stress test and pulmonary function test) and general work impairments (work productivity impairment and work instability) were recorded. WPAI and AS-WIS were selected as work outcomes. The most predictive factors were analyzed in work productivity and work instability. SPSS 14.0 statistics (descriptives, pearson correlation, and stepwise regressions were used for statistical analyses.
Results: Thirty-two patients (mean age: 42,6±11.7) were unemployed. Unemployed patients showed more female, less educated, low disease activity, and low fitness profile. The percentages of absenteeism (WPAI-1), presenteeism (WPAI-2), regular activity impairment (WPAI-3) and overall work impairment (WPAI-4) were determined as 8, 44, % 47, and % 37, respectively, in employee group. When affecting factors assessed with multiple stepwise linear regression analysed; the only determinant for absenteeism (WPAI-1) was the working day loss due to ilness at last year. Chest mobility, annual income level, AS quality of life (ASQoL), work change and co-morbid diseases were the determinants of presenteeism (WPAI-2), regular activity impairment (WPAI-3) and overall work impairment (WPAI-4). The score of mean work instability (AS-WIS) was 11.5±5.8, and 42.6% of patients had low and 57,4% of patients had moderate-high work instability. Multiple stepwise linear regression analysis showed that most predictive factors for work instability were regular activity impairment (WPAI-3) and AS-QoL. The factors affecting non-work status were older age, female sex and low annual income level in stepwise logistic regression.
Conclusions: The common predictive factor of work productivity and work stability was quality of life. For evaluation of work productivity; socioeconomic factors such as annual income level and frequent work change were determinative as well as clinical datas (chest expansion and comorbid diseases). We suggested both pharmacologic and nonpharmacologic interventions to improve quality of life should be enabled in early period to improve work productivity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2550

THU0619 PREVALENCE OF PNEUMOCOCCAL VACCINATION IN RHEUMATOLOGIC PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA. BIOBADASAR REGISTRY

G. Gómez, A. Brigante, A. Benitez, O. Cerda, S. Retamozo, I. Gandino, A. Quinteros, I. Exeni, B. Barrios, P. Astesana, C. Sanchez Andia, M.V. Collado, A. Granel, A.M. Cappuccio, R. Quintana, E. Mussano, A. Smichowski, M. de la Sota, K. Kirmayr, E. Velozo, M.S. Larroude, A. Bertoli, S. Agüero, C. Battagliotti, S. Soaures de Souza, E. Cavillon, A. Bohr, O. Rillo, L. Carlevaris, E. Bedoya, E. Kerzberg, B. Kisluk, I. Petkovic, D. Pereira, J.C. Barreira, L. Somma, C. Costi, F. Melo, B. Virasoro, S. Paira, L. Roa Perez, G. Casado, D.L.V. María Celina.
Sociedad Argentina de Reumatologia, Buenos Aires, Argentina

Background: Biobadasar is a registry that monitors adverse events in patients who use biological treatments in rheumatologic diseases conducted by the Argentine Society of Rheumatology. As in others international registries the community acquired pneumonia (CAP) has been detected as one of the most frequent infectological adverse events. Although all immunosuppressed patients should be vaccinated against streptococcus pneumoniae, there is a proportion of patients who are not.
Objectives: Evaluate the prevalence of pneumococcal vaccination in patients with CAP within the Biobadasar database. Assess factors associated with Severe CAP in these patients.
Methods: A cross-sectional, multicentric study was made in BIOBADASAR database from 2010 to2016.
In patients who reported CAP data of demographics, comorbidities and state of pneumococcal immunization was collected. Microbiological data, treatment and outcome of the event were considered. The severity of CAP was assessed according to the opinion of the attending physician, hospitalization, risk of life and/or death. Values are expressed as mean ± standard deviation, median (ranges) and frequencies (percentages), as appropriate. We performed bivariate and multivariate logistic regression analysis to identify variables associated with the event.
Results: Of the 4029 patients enrolled in the registry, the cumulative incidence of CAP was 4.2% (n 170), 72.4% (n 123) were women. The mean age was 57 (SD +/- 14.5). Biological treatment was found in 81.8% (n 139). Patient s that have received the pneumococcal vaccine were 40.6% (n=69). Severe CAP was detected in 7.1%. Streptococco Pneumoniae was the main pathogen isolated in 13% of the cases. Overall mortality was 4.1%. In the univariate analysis for severe CAP we found statistical significance for Smoking OR 3.88, CI95 1.063–14.22, p= 0.029 and chronic kidney disease (CKD) OR 31, CI95 2.6–376, p= 0.007. When performing a multiple logistic regression model, only renal failure OR 7.39 CI95 0.003–0.38 p= 0.007 was a predictor of severe CAP. Not significative association with immunosuppressive treatment (p: 0.09), age (p: 0.464), or vaccination (p: 0.937)
Conclusions: The annual incidence of CAP in Argentina varies between 0.5 - 1.1% while in our cohort it was four times higher. The prevalence of pneumococcal vaccination was less than 50%, showing that, although the literature and guidelines establish the need for vaccination, this is not so in the real world. In the multivariate analysis, only CKD was related to severe CAP. Although in the univariate analysis the CKD and the smoking habit represented factors associated with severity. We must emphasize the medical education in following the international vaccination guidelines.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5282

THU0620 PERSISTENCE WITH BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS – A RETROSPECTIVE DATABASE STUDY IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS

J. Mahlich [1], H. Kameda [2], R. Sruamsiri [1]. [1] *Health Economics, Janssen Pharmaceutical KK, Tokyo, Japan;* [2] *Toho University Ohashi Medical Center, Tokyo, Japan*

Background: Persistence rate is one of the key benefits of biological disease-modifying antirheumatic drugs (bDMARDs) in the treatment of rheumatoid arthritis (RA). Limited evidence of persistence has been found in Japan and the results are not transferrable across countries and cultures (1–3). In addition, the impact of persistence on healthcare cost is still questionable.
Objectives: To assess persistence rates of bDMARDs for the treatment of RA in Japan and compared resource utilization and treatment costs between persistence and non-persistence groups.
Methods: Data was extracted from a Japanese claims database that included 4,400,000 patients between 2009 and 2015. RA patients who initiated bDMARD treatment (bDMARD-naïve patients) were identified and included in the final analysis. Survival analysis was used to estimated 6-, 12-, and 18- month persistence rates for current bDMARDs. Propensity score matching was applied to control for potential treatment selection bias. Resource utilization and health care costs of treatments were calculated 12 months before and after initiation of bDMARDs treatment and compared between persistence and non-persistence groups.
Results: A total of 6,153 bDMARD-naïve patients were included in the final analysis. The overall 1-year persistence rate was 85% (95% CI, 84–86). Persistence of patients treated with golimumab was higher [92% (95% CI, 89–94)] than that with other bDMARDs. Overall, 1-year outpatient visits increased from 10 at baseline to 16 after bDMARD treatment, while the number of hospital admissions declined from 3.3 to 1.6. Hospital days decreased from 17 at baseline to 12 following treatment. The non-persistence group had a larger increase in outpatient visits after bDMARD initiation compared with the persistence group (8 to 16 vs. 10 to 16, respectively) and a smaller decrease in hospital admissions (3.1 to 1.9 vs. 3.5 to 1.4, respectively). Compared to non-persistence group, persistence was associated with a reduction in total healthcare costs of 760 USD.
Conclusions: Japanese bDMARD-naïve patients with RA have a high persistence rate of bDMARDs. The reduction in medication costs in non-persistent patients is offset by higher hospitalization costs, making non-persistence more expensive.
References:
[1] Dalén J et al. Rheumatol Int 2016;36(7):987–95.
[2] Tang B et al. Clin Ther 2008;30(7):1375–84.
[3] Meissner B et al. J Med Econ 2014;17(4):259–65.
Disclosure of Interest: J. Mahlich Employee of: Janssen Pharmaceutical KK, H. Kameda Grant/research support from: Abbvie GK, Astellas Pharma, Chugai Pharmaceutical Co, Ltd., Eisai Co. Ltd., Mitsubishi Tanabe Pharma Co., Nippon Kayaku Co. Ltd., Santen Pharmaceutical Co. Ltd., Takeda Pharmaceutical Co. Ltd, Consultant for: Eli Lilly Japan K.K., Novartis Pharma K.K. and Sanofi K.K., Speakers bureau: AbbVie GK, Astellas Pharma, Bristol– Myers K.K., Chugai Pharmaceutical Co. Ltd., Eisai Co. Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Nippon Kayaku Co. Ltd., Pfizer Japan Inc., Santen Pharmaceutical Co. Ltd. and Takeda Pharmaceutical Co. Ltd. and UCB Pharma, R. Sruamsiri Employee of: Janssen Pharmaceutical KK
DOI: 10.1136/annrheumdis-2017-eular.2102

THU0621 COMPARISON OF THE EFFECT OF ANTI-TNF THERAPY ON WORK DISABILITY BETWEEN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS OVER ONE YEAR– REAL LIFE DATA FROM THE CZECH BIOLOGICS REGISTRY ATTRA

J. Zavada [1], L. Szczukova [2], J. Vencovsky [1], P. Horák [3], K. Pavelka [1] on behalf of collaborators of the ATTRA registry. [1] *Rheumatology, Institute of Rheumatology, Prague;* [2] *Institute of Biostatistics and Analyses, Faculty of Medicine, Masaryk University, Brno;* [3] *Internal Medicine, Faculty of Medicine and Dentistry, Palacký University, Olomouc, Czech Republic*

Objectives: To compare the effect of anti-TNF therapy (a-TNF-th) on Work Disability (WD) between RA, PSA and AS. In the Czech Republic (CZ), a-TNF-th is reimbursed for RA if DAS28>5.1 despite therapy with csDMARDs, for PSA if disease is not "adequately controlled" with csDMARDs, and for AS if BASDAI>4 and CRP/ESR elevated above normal. More than 95% of anti-TNF treated patients in CZ are followed up in the ATTRA registry.
Methods: Bionäive patients with RA (n=1085), AS (n=1126) and PSA (n=351) starting a-TNF-th with available baseline data on demography, disease duration and physical function, and on working status at baseline and at 12 months were included in the analysis. Patients older than 60 years, on maternity leave or students were excluded. Work status was self-reported by patients as (A) able to work = [(i) employed, or (ii) unemployed and actively seeking employment], or (B) unable to work = [(iii) on sick leave, or (iv) on disability pension]. Regression analyses were performed to examine the predictors of improvement in WD (change B→A coded as 1, B→A as -1, no change as 0) over 1 year.

Table 1. Baseline characteristics

	RA (n=1085)	AS (n=1126)	PSA (n=351)	p-value
Female	836 (77.1%)	263 (23.4%)	161 (45.9%)	**<0.001**[ABC]
Disease duration	8.2±6.6	7.5±6.9	8.2±7.2	**0.002**[A]
Age at start of anti-TNF Therapy	46.6±9.0	38.2±8.8	44.1±9.3	**<0.001**[ABC]
HAQ	1.5±0.6	1.1±0.5	1.2±0.6	**<0.001**[ABC]
Calendar year of starting anti-TNF				
before 2008	420 (38.7%)	306 (27.2%)	90 (25.6%)	**<0.001**[AB]
2009–2012	394 (36.3%)	427 (37.9%)	156 (44.4%)	
2013–2015	271 (25.0%)	393 (34.9%)	105 (29.9%)	

Post-hoc analysis (with Bonferroni correction): statistically significant difference btw groups A) RA vs. AS, B) RA vs. PSA, C) AS vs. PSA. Values or N (%) or mean (SD).

Table 2. Prediction of improvement in work disability

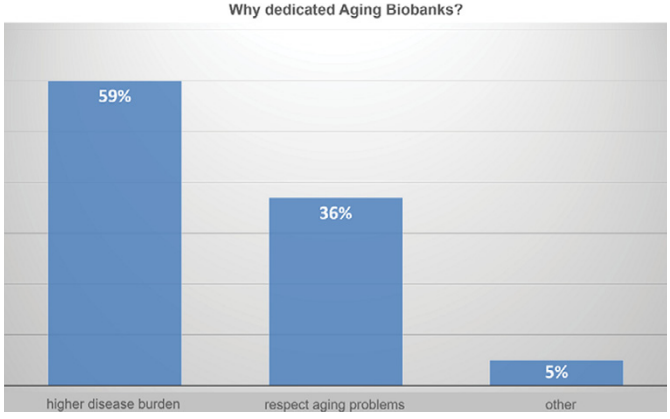
Independent variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Diagnosis				
RA	*reference*		*reference*	
AS	**1.477 (1.150; 1.898)**	**0.002**	**1.466 (1.044; 2.058)**	**0.027**
PSA	1.206 (0.840; 1.731)	0.310	1.226 (0.838; 1.792)	0.293
Female	0.821 (0.651; 1.034)	0.093	0.988 (0.754; 1.295)	0.932
Age at start of anti-TNF therapy	**0.983 (0.971; 0.994)**	**0.004**	0.987 (0.974; 1.001)	0.067
Disease duration	0.992 (0.975; 1.009)	0.341	0.998 (0.980; 1.016)	0.840
HAQ	1.024 (0.839; 1.251)	0.815	1.181 (0.949; 1.470)	0.135
Calendar year of starting anti-TNF				
before 2008	*reference*		*reference*	
2009–2012	0.843 (0.639; 1.113)	0.228	0.799 (0.601; 1.062)	0.122
2013–2015	1.075 (0.804; 1.438)	0.624	1.001 (0.741; 1.352)	0.995

Results: Baseline characteristic were significantly different between diagnoses (Table 1). In patients with RA, 60% were able to work at baseline and 61% at 12 month, with PSA 71% and 74% resp., and with AS 72% and 77% resp. The main driver of improvement of WD was a change in the sick leave (RA 6%→2%, PSA 7%→1%, AS 9%→2%). In univariate analyses, diagnosis of AS and younger age at start of a-TNF-th were predictive of improvement in WD. In multivariate analysis, only diagnosis of AS was significantly associated with improvement in WD.
Conclusions: These real life data from CZ show that for improvement of WD, a-TNF-th was most effective in patients with AS. This may be a sequel of disease specific factors or reimbursement policy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4056

THU0622 PATIENT-CENTERED AGING BIOBANKS - A SURVEY ON PUBLIC PERCEPTIONS AND PATIENT CHOICE AMONG RHEUMATOLOGY OUTPATIENTS

J.V. Cordeiro[1], A. Fernandes[2], C.D. Lopes[3], G. Victorino[4], P. Lobato Faria[1], M.J. Cercas[4], J.C. Branco[5], F.M. Pimentel-Santos[3,5]. *[1]Centro de Investigação em Saúde Pública (CISP), Escola Nacional de Saúde Pública; [2]CICS.NOVA – Centro Interdisciplinar de Ciências Sociais, Faculdade de Ciências Sociais e Humanas, NOVA University of Lisbon; [3]Rheumatology, CHLO, Hospital Egas Moniz; [4]NOVA Information Management School (NOVAIMS); [5]CEDOC, NOVA Medical School|Faculdade Ciências Médicas, NOVA University of Lisbon, Lisboa, Portugal*

Background: Biobanks for research (BBR) are organized repositories of biological materials and associated health information with enormous potential and value for scientific research. In consonance with increasing attention to healthy aging research, BBR specifically oriented to chronic diseases and aging populations have gathered heightened attention. Public perceptions and patient choices are key to design, develop and implement patient-centered BBR. Public awareness, education and involvement are confidence building and unequivocally lead to higher participation in scientific enterprises.
Objectives: To assess patient awareness, perception and choices regarding aging biobanking activities.
Methods: We developed and applied a standard anonymous questionnaire to rheumatology terciary outpatients, aged 50 or older, between March-October 2016. Demographic data and perceptions about biobanking were collected. Data analysis was performed using Stata 14® software.
Results: We obtained a total of 131 valid responses [age (min-max, 50–93), mean (64); sex ratio (M/F) (40/91, 44%), education years (min-max, 0–20), mean (8.5)]. 69% of respondents did not know the specific term "biobank" but 57% were aware about the possibility of donating their biological material for research purposes. Furthermore, 77% of respondents indicated they were willing to contribute with their biological material to BBR, stating they had no particular preference whether these infrastructures were of private or public nature. However, they expressed a clear preference for these to be based at scientific research institutes (50%), instead of hospitals (23%), universities (16%) or biotechnology companies (7%). Moreover, respondents highlighted diferent requirements for their participation with anonymity (31%) and confidentiality (27%) ranking as top priorities. Most importantly, a majority of respondents (70%) expressed their agreement with a biobank exclusively dedicated to the study of aging, considering that people of older ages have higher disease burdens and that such research infrastructures and practices expressed respect for the particular problems of the elderly (Figure).



Conclusions: Our study constitutes a comprehensive assessment of public perceptions and patient choices regarding biobanks for aging research purposes among rheumatology outpatients. Although awareness is still suboptimal, BBR are highly regarded health infrastructures with enormous potential for further patient-centered development.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6527

THU0623 DECREASE IN THE TEMPORARY WORK INCAPACITY DUE TO MUSCULOSKELETIC DISEASES: UTILITY OF A PREVENTIVE PROGRAM IN VALENCIA-LA FE HEALTH AREA

J.E. Oller Rodríguez[1], M.T. Fuente Goig[2], F. Ortiz Sanjuan[1], J. Ivorra Cortés[1], E. Grau García[1], E. Vicens Bernabéu[1], E. Labrador Sánchez[1], K.R. Arévalo Ruales[1], J. Fragio Gil[1], R. González Mazario[1], C.P. Alcañiz Escandell[1], I. Cánovas Olmos[1], I. Chalmeta Verdejo[1], C.M. Feced Olmos[1], L. González Puig[1], I. Martínez Cordellat[1], C. Nájera Herranz[1], R. Negueroles Albuixech[1], J. Andani Cervera[2], J.A. Román Ivorra[1] on behalf of Rheumatology Service. *[1]Rheumatology; [2]Service of Prevention of Occupational Hazards, Hospital Universitari I Politècnic la Fe, Valencia, Spain*

Background: Musculoskeletal diseases are nowadays a frequent cause of temporary work incapacity (TWI). The implementation of specific programs for the care of these patients can be an important cornerstone in the resolution of these TWI processes.
Objectives: Our aim is to analyze the usefulness of an Early Intervention Program (EIP) in patients with TWI of musculoskeletal origin.
Methods: Case-control study, including patients from HUP La Fe area, which were referred from Primary Care since April 2012 to April 2016 to our Early intervention program (EIP) addressed to patients with TWI of musculoskeletal origin. The patients were evaluated in our consultation within a maximum of 15 days after the start of TWI. The intervention consisted in an evaluation, including complementary tests if necessary, diagnosis and treatment by the rheumatologist in consultation. The patient was followed in consultation continuously until discharge. Patients whose disabilities were of traumatic or surgical origin were excluded. A comparative study was carried out against a control group of patients with ILT of musculoskeletal origin.
Results: A total of 666 patients were recruited; 508 (76.3%) belonged to EIP group (46.1% male; 53.9% female) and 158 patients (23.7%) belonged to the control group (44.3% male; 55.7% female).
The average age was 47,6±10.5 years for the EIP ones and 46.7±10 years in the control group.
The most frequent diagnoses were low back pain (23.3%), neck pain (18%) y lumbosciatica (12.3%). In EIP group, 100% of the patients received medical treatment, a 54.5% received instructions for doings physical therapy at home, an ultrasound scan was performed to the 26,4% of the patients while the 19.9% received at least one local infiltration. The longest TWI corresponded to knee meniscopathy (203 days), painful shoulder syndrome (173 days) and lumbosciatica (170.5 days). No statistically significant differences were found between the duration of the TWI attending to sex, age group, labour activity or diagnose. However, a significant association was found between TWI duration and the delay since the start of the symptons to the referral from Primary Care to our consultation, specially within the firdt 10 days (p=0.04). Furthermore, TWI duration was significantly shorter in the EIP group patients than in the control group patients (137.4±132.3 days vs 194.7±143.1 days; $p<0,001$).The period before relapse was longer in the EIP group, although the differences did not reach significance. In addition, an inverse relation was found between age and time to relapse (p=0,01).
Conclusions: The establishment of an early intervention program specifically addressed to patients with temporary work incapacity of musculoskeletal origin shortens the duration of this situation, allowing the patient to rejoin his work activity, with the resulting cost savings related to work incapacity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5486

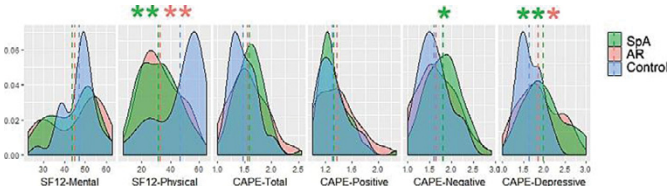
THU0624 ASESSMENT OF PSYCHIC EXPERIENCES IN PATIENTS WITH RHEUMATIC DISEASES

J.L. Prados-Ojeda[1], J.L. Garrido-Castro[2], R. Segura-Ruiz[1], C. González-Navas[2], P. Font-Ugalde[2], E. Collantes-Estevez[2], A. Escudero-Contreras[1]. *[1]Reina Sofia University Hospital; [2]Maimonides Institute for Biomedical Research of Cordoba, Cordoba, Spain*

Background: There are several studies that report psychiatric comorbidity in patients with rheumatic disease, mainly the presence of mood disorders. Some of them describe non-affective psychosis related with inflammatory processes. Population with chronic inflammatory disease could present subclinical psychotic experiences that can interfere in the patient's functional status. The Community Assessment of Psychic Experiences (CAPE) scale is a validated and widely used tool for the evaluation of these experiences in the general population.
Objectives: To identify the presence of psychic experiences in different populations with a diagnosis of rheumatic disease, and to compare it with a sample of healthy subjects.
Methods: 124 subjects completed surveys including SF-12 and CAPE questionnaires, as well as other demographic and behavioral variables. Among them, 70 had Spondylarthritis (SpA) (age 44.3±13 years, 62% female), 23 rheumatoid arthritis (RA) (age 51.2±13 years, 82% female) and the rest were individuals without rheumatic diseases (47.6±12 years, 58% female).
Results: Results of the SF-12 test in their mental and physical domains, and the CAPE questionnaire in their dimensions (positive, negative, depressive and total symptoms) are shown in the table, expressed as mean value (SD) and in the graph expressed as density histograms with mean values. Significant statistical

	SF-12		CAPE			
	Physical	Mental	Positive	Negative	Depressive	Total
SpA	31.8 (13.6)**	43.8 (10.6)	1.32 (0.2)	1.81 (0.4)*	1.98 (0.5)**	1.59 (0.3)*
RA	33.1 (13.1)**	44.9 (12.7)	1.37 (0.3)	1.66 (0.4)	1.86 (0.5)*	1.55 (0.3)
Control	47.0 (16.1)	47.2 (7.5)	1.30 (0.2)	1.61 (0.4)	1.65 (0.3)	1.47 (0.2)

differences, according a t de Student test with control group is shown in both (* $p<0.05$, ** $p<0.01$).
There were no significant differences in the mental component of the SF-12. These differences appear at the physical component, since patients have impaired their mobility and function due to their disease. About the CAPE questionnaire, patients had a little bit higher score due mainly to the appearance of depressive symptoms. The values of positive symptoms of psychosis remained within the normal range for diseases analyzed.



Conclusions: In our study, we found significant differences in the dimensions, especially depressive, of the CAPE scale among patients with rheumatic diseases (especially in SpA) and healthy subjects. This gives us an idea of the importance of considering the psychological problems of patients (anxiety, depression, ...) to improve the treatment of rheumatic disease.
Acknowledgements: We would like to thank these patients' organizations for their collaboration in our study: Coordinadora Española de Asociaciones De Espondiloartritis (CEADE), Asociación Cordobesa de Enfermos de Espondilitis (ACEADE), Asociación Cordobesa de Enfermos de Artritis Reumatoide (ACOARE).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3505

THU0625 DESIGN OF AN INFORMATION AND COMMUNICATIONS TECHNOLOGY PLATFORM TO SUPPORT COORDINATION OF CARE FOR RHEUMATOID ARTHRITIS PATIENTS WITH CARDIOVASCULAR CO-MORBIDITIES – FIRST EXPERIENCES

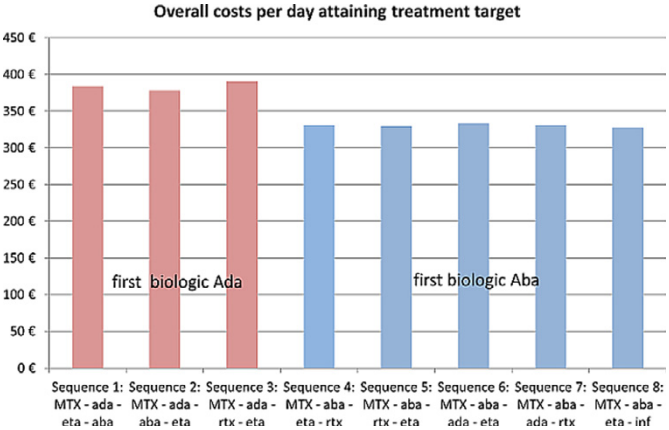
J.G. Richter, G. Chehab, M. Schneider on behalf of the PICASO Consortium (www.picaso-project.eu). *Policlinic & Hiller Research Unit for Rheumatology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany*

Background: Coordination of care plans between healthcare sectors and efficient management of patients (pts) with co-morbidities is of large demand. Rheumatoid arthritis (RA) pts are at increased risk of cardiovascular diseases (CVD). Different stakeholders are potentially involved in the EULAR recommended management processes. Optimized orchestration of accumulated information is of major importance to ensure data quality, meaningful management processes and cost effectiveness. A newly developed information and communications technology (ICT) platform within the Horizon2020-funded PICASO-project (www.picaso-project.eu) will support a continuum of care from hospitals and outpatient clinics to the home.
Objectives: Explore challenges to provide an efficient ICT integrated solution across many healthcare professionals working for various organisations and potentially crossing national borders that complies to privacy and regulatory constraints allowing more efficient care management. Suitable system architecture and appropriate features require identification of target users' user requirements. PICASO platform will be developed and trialed with pts and clinician. The proposed system architecture will be evaluated for suitability for a larger scale rollout.
Methods: Projects' pre-defined clinical and technological driven work packages started. Various stakeholders (e.g. pts, local data security and IT representatives, health care insurances' representatives, clinicians) were integrated in the design phase. A PICASO ethical board including external members (e.g. Chair of the Standing Committee of PARE) addressed ethical and legal concerns.
Results: Current work-flows for the care plan management including stakeholders' hand-over procedures were elaborated. Vision scenarios (n=11) and To-Be Use Cases (n=18) addressing solutions including home monitoring were developed (1). A comprehensive list of user requirements (currently n=87) resulted. Detailed system architecture descriptions are stipulated. Ethical issues and how to handle these, in particular data-protection and -privacy challenges were pre-assigned as these affect platforms' architecture. PICASO ethical principles and guidelines were stated (2). The platform is under development. The first trial running over nine months including RA-pts will start in spring 2017. First experiences will be reported at EULAR.
Conclusions: Considering the needs of a highly valued, specialised health care system relevant To-Be Use Cases, numerous user requirements and EU-wide ethical and legal issues were gathered to serve as basis for appropriate design, development and implementation of the ICT platform. Software development will take place in iterative cycles followed by prototypes' thoroughly evaluated by real end users investigating usability and acceptance. The platform will become available for RA-pts in routine care but also for wider applicability in Rheumatology and other chronic diseases.
References:
[1] PICASO Consortium (2016), D2.1 Scenarios and Use Cases for Integrated Care. http://www.picaso-project.eu/download/4894.
[2] PICASO Consortium (2016), D3.3 PICASO Ethical Guidelines. http://www.picaso-project.eu/download/520/; both last accessed 27/01/2017.
Acknowledgements: This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 689209.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4001

THU0626 COST-EFFECTIVENESS OF EARLY TREATMENT OF ACPA POSITIVE RHEUMATOID ARTHRITIS PATIENTS WITH ABATACEPT

A.S. Neubauer[1], C. Minartz[1], K.H. Herrmann[2], R. Postema[3], C. Baerwald[4]. *[1]Institute for Health Economics (IfG, IfGPh); [2]Bristol-Myers Squibb, Muenchen, Germany; [3]Bristol-Myers Squibb, London, United Kingdom; [4]Rheumatology Unit, University of Leipzig, Leipzig, Germany*

Background: Studies have reported that the presence of elevated anti-citrullinated protein antibodies (ACPA)/RF levels, together with joint erosions, is associated with higher disease burden in terms of disability, and mortality in rheumatoid arthritis (RA). Abatacept has been shown to be effective in this patient population with favorable comparative data against adalimumab.(1) However, few studies have investigated the cost effectiveness of abatacept in this population to similar treatments such as TNFs.
Objectives: The objective of the study was to compare the cost-effectiveness of abatacept to adalimumab as a first bDMARD in ACPA positive RA patients who failed treatment with methotrexate (MTX) in Germany.
Methods: A decision tree model was used to estimate the cost-effectiveness, from a payer's perspective, of different treatment sequences in RA over a two year time frame. The effectiveness criteria were defined as achieving the treatment target measured by the Disease Activity Score 28 (DAS28 (CRP)<2.6; "remission"). A treatment switch to a different biologic as 2nd line and 3rd line bDMARD was allowed -in case of not achieving remission with therapy- every 6 months over a two year time period. Effectiveness data was based on randomized controlled trials (RCT) identified by an updated previous systematic literature search by the Institute for Quality and Efficiency in Health Care (IQWiG). Costs of medication and other direct medical costs were taken from a recent publication (2) and included in the analysis. Cost-effectiveness of RA treatment was investigated in ACPA positive patients in this study and presented as overall costs per day in remission. To manage uncertainty in the model, a fully probabilistic approach was used with 10,000 runs.
Results: For ACPA positive patients, treatment strategies including early treatment with abatacept had lower total costs per clinical outcome compared to later use. Figure 1 summarizes the costs per day in remission for the treatment sequences investigated: treatment sequences starting with abatacept resulted in lower costs for reaching remission (mean 330 €/day, range 328 €-333 €/day) compared to sequences starting with adalimumab (mean 384 €/day, range 378 €-390 €/day). Choice of the second or third biologic in the treatment sequences appears to have little impact on the costs per outcome.



Conclusions: The results of this analysis suggest that in ACPA positive RA patients treatment with abatacept appears to be more cost-effective compared to treatment with adalimumab as a first bDMARD.
References:
[1] Sokolove J, Schiff M, Fleischmann R, et al. Annals of the rheumatic diseases. 2016 Apr;75(4):709–14.

[2] Beresniak A, Baerwald C, Zeidler H et al. Clin Exp Rheumatol. 2013 May-Jun;31(3):400–8.
Disclosure of Interest: A. Neubauer Grant/research support from: BMS, Intercept, Roche, Santen, C. Minartz Grant/research support from: BMS, Intercept, Roche, K. Herrmann Employee of: BMS, R. Postema Employee of: BMS, C. Baerwald Grant/research support from: Abbvie, Biogen, BMS, Chugai, Hexal, Medac, Pfizer, Roche, Sanofi Aventis, UCB
DOI: 10.1136/annrheumdis-2017-eular.4312

THU0627 TREATMENT OF RHEUMATOID ARTHRITIS: ADHERENCE TO GUIDELINES IN PRIVATE PRACTICE

L.B. Fernandes, F.A. Palacios, P.G. Lerner, C.G. Macedo, F. Omura, E.A.K. Azeka, I.M.M. Laurindo, P. Toth, R.C. Ferreira, R.A.O. Aurichio, A.P. Bazilio, J. Brudniewski, A.L. Hayata. *Private Office, São Paulo, Brazil*

Background: Guidelines and therapeutic strategies in the treatment of rheumatoid arthritis (RA) have been developed and adopted by most Societies of Rheumatology. However, the extent to which they have been supported by rheumatologists in their individual clinical practice is unclear.
Objectives: Our aim was to analyze, at private offices, adherence to guidelines and characteristics of RA patients in regular follow-up.
Methods: This was a cross-sectional study developed by a group of rheumatologists (n=13) working exclusively in private offices and hospitals in São Paulo, Brazil. It consisted of a web-based questionnaire addressing patient's demographics, social characteristics and treatment. Patients having the diagnosis of RA should be included sequentially. As Brazil's private health has no reference flowchart, patients can consult any physician from their insurance health program, or any physician at all if bearing the costs. Insurance programs can be either personal or tied to employers, in which case job changes imply in insurance and health professional changes.
Results: Data from 235 RA patients were collected, 84% were female, mean age (SD) 57.3 (13.3) yrs., disease duration 9.5 (1–54) yrs., 73% RF positive (74% of the 61 RF negative patients had an anti-CCP test and 8 were positive), The mean duration of symptoms until diagnosis was 1.7yrs (0–23), number of physicians until diagnosis 2.4 (1 – 12), including GP (102 patients), orthopedists (110 patients) and rheumatologists (129 patients). Even after diagnosis, patients switched professionals at a mean number of 2 physicians (1–6), justified by shift of health insurance (66 patients), lack of resolution (33 patients), dislike of the physician (26 patients) and cost (11 patients). Regarding treatment, 51% of patients were on biologic agents: 23% adalimumab, 15% abatacept and rituximab, 14% etanercept, 12% tocilizumab, 7.6% golimumab, 5% certolizumab and infliximab and 4% tofacitinib. Interestingly, most patients (75%) using abatacept, tofacitinib and tocilizumab were not on methotrexate (MTX), while from the 65 patients on an anti-TNF agent, 75% were also using MTX or leflunomide (LFN). Regarding traditional DMARDs, 91% of patients were on (n=94) or had used MTX (n=120); 43% were on (n=37) or had used (n=64) LFN. Concerning treatment and disease activity, 91% of patients were considered adherent to the treatment with a mean number of 4 annual visits, 82% were also deemed to be in regular monitoring. According to rheumatologist's assessment, 63% of patients had RA "under control". In fact, 72% of patients were on low disease activity (22%) or on remission (50%), according to the DAS28. However, when patients in disease activity were analyzed, few of them (0.28 CI 0.18–0.40) were on biologic or target DMARDS, pointing to a possible therapeutic transitional moment. Only 3 of these could be labeled "refractory", having previously used 3 biologic agents.
Conclusions: *Treat-to-target* strategy seems to have been adopted by most rheumatologists in their individual practice, although there is room for improvement and optimization of therapy. While treatment guidelines are roughly followed, the delay in diagnosis and changes of healthcare are particularly worrisome and need to be addressed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5521

THU0628 PATTERNS OF ETANERCEPT DOSE ADJUSTMENTS IN A REAL–WORLD SETTING: A CANADIAN RETROSPECTIVE COHORT STUDY

M. Khraishi[1], Y. Zhang[2], J. Ivanovic[2], B. Millson[2], E. Singh[3], J. Woolcott[4], H. Jones[3]. [1]*Faculty of Medicine, Memorial University of Newfoundland, St. Johns;* [2]*Health Access & Outcomes, QuintilesIMS, Kanata, Canada;* [3]*Inflammation and Immunology, Global Medical Affairs, Pfizer Inc., Collegeville, United States;* [4]*Health Economics and Outcomes Research, Pfizer Inc., Kirkland, Canada*

Background: Etanercept is a soluble TNF receptor (humanized protein) indicated for treatment of immune-mediated inflammatory diseases, including rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis (PsO), and ankylosing spondylitis (AS). Canadian monograph recommended dosing of etanercept is 50mg/week, with select indications also requiring an initial loading phase of 100mg/week for 12 weeks. Evidence suggests that real-world practices differ from monograph, with patients titrating to lower or higher weekly dosing as needed. Limited research exists on how etanercept patients are dose optimized in the real-world Canadian setting.
Objectives: To describe etanercept treatment dynamics, including dose de-escalation/escalation in the Canadian real-world setting.
Methods: A retrospective cohort study was conducted utilizing claims-level data from QuintilesIMS Private Drug Plan database, Ontario Public Drug Plan database, and Quebec Public Drug Plan database. Between 07/2013–06/2015, bio-naïve patients who initiated etanercept and who retained on therapy for 12 months were identified. Weekly dosing of each patient was calculated and analyzed for the prevalence and magnitude of dose de-escalation/escalation. Patients with at least 20% lower/higher average dose than monograph recommended dose (50mg/week) were flagged as dose de-escalators/dose escalators, respectively. The first 3 claims of etanercept were excluded from average dose calculations to exclude a possible loading phase.
Results: The study identified 3,051 etanercept patients (60% female, 77% aged between 18 and 65, 87% rheumatic diseases, and 13% PsO) across Canada in the selection period. Overall, 11% (n=332) of patients de-escalated during their first year of therapy, led by AS (15%, n=24) and RA (12%, n=286); 15% (n=449) of patients escalated, led by PsO (64%, n=262) versus 7% (n=168) in RA; 74% (n=2,270) of patients maintained a consistent dose. Average dosing across rheumatic disease patients stabilized to monograph levels by week 20 of their therapy; PsO patients' dosing was observed to be lower than monograph during the loading phase, while higher than monograph in the maintenance phase.
Conclusions: In Canadian real-world practice, the average patient utilization of etanercept remained consistent over the first year in majority of patients, with the exception of those with PsO. A notable proportion of etanercept patients with rheumatic diseases reduced their average dosing over time while on therapy, with almost twice as many patients titrating their dose downwards than upwards. However, in PsO patients, a majority of patients increased their etanercept.
Disclosure of Interest: M. Khraishi Consultant for: Pfizer Canada and Amgen Canada, Y. Zhang: None declared, J. Ivanovic: None declared, B. Millson: None declared, E. Singh: None declared, J. Woolcott: None declared, H. Jones: None declared
DOI: 10.1136/annrheumdis-2017-eular.6959

THU0629 THE PERSPECTIVES OF PATIENTS, THEIR FIRST DEGREE RELATIVES, AND RHEUMATOLOGISTS AROUND PREVENTATIVE TREATMENTS FOR RHEUMATOID ARTHRITIS

L. Spooner[1], K. Milbers[2], S. Munro[1], N. Tsao[1], M. Hudson[3], C. Koehn[4], N. Bansback[1], M. Harrison[1,2]. [1]*University of British Columbia;* [2]*Centre for Health Evaluation and Outcome Sciences, Vancouver;* [3]*McGill University, Montreal;* [4]*Arthritis Consumer Experts, Vancouver, Canada*

Background: Ongoing randomized controlled trials are looking at the efficacy of preventing RA through treatment with anti-rheumatic medications. However even if these trials are successful, uncertainty around the potential benefits of preventative programs in practice will affect the uptake of a preventative treatment program. The views of rheumatologists, patients with RA and people considered at-risk of RA (potential recipients) will be important to consider.
Objectives: To identify relevant attributes for a discrete choice experiment (DCE) representing the factors that influence the preferences of patients, first-degree relatives (FDRs), and rheumatologists about preventative treatment for rheumatoid arthritis (RA).
Methods: Semi-structured focus groups were conducted with 1) RA patients in British Columbia (BC), Canada 2) FDRs of people with RA, and 3) rheumatologists from across Canada. Participants were recruited through a combination of convenience and homogenous sampling. Focus group guides were adapted from a previous study which used a DCE to represent an RA treatment decision. In the first round of focus groups, moderated discussions with RA patients, FDRs, and rheumatologists elicited open-ended responses to the interview guide questions. Findings from analysis of these discussions were reduced to a list of potential attributes for the DCE. In the second round, RA patients and FDRs provided feedback to improve the validity and representation of the potential attributes. All focus groups were audio recorded, transcribed, and analyzed using Framework Analysis.
Results: Five focus groups were conducted with 13 RA patients, 5 FDRs, and 7 rheumatologists from four Canadian provinces. Analysis of the discussions revealed that all groups considered competing risks when considering a preventative treatment decision: risks of developing RA and when it might occur; accuracy of predictive tests and the risk of a false positive; and the risks of treatment itself. For rheumatologists, the empirical evidence supporting preventative tests and preventative treatments for RA, as well as treatment side effects were of significant importance. Interestingly, some rheumatologists did not consider prevention to be part of their role. FDRs frequently mentioned the impact that a preventive treatment would have on their lifestyle, the accuracy of predictive test, and weighing the potential benefits against side effects of treatment as key factors in decisions to take a preventative treatment. The health care provider's (nurse/family physician/rheumatologist) knowledge of RA and perceived trustworthiness was also important to FDRs in considering a heath care provider's recommendation for preventative treatment.
Conclusions: Our Framework Analysis highlighted key themes in this discussion which informed the attributes to be included in a DCE. Our findings suggest there are important differences in how patients, FDRs and rheumatologists value the uncertainties surrounding the potential benefits of a preventative treatment for RA.

Acknowledgements: This work was supported by a grant from the Canadian Rheumatology Association through the Canadian Initiative for Outcomes in Rheumatology Care (CIORA).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2007

THU0630 OPIOID USE IN PATIENTS WITH POLYMYALGIA RHEUMATICA

M.D. Richter[1], S.J. Achenbach[2], J.A. Zamora-Legoff[3], C.S. Crowson[2], E.L. Matteson[3]. *[1]Graduate Medical Education; [2]Division of Biomedical Statistics and Informatics; [3]Division of Rheumatology, Mayo Clinic, Rochester, United States*

Background: Polymyalgia rheumatic (PMR) is a systemic rheumatic inflammatory disease characterized primarily by musculoskeletal pain and stiffness. Glucocorticoid treatment is the current standard of care however the need for additional pain management, in particular the need for opioid therapy, has not been studied.
Objectives: To examine the trends of chronic opioid use in patients with PMR over an 11 year period in Olmsted County, Minnesota, USA and compare this to subjects without the disease.
Methods: Retrospective data on opioid prescriptions were collected from 2005 to 2015 in a population-based incidence cohort of patients meeting the 2012 American College of Rheumatology classification criteria for PMR alongside comparison subjects. Poisson regression methods were used to compare opioid use between these groups.
Results: 244 patients with PMR and 211 non-PMR comparator subjects were included in the study. Rates of chronic opioid use were not significantly different between the two groups. 7.5% of patients with PMR were identified as chronic users by the end of the study period compared with 5.2% of non-PMR subjects. Any opioid use was also not significantly higher in PMR, with relative risk of 1.10 (95% CI 0.97, 1.26, p=0.14). There were higher rates of chronic use among patients over 80 years in both groups.
Conclusions: PMR does not appear to be associated with increased rates of opioid use when compared with the general population.
Acknowledgements: This study was made possible by the Rochester Epidemiology Project, which receives support from the National institute on Aging of the NIH.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1237

THU0631 DIRECT FINANCIAL BURDEN OF RHEUMATOID ARTHRITIS ON PATIENTS' LIFE IN A DEVELOPING NATION OF PAKISTAN, ONE YEAR PROSPECTIVE STUDY

M.S. Ahmad. *Orthopedic Surgery, Fazle Omar Hospital, Chenab Nagar, Pakistan*

Background: Rheumatoid Arthritis is chronic inflammatory disease. Early diagnosis and management is necessary to ovoid joint destruction and to minimize disability. It effects 0.5 to 1 percent population. The female to male ratio is 3 to 1. Health care cost is of great concern to patients, physicians and health care policy makers. The financial impact of rheumatoid arthritis treatment like any chronic illness is of great significance in developing society like Pakistan where 30 percent population lives below poverty line and annual per capita incomes are very low. Whereas prevalence is same with high medicines prices with poorly developed health insurance system and government funded hospitals are scanty.
Most of times attention in the field of health economy is focused on direct medical in general and hospital cost in particular but however there are some social societal customs which also increases the burden of direct cost. The direct cost includes expenditures like physician visit cost, diagnostic tests, medications. There are also some hidden charges to this direct cost which are not included in studies like transport charges, food bills during hospital stay and accompany person, female are companied by males. All included puts strain on economy and major share of annual income of patient is paid on management of disease. The worst scenario is when patient stops treatment and if lucky gets support from other sources like patient welfare societies or from relatives.
Objectives: To assess the direct cost of patient's every visit to hospital outpatient department prospectively for one year and total cost of one year was summed up and percentage to annual income spend on treatment was calculated.
Methods: Study carried out from January to December 2015 at Fazle Omar Hospital Rabwah Chenab Nagar and 150 patients either newly diagnosed or already on treatment of rheumatoid Arthritis were included. Data collected for next 1 year for each visit, patients with any other disease along with rheumatoid were excluded. The estimated annual income of patient or the person bearing the expenses was recorded before start of study. Every time patient visit hospital outpatient department, prescription copy kept and cost of medicines, laboratory investigations and consultation fee is calculated and a questionnaire is filled how much it cost coming hospital and going back home and during hospital stay on any other things. The total cost of every visit was recorded for one year.
Results: The mean total per patient income after conversion from local currency was 3000 US dollars against 1474 US dollars per capita income in 2015. The annual average cost per patient including consultation fee, medicines purchased, laboratory investigations and other overhead expenses like transportation of patient and accompanied person and food bills during hospital stay was 1194 US dollars. 41% of patient gross income was spend on management of rheumatoid arthritis. Investigations cost 12%, medicines purchased 16%, consultation 2% and over head visit charges cost 10% of the total mean of per patient annual income.
Conclusions: RA management consumes large portion of patients annual income and it has significant burden on developing world economy.
References:
[1] The economic burden of rheumatoid arthritis in a developing nation: result from one year prospective cohort study in Thailand, Osiri M, Maetzel A, Tugwell P. J Rheumatol 2007 Jan.34(1):57–63.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5571

THU0632 VALIDATION OF INTERNET-BASED REPORTING OF PATIENT REPORTED OUTCOMES WITHIN THE SWEDISH RHEUMATOLOGY QUALITY REGISTER

O.E. Hofstedt[1], D. Di Giuseppe[2], G.-M. Alenius[1], N. Stattin[3], H. Forsblad-d'Elia[1], L. Ljung[1]. *[1]Department of Public Health and Clinical Medicine, Umeå University, Umeå; [2]Department of Medicine Solna, Karolinska Institutet, Stockholm; [3]Swedish Rheumatism Association, Sundsvall, Sweden*

Background: Previous studies have validated the use of clinic based touch-screens for registering patient reported outcome measures (PROMs) (1–3). The Swedish Rheumatology Quality (SRQ) register has implemented an internet-based method (PER (Patientens Egen Registrering, or Patients' sElf Registration)) for collecting PROMs.
Objectives: The aim of this study was to investigate the feasibility of the internet-based method as well as the validity of reported outcomes and disease activity scores compared to the gold standard paper format.
Methods: We recruited patients (n=44, mean age =51.0, standard deviation =13.2 years, 69.6% women) included in SRQ with a diagnosis of rheumatoid arthritis, psoriatic arthritis, juvenile arthritis, spondyloarthritis or ankylosing spondylitis. Before a planned visit at the rheumatology clinic the patients registered Visual Analog Scales (VAS) for global health, pain and fatigue, both electronically by PER and on paper. Patients with axial disease also registered BASDAI and BASFI related variables (n=6). For patients with peripheral arthritis (n=38), DAS28 was calculated using both methods. The differences between the methods were compared by T-test and Intra-class correlation (ICC). Agreement was visualized using Bland-Altman plots for all VAS registrations. The patients also answered a questionnaire regarding the used device and preferred method.
Results: No differences between PER or paper based VAS scores were found for VAS Global, VAS Pain and VAS Fatigue (p=0.086, p=0.691 and p=0.197, respectively). ICC scores ranged from 0.930 to 0.971. Bland-Altman plots for VAS assessments showed good agreement and no proportional bias was detected (Fig 1). Mean difference for DAS28 was - 0.04 (p=0.177). Of the recruited patients, 78%, preferred the Internet based method. BASDAI and BASFI could not be evaluated due to a limited number of observations.

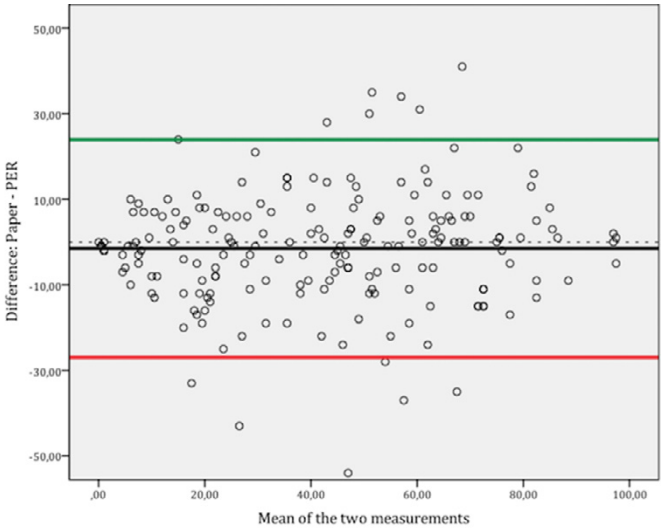


Fig. 1 Bland-Altman plot showing level of agreement of all VAS (VAS Global, VAS Pain, VAS Fatigue, VAS included in BASFI and BASDAI) between paper and PER method. BASDAI and BASFI scores multiplied by 10 for comparability.

Conclusions: Internet based reporting of PROMs supply valid VAS data. DAS28 scores from the internet-based method presents an acceptable alternative to the traditional paper formats.
References:
[1] Greenwood MC, et al. Rheumatology (Oxford). 2006.
[2] Schefte DB, et al., Rheumatology (Oxford). 2010.
[3] Cunha-Miranda L, et al Rheumatol Int. 2015.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2590

THU0633 TEMPERATURE SENSITIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

P. Mandl[1], F. Alasti[1], A. Kerschbaumer[1], R. Kaltenberger[2], T. Krennert[2], G.M. Supp[1], U. Landesmann[1], J.S. Smolen[1], D. Aletaha[1]. [1]*Department of Rheumatology, Medical University of Vienna;* [2]*Central Institute for Meteorology and Geodynamics, Vienna, Austria*

Background: Studies evaluating weather sensitivity among patients with rheumatoid arthritis (RA) have yielded conflicting results.
Objectives: To evaluate whether patients with RA exhibit sensitivity to outside temperature.
Methods: We assessed correlation between mean daily temperature and self-reported pain (by visual analogue scale), and patient's global assessment of disease activity (PGA). Assessments documented in the RA database of our department as well as the average temperature obtained from the Central Institute for Meteorology and Geodynamics, were matched on a daily basis for a period of 10 years between 2005 and 2015 and analyzed using generalized estimating equation (GEE) and a mixed model analysis (MM). Patients with <5 visits in the study period, or with <1 visit/quarter or with pain=0 in ≥ 3 consecutive visits and those living outside of the catchment area were excluded. Overlap between responsiveness of pain or PGA to temperature was calculated by Cohen's kappa.
Results: A total of 399 patients with RA (average disease duration at first visit: 6.0±7.6 years, average age: 57.7±13.9 years, 82% female, mean CDAI 19.7±11.5, 59.9% rheumatoid factor positive) were analyzed. Lower temperatures correlated significantly with higher pain levels (estimate: -0.07, p=0.021) in GEE, however the effect size was very small. When we performed MM with temperature as independent variable and VAS pain or PGA as dependent variable, the majority of patients showed no sensitivity to temperature, however 22% of patients were significantly sensitive to cold temperature with an estimate of -0.29 ($p<0.0001$) for pain and -0.21 (p=0.0005) for PGA (Figure 1). When we evaluated whether patients who demonstrate temperature-sensitivity to pain also exhibit temperature-sensitivity to PGA, we found an excellent overlap between the two patient groups (kappa: 0.81).

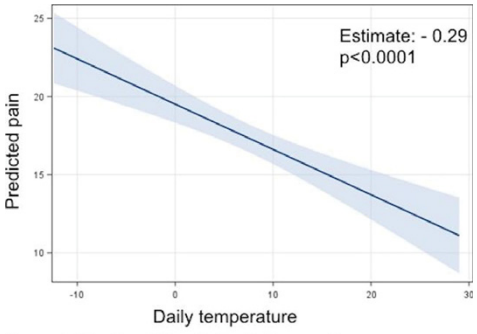


Figure 1. Mixed model analysis of influence of temperature on pain of patients demonstrating sensitivity to cold temperature

Conclusions: Our results indicate that a subgroup of patients with RA show significant sensitivity to cold temperature, and that these patients are characterized by higher pain and PGA levels at lower daily temperatures. These aspects may have to be taken into account in longitudinal analyses of disease activity of RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5134

THU0634 COMPARING PREFERENCES OF PATIENTS WITH RHEUMATIC DISEASES, OF RHEUMATOLOGISTS, NURSES AND PHARMACISTS TOWARD THE TREATMENT OF RHEUMATIC DISEASES WITH BIOLOGICAL AGENTS: RESULTS FROM THE CARA STUDY

P. Sarzi-Puttini[1], P.A. Cortesi[2,3], L. Sinigaglia[4], C.M. Montecucco[5], R. Giacomelli[6], G. Lapadula[7], I. Olivieri[8], A. Giardino[9], G. DIdoni[10], L. Scalone[2,3], L.G. Mantovani[3,11], M. Mecchia[10] on behalf of CARA Working group. [1]*Rheumatology Unit, L. Sacco University Hospital, Milano;* [2]*Univeristy of Milano-Bicocca, Monza;* [3]*CHARTA Foundation;* [4]*Rheumatology Unit, G. Pini Hospital, Italy, Milano;* [5]*University of Pavia School of Medicine, IRCCS Policlinico San Matteo Foundation, Pavia;* [6]*Rheumatology Unit School of Medicine, University of L'Aquila, L'Aquila;* [7]*Rheumatology Unit, University of Bari, Bari;* [8]*San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, and the Basilicata Ricerca Biomedica (BRB) Foundation, Potenza and Matera;* [9]*MSD;* [10]*MSD Italia, Roma;* [11]*University of Milano Bicocca, Monza, Italy*

Background: The management of patients with rheumatologic diseases (RDs) involves a complex interaction between different parties such as patients, physicians, pharmacists. The development of biologic therapies has created a more complex decision-making process to select the treatment option for patients. To optimize the appropriateness of the decisions, it is necessary to be informed and aware of the preferences of the interested parties.
Objectives: To estimate preferences of relevant treatment characteristics with biological agents valued by the different subjects involved in the management of patients with rheumatic diseases.
Methods: We involved patients with RDs, rheumatologists, nurses and pharmacists with experience in the treatment with/provision of biological drugs of these patients. Through a Discrete-Choice-Experiment, the participants valued 16 possible scenarios in which pairs of similarly effective treatments were described with 6 characteristics including 2–4 possible levels each: (1) frequency of administration; (2) mode and place of administration; (3) hospitality, service, efficiency and courtesy of health personnel; (4) frequency of reactions at the site of drug administration; (5) generalized undesired/allergic reactions; (6) additional cost: since the Italian NHS pays treatment costs, we included possible additional cost as monthly healthcare taxes for all the citizens, to make available the treatment to all target patients. relative importance of each characteristic was estimated through a random-effects conditional logistic regression model.
Results: 513 patients, 110 rheumatologists, 51 nurses and 46 pharmacists from 30 centres through Italy participated. Characteristics (3), (4) and (6) were the most important for every subgroup, while (1) was the least important for patients and rheumatologists, (2) the least important for the pharmacists, (2) and (5) the least important for the nurses. The four subgroups were consistent in preferences towards the specified levels of characteristics (1) and (3) to (6). However, as for characteristic (2), pharmacists preferred autonomous subcutaneous injection with syringe, nurses preferred assisted infusion at an infusional center close to patient's place, patients and rheumatologists preferred autonomous subcutaneous injection with pen.
Conclusions: Different subjects show different preferences for some treatment characteristics, which together with pure clinical aspects can play an important role in the choice and consequent success of treatments.
Disclosure of Interest: P. Sarzi-Puttini: None declared, P. Cortesi Grant/research support from: Gilead, L. Sinigaglia: None declared, C. Montecucco: None declared, R. Giacomelli Grant/research support from: MSD, G. Lapadula: None declared, I. Olivieri: None declared, A. Giardino Employee of: MSD Italia, G. DIdoni Employee of: MSD Italia, L. Scalone: None declared, L. Mantovani: None declared, M. Mecchia Employee of: MSD Italia
DOI: 10.1136/annrheumdis-2017-eular.4833

THU0635 PRECISE AND SIMPLE ALGORITHM TO IDENTIFY RA CASES IN ELECTRONIC MEDICAL RECORDS

R. Knevel[1,2,3,4], S. Raychaudhuri[1,2,4], K. Liao[1,2], T.W. Huizinga[3]. [1]*Rheumatology, Brigham and Women's Hospital, Boston;* [2]*Harvard Medical School, Cambridge, United States;* [3]*Rheumatology, Leids Universitair Medisch Centrum, Leiden, Netherlands;* [4]*Broad Institute, Cambridge, United States*

Background: Electronic medical records (EMR) have emerged as a large-scale data collection option for observational studies. These huge data registries create new opportunities to study the rheumatologic phenotype and the real-life implications for these diseases. EMR usage poses new questions of quality management, such as how to reliably identify patients with the disease or phenotype of interest, as well as bioinformatic tools to handle the magnitude of data.
Thusfar, the algorithms used to identify cases are often not validated and overly simplify by using one financial code, or they are well-validated but require very specific information which hampers the applicability to other datasets.
Objectives: *Aim I:* Test the accuracy of the identification of patients with rheumatoid arthritis (RA) using the financial coding system.
Aim II: Develop a simple and precise algorithm to select patients with RA that is easy to implement at other centers.
Methods: *Aim I:* Out of the 16,183 Rheumatology patients in the Leiden out-patient EMR system 400 charts were randomly selected and reviewed for the rheumatologic diagnosis. Next, the charts were reviewed for 200 randomly selected patients that were labeled as RA in the financial system.
Aim II: To enable generalizability, only codified data that was obtained at regular outpatient clinic visits was used. Lasso regression was applied to identify the most discriminative variables.
Results: *Aim I:* Since 2008, 16,183 patients were enrolled in the EMR system of the Leiden rheumatology outpatient clinic. 2,845 of these patients were classified as having RA in the financial system. 63/400 (16.3%) of the reviewed charts concerned patients with RA. The majority (n=57) were registered as having RA in the financial system. Still, 33% of the patients with the financial code RA did not have RA.
Aim II: Using Least Absolute Shrinkage and Selection Operator (LASSO) regression anti CCP, MTX prescription and number of visits were identified as the most discriminative variables. Combining these with the presence of the financial code for RA improved the algorithm from an accuracy of 67% to 90%.
Conclusions: The vast majority of patients that are classified as having RA are registered as such in the financial system. However, a substantial number of patients are registered as RA in the financial system are not classified as RA in clinical charts. Using widely available data on anti-CCP status, MTX prescription

and visit count improved the selection of RA patients from a 67% to 90% accuracy. The combination of these variables provides a widely applicable algorithm, as they are broadly registered in Rheumatology clinics.
Subsequent replications are ongoing.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6464

THU0636 INFLUENZA AND MENINGOCOCCAL C VACCINATIONS IN A COHORT OF PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES: ADHERENCE, SAFETY AND IMMUNOGENICITY

R. Vagelli, C. Tani, L. Maggi, E. Elefante, A. Parma, E. Cioffi, S. Talarico, C. Baldini, C. Stagnaro, A. Delle Sedie, S. Vagnani, M. Mosca. *Department of Clinical and Experimental Medicine, Rheumatology Unit, University of Pisa, Pisa, Italy*

Background: The EULAR recommendations for vaccination in adult patients with autoimmune rheumatic diseases strongly recommend inactivated influenza vaccination.Insufficient data are available about safety and efficacy of meningococcal C vaccination.In 2015–2016,after an increased incidence of meningitidis C infections in our country,the health care system has promoted a free meningococcal vaccination campaign
Objectives: To evaluate the adherence to the EULAR recommendations for influenza vaccination and to the meningococcal C vaccination campaign in a cohort of patients with autoimmune rheumatic diseases and to assess their safety.The efficacy in term of immune response to meningococcal C vaccination has been also evaluated
Methods: Consecutive in- and out-patients seen at our unit from February to December 2016 were enrolled in the study.Using a questionnaire created *ad hoc* the following data were collected:the percentage of patients who underwent influenza and/or meningococcal C vaccinations in the previous 12 months,the occurrence of adverse events and of disease flares after vaccinations,according with the report from the patients and with the rheumatologist clinical evaluation.Seroconvertion rates in patients and healthy controls were assessed using ELISA kits for human anti-meningococcal ACWY IgG antibodies.Antibody titres were expressed in U/ml and according with kit reference value were classified in absent,low,medium and high titre
Results: 286 patients (91% female) (143 SLE, 68 RA,60 Scleroderma,11 Sjögren Syndrome,3 Behcet disease and 1 Dermatomyositis) were included in the analysis.The mean age at evaluation was 52.9±16.1 years,mean disease duration was 15.3±10 years.The 53.1% of patients was taking steroids,at an average dose of 4.2 mg of 6-metilprednisolone/day,134/286 (46.9%) patients were on immunosuppressive therapies,of which 49/134 (36.6%) on biologic agents.The 19.9% (57/286) of patients underwent influenza vaccinations and the 13.3% (38/286) meningococcal C vaccination,8 patients underwent both vaccinations.No disease flares were observed after vaccination;seven patients reported non-specific adverse events after influenza (fever,discomfort,nausea,arthralgia) and 2 patients after meningococcal C vaccination (fever,rash at the injection site,discomfort).Seroconversion after meningococcal vaccination was analysed in 27 patients and 9 healthy subjects,no statistically significant differences in terms of antibody response to meningococcal vaccination were observed between these two groups.Treatment (steroids and immunosuppressive drugs) did not influence antibody titres
Conclusions: These data highlight the poor adherence to international recommendations on influenza vaccination in patients with autoimmune rheumatic disease at our Unit.The adherence to the meningococcal C vaccination campaign conducted in our country in 2015–2016 was also low.Our data confirm the safety of these vaccination and show that the immune response elicited by meningococcal C vaccination is comparable to healthy controls and is not influence by therapy
References:
[1] van Assen S, Agmon-Levin N, Elkayam O, et al.EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases.Annals of the rheumatic diseases 2011; 70(3): 414–22.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6123

THU0637 PATIENT'S AND RHEUMATOLOGIST'S PERSPECTIVES ON THE FOLLOW-UP INTERVAL AS A TOOL FOR OPTIMIZED OUTPATIENT TREATMENT

S. Hermann, S. Fügner, E. Wiebe, T. Alexander, G.R. Burmester, F. Buttgereit. *Dept. of Rheumatology, Charite, Berlin, Germany*

Background: Scientific progress and better disease awareness constantly lead to increasing patient numbers in rheumatology which requires optimization of patient care.
Objectives: The aim of this study was to evaluate and to optimize the procedures of patient care in an university-based outpatient rheumatology setting in Berlin, Germany.
Methods: One hundred patients with rheumatoid arthritis (80 women, 20 men, mean age 61.2 years, mean disease duration 12.9 years) were independently assessed both by a rheumatologist and via patient-reported self-assessment questionnaires. Current follow-up interval (usually 3 months), patient's perspective on follow-up intervals, signs of disease activity as well as individual patient concerns were recorded. Satisfaction with follow-up intervals was grouped into three categories: too early, just right/optimal, too late.
Results: Based on the physicians perspective, 46 patients presented at the optimal time point, 51 too early, and three too late. The patients reported the category "just right" in 82 cases, too early follow-up in 10 cases and too late in 8 cases. Of note, 51% (42 individuals) of all patients with self-reported satisfactory follow-up interval were judged to visit the out-patient department too early by the expert rheumatologist. When taking into account the follow-up interval and optimal satisfactory levels, 62% of patients were concluded to visit the department too early in those revisited after 3–4 months (n=65), and in 12% of those who were seen again after 5–6 months (n=17). 82% of patients in the latter group were judged to revisit just right by the physician.
Conclusions: There was a high proportion of overlap in the views on the satisfaction with follow-up intervals between physicians and patients. Especially in patients who were seen every 3–4 months, a high proportion was deemed to could have come later to the out-patient care unit from a purely medical point of view. Here we see a way to stretch the interval to 5–6 months without risking a long-term deterioration in patient care. However, this measure should be flanked by patient education and good collaboration with the general practitioners.
Acknowledgements: We thank AbbVie for financial support in the development of measures to optimize out-patient management in patients with rheumatoid arthritis. The sponsor did not influence the scientific results.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4748

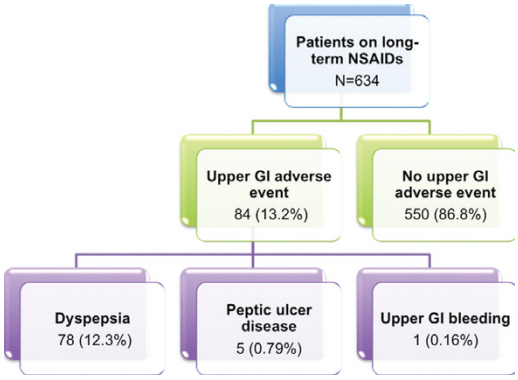
THU0638 PREVALENCE AND DIRECT HEALTHCARE COSTS OF UPPER GASTROINTESTINAL (UGI) ADVERSE EVENTS IN ASIAN RHEUMATIC PATIENTS ON LONG-TERM NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

S.L. Pok[1], F.H. Shabaruddin[2], J.Y. Teng[2], M. Dahlui[3], C.T. Ng[1], S. Sockalingam[1], M.S. Said[4], A. Rosman[5], I.S. Lau[5], L. Mohd Isa[6], H. Hussain[6], S. Mahadeva[2]. *[1]Dept. of Rheumatology; [2]Dept. of Medicine; [3]Dept. of Social & Preventive Medicine, University of Malaya; [4]Dept. of Rheumatology, National University of Malaysia, Kuala Lumpur; [5]Dept. of Rheumatology, Selayang Hospital, Selangor; [6]Dept. of Rheumatology, Putrajaya Hospital, Kuala Lumpur, Malaysia*

Background: NSAIDs are frequently used in patients with rheumatoid arthritis (RA) and osteoarthritis (OA). NSAID-induced UGI adverse events are well described in the Western population but data is lacking in Asian patients.
Objectives: To describe the prevalence and direct healthcare costs of NSAID-induced UGI adverse events in a large cohort of RA and OA patients in Malaysia.
Methods: A retrospective cohort study of RA and/or OA patients who received long-term NSAIDs (minimum 4 weeks prescription of any NSAID) between 2010 and 2013 was conducted in 4 large tertiary care centres with rheumatology units in Malaysia. Electronic clinical records and pharmacy prescriptions were reviewed. Resource use data was collected in patients who developed UGI adverse events within the 24 months follow up period. Unit costs were estimated by combining top down (general overheads for hospital services) and bottom up (activity-based costing for clinic visits, hospitalisation, diagnostic investigations, medications) approaches.
Results: 634 patients were included in the final analysis with mean age 53.4±12.5 years, 90% female, diagnosis of RA in 60%, OA in 10% and both RA and OA in 30%. 45% and 8% of patients were on concomitant prednisone and aspirin respectively. 89% of patients had no previous upper GI disease. 59% and 41% of patients were grouped under non-selective and COX-2 inhibitor respectively. 84 (13.2%) patients developed UGI adverse events (Figure 1), consisting of 78 (12.3%) patients with dyspepsia, 5 (0.79%) with peptic ulcer disease (PUD) and 1 (0.16%) with upper GI bleeding (UGIB). The total direct cost was RM37,352 (USD 11,419) with a mean cost of RM447±535 (USD 137±163) per patient (Table 1). The largest cost components were pharmacotherapy (34%), oesophagoduodenoscopies (OGD) (23%) and outpatient visits (18%). The mean cost of dyspepsia was RM409±513 (USD 125±157) per patient. The mean cost of PUD and UGIB was approximately double (RM806±579) (USD 246±177) and quadruple (RM1,602) (USD 490) of dyspepsia respectively.

Healthcare resource	Mean cost per patient in RM (USD)			
	Dyspepsia (n=78)	PUD (n=5)	UGIB (n=1)	All patients with UGI adverse events (n=84)
Outpatient visits	77 (23)	146 (45)	146 (45)	82 (25)
Emergency Dept visits	28 (9)	0	146 (45)	28 (9)
Inpatient stay	46 (14)	136 (41)	679 (207)	59 (18)
OGD	85 (26)	253 (77)	211 (65)	103 (32)
Blood tests	4 (1)	32 (10)	57 (17)	6 (2)
Radiology	8 (3)	0	0	8 (3)
Blood transfusion	4 (1)	56 (17)	280 (86)	10 (3)
Pharmacotherapy	150 (46)	183 (56)	84 (26)	151 (46)
Mean cost per patient in RM ±SD (USD)	409 ±513 (125±157)	806±579 (246±177)	1602 (490)	447±535 (137±163)

Conclusions: The low prevalence of UGI adverse events in Malaysian rheuma-



tology patients suggests judicious use of NSAIDs in tertiary care setting resulting in a low cost implication for the management of these events.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3523

THU0639 RHEUMATOLOGICAL MEDICATION USE IN PREGNANCY, PLANNING PREGNANCY, AND BREASTFEEDING AT MOTHERSAFE DURING THE YEARS 2010 TO 2015

S.-N. Luong[1], D. Kennedy[2], J.V. Bertouch[1]. [1]*Rheumatology, Prince of Wales Hospital;* [2]*Clinical Genetics, Royal Hospital for Women, Randwick, Australia*

Background: MotherSafe is a free, statewide, phone based counselling service for the general public and healthcare professionals concerned about exposures during pregnancy, pregnancy planning and breastfeeding (1). Obstetric drug information services such as MotherSafe are important in guiding decision-making in pregnancy, breastfeeding and planning of future pregnancies, and are increasingly used worldwide by both patients and healthcare providers (1, 2). At MotherSafe, phone advice is provided by trained telephone counsellors who are generally pharmacists. Data from each phone call is entered onto an electronic document. Some patients are then referred onto the MotherSafe clinic for specialised counselling by a clinical geneticist.

Objectives: To analyse data including patient and medication characteristics and trends from phone calls made to MotherSafe regarding disease modifying antirheumatic drugs (DMARDs) and biologic DMARDs (bDMARDs) from January 2010 to December 2015 inclusive.

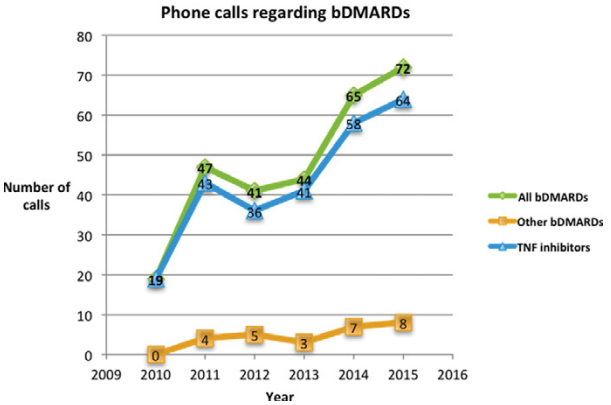
Methods: Retrospective study of phone calls made to MotherSafe from January 2010 to December 2015 regarding conventional DMARDs and biologic DMARDs. SPSS software facilitated statistical analysis.

Results: A total of 135,115 phone calls were made to MotherSafe from 2010–2015 with 2611 (1.93%) phone calls pertaining to DMARDs and bDMARDs.

Of these 2611 phone calls, 65.4% were made by patients and 13.5% by general practitioners. Most phone calls were made in metropolitan New South Wales (69.3%). 43% of phone calls were concerning exposures during breastfeeding, followed by exposures during pregnancy (32.9%), exposures whilst planning pregnancy (17.7%) and paternal exposures (2.9%). Where a specific diagnosis was given, inflammatory bowel disease was the most common indication (18.4%), followed by rheumatoid arthritis (8.2%). Corticosteroids were the most common medication exposure (37.3%), followed by azathioprine (18.8%), sulfasalazine (11.2%) and methotrexate (8.5%).

Most callers just received phone advice, especially if the call was just regarding breastfeeding exposures (73.4%). 383 callers (14.7%) were referred onto the MotherSafe clinic, which is run by a clinical geneticist.

bDMARDs made up 9.5% of calls with calls tending to increase over the years, but there was a slight decrease in 2012 and 2013 albeit with small numbers. TNF inhibitors still made up the majority of calls regarding bDMARDs.



Conclusions: This study evaluated the only obstetric medicine exposure information service in New South Wales, Australia. It is the first time that DMARDs and bDMARDs have been analysed for MotherSafe. There was a trend to increasing number of calls regarding bDMARDs over 2010 to 2015, which presumably reflects change in prescribing patterns. This study highlights the need for services like MotherSafe so patients and health care professionals can receive evidence based information and make choices about treatment in pregnancy.

References:

[1] Kennedy D, Eamus M, Hill M, Oei JL. Review of calls to an australian teratogen information service regarding psychotropic medications over a 12 year period. Aust N Z J Obstet Gynaecol. 2013;53(6):544–52. doi: 10.1111/ajo.12129.

[2] De Santis M et al. Prenatal drug exposure and teratological risk one year experience of an italian teratology information service. Med Sci Monit 20–8;14:PH1–8.

Acknowledgements: MotherSafe staff.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5560

THU0640 SECOND LINE TREATMENT PERSISTENCE AND COSTS AMONG PATIENTS WITH IMMUNE-MEDIATED RHEUMATIC DISEASES TREATED WITH SUBCUTANEOUS TNF-ALPHA INHIBITORS

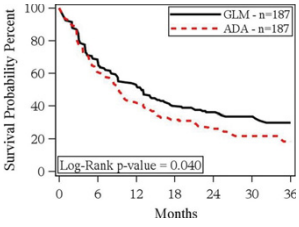
J. Dalén[1], A. Svedbom[1], C.M. Black[2], S. Kachroo[2]. [1]*Mapi group, Stockholm, Sweden;* [2]*Merck & Co., Inc., Kenilworth, United States*

Background: For some patients with Immune Mediated Rheumatic Disease (IMRD) discontinuing 1st line treatment with a subcutaneous Tumor Necrosis Factor-alpha inhibitor (SC-TNFi), 2nd line treatment with another SC-TNFi may be appropriate.

Objectives: The primary objective of this study was to describe treatment persistence with 2nd line SC-TNFi stratified by agent in patients with IMRD in Sweden. The secondary objective was to explore the impact of non-persistence with a second SC-TNFi on health care costs.

Methods: We conducted a retrospective study on treatment persistence and health care costs using data from health registers. Adults (≥18 years old) previously treated with one SC-TNFi and subsequently prescribed a second SC-TNFi were identified through prescriptions for adalimumab (ADA), etanercept (ETA), certolizumab pegol (CZP) and golimumab (GLM) between 5/6/2010 and 12/31/2012. Prescriber specialty and department were used to exclude patients treated for diseases other than IMRD. Persistence up to 3 years was estimated using non-parametric survival analysis. Given differences in baseline characteristics, analyses were conducted on propensity score matched (PSM) cohorts. Matching was based on age, gender, index year, diagnosis, Charlson Comorbidity Index and non-biologic DMARD use. Non-treatment health care costs were captured 12 months pre and post initiation of 2nd line SC-TNFi treatment and stratified by persistence status at 6 months.

Results: In total, 845 patients were identified (ADA: 316, ETA: 202, CZP: 140, GLM: 187). PSM cohorts were generated as GLM vs ADA, GLM vs ETA and GLM vs CZP, with 187, 164, and 113 matched pairs, respectively. GLM exhibited statistically significant higher persistence than ADA over 3 years (Figure; p=0.040) and numerically, but not statistically significant, higher persistence than ETA and CZP at 12 and 24 months. Persistent and non-persistent patients had similar mean total cost 12 months pretreatment initiation (USD 5,185 vs USD 5,064, p=0.750). During the 12 months post treatment initiation, persistent patients had lower mean total costs (USD 4,377 vs USD 6,605), corresponding to a difference in difference of USD 2,228 (p<0.001).



Conclusions: In patients previously treated with a SC-TNFi, GLM exhibited significantly better persistence than ADA and numerically higher persistence than ETA and CZP at 12 and 24 months, findings that are similar to results observed in 1st line SC-TNFi patients[1]. Given the lower healthcare costs for persistent patients, the choice of 2nd line SC-TNFi among eligible patients may merit careful consideration given its impact on patients and payers.

References:

[1] Dalén, J, et al. Treatment persistence among patients with immune-mediated rheumatic disease newly treated with subcutaneous TNF-alpha inhibitors and costs associated with non-persistence. Rheumatol International (2016): 1–9.

Disclosure of Interest: J. Dalén Consultant for: Merck & Co., Inc., Employee of: Mapi group, A. Svedbom Consultant for: Merck & Co., Inc., Employee of: Mapi group, C. Black Shareholder of: Merck & Co., Inc., Employee of: Merck & Co., Inc., S. Kachroo Shareholder of: Merck & Co., Inc., Employee of: Merck & Co., Inc.

DOI: 10.1136/annrheumdis-2017-eular.2654

THU0641 THE DISEASE BURDEN OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS FOR PATIENTS AND CAREGIVERS: AN INTERNATIONAL HEALTH RELATED QUALITY OF LIFE SURVEY AND RETROSPECTIVE CHART REVIEW

S. Shenoi[1], G. Horneff[2], M. Cidon[3], A. Ramanan[4], Y. Kimura[5], P. Quartier[6], I. Foeldvari[7], A. Zeft[8], K.G. Lomax[9], J. Gregson[10], A. Tineke[11], S. Campbell[12], J. Weiss[13], N. Marinsek[12], D. Patel[12], N. Wulffraat[14]. *[1]Seattle Children's Hospital, Seattle, United States; [2]Asklepios Kliniken GmbH, Hamburg, Germany; [3]Stanford University, Palo Alto, United States; [4]University Hospitals Bristol, Bristol, United Kingdom; [5]Hackensack University Medical Center, New Jersey, United States; [6]Paris-Descartes University Necker-Enfants Malades Hospital, Paris, France; [7]Hamburger Zentrum für Kinder-und Jugend Rheumatologie, Hamburg, Germany; [8]Pediatrics Rheumatology, Cleveland Clinic, Cleveland; [9]Novartis Pharmaceutical Corporation, New Jersey, United States; [10]Novartis Pharma AG, Basel, Switzerland; [11]VU University Medical Centre, Amsterdam, Netherlands; [12]Navigant Consulting Inc., London, United Kingdom; [13]Navigant Consulting Inc., San Francisco, United States; [14]Wilhelmina Kinderziekenhuis, Utrect, Netherlands*

Background: Systemic juvenile idiopathic arthritis (SJIA) is a severe autoinflammatory disease characterised by systemic features including high fevers, rash and arthritis. SJIA can impose a high physical, psychosocial, behavioral and financial burden on patients (pts) and their families.
Objectives: To analyse the impact of the burden of SJIA by evaluating caregiver perspectives of disease burden utilising a SJIA-specific questionnaire combined with physician data about disease severity and treatment in an international, real-world study.
Methods: SJIA treatment centers in France, Germany, Netherlands, UK and the US participated. Pts (aged 4–18 years) with confirmed SJIA received one of the following biologic treatments for ≥2 months: anakinra (ANA), canakinumab (CAN), or tocilizumab (TOC). SJIA burden in patients on biologics was assessed using a caregiver questionnaire and retrospective chart review. Validated measures included: Child Health Questionnaire Parent-Form 50 (CHQ-PF50), 36-Item Short-Form Health Survey (SF-36v2) and Work Productivity and Activity Impairment questionnaire: Specific Health Problem (WPAI:SHP). Caregivers completed function, treatment satisfaction and resource utilization questions.
Results: Sixty-one pts enrolled from June 2015- June 2016: 12 on ANA, 25 on CAN, 24 on TOC; 46% from the US; 48% female; mean age at survey was 11.3 years. Mean age at SJIA diagnosis was 6.4 years, mean age at start of ANA, CAN, and TOC treatment was 9.9, 9.1, and 7.5 years, respectively. Caregivers were 79% female, mean age 41.2 years, and 36% reduced or stopped working due to their child's SJIA. Of the pts enrolled on CAN and TOC, 72% and 46% respectively had previously been on ANA. Baseline CHAQ, CHQ-PF50, and WPAI scores were worse in CAN and TOC than ANA pts. Mean (±SD) CHQ-PF50 physical (PhS) and psychosocial (PsS) summary scores were significantly lower in SJIA patients than a normative population (PhS: 40.0±18.2 vs. 53.0±8.8; PsS: 46.6±11.3 vs. 51.2±9.1) as was caregivers' mean SF-36v2 mental component score (46.2±10.7 vs. 50.0+10). Highest caregiver stressors were worry over long-term SJIA impact on their child (45%) and uncertainty about the future (28%).
Conclusions: Treatment sequencing and patient-reported outcome measures indicate ANA is used as 1st line for less severe SJIA while CAN and TOC are used as 2nd/3rd line for severe SJIA. Caregivers expressed stress over the long-term impact of SJIA and fear for the future and had variable treatment satisfaction and resource utilisation levels.
Disclosure of Interest: S. Shenoi: None declared, G. Horneff Grant/research support from: Abbvie, Chugai, Novartis, Pfizer, Roche, M. Cidon: None declared, A. Ramanan: None declared, Y. Kimura Grant/research support from: Novartis, SOBI, CARRA, Inc (salary support), P. Quartier Grant/research support from: Abbvie, Novartis, Pfizer, Chugai-Roche, Consultant for: Abbvie, Novartis, Pfizer, Roche, Sobi, Speakers bureau: Abbvie, Novartis, Sobi, Roche, I. Foeldvari Speakers bureau: Novartis, Abbvie, Chugai, A. Zeft Shareholder of: Merck, OPKO, ARNI, K. Lomax Employee of: Novartis Pharmaceuticals Corporation, J. Gregson Employee of: Novartis, A. Tineke: None declared, S. Campbell Consultant for: Novartis, J. Weiss Consultant for: Novartis, N. Marinsek Consultant for: Novartis, D. Patel Consultant for: Novartis, N. Wulffraat Grant/research support from: AbbVie, Roche, Sobi, Consultant for: Novartis, Pfizer, Sobi
DOI: 10.1136/annrheumdis-2017-eular.3347

THU0642 THERE IS A COMMUNICATION PROBLEM BETWEEN PATIENT AND PHYSICIAN DURING PRE-CONCEPTIONAL PERIOD: HUR-BIO REAL LIFE RESULTS

O.A. Uyaroglu[1], E. Seyhoglu[1], A. Erden[2], L. Kılıç[2], B. Armagan[2], A. Sarı[2], Ö. Karadağ[2], A. Akdoğan[2], S. Apraş Bilgen[2], S. Kiraz[2], I. Ertenli[2], U. Kalyoncu[2]. *[1]İnternal Medicine; [2]Division of Rheumatology, Hacettepe University School of Medicine, Ankara, Turkey*

Background: A significant part of patients with inflammatory arthritis are at their reproductive ages. Biological drugs are one of the important treatment options for inflammatory artritis which can cause fetal morbidity and mortality. Management of arthritis during pre-conceptional period is one of the challenges in rheumatology.
Objectives: This study aims to assess whether patients under biological treatment share their conception intents with their physicians.
Methods: 1580 patients admitted to our outpatient clinic between July 2015 and July 2016 who were received biological treatment. A questionnaire was performed to 373 patients who are at their reproductive ages. Patients were asked whether they or their wifes had got pregnant after the start of biological agent. If they had got, they were asked;
1. Was the pregnancy intented?
2. Did your physician know if you were going to get pregnant while taking a biological agent?
Results: There were total of 79 patients who or whose wifes had got pregnant after the start of biological agent. 34 (%43) out of 79 were female and 45 (%57) out of were male. Mean age of patients were 35.1 (5.3). Median disease duration was 10 (IQR=9) years. 24 (30.4%) pregnancies out of 79 were not planned [15 female (44.1%), 9 male (20%), p=0.021]. In addition, 43 (54.4%) out of 79 patients did not share their pregnancy plans with their physicians [15 (44,1%) female and 28 (62,2%) male (p=0.110)]. 28 (35.4%) of all patients stated that their disease was active during pre-conceptional period [20 (58,8%) female patients, 8 (17,8%) male patients, (p<0,001)].
Conclusions: In our study group, almost one third of the patients had unplanned pregnancies particularly with in female patients. One third of the patients were in active state before conception according to patients' report. Almost half of the patients did not share their plan of pregnancy with their physicians. We suggest that in routine practise, physicians should ask plan of pregnancy in every clinical visit.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4101

THU0643 WHAT FACTORS RELATE TO PATIENTS CONTRIBUTING LONGITUDINAL DATA USING SMARTPHONE TECHNOLOGY? FINDINGS FROM RA PATIENTS PARTICIPATING IN ARTHRITISPOWER REGISTRY

W.B. Nowell[1], H. Yun[2], J. Willig[3], J. Beaumont[4], B. Johnson[3], S. Ginsberg[5], C. Wiedmeyer[5], R. Crow-Hercher[5], B.J. Johnson[5], S. Yang[3], J.R. Curtis[3]. *[1]Global Healthy Living Foundation, Upper Nyack; [2]University of Alabama at Birmingham School of Public Health; [3]University of Alabama at Birmingham, Birmingham; [4]Northwestern University Feinberg School of Medicine, Evanston; [5]CreakyJoints, Global Healthy Living Foundation, Upper Nyack, United States*

Background: Data capture of patient reported outcomes (PROs) is gradually shifting from data collection on paper in medical office settings to use of computer or mobile based technologies between doctor visits. Concerns have been raised that patients may have limited interest in contributing data over time or that they may only record new data when there has been a change in their clinical status.
Objectives: The objective of this study was to evaluate the patterns and factors associated with longitudinal PRO data capture among participants in the PCORI-funded Patient Powered Research Network for adult rheumatologic conditions, ArthritisPower.
Methods: Patients in the registry were asked to voluntarily complete PROs including the RAPID3 and 4 PROMIS instruments plus disease-specific information via a mobile application (App) on their smartphone or computer. We evaluated the average time it took the patient to record each of the instruments and the total number of unique days that patients recorded PROs on the smartphone. Given the newness of the registry (launched late 2015), longitudinal data was defined as contributing at least 2 sets of PROs on unique calendar days. We tested the hypothesis that patients would contribute longitudinal data only when at least one of their scores exceeded a minimally important difference (MID) of any of the 5 PROs examined (generally 2–3 units for PROMIS instruments; 3.6 units for RAPID3). Demographic factors associated with multiple PRO reports were identified using logistic regression among patients who had been enrolled in the registry for at least 3 months.
Results: At the time of analysis, ArthritisPower had recruited 2,103 patients, most (approximately 68%) had RA, and 20% provided their Twitter handle. Average (SD) age was 50 (12); 87% were women. The mean assessment time for each of the PROMIS instruments ranged from a low of 16 seconds (Sleep Disturbance) to a high of 105 seconds (RAPID3). The average score for Pain Interference was 64.3 (SD: 6.3), Physical Function 37.5 (6.5), Sleep Disturbance 59.3 (8.4), Fatigue 64.2 (8.4), and RAPID3 15.7 (5.3). Of 1,946 patients who registered the Smartphone App more than 3 months prior to analysis, 20.6% never contributed any PRO information, 53.3% answered once, and 26.1% answered at least twice. Among patients with longitudinal data (≥2 assessments), the mean change score of PROs between pairwise PRO assessments was <1 point for all instruments

Table: Mean change between 1st and 2nd visit among ArthritisPower patients with longitudinal data

	Mean change from 1st to 2nd visit	Absolute mean change from 1st to 2nd visit	% of patients exceeding change > MID
PROMIS Physical Function	-0.4 (3.8)	2.7 (2.7)	34.2%
PROMIS Pain Interference	-0.4 (5.4)	3.9 (3.6)	52.3%
PROMIS Sleep Disturbance	0.2 (6.1)	4.6 (4.0)	56%
PROMIS Fatigue	-0.03 (6.6)	4.8 (4.4)	55.6%
RAPID3	0.2 (3.8)	2.8 (2.6)	29.8%
MID: Minimally important difference (using 3 points for PROMIS instruments and 3.6 for RAPID3)			

(Table). Only 23.1% of patients contributing longitudinal data had a change greater than the MID in any of the 5 PRO measures. Patients with RA (OR: 1.54, 95% CI: 1.14–2.06), biologic use (2.12, 1.43–3.15), and those with Twitter accounts (1.40, 1.08–1.82) were more likely to contribute longitudinal PRO data in the absense of regular reminders.
Conclusions: Multiple factors were associated with patients contributing longitudinal PRO data. Patients were willing to contribute longitudinal PRO data even in the absence of a change in their health state exceeding any MID. Additional efforts are needed to engage patients to contribute PRO data over time.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5370

THU0644 PATIENT DECISIONS RELATED TO HIP AND KNEE ARTHROPLASTY AND THE FACTORS INFLUENCING THEM

W.B. Nowell[1], S. Venkatachalam[2], E. Harden[2], T. Concannon[3,4,5]. *[1]Global Healthy Living Foundation, Upper Nyack, United States; [2]CreakyJoints, Global Healthy Living Foundation, Upper Nyack; [3]Tufts Clinical and Translational Science Institute; [4]Tufts University School of Medicine; [5]The RAND Corporation, Boston, United States*

Background: Patient-engaged research can improve the safety and satisfaction outcomes of hip and knee arthroplasty (joint replacement surgery).
Objectives: The objective of this study was to identify the decisions that are most important to patients when undergoing hip or knee arthroplasty and the factors they view as important in making those decisions.
Methods: Forty-nine U.S. participants were recruited from ArthritisPower Patient-Powered Research Network and CreakyJoints arthritis patient community to participate in structured one-hour discussions held via webinar during January to April 2016 to understand patients' experiences with joint replacement. Patients described decisions that were most important to them and the factors they used to make those decisions. Discussions were transcribed and coded to identify themes; patient decisions and factors were identified and categorized and co-occurrence of decisions and factors was tabulated. Demographic and procedure-related characteristics were captured.
Results: Eight decisions emerged that were influenced by at least ten factors (Table). The most important decisions involved whether to have surgery, selection of surgery date, surgeon, facility, implant device, and ancillary health care professionals (HCPs) and services. Factors included current situation, expectations of having or not having surgery, professional and word-of-mouth familiarity with surgeon/HCP, procedure, services and device, and perceived value. Patients' current situation and health status and their expectations of surgery were most commonly used to make decisions about whether and when to have surgery. Patients' trust of and communication with doctors was the most commonly factor used when deciding on arthroplasty surgeon.

Table 1: Arthroplasty Decisions Important to Patients and the Most Common Factors Influencing Them

Decisions Important to Patients	Most Common Factors Influencing Decisions
Surgery: Whether to have partial or total hip/knee joint replacement surgery (arthroplasty)	Current life situation / health status (44%), Expectations of surgery (11%), Information provided to patient by doctor/HCP (11%), Alternatives to surgery (11%)
Timing: When to have surgery	Current life situation and health status (38%), Expectations of surgery (19%), Alternatives to surgery (19%)
Surgeon: Which surgeon will perform surgery	Trust and communication with surgeon (45%), Perceived value of surgeon's expertise (19%), Expectations of surgery (16%), Information accessed by patient (10%)
Facility: Where surgery will be performed (e.g., location, specific hospital or medical center)	Information provided to patient by doctor/HCP (28%), Trust and communication with HCP (18%), Firsthand familiarity with facility (18%), Expectations of surgery (18%), Information accessed by patient (9%), Perceived value of facility expertise (9%)
Device: Which implant device will be installed during surgery	Expectations of surgery (39%), Information provided to patient by doctor/HCP (18%), Perceived value of device (16%), Trust and communication with HCP (11%)
Approach: Specific approach to surgery (e.g., anterior vs. posterior, bilateral joint replacement)	Expectations of surgery (45%), Trust and communication with surgeon (42%), Firsthand familiarity with other HCPs (18%)
Other HCPs: Who/which other health care professionals (HCPs) besides the surgeon will be involved in care during and after surgery	Expectations of surgery (30%), Trust and communication with HCP (20%), Current life situation / health status (20%), Perceived value of / familiarity with other HCPs (20%)
Other Services: What other services will be necessary before, during or after surgery	Expectations of surgery (71%), Trust and communication with HCP (14%), Current life situation / health status (14%)

Conclusions: Arthroplasty patients are concerned about a variety of decisions. Patient-centered research should maximally address questions of importance to patients and this study is a first step in identifying and prioritizing topics that matter most to patients and the information that patients currently use to make joint replacement decisions.
Acknowledgements: This project was funded through a Patient-Centered Outcomes Research Institute (PCORI) Eugene Washington PCORI Engagement Award (2228-GHLF).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5291

THU0645 OPTIMIZING THE EFFICIENCY OF PATIENT DATA CAPTURE USING SMARTPHONE TECHNOLOGY: EVALUATION OF THE CORRELATION BETWEEN PROMIS INSTRUMENTS FOR PRO DATA CAPTURE

W.B. Nowell[1], H. Yun[2], J. Beaumont[3], S. Yang[4], J. Willig[4], S. Ginsberg[5], K.V. Clayton[5], S. Hazel[5], C. Wiedmeyer[5], J.R. Curtis[4]. *[1]Global Healthy Living Foundation, Upper Nyack; [2]University of Alabama at Birmingham School of Public Health, Birmingham; [3]Northwestern University Feinberg School of Medicine, Evanston; [4]University of Alabama at Birmingham, Birmingham; [5]CreakyJoints, Global Healthy Living Foundation, Upper Nyack, United States*

Background: Patient-reported outcomes (PROs) are key to enabling the comprehensive assessment of patient-centered benefits in comparative effectiveness research (CER). However, the relationships between different PROMIS instruments and condition-specific disease activity measures in diseases such as rheumatoid arthritis (RA) have not been well studied.
Objectives: The objectives of this analysis were to evaluate the longitudinal relationship between different PROMIS instruments and the RAPID3, a measure of self-reported patient disease activity.
Methods: Four NIH PROMIS instruments (Pain Interference, Physical Function, Sleep Disturbance and Fatigue) and the RAPID3 were administered to participants in the PCORI-funded ArthritisPower patient registry. After descriptive analytics, we estimated multiple correlations between PROMIS instruments and the RAPID3. For each PRO instrument and with each assessment used as the unit of measure, we calculated the R-squared using mixed models to evaluate how the PROs were related to each other. Using Pain Interference as an example, we evaluated R-squared for each model with additional PROs and demographic factors including enrollment age, sex, race, Twitter account, region, and visit times.
Results: A total of 1,590 unique participants who answered the survey one or more times were included in the analysis, with mean (SD) age of 49 (12) years. The mean score for Pain Interference was 63.7 (SD: 7.0), Physical Function 37.5 (8.7), Sleep Disturbance 58.4 (8.7), Fatigue 63.8 (8.8), and RAPID3 15.5 (5.7). Most PROMIS instruments were low to moderately correlated (around 0.2) with each other and the RAPID3. Using Pain Interference as an example, R-squared measures revealed a high total variance explained (R^2=49%) between Pain Interference and Physical Function (Table); those involving Pain Interference, Physical Function, Fatigue, Sleep Disturbance and RAPID3 also revealed a higher variance contribution with these additional PROs (66%). Additional adjustment for demographic factors added little variance explanation (1.4%).

Table: Total variance explained by predictors (R-Squared) with PROMIS Pain Interference as the dependent variable

Models with PROMIS Pain Interference as the dependent variable	Pain variance that could not be explained by predictors	Total variance that could be explained by predictors (R-Squared)
Baseline model: no predictors	42.6	-
Model with predictors: PROMIS Physical Function	22.6	46.9%
Model with predictors: PROMIS Physical Function, Sleep Disturbance	20.7	51.6%
Model with predictors: PROMIS Physical Function, Sleep Disturbance, Fatigue	18.7	56.1%
Model with predictors: PROMIS Physical Function, Sleep Disturbance, Fatigue, RAPID3	15.3	64.1%
Model with predictors: PROMIS Physical Function, Sleep Disturbance, Fatigue, RAPID3 and demographic predictors (age, gender, race, region, etc.)	15.1	64.7%
Model with only demographic predictors: age, gender, race, region, etc.	42.3	0.7%

Conclusions: PROMIS Pain Interference, Physical Function, Sleep Disturbance, Fatigue instruments and RAPID3 are reasonably correlated to each other. Age, gender, race and other demographic factors play little role in explaining variance in PROs. These results suggest potential efficiencies in using some measures to predict or impute the values for other measures and to optimize the frequency of patient data collection using at-home technologies including Smartphone Apps like ArthritisPower.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5329

THU0646 INTERCHANGEABILITY FROM INFLIXIMAB ORIGINATOR TO INFLIXIMAB BIOSIMILAR: EFFICACY AND SAFETY IN A PROSPECTIVE OBSERVATIONAL STUDY ON 89 PATIENTS

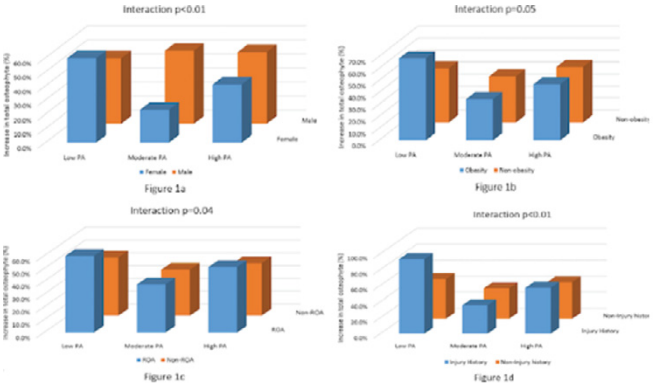
Y. Presberg[1], V. Foltz[2], C. L'Amour[2], P. Tilleul[1], D. Zerkak[2], C. Gard[1], B. Fautrel[2,3]. [1]*Pharmacy;* [2]*Rheumatology, AP-HP pitié salpetrière hospital;* [3]*Université Pierre et Marie Curie (UPMC)-Paris 6, Paris, France*

Background: Biosimilar biologic disease modifying anti-rheumatic drug (bsDMARD) are supposed to offer a real economic advantage for these diseases for the same health benefit. While the administration of a biosimilar to a new patient is widely accepted, the switch from a biologic originator DMARD (boDMARD) to its biosimilar remains questioned.
Objectives: This study aimed to assess the safety and efficacy of switching from an IV anti-TNF boDMARD to its bsDMARD in patients with rheumatic arthritis, spondyloarthritis, psoriatic arthritis, juvenile arthrtitis and uveitis.
Methods: Prospective real-life study in the rheumatology unit of La Pitié-Salpêtrière Hospital, from February 2016 to December 2016. Patients initially treated with the boDMARD infliximab (RemicadeÒ), all switched to infliximab bsDMARD (InflectraÒ) after patient's information by a rheumatology nurse. The dose and administration schedule remained unchanged at the switch. Our primary endpoint was infliximab maintenance rate. Secondary endpoints were evolution of disease activity, as well as evolution of both infliximab trough levels and anti-drug antibody (ADA) serum levels before and after the switch. In addition, safety events were also monitored.
Results: We identified 89 patients – spondyloarthritis (61%), rheumatic arthritis (27%), psoriatic arthritis (11%), juvenile arthritis and uveitis (1%) – in rheumatology who have been switched to boDMARD infliximab to its bsDMARD. Clinical assessment was based on DAS28 (peripheral joint involvement) or BASDAI (axial involvement) scores. 93% of patients remained treated with infliximab: 6 patients (7%) stopped the treatment due to a loss of efficacy. As shown in Figure 1, there is no significant change in disease activity before and after having switched patients to infliximab biosimilar.The ADAdosage were detected in 10 patients, 7 with high titer (>200ng/mL) and 3 with moderate titer (between 50 and 200 ng/mL). It was significantly correlated with low trough levels of IFX (<0,3µg/mL). Among them, 6 (4 with high titer; 2 with moderate titer) also had a poor clinical response before switch (refractory patients). 4 ADA-positive patients (3 with high titer; 1 with moderate titer) were still good clinical responders.
Conclusions: The interchangeability of infliximab boDMARD to its bsDMARD does not rise any efficacy and safety concern in our experience. The role of drug and ADA monitoring during the switch remains to be further explored.
References:
[1] Jørgensen K et al. (2016) LB15 - Biosimilar infliximab (CT-P13) is not inferior to originator infliximab: results from the 52-week randomized NOR-SWITCH trial. BioDrugs 2017 Jan 24. doi: 10.1007/s40259-017-0210-0,
[2] Interchangeability of Biosimilars: A European Perspective, Kurki P, van Aerts L, Wolff-Holz E, Giezen T, Skibeli V, Weise M.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6586

THU0647 INTERACTIONS BETWEEN STEPS PER DAY AND RISK FACTORS FOR OSTEOARTHRITIS ON MRI-DETECTED OSTEOPHYTES IN A POPULATION BASED COHORT STUDY

Z. Zhu[1,2], W. Han[1], S. Zheng[1], K. Wang[1], T. Winzenberg[1], F. Cicuttini[3], C. Ding[1], G. Jones[1] on behalf of Musculoskeletal Uni, Menzies Institute for Medical Research. [1]*Musculoskeletal Unit;* [2]*12779, Hobart;* [3]*Department of epidemiology and Preventive Medicine, Monash University, Melbourne, Australia*

Background: It is clear that exercise helps the symptoms of osteoarthritis. However, the relationship between physical activity (PA) and progression of knee osteoarthritis (OA) remains controversial. Moreover, no guideline on the amount of PA to prevent OA progression in general older population has been recommended, and it is still uncertain whether PA should be promoted among subgroups with knee OA such as female gender, obesity, radiographic osteoarthritis (ROA) and knee injury history. Osteophyte (OP) has long been viewed as a defining structural feature of knee OA. Recently, MRI-detected OPs have been shown to be more sensitive to change than radiographs.
Objectives: The aims of this study were to describe the longitudinal association between objectively-measured PA and knee MRI-detected (OPs), and to test the interactions between PA and gender, obesity, ROA or knee injury history on the increases in MRI-detected OPs.
Methods: 408 community-dwelling adults aged 51–81 were randomly selected from local community and measured at baseline and 2.6 years later. T1-weighted fat suppressed MRI was used to evaluate knee OPs at baseline and after 2.6 years. PA was assessed at baseline by pedometers (steps per day) and categorized as 3 groups: low PA (≤7499 steps per day), moderate PA (7500 to 9999 steps per day) and high PA (≥10000 steps per day). Radiographs were obtained and scored for individual features of radiographic osteoarthritis (ROA). Knee injury history was recorded by questionnaire and body mass index (BMI) was calculated. Logistic regression and log binomial regression were used in longitudinal analyses.
Results: In total study sample, doing moderate PA was associated with reduced risk of an increase in MRI-detected OPs, comparing to low PA (RR=0.73, p=0.03). There were significant interactions between PA and gender, obesity, ROA or knee injury history (all p<0.05) for an increase in MRI-detected OPs. In stratified analyses, moderate PA was protective against an increase in MRI-detected OPs in females (OR=0.23, p<0.01), obese participants (OR=0.23, p<0.01), participants with ROA (OR=0.45, p=0.02) and participants with knee injury history (OR=0.05, p=0.02). These significant associations still existed after further adjustments for age, sex, BMI, ROA and/or knee injury history (where appropriate). High PA was not associated with an increase in MRI-detected OPs in total sample or the stratified analyses but there were relatively few in this category.



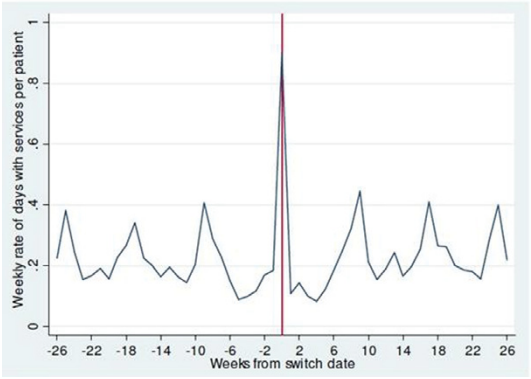
Conclusions: Moderate PA is protective for change in MRI-detected OPs in older adults, especially in those with female gender, ROA, obesity and knee injury history. This implies older people with above risks of knee OA may need to aim for a range from 7500 to 9999 steps per day.
References:
[1] Dore DA, Winzenberg TM, Ding C, Otahal P, Pelletier JP, Martel-Pelletier J, et al. The association between objectively measured physical activity and knee structural change using MRI. Ann Rheum Dis 2013; 72: 1170–1175.
Acknowledgements: The authors thank the participants who made this study possible, and acknowledge the role of the staff and volunteers in collecting the data, particularly research nurses Boon C and Boon P. Warren R assessed MRIs and Dr Srikanth V and Dr Cooley H assessed radiographs.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1162

THU0648 USE OF OUTPATIENT RHEUMATOLOGIC HEALTH CARE SERVICES BEFORE AND AFTER SWITCH FROM ORIGINATOR TO BIOSIMILAR INFLIXIMAB

B. Glintborg[1], J. Sørensen[2,3], M.L. Hetland[1]. [1]*The DANBIO registry and Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre of Head and Orthopaedics, Glostrup;* [2]*University of Southern Denmark, Odense, Denmark;* [3]*Royal College of Surgeons in Ireland, Dublin, Ireland*

Background: According to Danish national guidelines issued in 2015, pts (pts) with inflammatory rheumatic diseases in routine care treatment with originator infliximab (INX) must switch to the cheaper biosimilar infliximab (CT-P13). This switch was done for economic reasons (CT-P13 64% cheaper than INX). Since any treatment change potentially induces additional guidance of pts and use of hospital services, it is relevant to investigate whether the switch affected use of hospital resources.
Objectives: To study difference in rates of outpatient activities and services provided 6 months before vs after the switch to CT-P13 for pts treated at rheumatologic departments which provide infliximab treatment.
Methods: The switch population and switch dates were identified in the Danish quality registry, DANBIO (1). Vital status was validated in the Central Person Registry. The Danish National Patient Registry (NPR) provided information regarding outpatient contacts and services. The use of 16 types of services relevant to the rheumatologic specialty was identified and included outpatient visits, infliximab infusion, nurse counselling, phone consultation, and rheumatologic ultrasound. Number of days with these services was counted. Services performed on the switch date were analyzed separately. Thus, for each patient the following rates were calculated 6 months before and after the switch: 1) days with at least one outpatient service provided, and 2) number of services provided. In addition, the weekly rate of days with services was calculated.
Only pts who were alive and could be followed in the NPR for 6 full months after the switch were included.
Paired t-tests were used to compare rates before and after switch. A graphical interrupted time series analysis was conducted for weekly number of services provided.
Results: Among 802 pts identified, 769 had available NPR outpatient data from hospital departments of rheumatology. The 769 pts had 1484 outpatient treatment contacts at the included rheumatology departments with a total of 9243 days with services provided (including 693 on the switch date). The mean rate of days with services provided was 5.4 before the switch and 5.7 after switch (p=0.0003). The

Figure Weekly rate of days with services per patient according to switch date



weekly rate of days with services showed no obvious differences before and after the switch but had a clear 8-week pattern (corresponding to the average infusion interval) (Figure).

The total number of services provided was 19,752 (2,019 of these on the switch date). There were significant increases in the rates before vs after switch for 6 of the 16 service categories, although the mean rates were small: telephone consultations (mean rate 1.0 before vs. 1.2 after), patient guidance (0.5 vs. 0.4), intravenous medication (0.0 vs. 0.1), clinical controls (2.1 vs. 2.3) and clinical investigations (0.3 vs. 0.5), whereas the rate of infliximab treatment decreased (3.1 vs 3.0) (all $p<0.05$, insignificant results not shown).

Conclusions: This analysis showed that there were only small differences in the rates of days with outpatient services and rates of services 6 months before and after the switch from original to biosimilar infliximab. Thus, it is unlikely that the switch is associated with substantially higher cost of health care resources.

References:

[1] Glintborg et al. Arthritis Rheumatol. 2016; 68 (suppl 10).

Disclosure of Interest: B. Glintborg Grant/research support from: Abbvie, J. Sørensen Grant/research support from: Abbvie, M. Hetland Grant/research support from: Orion, BMS, AbbVie, Biogen, Pfizer, MSD

DOI: 10.1136/annrheumdis-2017-eular.3008

THU0649 MANDATORY CHOICE OF FIRST BDMARD IN DENMARK – AN OPPORTUNITY TO STUDY REAL-LIFE EFFECTIVENESS? RESULTS FROM THE DANBIO REGISTRY

K.L. Grøn[1], B. Glintborg[1], M. Nørgaard[2], F. Mehnert[2], M. Østergaard[1], L. Dreyer[1], N.S. Krogh[3], M.L. Hetland[1]. *[1]DANBIO, COPECARE; [2]Department of Clinical Epidemiology, Aarhus; [3]Zitelab Aps, Copenhagen, Denmark*

Background: In Denmark, biological treatments (bDMARDs) are tax paid. Since year 2013, The Danish Council for the Use of Expensive Hospital Medicines (RADS) has issued recommendations with annual updates regarding RA patients (pts) initiating biological treatment, dictating a mandatory choice of the cheapest bDMARD (1). Furthermore, the percentage of pts expected to be treated according to the RADS recommendation per year is stated. For pts treated with concomitant methotrexate (MTX) recommendations on first line, first choice bDMARD were: Jan 1th 2013-June 30th 2014: certolizumab pegol (in 80% of pts); July 1th 2014 - June 30th 2015: abatacept (80%); July 1th 2015-June 30th 2016: biosimilar infliximab (CT-P13) (50%). The nationwide Danish DANBIO registry collect data prospectively and covers >90% of adults with rheumatological diseases treated with bDMARDs in routine care (2).

Objectives: To characterize Danish RA pts initiating first line, first choice treatment with a bDMARD in combination with MTX in the three RADS periods and to explore the degree of compliance to RADS recommendations. Furthermore, to investigate differences in baseline characteristics between those pts who were compliant to RADS guidelines and those who were not.

Methods: For each of the three RADS' periods bio-naive pts with RA were identified in DANBIO and compliance to RADS recommendations was assessed. Baseline characteristics of those who started first choice bDMARD treatment according to RADS were compared with those who started another biologic instead. Comorbidities and previous hospitalized infections were identified in the Danish National Patient Registry. Comorbidities from Charlson Comorbidity Index were summarized except category number 7, connective tissue disease.

Results: For all three RADS periods, age, gender, functional status and disease activity were typical for pts with RA. Age was median: 57 years, range 18–88 years and disease duration: 3 years, range 0–54 years. 16–22% of pts had ≥1 comorbidity and 7–9% had ≥1 hospitalized infection the previous year. In each of the three RADS periods, 71%, 66% and 60% of pts followed the RADS recommendations, respectively (Table). The table shows differences between those who started first choice bDMARD treatment according to RADS, and those who did not. Overall, pts who complied to RADS had higher DAS28 and patient VAS global. Characteristics of pts who followed RADS recommendations in the three periods appeared similar.

Conclusions: In this nationwide study of >600 RA pts, pts' clinical characteristics were more heterogeneous than in clinical trials, reflecting routine care. Overall, compliance to recommendations was good. Thus, the national guidelines in Denmark with mandatory choice of the first biological drug may provide an interesting opportunity to study effectiveness of bDMARDs in routine care. This highlights observational studies as a valuable supplement to RCTs.

Table 1: Characteristics of RA pts initiating treatment with first bDMARD in combination with MTX stratified by compliance to the recommendations of RADS or not in the three time periods.

	Certolizumab pegol		Abatacept		CT-P13	
Time periods, MM.YY	01.13-06.14		07.14-06.15		07.15-06.16	
Recommended compliance (%)	80		80		50	
Actual compliance to RADS (%)	71		66		60	
Baseline characteristics	RADS	Not RADS	RADS	Not RADS	RADS	Not RADS
Number of pts	328	135	210	109	200	131
Age (years)	**57**	**58**	57	59	59	56
Female (%)	**71**	**80**	73	71	69	71
IgM-RF positive (%)	61	61	67	69	64	70
Anti-CCP positive (%)	74	73	77	83	70	71
Disease duration (years)	3	5	3	4	**4**	**2**
DAS28	**4.6**	**4.3**	**4.5**	**4.3**	4.6	4.5
HAQ	1.1	1.1	**1.1**	**0.9**	1.0	1.0
Patient global VAS (mm)	**70**	**57**	**73**	**53**	69	67
Comorbidities ≥1 (%)*	**22**	**33**	**16**	**28**	24	20
No. of comorbidities (mean)**	1.3	1.5	**1.2**	**1.6**	1.3	1.4
Hosp. infections ≥1 (%) ***	8	10	7	9	9	9

Variables are medians unless otherwise mentioned. **Numbers in bold:** p<0.05 for comparison between RADS/not RADS, (Mann Whitney and Chi-square test) *From baseline and 10 years back; **In pts with ≥1 comorbidity; *** From baseline and 1 year back; Abbreviations: DAS28 Disease activity score in 28 joints; HAQ health assessment questionnaire; VAS: visual analogue scale

References:

[1] The Danish Council for the Use of Expensive Hospital medicines (RADS), http://www.regioner.dk/media/28308/radsfolder-engelsk.pdf.
[2] Hetland ML. Rehumatology 2011;50:69–77.

Disclosure of Interest: K. Grøn Grant/research support from: BMS, B. Glintborg Grant/research support from: Abbvie, M. Nørgaard Grant/research support from: Department of Clinical Epidemiology is involved in studies with funding from various companies as research grants to (and administered by) Aarhus University, Denmark, F. Mehnert Grant/research support from: Department of Clinical Epidemiology is involved in studies with funding from various companies as research grants to (and administered by) Aarhus University, Denmark, M. Østergaard Grant/research support from: Consultation fees from: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, and Wyeth; Research support and grants from: Abbvie, BMS, Janssen and Merck, L. Dreyer Grant/research support from: MSC, UCB, Janssen Pharmaceutical, N. Krogh: None declared, M. Hetland Grant/research support from: Abbvie, BMS, MSD, Orion, Novartis, UCB, Pfizer

DOI: 10.1136/annrheumdis-2017-eular.4116

THU0650 THE EFFECT OF ANTI-TNF THERAPY ON WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS OVER ONE YEAR – REAL LIFE DATA FROM THE CZECH BIOLOGICS REGISTRY ATTRA

J. Zavada[1], L. Szczukova[2], K. Pavelka[1], P. Horák[3], J. Vencovsky[1] on behalf of collaborators of the ATTRA registry. *[1]Rheumatology, Institute of Rheumatology, Prague; [2]Institute of Biostatistics and Analyses, Faculty of Medicine, Masaryk University, Brno; [3]Internal Medicine, Faculty of Medicine and Dentistry, Palacký University, Olomouc, Czech Republic*

Objectives: To assess the effect of anti-TNF therapy on work productivity using the Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP) questionnaire in patients with RA, PSA and AS in the real life setting. In the Czech Republic, anti-TNF-therapy is reimbursed for RA if DAS28>5.1 despite therapy with csDMARDs, for PSA if disease is not "adequately controlled" with csDMARDs, and for AS if BASDAI>4 and CRP/ESR elevated above normal.

Methods: WPAI-SHP scores were collected for all patients enrolled in ATTRA since 2012 at baseline and after 12 months of anti-TNF exposure. Bionäive patients with RA (n=352), AS (n=442) and PSA (n=133) starting anti-TNF therapy with available baseline data on demography, disease duration and physical function, and WPAI-SHP at baseline and at 12 months were included in this analysis. Patients older than 60 years, on maternity leave or students were excluded. Only patients working for pay at baseline were assessed for WPAI-SHP summary scores: absenteeism (mean % work time missed), presenteeism (mean % productivity loss at work), overall work impairment (mean % overall work productivity loss), and activity impairment (mean % productivity loss in regular activities).

Results: Baseline characteristic were significantly different between diagnoses (Table 1). Working status changed significantly only in patients with RA (employed

Table 1

	RA (n=352)	AS (n=442)	PSA (n=133)	p-value*
Female	257 (73.0%)	104 (23.5%)	58 (43.6%)	<0.001 ABC
Disease duration	7.1±5.7	7.0±6.7	7.5±7.2	0.245
Age at start of anti-TNF therapy	47.2±8.9	39.5±8.6	44.4±9.1	<0.001 ABC
HAQ	1.5±0.5	1.2±0.5	1.2±0.6	<0.001 AB

Post-hoc analysis (with Bonferroni correction): statistically significant difference btw groups A) RA vs. AS, B) RA vs. PSA, C) AS vs. PSA. Values or N (%) or mean (SD).

Table 2

Dg.	WPAI-SHP component	Baseline	12 months	Mean change after 12 months	N†	P-value*
RA	Absenteeism	12.8 (27.9)	5.1 (18.5)	7.7 (30.3)	203	<0.001
	Presenteeism	52.1 (21.9)	27.6 (20.9)	24.5 (26.3)	183	<0.001
	Overall work impairment	53.9 (22.8)	28.7 (22.0)	25.2 (26.9)	183	<0.001
	Activity impairment	62.4 (21.4)	36.0 (23.0)	26.4 (27.7)	352	<0.001
AS	Absenteeism	10.6 (25.6)	3.5 (15.8)	7.1 (28.0)	307	<0.001
	Presenteeism	53.1 (22.2)	21.1 (18.0)	32.0 (24.9)	282	<0.001
	Overall work impairment	54.8 (22.6)	21.8 (18.8)	33.0 (25.5)	281	<0.001
	Activity impairment	60.7 (22.1)	27.3 (21.4)	33.5 (26.4)	442	<0.001
PSA	Absenteeism	5.7 (17.3)	4.2 (18.4)	1.5 (24.6)	90	0.135
	Presenteeism	43.9 (24.0)	15.3 (16.2)	28.6 (24.5)	84	<0.001
	Overall work impairment	45.2 (25.0)	15.9 (16.8)	29.3 (25.1)	84	<0.001
	Activity impairment	57.4 (24.6)	26.2 (21.3)	31.2 (26.5)	133	<0.001

†N = Number of assessed patients. Values are mean % (SD). *Wilcoxon paired test for difference between baseline and 12 months within each WPAI score.

69→64%, p=0.013), but not in AS (77→78%) or PSA (77→73%). In patients employed for pay both at baseline and after 12 months, all WPAI-SHP scores improved significantly over one year of anti-TNF therapy (Table 2).

Conclusions: In the real life setting of the Czech Republic, anti-TNF therapy effectively reduced absenteeism, presenteeism, activity impairment and work impairment over one year in employed patients with RA, AS and PSA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4339

THU0651 SHOULD WE REDUCE THE DOSE OF BIOLOGICAL THERAPY TO ALL PATIENTS WITH INFLAMMATORY ARTHRITIS ACHIEVING SUSTAINED THERAPEUTIC GOAL?

I. Gonzalez-Alvaro[1], C. Sánchez-Piedra[2], R. Almodovar[3], J. Bachiller[4], A. Balsa[5], A.J. Blasco[6], R. Caliz[7], G. Candelas[8], C. Fernández-Carballido[9], A. García-Aparicio[10], B. García-Magallón[11], R. García-Vicuña[1], A. Gomez-Centeno[12], A.M. Ortiz[1], R. Sanmartí[13], J. Sanz[14], B. Tejera[15], I. Notario[7], M.J. Soto[7], C. Plasencia[5], V. Hernández[15], M. Espinosa[14], C. Ramos[14], P. Lazaro[6]. *[1]Rheumatology, HU la Princesa; [2]Research Unit, SER, Madrid; [3]Rheumatology, HU Fundación Alcorcón, Alcorcón; [4]Rheumatology, HU Ramon y Cajal; [5]Rheumatology, HU la Paz; [6]Independent Health Services Researcher, Madrid; [7]Rheumatology, HU Virgen de la Nieves, Granada; [8]Rheumatology, Hospital Clínico San Carlos, Madrid; [9]Rheumatology, Hospital General Universitario, Elda; [10]Rheumatology, Hospital Virgen de la Salud, Toledo; [11]Rheumatology, Hospital Gral San Jorge, Huesca; [12]Rheumatology, HU Parc Taulí, Sabadell; [13]Rheumatology, Hospital Clinic, Barcelona; [14]Rheumatology, HU Puerta de Hierro, Majadahonda; [15]Rheumatology, HU Canarias, Sta Cruz Tenerife, Spain*

Background: Dose tapering of biological therapies (BT) in patients with rheumatoid arthritis (RA) or spondyloarthritis (SpA) is frequent in Spain. However, there is variability in BT optimization (BTO). So, Spanish Society of Rheumatology published in 2015 recommendations on how to optimize BT (1). Nevertheless, there is no solid evidence on which patient profiles BTO is appropriated.

Objectives: To develop appropriateness criteria for BTO in patients with RA, axial SpA (axSpA) or peripheral SpA (pSpA)

Methods: The RAND/UCLA appropriateness method was used. Five rheumatologists experienced in RA and/or SpA clinical research selected and defined the variables considered relevant when deciding reduction of BT in order to define patient profiles. Ten BT experienced rheumatologists anonymously rated 1 (completely inappropriate) to 9 (completely appropriate) each profile after reading evidence synthesis. Then, in a meeting, classification variables and profiles with disagreement were revised and all profiles were scored again. Profiles with a median score >6 were considered appropriate, those with a median score <3.5 were considered inappropriate and the remaining uncertain. In addition, a study of the prevalence of these profiles was performed in 9 Spanish hospitals.

Results: Combining the options of variables 2,304 different profiles were obtained for RA, 768 for axSpA, and 3,072 for pSpA. 327 (14.2%) profiles in RA, 80 (10.4%) in axSpA, and 154 (5%) in pSpA were considered appropriate for BT dose reduction. By contrast, 749 (53.3%) profiles in RA, 270 (54.4%) in axSpA, and 1243 (54.5%) in pSpA were considered inappropriate. The remaining profiles were considered uncertain. In the preliminary study to determine profiles prevalence, we collected information from 242 RA, 171 axSpA and 172 pSpA patients that underwent BTO. We found that BTO was performed appropriately in 23% RA, 67% axSpA and 61% pSpA patients. BTO was indicated in uncertain profiles in 67% RA, 23% axSpA and 37% pSpA patients. Only in RA we detected BT dose reduction in patient profiles considered inappropriate (2%).

Conclusions: Appropriateness criteria for BT dose reduction in three inflammatory conditions were developed and the preliminary prevalence study suggests that BTO was wisely applied. However, further research in this field is needed to determine the real prevalence of clinical profiles of patients undergoing BTO in daily clinical practice and validate these criteria in real life.

References:

[1] Gonzalez-Alvaro I et al. Rheumatology 2015; 54: 1200–1209.

Disclosure of Interest: I. Gonzalez-Alvaro: None declared, C. Sánchez-Piedra Grant/research support from: Unrestricted grant from Abbvie, R. Almodovar: None declared, J. Bachiller: None declared, A. Balsa: None declared, A. Blasco Grant/research support from: Unrestricted grant from Abbvie, R. Caliz: None declared, G. Candelas: None declared, C. Fernández-Carballido: None declared, A. García-Aparicio: None declared, B. García-Magallón: None declared, R. García-Vicuña: None declared, A. Gomez-Centeno: None declared, A. Ortiz: None declared, R. Sanmartí: None declared, J. Sanz: None declared, B. Tejera: None declared, I. Notario: None declared, M. Soto: None declared, C. Plasencia: None declared, V. Hernández: None declared, M. Espinosa: None declared, C. Ramos: None declared, P. Lazaro Grant/research support from: Unrestricted grant from Abbvie

DOI: 10.1136/annrheumdis-2017-eular.3836

THU0652 ASSESSMENT OF BIOSIMILARS USING REAL WORLD DATA: THE COMPLEXITY OF CHOOSING A COMPARATOR AND UNDERSTANDING UPTAKE

D. Di Giuseppe[1], T. Frisell[1], S. Ernestam[1], H. Forsblad-d'Elia[2], E. Lindqvist[3], U. Lindström[4], C. Sjöwall[5], J. Askling[1] on behalf of the ARTIS group. *[1]Department of Medicine Solna, Karolinska Institutet, Stockholm; [2]Umeå University, Umeå; [3]Lund University and Skåne University hospital, Lund; [4]Sahlgrenska Academy, University of Gothenburg, Göteborg; [5]Linköping University, Linköping, Sweden*

Background: The introduction of biosimilars has been linked with concerns regarding how to best monitor their similarity vs. the originator product using real world data.

Methods: Data from the Swedish Rheumatology Quality register (SRQ) was used to identify all patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatric arthritis (PsA), and other spondyloarthropathy (SpA), who started a treatment with infliximab (originator Remicade or biosimilars Remsima or Inflectra) between 1st Mar 2015 and 30th Sept 2016 or with etanercept (originator Enbrel or biosimilar Benepali) between 1st April 2016 and 30th Sept 2016.

Results: During the study period, a total of 1833 patients started an infliximab treatment and 1793 started etanercept. These patients were either bDMARD-naïve (patients without a history of any biological treatment), non-medical switchers (patients who switched from the originator product), or patients who had a history of a previous (but not the same) bDMARD (Table 1). These three groups were not evenly distributed across originators or biosimilars, and had different baseline demographic and disease characteristics.

The uptake in terms of *treatment starts* was faster for Benepali (it covered more than 90% of this part of the etanercept market after only 3 months) as compared to Remsima and Inflectra (together they accounted for 88% of this section of the infliximab market after 10 months). The uptake of biosimilars in terms of proportion of all patient *on treatment* was, at the end of September 2016, 27%

Table 1. Number of patients starting infliximab (from 1 March 2015 to 30 September 2016) or etanercept (from 1 April 2016 to 30 September 2016) originator or biosimilar, by line of treatment

	Infliximab		Etanercept	
	Originator	Biosimilars	Originator	Biosimilar
Total	570	1263	186	1607
Bio- naïve	379 (66%)	508 (40%)	89 (48%)	581 (36%)
Non-medical switchers	–	524 (42%)	–	710 (44%)
Switchers from other biologics	191 (34%)	231 (18%)	97 (52%)	316 (20%)

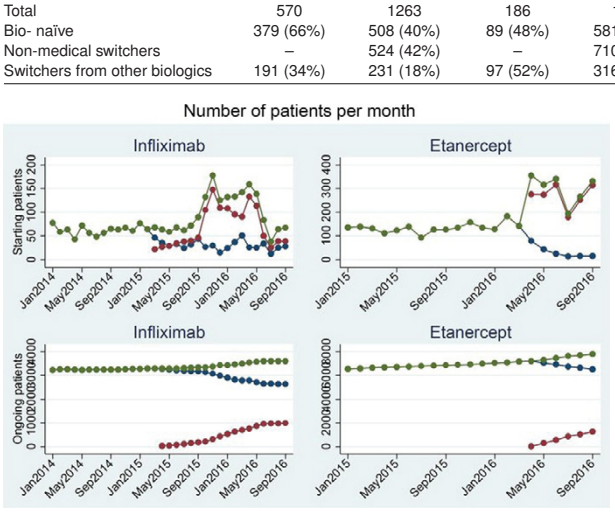


Figure 1. Number of patients *starting*, and *on*, respectively, infliximab or etanercept by month. Green: total, red: biosimilar, blue: originator.

of all infliximab (after 18 months of marketing) and 16% of etanercept (after 5 months since marketing).
In contrast to the bio-naïve group and those with a history of a previous (but not the same biologic), there was no readily available comparator group for the non-medical switcher group. To this end, we assessed three tentative definitions for a comparator; i) a historical comparison, i.e., same patients 18 months before the switch, ii) an individually matched sample of those patients still on originator treatment at the time of the switch, and iii) the total cohort of those who had not switched.
Conclusions: "Uptake" of biosimilars can be expressed both as proportion of all new starts and as proportion of ongoing treatments. Assessments of uptake, and any comparison between biosimilars and their originators, need to be based on line of therapy in order to avoid mixing up effects of channeling with true differences between originator and similar. For the same reason, any originator comparator for non-medical switchers needs to be reflective of those patients who stood the same chances of switching, but did not switch.
Disclosure of Interest: D. Di Giuseppe: None declared, T. Frisell: None declared, S. Ernestam: None declared, H. Forsblad-d'Elia: None declared, E. Lindqvist: None declared, U. Lindström: None declared, C. Sjöwall: None declared, J. Askling Grant/research support from: Abbvie, BMS, Pfizer, MSD, Roche, Samsung, Lilly
DOI: 10.1136/annrheumdis-2017-eular.4651

THU0653 PREVENTING RHEUMATOID ARTHRITIS: A GENERAL POPULATION PILOT STUDY ON PERSPECTIVES OF THE RISK OF DEVELOPING THE DISEASE AND POTENTIAL PREVENTATIVE INTERVENTIONS

M. Harrison[1,2], N. Bansback[1,2], L. Spooner[1], K. Milbers[2], C. Koehn[3], M. Hudson[4]. *[1]University of British Columbia; [2]Centre for Health Evaluation and Outcome Sciences; [3]Arthritis Consumer Experts, Vancouver; [4]McGill University, Montreal, Canada*

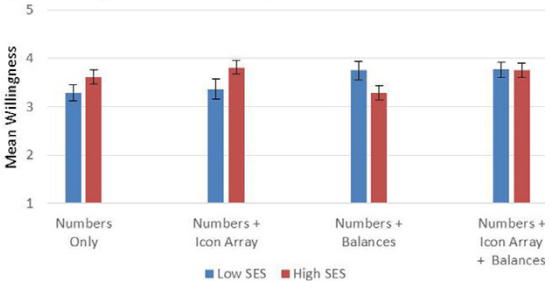
Background: Evidence suggests that treatment of people at risk of rheumatoid arthritis (RA) with anti-rheumatic drugs could prevent the onset of disease, and there are ongoing randomized controlled trials on the efficacy of preventing RA. However even if these trials are successful, there will be uncertainty around the potential benefits of these programs in practice; namely, the ability to predict those at risk of RA, exact benefits and risks, and inconvenience of treatment.
Objectives: To determine the features of a preventative treatment program that are likely to be acceptable to pre-symptomatic people at high risk of RA. Our focus is on preferences for treatment, the values and most important attributes of a preventative treatment program, and the likely uptake of preventative treatment. In this pilot study we sought general population preferences.
Methods: A discrete choice experiment was administered to a US general population sample, asking participants to choose between sets of 2 hypothetical preventative RA treatments, then between their preferred treatment and "no treatment for now". The treatment (risk of developing RA, how treatment is taken, chance of side effects, certainty in estimates, health care provider's opinion) and test attributes (chance test is wrong, who recommends treatment) were identified in focus groups with RA patients, first-degree relatives of RA patients and rheumatologists. An efficient experimental design was developed using SAS and included 2 consistency checks. Responses were analyzed using a conditional logit regression model to estimate the significance and relative importance of attributes in influencing preferences.
Results: 201 respondents completed the survey. The majority of the sample was 25–54 years old (modal age category: 30–39 years (38%)) and 50% were female. 23 members (11%) reported having a physician diagnosis of RA, and 91 (45%) had a family member or close friend with RA. All attributes' levels significantly influenced treatment preferences, but risk reduction, how treatment is taken, and health care provider preference were most influential. Respondents were most willing to trade a reduction in risk of RA for a treatment preferred by their health care professional and an oral route of administration. Respondents had a similar strength of preference for reducing uncertainty in evidence and reducing the risk of side effects. The preferred preventative treatment was chosen over no treatment in 67% of choices.
Conclusions: Our survey suggests that people value the potential benefits of treatments, but equally values how the treatment is taken and the preference of their health care provider. The degree of confidence in the estimates of a treatment's risks and benefits is as important to people as the risk of side effects. The uptake of a preventative strategy will depend on these key factors. This evidence will help policymakers understand whether different preventative treatment strategies are likely to be acceptable to people they are offered to.
Acknowledgements: This work was supported by a grant from the Canadian Rheumatology Association through the Canadian Initiative for Outcomes in Rheumatology Care (CIORA).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2170

THU0654 THE INFLUENCE OF RISK PRESENTATION FORMAT ON WILLINGNESS TO START A MEDICATION

R. Cozmuta[1], L. Fraenkel[2], E. Wilhelms[3], V. Reyna[4], J. Nolte[4]. *[1]Emory University, Atlanta; [2]Yale University, New Haven; [3]Vasser College, Poughkeepsie, NY; [4]Cornell University, Ithica, NY, United States*

Background: Patients with rheumatoid arthritis frequently refuse to escalate care because they overweight the probability of adverse events. Effectively communicating risk information to patients is difficult. Several approaches have been developed to facilitate comparative risks; however, recent data suggest that current approaches have a limited impact on risk perceptions and willingness to take medication.
Objectives: The objective of this study was to examine whether an icon array (IA), an illustration of the gist of how medications regulate the immune system (a series of balance beams), or both influence willingness to start a medication.
Methods: Patients with a rheumatic disease were mailed a survey in which they were asked to imagine that their symptoms had worsened and that their physician was recommending a new medication. We varied the probability of an adverse event (pneumonia requiring hospitalization): 2% or 0.2%, and the risk presentation format: numbers, numbers + IA, numbers + balance beams (BB), or numbers + both. Route of administration, benefit, and cost were held constant. Each subject responded to a single, randomly-assigned scenario. We controlled for socioeconomic status (SES), using a variable including both difficulty paying for medications as well as education, in a full-factorial model testing willingness to take the medication (measured on a 5-point scale).
Results: Of 1453 surveys, 465 patients completed the survey. Overall, the mean (SD) age was 59.0 (14.8); 79.7% were female; 83.2% White and 39.1% were classified as having low SES. There were no statistical differences in patient characteristics across the risk presentation formats. Willingness to start the medication was predicted by the interaction between the risk presentation format and SES (F =2.9, p=0.03). Willingness by SES status is described in the Figure 1. Among low SES subjects, addition of an IA did not affect willingness compared to the numbers-only format. In contrast, addition of BB (mean difference =0.47, p=0.07), or both IA and BB increased willingness (mean difference =0.48, p=0.04). Among high SES subjects, addition of an IA or BB or both did not influence willingness compared to the numbers only format. However, both formats including an IA increased willingness compared to the BB format among high SES subjects (mean difference IA vs BB = 0.53, p=0.01; mean difference IA vs IA + BB = 0.48, p=0.02).

Figure 1. Willingness across Formats by SES



Conclusions: SES affects how subjects respond to risk presentation formats. IA marginally increases willingness in high SES subjects, while BB increases willingness in low SES subjects; when both IA and BB are present, SES differences disappear. BB, when not accompanied by an IA, may decrease willingness in high SES subjects. These results demonstrate the differential effects of risk presentation formats, and highlight the need to identify mechanisms underlying their effects when implementing decision-support tools.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5169

THU0655 DO VISUAL DECISION AIDS HELP PATIENTS CORRECTLY DIFFERENTIATE BETWEEN A 2% AND A 0.2% RISK?

R. Cozmuta[1], L. Fraenkel[2], E. Wilhelms[3], V. Reyna[4], J. Nolte[4]. *[1]Emory University, Atlanta; [2]Yale University, New Haven; [3]Vasser College, Poughkeepsie, NY; [4]Cornell University, Ithica, NY, United States*

Background: Studies have found that patients ignore probabilities when making treatment decisions.
Objectives: The objective of this study was to examine whether addition of an icon array (IA), a series of three consecutive balance-beam (BB) illustrations depicting how medications regulate the immune system, or both resulted in patients being able to better differentiate between an uncommon (2%) and rare (0.2%) adverse event (AE).
Methods: Patients currently being treated for a chronic inflammatory rheumatic disease were mailed a survey in which they were asked to imagine that their symptoms had recently worsened and that their physician was recommending a new medication. The medication was described using eight scenarios (manipulated using a 2x4 design). We varied the probability of a serious AE (pneumonia

requiring hospitalization): 2% vs 0.2% and the risk presentation format: numbers only, numbers + IA, numbers + BB, and numbers + IA + BB. Route of administration, benefit, and cost were held constant. Each subject responded to a single, randomly-assigned scenario. Dependent variables included perceived riskiness, worry, global gist related to the acceptability of the AE, and willingness to take the medication (all measured on 5-point ordinal scales). We hypothesized that the IA and BB formats would result in 1) lower perceived riskiness and worry, and 2) greater acceptability of the AE and willingness to take the medication in the 0.2% vs 2% scenarios. Socioeconomic status (SES) was defined based on difficulty paying for medication and education level.

Results: We mailed 1453 surveys. 465 patients completed and mailed the survey back (32% response rate). Overall, the mean age of responders was 58.99 (SD=14.85); 79.7% of were female; 83.2% White and 39.1% had a low SES. There were no statistical differences in demographic or clinical characteristics across the four risk presentation formats. Mean (SD) perceived riskiness, worry, global gist, and willingness to take the medication for 2% versus 0.2% chance of the AE, by SES level, are presented in the Image.

Perceived riskiness was lower for a 0.2% versus 2% risk of the AE in the numbers + IA condition in higher SES subjects. Lower SES subjects who viewed both IA and BB were more worried about the AE and found the AE to be less acceptable in the 0.2% versus 2% condition.

Risk Presentation Format		Riskiness Mean (SD)	Worry Mean (SD)	Gist Mean (SD)	Willingness Mean (SD)
Low SES					
Numbers Only					
AE probability	2%	3.12 (0.18)	3.16 (0.23)	3.12 (0.22)	3.20 (0.24)
	0.20%	3.04 (0.19)	3.38 (0.23)	3.69 (0.22)	3.38(0.25)
	p-value	0.77	0.51	0.07	0.61
Numbers + IA					
AE probability	2%	3.4 (0.24)	3.4 (0.29)	3.07 (0.28)	3.20 (0.31)
	0.20%	2.79 (0.21)	3.05 (0.26)	3.61 (0.25)	3.53 (0.28)
	p-value	0.06	0.37	0.15	0.43
Numbers + BB					
AE probability	2%	3.06 (0.23)	3.13 (0.28)	3.32 (0.27)	3.69 (0.30)
	0.20%	3.17 (0.19)	3.17 (0.23)	3.55 (0.22)	3.82 (0.25)
	p-value	0.72	0.91	0.52	0.74
Numbers + IA + BB					
AE probability	2%	2.83 (0.17)	**2.83 (0.21)**	**3.67 (0.2)**	4.03 (0.22)
	0.20%	3.20 (0.17)	**3.40 (0.21)**	**2.99 (0.2)**	3.50 (0.22)
	p-value	0.12	**0.05**	**0.02**	0.09
High SES					
Numbers Only					
AE probability	2%	2.95 (0.15)	3.03 (0.18)	3.52 (0.18)	3.50 (0.20)
	0.20%	2.77 (0.17)	2.71 (0.20)	3.83 (0.20)	3.74 (0.22)
	p-value	0.44	0.25	0.24	0.41
Numbers + IA					
AE probability	2%	**3.29 (0.16)**	3.06 (0.19)	3.61 (0.19)	3.82 (0.21)
	0.20%	**2.78 (0.15)**	2.73 (0.18)	3.82 (0.17)	3.80 (0.19)
	p-value	**0.02**	0.21	0.41	0.93
Numbers + BB					
AE probability	2%	3.25 (0.15)	3.43 (0.18)	3.48 (0.17)	3.43 (0.19)
	0.20%	3.00 (0.16)	3.28 (0.20)	3.49 (0.19)	3.14 (0.21)
	p-value	0.25	0.59	0.97	0.33
Numbers + IA + BB					
AE probability	2%	2.79 (0.15)	2.76 (0.18)	3.89 (0.18)	4.03 (0.20)
	0.20%	3.2 (0.17)	3.27 (0.21)	3.40 (0.2)	3.50 (0.22)
	p-value	0.07	0.07	0.07	0.08

Conclusions: With the exception of the IA's impact on perceived riskiness among subjects with higher SES, the risk formats used did not enable subjects to correctly differentiate between a 0.2% and a 2% risk of a serious AE. These results highlight the lack of impact of quantitative risk information on patients' risk perceptions.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5618

THU0656 ETANERCEPT BIOSIMILAR USAGE AND ASSOCIATED COST SAVINGS IN GERMANY

K. Thakur, A. Handrich, E. Psachoulia. *Biogen, Zug, Switzerland*

Background: The first etanercept biosimilar was approved by the European Commission in January 2016. Of the 27,000 patients* estimated to be treated with etanercept biosimilar in the Europe, 5,122 patients* are estimated to be on the etanercept biosimilar in Germany at the end of the analysis period. Its usage in Europe may support healthcare sustainability by reducing costs, thereby relieving the burden on healthcare budgets and improving patient's ability to get the right care at the right time.

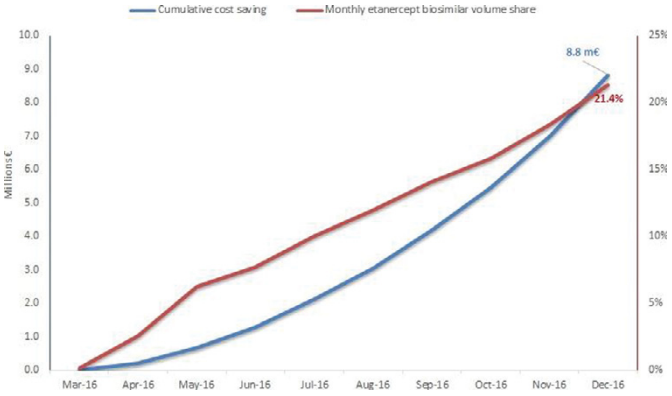
Objectives: The analysis aimed to estimate the pharmacoeconomic impact of etanercept biosimilar use in Germany between March and December 2016.

Methods: The volume of etanercept biosimilar prescribed in Germany was calculated using sell-out data from retail pharmacies to patients sourced from INSIGHT Health. For this analysis, only the pre-filled syringe (PFS) and pre-filled pen (PFP) presentations of 50 mg etanercept were considered. The biosimilar volume share was calculated by dividing the total etanercept biosimilar 50 mg units prescribed by total etanercept 50 mg units prescribed. The cost savings realized through the use of the biosimilar was calculated using the INSIGHT Health volume data and the pharmacies selling price (source: Lauertaxe) of the etanercept reference product and the etanercept biosimilar. (Note: volume, volume share, patient and price data will be updated at time of presentation to reflect most current impact of etanercept biosimilars use).

Results: Based on 5,122 patients currently estimated to be treated with etanercept biosimilar (volume share of 21.4% in Dec 2016) in Germany and on the price differential between etanercept biosimilar and the reference product, a total cost saving of 8.8 million EUR was realized during the analysis period. Assuming these patients remain on etanercept biosimilar treatment, a total savings of 21.1 million EUR** can be returned annually to the healthcare system, compared to using only the reference product. This annual cost savings could be utilized to provide treatment to additional 1,208 patients with etanercept biosimilar.

Table 1. No. of 50 mg Pen/PFS etanercept prescribed: March–Dec 16

Product	Pen	PFS	Total
Reference product	318,317	580,563	898,880
Biosimilar	71,408	40,658	112,066



Conclusions: Experience with etanercept biosimilar has been growing in Germany, as reflected by the growing market share. Based on the current number of patients treated with etanercept biosimilar, savings of 21.1 million EUR are projected to be returned to the health system in Germany annually. The economic burden associated with etanercept treatment is expected to decrease further with an increase in market share for the etanercept biosimilar. These savings can have a significant impact on broadening patient access to biologic treatment in Germany.

References:

[1] http://www.ema.europa.eu/.
[2] INSIGHT Health GmbH & Co.KG.
[3] WHO ATC/DDD classification (final) for etanercept in: WHO Drug Information Vol 15, No 2, 2001.

Disclosure of Interest: K. Thakur Shareholder of: Biogen, Grant/research support from: Biogen, Employee of: Biogen, A. Handrich Shareholder of: Biogen, Grant/research support from: Biogen, Employee of: Biogen, E. Psachoulia Shareholder of: Biogen, Grant/research support from: Biogen, Employee of: Biogen

DOI: 10.1136/annrheumdis-2017-eular.3380

THU0657 A TELE-HEALTH FOLLOW-UP STRATEGY FOR TIGHT CONTROL OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: RESULTS OF THE NON-INFERIORITY RANDOMISED CONTROLLED TRAIL (THE TERA STUDY)

A. Thurah[1,2], K. Steengaard-Pedersen[1,2], M. Axelsen[3], U. Fredberg[3,4], L.M.V. Schougaard[5], N.H.I. Hjøllund[5,6], M. Pfeiffer-Jensen[1,2], T.B. Laurberg[1], K. Lomborg[6,7], T. Maribo[8,9]. *[1]Department of Rheumatology, Aarhus University Hospital; [2]Clinical Medicine, Aarhus University, Aarhus; [3]Diagnostic Centre, Silkeborg Regional Hospital, Silkeborg; [4]Department of Rheumatology, Odense University Hospital, Odense; [5]WestChronic, Department of Occupational Medicine, University Clinic, Health, Aarhus University, Herning; [6]Clinical Epidemiology, Aarhus University; [7]The Research Programme in Patient Involvement, Aarhus University Hospital; [8]Defactum, Central Denmark Region; [9]Department of Public Health, Section for Clinical Social Medicine and Rehabilitation, Aarhus University, Aarhus, Denmark*

Background: Despite the increased prevalence of rheumatoid arthritis (RA) in recent years, no studies have yet investigated the effect of monitoring disease activity through a standardized tele-health strategy in patients with RA (1).

Objectives: To test the effect of patient-reported outcome (PRO) based tele-health follow-up for tight control of disease activity in patients with RA, and the differences between tele-health follow-up performed by rheumatologists or rheumatology nurses.

Methods: A total of 294 patients were randomized (1:1:1) to either PRO-based tele-health follow-up carried out by a nurse (PRO-TN) or a rheumatologist (PRO-TR), or conventional out-patient follow-up by physicians. The Flare-RA (2) was used as decision aid for assessing disease activity.
The primary outcome was change in DAS28 after week 52. Secondary outcomes were: physical function, quality of life and self-efficacy. The non-inferiority margin was a DAS28 change of 0.6. Mean differences were estimated following per-protocol, intention to treat (ITT) and imputation (IMP).
Results: Overall patients had low disease activity at baseline and end follow-up. Demographics and baseline characteristics were similar between groups. Non-inferiority was established for DAS28. In the ITT analysis mean difference in DAS28 between PRO-TR vs. control were -0.10 (90% CI -0.30; 0.13) and -0.19 (-0.41; 0.02) between PRO-TN vs. control. When including one yearly visit to the outpatient clinic, patients in PRO-TN had a total of 1.72 (SD 1.03) visit/year, PRO-TR 1.75 (SD 1.03) vist/year and control 4.15 (SD 1.0) visits/year. This included extra visits due to inflammatory flare.
Overall more than 80% of the patients in all three groups answered that they were "very satisfied" with the consultation form they received and no differences were found between the three groups.
Conclusions: Among RA patients with low disease activity or remission a PRO-based tele-health follow-up for tight control of disease activity in RA can achieve similar disease control as conventional outpatient follow-up. The degree of disease control did not differ between patients seen by rheumatologists or rheumatology nurses.
References:
[1] References.
[1] Ward IM, Schmidt TW, Lappan C, Battafarano DF. How critical is tele-medicine to the rheumatology workforce? Arthritis Care Res (Hoboken). 2016 Feb 11.
[2] Berthelot JM, De Bandt M, Morel J, Benatig F, Constantin A, Gaudin P, et al. A tool to identify recent or present rheumatoid arthritis flare from both patient and physician perspectives: The 'FLARE' instrument. Ann Rheum Dis. 2012 Jul;71(7):1110–6.
[2] ClinicalTrails.gov identifier: NCT02155894.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2995

THURSDAY, 15 JUNE 2017

Validation of outcome measures and biomarkers

THU0658 WNT/β-CATENIN PATHWAY IS AFFECTED IN PRIMARY SJÖGREN'S SYNDROME

Z. Omercikoglu[1], A. Karatas[2], O. Catak[3], B. Oz[2], F. Erman[4], K. Sahin[5], A.F. Dagli[6], N. Gozel[1], S.S. Koca[2]. *[1]Department of Internal Medicine; [2]Department of Rheumatology; [3]Department of Ophthalmology, Faculty of Medicine, Firat University; [4]Elazıg Health High School, Firat University; [5]Department of Animal Nutrition, Faculty of Veterinary Medicine, Firat University; [6]Department of Pathology, Faculty of Medicine, Firat University, Elazığ, Turkey*

Background: Sjögren's syndrome (SS) is a chronic autoimmune disease that causes salivary and lacrimal gland dysfunction, resulting in oral and ocular dryness. The pathogenesis of SS is still unknown. The Wingless (Wnt)/β-catenin pathway has been recently shown to play an important role in inflammation.
Objectives: The aim of the present study was to determine serum and salivary levels of *Dickkopf-related protein 1* (DKK1) and sclerostin those are inhibitor of Wnt/β-catenin signaling pathway and to evaluate the expression of Wnt-1 and Wnt-3a in the salivary gland, in patients with primary SS.
Methods: 30 patients with primary SS, 30 patients with systemic lupus erythematosus (SLE) and 29 healthy controls were enrolled in the study. Fasting blood and saliva samples were obtained from the participants. Serum and salivary levels of DKK1 and sclerostin were measured by enzyme-linked immunosorbent assay. Wnt-1 and Wnt-3a expression were also immunohistochemically assessed in salivary gland. EULAR SS Disease Activity Index (ESSDAI), and EULAR SS Patient Reported Index (ESSPRI) in the SS group and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) in the SLE group were recorded.
Results: Serum DKK1 and sclerostin levels were decreased in the SS and SLE groups compared to the controls (Table 1) ($p<0.001$ for both). Salivary sclerostin levels were similar among the study groups ($p>0.05$ for all). Salivary DKK1 levels were higher in the SS group compared to the control and SLE group ($p=0.004$ and $p=0.009$, respectively). Moreover, serum DKK1 level was higher in the SS group than in the SLE group ($p=0.046$). Serum DKK1 level was positively correlated with serum sclerostin level in the SS, SLE and control groups ($r=0.677$; $p<0.001$, $r=0.783$; $p<0.001$, and $r=0.829$; $p<0.001$, respectively). ESSPRI was negatively correlated with serum DKK1 and sclerostin levels ($r=-0.363$; $p=0.049$ and $r=-0.416$; $p=0.022$, respectively) in the SS group.
Moreover, in the salivary gland tissues, the positivities of Wnt-1 (71.4% vs. 46.2%, $p=0.182$) and Wnt-3a (71.4% vs. 53.8%, $p=0.345$) were relatively higher in the SS group compared to the control group, respectively.
Conclusions: According to the best of our knowledge, this study is the first study evaluating the activity of Wnt/β-catenin pathway in the primary SS. The altered serum levels of DKK1 and sclerostin in primary SS and SLE is suggest that Wnt/β-catenin pathway is affected in these inflammatory diseases. Salivary DKK1 level is increased in primary SS in contrast to SLE. On the other hand, Wnt-1 and Wnt-3a expressions on the salivary gland are increased in primary SS. Therefore, it may be concluded that Wnt/β-catenin pathway acts pathogenic roles on the glandular inflammation.

Table 1. Demographics and clinical variables in the study groups

	HC	SLE	SS	P_1 (SLE vs. HC)	P_2 (SS vs. HC)	P_3 (SS vs. SLE)
Serum DKK1, ng/ml	49.8±14.9	27.8±11.8	35.2±8.8	<0.001	<0.001	0.046
Salivary DKK1, ng/ml	30.6±5.9	31.1±6.9	36.3±6.9	0.944	0.004	0.009
Serum Sclerostin, ng/ml	12.9±5.1	5.7±4.1	5.5±3.8	<0.001	<0.001	0.984
Salivary Sclerostin, ng/ml	16.1±3.4	15.7±2.5	15.6±3.7	0.877	0.838	0.996

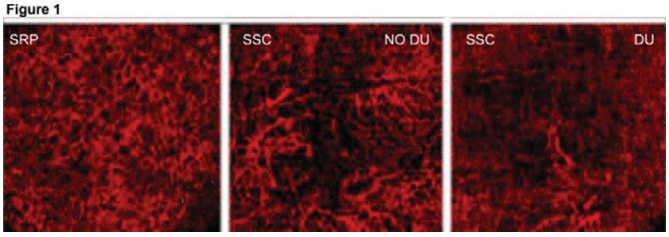
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5769

THU0659 SKIN MICROVASCULAR FLOW ASSESSED BY DYNAMIC OPTICAL COHERENCE TOMOGRAPHY: FIRST NON-INVASIVE QUANTITATIVE OUTCOME MEASURE OF MICROVASCULAR DAMAGE IN SYSTEMIC SCLEROSIS

A. Daniel[1,2], G. Abignano[2,3], S. Eng[2,3], L. Green[2,3], P. Emery[2,3], F. Del Galdo[2,3]. *[1]Rheumatology Unit, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal; [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [3]NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Reduction in capillaries number is the defining feature of microvascular disease in Systemic Sclerosis (SSc) and it concurs to the ischemic manifestations of the disease. Digital Ulcers (DUs) are the major complication of ischemic peripheral vasculopathy.
Dynamic optical coherence tomography (D-OCT) is a recently developed imaging technique that allows non-invasive in vivo study of the microvasculature of the skin. In addition to the skin architecture and vessels morphology, it offers information about flow status, allowing the functional and quantitative evaluation of the microcirculation.[1]
Objectives: To determine the face and content validity of D-OCT as outcome measure of the skin microvascular disease, assuming the presence of current DUs, distal to the DIP joints, as gold standard for ischemic peripheral vasculopathy in SSc.
Methods: A total of 54 patients were enrolled in this cross-sectional study, including 18 SSc patients with current DUs (DU group); 18 SSc patients without current DUs (no DU group) and 18 patients with Raynaud's phenomenon and SSc specific ANA, who did not fulfilled ACR/EULAR 2013 classification criteria (SRP group).
For each patient, we performed a D-OCT scan on both index and middle fingers, on the dorsal aspect of the second phalanx, employing *Vivosight Scanner (Michelson Diagnostics)*. The speckle variance signal of D-OCT images within the first mm of skin depth was extracted, quantified as area under the curve (AUC) and defined as Micro Vascular Flow (MVF).
MVF comparison between the groups was done using parametric or non-parametric tests as appropriate. Statistical Analysis was performed with SPSS V.22.
Results: All three groups were comparable in terms of age and gender distribution ($p>0.80$ for both) as well as disease duration and clinical subset between the two SSc groups ($p=0.839$ and $p=0.646$, resp.). With a scan time <1 minute, D-OCT allowed the visualization and quantification of capillaries within the first millimeter of skin depth (Figure 1).
The distribution of MVF was not significantly different among the four fingers within each group (DU group: $p=0.459$, no DU group: $p=0.953$ and SRP group: $p=0.616$). On the contrary, the distribution and median MVF for all fingers was significantly different among the 3 groups: DU group=0.134 (IQR 0.121–0.134), no DU group=0.153 (IQR 0.132–0.153) and SRP group=0.167 (IQR 0.148–0.167) ($p<0.0001$), as well as in the DU group vs. no DU group ($p<0.001$) or DU vs SRP group ($p<0.001$).
Further, sub analysis of the DU group showed that 10 of the total 20 DUs were on the left index finger. Within this subgroup the MVF of patients on Sildenafil (n=6) was significantly higher than the rest of the group (0.148±0.021 vs. 0.113±0.019, $p=0.03$).

Figure 1



Conclusions: MVF assessed by D-OCT is a quantitative, non-invasive surrogate outcome measure of severe peripheral ischemic vasculopathy in SSc. Longitudinal

studies assessing its sensitivity to change will inform whether MVF can be used as end point of skin microvascular involvement in SSc.

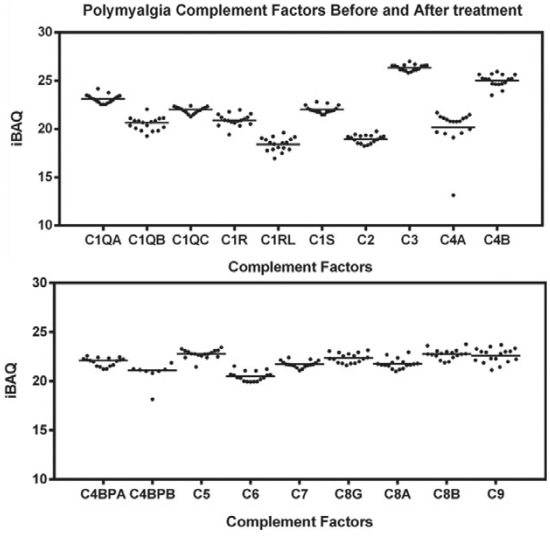
References:
[1] C. Tolosa-Vilella et al. Semin Arthritis Rheum 46(2016):200–208.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6582

THU0660 POLYMYALGIA RHEUMATICA TREATMENT SERUM BIOMARKERS VERSUS RHEUMATOID ARTHRITIS

M.K. Meyer[1], M. Andersen[1], T.V. Stausbo[2], K.J. Elbæk[2], G.N. Andersen[1], A. Stensballe[2]. [1]*Department of Rheumatology, Nortmark Regional Hospital, Hjørring;* [2]*Department of Health Science and Technology, Aalborg University, Aalborg, Denmark*

Background: Polymyalgia rheumatica (PMR) is a systemic inflammatory disorder with unknown etiology and overlapping symptoms with giant cell arthritis and late-onset rheumatoid arthritis (RA). To date, no proteomics studies have been performed on PMR patients, and the number of biomarker studies remain limited.
Objectives: The primary aim of this study was to thoroughly investigate the corticosteroid treatment serum proteome of PMR with a focus on acute-phase reactions, complement system, and cytokines.
Methods: Filter-aided sample preparation for mass spectrometry, cell free DNA (cfDNA) assay, and 10plex cytokine assay were applied to PMR serum samples from the same patients before and after treatment, DMARD-naïve RA patients, and healthy controls.
Results: The core serum proteomes of the four groups were remarkably similar, and consisted of >200 proteins, which included acute-phase reactants, coagulation and complement proteins (figure), immunoglobulins, and apolipoproteins, and several more. Acute Phase Serum Amyloid A (SAA1) was differentially less abundant after PMR treatment, and CRP (after adjusting for two patients with low baseline CRP). cfDNA were more abundant in both groups of PMR compared to healthy controls. Complement factors were narrowly distributed and not affected by PMR treatment. The individual serum proteome of each PMR patient provided more than 100 differentially abundant proteins, and highlights the heterogeneity of patients.



Conclusions: We have established the core serum proteome of PMR in response to treatment, and compared it with RA and healthy controls. The results suggest a functional role of SSA1, and increased cfDNA in the pathogenesis of PMR indicates the activation of NETs.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5844

THU0661 CLINICAL RELEVANCE OF DETECTING ANTI-ADALIMUMAB ANTIBODIES WITH A DRUG-TOLERANT ASSAY

A. Martinez-Feito[1], L.Y. Bravo Gallego[2], B. Hernandez-Breijo[1], C. Plasencia[1], A. Jochems[1], M.A. Gonzalez[2], I. Monjo[1], D. Peiteado[1], G. Bonilla[1], P. Nozal[2], A. Balsa[1], D. Pascual-Salcedo[1]. [1]*Immuno-Rheumatology research group;* [2]*Immunology, University Hospital la Paz, madrid, Spain*

Background: Adalimumab (Ada) has proven effective in treating rheumatoid arthritis (RA) and spondyloarthropathies (SpA), although approximately 30% of responders will present secondary clinical failure. Immunocomplex formation between antibodies to Ada (ATA) and Ada can increase drug clearance. Most of the assays to measure ATA present drug interference. Currently, different assays are available to measure total ATA (free and complexed).
Objectives: To compare the detection of ATA along Ada treatment between two assays: one drug-sensitive and another drug-tolerant assay. Study the association of ATA with the clinical status.
Methods: This is a prospective observational study with 63 patients with rheumatic diseases under Ada treatment enrolled at Biological Therapy Unit of Hospital La Paz. Serum Ada levels were measured by ELISA and serum ATA levels by two assays: an in-house two-site (bridging) ELISA (bELISA) to detect uncomplexed ATA (free ATA) and a drug-tolerant assay developed by ImmundiagnostikÒ (Bensheim, Germany) (IDK) to measure simultaneously free and complexed ATA (total ATA). Samples were evaluated at 0, 0.2, 0.5, 1, 1.5 and 2 years after Ada initiation.
Results: Out of the 63 studied patients, 12 (19%) had RA and the rest (51, 81%) had different spondyloarthropathies (24, 38%) ankylosing spondylitis, 9 (14%) psoriatic arthritis, 14 (22%) undifferentiated spondyloarthritis and 4 (6%) spondyloarthritis associated with inflammatory bowel disease).Thirty-one patients (49%) received concomitant methotrexate (26% RA patients and 74% SpA patients), 13 (21%) received another DMARDs associated to Ada and 19 (30%) were on monotherapy.Out of the 63 patients, in 27 (43%) no ATA were detected. Thirty six patients (57%), were IDK+ and 12 patients (19%) were bELISA+ (all of them IDK+).The presence of ATA by bELISA was associated with absence of serum Ada levels. However, most (78%) samples with complexed ATA had low circulating Ada levels (1.65 mg/ml in ATA+ vs 6.25 mg/ml in ATA-, $p<0.0001$). ATA appeared by IDK at earlier treatment stages than by bELISA, statistically different at all studied time points.In patients who dropped-out (30 patients, 48%) ATA detection was frequent and significant by both methods.Ten patients (33%) bELISA ATA+ dropped-out vs 2 patients bELISA ATA+ in those who continued treatment ($p<0.0001$). Twenty four patients (80%) IDK ATA+ dropped-out vs 12 patients (36%) who continued treatment ($p<0.0001$). The percentage of ATA detected by IDK was higher than by bELISA, with a tendency of more IDK ATA+ among patients with less survival (24,80% IDK positive vs 10,33% bELISA +; p=0.06)
Conclusions: ATA are detected by a drug-tolerant assay at earlier stages of treatment than by bELISA. The antibodies formed early are associated with lower levels of circulating Ada, indicating higher drug clearance. This information might be useful to implement the Therapeutic Drug Monitoring. However, the detection of early complexed ATA has not demonstrated a significant advantage over the bELISA to predict treatment survival.
Acknowledgements: This work has been supported by a collaboration with Leti laboratories.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2864

THU0662 COMPARING ELECTRONIC COLLECTION OF PATIENT REPORTED OUTCOMES AT HOME VERSUS TOUCH-SCREENS IN THE WAITING AREA AMONG PATIENTS WITH ARTHRITIS IN CLINICAL PRACTICE: A RANDOMISED AGREEMENT STUDY WITH ONLINE RECRUITMENT USING DANBIO

A.E. Secher[1], B. Glintborg[1], H. Gudbergsen[2], N.S. Krogh[3], D.V. Jensen[1], I.J. Sørensen[1], R. Christensen[2], M. Skougaard[2], M.L. Hetland[1]. [1]*DANBIO registry, Glostrup;* [2]*The Parker Institute;* [3]*Zitelab Aps, Frederiksberg, Denmark*

Background: Collection of patient-reported outcomes (PROs) is an important aspect of modern treatment strategies. Electronic capture in waiting areas by touch screens is part of routine care in the Danish DANBIO registry[1]. It is not known whether this data collection can be replaced with electronic data entry from home.
Objectives: To test the feasibility of online patient recruitment via touch screens and to investigate if electronic reporting of PROs from home (ELECTOR IT-platform) is comparable to reporting completed at the hospital among patients with rheumatoid arthritis (RA) or axial spondyloarthritis (AS).
Methods: Patients with RA or AS were recruited via touch screens and randomized to one of two groups by a pre-computed list generated through DANBIO; the first group completing the PROs at home and then at the hospital-site, and vice versa for the second group. All patients completed the Health Assessment Questionnaires (HAQ), the Visual Analogue Scales (VAS) for fatigue, pain and global health and the annual visit questions. Furthermore, AS patients completed the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the BAS Function Index (BASFI). Pearson's Chi-square test, independent samples t-test and Mann-Whitney U test were calculated. Smallest detectable differences (SDDs), 95% confidence intervals (CIs) and intra-class correlation coefficients (ICCs) were calculated.
Clinicaltrials.gov identifier: NCT02818478.
Results: A total of 952 patients received invitation, 45% accepted, 127 patients were contacted by phone, and 56 (44%) gave consent to participate. 22 patients with RA and 20 patients with AS completed the trial.
All differences between scores from home vs hospital were smaller than SDD, and all were non-significant ($p<0.05$), except for BASFI and BASDAI item 5. ICC ranged from 0.947–0.990 ($p<0.00001$). Annual visit questions showed 96% concordance between the two methods. 50% of the patients preferred from home data entry over hospital and 10% vice versa.
Conclusions: Recruitment of patients for a randomized trial via touch screens was feasible. PROs collected from patients' own devices at home generated

Table: Scores, differences, SDD and ICC for hospital and home PROs.

	Hospital, mean (SD)	Home, mean (SD)	Difference, mean (95% CI)*	SDD	ICC (95% CI)
Rheumatoid arthritis (RA)					
HAQ (0-3)	0.580 (0.499)	0.619 (0.531)	-0.040 (-0.283, 0.204)	0.244	0.984 (0.962, 0.994)
VAS pain, mm	25.5 (24.2)	24.2 (23.8)	1.3 (-15.3, 17.7)	16.4	0.969 (0.927, 0.987)
VAS fatigue, mm	35.6 (30.4)	33.1 (30.3)	2.4 (-15.8, 20.7)	18.2	0.975 (0.942, 0.990)
VAS global, mm	34.0 (29.8)	34.8 (30.7)	-0.81 (-18.3, 15.4)	16.1	0.982 (0.955, 0.993)
Spondyloarthritis (AS)					
HAQ (0-3)	0.356 (0.307)	0.319 (0.276)	0.038 (-0.215, 0.290)	0.253	0.947 (0.868, 0.979)
VAS pain, mm	25.2 (22.6)	23.5 (21.6)	1.7 (-10.6, 14.0)	12.3	0.979 (0.948, 0.992)
VAS fatigue, mm	33.8 (23.8)	32.4 (23.7)	1.4 (-11.6, 14.4)	13.0	0.980 (0.951, 0.992)
VAS global, mm	30.9 (25.9)	30.3 (28.2)	0.6 (-17.3, 18.4)	17.8	0.972 (0.930, 0.989)
BASDAI, mm	26.0 (20.7)	24.4 (21.1)	1.6 (-8.6, 11.8)	10.2	0.983 (0.959, 0.993)
BASFI, mm	27.8 (22.7)	25.9 (23.8)	1.9** (-6.4, 10.2)	8.3	0.990 (0.974, 0.996)

**Spearman's rho>0.9 for all items*
***p<0.05 (Wilcoxon rank sum test for difference between hospital and home scores)*

results comparable to results obtained from the existing touch-screen solution and were preferred by the patients.

References:

[1] Schefte et al. (2010).

Disclosure of Interest: A. E. Secher: None declared, B. Glintborg Grant/research support from: AbbVie, H. Gudbergsen Speakers bureau: MSD and Pfizer, N. Krogh: None declared, D. Jensen: None declared, I. Sørensen: None declared, R. Christensen: None declared, M. Skougaard: None declared, M. Hetland Grant/research support from: AbbVie, BMS, MSD, Pfizer, UCB, Biogen, Orion

DOI: 10.1136/annrheumdis-2017-eular.3726

THU0663 SERUM GALECTIN-3 BINDING PROTEIN IS A NOVEL PREDICTOR OF VENOUS THROMBOEMBOLISM IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

A.S.R. Peretz[1], N.S. Rasmussen[2], N.H.H. Heegaard[3], S. Jacobsen[2], C. Sjöwall[4], C.T. Nielsen[2]. *[1]Centre for Rheumatology and Spine Diseases, Gentofte, Copenhagen University Hospital, Denmark., Gentofte; [2]Copenhagen Lupus and Vasculitis Clinic, Centre for Rheumatology and Spine Diseases, Rigshospitalet; [3]Department of Autoimmunology and Biomarkers, Statens Serum Institut, Copenhagen, Denmark; [4]Rheumatology/AIR, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden*

Background: SLE patients have a marked increased risk of venous (VTE) and arterial (AT) thrombosis, which is not fully explained by traditional risk factors or the presence of anti-phospholipid antibodies. Thrombosis is a major cause of damage accrual, morbidity, and mortality in SLE. A better understanding of the pathogenesis and development of new biomarkers to identify patients at risk are needed. Recent studies link leptin and tumor necrosis factor-like weak inducer of apoptosis (TWEAK) to subclinical atherosclerosis and galectin-3-binding protein (G3BP) to type I interferon activation and a pro-thrombotic environment.

Objectives: To explore G3BP, interferon gamma-induced protein 10 (IP-10), soluble CD163 (sCD163), TWEAK, and leptin serum levels as predictors of venous and arterial thrombotic events, damage accrual, and all-cause mortality during long-term follow-up in a large cohort of Swedish SLE patients.

Methods: Baseline clinical and paraclinical data including disease activity and damage scores (SLICC) were available from 167 SLE patients. VTE (deep vein thrombosis and/or pulmonary embolism) and AT (myocardial infarction and/or cerebrovascular incident) data were available with a median follow-up period of six years. Baseline serum G3BP, IP-10, sCD163, TWEAK, and leptin were quantified using ELISA. Univariate and multivariate analyses were conducted to asses associations between the serum biomarkers and the occurrence of VTE/AT, damage accrual, and death.

Results: In the follow-up period 11 (7%) VTE and 12 (7%) AT events occurred. SLICC-scores increased in 79 (47%) patients, and 19 (11%) patients died. In the univariate Cox regression analysis G3BP levels were significantly associated with an increased risk of VTE (hazard ratio (HR) 1.10, 95% confidence interval (CI): 1.01–1.2, *P*=0.03). This persisted in the multivariate cox regression analyses when adjusting for age, gender, diabetes, antiphospholipid syndrome, and treatment with warfarin (HR 1.16, 95% CI: 1.04–1.31, *P*=0.01). None of the other serum biomarkers were associated with AT and VTE. No significant associations were observed between the biomarkers and changes in SLICC-scores or all-cause mortality.

Conclusions: Our study identifies serum G3BP as a novel independent predictor of VTE in SLE. This may improve our understanding of VTE pathogenesis in SLE and aid future VTE risk stratification and prophylaxis. Further studies are needed to translate this into clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4287

THU0664 TRANSLATION, CULTURAL ADAPTATION AND VALIDATION OF THE SYSTEMIC LUPUS ACTIVITY QUESTIONNAIRE (SLAQ) IN A COHORT OF ITALIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

C. Tani[1], R. Vagelli[2], L. Carli[2], C. Stagnaro[1], F. Drago[1], V. Lorenzoni[3], G. Turchetti[3], M. Mosca[1]. *[1]Rheumatology Unit, University of Pisa, Pisa, Italy; [2]Via Roma 67, Pisa, Rheumatology Unit, University of Pisa; [3]Institute of Management, Scuola Superiore Sant'Anna, Pisa, Italy*

Background: Evaluation of disease activity is one of the most important assessments in SLE; several instruments have been developed based on clinical and laboratory information recorded by the physician. Patient-administered questionnaires provide useful information with significant time and cost saving. Indeed, patient-reported outcomes are gaining a central role as outcome measures.SLAQ is a patient-reported instrument for the assessment of disease activity in SLE. It consists of three scores: Patient Global Assessment question (PGA) about presence and severity of lupus activity over the past month, questions on 24 symptoms (SLAQscore) and a single Numerical Rating Scale (NRS) for disease activity (0 – 10).

Objectives: The aim of the study was to translate and to validate the SLAQ in Italian.

Methods: The process of translation and cultural adaptation followed published guidelines (1). The final version of the questionnaire (SLAQit) was pretested in a group of 35 SLE patients to assess acceptability, comprehension and feasibility. The validity of the SLAQit was evaluated by its administering to consecutive SLE patients attending the outpatient's clinic or the inpatients wards. Internal consistency between the three components of the score was evaluated by Chronbach's alpha; the external validity was tested toward validated activity indices (SLEDAI and ECLAM) scored by a physician blinded to the SLAQ results. In a subgroup of 30 patients the questionnaire was administered twice at 2 weeks' interval to assess its reliability.

Results: 137 patients were enrolled (92% female, mean age 43.1 years, mean disease duration 15.3 years). At enrollment, the median SLEDAI score was 2 (range 1–18) and 45% of patients had at least one organ damage (median 2, 1–8). The pilot test provided a good acceptability (99.9% of response rate) and feasibility (mean of 4.6±2.3 minutes to be completed, 1–10); moreover, the 100% of patients declared to comprehend the scope of the SLAQ and 67.5% declared no content comprehension problems. Internal consistency was very good between (NRS vs PGA vs SLAQscore (α=0.79). NRS and PGA showed a linear correlation with both ECLAM and SLEDAI scores (ρ=0.24, p=0.004 and ρ=0.45, p<0.001 respectively), while the correlation with the SLAQscore didn't reach the statistical significance. SLAQit showed a very high reliability by comparing the test-retest results (α>0.8 for NRS, PGA and SLAQscore). SLAQit scores resulted directly related to the patients age (p=0.002) and the SLICC score (p=0.003) while no correlation with disease duration was observed.

Conclusions: SLAQit demonstrated to be acceptable, comprehensible and feasible in our routine clinical setting; it also showed good internal consistency; correlation with physician's driven instruments is weaker and the SLAQit was influenced by epidemiological and disease-related factors (i.e. damage), thus confirming that the disease perception from the patient's perspective can be different from physicians and influenced by several factors. The SLAQit can be considered a useful screening tool for the first assessment of the disease activity before the standard visit.

References:

[1] Guillemin F, et al. Journal of Clinical Epidemiology 1993; 46: 1417–1432.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4207

THU0665 CAN ONE GIVE UP BASDAI IN FAVOR OF ASDAS IN MONITORING SPONDYLOARTHRITIS PATIENTS ON BIOLOGICS?

C. Cobilinschi, D. Opris-Belinski, R. Ionescu. *Sfanta Maria Clinical Hospital, Bucharest, Romania*

Background: Disease activity in SpA is widely evaluated through BASDAI or ASDAS with no proven superiority between the two, in spite the more objective evaluation of ASDAS through the inflammatory markers.

Objectives: The aim of this study was to evaluate the clinical quality and discriminating power between the above indices when subdividing patients with anti-TNF therapy according to their disease status indicated by BASDAI, ASDAS or PtGA.

Methods: This prospective, observational study included 100 patients with definite SpA on biological therapy.Demographic, clinical and laboratory data was collected. Statistical analysis was performed with SPSS 20.0.

Results: When used as an external criterion PtGA showed that 12% of patients had active disease with a PtGA of over 5 while 88% were classified as low disease activity.Mean ASDAS-CRP and ASDAS-ESR in the active group were 3.39 and 3.24.Mean BASDAI score in the high activity group according to PtGA was 5.66.We showed that both ASDAS scores had good discriminating capacities, with similar values when using the SMD (2.0034 [95% CI 1.29–2.71]).Based on PtGA,BASDAI outperformed ASDAS scores with a SMD of 3.3391 [95% CI 2.5334–4.1447]. ROC curves of the disease activity scores by using the PtGA $\geq$5

as variable of high disease activity state showed the following: for ASDAS-CRP, ASDAS-ESR and BASDAI the AUCs (*area under curve*) were 0.89 (P=0.05; 95% CI 0.80–0.99), 0.88 (P<0.001; 95% CI 0.77–0.99), and 0.99 (P=0.009; 95% CI 0.97–1.00).For CRP and ESR the AUCs were 0.81 and 0.79. This shows the high accuracy of the three scores in assessing SpA activity,but with a lower fidelity of the inflammatory markers alone.When dividing patients according to BASDAI score,14% showed a more active disease than the rest of 86% who had low disease activity.Mean ASDAS-CRP scores in the first group was 3.31.When correlating disease activity scores for the entire study group we observed that BASDAI correlated to both ASDAS scores (r=0.65 and 0.71, P<0.001) and that PtGA showed a stronger correlation to BASDAI (r=0.912, P<0.01) than ASDAS and to acute phase reactants.

Conclusions: This study shows that disease activity scores have good discriminatory powers. BASDAI surpassed ASDAS scores when relating to the PtGA. According to Van der Heijde et al.(1), the only situation in which BASDAI can outperform ASDAS is when assessing the PASS (*patient acceptable symptom state*). However, ASDAS-CRP had better discriminatory power than ASDAS-ESR or acute phase reactants. This demonstrates that ASDAS-CRP is a more objective evaluation that can better differentiate patients with high or low disease activity.

References:

[1] D van der Heijde,ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis, Ann. Rheum. Dis,vol. 68,Dec 2009.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5326

THU0666 PATIENT GLOBAL ASSESSMENT IS MORE SENSITIVE TO CHANGE THAN HEALTH-RELATED QUALITY OF LIFE INSTRUMENTS IN EARLY AXIAL SPONDYLOARTHRITIS OVER 3 YEARS: DATA FROM THE DESIR COHORT

D. Puyraimond-Zemmour[1,2], C. Desthieux[1,2], A. Ruyssen-Witrand[3], B. Fautrel[1,2], L. Gossec[1,2]. *[1]Pitie Salpetriere Hospital; [2]Paris 06 university, Pierre and Marie Curie, Paris; [3]CHU de Toulouse, Hôpital Pierre-Paul Riquet, Toulouse, France*

Background: Several questionnaires assess similar constructs of global patient-reported state or Health-Related Quality of Life (HRQoL).

Objectives: To evaluate sensitivity to change (ie, discriminance) of several questionnaires in early axial spondyloarthritis (axSpA) over 3 years of follow up: the SF36, axial spondyloarthritis quality of life (ASQoL), axial spondyloarthritis health assessment questionnaire (AS-HAQ) and patient global assessment (PGA).

Methods: DESIR is an ongoing prospective, multicenter, longitudinal, observational French cohort (1). Patients had inflammatory back pain of more than 3 months and less than 3 years suggestive of axSpA. For our analysis, only patients with no missing data for MCS and PCS SF36 values during the first 3 years were included. A global construct of patient global state was assessed by the SF36 questionnaire and its 2 subscales (scored 0–100 with higher scores indicating better status): the physical composite score (PCS) and the mental composite score (MCS), AsQoL, a disease-specific HRQoL scale, PGA and AS-HAQ. ASDAS-CRP was used as comparator. Each outcome was assessed at baseline, 6 months, 12 months, 24 months and 36 months. Standardized mean differences (SMD) were calculated using Cohen's effect size with confidence intervals, between each time point for each outcome. A SMD <0.5 is usually considered small, between 0.5 and 0.8 moderate and >0.8 as important.

Results: In all, 442 patients were analyzed: at baseline, mean age was 34.2±8.6 years; mean disease duration was 18.6±10.7 months; 239 (54%) were females, 274 (62%) had HLAB27 and 124 (28%) had radiological sacroiliitis. At baseline, patients were not in an optimal state; improvement was clear up to month 6 then minimal (at the group level): Table. Sensitivity to change was greatest for PGA, then ASQoL whereas AS-HAQ, MCS and PCS appeared the least discriminant measure (Table).

Conclusions: PGA was more sensitive to change than HRQoL measures in early axSpA. ASDAS appeared also sensitive to change. Changes in all the measures were very small at the group level after 6 months of follow-up indicating the concepts convered may be as much patient- as disease-related.

References:

[1] Dougados M. et al. Clinical presentation of patients suffering from recent onset chronic inflammatory back pain suggestive of spondyloarthritis: The DESIR cohort.Joint Bone Spine. 2015;82(5):345–51.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4866

THU0667 A QUALITATIVE AND QUANTITATIVE COMPARISON OF SYNOVIAL BIOPSY TECHNIQUES DURING CLINICAL TRIALS OF INFLAMMATORY ARTHRITIS

F. Humby[1], S. Bugatti[2], A. Filer[3], S. Kelly[4], A. Manzo[2], E. Souza[5], V. Romao[5], V. Rocher[1], R. Hands[1], M. Wechalekar[6], J. Fonseca[5], C. Montecucco[2], C. Pitzalis[1]. *[1]Experimental Medicine and Rheumatology, Barts and the London School of Medicine and Dentistry, London, United Kingdom; [2]Division of Rheumatology, University of Pavia, Pavia, Italy; [3]Institute of Inflammation and Ageing, University of Birmingham, Birmingham; [4]Department of Rheumatology, Barts Health NHS Trust, London, United Kingdom; [5]Department of Rheumatology, Lisbon Academic Medical Centre, Lisbon, Portugal; [6]Rheumatology Unit, Repatriation General Hospital, Adelaide, Australia*

Background: Synovial tissue is an attractive area of research for biomarkers of disease outcome in RA. Currently acquisition of synovial tissue using an arthroscopic approach in clinical trials is recommended though two US-guided techniques have been described, a portal and forceps (P&F) approach and an adaptation using a quick core needle (NB). However before US-guided biopsy techniques are widely adopted into clinical trials validation of performance against arthroscopy is required.

Objectives: To evaluate whether there were significant differences in synovial sampling quality and quantity between arthroscopic, US-P&F and US-NB procedures within the context of clinical trials.

Methods: This was a multicentre retrospective analysis of inflammatory arthritis patients recruited to clinical trials utilizing US-guided NB (Barts Health NHS Trust), US-guided P&F (ICRSS Policlinico San Matteo and University Hospital Birmingham) and arthroscopic biopsy (Repatriation General Hospital).

Paraffin embedded synovial sections from each procedure underwent H&E staining and sections examined for intact cell lining layer (graded sections). Biopsy procedures were segregated into large (knee) and small joint procedures (wrist/MCP) for analysis. Proportion of samples yielding graded tissue per procedure was recorded. Using CellSens Dimensions software the mean area of synovial tissue obtained per procedure was determined. In addition the degree of synovitis was assessed using semi-quantitiative scoring (0–9).

Results: 78 patient procedures were evaluated, 22 on small joints (11 US-NB, 11 US P&F) and 56 on large joints (11 US-NB, 35 US-P&F, 10 arthroscopic). 47 patients had RA, 11 undifferentiated arthritis and 10 psoriatic arthritis. Arthroscopic sampling resulted in a significantly higher area of tissue retrieved per procedure than US P&F or US-NB. There were no significant differences in proportion of graded samples per procedure suggesting quality of synovial tissue was preserved between techniques. Finally no significant differences in degree of histological synovitis were demonstrated between sampling techniques.

Conclusions: The results suggest that US-guided biopsy provides a reliable method for sampling synovial tissue of comparable quality to that obtained from arthroscopy. However when sampling large joints arthroscopic techniques, and when sampling small joints US-P&F yield a significantly higher quantity, though not quality, of tissue per procedure than US-NB. These results may influence choice of biopsy technique when designing clinical trial protocols in inflammatory arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1918

Abstract THU0666 – Table 1. Sensitivity to change (SMD (95% CI)) of different outcomes in early axSpA over 3 years

	Baseline value (mean ± SD)	SMD between baseline and M6 [95% confidence interval (CI)]	SMD between M6 and M12 [95% CI]	SMD between M12 and M24 [95% CI]	SMD between M24 and M36 [95% CI]
PCS	40.5±9.2	0.27 [-0.41;-0.14]	0.02 [-0.11; 0.15]	0.02 [-0.11; 0.16]	-0.02 [-0.15; 0.11]
MCS	40.4±11.0	-0,26 [-0,39; -0,13]	0.02 [-0.11; 0.16]	-0.08 [-0.21; 0.05]	0.00 [-0.13; 0.13],
PGA	6.1±2.2	0.69 [0.56;0.83],	0.09 [-0.04; 0.22]	0.06 [-0.07; 0.19]	0.05 [-0.08; 0.18]
ASQoL	9.1±5	0.36 [0.22;0.49]	-0.01 [-0.14; 0.12]	0.02 [-0.12; 0.15]	0.00 [-0.14; 0.13]
AS-HAQ	0.63±0.5	0.24 [0.11;0.38],	-0.04 [-0.17; 0.09]	0.02 [-0.11; 0.15]	0.00 [-0.13; 0.13]
ASDAS-CRP	2.6±0.98	0.52 [0.38;0.65].	-0.03 [-0.17; 0.10]	0.06 [-0.08; 0.20]	0.10 [-0.04; 0.24]

Abstract THU0667 – Table 1

Mean (SD)	Small joint biopsies				Large joint biopsies		
	US –NB (n=11)	US P&F (n=11)	P value	US-NB (n=11)	US P&F (n=35)	Arthroscopic (n=10)	P value
Joint biopsied	7 wrist 5 MCP	1 wrist 10 MCP		10 knee	32 knee 3 ankle	10 knee	
% graded samples per procedure	82.3 (22.4)	91 (10)	0.34	89.8 (17.5)	83.23 (19)	97 (11)	0.08
Mean area of tissue (mm^2) per procedure	3.19 (1.75)	7.95 (4.91)	<0.005*	4.66 (3.19)	8.8 (8.17)	17.64 (7.56)	<0.0001*
Synovitis score	4.9 (3.2)	NA	NA	3.8 (2.6)	4.53 (2.26)	4.5 (1.71)	0.35

THU0668 RELIABILITY OF PATIENT GLOBAL ASSESSMENT IN RHEUMATOID ARTHRITIS PATIENTS

G. Kageyama[1], A. Onishi[2], Y. Ueda[2], J. Saegusa[2], A. Morinobu[2]. *[1]Department of Rheumatology, Hyogo Prefectural Amagasaki General Medical Center, Amagasaki; [2]Department of Rheumatology, Kobe University Hospital, Kobe, Japan*

Background: Patient's global assessment (PtGA) is one of the most widely used patient reported outcomes in rheumatoid arthritis (RA) that reflects both disease activity and other factors. PtGA is onymous and obtained at hospital, which may cause a conscious or unconscious bias, whereas PtGA obtained anonymously may be free from any bias. The credibility of PtGA to report RA patient outcomes has been usually investigated by assessing test-retest reliability. There has been no study comparing routine PtGA and PtGA where patients answered anonymously.

Objectives: The aim of this study was to compare routinely obtained in-hospital PtGA before clinical examination with those answered anonymously at home. Additionally, physician's global assessment (PhyGA) was compared with routine PtGA and anonymized PtGA

Methods: We asked RA patients (n=389) to answer and mail the PtGA test anonymously, Clinical data regarding disease duration, stage, class, swollen joint counts, tender joint counts, pain visual analog scale (VAS), PhyGA, Health Assessment Questionnaire (HAQ), EuroQOL five dimensions questionnaire (EQ5D), Kessler 6 scale (anxiety/ depression), treatment data, laboratory data, and socioeconomic factors were collected simultaneously. We compared the PtGA that is routinely surveyed at hospital before clinical examination with those surveyed anonymously at home. We calculated a discrepancy score by subtracting anonymized PtGA from routine in-hospital PtGA. We defined (1) positive discrepancy when routine PtGA was over-rated relative to the anonymized PtGA; (2) negative discrepancy when routine in-hospital PtGA was under-rated relative to the anonymized PtGA.

Results: The anonymized PtGA score was higher than routinely evaluated in-hospital PtGA ($p<0.0001$). The anonymized PtGA poorly correlated with routine in-hospital PtGA ($r=0.426$, $p<0.0001$). We compared patients who had discordance between in-hospital PtGA and anonymized PtGA. We used 3 models in which the discordance between both PtGAs was set at 10 mm, 20 mm, or 30 mm. If we adopted 30 mm as discordance, the pain scale remained to be a risk factor of positive discrepancy (higher in-hospital PtGA than anonymized PtGA). If we adopted 20 mm or 10 mm as discordance, the pain scale remained to be a risk factor of positive discrepancy and remaining low quality of life (QOL) negative discrepancy (lower in-hospital PtGA than anonymized PtGA) after multivariate analysis. The discordance between PhyGA and routine PtGA are associated with high pain VAS. The discordance between PhyGA and anonymized PtGA is associated with tender joint counts, swollen joint counts, and low QOL.

Discordance Model	Difference between in-hospital PtGA and anonymized PtGA		
	30mm	20mm	10mm
Household income	-0.074 ± 0.18	0.14 ± 0.14	0.09 ± 0.082
Married (yes)	1.0 ± 1.2	1.3 ± 1.0	-0.057 ± 0.06
Tender Joint Counts	-0.3 ± 0.3	-0.12 ± 0.18	0.011 ± 0.14
Swollen Joint Counts	0.5 ± 0.66	0.32 ± 0.37	0.2 ± 0.18
CRP (mg/dl)	-0.42 ± 0.51	-0.26 ± 0.40	-0.18 ± 0.26
Pain VAS	0.11 ± 0.035 **	0.12 ± 0.026 ***	0.081 ± 0.013 ***
Physician's Global Assessment	0.028 ± 0.066	-0.017 ± 0.045	-0.0089 ± 0.026
EQ5D	0.093 ± 0.056	0.093 ± 0.037 *	0.043 ± 0.018 *
K6 scale(Anxiety/Depression)	-0.15 ± 0.14	0.0027 ± 0.091	0.56 ± 0.59

Value are expressed as Estimate ± Standard Error. * p<0.05, *** p<0.0001

Conclusions: Discrepancy exists between routine in-hospital PtGA and anonymized PtGA.

The high pain VAS scale and low QOL are risk factors that could make the difference between routine PtGA from anonymized PtGA. There is a possibility that high pain VAS score and low QOL influence the reliability of PtGA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1488

THU0669 THE ASSOCIATION BETWEEN HARRIS HIP SCORE AND DISEASE ACTIVITY OR HIP MRI FEATURES IN ANKYLOSING SPONDYLITIS

Z. Wu[1], L. He[2], M. Yang[3], Y. Liu[4], D. He[5], Y. Zhang[6], C. Wang[7], H. Xu[8]. *[1]Department of Rheumatology, Xijing Hospital; [2]Department of Rheumatology, The First Affiliated Hospital of Xi'An JiaoTong University Hospital, Xi'An; [3]Department of Rheumatology, Nanfang Hospital, Guangzhou; [4]Department of Rheumatology, West China Hospital, Sichuang; [5]Department of Rheumatology, GuangHua Hospital, Shanghai; [6]Department of Rheumatology, Tangdu Hospital; [7]Medical Affairs, Xian-Janssen Pharmaceutical Ltd, Xi'An; [8]Department of Rheumatology and Immunology, Shanghai Changzheng Hospital, Shanghai, China*

Background: Hip involvement is a common clinical feature observed in ankylosing spondylitis (AS) patients and it often leads to substantial restriction of the body functions.[1] Hip involvement in AS is mainly assessed by radiographic changes, clinical symptoms or MRI. The Harris hip score (HHS) is a valuable assessment tool to measure health status of AS patients. However, the relationship between HHS and other clinical indices is unknown.

Objectives: To evaluate relationship between HHS and other commonly used clinical indices.

Methods: In this multicentre, observational study, AS patients with hip clinical manifestation are enrolled and randomly assigned to infliximab treatment (group I, with/without DMARDs and/or NSAIDs) or conventional therapy (group II, DMARDs and/or NSAIDs). Primary endpoint: to compare functional improvement of hip joint (HHS) between two treatment groups (infliximab and conventional therapy) at week 30. Secondary endpoint: to compare disease activity and functional improvement of AS and radiologic progression of hip joint between two treatment groups at week 30 and 52. Association between baseline HHS and disease activity measures such as Bath ankylosing spondylitis (BAS)-functional index (BASFI), BAS disease activity index (BASDAI), AS disease activity score (ASDAS), CRP and ESR was analysed using Pearson correlation coefficient. BAS metrology index (BASMI) and hip imaging functions (MRI of hip, BAS radiology hip index [BASRI-h]) were analysed using independent two-sample t-test or ANOVA based on data characteristics.

Results: Study is ongoing; currently, only baseline information is analyzed. Baseline demographics and disease characteristics did not show any significant difference between groups. Almost all baseline disease activity measures showed significant Pearson correlation (high correlation in BASFI=0.646) with HHS, except for BASDAI (table 1). Significant association between HHS and three MRI scores (articular cartilage stripping, bone destruction under joint surface, femoral head bone marrow cavity edema) and BASRI-h was shown (table 2). Also, significant correlation was shown between BASMI and HHS (F value [degree of freedom]=4.70 [4]; p=0.0022).

Table 1. Association between HHS and disease activity measures at baseline

	Mean (SD)	Pearson correlation-HHS	P Value
ASDAS	2.81 (0.904)	-0.449	0.0004
BASDAI	4.60 (1.109)	-0.169	0.1691
BASFI	3.79 (2.050)	-0.646	<0.0001
CRP	12.270 (19.4810)	-0.348	0.0074
ESR	22.1 (24.06)	-0.386	0.0023

Table 2. Association between HHS and hip imaging functions at baseline

		N	HHS, mean (SD)	T-test (degree of freedom)	P value
Articular cartilage stripping	No	29	62.5 (9.13)	2.27 (54.97)	0.0271
	Yes	32	55.9 (13.39)		
Bone destruction under joint surface	No	22	63.8 (4.66)	3.08 (49.29)	0.0034
	Yes	38	56.2 (14.02)		
Femoral head bone marrow cavity edema	No	29	62.4 (9.37)	2.18 (58.00)	0.0332
	Yes	31	55.8 (13.46)		
BASRI-h (at least one Hip ≥1)	_	29	54.7 (14.01)	-3.00 (37.55)	0.0048

Conclusions: The baseline results of HHS were found to be well associated with disease activity scores like BASFI, ASDAS and BASMI and four hip imaging features in AS patients with hip involvement.

References:

[1] Jeong H, et al. Korean J Intern Med. 2017; 32(1): 158–164.

Disclosure of Interest: Z. Wu: None declared, L. He: None declared, M. Yang: None declared, Y. Liu: None declared, D. He: None declared, Y. Zhang: None declared, C. Wang Employee of: Xi'an Janssen pharmaceuticals Ltd., H. Xu: None declared

DOI: 10.1136/annrheumdis-2017-eular.3724

THU0670 DETECTION OF SERUM ANTI-DNASE I ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS USING IMPROVED IMMUNOSORBENT ASSAY

A.S. Trofimenko[1,2], I.P. Gontar[1], I.A. Zborovskaya[1], L.N. Shilova[2], E.G. Korenskaya[2]. *[1]Research Institute for Clinical and Experimental Rheumatology; [2]Volgograd State Medical University, Volgograd, Russian Federation*

Background: Diagnosis of systemic lupus erythematosus (SLE) is a sophisticated problem in most of the disease cases. The reasons of this include common diagnostic markers of SLE (ANA, anti-dsDNA, anti-Sm), that are insufficiently reliable itself as well. One of possible ways to overcome these difficulties is searching for new SLE markers. These emerging diagnostic tools are not only to be valuable for diagnosis establishment, but also to provide economical efficiency and facility in common use.

Objectives: To compare diagnostic efficiency of anti-DNase I antibodies measured by conventional ELISA and by originally modified enzyme immunosorbent assay using magnetic polyacrylamide beads as an antigen carrier.

Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles, it was approved by the Regional Committee on Medical Ethics. All the patients signed the informed consent. We have enrolled 54 in-hospital adult patients with SLE, verified by the ACR criteria (1997). Control group (n=52) was comprised of patients with rheumatoid arthritis, systemic sclerosis, systemic vasculitides, dermatomyositis, and Sjogren's disease. Serum

anti-DNase I concentrations were evaluated by conventional ELISA, as described elsewhere [1]. The beads were synthesized using original technique [2], modified ELISA and recovery of the beads for repeating use was performed according to the previously published protocols [2]. Antibody concentrations were expressed as relative optical density units (ODU). The cutoff values for conventional and modified ELISA were 0.061 and 0.057 ODU, respectively. All the means and operation characteristics were expressed as values (95% confidence intervals). Differences were considered significant when $p<0.05$.

Results: Mean anti-DNase I concentrations in SLE patients (negative and positive together) were 0.088 (0.031–0.145) and 0.079 (0.033–0.125) ODU for conventional and modified ELISA, respectively; in the control group they were 0.068 (0.020–0.116) and 0.063 (0.019–0.107) ODU, respectively. Differences within these couples were not significant. Diagnostic sensivity and specificity of modified ELISA were 64.74 (53.09–76.39) and 85.01 (72.95–97.07)%, coinciding with those for conventional ELISA. LOQ for the modified ELISA was slightly lower than for the conventional one. Accuracy and repeatability of modified ELISA were also insignificantly higher than those for conventional approach. There was no substantial change in all the parameters of modified ELISA after single recovery of beads.

Conclusions: The newly developed ELISA for anti-DNase I antibodies was demonstrated to have equivalence or advantage in some analytical parameters over conventional ELISA. Considering some economic and maintenance benefits, our innovation can be an alternative tool to improve SLE diagnostics.

References:

[1] Trofimenko AS, Gontar IP, Zborovsky AB, Paramonova OV. Anti-DNase I antibodies in systemic lupus erythematosus: diagnostic value and share in the enzyme inhibition. Rheumatol Int. 2016;36(4):521–9.

[2] Gontar IP, Simakova ES, Trofimenko AS, Zborovskaya IA. An approach for removal of DNA-containing immune complexes from blood using composite sorbent. Patent RU2441674 (2010) [in Russian].

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2598

THU0671 CAN AN INNER DISPOSABLE GLOVE BE USED UNDER AN ELECTROGONIOMETRIC GLOVE FOR MEASURING FINGER MOVEMENT WITHOUT LOSS OF ACCURACY?

J. Connolly[1], P. Gardiner[2], J. Condell[3], K. Curran[3], D. Small[2]. *[1]Computing, Letterkenny Institute of Technology, Letterkenny, Ireland; [2]Rheumatology, Altnagelvin hospital; [3]Computing, Ulster University, Londonderry, United Kingdom*

Background: Improving joint mobility is an important outcome for patients with arthritis, but finger joint range of motion is rarely measured in clinic. Electronic gloves with movement sensors have been developed to measure joint movement accurately and it is now possible to assess dynamic mobility of the finger joints. However these gloves are expensive and it is likely that when carrying out measurements in the patient population they would be used with inner disposable gloves to avoid nonsocomical infection. Establishing accuracy and usability of electronic gloves whilst wearing disposable inner gloves is therefore an important pre-requisite for studies in patients with arthritis.

Objectives: To establish the accuracy and repeatability of measurements of finger movement obtained using two different electrogoniometric gloves worn with and without an inner disposable glove.

Methods: We used two different types of electrogoniometric glove for the purpose of this study. One is the commercially available 5DT dataglove 14 Ultra (5DT, 2011) and the other was produced to our specifications by Tyndall National Institute, University College Cork. We called this the “IMU glove”. We developed a graphical interface for both devices to facilitate detailed evaluation of joint movement in each finger. Both gloves were tested using a protocol adapted from Dipietro, Sabatini, & Dario, (2003).

Results: Table 1 displays comparison of Coefficient of Variation (CV) readings for both data gloves. Figure shows this information graphically.

Sensor	No surgical glove		Surgical glove underneath	
	5DT	IMU	5DT	IMU
Index MCP	2.97	2.86	3.22	3.88
Middle MCP	7.01	6.77	9.02	6.39
Ring MCP	6.10	4.37	6.28	4.32
Little MCP	24.17	6.07	9.55	8.25
Index PIP	1.96	9.72	2.92	14.69
Middle PIP	4.40	10.29	2.98	12.53
Ring PIP	5.38	9.95	5.00	11.03
Little PIP	9.11	3.71	10.07	5.46

Results show no significant change for 5DT angular readings with and without a surgical glove worn underneath the data glove. Results for PIP sensors show an improvement in repeatability with a surgical glove. CV variance was smaller for MCP sensors with a surgical glove worn underneath the data glove compared with no surgical glove.

CV for the IMU data glove show negligible changes in MCP readings when a surgical glove is worn underneath. PIP readings show small changes when using a surgical glove.

Conclusions: Inner disposable gloves can be worn when using electrogoniometric gloves for testing finger movement without loss of accuracy or any significant discomfort in patients with arthritis.

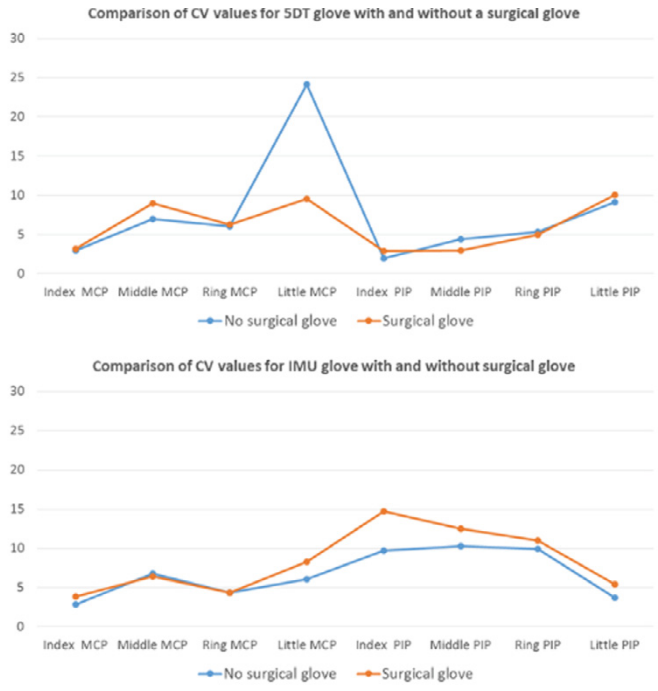


Figure 1: Comparison of Coefficient of Variation (CV) values for mean angular readings for both data gloves, with and without a surgical glove worn underneath.

References:

[1] 5DT, 2011. 5DT Data Glove 14 Ultra [WWW Document]. URL http://www.5dt.com/products/pdataglove14.html (accessed 1.10.12).

[2] Dipietro, L., Sabatini, A.M., Dario, P., 2003. Evaluation of an instrumented glove for hand-movement acquisition. J. Rehabil. Res. Dev. 40, 179–89.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4429

THU0672 REAL WORLD EVIDENCE COMPARING THE PATIENT REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM TO THE CDAI IN RHEUMATOID ARTHRITIS PATIENTS

J.R. Curtis[1], S. Kafka[2], D. Parenti[2], S. Black[2], S. Xu[3], Y. Wang[3], C.O. Bingham III[4]. *[1]University of Alabama at Birmingham, Birmingham; [2]Janssen Scientific Affairs, LLC, Horsham; [3]Janssen Research & Development, LLC, Springhouse; [4]Johns Hopkins University, Baltimore, United States*

Background: Patient (Pt) reported outcomes (PROs) play a role in overall disease evaluation, therapeutic response assessment and care of rheumatoid arthritis (RA) patients (Pts). The Pt Reported Outcomes Measurement Information System (PROMIS [P]) questionnaires developed by the NIH have been validated and are a feasible assessment tool in RA (Bartlett 2015).

Objectives: AWARE (Comparative and Pragmatic Study of Golimumab Intravenous (IV) Versus Infliximab in RA) is a real-world study of golimumab IV (G-IV) vs. infliximab (IFX) in RA and will assess infusion reactions, disease activity and multiple PROs as outcomes measures.

Methods: AWARE is a prospective, noninterventional, ongoing US-based study in which 1,200 adult Pts will be enrolled on initiation of treatment with G-IV or IFX. Objectives include PRO assessments of Pt response to treatment using the PROMIS-29 Profile v2.0 (P29v2), P Pain Interference Short Form-6b (PISF) and P Fatigue Short Form-7a (FSF), 36-Item Short Form Health Survey (SF-36v2) and the Clinical Disease Activity Index (CDAI). We report an interim analysis from the first 353 Pts of baseline PROMIS questionnaire and CDAI scores, and their inter-relationships. PROMIS questionnaire results are scored on a 0 to 100 scale, normed to the US population and reported as a “T-score” (mean of 50 and standard deviation (SD) of 10). PROMIS T scores were compared across CDAI disease activity (DA) categories.

Results: Baseline mean (SD) CDAI score was 33.46 (±15.79), with 73.4% of pts with high DA (HDA), 22.1% with moderate disease activity (MDA), 3.7% with low disease activity (LDA) and 0.8% pts in remission. PROMIS scores are shown below. All P29v2 domains, PISF and FSF scores were significantly worse in pts with CDAI>22 vs. CDAI≤22 ($p<0.05$). The same was true for SF-36 domains (data not shown). PROMIS scores are shown below for all pts, and also based on CDAI DA category. PROMIS T scores across all domains (P29v2 domains, PISF and FSF) were compared to CDAI disease activity category (below). As shown, PROMIS T scores correlated with CDAI disease category, with HDA Pt T scores significantly (*, $p<0.05$) greater than those of MDA, LDA and Remission pts (excepting the Sleep Disturbance domain).

Mean PROMIS T Score of All Patients in Interim Analysis Dataset and a Comparison of T Scores of PROMIS-29 Domains, Fatigue Short Form and Pain Interference Short Form to CDAI Disease Activity Category

	All Patients (n=353)	Remission CDAI</=2.8 (n=3)	LDA 2.8<CDAI</=10 (n=13)	MDA 10<CDAI</=22 (n=78)	HDA CDAI>22 (n=259)
P29-Physical Function	37.5 ± 6.4	50.1 ± 6.07	43.5 ± 7.37	39.7 ± 6.83	36.4 ± 5.66*
P29-Anxiety	54.5 ± 10.3	44.8 ± 7.74	50.4 ± 9.12	51.6 ± 10.0	55.7 ± 10.24*
P29-Depression	52.7 ± 10.1	43.7 ± 4.62	46.2 ± 7.25	49.8 ± 10.18	54.0 ± 9.91*
P29-Fatigue	59.9 ± 9.6	41.8 ± 7.53	51.1 ± 9.57	56.9 ± 9.55	61.5 ± 9.04*
P29-Sleep Disturbance	56.0 ± 8.3	52.8 ± 14.36	52.3 ± 6.41	54.1 ± 8.48	56.8 ± 8.17
P-29 Ability to participate in Social Roles and Activities	42.3 ± 8.2	56.2 ± 9.18	49.9 ± 8.43	44.5 ± 8.84	41.2 ± 7.50*
P29-Pain Interference	64.0 ± 7.5	45.7 ± 7.1	54.3 ± 7.81	61.0 ± 8.10	65.5 ± 6.35*
Fatigue SF 7a	60.3 ± 8.3	43.0 ± 10.19	54.3 ± 7.65	57.5 ± 7.22	61.7 ± 8.02*
Pain Interference SF 6b	63.0 ± 7.7	43.5 ± 4.33	54.6 ± 9.29	59.9 ± 8.03	64.5 ± 6.62*
P29 Pain Intensity (scored 0-10 scale)	6.2 ± 2.2	2.0 ± 3.46	3.5 ± 1.71	5.4 ± 2.32	6.6 ± 1.91*

T scores > 50 indicate worsening of the domain relative to the general population, except "Physical Function" and "Ability to participate in Social Roles and Activities", where T-scores < 50 indicate worsening of these domains relative to the general population. * = p<0.05 vs respective scores in MDA, LDA and remission DA categories

Conclusions: These interim data further support the viability of using PROMIS questionnaires to evaluate RA pts, and indicate in this predominantly HDA population of RA pts correlations between PROMIS and CDAI disease activity category. Confirmation of the baseline interim analysis findings with the fully enrolled AWARE study, as well as inclusion of longitudinal and subset analyses based on disease activity levels, will further define the role of PROMIS relative to CDAI in RA patients in a real world setting.

Disclosure of Interest: J. Curtis Consultant for: Janssen, AbbVie, Roche/Genentech, BMS, UCB, Myriad, Lilly, Amgen, Pfizer, Corrona, S. Kafka Employee of: Janssen Scientific Affairs, LLC, D. Parenti Employee of: Janssen Scientific Affairs, LLC, S. Black Employee of: Janssen Scientific Affairs, LLC, S. Xu Employee of: Janssen Research & Development, LLC, Y. Wang Employee of: Janssen Research & Development, LLC, C. Bingham III Grant/research support from: Janssen, PCORI, NIH, Pfizer, Consultant for: Janssen, AbbVie, Amgen, BMS, Celgene, Genentech/Roche, Lilly, Macrogenics, Meoblast, Novartis, NovoNordisk, Pfizer, Regeneron, UCB

DOI: 10.1136/annrheumdis-2017-eular.5225

THU0673 THE EUROPEAN CONSENSUS FINDING STUDY GROUP (ECFSG) HELPS CHARACTERIZING NEW TENTATIVE REFERENCE STANDARDS FOR AUTOANTIBODY MEASUREMENT

J. Rönnelid[1], C. Dahle[2], M. Blüthner[3], E. Feist[4], C. Dolman[5], S.J. Thorpe[5], E. Monogioudi[6], I. Zegers[6], P.L. Meroni[7], D. Hamann[8] on behalf of ECFSG.
[1]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala; [2]Department of Clinical Immunology and Transfusion Medicine, Linköping University Hospital, Linköping, Sweden; [3]MVZ Laboratory PD Dr. Volkmann & colleagues, Department of autoimmune diagnostics, Karlsruhe; [4]Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin, Berlin, Germany; [5]National Institute for Biological Standards and Control, Biotherapeutics Group, Potters Bar, Herts, United Kingdom; [6]Joint Research Centre, European Commission, Geel, Belgium; [7]Department of Clinical Sciences & Community Health, University of Milan, Milan, Italy; [8]Department of Immunopathology and Blood Coagulation, Sanquin Diagnostic Services, Amsterdam, Netherlands

Background: Since 1988, the European Consensus Finding Study Group on autoantibodies in rheumatic diseases (ECFSG), also known as the EULAR autoantibody study group, has been distributing sera with unspecified antibodies to European laboratories (presently n=43) for evaluation of different autoantibody measurement techniques in a clinical context. Use of reference materials helps to align test results by adopting internationally used measurement units, but reference materials are missing for many autoantibody specificities.

Objectives: Recently the scope for ECFSG was expanded to also include unbiased autoantibody characterization of serum/plasma specimens planned to constitute raw material for production of future autoantibody reference materials.

Methods: Four samples were included to be evaluated as future tentative international reference materials for four different autoantibody specificities: double stranded/native DNA (dsDNA, evaluated in 2013/14), IgG anti-b2GP1, proteinase 3 (PR3) and myeloperoxidase (MPO, evaluated in 2015/16). The samples were included "blind", and evaluated broadly for multiple autoantibody specificities by participating laboratories.

Results: All or almost all participating laboratories detected the target specificities, and all four samples showed restricted autoantibody specificities related to the target specificity. Anti-dsDNA was detected by all laboratories using *Crithidia luciliae*, ELISA/EIA, FARR assay or ALBIA and all labs reported a homogenous ANA pattern. Other specificities were restricted to histones, nucleosomes and anti-Ku. All laboratories but one detected IgG anti-b2GP1 and IgG anti-cardiolipin, mostly in high levels, in the tentative IgG anti-b2GP1 reference standard, whereas corresponding IgA and IgM antibodies were absent. All laboratories detected anti-MPO, mostly monospecific and in high levels together with P-ANCA pattern in the anti-MPO reagent. Anti-PR3 and C-ANCA pattern, mostly in high levels/titers were detected by all laboratories in the tentative anti-PR3 reagent, irrespective of method used.

Conclusions: The expanded scope of ECFSG has enabled broad characterization of new tentative autoantibody reference standards. The anti-dsDNA specimen has been processed by the National Institute for Biological Standards and Control (NIBSC) for consideration as the 2nd WHO anti-dsDNA reference standard. The other materials are basis for certified reference material for IgG anti-myeloperoxidase (ERM-DA476/IFCC), and the candidate reference materials for IgG anti-proteinase 3 (in certification) and for IgG anti-b2PG1 (in evaluation) from the Joint Research Centre.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1743

THU0674 ANTI-DFS70 ANTIBODY – A BIOMARKER THAT AID IN THE EXCLUSION OF ANA ASSOCIATED RHEUMATIC DISEASES

K. Conrad[1], N. Röber[1], M. Achtleitner[1], M. Aringer[2], S. Rudolph[3], L. Unger[4], A. Gräßler[5], K. Lüthke[6], M. Mahler[7]. *[1]Medical Faculty of the TU Dresden, Institute of Immunology; [2]University Hospital Carl Gustav Carus, Department of Internal Medicine and Rheumatology, Dresden; [3]Admedia MVZ, Immune Center Chemnitz, Chemnitz; [4]Municipal Hospital Dresden-Friedrichstadt, Department of Medicine I, Dresden; [5]Medical Practice, Pirna; [6]Medical Practice of Rheumatology, Dresden, Germany; [7]Inova Diagnostics, San Diego, United States*

Background: Positive ANA may lead to additional testing and potentially even inappropriate treatment in patients with rheumatic symptoms not caused by ANA associated rheumatic diseases (AARD).

Objectives: It has been shown that autoantibodies directed against lens epithelial derived growth factor (LEDGF), also named DFS70 according to the staining pattern (dense fine speckled) and molecular weight of the target antigen (70 kDa), are common among ANA positive individuals with no evidence of AARD [1,2]. The aim of our study was to evaluate if autoantibodies directed against DFS70 can be used to exclude AARD in ANA positive patients.

Methods: Anti-DFS70 antibody were determined by chemoluminescence assay (CIA) in sera of 352 apparently healthy controls (AHI), 1048 patients of an ANA positive routine cohort, 579 patients with AARD (300 SLE, 76 idiopathic inflammatory myopathies, 167 systemic sclerosis, 36 Sjögren's syndrome), 56 patients with undifferentiated connective tissue disease (UCTD), and 660 non-AARD patients (302 rheumatoid arthritis, 94 ANCA-associated vasculitis, 87 atopic rhinitis, 135 pediatric patients with celiac disease, and 42 autoimmune liver diseases).

Results: In AHI and in the non-AARD cohort, anti-DFS70 antibodies occur with a prevalence of 5.1% and 2%, respectively. Of the 1048 selected routine sera, 205 (19.6%) were positive for anti-DFS70 antibodies. Up to now, clinical reports are available for 116 of anti-DFS70 positive patients in this group. The diagnoses were widely scattered (nonspecific rheumatic symptoms, arthritis, thyreoiditis, asthma, psoriasis, tumor, infections, inflammatory bowel disease), but no definite AARD could be diagnosed. In the AARD group, only 6 of 579 patients (1.2%) were positive for anti-DFS70 antibodies, all of them also show disease specific autoantibodies (two anti-Scl70 antibody positive SSc, one anti-RNAPIII antibody positive SSc, one Ro-52 positive SSc, one anti-Mi-2 antibody positive IIM, one SLE patient with multiple autoantibodies including dsDNA antibodies). In patients with UCTD, 6 (10.7%) were anti-DFS70 antibody positive in the absence of disease specific autoantibodies. Up to now, no development of an AARD was observed in these patients.

Conclusions: Anti-DFS70 antibodies are frequently observed in sera with chromatin binding antibodies in the absence of disease specific autoantibodies. If anti-DFS70 antibodies are positive in the absence of AARD specific autoantibodies, an AARD can be excluded with high certainty.

References:

[1] Dellavance A, Viana VS, Leon EP, Bonfa ES, Andrade LE, Leser PG. The clinical spectrum of antinuclear antibodies associated with the nuclear dense fine speckled immunofluorescence pattern. J Rheumatol 2005;32,2144–49.
[2] Mahler M, Hanly JG, Fritzler MJ. Importance of the dense fine speckled pattern on HEp-2 cells and anti-DFS70 antibodies for the diagnosis of systemic autoimmune diseases. Clin Dev Immunol 2012; Article ID 4943356.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5915

THU0675 DEVELOPMENT AND PSYCHOMETRIC VALIDATION OF A TOOL TO ASSESS THE FEARS OF PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: THE FAIR SCALE

L. Gossec[1,2], P. Chauvin[3], C. Hudry[4], G. Cukierman[5], V. Saulot[6], F. Russo-Marie[6], T. de Chalus[5], J.M. Joubert[5], A. Saraux[7], F. Berenbaum[8]. *[1]UPMC Univ Paris 06; [2]AP-HP, Hôpital Pitié Salpêtrière; [3]INSERM, UPMC Univ Paris 06; [4]AP-HP, Hôpital Cochin, Paris; [5]UCB Pharma, Colombes; [6]Arthritis Fondation Courtin, Neuilly-sur-Seine; [7]CHU la Cavale Blanche and Université de Bretagne Occidentale, Brest; [8]UPMC Univ Paris 06, AP-HP, Hôpital Saint-Antoine, Paris, France*

Background: Patients (pts) with chronic inflammatory rheumatic diseases (CIRDs) such as rheumatoid arthritis (RA) and axial spondyloarthritis (axSpA) have fears related to their disease that can negatively impact health-related quality of life and compromise treatment adherence.

Objectives: To develop and validate a patient-reported outcome (PRO) ques-

tionnaire to explore fears related to CIRDs using the Fears Assessment in Inflammatory Rheumatic Diseases (FAIR) Scale.

Methods: The preliminary questionnaire included 44 items (23 related to fears) most frequently cited by pts in a qualitative study of 50 French pts.[1] Each item was formulated as an affirmative sentence and scored from 0 (completely disagree) to 10 (totally agree). Item scores were summed to provide a total score. The questionnaire was finalised and validated. Pts diagnosed with RA (EULAR/ACR criteria) or axSpA (ASAS criteria), recruited during routine visits by 100 participating rheumatologists across France, completed the preliminary questionnaire, HAD (Hospital Anxiety and Depression) and AHI (Arthritis Helplessness Index) scores. Redundant items (inter-item correlation coefficient >0.65) were eliminated. For the others, internal consistency (Cronbach alpha) and the factorial structure of the scale (principal component analysis) were assessed. Pts were classified according to their level of fears (cluster analysis) and corresponding score thresholds were determined (ROC analysis). The final questionnaire was independently translated into English and back into French twice, with reconciliation of the translated texts.

Results: 672 pts were included: 432 RA pts (mean±SD disease duration was 13.1±11.4 years, DAS28[ESR] was 2.6±1.2, 77.3% were taking biologics) and 240 axSpA pts (disease duration was 13.8±10.6 years, BASDAI was 3.3±2.2, 72.7% were taking biologics). The final FAIR Scale included 10 questions (Table) with total scores ranging 0–100. Mean±SD scores were 51.2±25.4 in RA and 60.5±22.9 in axSpA. Three pt groups were identified, characterised by high, moderate and low level of fears (17.2%, 41.1% and 41.7% of the population, respectively). The corresponding thresholds of the total score were 77 and 51, respectively. Fear scores were correlated with HAD scores for anxiety (r=0.47) and depression (r=0.40) and with the AHI (r=0.50).

Table: FAIR Scale – 10 items [a]

Fears about the progression and consequences of the disease:
B-7: I am afraid of suffering like I did in the past.
D-3: I am afraid that my disease is rapidly getting worse.
D-5: I am afraid that my spinal column or some of my bones will fuse.
D-7: I am afraid of not having anyone to help me if I lose my autonomy.
E-1: I am afraid that I will no longer be able to carry out my daily activities.
E-5: I am afraid that people will think of me as disabled.
C-6: I am afraid that at some point there will be no more effective treatments for my disease.
Fears about treatments:
C-2: I am afraid of the side effects of treatments for my disease.
C-3: I am afraid that the treatments of my disease may cause cancer.
C-4: I am afraid that the treatments of my disease will become less effective.

[a] Each item is scored between 0 (strongly disagree) and 10 (strongly agree); total score of 100.

Conclusions: The FAIR Scale is a 10-question PRO to evaluate disease-related fears in CIRD pts. In this pt population, 17.2% had high fear scores, contrasting with a disease that is often well-controlled. The FAIR Scale was associated with psychological distress. This psychometrically-validated and easy to use questionnaire could be used to improve pt-physician dialogue in CIRDs and also be of value in clinical studies. Further validation in other populations is needed.

References:

[1] Berenbaum F. PloS One 2014; 9(12):e114350.

Acknowledgements: The authors acknowledge Costello Medical Consulting, funded by UCB Pharma, for editorial assistance. This study was funded by UCB Pharma and Arthritis Foundation Olivier Courtin.

Disclosure of Interest: L. Gossec Grant/research support from: UCB Pharma, Lilly, Consultant for: AbbVie, BMS, Celgene, Janssen, Novartis, MSD, UCB, P. Chauvin: None declared, C. Hudry: None declared, G. Cukierman Employee of: UCB Pharma, V. Saulot: None declared, F. Russo-Marie: None declared, T. de Chalus Employee of: UCB Pharma, J. M. Joubert Employee of: UCB Pharma, A. Saraux Consultant for: UCB Pharma, F. Berenbaum: None declared

DOI: 10.1136/annrheumdis-2017-eular.1282

THU0676 ANTI-RO/SS-A 52-KDA ANTIBODIES: A MARKER FOR LUNG FIBROSIS IN RHEUMATIC DISEASES

L. Garcia Montoya, C.N. Sáenz-Tenorio, R.D. González-Benítez, M. Correyero-Plaza, J.C. Nieto, I. Janta, J.G. Ovalles-Bonilla, J. Martínez-Barrio, B. Serrano, L. Valor, D. Hernández-Flórez, C.M. González, I. Monteagudo, F.J. López-Longo. *Rheumatology, Hospital General Universitario Gregorio Marañon, Madrid, Spain*

Background: Lung fibrosis (LF) is a type of interstitial disease that leads to lung scarring, respiratory failure and later on, death. There are 2 main types of LF: idiopathic and secondary; and the prognosis is very different. LF becomes relevant in connective tissue diseases (CTD) and some studies have suggested that there could be an association between anti-Ro/TRIM21 antibodies and the development of interstitial lung disease in these patients.

Objectives: The aim of this study was to assess if the presence of anti-Ro52/TRIM21 antibodies is an independent risk factor for developing CTD-associated LF. We also aimed to evaluate the initial manifestations of systemic diseases and clinical characteristics linked to certain antibodies.

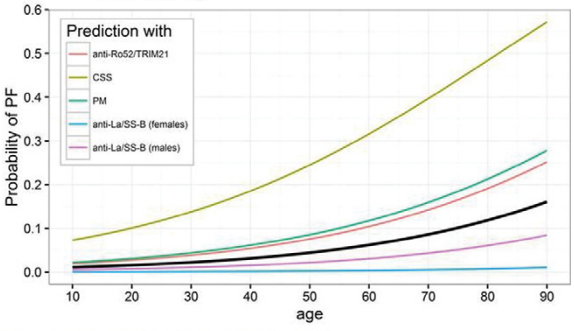
Methods: It is a prospective, observational, longitudinal, single-center study conducted among unselected patients with CTD (rheumatoid arthritis, systemic lupus erythematosus (SLE), systemic sclerosis (SSc), polymyositis (PM), overlap CTD syndrome (OCTD), MCTD, primary Sjögren's sd (PSS), primary antiphospholipid sd, systemic vasculitis, and undifferentiated connective tissue disease).

We analysed data from 1,432 caucasian patients included in the "Systemic Autoimmune Diseases (SAD) Registry" from 1988 to 2014. They were all checked at least biannually and blood samples were taken according to clinical practice. Exclusion criteria were LF as the initial manifestation of the SAD, LF already diagnosed at the first visit and also LF secondary to drugs or a specific environment.

Results: 10% of patients included in the study developed LF. The OR for LF in patients with anti-Ro52/TRIM21 antibodies was 1.757 (95%*CI*=1.1–2.7). The OR for LF increased with every year of age (*OR*=1.03, 95%*CI*=1.02–1.04). Only 9 out of 146 patients with LF were positive for Anti-La/SS-B antibodies, and the OR for males was 8.6 compared to women (95%*CI*=1.8–39.5). Patients with SSc and PM showed a higher OR for the development of LF (6.9 95%*CI*=4.6–10.4 and 2.0, 95% CI=1.2–2.8 respectively) compared to those diagnosed with other CTD. The time passed from the first symptoms to the diagnosis of LF was inversely related to the age of onset (r=-.230; p=0.013). The average time was 60 months for patients with anti-Ro52/TRIM21 antibodies (29 patients) and 138 months for patients without them.

	LF				p	OR	OR 95% CI
	Yes (*n*=146)		No (*n*=1286)				
	Mean (Sd)	*n* (%)	Mean (Sd)	*n* (%)			
anti-Ro/SS-A 60 kDa	39	26.7	307	23.9	0.47	1.16	0.78–1.71
anti-Ro52/TRIM21	36	24.7	205	15.9	0.01	1.72	1.15–2.58
anti-La	9	6.2	129	10.1	0.14	0.58	0.29–1.17
SLE	25	17.1	398	30.9	<0.001	0.46	0.29–0.72
MCTD	13	8.9	71	5.5	0.13	1.67	0.90–3.10
OCTD	13	8.9	52	4.0	0.01	2.32	1.23–4.37
SSc	52	35.6	107	8.3	<0.001	6.09	4.11–9.02
PM	26	17.8	126	9.8	0.006	1.99	1.25–3.16
SSc-PM	8	5.5	16	1.2	0.002	4.60	1.93–10.9
PSS	8	5.5	100	7.8	0.408	0.68	0.32–1.44
Female	30	20.5	229	17.8	0.42	1.19	0.78–1.82
Age (y.)	65.25	14.5	58.3	17.2	<0.001	1.02	1.01–1.03

Figure 1. **Multiple logistic regression predictions (the black line represents the base prediction)**



CSS: cutaneous systemic sclerosis; PM: polymyositis

Conclusions: Anti-Ro52/TRIM21 antibodies have been proved to be a risk factor for developing LF. The earlier the age of onset, the slower the progression to fibrosis. However, patients with anti-Ro52/TRIM21 antibodies tend to have a faster development, independent of the age of onset. Anti-La-SS-B antibodies seem to be a protective factor for the development of LF in both genders; but the association is stronger in women.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2890

THU0677 OUTCOME MEASUREMENT INSTRUMENTS FOR SAFETY IN RHEUMATOLOGY: A SCOPING REVIEW OF AVAILABLE INSTRUMENTS TO INFORM THE OMERACT SAFETY WORKING GROUP

L. Klokker[1], T. Woodworth[2], D.E. Furst[2], P. Tugwell[3], D. Devoe[4], P. Williamson[5], C.B. Terwee[6], M.E. Suarez-Almazor[7], V. Strand[8], A.L. Leong[9], N. Goel[10], M. Boers[11], P.M. Brooks[12], L.S. Simon[13], R. Christensen[1] on behalf of OMERACT working group. *[1]The Parker Institute, Bispebjerg & Frederiksberg Hospital, Copenhagen, Denmark; [2]David Geffen School of Med., Division Rheumatology, UCLA, Los Angeles, United States; [3]Dept of Medicine, School of Epidemiology, Public Health and Community Medicine, University of Ottawa, Ottawa; [4]Department of Medicine, University of Calgary, Cumming School of Medicine, Calgary, Canada; [5]Institute of translational medicine, University of Liverpool, Liverpool, United Kingdom; [6]Department of Epidemiology and Biostatistics, the EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, Netherlands; [7]Section of Rheumatology and Clinical Immunology, University of Texas MD Anderson Cancer Center, Houston; [8]Div Imm/Rheum, Sanford University, San Fransisco; [9]Healthy Motivation, Global Alliance for Musculoskeletal Health, Bone and Joint Decade, Santa Barbara; [10]Advisory Services, Strategic Drug Development, Quintiles IMS, Morrisville NC, United States; [11]Department of Epidemiology and Biostatistics, Amsterdam Rheumatology and immunology Center, VU University Medical Center, Amsterdam, Netherlands; [12]Centre for Health Policy Melbourne School of Population, Global Health University of Melbourne, Melbourne, Australia; [13]SDG LLC Cambridge, Cambridge MA, United States*

Background: International scientific networks have raised concerns about inadequate reporting of safety outcomes in randomised trials and systematic reviews. Outcome Measures in Rheumatology (OMERACT) has previously developed an adaptation of the US National Cancer Institute (US NCI) Common Terminology Criteria for Adverse Events (CTCAE), the RCTC (Rheumatology Common Toxicity Criteria) to collect adverse events in rheumatology clinical trials. To respond to the need to also report safety outcomes from the patient perspective, the Safety Working Group is developing a core outcome set, followed by a core outcome measurement set. A scoping review of available instruments for measuring safety outcomes is needed to inform this work.

Objectives: To identify candidate measurement instruments for safety outcomes in rheumatology clinical trials.

Methods: A systematic search was performed in the MEDLINE database (via PubMed) in January 2017 using MeSH terms covering synonyms for adverse events, rheumatology and measurement instruments and the Boolean operator AND to combine them. Full-text articles about the development or evaluation of instruments for measuring safety in rheumatology were eligible. One reviewer (LK) screened for eligibility based on title and abstracts. Two reviewers (LK and RC) screened the full text articles.

Results: Of 434 unique references identified, 19 were read in full-text, and 8 were included (see figure). The instruments identified were: Glucocorticoid Toxicity Index (GTI), Patient Reported Experiences and Outcomes of Safety in Primary Care (PREOS-PC), Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI flare index (cSFI), the BioSecure questionnaire, Rheumatology Common Toxicity Criteria (RCTC), OMERACT 3x3, and the Stanford Toxicity Index (STI). These instruments were specific for substance (GTI, BioSecure questionnaire), setting (PREOS-PC), condition (cSFI), or not fully validated (RCTC, OMERACT 3x3, STI).

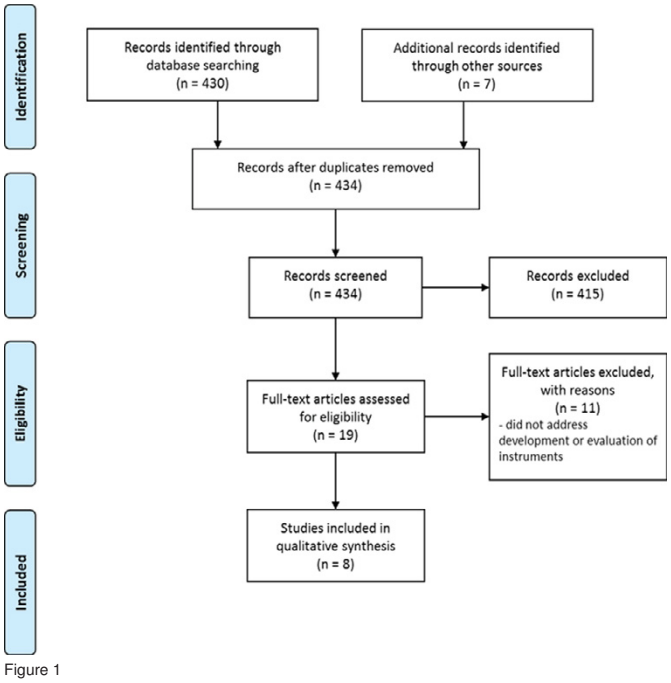


Figure 1

Conclusions: The instruments identified are either too specific, or require further development/evaluation, for the purpose of standardizing measurement of safety in rheumatology clinical trials. Thus, we will proceed to gain consensus on the domains that must be measured to develop a core outcome set.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6141

THU0678 EXPRESSION OF ADHESION MOLECULES CD44V3 AND CD44V6 ON T CELLS IN SLE PATIENTS: CORRELATION WITH CLINICAL PHENOTYPE AND DISEASE ACTIVITY

L. Novelli[1], C. Barbati[1], F. Ceccarelli[1], C. Perricone[1], F.R. Spinelli[1], C. Alessandri[1], G. Valesini[1], R. Perricone[2], F. Conti[1]. *[1]Lupus Clinic, Sapienza University of Rome, Italy; [2]Rheumatology, Allergology and Clinical Immunology, Tor Vergata University, Rome, Italy*

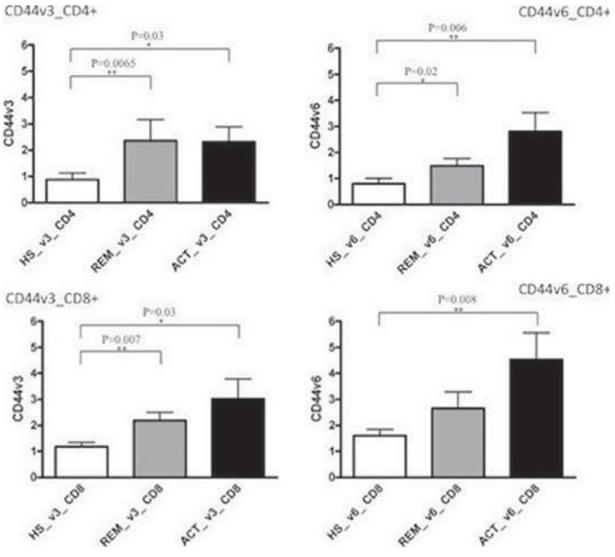
Background: Adhesion molecule CD44 enables T lymphocytes' adhesion to endothelium. During inflammation, increased expression of CD44 contributes to T cell migration into target organs. Infiltration of peripheral tissues is crucial in the development of SLE organ damage and the different isoforms of CD44 seem to be involved in this process. Both CD44v3 and CD44v6 isoforms have been found in kidney biopsies of SLE patients, and CD44v3 in the skin only[1,2]. A higher expression of CD44v3 and v6 has been identified on T cells from SLE patients compared to healthy subjects (HS) and the expression levels seem to correlate with disease activity[3].

Objectives: The aim of this study was to investigate the expression of the CD44v3/v6 isoforms on T cells of SLE patients and their correlation with disease activity and clinical phenotype.

Methods: We enrolled 23 patients (23F, mean age±SD 45.7±13 years, mean disease duration±SD 13±8years) affected by SLE according to the 1997 ACR criteria, and 14 HS (14F, mean age±SD 34.28±12.7 years). Disease activity was measured by SLEDAI-2K. 10 patients were in remission (SLEDAI-2K=0) and 13 patients had an active disease (SLEDAI-2K≥4). Expression of CD44v3 and v6 on T cells was determined by flow cytometry analysis.

Results: Expression of CD44v3 and v6 was significantly higher in active and remission patients compared to HS on CD4+ and CD8+ T cells. SLE patients with active disease showed a trend of major expression of CD44v3 and v6 on CD4+ and CD8+ cells compared to patients in remission (Fig.1). CD44v3/CD44v6 expression ratio on CD4+ and CD8+ T cells was shifted towards isoform v3 on CD4+ cells and towards isoform v6 on CD8+ cells in SLE patients in remission and HS. In active disease this ratio was shifted towards isoform v6 on both T cells populations (Table 1). By using a ROC curve analysis, CD44v6 on CD4+ T cells resulted the most sensitive and specific one (sensitivity 82.6%, specificity 78.6%). Finally, we observed a significant correlation between CD44v3 on CD4+ cells and skin involvement (P=0.027, r=0.632).

Ratio	CD4 CD44v3/CD4 CD44v6	CD8 CD44v3/CD8 CD44v6
Healthy subjects	1.14	0.74
SLE SLEDAI-2k=0	1.58	0.82
SLE SLEDAI-2k≥4	0.82	0.67



Conclusions: Our study confirms previous evidences suggesting a higher expression of CD44v3 and v6 on T cells from SLE patients compared to HS. Higher expression of CD44v3 and v6 on patients with active disease suggests their possible use as biomarkers of disease activity. The good specificity and sensitivity of CD44v6 on CD4+ T cells, and the shift of the ratio towards this

isoform in active patients, suggest a stronger value of this isoform as a biomarker of disease activity.

References:
[1] Cohen RA, Bayliss G, Crispín JC et al. T cells and in situ cryoglobulin deposition in the pathogenesis of lupus nephritis. Clin Immunol 2008;128:1–7.
[2] Seiter S, Schadendorf D, Tilgen et al. CD44 variant isoform expression in a variety of skin-associated autoimmune diseases. Clin Immunol Immunopathol 1998;89:79–93.
[3] Crispín JC, Keenan BT, Finnell MD et al. Expression of CD44 variant isoforms CD44v3 and CD44v6 is increased on T cells from patients with systemic lupus erythematosus and is correlated with disease activity. Arthritis Rheum 2010;62:1431–7.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3671

THU0679 CAN THE USE OF NEW TECHNOLOGIES IMPROVE THE USE OF PATIENT REPORTED OUTCOMES (PROS) AND PATIENT PARTICIPATION IN A NATIONAL REGISTRY?

L. Cunha-Miranda[1], H. Santos[1], F. Barcelos[1], N. Madeira[1], S. Fernandes[1], J. Borges[1], R. Marques[1], C. Silva[1], C. Miguel[1], A. Cardoso[2], R. Trinca[3], A. Faustino[1]. *[1]Rheumatology; [2]Nutrition; [3]Nurse Day Hospital, Instituto Português de Reumatologia, Lisboa, Portugal*

Background: PROs are especially useful in the management of rheumatic diseases in complement to physician evaluation. However they are time consuming and used in a limited manner in the daily clinical practice.
Reuma.pt is the Portuguese national rheumatic diseases register and one of the few registries in Europe that allows the patient to do at home the PROs before the appointment. In our institute we have complemented that with the creation of a paper free day hospital with the use of touch screen computers that also allows the patient to do the PROs before the clinical evaluation by the rheumatologist.
Objectives: to compare the impact of the use off Reuma.pt at home PROs completion platform before and after the utilization of touch screen computers in the day hospital.
Methods: We determined the number of patients and appointments with the use at home of the PROs platform one year prior to the introduction of the touch screen computer at our day hospital (October 2014 –October 2015) and one year after the paper free day hospital was installed (November 2015-November 2016). To determine any change of pattern of the use at home of the platform and the relations between that and patients characteristics.
Results:

Table 1. Diferences between previous use of touchscreen computers in the use at home PROs

	T0 October 2014 to October 2015	T1 November 2015 to November de 2016
Number of appointments with PROs done at home/total of appointments with completed PROs/percentage	93/419 /22.1%	216/448/48,2%
Number of patients with PROs done at home	57	106
Age	45.19±10.33	49.82±11.54
Sex	40F + 17M	75F + 31M
Mean school years	11.79±3.96 (N=29)	10.35±4.3 (N=68)
Under biologics	53 appointments (56.99%)	162 appointments (75%)
Diagnosis	43 AS, 11 RA e 3 PsA	61 AS, 33 RA e 12 PsA

When we analyse the available variables between the patients that performed the PROs at home we found for both periods considered that they were younger (45,2/49,8 vs 53,4/55,1 $p<0.001$) they have more education (11.8/10.35 vs 8.2/7,9) no differences were found regarding gender. There is a tendency that with the continuous use of touchscreen computers at the day hospital less educated (T0 -11.8, T1–10.35 school years) and older patients (T0- 45,2/ T1 -49,8 years) are using more at home platform of Reuma.pt.
Conclusions: The use of technology could have a consider impact on the way we collected data from our patients. With the use of a touchscreen computer we have improved not only the overall completion of PROs but also increased the familiarity of patient to the online questionnaires. Number of appoitments with previous at home completion of the questionnaires more than double. This has a clear impact on patient participation, quality of data in the registry but even more impact on time and human resources at a day hospital.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7001

THU0680 VALIDATION OF EQ-5D, RAPID-3 AND HADS QUESTIONNAIRES FOR THE ASSESSMENT OF THERAPY EFFICACY IN PANNICULITIS PATIENTS

N. Savushkina, V. Amirdjanova, O. Egorova, B. Belov. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Pn is a group of heterogeneous inflammatory diseases characterized by involvement of the subcutaneous fat (SF), locomotor system and viscera, *and* the number of panniculitis (Pn) cases is increasing in everyday practice of a rheumatologists. There are no specific scales available to assess efficacy of Pn therapy. EQ-5D, RAPID-3 and HADS validity, sensitivity and specificity were proven for some rheumatic diseases. Thus, evaluation of EQ-5D, RAPID-3 and HADS psychometric properties in Pn patients has become the objective of this study.
Objectives: Evaluate psychometric properties of questionnaires EQ-5D, RAPID-3 and HADS in Pn patients.
Methods: The study group included 83 Pn pts (80 females, 3males) aged 43,4±13,9 years with median disease duration of 5 [2;24] months who were at the record of V. A. Nasonova Research Institute of Rheumatology during 2009–2015 yy. All patients filled in EQ-5D, RAPID-3 and HADS questionnaires during the first and the control visits at 12 months. Questionnaires' sensitivity was assessed by comparing patient's answers and objective response to therapy measured by achievement of complete regression of the nodules on the control visit. The construct validity was measured based on correlation with "external criteria", including presence of arthritis and arthralgias, tenderness of nodules at palpation measured by VAS, ESR and CRP values.
Results: Positive dynamics (nodule regression) correlated with improved EQ-5D (EQ-5D-scale - p=0,005, EQ-5D-VAS - p=0,004) and RAPID-3 (p=0,0011). Median Δ EQ-5D and HADS-depression after therapy were 0,27 [0,12; 0,45] (p=0,005), and 2 [1;5] (p=0,13) scores, respectively, while average decline in RAPID-3 and HADS-anxiety scores after therapy was 9,2±5,2 (p=0,0011) and 4±3 (p=0,15), respectively. EQ-5D showed the greatest power in Pn patients' quality of life assessment. EQ-5D-scale and VAS-"thermometer" showed moderate correlation with nodule tenderness at baseline (r= -0,23, p=0,036) & (r= -0,45, p=0,0003), and control visits (12 months) (r= -0,38, p=0,0002) & (r= -0,41, p=0,0002); EQ-5D-scale showed moderate correlation with ESR and CRP values at the control visit (r= -0,23, p=0,03) & (r= -0,25, p=0,005), and EQ-VAS – with CRP value at 12 months (r= -0,33, p=0,002), demonstrating clear correlation with patient's objective health status and lab parameters values. Moderate correlation between functional RAPID-3 values and nodule tenderness at baseline (r=0,34, p=0,0015) and after 12 months (r=0,5, $p<0,0001$) are also indicative of close links between the questionnaire data and pts' objective health status. As for the HADS scale, moderate correlation was found only between HADS-depression and nodule tenderness at baseline (r= -0,24, p=0,026) and 12 months (r=0,28, p=0,014) visits. There were no other significant correlations identified.
Conclusions: EQ-5D and RAPID-3 questionnaires should be considered as valid and sensitive instruments for the assessment of the quality of life and efficacy of therapy in Pn pts.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2518

THU0681 BASELINE ESSDAI/DAS SCORES IN 8061 PATIENTS WITH PRIMARY SJÖGREN SYNDROME: CHARACTERIZATION OF SYSTEMIC DISEASE

P. Brito-Zerón[1,2], N. Acar-Denizli[3], M. Zeher[4], A. Rasmussen[5], X. Li[6], C. Baldini[7], J.-E. Gottenberg[8], D. Danda[9], L. Quartuccio[10], G. Hernandez-Molina[11], A.A. Kruize[12], S.-H. Park[13], M. Kvarnström[14], S. Praprotnik[15], D. Sene[16], A. Alunno[17], R. Solans[18], T. Mandl[19], Y. Suzuki[20], M. Rischmueller[21], G. Nordmark[22], G. Fraile[23], P. Wiland[24], H. Bootsma[25], T. Nakamura[26], V. Valim[27], R. Giacomelli[28], R. Seror[29], V. Devauchelle-Pensec[30], B. Hofauer[31], M. Bombardieri[32], V. Trevisani[33], D. Hammenfors[34], A. Minniti[35], S.G. Pasoto[36], J. Morel[37], S. Retamozo[38], T.A, Gheita[39], F. Atzeni[40], C. Vollenveider[41], X. Mariette[29], M. Ramos-Casals[2] on behalf of EULAR-SS TF Big Data Consortium. *[1]Hosp CIMA-Sanitas; [2]Hosp Clínic, Barcelona, Spain; [3]Msgsü, Istanbul, Turkey; [4]Univ, Debrecen, Hungary; [5]OMRF, Oklahoma, United States; [6]Anhui Hosp, Hefei, China; [7]Univ, Pisa, Italy; [8]Univ, Strasbourg, France; [9]CMC, Vellore, India; [10]Santa Maria, Udine, Italy; [11]INCMNSZ, México, Mexico; [12]UMC, Utrecht, Netherlands; [13]Catholic Univ, Seoul, Korea, Republic Of; [14]Karolinska Instit, Stockholm, Sweden; [15]UMCL, Ljubljana, Slovenia; [16]Lariboisière Hosp, Paris, France; [17]Univ, Perugia, Italy; [18]Hosp Vall Hebron, Barcelona, Spain; [19]Lund Univ, Malmö, Sweden; [20]Univ, Kanazawa, Japan; [21]TQEH, Adelaide, Australia; [22]Univ, Uppsala, Sweden; [23]Hosp Ramón Cajal, Madrid, Spain; [24]Med Hosp, Wroclaw, Poland; [25]Univ, Groningen, Netherlands; [26]Univ, Nagasaki, Japan; [27]UFES, Vitória, Brazil; [28]Univ, L'Aquila, Italy; [29]Univ Sud, Paris; [30]Univ, Brest, France; [31]TUM, München, Germany; [32]QMUL, London, United Kingdom; [33]UNIFESP, Sao Paulo, Brazil; [34]Haukeland Hosp, Bergen, Norway; [35]Sapienza Univ, Rome, Italy; [36]USP, Sao Paulo, Brazil; [37]Univ, Montpellier, France; [38]INICSA, Cordoba, Argentina; [39]Univ, Cairo, Egypt; [40]L.Sacco Univ, Milan, Italy; [41]German Hosp, Buenos Aires, Argentina*

Objectives: To characterize and quantify systemic involvement at diagnosis in a large international cohort of patients with primary Sjögren's syndrome (SS).
Methods: The Big Data Sjögren Project was formed in 2014 to take a "high-definition" picture of primary SS at diagnosis by merging international databases (9302 consecutive patients from 21 countries of the 5 continents). The main features (including ESSDAI/DAS) at diagnosis were analysed.
Results: Baseline ESSDAI was available in 8061 patients (93% female, mean age 53yrs). The mean ESSDAI score at diagnosis of the entire cohort was 6.4±7.9. In 1498 patients (19%), score at diagnosis was 0, while 681 (8%) presented with high activity in at least one domain. The main systemic features at diagnosis were

biological (51%), articular (38%), haematological (24%) and glandular (22%). Low DAS was reported in 4480 (56%) patients, moderate DAS in 2483 (31%) and high DAS in 1098 (14%) patients. The mean baseline ESSDAI was higher the younger the patient was ($p<0.001$), higher in White patients (6.9 vs 5.1, $p<0.001$), males (8.4 vs 6.2, $p<0.001$), those with positive ocular (6.7 vs 4.9, $p<0.001$) or oral (6.8 vs 6.2, $p=0.016$) tests, and those with ANA (6.9 vs 4.5, $p<0.001$), RF (7.5 vs 5.8, $p<0.001$) and anti-Ro/La antibodies (7.2 vs 4.4, $p<0.001$). Logistic regression identified as independent variables White ethnicity (OR 3.07), abnormal ocular tests (OR 2.14), ANA (OR 1.67) and Ro/La autoantibodies (OR 2.78).

Conclusions: This is the largest series of patients with primary SS in whom the ESSDAI score has been evaluated. Primary SS is undeniably a systemic disease even at the time of diagnosis, with nearly 80% of patients showing an ESSDAI score >0.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4472

THU0682 POPGEN-OSSA: DEVELOPMENT OF AN ORGAN SPECIFIC SELF ASSESSMENT (OSSA) FOR INTERDISCIPLINARY DOCUMENTATION OF PATIENT REPORTED CLINICAL OUTCOMES

R. Zeuner[1], U. Gsell[2], M. Hübenthal[3], S. Schreiber[4], A. Franke[3], M. Laudes[4], J.O. Schröder[1]. *[1]Section of Rheumatology, Clinic for Internal Medicine I, University Hospital Schleswig-Holstein, Campus Kiel, Kiel; [2]Klinik Eichstätt, Eichstätt; [3]Institute of Clinical Molecular Biology; [4]Clinic for Internal Medicine I, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany*

Background: Patient reported outcome measures are comprised of either sets of questionnaires or patient global assessment based on visual analogue scale (VAS). These patient-reported outcome measures lack accuracy and/or clinical feasibility when comparing heterogeneous patient groups with different diseases, or when characterizing patients with systemic disease involving different organ systems.

Objectives: Developing a clinical feasible patient-reported outcome measure based VAS assessment of different organ systems.

Methods: Patients were asked to rate their health status in a 10cm VAS (0–100%) concerning their global health as well as of different organ systems, namely heart, lung, muscle and joints, gastro-intestinal, metabolic, uro-genital, skin, neuro-psychiatric, eyes and ears. All VA-scales were "anchored". Patients were advised to rate their health status below 75% if they felt "medical action is needed", they should rate the health status <50% in case of a "strong need for medical action" and <25% in case of a "medical emergency".

336 patients from different outpatient clinics (cardiologic, pneumologic, gastro-intestinal, nephrologic, neurologic, dermatologic, rheumatologic, ophthalmologic and obesity outpatient clinic) as well as patients from internal emergency clinics and a general practitioner clinic were evaluated. Both, patients and the attending physicians completed the Popgen-OSSA. In addition the attending physician was asked to document ranking of the 5 most important diagnoses of the patient.

Statistical analysis was carried out using non-parametric testing. Furthermore, to predict main diagnoses based on patients's as well as physician's OSSA state-of-the-art machine learning tools, namely support vector machines (SVMs), were applied. To assess model performance multi-class AUC (area under the ROC curve) according to Hand and Till (2001) was estimated based on repeated cross validation (10 folds, 5 repeats), optimizing the SVM's hyperparamters using grid search.

Results: The test showed a good reproducibility. With a mean percentage of 74±0.98 SE and 66±1.17 SE, respectively, the physicians OSSA rating was significantly higher than the rating of the patients ($p_{wilcoxon}<0.001$). Models predicting main diagnoses were constructed and estimated to perform with multi-class AUCs of 63.5% and 73.4% based on patient's and physician's OSSA, respectively.

Conclusions: In this preliminary trial with low sample size the Popgen-OSSA showed a good reproducibility and allowed a correct allocation of the patient's clinical problem to involved organ system by SVM analysis with multi-class AUC of up to 73.4%. These data merit further investigation and development of the Popgen-OSSA on larger patient cohorts.

References:

[1] David J. Hand and Robert J. Till (2001). A Simple Generalisation of the Area Under the ROC Curve for Multiple Class Classification Problems. Machine Learning 45(2), p. 171–186. DOI: 10.1023/A:1010920819831.

Disclosure of Interest: R. Zeuner Grant/research support from: Pfizer, Novartis, UCB, U. Gsell: None declared, M. Hübenthal: None declared, S. Schreiber: None declared, A. Franke: None declared, M. Laudes Grant/research support from: Roche, Lilly, MSD, J. Schröder: None declared

DOI: 10.1136/annrheumdis-2017-eular.4325

THU0683 RAPID DETERMINATION OF THE INFLAMMATION MARKER CALPROTECTIN IN SERUM FROM PATIENTS WITH INFLAMMATORY ARTHRITIS AT THE POINT OF CARE

N. Ryter[1], A. Szentpetery[2], S.R. Pennington[3], R. Cotti[1], O. FitzGerald[2], J.M. Weber[1]. *[1]BÜHLMANN Laboratories AG, Schoenenbuch, Switzerland; [2]St Vincent's University Hospital; [3]University College, Dublin, Ireland*

Background: A Treat-to-Target (T2T) strategy for inflammatory arthritis, targeting remission or minimal disease activity, is the recommended treatment approach by EULAR and ACR. This strategy relies on "tight monitoring" which necessitates regular clinical examination and measuring acute-phase reactants such as C-reactive protein. Calprotectin (MRP8/14; S100A8/A9), a relatively novel inflammation and disease activity marker in the arthritis field, exhibits several features which fit the "theranostic needs" for accurate therapy monitoring. Those features include discrimination between responders and non-responders [1], detection of subclinical disease activity [2] and prediction of relapse or radiographic progression [3]. The classical method to determine calprotectin in serum (sCAL) is ELISA which is used in service or central laboratories. A rapid and simple determination of sCAL at the point of care is a substantial step forward in supporting clinicians to deliver an efficient T2T strategy. Here, we report on the validation of a quantitative, rapid test which can measure sCAL within 15 minutes.

Objectives: (1) To demonstrate the performance evaluation of a quantitative lateral flow assay combined with a dedicated test reading device for the rapid quantification of calprotectin in serum; and (2) to compare results to a well-established laboratory reference method using patient samples.

Methods: The Quantum Blue® sCAL sandwich lateral flow immunoassay uses two highly specific monoclonal antibodies immobilized on the test membrane and on the gold label. 10μL of serum was diluted in 90μL of chase buffer, 60μL of this mixture was applied onto the lateral flow test cassette, which was incubated for 12 minutes at ambient temperature and then measured with the BÜHLMANN Quantum Blue® Reader. Performance evaluation (sensitivity, linearity, high-dose hook effect, interferences) was carried out according to CLSI guidelines. A method comparison based on 178 serum samples from RA and PsA patients was performed against the BÜHLMANN sCAL (MRP8/14) reference ELISA.

Results: The linearity study over the complete measuring range together with the observed limit of quantification (LoQ) of <0.5 μg/mL allowed a quantitative measurement in the clinically relevant range from 0.5 to 10.0 μg/mL calprotectin. No high dose hook effect was observed up to a concentration of 200 μg/mL. Moreover, no interferences were detected with triglycerides (37mmol/L), conjugated bilirubin (342μmol/L), unconjugated bilirubin (342μmol/L), and hemoglobin (200mg/dL). The Quantum Blue® sCAL lateral flow assay showed an excellent linear correlation (r=0.94, slope=1.05) to the BÜHLMANN sCAL (MRP8/14) reference ELISA. There was a negligible bias of -3.1% by Bland-Altman difference plot between the sCAL lateral flow assay and ELISA.

Conclusions: Rapid quantification of serum calprotectin using the Quantum Blue® sCAL assay represents a fast and reliable method for the determination of inflammation and the disease activity of a patient with inflammatory arthritis at the point of care. This rapid test shows excellent agreement to a corresponding laboratory reference method.

References:

[1] Anink J. Arthritis Res Ther (2015);15:200.
[2] Inciarte-Mundo J. Arthritis Res Ther (2016);18:160.
[3] Hurnakova J. Arthritis Res Ther (2015);17:252.

Disclosure of Interest: N. Ryter Employee of: Employee of BÜHLMANN Laboratories AG, A. Szentpetery: None declared, S. Pennington: None declared, R. Cotti Employee of: Employee of BÜHLMANN Laboratories AG, O. FitzGerald: None declared, J. Weber Employee of: Employee of BÜHLMANN Laboratories AG

DOI: 10.1136/annrheumdis-2017-eular.4722

THU0684 WORK IMPACT IN AXIAL SPONDYLOARTHRITIS: THE AS-WIS QUESTIONNAIRE PREDICTS THE RISK OF WORK IMPACT: A LONGITUDINAL STUDY OF 101 PATIENTS

S. Dadoun[1], C. Jacquemin[1], S. Kreis[1], S. Fabre[1], C. Rein[1], C. Hudry[2], E. Pertuiset[1], B. Fautrel[1], L. Gossec[1]. *[1]Rheumatology, Pitié Salpétrière Hospital; [2]Rheumatology, Cochin Hospital, Paris, France*

Background: Axial spondyloarthritis (axSpA) mainly affects the working-age subject and can have a moderate (short-term sick leave) or significant (long-term sick leave, disability status, unemployment) work impact.

Objectives: To evaluate the value of a simple and short (2 minutes) questionnaire, the AS-Work instability scale (AS-WIS) to predict the work impact of axSpA after 1–2 years.

Methods: Longitudinal study in 3 centers in Paris, France. Patients with axSpA according to the rheumatologist and the ASAS criteria were included. Patients were asked twice (1 to 2 year interval) to answer questionnaires evaluating: disease activity, demographic characteristics, impact on work (short-term and long-term sick leave, disability, unemployment), and the ASWIS questionnaire (1): a 20 item, simple screening tool for Work Instability (the consequences of a mis-match between an individual's functional ability and their work tasks). The risk of disability is assessed as low if the score is <11, medium between 11–18 and high>18. Only patients who answered both questionnaires were included for analyses. Statistical analyses included descriptive analyses and univariate/ multivariate

analyses to search for baseline factors of work impact at 1–2 years (including a medium/high ASWIS score, gender, age, schooling level, BASDAI, BASFI).
Results: Among the 188 patients who answered the first questionnaire, 144 were currently working and were asked to answer the second questionnaire. A total of 101 patients answered both questionnaires. Mean age at inclusion was 45 (SD 9) years, 52% were male, disease duration was 14 (SD 8) years and 62% had an education level equivalent to more than high school. The BASDAI and the BASFI were respectively 34 (SD 21) and 23 (SD 23). At baseline, median ASWIS was 10, a low-risk score was found in 55 patients (54%), and a medium/high risk score in 46 (46%).
1 -2 years later, 37 patients (36%) had work impact: 25 patients (25%) a short-term sick leave, and 12 patients (12%) a significant work impact (long-term disability or unemployment due to Ax-SpA).
Among patients with a low ASWIS score at baseline (n=55), only 13 (24%) had a work impact (including only 2 with a significant impact). Among patients with a medium/high ASWIS score (n=46), 24 (52%) had a work impact (including 10 patients of a significant impact).
In univariate analysis, baseline factors associated with work impact (moderate or significant) were a medium/high ASWIS score, a high BASFI and a shorter disease duration. In multivariate analysis, medium/high ASWIS (odds ratio, OR 2.71 (1.04–7.22)) and a lower disease duration (0.94 (0.89–0.99)) were independent predictive factors of work impact.
Conclusions: In patients with axSpA, a medium/high ASWIS score was followed by a work impact in 50% of cases within 2 years in this well-controlled population. This short questionnaire can be helpful to screen for future difficulties at work, whatever the stage of disease.
References:
[1] Gilworth G, et al. Reducing work disability in ankylosing spondylitis: development of a work instability scale for AS. BMC Muskuloskelet Disorders 2009 Jun 16;10:68.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3280

THU0685 ASAS HEALTH INDEX FOR PATIENTS WITH SPONDYLOARTHRITIS: TRANSLATION INTO PORTUGUESE, VALIDATION, AND RELIABILITY

S. Rodrigues Manica[1,2], E. Cruz[3], S. Ramiro[4], S. Sousa[5], R. Aguiar[6], A. Sepriano[1,4], P.M. Machado[7], U. Kiltz[8], J.C. Branco[1,2], F.M. Pimentel-Santos[1,2]. *[1]CEDOC - NOVA Medical School | Faculdade de Ciências Médicas, NOVA University of Lisbon; [2]Rheumatology Department, Hospital Egas Moniz, Centro Hospitalar de Lisboa Ocidental, Lisbon, Lisbon; [3]Escola Superior de Saúde de Setúbal, Instituto Politecnico de Setúbal, Setúbal, Portugal; [4]Rheumatology, Leiden University Medical Center, Leiden, Netherlands; [5]Hospital Garcia de Orta, Almada; [6]Centro Hospitalar Baixo Vouga, Hospital de Aveiro, Aveiro, Portugal; [7]Centre for Rheumatology Research & MRC Centre for Neuromuscular Diseases, University College London, London, United Kingdom; [8]Rheumazentrum Ruhrgebiet, Herne, Germany*

Background: The Assessment of SpondyloArthritis international Society Health Index (ASAS HI), is a unidimensional questionnaire, that includes 17 items, measuring functioning and health in patients with spondyloarthritis (SpA) (1). At the beginning of this project, only an English version of the instrument existed.
Objectives: The aim of this study was to conduct the cross-cultural adaptation of the ASAS-HI into European Portuguese language and investigate its reliability and validity in a sample of Portuguese patients with SpA.
Methods: The ASAS-HI has a range from 0 (best health state) to 17 (worst health state). The questionnaire was first translated and then back translated following published guidelines. Patients fulfilling ASAS classification criteria for either axial (axSpA) or peripheral SpA (pSpA) were included. Reliability was assessed through internal consistency coefficient, and internal consistency was assessed using Cronbach's alpha. Construct validity was assessed through Spearman's correlation analyses between the ASAS-HI and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Disease Activity Score-CRP (ASDAS-CRP), and the Short Form (36) Health Survey (SF-36) (physical) SF-36 (physical) for convergent validity and between the ASAS-HI and the HAD-S Anxiety/Depression, and SF-36 (mental) for divergent validity. Discriminative validity was tested comparing the ASAS-HI across ASDAS-CRP disease activity states using the Kruskal–Wallis test.
Results: In total, 86 patients were included: 65% male, mean (SD) age 47.1 (12.9) years, symptom duration 11.4 (11.0) years, BASDAI 3.1 (2.1), BASFI 2.2 (2.6), ASDAS-CRP 2.2 (0.8). The diagnosis of axSpA was established in 58 patients (AS =45, nr-axSpA =13) and of pSpA in 28 patients. The forward backward translation was successful and qualitative interviews raised no further comments of the patients. The total mean score of the ASAS-HI was 4.6 (3.8). The ASAS- HI showed an excellent test-retest reliability (n=72) (ICC=0.93: 95% CI=0.89;0.96, $p<0.001$) and a good internal consistency (Cronbachs-α of 0.87). According to the predefined hypothesis, the ASAS-HI correlated strongly with the BASDAI (0.76, $p<0.001$), SF-36 (physical) (-0.75, $p<0.001$), moderately well with the HAD-S Anxiety (0.41, $p<0.001$), and SF-36 (mental) (-0.44, $p<0.001$) (Table 1), and showed a good discriminatory capacity across the different levels of disease activity ($p<0.001$) (Table 2).

Table1 – Correlation between ASAS-HI at baseline and other health outcomes

Characteristics		R	P value
BASDAI	(0-10)	0.76	<0.001
BASFI	(0-10)	0.63	<0.001
ASDAS-CRP		0.64	<0.001
SF-36 (physical)	(0-100)	-0.75	<0.001
SF-36 (mental)	(0-100)	-0.44	<0.001
HAD-S Anxiety		0.41	<0.001
HAD-S Depression		-0.05	0.660

Table 2 - Discriminant ability of ASAS-HI (at baseline) stratified by disease activity (mean±SD)

	ASDAS-CRP				
	Inactive (N=9)	Moderate (N=30)	High (N=32)	Very high (N=6)	p-value
ASAS-HI	1.6 (1.5)	2.3 (2.0)	6.2 (4.1)	8.1 (3.3)	<0.001

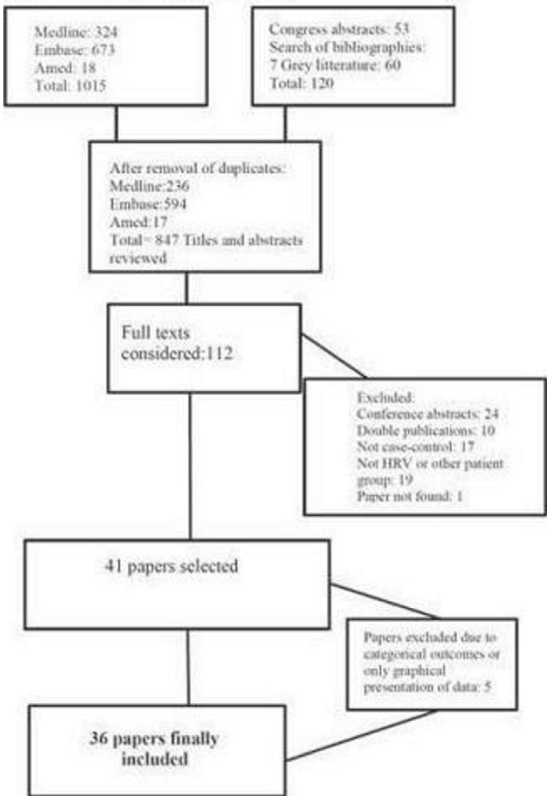
Conclusions: The findings of this study showed that the Portuguese version of the ASAS –HI is a comprehensible questionnaire that is reliable and valid. Therefore, its use can be recommended, both for clinical practice and research purposes, to assess the state of health and functioning in Portuguese SpA patients. Future research is needed to evaluate the responsiveness of the ASAS-HI in SpA patients.
References:
[1] Kiltz U et al. Ann Rheum Dis. 2015;74(5):830–5.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3927

THU0686 HEART RATE VARIABILITY IN INFLAMMATORY JOINT DISEASE. A META-ANALYSIS

S.A. Provan[1], D.S. Olstad[2], E.E. Solberg[3], G. Smedslund[2], H. Dagfinrud[2]. *[1]Rheumatology, Diakonhjemmet Hospital; [2]Rheumatology, National Resource Centre for Rehabilitation in Rheumatology, Diakonhjemmet Hospital; [3]Medicine, Diakonhjemmet Hospital, Oslo, Norway*

Background: Autonomic dysfunction is an established predictor of all-cause mortality and post-myocardial infarction mortality. It has been suggested to be a pathogenic factor for the development of cardiovascular disease (CVD) in the general population, possibly acting through the impact of the autonomic nervous system on inflammation [1]. Heart rate variability (HRV) is a marker of cardiac autonomic function and is increased in many conditions including chronic widespread pain. HRV is responsive to physical exercise. Inflammatory joint diseases (IJD) are characterised by joint inflammation and symptoms include pain, functional decline and restricted movement. Patients with IJD have an increased risk of premature death due to CVD.
Objectives: To compare HRV between adult patients with IJD and healthy controls, using the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) methodology, and to describe the associations between IJD disease activity, pain and physical activity, and HRV.

Figure 1 Flow chart literature search



Methods: A research librarian conducted systematic searches in Medline, Embase and Amed from earliest date until August 2016. Inclusion criteria were adult human case-control studies published in English or a Scandinavian language, presenting data on HRV in patients with IJD (Rheumatoid Arthritis (RA) or Spondyloarthritis (SpA)). Included under the SpA diagnosis were patients with psoriatic arthritis or ankylosing spondylitis. Six established measures of HRV were selected: the Square root of mean squared difference of successive R-R interval (rMSSD), high frequency (HF), total power (TP), Ewing protocol standing (E-S), breathing (E-B) and Valsalva (E-V). Patients with RA, SpA and healthy controls were compared separately using random-effects meta-analyses of standardized mean differences (SMD).
Results: 847 titles and abstracts were reviewed, 36 papers were eligible for inclusion (Figure 1). For rMSSD the pooled SMD (95% CI) RA vs. controls was -0.90 (-1.35 to -0.44), for SpA vs. controls; -0.34 (-0.73 to 0.06). For HF, the pooled SMD RA vs. controls was -0.78 (-0.99 to -0.57), for SpA vs. controls; -0.04 (-0.22 to 0.13). For TP the pooled SMD RA vs. controls was -0.60 (-1.26 to 0.06), SpA vs. controls; -0.27 (-0.51 to -0.03). All pooled Ewing parameters were significantly lower in cases compared to controls, except for E-V which was comparable between cases and controls in patients with RA. 18/36 papers examined the relationship of IJD disease activity to HRV, of which the majority, 13, describe an inverse association between the parameters. The impact of pain on HRV was not explored in any study, and only one study explored the impact of physical activity on HRV, finding no cross-sectional association.
Conclusions: Patients with IJD have lower cardiac parasympathetic modulation compared to healthy controls and this may be a risk factor for CVD. There is an inverse relationship between IJD disease activity and HRV. The relationship between pain, physical activity and HRV should be further explored.
References:
[1] Kosek E, Altawil R, Kadetoff D, et al. Evidence of different mediators of central inflammation in dysfunctional and inflammatory pain–interleukin-8 in fibromyalgia and interleukin-1 beta in rheumatoid arthritis. J Neuroimmunol. 2015; 280:49–55.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2897

THU0687 FEASIBILITY AND VALIDITY OF PROMIS® GLOBAL HEALTH SHORT FORM (PROMIS10) IN OUTPATIENTS WITH SLE

S. Kasturi[1], J. Szymonifka[1], J. Burket[2], J. Berman[1], K. Kirou[1], A. Levine[1], L. Sammaritano[1], L.A. Mandl[1]. *[1]Medicine; [2]Healthcare Research Institute, Hospital for Special Surgery, New York, United States*

Background: Routine measurement of patient reported outcomes (PROs) is a priority for improving quality of care and outcomes in chronic rheumatic conditions including systemic lupus erythematosus (SLE). Measuring PROs at the point of care requires validated instruments with minimal responder burden. PROMIS10 is a 10 question universal (non-disease specific) PRO instrument measuring physical and mental health domains with T-scores normalized to the general population (mean score =50). The feasibility and validity of PROMIS10 have not been demonstrated in SLE.
Objectives: To evaluate: 1) feasibility and 2) validity of PROMIS10 in outpatients with SLE.
Methods: Adults meeting 1997 ACR SLE classification criteria were recruited from an SLE Center of Excellence. Subjects completed SF-36, LupusQoL-US, selected PROMIS Computerized Adaptive Tests (CATs), and PROMIS10. Construct validity was evaluated using Spearman's correlations comparing PROMIS10 physical and mental health scores with PROMIS CATs and legacy instruments. Test-retest reliability was evaluated in subjects reporting stable SLE activity at 2 assessments a week apart with intraclass correlation coefficients (ICCs). Focus groups of participants evaluated the relevance and utility of PROMIS10.

Table 1. Spearman's Correlations of PROMIS10 with PROMIS CATs, SF-36, and LupusQOL

	PROMIS10 Physical Health (n=199)	PROMIS10 Mental Health (n=187)
PROMIS CAT- Physical Function	**0.77**	0.54
PROMIS CAT- Pain Interference	**-0.80**	-0.59
PROMIS CAT- Fatigue	-0.65	-0.60
PROMIS CAT- Anxiety	-0.41	-0.61
PROMIS CAT- Depression	-0.48	**-0.73**
PROMIS CAT- Ability to Participate in Social Roles	**0.74**	0.65
SF-36- Physical Function	**0.76**	0.47
SF-36- Role Physical	0.60	0.46
SF-36- Physical Component Summary	**0.77**	0.41
SF-36- Mental Health	0.42	**0.72**
SF-36- Role Emotional	0.49	0.61
SF-36- Mental Component Summary	0.41	0.72
SF-36- Bodily Pain	**0.79**	0.56
SF-36- Social Function	**0.70**	0.66
LupusQoL-US- Physical Health	**0.77**	0.59
LupusQoL-US- Emotional Health	0.52	**0.70**
LupusQoL-US- Pain	**0.74**	0.56
LupusQoL-US- Fatigue	0.62	0.62
LupusQoL-US- Planning	0.69	0.62

$p<0.01$.

Results: 204 (86%) of 238 patients approached, enrolled. There were no statistically significant differences in demographic characteristics between participants and non-participants. SLE patients scored worse than the general population in PROMIS10 physical health (mean T-score 41.6 +/- SD 8.8; range 19.9 - 67.7) and mental health (mean T-score 43.7 +/- SD 8.7; range 25.1 - 67.6). PROMIS10 physical health scores correlated strongly with physical function, pain, and social health domains in PROMIS CATs, SF-36, and LupusQoL, while PROMIS10 mental health scores correlated strongly with PROMIS depression CAT and SF-36 and LupusQoL mental health domains (Table 1). Test-retest reliability for both PROMIS10 physical and mental health scores was high with ICCs of 0.89 and 0.85 respectively. Median time to complete PROMIS10 was <2 minutes. Focus group participants found PROMIS10 relevant and useful.
Conclusions: PROMIS10 is feasible to administer to outpatients with SLE and valid compared to legacy instruments. PROMIS10 can be used to quickly, accurately, and reliably screen for impaired physical function, pain, and depression and could be an important tool in the measurement of patient centered outcomes and improvement of quality of care in SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2143

THU0688 DISEASE FLARES, DAMAGE ACCRUAL AND SURVIVAL IN ANCA-ASSOCIATED VASCULITIS

S. Paramalingam[1], G. Dogra[2], A. Mclean-Tooke[3], J. Nossent[1,4]. *[1]Rheumatology; [2]Renal Medicine; [3]Immunology, Sir Charles Gairdner Hospital; [4]School of Medicine, University of Western Australia, Perth, Australia*

Background: ANCA- associated vasculitis (AAV) is a potentially life threatening condition requiring careful monitoring and balancing of treatment options to minimize morbidity and mortality.
Objectives: To investigate the influence of baseline disease characteristics and induction therapy on the disease course and outcome in ANCA- associated vasculitis.
Methods: Single centre longitudinal cohort study of all adult patients with an EMEA algorithm based diagnosis of AAV followed up to August 2016. Clinical data including disease activity (BVAS), ANCA type and level, treatment, relapses (BVAS >3) and organ damage (VDI) and other complications (e.g. infections) during the disease course were recorded. Predictors for ESRD, death, cancer and damage accrual were analysed by multivariate logistic regression presented as Odds Ratios (OR).
Results: A total of 63 patients (59% male) (mean age at diagnosis 57 years, 59% with GPA, 24% MPA and 16% EGPA) were included. Fluorescence ANCA was positive in 92%, while 47% had MPO-ANCA and 43% PR3-ANCA. Induction therapy included corticosteroids (92%), Cyclophosphamide (57%), Rituximab (35%) and Plasmapheresis (6%). During 46 months of follow-up 34 patients (54%) experienced 71 relapses (rate 2.5/100 months) and 55 serious complications occurred (rate 2/100 months). Mean VDI at last follow-up was 2.1 with only 11 patients (17.4%) not developing organ damage. Averaged BVAS correlated with last VDI scores (Rs 0.25,p=0.012). Overall, 4 patients (6.3%) died, 19 (27%) developed renal insufficiency of which 2 (3.1%) required chronic dialysis, while 6 (9.5%) developed a new cancer. Age was an independent predictor (OR 1.09, p=0.05) for patient survival (95% and 91% at 1 and 5 years), but no effect was seen for baseline BVAS, gender, AAV or ANCA subtype (all $p>0.1$).
Conclusions: While current treatment reduces the risk of death, AAV is still associated with a high rate of disease relapse, organ damage accrual and serious complications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4846

THU0689 MODERATE TO GOOD CONSTRUCT VALIDITY OF GLOBAL PRESENTEEISM MEASURES WITH MULTI-ITEM PRESENTEEISM MEASURE AND PATIENT REPORTED HEALTH OUTCOMES: EULAR-PRO WORKER PRODUCTIVITY STUDY

S. Leggett[1], A. Boonen[2], D. Lacaille[3], S. Talli[4], M. Bojinca[5], J. Karlson[6], D. Beaton[7], B. Fautrel[8], J. Canas da Silva[9], C. Hoffstetter[10], S. Verstappen[1,11] on behalf of EULAR-PRO at-work productivity co-investigators. *[1]Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, United Kingdom; [2]Department of Internal Medicine, Division of Rheumatology, Maastricht University Medical Centre, and Caphri Research Institute, Maastricht University, Maastricht, Netherlands; [3]Arthritis Research Centre of Canada, University of British Columbia, Vancouver, Canada; [4]Rheumatology, East Tallinn Central Hospital, Tallinn, Estonia; [5]Internal Medicine and Rheumatology Clinic, Dr. Ion Cantacuzino Hospital, Bucharest, Romania; [6]Section of Rheumatology, Lund University and Skane University hospital, Lund, Sweden; [7]St. Michael's Hospital, Mobility Program Clinical Research Unit, Toronto, Canada; [8]All - APHP Pitie-Salpetriere Hospital, Department of Rheumatology, Paris, France; [9]Hospital Garcia de Orta, Almada, Portugal; [10]OMERACT, Toronto, Canada; [11]NIHR Manchester Musculoskeletal BRU, Central Manchester Univ. Hospitals NHS Foundation Trust, Manchester, United Kingdom*

Background: Inflammatory arthritis (IA) and osteoarthritis (OA) often impact on

the worker's performance whilst at work due to ill health (i.e. presenteeism). A number of global measures have been developed to assess presenteeism in clinical studies. However, limited information is available on the correlation between these measures and the construct validity of these measures.

Objectives: To i) determine the correlation between four global measures of presenteeism and ii) to evaluate the construct validity of these measures.

Methods: The main aim of this international observational study (7 countries in Europe and Canada), recruiting patients with IA (RA, PsA or AS) or OA in paid employment, was to investigate content and construct validity of global presenteeism measures. Patients completed 4 global measures (Work Productivity Scale – Arthritis (WPS-A), Work Productivity and Activity Impairment Questionnaire (WPAI), Work Ability Index (WAI), and both the Quality and Quantity scales of the QQ questionnaire) (see table legend for descriptions individual scales). Spearman correlations were applied to test the correlation between individual presenteeism scales and to test construct validity with the 11-item Workplace Activity Limitation presenteeism Scale (WALS) and several health related patient reported outcome measures. Interpretation of correlation coefficients: (very) weak (r_{range}=0.0–0.39), moderate (r_{range}=0.40–0.59) to strong (r_{range}=0.60–1.0).

Results: 468 patients with a median disease duration of 10 [IQR 5–18] yrs were included; 62% were female. Median [IQR] presenteeism scores were, respectively: 2 [0–5] for WPS-A, 3 [1–5] for WPAI, 8 [6–9] for WAI, 81 [49–100] QQ-total, with WAI and QQ having reversed scales (Legend table). Correlations between the 4 global measures were moderate to strong, ranging from -0.49 for the correlation between WPS-RA and QQ-Quality to 0.83 between WPAI and WPS-RA. The multi-item presenteeism scale WALS, measuring difficulty at work, strongly correlated with both WPAI (r=0.65, $p<0.05$) and WPS-RA (r=0.64, $p<0.05$), both measures capturing the affect and interference of arthritis on work productivity. Moderate correlations were achieved between all six global presenteeism measures and health outcomes ($r_{range\ irrespective\ direction}$: $|r_{presenteeism\text{-}VAS\ Well\text{-}being}|$ =0.36 to 0.54; $|r_{presenteeism\text{-}EQ\text{-}5D}|$ =0.37 to 0.54; and $|r_{presenteeism\text{-}HAQ}|$ =0.40 to 0.58).

		WPAI	WPS-RA	WAI	QQ-Quantity	QQ-Quality	QQ-Total
Global presenteeism scales	WPAI	1.0					
	WPS-RA	0.83	1.0				
	WAI	-0.65	-0.62	1.0			
	QQ-Quantity	-0.58	-0.53	0.60	1.0		
	QQ-Quality	-0.52	-0.49	0.58	0.75	1.0	
	QQ-Total	-0.60	-0.56	0.63	0.95	0.88	1
Multi-item presenteeism scale	WALS	0.65	0.64	-0.55	-0.50	-0.49	-0.54
Health related patients reported outcomes	VAS Well being	0.54	0.51	-0.43	-0.39	-0.36	-0.42
	EQ-5D	-0.54	-0.54	0.48	0.37	0.39	0.42
	HAQ	0.57	0.58	-0.52	-0.40	-0.41	-0.45

WPAI (0= condition no effect on work – 10=condition completely prevented work); WPS-IA/OA (0=no interference – 10=complete interference; WAI (0=completely unable to work – 10=work ability at its best); QQ-Quantity/Quality (0=normal quantity/good quality – 10=normal quantity/good quality); QQ-Total=$Q_{quantity} * Q_{quality}$; VAS well-being = Visual Analogue Scale general Well being; EQ-5D=EuroQol 5D measurement; HAQ= health assessment questionnaire.

Conclusions: Global measures of presenteeism show good to moderate construct validity, with the WPAI and WPS-IA/OA showing slightly better construct validity compared to the WAI and QQ. The information obtained in this study will further inform research on instrument use for a standardized approach to estimate presenteeism in future clinical studies.

Acknowledgements: Funding: EULAR, AbbVie, BMS

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5125

THU0690 SERUM AMYLOID A LEVELS AS A POTENTIAL BIOMARKER TO MONITOR PSORIATIC ARTHRITIS PATIENTS ON BIOLOGICS – A RETROSPECTIVE OBSERVATIONAL STUDY

T. Martins Rocha, R. Fonseca, D. Rosa-Goncalves, F. Aguiar, R. Ferreira, A. Bernardo, M. Bernardes, L. Costa. *Rheumatology, Centro Hospitalar de São João, Porto, Portugal*

Background: According to previous studies, serum amyloid A (SAA) is involved in the pathophysiology of several conditions including inflammatory arthritis and psoriasis. Recent evidence suggests its valuable role in monitoring disease activity in Rheumatoid Arthritis, but its role is yet to be determined in Psoriatic Arthritis (PsA).

Objectives: To study the association between SAA levels and its variation with other biomarkers and disease activity/functional parameters in a cohort of PsA patients under biologic therapy.

Methods: Observational retrospective study was conducted including PsA patients (according to CASPAR criteria) followed at our Rheumatology department with at least one measurement of SAA levels from January 2015 until December 2016. Demographic and clinical data were obtained by consulting the national database (Reuma.pt). The disease activity/functional scores from at least one visit and corresponding measurements of SAA, ESR and CRP levels were collected. The difference (Δ) between 2 evaluations separated by a median time of 6 months [6–18] was calculated for all variables. Agreement between dichotomized biomarkers was calculated using kappa coefficients. Correlations were studied using Pearson and Spearman coefficient analysis. Significance level was set as 0.05.

Results: 53 PsA patients were included. 31 (59%) patients were females with a mean (SD) age of 50 (11.2) years and a median disease duration of 9 years [1–43]. 28% had axial involvement, 34% peripheral involvement and 38% had both types. All patients were under biologic DMARD. 100 SAA measurements were collected. Median SAA and ESR levels were significantly superior in female patients (23 vs 6mm/1sth and 8.6 vs 4.4mg/L, respectively, $p<0.05$) and only ESR levels correlated with age (r=0.20, p=0.05). The three biomarkers showed a weak association with serum creatinine levels, with greater correlation for SAA (r=0.46, $p<0.001$). SAA levels had a stronger correlation with CRP (r=0.75, $p<0.001$) than with ESR levels (r=0.26, $p<0.01$). SAA and CRP (dichotomized as negative/positive) had a greater level of agreement (κ=0.40) compared to ESR (κ=0.26 and κ=0.32, respectively). No significant correlations were found between the biomarkers and the tender/swollen joint count or the pain/global disease activity VAS. SAA levels correlated with ASDAS CRP (r=0.43, $p<0.001$) and weakly with ASDAS ESR and DAS28 CRP (r=0.20 and r=0.24, respectively, $p<0.05$). Only ESR had a significant weak correlations with BASDAI, MASES and SPARCC scores (r=0.25, r=0.21, r=0.35; $p<0.05$). All the biomarkers had weak correlations with BASFI and HAQ scores. ΔSAA levels had a weak correlation with ΔCRP (r=0.32, p=0.03; n=47) and no significant association was found with ΔESR. ΔSAA correlated significantly with ΔASDAS CRP and ΔBASMI (r=0.32, r=0.39; $p<0.05$).

Conclusions: This study showed that SAA levels and its variation had a significant correlation with CRP levels and its variation, respectively. Significant association with ASDAS CRP variations suggests that serial measurements of SAA may represent an additional marker for monitoring disease activity over time in PsA patients.

References:

[1] Connolly M et al. Arthritis Rheum. (2012);64(4):1035–45.
[2] Hwang et al. Arthritis Res Ther (2016) 18:108.
[3] Morizane S. et al. J Invest Dermatol. (2016) Oct 20. pii: S0022-202X(16)32533-7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5466

THU0691 IS SERUM AMYLOID A PROTEIN AN USEFUL BIOMARKER TO MONITOR TREATMENT WITH ANTI-TUMOUR NECROSIS FACTOR-ALPHA AGENTS IN SPONDYLOARTHRITIS PATIENTS?

F. Aguiar, D. Rosa-Gonçalves, T. Martins-Rocha, R.M. Ferreira, A. Bernardo, I. Brito, M. Bernardes. *Rheumatology, Centro Hospitalar São João, Oporto, Portugal*

Background: Quantitating the degree of inflammation has become essential to tailor the treatment strategy of various rheumatic diseases. Traditionally used measures to assess disease activity and treatment response in spondyloarthritis (SpA) are ESR, CRP and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS). Serum amyloid A (SAA) is an acute-phase reactant predominantly synthesized in the liver by hepatocytes in response to proinflammatory cytokines. Some studies have shown that SAA can be a valuable indicator of disease activity, damage and functional impairment, however it has not been extensively used in clinical practice.

Objectives: To investigate if SAA levels have better correlation with conventional assessments used to monitor anti–tumor necrosis factorα (anti-TNF) treatment in SpA than CRP and ESR.

Methods: Prospective study, including SpA patients under anti-TNFα treatment at a Rheumatology Department of a Portuguese Universitary Hospital. The following parameters were collected and registered in two different evaluations 6 months apart from each other: SAA, CRP and ESR levels, BASDAI, ASDAS-PCR, ASDAS-VS, BASFI, BASMI, swollen and tender joints counts (SJC and TJC), MASES, SPARCC, and patient global assessment (PtGA), physician global assessment (PGA), total back pain (TBP), nocturnal back pain (NBP) measured in a visual analogue scale (VAS). The variation of each parameter was calculated as the difference between the levels registered at each evaluation (baseline and 6 months) and presented as Δ(parameter). We compared the correlation between ΔSAA, ΔCRP and ΔESR levels with ΔBASDAI, ΔASDAS-PCR, ΔASDAS-VS, ΔBASFI, ΔBASMI, ΔSJC, ΔTJC, ΔMASES, ΔSPARCC, ΔPtGA-VAS, ΔPGA-VAS, ΔTBP-VAS, ΔNBP-VAS. The statistical analysis was performed using SPSS 21.0 software, and *$p<0.05$* was taken to indicate statistical significance. Correlation was calculated using the Spearman rank correlation (r).

Results: 89 patients were included, 58.4% (n=52) were male. On baseline the median age was 44.0 years (range 21.0–74.6) and median disease duration was 18.8 years (2- 51.6). ΔSAA was moderately correlated with ΔCRP (r=0.65,

p<0.001) and had lower correlation with ΔESR (r=0.28, p=0.009). ΔSAA correlated with ΔNBP-VAS (r=0.260, p=0.016), but ESR and CRP did not correlate with this parameter. We also found statistically significant correlation between ΔSAA and ΔASDAS-VS (r=0.257, p=0.017), ΔASDAS-CRP (r=0.387, p<0.001), ΔBASFI (r=0.301, p=0.005). ΔCRP also showed significant correlation with ΔBASFI, but it was weaker than that observed with ΔSAA (r=0.230, p=0.033). There was no statistically significant correlation between ΔSAA levels and ΔMASES, although ΔCRP had a weak correlation (r=0.217, p=0.041). There was no significant correlation between neither ΔSAA, ΔCRP or ΔESR and the following parameters: ΔTBP-VAS, ΔPtGA-VAS, ΔPGA-VAS ΔBASDAI, ΔBASMI, ΔSPARCC, ΔTJC or ΔSJC.

Conclusions: This study suggests that SAA can be an useful tool in monitoring treatment with anti-TNFα and that could be introduced in clinical practice. However more studies, with larger sample sizes, should be undertaken to better assess this subject.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5492

THU0692 THE TURKISH VALIDATION AND RELIABILITY OF DISEASE-SPECIFIC, PATIENT REPORTED OUTCOME MEASURE IN RHEUMATOID ARTHRITIS: TR AIMS2-SF

T. Duruoz[1], C. Unal Ertekin[2], C. Sanal Top[2]. [1]*PM&R Department, Rheumatology Division;* [2]*PM&R Department, Marmara University, School of Medicine, Istanbul, Turkey*

Background: Rheumatoid arthritis (RA) can have a major impact on health related quality of life (HRQoL). The revised AIMS-2 is the main outcome measure that has been used for measuring HRQoL in patients with rheumatic diseases. Guillemin et al. developed a short form of AIMS-2 (AIMS-2 SF) (1) which is more practical and less time consuming compared to AIMS-2.

Objectives: The purpose of this study was to investigate validity and reliability of the Turkish version of AIMS2-SF (TR AIMS-2 SF).

Methods: Turkish AIMS2-SF was developed after translation and back-translation method. Culturally adapted version preserved 5 component-structure (upper limb function, lower limb function, affect, pain and social interaction) with 26 items according to the original article (1). Subjects fulfilling ACR/EULAR 2010 classification criteria for RA were consecutively enrolled into the study. Patients with malignancy, fibromyalgia syndrome and other systemic inflammatory diseases were excluded. Demographic data, the body mass index (BMI), severity of pain (VAS), disease duration (month) and other clinical features was evaluated. Reliability was investigated with test-retest reliability (intraclass correlation coefficient-ICC) and internal consistency (Cronbach's alpha). Spearman's rank correlation coefficient was used to evaluate the relation between quantitative parameters and the validity. Construct validity was assessed by the correlation of TR AIMS2-SF with other clinical parameters (age, disease duration, VAS pain, DAS-28) and functional parameters such as Nottingham Health Profile (NHP), Health Assessment Questionnaire (HAQ), Beck Depression Inventory (BDI), Duruoz Hand Index (DHI). Statistical analyses were performed with SPSS version 20 and a value of p<0.05 was considered as statistically significant.

Results: Sixty patients (6 males) were recruited into the study. The mean ± standart deviation (SD) of age (years) and disease duration (months) were 51.8±12.5 and 71.4±69.3, respectively. Mean scores of TR AIMS2-SF were; upper limb function 7.3±6.9, lower limb function 7.7±4.7, affect 7.4±3.2, pain 6±3.1, social interaction 4±2.3 and total score 35.5±16.6. The floor and ceiling effects of TR AIMS2-SF were 1.6 and 3.3, respectively. Both Cronbach's alpha and ICC were 0.83 indicating good reliability. There was significant correlation (rho, p value) with parameters that were directly related to HRQoL which were NHP subscales (energy level: 0.46, pain: 0.63, emotional reaction: 0.55, sleep 0.33, social interaction: 0.60, physical activity: 0.63; p<0.0001), HAQ (0.70, p<0.0001), BDI (0.54, p<0.0001), DHI (0.60, p<0.0001). Poor or not significant correlation was found with parameters that were not directly related to HRQoL such as age (-0.004, p=0.97), disease duration (0.21, p=0.09), vas pain (0.37, p<0.05); on the other hand, disease activity (DAS-28) correlated moderate (0.49, p<0.0001).

Conclusions: Turkish version of AIMS2-SF is a reliable and valid tool that can be used to evaluate the quality of life in RA. This is a feasible measure that can be used in daily practice easily.

References:

[1] Guillemin F, Coste J, Pouchot J et al. The AIMS2-SF: a short form of the Arthritis Impact Measurement Scales.

[2] French Quality of Life in Rheumatology Group. Arthritis Rheum 1997, 40:1267–74.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6351

THU0693 FEASIBILITY AND RELIABILITY OF THE SPONDYLOARTHRITIS RESEARCH CONSORTIUM OF CANADA SACROILIAC JOINT INFLAMMATION SCORE FOR CHILDREN WITH SPONDYLOARTHRITIS

N.A. Chauvin[1], W.P. Maksymowych[2], R.G. Lambert[3], J.L. Jaremko[3], D.M. Biko[1], J. Paschke[4], T.G. Brandon[5], P.F. Weiss[5]. [1]*Radiology, Children's Hospital of Philadelphia, Philadelphia, United States;* [2]*Rheumatology;* [3]*Radiology, University of Alberta;* [4]*Care Arthritis, Alberta, Canada;* [5]*Rheumatology, Children's Hospital of Philadelphia, Philadelphia, United States*

Background: Clinical trials in children with pediatric spondyloarthritis and axial disease are lacking. In order to assess the effectiveness of medications we need an objective measure to quantify severity of inflammation in the pediatric sacroiliac joint.

Objectives: We evaluated the reliability and construct validity of the Spondyloarthritis Research Consortium of Canada (SPARCC) sacroiliac joint inflammation score (SIS) in children with suspected or confirmed juvenile spondyloarthritis (SpA).

Methods: The SIS divides the joint into quadrants and scores the presence, depth, and intensity of bone marrow edema (BME) on short tau inversion recovery (STIR) magnetic resonance imaging (MRI). Six consecutive semicoronal slices through the cartilaginous portion of the joint are scored for BME (total score 0–72). We developed a pediatric training module that included scoring instructions and examples of bright subchondral signal on STIR scans easily confused with inflammation (Figure). After reviewing the module, 6 readers (1 adult and 3 pediatric radiologists, 1 adult rheumatologist, and 1 pediatric rheumatologist), blinded to clinical details except age, scored 30 studies that included semicoronal T1-weighted and STIR sequences. Pain was recorded on a visual analogue scale (0–10). Disease activity was evaluated using the juvenile SpA disease activity (JSpADA) index (range 0–8). Inter-observer reliability was assessed using intraclass correlation (ICC). Correlation (convergent validity) of the mean SPARCC SIS developers' score with disease activity was tested using Spearman correlation. Discrimination was tested by comparing the mean SPARCC SIS developers' score between children with and without inflammatory back pain using the Mann-Whitney test.

Results: The SIS had face validity and was feasible to score in the 30 pediatric cases. 21 (70%) were male. Median age at the time of imaging was 15.5 years (IQR: 12.7–16.8). Median pain score and JSpADA index were 2 (IQR 0.5–6) and 2 (IQR: 0.5–3), respectively. Of the 180 scores submitted by 6 readers, 140 (78%) of the studies had a SIS ≥2. Median SIS was 14 (IQR: 3–29). ICCs for all readers (N=6), SPARCC developers (N=2), rheumatologists (N=2), and pediatric radiologists (N=3) were 0.63 (95% CI: 0.45–0.78), 0.89 (95% CI: 0.75–0.95), 0.43 (95% CI: -0.02–0.71), and 0.85 (95% CI: 0.72–0.92), respectively. SIS had low correlation with disease activity as measured by the JSpADA (r=-0.08) and C-reactive protein (r=0.14). SIS score did not discriminate between those with and without inflammatory back pain (p=0.16).

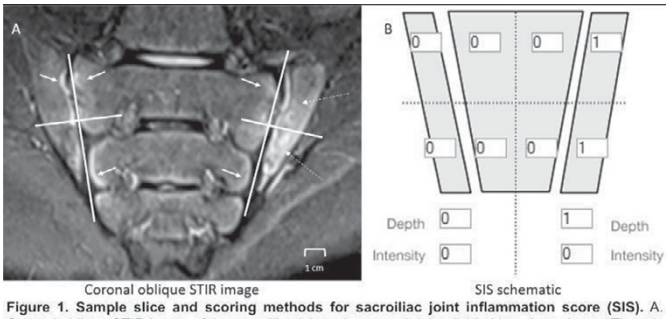


Figure 1. Sample slice and scoring methods for sacroiliac joint inflammation score (SIS). A. Coronal oblique STIR image of the sacroiliac joints shows each joint divided into 4 quadrants. There is normal bright subchondral signal along both sides of the right sacroiliac joint and along the periarticular region of the left sacrum (solid arrows) in this skeletally immature patient. On the left, there is abnormal signal consistent with bone marrow edema within periarticular region of the left ilium in both the upper and lower quadrants (dashed arrows). B. Scoring schematic demonstrates a "1" within the left iliac bone in both the upper and lower quadrants representing bone marrow edema. An additional score of "1" is given as the depth of the bone marrow edema extends >1cm from the articular surface. The patient received a total score of "3" for this image slice.

Conclusions: The SIS was feasible to score and had near excellent reliability, even with limited calibration. SIS did not have convergent validity with clinical measures of disease activity, highlighting that imaging and clinical evaluations provide complimentary but non-overlapping information. Responsiveness of the SIS should be evaluated in a prospective cohort of children who start biologic therapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6328

THU0694 EFFECTS OF ANTI-TNF THERAPY ON SOLUBILE UROKINASE PLASMINOGEN ACTIVATOR RECEPTOR (SUPAR) LEVELS IN ARTHRITIS

A. Pusztai, E. Végh, Á. Horváth, A. Hamar, S. Szántó, Z. Szekanecz, G. Szücs. *Department of Rheumatology, University of Debrecen, Faculty of Medicine, Debrecen, Hungary*

Background: The urokinase plasminogen activator receptor (uPAR) is expressed mainly on immune cells, smooth muscle cells and endothelial cells, favoring extracellular matrix degradation, cell adhesion, cell proliferation and regulates cell migration. The suPAR is the soluble form of the cell membrane-bound protein

uPAR, elevated levels may reflect increased activation of immune system which observed in the autoimmune diseases.
Objectives: The aim of this study was to assess the effects of anti-TNF therapy on uPAR production in rheumatoid arthritis (RA) and ankylosing spondylitis (AS). We also wished to correlate suPAR levels with various autoimmune-inflammatory biomarkers.
Methods: Altogether 33 arthritis patients including 22 RA patients treated with either etanercept (ETN) or certolizumab pegol (CZP) and 11 AS patients treated with ETN were included in a 12- month follow-up study. Circulating suPAR levels were assessed by suPARnostic Quick Test Reader. In addition,disease activity (DAS28 or BASDAI), CRP, IgM rheumatoid factor, anti-CCP were also assessed. Assessment were performed at baseline, as well as 6 and 12 months after treatment initation.
Results: Anti-TNF treatment was highly effective in both disease, as the mean DAS28 decreased in RA, mean BASDAI decresead in AS. There were no significant change in the suPAR levels after 12 months of anti-TNF therapy, although resulted non-significant decrease ($p<0,18$) in RA patients with critical suPAR levels (>9ng/ml). Baseline suPAR levels positively correlated with anti-CCP ($p<0,001$) and rheumatoid factor (p=0,024) in RA patients. Circulating suPAR levels did not correlate with DAS28, BASDAI or CRP.
Conclusions: In a mixed cohort of RA and AS patients, anti-TNF therapy did not affect the suPAR levels after 12 months. suPAR levels correlated with rheumatoid factor and anti-CCP. Based on these results suPAR may be a marker of autoimmunity rather than that of disease activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3428

THU0695 THE RA FLARE QUESTIONNAIRE (RA-FQ) IS RESPONSIVE TO CHANGE IN RA SYMPTOMS AND IMPACTS IN CLINICAL AND OBSERVATIONAL TRIALS

S.J. Bartlett[1,2], V.P. Bykerk[3], B. Fautrel[4], F. Guillemin[5], A. den Broeder[6], R. Alten[7], R. Christensen[8], E. Choy[9], D. Furst[10], S. Hewlett[11], A. Leong[12], L. March[13], T. Woodworth[10], B.I.O. Clifton[1] on behalf of CATCH, STPR, & DRESS Investigators. *[1]Johns Hopkins, Baltimore, United States; [2]McGill University, Montreal, Canada; [3]HSS, New York, United States; [4]Pierre & Marie Curie Universite, Paris; [5]Universite de Lorraine, Nancy, France; [6]Maartens Kliniek, Nijmegen, Netherlands; [7]Schlosspark Klinik, Berlin, Germany; [8]Parker Institute, Copenhagen, Denmark; [9]Cardiff University, Cardiff, United Kingdom; [10]UCLA, Los Angeles, United States; [11]University of the West of England, Bristol, United Kingdom; [12]Healthy Motivation, Santa Barbara, United States; [13]University of Sydney, Sydney, Australia*

Background: The RA-FQ is a new tool to measure RA flares. We have previously provided evidence of construct validity and reliability.1
Objectives: We evaluated sensitivity to change of the RA-FQ in clinical trials and observational studies of RA patients with low disease activity.
Methods: RA patients in observational studies [CATCH-Canada (n=896) and STPR-France (n=138)], and an RCT (DRESS-Netherlands; n=178) completed 5 items asking whether they were in flare (yes/no), and if so, the severity and duration. We selected patients who said they were not in flare and had a DAS28 <3.2 at thefirst visit (V1). Flare at the next study visit (V2) was defined three ways: 1) patient report (yes/no); 2) patient report-stringent (Boolean: patient report yes AND severity ≥4/10 AND duration >7 days [to increase this reflected increased inflammatory disease activity]; and c) DAS definition often used in studies (DAS28<3.2 at V2 required increase of 1.2; DAS≥3.2 at V2 required increase of 0.6). We compared RA-FQ scores with other PROs and disease activity indicators between flaring and non-flaring patients at V2. Effect size was estimatedusing Cohen's SMD. We hypothesized that at V2, RA-FQ scores would be similar in patients not flaring at both visits, and would be significantly higher in those flaring at V2.
Results: The mean difference in RA-FQ scores at V2 ranged from 7.3 (95% CI 1.4, 13.2) in STPR (DAS def) to 19.6 (95% CI 16.7, 22.6) in CATCH (patient report-stringent). The standardized mean difference effect sizes (SMDES) ranged from 0.82–1.95, and were largest for patient report-stringent in 2 studies. SMDE were strong (range 0.84–2.42) for patient global, MD global, HAQ, DAS28, and other clinical indicators except ESR.
The mean difference in RA-FQ scores at V2 ranged from 7.3 (95% CI 1.4, 13.2) in STPR (DAS def) to19.6 (95% CI 16.7, 22.6) in CATCH (patient report-stringent). The standardized mean difference effect sizes (SMDES) ranged from 0.82–1.95, and were largest for patient report-stringent in 2 studies. SMDE were strong (range 0.84–2.42) for patient global, MD global, HAQ, DAS28, and other clinical indicators except ESR.
Conclusions: Data from clinical and observational studies support the responsiveness of the RA-FQ in detecting change over time. The robust psychometric properties of the RA-FQ suggest it reliably detects clinically relevant worsening of RA symptoms consistent with increased disease activity and support its use in research and clinical care.

	Flare (Second Visit)		No Flare (Second Visit)		Mean difference RA-FQ Score (95% CI)	Effect Size
	V1	V2	V1	V2		
CATCH[1] (Canada)						
Patient Report	13.4	22.5	9.8	8.5	14.0 (11.4,16.5)	1.39
Patient Report - Stringent*	16.6	29.0	9.9	9.4	19.6 (16.7, 22.6)	1.95
DAS-defined flare#	11.8	26.8	10.0	9.3	17.5 (13.6, 21.5)	1.73
DRESS[2] (Netherlands)						
Patient Report	17.4	22.4	11.6	12.2	10.2 (5.6, 14.8)	1.10
Patient Report - Stringent*	16.7	31.3	12.2	12.9	18.3 (8.9, 27.8)	1.10
DAS-defined flare#	18.7	24.6	11.6	12.2	12.4 (7.7, 17.2)	1.37
STPR[3] (France)						
Patient Report	17.5	22.7	13.0	13.0	9.6 (3.6,15.6)	1.10
Patient Report - Stringent*	17.1	25.3	13.3	13.7	11.5 (2.3, 20.8)	1.30
DAS-defined flare#	16.5	20.5	13.9	13.2	7.3 (1.4,13.2)	0.82

[1]Canadian Early Arthritis Cohort; [2]Dose Reduction Strategy of Subcutaneous TNF Inhibitors in Rheumatoid Arthritis; [3]Strategy of Treatment in Patients with Rheumatoid Arthritis
*Stringent = Boolean: patient report flare yes AND severity ≥ 4/10 AND duration > 7 days.
#DAS28 < 3.2 at V2 required increase of 1.2; DAS ≥ 3.2 at V2 required increase of 0.6

References:
[1] Bykerk V et al. RMD Open 2016;2(1):e000225.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6921

THU0696 ANTI-CARBAMYLATED PROTEINS ANTIBODIES IN SLE PATIENTS WITH JOINT INVOLVEMENT: A POSSIBLE NEW BIOMARKER FOR EROSIVE DAMAGE

F. Ceccarelli[1], C. Perricone[2], L. Massaro[1], T. Colasanti[1], E. Cipriano[1], M. Pendolino[1], F. Natalucci[1], G. Capalbo[1], R. Mancini[1], F.R. Spinelli[1], C. Alessandri[1], G. Valesini[1], F. Conti[1]. *[1]Lupus Clinic, Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Roma; [2]Lupus Clinic, Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Rome, Italy*

Background: The traditional concept of non-erosive arthritis in Systemic Lupus Erythematosus (SLE) patients changed during the last years, thanks to the use of more sensitive imaging techniques, such as ultrasonography (US). The predictive role of Rheumatoid Arthritis (RA)-specific autoantibodies for bone loss in SLE patients has been investigated. In particular, anti-citrullinated peptide antibodies (ACPA) have been identified in about 50% of SLE patients with x-Ray detected erosive arthritis. More recently, anti-carbamylated proteins (anti-CarP) antibodies have been demonstrated in seronegative RA patients, with a prevalence of about 16% and a significant association with erosive damage.
Objectives: In the present cross-sectional study, we aimed at assessing the association between anti-CarP antibodies and erosive damage in a large cohort of SLE patients with joint involvement.
Methods: For this purpose, we evaluated 152 SLE patients (1997 ACR criteria; M/F 11/141, mean±SD age 46.4±11.3 years, mean±SD disease duration 144.9±110.5 months) with joint involvement (arthralgia/arthritis). The clinical and laboratory data were collected in a standardized computerized electronically filled form. All patients underwent blood draws to detect Rheumatoid Factor (RF) and ACPA, by using commercial ELISA kits according to the manufacturer's instructions, and anti-CarP antibodies by home-made ELISA (results were expressed in arbitrary units (AU)/ml and values above 340 IU/ml were considered positive). US was performed to assess the bone surfaces of metacarpophalangeal and proximal interphalangeal. At each joint, according with OMERACT definition, the presence of erosions was registered with a dichotomous value (0/1), allowing the possibility to obtain a total score, ranging from 0 to 20.
Results: The prevalence of anti-CarP antibodies was 28.3%, similar to RF (27.6%) and significantly higher to ACPA (11.2%, p=0.003). The mean±SD titer of anti-CarP antibodies was 890.5±794.9 IU/ml. Thirty-nine patients (25.6%) showed erosive arthritis: all the patients referred the occurrence of at least one episode of clinical synovitis. Erosive arthritis was significantly associated with anti-CarP antibodies (p=0.004) and ACPA (p=0.0008). Moreover, a significant correlation between anti-CarP antibody titer and US-erosive score was observed (r=0.2, p=0.01). Of note, anti-CarP antibodies were identified in 24.5% of double negative (ACPA-/RF-) patients, with erosive damage in 25% of them. Interestingly, anti-CarP antibodies resulted significantly associated with the presence of anti-dsDNA (P=0.01).
Conclusions: In the present study, for the first time, we identified a significant association between anti-CarP antibodies and erosive damage in SLE-related arthritis, in terms of frequency and severity. We found these antibodies in about 25% of $ACPA^-/RF^-$ SLE patients, a prevalence higher than that described in seronegative RA patients. Taken together, our results suggest that anti-CarP antibodies could be considered as a candidate biomarker of severity in SLE patients with joint involvement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5307

THU0697 FEASIBILITY AND RELIABILITY OF THE SPARCC SACROILIAC JOINT STRUCTURAL SCORE FOR CHILDREN WITH SPONDYLOARTHRITIS

N.A. Chauvin[1], W.P. Maksymowych[2], R.G. Lambert[3], J.L. Jaremko[3], D.M. Biko[1], J. Paschke[4], T.G. Brandon[5], P.F. Weiss[5]. *[1]Radiology, Children's Hospital of Philadelphia, Philadelphia, United States; [2]Rheumatology; [3]Radiology, University of Alberta; [4]CARE Arthritis, Alberta, Canada; [5]Rheumatology, Children's Hospital of Philadelphia, Philadelphia, United States*

Background: Clinical trials in juvenile spondyloarthritis (JSpA) and axial disease are lacking. To assess the effectiveness of medications, we need measures to evaluate structural progression in the pediatric sacroiliac joint (SIJ).
Objectives: To evaluate the reliability of the SPARCC sacroiliac joint structural score (SSS) in children with suspected or confirmed JSpA.
Methods: The SSS assesses a spectrum of structural lesions of the SIJ on MRI including fat metaplasia, erosion, backfill, and ankylosis on 5 consecutive slices through the cartilaginous part of the joint. These components are scored 0–20 (backfill and ankylosis) or 0–40 (fat metaplasia, erosion). We developed a pediatric training module that included a detailed description of each SSS component plus sclerosis (0–40), scoring methodology, and numerous examples. After reviewing the module, 6 readers (mix of adult and pediatric radiologists and rheumatologists) scored 30 studies (Exercise 1). All readers then reviewed a second training module based on DICOM images and scored an additional 29 studies (Exercise 2). Inter-observer reliability was assessed using intraclass correlation (ICC).
Results: The SSS had face validity and was feasible to score in the 59 pediatric cases. 35 (59%) were male and median age was 15 years (IQR 12–16). The ICCs for the SSS components from both calibration exercises are shown in the Table. In the 1st exercise, fat metaplasia and sclerosis had good reliability ($\geq$0.4) while reliability for erosion, backfill, and ankylosis were low. During the first exercise, 31 (17%), 131 (73%), 56 (31%), 100 (56%), and 21 (12%) of the 180 ratings from 6 readers had a score$>$0 for fat metaplasia, erosion, backfill, sclerosis, and ankylosis, respectively. In the second exercise, the ICC for erosion, backfill, and sclerosis improved and had good reliability. Of the 174 ratings from 6 readers, 91 (52%), 18 (10%), and 49 (28%) of scores were $>$0 for erosion, backfill, or sclerosis in exercise 2, respectively. Reliability for fat metaplasia and ankylosis were not calculated due to low frequency of lesions (8 (5%) and 3 (2%), respectively).

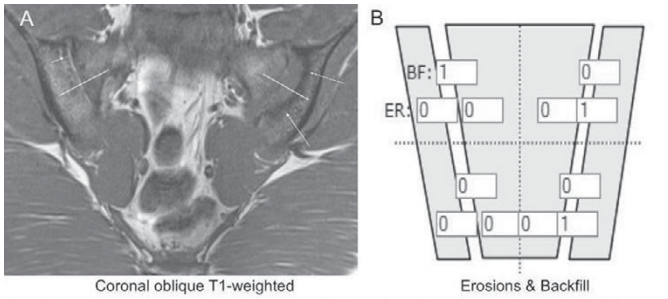


Figure 1. Sample slice and scoring methods for the sacroiliac joint structural score. A. Coronal oblique T1-weighted image of the sacroiliac joints shows each joint divided into 4 quadrants. There is backfill along the superior aspect of the right sacroiliac joint, as demonstrated by increased T1 signal in the joint space (short arrow). There is an extended erosion of the left iliac cortex affecting both upper and lower quadrants of the left iliac bone (long arrows). No sclerosis, ankylosis or fat metaplasia. B. Scoring schematic demonstrates a "1" for backfill (BF) within the R upper SIJ quadrant and "1" in both the upper and lower quadrants of the left SIJ representing erosions (ER).

Conclusions: The SSS was feasible to score and had acceptable reliability for pediatric SIJ MRI evaluation. ICC improved with additional calibration exercises based on DICOM, even for readers with limited experience.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6146

THU0698 MEASUREMENT PROPERTIES OF PRESENTEEISM MEASURES WITH DUAL ANSWER KEYS IN INFLAMMATORY ARTHRITIS

M. Donaldson[1], A. Kobza[1], D.E. Beaton[2], M.A. Gignac[2], D. Lacaille[1,3]. *[1]Arthritis Research Canada, Richmond; [2]Institute for Work and Health, Toronto; [3]University of British Columbia, Vancouver, Canada*

Background: Employment studies in arthritis have emphasised the importance of decreased productivity at work, or presenteeism. Yet, how to best measure presenteeism remains challenging. The "Work Limitations Questionnaire" (WLQ) is frequently used. A drawback is that it measures the amount of time people are limited, but not the degree to which they are limited. In contrast, the "Workplace Activity Limitations Scale" (WALS) measures the degree of limitation, but not the time. We modified the response keys to the WALS and WLQ to measure both degree of difficulty and amount of time with difficulty.
Objectives: Our objective was to evaluate measurement properties, i.e. internal consistency and construct validity, of the WALS and WLQ with combined scores from dual answer keys.
Methods: A cross-sectional study used baseline data from the RCT of an employment intervention, the "Making It Work" Program. Participants were recruited from BC, Alberta and Ontario. Inclusion criteria included: having inflammatory arthritis, currently employed, age 19–59, and having concerns about arthritis affecting ability to work. 364 participants were included (RA:195, PsA:54, SLE:46, AS:69; 77% female, mean (SD) age: 45.9 (9.8) yrs). Combined scores were obtained by i) multiplying, and ii) adding, the scores of difficulty and time answer keys at the item level. No significant differences were observed between the additive and multiplicative models. Hence, we report on the multiplicative model, which reflects consumers' preference. Internal consistency was analyzed using Cronbach's alphas; construct validity by measuring correlation (Spearman coefficients) between WALS or WLQ subscales and constructs such as work productivity activity impairment (WPAI), risk of impending work loss (work instability, RA-WIS), disease measures, and job characteristics.
Results: Analyses at the item level revealed a strong floor effect (WALS: 16% to 56%; WLQ: 27% to 81% of answers for all items except one) but no ceiling effect, likely reflecting the relatively low limitation expected in a working sample. High (i.e. $\geq$0.7) internal consistency (α 0.70–0.82) was found for WALS and all WLQ subscales except WLQ Physical Demands (0.67). As a priori hypothesized, moderate correlation was observed between the time (0.33–0.57), or combined (0.44–0.61), scores of WLQ subscales and WPAI, or WIS; and correlation was consistently higher for combined than time scores. Moderate correlation was also observed between degree of difficulty (0.70–0.77), or combined (0.60–0.69), scores of the WALS and WPAI, or WIS. Contrary to our hypothesis, the WALS combined score did not have a higher correlation with WPAI, or WIS, than degree of difficulty score. Correlations with disease (fatigue, pain, physical function, depression) and job characteristics (job demand, autonomy, social support at work, commuting difficulty) with time, difficulty, or combined scores of the WALS and WLQ met the a priori hypothesized correlation levels.
Conclusions: Our previous research confirmed the value of measuring both degree of difficulty and amount of time, showing they measure different concepts, which can serve different purposes and are both important to patients. This research demonstrates that applying a dual answer key to two validated instruments shows good initial indicators of internal consistency and construct validity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3031

THU0699 CHARACTERIZING AND VALIDATING THE PHENOTYPE OF KNEE PAIN: A LATENT CLASS ANALYSIS

F. Pan[1], J. Tian[2], D. Aitken[1], F. Cicuttini[3], C. Ding[1], G. Jones[1]. *[1]Musculoskeletal Unit; [2]Public Health, Menzies Institute for Medical Research, University of Tasmania; [3]Department of Epidemiology and Preventive Medicine, Monash University Medical School, Hobart, Australia*

Background: Pain in osteoarthritis (OA) is very common and often involves multiple joints. It is multifactorial and individualised with multiple factors involved in the genesis and pain experience, such as structural pathology, psychological factors and pain coping strategies. Thus it may be possible to group people together based on specific factors which are linked to experiencing pain.
Objectives: To identify and validate the phenotype of knee pain over 10.7 years.
Methods: 1099 participants (mean age 63 years; range 51–81 years) from the population-based Tasmanian Older Adult Cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Demographic, psychological, lifestyle and comorbidities data were obtained at baseline. T1-weighted or T2-weighted fat saturated MRI of the right knee was performed to measure knee structural pathology–cartilage defects, bone marrow lesions (BMLs) and effusion-synovitis at baseline. Knee pain was assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at each time-point. Presence of pain (yes/no) at the neck, back, hands, shoulders, hips, knees and feet was also assessed by questionnaire at each time-point. Latent class analysis, which can identify unmeasured class membership

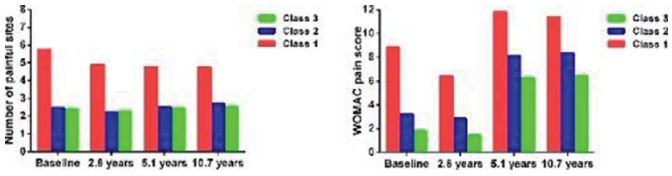
Abstract THU0697 – Table 1

	Exercise 1 ICC (95% CI)				Exercise 2 ICC (95% CI)			
	All	Pediatric Radiologists	SSS developers	Rheumatologists	All	Pediatric Radiologists	SSS developers	Rheumatologists
Fat metaplasia	0.40 (0.25–0.58)	0.46 (0.25–0.67)	0.89 (0.77–0.95)	0.82 (0.65–0.91)				
Erosion	0.37 (0.22–0.55)	0.39 (0.15–0.61)	0.72 (0.48–0.86)	0.16 (-0.17–0.47)	0.54 (0.34- 0.72)	0.51 (0.16–0.74)	0.96 (0.89–0.98)	0.61 (0.32–0.79)
Backfill	0.39 (0.25–0.58)	0.36 (0.14–0.58)	0.82 (0.56–0.92)	0.45 (0.12–0.69)	0.47 (0.31- 0.64)	0.12 (-0.08–0.38)	0.90 (0.80–0.95)	0.98 (0.95–0.99)
Sclerosis	0.42 (0.25–0.60)	0.42 (0.17–0.65)	0.61 (0.08–0.83)	0.72 (0.49–0.86)	0.47 (0.30- 0.65)	0.35 (0.13–0.58)	0.88 (0.75–0.94)	0.81 (0.63–0.90)
Ankylosis	0.31 (0.17–0.49)	0.46 (0.24–0.66)	0.72 (0.49–0.85)	0.19 (-0.16–0.51)				

Legend: ICC$<$0.40 is poor, 0.40$\leq$ICC$<$0.75 is good, ICC$\geq$0.75 is excellent.

among participants using observed variables, was used to differentiate "pain phenotypes" considering sex, body mass index (BMI), emotional problems, comorbidities, number of painful sites and knee structural damage on MRI.

Results: Three pain phenotypes were identified: Class 1: high levels of emotional problems and low levels of structural damage (24%); Class 2: high levels of structural damage and low levels of emotional problems (20%); Class 3: relatively low levels of emotional problems and low levels of structural damage (56%). People within Class 1 were more likely to be female, had greater BMI, lower education level, more comorbidities, more severe knee pain and more painful sites as compared to Class 2 and Class 3. Furthermore, WOMAC pain scores and number of painful sites were consistently greater at baseline, 2.6, 5.1 and 10.7 years in Class 1 than Class 2 and Class 3 (all $P<0.05$).



Conclusions: Psychological and structural factors interact with each other to influence pain perception.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3033

THU0700 IMMUNOGENICITY IN PATIENTS SWITCHING FROM STABLE ORIGINATOR INFLIXIMAB TREATMENT TO CT-P13: ANALYSES ACROSS SIX DISEASES FROM THE 52-WEEK RANDOMIZED NOR-SWITCH STUDY

G.L. Goll[1], I.C. Olsen[1], K.E.A. Lundin[2], K.K. Jørgensen[3], M. Lorentzen[4], R.A. Klaasen[5], D.J. Warren[5], C. Mørk[6], J. Jahnsen[3], E.A. Haavardsholm[1], T.K. Kvien[1], N. Bolstad[5] on behalf of The NOR-SWITCH study group. *[1]Dept of Rheumatology, Diakonhjemmet Hospital; [2]Gastroenterology, Oslo University Hospital, Oslo; [3]Gastroenterology, Akershus University Hospital, Lørenskog; [4]Dermatology; [5]Biochemistry DNR, Oslo University Hospital, Oslo; [6]Dermatology, St Olav University Hospital, Trondheim, Norway*

Background: TNF-inhibitors (TNFi) have improved treatment of Crohn's disease (CD), ulcerative colitis (UC), spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA) and chronic plaque psoriasis (Ps). The NOR-SWITCH study was funded by the Norwegian government to investigate if switching from originator infliximab (Remicade®, INX) to biosimilar CT-P13 (Remsima®), is safe. Previously, the primary analyses of the pooled indications have been published[1]. Immunogenicity is associated with treatment failure and has been of particular concern in switching [2].

Objectives: The NOR-SWITCH study aimed to assess if immunogenicity to infliximab differed between patients treated with continous INX vs patients switched to CT-P13.

Methods: The study was designed as a 52-week randomized, double-blind, non-inferiority, phase IV trial. Adult patients with a diagnosis of CD, UC, SpA, RA, PsA or Ps on stable treatment with the originator infliximab were eligible. Patients were randomized 1:1 to either continued INX or switch to CT-P13 treatment, using unchanged dosing regimen. Trough drug levels and neutralizing anti-drug antibodies (ADAb) measurements were done prior to every infusion, but results were not reported during the study. Assays for drug serum levels and ADAb are fully automated on the AutoDELFIA® (PerkinElmer, Waltham, MA) immunoassay platform.

Results: Twenty patients entered the study with detectable ADAb (9 in INX arm, 11 in CT-P13 arm). 36 additional patients developed detectable incident ADAb during the 52-week study period (17 in INX arm, 19 in CT-P13 arm). Incident ADAb in each disease are shown in the table. Patients with detectable ADAb at any time during the study period were more likely to discontinue study drug treatment (7/26 (26.9%) in INX arm, 5/30 (16.7%) in CT-P13 arm) than patients without detectable ADAb (17/214 (7.9%) in INX arm, 13/210 (6.2%) in CT-P13 arm) (p=0.001).

Incident ADAb during study period (total number of patients), Full Analysis Set

	INX	CT-P13
All patients in study	17 (241) 7.1%	19 (240) 7.9%
RA patients	6 (39) 15.4%	2 (38) 5.3%
SPA patients	2 (45) 4.4%	5 (46) 10.9%
PSA patients	1 (14) 7.1%	0 (16)
UC patients	5 (47) 10.6%	8 (46) 17.4%
CD patients	3 (75) 3.9%	4 (77) 5.2%
Ps patients	0 (18)	0 (17)

Conclusions: The NOR-SWITCH study demonstrated similar immunogenicity in patients switched to CT-P13 vs those who continued INX treatment, supporting that switch does not influence ADAb formation. Presence of ADAb was associated with termination of study treatment.

References:

[1] Jørgensen KK, Olsen IC, Goll GL et al. Switching from originator infliximab to biosimilar CT-P13 compared to maintained treatment with originator infliximab (NOR-SWITCH): a 52-week randomised double-blind non-inferiority trial. The Lancet, in press.

[2] Dörner T, Kay J. Biosimilars in rheumatology: current perspectives and lessons learnt. Nat Rev Rheumatol 2015 Dec;11(12):713–24.

Disclosure of Interest: G. Goll Consultant for: Novartis, Pfizer, Orion Pharma, AbbVie, I. Olsen: None declared, K. Lundin Consultant for: Orion Pharma, MSD, Takeda, K. Jørgensen Consultant for: Orion Pharma, AbbVie, Tillott, Intercept, M. Lorentzen: None declared, R. Klaasen: None declared, D. Warren: None declared, C. Mørk Consultant for: Novartis, LeoPharma, ACOhud, AbbVie, Galderma Nordic, Cellgene, J. Jahnsen Consultant for: Orion Pharma, Celltrion, Pfizer, MSD, AbbVie, Takeda, Napp Pharm, AstroPharma, E. Haavardsholm Consultant for: AbbVie, UCB, Pfizer, MSD, Roche, T. Kvien Consultant for: Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lily, Epirus, Hospira, Merck-Serono, Novartis, Orion Pharma, Pfizer, Sandoz, UCB, N. Bolstad: None declared

DOI: 10.1136/annrheumdis-2017-eular.4112

THU0701 THE EFFECTS OF STRUCTURAL DAMAGE ON FUNCTIONAL DISABILITY IN PSORIATIC ARTHRITIS

A. Kerschbaumer, F. Alasti, J.S. Smolen, D. Aletaha. *Department of Medicine III (Chairman: Prof. Josef Smolen, MD), Medical University of Vienna, Vienna, Austria*

Background: Functional outcomes are central in patients with chronic inflammatory musculoskeletal diseases. It has been shown in rheumatoid arthritis that functional outcomes are impaired in the presence of structural damage, a finding that has not yet been investigated in psoriatic arthritis (PsA), which has a more complex phenotype than rheumatoid arthritis (RA).

Objectives: To quantify the association of radiographic damage with physical function in PsA patients.

Methods: We analysed patients enrolled in the GO-REVEAL study[1] who had received golimumab. We obtained modified Sharp-van-der-Heijde scores (mSvDHS) from X-rays, performed at week 0, 24, 52 and week 104 (n=262). In longitudinal data analysis, we then used generalized estimating equations (GEE) on all patients in DAPSA remission (n=96), utilising all their remission visits, whereby the health assessment questionnaire (HAQ) disability index of each patients visit was used as dependent variable and mSvDHS, joint space narrowing (JSN) and erosion (ERO) scores, respectively, were used as independent variables in separate models.

To analyse effects of structural damage on changeability of functional limitations, we identified a subgroup of patients who had functional limitations at baseline (HAQ$\geq$1) and who showed a major response of DAPSA (improvement of $\geq$85% from baseline). In this model we assess the effect of mSvDHS on changes in HAQ, while adjusting for HAQ at baseline (n=54).

As validation cohort, we analysed a routine clinic PsA cohort with complete cDAPSA (the clinical version of the DAPSA without CRP) and mSvDHS (n=99). A cDAPSA cutoff of $\leq$4 was used to define the remission cohort in an analogous way as decribed above (n=32).

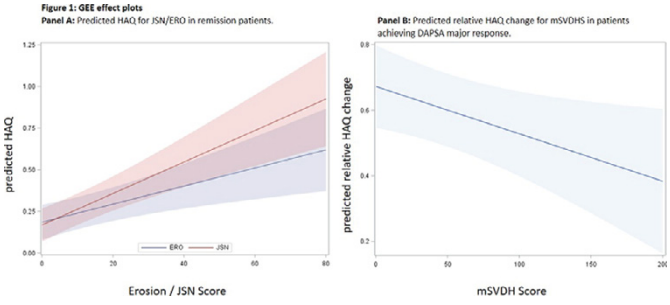
Results: As shown in table 1 and visualised in figure 1A, for patients in DAPSA remission, significant effects were seen for mSvDHS, JSN and ERO. These results could be confirmed in the validation cohort with patients achieving cDAPSA remission and showed a significant association of HAQ and mSvDHS (Estimate=0.0044, p=0.0176) as well as JSN (Estimate=0.0078, p=0.0165).

In the second analysis, looking at patients achieving DAPSA major response, again, results were significant for the association total mSVDHS and JSN. Additionally, higher estimates of JSN, compared to mSvDHS could be observed, with relative HAQ change as outcome parameter (see table 1 and figure 1B).

Table 1. Association of radiographic damage and HAQ in separate GEE models

Dependent variable	DAPSA remission (n=96) HAQ		DAPSA Major Response (n=54) relative HAQ change*	
Independent variable	Estimate	p	Estimate	p
mSVDHS	0.0037 (0.0018 to 0.0055)	**<0.001**	-0.0014 (-0.0027 to -0.0002)	**0.024**
Erosion	0.0054 (0.0021 to 0.0088)	**0.001**	-0.0021 (-0.0043 to 0.0002)	0.075
JSN	0.0095 (0.0057 to 0.013)	**<0.001**	-0.0039 (-0.0067 to -0.0012)	**0.005**

*Adjusted for HAQ at baseline.



Conclusions: Our results suggest that in JSN is functionally more important than

erosions. Functional outcomes have an irreversible component that is strongly related to the amount of structural damage. This needs to be considered when targeting functional outcomes in clinical practice.

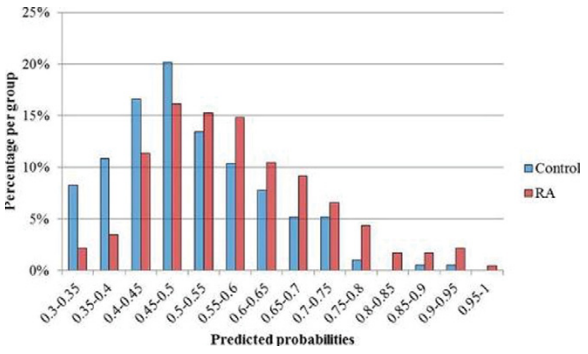
References:
[1] Kavanaugh A, van der Heijde D, McInnes IB, et al. Golimumab in psoriatic arthritis: one-year clinical efficacy, radiographic, and safety results from a phase III, randomized, placebo-controlled trial. Arthritis Rheum 2012; 64: 2504–2517.

Acknowledgements:.
We thank Janssen for provision of an 80% random data cut of patients in the GO-REVEAL trial for our analyses.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2835

THU0702 ARE MRI-DETECTED EROSIONS SPECIFIC FOR RA? A LARGE EXPLORATIVE CROSS-SECTIONAL STUDY

D. Boeters[1], W. Nieuwenhuis[1], H. van Steenbergen[1], R. Landewé[2], M. Reijnierse[3], A. van der Helm-van Mil[1]. *[1]Department of Rheumatology, LUMC, Leiden; [2]Department of Clinical Rheumatology and Immunology, AMC and Atrium MC, Amsterdam and Heerlen; [3]Department of Radiology, LUMC, Leiden, Netherlands*

Background: Magnetic resonance imaging (MRI) is recommended in the diagnostic process of rheumatoid arthritis (RA), as it can detect damage at an earlier time point than conventional radiographs. However, MRI-detected erosions as defined by EULAR and included in RAMRIS are also observed in symptom-free controls, especially at older age. It is unclear how RA-specific erosions on MRI can be distinguished from physiological erosions in symptom-free individuals. Therefore this study compared MRI-detected erosions between RA-patients and healthy controls, including evaluation of the effect of age.
Objectives: To compare characteristics of MRI-detected erosions (total erosion score, location and severity of erosions and simultaneous presence of MRI-detected inflammation) in metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints between RA-patients and healthy controls.
Methods: 422 subjects (229 newly presenting patients with a clinical diagnosis of RA and fulfilling the 2010-criteria and 193 symptom-free controls) underwent contrast enhanced 1.5T MRI of unilateral MCP and MTP joints. The readers were blind to the clinical information. Total erosion score according to the RAMRIS method (hence a combination of number and severity), location and severity of erosions and simultaneous presence of MRI-detected inflammation (synovitis and/or bone marrow edema) were compared between groups, also in relation to age.
Results: First total erosion scores were analyzed. Both in RA-patients and in controls this score was associated with age ($p<0.001$ in both groups). In addition, at all ages and on group level, RA-patients had 1.2 (95% CI 1.1–1.3) times higher erosion scores than controls. Despite this difference, total erosion scores could not differentiate RA-patients from controls on the individual level, as there was large overlap (Figure). Next different characteristics of erosions were explored within age groups (<40, 40–59, ≥60) to search for RA-specific features. With respect to location, erosions found in MTP5 were specific for RA (spec 90–98% for different age groups). Erosions found in MTP1 were specific for RA if subjects were aged <40 (spec 98%), but specificity decreased by increasing age (spec 86% if aged 40–59 and 63% if aged ≥60). Evaluating the severity revealed that "severe erosions" (scores ≥2) were infrequent in all subjects, but almost exclusively present in RA (spec 98–100%). Finally the simultaneous presence of erosions with inflammation was studied. In the age group <40 years, the simultaneous presence was exclusively observed in RA-patients (specificity 100%); but specificity decreased by age since the combined presence was also seen in symptom-free controls (spec 91% if aged 40–59 and 71% if aged ≥60 years).



Conclusions: Whilst the group of RA-patients at disease presentation had significantly higher erosion-scores than healthy controls, scores of individual subjects were largely overlapping. Some erosion characteristics were specific for RA, but these were present in only a minority of all RA-patients (22%).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4026

THU0703 SYSTEMATIC REVIEW OF RHEUMATOID ARTHRITIS CLINICAL STUDIES: SUBOPTIMAL STATISTICAL ANALYSIS OF RADIOLOGICAL DATA

S. Mahmood[1,1], L. van Tuyl[1], L. Schoonmade[2], R. Landewé[1], D. van der Heijde[3], J. Twisk[2], M. Boers[1]. *[1]Amsterdam Rheumatology and immunology Center; [2]VUmc, Amsterdam; [3]LUMC, Leiden, Netherlands*

Background: Radiography is an inexpensive, reliable and reproducible method to detect and quantify progression of damage, an important outcome in rheumatoid arthritis (RA) trials and observational studies. However, the distribution of progression scores is skewed with many low or zero scores. Analysis of such data is challenging, and the choice of analysis technique may influence the result. Current analysis practice is unknown.
Objectives: We systematically searched the literature to identify current practice for the analysis of radiographic progression in clinical trials and observational studies of RA.
Methods: PubMed Embase and Cochrane databases were searched (2006–2016) to identify studies that described analysis techniques to compare radiographic progression in at least two groups. Studies in animals, children as well as conference abstracts and studies not written in English were excluded. Titles and abstracts were screened by one researcher (SM); a second investigator (LvT) evaluated the included cases, doubtful cases and a random sample of the excluded cases.
Information on study design, sample size, assessment methods and analysis technique was extracted by one researcher (SM), in consultation with 3 others (LvT; MB and JT).
Results: Of 5980 identified papers, 252 were eligible. 226 of these reports were on a single study while 26 were on multiple studies in one paper.
Of the 226 studies, 75 studies used parametric techniques, such as t-tests, ANOVA or linear regression to analyze the data. Of these only 12% took the skewed distribution into account. In 78 studies, the continuous data was categorized into two or more groups and analyzed with binomial or ordinal methods, such a chi-square tests or logistic regression analyses. 4 studies treated the outcome as a "count" outcome variable (2 studies applied a Poisson regression, 1 a negative binomial regression and 1 a zero-inflated binomial regression).
43% compared more than two groups. Median (IQR) sample size was 351 (range 163–608). 30% had one reader, 57% two readers, and 2% more than two; in 10% the number of readers was not recorded. Order of reading was random in 43%, sequential in 31%, and unknown in 26%. Most applied the Sharp van der Heijde scoring method (75%); 9% the Genant modification, and 16% other methods.
Conclusions: There is large heterogeneity in the analysis strategy of radiographic progression in recent RA clinical trials and observational studies: a large number of studies apply simple, suboptimal or inappropriate methods. In addition, key information (i.e. number of readers and order of readings) is poorly documented.
Disclosure of Interest: S. Mahmood: None declared, L. van Tuyl: None declared, L. Schoonmade: None declared, R. Landewé Employee of: director of Rheumatology Consultancy BV, D. van der Heijde Employee of: director of Rheumatology Consultancy BV, J. Twisk: None declared, M. Boers: None declared
DOI: 10.1136/annrheumdis-2017-eular.1829

THU0704 EVALUATION OF THE ACCURACY OF HAND AND FOOT MRI IN THE EARLY IDENTIFICATION OF RA: USING THE PREVALENCE OF LOW-GRADED INFLAMMATION IN THE SYMPTOM-FREE POPULATION AS REFERENCE REDUCES FALSE-POSITIVE MRI RESULTS

A.C. Boer[1], L.E. Burgers[1], L. Mangnus[1], R.M. Ten Brinck[1], W.P. Nieuwenhuis[1], H.W. Van Steenbergen[1], M. Reijnierse[2], T.W. Huizinga[1], A.H. van der Helm van Mil[1]. *[1]Rheumatology; [2]Radiology, LUMC, Leiden, Netherlands*

Background: Early identification of rheumatoid arthritis (RA) is important, because it allows early treatment initiation and is associated with better disease outcomes. In this perspective, the use of hand and foot MRI in the diagnostic process of rheumatoid arthritis (RA) has been advocated. Recent studies showed that MRI is helpful in predicting progression from clinically suspect arthralgia (CSA) to clinical arthritis, and from undifferentiated arthritis (UA) to RA. However, the diagnostic value of MRI is still undetermined. Most studies focussed on the sensitivity rather than the specificity of inflammation detected on MRI. It is known that symptom-free persons can also show inflammation on MRI. Consequently, it has been questioned if MRI-findings in symptom-free volunteers are relevant to consider as a reference when defining a "positive MRI".
Objectives: To determine the value of considering MRI-findings in a control group for the predictive accuracy of MRI when defining a positive MRI.
Methods: 225 patients with CSA and 201 patients with UA underwent MRI of MCP-, wrist- and MTP-joints at baseline and were followed for 1 year on progression to arthritis and RA respectively. MRI was considered positive either if ≥1 joint showed inflammation (called "uncorrected definition"), or if ≥1 joint had inflammation that was present in <5% of persons of the same age-category at the same location in a symptom free reference population (called "5% corrected definition"). MRI scans were scored according to RAMRIS method. Test characteristics were compared for both definitions, hence with and without the incorporation of a reference population when defining a "positive MRI".
Results: By using MRI-data of symptom-free volunteers as reference, the

specificity of MRI-detected inflammation increased from 22% to 56% in CSA-patients, and from 10% to 36% in UA-patients. The sensitivity was not affected; it was 88% and 85% in CSA-patients and 93% and 93% in UA-patients. The accuracy also increased, from 32% to 60% in CSA-patients and 22% to 44% in UA-patients.

Conclusions: The use of a reference population resulted in a substantial reduction of false-positive results, without affecting the sensitivity. This is of high importance because of the potential risks of false-positive MRI-results, for example in the setting of UA as a positive MRI-result may influence the decision to initiate disease modifying medication. Although a reference population is generally used in medicine for other tests to derive a definition of a positive test result, this is the first study demonstrating the value of a reference population to define a "positive MRI".

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1559

THURSDAY, 15 JUNE 2017

Rehabilitation

THU0705 EXPERIMENTAL USE OF 3D PRINTING TECHNOLOGY FOR THE CONSTRUCTION OF DEVICES AS INTEGRATION OF OCCUPATIONAL THERAPY INTERVENTION WITH RHEUMATOID ARTHRITIS PATIENTS (RA)

G. Sandri[1], A. Bottini[2], F. Franchi[3], M.T. Mascia[2]. *[1]Department of Clinical, Diagnostic and Public Health, Service of Rheumatology; [2]Department of Clinical, Diagnostic and Public Health, Occupational Therapy Unit; [3]Orthopedic, Hand Rehabilitation, Modena, Italy*

Background: RA is a chronic inflammatory disease that can interfere with the ability to perform activities of daily living. The adoption of aid devices allows to maintain and/or improve employment performance, reducing the pain preventing further joint damage. However, it is known that the abandonment rate of such devices is quite high, resulting in failure of the rehabilitation project, and waste of resources. The reasons people give for abandoning support technology are that they have not been involved in the process of provision, and that the devices do not have the intended effect (1).

Objectives: technology may allow customization of 3D printing devices agreed together with patients, utilizing materials which are cheap, fast and easily adjustable.

Methods: The study was organized into the following phases: recruitment of RA patients for the "joint protection laboratories"; sessions of the "joint protection laboratories"; recruitment of patients for the identification of needs for customized aid devices; co-design of customized aid devices; printing of customized aid devices; delivery of customized aid devices; detection using customized aid devices.

We have collected a list of needs to be able to develop such customized aid devices at the end of a course to educate on joint protection covering: ergonomic gestures, management of fatigue and pain, environmental adaptations and aid devices.

18 patients (17 women and 1 man), age between 30 and 75 years old, were organized into small groups for the "joint protection laboratories". 9 patients expressed their specific needs regarding the aid devices and therefore subsequent meetings were organized that have allowed us to produce and deliver customized objects.

Autodesk® Fusion360 for object modeling; Ultimaker Care for slicing; 3D printing DeltaWASP 20 40. For the collection of the design features we used the PA board (product analysis) of the USERfit tool. For the psycho-social impact assessment of the assistance, the PIADS (Psychosocial Impact of Assistive Devices Scale – scale -3+3) was used, and for the evaluation of the patient's satisfaction with respect to the aid device, QUEST (Quebec User Evaluation of Satisfaction with Technical Aids, scale 1–5) was used.

Results: 6 aid devices were customized: hand grip holder for chalk, toothbrush, ignition key, tablespoon, iron, as well as a handle to open the moka coffee machine.

The psychosocial assessment of 6 delivered aid devices, collected through PIADS, showed an overall positive outcome (mean competence +1.488; adaptability: +1.690; self-esteem: +1.375). The assessment of patient satisfaction through QUEST, was good overall (scale 1–5: satisfaction aid: 4.75; service satisfaction: 4.68).

Conclusions: This work also demonstrated, over a range of small numbers, that the path of co-design and production of customized aid devices via rapid manufacturing with 3D printing technology is feasible and fulfilling.

References:

[1] Tuntland H, Kjeken I, Nordheim L, Falzon L, Jamtvedt G, Hagen K. The Cochrane review of assistive technology for rheumatoid arthritis Eur J Phys Rehabil Med. 2010 Jun;46(2):261–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2591

THU0706 LOW DISEASE ACTIVITY AFTER A SHORT COURSE OF DRUG THERAPY AND REHABILITATION IS ASSOCIATED TO A GREATER IMPROVEMENT IN FUNCTIONAL CAPACITY IN RHEUMATOID ARTHRITIS

B. Cunha, B. Ferreira, L. Moreira, C. Barros, A. Gushikem, J. Kauer, T. Ferreira on behalf of SARAR 2 cohort. *Rheumatology, SARAH Network of Rehabilitation Hospitals, Brasíia, Brazil*

Background: Patients with rheumatoid arthritis (RA) have lower funcional capacity than general population (1). Studies have shown that patients are able to improve their functional capacity after adequate treatment with disease-modifying antirheumatic drugs (DMARDs) (1–2), but it is unclear which other factors are involved in rehabilitation settings.

Objectives: To investigate which clinical factors are associated to improvement in funcional capacity in patients with RA in the context of DMARD therapy and rehabilitation.

Methods: It was a case-control study. Patients with RA admitted between june 2014 and july 2016 were included. Assessments were carried out just before and after completion of rehabilitation program. Functional capacity was assessed with Health Assessment Questionnaire-Disability Index (HAQ-DI). Disease activity was evaluated with Clinical Disease Activity Index (CDAI). It was allowed to change DMARD treatment or dose during the follow-up period. Interventions were carried out at the discretion of the rehabilitation team and could include joint injections, exercises, orthoses, insoles, educational interventions and assistive devices. Patients that were operated in the follow-up period were excluded.

An improvement in HAQ-DI was defined as a difference of -0,22. Patients that improved after treatment were compared with those who did not, regarding clinical caracteristics and modalities of treatment that were employed. Chi-square or Fisher exact test analyses were employed.

Results: Forty-six women and two men were included, with average age of 56 (11) years old and 10,8 years of diagnosis, Rheumatoid factor was positive in 58% (mean title 242,3 U/L); anti-CCP was positive in 48% (mean title 283,8 U/L). Patients were followed for 6–12 months.

HAQ-DI improved 0,51 (0,3–0,71; $p<0,001$) and CDAI improved 12,8 (7,6–17,9). Patients who were able to improve HAQ-DI had a better average CDAI in the second assessment (16 vs. 7, p=0,011). There was no association between improvement of HAQ-DI and other clinical and laboratorial variables, including drug and rehabilitation modalities.

Conclusions: Low disease activity after a short course of drug therapy and rehabilitation is related to a greater improvement of functional capacity in patients with RA. Therefore, patients with RA may have better outcomes in rehabilitation if disease activity is controlled.

References:

[1] Mota LM, Laurindo IM, dos Santos Neto LL. Prospective evaluation of thequality of life in a cohort of patients with early rheumatoid arthritis. Rev BrasReumatol. 2010 May-Jun;50(3):249–61.

[2] Norton S, Fu B, Scott DL, Deighton C, Symmons DP, Wailoo AJ, Tosh J, Lunt M. Davies R, Young A, Verstappen SM. Health Assessment Questionnaire disabilityprogression in early rheumatoid arthritis: systematic review and analysis of two inception cohorts. Semin Arthritis Rheum. 2014 Oct;44(2):131–44.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1670

THU0707 RACE & REHABILITATION DESTINATION AFTER TOTAL HIP REPLACEMENT

E.R. Vina[1], M. Kallan[2], A. Collier[2], C. Nelson[2], S. Ibrahim[2]. *[1]University of Arizona, Tucson; [2]University of Pennsylvania, Philadelphia, United States*

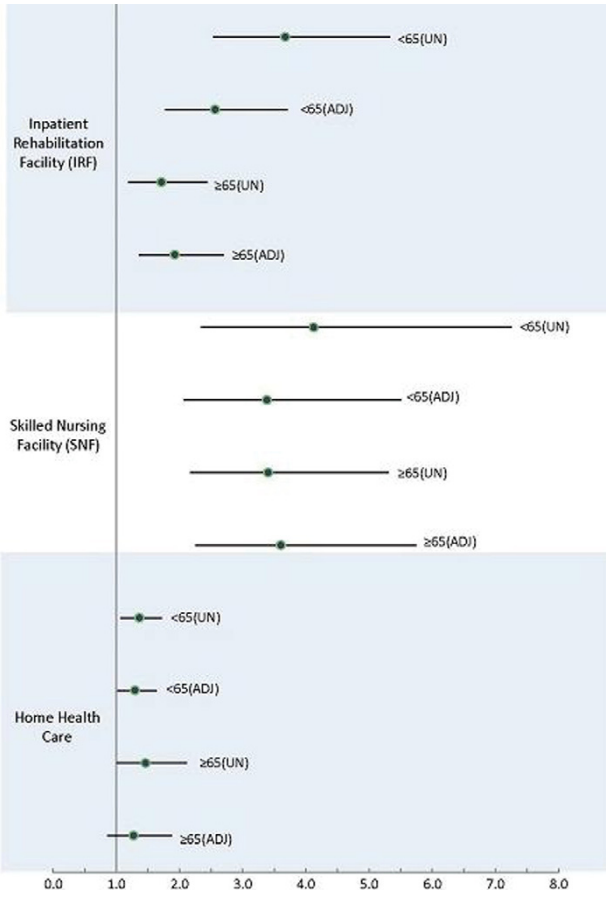
Background: There are marked racial/ethnic disparities in the utilization of hip joint replacement in the US. Differences in post-surgical rehabilitation care may influence this disparity. There is relatively little research on racial variations in post-hip joint replacement surgery care processes.

Objectives: The main objective of this analysis was to examine racial differences in where patients go for post-acute care rehabilitation after elective hip replacement surgery. We also assessed whether or not where patients go for post-surgery rehabilitation care impacts quality of care markers such as 90-day hospital readmission.

Methods: A retrospective, large regional dataset analysis using the Pennsylvania Health Care Cost Containment Council database was performed. Patients who underwent elective hip replacement surgery and discharged from Pennsylvania hospitals between fiscal years 2008–2012 were selected. Post-surgery rehabilitation destinations options included: home with self-care, home with home health (HH) care; skilled nursing facility (SNF) and in-patient rehab facility (IRF).

We used multinomial logistic regression models to estimate unadjusted and adjusted relative risk ratios (aRRRs) of being discharged home with HH care, to a SNF or to an IRF (vs. home with self-care) after surgery, comparing African-American (AA) to white patients. Multivariable models adjusted for patient-level and facility-level variables associated ($p<0.10$) with post-surgical discharge destination based on bivariate analyses. Unadjusted and adjusted odds ratios (aORs) of 90-day hospital readmission were estimated using binary logistic regression models. Multivariable models adjusted for patient-level and facility-level variables associated

(p<0.10) with 90-day hospital readmission. In all models, patients were stratified by age group (<65 and ≥65 years) to account for differences in Medicare eligibility.
Results: Among all patients analyzed, 4,391 self-identified as AA and 63,625 self-identified as white. Among those <65 years of age, AAs, in comparison to whites, were less likely to have private insurance (52.5% vs. 82.7%) and more likely to rely on Medicare or Medicaid (47.5% vs. 17.3%) (both p<0.001). For those age ≥65, ~90% of both AAs and whites relied on Medicare. Co-morbidities such as hypertension, diabetes and renal failure were more common among AAs than whites (p<0.001, all comparisons, both age groups).
The Figure summarizes the unadjusted (UN) and adjusted (ADJ) RRRs of referral to an IRF, SNF and HH care (vs. home self-care) in AAs (vs. whites) by age group. Among patients <65 years of age, compared to whites, AAs had higher risk of discharge to an IRF (aRRR 2.56, 95% CI, 1.77–3.71) and a SNF (aRRR 3.37, 95% CI, 2.07–5.49). Among those ≥65 years of age, AA patients also had higher risk of discharge to an IRF (aRRR 1.96, 95% CI, 1.39–2.76) and a SNF (aRRR 3.66, 95% CI, 2.29–5.84). Discharge to either IRF (<65 years: aOR 4.06, 95% CI, 3.49–4.74; ≥65 years: aOR 4.32, 95% CI, 3.67–5.09) or SNF (<65 years: aOR 2.05, 95% CI, 1.70–2.46; aOR 1.74, 95% CI, 1.46–2.07), instead of home with self-care, was significantly associated with higher odds of hospital readmission within 90 days.



Conclusions: Compared to whites, AA patients who underwent hip replacement were more likely to be discharged to an IRF or SNF. Furthermore, discharge to either IRF or SNF was associated with higher risk of hospital readmission.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2168

THU0708 LONG-TERM OUTCOME AND RISK FOR TOTAL ARTHROPLASTY OF KNEE OSTEOARTHRITIS AFTER COMPREHENSIVE REHABILITATION

F. Angst[1,1], T. Benz[1], A. Aeschlimann[1], S. Lehmann[1], B. Winteler[2], M.L. Verra[2]. *[1]Research, Rehabilitation Clinic "REHACLINIC", Bad Zurzach; [2]Physiotherapy, Bern University Hospital, Bern, Switzerland*

Background: Knee osteoarthritis affects mobility leading to substantial loss of perceived health and quality of life. Our previous study showed that aged persons with various comorbidities may profit from comprehensive rehabilitation in the short-term by corrected effect sizes up to 0.62 in pain, 0.51 in physical function, and 0.32 in psychosocial health (1).
Objectives: To follow-up those patients to 5 years by 1) quantifying observed effects in pain, function, and psychosocial health and 2) associating risk factors to total knee arthroplasty during the observation period.
Methods: Prospective cohort study with assessments at baseline (start of rehabilitation) and 1, 2, 3, 4, 5 years after. Comprehensive rehabilitation lasted 2–3 weeks for inpatients and 6 weeks for outpatients. Changes between baseline and the follow-ups were measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Short Form 36 Health Survey (SF-36). They were expressed as effect sizes (ES) according to Kazis (2). Multivariate logistic regression included various sociodemographic and disease-modifying confounders and provided adjusted odds rations (OR) for the risk of getting total knee arthroplasty.
Results: At baseline, n=205 knee osteoarthritis patients were included: 77.1% women, mean age 65.7 years (sd=10.3y), 81.5% having 3 or more comorbidities. Up to the 5 year follow-up, n=83 (40.5%) remained with complete data, 48 (23.4%) received arthroplasty. At 5 years, ES were 0.13 to 0.79 for pain, –0.12 (worsening) to 0.42 (improvement) for function, and –0.25 to 0.21 for psychosocial health. At the last follow-up before surgery, WOMAC pain had worsened by ES=–0.42 (p=0.001) and WOMAC function by ES=–0.54 (p=0.002) in the total knee arthroplasty group. Getting total knee arthroplasty was statistically significantly associated with female sex (OR=3.30), educated at university (OR=3.54), minus 1 comorbidity less (OR=1.41), and 10 (of 100 possible) points worsening on the WOMAC factor ascending/descending (OR=1.60).
Conclusions: Moderate to small improvements on pain, function, and psychosocial health were observed up to 5 years after comprehensive rehabilitation of knee osteoarthritis. Nevertheless, almost one quarter of the participants were referred to total knee arthroplasty suffering from significant deterioration in pain and function. The WOMAC seems to be sensitive to predict the need for arthroplasty. Highly educated women with low number of comorbidities and high disability to manage stairs were more likely to receive total knee arthroplasty (3).
References:
[1] Angst F, Verra ML, Lehmann S, Benz T, Aeschlimann A. Effects of inpatient rehabilitation in hip and knee osteoarthritis. A naturalistic prospective cohort study with intra-individual control of effects. Arch Phys Med Rehabil 2013;94;2139–45.
[2] Kazis ES, Anderson JJ, Meenan RF. Effect sizes for interpreting changes in health status. Med Care 1989;27(3 Suppl):S178–89.
[3] Verra ML, Benz T, Lehmann S, Aeschlimann A, Winteler B, Angst F. Long-term outcome of knee osteoarthritis after comprehensive rehabilitation – 5 year follow up and risk for total knee arthroplasty. Journal 2017;in preparation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1822

THU0709 DOES THE USE OF ANALGESIC CURRENT THERAPIES INCREASE THE EFFECTIVENESS OF NECK STABILIZATION EXERCISES FOR IMPROVING PAIN, DISABILITY, MOOD, AND QUALITY OF LIFE IN CHRONIC NECK PAIN? A RANDOMIZED, CONTROLLED, SINGLE-BLIND STUDY (A PILOT STUDY)

H. Yesil[1], S. Hepguler[2], U. Dundar[1], S. Taravati[2], B. Isleten[3]. *[1]Physical Medicine and Rehabilitation, Afyon Kocatepe University, Faculty of Medicine, Afyonkarahisar; [2]Physical Medicine and Rehabilitation, Ege University, Faculty of Medicine, Izmir; [3]Physical Medicine and Rehabilitation, Yalova Aktif Hastanesi, Yalova, Turkey*

Background: Analgesic therapies; such as interferential current (IFC) and transcutaneous electrical nerve stimulation (TENS) have been applied solo or combined with exercise for management of neck pain (NP), however, the efficacy of these combinations are unclear.
Objectives: To determine if TENS or IFC increase the effectiveness of neck stabilization exercises on pain, disability, mood, and quality of life for chronic NP.
Methods: 60 patients with chronic NP were included in the study. Patients were randomly assigned into 3 groups; Group I: neck stabilization exercise, Group II: TENS+ neck stabilization exercise and Group III: IFC+ neck stabilization exercise. Patients' pain levels (visual analogue scale (VAS)), quality of life (short form-36), mood (Beck depression inventory (BDI)), levels of disability (Neck Pain and Disability Index) and the need for analgesics were evaluated prior to treatment, at 6th and 12th week follow-up. All participants had group exercise accompanied by a physiotherapist for 3 weeks and an additional 3 weeks of home exercise program.
Results: All three groups had statistically significant improvement regarding their VAS, neck disability index and most sub-scores of short form-36 (p<0,05). At 12th- week follow-up, no difference was found between groups regarding pain, disability, and quality of life (p>0,05). On the other hand, analyses indicated significantly lower scores of neck disability index (p=0.004) and less need for paracetamol (p=0.036) in TENS group 6th-week follow-up when compared to exercise and IFC groups.
Conclusions: All treatment modalities improved pain, disability, mood and quality of life in patients with chronic NP. Besides, results suggest TENS enhanced the efficacy of exercise therapy on pain, disability and need for analgesics in acute phase but not in long term, since there was no difference at 12th week follow-up. To conclude, we think exercise protocols can be of choice since they are inexpensive, easy and effective in the management of chronic NP.
References:
[1] Acedo AA, Luduvice Antunes AC, Barros dos Santos A, Barbosa de Olveira C, Tavares dos Santos C, Colonezi GL, Fontana FA, Fukuda TY. Upper trapezius

relaxation induced by TENS and interferential current in computer users with chronic nonspecific neck discomfort: An electromyographic analysis. J Back Musculoskelet Rehabil. 2015;28(1):19–24.
[2] Kroeling P, Gross A, Graham N, Burnie SJ, Szeto G, Goldsmith CH, Haines T, Forget M. Electrotherapy for neck pain. Cochrane Database Syst Rev. 2013 Aug 26;(8):CD004251.
[3] Dusunceli Y, Ozturk C, Atamaz F, Hepguler S, Durmaz B. Efficacy of neck stabilization exercises for neck pain: a randomized controlled study. J Rehabil Med. 2009 Jul;41(8):626–31.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5843

THU0710 VALIDATION OF NEW WEIGHTED SCORING SYSTEM TO PREDICT MODIFIED HEALTH ASSESSMENT QUESTIONNAIRE SCORES IN PATIENTS WITH RHEUMATOID ARTHRITIS USING NATIONAL DATABASE OF RHEUMATIC DISEASES IN JAPAN DURING 2009 AND 2014

K. Ono[1], S. Ohashi[2], Y. Kadono[3], H. Oka[4], J. Hirose[5], T. Matsumoto[5], N. Izawa[5], M. Naito[5], J. Nishino[5], S. Tanaka[5], S. Tohma[6]. *[1]Joint Surgery, Research Hospital, The institute of Medical Science, The university of Tokyo, Tokyo; [2]Orthopaedic sugery, Satamihara Hospital, National Hospital Organization, Kanagawa; [3]Orthopaedic sugery, Saitama medical university, Saitama; [4]22nd century Medical and Research center; [5]Orthopaedic sugery, Faculty of medicine, The university of Tokyo, Tokyo; [6]Clinical Research center for allergy and rhuematology, Satamihara Hospital, National Hospital Organization, Kanagawa, Japan*

Background: We reported the impact of joint diseases on modified health assessment questionnaire (MHAQ) scores determined using 2011 data from NinJa (National Database of Rheumatic Diseases by iR-net in Japan). The MHAQ score was significantly associated with disease in almost all joints and physical ability tended to become aggravated. We also developed a joint-weighted scoring system from odds ratios. Respective integer scores assigned to disease in bilateral and unilateral joints comprised shoulder, 4 and 2; elbow, 3 and 2; wrist, 2 and 2; hip, 0 and 3; knee, 3 and 2; ankle, 2 and 2; finger, 1 and 1. Statistical analyses indicated a cut-off at 3 points using this system (Ono K, et al., Modern Rheumatology, 2016).
Objectives: To validate the weighted scoring system using NinJa data from 2009 and 2014.
Methods: We analyzed data from 7,189 and 13,459 patients listed in the NinJa database during 2009 and 2014. The presence or absence of disease in each joint (swelling and/or tenderness were considered to indicate active disease) and whether the disease was bilateral or unilateral were investigated. We calculated joint scores for each patient using a weighted scoring system and then created ROC curves for each patient based on total scores.
Results: Patients in the 2009 and 2014 groups were aged 62.4±12.6 and 64.1±12.8 years, median DAS28 CRP values were 2.9 and 2.4, and total joint scores were 3.4 and 2.4 with a significant difference ($p<0.05$; Wilcoxon signed-rank test) between the two groups. Analyses of ROC curves generated from scores derived using the new system and MHAQ revealed a cut-off of 3 points (same as 2011); AUC, 0.72, 0.68 (Table 1).

Variable	2009 (n=7,189)	2014 (n=13,459)	P value
Age (mean ± SE, years)	62.4±12.6	64.1±12.8	<0.05
Duration of disease (mean ± SE, years)	12.7±10.7	13.0±12.9	0.68
MHAQ score (median)	0.25	0.13	<0.05
DAS28 CRP (median)	2.9	2.4	<0.05
DAS28 ESR (median)	3.6	3.0	<0.05
Total joint score (median)	3.4	2.4	<0.05
Joint score: ROC analysis' cut-off value	3.0	3.0	
AUC	0.72	0.68	

Conclusions: Disease activity changed from moderate to low in the NinJa cohorts and the scoring system was validated for the years 2009 and 2014. The weighted scoring system appears useful to predict functional disability in a simpler way by examining each joint rather than changes in disease activity among patients with RA.
References:
[1] Ono K, et al., The impact of joint disease on the Modified Health Assessment Questionnaire scores in rheumatoid arthritis patients: A cross-sectional study the National Database of Rheumatic Diseases by iR-Net in Japan. Modern Rheumatology, 2016(4): 529–533.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3605

THU0711 IMPACT OF SPORTS PRACTICE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED STUDIES

L. Bouleau[1,2,3], C. Palazzo[4,5], M. Kerzoncuf[1,3], T. Pham[2,3]. *[1]Physical Medicine and Rehabilitation Department, la Timone Hospital, AP-HM; [2]Rheumatology Department, Sainte-Marguerite Hospital, AP-HM; [3]Aix-Marseille University, Marseille; [4]Service de rééducation et de réadaptation de l'appareil locomoteur et des pathologies du rachis, Cochin Hospital, AP-HP; [5]ECaMO, INSERM U1153, Paris, France*

Background: The recent update of the ASAS-EULAR management recommendations for axial spondyloarthritis highlights effectiveness of home exercises and physical therapy. However, the adherence rates to these structured exercises are low, what could limit their long-term effectiveness. An option could be to replace or to complete the practice of specific exercises with the regular practice of a recreational sport activity. Data concerning the effectiveness and tolerance of sports in ankylosing spondylitis (AS) are scarce.
Objectives: To assess the tolerance and effectiveness of recreational sports practice on function, spinal mobility, disease activity, pain and quality of life in patients with AS.
Methods: A systematic review was performed according the PRISMA guidelines, using the following search engines: MEDLINE (Pubmed), COCHRANE Library, Google Scholar and Physiotherapy Evidence Database (PEDro), completed by a manual research. We included randomized controlled trials (RCTs) from 1984 to September 2016, with participants with AS fulfilling the New York modified criteria, and interventions involving sports practice. We defined "sports" according to the MeSH definition as "Activities or games, usually involving physical effort or skill [with purpose of] pleasure, competition, and/or financial reward." Exercise therapy and physiotherapy were not included in the research. The outcomes measured were the followings: stiffness/spinal mobility, function, disease activity, quality of life, pain, side effects. Methodological quality was assessed using the PEDro scale.
Results: From the 40 studies identified after screening, only 5 articles were selected for eligibility. One study was excluded (poor quality). The 4 RCTs concerned a total of 187 AS patients. Interventions were Pilates, Tai Chi, swimming, walking, and exergames. Control groups received either no specific intervention or standard exercise therapy. The studies were too heterogeneous to be pooled but the comparisons inter and intra-groups in each study tended to show significant effectiveness of sports practice on function, activity and spinal mobility. Data on tolerance were scarce, but no significant side effect was reported.
Conclusions: Recreational sports practice may improve function, activity and spinal mobility in patients with AS. However, there are very few studies available, and evidence-level is low. More controlled randomized clinical trials should be conducted in the future to confirm the effectiveness and safety of sports in AS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4968

THU0712 DUTCH NORM SCORES FOR FOUR DUTCH-FLEMISH PROMIS ITEM BANKS IMPORTANT FOR PATIENTS WITH RHEUMATOID ARTHRITIS

M.H. Crins[1], L.D. Roorda[1], H.C. de Vet[2], R. Westhovens[3,4], M. Boers[2,5], J. Dekker[6], C.B. Terwee[2]. *[1]Amsterdam Rehabilitation Research Center, Reade; [2]Department of Epidemiology and Biostatistics, The EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, Netherlands; [3]Rheumatology, University Hospitals; [4]Department of Development and Regeneration, Skeletal Biology and Engineering Research Center, KU Leuven, Leuven, Belgium; [5]Amsterdam Rheumatology and immunology center; [6]Department of Rehabilitation Medicine and Department of Psychiatry, VU University Medical Center, Amsterdam, Netherlands*

Background: In the assessment of patients with rheumatoid arthritis (RA) it is important to measure physical function, fatigue, pain behavior and pain interference. The Patient-Reported Outcomes Measurement Information System (PROMIS) initiative developed item banks for measuring these concepts. These item banks were translated into Dutch-Flemish language.
Objectives: To facilitate interpretation and implementation of PROMIS in the Netherlands, we aimed to calibrate and validate the Dutch-Flemish PROMIS Physical Function (DF-PROMIS-PF), Fatigue (DF-PROMIS-FA), Pain Behavior (DF-PROMISPB) and Pain Interference (DF-PROMIS-PI) Item Banks in the general Dutch population, to obtain Dutch norm scores for these item banks.
Methods: 3365 persons of the general Dutch population completed a web-based survey, of which 1309 persons completed the full DF-PROMIS-PF (121 items), 1007 persons completed the full DF-PROMIS-FA (95 items), and 1049 persons completed the full DF-PROMIS-PB (39 items) and the full DF-PROMIS-PI (40 items). The sample was stratified for gender, age, education, and ethnicity according to the distribution of the 2015 census of the general Dutch population. A one-factor confirmatory factor analysis (CFA) was performed per item bank to assess unidimensionality. A graded item response model (GRM) was fitted per item bank to evaluate the item characteristics of the item banks and to facilitate future development of computer adaptive tests (CATs). Ordinal regression models were used to evaluate Differential Item Functioning (DIF) for language (Dutch vs. English) as a measure of cross-cultural validity.
Results: All four item banks showed good fit to the GRM: they showed good fit indices for CFA and high percentages of explained variance by first factor. The item banks showed only little local dependency and the scalability coefficients suggested strong scalability for all four item banks. The item characteristics

showed good coverage across the range of the four concepts. DIF analyses are in progress.
Conclusions: The item banks exhibited good psychometric properties in the general Dutch population. The four Dutch-Flemish PROMIS item banks can be used to develop CATs for measuring physical function, fatigue, pain behavior and pain interference in the Netherlands. Dutch norm scores are presented.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1247

THU0713 HOW THE VARIATION IN THE LUMBOPELVIC PATTERNS OF MOVEMENT AFFECTS THE NEUROMOTOR CONTROL OF THE BICEPS FEMORIS DURING TRUNK FORWARD BENDING

M. Sarti[1], R. Expositor-Rodríguez[2], R. Borona-Carvajal[1], M. Ybañez-García[3], M. Fuster-Ortí[4]. *[1]Human Anatomy and Embryology, Universidad de Valencia (UVEG); [2]Inst, for Research on Musculoskeletal Disorders, Catholic University of Valencia; [3]Rheumatology Section, Pesset Hospital; [4]Department of Statistics and Operations Research, Universidad de Valencia (UVEG), Valencia, Spain*

Background: Trunk forward bending is one of the most common activities in daily living; it is a two-part movement involving the lumbar spine flexion and pelvis rotation at hip joint. The pattern of movement during forward bending was defined as the relative contribution of the lumbar spine to pelvis motion, and was expressed as the ratio between the ranges of lumbar spine motion to pelvis motion (L/P), which, calculated at certain degrees of trunk flexion during the entire movement, provides the lumbo-pelvic rhythm. This is associated with a specific pattern of activation for back and hip extensor muscles which was coined as flexion relaxation phenomenon, observed either in the erector spinae and biceps femoris (BF). It has been shown that in healthy people lumbopelvic pattern of movement for entire flexion varies, showing both lumbar spine dominant and pelvis dominant-patterns of movement.
Objectives: To find out whether the variation in the lumbopelvic pattern of movement (lumbar spine or pelvis dominant) affects the appearance of the relaxation of the BF during trunk forward bending.
Methods: Surface electrodes were applied to the skin on right BF, midway between ischial tuberosity and head of fibula to record EMG during a trunk flexion movement from the upright position. The EMG signal was full-wave rectified and averaged (40ms) to produce a linear envelope. An electrogoniometer measured the differential lumbar spine - pelvis sagittal angular displacement during trunk flexion in asymptomatic subjects. Both signals (EMG and degrees) were synchronously and continuously captured during the movement. Ranges of flexion (ROF) for the lumbar spine, pelvis and trunk motion were calculated for the entire movement. The subjects (both sexes) were assigned to group-L (n=11) and group-P (n=15) according to exhibiting lumbar spine and pelvis dominant patterns of movement (average age,24.5±3.3years).The myoelectric relaxation (MR) appearance was defined in terms of degrees of flexion where the electrical activity of the BF was less than that in upright posture (EMG basal), at this point the degrees of flexion for the pelvis and spine were determined; and their respective "range of motion" (ROM) was calculated and normalized to range of trunk flexion. One-way MANOVA was used to determine differences in range of flexion at the appearance of the myoelectric relaxation between groups.
Results: ROF for MR of the BF was significantly greater in group-P (77,3%±3,4%) ($p<0.01$) than in group-L (47,8%±2,4%) for the pelvis, whereas ROF for the lumbar spine was significantly greater in group-L 95%±1,2% ($p<0.01$) than in group-P 40,41%±1,7%.
Conclusions: In healthy subjects, differences in lumbopelvic patterns of movement during trunk flexion vary the appearance of the relaxation of the biceps femoris in the range of flexion. Present results show that the variance of the lumbar spine and pelvis Kinematics is associated with the neuromotor control of the biceps femoris.
Acknowledgements: Grants supporting present study: Ref. FIS2001–0070–01, Ref. TIC2001–2786- C02–02, Ref. AP2001–376
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6855

THU0714 INVESTIGATING THE EFFECTS OF HYPERMOBILITY ON BALANCE VARIABLES

M. Selmani[1], A. Elvan[1], B. Akcay[1], G. Kenar[2], A.M. Birlik[2], S. Angin[1], I.E. Simsek[1]. *[1]School of Physical Therapy and Rehabilitation, Dokuz Eylul University Institute of Health Sciences; [2]Department of Internal Medicine, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey*

Background: Hypermobility syndrome (HMS) is a clinical syndrome in which the range of motion of the joint is observed above normal ranges without being associated with a rheumatic disease. Excessive joint motion in HMS reduces joint stability and joint position sense and also can cause pain. Decreased muscle tone and tensile forces of the tendons cause decreased locomotor system stiffness and impairment of proprioception mechanisms. These problems in proprioceptive mechanisms can lead to balance-related disorders in individuals with hypermobility syndrome
Objectives: The aim of this study was to investigate the possible effects of hypermobility on balance variables.
Methods: 50 hypermobile (5 males and 45 females) volunteers diagnosed with Brighton Scale and 50 healthy (21 males and 29 females) volunteers were included in this cross sectional study. Participants with a score of 4 or over according to the Beighton scale were referred to a rheumatologist and were administered Brighton scale. Participants who were diagnosed by the physician were included in the hypermobile group. The objective balance evaluation was conducted using a balance platform. Evaluation variables were; static balance on single foot, static balance on both feet, limits of stability test and tandem walking. analysis was performed using independent samples t-test.
Results: The mean age was found 21,69±2,13 years old for the control group and 20,09±2,65 years old for the HMS group. Body Mass Index was found 22,13±3,54 kg/m^2 in the control group and 21,54±3,50 kg/m^2 in the HMS group. HMS group showed significant wider step width in tandem walking (p=0,001), significantly longer reaction time (p=0,23, p=0.030), significantly higher end-point excursion (p=0.003, p=0,026, p=0,049), significant higher mean maximum excursions (p=0.018) (Table 1).

Table 1. Comparison of Groups About Balance Variables

	HMS Group (Mean ± SD)	Control Group (Mean ± SD)	p
Tandem Walking			
Step-Width (cm)	6,52±0,89	7,20±1.10	0.001*
Limits Of Stability			
Reaction Time 2 (sec)	0,91±0.44	0,72±0.37	0.023*
Reaction Time 6 (sec)	0,78±0,36	0,64±0,25	0.030*
End-Point Excursion 1 (°/sec)	86,69±17,73	73,19±26,17	0.003*
End-Point Excursion 4 (°/sec)	76,56±17,36	83,92±14,91	0.026*
Maximum Excursion 5 (°/sec)	76,54±18,31	82,69±11,50	0.049*
Mean Maximum Excursion (°/sec)	94,56±6,51	97,25±4,29	0.018*

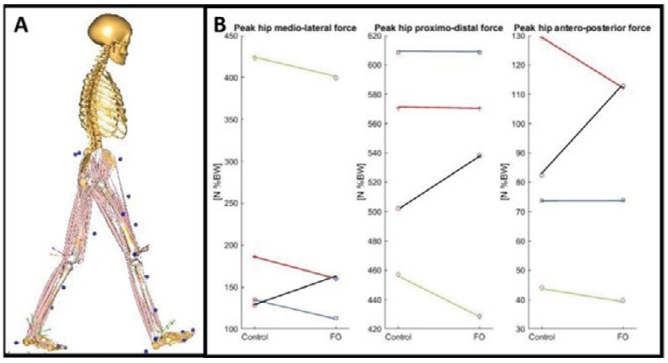
*$p<0.05$.

Conclusions: In this study it was found that hypermobility has significant effects on the stability limits test and tandem walking. In previous studies it was found that hypermobility affects the static balance assessment variables (1, 2), but in this study dynamic balance assessment variables were affected.
References:
[1] Iatridou K, Mandalidis D, Chronopoulos E, Vagenas G, Athanasopoulos S. Static and dynamic body balance following provocation of the visual and vestibular systems in females with and without joint hypermobility syndrome. J Bodyw Mov Ther. 2014 Apr;18(2):159–64. doi: 10.1016/j.jbmt.2013.10.003.
[2] Juul-Kristensen B, Johansen K, Hendriksen P, Melcher P, Sandfeld J, Jensen BR. Girls with generalized joint hypermobility display changed muscle activity and postural sway during static balance tasks. Scand J Rheumatol. 2015 Sep 1:1–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6256

THU0715 ESTIMATION OF THE EFFECT OF FOOT ORTHOTICS ON HIP JOINT LOADING FOR RHEUMATOID ARTHRITIS PATIENTS USING MRI-BASED MUSCULOSKELETAL MODELS: A PILOT STUDY

M.B. Simonsen[1], K. Næsborg-Andersen[2], M.R. Kowalski[3], K. Hørslev-Petersen[4], M.S. Andersen[1]. *[1]Department of Mechanical and Manufacturing Engineering, Aalborg University, Aalborg; [2]Bandagist-Centret A/S, Haderslev; [3]Department of Rheumatology, Hjørring Hospital, Hjørring; [4]King Christian 10th Hospital for Rheumatic Diseases, Gråsten, Denmark*

Background: Over 85% of rheumatoid arthritis (RA) patients experience feet and ankle problems during the course of the disease. Persistent foot and ankle problems still occur even after clinical remission is reached [1]. In RA, synovitis, effusion, and eventually erosive arthritis are thought to cause clinically recognizable planovalgus or valgus heel [1]. With the intention to stabilize and align the foot, patient-specific foot orthotics (FO) are commonly prescribed to this patient group. A limitation of the previous literature on FO to treat RA and related diseases is that it has focused exclusively on clinical outcomes of FO such as pain and physical function, while overlooking the biomechanical principles on which the rationales for FO is based [2].
Objectives: The aim of this study was to investigate the effect of patient-specific FO on hip loading during gait. This was accomplished by developing patient-specific (PS) musculoskeletal models (MS) capable of estimating joint mechanics with and without the FO.
Methods: Four early stage RA patients were recruited for this study. A pair of FO was developed for each patient using a weight bearing casting technique. PS bone geometry was obtained from magnetic resonance imaging (MRI) images and segmented in an image analysis package (Mimics 19, Materialse, Belgium). Motion capture was performed with an eight-camera setup (Qualysis, Sweden) with reflective markers together with three force plates (AMTI, USA) sampling at 100 and 1000 Hz, respectively. The gait trials consisted of two conditions: one with the PS FO and one with a control insole (C). PS MS models of each patient were developed using the AnyBody Modeling System (AnyBody Technology, Denmark), Figure 1A. Muscle attachments were made PS based on the Twente Lower Extremity Model version 2.0 dataset using advanced morphing to customize a generic cadaver-based model with respect to PS morphology



acquired from MRI [3]. Accurate joint centers and axes were calculated with analytical surface fits to the segmented MRI bones for the hip, knee and ankle.
Results: Peak hip force for medio-lateral (ML) proximo-distal (PD) and antereo-posterior (AP) is presented in Figure 1B for the C and FO with values for each subject.
Conclusions: The results of this study indicate that FO can change the load distribution in the hip joint. A reduction or similar values for ML, DP and AP force was found for all but one participant. These changes may potentially contribute to the reduction in pain. Further studies are needed to investigate if there is a relationship between changed loading and pain for RA patients. This knowledge can potential be used for design of better FO and clinical guidelines for use of FO.
References:
[1] Hennessy K. et al, Arthritis Care Res, 64: 311–320, 2012.
[2] Lewinson R. et al., Ann Biomed Eng, 44: 3173–3185, 2016.
[3] Marra M, et al., J Biomech Eng. 137: BIO-14–1490, 2015.
Acknowledgements: The study is financially supported by The Danish Rheumatism Association [R142-A4113].
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2169

THU0716 LONGITUDINAL OUTCOME OF AEROBIC FITNESS IN ADOLESCENTS AND YOUNG ADULTS WITH JIA

P.V. Pelt[1,2], T. Takken[3], M.V. Brussel[4], R. Dolhain[1], J. Hazes[1], J. Bijlsma[5], N. Wulffraat[6], A. Kruize[5]. *[1]Department of Rheumatology, Erasmus MC, University Medical Center Rotterdam, Rotterdam; [2]Department of Pediatric Immunology, Wilhelmina Children's Hospital, University Medical Center Utrecht; [3]Child Development and Exercise Center, Wilhelmina Children's Hospital, University Medical Center Utrecht; [4]Child Development and Exercise Center, Wilhelmina Children's Hospital, University Medical Center Utrecht; [5]Department of Rheumatology and Immunology, University Medical Center Utrecht; [6]Department of Pediatric Immunology, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, Netherlands*

Background: Aerobic fitness may serve as an important health-related outcome measure in JIA. A reduced aerobic fitness is associated with cardiovascular morbidity, mortality and osteoporosis in adult patients with chronic diseases. However, in adolescents and young adults, long-term outcome data of aerobic fitness are unknown. Reduced aerobic fitness was described in cross-sectional studies in children and adolescents with JIA, and was more impaired in active disease
Objectives: Our objectives are to describe course of the aerobic fitness in a longitudinal cohort of adolescents and young adult JIA-patients who are intensively treated including the possibility of biologics and to identify the association of clinical variables with aerobic fitness.
Methods: In a longitudinal cohort, all consecutive JIA patients aged 10–24 years were included after informed consent. Annual examinations were obtained from demographic and disease-related items. At baseline and end of the study, aerobic fitness (VO2peak) was assessed using a graded cardiopulmonary exercise test (CPET) to volitional exhaustion performed on an electronically braked cycle ergometer. Absolute and relative VO2-peak values were measured and related to healthy controls (Z-scores), using one-sample T-tests. Non-parametric tests were used to evaluate results
Results: Paired Z-scores were available from 27 patients. 44% were male, median age at baseline was 13,0yrs (IQR 4,3), disease duration 7,6yrs (6,7), JADAS27 4,0 (5,9), DAS28 2,2 (1,2). 76% of the patients were in DAS28-remission. 11% had systemic JIA, 7% persistent oligoarticular and 82% had a polyarticular course. Baseline and end Z-scores were reduced compared to healthy controls (ZAbs_base -0,68, IQR2,3 p=0,01; Zrel_base -1,33, IQR 2,0, p<0,01; Zabs_end -0,23, IQR 1,7, p=0,06; Zrel_end -0,87, IQR 2,2, p=0,01) and did not change significantly over time (change Zabs_change 0,45, p=0,34; Zrel_change 0,46, p=0,31). At baseline, MTX-use (p=0,04) and a higher DAS28 (p=0,015) and ESR (p=0,013) are associated with a worse outcome of aerobic fitness. The greatest improvement of aerobic fitness over time was seen in patients with a higher ESR (p<0,01) and thrombocytes (p<0,01) at baseline. Multivariate analysis showed that a higher DAS28 and male gender were the most important variables for worse aerobic fitness at baseline, a higher ESR at baseline was the most important predictor for improving aerobic fitness over time
Conclusions: Aerobic fitness is significantly reduced in adolescents and young adults with JIA and does not improve over time, despite intensive treatment. Be aware of a reduced quality of life due to a persistent reduced aerobic fitness during disease course of JIA, despite low disease activity
References:
[1] Aerobic capacity and disease activity in children, adolescents and young adults with juvenile idiopathic arthritis (JIA). Ph.A. van Pelt MD, T. Takken PhD, M.van Brussel PhD, M. de Witte. A.A. Kruize*, MD, N.M.Wulffraat* MD, PhD. Pediatr Rheumatol Online J. 2012 Aug 27;10(1):27. doi: 10.1186/1546–0096–10–27.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4756

THU0717 MIRROR VISUAL FEEDBACK THERAPY IMPROVES CLINICAL OUTCOMES AND THE ACTIVITY OF DAILY LIVING TO PATIENTS WITH HAND COMPLEX REGIONAL PAIN SYNDROME

S. Patru[1], I.R. Marcu[2], D. Matei[1], A.M. Bumbea[1], A.C. Bighea[1]. *[1]Physical Medicine and Rehabilitation; [2]University of Medicine and Pharmacy of Craiova, Craiova, Romania*

Background: Wrist osteoporotic fractures may be as disabling as vertebral or hip fractures and the functional decline attributed to them is similar to that seen for arthritis and diabetes mellitus. Sometimes these fractures will lead to a painful, debilitating condition with sensory and motor disturbances, changes in vascular tone, temperature and edema- complex regional pain syndrome (CRPS). We found some clinical trials and case reports which conclude that mirror visual feedback therapy (MVFT) improves clinical outcomes and the activity of daily living to patients with hand neurological disorders, including CRPS.
Objectives: In this controlled randomized clinical study we tried to investigate the effects of (MVFT) in CRPS type I following osteoporosis wrist fracture.
Methods: We included 21 subjects with osteoporotic wrist fracture and early CRPS (duration of 3–4 weeks), with a single hand affected by allodynia, stiffness and vasomotor disturbances, from Physical Medicine and Rehabilitation outpatient clinic. They are randomly assigned into two groups: MVFT group (n=11, simply place a mirror between their two hands and train the patient by asking them to move both hands while watching the reflection of the non-affected hand in the mirror, 10 minutes for each session, four times a day) and Control group (n=10, moved both hands separated by an opaque partition between the arms). All subjects also received conventional therapy. On presentation and after 4 weeks of rehabilitation programme we assessed the wrist flexion and extension with a goniometer and the Patient-Rated Wrist Evaluation (PRWE) a 15-items questionnaire designed to measure wrist pain and disability in activities of daily living.
Results: Subjects in the mirror therapy group showed significant improvement in range of motion: extension increased with 50.4% vs. 41.7% and for flexion MVFT achieved 33.2% and Control group 16.8% ($P<.001$). The rehabilitation programme also increased hand function with better results to 4 weeks PRWE for MVFT group (40.4 vs. 51.8, $P=0.003$).
Conclusions: MVF is a simple, inexpensive, without adverse events treatment option that significantly reduces pain and stiffness and improves hand mobility in early CRPS after osteoporosis wrist fracture.
References:
[1] Vladimir Tichelaar YI, et al. Mirror box therapy added to cognitive behavioural therapy in three chronic complex regional pain syndrome type I patients: a pilot study. Int J Rehabil Res 2007; 30: 181–8.
[2] Bache SJ, Ankcorn L, Hiller L, Gaffrey A. Two different approaches to physiotherapy management of patients with distal radius fractures. Physiotherapy. 2000;86:383.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2339

THU0718 DIFFERENCES IN THE COURSE OF ITALIAN- AND GERMAN-SPEAKING PATIENTS' OUTCOME AFTER INTERDISCIPLINARY PAIN PROGRAM

T. Benz[1,2], S. Lehmann[2], R. Brioschi[2], A. Elfering[1], A. Aeschlimann[2], F. Angst[2]. *[1]Institute of Psychology, University of Bern, Bern; [2]Research Department, RehaClinic, Bad Zurzach, Switzerland*

Background: Available evidence shows that the experience and perception of pain varies among different populations. Further, inequalities are reported in pain treatment across various types of pain and in different settings (1). In particular, it is unknown how much immigrants in Western European countries profit from pain management programs.
Objectives: The aim of this study was to detect differences in the course of Italian- and German-speaking patient's state of health and quality of life after a 4-week standardized interdisciplinary pain management program in German or in Italian.
Methods: The prospective cohort study with 61 Italian-speaking and 63 German-speaking patients with fibromyalgia or chronic back pain measured health-related quality of life, pain, anxiety and depression comparing at baseline, after 4 weeks of pain program and at 1 year follow-up. Differences between the two groups

were tested on significance by generalized estimation equations (GEE) (2). This method modeled changes of health by multivariate logistic regression adjusting for sex, education, number of comorbidities and the baseline score over both follow-ups for each scale.

Results: Italian-speaking patients (n=61) showed higher proportions of males, lower educated and less burdened by comorbidities than German-speaking patients (n=63). At baseline, physical and psychosocial health, depression and anxiety of the Italian-speaking patients were worse than German-speaking patients, with the exception of less pain in the Italian-speaking patients on the SF-36. Changes of health showed more improvement in German- than in Italian-speaking patients on all scales and at both follow-ups. In GEE, the highest differences were observed in SF-36 physical functioning (p=0.035), HADS anxiety (p=0.038) and HADS depression (p=0.023). On SF-36 bodily pain, the difference was not significant (p=0.166).

Conclusions: This study detected that short- and midterm outcome of Italian-speaking patients was worse than that of German-speaking patients, even after adjustment for baseline differences. The reasons for this study's results remain unclear, but may have consequences for future management of Italian-speaking patients in interdisciplinary pain management programs. Considering language as a proxy for acculturation, this supports the hypothesis that patients with lower level of acculturation may have special needs in therapeutic management. A cultural sensitive approach in a multidisciplinary pain program might enhance the positive outcome in the short- and mid-term (3).

References:

[1] Green CR, Anderson KO, Baker TA, Campbell LC, Decker S, Fillingim RB, Kalauokalani DA, Lasch KE, Myers C, Tait RC, Todd KH, Vallerand AH. The unequal burden of pain: confronting racial and ethnic disparities in pain. Pain Med 2003;4:277–94.

[2] Twisk JW. Generalized estimating equations. Applied longitudinal data analysis for epidemiology. 2nd ed. Cambridge: Cambridge University Press; 2013: p 57–68.

[3] Benz T, Lehmann S, Brioschi R, Elfering A, Aeschlimann A, Angst F. Comparison of short- and mid-term outcome of Italian- and German-speaking patients after an interdisciplinary pain management program. Disabil Rehabil 2017; in preparation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5888

THU0719 LONG-TERM COURSE OF HEALTH AND WORKING CAPACITY AFTER A REHABILITATION PROGRAM FOR WHIPLASH INJURY

T. Benz[1], P. Haiduk[1], S. Lehmann[1], F. Gysi-Klaus[1], B.A. Michel[2], A. Aeschlimann[1], F. Angst[1]. *[1]Research Department, RehaClinic, Bad Zurzach; [2]Clinic of Rheumatology, University Hospital of Zurich, Zurich, Switzerland*

Background: Persistent pain and disability of whiplash injury associated disorders (WAD) cause high burden for the individual and costs for healthcare.

Objectives: The aim of this study was to determine state and change of health and working-capacity five years after a standardized inpatient pain management program of four weeks.

Methods: This prospective cohort study quantified health and quality of life by the generic Short Form 36 (SF-36, 100=best), the neck-specific Northern American Spine Society (NASS) form, and the Coping Strategies Questionnaire (CSQ). SF-36 data were compared to age-, sex-, and comorbidity-specific German population norms (1). Changes of health were determined using effect sizes (ES) at the 6 month and the 60 month follow-up. Changes of health were determined using effect sizes (ES) (2).

Results: The 59 participants had mean age of 40.3 years (sd=12.3), 83% were women, and 37% had one or more comorbidites. At 5 years, health was worse on all SF-36 scales when compared to the norms ($p<0.001$), varying from mean 41.5, norm 82.3 on role physical to mean 65.7, norm 71.0 on mental health (all $p<0.001$).

Table 1

Effect sizes (ES)	Entry to 60 months	6 months to 60 months
SF-36 Physical functioning	0.99	0.16
SF-36 Role physical	2.22	0.83
SF-36 Bodily pain	1.61	0.78
SF-36 Vitality	0.89	0.32
SF-36 Social functioning	0.71	0.47
SF-36 Mental health	0.61	0.30
NASS Pain	1.12	0.56
NASS Function	0.78	0.26
CSQ Catastrophizing	1.03	0.62

Median working capacity improved from 0 at entry to 21 at 6 months and to 30 hours/week at 5 years.

Conclusions: Moderate to large long-term effects were observed. Substantial improvements still occurred between 6 and 60 months after start of the pain program, especially in pain, catastrophizing, and physical role performance. Improvements observed after the inpatient pain program can be maintained and expanded in the long-term at home (3).

References:

[1] Kurth BM, Ellert U. The SF-36 questionnaire and its usefulness in population studies: Results of the German Health Interview and Examination Survey 1998. Soz Praeventivmed 2002;47:266–277.

[2] Kazis ES, Anderson JJ, Meenan RF. Effect sizes for interpreting changes in health status. Med Care 1989;27(3 Suppl):S178–89.

[3] Haiduk P, Benz T, Lehmann S, Gysi-Klaus F, Aeschlimann A, Michel BA, Angst F. Interdisciplinary rehabilitation after whiplash injury: An observational prospective five year outcome study. Medicine 2017;in press.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6178

FRIDAY, 16 JUNE 2017

Cartilage, synovium and osteoimmunology

FRI0001 ALL STAGES OF SYNOVIAL MESENCHYMAL STEM CELL ACTIVITY INCLUDING ADHESION, PROLIFERATION, MIGRATION AND CHONDROGENIC DIFFERENTIATION ARE SUPPORTED BY HUMAN PLATELET LYSATE- IMPLICATIONS FOR NOVEL ONE STAGE JOINT REGENERATIVE PROCEDURES

A. Altaie, T.G. Baboolal, E. Jones, O. Wall, D. McGonagle. *Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*

Background: Both synovial and related synovial fluid-derived mesenchymal stem cells (SF-MSC) are highly proliferative and chondrogenic and have direct access to superficial cartilage injuries [1]. Human platelet lysate (PL) is being increasingly used for joint regenerative approaches [2,3] but the biological basis for in vivo effect, if any is lacking.
Objectives: The study evaluated the effect of PL on adhesion, proliferation, migration and trilineage differentiation of synovial cavity derived MSCs in comparison to "gold standard" foetal calf serum (FCS) based stem cell media.
Methods: MSCs were derived from joint cavity washout in patients undergoing anterior cruciate ligament reconstruction or meniscal repairs. Cells were plated in StemMACS (FCS media) or with DMEM Supplemented with 10% Stemulate (PL media, Cook Regentec). Standard MSC proliferation, trilineage differentiation assays, and transwell migration assays were performed for both conditions.
Results: PL enhanced MSC colonies sizes (CFU-F) by 2.5 folds compared to FCS (p=0.0023, n=5). PL shortened MSC doubling times (p=0.0411, n=6). However, PL had no impact on CFU-F numbers (p=0.5973, n=5). In transwell migration assays, MSC migration was significantly increased toward 10%PL compared to 10%FCS (p=0.0286, n=6). Under standard chondrogenic induction conditions, PL-expanded MSC showed 30% more sulphated GAG (sGAG) production compared to FCS-expanded cells (n=4). In osteogenic and adipogenic induction, Alizarin red staining Ca++ assay and Nile Red showed no significant difference compared to FCS expanded cells (p=0.3429, n=4). Interestingly, replacing TGFβ with 20% PL was as good as standard chondrogenic media and with increasing PL percentage sGAG production increased (n=4). In same time using PL with high glucose media in 1:1 ratio was efficient to produced sGAG as compared to negative control (media only) (p=0.0286, n=4, figure 1). Moreover, substituting FCS with PL in the osteogenic media resulted in increased Ca++ deposition in both PL and FCS expanded cells by 90% and 100% compared standard osteogenic media.

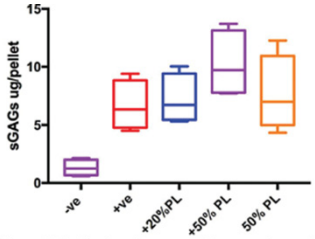


Figure 1: Evaluation the use of PL as an alternative TGFBeta in chondrogenic media. A: sGAGS activity of SF-MSC in different chondrogenic media; -ve: high glucoase+10% FCS, +ve: complete chondrogenic media, +20%PL: complete media with no TGFBeta and with 20%PL, +50%PL: complete media with nc TGFBeta and with 50%PL, 50%PL: high glucose DMEM with 50%PL. (N=4), Mann-Whitney test.

Conclusions: This is the first study that assessed joint cavity MSC responses to PL. All aspects of joint cavity derived MSC biology towards cartilage repair were augmented in vitro with PL based media over "gold standard" MSC media. This work provides biological plausibility for the combination of PL with joint resident MSC towards endogenous joint repair strategies.
References:
[1] Jones, E.A., et al., Synovial fluid mesenchymal stem cells in health and early osteoarthritis: detection and functional evaluation at the single-cell level. Arthritis Rheum, 2008. 58(6): p. 1731–40.
[2] Morito, T., et al., Synovial fluid-derived mesenchymal stem cells increase after intra-articular ligament injury in humans. Rheumatology (Oxford), 2008. 47(8): p. 1137–43.
[3] Ben Azouna, N., et al., Phenotypical and functional characteristics of mesenchymal stem cells from bone marrow: comparison of culture using different media supplemented with human platelet lysate or fetal bovine serum. Stem Cell Res Ther, 2012. 3(1): p. 6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5958

FRI0002 DEVELOPMENT OF AN IN VITRO MULTI-COMPONENT 3D JOINT MODEL TO SIMULATE THE PATHOGENESIS OF ARTHRITIS

A. Damerau[1], A. Lang[1,2,3], M. Pfeiffenberger[1], F. Buttgereit[1,2], T. Gaber[1,2]. *[1]Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin Berlin; [2]German Arthritis Research Center; [3]Berlin-Brandenburg School of Regenerative Therapies, Charité-Universitätsmedizin Berlin, Berlin, Germany*

Background: Our ultimate goal is to develop a valid *in vitro* 3D model to simulate the immune mediated pathogenesis of arthritis in order to present an alternative experimental setup for the traditional animal models. Therefore, we work to establish an *in vitro* simulation of a healthy joint, followed by the depiction of an inflamed arthritic joint to finally study the efficacy of drug treatment. The *in vitro* 3D joint model consists of different components including an (1) osteogenic and (2) chondrogenic part, (3) the joint space with synovial fluid and (4) the synovial membrane. The model is suggested to include all involved cell types and thus, to allow interactions between cells by cell contacts and signaling molecules. To our knowledge, there is currently no valid 3D model which is able to mimic an inflamed arthritic joint.
Objectives: Here, we aim to mimic the (1) osteogenic and (2) chondrogenic part of the joint for our *in vitro* multi-component 3D joint model.
Methods: We used β-tricalcium phosphate (TCP) particles as a mineralized 3D bone scaffold and human bone marrow derived mesenchymal stem cells (hMSCs), non- and pre-differentiated towards osteoblastic lineage. Both were cultured up to 21 days on β-TCP. Osteogenic differentiation was performed in the presence of osteogenic supplements under normoxic conditions (37 °C, 18% O2). Adhesion and proliferation of hMSCs on β-TCP were evaluated by immunofluorescence and histological analysis. To confirm cell attachment and biocompatibility of β-TCP particles cellular release of LDH was assessed. Osteogenic differentiation was analyzed on gene expression level using qRT-PCR. The chondrogenic model, a scaffold-free 3D cartilage construct (fzmb GmbH) was generated using hMSCs. Chondrogenic differentiation was performed under hypoxia (37 °C, 1% O2) with intermittent mechanical stimulation and analyzed by histology.
Results: We developed an *in vitro* 3D trabecular bone model by seeding hMSCs on β-TCP scaffold after pre-incubation for 24 hours. The analysis of cell viability via LDH detection showed no toxic effects on the cells seeded as compared to the corresponding control. Furthermore, we assessed cell attachment and proliferation by measurement of LDH activity after scaffold crushing. As a result, samples showed higher LDH activity compared to the controls. Histological and immunofluorescence analysis based on DNA and actin staining demonstrated cell attachment until day 21. After 21 days, cells were located more inside the scaffold compared to day 1. qRT-PCR expression of bone-related genes such as RUNX2, SPP1 and COL1A1 confirmed the phenotypic change during osteogenic differentiation on the scaffold. Furthermore, the scaffold-free 3D chondrogenic structure was confirmed by HE staining representing the different zones. Cartilage phenotype was confirmed by the reduced expression of Col1a1, an abundant expression of Col2a1 and Aggrecan.
Conclusions: The initial results from our *in vitro* 3D osteogenic and chondrogenic model confirm good cell vitality which indicates successful progression. To confirm the exchange of β-TCP through cellular matrix, we will now extend the assay co-cultivation time for up to 6 weeks. This 3D multi-component joint model should enable us to simulate arthritis and to study the efficacy of drug treatment *in vitro.*
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5889

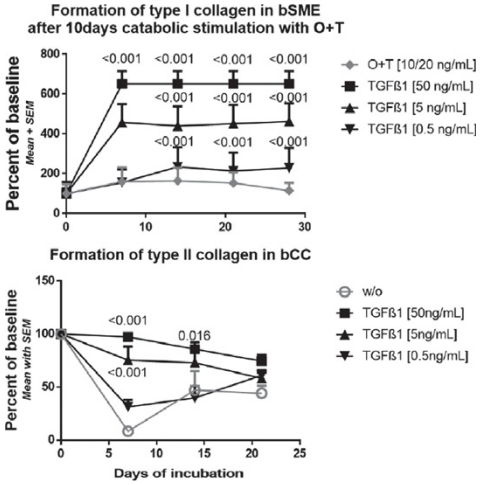
FRI0003 MODULATION OF ARTICULAR JOINT TISSUE TURNOVER IN BOVINE EXPLANT MODELS OF CARTILAGE AND SYNOVIAL MEMBRANE: DEVELOPMENT OF NOVEL DRUG DEVELOPMENT TOOLS

A.S. Siebuhr, C.A. Cabanes, S. Dahab, M.A. Karsdal, A.-C. Bay-Jensen, C.S. Thudium. *Biomarkers and Research, Nordic Bioscience, Herlev, Denmark*

Background: There is currently a lack of disease modifying OA drugs approved by the drug administration agencies. One of the obstacles in the development of DMOADs that can effectively halt or reverse cartilage degradation is the lack of robust and reproducible model systems for early drug testing.
Objectives: To develop inducable anabolic bovine ex vivo models of 1) synovial membrane explants and 2) synovial membrane explants in co-culture with cartilage explants.
Methods: Synovium (bSME) from healthy bovine (<24months old) hind knees were isolated and cut into explants of 30±5 mg. Bovine cartilage (BEX) was cut into equally sized explants using a 6mm diameter biopsy puncher. bSME and BEX were cultured together (bCC) or alone for 14–35 days in DMEM-GlutaMAX™ with or without continuous stimuli in 4 replicates per treatment: Oncostatin M [10 ng/mL] + TNF-α [20 ng/mL] (O+T), O+T + GM6001 [1uM], IGF-1 [100ng/mL] or TGFβ-1 [50–0.5 ng/mL]. Media were changed 3 times a week and the viability was assessed with Alamar Blue every week. The reversibility of synovial membrane degradation was investigated by 10 days incubation with O+T followed by 21 days of TGFβ-1 [50–0.5 ng/mL] treatment. The following biomarkers were assessed in the conditioned media by competitive ELISA: Type I, II and III collagen degradation (C1M, C2M and C3M), formation of type I and II collagen (P1NP

and PRO-C2), aggrecanase degraded aggrecan (AGNxI) and MMP degraded aggrecan (exFFGV). C1M and C3M are synovial membrane biomarkers and C2M, AGNxI and exFFGV are cartilage biomarkers.

Results: Explants were viable throughout the experiments, albeit the bSME lost some viability with time. bSME treated with O+T showed increased C1M and C3M (>400% and >200%) from day 10, compared to w/o, whereas in bCC O+T increased C1M from day 21 and C3M from day 14 (>800%, >1900%). O+T treatment increased C2M was increased from day 21 (>400% and >1000%) in both BEX and bCC. The release was blocked by the generic MMP inhibitor GM6001 which also decreased the C1M and C3M compared to w/o. O+T treatment increased AGNxI at day 7 and 10 (>600%) and exFFGV from day 21 (>650%) in both BEX and bCC. In bSME, TGF-b1 continuously and dose-dependently increased P1NP from day 7 compared to w/o (250%). O+T pre-treatment for 10 days followed by TGF-b1 stimulation increased P1NP after 7 days of TNF-b1 treatment (150%, figure). IGF-1 did not affect the P1NP level at any time point in bSME. In bCC both TGF-b1 (dose-dependently) and IGF-1 sustained the PRO-C2 level at the level of baseline throughout the study periods (figure), whereas O+T decreased PRO-C2 compared to with w/o. The PRO-C2 level in BEX with TGF-b1 was unaltered compared to w/o.



Conclusions: We here show that bovine synovium can be anaobolic and catabolic stimulated, both alone and in co-culture with cartilage. Anabolic stimulation was achieved with TGF-b1 in both bSME and bCC, while IGF-1 only showed an anabolic effect in the bCC. Previous human explant models using human tissuehave lacked the anabolic capacity. These translational explants models may be applied in the early development of anabolic drugs for cartilage degenerative diseases.

Disclosure of Interest: A. S. Siebuhr Employee of: Nordic Bioscience, C. Cabanes: None declared, S. Dahab: None declared, M. Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, A.-C. Bay-Jensen Employee of: Nordic Bioscience, C. Thudium Employee of: Nordic Bioscience

DOI: 10.1136/annrheumdis-2017-eular.5737

FRI0004 14-3-3ETA AS A NOVEL INVADOSOME REGULATORY MOLECULE IN RHEUMATOID ARTHRITIS

C. Lalanne[1], R.R. Lavoie[1], M. Charbonneau[1], J. Savill[2], A. Marotta[2], C. Dubois[1]. *[1]University of Sherbrooke, Sherbrooke; [2]Augurex Life Sciences Corp, Vancouver, Canada*

Background: Progressive cartilage destruction, mostly mediated by invasive fibroblast-like synoviocytes (FLS), is a central feature in the pathogenesis of rheumatoid arthritis (RA). We have reported that the ability of arthritic FLS to degrade the extracellular matrix depends on the formation of actin-rich plasma membrane invadosomal structures detected in cells strategically located at the cartilage-synovial membrane interface. Interference with the formation of invadosomes in RA FLS impeded matrix degradation in vitro and cartilage degradation in a model of collagen-induced arthritis, suggesting that invadosomes are important physiological structures involved in cartilage destruction.

The chaperonin molecule 14–3-3η has been detected in the joints of patients with early and established RA and that its concentration in both serum and synovial fluid correlated with elevated expression of extracellular matrix (ECM) degrading enzymes and erosive damage. Extracellular 14–3-3η has therefore been proposed to be a novel biomarker for joint damage and a potential drug target for the personalized treatment of connective tissue-associated diseases but the direct relationship between 14–3-3η and joint damage remains a key area of research.

Objectives: To evaluate the role of 14–3-3η in the ability of synoviocytes to degrade the ECM.

Methods: mRNA from primary synoviocytes of healthy individuals (N=3) and RA patients (N=5) was extracted and the relative level of 14–3-3 isoforms and MMP gene expression was determined by qPCR. The ability of the synovial cell lines to degrade ECM was assessed by in situ invadosome assays using fluorescent cross-linked gelatine. Confocal microscopy was used to determine the cellular localization of 14–3-3η.

Results: We found a significant increase in 14–3-3η, MMP1 and MMP3 mRNA levels in synoviocytes from rheumatoid arthritis patients compared to cells from non-arthritis individuals. A strong correlation between 14–3-3η expression levels and the ability of synoviocyte cell lines to form invadosomes was observed (r2=0.8299). Knockdown of 14–3-3η decreased the ability of arthritic synoviocytes to form invadosomes indicating a role of 14–3-3η in extracellular matrix degrading ability. Confocal microscopy revealed that 14–3-3η staining was mostly found as small punctated structures in the cytoplasm and at the cell periphery of arthritic synoviocytes where they colocalized with leading edge F-actin and discrete patches of the exocyst component, Exo70.

Conclusions: The finding of the role of 14–3-3η in invadosome formation points to a previously unappreciated facet of how 14–3-3η influences joint ECM remodelling and reinforces its role as a marker of RA progression and joint damage. How 14–3-3η is involved in the regulation of MMP production/secretion and the possible role it plays in remodelling of actin-rich subcellular structures is the subject of ongoing studies.

Disclosure of Interest: C. Lalanne: None declared, R. Lavoie: None declared, M. Charbonneau: None declared, J. Savill Employee of: Augurex Life Sciences Corp., A. Marotta Employee of: Augurex Life Sciences Corp., C. Dubois: None declared

DOI: 10.1136/annrheumdis-2017-eular.5531

FRI0005 TARGETING CARTILAGE AGING AS OSTEOARTHRITIS THERAPEUTICS BY DRUG REPURPOSING

B. Carames[1], U. Nogueira-Recalde[1], M.I. Loza[2], F.J. Blanco[1], E. Dominguez[2]. *[1]Rheumatology Division. Cartilage Biology Group, The Institute of Biomedical Research of A Coruña (INIBIC), A coruña; [2]Biofarma Research Group, Center for Research in Molecular Medicine and Chronic Diseases (CIMUS), University of Santiago de Compostela, Santiago de Compostela, Spain*

Background: Effective treatments for Osteoarthritis (OA) are not available. In aging-related diseases, including OA, failure of cellular homeostasis mechanisms, such as autophagy can cause extracellular matrix destruction and cell death (1). With aging, chondrocyte function is diminished, contributing to a cellular senescence phenotype often observed in OA chondrocytes. In addition, a defect in autophagy is observed in both aging and cartilage degeneration (2,3).

Objectives: The objective of this study was to identify anti-senescence and pro-autophagy molecules by a cell-based high-throughput screening (HTS) in human chondrocytes.

Methods: To induce cellular senescence or reduced autophagy, immortalized human chondrocytes (TC28a2) were seeded (2500 cells/well) in 384 well plates, and treated with IL-6 (20 ng/ml) for 72 or 18 hours, respectively. Then, chondrocytes were incubated with Prestwick Chemical Library (1120 approved drugs with chemical and pharmacological diversity, as well as bioavailability and safety in humans) at 10 μM for 72 hours. To identify anti-senescence hits, nuclei was stained with Hoechst 33342 (2,5μg/ml), while β–galactosidase subcellular structures was stained by using Imagene Green C12FDG substrate (30 μM). To evaluate autophagic flux, a reporter cell line was generated by retrovirus transfection of pBABE-mCherry-EGFP-LC3 plasmid in TC28a2 chondrocytes. Plates were imaged by using Operetta® High Content Screening (HCS) system in non-confocal mode using the 20x WD objective. For each well, 4 fields and 4 planes of bright field, Hoechst and fluorescein channels were obtained. Relative intensity of C12FDG in cytoplasm and number of autophagosomes/autolysosomes per area of cytoplasm were determined to quantitate β–galactosidase activity and autophagy flux respectively. Compound validation was performed in TC28a2 chondrocytes and in primary human chondrocytes by evaluating cell senescence, autophagy pathway and cell death by apoptosis.

Results: A primary screening was performed to identify anti-senescence compounds by measurement of senescence-associated β-galactosidase activity. 283 compounds with anti-senescence effects were identified. The anti-senescence hits were analyzed by monitorizing autophagic flux. 29 compounds with both anti-senescence and pro-autophagy effects were selected. Then, one compound was selected for further validation. The compound reduced chondrocyte senescence, increased autophagy ($p<0.0001$) and protected against inflammation and cell death by apoptosis in human chondrocytes ($p<0.05$) in response to IL-6. Interestingly, this protective effect was partially mediated by mTOR inhibition, a proposed mechanism to prevent cartilage aging.

Conclusions: Our screening methodology provides a unique opportunity to repurpose drugs and mechanisms to prevent cartilage aging. Autophagy activation and protection against senescence in chondrocytes may provide benefits for delaying cartilage degeneration.

References:

[1] Lotz MK and Caramés B. Nat Rev Rheumatol 2011;7:579–587.
[2] Caramés B, et al. Arthritis Rheumatol 2015;67:1568–76.
[3] Caramés B et al. Arthritis Rheum 2010;62:791–801.

Acknowledgements: This study was supported by Instituto de Salud Carlos III-Ministerio de Economía y Competitividad, Spain-PI14/01324 and Fondo Europeo de Desarrollo Regional (FEDER).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3658

FRI0006 PROTEIN CITRULLINATIONS BY PAD ENZYMES PROMOTE DENDRITIC CELL TRANSDIFFERENTIATION INTO OSTEOCLAST AND GENERATE TARGETS FOR RA-SPECIFIC ANTIBODIES

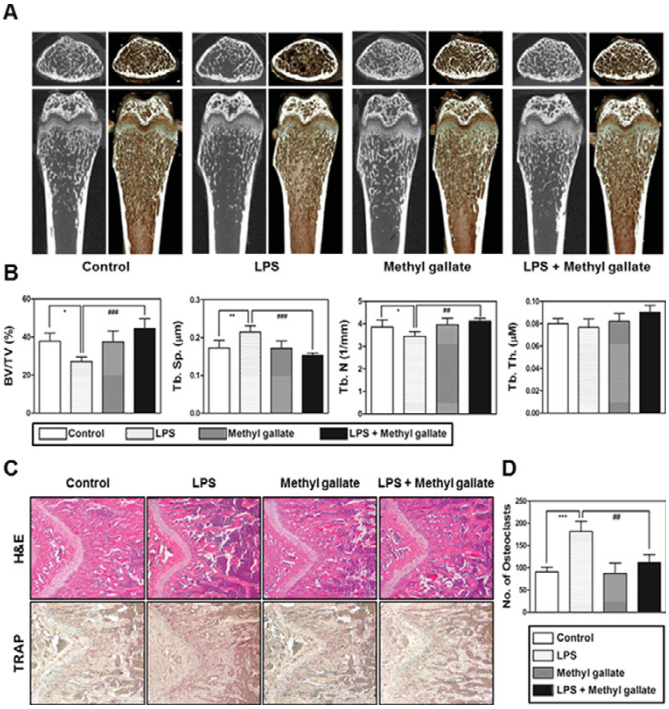
B. Réthi[1], A. Krishnamurthy[1], J. Ytterberg[1], M. Sun[1], V. Joshua[1], H. Wähämaa[1], N. Tarasova[2], J. Steen[1], V. Malmström[1], A.I. Catrina[1].
[1]Department of Medicine, Center for Molecular Medicine, Karolinska Institutet & Karolinska University Hospital; [2]Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden

Background: Immature dendritic cells (DCs) are able to trans-differentiate into osteoclasts (OCs) although the mechanisms regulating this process are little understood. We have recently described an important role for protein citrulliantion and peptidylarginine deiminase (PAD) enzyme activity in the regulation of OC development (1).
Objectives: We studied the molecular bases of DC-OC trans-differentiation and aimed at understanding the role of protein citrullination in this process.
Methods: Monocyte-derived DCs and peripheral blood CD1c+ DCs were cultured in the presence of osteoclastogenic cytokines. Polyclonal ACPAs were isolated from the serum of RA patients and applied in OC cultures. DC and OC differentiation was analyzed *in vitro* using gene expression analyses, flow cytometry-based methods, DC-T cell co-culture experiments, tartrate-resistant acid phosphatase stainings and osteolysis assays. Protein citrullination was monitored with the help of mass spectrometry. PAD activity was measured by ELISA.
Results: Different DC types showed different capacities to develop into OCs. OC-prone DCs were characterized by little immunogenicity and their development was potentiated by the increase of lactic acid, a side product of glycolytic metabolism. The more immunogenic DC types, characterized by prominent ability to migrate towards secondary lymphoid tissues and trigger T cell activation, showed a limited capacity to develop into OCs (2). The differentiation switch towards the OC lineage was associated with increased activity of the Protein Arginine Deiminase (PAD) enzymes and with higher level of protein citrullination in DCs. The PAD inhibitor Cl-Amidine efficiently interfered with OC development form DC precursors. In addition, the deposition of citrullinated proteins on the cell surface made the cells sensitive for anti-citrullinated protein autoantibodies, which could further stimulate DC-OC trans-differentiation through inducing the cytokine IL-8.
Conclusions: Our results indicated that DCs are heterogenic in their ability to form OCs and lineages for immunostimulatory and OC-prone DCs might separate early during DC differentiation. Plasticity towards OC differentiation might be influenced by the metabolic environment and the upregulation of PAD activity in DCs.
References:
[1] Krishnamurthy A et al. Ann Rheum Dis 2016.
[2] Nasi A et al. J Immunol 2013.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5971

FRI0007 METHYL GALLATE INHIBITS OSTEOCLAST FORMATION AND FUNCTION THROUGH SUPPRESSING THE AKT AND BTK-PLCγ2-CA2+ SIGNALING, AND PREVENTS LPS-INDUCED BONE LOSS

M.-S. Lee[1], J.M. Baek[2], J.-Y. Kim[2], W.-H. Yoo[3], S.-J. Hong[4], C.-H. Lee[1].
[1]Internal Medicine, Wonkwang University Hospital; [2]Anatomy, School of Medicine, Wonkwang University, Iksan; [3]Internal Medicine, Chonbuk National University Medical School, Jeonju; [4]Internal Medicine, Kyung Hee University School of Medicine, Seoul, Korea, Republic Of

Background: Methyl gallate, a plant-derived phenolic constituent has been known to possess numerous pharmacological features against inflammation, oxidation, and cancer. But so far, there have been no evidences to describe relationship between methyl gallate and bone metabolism.
Objectives: In order to propose a promising candidate for osteoporosis, we performed experiments in this study by using methyl gallate.
Methods: we performed screening of methyl gallate utilizing TRAP staining and revealed intracellular mechanisms responsible for methyl gallate-mediated regulation of osteoclastogenesis through western blotting and quantitative RT-PCR. Also, we assessed the role of methyl gallate on characteristics of mature osteoclasts. we used LPS-induced bone loss mice as a model of osteoporosis and analyzed using micro-CT system and the right femurs were stained with TRAP and H&E.
Results: we observed that methyl gallate significantly suppressed osteoclast formation through Akt and Btk-PLCγ2-Ca^{2+} signaling. The blockade of these pathways was reconfirmed through transduction of CA-Akt retrovirus and evaluation of Ca^{2+} influx intensity stained with Fluo-3/AM. Indeed, methyl gallate down-regulated the formation of actin ring-positive osteoclasts and resorption pit areas. In agreement with in vitro results, we found that the administration of methyl gallate restored osteoporotic phenotype stimulated by acute systemic injection of LPS in vivo through micro-CT and histology.



Conclusions: Consequently, the overall data strongly indicated that methyl gallate could be a useful substance for development of plant-based anti-osteoporotic agent.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2141

FRI0008 EFFECTS OF THE HUMAN IL4-10 FUSION PROTEIN IN THE CANINE GROOVE MODEL OF OSTEOARTHRITIS

E.M. Van Helvoort[1], J. Popov-Celeketic[1], K. Coeleveld[1], M.A. Tryfonidou[2], F.P. Lafeber[1], S.C. Mastbergen[1]. *[1]Rheumatology and Clinical Immunology, University Medical Centre Utrecht; [2]Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, University Utrecht, Utrecht, Netherlands*

Background: Ideally a disease modifying osteoarthritis drug (DMOAD) combines treatment for pain, tissue damage and inflammation, all in one molecule. Intra-articular application of a DMOAD brings additional value to treatment for two reasons, (i) lower risk of systemic side effects and (ii) higher drug concentration and potentially improved penetration of non-vascularized articular cartilage. Interleukin-4 (IL-4) and Interleukin-10 (IL-10) have been shown to prevent joint degeneration and can work synergistically[1].
Objectives: This study evaluates the DMOAD activity of repetitive intra-articular injections with a human fusion protein of IL-4 and IL-10 (hIL4–10FP) in the canine Groove model of osteoarthritis (OA).
Methods: In 8 dogs joint degeneration was induced according to the Groove model. Six weeks after surgery dogs were treated with ten weekly intra-articular injections of either hIL4–10FP (n=4) or PBS (n=4). Subsequently, dogs were euthanized and cartilage and synovium were harvested. Cartilage damage and synovial inflammation were macroscopically evaluated. Proteoglycan release and content were determined ex vivo by staining of glycosaminoglycans (GAGs) with Alcian Blue. Proteoglycan synthesis was measured by $^{35}SO_4^{2-}$ incorporation and precipitation with cetylpyridium chloride and liquid scintillation analysis of $^{35}SO_4^{2-}$-labeled GAGs. Potential antibody formation against hIL4–10FP was evaluated with ELISA and a cell based assay. Immunohistochemistry of CD79α and CD10 was used to evaluate the presence of B-cells in synovium.
Results: Affected knees of PBS treated dogs showed enhanced macroscopic cartilage damage compared to their controls (0.31 vs 2.44, p=0.068). Also differences in proteoglycan release, content and synthesis indicated a degenerative state in the affected knees.
Unexpectedly, enhanced synovial inflammation was observed in hIL4–10FP treated joints compared to PBS treated joints, demonstrated by enhanced macroscopic (3.5 vs 2.3 out of 5) and histologic (2.5 vs 1.8 out of 6) scores. CD79α and CD10 showed enhanced expression in synovium of the hIL4–10FP group compared to the PBS group, although not statistically significant (fig 1). Additional analyzes showed that hIL4–10FP was immunogenic in dogs after multiple injections. Formation of neutralizing antibodies was shown in a cell based assay where the activity of hIL4–10FP was inhibited in the presence of serum of hIL4–10FP treated dogs (fig 2). Despite the enhanced inflammatory response

in hIL4–10FP group there was no enhanced cartilage degeneration detected compared to the PBS group (fig 3).

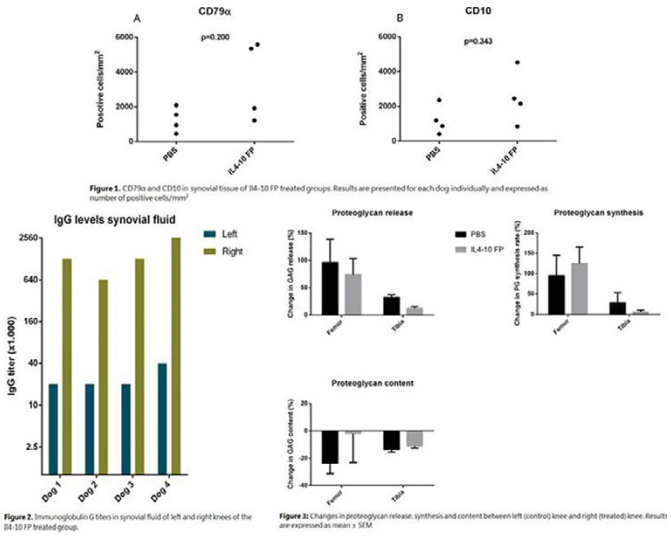


Figure 1. CD79α and CD10 in synovial tissue of Il4-10 FP treated groups. Results are presented for each dog individually and expressed as number of positive cells/mm²

Figure 2. Immunoglobulin G titers in synovial fluid of left and right knees of the Il4-10 FP treated group.

Figure 3: Changes in proteoglycan release, synthesis and content between left (control) knee and right (treated) knee. Results are expressed as mean ± SEM

Conclusions: Repetitive intra-articular injection of human IL4–10FP led to antibody formation in a non-inflammatory canine model of OA. Despite the immune response, proteoglycan turnover parameters were comparable between the two treatment groups, suggesting a beneficial effect of hIL4–10FP. This study also shows that it is not evident to use a human protein in a (canine) animal model, although this is often done. Instead, a species specific protein is warranted. Therefore a canine version of IL4–10FP will be developed to study its DMOAD activity in this model.

References:

[1] van Roon JA, Lafeber FP, Bijlsma JW. Synergistic activity of interleukin-4 and interleukin-10 in suppression of inflammation and joint destruction in rheumatoid arthritis. Arthritis and rheumatism. 2001;44(1):3–12.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1498

FRI0009 ACCELERATED DEVELOPMENT OF AGING-ASSOCIATED AND INSTABILITY-INDUCED OSTEOARTHRITIS IN 12/15-LIPOXYGENASE DEFICIENT MICE

L. Habouri, F. El Mansouri, Y. Ouhaddi, J.-P. Pelletier, J. Martel-Pelletier, M. Benderdour, H. Fahmi. *Medicine, CRCHUM, Montreal, Canada*

Background: 12/15-Lipoxygenase (12/15-LOX) catalyzes the generation of various anti-inflammatory lipid mediators, and has been implicated in several inflammatory and degenerative diseases. However, there is currently no evidence that 12/15-LOX has a role in osteoarthritis (OA).

Objectives: The aim of this study was to investigate the role of 12/15-LOX in the pathogenesis of OA

Methods: The development of aging-associated and destabilization of the medial meniscus (DMM)-induced OA were compared in 12/15-LOX-deficient (12/15-LOX-/-) and wild-type (WT) mice. The extent of cartilage damage was evaluated by histology. The expression of OA markers was evaluated by immunohistochemistry and RT-PCR. Cartilage explants were stimulated with IL-1α in the absence or presence of the 12/15-LOX metabolites, 15-HETE, 13-HODE or LXA4, and the levels of MMP-13, NO and PGE_2 were determined. The effect of LXA4 on the progression of OA was evaluated in WT mice.

Results: The expression of 12/15-LOX in cartilage increased during the progression of DMM-induced OA and with aging in WT mice. Cartilage degeneration was more severe in 12/15-LOX-/- mice compared to WT mice in both models of OA, and this was associated with increased expression of MMP-13, ADAMTS5, iNOS, and mPGES-1. Treatment of cartilage explants with 12/15-LOX metabolites, suppressed IL-1α-induced production of MMP-13, NO and PGE_2, with LXA4 being the most potent. Intra-peritoneal injection of LXA4 reduced the severity of DMM-induced cartilage degradation.

Conclusions: These data demonstrate an important role of 12/15-LOX in OA and suggest that activation of this pathway may provide a novel strategy for prevention and treatment of OA.

Acknowledgements: This work was supported by the Canadian Institutes of Health Research (CIHR) Grant MOP-130293, the Arthritis Society, and the Fonds de la Recherche du Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6184

FRI0010 METABOLIC DYSREGULATION ACCELERATES JOINT DEGENERATION UPON MECHANICALLY INDUCED CARTILAGE DAMAGE, DRIVEN BY LOCAL INFLAMMATION; AN IN VIVO RAT STUDY

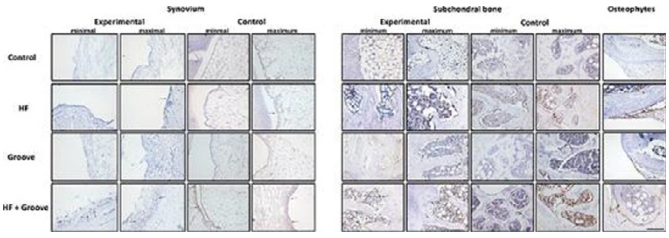
H.D. Visser[1,2], S. Mastbergen[2], A. Kozijn[2], K. Coeleveld[2], M.V. Rijen[1], H. Weinans[1,2,3], F. Lafeber[2]. *[1]Orthopaedics; [2]Reumatology & Clinical Immunology, UMC Utrecht, Utrecht; [3]Biomechanical Engineering, Delft University of Technology, Delft, Netherlands*

Background: Obesity is a well-known and important risk factor for osteoarthritis (OA). Moreover, obesity is highly associated with the metabolic syndrome (MetS)[1]. Growing evidence indicates that both OA and MetS are low-grade inflammatory conditions with elevation in systemic inflammatory markers. Nonetheless, it is unclear whether MetS low-grade inflammation induces OA, or contributes to the disease.

Objectives: To determine the contribution of metabolic alterations, induced by a High-Fat Diet (HFD), on the onset or progression of OA in a rat model of local cartilage damage.

Methods: Forty Wistar rats (12 weeks old, male), were randomly divided over two groups: twenty rats were fed a HFD (60% of the kcal contained fat:D12492i, Research Diets Inc.) while the other animals received a standard diet. After 12 weeks, local articular cartilage damage was induced on the femoral condyles, in one knee joint according to the groove model in 14 rats of each diet group. Remaining animals served as a control group in each arm. At week 24, serum was collected, subchondral bone was assessed by μCT scan (Quantum FX, PerkinElmar,USA), OA severity was evaluated by rat OARSI histopathology score and macrophage presence with CD68 immunostaining from histological sections was assessed.

Results: HFD feeding resulted in metabolic dysregulation as indicated by significantly increased metabolic parameters (weight, fasting insulin and total cholesterol) compared to the standard fed rats. HFD feeding alone resulted in mild cartilage degeneration (2±1.1 vs 0.58 ±0.7; p=0.06) and synovial membrane inflammation (1.0±0.6 vs 0.3±0.5; p=0.075) both subscores of the rat OARSI histopathology score. However, when HFD feeding is combined with the surgical model of applied local cartilage damage, OA severity is statistically significant increased compared to the local cartilage damage group on a standard diet (6.2±2.1 vs 3.4±1.4; p=0.001). Synovial membrane inflammation (1.3±0.9vs 0.5±0.5; p=0.011) and multiple large osteophyte formation, demonstrated by histology (0.9±1 vs 0.2±0.4; p=0.04) and quantified on μCT (328±349 μm^3 vs 7±14 μm^3; p=0.0001), contributes most to this increased OA severity. Immunohistochemical CD68 expression as observed on both the synovial membrane as well as in the subchondral bone and around the formed osteophytes can explain the increase in selected inflammatory parameters when groove surgery is combined with a HFD (Figure 1).



Conclusions: This study shows that a HFD induces metabolic alterations and increases the inflammatory state of the joint. This by itself does not result in severe OA. However, when adding a HFD to a mild cartilage damage model of OA, joint degeneration is significantly increased. This progression of joint degeneration appears to be driven mainly by inflammatory responses as demonstrated by an increased CD68 expression in both the subchondral bone and synovium membrane with increased osteophytosis. Hence, our findings indicate that systemic metabolic and subsequent inflammatory factors need an additional trigger to contribute to the progression of the OA.

References:

[1] Zhuo Q, Yang W, Chen J and Wang Y, Metabolic syndrome meets osteoarthritis. Nat Rev Rheumatol, 2012. 8(12): p. 729–37.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1639

FRI0011 TARGETING NEUTROPHIL MICROVESICLES TO DAMAGED CARTILAGE USING ANTIBODIES TO POST TRANSLATIONALLY MODIFIED COLLAGEN II

L.M. Topping, H. Rhys, L. Norling, A. Nissim. *Biochemical Pharmacology, William Harvey Research Institute, Queen Mary University of London, London, United Kingdom*

Background: Microvesicles (MV) are double membrane-bound extracellular vesicles released from the plasma membrane of cells. MV derived from polymorphonuclear neutrophils (PMN) promote tissue protection, and have been demonstrated to penetrate cartilage during inflammatory arthritis and provide protection to the tissue [1].

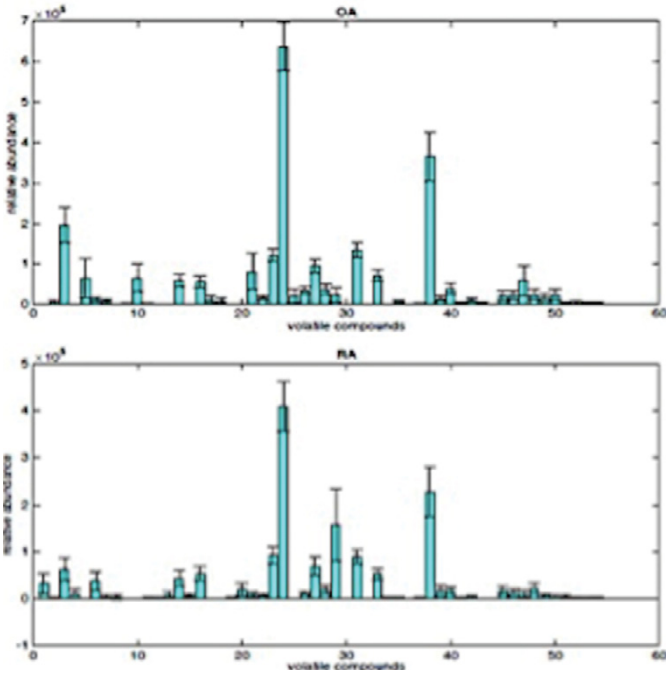
Collagen type II (CII) is the most abundant protein found in cartilage. We have produced a single chain variable fragment (scFv) antibodies specific to CII modified by reactive oxygen species (ROS), namely anti-ROS-CII_{scFv}. Previously, we have demonstrated the ability of anti-ROS-CII_{scFv} to localise exclusively and deliver payload drugs to the arthritic joint in mice models of rheumatoid arthritis[2].
Objectives: To test our hypothesis that anti-ROS-CII association with MV might i) target delivery of MV to inflamed joint and/or ii) enhance the avidity of the scFv (several scFv can be loaded in each MV) and may thus increase localisation and enhance therapeutic efficacy.
Methods: Cy5.5 labeled Anti-ROS-CII_{scFv} were loaded on fluorescently labelled human PMN MV by aqueous energy dissemination using a sonic dismembrator [3–4]. Anti-ROS-CII_{scFv} MV incorporation was confirmed by Imagestream^X analysis. Anti-ROS-CII_{scFv} MV were tested by ELISA to assess the retention of antibody binding capabilities.
Results: Positive incorporation of Anti-ROS-CII_{scFv} upon MV was observed by flow cytometric analysis. ELISA demonstrated the ability of the anti-ROS-CII loaded MV to bind strongly to ROS-CII following incorporation into MV.
Conclusions: In this study, we have demonstrated a simple, efficient and cost effective way of antibody targeting that retains antibody function. Such technology has the potential to increase efficacy of existing therapies by ensuring specific targeting. Future *in vivo* studies will assess the ability of the Anti-ROS-CII_{scFv} MV to localise to arthritic joints.
References:
[1] Headland, S. E. et al. Neutrophil-derived microvesicles enter cartilage and protect the joint in inflammatory arthritis. Science Translational Medicine, 7(315), (2015).
[2] Hughes, C. et al. Human single-chain variable fragment that specifically targets arthritic cartilage. Arthritis and Rheumatism 62(4), 1007–1016 (2010).
[3] Dalli, J. et al. Microparticle alpha-2-macroglobulin enhances pro-resolving responses and promotes survival in sepsis. EMBO Molecular Medicine 6(1), 27–42 (2014).
[4] Norling, L.V. et al. Cutting Edge: Humanized Nano-Proresolving Medicines Mimic Inflammation-Resolution and Enhance Wound Healing. The Journal of Immunology 186(10), 5543–5547 (2011).
Acknowledgements: The author would like to acknowledge Timothy Harrison and Amit Gupta for their contrabutions to preliminary results. The author would also like to acknowledge Dr Jesmond Dalli for his guidance on methodology.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4842

FRI0012 ROLE OF VOLATILE COMPOUNDS RELEASED BY SYNOVIAL FLUID IN THE DIAGNOSIS OF OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS OF THE KNEE JOINT

R. Capuano[1], M.S. Chimenti[2], F. Dini[1], A.C. Domakoski[3], E. Martinelli[1], P. Conigliaro[2], R. Paolesse[3], C. Di Natale[1], R. Perricone[2], A. Bergamini[2]. *[1]Department of Electronic Engineering; [2]Department of system medicine, Rheumatology, Allergology and Clinical Immunology; [3]Department of Chemical Science and Technology, University of Rome Tor Vergata, Rome, Italy*

Background: Synovial fluid (SF) receives protein contribution from the tissue around: cartilages, synovial membranes and bones. The presence of inflammation and oxidative stress alters the its chemical composition. In particular, inflammation modulates the release of volatile organic compounds (VOCs) that are the product of reactive oxygen species and free radicals excreted by mithocondria during oxydative stress (1). Articular inflammation plays a major role both in Osteoarthritis (OA) and Rheumatoid arthritis (RA), thus, the identification of specifics VOCs associated with inflammation in the SF may represent a suitable procedure to facilitate a diagnosis and a better characterization of these diseases. E-noses are versatile instruments based on arrays of partially selective gas sensors system that do not provide specific information about the individual molecules but can detect a large spectrum of VOCs to provide a discrimination among samples classified according to their chemical composition (VOC pattern) (2).
Objectives: Aim of this study was to prospectively investigate whether analysis of volatile compounds (VOCs) emitted from knee synovial fluid can identify differences between osteoarthritis (OA) and rheumatoid arthritis (RA).
Methods: VOCs Profile emitted by knee synovial fluid of 10 OA patients was compared with that of 25 RA patients using gas chromatography and mass spectrometry (GC-MS) and a gas sensor array (electronic nose) made by an ensemble of metalloporphyrins coated quartz microbalances. Patients' data are summarized in Table 1. Data were analyzed by principal component analysis (PCA), partial least squares discriminant analysis (PLSDA). Permutation analysis and area under curve (AUROC) of receiver operating characteristics (ROC) curves were used to characterize the classifier performance.
Results: GC-MS analysis identified 55 VOCs in the headspace of synovial fluids. The ANOVA analysis of the relative abundance indicated five VOCs significantly different between OA and RA. The abundance of five compounds allowed to identify OA with respect to RA with an accuracy of 82% (sensitivity: 0.90, specificity: 0.80, AUROC=0.92, 99.7% CI). The signals of the electronic nose sensors allowed to classify the studied subjects in OA or RA. In particular, OA patients could be distinguished from that of RA patients with an accuracy of 100% (sensitivity: 1, specificity: 1, AUROC=1, 99.9% CI).) (Figure 1). However, no single VOC was specific for OA or RA.

Figure 1. Mean and standard deviation of relative abundance of the 54 compounds.



Conclusions: This study shows that OA and RA patients exhibit qualitative and quantitative differences in the chemical compositions of knee synovial fluid. These differences may be attributed to five volatile compounds and can be detected by an electronic nose which may represent a suitable diagnostic tool for diagnosis and characterization of OA vs. RA.
References:
[1] Hakim M, Broza YY, Barash O, Peled N, Phillips M, Amann A, et al. Volatile organic compounds of lung cancer and possible biochemical pathways. Chem Rev. 2012;112:5949–66.
[2] Stitzel S, Arnecke M, Walt D. Artificial noses. Ann Rev Biomed Eng. 2011;13:1–25.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3695

FRI0013 ACPA-INDUCED MOBILITY OF PRIMED SYNOVIAL FIBROBLASTS: THE MISSING LINK BETWEEN ACPA-INDUCED BONE LOSS AND SYNOVIAL CHANGES

M. Sun[1], V. Joshua[1], A. Krishnamurthy[1], A.H. Hensvold[1], Y. Liu[2], S.B. Catrina[3], C. Ospelt[4], V. Malmström[1], J. Steen[1], M. Engström[1], H. Wähämaa[1], B. Rethi[1], A.I. Catrina[1]. *[1]Rheumatology unit, Department of Medicine, Karolinska Institute, Stockholm, Sweden; [2]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China; [3]Department of Molecular Medicine and Surgery, Diabetes Center Karolinska, Karolinska Institute, Stockholm, Sweden; [4]Centre of Experimental Rheumatology, Department of Rheumatology, University Hospital Zürich, Zurich, Swaziland*

Background: Anti-citrullinated proteins antibodies (ACPAs) injected in mice induce IL-8 dependent bone loss and arthralgia, but no synovial changes. We hypothesized that additional stimulus, sensitizing the synovial compartment to ACPA effects, is needed for the transition from bone to synovial pathology.
Methods: Synovial fibroblasts (SFs) were isolated from synovial tissue of RA patients by enzymatic digestion. Polyclonal ACPA and other non-ACPA IgGs were separated from peripheral blood of RA patients by affinity purification on a cyclic citrullinated peptide (CCP)-2 column. SF migration capacity was tested by scratch-assays in starved and non-starved cultures treated with ACPAs, with or without presence of IL-8. The results were evaluated by NIH ImageJ software. SF adhesion was analyzed by xCELLigence System Real-Time Cell Analyzer (ACEA bioscience). Peptidylarginine deiminases (PAD) expression and protein citrullination were evaluated by immunohistochemistry. The role of signaling pathways in the ACPA-mediated SF modulation was analyzed by using specific signal inhibitors and by monitoring protein phosphorylations using western blot.
Results: Serum starvation of SF increased citrullinated proteins and PAD expression. Starved but not non-starved SF showed an increased mobility index following polyclonal ACPA stimulation to a mean±SD fold increase of 2.6±0.5. This effect was abolished by PAD inhibition as well as ACPA blocking with citrullinated but not native fibrinogen. Exogenous pro-inflamamatory cytokines (IL-8 and TNF) synergistically increased SF mobility when added together with ACPA. Phosphorylation and inhibition studies of intracellular signalling pathways

in starved SF indicated an important role for PI3K-mediated signals in the ACPA-induced increase of SF mobility.
Conclusions: We demonstrated that additional stimuli (such as stress-induced citrullination and cytokine priming) were needed for SF to react upon ACPA stimulation. This is an indirect proof supporting the idea that a synovial insult that will normally resolve unobserved, might be essential for the transition towards chronic synovial changes in the presence of ACPA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6448

FRI0014 ANTIOXIDANT ROLE OF MICROVESICLES FROM ADIPOSE TISSUE-DERIVED MESENCHYMAL STEM CELLS IN HUMAN OSTEOARTHRITIC CHONDROCYTES

M. Tofiño-Vian[1], I. Guillen[1,2], M.D. Perez del Caz[3], A. Silvestre[4], M.J. Alcaraz[1]. *[1]Pharmacology and IDM, University of Valencia, Burjasot, Valencia; [2]Dpt. Pharmacy, CEU-Cardenal Herrera; [3]Department of Burn and Plastic Surgery, la Fe University Hospital; [4]Orthopaedic Surgery and Traumatology, Clinical University Hospital, Valencia, Spain*

Background: Oxidative stress results in the disruption of normal physiologic signaling leading to inflammatory changes, cartilage degradation and osteoarthritis (OA) progression (1). Recent advances have revealed the role of cell-derived microvesicles (MV) as a new mechanism of cell-to-cell communication with potential therapeutic applications. We have shown previously the antiinflammatory effects of human adipose tissue-derived mesenchymal stem cells (AD-MSC) conditioned medium in OA chondrocytes (2).
Objectives: We have isolated the MV fraction from the secretome of AD-MSC to investigate its activity on oxidative stress and inflammation in OA chondrocytes stimulated with interleukin (IL)-1β. Furthermore, we have characterized the MV protein content by proteomic analysis.
Methods: AD-MSC were isolated from fat of patients who undergone abdominoplasty (without obesity). MV were isolated from AD-MSC conditioned medium by differential centrifugation with size filtration. MV size and concentration were determined by resistive pulse sensing. Proteomic analysis was performed by LC-MS/MS, with ProteinPilot and PeakView software and the bioinformatic tools UNIPROT and PANTHER. OA chondrocytes were isolated from knee specimens of advanced OA patients, stimulated with IL-1β (10 ng/mL) and treated with MV ($3.6x10^7$ particles/mL) for 24h. Accumulation of 4-hydroxy-2-nonenal (HNE)-modified proteins and cytokines were measured by ELISA, NO production and MMP activity by fluorometry. Expression of specific proteins was evaluated by confocal microscopy or immunostaining. The data were analysed by ANOVA followed by Dunnett's test.
Results: MV reduced the accumulation of HNE-modified proteins, a biomarker of oxidative stress–induced lipid peroxidation, in OA chondrocytes stimulated with IL-1 β. The production of NO, IL-6 and TNFα, as well as MMP activity were also significantly reduced by MV treatment, whereas IL-10 and collagen II were enhanced. Proteomic analysis of MV showed high levels (5.89-fold upregulation) of peroxiredoxin 6 (Prdx6), a member of the peroxiredoxin family of antioxidant proteins which is downregulated in OA cartilage (3). MV treatment increased the expression of Prdx6 in OA chondrocytes suggesting a protective role against oxidative stress in these cells.
Conclusions: MV from AD-MSC downregulate the production of oxidative stress and inflammatory mediators in OA chondrocytes. Prdx6, an antioxidant enzyme, may contribute to the protective effects of MV. Our data support the interest of these MV to develop new therapeutic approaches.
References:
[1] Loeser RF et al. (2002) Detection of nitrotyrosine in aging and osteoarthritic cartilage: Correlation of oxidative damage with the presence of interleukin-1beta and with chondrocyte resistance to insulin-like growth factor 1. Arthritis Rheum 46: 2349–2357.
[2] Platas J et al. (2016) Paracrine effects of human adipose-derived mesenchymal stem cells in inflammatory stress-induced senescence features of osteoarthritic chondrocytes. Aging 8: 1703–17.
[3] Ikeda D et al. (2013) iTRAQ-based proteomics reveals novel biomarkers of osteoarthritis. Biomarkers 18: 565–572.
Acknowledgements: Funded by SAF2013–48724-R (MINECO, FEDER) and PROMETEOII/2014/071 (Generalitat Valenciana).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3682

FRI0015 MODELLING THE INITIAL PHASE OF FRACTURE HEALING IN VITRO – 3D BONE-LIKE MODELS OF ENDOCHONDRAL OSSIFICATION

M. Pfeiffenberger[1], A. Lang[1], I. Ponomarev[2], D. Barnewitz[2], F. Buttgereit[1], T. Gaber[1]. *[1]Charité University Hospital, Berlin, Germany, Berlin; [2]Research Center of Medical Technology and Biotechnology, Bad Langensalza, Germany*

Background: Immunosuppressed patients with ongoing inflammation experience more often difficulties in the process of fracture healing. Hereby amongst others immunomodulated activation of osteoclasts leads to augmented osteolysis. Most notably numerous cytokines and invading lymphocytes provide an inflammatory environment within the fracture gap, utmost during the first phase of fracture healing. Nowadays researchers, whilst investigating fracture healing, use small rodent models, facing the problem of translation towards the human system. Hence, there is a lack of valid *in vitro* models to examine the first phase of fracture healing. To test new therapeutic strategies, we develop a valid 3D-model using human cells to mimic the first phase of fracture healing *in vitro* which is characterized by the formation of a fracture hematoma, a hypoxic microenvironment as well as inflammation that initiate the healing cascade and the process of endochondral ossification.
Objectives: To develop 3D bone-like models displaying endochondral ossification.
Methods: As a first step, we focus on establishing 3D bone-like, matrix-free models consisting of human mesenchymal stromal cells (hMSC). MSC were isolated from bone-marrow samples of patients undergoing total hip replacement and characterized with regard to their typical surface markers as well as their differentiation potential towards osteogenic, adipogenic and chondrogenic lineage. 3D bone-like models were generated from micro-mass culture of hMSC (Research Center of Medical Technology and Biotechnology, Bad Langensalza). After initial maturation, 3D bone-like models were cultured under hypoxic conditions (37°C, 1% O2) in osteogenic medium for up to 3 months. *In vitro* μCT analyses were performed at day 0, after one and two months focusing on the total volume (TV) and bone volume (BV). Additionally osteogenic-relevant genes/factors (Runx2, SPP1, Dlx5, ALP, RANKL, SPI1) as well as exclusion markers (SOX9, PPARg2) were investigated after 3 months of cultivation using qRT-PCR. Finally, we implemented histological/immunohistochemical methods (van Kossa, ALP, Col1 staining).
Results: The 3D bone-like models achieved diameters between 0.5 and 0.7 and a thickness of 0.3 cm. *In vitro* μCt analysis revealed a high amount of mineralized tissue at day 0 and substantial increase in the bone volume (BV/TV) after cultivation. At day 0 *in vitro* μ Ct analysis implied mineralization mostly at the margin but penetrated the tissue within further cultivation. These results are also supported by positive van Kossa staining. Additionally, qRT-PCR results yielded higher expressions of *RUNX2, SPP1, SPI1, RANKL* and *DLx5*. Furthermore, immunohistochemistry showed high ALP-activity and CoII-expression.
Conclusions: Preliminary results of our study focusing at developing a 3D bone-like model displayed a promising trend towards modelling endochondral ossification *in vitro* by increased mineralization (*in vitro* μCt analysis and van Kossa staining), and upregulation of osteogenic-relevant *RUNX2* and *SPP1* expression as well as ALP-activity and CoII-expression. High expression of *SPI1* and *RANKL* could refer to osteoclast-like activities, which will be in the focus of further investigations. Finally, the complete 3D model will leave us the opportunity for studying the first phase of fracture healing under *in vitro* conditions.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5899

FRI0016 INVOLVEMENT OF RUNX-2 AND β-CATENIN SIGNALING IN THE PRODUCTION OF ADAMTS-7 AND ADAMTS-12 IN OSTEOARTHRITIC SYNOVIAL FIBROBLASTS

S. Pérez-García[1], I. Gutiérrez-Cañas[1], R. Villanueva-Romero[1], J. Leceta[1], J. Fernández[2], I. González-Álvaro[3], Y. Juarranz[1], R.P. Gomariz[1]. *[1]Cell Biology, Faculty of Biology, Complutense University of Madrid; [2]Traumatology Service; [3]Rheumatology Service, la Princesa University Hospital, Princesa Medical Research Institute, Madrid, Spain*

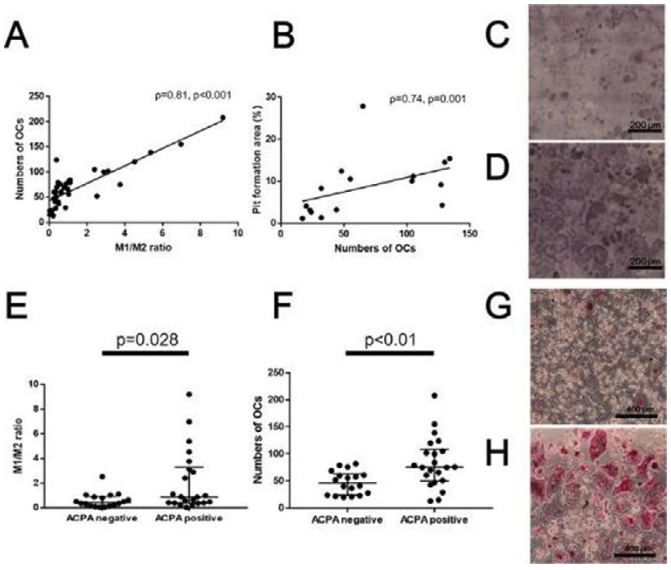
Background: Proteinases released from synovial membrane of osteoarthritis (OA) patients contribute to cartilage damage. We recently reported in synovial fibroblasts (SF) the expression of ADAMTS (a disintegrin and metalloproteinase domain with thrombospondin motifs)-7 and -12, involved in the destruction of the cartilage oligomeric matrix protein (COMP) (1). Signaling pathways regulating these ADAMTS are poorly understood. As Runx2 and β-catenin are two transcription factors involved in chondrocytes metabolism and OA pathology (2–5), we studied whether these factors are implicated in the production of ADAMTS-7 and 12 in SF. Moreover, we analyzed the induction by two inflammatory mediators present in OA joints: interleukin-1β (IL-1β), and fibronectin fragments (Fn-fs), previously described in ADAMTS expression (1).
Objectives: To elucidate the signaling pathways involved in the production of ADAMTS-7 and -12 in healthy donors (HD) - and OA-SF.
Methods: ADAMTS-7 and -12 were detected in HD- and OA-SF protein extracts by Western blot. Blockade experiments were performed after stimulation with IL-1β or 45-kDa Fn-fs. We used inhibitors for two mitogen-activated protein kinases (MAPKs), ERK and p38, implicated in the activation of Runx2, PD98059 and SB203580, respectively. We also used an inhibitor of Wnt/β-catenin signaling, DDK-1. Levels of ADAMTS-7 and -12 were analyzed by quantitative RT-PCR and ELISA in SF culture supernatants.
Results: Intracellular presence of ADAMTS-7 and -12 was confirmed in HD- and OA-SF, with higher levels of ADAMTS-7 in OA. After IL-1β or Fn-Fs stimulation, DDK-1 decreased ADAMTS-7 transcript in HD and OA-SF that was translated to a protein reduction in OA. Besides, ERK inhibitor decreased ADAMTS-12 mRNA and protein exclusively in OA-SF.
Conclusions: We reported that ADAMTS-7 protein expression is higher in OA-SF compared to HD confirming previous data at mRNA level (1). As DKK decreased ADAMTS-7, Wnt-β-catenin signaling seems to be implicated in its expression. By contrast, the expression of ADAMTS-12 is regulated by ERK, pointing to a possible implication of ERK-Runx2 axis, exclusively in OA-SF.

References:
[1] Pérez-Garcia S, Gutiérrez-Cañas I, Seoane IV, et al. Am J Pathol. 2016; 186(9):2449–61.
[2] Yuasa T, Otani T, Koike T, et al. Laboratory Investigation. 2008;88(3):264–74.
[3] Luyten FP, Tylzanowski P, Lories RJ. Bone. 2009;44(4):522–7.
[4] Ji Q, Xu X, Xu Y, Fan Z, Kang L, Li L, et al. J Mol Med (Berl). 2016;94(6):681–94.
[5] Komori T. Cell and tissue research. 2010;339(1):189–95.
Acknowledgements: This work has been supported by Instituto de Salud Carlos III, Spain, cofinanced by FEDER, European Union: RETICS program, Red de Investigación en Inflamación y Enfermedades Reumáticas (RD16/0012/0008 (RPG) and RD16/0012/0011 (IGA) and the projects PI12/00758 (RPG), PI14/00477 (CMM) and PI14/00442 (IGA).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5808

FRI0017 A NOVEL CONCEPT OF M1 AND M2 MONOCYTES IN RHEUMATOID ARTHRITIS: PRO-INFLAMMATORY MONOCYTE POLARIZATION IMBALANCE, ANTI-CITRULLINATED PROTEIN ANTIBODY AND OSTEOCLASTOGENESIS

S. Fukui[1], N. Iwamoto[1], R. Masuyama[2], K. Kosai[3], K. Yanagihara[3], A. Kawakami[1]. *[1]Immunology and Rheumatology; [2]Molecular Bone Biology; [3]Laboratory Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan*

Background: Monocytes can differentiate into either proinflammatory, microbicidal M1 macrophage or anti-inflammatory M2 macrophage subtypes. In addition to macrophages, regarding monocyte subsets, M1 monocytes and M2 monocytes mirroring the M1/M2 macrophage polarization concept were suggested.
Little is known regarding the relationships between osteoclastogenesis and M1/M2 monocyte subsets.
Objectives: We investigated the relationships among M1 monocytes, M2 monocytes, osteoclast differentiation ability and clinical characteristics in patients with rheumatoid arthritis (RA).
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from RA patients and healthy donors, and we then investigated the number of M1 monocytes or M2 monocytes by fluorescence-activated cell sorting. We defined positive CD14, CD68 and CCR2 monocytes as M1 monocytes, and in separate tubes, we defined positive CD14, CX3CR1 and CD163 or CD206 monocytes as M2 monocytes.
We also obtained and cultured CD14-positive cells from PBMCs from RA patients and healthy donors to investigate osteoclast differentiation in vitro. We defined osteoclasts as tartrate-resistant acid phosphatase (TRAP) staining-positive cells with >3 nuclei. We counted the osteoclasts in the whole wells of a 96-well dish. Pit formation assays were performed to evaluate function of osteoclasts.
Results: Forty RA patients and 20 healthy donors were included. Twenty-two patients (55%) were ACPA-positive.
The median M1/M2 ratio was 0.59 (0.31–1.11, IQR). There were no significant differences between the RA patients and healthy donors.
There was a positive correlation between the M1/M2 ratio and the differentiated osteoclast number in vitro in RA patients (ρ=0.81, p<0.01) (A). The numbers of osteoclasts in vitro were significantly correlated with the area percentage of the pit formation area (ρ=0.74, p=0.001) (B).We demonstrated that the RA patients who had lower M1/M2 ratio and fewer osteoclasts (C) had smaller resorbed areas compared to the RA patients who had higher M1/2 ratio and greater numbers of osteoclasts (D).
The ACPA-positive patients had significantly higher M1/M2 ratio in vivo (p=0.028) (E) and significantly greater numbers of osteoclasts in vitro (p<0.01) (F) than the ACPA-negative patients. We show an ACPA-negative patient's osteoclasts in vitro (G) and those of an ACPA-positive patient (H).



Multivariable regression analysis revealed that the M1/M2 ratio was the sole significant contribution factor to in vitro osteoclastogenesis (β-coefficient 16.3, p<0.0001).
RA patients with M1/M2 ratio >1 (having relatively more M1 monocytes) had higher erythrocyte sedimentation rates (p=0.011) and C-reactive protein (p=0.032) than RA patients with M1/M2 ratio ≤1.
M1-dominant monocytes in vitro produced higher concentrations of IL-6 upon stimulation with lipopolysaccharide than M2 monocytes (p=0.032).
Conclusions: The M1/M2 ratio is strongly correlated with the in vitro differentiation of osteoclasts in patients with RA. The RA patients with positive ACPA had higher M1/M2 ratio and higher numbers of osteoclasts.
M1 and M2 monocyte subsets may become a new target of treatments for RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2083

FRI0018 TARGETED INHIBITION OF JANUS KINASES ABATES IFN-GAMMA-INDUCED INVASIVE BEHAVIOR OF FIBROBLAST-LIKE SYNOVIOCYTES

T. Karonitsch[1], D. Beckmann[2], K. Dalwigk[1], R. Byrne[1], B. Niederreiter[1], J. Holinka[3], F. Sevelda[3], A. Korb-Pap[4], G. Steiner[1], J. Smolen[1], T. Pap[2], H. Kiener[1]. *[1]Division of Rheumatology, Medical Universitiy of Vienna, Vienna, Austria; [2]Institute of Experimental Musculoskeletal Medicine, University Hospital Muenster, Muenster, Germany; [3]Department of Orthopaedics, Medical Universitiy of Vienna, Vienna, Austria; [4]University Hospital Muenster, Muenster, Germany*

Background: Emerging evidence suggests that fibroblast-like synoviocytes (FLS) are key effector cells in rheumatoid arthritis (RA) and research into the mechanisms defining FLS activity in RA indicate that cytokines secreted by leukocytes play a crucial role. Nevertheless, the contribution of IFNγ, which is increased in rheumatoid synovitis, to the inflammatory synovial tissue reaction is not known.
Objectives: To explore the function of the T-cell cytokine IFNγ for mesenchymal tissue remodeling in RA, and to determine whether IFNγ-signaling controls the invasive potential of FLS.
Methods: To assess architectural responses, FLS were cultured in three-dimensional micromasses. FLS motility was analyzed in migration-, spreading- and invasion assays. Signaling events relevant to cellular motility were defined by western blots. Baricitinb and siRNA pools were used to suppress Janus Kinase (JAK) functions.
Results: Histological analyses of micromasses revealed unique effects of IFNγ on FLS shape and tissue organization. This was consistent with accelerated migration, pronounced actin and focal adhesion (FA) re-organization upon IFNγ stimulation. Since actin and FA dynamics and, thus, cell motility are integrated by the focal adhesion kinase (FAK), we next analyzed its activity. Indeed, IFNγ stimulation induced the phosphorylation of FAK-Y925, a phosphosite implicated in FAK-mediated cell migration. siRNA knockdown of JAK2, but not JAK1, abrogated FAK activation by IFNγ. Correspondingly, IFNγ-inudced FAK activation and invasion of FLS was abrogated by the JAK-inhibitor baricitinib.
Conclusions: Our study contributes insight into the synovial response to IFNγ and reveals JAK2 as a potential therapeutic target for FLS-mediated joint destruction in arthritis, especially in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4862

FRI0019 HUMAN MESENCHYMAL STROMAL CELLS REDUCE TNFα SECRETION OF ACTIVATED PBMC VIA CTLA-4

T. Gaber[1,2], K. Schönbeck[3], C.L. Tran[2], C. Strehl[1,2], E. Röhner[4], G. Matziolis[4], G.-R. Burmester[1], F. Buttgereit[1,2], P. Hoff[1,2]. *[1]Department of Rheumatology and Clinical Immunology, Charité – Universitätsmedizin Berlin; [2]German Rheumatism Research Center (DRFZ); [3]Department of Pediatric Oncology and Hematology, Charité – Universitätsmedizin Berlin, Berlin; [4]Department of Orthopaedics, Friedrich-Schiller-University, Jena, Germany*

Background: The inhibitory costimulatory molecule Cytotoxic T-Lymphocyte Antigen-4 (CTLA-4) plays a crucial role in conveying immune tolerance in both inflammatory disorders and regenerative processes such as bone healing. During regenerative processes, mesenchymal stromal cells (MSC) provide the building bricks for reestablishing structural integrity but do also control inflammation by their immunomodulatory activities under restrictive microenvironmental conditions such as hypoxia. Here, we hypothesize these cells to support the control of inflammation via CTLA-4 in order to facilitate tissue regeneration such as bone fracture healing.
Objectives: Therefore, we analyzed expression of CTLA-4 by human MSC and their ability to convey immune suppression.
Methods: MSC were isolated from bone marrow of patients undergoing total hip replacement and characterized (i) by surface marker staining using flow cytometry and (ii) via assessing their osteogenic and adipogenic differentiation potential. MSC were cultured under normoxic (~18% O_2) and hypoxic (<1.5% O_2) con-

ditions, respectively. CTLA-4 expression in MSC was analyzed on protein and on transcriptional levels by flow cytometry, immunoblotting, ELISA and by quantitative PCR, respectively. To assess the functionality of CTLA-4 expression, MSC were co-cultured with peripheral blood mononuclear cells (PMBC) isolated by density gradient centrifugation from venous blood of healthy donors. The cells were stimulated for 48h with PHA (5μg/ml) or left untreated and challenged using either CTLA-4-Ig or anti-CTLA-4-antibody, incubated under normoxic (~18% O_2) or hypoxic (<1.5% O_2) conditions and analyzed for TNFα secretion by suspension assay.
Results: The MSC phenotype of bone-marrow derived cells could be verified according to their surface marker expression and their osteogenic and adipogenic differentiation capacity. On transcriptional level, MSC express both the full-length and - to a higher extent - the soluble CTLA-4 isoforms with a higher mRNA abundance under normoxic as compared to hypoxic conditions. Extra- and intracellular analysis of CTLA-4 expression on protein level, demonstrated a significant shift of the whole MSC population ($p<0,01$). CTLA-4 expression and secretion by MSC was confirmed using immunoblot and ELISA, respectively. Co-culture of MSC with PHA-activated PBMC significantly reduced the amount of secreted TNFα ($p<0,05$) which could be reversed by anti-CTLA-4-antibody ($p<0,05$), under both normoxic and compared to hypoxic conditions, respectively.
Conclusions: We clearly demonstrate the existence of CTLA-4 on hMSC and its functionality with regard to the inhibition of PHA-induced TNFα secretion by PBMC. We also demonstrate that the expression of CTLA-4 (i) contributes to the immunomodulatory capacity of hMSC and (ii) supports the '*immune privileged*' status of these cells.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4078

FRI0020 ALTERED BIOENERGETICS, MITOCHONDRIAL FUNCTION AND PRO-INFLAMMATORY PATHWAYS IN RA SYNOVIUM IN RESPONSE TO TOFACITINIB

C. Orr[1], T. Mcgarry[2], S. Wade[3], M. Biniecka[4], S. Wade[5], D.J. Veale[4], U. Fearon[5]. *[1]Translational Rheumatology, St. Vincent's University Hospital; [2]Clinical Medicine, Trinity Biomedical Sciences Institute; [3]Molecular Rheumatology, Trinity Biomedical Sciences Centre; [4]Center for Arthritis and Rheumatic Diseases, St Vincent's University Hospital; [5]Molecular Rheumatology, Trinity Biomedical Sciences Center, Dublin, Ireland*

Background: Rheumatoid arthritis (RA) is a chronic joint disease, characterised by synovial inflammation and a shift in the metabolic profile of cells to a more destructive phenotype. The JAK-STAT signalling pathway is implicated in the pathogenesis of RA.
Objectives: To examine the effect of tofacitinib, a selective JAK inhibitor, on synovial cellular bioenergetics, mitochondrial function and subsequent pro-inflammatory mechanisms in RA.
Methods: *Ex-vivo* RA whole tissue synovial explants and primary RA synovial fibroblasts (RASFC) and were cultured with tofacitinib (1μM) for 24–72hrs. RASFC metabolism was assessed by the XF24-Flux-analyser and mitochondrial mutagenesis was quantified using a mitochondrial random mutation capture assay. Mitochondrial function was assessed for reactive oxygen species (ROS), mitochondrial membrane potential (MMP) and mitochondrial mass (MM) using the specific cell fluorescent probes and differential gene expression by mitochondrial gene arrays or RT-PCR. Mitochondrial structural morphology was assessed by transmission electron microscopy. Lipid peroxidation (4HNE) was measured by specific ELISA. Dual staining of pSTAT3 and mitochondrial marker Cox-IV was demonstrated by confocal microscopy. The effect of tofacitinib (1μM) in RA synovial explant on markers of cellular bioenergetics and pro-inflammatory mediators, including cytokines and growth factors were quantified by ELISA, MSD multiplex assays and Real-time PCR.
Results: An initial screen demonstrated alterations in 18 key genes involved in mitochondrial function in RA synovial tissue in response to tofacitinib. Supporting this, tofacitinib inhibited ROS production, decreased the MMP and MM (all $p<0.05$), coupled with altered mitochondrial morphology. No effect observed for mtDNA mutations or 4HNE levels. Tofacitinib significantly inhibited the expression of glycolytic genes HIF1α, HK2, LDHA, GSK3A and PDK1 (all $p<0.05$) suggesting altered energy metabolism. This was paralleled by inhibition of baseline ECAR (glycolysis) with a concomitant increase in baseline OCR (oxidative phosphorylation), ATP production, maximal respiratory capacity and in the respiratory reserve in RASFC, confirming a bioenergetic switch in synovial cells in response to tofacitinib. Furthermore, we demonstrated co-localisation of pSTAT3 with Cox-IV in RASFC, suggested that in addition to nuclear transcription, pSTAT3 may also act as a mitoTF, regulating mitochondrial function directly. Finally, in RA whole tissue explants, tofacitinib significantly inhibited glycolytic genes HK2, GSK3A and PDK1 which was paralleled by a significant decrease in the spontaneous secretion of inflammatory mediators IL-6, IL-8, IL-1β, ICAM-1, VEGF, Tie2 and MMP1 (all $p<0.05$).
Conclusions: In this study, we describe a potential mechanism of action for tofacitinib, through reversing mitochondrial dysfunction and subsequent switch in cellular bioenergetics, in favour of a less glycolytic microenvironment leading to the reduction of inflammatory mediators. Thus, we have demonstrated that pathological cellular metabolism may be reversed by therapeutic treatment with tofacitinib.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6209

FRI0021 INTRAVENOUS INFUSION OF FUCOSYLATED BONE MARROW MESENCHYME CELLS IN PATIENTS WITH OSTEOPOROSIS. PRECLINICAL STUDY IN A MURINE MODEL

N. Lozano-Rivas[1], V. Cabañas-Perianes[2], L. Linares-Ferrando[1], C. Marras Fernández-Cid[1], M.D. Lucas López[2], F.A. Martínez-Angosto[1], M. Blanquer[2], J. Martínez Ferrín[1], A. García Hernández[2], R. Sackstein[3], J.M. Moraleda[2]. *[1]Rheumatology; [2]Hematology, University Hospital Virgen de la Arrixaca, Murcia, Spain; [3]Harvard Medical School, Cambridge, United States*

Background: Osteoporosis is a skeletal disease characterized by systemic bone loss with an increased risk to bone fractures, associated with high morbidity and mortality[1]. Mesenchymal stem cells (MSC) from bone marrow (BM) are ideal candidates for the treatment of osteoporosis because they are able to differentiate to osteoblasts although its osteotropism is low[2]. Ex vivo fucosylation (adding a fucose residue) in α1–3 position of the CD44 antigen by use of the enzyme fucosyltransferase VI (FTVI) yields Hematopoietic cell E and L-selectin ligand (HCELL) in MSC increasing the affinity for E-selectin and osteotropism.
Objectives: To describe the safety and efficacy of human fucosylated MSC infused in an immunocompromised mice model (NOD/SCID).
Methods: 31 NOD/SCID mice were randomized to by tail vein injection: $1x10^6$ fucosylated MSC (n=13), $1x10^6$ MSC (n=14) or saline (n=4). Toxicities were evaluated by a clinical score, weight and histological assessment (heart, lung, liver, spleen, kidney, gonads, brain, bone and BM). RT-PCR array-based evaluation of the expression of human β-actin and β2-microglobulin genes was performed to study biodistribution of MSC. The maintenance of genetic integrity was evaluated during in vitro culture by karyotype. Additional samples of tibia and calota were to immunostained with a polyclonal Rabbit anti-human osteocalcina to demonstrate efficacy. Osteocalcin-positive cells were identified by a dark-brown cytoplasmic precipitate.
Results: There was no unexpected death and none of the mices had any acute toxicity. The histology of heart, liver, kidney, spleen, gonads, brain, bone and bone marrow was normal in all mice. There were localized areas of lung inflammation in 15%, 42% and 25% of mice infused with fucosylated MSC, MSC, and saline, respectively without significance differences (p=0.28). Biodistribution was normal with except one mice (infused with MSC non-fucosylated) showed an expression of human RNA β-actin and β2-microglobulin in the lung sample taken after 12 weeks of intravenous infusion. Osteoblasts were seen in 100% of mices infused with fucosylated MSC, in 62.5%% of animals infused with MSC alone, and none in saline group (p=0.01). NOD/SCID mice infused with fucosylated MSC presented a higher number of osteoblasts positive for osteocalcin in 10 high-power fields (400x) of tibia and calvarium sections that non-fucosylated (32 vs 5.5) (p=0.0082). Human osteoblasts were detected inside the bone from the fifth to the twelfth week after infusion.
Conclusions: Intravenous infusion of human fucosylated MSC is safe and effective in guiding the cells to bone with a higher potential to ossification in NOD/SCID mices that non-fucosylated MSC. These results are allowing to start a human clinical trial with intravenous fucosylated MSC as treatment in patients with osteoporosis.
References:
[1] Johnell O, Kanis JA. An estímate of the worldwide prevalence and disability associated with osteoporotic fractures.Osteoporos Int 2006 Dec;17(12):1726–33.
[2] Connolly JF. Injectable bone marrow preparations to stimulate osteogenic repair. Clin Orthop Relat Res 1995 Apr;(313):8–18.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2945

FRIDAY, 16 JUNE 2017

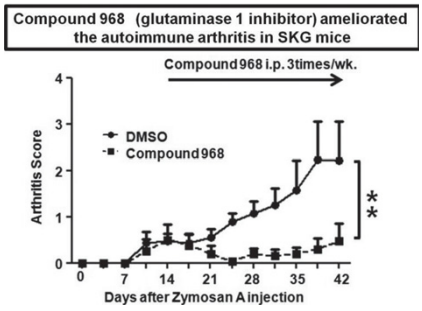
Rheumatoid arthritis - etiology, pathogenesis and animal models

FRI0022 GLUTAMINE METABOLISM PLAYS A KEY ROLE IN THE CELL GROWTH OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS

S. Takahashi, J. Saegusa, H. Yamada, Y. Ichise, I. Naka, T. Okano, K. Akashi, S. Sendo, Y. Ueda, A. Onishi, A. Morinobu. *Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe, Japan*

Background: Many signaling pathways activated under inflammatory and hypoxic conditions have profound effects on intracellular metabolism to support cell growth and survival. The recent findings of cancer-specific metabolic changes, including increased glucose and glutamine consumption, has provided new therapeutic targets for consideration. The microenvironment in inflamed joints in RA is also characterized by hypoxia and low concentration of nutrients, and fibroblast-like synoviocytes from RA patients (RA-FLS) is known to have several tumor-like characteristics. However, the role of glucose and glutamine metabolism in the aberrant proliferation of these cells is unclear.

Objectives: We evaluated the role of these metabolic pathways in RA-FLS proliferation and in autoimmune arthritis in SKG mice.
Methods: The expression of glycolysis- or glutaminolysis-related enzymes was evaluated by real-time PCR and Western blotting, and the intracellular metabolites were evaluated by metabolomic analyses. The effects of glucose or glutamine on RA-FLS cell growth were investigated using glucose- or glutamine-free medium. Glutaminase 1 (GLS1) siRNA and the GLS1 inhibitor compound 968 were used to inhibit GLS1 in RA-FLS. Arthritis was induced in SKG mice by zymosan A injection. Compound 968 was used to study the effect of GLS1 inhibition on Zymosan A-injected SKG mice. Ki-67-positive cells were analyzed by immunohistochemistry.
Results: GLS1 expression was increased in RA-FLS, and metabolomic analyses revealed that glutamine and glutamate consumption were increased in RA-FLS. RA-FLS proliferation was reduced under glutamine-deprived, but not glucose-deprived conditions. Cell growth of RA-FLS was inhibited by GLS1 siRNA transfection or GLS1 inhibitor treatment. Silencing of GLS1 in RA-FLS did not affect IL-6 or MMP-3 production in supernatants. GLS1 expression in RA-FLS was not affected by pro-inflammatory cytokine stimulation. Compound 968 ameliorated the autoimmune arthritis and decreased the number of Ki-67-positive synovial cells in SKG mice.



Conclusions: Our findings suggested that glutamine metabolism plays an important role in regulating RA-FLS proliferation, without being affected by pro-inflammatory cytokine stimulation or affecting cytokine production, and may be a novel therapeutic target for RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2804

FRI0023 ARTESUNATE CAN INHIBIT MIGRATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES VIA SUPPRESSION OF MATRIX METALLOPROTEINASE 9 IN RHEUMATOID ARTHRITIS PATIENTS

J. Jing[1], T. Yan[2], J.-D. Ma[1], Y.-Q. Mo[1], L. Dai[1]. [1]*Rheumatology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University;* [2]*Zhongshan School of Medicine, Sun Yat-Sen University, Guangzhou, China*

Background: Evidences show that antimalarial agents of artemisinin and its derivatives such as artesunate may inhibit proinflammatory cytokines secretion from human rheumatoid arthritis (RA) fibroblast-like synoviocytes (FLS) in vitro. It has also been demonstrated that artesunate may ameliorate the symptoms of arthritis and prevent joint damage in collagen induced arthritis rat, which suggests that artesunate may be used for RA treatment. Recent studies show that RA-FLS is critical for joint destruction in RA because it can migrate and attach to cartilage and bone, and then invade them by secreting proteases such as matrix metalloproteinases (MMP) 9 in RA. However, effects of artesunate on migration and invasion of RA-FLS are poorly understood.
Objectives: To investigated the effects of artesunate on migration and invasion of RA-FLS and its underlying mechanism.
Methods: Synovial tissues were obtained from active RA patients as well as osteoarthritis (OA) and noninflammatory orthopedic arthropathies (Orth.A) patients and immumohistochemical (IHC) staining were performed for MMP9 expression. FLS isolated from these patients were analyzed for MMP9 exprssion by western blot (WB) and incubated with artesunate at different concentrations (0μM, 20μM, 40μM and 60μM), methotrexate (MTX, 10nM) or hydroxychloroquine (HCQ, 20μM) for 24 hours. Effects of artesunate on migration and invasion capacity were detected by transwell and wound healing assays. MMP9 and PI3K/Akt signal transduction protein expression after artesunate treatment was measured by WB.
Results: (1) IHC staining showed that synovial MMP9 expressed in lining and sublining area with intense nuclear and endochylema staining in RA synovium and the percentage of MMP9+ cells was significantly higher in RA (n=32) than that in OA (n=6) or Orth.A (n=6, Figure 1A, B).
(2) Migration and wound healing assays for 12 hours and invasion assay for 24 hours showed that RA-FLS possessed stronger capacity in migration and invasion than OA-FLS or Orth.A-FLS (Figure 1E, F). Artesunate inhabits the migration and invasion capacity of RA-FLS in a dose-dependent manner. MTX also has an inhibition effect on the migration and invasion of RA-FLS, but not HCQ (Figure 2A).
(3) MMP9 expression in RA-FLS was significantly higher than that in OA-FLS or Orth.A-FLS (Figure 1C, D). 40μM or 60μM artesunate markedly inhibited the expression of MMP9 in RA-FLS by WB (Figure 2B).
(4) WB analysis showed artesunate suppressed generation of phophso-Akt in a dose-dependent manner which indicated that Akt activity (phophso-Akt/Akt) in 40μM and 60μM artesunate treatment groups were significantly lower than that in untreated group (Figure 2C).

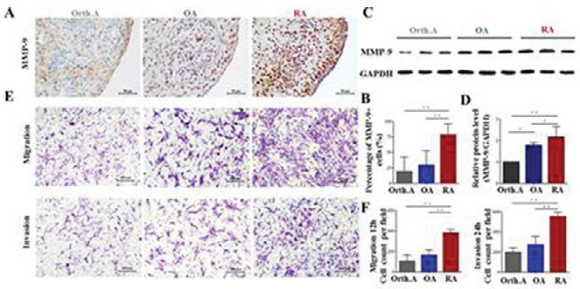


Figure 1 Expression of MMP9 in synovium and FLS and migration and invasion capacity of FLS. **(A and B)** IHC analysis showed that expression of MMP9 from RA patients was significantly higher than OA and Orth.A patients. Data are representative as means ± SD **P<0.01, ***P<0.001. **(C and D)** WB analysis showed that expression of MMP9 from RA-FLS was significantly higher than Orth.A-FLS or OA-FLS. Data were representative as means ± SD, *P<0.05, **P<0.01. **(E and F)** Transwell assays showed that RA-FLS possess stronger capacity of migration and invasion than OA-FLS or Orth.A-FLS. Data were representative as means ± SD, **P<0.01.

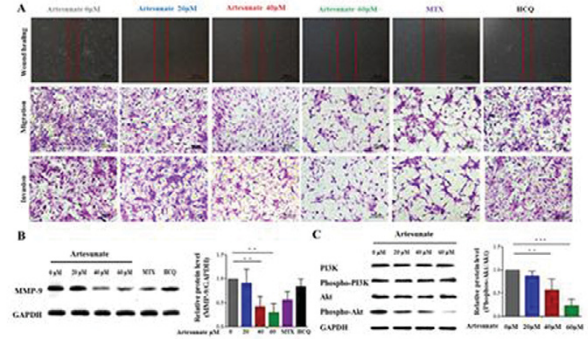


Figure 2 Effects of artesunate on the migration and invasion capacity and MMP9, PI3k/Akt pathway expression. (A) Artesunate inhabits the migration and invasion capacity of RA-FLS in a dose-dependent manner. **(B)** WB analysis of RA-FLS showed that MMP9 expression was siginificantly inhibited with treatment with 40 μM and 60 μM artesunate. **(C)** WB analysis showed that artesunate suppressed the expression of phophso-Akt in a dose-dependent manner. Bar are representative as means ± SD, **P<0.01, ***P<0.001.

Conclusions: Artesunate could inhibit the migration and invasion capacity of RA-FLS and the expression of MMP9 through suppressing Akt activity.
Acknowledgements: This work was supported by National Natural Science Foundation of China (81671612 and 81471597), Research Project of Traditional Chinese Medicine Bureau of Guangdong Province (20161058) and Guangdong Natural Science Foundation (2014A030313074).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2039

FRI0024 MICRORNA-146A CONTROLS LOCAL BONE DESTRUCTION BY REGULATING FIBROBLAST INDUCED OSTEOCLASTOGENESIS IN INFLAMMATORY ARTHRITIS

V. Saferding[1], A. Puchner[1], E. Goncalves-Alves[1], M. Hofmann[1], M. Bonelli[1], S. Hayer[1], H.P. Kiener[1], P. Georgel[2], M.I. Koenders[3], G. Steiner[1], J.S. Smolen[1], K. Redlich[1], S. Blueml[1]. [1]*Medical University of Vienna, Vienna, Austria;* [2]*Université de Strasbourg, Strasbourg, France;* [3]*Radboud University Nijmegen, Nijmegen, Netherlands*

Background: MicroRNA (MiR-) 146a plays an important role in the regulation of the innate immune response and has also been shown to suppress cancer development in myeloid cells. Although in late stages of arthritis elevated expression of miR-146a in synovial tissue of rheumatoid arthritis patients was detected, the level of this miRNA was found to be down regulated in early disease, but its role in the development of inflammatory arthritis is still elusive.
Objectives: The objective of this study is to analyse the role of miR-146a in arthritis by the use of a chronic arthritis disease model. We aim to investigate the regulatory function of this miRNA in the pathogenic stroma, therefore in fibroblasts but also in immune cells.
Methods: To induce arthritis we used the chronic inflammatory hTNFtg disease model, therefore we crossed miR-146a deficient into hTNFtg mice. Disease severity was assessed clinically and histologically. Blood of arthritis animals was analysed by flow cytometry. Serum cytokine levels were measured by Elisa. Synovial fibroblasts were isolated from metatarsal bones and their proliferation

was analysed histologically and by ^{3}[H]thymidine incorporation. RNA expression levels were measured by qPCR.
Results: When we crossed miR-146a$^{-/-}$ into hTNFtg mice, histological examination revealed a significant increase in synovial inflammation and even more striking a more than twofold increase in local bone destruction, due to increased generation of osteoclasts in the tarsal joints of miR-146a$^{-/-}$/hTNFtg mice compared to hTNFtg mice. Interestingly, systemic bone loss was comparable in hTNFtg compared to miR-146a$^{-/-}$/hTNFtg mice, suggesting an important local role of miR-146a. Indeed, we detected increased levels of IL-1β, TRAF6, a major target of miR-146a and RANKL, in addition the expression level of OPG was decreased locally in the paws of miR-146a$^{-/-}$/hTNFtg compared to hTNFtg mice. By performing bone marrow transplants we could indeed show a pivotal role for miR-146a in mesenchymal cells in controlling local osteoclast generation and bone destruction. Analysis of important mesenchymal cells in arthritis, the synovial fibroblasts exhibited enhanced proliferation if miR-146a is missing, *in vitro* and *in vivo*. Moreover stimulation of these cells with IL-1β, a prominent cytokine in arthritis which was also shown to be negatively regulated by miR-146a, led to increased expression of RANKL and TRAF6 in miR-146a deficient synovial fibroblasts.
Conclusions: These data demonstrate an important mitigating role of the miR-146a in inflammatory arthritis, most importantly in local bone destruction, by controlling mesenchymal expression of osteoclastogenic factors. This shows an important anti-inflammatory role of miR-146a, which might possibly be exploited for therapeutic purposes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3384

FRI0025 THE TAM RECEPTORS AXL AND MER PLAY A PROTECTIVE ROLE IN A TEMPORAL AND SPATIAL MANNER IN INFLAMMATORY ARTHRITIS

C.E.J. Waterborg[1], P.G. Través[2], S. Beermann[1], M.I. Koenders[1], P.L.E.M. van Lent[1], F. den Hoogen[1], P.M. van der Kraan[1], F.A.J. van de Loo[1]. *[1]Experimental Rheumatology, Radboudumc, Nijmegen, Netherlands; [2]Molecular Neurobiology Laboratory, The Salk Institute for Biological Studies, la Jolla, CA, United States*

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by an inflammatory response in synovial joints. One family of tyrosine kinase receptors that mediates a natural anti-inflammatory feedback mechanism are Tyro3, Axl and Mer (gene *Mertk*; TAM). The two principal TAM receptor protein ligands are Growth Arrest-Specific 6 (Gas6) and Protein S (Pros1). Targeting the TAM receptors by adenoviral overexpression of their ligands alleviates experimental arthritis pathology. Notably, Gas6 is a ligand for all three receptors but with the highest affinity for Axl. In contrast, Pros1 can only activate Tyro3 and Mer but not Axl. The role of the separate TAM receptors in RA has not been elucidated.
Objectives: To reveal the individual role of the TAM receptors Axl and Mer in an experimental inflammatory model of RA.
Methods: The KRN serum transfer model of arthritis was induced by two intraperitoneal injections of arthritic K/BxN serum in *Axl*$^{-/-}$, *Mertk*$^{-/-}$, *Axl*$^{-/-}$*Mertk*$^{-/-}$ and wild-type (WT) mice. Ankle joints were macroscopically scored for 7 days. At day 0, 2 and 7, ankle and knee joints were isolated for histology and immunohistochemistry.
Results: The course of arthritis was studied macroscopically and *Mertk*$^{-/-}$ mice had increased macroscopic ankle scores until day 4, compared to WT. Thereafter, *Axl*$^{-/-}$ mice developed more severe arthritis as compared to WT with enhanced macroscopic scores from day 4 until day 7. Histology of ankle joints showed significantly more inflammation in *Mertk*$^{-/-}$ mice at day 2 and increased arthritis pathology in *Axl*$^{-/-}$ mice at day 7, reflecting the macroscopic ankle scores. Histological analysis of ankle joints of *Axl*$^{-/-}$*Mertk*$^{-/-}$ mice at day 7 showed enhanced pathology compared to both *Axl*$^{-/-}$ and WT mice, indicating an additive effect of Axl and Mer deficiency. In contrast to the ankle joints at day 7, enhanced macroscopic scores and arthritis pathology in knee joints of *Mertk*$^{-/-}$ mice, compared to WT mice, was observed at both day 2 and day 7. *Axl*$^{-/-}$ mice had comparable knee joint pathology compared to WT. To explain the discrepancy of Axl involvement between ankle and knee at day 7, we examined Axl expression in synovium before the onset of arthritis. The cells in the lining layer of ankle synovium were strikingly Axl positive whereas the synovium of the knee joints was Axl negative.
Conclusions: The Mer receptor plays a protective role at the onset of arthritis whereas the Axl receptor takes over this role in established disease in ankle joints. In the knee joints, however, Mer but not Axl, plays a prominent protective role, likely due to the lack of Axl in naïve knee joints. These findings identify the TAM receptors Axl and Mer as protective in arthritis, dependent on the distinct anatomic location. It is tempting to speculate that these differences in topographically distinct synovial joints could, at least in part, explain the differential joint involvement in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4887

FRI0026 IDENTIFICATION OF MICRORNAS CANDIDATES SPECIFICALLY EXPRESSED IN MONOCYTES OF UNDIFFERENTIATED ARTHRITIS PATIENTS WHO PROGRESSED TO RHEUMATOID ARTHRITIS

W. Kurowska[1], E. Kuca-Warnawin[1], A. Radzikowska[1], M. Ciechomska[1], U. Skalska[1], M. Jakubaszek[2], B. Kwiatkowska[2], W. Maslinski[1]. *[1]Department of Pathophysiology and Immunology; [2]Early Arthritis Clinic, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland*

Background: Monocytes are central to the initiation of inflammation and bone erosion in rheumatoid arthritis (RA). Therefore, understanding of molecular pathways regulation in monocytes, especially at the early stages of RA development, is of crucial importance as it may help to predict the progression to the full-blown disease. However, mechanisms of gene regulation in monocytes, particularly the pattern of microRNA molecules (miRNAs) expression which can be involved in regulation of several cellular inflammatory pathways, in early phases of RA (i.e. at undifferentiated arthritis-UA stage) are not fully characterized.
Objectives: To investigate the pattern of miRNAs expression in monocytes that could serve as new biomarkers for RA development.
Methods: Magnetically sorted monocytes from peripheral blood of 19 patients with UA served for total RNA isolation. Total RNA from both sample and reference was labelled with Hy3 and Hy5 fluorescent label, respectively, using the miRCURY LNA microRNA Hi-Power Labeling Kit (Exiqon, Denmark). Fluorescent labelled samples and a reference RNA sample were hybridized to the miRCURY LNA microRNA Array 7th Gen (Exiqon), followed by scanning by Microarray Scanner System (Agilent Technologies, USA). The image analysis was carried out using ImaGene 9 Software (Exiqon).
Results: Out of 19 patients with UA enrolled in the study, 12 were verified for diagnosis after 4 years of follow-up (7 patients did not respond to the call for re-evaluation). Four patients developed full-blown RA (UA→RA patients), 6 patients remained still in UA phase (UA→UA patients), 1 patient was diagnosed as having Sjögren's Syndrome, and 1 undifferentiated connective tissue disease. Baseline characteristics of UA→RA *vs* UA→UA patients were as follows: age (median: 50.5, range 37–59 years *vs* 52.5, range 32–63 years), CRP (median: 9.0, range 1–22 mg/l *vs* 8.0, range 1–21 mg/l), ESR (median: 37.0, range 4–47 mm/h *vs* 34.0, range 15–44 mm/h) and swollen joins count (median: 3.0, range 1–9 *vs* 2.5, range 1–4). Following computational unsupervised analysis we identified 50 miRNAs in monocytes that have the largest variation across all patients samples. From these 50 miRNAs we selected several specific miRNA candidates on the basis of significantly changed expression in monocytes of UA→RA *vs* UA→UA patients. Predicted specific miRNAs targeting inflammatory genes in monocytes of UA→RA patients are: miR-483–3p (2.7-fold increased, p=0.009), miR-378d (4.1-fold decreased, p=0.0059), miR-371b-5p (52.8-fold increased, p=0.0381) miR-642b-5p (13.7-fold increased, p=0.0380), and miR-25–3p (1.8-fold decreased, p=0.0317). Additional validation of selected miRNAs candidates will be further performed using qPCR analysis.
Conclusions: Our results indicate new miRNA candidates differentially expressed in peripheral blood monocytes from patients with UA who subsequently developed RA, in comparison to patients with UA who did not progress to RA after 4 years follow-up.
Acknowledgements: Supported by NCN Poland (grant 2012/06/A/NZ5/00059).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5703

FRI0027 TNF EXPRESSION ON MICROPARTICLES FROM RHEUMATOID ARTHRITIS PATIENTS MEDIATES ENDOTHELIAL CELL FATE IN VITRO

C. Barbati, M. Vomero, T. Colasanti, L. Novelli, F.R. Spinelli, F. Miranda, F. Ceccarelli, A. Finucci, C. Perricone, R. Scrivo, F. Conti, G. Valesini, C. Alessandri. *Department of Internal Medicine and Medical Specialties, Arthritis Center, Sapienza University of Rome, Rome, Italy, roma, Italy*

Background: Microparticles (MPs) are small membrane vesicles released by many cell types under physiological conditions or pathological situations. Increased levels of MPs have been reported in patients with autoimmune diseases, such as Rheumatoid Arthritis (RA) (1) which is characterized by an accelerated atherosclerosis. TNF, a key cytokine involved in the pathogenesis of RA, has been associated to RA atherosclerosis (2). Moreover, MPs could also have a role in endothelial dysfunction contributing to atherosclerosis in RA patients.
Objectives: The aim of this study was: 1) to evaluate TNF expression on RA-MPs. 2) to estimate the effects of serum RA-MPs on endothelial apoptosis and autophagy before and after in *vivo* and in *vitro* treatment with Etanercept.
Methods: 15 RA patients were recruited from the Department of Rheumatology Sapienza University of Rome at baseline (T0) and after three months of therapy (T3) with Etanercept. A fasting blood sample was collected and centrifuged two times to obtain platelet-poor plasma rich in MPs. The resulting plasma was stained with Ab anti-TNF and analized by flow cytometry. In *vitro* effects of serum RA-MPs on endothelium were evaluated using human umbilical vein cell line *EA.hy926*. Cells were treated with RA-MPs purified at T0 and T3 and with RA-MPs in *vitro* treated with Etanercept. At the end of experiments apoptosis and autophagy were evaluated. Apoptosis was analyzed by flow cytometry using a FITC-conjugated

annexin V and propidium iodide apoptosis detection kit; autophagy was analyzed by western blot for the expression level of the autophagic marker LC3-II.
Results: Our results showed that MPs purified from RA patients at T0 expressed TNF on their surface and this expression decreased after three months of treatment with Etanercept (p=0.04). Moreover, serum RA-MPs at T0 significantly increased, in a dose-dependent manner, both apoptosis and autophagy levels in the human umbilical vein cell line *EA. hy926* (p=0.005 and p=0.02, respectively *versus* untreated cells). After three months of treatment with Etanercept, RA-MPs were not able to significantly change these parameters.Finally, in *vitro* studies showed that RA-MPs treated with Etanercept significantly decreased surface expression of TNF and were no longer able to modulate apoptosis and autophagy in *EA.hy926* cells.
Conclusions: Our data demonstrate that serum RA-MPs express TNF on their surface. Moreover, both in *vivo* and in *vitro* treatment with Etanercept interfere with the ability of MPs to significantly modulate apoptosis and autophagy of endothelial cells by decreasing surface expression of TNF.
References:
[1] Beyer C and Pisetsky DS.The role of microparticles in the pathogenesis of rheumatic diseases. Nat. Rev. Rheumatol. 2010;6:21–9.
[2] Feldmann M, Brennan FM, Foxwell BM and Maini RN.The role of TNF alpha and IL-1 in rheumatoid arthritis Curr. Dir. Autoimmun. 2001;3:188–99.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3434

FRI0028 IN VITRO INHIBITORY EFFECT OF ETANERCEPT ON AUTOPHAGY: A NEW MECHANISM OF ACTION OF TNF INHIBITORS IN RHEUMATOID ARTHRITIS

M. Vomero[1], A. Capozzi[2], C. Barbati[1], T. Colasanti[1], V. Manganelli[2], F. Ceccarelli[1], F.R. Spinelli[1], F. Conti[1], C. Perricone[1], A. Finucci[1], M. Pendolino[1], R. Scrivo[1], R. Misasi[2], M. Sorice[2], G. Valesini[1], C. Alessandri[1]. *[1]Department of Internal Medicine and Medical Specialties, Arthritis Center, Sapienza University of Rome; [2]Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy*

Background: Autophagy has emerged as a key mechanism in the development, survival and function of immune cells and dysregulation of autophagic pathway has been implicated in the pathogenesis of several autoimmune diseases including Rheumatoid Arthritis (RA) (1). In fact, autophagy seems to be involved in the generation of citrullinated peptides, with consequent breakage of tolerance in RA (2). Moreover, increased autophagy levels and a reduction of apoptosis-related molecules have been found in RA synovial tissues and a role of TNF-induced autophagy in RA development has been proposed (3).
Objectives: The aim of the study was to analysed the effect of TNF and anti-TNF inhibitor etanercept on autophagy and apoptosis in cells involved in RA pathogenesis.
Methods: Peripheral blood mononuclear cells (PBMCs) and fibroblast-like synoviocytes (FLS) isolated from RA patients were cultured in presence of TNF and in serum deprivation state (starvation) for 4 hours and then etanercept, at concentration of 15 ug/mL, were added to the culture. After 24h cells were analyzed for levels of autophagy marker LC3-II by western blot and for percentage of annexin V-positive apoptotic cells by flow cytometry.
Results: As expected, TNF and starvation induced autophagy on RA PBMC and FLS in dose-dependent manner after 24h of culture ($p<0.05$ in all experimental conditions). Moreover, the adding of etanercept caused a significant reduction of LC3-II levels (p=0.004) and an increase of apoptosis rate (p=0.002) after both pro-autophagic stimuli ($p<0.05$).
Conclusions: We demonstrated for the first time an inhibitory effect of etanercept on autophagy activation of cells involved in RA pathogenesis. In addition, our findings suggest a crucial role of autophagy in RA cells survival.
References:
[1] Pierdominici M, Vomero M, Barbati C et al. Role of autophagy in immunity and autoimmunity, with a special focus on systemic lupus erythematosus. FASEB J. 2012; 26:1400–12.
[2] Sorice M, Iannuccelli C, Manganelli V et al. Autophagy generates citrullinated peptides in human synoviocytes: a possible trigger for anti-citrullinated peptide antibodies. Rheumatology. 2016;55:1374–85.
[3] Rockel JS, Kapoor M. Autophagy: controlling cell fate in rheumatic diseases. Nat Rev Rheumatol. 2016;12:517–31.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5061

FRI0029 THE OXYGEN SENSOR PHD1 IS AN INDISPENSABLE REGULATOR OF ARTHRITIS DEVELOPMENT

K. De Wilde[1,2], D. Gaublomme[1,2], J. Coudenys[1,2], F. Windels[1,2], S. Van Welden[3], A. De Muynck[4], D. Elewaut[1,2]. *[1]Department of Rheumatology, Department of Internal Medicine, Ghent University; [2]Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center; [3]Department of Gastroenterology; [4]Department of Physics and Astronomy, Ghent University, Ghent, Belgium*

Background: Oxygen supply is a fundamental requirement for all living tissues. Some tissues such as articular joints are characterized by a physiological state of hypoxia. Interestingly, under conditions of inflammation such as in arthritic disease, this level of hypoxia is even further enhanced. However, the functional significance of these observations and the molecular mechanisms involved remain poorly characterized to date. Our goal was therefore to examine the role of 3 known oxygen sensors, prolyl hydroxylase domain (PHD) proteins: PHD1, PHD2 and PHD3. They are enzymes whose function is essentially controlled by oxygen. Their expression pattern varies between either of them and all of them have been ascribed specific roles in a myriad of biological processes. [1]
Objectives: Our goal was to examine the role of oxygen sensors PHD1, PHD2 and PHD3 in preclinical models of rheumatoid arthritis, and to delineate the cellular source involved.
Methods: We subjected the collagen antibody induced arthritis (CAIA) model (resembling rheumatoid arthritis) to hypoxic (10% O_2) and normoxic conditions (21% O_2), respectively. Furthermore, the CAIA-model was induced in mice with germline deficiency of the specific PHD's and in mice with a myeloid cell-specific PHD1 deficiency versus controls. Arthritis development was assessed by clinical scoring of paw swelling, histopathology of knee joints and μCT.
Results: Mice kept in hypoxic conditions during CAIA experiments showed markedly less arthritis (both by clinical and histopathological assessment) compared to mice in normoxic conditions. Furthermore, we demonstrated that PHD1 knock-out (KO) mice had significantly less joint inflammation compared to wildtype mice. PHD1 KO mice were also protected against inflammation induced bone loss as evidenced by μCT. By contrast, no differences were found between PHD2 heterozygous (PHD2 KO mice are not viable) or PHD3 KO mice and littermate controls. Because myeloid cells are considered critical effector cells upon passive transfer of arthritogenic antibodies in the CAIA model we also generated myeloid cell specific ko mice ($PHD1^{myelKO}$). Of interest, $PHD1^{myelKO}$ mice developed less arthritis compared to wildtype mice and were protected against inflammation induced bone loss.
Conclusions: Our data are consistent with a new paradigm that the oxygen sensor PHD1 is a critical regulator of myeloid cell function in arthritic disease. Overall, the data suggest that PHD1 is a potential target in the treatment of arthritis.
References:
[1] Fong G-H, Takeda K. Role and regulation of prolyl hydroxylase domain proteins. Cell Death Differ 2008;15:635–41. doi:10.1038/cdd.2008.10.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5194

FRI0030 SYNOVIAL MAST CELLS IDENTIFY PATIENTS WITH A SEVERE PHENOTYPE IN A COHORT OF DMARD NAÏVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

F. Rivellese[1], F. Humby[1], A. Nerviani[1], S. Pagani[1], D. Mauro[1], A. de Paulis[2], G. Marone[2], C. Pitzalis[1]. *[1]Centre for Experimental Medicine & Rheumatology, William Harvey Research Institute, Barts and the London School of Medicine & Dentistry, London, United Kingdom; [2]Department of Translational Medical Sciences (DiSMeT) and Center for Basic and Clinical Immunology Research (CISI), University of Naples Federico II, Naples, Italy*

Background: Mast cells (MCs) are among the immune cells participating to the inflammatory response in Rheumatoid Arthritis (RA), but their exact contribution to disease development and progression is unclear.
Objectives: To evaluate the presence of MCs in the synovia of patients with early RA naïve to treatment and their correlation with baseline clinical phenotype, response to DMARDs and disease progression.
Methods: DMARD-naïve patients with early (<12 months) RA (n=99) fulfilling the 2010 ACR/EULAR criteria were recruited as part of the Pathobiology of Early Arthritis Cohort at Barts Health NHS Trust. Sections of paraffin embedded synovial tissue obtained by ultrasound-guided synovial biopsy were stained by immunohistochemistry for CD117 (c-kit) and patients were classified into MC+ and MC- groups. Differences in clinical parameters at baseline and 6 months and progression in radiographic damage at 12 months were evaluated. The expression of Receptor Activator of Nuclear factor Kappa-B Ligand (RANKL) by human primary MCs was assessed by western blot and immunofluorescence.
Results: The presence of synovial CD117+ MCs was significantly associated with highly active disease (DAS28, ESR, CRP, tender and swollen joint counts, $p<0.05$). At the 6 months follow-up, there were no differences in terms of response to treatment with synthetic DMARDs (e.g. DAS28 remission 38.8% in MC+ vs 42.9% in MC-, p=0.725). Nonetheless, MC+ patients showed a significantly higher prevalence of radiographic progression at 12 months (progressors/non progressors 13/38 in MC+ vs 0/28 in MC-, p=0.003, n=79). When progressors were compared with non progressors, there were no differences in clinical parameters at baseline (inflammatory markers, DAS28, ACPA or RF positivity). Because of the observed association of MCs with radiographic progression, we looked for mechanisms that could link MCs to bone erosions, and we found that human primary MCs express the osteoclast activator RANKL.
Conclusions: We show that synovial MCs identify patients with a severe clinical phenotype in a DMARD-naïve early RA cohort. In particular, despite a similar rate of response to DMARDs at 6 months, the presence of synovial MCs at baseline was significantly associated with radiographic progression at 12 months. As clinical parameters at baseline showed no association with radiographic

progression, our work suggests that the analysis of synovial MCs could help to identify patients at high risk of progression in radiographic damage, warranting further investigations to confirm the association of MCs with the development of joint damage and their direct contribution to bone erosion, possibly via a RANKL-mediated activation of osteoclasts.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6393

FRI0031 DNA OXIDASE ENZYME TET3 EXACERBATES SYNOVIAL INFLAMMATION AND BONE DESTRUCTION

A. Kawabe[1], K. Naknao[1], K. Sakata[1,2], K. Yamagata[1], S. Nakayamada[1], Y. Tanaka[1]. [1]*The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu;* [2]*Mitsubishi Tanabe Pharma, Yokohama, Japan*

Background: In rheumatoid arthritis (RA), fibroblast-like synoviocytes (FLSs) play an important role in joint destruction. We have shown a disease-specific DNA methylation pattern in RA patient-derived FLSs (RA FLSs). In 2009, active demethylation enzymes, Ten-Eleven translocation (TET) 1/2/3, were demonstrated. However, little is known about the role of the TET protein family in RA FLSs

Objectives: The aim of this study was to examine the role of the TET protein family in the pathological process of RA from an *in vivo* perspective with a mouse model, and from an *in vitro* perspective using human synovial tissue.

Methods: K/BxN serum-induced arthritis was induced in *Wild-type* (*WT*) and TET3 heterozygous-deficient (*TET3*$^{+/-}$) C57BL/6 mice. Synovial tissues were obtained from patients with RA and Osteoarthritis (OA) who had received joint replacement surgery. FLSs were transfected with siRNA and knocked down (KD). Gene expression was determined by qPCR and protein expression by western blot and immunostaining. 5-hydroxymethylcytosine (5hmC) was determined by dot blot and hMeDIP assay. Cell migration were assessed using a scratch assay.

Results: TET3 was expressed in particularly infiltrative synovial areas in K/BxN-*WT* mice. The arthritis score of K/BxN-*TET3*$^{+/-}$ was not increased after day 8. Histologically, synovial inflammation and proliferation, and bone destruction were significantly suppressed in the K/BxN-*TET3*$^{+/-}$ mice. In the RA synovial membrane, TET3 was more highly expressed in RA than in OA. In cultured FLSs, the expression of *TET3* mRNA tended to be slightly higher in RA than in OA. After 2 h of stimulation with various cytokines, the expression level of *TET3* mRNA was increased by stimulation with TNFα, interleukin (IL)-1, or IL-17. Assessment of the protein expression of TET3 after stimulation by TNFα using extracted intranuclear proteins of FLSs showed an increase in the expression level of TET3 protein over time. Similarly, the expression level of 5hmC was increased after stimulation by TNFα. Next, the function of TET3 in the FLSs was examined using TNF stimulation follwoing TET3-KD. A scratch assay of cell migration and invasion demonstrated that the TNFα-dependent migration and invasion of FLSs was completely inhibited by TET3-KD. The protein levels of CCL2 were strongly induced by TNFα stimulation, and inhibited by TET3-KD. In addition, flow cytometry of the expression of intercellular adhesion molecule-1 (ICAM-1) revealed that the expression of ICAM-1 was TNFα-dependent and was inhibited by TET3-KD. Assessment of gene expression changes showed that the induction of TNFα-dependent *CCL2* and *ICAM-1* mRNA expression was significantly inhibited by TET3-KD. Subsequently, although 5hmC level on the *ICAM-1* promoter was increased by TNF stimulation, it was strongly inhibited by TET3-KD.

Conclusions: *In vivo*, the arthritis and bone erosion were significantly decreased in the *TET3*$^{+/-}$ mice. *In vitro*, TET3 was induced by inflammatory cytokine stimulation, and TET3 knockdown inhibited the cytokine-induced expression of CCL2 and ICAM-1 in RA FLSs. In addition, hydroxymethylation of the ICAM-1 promoter region was dependent on TET3. These results suggest that continuous exposure to inflammatory cytokines results in leaving an inflammatory memory in FLS in a TET3-dependent manner, thereby promoting pannus formation and increasing the probability of joint destruction.

Disclosure of Interest: A. Kawabe: None declared, K. Naknao: None declared, K. Sakata: None declared, K. Yamagata: None declared, S. Nakayamada: None declared, Y. Tanaka Grant/research support from: Y. Tanaka, has received consulting fees, speaking fees, and/or honoraria from Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, GlaxoSmithKline and has received research grants from Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai

DOI: 10.1136/annrheumdis-2017-eular.3613

FRI0032 CURATIVE EFFECT OF CAMELLIA SINENSIS (CS) AGAINST OPPORTUNISTIC INFECTION IN VULNERABLE ANIMAL MODEL OF RHEUMATOID ARTHRITIS

A. Tanwar[1,2], R. Chawla[2], M. Basu[2], R. Arora[3], H.A. Khan[1]. [1]*Heavy metal and Clinical Toxicology Laboratory, Department of Medical Elementology and Toxicology, Jamia Hamdard, New Delhi;* [2]*Division of CBRN Defence, Institute of Nuclear Medicine and Allied Sciences (INMAS);* [3]*Office of DG (LS), Defence Research and Development Organisation, DRDO Bhawan, Delhi, India*

Background: Rheumatoid arthritis (RA) is an autoimmune disease characterised by chronic inflammation of pro-inflammatory cytokines. Opportunistic infection plays a significant role in loss of tolerance to citrullinated proteins along with inflammatory progression of RA. Due to the immunosuppressive property of anti-rheumatic drugs, the patients of RA become highly vulnerable to microbial infections [1]. Thus, the present study employed an *in vivo* animal model to explore the holistic remedies for the effective treatment of RA.

Objectives: To study the immunomodulatory effect of *Camellia sinensis (Cs)* against inflammatory disorder

Methods: Study utilized collagen induced arthritis (CIA) rat model with *Salmonella typhimurium* (10^8 CFU/ml, p.o) as an opportunistic infectious agent which was introduced to enhance disease severity (on 21st day)[2]. Treatment with Cs at oral dose 400 mg/kg/body wt. (p.o) was started from 21st day for 14 days to explore its curative, anti-edematogenic effect and quantitation of oxidative stress markers. To validate biochemical changes, the histopathologiy and level of cytokines were also studied in joint tissue followed by 7 Tesla Magnetic Resonance Imaging (7T MRI).

Results: Treatment groups significantly restored the level of oxidative stress markers (Table-1). Furthermore, there was significant reduction in the number of bacterial colonies in blood and fecal matter in the treatment group as compared to infected group, while pro-inflammatory cytokine level of TNF-α, IL-1, IL-6 was significantly lower in joint tissue. Histological & 7T-MRI changes in the treatment group included significant reduction of cartilage erosion & pannus formation and there were no signs of inflammation in the small intestine as compared to arthritic and infected group (Figure 1).

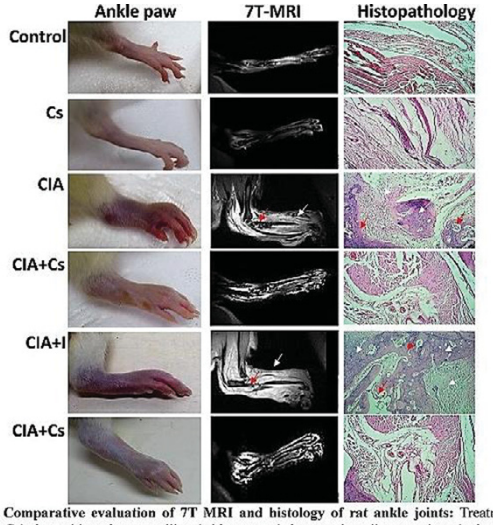


Fig 1: Comparative evaluation of 7T MRI and histology of rat ankle joints: Treatment group (CIA+Cs, CIA+I+Cs) showed less tissue swelling (white arrows), bone and cartilage erosions (red arrows) as compared to infected groups (CIA , CIA+I) and there was no significant change in between control and Cs only groups.

Conclusions: The present study demonstrated that Cs has anti-inflammatory effect and could also be used as potent immunomodulator to manage RA.

References:

[1] R. Fleischmann, et al, Efficacy and safety of tofacitinib in patients with active rheumatoid arthritis: review of key Phase 2 studies, Int. J. Rheum. Dis. (2016). doi:10.1111/1756–185X.12901.

[2] D.D. Brand, et al Rosloniec, Collagen-induced arthritis, Nat. Protoc. 2 (2007) 1269–1275. doi:10.1038/nprot.2007.173.

Acknowledgements: Authors are greatful to VC, Jamia Hamdard and Director, INMAS for providing research facility and support.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1057

Abstract FRI0032 – Table 1. Effect of Cs on oxidative stress markers

S. No	Control	Cs	CIA (Arthritic)	CIA+Cs (Treatment)	CIA+I (Infected)	CIA+I+Cs (Treatment)
Glutathione (μmoles of GSH/g tissue)	1.29±0.042	1.69±0.02	0.51±0.26*	1.40±0.06##	0.56±0.032*	1.45±0.034#
Lipid peroxidation (μmoles of TBARS formed/hr/g tissue)	1.40±0.0095	1.33±0.023	2.09±0.073*	1.80±0.055##	2.32±0.043*	1.73±0.073##
Articular elastase (ng/g protein)	135±5.00	136±4.50	250±0.13*	182±1.00##	242±0.3*	193±2.5##
Superoxide dismutase (nmoles of epinephrine protected from oxidation /min/mg protein)	2.20±0.085	2.21±0.082	1.84±0.135*	2.35±0.80#	1.69±0.05*	2.63±0.1##
Nitric oxide (μmoles nitrite/mg wet tissue)	0.44±0.03	0.39±0.065	0.97±0.1*	0.66±0.2#	0.95±0.4*	0.73±0.03#
Catalase (μmoles of H2O2 consumed/min/mg protein)	161±2.94	144±3.10	39±0.005*	106±1.00##	37±2.00*	82±1.50##

All the values expressed in Mean ± SD (n=6); Significant differences indicated by #p<0.05 and ##p<0.01 as compared to CIA and CIA+I group and *p<0.001 as compared to control group.

FRI0033 IMPORTANT ROLE OF CD11C+ DENDRITIC CELLS IN INFLAMMATORY ARTHRITIS

A. Puchner[1], V. Saferding[1], M. Bonelli[1], H. Leiss[1], R. Pfeifle[2], G. Kroenke[2], M. Koenders[3], J. Smolen[1], K. Redlich[1], S. Blüml[1]. *[1]Medizinische Universität Wien, Wien, Austria; [2]University Hospital Erlangen, Erlangen, Germany; [3]Radboud University Nijmegen Medical Center, Nijmegen, Netherlands*

Background: Dendritic cells (DCs) are important antigen presenting cells (APCs) and therefore they play an important role in bridging the innate and the adaptive immune response. DCs can be divided in different subsets with specific functions. As powerful APCs, DCs are thought to play an important role in the induction of autoimmune diseases such as rheumatoid arthritis. However, the active role of DCs in joint inflammation is not known yet.
Methods: We analyzed histological sections of K/BxN serum transfer arthritis as well as hTNFtg arthritis for the presence of $CD11c^+$ cells by immunohistochemistry. We also performed synovial biopsies and analyzed the cellular composition of the inflammatory infiltrate with respect to DCs. We used CD11c-diphteria toxin receptor (DTR) transgenic mice, which express the human diphtheria-toxin receptor under the CD11c promoter, allowing for specific depletion of $CD11c^+$ cells by administration of diphtheria toxin (DT). K/BxN serum transfer arthritis was induced, and mice were given either DT or PBS or in wt and BARF3 deficient mice. In addition CD11c DTR mice were crossed into hTNFtg animals and also received either DT or PBS. The severity of arthritis was determined clinically and histologically.
Results: We show that $Cd11c^+$ cells are present in significant numbers in the synovia of K/BxN and TNF driven arthritis. Both $CD8^+CD11c^+$ and $CD11b^+CD11c^+$, can be found in synovial tissue. Upon depletion of CD11c+ cells clinical signs of K/BxN serum transfer arthritis were significantly reduced. Histological analysis found reduced synovial inflammation after the depletion of $CD11c^+$ cells in K/BxN arthritis. In addition, local bone destruction and the number of osteoclasts was also significantly reduced. Analysis of K/BxN arthritis in wt mice and $BATF3^{-/-}$ mice, which lack a subset of DCs, namely $CD8^+CD11^+$ DCs, revealed no difference in arthritis severity between the two groups. In addition to K/BxN arthritis, we found that also in TNF-driven arthritis depletion of $CD11c^+$ cells led to a striking reduction of synovial inflammation and a complete depletion of osteoclasts.
Conclusions: These data show that in addition to initiating an adaptive immune response, $CD11c^+$ dendritic cells, are also involved in innate effector mechanisms of inflammatory arthritis. Especially $CD11b^+CD11c^+$ and monocyte derived inflammatory seem to play a role in inflammatory arthritis, suggesting that they could be an important therapeutic target for patients suffering from inflammatory arthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6625

FRI0034 ADALIMUMAB REDUCES CXCR4 EXPRESSION DURING INFLAMMATORY ARTHRITIS AND IN FIBROBLAST-LIKE SYNOVIOCYTES AND OSTEOCLASTS UNDER CHRONIC TNF EXPOSURE

B.P. Harvey[1], L. Li[2], M. Konrad[2], H. Knight[3], S. Westmoreland[3], M. Ruzek[2], Z. Kaymakcalan[1]. *[1]Biologics; [2]Translational Research; [3]Immunology Pharmacology, Abbvie Bioresearch Center, Worcester, United States*

Background: The CXCL12/CXCR4 chemokine axis has been implicated in the pathogenesis of RA. The expression of this chemokine and receptor has been shown to be increased in RA synovium, and moreover, CXCR4 levels in synovium have been correlated with joint destruction in RA patients.
Objectives: Given that high levels of CXCR4 are associated with RA pathogenesis, we sought to determine whether CXCR4 levels are altered by adalimumab (ADA) both *in vivo* in RA patients and in the human TNF transgenic mouse model (huTNF Tg197) of arthritis, as well as *in vitro* with RA fibroblast-like synoviocytes (RA-FLS) and human osteoclast precursors (OCP) following TNF exposure. In addition, we investigated the role of CXCR4 in human osteoclastogenesis (OCgenesis) under chronic TNF exposure.
Methods: Public DNA microarray data of synovial tissue from ADA treated RA patients was analyzed for changes in the expression level of various chemokines and their cognate receptors. PBMC populations from ADA treated RA patients taken at baseline, wks. 4 & 12 were assessed by CyTOF for CXCR4. IHC staining was performed on formalin paw sections from wk. 13 placebo control and ADA treated (1 mg/kg i.p.) huTNF Tg197 mice to evaluate CXCR4 expression in various pannus-associated cells. To assess the role of TNF and concomitant ADA treatment on human cultures *in vitro*, CXCR4 RNA expression was evaluated in RA-FLS treated with conditioned media from PBMCs +/-ADA for 6 hrs., and CXCR4 protein on OCP by flow cytometry in response to 72 hr. M-CSF+RANKL+/-TNF+/-ADA. To demonstrate the role of CXCR4 in OCgenesis, OCP were cultured for 6 d. in M-CSF+RANKL+/-TNF following 30 min. pretreatment with CXCR4 neutralizing antibody. OC maturation and activity were assessed by measuring TRAcP 5b activity and CTX-I release, respectively.
Results: Preliminary microarray data analysis of RA synovial tissue demonstrated that active RA patients over-expressed CXCR4 while CXCR4 was significantly normalized (two-fold reduction) in the responders to ADA therapy. In addition, CyTOF analysis of PBMC from ADA treated RA patients indicated a significant 2-fold reduction from baseline in CXCR4 expression on B cells with a modest trend of reduction on CD4+ T cells by wk. 4. In huTNF Tg197 mice, CXCR4 expression in the inflamed pannus (most notably in FLS, lymphocytes and OC) was also decreased by ADA therapy. *In vitro* human cultures of similar cell types including RA-FLS and OCP were subjected to conditioned media or TNF, respectively, and found to express higher levels of CXCR4 that was reduced with concomitant ADA treatment. Finally, antibody-mediated blockade of CXCR4 on human OCP decreased both TNF-enhanced OC maturation and activity.
Conclusions: Our findings demonstrate that ADA therapy reduces CXCR4 expression *in vivo* both in RA patient PBMCs and in the pannus of huTNF Tg mice with inflammatory arthritis especially in lymphocytes, FLS and OC. Similar results were also observed with our *in vitro* human cultures of equivalent cell types. More importantly, we've shown that inhibition of CXCR4 can reduce TNF-enhanced OCgenesis *in vitro*, suggesting that CXCR4 may be a contributing factor to TNF-mediated osteolysis in RA.
Acknowledgements: Dr. J. Salfeld and J. Min
Disclosure of Interest: B. Harvey Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., L. Li Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., M. Konrad Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., H. Knight Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., S. Westmoreland Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., M. Ruzek Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., Z. Kaymakcalan Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc.
DOI: 10.1136/annrheumdis-2017-eular.2982

FRI0035 SPECIFIC MONOCYTE SUBSETS IN PATIENTS WITH RHEUMATOID ARTHRITIS ARE ASSOCIATED WITH THE PROGRESSION OF THE DISEASE ALONG WITH THEIR AUTOIMMUNE AND PRO-ATHEROTHROMBOTIC PROFILE

N. Barbarroja[1], P. Ruiz-Limon[1], C. Pérez-Sánchez[1], Y. Jimenez-Gomez[1], M.C. Abalos[1], P. Segui[2], R. Ortega[1], E. Collantes[1], A. Escudero[1], M. Alarcon-Riquelme[3], L. Lelann[4], C. Jamin[4], J.O. Pers[4], C. Lopez-Pedrera[1] on behalf of PRECISESADS Clinical Consortium. *[1]GC-5/Rheumatology; [2]Radiology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba; [3]Genetic, Centro de Genomica e Investigación Oncológica (GENYO), Granada, Spain; [4]Université de Brest, Brest, France*

Background: Circulating monocytes play a key role in the pathogenesis of cardiovascular disease (CVD). Three monocyte subsets have been described based on their CD14 and CD16 expression profiles, with different actions in vascular pathology. The distribution of these monocyte subsets and their inflammatory profile associated with CVD in rheumatoid arthritis (RA) remain unknown.
Objectives: This study, developed within the Innovative Medicines Initiative Joint Undertaking (IMI JU) project PRECISESADS framework, aimed at: 1) determine which of the two CD16+ monocyte subpopulations is expanded in RA patients and to investigate their possible role in disease pathogenesis. 2) Functionally characterize the CD16+ monocyte subsets in RA patients and analyze their role in the pro-atherothrombotic profile associated to RA.
Methods: The frequencies of monocyte subpopulations in the peripheral blood of 50 healthy donors and 50 RA patients included in the PRECISESADS study were determined by flow cytometry. A second cohort of 30 RA patients was included, of which CD16+ monocyte subpopulation was isolated using immuno-magnetic selection. Proinflammatory circulating cytokines, as well as peroxide levels and cellular activation markers were analyzed. The expression of 84 genes related to atherosclerosis was analyzed by PCR-array. Endothelial function was measured through post occlusive hyperaemia using Laser-Doppler. Carotid intima media thickness (CIMT) was evaluated as atherosclerosis marker.
Results: CD14highCD16+ monocyte subset was expanded in RA patients belonging to the PRECISESADS study. Their frequency correlated with the evolution of the disease as well as with the positivity for RF and anti-CCP autoantibodies. Correlation studies further indicated a link between the increased frequency of these monocytes and increased levels of circulating cytokines such as IL-17F and IL-10.
CD14highCD16+ monocytes were also significantly extended in RA patients of the second cohort. Those patients had impaired endothelial function, with a reduced perfusion value after ischemia. Increased CD14highCD16+ monocyte proportions were associated with both endothelial dysfunction and the presence of a pathologic CIMT. CD16+ monocyte subsets showed increased protein and gene expression of proinflammatory cytokines, markers of atherosclerosis and peroxide levels.
Conclusions: RA patients exhibit an increased number of CD14highCD16+ monocytes, which display a specific atherogenic and inflammatory pattern directly associated to the autoimmune profile, the progression of the disease and the altered microvascular function. That data suggest that CD16+ subpopulation might play a key role in the CVD pathogenesis associated with RA.
Acknowledgements: Supported by the Innovative Medicines Initiative Joint Undertaking under grant agreement n°115565, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007–2013) and EFPIA companies' in kind contribution, the Instituto de Salud Carlos III (FIS PI15/1333; RIER Rd16/0012/0015) and the JA (CTS-7940).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4918

FRI0036 ASSOCIATION BETWEEN THE 18FDG-PET IMAGING AND THE PATHOLOGICAL FINDINGS OF RHEUMATOID SYNOVITIS

C. Okura, Y. Yonemoto, K. Okamura, T. Suto, M. Tachibana, H. Chikuda. *Orthopaedic Surgery, Gunma University Graduate School of Medicine, Maebashi, Japan*

Background: It has been reported that 18FDG-PET (PET) is useful in the evaluation of RA and for monitoring the effects of treatment on the disease activity, so its utility for the evaluation of arthritis is expected. However, the mechanism underlying the uptake of FDG into the inflamed joint is still unclear.
Objectives: The aim of this study was to investigate the associations among the amount of FDG uptake in RA joints, the inflammatory findings with regard to the pathology of the synovium and the clinical findings.
Methods: We performed PET in 18 RA patients who underwent Total Knee Arthroplasty surgery in our hospital just prior to surgery. We calculated the FDG uptake as the standardized uptake value (SUV)max and scored it using the Rooney score, with the degree of inflammation of the synovial tissues used for the pathological evaluation. We evaluated the associations among the SUVmax, Rooney score, CRP level, ESR and MMP-3 level just before surgery.
Results: The subjects were 18 cases with 20 joints, which were in four females and 14 males. At the time of surgery, the average age of the patients was 66.7±7.9 years old, and the mean disease duration was 20.8±14.0 years. Significant correlation was not observed between SUVmax and total Rooney score (r =0.056, p=0.814). But there were strong correlations between SUVmax and some of the individual items in Rooney score, including the "Synoviocyte hyperplasia", and also between SUV max and "Diffuse infiltrates of lymphocytes" (r=0.512, p=0.021 and r=0.581, p=0.007, respectively).
Conclusions: The accumulation of FDG was associated with the extent of "synoviocyte hyperplasia" and "diffuse infiltrates of lymphocytes". It is estimated that accumulation of FDG is associated with relatively early stage of active inflammation of RA.
References:
[1] McQueen FM, et al. Clin Rheumatol: 2007.
[2] Beckers C, et al. Eur J Nucl Med Mol Imaging; 2006.
[3] Okamura K, et al. Rheumatology (Oxford); 2012.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7021

FRI0037 MER-MEDIATED EFFEROCYTOSIS TEMPERS ARTHRITIS BY PREVENTING NEUTROPHILS TO GO INTO SECONDARY NECROSIS AND SPILL THEIR INFLAMMATORY CONTENT IN THE JOINT

C.E.J. Waterborg, S. Beermann, M.B. Bennink, M.I. Koenders, P.L.E.M. van Lent, F. van den Hoogen, P.M. van der Kraan, F.A.J. van de Loo. *Experimental Rheumatology, Radboudumc, Nijmegen, Netherlands*

Background: Rheumatoid arthritis is characterized by an inflammatory response in synovial joints, showing a predominant influx of neutrophils. These cells are cytotoxic and contribute to matrix degradation. In addition, they are implicated as a source of citrullinated auto-antigens, leading to the production of anti-citrullinated protein antibodies. Neutrophils have a relative short life span and many of them undergo apoptosis. If they are not cleared, they undergo secondary necrosis and release their cell content. A key mediator in the resolution of inflammation and the uptake of apoptotic cells, or efferocytosis, is the receptor tyrosine kinase Mer.
Objectives: To elucidate the local role of Mer during gonarthritis.
Methods: Macrophages were transduced by adenoviruses encoding the Mer ligand *Pros1* or *Luciferase*. One day after the collagen booster injection in mice, Mer-specific antibodies or IgG antibodies, or adenoviruses overexpressing *Pros1* or *Luciferase* were injected intravenously. Mice were euthanized at day 30 or 36, respectively. The KRN serum transfer arthritis model was induced by two intraperitoneal injections of arthritic K/BxN serum in either Mer-deficient or wild-type (WT) mice, or in mice that overexpress *Pros1* or *Luciferase* in their knee joints. Mice were euthanized at day 7 or day 14, respectively. From all mice, serum was taken for cytokine profiling and knee joints were isolated for either synovial gene expression or histology and immunohistochemistry.
Results: Adenoviral overexpression of the Mer ligand *Pros1* resulted in reduced production of pro-inflammatory cytokines and chemokines by macrophages, compared to *Luciferase*. In addition, local *Pros1* overexpression resulted in reduced expression of pro-inflammatory and pro-destructive mediators by synovial cells of arthritic mice. Systemic and local *Pros1* overexpression diminished joint pathology, reduced the number of cleaved Caspase 3-positive apoptotic cells and secondary necrotic neutrophils. Conversely, inhibiting Mer-mediated efferocytosis by either Mer-specific antibodies or *Mertk* gene ablation resulted in aggravation of arthritis compared to controls, as evidenced by increased inflammation and tissue destruction. Additionally, Mer-inhibited mice had increased numbers of apoptotic cells in their knee joints, and higher serum levels of IL-16C, a cytokine released by secondary necrotic neutrophils.
Conclusions: Together, these results demonstrate that Mer locally plays a unique protective role in knee joint disease by enhancing resolution of arthritis. Our data suggest that promoting and/or restoring Mer-mediated uptake of apoptotic cells in the arthritic joint might be therapeutically beneficial.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4902

FRI0038 RELEASE OF PEPTIDYLARGININE DEIMINIASE 2 FROM ACTIVATED NEUTROPHILS

M.A. Steffensen, D. Damgaard, M. Bassi, C.H. Nielsen. *Institute for Inflammation Research, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark*

Background: Extracellular citrullination catalyzed by peptidylarginine deiminase (PAD) is thought to play a central role in the pathogenesis of rheumatoid arthritis. Neutrophils are a major reservoir of PAD2 and PAD4. Cellular release of PAD2 and PAD4 is usually considered a consequence of cell death.
Objectives: We aimed to determine if PAD2 can be released from live, activated neutrophils as an active process.
Methods: Whole blood cells were purified from healthy blood were stimulated with phorbol 12-myristate 13-acetate (PMA). To capture PAD2 released from neutrophils and detect it by flow cytometry, we used biotinylated anti-CD15 and anti-PAD2 (mAb DN6) mAbs linked by streptavidin, and a different PE-labelled anti-PAD2 amtibody (mAb DN2). In addition, intracellular PAD2 was quantified by intracellular staining with PE-anti-PAD2. PAD2 released from leukocytes and subcellular fractions of human granulocytes were assessed for content of PAD2 using an in-house luminex-based assay.
Results: On incubation of whole blood cells with PMA, PAD2 was detectable in the supernatants after 30 minutes, and levels increased thereafter in parallel with increasing cell death. However, using PAD2 catch reagent, we found that live neutrophils released PAD2 in the 30 minutes after stimulation. Intracellular staining for PAD2 showed that the content of PAD2 in live neutrophils decreased correspondingly. Upon subcellular fractioning of granulocytes, the majority of PAD2 was found in cytosol and, in 25 times lower quantities, in the fraction containing plasma membranes and secretory vesicles. Sparse amounts of PAD2 were also observed in gelatinase granules.

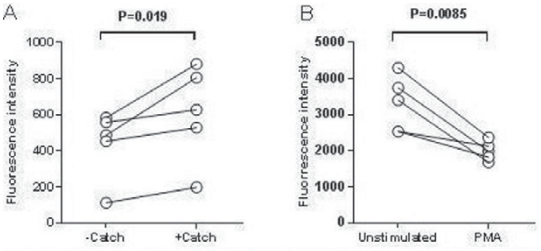


Figure 1: Release of PAD2 by live neutrophils following activation. (A) Whole blood cells were stimulated with PMA for 30 minutes in presence of a catch reagent consisting of co-conjugated anti-CD15 and anti-PAD2 antibodies, and PAD2 caught on the surface of CD15- granulocytes was detected by flow cytometry using PE-conjugated anti-PAD2 antibody (+Catch). Cells not exposed to catch reagent (-Catch) were included as controls. (B) Whole blood cells were incubated with or without PMA for 30 minutes, and the content of PAD2 in granulocytes was assessed using flow cytometry with a PE-conjugated anti-PAD2 antibody (DN2). In both A and B, granulocytes were gated on the basis of forward and side light scatter characteristics, and dead cells staining positive for a near-IR dead-cell stain were excluded.

Conclusions: In conclusion, PAD2 can be released from live, activated neutrophils, which may contribute to extracellular citrullination and thereby play a role in driving inflammatory processes in RA patients with immune responses to citrullinated proteins.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5964

FRI0039 ENDOTHELIAL DYSFUNCTION IN RHEUMATOID ARTHRITIS: WHICH EFFECT OF METHOTREXATE? A STUDY IN ADJUVANT INDUCED ARTHRITIS MODEL

R. Bordy [1], P. Totoson [1], F. Verhoeven [2], C. Prati [1,2], J. Moretto [1], M. Tournier-Nappey [1], C. Demougeot [1]. *[1]Pepite Ea4267, Université de Franche-Comté; [2]Rhumatologie, CHRU Besançon, Besançon, France*

Background: Rheumatoid arthritis (RA) is associated with increased cardiovascular (CV) risk [1] secondary to endothelial dysfunction (ED) [2]. There is accumulating evidence that methotrexate (MTX), first intention DMARD, reduces CV risk in RA [3], but the mechanisms involved are still unknown.
Objectives: The aim of this study was to determine the effect of MTX on endothelial function in arthritis and to investigate its effect on endothelial pathways.
Methods: Experiments were conducted in the adjuvant-induced arthritis (AIA) model in Lewis rat. At onset of arthritis, rats were treated by a sub-cutaneous injection of MTX (1 mg/kg/week) or phosphate buffer saline (vehicle) for 3 weeks. Arthritis score was daily monitored. At the end of treatment, thoracic aorta was harvested to measure the relaxation to acetylcholine on pre-constricted aortic rings in the presence or not of inhibitor of nitric oxide (NO) synthase (L-NAME), arginase (nor-NOHA), EDHF (Apamin/Charybdotoxin), or a superoxide dismutase analog (Tempol). The effect of norepinephrine (NE) and sodium nitroprusside

(SNP) was studied on endothelium-denuded aortic rings. The effect of MTX on hind paw radiographic score, serum lipids and plasma pro-inflammatory cytokines (TNFα and IL-1β) levels was measured.

Results: As compared to Vehicle rats, MTX significantly reduced arthritis score ($p<0.01$) but did not change radiographic score. It reduced plasma cytokines levels ($p=0.02$) but not total cholesterol and triglycerides levels. MTX did not change Ach-induced relaxation as compared to Vehicle. As regards endothelial pathways, MTX increased vascular NOS activity ($p<0.0001$) and decreased superoxide anions production but did change neither COX-2 and arginase activities nor EDHF production. Vascular smooth muscle reactivity to NE and SNP was unchanged by the treatment.

Conclusions: Despite a reduction of clinical and biological inflammation, MTX did not improve endothelial function in AIA rats. The study of endothelial mechanisms highlights the role of COX and arginase as seminal targets for reducing ED in RA. This study suggests that other mechanisms than improvement of endothelial function are involved in the CV benefits of MTX in RA that remain to be elucidated. Our data also suggest that the adjunction of drugs targeting endothelial function to MTX in RA patients might improve their CV prognostic.

References:

[1] Agca R, Heslinga SC, Rollefstad S, et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Ann Rheum Dis 2016:annrheumdis-2016–209775. doi:10.1136/annrheumdis-2016–209775.

[2] Prati C, Demougeot C, Guillot X, et al. Endothelial dysfunction in joint disease. Joint Bone Spine Rev Rheum 2014;81:386–91. doi: 10.1016/j.jbspin.2014.01.014.

[3] Roubille C, Richer V, Starnino T, et al. The effects of tumour necrosis factor inhibitors, methotrexate, non-steroidal anti-inflammatory drugs and corticosteroids on cardiovascular events in rheumatoid arthritis, psoriasis and psoriatic arthritis: a systematic review and meta-analysis. Ann Rheum Dis 2015;74:480–9. doi: 10.1136/annrheumdis-2014–206624.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3234

FRI0040 CHARACTERIZATION OF ANTI-CARBAMYLATED SYNOVIAL PROTEIN ANTIBODIES (ANTI-CARPS) IN RHEUMATOID ARTHRITIS PATIENTS

C. Regueiro[1], A. Montes[1], M.D. Boveda[2], S. Amhaz-Escanlar[3], E. Perez-Pampin[4], A. Mera-Varela[4], A. Gonzalez[1]. *[1]Experimental and observational Rheumatology; [2]Unit of Diagnosis and Treatment of Congenital Metabolic Diseases; [3]Orthopedic Surgery and Traumatology; [4]Rheumatology Unit, Instituto Investigacion Sanitaria- H. Clinico Universitario de Santiago, Santiago de Compostela, Spain*

Background: Anti-carbamylated protein antibodies (anti-CarP) are a new type of autoantibodies specific of patients with RA. Reactivity has generally been tested with *in vitro* carbamylated proteins from fetal calf serum (FCS) as anti-CarPF. It is likely that other sources of antigens could be more suitable than FCS unless the reactivity of the autoantibodies is directed primarily against the carbamylated residues independently of the protein.

Objectives: To evaluate the anti-CarP antibodies against *in vitro* carbamylated synovial tissue proteins (anti-CarPS) and to compare them with anti-CarPF antibodies.

Methods: A pool of sinovial tissue proteins from 3 osteoarthritis patients was *in vitro* carbamylated and used as antigen for ELISA. Anti-CarPS antibodies were determined in 520 sera from patients with RA and 278 healthy controls, which have been previously tested for anti-CarPF antibodies (1). Logistic regression analysis was used to evaluate the association of the antibodies with SE alelles, *PTPN22,* smoking and erosions. Relationship between antibodies titers was analyzed with Spearman rank correlation (r_s) and concordance between positivity of the different antibodies was analyzed with the Goodman and Kruskal γ.

Results: Similar percentages of patients were positive for anti-CarPS (31.7%) and for anti-CarPF antibodies (29.4%). However, many patients were discordant (28.9%). Notably, the concordance between anti-CarPS and anti-CCP antibodies was higher than the concordance between anti-CarPS and anti-CarPF antibodies (γ =0.73, 95% CI: 0.60–0.86 *vs.* γ =0.60, 95% CI: 0.47–0.73, respectively). Moreover, titers of anti-CarPS antibodies were more correlated with anti-CCP than with anti-CarPF antibodies (r_s =0.41, 95% CI: 0.33–0.48 *vs.* r_s=0.29, 95% CI: 0.21–0.37, respectively). Accordingly, presence of anti-CarPS antibodies showed a clearer trend to be associated with the genetic and environmental RA risk factors than anti-CarPF antibodies, although only the association with smoking was significant (smoking OR=2.0, p=0.02 *vs.* OR=1.1, p=0.8, respectively; OR=1.3 *vs.* OR=1.1 for HLA-SE and OR=1.3 *vs.* OR=0.9 for PTPN22). There were no differences in the association with erosions, which was significant for both antibodies analyzed separately (OR=2.3, $p=6.8 \times 10^{-4}$ for anti-CarPS and OR=2.4 $p=2.0 \times 10^{-4}$ for anti-CarPF) and together (OR=1.8, p=0.02 and OR=2.0, p=0.005, respectively).

Conclusions: Our results indicate that the proteins used as antigens in the determination of anti-CarP antibodies are relevant for the obtained positivity and titer. The differences could affect the pattern of characteristics associated with these antibodies, making it necessary to identify the specific carbamylated autoantigens targeted by them *in vivo*.

References:

[1] Montes A, et al. PLoS One 2016;11:e0161141.

Acknowledgements: Supported by PI14/01651 and RD12/0009/0008 of the ISCIII (Spain) with participation of FEDER.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4789

FRI0041 IN VIVO MONITORING OF ANTI-FOLATE THERAPY IN ARTHRITIC RATS USING [18F]FLUORO-PEG-FOLATE AND PET

D.M.S.H. Chandrupatla[1], C.J. van der Laken[1], R. Vos[2], M. Verlaan[2], R. van Kooij[2], A.D. Windhorst[2], Q. Chen[3], P.S. Low[3], A.A. Lammertsma[2], G. Jansen[1], C.F.M. Molthoff[2]. *[1]Amsterdam Rheumatology and immunology Centre – location VUmc; [2]Radiology and Nuclear Medicine, VU University Medical Center, Amsterdam, Netherlands; [3]Department of Chemistry, Purdue University, West Lafayette, United States*

Background: Macrophages play a key role in the pathophysiology of rheumatoid arthritis (RA). The folate receptor β (FR-β) is expressed on these macrophages [1] and [^{18}F]fluoro-PEG-folate positron emission tomography ([^{18}F]fluoro-PEG-folate PET) can be used to visualize arthritis *in vivo* [2]. In addition, [^{18}F]fluoro-PEG-folate PET could be a highly interesting tool for therapeutic monitoring of MTX therapy, the corner stone for RA therapy.

Objectives: To study the potential of [^{18}F]fluoro-PEG-folate PET for monitoring response to MTX in a rat model of RA.

Methods: Arthritic rats [3] (n=3–6 per group) received interventions with either MTX [i.p., 1mg/kg; 2 times (group A) or 4 times (group B)] or PBS (control group)] with a time interval of 3–4 days. Healthy rats didn't receive any arthritic induction or MTX therapy. [^{18}F]fluoro-PEG-folate PET-CT were acquired for one hour after tracer injection [2]. Scans were analysed using the region of interest method and standardized uptake values (SUVs) were determined (50–60 min time frame). Sixty minutes after the PET scan, *ex-vivo* tissue distribution was performed and the amount of radioactivity measured in a gamma counter (expressed as percentage of the injected dose/gram tissue (%ID/g)) [2]. For histopathology (Haematoxylin-Eosin (HE) and immunohistochemistry with macrophage specific antibodies ED1 (∼CD68) and ED2 (∼CD163) were applied. Synovial macrophages were counted in predefined areas of the knees [3].

Results: PET scans clearly visualized significantly lower SUVs (1.5-fold, $p<0.01$) in arthritic knees of both MTX-treated groups, approximating the levels observed in healthy rats. Corroborating [^{18}F]fluoro-PEG-folate PET, *ex vivo* tissue distribution [^{18}F]fluoro-PEG-folate demonstrating a 2- and 4-fold decrease (group A and B, respectively) in tracer uptake in arthritic knees after MTX therapy (0.12 and 0.06 for groups A and B, and 0.22%ID/g for controls, respectively) (Figure). This reduction in uptake of [^{18}F]fluoro-PEG-folate in arthritic knees was also associated with a significant decrease in ED1 and ED2 positive synovial macrophages in arthritic knees (∼4 fold) for both treated groups compared with control rats knees ($p<0.01$).

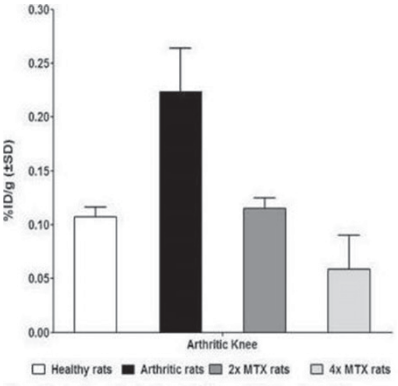


Figure. Ex vivo tissue distribution of [^{18}F]fluoro-PEG-folate in arthritic knee of healthy (white bars) (n=3), arthritic (black bars) (n=3), 2x-MTX (dark grey) (n=4) and 4x-MTX (light grey) (n=4) treated rats at 60 min post tracer injection. Results are expressed as mean percentage injected dose per gram (%ID/g ± SD).

Conclusions: This study in arthritic rats underscores the potential and usefulness of [^{18}F]fluoro-PEG-folate PET as tool to monitor of MTX therapy and potentially other anti-folate treatments of RA.

References:

[1] Van der Heijden et al, Arthr & Rheum (2009).

[2] Gent et al, Arthr Res Ther (2013).

[3] Chandrupatla et al, BioMed Res Int (2015).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4803

FRI0042 BAFF-R EXPRESSION IN NAÏVE CD5+IGM+ B CELLS IN RHEUMATOID ARTHRITIS PATIENTS REPOPULATING AFTER RITUXIMAB

E. Becerra[1,2], I. de la Torre[2], M.J. Leandro[2], G. Cambridge[2]. *[1]Rheumatology, Hospital universitario de Torrevieja, Alicante, Spain; [2]Rheumatology, University College London, London, United Kingdom*

Background: Serum levels of B cell activating factor (BAFF) rise following Rituximab (RTX) therapy in patients with Rheumatoid arthritis (RA). CD5+IgM+B cells are present within transitional and naïve B cell subsets and their increased production or accumulation is associated with some autoimmune diseases. Previous studies have shown that BAFF does not enhance their survival compared with CD5- naïve B cells, suggesting that signalling pathways are important in promoting their survival.
Objectives: To determine serum BAFF levels and BAFF-receptor (BAFF-R) expression in CD5+IgM+B cells in healthy controls (HC), RTX-naïve RA patients (pre-RTX), and relapsing at different time points after peripheral B cell repopulation post-RTX treatment, divided into 2 groups: early relapsers (0–3 months post-B cell return) and later relapsers (>4 months post-B cell return).
Methods: Immunophenotyping of peripheral blood mononuclear cells was used to determine %CD5+IgM+B cells and BAFF-R (% and expression, mean fluorescence intensity (MFI)) in 5 HC, 13 pre-RTX and 12 post-RTX RA patients. Results were analyzed with respect to timing of relapse after peripheral B cell return (≥5 B cells/μL) and serum BAFF levels.
Results: %CD5+IgM+B cells, but not absolute numbers, were significantly higher in post-RTX early relapsers compared to HC ($p<0.01$), pre-RTX patients ($p<0.001$) and post-RTX later relapsers ($p<0.01$). There was a strong inverse correlation between %CD5+IgM+B cells and time after B cell return ($r^2=0.88$, $p<0.0001$). BAFF-R+ expression was significantly lower in both post-RTX groups compared to HC and pre-RTX patients; early relapsers showed the lowest % and MFI BAFF-R+ expression, compared with later relapsers ($p<0.01$). BAFF-R+ expression increased with time after B cell return, both % ($r^2=0.47$, $p<0.002$) and MFI ($r^2=0.76$, $p<0.0004$). BAFF levels were significantly higher in both post-RTX groups compared to HC and pre-RTX patients, with the highest BAFF levels in early relapsers ($p<0.05$ compared to later relapsers). There was a significant inverse correlation between BAFF levels and % ($r^2=0.51$, $p<0.01$) and MFI ($r^2=0.4$, $p<0.05$) BAFF-R+ expression.
Conclusions: Early relapsers show increased %CD5+IgM+ naïve B cells, and decreased BAFF-R expression, similar to ontogeny and what is seen in cord blood B cells. Whether the increased numbers of CD5+ naïve cells were contributing to relapse was not determined but they have the capacity to rapidly mature into autoantibody producing plasma cells, independent of the BAFF/BAFFR system. BAFF-R expression was found to increase with time after B cell return, again mirroring ontogeny with a later relapse showing more normalized BAFF/BAFF-R levels, suggesting their mechanism of relapse may follow a more conventional B cell differentiation pathway.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6604

FRI0043 PEPTIDES HIGHLY SPECIFIC TO THE VARIABLE REGION OF TNF-ALFA-SPECIFIC REFERENCES LICENSED (RL) MONOCLONAL ANTIBODIES (MAB), AS POTENTIAL TOOL TO EFFECTIVELY ASSESS SIMILARITY BETWEEN BIOSIMILARS AND THE CORRESPONDIG RL MAB

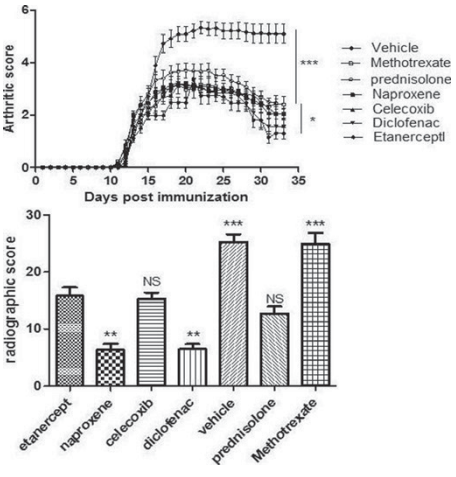
E. Favoino, C. Ionescu, F. Perosa. *Department of Biomedical Sciences and Human Oncology, Systemic Rheumatic and Autoimmune Disease Unit, University of Bari Medical School, Bari, Italy*

Background: Monoclonal antibodies (mAb) have greatly facilitated the development of highly specific immunotherapy, with a significant improvement of clinical outcome in certain rheumatologic diseases. However, the approaching of many references licensed mAb (RLM) to the end of their licensing period, have stimulated a tremendous interest in the synthesis of a new generation of low-cost mAb referred to as biosimilars (BS) mAb (BSM), because of their similarity to the RLM. An essential requirement imposed by Regulatory Agencies for a mAb to be considered BS is that its variable region (VR) primary sequence must be highly similar to that of RLM. However, epitope recognition and affinity of a mAb very much depends on its VR conformational structure, which may differ even between two mAb bearing highly similar (but not identical) VR. The availability of reagents highly specific to the RLM VR may offer an unique opportunity to define whether a mAb can or cannot be considered BS to a given RLM.
Objectives: To isolate and characterize phage clone-expressing peptide (pc) which are highly specific for the VR of two anti-TNF-α RLP namely mAb Infliximab (Inf) and Golimumab (Gol).
Methods: Cross-inhibition ELISA on recombinant TNF-α (rTNF-α) was performed to define the spatial relationship among the epitopes detected by mAb. mAb-specific phage clones expressing peptide (pc) were obtained by the panning of a phage peptide display library with TNF-a specific mAb. Characterization of pc-specificity and of the spatial relationship between pc- and the TNF-a-binding site on the variable region of mAb was assessed by binding and inhibition assay.
Results: mAb Inf and Gol specifically and dose-dependently cross-inhibited each to the other in the binding to rTNF-a, indicating the recognition by these 2 mAb of the same or two distinct spatially related epitopes on TNF-a. The panning of mAb Inf and Gol with a phage peptide display library resulted in the isolation of one Inf-specific pc (pcInf) and three Gol-specific pc (pcGol1 to 3). Binding assay showed that pcInf and the three pcGol specifically reacted with the corresponding mAb. Furthermore, pcInf and pcGol3 specifically and dose-dependently inhibited the binding of the corresponding mAb to rTNF-α, suggesting the recognition by the pc of the corresponding mAb antigen-combining site. Finally, pcInf and all three pcGol did not react with two additional TNF-a antagonists, suggesting that they are highly specific for mAb Inf and Gol respectively.
Conclusions: The highly specificity of the pc described indicates that they can be eventually employed to predict similarity between a newly synthesized BSM and the claimed RLM, based on the BSM reactivity (or the lack of reactivity) with RLM-specific pc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6358

FRI0044 NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ARE MORE BENEFICIAL THAN ANTI-TNFα DRUGS ON THE RADIOGRAPHIC DAMAGE IN ARTHRITIS: A STUDY IN ADJUVANT INDUCED ARTHRITIS

F. Verhoeven[1], C. Prati[2], P. Totoson[3], R. Bordy[3], D. Wendling[1], C. Demougeot[3]. *[1]Rhumatologie; [2]CHRU de Besançon; [3]Ea 4267 "Pepite", université de Bourgogne Franche Comté, Besançon, France*

Background: The management of the chronic inflammatory rheumatisms has dramatically evolved in the last decade with a concept of "treat to target". The theory of a window of opportunity with more beneficial effects of an early intensive treatment is supported by several evidences. The positive impact of an early treatment with a TNFα blocker is expected but the place and the interest of non-steroidal anti-inflammatory treatments (NSAIDs) and glucocorticoids is not clear.
Objectives: The aim of this study was to evaluate the radiological outcomes after an early treatment during 21 days by Etanercept, or Naproxene, or Celecoxib, or Prednisone, or Diclofenac or Methotrexate in adjuvant induced arthritis in rats.
Methods: Adjuvant-induced arthritis (AIA) was induced in 6 weeks old male Lewis rats by injection of *Mycobacterium butyricum* in adjuvant at the basis of the tail. At the onset of arthritis, rats were daily treated with Naproxene (10 mg/kg/d i.p), or Diclofenac (5mg/kg i.p twice a day), or Celecoxib (3 mg/kg/d i.p) or Prednisone (10 mg/kg/d i.p), or Etanercept (10 mg/kg/3 days, s.c.), or Methotrexate (1mg/kg/3 days, s.c.), or saline solution (Vehicle), for 21 days. Arthritic score was daily monitored. At the end of treatment, paws' radiological exam was performed with a BMA High Resolution Digital X Ray (40mV, 10mA). A score of 0 to 20 was determined for each paw using a grading scale modified from Ackerman *et al (1979)*.



Abstract FRI0042 – Table 1

	%CD5+IgM+ (median;range)	%BAFF-R+ve	BAFF-R+ve (MFI)	BAFF levels (ng/ml) (median;range)
HC	18.5 (9.1–26.8)	98.7 (97.9–99.5)	62.5 (50.5–82.4)	1.1 (0.9–1.2)
Pre-RTX	5.4 (1.9–21.4)	97.3 (85.8–100)	58 (34.2–139)	1.4 (0.9–1.7)
Post-RTX early relapse	44.4 (39.6–55.8) **###$$	60.6 (12.9–71.2)**###$$	15.6 (11.8–17.5)**###$$	2.4 (2–6.4)**###$
Post-RTX late relapse	12.7 (2.3–27.9)$$	93.1 (81.5–97.9)**$$	30.2 (19.9–36)**##$$	1.7 (1.3–2.4)**#$

*p<0.05; **p<0.01; ***p<0.001 compared with NC; #p<0.05; ##p<0.01; ###p<0.001 compared with pre-RTX; $p<0.05; $$p<0.01; $$$p<0.001 for comparisons between post-RTX groups.

Results: Compared to the Vehicle, all treatments significantly reduced ($p<0.001$) arthritic score with a reduction of the arthritic score evaluated between 40% (for methotrexate) and 70% (for diclofenac) (figure 1. Compared to the vehicle, the radiographic score was improved by Naproxene, Diclofenac, Celecoxib, Glucocorticoids, Etanercept ($p<0.001$) but not by methotrexate. Compared to Etanercept, Naproxene and diclofenac showed less radiological structural changes ($p<0.01$) (figure 2).
Conclusions: Our study demonstrates for the first time that an early treatment with NSAIDs, excluding COX2 selective inhibitor, is more beneficial than Etanercept on the radiological damages in adjuvant induced arthritis. The close efficacy of all drugs on the arthritis score suggests that the beneficial impact of NSAID is not only driven by their impact on the systemic inflammation. NSAIDs should be used during the window of opportunity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2611

FRI0045 ORAL MICROBIOME PROFILE IN RHEUMATOID ARTHRITIS PATIENTS: ASSOCIATION BETWEEN TONGUE BIOFILM PORPHYROMONAS GINGIVALIS AMOUNT AND DISEASE ACTIVITY

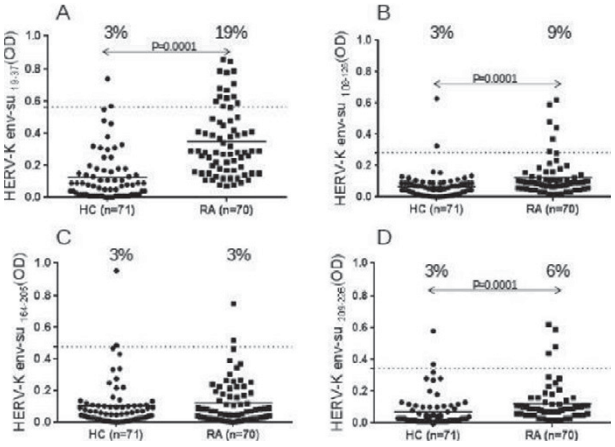
F. Ceccarelli[1], G. Orrù[2], A. Pilloni[3], I. Bartosiewicz[4], C. Perricone[4], E. Martino[5], R. Lucchetti[6], S. Fais[2], M. Vomero[4], M. Olivieri[4], M. Di Franco[4], R. Priori[4], V. Riccieri[4], A. Sili Scavalli[4], R. Scrivo[4], C. Alessandri[4], F. Conti[4], A. Polimeni[4], G. Valesini[4]. *[1]Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Rome; [2]Molecular Biology Service, University of Cagliari "Ospedale S. Giovanni di Dio", Cagliari; [3]Odontoiatria, Dipartimento di Scienze Odontostomatologiche e Maxillo Facciali, Sapienza Università di Roma, Rome; [4]Reumatologia, Dipartimento di Medicina Interna e Specialità Medica; [5]Odontoiatria, Dipartimento di Scienze Odontostomatologiche e Maxillo Facciali, Sapienza Università di Roma; [6]Reumatologia, Dipartimento di Medicina Interna e Specialità Medica, Sapienza, Università di Roma, Roma, Italy*

Background: *P. gingivalis* is a Gram-negative anaerobic bacterium usually located in the oral cavity, as component of microbiome. Next to the established association with oral cavity diseases, such as periodontitis and halitosis, in the last years a growing interest has been addressed to its implication in the development of autoimmune diseases, such as Rheumatoid Arthritis (RA). The ability of *P. gingivalis* to citrullinate peptides is the most relevant link with RA. Indeed, this bacterium has several virulence factors directly contributing to its chronic inflammation regardless of citrullination. Data from the literature demonstrated the ability of *P. gingivalis* in inducing the production of several inflammatory cytokines, such as TNF, IL6 and IL17, through the TLR signaling pathways.
Objectives: In the present case-control study, we aimed at analysing tongue microbiome in a large RA cohort, focusing on the evaluation of *P. gingivalis* presence and quantification.
Methods: We enrolled 143 RA patients (1987 ACR criteria; M/F 32/111, mean±SD age 57.5±19.8 years, mean±SD disease duration 155.9±114.7 months); 36 periodontitis (M/F 11/25, mean±SD age 56±9.9 years, mean±SD disease duration 25.5±20.9 months); 57 (M/F 12/45, mean ±SD age 61.4±10.9 years, mean ±SD disease duration 62.3±66.9 months) affected by knee osteoarthritis or fibromyalgia (control subjects – CS). All subjects underwent a clinical evaluation in order to assess disease activity by DAS28. Blood serum samples were obtained to evaluate the presence of ACPA by a commercial ELISA kit. Finally, a standard cytologic swab to collect tongue biofilm samples was performed and the presence of *P. gingivalis* was evaluated by PCR method.
Results: The prevalence of *P. gingivalis* resulted significantly higher in RA and PD patients in comparison with CS (P=0.01 and P=0.003, respectively). No correlation between bacterium presence and ACPA was found. When evaluating the percentage of *P. gingivalis* on the total tongue biofilm, we observed a significant correlation between this measure and DAS28 values (r=0.4, P=0.01). Furthermore, RA patients in DAS28 remission showed a significantly lower prevalence of *P. gingivalis* in comparison with non-remission patients (P=0.02).
Conclusions: In the present study, for the first time we assessed the prevalence of *P. gingivalis*, i.e. its percentage on the total tongue biofilm, in a large RA cohort. A significant correlation between the amount of *P. gingivalis* on total tongue biofilm and disease activity was observed. There was no association with ACPA, suggesting that this bacterium, beyond citrullination, could be implicated in triggering a pro-inflammatory state in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5034

FRI0046 IDENTIFICATION OF HERV-K ENV SURFACE PEPTIDES HIGHLY RECOGNIZED IN RA PATIENTS

G.L. Erre[1], G. Mameli[2], D. Cossu[2], S. Mura[3], A. Piras[3], M.L. Cadoni[1], G. Buscetta[3], N. Mundula[3], E. Colombo[3], M.G. Longu[1], L.A. Sechi[2], G. Passiu[3]. *[1]UOC Reumatologia, Dipartimento di Medicina Clinica e Sperimentale, Azienda Ospedaliero-Universitaria di Sassari; [2]Scienze Biomediche, Istituto di Microbiologia; [3]UOC Reumatologia, Dipartimento di Medicina Clinica e Sperimentale, Università degli Studi di Sassari, Sassari, Italy*

Background: Endogenous Retroviruses (HERV) are believed to be pathogenic in several autoimmune diseases. Among them, HERV-K viruses have been recently reported to be involved in the pathogenesis of rheumatoid arthritis (RA).
Objectives: In this study we have explored the role of humoral immune response against HERV-K as a potential pathogenetic mechanism in RA.
Methods: Four different peptides from the extracellular portion of the *env* protein of HERV-K (env-su $_{19–37}$, env-su $_{109–26}$, env-su $_{164–205}$, env-su $_{209–226}$) were selected by bioinformatic analysis on the basis of their putative immunogenicity. Indirect ELISA was then carried out to quantify antibodies against those peptides on blood samples from RA patients and healthy controls (HC). Differences between the two groups were analysed using the Mann-Whitney rank-sum and chi-square tests. Potential correlations between RA laboratory, clinical descriptors and IgGs levels were explored by bivariate regression analysis.
Results: Seventy consecutive RA patients and seventy-one HC crossed by age and sex were enrolled in the study. Serum autoantibodies against three out of the four tested peptides, anti HERV-Ksu$_{19–37}$, HERV-K env-su$_{109–126}$ and HERV-K env-su$_{205–226}$, were significantly more prevalent in RA than in HC (19% vs 3%,p=0.0001;9% vs 3%, p=0.0001; and 6% vs 3%, p=0.0001 respectively) (See Fig. 1)
Subgroup analysis showed no association between anti-HERV-K peptide humoral response and clinical, serological and clinimetric RA disease descriptors.



Conclusions: Serum from RA patients in our series significantly reacted against different HERV-K peptides in comparison to the general population suggesting a role for the HERV-K related, secondary antigenic driven immune response in the pathogenesis of RA. Further studies are needed to confirm these results and to explore the role of HERV-K surface peptides as potential therapeutic targets.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2043

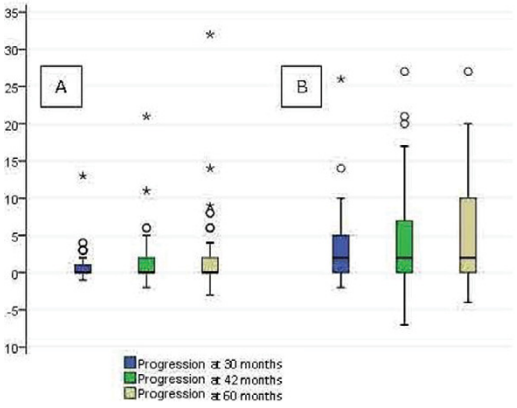
FRI0047 ELEVATED 14-3-3ETA LEVELS PREDICT WORSE RADIOGRAPHIC OUTCOMES IN PATIENTS WITH RECENT-ONSET INFLAMMATORY ARTHRITIS IN CLINICAL REMISSION

N. Carrier[1], M.-P. Garant[2], A. Marotta[3], A.J. De Brum Fernandes[4], P. Liang[4], A. Masetto[4], Y. Gui[5], J. Savill[5], S. Michienzi[5], W.P. Maksymowych[6], G. Boire[4]. *[1]Division of Rheumatology, CIUSSS de l'Estrie-CHUS; [2]Biostatistics, Centre de recherche du CHUS, Sherbrooke; [3]Auguex Life Sciences Crop., Vancouver; [4]Medicine, Division of Rheumatology, Université de Sherbrooke, Sherbrooke; [5]Augurex Life Sciences Corp., Vancouver; [6]Medicine, University of Alberta, Edmonton, Canada*

Background: 14–3-3η is a joint-derived serum protein that up-regulates pro-inflammatory factors. We have previously reported that baseline 14–3-3η levels ≥0.50 ng/ml (HIGH 14–3-3η) were predictive of radiographic progression over 5 years.
Objectives: Our objective was to verify if the persistence of HIGH 14–3-3η at 18 months in recent-onset polyarthritis patients in REMISSION predicts more rapid radiographic progression over the following years, up to 42 months.
Methods: Serum 14–3-3η titres were assessed at baseline and at 18 months into disease, a median of 14 months after diagnosis and initiation of treatment. Three definitions of "clinical remission" at 18 months were used: Swollen Joint Count (SJC) =0; SJC + Tender Joint Count (TJC) =0; ACR/EULAR Boolean definition. The progression of radiographic damage (Erosion and Total Sharp/van der Heijde (SvH) scores) in patients with LOW (<0.50 ng/ml) or HIGH (≥0.50 ng/ml) 14–3-3η were compared using the Mann-Whitney test. P values <0.05 were considered significant.
Results: Out of 331 patients, 36.0% of which had HIGH 14–3-3η at Baseline, 308 had complete data up to 5 years. Median age was 60 years, 62% women. Depending on the stringency of the definition used, variable numbers of patients reached remission at 18 months: 162 (53%) had SJC=0; 108 (35%) SJC+TJC=0; and 56 (18%) Boolean.
Remission at 18 months was negatively associated with persistence of HIGH

14–3-3η since HIGH 14–3-3η were then present in 32/162 (19.7%) SJC=0 patients; 22/108 (20.4%) SJC+TJC=0 and 13/56 (23.2%) Boolean.
Compared to patients in remission with LOW 14–3-3η, patients in remission with HIGH 14–3-3η at 18 months had numerically faster subsequent progression with all definitions. For example, in patients with Boolean remission, mean (SD) erosion progression over 42 months was 7.2±13.1 vs 1.5±3.3 and mean (SD) progression of Total score 9.2±14.5 vs 2.8±4.4 units (Figure).
However, due to low numbers and limited power, differences in progression were statistically significant only for the less strict definitions of remission and only over the following year: Erosions (SJC=0, p=0.0042, SJC+TJC=0, p=0.0236), Total score (SJC=0, p=0.0146; with a trend for SJC+TJC=0, p=0.077).
None of the comparisons over 42 months or of those involving Boolean reached significance.

Figure. Progression of Erosion Sharp/van der Heijde score in patients in Boolean remission at 18 months.
A. 14-3-3η <0.50 ng/ml at 18 months. **B.**14-3-3η ≥0.50 ng/ml at 18 months.



Conclusions: The persistence of 14–3-3η levels ≥0.50 ng/ml appears to be associated with a lower probability of reaching remission in polyarthritis patients. 14–3-3η levels ≥0.50 ng/ml in patients in clinical remission appear to be associated with more rapid radiographic (especially erosive) progression over the following year. A larger study is required to validate these findings, especially with the most stringent criterion of Boolean remission.
Disclosure of Interest: N. Carrier: None declared, M.-P. Garant: None declared, A. Marotta Employee of: Augurex Life Sciences Corp., A. De Brum Fernandes Grant/research support from: AJdBF is part of the Centre de Recherche Clinique from the CHUS, which received a team grant from the Fonds de Recherche en Santé-Québec, P. Liang: None declared, A. Masetto: None declared, Y. Gui Employee of: Augurex Life Sciences Corp., J. Savill Employee of: Augurex Life Sciences Corp., S. Michienzi Employee of: Augurex Life Sciences Corp., W. Maksymowych Consultant for: Augurex Life Sciences Corp., G. Boire Grant/research support from: GB is part of the Centre de Recherche Clinique from the CHUS, which received a team grant from the FRSQ. GB is the recipient of CIHR grant MOP-110959. Since 2007, the Sherbrooke EUPA cohort has also received financial support from the Canadian ArTritis CoHort (CATCH), a study designed and implemented by investigators and financially supported via unrestricted research grants initially by Amgen Canada Inc
DOI: 10.1136/annrheumdis-2017-eular.4085

FRI0048 THE ANTI-CD20 ANTIBODY RITUXIMAB REDUCES THE INFLAMMATORY AND PROTHROMBOTIC PROFILE OF LEUKOCYTES FROM RHEUMATOID ARTHRITIS PATIENTS AND MODULATES THE ACTIVITY OF ENDOTHELIAL CELLS

I. Cecchi[1], C. Perez-Sanchez[2], P. Ruiz-Limon[2], I. Arias de la Rosa[2], M.C. Abalos-Aguilera[2], Y. Jimenez-Gomez[2], R. Ortega[2], E. Collantes-Estevez[2], A. Escudero[2], N. Barbarroja[2], S. Sciascia[1], C. Lopez-Pedrera[2]. *[1]Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases - Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Turin, Italy; [2]GC-5/Rheumatology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain*

Background: Rituximab (RTX) has been shown to be successful in the treatment of rheumatoid arthritis (RA), indicating that B cells have an important role in this disease.
Objectives: The present study was undertaken to investigate the mechanisms of action of RTX on the immune and endothelial cells (EC) of the vascular system in the setting of RA.
Methods: Purified lymphocytes from five RA patients with high disease activity were treated with RTX (1ug/mL) for 24 hours. Then, the depletion of B cells was assessed by flow cytometry, and the changes occurred in the inflammatory profile of T-lymphocytes was analysed by RT-PCR. In a second set of experiments, to evaluate the influence of B-cell depletion on the inflammatory/prothrombotic profile of cells belonging to the vascular system, supernatants from cultured lymphocytes of RA patients in the presence or in the absence of RTX were added to isolated monocytes from AR patients and to cultured endothelial cells. The response to RTX was then examined.
Results: As expected, RTX promoted a significant depletion of B-cells. In parallel, the inflammatory profile of T lymphocytes from RA patients was downregulated, as shown by a significant drop of IL-1, IL-6, IL-17, IFN and TNF expression levels, thus suggesting that the anti-inflammatory effects of RTX might be related to B cell depletion. Supernatants from RTX-treated lymphocytes further abridged the prothrombotic profile of RA-monocytes, promoting a significant inhibition of TF, MCP-1, IL-8, IL-1 and VEGF-A gene expression. Moreover, endothelial cells, activated after treatment with supernatants from cultured RA-lymphocytes, showed reduced expression of cell-adhesion molecules (i.e. V-CAM, I-CAM, E-Selectin) and pro-thrombotic factors (i.e. TF, VEGF, IL-8) after treatment with supernatants from cultured RA-lymphocytes in the presence of RTX.
Conclusions: Overall, these results reveal that depletion of B-cells by RTX in RA influences the inflammatory profile of T lymphocytes, as well as their interaction with monocytes and ECs, thus modulating the inflammatory and prothrombotic shape of vascular cells in the setting of RA.
Acknowledgements: Supported by CTS-794, ISCIII (PI15/01333; RIER RD16/0012/0015)
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4916

FRI0049 FC GAMMA RECEPTOR IV ENHANCES BONE EROSION IN EXPERIMENTAL ARTHRITIS BY PROMOTING INFLUX OF PMNS

I. Di Ceglie[1], G. Ascone[1], M. van den Bosch[1], J.S. Verbeek[2], P. van der Kraan[1], P. van Lent[1]. *[1]Experimental Rheumatology, Radboud University Medical Center, Nijmegen; [2]Leiden University Medical Center, Leiden, Netherlands*

Background: FcγRs are involved in regulation of synovial activation and bone destruction during immune complex (IC)-mediated arthritis. The balance between activating FcγRs (FcγRI,III and IV) and inhibiting FcγRII determines synovial activation. Here we investigated the particular role of activating FcγRIV in bone erosion in IC-mediated antigen induced arthritis (AIA) by comparing FcγRI,II,III,IV$^{-/-}$ mice, FcγRI,II,III$^{-/-}$ mice and wild type controls (WT).
Objectives: To investigate the role of FcγRIV in bone erosion during experimental arthritis.
Methods: AIA was induced by injection of mBSA into knee joints of mice previously immunized with mBSA/CFA. Joint inflammation, bone destruction, number of TRAP^{+} osteoclasts and S100A8/A9 positive cells was determined using histology and immunohistochemistry. *In vitro* osteoclastogenesis was assessed using TRAP staining.
Results: Seven days after induction of AIA, we observed decreased inflammation and bone erosion in the knee joints of FcγRI,II,III,IV$^{-/-}$ mice compared to WT. The ability of bone marrow cells of FcγRI,II,III,IV$^{-/-}$ mice to differentiate into osteoclasts *in vitro* was comparable to the one of WT controls. Moreover, we observed comparable numbers of TRAP^{+} osteoclasts on the bone surface of FcγRI/II/III/IV$^{-/-}$ and WT arthritic mice, suggesting that the observed decrease in bone erosion is mainly caused by a reduced osteoclast activity, rather than decreased osteoclast number. However, in contrast to FcγRI/II/III/IV$^{-/-}$, AIA induction in knee joints of FcγRI/II/III $^{-/-}$ resulted in increased bone erosion and inflammation compared to WT, highlighting the possible crucial role of FcγRIV in the pathology. Interestingly, the number of PMNs infiltrated in the knee joint of FcγRI/II/III$^{-/-}$ resulted increased, whereas it was decreased in the knee joints of FcγRI/II/III/IV$^{-/-}$ compared to their WT controls. This observation suggests that particularly FcγRIV is involved in regulating influx of PMNs. PMNs are potent producers of alarmins S100A8/A9 which are described to promote osteoclast activity. In line the number of S100A8/A9 positive cells in synovium was increased in FcγRI/II/III$^{-/-}$ while decreased in FcγRI/II/III/IV$^{-/-}$, compared to their WT control.
Conclusions: FcγRIV promotes bone erosion in AIA by enhancing influx of PMNs within the synovium. PMNs are potent producers of S100A8/A9 which has been described to induce osteoclast activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5386

FRI0050 TYPE II COLLAGEN SECRETED FROM ARTICULAR CHONDROCYTES IS MAINLY DESTROYED BY CATHEPSIN S IN RA MICE

J. Zhao, Q. Huang, H. Ren, M. Yang. *Department of Rheumatology, Nanfang Hospital, Southern Medical University, Guangzhou, China*

Background: Mast cells have long been recognized to increase strikingly in number in the synovial membrane of rheumatoid arthritis (RA), accounting for 5% of the surface synovial membrane cells. Type II collagen has the longest half-life in cartilage matrix. The main cells which might affect articular cartilage in RA are synovial fibroblasts, synovial macrophages and mast cells. The latter two could express cathepsin S.
Objectives: We aimed to find the cells which have the biggest influence on type II collagen secreted from articular chondrocytes and the possible mechanisms in RA mice.
Methods: Four types of cells from collagen-induced arthritis model-established C57BL/6 mice were primary cultured, including synovial fibroblasts, peritoneal

macrophages, bone marrow-derived mast cells and articular chondrocytes. The first three were co-cultured with articular chondrocytes separately. LHVS, a specific inhibitor of cathepsin S, and E64, a broad-spectrum inhibitor of cysteine protease, were added into the cocultures of macrophages and articular chondrocytes separately. Also, C48/80, an activator of mast cells, LHVS, and E64 were added into the cocultures of mast cells and articular chondrocytes separately. The culture supernatant fluid was collected. The concentration of cathepsin S and type II collagen were measured by ELISA. The expression of type II collagen mRNA in each group was detected with RTPCR.

Results: Macrophages and mast cells expressed cathepsin S, while synovial fibroblasts did not express cathepsin S. Synovial fibroblasts had little effect on the expression of type II collagen from articular chondrocytes. When articular chondrocytes were co-cultured with macrophages, the expression of type II collagen decreased (8.79±2.79ng/ml),compared with the control group (17.75±7.84ng/ml). The secretion of type II collagen could return to normal by the inhibitors of cathepsin S, both LHVS (16.15±8.05 ng/ml) and E64 (12.55±6.64 ng/ml). When articular chondrocytes were co-cultured with mast cells, the type II collagen could be restrained by C48/80 (9.82±0.42ng/ml), compared with the control group (26.09±9.34ng/ml). Similarly, the secretion of type II collagen could return to normal by LHVS and E64 (16.15±8.05 ng/ml, 12.55±6.64 ng/ml, respectively). There was no significant difference in the expression of type II collagen mRNA between different groups. It showed that the type II collagen was not suppressed at the transcription level, but was mainly destroyed by cathepsin S after secretion.

Conclusions: Macrophages and mast cells are the major sources of cathepsin S, which might be the main factor that destroys type II collagen secreted from articular chondrocytes in RA mice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5664

FRI0051 EARLY ARTHRITIS INDUCES DISTURBANCES AT BONE NANOSTRUCTURAL LEVEL REFLECTED IN DECREASED TISSUE HARDNESS

B. Vidal[1], R. Cascão[1], M. Finnilä[2,3], I. Lopes[1], S. Saarakkala[2,4,5], P. Zioupos[6], H. Canhão[7], J. Fonseca[1,8]. *[1]Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal; [2]Research Unit of Medical Imaging, Physics and Technology, Faculty of Medicine, University of Oulu, Oulo; [3]Department of Applied Physics, University of Eastern Finland, Kuopio; [4]Medical Research Center Oulo, Oulu University; [5]Department of Diagnostic Radiology, Oulu University Hospital, Oulo, Finland; [6]Biomechanics Labs, Cranfield Forensic Institute, Cranfield University, Swindon, United Kingdom; [7]EpiDoC Unit, CEDOC, NOVA Medical School, NOVA University; [8]Rheumatology Department, Centro Hospitalar de Lisboa Norte, EPE, Hospital de Santa Maria, Lisbon Academic Medical Centre, Lisboa, Portugal*

Background: Arthritis induces joint erosions and skeletal bone fragility.

Objectives: The main goal of this work was to analyze the early arthritis induced events at bone tissue level.

Methods: Eighty-eight Wistar rats were randomly housed in experimental groups, as follows: adjuvant induced arthritis (N=47) and a control healthy group (N=41). Rats were monitored during 22 days for the inflammatory score, ankle perimeter and body weight and sacrificed at different time points (11 and 22 days post disease induction). Bone samples were collected for histology, micro-CT, 3-point bending, nanoindentation and Fourier transformed infrared spectroscopy (FTIR) analysis. Blood samples were also collected for bone turnover markers and systemic cytokine quantification.

Results: At bone tissue level, measured by FTIR analysis and nanoindentation, there was a reduction of the mineral and collagen content and of hardness in the arthritic group, associated with an increase of the ratio of bone concentric to parallel lamellae and of the area of the osteocyte lacuna. In addition, increased bone turnover and changes in the microstructure and mechanical properties were observed in arthritic animals, since the early phase of arthritis, when compared with healthy controls.

Conclusions: Arthritis induces very early changes at bone tissue level characterized by decreased tissue hardness and of collagen and mineral content. These observations highlight the pertinence of immediate control of inflammation in the initial stages of arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3509

FRI0052 SALIVARY PEPTIDYL-ARGININE DEIMINASE AND TANNERELLA FORSYTHIA ARE ASSOCIATED WITH CLINICAL ACTIVITY OF RHEUMATOID ARTHRITIS

D.-X. Xibillé-Friedmann[1], J.-I. Martínez-Rivera[2], M.-A. De la Garza-Ramos[3], J. González-Christen[4], S.-M. Carrillo-Vázquez[5], J.-L. Montiel-Hernandez[4]. *[1]SEIC, Servicios de Salud de Morelos; [2]CISEI, Instituto Nacional de Salud Pública, Cuernavaca; [3]CIDICS/Facultad de Odontología, Universidad Autonoma de Nuevo Leon, Monterrey; [4]Facultad de Farmacia, Universidad Autonoma del Estado de Morelos, Cuernavaca; [5]Hospital Regional 1o. Octubre, ISSSTE, Mexico city, Mexico*

Background: Although the expression of bacterial Peptidyl-Arginine Deiminase (PAD) derived from *P. gingivalis* seems critical in explaining the potential effects of severe periodontitis in the development of Rheumatoid arthritis (RA), the association with the presence of the bacteria or anti-P. gingivalis/anti-PPAD antibodies is not always evident suggesting that other bacteria could be involved in the link between oral microbiota and citrullination of host proteins.

Objectives: To confirm the association between RA disease activity in a homogeneous population (aCCP+ RA patients), oral PAD activity and the prevalence of other bacterial strains such as *T. forsythia*.

Methods: RA patients fulfilling ACR/EULAR 2010 criteria were evaluated from a periodontal (Periodontal Screening Recoding Index) and rheumatologic standpoint. Patients with Sjögren's syndrome or sicca symptons were excluded. Disease activity was measured using DAS28 (ESR). Oral PAD activity was measured by colorimetric assay and presence of *Porphyromonas gingivalis, Tannerella forsythia* and *Prevotella intermedia* was evaluated by PCR. Autoantibody levels were determined by ELISA. Multivariate analysis adjusted for gender, age, time since onset of disease, RF and ESR. Comparisons between groups were performed by Mann-Whitney U testing or Kruskal–Wallis testing per the t variables. Spearman correlation testing was employed to correlate PAD activity and DAS28. Statistical significance was set at 0.05%.

Results: 132 patients were included. After a multivariate analysis an association was observed between severe periodontitis/dental mobility with moderate/high RA disease activity (OR: 4.4 (1.8–14.0), p=0.04 and 3.4 (1.1–13.4), p=0.03, respectively). Additionally, presence of *P. gingivalis* and *T. forsythia*, but not *P. intermedia*, was significantly associated with moderate/high RA disease activity (3.4 (1.1–10.5), $p<0.05$ and 4.4 (1.2–10.9), $p<0.05$). Comparing PAD activity in saliva samples of RA patients we found significant differences between the low (2.3±0.5), moderate (3.4±0.8) and high (4.3±0.3) disease activity subgroups ($p<0.01$%), whereas patients in remission demonstrated a PAD activity similar to the low disease activity group (1.9±0.39). Additionally, we found a significant correlation between oral PAD activity and RA activity, but not with autoantibody titers.

Conclusions: These results show that RA activity is associated with severe periodontitis, high oral PAD activity and the presence of *T. forsythia* and *P. gingivalis*, suggesting that both bacteria equally participate in PAD activity present in the oral microenvironment.

Acknowledgements: Disclosure: This work was supported by a grant from SEP/CONACYT CB-2010 (#155392).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3894

FRI0053 ANTIBODIES TO A SUBSET OF CITRULLINATED PEPTIDE ANTIGENS CORRELATE WITH NEUTROPHIL EXTRACELLULAR TRAP LEVELS IN THE SPUTUM OF SUBJECTS AT-RISK FOR FUTURE RA

K.D. Deane[1], M. Purmalek[2], N.L. Seto[2], E. Bowers[1], J.M. Norris[3], V.M. Holers[1], W. Robinson[4], M. Kaplan[2], M.K. Demoruelle[1]. *[1]Division of Rheumatology, University of Colorado Denver, Aurora; [2]Systemic Autoimmunity Branch, National Institutes of Health/NIAMS, Bethesda; [3]Epidemiology, Colorado School of Public Health, Aurora; [4]Division of Immunology and Rheumatology, Stanford University, Palo Alto, United States*

Background: Prior data suggest that anti-citrullinated protein/peptide antibodies (ACPA) may originate in the lung prior to the onset of synovitis in rheumatoid arthritis (RA) (1). Neutrophil extracellular trap (NET) formation is one potential mechanism that could trigger or be associated with local ACPA generation because NETs externalize citrullinated proteins and release peptidylarginine deiminase that could citrullinate nearby proteins (2–4).

Objectives: Using induced sputum, we recently identified a significant correlation between NETs and anti-cyclic citrullinated peptide (CCP) antibodies in subjects at-risk for future RA. Herein, we sought to explore associations of individual ACPAs and NETs in these subjects.

Methods: From the Studies of the Etiology of RA (SERA) cohort, we included 24 RA-free subjects At-Risk for future RA based on familial (i.e. first-degree relative of RA patient) or serologic (i.e. serum anti-CCP positive identified at health fairs) risk. Induced sputum was tested using a bead-based ACPA array for IgG reactivity to 29 individual citrullinated proteins/peptides. Levels of NET complexes in sputum were measured using a deoxyribonucleic acid (DNA)-myeloperoxidase (MPO) and DNA-neutrophil elastase (NE) sandwich ELISA. Analyses included Spearman's correlation and linear regression. Using Bonferonni's correction, results were considered significant if both DNA-MPO and DNA-NE assays had a $p<0.002$.

Results: Subjects had a median age of 51 years, were 67% female and 38% ever-smokers. Increasing sputum NET levels significantly correlated with increasing ACPA levels for 27/29 ACPAs, including proteins/peptides of cit-vimentin, cit-fibrinogen, cit-fibronectin, cit-apoliporoteins and cit-alpha-enolase. After adjusting for ever-smoking, sputum NET levels remained significantly associated with 17/29 ACPAs. The strongest associations ($p\leq0.001$ for both NET assays) were cit-H2A/a2$_{1–20}$, cit-vimentin$_{58–77\ \text{cyclic}}$, cit-alpha-enolase$_{5–21}$, cit-fibrinogen$_{27–43}$, cit-fibrinogen$_{211–230\ \text{cyclic}}$, cit-fibrinogen$_{616–635\ \text{cyclic}}$, cit-fibrinogenB$_{54–72}$, and cit-apolipoprotein E$_{277–269\ \text{cyclic}}$.

Conclusions: In subjects At-Risk for future RA, we identified a strong corre-

lation between sputum NET complexes and multiple sputum ACPAs that was independent of smoking exposure. These data suggest that in the lung, NET formation may be associated with the production of multiple ACPA reactivities locally. Additional studies are needed to determine if NET-associated cit-proteins are an initial trigger or a self-perpetuating stimulus of sputum ACPA generation as well as contributions of other local mechanisms of citrullination.

References:
[1] Willis VC, Demoruelle MK, Derber LA, Chartier-Logan CJ, Parish MC, Pedraza IF, et al. Sputum autoantibodies in patients with established rheumatoid arthritis and subjects at risk of future clinically apparent disease. Arthritis Rheum. 2013;65(10):2545–54.
[2] Brinkmann V, Reichard U, Goosmann C, Fauler B, Uhlemann Y, Weiss DS, et al. Neutrophil extracellular traps kill bacteria. Science. 2004;303(5663):1532–5.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6757

FRI0054 A NOVEL PHARMACOLOGICAL ACTION OF MTX THROUGH CIRCADIAN CLOCK GENES IN RA FIBROBLAST-LIKE SYNOVIAL CELLS

K. Suzuki[1], K. Yoshida[1], T. Hashimoto[2], K. Kaneshiro[1], A. Nakai[1], N. Hashimoto[1], Y. Kawasaki[3], N. Shibanuma[4], N. Nakagawa[5], Y. Sakai[6], A. Hashiramoto[1]. *[1]Biophysics, Kobe University Graduate School of Health Sciences; [2]Rheumatology; [3]Kobe Kaisei Hospital, Kobe, Japan; [4]Orthopaedic Surgery, Kobe Kaisei Hospital, Kobe; [5]KonanKakogawa Hospital, Kakogawa; [6]Kobe University Graduate School of Medicine, Kobe, Japan*

Background: Methotrexate inhibits the proliferation of RA fibroblast-like synovial cells (RA-FLS) by folate anti-metabolism. We previously reported that disruptions of circadian clock genes were involved in the pathogenesis of inflammatory arthritis (1,2).
Objectives: To explore pharmacological effects of MTX on circadian clock genes of RA-FLS.
Methods: Under treatments of MTX on RA-FLS, cell viabilities were determined by WST-8 assay, expressions of circadian clock genes (*Clock, Bmal1, Cry1* and *Per2*), circadian transcriptional factor PAR bZip (*Dbp, Tef* and *Hlf*), and pro-apoptotic Bcl-2 interacting killer (*BIK*) were examined by real time PCR, and expressions of PER2 and CYTOCHROME C were examined by western blotting. The expressions of PER2, BIK, CYTOCHROME C and morphological changes of the nucleus were observed by fluorescent immunostaining. RA-FLS were transfected with *Per2* and *BIK* siRNAs and successively treated with MTX to determine cell viabilities by WST-8 assay.
Results: MTX (1,10 nM) treatment significantly decreased the cell viabilities. MTX (10nM) have increased mRNA expression of *Per2, Dbp, Tef, Hlf*, and *BIK*, and protein expressions of PER2 and CYTOCHROME C, as well. In fluorescent observations, PER2, BIK, and CYTOCHROME C were increased in apoptotic cells. Cytotoxicity of MTX was attenuated by knockdowns of *Per2* or *BIK* in RA-FLS.
Conclusions: The transcriptional factor PAR bZip binds to the D-box elements of *Per2* and *BIK* promoters (3,4). Here, we propose a novel action of MTX that up-regulates the expressions of *Per2* and *BIK* via PAR bZip to induce apoptosis in RA-FLS.

References:
[1] Hashiramoto A, J Immunol. 2010 Feb 1;184(3):1560–5.
[2] Hand LE, FASEB J. 2016 Nov;30(11):3759–3770.
[3] Yoshida K, Scand J Rheumatol. 2013;42(4):276–80.
[4] Ritchie A, Cell Death Differ. 2009 Jun;16(6):838–46.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3351

FRI0055 HISTONE DEACETYLASE 1 (HDAC1): A NOVEL THERAPEUTIC TARGET IN RHEUMATOID ARTHRITIS

L. Göschl[1], M. Bonelli[1], V. Saferding[1], T. Preglej[2], C. Seiser[3], S. Knapp[4], J. Backlund[5], C. Bock[6], P. Mathias[7], K. Hirahara[8], C. Scheinecker[9], G. Steiner[1], W. Ellmeier[10]. *[1]Division of Rheumatology, Medical University of Vienna; [2]Division of Immunobiology, Medical University of Vienna; [3]Department of Medical Biochemistry, Medical University of Vienna; [4]Research Center for Molecular Medicine (CeMM), Austrian Academy of Sciences, Vienna, Austria; [5]Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden; [6]Research Center for Molecular Medicine (CeMM), Austrian Academy of Sciences, Wien, Austria; [7]Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland; [8]Department for Cell Biology, Chiba University, Chiba, Japan; [9]Internal Medicine III, Division of Rheumatology; [10]Division of Immunobiology, Medical University of Vienna, Vienna, Austria*

Background: Autoreactive T cells have been shown to play a major role in Rheumatoid Arthritis, which drive the inflammatory process leading to an irreversible destruction of the joints. Gene transcription and regulation of proinflammatory cytokine production in T cells is regulated by epigenetic mechanisms. Histone deacetylases (HDACs) modify the epigenetic landscape by removing acetyl groups of lysine residues of histones, resulting in chromatin condensation and repression of transcription. The application of pan-HDAC inhibitors has been shown to be a potential therapeutic strategy. However, major side effects limited the clinical use and underline the need of more specific HDAC inhibitors.
Objectives: Our aim was to to investigate whether HDAC1 is linked with the development of autoimmune diseases. Therefore we were using the collagen-induced arthritis model (CIA) and the experimental autoimmune encephalomyelitis model (EAE).
Methods: Mice with a T cell specific deletion of HDAC1 (HDAC1cKO) were generated by using the CD4Cre/LoxP system. The clinical and the histological phenotype were assessed in the CIA and the EAE. Anti-collagen antibody levels were determined by ELISA. Qualitative and quantitative analysis of T cell subsets of the spleen and draining LN were assessed using flow cytometry. Additionally comparative RNA-sequencing of $CD4^+$ T cells from wild type (WT) and HDAC1cKO mice was performed.
Results: To address whether HDAC1 is involved in the pathogenesis of autoimmune diseases we induced the CIA and the EAE in WT and HDAC1cKO mice. Unexpectedly, HDAC1cKO mice did not develop any clinical or histological signs of inflammation, despite the presence of serum anti-CII antibodies. A similar protection against disease development was also observed in the context of EAE. A molecular analysis of HDAC1cKO $CD4^+$ T cells revealed increased STAT1 phosphorylation in activated HDAC1cKO $CD4^+$ T cells in comparison to WT cells. This was accompanied with an impaired expression of CCR6 in activated HDAC1cKO $CD4^+$ T cells, which is an essential chemokine receptor for the development of arthritis and EAE. In line with this finding we observed increased expression of CCR6 in $STAT1^{-/-}$ $CD4^+$ T cells. This indicates a negative role of STAT1 in the regulation of CCR6 expression.
Conclusions: Our data show the importance of HDAC1 as a key immune regulator in the pathogenesis of collagen induced arthritis. Therefore it might be considered as an interesting novel therapeutic target in RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5162

FRI0056 INCREASED EXPRESSION OF THE COLLAGEN INTERNALIZATION RECEPTOR ENDO180 IN FIBROBLAST-LIKE SYNOVIOCYTES OF PATIENTS WITH RHEUMATOID ARTHRITIS

L. Yan, Y. Wen. *Department of Rheumatology, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Hyperproliferative and invasion are the characteristics of fibroblast-like synoviocytes in rheumatoid arthritis (RA-FLSs), which contribute mainly to RA disease progression and ultimately to joint destruction. Endo180 is a recycling endocytic receptor that has functions to regulate cell migration and bind and internalize collagens. However, the expression of Endo180 in RA-FLSs and its underlying mechanisms remain unclear.
Objectives: To examine the expression of Endo180 in RA-FLSs and the role it played in RA.
Methods: Tissues were collected from RA patients with joint replacement surgery or arthroscopy and RA-FLSs were obtained by tissue culture; Westren blot was used to measure the expression of Endo180 in RA-FLSs. Chemically synthesized small interference RNA (siRNA) specifically targeting Endo180 gene was transfected into RA-FLSs by cationic liposome; The interference efficiency of Endo180-siRNA on the production of Endo180 mRNA and protein was determined by RT-qPCR and Western blot respectly; The proliferative inhibition rate was examined by CCK8 assay and the migration of RA-FLSs were examined by Transwell assay.
Results: Expression of Endo180 was obviously higher in fibroblast-like synoviocytes in RA than OA and the traumatic patients. And its expression level has positive correlation with disease activity. The proliferative inhibition rate was obviously higher in the Endo180-siRNA group than the control groups ($P<0.05$) after transfection for 48h (8.31%±1.17%), 72h (15.93%±2.12)%), 96h (18.01%±2.78%). Transwell migration assay demonstrated the RA-FLSs through the transwell membrane in Endo180-siRNA group (21.27±6.35) were lesser than the NC-siRNA group (80.20±11.12) ($P<0.05$)and the blank control group (82.17±10.36) ($P<0.05$).
Conclusions: Endo180 may play a role in the regulation of proliferation and migration of RA-FLSs, which may provide beneficial therapeutic effects in RA.

References:
[1] Melander MC, Jürgensen HJ, Madsen DH,et al. The collagen receptor uPARAP/Endo180 in tissue degradation and cancer (Review).Int J Oncol. 2015 Oct;47(4):1177–88. doi: 10.3892/ijo.2015.3120. Epub 2015 Aug 12.
[2] Madsen DH, Jurgensen HJ, Ingvarsen S, et al. Endocytic collagen degradation: a novel mechanism involved in protection against liver fibrosis. J Pathol. 2012 May;227(1):94–105. doi: 10.1002/path.3981. Epub 2012 Feb 17.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5667

FRI0057 EVALUATION OF THE IMMUNODOMINANCE OF A HISTONE H4 PEPTIDE IN ANTI-CCP ANTIBODIES FROM RHEUMATOID ARTHRITIS PATIENTS

L. Rodriguez-Martinez[1], C. Regueiro[1], A. Montes[1], E. Perez-Pampin[2], A. Mera-Varela[2], A. Gonzalez[1]. *[1]Experimental and Observational Rheumatology; [2]Rheumatology Unit, Instituto Investigacion Sanitaria- H. Clinico Universitario de Santiago, Santiago de Compostela, Spain*

Background: The anti-CCP assay identifies antibodies against endogenous citrullinated proteins that are not completely characterized. The histone H4 seems to be a prominent one according to a recent study (1), which found this protein specifically in the immune complexes from synovial fluid of anti-CCP positive RA patients. Only vimentin, among the previously proposed autoantigens, was present in those immune complexes, but its abundance was much lower than that of histone H4. In addition, a citrullinated H4-derived peptide, H4-c39/40, showed marked immunodominance since antibodies directed against this peptide were present in 100% of synovial fluid samples and in 92–94% of anti-CCP positive sera. These frequencies are much larger than the reported with other autoantigens.
Objectives: To confirm the immunodominance of the H4-c39/40 peptide in anti-CCP antibodies from RA patients by direct comparison with citrullinated peptides of two other potential autoantigens.
Methods: Five hundred and thirteen patients with established RA and 273 healthy controls were included. Antibodies against H4-c39/40, cFibB36–52 and cVim60–75 were evaluated using indirect ELISA. Concordance between positives and negatives was analyzed with the Goodman and Kruskal's gamma coefficient (γ). In addition, Spearman's rank correlation (r_s) was used to analyze the correlation between levels of antibody titers.
Results: In contrast to the previous report (1), only 68.5% of the anti-CCP positive patients carried anti-H4-c39/40 antibodies. However, this frequency was higher than the observed with the other two peptides, 50.5% of anti-cFibB36–52 and 28.8% of anti-cVim60–75 positive patients. Consequently, a high concordance was found between anti-CCP and anti-H4-c39–40 antibodies (γ =0.95), which was moderately larger than that observed between anti-CCP and anti-cFibB36–52 antibodies (γ =0.86). In addition, anti-H4-c39/40 antibody titers were correlated with anti-CCP titers, but this correlation was similar to the observed between anti-cFibB36–52 and anti-CCP titers (r_s =0.34 and 0.33, respectively). The anti-cVim60–75 antibodies, in turn, showed notably low concordance and low correlation with the anti-CCP antibodies.
Conclusions: Our results confirm that anti-H4-c39/40 antibodies are a significant component of the antibodies detected with the anti-CCP assay. However, immunodominance of this peptide was not as marked in our patients as the described in the original study.
References:
[1] Meng X, et al. PLoS One. 2016; 11(10):e0165501.
Acknowledgements: Funding was provided by grants of the Instituto de Salud Carlos III (Spain) PI14/01561 and RD12/009/008 with participation of FEDER.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5739

FRI0058 EFFECT OF MIF GENE HAPLOTYPES ON RHTNF-A AND RHMIF RESPONSE IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF RHEUMATOID ARTHRITIS PATIENTS

L.A. Hernandez-Palma[1], S. Garcia-Arellano[1], S. Cerpa-Cruz[2], J.F. Muñoz-Valle[1]. *[1]Research Institute in Biomedical Sciences, University of Guadalajara; [2]Division of Rheumatology, Guadalajara Civil Hospital "Fray Antonio Alcalde", Guadalajara, Mexico*

Background: Macrophage migration inhibitory factor (MIF) is a pro-inflammatory cytokine that plays important role in the development and pathogenesis of rheumatoid arthritis (RA). MIF promotes the expression of cytokines related to RA development, as tumor necrosis factor alpha (TNF-α), interleukin (IL)-6 and IL-17. Two polymorphisms in the promoter of the *MIF* gene have been associated with increased production of protein and it has been shown that TNF-α is involved in the regulation of *MIF* mRNA expression and protein secretion in a dose-dependent manner.
Objectives: To evaluate the effect of *MIF* gene haplotypes on rhTNF-α and rhMIF response in peripheral blood mononuclear cells (PBMC) of RA patients
Methods: Genotyping was performed for *MIF* gene haplotypes in 230 RA patients. Cell culture of PBMC from two patients per homozygous haplotype (5G, 6G and 7C) was performed and stimulated with rhTNF-α and rhMIF. Cytokine levels were analyzed by a microsphere-based ELISA method (Bio-Plex® MAGPIX™).
Results: rhTNF-α and rhMIF-induced IL-6, IL-17A and IL-17F secretion in PBMC of RA patients. We observed that PBMC extracted from patients with MIF 7C haplotypes stimulated with rhTNF showed higher secretion of IL-17A and IL-17F than patients with 5G and 6G haplotypes. IL-6 production with rhMIF stimulation was more pronounced in the 5G haplotype group than 6G or 7C haplotype groups.
Conclusions: rhTNF-α and rhMIF promote differential secretion of IL-6, IL-17A and IL-17F according to *MIF* haplotypes presence. IL-17A and IL-17F secretion of stimulated PBMC with rhTNF-α are higher in patients with 7C haplotype than non-7C haplotypes. Furthermore, IL-6 levels are higher in PBMC from patients with 5G haplotype stimulated with MIF than non-5G haplotypes.
References:
[1] McInnes IB, Buckley CD, Isaacs JD. Cytokines in rheumatoid arthritis - shaping the immunological landscape. Nat Rev Rheumatol 2016;12(1):63–68.
[2] Llamas-Covarrubias MA, Valle Y, Navarro-Hernández RE, Guzmán-Guzmán IP, Ramírez-Dueñas MG, Rangel-Villalobos H, Estrada-Chávez C, Muñoz-Valle JF. Serum levels of macrophage migration inhibitory factor are associated with rheumatoid arthritis course. Rheumatol Int 2012;32(8):2307–2311.
[3] Stojanović I, Cvjetićanin T, Lazaroski S, Stosić-Grujicić S, Miljković D. Macrophage migration inhibitory factor stimulates interleukin-17 expression and production in lymph node cells. Immunology. 2009;126(1):74–83.
[4] Gregersen PK y Bucala R. Macrophage migration inhibitory factor, MIF alleles, and the genetics of inflammatory disorders: incorporating disease outcome into the definition of phenotype. Arthritis Rheum. 2003;48(5):1171–6.
[5] Xiong C1, Huang B, Cun Y, Aghdasi BG, Zhou Y. Migration inhibitory factor enhances inflammation via CD74 in cartilage end plates with Modic type 1 changes on MRI. Clin Orthop Relat Res. 2014;472(6):1943–54.
Acknowledgements: This study was supported by funding from the National Council of Science and Technology (CONACYT) Grant #161749 assigned to JFMV.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4566

FRI0059 CARDIAC, PULMONARY AND PERIODONTAL DISEASE AS COMORBIDITIES IN TNF-DRIVEN MODELS OF CHRONIC POLYARTHRITIS

M.C. Denis[1], L. Ntari[2], M. Sakkou[2], P. Chouvardas[2], A. Prados[2], G.M.C. Consortium[3], H. Fuchs[3], V. Gailus-Durner[3], M. Hrabě de Angelis[3], B. Simic[4], M. Crucet[4], T.F. Lüscher[4], K. Mitchell[5], C. Schwarzwald[5], N. Karagianni[1], G. Kollias[2,6]. *[1]Biomedcode Hellas SA; [2]Department of Immunology, Biomedical Sciences Research Center (BSRC), "Alexander Fleming", Vari, Greece; [3]German Mouse Clinic, Institute of Experimental Genetics, Helmholtz Zentrum München, German Research Center for Environmental Health (GmbH), Neuherberg, Germany; [4]Center for Molecular Cardiology; [5]Clinic for Equine Internal Medicine, Equine Department Vetsuisse Faculty, University of Zurich, Zurich, Switzerland; [6]Department of Physiology, School of Medicine, National Kapodistrian University, Athens, Greece*

Background: Patients with RA exhibit an increased risk of developing multiple extraarticular pathologies. The link between co-manifested pathologies and RA at the level of common molecular and cellular mechanisms remains to be further elucidated.
Objectives: We aimed to identify comorbidities developing in models of TNF-driven chronic polyarthritis and further explore their aetiopathogenesis.
Methods: Through detailed phenotyping, clinical, histopathological and functional analysis we investigated the development of comorbidities in the Tg197 and $Tnf^{\Delta ARE/+}$ mouse models that overexpress respectively human and mouse TNF and develop spontaneous chronic polyarthritis with the concomitant development of Crohn's-like IBD in the case of the $Tnf^{\Delta ARE/+}$ animals. Targeting mesenchymal origin cells, *ex vivo* cellular analyses and RNA sequencing expression profiling allowed us to further explore the key cellular instigators of RA related comorbidities.
Results: Histopathological evaluation and echocardiography assessment of both arthritis models showed thickening of the aortic valve and cardiac dysfunction characterized by mild decreased fractional shortening, decreased heart rate and increased velocities in ascending aorta hinting towards aortic valve disease. The aortic valve pathology, similarly to arthritis, was ameliorated with anti-TNF treatment. The thickening of the aortic valve leaflets was due to fibrosis which consisted almost entirely of mesenchymal origin Valve Interstitial Cells (VICs). VICs from mutant mice expressed high levels of TNF and exhibited a proliferative and migratory phenotype resembling the activated phenotype of pathogenic Synovial Fibroblasts (SFs) isolated from the joints of the same mice. RNA-seq analysis further supported a significant correlation between pathogenic SFs and VICs highlighting a common cellular mechanism linking RA and aortic valve pathology. Furthermore, we show that TNF deregulation leads to additional RA related comorbidities, as described in human disease, including periodontitis with early onset alveolar bone loss and pulmonary inflammation with mild to severe bronchus-associated lymphoid tissue (BALT).
Conclusions: Similarly to human RA patients, TNF-driven arthritis models develop multiple RA-associated comorbidities, offering novel insights into potential molecular and cellular mechanisms commonly underlying these complex pathologies.
References:
[1] Keffer, J. et al. Transgenic mice expressing human tumour necrosis factor: a predictive genetic model of arthritis. EMBO J. 10, 4025–4031 (1991).
[2] Kontoyiannis, D. et al. Impaired on/off regulation of TNF biosynthesis in mice lacking TNF AU-rich elements: implications for joint and gut-associated immunopathologies. Immunity 10, 387–398 (1999).
[3] Armaka, M. et al. Mesenchymal cell targeting by TNF as a common pathogenic principle in chronic inflammatory joint and intestinal diseases. J. Exp. Med. 205, 331–7 (2008).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5142

FRI0060 MONOCYTE-DERIVED MICROPARTICLES IN CIRCULATION OF PATIENTS WITH RHEUMATOID ARTHRITIS: A NOVEL BIOMARKER FOR THE DISEASE ACTIVITY

M. Koseki, H. Yasuoka, K. Sakata, K. Yoshimoto, K. Yamaoka, T. Takeuchi.
Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan

Background: Rheumatoid arthritis (RA) is a systemic connective tissue disease and characterized by inflammation of synovium of multiple joints, however, its pathogenesis is still unclear (1). Physiologically, microparticle (MP) is categorized as a membrane microvesicle which contains various humoral factors such as cytokines or growth factors and 0.1–1 μm in size (2). And MPs can distribute systemically through circulation. MP is released from almost all cell types and induced by stimulation, stress or apoptosis (3). Thus, we hypothesized that MPs derived from various cells can distribute to the lesion of RA and be associated with systemic disease process of RA.
Objectives: To clarify the source of MPs in circulation of RA and elucidate their role in the pathogenesis and the possibility for application as a novel disease marker.
Methods: Twenty patients with RA and 13 healthy controls were involved. Using gradient centrifugation, platelet-rich plasma was isolated from whole blood and applied to flow cytometry. MP is defined as a vesicle less than 1 mm in diameter and Megamix® was used to set a gating condition to detect microparticles (4). Sources of MP (MP subsets) were identified by the expression of cell-specific markers using flow cytometry with fluorescence-conjugated antibodies as follows; platelets MP: $CD41^+CD31^+$ MP, endothelial cell MP: $CD41^-CD31^+$ MP, immune cell MP: $CD45^+CD41^-$ MP, MP derived other cells: $CD41^-CD31^-CD45^-$ MP. Correlation between clinical information and proportion of MP subsets was also analyzed. Comparisons between two groups were examined by Mann-Whitney U-test with Bonferroni correction. Significant difference was defined as corrected *p* value (*Pc*) <0.05.
Results: Mean age of 20 patients with RA was 56±14 years, 95% was female, disease duration was 8.5±8.0 years, and DAS28-ESR was 2.0±1.1. Methotrexate was administered to 75% and average dose was 8.0±2.4 mg/week. Platelet-derived MP covered the largest proportion in all groups. Interestingly, proportion of immune-cell-derived MP was higher ($Pc<0.006$) in patients with RA compared to controls. Proportion of immune-cell-derived MP was positively correlated with inflammatory markers such as CRP and composite disease markers such as DAS28-ESR. Furthermore, when stratified by monocyte fraction and non-monocyte fraction based on CD14 expression, proportion of monocyte-derived MP showed higher ($Pc<0.01$) in patients with RA compared to controls, but non-monocytes MP did not, and that of monocyte-derived MPs was also correlated with disease markers for activity of RA.
Conclusions: Proportion of circulating immune-cell-derived MPs, especially monocyte-derived MPs, increased in RA and correlate with disease activity. These results suggest that monocyte-derived MPs can be measured as a novel biomarker and involved in the disease process of RA.
References:
[1] Smolen JS et al. Lancet 388: 2023–2038, 2016.
[2] van der Pol E et al. 64: 676–705, 2012.
[3] Buzas EI et al. Nat Rev Rheumatol 10: 356–364, 2014.
[4] Chandler WL et al. J Thromb Haemost 9:1216–1224, 2011.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4599

FRI0061 IDENTIFICATION OF CITRULLINATION SITES SPECIFIC FOR PEPTIDYLARGININE DEIMINASE 2 (PAD2) AND PAD4 IN FIBRINOGEN FROM SYNOVIAL FLUID OF PATIENTS WITH RHEUMATOID ARTHRITIS

M. Sharma[1], D. Damgaard[2], L. Senolt[3], B. Svensson[1], A.C.B. Jensen[4], C.H. Nielsen[2], P. Hägglund[1]. *[1]Department of Biotechnology and Biomedicine, Technical University of Denmark; [2]Center for Rheumatology and Spine Diseases, Copenhagen University Hospital, Rigshospitalet, Institute for Inflammation Research, Copenhagen, Denmark; [3]Department of Rheumatology and Faculty of Medicine, Charles University, Institute of Rheumatology and Department of Rheumatology, Prague, Czech Republic; [4]Rheumatology, Biomarkers and Research, Nordic Biosciences, Copenhagen, Denmark*

Background: Protein citrullination, i.e. conversion of arginine residues into citrulline residues, is a post-translational modification catalyzed by PAD, and is an important pathophysiological determinant in conditions such as Rheumatoid arthritis (RA). Identification of citrullination sites on putative autoantigens is likely to enhance our understanding of PAD's substrate specificity.
Objectives: Citrullinated fibrinogen is an autoantigen linked to the pathophysiology of RA.We have applied a novel MS-based proteomics approach to estimate the degree of citrullination in synovial fluid (SF) from RA patients, and compare to fibrinogen citrullinated *in vitro* by PAD2/4, the most important PAD isoforms involved in RA. The estimated degree of citrullination induced by the two isoforms is also compared to evaluate their relative impact.
Methods: Fibrinogen was citrullinated *in vitro* by PAD2/4 and citrullination sites were identified by LC-MS/MS on a Q-exactive orbitrap following proteolytic digestion with Lys-C. These *in vitro* citrullination profiles were compared to those observed in SF fibrinogen of four RA patients with varying DAS28 scores, CRP levels and leukocyte counts. DAS28 scores >5.1 and ≤ 2.4 correspond to moderate to severe and low activity of disease respectively. Patients with high inflammatory activity gave high CRP level and leukocyte count values.
Results: A total of 52 citrullination sites were identified. Overall, PAD2 generated higher number of identified sites and higher degree of citrulline occupancy at given sites than PAD4. In fibrinogen from SF, 38 citrullination sites were identified, of which 23 have not been previously reported. Several of these sites were identified in more than one patient, and were regarded as hotspots. Fibrinogen from patients with high DAS28 levels contained markedly more citrullination sites and higher citrulline occupancy.
Conclusions: Study suggests that PAD2 citrullinates fibrinogen more efficiently than PAD4 and citrullination of certain sites in fibrinogen from SF reflects disease activity. Identification of such sites may have diagnostic or prognostic value in RA and other inflammatory disorders.
References:
[1] D Makrygiannakis, E af Klint, I E Lundberg, R Lofberg, A-K Ulfgren, L Klareskog, A.I.C. Citrullination is an inflammation-dependent process. Ann. Rheum. Dis. 2006, 65 (9), 1219–1222.
[2] Foulquier,C.; Sebbag, M.; Clavel, C.; Chapuy-Regaud, S.; Al Badine, R.; Mechin, M. C.; Vincent, C.; Nachat, R.; Yamada, M.; Takahara, H. Peptidyl arginine deiminase type 2 (PAD-2) and PAD-4 but not PAD-1, PAD-3, and PAD-6 are expressed in rheumatoid arthritis synovium in close association with tissue inflammation. Arthritis Rheum. 2007, 56 (11), 3541–3553.
[3] Gestel, A.; Haagsma, C.; Riel, P. Validation of rheumatoid arthritis improvement criteria that include simplified joint counts. 1998, 41 (10), 1845–1850.
Acknowledgements: The Danish Council for Independent Research Natural Sciences (grant number 11–106246) and the Velux foundation. The Danish Research Foundation, Nordic Bioscience A/S and DTU are acknowledged for a joint PhD scholarship. LS was supported by the Ministry of Health of the Czech Republic (grant #00023728).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5950

FRI0062 SYNOVIAL FLUID TREG CELLS SECRETE IL-17 AND AT THE SAME TIME ARE POTENT SUPPRESSORS OF TRESP CELL PROLIFERATION, TNF ALPHA AND IFN GAMMA PRODUCTION

M. Benito-Miguel[1,2], A. Villalba[1], M.-G. Bonilla-Hernán[1], D. Peiteado[1], A. Balsa[1], P. Aguado[1], P. Sánchez-Mateos[3], A. Puig-Kröger[3], E. Martin-Mola[1], M.E. Miranda Carus[1]. *[1]Rheumatology, HOSPITAL LA PAZ - IdiPAZ; [2]Biochemistry, Centro de Ciencias de la Salud San Rafael. Universidad Antonio de Nebrija; [3]Immunology, Hospital Gregorio Marañon, Madrid, Spain*

Background: IL-17-expressing FoxP3 regulatory T cells have been described, and their suppressive capacity has been questioned. An inflammatory environment seems to favor IL-17 secretion by regulatory CD4+CD25+FoxP3+ T cells.
Objectives: To assess the suppressive function and IL-17 producing capacity of CD4+CD25+CD127-FoxP3+ T cells in the synovial fluid of RA patients (RASFd).
Methods: Synovial fluid was drawn from 35 patients with established RA who were receiving methotrexate and low-dose oral prednisone. The frequency of CD4+CD25+CD127-FoxP3+ T cells was assessed by flow cytometry. Total CD4+ T cells, CD4+CD25+CD127- T reg cells and CD4+CD25- Tresp cells were isolated by Ficoll-Hypaque gradient, followed by sorting. After isolation, cells were stimulated for 5 hours with PMA+ionomycin or cultured for 5 days in flat-bottom 96-well plates coated with an anti-CD3 monoclonal antibody. Treg cell function was assessed using two different approaches: A.The regulatory function of natural proportions of Tregs was inferred by comparing the proliferative and cytokine responses of total CD4+ T cells (TCD4T) versus CD25+ depleted CD4+ T cells (CD4+CD25-T cells or Tresp cells); B. The per cell suppressor potency of Tregs was assessed in cocultures of isolated Tregs with Tresp, established at different Treg/Tresp ratios. Proliferation was determined by 3Hthymidine incorporation and CFSE dilution; cytokine secretion was measured by ELISA of culture supernatants.
Results: A high proportion of CD4+CD25+CD127- T cells was present in RASFd (mean ± SD, 21.1%±6.2), which is significantly higher than reported frequencies of this cell population in the peripheral blood of both RA and healthy subjects. These RASFd CD4+CD25+CD127- T cells expressed FoxP3 but did not express CD69. The proliferation rate, TNFα and IFNγ secretion were significantly higher for isolated Tresp as compared with TCD4T cells, indicating that natural proportions of Treg cells present in the synovial fluid of RA are funcionally suppressive. Surprisingly, TCD4T cells secreted higher amounts of IL-17 as compared with Tresp cells, although the difference did not reach statistical significance. On a per cell basis, RAPB Tregs were potent suppressors of Tresp proliferation, TNFα and IFNγ but not of IL-17 secretion; in fact IL-17 secretion did not decrease but was enhanced in the presence of increasing proportions of Treg cells. Isolated Treg cells did not proliferate or produce cytokines when cultured alone in anti-CD3 coated plates. However, in the presence of plate-bound anti-CD3 plus anti-CD28 and recombinant human IL-2, isolated Treg cells secreted significant amounts of IL-17 whereas no TNFα or IFNγ could be detected in supernatants.
Conclusions: CD4+CD27+CD127- FoxP3+ Treg cells present in the synovial fluid of RA patients are potent suppressors of Tresp proliferation, TNFα and IFNγ secretion, and at the same time produce significant amounts of IL-17.

References:
[1] Voo KS, et al. Proc Natl Acad Sci U S A. 2009;106:4793.
[2] Beriou G et al. Blood. 2009;113:4240.
[3] Wang T, et al. Ann Rheum Dis. 2015;74:1293.
[4] Komatsu N, et al. Nat Med. 2014;20:62.
[5] Yang BH, et al. Mucosal Immunol. 2016;9:444.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4088

FRI0063 RESVERATROL ATTENUATES SYNOVIAL HYPERPLASIA IN AN ACUTE ANTIGEN-INDUCED ARTHRITIS MODEL BY AUGMENTING AUTOPHAGY AND DECREASING ANGIOGENESIS

M. Almonte-Becerril[1], J.A. Fernandez-Rodriguez[1], J.A. Fernandez-Rodriguez[1], O. Ramil-Gomez[1], R.R. Riveiro-Naveira[1], L. Hermida-Carballo[1], A. Concha[2], A. Vela-Anero[3], S. Viñas[1], F.J. Blanco[4], M.J. Lopez-Armada[1]. *[1]Aging and Inflammatory Research Lab; [2]Servicio de Patología; [3]Terapia Celular y Medicina Regenerativa; [4]Laboratorio de Investigacion Osteoarticular y Envejecimiento, SERGAS, A Coruña, Spain*

Background: Previously, we have demonstrated that dietary supplementation with resveratrol lowers synovial hyperplasia, inflammatory markers and oxidative damage in an acute antigen-induced arthritis (AIA) model.
Objectives: In this work, we investigated whether resveratrol can also regulate this abnormal proliferation of synovial tissue in an acute AIA model by inducing cell death pathways and by modifying the angiogenesis in the synovial membrane.
Methods: Animals were randomly divided into 3 groups: control, AIA, and resveratrol-treated AIA group. Resveratrol (12,5 mg/kg/day) was given orally 8 weeks before AIA induction until sacrifice day (48 h after intra-articular injection). Control and AIA animals were administered 100 μl of water. Resveratrol effects on autophagy and apoptosis were evaluated by LC3 and active caspase-3 expression (confocal and immunohistochemistry, respectively). Angiopoietin 1 (Ang-1), vascular endothelial growth factor (VEGF), and the nuclear factor NF-*kappa*-B p65 subunit (p65) were also determined by immunohistochemistry and cartilage degradation with Safranin-O.
Results: Resveratrol significantly reduced the histological score of synovial tissue. Results showed a significant higher expression of LC3 signals in the AIA synovial membranes, compared with control samples, in which the presence of vesicles was easily observed. Interestingly, the synovial tissues from the resveratrol group showed a significantly ($p \leq 0.001$) higher signal for LC3, compared with the AIA samples. Active caspase-3 expression was up-regulated at the same level in the synovial membranes of AIA group than in resveratrol-treated AIA group; however, in resveratrol-treated AIA group active caspase-3 signal was mainly located in the inflammatory cells. Resveratrol consumption significantly attenuated Ang-1 signal, whereas expression of VEGF showed a non significant reduction. Resveratrol administration also mitigated, even not significantly, p65 expression that was significantly higher in the AIA animals than those from the control animals. In addition, resveratrol decreased articular cartilage degradation.
Conclusions: These data suggest that resveratrol is able to modulate synovial hyperplasia by increasing autophagic cell death and limiting angiogenic response in an acute AIA model, which could also modulate the inflammatory and destructive processes for rheumatoid arthritis.
Acknowledgements: Instituto de Salud Carlos III-Ministerio de Economía y Competitividad N° Expediente PI12/02771. Unión Europea-Fondo Europeo de Desarrollo Regional (FEDER) "Una manera de hacer Europa"
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6270

FRI0064 CHEMOKINE RECEPTOR 6 MODULATES ARTHRITIS IN A T CELL DEPENDENT MANNER

M. Bonelli, A. Puchner, L. Goeschl, S. Hayer, B. Niederreiter, J.S. Smolen, C. Scheinecker, S. Blueml. *Devision of Rheumatology, Medical University of Vienna, Vienna, Austria*

Background: Rheumatoid arthritis (RA) is an inflammatory autoimmune disease, characterized by synovial infiltration of various cells. Chemokines are involved in the recruitment of different cell types into the synovial membrane. Accumulation of CCR6 expressing mononuclear cells can be found in joints of RA patients. CCR6 expression has also been reported on $CD4^+$ T cells, in particular regulatory as well as Th17 cells. In addition, a subset of regulatory T cells, namely $CD25^-Foxp3^+$ T cells, can upregulate CCR6 and RANKL and thereby can promote osteoclastogenesis.
Objectives: In this study, we investigated the role of CCR6 in the pathogenesis of arthritis using different arthritis models.
Methods: Clinical as well as histological signs of arthritis were investigated in the collagen-induced arthritis (CIA), K/BxN serum transfer arthritis and in the human tumor necrosis factor (hTNFtg) arthritis model, comparing *wt* and *CCR6-/-* mice. We analyzed the phenotype of lymph node cells by flow cytometry and cytokine concentrations in serum. Anti-collagen antibodies and cytokines were measured by enzyme-linked immunosorbent assay.
Results: The K/BxN serum transfer arthritis and hTNFtg arthritis model are known to be T cell independent. Since CCR6 is an important component of the innate immune system we compared the development of arthritis in both models. We did not detect any significant differences in clinical signs of inflammation or histological severity of arthritis between *wt* and *CCR6-/-* mice. In addition, bone volume was similar between *wt* and *CCR6-/-* mice. To investigate the role of CCR6 as part of the adaptive immune system in the development of arthritis we induced CIA in *wt* and *CCR6-/-* mice, which is known to be T cell dependent. *CCR6-/-* mice were almost completely protected from CIA. Indeed, analyses of T cell subsets by flow cytometry revealed a significant reduction of $CD25^-Foxp3^+$ T cells.
Conclusions: CCR6 is necessary for the generation of pathogenic $CD25^-Foxp3^+$ T cells in CIA, suggesting an important function of CCR6 on T cells in the development of autoimmune arthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5107

FRI0065 HELMINTHES BASED NOVEL COMPOUND, TUFTSIN-PHOSPHORYLCHOLINE (TPC) AMELIORATES ESTABLISHED MURINE ARTHRITIS

T. Bashi[1], J. Lachnish[1], M. Fridkin[2], Y. Shoenfeld[3], M. Blank[1]. *[1]Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Ramat Gan; [2]Organic Chemistry, Weizmann, Rehovot; [3]Zabludowicz Center for Autoimmune Diseases, Sheba.health.gov.il, Ramat Gan, Israel*

Background: In areas where helminthes infections are common, autoimmune diseases are rare. Treatment with helminthes or their ova, improved clinical findings of several autoimmune diseases. Based on the helminthes biological activity, a novel chimeric be-specific molecule was synthetized of tuftsin-phosphoryl-choline (PC)-TPC.
Objectives: To study TPC treatment in established collagen induced arthritis (CIA) mice, and the mechanism of activity.
Methods: Arthritis was induced in DBA male mice by immunization with collagen emulsified in TB-mycobacteria at the tail base. Boost was given 3 weeks later. Treatment with TPC started when the clinical score was 2. Cytokines were measure in culture-fluid of splenocytes in-vitro. T regulatory cells and B regulatory cells were measured by FACS. TPC effect on TLR4 expression was studied using HEKTM-mTLR4 cells system and its inhibitor. M1 shift to M2 was performed in RAW macrophages differentiated to M1 by PMA followed by LPS. TPC was added and IL-6, TNFalpha, IL-10 were tested by ELISA.
Results: Starting TPC treatment of CIA mice after disease establishment, had a significant lower arthritis score in comparison with control vehicle subjected mice (i.e. TPC-6.8±0.8 vs vehicle-13.8±0.45; $p<0.0001$). Joints staining revealed normal joint structure in TPC treated mice, whereas, control mice treated with PBS, PC or tuftsin had severe inflamed joints. Likewise, TPC enhanced anti-inflammatory response by enhanced IL-10 secretion, reduced pro-inflammatory cytokines secretion (IL-1β, IL-17, IL-6, and TNF-α) ($p<0.001$). Furthermore, TPC induced expansion of splenic CD4+CD25+FOXP3+ T regulatory cells (Tregs) and IL-10+CD5+CD1d+ B regulatory cells (Bregs). The mechanism underling the TPC related immunomodulatory activity was attributed to its bi-specific activity: a) Shift of Raw cells macrophages from pro-inflammatory macrophages M1 to anti-inflammatory M2 secreting anti- IL-10 ($p<0.001$), through the tuftsin part of TPC. b) TPC inhibited significantly TLR4 expression by HEKTM-mTLR4 cells ($p<0.02$) *via* the phosphorylcholine end. Our data indicated that TPC significantly ameliorated established CIA by anti-inflammatory immunomodulatory activity.
Conclusions: Our data may lead to a novel bi-specific self small molecule for therapy of patients with advanced RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3065

FRI0066 GASTRIN-RELEASING PEPTIDE AND ITS RECEPTOR INCREASE ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTE INVASIVENESS OVER THE PI3K/AKT PATHWAY

M. Farinon[1,2], V.S. Clarimundo[1], R.T. Pedó[1,2], V.O.N. Teixeira[1], C. Nör[3], P.S. Gulko[4], R.M. Xavier[1,2], P.G. Oliveira[1,2]. *[1]Hospital de Clínicas de Porto Alegre; [2]Universidade Federal do Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil; [3]Peter Gilgan Centre for Research and Learning, Toronto, Ontario, Canada; [4]Icahn School of Medicine at Mount Sinai, New York, United States*

Background: Rheumatoid arthritis (RA) is an autoimmune disease where the chronic inflammation and subsequent cartilage and bone erosion lead to joint destruction. The fibroblast-like synoviocytes (FLS) have a central role in disease pathogenesis and *in vitro* FLS invasiveness correlates with articular damage in RA patients. Gastrin-releasing peptide (GRP) plays an important role in the immune and inflammatory response. GRP is found in synovial fluid of RA patients and its receptor (GRPR) is found in synovial membrane of murine arthritis. RC-3095 in an antagonist of GRPR.
Objectives: To evaluate the role of GRP and GRPR on invasive behavior of mice FLS and to evaluate the GRP-induced signaling on PI3K/AKT pathway.
Methods: FLS were isolated from joints of DBA/1J mice with collagen-induced arthritis. Expression of GRPR in FLS was investigated by immunocytochemistry and western blot (WB). Proliferation of FLS treated with GRP (0.1 μM – 10 μM)

(n=3) and RC-3095 (0.05 μM – 10 μM) (n=4) was assessed by Sulforhodamine B assay in 24h, 48h and 72h. Invasion assay with FLS was performed using a Matrigel-coated transwell system over 24h in two different experimental arms: first, FLS were treated with GRP (10 μM), RC-3095 (1 μM) or GRP+RC-3095 (GRP 10 μM and RC-3095 1 μM) (n=6) and after, FLS were treated with GRP (10 μM), Ly294002 (10 μM), or GRP+Ly294002 (GRP 10 μM and Ly294002 10 μM) (n=4). Akt phosphorylation was assessed by WB.

Results: GRPR protein was detected in FLS both by immunocytochemistry and WB. GRP and RC-3095 treatments did not affect FLS proliferation. Exposure to GRP increased FLS invasion (5356±1027) by nearly two-fold compared with untreated cells (2845±532) ($p<0.02$), while the treatment with RC-3095 reduced FLS invasion (1723±271) compared with untreated cells. Treatment with GRP+RC-3095 (2670±499) reversed the invasiveness effect of GRP ($p<0.0001$). GRP also increased phosphorylated AKT expression in FLS by 30% ($p<0.001$). When Ly294002 was added with GRP (7772±1200), it prevented the GRP-induced increased cell invasiveness (11036±953.6) ($p<0.001$) (Figure 1).

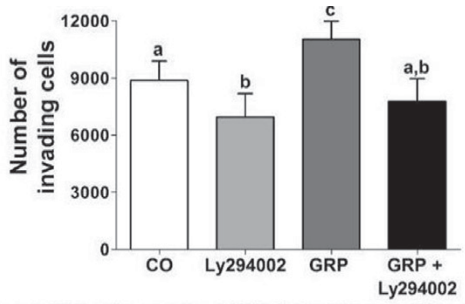


Figure 1. FLS invasion assay (n = 4). GRP significantly increased FLS invasion compared with untreated cells, whereas Ly294002 present opposite effect. Bars represent mean ± SEM. Data were analyzed by generalized estimating equation (GEE) followed by Bonferroni. a) p<0.008 versus Ly294002; p<0.026 versus GRP; b) p<0.001 versus GRP; c) p<0.001 versus GRP+Ly294002.

Conclusions: Our group demonstrated for the first time GRPR expression in FLS and that GRP are able to activate FLS invasion through AKT pathway. Finally, our results suggest that GRP/GRPR pathway could be relevant in the development of FLS-targeted therapy for RA.

References:

[1] Scott TL et al. Lancet 376;9746:1094–108.
[2] Bottini N, Firestein GS. Nat Rev Rheumatol 2013;9:24–33.
[3] Grimsholm O et al. Arthritis Res Ther 2005;7:R416–26.
[4] Oliveira PG et al. Arthritis Rheum 2011;63:2956–2965.

Acknowledgements: FIPE-HCPA, CAPES, CNPq.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2484

FRI0067 MICRORNA PROFILING OF MTX-TREATED FIBROBLAST-LIKE SYNOVIAL CELLS IN RHEUMATOID ARTHRITIS REVEALED A POSSIBILITY OF MICRORNA-887-3P AS NOVEL THERAPEUTIC TARGET OF RA

N. Iwamoto, S. Fukui, T. Koga, S.-Y. Kawashiri, K. Ichinose, M. Tamai, H. Nakamura, T. Origuchu, A. Kawakami. *Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Nagasaki, Japan*

Background: The hallmarks of rheumatoid arthritis (RA) is the expansive of fibroblast-like synovial cells (FLS) in affected joints, causing joint destruction. FLSs are resistant to programmed cell death resulting in aggressive, invasive phenotype like a cancer invades and the hyperplastic synovial tissue destroys cartilage and bone. Therefore inhibition of FLS proliferation and is one of the therapeutic targets of RA. MicroRNAs (miRNAs), a group of small non-coding RNAs, have been shown to regulate cell differentiation through regulation of gene expression post-transcriptionally. Recently, several studies reported anti-cancer drugs modulate miRNA expression and that have been considered as one of important mechanism of cellular action to drug[1,2].

Objectives: To investigate the changes in microRNA expression profiles in response to MTX.

Methods: RA-FLS was treated with MTX with 1nM 48 hours, that could inhibit IL-6 production from RA-FLS. To investigate differentially expressed miRNAs in response to MTX, we performed miRNA array analysis. Expression of miR-887–3p in response to MTX of RA-FLS was analyzed by quantitative real-time PCR. To investigate the functional role of miR-887–3p, RA-FLS was transfected with synthetic precursor miRNA (pre-miR)/inhibitors of miRNA (anti-miR) of miR-887–3p using Lipofectamine and then gene expression microarray was performed. The cytokine/ chemokine production was screened by Multiplex cytokine/chemokine bead assays and confirmed by ELISA. Finally, we analysed migratory activities of RA-FLS by scratch assay.

Results: After 48 h of treatment with MTX, 7 miRNAs were up-regulated and 6 miRNAs were down-regulated as compared with that of untreated control. Among them quantitative real-time PCR with additional samples confirmed that miR-887–3p was up-regulated in response to MTX treatment of RA-FLS (1.79±0.46 -fold, $p<0.05$, n=7). To elucidate the functional consequence of the deregulation of miR-887–3p of RA-FLS, we performed gain-and-loss of function assays with miR-887–3p. Microarray analysis with gene ontology analysis revealed several genes correlated with cell signalling was modulated by miR-887–3p. Multiplex bead assay showed that overexpression of miR-887–3p decreased cytokine/chemokine production of RA-FLS such as TNF-a, GM-CSF, CCL4. Among these candidates, the secretion of GM-CSF was consistently and strongly decreased from RA-FLS transfected with pre-miR-887–3p. Furthermore overexpression of miR-887–3p reduced migratory activity of RA-FLS in scratch assay.

Conclusions: Our result showed that MTX altered micro RNA expression profiles in RA-FLS. MiR-887–3p might be downstream effector of MTX in suppression of its cytokine production and invasive phenotype. This knowledge may also be useful for the development of novel therapeutic strategies for RA based on other treatments able to boost the cellular reservoir of miR-877–3p.

References:

[1] Potenza N, Mosca N, Zappavigna S et al. MicroRNA-125a-5p Is a Downstream Effector of Sorafenib in its Antiproliferative Activity Toward Human Hepatocellular Carcinoma Cells. J Cell Physiol. 2016 Dec 16.
[2] Shah MY, Pan X, Fix LN et al. 5-Fluorouracil drug alters the microRNA expression profiles in MCF-7 breast cancer cells. J Cell Physiol. 2011; 226(7):1868–1878.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3327

FRI0068 REDUCTION OF PROLIFERATION, MIGRATION AND INVASION OF RHEUMATOID SYNOVIOCYTES BY ALL-TRANS RETINOIC ACID

N. Mosquera[1], Á. Rodríguez-Trillo[1], S.B. Bravo[2], A. Mera[1], C. Conde[1]. *[1]Experimental and Observational Rheumatology; [2]Proteomic Unit, IDIS, CHUS, Santiago de Compostela, Spain*

Background: Fibroblast-like synoviocytes (FLS) are pivotal in inflammation and joint damage of rheumatoid arthritis (RA). These cells proliferate, become resistant to apoptosis, migrate and invade, contributing to perpetuate synovial inflammation and destruction of cartilage and bone. Current treatments of RA are focused against inflammatory factors and immune cells, however, a significant percentage of patients do not successfully respond. Combined treatments with drugs that control inflammation and with others that reverse the pathogenic phenotype of FLS could improve the prognosis of these patients. An unexplored area includes vitamin A and its metabolites. These compounds modulate differentiation, development, apoptosis and proliferation. Indeed, retinoids are being successfully used in the treatment of several cancers for their anti-proliferative and pro-differentiative actions. In addition, several studies have shown a notable reduction of cell migration and invasion in different cell types after treatment with all-trans retinoic acid (ATRA). However, it is not known if ATRA could modify the migratory and invasive ability of rheumatoid synoviocytes.

Objectives: To analyse the effect of treatment with the retinoid all-trans retinoic acid in proliferation, migration and invasion of rheumatoid synoviocytes.

Methods: FLS were obtained from 8 RA patients. Cellular proliferation was determined using the CellTiter-Glo luminescent viability assay (Promega). Migration was analysed by wound healing assay, using Ibidi inserts. Percentage of migrating cells was determined by Image J. Invasion was tested by the Boyden chamber method using inserts (Millicell) coated with Matrigel (BD Biosciences). Invasion was determined by quantification of Giemsa stained cells on the bottom side of the inserts under the microscope. Proteomic analysis was performed using LC-MALDI-TOF/TOF and 1-DE and 2-DE gels. MS and MS/MS data was searched against the UniProt/Swiss-Prot database of protein sequences.

Results: We analysed the effect of ATRA in the spontaneous proliferation of FLS from 8 RA patients. ATRA treatment significantly reduced proliferation at 48, 72 and 96 h (p=0,005; p=0,002; p=0,04; respectively). Next, we analysed the effect of ATRA on RA FLS migration and invasion. Migration of RA FLS treated with ATRA for 96 h was reduced by 46% when compared with cells treated with vehicle control (p=0,002). In addition, RA FLS invasion was also impaired after ATRA treatment, as the invaded area was 31% lower than in controls (p=0,018). To elucidate the mechanisms underlying the effects of ATRA on RA FLS a proteomic analysis was performed. We compared the proteome of FLS from 5 RA patients treated with ATRA or with vehicle using LC-MALDI analysis. The differentially identified proteins in ATRA-treated FLS *vs* control FLS were Septin, Rho GTPase activating protein (ARHGAP1) and actin related protein 2 (ARP2). Validation experiments using 1-DE and 2-DE gels were performed.

Conclusions: Overall these results reveal that retinoid treatment reduces the proliferative, migratory and invasive capacity of RA FLS, indicating that this treatment could decrease joint damage and loss of function in RA patients.

Acknowledgements: Supported by grant PI14/01153 of the ISCIII (Spain), partially financed by FEDER.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3139

FRI0069 **NEUTROPHILS PLAY A KEY ROLE IN THE REGULATION OF THE CHRONIC INFLAMMATION ASSOCIATED WITH RHEUMATOID ARTHRITIS THROUGH EPIGENETIC MECHANISMS MODULATED BY ANTI-CCPS ANTIBODIES AND REVERSED BY BIOLOGIC THERAPIES**

P. Ruiz-Limon, I. Arias de la Rosa, M.C. Abalos, C. Perez-Sanchez, Y. Jimenez-Gomez, M. Caracuel, J. Calvo, R. Ortega, M. Castro, E. Collantes, A. Escudero, C. Lopez-Pedrera, N. Barbarroja. *Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain*

Background: MicroRNAs (miRNA) are as a new class of modulators of gene expression, regulating inflammation, degradation of extracellular matrix and invasive behavior of the resident cells in rheumatoid arthritis (RA).
Objectives: 1) To investigate the miRNA expression profile in synovial and blood neutrophils in RA and its role in the pathogenesis of this disorder. 2) To study the effects of biological therapies on the miRNA profile in neutrophils.
Methods: Neutrophils were isolated from peripheral blood (PB) of 25 healthy donors (HD) and 25 RA patients. Neutrophils were isolated from paired synovial fluid (SF) of 15 RA patients. nCounter microRNA Assay was used to detect 800 human microRNAs simultaneously. Altered miRNAs were analyzed for potential mRNA targets using Ingenuity pathways analysis (IPA) software. mRNA targets and genes involved in miRNA biogenesis were evaluated. RA neutrophils were treated in vitro with tocilizumab and infliximab.Healthy neutrophils were treated in vitro with anti-CCPs isolated from RA patients alone or combined with tocilizumab or infliximab. RA neutrophils were cotransfected with the pre-miRNAs 126 and 148.
Results: 94 miRNAs were downregulated and 3 upregulated in PB neutrophils from RA patients compared to HD.Among the miRNAs deregulated in blood, 34 miRNAs were even more significantly reduced in SF neutrophils. Accordingly, RA neutrophils showed a downregulation of the proteins participating in miRNA biogenesis and upregulation of its mRNA targets. Altered miRNAs were mainly involved in immunological disease and inflammatory response, suggesting the abnormal activation of this cell subtype in RA. In vitro treatment of RA neutrophils with infliximab reversed the expression of miRNAs, genes involved in their biogenesis and reduced the inflammatory profile in these cells.In addition, treatment of healthy neutrophils with IgGs anti-CCPs isolated from RA patients decreased the expression of the miRNAs, proteins involved in the biogenesis machinery and increase its inflammatory targets. Finally, cotransfection of RA neutrophils with the pre-miRNAs 126 and 148 reduced the levels of their target proteins.
Conclusions: 1)RA neutrophils exhibit a defect in the miRNAs processing, showed by a decrease in most of the detected miRNAs and the downregulationof proteins involved in their biogenesis. This defect seems to be modulatedby anti-CCPs antibodies.2)miRNA downregulation is even more pronounced in synovial fluid neutrophils, which may contribute to the high inflammatory profile of these cells in the joint. 3) Infliximab reverses the altered miRNA profile and the defect in the biogenesis machinery, reducing the proinflammatory pattern in these cells. 4)miRNAs 126 and 148 regulate the expression of numerous inflammatory proteins in RA neutrophils.In sum, this study shows that the neutrophils play a key role in the regulation of the chronic inflammation link to RA. The effect, associated to epigenetic mechanisms, seems to be mediated by the anti-CCPs and is reversed by biologic therapies.
Acknowledgements: Funded by CTS7940, PI2013–0191, ISCIII (CP15/00158, PI15/001333), RD16/0012/0015
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4689

FRI0070 **ANGIOTENSIN II TYPE 2 RECEPTOR (AT2R) IS OVEREXPRESSED IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS SYNOVIUM AND INCREASES STEADILY WITH INFLAMMATORY STIMULI: A POTENTIAL NEW TARGET FOR PAIN AND ANTI-INFLAMMATORY THERAPIES**

R. Terenzi[1], M. Manetti[2], I. Rosa[2], E. Romano[1], F. Galluccio[1], S. Guiducci[1], L. Ibba-Manneschi[2], M. Matucci-Cerinic[1]. *[1]Department of Medicine, Division of Rheumatology; [2]Department of Anatomy, Università degli Studi di Firenze, Firenze, Italy*

Background: Despite increasing evidence suggesting that angiotensin II type 2 receptor (AT2R) antagonism might be a feasible strategy for the treatment of chronic inflammation and pain, no study has yet analyzed the synovial expression of AT2R.
Objectives: To investigate the expression of AT2R in rheumatoid arthritis (RA) and osteoarthritis (OA) synovium and its possible modulation in fibroblast-like synoviocytes (FLS) by proinflammatory stimuli.
Methods: The expression of AT2R in RA and OA synovium was investigated by immunohistochemistry. AT2R expression in synovial T cells, B cells, macrophages and FLS was assessed by double immunofluorescence. FLS were isolated from healthy (H), OA and RA synovium and treated with tumor necrosis factor (TNF)-α and interleukin (IL)-1β, alone or in combination. Immunocytochemistry and Western blotting were performed to study AT2R expression in cultured FLS.
Results: RA synovium showed stronger AT2R immunostaining than OA synovium in the lining and sublining layers. In RA synovium, AT2R was strongly expressed in CD3+ T cells, CD20+ B cells, CD68+ macrophages and vimentin+ FLS. High levels of AT2R were found in OA-FLS and RA-FLS at baseline, while AT2R expression was negligible in basal H-FLS. AT2R expression was higher in RA-FLS than OA-FLS. Treatment with TNF-α and IL-1β was able to foster the expression of AT2R not only in OA-FLS and RA-FLS, but also in H-FLS.
Conclusions: AT2R is strongly expressed in different cell types of the inflamed synovium and proinflammatory stimuli may foster the expression of AT2R in FLS. AT2R might represent a novel potential therapeutic target in chronic arthritides.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1338

FRI0071 **TOFACITINIB RESTORES THE INHIBITION OF REVERSE CHOLESTEROL TRANSPORT INDUCED BY INFLAMMATION: UNDERSTANDING THE LIPID PARADOX ASSOCIATED WITH RHEUMATOID ARTHRITIS**

S. Pérez Baos, J.I. Barrasa, P. Gratal, A. Larrañaga-Vera, I. Prieto-Potin, G. Herrero-Beaumont, R. Largo. *Bone and Joint Research Unit, Rheumatology Dept., IIS-Fundación Jiménez Díaz UAM, Madrid, Spain*

Background: Patients with active rheumatoid arthritis (RA) have increased cardiovascular mortality, paradoxically associated with reduced serum lipid levels. In fact, an inverse relationship between C-reactive protein (CRP) and circulating lipid levels has been observed [1,2]. The Jak inhibitor tofacitinib ameliorates systemic and joint inflammation in RA with a concomitant increase in serum lipids [3].
Objectives: Our aim was to analyze the effect of tofacitinib on the lipid and inflammatory profile of hyperlipidemic rabbits with chronic arthritis (CA), and on the regulation of reverse cholesterol transport (RCT) during chronic inflammation.
Methods: New Zealand male rabbits were randomly assigned to three groups: control group (*n*=6), chronic arthritic rabbits (CA, *n*=9) and CA rabbits receiving tofacitinib (CA+TOFA, *n*=9). All animals were fed *ad libitum* with a high-fat diet (0.5% cholesterol, 4% peanut oil). CA was induced in previously immunized rabbits by administering four intra-articular injections of ovalbumin. A group of rabbits received tofacitinib (10mg/kg/day) for two weeks. All animals were euthanized 6 weeks after challenge, when synovial and serum samples were collected. For *in vitro* studies, vehicle and ABCA1 siRNA-treated THP-1-derived macrophages were exposed to high lipid concentrations, and then stimulated with interferon gamma (IFNγ) in the presence or absence of tofacitinib, in order to assess their cholesterol efflux capacity and the involved mediators.
Results: CA rabbits showed lower levels of serum TC and LDL-C compared to controls (p=0.001, p=0.012), while TC/HDL-C ratio was higher in CA+TOFA rabbits when compared to CA animals (150±15 vs 231±17, p=0.004). Synovial inflammation and CRP levels were increased in CA animals, and a significant reduction was shown in CA+TOFA rabbits in both parameters. We also observed an inverse correlation between serum TC and CRP (R=-0.454, p=0.029). Tofacitinib was able to reduce the lipid content within synovial macrophages up to a 58% (p=0.041), although it did not modify synovial macrophage density. In foam macrophages in culture, an inflammatory milieu induced by IFNγ further stimulated the intracellular lipid accumulation (p=0.041) along with a decrease in the protein levels of the nuclear factor LXRα (liver X receptor α) and the cholesterol transporter ABCA1 (ATP-binding cassette transporter 1) (p=0.002 and p=0.0047, respectively). Tofacitinib prevented the lipid accumulation within macrophages (p=0.029) by increasing LXRα (p=0.047) and ABCA1 synthesis (p=0.004) in a Jak/STAT-dependent manner, while it was unable to reduce lipid accumulation in ABCA1 silenced macrophages.
Conclusions: Our results suggest that active inflammation could be associated with lipid accumulation within macrophages – in the synovium and probably in other tissues – thus inducing a decrease in serum lipid levels. Tofacitinib may prevent this phenomenon, at least partially, by increasing RCT pathways in macrophages. Taken together, these findings further explain how serum lipid levels are diminished in RA and partially justify the effect of tofacitinib on the lipid profile in RA patients.
References:
[1] Choy E, Sattar N. Ann Rheum Dis 2009;68:460–9.
[2] Johnsson H et al. Ann Rheum Dis 2013;73:1495–9.
[3] van Vollenhoven RF et al. N Engl J Med 2012;367:508–19.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2693

FRI0072 **ALTERATION OF THE INTESTINAL MICROBIOME IN THE PRECLINICAL PHASE OF EXPERIMENTAL ARTHRITIS AND THE EFFICACY OF MICROBIOTA MODULATION IN ESTABLISHED ARTHRITIS IN MICE**

R. Rogier[1], H. Evans-Marin[2], P. van der Kraan[1], W. van den Berg[1], M. Koenders[1], J. Scher[2], S. Abdollahi-Roodsaz[1,2]. *[1]Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands; [2]Medicine, New York University School of Medicine, New York, United States*

Background: The composition of intestinal microbiota is perturbed in patients with new-onset rheumatoid arthritis (RA) and those with chronic RA. However, it is not known whether the changes in the intestinal microbiome precede

the development of arthritis or are rather a consequence of the inflammatory processes. Furthermore, while both germ-free condition and administration of oral antibiotics prevent arthritis in mice, it is unclear whether modulation of the intestinal microbiota after the onset of arthritis may still suppress the disease.
Objectives: We aimed to assess potential alterations of the intestinal microbiome in the preclinical phase of inflammatory arthritis, and to determine the efficacy of microbiota modulations in the treatment of established disease in mice.
Methods: We sequenced fecal bacterial 16S rRNA to define the intestinal microbiome in mice before immunization with collagen and 21 days later before the booster injection for the induction of collagen-induced arthritis (CIA). To assess the efficacy of microbiota modulation during arthritis, mice with ongoing CIA were treated orally by a broad-spectrum antibiotic cocktail for one week to partially eliminate the intestinal microbiota. T cell differentiation and production of cytokines in intestinal lamina propria and joint-draining lymph nodes were assessed by flow cytometry and Luminex. Arthritis was assessed macroscopically and by histology. Serum-transfer arthritis induced by intraperitoneal injections of arthritogenic K/BxN mouse serum was used as a control, T cell-independent, model.
Results: The preclinical phase of inflammatory arthritis in mice was characterized by marked changes in the intestinal microbiome, represented by a significant increase of the phylum *Bacteroidetes* and a decrease of *Firmicutes* and *Proteobacteria*. Among the most abundant bacterial families, S24–7 and *Staphylococcaceae* were expanded, whereas *Lachnospiraceae* were reduced during the immune priming phase of CIA. Several operational taxonomic units associated with S24–7 family increased, while those assigned to *Lachnospiraceae* and *Ruminococcaceae* decreased in the intestinal microbiota before the clinical onset of arthritis. The abundance of intestinal lamina propria Th17 cells significantly correlated with the severity of CIA; however, intestinal Th1 cells were not correlated with the disease. Elimination of intestinal microbiota in mice with ongoing CIA specifically suppressed intestinal Th17 cell differentiation without affecting Th1 and Treg cells. Importantly, elimination of intestinal microbiota suppressed Th17 cell differentiation and IL-17 production in joint-draining lymph nodes, and reduced the severity of established CIA. In contrast, the T cell-independent serum-transfer arthritis was not affected by this strategy.
Conclusions: These observations suggest that perturbations of the intestinal microbiome may precede the development of inflammatory arthritis. Similar studies are warranted in human pre-RA or at-risk individuals to shed light on the functional role of the microbiome in the development of RA. Our studies also suggest that modulation of the intestinal microbiota after the onset arthritis may still provide opportunities to treat inflammatory arthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5533

FRI0073 RAGE ACTIVITY INFLUENCES CO-DEVELOPMENT OF JOINT AND VASCULAR DISEASE IN RA

S. Yu[1], L.-S. Tam[2]. *[1]Rheumatology, The Second Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; [2]Rheumatology, Medicine & Therapeutics, Hong Kong, Hong Kong*

Background: RAGE is expressed by many cells in blood and joints of RA and interacts with a variety of pro-inflammatory ligands, especially HMGB1 that are enriched in inflamed joint. The RAGE-ligand interaction leads to a sustained inflammatory response. Soluble RAGE (sRAGE) lacks the transmembrane and cytoplasmic domain of the cell surface full-length RAGE (flRAGE) and function as a decoy for RAGE ligand. Relatively little is known about factors that regulate sRAGE levels in human subjects and whether circulating levels reflect tissue RAGE expression and activity is unclear. The relationship between the up-regulation of flRAGE/HMGB1 and the level of "protective" sRAGE levels in RA is of obvious clinical interest.
Objectives: To elucidate the balance between the expression of flRAGE on peripheral blood monocyte and dendritic cell (DC), and the plasma concentration of sRAGE and HMGB1 in patients with active RA compare to controls; To ascertain whether flRAGE expression profiles, plasma sRAGE and HMGB1 level correlated with disease activity or inflammatory markers in RA patients.
Methods: 40 consecutive patients attending the rheumatology clinic at Prince of Wales Hospital, who fulfilled the 2010 ACR/RULAR classification criteria with active RA (28 joint disease activity score 28–4 [CRP] (DAS28)$>$3.2) and 40 age- and sex-matched healthy volunteers were recruited for this cross-sectional study. The expression profile of cellular transmembrane RAGE on peripheral blood monocyte ($ILT3^+CD123^-$), total DC ($ILT3^+CD14^-CD16^-$), myeloid DC ($ILT3^+CD14^-CD16^-CD123^-$) and plasmacytoid DC ($ILT3^+CD14^-CD16^-CD123^+$), plasma levels of HMGB1 and soluble RAGE in all RA patients and healthy controls were measured at baseline using flow cytometry and ELISA. In RA patients, associations with disease activity and severity variables were analyzed by simple and multiple linear regressions.
Results: Protein expression of flRAGE on peripheral blood monocytes ($ILT3^+CD123^-$), total DCs ($ILT3^+CD14^-CD16^-$) and myeloid DCs ($ILT3^+CD14^-CD16^-CD123^-$) were significant increased in RA patients with active disese compared with control subjects (all $p<0.01$) (no enough cells for flRAGE detection on plasmacytoid $ILT3^+CD14^-CD16^-CD123^+$ DCs). Also, the flRAGE was more common in patients with cardiac affection. There was no statistically significant difference of the plasma level of HMGB1 from active RA patients as compared healthy controls ($p>0.05$). The plasma sRAGE level was significantly lower in patients compared to healthy controls ($p<0.001$), which correlated negatively with serum levels of CRP, ESR, DAS28 and high-density lipoprotein (HDL) (all $p<0.05$). Linear regrssion analysis detected CRP as significant predictors for sRAGE level.
Conclusions: Autoimmunity-mediated inflammation might induce aberrant expression and activation of flRAGE while decreasing the plasma level of sRAGE in RA patients, subsequently leading to the augmented inflammatory response. Moreover, membrance flRAGE and sRAGE were associated not just with RA inflammation and autoantibody protein, but also with classical vascular risk factors for end-organ damage. These data suggest that RAGE activity influences co-development of joint and vascular disease in RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1701

FRI0074 ANTI-INFLAMMATORY EFFECT OF RESVERATROL IN VITRO; POTENTIAL ROLE IN MANAGING LOW DISEASE ACTIVITY IN ARTHRITIS?

S. Lomholt[1], A. Mellemkjaer[2], M.B. Iversen[2], S.B. Pedersen[3], T.W. Kragstrup[4]. *[1]Aarhus University, Aarhus C, Denmark; [2]Department of Biomedicine, Aarhus University; [3]Department of Endocrinology and Internal Medicine; [4]Department of Rheumatology, Aarhus University Hospital, Aarhus C, Denmark*

Background: Resveratrol (RSV), a non-toxic polyphenol found in grapes, certain nuts, roots etc., have received increased attention in the last decade due to its anti-inflammatory modulation of a number of pathways, including cyclooxygenase-1/-2, nuclear factor kappa-beta and cytokine production. In vitro, RSV has been shown to reduce production of interleukin 1-beta and tumor necrosis factor alpha in monocytes and inhibit T-cell activation and synoviocyte proliferation. In vivo, intra-articular injections of RSV have demonstrated anti-inflammatory and pannus inhibiting effects in rats with induced arthritis.
Objectives: Here, we tested whether the anti-inflammatory effect of RSV in arthritis patients depends on the degree of systemic inflammation and the cellular composition of extracted synovial fluid. Furthermore, we evaluated the anti-inflammatory effect of RSV in combination with methotrexate (MTX) and adalimumab.
Methods: Synovial fluid mononuclear cells (SFMCs) from patient with rheumatoid arthritis (n=7) and spondyloarthritis (n=7) were cultured in monoculture for 48 hours (in vivo activated lymphocytes and monocytes) or 21 days (spontaneous generation of osteoclasts). Cultures were either left untreated or treated with RSV (25 μM), methotrexate (0.5 μg/ml), adalimumab (5 μ g/ml) or in combination. Supernatants were analysed for the production of monocyte chemoattractant protein-1 (MCP-1) and matrix metalloproteinase 3 (MMP3). Osteoclast differentiation was analysed with a tartrate resistant acidic phosphatase (TRAP) enzymatic assay.
Results: In the SFMC cultures, RSV reduced MCP-1 production by 25% compared with untreated cells (P=0.032). When grouping results by c-reactive protein (CRP), i.e. $<$ median vs. $\geq$ median, the inhibitory effect of RSV was primarily seen in cultures from patients with CRP $<$21 mg/l. In this group, RSV reduced MCP-1 production by 63%. Combining MTX and RSV reduced MCP-1 production compared to MTX alone, but only in the group of patients with CRP $<$21 mg/l (P=0.002). Combining adalimumab and RSV seemed to reduce MCP-1 in the group of patients with CRP $<$21 mg/l, but increase production in patients with CRP $\geq$21 mg/l (P=0.03). Similar grouping based on lymphocyte count showed RSV, MTX and adalimumab, alone or in combination, all reduced MCP-1 significantly compared to untreated cells in cultures from patients with $\geq$62% lymphocytes in the synovial fluid. RSV, MTX and adalimumab did not affect MMP3 production in the SFMC cultures. In the osteoclast cultures, RSV alone did not affect MCP-1 or TRAP. However, the combination of RSV and MTX reduced MCP-1 compared to no treatment (P=0.004). Adalimumab alone or combined with RSV reduced TRAP compared with untreated cultures ($P<0.027$).
Conclusions: RSV exhibits an anti-inflammatory effect on SFMCs. Interestingly; our data suggest that this effect is most pronounced in patients with relatively low CRP. Further, RSV produces an additive anti-inflammatory response in combination with MTX in the group of patients with low CRP and a synovial fluid dominated by lymphocytes. Together, this suggests that RSV may possess an additive potential when added to MTX treatment of arthritis patients with low disease activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2635

FRI0075 RHEUMATOID ARTHRITIS PATIENTS RECEIVING GLUCOCORTICOID EXHIBITS SIGNIFICANT BONE QUALITY ABNORMALITIES, LEADING TO SEVERE BONE FRAGILITY REGARDLESS OF BISPHOSPHONATE TREATMENT

T. Shimizu[1,2], M. Takahata[1], H. Hamano[1], M. Ota[1], S. Hiratsuka[1], N. Iwasaki[1]. *[1]Department of Orthopeadic Surgery, Hokkaido University School of Medicine, Sapporo, Japan; [2]Department of Radiology & Biomedical Imaging, Musculoskeletal Quantitative Imaging Research, University of California San Francisco, San Francisco, United States*

Background: Patients with rheumatoid arthritis (RA) receiving glucocorticoids

develop particularly severe bone fragility accompanied with high risk factors for fragility fractures[1,2]. Although bisphosphonate is recommended for treatment of osteoporosis related RA and glucocorticoid-induced-osteoporosis[3], there are more frequently fractures than expected from bone mineral density based prediction even after used bisphosphonate.

Objectives: To clarify the pathological mechanisms of bone fragility of these RA patients, we investigated bone biopsy samples obtained from RA and normal postmenopausal patients.

Methods: We examined 10 female postmenopausal RA patients receiving glucocorticoid and bisphosphonate therapy (RA group) and 10 age-matched female patients with postmenopausal osteoporosis (Ctl group) selected from patients who required autologous iliac bone grafts. Analyses of clinical data, bone mineral density, serum metabolic markers, bone quality and material mechanical property of biopsy sample were performed.

Results: Although bone mineral density didn't show significant differences, RA group had significantly higher score of fracture risk assessment tool (FRAX), number and severity of existing vertebral fractures.

	Control	RA	p
FRAX score (%)			
Major osteoporosis fx.	10.7±4.8	33.4±8.0	<0.001
Femoral neck fx.	2.8±2.4	9.9±6.1	0.002
Clinical fragility fx.			
Number	4	16	
Severity (# x grade)	4	29	
Mechanical strength (N/mm)	218.8±24.6	164.9±36.5	0.001

RA group exhibited significant bone quality abnormalities including deterioration of the bone microstructure, decreased calcification of the bone matrix, increased osteocyte atrophy and empty lacunae (Figure), and an impairment bone material strength properties.

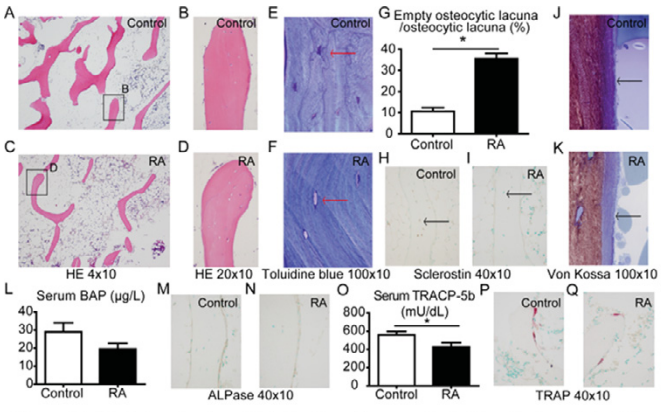


Figure: Histological mechanism of deterioration of bone quality in RA patients receiving GCs. (A-D) Representative photomicrographs of HE stained sections of the specimen. Images show sections from Control (A, C) and RA groups (B, D). Boxed areas in B and D are shown at higher magnification in the indicated images. (E, F) Representative micrographs focused on osteocytes of Control (E) and RA groups (F) with toluidine blue staining. Osteocytic lacunas (red arrows) are out of shape and emptiness in RA patients. (G) Comparison of ratio of empty osteocytic lacuna is shown. (H, I) Representative micrographs of Control (H) and RA groups (I) with immunostaining of sclerostin (black arrow). (J, K) Representative micrographs of Control (J) and RA group (K) with von Kossa staining. Black arrows show the cement lines. (L) Comparison of serum BAP is shown. (M, N) Representative micrographs of Control (M) and RA groups (N) with immunostaining of sclerostin ALP ase. (O) Comparison of serum TRACP-5b is shown. (P, Q) Representative micrographs of Control (P) and RA group (Q) with TRAP staining. Osteoclasts are stained red. Values shown are means ± SD (* p<0.05).

Conclusions: Our findings showed that RA patients receiving glucocorticoid treatment have severe bone fragility regardless of increased bone quantity by using bisphosphonate. The functional deteriorations of the osteocyte system and the abnormalities of bone quality might induce bone fragility fracture. Therefore, management of osteoporosis associated with RA should be targeted about bone quality as well as bone quantity.

References:

[1] Kanis JA et al. J Bone Miner Res 2004.
[2] Takaha M et al. Arthritis Rheum 2012.
[3] Grossman, J.M. et al. Arthritis Care Res 2010.

Acknowledgements: This project was supported in part by a Grant-in-Aid for Scientific Research (C) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan 25462357 (M. Takahata).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3514

FRI0076 LACTATE/SLC5A12-INDUCED METABOLIC SIGNALLING NETWORK: A NEW TARGET IN RHEUMATOID ARTHRITIS

V. Pucino[1,2], J. Smith[1], D. Cucchi[1], K. Blighe[3], M. Bombardieri[2], C. Pitzalis[2], C. Mauro[1]. *[1]Centre of Biochemical Pharmacology; [2]Centre for Experimental Medicine and Rheumatology, William Harvey Research Institute, Barts and The London SMD, Queen Mary University of London, London, United Kingdom; [3]Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, United States*

Background: RA is a systemic-autoimmune-disease characterized by chronic inflammation of the synovial-joints. Up to 30–40% of patients do not respond to treatment and current biomarkers are largely insensitive at predicting disease progression and response to treatment. It is well recognised that RA-synovitis is a heterogeneous pathology with different histological phenotypes i.e. lymphoid-(L), myeloid-(M) and fibroid-(F). As a result of inflammation the RA synovial microenvironment is hypoxic and acidic partly due to the accumulation of lactate, the end product of anaerobic glycolysis. Exposure of $CD4^+$ T cells to lactate inhibits their migratory capabilities and induces their shift toward a Th17 phenotype[1,2]. These effects are mediated via the interaction of lactate with its transporter SLC5A12, which is expressed on the $CD4^+$ T cell surface[1,2].

Objectives: To characterize whether the newly identified lactate/SLC5A12-induced metabolic signalling pathway can be harnessed in the stratification of RA patients in the different histological phenotypes and to modulate inflammatory responses *in vitro* and *in vivo*.

Methods: RA peripheral blood cells, RA synovial tissues (ST, 21 lymphoid and 8 myeloid) and mononuclear cells from tonsil of patients undergoing tonsillectomy were included in the analysis. RNA sequencing of RA-ST was performed and data analysed for the expression of metabolic genes. SLC5A12 expression and IL17 production was performed by flow-cytometry. Cytokines and transcription factors mRNA relative expression was evaluated by RT-PCR. Seahorse and western blot analysis was performed for the evaluation of metabolic pathways. Transwell plates were used for migration assays. Human-glucose-6-phosphate-isomerase (hG6PI) induced arthritis model was used to evaluate the impact of anti-SLC5A12 on the clinical and histological score.

Results: We showed that: i) the expression of SLC5A12 is up-regulated by $CD4^+$ T cells upon inflammation; ii) SLC5A12 is up-regulated in anti-CD3 stimulated RA $CD4^+$ T cells cultured in autologous synovial fluid; iii) the lactate/SLC5A12 induced metabolic pathway is differentially activated in RA patients with distinctive synovial "pathotypes"; iv) SLC5A12 antibody reduces lactate-induced pro-inflammatory cytokines, limits Th17 and follicular helper T cell differentiation, reverses lactate impaired $CD4^+$ T cell migration and restores lactate-mediated inhibition of glycolysis *in vitro*; v) antibody-mediated blockade of SLC5A12 ameliorates the clinical course in human-glucose-6-phosphate-isomerase (hG6PI)-induced arthritis.

Conclusions: Targeting lactate/SLC5A12-induced metabolic signalling pathway may provide a novel therapeutic strategy to reduce inflammation in RA patients.

References:

[1] Haas R. et al. PLoS Biology 2015.
[2] Pucino V. et al. Eur J Immunol 2017.

Acknowledgements: This work is supported by a fellowship from the Arthritis Research UK (ARUK) to V.P. by a fellowship from the British Heart Foundation, a project grant from the CARIPLO Foundation, a Proof of Concept award from Queen Mary Inno-vation, Ltd., to C.M. and MRC ARUK founded project "The Pathobiology of Early Arthritis Cohort (PEAC)" to C.P.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3993

FRI0077 GUT COMMENSALS MODULATE INFLAMMATION VIA T REGULATORY CELLS

V. Taneja. *Mayo Clinic, Rochester, United States*

Background: Role of environmental factors in predisposition to develop rheumatoid arthritis (RA) have gained interest due, in part, to the studies showing an association of gut microbiota with immune homeostasis. Although the etiology of RA is unknown, recent studies on the role of gut microbiota in inflammatory adaptive immune response have led to the concept that interaction between the host microbiome and genetic factors influences autoimmunity. We have recently shown an association of Collinsella aerofaciens with RA

Objectives: In this study, we aimed to determine how human gut commensals modulate arthritis phenotype in humanized mice expressing RA-susceptible HLA-DQ8.

Methods: DQ8 mice following immunization with type II collagen develop arthritis and antigen-specific cellular and humoral response. DQ8 mice orally gavaged with RA-associated Collinsella aerofaciens and non-associated Prevotella histicola on alternate days for one week and were induced for arthritis. Gavage with microbes continued for 4 weeks. Mice were monitored for onset and progression of arthritis. Th17 regulatory network and cells involved in regulation were analyzed. DQ8 mice were gavaged with fecal homogenates supernatants from arthritis-resistant mice, induced for arthritis and monitored for disease.

Results: Mice gavaged with C. aerofaciens enhanced disease severity while P. histicola protected mice from arthritis. While treatment with *P. histicola* reduced intestinal permeability by increasing expression of tight junction proteins, C.

aerofaciens had a complete opposite effect. Suppression of arthritis by P histicola was dependent on an increase in the numbers of CD103+ dendritic cells, myeloid suppressors, CD11b+Gr-1, and T regulatory cells, CD4+CD25+FoxP3+, in the gut as well as systemically. This led to reduction in TH17 response while increasing IL-10. On the other hand, C. aerofaciens gavage increased expression of IL-17 and regulatory chemokines as compared to controls. DQ8 mice gavaged with intestinal microbes of arthritis-resistant mice developed arthritis with lower incidence and had skewed Th17/Th2 response.

Conclusions: Our studies suggest that gut commensals influence immune response in and away from the gut. Commensals and their products may provide novel targets for therapeutic strategies in arthritis.

Acknowledgements: Funds were provided by the Department of Defense and Mayo Center of Individualized Medicine

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2307

FRI0078 ADENOSINMONOFOSFAT-AKTIVACTIVATING PROTEIN KINASE (AMFK) – THE BIOPOWER REGULATOR OF AN AUTOPHAGY IN RHEUMATOID ARTHRITIS (PA)

V.I. Shihkin, G.V. Kudriavtseva, V.V. Shishkin, Y.A. Malenkov. *Saint Petersburg state University, Saint Petersburg, Russian Federation*

Background: Rheumatoid arthritis is an autoimmune disease characterized by altered cellular homeostasis. A great role of an autophagy is expected in the pathogenesis of these changes.

Objectives: To assess the functional activity of AMFK as a strategic biopower regulator of an autophagy and specific indicator of red-ox potential of cells in the sinovial fluid (SF) of patients with rheumatoid arthritis (RA).

Methods: SF of knee joints of 7 RA patients with active synovitis and 5 donors were investigated. Activity of enzymes was measured in cytosol of SF cells after ultracentrifugation. Activity of AMFK was estimated with the Western blotting method. The consumption speed of oxygen by SF cells was recorded polarographycally using as the substrate glutamic acid (5 μ mol/ml in incubation fluid). Registration of the active forms of oxygen was carried out by EPR (electronic paramagnetic resonance). Levels of adenylic nucleotides were determined chromatographically.

Results: In RA SF we noted activation of AMFK (on average by 2,5 times) at the considerable increase of the AMP level and decrease in ADP and ATP.

Conclusions: These data demonstrate transition of cells of SF in RA to the energy saving mode of functioning that is followed by strengthening of oxidizing processes, deep dissociation of respiration with oxidizing phosphorylation and sharp increase of oxigen consumption speed by SF cells in vitro against the background of the progressing hypoxia of synovial cells and chondrocytes in vivo. Destabilization of mitochondrial and lysosomal membranes of SF cells appears against the background of shift of pH in RA in more acidic zone. It leads to the reinforced formation of the active forms of oxygen (short-lived toxiferous hydroxyl radicals), shift of red-ox potential of cells, activation of lysosomal hydrolyzing enzymes that forms biochemical mechanisms of development of an autophagy in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5025

FRI0079 TAS5315, A NOVEL BRUTON'S TYROSINE KINASE INHIBITOR, IMPROVE BONE MINERAL DENSITY (BMD) AND BONE EROSION VIA INHIBITION OF OSTEOCLAST ACTIVATION IN MURINE MODEL FOR RHEUMATOID ARTHRITIS

Y. Yoshiga, F. Hosoi, S. Iguchi, R. Kaneko, Y. Nakachi, D. Akasaka, K. Tanaka, K. Yonekura, T. Utsugi, E. Sasaki, Y. Iwasawa. *Taiho Pharmaceutical, Ibaraki, Japan*

Background: The erosions of bone and cartilage are a cardinal feature of rheumatoid arthritis (RA) and associated with disease severity and poor functional outcome[1]. Although several anti-inflammatory drugs improve symptoms of articular inflammation, they are less effective against bone erosion. The bone erosions in RA are associated with aberrant activations of osteoclasts induced by pro-inflammatory cytokines and receptor activator of nuclear factor κB ligand (RANKL)[2]. Bruton's tyrosine kinase (BTK), which is expressed in immune cells and mature osteoclast, is reported to be a key molecule in inflammatory response and bone resorption[3,4]. Thus, targeting BTK may be efficacious against not only inflammation but also bone erosion through direct regulation of activation of effector cells such as B cells, macrophages and osteoclasts in RA.

Objectives: In this study, we evaluated the effect of TAS5315, a novel BTK inhibitor, on *in vitro* osteoclasts activation and bone erosion in mouse collagen-induced arthritis.

Methods: Kinase selectivity of TAS5315 was assessed by available kinase assay panels. The effects of TAS5315 on macrophages and osteoclasts were assessed by examining phosphorylation of BTK, cytokine productions, osteoclast differentiation and bone resorptions. The effects of TAS5315 were investigated in mouse collagen-induced arthritis (CIA). Disease severity was evaluated by clinical score of paw swelling. Changes in bone mineral density (BMD) and bone erosion were assessed using microCT. TNF blocker was used as a control drug.

Results: TAS5315 selectively inhibited the enzyme activity of BTK and had less off target inhibition against other kinases. TAS5315 dose-dependently inhibited cytokine productions by macrophages, phosphorylation of BTK, osteoclastogenesis and bone resorbing activity in osteoclasts. In established mouse CIA, TAS5315 significantly ameliorated paw swelling in a dose dependent manner and the anti-inflammatory effect of TAS5315 (0.3 mg/kg, once daily) was comparable to that of TNF blocker. Most importantly, improvement of BMD and bone erosion were observed in TAS5315 treated mice at a doses of higher than 0.1 mg/kg within 13 days from treatment initiation, but not in TNF blocker-treated mice. The onset of action of TAS5315 on BMD and bone erosion was earlier and stronger compared with that of TNF blocker. These data suggest that TAS5315 had direct effect against osteoclasts function and led to improvement of bone erosion in murine model for RA.

Conclusions: Our study demonstrates that TAS5315, a novel BTK inhibitor, would be an ideal RA therapeutic agent that could inhibit bone destruction as well as inflammation.

References:

[1] Nat Rev Rheumatol. 2012;8,656–64.
[2] Nat Rev Rheumatol. 2015;11,189–94.
[3] Cell. 2008;132,794–806.
[4] Drug Discov Today. 2014;19,1200–4.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1761

FRI0080 CD11B+GR1DIM TOLEROGENIC DENDRITIC CELL-LIKE CELLS ARE EXPANDED IN INTERSTITIAL LUNG DISEASE IN SKG MICE

S. Sendo, J. Saegusa, Y. Ichise, H. Yamada, I. Naka, T. Okano, S. Takahashi, Y. Ueda, K. Akashi, A. Onishi, A. Morinobu. *Department of Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine, Kobe City, Japan*

Background: SKG mice develop interstitial lung disease (ILD) resembling human rheumatoid arthritis (RA)–associated ILD. We identified a unique cell population of $CD11b^{+}Gr1^{dim}$ cells in the severely inflamed lungs in SKG mice.

Objectives: The aims of this study are to clarify the mechanism behind the lung pathology, and to elucidate the phenotype and function of $CD11b^{+}Gr1^{dim}$ cells in ILD-induced SKG mice.

Methods: We assessed the severity of zymosan A-induced ILD in SKG mice histologically, and examined lung-infiltrating cells by Giemsa stain and flow cytometry. Total lung cells and isolated monocytic myeloid-derived suppressor cells (M-MDSCs) were cultured in vitro with GM-CSF (and IL-4). The proliferation of CSFE-labeled naïve T cells co-cultured with isolated $CD11b^{+}Gr1^{dim}$ cells and MDSCs was evaluated by flow cytometry.

Results: MDSCs, Th17 cells, and group 1 and 3 innate lymphoid cells (ILC1s and ILC3s) were increased in the lungs; the proportion of these cells varied with ILD severity. In this process, we found that a unique cell population, $CD11b^{+}Gr1^{dim}$ cells, were expanded in the severely inflamed lungs (Figure). About half of the $CD11b^{+}Gr1^{dim}$ cells expressed CD11c and Giemsa stain revealed that they were morphologically dendritic cell (DC)-like. The $CD11b^{+}Gr1^{dim}$ cells were induced from M-MDSCs with GM-CSF in vitro and were considered tolerogenic because they expressed high levels of PD-L1 and suppressed T-cell proliferation. The $CD11b^{+}Gr1^{dim}$ cells have never described previously and termed $CD11b^{+}Gr1^{dim}$ tolerogenic DC-like cells ($CD11b^{+}Gr1^{dim}$tolDC-LCs). Th17 cells, ILC1s and ILC3s in the inflamed lung produced GM-CSF, which in turn could induce $CD11b^{+}Gr1^{dim}$tolDC-LCs to reduce inflammation.

Conclusions: We identified a unique cell population, termed $CD11b^{+}Gr1^{dim}$tolDC-LCs, in ILD-induced lungs in SKG mice.

References:

[1] Nishimura K, Saegusa J, Matsuki F, Akashi K, Kageyama G, Morinobu A. Tofacitinib facilitates the expansion of myeloid-derived suppressor cells and ameliorates arthritis in SKG mice. Arthritis Rheumatol 2015;67:893–902.
[2] Shiomi A, Usui T, Ishikawa Y, Shimuzu M, Murakami K, Mimori T. GM-CSF but not IL-17 is critical for the development of severe interstitial lung disease in SKG mice. J. Immunol 2014;193:849–59.
[3] Takenaka MC, Quintana FJ. Tolerogenic dendritic cells. Semin. Immunopahol 2016. doi:10.1007/s00281–016–0587–8.

Acknowledgements: The authors thank Shino Tanaka (Department Rheumatology and Clinical Immunology, Kobe University Graduate School of Medicine) for providing technical assistance.

Abstract FRI0078 – Table 1 AMPK activity (units/mg of protein), oxygen uptake rate (OUR, natoms of oxygen/min/mg of protein), the level of active free radical form of oxygen (AFRF, units/mg of protein), the content of adenine nucleotides in SF (nmol/ml) and pH in SF in RA

	AMPK	OUR	AFRF	AMP	ADP	AFP	pH of SF
RA SF	2,5±0,4	86,3±4,3	32,8±4,6	120–135 (127,5)	97–123 (110)	735–990 (862,5)	66,4–6,97 (6,81)
Donor SF	1,1±0,2	42,4±3,7	10,9±2,1	45–81 (63)	157–294 (222,5)	1490–1547 (1518,5)	7,43–7,65 (7,54)

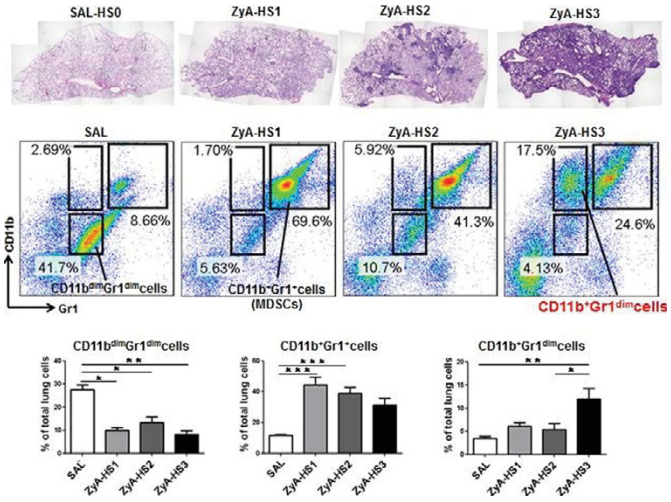


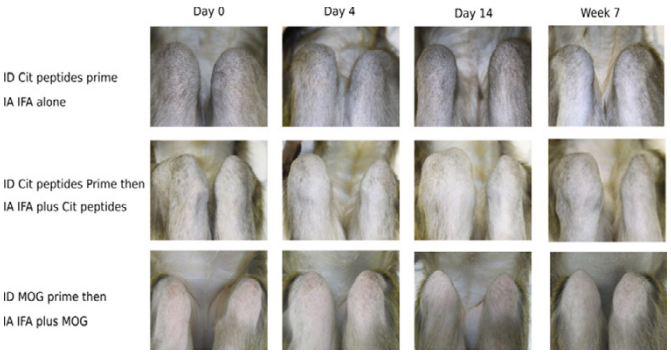
Figure 1

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1429

FRI0081 A MACAQUE MODEL OF RHEUMATOID ARTHRITIS BY IMMUNIZATION WITH CITRULLINATED PEPTIDES: LESSONS FOR THE HUMAN DISEASE

S. Bitoun[1], P. Roques[2], T. Larcher[3], G. Nocturne[1], C. Serguera[4], P. Chretien[5], G. Serre[6], R. Le Grand[7], X. Mariette[1]. *[1]Université Paris-Sud, Hôpitaux Universitaires Paris-Sud, INSERM U1184, le Kremlin Bicêtre; [2]Immunology of viral infections and autoimmune diseases, CEA, Fontenay aux Roses; [3]INRA UMR703 Veterinary School of Nantes, Nantes; [4]MIRCEN, CEA/INSERM, Fontenay aux Roses; [5]AP-HP, Hôpitaux Universitaires Paris-Sud, le Kremlin Bicêtre; [6]INSERM U1056 - Université de Toulouse Paul, Toulouse; [7]CEA - Université Paris Sud 11 - INSERM U1184, Fontenay aux Roses, France*

Background: Recent evolution in the understanding of rheumatoid arthritis (RA) mechanisms is the role of antibodies directed against citrullinated (cit) proteins (ACPAs). The shared epitope (SE) on the MHC class II is the main genetic risk factor of RA and favors presence of ACPAs. Mouse models dependent on cit peptides immunization require transgenic expression of the SE and are controversial. Non-human primates are ideal to study the interaction between ACPA and RA since 8% carry, similarly to humans, the SE called the H6 haplotype.
Objectives: The goal of this study was to develop a new animal model of RA based on immunization of genetically predisposed macaques against cit peptides to generate an ACPA-mediated model of arthritis.
Methods: Six macaques were intra dermally (ID) immunized with 4 peptides: vimentin (59–71) and (66–78), α fibrinogen (79–91) and aggrecan (89–103). H6 animals were immunized with either cit (n=2) or arginine (arg) (n=2) containing peptides. Two non H6 animals were immunized with cit peptides. These peptides are known to induce a T cell response in RA patients carrying the SE. T-cell response was assessed with Interferon γ ELISPOT and B-cell response by ELISA. An intra articular (IA) boost was done 30 weeks after initial immunization with either incomplete Freud's adjuvant (IFA) alone, IFA and cit peptides and IFA plus non relevant peptides.
Results: In the macaques, the T-cell response was specific to cit or arg peptides (depending on the peptides used for immunization). Surprisingly, the presence of the H6 epitope did not influence the response. Conversely the antibodies generated in response to the peptides were cross-reactive between the cit and arg peptides. Since no clinical response was observed, an IA boost was performed with the same 4 cit peptides and IFA adjuvant. This led to a prolonged neutrophil-rich mono-arthritis preferentially in H6 animals (Figure). Conversely, animals boosted with IFA alone only or with IFA plus myelin oligodendrocyte glycoprotein (MOG) peptides and previously immunized with MOG peptides presented with a transient mono-arthritis. Histological analysis revealed a local mononuclear infiltrate in one of the two animals that had prolonged knee monoarthritis. There was no clinical polyarthritis but 2 animals displayed synovial proliferation in 1 MCP and 1 MTP, respectively.
Conclusions: Immunization of macaques with cit peptides, then IA boost with the same cit peptides plus IFA, induced a prolonged monoarthritis. Shared epitope bearing did not restrict the T-cell response but seemed to favor the prolonged swelling after the IA boost. Neutrophil infiltration of the joint occurred similarly to what is seen in RA. Further use of neutrophil chemo-attractant might lead to a poly-articular disease. This macaque model of RA appears unique to study the events occurring during the pre-clinical phase of RA.



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2843

FRI0082 RAS SIGNALING INHIBITORS ATTENUATE ARTHRITIS IN ANIMAL MODELS OF RHEUMATOID ARTHRITIS BY DOWN MODULATING THE PATHOGENIC TH17 CELL RESPONSE

M. Zayoud[1,2], E. Vax[1], G. Elad Sfadia[3], V. Marcu-Malina[1], Y. Kloog[3], I. Goldstein[1,2,4]. *[1]Immunology Core Laboratory, Chaim Sheba Academic Medical Center, Ramat Gan; [2]Medicine, Sackler Faculty of Medicine, Tel Aviv University; [3]Faculty of Life Sciences, Tel Aviv University, Tel Aviv; [4]Rheumatology, Chaim Sheba Academic Medical Center, Ramat Gan, Israel*

Background: Ras-GTPases are vital for normal T cell activation, and downstream effectors of Ras include the MEK/ERK, PI3-kinase/AKT, mTOR/p70S6-kinase, and NF-kB pathways. Somatic mutations in *NRAS* cause an autoimmune lymphoproliferative disorder and T cells from Rheumatoid Arthritis (RA) patients exhibit perturbation of the Ras/MEK/ERK pathway. The small molecule Farnesylthiosalicylic acid (FTS) inhibits the interaction between Ras-GTPases and prenyl-binding chaperones vital for proper plasma membrane localization and downstream signaling [1]. Previous pre-clinical studies suggest that FTS has an immunomodulatory effect in various animal models of autoimmunity [2].
Objectives: To test in the Lewis rat adjuvant induced arthritis (AIA) and in the DBA/1 mouse collagen type-II induced arthritis (CIA) models the therapeutic immunomodulatory effect of FTS alone or combined with methotrexate (MTX).
Methods: Arthritis was induced in 8–12 week old male Lewis rats by complete Freund's adjuvant (CFA) injection and in male DBA/1 mice by collagen type-II (CII) immunization. Animals were treated prophylactically with once daily oral FTS (100 mg/kg); weekly i.p injection of MTX (0.5 mg/kg), oral FTS combined with MTX, or daily oral vehicle solution (0.5% carboxy methyl cellulose; CMC). Arthritis severity was scored daily from disease onset until study termination. In addition, we measured multiple disease- and drug-related immunological/molecular biomarkers.
Results: AIA severity was significantly reduced by FTS treatment compared to CMC controls (Figure 1A, $P<0.001$). Combining FTS and low dose MTX significantly increased its therapeutic efficacy compared to each drug alone (Figure 1A, $P<0.05$). FTS or FTS+MTX treatment also suppressed the upsurge in serum IL-17 and CRP compared to ailing controls. Global gene expression analysis of relevant splenic CD4+ T cells revealed that FTS is a potent inhibitor of pro-inflammatory and TH17 related gene networks. Next, our data from the mouse CIA model show that the therapeutic efficacy of FTS was non-inferior to MTX and it significantly reduced arthritis severity compared to controls (Figure 2, $P<0.001$). Importantly, FTS significantly inhibited the production of pathogenic anti-CII autoantibodies and upregulation of serum IL-6 and IL-17A compared to control arthritic mice. The in depth, multiplex, analysis of the effect of FTS on the T cell cytokine response to CII, revealed strong suppression of IL-22, IL-17, IL-9, GM-CSF and TNF production. Noteworthy, FTS therapy positively correlated with reduced Ras-GTP, p-ERK and p-AKT levels in splenic lymphocytes (drug related biomarkers).

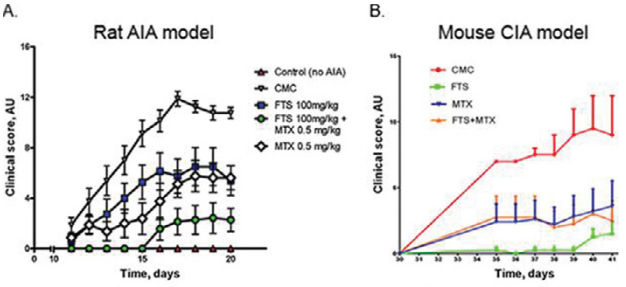


Figure 1. FTS attenuates arthritis severity in the (A) rat AIA and (B) mouse CIA models

Conclusions: FTS, a first-in-class oral selective Ras-GTPases inhibitor, exhibits a potent immunomodulatory effect in two classical murine model of arthritis, coupled with the inhibition of the TH17 response to relevant arthritogenic-antigens. Thus, Ras-signaling-blockade is a promising novel therapeutic approach for RA.

References:

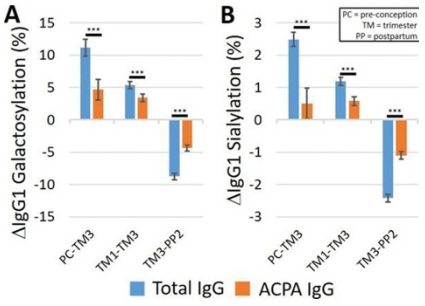
[1] Kloog Y, Cox AD. Prenyl-binding domains: potential targets for Ras inhibitors and anti-cancer drugs. Semin Cancer Biol. 2004 Aug; 14(4):253–261.

[2] Mor A, Aizman E, Chapman J, Kloog Y. Immunomodulatory properties of farnesoids: the new steroids? Curr Med Chem. 2013; 20(10):1218–1224.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1083

FRI0083 REDUCED INCREASE OF ACPA IGG-FC GALACTOSYLATION DURING PREGNANCY IN COMPARISON TO TOTAL IGG: AN EXPLANATION WHY AUTOANTIBODY POSITIVE RA-PATIENTS IMPROVE LESS DURING PREGNANCY?

A. Bondt[1,2,3], L. Hafkenscheid[3], D. Falck[2], T.M. Kuijper[1], Y. Rombouts[3], J.M. Hazes[1], M. Wuhrer[2], R.J. Dolhain[1]. *[1]Rheumatology, Erasmus University Medical Center, Rotterdam; [2]Center for Proteomics and Metabolomics; [3]Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

Background: Rheumatoid arthritis (RA) disease activity (DAS28-CRP) improves less during pregnancy in autoantibody positive patients.[1] The most specific autoantibodies for RA are anti-citrullinated protein antibodies (ACPAs), which mainly occur as the immunoglobulin (Ig) G isotype. An association with DAS28-CRP and the pregnancy-associated improvement is well established for the Fc glycosylation of total IgG, in particular for galactosylation (Gal) and sialylation (SA).[2] The Fc glycosylation of ACPAs – mainly present as IgG – has been reported to be different from the total IgG Fc glycosylation.[3]
Objectives: We sought to determine whether the change in ACPA IgG glycosylation during pregnancy is different from that of total IgG, and whether this relates to the improvement of RA during pregnancy.
Methods: ACPA positive patient sera (*n*=152) were obtained within the framework of the PARA cohort, a prospective study designed to investigate pregnancy-associated improvement of RA. ACPA IgG was isolated using microscale affinity chromatography. Trypsin digested ACPA IgG was measured using nano-liquid chromatography mass spectrometry, and compared to total IgG.
Results: Pregnancy-associated changes in the levels of glycosylation were observed for all ACPA IgG subclasses. Pregnancy-associated glycosylation changes were less pronounced during pregnancy and after delivery in ACPA IgG (Gal +5%; SA +0.5%) compared to total IgG (Gal +11%; SA +2.5%; Figure 1), but – for total IgG – not different between ACPA+ and ACPA- patients. No association of the change in DAS28-CRP with the change in ACPA IgG or total IgG galactosylation was observed for ACPA+ patients, whereas a strong association of total IgG galactosylation was observed for ACPA- patients.



Conclusions: During pregnancy the increase in galactosylation of ACPA IgG was less pronounced than that of total IgG, whereas the increase in the galactosylation of total IgG was not different between ACPA+ and ACPA- patients. Since it is known that changes in IgG galactosylation are associated with improvement of RA during pregnancy and since ACPA is thought to be of pathogenic significance in RA, our data might provide an explanation why ACPA+ RA patients are less likely to improve during pregnancy.
References:
[1] Ince-Askan H, Hazes JM, Dolhain RJ. Identifying clinical factors associated with low disease activity and remission of rheumatoid arthritis during pregnancy. Arthritis Care Res (Hoboken) 2016 doi: 10.1002/acr.23143.
[2] Bondt A, Selman MHJ, Deelder AM, et al. Association between galactosylation of immunoglobulin G and improvement of rheumatoid arthritis during pregnancy is independent of sialylation. Journal of Proteome Research 2013;12(10):4522–31. doi: 10.1021/pr400589m.
[3] Scherer HU, van der Woude D, Ioan-Facsinay A, et al. Glycan profiling of anti-citrullinated protein antibodies isolated from human serum and synovial fluid. Arthritis Rheum 2010;62(6):1620–29. doi: 10.1002/art.27414.
Acknowledgements: This project is funded by the Dutch Arthritis Foundation (NR 10–1-411) and by the European Union's Seventh Framework Program (FP7-Health-F5–2011) under grant agreement no°278535 (HighGlycan). We thank Dr Jan Wouter Drijfhout (LUMC, Leiden) for providing the CCP2 peptide.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6229

FRI0084 THE TONSIL MICROBIOME IS INVOLVED IN RHEUMATOID ARTHRITIS

J. Li[1], J. He[1], K. Deng[2], J. Qin[2], Y. Jin[1], J. Chen[1], Z. Li[1]. *[1]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing; [2]Digital Microbiota Technology Co. Ltd., Shenzhen, China*

Background: Rheumatoid arthritis (RA) is a prevalent systemic autoimmune disease characterized by the production of autoantibodies[1]. The tonsil has been demonstrated to be a site of citrullination, and tonsillectomy has been reported to be a potential treatment of RA, suggesting the possibility that the tonsil could be a site of autoimmunity generation in RA[2,3]. The dysbiosis of gut microbiome and the associated host immune response has been implicated in the initiation and progression of RA[4–6]. However, there is no in-depth studies on the role of tonsil microbiota in RA. Thus, studies of the characteristics of tonsil microbiome in RA patients, the underlying mechanisms, as well as specific markers for the diagnosis and therapeutic evaluation for RA, are critical for the early diagnosis and prevention of RA.
Objectives: Therefore, we aimed to define the association of RA with tonsil microbiome as well as a microbial and metabolite profile that could predict disease status.
Methods: 16S rRNA gene sequencing was utilized on 220 tonsil swab samples (121 RA patients and 99 healthy controls) as well as 78 fecal samples (68 RA and 10 controls). Analysis of microbial taxa and metabolic pathway were performed to characterise and compare the tonsil microbiome of RA patients and healthy subjects
Results: Results showed that the tonsil harbored a unique microbiome relative to that present in the fecal samples. Patients with RA exhibited different tonsil microbiome from controls. A taxon-level analysis suggested that the relative abundance of 26 microbial clades were significantly altered, with 7 taxa increased and 19 taxa decreased in RA samples. Noticeably, we observed an expansion of rare microbial lineages as well as an alteration in microbial cladogenesis within RA patients. RA tonsil microbiota was associated with smoke, anti-peripheral factor, rheumatoid factors, disease duration and activity. Furthermore, we identified that 86 genes associated with bacterial metabolic pathway were enriched in RA tonsil microbiome.
Conclusions: Our results demonstrated that the RA tonsil microbiome differs from that of healthy controls, which correlates with systemic autoimmune changes and may potentially drives initiation of RA.
References:
[1] McInnes IB, and Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med. 2011, 365(23): 2205–2219.
[2] Kawano M, Okada K, Muramoto H, et al. Simultaneous, clonally identical T cellexpansion in tonsil and synovium in a patient with rheumatoid arthritis and chronic tonsillitis. Arthritis Rheum. 2003, 48(9): 2483–2488.
[3] Makrygiannakis D, af Klint E, Lundberg IE, et al. Citrullination is an inflammation-dependent process. Ann Rheum Dis. 2006, 65(9): 1219–1222.
[4] Scher JU and Abramson SB. The microbiome and rheumatoid arthritis. Nat Rev Rheumatol, 2011, 7(10): 569–578.
[5] Scher JU, Sczesnak A, Longman RS, et al. Expansion of intestinal Prevotella copri correlates with enhanced susceptibility to arthritis. Elife, 2013, 2:e01202.
[6] Zhang X, Zhang D, Jia H, et al. The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment. Nat Med, 2015, 21(8): 895–905.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4707

FRIDAY, 16 JUNE 2017

Rheumatoid arthritis - prognosis, predictors and outcome

FRI0085 NUMBER OF PEPTIDE-SPECIFIC ANTI-CITRULLINATED PEPTIDE ANTIBODIES IN SYNOVIAL FLUID AND IN SYNOVIAL FLUID IMMUNE COMPLEXES ASSOCIATE WITH DEGREE OF RADIOLOGICAL DESTRUCTION AND RESPONSE TO TRIAMCINOLONE HEXACETONIDE FOR KNEE SYNOVITIS IN RHEUMATOID ARTHRITIS

A. Sohrabian[1], L. Mathsson Alm[1,2], M. Hansson[3], J. Lysholm[4], M. Cornillet[5], A. Knight[6], K. Skriner[7], G. Serre[5], A. Larsson[8], T. Weitoft[9], J. Rönnelid[1]. *[1]Department of Immunology, Genetics and Pathology, Uppsala university; [2]ImmunoDiagnostic Division, Thermo Fisher Scientific, Uppsala; [3]Rheumatology Unit, Department of Medicine, Karolinska Institutet, Stockholm; [4]Clinic of Rheumatology, Falun Hospital, Falun, Sweden; [5]Epithelial Differentiation and Rheumatoid Autoimmunity, U 1056 Inserm Toulouse University, Toulouse, France; [6]Rheumatology, Department of Medical Sciences, Uppsala university, Uppsala, Sweden; [7]Department of Medicine, Charité University Hospital, Berlin, Germany; [8]Section of Clinical Chemistry, Department of Medical Sciences, Uppsala university, Uppsala; [9]Section of Rheumatology, Center for Research and Development, Uppsala university, Gävle, Sweden*

Background: We have described a planar microarray for the determination

of antibodies against individual citrullinated peptides (ACPA; Hansson M et al. Arthritis Res Ther 2012;14:R201). We have also developed a method for the quantification of autoantibodies in immune complexes (IC; Sohrabian et al. Ann Rheum Dis 2015;74(Suppl 1):A74). Here we have combined these techniques to determine ACPA profiles in RA IC.

Objectives: To investigate if measurement of specific ACPA in synovial fluids (SF) and in IC from sera and SF can provide more prognostic information than conventional measurement of total ACPA and rheumatoid factor (RF) in serum.

Methods: Seventy-seven RA patients with knee synovitis were treated with intra-articular triamcinolone hexacetonide, and followed until relapse. DAS28 and radiographic joint damage according to Larson-Dale were recorded. Anti-CCP2, IgM and IgA RF and circulating C1q-binding immune complexes (CIC) were determined in paired sera and SF. IC were purified from sera and SF by binding to C1q-coated beads, and thereafter eluted with a procedure developed in our laboratory. Antibodies against 19 citrullinated peptides were investigated with a custom-made microarray assay based on the ImmunoCAP ISAC system (Phadia AB, Sweden) in sera and SF as well as in IC from sera and SF. The target peptides were filaggrin 307–324 (CCP1), vimentin peptides 60–75 and 2–17, fibrinogen peptides α36–50„ α563–583, α580–600, α621–635, β36–52, β60–74, β62–81 (with citrullination in positions 72 and 74, respectively), α-enolase 5–21 (CEP-1), peptides 1, 5, Z1, Z2 and Bla26 from hnRNP, and histone 4 peptides 14–34 and 31–50. Cutoffs were established in relation to healthy controls. Backward stepwise regression was used to investigate what factors determined Larsen Dale index, DAS28, and duration of remission after steroid treatment. Independent factors were anti-CCP2, IgM RF, IgA RF, CIC, number of ACPA peptide reactivities, and number of ACPA reactivities in IC, all measured both in serum and paired SF.

Results: A considerable proportion of anti-CCP2 negative patients had multiple ACPA in SF, and in IC fractions. High DAS28 associated with reactivity against 7/19 peptides in serum and 9/19 in SF. High Larsen score associated with number of specific ACPA in SF IC and with CIC in SF. DAS28 levels associated with IgM RF in SF and with CIC in SF, and steroid response duration with number of specific ACPA in serum and in SF IC.

Conclusions: We found ACPA in SF, and especially in the IC fraction of SF, in a sizeable fraction of anti-CCP2 negative patients. Number of peptide-specific ACPA (but not anti-CCP2 levels) associated with radiological destruction and length of remission after intra-articular steroid therapy. Our data do not support a role for any unique ACPA specificity in RA pathogenesis. Instead, the number of individual ACPA specificities may be important.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3222

FRI0086 EFFICACY AND SAFETY DATA BASED ON HISTORICAL OR PRE-EXISTING CONDITIONS AT BASELINE FOR PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS WHO WERE TREATED WITH BARICITINIB

B. Combe[1], A. Balsa[2], P. Sarzi-Puttini[3], H.-P. Tony[4], I. de Torre[5], V. Rogai[5], F. Durand[6], A. Jahangir[5], S. Witt[5], J. Zhong[7], M. Dougados[8]. *[1]Hopital Lapeyronie, Montpellier, France; [2]Hospital Universitario la Paz, Madrid, Spain; [3]Sacco Hospital, Milano, Italy; [4]University Hospital of Würzburg, Würzburg, Germany; [5]Eli Lilly and Company, Indianapolis; [6]Eli Lilly and Company, Madrid; [7]QuintilesIMS, Morrisville, United States; [8]Rene Descartes Univ/ Cochin Hospital, Paris, France*

Background: Patients (pts) with rheumatoid arthritis (RA) often experience comorbidities that may affect efficacy and safety when treated with different drugs.[1] Baricitinib (BARI) is a selective inhibitor of Janus kinase[2,3] 1 and 2 that improves disease activity in pts with RA with an acceptable safety profile.[4–6]

Objectives: To investigate the effect of selected comorbidities on safety and efficacy outcomes in pts treated with BARI.

Methods: Pts were selected for this post hoc analysis on the basis of historical or ongoing conditions defined by Medical Dictionary for Regulatory Activities and divided by the following comorbidity subgroups: depression, osteoporosis, hepatic disorders, and previous cardiovascular events. Efficacy outcomes included 20% and 50% improvement in American College of Rheumatology 20 Response (ACR20) and American College of Rheumatology 50 Response (ACR50) criteria, respectively; the proportion of pts who achieved a Disease Activity Score for 28-joint count using high-sensitivity C-reactive protein (DAS28-hsCRP) score ≤3.2; and change from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) at week 12. Pts who had an inadequate response (IR) to conventional disease-modifying antirheumatic drugs (cDMARDS) from 5 studies with BARI 4 mg and placebo (PBO) were included in efficacy analyses (N=1684) and safety analyses (N=1683). The interaction of comorbidity by treatment was analysed using logistic regression or analysis of variance modelling. Interaction tests were performed within each comorbidity subgroup, and the effect size in pts with and without the comorbidity was analysed.

Results: Pts in the efficacy set had similar baseline demographic and disease-activity characteristics across treatments within each comorbidity subgroup. The presence of a comorbid condition did not affect the incidence of treatment-emergent adverse events (TEAEs), serious adverse events (AE), discontinuations, or deaths caused by AEs for BARI 4 mg vs PBO (Table 1). The most common TEAEs across the subgroups for BARI and PBO were nasopharyngitis and upper respiratory tract infection. For cDMARD-IR pts, change from baseline for each comorbidity subgroup for ACR20, ACR50, DAS28-hsCRP ≤3.2 response, and HAQ-DI was higher for BARI 4 mg compared with PBO. Within each comorbidity subgroup, BARI responses compared with PBO were similar (interaction $P > 0.1$) (Table 2).

Table 1: Adverse Events Reported by Selected Comorbidity up to Week 16

Baricitinib 4 mg n (%)	Depression (N=64)	Osteoporosis (N=113)	CV Event (N=350)	Hepatic Event (N=222)	Overall (N=802)
Any TEAE	45 (70.3)	70 (61.9)	227 (64.9)	152 (68.5)	495 (61.7)
Serious AE	0	9 (8.0)	14 (4.0)	8 (3.6)	25 (3.1)
Discon due to AEs	1 (1.6)	7 (6.2)	14 (4.0)	9 (4.1)	25 (3.1)
Deaths	0	0	0	0	0
Placebo	**(N=69)**	**(N=134)**	**(N=381)**	**N=202**	**(N=881)**
Any TEAE	57 (82.6)	91 (67.9)	228 (59.8)	119 (58.9)	494 (56.1)
Serious AE	6 (8.7)	9 (6.7)	16 (4.2)	5 (2.5)	31 (3.5)
Discon due to AEs	3 (4.3)	9 (6.7)	12 (3.1)	6 (3.0)	24 (2.7)
Deaths	1 (1.4)	1 (0.7)	1 (0.3)	0	1 (0.1)

Abbreviations: AE=adverse event; CV=cardiovascular; Discon=discontinuations; TEAE=treatment-emergent adverse event.

Table 2: Efficacy Outcomes Reported by Selected Subgroup at Week 12

Baricitinib 4 mg	Depression (N=64)	Osteoporosis (N=113)	CV Event (N=350)	Hepatic Event (N=222)	Overall (N=803)
ACR20, NRI, n (%)	38 (59.4)	74 (65.5)	239 (68.3)	149 (67.1)	542 (67.5)
ACR50, NRI, n (%)	22 (34.4)	46 (40.7)	143 (40.9)	90 (40.5)	330 (41.4)
DAS-hsCRP≤3.2, mLOCF, n (%)	20 (31.3)	53 (46.9)	157 (44.9)	95 (42.8)	352 (43.8)
ΔHAQ-DI,mLOCF* N-Obs, LSM (SE)	63,-0.46 (0.14)	111,-0.36 (0.07)	347, -0.54 (0.04)	219 -0.58 (0.08)	792, -0.53 (0.03)
Placebo	(N=69)	(N=134)	(N=381)	(N=202)	(N=881)
ACR20, NRI, n (%)	22 (31.9)	43 (32.1)	155 (40.7)	75 (37.1)	345 (39.2)
ACR50, NRI, n (%)	6 (8.7)	16 (11.9)	55 (14.4)	23 (11.4)	127 (14.4)
DAS28-hsCRP ≤3.2, mLOCF, n (%)	9 (13.0)	17 (12.7)	60 (15.7)	26 (12.9)	146 (18.2)
ΔHAQ-DI, mLOCF* N-Obs, LSM (SE)	68, -0.20 (0.13)	131, -0.08 (0.07)	374 -0.27 (0.04)	201, -0.28 (0.08)	868, -0.25 (0.03)

Abbreviations: ACR20 = 20% improvement in American College of Rheumatology 20 Response criteria; ACR50 = 50% improvement in American College of Rheumatology 50 Response criteria; CV = cardiovascular; DAS28-hsCRP = Disease Activity Score for 28-joint count using high-sensitivity C-reactive protein; HAQ-DI = Health Assessment Questionnaire-Disability Index (patient-reported questionnaire with 24 questions in 8 domains: dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities); LSM = least squares mean; mLOCF = modified last observation carried forward; N-obs = number of patients in the analysis; NRI = nonresponder imputation; SE = standard error
*LSM and SE were calculated using analysis of variance model.

Conclusions: Treatment with BARI 4 mg showed similar effect in selected comorbidity subgroups with depression, osteoporosis, cardiovascular events, and hepatic impairment for efficacy and safety. No trends were noted for pts in each comorbidity subgroup for increased risk of events after treatment with BARI 4 mg compared with PBO.

References:

[1] Gossec L et al. Joint Bone Spine. 2016.
[2] Taylor et el. 2015 ACR Meeting. Abstract 2L.
[3] Kremer et al. 2015 ACR Meeting. Abstract 1050.
[4] Dougados M et al. Ann Rheum Dis. 2017.
[5] Smolen et al. Ann Rheum Dis. 2016.
[6] Fleischmann R et al. Arthritis Rheumatol. 2016.

Disclosure of Interest: B. Combe Grant/research support from: Pfizer, Roche, UCB, Consultant for: Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, UCB, Speakers bureau: BMS, MSD, Pfizer, Roche, Regeneron, UCB, A. Balsa Consultant for: Eli Lilly & Company, P. Sarzi-Puttini Grant/research support from: Eli Lilly & Company, Speakers bureau: Eli Lilly & Company, H.-P. Tony Consultant for: Eli Lilly & Company, I. de Torre Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, V. Rogai: None declared, F. Durand Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, A. Jahangir Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, S. Witt Shareholder of: Eli Lilly & Company, Employee of: Eli Lilly & Company, J. Zhong Consultant for: Eli Lilly & Company, M. Dougados Grant/research support from: Lilly, Pfizer, UCB, Merck, BMS, Roche, Abbvie, Consultant for: Lilly, Pfizer, UCB, Merck, BMS, Roche, Abbvie

DOI: 10.1136/annrheumdis-2017-eular.2227

FRI0087 LOW RATES OF RADIOGRAPHIC PROGRESSION OF STRUCTURAL JOINT DAMAGE OVER 2 YEARS OF BARICITINIB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

D. van der Heijde[1], M. Schiff[2], Y. Tanaka[3], R. Klar[4], L. Xie[5], G. Meszaros[5], T. Ishii[5], M. Casillas[5], R. Ortmann[5], P. Emery[6]. *[1]Leiden University Medical Center, Leiden, Netherlands; [2]University of Colorado, Denver, United States; [3]School of Medicine, Kitakyushu, Japan; [4]Quintiles IMS Holdings, Inc, Durham; [5]Eli Lilly and Company, Indianapolis, United States; [6]University of Leeds, Leeds, United Kingdom*

Background: In ph3 studies, baricitinib (bari) inhibited progression of radiographic joint damage for up to 1 year in patients (pts) with active rheumatoid arthritis (RA) who were DMARD-naïve or who had an inadequate response to conventional synthetic DMARDs (csDMARD-IR).

Objectives: To evaluate radiographic progression of structural joint damage in pts with RA over 2 years of treatment.

Methods: Upon completion of a bari ph 3 study, pts could enter a long-term extension (LTE) study, in which they continued to receive the same bari dose as in the original ph3 study. At 52 wks, DMARD-naïve pts receiving methotrexate (MTX) or combination therapy (bari 4mg + MTX) were switched to bari 4mg monotherapy; MTX-IR pts receiving adalimumab (ADA) were switched to bari

4mg on background MTX. At 24 wks, csDMARD-IR pts receiving placebo (PBO) were switched to 4mg on background csDMARD. Radiographs at baseline, year 1 and year 2 were scored using the van der Heijde modified total sharp score (mTSS). Data are least squares mean change from baseline using mixed model repeated measures on observed data.

Results: Of all pts randomised, 82.5% entered the LTE, and 87.6% of those could be entered in this analysis. At year 2, progression was significantly lower with initial bari (including monotherapy) vs. initial MTX in DMARD-naïve pts. In MTX/csDMARD-IR pts, progression with initial bari was significantly lower than initial PBO, and similar to initial ADA.

	1 year (52 weeks)			2 years (100 weeks)		
DMARD-naïve	MTX N=136	Bari 4 mg mono N=120	Bari 4 mg + MTX N=150	MTX → Bari 4 mg mono† N=136	Bari 4 mg mono N=117	Bari 4 mg + MTX → Bari 4 mg mono† N=150
Change in (Δ) mTSS	1.62	1.14	0.37***	1.97	1.35	0.61***
Δ mTSS ≤0.5, n (%)	85 (63)	89 (74)*	126 (84)***	77 (57)	83 (71)*	120 (80)***
	1 year (52 weeks)			2 years (100 weeks)		
MTX-IR	PBO → Bari 4 mg¶ N=358	Bari 4 mg N=380	ADA‡ N=260	PBO → Bari 4 mg¶ N=357	Bari 4 mg N=376	ADA → Bari 4 mg‡ N=260
Δ mTSS	1.64	0.81***	0.81**	2.20	1.13***	1.14**
Δ mTSS ≤0.5, n (%)	228 (64)	287 (76)***	196 (75)**	212 (59)	269 (72)***	190 (73)***
	1 year (48 weeks)			2 years (96 weeks)		
csDMARD-IR	PBO → Bari 4 mg§ N=143	Bari 2 mg N=157	Bari 4 mg N=144	PBO → Bari 4 mg§ N=153	Bari 2 mg N=163	Bari 4 mg N=149
Δ mTSS	1.09	0.70	0.44*	1.42	0.98	0.68*
Δ mTSS ≤0.5, n (%)	104 (73)	125 (80)	120 (83)*	105 (69)	119 (73)	122 (82)**

Missing scores at 2 years were imputed using linear extrapolation based on data collected between 1 and 2 years; Time point=time from randomisation in originator study; N=number of pts with non-missing baseline and non-missing postbaseline mTSS data.
†Pts switched to bari 4mg at entry to LTE (at Week 52).
¶Pts switched to bari 4mg at rescue or at Week 24.
‡Pts switched to bari 4mg at rescue or at entry to LTE (at Week 52).
§Pts switched to bari 4mg at rescue or at entry to LTE (at Week 24). Comparisons analysed using MMRM.
*p≤0.05, **p≤0.01, ***p≤0.001 vs. PBO or MTX.

Conclusions: Treatment with once-daily oral bari resulted in low rates of radiographic progression for up to 2 years. Pts starting with bari showed progression that was significantly less than those starting with PBO or MTX, and comparable to those starting with ADA. The most robust benefit was seen with the 4mg dose.

Disclosure of Interest: D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boeringer Ingelheim, Celgene, Daiichi Sankyo, Eli Lilly and Company, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, UCB, Employee of: Director of Imaging Rheumatology bv, M. Schiff Consultant for: Abbvie, BMS, Eli Lilly and Company, Johnson & Johnson, Speakers bureau: Abbvie, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, BMS, MSD, Astellas, Abbvie, Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, BMS, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly and Company, GlaxoSmithKline, R. Klar Employee of: Quintiles IMS Holdings, Inc., L. Xie Employee of: Eli Lilly and Company, G. Meszaros Employee of: Eli Lilly and Company, T. Ishii Employee of: Eli Lilly and Company, M. Casillas Employee of: Eli Lilly and Company, R. Ortmann Employee of: Eli Lilly and Company, P. Emery Consultant for: Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company

DOI: 10.1136/annrheumdis-2017-eular.1324

FRI0088 SYNOVIAL PATHOBIOLOGY CORRELATES WITH DIAGNOSTIC SUBGROUPS IN EARLY INFLAMMATORY ARTHRITIS: RESULTS FROM THE PATHOBIOLOGY OF EARLY ARTHRITIS COHORT (PEAC)

G. Lliso-Ribera[1], F. Humby[1], S. Kelly[1], M. Bombardieri[1], M. Lewis[1], R. Hands[1], V. Rocher[1], F. Bene[1], A. Nerviani[1], C. Buckely[2], P. Taylor[3], I. McInnes[4], C. Pitzalis[1]. *[1]Experimental Medicine and Rheumatology, Queen Mary University London, London; [2]Centre for Translational Inflammation Research, University of Birmingham, Birmingham; [3]Kennedy Institute of Rheumatology, University of Oxford, Oxford; [4]Experimental Medicine and Rheumatology, University of Glasgow, Glasgow, United Kingdom*

Background: Application of the 2010 ACR/EULAR Criteria for RA to early inflammatory arthritis cohorts permits an enhanced sensitivity for diagnosis compared to the historic 1987 ACR criteria but risks loss of diagnostic specificity. Heterogeneity in RA synovial pathobiology is well recognised with differences in qualitative and quantitative degree of immune cell infiltration, whether such heterogeneity correlates with classification criteria in early inflammatory arthritis is unknown, offering the potential to refine early diagnostic criteria.

Objectives: The aim of this study was to examine in a cohort of therapy naïve, early inflammatory arthritis patients whether synovial immune cell infiltration differed significantly between diagnostic categories of early inflammatory arthritis (ACR/EULAR 2010 vs ACR 1987 vs undifferentiated).

Methods: A total of 200 consecutive DMARD naïve early arthritis patients (disease duration <1 year) recruited as part of the multicentre PEAC study at Barts Health NHS Trust were categorised according to the following criteria: i. RA 1987 ACR, ii. RA 2010 ACR/EULAR, and iii. Undifferentiated Arthritis (UA). All patients underwent a baseline synovial biopsy of a clinically active joint along with collection of demographic data. Following H&E staining, degree of synovitis was assessed. Sections underwent immumohistochemical staining and semi-quantitative scoring (0–4) to determine the degree of CD20+Bcells, CD3+T cells, CD68+ lining (l) and sublining (sl) macrophage and CD138+ plasma cell infiltration. Sections were categorised into three pathotypes: (i) Fibroid: (CD68 SL<2 and or CD3, CD20, CD138<1), (ii) Myeloid: (CD68SL>2, CD20<1 and or CD3>1) and (iii) Lymphoid: (grade 2–3 CD20+ aggregates, CD20>2).

Results: 166/200 samples were suitable for analysis. 115 patients were classified as RA1987, 16 patients as RA 2010 ACR/EULAR and 35 as UA. 80% of synovial samples were collected from small joints (wrist, MCP, PIP). Although there were no significant differences in disease duration between diagnostic subgroups, patients classified as RA1987 criteria had significantly higher levels of CRP, tender and swollen joints, DAS28 and sero positivity for ACPA and RF. When patients were stratified into pathotypes, a numerically higher proportion of patients within the RA1987 group were categorised as lymphoid. Further, patients within the RA 1987 group had a significantly higher synovitis score and degree of immune cell infiltration.

N=166	RA1987 (115)	RA2010 (16)	UA (35)	P value
Fibroid 47 (%)	27 (23.5%)	6 (37.5%)	14 (40%)	
Myeloid 57 (%)	38 (33%)	5 (31.2%)	14 (40%)	0.10
Lymphoid 62 (%)	50 (43.5%)	5 (31.2%)	7 (20%)	
CD3 T cells	3.19	1.21	0.60	<0.001
CD20 B cells	2.88	0.80	0.75	<0.05
CD68L macrophages	3.60	1.86	1.34	<0.001
CD68SL macrophages	3.60	2.18	1.79	<0.05
CD138 Plasma Cells	2.85	1.06	0.73	<0.05
Synovitis Score	6.17	3.26	3.24	<0.001

Conclusions: Stratifying patients according to baseline clinical diagnosis translates into differences in synovial pathobiology. The capacity to refine early clinical classification criteria through application of synovial pathobiological markers offers the potential to predict disease outcome and stratify therapeutic intervention.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2927

FRI0089 EFFECT OF STARTING DOSE OF BARICITINIB IN ACHIEVING SUSTAINED LOW DISEASE ACTIVITY

J.R. Curtis[1], A. Kavanaugh[2], D. van der Heijde[3], D. Muram[4], J. Alam[4], S. Beattie[4], J.S. Smolen[5]. *[1]Univ of Alabama at Birmingham, Birmingham; [2]UC San Diego School of Medicine, la Jolla, United States; [3]Leiden University Medical Centre, Leiden, Netherlands; [4]Eli Lilly and Company, Indianapolis, United States; [5]Medical University of Vienna, Vienna, Austria*

Background: In Phase 3 studies, baricitinib (bari) treatment with 2 different doses (2 mg and 4 mg once daily) demonstrated significant improvements across multiple measures of disease activity in patients (pts) with active RA and an inadequate response (IR) to conventional synthetic (cs) DMARDs (RA-BUILD[1]) or biologic (b) DMARDs (RA-BEACON[2]).

Objectives: To determine the effect of starting dose of bari on achieving and sustaining low disease activity (LDA).

Methods: RA-BUILD and RA-BEACON trials were 24 week (wk), placebo (PBO) controlled studies. Pts completing the studies on bari treatment could enter a long-term extension (LTE) study, RA-BEYOND, continuing blinded treatment with the same dose, while pts on PBO switched to bari 4 mg. This post hoc analysis assessed disease activity in pts who achieved CDAI ≤10 at ≥1 visit (LDA) or at ≥2 consecutive visits (sustained LDA) within the originating study (24 wks) and continued into the LTE. The length of time required by pts to achieve LDA was determined by the incidence rate (percent pts responding per month) for each group.

Results: Treatment with bari 2 mg and 4 mg, when compared to PBO, resulted in higher rates of LDA and sustained LDA, as well as higher incidence rates (shorter time to achieve LDA/sustained LDA) within 24 wks of each originating study. Across studies, treatment with bari 4 mg demonstrated higher incidence rates when compared to bari 2 mg, both in achieving LDA and sustained LDA, indicating that these pts reached the desired LDA state faster. Incidence rates were lower in all treatment groups in bDMARD-IR pts compared with csDMARD-IR pts.

Conclusions: The most robust benefit in terms of achieving LDA and sustained LDA was observed with bari 4 mg treatment, which required shorter time to response, than treatment with 2 mg. This was observed in both the short (24 wks) and in the long-term in pts with IR to csDMARDs or bDMARDs.

References:

[1] Dougados M et al. Ann Rheum Dis 2017; 76(1):88–95.

Table 1. Proportions and Rates of LDA/sustained LDA by Treatment Group

			csDMARD-IR pts[a]			bDMARD-IR pts[b]		
Pts achieving CDAI ≤10			PBO	Bari 2 mg	Bari 4 mg	PBO	Bari 2 mg	Bari 4 mg
Time	# of visits	Category	N=228	N=229	N=227	N=176	N=174	N=177
Original study (24 wks)	≥1	%	44.7	60.7	65.6	26.7	39.7	48.6
		i-rate	12.06	18.79	21.50	6.36	10.08	13.38
	≥2	%	32.0	48.5	52.9	15.9	28.7	35.6
		i-rate	7.32	12.11	13.95	3.50	6.42	8.29
Original study + LTE	≥1	%	56.6	70.7	71.4	39.8	47.7	53.1
		i-rate	4.93	8.14	9.40	2.85	3.81	4.85
	≥2	%	48.2	61.6	61.2	27.8	39.1	44.1
		i-rate	3.41	5.33	5.78	1.66	2.57	3.13

Pts were defined as responders if they met the response criterion within the stated time frame, prior to any rescue or discontinuation. % = percent of pts meeting response criteria; ≥2 = at least 2 consecutive visits with CDAI ≤10; i-rate = exposure-adjusted incidence rate (% pts/month); N = number of randomised and treated pts; PBO = placebo treated pts in original study, Bari 4 mg treated pts in LTE. [a]RA-BUILD, [b]RA-BEACON.

[2] Genovese M et al. N Engl J Med 2016; 374(13):1243–52.

Disclosure of Interest: J. Curtis Grant/research support from: Abbvie, Amgen, BMS, Corrona, Eli Lilly and Company, Janssen, Myriad, Pfizer, Roche/Genentech, UCB, Consultant for: Abbvie, Amgen, BMS, Corrona, Eli Lilly and Company, Janssen, Myriad, Pfizer, Roche/Genentech, UCB, A. Kavanaugh Consultant for: Eli Lilly and Company, D. van der Heijde Consultant for: Abbvie, Amgen, Astellas, Astra-Zeneca, BMS, Boeringer Ingelheim, Celgene, Daiichi Sankyo, Eli Lilly and Company, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, UCB, Employee of: Director of Imaging Rheumatology bv, D. Muram Employee of: Eli Lilly and Company, J. Alam Employee of: Eli Lilly and Company, S. Beattie Employee of: Eli Lilly and Company, J. Smolen Grant/research support from: Abbvie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, Speakers bureau: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB

DOI: 10.1136/annrheumdis-2017-eular.1339

FRI0090 ANALYSIS OF NEUTROPHILS, LYMPHOCYTES, AND PLATELETS IN POOLED PHASE 2 AND PHASE 3 STUDIES OF BARICITINIB FOR RHEUMATOID ARTHRITIS

J. Kremer[1], T.W.J. Huizinga[2], L. Chen[3], C.G. Saifan[3], M. Issa[3], S.L. Witt[3], C.D. Walls[3], I. de la Torre[3]. *[1]Albany Medical College, New York, United States; [2]Leiden University Medical Center, Leiden, Netherlands; [3]Eli Lilly and Company, Indianapolis, United States*

Background: Rheumatoid arthritis (RA) is associated with increased neutrophil levels[1] and platelet[2] counts and decreased lymphocyte levels.[1,3] Baricitinib (bari) is a selective and reversible Janus kinase (JAK)1/JAK2 inhibitor in development for patients (pts) with moderate to severe RA.[4]

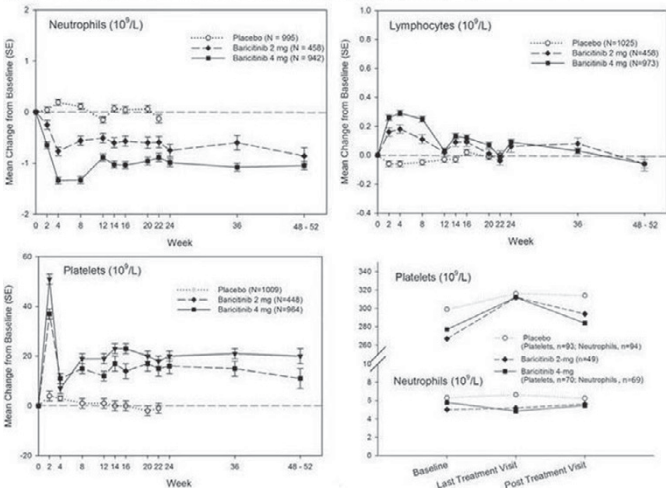
Objectives: To characterize changes in absolute neutrophil counts (ANC), absolute leukocyte counts (ALC), and platelet counts following once daily oral administration of bari.

Methods: Data were pooled from 6 placebo-controlled phase 2 and 3 studies of bari (2 and 4 mg). Changes in ANC, ALC, and platelets were evaluated for up to 52 weeks (wks) including data from a long-term extension study. Reversibility was evaluated in a subgroup of pts who discontinued treatment by wk 24.

Results: Mean ANC decreased within 1 month of administration of bari, followed by stabilization and an increase to baseline after treatment discontinuation (Figure 1). ANC <1000 cells/mm^3 were reported in <1% of pts, and 2 bari-treated pts (0.1%) reported permanent discontinuation of study drug due to neutropenia. Incidence of neutropenia was not associated with higher risk of overall or serious infections (Table 1).

Mean ALC increased within 1 month of bari administration and then decreased to baseline level in wks 12 to 24 (Figure 1). Lymphopenia appeared to be associated with slightly higher rate of overall infections (Table 1).

Figure 1: Longitudinal Profiles of Neutrophils, Lymphocytes, and Platelets



Mean platelet counts increased to peak at wk 2, returned towards baseline, stabilized over time, and returned to baseline after treatment discontinuation (Figure 1). Permanent study drug discontinuations from thrombocytosis occurred in 2 bari-treated pts (0.1%). No clear association between platelet increase and thromboembolic events was observed.

Conclusions: Treatment with bari was associated with a decrease in ANC and an increase in ALC and platelets, which stabilized over time and returned to baseline with prolonged treatment (ALC) or treatment discontinuation (ANC and platelets). No associations between ANC decrease and infections or between thrombocytosis and thromboembolic events were observed.

References:

[1] Schulze-Koops H et al. Rheumatology. 2017;56(1):46–57.
[2] Farr M et al. Ann Rheum Dis. 1983;42(5):545–549.
[3] Symmons DP et al. J R Soc Med. 1989;82:462–463.
[4] Fridman JS et al. J Immunol. 2010;184:5298–5307.

Disclosure of Interest: J. Kremer Grant/research support from: Abbvie, Genentech, Eli Lilly and Company, Novartis, Pfizer, Consultant for: Abbvie, Amgen, BMS, Genentech, GSK, Eli Lilly and Company, Novartis, Pfizer, Employee of: Corrona, Speakers bureau: Genentech (non-promotional), T. W. J. Huizinga Grant/research support from: Eli Lilly and Company, Pfizer, Consultant for: Eli Lilly and Company, Pfizer, Speakers bureau: Eli Lilly and Company, Pfizer, L. Chen Employee of: Eli Lilly and Company, C. Saifan Employee of: Eli Lilly and Company, M. Issa Employee of: Eli Lilly and Company, S. Witt Employee of: Eli Lilly and Company, C. Walls Employee of: Eli Lilly and Company, I. de la Torre Employee of: Eli Lilly and Company

DOI: 10.1136/annrheumdis-2017-eular.1325

FRI0091 PATIENT-PROVIDER DISCORDANCE MAY BE ASSOCIATED WITH INCREASED RISK OF SUBSEQUENT FLARES IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Myasoedova, C.S. Crowson, K. McCarthy-Fruin, E.L. Matteson, J.M. Davis III. *Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, MN, United States*

Background: Patient-provider discordance in assessment of disease status has been linked to lower patient satisfaction with potential implications on patient compliance and outcomes of care. Global assessment (GA) of disease activity in rheumatoid arthritis (RA) is discordant between patient and provider in about one third of cases. Prospective studies evaluating the implications of patient-provider discordance on RA disease course are lacking.

Abstract FRI0090 – Table 1. Infection by Worst Neutropenia and Lymphopenia CTCAE Grade in Placebo-Controlled Period up to Week 24

	Placebo			Baricitinib 4-mg		
	Total Pts	Pts (%) with Overall Infection	Pts (%) with Serious Infection	Total Pts	Pts (%) with Overall Infection	Pts (%) with Serious Infection
Neutropenia CTCAE Grade						
0 (≥2x10^9 cells/L)	985	279 (28.3)	16 (1.6)	853	313 (36.7)	13 (1.5)
1 (<2 and ≥1.5x10^9 cells/L)	34	10 (29.4)	0	74	32 (43.2)	1 (1.4)
2 (<1.5 and ≥1.0x10^9 cells/L)	9	0	0	27	11 (40.7)	0
3 (<1.0 and ≥0.5x10^9 cells/L)	1	1 (100.0)[1]	0	3	1 (33.3)[2]	0
4 (<0.5x10^9 cells/L)	0	0	0	0	0	0
Lymphopenia CTCAE Grade						
0 (≥1.1x10^{9}cells/L)	710	201 (28.3)	12 (1.7)	704	246 (34.9)	8 (1.1)
1 (<1.1 and ≥0.8x10^9 cells/L)	233	65 (27.9)	2 (0.9)	205	81 (39.5)	2 (1.0)
2 (<0.8 and ≥0.5x10^9 cells/L)	103	30 (29.1)	1 (1.0)	71	31 (43.7)	3 (4.2)
3 (<0.5 and ≥0.2x10^9 cells/L)	13	3 (23.1)	1 (7.7)	8	4 (50.0)	1 (12.5)
4 (<0.2x10^9 cells/L)	0	0	0	0	0	0

CTCAE=common terminology criteria for adverse events; pts = patients. [1]Upper respiratory tract; [2]Pharyngitis.

Objectives: We aimed to assess the occurrence and severity of patient-reported flares of RA in patients who had discordant estimates of RA disease activity with their provider at baseline compared to those who had concordant estimates.
Methods: Patients with RA (age≥18 years; 2010 ACR criteria) participating in an ongoing prospective study underwent clinical evaluation by a rheumatology provider (MD/NP/PA) at baseline with assessment of tender (TJC28) and swollen joint counts (SJC28), C-reactive protein (CRP), patient and provider GA of RA disease activity, disease activity score (DAS28-CRP), clinical disease activity index (CDAI), completion of Health Assessment Questionnaire-II (HAQ-II), visual analogue scales (0–100 mm) for pain (VAS-pain) and the flare-assessment in RA (FLARE) questionnaire. Patient-provider discordance was defined as ≥25 mm difference in GA between the patient and provider. Occurrence of patient-reported RA flares was compared between patients with and without discordance in GA. Flare was defined based on patient report when answered "Yes" to the question "Are you having a flare of your RA at this time?" or a predefined cut-off ≥2.5 on FLARE questionnaire (1,2).
Results: The study included 55 patients with RA (mean age 60.7 years; 65% female), of whom 40 had GA concordant with their provider and 15 had higher GA than their provider. Table 1 summarizes patient characteristics depending on GA discordance at baseline. Patients with discordance were similar in age, sex, duration of follow-up, had similar TJC28 and SJC28, but had significantly higher HAQ-II, VAS-pain, CRP, DAS28, CDAI, provider GA and FLARE scores at baseline vs patients with concordant GA. During the follow up, patients with discordance had significantly higher numbers and rates of flares, and tended to have more visits with discordant GAs compared to patients who had concordant GA with their provider at baseline.

Table. Characteristics of patients with rheumatoid arthritis (RA) depending on the presence of discordance in general assessment of RA disease activity

Characteristics*	Patients with concordant baseline GA (n=40)	Patients with discordantly high baseline GA (n=15)	p-value
Age	59.5 (10.3)	64.0 (7.4)	0.22
Sex, female	26 (65%)	10 (67%)	0.91
Duration of follow up, months	6.5 (4.0)	8.2 (5.8)	0.37
TJC28, baseline	2.0 (4.2)	2.6 (6.2)	0.91
SJC28, baseline	0.6 (1.5)	1.1 (2.4)	0.92
HAQ-II, baseline	0.5 (0.5)	1.0 (0.5)	0.001
VAS pain, baseline	26 (27)	54 (14)	<0.001
CRP, mg/L	7.0 (12.8)	10.5 (10.6)	0.020
DAS-28 CRP, baseline	2.3 (1.2)	3.0 (1.0)	0.006
CDAI, baseline	6.2 (9.0)	10.9 (8.5)	0.002
Patient GA, baseline	20.7 (23.1)	56.5 (12.6)	<0.001
Provider GA, baseline	15.0 (22.5)	17.0 (11.3)	0.044
Patient-reported flare, baseline	6 (15%)	5 (33%)	0.13
Number of patient-reported flares during the follow up	0.6 (0.9)	2.0 (2.9)	0.010
Flare rate based on patient-reported flares (% of subsequent months with flare)	8.4 (15.1%)	25.4 (29.3%)	0.009
FLARE score, baseline			
- Overall FLARE	1.9 (2.6)	4.4 (2.6)	0.002
- Systemic subscale	1.6 (2.5)	4.3 (2.9)	0.001
- Joint subscale	2.3 (2.8)	4.5 (2.7)	0.006
Number of FLARE questionnaire reports scoring ≥2.5 during the follow up			
- Overall FLARE	0.7 (1.2)	3.2 (3.6)	0.001
- Systemic subscale	0.6 (1.0)	2.5 (3.3)	0.002
- Joint subscale	1.1 (1.5)	3.4 (3.5)	0.007
Number of visits with discordant GA during the follow up	0.1 (0.2)	0.3 (0.6)	0.076
Rate of discordance (% of subsequent months with discordance)	0.5 (2.5%)	2.9 (6.2%)	0.070

*All measures are shown as mean (standard deviation) or as number (%)

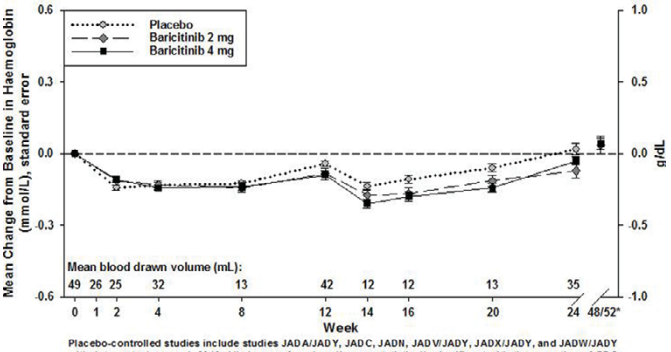
Conclusions: Patients with patient-provider discordance at baseline were more likely to report flares of RA during follow-up. Patient-provider discordance tended to persist at follow-up visits. Disease activity assessments with patient-reported component (i.e., HAQ-II, VAS-pain, DAS28, CDAI, FLARE score), as well as CRP and provider GA, but not joint counts, were higher at baseline in patients with discordance. Consideration of the results of clinical and laboratory assessment in combination with patient-reported measures of RA disease activity may be important to inform future risk of flares in patients with RA and help improve patient-provider communication and shared decision making.
References:
[1] Myasoedova E, et al. Identifying Flare in Rheumatoid Arthritis: What Is the Threshold? [abstract]. Arthritis Rheumatol. 2016; 68 (suppl 10).
[2] De Thurah A, et al. Patient self-assessment of flare in rheumatoid arthritis: criterion and concurrent validity of the Flare instrument. Clin Rheum. 2016; 35: 467–71.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1925

FRI0092 EFFECTS OF BARICITINIB ON HAEMOGLOBIN AND RELATED LABORATORY PARAMETERS IN RHEUMATOID ARTHRITIS PATIENTS

J. Kay[1], M. Harigai[2], J. Rancourt[3], C. Dickson[3], Y. Isaka[3], L. Chen[3], T. Carmack[3], D. Hyslop[3], D. Muram[3], W. Macias[3], J. Bradley[3], E. Keystone[4].
[1]Division of Rheumatology, U Mass Memorial Med Ctr and Med School, Worcester, United States; [2]Tokyo Women's Medical Univ., Tokyo, Japan; [3]Eli Lilly and Company, Indianapolis, United States; [4]Mt. Sinai Hospital, Ontario, Canada

Background: Baricitinib (bari), a selective, transient and reversible inhibitor of Janus kinase (JAK)1 and JAK2, improved signs and symptoms of active rheumatoid arthritis (RA) in multiple phase 3 studies. Since erythropoietin (EPO) stimulates erythrocyte production via the JAK2 signaling pathway, haemoglobin (Hgb) and other haematologic parameters were thoroughly evaluated in the bari RA clinical development program.
Objectives: To evaluate baseline and subsequent changes in Hgb and related laboratory parameters in RA patients (pts) treated with bari (2 or 4 mg once daily), placebo (PBO), or active comparator (methotrexate [MTX] or adalimumab [ADA]).
Methods: Blood samples were analyzed at baseline and at each study visit for complete blood count, with more extensive phlebotomy at baseline (Wk 0) and Wks 12, 24, and 52 (Figure 1). Data were aggregated from completed Phase 2 and 3 RA studies and one ongoing long-term extension study. EPO and reticulocyte (RET) data were collected from a Phase 2 RA study in Japan.
Results: Hgb levels below the gender-adjusted lower limit of normal (LLN) were often observed at baseline (25%). Small declines in Hgb were observed at Wk 2 and again at Wk 14 in bari (2 and 4 mg) and PBO-treated RA pts consistent with the volume and frequency of phlebotomy (Figure 1). Initial decreases in Hgb were accompanied by declines in RET counts in bari-treated RA pts. Subsequent increases in Hgb were associated with increases in RET after Wk 8 and statistically significant dose-dependent increases vs. PBO in total iron (Fe), total iron binding capacity (TIBC) and EPO. Treatment-emergent (TE) shifts in Hgb from normal to <LLN were very common in all groups without differences across groups except for ADA, which was associated with a lower incidence of TE low Hgb. TE Common Terminology Criteria for Adverse Events (CTCAE) shifts in Hgb from <grade 3 to ≥grade 3 (<4.9 and ≥4.0 mmol/L; <8.0g/dL and ≥6.5g/dL) were uncommon and occurred in similar proportions of RA pts across groups (Table 1). Permanent discontinuation of study drug due to CTCAE ≥grade 3 Hgb shifts was uncommon (0.2%).

Figure 1. Mean Change from Baseline in Haemoglobin Over 52 Weeks in Placebo-Controlled Studies



Placebo-controlled studies include studies JADA/JADY, JADC, JADN, JADV/JADY, JADX/JADY, and JADW/JADY with data up to January 1, 2016. All changes from baseline are statistically significant with the exception of PBO and BARI 4-mg at Week 24 and BARI 2-mg and 4-mg at Week 52.
*Last blood draw prior to Week 48/52 data was up to 12 weeks prior.

Table 1. Summary of Treatment-Emergent Changes in Haemoglobin

	Treatment-emergent abnormally low, n/NAR (%)	Shift from <grade 3 to ≥grade 3[a], n/NAR (%)
RA bari PBO-controlled studies through Week 24[b]		
PBO (N=1070) [PYE=393.8]	193/747 (25.8)	2/1059 (0.2)
Bari 4 mg (N=997) [PYE=409.4]	204/696 (29.3)	1/988 (0.1)
RA bari studies containing 2- and 4-mg doses[c,d]		
Bari 2 mg (N=479) [PYE=434.8]	106/343 (30.9)	3/478 (0.6)
BARI 4 mg (N=479) [PYE=477.7]	126/360 (35.0)	1/474 (0.2)
All RA bari studies[d]		
N=3464 [PYE=4214.1]	829/2451 (33.8)	16/3407 (0.5)

Abbreviations Bari=baricitinib; NAR=number at risk; PYE=patient years of exposure; RA=rheumatoid arthritis.
[a]Grade 3 is <4.9 and ≥4 mmol/L (<8.0 and ≥6.5 g/dL).
[b]Includes Studies JADA, JADC, JADN, JADV, JADW and JADX.
[c]Includes Studies JADA/JADY, JADN, JADW/JADY and JADX/JADY.
[d]Includes data up to August 10, 2015.

Conclusions: The proportions of RA pts with TE abnormally low Hgb did not differ significantly between bari and PBO. Reductions in Hgb, including to ≥grade 3, were generally not associated with adverse outcomes. Despite concerns about the impact of JAK2 inhibition on EPO signaling, following initial declines incident to phlebotomy, dose-dependent increases in EPO, Fe, and TIBC with return to baseline in RET and Hgb were observed with bari. This suggests that homeostatic mechanisms counterbalance the pharmacologic effect of JAK inhibition on EPO signaling and that bari treatment enhances iron utilisation markers associated with anaemia of chronic disease.
Disclosure of Interest: J. Kay Grant/research support from: AbbVie, Eli Lilly and Company, Pfizer, Genentech, Roche, UCB, Consultant for: Amgen, AbbVie, BMS, Eli Lilly and Company, Genentech, GlaxoSmithKline, Janssen Biotech, Merck, Novartis, Pfizer, Samsung Bioepis, Sandoz, Roche, UCB, M. Harigai Grant/research support from: BMS KK, Eisai Ltd, Ono Pharma, Takeda Ltd,

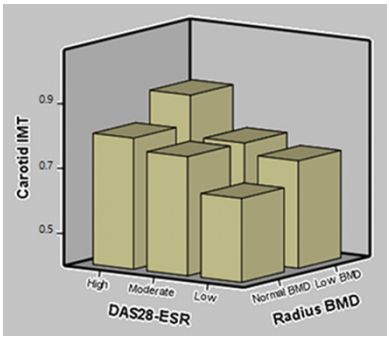
Consultant for: Eli Lilly and Company, J. Rancourt Employee of: Eli Lilly and Company, C. Dickson Employee of: Eli Lilly and Company, Y. Isaka Employee of: Eli Lilly and Company, L. Chen: None declared, T. Carmack Employee of: Quintiles, D. Hyslop Employee of: Eli Lilly and Company, D. Muram Employee of: Eli Lilly and Company, W. Macias Employee of: Eli Lilly and Company, J. Bradley Employee of: Eli Lilly and Company, E. Keystone Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Hoffmann-LaRoche, Janssen, Eli Lilly and Company, Novartis, Pfizer, Sanofi-Aventis,UCB, Consultant for: Abbott, AstraZeneca, Biotest, BMS, Crescendo Biosciene, Hoffmann-LaRoche, Genentech, Janssen, Eli Lilly and Company, Merck, Pfizer, UCB, Speakers bureau: Abbott, AstraZeneca, BMS Canada, Hoffmann-laRoche, Janssen, Pfizer, UCB, Amgen

DOI: 10.1136/annrheumdis-2017-eular.1335

FRI0093 CAROTID ATHEROSCLEROSIS IS ASSOCIATED WITH DISEASE ACTIVITY AND BONE MINERAL DENSITY IN RHEUMATOID ARTHRITIS

J.W. Kang, E.S. Lee, J.S. Eun, J.H. Kim, J.Y. Kang, G.B. Bae, N.R. Kim, S.J. Lee, E.J. Nam, Y.M. Kang. *Kyungpook National University School of Medicine, Daegu, Korea, Republic Of*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease which causes juxta-articular and generalized bone loss. Several studies revealed that bone mineral density (BMD) is associated with atherosclerosis.
Objectives: In the present study, we investigated the association between BMD and RA disease activity and the carotid atherosclerosis in RA patients based Kyungpook National University Hospital Atherosclerosis Risk in Rheumatoid Arthritis (KARRA) cohort study.
Methods: A total of 323 patients with RA, who performed dual-photon x-ray absorptiometry and carotid ultrasound, were included. We assessed RA disease activity, risk factors for atherosclerosis including hypertension, diabetes mellitus and dyslipidemia, presence of carotid plaque, carotid intima-media thickness (IMT), and BMD. BMD was measured at the lumbar spine (L-spine, L1-L4), femur neck (total femur neck) and distal forearm (total radius), and low BMD was defined as a T score of -1.0 or less.
Results: The BMD in the L-spine, femur, and radius was significantly lower in patients with carotid plaques (n=152), compared to patients without plaques (n=171) (1.014 g/cm^2 ± 0.21 vs. 1.066 g/cm^2 ± 0.18, p=0.016 for L-spine; 0.816 g/cm^2 ± 0.16 vs. 0.863 g/cm^2 ± 0.13, p<0.001 for femur; 0.542 g/cm^2 ± 0.13 vs. 0.603 g/cm^2 ± 0.12, p<0.001 for radius). The frequency of low BMD in these areas was also higher in patients with carotid plaques, compared to patients without plaques (52.7% vs. 47.5%, p=0.045 for L-spine; 56.0% vs. 44.0%, p=0.001 for femur; 60.6% vs. 39.4%, p<0.001 for radius). Carotid IMT showed a significant difference between patients with low BMD and those with normal BMD (0.84 mm ± 0.14 vs. 0.80 mm ± 0.19, p=0.025 for L-spine; 0.83 mm ± 0.15 vs. 0.80 mm ± 0.18, p=0.045 for femur; 0.85 mm ± 0.15 vs. 0.77 mm ± 0.18, p <0.001 for radius). In subgroup analysis, patients with the highest IMT quartile had a significantly lower BMD in all the regions than those with the lowest IMT quartile (61.2% vs. 37.7%, p=0.004 for L-spine; 59.5% vs. 35.1%, p=0.003 for femur; and 71.4% vs. 28.6%, p<0.001 for radius). Multivariate logistic regression analysis demonstrated that BMD at radius (OR 4.995, 95% CI [1.067–10.276], p<0.001), DAS28-ESR (OR 1.906, 95% CI [1.042–3.046], p=0.036), and dyslipidemia (OR 2.334, 95% CI [1.164–3.156], p=0.02) were risk factors for presence of carotid plaques.



Conclusions: The present study showed that carotid atherosclerosis was influenced by both disease activity and impaired bone health.
References:
[1] Im CH et al. Inflammatory burden interacts with conventional cardiovascular risk factors for carotid plaque formation in rheumatoid arthritis. Rheumatology (Oxford). 2015 May;54(5):808–15.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6387

FRI0094 TIME TO AND FACTORS ASSOCIATED WITH INITIATION OF BIOLOGICAL THERAPY WITH DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN COLOMBIA

J.E. Machado-Alba, L.F. Calvo-Torres, A.M. Bañol-Giraldo, S. Garcia-Betancurt on behalf of Grupo de Investigación en Farmacoepidemiología y Farmacovigilancia. Universidad Tecnológica de Pereira- Audifarma S.A. *Grupo de Investigación en Farmacoepidemiología y Farmacovigilancia, Universidad Tecnológica de Pereira-Audifarma S.A, Pereira, Colombia*

Background: Rheumatoid arthritis (RA) treatment is usually done with non-biological disease-modifying antirheumatic drugs (DMARDs), but the addition of a biological DMARD can be necessary. Biological drug therapy is usually prescribed following failure to achieve remission of the morbidity with one or more non-biological DMARDs. However, there is the possibility of using them as a first line in the initial phase, which there is the possibility of potentially altering its course or even reverting it to normality.
Objectives: To determine the time Colombian patients with rheumatoid arthritis (RA) are treated with non-biological disease-modifying antirheumatic drugs (DMARDs) before changing to biological therapy.
Methods: A retrospective cohort study that collected information about the start of antirheumatic treatment in patients of all ages with a diagnosis of RA until the change to biological DMARD therapy. Survival analysis using Kaplan–Meier curves, from 1 January 2007 until 31 December 2013 by SPSS 23.0 for Windows, was made.
Results: A total of 3880 patients (75.3% women) with a mean age of 51.3 years started non-biological DMARDs. After 5 years, 234 patients (6.0%) initiated biological DMARD therapy in 17.5±13.9 months. Differences in the socio demographic and pharmacological characteristics between the two groups of treatment are shown in the table 1. The use of glucocorticoids was associated with a greater risk of biological DMARD initiation (OR: 2.49; 95% CI: 1.658–3.732; p<0.001), while the use of methotrexate (OR: 0.04; 95% CI: 0.014–0.108; p<0.001) and chloroquine (OR: 0.13; 95% CI: 0.092–0.187; p<0.001) reduced the risk of initiation.

Variables	Non biological DMARDs (n: 3646)	%	Biological DMARDs (n: 234)	%
Sociodemographic				
Aged (mean ± SD)	52.2± 14.8		51.2± 16.2	
Sex (Male/Female, %)	74/160	31.6/68.4	884/2762	24.3/75.7
Women > 55 años	1364	37.4	79	33.8
Men > 45 años	580	15.9	46	19.6
Initial therapy				
Chloroquine	1485	40.7	44	18.8
Sulfasalazine	945	25.9	0	0
Methotrexate	493	13.5	4	1.7
Azatriopine	300	8.2	21	9.0
Cyclophosphamide	117	3.2	9	3.8
Cyclosporine	112	3.1	8	3.4
Others	59	1.6	4	1.7
Comedication				
Glucocorticoids	2183	59.9	199	85.0
Antihypertensives	582	16.0	52	22.2
Diuretics	281	7.7	19	8.1
Hipolipemiants	414	11.3	33	14.1
Antiplatelets	298	8.2	20	8.5
Antidiabetics	170	4.7	11	4.7
Nonsteroidal anti-inflammatory drugs	298	8.2	34	14.5
Antiulcer drugs	623	17.1	91	38.9
Thyroid hormone	200	5.5	21	9.0
Vitamin D and Calcium	283	7.8	43	18.4

Conclusions: After 5 years of non-biological DMARD therapy, 6.0% of people with RA started biological DMARDs. Receiving glucocorticoids, having any comedication, being treated in Bogota City or cities of the Colombian Atlantic coast affected the probability of switching to biological therapy in these patients.
References:
[1] Nam JL, Emery P. Is there a place for initial treatment with biological DMARDs in the early phase of RA? Best Pract Res Clin Rheumatol. 2013;27(4):537–54.
[2] Emery P, Breedveld FC, Hall S, Durez P, Chang DJ, Robertson D, et al. Comparison of methotrexate monotherapy with a combination of methotrexate and etanercept in active, early, moderate to severe rheumatoid arthritis (COMET): a randomised, double-blind, parallel treatment trial. Lancet. 2008;372(9636):375–82.
[3] Tak PP, Rigby WF, Rubbert-Roth A, Peterfy CG, van Vollenhoven RF, Stohl W, et al. Inhibition of joint damage and improved clinical outcomes with rituximab plus methotrexate in early active rheumatoid arthritis: the IMAGE trial. Ann Rheum Dis. 2011;70(1):39–46.
Acknowledgements: To Universidad Tecnológica de Pereira and Audifarma S.A.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4986

FRI0095 PILOT STUDY OF THE EARLY RHEUMATOID ARTHRITIS DIAGNOSIS PROGRAM WITH A STRUCTURED REFERRAL FORMAT

J. Jaimes-Hernandez[1], P. Aranda-Pereira[2], C.I. Melendez-Mercado[2], A. Mendoza-Fuentes[2], I. Guzman-Sanchez[2], R.M. Rodriguez-Romo[3].
[1]Rheumatology Department, ISSEMYM Toluca Medical Center, Toluca, State of Mexico; [2]Rheumatology Department, ISSEMYM, Toluca; [3]Rheumatology, Mexican College of Rheumatology, Mexico City, Mexico

Background: The delay in referral of patients with suspicion of Undifferentiated Inflammatory Arthritis (UIA), especially the Rheumatoid Arthritis (RA), from the primary care physician (PCP) to the Rheumatologist prevents diagnosing and treatment in a timely manner. Early diagnosis and treatment decreases progression and permanent joint damage. Several strategies have been proposed to improve the time to referral of patients with UIA, however there is none for early RA in specific.
Objectives: We present a pilot study for the use of a weighted construct format for the improvement of the time to referral of patients with suspicion of early RA.
Methods: Since June 2005, in clinics and hospitals, PCPs were trained for the use of the weighted construct format tool. Adult patients with less than 1year of symptoms were considered for the referral. The criteria for reference of suspicion of early RA are shown in Table 1. The patient referral was made through the counter-reference system, including the complete format and laboratory results. The patient's appointment was given within 15 business days. Once the patients were evaluated and studied in the Department of Rheumatology, they were classified with RA according to 2010 ACR/EULAR criteria when was available this criteria classification. For the demographic variables, we used descriptive and inferential statistics and for the format validation we verified the reliability, and validity of the construct and criterion tool.
Results: Between July 2005 and July 2015, 298 patients were referred to our clinic. The average referral time in the first year (2005–2006) was 34.3±20.4 days, maintaining an average of 32.1±16.8 days until 2015. There was a reduction of 74% of referral time compared to a historical reference (mean time of referral was 127.4±51.8 days, in 122 patients). 182 (62%) patients filled out the 2010 ACR/EULAR criteria. The referral format for early RA had a Cronbach alpha of 0.49, Sensitivity 85.1%, Specificity 93.5% and PPV 92.2%. The correlation between patients with early RA and the 2010 ACR/EULAR criteria was 0.765 with a $p<0.000$.
Conclusions: In this pilot study, we observed that the construct had a suitable sensitivity, specificity and PPV for a referral format. Therefore, on suspicion of early RA the referral format could be useful as a simple clinical tool for the timely referral to the Rheumatologist. On the other hand, the program implementation allowed the reduction in the referral time substantially. To implement the use of this tool in the daily clinical practice it needs to be validated with an open population and an adequate sample size

Table 1

	Criteria	Score	Total
Clinical	Polyarticular arthritis: >5 joints Small joints: proximal interphalangeal joints, metacarpophalangeal joints, metatarsophalangeal or wrist joints+ any large joint (shoulders, elbows, knees or ankles)	4	
	Morning stiffness greater than 30 minutes (>30').	3	
	Oligoarticular arthritis: < 5 joints (small and large joints).	0	
Laboratory	Rheumatoid factor (+): dilution > 1:160 or 20 IU for nephelometry or turbidimetry.	4	
	Erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP): positive (> than normal reference parameter).	3	
	Anemia: hemoglobin (Hb) ≤12.5g/dl or thrombocytosis>40x10 ^{3}/µl platelets.	1	
	Total	15	

≤ 5points low suspect, between ≥6 and ≤10 suspect, and ≥11 points highly suspect.
Clinical criteria: obtained through complete clinical history (morning stiffness: time it takes to mobilize a joint after waking up). Musculoskeletal examination should show joint swelling (swelling, tenderness, temperature increase and difficulty to mobilize).
Laboratory: obtained within the protocol that caused the patient's visit (no > 2 weeks) results must be attached.

References:
[1] Emery P,Breedveld F C,Dougados M,Kalden J R,Schiff M H,Smolen J S. Early referral recommendation for newly diagnosed rheumatoid arthritis:evidence based development of a clinical guide. Ann Rheum Dis 2002;61:290–297.
[2] Villeneuve E,Nam JL,Bell MJ,Deighton CM,Felson DT, Et al, A systematic literature review of strategies promoting early referral and reducing delays in the diagnosis and management of inflammatory arthritis. Ann Rheum Dis 2013;72:13–22.
[3] Deane KD,Striebich CC,Goldstein BL, et al. Identification of undiagnosed inflammatory arthritis in a community health fair screen. Arthritis Rheum 2009;61:1642–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2561

FRI0096 DURABILITY AND MAINTENANCE OF EFFICACY FOLLOWING PROLONGED TREATMENT WITH BARICITINIB

J.S. Smolen[1], Z. Li[2], R. Klar[3], L. Xie[4], D. Walker[4], A. Ghizdavescu[4], R. Ortmann[4], M. Dougados[5]. *[1]Medical University of Vienna, Vienna, Austria; [2]Peking University People's Hospital, Beijing, China; [3]Quintiles IMS Holdings, Inc., Durham; [4]Eli Lilly and Company, Indianapolis, United States; [5]Hôpital Cochin, Paris Descartes University, Paris, France*

Background: Baricitinib (bari) demonstrated clinical efficacy in Ph3 trials in RA patients (pts) naïve to DMARDs (RA-BEGIN[1]); and in RA pts with inadequate response to conventional synthetic DMARDs (RA-BEAM[2] and RA-BUILD[3]) or biologic DMARDs (RA-BEACON[4]).
Objectives: To evaluate durability and maintenance of efficacy over an additional 96 weeks (wks) of bari treatment.
Methods: Pts included were those randomised to bari in an originating study (OS), completed that study without rescue (52 wks in RA-BEGIN or RA-BEAM; 24 wks in RA-BUILD or RA-BEACON), and entered the long-term extension (LTE) study ≥96 wks prior to data cut-off. Durability of response was evaluated as pts achieving low disease activity (LDA) of SDAI ≤11 and minimal clinically important difference (MCID) of HAQ-DI improvement ≥0.22. Maintenance of response was evaluated as proportion of pts who had responded to bari at entry into LTE and maintained response at wk 96. Data are also provided for pts who had not responded to bari at entry into LTE who achieved response.
Results: Approximately half the pts in the durability analyses were categorised as LDA by wk 24 and the proportion of pts in the LDA category were similar or higher at wk 96. Three quarters of pts across groups demonstrated HAQ-DI improvement by wk 12 and more than half achieved MCID at wk 96. Most responders at entry into LTE maintained their response through wk 96. More than 25% of SDAI and HAQ-DI nonresponders at entry into LTE achieved response after 96 wks of treatment.
Conclusions: These data provide further evidence of the effectiveness of bari treatment in achievement of meaningful clinical control of disease activity long term.

References:
[1] Fleischmann R et al. Arthritis Rheumatol 2016.
[2] Taylor P et al. Arthritis Rheumatol 2015;67(Suppl10).
[3] Dougados M et al. Ann Rheum Dis 2017.
[4] Genovese MC et al. N Eng J Med 2016.

Abstract FRI0096 – Table 1

		RA-BEGIN Bari 4mg N=30	RA-BEAM Bari 4mg N=104	RA-BUILD Bari 2mg N=154	RA-BUILD Bari 4mg N=164	RA-BEACON Bari 2mg N=117	RA-BEACON Bari 4mg N=124
Durability of Response, n (%)							
SDAI ≤11	Wk12 OS	13 (43.3)	48 (46.2)	59 (38.3)	69 (42.1)	31 (26.5)	46 (37.1)
	Wk24 OS	18 (60.0)	59 (56.7)	87 (56.5)	106 (64.6)	40 (34.2)	56 (45.2)
	Wk52 OS	23 (76.7)	74 (71.2)				
	Wk48 LTE	23 (76.7)	77 (74.0)	98 (63.6)	106 (64.6)	54 (46.2)	62 (50.0)
	Wk96 LTE	25 (83.3)	73 (70.2)	86 (55.8)	92 (56.1)	54 (46.2)	62 (50.0)
HAQ-DI imp≥0.22	Wk12 OS	28 (93.3)	80 (76.9)	118 (76.6)	118 (72.0)	85 (72.6)	97 (78.2)
	Wk24 OS	27 (90.0)	85 (81.7)	121 (78.6)	121 (73.8)	88 (75.2)	92 (74.2)
	Wk52 OS	24 (80.0)	86 (82.7)				
	Wk48 LTE	25 (83.3)	77 (74.0)	113 (73.4)	115 (70.1)	75 (64.1)	80 (64.5)
	Wk96 LTE	26 (86.7)	80 (76.9)	98 (63.6)	105 (64.0)	58 (49.6)	79 (63.7)
Maintenance of Response at 96 wks, % (n/N')							
SDAI ≤11	R	82.6 (19/23)	81.1 (60/74)	70.9 (61/86)	66.7 (68/102)	77.5 (31/40)	77.8 (42/54)
	NR	85.7 (6/7)	43.3 (13/30)	36.9 (24/65)	36.2 (21/58)	27.8 (20/72)	27.7 (18/65)
HAQ-DI imp≥0.22	R	87.5 (21/24)	84.9 (73/86)	72.7 (88/121)	71.9 (87/121)	56.8 (50/88)	71.7 (66/92)
	NR	83.3 (5/6)	38.9 (7/18)	30.3 (10/33)	39.0 (16/41)	27.6 (8/29)	40.6 (13/32)

Data were analysed using nonresponder imputation without considering rescue status in LTE. N = number of mITT pts; N' = number of responders (R) or nonresponders (NR) at entry into LTE; n = number of pts in the specific category.

Disclosure of Interest: J. Smolen Grant/research support from: Abbvie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Speakers bureau: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Z. Li: None declared, R. Klar Employee of: Quintiles IMS Holdings, Inc., L. Xie Employee of: Eli Lilly and Company, D. Walker Employee of: Eli Lilly and Company, A. Ghizdavescu Employee of: Eli Lilly and Company, R. Ortmann Employee of: Eli Lilly and Company, M. Dougados Grant/research support from: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, Consultant for: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS
DOI: 10.1136/annrheumdis-2017-eular.1311

FRI0097 REPAIR OF JOINT DAMAGE IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS PATIENTS OCCURS BUT DOES NOT RELATE TO PREVIOUS SUPPRESSION OF INFLAMMATION; AN 8-YEARS SUB ANALYSIS IN THE BEST-COHORT

J.A. van der Pol[1], G. Akdemir[1], M. van den Broek[1], L. Dirven[1], P. Kerstens[2], W.F. Lems[3], I.M. Markusse[1], T.W. Huizinga[1], C.F. Allaart[1]. *[1]Department of Rheumatology, Leiden University Medical Center, Leiden; [2]Department of Rheumatology, Westfries Gasthuis, Hoorn; [3]Department of Rheumatology, VU Medical Center, Amsterdam, Netherlands*

Background: Joint damage in rheumatoid arthritis (RA) is thought to be irreparable. We hypothesized that in patients where inflammation is well suppressed for a long time, repair may be possible.
Objectives: To investigate whether reversal of erosions and joint space narrowing (JSN) in RA occurs and whether clinical variables predict repair.
Methods: In the BeSt study, patients with active early RA (ACR 1987 criteria, arthritis symptoms <2 years) were randomized to 4 treatment strategies, each with the aim to ensure and maintain suppression of disease activity by adjusting medication based on three-monthly calculations of the 44-joint Disease Activity Score (DAS), target ≤2.4. Radiographic joint damage was assessed yearly, using the Sharp/van der Heijde score (SHS). In this analysis, 8-years data of the study were used. Repair of erosions or JSN was defined at the individual joint level as a reduction of ≥1 SHS point compared to the previous available X-ray, present in ≥2 consecutive visits and with ≥3 out of 4 independent scorers agreeing. Radiographs were scored in random order per patient, blind for patient identity and treatment arm. Multiple logistic regressions were applied at the patient level for associations between achieving repair and maximum duration of previous remission, mean DAS until repair, previous prednisone use, previous infliximab use, anti-citrullinated protein antibody (ACPA), gender, age and randomization arm. All models were adjusted for mean joint damage over time in the group with repair. In the group without repair, the models were corrected for mean damage over time until mean time point of repair in the group with repair.
Results: Seven out of 508 patients did not have any X-ray images taken in the study. Of the remaining 501 patients, 320 had damage in at least 1 joint and thus could potentially show repair. In total, 2395 X-rays were available, on average 7.5 per patient (range 2–9). Median SHS after 8 years in these patients was 10 (IQR 4–21, range 0–234), and mean (SD) DAS from month 3 was 2.00 (0.67). Repair was seen in 17 patients, 3.3%; 10 had reduction of JSN, 6 of erosions, 1 had repair of both JSN and erosions. In 14 patients repair was seen in 1 joint, in 3 patients repair was seen in 2 joints (same time point). Mean (SD) time to repair was 44.1 (20.1) months. Ten of 17 patients (59%) had previously achieved DAS-remission, compared to 100% of the patients who at a matching time point showed no repair. Adjusted for mean SHS until repair, we found no associations with repair for duration of remission, mean DAS until repair, gender, age, presence of ACPA, or previous exposure to prednisone or infliximab (table 1). Apart from a trend towards fewer patients with repair in the initial infliximab study arm, there were no differences in any of the groups in any of the regression analyses.

Table 1. Results of multiple logistic regression models to investigate associations with repair (n=17)

	OR	95% CI	P
Duration of previous remission*	-	-	-
Mean DAS from month 3 to time of repair	1.39	0.77 - 2.51	0.270
Previous prednisone	1.09	0.385 - 3.09	0.871
Previous infliximab	0.599	0.206 - 1.74	0.347
ACPA	1.51	0.413 - 5.53	0.533
Gender	1.13	0.401 - 3.16	0.822
Baseline age	1.01	0.975 - 1.05	0.548
Randomization arm			
Sequential monotherapy	ref	-	-
Step-up combination therapy	0.797	0.231 - 2.75	0.721
Initial combination with prednisone	0.597	0.158 - 2.26	0.448
Initial combination with infliximab	0.147	0.0173 - 1.25	0.080

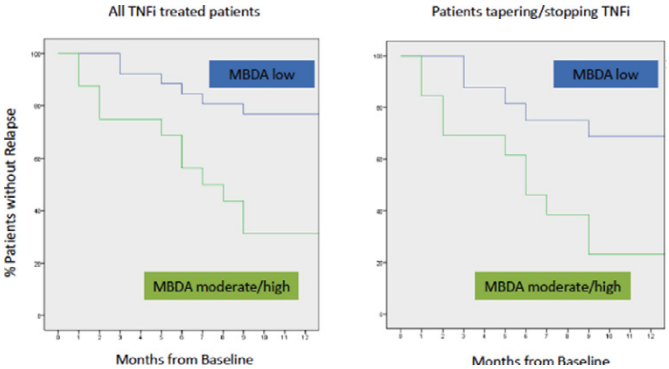
All models were adjusted for mean Sharp/van der Heijde score until repair
DAS: disease activity score, ACPA: anti-citrullinated peptide antibody
*No results due to 100% remission in non-repair comparator group

Conclusions: In this early RA cohort, during 8 years treated to target DAS ≤2.4, repair of JSN and erosions was seen in 17 patients (3.3%), which supports that repair occurs in early RA. However, repair is a rare phenomenon, and does not seem to relate to previous inflammation or other predictors in this cohort.
Disclosure of Interest: J. van der Pol: None declared, G. Akdemir: None declared, M. van den Broek: None declared, L. Dirven: None declared, P. Kerstens: None declared, W. Lems Speakers bureau: Speakersfee/advosory boards Pfizer, MSD, Eli Lilly, Abbvie, I. Markusse: None declared, T. Huizinga: None declared, C. Allaart Grant/research support from: The BeSt study was supported by a government grant from the Dutch Insurance Companies, with additional funding from Schering-Plough B.V. and Janssen B.V.
DOI: 10.1136/annrheumdis-2017-eular.2270

FRI0098 ELEVATED MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) PREDICTS RELAPSES IN RA PATIENTS IN SUSTAINED REMISSION TAPERING TUMOUR NECROSIS FACTOR INHIBITOR THERAPY- RESULTS FROM THE RANDOMIZED CONTROLLED RETRO STUDY

J. Rech[1,1], M. Hagen[1], M. Englbrecht[1], J. Haschka[2], M. Reiser[1], A. Kleyer[1], A. Hueber[1], B. Manger[1], C. Figuereido[3], J. Fogagnolo Cobra[3], H.-P. Tony[4], S. Finzel[5], S. Kleinert[6], J. Wendler[6], F. Schuch[6], M. Ronneberger[6], M. Feuchtenberger[7], M. Fleck[8], K. Manger[9], W. Ochs[10], M. Schmitt-Haendle[10], H.-M. Lorenz[11], H. Nuesslein[12], R. Alten[13], J. Henes[14], K. Krueger[15], G. Schett[1]. *[1]University of Erlangen-Nuremberg, Erlangen, Germany; [2]St.Vincent Hospital, Vinforce Study Group, Medical University of Vienna, Vienna, Austria; [3]Institutio de Rheumatologia, Sao Paolo, Brazil; [4]University of Wuerzburg, Internal Medicine 2, Wuerzburg; [5]University Medical Center Freiburg, Rheumatology and Clinical Immunology, Freiburg; [6]Rheumatology Clinical Practice Erlangen, Erlangen; [7]Rheumatology Practice and Department of Internal medicine 2, Clinic Burghausen, Burghausen; [8]Asklepios Medical Center, Department of Rheumatology and clinical Immunology, Bad Abbach; [9]Rheumatology Practice Bamberg, Bamberg; [10]Rheumatology Practice Bayreuth, Bayreuth; [11]University of Heidelberg, Medicine 5, Heidelberg; [12]Rheumatology Practice Nuremberg, Nuremberg; [13]Schlosspark Klinik, Internal Medicine/Rheumatology, Berlin; [14]University of Tuebingen, Centre for Interdisciplinary Clinical Immunolog, Tuebingen; [15]Praxiszentrum St.Bonifatius, Munich, Germany*

Background: Tumor necrosis factor inhibitors (TNFi) are the most frequently used bDMARDs in RA patients. TNFi induces remission in a substantial numbers of patients. Once remission, particularly sustained remission is achieved the question arises whether TNFi can be successfully tapered. To date biomarkers, which can help to predict if TNFi can be tapered or stopped, remain to be developed.
Objectives: To test whether residual subclinical inflammation assessed by multi-biomarker disease activity (MBDA) predicts the risk of disease relapse after tapering or stopping TNFi treatment in RA patients in sustained remission.
Methods: Sub-analysis of TNFi treated patients of the RETRO study, a randomized-controlled study in RA patients in sustained (>6 month) DAS28 remission comparing 3 different DMARD treatment strategies (continuation of full dose, 50% dose tapering, stopping after 50% dose tapering). Patients were followed over one year for the occurrence of relapses as defined by leaving DAS28-ESR remission (>2.6 units) (1). Vectra-DA tests were done in the baseline samples of all patients included into the RETRO study. MBDA score was calculated according to previously defined algorithms with low MBDA score defined as <30 units and moderate to high scores as ≥30 units (2).
Results: Of the 151 patients included in the RETRO study, 42 received TNFi treatment (mean age: 56 ys, 25 (60%) females, 78% concomitant csDMARDs; 69% ACPA/RF positive. Baseline demographic and disease specific characteristics of these patients were comparable to the non-TNFi treated patients of the RETRO study. 26/42 patients (62%) had low MBDA scores at baseline, while 16/42 (38%) had moderate/high scores. Relapse rates were significantly (chi square p=0.016) lower in RA patients with low MBDA scores (N=8 of 26; 31%) than in those with moderate/high scores (N=11 of 16; 69%) (Figure; left graph). When separately analyzing only patients tapering TNFi (N=29), relapse rates were moderate in



RA patients with low MBDA scores (N=6 of 16; 37%) but high in those with moderate/high scores (N=10 of 13; 77%) (chi square p=0.015) (Figure; right graph).

Conclusions: These data show that the majority of RA patients in sustained clinical remission with low MBDA scores can successfully taper TNFi. In contrast tapering cannot be recommended in patients with moderate to high MBDA scores, as relapse rates are high in these patients.

References:
[1] Haschka J et al. Ann Rheum Dis 2016,75;45–51.
[2] Curtis JR et al. Arthritis Care Res 2012;64:1794–803.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4787

FRI0099 PAIN REDUCTION IS ASSOCIATED WITH IMPROVED WORK PRODUCTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Michaud[1,2], B. Zhu[3], C. Gaich[3], A.M. DeLozier[3], V. Arora[3], C. Dickson[3], J.S. Smolen[4]. *[1]University of Nebraska Medical Center, Omaha; [2]NE & National Data Bank for Rheumatic Diseases, Wichita; [3]Eli Lilly and Company, Indianapolis, United States; [4]Division of Rheumatology, Medical University of Vienna, Vienna, Austria*

Background: Patients with rheumatoid arthritis (RA) indicate pain is an important aspect of disease burden and may persist despite control of disease. In a randomized, double-blind phase 3 clinical trial of baricitinib (RA-BEAM),[1] baricitinib provided significant improvement in pain reduction. It is not clear, however, how much reductions in pain impacted other aspects of life, such as work productivity.

Objectives: To assess the relationship between pain reduction and improvements, regardless of treatment, in daily activity and work productivity in patients with RA.

Methods: In this post-hoc analysis of RA-BEAM[1], pain for the intention-to-treat patients was assessed using the patient's assessment of pain (0–100 mm visual analogue scale). The Work Productivity and Activity Impairment Questionnaire-RA (WPAI-RA) instrument was used to evaluate the percentage of activity impairment due to RA (impairment in regular daily activities, N=1302), percentage of work-time missed due to RA (absenteeism, N=521), percentage of impairment while working due to RA (presenteeism, N=490), and percentage of overall work impairment due to RA (impairment in work productivity, N=490). Pain was divided into pain reduction groups (<30%, 30% – <50%, ≥50% at Weeks 12 and 24; ≥30% [Y/N] and ≥50% [Y/N] at Weeks 1 and 2). Pairwise comparisons on improvement in WPAI-RA scores between pain reduction groups at Weeks 12 and 24 were assessed by ANCOVA adjusting for region, baseline joint erosion status, and baseline values of outcome variables. Missing values were imputed using the modified last-observation carried forward method.

Results: At baseline across treatment groups, the mean values ranged from 56–58 for daily activity impairment, 12–13 for absenteeism, 42–46 for presenteeism, and 45–49 for work productivity impairment. A ≥30% reduction in pain as early as Week 1 was associated with significantly greater (p<0.001) improvement than <30% pain reduction in regular daily activity (-22.8 vs -16.0), presenteeism (-17.5 vs. -12.1), and work productivity (-16.8 vs. -11.6) at Week 12. Greater improvement was observed in most WPAI-RA scores in patients who had more pain reduction at Weeks 12 and 24; with a reduction of ≥50% in pain from baseline, the WPAI-RA scores were substantially improved at Weeks 12 or 24 for daily activity, presenteeism, and work productivity (Table).

	Pain (VAS) % reduction from baseline at Week 12			Pain (VAS) % reduction from baseline at Week 24		
Mean (SD)%	**<30%**	**30% - <50%**	**≥50%**	**<30%**	**30% - <50%**	**≥50%**
Improvement in WPAI-RA	**WPAI-RA at Week 12**			**WPAI-RA at Week 24**		
Impairment in Regular Daily Activity	-5.6 (22.2)	-17.8 (21.8)[c]	-30.1 (25.4)[cd]	-3.5 (23.6)	-17.1 (22.4)[c]	-33.2 (25.3)[cd]
Absenteeism	0.7 (28.0)	-5.2 (29.7)[b]	-3.0 (18.2)[c]	-1.8 (28.5)	-2.1 (36.1)	-2.5 (21.8)
Presenteeism	-2.8 (24.6)	-12.9 (21.1)[c]	-23.4 (24.6)[cd]	-0.2 (25.1)	-7.7 (23.1)[a]	-26.0 (25.1)[cd]
Impairment in Work Productivity	-2.3 (24.4)	-11.3 (23.5)[c]	-23.1 (26.5)[cd]	0.5 (25.6)	-5.7 (26.2)	-25.2 (28.1)[cd]

[a]p≤0.05; [b]p≤0.01; [c]p≤0.001 vs. pain reduction <30%; [d]p<0.001 vs. pain reduction 30-<50%

Conclusions: Regardless of treatment, pain reduction was associated with improved regular daily activity and work productivity in patients with RA, with larger levels of reduction related to more improvement.

References:
[1] Taylor PC, Keystone E, van der Heijde D, et al. Baricitinib Versus Placebo or Adalimumab in Patients with Active Rheumatoid Arthritis (RA) and an Inadequate Response to Background Methotrexate Therapy: Results of a Phase 3 Study. Arthritis Rheum 2015;67(Suppl 10):3928.

Disclosure of Interest: K. Michaud Grant/research support from: Pfizer, B. Zhu Employee of: Eli Lilly and Company, C. Gaich Employee of: Eli Lilly and Company, A. DeLozier Employee of: Eli Lilly and Company, V. Arora Employee of: Eli Lilly and Company, C. Dickson Employee of: Eli Lilly and Company, J. Smolen Grant/research support from: Abbvie, Janssen, Lilly, MSD, Pfizer, Roche and has provided expert advice to and/or had speaking engagements for Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Lilly, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB
DOI: 10.1136/annrheumdis-2017-eular.1345

FRI0100 DETERMINING MINIMUM CLINICALLY IMPORTANT CHANGE IN MULTI BIOMARKER DISEASE ACTIVITY SCORE ASSOCIATED WITH CLINICAL IMPROVEMENT IN METHOTREXATE NAÏVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

K. Chatzidionysiou[1], A.H. Hensvold[1], S. Saevarsdottir[1], R.J. Bolce[2], D. Chernoff[2], C.C. Hwang[2], X. Wang[2], A.I. Catrina[1]. *[1]Karolinska University and Institutet, Stockholm, Sweden; [2]Crescendo Bioscience Inc., South San Francisco, United States*

Background: The Multi-Biomarker Disease Activity (MBDA) score is a validated tool that quantifies 12 biomarkers to assess disease activity in rheumatoid arthritis (RA) patients. Many studies have demonstrated usefulness of the score for assessing RA disease activity.

Objectives: To determine minimum clinically important change in MBDA score (ΔMBDA) from baseline (BL) to Month 3 (M3) associated with clinical improvement (decrease in DAS-ESR >1.2) in early RA patients after initiating methotrexate (MTX).

Methods: We evaluated the MBDA test in patients from one of the sites participating in the Solna Epidemiological Investigation of RA (EIRA) cohort. EIRA patients were eligible if they were ≥18 years; RA diagnosis within 12 months of symptom duration; had serum and clinical assessments at BL and M3; and clinical follow-up data in the Swedish Rheumatology Quality Register. Patients naïve to disease modifying anti-rheumatic drugs who received MTX were included. Kruskal-Wallis was used to test the null hypothesis that medians of ΔMBDA scores of 3 EULAR response groups are equal. Receiver operating characteristic (ROC) analysis was performed. The optimal threshold of ΔMBDA associated with DAS28-ESR improvement (decrease in DAS-ESR >1.2 at M3) was determined by Youden criterion maximizing sum of sensitivity and specificity.

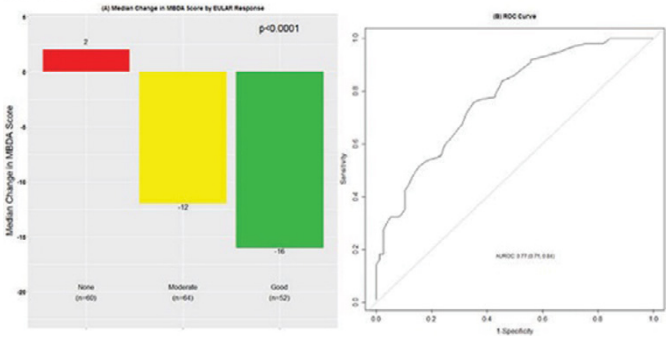
Results: 176 patients were included: 72% women, mean age 51 (SD: 11.7) years, mean DAS28-ESR score 5.6 (SD: 0.99); 51% had ESR <28 mm/hr, 66% were anti-CCP2+, and 22% received prednisone. Mean BL MBDA score was 56.8 (SD: 14.7) with 8 (5%) patients in low (<30), 29 (16%) patients in moderate (30–44) and 139 (79%) patients in high MBDA disease activity categories. Median MBDA scores for patients with no EULAR response worsened by 2 points and for patients with moderate and good response improved by 12 and 16 points, respectively (p<0.0001 across groups, Fig 1A). Median MBDA scores improved by 10 points for all patients and 15 points in patients with a DAS28-ESR decrease >1.2. The best combination of sensitivity and specificity to achieve a DAS28-ESR decrease >1.2 was provided by a ≥8 point MBDA score improvement (Fig 1B). A similar result was obtained using the bootstrap method. AUROC was 0.77 (95% CI: 0.71, 0.84). 125 patients (71%) had concordance between DAS28-ESR improvement and ΔMBDA improvement at the optimal threshold (Table 1).

Table 1. Performance Measures (95% CI) Based on Optimal Threshold of ΔMBDA Score from BL to M3 Associated with DAS28-ESR Improvement

Improvement		DAS28-ESR (decrease >1.2)		
		Yes	No	Total
MBDA (optimal threshold: improvement ≥8 points)	Yes	75	27	102
	No	24	50	74
	Total	99	77	176

Sensitivity: 0.76 (0.66, 0.83); Positive predictive value: 0.74 (0.64, 0.81); Specificity: 0.65 (0.54, 0.75); Negative predictive value: 0.68 (0.56, 0.77).r Concordance rate: 71%.

Figure A) Median Change in MBDA Score by EULAR Response; B) Receiver Operating Curve (ROC) to Determine the Optimal Threshold of Change in the MBDA Score Associated with Clinical Improvement (ΔDAS28-ESR Decrease >1.2)



Conclusions: The optimal threshold of ΔMBDA score associated with a clinically relevant decrease of DAS28 was 8 points. Using this threshold, the MBDA test is informative to detect clinical improvement. Thus, based on these results improvement in MBDA score ≥8 points at M3 after initiating MTX is indicative of meaningful clinical improvement.

Disclosure of Interest: K. Chatzidionysiou Consultant for: AbbVie, Pfizer, Eli Lilly, UCB, Roche, A. Hensvold: None declared, S. Saevarsdottir: None declared, R. Bolce Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., D. Chernoff Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., C. Hwang Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., X. Wang Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., A. Catrina Grant/research support from: Roche, Abbvie, Consultant for: BMS, GSK, Pfizer, Roche, Lilly, Abbvie
DOI: 10.1136/annrheumdis-2017-eular.5534

FRI0101 RA IN MALE CARPENTERS: OCCUPATIONAL WOOD DUST EXPOSURE INCREASES ACPA AND RF SEROPOSITIVITY AND SIGNIFICANTLY RAISES RF TITRES

K. Bellis[1], M. Whallett[2], D. Murphy[1,2], D. Hutchinson[1,2]. [1]*Rheumatology, Royal Cornwall Hospital;* [2]*University of Exeter Medical School, Cornwall Campus, Truro, Cornwall, United Kingdom*

Background: Wood dust has been hypothesised as a trigger in RA. Exposure may activate peptidyl arginine deaminase through exposure to silica and carbon nanoparticles,[1] stimulating RF autoantibody production.[2] Though non-silica dusts have shown increased RA risk in construction workers, wood dust exposed individuals were excluded from analysis in a recent large registry study.[3]
Objectives: To analyse the autoantibody status of male RA wood workers in Cornwall, UK, compared to matched RA controls with no occupational dust or fume exposure.
Methods: All male RA patients were sent an occupational questionnaire, detailing current occupation, last occupation (if retired) and other occupations for >1 year. Telephone follow up was completed to minimise missing data. 41/720 (6%) patients died during the study period (22 months). 39/720 (5%) were excluded due to incomplete data. 147/640 (23%) had exposure to wood dust including other dust co-exposures, with 44/147 (30%) indentifying wood dust as their primary occupational exposure as carpenters, approximately seven times higher than expected given UK employment census data. This cohort was matched to 102 RA controls with no dust or fume exposure for age +/- 5 years, sex and index of multiple deprivation (IMD) +/- 1 decile. RF titres were compared via 2 tailed Mann Whitney U test, and ACPA seropositivity was compared using a Z test of 2 proportions.
Results: No significant differences were seen in median age between woodworker cases (median 59 years IQR 50–63), and controls (median 58 years IQR 48–65). Woodworker never smokers demonstrated significantly higher seropositivity rates for both RF and ACPA than respective controls, and RF titres were significantly higher amongst woodworkers irrespective of smoking (Table 1). Median smoking rates were not significantly different between cohorts: woodworkers median pack years 23.5 (IQR 14.75–36), control median pack years 20.5 (IQR 10.25–32.75).

Table 1. Seropositivity rates and RF levels for woodworkers vs. controls

	Median RF (IQR)	ACPA+ (%)
Control never smokers (n=40)	16 (IQR 6.7–47.2)*	19/40 (48%)***
Control ever smokers (n=62)	68.9 (IQR 20.65–167.58)**	46/62 (74%)****
Wood worker never smokers (n=8)	86.4 (IQR 19.5–230.3)*	7/8 (88%)***
Wood worker ever smokers (n=36)	156.1 (IQR 54–321.1)**	29/36 (81%)****

*p<0.04; **p<0.01; ***p<0.04; ****p= not sig.

Conclusions: Wood dust exposed RA patients are more likely to be seropositive. Sequential environmental insults of smoking and wood dust exposure have an additive effect on rheumatoid factor levels, conferring increased disease severity. Further studies are needed to determine if occupational wood dust exposure causes RA.
References:
[1] Murphy D, Sinha A, Hutchinson D. Wood Dust: A Trigger for Rheumatoid Arthritis? Am J Med 2015;128:e35.
[2] Hubbard R, Lewis S, Richards K, Johnston I, Britton J. Occupational exposure to metal or wood dust and aetiology of cryptogenic fibrosing alveolitis. Lancet 1996;347:284–9.
[3] Blanc PD, Jarvholm B, Toren K. Prospective risk of rheumatologic disease associated with occupational exposure in a cohort of male construction workers. Am J Med 2015;128:1094–101.
Acknowledgements: Cornwall Arthritis Trust.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3733

FRI0102 ULTRASOUND AND MRI DURING FLARES OF PALINDROMIC RHEUMATISM REVEAL A DISTINCT PHENOTYPE EVEN IN IMMINENT RA

K. Mankia[1], M.-A. D'Agostino[1], R. Wakefield[1], G. Eugenio[1], L. Horton[1], J. Nam[1], A. Grainger[2], P. Emery[1]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine and Nihr Leeds Musculoskeletal Biomedical Research Unit;* [2]*Radiology, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Palindromic rheumatism (PR) is a recurrent, self-abortive arthritis and/or peri-arthritis which progresses to RA in up to 50% of patients, especially those that are anti-CCP positive (1). Whether PR is truly a prodrome of RA or a distinct syndrome is unclear; the pathological phenotype of PR flare, and whether this changes when RA is imminent, remains unknown
Objectives: To describe the clinical and imaging (US and MRI) phenotype during PR flares and to determine whether this changes in PR patients with imminent RA. We hypothesised PR patients with imminent RA would have a RA phenotype during flare
Methods: Patients were recruited from a prospective PR cohort. PR flares were defined as ≥2 of pain, swelling, erythema in or around ≥1 joint, that later normalised. Clinical details were recorded during flares. Blinded US assessment (wrists, MCPs, PIPs, elbows, knees, MTPs, ECUs and 2nd-5th finger flexor tendons) was performed during and between flares. Synovitis, tenosynovitis, subcutaneous oedema, peri-articular inflammation and peri-tendinous oedema were reported at each joint. Where possible, MRI was also performed on the most symptomatic region during flare. Patients were followed for progression to RA
Results: US was performed in 22 patients during flare. 19 patients also had non-flare US. Mean age was 49 yrs. 16/22 (73%) were anti-CCP+ and 6/22 (27%) anti-CCP-. Six (27%) patients developed RA (mean 23 weeks post flare); these patients had higher frequency of flares and absence of flare trigger (figure) but no difference in distribution of flaring joints. *The flare US* showed grey scale (GS) synovitis in 13/22 (59%) patients, power Doppler (PD) synovitis in 4/22 (18%) and no erosions. 12/22 (55%) patients had peri-articular inflammation and/or subcutaneous oedema; in 6 patients this was without synovitis/tenosynovitis. Tenosynovitis and/or peri-tendinous oedema were present in 6/22 (27%) patients. Non-flare US demonstrated fewer abnormalities with improvement post flare. In 5 patients multiple flares were imaged with variable US abnormalities identified. The US flare phenotype did not differ (from non-progressors) in patients who progressed to RA, with PD synovitis present in only 17% (table 1) contrasting with our early RA cohort where PD synovitis occurred in 73% of patients (2). MRI was performed on 8 patients (2 flares imaged in 1 patient) and detected more pathology than US. Bone marrow oedema (BME) was found in only 1 patient. No erosions were seen.

Table 1

US abnormality	Progressed to RA (n=6)	Not progressed to RA (n=16)
PD synovitis	1 (17%)	3 (19%)
GS synovitis	2 (33%)	10 (63%)
Tenosynovitis	1 (17%)	4 (25%)
Peri-tendinous oedema	0 (0%)	2 (13%)
Peri-articular inflammation	1 (17%)	7 (44%)
Subcutaneous oedema	3 (50%)	6 (38%)

		Progressed to RA (n=6)	Not progressed to RA (n=16)
Anti-CCP positive		5 (83%)	11 (69%)
Disease duration (yrs), median (IQR)		2.6 (1.8-9.2)	3.1 (1.1-7.4)
Frequency of flares (per yr), median (IQR)		25 (12-50)	9 (5-23)
Flare Trigger identifiable?		0 (0%)	7 (44%)
	Mechanical	0 (0%)	4 (57%)
	Emotional Stress	0 (0%)	3 (43%)
Flare symptoms			
	Joint pain	6 (100%)	15 (94%)
	Joint swelling	5 (83%)	15 (94%)
	Skin colour change	6 (100%)	14 (88%)
Number of joints involved in the flare, median (IQR)		2 (1-5)	2 (1-4)
CRP (mg/L), median (IQR)		10.8 (6.0-31)	9.0 (2.2-41.3)

Conclusions: PR flares have a distinct imaging phenotype characterised by peri-articular inflammation and subcutaneous oedema, often without synovitis. The low prevalence of PD synovitis, BME and erosions distinguishes PR from RA. PR patients with imminent RA have no triggers and more frequent flares, but retain the distinct PR phenotype. This suggests distinct pathological mechanisms in PR and should be of value for potential therapeutic interventions.
References:
[1] Russell AS et al.J Rheumatol 2006.33(7):1240–2.
[2] Horton SC et al.Rheumatol 2016;55:1177–87.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6237

FRI0103 CONTRIBUTION OF SUBJECTIVE DISEASE ACTIVITY SCORE 28 (DAS28) COMPONENTS TO THE RESPONSE TO TREATMENT OF RHEUMATOID ARTHRITIS

K.M. Son[1], S.Y. Lee[2], Y.I. Seo[2], J.-E. Choi[3], H.A. Kim[2]. [1]*Hallym University Dongtan Sacred Heart Hospital;* [2]*Hallym University Sacred Heart Hospital, Gyeonggi-Do;* [3]*Ewha womans University, Seoul, Korea, Republic Of*

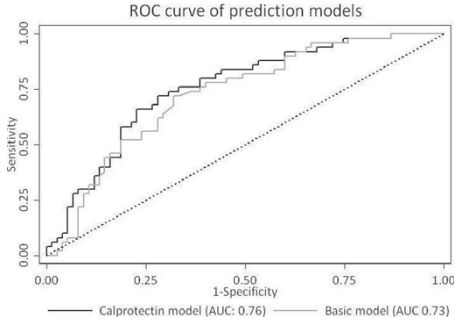
Background: Some patients with rheumatoid arthritis (RA) do not respond adequately to treatment.
Objectives: We investigated the contributions made by the subjective components of the disease activity score 28 (DAS28) to the treatment response of RA. In addition, factors associated with poor response to treatment at 6 months, despite normalization of objective measures, were examined.

Methods: A total of 426 newly diagnosed RA patients treated from August 2011 to December 2014 were included. The DAS28-P score (the subjective components of the DAS28 relative to the total components) was calculated as DAS28-P = 0.56*sqrt(TJC28) + 0.014*(VAS-GH) / 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.78ln(ESR) + 0.014*(VAS-GH). The EULAR response was assessed after 6 months of treatment. Of those who failed to attain good EULAR responses, those for whom the objective measures (the ESR, the CRP level, and swollen joints) were normalized were defined as having failed treatment because of subjective measures.
Results: The mean age of all patients was 54 years and 79% were female. The median (IQR) DAS28 score at baseline was 4.8 (4.04–5.49) and that after 6 months of treatment 3.21 (2.41–3.95). Good responders (according to the EULAR criteria) numbered 180 (38.9%), moderate responders 150 (32.4%), and non-responders 96 (20.7%). The DAS28-P score fell significantly from baseline to 6 months in good (0.43 versus 0.28, $p<0.001$) and moderate responders (0.44 versus 0.4, $p=0.003$), but not in non-responders (0.43 versus 0.45, $p=0.727$). Younger age, a lower DAS28 score, and a lower DAS28-P score at baseline were related to a good EULAR response. Subjects who failed to respond because of subjective measures tended to have higher DAS28-P scores at baseline.
Conclusions: We found that RA patients with high DAS28-P scores, reflecting subjective measures, were less likely to achieve good EULAR responses 6 months after treatment initiation and tended not to be classified as good responders despite normalization of objective measures.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1588

FRI0104 NO ADDED PREDICTIVE VALUE OF SERUM CALPROTECTIN FOR TREATMENT RESPONSE TO ADALIMUMAB OR ETANERCEPT IN RA PATIENTS

L. Tweehuysen[1], N. den Broeder[1], L.A.B. Joosten[2], T. Vogl[3], F.H.J. van den Hoogen[1,4], R.M. Thurlings[4], A.A. den Broeder[1,4]. *[1]Rheumatology, Sint Maartenskliniek; [2]Internal Medicine, Radboudumc, Nijmegen, Netherlands; [3]Immunology, University of Münster, Münster, Germany; [4]Rheumatology, Radboudumc, Nijmegen, Netherlands*

Background: Approximately 60% of RA patients do not achieve good clinical response after 6 months of treatment with a TNF inhibitor (TNFi).[1] To date, no clinically useful baseline biomarkers have been found to predict response.[2] Calprotectin (a heterodimer of S100A8/S100A9) was shown to be modestly predictive for treatment response to adalimumab (ADA) (area under the curve (AUC): 0.69) while no difference in calprotectin levels was found between responders and non-responders in RA patients treated with etanercept (ETN) and methotrexate.[3,4]
Objectives: To assess the added predictive value of serum calprotectin for clinical response after 6 months treatment with ADA or ETN in RA patients.
Methods: RA patients starting treatment with ADA or ETN in the BIO-TOP study (a prospective cohort study) were included. Patients who discontinued TNFi treatment within 2 months were excluded from analysis. Serum calprotectin was measured at baseline using ELISA. EULAR response was measured at 6 months (good versus moderate/no response). Discontinuation of TNFi before 6 months was regarded as non-response (in case of lack of effect) and clinical response at 3 months was carried forward (when stopped for other reasons). First calprotectin levels were correlated cross-sectionally with several clinical baseline markers. Thereafter receiver-operator-characteristic (ROC) curves were created for ADA and ETN separately. Finally logistic prediction models (basic model and calprotectin added model) were created using backward selection, including baseline characteristics and calprotectin levels to examine the added predictive value of calprotectin.
Results: Data on calprotectin levels and EULAR response were available for 125 patients (ADA (n=50), ETN (n=75)) with 40% of patients achieving EULAR good response. Responders showed significantly higher calprotectin levels at baseline: 985 ng/mL (p25-p75: 558–1417) versus 645 ng/mL (p25-p75: 415–973) (p=0.04). Calprotectin levels were significantly correlated to DAS28-CRP (Spearman $\rho=0.32$, $p<0.01$) and C-reactive protein (CRP) levels (Spearman $\rho=0.57$, $p<0.01$) and significantly higher in rheumatoid factor positive patients (p=0.03). No significant correlation was found between calprotectin and age, gender or ACPA positivity. The AUC for serum calprotectin in the ADA and ETN group were 0.68 (95% CI: 0.49–0.88) and 0.49 (95% CI: 0.35–0.63), respectively. The basic model (backward selected variables: baseline DAS28-CRP and medication used (ADA versus ETN)) showed an AUC of 0.73 (95% CI: 0.64–0.82). The calprotectin added model performed similarly with an AUC of 0.76 (95% CI: 0.67–0.84) (p=0.27).



Conclusions: Serum calprotectin is modestly predictive for EULAR good response to ADA but not ETN treatment after 6 months in RA patients. However, calprotectin does not provide additional predictive value over a basic clinical prediction model.
References:
[1] Hetland et al. Arthritis Rheum 2010;62(1):22–32.
[2] Cuppen et al. Rheumatology (Oxford) 2016;55(5):826–39.
[3] Choi IY et al. Ann Rheum Dis 2015;74(3):499–505.
[4] Obry A et al. PLoS One 2014;9(12):e115800.
Disclosure of Interest: L. Tweehuysen: None declared, N. den Broeder: None declared, L. Joosten: None declared, T. Vogl: None declared, F. van den Hoogen Consultant for: Biogen, Celltrion, Janssen, Mundipharma and Sandoz, R. Thurlings: None declared, A. den Broeder Consultant for: Amgen
DOI: 10.1136/annrheumdis-2017-eular.3751

FRI0105 FLUCTUATING, UNPREDICTABLE AND CHALLENGING: HOW PAIN, FATIGUE AND SLEEP DISTURBANCE IMPACT QUALITY OF LIFE IN PEOPLE WITH RHEUMATOID ARTHRITIS

V. Short[1], J. McBeth[1], K.L. Druce[1], S. Moore[2], W. Dixon[1], S. Kyle[3], M. Lunt[1], L. Cordingley[4]. *[1]Arthritis Research UK Centre for Epidemiology, University of Manchester; [2]Research User Group, NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester University Hospitals NHS Foundation Trust, Manchester; [3]Sleep & Circadian Neuroscience Institute, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford; [4]Division of Musculoskeletal and Dermatological Sciences, University of Manchester, Manchester, United Kingdom*

Background: Qualitative studies of patient experiences have provided useful insights into how rheumatoid arthritis (RA) affects quality of life (QoL). RA threatens self-image and feelings of independence, reduces personal control, and is associated with difficulty in juggling self-management alongside pre-existing demands of work, home and family life. Pain, fatigue, sleep problems and low mood are commonly reported by patients and perceived as particularly troublesome aspects of RA. We wanted to know whether these symptoms of RA were viewed as the key drivers of reported changes to QoL.
Objectives: To explore RA patients' perceptions of RA-related pain, fatigue, sleep problems and mood, and their impact on QoL.
Methods: Participants, recruited through RA charities across England, were purposively sampled to include a broad range of current ages and ages at onset of RA. Eleven individuals with RA were interviewed either in a group interview (three participants) or individual semi-structured interviews (eight participants). The interview topic guide was developed in consultation with patient representatives. Interviews were audio-recorded and transcribed in full. Interview data were analysed using inductive latent thematic analysis.
Results: All participants were female, aged 36–75 years. Disease duration ranged from five months to 31 years.
Pain, fatigue, poor sleep and low mood were all attributed to RA, and viewed as having wide-ranging impacts on QoL. Participants saw the bidirectional nature of relationships between these four symptoms as particularly challenging. For example, reduced sleep led to increased pain and vice versa.
Themes included: "*Fluctuating symptoms*" referring to the impact of the significant changes in mood, fatigue or pain which can occur within a single 24 hour period during "an RA flare"; "*The unpredictability of symptoms*" was viewed as emotionally draining, anxiety-provoking and undermined both short and long-term plans; "*Challenging*" described both the symptoms and the need to anticipate potential daily challenges in the context of current levels of symptoms.
Most were able to articulate the attitudinal, practical and emotional strategies which could facilitate adaptation to living with RA such as the need to maintain optimism, a focus on what could realistically be achieved, day-to-day cognitive flexibility and practical support.
Pain, fatigue and changes to sleep patterns were viewed as affecting the following aspects of QoL; ability to work effectively, family and social relationships, self-worth, ability to feel "in control", threats to future plans and appearance. The appearance theme included a desire not to be viewed as ill or "disabled", weight-gain and self-consciousness.
Conclusions: Daily and hourly variations in pain, fatigue and low mood are challenging for individuals with RA. The unpredictable nature of RA often was associated with anticipatory anxiety and mood fluctuations within the day. However, despite this the importance of positivity and acceptance were identified as mitigating some of the impact RA was having on QoL.
Acknowledgements: This study was funded by an Arthritis Research UK project grant (Project number 21188)
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1849

FRI0106 RESULTS OF A SYSTEMATIC LITERATURE REVIEW OF PROGNOSTIC FACTORS IN RHEUMATOID ARTHRITIS AS A BASIS FOR A PROSPECTIVE RHEUMATOLOGISTS SURVEY

L. Carmona[1], T. Otón[1], A. Royo[2], J.L. Baquero[3], S. Luján[2], S. Muñoz-Fernández[4]. *[1]Instituto de Salud Musculoesquelética; [2]Medical Dpt., Bristol-Myers Squibb; [3]Departamento Científico, Scientia Salus; [4]Rheumatology, Hospital Universitario Infanta Sofía, Universidad Europea, Madrid, Spain*

Background: Selecting the most appropriate therapy for each patient with rheumatoid arthritis (RA) is crucial in order to prevent joint damage, particularly in patients with rapidly progressing disease. The literature on prognostic factors is tremendous, being practical to summarize which factors are most strongly associated with a particular outcome and what is the utility that rheumatologists assign to these factors.
Objectives: To identify well established factors predicting long-term outcomes in RA, as the basis for a survey.
Methods: The identification of the factors was performed via an overview of systematic reviews studying prognostic factors in RA, followed by scoping reviews for individual factors. All searches were conducted in PubMed. In order to be included in the overview, the study had to be a systematic review of prognostic factors of any of the following outcomes: disability, mortality, remission, response to treatment, or radiological damage. All factors identified, in positive or negative association with the selected outcomes, were compiled in a matrix of factors * outcomes. Subsequent scoping literature reviews were performed for each combination of the matrix.
Results: The overview of systematic reviews allowed the identification of 36 prognostic factors (see Table 1).

Table 1. Prognostic factors identified in the overview of systematic reviews

Outcomes	Prognostic factors	
Disability	Genetic markers	Genetic polymorphisms
	Quality of life index	HAQ
Mortality	Genetic markers	Shared epitope
	Medical history	Lung disease
No remission	Medical history	Clinical Presentation
		Advanced age
		Age at disease onset
		Duration of disease
		Tobacco
		Obesity
		Comorbidities
		Disease activity
		Monotherapy
		Biological treatment
		Response to treatment
	Biomarkers	RF
		ACPA
		RFA
		IL2
		RANKL
		Vitamin D
	Radiological data	Residual synovitis by US
		Scintigraphy
		MRI
	Treatment	Treat to target
		Remission
No response to treatment	Biomarkers	Calprotectin
		RF
	Treatment	Treatment Failure
Structural damage	Genetic markers	Shared epitope
		Polymorphisms
	Radiological data	Erosions
	Biomarkers	Calprotectin
		RF
		ACPA
		Composite activity indices
	Treatment	Minimum treatment
		Combination Therapy Effect
		Recruitment time in clinical trials

After a round of discussions, we decided to remove all factors depending on treatment or study methodology for the scoping reviews, considering that they could not properly be considered prognostic factors but modifiers. Following the scoping reviews, we obtained a list of studies of prognostic factors, with methodological characteristics and 27 reviews of specific prognostic factors and outcomes. With this information, a survey addressed to practicing rheumatologists was developed to test how often they use the various factors to make long-term predictions, and how strong they think the association with outcome is.
Conclusions: We have analyzed and compiled a summary of prognostic factors published in RA and their predictability of long-term outcomes. This may act as a reference for cross-factor comparison and evidence-based risk assimilation and serve as a basis of surveying the value of such factors.
Acknowledgements: This study was funded by Bristol-Myers Squibb.
Disclosure of Interest: L. Carmona Grant/research support from: BMS, T. Otón Grant/research support from: BMS, A. Royo Employee of: BMS, J. L. Baquero Grant/research support from: BMS, S. Luján: None declared, S. Muñoz-Fernández Grant/research support from: BMS
DOI: 10.1136/annrheumdis-2017-eular.4765

FRI0107 DEVELOPMENT OF A PREDICTIVE MODEL FOR RHEUMATOID ARTHRITIS MORTALITY USING RANDOM SURVIVAL FOREST

L. Rodriguez-Rodriguez[1,2], J.M. Lezcano[3], E. Soudah[4], J.Á. Jover[1], I. González-Álvarez[5,6], F. Salazar[4], L. Abásolo[1,2]. *[1]Rheumatology, Hospital Clínico San Carlos; [2]San Carlos Health Research Institute, Madrid, Spain; [3]Rheumatology, San Carlos Health Research Institute; [4]CIMNE-Madrid; [5]La Princesa Health Research Institute; [6]Rheumatology, Hospital de la Princesa, Madrid, Spain*

Background: Different machine learning methods have been used to develop predictive models of high quality and precision [1]. Among them, Random Survival Forests (RSF) has been proposed as an alternative to traditional survival models [2], being able to overcome most of the limitation of traditional survival techniques, such as Cox proportional hazards models.
Objectives: Our objective was to develop and internally validate a predictive model for rheumatoid arthritis (RA) mortality using Random Survival Forests (RSF).
Methods: Retrospective longitudinal study involving 1,461 patients diagnosed with RA between January 1994 and August 2011, and followed at the outpatient clinic of the Rheumatology Department of the Hospital Clínico San Carlos (Madrid, Spain) until death or September 2013. Demographic and clinical-related variables collected during the first two years after disease diagnosis were used. RSF models were developed, based on 1,000 trees. 100 iterations of each model were performed to measure the mean and standard deviation (SD) of the predictive error and the integrated Brier score (IBS). Missing values were imputed using the function implemented by the *randomForestSRC* package [3]. The predictive capacity of the variables was assessed using the "variable importance" (VIMP). Two models were constructed using the log-rank (M_{LG}) or log-rank score (M_{LGS}) splitting rules. The model with the lowest prediction error was selected. Next, those variables with negative VIMP were excluded and a final model developed.
Results: 148 patients died (10.1%). M_{LG} showed the lowest prediction error. All variables exhibited a positive VIMP. Final model showed a mean (SD) prediction error and IBS of 0.187 (0.002) and 0.150 (0.003) respectively. The most important predictor variables were age at diagnosis, median erythrocyte sedimentation rate and number of hospital admissions in the first 2 years after RA diagnosis.
Conclusions: We developed an accurate and precise model for RA mortality using RSF. Age and disease activity showed the highest influence in mortality.
References:
[1] Churpek MM, Yuen TC, Winslow C, Meltzer DO, Kattan MW, Edelson DP. Multicenter Comparison of Machine Learning Methods and Conventional Regression for Predicting Clinical Deterioration on the Wards. Crit Care Med. 2016;44: 368–74.
[2] Ishwaran H, Kogalur UB, Blackstone EH, Lauer MS. Random survival forests. Ann Appl Stat. 2008;2: 841–860.
[3] Ishwaran H, Kogalur U. Random Forests for Survival, Regression and Classification (RF-SRC) [Internet]. 2016 [cited 15 Dec 2016]. Available: https://cran.r-project.org/package=randomForestSRC.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6139

FRI0108 TIME TO FIRST TREATMENT IS ASSOCIATED WITH A REFRACTORY COURSE OF RHEUMATOID ARTHRITIS

M. Bécède[1], F. Alasti[1], L. Haupt[2], A. Kerschbaumer[1], U. Landesmann[1], G. Supp[1], J. Smolen[1], D. Aletaha[1]. *[1]Department of Internal Medicine 3, Division of Rheumatology, Medical University of Vienna; [2]Hietzing Hospital, Vienna, Austria*

Background: It is an ongoing matter of research, whether the natural course of rheumatoid arthritis (RA) can be altered by an early intervention, a concept historically referred to as the "window of opportunity" (1). So far, only short-term disease activity outcomes have been investigated (e.g. "remission off drugs"), which are, however, inherently affected by the unknown rate of underlying rate self-limiting disease. It is unclear, whether among those, who eventually develop RA, the disease course is really affected by the timing of their initial treatment.
Objectives: To explore whether the long-term course of RA is different according to the delay of initial treatment.
Methods: Based on a longitudinal observational dataset, we initially identified a group of patients with an observed refractory disease, we defined presenting with ongoing moderate or high disease activity (by the Simplified Disease Activity Index, SDAI), despite at least three courses of DMARDs, of which at least on course was a biological compound. To ensure that sufficient time had been allowed for the previous treatments to be exert their non-effects, we also required these patients to have total treatment time of at least 18 months in accordance with treat to target strategy (3 x 6 months).
We identified 399 patients with a treatment time of at least 18 months. 48 patients were excluded despite fulfilling the disease activity criteria, because they haven't experienced enough treatment courses, or had received a biological compound yet, to claim refractory disease as per our criteria above. We could include 69 refractory and 282 non-refractory patients in our analyses and then performed

logistic regression analysis to assess the effects of different characteristics at baseline, including disease duration, on becoming refractory.

Results: By comparing patient characteristics (Table 1), more of the patients, who later will become refractory, are female (94.2% Vs 73.4%, p>0.001), have higher baseline disease activity (SDAI of 25.5 vs 17.7, p<0.001), and longer delay of the initial treatment from symptom onset (3.17 Vs 1.34 years, p=0.001).

The multivariable logistic regression model confirmed that a longer delay of first treatment is independently afflicted with a higher probability of a refractory disease course at a later stage. This model was adjusted for disease activity at baseline and gender (p<0.001, Figure 1). With increasing treatment delay, the chance of a dire disease course rises by approximately 1% every 6 months.

Table 1. Baseline characteristics in refractory and non-refractory patients

Baseline Descriptive	ReRA (n=69)	non-ReRA (n=282)	Sig.
% Female	94.2	73.4	<0.001
% RF +	56.5	62.1	0.398
% ACPA +	60.9	61.0	0.985
Time to Treatment*	3.17 (4.10)	1.34 (2.70)	0.001
SDAI	25.54 (12.24)	17.70 (12.17)	<0.001
CRP†	2.02 (2.30)	1.80 (2.02)	0.435
SJC 28	6.42 (5.35)	4.64 (4.72)	0.009
TJC 28	9.22 (6.98)	4.35 (5.40)	<0.001
EGA‡	37.78 (20.49)	28.77 (21.40)	0.002
PGA‡	55.19 (26.67)	41.42 (26.67)	<0.001

*years; †mg/dl; ‡100mm VAS scale.

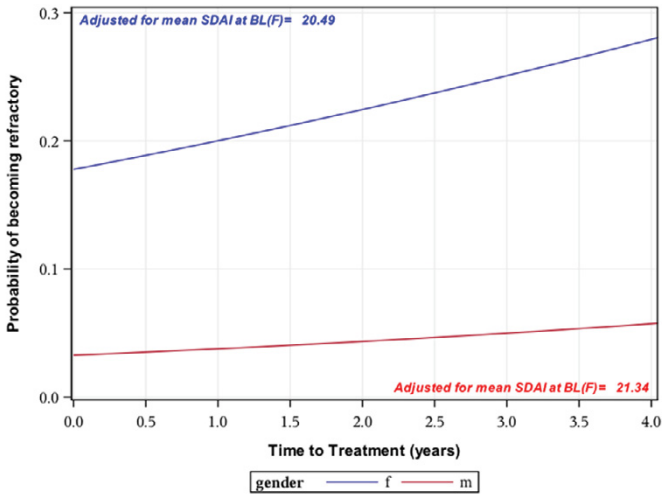


Figure 1: Predicted probabilities for becoming refractory depending on time to first treatment adjusted for baseline disease activity levels and gender.

Conclusions: Our data suggest that delay to initial treatment in RA affects the long-term course of RA. Earlier treatment initiation thus may change the severity of RA.

References:

[1] van Nies, J.A., et al., What is the evidence for the presence of a therapeutic window of opportunity in rheumatoid arthritis? A systematic literature review. Ann Rheum Dis, 2014. 73(5): p. 861–70.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3946

FRI0109 SHORT-TERM MONITORING OF SONOGRAPHIC CHANGES INDUCED BY A CORTICOSTEROID INJECTION IN METACARPOPHALANGEAL JOINT OF RHEUMATOID ARTHRITIS PATIENTS: A PILOT STUDY

M. Di Carlo, D. Roia, A. Di Matteo, F. Salaffi, E. Filippucci, W. Grassi.
Rheumatology Department, Università Politecnica delle Marche, Jesi, Italy

Background: Intra-articular corticosteroid injection is a well-established procedure in the daily practice since many decades [1]. High-resolution ultrasound (US), considered as *in vivo* microscopy, has the potential to help to understand how drugs develop their anti-inflammatory properties inside the articular space [2].

Objectives: To provide a very tight sonographic monitoring of the changes in a single metacarpophalangeal (MCP) joint in rheumatoid arthritis (RA) patients after the administration of intra-articular corticosteroid.

Methods: In this study we consecutively enrolled RA patients with active disease (Composite Disease Activity Index - CDAI >10), at least one tender and swollen MCP joint, and without contraindication to intra-articular corticosteroid injection (e.g. poor controlled diabetes). After the clinical evaluation that established the most clinically involved MCP joint to inject, patients underwent an US examination of the joint by an experienced sonographer. Synovitis was scored in grey scale (GS) in terms of joint space enlargement (measured at the level where the distance between the bone diaphysis and the joint capsule was greater), and power Doppler (PD) signal (scored by a semiquantitative method: 0 = no intra-articular flow, 1 = single vessel signal, 2 = confluent vessels, and 3 = vessel signal in more than 50% of the intra-articular area). After the baseline US assessment (T0), the MCP joints were injected with 20 mg triamcinolone acetonide under sonographic guidance. Sonographic follow-up was performed in five timepoints: two hours (T1) after the injection, four hours (T2), eight hours (T3), 24 hours (T4), and 48 hours after the injection (T5).

Results: Fifteen patients (13 women), with a mean age of 62.5 years, completed the follow-up. The mean CDAI was 28.9, anti-citrullinated protein antibodies were present in 9 patients. At T5, in all the patients was detectable a global reduction of joint space enlargement, of intra-articular PD signal, and of the numerical rating scale (NRS) of pain at the joint injected (Table). However, in majority of the patients (n: 13), the joint space enlargement showed an increase in the T1 and T2 US examinations, and in four patients PD signal, compared to T0, increased within the eight hours after the injection. No major adverse events were registered.

	Power Doppler grade (0–3)			Joint space enlargement (mm)			NRS pain (0–10)		
Case ID	First	Last	Maximum	First	Last	Maximum	First	Last	Maximum
1	2	1	3	3,4	2,4	4,2	3	1	5
2	2	0	2	4,4	3,7	5,7	8	1	8
3	2	0	2	2,1	1,3	3	7	2	7
4	3	1	3	2,1	1,8	2,9	9	0	9
5	3	2	3	4	4	4,9	10	0	10
6	3	1	3	6,5	2,7	6,5	2	1	2
7	2	0	2	3,5	1,2	3,6	6	0	6
8	1	1	3	4,6	3,3	4,6	3	0	3
9	3	0	3	2,5	2,1	3,6	2	0	2
10	2	1	3	4,3	3,9	5,6	7	3	7
11	3	1	3	5,3	3,3	5,7	8	3	8
12	3	1	3	3,3	2,6	3,3	7	3	7
13	2	1	2	2,6	2,3	3	7	2	7
14	3	1	3	3,1	2,2	4	7	2	7
15	2	1	3	4,5	3,7	4,5	7	0	7

Conclusions: A single intra-articular corticosteroid injection, performed under US guidance, is a very fast treatment to reduce synovitis of the injected joint. In the hours next to the injection is common to reveal a rise of joint space enlargement together with that of PD signal score.

References:

[1] Courtney P, Doherty M. Joint aspiration and injection and synovial fluid analysis. Best Pract Res Clin Rheumatol 2013;27:137–69.
[2] Filippucci E, Iagnocco A, Salaffi F, et al. Power Doppler sonography monitoring of synovial perfusion at the wrist joints in patients with rheumatoid arthritis starting adalimumab treatment. Ann Rheum Dis 2006; 65:1433–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5357

FRI0110 METHOTREXATE MONOTHERAPY IN REAL LIFE: A DRUG SURVIVAL ANALYSIS. COMPARISON BETWEEN VERY EARLY ARTHRITIS AND EARLY ARTHRITIS COHORTS

M.G. Anelli[1], C. Rotondo[2], G. Righetti[2], A. Rinaldi[2], S. Perniola[2], M. Nivuori[2], S. Lopriore[2], G. Lopalco[2], G. Laselva[2], C. Scioscia[1], F. Cacciapaglia[2], G. Lapadula[2], F. Iannone[2]. *[1]DIM; [2]DETO, Unit of Rheumatology, Bari, Italy*

Background: Methotrexate (MTX) is the first line drug suggested in the ACR/EULAR guidelines to treat the rheumatoid arthritis (RA) (1) and spondylarthritis (SpA). Although MTX efficacy is demonstrated by high levels of evidences, maximum benefit might require interventions even earlier. For this reason, it is suggested to identify the patients (pts) with symptom onset of less than 12 weeks, that is very early arthritis, to obtain better outcomes. Few data are available by the clinical practice on MTX monotherapy (MTXm) survival in very early or early arthritis pts.

Objectives: We aim to evaluate the presence of different outcomes in MTXm drug survival and MTX efficacy between Very Early arthritis (VEA) pts (less than 12 weeks from symptom onset) and Early arthritis (EA) pts (12–52 weeks from symptom onset), and between early RA pts and early SpA pts.

Methods: On 305 pts, we selected 219 pts (30 pts diagnosed as VEA (4,2 (4) weeks from symptom onset) and 155 pts as EA (25,7 (25) wks from symptom onset) in which MTXm could be started. The RA pts were 93 and SpA pts were 126. To assess the MTXm persistency the Kaplan-Meier survival curves analysis was performed and Cox regression analysis was used to assess clinical predictors of MTXm suspension. The results are expressed as mean±standard deviation or median (interquartile range). A p≤0.05 was set for statistically significant.

Results: No difference in MTXm survival was found between VEA pts 95,5 (36) wks and EA 92,5 (10) wks (p=0,38) (Fig.1a). We observed a significant difference in drug survival between early RA pts 63 (16) wks) and early SpA pts 112,7 (15,8) wks (p=0,001) (Fig.1b). In 55% early RA pts and in 45% early SpA pts the biotechnology drug needs to be added because of disease flare. In the remaining pts a low disease activity (DAS≤3,2) was observed. No adverse events were recorded in follow-up period. In early RA pts predictors of shorter MTXm survival were younger age at diagnosis (p=0,004), lower dose of MTX (p=0,032),

Fig. 1a

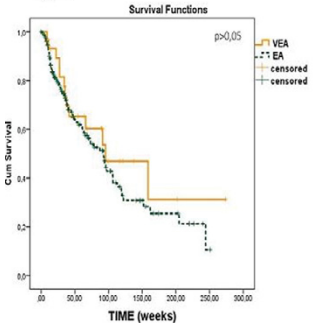
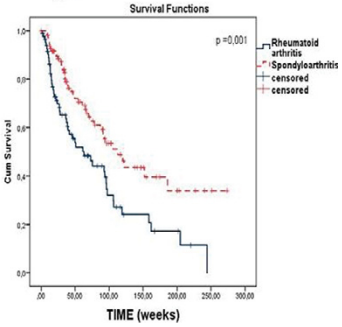


Fig. 1b



earlier diagnosis from symptom onset (p=0,0001), higher titer of rheumatoid factor (p=0,037) and female gender (p=0,019). In early SpA pts the only predictor of shorter MTXm survival was younger age at diagnosis (p=0,0,37). Smoking, disease activity at diagnosis and BMI were not predictors of MTXm survival.

Conclusions: The MTXm survival is not influenced by VEA or EA diagnosis. The RA seems to be less responder to MTXm than SpA. It might be due to the difficult to capture the earliest phase of disease, as circulating antibodies might appear years before the onset of symptoms in RA, and biomarkers reflecting bone destruction are elevated before arthritis is present, as described in previous studies. In particular, might be pay attention to younger pts, female gender and pts with higher titer of rheumatoid factor as they seem to present a more resistant RA disease. A high dose of MTX and earlier interventions are suggested in RA to improve the clinical outcome of patients and the MTXm survival.

References:

[1] Smolen JS et. Al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis 2014;73:492–509.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4237

FRI0111 ANTI-CITRULLINATED PROTEIN ANTIBODY REACTIVITIES IN TREATMENT NAÏVE EARLY RHEUMATOID ARTHRITIS

M.K. Jonsson[1,2], A.H. Hensvold[3], M. Hansson[3], L. Mathsson-Alm[4], A.-B. Aga[2], J. Sexton[2], B.-T.S. Fevang[1,5], S. Lillegraven[2], A.I. Catrina[3], E.A. Haavardsholm[2,6]. *[1]Haukeland University Hospital, Bergen; [2]Diakonhjemmet Hospital, Oslo, Norway; [3]Karolinska Institute, Stockholm; [4]Thermo Fisher Scientific, Uppsala, Sweden; [5]University of Bergen, Bergen; [6]University of Oslo, Oslo, Norway*

Background: An increase in the number of anti-citrullinated protein antibodies (ACPA) reactivities precede RA onset, and may be involved in the pathogenesis of the disease. The presence of ACPA is associated with radiographic progression in RA, and it has been suggested that ACPAs with different reactivities may be associated with different phenotypes of RA.

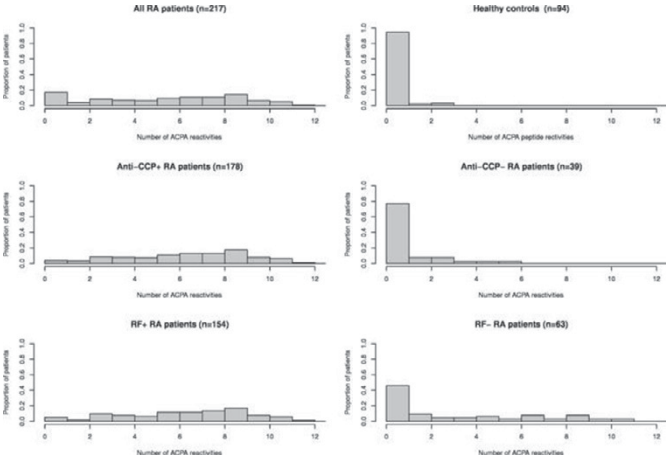
Objectives: To assess the prevalence of baseline ACPA reactivities in an inception cohort of early RA patients, including subgroups based on anti-CCP/RF status, and to compare the findings to healthy controls.

Methods: 217 DMARD-naïve early RA patients from the ARCTIC trial (1) were analysed. Radiographs were scored according to van der Heijde Sharp (vdHS) score. Anti-CCP status was analysed by FEIA (pos. if ≥10 IU/mL) and RF by ELISA (pos. if ≥25 IU/mL). ACPA titres (AU/ml) were considered pos. if above the 98-perc. of values in 619 non-RA subjects. Analysis of 13 ACPA reactivities targeting citrullinated peptides from fibrinogen, alpha-1 enolase, vimentin, fillagrin and histone was performed at baseline in patients and 94 controls (blood donors matched for age/gender/smoking), using a multiplex chip-based assay (2).

	anti-CCP+, n=178	anti-CCP-, n=39	RF+, n=154	RF-, n=63	All RA, n=217	Controls, n=94
Age, years[1]	50.8 (13.2)	55.0 (14.9)	51.9 (13.3)	50.8 (14.2)	51 (14)	52 (9.4)
Female[2]	109 (61)	22 (56)	91 (59)	40 (64)	131 (60)	63 (59)
Ever-smoker[2]	122 (69)	26 (67)	109 (71)	39 (62)	148 (68)	81 (64)
DAS[1]	3.4 (1.1)	4.0 (1.3)	3.5 (1.2)	3.5 (1.2)	3.5 (1.2)	NA
vdHS score[3]	4.0 [1.5–8.0]	4.5 [2.0–10.0]	4.5 [2.0–8.0]	3.5 [1.5–10.0]	4.0 [1.5–8.0]	NA
Vim60–75 cit[4]	152 (85)	7 (18)	130 (84)	29 (46)	159 (73)	5 (5)
H4 31–50 cit[4]	142 (80)	3 (8)	119 (77)	26 (41)	145 (67)	1 (1)
CEP1[4]	137 (77)	3 (8)	117 (76)	23 (37)	140 (65)	1 (1)
Fil307–324 cit[4]	134 (75)	2 (5)	113 (73)	23 (37)	136 (63)	0 (0)
Fib573 cit[4]	121 (68)	2 (5)	99 (64)	24 (38)	123 (57)	0 (0)
Fib36–52 cit[4]	116 (65)	1 (3)	96 (62)	21 (33)	117 (54)	2 (2)
H3 1–30 cit[4]	106 (60)	1 (3)	93 (60)	14 (22)	107 (49)	0 (0)
H4 14–34 cit[4]	103 (58)	2 (5)	90 (58)	15 (24)	105 (48)	3 (3)
H3 21–44 cit[4]	94 (53)	2 (5)	80 (52)	16 (25)	96 (44)	1 (1)
Vim2–17 cit[4]	87 (49)	1 (3)	80 (52)	8 (13)	88 (41)	0 (0)
Fib591 cit[4]	66 (37)	3 (8)	56 (36)	13 (21)	69 (32)	1 (1)
Fib74 cit[4]	60 (34)	6 (15)	54 (35)	12 (19)	66 (30)	3 (3)
Fib72 cit[4]	24 (14)	3 (8)	21 (14)	6 (10)	27 (12)	2 (2)

[1]Mean (SD), [2]n (%), [3]Median [IQR], [4]ACPA reactivity, n positive (%).

Results: Baseline characteristics are presented in the table. The figure shows the prevalence of ACPA reactivities in the subgroups, with median [IQR] number of antibody reactivities in all patients 7 [3,10], compared to 0 [0,0] in controls (p<0.001). The corresponding numbers were 8 [5,10] and 0 [0,1] for the anti-CCP+ vs. anti-CCP- patients (p<0.001), and 8 [5,10] and 2 [0,7.5] for the RF+ vs. RF- patients (p<0.001). Positivity for ACPA reactivities was seen mainly in the anti-CCP+ and RF+ patients, but also occurred more frequently in RF- and anti-CCP- patients (table) than in controls (anti-CCP- vs controls p=0.037, RF- vs controls p<0.001).



Conclusions: Prevalence of ACPA reactivities differed in subgroups of DMARD-naïve early RA patients according to anti-CCP and RF status. All RA subgroups, including RF- and anti-CCP- patients, had higher prevalence of ACPA reactivities compared to healthy controls.

References:

[1] Haavardsholm et al BMJ 2016.
[2] Hansson et al Arthr Res Ther 2012.

Disclosure of Interest: M. Jonsson: None declared, A. Hensvold: None declared, M. Hansson: None declared, L. Mathsson-Alm Employee of: Thermo Fisher Scientific, A.-B. Aga: None declared, J. Sexton: None declared, B.-T. Fevang Grant/research support from: Novartis, S. Lillegraven: None declared, A. Catrina: None declared, E. Haavardsholm Grant/research support from: AbbVie, MSD, Pfizer, Roche, UCB

DOI: 10.1136/annrheumdis-2017-eular.2915

FRI0112 SERUM LEVELS OF IL-33 AND SST2 ARE ASSOCIATED WITH FUNCTIONAL DISABILITY IN RHEUMATOID ARTHRITIS

M.R. Pinto[1], A. Kakehasi[2], M.V. Andrade[3]. *[1]Rheumatology, Hospital das Clínicas da UFMG; [2]Aparelho Locomotor; [3]Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil*

Background: Interleukin 33 (IL-33) is a cytokine related to amplification of the articular inflammation in rheumatoid arthritis (RA) animal models. Elevated IL-33 serum levels have been described in RA patients, suggesting a possible participation of this cytokine in the physiopathology of the disease.[1,2] IL-33 soluble receptor (sST2) is a decoy receptor that functions as an inhibitor of the interaction of the transmembrane receptor with IL-33.[3]

Objectives: To identify the association between serum levels of IL-33 and its soluble receptor (sST2) with clinical and laboratory characteristics of RA.

Methods: Cross-sectional observational study in which RA patients were submitted to clinical and laboratorial evaluation. IL-33 and sST2 serum levels were measured by ELISA (R&D System Inc, Minneapolis, MN, USA).

Results: 102 RA patients were included, 92,5% women, mean age of 55,5±10 years and mean disease duration of 17,6±9,5 years. Eighty-four (82,4%) patients had seropositive RA. The median (interquartile range) IL-33 serum level was 69.1 pg/ml (31.6 - 114.5). Higher scores on the visual analogue scale (VAS) of disease activity assessed by the examiner were associated with higher IL-33 values (CI95%: 0.01–0.05). In the group of patients with high titres of rheumatoid factor (RF), IL-33 levels were higher, compared to the group with negative RF (95% CI: 0.55 - 2.34). In 34 (33.3%) patients, IL-33 was undetectable and the presence of metabolic syndrome[4] represented a 63% lower chance (OR =0.37, 95% CI: 0.15–0.90) of having IL-33 detected. In addition, 1-unit increase in HAQ-DI increased by 2.43 times the chance of detecting IL-33 (95% CI: 1.23 - 4.80). The median sST2 serum level was 469.8 pg/ml (336.3–651). sST2 was associated with worse functional capacity by the classification of Steinbroker[5] (IC95%: 0.09 - 0.5), use (current or in the past) of tobacco (95% CI: 0.02 - 0.53) and use of leflunomide (95% CI: 0.05 - 0.53). There was no correlation between IL-33 and sST2 levels.

Conclusions: These findings may suggest that both IL-33 and its soluble receptor play a role as a marker of RA severity and functional disability. The negative association of IL-33 with metabolic syndrome is in agreement with the possible protective role of this cytokine in relation to lipid metabolism.[6]

References:
[1] Xu D, Jiang HR, Li Y, et al. IL-33 exacerbates autoantibody-induced arthritis. J Immunol. 2010;184(5):2620–2626.
[2] Matsuyama Y, Okazaki H, Tamemoto H, et al. Increased levels of interleukin 33 in sera and synovial fluid from patients with active rheumatoid arthritis. J Rheumatol. 2010;37(1):18–25.
[3] Schmitz J, Owyang A, Oldham E, et al. IL-33, an interleukin-1-like cytokine that signals via the IL-1 receptor-related protein ST2 and induces T helper type 2-associated cytokines. Immunity. 2005;23(5):479–490.
[4] Alberti KG, Zimmet P, Shaw J. Metabolic syndrome–a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med. 2006;23(5):469–480.
[5] Steinbrocker O, Traeger CH, Batterman RC. Therapeutic criteria in rheumatoid arthritis. JAMA 1949;140:659–62.
[6] Kunes P, Holubcová Z, Kolácková M, Krejsek J. The counter-regulation of atherogenesis: a role for interleukin-33. Acta Medica (Hradec Kralove). 2010;53(3):125–129.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5565

FRI0113 VALIDATION AND RESULTS OF THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS (SPARRA) QUESTIONNAIRE

M.V. Beers-Tas[1], M. Ter Wee[2], B. Maat[1], W. Hoogland[1], A. Hensvold[3], A. Catrina[3], E. Mosor[4], A. Finckh[5], D. Courvoisier[6], K. Raza[7], D.V. Schaardenburg[1]. *[1]Amsterdam Rheumatology and immunology Center, Reade; [2]Amsterdam Rheumatology and immunology Center, VUMC, Amsterdam, Netherlands; [3]Rheumatology, Karolinska university, Stockholm, Sweden; [4]Rheumatology, Section for Outcomes Research, CeMSIIS, Medical University of Vienna, Vienna, Austria; [5]Rheumatology; [6]University hospital of Geneva, Geneva, Switzerland; [7]Rheumatology, Institute of Inflammation and Ageing, Birmingham, United Kingdom*

Background: A range of symptoms can be present in persons at risk of rheumatoid arthritis (RA). However, information on the nature, location, timing, severity and predictive value of these symptoms is largely lacking. The Symptoms in Persons At Risk of Rheumatoid Arthritis (SPARRA) questionnaire has been developed with support from EULAR, informed by data from a qualitative study[1] and with input from patient research partners.
Objectives: To test the psychometric properties of the SPARRA questionnaire in an international group of arthralgia patients at risk of RA and to quantify these symptoms.
Methods: The SPARRA questionnaire contains questions about presence, severity, impact and location of 13 symptoms. 240 individuals (69% rheumatoid factor and/or ACPA positive, 23% seronegative with clinically suspect arthralgia and 8% first degree family members of patients with RA) completed the questionnaire in the Netherlands (N=125), United Kingdom (N=70), Sweden (N=15), Austria (N=11) and Switzerland (N=19). Individuals had no history or presence of clinically diagnosed arthritis at the time of first physical examination. Reliability (test-retest) and validity (face, content and construct validity) were tested.
Results: Face validity was tested by a group of experts on the at-risk phase of RA and feedback on the questionnaire was asked and received from 30 arthralgia patients, leading to only minor comments. The test-retest within 7–14 days (N=51) showed moderate to good agreement (kappa mean 0.565, range 0.309–1; agreement mean 71%, range 59–100%). The content validity was high, in line with the fact that the items were derived from a qualitative study in seropositive arthralgia patients. In contrast, the construct validity (relation to visual analog scale scores (VAS) for pain and well-being) was low (R-square 0.040–0.199), suggesting that the questions measure different elements in different time frames and grasp symptom content not captured with regular VAS pain/well-being. Most symptoms were present in a high percentage of individuals, with pain, stiffness and fatigue as the most common ones. When a symptom was present, it was usually experienced as moderate to severe, and with moderate impact. ACPA positive individuals reported lower presence of symptoms then ACPA negative individuals (mean 47% for ACPA-positive (N=118), 41% for only RF positives (N=53) and 59% in seronegative individuals (N=69)), but functional impact was higher in ACPA positive individuals (51%, versus 42% in seronegatives, NS). Note that the inclusion criteria for the seronegative individuals was presence of symptoms.
Conclusions: This study provides evidence of good psychometric properties of the SPARRA questionnaire, except for low construct validity. This means the questionnaire adds information to currently available clinical measures in persons at risk of RA. Future studies are needed to evaluate whether SPARRA data can help to improve the prediction of RA.
References:
[1] Stack, Rheumatology 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2450

FRI0114 ALLOGRAFT INFLAMMATORY FACTOR 1 (AIF1) POLYMORPHISMS RS4711274 (G/A) AND RS2269475 (C/T) MAY PREDICT ETANERCEPT PLUS METHOTREXATE RESPONSE IN FRENCH CAUCASIAN PATIENTS WITH RHEUMATOID ARTHRITIS

D.F. Azzouz[1], M. El Haddad[1], S. Kanaan[1], N. Balandraud[1,2], M. Martin[1], C. Picard[3], J. Roudier[1,2], I. Auger[1], N.C. Lambert[1]. *[1]INSERM UMRs1097; [2]Rheumatology, AP-HM; [3]HLA Laboratory, Etablissement Français du Sang, Marseille, France*

Background: Several risk loci for Rheumatoid Arthritis (RA) have been identified by Genome Wide Association Studies (GWAS), but they do not include Allograft Inflammatory Factor 1 (AIF1). Nevertheless, a few studies have shown that AIF1 rs2269475 (C/T) is associated with RA[1,2].
Objectives: We propose 1) To examine associations in French Caucasian patients with RA, of the seven most described AIF1 SNPs; 2) To study their linkage disequilibrium with HLA-DRB1 alleles; 3) To evaluate whether AIF1 single nucleotide polymorphisms (SNPs) could predict first line treatment responses in RA.
Methods: We amplified the AIF1 gene region containing the 7 SNPs and sequenced PCR products on a total of 469 individuals, including 95 Anti-Citrullinated Protein Antibody (ACPA) positive RA patients, 146, patients with scleroderma, 132 healthy controls and 96 additional healthy controls selected from a large database of volunteer bone marrow donors (VBMD) for carrying at least one RA-associated allele. Patients and controls were HLA-DRB1 genotyped. Patients with RA were divided into 2 groups, a first group called "*non responders*" was defined as patients who did not respond to first-line methotrexate (MTX) combined with Etanercept and a second group called "*good responders*" was defined as patients who did respond to methotrexate combined with Etanercept.
Results: Two SNPs were associated with RA: *rs4711274 (G/A)* and *rs2269475 (C/T)*. The frequency of minor allele carriers was respectively 37% (A) and 36% (T) in patients with RA versus 18% among controls (p=0.0014 and p=0.001). Furthermore, patients with RA-associated HLA-DRB1 alleles carried more often minor alleles for both SNPs (p=0.0005). Preliminary clinical data show that 56% of non-responders (N=16) carried the minor alleles of both rs4711274 and rs2269475 compared to only 21% of good responders (N=24, p=0.02).
Conclusions: AIF is an inflammation-responsive protein encoded within the HLA class III region on chromosome 6 (6p21.3). As already described in British and Polish Caucasians, we found a significant AIF1 Rs2269475 association with RA. We also found an association with Rs4711274 in linkage disequilibrium with the former. The increased frequency of minor AIF1 alleles in RA was not associated with a particular HLA-DRB1 allele, but to any HLA-DRB1 allele carrying the shared epitope.
Finally, patients who failed to respond to Etanercept and MTX carried more often minor alleles of the 2 described AIF1 SNPs.
Further analysis on a larger groups of patients is required to confirm whether AIF1 SNPs can predict response to therapy with Etanercept and Methotrexate.
References:
[1] Harney SM, Vilarino-Guell C, Adamopoulos IE, Sims AM, Lawrence RW, et al. (2008) Fine mapping of the MHC Class III region demonstrates association of AIF1 and rheumatoid arthritis. Rheumatology 47: 1761–1767.
[2] Pawlik A, Kurzawski M, Szczepanik T, Dziedziejko V, Safranow K, et al. (2008) Association of allograft inflammatory factor-1 gene polymorphism with rheumatoid arthritis. Tissue antigens 72: 171–175.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4872

FRI0115 EVER-SMOKING IS ASSOCIATED WITH DISEASE SEVERITY AND OPIOID USE IN RHEUMATOID ARTHRITIS

A. Karellis[1], E. Rampakakis[1,2], J.S. Sampalis[1,2], M. Cohen[3], M. Starr[3], P. Ste-Marie[4], Y. Shir[4], M. Ware[4], M.-A. Fitzcharles[3,4]. *[1]JSS Medical Research, St-Laurent; [2]Jewish General Hospital; [3]Rheumatology; [4]Alan Edwards Pain Management Unit, McGill University Health Centre, Montreal, Canada*

Background: Cigarette smoking, both current and past, is a risk for incident rheumatoid arthritis (RA), even for those with low exposure rates of 1–10 pack years. Current smoking is also associated with severity of disease and poorer response to treatments. It is however not known whether any exposure to cigarettes impacts disease expression, especially for those who have discontinued smoking.
Objectives: To assess the disease severity in RA according to smoking status (ever-, past-, current-, non-smoker).
Methods: As part of a study to examine cigarette and marijuana smoking in rheumatic disease patients, consecutively attending rheumatology patients completed an anonymous self-administered questionnaire including: pain severity on visual analog scale (VAS), patient global assessment (PtGA) and cigarette or marijuana smoking status. Concomitant physician recorded information included: sociodemographics, co-morbidities, treatments for RA, physician global assessment (PGA). Patients were categorized according to smoking status. Categorical variables were compared between groups with the Chi-Square test and continuous variables with the Student's t-test. Variables showing a statistical trend ($p<0.15$) in univariate analysis were considered in multivariate logistic regression.

Results: Over a 2-month period (April-May 2014), there were 248 (25%) RA attendees of 1000 participants. Significant differences were observed between current, past and non-smokers in regard to age [mean (SD): 59.5 (10.0) vs. 65.2 (10.6) vs. 61.0 (18.2) years; p=0.034], gender (male: 23.9% vs. 30.3% vs. 14.6%; p=0.027), unemployment due to disability (13.3% vs. 3.1% vs. 4.9%; p=0.044), number of RA medications [mean (SD): 2.3 (1.1) vs. 2.1 (1.1) vs. 1.8 (1.1); p=0.019], DMARD use (78.3% vs. 82.8% vs. 64.1%; p=0.008), opioid use (19.6% vs. 10.1% vs. 3.9%; p=0.009), pain [mean (SD): 5.0 (3.3) vs. 4.0 (2.9) vs. 3.7 (2.6) cm; p=0.040] and PGA [mean (SD): 3.8 (2.8) vs. 3.1 (2.8) vs. 3.0 (2.4); p=0.039]. Recreational marijuana was used by 3 non cigarette smokers only, with 1 also reporting medicinal marijuana use. Ever smokers vs. non-smokers used a greater number of RA medications [mean (SD): 4.3 (3.0) vs. 3.7 (2.6); p=0.081], were more likely to use DMARDs (81.4% vs. 64.1%; p=0.003) and opioids (13.1% vs. 3.9%; p=0.014), and showed a trend towards more pain [mean (SD): 4.3 (3.0) vs. 3.7 (2.6); p=0.081]. In multivariate analysis, male gender (OR=2.193; p=0.025) and DMARD use (OR=2.376; p=0.010) were significantly associated with ever smoking while opioid use (OR=2.784, p=0.103 for ever smoking; OR=3.561, p=0.074 for current smoking) showed a statistical trend.
Conclusions: Current, but also ever cigarette use, was associated with worse RA disease as indicated by the use of more drug categories, and more likely use of DMARDs to treat RA, and a trend to more pain and opioids. The combination of opioids and cigarettes may be a manifestation of a patient "chemical coping" strategy in RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3777

FRI0116 A HIGH LEVEL OF CLINICAL RESPONSE BASED ON COMPOSITE INDICES IS ASSOCIATED WITH IMPROVED HEALTH-RELATED QUALITY OF LIFE: ANALYSES FROM A PHASE 3 CLINICAL TRIAL IN PATIENTS WITH RHEUMATOID ARTHRITIS

M. Dougados[1], B. Zhu[2], A.C. Tang[2], A. Quebe[2], I. Stoykov[2], Z. Cai[2], M. Ishida[2], C. Gaich[2]. *[1]Hopital Cochin, Paris, France; [2]Eli Lilly and Company, Indianapolis, United States*

Background: Rheumatoid arthritis (RA) is a chronic disease associated with inflammatory activity and joint damage that result in disability, pain, and other impairments. The current recommendation is to assess disease activity based on composite indices with objective signs of inflammation (e.g. synovitis, acute phase reactants) and patient's assessment of disease activity. The patient's perception of disease impact and its treatment also facilitate shared decision-making about treatment.
Objectives: To compare patient-reported outcomes (PROs) for RA patients who achieved low disease activity (LDA) or remission based upon the DAS28-ESR compared to those with moderate and high disease activity (MDA and HDA) in this post-hoc analysis of a randomized, double-blind phase 3 clinical trial, RA-BEAM[1].
Methods: 1305 patients were randomized to placebo (N=488), adalimumab (N=330) or baricitinib 4 mg (N=487). Patients with observed DAS28-ESR values at Week 24 (N=1,010) were divided into 4 disease activity groups: HDA (DAS28-ESR>5.1), MDA (3.2<DAS28-ESR≤5.1), LDA (2.6≤DAS28-ESR≤3.2), or remission (DAS28-ESR<2.6). Change from baseline to Week 24 were assessed for the pain visual analogue scale (VAS, 0–100 mm), Health Assessment Questionnaire-Disability Index (HAQ-DI) and SF-36 physical and mental component score (PCS and MCS) for the intent-to-treat (ITT) patients.
Results: Patients with HDA and MDA at Week 24 had greater baseline pain and HAQ-DI scores and lower PCS and MCS scores than patients achieving LDA or remission at Week 24. Lower disease activity at Week 24 was associated with improvement in pain, HAQ-DI, SF-36 PCS and MCS at Week 24. Among patients who achieved remission, residual pain was observed, with close to 40% still experiencing some level of pain and 20% of patients in remission at Week 24 had a residual pain score>20. Sensitivity analyses using other clinical measures (DAS28-CRP, SDAI, CDAI) to define disease activity confirmed the findings.
Conclusions: Improving patient disease activity is associated with improved health-related quality of life. Patients who achieved remission had greater improvement in PROs but residual pain remained. Further research is needed to understand the treatment differences in the association between disease activity and PROs among different therapies.

Table 1. Improvement in disease activity is associated with improved PROs.

PRO Measures	Outcomes at Week 24	Disease Activity at Week 24			
		HDA DAS28-ESR>5.1 N=210	MDA 3.2<DAS28-ESR≤5.1 N=490	LDA 2.6≤DAS-28-ESR≤3.2 N=142	Remission DAS28-ESR<2.6 N=168
Pain VAS	Baseline	65.8	61.3	56.6	51.9
	LSM Change	-10.6	-31.0[a]	-43.2[ab]	-46.7[ab]
	Pain VAS≤10, %	1.4	19.0[a]	48.6[ab]	60.7[ab]
	Pain VAS≤20, %	7.6	37.1[a]	70.4[ab]	79.2[ab]
HAQ-DI	Baseline	1.8	1.6	1.4	1.2
	LSM Change	-0.3	-0.7[a]	-1.0[ab]	-1.0[ab]
SF-36 PCS	Baseline	29.7	32.1	34.3	37.2
	LSM Change	3.3	8.0[a]	12.9[ab]	13.6[ab]
SF-36 MCS	Baseline	44.3	46.2	46.7	49.8
	LSM Change	1.8	4.1[a]	5.6[a]	5.2[a]

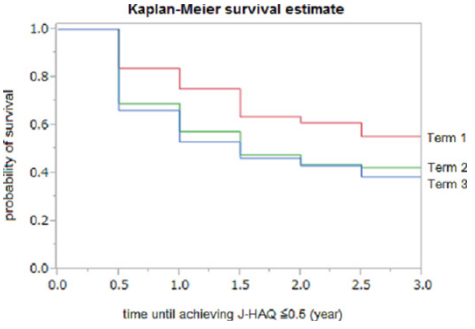
[a]p≤0.05 compared to DAS28-ESR>5.1; [b]p≤0.05 compared to 3.2<DAS28-ESR≤5.1; LSM=least squares mean

[1] Taylor PC, Keystone E, van der Heijde D, et al. Baricitinib Versus Placebo or Adalimumab in Patients with Active Rheumatoid Arthritis (RA) and an Inadequate Response to Background Methotrexate Therapy: Results of a Phase 3 Study. Arthritis Rheum 2015;67(Suppl 10):3928.
Disclosure of Interest: M. Dougados Grant/research support from: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, Consultant for: Abbvie, Pfizer, Eli Lilly and Company, Novartis, UCB, Merck, Roche, BMS, B. Zhu Employee of: Eli Lilly and Company, A. Tang Employee of: Eli Lilly and Company, A. Quebe Employee of: Eli Lilly and Company, I. Stoykov Employee of: Eli Lilly and Company, Z. Cai Employee of: Eli Lilly and Company, M. Ishida Employee of: Eli Lilly and Company, C. Gaich Employee of: Eli Lilly and Company
DOI: 10.1136/annrheumdis-2017-eular.1344

FRI0117 CHRONOLOGICAL CHANGES IN ACHIEVING J-HAQ REMISSION IN PATIENTS WITH EARLY-STAGE RHEUMATOID ARTHRITIS IN THE IORRA COHORT

M. Ochiai[1], E. Tanaka[1], E. Inoue[1,2], R. Yamaguchi[1], Y. Shimizu[1], N. Sugimoto[1], K. Ikari[1], A. Nakajima[1], A. Taniguchi[1], H. Yamanaka[1]. *[1]Rheumatology, Institute of Rheumatology Tokyo Women's Medical University; [2]Center for Clinical Research for Development, National Center for Child Health and Development, Tokyo, Japan*

Background: With the introduction of biologic disease-modifying antirheumatic drugs (DMARDs) and the increase in the approved maximum dose of methotrexate in our country, the treatment of rheumatoid arthritis (RA) has advanced dramatically in the past 2 decades. Consequently, many patients were able to achieve clinical remission and low radiographic progression rates[1–3]. In view of these dramatic changes in RA treatment, we investigated whether the Japanese version of the Health Assessment Questionnaire (J-HAQ) improved chronologically due to improved treatment over time.
Objectives: To investigate chronological changes in achieving J-HAQ remission and the factors related to J-HAQ remission in Japanese patients with an early stage of RA.
Methods: RA patients who enrolled in the IORRA cohort for the first time between 2000–2002 (Term 1), 2005–2007 (Term 2), and 2010–2012 (Term 3) and were within 2 years of disease onset were examined. For each patient in Term 3, one patient was extracted from Term 1 and Term 2 by matching the sex, age, and J-HAQ score. Among them, patients with J-HAQ >0.5 at study entry (baseline) were selected; the time to achieve J-HAQ remission (J-HAQ ≦0.5) and the J-HAQ remission rate at 3 years were analyzed. Multivariate analysis was performed to assess factors related to achieving J-HAQ remission.
Results: In each term, 348 RA patients were extracted. At baseline, the average J-HAQ of all 1,044 patients was 0.52. Baseline characteristics of 408 patients with baseline J-HAQ >0.5 were as follows: female, 89.0%; mean age, 56.3 years; anti-cyclic citrullinated peptide (anti-CCP) antibody positivity, 78.0%; mean Disease Activity Score with 28-joint count (DAS28), 4.37; and mean J-HAQ, 1.11. The mean time from baseline to achieving J-HAQ remission became significantly shorter chronologically (Term 1: 2.2 years; Term 2: 1.8 years; Term 3: 1.7 years; p<0.005, Fig.1). J-HAQ remission rates significantly increased in both Term 2 (55.2%) and Term 3 (57.4%) compared with Term 1 (37.5%; p<0.005). The factors significantly related to achieving J-HAQ remission at 3 years were younger age (OR 1.02; 95% CI 1.00–1.04) and enrollment in Term 2 (OR 2.0; 95% CI 1.2–3.5) or Term 3 (OR 2.3; 95% CI 1.3–4.1) compared with enrollment in Term 1.



Conclusions: Along with the improvement in RA treatment, patients were able to achieve J-HAQ remission more frequently and more quickly.

[1] Mod Rheumatol. 2007;17:283–9.2) J Rheumatol. 2015; 42:2279–87.3) Rheumatology. 2016;55:1053–1065.

Disclosure of Interest: M. Ochiai: None declared, E. Tanaka Consultant for: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical., Speakers bureau: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical., E. Inoue: None declared, R. Yamaguchi: None declared, Y. Shimizu: None declared, N. Sugimoto Speakers bureau: Takeda Pharmaceutical and Bristol Myers Squibb., K. Ikari Grant/research support from: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., Speakers bureau: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., A. Nakajima Consultant for: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company, Speakers bureau: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company, A. Taniguchi Grant/research support from: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., Speakers bureau: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., H. Yamanaka Grant/research support from: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Consultant for: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Speakers bureau: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers.
DOI: 10.1136/annrheumdis-2017-eular.1902

FRI0118 CLINICAL UTILITY OF AREA-UNDER-CURVE (AUC) OF PATIENT-DERIVED DISEASE ACTIVITY SCORE (PDAS2) BETWEEN CLINIC VISITS ON REMISSION, FLARE UP AND RHEUMATOLOGIST'S DECISION TO ESCALATE ANTI-RHEUMATIC DRUGS

M.-H.A. Leung [1], E. Choy [2], C.S. Lau [3]. *[1]Department of Medicine, Queen Elizabeth Hospital, Kowloon, Hong Kong; [2]Arthritis Research UK, Health and Care Research Wales CREATE Centre, Institute of Infection and Immunity, Cardiff University, Cardiff, United Kingdom; [3]Department of Medicine, LKS Faculty of Medicine, University of Hong Kong, Hong Kong, Hong Kong*

Background: The standard of care in RA is treat-to-target of remission or low disease activity state (LDAS). Integral to this is the regular assessment of disease activity. Patient-derived Disease Activity Score 2 (PDAS2) was developed to allow RA patients to self-assess. Validation, corresponding disease activity statuses cut-points and response criteria had been published. PDAS2 scores <3.8, 3.8–4.5, 4.6–5.0, >5.0 correspond to remission, LDAS, moderate and high disease activities respectively. PDAS2 can be recorded by patients in-between clinic visits.
Objectives: To explore the clinical utility of PDAS2 on remission, flare and need of drug adjustment
Methods: A cohort of 100 consecutive RA patients was recruited to complete PDAS2 score at home fortnightly in between two consecutive rheumatology clinics. Patients would return the forms when they attended the second clinic. Rheumatologists adjusted treatment according to disease activity while blinded to the scores of PDAS2 recorded at home. AUC of PDAS2 was calculated from the mean of (PDAS2 score multiplied by the time interval between scores). They were compared with disease activity at the first and second visits. The change of PDAS2 score for those patients having SDAI flare-up (from remission/LDAS to moderate/high disease activity) was compared to those didn't flare-up using unpaired T-test. Receiver Operator Characteristic curve was used to determine the cut-point for AUC-PDAS2 increment to predict flare-up and the cut-point of PDAS2 score for rheumatologists to escalate anti-rheumatic drugs.
Results: Mean age of the cohort was 60 years, mean RA duration 14 years, 90% female, 71% sero-positive and 48% in remission/low disease activity. 89 patients (89%) returned written questionnaires which were done 7.8±3.5 times (mean±standard deviation) (range 1–16) for a follow-up interval of 17.5±9.4 weeks (range 3.9–60.3). Disease activities in first and second visits are shown in Table. *Remission:* For the 14 patients in SDAI remission in both visits, 13/14 were in AUC-PDAS2 remission, and 1/14 in LDAS. There were 47, 45 and 37 out of 89 patients in SDAI, CDAI and DAS28 remission/LDAS respectively – they were all in AUC-PDAS2 remission/LDAS. *Flare-up:* There were 10/89 patients in SDAI remission/LDAS in first visit and moderate/high activity in second visit. Their AUC-PDAS2 score rose by 0.33±0.35 points compared to 0.01±0.32 who had no flare-up (p=0.002). ROC curve AUC was 0.80 (95% CI: 0.64, 0.95) (p=0.002), with optimal cut-point at increment of AUC-PDAS2 score by 0.11 to predict flare, sensitivity and specificity both being 80%. Moreover, rheumatologists decided to *escalate anti-rheumatic drugs* in 15/89 patients. ROC curve AUC was 0.71 (95% CI: 0.56, 0.86) (p=0.01), with optimal cut-point at PDAS2 score 4.33 to predict the need of escalating anti-rheumatic drugs, sensitivity being 60% and specificity 77%.

		First visit		*Second visit*	
		N (%)	AUC-PDAS2 (SD)	N (%)	AUC-PDAS2 (SD)
SDAI	Remission	22 (24.7%)	3.23(0.40)	22 (24.7%)	3.22(0.43)
	LDAS	36 (40.4%)	3.72(0.52)	35 (39.5%)	3.80(0.55)
	Moderate	29 (32.6%)	4.50(0.60)	30 (33.7%)	4.40(0.66)
	High	2 (2.2%)	5.26(1.08)	2 (2.2%)	5.21(1.15)

Table. Simplified Disease Activity Index (SDAI) disease activities of RA patients (N=89) in first and second visits, and corresponding mean area-under-curve of Patient Disease Activity Score 2 (AUC-PDAS2)

Conclusions: PDAS2 scoring by patients in-between follow-up is feasible and useful in reassuring RA patients kept in remission/LDAS, informing a potential flare from previous remission/LDAS state, and predicting rheumatologists' decision to escalate anti-rheumatic drugs. AUC-PDAS2 concept is useful in development of smartphone application for patient use.
References:
[1] A&R 2008 Feb 15;59(2):192–9.
[2] Rheumatology 2016 Nov;55(11):1954–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2788

FRI0119 A PROPOSAL FOR A SDAI, CDAI, AND RAPID3-BASED DEFINITION OF MINIMAL DISEASE ACTIVITY FOR USE IN ROUTINE CARE OF RHEUMATOID ARTHRITIS: RESULTS FROM A JAPANESE NATIONAL DATABASE

N. Yokogawa [1], A. Komiya [2], K. Shimada [1], S. Sugii [1], J. Nishino [3], S. Tohma [4]. *[1]Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Tokyo; [2]Department of Clinical Laboratory, Sagamihara National Hospital, National Hospital Organization, Kanagawa; [3]Department of Orthopaedic Surgery and Spinal Surgery, he University of Tokyo, Tokyo; [4]Clinical Research Center for Allergy and Rheumatology, Sagamihara National Hospital, National Hospital Organization, Kanagawa, Japan*

Background: The OMERACT group proposed minimal disease activity (MDA) as a treatment target, given the current treatment possibilities and limitations. Whereas a Disease Activity Score 28 (DAS28)-based definition of MDA has been proposed[1], definitions based on the Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), and Routine Assessment of Patient Index Data 3 (RAPID3) have not, despite the increasing use of these indices.
Objectives: To define SDAI, CDAI, and RAPID3-based definition of MDA for use in routine care.
Methods: We analyzed 15,101 patients registered in the Japanese National Database (NinJa 2015). As the OMERACT group proposed, patients with tender joint count (TJC) of 0, swollen joint count (SJC) of 0, and erythrocyte sedimentation rate (ESR) $\leq$10 mm/hour or patients with five of the following seven criteria, namely, pain $\leq$2, SJC $\leq$1, TJC $\leq$1, HAQ $\leq$0.5, physician's global $\leq$1.5, patient's global $\leq$2, and ESR $\leq$20, were considered to be in MDA.[1] The ROC curve was used to obtain the best cut-off points for the SDAI, CDAI, and RAPID3-based definitions of MDA, which emerged as good predictors of MDA as defined by the core dataset. To compare the usefulness of the indices, the interclass correlation of MDA in DAS28, SDAI/CDAI, and RAPID3 was compared to that of low disease activity (LDA).
Results: 57.6% of patients (5,629/9,767) were categorized as having MDA, and 29% of patients (4,003/13,781) were categorized as Boolean remissions. In the ROC analysis, the area under the curve for DAS28, SDAI, CDAI, and RAPID3 was 0.911, 0.955, 0.953, and 0.930, respectively. Based on the Youden index, SDAI $\leq$5.3, CDAI $\leq$4.8, and RAPID3 $\leq$5 were defined as SDAI, CDAI, and RAPID3-based MDA, respectively. The sensitivity and specificity of the DAS28, SDAI, CDAI, and RAPID3-based definitions were higher than those of the DAS28-based definition, with a sensitivity of 81.5%, 89.2%, 88.8%, and 90.0%, respectively, and a specificity of 83.5%, 89.4%, 89.9%, and 88.4%, respectively. Each index-based definition of MDA showed better interclass correlation than that of LDA; DAS28 vs CDAI/SDAI: MDA of 0.643/0.662 and LDA of 0.540/0.540; DAS28 vs RAPID3: MDA of 0.541 and LDA of 0.482; CDAI/SDAI vs RAPID3: MDA of 0.677/0.671 and LDA of 0.433/0.425.
Conclusions: SDAI $\leq$5.3, CDAI $\leq$4.8, and RAPID3 $\leq$5, values two points higher than each remission criterion, may provide a more stringent therapeutic goal than LDA in clinical practice.
References:
[1] Wells GA, et al. Minimal disease activity for rheumatoid arthritis: a preliminary definition. J Rheumatol 2005;32:2016–24.
Acknowledgements: Supported in part by a Health and Labor Sciences Research Grant from the Ministry of Health, Labor, and Welfare of Japan.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3339

FRI0120 SERUM CALPROTECTIN IS NOT PREDICTIVE FOR SUCCESSFUL DOSE REDUCTION OR DISCONTINUATION OF TNF INHIBITORS IN RA PATIENTS WITH LOW DISEASE ACTIVITY

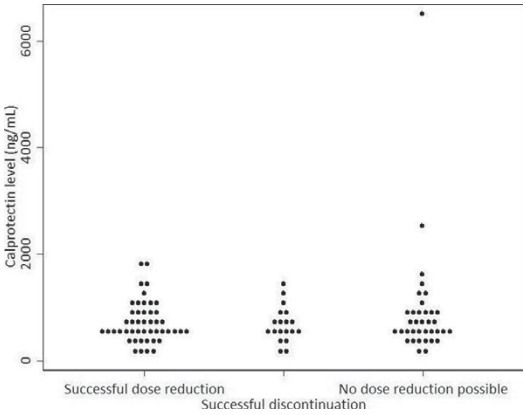
N. Den Broeder[1], L. Tweehuysen[1], T. Vogl[2], N. van Herwaarden[1], F.H.J. van den Hoogen[1,3], R.M. Thurlings[3], A.A. den Broeder[1]. *[1]Rheumatology, Sint Maartenskliniek, Nijmegen, Netherlands; [2]University of Münster, Münster, Germany; [3]Rheumatology, Radboudumc, Nijmegen, Netherlands*

Background: Dose reduction and discontinuation of TNF inhibitors (TNFi) have been shown feasible in a large proportion of RA patients with low disease activity.[1] However, to date, no predictors for successful dose reduction or discontinuation have been identified.[2] Calprotectin (a heterodimer of S100A8/S100A9) might be a promising biomarker in this context, as preliminary data showed this pro-inflammatory marker to be associated with disease activity and radiographic progression in RA and to be predictive for response in RA patients starting treatment with a TNFi.[3,4]

Objectives: To investigate the predictive value of baseline serum calprotectin for successful TNFi dose reduction or discontinuation in RA patients with low disease activity.

Methods: Data was derived from the intervention arm of the DRESS (Dose REduction Strategies of Subcutaneous TNFi) study, which showed non-inferiority of a dose reduction strategy of adalimumab or etanercept compared to usual care.[1] TNFi dose interval was reduced stepwise every 3 months until flare (DAS28-CRP increase >1.2 or >0.6 if current DAS28-CRP ≥ 3.2) or discontinuation. Patients were classified at 18 months as being successfully dose reduced, discontinued or not able to reduce the TNFi dose. At baseline, quantification of calprotectin was carried out on serum samples using ELISA. To assess the predictive value, calprotectin levels were compared between each group and receiver-operator-characteristic (ROC) curves were created. In addition, calprotectin was correlated cross-sectionally with several clinical markers for disease activity.

Results: Calprotectin levels were available for 102 of 121 patients randomised to the intervention group; 61% were women, 63% received etanercept and 37% received adalimumab. Overall, 46% of patients successfully reduced their TNFi dose, 19% of patients successfully discontinued their TNFi and 35% of patients could not reduce their TNFi dose. In these groups, median calprotectin levels were 599 ng/ml (p25-p75: 473–965), 629 ng/mL (p25-p75: 453–896) and 624 ng/mL (p25-p75: 514–931) (p=0.801) (Figure 1). The area under the ROC-curve was 0.52 (95% CI: 0.40–0.63) for predicting successful TNFi dose reduction, 0.53 (95% CI: 0.38–0.67) for successful TNFi discontinuation and 0.54 (95% CI: 0.42–0.66) for no dose reduction possible. Calprotectin levels were significantly but weakly correlated with C-reactive protein (CRP) levels with a Spearman ρ of 0.21 (p=0.03). No significant correlation was found between calprotectin and age, gender, DAS28-CRP, rheumatoid factor or ACPA positivity.



Conclusions: Serum calprotectin is not predictive for successful TNFi dose reduction or discontinuation in the context of RA patients with low disease activity, and calprotectin was only weakly correlated to CRP levels. These results might be caused by the lack of variability in calprotectin levels at baseline as all patients were in low disease activity state.

References:

[1] van Herwaarden et al. BMJ 2015;350:h1389.
[2] Tweehuysen et al. Arthritis Rheumatol 2016.
[3] Berner Hammer et al. Ann Rheum Dis 2010;69(1):150–4.
[4] Choi et al. Ann Rheum Dis 2015;74(3):499–505.

Disclosure of Interest: N. Den Broeder: None declared, L. Tweehuysen: None declared, T. Vogl: None declared, N. van Herwaarden: None declared, F. van den Hoogen Consultant for: Biogen, Celltrion, Janssen, Mundipharma and Sandoz, R. Thurlings: None declared, A. den Broeder Consultant for: AMGEN
DOI: 10.1136/annrheumdis-2017-eular.1729

FRI0121 REMISSION AT 6 MONTHS AND IDENTIFICATION OF FUTURE GOOD RADIOGRAPHIC AND PHYSICAL OUTCOME IN EARLY RHEUMATOID ARTHRITIS

N.P. Sundlisater[1], A.-B. Aga[1], I.C. Olsen[1], H.B. Hammer[1], T. Uhlig[1], D. van der Heijde[2], T.K. Kvien[1], S. Lillegraven[1], E.A. Haavardsholm[1] on behalf of the ARCTIC study group. *[1]Diakonhjemmet Hospital, Oslo, Oslo, Norway; [2]Leiden University Medical Center, Leiden, Netherlands*

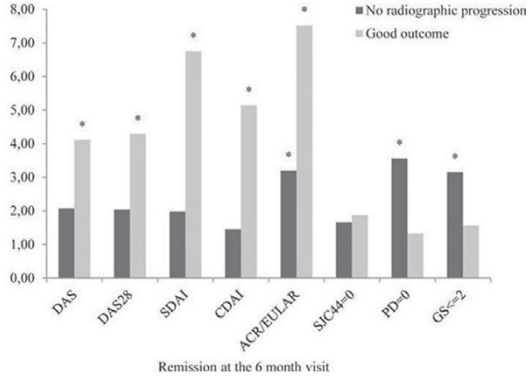
Background: Treat-to-target strategies with achievement of clinical remission within 6 months minimize radiographic progression and physical impairment in RA.(1) The preferred target, ACR/EULAR Boolean remission criteria, was developed to optimize a combination of radiographic and functional outcome.(2) However, clinical remission does not exclude subclinical inflammation, associated with progression of radiographic damage.(3)

Objectives: Our aim was to assess the association between definitions of remission at six months, including absence of ultrasound inflammation, and future absence of joint damage and physical disability.

Methods: DMARD-naïve RA patients with <2 years since first swollen joint and indication for DMARD treatment were included in the treat-to-target ARCTIC trial.(4) Patients followed with ultrasound (treatment target DAS <1.6 + SJC44=0 + no PD signal in 32 joints) were analyzed. We assessed remission at 6 months according to the following criteria: DAS-ESR, DAS28-ESR, SDAI, CDAI, ACR/EULAR Boolean remission (based on 44 joints), no swollen joints (SJC44), no ultrasound PD signal in any joint (0–96), and minimal greyscale (GS) score (GS ≤ 2, 0–96). Radiographs were scored by two readers using van der Heijde-Sharp score, with no radiographic progression defined as <1 unit change between 12–24 months based on the average score of the readers. We defined good outcome as a combination of no radiographic progression and physical function (PROMIS) $\geq$ median of the general population.(2) Odds ratios of reaching both outcomes were calculated according to various remission states at 6 months.

Results: Of the 103 patients included, 74% were female, mean [SD] age 51.4 [12.9], disease duration 6.7 [5.3] months, DAS 3.5 [1.1] and PROMIS 39 [8]. Median [25th, 75th percentile] radiographic progression 12–24 months was 0.49 [0.0, 1.03], and 71% had no progression. DAS remission was achieved by 59% at the 6-month visit, while 42% were in ACR/EULAR Boolean remission. Patients in ACR/EULAR Boolean remission had significantly higher odds ratio of no radiographic progression from 12–24 month than patients not in Boolean remission, as had patients with no PD signal or minimal GS findings (fig). Being in remission at six months according to each composite score separately or ACR/EULAR Boolean remission (OR 7.52, CI 3.06 –18.49) predicted a good outcome, while criteria based on ultrasound or no swollen joints did not (fig). No statistically significant association was found between remission according to composite scores and radiographic progression (Fig).

Figure: OR of no radiographic progression at 12-24 months compared to OR of a good outcome (no radiographic progression + physical function ≥ median in the general population) at 12-24 months. P-values ≤0.05 marked with an asterix.



Conclusions: Our data show that being in ACR/EULAR Boolean remission after six months of treat-to-target therapy increases both the odds of no radiographic progression and good physical function, supporting current recommendations stating that ACR/EULAR remission should be the preferred treatment target in early RA.(1) Additionally, our analyses support that absence of ultrasound inflammation is associated with no future radiographic progression.

References:

[1] Smolen JS, et al. ARD. 2016;75:3–15.
[2] Felson DT, et al. ARD. 2011;70:404–13.
[3] D'Agostino M, et al. ARD. 2016;75:1902–1908.
[4] Haavardsholm E, et al. BMJ. 2016;354:i4205.

Disclosure of Interest: N. Sundlisater: None declared, A.-B. Aga: None declared, I. Olsen: None declared, H. Hammer Consultant for: AbbVie, Pfizer, BMS, Roche, UCB, T. Uhlig: None declared, D. van der Heijde: None declared, T. Kvien: None declared, S. Lillegraven: None declared, E. Haavardsholm Grant/research support from: AbbVie, Pfizer, MSD, Roche, UCB
DOI: 10.1136/annrheumdis-2017-eular.2834

FRI0122 PREDICTING FACTORS FOR DISAPPEARANCE OF ANTI-MUTATED CITRULLINATED VIMENTIN ANTIBODIES IN SERA FROM PATIENTS WITH RHEUMATOID ARTHRITIS

N. Ishigooka[1], T. Fujii[1,2], S. Kondo-Ishikawa[1], M. Hashimoto[3], M. Furu[3], M. Tanaka[3], H. Ito[4], R. Nakashima[1], K. Murakami[1], Y. Imura[1], H. Yoshifuji[1], K. Ohmura[1], T. Mimori[1]. *[1]Department of Rheumatology and Clinical Immunology, Kyoto University Graduate School of medicine, Kyoto; [2]Department of Rheumatology and Clinical Immunology, Wakayama Medical University, Wakayama; [3]Department of the Control for Rheumatic Diseases; [4]Department of Orthopaedic Surgery, Kyoto University Graduate School of medicine, Kyoto, Japan*

Background: Mutated citrullinated vimentin (MCV) is one of the important targets of anti-citrullinated protein/peptide antibodies (ACPA) and is found in synovial fluid in patients with rheumatoid arthritis (RA). Serum anti-MCV antibody (anti-MCV) titer may be better correlated with RA disease activity and radiographic progression than anti-cyclic citrullinated peptide antibody (anti-CCP) titer.
Objectives: In the present study, we tried to determine the predicting factor of anti-MCV disappearance in sera from RA patients.
Methods: Both anti-MCV (ORGENTEC Diagnostika, Germany) and anti-CCP (MESACUP^{TM}-2 test CCP, MBL, Japan) in sera from 280 RA patients who met 2010 ACR/EULAR classification criteria in Kyoto University RA Management Alliance (KURAMA) cohort 2013 and 2014 were measured by ELISA. Then, we determined retrospectively the predicting factors of anti-MCV disappearance using multivariate logistic analysis.
Results: In 2013 cohort, anti-MCV and anti-CCP positivities were 64.6 and 84.6%, respectively. The majority (97.8%) of anti-MCV-positive patients was also anti-CCP-positive and there was significant correlation between anti-MCV and anti-CCP titers (r=0.63, $p<0.001$). In 2013 baseline, there was no difference in patients' age, gender and disease duration between anti-MCV-positive (n=181, 64.6%) and -negative (n=99, 35.4%) groups. DAS28, however, was higher in anti-MCV-positive group than in -negative group (3.08±1.22 vs. 2.68±1.07, p=0.011), while anti-CCP-positive (n=237, 84.6%) and -negative (n=43,15.4%) groups had no significant difference of DAS28. Of note, whereas anti-CCP positivity rate did not change during 2013 and 2014, anti-MCV changed to positive and to negative were recognized in 20 (=7.2%) and 41 (=14.6%, disappeared group) patients. So we next compared anti-MCV disappeared and sustained-positive groups (n=140, 50.0%). There was no difference in patients' age, gender, disease duration and DAS28 in 2013. While decrease of DAS28 from 2013 to 2014 (=ΔDAS28) in disappeared group was more apparent than that in sustained-positive group (-0.58±1.1 vs. +0.02±0.34, p=0.028). Methotorexate monotherapy was rarer in disappeared group than in sustained-positive group (26.5% vs. 53.8%, p=0.015), while continuous use of biological disease modifying antirheumatic drug (bDMARD) was more frequent in disappeared than sustained-positive group (64.7% vs. 25.2%, $p<0.0001$). Also serum levels of KL-6, a serum marker of interstitial lung disease, were lower in disappeared than in sustained-positive group (255±146 vs. 315±183, p=0.006). To clear the most effective factor in anti-MCV disappearance, we choose variables including anti-MCV titers in baseline, KL-6 levels, ΔDAS28 and bDMARD use, and performed multivariable analysis. Analysis showed that anti-MCV titers and bDMARD use, especially TNF inhibitor (Odds Ratio =7.2, $p<0.001$) were observed as the predicting factors of anti-MCV disappearance. On the other hand, no predicting factor for newly anti-MCV appearance was recognized in our cohort.
Conclusions: Anti-MCV, but not anti-CCP, can be disappeared in a year by continuous bDMARD use regardless of disease activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1589

FRI0123 DOES THE BODY MASS INDEX HAVE ANY INFLUENCE IN THE CHARACTERISTICS OF EARLY ARTHRITIS PATIENTS?

P. Moreno Fresneda, L. Martínez-Quintanilla, A.M. Ortiz, E. Tomero, R. García Vicuña, I. González Álvaro. *Rheumatology Deparment, Hospital Universitario de la Princesa, Madrid (Madrid), Spain*

Background: Obesity has been proposed as a risk factor to develop rheumatoid arthritis (RA) and it has been associated with a worse response to several disease modifying anti-rheumatic drugs (DMARDs).
Objectives: To study the differences in baseline characteristics according to the body mass index (BMI) of patients in the PEARL (Princesa Early Arthritis Register Longitudinal) study.
Methods: A total of 432 patients (69.1% female) of the PEARL cohort were included for this study. The register protocol comprises the collection of sociodemographic, disease-related and treatment data in five visits (baseline, 6, 12, 24 and 60 months). The local ethics and clinical research committee approved the protocol and all patients sign an informed consent prior to their inclusion. For this study it was analyzed the baseline visit data from the 304 (70.37%) patients that met ACR 1987 criteria for RA after 2 years of follow-up, as well as those considered undifferentiated arthritis (UA) since other diagnoses were excluded. The WHO definition for low, normal weight, overweight and obesity (BMI $<$18.5, 18.5–25, 25–30 or $\geq$30 kg/m^2 respectively) was applied. ACPA (anticitrullinated peptide antibodies) were assessed by enzyme immunoassay (CCP2 Eurodiagnostica). HLA-DRB1 genotype was determined in 219 patients using specific HLADRB1 typing kits (Dynal RELI SSO). The presence of shared epitope (SE) was determined based on this genotyping. The statistical analysis was performed by using Stata 12.1. Chi-Square and Kruskal-Wallis tests were used for the bivariate analysis. A multivariate logistic regression was performed to determine which factors may be related to ACPA positivity, including BMI, age, sex, smoking habit, number of SE alleles and study level as independent variables.
Results: Patients were 54.9 years old [44.2–67.5] (median [p25-p75]); disease duration was 5.3 months [3–8.4]. Table 1 shows the main variables significantly associated to BMI. In addition, we observed less ACPA positivity with increasing BMI (57% low weight vs. 43% in obese [p =0.08]), as well as a lower frequency of SE in patients with a higher BMI. The multivariate analysis confirmed that being smoker (ever or current) and carrying SE alleles is associated with the presence of ACPA. Adjusted by these variables, overweight and obesity were associated with lower probability of suffering an ACPA positive disease (OR 0.49, p=0.027 and OR 0.39, p=0.019 respectively).

Table 1. Variables significantly different according to BMI

BMI	Age (years)	Sex (W/M)	Level of studies (N/P/Se/U; %)	HAQ	VAS pain	TJC28
Low weight	52.3 [22.2–64]	7/0	0/14.3/42.9/42.9	1.25 [0.9–2.2]	50 [26–75]	7 [2–19]
Normal weight	50 [38.6–64]	145/24	1.2/21.4/35.1/42.3	0.87 [0.4–1.4]	41 [20–61]	3 [0–7]
Overweight	57.9 [47–69.6]	120/45	8.5/35.4/32.9/23.2	0.87 [0.5–1.6]	49 [20–62]	3 [0–9]
Obesity	59 [50.7–69.8]	68/23	12/38.5/26.5/22.9	1.3 [0.7–1.9]	50 [36–65]	5 [2–12]
	p$\leq$0.001	p=0.01	p$\leq$0.001	p=0.0018	p=0.031	p=0.047

*HAQ: Health Assessment Questionnaire; VAS: visual analogic scale (mm); TJC28: tender joints count (28 joints); W: women; M: men; N: no studies; P: primary studies; Se: secondary studies; U: universitary studies.

Conclusions: In our early arthritis register, patients with a higher BMI have predominantly ACPA negative disease, a more intense perception of pain and higher disability. These findings should be validated in other populations.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4458

FRI0124 TEMPORARY INTERRUPTIONS OF STUDY DRUG DURING THE BARICITINIB PHASE 3 RHEUMATOID ARTHRITIS PROGRAM

P. Emery[1], Y. Tanaka[2], T.E. Cardillo[3], D.E. Schlichting[3], S. Beattie[3], L. Chen[3], T.P. Rooney[3], J.S. Smolen[4]. *[1]Leeds MSK Biomed/Chapel Allerton Hosp, Leeds, United Kingdom; [2]University of Occupational & Environmental Health, Kitakyushu, Japan; [3]Eli Lilly and Company, Indianapolis, United States; [4]Medical University of Vienna, Vienna, Austria*

Background: Temporary interruption of RA therapy is common in clinical practice; therefore, rapid clearance and low immunogenicity may be useful DMARD attributes. Baricitinib (bari) is a non-biologic Janus kinase (JAK) 1 /JAK2 selective inhibitor with a pharmacokinetic half-life in RA patients of approximately 13 hours. It has demonstrated improved clinical efficacy compared to MTX, adalimumab and placebo (pbo) with a satisfactory safety profile when administered once daily to RA patients in 4 completed Phase 3 studies.
Objectives: These analyses aimed to characterize temporary interruptions of study drug during these studies and explore the kinetics of RA symptoms during and following interruption.
Methods: During bari Phase 3 studies, investigators were required to document temporary interruptions of study drug, including timing, reason and duration, using electronic case report forms. In 2 studies, patients recorded RA symptoms (duration and severity of morning joint stiffness, worst tiredness and worst joint pain) daily for 12 weeks. Post hoc analyses investigated changes in these scores among patients randomized at least 7 days prior to interruption, having an interruption that lasted at least 3 days, and retreated.
Results: Across the 3 pbo-controlled studies, interruptions occurred in a larger proportion of patients with bari than pbo only in the biologic DMARD-inadequate responder (IR) study RA-BEACON. In the 2 active comparator-controlled studies, the lowest rates of interruption were in the bari monotherapy arm of the DMARD-naïve MTX-controlled RA-BEGIN study, and proportions were similar for bari and adalimumab in the MTX-IR study, RA-BEAM (Table 1). Adverse events (predominantly non-serious, mild or moderate infections, most commonly of the respiratory tract) were the most frequent reason for interruption. Few patients interrupted for the reason of abnormal laboratory results. Most interruptions lasted for 2 weeks or less; in RA-BEAM, interruptions appeared shorter in duration for bari than for adalimumab. Diary measures indicated modest symptom increases during interruption compared to the last pre-interruption value, with a return to pre-interruption values or better after resumption of study drug (Table 2).
Conclusions: Consistent with its pharmacologic properties, brief temporary interruptions of bari during Phase 3 studies were associated with minor increases in RA symptoms, which resolved following resumption of therapy. A small molecule with a short half-life may offer advantages over injectable biologic therapies with respect to drug interruption for clinical cause in RA patients.
Disclosure of Interest: P. Emery Consultant for: Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company, Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin,

Table 1. Summary of temporary interruptions during completed baricitinib Phase 3 studies in RA[a,b]

	Study RA-BEAM (0-24/0-52, data up to rescue)			Study RA-BUILD (0-24, data up to rescue)		
	PBO (N=488)	BARI 4 mg (N=487)	ADA (N=330)	PBO (N=228)	BARI 2 mg (N=229)	BARI 4 mg (N=227)
Total number of dose interruptions, I	67	62/103	30 /46	32	24	40
Patients with ≥1 interruption, n (% of N)	54 (11.1)	50 (10.3)/75 (15.4)	28 (8.5)/40 (12.1)	29 (12.7)	21 (9.2)	34 (15.0)
Number of interruptions per interrupted patient, mean	1.2	1.2/1.4	1.1/1.2	1.1	1.1	1.2
Time from first dose to first interruption, mean, days	68.9	70.6/126.9	73.2/112.3	53.1	41.0	53.6
Duration of individual interruptions, mean (SD), days	11.7 (13.2)	11.4 (9.4)/15.1 (15.7)	19.4 (24.6)/23.1 (29.1)	11.6 (10.2)	12.3 (12.6)	10.7 (9.8)
Interruption duration categories, m (% of I)						
0-7 days	35 (52.2)	26 (41.9)/44 (42.7)	10 (33.3)/15 (32.6)	16 (50.0)	10 (41.7)	20 (50.0)
8-14 days	14 (20.9)	15 (24.2)/26 (25.2)	10 (33.3)/16 (34.8)	7 (21.9)	8 (33.3)	10 (25.0)
15-21 days	6 (9.0)	5 (8.1)/6 (5.8)	4 (13.3)/4 (8.7)	5 (15.6)	4 (16.7)	4 (10.0)
22-28 days	3 (4.5)	5 (8.1)/14 (13.6)	0/1 (2.2)	1 (3.1)	0 (0.0)	3 (7.5)
>28 days	5 (7.5)	4 (6.5)/13 (12.6)	5 (16.7)/10 (21.7)	3 (9.4)	2 (8.3)	3 (7.5)
Reason for interruptions, n (% of N)						
Adverse event	44 (9.0)	46 (9.4)/68 (14.0)	26 (7.9)/37 (11.2)	24 (10.5)	16 (7.0)	26 (11.5)
Abnormal lab result	10 (2.0)	3 (0.6)/6 (1.2)	0/0	4 (1.8)	5 (2.2)	6 (2.6)
Investigator decision	3 (0.6)	2 (0.4)/2 (0.4)	2 (0.6)/3 (0.9)	2 (0.9)	0	2 (0.9)

Abbreviations: ADA=adalimumab; BARI=baricitinib; m=number of interruptions in the specified category; N=number of patients in safety population; n=number of patients in the specified category; PBO=placebo.
[a]Interruptions are based on daily tablet study drug. [b]Temporary interruption is defined as a temporary with holding of study drug that is followed by resumption of study drug during the study.

Table 2. Summary of ePRO daily diary scores among patients retreated following study drug interruptions[a]

	Placebo 25 (25)[b,c]				Baricitinib[c] 54 (52)[b]			
Mean (SD)	Study drug initiation[a]	Pre-interruption[f]	Last during interruption[g]	Post-interruption[h]	Study drug initiation[a]	Pre-interruption[f]	Last during interruption[g]	Post-interruption[h]
MJS Duration	106 (87)	118 (157)	126 (159)	116 (159)	160 (167)	137 (164)	135 (171)	121 (188)
MJS Severity	5.5 (2.1)	4.3 (2.0)	4.5 (2.0)	4.2 (1.9)	5.8 (2.0)	4.2 (2.2)	4.4 (2.2)	3.8 (2.1)
Worst Joint Pain	5.8 (1.7)	4.6 (2.0)	4.9 (2.0)	4.4 (1.9)	6.1 (2.0)	4.6 (2.2)	4.7 (2.1)	4.2 (2.1)
Worst Tiredness	5.5 (2.5)	4.7 (2.2)	4.7 (2.2)	4.1 (2.0)	5.5 (2.0)	4.7 (2.3)	4.9 (2.5)	4.2 (2.4)

Abbreviations: ePRO=electronic patient reported outcome; MJS=morning joint stiffness.
[a]Data presented are combined from studies RA-BEAM and RA-BUILD. [b]Number of interruptions (number of patients); excludes interruptions without at least 3 diary entries during interruption. [c]For MJS severity, it is 26 (26). [d]Includes combined doses of baricitinib (2 mg and 4 mg). [e]Average of values obtained within the first 3 days following randomization. [f]Average of up to 3 most recent values obtained in the 7 days prior to interruption. [g]Average of 3 most recent values in the last 7 days of the interruption. [h]Average of last 3 available values obtained following interruption and prior to any subsequent interruption or Week 12 study visit.

Asahi-kasei, YL Biologics, Sanofi, janssen, Eli Lilly and Company, GlaxoSmithKline, T. Cardillo Employee of: Eli Lilly and Company, D. Schlichting Employee of: Eli Lilly and Company, S. Beattie Employee of: Eli Lilly and Company, L. Chen Employee of: Eli Lilly and Company, T. Rooney Employee of: Eli Lilly and Company, J. Smolen: None declared
DOI: 10.1136/annrheumdis-2017-eular.1326

FRI0125 RHEUMATOID ARTHRITIS PATIENTS WITH ANTI-ACETYLATED PEPTIDE ANTIBODIES STARTING THEIR FIRST TUMOR-NECROSE-FACTOR-INHIBITOR TREATMENT SHOW GREATER RESPONSE

P. Studenic[1], S. Blüml[1], H. Bang[2], D. Sieghart[1], D. Aletaha[1], H. Haslacher[3], T. Perkmann[3], J.S. Smolen[1,4], G. Steiner[1]. *[1]Internal Medicine 3, Division of Rheumatology, Medical University Vienna, Vienna, Austria; [2]Orgentec Diagnostika, Mainz, Germany; [3]Department of Laboratory Medicine, Medical University Vienna; [4]Internal Medicine 2, Hietzing Hospital, Vienna, Austria*

Background: Anti-acetylated-peptide antibodies (AAPA) have recently been described in rheumatoid arthritis (RA) patients.[1] Patients that show multiple autoantibody positivity have a higher likelihood to flare when stopping biological treatment. The role of AAPA antibodies for response to Tumor-Necrose-Factor-inhibitor treatment (TNFi) has not been explored.
Objectives: To determine the prevalence and serological overlap of AAPA to rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) in a cohort of RA patients starting their TNF-inhibitor, and to assess their relation of autoantibody status to response to therapy.
Methods: We measured AAPA by ELISA using two acetylated peptides derived from vimentin, as well as RF and ACPA. We evaluated the prevalence of autoantibodies, baseline characteristics of autoantibody positive and negative patients, and their association with a 50% response by the Simplified disease activity index (SDAI50), and with achieving of SDAI low disease activity or remission at 6 months after starting the first TNFi. Likelihood ratios were calculated from logistic regression analyses. To better determine differences in SDAI change over time General Estimated Equation analyses (GEE) was used.
Results: Among our 93 patients starting treatment on a TNFi (85% female, mean disease duration: 7.7±7 years mean SDAI20±13), 50% were positive for AAPA, 57% for ACPA and 61% for RF (for overlap of antibodies see figure). There were no significant differences in baseline characteristics found between AAPA positive and negative patients. 61% of patients reached LDA or REM and 33% achieved an SDAI50 response after 6 months of TNFi treatment. AAPA positive patients showed a likelihood ratio (LR+) of 5.3 (p=0.022) to achieve an SDAI50 response and 3.9 (p=0.048) to reach LDA/REM. In contrast, being RF or ACPA positive did not coincide with a higher likelihood of achieving SDAI50 (LR+ of 0.08; p=0.773 and 1.09; p=0.297, respectively) or LDA/REM (LR+ of 1.83; p=0.177 and 1.55; p=0.213). Relative changes upon treatment with TNFi in composite scores were neither different between RF+ vs. RF- patients, nor between ACPA+ vs ACPA-patients; however AAPA+ showed significantly higher relative changes in SDAI (p=0.021), CDAI (p=0.025) and DAS (p=0.022) compared to AAPA- patients. Of note, relative changes in CRP were similar between the groups.
GEE on up to 230 days of TNFi treatment or until change of treatment, showed no significant difference in SDAI courses comparing RF+ vs RF- or ACPA+ vs ACPA-

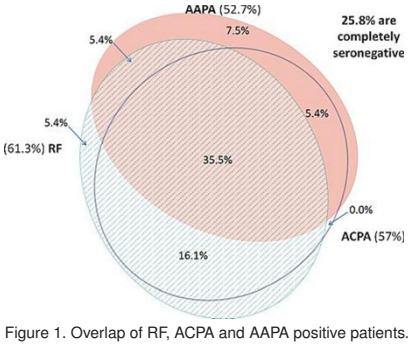


Figure 1. Overlap of RF, ACPA and AAPA positive patients.

patients; but for AAPA+ vs. AAPA- patients the difference in change in SDAI was significant (p=0.045) over time.
Conclusions: AAPA positivity, in contrast to RF and ACPA positivity, appears to have a tighter association with greater levels of response in patients who are initiating TNFi-treatment. Therefore, AAPA might add additional information to estimate the chances of RA patients for responding to TNF-inhibitors.
References:
[1] Juarez M, Bang H, Hammar F, et al. Identification of novel antiacetylated vimentin antibodies in patients with early inflammatory arthritis. Ann Rheum Dis 2016;75(6):1099–107.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5374

FRI0126 AIMING FOR REMISSION ACCORDING TO ANY OF THE RHEUMATOID ARTHRITIS DISEASE ACTIVITY INDICES IS MORE IMPORTANT FOR PHYSICAL FUNCTION THAN THE ACTUAL CHOICE OF INDEX: A LONGITUDINAL ANALYSIS IN A CLINICAL PRACTICE SETTING (METEOR COHORT)

P.D. Carvalho[1], R. Ferreira[1], R. Landewé[2], D. Vega-Morales[3], K. Salomon-Escoto[4], D.J. Veale[5], J. da Silva[1], P.M. Machado[6]. *[1]CHUC, Coimbra, Portugal; [2]ARC, Amsterdam, Netherlands; [3]HU/UANL, Monterrey, Mexico; [4]UMass, Massachusetts, United States; [5]DAMC, Dublin, Ireland; [6]UCL, London, United Kingdom*

Background: The association between remission and disability in patients with rheumatoid arthritis (RA) has been established mainly in clinical trial cohorts and not in "real-life" patients. Moreover, only a limited number of remission definitions have been tested.
Objectives: To compare the association between different remission criteria and physical function in patients with RA followed in clinical practice.
Methods: Longitudinal data from the METEOR database were used. Fifteen definitions of remission were tested: ACR-EULAR boolean-based; Simplified Disease Activity Index (SDAI); Clinical Disease Activity Index (CDAI); Disease Activity Score (DAS) and 28-joint count DAS (DAS28), both with ESR/CRP, with 3/4 variables (3v/4v), and various cut-offs tested. Disability was measured by the Health Assessment Questionnaire (HAQ) and HAQ≤0.5 was defined as a good outcome. Associations were investigated using generalised estimating equations (GEE), using HAQ≤0.5 as dependent variable and the various remission criteria as independent variables. Potential confounding factors (age, body mass index, gender, rheumatoid factor positivity, erosions and biologic treatment) were also tested. Sensitivity analyses were performed using first visits only and using patients with no missing data for all definitions of remission.
Results: Data from 32,915 patients and 157,899 visits were available. The most stringent definition of remission (table 1) was the ACR-EULAR boolean definition (4.5%). The proportion of patients with HAQ≤0.5 among patients in remission

Table 1. Remission rates (%) and association with HAQ≤0.5

Remission definition		Remission rate	HAQ≤0.5 (%)		Adjusted OR (95%CI) for HAQ≤0.5 (GEE)
			Among patients in remission	Among patients in non-remission	
ACR-EULAR boolean		4.5	87.0	34.1	2.6 (2.3-2.9)
CDAI≤2.8		13.4	78.5	27.4	3.2 (2.9-3.5)
SDAI≤3.3		17.1	78.1	25.7	3.4 (3.0-3.7)
DAS-CRP<1.6	4v	38.6	59.1	19.3	3.2 (2.9-3.5)
	3v	39.1	56.4	20.7	2.8 (2.6-3.0)
DAS-ESR<1.6	4v	31.7	63.2	22.6	3.0 (2.7-3.2)
	3v	30.4	60.4	24.3	2.6 (2.4-2.8)
DAS28-CRP<2.6	4v	34.8	62.8	20.2	3.3 (3.0-3.6)
	3v	37.5	57.7	21.3	2.8 (2.6-3.0)
DAS28-ESR<2.6	4v	25.2	68.1	26.5	2.8 (2.6-3.1)
	3v	24.4	62.5	28.7	2.3 (2.2-2.5)
DAS28-CRP≤1.9*	4v	20.0	72.8	26.1	2.9 (2.7-3.2)
	3v	21.7	64.5	27.4	2.3 (2.2-2.5)
DAS28-ESR≤2.2*	4v	18.4	71.3	29.9	2.6 (2.4-2.8)
	3v	17.3	64.4	31.8	2.1 (1.9-2.2)

*Fleischmann 2015 (PMID: 25143522)

was higher for the most stringent definitions. However, this also meant that, for the most stringent criteria, many patients in non-remission had HAQ≤0.5. The strongest degree of association between remission and HAQ≤0.5 was observed for the SDAI. However, only minor differences were noted between definitions (table 1). Sensitivity analyses yield similar results (not shown).
Conclusions: The various remission definitions confirmed their validity in terms of physical function in a large international clinical practice setting. However, many patients in non-remission will still have good functional status and being in clinical remission does not equate to having HAQ≤0.5. A multidimensional approach should be taken to help patients achieve this functional goal. Achievement of remission according to any of the indices is more important than the use of a specific index.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3929

FRI0127 OUTCOMES OF DISEASE ACTIVITY IN A 5-YEAR LARGE COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED UNDER TREAT TO TARGET RECOMMENDATIONS AND A MULTIDISCIPLINARY CARE MODEL – A REAL-LIFE EXPERIENCE

P. Santos-Moreno[1], D. Gomez[1], E. Castillo[1], R. Giraldo[1], G. Ballesteros[1], L. Villarreal[2], J. Bello[3], D. Buitrago-Garcia[3]. *[1]Rheumatology; [2]Psychology and processes; [3]Epidemiology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: Treat to Target (T2T) strategy becomes from the need to develop therapeutic targets and tools to achieve defined outcomes in rheumatoid arthritis (RA), this strategy has become recognized as a standard of good practice embodying the principle that rapid attainment of remission, or low disease activity, can halt joint damage and maintain good quality of life.
Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy for a 60 month period in a large cohort of patients from a Colombian specialized in RA center.
Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed; those patients were followed-up under T2T standards and a multidisciplinary approach. Each patient had a minimum of 6 follow-up visits. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it; we considered this follow-up type as implementation of a T2T strategy in patients with RA. We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. Descriptive epidemiology was done, percentages and averages were calculated; the median of each variable was analyzed using t-Student assuming normality for DAS28 distribution and the level activity disease was analyzed using Pearson's statistics.
Results: 3618 patients meet the inclusion criteria. 72% were receiving conventional DMARDs therapy and 28% were receiving biological therapy. 83% were woman and 17% were men. Mean age was 61 years ±11. Mean DAS28 at beginning was 3.3±1.3 and at the end of five year period was 2.8±0.7. The difference of medians for DAS28 at begging and at the end showed improvement with statistical significance (p<0.00). It was found a global increase in the percentage of patients in remission and LDA and decrease in moderate and severe disease activity groups (from 31% to 19% and from 12% to 2% respectively) with statistical significance.

ACTIVITY LEVEL	TIME 0 n(%)	2011-2012 n(%)	2013-2014 (%)	2015-2016 (%)
REM	1512 (42)	1548 (43)	1751 (48)	1826 (50)
LDA	536 (15)	955 (26)	969 (27)	1033 (29)
MDA	1128 (31)	875 (24)	809 (22)	694 (19)
SDA	442 (12)	240 (7)	89 (2)	65 (2)

Conclusions: This study show evidence of an improvement in DAS28 and level of disease activity in a cohort of RA patients from a specialized center in Colombia treated under recommendations of T2T strategy; it was found a global increase in the percentage of patients in remission (REM) and decrease in moderate and severe disease activity groups. This revision shows the importance of T2T follow-up and a multidisciplinary treatment for the management or RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5589

FRI0128 PRISM – PICTORIAL REPRESENTATION OF ILLNESS AND SELF MEASURE: THE USE OF A SIMPLE NON-VERBAL TOOL AS A PATIENT-CENTRED OUTCOME MEASURE IN EARLY RHEUMATOID ARTHRITIS COHORTS

P.C. Taylor[1], R. Alten[2], B. Haraoui[3], B. Amess[1], J. Macdonald[1], M. Truchon[4], C. Pohl[2], C. Swales[1], Y. Kaneko[5], T. Sensky[6]. *[1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom; [2]Schlosspark-Klinik Charité, University Medicine Berlin, Berlin, Germany; [3]Université de Montréal, Montreal; [4]l'institut de Rhumatologie de Montréal, Montréal, Canada; [5]Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan; [6]Centre for Mental Health, Imperial College London, London, United Kingdom*

Background: Treatment recommendations in early RA advocate a treat to target approach with the ideal goal of remission. But not all patients attain this goal. There is a need for outcome measures that are meaningful to patients and inform management of which alleviation of suffering is a key aim. PRISM[1] is a novel, validated, brief method of measuring suffering consistent with Cassell's seminal conceptualisation[2].
Objectives: To understand the relationships between a patient's perception of the totality of the impact of RA and commonly used clinical assessments of disease activity, depression and illness intrusiveness.
Methods: Basic sociodemographic and clinical data were collected from 182 RA patients from 3 international centres, assigned to one of four cohorts (two early RA and two established RA), at baseline, weeks 12 and 24. The two early RA cohorts (diagnosis <2 yr) comprised Group 1 on stable treatment (n=37) and Group 2 requiring csDMARD adjustment (n=34). Using the iPRISM App on a tablet, all patients were asked to complete the basic PRISM task to measure self-illness separation (SIS). The smaller the SIS, the greater the person's perceived suffering. In the PRISM+ task, patients were asked to identify two valued aspects of their life at the moment (X and Y) which bring pleasure, satisfaction, a sense of achievement, or a sense of purpose. The iPRISM App automatically records the distance between the centres of each of these disks and the Self disk to measure patients' perceptions of the intrusiveness of their illness on two personally valued aspects of their lives.
For both groups, direction of change in SIS and the PRISM+ measures were compared with direction of change in disease activity measures and patient global disease activity (ptGbl), assessed at wks 12 and 24, using the sign test.
Results: PRISM was easy to use and most patients understood the simple instructions. Of 182 patients at baseline, SIS showed significant correlations with ptGbl (r_s=-0.48, p<0.0001), pain VAS (r_s=-0.45, p<0.0001), PHQ9 (r_s=-0.45, p<0.0001) and illness intrusiveness scale (r_s=-0.51, p<0.0001). Suffering was inversely correlated with the perceived controllability of the symptoms of RA; for Group 1, r_s=0.41, p<0.0001, for Group 2, r_s=0.32, p<0.0001.
In Group 2, SIS and DAS28-ESR showed small trends to improvement by wk 12 (DAS28-ESR Δ=-0.11, p=0.557; SIS Δ=1.7, p=0.296) with significant improvement by wk 24 (DAS28-ESR Δ=-0.82, p=0.002; SIS Δ=3.85, p=0.029). However, there was no significant improvement in the intrusiveness of the illness on the valued aspects of life over this time period (Actual X, Δ=-0.25, p=0.557; Actual Y, Δ=1.89, p=0.169).
Conclusions: PRISM is a novel PRO that quantifies factors salient to each individual with respect to the impact of RA and its treatment while allowing for incorporation of a wide range of such influences. It may have utility as an adjunct to disease activity measures in setting agreed personalised therapeutic targets.
References:
[1] T Sensky & S Buchi. PLoS ONE 11(5):e0156284, 2016.
[2] EJ Cassell. NEJM 306:639–645,1982.
Acknowledgements: This work was financially supported by UCB in the context of an Investigator Initiated Study.
Disclosure of Interest: P. Taylor Grant/research support from: Celgene, Galapagos, GlaxoSmithKline, UCB, and Janssen, Consultant for: AbbVie, Bristol Myers Squibb, Eli Lilly and Company, GlaxoSmithKline, Merck, Pfizer, UCB, Biogen, Sandoz and Janssen, R. Alten: None declared, B. Haraoui: None declared, B. Amess: None declared, J. Macdonald: None declared, M. Truchon: None declared, C. Pohl: None declared, C. Swales: None declared, Y. Kaneko Grant/research support from: Eisai, AbbVie, Daiichisankyo, Speakers bureau: Astellas Pharma, Chugai Pharmaceutical Co, Ltd., Bristol–Myers K.K., Eisai Co., Ltd., Kissei Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Taisho Toyama Pharma Co., and UCB, T. Sensky: None declared
DOI: 10.1136/annrheumdis-2017-eular.4450

FRIDAY, 16 JUNE 2017

Rheumatoid arthritis - comorbidity and clinical aspects

FRI0129 COMPARATIVE SAFETY OF BIOLOGIC DMARD INITIATION IN RA: A POPULATION-BASED OBSERVATIONAL STUDY OF MALIGNANCY RISK

S. Suissa[1], S. Dell'Aniello[1], T. Simon[2]. *[1]McGill University, Montreal, Canada; [2]Bristol-Myers Squibb, Princeton, United States*

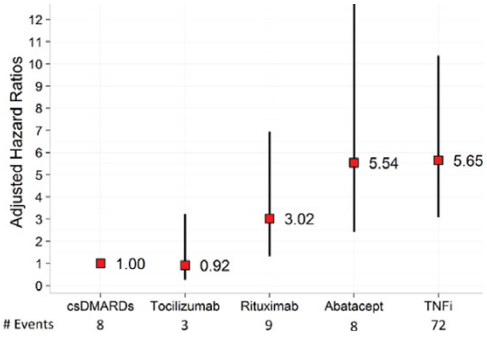
Background: Patients (pts) with RA are at increased risk for some malignancies and the use of biologic (b)DMARDs has been reported to further increase this risk.[1] Abatacept (ABA), the first selective T-cell co-stimulation modulator for RA treatment, is now often prescribed as a first-line bDMARD, but long-term effects are unknown.

Objectives: To assess in a real-world, observational study whether treatment with ABA had a similar malignancy risk as other biologics, with or without MTX, when used as the initial bDMARD for RA.
Methods: The Truven MarketScan® Commercial and Supplemental Medicare databases were used to identify adult pts diagnosed with RA who initiated bDMARD treatment with ABA or another bDMARD between Jan 2007 and Dec 2014. Other bDMARDs included adalimumab, anakinra, certolizumab, etanercept, golimumab, infliximab, rituximab and tocilizumab. Pts were required to have ≥6 months (M) of continuous health plan enrolment before bDMARD initiation (index date) and deemed to have initiated a treatment if there was no claim for any bDMARD in the limited 6M period before bDMARD initiation. Pts who had a malignancy in the baseline 6M period were excluded. Pts were followed up from the date of the first bDMARD prescription initiation, either ABA or another bDMARD, until occurrence of a malignancy (identified by ICD-9 diagnosis code), end of enrolment in the database or end of data collection, whichever occurred first. A 6M latency period was included. Propensity scores of ABA initiation were estimated from the baseline covariates using a logistic regression model, and trimmed to include only pts with ranges common to both ABA-exposed and comparator bDMARD cohorts. The Cox proportional hazard regression model was used to provide an estimate of the hazard ratio (HR) of malignancy associated with ABA initiation compared with initiation of another bDMARD, adjusted for age and deciles of the propensity score after trimming.
Results: A total of 5391 pts were identified as above as having initiated bDMARD therapy with ABA and 74,315 initiated with another bDMARD, with follow-up of <8 yrs (mean 2.1 yrs). Pts who initiated ABA vs other bDMARDs were older (mean 55 vs 52 yrs), had more co-morbidity, used less MTX (49 vs 57%) and more other non-bDMARD (41 vs 36%) at baseline. After trimming on propensity scores, 565 pts developed a malignancy after ABA (incidence rate 5.0 per 100/yr) compared with 5750 after another bDMARD (incidence rate 3.6 per 100/yr). The adjusted HR (95% CI) of any malignancy with ABA initiation relative to other bDMARDs was 1.18 (1.06, 1.30), while for any malignancy excluding non-melanoma skin cancer it was 1.17 (1.02, 1.34). The risk (HR; 95% CI) was not significantly elevated for lung cancer (1.11; 0.70, 1.76), female breast cancer (1.21; 0.91, 1.62) and lymphoma (1.21; 0.77, 1.90).
Conclusions: In this large, real-world study of pts treated for RA, the incidence of the most common malignancies of breast, lung and lymphoma were not significantly increased in pts using abatacept as first-line bDMARD treatment compared with other bDMARDs, though the confidence intervals were wide. The slight increase in the risk of overall malignancy with abatacept needs further investigation, particularly to assess the potential for residual confounding and the impact of the short baseline period.
References:
[1] Mercer LK, et al. Ann Rheum Dis 2015;74:1087–93.
Disclosure of Interest: S. Suissa Consultant for: Bristol-Myers Squibb, S. Dell'Aniello: None declared, T. Simon Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb
DOI: 10.1136/annrheumdis-2017-eular.2887

FRI0130 RATES AND RISK FACTORS OF NEW-ONSET PSORIASIS UNDER DIFFERENT BIOLOGIC AGENTS AND CONVENTIONAL SYNTHETIC DMARD TREATMENT

A. Strangfeld[1], L. Baganz[1], A. Richter[1], B. Manger[2], G.-R. Burmester[3], C. Eisterhues[4], S. Wassenberg[5], A. Zink[1,3], J. Listing[1]. *[1]German Rheumatism Research Center, Berlin; [2]Scientific Advisory Board, Erlangen; [3]Charité University Medicine, Berlin; [4]Rheumatologist, Braunschweig; [5]Rheumatologist, Ratingen, Germany*

Background: Psoriatic skin disease is a burdensome, sometimes painful, dermatologic condition which was reported to occur as an adverse event (AE) during TNF-inhibitor (TNFi) treatment of rheumatoid arthritis (RA). Single case reports revealed the occurrence of psoriasis also during treatment with non-TNFi, but the magnitude under those agents remains unclear.
Objectives: To compare incidence rates of psoriasis in RA under treatment with different biologic and conventional synthetic (b/cs)DMARDs and to investigate risk factors.
Methods: We used data of 12,722 patients (53,585 patient years (py)) enrolled with the start of a b/csDMARD in the German biologics register RABBIT. Patients were required to have no psoriasis at baseline and at least one follow-up. All psoriatic events (PsE) reported until 30 April 2016 were selected and assigned to treatments administered within 3 months prior to the event. Crude incidence rates (IR) of PsE were calculated per 1,000py. Cox regression was applied to investigate risk factors for the occurrence of PsE with and without inverse probability weights (IPW) to adjust for confounding by indication.
Results: 96 PsE were reported, with only 6 of them categorized as being serious. The median time between enrollment in the cohort and onset of psoriasis was 19 months (IQR:11–45 months). 21 of all PsE (22%) were palmoplantar manifestations of which 9 were reported as pustular type.
Compared to csDMARD treatment with a crude IR of 0.44/1,000py (95% CI 0.2;0.9), the IRs found under TNFi (IR 2.99 (95% CI 2.3;3.8)) and abatacept (IR 3.99 (95% CI 1.7;7.9)) were significantly higher. In patients treated with rituximab (IR 1.8 (95% CI 0.8;3.4)) or tocilizumab (IR 0.7 (95% CI 0.1; 2.0)) IRs for PsE were not significantly different from csDMARD patients. Across TNFi, the IR varied insignificantly.
Adjusted regression analysis showed higher risk for PsE with TNFi, abatacept and rituximab (graph). Female sex (adjusted hazard ratio (HR) 1.8 (1.0;3.3)) and being rheumatoid factor negative (HR 1.6 (1.0;2.6)) were additional significant risk factors. Smoking (HR 1.6 (1.0; 2.5)), age (HR 1.0 (0.98;1.01)), glucocorticoids per 5 mg/d increase (HR 1.1 (1.0;1.2)), and prior (≤6months) skin infections (HR 2.2 (0.5;9.7)) were not significantly associated. Replacing glucocorticoids with DAS28 did not show differing results. Adjustment with IPW attenuated the effect of rheumatoid factor (p=0.4) but smoking was significantly associated with a higher risk (p<0.01).



Conclusions: This is the first analysis comparing the incidence of psoriasis under biologics with different modes of action within one cohort. Our results confirmed a higher risk for TNFi [1] and showed a similar result for abatacept. A lower but still significant increased risk was found for rituximab, whereas there was no difference for tocilizumab compared to csDMARDs. New onset psoriasis is a rare and most often non-serious event. The number needed to harm is 334 patients treated with TNFi for one year to observe one PsE.
Acknowledgements RABBIT is supported by a joint, unconditional grant from AbbVie, BMS, Celltrion, MSD, Pfizer, Roche, Samsung and UCB.
References:
[1] Hernandez et al., Arthritis Care Res 2013; 65:2024–31.
Disclosure of Interest: A. Strangfeld Speakers bureau: BMS, MSD, Pfizer, Roche, Sanofi-Aventis, L. Baganz: None declared, A. Richter Consultant for: Pfizer, B. Manger Consultant for: Abbvie, BMS, MSD, Pfizer, Roche, UCB, G.-R. Burmester Consultant for: AbbVie, BMS, MSD, Pfizer, Roche, UCB, C. Eisterhues: None declared, S. Wassenberg Consultant for: AbbVie, Pfizer, Novartis, Janssen, Roche-Chugai, Celltrion, BMS, Fuji, Speakers bureau: AbbVie, Celgene, Novartis, Pfizer, MSD, Lilly, Janssen, UCB, A. Zink Speakers bureau: AbbVie, BMS, MSD, Pfizer, Roche, UCB, J. Listing Consultant for: Sandoz, Pfizer
DOI: 10.1136/annrheumdis-2017-eular.5092

FRI0131 THE 2010 ACR/EULAR CRITERIA ARE INSUFFICIENTLY ACCURATE IN THE EARLY IDENTIFICATION OF AUTOANTIBODY-NEGATIVE RHEUMATOID ARTHRITIS: RESULTS FROM THE LEIDEN-EAC AND ESPOIR COHORTS

D. Boeters[1], C. Gaujoux-Viala[2], A. Constantin[3], A. van der Helm-van Mil[1]. *[1]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; [2]Department of Rheumatology, Nîmes University Hospital; EA2415, Montpellier University, Nîmes; [3]Department of Rheumatology, Centre Hospitalier Universitaire de Toulouse, Hôpital Purpan, Toulouse, France*

Background: The 2010-ACR/EULAR criteria were derived to classify RA earlier in time. Previous studies indeed observed that the 2010-criteria were fulfilled earlier than the 1987-criteria. This study determined whether the 2010-criteria perform equally in the early detection of autoantibody-positive and autoantibody-negative RA.
Objectives: To compare the performance of the 2010-criteria between autoantibody-positive and autoantibody-negative RA within two different early arthritis cohorts.
Methods: From the total Leiden-EAC (n=3448) and ESPOIR (n=813) RA-patients who fulfilled the 1987-RA criteria at 1-year but not at presentation were selected (n=515 and n=53, respectively). These RA-patients were studied on the presence of ACPA and RF, and on fulfilling the 2010-criteria at baseline, as 2010-positivity indicated that these RA-patients were earlier identified.
Results: In the EAC, 67% of the selected RA-patients did already fulfil the 2010-criteria at baseline. In ESPOIR this was 57%, indeed demonstrating early classification with the 2010-criteria. Among the selected autoantibody-positive RA-patients of the EAC, 85% was identified at baseline already with the 2010-criteria. Within autoantibody-negative RA this was 45% (p<0.001). Similarly within autoantibody-positive RA-patients in ESPOIR 92% was 2010-positive at baseline, whereas this was only 25% within autoantibody-negative RA (p<0.001).
Conclusions: The 2010-criteria perform well in the early identification of autoantibody-positive RA, but autoantibody-negative RA-patients are still frequently missed with these criteria. As it has been demonstrated that early

treatment initiation is beneficial for the outcome of ACPA-negative RA as well, other diagnostics are required for the early identification of ACPA-negative RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3994

FRI0132 HIGH DISEASE ACTIVITY IS A PREDICTOR OF DEPRESSION AND PERSISTENT DEPRESSION IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE (OBRI)

R. Joshi[1], M. Movahedi[2,3], E. Rampakakis[2], A. Cesta[3], X. Li[3], S. Couto[3], J. Sampalis[2], C. Bombardier[3,4,5], B. Kuriya[6] on behalf of OBRI investigators. *[1]Department of Rheumatology, Brampton Civic Hospital, William Osler Health System, Brampton; [2]JSS Medical Research, Montreal; [3]Ontario Best Practices Research Initiative, Toronto General Hospital, University Health Network; [4]Division of Rheumatology, Mount Sinai Hospital; [5]Department of Medicine (DOM) and Institute of Health Policy, Management, and Evaluation (IHPME); [6]Sinai Health System, University of Toronto, Toronto, Canada*

Background: The prevalence of depression among individuals with rheumatoid arthritis (RA) may be as high as 40% but persistence of depression over time is relatively unknown. Uncontrolled inflammation may drive severe disease and, in turn, inflammation and high disease activity are hypothesized to mediate depressive symptoms.
Objectives: The aims of this analysis were to: (1) describe the prevalence of depression at baseline and determine how often depression persists over time; (2) determine whether there is an association between changes in disease activity and depression over time among individuals with early RA (ERA).
Methods: ERA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) with ERA ($\leq$1 year disease duration) and $\geq$2 years of follow-up were included. Persistent depression was defined as self-reported depression at baseline and at >50% of visits over the first 2 years. The association between baseline disease activity, measured by the Clinical Disease Activity Index (CDAI), and depression at baseline or persistent depression was evaluated with multivariate logistic regression. The General Estimation Equation was also used to explore the association between changes in CDAI disease activity over time and risk of depression.
Results: 469 patients with ERA (72.9% female) were included with a mean (SD) age of 56.8 (13.6) years. Mean (SD) disease parameters were: CDAI: 22.9 (14.1); DAS28: 4.6 (1.5); and HAQ disability Index: 1.1 (0.75). At baseline, the prevalence of depression was 26%, and 23% reported persistent depression. Persistent depression was significantly higher in patients with moderate CDAI (19%) and high CDAI (29%) compared to those in CDAI low disease activity (LDA) or remission (16%, p=0.02). After adjusting for potential confounders (sex, rheumatoid factor status, prior use of csDMARDs, current use of bDMARDs, HAQ disability index, number of comorbidities), increased CDAI at baseline was significantly associated with both baseline depression and persistent depression (OR: 1.04; 95% CI: 1.01–1.06, p=0.002). Female gender (OR: 3.17; 95% CI: 1.50–6.68 p=0.002) and greater number of comorbidities at baseline (OR: 1.68; 95% CI: 1.47–1.93, p<0.001) were also associated with persistent depression. Over the course of follow-up, the risk of depression was significantly higher among patients with moderate disease activity compared to those in CDAI LDA or remission (OR: 1.16; 95% CI: 1.04–1.29, p=0.006). The risk of depression was substantially greater for those with high disease activity (OR: 1.32; 95% CI: 1.15–1.52) over time compared to those achieving LDA or remission states.
Conclusions: Depression in ERA is common and initial high disease activity increases the risk of depression as well as its persistence. High CDAI during the early years of follow-up was also an independent predictor of depression. This highlights the importance of intervening during the "window of opportunity" to control disease activity and the potential to mitigate adverse health outcomes, including depression.
Disclosure of Interest: R. Joshi Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Novartis, Merck, Pfizer, Roche, Sanofi, & UCB, M. Movahedi Employee of: OBRI/JSS Medical Research, E. Rampakakis Employee of: JSS Medical Research, A. Cesta Employee of: OBRI, X. Li Employee of: OBRI, S. Couto Employee of: OBRI, J. Sampalis Employee of: Head of JSS Medical Research, C. Bombardier Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Novartis, Merck, Pfizer, Roche, Sanofi, & UCB, B. Kuriya Grant/research support from: OBRI was funded by peer reviewed grants from CIHR (Canadian Institute for Health Research), Ontario Ministry of Health and Long-Term Care (MOHLTC), Canadian Arthritis Network (CAN) and unrestricted grants from: Abbvie, Amgen, Celgene, Hospira, Janssen, Lilly, Novartis, Merck, Pfizer, Roche, Sanofi, & UCB
DOI: 10.1136/annrheumdis-2017-eular.2311

FRI0133 IS THERE INCREMENTAL MENTAL HEALTH BURDEN ASSOCIATED WITH RHEUMATOID ARTHRITIS?

V. Strand[1], M. Kosinski[2], R. Rendas-Baum[2], D. Brooks[3], R. Ganguly[3]. *[1]Stanford University, Palo Alto, CA; [2]Optum, Inc., Eden Prairie, MN; [3]GlaxoSmithKline, Collegeville, PA, United States*

Background: Rheumatoid arthritis (RA) patients are more likely to experience depression.[1] This comorbidity is associated with increased disability, use of healthcare services, and mortality risk.[2,3] The association between RA and other mental health disorders has received limited attention and there remains a need to further demonstrate and understand the impact of RA on mental health.
Objectives: Evaluate the mental health burden of RA patients based on the analysis of Short Form-36v2 Health Survey (SF-36v2) mental health (MH) and role emotional (RE) domain scores from two independent general population databases in the US and Europe.
Methods: The mental health burden associated with RA was analyzed by comparing mean SF-36v2 MH and RE scores of individuals self-reporting RA (with or without depression) and the scores from 2 benchmark samples (individuals without RA, individuals with depression and no RA) in two large cross-sectional survey studies (QualityMetric's 2009 General US Population Norming Study of the SF-36v2 and the 2014 European National Health and Wellness Survey). Multivariate regression methods were used to adjust each benchmark sample to the distribution of the RA sample in terms of age and gender. Differences between samples were interpreted with respect to minimally important differences: 3 points for MH; 4 points for RE.
Results: The US (2009) and European (2014) samples included 4,042 and 81,366 individuals, respectively. Compared with individuals without RA or depression, mean RE scores were significantly (P<0.001) lower for RA patients without depression in the US (-7.75 points) and Europe (-5.31 points). Likewise, mean MH scores were significantly (P<0.001) lower among RA patients without depression in the US (-4.85 points) and Europe (-5.03 points) compared with individuals without RA or depression. Compared to individuals with depression and no RA, mean RE and MH scores were 5 to 10 points higher (P<0.001) for RA patients without depression in both the US and Europe. Comparisons of RE and MH scores between RA patients with and without comorbid depression showed that comorbid depression was associated with 2 to 6 points lower scores (P<0.01) in RE and MH domains, in both the US and Europe.
Conclusions: RA is associated with significant and clinically meaningful mental health burden as measured by SF-36v2 MH and RE domains. Results comparing scores between RA patients with and without comorbid depression suggest that there is an incremental mental health burden associated with RA, often exceeding minimally important differences among US patients.
References:
[1] Dickens C, et al. Psychosomatics. 2003;44(3):209–215.
[2] Ang DC, et al. J Rheumatol. 2005;32(6):1013–1019.
[3] Kessler RC, et al. J Occupat Environ Med. 2003;45(12):1257–1266.
Disclosure of Interest: V. Strand Consultant for: Abbvie, Amgen, AstraZeneca, BiogenIdec, Boehringer Ingelheim, Celltrion, Crescendo, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi and UCB, M. Kosinski Employee of: Optum, R. Rendas-Baum Employee of: Optum, D. Brooks Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, R. Ganguly Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline
DOI: 10.1136/annrheumdis-2017-eular.3575

FRI0134 CLUSTER ANALYSIS OF PULMONARY LESIONS IN RHEUMATOID ARTHRITIS (RA); AIRWAY DISEASE IS SHARED AND CRITICAL PULMONARY ABNORMALITY IN RA

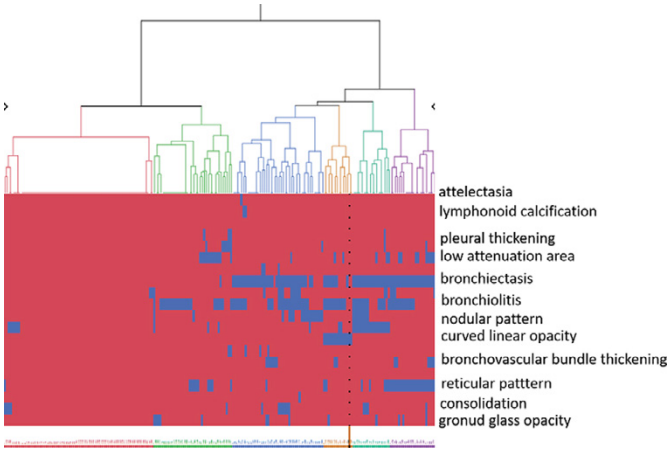
A. Tanaka, Y. Namiki, R. Yamazaki, H. Okada, S. Arai, T. Owada, R. Maezawa, M. Arima, K. Kurasawa. *Departoment of Rheumatology, Dokkyo Medical University, Shimotuga-Gun, Japan*

Background: Rheumatoid arthritis (RA) is a systemic inflammatory disease that affects joints and various organs including the lung. The pulmonary involvement is critical for prognosis of the patients and decision of the treatment. Moreover, the pulmonary involvement showed various abnormalities such as interstitial pneumonia (ILD) and airway disease (AD). Importantly, a pulmonary abnormality coexists with other ones in RA patients. There have been large numbers of studies on the prevalence of pulmonary abnormalities and clinical features of patients with these lesions. However, it remains to be elucidated what existence pattern of pulmonary abnormalities RA patients have.
Objectives: To reveal the existence pattern of the pulmonary abnormalities in RA patients using cluster analysis, and to clarify the clinical features of patients with multiple pulmonary abnormalities.
Methods: Subjects were consecutive 208 RA patients who were treated with bDMARDs as the first one from Feb. 2004 to Sep. 2015 in our department and received HRCT scan before and after the therapy. Pulmonary abnormalities were classified into 4 categories (ILD, nodular lesions, AD and other) and 20 lesions such as ground-glass opacity, reticular pattern, bronchiolitis and bronchiectasis and were examined their existence and distribution. Cluster analysis was conducted according to the existence of the lesions by Ward method. Clinical features were analyzed through reviewing medical records.
Results: Subjects were 208 RA cases (M/F; 64/144, mean age 59.2 year-old,

disease duration 13.1 years). Pulmonary lesions were found in 146 (70.2%) of RA patients before treatment Imaging findings were 81of ILD (39%),45 of nodular lesion (21.6%) and 115 of AD (55%). Cluster analysis showed 6 clustered (Fig.), 1; no pulmonary lesions, 2; AD without bronchoectasia, 3; AD with bronchoectasia, 4; AD with curved linear opacities, 5; AD with nodular lesions, and 6; reticular pattern with AD.

AD was common abnormalities and coexisted with other pulmonary lesions in RA. AD was found in 79%, 78% and 71% of patients with pulmonary abnormalities, ILD and nodular lesions, respectively. AD alone, AD with ILD, and AD with nodular pattern were found in 16.3%, 8.6% and 28.9%, respectively, while patients without pulmonary lesions were 29.8% in RA. AD was frequently associated with ILD and nodule compare to non-AD.

No differences were found in gender, smoking history, disease duration and disease activity between patients with and without AD. New emergence or exacerbation of pulmonary abnormalities developed in AD patients compared to those without pulmonary abnormalities or AD. No significant differences were found in clinical features, among AD alone, AD with ILD and AD with nodules.



Conclusions: Pulmonary abnormalities were found in 70% in RA. AD was found in 55% of RA patients and coexisted with other pulmonary lesions such as ILD and nodular lesions. Patients with AD frequently showed newly emerging or worsening pulmonary lesions, regardless of the coexistence of other pulmonary lesions. Thus, AD is shared and critical pulmonary abnormality in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5828

FRI0135 TREATMENT OF JAPANESE EARLY RHEUMATOID ARTHRITIS PATIENTS WITH LOW-DOSE PREDNISOLONE FOR MAXIMUM 1 YEAR LEADS TO EARLIER IMPROVEMENT OF DISEASE ACTIVITY AND DOES NOT WORSEN BONE METABOLISM STATUS AND RATES OF NEW COMPLICATIONS

E. Torikai, M. Suzuki, Y. Matsuyama. *Orthopaedic Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan*

Background: Glucocorticoid (GC) therapy for rheumatoid arthritis patients improves joint inflammation and destruction; however, it is associated with risk of complications such as osteoporosis, diabetes (DM), and cardiovascular (CV) disease. Although EULAR recommends that low-dose GC should be administered for up to 6 months, the ideal dose and duration of GC use remain unresolved.

Objectives: To investigate the efficacy and safety of low-dose GC therapy in addition to other disease-modifying antirheumatic drugs (DMARDs) for maximum 1 year in Japanese early RA patients.

Methods: Ninety-six Japanese RA patients with disease duration of <2 years were included. Patients were treated with a T2T strategy; if disease activity did not improve within 3 months, their DMARDs were replaced with alternatives or additional DMARDs were added. We excluded patients with a history of prior complications, including CV disease, DM, or vertebral fracture. We classified patients into two groups, one was group treated with DMARDs alone (N group; 35 females and 10 males) and the other with maximum 5 mg of GC for maximum 1 year along with DMARDs (GC group; 40 females and 11 males). The mean ages of the N and GC groups were 56.3 and 60.9 years, respectively. Thirty-four percent of patients were treated with MTX monotherapy, 20.9% were treated with combined conventional synthetic DMARD with MTX, and 31.3% were treated with a biological agent. Regarding MTX or biological agent use rates, no significant statistical differences were observed between the groups. We evaluated the change of DAS28-CRP scores for 3 years, bone metabolism makers [urine type I collagen cross-linked N-telopeptide (NTX), serum tartrate-resistant acid phosphatase 5b (TRACP5b), serum bone-specific alkaline phosphatase (BAP), and serum osteocalcin (OC)], bone mineral density (BMD) of lumber spine (L-spine) and femoral neck (FN) and the rate of new complications. Comparisons of BMD and the rate of new complications were made at baseline and 3 years after initiating GC treatment.

Results: There were no significant differences in DAS28-CRP scores at baseline. In the GC group, the mean GC dose was 2.46 mg/day. At 1 month after treatment, there was a significant difference in the improvement rate of DAS28-CRP scores in the GC group compared with the N group. However, no significant difference was observed between the two groups at 3 months or more post-treatment (Fig.1). None of the bone metabolism makers and BMD deteriorated in the GC group and there were no statistical differences between both groups (Table.1, Fig.2). New complications occurred in four cases in the N group (one, vertebra fracture; one, CVD; and two, high HbA1c levels) and four cases in the GC group (two, vertebrae fractures and two, high HbA1c levels). There were no significant differences in the rate of new complications between both groups.

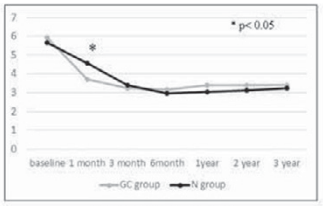


Fig.1 DAS28ESR score

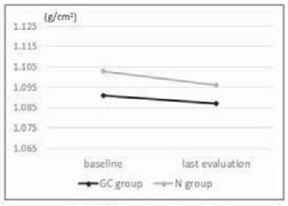


Fig.2(a) BMD of L-spine

(GC group)	baseline	1 year	3 year
NTX (nmolBCE/mmolCr)	45.9± 24.5	48.3± 25.1	46.5± 23.9
TRCP5b (mU/dL)	376± 181	388± 176	369± 169
BAP (μg/L)	17.1± 6.5	16.1± 6.0	17.6± 6.4
OC (ng/mL)	13.4± 6.5	12.6± 6.4	13.9± 6.9
(N group)	**baseline**	**1 year**	**3 year**
NTX (nmolBCE/mmolCr)	44.1± 22.9	44.7± 23.5	44.0± 23.0
TRCP5b (mU/dL)	359± 172	364± 165	365± 164
BAP (μg/L)	17.9± 6.5	17.4± 6.0	17.0± 6.4
OC (ng/mL)	13.7± 6.1	13.6± 6.2	14.1± 6.5

Table. bone metabolism makers

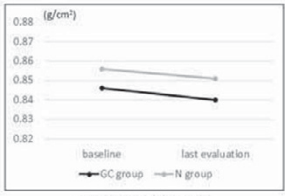


Fig.2(b) BMD of FN

Conclusions: The treatment of early rheumatoid arthritis by low-dose GC for maximum one year enables earlier improvement of disease activity and does not worsen bone metabolism status or the rate of new complications. The therapy does not pose a problem in the middle term. This study confirms that use of GC in RA patients leads to patient satisfaction.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2092

FRI0136 OVARIAN RESERVE, AS ASSESSED BY MEASURING SERUM ANTI-MÜLLERIAN HORMONE LEVELS, DECLINES MORE RAPIDLY OVER TIME IN RHEUMATOID ARTHRITIS PATIENTS COMPARED TO CONTROLS

J. Brouwer[1,2], J.S. Laven[1], J.M. Hazes[2], N.S. Erler[3], J.A. Visser[4], R.J. Dolhain[2]. *[1]Division of Reproductive Medicine - Department of Obstetrics and Gynaecology; [2]Department of Rheumatology; [3]Department of Biostatistics; [4]Department of Internal Medicine, Erasmus MC University Medical Center Rotterdam, Rotterdam, Netherlands*

Background: The ovarian reserve in women with rheumatoid arthritis (RA) may be compromised, based on a reduced fertility[1] and a younger age at menopause[2]. Serum anti-Müllerian hormone (AMH) levels are a proxy for the ovarian follicle pool, and are the most reliable predictor of the age at which menopause sets in.

Objectives: Our objectives were to study the intra-individual change in AMH levels in female RA patients, and to study the effect of RA-related factors on the decline of AMH levels over time.

Methods: Female RA patients from a nationwide prospective cohort study (PARA study) in 2002–2008, were re-assessed in 2015–2016. Serum AMH levels were measured using the pico AMH assay (provided by Ansh Labs, Texas, USA) and compared to healthy controls (Lie Fong, 2012)[3]. A linear mixed model was built to assess the effect of RA-related clinical factors on the decline of serum AMH levels over time.

Results: 128 women were re-assessed at a mean age of 42.6±4.4 years, with a median disease duration of 15.8 (IQR 12.7–21.5) years. The participants appeared a more fertile selection of the original PARA cohort. The mean time between the first and the follow-up assessments was 10.7±1.8 years. At follow-up, more patients had AMH levels below the 10th percentile of controls (39%; 95% CI 31 – 48%), than at baseline (16%; 95% CI 9.3–22%). The linear mixed model showed only a significant effect of age, and no significant effect of RA-related factors on the decline of serum AMH levels over time.

Conclusions: This is the first longitudinal study on AMH levels in women with RA, and is showing that AMH levels in RA patients decline more rapidly over time compared to healthy controls. This indicates that the disease process of RA has a negative impact on the ovarian reserve of young pre-menopausal RA women.

References:

[1] Brouwer J, Hazes JM, Laven JS, Dolhain RJ. Fertility in women with rheumatoid arthritis: influence of disease activity and medication. Ann Rheum Dis 2015;74:1836–41.

[2] Del Junco D. The relationship between rheumatoid arthritis and reproductive function [Dissertation]. Houston, Texas: The University of Texas Health Sciences Center at Houston School of Public Health; 1988.

[3] Lie Fong S, Visser JA, Welt CK, et al. Serum anti-mullerian hormone levels in healthy females: a nomogram ranging from infancy to adulthood. J Clin Endocrinol Metab 2012;97:4650–5.

Acknowledgements: This study was funded by the Dutch Arthritis Foundation (Reumafonds). The pico AMH assays were generously provided by Ansh Labs (Houston, Texas, USA).
Furthermore, we would like to thank all patients and rheumatologists who contributed to the PARA study, as well as all researchers and laboratory workers who have worked on this project.

Disclosure of Interest: J. Brouwer: None declared, J. Laven: None declared, J. Hazes: None declared, N. Erler: None declared, J. Visser: None declared, R. Dolhain Grant/research support from: unrestricted research grant by UCB Pharma BV

DOI: 10.1136/annrheumdis-2017-eular.4270

FRI0137 PRESENCE OF THYROID DISEASE IN RHEUMATOID ARTHRITIS PATIENTS IS PREDICTOR OF WORSE INITIAL TREATMENT RESPONSE: AN OBSERVATIONAL, COHORT STUDY

A. Emamifar[1], R. Hviid Larsen[2], R. Asmussen Andreasen[1], I.M. Jensen Hansen[1,3]. *[1]Rheumatology; [2]Medicine, Svendborg Hospital, Odense University Hospital, Svendborg; [3]DANBIO, Copenhagen, Denmark*

Background: Rheumatoid Arthritis (RA) should be treated instantly to prevent further joint destruction. The first few months after treatment initiation are critical for long-term treatment outcome.[1]Patients with RA are at increased risk of thyroid disease with direct effect on initial treatment response.[2]

Objectives: To define the prevalence of thyroid disease among RA patients as well as to evaluate the correlation between presence of thyroid disease in RA patients and initial treatment response.

Methods: All RA patients who were registered in the local part of Danish Danbio registry were included in this study. Patients' demographic data, serology results including rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (anti-ccp) as well as disease activity score in 28 joints-C-reactive protein (DAS28-CRP) at the time of diagnosis and after 4 months (±1–2 months) of treatment initiation were extracted. ∆DAS28 was calculated as follows: DAS28 at the time of diagnosis – DAS28 after 4 months (±1–2 months) of treatment initiation. Patients' electronic hospital records including laboratory results were reviewed to reveal if they had been diagnosed with thyroid disease.

Results: 1035 patients were included in the study (Table 1). Prevalence of thyroid disease was 11.8% (122/1035). Multiple linear regression analysis showed a negative correlation between ∆DAS28 and presence of thyroid disease adjusted for age, gender, disease duration, RF, anti-ccp and DAS28 at the time of diagnosis (Regression coefficient (95% Confidence Interval): -0,157 (-0.312 to -0.002), P=0.047) (Table 2). RA patients with thyroid disease had significantly poorer initial response to RA treatment compared to patients with isolated RA after 4 months of treatment (P=0.002).

Table 1. Demographic and disease characteristics of the included (N=1035) patients

Age (years), Mean ± SD:	67,1±14,5
Gender (%) Female	656 (63.4%)
DAS28 at time of diagnosis, Mean ± SD:	4.5±0.9
DAS28 after 4 months of treatment, Mean ± SD:	3.1±0.8
∆DAS28, Mean ± SD:	1.4±1.0
IgM Rheumatoid Factor (%) Positive	607 (58.6%)
Anti-ccp (%) Positive	532 (51.4%)

Table 2. Results of Multiple linear regression analysis

Variables	Coefficient	t-stat	Confidence Interval		P value
			Lower 95%	Upper 95%	
Age	0,002	1.427	-0.001	0.006	0.154
Male gender	0,056	1.051	-0.049	0.161	0.293
disease duration	-0,003	-1.093	-0.009	0.002	0.275
Rheumatoid Factor positivity	0,010	0.159	-0.118	0.139	0.873
Anti-ccp positivity	-0,030	-0.456	-0.158	0.098	0.649
DAS28 at diagnosis	0,717	26.173	0.664	0.771	>0.001
Presence of Thyroid Disease	-0,157	-1.988	-0.312	-0.002	0.047

Conclusions: Presence of thyroid disease in RA patients worsens initial treatment response and is suggestive of poor long-term prognosis. The authors propose routine measurement of serum thyroid stimulating hormone (TSH) in all RA patients at the time of diagnosis and with yearly interval.

References:

[1] Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet 2016; 388:2023–2038. doi: 10.1016/S0140–6736(16)30173–8.
[2] Joshi P, Agarwal A, Vyas S, et al. Prevalence of hypothyroidism in rheumatoid arthritis and its correlation with disease activity. Trop Doct 2017;47:6–10.

Acknowledgements: We thank Mrs. Maryam Mousavi for her contribution to data collection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3271

FRI0138 LUNG INVOLVEMENT IN RHEUMATOID ARTHRITIS – A PORTUGUESE REALITY

A.C. Duarte, S. Sousa, A. Cordeiro, M.J. Santos, J. Canas da Silva. *Rheumatology, Hospital Garcia de Orta, Almada, Portugal*

Background: Rheumatoid arthritis (RA) is associated with a wide range of extra-articular manifestations. Non-cardiac thoracic manifestations occur in approximately 5–20% and can affect the pleura, pulmonary parenchyma, airways and vasculature[1]. Besides, patients can also experience drug-induced pulmonary disease related to RA medication[2].

Objectives: To characterize lung involvement and factors associated with lung disease in a cohort of RA patients.

Methods: Retrospective analysis of RA patients followed in our Rheumatology department. Lung involvement was defined by the presence of imagiological/histopathological alterations described in the spectrum of rheumatoid arthritis-associated lung disease in either symptomatic or asymptomatic patients. Logistic regression analysis was used to evaluate demographic and clinical features independently associated with lung disease.

Results: In total, 532 RA patients were analysed, 400 females, mean age of 63.6 (±13.8) years and mean disease duration of 11.8 (±9.5) years. Rheumatoid factor (RF) was positive in 69% and anti-cyclic citrullinated peptide antibodies (ACPA) in 60%; 8.8% were current smokers and 7.5% past smokers. Methotrexate (MTX) was the most prescribed synthetic DMARD (85.9%) and biologics were used in 32.3% of patients.

Lung involvement was documented in 38 patients (7.1%; 95% CI 5.2%>9.7%). The specific types of lung disease are presented in figure 1. The mean interval between articular and pulmonary symptoms was 6.1 (±6.4) years, with only 1 patient having lung involvement diagnosed prior to joint manifestations. Most patients were female (73.7%), 78.9% RF positive, 68.4% ACPA positive and 29% current/previous smokers. Secondary Sjögren's Syndrome was present in 5 patients. Eighteen (47%) patients were medicated with MTX, 16 of them initiated therapy before developing respiratory symptoms and 10 (26.5%) with biologics (4 with TNF antagonists, 3 with tocilizumab, 2 with rituximab and 1 with abatacept). Most patients (92.1%) had abnormal chest x-rays, but only 47.4% were symptomatic. Pulmonary function tests (PFT) were abnormal in 31.6% of patients and 47.4% had diffusing capacity for carbon monoxide (DLCO) less than 75% predicted (7 had no DLCO estimated). Respiratory insufficiency was present in 7 (18.4%) patients. In multivariate logistic regression analysis, current MTX use (OR: 2.1 [1.02–4.33]), RF positivity (OR: 3.48 [1.18–10.25]) and older age (OR: 1.03 [1.00–1.06)] were independently associated with lung involvement.

Type of lung involvement	**UIP** (n=10)	**NSIP** (n=8)	**Bronchiectasis** (n=16)	**Follicular bronchiolitis** (n=1)	**Pleural involvement** (n=3)
Female	7	6	14	1	0
RF positive	8	7 (1 missing)	12 (1 missing)	1	2 (1 missing)
Smoking	4 (1 missing)	3	3	0	1
PFT	4 normal	5 normal	9 normal	1 normal	3 normal
	3 restrictive	1 restrictive	4 restrictive		
	1 obstructive	1 restrictive + obstructive	2 obstructive		
DLCO < 75%	7	3 (2 missing)	7 (3 missing)	0	2

UIP – usual interstitial pneumonia; NSIP – nonspecific interstitial pneumonia

Figure 1 – Specific types of lung involvement and its characteristics

Conclusions: Lung involvement was present in 7.3% of our cohort and was diagnosed in average 6.1 years after the first joint manifestations. RF positivity, older age and current MTX use are associated with lung disease.

As most patients remain asymptomatic, lung involvement is probably under-diagnosed in RA patients. Besides, in clinical practice exams that can detect preclinical disease, such as high-resolution chest computed tomography, are usually reserved for symptomatic patients or with an abnormal chest x-ray.

References:

[1] Chansakul T, Dellaripa, Doyle TJ, Madan R. Intra-thoracic rheumatoid arthritis: imaging spectrum and treatment related complications. Eur J Radiol. 2015 October; 84(10): 1981–1991.
[2] Megan Shaw, Bridget F. Collins, Lawrence A. Ho and Ganesh Raghu. Rheumatoid arthritis-associated lung disease. Eur Respir Rev 2015; 24: 1–16.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4513

FRI0139 PREVALENCE OF HYPERPARATHYROIDISM IS HIGHER AMONG RHEUMATOID ARTHRITIS PATIENTS COMPARED TO THE GENERAL POPULATION: AN OBSERVATIONAL, COHORT STUDY

A. Emamifar[1], L. Stilgren[2], R. Hviid Larsen[3], R. Asmussen Andreasen[1], I.M. Jensen Hansen[1,4]. *[1]Rheumatology; [2]Endocrinology; [3]Medicine, Svendborg Hospital, Odense University Hospital, Svendborg; [4]DANBIO, Copenhagen, Denmark*

Background: Patients with Rheumatoid Arthritis (RA) are at increased risk of different comorbidities which may affect long-term prognosis.[1] Primary hyperparathyroidism (PHP) is a metabolic disorder of one or more of the parathyroid glands with a prevalence of 1–7 per 1000 adults.[2]

Objectives: To define the prevalence of PHP in patients with RA.
Methods: All RA patients who were registered in the local part of Danish Danbio registry were included in this study. Patients'demographic data and serology results (rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (anti-ccp)) were extracted from Danbio. Patients' electronic hospital records including laboratory results (Parathyroid hormone (PTH) and calcium levels) were reviewed to reveal if they had been diagnosed with PHP as well.
Results: 1035 RA patients were included in this study [table 1]. Prevalence of PHP was 2.8% (29/1035). RA Patients with PHP had significant longer disease duration compared to patients with isolated RA (p=0.003). There was no significant difference between RA patients with and without PHP with respect to age, gender, RF and anti-ccp positivity (Table 1).

Table 1. Association of PHP with age, gender, disease duration, Rheumatoid Factor and Anti-ccp in RA patients

Variables:	RA patients with PHP N=29	RA patients without PHP N=1006	P value
Age	69.9±10.6	67.0±14.6	0.170
Gender, Female	23 (79.3%)	633 (62.9%)	0.107
Disease Duration	15.2±9.5	9.4±9.6	0.003
Rheumatoid Factor, Positive	20 (69%)	587 (58.3%)	0.393
Anti-ccp, Positive	19 (65.6%)	513 (51%)	0.241

RA: Rheumatoid Arthritis, PHP: Primary Hyperparathyroidism.

Conclusions: Clinicians should pay special attention to higher prevalence of PHP among RA patients compared to the general population. Presence of PHP in RA patients may aggravate the effect of RA on bones and joints by means of interaction with cytokines and inflammatory markers involved in RA. Concurrent PHP can be diagnosed at early stage by testing PTH and calcium levels which minimize the future morbidities e.g. fracture due to osteoporosis.
References:
[1] Dougados M, Soubrier M, Antunez A, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis 2014;73:62–8.
[2] Yeh MW, Ituarte PH, Zhou HC, et al. Incidence and prevalence of primary hyperparathyroidism in a racially mixed population. J Clin Endocrinol Metab 2013;98:1122–9.
Acknowledgements: We thank Mrs. Maryam Mousavi for her contribution to data collection.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5304

FRI0140 COMORBIDITY AND SURGERY HISTORY OF RHEUMATOID ARTHRITIS PATIENTS WHO ARE RECEIVING BIOLOGICAL AGENT

B. Armagan[1], A. Sari[1], A. Erden[1], L. Kilic[1], E.C. Erdat[2], O. Karadag[1], A. Akdogan[1], S. Apras Bilgen[1], U. Kalyoncu[1], I. Ertenli[1], S. Kiraz[1]. *[1]Hacettepe University, Department of Internal Medicine, Division of Rheumatology; [2]Department of Internal Medicine, Hacettepe University, Ankara, Turkey*

Background: Rheumatoid artritis (RA) is a chronic and autoimmune disorder that primarily affects middle and older ages. Comorbidities are important during RA treatment.
Objectives: We aim to determine the frequency of comorbidites and surgical history in the RA patients who receive biological agents.
Methods: Hacettepe University Biologic Registry (HUR-BIO) includes demographic and clinical data of patients treated with biological agent since 2005. By August 2016, 1235 RA patients were recorded in the database. Age, gender, smoking habits, disease duration, rheumatoid factor, anti citrullinated peptide (CCP), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), current and previous treatments, comorbidites and surgical history of patients were analyzed. Comorbidites and surgery history were determined by patients medical records. Disease activity was estimated by the 28-joint activity calculator- C reactive protein (DAS28-CRP). Functional assessment was evaluated by the Health Assessment Questionnaire (HAQ).
Results: Mean age (SD) of the patients (79,8% women) was 53,1 (12,6) and the mean disease duration was 11,0 (7,7) years. Of patients, 166 (16,6%) were older than 65 years. A total of 630 (63%) patients education level were less than high school, 197 (19,7%) of the patients were graduated from university. Smoking habitus of patients was as follows, 599 (59,9%) never smoked, 189 (18,9%) current smoker and 212 (21,2%) ex-smoker. At least one cardiovascular risk factor was detected in 699 (69,9%) patients. Comorbidities and surgical history of patients were shown in the table below. Patients with at least one comorbidity had less frequently female (77.3% vs 84.5%, p=0.007), high seropositivitly of RF (66% vs 57.1%, p=0.004), high patient global assessment (4.4±2.5 vs 3.9±3.9, p=0.007), high fatique score (4.6±3 vs 3.9±3.1, p=0.001), high pain score (4.8±2.5 vs 4.0±2.8, p=0.009), DAS-28 (3.43±1.39 vs 3.17±1.48, p=0,009) and high HAQ score (0.72±0.59 vs 0.58±0.54, p=0.001) than patients without comorbidities.
Conclusions: Comorbidities and past surgical history should be considered in RA patients when biological therapy is indicated. Comorbidities is one of the important conditions for physicians to manage patients. Cardiovascular, chronic viral infection such as hepatitis B and C, tuberculosis and cancer have to be investigated to start biological treatments. Surgical history such as cataracts, ortopedic surgery were also important for clinicians. HURBIO data demonstrated that patients with at least one comorbidities reflects more negative patient outcome measures.

Table: Comorbidity and surgery details in RA patients

	Female	Male	Total	p
Comorbidity				
Obesity [kilo >30]	382 (46,3)	64 (30,2)	446 (44,4)	0,00
Hypertension	368 (33,4)	41 (19,3)	409 (30,9)	0,00
Diabetes mellitus	93 (11,2)	15 (7,4)	108 (10,3)	0,000
Thyroid disease	129 (16,2)	8 (4)	137 (13,7)	0,000
Asthma	35 (4,4)	11 (5,4)	46 (4,6)	0,325
COPD	4 (0,5)	0 (0)	4 (0,4)	0,313
Amiodaron	5 (0,6)	2 (1)	7 (0,7)	0,584
Tuberculosis history	19 (2,4)	10 (5,4)	29 (3,9)	0,012
Hepatit B	17 (2,1)	7 (3,5)	24 (2,4)	0,215
Hepatit C	18 (2,3)	6 (3)	24 (2,4)	0,215
Cancer	20 (2,5)	5 (2)	25 (2,5)	0,547
Surgery history				
Spinal surgery	79 (9,9)	8 (4)	87 (8,7)	0,000
Orthopedic extremity surgery	72 (9)	18 (8,9)	90 (9)	0,968
Knee prosthesis	58 (7,3)	5 (2,5)	63 (6,3)	0,14
Hip prosthesis	36 (4,4)	10 (5)	45 (4,5)	0,805
CNS surgery	30 (3,8)	2 (1)	32 (3,2)	0,044
Cholecystectomy	72 (9)	7 (3,5)	79 (7,9)	0,000
Appendectomy	79 (9,9)	10 (5,0)	89 (8,9)	0,027
Hernia repair	25 (3,1)	15 (7,4)	40 (4,0)	0,005
GIS surgery	31 (3,9)	12 (5,9)	43 (4,3)	0,158
Cataract	64 (8)	15 (7,4)	79 (7,9)	0,708
Gynecologic surgery	137 (35,9)	-	137 (32,7)	
Renal surgery	16 (2)	0 (0)	16 (1,6)	0,042
Thyroid surgery	57 (7,1)	3 (1,5)	60 (6,0)	0,002
ENT surgery	62 (7,8)	15 (7,5)	77 (7,7)	0,895
Urological surgery	78 (2,5)	16 (7,9)	94 (3,4)	0,00
Pulmonary surgery	8 (0,8)	4 (2)	12 (1,2)	0,03
Cardiovascular surgery	20 (2,5)	8 (4)	28 (2,8)	0,438

CNS: Cerebrovascular diseases, CTS: Carpal tunnel syndrome, GIS: Gastrointestinal surgery, ENT: Ear, nose and throat

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4282

FRI0141 LEFT VENTRICULAR CONCENTRIC REMODELING IS MORE PREVALENT IN RHEUMATOID ARTHRITIS: A CASE-CONTROL STUDY

D.Á. Galarza-Delgado[1], J.R. Azpiri-López[2], I.J. Colunga-Pedraza[1], F.J. Torres-Quintanilla[2], R.E. Ramos-Cázares[1], A. Valdovinos-Bañuelos[1], A. Martínez-Moreno[3], R.I. Arvizu-Rivera[3], R. Vera-Pineda[3], J.A. Cárdenas-de la Garza[3], M.A. Garza-Elizondo[1], M.A. Benavides-González[2], J.A. Silva-Ortiz[2]. *[1]Rheumatology; [2]Cardiology; [3]Internal Medicine, Hospital Universitario "Dr. José Eleuterio González", UANL, Monterrey, Mexico*

Background: Patients with rheumatoid arthritis (RA) have a higher risk to develop cardiovascular complications than general population (1), leading to a decrease in life expectancy of 3 to 10 years (2). RA is associated to increased left ventricle mass, pericardial effusion and diastolic dysfunction (3).
Objectives: The aim of this study was to assess the structure and function of the left ventricle in patients with RA and compare the results with matched controls.
Methods: We designed an observational cross-section case-control study. Patients diagnosed with RA according to the 1987 ACR and/or 2010 ACR/EULAR classification criteria, 40–75 years old, with no overlap syndromes, atherosclerotic cardiovascular disease or hypertension were included. Subjects for the control group were matched by sex, age and comorbidities. A board-certified cardiologist performed a transthoracic echocardiogram.
Results: We included a total of 44 RA-patients and 26 control subjects. Table 1 summarizes the demographic characteristics for each group. Left ventricular concentric remodeling (LVCR), defined as a relative wall thickness (RWT) >0.42 cm and a left ventricular mass index (LVMI) ≤ 95 gm/m^2 in women and ≤ 115 gm/m^2 in men, was found in 14 patients (32.6%) of the RA-group and 2 subjects (8%) of the control group; this difference was statistically significant (p=0.021).
When we analyzed general abnormalities of left ventricle (either LVCR or left ventricular concentric hypertrophy [RWT >0.42 cm and LVMI >95 gm/m^2 in women, >115 gm/m^2 in men]) we found 15 RA patients (34.1%) with abnormalities and 3 subjects in the control group (11.5%) (p=0.037). There were no statistically significant differences among the groups in LVMI, diastolic dysfunction, global longitudinal strain or ejection fraction.

Table 1. Demographic characteristics

	RA group (n=44)	Control group (n=26)	*p*
Age, mean ± SD	52.35±7.34	53.94±6.81	0.371
Disease duration (years), mean ± SD	10.682±8.3321	–	–
DAS-28 CRP, mean ± SD	3.36±1.42	–	–
Women, n (%)	43 (97.7)	24 (92.3)	0.279
Body Mass Index, mean ± SD	26.98±6.13	28.3±4.12	0.956
Active smoking, n (%)	4 (9.1)	0 (0)	0.113
Type 2 Diabetes mellitus, n (%)	2 (4.5)	2 (7.7)	0.584

DAS-28 CRP - Disease activity score 28 using C-reactive protein.

Conclusions: Left ventricle concentric remodeling is more prevalent in RA-patients when compared to controls. Further research is needed to determine the impact of these findings in the clinical prognosis of RA-patients.
References:
[1] Solomon DH, Curhan GC, Rimm EB, Cannuscio CC, Karlson EW. Cardiovas-

Table 2

	RA group (n=44)	Control group (n=26)	*p*
LVCR, n (%)	14 (32.6)	2 (8)	**0.021**
LVCR or LVH, n (%)	15 (34.1)	3 (11.5)	**0.037**
Diastolic dysfunction, n (%)	20 (45.5)	9 (34.6)	0.374
Left ventricular mass index (g/m²), mean ± SD	66.77 ± 17.11	68.65 ± 18.31	0.668
EF (%), mean ± SD	60.85 ± 4.94	62.62 ± 6.67	0.228
GLS (%), mean ± SD	-20.66 ± 2.63	-21.6 ± 2.52	0.189
TAPSE (mm), mean ± SD	23.23 ± 4.34	23.84 ± 2.71	0.485

LVCR - Left ventricular concentric remodeling, LVH - Left ventricular hypertrophy, GLS - Global longitudinal strain, TAPSE - Tricuspid annular plane systolic excursion.

cular risk factors in women with and without rheumatoid arthritis. Arthritis & Rheumatism. 2004;50(11):3444–9.
[2] Myasoedova E, Davis JM, Crowson CS, Gabriel SE. Epidemiology of Rheumatoid Arthritis: Rheumatoid Arthritis and Mortality. Current Rheumatology Reports. 2010;12(5):379–85.
[3] Corrao S, Messina S, Pistone G, Calvo L, Scaglione R, Licata G. Heart involvement in Rheumatoid Arthritis: Systematic review and meta-analysis. International Journal of Cardiology. 2013;167(5):2031–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5623

FRI0142 NEUTROPENIA IN RHEUMATOID ARTHRITIS. INCIDENCE, PROGNOSTIC FACTORS, NATURAL HISTORY AND OUTCOME

G.E. Fragoulis[1], I.B. McInnes[1], D. Porter[2], S. Siebert[1] on behalf of SERA collaborators. *[1]Institute of Infection, Immunity and Inflammation, University of Glasgow; [2]Rheumatology, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom*

Background: Neutropenia is an uncommon finding in the context of rheumatoid arthritis (RA). The incidence and association with RA features is not yet well-defined.
Objectives: To determine the incidence and severity of neutropenia in an early RA inception cohort, explore possible association with RA features and describe its impact on patient's management.
Methods: The Scottish Early Rheumatoid Arthritis (SERA) inception cohort prospectively recruited newly diagnosed RA patients (ACR-EULAR 2010 criteria), who were followed-up every 6 months. Patients who developed at least one episode of neutropenia (grade 1: <2000/μL, grade 2: <1500/μL, grade 3: <1000/μL, grade 4: <500/μL) were compared with patients who never developed neutropenia. Binominal logistic regression was performed, exploiting the enter model and using the occurrence of neutropenia as dependent variable.
Results: 77 episodes of neutropenia were observed in 60 (8.6%) out of 698 RA patients, who were followed up for a median (range) time of 18 (6–48) months. Neutropenia occured in 12 (0–120) [median (range)] months after RA diagnosis. The majority had mild neutropenia (grade 1: n=49, grade 2: n=9, grade 3: n=0, grade 4: n=2) and the mean ± SD number of neutrophils/μL was 1.68±0.35. Of the 77 neutropenic episodes recorded, coexistent lymphopenia was found in 13.0%, leukopenia in 70.1%, thrombocytopenia in 1.3% and anaemia in 32.5%. At the time of the neutropenia, most of the patients were in remission (DAS28<2.6: 53%, DAS28<3.2: 15.5%, DAS28≤5.1: 22.4%, DAS28>5.1: 8.6%). Neutropenia was a single episode in the majority (76.7%) of the patients and led to treatment discontinuation in 11.7% of them.
Patients who subsequently developed neutropenia, were more likely females (p=0.03) and non-smokers (p=0.0009) (Table 1). Treatment received for RA was comparable between the two groups. Binominal regression analysis confirmed female gender [p=0.017, Exp(B): 2.587] and not smoking [p=0.032, Exp(B): 2.880] as predictors of neutropenia development.
During total follow-up time, patients who had at least one episode of neutropenia they also manifested more commonly anaemia (p=0.04) and lymphopenia (p=0.03). The rate of infections/1000 person-months did not differ between patients who developed neutropenia and those who did not [5.75 (2.47–11.33) vs 4.1 (3.13–5.47), p=0.399].

Table 1. Baseline patients characteristics

	Neutropenia	No Neutropenia	p value
Patients characteristics	N=60	N=638	
Age, mean (mean±SD)	58.7±14.5	58.7±13.2	0.978
Female gender, No (%)	50 (83.3%)	414 (64.9%)	0.03
Total follow-up (months), median (range)	18 (6–48)	18 (6–48)	0.173
Smoking, No (%)	5 (8.3)	172 (27.0)	0.0009
Smoking (present/past/never)	5/23/32	172/240/225	0.002
Anaemia[a], No (%)	8/57 (14.0)	133/631 (21.1)	0.235
Thrombocytopenia[b], No (%)	0/57 (0.0)	0/631 (0.0)	1.000
Leukopenia[c], No (%)	1/57 (1.7)	3/631 (0.4)	0.293
Lymphopenia[d], No (%)	4 (7.0)	34/631 (5.4)	0.545
RF positive, No (%)	28/36 (77.8)	295/401 (73.5)	0.693
Anti-CCP positive, No (%)	34/48 (70.8)	410/527 (77.8)	0.282
Baseline DAS28 (mean±SD)	4.8±1.6	5.02±1.42	0.408

[a]Hb<120 g/L, [b]platelets <100000/μl, [c]white blood cells: $<4x10^9$/L, [d]lymphocytes: $<1x10^9$/L.

Conclusions: Neutropenia was observed in about 9% of patients in this early RA cohort. It was usually mild, transient and not associated with increased infection rates. Interestingly, not-smoking and female gender were associated with neutropenia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6725

FRI0143 PREVALENCE AND DETERMINANTS OF PERIPHERAL ENDOTHELIAL DYSFUNCTION IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS: PRELIMINARY RESULTS FROM A MULTICENTER CROSS-SECTIONAL STUDY

G.L. Erre[1,1], M. Piga[2], A.L. Fedele[3], M.L. Cadoni[1], G. Di Sante[3], I. Cangemi[2], A. Piras[4], M. Dessì[2], S. Mura[4], B. Tolusso[3], M.G. Longu[1], P.S. Saba[5], E. Gremese[3], A. Cauli[2], G. Ferraccioli[3], A. Mathieu[2], G. Passiu[4]. *[1]UOC Reumatologia, Dipartimento di Medicina Clinica e Sperimentale, Azienda Ospedaliero-Universitaria di Sassari, Sassari; [2]UOC Reumatologia, Azienda Ospedaliero-Universitaria di Cagliari, Cagliari; [3]UOC Reumatologia, Policlinico Gemelli, Roma; [4]UOC Reumatologia, Dipartimento di Medicina Clinica e Sperimentale, Università degli Studi di Sassari; [5]UO Cardiologia, Azienda Ospedaliero-Universitaria di Sassari, Sassari, Italy*

Background: RA patients suffer of a life expectancy significantly reduced with respect to the general population mainly due to cardiovascular (CV) disease. Endothelial dysfunction (ED), the early step in atherosclerotic process, is more evident in RA than in the general population. Peripheral arterial tonometry (PAT), a simple, rapid, and objective tool for evaluation of ED, measures small digital artery reactive hyperaemia after an ischemic stimulus in forearm. PAT shows high grade of correlation with coronary ED and predicts future CV events in the general population.
Objectives: To define prevalence and determinants of peripheral ED in RA.
Methods: Data from 633 RA patients free of previous CV events prospectively enrolled in the EDRA study* (ClinicalTrials.gov: NCT02341066) were analysed. Reactive hyperemia index (LnRHI) was evaluated by PAT using the EndoPAT2000 device: ED was defined by LnRHI <0.51. Linear and logistic regression analysis were performed to define independent predictors of ED in RA patients. A p-value <0.05 was considered statistically significant.
Results: Peripheral ED was documented in 212 out of 633 RA patients (33.3%). A linear regression for multiple variables (stepwise method) performed including into the models variables showing significant association with LnRHI at the univariate regression analysis (systolic blood pressure, HDL cholesterol levels, triglycerides levels, smoking habit and ACPA positivity; Age and gender were forced) showed that only higher levels of triglycerides [B coefficient (95%IC) = -0,001 (-0,001–0,00); $p<0.05$] negativity for ACPA [B coefficient (95%IC) = -0,070 (-0,135–0,005); $p<0.05$] and smoking habit [B coefficient (95%IC) =0,01 (0,043–0,156); $p<0.05$] were independently related to lower values of LnRHI. No significant correlation between peripheral ED and RA activity (DAS-28, CDAI, SDAI, HAQ), burden of systemic inflammation (CRP, ESR) and type of immunosuppressive treatment (steroids, NSAIDs, DMARDs and bDMARDs) was found. At logistic regression analysis ACPA negativity [OR ((95%IC) = 1.57 (1.04–2.21); $p<0.05$] and smoking habit [OR ((95%IC) = 1.64 (1.06–2.53); $p<0.05$] indipendently conferred a major risk of peripheral ED.
Conclusions: This study demonstrates for the first time a very high prevalence of peripheral ED in patient with RA free of previous CV events. Triglycerides levels and smoking habit, among traditional cardiovascular risk factor, showed a significant correlation with lower peripheral ED. Surprisingly ACPA negativity confers an increased risk for ED in RA population. Moreover, other than expected, systemic inflammation does not appear to influence peripheral ED in RA population. In conclusion our data further support the notion that atherogenesis in RA is only partially driven by traditional CV factors. The negative association between ACPA and ED warrants further investigation.
Acknowledgements: *The EDRA study is a project funded by Italian Ministry of Health and by Regione Sardegna (RAS) (GR-2011–02352816; Ricerca Finalizzata 2011).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2234

FRI0144 EVALUATION OF FACTORS AFFECTING FATIGUE IN PATIENTS WITH RHEUMATOID ARTHRITIS

G. Kilinc Kamaci[1], S. Unsal Delialioglu[1], S. Ozel[1], F. Yurdakul[2], H. Bodur[2]. *[1]Ankara Physical Therapy and Rehabilitation Training and Research Hospital; [2]Ankara Numune Training and Research Hospital, Ankara, Turkey*

Background: Fatigue is a common and disturbing symptom in patients with Rheumatoid arthritis (RA) (1,2). Measuring fatigue, understanding its contributory factors, and treating it lead to better patient outcome (3).
Objectives: The aim of this study is to investigate the relation between fatigue and pain, functional status, disease activity in patients with RA and to determine the effect of fatigue on the quality of life of patients with RA.

Methods: A total of 141 patients (103 female, 38 male) who were diagnosed RA according to ACR (American College of Rheumatology) diagnostic criteria were included in the study. Fatigue Symptom Inventory (FSI) was used for evaluation of fatigue. While the disease activity was determined using the Disease Activity Score-28 (DAS28), the Health Assessment Questionnaire (HAQ) was used to determine the functional status. The pain intensity was determined using 10 cm Visual Analogue Scale-Pain (VAS-pain).
Results: The mean age of the patients is 54.67±10.70 years and the mean duration of illness is 14.31±10.89 years. When the relationship between fatigue and other factors was examined, a statistically significant relationship was found between FSI fatigue severity scores (maximum, minimum, mean, current), FSI duration scores (number of days felt tired, amount of time felt tired), FSI interference score and HAQ, number of swollen joints, number of tender joints, VAS rest and VAS motion values ($p<0.05$). There was a statistically significant lower correlation between FSI fatigue severity scores (at least, mean) and DAS28 (r: 0.216, r: 0.181, respectively). There was no significant relationship between FSI scores and age, duration of illness, steroid use
Conclusions: Fatigue affects patients independently of disease duration in patients with RA. Fatigue is associated with disease activity, functional status, and pain. For this reason, fatigue in RA patients should be considered as an important symptom that should not be overlooked and should be struggled.
References:
[1] Steenbergen HW, Tsonaka R, Huizinga TWJ, Boonen A, Helm-van Mill AHM. Fatigue in rheumatoid arthritis; a persistent problem: a large longitudinal study. RMD Open 2015;1:e000041.
[2] Dartel SAA, Repping-Wuts JWJ, Hoogmoed D, Bleijenberg G, Riel PLCM, Fransen J. Association between fatigue and pain in rheumatoid arthritis: does pain precede fatigue or does fatigue precede pain? Arthritis Care Res (Hoboken). 2013 Jun;65(6):862–9.
[3] Singh H, Arya S, Talapatra P, Lather K, Mathur R, Singhania A, Chaudhary V. Assessment of Fatigue in Rheumatoid Arthritis (by Functional Assessment of Chronic Illness Therapy-Fatigue Score) and Its Relation to Disease Activity and Anemia. J Clin Rheumatol. 2014 Mar;20(2):87–90.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1689

FRI0145 DOES PAIN HAVE INFLUENCE ON HEALTH ASSESSMENT QUESTIONNAIRE DISABILITY INDEX (HAQ-DI) IN RHEUMATOID ARTHRITIS PATIENT? AN ATTEMPT TO EVALUATE EFFECTIVENESS OF PAIN VAS (PS-VAS) ON HAQ-DI IN REAL CLINICAL PRACTICE –

I. Yoshii[1], T. Chijiwa[2]. [1]*Rheumatology, Yoshii Hospital, Shimanto City;* [2]*Rheumatology, Kochi Memorial Hospital, Kochi, Japan*

Background: Health Assessment Questionnaire Disability Index (HAQ-DI) is the most important index in treatment for rheumatoid arthritis (RA) patient. HAQ-DI expresses patient's disability in daily life (ADL), and this is influenced by disease activity (ACT-HAQ) and joint structural damage (DAM-HAQ), and aging when patient gets older in senectitude (AGE-HAQ) (1–3). One more factor that possibly makes influence on HAQ-DI is patient's pain. However, this problem is not discussed at all.
Objectives: We have investigate patient's pain and its effect on HAQ-DI in our clinical data in order to evaluate whether pain influences on HAQ-DI, and to make assessment existence of pain related HAQ-DI (PAIN-HAQ)
Methods: RA patients who have been treated continuously for more than five years, who had visited later than October 31th, 2016, were picked up in this study. Patients average 28-joints disease activity score with C-reactive protein (DAS28-CRP), modified HAQ (mHAQ), Sharp/van der Heijde Score (SvdHS), age, and pain score calculated by visual analogue scale (PS-VAS) were calculated in fifth treatment year. Average values of these parameters have been calculated. Relationships among these factors have been investigated statistically using multiple linear regression analysis (MLR). After evaluation of relationship of each pairs of these factors, the relationship between HAQ-DI and the other factors had been evaluated from modified data of these patients in minimize the effect of parameters other than PS-VAS and data that minimized effectiveness of PS-VAS with MLR.
Results: 382 patients had been picked up. Their sex distribution was 87 for male and 295 for female, and their average values and standard deviations of age, DAS28-CRP, HAQ-DI, SvdHS, and PS-VAS were 68.99 and 13.47, 1.91 and 0.54, 0.43 and 0.55, 54.97 and 67.30, and 22.96 and 17.85, respectively. HAQ-DI demonstrated significant regression with all of DAS28-CRP, SvdH, age, and PS-VAS (<0.01). DAS28-CRP demonstrated positive correlation with PS-VAS, HAQ-DI, and SvdHS, but negatively correlated significantly with age (<0.01). PS-VAS demonstrated positive correlation with HAQ-DI and DAS28-CRP, but negatively correlated with SvdHS significantly (<0.01), while no significant correlation demonstrated with age. SvdHS demonstrated positive correlation with DAS28-CRP and HAQ-DI, but negative correlation with PS-VAS significantly (<0.01), while no significant correlation demonstrated with SvdHS. Age demonstrated positive correlation with HAQ-DI, but negatively correlated with DAS28-CRP (<0.01), while no significant correlation demonstrated with PS-VAS and SvdHS (Figure 1).
After minimizing the data effectiveness of DAS28-CRP, Age, and SvdHS on HAQ-DI, HAQ-DI demonstrated significant regression only with PS-VAS. When the effectiveness of PS-VAS was minimized, HAQ-DI demonstrated significant regression with parameters other than PS-VAS. Threshold of PS-VAS was 15mm.

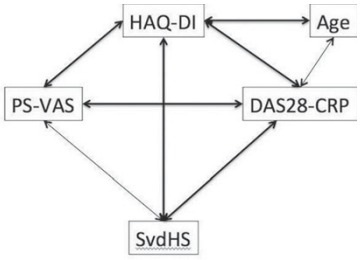


Figure 1: Schematic relationship among HAQ-DI, DAS28-CRP, SvdHS, Age, and PS-VAS. Thick lines demonstrate significant positive correlations, and thin lines demonstrate significant negative correlations.

Conclusions: These results suggested that HAQ-DI is influenced PS-VAS when it is no less than 15mm. Therefore, we conclude that HAQ-DI consists with PAIN-HAQ in adding with ACT-HAQ, DAM-HAQ, and AGE-HAQ.
References:
[1] Smolen JS, et al. Ann Rheum Dis 2010;69:1058–1064.
[2] Vita AJ, et al. N Engl J Med 1998; 338:1035–1041.
[3] Yoshii I, et al. Arthritis Rheumatol. 2015; 67 (suppl 10).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3977

FRI0146 ANTI-ELASTIN AND ANTI-ELASTASE AUTOANTIBODIES: POTENTIAL CLINICAL AND DIAGNOSTIC IMPLICATIONS IN RHEUMATOID ARTHRITIS

N.V. Nenasheva[1], A.S. Trofimenko[1,2], I.P. Gontar[1], L.A. Maslakova[1], O.A. Rusanova[1], O.V. Paramonova[2]. [1]*Research Institute for Clinical and Experimental Rheumatology;* [2]*Volgograd State Medical University, Volgograd, Russian Federation*

Background: Elastin is an ubiquitous molecule, presented in connective tissue matrix, including skin, ligaments, lungs, and blood vessels. Elastase is a characteristic protease, considerably presented in neutrophils and in pancreas. Autoantibodies (Ab) to elastin and to elastase are promising candidate biomarkers in rheumatoid arthritis (RA).
Objectives: To explore potential clinical and diagnostic utility of anti-elastin and anti-elastase Ab in RA.
Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles and was approved by Volgograd Regional Committee on Medical Ethics. All the patients signed the informed consent. We enrolled 106 adult patients with definite RA in Volgograd Municipal Hospital #25, the diagnosis have been established using ACR-EULAR criteria (2010). For ROC analysis calculations we used mixed control group consisted of 19 patients with ankylosing spondylitis, 32 with gout, 11 with psoriatic arthritis, and 22 with reactive arthritis. Serum anti-elastin and anti-elastase Ab concentrations were evaluated by ELISA, using antigens immobilized on magnetic polyacrylamide beads, which were previously described by our group [1]. Antibody concentrations were expressed as relative optical density units (ODU). The cutoff values for anti-elastin and anti-elastase Ab presence were 0.104 and 0.113 ODU, respectively; the calculations were performed using 34 healthy control sera. All the means and operation characteristics were expressed as values (95% confidence intervals). Differences were considered significant when $p<0.05$.
Results: In RA anti-elastin Ab were found in 37 (34.9%) patients, and the mean concentration was 0.128 (0.118–0.138) ODU. There was no significant correlation between DAS28 and anti-elastin concentrations, but the least marker was increased in patients with heart and kidney involvement, as well as in vasculitis patients, comparing to those who have no such manifestations (p=0.017, 0.046, and 0.009, respectively). We detected 58 (54.72%) anti-elastase positive RA patients, with the mean concentration 0.137 (0.103–0.171) ODU. Anti-elastase positive patients had significantly increased frequencies of anemia (p=0.025) and vasculitis (p=0.017) comparing to the negative subgroup. The prevalence of anti-elastase Ab was also increased along with RA activity. Concentrations of these two Ab were positively correlated (r=0.866, $p<0.001$).For anti-elastin Ab assay (cutoff point 0.112 ODU) diagnostic sensivity in RA patients was 72 (62–87)%, specificity 50 (41–64)%, AUC of ROC curve 0.703 (0.590–0.797). For anti-elastase Ab assay (cutoff point 0.115 ODU) the respective values were 77 (62–87)%, 81 (59–91)%, and 0.822 (0.675–0.923).
Conclusions: Anti-elastin and, increasingly, anti-elastase antibodies are valuable candidate markers to improve diagnosis of RA and, particularly, rheumatoid vasculitis and heart involvement. Further investigations are needed to assess sensivity and specificity of these markers being included in the comprehensive diagnostic algorithms.
References:
[1] Gontar IP, Simakova ES, Trofimenko AS, Zborovskaya IA. An approach for

removal of DNA-containing immune complexes from blood using composite sorbent. Patent RU2441674 (2010) [in Russian].

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2593

FRI0147 ANTI-MÜLLERIAN HORMONE LEVELS IN FEMALE RHEUMATOID ARTHRITIS PATIENTS TRYING TO CONCEIVE – THE ROLE OF OVARIAN FUNCTION IN TIME TO PREGNANCY IN A NATIONWIDE COHORT STUDY

J. Brouwer[1,2], J.S. Laven[1], J.M. Hazes[2], J.A. Visser[3], R.J. Dolhain[2]. *[1]Division of Reproductive Medicine - Department of Obstetrics & Gynaecology; [2]Department of Rheumatology; [3]Department of Internal Medicine, Erasmus MC University Medical Center Rotterdam, Rotterdam, Netherlands*

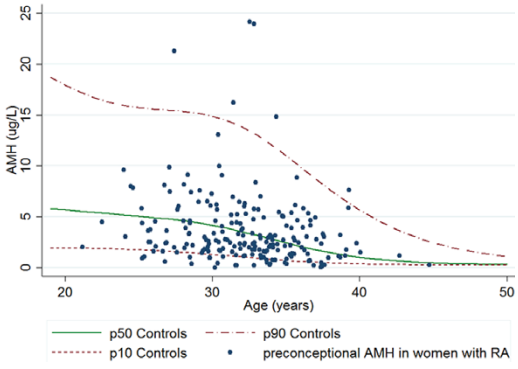
Background: Subfertility, a time to pregnancy (TTP) >12 months, is present in 40% of women with rheumatoid arthritis (RA) actively trying to conceive.[1] Since RA patients appear to reach menopause at a younger age[2], the reduced fertility may be caused by a lower ovarian reserve (OR). Serum anti-Müllerian hormone (AMH) levels are currently the most reliable way to measure the OR.

Objectives: Our objective was to study preconception AMH levels and their association with TTP in women with RA.

Methods: A post-hoc analysis was performed in patients of the Pregnancy-induced Amelioration of RA (PARA) cohort who were visited preconceptionally. Serum AMH levels were measured using the pico AMH ELISA assay (Ansh Labs, Texas, USA), and compared to converted[3] AMH values from a cohort of 554 healthy adult controls[4].

Results: Preconception serum was available in 209 women aged 32.1±3.9 years, of whom 45% were subfertile. The median AMH level was 2.5 ug/L (IQR 1.5–4.6). AMH levels were significantly lower compared to healthy controls ($p<0.001$), with 17.2% (95% CI 10.7 – 23.8%) of patients having levels below the age-specific 10th percentile.

Log-transformed AMH levels were negatively associated with age (-0.070 (95% CI -0.11;-0.031), p=0.001), and with the presence of anti-citrullinated protein antibodies (ACPA) (-0.38 (95% CI -0.71;-0.056), p=0.022). The associations remained significant in the multivariable analyses. AMH levels showed no significant association with TTP (HR 1.09 (95% CI 0.94;1.27), p=0.26).



Conclusions: Women with RA have lower AMH levels than healthy controls. Reduced AMH levels were more pronounced in ACPA positive patients, suggesting that the OR may be compromised more strongly in patients with a more severe disease. However, since preconception AMH levels were not associated with TTP, the reduced levels do not explain the reduced fertility in women with RA.

References:

[1] Brouwer J, Hazes JM, Laven JS, Dolhain RJ. Fertility in women with rheumatoid arthritis: influence of disease activity and medication. Ann Rheum Dis 2015;74:1836–41.

[2] Del Junco DJ, Annegers JF, Coulam CB, Luthra HS. The relationship between rheumatoid arthritis and reproductive function. Br J Rheumatol 1989;28 Suppl 1:33; discussion 42–5.

[3] Su HI, Sammel MD, Homer MV, Bui K, Haunschild C, Stanczyk FZ. Comparability of antimullerian hormone levels among commercially available immunoassays. Fertil Steril 2014;101:1766–72 e1.

[4] Lie Fong S, Visser JA, Welt CK, et al. Serum anti-mullerian hormone levels in healthy females: a nomogram ranging from infancy to adulthood. J Clin Endocrinol Metab 2012;97:4650–5.

Acknowledgements: This study was funded by the Dutch Arthritis Foundation (Reumafonds).

The pico AMH assays were generously provided by Ansh Labs (Houston, Texas, USA).

Furthermore, we would like to thank all patients and rheumatologists who contributed to the PARA study, as well as all researchers and laboratory workers who worked on this project.

Disclosure of Interest: J. Brouwer: None declared, J. Laven: None declared, J. Hazes: None declared, J. Visser: None declared, R. Dolhain Grant/research support from: unrestricted research grant by UCB Pharma BV

DOI: 10.1136/annrheumdis-2017-eular.2105

FRI0148 THE EFFECT OF TNF INHIBITORS, METHOTREXATE (MTX), AND THE OTHER DMARDS THERAPIES ON DIABETIC CONTROL IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA): TREATMENT WITH MTX ALONE IMPROVED DIABETES CONTROL MORE THAN TNF INHIBITORS PLUS MTX

K. Fujioka, M. Tangiku, M. Fuwa, I. Mori, T. Ishizuka. *Center of General Internal Medicine and Rheumatology, Gifu Municipal Hospital, Gifu City, Japan*

Background: It has been shown that inflammation directly influences insulin and glucose metabolism through cytokines such as TNFα and IL-6. It has also been reported that certain RA drugs such as TNF inhibitors, hydroxychloroquine, and MTX were associated with lower diabetes risk among people with RA, but it is still clinically unknown. On the other hand, it has been shown that MTX is involved in activation of intracellular AMP-kinase and promotes glucose uptake in skeletal muscle (Diabetes, 2015).

Objectives: We examined medical records of patients with new RA patients complicated with glucose intolerance to measure in HbA1c, body weight, and DAS28-ESR for 6 and 12 months treated with TNF inhibitors, MTX, and the other DMARDs.

Methods: Newly registered 20 RA patients complicated with glucose intolerance (HbA1c ≥5.6%) at our hospital from May 2013 to December 2015, have treated with as follows; Treatment with infliximab (1 case), golimumab (3 cases), and etanercept (2 cases) in combination with 4–12mg/week of MTX (group A: 6 cases, TNF inhibitors + MTX), MTX (4–10 mg/week) alone (group B: 8 cases MTX alone). The other DMARDs (group C: 6 cases, the other DMARDs including bucillamine (BCL) + salazosulfapyridine (SASP) + tacrolimus (TAC); 1case, BCL+SASP; 1case, BCL alone; 2 cases and SASP alone; 2 cases) had been registered. We have compared the changes of HbA1c levels, body weight, DAS 28-ESR from the beginning of the treatments and 6 and 12 months later. RA patients treated with glucocorticoid were excluded. Diabetic treatment were diet and exercise in all cases, but metformin (500 mg) and DPP4 inhibitor were used in 4 cases (Group A and C). However, each patient in Group B did not use antidiabetic agents. We analyzed these results with paired and unpaired *t* test using JMP12.2.0.

Results: These registered RA patients with female were 60.0%. The mean age were 62.1, 53.5 and 63.8 for group A, B, and C, respectively. There were significant changes in DAS28-ESR after treatment for 6 months in group A and B, respectively ($p<0.01$ in group A and $p<0.05$ in group B).

Groups A and B showed significant improvement of DAS 28-ESR after treatment with 12 months ($P<0.0001$ in group A, $p<0.01$ in group B), but no significant difference of DAS28-ESR in group C was observed. The mean reduction in HbA1c showed a significantly decreases only in the group B ($P<0.01$). There were no significant differences in body weight between the each group, but slightly an increase in body weight was observed in group B. There were no significant correlations between body weight and DAS28-ESR and its changes.

Conclusions: In this study, MTX was thought to contribute not only to suppress chronic inflammation but also to improve the glucose tolerance as compared with TNF inhibitors plus MTX and the other DMARDs. Further studies concerns about the interrelationship between glucose tolerance and RA treatments may require.

References:

[1] Sergej Pirkmajer, et al. Diabetes 2015;64:360–369.

[2] Laura R. Rekedal, et al. Arthritis Rheum.2010;62(12):3569–3573.

[3] Daniel H. Solomon, et al. JAMA.2011;305(24):2525–2531.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4914

FRI0149 DOES THYROXIN SUBSTITUTION PREDICT NON-RESPONSE TO METHOTREXATE IN EARLY RA?

K. Waldenlind[1], S. Saevarsdottir[1], C. Bengtsson[2], J. Askling[1]. *[1]Rheumatology Unit, Department of Medicine, Solna, Karolinska Institute; [2]Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden*

Background: Response to treatment varies widely between RA-patients. Our means to predict disease course and treatment response is limited, leading to substantial over- as well as under- treatment. Whereas female gender and smoking have been identified as predictors of non-response, the impact of autoimmune co-morbidities remains largely unknown. Autoimmune thyroid disease (AITD) is one of the most frequent autoimmune diseases in the population. AITD is more prevalent in RA-patients and has also been identified as a risk factor for RA. AITD can be readily identified via thyroxin substitution. We aimed at assessing the impact of prevalent AITD in relation to 3- and 6-month EULAR response to methotrexate in early RA.

Objectives: To investigate whether thyroxin substitution impacts response to methotrexate as the first-line therapy in RA.

Methods: We identified patients with incident RA (symptom duration <1 year), included in the Swedish Rheumatology Quality Register, July 2006 through 2015 (n=7009). All patients starting treatment with methotrexate and who had a follow-up visit at 3 months (n=4364) and/or at 6 months (n=3148) were included. Prevalent AITD was defined as prescription of thyroxin substitution before RA-diagnosis (n=347), based on linkage to the Swedish Prescribed Drug register,

and excluding participants with prescriptions for iodine-containing drugs or history of thyroid cancer (e.g. non-autoimmune cause of thyroxin use). We used a case-control design with thyroxin substitution as exposure, cases defined as EULAR DAS28 3- and 6-month non-responders, and controls defined as moderate/good responders at these time-points. Odds Ratios (OR) were calculated adjusted for sex, age, and HAQ.

Results: At 3 months, the proportion of thyroxin users did not differ between responders and non-responders 12% vs. 11%, (OR non-response =1.1, 95% CI 0.9–1.4). At 6 months, the corresponding figures were 13% vs. 11%, respectively, (OR non-response =1.3, 95% CI 1.0–1.7). However, a significant difference was observed in RF and/or ACPA positive patients at 6 months, where 15% of non-responders and 10% of responders used thyroxin (OR non-response=1.6, 95% CI 1.1–2.1), while no such difference was observed for seronegative RA. When stratified for gender, thyroxin substitution was significantly associated with non-response in men but not in women.

Table 1. Relative risk of prevalent AITD before RA-diagnosis in *non-responders* compared to *moderate and good responders* according to EULAR response criteria, at the 6 month follow-up visit among 3148 RA-patients starting methotrexate as first ever DMARD

	No of AITD in non-responders (718)/ moderate and good responders (887+1543)	Adj. OR (95% CI)
Overall	93 (13%)/254 (11%)	1.28 (0.98–1.66)
Sex		
Women	81 (16%)/231 (14%)	1.19 (0.89–1.57)
Men	12 (5.6%)/23 (2.8%)	2.20 (1.05–4.60)
Serostatus		
RF and/or ACPA positive	73 (15%)/163 (10%)	1.57 (1.14–2.14)
RF and ACPA Negative	20 (8.9%)/80 (11%)	0.82 (0.48–1.42)
Serostatus unspecified	0/11	NA

Values are the number. RA = rheumatoid arthritis; AITD = autoimmune thyroid disease; OR = odds ratio; 95% CI = 95% confidence interval.

Conclusions: This large real-life study of response to methotrexate in early RA suggests that AITD, measured as thyroxin replacement therapy, may be linked to treatment response in seropositive patients (and among males). Exploratory by nature, these findings call for replication.

Disclosure of Interest: K. Waldenlind: None declared, S. Saevarsdottir: None declared, C. Bengtsson: None declared, J. Askling Grant/research support from: Abbvie, Pfizer, Lilly, Samsung, MSD, UCB, Roche, Janssen

DOI: 10.1136/annrheumdis-2017-eular.3725

FRI0150 EPIDEMIOLOGICAL DESCRIPTION OF PSYCHOLOGICAL, SEXUAL AND SLEEP DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND CORRELATION BETWEEN THEM AND DISEASE ACTIVITY

L. Villarreal[1], S. Henao[2], D. Buitrago-Garcia[3], P. Santos-Moreno[4]. *[1]Psychology and processes; [2]Patient service; [3]Epidemiology; [4]Rheumatology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: Rheumatoid arthritis (RA) is the prevalent autoimmune inflammatory arthritis found in adults, with the worldwide prevalence ranging from 0.4% to 1.3%. Psychological disorders can be underestimated in this population; on the other hand studies had shown that the daily experience with RA can lead to sleep, psychological and sleep disorders.

Objectives: To characterize a population with RA and to describe the psychological, sexual and sleep disorders in a specialized rheumatology center in Bogotá Colombia.

Methods: We perform a cross-sectional study of patients attending to our psychology consultation the information was collected through semi-structured interviews, also using classificatory criteria of pathologies described in CIE 10 diagnostic manual, applying descriptive epidemiology for continuous variables, measure of central tendency and dispersion for qualitative and categorical variables through percentages and averages.

Results: We included 1398 patients attending to our psychology consultation. Mean age was 55 years ± 8; 80% were female and 20% male. Mean DAS28 was 2.6±1.3, mean HAQ was 1.6±1.6; patients had the disease for an average of 12 years ± 8; 41% of patients had comorbidities associated with non-autoimmune disease, 14% comorbidities related to autoimmune disease; 35% of our patients did not report other comorbidities. Most of patients were married 60%, followed by divorced 19%, single 14% and widowed 7%. Regarding occupation 33% were employees, 25% were housekeepers or retired due to age, 12% were retired due to disabilities, and 3% unemployed. Of the total population 45% had elementary school, 32% high school, 8% college education, 7% graduate education and 7% were illiterate. 17% of patients lived alone. Regarding psychological factors 25% had any mood disorders, 13% sleep disorders, 12% somatomorphic disorders, 6% sexual dysfunction, 2% dementia, 4% eating disorders and 38% reported no to have any of the above. Concerning sexual disorders, 38% reported no to have any sexual activity, 32% reported to have a satisfactory sexual life, 11% dyspareunia, 9% had an unsatisfactory sexual life, 5% loss of desire, 3% premature ejaculation and 2% orgasmic decrease. When the psychologist asked about sleep disorders 69% reported no to have any, 25% primary insomnia, 1% hypersomnia, 3% OSAS and 2% alterations on the circadian rhythm. There was a statistical association between psychological and sexual disorders, sleep and sexual disorders and, psychological and sleep disorders. Disease activity was associated only with sleep disorders.

Conclusions: Not only DMARDs disease management should be a priority for RA patients, factors such as sleep, sexual and psychological are important because one third of patients have it; on the other hand there is a interdependence between them and disease activity. Thus, it is important to have a multidisciplinary care team for the patient with RA, including a psychologist that can manage this kind of conditions and if necessary refer to a psychiatrist consultation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5622

FRI0151 DISEASE COURSE IN SERONEGATIVE RA PATIENTS CLASSIFIED ACCORDING TO THE 2010 ACR/EULAR CRITERIA

L.B. Nordberg[1], S. Lillegraven[1], A.-B. Aga[1], I.C. Olsen[1], E. Lie[1], H.B. Hammer[1], T. Uhlig[1], D. van der Heijde[2], T.K. Kvien[1], E.A. Haavardsholm[1] on behalf of the ARCTIC study group. *[1]Diakonhjemmet Hospital, oslo, Norway; [2]Leiden University medical center, Leiden, Netherlands*

Background: The development of the 2010 classification criteria for rheumatoid arthritis (RA) has led to a redefinition of the patient population, including classification of seropositive versus seronegative patients. In our recently published study of DMARD naïve early RA patients fulfilling the 2010 ACR/EULAR criteria, we found seronegative patients to have markedly higher disease activity at time of diagnosis, compared to seropositive patients.[1] There is very limited information about the disease course of seronegative patients classified according to the new criteria.

Objectives: Our aim was to examine the disease course of seronegative early RA patients fulfilling the 2010 ACR/EULAR criteria.

Methods: In the treat-to-target ARCTIC trial, DMARD-naive RA patients classified according to the 2010 EULAR/ACR criteria were randomised 1:1 to follow-up with or without ultrasound. Patients in both arms were treated according to the same DMARD escalation strategy. Patients were assessed at 13 visits during two years of follow-up.[2] We stratified the patients as seropositive (rheumatoid factor (RF)+, anti-citrullinated peptide antibody (ACPA)+, or both) or seronegative (RF- and ACPA-). At 24-month follow-up, measures of disease activity were compared across the groups using independent samples t-test, Mann-Whitney U test or chi square test as appropriate.

Results: A total of 230 patients were included, the mean (SD) age was 51.4 (13.7) years and 61.3% were female; 34 patients (14.8%) were seronegative. The mean age (SD) was 55.4 (2.7)/ 50.8 (0.9) years (p=0.07), mean (SD) disease duration was 7.7 (6.8)/7.0 (5.1) months (p=0.46), and 56/62% were females (p=0.48) in the seronegative/seropositive groups. At 24-month follow-up, measures of disease activity were similar between groups (table). There was a tendency towards more radiographic damage in the seronegative patients. Seronegative patients had a significantly greater reduction (0–24 months) in disease activity measures in terms of DAS, number of swollen joints, physician global and ultrasonography scores (table).

Table: Measures of disease severity at follow-up compared across serology status

Variable	Baseline			State at 24 months			p-value Δ0-24 months
	Seronegative N=34	Seropositive N=196	p-value	Seronegative N=34	Seropositive N=196	p-value	
DAS*	3.86 (1.2)	3.39 (1.2)	**0.029**	1.18 (0.15)	1.32 (0.06)	0.40	**0.007**
44-SJC	18 (11-25)	8 (4-13)	**<0.001**	0 (0-0)	0 (0-1)	0.73	**<0.001**
CRP	7 (3-27)	7 (3-18)	0.50	2.5 (1-4)	3 (1-5)	0.42	0.50
ESR	13 (10-29)	21 (12-33)	0.14	6.5 (4-12)	8 (5-15)	0.11	0.44
Ritchie articular index	7 (3-14)	7 (4-13)	0.92	0 (0-1)	0 (0-2)	0.57	0.59
Physician GlobalVAS*	49.2 (21.7)	39.1 (20.1)	**0.008**	7.4 (1-6)	9.7 (0.8)	0.28	0.003
Patient Global VAS*	50.2 (26.9)	49.7 (1.7)	0.90	18.1 (3.5)	18.1 (1.6)	0.99	0.91
US PD joint score	13 (7-22)	6 (2-12.5)	**<0.001**	0 (0-1)	0 (0-0)	0.68	**0.002**
US GS joint score	33 (21-51)	17 (10-25)	**<0.001**	3.5 (0-7)	4 (1-7)	0.73	**<0.001**
Total van der Heijde Sharp score	5.5 (2-13)	4 (1.5-8)	0.17	9.5 (2.5-16.0)	5.5 (3-10.3)	0.17	0.92
Joint space narrowing	1.5 (0-6)	1 (0-3)	**0.047**	2.5 (1-7.5)	1 (0-4)	0.059	0.31
Erosion score	3 (1-6.5)	3 (1-4.5)	0.42	4 (2-9)	4 (2-7)	0.34	0.42
Pain VAS	44 (25-71)	48 (29-70)	0.58	14 (4-27)	8 (2-28)	0.22	0.35
Fatigue VAS	36 (22-67)	38 (14-65)	0.88	9 (2-38)	13 (3-38)	0.56	0.76
PROMIS Physical function	39.2 (30-46)	39.3 (33-44)	0.86	51 (44-63)	50 (43-63)	0.50	0.47
ACR/EULAR remission n (%)	-	-	-	53%	48%	0.59	-

Values are median (25-75 percentiles) if not otherwise indicated. *Mean(SD).

Conclusions: In this study of early RA patients, seronegative patients had more inflammatory activity at baseline and a tendency to more radiographic damage, but disease activity after two years of treat-to-target therapy was similar to the seropositive patients. Our findings suggest that seronegative patients classified according to the new criteria respond to modern treatment strategies, with similar rates of patients reaching remission compared to seropositive patients.

References:

[1] Nordberg LB et al. Annals of the rheumatic diseases 2017;76:341–345.
[2] Haavardsholm EA et al., BMJ 2016;354:i4205.

Disclosure of Interest: L. Nordberg: None declared, S. Lillegraven: None declared, A.-B. Aga: None declared, I. Olsen: None declared, E. Lie: None declared, H. Hammer Consultant for: AbbVie, Pfizer, BMS, Roche, UCB, T. Uhlig: None declared, D. van der Heijde: None declared, T. Kvien: None declared, E. Haavardsholm Grant/research support from: Pfizer, MSD, UCB, AbbVie, Roche

DOI: 10.1136/annrheumdis-2017-eular.4967

FRI0152 RHEUMATOLOGISTS' EXPERIENCES AND VIEWPOINTS TOWARDS MANAGING RHEUMATOID ARTHRITIS IN ELDERLY PATIENTS: A QUALITATIVE STUDY

J. Nawrot[1], A. Boonen[1,2], R. Peeters[3], M. Starmans[3], M. Van Onna[1,2].
[1]Department of Internal Medicine, division of Rheumatology, Maastricht University Medical Center +; [2]School for Public Health and Primary Care, Maastricht University, Maastricht; [3]Rheumatology, Zuyderland Hospital, Heerlen, Netherlands

Background: The number of elderly individuals with rheumatoid arthritis (RA) is expanding in Europe, mainly due to an increase in life expectancy. As a result, management of these patients, e.g. the application of the treat-to-target and tight control principles, shall have to account for frailty and comorbidity. However, knowledge about how rheumatologists perceive and manage RA in the elderly patient population is limited.
Objectives: To explore the viewpoints of rheumatologists on management goals in elderly RA patients and the influence of factors such as age, frailty and comorbidity on these goals. Furthermore, experiences of rheumatologists with regard to outcome instruments to guide management in elderly patients were assessed.
Methods: A qualitative study involving semi-structured interviews with rheumatologists was conducted. Two readers independently annotated the transcripts of the interviews. Important concepts were taxonomically categorized and later combined in overarching themes by using NVivo 11.
Results: Seventeen rheumatologists were purposively sampled from nine medical centres (mean age: 44.8 years (SD 7.7 years); 29% male). High levels of frailty and comorbidity frequently influenced management goals of rheumatologists: in these cases, preserving an acceptable functional status prevailed over the treat-to-target and tight control principles. For instance, most rheumatologists accepted the presence of tender and swollen joints when overall functioning and social participation were not or only minimally impaired. In patients ≥80 years, age instead of frailty and comorbidity was the most prominent factor that steered management. On that line, almost all rheumatologists admitted that their management strategy is less driven by the result of the Disease Activity Score-28 (DAS28), since comorbidity (e.g. osteoarthritis) and an age-related physiological Erythrocyte Sedimentation Rate (ESR)-elevation might distort the DAS28 value. Instead, before adapting anti-rheumatic therapy, rheumatologists weighted the frailty and comorbidity levels of a patient and the functional consequences of these factors such as cognitive and physical decline, dependency and polypharmacy (quote 1, Table 1). This frequently resulted in a less future-oriented management approach that was not aimed at the maximal prevention of joint erosions and deformities (quote 2, Table 1). Rheumatologists reported that a lack of time to evaluate all comorbid conditions, as well as contradictory advices of other medical specialists often complicated the management of elderly RA patients.

Table 1. Illustrative quotes made by rheumatologists.

Quote	
1	'I sometimes ask my patients: what physical complaint bothers you the most? The RA, the heart failure or something else? Treat what actually limits an elderly patient.'
2	'I wonder if low-dosage prednisone for the rest of their lives is considerably worse than to initiate biological therapy and cause a life-threatening infection?'

Conclusions: Commonly accepted RA treatment paradigms such as treat-to-target and tight control are not automatically adopted in the elderly patient population. Maintaining a patient acceptable functional status prevails. Future RA management recommendations for elderly RA patients are needed and should account for factors such as frailty and comorbidity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2291

FRI0153 COMPARISON OF CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS VERSUS METHOTREXATE: RESULTS AT 24-MONTHS OF FOLLOW-UP

M. Khraishi[1], M. Stutz[2], A. Lewis[3], C. Molta[4], E. Rampakakis[2]. *[1]Rheumatology, Memorial University of Newfounbdland, St. John's; [2]JSS Medical Research, St-Laurent; [3]Epidemiology, Memorial University of Newfoundland, St.John's, Canada; [4]Rheumatology, MainLine Rheumatology Lankenau Medical Center, Philadelphia, United States*

Background: Rheumatoid arthritis (RA) is associated with increased risk of atherosclerotic cardiovascular (CV) disease. Treatment with conventional systemic disease modifying drugs (csDMARDs) such as methotrexate (MTX), as well as biological DMARDs (bDMARDs), has been shown to decrease CV risk. Although bDMARDs specifically target inflammation common to RA and atherosclerosis, whether or not cardioprotective effects associated with bDMARD use is superior to csDMARDs, remains to be determined.
Objectives: To investigate 10 year-CV risk, and incidence of new myocardial infarctions (MI), in RA patients treated with either MTX or bDMARD mono/combination therapy, in a Canadian routine clinical care setting
Methods: RA patients were prospectively followed between January 2011-March 2014. Parameters collected were patient demographics, RA disease activity parameters, traditional CV risk factors, lipid parameters, and 10-year CV risk, assessed using the Framingham Risk Score (FRS). Between-group differences in change from baseline to month 24 in FRS, disease activity, and lipid parameters were assessed with the two sample t-test or the Chi-Square statistic; within-group differences were assessed with the paired-samples t-test or the McNemar-Bowker test. Adjusted change in FRS was ascertained using general linear models, and logistic regression identified predictors of MI.
Results: A total of 517 RA patients receiving bDMARDs (n=313) or MTX (n=199), were included. Mean (SD) age was comparable between cohorts [57.57 (12.11) years vs. 59.58 (12.60), p=0.11; bDMARD vs. MTX, respectively], as was female gender (76.7% vs. 73.9%, p=0.268). Patients receiving bDMARDs had significantly ($p<0.05$) longer mean (SD) RA duration [12.63 (9.95) vs. 7.88 (6.94) years] and higher total comorbidities [3.96 (2.53) vs. 3.38 (2.32)]. Mean (SD) baseline FRS was 11.84 (9.38) vs. 12.36 (9.19) percent (p=0.564; bDMARDs vs. MTX, respectively), and patient distribution across low (62.3% vs. 54.8%), intermediate (9.9% vs. 12.2%) and high (27.8% vs. 33.2%) FRS risk categories was comparable (p=0.239).
At month 24, FRS category remained stable in bDMARD patients (low: 58.8%; intermediate: 14.2%; high: 27.0%; p=0.380), whereas a shift in FRS category was observed in MTX patients (low: 69.6%; intermediate: 10.1%; high: 27.0%, p=0.006). Within-group changes in FRS were significant for both MTX ($p<0.001$) and bDMARD patients (p=0.016). Adjusted mean change (SE) in FRS was higher in MTX patients [-1.37 (0.30) vs. -0.72 (0.25)], although not statistically different (p=0.098). Incidence of new MI was similar between groups (MTX: 3.8% vs. dDMARD: 3.0%; p=0.421), and predictors [OR (95% CI)] identified were: higher total comorbidities [1.45 (1.24, 2.20), $p<0.001$], age [1.07 (1.00, 1.13), p=0.037], and male gender [4.00 (1.38, 11.57), p=0.011].
Conclusions: Significant improvement in CV risk at 24 months was observed during treatment with both MTX and bDMARDs. As predictors of MI did not include several established CV risk factors, longer studies, as well as the development of an RA-specific tool, may permit better assessment of CV risk in RA patients.
Disclosure of Interest: M. Khraishi Grant/research support from: Roche Canada, M. Stutz: None declared, A. Lewis: None declared, C. Molta: None declared, E. Rampakakis: None declared
DOI: 10.1136/annrheumdis-2017-eular.2789

FRI0154 THE TOLERABILITY OF VACCINATION AGAINST PNEUMOCOCCUS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

M. Soloshenko[1], E. Alexeeva[1,2], T. Bzarova[1,2], S. Valieva[1], R. Denisova[1], O. Lomakina[1], K. Isaeva[1], E. Kashchenko[1], A. Karaseva[1]. *[1]Federal State Autonomous Institution "National Scientific and Practical Center of Children's Health"; [2]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Background: Children with chronic rheumatic diseases, including juvenile idiopathic artritis, are at high risk of bacterial and viral infections. The risk of complications and severity of infectious diseases are increased in immunosuppressive therapy due to given the long-term use.
Objectives: To evaluate the safety and tolerability of vaccination against pneumococcus in children with juvenile idiopathic arthritis.
Methods: The analysis included 39 patients with juvenile idiopathic arthritis who were in remission. Patients were divided into two groups, depending on the type of immunosuppressive therapy. Group 1 (n=24) consisted of patients receiving etanercept, mean age 5,4±2,5, observed 48 patient-years; Group 2 (n=15), patients who received methotrexate mean age 6,8±3,2, observed 30 patient-years. All patients had been vaccinated by 13-valent pneumococcal polysaccharide conjugate vaccine (13PPV). Recorded the incidence of infection diseases (such as pneumonia, tonsillitis, otitis media, etc.) in the 12 months prior to vaccination and 12 months after vaccination. All patients monitored the development of adverse events against the background of vaccination.
Results: The study showed a decrease in the incidence ofinfection diseases after vaccination in the first group from 5,4±1,66 to 1,7±0,77, in second group from 4,4±1,05 to 1,6±0 73, ($p<0.05$). Adverse events related to vaccination are presented in the table. Results of the study showed no relapse of the underlying disease following immunization. Adverse events related to vaccination are presented in the table.
Conclusions: The results showed a good tolerability of the vaccine, no relapse of the underlying disease following immunization, as well as a statistically significant ($p<0.05$) reduction in the incidence following immunization.
Disclosure of Interest: M. Soloshenko: None declared, E. Alexeeva Grant/research support from: Roche, Abbott, Pfizer, Bristol-Myers Squibb, Centocor, Novartis., Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Bristol-Myers Squibb, Medac, Novartis, Pfizer, T. Bzarova Grant/research support

Adverse events	Group I: Methotrexate	Group II: Etanercept
Total, n	6	3
Hyperemia and soreness at the injection site	3	2
Swelling at the site of vaccine injection	1	1
Fever	1	–
Headache	1	–

from: Roche, Pfizer, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Pfizer, S. Valieva Grant/research support from: Roche, Bristol-Myers Squibb, Speakers bureau: Roche, Merck Sharp & Dohme, Bristol-Myers Squibb, Medac, Novartis, R. Denisova Grant/research support from: Roche, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Medac, O. Lomakina: None declared, K. Isaeva: None declared, E. Kashchenko Grant/research support from: Novartis, A. Karaseva: None declared

DOI: 10.1136/annrheumdis-2017-eular.5944

FRI0155 PREVALENCE OF HBV INFECTION AND RISK OF REACTIVATION ON BIOLOGIC TREATMENT: A POPULATION-BASED OBSERVATIONAL STUDY OF RHEUMATOID ARTHRITIS SUBJECTS IN A NORTHERN ITALY AREA

M. Meroni [1,2], L. Sangiovanni [3], E. Lupi [1], S. Fagiuoli [3], M. Limonta [1]. *[1] Rheumatology Unit, ASST Papa Giovanni XXIII, Bergamo; [2] Research Laboratory and Academic Division of Clinical Rheumatology, Internal Medicine Dept., University of Genova, Genova; [3] Gastroenterology and Transplant Hepatology Unit, ASST Papa Giovanni XXIII, Bergamo, Italy*

Background: The introduction of biologic agent's treatment in rheumatic diseases dramatically changed their outcome, but raised some concerns about infections recrudescence. Due to the prevalence of hepatitis B virus (HBV) among Italian general population (2–6%), the possibility of a disease reactivation in case of an immunosuppressive treatment has to be considered.
Objectives: Aim of this prospective, population-based observational study was to assess the prevalence of HBV (both in chronic carriers and recativated) rheumatoid arthritis (RA) patients in our setting; to verify if these findings were in line to the Italian and European-reported data; finally, to evaluate the final outcome of HBV RA subjects.
Methods: We enrolled the totality of RA patients treated by biologics and, therefore, consulting our Unit at least every 12 weeks, from December 2015 to January 2017. According to the current (ACR/EULAR and AASLD) guidelines, every subject was screened for HBV before starting biologic treatment. Descriptive statistics was performed. Acute infection; previous (resolved) infection; inactive and active carrier; and vaccine-immunized subjects were defined according to Tab. I.
Results: A totality of 265 RA patients (female 56.3%; male 43.7%; mean age 36+/-20 years) underwent biologic treatment after succeeding the screening (HBsAg+ subjects were excluded). The huge majority of them (82%) was treated by TNF-alpha inhibitors (TNFi), since the remaining received biologic agents with different mechanisms of action. We overall detected 33 (12.5%) inactive carriers, for whom HBsAg and HBV DNA periodical monitoring was suggested; in 3 of them (1.1% of the study population), HBV DNA became detectable, with a low viral load (<2000 UI/ml): they prosecute the biologic therapy after the introduction of the standard prophylaxis (lamivudine 100 mg daily) and a more strictly (periodic liver enzymes and liver ETG evaluation) monitoring.
In occasion of the screening, we observed 6 (2.3%) HBV-immunized (due to vaccine) and 6 (2.3%) previously infected (HBcAb+) patients: for the first ones no action is required, since the latter were put on standard prophylaxis before undergoing biologic agent and monitored. One of them (0.38%) developed, after 6 months of treatment, HBV reactivation with high-level (>2000 UI/ml) detectable DNA and liver enzymes elevation (>normality x3). She was therefore stopped from receiving biologic agent and put on entecavir 1 mg daily.

Interpretation of HBV serologic test results

	HBsAg	HBsAb	HBcAb IgM	HBcAb IgG	HBeAg	HBV DNA
Acute infection	POS	neg	POS	neg	POS	POS
Past infection (resolved)	neg	POS	neg	POS	neg	neg
Inactive carrier	POS	neg	neg	POS/neg	neg	neg
Active carrier	POS	neg	neg	POS	POS/neg	POS
Vaccine induced immunity	neg	POS	neg	neg	neg	neg

POS: positive; neg: negative; HBsAg: hepatitis B surface antigen; HBsAb: hepatitis B surface antibody;
HBcAb: hepatitis B core antibody; HBeAg: hepatitis B envelope antigen.

Conclusions: Our prospective, population-based observational study, performed in a first-level referring Hospital in a highly populated area, suggests some considerations. In a way, our data reported a significantly higher prevalence of HBV infection "contact" among our RA population, in comparison to the general one ($p<0.05$). This issue has previously been reported and could be justified but the generally higher HBV diffusion in certain area (i.e., Italy); by the age/ethnicity of the sample; and, finally, by the bias consisting in an extensive screening of these patients. On the other hand, our experience suggests that a tight monitoring of parameters predicting infectious flare should lead to a prompt diagnosis and a lower number of complications for these peculiar patients, as observed in our population.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2572

FRI0156 DO CHANGES IN ADIPOCYTOKINES CORRELATE WITH CHANGES TO DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS? FINDINGS FROM THE TOMORROW STUDY

M. Tada [1], K. Inui [2], Y. Sugioka [3], T. Okano [2], K. Mamoto [2], T. Koike [3], H. Nakamura [2]. *[1] Orthopaedic Surgery, Osaka City General Hospital; [2] Orthopaedic Surgery; [3] Center of Senile Degenerative Disorders, Osaka City University Graduate School of Medicine, Osaka, Japan*

Background: Cytokines released from mast cells evoke inflammation and correlate with arteriosclerotic lesions and autoimmune disease[1]. The relationship between disease activity and lipid metabolism is a notable in research surrounding rheumatoid arthritis (RA). RA patients without disease control reportedly show high titers of leptin or adiponectin as adipocytokines[2].
Objectives: We analyzed the interaction between changes in disease activity and adipocytokines using data from the TOMORROW (TOtal Management Of Risk factors in Rheumatoid arthritis patients to lOWer morbidity and mortality clinical trial) study, a 10-year prospective study (registration number, UMIN000003876).
Methods: We analyzed data collected from the cohort of the TOMORROW study including 193 patients with RA and age- and sex-matched 194 healthy individuals (controls). We compared changes in leptin and adiponectin (Δleptin and Δadiponectin) in both groups between baseline and after 3 years. Correlations with the change in disease activity (ΔDAS28ESR) during 3 years and changes in Δleptin and Δadiponectin in RA were investigated by univariate analysis.
Results: Leptin levels increased in both groups. No significant differences in Δleptin were seen between RA (0.21 ng/ml) and controls (0.18 ng/ml; p=0.37). On the other hand, adiponectin was significantly decreased in controls (-3.3 μg/ml) compared to RA (-1.8 μg/ml; p=0.01). Negative correlations between Δleptin and Δadiponectin were detected in the RA group ($r=-0.29$, $p<0.01$). The correlation between adiponectin and DAS28ESR was positive both at baseline ($r=0.22$, p=0.01) and after 3 years ($r=0.18$, p=0.01). However, no such tendencies were seen for leptin. Table 1 shows details of the correlations with changes in adipocytokine. In terms of the relationship with ΔDAS28ESR, no correlation was seen with Δleptin ($r=0.07$, p=0.31) or Δadiponectin ($r=-0.01$, p=0.91). Changes in lipid metabolic markers and fat percentages were detected as predictive factors for Δadipocytokines.

Table 1. Correlations with changes in adipocytokine by univariate analysis

	R	*P*
ΔAdiponectin		
Baseline age	-0.199	0.006
ΔHigh-density lipoprotein	0.265	0.001
ΔFat percentage	-0.144	0.046
ΔDAS28ESR	-0.009	0.906
ΔLeptin		
Baseline age	0.258	0.001
ΔLow-density lipoprotein	0.347	0.001
Δfat percentage	0.554	0.001
Fall	-0.145	0.045
ΔDAS28ESR	0.074	0.311

Conclusions: Leptin increased and adiponectin decreased over the course of 3 years. Correlations between Δadipocytokines and ΔDAS28ESR were not detected. RA patients with high disease activity show higher adiponectin titers.
References:
[1] Benoist C., Mathis D. Mast cell in autoimmune disease. Nature. 2002; 420: 875–8.
[2] Cho H., Lin J., Chen W., et al. Baseline adiponectin and leptin levels in predicting an increased risk of disease activity in rheumatoid arthritis: a meta-analysis and systematic review. Autoimmunity. 2016; 49: 547–53.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2833

FRI0157 FERTILITY IN WOMEN WITH RHEUMATOID ARTHRITIS COMPARED TO HEALTHY CONTROLS

M.E.B. Clowse, G. McDaniel, A.M. Eudy. *Rheumatology, Duke University Medical Center, Durham, United States*

Background: Data suggest infertility is increased in women with rheumatoid arthritis (RA) compared to healthy women. Therefore, it is possible that diminished ovarian reserve and ovulatory dysfunction may be more common among women with RA.
Objectives: To compare differences in ovarian reserve and ovulatory frequency, as well as in self-reported infertility, between women with and without RA.
Methods: Women with RA aged 20–40 seen in a university clinic without a history of ovarian surgery or prior exposure to possible ovary-toxic medications were invited to participate in a cross-sectional survey. Healthy controls were women aged 20–40 without an autoimmune disease, matched for age and current use of hormonal contraceptives. Infertility was defined as a patient reporting physician-diagnosed infertility or being unable to get pregnant after 12 months of trying. Ovarian reserve was assessed by measuring anti-Müllerian hormone (AMH). In women who were not taking hormonal contraceptives, progesterone level was measured from a serum sample drawn between days 21 and 23 of the menstrual cycle. Anovulation was defined as a progesterone level <3 ng/mL. In

descriptive comparisons, differences in proportions were determined by Fisher's exact test, and ANOVA determined differences in means for continuous variables. Multivariate linear models estimated the effect of RA on AMH. In women with RA, the effect of RA medication use on AMH and anovulation was explored.

Results: There were 75 RA patients (83% Caucasian, 4% Hispanic, 77% with at least a college education) and 75 controls (64% Caucasian, 5% Hispanic, 88% with at least a college education). The majority of RA patients were married (60%), compared to 31% of controls. The mean age of both RA patients and controls was 32 years. Mean AMH in RA patients was 3.0 (SD: 2.6) compared to 3.9 (SD: 3.9) in controls (p-value: 0.1). In linear regression models adjusted for age, hormonal contraceptives and race (nonwhite vs. white), RA patients had a lower AMH than healthy controls (β: -1.05; 95% CI: -2.09, -0.005; p=0.05). There was no observed difference in the proportion of RA patients and controls with anovulation (19% in RA and 21% in controls). Infertility was reported by 12% of RA patients and 7% of controls (p=0.4).

Among RA patients, 81% reported having ever used methotrexate (MTX). The mean AMH for MTX users was 2.8 (SD: 2.4) compared to 4.0 (SD: 3.1) in never users (p=0.1). In linear regression models adjusted for age, hormonal contraceptives and race, RA patients who had ever taken MTX had a lower AMH than those who had never taken MTX (β: -1.49; 95% CI: -2.83, -0.15; p=0.03). However, when the cumulative dose of MTX was analyzed, there was no effect of cumulative MTX and AMH. Ever use of prednisone or NSAIDs did not appear to affect AMH levels in RA patients. Methotrexate, prednisone, and NSAIDs use did not have an observed effect on anovulation.

Conclusions: In this cross-sectional study, women with RA appeared to have a lower AMH level than healthy controls, suggesting ovarian reserve may be lower in these patients. In RA patients, previous use of methotrexate was associated with lower AMH, although no dose response of cumulative methotrexate exposure was observed. We did not observe a difference in anovulation between RA patients and controls. This suggests women with RA may have reduced fertility for reasons other than anovulation.

Acknowledgements: This study was funded by Pfizer.

Disclosure of Interest: M. Clowse Grant/research support from: Pfizer, Janssen, Consultant for: UCB, G. McDaniel: None declared, A. Eudy: None declared

DOI: 10.1136/annrheumdis-2017-eular.6376

FRI0158 CAROTID ENLARGEMENT, BRACHIAL ARTERY FLOW-MEDIATED VASODILATATION AND SERUM LEVELS OF VON WILLEBRAND FACTOR IN RHEUMATOID ARTHRITIS

M. Veselinovic, A. Tomic-Lucic, V. Grbovic, V. Jakovljevic. *KC Kragujevac, Kragujevac, Serbia*

Background:

In rheumatoid arthritis (RA), higher mortality is mainly due to cardiovascular disease, as a consequence of accelerated atherosclerosis found in this diseases (1). Finding methods for assessing vascular dysfunction during the early stages of the disease is important, particularly in patient groups at high CV risk (2).

The use of noninvasive imaging techniques may help identify high-risk individuals who may benefit from active therapy to prevent clinical disease. Two of them, brachial ultrasonography to determine the presence of endothelial dysfunction and carotid ultrasonography to assess carotid intima-media wall thickness (IMT) have been found to be useful in the assessment of the cardiovascular risk of patients with RA (3). Prothrombotic markers have been shown to be able to predict cardiovascular risk in patients with RA (4).

Objectives: The first aim of the study was to investigate whether early signs of atherosclerosis and endothelial dysfunction, as measured by IMT and brachial artery flow-mediated (FMD) vasodilatation, were present in patients with RA compared with controls. The second aim was to analyze correlation between serum levels of vWf and IMT and FMD in patients with RA.

Methods: Fifty-two patients with RA and 30 matched healthy controls without clinically evident CV disease were studied. Brachial and carotid ultrasonography was performed to determine FMD and IMT, respectively. We also assayed immunological, inflammatory and metabolic laboratory markers.

Results: IMT was significantly higher in RA patients (1.00±0.16 mm) patients than in controls (0.89±0.13 mm) (P=0.001). FMD% was significantly lower in RA (9.16±7.03) as compared to controls (12.60±5.49) (p=0.005). It showed statistically higher values of vWF in the RA patients compared to the control group (p=0.01).

Patients with RA is divided into two groups according to the value of the IMT, below 9mm and 0.9mm and above. vWFact is statistical significantly higher in the group with thicker IMT (p=0.046), as well as the percentage of men (p=0.030). Other parameters did not show statistical significance in relation to the value of the IMT.

Conclusions: In patients with RA, increased serum levels of vWF and impaired FMD and IMT, indicating endothelial dysfunction and accelerated atherosclerosis. IMT measurement is the first candidate to evaluate against conventional evaluation of cardiovascular risk in prospective studies.

References:

[1] Dessein PH, Joffe BI, Singh S. Biomarkers of endothelial dysfunction, cardiovascular risk factors and atherosclerosis in rheumatoid arthritis. Arthritis Res Ther 2005;7:634–643.

[2] Tousolis D, Antoniades C, Bosinakou E et a. Differences in inflammatory and thrombotic markers between unstable angina and acute myocardial infarction. Int J Cardiol 2007;115:203–207.

[3] Fuchs I, Frossard M, Spiel A, Riedmuller E, Laggner AN, Jilma B. Platelet function in patients with acute coronary syndrome (ACS) predicts recurrent ACS. J Thromb Haemost 2006;4:2547–2552.

[4] Jonsson SW, Backman C, Johnson O et al. Increased prevalence of atherosclerosis in patients with medium term rheumatoid arthritis. J Rheumatol 2001;28:2597–2602.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1216

FRI0159 INFECTION AND MALIGNANCY ARE NOW THE MAJOR CAUSES OF DEATH IN AGGRESSIVELY TREATED RHEUMATOID ARTHRITIS PATIENTS

N. Chaplin[1], J. McNally[2], J. Kitchen[2]. *[1]St George's University of London, London; [2]Rheumatology, Royal Berkshire NHS Foundation Trust, Reading, UK*

Background: Patients with rheumatoid arthritis (RA) have an increased mortality compared to the general population. Previous studies have shown that this is attributable to cardiovascular and respiratory disease. Over recent years earlier and more aggressive treatment with higher dosage of methotrexate and the earlier use of biologic drugs has improved disease outcomes. The effect on cause of death is unknown. In this retrospective cohort study we found the major cause of death was infection followed by malignancy and found no correlation with seropositivity or gender.

Objectives: To analyse the causes of death in RA patients treated with aggressive disease modifying anti rheumatic drugs (DMARD) and Biologic therapies in Berkshire, UK.

Methods: Patients with RA who died between 2010 and 2016 were identified using the DAWN software DMARD monitoring database. A cohort of 3106 patients with RA are monitored using DAWN software in Berkshire, UK. The causes of death were identified from medical records, general practice records or the local coroners office.

Results: 198 patients on DAWN monitoring died during the 6 year study period. Treatment details and cause of death was identified for 131 RA patients. 71% were seropositive for rheumatoid factor and 61% were female.

91 patients (69%) were treated with methotrexate, 28 hydroxychloroquine (21%), 14 sulphasalazine (21%) and 7 with leflunomide (5%). The majority of patients (81) were on monotherapy (61%), 32 were on 2 DMARDS (24%) and only one was on triple therapy.

4 patients with RA who died were on biologic monotherapy, 10 were treated with biologic and combination DMARD. The most commonly prescribed biologics were etanercept (35%) and rituximab (35%).

The leading causes of death in this cohort were pneumonia (39 patients 29%), cerebrovascular disease (16 patients 12%), septicaemia (11 patients 8%) and lung cancer (6 patients 4%).

Infection accounted for 57 patients' deaths (43%) followed by malignancy in 24 patients (18%). Cerebrovascular disease (20 patients, 15%) and cardiovascular disease (13 patients, 9%) were less frequent causes of death in our cohort.

Comorbidity data for the cohort was recorded premortem. 49 patients (37%) had cardiovascular disease of any kind. 25% had respiratory disease and 23% had an endocrine comorbidity (predominantly diabetes).

Conclusions: In our large cohort of aggressively treated RA patients, infection followed by malignancy and not cardiovascular disease, was the leading cause of death. Larger prospective studies will be required to see if cumulative drug toxicity of more aggressive early treatment improves outcome from RA but changes mortality from comorbidities over time.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5442

FRI0160 EVALUATION OF INFLAMMATORY CARDIOVASCULAR (CV) RISK FACTORS IN PRE- AND POST-MENOPAUSAL FEMALE PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

O.O. Garmish, V. Levchenko, V. Kovalenko. *NSC "Institute of Cardiology named by M.D.Strazhesko NAMS of Ukraine", Kiev, Ukraine*

Objectives: To assess inflammatory factors and peripheral vessels involvement as markers of cardiovascular risk in female patients with RA

Methods: 105 female patients who fulfill ACR/EULAR 2010 criteria were examined. Laboratory assessments consisted of biochemistry and hematology analysis, measuring of CRP level, rheumatoid factor, anti-CCP level, total cholesterol, HDL, LDL, thyroglobulin, apoliprotein, A1, apoliprotein B, uric acid, HbA1c, microalbuminuria. DAS28 was used in characterizing RA activity. CV risk was defined per mSCORE. Tibial artery and carotid artery ultrasonography examination included the measurement of cIMT in 3 points, detection of focal plaques in the extracranial carotid tree, blood flow velocity and morphology of the intima was performed

Results: 83.3% reproductive age patients were without CV risk, 11.1% experienced middle level and 5.6% low level of CV risk on mSCOR. In 96.1% postmenopausal patients moderate, high and very high CV risk was detected. According to multiple logistic regression analysis we identified CV risk factors:

high CRP and DAS28, swollen joint count, LDL cholesterol level, menopause, thickness of cIMT and tibial artery. Were identify a significant correlation between tibial artery thickness and age, BMI, RA duration, systolic and diastolic blood pressure, cholesterol, menopause ($p<0.01$, $\chi2=26.18$). Also, we identified a significant relationship between tibial artery thickness and changes of the intima morphology ($\chi2=31,64$; $p<0,01$), carotid plaques ($\chi2=26,179$; $p<0,01$), sclerosis of the heart valves ($\chi2=25,78$; $p<0,01$). A less significant relationship was between cIMT ($\chi2=8,507$; $p<0,01$). The DAS28, age ($p<0.001$), thickness of cIMT and tibial artery ($p<0.001$) are predictive factors for the development of carotid plaques. The predictive factors for tibial artery thickness in female patients <45 age are: high CRP ($p<0.004$) and DAS28 ($p<0.03$), anti-CCP positivity ($p<0.04$), Vps internal carotid artery ($p<0.04$)

Conclusions: The results of our study indicate that high CRP and DAS28 score, swollen joint count, LDL cholesterol level, menopause, thickness of cIMT and tibial artery associated with the increased cardiovascular risk. Tibial artery thickness and Vps internal carotid artery may be assessed like the new predictive factors of CV diseases in RA female patient

Acknowledgements: None

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6388

FRI0161 NON-INVASIVE ASSESSMENT OF MYOCARDIAL PERFUSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

P. Anyfanti [1], N. Koletsos [1], A. Triantafyllou [1], S. Chatzimichailidou [2], G. Triantafyllou [1], P. Panagopoulos [1], E. Gkaliagkousi [1], S. Aslanidis [2], S. Douma [1]. *[1]3rd Department of Internal Medicine, Papageorgiou Hospital; [2]2nd Propedeutic Department of Internal Medicine, Hippokration Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Background: Cardiac involvement among patients with rheumatoid arthritis (RA) is common, potentially life-threatening, but often underdiagnosed at presymptomatic stages. Subendocardial viability ratio (SEVR) reflects microvascular coronary perfusion, as it correlates with the ratio of subepicardial to subendocardial blood flow, that can be non-invasively estimated by applanation tonometry. Although it has been studied as a surrogate measure of myocardial perfusion in high-cardiovascular risk populations, it remains unclear whether it is affected in RA patients.

Objectives: The purpose of the study was to compare SEVR between RA patients and healthy controls. We additionally sought predictors of SEVR in RA among a wide range of disease-related parameters, hemodynamic factors, and markers of atherosclerosis, arteriosclerosis, and endothelial dysfunction.

Methods: Consecutive patients with RA and healthy, nontreated volunteers were recruited. SEVR was estimated from applanation tonometry with the Sphygmocor device (AtCor Medical, Sydney, Australia), which was also used to evaluate arterial stiffness (aortic index, AIx; pulse wave velocity, PWV). In the RA group, carotid atherosclerosis was additionally evaluated by ultrasound (carotid intima-media thickness, cIMT); cardiac and hemodynamic parameters by impedance cardiography, and endothelial dysfunction by measurement of asymmetric dimethylarginine (ADMA) in serum samples.

Results: A total of 122 participants, 91 RA patients and 31 controls, were studied. SEVR was significantly lower among RA patients compared to controls (141.4±21.9 vs 153.1±18.7%, p=0.005), and the same was observed when the subgroup of RA patients without cardiovascular comorbidities (n=29) was studied separately (139.7±21.7 vs 153.1±18.7%, p=0.013). In the univariate analysis, SEVR significantly correlated with cardiac and hemodynamic parameters, but not with PWV, AIx, cIMT, ADMA, or disease-related parameters. In the linear regression analysis accounting for sex, statin use, markers of atherosclerosis, cardiac, and hemodynamic parameters, female gender (p=0.007), blood pressure (p=0.028), heart rate (p=0.025), cholesterol levels (p=0.008), cardiac index ($p<0.001$), and left ventricular ejection time (p=0.004) were identified as independent predictors of SEVR among patients with RA.

Conclusions: Patients with RA exhibit lower values of SEVR compared to healthy individuals, suggesting a disturbed balance between oxygen supply and demand that might provide an additional pathophysiological link for the increased cardiovascular burden in RA. Cardiac and hemodynamic parameters, rather than markers of atherosclerosis, arteriosclerosis, and endothelial dysfunction, may be useful as predictors of impaired myocardial perfusion in RA.

References:

[1] Buckberg GD, et al. Experimental subendocardial ischemia in dogs with normal coronary arteries. Circ Res 1972;30:67–81.

[2] Sarnoff SJ, et al. Hemodynamic determinants of oxygen consumption of the heart with special reference to the tension-time index. Am J Physiol 1958;192:148–56.

[3] Tsiachris D, et al. Subendocardial viability ratio as an index of impaired coronary flow reserve in hypertensives without significant coronary artery stenoses. J Hum Hypertens 2012;26:64–70.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4903

FRI0162 ANTIBODY RESPONSE TO 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IS NOT IMPAIRED IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) OR SJOGRENS SYNDROME WITHOUT DMARD TREATMENT COMPARED TO CONTROLS

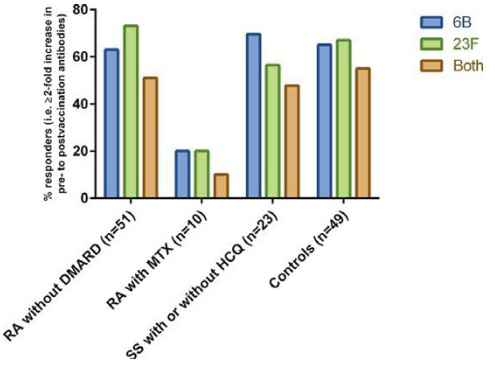
P. Nived [1,2], J. Nagel [1], T. Saxne [1], P. Geborek [1], T. Mandl [3], L. Skattum [4,5], M.C. Kapetanovic [1]. *[1]Department of Clinical Sciences Lund, Section of Rheumatology, Skåne University Hospital, Lund University, Lund; [2]Clinic for Infectious Diseases, KRYH, Kristianstad; [3]Department of Clinical Sciences Malmö, Section of Rheumatology, Skåne University Hospital, Lund University, Malmö; [4]Clinical Immunology and Transfusion Medicine, Region Skåne; [5]Department of Laboratory Medicine, Section of Microbiology, Immunology and Glycobiology, Lund University, Lund, Sweden*

Objectives: To investigate if antibody response and functionality of antibodies following immunization with 13-valent pneumococcal conjugate vaccine (PCV13) is impaired in patients with rheumatoid arthritis (RA) and primary Sjogrens syndrome (pSS) without treatment, with methotrexate (MTX) or hydroxychloroquine (HCQ), compared to healthy controls.

Methods: In total, 61 patients with RA (51 without DMARD and 10 on MTX), 23 patients with pSS (18 without DMARD and 5 on HCQ) and 49 controls were vaccinated with a single dose (0.5 ml) PCV13 intramuscularly. Pre- and postvaccination serotype-specific antibody concentrations for pneumococcal serotypes 6B and 23F and functionality of antibodies (23F) were determined in serum samples taken immediately before and 4–6 weeks after vaccination using ELISA and opsonophagocytic activity (OPA) assay, respectively. Proportions of individuals with positive antibody response (i.e. ≥2-fold increase from prevaccination concentrations) for both serotypes were calculated and groups were compared using Chi2 test. Percentage change (pre- to postvaccination) in OPA was calculated and groups were compared using Mann-Whitney U test.

Results: Pre- to postvaccination antibody concentrations (Table) increased significantly for both serotypes and in both patient and control groups ($p<0.001$). Antibody response to serotypes 6B and 23F was decreased in patients with RA on MTX treatment (both $p<0.01$), but not in RA without DMARD or pSS with or without HCQ, compared to controls (Figure). Proportions of antibody responders to both serotypes did not differ significantly between groups RA without DMARD (51%), pSS (48%) and controls (55%). After vaccination, OPA increased in groups RA without DMARD ($p<0.001$), pSS without DMARD ($p=0.01$) and controls ($p<0.001$), but did not change significantly in patients with RA on MTX and pSS on HCQ. The mean percentage change in OPA was lower in RA on MTX (1.8%, $p=0.01$), RA without DMARD (8.9%, $p<0.01$) and pSS on HCQ (-1.5%, $p=0.01$), but not in pSS without DMARD (11.0%), compared to controls (17.9%).

Figure. Antibody response to vaccination.



Conclusions: Pneumococcal conjugate vaccine is immunogenic in patients with RA and pSS without DMARD treatment. Both antibody response and functionality of antibodies is impaired in patients with RA on MTX.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2146

Abstract FRI0162 – Table 1. Group characteristics and serotype-specific antibody geometric mean levels (GMLs, μg/mL)

	RA without DMARD (n=51)	RA on MTX (n=10)	Sjogrens syndrome without DMARD (n=18)	Sjogrens syndrome on HCQ (n=5)	Controls (n=49)
Age (mean; range) years	65.2 (35–87)	65.3 (39–79)	58.9 (26–90)	61.0 (33–80)	50.6 (17–85)
Sex (% female)	78.4	70.0	88.9	100.0	63.3
GML 6B prevaccination (95% CI)	0.6 (0.4–1.0)	1.3 (0.5–2.9)	0.6 (0.2–1.5)	0.6 (0.2–1.7)	0.8 (0.5–1.3)
GML 6B postvaccination (95% CI)	3.3 (1.8–6.0)	2.1 (0.8–5.6)	2.4 (1.1–5.4)	1.7 (0.2–11.4)	3.1 (1.9–5.0)
GML 23F prevaccination (95% CI)	0.5 (0.3–0.8)	1.0 (0.3–3.5)	0.8 (0.4–1.6)	0.4 (0.2–1.2)	0.6 (0.4–0.9)
GML 23F postvaccination (95% CI)	2.4 (1.5–3.9)	1.7 (0.7–3.9)	3.6 (1.4–9.1)	1.1 (0.2–6.6)	3.3 (2.0–5.5)

FRI0163 INVESTIGATION OF THE PERIODONTAL CONDITION AMONG RHEUMATOID ARTHRITIS (RA) PATIENTS AND ANALYSIS OF INFLAMMATORY MEDIATOR IN THEIR SERUM AND GINGIVAL CREVICULAR FLUID (GCF)

F. Xiao, P. Zhang, X. Li, Y. Mou, H. Chen, Z. Chen. *The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China*

Background: Rheumatoid arthritis (RA) and periodontitis (PD) are common chronic inflammatory diseases with remarkable pathological and clinical similarities.A lot of similarities exist between RA and PD at cellular and molecular levels.
Objectives: To analyse the PD incidence among RA patients, measure the level of tumor necrosis factor-alpha (TNF-α), Interleukin-1β(IL-1β) and Interleukin-6 (IL-6)in their serum and gingival crevicular fluid (GCF), and to investigate their relationship.
Methods: The experimental group was composed of 350 patients with RA and the control group consisted of 426 age and gender matched healthy individuals,check and record periodontal condition by dentist,analyse the PD incidence of the two groups,then select 64 PD patients without systematic diseases and 47 PD patients with a stable condition of RA,Detect and compare their periodontal status and the level s of TNF-α, IL-1β and IL-6 in their serum and GCF.
Results: The percentage of PD was 67.7%,which was statistically significant higher than control group (43.6%) ($P<0.001$). The periodontal disease index (PDI),Probing depth (PD)and Clinical attachment loss (CAL) in patients with PD and RA are all significantly higher than those with simple PD ($P<0.05$). But the bleeding on probing (BOP) in the two groups was not statistically significant ($P>0.05$). Meanwhile, the level of TNF-α, IL-1β and IL-6 in serum and GCF are significantly higher in all PD patients than oral healthy individuals ($P<0.01$).Although those inflammatory mediators in serum are much higher in patients with PD and RA than in those with simple PD ($P<0.01$), there is no difference in the two group about those inflammatory mediators in GCF. The serum level of TNF-α,IL-1β and IL-6 in patients with PD and RA are positively correlated with the corresponding inflammatory mediators in their GCF (r value was 0.531,0.422 and 0.770 respectively,$p<0.01$).
Conclusions: Individuals with RA are more likely to experience periodontitis compares to healthy subjects, and the periodontitis is much more serious in patients with RA and PD than those with simple PD. the serum and GCF inflammatory factors' level increased significantly in patients with RA and PD,even during their RA stable period. The serum level of inflammatory factors in patients with PD and RA are positively correlated with the corresponding inflammatory mediators in their GCF. There is correlation between periodontitis and RA,and they may be the risk factors for eachother, the improvement of the periodontal status in patients with RA and PD may help to control systemic inflammation level and to make comprehensive treatment measure for RA patients.
References:
[1] Venkataraman A, Almas K.Rheumatoid Arthritis and Periodontal Disease. An Update.N Y State Dent J. 2015 Aug-Sep;81(5):30–6.
[2] Araújo VM, Melo IM, Lima V.Relationship between Periodontitis and Rheumatoid Arthritis: Review of the Literature.Mediators Inflamm. 2015;2015:259074. doi: 10.1155/2015/259074. Epub 2015 Aug 4.
[3] Javed F, Ahmed HB, Mikami T, Almas K, Romanos GE, Al-Hezaimi K.Cytokine profile in the gingival crevicular fluid of rheumatoid arthritis patients with chronic periodontitis.J Investig Clin Dent. 2014 Feb;5(1):1–8. doi: 10.1111/jicd.12066. Epub 2013 Dec 20.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5919

FRI0164 DIFFERENCES BETWEEN RA PATIENTS WITH AND WITHOUT ILD FROM A UNITED STATES TERTIARY REFERRAL CENTER

R. Meehan[1], J. Solomon[1], J. Crooks[1], D. Muram[2], E. Hoffman[1], P. Zelarney[1]. [1]*National Jewish Health, Denver;* [2]*Eli Lilly and Company, Indianapolis, United States*

Objectives: To describe the characteristics of RA patients with and without ILD and to determine if medication use constitutes a risk factor for the development of ILD.
Methods: The medical records of RA patients with and without ILD treated at one academic center between 2008 and 2016 were analyzed. Data extracted include: patient demographics, serology, medication use (prednisone, DMARDs, biologics or small molecule drugs), and self-reported disease activity as MDHAQ and RAPID 3 scores. The subtype of ILD was based upon HRCT imaging, and some patients through histology. Differences between RA-ILD patients and RA patients without ILD were determined by Fishers exact test, and t-tests with a $p<0.05$ were considered statistically significant.
Results: The demographics and clinical data of 1,024 RA non-ILD patients and 96 RA-ILD patients indicate ILD patients were older males, had a higher mortality and were less likely to have been never smokers (Table 1). At the onset of ILD diagnosis, 31% were on no medication, 56% on monotherapy (MTX 16%, prednisone 13%, Etanercept 7%, adalimumab or LEF 5%, Rituximab 4%, HCQ 3%, and <1% on infliximab, SSZ or tofacitinib) and 11% received combination therapy. Twenty five percent of the RA-ILD patients developed ILD preceding or coinciding with the diagnosis of RA. After the onset of ILD those patients were more likely to receive prednisone and less likely to receive MTX than those without ILD ($p<0.05$). The predominant types of ILD were as follows: UIP 27%, NSIP 15%, NSIP vs UIP 14%, and unclassifiable 9%.

Table 1

	RA-ILD	RA-without ILD	P values
Total number of patients	96	1,024	
Gender (Male)	48 (50%)	238 (23%)	<0.001
Age >65	57 (59%)	337 (33%)	<0.001
Never smoker	33 (34%)	504 (50%)	<0.001
Fatalities	15 (16%)	38 (4%)	<0.001
BMI (>25)	64 (67%)	671 (66%)	NS
RF+ (>14 units)	67 (74%)	678 (69%)	NS
CCP+ (>20 units)	62 (65%)	617 (61%)	NS
MDHAQ	0.7	0.7	NS
Rapid3	10.6	12.0	NS

Conclusions: RA-ILD patients differed from RA patients without ILD in demographic characteristics, but not in self-reported measures of disease activity or serology. Thirty one percent of RA-ILD patients were not on any immunomodulatory medications at the time of ILD diagnosis, and 25% of RA-ILD patients developed ILD preceding, or coinciding with, the onset of active RA. Our results did not identify a specific drug class or biologic agent as a risk factor for developing ILD in RA patients.
Disclosure of Interest: R. Meehan Grant/research support from: Eli Lilly and Company, J. Solomon: None declared, J. Crooks: None declared, D. Muram Employee of: Eli Lilly and Company, E. Hoffman: None declared, P. Zelarney: None declared
DOI: 10.1136/annrheumdis-2017-eular.4134

FRI0165 SERUM FREE LIGHT CHAINS OF IMMUNOGLOBULINS IN RHEUMATOID ARTHRITIS: CORRELATION WITH INTERSTITIAL LUNG DISEASE

S. Belghali[1], S. Lataoui[1], S. Ferchichi[2], K. Baccouche[1], N. Elamri[1], K. Limam[2], H. Zeglaoui[1], E. Bouajina[1]. [1]*Rheumatology Department;* [2]*Laboratory of Biochemistry, Farhat Hached Hospital, Sousse, Tunisia*

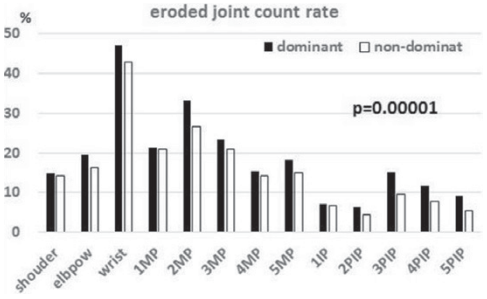
Background: Lungs in Rheumatoid arthritis (RA) seem to play an important role, not only as an extra-articular manifestation but also as a site of initiation of the disease and activation for the immune response. B lymphocytes are thought to be involved in the pathophysiology of RA and interstitial lung disease (ILD). The encouraging results of the use of Anti-CD20 treatments to stabilize articular symptoms and lung involvement reinforce this theory. Serum Free immunoglobulin Light Chains (FLC) might represent, in this context, an interesting marker of B lymphocytes activation during this disease.
Objectives: To determine the serum FLC levels in RA patients with and without ILD and to study their possible association with disease characteristics and activity.
Methods: Fifteen RA patients with clinically symptomatic interstitial lung disease, confirmed by computed tomography (RA-ILD) (53.3% females; mean age 61,27±6,48 years) and age matched RA patients (66.7% females) with no clinically evident interstitial disease (non-ILD) were studied. Clinical and immunological inflammatory characteristics were assessed for all the patients. FLC levels were quantified by turbidimetry (Freelite TM Kappa and Lambda Kits, The Binding Site, UK).
Results: The mean serum FLC-κ levels (RA-ILD: 40,74±16,94 ng/ml *vs* non-ILD 24,88±8,87 ng/ml, p=0,003) and FLC-λ levels (RA-ILD: 37,34±16,56 ng/ml *vs* non-ILD 26,28±7,22 ng/ml, p=0,028) were significantly higher in patients with ILD compared to non-ILD, while the serum FLC-ratioκ/λ (RA-ILD: 1,15±0,38 *vs* non-ILD 1,00±0,43, p=0,304) were comparable.
There was no significant difference for the DAS28 disease activity score between both groups (RA-ILD: 4,6±1,5 vs non-ILD 4,38±1,46, p=0,69). No significant correlations were found between the DAS28-score and FLCκ, FLCλ and FLC-ratioκ/λ ($p>0,05$). FLC-κ levels correlated significantly with ESR and CRP levels ($p<0.001$), FLC-λ levels with CRP (p=0,005) but not with ESR (p=0,247) and FLC-ratioκ/λ did not correlate with both ESR and CRP levels.
Conclusions: High levels of serum FLC are associated with RA-ILD and with a higher degree of inflammation, supporting the role of B cell activation in the pathophysiology of RA with ILD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6364

FRI0166 RADIOGRAPHIC STRUCTURAL DAMAGE IS WORSE IN THE DOMINANT THAN THE NON-DOMINANT UPPER EXTREMITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Nakazaki[1], T. Murayama[1], S. Kato[2]. [1]*Rheumatology, Johoku Hospital;* [2]*Rheumatology, Kamiaraya Clinic, Kanazawa, Japan*

Background: The relationship between mechanical stress and radiographic damage in rheumatoid arthritis (RA) has been detected in patients with hemiplegia[1)] or poliomyelitis[2)]. In patients without neurological disorder, Koh reported that radiographic damage was worse and progressed faster in the dominant hand in

individuals with early RA[3]. However, few studies have detected the radiographic damage in the whole upper extremity on the mechanical stress.
Objectives: To examine the relationship between mechanical stress and radiographic damage in RA, we evaluated the joint destruction of the dominant and non-dominant upper extremity.
Methods: The joint destruction of the upper extremity (shoulder, elbow, wrist, metacarpo-phalangeal, interphalangeal, proximal interphalangeal) in 295 patients with RA, who were from 25 years to 91 years (mean age 64 years, mean disease duration 183 months, 86% females and 97% right-handed), was assessed according to the eroded joint, which was defined as ≥2 by Larsen scores for radiographic damage. These were divided into the dominant and non-dominant upper extremity. The Wilcoxon signed-rank test was used to examine the difference between the eroded joint count (EJC) in the dominant and the non-dominant upper extremity.
Results: The mean EJC in the dominant and the non-dominant upper extremity was 2.4 and 2.05 respectively. The EJC was significantly more in the dominant than the non-dominant upper extremity. And, in regards to every joint of upper extremity, the eroded joint rate was higher in the dominant than the non-dominant



Conclusions: The eroded joint count of the upper extremity was significantly more in the dominant than the non-dominant one, therefore it was suggested that the mechanical stress influenced the radiographic damage in patients with RA
References:
[1] John H Bland, et al.: Hemiplegia and rheumatoid hemiarthritis. Arthritis Rheum (11) 1: 72–80, 1968.
[2] E N Glick, et al.: Asymmetrical rheumatoid arthritis after poliomyelitis. Br Med J 3: 26–28, 1967.
[3] Jung Hee Koh, et al.: Radiographic structural damage is worse in the dominant than the non-dominant hand in individuals with early rheumatoid arthritis. PLOS ONE, doi: 10. 1371/journal. Phone.0135409 August 6, 2015.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3621

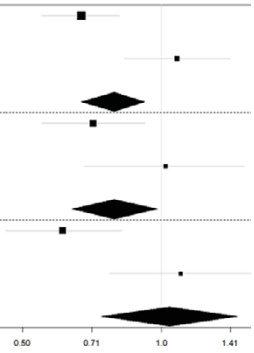
FRI0167 COMPARATIVE CARDIOVASCULAR SAFETY OF ABATACEPT AND TUMOR NECROSIS FACTOR INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT CARDIOVASCULAR DISEASE: A POPULATION-BASED COHORT STUDY

Y. Jin[1], E.H. Kang[1,2], G. Brill[1], R.J. Desai[1], S.C. Kim[1,3]. *[1]Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Harvard Medical School, Boston, United States; [2]Division of Rheumatology Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea, Republic Of; [3]Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, United States*

Background: Rheumatoid arthritis (RA) patients have an increased risk of cardiovascular disease (CVD). Recent studies suggested that treatment of RA with tumor necrosis inhibitors (TNFi) can reduce the risk of cardiovascular events. However, it is unclear how abatacept, a selective costimulation modulator, affects cardiovascular risk among RA patients compared with TNFi.
Objectives: To evaluate the comparative cardiovascular safety of abatacept versus TNFi in RA patients with and without underlying CVD.
Methods: We identified RA patients aged ≥18 with ≥2 RA ICD-9 codes (714.xx) separated by ≥7 days but <365 days, from two large insurance claims data across the U.S.: Medicare (2008–2013) and Truven MarketScan (2006–2015). Only new users of abatacept or TNFi (adalimumab, etanercept, certolizumab, golimumab, and infliximab) were included. The primary outcome of interest was a composite endpoint of CVD including myocardial infarction (MI), stroke/transient ischemic stroke, or coronary revascularization. Secondary outcomes were each component of the primary outcome, incident heart failure (HF), and venous thromboembolism (VTE). 1:1 propensity score (PS) matching was performed separately in each database and each subgroups (with or without baseline CVD). Then the PS-matched subgroups were aggregated to form the overall matched cohort. Cox regression model was used to estimate the hazard ratio (HR) and 95% confidence interval (CI) of risk of each outcome. Estimates from two different databases were combined through an inverse variance-weighted fixed-effects model.
Results: After 1:1 PS matching, there were 6,102 patient pairs from Medicare and 6,934 pairs from MarketScan. Among them, patients with baseline CVD were 35.3% in Medicare and 14.0% in MarketScan. Baseline characteristics were well balanced between two treatment groups after matching (standardized mean difference <0.1). In Medicare cohort, abatacept consistently showed a decreased risk of composite CVD compared with TNFi in overall and each subgroup (Figure). However, in MarketScan cohort, where the population was younger than Medicare cohort, there was no association between abatacept and CVD compared to TNFi. After combining the two databases, abatacept was significantly associated with reduced risk of composite CVD outcome vs. TNFi in overall cohort (HR =0.79, 95% CI=0.67–0.92) and baseline CVD subgroup (HR =0.79, 95% CI=0.64–0.98). We also observed similar trend for secondary outcomes, where abatacept had decreased risk than TNFi.

Figure. Risk of composite CVD outcome in Abatacept initiators versus TNF inhibitors: PS-matched analysis

Subgroup	Database	Exposure	Total N	Number of event	IR per 100 person-years	HR (95% CI)
	Medicare	Abatacept	6102	185	2.38	0.67 (0.55, 0.81)
		TNFi	6102	248	3.58	Ref
Overall	MarketScan	Abatacept	6934	114	1.38	1.08 (0.83, 1.41)
		TNFi	6934	113	1.27	Ref
	Pooled					**0.79 (0.67, 0.92)**
	Medicare	Abatacept	2156	107	4.18	0.71 (0.55, 0.92)
With		TNFi	2156	134	5.92	Ref
baseline	MarketScan	Abatacept	968	49	4.6	1.02 (0.68, 1.51)
CVD		TNFi	968	49	4.35	Ref
	Pooled					**0.79 (0.64, 0.98)**
	Medicare	Abatacept	3946	78	1.5	0.61 (0.46, 0.82)
Without		TNFi	3946	114	2.44	Ref
baseline	MarketScan	Abatacept	5966	65	0.91	1.10 (0.77, 1.57)
CVD		TNFi	5966	64	0.82	Ref
	Pooled					**1.04 (0.74, 1.46)**



Conclusions: In this large multi-database population-based study of RA patients, abatacept treatment was associated with reduced risk of CVD compared to TNFi, especially among older population and patients with prior CVD conditions.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2727

FRI0168 RESTORATION OF DECREASED LYMPHOCYTES, CD8+T CELL SUBSETS WITH TH1 SKEWED PHENOTYPE ASSOCIATE WITH SPONTANEOUS REGRESSION OF LYMPHO-PROLIFERATIVE DISORDERS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH METHOTREXATE

S. Saito[1], K. Suzuki[1], K. Yamaoka[1], K. Amano[2], M. Tokuhira[3], T. Takeuchi[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo; [2]Division of Rheumatology, Saitama Medical Center, Saitama Medical University; [3]Division of Hematology, Saitama Medical Center, Saitama Medical University, Saitama, Japan*

Background: Lympho-proliferative disorder (LPD) is known as a relatively rare but life-threatening complication in RA patients under MTX administration. Spontaneous regression of LPD after MTX withdrawal is regarded as a distinct character of LPD under MTX administration. Previous study from our institution [1] and others [2] reported the link between decreased lymphocyte counts at LPD diagnosis and restoration after MTX cessation and the regression of LPD.
Objectives: To investigate the immunological factors including lymphocyte subsets which involved in spontaneous regression of LPD following MTX withdrawal.
Methods: We studied 35 RA patients complicated with LPD under MTX administration in our institution. Age, sex, RA disease duration matched control MTX-treated patients (N=35) were selected. LPD patients were divided into two groups regarding to the status of LPD after MTX cessation; regressive group (N=22) and persistent group (N=13). Clinical features were compared among 3 groups. Flowcytometric analysis of the whole blood sample and measurement of cytokine concentration in ELISA were conducted in a part of the LPD patients (N=10, 7 regressive, and 3 persistent LPD) and controls (N=10). The time of MTX cessation, which was simultaneous with LPD diagnosis, was defined as week 0, and blood sample was collected at week 0, 4 and 12.
Results: At week 0, number of peripheral lymphocytes was significantly decreased in regressive group, compared to persistent group and control group. Flowcytometric analysis revealed significant decrease in proportion of effector memory CD8+ T cells (EMCD8+T), Epstein Barr Virus specific CD8+ T cells (EBV specific CD8+) and T helper 1 cells (Th1 cells) subset in regressive group compared to control group. Following MTX cessation, significant increase in proportion and absolute number of these subsets were observed only in the regressive group, but not in persistent group. Expansion of Th1 cells and EMCD8+ T cells significantly correlated with increase of serum IFN-γ, and expansion of EMCD8+ T cells inversely correlated with change of serum IL-15.
Conclusions: Restoration in proportion and absolute number of Th1 cells, EMCD8+T cells and EBV specific CD8+ T cells coincided with increase of IFN-γ, and associated with regression of LPD developed under MTX administration. Since changes of those immunological factors were not observed in persistent LPD, this study would be the first report to demonstrate the difference of

immune status between regressive and persistent LPDs developed under MTX administration.

References:
[1] Saito S, et al. Rheumatology. 2017; in press.
[2] Inui Y, et al. Leuk Lymphoma. 2015; 56(11):3045–3051.

Acknowledgements: None.

Disclosure of Interest: S. Saito: None declared, K. Suzuki: None declared, K. Yamaoka Speakers bureau: Pfizer, Chugai Pharma, Mitsubishi-Tanabe Pharma, Takeda Industrial Pharma, GlaxoSmithKline, Nippon Shinyaku, Eli Lilly, Janssen Pharma, Eisai Pharma, Astellas Pharma and Actelion Pharmaceuticals, K. Amano: None declared, M. Tokuhira Speakers bureau: Eisai Co., T. Takeuchi Grant/research support from: Astellas Pharma, Bristol–Myers K.K., Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Eisai Co.,Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co.,Ltd., Teijin Pharma Ltd., AbbVie GK, 2,Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K.,

DOI: 10.1136/annrheumdis-2017-eular.4662

FRI0169 GLOMERULAR FILTRATION RATE IS LOW IN RHEUMATOID ARTHRITIS COMPARED TO HEALTHY POPULATION: ESSENTIAL ROLE OF INFLAMMATION

S. Hannawi[1], I. AlSalmi[2]. [1]*Rheumatology, Ministry of Health and Prevention of UAE, Dubai, United Arab Emirates;* [2]*Nephrology, Royal Hospital, Muscat, Oman*

Background: Rheumatoid Arthritis is associated with subclinical renal impairment which contributes to increase mortality and morbidity. The role of inflammation on kidney function in inflammatory arthritis is not well studied.

Objectives: To investigate the associations between estimated glomerular filtration rates (eGFR), traditional cardiovascular risk factors, and markers of inflammation in rheumatoid arthritis compared to healthy controls.

Methods: RA patient were recruited through a specialized rheumatology clinic at the Ministry of Health and Prevention of UAE, from January 2013 to January 2016. Healthy subjects recruited from the community through brochure advertisement. The Modification of Diet in Renal Disease Study (MDRD) formula was used to calculate the eGFR. ttest was used to compare the laboratory values and renal function parameters between two groups. Linear regression analysis used to look for the correlation between the eGFR and each of the traditional cardiovascular risk factors and inflammatory markers

Results: 98 RA patients and 82 controls were recruited. None of the patients has history of diabetes, atherosclerosis or renal impairment. The mean age for the total participants was 49±13 years (Min16 –Max 82). The mean eGFR of the inflammatory arthritis patients was 118±30 ml/min (range 60–227) and 128±37 ml/min (range 62–286) for the controls. Patients and control had no significant difference in Systolic and diastolic blood pressure.

Inflammatory arthritis patients had lower GFR, albumin ($P<0.001$), and total protein (p=0.03) levels, and had higher Erythrocyte Sedimentation Rate (ESR) ($P<0.001$), C-reactive protein (CRP) ($P<0.001$), and uric acid level (p=0.01),

Negative linear relationships were found as follows:

Among RA patients and controls: There was a negative linear relationship between GFR and each of the age of the participants; ($p<0.001$, CI: -1.24, -0.40 for the patients and p=0.01, CI: -1.82, -0.26 for the controls), and the systolic blood pressure; (p=0.04, CI: -0.61 for the patients and, -.00 and p=0.022, CI: -0.61, -0.05 for the controls).

Among RA patiens: The GFR had a negative linear relationship with the age of the participants, age at RA onset (p=0.002, CI: -1.18, -0.29), diastolic blood pressure (p=-2.14, CI: -1.24, -0.05), ESR level (p=0.04, CI: -0.24,-0.01), C-reactive protein; CRP level (p=0.02, CI: -0.47, -0.04), uric acid level ($p<0.001$, CI -0.18, -0.05), and total protein (p=0.01, CI: -0.91, -0.16). There was a positive linear relationship between eGFR and albumin level (p=0.03, p=0.14, 2.35),

Conclusions: In RA non-traditional cardiovascular risk factors such as inflammatory markers are associated with sub-clinical presence of renal injury. Our data indicate that in RA, inflammation is involved in the early stages of impaired kidney function. Whether anti-inflammatory therapies are effective in slowing down the deterioration of kidney function in the arthritis diseases remain to be established.

References:
[1] Puttevils, D., et al., Increased cardiovascular risk in patients with rheumatoid arthritis: an overview. Acta Cardiol, 2014. 69(2): p. 111–118.
[2] Nordin, H. and L.M. Pedersen, Kidney function problems in rheumatoid arthritis. Ugeskr Laeger, 1996 158(22): p. 3137–40.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1658

FRI0170 CARDIOVASCULAR RISK FACTORS AND DISEASE CHARACTERISTICS ARE CONSISTENTLY ASSOCIATED WITH ARTERIAL STIFFNESS IN RHEUMATOID ARTHRITIS

S. Gunter[1], C. Robinson[1], G. Norton[1], A. Woodiwiss[1], L. Tsang[1], A. Millen[1], P. Dessein[1,2]. [1]*Cardiovascular Pathophysiology and Genomics Research Unit, University of Witwatersrand, Johannesburg, South Africa;* [2]*Rheumatology Division, Universitair Hospital Brussels, Brussels, Belgium*

Background: In the non-rheumatoid arthritis (RA) population, arterial stiffness contributes to cardiovascular disease risk beyond brachial blood pressure and other established cardiovascular risk factors. The increased cardiovascular disease risk in RA is now well documented. In this regard, how RA impacts on arterial stiffness remains uncertain.

Objectives: The aim of the present study was to identify potential determinants of comprehensively assessed arterial stiffness in a relatively large group of ethnically diverse patients with RA.

Methods: Relationships of traditional cardiovascular risk factors and RA characteristics with 9 arterial stiffness markers including central systolic and pulse pressure, pulse wave velocity, augmentation index, forward and reflected wave pressure, reflection magnitude, brachial-to-aortic pulse pressure amplification (a marker of reduced wave reflection) and peripheral pulse pressure were identified in multivariable backward regression models among 177 (118 white, 32 Asian, 22 black, 5 mixed ancestry) patients without established cardiovascular disease.

Results: Recorded characteristics explained 37% (pulse wave velocity) to 71% (reflected wave pressure) of the variability in arterial stiffness. RA duration (partial r=0.17, p=0.04), rheumatoid factor status (partial r=-0.19 to 0.20, p=0.01 to 0.03), leukocyte counts (partial r=0.16 to 0.19, p=0.02 to 0.05) and total cholesterol (-0.18 to 0.26, p=0.00 to 0.03) were associated with enhanced central systolic blood pressure or/and wave reflection markers. C-reactive protein (partial r=-0.24, -0.17 and -0.20, respectively, $p\leq0.05$) was paradoxically related to reduced central pulse pressure, pulse wave velocity and forward wave pressure, and body mass index (partial r=-0.39 to 0.42, p=0.00 to 0.02) and insulin resistance (partial r=-0.21 to -0.20, p=0.00 to 0.01) to reduced wave reflection and peripheral pulse pressure. Exercise (partial r=0.19, p=0.02) and alcohol (partial r=-0.27, p=0.00) consumption were associated with increased pulse pressure amplification and decreased peripheral pulse pressure, respectively. Tumour necrosis factor-α inhibition (partial r=-0.25, p=0.00) was related to reduced pulse wave velocity and tetracycline use (partial r=-0.20, p=0.02) to reduced peripheral pulse pressure.

Conclusions: Traditional cardiovascular risk factors and disease characteristics are consistently associated with vascular hemodynamic alterations in RA. The role of arterial stiffness in cardiovascular disease risk in RA needs further study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4277

FRI0171 OBESITY CONTRIBUTES TO SUBOPTIMAL PHYSICAL FUNCTION IN RHEUMATOID ARTHRITIS

A. Sirois[1], N. Chiarlitti[1], M. Inceer[1], M. Jones[2], C.O. Bingham III[2], S.J. Bartlett[1]. [1]*McGill University, Montreal, Canada;* [2]*Johns Hopkins, Baltimore, United States*

Background: Aggressive, early treatment of RA with new therapeutic agents has dramatically improved the management of RA. However, many studies have failed to show greater improvements in function or disability reduction between targeted control vs. less-aggressive care. The prevalence of obesity is increasing dramatically globally, and may be even higher in RA patients.[1]

Objectives: Because obesity is also a risk factor for disability, we evaluated the extent to which excess weight may independently contribute to poorer physical function (PF) in RA.

Methods: RA patients enrolled in an observational study at an academic Inflammatory Arthritis Clinic in Baltimore USA completed the patient global, pain VAS, and PROMIS measures assessing PF, pain, fatigue, sleep, and depression. RA clinical indicators were also collected at the visit. Outcomes were compared in obese and non-obese patients using t-tests and chi-square. Multiple regression was used to evaluate the effects of pain, fatigue, and BMI on PF, after controlling for age and disease activity.

Results: Participants were mostly female (82%) and white (83%) with mean (SD) age of 55 (13) years; 24% had $\leq$ high school; RA duration 12 (9). Mean CDAI was 8.1 (8.1). Most were in CDAI remission (n=57; 32%) or LDA (n=64; 36%); 40 (23%) were in MDA and 16 (9%) in HDA. 49 (28%) were classified as normal weight (BMI 18.5–24.9), 46 (26%) were overweight (BMI 25–29.9), and 82 (46%) were obese (BMI$\geq$30). Men had a significantly higher mean BMI than women (33.6 [8.4] vs. 29.5 [7.2], p=0.006).

As compared to non-obese participants, obese participants had a significantly ($p<.05$) higher CDAI (6.1 [6.9] vs. 10.4 [8.9]; p=.000, respectively) and worse PF, pain, fatigue, sleep, and depression (mean differences -5.0, -4.6, 4.6, 3.8, 2.9, 3.6, and -4.7, respectively). In regression analyses, pain, fatigue, and BMI (but not sleep or depression) were inversely related to PF, after controlling for age and disease activity. In the final model, pain, fatigue and BMI were significantly and inversely related to PF (β=-.39, -.24, and -.153, respectively) after controlling for age and disease activity ($F(5, 170) = 55.5$, p=.000, adjusted r^2=.61).

Table. Independent Contributors of Function in RA.

	Coefficient		Std		Collinearity	
	B	SE	Beta	Sig.	Tol	VIF
Pain	-.386	.064	-.405	.000	.500	2.001
Fatigue	-.240	.060	-.266	.000	.509	1.965
BMI	-.153	.058	-.128	.010	.932	1.073
Adjusted for age and CDAI.						

Conclusions: Our results suggest that excess weight also contributes to poorer PF in addition to pain and fatigue. As the prevalence of obesity continues to

escalate in RA populations, weight loss may be increasingly important to improve not only physical health, disease activity, and response to treatment, but also pain, fatigue, and PF.

References:
[1] Colmegna et al. High rates of obesity and greater associated disability among people with rheumatoid arthritis in Canada. Clin Rheumatol 2016;35(2):457–60.

Acknowledgements: Funding: PCORI IP2-PI0000737 and SC14–1402–10818, CIHR 312205.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5600

FRI0172 PREVALENCE AND FEATURES OF THE "MASKED" ARTERIAL HYPERTENSION IN WOMEN WITH RHEUMATOID ARTHRITIS WITHOUT CARDIOVASCULAR DISEASES BASED TO AMBULATORY BLOOD PRESSURE MONITORING

T.A. Romanova, N.M. Nikitina, A.P. Rebrov. *Hospital Therapy Department, State Medical University of Saratov, Saratov, Russian Federation*

Background: Cardiovascular (CV) events are the main reason of increased mortality at patients with rheumatoid arthritis (RA). Arterial hypertension (AH) takes a leading position among CV risk factors in RA. Ambulatory blood pressure monitoring (ABPM) has to be executed for persons with high cardiovascular risk and can be used for evaluation of "masked" arterial hypertension (MAH), according to the current recommendations.
Objectives: to estimate the frequency of identification and peculiarities of the MAH according to ambulatory blood pressure monitoring in women with RA without CV diseases.
Methods: The study included 36 women with RA (ACR 1987 and/or EULAR/ACR 2010 criteria) without CV diseases and AH (according to the anamnesis and 3-fold "office" blood pressure (BP) measurement). Mean age of RA patients was 55±7.15 years; mean duration of RA was 10 [3; 17] years, mean DAS 28 – 5.25 [4.6; 5.7]. As controls were involved 39 women with RA and AH (mean age- 58.3±6.08 years; mean duration of RA - 8 [4;14] years, mean DAS 28- 5.08 [4.04; 5.85]) and 30 women with AH without inflammatory joint diseases (mean age 55.9±6.2). Exclusion criteria were smoking, diabetes mellitus, symptomatic AH (except controls), cardiovascular diseases.
ABPM was measured using the BPlab with the program VASOTENSE (Russian). Criteria for MAH were out-of-office BP $\geq$135/85 mmHg and/or average daily out-of-office BP $\geq$130/80 mmHg according to ABPM and considering optimal office BP.
The anamnesis, laboratory and instrumental methods of inspection were considered. Statistical analyze was performed with STATISTICA 7.0 (State Soft, USA).
Results: According to ABPM 24 of the 36 (66.6%) RA patients had optimal BP, 12 (33.3%) patients had the MAH phenomenon.
The patients with RA + AH and AH patients had the comparable levels of a daily BP [132.1/80.7 and 126.9/78.0 mmHg respectively, $p>0.05$].
The RA patients with MAH had statistically significant differences of BP in day and night hours [137.58/87 mmHg and 137/84 mmHg, respectively] compared to the RA + AH patients [132.1/80.7 mmHg and 128.3/73.8 mmHg, respectively, p=0.004] and AH patients [126.9/78 and 118/68.5 mmHg, respectively, p=0.001], what it is can be bound to absence of anti-hypertensive therapy at RA patients with MAH.
Nocturnal systolic BP correlated with ESR (Spearmen's r=0.64, $p<0.05$). Daily diastolic BP interrelated with SCORE/EULAR (r=0.86, $p<0.05$) and arterial stiffness index (r=0.86, $p<0.05$) in RA patients with MAH; nocturnal systolic BP correlated with C-reactive protein (r=0.36, $p<0.05$) in RA+AH patients.
More than 60% of the RA+AH patients and RA+MAH had high variability of BP. High variability of nocturnal systolic BP occurred at 34.3% and 44.4% of RA+AH and RA+MAH patients, respectively.
In RA patients were found correlations between indices of a BP variability, duration of RA (r=0.33, $p<0.05$); C-reactive protein (r=0.36, $p<0.05$); daily diastolic BP (r=0.35, $p<0.05$); pulse BP (r=0.31, $p<0.05$); and frequency of non-steroidal anti-inflammatory drugs intake (r=0.42, $p<0.05$).
Conclusions: In RA patients AH can proceed subclinically. Activity of RA and increased arterial stiffness can predict the masked arterial hypertension's development in RA patients.
ABPM measurement can be use full in early evaluation of AH and optimization of RA treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5707

FRI0173 CORRELATION BETWEEN ASSYMETRIC DIMETHYLARGININE AND HOMOCYSTEINE LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

T. Dimitroulas[1,2], J. Hodson[3], A. Sandoo[4], K. Douglas[1], J. Smith[1], G. Kitas[5]. *[1]Department of Rheumatology, Dudley Group of Hospitals NHS Trust, Russells Hall Hospital, Dudley, United Kingdom; [2]4th Department of Internal Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]Wolfson Computer Laboratory, University Hospital Birmingham NHS Foundation Trust, Queen Elizabeth Hospital Birmingham, Mindelsohn Way, Birmingham; [4]School of Sport, Health and Exercise Sciences, Bangor University, George Building, Bangor; [5]Arthritis Research UK Epidemiology Unit, University of Manchester, Manchester, United Kingdom*

Background: Rheumatoid Arthritis is a chronic inflammatory condition associated with increased cardiovascular disease (CVD) morbidity and mortality due to high coronary and cerebral atherosclerotic burden. Assymetric dimethylarginine (ADMA) – the most potent endogenous inhibitor of nitric oxide synthase - is an emerging marker of endothelial dysfunction and CVD in several conditions such as coronary artery disease and diabetes mellitus. ADMA levels are higher in RA patients compared to controls suggesting a role in the development of atherosclerosis. In addition ADMA is involved in the metabolism of honocysteine (Hcy) which is considered a novel, non-traditional CVD risk factor contributing to excess CVD risk in this population.
Objectives: The aim of our study was to determine whether asymmetric dimethylarginine (ADMA) levels are associated with Hcy and methylenetetrahydrofolate reductase (MTHFR) C677T (rs1801133) gene variants in patients with RA.
Methods: Serum ADMA and Hcy levels were measured in 201 RA individuals [155 (77.1%) females, median age 67 years (interquartile range 59–73)]. The MTHFR C677T polymorphism was assessed by using the LightCyclerTM System. Initially, ADMA was compared across the categories of MTHFR using a one-way analysis of variance (ANOVA), followed by a multivariate model, which accounted for Hcy, age, erythrocyte sedimentation rate (ESR), and homeostatic model assessment (HOMA).
Results: In univariable analysis, ADMA differed significantly across the categories of MTHFR (p=0.037). Patients with the MTHFR 677TT genotype had the highest ADMA levels, with a mean of 0.62 (SE =0.03), significantly higher than either those patients carrying the MTHFR 677CT (0.55, SE =0.01) or the MTHFR 677CC (0.55, SE=0.01) genotype (p=0.042) in both cases. In the multivariable model, Hcy (p=0.022) and ESR ($p<0.001$) were found to have significant positive associations with ADMA but the relationship between MTHFR gene variants and ADMA was found to be non-significant (p=0.102).
Conclusions: The results of our study indicate an association between ADMA and Hcy in patients with RA without any genetic background as no relationship was established between ADMA and MTHFR gene variants. Abnormal metabolism of Hcy and dimethylarginines may interfere with each other resulting in endothelial dysfunction and accelerated atherosclerosis in RA individuals.

References:
[1] Dimitroulas T, Sandoo A, Hodson J, Smith J, Douglas K, Kitas G. MTHFR C677T Polymorphism but not DDAH gene variants are associated with Assymetric Dimethylarginine (ADMA) in RA. Ann Rhem Dis 2014;72(Suppl 2):333.
[2] Perna M, Roman MJ, Alpert DR, Crow MK, Lockshin MD, Sammaritano L, et al. Relationship of asymmetric dimethylarginine and homocysteine to vascular aging in systemic lupus erythematosus patients. Arthritis Rheum 2010;62:1718–22.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2512

FRI0174 A POPULATION BASED COHORT STUDY OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: COMORBIDITY AND MORTALITY

C. Hyldgaard[1], O. Hilberg[2], A.B. Pedersen[3], S.P. Ulrichsen[3], A. Løkke[1], E. Bendstrup[1], T. Ellingsen[4]. *[1]Department of Respiratory Diseases, Aarhus University Hospital, Aarhus C; [2]Department of Medicine, Vejle Hospital, Vejle; [3]Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus; [4]Department of Rheumatology, Odense University Hospital, Odense, Denmark*

Background: Interstitial lung disease (ILD) is an important reason for excess mortality among patients with rheumatoid arthritis.
Objectives: The aim of this study was to compare mortality risks in patients with rheumatoid arthritis-associated interstitial lung disease (RA-ILD) and patients with RA without ILD.
Methods: The study was conducted in Denmark, using nationwide, prospectively collected data from the national medical registries. Among patients with RA, diagnosed between 2004 and 2016, 679 patients with RA-ILD were matched for age, gender, and age at RA diagnosis with 11,722 patients with RA but without ILD. Mortality risks were assessed using Kaplan-Meier survival curves, and hazard rate ratios (HRR) for death were estimated using Cox proportional hazards regression models.
Results: The number of prevalent RA patients more than doubled from 15,352 to 35,362 individuals during the study period. RA-ILD was seen in 2.2% of incident RA patients. 34.0% of RA-ILD cases were diagnosed within one year prior to and one year after the RA diagnosis. One-year mortality was 13.9% in RA-ILD and 3.8% in non-ILD RA, three-year mortality was 28.0% and 10.9%, and five-year mortality was 39.0% and 18.2%, respectively. The HRRs for death were two to 10 times increased for RA-ILD compared with non-ILD RA, irrespective of follow-up period. Stratified analysis showed that the HRR for death was highest in the first months after the diagnosis of RA-ILD was made, especially in patients diagnosed with RA before diagnosis of ILD. HRR was higher in males and in patients without comorbidity as assessed by the Charlson Comorbidity Index.

Conclusions: ILD is a serious complication in RA with a significantly increased mortality compared with a large matched cohort of RA comparisons without ILD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2848

FRI0175 USING SMARTPHONES TO IMPROVE REMOTE MONITORING OF RHEUMATOID ARTHRITIS: COMPLETENESS OF PATIENTS' SYMPTOM REPORTS

S. Van Der Veer[1], L. Austin[1,2], C. Sanders[2], W. Dixon[1]. [1]*Arthritis UK Centre for Epidemiology, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, University of Manchester;* [2]*Centre for Primary Care, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom*

Background: Clinical decisions about management of rheumatoid arthritis (RA) happen at intermittent clinic visits. In the absence of objective measures of disease severity between visits, understanding fluctuating disease severity largely relies on patients' symptom reports, and thus on patients' recall, eloquence, stoicism and willingness to discuss symptoms.
The Remote Monitoring of Rheumatoid Arthritis (REMORA) study aims to improve monitoring of disease severity in RA. Patients, clinicians and researchers co-designed a smartphone app to enable RA patients to report daily symptoms in between clinic visits with data integrated into the electronic health record. The data presented here were collected as part of the REMORA feasibility evaluation.
Objectives: To evaluate the completeness of patient-reported symptom data submitted through the REMORA smartphone app over three months.
Methods: We invited 23 RA patients treated at the outpatient clinic of Salford Royal Foundation Trust (UK) to record their symptoms for three months using the REMORA smartphone app. Participants received notifications to record: daily scores for the seven items of the RA Impact of Disease score, as well as morning stiffness on a scale from 0 to 10; weekly scores for thirteen items on 28 tender and swollen joint self-assessments, global assessment, impact on work and activity, and flare occurrence; and monthly scores for the Health Assessment Questionnaire (HAQ) 20-item disability scale. We calculated the time that participants were in the study as the number of days between the first and last day of submitting daily scores. We then explored patterns of data entry, as well as entry completeness.
Results: Twenty patients accepted the invitation to participate. Eight (40%) were male, all but one were white British, and their mean age was 56.9±11.1 years. The median number of days in the study was 82 (interquartile range [IQR], 80 to 82). While being in the study, participants submitted daily scores on almost all days (median, 91% of days; IQR, 78 to 95), with four doing this on <60% of study days. Across participants, almost all of 1325 daily entries were complete, with only nine (<1%) having missing values for up to two individual items. Participants submitted weekly scores for a medium of 11 out of 13 weeks (IQR, 10 to 12). Of all 213 weekly entries, fifteen (7%) had missing values, but never more than two. Lastly, 8/20 participants provided monthly HAQ scores only once, while a further 9/20 and 3/20 participants did this for two and all three months, respectively. No monthly entries had any missing values.
Conclusions: Our feasibility study showed that smartphones have the potential to support collection of daily patient reports of symptoms with high levels of completeness over three months. Lengthier monthly question sets were less likely to be completed compared to briefer daily and weekly ones. Future steps include exploring methods for adapting data entry frequency to (fluctuations in) disease severity in order to support sustained symptom reports over longer time periods and in a wider group of patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4243

FRI0176 CORRELATION BETWEEN DISEASE ACTIVITY AND MENTAL HEALTH IN CHINESE PATIENTS WITH RHEUMATOID ARTHRITIS -ASSESSMENT WITH SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILES TOOLS

X. Li[1], H. Sun[2], R. Wu[3], H. Wei[4], W. Fan[5], C. Zhao[6], Z. Zhang[7], Z. Wu[8], Y. Wang[9], J. Huang[10], F. Xiao[11], H. Xiao[11], Y. Jia[11], M. Zhang[12]. [1]*Dept. of Rheumatology, Anhui Medical University Affiliated Provincial Hospital, Hefei;* [2]*Dept. of Rheumatology, Shandong Provincial Hospital, Jinan;* [3]*The First Affiliated Hospital of Nanchang University, Nanchang;* [4]*Dept. of Rheumatology, Northern Jiangsu People's Hospital, Yangzhou;* [5]*Dept. of Rheumatology, Central Hospital of XinXiang, XinXiang;* [6]*Dept. of Rheumatology and Immunology, The First Affiliated Hospital of Guangxi Medical University, Nanning;* [7]*Linyi people's Hospital, Linyi;* [8]*Dept. of Rheumatology and Immunology, The First Affiliated Hospital of The Fourth Military Medical University, Xi'an;* [9]*Dept. of Rheumatology and Immunology, The First Affiliated Hospital of BaoTou Medical College, Baotou;* [10]*Dept. of Rheumatology and Immunology, The sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou;* [11]*Medical Dept., Shanghai Gothic Internet Technology Co., Ltd., Shanghai;* [12]*Dept. of Rheumatology and Immunology, Jiangsu Province Hospital, Nanjing, China*

Background: Rheumatoid arthritis (RA) patients can cause joint swelling and tenderness, and affect the patient's mental health. Previous studies showed that 13–47% of RA patients suffered from anxiety and/or depression. Hospital anxiety and depression scale (HADS) is usually used to evaluate patients' mental health, which consists of 14 items divided into an anxiety subscale (HADS-A) and a depression subscale (HADS-D). Disease activity score in 28 joints (DAS28) is one of the most used tool to assess RA patients' disease activity. Both HADS and DAS28 assessments were commonly led by health professionals with paper questionaire. This study applies the mobile platform of Smart System of Disease Management (SSDM) for evaluating DAS28 and HADS by RA patients.
Objectives: The purpose of this study is to describe the morbidity of mental comorbidity in Chinese patients with RA and analyze the potential association among DAS28 and HADS.
Methods: SSDM is a mobile application includes physicians' and patients' interfaces. The patient's terminal system includes self-assessment (DAS28, HADS), lab test results and medication management. After data entry, patients can synchronize data to the mobile terminal of their authorized rheumatologist. A cohort study was conducted with patients who were diagnosed with RA in tertiary hospital across China. All participants self-assessed both DAS28 and HADS with SSDM at least one time. Descriptive statistics were performed for patient and disease characteristics, assuming normality for DAS28 distribution and the level of disease activity was analyzed using Pearson's statistics. One-way analysis of variance was employed to explore for difference between sub-groups. Bivariate correlation and linear logistic analysis were employed to explore for potential correlation between DAS28 and HADS.
Results: From June 2016 to January 2017, 230 patients (male 66, female 164) from 12 hospitals performed 311 times HADS and 517 times DAS28 self-assessment. The mean (±SD) age was 34.17±13.11 (11–71) years, with the median disease duration of 24.70 (0–572) months. As the standard of HADS score higher than 10, 31% and 37% patients could be diagnosed as anxiety and depression respectively. According to the DAS28 assessment results, the proportion of patients with remission, low disease activity, moderate activity and high activity were 18%, 19%, 46% and 18% respectively. Bivariate correlation showed that DAS28 was positively correlated with HADS, $p<0.001$. Both HADS-A and HADS-D showed linear regression association with DAS28 score, the regression equation as "HADS-A = 5.962 + 0.435*DAS28" and "HADS-D = 6.379 + 0.694*DAS28" respectively, $p<0.001$.
Conclusions: DAS28 was positively correlated with HADS. SSDM is an effective mobile interface to serve for RA patients performing self-management of both disease activity and mental health as well as to supply physicians with valuable data.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4032

FRI0177 THE UNDERRATED PREVALENCE OF DEPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

R. Sruamsiri[1], Y. Kaneko[2], J. Mahlich[1]. [1]*Health Economics, Janssen Pharmaceutical KK, Tokyo, Japan;* [2]*Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan*

Background: Significant evidence in the scholarly literature suggests that depression is a common comorbidity among patients with rheumatoid arthritis (RA) (1) Comorbid depression in RA patients is especially troublesome because it often goes unrecognized and untreated (2) often because rheumatologists and their patients seldom communicate about depression (3). In addition, evidence of depression in RA patients is limited in Asia studies.
Objectives: To determine the prevalence of depression among patients with RA and explore the relationships between depression and an array of variables.
Methods: Cross-sectional online survey (n=500) of RA patients including the Patient Health Questionnaire [PHQ-9] (4) to measure the presence and severity of depressive symptoms were performed. The survey contained patient demographic, clinical characteristics such as functional impairment as assessed using the Japanese version of the Stanford Health Assessment Questionnaire (J-HAQ score), and the participant's current medical treatment. Ordered logistic regression was used to identify the determinants of depression conditions among survey respondents.
Results: The mean age of the 500 patients with RA was 54.3 years old and 67% were female. While only 25 (5%) of the population studied had been officially diagnosed with depression, 176 (35%) had PHQ-9 scores indicating depression was present. Comorbidity conditions, except for migraine and heart conditions, were not different between patients with depression and those without. Logistic regression analysis revealed a negative correlation between the prevalence of depression and younger age with odds ratio (OR) of 0.96 (95% confidence interval (CI); 0.93–0.98), higher education (OR, 0.60; 95% CI, 0.36–0.98 for a bachelor's degree or higher) and an income level of 0.8–1.6 million yen (OR, 0.45; 95% CI, 0.22–0.91). Positive correlations with depression was found in RA patients with high J-HAQ score (OR, 1.99; 95% CI, 1.47–2.71). Patients treated with biologic monotherapy were significantly less likely to have depression compared to those treated with non-biologic anti-rheumatic drugs (OR, 0.36; 95% CI, 0.17–0.75)
Conclusions: It is a potential risk of under-diagnosis and under-reporting of Depression in patients with RARA patients are more likely to experience depression if they are younger, have greater functional impairment, or whose treatment regimen includes pain medications without biologic drugs.

References:
[1] Dickens C et al. (2002). Psychosom Med. 64(1), 52–60.
[2] Nagyova I et al. (2005) Patient Educ Couns. 58(1), 55–62.
[3] Sleath B et al. (2008) Arthritis Rheum. 59(2), 186–91.
[4] Suzuki K et al. (2015) PLoS One. 10(3), e0119147.
Acknowledgements: None.
Disclosure of Interest: R. Sruamsiri Employee of: Janssen Pharmaceutical KK, Y. Kaneko Paid instructor for: YK has received lecture fees from AbbVie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Pfizer, Janssen, and UCB., J. Mahlich Employee of: Janssen Pharmaceutical KK
DOI: 10.1136/annrheumdis-2017-eular.4542

FRIDAY, 16 JUNE 2017

Rheumatoid arthritis - anti-TNF therapy

FRI0178 RITUXIMAB IS EFFECTIVE IN THE TREATMENT OF RHEUMATOID ARTHRITIS REGARDLESS OF BODY MASS INDEX

D.H. Yoo[1], W. Park[2], C.H. Suh[3], S.C. Shim[4], S.J. Lee[5], Y.J. Bae[5], C. Park[5], J.H. Koo[5]. *[1]Hanyang University Hospital for Rheumatic Diseases, Seoul; [2]IN-HA University, School of Medicine, Incheon; [3]Ajou University School of Medicine, Suwon; [4]Chungnam National University Hospital, Daejeon; [5]Celltrion Inc., Incheon, Korea, Republic Of*

Background: High body mass index (BMI) is known to be associated with inadequate clinical response to anti-TNF agents in rheumatoid arthritis (RA) patients.[1] However, there are limited data on the effect of high BMI on the response to rituximab in RA patients, who showed an inadequate response or intolerance to anti-TNF agents.
Objectives: To investigate the impact of BMI on clinical response in the post-hoc analysis of randomized controlled trial that demonstrated clinical equivalence between a biosimilar of rituximab, CT-P10 and innovator rituximab, RTX[2] (NCT02149121).
Methods: A total of 332 patients who received two courses of either CT-P10 or RTX were included in this analysis. Patients were classified into 3 groups; normal weight (<25kg/m^2), overweight (≥25 kg/m^2 ~<30 kg/m^2) and obesity (≥30 kg/m^2) as per WHO BMI category. Improvement in disease activity by the Disease Activity Score using C-reactive protein (DAS28-CRP), remission (≤2.6), low disease activity rate (LDA, ≤3.2) and ACR response at Week 24 (Week 24 of 1st course) and Week 48 (Week 24 of 2nd course) and duration of sustained LDA (from the first LDA observed to the last LDA observed up to Week 48) were analysed by BMI categories in the each and combined group of CT-P10 and RTX.
Results: In the pooled group of CT-P10 and RTX, the mean weights were 59 kg in normal weight, 73kg in overweight and 91kg in obesity. All other baseline characteristics were comparable among BMI groups including baseline disease activity based on DAS28; Moderate disease activity, 22.3% vs. 22.8% vs. 25.7%, respectively; High disease activity, 77.7% vs. 77.2% vs. 74.3%, respectively. There was no statistical difference among BMI groups in terms of DAS28 change from baseline and ACR 20/50/70 response (Table). No particular trend was observed in remission and LDA rate by DAS28 at Week 24 and Week 48 among BMI groups (Figure). Mean duration of sustained LDA (months) were also comparable among the groups (4.5 vs. 4.7 vs. 5.0, respectively). Additionally, similar trends in all analyses were observed in each treatment group; CT-P10 and RTX.
Conclusions: The BMI does not affect the clinical response in RA patients with rituximab treatment. Therefore, this result supports that rituximab could be a reasonable therapeutic option for obese RA patients with inadequate response to anti-TNF agents.

Table 1. DAS28, ACR responses by BMI subgroups

Parameter	Visit	Normal (N=148)	Over weight (N=114)	Obesity (N=70)
DAS28, mean (SD)	Baseline	5.88 (0.95)	5.81 (0.89)	5.69 (0.78)
	Week 24*	-2.43 (1.12)	-2.13 (1.19)	-2.39 (0.99)
	Week 48*	-2.76 (1.31)	-2.47 (1.32)	-2.74 (1.01)
ACR20, n (%)	Week 24	122 (82.4%)	86 (75.4%)	56 (80.0%)
	Week 48	119 (80.4%)	88 (77.2%)	60 (85.7%)
ACR50, n (%)	Week 24	80 (54.1%)	56 (49.1%)	39 (55.7%)
	Week 48	76 (51.4%)	62 (54.4%)	43 (61.4%)
ACR70, n (%)	Week 24	51 (34.5%)	33 (28.9%)	21 (30.0%)
	Week 48	47 (31.8%)	36 (31.6%)	26 (37.1%)

*Change from baseline.

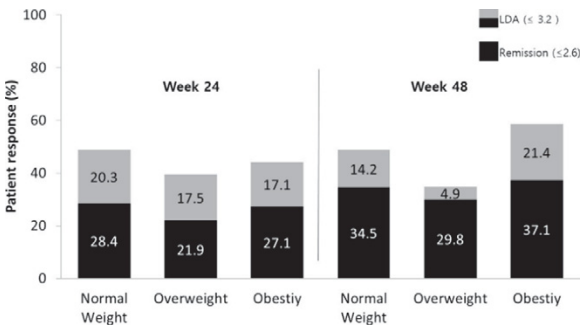


Figure 1. Remission and LDA by DAS28 by BMI group.

Disclosure of Interest: D. H. Yoo Consultant for: Celltrion Inc., W. Park Consultant for: Celltrion Inc., C. H. Suh Consultant for: Celltrion Inc., S. C. Shim Consultant for: Celltrion Inc., S. J. Lee Employee of: Celltrion Inc., Y. J. Bae Employee of: Celltrion Inc., C. Park Employee of: Celltrion Inc., J. H. Koo Employee of: Celltrion Inc.
DOI: 10.1136/annrheumdis-2017-eular.5591

FRI0179 MINIMAL TO NO TRANSFER OF CERTOLIZUMAB PEGOL INTO BREAST MILK: RESULTS FROM CRADLE, A PROSPECTIVE, POSTMARKETING, MULTICENTER, PHARMACOKINETIC STUDY

M.E.B. Clowse[1], F. Förger[2], C. Hwang[3], J. Thorp[4], R.J.E.M. Dolhain[5], A. van Tubergen[6], L. Shaughnessy[7], J. Simpson[7], M. Teil[8], N. Toublanc[9], M. Wang[7], T.W. Hale[10]. *[1]Duke University Medical Center, Durham, United States; [2]Inselspital, University of Bern, Bern, Switzerland; [3]Keck Hospital of USC, Los Angeles; [4]University of North Carolina at Chapel Hill, Chapel Hill, United States; [5]University Medical Centre Rotterdam, Rotterdam; [6]Maastricht University Medical Center, Maastricht, Netherlands; [7]UCB Pharma, Raleigh, United States; [8]UCB Pharma, Slough, United Kingdom; [9]UCB Pharma, Brussels, Belgium; [10]Texas Tech University School of Medicine, Amarillo, United States*

Background: Women with active chronic rheumatic inflammatory conditions (RA, PsA, AxSpA) often face uncertainty regarding the safety of the use of biologics during breastfeeding.[1] Limited and non-validated data exist on the potential transfer of anti-TNFs into breast milk.[2] CRADLE (NCT02154425) was the first sponsored study to evaluate certolizumab pegol (CZP) concentrations in breast milk, and to estimate the Average Daily Infant Dose (ADID) of maternal CZP.
Objectives: To determine the concentration of CZP in breast milk and calculate the ADID of maternal CZP.
Methods: CRADLE was a pharmacokinetic study of lactating mothers (≥6 weeks postpartum) receiving commercial CZP. Decision to treat with CZP and breastfeed was independent of study participation. At steady state (≥3 CZP doses), breast milk samples were collected on Days 0, 2, 4, 6, 8, 10, 12, 14 (±28) from each mother across 1 dosing period. CZP was detected using a highly sensitive, CZP-specific electrochemiluminescence immunoassay validated in milk (lower limit of quantification [LLOQ]=0.032 μg/mL; 10-fold lower than previous assays). CZP stability in milk was confirmed.
Results: 18 CZP-treated mothers were screened: 17 entered the sampling period; 16 on CZP 200 mg Q2W; 1 on CZP 400 mg Q4W (7 RA; 5 SpA; 5 CD; Table A). Samples from 4/17 mothers had no measurable CZP in breast milk; 13/17 had quantifiable levels for at least 1 time point (highest concentration: 0.076 μg/mL; Table B). Estimated ADID ranged 0–0.0104 mg/kg/day; median Relative Infant Dose (RID; calculated post hoc[3]): 0.15%. Infants of CZP-exposed mothers had a

Table A: Baseline characteristics of mothers and infants

Mean (SD), unless otherwise stated	All mothers (N=18) [a]
Age, years	33.7 (4.2)
Weight, kg	68.9 (9.6)
BMI, kg/m²	23.6 (3.0)
Indication for CZP treatment, n [b]	
Rheumatoid arthritis	7
Psoriatic arthritis	3
Axial spondyloarthritis/ankylosing spondylitis	2
Crohn's disease	5
Infant age at mother's first sample, n (%)	**All infants (N=17)**
≤6 months	13 (76.5)
>6 months–≤12 months	2 (11.8)
>12 months–≤18 months	2 (11.8)

[a] Includes 1 screen failure; [b] n=17.

Table B: Concentrations of CZP (μg/mL) in breast milk

Mother no.	Relative time (days) 0	2	4	6	8	10	12	14	28
5	0.056	0.069	0.074	0.076	0.076	0.069	0.069	0.06	–
1	0.057	0.051	0.066	0.065	0.062	0.056	0.052	0.041	–
9	0.039	0.04	0.047	0.045	0.042	0.043	0.038	0.035	–
3	BLQ	0.032	0.049	0.053	0.037	0.037	0.033	0.033	–
16	0.04	0.033	0.036	0.037	0.043	BLQ	BLQ	BLQ	–
11	BLQ	BLQ	0.051	0.038	0.042	BLQ	0.033	BLQ	–
2	BLQ	BLQ	0.035	0.037	0.041	BLQ	0.043	BLQ	–
15	BLQ	BLQ	0.041	0.034	0.033	BLQ	0.037	BLQ	–
10	BLQ	BLQ	BLQ	0.033	0.042	0.042	BLQ	BLQ	–
8	BLQ	BLQ	0.035	0.034	0.043	BLQ	BLQ	BLQ	–
12	BLQ	BLQ	0.034	0.037	0.033	BLQ	BLQ	BLQ	–
6	BLQ	BLQ	0.044	0.048	BLQ	BLQ	BLQ	BLQ	–
7	BLQ	BLQ	BLQ	BLQ	BLQ	0.035	BLQ	BLQ	–
4	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	–
13	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	–
14	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	–
17	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ

Less than 3×LLOQ (<0.096 μg/mL)
Less than 2×LLOQ (<0.064 μg/mL)
BLQ (<0.032 μg/mL)
CZP plasma C_{trough} from the RAPID2 study: 15.7 μg/mL

BLQ: below the lower limit of quantification; LLOQ: lower limit of quantification.

safety profile consisting of events occurring in unexposed infants of similar age.
Conclusions: CZP was below the lower limit of quantification in 56% of the milk samples. When detectable, CZP concentrations were less than 3x LLOQ (<1% of expected plasma concentration of a therapeutic dose[4]), indicating no to minimal transfer of CZP from plasma to breast milk. RID was below 0.5% of maternal dose; <10% is unlikely to be of clinical concern.[3] CZP absorption via breast milk is unlikely, due to low bioavailability and its Fc-free molecular structure. These findings support continuation of CZP treatment during breastfeeding.
References:
[1] Gõtestam Skorpen C. Ann Rheum Dis 2016;75:795–810.
[2] Ben-Horin S. J Crohns Colitis 2011;5:555–8.
[3] Hale TW. Textbook of Human Lactation. Amarillo, TX: Hale Publishing, 2007.
[4] Lacroix BD. Gastroenterology 2010;138:S163–4.
Acknowledgements: This study was funded by UCB Pharma. We are indebted to the mothers and their infants for their altruistic participation. We thank the nurses, investigator teams and Nicole Hurst, PPD, and acknowledge Amanda Golembesky and Gerry Parker, UCB Pharma. Editorial services were provided by Costello Medical Consulting.
Disclosure of Interest: M. Clowse Grant/research support from: Pfizer, Janssen, Consultant for: UCB Pharma, F. Förger Grant/research support from: UCB Pharma, Speakers bureau: Mepha, Roche, UCB Pharma, C. Hwang Grant/research support from: AbbVie, UCB Pharma, Consultant for: Janssen, J. Thorp Grant/research support from: UCB Pharma, Consultant for: Genentech/Roche, UCB Pharma, R. Dolhain Grant/research support from: UCB Pharma, A. van Tubergen Grant/research support from: Pfizer, AbbVie, UCB Pharma, Janssen-Cilag, Celgene, Novartis, MSD, Consultant for: AbbVie, Novartis, Janssen-Cilag, Pfizer, Speakers bureau: MSD, Janssen-Cilag, Pfizer, L. Shaughnessy Employee of: UCB Pharma, J. Simpson Employee of: UCB Pharma, M. Teil Employee of: UCB Pharma, N. Toublanc Employee of: UCB Pharma, M. Wang Employee of: UCB Pharma, T. Hale Consultant for: UCB Pharma
DOI: 10.1136/annrheumdis-2017-eular.2467

FRI0180 MULTIPLE SCLEROSIS RISK-ALLELES STUDY IN PATIENTS WITH DEMYELINATING SIDE EFFECTS ON ANTI TNF ALPHA THERAPY

S. Bitoun[1], C. Verstuyft[2], C. Miceli-Richard[1], J.-M. Berthelot[3], C. Richez[4], C. Cauquil[5], C. Sordet[6], S. Melac-Ducamp[7], L. Gossec[8], B. Beatrice[9], E. Dernis[10], E. Houvenagel[11], M.-A. Boutry-Bacle[12], X. Mariette[1], R. Seror[1]. *[1]Université Paris-Sud, Hôpitaux Universitaires Paris-Sud, INSERM U1184, le Kremlin Bicètre; [2]Department of Pharmacogenetics, Hôpitaux Universitaires Paris-Sud, le Kremlin Bicêtre; [3]C.H.U. Hôtel Dieu, Nantes; [4]C.H.U Pellegrin, Bordeau; [5]Hôpitaux Universitaires Paris-Sud, le Kremlin Bicètre; [6]Hôpitaux Universitaires Strasbourg, Strasbourg; [7]C.H.I, Nevers; [8]Pitie-Salpétrière Hospital, Paris; [9]CHU, Angers; [10]Centre Hospitalier du Mans, le Mans; [11]Hôpital Saint Philibert, Lomme; [12]C.H., Abbeville, France*

Background: Tumor Necrosis Factor alpha (TNFα) is a key cytokine in inflammatory rheumatic diseases. TNF inhibitors (TNFi) has revolutionized treatment of rheumatic diseases, but may cause flares of multiple sclerosis (MS). Two Single Nucleotide Polymorphisms, (SNPs) *rs1800693* and *rs4149584*, located within *TNF receptor superfamilly 1* (*TNFRSF1A*) locus have been shown to increase the risk of developing MS [1]. The rs1800693*G allele leads to a dysfunctional TNFα soluble receptor that inhibits TNFα signaling while *rs4149584* is involved in TNF receptor associated periodic syndrome.
Objectives: The aim of this study was to look for a possible the association between *TNFRSF1A* polymorphisms and demyelinating complications occurring during TNFi therapy.
Methods: Patients who presented with a demyelinating disorder (central or peripheral involvement) while treated with TNFi (cases), were recruited between March 2013 and December 2015, through the physicians involved in the CRI ("Club Rhumatismes et Inflammation") a nationwide network of the French Society of Rheumatology. Rheumatoid arthritis patients treated with TNFi, from the French ReAct cohort, and who did not develop demyelinating complication constituted the control population (n=294). The frequency of *rs1800693* and *rs4149584* TNFRSF1A SNPs were compared between cases and controls.
Results: Twenty-four cases with demyelinating disorders, recruited from 11 centers with a median age of 39.7 years (range 30.4–75.8); of which 16 (67%) were females were included in the study. Neurological symptoms occurred after a median of 18.3 (1–66) months of anti TNFi; 15 (62.5%) had central neurologic involvement and 9 (37.5%) had peripheral involvement. The median follow-up was 26 (4–54) Months. No significant difference in the frequency of the *rs1800693* MS risk-alleles (39,5% for cases vs 38,6% for controls) was observed. Similarly no difference was observed between cases (2%) and controls (4%) for *rs4149584.*
Conclusions: This study was unable to show an association between MS-associated SNPs within *TNFRSF1A* locus and the occurrence of demyelination while taking TNFi, suggesting that demyelination might be linked to other genetic factors or other pathways.
References:
[1] De Jager PL, Jia X, Wang J, et al. Meta-analysis of genome scans and replication identify CD6, IRF8 and TNFRSF1A as new multiple sclerosis susceptibility loci. Nat Genet 2009;41:776–82. doi:10.1038/ng.401.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4710

FRI0181 TAPERING OR CESSATION OF ANTIVIRAL AGENT IN HEPATITIS B VIRUS-INFECTED PATIENTS CONCOMITANTLY TREATED WITH BIOLOGIC AGENTS

B. Ghang[1], D.-H. Lim[2], W.J. Seo[3], Y.-G. Kim[1], B. Yoo[1]. *[1]Rheumatology, Asan Medical Center, Seoul; [2]Rheumatology, Ulsan University Hospital, Ulsan; [3]Rheumatology, Seoul Veterans Hospital, Seoul, Korea, Republic Of*

Background: Clinicians generally prescribe antiviral agents to patients with chronic hepatitis B (CHB) or to inactive carriers of the virus until 6–12 months after the cessation of biologic agents. However, the current antiviral prophylaxis regimen, in addition to biological therapy, is expensive and poses an economic burden to both patients and societies. We have had patients in our medical center quit or reduce antiviral prophylaxis due to economic reasons.
Objectives: To assess the outcome of tapering or discontinuation of antiviral agents in patients who were infected with hepatitis B virus (HBV) during biologic therapy.
Methods: We identified 45 patients who were infected with HBV and treated with biologic agents concomitantly from January 2005 to December 2016. They were diagnosed with rheumatoid arthritis (n=20), Crohn's disease (n=13), ankylosing spondylitis (n=8), ulcerative colitis (n=3), and psoriatic arthritis (n=1). The criteria of HBV reactivation was a 10-fold rise in HBV DNA compared with previous HBV DNA titers, resulting in HBV DNA of greater than 20,000 IU/ml (HBeAg-positive patients) or 2,000 IU/ml (HBeAg-negative patients), and an increase in AST or ALT to more than twice the upper normal limit (40 IU/l).
Results: Sixteen CHB patients and 29 inactive carriers were treated with biologic agent for 4.1±2.7 years. No reactivation case was observed in 23 patients (10 of CHB and 13 of inactive carrier) who maintained antiviral prophylaxis for 4.0±2.3 years. Among them, 4 patients (3 treated with infliximab and 1 with adalimumab) taking antiviral prophylaxis regimen on alternate days did not experience HBV reactivation for 28–42 months of follow-up period. In the discontinuation group (n=9), no reactivation case was observed in all inactive carrier patients (2 treated with etanercept, 1 with infliximab, and 1 with rituximab) after discontinuation of antiviral prophylaxis for 6–33 months of follow-up period. In contrast, 3 patients (2 treated with etanercept and 1 with adalimumab) among the 5 patients with CHB experienced reactivation after discontinuation of antiviral prophylaxis for 3–29 months of follow-up period.
Conclusions: During biologic therapy, HBV reactivations were frequently found in CHB patients who ceased to take antiviral prophylaxis. However, no reactivation after the cessation of prophylaxis was found in inactive carrier patients who were previously treated with prophylaxis. Based on our experience, tapering or discontinuation of antiviral agent in inactive carriers with economic problem undergoing concomitant biologic agent therapy could be considered viable, albeit with caution.
References:
[1] Perez-Alvarez R, Diaz-Lagares C, Garcia-Hernandez F, Lopez-Roses L, Brito-Zeron P, Perez-de-Lis M, et al. Hepatitis B virus (HBV) reactivation in patients receiving tumor necrosis factor (TNF)-targeted therapy: analysis of 257 cases. Medicine (Baltimore). 2011;90(6):359–71.2.
[2] Mori S, Fujiyama S. Hepatitis B virus reactivation associated with antirheumatic therapy: Risk and prophylaxis recommendations. World J Gastroenterol. 2015;21(36):10274–89.
[3] Ryu HH, Lee EY, Shin K, Choi IA, Lee YJ, Yoo B, et al. Hepatitis B virus reactivation in rheumatoid arthritis and ankylosing spondylitis patients treated with anti-TNFalpha agents: a retrospective analysis of 49 cases. Clin Rheumatol. 2012;31(6):931–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3186

FRI0182 DISEASE WORSENING AND SAFETY IN PATIENTS SWITCHING FROM ORIGINATOR INFLIXIMAB TO BIOSIMILAR INFLIXIMAB (CT-P13) IN THE NOR-SWITCH STUDY: EXPLORATIVE ANALYSIS OF RA PATIENTS

G.L. Goll[1], I.C. Olsen[1], N. Bolstad[2], K.K. Jørgensen[3], M. Lorentzen[4], C. Mørk[5], J. Jahnsen[3], E.A. Haavardsholm[1], T.K. Kvien[1] on behalf of The NOR-SWITCH study group. *[1]Dept of Rheumatology, Diakonhjemmet Hospital; [2]Biochemistry DNR, Oslo University Hospital, Oslo; [3]Gastroenterology, Akershus University Hospital, Lørenskog; [4]Dermatology, Oslo University Hospital, Oslo; [5]Dermatology, St Olav University Hospital, Trondheim, Norway*

Background: The NOR-SWITCH study was a 52-week randomized, double-blind, non-inferiority, phase IV switch trial in patients with Crohn's disease (CD), ulcerative colitis (UC), spondyloarthritis (SpA), rheumatoid arthritis (RA), psoriatic arthritis (PsA) and plaque psoriasis (Ps) on stable treatment with originator infliximab (Remicade®, INX) and was funded by the Norwegian government. Previously, the primary analyses of the pooled indications have been published[1].
Objectives: To investigate efficacy, safety and immunogenicity in RA patients treated with continous INX vs patients switched to CT-P13 (biosimilar infliximab, Remsima®) in the NOR-SWITCH study (explorative analyses).
Methods: Patients were randomized 1:1 to continued INX or switch to CT-P13. Serum drug levels were analysed in automated in-house assay. The primary

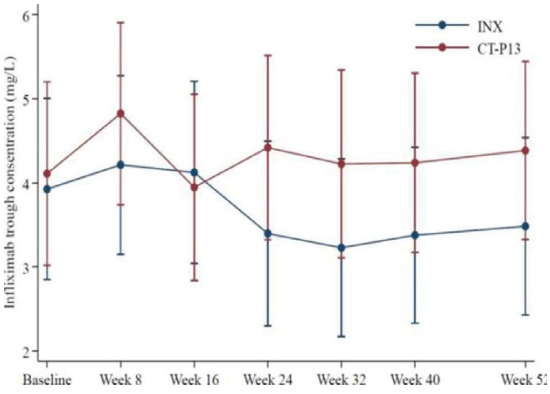
Abstract FRI0182 – Table 1. Demographic and baseline characteristics (FAS), percentage of RA patients with disease worsening and change in disease measures during 52 weeks follow-up (PPS)

Demographics and baseline characteristics	INX	CT-P13	
Total number of RA patients PPS/FAS	30/39	30/38	
Age (years) mean (SD)	59.9 (11.5)	60.4 (11.4)	
Females	31 (79%)	25 (66%)	
Duration of ongoing infliximab treatment (years) mean (SD)	8.2 (3.7)	9.9 (3.4)	
Concomitant immunosuppressive medication	27 (69%)	34 (89%)	
ACPA pos	25 (83%)	20 (74%)	
Disease worsening			95% CI of group difference after 52 weeks
All study patients	53 (26.2%)	61 (29.6%)	-12.7–3.9%
RA	11 (36.7%)	9 (30.0%)	-20.3–29.3%
Change in disease measures from baseline			
Physician Global Assessment of Disease Activity (0–10)	-0.1 (1.3)	0.1 (1.4)	-0.58–0.68
Patient Global Assessment of Disease Activity (0–10)	1.1 (1.4)	0.4 (1.9)	0.21–1.91
Log_{10} erythrocyte sedimentation rate (mm/h)	0.0 (0.3)	0.0 (0.3)	-0.08–0.16
Log_{10} C-reactive protein (mg/L)	0.1 (0.3)	0.0 (0.5)	-0.11–0.22
DAS28	0.2 (0.9)	0.2 (0.9)	-0.30–0.50
TEAE (FAS)	94	62	

Data are n (%), mean (SD) or median (25–75 percentiles). 95% CI, 95% confidence interval of the adjusted treatment difference. DAS28, Disease Activity Score in 28 joints. FAS, Full Analysis Set. PPS, Per Protocol Set. TEAE, treatment emergent adverse events.

endpoint was disease worsening according to disease-specific composite measures and/or consensus between investigator/patient leading to major treatment change. Exploratory subgroup analyses examined disease worsening and safety in RA. The primary endpoint was analysed using logistic regression, adjusted for diagnosis and disease duration.

Results: Demographics, occurence of disease worsening, change in disease measures and treatment-emergent adverse events (TEAE) were similar (Table). Serum drug levels for INX and CT-P13 were similar throughout the study (Figure)



Conclusions: Explorative analyses in the NOR-SWITCH study showed similar efficacy, serum drug levels and safety in RA patients switched to CT-P13 as those on continuous INX. The study was not powered to show non-inferiority within each diagnosis.

References:

[1] Jørgensen KK et al Switching from originator infliximab to biosimimlar CT-P13 compared to maintained treatment with originator infliximab (NOR-SWITCH): a 52-week randomized double-blind non-inferiority trial. The Lancet, in press.

Disclosure of Interest: G. Goll Consultant for: Orion Pharma, Pfizer, Novartis, Boeringer Ingelheim, AbbVie, I. Olsen: None declared, N. Bolstad: None declared, K. Jørgensen Consultant for: Intercept, Celltrion, Tillot, M. Lorentzen: None declared, C. Mørk Consultant for: Cellgene, AbbVie, Novartis, LeoPharma, ACOhud, Galdena Nordic, J. Jahnsen Consultant for: OrionPharma, Celltrion, Pfizer, MSD, AbbVie, Takeda, NappPharma, AstroPharma, E. Haavardsholm Consultant for: AbbVie, UCB, Roche, MSD, Pfizer, T. Kvien Consultant for: Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lily, Epirus, Hospira, Merck-serono, Novartis, Orion Pharma, Pfizer, Sandoz, UCB

DOI: 10.1136/annrheumdis-2017-eular.2319

FRI0183 ASSESSING ADHERENCE OF RA PATIENTS TREATED WITH ETANERCEPT USING ETANERCEPT SERUM TROUGH CONCENTRATIONS AND PATIENT SELF-REPORT

E. Vogelzang[1], R. Hebing[2], M. Nurmohamed[1], M. L'Ami[1], C. Krieckaert[1], G. Wolbink[1,3]. *[1]Rheumatology; [2]Rheumatology, Pharmacy, Amsterdam Rheumatology and immunology Center | Reade; [3]Immunopathology, Sanquin Research and Landsteiner Laboratory, Amsterdam, Netherlands*

Background: The EULAR recommendations for the management of rheumatoid arthritis (RA) update 2013 contained the following research question: "How good is patient adherence to biological agents and can lack of adherence be related to loss of efficacy?" [1]. Limited studies are published in which adherence of RA patients treated with biological disease-modifying anti rheumatic drugs (bDMARDs) has been assessed. Previous studies regarding adherence of RA patients treated with etanercept did not take into account that patients are instructed to temporarily discontinue bDMARDs therapy during e.g. a serious infection. In addition, etanercept concentrations have never been utilized in determining adherence to etanercept in RA patients.

Objectives: The aim of our study was to determine the percentage of non-adherent RA patients treated with etanercept, using etanercept concentrations and patient self-report, and to assess the relationship between adherence and clinical outcome during 52 weeks.

Methods: Non-adherence was defined as an etanercept trough concentration <0.1ug/mL at least once and no valid/medical reason to miss an etanercept dose. In this retrospective cohort study patients visited our clinic at baseline and 4, 16, 28, 40 and 52 weeks after initiation of etanercept treatment. At baseline and following visits disease activity score of 28 joints (DAS28) was calculated and blood was drawn to measure etanercept concentrations. During each visit patients were asked if they missed an etanercept dose, at which date and for which reason. Remission was defined as DAS28 <2.6 at least for two consecutive visits. Low disease activity (LDA) was defined as DAS28 <3.2 during a minimal of two consecutive visits.

Results: In total 292 patients were included. Mean age was 53 years (SD 12.7), 82% was women and median disease duration was 8 years (IQR 3–16). In total 24 patients had an etanercept concentration <0.1ug/mL. Most patients had a medical reason to miss an etanercept dose, see table 1.

Table 1. Reasons for patients to miss an etanercept dose

Reason	Number of patients
Medical	10
Did not start	3
Logistical problem	1
Stopped due to inefficacy	1
Unknown	9

Only ten patients (3.4%) were non-adherent during the follow-up of 52 weeks. Of the adherent patients 82 out of 282 (29%) reached LDA versus 1 out of 10 non-adherent patients. A total of 127 of 282 (45%) adherent patients achieved MDA versus 3 out of 10 non-adherent patients.

Conclusions: Most patients had a medical reason to miss an etanercept dose. The percentage of patients who are non-adherent to etanercept therapy is very low (3.4%).

References:

[1] Smolen JS, Landewe R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis 2014;73:492–509.

Disclosure of Interest: E. Vogelzang: None declared, R. Hebing: None declared, M. Nurmohamed Speakers bureau: Abbvie, Bristol-Myers Squibb, Merck Sharp & Dohme, Celgene, Pfizer, Roche, Janssen, UCB and Sanofi, M. l'Ami: None declared, C. Krieckaert Speakers bureau: Pfizer and Abbvie, G. Wolbink Grant/research support from: Pfizer, Speakers bureau: Pfizer, UCB and Abbvie

DOI: 10.1136/annrheumdis-2017-eular.1652

FRI0184 THE PROFILES OF PATIENTS WITH RHEUMATOID ARTHRITIS ACCORDING TO THEIR BELIEFS IN THEIR BIOLOGICAL DRUGS. ARCO STUDY

E. Raya[1], I. Monteagudo[2], J. Calvo-Alén[3], G. Salvador[4], T. Vázquez-Rodriguez[5], J. Tovar[6], T. Salman-Monte[7], V. Torrente-Segarra[8], P. Vela[9], C. Díaz-Miguel[10], E. Giner[11], L. Cea-Calvo[12], N. Lozano-Rivas[13], C. Marras[13]. *[1]HU San Cecilio, Granada; [2]HGU Gregorio Marañon, Madrid; [3]HU Araba, Vitoria; [4]HU Mútua Terrassa, Barcelona; [5]HU Lucus Augusti, Lugo; [6]HGU, Elche; [7]H del Mar, Barcelona; [8]H Moisès Broggi-General, Barcelona; [9]HGU, Alicante; [10]HU Ramón y Cajal, Madrid; [11]H Obispo Polanco, Teruel; [12]Medical Affairs, Merck Sharp & Dohme, Madrid; [13]HCUV Arrixaca, Murcia, Spain*

Objectives: To describe profiles of rheumatoid arthritis (RA) patients according to their beliefs in their subcutaneous biological medication (SC).

Abstract FRI0184 – Table 1

		Accepting (n=116)	Ambivalent (n=182)	Indifferent (n=16)	Skeptical (n=7)	p
Mean age (SD)		55.5 (12.6)	54.2 (12.5)	58.8 (13.2)	53.6 (10.2)	0.459
		%	%	%	%	
Sex	Men	19.0	23.1	43.8	43.9	0.090
	Women	81.0	76.9	56.2	57.1	
RA duration	> median	51.8	50.3	43.8	28.6	0.651
	≤ median	48.2	49.7	56.2	71.4	
Satisfaction						
Symptoms control	Very/quite satisfied	93.1	82.9	68.8	85.7	0.009
	Indifferent, quite/very unsatisfied	6.9	17.1	31.2	14.3	
Tolerance/side effects	Very/quite satisfied	79.7	57.0	50.0	57.1	<0.001
	Indifferent, quite/very unsatisfied	20.3	43.0	50.0	42.9	
Expectations						
Effect of the drug on symptoms	Much/quite greater than expected	69.6	53.3	75.0	57.1	0.031
	+/– As expected	23.5	39.0	12.5	28.6	
	Quite/lower than expected	7.0	7.7	12.5	14.3	
Side effects/discomfort	Much/quite greater than expected	7.0	17.0	12.5	0.0	0.004
	+/– As expected	27.0	39.6	25.0	57.1	
	Quite/lower than expected, or no side effects/discomfort	66.0	43.4	62.5	42.9	

Methods: ARCO was a study carried out on RA Spanish patients who initiated a SC biological drug 11–18 months prior to the study visit. Patients completed the Beliefs About Medication Questionnaire (BMQ). According to the scores obtained in the necessity (N) and concerns (C) sub-scales, patients were classified into 4 groups: accepting (high N [>3]/low C [≤3]), ambivalent (N>3/C>3), indifferent (N≤3/C≤3) and skeptical (low N [≤3]/high C [>3]). We studied demographic characteristics, expectations and satisfaction with the treatment by group.
Results: 321 patients (77% women) completed the BMQ, 92.8% scored N>3 and 58.9% C>3. A higher % of men than women scored N≤3 (13.5% vs. 5.2%, p=0.031). The % who scored C>3 was higher in those with low satisfaction with symptom control (71.1% vs. 56.7% in satisfied/very satisfied, p=0.098), or side effects (72.1% vs. 52.0%, p<0.001), and in those with lower fulfillment of expectations of efficacy and tolerance (p=0.006 and p<0.001). The combination of N and C scores identified 116 accepting (36.1%), 182 ambivalent (56.7%), 16 indifferent (5.0%) and 7 skeptical patients (2.2%). There were no differences in age, gender, or RA duration among the groups, but differences were seen in the satisfaction with the treatment and in the fulfillment of the expectations (table). Ambivalent patients showed less satisfaction and lower fulfillment of expectations with the treatment received than accepting patients.
Conclusions: Patients with RA have strong beliefs about the need of their biological SC medication, but a high % also expresses concerns. Beliefs, and especially concerns, seem to relate to the satisfaction and fulfillment of expectations of efficacy and tolerability or the drug, rather than to demographics or RA characteristics. Discussing expectations may be important when initiating a biological treatment.
Acknowledgements: Funded by MSD, Spain.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3099

FRI0185 A SYSTEMATIC REVIEW AND BIVARIATE META-ANALYSIS OF STUDIES THAT MEASURED ADALIMUMAB DRUG LEVELS BY ELISA TO DETECT TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS

S. Gavan[1,2], K. Payne[1], A. Barton[2,3]. *[1]Manchester Centre for Health Economics, The University of Manchester; [2]National Institute for Health Research Manchester Musculoskeletal Biomedical Research Unit at Central Manchester University Hospitals NHS Foundation Trust; [3]Centre for Musculoskeletal Research, The University of Manchester, Manchester, United Kingdom*

Background: Previous research has demonstrated an association between circulating drug levels and treatment response in patients with rheumatoid arthritis that received the anti-TNF therapy adalimumab. Commercial ELISA assays are now available for use in routine practice to monitor anti-TNF drug levels at regular intervals. However, the ability to detect treatment response by measuring adalimumab drug levels using an ELISA is uncertain.
Objectives: The objectives of this research were to identify and synthesise all published studies that investigated the accuracy of measuring adalimumab drug levels by ELISA to detect treatment response in patients with rheumatoid arthritis.
Methods: A systematic review identified all published studies that performed a receiver operating characteristic (ROC) analysis to detect treatment response in patients with rheumatoid arthritis by measuring adalimumab drug levels using an ELISA. Medline and Embase were searched electronically from inception to August 2016. Two researchers independently identified studies for the review using a pre-defined inclusion criteria. Assay results were classified as positive if adalimumab drug levels exceeded the cut-point reported in each study. Study design characteristics, sample characteristics, and test outcomes from 2x2 tables (true-positive; false-positive; true-negative; false-negative) were extracted from each study. The quality of each study was assessed using the QUADAS-2. A hierarchical bivariate meta-analysis synthesised the findings of the ROC analyses to account for between-study heterogeneity and correlation between assay sensitivity and specificity.
Results: The search strategy identified 4,006 abstracts and four studies met the inclusion criteria of the systematic review. Patients received 40mg adalimumab every two weeks in all studies. Studies varied in their design and sample characteristics, but had low risk of bias and low concern of applicability to the research objective. The hierarchical bivariate meta-analysis estimated that measuring high adalimumab drug levels by ELISA detected treatment response with an average sensitivity of 0.95 (95% CI: 0.85–0.98) and specificity of 0.68 (95% CI: 0.28–0.92).
Conclusions: Measuring high adalimumab drug levels by ELISA in patients with rheumatoid arthritis appeared to be predictive of treatment response. However, the measurement of low adalimumab drug levels was less predictive of no response to treatment. In practice, test accuracy may be improved by measuring anti-drug antibodies alongside adalimumab drug levels. Given the imperfect accuracy of ELISA assays, the relative cost-effectiveness of drug level monitoring should be evaluated before being recommended for use in routine practice.
Acknowledgements: SG acknowledges support from a National Institute for Health Research Manchester Musculoskeletal Biomedical Research Unit Ph.D studentship. We also acknowledge support from MATURA, a stratified medicine initiative funded jointly by the Medical Research Council and Arthritis Research UK (MR/K015346/1).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6242

FRI0186 INFLUENCE OF IMMUNOGENICITY TO THE FIRST TNF-I THERAPY ON RESPONSE TO THE SECOND BIOLOGIC AGENT IN RA PATIENTS

P. Bogas[1], C. Plasencia[1], D. Pascual-Salcedo[2], G. Bonilla[1], E. Moral[1], C. Tornero[1], L. Nuño[1], A. Villalba[1], D. Peiteado[1], A. Martinez[2], B. Hernandez[2], A. Balsa[1]. *[1]Rheumatology; [2]Immunology, Hospital Universitario la Paz, Madrid, Spain*

Background: There is currently no consensus on selecting a therapeutic target in patients (pts) non-responsive to their first TNF-inhibitors (TNF-i). The development of anti-drug antibodies (ADA) is a frequent cause of secondary inefficacy in our pts with TNF-i and there is evidence that those who develop ADA at their 1st TNF-i achieve a higher degree of response to the second one, compared to ADA- pts. Thus ADA measurement can help in choosing a therapeutic target in pts who failed to respond to their 1st TNF-i
Objectives: To assess if development of ADA to the 1st TNF-i determines better response when switching to a 2nd TNF-i versus a nonTNF-i. As secondary objective, analyze whether the presence or absence of ADA to a 1st TNF-i influences the efficacy of a 2nd TNF-i
Methods: Of a total of 144 pts that switched from infliximab or Adalimumab to a 2nd biologic agent (Etanercept, Rituximab, Tocilizumab, Adalimumab, Abatacept, Certolizumab and Infliximab), only 60, who had measured drug levels (DL)/ADA at discontinuation of the 1st TNF-I, were included. Clinical response was evaluated with DAS28, Delta-DAS28 (ΔDAS28) and EULAR response (E-resp) at 6 (v-6) and 12 (v-12) months after initiating 2nd biologic agent and at the last visit prior to drug discontinuation or ending of the study for those who did not interrupt the biological therapy (v-end). DL/ADA levels were measured by ELISA. Statistical analysis was performed using SPSS version 20.0
Results: Within the 60 pts who had measured DL/ADA at suspension of the 1st TNF-i, 26 (43%) were ADA- (i.e. DL +). In this ADA- subpopulation, 50% changed to a 2nd TNF-i; at v-6 there were no differences between switchers to a 2nd TNF-i and switchers to a nonTNF-i in DAS28 (3.7±2.1 TNF-i vs 4.2±1.1 nonTNF-i, p=0.286), ΔDAS28 (1,4±2 TNF-i, 1±1,2 nonTNF-i, p=0,374) and resp-E (75% good/moderate resp in TNF-I, 40% in nonTNF-i, p=0,064). At v-12, switchers to a 2nd TNF-i showed a lower DAS28 (2.5±0.6 TNF-i, 3.9±0.9 nonTNF-i, p=0.009) and a higher good E-resp rate with a marginally significant difference (80% in TNF-i, 22% in nonTNF-i, p=0.071). However, at v-end, pts with a 2nd nonTNF-i had better response (DAS28 >5,1 in 50% of TNF-i pts, 0% of nonTNF-i, p=0.044). Likewise ΔDAS28 at v-end was higher in the nonTNF-i group with trend to significance (0,7±1,7 TNF-i, 1,7±0,8 nonTNF-i, p=0,06). Along these lines, the

good/moderate E-resp rate was higher in switchers to a nonTNF-i (70% in TNF-i, 8.3% in nonTNF-i, p=0.006). In ADA+ subpopulation (n=34), no differences were found in clinical response at v-end in DAS28 (3.7±1.2 TNF-i, 3.9±1.1 non-TNF-i, p=0.64), ΔDAS28 (0,63±1,6 in TNF-i, 1,4±1,4 in nonTNF-i, p=0,35) and good/moderate E-resp rate (30% in TNF-i, 91% in nonTNF-i, p=0,703). In pts who changed to a 2nd TNF-i, those with ADA to 1st TNF-i had a higher good response rate than ADA- pts (65% in ADA +, 30% in ADA-, p=0.07)

Demographic characteristics	ADA+ subpopulation	ADA- Subpopulation	p
Age (years)	62,3±14,6	65,7±14,9	0,203
Sex (female)	28 (82%)	23 (88%)	0,719
Smokers	7 (20,6%)	4 (26%)	0,537
BMI	26,9±8,9	23,9±4,2	0,39
Disease duration (years)	19,3±8,05	24,1±8,2	0,844
RF +	32 (94%)	20 (77%)	0,067
Anti-CCP +	32 (94%)	22 (88%)	0,641
Basal CPR	15,1±18,2	20,4±21,7	0,46
Basal ESR	41±27,9	38±20	0,28
Basal DAS	5,31±1,4	5,51±1,3	0,18

Conclusions: The development of ADA to the first TNF-i entails a better response when switching to a 2nd TNF-i, with a similar efficacy to the pts who switched to a nonTNF-i. In those pts who did not develop immunogenicity to the 1st TNF-I, there is a better response when changing therapeutic target. The ADA measurement can help to select the pts who can benefit from a 2nd TNF-i

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6688

FRI0187 RADIOGRAPHIC PROGRESSION BY DISEASE ACTIVITY STATES IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SB2 OR REFERENCE INFLIXIMAB

J.S. Smolen[1], J.-Y. Choe[2], E. Keystone[3], Y.H. Rho[4], Y. Lee[4], S. Lee[4]. *[1]Medical University of Vienna, Vienna, Austria; [2]Daegu Catholic University Medical Center, Daegu, Korea, Republic Of; [3]Mount Sinai Hospital, University of Toronto, Toronto, Canada; [4]Samsung Bioepis Co., Ltd., Incheon, Korea, Republic Of*

Background: Based on the totality of evidence, SB2 has shown to be similar with reference infliximab (INF) and has been approved as a biosimilar by the European Medical Agency. It is, however, hitherto unknown, if SB2 also shares similar structural efficacy in the different disease activity states when compared with INF.

Objectives: To evaluate the disease activity by simplified disease activity index (SDAI) and clinical disease activity index (CDAI) at weeks 14, 30 and 54 in patients with rheumatoid arthritis (RA) treated with SB2 or INF from a phase III study and to assess the radiographic progression at week 54 in patients by disease activity states (remission, low disease activity [LDA], moderate disease activity [MDA], or high disease activity [HDA]).

Methods: Patients with RA were randomised to receive either SB2 or INF 3 mg/kg at weeks 0, 2, 6, and then every 8 weeks thereafter until week 46 with background methotrexate. Dose increments were allowed after week 30 by 1.5 mg/kg up to a maximum dose of 7.5 mg/kg. Disease activities by SDAI, and CDAI were compared at weeks 14, 30, and 54. The radiographic progression was measured by modified Total Sharp Score (mTSS) at weeks 0 and 54.

Results: Up to week 54, comparable proportions of patients achieved ACR-EULAR-index remission between SB2 and INF (by SDAI: 13/279 [4.7%] vs. 13/283 [4.6%] at week 14; 24/250 [9.6%] vs. 29/263 [11.0%] at week 30; 34/226 [15.0%] vs. 24/224 [10.7%] at week 54; by CDAI: 12/279 [4.3%] vs. 12/283 [4.2%] at week 14; 22/253 [8.7%] vs. 31/265 [11.7%] at week 30; 33/227 [14.5%] vs. 24/225 [10.7%] at week 54 in SB2 and INF, respectively). The proportions of radiographic non-progressors (defined as change in mTSS ≤0) by disease activity were comparable between SB2 and INF at week 14, 30 and 54 (Table 1). Patients treated with SB2 as well as INF also exhibited the lowest progression of radiographic damage in remission and the largest progression in HDA, but also very small increases in mTSS in LDA and MDA, in line with previous findings on INF.

Table 1. The proportion of radiographic non-progressors (mTSS progression ≤ 0) and mean change from baseline in mTSS at week 54 by disease activity states at weeks 14, 30, and 54

Disease activity state at each visit		CDAI				SDAI			
		SB2		INF		SB2		INF	
		Radiographic non-progressors	Mean change	Radiographic non-progressors	Mean change	Radiographic non-progressors	Mean change	Radiographic non-progressors	Mean change
Week 14	HDA	43/62 (69.4)	0.44	42/59 (71.2)	0.61	25/41 (61.0)	0.80	31/45 (68.9)	1.03
	MDA	64/86 (74.4)	0.27	57/82 (69.5)	0.64	81/105 (77.1)	0.10	63/89 (70.8)	0.45
	LDA	43/56 (76.8)	0.54	49/58 (84.5)	-0.38	44/58 (75.9)	0.63	53/64 (82.8)	-0.27
	Remission	7/9 (77.8)	0.17	6/8 (75.0)	1.44	7/9 (77.8)	0.17	7/9 (77.8)	1.00
Week 30	HDA	29/43 (67.4)	0.93	33/47 (70.2)	1.20	25/37 (67.6)	0.79	24/33 (72.7)	1.32
	MDA	57/76 (75.0)	0.14	49/71 (69.0)	0.43	59/80 (73.8)	0.24	58/84 (69.0)	0.54
	LDA	55/74 (74.3)	0.40	52/67 (77.6)	-0.10	56/74 (75.7)	0.42	54/69 (78.3)	-0.23
	Remission	16/20 (80.0)	0.05	22/24 (91.7)	-0.13	17/21 (81.0)	0.07	20/22 (90.9)	0.07
Week 54	HDA	31/43 (72.1)	0.39	25/42 (59.5)	1.59	25/36 (69.4)	0.65	23/36 (63.9)	1.71
	MDA	47/69 (68.1)	0.69	46/66 (69.7)	0.30	50/73 (68.5)	0.57	44/68 (64.7)	0.35
	LDA	51/67 (76.1)	0.20	62/78 (79.5)	0.29	54/69 (78.3)	0.18	66/82 (80.5)	0.24
	Remission	28/33 (84.8)	-0.11	23/23 (100.0)	-1.39	27/33 (81.8)	-0.08	23/23 (100.0)	-1.22

Disease activity was defined as following:
by CDAI: remission, CDAI ≤ 2.8; LDA, 2.8 < CDAI ≤ 10.0; MDA, 10 < CDAI ≤ 22.0; HDA, 22.0 < CDAI
by SDAI: remission, SDAI ≤ 3.3; LDA, 3.3 < SDAI ≤ 11.0; MDA, 11 < SDAI ≤ 26.0; HDA, 26.0 < SDAI
Patients with available mTSS at both baseline and week 54 were included.

Conclusions: The proportion of patients achieving remission or LDA was comparable up to week 54 upon treatment with both SB2 and INF. Inhibition of radiographic progression was also comparable in each disease activity state. The proportion of radiographic non-progressors was also similarly high in patients achieving remission, and overall very low radiographic progression rates were seen even in LDA and MDA in both treatment arms. These data further confirm the comparability of SB2 and INF.

Disclosure of Interest: J. S. Smolen Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, Celgene, Glazo, Janssen, Lilly, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung Bioepis, Sanofi, UCB, J.-Y. Choe Consultant for: Samsung Bioepis, E. Keystone Consultant for: Pfizer, Roche, Janssen, Amgen - consultant/Pfizer, Roche, Janssen, Amgen, BMS, Merck. Merck, Celltrion, Samsung Bioepis, Y. H. Rho Employee of: Samsung Bioepis, Y. Lee Employee of: Samsung Bioepis, S. Lee Employee of: Samsung Bioepis

DOI: 10.1136/annrheumdis-2017-eular.5524

FRI0188 EFFECTIVENESS OF ADALIMUMAB COMBINATION THERAPY WITH METHOTREXATE AND NON-METHOTREXATE CSDMARDS: RESULTS FROM THE CORRONA RHEUMATOID ARTHRITIS REGISTRY

D. Pappas[1,2], J. Griffith[3], C.A. Schlacher[3], J.L. Subotcki[3], R.W. Harrison[2], Y. Shan[2], C. Karki[2], J.M. Kremer[4]. *[1]Columbia University, New York; [2]Corrona, LLC, Southborough; [3]AbbVie, Inc., Abbott Park; [4]Albany School of Medicine, Albany, United States*

Background: Combination therapy of methotrexate (MTX) with biologics results in superior outcomes vs. monotherapy. However, little is known on the effectiveness of adalimumab (ADA) combination therapy with non-MTX conventional synthetic disease modifying anti-rheumatic drugs (csDMARD).

Objectives: To evaluate whether ADA in combination with non-MTX csDMARD has similar effectiveness as MTX combination therapy on clinical and patient report outcomes (PROs).

Methods: Adult RA patients, naïve to other monoclonal antibodies, who initiated standard dose ADA (40mg q2w) in combination with MTX or ≥1 non-MTX csDMARD between 2003–2016 and had a 6 month follow-up visit were included. The primary outcomes were mean change in clinical disease activity index (CDAI) and mean change in PROs (mHAQ, pain, fatigue, morning stiffness) from baseline to 6 months. Secondary outcomes included achievement of remission (CDAI≤2.8)/low disease activity (LDA: CDAI≤10). Outcomes were evaluated adjusting for covariates that differed at the time of initiation using mixed model linear regression. Kaplan-Meier survival analysis was used to examine the persistency of ADA between the two groups.

Results: A total of 754 patients were included: N=519 ADA+MTX and N=235 ADA+non-MTX csDMARD. Patients on ADA+MTX were slightly younger (mean age: 54.5 vs 57.4 years), with shorter disease duration (median: 3 vs 5 years), more likely to be biologic naïve (77% vs 69%) compared to patients on ADA+nonMTX csDMARD (all p<0.05). Disease activity and PROs were comparable in both groups at the time of initiation (mean CDAI: 20.4 vs 22.8; mean pain: 45.3 vs 45.9; mean fatigue: 46.3 vs 47.8; mean patient global assessment: 42.8 vs 42.9 (on a VAS 0–100) in ADA+MTX and ADA+nonMTX csDMARD group respectively. Adjusted analysis showed that patients on ADA+MTX had significantly lower mean CDAI at 6 months and higher change in CDAI vs patients in the ADA+non-MTX csDMARD group (p<0.05). In addition, patients on ADA+MTX were more likely to achieve LDA compared to the ADA+non-MTX csDMARD group (Table). Change in PROs and persistency of ADA was comparable in both groups.

Table: Outcomes at 6 months among ADA+MTX and ADA+nonMTX csDMARD therapy

	ADA +MTX	ADA + nonMTX csDMARD[a]	Unadjusted[b]	Adjusted[b,c]
6 month outcomes	Mean (SD)	Mean (SD)	β (95% CI)	β (95% CI)
Mean CDAI at 6 months	11.9 (11.5)	15.7 (13.1)	4.07 (2.09 to 6.04)	3.15 (1.11 to 5.18)
Change in CDAI	-8.8 (13.4)	-7.4 (13.4)	1.72 (-0.85 to 4.29)	3.15 (1.11 to 5.18)
Change in mHAQ	-0.11 (0.39)	-0.1 (0.4)	0.01 (-0.07 to 0.08)	0.01 (-0.07 to 0.08)
Change in pain	-10.1 (26.5)	-9.7 (30.7)	0.68 (-4.51 to 5.88)	1.61 (-3.58 to 6.80)
Change in fatigue	-2.7 (25.9)	-5.3 (25.1)	-2.64 (-9.13 to 3.84)	-2.58 (-9.22 to 4.07)
	Response rate n (%)	Response rate n (%)	Odds Ratio[†] (95% CI)	Odds Ratio[††] (95% CI)
Achievement of Remission (CDAI≤2.8)	46 (15.5%)	13 (8.6%)	0.52 (0.26, 1.06)	0.58 (0.27, 1.26)
Achievement of LDA (CDAI≤10)	136 (45.9%)	47 (31.1%)	0.51 (0.32, 0.80)	0.59 (0.37, 0.96)

mHAQ: modified Health Assessment Questionnaire; LDA: Low Disease Activity; nonMTX csDMARD: non-methotrexate conventional synthetic disease modifying anti-rheumatic drug. [a] Includes leflunomide, sulfasalazine, and hydroxychloroquine. [b] Compared with MTX combination therapy as a reference; [c]Adjusted for age, duration of RA, work status (part-time, full-time, disabled, retired, other), insurance status (none, private, Medicare), prior biologic count, MTX continuation, baseline CDAI, baseline patient pain.

Conclusions: In this real world study, patients on ADA+MTX had significantly greater improvements in disease activity compared to patients on ADA+nonMTX

csDMARD therapy but had comparable improvements in PROs at 6 months from initiation.

Acknowledgements: This study is sponsored by Corrona, LLC. The Corrona, LLC. has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB. The design, study conduct, and financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.

Disclosure of Interest: D. Pappas Grant/research support from: AbbVie, Consultant for: AbbVie, Employee of: Corrona, LLC, J. Griffith Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc, C. Schlacher Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc, J. Suboticki Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc, R. Harrison Employee of: Corrona, LLC, Y. Shan Employee of: Corrona, LLC, C. Karki Employee of: Corrona, LLC, J. Kremer Shareholder of: Corrona, LLC, Grant/research support from: AbbVie, Genentech, Lilly, Novartis, Pfizer, Consultant for: AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, Employee of: Corrona, LLC

DOI: 10.1136/annrheumdis-2017-eular.1924

FRI0189 SIMILAR EFFICACY AND SAFETY OF BIOSIMILAR CANDIDATE BI 695501 AND ADALIMUMAB ORIGINATOR REFERENCE PRODUCT IN PATIENTS WITH MODERATE TO SEVERE ACTIVE RHEUMATOID ARTHRITIS: 24 WEEK RESULTS FROM A PHASE III CLINICAL STUDY (VOLTAIRE®-RA)

S. Cohen[1], A. Alonso-Ruiz[2], P.A. Klimiuk[3], E. Lee[4], N. Peter[5], I. Sonderegger[5], D. Assudani[5]. *[1]Metroplex Clinical Research Center, Dallas, United States; [2]Hospital de Cruces, Barakaldo, Spain; [3]Medical University of Bialystok and Gabinet Internistyczno-Reumatologiczny, Bialystok, Poland; [4]Inland Rheumatology, Upland, United States; [5]Boehringer Ingelheim, Ingelheim a.R., Germany*

Background: PK bioequivalence of BI 695501, a biosimilar candidate, and the adalimumab originator was demonstrated previously (VOLTAIRE®-PK: Wynne et al., Expert Opin Investig Drugs 2016;25:1361–70) and led to further clinical development.

Objectives: To demonstrate clinical equivalence of BI 695501 with the adalimumab originator by comparing efficacy, safety and immunogenicity using a clinical model sensitive to detect potential differences between the two biologics.

Methods: In this 58-week, multi-national, multicentre, randomised, double-blind, parallel arm Phase III study (NCT02137226), 645 pts (18–80 years) with moderate to severe active RA on stable treatment with methotrexate were randomised to receive US-licensed SC adalimumab originator or BI 695501 40mg Q2W for 24 weeks. At Wk 24, pts on adalimumab originator were re-randomised to continue the adalimumab originator or switch to BI 695501 until Wk 48. Pts on BI 695501 were dummy re-randomised. Co-primary end points were proportion of pts achieving ACR20 at Wks 12 and 24. Equivalence between BI 695501 and the adalimumab originator was demonstrated if the relevant confidence intervals (CI) for differences in ACR20 response rate at Wks 12 and 24 were within the predefined margins (Wk 12: 90% CI –12%, 15%; Wk 24: 95% CI –15%, 15%). The secondary efficacy end point was change from baseline in DAS28-ESR at Wks 12 and 24. Safety and immunogenicity were exploratory objectives. Wk 48/58 data will be reported later.

Results: The co-primary end points of ACR20 response at Wks 12 and 24 were within the pre-defined criteria for equivalence, demonstrating clinical equivalence between BI 695501 and the adalimumab originator (Table 1).

The proportion of pts with treatment-emergent adverse events (TEAE) was similar between the BI 695501 and the adalimumab originator treatment groups (Table 2).

Table 1. Response at Weeks 12 and 24

ACR, %	Week 12		Week 24	
	BI 695501 n=321	Adalimumab originator n=318	BI 695501 n=321	Adalimumab originator n=318
ACR20*	67.0	61.1	69.0	64.5
ACR50	29.3	31.0	36.8	36.8
ACR70	10.1	11.1	13.6	18.2
DAS28-ESR#, mean change from baseline (95% CI)	–2.1 (–2.28, –2.01)	–2.0 (–2.18, –1.91)	–2.4 (–2.51, –2.21)	–2.4 (–2.54, –2.24)

*Week 12 risk difference (RD) and 90% CI for BI 695501-adalimumab originator are 5.9% and 90% CI (–0.9%, 12.7%); #Week 24: RD and 95% CI are 4.5% and (–3.4%, 12.5%).

Table 2. Overview of TEAEs up to Week 24

Pts, n (%)	BI 695501 (n=324)	Adalimumab originator (n=321)
≥1 TEAE	138 (42.6)	148 (46.1)
≥1 TEAE related to trial drug	36 (11.1)	44 (13.7)
≥1 Non-serious TEAE	135 (41.7)	141 (43.9)
≥1 serious TEAE	12 (3.7)	18 (5.6)
≥1 serious TEAE related to trial drug	1 (0.3)	5 (1.6)
A TEAE leading to trial drug discontinuation	8 (2.5)	11 (3.4)
A TEAE leading to death	0 (0.0)	0 (0.0)

Rates of serious AEs and discontinuation due to TEAEs were similar across the groups. No deaths were reported during the study. Similar frequencies of pts tested positive for anti-drug antibodies (BI 695501 43.2%; adalimumab originator 47.8%), and neutralising antibodies (BI 695501 16.0%; adalimumab originator 20.6%) in both groups at Week 24.

Conclusions: This study in pts with RA demonstrated that BI 695501 and the adalimumab originator are highly similar in terms of efficacy, safety and immunogenicity.

Disclosure of Interest: S. Cohen Grant/research support from: Amgen, Boehringher Ingelheim, Coherus, Pfizer, Consultant for: Amgen, Boehringher Ingelheim, Celltrion, Merck, Pfizer, Sandoz, A. Alonso-Ruiz: None declared, P. Klimiuk: None declared, E. Lee: None declared, N. Peter Employee of: Boehringer Ingelheim, I. Sonderegger Employee of: Boehringer Ingelheim, D. Assudani Employee of: Boehringer Ingelheim

DOI: 10.1136/annrheumdis-2017-eular.3405

FRI0190 CLINICAL OUTCOMES FROM A NATIONWIDE NON-MEDICAL SWITCH FROM ORIGINATOR TO BIOSIMILAR ETANERCEPT IN PATIENTS WITH INFLAMMATORY ARTHRITIS AFTER 5 MONTHS FOLLOW-UP. RESULTS FROM THE DANBIO REGISTRY

B. Glintborg, I.J. Sørensen, A.G. Loft, J. Esbesen, H. Lindegaard, D.V. Jensen, K. Danebod, S. Dieperink, O. Hendricks, I.M.J. Hansen, A. Linauskas, S. Kristensen, L.S. Andersen, M. Hossein, H. Nordin, B.L. Andersen, S. Chrysidis, J.L. Raun, N. Manilo, J. Grydehøj, E.B. Dalgaard, D.D. Pedersen, N.S. Krogh, M.L. Hetland. *The DANBIO registry and the Danish Departments of Rheumatology, Copenhagen, Denmark*

Background: In Denmark, biological drugs are provided free by the hospitals to the patients via a tax-based system. In 2015 a non-medical switch from originator infliximab to CT-P13 was conducted (1). According to national guidelines in April 2016, a non-medical switch from originator (ETA, Enbrel® 50 mg/week) to biosimilar etanercept (SB4, Benepali®) was dictated when SB4 was marketed, including patients with inflammatory rheumatic diseases treated in routine care.

Objectives: To investigate 3 months' disease activity and 5 months' treatment withdrawal in ETA-treated patients (pts) with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthrits (SpA), who were switched to SB4 and monitored prospectively in the DANBIO registry.

Methods: Pts with RA/PsA/SpA followed in DANBIO since start of first bDMARD were included. Disease activity at 3 months before switch (pre-switch), at the switch and after 3 months (post-switch) and changes over time (∆pre-switch and ∆post-switch) were calculated. Disease flare was defined as ∆DAS28≥1.2 (RA/PsA) or ∆ASDAS≥1.3 (SpA). Factors associated with withdrawal (gender/age/diagnosis/bDMARD-treatment-no/comedication methotrexate/baseline CRP/patient's global score) were explored by multivariable Cox regression analysis.

Results: In total, 1548 switch pts were identified (891 RA, 335 PsA, 322 SpA). 60% were women, age (median (IQR) 56 (44–65) yrs)). Prior ETA treatment duration was 5.2 (3.2–8.0) yrs. ETA was the first biological treatment in 49%, and the second in 33% of pts. Concomitant MTX was given in 60% (RA)/49% (PsA)/15% (SpA). Median follow-up time was 154 (110–178) days.

Disease activity remained largely unchanged 3 months prior to vs. after the switch (Table). The proportion of patients with disease flare pre-/post switch was 8%/13% (RA), 9%/13% (PsA), 5%/5% (SpA).

Overall, 129 pts (9%) stopped SB4 treatment during 5 months' follow-up (Table). Prior ETA treatment duration in these patients was 4.5 (2.7–7.1) years.

Higher patient's global score (HR 1.12/cm, 95% CI (1.05–1.21), p=0.002) and no concomitant methotrexate (HR 2.28 (1.48–3.52), p<0.001) at baseline were associated with withdrawal.

Table Disease activity 3 months pre/post-switch and changes in patients switched from originator to biosimilar etanercept. Reasons for withdrawal after 5 months' follow-up are also shown

	Disease activity, median(IQR)			Changes, median(IQR)		P*
	pre-switch	switch	post-switch	Δpre-switch	Δpost-switch	
RA, n=891						
DAS28	2.1 (1.7-2.9)	2.1 (1.6-2.9)	2.2 (1.6-3.1)	0.0 (-0.4-0.5)	0.0 (-0.4-0.5)	0.2
HAQ	0.6 (0.2-1.3)	0.8 (0.1-1.3)	0.8 (0.3-1.3)	0.0 (-0.1-0.1)	0.0 (-0.1-0.1)	0.7
CRP, mg/l	3 (1-7)	2 (1-6)	3 (1-6)	0 (-2-1)	0 (-1-1)	0.02
VAS global, mm	30 (13-57)	28 (13-55)	31 (11-62)	0 (-11-9)	0 (-9-11)	0.1
PsA, n=335						
DAS28	2.0 (1.5-2.6)	2.0 (1.6-2.8)	2.1 (1.5-3.0)	0.0 (-0.2-0.5)	0.0 (-0.6-0.5)	0.7
HAQ	0.5 (0.1-1.1)	0.5 (0.0-1.1)	0.5 (0.1-1.1)	0.0 (-0.1-0.1)	0.0 (-0.1-0.1)	0.7
CRP, mg/l	2 (1-4)	2 (1-4)	2 (1-4)	0 (-2-1)	0 (-1-1)	0.04
VAS global, mm	31 (12-58)	30 (13-54)	32 (13-59)	0 (-9-7)	0 (-7-12)	0.2
SpA, n=322						
BASDAI, mm	33 (15-51)	27 (12-48)	29 (16-47)	-1 (-7-5)	1 (-5-8)	0.03
CRP, mg/l	3 (1-6)	3 (1-5)	3 (1-5)	0 (-2-1)	0 (-1-1)	0.4
VAS global, mm	34 (16-59)	30 (12-53)	31 (15-53)	-1 (-12-6)	2 (-6-14)	0.04
ASDAS	2.0 (1.3-2.8)	1.9 (1.2-2.7)	1.9 (1.3-2.7)	-0.1 (-0.4-0.2)	0.1 (-0.4-0.5)	0.1
Reasons for withdrawal during ≈ 5 months follow-up (n= 129)						
Lack of effect 59, Adverse event 42 (rash 5, diarrhea 3, unspecific/other 34), remission 2, cancer 4, death 1, other/unknown 21						
*Delta values for disease activity pre-switch vs. post-switch, Wilcoxon matched-pair signed rank test						

Conclusions: In 1548 patients with inflammatory rheumatic diseases treated with ETA for >5 years, disease activity was largely unaffected in the majority of patients 3 months after non-medical switch to SB4 and comparable to the fluctuations observed in the 3 months prior to the switch. Several patients (≈9%)

stopped treatment during 5 months follow-up. Higher patient's global score and no use of methotrexate were associated with withdrawal. Longer follow-up will offer additional understanding of the potential efficacy and safety consequences of the non-medical switch.

References:
[1] Glintborg et al. Arthritis Rheumatol. 2016; 68 (suppl 10): Abstract no 951.

Acknowledgements: Data analysis was partly financially supported by Biogen.

Disclosure of Interest: B. Glintborg Grant/research support from: Abbvie, Biogen, I. Sørensen: None declared, A. G. Loft: None declared, J. Esbesen: None declared, H. Lindegaard: None declared, D. Jensen: None declared, K. Danebod: None declared, S. Dieperink: None declared, O. Hendricks: None declared, I. M. Hansen Grant/research support from: Roche, A. Linauskas: None declared, S. Kristensen: None declared, L. Andersen: None declared, M. Hossein: None declared, H. Nordin: None declared, B. Andersen: None declared, S. Chrysidis: None declared, J. Raun: None declared, N. Manilo: None declared, J. Grydehøj: None declared, E. Dalgaard: None declared, D. Pedersen: None declared, N. Krogh: None declared, M. Hetland Grant/research support from: Orion, BMS, AbbVie, Biogen, Pfizer, MSD, Eli Lilly

DOI: 10.1136/annrheumdis-2017-eular.1703

FRI0191 INCIDENCE OF DISEASE WORSENING IN INFLAMMATORY ARTHRITIS PATIENTS ON LONG-TERM INNOVATOR INFLIXIMAB THERAPY

A.M. Marrache[1], E. Psaradellis[2], J. Vaillancourt[2], E. Rampakakis[2], F. Nantel[1]. *[1]Medical Affairs, Janssen Inc., Toronto; [2]JSS Medical Research, Montreal, Canada*

Background: A recent randomized controlled study in a single country reported rates of disease worsening over a one-year follow-up period for innovator infliximab (REMICADE®, IFX) and a comparator in various diseases including AS and RA. After a mean duration of treatment of 6.7 years of innovator IFX, rates for disease worsening post-one year follow-up were 39.5% in AS and 36.7% in RA[1]. Other such data reporting disease worsening rates are rare.

Objectives: Using data from a longitudinal database, the objective was to determine the incidence of disease worsening in AS and RA patients on long-term therapy with innovator IFX. PsA patients were not included in this study due to low numbers (n=49).

Methods: BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients initiating treatment with infliximab, golimumab or ustekinumab that has been ongoing since 2002 in Canada. We included AS and RA patients who had been on innovator IFX therapy for at least two, four or six years. Disease worsening endpoint was defined as follows: for AS patients; an increase in ASDAS $\geq$1.1 from baseline and a minimum score of 2.1. For RA patients; an increase in DAS28 $\geq$1.2 from baseline and a minimum score of 3.2.

Results: This analysis included a total of 196 AS and 425 RA patients. Among AS patients, 36.1% were female, 90.8% were bio-naïve at IFX initiation and 50% were on concomitant NSAID(s) at the 2-year index. The mean (SD) ASDAS score was 2.17 (1.05). As for the RA patients, 75% were female, 88.5% were bio-naïve, and 93% were on concomitant DMARD(s) while 35% were on corticosteroids at the 2-year index. The mean (SD) DAS28 ESR and DAS 28 CRP were 3.37 (1.40) and 3.00 (1.24), respectively.

As shown in table 1, the incidence of disease worsening in AS and RA patients on stable IFX for 2–6 years was low and varied from 2.7% to 11.5% at the subsequent 12 and 24 months visit.

Table 1. Incidence of disease worsening in AS and RA patients at the 2, 4, and 6-year index

Disease	Outcome	Index date post IFX initiation	Disease worsening at subsequent visits, n/N (%)	
			12 months	24 months
AS	ASDAS	2 years	9/79 (11.4%)	6/59 (10.2%)
		4 years	2/42 (4.8%)	1/37 (2.7%)
		6 years	1/25 (4.0%)	2/18 (11.1%)
RA	DAS28 ESR	2 years	20/184 (10.9%)	17/148 (11.5%)
		4 years	9/121 (7.4%)	7/106 (6.7%)
		6 years	8/73 (11.0%)	5/47 (10.6%)
	DAS28 CRP	2 years	16/160 (10.0%)	11/124 (8.9%)
		4 years	8/115 (7.0%)	6/104 (5.9%)
		6 years	6/80 (7.5%)	4/54 (7.4%)

Conclusions: In this prospective longitudinal cohort, patients on long-term innovator IFX therapy show low rates of disease worsening of 2.7% to 11.5% at 1 and 2 years in AS and RA. Additional studies may elucidate the true rate of and reasons for disease worsening in rheumatologic populations.

References:
[1] Goll et al. Biosimilar Infliximab (CT-P13) Is Not Inferior to Originator Infliximab: Results from a 52-Week Randomized Switch Trial in Norway. Arthritis Rheum 2016;68(S10). Abstract 19L.

Disclosure of Interest: A. M. Marrache Employee of: Janssen Inc., E. Psaradellis Employee of: JSS Medical Research, J. Vaillancourt Employee of: JSS Medical Research, E. Rampakakis Employee of: JSS Medical Research, F. Nantel Employee of: Janssen Inc.

DOI: 10.1136/annrheumdis-2017-eular.4545

FRI0192 CLINICAL PRACTICE GUIDE FOR THE TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA). SYSTEMATIC REVIEW: IN PATIENTS WITH RA, WHICH IS THE SAFEST THERAPY FOR PATIENTS WITH PREVIOUS CANCER?

M.B. Nishishinya[1], C.A. Pereda[2], P. Diaz del Campo[3], A. Balsa[4] on behalf of GUIPCAR, Evidence based Rheumatology Working Group (SER) and GUIPCAR Working Group. *[1]Traumatology Institute Quirón, Barcelona; [2]Rheumatology, Hospital Mediterraneo, Almeria; [3]Investigation Unit, Spanish Rheumatology Society; [4]Rheumatology, Hospital Universitario la Paz, Madrid, Spain*

Background: Anti TNF therapy, has been used for the treatment of RA patients for several years. Yet, cancer and infections are among the most serious adverse effects described. Unfortunately, little is known about the effect of anti TNF therapy amongst patients with RA and previous cancer, mainly when synthetic DMARds treatment fails.

Objectives: To review the evidence on the safety of biological therapy in RA patients with previous neoplasia.

Methods: we performed a systematic review through Medline, Cochrane Library, and EMBASE databases. Studies written in English, French and Spanish were considered. Patients 18 years or older, with RA diagnosis (ACR 1987 o ACR/EULAR 2010 criteria), and cancer diagnosis before starting biologic therapy were included. While Systematic reviews, clinical trials and or observational studies with a minimal follow –up of 6 months were considered; case reports or narrative reviews were excluded.

Results: 1077 studies were potentially identified, and 6 cohort studies were finally included, (Aaltonen 2015, Dixon 2010, Phillips 2015, Raaschou 2015, Silva-Fernández 2016, Stranfeld 2010). Studies were based on registries of patients with RA treated with DMARds and biological therapy. Registries evaluated between 3.762 and 14.168 patients. The number of patients with documented previous cancer was around 122 to 425 as a whole. Biological therapies evaluated were: IFX, ETN, ADA, RTX, certolizumab pegol, Golimumab, ANAKinRA and synthetic DMARDs. Studies results were organized as anti TNF vs. DMARDs. All studies assessed were cohort trials, SIGN 2+ (Quality Scale). They included solid tumours as breast cancer, lymphoproliferative tumours, skin cancer, neck and brain tumours, as well as in situ uterus cancer.

There was no increment in the risk of incidence of previous cancer in patients treated both with synthetic DMARDs and with anti TNF therapy in all studies assessed.

We point out, that 1 SR (LaForest Divonne 2016) evaluated biological therapy safety in patients with RA. It included 124 trials, while in 27 metanalysis was performed. From these 27, only 3 (Dixon 2010, Mercer 2013 and Strangfeld 2010) where the only studies which assessed risk of recurrence of previous cancer in patients with RA. The RR 0, 77 (IC 95% 0, 29–2,03), did not exhibit an increment in the risk of cancer in these patients.

Conclusions: - Studies showed no differences in the incidence of previous cancer in patients treated either with synthetic DMARds or with anti TNF. However, we suggest precaution in the use of these therapies, as the real risk in this population is still unknown.

- The final decision of treating or not treating these patients (risk factors, limitations etc.) needs to be performed in accordance with oncologists.
- There is no strong evidence that could identify the real risk of anti TNF therapies in RA patients, with previous cancer.
- The Individual impact risk of different anti-TNF therapies in this population could not be performed due to incomplete data. Yet, there is not real time schedule considering time since previous cancer and the start of anti TNF therapy.

Well design studies with long follow-up periods are needed to answer these questions

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5953

FRI0193 EFFECT OF VALENCY OF ANTI-TNFS ON ELIMINATION MEDIATED BY ANTI-DRUG ANTIBODIES

J. Silva, A. Nesbitt. *UCB Pharma, Slough, United Kingdom*

Background: There are five different anti-TNF biologics: three are bivalent full length (FL) antibodies (adalimumab, golimumab, and infliximab), one a bivalent fusion protein (etanercept), and one a univalent PEGylated Fab' (PF) (certolizumab pegol [CZP]). Administration of such protein biologics can induce anti-drug antibodies (ADAbs), of which the majority are anti-idiotypic antibodies (anti-ID).[1] The potential cross-linking of bivalent anti-IDs with bivalent biologics can result in the formation of large immune complexes (ICs), which are subsequently cleared by mechanisms using the multiple Fc domains, thereby resulting in a decrease in the efficacy of the biologic. Since univalent biologics, such as CZP, only have one binding Fab' arm, such large cross-linked anti-ID-mediated ICs are unlikely to form. Therefore, anti-IDs may have a different effect on the elimination and bioavailability of univalent and bivalent biologics *in vivo*.

Objectives: To determine if the valency of a biologic will affect the *in vitro* size and *in vivo* elimination from the plasma of ICs formed with an anti-ID following intravenous (IV) administration to BALB/c mice.

Methods: An anti-ID antibody to CZP was generated and used for subsequent studies to mimic an ADAb response. Univalent PF CZP was reengineered as a bivalent FL humanized IgG1 antibody (similar to adalimumab) to directly

compare the effect of valency on IC-mediated clearance. This FL antibody showed very similar TNF neutralization compared to the conventional PF molecule in a bioassay. To generate ICs, the anti-ID was incubated overnight with either PF or FL CZP, and the size of the resultant ICs determined by analytical ultracentrifugation (AU). The anti-ID complexes and PF and FL CZP alone were then administered IV to the mice, and the elimination of the anti-TNFs from the circulation was monitored by quantitative liquid chromatography-mass spectrometry (LC-MS) in serial plasma samples.

Results: AU analysis of the immune complexes formed between PF CZP and the anti-ID showed the presence of one peak corresponding in size to one anti-ID molecule bound to two PF molecules (~$3.5x10^5$ Da). In contrast, the FL CZP/anti-ID mixture showed ICs of various sizes up to very large molecular weights (>$1x10^6$ Da), with the predominant species corresponding to a complex of two anti-IDs bound to two FL CZP molecules (~$6x10^5$ Da). The *in vivo* studies showed that the FL CZP/anti-ID ICs were eliminated much faster ($t_{1/2}$=0.3 hours) than the FL CZP alone ($t_{1/2}$=44.5 hours), whereas the PF CZP/anti-ID ICs were eliminated more slowly ($t_{1/2}$=60.5 hours) than the PF CZP alone ($t_{1/2}$=19.7 hours).

Conclusions: The FL CZP molecule formed large ICs with the anti-ID, which led to much faster elimination than the FL molecule alone. This result suggests that an ADAb response to a FL antibody could lead to rapid elimination and loss of efficacy of the drug in patients. In contrast, the PF CZP/anti-ID complex had a longer half-life than the PF CZP alone, presumably because this molecule was not seen as an IC due to the presence of only one Fc. These results showed that an ADAb to a univalent biological reagent may not lead to elimination and instead, may actually increase the *in vivo* half-life of the molecule.

References:

[1] van Schouwenburg PA. Ann Rheum Dis 2013;72:104–9.

Acknowledgements: This study was funded by UCB Pharma. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: J. Silva Employee of: UCB Pharma, A. Nesbitt Employee of: UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.2241

FRI0194 USE OF GLORESPONSETM NF-κB-RE-LUC2P HEK293 CELLS TO MONITOR DRUG AND ANTI-DRUG ANTIBODY LEVELS IN SERUM

B. Hernandez-Breijo[1], L.Y. Bravo Gallego[2], A. Martinez-Feito[1], A. Jochems[1], E. Olariaga[1], J. Cheng[3], L. Delaurière[4], F. Fan[3], T. Schagat[3], C. Plasencia[1], A. Mezcua[2], P. Nozal[2], A. Balsa[1], D. Pascual-Salcedo[1].

[1]Immuno-Rheumatology research group; [2]Immunology, University Hospital la Paz, Madrid, Spain; [3]Promega Corporation, Madison (WI), United States; [4]Promega Europe Training and Applications Laboratory (PETAL), Promega Corporation, Charbonnières-les-Bains, France

Background: Rheumatoid Arthritis (RA) is often treated with anti-TNFα such as infliximab (Ifx) which in a long-term treatment can lead to the development of anti-Ifx antibodies (ATI), resulting in an interference with the drug activity. The investigation of the bioactivity of the circulating drug and antibodies present in patients sera with inflammatory diseases will allow to harmonize the different published data using both bioassays as well as immunoassays.

Objectives: To evaluate the ability of the Promega bioassay in the quantification of both Ifx and ATI in serum from RA patients.

To compare the bioassay performance between capture- and bridging-ELISA.

Methods: Serum Ifx-trough levels were determined in 50 samples from patients with RA. To measure Ifx, the *bioassay* uses GloResponse™ NF-κB-RE-luc2P HEK293 cell line, which responses to TNFα resulting in modulation of NF-κB activity (Promega Corp., Madison, USA). This is an ease on performing reporter assay (add-mix-read) that detects the serum Ifx by inhibition of the luminiscent signal due to TNFα. The inhibition of the Ifx-driven luminescent signal is reverted by the presence of ATI in the serum. ATI concentration is determined using a standard curve obtained with a serial dilution of a serum sample known to have ATI. A relative luminescent unit (RLU) is arbitrarily defined. The *immunoassay* for Ifx (ELISA) captures recombinant TNFα, via a monoclonal antibody that does not interfere with the serum Ifx binding to TNFα. The reaction is developed with a biotinylated anti-idiotype antibody[1] (Cut-off for Ifx: 0.050 μg/ml). The ELISA to detect ATI takes advantage of the bivalency of most IgG subclasses, allowing the antibodies present in serum to bridge between Ifx-coated onto the plate with biotinylated Ifx in fluid phase[1] (Cut-off for ATI 50 AU/ml).

Results: Addition of TNFα on GloResponse cells induces the production of luciferase resulting in an increase of the luminescent signal in a dose-response. Addition of Ifx on GloResponse cells +TNFα decreases the production of luciferase and therefore the luminescent signal falls (r^2=0.99). Addition of anti-Ifx (in relative units) on GloResponse cells +TNFα + Ifx restore the production of luciferase resulting in an increase of the luminescent signal (r^2=0.98).

Serum Ifx concentrations were sorted into 3 groups (low, medium and high following ELISA levels). Similar number of positive Ifx results was found (30 samples, 55% by ELISA vs 28 samples, 52% by bioassay; κ=0.92; p=0.56) along with a significant Pearson correlation (r=0.8) between methods. The bioassay to measure ATI activity showed lower sensitivity than ELISA (9/31, 29% by ELISA vs 4/31, 13% by bioassay, κ=0.53, p=0.22) with a slightly less correlation for ATI levels by both methods (r=0.26).

Conclusions: Bioassay using GloResponse NF-κB cell line can be performed to monitor therapeutic drug of TNFα blocker and are useful to detect the presence of anti-drug antibody in serum samples treated with anti-TNFα antibodies. Comparison with ELISA method shows in most of the case the same data.

References:

[1] Pascual-Salcedo D. et al, Rheumatology, 2011.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6352

FRI0195 POINT-OF-CARE MONITORING OF ANTI-INFLIXIMAB ANTIBODIES IN PATIENTS TREATED WITH THE REFERENCE INFLIXIMAB OR CT-P13 IN ROUTINE CLINICAL PRACTICE

A. Ametzazurra[1], N. Rivera[2], A. Balsa[3], M.P. Arreba[4], E. Ruiz[2], C. Plasencia[3], J. Ortiz[4], D. Pascual-Salcedo[5], M.C. Muñoz[4], C. De Aysa[3], M.J. Allande[2], N. Torres[1], A.M. Hernández[1], X. Recalde[1], A. Martínez[1], D. Nagore[1]. *[1]R&D, Progenika-Grifols, Derio; [2]Rheumatology, Basurto University Hospital, Bilbao; [3]Rheumatology, la Paz University Hospital, Madrid; [4]Gastroenterology, Basurto University Hospital, Bilbao; [5]Immunology, la Paz University Hospital, Madrid, Spain*

Background: Loss of clinical response and infusion reactions to infliximab (IFX) are associated to the development of antibodies to IFX (ATI). ATI detection is a key step of patient management. However, current techniques may require additional patient appointments for sample collection, processing and batching in centralised facilities. Test reporting usually takes several days or weeks impairing effective decision making.

Objectives: To clinically validate the use of a new rapid test to detect ATI in capillary blood in a real-life point-of-care (POC) setting where patients attend the infusion center for the reference IFX (Remicade®, RMC) or CT-P13 (Inflectra®, IFT, or Remsima®) infusions.

Methods: PQ-EF1 and PQ-EF2 are prospective, observational studies designed to evaluate and compare the performance of a rapid POC test (CE-marked Promonitor® Quick Anti-IFX, Progenika, Spain) to detect ATI in routine clinical practice in rheumatic and gastroenterology patients treated with the reference IFX or the biosimilar CT-P13 attending the infusion center with the ELISA technique as a reference. The POC test is a qualitative immunochromatographic assay based on lateral flow technology to detect ATI (including biosimilar CT-P13) in either fingerprick or serum or venous whole blood. Consecutive patients (initiating or under maintenance therapy) were recruited and tested in La Paz and Basurto University hospitals with the rapid test in capillary and venous whole blood specimens immediately before the infusion. ATI test results were read visually with the POC test in 30 min, just before the patient started the infusion. Trough sera were also collected for subsequent analysis with the rapid test and benchmarked with Promonitor®-Anti-IFX ELISA (Progenika, Spain). Follow-up time was 6 months. ELISA quantitative results were categorized as positive and negative to allow comparisons with the qualitative rapid test.

Results: Ninety consecutive patients were recruited (a total of 137 visits in the 6 months follow-up) accounting for a total of 137 sera, 137 fingerpricks and 71 venous whole blood samples. Overall, 8 (8.9%) patients developed ATI (5 ankylosing spondylitis, 1 Crohn's disease, 1 ulcerative colitis and 1 juvenile idiopathic arthritis). ATI were detected in 5 patients treated with Remicade® and 3 treated with Inflectra®. Overall agreements between fingerprick vs venous whole blood and fingerprick vs serum measured with the rapid POC test were 100% and 99%, respectively. Positive (PPA) and negative (NPA) agreements between the POC test and ELISA were 91% and 99%, respectively. PPA and NPA between the ELISA and the POC test in serum was 100% and 99%, respectively.

Conclusions: ATI can be reliably detected in either venous or capillary circulation. Results show an almost perfect agreement between specimens and with the reference ELISA technique. ATI measurement with the POC test allows the clinician to detect ATI in a quick and fully decentralised mode facilitating immediate POC decision making.

Disclosure of Interest: A. Ametzazurra Employee of: Employee of Progenika Grifols, N. Rivera: None declared, A. Balsa: None declared, M. Arreba: None declared, E. Ruiz: None declared, C. Plasencia: None declared, J. Ortiz: None declared, D. Pascual-Salcedo: None declared, M. Muñoz: None declared, C. De Aysa: None declared, M. Allande: None declared, N. Torres Employee of: Employee of Progenika Grifols, A. Hernández Employee of: Employee of Progenika Grifols, X. Recalde Employee of: Employee of Progenika Grifols, A. Martínez Employee of: Employee of Progenika Grifols, D. Nagore Employee of: Employee of Progenika Grifols

DOI: 10.1136/annrheumdis-2017-eular.5056

FRI0196 BIOSIMILARS IN THE UK: EARLY REAL WORLD DATA FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTERS FOR RHEUMATOID ARTHRITIS

D. De Cock[1], K. Watson[1], K.L. Hyrich[1,2] on behalf of BSRBR-RA Control Centre Consortium. *[1]Arthritis Research UK Centre for Epidemiology, University of Manchester; [2]National Institute of Health Research Manchester Musculoskeletal Biomedical Research Unit, Central Manchester NHS Foundation Trust, Manchester Academic Health Science, Manchester, United Kingdom*

Background: Biosimilars, biopharmaceuticals assessed by regulatory agencies

to have efficacy and safety similar to their reference products, were introduced to the UK market in February 2015 for rheumatoid arthritis (RA). Most research on RA biosimilars has been done in the context of clinical trials, but real world data are lacking. No national mandate exists in the UK to switch all patients from originator to biosimilars, but there are regional variations.

Objectives: This analysis aims to describe the characteristics of the first UK patients starting RA biosimilars registered with the British Society for Rheumatology Biologics Register for RA (BSRBR-RA).

Methods: Since 03/08/2015, the BSRBR-RA has captured data on patients starting biosimilars available in the UK: infliximab (Inflectra and Remsima) and etanercept (Benepali). At biosimilar start, information is captured from the hospital including demographic and clinical data, previous biologic exposure and if switching therapies, the reason for switch (as a tick box and free text). Follow-up data, including disease activity, occurrence of adverse events and changes to treatment is captured 6-monthly for 3 years and annually thereafter. Descriptive data are presented.

Results: To 15/12/2016, 417 RA patients were recruited to the BSRBR-RA at point of starting a biosimilar for whom data were available for analysis on 414 participants: 47 (11%) Inflectra, 78 (19%) Remsima and 289 (70%) Benepali. Of these, 138 started a biosimilar as first biologic, 242 switched directly from the originator product and 34 switched from an alternative biologic (Table). Patients switching from the originator did so after a median (IQR) of 6.7 (3.0–9.5) years and the majority had low disease activity (median DAS28 2.7 (IQR 2.0–3.9)). The switch reason was reported in 33% of patients, with cost listed as the main reason and "trust policy" included in 63% of 30 free text comments. Six-month follow-up data were available in 41 patients. Three patients on Remsima and 1 patient on Inflectra reported drug hypersensitivity reactions (rash, pruritus, hyperpigmentation), and 18% (6/34) of patients experienced a deterioration in their DAS28 of >1.2 after 6 months.

Table

	Biological naive	Switched from reference product	Not switched from reference product
Number	138	242	34
Biosimilar, n (%)			
Inflectra	3 (2%)	40 (16%)	4 (12%)
Remsima	9 (6.5%)	65 (27%)	4 (12%)
Benepali	126 (91%)	137 (57%)	26 (76%)
Women, n (%)	108 (78%)	181 (75%)	28 (82%)
Age (years)	56.0 (48.0-64.5)	67.0 (57.0-72.0)	59.5 (44.5-68.0)
Disease Duration (years)	4.0 (1.0-10.0)	17.0 (10.0-24.0)	9.5 (6.0-14.0)
DAS28(CRP)	5.9 (5.3-6.5)	2.7 (2.0-3.9)	5.1 (3.5-6.2)
Comorbidities			
0	52 (38%)	84 (35%)	12 (35%)
1	47 (34%)	84 (35%)	11 (32%)
2	32 (23%)	32 (13%)	5 (14%)
3+	7 (5%)	42 (17%)	6 (19%)
Previous biological on n (%)			
Enbrel	-	137 (57%)	1 (3%)
Remicade	-	105 (43%)	4 (12%)
Kineret	-	-	1 (3%)
Humira	-	-	7 (21%)
Mabthera	-	-	1 (3%)
Orencia	-	-	4 (12%)
Simponi	-	-	4 (12%)
RoActemra	-	-	6 (18%)
Cimzia	-	-	6 (18%)
Reasons to switch, n (%)			
Cost factors	6 (86%)	107 (86%)	2 (50%)
Clinical indication	-	5 (4%)	1 (25%)
Patient choice	-	1 (1%)	1 (50%)
Other	1 (11%)	11 (9%)	-
Follow-up data available, n	5	35	1
DAS28 at 6 months	3.9 (3.1-7.1)	2.8 (2.2-3.9)	5.3

All data presented are numbers (percentages) or median (IQR).

Conclusions: This preliminary study gives an early review of biosimilar use in the UK, showing that these drugs are used in patients with active disease as both first-line and subsequent-line biologics. Many patients with low disease activity are also being switched from originators primarily for cost reasons. Outcome data are limited but data capture will continue and updated reports from the BSRBR-RA will continue to be presented.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3497

FRI0197 ADHERENCE, SATISFACTION AND FULFILLMENT OF EXPECTATIONS OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS BIOLOGICALS. ARCO STUDY

J. Calvo-Alén[1], C. Marras[2], I. Monteagudo[3], G. Salvador[4], T. Vázquez-Rodríguez[5], J. Tovar[6], P. Vela[7], F. Maceiras[8], M. Bustabad[9], E. Peiró[10], J. Rosas[11], M. Arteaga[12], S. Fernández[12], L. Cea-Calvo[12], Y. Mestre[12], E. Raya[13]. *[1]H Txagorritxu, Vitoria; [2]HUV Arrixaca, Murcia; [3]HGU Gregorio Marañón, Madrid; [4]HU Mútua Terrasa, Barcelona; [5]HU Lucus Augusti, Lugo; [6]HGU, Elche; [7]HGU, Alicante; [8]CHU, Vigo; [9]HU, Tenerife; [10]HU Marqués de Valdecilla, Santander; [11]H Marina Baixa, Alicante; [12]Medical Affairs, Merck Sharp & Dohme, Madrid; [13]HU San Cecilio, Granada, Spain*

Background: In patients with rheumatoid arthritis (RA), we previously described that adherence to the subcutaneous (SC) biological treatment is better with monthly administration.

Objectives: We further assessed if there are differences in patients expectations and satisfaction with efficacy and tolerance that could contribute to explain such finding.

Methods: ARCO was a retrospective study on RA patients who had been prescribed a SC biological 11–18 months prior to the study. Adherence was calculated with the medication possession ratio (MPR). Satisfaction and expectations were assessed with the Spanish validated Carbonell questionnaire [1].

Results: We included 364 patients (age 54.9 years [SD 12.5], 77.5% women, median duration of RA 7.8 years, period studied for the SC biological 14.8 months). Non-adherence (MPR ≤80%) was lower in patients with monthly (6.4%) than with weekly (17.4%, p=0.034) or every 2 weeks administration (14.4%, p=0.102). The % of satisfied patients (quite/very satisfied) was 86.2% for efficacy and 64.4% for side effects or tolerance. Non-adherence was similar in satisfied with efficacy and in neutral/unsatisfied patients (14.7% vs. 8.3%, p=0.399), or in patients satisfied/not satisfied with side effects (13.1% vs. 15.4%, p=0.504). The fulfillment of expectations is shown in the table. With regard to expectations on the effect, non-adherence was 15.5% (higher than expected), 12.6% (as expected) and 10.7% (lower than expected) (p=0.677), and with regard to discomfort/side effects, it was 15.6% (greater than expected), 18.5% (as expected) and 11.1% (lower than expected, or no side effect) (p=0.189). Fulfilment of expectation on efficacy was similar for the 3 dosing schemes, but the % reporting lower than expected discomfort or no discomfort was greater with fewer SC injections (table). In particular, the % reporting no discomfort/side effects with the administration were 17.8% (weekly), 29.3% (every 2 weeks), and 35.0% (monthly) (p=0.013).

	All %	Weekly %	Every 2 weeks %	Monthly %	p
Effect of the treatment					
Much/quite higher than expected	59.9	59.2	57.2	66.7	0.573
More or less as expected	32.1	33.6	33.8	25.0	
Quite/much lower than expected	8.0	7.4	9.0	8.3	
Discomfort					
Much/quite higher than expected	13.0	15.8	11.5	10.1	0.048
More or less as expected	34.4	38.2	35.3	23.3	
Quite/much lower than expected or there were no discomfort	52.5	46.0	53.2	66.6	

Conclusions: RA patients on SC biological therapy show high satisfaction and fulfillment of expectations on efficacy, although both aspects lower for tolerance. Dosing regimen with lower number of SC injections seems to be associated with better fulfillment of expectations of tolerance. This finding, added to the lower number of injections itself, might explain the better adherence observed with monthly administration.

References:

[1] Carbonell J, Badia X; Grupo Expresar. Development and validation of a satisfaction questionnaire in patients with rheumatoid arthritis. Reumatol Clin 2006;2:137–45.

Acknowledgements: Funded by MSD, Spain.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3176

FRI0198 USABILITY AND SAFETY OF SB5 (AN ADALIMUMAB BIOSIMILAR) PRE-FILLED SYRINGE AND PRE-FILLED PEN IN PATIENTS WITH RHEUMATOID ARTHRITIS

J. Ghil[1], J. Niebrzydowski[2], A. Zielińska[3], Y. Lee[1]. *[1]Samsung Bioepis Co., Ltd., Incheon, Korea, Republic Of; [2]Medica Pro Familia Sp. z o.o. S.K.A., Gdynia; [3]Medica pro Familia Sp z o.o. S.K.A, Warszawa, Poland*

Background: SB5 is developed as a biosimilar of the reference adalimumab (ADL). Equivalence in pharmacokinetics (PK) and efficacy between SB5-pre-filled syringe (PFS) and ADL-PFS has been demonstrated in a phase I and phase III study.[1,2] The PK equivalence between SB5-PFS and SB5-pre-filled pen (PFP) in healthy subjects has been reported previously.[3]

Objectives: To compare the usability and safety of SB5-PFS and SB5-PFP from a phase II study.

Methods: This was an open-label, single-arm study in patients with rheumatoid arthritis (RA). Patients with RA self-administered a total of 6 injections of 40 mg SB5 every other week; the first two injections were through PFS and the following four injections were through PFP. The primary objective of this study was to demonstrate comparability between PFS (at week 2) and PFP (at week 6) in terms of injection site pain score. Patients completed a pain evaluation questionnaire using an 11-point numeric rating scale at two time points (immediately and 15–30 minutes post-injection) after the first four injections. Equivalence between PFS and PFP was concluded if the 97.5% confidence interval (CI) of the difference in the injection site pain score was contained within the equivalence margin of ±5. Other usability (overall impression and patient preference) and safety endpoints were also measured.

Results: A total of 49 patients were enrolled and 48 patients completed the study. The mean injection site pain score was 2.3 in PFS vs. 2.0 in PFP immediately post-injection and 0.8 in PFS vs. 0.7 in PFP at 15–30 minutes post-injection. At both time points the score was equivalent between PFS and PFP: the 97.5% CI was (–0.99, 0.30) and (–0.47, 0.25) immediately and 15–30 minutes post-injection, respectively.
The overall impression was also comparable between PFS and PFP. There were no patients who had an overall impression of extremely unfavorable and the proportion of patients who had a favorable impression was higher than that of unfavorable impression in both PFS and PFP. The overall preference for PFP (56.5%) was higher than PFS (30.4%) as presented in the Table.
Both PFS and PFP were well tolerated and there were no serious treatment-emergent adverse events. Only one patient after administration of PFS experienced injection site reaction.

Table. Preference between Pre-filled Syringe and Pre-filled Pen

Preference	Pre-filled Syringe n/n' (%)	Pre-filled Pen n/n' (%)	No Preference n/n' (%)
Overall preference	14/46 (30.4)	26/46 (56.5)	6/46 (13.0)
Preference categories			
Ease to use	10/46 (21.7)	33/46 (71.7)	3/46 (6.5)
Convenience	6/46 (13.0)	35/46 (76.1)	5/46 (10.9)
Time to administration injection	9/46 (19.6)	30/46 (65.2)	7/46 (15.2)
Safety	6/46 (13.0)	31/46 (67.4)	9/46 (19.6)
Less pain	17/46 (37.0)	21/46 (45.7)	8/46 (17.4)

Conclusions: The injection site pain score of PFS and PFP was comparable with overall preference rate higher for PFP. Both PFS and PFP were well tolerated with similar safety profiles.
References:
[1] Shin D et al. Ann Rheum Dis. 2015; 74 (Suppl2: 459–460), FRI0110.
[2] Weinblatt ME et al. Arthritis Rheumatol. 2015; 67 (suppl 10).
[3] Shin D et al. Ann Rheum Dis 2016;75(Suppl2): 1005.
Disclosure of Interest: J. Ghil Employee of: Samsung Bioepis Co., Ltd., J. Niebrzydowski Grant/research support from: Samsung Bioepis Co., Ltd., A. Zielińska Grant/research support from: Samsung Bioepis Co., Ltd., Y. Lee Employee of: Samsung Bioepis Co., Ltd.
DOI: 10.1136/annrheumdis-2017-eular.3350

FRI0199 SYSTEMATIC REVIEW AND META-ANALYSIS ON CERTOLIZUMAB PEGOL FOR RHEUMATOID ARTHRITIS IN ADULTS

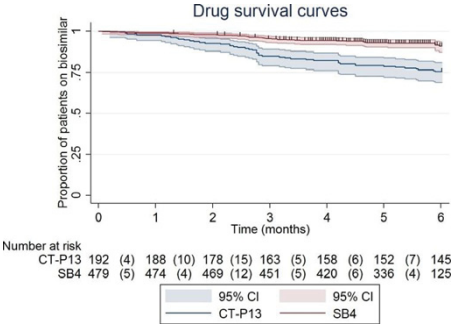
J.A. Bernal[1], P. Vela[1], V. Ruiz García[2], A. Burls[3], J.B. Cabello[4], S. Bort-Martí[5]. *[1]Rheumatology, Hospital General Universitario de Alicante, Alicante; [2]Hospital at Home Unit, la Fe University Hospital, Valencia, Spain; [3]School of Health Sciences, University of London, London, United Kingdom; [4]Cardiology & CASP Spain, Hospital General Universitario de Alicante, Alicante; [5]Acella Incubator, Paterna, Valencia, Spain*

Background: The appearance of tumor necrosis factor-alpha (TNFalpha) inhibitors dramatically changed the prognosis of rheumatoid arthritis. Certolizumab pegol (CZP) is a human Fab fragment of anti-TNFalpha monoclonal antibody which is approved for the treatment of rheumatoid arthritis. We performed a systematic review and meta-analysis, with Cochrane methodology, of the effects of CZP in rheumatoid arthritis.
Objectives: To assess the clinical benefits and harms of CZP in patients with rheumatoid arthritis.
Methods: We performed a search of electronic database (Cochrane Database, MEDLINE, EMBASE, Web of Knowledge and clinicaltrials.gov) until 26th September 2016. We searched for randomized controlled trials of CZP in rheumatoid arthritis compared to any other agent including placebo.
Results: 14 trials were included for the meta-analysis, 12 (5422 patients) in the pooled analysis for benefits and 14 (5499 patients) in the pooled analysis for safety. The overall possibility of bias seemed to be low but the quality of the evidence was low due to the risk of attrition bias.
With the approved dose - CZP 200 mg subcutaneous every other week with the first three doses of 400 mg - CZP showed statistically significant improvements at 24 weeks compared to placebo in: ACR50 absolute improvement 27% (95% CI 20% to 33%), RR 3.8 (95% CI 2.42 to 5.95) and NNT=4 (95% CI 3 to 8); DAS28 $<$2.6 - original definition of remission - with RR 3.79 (95% CI 1.90 to 7.56); HAQ with -12% absolute improvement (95% CI -9% to -14%); and erosion score with -0.29% (95% CI -0.42% to -0.17%). There are also data available at 12 weeks with RR of 1.99 (95% CI 1.44 to 2.76) of achieving DAS28$<$2.6 with CZP 200 mg dose. The proportion of patients achieving DAS28$<$2.6 was still higher with CZP at 52 weeks with RR of 1.83 (95% CI 1.53 to 2.18).
Serious adverse events were more frequent for CZP 200 mg dose with a RR of 1.47 (95% CI 1.13 to 1.91) and NNH of 32. There have been eight adverse events leading to death in CZP 200 mg group versus two in the control group (not statistically significant) and 10 patients developing tuberculosis versus two in the control group (not statistically significant).
Conclusions: There is low level evidence from randomized controlled trials that CZP as monotherapy or combined with methotrexate improved ACR50, DAS28, HAQ and joint damaged on x-ray. Adverse events were more frequent with active treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6433

FRI0200 HIGHER ACCEPTANCE AND PERSISTENCE RATES AFTER BIOSIMILAR TRANSITIONING IN PATIENTS WITH A RHEUMATIC DISEASE AFTER EMPLOYING AN ENHANCED COMMUNICATION STRATEGY

L. Tweehuysen[1], V.J.B. Huiskes[2], B.J.F. van den Bemt[2,3], F.H.J. van den Hoogen[1,4], A.A. den Broeder[1,4]. *[1]Rheumatology; [2]Pharmacy, Sint Maartenskliniek; [3]Pharmacy; [4]Rheumatology, Radboudumc, Nijmegen, Netherlands*

Background: In blinded trials, transitioning from an innovator to a biosimilar has shown to be equivalent to maintenance on innovator biologic treatment in rheumatic diseases. However, data on open label transitioning to a biosimilar are scarce. Recently, we sequentially implemented two biosimilar transition projects (from innovator infliximab (REM) to biosimilar infliximab (CT-P13) and from innovator etanercept (ENB) to biosimilar etanercept (SB4)) in patients with a rheumatic disease using different communication strategies.
Objectives: To investigate the impact of different communication strategies on the acceptance and persistence rates after transitioning from ENB to SB4 in 2016 and transitioning from REM to CT-P13 in 2015.
Methods: Adult patients treated with REM or ENB were informed by letter about the request to transition to a biosimilar. Subsequently, patients were approached by telephone to ask whether they agreed. After the transition of REM to CT-P13 had finished, communication was enhanced for the transition of ENB to SB4 by 1) informing all patients at the same time directly followed by a national media item, 2) reporting that lower costs and fewer injection site reactions (demonstrated in a previous trial) were the reason for transitioning, 3) providing a "soft skills" training for rheumatology and pharmacy staff about how to assuage patient concerns regarding a biosimilar and how to act if a patient has objective or subjective health complaints (discuss possible nocebo response and incorrect causal attribution). Also, group think effects did not play a role during SB4 treatment (individual subcutaneous versus group intravenous administration). Transitioning patients were eligible for inclusion in the BIO-SWITCH study (switch REM to CT-P13) and BIO-SPAN study (switch ENB to SB4)[1]. Demographic, disease and treatment specific characteristics at baseline and disease activity and adverse events (AEs) during 6 months follow-up were collected.
Results: 196 of 222 (88%) REM-treated patients and 636 of 643 (99%) ENB-treated patients transitioned to respectively CT-P13 and SB4 (delta 11%, 95% CI 7% to 16%). Until January 1st 2017, 479 of 636 (75%) patients gave informed consent for the BIO-SPAN study. Baseline characteristics were similar, except for disease duration and innovator treatment duration (both shorter in the BIO-SPAN cohort; p$<$0.01). Drug survival of patients on SB4 was adjusted for confounders greater than patients on CT-P13 (Figure 1; adjusted Hazard Rate 0.21, 95% CI 0.13 to 0.34). During 84 person-years of follow-up 47 patients discontinued CT-P13 (56/100 person-years; 26% due to inefficacy, 74% due to AEs). In contrast, 36 patients discontinued SB4 during 230 person-years of follow-up (16/100 person-years; 53% due to inefficacy, 42% due to AEs and 5% due to remission).



Conclusions: Use of an enhanced communication strategy, together with more experience and absence of group think effects, resulted in much higher acceptance and persistence rates after open label shared decision making biosimilar transitioning in patients with a rheumatic disease.
Acknowledgements: This study was funded by Biogen
Disclosure of Interest: L. Tweehuysen: None declared, V. Huiskes: None declared, B. van den Bemt Speakers bureau: Pfizer, AbbVie, Mundipharma, F. van den Hoogen Consultant for: Biogen, Celltrion, Janssen, Mundipharma and Sandoz, A. A. den Broeder Consultant for: AMGEN
DOI: 10.1136/annrheumdis-2017-eular.2889

FRI0201 ETANERCEPT RETENTION PATTERNS AND FACTORS ASSOCIATED WITH TREATMENT DISCONTINUATION: A RETROSPECTIVE COHORT STUDY USING CANADIAN CLAIMS-LEVEL DATA

M. Khraishi[1], Y. Zhang[2], J. Ivanovic[2], B. Millson[2], M.-J. Brabant[2], K. Charland[2], E. Singh[3], J. Woolcott[4], H. Jones[3]. [1]*Faculty of Medicine, Memorial University of Newfoundland, St. Johns;* [2]*Health Access & Outcomes, QuintilesIMS, Kanata, Canada;* [3]*Inflammation and Immunology, Global Medical Affairs, Pfizer Inc., Collegeville, United States;* [4]*Health Economics and Outcomes Research, Pfizer Inc., Kirkland, Canada*

Background: Etanercept is a soluble TNF receptor (humanized protein) indicated for the treatment of immune-mediated inflammatory diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and psoriasis (PsO). Limited information exists on the factors associated with long-term retention and use of etanercept in Canada in a real-world setting.
Objectives: To evaluate the 6-year retention rates of etanercept patients in Canada, and to identify factors associated with discontinuation.
Methods: A retrospective cohort study was conducted using longitudinal prescription drug claims data from QuintilesIMS Private Drug Plan database (PDP), Ontario Public Drug Plan database (OPDP), and Quebec Public Drug Plan database (RAMQ). Between 07/2008 and 06/2010, bio-naïve patients who initiated etanercept were identified and followed for 72 months. 12-month retention rates were evaluated in 1-year increments for all patients retained on therapy at years 1, 2, 3, 4 and 5 and compared to retention rates in the first year. The covariates associated with time to discontinuation over the entire 72 month period were identified using a Cox proportional hazards regression model.
Results: The study identified 4,528 etanercept patients (61% female, 85% rheumatic diseases, and 15% PsO) across Canada who started their therapy during the selection period. Overall, 12-month retention rates on etanercept increased significantly for patients following their first year on therapy ($p<.0001$), with 66% of patients retained at year 1 vs. 12- month retention rates of 79%, 82%, 84%, 83% and 79% at year 2, 3, 4, 5 and 6, respectively. A total of 17.1% (n=771) of patients were retained for the entire 72 month study. Regression analysis showed PsO patients were less likely to be retained on therapy than other indications (HR 1.199; $p<.0001$), older patients (65+) were more likely to be retained than younger patients (HR 0.802; $p<.0001$), and public plan patients (ODB HR 0.735, RAMQ HR 0.55; $p<.0001$) were more likely to be retained than private plan patients.
Conclusions: Etanercept patient retention likelihood increased the more years a patient was retained on therapy. This pattern was consistent across therapeutic areas, sex, age, and payers. Age, indication, and payer were found to have a significant impact in determining etanercept patients' time to therapy discontinuation. With better understanding of factors associated with retention, patient support programs can be designed to address the specific needs of at-risk groups while supporting patients stable on therapy.
Disclosure of Interest: M. Khraishi Consultant for: Pfizer Canada and Amgen Canada, Y. Zhang: None declared, J. Ivanovic: None declared, B. Millson: None declared, M.-J. Brabant: None declared, K. Charland: None declared, E. Singh: None declared, J. Woolcott: None declared, H. Jones: None declared
DOI: 10.1136/annrheumdis-2017-eular.6312

FRI0202 THE DIFFERENT EFFECT OF TNFα BLOCKERS AND SDMARDS ON LIPOPROTEIN SUBCLASSES IN RA PATIENTS. A PERSPECTIVE CONTROLLED LONGITUDINAL STUDY

M. Zakalka[1], M. Karakota[2], G. Koliakos[3], L. Settas[1]. [1]*Division of Clinical Immunology/Rheumatology, 1st Internal Medicine Department, AHEPA University Hospital, Medical School, Aristotle University;* [2]*Laboratory of Biological Chemistry;* [3]*Laboratory of Biological Chemistry, Aristotle University, Thessaloniki, Greece*

Background: The different antirheumatic drugs reduce inflammation in RA patients, causing alterations in cholesterol levels (mainly decreasing LDL and increasing HDL cholesterol levels), but HDL and LDL structure and function predict cardiovascular disease better than LDL and HDL cholesterol levels.
Objectives: The investigation of the qualitative changes of LDL and HDL lipoprotein subclasses in RA patients who are good responders, depending on the anti-inflammatory treatment (sDMARDs vs anti-TNFa+sDMARDs) and their in between associations.
Methods: 85 patients ((89%) 76females) with established RA (mean disease duration ≥5 yrs), mean age 57 yrs (SD: 12yrs), without known cardiovascular disease, D/M and thyroid disorders, on sDMARD (MTX, LEF, SSZ, low dose prednisolone or combination) and naïve to biologic treatment, were divided into two groups: the 1st one of 43 patients who had $DAS_{28}>3.2$ and were given in addition a TNFα inhibitor (23 patients had golimumab and 20 patients had certolizumab-pegol) for at least 54weeks (mean treatment duration 18 months) with good clinical response according to Eular and the 2nd group of 42 patients (disease control group) with $DAS_{28}\leq3.2$,who continued on sDMARDs and followed closely the same time period so as to ensure, as well, good clinical response without biologic therapy. Plasma electrophoresis was performed in two time points, before and after anti-TNFα administration and on the same time for the control group, with non-denaturing polyacrylamide gel (ND-PAGE) for size-based separation of lipoprotein subclasses, a standard laboratory technique that indentify various HDL subspecies separable on the basis of average diameter/size into 6 distinct subclasses (HDL-1, HDL2a, HDL2b, HDL3a, HDL3b, HDL3c), as well as LDL lipoprotein into 2 subfractions (LDL-B, LDL-A.)
Results: The RA patients on DMARDs had a percent reduction of LDL-B subfraction by 11.9% (p=0.014), but a significant increase of HDL-3c subclass by 2.38% (p=0.049). In a multivariate model of stepwise logistic regression the after (treatment)-LDL-B subfraction in these patients was found to have significant positive association only with pro-LDL-B subfraction (odds ratio: 10.95, %CI (1.59–62.79)). In the RA patients who took TNFα inhibitors was observed a prominent percent decrease of the more lipoprotein subclasses: LDL-B by 2.33% (p=0.005), LDL-A by 2.33% (p=0.0001), HDL3a by 11.63% (p=0.072) and HDLc by 4.65% (p=0.035). Accordingly, in stepwise logistic regression the after-(treatment) LDL-B subfraction had a significant positive association only with pro-LDL-B subfraction (odds ratio: 12.91,95% CI (2.2–75.83)), as well as, after-LDL-A with pro-LDL-A subfraction (odds ratio:36.16, 95% CI (5.05–258.89)), whereas the reduced after (treatment)-HDL3c subclass was significantly positively associated with pro-HDL3a subclass (odds ratio:8.15, 95% CI (1.04–63.65)) and after-HDLa subclass (odds ratio:22.09, 95% CI (3.56–137.18)).
Conclusions: The discrepancy of qualitative modification of lipoprotein subclasses (LDL and HDL) after treatment with different antirheumatic drugs (sDMARDs, anti-TNFa+sDMARDs) demonstrate their different effect on RA dyslipidemia and their subsequent antiatherogenic prospective.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4507

FRI0203 GOLIMUMAB IN BIOLOGIC-NAÏVE PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS (RA), PSORIATIC ARTHRITIS (PSA) OR ANKYLOSING SPONDYLITIS (AS) - SUBANALYSIS FROM THE NON-INTERVENTIONAL EVALUATION GO-NICE

K. Krüger[1], G.R. Burmester[2], S. Wassenberg[3], M. Bohl-Bühler[4], M.H. Thomas[5]. [1]*Rheumatologisches Praxiszentrum, München;* [2]*Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin, Berlin;* [3]*Rheumazentrum Ratingen, Ratingen;* [4]*Rheumahaus Potsdam GbR, Potsdam;* [5]*Medical Affairs, MSD Sharp & Dohme GmbH, Haar, Germany*

Background: Golimumab (GLM) has demonstrated efficacy and safety in several randomized clinical trials with biologic-naïve patients. However, data from effectiveness and patient-reported outcomes (PROs) parameters in daily clinical practice in Germany are still lacking
Objectives: The aim of this subanalysis is to assess Golimumab on the effectiveness, and PROs in biologic-naïve patients with established RA, PsA or AS
Methods: This is a subanalysis of the non-interventional, prospective, 24-month study GO-NICE. Biologic-naïve patients with established RA, PsA or AS starting with GLM 50mg SC once monthly in a real life setting in Germany. Endpoint measures: disease activity DAS28, PsARC and BASDAI. PROs included QoL (EQ-5D-3L), functionality (FFbH), fatigue (FACIT-F). Safety data were also collected
Results: *RA patients* (n=265): Mean age 54.5 yr, 82.1% of the patients were female, 77.3% (n=204) were rheumatoid factor (RF) positive, and 76.4% (n=201) had anti-ccp antibodies at BL.
The DAS28 score at BL was 5.0 and dropped significantly to 2.9 within 24 months ($p<0.0001$ v. BL). After 3 months of treatment, 45.2% of patients had LDA (DAS28 ≤3.2), which increased to 50.8% after 6 month and 64.9% after 24 months.
PsA patients (n=247): Mean age 49.7 yr, 53.8% of the patients were female, 42.1% (n=104) had a nail involvement, 25.5% (n=63) dactylitis and 13.8% (n=34) enthesitis at BL. The proportion of patients achieving a response (mod PsARC) was 64%, 72.2% and 77.7% at 3, 6 and 24 months, respectively.
AS patients (n=246): Mean age 41.9 yr, 70.7% of the patients were male, 80.5% (n=198) were HLA-B27 positiv. Most common extraarticular manifestations were: enthesitis (12.6%), iritis (12.2%), IBD (3.7%), and dactylitis (2.8%) at BL.
The BASDAI at BL was 5.0 and dropped significantly to 2.0 within 24 months ($p<0.0001$ vs. BL). The proportion of patients achieving a response (BASDAI 50) was 62.2%, 66.9% and 76.9% at 3, 6 and 24 months, respectively.
An improvement of quality of life (QoL) by EQ-5D-3L was seen after 6 months and was maintained over 24 months. The patients' health state today (EQ VAS) improved from 52.3 at BL to 64.9 (RA), from 49.0 to 66.3 (PsA) and from 49.2 to 70.6 (AS). The functional ability (FFbH) improved significantly ($p<0.0001$ vs. BL) from 73.1 to 80.4 points (RA), from 73.0 to 82.2 (PsA) and from 72.8 to 81.2 (AS). The mean Fatigue score (FACIT-F) increased from BL: 33.3 to 39.5 points (RA), from 31.6 to 38.4 points (PsA), and from 31.6 to 40.2 points (AS) (each $p<0.001$ vs BL) within 24 months.
No new safety signals were detected.
Conclusions: GLM SC once-monthly showed after 3 months remarkable improvements in clinical effectiveness, patient-reported quality of life, functionality, and fatigue parameters and were maintained over 24 months in biologic-naive patients with established RA, PsA or AS.
At month 24, 64.9% of RA patients achieved LDA status, 77.7% of PsA achieved positive PsARC response and 76.9% of AS patients achieved BASDAI 50.
No new safety signals were detected.

Disclosure of Interest: K. Krüger Consultant for: AbbVie, BMS, Celgene, Janssen Biologics, MSD, Pfizer, Roche, and Sanofi-Aventis, G. Burmester Consultant for: AbbVie, BMS, MSD, Pfizer, Roche, and UCB, S. Wassenberg Consultant for: AbbVie, Chugai, Janssen Biologics, MSD, Novartis, Pfizer, Roche, and UCB, M. Bohl-Bühler Consultant for: AbbVie, Hexal, MSD, Roche, and UCB, M. Thomas Employee of: MSD Sharp & Dohme GmbH Germany
DOI: 10.1136/annrheumdis-2017-eular.5154

FRI0204 COMPARISON THE LONG-TERM CLINICAL OUTCOMES BETWEEN NONTNF-INHIBITORS VERSUS TNF-I IN RA PATIENTS WHO FAILED TO A FIRST TNF-I

P. Bogas[1], C. Plasencia[1], D. Pascual-Salcedo[2], G. Bonilla[1], E. Moral[1], C. Tornero[1], L. Nuño[1], A. Villalba[1], D. Peiteado[1], A. Martinez[2], B. Hernandez[2], A. Balsa[1]. *[1]Rheumatology; [2]Immunology, Hospital Universitario la Paz, Madrid, Spain*

Background: There are many biological therapies for Rheumatoid Arthritis (RA) with different mechanisms of action and good efficacy rate; however, up to 40% of patients (pts) fail to respond to the 1st biologic agent, and it is still not clear what strategy to follow after showing inadequate response to tumor necrosis factor α inhibitors (TNF-i)
Objectives: To assess the clinical response and survival (SVV), in our cohort of RA pts that discontinued the 1st TNF-i, of a 2nd TNF-i vs a nonTNF-i, both in the global cohort and in the subpopulation that dropped out the 1st TNF-I due to inefficacy
Methods: This observational study included 110 pts in the RA-Paz cohort who previously suspended Ifx (68%) or Ada (32%) between 1999–2016. Two groups were established as they switched to a TNF-i or nonTNF-i. Clinical response was evaluated by DAS28, Delta-DAS28 (∆DAS28) and EULAR response (E-resp). The assessments were performed at 6 (v-6) and 12 months (v-12) since initiating 2nd biological agent and during the last visit prior to drug discontinuation or ending of the study for those who did not interrupt the drug (v-end). Statistical analysis was performed using SPSS version 20.0
Results: Of the 110 pts who had stopped Ifx or Ada as 1st TNF-i, 65% changed to a 2nd TNF-i. The 84% of the overall pts were women. The mean age was 64±14 years and the mean time of 2nd biologic drug was 3.71±3.51 years. 61% associated methotrexate at the beginning of 2nd biologic agent and 56% at the v-end, without differences between those who switched to TNF-i and those who did to nonTNF-i. At v-6 and v-12, there was no difference in ∆DAS28 [at v-6:1.3±1.4 in TNF-i and 1.2±1.2 in nonTNF-i (p=0.919), at v-12: 1.3±1.5 in TNF-I and 1.2±1.1 in nonTNF-i (p=0.852)]. In contrast, at v-end, pts with nonTNF-i showed a higher clinical improvement (∆DAS28: 0.68±1.7 in TNF-i, 1.8±1.1 in nonTNF-i, p=0.002). At v-6, the TNF-i group achieved higher good E-resp rate (41% vs 18%, p=0.035), but there was no difference at v-12 (36% in TNF-I vs 23% in nonTNF-i, p=0.435). However, at v-end, the nonTNF-I group achieved better E-resp (good resp: 38% in nonTNF-i vs 25% in TNF-I, no resp 18% in nonTNF-i vs 50% in TNF-i, p=0.01). Likewise, 100% (n=7) of the pts that finished 2nd biologic agent by remission, had changed to a nonTNF-i (p<0.00001). There were no differences regarding 2nd biologic drug SVV (mean SVV time of 5.7±0.66 in TNF-I, 4.3±0.59 in nonTNF-i, p=0.797). When analyzing the cohort that discontinued 1st TNF-I because of inefficacy, at v-6 and v-12 there were no differences between switchers to TNF-I and nonTNF-i in ∆DAS28 [v-6: 1.4±1.4 vs 0.9±1 p=0.164); v-12: 1.5±1.4 vs 1±1, p=0.192)], but at v-end, the nonTNF-i group reached a higher ∆DAS28 (0.9±1.5 in TNF-i, 1.6±1 in nonTNF-i, p=0.031)

Demographic characteristics	
Age (years)	64±13,9
Sex (female)	92 (84%)
Smokers	18 (16%)
BMI	26,6±7,7
Disease duration (years)	16,7±8,04
RF +	94 (85%)
Anti-CCP +	96 (89%)
Duration of treatment 1st biological (years)	3,2±3,1
Basal DMARDs (2º biological)	99 (90%)
Basal MTX (2º biological)	67 (61%)
v-Final FAMEs (2º biological)	93 (86%)
v-Final MTX (2º biological)	60 (56%)
Basal CPR (2º biological)	15,2±18,7
Basal ESR (2º biological)	42±24,1
Basal DAS (2º biological)	5,55±1,3

Conclusions: In our sample of RA patients who suspended Ifx/Ada as 1st TNF-i, switching to a 2nd biologic agent did not show relevant clinical differences between a TNF-i and a nonTNF-i within the 1st year of treatment. However, in the long-term, switching to a nonTNF-i shows enhanced clinical benefits with no impact on survival vis-à-vis a 2nd TNF-i. Despite the efficacy of TNF-i, new therapeutic targets are needed for those who fail to respond to these biological agents
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4383

FRI0205 CORRELATION OF PATIENT PREFERENCES TO TREATMENT OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) TREATED WITH ANTI-TNF AGENTS IN GREECE. THE PANORAMA STUDY

P. Sidiropoulos[1], A. Bounas[2], P. Athanassiou[3], A. Andrianakos[4], E. Petrikkou[5], A. Drosos[6], D. Vassilopoulos[7]. *[1]Department of Rheumatology, Clinical Immunology and Allergy, University of Crete, Heraklion; [2]Private practice, Patras; [3]Rheumatology Division, General Hospital of Thessaloniki St. Paul, Thessaloniki; [4]IASO General Hospital; [5]Medical Affairs, MSD, Athens; [6]Rheumatology Clinic, University of Ioannina, Ioannina; [7]Joint Rheumatology Program, Clinical Immunology-Rheumatology Unit, 2nd Department of Medicine and Laboratory, National and Kapodistrian University of Athens, Athens, Greece*

Background: Route and frequency of administration of treatment options may be an important differentiator between drugs that are used to treat RA and patient preferences may influence adherence to and outcomes of therapy.
Objectives: The objective of this study was to assess the correlation between the fulfillment of patient preferences and clinical and patient reported outcomes.
Methods: PANORAMA was a non-interventional, prospective, multicenter, cohort study. Patients were either biologic naïve or experienced who initiated/switched to anti-TNF at enrollment. Post physician's anti-TNF choice, patients completed a preferences questionnaire over attributes related to anti-TNF treatment. Satisfaction with treatment was assessed with the TSQM questionnaire and compliance (proportion of full doses/planned) was recorded via the use of a patient diary. Persistence was defined as the time period between first and last anti-TNF administration. The observational period was 12 months, with study visits every 3 months.
Results: A total of 254 patients were enrolled in the study. The mean patient age was 58.3±13.4 years, 82.7% were female, 65.4% were biologic naïve and 66.1% had severe disease (DAS-28 ESR>5.1).The mean DAS-28 and HAQ-DI scores at enrollment were 5.5±1.1 and 1.4±0.6 respectively, while mean disease duration was 6.7±6.2 years with 53.2% of patients being seropositive (RF (+):49.2%, Anti-CCP (+): 40.5%). A monthly administration was most preferred by patients (65.7% vs. 20.1% for twice per month, 11.8% for once per week and 3.9% for twice per week), and the large majority of patients (75.2%) preferred the subcutaneous mode of administration. The mean compliance and 12-month persistence rates were 97.0% and 72.3% respectively. At 12 months, good EULAR response rate was achieved by 56.5% of patients and 40.8% were in DAS-28 remission. Univariate analysis demonstrated that fulfillment of patient preferences was correlated to good EULAR response (p<0.001), increased probability of being persistent (p=0.019) and satisfaction with treatment (p=0.063). Multivariate logistic regression analysis revealed that a good EULAR response was associated with satisfaction of patient preferences (OR 5.560, p<0.001), good patient knowledge of the disease (OR 1.327, p=0.006), absence of history of comorbidities (OR 2.42, p=0.014) and lower SJC (OR 1.10, p=0.021), whereas anti-TNF persistence at 12 months was associated (Cox regression analysis) with seropositivity (HR 0.566, p=0.047) and a high baseline ESR (>35 mm/h (HR 0.587, p=0.071)).
Conclusions: In anti-TNF treated RA patients, fulfillment of expressed treatment preferences was independently associated with a good EULAR response and correlated with drug persistence at 12 months, emphasizing the importance of patient preferences in treatment outcomes.
Acknowledgements: The study was funded by Merck Sharp & Dhome S.A., Greece
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4920

FRI0206 CORRELATION BETWEEN THE SERUM ETANERCEPT LEVEL AND RESPONSE TO ETANERCEPT TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

S.M. Zivojinovic[1], M. Sefik-Bukilica[2], N.S. Damjanov[3]. *[1]Clinical IV; [2]Laboratory department; [3]Head of Institute of rheumatology, Institute of Rheumatology, Belgrade, Serbia*

Background: It is well documented that the blockade of TNF-α significantly reduces disease activity in patients with rheumatoid arthritis (RA). However, at least one third of patients receiving etanercept either do not respond to treatment, or lose initial responsiveness [1]. Recent findings indicate that lack of clinical response may be related with lowering the serum drug levels.
Objectives: To investigate the relationship between serum etanercept levels and response to etanercept treatment in patients with RA.
Methods: The study population consisted of fifty eight patients with rheumatoid arthritis (RA), all treated with etanercept. Disease activity was assessed according to the 28-joint count *Disease Activity* Score (*DAS28*) at baseline and 6 months of

therapy. Clinical response was assessed using the European League Rheumatism (EULAR) response criteria [2]. Serum etanercept levels were measured by sandwich ELISA based on the ability of etanercept to bind TNF. Antibodies against etanercept were measured by bridging ELISA (Promonitor).

Results: The 47 female and 11 male were of a mean age 52.1±11.2 years (22–87) and have been living with RA for a mean of 13.2±8.2 years (2–24). At baseline the DAS28-$_{ESR}$ mean score was 6.1±1.0. After six months of etanercept treatment, 20 (34.5%) patients were in remission, 20 (34.5%) were in low disease activity and 18 (31%) were in moderate disease activity. The serum etanercept levels were significantly higher in patients in remission compared with patients in moderate disease activity (p=0.05). According to the EULAR response criteria, RA patients were divided into responders (52pts, 89.7%) and non-responders (6 pts, 10.3%). Median etanercept levels in all patients were 3.937mcg/ml. There were no statistical differences in etanercept levels between responders and non-responders patients (p=0.41). In addition, we stratified all patients into quartiles according to height of the etanercept level. The percentage of EULAR good responders was significantly different between the highest and the lowest quartiles ($p<0.05$).

Anti-etanercept antibodies were not found in any of the studied patients (0/58).

Conclusions: Patients with RA who did not respond to etanercept treatment achieved lower etanercept levels compared with responding patients. Higher concentrations of the drug were associated with a better response to treatment. Further studies are needed to provide evidence for this approach.

References:

[1] Morand EF, Murphy K, Mackay F, Mariette X, Marcelli C. Antidrug antibodies (ADAb) to tumour necrosis factor (TNF)-specific neutralising agents in chronic inflammatory diseases: a real issue, a clinical perspective. Ann Rheum Dis. 2013 Feb;72(2):165–78.

[2] Van Gestel AM, Anderson JJ, van Riel PL, et al. ACR and EULAR improvement criteria have comparable validity in rheumatoid arthritis trials. American College of Rheumatology European League of Associations for Rheumatology.J Rheumatol 1999; 26:705–11.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5957

FRI0207 INDUCTION OF SUSTAINED REMISSION IN EARLY INFLAMMATORY ARTHRITIS WITH THE COMBINATION OF INFLIXIMAB PLUS METHOTREXATE, METHOTREXATE ALONE OR PLACEBO: THE DINORA TRIAL

T.A. Stamm[1], K. Machold[2], D. Aletaha[2], F. Alasti[2], P. Lipsky[3], D. Pisetsky[4], R. Landewe[5], D. van der Heijde[5], A. Sepriano[5], M. Aringer[6], D. Boumpas[7], G. Burmester[8], M. Cutolo[9], W. Ebener[10], W. Graninger[11], T. Huizinga[5], G. Schett[12], H. Schulze-Koops[13], P.P. Tak[14], F. Breedveld[15], J. Smolen[16].

[1]Center for Medical Statistics, Informatics, and Intelligent Systems, Section for Outcomes Research, Medical University of Vienna, Vienna; [2]Rheumatology, Medical University of Vienna, Wien, Austria; [3]-, -, Charlottesville, Virginia; [4]Duke University Medical Center, Durham, North Carolina, United States; [5]Rheumatology, Leiden University Medical Centre, Leiden, Netherlands; [6]Rheumatology, University Medical Center and Faculty of Medicine Carl Gustav Carus at the TU Dresden, Dresden, Germany; [7]Rheumatology, University of Crete, Athens, Greece; [8]Rheumatology, Charité, Berlin, Germany; [9]Rheumatology, University of Genova, Genova, Italy; [10]Rheumatology, Hietzing Hospital, Vienna; [11]Rheumatology, Medical University Graz, Graz, Austria; [12]Internal Medicine 3, Friedrich-Alexander University, Erlangen; [13]Rheumatology, Ludwig Maximilians University of Munich, Munich, Germany; [14]Rheumatology, University of Amsterdam, Amsterdam; [15]Leiden University Medical Centre, Leiden, Netherlands; [16]Rheumatology, Medical University of Vienna, Vienna, Austria

Background: Rheumatoid arthritis is a chronic form of inflammatory arthritis that is thought to have an early stage or reversibility with effective therapy ("window of opportunity").

Objectives: In the present study, we explored the effects of induction therapy with anti-TNFα antibody infliximab (IFX) plus methotrexate (MTX) compared with MTX alone and with placebo (PL) in patients with very early inflammatory arthritis.

Methods: In an investigator-initiated, double-blind, randomized, placebo-controlled, multi-center trial, patients with synovitis of 12–16 weeks duration in at least 2 joints underwent one year of treatment with IFX in combination with MTX, MTX monotherapy or PL randomized in a 2:2:1 ratio. The primary endpoint was clinical remission after 1 year (sustained for at least two consecutive visits 8 weeks apart including week 54) with remission defined as no swollen joints, 0 - 2 tender joints and a C-reactive protein (CRP) level within the normal range (<0.5 mg/dl) or a normal ESR (<25 mm/h). Further, sustainability of remission was assessed during the second year of the study, during which patients received no treatment. The trial was registered at www.isrctn.com (ISRCTN21272423).

Results: See Table 1.

Table 1. Number of patients in clinical remission at 6 months, one year and two years

	1: IFX+MTX (N=38)	2: MTX (N=36)	3: PL (N=16)
6 Mo	10 (26%)	6 (17%)	0
1 Year*	12 (32%)	5 (14%)	0
2 Years*	9 (24%)	1 (3%)	3 (19%)

*$p<0.05$ across the three groups.

90 patients participated in the present study. At week 54 (primary endpoint), 32% of the patients in the IFX+MTX group achieved sustained remission compared with 14% on MTX alone and 0% on PL (Table). This difference was statistically significant for all three groups ($p<0.05$) and for IFX+MTX vs PL ($p<0.05$) separately, but not for IFX+MTX vs MTX (p=0.10), nor for MTX vs PL (p=0.31). Remission was maintained during the second year on no therapy in 75% of the IFX+MTX patients but was lost in 80% of the MTX-only-patients (Table). The analysis of radiographic progression did not reveal significant differences between the three treatment groups. The number needed to treat (NNT) to achieve one additional sustained remission at 52 weeks with IFX+MTX was 3 compared to placebo; the NNT for MTX alone versus placebo was 7 (NNT=6 for IFX+MTX vs MTX alone).

Conclusions: These results indicate that patients with early arthritis can benefit from induction therapy with anti-TNF plus MTX compared to MTX alone, suggesting the existence of a window of opportunity where intensive treatment can alter the disease evolution

Disclosure of Interest: T. Stamm Grant/research support from: For all authors: DINORA was partly funded by a grant from Janssen (previously Centocor). TS: AbbVie, Consultant for: AbbVie, Novartis, Speakers bureau: AbbVie, Janssen, MSD, Novartis and Roche, K. Machold: None declared, D. Aletaha Grant/research support from: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen and Roche, Consultant for: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen and Roche, F. Alasti: None declared, P. Lipsky Consultant for: Janssen, EMD Serono, Astra Zeneca, UCB, Roche, Celgene, Sanofi and Horizon, but none of them relates to the content of this manuscript, D. Pisetsky: None declared, R. Landewe Grant/research support from: Abbott, Amgen, Centocor, Novartis, Pfizer, Roche, Schering-Plough, UCB and Wyeth, Consultant for: Abbott/AbbVie, Ablynx, Amgen, Astra-Zeneca, Bristol Myers Squibb, Celgene, Janssen (formerly Centocor), Galapagos, Glaxo-Smith-Kline, Novartis, Novo-Nordisk, Merck, Pfizer, Roche, Schering-Plough, TiGenix, UCB and Wyeth, Employee of: RL is director of Rheumatology Consultancy BV which is a registered company under Dutch law., Speakers bureau: Abbott/AbbVie, Amgen, Bristol Myers Squibb, Janssen (formerly Centocor), Merck, Pfizer, Roche, Schering-Plough, UCB and Wyeth, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boeringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi and UCB, Employee of: DH is director of Imaging Rheumatology bv., A. Sepriano: None declared, M. Aringer Grant/research support from: MA's institution is clinical trial site for AbbVie, Astra Zeneca, Boehringer Ingelheim, Novartis, Pfizer and Roche., Consultant for: AbbVie, Astra Zeneca, BMS, Chugai, GSK, Hexal, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi and UCB, Speakers bureau: AbbVie, Astra Zeneca, BMS, Chugai, GSK, Hexal, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi and UCB, D. Boumpas: None declared, G. Burmester Grant/research support from: AbbVie, BMS, UCB and Roche, Speakers bureau: MSD, UCB and Roche, M. Cutolo Grant/research support from: BMS, Horizon, Actelion, Celgene and MSD, Speakers bureau: Biogen, Mundipharm, Pfizer and Menarini, W. Ebener Consultant for: Novartis and Abbvie, W. Graninger: None declared, T. Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience, Nycomed, Boeringher, Takeda, Epirus and Eli Lilly, G. Schett Speakers bureau: BMS, Celgene, Chugai, Lilly, Roche and UCB, H. Schulze-Koops Speakers bureau: AbbVie, Actelion, AstraZeneca, Biogen International, Boehringer Ingelheim, BMS, Celgene, Celltrion, Chugai, Cinfa Biotech, GSK, Hospira, Janssen-Cilag, Lilly, MSD, Medac, Merck, Mundipharma, Novartis, Pfizer, Hexal Sandoz, Roche and UCB, P. P. Tak Employee of: PPT has become an employee of GlaxoSmithKline. GSK has not been involved in this study., F. Breedveld: None declared, J. Smolen Grant/research support from: Abbvie, Lilly, MSD, Pfizer and Roche, Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Boehringer-Ingelheim, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Lilly, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi and UCB

DOI: 10.1136/annrheumdis-2017-eular.3743

FRI0208 COMPARISON OF EFFICACY, SAFETY AND PHARMACOKINETICS OF INFLIXIMAB BIOSIMILAR (BCD-055) AND INNOVATOR INFLIXIMAB

L. Denisov[1], I. Gordeev[2], V. Mazurov[3], A. Lila[3], E. Zonova[4], O. Nesmeyanova[5], E. Ilivanova[6], T. Plaksina[7], A. Eremeeva[8], A. Artemeva[8], E. Chernyaeva[8], R. Ivanov[8], S. Pimanov[9], E. Kunder[10], N. Soroka[11]. *[1]V.A. Nasonova Research Institute of Rheumatology; [2]O.M. Filatov City Clinical Hospital No. 15, Moscow; [3]I.I. Mechnikov North-Western State Medical University, Saint-Petersburg; [4]Novosibirsk State Medical University, Novosibirsk; [5]Chelyabinsk Regional Clinical Hospital, Chelyabinsk; [6]Leningrad Regional Clinical Hospital, Saint-Petersburg; [7]N.A. Semashko Nizhny Novgorod Regional Clinical Hospital, Nizhny Novgorod; [8]Jcs Biocad, Saint-Petersburg, Russian Federation; [9]Vitebsk Regional Clinical Hospital, Vitebsk; [10]1st City Clinical Hospital; [11]9th City Clinical Hospital, Minsk, Belarus*

Background: Infliximab (IFX) was one of the first genetically engineered biologics successfully applied for medical use in patients with active RA and patients with AS. Previous preclinical studies showed that BCD-055 is highly similar to innovator IFX.

Objectives: This abstract presents results from three clinical trials of infliximab biosimilar, BCD-055, including comparative data on pharmacokinetics (PK), efficacy and safety in a variety of patient populations.
Methods: All three studies were conducted as international multicenter randomized double-blind studies in direct comparison with innovator IFX. ASART-1 study (Phase 1, PK study) and ASART-2 study (Phase 3, efficacy and safety study) were conducted in patients with AS. After the screening patients were stratified by CRP and BASDAI score, randomized (1:1 ratio in ASART-1; 2:1 ratio in ASART-2) into 2 arms and received BCD-055 or innovator IFX at a dose 5 mg/kg IV on day 1 wk 0, 2, 6 and then every 8 wks (up to wk 54). LIRA study (Phase 3 study) was conducted in patients with active RA who were stratified by age and DAS28 score, randomized (2:1) into 2 arms and received BCD-055 or innovator IFX at a dose 3 mg/kg IV on day 1 wk 0, 2, 6 and then every 8 wks (up to wk 54).
Results: A total of 91 patients were enrolled in ASART-1 study, 198 patients - in ASART-2 study and 195 patients - in LIRA study in Russia and Belarus.
PK characteristics were equivalent for BCD-055 and innovator IFX. After the single administration 90%CI for the ratio of geometric means for $AUC_{0–336}$ was 86.40% – 110.09%, for C_{max} – 82.70% – 109.83%. After multiple-dose administration 90%CI for the ratio of geometric means for $AUC_{0\text{-}tau}$ was 81.35% – 121.13%, for $C_{max,ss}$ – 90.16% – 117.32%.
Efficacy: BCD-055 is non-inferior to innovator IFX both in RA and AS patients: ACR20 at wk 14 was reached by 75.83% of patients in BCD-055 group and 74.19% in innovator IFX group (p=0.951, 95% CI for difference in proportion [-12.90%; 16.18%], margin -20%), ASAS20 at wk 30 - by 81.30% and 67.74% respectively (p=0.061, 95% CI for difference in proportion [-1.18%; 28.28%], margin -17.5%).
Safety: BCD-055 and innovator IFX showed highly similar safety profiles in all three studies without cases of unexpected toxicity. The rates of AEs were equivalent for both drugs and varied from 47% in patients with AS to 53% in patients with RA. Immunogenicity assessment didn't find any significant difference between BCD-055 and innovator IFX, anti-drug antibodies occurred at the same rate irrespectively to the group.
Conclusions: BCD-055 is highly similar to innovator IFX in patients with active RA and in patients with AS in terms of efficacy, safety and PK.
References:
[1] EMA/CHMP/BMWP/403543/2010.
Disclosure of Interest: L. Denisov: None declared, I. Gordeev: None declared, V. Mazurov: None declared, A. Lila: None declared, E. Zonova: None declared, O. Nesmeyanova: None declared, E. Ilivanova: None declared, T. Plaksina: None declared, A. Eremeeva Employee of: JCS BIOCAD, A. Artemeva Employee of: JCS BIOCAD, E. Chernyaeva Employee of: JCS BIOCAD, R. Ivanov Employee of: JCS BIOCAD, S. Pimanov: None declared, E. Kunder: None declared, N. Soroka: None declared
DOI: 10.1136/annrheumdis-2017-eular.4723

FRI0209 REAL-LIFE SAFETY PROFILE OF BIOSIMILAR ADALIMUMAB IN PATIENTS WITH INFLAMMATORY ARTHRITIC CONDITIONS

V. Kaushik, S. Apparao. *Arthritis & Rheumatism Centre, Chennai, Chennai, India*

Background: Biologic therapies have dawned a new era in the management of patients with chronic inflammatory arthritis by nudging the goal post from control to induction of remission. Adalimumab, a TNF-α inhibitor, has proven to be safe and effective in improving the disease activity and quality of life in patients with conditions like rheumatoid arthritis (RA) and ankylosing spondylitis (AS).[1,2] A biosimilar adalimumab (developed by *Cadila Healthcare Ltd., India*) has been approved for clinical use in 2014 in India. While the initial biosimilarity has been established for physicochemical, functional as well as clinical efficacy and safety aspects;[3,4] ongoing evaluation of safety in real-life patients is crucial for such biosimilar therapies.
Objectives: We share our experience on the real-life safety profile of biosimilar adalimumab following its clinical use in patients with RA and AS.
Methods: Patients with RA or AS treated with biosimilar adalimumab in our outpatient clinic at Arthritis and Rheumatism Centre during the period of 17 Dec 2014 to 30 Mar 2016 were considered for this analysis. The patients were prescribed biosimilar adalimumab 40 mg subcutaneously every fortnight for a minimum of 6 months. The patients were followed up till the end of the treatment, and any safety signals or adverse events reported were collected and analysed.
Results: A total of 200 patients - 119 patients with AS and 81 patients with RA - who received biosimilar adalimumab therapy for a period of 6 months were included. The median age for the group was 36 (17–68 years); and 138 patients were males. The mean BMI was 25.74±3.83; and the median duration of disease for the entire group was 4.54 (0.5–13.5) years - 4.54 (0.5–9.58) years for the patients with AS, and 4.58 (2.5–13.5) years for the patients with RA. About 90% (181 out of 200 patients) received concomitant therapy with methotrexate. Biosimilar adalimumab therapy was well tolerated by all patients, with no serious adverse events. Adverse events were noted in only 2 patients - one patient had developed pulmonary tuberculosis in the 4th month of treatment, biosimilar adalimumab was discontinued and AKT treatment was started; while another patient experienced rise in transaminases for which, the dose of methotrexate was reduced. Overall assessment of tolerability as "Excellent" was 65.5% by the treating physician and 82% by patients.
Conclusions: To the best of our knowledge, this is the first report on "real-life" use of biosimilar adalimumab in such a large number of patients. The analysis reveals a safety and tolerability profile of biosimilar adalimumab comparable to that of the innovator product.
References:
[1] Voulgari PV, Drosos AA. Expert Opin Biol Ther. 2006; 6(12):1349–1360.
[2] Papagoras C, Voulgari PV, Drosos AA. Open Access Rheumatol. 2009 May 18;1:51–68.
[3] Bandopadhyay S, et al. Biosimilars. 2015;5:1–18.
[4] Jani RH, et al. Int J Rheum Dis. 2015 Jul 14.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2357

FRI0210 REAL-WORLD HAWK STUDY: LONG-TERM SAFETY AND EFFECTIVENESS OF ADALIMUMAB WITH HIGHER-DOSE METHOTREXATE IN JAPANESE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

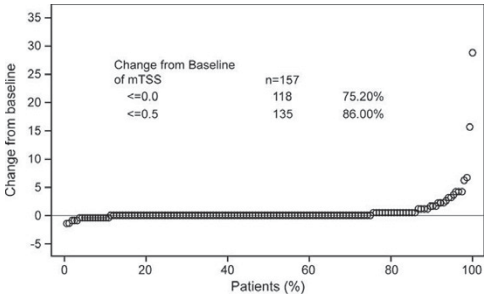
Y. Tanaka[1], T. Mimori[2], H. Yamanaka[3], R. Nakajima[4], K. Morita[4], J. Kimura[4], T. Takeuchi[5]. *[1]The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Kitakyushu; [2]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Kyoto; [3]Institute of Rheumatology, Tokyo Women's Medical University; [4]AbbVie GK; [5]Division of Rheumatology, Department of Internal Medicine, School of Medicine, Keio University, Tokyo, Japan*

Background: TNF inhibitors are first-line biologic therapy used in combination with MTX for treatment of RA. However, in Japan, limited real-world data exist on this combination with relatively higher doses of MTX (>8 to ≤16 mg/week).
Objectives: The HAWK study was designed to assess real-world, long-term safety and effectiveness of the TNF inhibitor ADA with MTX (≥12 mg/week) in Japan. Week 52 results are presented.
Methods: This multicenter, prospective, observational study, enrolled biologic-naïve, early (≤2 years) RA patients with DAS28-CRP>3.2 despite MTX therapy for ≥3 months. Eligible patients received ADA + MTX (≥12 mg/week at beginning of ADA) for 104 weeks. Primary endpoint was DAS28-CRP <2.6 at week 52. Secondary endpoints included CDAI, SDAI, HAQ-DI and inhibition of structural joint damage using the mTSS. ADRs and dosage of ADA and MTX were recorded.
Results: As of April 15, 2016, 346 patients were enrolled (safety set 301; effectiveness set 293). Effectiveness set comprised 73% women; mean (±SD) age, 54.3 (13.9) years; duration of RA, 12.1 (6.2) months; MTX dosage, 13.4 (1.8) mg/week; DAS28-CRP, 4.5 (0.9); and mTSS, 7.7 (10.0) at baseline. At week 52, DAS28-CRP <2.6 and low disease activity (<3.2) were achieved in 77% and 92% patients, respectively. Remission rates in CDAI (≤2.8), SDAI (≤3.3), and HAQ-DI (≤0.5) were 49%, 51%, and 82%, respectively. Although average MTX dosage was decreased (≤2 mg/week), unchanged, and increased (≥2 mg/week) from baseline in 19.6%, 78.9%, and 1.4% patients over 52 weeks, respectively, there was no significant difference in disease activity improvement across these MTX dosage groups at week 52 (p=0.350). Structural remission rate at week 52 was 86% (ΔmTSS ≤0.5) (Figure). A total 110 ADRs occurred in 80 (26.6%) patients, 23 were serious in 21 (7.0%) patients (Table).

	All (N=301)		Serious (N=301)	
ADR				
Total	80	26.6%	21	7.0%
ADRs by SOC				
Infections and infestations	29	9.6%	9	3.0%
Investigations	16	5.3%	1	0.3%
Respiratory, thoracic and mediastinal disorders	13	4.3%	3	1.0%
Hepatobiliary disorders	9	3.0%	0	
ADRs of particular interest				
Tuberculosis	0		0	
Pneumocystis jirovecii pneumonia	4	1.3%	4	1.3%
Pneumonia bacterial*	6	2.0%	4	1.3%
Herpes zoster	4	1.3%	0	
Malignancy (1)	4	1.3%	4	1.3%
Interstitial lung disease	2	0.7%	2	0.7%
Sepsis	0		0	
Pancytopenia	0		0	
Reactivation of hepatitis B	0		0	

*Pneumonia, Pneumonia bacterial, Pneumonia pneumococcal, Pneumonia legionella, Pneumonia streptococcal. (1) Colon cancer, diffuse large B-cell lymphoma, ovarian cancer metastatic, lung neoplasm malignant.

Conclusions: Results show that ADA with MTX (≥12 mg/week at the beginning) displayed a consistent safety profile and was effective with a DAS28-CRP remission rate of 77% in routine clinical practice. The ADR rate of 26% was similar to a previous, short-term (28 weeks) postmarketing surveillance report (1).
References:
[1] Koike et al. Mod Rheumatol 2014; 24:390–8.
Acknowledgements: This study (NCT01736189) was funded by AbbVie GK and Eisai Co., Ltd. AbbVie participated in the collection, analysis, and interpretation of the data, and in the drafting, review, and approval of the abstract.
AbbVie GK and Eisai Co., Ltd. provided funding to EPS Corporation for data analysis and to Cactus Communications for editorial assistance.
Disclosure of Interest: Y. Tanaka Grant/research support from: Mitsubishi-



Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, Consultant for: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, GlaxoSmithKline, T. Mimori Grant/research support from: Acterion, Ayumi, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi Tanabe, Speakers bureau: Chugai, Mitsubishi Tanabe, H. Yamanaka Grant/research support from: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer, UCB. Nippon Kayaku, YL biologics, Bayer, Bristol-Meyers, Consultant for: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer, UCB, Nippon Kayaku, YL biologics, Bayer, Bristol-Meyers, R. Nakajima Employee of: AbbVie GK, K. Morita Employee of: AbbVie GK, J. Kimura Employee of: AbbVie GK, T. Takeuchi Grant/research support from: AbbVie, Astellas, Bristol-Myers, Chugai, Daiichi Sankyo, Eisai, Janssen, Mitsubishi Tanabe, Nippon Shinyaku, Pfizer, Sanofi, Santen, Takeda, Teijin, Consultant for: AstraZeneca, Eli Lilly, Novartis, Mitsubishi Tanabe, Asahi Kasei Medical, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi Tanabe, Pfizer, Takeda

DOI: 10.1136/annrheumdis-2017-eular.4579

FRI0211 **A DESCRIPTIVE ANALYSIS OF REAL-WORLD TREATMENT PATTERNS OF INNOVATOR INFLIXIMAB (REMICADE) AND BIOSIMILAR INFLIXIMAB IN A TREATMENT NAÏVE TURKISH RHEUMATOLOGIC DISEASE POPULATION**

Y. Yazici[1], L. Xie[2], A. Ogbomo[2], D. Parenti[3], K. Goyal[3], A. Teeple[3], L. Ellis[3], I. Simsek[4]. *[1]NYU Hospital for Joint Diseases, New York; [2]STATinMED Research Inc, Ann Arbor; [3]Janssen Scientific Affairs, LLC, Horsham, United States; [4]Guven Hospital, Ankara, Turkey*

Objectives: This retrospective healthcare claims analysis examined treatment patterns of innovator infliximab (IFX) and biosimilar infliximab (CT-P13) in a Turkish rheumatologic disease population after CT-P13 availability in July, 2014.
Methods: Adult patients (pts) with ≥1 diagnosis code (ICD-10-CM) for rheumatoid arthritis (RA) were identified in a national Turkish healthcare database during the study period (01DEC2010–01DEC2015). Eligible pts had continuous medical/pharmacy enrollment ≥12 months before and ≥6 months after IFX or CT-P13 initiation (index date). Patients were naïve to IFX or CT-P13 (i.e. had no IFX or CT-P13 within 12 months before the index date). Demographics, concomitant diseases and medications, and treatment patterns, eg., dose, interval, discontinuation, and switch were summarized. Confirmed discontinuation was defined as a switch to another biologic medication or the absence of an index biologic claim for ≥120 days without censoring.
Results: Key results are shown in the Table. A total of 1044 patients initiated either medication. The majority (80%; n=831) initiated IFX. The IFX cohort had a mean age of 42 years; 56% were women and mean follow up was 12 months. The CT-P13 cohort consisted of 213 pts with mean age of 43 years; 58% women; and mean follow up of 9 months. Approximately one-third of pts in each cohort had a concomitant diagnosis of ankylosing spondylitis (AS; TABLE). Other concomitant diseases and medications appeared balanced between cohorts. Pts in the IFX cohort had an average of 5.2 infusions and mean dose of 4.7 vials per infusion approximately every 8 weeks. Pts in the CT-P13 cohort had an average of 3.6 doses and mean dose of 5.8 vials per dispensing approximately 9 weeks apart.
A confirmed discontinuation occurred in 55% of the IFX cohort; driven in part by switching. 24% of IFX pts had ≥1 biologic switch with 8% initially switching to CT-P13. Time to any discontinuation or censoring of IFX is shown in the Table.
In the CT-P13 cohort, a confirmed discontinuation was observed in 63%; 31% switched to another biologic therapy; and 20% initially switched to IFX. Time to any discontinuation or censoring of CT-P13 is shown in the Table.
Conclusions: These findings in a single country indicate that real world utilization patterns may differ between innovator IFX and CT-P13, with predominantly more patients initiating IFX; greater overall CT-P13 discontinuation and a higher proportion of patients switching from CT-P13 to IFX. Further studies are needed to understand the reasons for these observed differences.
Disclosure of Interest: Y. Yazici Grant/research support from: Janssen Scientific Affairs, LLC, L. Xie Consultant for: Janssen Scientific Affairs, LLC, A. Ogbomo Consultant for: Janssen Scientific Affairs, LLC, D. Parenti Employee of: Janssen Scientific Affairs, LLC, K. Goyal Employee of: Janssen Scientific Affairs, LLC, A. Teeple Employee of: Janssen Scientific Affairs, LLC, L. Ellis Employee of: Janssen Scientific Affairs, LLC, I. Simsek Grant/research support from: Janssen Scientific Affairs, LLC

	Innovator IFX Cohort (N= 831)		CT-P13Cohort (N=213)	
	N/Mean	%/SD	N/Mean	%/SD
Age (Mean)	42	13	43	12
Gender				
Female	465	56%	124	58 %
Average Length of Follow up Period (in Months)	12	3	9	2
Concomitant Disease During Baseline Period				
Ankylosing Spondylitis	230	28%	70	33%
Psoriatic Arthritis	130	16%	24	11%
Crohn's Disease	65	8%	11	5%
Ulcerative Colitis	64	8%	10	5%
Concomitant RA-Medications During Follow up Period				
Methotrexate	253	30%	69	32%
Sulfasalazine	147	18%	46	22%
Dosing Characteristics				
Average # of doses within follow up period	5.2	2.6	3.6	1.8
Mean # of weeks between doses	8.2	4.2	9.0	4.7
Mean # of days between 1st and 2nd dose	38	37	50	41
Mean # of days between 2nd and 3rd dose	53	33	60	38
Mean # of days between 3rd and 4th dose	65	34	67	31
Switching				
# and % of patients with ≥1 switch	203	24%	66	31%
# of patient switches between Infliximab Types				
Switch to CT-P13	64	8%		
Switch to Innovator Infliximab			42	20%
Discontinuations				
# of Patients Confirmed to Have Discontinued	453	55%	134	63%
Time to confirmed discontinuation (days)	155	93	107	66
Time to any discontinuation or censoring (days):	239	130	169	102

DOI: 10.1136/annrheumdis-2017-eular.1117

FRIDAY, 16 JUNE 2017

Rheumatoid arthritis - other biologic treatment

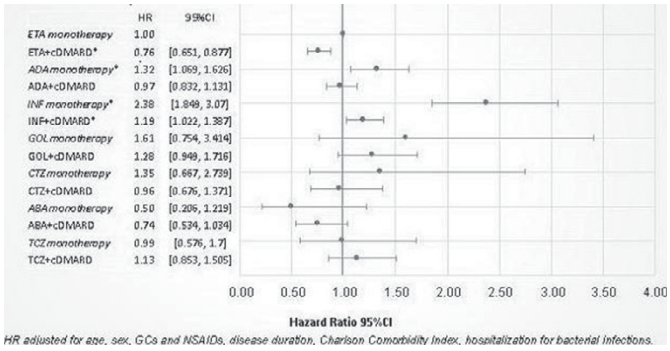
FRI0212 **COMPARATIVE EFFECTIVENESS OF FIRST-LINE BIOLOGIC MONOTHERAPY IN RHEUMATOID ARTHRITIS**

E. Silvagni[1], A. Bortoluzzi[1], G. Carrara[2], M. Govoni[1], C. Scirè[1,3]. *[1]1Department of Medical Science, Rheumatology Unit, University of Ferrara and Azienda Ospedaliero-Universitaria Sant'anna, Cona (Ferrara), ITALY, Ferrara (FE); [2]Epidemiology Unit, Italian Society for Rheumatology; [3]Epidemiology Unit, Italian Society for Rheumatology, Milan, Italy*

Background: Non-Biological disease modifying antirheumatic drugs (csDMARDs) are recommended in association to biologics (bDMARDS) in the treatment of Rheumatoid Arthritis (RA) and combination therapy is superior than bDMARD monotherapy with a better drug survival. Limited data are available in literature about the best biological treatment choice when a monotherapy is necessary in biologic-naïve patients.
Objectives: To assess comparative effectiveness (drug survival) of different first-line bDMARDs when administered in monotherapy in a large population-based sample of RA deriving from the administrative health database of the Lombardy region in Italy.
Methods: Data were obtained from health database of the Lombardy Region between 1/1/2004 and 31/12/2013. Patients with RA, diagnosed by a rheumatologist, with a certified diagnosis (exemption code 006.714.0) and treated with first-line approved bDMARDs (Abatacept [ABA], Adalimumab [ADA], Certolizumab [CTZ], Etanercept [ETA], Golimumab [GOL], Infliximab [INF] and Tocilizumab [TCZ]) were included; the presence of a combination therapy of any duration with a concomitant csDMARD (Methotrexate, Leflunomide, Sulfasalazine, Cyclosporine and Hydroxychloroquine) was compared to monotherapy. Clinical characteristics recorded were age, sex, disease duration, Charlson Comorbidity Index, hospitalization for bacterial infections, use of concomitant glucocorticoid (GCs) or Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Propensity to treatment with monotherapy was assessed by logistic models and results were presented as odds ratios and 95%confidence intervals (CI) Effectiveness was evaluated as drug survival using Cox proportional hazard models.
Results are presented as hazard ratios (HR) and CI, crude and adjusted for pre-specified confounders.
Results: 4478 RA patients who started a first-line bDMARD were included; 840 (18.8%) in monotherapy and 3638 (81.2%) in association to at least one csDMARD. Among biologic-naïve monotherapy patients, N.398 (47.4%) received ETA, N.215 (25.6%) ADA, N.92 (10.9%) INF, N.48 (5.7%) TCZ, N.35 (4,2%) ABA, N.30 (3,6%) CTZ, N.22 (2,6%) GOL. Median survival on treatment was 19.9 months (7.9–45.1).
Monotherapy was associated with a lower age, longer disease duration, a consistently higher Charlson Comorbidity Index (in particular hepatic or renal disease), lower GCs and NSAIDs intake.

Compared to monotherapy, combination therapy was associated with a lower drug failure (crude HR 0.75 [95% CI 0.68–0.82]; adjusted HR 0.78 [95% CI 0.70–0.86]; $p<0.0001$).

In patients in monotherapy, considering ETA as reference and adjusting for the above mentioned clinical characteristics, the HR for bDMARD failure was 1.32 for ADA (95% CI 1.07–1.63) and 2.38 for INF (95% CI 1.85–3.07).



HR adjusted for age, sex, GCs and NSAIDs, disease duration, Charlson Comorbidity Index, hospitalization for bacterial infections.

Conclusions: Monotherapy with bDMARDs is consistenly associated with lower retention rate in first-line therapy for anti-TNF drugs. Comparing bDMARDs administered in monotherapy, INF and ADA show a higher risk of withdrawal than ETA. Real life data support the currently recommended use of bDMARDs in association to csDMARDs.

References:
[1] Souto et al. Rheum (Oxford)2016;55(3):523–34.
[2] Choy et al. Rheum (Oxford)2016; 21.

Acknowledgements: None declared.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5236

FRI0213 COMPARATIVE EFFECTIVENESS OF ABATACEPT, RITUXIMAB, TOCILIZUMAB AND ANTI-TNF BIOLOGICAL DMARDS IN RA: RESULTS FROM THE NATIONWIDE SWEDISH REGISTER

T. Frisell[1], M. Dehlin[2], D. Di Giuseppe[1], N. Feltelius[3], A. Kastbom[4], C. Turesson[5], J. Askling[1] on behalf of the ARTIS Study Group. *[1]Karolinska Institutet, Stockholm; [2]Sahlgrenska Academy, University of Gothenburg, Göteborg; [3]Medical Products Agency, Uppsala; [4]Rheumatology/AIR, Linköping; [5]Rheumatology, Department of Clinical Sciences, Malmö, Lund University, Malmö, Sweden*

Background: Many current guidelines rank abatacept (ABA), rituximab (RTX), tocilizumab (TOC), and the TNFi bDMARDs as equal in effectiveness for the treatment of RA, at least as second line therapies. This is mainly based on evidence from separate RCTs, with few direct comparisons and limited comparative effectiveness data from clinical practice.
Objectives: To describe outcomes in clinical practice among RA patients starting different bDMARDs as first bDMARD, and after switch from initial TNFi.
Methods: The Swedish Rheumatology Register was linked to nationwide registers with data on demographics and medical history. We included all patients with RA starting a first ever bDMARD, or switching to a new bDMARD after a TNFi as first bDMARD, in 2010 - 2014, with follow-up through 2015. Effectiveness was assessed at 1 year (±90 days) after starting therapy, and measured as 1) the proportion remaining on therapy, or the proportion remaining on therapy and with 2) Good EULAR response, 3) HAQ improvement >0.2, 4) no swollen or tender joints. Relative response was estimated with log-binomial regression adjusting for potential confounders.
Results: Patients starting non-TNFi were older than those starting a TNFi, had lower socioeconomic status, and more often a history of diseases including malignancy, serious infections, and diabetes. After switch from TNFi, those starting non-TNFi also had higher disease activity.
Non-TNFi were associated with better drug survival and higher proportion reaching response outcomes compared to TNFi as first bDMARD. After switch from TNFi, RTX and TOC, but not ABA, were associated with significantly better drug survival and response. Differences remained after adjusting for identified potential confounders.
Conclusions: Despite channeling of older and sicker individuals to non-TNFi-bDMARDs, treatment outcomes were in general better in these groups, particularly for TOC and RTX. In interpreting this, the risk of residual confounding should be remembered, and that we did not include safety or long term outcomes.
Acknowledgements: The ARTIS registry has been, or is, supported by agreements with Abbvie, BMS, MSD, Pfizer, Roche, Samsung, and UCB.
Disclosure of Interest: T. Frisell: None declared, M. Dehlin: None declared, D. Di Giuseppe: None declared, N. Feltelius: None declared, A. Kastbom Consultant for: Bristol-Myers Squibb, Pfizer, Roche, UCB, Paid instructor for: Bristol-Myers Squibb, Pfizer, Roche, UCB, C. Turesson Grant/research support from: Abbvie, Pfizer, Roche, Consultant for: MSD, Pfizer, Roche, Paid instructor for: Abbvie, Bristol-Myers Squibb, Janssen, MSD, Pfizer, Roche and UCB, J. Askling Grant/research support from: Abbvie, UCB, Pfizer, Merck, Samsung, Roche, Lilly
DOI: 10.1136/annrheumdis-2017-eular.1307

FRI0214 LONG-TERM EFFICACY AND SAFETY OF SIRUKUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS DESPITE ANTI-TUMOR NECROSIS FACTOR THERAPY: RESULTS OF THE RANDOMIZED, PHASE 3 SIRROUND-T STUDY

Y. Tanaka[1], D. Aletaha[2], P. Agarwal[3], R. Kurrasch[4], P.P. Tak[5], S. Popik[3]. *[1]Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan; [2]Division of Rheumatology, Medical University of Vienna, Vienna, Austria; [3]Janssen Research & Development, LLC, Spring House, PA; [4]GlaxoSmithKline, Collegeville, PA, United States; [5]GlaxoSmithKline, Stevenage, United Kingdom*

Background: Sirukumab, a selective, high-affinity human monoclonal antibody to the interleukin-6 (IL-6) cytokine, is under development for rheumatoid arthritis (RA) and other diseases.
Objectives: To evaluate long-term efficacy and safety of sirukumab in patients (pts) with RA refractory or intolerant to anti-tumor necrosis factor (TNF) agents.
Methods: This phase 3 study included pts ≥18 years with moderate to severe active RA, and a lack of benefit to ≥1 anti-TNF or intolerance to ≥2 anti-TNFs. Eligible pts were initially randomized 1:1:1 to sirukumab subcutaneous (SC) 50mg q4w, sirukumab SC 100mg q2w, or placebo SC q2w for 24 wks. Placebo-treated pts with <20% improvement in tender and swollen joints at Wk 18 (early escape [EE]) and those remaining on placebo at Wk 24 (crossover) were re-randomized to sirukumab through Wk 52. Efficacy endpoints included ACR response, HAQ-DI scores, DAS28 (CRP) remission rates, and SF-36 scores. Results are presented for these key endpoints at Week 52.
Results: 878 pts were initially randomized to placebo (n=294), sirukumab 50 mg q4w (n=292), or sirukumab 100 mg q2w (n=292). Of placebo-treated pts, 94 met EE criteria at Wk 18 and 158 crossed over at Wk 24 and were re-randomized to sirukumab. 60% of pts had received ≥2 prior biologics, including non-TNF–targeted biologics. RA signs and symptoms and patient-reported outcomes (PROs [SF-36 scores]) improved significantly with sirukumab versus placebo through Wk 24. Improvements were maintained through Wk 52 with no dose response (Table 1). Through Wk 52 in the combined sirukumab 50mg q4w and 100mg q2w groups, respectively, an adverse event (AE) was reported for 79.6% and 81.3% of pts and a serious AE was reported for 14.2% and 13.2% of pts; injection-site reactions and alanine aminotransferase increases were the most commonly reported AEs.
Conclusions: In this population intolerant or refractory to anti-TNFs/other biologics, sirukumab SC 50mg q4w and 100mg q2w were well tolerated and reduced signs and symptoms of RA and improved PROs through 52 wks of treatment, also among pts who switched from placebo to sirukumab.
Disclosure of Interest: Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, and Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, and GlaxoSmithKline, D. Aletaha Grant/research support from: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, Consultant for: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, P. Agarwal Shareholder of:

Abstract FRI0213 – Table 1. Status at 12 months among all patients with RA initiating a biologic DMARD 2010–2014 in Sweden

	TNFi	RTX		TOC		ABA	
	%	%	RR†	%	RR†	%	RR†
First bDMARD	N=5568	N=654		N=202		N=240	
On drug	68.4	87.8	1.34 (1.27–1.41)	75.5	1.20 (1.09–1.31)	77.7	1.15 (1.05–1.27)
On drug + EULAR Good resp.	26.1	31.1	1.42 (1.19–1.69)	53.1	2.03 (1.70–2.42)	34.3	1.37 (1.10–1.72)
On drug + HAQ Improvement	26.7	39.2	1.64 (1.40–1.93)	45.0	1.54 (1.27–1.87)	36.8	1.37 (1.09–1.71)
On drug + 28 Joint count = 0	20.3	22.4	1.13 (0.89–1.43)	30.9	1.60 (1.21–2.11)	22.8	1.26 (0.91–1.74)
Switch from TNFi	N=1840	N=408		N=320		N=256	
On drug	57.7	80.2	1.48 (1.37–1.60)	73.0	1.36 (1.23–1.49)	65.1	1.11 (0.98–1.26)
On drug + EULAR Good resp.	11.4	24.0	1.87 (1.41–2.49)	36.8	3.06 (2.37–3.94)	14.6	1.16 (0.76–1.76)
On drug + HAQ Improvement	16.6	34.3	1.85 (1.49–2.30)	32.4	1.71 (1.33–2.19)	20.4	1.10 (0.78–1.53)
On drug + 28 Joint count = 0	12.3	20.8	1.96 (1.43–2.70)	19.9	2.12 (1.48–3.02)	11.2	0.86 (0.48–1.52)

†Adj. for region, sex, age, birth country, RF, dis. dur., HAQ, DAS28, co-medication, recent history of malignancy, infection, SSRI, and hospital days last 5 yrs.

Abstract FRI0214 – Table 1. Key Endpoints at Wk 52

Endpoints	Sirukumab 50 mg q4w			Sirukumab 100 mg q2w		
	Placebo to 50 mg q4w (n=124)	50 mg q4w (n=235)	Combined 50 mg q4w (n=359)	Placebo to 100 mg q2w (n=123)	100 mg q2w (n=241)	Combined 100 mg q2w (n=364)
ACR20 response, n (%)	68 (54.8)	127 (54.0)	195 (54.3)	71 (57.7)	145 (60.2)	216 (59.3)
ACR50 response, n (%)	41 (33.1)	74 (31.5)	115 (32.0)	38 (30.9)	77 (32.0)	115 (31.6)
HAQ-DI change from baseline, mean (SD)	-0.30 (0.55)	-0.39 (0.58)	-0.36 (0.57)	-0.43 (0.51)	-0.43 (0.60)	-0.43 (0.57)
DAS28 (CRP) <2.6, n (%)	36 (29.0)	63 (26.8)	99 (27.6)	42 (34.1)	71 (29.5)	113 (31.0)
SF-36 summary scores						
PCS change from baseline, mean (SD)	4.47 (7.70)	6.33 (7.23)	5.69 (7.44)	5.45 (7.22)	5.98 (7.25)	5.80 (7.24)
MCS change from baseline, mean (SD)	3.64 (8.48)	5.19 (10.84)	4.65 (10.10)	5.60 (10.62)	4.46 (10.45)	4.85 (10.51)

Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, R. Kurrasch Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, P. Tak Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, S. Popik Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC
DOI: 10.1136/annrheumdis-2017-eular.6486

FRI0215 COMPARATIVE EFFICACY AND RETENTION RATE OF TOCILIZUMAB AND TNF INHIBITORS USED IN COMBINATION WITH METHOTREXATE AS FIRST-LINE BIOLOGIC THERAPY IN RHEUMATOID ARTHRITIS: DATA FROM A MULTICENTRE OBSERVATIONAL REGISTRY

E.G. Favalli[1], M. Biggioggero[1], P. Sarzi Puttini[2], F. Atzeni[2], E. Fusaro[3], V. Grosso[4], R. Pellerito[5], R. Gorla[6], C. Bazzani[6], A. Marchesoni[1], R. Caporali[4]. *[1]Department of Rheumatology, Gaetano Pini Institute; [2]Rheumatology Unit, University Hospital L. Sacco, Milano; [3]Rheumatology, Azienda Ospedaliera Universitaria Città; della Salute e della Scienza, Torino; [4]Rheumatology, University of Pavia, IRCCS Policlinico San Matteo Foundation, Pavia; [5]Rheumatology, Ospedale Mauriziano, Torino; [6]Rheumatology Unit, Spedali Civili, Brescia, Italy*

Background: Despite a demonstrated superiority of interleukin-6 over tumour necrosis factor (TNF) blockade when used as monotherapy, the choice of the first biologic agent (bDMARD) for treating rheumatoid arthritis (RA) in combination with methotrexate (MTX) is still a challenge for rheumatologist.
Objectives: To retrospectively evaluate in a multicentre observational cohort of Northern Italy (the LORHEN registry) the 6- and 12-month comparative drug survival and remission rate of tocilizumab (TCZ) and TNF inhibitors (TNFis) used as first bDMARD in combination with MTX.
Methods: All RA patients treated with TCZ or a TNFi as first-line bDMARD with at least 12-month follow-up were selected from the LORHEN registry. The analysis was limited to the period from January 2009 to May 2016 and to patients receiving either TCZ or TNFi in combination with MTX, excluding bDMARD monotherapy. Six- and 12-month clinical remission rate was defined as achievement of disease activity score 28 calculated by using erythrosedimentation rate (DAS28-ESR) <2.6. Drug persistence was calculated by Kaplan-Meier method. The comparison between treatment subgroups was performed by a chi-square test for remission data and by a log-rank test for drug survival. Moreover, DAS28-ESR remission rate has been corrected for drug discontinuation by using the LUNDEX formula [(1)].
Results: The overall study population included 591 patients (female 77.3%, mean age [± standard deviation, SD] 54.2±13.2 years, mean disease duration [±SD] 7.4±7.7 years, positive rheumatoid factor 67.5%, positive anti-citrullinated peptide antibodies 77.6%, mean baseline DAS28-ESR 5.1±1.2) treated with TCZ (n=61) or TNFis (n=530; infliximab 43, adalimumab 163, etanercept 195, golimumab 60, certolizumab pegol 69). Baseline characteristics were similar in the two groups, with the exception of mean age (TCZ 58.2 vs TNFis 53.7 years; p=0.021). No significant differences (p=0.361) emerged in the 6- (TCZ 88% vs TNFis 84.3%; p=0.752) and 12-month (TCZ 76.4% vs TNFis 71.5%;) retention rate. Clinical remission was achieved in overall 35.7% patients at 6 months (TCZ 59% vs TNFis 33%; p<0.001) and in 36.8% patients at 12 months (TCZ 58.8% vs TNFis 34.5%; p<0.001). Similar trends were observed after correction by LUNDEX formula at 6 (TCZ 51.9% vs TNFis 27.8%) and 12 months (TCZ 44.9% vs TNFis 24.6%).
Conclusions: Despite a similar 1-year retention rate, the proportion of patients achieving DAS28-ESR remission was significantly higher in TCZ+MTX treated group compared with TNFis+MTX, suggesting a deeper clinical response in patients receiving IL6 blockade.
References:
[1] Kristensen LE, et al. Arthritis Rheum 2006;54:600–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4771

FRI0216 RESULTS OF A LONGITUDINAL REVIEW OF PULMONARY FUNCTION AND SAFETY DATA IN A PHASE IIB CLINICAL PROGRAMME TESTING GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR (GM–CSF) RECEPTOR ANTAGONIST MAVRILIMUMAB FOR TREATMENT OF RHEUMATOID ARTHRITIS (RA)

G. Burmester[1], M.A. Michaels[2], D. Close[3], A. Godwood[3], K. Middleton[3], P. Miranda[4], J. Vencovský[5], J. Kremer[6], I.B. McInnes[7], M. Albulescu^[3], M. Weinblatt^[8]. *[1]Charité – University Medicine Berlin, Berlin, Germany; [2]MedImmune, Gaithersburg, United States; [3]MedImmune, Cambridge, United Kingdom; [4]Centro de Estudios Reumatológicos, Santiago, Chile; [5]Institute of Rheumatology, Prague, Czech Republic; [6]The Albany Medical College, Albany, United States; [7]University of Glasgow, Glasgow, United Kingdom; [8]Brigham and Women's Hospital, Boston, United States*

Background: RA is associated with pulmonary comorbidity and lung function decline over time, but longitudinal assessment of pulmonary abnormalities in the context of RA treatment needs further characterisation. Mavrilimumab, an investigational human monoclonal antibody, inhibits GM-CSF by binding to the GM-CSF receptor α subunit.
Objectives: To investigate the pulmonary safety of mavrilimumab because of the theoretical risk of inhibiting alveolar macrophage function and causing pulmonary alveolar proteinosis (PAP).
Methods: Pulmonary monitoring included standardised serial pulmonary function testing (spirometry and diffusing capacity of lung carbon monoxide [DLCO]), chest X-rays, assessments of dyspnoea and pulmonary adverse events (AEs) in two randomised, double-blind studies (NCT01706926; NCT01715896) where patients (pts) with moderate to severe RA received mavrilimumab 30, 100 or 150 mg every other week (eow), or placebo and mavrilimumab 100 mg eow or golimumab 50 mg every 4 weeks, respectively. Eligible pts transferred to the open-label extension study (NCT01712399) and received mavrilimumab 100 mg eow. All studies excluded pts with clinically significant uncontrolled pulmonary disease. An Independent Pulmonary Evaluation Committee (IPEC), blinded to treatment, adjudicated pulmonary AEs and lung function abnormalities.
Results: Mavrilimumab was received by 442 pts with cumulative safety data exposure of approximately 900 pt-yrs and a median (range) exposure time of 2.5 (0.1–3.3) yrs. Baseline (BL) characteristics are shown (Table). Mean dyspnoea (Table), forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC) and DLCO were mostly maintained within 5% of BL values for pts treated with mavrilimumab during the clinical programme. Clinically relevant decreases in predicted FEV_1 and FVC (>20% from BL and <80% predicted) were demonstrated by ≤6.2% of pts at any visit (Table); decreases were mostly transient with no apparent trends. Overall, 83 pts (9.24/100 pt-yrs) reported ≥1 pulmonary AE; bronchitis was reported most frequently (34 pts [3.78/100 pt-yrs]); one AE was considered serious and treatment-related (acute bronchitis). The reported pulmonary AE rate was generally stable over time. No suspected or confirmed PAP cases were found by IPEC and no pulmonary-related deaths were reported.
Conclusions: We believe this is the most comprehensive longitudinal study of pulmonary function in a clinical RA programme. The BL pulmonary function profile indicates that this is not a normal population from a pulmonary health perspective. Mavrilimumab was not associated with substantial decline in pulmonary function or PAP in pts treated up to 3.3 years; its acceptable safety profile advocates initiation of Phase III studies with mavrilimumab. Further studies are now required to fully characterise pulmonary function over time in RA.
Acknowledgements: Funded by MedImmune. Medical writing support: R Plant, QXV Comms, an Ashfield company, funded by MedImmune.
^Senior author.
Disclosure of Interest: G. Burmester Consultant for: MedImmune, M. Michaels Employee of: MedImmune, D. Close Employee of: MedImmune, A. Godwood Shareholder of: AstraZeneca, Employee of: MedImmune, K. Middleton Employee of: MedImmune (contracted employment at time of study), P. Miranda Grant/research support from: Amgen, Medimmune, Janssen, Pfizer, Celltrion, Abbott, Sanofi, Actelion, Merck & Co, Boehringer, BMS, Consultant for: Pfizer [Etanecept: Fee less than USD5000], J. Vencovský Consultant for: Pfizer, Elli Lilly, MSD, Novartis, Speakers bureau: Biogen, Pfizer, MSD, Abbvie, Novartis, Boehringer, UCB, BMS, J. Kremer Shareholder of: Corrona, Grant/research support from: Abbvie, Amgen, Genentech, Lilly, Pfizer, Consultant for: Abbvie, Amgen, BMS, Genentech, Lilly, Pfizer, Employee of: Corrona, I. McInnes Grant/research support from: MedImmune [The University of Glasgow is a charity registered in

	Mavrilimumab total[a] (n=442)
Demographics	
Age, years, median (min–max)	52 (19–79)
Sex, % female	85.1
BL disease characteristics	
Years since RA diagnosis, mean (SD)	7.91 (6.85)
MTX dose, mg/week, mean (SD)	15.00 (6.84)
DAS28-CRP, mean (SE)	5.77 (0.04)
Concomitant pulmonary disease, n (%)[b]	
Asthma COPD Other	17 (3.8) 8 (1.8) 21 (4.8)
Ever smoked, n (%)	134 (30.3)
Current smokers, n (%)	76 (17.2)
RF and ACPA positive, n (%)	359 (81.2)
BL pulmonary function	
% predicted FEV_1, mean (SD)	93.9 (14.7)
% predicted FVC, mean (SD)	94.0 (14.6)
% predicted DLCO, mean (SD) [n]	72.4 (9.3) [48]
Borg dyspnoea score, mean (SE)	0.4 (0.0)
Efficacy results	
Borg dyspnoea score, mean (SE) [N]	
Week 12[c,d]	NA
Week 74	0.3 (0.0) [279]
Week 134	0.3 (0.0) [58]
>20% reduction from BL to 80% predicted FEV_1, n/N (%)	
Week 12[c,d]	2/298 (0.7)
Week 74	8/231 (3.5)
Week 104	11/178 (6.2)
Week 130	1/29 (3.4)
>20% reduction from BL to 80% predicted FVC, n/N (%)	
Week 12[c,d]	2/298 (0.7)
Week 74	7/239 (2.9)
Week 104	3/177 (3.4)
Week 130	0/32 (0.0)

[a]Mavrilimumab total=all patientswho received mavrilimumab in either of the two randomised studies or in the OLE study. [b]Clinically significant uncontrolled pulmonary disease was an exclusion criterion for all three studies. [c]Between weeks 12 and 24, 3(3.8%), 8(9.4%), 12(14.8%) and 37 (45.7%) pts receiving mavrilimumab 150 mg, 100 mg, 30 mg eow, and placebo, respectively, transferred from NCT01706926 to the OLE study because of lack of efficacy. [d]Between Weeks 12 and 24, 2 (2.9%) and 0 (0.0%) pts receiving mavrilimumab 100 mg and golimumab 50 mg, respectively, transferred from NCT01715896 to the OLE study because of lack of efficacy.
ACPA, anti-citrullinated protein antibody; BL, baseline; COPD, chronic obstructive pulmonary disease; DAS28–CRP, disease activity score 28 C-reactive protein; DLCO, diffusing capacity of the lung for carbon monoxide; eow, every other week; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; MTX, methotrexate; NA, not available; OLE, open-label extension; pts, patients; RA, rheumatoid arthritis; RF, rheumatoid factor; SD, standard deviation; SE, standard error

Scotland, charity number SC004401 Grant/research support: Research award to University of Glasgow], Consultant for: MedImmune, M. Albulescu Shareholder of: MedImmune, Employee of: MedImmune, M. Weinblatt Grant/research support from: BMS, UCB, Crescendo Bioscience. Amgen, dxterity, Consultant for: MedImmune, Astra Zeneca, Amgen, Abbvie, BMS, Crescendo bioscience, Lilly, Pfizer, UCB, Roche, novartis

DOI: 10.1136/annrheumdis-2017-eular.3131

FRI0217 IMPACT OF RITUXIMAB IN COMBINATION WITH LEFLUNOMIDE AND RITUXIMAB RETREATMENT WITH TWO DIFFERENT DOSAGES ON PATIENT-REPORTED OUTCOMES: RESULTS FROM A MULTICENTER RANDOMIZED PLACEBO CONTROLLED INVESTIGATOR INITIATED CLINICAL TRIAL IN ACTIVE RHEUMATOID ARTHRITIS (AMARA-STUDY)

M. Köhm[1,2], T. Rossmanith[2], S. Dauth[2], R. Alten[3], M. Aringer[4], M. Backhaus[5], G. Burmester[6], E. Feist[6], H. Kellner[7], K. Krüger[8], U. Müller-Ladner[9], A. Rubbert-Roth[10], H.-P. Tony[11], S. Wassenberg[12], H. Burkhardt[1,2], F. Behrens[1,2] on behalf of AMARA study group. *[1]Rheumatology, Goethe-University Frankfurt/Main, Frankurt/Main; [2]Clinical Research, Fraunhofer IME-TMP, Frankfurt; [3]Rheumatology, Schlosspark-Klinik, Berlin; [4]Medizinische Klinik und Poliklinik III, Universitätsklinik, Dresden; [5]Rheumatologie, Park-Klinik Weißensee; [6]Rheumatologie, Charité Universitätsmedizin, Berlin; [7]Rheumatologische Fachpraxis; [8]Praxiszentrum St. Bonifatius, München; [9]Abteilung Rheumatologie und klinische Immunologie, Kerckhoff-Klinik, Bad Nauheim; [10]Rheumatologie, Universitätsklinik, Köln; [11]Abteilung Rheumatologie/Immunologie, Universitätsklinik, Würzburg; [12]Rheumazentrum, Ratingen, Germany*

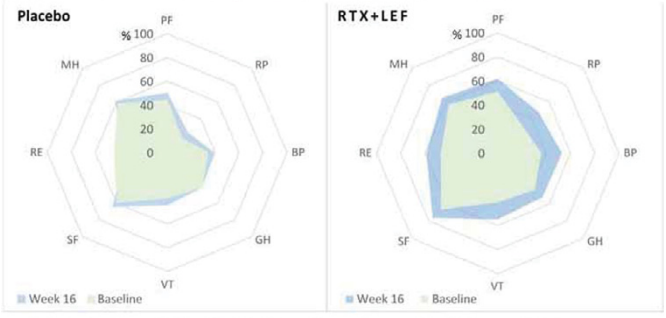
Background: Use of biologicals such as Rituximab (RTX) in Rheumatoid Arthritis (RA) is effective and often only licensed in combination with Methotrexate (MTX). In cases of contraindications to or intolerances of MTX other cDMARDs are frequently used without robust data from RCTs. In addition, different strategies of retreatment of RTX are available.

Objectives: To demonstrate efficacy on patient-reported outcomes (PROs) of RTX in combination with leflunomide (LEF) in a multicenter investigator-initiated placebo (PLA)-controlled RCT in Germany.

Methods: A total of 189 patients with active RA (DAS28>3.2 and at least 3 SJC and 3 TJC) despite stable LEF treatment were screened for a 52-weeks double-blind placebo controlled RCT. Patients were randomized to receive either two-times 1000mg RTX i.v. followed by a retreatment at week 24 with two-times 1000 (RTX-RTXhigh) or 500mg (RTX-RTXlow) or two times PLA at baseline, followed by a retreatment of RTX of either two-times 1000 (PLA-RTXhigh) or 500mg (PLA-RTXlow) at week 24. Adult patients who had inadequate response to more than one antiTNF or failed more than three cDMARDs were excluded. PROs (HAQ, FACIT-F, SF36) were measured at each visit until week 52. Treatment effects on PROs were determined by differences from baseline to week 16, 24 and week52.

Results: Of 189 screened patients 148 were randomized (mean age 56 years; mean proportion of RF-and antiCCP-positivity 58.4% and 55.7% in the RTX-group; 74% female). DAS28 at baseline was 5.55 for RTX and 5.53 in the PLA-group. All baseline-characteristics were well balanced between treatment groups. An improvement in HAQ from baseline to week 16 was seen with a mean delta of -0.23 in the RTX-group (MCID) vs. -0.11 for PLA. In the RTX-group, retreatment until week 52 resulted in stable HAQ-values compared to week24 independent from its dosage. FACIT-F values increased in the RTX-group from baseline to weeks 16, 24 and 52 by 11.87, 12.3 and 14.25, respectively. All physical and mental domains of the SF36 showed a pronounced increase of levels at week 16 compared to baseline in the RTX-group (Figure 1). A total of 372 adverse events (AE) were observed during the one-year studyperiod, only 14 classified as severe (10 in RTX and 4 in PLA). 43 serious adverse events were reported, 28 of them in the RTX-group during the placebo-controlled period.

Figure 1: SF36 domains at baseline and week 16 after placebo or RTX+LEF treatment



PF: physical functioning; RP: physical role limitations; BP: pain; GH: general health; VT: energy/vitality; SF: social functioning; RE: emotional role limitations; MH: mental health

Conclusions: Efficacy of LEF plus RTX was demonstrated not only by measurements of disease activity (as presented previously) but also by measurements of PROs (HAQ, FACIT-F, SF36). This treatment regime showed equal effect sizes compared to the combinational therapy of MTX plus RTX. The treatment with LEF plus RTX illustrated an acceptable safety profile.

Disclosure of Interest: M. Köhm Grant/research support from: Pfizer, Janssen, Consultant for: Janssen, T. Rossmanith Grant/research support from: Janssen, Pfizer, Roche, S. Dauth: None declared, R. Alten Grant/research support from: Roche, M. Aringer Grant/research support from: Roche, M. Backhaus Grant/research support from: Roche, G. Burmester Grant/research support from: Roche, E. Feist Grant/research support from: Roche, H. Kellner Grant/research support from: Roche, K. Krüger Grant/research support from: Roche, U. Müller-Ladner Grant/research support from: Roche, A. Rubbert-Roth Grant/research support from: Roche, H.-P. Tony Grant/research support from: Roche, S. Wassenberg Grant/research support from: Roche, H. Burkhardt Grant/research support from: Roche, Pfizer, Speakers bureau: Pfizer, BMS, F. Behrens Grant/research support from: Roche, Pfizer, Janssen, Speakers bureau: BMS, Janssen, Pfizer, AbbVie

DOI: 10.1136/annrheumdis-2017-eular.6238

FRI0218 SHARED EPITOPE POSITIVITY IS RELATED TO EFFICACY OF ABATACEPT IN RHEUMATOID ARTHRITIS

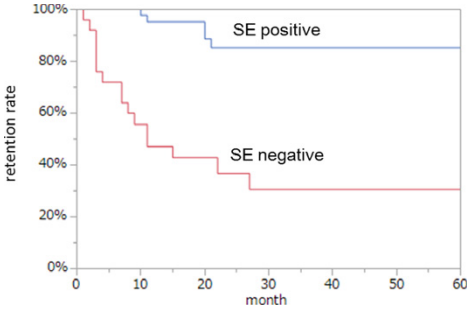
K. Oryoji, K. Yoshida, S.-I. Mizuki. *Matsuyama Red Cross Hospital, JAPAN, Matsuyama-Shi, Japan*

Background: Abatacept, a soluble fusion protein composed of the extracellular domain of CTLA-4 molecule and the Fc portion of human IgG1, is approved therapy for RA by the mechanism of binding to CD80/86 (B7–1/B7–2) on antigen presenting cell (APC), and blocking the B7:CD28 interaction. Meanwhile, it is suggested that HLA-DRB1 shared epitope (SE) associates with the production of ACPA through MHC molecule-based antigen presentation. Moreover, the association between the efficacy of abatacept and the positivity for anti-cyclic citrullinated peptide antibody (ACPA) was reported. Thus, we speculated that there may be correlation between the efficacy of abatacept and patients' HLA-DRB1 SE positivity, so we investigated correlation between the clinical efficacy of abatacept in RA patients and their HLA-DRB1 genotype.

Objectives: To identify the relation between the efficacy of abatacept on patients with rheumatoid arthritis (RA) and their HLA-DRB1 phenotype including whether having shared epitope (SE).

Methods: HLA-DRB1 phenotype of 72 patients treated with abatacept was identified, and divided into 2 group, SE (HLA-DRB1 0101, 0401, 0404, 0405,

0408, 1001) positive and SE negative. To overcome potential bias, multivariate logistic regression analysis was done in this retrospective cohort.
Results: They were divided into 47 SE positive patients (65.3%) and 25 SE negative patients (34.7%). The retention rate of abatacept treatment at week 52 were 95.3%/47.1% (SE positive/SE negative, p<0.0001, log-rank test), respectively. Adjusted hazard ratio for abatacept discontinuation due to lack of efficacy was 8.94 (95% CI: 2.95–34.1, p<0.0001, Multivariable Cox proportional hazards regression model) in SE negative group compared to SE positive group. The EULAR good response rate at week 24 were 74.5%/20.0% (SE positive/SE negative, p<0.0001, Fisher's exact test), respectively. Simplified Disease Activity Index (SDAI) remission rate at week 24 were 55.3%/20.0% (SE positive/SE negative, p=0.004, Fisher's exact test), respectively. Multivariate logistic regression revealed the odds ratio of EULAR good response and SDAI remission achievement in SE positive patients was 23.2 and 6.73 (95% CI: 5.10–152.0, p<0.0001 and 1.70–32.3, p=0.006), respectively.



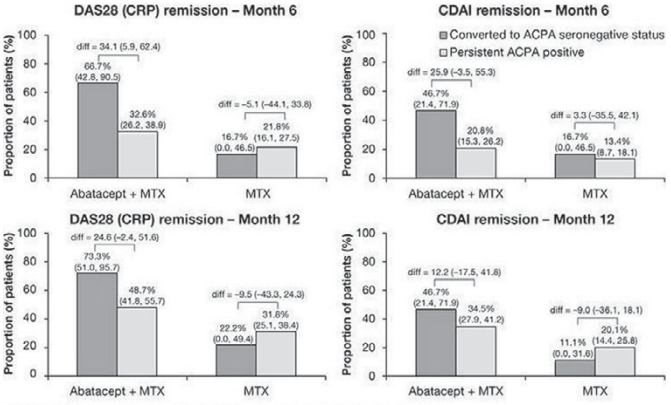
Conclusions: Abatacept is strictly effective to SE positive RA patients.
Disclosure of Interest: K. Oryoji Grant/research support from: Ono, Speakers bureau: Abbvie, Chugai, Astellas, Mitsubishi-Tanabe, Pfizer, Janssen, Eisai, UCB and Ono, K. Yoshida: None declared, S.-I. Mizuki Speakers bureau: Abbvie, Astellas, Mitsubishi-Tanabe, Pfizer, Janssen, Eisai, UCB and Ono
DOI: 10.1136/annrheumdis-2017-eular.5586

FRI0219 ASSOCIATION BETWEEN CONVERSION TO ACPA/RF SERONEGATIVE STATUS AND CLINICAL OUTCOMES FOLLOWING TREATMENT WITH ABATACEPT IN COMBINATION WITH METHOTREXATE COMPARED WITH METHOTREXATE ALONE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AND POOR PROGNOSTIC INDICATORS

D. Jansen[1], P. Emery[2], J. Smolen[3], R. Westhovens[4], M. Le Bars[5], S. Connolly[6], J. Ye[6], R. Toes[1], T. Huizinga[1]. *[1]Leiden University Medical Center, Leiden, Netherlands; [2]University of Leeds and Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom; [3]Medical University of Vienna, Vienna, Austria; [4]UZ Gasthuisberg, Leuven, Belgium; [5]Bristol-Myers Squibb, Rueil-Malmaison, France; [6]Bristol-Myers Squibb, Princeton, United States*

Background: RA is characterized by the production of autoantibodies, including anti-citrullinated protein antibodies (ACPA) and RF, which are associated with poor prognosis in RA.[1–3] More data on the clinical significance of ACPA/RF seroconversion in response to treatment are needed. Evidence suggests a role for T cells in ACPA production.[2,3]
Objectives: This *post hoc* analysis investigated the effect of the T-cell co-stimulation modulator abatacept (ABA) in combination with MTX vs MTX alone on conversion of ACPA positive (+) and RF+ patients (pts) to seronegative status, and the relationship between conversion to seronegative status and clinical response.
Methods: Data from a double-blind, randomized, Phase III study (AGREE; NCT00122382) conducted in MTX-naïve pts with early RA (≤2 years) and poor prognostic factors (ACPA+ and/or RF+ with evidence of erosions) were included.[4] Pts were randomized to ABA (~10 mg/kg IV according to weight)+MTX or placebo+MTX (MTX alone) in a 12-month (M) double-blind phase followed by 12M of open-label ABA+MTX. Autoantibody titres were assessed at baseline and 6M and 12M of the double-blind phase by ELISA. Pts with titres below the threshold for positivity (ACPA 5 AU/mL; RF [IgM] 15 IU/mL) at M6 or M12 were considered to have converted to seronegative status. The relationship between conversion to ACPA seronegative status and clinical response at M6 and M12 was determined. All analyses were descriptive and based on pts with available DAS28 (CRP) and CDAI data at baseline and M6 and M12.
Results: A total of 435 and 461 pts, respectively, were ACPA+ or RF+ at baseline and had known serostatus at M6 and M12. At 6M, 6.6% (15/227) and 17.0% (39/230) of ABA+MTX pts were ACPA and RF negative, respectively, vs 2.9% (6/208) and 9.5% (22/231) of MTX pts. At 12M, 7.1% (15/212) and 18.5% (41/222) of ABA + MTX pts were ACPA and RF negative, respectively, vs 4.5% (9/198) and 14.6% (32/219) of MTX pts. A higher proportion of pts receiving ABA + MTX who converted to ACPA seronegative status achieved remission (DAS28 [CRP] <2.6 or CDAI ≤2.8) compared with ABA + MTX-treated pts who remained ACPA+ or with pts treated with MTX alone regardless of whether they converted to seronegative status or not (Figure). Pts receiving ABA + MTX who converted to ACPA seronegative status also had a numerically higher cumulative probability of achieving sustained remission (DAS28 [CRP] <2.6) and lower radiographic progression than pts receiving MTX who converted to seronegative status or pts in either treatment group who remained ACPA+ (data not shown).

Figure. Proportion of Patients Achieving Remission, According to DAS28 (CRP)-Defined or CDAI Criteria, by ACPA Seronegative/Seropositive Status



Baseline to Month 6 and baseline to Month 12 were carried out as separate analyses.

Conclusions: Compared with MTX alone, treatment with abatacept + MTX was more likely to result in conversion to ACPA/RF seronegative status in pts with early erosive RA. Conversion to ACPA seronegative status was associated with better clinical and radiographic outcomes.
References:
[1] Scott DL, et al. Lancet 2010;376:1094–108.
[2] Hecht C, et al. Ann Rheum Dis 2015;74:2151–6.
[3] Aletaha D, et al. Arthritis Res Ther 2015;17:229.
[4] Rombouts Y, et al. Ann Rheum Dis 2016;75:578–85.
Disclosure of Interest: D. Jansen: None declared, P. Emery Grant/research support from: AbbVie, Merck, Pfizer, Roche, Consultant for: AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, Lilly, Novartis, Samsung Bioepis, J. Smolen Grant/research support from: AbbVie, Janssen, Lilly, MSD, Pfizer, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, GSK, ILTOO, Janssen, Lilly, MedImmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, R. Westhovens Grant/research support from: Roche, Consultant for: Janssen, Celltrion, Galapagos, Speakers bureau: Bristol-Myers Squibb, M. Le Bars Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, J. Ye Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, R. Toes: None declared, T. Huizinga Grant/research support from: EU & Dutch Arthritis Foundation, Consultant for: Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Crescendo Bioscience, Inc, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, UCB, Inc., Eli Lilly, Speakers bureau: Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough
DOI: 10.1136/annrheumdis-2017-eular.1716

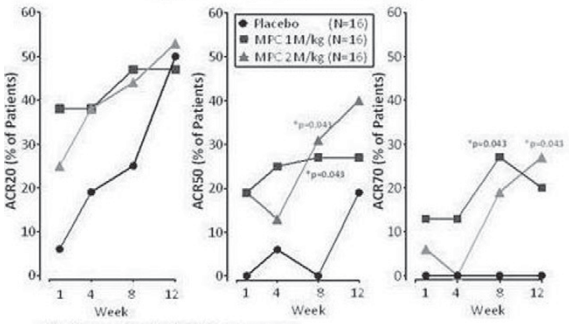
FRI0220 ALLOGENEIC MESENCHYMAL PRECURSOR CELLS (MPCS): A NOVEL APPROACH TO TREATING BIOLOGIC REFRACTORY RHEUMATOID ARTHRITIS

S. Kafaja[1], K.R. Segal[2], D. Skerrett[3], S. Itescu[4], D.E. Furst[5]. *[1]Division of Rheumatology, David Geffen School of Rheumatology, University of California Los Angeles, Los Angeles; [2]Mesoblast, Inc; [3]Mesoblast, Inc, New York, United States; [4]Mesoblast, Inc, Melbourne, Australia; [5]Arthritis Associates of Southern California, Los Angeles, United States*

Background: Allogeneic STRO-3 immunoselected mesenchymal precursor cells (MPCs) derived from bone marrow of healthy donors are a potent, homogeneous cell population which can be activated by pro-inflammatory cytokines to release factors which polarize pro-inflammatory monocytes and T cells to an anti-inflammatory state. This is the first in human trial to assess MPC therapy in biologic refractory RA, a disease driven by monocyte and T cell activation.
Objectives: To assess the safety and tolerability and to explore the clinical efficacy of MPC therapy in RA.
Methods: MSB-RA001 is a phase 1B/2A randomized, double-blind, placebo-controlled, sequential, dose-escalation trial to assess the safety and explore efficacy of a single intravenous (IV) infusion of MPCs in patients with active RA who had failed to respond to at least one biologic. Efficacy endpoints included ACR 20,50,70, ACR core components, HAQ and DAS28. Patients were randomized to receive one IV infusion of MPC 1 million cells/kg (n=16), 2 million cells/kg (n=16), or placebo (n=16) in 2 sequential dose cohorts. The primary study period was 12 weeks.
Results: Patients in all 3 treatment groups (N=16 per group) were comparable in mean age (55 y), gender (73% women), duration of RA (14 years) and

prior biologic exposures. Importantly, MPC infusions were well-tolerated with no adverse infusion reactions or serious adverse events (SAE) noted over 12 weeks. At 4 and 8 weeks, both MPC groups achieved higher ACR20 levels than placebo, with the placebo group reaching similar levels by 12 weeks. Notably, at 12 weeks both ACR50 rates (31, 27, 19%) and ACR70 rates (27, 20, 0%) were higher for the 2M/kg and 1M/kg MPC groups than placebo (Figure 1); p=0.04 for ACR70 in 2M/kg vs. placebo. The MPC groups showed dose-related greater improvement in pain, patient global assessment (PGA) of disease and physical function vs. placebo with greater efficacy in the 2M/kg group (Table 1). At 12 weeks PGA and Pain were significantly reduced in 2M/kg MPC group vs. placebo (both p=0.04). MPC treatment was associated with significantly improved health-related physical function by the HAQ. Minimal clinically important difference in HAQ defined as reduction of at least -0.22 points was achieved in 93% of 2M/kg MPC vs. 25% of placebo at 12 weeks (p=0.003).

Figure 1. ACR20/50/70 Over 12 Weeks



*P values vs. Placebo by Fisher's exact test

Table 1 Summary of Week 12 Efficacy Assessments

	Placebo	MPC 1M/kg	MPC 2M/kg
	N=16	N=16	N=16
ACR20 (%)	50%	47%	50%
ACR50 (%)	19%	27%	31%
ACR70 (%)	0%	20%	27%*
DAS-28 CRP (%)			
Response: ≤3.2	19%	27%	36%
Remission: <2.6	13%	20%	21%
HAQ Change from baseline ≤-0.22 (%)	37.5%	53%	93%**
ACR Core Components [Change (SE) from baseline]			
Tender joints	-9.8 (1.9)	-5.8 (1.9)	-11.2 (1.9)
Swollen joints	-7.7 (1.6)	-6.1 (1.6)	-10.1 (1.6)
Investigator global assessment	-21.6 (6.5)	-32.6 (6.5)	-35.6 (6.6)
Patient global assessment	-6.7 (6.5)	-17.5 (6.5)	-25.7 (6.5)*
Patient pain	-8.4 (6.6)	-16.2 (6.6)	-28.6 (6.7)*

*P<0.05; **P<0.005

Conclusions: A single infusion of MPCs was well-tolerated in RA patients. While the efficacy results are encouraging, further assessment including dose optimization is needed. The current trial is a unique early phase trial that shows promise of a future role for MPCs as a therapeutic option in biologic-refractory RA patients, a subset of the RA population with substantial remaining medical need.
Disclosure of Interest: S. Kafaja: None declared, K. Segal Employee of: Mesoblast, Inc., D. Skerrett Employee of: Mesoblast, Inc., S. Itescu Employee of: Mesoblast, Inc., D. Furst: None declared
DOI: 10.1136/annrheumdis-2017-eular.1106

FRI0221 DOES SEROPOSITIVITY INFLUENCE DIFFERENTIALLY DRUG DISCONTINUATION OF BIOLOGIC ANTIRHEUMATIC AGENTS WITH NON-ANTI-TNF MODE OF ACTION?

A. Finckh[1], D. Courvoisier[1], J.-E. Gottenberg[2], X. Mariette[3], J. Morel[4], S.A. Bergstra[5], V. Hernandez[6], C. Codreanu[7], T.K. Kvien[8], M.J. Santos[9], K. Pavelka[10], M. Hetland[11], K. Chatzidionysiou[12], J. Askling[12], C. Turesson[13], C. Gabay[1], R. Van Vollenhoven[14]. *[1]HUG, Geneva, Switzerland; [2]CHU, Strassbourg; [3]Paris-S University, le Kremlin-Bicêtre; [4]CHU, Montpellier, France; [5]University Medical Center, Leiden, Netherlands; [6]Hospital Clinic, Barcelona, Spain; [7]Univ of Medicine and Pharmacy, Bucharest, Romania; [8]Diakonhjemmet Hospital, Oslo, Norway; [9]Rheuma.PT, Lisbon, Portugal; [10]Institute of Rheumatology, Prague, Czech Republic; [11]Glostrup Hospital, Glostrup, Denmark; [12]Karolinska Institute, Stockholm; [13]Lund University, Lund, Sweden; [14]AMC, Amsterdam, Netherlands*

Background: Rheumatoid factor (RF) and anti-citrulinated protein antibodies (ACPA) are used as diagnostic tools, but may also be used as prognostic factors or as predictors of response to therapy, as these biomarkers have been associated with better clinical responses to some bDMARDs.
Objectives: To examine whether seropositivity has a similar impact on drug discontinuation of different bDMARDs with a non-anti-TNF mode of action (non-aTNF bDMARDs).
Methods: This is a pooled analysis of 10 observational European RA registries (FR, CZ, DK, NO, PT, RO, ES, SE, CH, NL). Inclusion criteria were a diagnosis of RA, initiation of treatment with abatacept (ABA), rituximab (RTX) or tocilizumab (TCZ) and available information on RF and/or ACPA status. The exposure of interest was seropositivity, which was defined as positive if RF or ACPA was positive and negative if both were negative. The primary endpoint was overall drug discontinuation, defined as the period between treatment initiation and treatment discontinuation. Because national differences may constitute a potential confounder, we only included national registries with information for all 3 bDMARD and pooled data across registries only after excluding significant effect modification by country. Drug discontinuation was analyzed using a Cox proportional hazard model, including drug, seropositivity, and their interaction, adjusting for age, gender, disease duration, baseline DAS28, concomitant synthetic DMARD (sDMARDs), number of previous sDMARDs and bDMARDs, and stratifying by country and calendar year.
Results: We found no effect modification by country, allowing us to pool data from 12040 patients (Table). In crude analyses, seropositivity was associated with a lower drug discontinuation with all 3 bDMARD (*p*-value interaction 0.22), with a hazard ratio for seropositive vs. seronegative (HR) 0.89 (95% CI: 0.82–0.97). In adjusted analyses, seropositivity remained associated with a lower drug discontinuation, but the effect differed by drug (*p* interaction 0.01): ABA: HR for seropositive vs. seronegative: 0.76 (95% CI 0.66–0.88), RTX: 0.88, (95% CI: 0.70–1.10), and TCZ: 1.08, (95% CI: 0.89–1.31). Two-by-two drug to drug comparisons showed that the effect of seropositivity differed between ABA and TCZ (*p*=0.004), but not between ABA and RTX (*p*=0.29), or between TCZ and RTX (*p*=0.16). Other factors associated with discontinuation were higher baseline disease activity and more previous bDMARD.

Table 1: Baseline demographic and treatment characteristics

	ABA N=3089	RTX N=5539	TCZ N=3412
Seropositivity, N (%)	2602 (84.2%)	5176 (93.4%)	2920 (85.6%)
• RF+	2234 (73.0%)	4655 (84.1%)	2682 (79.3%)
• ACPA+	1861 (68.5%)	3703 (85.0%)	1826 (73.7%)
Female sex, N (%)	2463 (79.7%)	4543 (82.0%)	2692 (78.9%)
Age [yr], mean (SD)	56.8 (13.2)	58.9 (12.1)	55.9 (12.8)
Disease duration [yr], mean (SD)	11.8 (9.3)	12.5 (9.3)	11.2 (9.6)
DAS28 at baseline, mean (SD)	4.9 (1.5)	5.2 (1.5)	4.7 (1.4)
N previous sDMARD, N (%)			
≤1	917 (32.3%)	1988 (40.1%)	1245 (39.2%)
≥2	1925 (67.7%)	2972 (59.9%)	1928 (60.8%)
N previous bDMARD, N (%)			
≤1	1903 (62.1%)	3818 (69.2%)	1733 (52.5%)
≥2	1163 (37.9%)	1699 (30.8%)	1569 (47.5%)
Concomitant sDMARD, N (%)	1657 (53.6%)	3899 (70.5%)	2251 (66.1%)
Median follow-up time [yrs]	0.96	2.00	1.12
Calendar year of treatment initiation, 10th - 90th percentile	2008-2014	2006-2012	2009-2015

Conclusions: Data from this pooled european registry analysis suggests that seropositivity is associated with lower drug discontinuation of non-aTNF bDMARDs. This effect differed between drugs and was significant for ABA, but not for TCZ or RTX. The impact of seropositivity on other measures of effectiveness still needs to be investigated.
Disclosure of Interest: A. Finckh Grant/research support from: BMS, Speakers bureau: Abbvie, Roche, Pfizer, UCB, D. Courvoisier: None declared, J.-E. Gottenberg: None declared, X. Mariette: None declared, J. Morel: None declared, S. A. Bergstra: None declared, V. Hernandez: None declared, C. Codreanu Grant/research support from: Abbvie, Pfizer, Roche, Consultant for: MSD, Pfizer, Roche, Paid instructor for: Abbvie, Bristol-Myers Squibb, Janssen, MSD, Pfizer, Roche and UCB, T. K. Kvien: None declared, M. J. Santos: None declared, K. Pavelka: None declared, M. Hetland Grant/research support from: AbbVie, BMS, MSD, Biogen, UCB, Pfizer, Eli Lilly, Roche, Speakers bureau: Orion, K. Chatzidionysiou Consultant for: AbbVie, Pfizer, Eli Lilly, UCB, Roche, J. Askling Grant/research support from: Abbvie, UCB, Lilly, Janssen, Samsung, Pfizer, MSD, Roche, C. Turesson Grant/research support from: Abbvie, Pfizer, Roche, Consultant for: MSD, Pfizer, Roche, Paid instructor for: Abbvie, Bristol-Myers Squibb, Janssen, MSD, Pfizer, Roche and UCB, C. Gabay: None declared, R. Van Vollenhoven: None declared
DOI: 10.1136/annrheumdis-2017-eular.6006

FRI0222 SUSTAINED RESPONSE FOLLOWING DISCONTINUATION OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB: RESULTS FROM A RANDOMIZED CONTROLLED TRIAL (COMP-ACT)

J. Kremer[1], W. Rigby[2], N. Singer[3], C. Birchwood[4], D. Gill[4], W. Reiss[4], J. Pei[4], M. Michalska[4]. *[1]Albany Medical College and The Center for Rheumatology, Albany, NY; [2]Geisel School of Medicine, Dartmouth College, Lebanon, NH; [3]School of Medicine, MetroHealth System, Case Western Reserve University, Cleveland, OH; [4]Genentech, Inc., South San Francisco, CA, United States*

Background: Methotrexate (MTX) is frequently administered in combination with biologics for the treatment of rheumatoid arthritis (RA). MTX may be subsequently discontinued due to intolerance or nonadherence, and/or to reduce medication burden once disease control is achieved. Previous studies have established the efficacy of tocilizumab (TCZ) initiated as monotherapy (MONO), but the impact

of MTX withdrawal in patients achieving good clinical response to TCZ+MTX (COMBO) has not been evaluated.

Objectives: To evaluate whether TCZ-MONO is non-inferior to TCZ-COMBO in maintaining clinical response in patients who achieve low disease activity with TCZ-COMBO.

Methods: US patients with RA who were inadequate responders to MTX were enrolled: initial combination therapy included MTX (15 mg/week orally) plus TCZ 162 mg subcutaneous (SC) either weekly (qw; for patients ≥100 kg) or every 2 weeks (q2w; for patients <100 kg). Dose escalation from q2w to qw was allowed at week 12 in patients who had not achieved low disease activity (DAS28 ≤3.2). If patients achieved DAS28-ESR ≤3.2 at week 24, they were randomized (double-blind) 1:1 to receive either TCZ-MONO or continue TCZ-COMBO until week 52. Patients who did not achieve DAS28 ≤3.2 were assigned to an open-label arm and continued TCZ-COMBO until week 52. The primary outcome measured was the comparison of mean change in DAS28-ESR score in the randomized cohort between weeks 24 and 40, between the TCZ-MONO or TCZ-COMBO arms (noninferiority margin of 0.6). Secondary outcomes included the proportion of patients achieving DAS28 <2.6, DAS28 ≤3.2 and American College of Rheumatology 20%/50%/70% (ACR20/50/70) responses at weeks 40 and 52, and safety. Trial registration number: NCT01855789.

Results: Of 718 patients enrolled, 296 were randomized at week 24 (TCZ-MONO, n=148; TCZ-COMBO, n=148). Early discontinuation in the randomized cohort occurred in 12.2% of patients in the TCZ-MONO group and 10.2% in the TCZ-COMBO group. Baseline characteristics were balanced between treatment groups (mean age 55.5 years; 74.8% female; mean RA duration 6.8 years; mean DAS28-ESR 6.3). At week 24, DAS28 scores were similar in both groups, but ACR responses were ~8–11% lower in the TCZ-MONO group prior to MTX withdrawal (randomization). The mean change in DAS28 was similar between the randomized treatment groups (Table 1). For the primary efficacy analysis, the mean changes in DAS28 from week 24 to week 40 were 0.46 and 0.14 in the TCZ-MONO and TCZ-COMBO groups, respectively (95% CI: 0.045–0.592). This study met the primary endpoint by demonstrating that discontinuing MTX in TCZ responders was noninferior to continuing MTX. The safety of TCZ-SC in this study was consistent with the known safety profile with no new safety signals observed (Table 2). The most common SAE was infection, occurring in 4.1% of patients. TCZ-COMBO had greater frequency of AEs, SAEs and serious infections than TCZ-MONO.

Table 1. Efficacy of TCZ as Monotherapy and in Combination With MTX

	TCZ-MONO n = 147	TCZ-COMBO n = 147	Difference (95% CI) (TCZ-MONO minus TCZ-COMBO)
ΔDAS28-ESR, Mean (SEM)*			
Week 24 to week 40	0.46 (0.123)	0.14 (0.126)	0.318 (0.045, 0.592)
Week 24 to week 52	0.43 (0.136)	0.20 (0.139)	0.232 (−0.068, 0.532)
Response at Week 40, n (%)			
DAS28 ≤ 3.2	94 (63.9)	113 (76.9)	−12.9 (−23.3, −2.6)
DAS28 < 2.6	74 (50.3)	87 (59.2)	−8.8 (−20.2, 2.5)
ACR20	103 (70.1)	116 (78.9)	−8.8 (−18.8, 1.1)
ACR50	76 (51.7)	94 (63.9)	−12.2 (−23.4, −1.0)
ACR70	51 (34.7)	62 (42.2)	−7.5 (−18.6, 3.6)
DAS28 Worsening ≥ 1.2, n (%)			
Week 24 to week 40	42 (28.6)	31 (21.1)	7.5 (−2.4, 17.3)

ACR, American College of Rheumatology criteria; AE, adverse event; ΔDAS28-ESR, change in Disease Activity Score-28 joints erythrocyte sedimentation rate; MTX, methotrexate; SAE, serious adverse events; SEM, standard error of the mean; TCZ-COMBO, tocilizumab plus MTX; TCZ-MONO, TCZ monotherapy.

* Adjusted means from ANCOVA model include week 24 DAS28 as a covariate, treatment group and the randomization stratification factors: DAS28 remission status at week 24 (< 2.6; ≥ 2.6 to ≤ 3.2), patient anti-TNF exposure (Yes/No), baseline weight-by-dosing group (< 80 kg q2w; < 80 kg qw; 80 to < 100 kg q2w; 80 to < 100 kg qw, ≥ 100 kg qw). Last observation carried forward (LOCF) was used to impute missing data at week 40 only.

Table 2. Safety of TCZ as Monotherapy and in Combination With MTX

Rate, per 100 PY (95%CI)	Total* N = 713 700.60 PY	TCZ-MONO† n = 144 92.44 PY	TCZ-COMBO† n = 139 90.56 PY
AEs	377.1 (362.9, 391.8)	238.0 (207.6, 271.6)	308.1 (273.0, 346.4)
SAEs	17.0 (14.1, 20.3)	8.7 (3.7, 17.1)	14.4 (7.6, 24.6)
Serious infections	5.0 (3.5, 7.0)	3.3 (0.7, 9.5)	4.4 (1.2, 11.3)

AE, adverse event; PY, patient-year; SAE, serious adverse event.

* Safety population from baseline to end of study.

† Includes all randomized patients who received TCZ+MTX or TCZ+PBO from week 24 to end of study.

Conclusions: These results demonstrate that patients receiving TCZ-COMBO who achieve low disease activity can discontinue MTX and maintain disease control.

Acknowledgements: This study was funded by F. Hoffmann-La Roche, Ltd.

Disclosure of Interest: J. Kremer Shareholder of: Corrona, LLC, Consultant for: AbbVie; Amgen; Bristol-Meyers Squibb; Genentech; GlaxoSmithKline; Eli Lilly; Pfizer; Regeneron; Sanofi, Employee of: Corrona, LLC, W. Rigby Consultant for: Roche, N. Singer Grant/research support from: Merck, EMD Serono, Consultant for: Pfizer, C. Birchwood Employee of: Genentech, Inc., D. Gill Employee of: Genentech, Inc., W. Reiss Employee of: Genentech, Inc., J. Pei Employee of: Genentech, Inc., M. Michalska Employee of: Genentech, Inc.

DOI: 10.1136/annrheumdis-2017-eular.2797

FRI0223 ANTI-CCP IS AN INDEPENDENT PREDICTOR OF 12-MONTH EULAR RESPONSE IN PATIENTS WITH RA TREATED WITH ABATACEPT

A. den Broeder[1], T. Kerstens[2], J. Fransen[2], C. van den Ende[1], L. Tweehuysen[3], R. Postema[4], E. Alemao[5], F. van den Hoogen[2]. *[1]Sint Maartenskliniek and Radboud UMC; [2]Radboud UMC; [3]Sint Maartenskliniek, Nijmegen, Netherlands; [4]Bristol-Myers Squibb, Uxbridge, United Kingdom; [5]Bristol-Myers Squibb, Princeton, United States*

Background: Although anti-cyclic citrullinated peptide (anti-CCP) positivity is regarded as a strong prognostic factor for untreated RA outcome, the benefit of anti-CCP tests for personalized medicine is controversial.[1] Illustratively, anti-CCP was not predictive for response to anti-TNF in RA, as shown in meta-analyses, although some predictive value was shown for rituximab.[2–4] There are, however, indications that better response to abatacept (ABA) is predicted by anti-CCP positivity.[5–7]

Objectives: To test whether anti-CCP level at baseline (BL) is an independent predictor for treatment response (DAS28 [CRP]-based EULAR response criteria) at 12 months (M) in patients (pts) with RA treated with ABA.

Methods: Consenting pts with RA from Radboud UMC and Sint Maartenskliniek were consecutively included if they started treatment with ABA (BL). The anti-CCP values closest before BL were used. DAS28 (CRP) was assessed at BL and at 12M by trained rheumatology nurses or rheumatologists. Demographic and disease-related variables, treatment history and co-morbidity were also assessed. Primary outcome was response to treatment based on DAS28 (CRP) EULAR response criteria at M12. Therapy cessation was regarded as non-response. Multiple imputation with 20 repetitions was used to replace missing predictors. Multivariate logistic regression was used to examine whether anti-CCP positivity was an independent predictor for treatment response, taking confounding BL covariates (Table variables) into account.

Results: Data were available for 200 pts with RA starting ABA. Mean (SD) age was 58 (13) years, 165 (83%) were female and median (p25–p75) disease duration was 12 (7–19) years (Table). Overall, 121 (61%) pts were anti-CCP positive at BL. At 12M, 86 (43%) pts remained on ABA. In the univariate model, anti-CCP was a predictor for treatment response (odds ratio 2.51; 95% CI 1.1, 6.0; p=0.038). No relevant confounding was present.

Table 1. Baseline Characteristics

	Abatacept (n=200)
Age, years, mean (SD)	58 (13)
Female, n (%)	165 (83)
RF+, n (%)	128 (64)
Anti-CCP+, n (%)	121 (61)
No. of previous bDMARDs*	3 (3–4)
No. of previous csDMARDs*	3 (2–4)
Oral glucocorticoids, n (%)	79 (40)
Disease duration, years*	12 (7–19)
Treatment duration, months*	8 (4–28)
NSAID, n (%)	117 (59)
Concomitant DMARD, n (%)	117 (59)
Overweight (BMI >25.0 kg/m^2), n (%)	98 (48)

*Median (p25–p75). RF+: IgM-Rheumatoid factor positivity. b/csDMARD=biologic/conventional synthetic DMARD.

Conclusions: Anti-CCP positivity was confirmed as an independent predictor for treatment response at 12M in pts with RA treated with abatacept. As indicated by meta-analysis and systematic reviews, anti-CCP is not predictive for the response to anti-TNFs.[2–4] Additional studies are needed to evaluate whether abatacept could be a preferable treatment in anti-CCP-positive pts.

References:

[1] Taylor P, et al. Autoimmune Dis 2011;2011:815038.
[2] Lv Q, et al. PLoS ONE 2014;9:e89442.
[3] Isaacs JD, et al. Ann Rheum Dis 2013;72:329–36.
[4] Cuppen BV, et al. Rheumatology (Oxford) 2016;55:826–39.
[5] Gottenberg JE, et al. Ann Rheum Dis 2012;71:1815–19.
[6] Sokolove J, et al. Ann Rheum Dis 2015;74(Suppl 2):675.
[7] Huizinga TWJ, et al. Ann Rheum Dis 2015;74(Suppl 2):234–5.

Disclosure of Interest: A. den Broeder Grant/research support from: CZ, Menzis, ZonMw, Consultant for: Amgen, Boehringer Ingelheim, Speakers bureau: Bristol-Myers Squibb, Pfizer, T. Kerstens: None declared, J. Fransen Grant/research support from: Bristol-Myers Squibb, C. van den Ende: None declared, L. Tweehuysen: None declared, R. Postema Employee of: Bristol-Myers Squibb, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, F. van den Hoogen Consultant for: Celltrion, Sandoz, Mundipharma and Biogen, Speakers bureau: Celltrion, Sandoz, Janssen, Egis

DOI: 10.1136/annrheumdis-2017-eular.2477

FRI0224 RITUXIMAB SELECTIVELY REDUCES IGG4 LEVELS IN RHEUMATOID ARTHRITIS PATIENTS

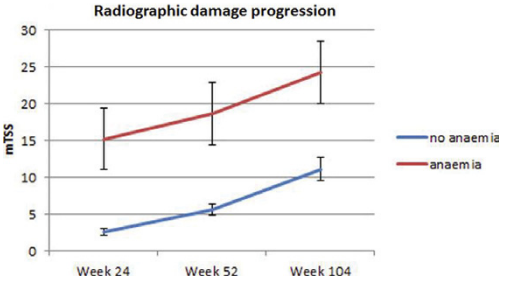
A. Sarantopoulos, I. Gkougkourelas, M. Mytilinaiou, P. Klonizakis, A. Georgiadou, P. Boura. *Clinical Immunology Unit, 2nd Dpt of Internal Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Background: Rituximab has been applied as a therapeutic strategy in a variety of diseases, including Rheumatoid Arthritis (RA) and IgG4-Related Disease (IgG4-RD)[1]. On IgG4-RD, it has been shown that apart from B-cell depletion, rituximab induces remission by reducing IgG4 levels[2].
Objectives: On this regard, we investigated weather B-cell depletion in RA is also associated with a selective reduction of any IgG subclass, especially IgG4.
Methods: 31 RA patients, 25/6 female/male, median age 59 years (34–73), duration of disease 9,5 years (1–30) on standard of care DMARD treatment and rituximab administration every 6 months for 2 years were investigated for alterations on disease activity along with Igs' and IgG subclasses levels. All parameters were assessed at enrollment (T0), and after 6, 12 and 24 months. On this 2-year period all patients had been periodically receiving rituximab every 6 months.
Results: After 2 years of rituximab administration, patients achieved a good response to treatment (EULAR criteria). Igs' levels were not statistically altered, though all of them declined (data for IgM and IgA not shown). Furthermore, from IgG subclasses, only IgG4 levels statistically declined.
Conclusions: This is the first time that IgG4 variations are investigated in a non-IgG4RD after rituximab administration. Our results imply that IgG4 may be actively implicated in RA pathophysiology, since disease remission is accompanied by only IgG4 level reduction among all classes and subclasses of Igs'. Furthermore, in RA patients, rituximab may exert its therapeutic results not only via B-cell depletion, but also via IgG4 levels reduction.
References:
[1] Carruthers MN, Topazian MD, Khosroshahi A, et al. Rituximab for IgG4-related disease: a prospective, open-label trial. Ann Rheum Dis. 2015 Jun;74(6):1171–7.
[2] Khosroshahi A, Bloch DB, Deshpande V, Stone JH. Rituximab Therapy Leads to Rapid Decline of Serum IgG4 Levels and Prompt Clinical Improvement in IgG4-Related Systemic Disease. Arthritis Rheum. 2010 Jun; 62(6): 1755–62.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6690

FRI0225 ANEMIA IS A BETTER PREDICTOR FOR RADIOGRAPHIC DAMAGE IN RHEUMATOID ARTHRITIS THAN DAS28 WHEN DETERMINED BEFORE START OF TOCILIZUMAB-TREATMENT – A SECONDARY ANALYSIS FROM THE ACT-RAY TRIAL

B. Möller[1], G. Scholz[1], M. Dougados[2], T. Huizinga[3], P.M. Villiger[1], A. Finckh[4]. *[1]Rheumatology, Immunology & Allergology, Inselspital - Bern University Hospital, Bern, Switzerland; [2]Rheumatology, Hôpital Cochin, Paris, France; [3]Rheumatology, Leiden University Medical Center, Leiden, Netherlands; [4]Rheumatology, University Hospital Geneva, Geneva, Switzerland*

Background: Clinical remission, or at least low disease activity, as measured by DAS28 or alternative compound indices is currently the goal of RA treatment. Anemia in the context of RA is mainly driven by tumor necrosis factor alpha (TNF-α) and interleukin-six (IL-6), and may serve as a simple biological marker of inflammation. Anemia was recently discovered as a largely DAS28-independent parameter to predict radiographic damage progression in RA, both with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or with anti-TNF agents.
Objectives: To study the predictive value of anemia in relation to DAS28 for radiographically detectable joint damage progression in patients treated with IL-6R inhibitor tocilizumab (TCZ) plus conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) when used in a treat to target concept.
Methods: In the ACT-RAY trial, all patients were methotrexate (MTX) inadequate responders and randomized to receive either TCZ plus MTX (add-on) or TCZ plus placebo (switch strategy) for at least one year. After week 24, open-label csDMARDs other than MTX could be added according to a treat-to-target approach in patients with moderate or high disease activity (DAS28≥3.2). After week 52, patients in sustained clinical remission (DAS28<2.6) could discontinue TCZ before stopping csDMARDs, and finally MTX/Placebo. The exposure of interest was anemia, defined using the WHO definition or the more liberal NHANES definition, both at baseline and over time. The primary outcome was the rate of joint damage progression measured by the change in the modified total Sharp score (ΔmTSS). We used longitudinal multivariate mixed effects models to test the impact of anemia on ΔmTSS. To examine the association of anemia to ΔmTSS independently from RA disease activity, the models were run with and without DAS28 at baseline and DAS28 over time.
Results: Of 556 randomised patients, complete datasets for fully adjusted models were available from 285 patients. Overall radiographic progression was regarded to be minimal, with insignificant differences in favor of the add-on strategy. Median annual ΔmTSS before inclusion was 2.9 (IQR 1.5 to 6.4) in patients without and 5.5 (IQR 2.7 to 11.1) in patients with baseline anemia, but evolved subsequently similar when being on TCZ. Anemia at baseline was a strong predictor of mTSS (per WHO definition: coefficient 14.8, 95% CI 7.6–21.9, p<0.001; per NHANES definition: coefficient 14.6 95% CI 7.6–21.5 p<0.001), as well as baseline DAS28 (coefficient 3.9, 95% CI 0.7–7.0, p=0.016). Mean DAS28 over time (p<0.001), in contrast to anemia data over time when obtained in patients already on TCZ, was significantly associated with subsequent ΔmTSS. Baseline anemia in contrast to baseline DAS28 remained a significant predictor of mTSS for up to two years on TCZ in fully adjusted multivariate analyses (p<0.05), including time-variant DAS28.



Conclusions: Anemia may be a strong and DAS28-independent long-term predictor of radiographic joint damage progression. Present data from patients on IL-6R blockade, a potent target-specific RA treatment with major impact also on erythropoiesis, add importantly to the growing body of evidence for the studied association.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6685

FRI0226 RITUXIMAB IN RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE: A MULTICENTER STUDY

C. Fernández-Díaz[1], M. Martin-Lopez[2], M. Carrasco-Cubero[3], D. Reina-Sanz[4], P. Rubio-Muñoz[5], A. Urruticoechea-Arana[6], J. Miranda-Filloy[7], N. Vegas-Revenga[1], L. Dominguez-Casas[1], M. Gonzalez-Gay[1], R. Blanco[1]. *[1]Rheumatology, Hospital Universitario Marques de Valdecilla, Santander; [2]Rheumatology, Hospital Universitario 12 de Octubre, Madrid; [3]Rheumatology, Hospital Infanta Cristina, Badajoz; [4]Rheumatology, Hospital Sant Joan Despi Moises Boggi; [5]Rheumatology, Hospital Universitario Germans Trias i Pujol, Barcelona; [6]Rheumatology, Hospital Can Misses, Ibiza; [7]Rheumatology, Hospital Universitario Lucus Augusti, Lugo, Spain*

Background: Anti-TNFα drugs and several conventional disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate (MTX) have been involved in the development of Interstitial Lung Disease (ILD).
Objectives: Our aim was to assess the efficacy and safety of Rituximab (RTX) in RA patients with ILD.
Methods: Multicenter study of RA patients with ILD treated with RTX. ILD was diagnosed by high-resolution computed tomography (HRCT). RTX was used at standard dose (1 gx2 and premedication with iv Methylprednisolone for a six month interval. We assess the the following variables: a) 1-point change in the degree of dyspnea according to the Modified Medical Research Council (MMRC); b) FVC improvement ≥10%; and improvement ≥10% in DLCO; c) radiological changes in HRCT scan, and d) changes in the joint assessment measured by DAS28 score.
Results: We studied 18 patients (13 women /5 men) with ILD associated to RA. The mean age±SD was 62.8±11.0 years. The median [IQR] to progression of RA was 5.25 [2–12.8] years. They had received the following DMARDs previously; MTX (n=11), Leflunomide (LFN) (n=9) mycophenolate (MMF) (n=1) sulfasalazine (SSZ) (n=5), hydroxichloroquine (HCQ) (n=4), azathioprine (AZA) (n=1), gold salts (n=1), D-penicillamine (n=1), cyclophosphamide (n=1). 7 patients had previously received biological drugs. RA was seropositive in 16 cases (89%). Besides HRCT, the diagnosis of ILD was confirmed by biopsy in 4 patients. In 2 patients ILD was drug-related: MTX (n=2). RTX was prescribed as monotherapy (n=7) and combined with DMARDs (11. The DMARDs prescribed were: LFD (4), SSZ (2),

Abstract FRI0224 – Table 1. DAS28 and IgG class and subclasses variations. Because of non-normal distribution of our sample, the results were expressed as median and range and statistical analysis was performed by using the Kruskal Wallis tests

	DAS28	IgG	IgG1	IgG2	IgG3	IgG4
T0	4,46 (2,06–6) *	12,2 (5,1–23,1)	7,7 (3,59–12,4)	2,7 (0,844–5,21)	0,573 (0,079–1,85)	0,451 (0,032–2,1)*
T6	3,8 (2,2–6,44)	11,1 (5,78–15)	7,28 (3,38–11,2)	2,7 (1,23–5,36)	0,445 (0,086–1,58)	0,35 (0,044–1,06)
T12	4,01 (1,68–5,77)	11,1 (5,36–19,2)	6,81 (3,35–12,2)	2,53 (0,876–4,67)	0,423 (0,07–1,88)	0,279 (0,036–1,24)
T24	3,27 (1,5–5,07) *	11,2 (4,92–14,5)	6,59 (3,34–10,3)	2,42 (0,92–4,7)	0,405 (0,08–0,823)	0,248 (0,025–1,08)*
	*p<0.05					*p<0.05

MTX (3), HCQ (1), AZA (1) MMF (1). A significant improvement of the dyspnea was observed. FVC and HRCT showed an improvement in the period between 6 and 12 months. DLCO remained stable in the majority of the patients (%). DAS28 also improved.
After a follow-up of 12 months, the only serious adverse effect was a severe Infection respiratory.

Table 1

	Baseline	3 months	6 months	12 months
MMRC, n (%)	18	15	16	16
– No change		10 (67)	10 (63)	10 (63)
– Improvement		5 (33)	6 (37)	6 (37)
– Worsening		0	0	0
CVF, n (%)	16	10	5	13
– No change		7 (70)	5 (100)	10 (77)
– Improvement		1 (10)	0	3 (23)
– Worsening		2 (20)	0	0
DLCO, n (%)	14	6	3	12
– No change		5 (83)	1 (33)	8 (66)
– Improvement		0	2 (67) 7 2 (17)	
– Worsening		1 (17)	0	2 (17)
HRCT, n (%)		7	9	7
– No change		6 (86)	7 (78)	4 (57)
– Improvement		1 (14)	1 (11)	3 (43)
– Worsening		0	1 (11)	0
JOINT, DAS28 – Mean	4.32±1.35	3,21±0.73	3,44±0.87	2.83±0.70
CRP (mg/dl)-, Mean	2.01±2.35	1.12±0.9	1.98±1.95	1.03±0.9
ESR (mm/1sth), Mean	49.0±30.64	37.79±37,73	38.63±30.63	24.50±22

Conclusions: RTX seems to be an effective and relatively safe treatment in RA patients with ILD. However, these data should be verified in prospective and randomized studies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3275

FRI0227 SARILUMAB SIGNIFICANTLY SUPPRESSES CIRCULATING BIOMARKERS OF BONE RESORPTION AND CARDIOVASCULAR RISK COMPARED WITH ADALIMUMAB: BIOMARKER ANALYSIS FROM THE PHASE 3 MONARCH STUDY

C. Gabay[1], J. Msihid[2], C. Paccard[2], M. Zilberstein[3], N.M. Graham[4], A. Boyapati[4]. *[1]University Hospitals of Geneva, Geneva, Switzerland; [2]Sanofi R&D, Chilly-Mazarin, France; [3]Sanofi R&D, Bridgewater; [4]Regeneron Pharmaceuticals, Inc, Tarrytown, United States*

Background: MONARCH (NCT02332590) was a randomized, active-controlled, double-blind, double-dummy, phase 3 superiority trial comparing sarilumab monotherapy with adalimumab monotherapy. Exploratory biomarkers associated with inflammation, bone erosion, and cardiovascular (CV) risk were evaluated in this study.
Objectives: To compare the effects of sarilumab monotherapy vs adalimumab monotherapy on circulating biomarkers associated with acute-phase response (CRP, serum amyloid A [SAA]), bone resorption (RANKL and osteoprotegerin [OPG]), and CV risk (lipoprotein (a) [Lp(a)]) in patients from MONARCH.
Methods: Sera were analyzed at baseline and posttreatment through wk 24 from patients who consented to biomarker analyses and received SC sarilumab 200 mg q2w (N=153) or adalimumab 40 mg q2w (N=154). Biomarkers were assessed using validated ELISAs. Nonparametric methods were used to evaluate differences in the percent change from baseline in biomarker levels between treatments at each time point. Percent change from baseline in biomarkers at wk 24 was also compared, separately by treatment group, between ACR50 responders and nonresponders at wk 24. The Benjamini-Hochberg procedure was used to correct *P* values for multiplicity and control false discovery rate. Significance level was $P<0.05$.
Results: A significant difference in RANKL was observed at wks 2 and 24 between sarilumab and adalimumab groups ($P<0.0001$; Table). Numerically, RANKL decreased after sarilumab and increased after adalimumab treatment. Significantly greater reductions in Lp(a), SAA, and CRP were observed at wks 12 and 24 after treatment with sarilumab vs adalimumab. The difference in OPG between groups was significant at wk 2 only.

Table 1. Median Percent Change From Baseline in Serum Concentrations of Circulating Biomarkers

		Sarilumab 200 mg q2w (N=153)	Adalimumab 40 mg q2w (N=154)
CRP	Wk 12	-94.2†	-29.7
	Wk 24	-94.0†	-24.0
SAA	Wk 12	-79.9†	-32.2
	Wk 24	-83.2†	-17.4
RANKL	Wk 2	-2.5†	4.4
	Wk 24	-18.3†	10.5
OPG	Wk 2	0.9*	-4.0
	Wk 24	2.2	3.3
Lp(a)	Wk 12	-35.0†	-0.4
	Wk 24	-41.0†	-2.8

*Adjusted $P<0.01$ vs adalimumab. †Adjusted $P<0.0001$ vs adalimumab.

At wk 24, change in OPG, RANKL, and Lp(a) did not differ between ACR50 responders and nonresponders at wk 24 in either treatment group. Responders in both groups demonstrated greater reductions vs nonresponders in CRP (sarilumab, -95.8% vs -87.3%; adalimumab, -47.6% vs -6.4%; all $P<0.01$); a trend was observed for SAA (sarilumab, -92.3% vs -73.2%; adalimumab, -33.0% vs 0.0%; unadjusted $P<0.05$, not significant after adjustment).
Conclusions: Sarilumab monotherapy significantly suppressed bone-resorptive and CV risk markers to a greater degree than adalimumab monotherapy. Reductions in CRP were significantly different in ACR50 responders vs nonresponders after either treatment. Analyses to assess predictive and prognostic effects of biomarkers (including markers of myeloid and lymphoid synovial phenotypes) are ongoing.
Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.
Disclosure of Interest: C. Gabay Consultant for: Roche, Merck, AbbVie, Pfizer, Bristol-Myers Squibb, Sanofi-Aventis, and AB2 Bio, J. Msihid Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, C. Paccard Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, M. Zilberstein Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, N. Graham Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Boyapati Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc
DOI: 10.1136/annrheumdis-2017-eular.4534

FRI0228 UGT1A1 GENETIC VARIANTS ARE ASSOCIATED WITH INCREASES IN BILIRUBIN LEVELS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH SARILUMAB

A. Damask[1], A. Boyapati[1], J.D. Hamilton[1], S. Hamon[1], C. Paccard[2], J. Parrino[1], J. van Adelsberg[1], N.M. Graham[1], J. Penn[1], A. Lopez[1], J. Reid[1], J. Overton[1], A. Baras[1], A.R. Shuldiner[1], C. Paulding[1]. *[1]Regeneron Pharmaceuticals, Inc, Tarrytown, United States; [2]Sanofi R&D, Chilly-Mazarin, France*

Background: Sarilumab is a human mAb that blocks IL-6 from binding to both membrane-bound and soluble IL-6Rα. Variants in the *UGT1A1* gene have been shown to be strongly associated with increased unconjugated bilirubin levels in patients treated with tocilizumab, another IL-6Rα inhibitor.[1,2] *UGT1A1* encodes the enzyme responsible for the glucuronidation of bilirubin and variation in this gene is also responsible for Gilbert's syndrome, a mild benign condition characterized by elevations in unconjugated bilirubin and jaundice. The underlying main genetic variation responsible for Gilbert's syndrome has been identified as a TA repeat located in the promoter of *UGT1A1* (UGT1A1*28 allele), which is in linkage disequilibrium with a single nucleotide polymorphism, rs6742078, previously associated with higher bilirubin levels after tocilizumab treatment.[1]
Objectives: To test for an association between rs6742078 and bilirubin levels in RA patients treated with sarilumab.
Methods: DNA was collected from patients enrolled in MOBILITY (NCT01061736), which evaluated the efficacy and safety of sarilumab + methotrexate (MTX) in RA patients with inadequate response to MTX. The pharmacogenetic analysis was conducted in 599 Caucasian patients treated with MTX + sarilumab (150 or 200 mg q2w) or placebo. Log-transformed unconjugated and total bilirubin levels were analyzed at baseline and over the treatment period (using maximum bilirubin).
Results: There was a strong association between the rs6742078 TT genotype and higher unconjugated bilirubin levels. The least squares mean (SE) for patients at baseline with the TT genotype was 0.48 (0.02) mg/dL vs 0.25 (0.009) and 0.21 (0.009) mg/dL for those with GT and GG genotypes, respectively ($p=1.02\times10^{-21}$). After sarilumab treatment, the difference between genotype groups increased over the course of the study ($p=4.3\times10^{-10}$; Figure). In the binary analysis of maximum total bilirubin in sarilumab-treated patients, the TT genotype was significantly associated with mild bilirubin elevations (OR =34.7; $p=1.2\times10^{-8}$; Table).

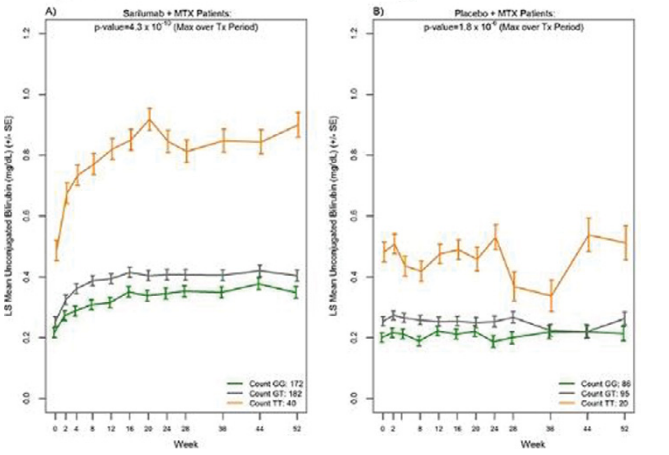
Table 1. Maximum Total Bilirubin in Sarilumab-Treated Patients by rs6742078 Genotype

	Maximum total bilirubin, n (%)		
Genotype, n (%)	≤1.5×ULN	>1.5×ULN	Total
GG/GT	352 (92)	4 (27)	356 (90)
TT	29 (8)	11 (73)[a]	40 (10)
	381	15	396

OR=34.7[b]; $p=1.2\times10^{-8}$. [a]Elevations remained ≤2×ULN. [b]Logistic regression with recessive genetic model, adjusting for ancestry covariates.

Conclusions: The association observed between the rs6742078 TT genotype in *UGT1A1* and unconjugated bilirubin elevations in sarilumab-treated patients is consistent with previous observations in tocilizumab-treated patients. These findings suggest that sarilumab-related increases in bilirubin levels are likely benign and caused by common genetic variation in *UGT1A1* and are not due to underlying liver injury.
References:
[1] Mori et al. Mod Rheumatol. 2012;22:515–523.
[2] Lee et al. Pharmacogenet Genomics. 2011;21:365–374.
Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Figure 1. Unconjugated bilirubin by UGT1A1 genotype (rs64742078) in patients treated with A) Sarilumab + MTX and B) Placebo + MTX



Disclosure of Interest: A. Damask Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Boyapati Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Hamilton Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, S. Hamon Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, C. Paccard Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, J. Parrino Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. van Adelsberg Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, N. Graham Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Penn Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Lopez Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Reid Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Overton Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Baras Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Shuldiner Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, C. Paulding Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc
DOI: 10.1136/annrheumdis-2017-eular.5016

FRI0229 SURVEY ON TRANSPORTATION AND STORAGE OF BIOLOGICAL THERAPIES BY PATIENTS

M. Arias Saavedra, C. Aimo, J.J. Astudillo Andrade, D. Alvarez, G. Sequeira, E.M. Kerzberg. *Servicio de Reumatologia, Hospital J. M. Ramos Mejia, Buenos Aires, Argentina*

Background: in order to ensure the pharmacological action of thermolabile drugs, it is mandatory to keep the cold chain unbroken from manufacturing to administration since lack of observance of these rules may compromise their efficacy. (1,2)
Objectives: to ascertain key aspects of transportation and storage of Biological Therapy (BT) on the part of the patients.
Methods: survey among outpatients who either were treated in the centre or attended the centre for the administration of a BT. Inclusion criteria encompassed patients of over 18 years of age, who were receiving a BT (at least one dose over the last 12 months) whose patient information leaflet indicated, "... must be refrigerated at 2℃ to 8℃ (36℉ to 46℉). Do not freeze." The survey comprised 31 questions about transportation and storage of the BT from the moment of collection from the pharmacy to its administration. This study was approved by the Bioethics Committee. Every patient signed an informed consent form.
Results: Eighty-three patients were interviewed (76% female and 24% males), their average age was 53 years old, 60% had Rheumatoid Arthritis, 24% Psoriatic Arthritis, and 16% sustained other conditions. Sixty-four percent were undergoing BT for the first time. Forty-eight percent were enrolled in a patient assistance programme.
Had patients been fully informed of the importance of proper transportation and storage of the drug? No, 20% acknowledged that the first time they dealt with a BT, they had not been made aware of the relevance of its correct preservation.
Are patients administered the BT immediately after collecting it from the pharmacy? No, 77% collected the drug at least 7 days before administration and though they received the BT in a cooler with ice packs (except in 5 cases) 71% was uninformed of how long it could be kept in this condition.
Is the BT duly stored in the patient's refrigerator? No, 28% misplaced the drug (65% in the freezer), and 90% did not know the temperature range at which it should be kept in the fridge. Only 1 patient used a thermometer to control the appliance temperature.
Is there another crucial point as to BT storage at home? Yes, 53% of the 83 patients had experienced frequent power cuts in summer; out of these, 59% on a weekly basis. Forty percent of the 83 patients had power cuts of over 12 hours, 28% of over 24 hours, and 22% of over 48 hours. Out of the 83 patients, 37% took the BT to another house to avoid wasting it, and 4 had to dispose of it due to a protracted power cut. Five patients were away from home for over 48 hours during which the BT was in the fridge and they had not assigned another person to take care of the drug during their absence.
Is the BT removed from the fridge only for its immediate administration? No, 46% of the respondents travelled to a centre, half of them for over an hour, carrying the BT.
Conclusions: before administering a BT, it is imperative to brief patients on suitable transportation and storage methods. Thus, treatment failure should prompt a thorough assessment of transportation and storage conditions.
References:
[1] Allegra JR, Brennan J, Lanier V, Lavery R, Markenzie B. Storage temperatures of out-of-hospital medications. Acad Emerg Med. 1999;6:1098–103.
[2] Marco JL, Cuéllar MJ, Pérez-Castelló I, Castelló A, Muelas J, Pelegrí J. La cadena del frío de los medicamentos termolábiles en el domicilio del paciente. Pharm Care Esp. 2008;10:40–3.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4150

FRI0230 RETENTION RATES OF TNF INHIBITORS AND ABATACEPT USED AS A FIRST BIOLOGIC DMARD IN THE TREATMENT OF RHEUMATOID ARTHRITIS: 8 YEARS OF EXPERIENCE FROM THE RHUMADATA® REGISTRY

D. Choquette[1], L. Bessette[2], E. Alemao[3], B. Haraoui[1], F. Massicotte[1], M. Mtibaa[4], E. Muratti[4], J.-P. Pelletier[1], R. Postema[5], J.-P. Raynauld[1], M.-A. Rémillard[1], D. Sauvageau[1], A. Turcotte[2], É. Villeneuve[1], L. Coupal[1]. *[1]Rheumatology, Institut de recherche en rhumatologie de Montréal (IRRM), Montréal; [2]Rheumatology, Centre d'ostéoporose et de rhumatologie de Québec (CORQ), Québec, Canada; [3]Bristol-Myers Squibb, Princeton, United States; [4]Bristol-Myers Squibb, Montréal, Canada; [5]Bristol-Myers Squibb, Uxbridge, United Kingdom*

Background: Sustainability of treatment is important to consider when selecting a therapy for chronic conditions such as RA. Sustainability is a useful clinical marker for both long-term efficacy and safety. A recently published randomized controlled trial has demonstrated similar efficacy and safety profiles between abatacept (ABA) and adalimumab over 2 years.[1,2]
Objectives: To assess the long-term sustainability of ABA and anti-TNFs following treatment failure with a conventional synthetic DMARD (csDMARD) in comparable cohorts of patients (pts) with RA.
Methods: Data from pts with RA seen at two tertiary centres and prescribed either ABA or a TNF inhibitor (adalimumab, certolizumab, etanercept, golimumab or infliximab) as their first biologic (b)DMARD after 1 January 2006 were extracted from the RHUMADATA® registry. The choice of therapy was a joint decision between the pt and the treating physician. Pts were followed until either they discontinued treatment, were lost to follow-up or the cut-off date of 9 January 2017. Pt baseline characteristics were compared using descriptive statistics and the cumulative incidence of biologic agent discontinuation using Kaplan-Meier methods. Overall differences in the discontinuation rates of biologic agents were tested using the log-rank test.
Results: Overall, 641 pts met study criteria; 82 pts received ABA and 559 TNF inhibitors (adalimumab=136, certolizumab=52, etanercept=226, golimumab=88 and infliximab=57) as first-line treatment following inadequate response to csDMARDs. No clinically significant differences in baseline characteristics were noted between treatment groups. Most pts were diagnosed after January 2000 (72.5%) and were women (77.5%). Average age at diagnosis was 47.1 (SD=13.4) years, with a mean disease duration of 7.2 (7.8) years, and a mean CDAI of 43.1 (32.5) at baseline. No significant differences in retention rates were observed in the ABA and anti-TNF groups (Table, Figure). On average, pts treated with anti-TNFs and ABA maintained their treatment for 1.59 (1.91) and 1.90 (2.08) years, respectively. Lack of efficacy (47.6%) and adverse effects (22.0%) were the most commonly cited reasons for treatment discontinuation.

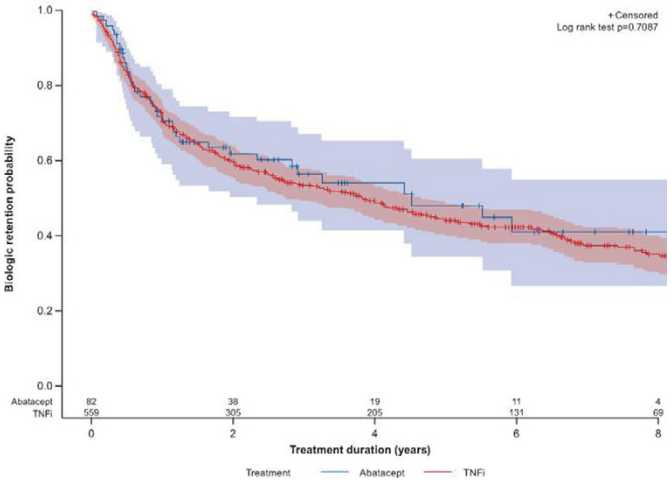
Table 1. Retention of the first bDMARD

	TNFi	Abatacept
Biologic retention probability at*:		
12 Months	71.66% (1.92%)	70.71% (5.15%)
24 Months	59.85% (2.11%)	62.16% (5.60%)
60 Months	44.28% (2.26%)	48.37% (6.75%)
96 Months	35.29% (2.46%)	41.17% (7.43%)
bDMARD retention time (years)		
Mean (SE)	4.83 (0.18)	4.71 (0.45)
Lower quartile, (95% CI)	0.86 (0.72–1.00)	0.86 (0.50–1.24)
Median, (95% CI)	3.83 (2.87–4.67)	4.53 (2.34-++)

*% (% standard error) survival.

Conclusions: Abatacept and TNF inhibitors demonstrate similar sustainability at 8-year, supporting studies[1,2] that demonstrate that abatacept used after csDMARDs inadequate response is as safe and effective as a TNF targeting agents in the long term.

Figure. Retention Rates of Abatacept and TNFi Groups



References:
[1] Schiff M, et al. Ann Rheum Dis 2014;73:86–94.
[2] Schiff M, et al. Ann Rheum Dis 2008;67:1096–1103.
Disclosure of Interest: D. Choquette Consultant for: BMS, Speakers bureau: BMS, L. Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant for: BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, E. Alemao Shareholder of: BMS, Employee of: BMS, B. Haraoui Grant/research support from: BMS, Janssen, Roche, Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Merck, Pfizer, Roche, Sandoz, UCB, Speakers bureau: Pfizer, UCB, F. Massicotte: None declared, M. Mtibaa Shareholder of: BMS, Employee of: BMS, E. Muratti Employee of: BMS, J.-P. Pelletier: None declared, R. Postema Shareholder of: BMS, Employee of: BMS, J.-P. Raynauld Speakers bureau: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, Sanofi, Novartis, UCB, M.-A. Rémillard: None declared, D. Sauvageau: None declared, A. Turcotte Consultant for: Amgen, Abbvie, BMS, Celegene, Janssen, Roche, Pfizer, Lilly, Novartis, Merck, Sanofi, UCB, Speakers bureau: Amgen, Abbvie, BMS, Celegene, Janssen, Roche, Pfizer, Lilly, Novartis, Merck, É. Villeneuve Consultant for: Celgene, Cimzia, Pfizer, Speakers bureau: Abbvie, Roche, BMS, L. Coupal: None declared
DOI: 10.1136/annrheumdis-2017-eular.2326

FRI0231 THE FIRST REPORT OF SIGNIFICANT INCREASE OF BODY MASS INDEX IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB DURING 12-MONTH FOLLOW-UP

D. Novikova, I. Kirillova, E. Luchikhina, E. Markelova, H. Udachkina, N. Demidova, A. Misiyuk, T. Popkova, A. Volkov, L. Denisov, D. Karateev.
V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

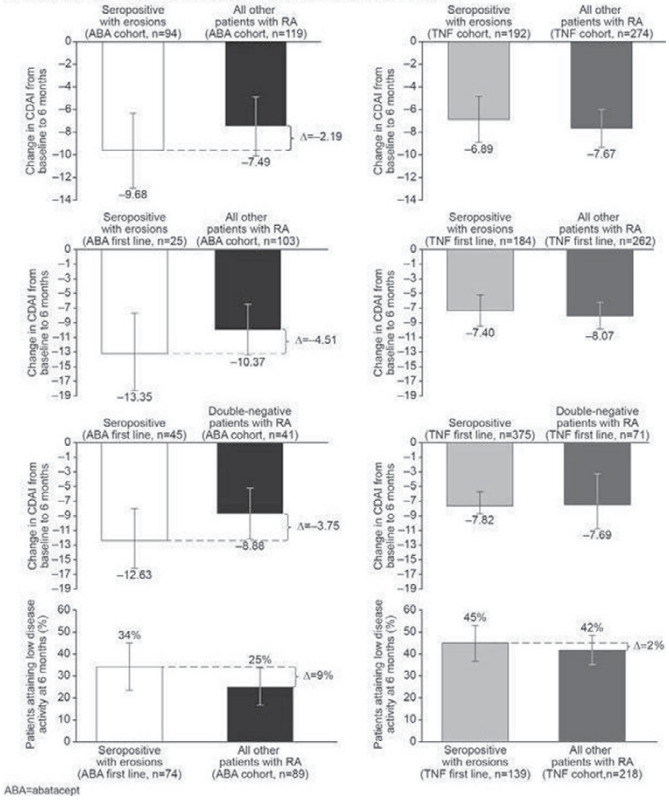
Objectives: to evaluate the effects of tofacitinib (TOFA) on cardiovascular risk factors (CVRF) in rheumatoid arthritis (RA) patients (pts).
Methods: After 12-m follow-up the CVRF dynamic was assessed in 28 RA pts treated with TOFA (22 women, median age 54 [40; 62] years, disease duration 39.5 [16.5; 60.0] m, moderate to high activity (DAS28 - 5.1 [4.6; 6.0], SDAI – 26 [21; 34]), positive for ACCP (75%)/RF (79%), who were non-responders to MTX at least 15 mg/week and/or other synthetic DMARDs and biologic DMARDs. TOFA therapy was started in all pts with dose 5 mg BID per os followed by the dose escalation to 10 mg BID in 8 (29%) pts. TOFA used in combination with MTX in 27 (96%) pts, leflunomide in 1 (4%). Low-dose oral corticosteroids (<10 mg/day prednisone or equivalent) were received by 9 (35%) pts. Remission or low disease activity was achieved in 55% pts (DAS28), 77% (SDAI). At baseline the most of pts had multiple CVRF and subclinical organ damage. Cardioprotective therapy received 16 (57%) pts (beta-blockers – 7, angiotensin II receptor type 2/ACE inhibitors – 11, statins – 11, dihydropyridine calcium channel blockers – 7).
Results: The incidence rate of arterial hypertension (67% vs 70%), overweight (57% vs 72%), abdominal obesity (61% vs 68%), physical inactivity (64% vs 47%), smokers/ex-smokers (25%/21% vs 21%/25%), menopausal status (59% vs 59%), DM type 2 (7% vs 7%), mSCORE≥5% (21% vs 28%), subclinical carotid atherosclerosis (64% vs 64%), cardiac heart failure with preserved ejection fraction (7% vs 7%) did not change significantly. Blood pressure remained stable over time except 1 pt. An increase in body mass index (BMI) was observed from 26.2 [22.9; 28.9] to 26.7 [24.0; 30.1], p<0.001, waist circumference from 86 [76;97] to 91 [80; 103], p=0,001. The increase of BMI <5% was observed in 11 (39%) pts, 5% - 10% - 7 (25%), >10% - 6 (21%). The normal BMI remained in 7 (25%) pts, overweight – 9 (32%), obese class I – 3 (11%), the rest of pts passed to a higher category of BMI (from normal BMI to overweight – 4 (14%), from overweight to obese class I – 1 (4%), from obese class I to obese class II – 1 (4%)) and only 1 pt went from underweight to normal BMI (4%). The change in BMI correlated negatively with DAS 28, SDAI at baseline (r=-0.6, p<0.001). BMI dynamic was independent of TOFA dose, achieving RA activity, dynamic of DAS 28, SDAI, use of cardioprotective therapy. Dynamic of lipid levels depended on statins treatment. An increase in HDL-C level from 1.35 [0.88; 1.91] to 1.90 [1.64; 2.17], p<0.05, a decrease in LDL-C level from 3.75 [3.11; 4.40] to 2.60 [2.55; 2.93], p<0.03 was observed in pts treated with statins (n=11). An increase in total cholesterol level from 4.60 [4.14; 6.41] to 5.45 [4.56; 6.64], p=0,001 was observed in pts who didn't receive statins (n=17). The change in HDL-C level correlated negatively with dynamic of DAS 28, SDAI (r=-0.4, p<0.05).
Conclusions: TOFA therapy of RA pts contributes to dramatical increase of BMI. Greater BMI dynamic associated with higher disease activity at baseline. BMI dynamic was independent of achieving RA activity and dynamic of DAS 28, SDAI. Co-administration TOFA and statins resulted in significant favorable changes of LDL-and HDL-cholesterol levels.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2968

FRI0232 TREATMENT EFFECTS OF ABATACEPT AND ANTI-TNF IN PATIENTS WITH RA WITH POOR PROGNOSTIC FACTORS: DATA FROM COMMUNITY RHEUMATOLOGY CLINICS

E. Alemao[1], K. Knapp[2], V. Anupindi[3], S. Annamalai[4], G. Craig[5]. *[1]Bristol-Myers Squibb, Princeton; [2]Discus Analytics, Spokane; [3]Mu Sigma, Princeton, United States; [4]Mu Sigma, Bangalore, India; [5]Arthritis Northwest, Spokane, United States*

Background: Poor prognostic factors (PPFs; e.g. elevated anti-citrullinated protein antibody/RF levels and erosions) are associated with higher disability and mortality in RA.[1–2] In addition, high seropositivity or CRP/ESR levels are correlated with erosive disease.[3]
Objectives: To evaluate if the presence of specific PPFs of seropositivity with erosions (PPF+) in patients (pts) with RA have an effect on treatment with abatacept (ABA) and anti-TNFs.
Methods: This retrospective study was based on electronic medical record data. This database includes >6500 pts with RA from 50+ rheumatologists. At each visit, data on diagnosis, medications and test results were collected. A homunculus was used to record joint tenderness, swelling, deformity or decreased range of motion. Disease activity was measured by DAS28 (ESR/CRP), SDAI, CDAI, RAPID3 and Vectra DA blood tests. For this analysis, pts aged ≥18 yrs with an RA diagnosis from 1 Jan 2009 to 3 Mar 2016 were followed until lost to follow-up, death or end of study period. Date of first ABA/anti-TNF prescription was designated as index date, preceded by the baseline (BL) period. The ABA cohort comprised pts with a record of ABA in the study period, while the anti-TNF cohort comprised pts with a record of anti-TNF and no record of ABA in the study period. Primary outcome was change (Δ) in CDAI at 6 months (M); other outcomes were SDAI, DAS28 (CRP), pain, RAPID3 and Patient Global Assessment. Descriptive statistics were used for BL characteristics. Univariate and multivariate regression analyses were

Figure. Changes in CDAI in Base Case Abatacept and TNF Cohorts and in Subgroups

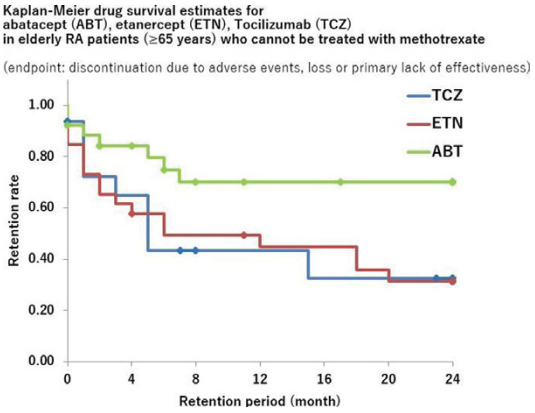


used to evaluate ΔCDAI. Subgroup analyses were conducted by line of therapy, after excluding switch pts.
Results: Overall, 3959 pts met inclusion criteria and 2045 had data on PPF; 344 and 814 pts received ABA and anti-TNF. Mean (SD) age of ABA pts was 60.3 (12.5) yrs and median (interquartile range; IQR) CDAI was 25.5 (18.1). Mean (SD) age of anti-TNF pts was 56.4 (13.3) yrs and median CDAI (IQR) was 19.8 (18.1). PPF+ pts treated with ABA (vs all other ABA pts) had a better CDAI outcome at 6M (–9.7 [16.1] vs –7.5 [14.4]). In sensitivity analyses, the difference persisted (–10.4 vs –8.4; Fig). PPF+ pts treated with ABA as first-line therapy (vs all other ABA pts) had a better CDAI outcome (–13.4 vs –10.3). Similar trends were not observed in the anti-TNF cohort (Fig). Adjusted mean (SE) ΔCDAI in PPF+ vs PPF– pts treated with ABA was –12.1 (2.01) vs –9.5 (0.79); covariates included in the model were age, sex and BL CDAI (p=0.24). During follow-up, more PPF+ pts treated with ABA changed from high/medium to LDA or remission vs all other pts (34% vs 25%), while this was not seen in anti-TNF pts (45 vs 42%).
Conclusions: Pts with RA treated with abatacept had higher disease activity at BL and a greater reduction in disease activity was observed in seropositive pts with RA and erosions compared with all other abatacept pts. Similar trends were not observed in anti-TNF pts. No direct comparisons between treatments were conducted in these cohorts.
References:
[1] Humphreys JH, et al. Arthritis Res Ther 2014;16:483.
[2] Quinn MA, et al. Rheumatology (Oxford) 2006;45:478–80.
[3] Dixey J, et al. J Rheumatol Suppl 2004;69:48–54.
Disclosure of Interest: E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, K. Knapp Employee of: Discus Analytics, V. Anupindi: None declared, S. Annamalai: None declared, G. Craig Shareholder of: Discus Analytics, Grant/research support from: Bristol-Myers Squibb, Consultant for: Premera Blue Cross/Blue Shield of Washington and Alaska, Employee of: Arthritis Northwest, Speakers bureau: Bristol-Myers Squibb, UCB, Genentech, Celgene, Novartis
DOI: 10.1136/annrheumdis-2017-eular.1517

FRI0233 THE RETENTION RATES OF ABATACEPT IN ELDERLY RA PATIENTS (65 YEARS AND ABOVE) WHO CANNOT BE TREATED WITH METHOTREXATE: COMPARISON WITH ETANERCEPT AND TOCILIZUMAB; A SINGLE-CENTER, RETROSPECTIVE, CASE-CONTROL STUDY

E. Kikuchi, N. Aoki, T. Yoshioka, T. Okai. *Center for Rheumatology and Joint Surgery, Kawakita General Hospital, Tokyo, Japan*

Background: There are many elderly rheumatoid arthritis (RA) patients who cannot be treated with methotrexate (MTX) for many reasons, but data about the therapeutic strategies by biologic agents for the patients are insufficient.
Objectives: To analyze the retention rate of abatacept in elderly patients with RA who cannot be treated with MTX.
Methods: Data were retrospectively collected from the medical records of patients with rheumatoid arthritis at our center. Abatacept (ABT), etanercept (ETN), or tocilizumab (TCZ) was administered to 68 elderly RA patients who could not be treated with MTX. We analyzed the retention rate of each group by Kaplan–Meier curves and the log-rank test. The primary end point was the 24-month retention rate of the biologics without discontinuation due to adverse events, loss or primary lack of effectiveness.
Results: In the ABT group (26 cases: a mean age of 77.8±6.3 years, ACPA positive 92.3%, oral steroid use 34.6%), the cumulative retention rates for both 12 and 24 months were 0.699. In the ETN group (26 cases: a mean age of 75.8±5.1 years, ACPA positive 92.0%, oral steroid use 73.1%), the cumulative retention rates for 12 and 24 months were 0.450 and 0.315, respectively. In the TCZ group (16 cases: a mean age of 73.7±5.6 years, ACPA positive 87.5%, oral steroid use 56.3%), the cumulative retention rates for 12 and 24 months were 0.433 and 0.325, respectively.
There was a significant difference in the retention rates between ABT groups and the other two groups [log-rank test, *p*=0.018 (ABT vs. ETN), 0.047 (ABT vs. TCZ)]. There are no significant retention rates between ETN groups and TCZ groups.
Three cases (11.5%) in the ABT group were discontinued the biologic agents by hospitalization for severe infection within 24 months. Five cases (19.2%) in the ETN group, six cases (37.5%) in TCZ group were hospitalized for severe infection, respectively.
Conclusions: Our data suggested that abatacept can be used for a period longer than etanercept or tocilizumab for elderly RA patients who cannot be treated with methotrexate.
References:
[1] Harigai, et al. Mod Rheumatol. 2016 Jul 3; 26(4): 491–498.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6045



FRI0234 CHOICE OF BIOLOGIC THERAPY FOLLOWING RITUXIMAB: INFLUENCING FACTORS IN A FRENCH MULTICENTER COHORT OF RHEUMATOID ARTHRITIS

G. Vial[1], A. De Pouilly[2], L. Scouppe[3], B. Pereira[4], C. Lukas[5], C. Daien[5], A. Ruyssen-Witrand[6], P. Vergne-Salle[2], A. Tournadre[1], C. Richez[3].
[1]Rheumatology, CHU, Clermont Ferrand; [2]Rheumatology, CHU, LIMOGES; [3]Rheumatology, CHU, Bordeaux; [4]DRCI, CHU, Clermont Ferrand; [5]Rheumatology, CHU, Montpellier; [6]Rheumatology, CHU, Toulouse, France

Background: In rheumatoid arthritis (RA), the long lasting effect of rituximab (RTX) on B lymphocyte depletion may influence the choice of biologic after RTX failure but there is currently no specific recommendation about the optimal strategy.
Objectives: We assessed factors which may have influenced the choice of biologic following failure to RTX in RA patients and analysed the effectiveness of these biologics.
Methods: A retrospective study of RA patients, who had started a new biologic during the year after RTX discontinuation, was conducted between 2009 and 2016 in 5 French rheumatology centers. We collected at baseline (at the time the biologic was introduced after RTX) and during follow-up (3, 6 and 12 months), data about patients and disease. Characteristics of the patients receiving tocilizumab (TCZ), abatacept (ABA) or anti-TNF following RTX, the EULAR response and retention rate were compared using univariate and multivariate analyses.
Results: 152 RA patients (117 women, mean age 56.9±13 years) were analysed. RA duration was 14.3 years [IQR 7.8–19.8], mean DAS28 ESR at baseline 4.8±1.3. 57 patients (37.5%) received TCZ, 47 (31%) anti-TNF and 48 (31.2%) ABA following RTX. 87% had received anti-TNF prior to RTX. No significant difference in the biologics prescription profile was noted across centers. At baseline, sex, disease characteristics and activity, use of concomitant DMARDs or prednisone were not different between the 3 groups. There was no difference in the number of cycles or dose of RTX received and the number of previous anti-TNF treatment. Patients receiving ABA were slightly older (59.8 years vs 54 years for TCZ and 57.8 years for anti-TNF, p=0.06). Multimorbidity index (MMI) assessing the number of comorbidities was higher in the group ABA but not significantly (MMI count 2±1.7 for ABA, 1.6±1.5 for TCZ, 1.7±1.4 for anti-TNF, p=0.5). At 3, 6 and 12 months, DAS28ESR was lower in patients with TCZ as compared to those with anti-TNF or ABA (Table) but tender and swollen joint counts did not differ. The EULAR good-or-moderate response rates were similar across groups (Table). After adjustment on age, sex, disease duration, MMI count,

Table 1. Change in DAS28-ESR score and EULAR response at 3, 6, 12 months according to the biologic following RTX treatment

	TCZ (n=57)	Anti TNF (n=47)	ABA (n=48)	p
DAS28 ESR (mean±SD)				
M3	2,7±1,2	3,5±1,7	3,7±1,3	0.002
M6	2,6±1,5	3,5±1,7	3,5±1,2	0.01
M12	2,5±1,2	3,1±1,7	3,3±1,3	0.04
EULAR Good-Moderate response n (%)				
M3	29 (76)	12 (63)	17 (52)	0.09
M6	22 (79)	8 (57)	19 (73)	0.34
M12	21 (75)	7 (70)	16 (73)	0.95

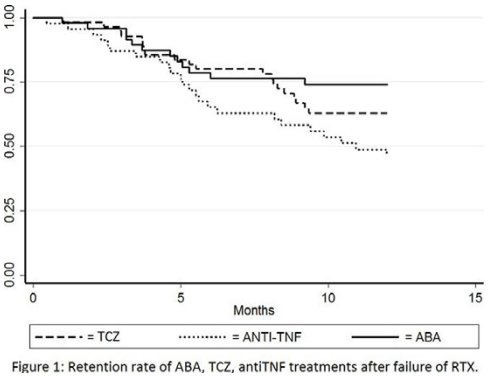


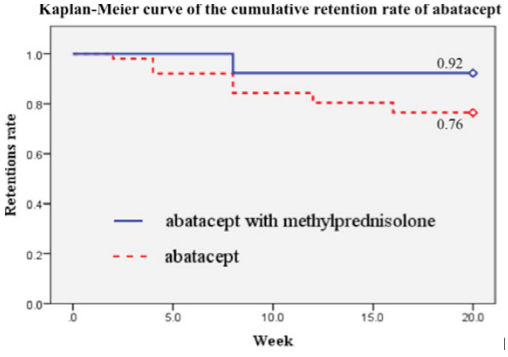
Figure 1: Retention rate of ABA, TCZ, antiTNF treatments after failure of RTX.

number of previous anti-TNF, use of concomitant DMARDs and prednisone, drug retention rate at 1 year was significantly better for ABA compared to anti-TNF (p=0.02) and for TCZ compared to anti-TNF (p=0.04), but no difference was found between TCZ and ABA (p=0.62) (Figure).
Conclusions: Patients who received ABA following failure of RTX, seem to be older and with more comorbidities. Similar rate of good-or-moderate EULAR response was observed between patients receiving TCZ, ABA or anti-TNF. However, drug retention rate was better with TCZ and ABA compared to anti-TNF after RTX discontinuation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5472

FRI0235 CNCOMITANT USE OF INTRAVENOUS METHYLPREDNISOLONE TO OBTAIN HIGHER RETENTION RATE OF ABATACEPT IN RHEUMATOID ARTHRITIS

H. Sawada, M. Suda, M. Kishimoto, M. Okada. *Immuno-Rheumatology Center, St Luke's International Hospital, Tokyo, Japan*

Background: Abatacept (ABT) is a widely used biologic for treating rheumatoid arthritis (RA).
Objectives: Concomitant use of intravenous corticosteroids with ABT infusion may contribute to achieve earlier remission and higher retention rates.
Methods: We conducted a retrospective cohort study at St. Luke's International Hospital, Tokyo, Japan, from January 2010 to June 2016. Patients who met the 2010 ACR/EULAR classification criteria for RA and treated with ABT were included in the study. We excluded patients who use two or more biologics prior to initiation of ABT. Our primary outcome was treatment retention rates of ABT at week 24. Secondary outcomes were changes in C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) during follow-up (week 0 vs. week 8). We compared these outcomes between the patients receiving concomitant intravenous methylprednisolone (mPSL) with first 3 consecutive doses of ABT and those not receiving it. Log-rank analysis and Fisher's exact test were applied for statistical analysis.
Results: 64 RA patients were included in the study. Mean age was 67.3 (± 14.2) and 55 (85.9%) were female. Among them, 13 (20.3%) received concomitant ABT with mPSL. The dosage of mPSL ranged from 30mg to 250mg (median dosage was 40mg). At week 24, the cumulative retention rates of the patients receiving mPSL (mPSL group) and those not receiving it (non-mPSL group) were 92.3% and 76.5%, respectively. There was no significant difference in the retention rates between the two groups (log-rank test, p=0.21) (figure). Changes in CRP between week 0 vs. week 8 were -1.56 mg/dl (± 2.92) in mPSL group and -1.08 mg/dl (± 2.17) in non-mPSL group (p=0.22), and those in ESR were -8.23 mm/h (± 18.40) in mPSL group and -6.61 mm/h (± 17.93) in non-mPSL group (p=0.75), respectively.



Conclusions: This is the first real world study to investigate whether ABT administrated with intravenous mPSL maintain higher retention rates in rheumatoid arthritis. Though there was no statistically significant difference, the retention rates of ABT at 24 weeks were higher among patients receiving ABT and mPSL concomitantly, compared with ABT mono-therapy group. It may reflect rapid improvement of the disease activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4716

FRI0236 AFTER DISCONTINUATION OF THE 1ST TUMOR NECROSIS FACTOR INHIBITOR (TNFI), NON-TNFI BIOLOGIC AGENTS HAVE SIMILAR RESPONSES BUT HIGHER SURVIVAL COMPARED TO A 2ND COURSE OF A DIFFERENT TNFI: LONG-TERM PROSPECTIVE OBSERVATIONAL STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS IN A TERTIARY HOSPITAL OF GREECE

I.D. Flouri[1], A. Repa[1], N. Avgoustidis[1], N. Kougas[1], A. Fanouriakis[1], I. Papalopoulos[1], C. Adamichou[1], P. Kyfonidou[1], E. Kampouraki[1], M. Terizaki[1], D.T. Boumpas[2], G. Bertsias[1], P. Sidiropoulos[1]. *[1]Rheumatology, Clinical Immunology and Allergy, Faculty of Medicine-University of Crete, Heraklion, Crete; [2]4th Internal Medicine Department, Attikon University Hospital, Athens, Greece*

Background: For rheumatoid arthritis (RA) patients who discontinue the first biologic agent (bDMARD), most commonly being a TNF inhibitor (TNFi), there is little evidence supporting the next best choice between a second TNFi course or a non-TNFi bDMARD in clinical practice.
Objectives: To compare the effectiveness and the adherence to therapy with non-TNFi versus TNFi administered as the second-line bDMARD in RA patients with one prior TNFi use.
Methods: All patients starting a bDMARD in the Rheumatology Department of the University Hospital of Heraklion, Crete, are included in a prospective observational study after their written informed consent. Data concerning disease activity at pre-specified time-points, drugs, comorbidities and any adverse events are recorded. For the present study we analyzed patients with RA starting their second course of a bDMARD after discontinuation of a TNFi. We compared DAS28 difference at 6 and 12 months using linear regression analysis and treatment retention using Kaplan-Meier survival curves with log-rank test.
Results: A total of 384 patients started a 2nd (different) TNFi [N=213 (Infliximab: 26, Adalimumab: 77, Etanercept: 89, Golimumab: 13 and Certolizumab: 8)] or a non-TNFi [N=171 (Rituximab:71, Abatacept:66, Tocilizumab:34)]. Patients' characteristics at baseline are described in the Table.
Two-year drug survival was higher for non-TNFi (64% vs. 39%, log rank $p<0.001$) due to lower frequency of discontinuations for primary failure ($p<0.001$) and adverse events (p=0.019).
δDAS28 was comparable between non-TNFi and TNFi patient groups both at 6 [mean (SD): -1.16 (1.29) and -1.07 (1.55) respectively, p=0.296] and at 12 months [-1.41 (1.29) and -1.39 (1.26) respectively, p=0.670]. In patients who did not receive co-therapy with methotrexate, significantly greater δDAS28 was observed with a non-TNFi (-1.25 (1.29) vs.-0.68 (1.61), p=0.006). When the first TNFi was discontinued due to primary failure, we observed a trend for greater δDAS28 in the non-TNFi patient group compared to the 2nd TNFi group (-1.4 vs. -1.0, p=0.12) while the opposite was observed in patients who have experienced secondary failure to the 1st TNFi (-0.81 vs -1.48, p=0.18), but this did not reach statistical significance, probably due to the low number of available patients.
Conclusions: In RA patients who need a 2nd bDMARD after discontinuation of a TNFi, administration of a non-TNFi results in similar clinical responses but higher treatment adherence compared to a second TNFi agent. In patients who do not receive methotrexate, responses are better with a non-TNFi bDMARD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6817

FRI0237 SAFETY OF BIOSIMILAR INFLIXIMAB USE IN A MEDICAL DAY HOSPITAL: A CASE-SERIES

J.M. Lopez Suarez[1], J.M. Lopez Chozas[2], E. Rubio Romero[3]. *[1]Family Doctor, CS Olivar de Quinto; [2]Interne Medicine; [3]Rheumatology, HU Virgen del Rocio, Sevilla, Spain*

Background: The first biosimilar anti-NTF (infliximab) approved by the EMA (European Medicines Agency) began to be used throughout Europe in 2015. Since then, it has been widely used throughout the world, even replacing the original treatment approved in 1999 Remicade® with Remsima®, a biosimilar drug. This medicine is currently approved to treat people who have been diagnosed with rheumatoid arthritis, ankylosing spondylitis or psoriatic arthritis in the field of reheumatology, in addition to ulcerative colitis (UC) or Crohn's disease (EC) in gastroenterology. However, safety data of the use of Remsima® infliximab in a medical day hospital (MDH) are lacking.
Objectives: To report intrainfusion and postinfusion adverse events related to intravenous Remsima® use in a medical day hospital. Besides, we will describe the rehospitalizations and continuity of treatment in the follow up.
Methods: We designed a prospective uncontrolled case-series study. Patients referred from March 2015 to October 2016 to our MDH to receive intravenous Remsima® were consecutively enrolled. Demographic data were collected, and a harmonised active monitoring strategy was applied. We recorded the indication for treatment, the doses administered and the number and symptoms of acute transfusion reactions (ATR) occurring both in the infusion period and during the 3 hour postinfusion observation interval
Results: 2828 doses were administered, 0.67% presented ATR, all of them during the infusion and reported to the Regional Pharmacovigilance Center. 53% of those ATR were women and they were on average 35.78 years (SD 14.71). The mean dose used was 4,809 mg/kg (SD 0.47). The indications for treatment in patients suffering ATR were: EC (47%), CU (26%), Spondylitis (21%) and Psoriasis (5%). As a predominant symptom during ATR we found: shortness of breath (36.89%), pruritus (15.75%), flushing sensation (15.75%), urticaria (10.4%), alopecia (5.2%), chest pain (5.2%), paresthesia (5.2%) and nausea (5.2%). 95% of ATR showed complete recovery of the symptoms, 47% disappeared with the pause of infusion. However, they had prolonged in MDH stay, the infusion was stopped for 30 minutes and restarted at a lower rate according to the protocol. 21% of patients presenting ATR dropped out because of the symptomatology, which represents 0.14% of the total infusions.
Conclusions: Biosimilar Inflximab seems to be safe in a MDH setting, given the

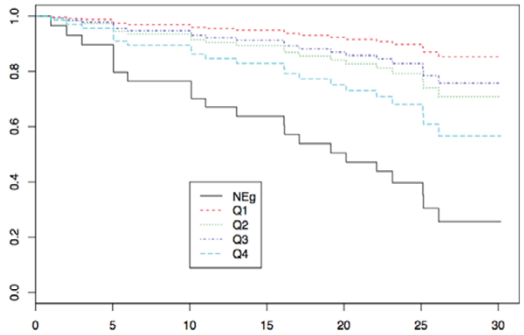
low rate of adverse transfusion reactions during the 18 months analyzed. The most frequent adverse reaction was shortness of breath.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6470

FRI0238 EFFECT OF BASELINE ANTI-CYCLIC CITRULLINATED PEPTIDE 3 ANTIBODY TITRE ON LONG-TERM DRUG SURVIVAL OF SUBCUTANEOUS ABATACEPT IN RHEUMATOID ARTHRITIS: A PROSPECTIVE COHORT STUDY

J.C. Sarmiento-Monroy[1,2], N. Molano-González[2], M. Rodríguez-Jiménez[2], R.D. Mantilla[1,2]. *[1]Rheumatology, Center of Dermatology and Rheumatology (FUNINDERMA); [2]Center for Autoimmune Diseases Research (CREA), Universidad del Rosario, Bogotá, Colombia*

Background: Clinical response to biologics varies widely between individuals with rheumatoid arthritis (RA). To date, there are few, and in some cases, conflicting results in the personalized approach of patients with RA treated with abatacept. Only the seropositive subphenotype (anti-cyclic citrullinated peptide, CCP) was validated in several populations, including a real-life registry (ORA) [1], and non-inferiority trial (AMPLE) [2].
Objectives: To assess whether baseline anti-CCP3 antibody status and concentration correlated with drug survival of subcutaneous (SC) abatacept among patients with RA in a real-world setting.
Methods: This was a prospective study in which well-characterized patients with RA (by 1987 ACR criteria) were included from April 2014 to December 2016. Patients were evaluated at a single rheumatology outpatient center in Bogotá, Colombia. Baseline anti-CCP3 antibody status (positive/negative) and concentration were determined using an anti-CCP3 IgG ELISA (INOVA Diagnostics). Patients with a baseline anti-CCP3 IgG concentration of ≥20 U were considered to be positive and were further divided into equal quartiles according to concentration [Q1–Q4 (highest concentration)]. The Cox proportional hazards regression model was used to test if there were any differences in drug survival curves according to baseline anti-CCP3 antibody status and concentration. The test was performed by the coxph function of the "survival" R package [3].
Results: A total of 129 patients were included. Baseline characteristics: female gender 86%, mean age 52±13 years, median disease duration 10 (IQR 11) years, and erosions 35%. Treatment background was as follows: biologic-naïve (n=54), switched from IV to SC abatacept administration (n=24), and inadequate response to at least 1 biologic disease-modifying antirheumatic drug (n=51). Forty-three patients (33%) discontinued treatment. The most frequent reasons for drug suspension were loss of efficacy. Rheumatoid Factor and anti-CCP3 was positive in 94%, and 89%, respectively. Median titre of anti-CCP3 was 248 U (IQR 352), and number of patients in each quartile group were Q1 (22–122)=21; Q2 (123–248)=20; Q3 (249–475)=19; Q4 (476–1544)=19. According to Cox proportional hazards regression model (Fig.1), there were significant differences between survival curves for Q1 (HR 0.1; 0.02–0.60 95% IC; p=0.011), Q2 (HR 0.2; 0.06–0.94 95% IC; p=0.041), and Q3 (HR 0.2; 0.04–0.85 95% IC; p=0.030), compared to negative group at month 32.

Figure 1. Subcutaneous abatacept survival by anti-CCP3 antibody status.



Antibody-positive patients were divided into equal quartiles (Q1-Q4), representing increasing antibody concentrations. The duration of follow-up was 32 months.

Conclusions: Baseline anti-CCP3 positivity was associated with a better response for SC abatacept in a real-world setting. Patients with lowest baseline anti-CCP3 antibody concentrations had better drug survival than patients with higher concentrations. Our results highlight the importance of identification of factors associated with response to biologics in order to optimize treatment and reduce costs.
References:
[1] Sokolove J, et al. Ann Rheum Dis. 2016;75(4):709–14.
[2] Gottenberg JE, et al. Ann Rheum Dis. 2012;71(11):1815–9.
[3] Therneau,T, Grambsch P. Modeling Survival Data: Extending the Cox Model. Springer-Verlag, 2000.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6682

FRI0239 RESULTS OF A PHASE 2B STUDY OF VOBARILIZUMAB, AN ANTI-INTERLEUKIN-6 RECEPTOR NANOBODY, AS MONOTHERAPY IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

T. Dörner[1], M. Weinblatt[2], K. Van Beneden[3], E.J. Dombrecht[3], K. De Beuf[3], P. Schoen[3], R.K. Zeldin[3]. *[1]Rheumatology and Clinical Immunology, Charité University Hospitals, Berlin, Germany; [2]Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, United States; [3]Ablynx Nv, Zwijnaarde, Belgium*

Background: Vobarilizumab is a Nanobody® consisting of an anti-IL6 receptor domain and an anti-human serum albumin domain in development for treatment of RA.
Objectives: To assess the efficacy and safety of several dose regimens of vobarilizumab monotherapy administered subcutaneously to patients with active RA.
Methods: Patients with active RA who were intolerant to methotrexate (MTX) or for whom continued MTX treatment was inappropriate were randomized in a 1:1:1:1 ratio to 1 of the 3 blinded dose groups of vobarilizumab or to open-label tocilizumab (TCZ), all of which were given subcutaneously. Efficacy was evaluated descriptively at Week 12 using a number of widely accepted clinical endpoints. Adverse events and routine safety parameters including laboratory assessments were recorded. TCZ administered weekly or biweekly according to local labeling was included to obtain parallel descriptive information.
Results: The study enrolled 251 patients in Europe, Latin America and the United States. Baseline demographics and disease characteristics were well balanced across groups with mean $DAS28_{CRP}$ between 5.9 and 6.2.

Week 12 (% of patients)	Vobarilizumab 150mg q4w (N=62)	Vobarilizumab 150mg q2w (N=62)	Vobarilizumab (N=63) 225mg q2w (N=63)	Tocilizumab 162mg q1w (N=60) q2w (N=4)
ACR20	73	77	81	78
ACR50	44	37	49	45
ACR70	16	24	21	23
HAQ-DI score decrease ≥0.25	65	68	71	72
$DAS28_{ESR}$ <2.6	34	21	40	25
$DAS28_{CRP}$ <2.6	26	27	41	27
SDAI remission	8	5	8	11
CDAI remission	10	5	6	9

At Week 12, 73% to 81% of the patients assigned to one of the vobarilizumab groups achieved an ACR20 response, while ACR50 and ACR70 response rates between 37 - 49% and 16 - 24%, respectively, were observed (see table). At the end of the 12-week treatment period, clinically meaningful improvement in HAQ-DI scores and remission based on $DAS28_{CRP}$ and $DAS28_{ESR}$ was observed in a substantial number of patients treated with vobarilizumab, either q4w or biweekly. Between 5% and 10% of the patients achieved remission defined by the more stringent CDAI or SDAI criteria. In total, 94% of patients randomized to open-label TCZ received drug weekly. In spite of this disparity in dosing frequency similar efficacy results were obtained in the vobarilizumab and TCZ groups.
One vobarilizumab treated patient (225mg q2w treatment group, 1.6%) experienced a SAE during the treatment period as did 2 patients in the TCZ group (3.1%). Frequencies of treatment-emergent adverse events were similar across the groups. Of the vobarilizumab treated patients, 2.1% discontinued study drug due to TEAEs compared with 6% in the TCZ group. One case of severe hypersensitivity, not considered serious, was reported in the 225mg q2w treatment group. Liver function abnormalities were infrequent across all study groups. Grade 3 neutrophil toxicities were less commonly observed with vobarilizumab (1.1%) than with TCZ (4.3%).
Conclusions: In patients with active RA, treatment with vobarilizumab monotherapy had a positive impact on disease activity with no unexpected safety findings.
Disclosure of Interest: T. Dörner Consultant for: Ablynx, M. Weinblatt Consultant for: Ablynx, K. Van Beneden Employee of: Ablynx, E. Dombrecht Employee of: Ablynx, K. De Beuf Employee of: Ablynx, P. Schoen Employee of: Ablynx, R. Zeldin Employee of: Ablynx
DOI: 10.1136/annrheumdis-2017-eular.3746

FRI0240 RHEUMATOID ARTHRITIS (RA) IMPACT FOLLOWING TREATMENT WITH SARILUMAB: PATIENT REPORTED OUTCOMES USING THE RAID SCALE FROM TWO RANDOMIZED PHASE III TRIALS

L. Gossec[1], V. Strand[2], C. Proudfoot[3], C. Chen[4], S. Guillonneau[5], T. Kimura[4], H. van Hoogstraten[6], E. Mangan[4], M. Reaney[3]. *[1]Université Pierre et Marie Curie and Hôpital Pitié-Salpêtrière, Paris, France; [2]Stanford University, Palo Alto, United States; [3]Sanofi, Guildford, United Kingdom; [4]Regeneron Pharmaceuticals, Inc, Tarrytown, United States; [5]Sanofi, Paris, France; [6]Sanofi, Bridgewater, United States*

Background: Patients with RA experience a variety of signs and symptoms and report significant physical and psychological impairment. The RA Impact of Disease (RAID) scale is a disease-specific measure of the impact of RA on patients' lives. RAID was assessed in two Phase 3 randomized trials of sarilumab,

a human monoclonal antibody directed against the IL-6 receptor-α (TARGET [NCT01709578]; MONARCH [NCT02332590]).

Objectives: To evaluate patient-perceived impact of sarilumab on RA using the RAID scale vs either placebo + conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or adalimumab.

Methods: TARGET assessed sarilumab 150mg and 200mg added to csDMARDs vs placebo in patients with RA intolerant of or not responding to anti-TNF therapy. MONARCH assessed sarilumab 200mg monotherapy vs adalimumab 40mg monotherapy in patients with RA either intolerant of, inadequate responders to, or considered inappropriate candidates for continued treatment with methotrexate. Treatments were administered subcutaneously every 2 weeks. RAID has 7 single-item domains, each rated by patients on an 11-point numeric rating scale from 0 (absence) to 10 (extreme). A total score from 0 to 10 (with lower scores indicative of less impact of disease) is calculated by weighting responses for each item based on patient assessment of the relative importance of the item. RAID was assessed at baseline (BL), Weeks 12 and 24. Least square mean (LSM) changes from BL in total score (Weeks 12 and 24) and domains (Week 24 only) were analysed with a mixed model for repeated measures, including treatment, region, visit, and treatment-by-visit interaction (and prior csDMARD therapy in TARGET) as fixed effects and BL as a covariate. RAID was tested outside of trial hierarchy and statistical significance is not claimed; nominal p-values are provided. Post-hoc categorical change analyses were conducted to identify "responders" in the total score (improvements ≥ minimum clinically important difference from BL to Week 24 [absolute change of 3 or relative change of 50% in total score]). Patients discontinuing therapy/requiring rescue medication prior to endpoint were classified as non-responders.

Results: Sarilumab was superior (nominal $p<0.05$) to placebo (TARGET) and adalimumab (MONARCH) at Weeks 12 and 24 for RAID total score (Table). There was a greater proportion of responders in both sarilumab dose groups vs placebo at both time points (TARGET) and in sarilumab 200mg vs adalimumab at Week 24 (MONARCH). The effect of sarilumab was consistent across all 7 individual RAID domains (nominal $p<0.05$) at Week 24, except for sleep difficulties vs placebo in TARGET. Effects of placebo were highest on pain and effects of sarilumab were lowest on emotional well-being (TARGET) and coping (MONARCH).

Table. RAID total and individual domain scores at Week 24

		TARGET study			MONARCH study	
		Placebo + csDMARD (n=181)	Sarilumab SC 150 mg q2w + csDMARD (n=181)	Sarilumab SC 200 mg q2w + csDMARD (n=184)	Adalimumab 40 mg q2w (n=185)	Sarilumab SC 200 mg q2w (n=184)
Week 24						
Total RAID score	LSM change (SE)	−1.80 (0.20)	−2.55 (0.19)	−2.80 (0.18)	−2.30 (0.17)	−3.08 (0.17)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.75 (−1.28, −0.22)**	−1.01 (−1.53, −0.48)**	–	−0.78 (−1.23, −0.32)**
	% of 'responders' (MCID = 3)	20.4	33.7**	41.8***	29.7	43.5**
	% of 'responders' (MCID = 50%)	18.8	32.0**	36.4***	28.1	39.7*
Pain	LSM change (SE)	−1.63 (0.20)	−2.66 (0.19)	−2.95 (0.19)	−2.34 (0.18)	−3.22 (0.18)
	LSM difference (95% CI) vs placebo/adalimumab	–	−1.04 (−1.56, −0.52)***	−1.32 (−1.84, −0.80)***	–	−0.87 (−1.36, −0.39)**
Functional disability	LSM change (SE)	−1.46 (0.19)	−2.34 (0.19)	−2.66 (0.19)	−2.25 (0.19)	−3.12 (0.19)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.88 (−1.39, −0.37)**	−1.20 (−1.71, −0.68)***	–	−0.87 (−1.38, −0.37)**
Fatigue	LSM change (SE)	−1.30 (0.20)	−2.21 (0.20)	−2.40 (0.20)	−2.33 (0.20)	−3.02 (0.20)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.91 (−1.44, −0.38)**	−1.11 (−1.64, −0.58)***	–	−0.69 (−1.22, −0.15)*
Sleep difficulties	LSM change (SE)	−1.56 (0.22)	−2.07 (0.22)	−2.53 (0.22)	−2.23 (0.21)	−2.94 (0.21)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.51 (−1.10, 0.07)	−0.97 (−1.56, −0.39)**	–	−0.70 (−1.25, −0.14)*
Physical well-being	LSM change (SE)	−1.58 (0.20)	−2.19 (0.20)	−2.36 (0.19)	−2.39 (0.19)	−3.13 (0.19)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.61 (−1.13, −0.08)*	−0.78 (−1.30, −0.26)**	–	−0.74 (−1.26, −0.22)**
Emotional well-being	LSM change (SE)	−1.24 (0.20)	−1.80 (0.20)	−2.20 (0.20)	−2.07 (0.20)	−2.65 (0.20)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.56 (−1.09, −0.03)*	−0.96 (−1.49, −0.43)**	–	−0.58 (−1.12, −0.04)*
Coping	LSM change (SE)	−1.32 (0.20)	−2.07 (0.20)	−2.50 (0.20)	−1.92 (0.19)	−2.56 (0.19)
	LSM difference (95% CI) vs placebo/adalimumab	–	−0.75 (−1.28, −0.22)*	−1.18 (−1.70, −0.65)***	–	−0.64 (−1.15, −0.12)*

*Nominal p≤0.05 vs placebo (TARGET)/adalimumab (MONARCH); **Nominal p≤0.01 vs placebo (TARGET)/adalimumab (MONARCH); ***Nominal p≤0.0001 vs placebo (TARGET)/adalimumab (MONARCH). CI = confidence interval; csDMARDS = conventional disease-modifying anti-rheumatic drugs; LSM = least square mean; MCID = minimum clinically important difference; q2w = every 2 weeks; RAID = Reumatoid Arthritis Impact of Disease; SC = subcutaneously; SD = standard deviation; SE = standard error of the mean

Conclusions: Assessed using RAID, sarilumab either with csDMARDs or as monotherapy reduced the impact of RA on patients' lives to a greater extent than placebo+csDMARDs or adalimumab monotherapy, with benefits shown on total RAID and all 7 individual domain scores.

Acknowledgements: This study was sponsored by Sanofi and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: L. Gossec Consultant for: Abbvie, Celgene, Janssen, Lilly, Novartis, MSD, Roche, and UCB, V. Strand Consultant for: AbbVie, Amgen, AstraZeneca, Biogen, BMS, Celltrion, CORRONA, Crescendo, Genentech/Roche, GSK, Janssen, Eli Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals, Sandoz, Sanofi, and UCB, C. Proudfoot Shareholder of: Sanofi, Employee of: Sanofi, C. Chen Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, S. Guillonneau Shareholder of: Sanofi, Employee of: Sanofi, T. Kimura Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, H. van Hoogstraten Shareholder of: Sanofi, Employee of: Sanofi, E. Mangan Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, M. Reaney Shareholder of: Sanofi, Employee of: Sanofi

DOI: 10.1136/annrheumdis-2017-eular.3448

FRI0241 THE EFFECT OF ABATACEPT ON CYTOKINE PROFILE IN PATIENTS WITH RHEUMATOID ARTHRITIS

M.A. Borisova, G.V. Lukina, Y. Sigidin, E.L. Luchihina, D.E. Karateev, A. Novikov, E. Alexandrova, E. Aronova, S. Glukhova, E. Nasonov. *Nasonova Reserch Institute of Rheumatology, MOSCOW, RUSSIA, Moscow, Russian Federation*

Background: Pathological activation of T-cells with the overproduction of pro-inflammatory cytokines is playing a major role in the pathogenesis of rheumathoid arthritis (RA). The influence of the selective co-stimulation modulator abatacept (ABA) on the dynamics of cytokine profile in patients with RA is not fully understood.

Objectives: To assess the changes in cytokine profile in patients treated with ABA.

Methods: 44 patients with RA and an inadequate response to synthetic DMARDs or biologics were enrolled in the study. Most of them were middle aged females (46,9±13,9 years) with median RA duration 2 years (1,4–3), high disease activity (DAS28=5,2±0,8), RF-positive (80%) and ACPA-positive (79,5%). 16 healthy individuals were included in the study as control. The serum levels of IL-1, IL-6, IL-17, TNF-α, VEGF, IP-10 (pg/ml) were measured by ELISA immunoassay, YKL-40 by MicroVue immunoassay at baseline and 24 weeks. Disease activity was measured by DAS28, results were assessed every 12 weeks by EULAR criteria. ABA was administered intravenously every 4 weeks.

Results: Levels of IL-6 (2.4 (1,1–6,4) vs 0.7 (0,62–1,0), p=0,0002), YKL-40 (97 (68,4–97, 9) vs. 64 (52,4–107,5), p=0,03), IP-10 (21 (12,9–49,8) vs 14 (9,2–15,2), p=0,005) were significantly higher in patients with RA compared to control. ABA significant reduced disease activity already after 12 weeks of therapy ($p<0,05$). After 24 weeks of ABA therapy good and moderate response by EULAR criteria was achieved in 86%, low disease activity by DAS28 in 52%. By the 6-th month ABA significant decreased levels of IL-6 (1,29 (0,9–2,2, p=0,0006), IP-10 (14 (7,5–28), p=0.007) as well as MMP3: before 30.1 (13–82), after 24 weeks 10 (7.4–55), p=0.0003 and RF: before 218 (9.6–187), after 24 weeks 159 (9.7–155), p=0.02. Lowering of the IL-6 (r=0,5) and IP-10 (r=0,32) levels were significantly ($p<0.05$) associated with a decrease of DAS28.

Conclusions: ABA therapy leads to a significant reduction in serum levels of IL-6, IP-10, MMP3 and RF. The serum levels of IL-6 and IP-10 correlate with decrease activity of RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6540

FRI0242 ASSOCIATION BETWEEN CLINICAL AND RADIOGRAPHIC RESPONSES, AND PHYSICAL FUNCTION IN A PHASE 3 STUDY OF SARILUMAB PLUS METHOTREXATE IN PATIENTS WITH ACTIVE, MODERATE-TO-SEVERE RHEUMATOID ARTHRITIS

M.C. Genovese[1], H. van Hoogstraten[2], W. Kampman[3], S. Jayawardena[2], T.W. Huizinga[4]. *[1]Stanford University Medical Center, Palo Alto; [2]Sanofi Genzyme, Bridgewater; [3]Regeneron Pharmaceuticals, Inc., Tarrytown, United States; [4]Leiden University Medical Centre, Leiden, Netherlands*

Background: In MOBILITY (NCT01061736), SC sarilumab (150 or 200 mg q2w) + MTX demonstrated efficacy in adults with RA and inadequate response to MTX. The most common TEAEs were infections, neutropenia, injection site reactions, and increased transaminases.

Objectives: To examine association between clinical response and radiographic progression and functional response (HAQ-DI) in MOBILITY.

Methods: In this post hoc analysis, associations between HAQ-DI and clinical efficacy categories (CDAI, DAS28-CRP, SDAI, and Boolean-based ACR/EULAR remission) were tested at wk 16. Trend for change from baseline (BL) in HAQ-DI across response categories was assessed using the Jonckheere-Terpstra test.

Results: Regardless of definition, percentage achieving remission (CDAI ≤2.8, DAS28-CRP <2.6, SDAI ≤3.3) or no x-ray progression was higher with sarilumab vs Pbo ($P<0.05$). Overall, there was a significant trend between magnitude of clinical response at wk 16 and improvement in physical function (Table). This trend was also observed for radiographic progression (mTSS change from BL),

Table. Change From BL in HAQ-DI at Wk 16 by Categories of Clinical and Radiographic Efficacy

	Pbo + MTX N=398		Sarilumab 150 mg q2w + MTX N=400		Sarilumab 200 mg q2w + MTX N=399		All patients* N=1197	
	n (%)	mean (SD)	n (%)	mean (SD)	n (%)	mean (SD)	n (%)	mean (SD)
CDAI								
≤2.8	13 (3)	-0.7 (0.5)	25 (7)†	-0.8 (0.6)	40 (11)†	-1.1 (0.7)	78 (7)	-0.9 (0.7)
>2.8 - ≤10	47 (12)	-0.8 (0.8)	92 (23)	-0.7 (0.6)	105 (26)	-0.8 (0.6)	244 (20)	-0.7 (0.6)
>10	315 (79)	-0.2 (0.5)	242 (61)	-0.5 (0.5)	218 (55)	-0.4 (0.5)	775 (65)	-0.3 (0.5)
DAS28-CRP								
<2.6	22 (6)	-0.7 (0.6)	88 (25)†	-0.8 (0.6)	109 (31)†	-0.9 (0.7)	219 (18)	-0.8 (0.6)
≥2.6 - ≤3.2	30 (8)	-0.6 (0.9)	59 (17)	-0.6 (0.6)	66 (19)	-0.5 (0.5)	155 (14)	-0.6 (0.6)
>3.2 - <5.1	154 (41)	-0.4 (0.5)	149 (42)	-0.5 (0.5)	149 (42)	-0.4 (0.6)	450 (38)	-0.4 (0.5)
>5.1	168 (45)	-0.1 (0.5)	61 (17)	-0.3 (0.5)	30 (8)	-0.2 (0.6)	259 (24)	-0.2 (0.5)
X-ray progression (≤0 cutoff)								
No	154 (39)	-0.3 (0.5)	191 (48)†	-0.5 (0.6)	222 (56)†	-0.6 (0.6)	550 (46)	-0.5 (0.6)
Yes	244 (61)	-0.3 (0.6)	209 (52)	-0.6 (0.5)	177 (44)	-0.5 (0.6)	555 (46)	-0.4 (0.6)
X-ray progression (≤0.5 cutoff)								
No	172 (43)	-0.4 (0.5)	219 (55)†	-0.5 (0.5)	257 (64)†	-0.6 (0.6)	648 (54)	-0.5 (0.6)
Yes	226 (57)	-0.2 (0.6)	181 (45)	-0.6 (0.5)	142 (36)	-0.4 (0.6)	549 (46)	-0.4 (0.6)

*$P<0.05$ for trend test. †$P<0.05$ vs Pbo for % with remission/no progression.

regardless of cutoff (≤0.5 and ≤0). In patients achieving remission, there was a numerically greater improvement in HAQ-DI with sarilumab vs placebo (Pbo). Even if patients did not achieve remission or LDA, the sarilumab group had generally greater numerical improvements in HAQ-DI vs Pbo.

Conclusions: Achieving LDA or remission, or absence of radiographic progression, was associated with overall greater improvement in physical function. Irrespective of whether patients achieved remission or LDA, sarilumab + MTX showed greater improvements in HAQ-DI than Pbo + MTX.

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: M. Genovese Grant/research support from: Roche, Sanofi, GlaxoSmithKline, R-Pharma, RuiYi, and Bristol-Myers Squibb, Consultant for: Roche, Sanofi, GlaxoSmithKline, R-Pharma, RuiYi, and Bristol-Myers Squibb, H. van Hoogstraten Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, W. Kampman Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, S. Jayawardena Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, T. Huizinga Consultant for: Sanofi, Roche, and Abblynx.

DOI: 10.1136/annrheumdis-2017-eular.3513

FRI0243 SIRUKUMAB TREATMENT REDUCES LEVELS OF IRON-REGULATORY PROTEINS AND AMELIORATES INFLAMMATION-ASSOCIATED ANEMIA IN RHEUMATOID ARTHRITIS PATIENTS

M. Loza[1], K. Campbell[1], K. Sweet[1], B. Hsu[1], S. Daga[2], B. Dasgupta[1].
[1]*Janssen Research & Development, LLC, Spring House, PA, United States;*
[2]*GlaxoSmithKline, Uxbridge, United Kingdom*

Background: Anemia of chronic disease, a common comorbidity of rheumatoid arthritis (RA), is detrimental to patients' (pts) quality of life, productivity, and long-term health.

Objectives: Sirukumab (SIR), a human monoclonal antibody that selectively binds to the IL-6 cytokine with high affinity, has recently demonstrated efficacy in RA. It was hypothesized that SIR, compared to placebo (pbo) and tumor necrosis factor-inhibitors (TNFi), increases hemoglobin (Hb) concentrations in RA pts by decreasing levels of iron-scavenging proteins and increasing transferrin levels, thus ameliorating anemia. This hypothesis was tested in post hoc analyses of 4 phase 3 studies of SIR in RA: SIRROUND-M (methotrexate [MTX] inadequate responders [IR]); -D (disease-modifying antirheumatic drug [DMARD] IR); -T (TNFi-IR); -H (MTX-IR, monotherapy).

Methods: Standard hematology measurements, including Hb levels, were made throughout the studies by a central laboratory. Anemia was defined as Hb levels <125 g/L (males) and <115 g/L (females). In a subset of pts, iron-regulatory proteins (hepcidin, haptoglobin, hemopexin, transferrin) were measured in serum at baseline (BL) and Wk 4 using the SomaLogic SOMAscan™ platform (for SIRROUND-M, -D, -T, and -H studies, respectively: SIR 100mg q2w, n=61, 205, 136, 0; SIR 50mg q4w, n=61, 201, 128, 100; pbo, n=0, 118, 56, 0; adalimumab [ADA], n=0, 0, 0, 98).

Results: SIR consistently reduced the prevalence of anemia to a greater extent than was observed for pbo ($p<0.05$; eg, in SIRROUND-D, anemia decreased from 25% of pts at BL to 10% at Wk 16 post-treatment with SIR 50mg q4w vs increase from 24% of pts to 28% with pbo) and ADA (SIRROUND-H). Across studies on SIR 50mg q4w, increases in Hb levels ranged from 7±10 to 10±11 g/L (mean±SD) through Wk 16; however, greater changes were seen in pts anemic at BL (13±13 to 16±12 g/L increase). Significant Hb elevations were observed by Wk 2, with comparable results for SIR 100mg q2w. Statistically significant increases in Hb levels were not observed with ADA (Fig.1) or pbo, regardless of BL anemia status. Changes in Hb levels with SIR were independent of changes in RA disease activity. Mean haptoglobin levels were modestly higher at BL in RA pts with anemia compared to pts without anemia. Across studies, both SIR doses similarly strongly decreased levels of hepcidin, haptoglobin, and hemopexin and increased transferrin levels at Wk 4, regardless of BL anemia status. The modulation of these proteins by ADA was considerably less (Fig.1) and by pbo non-significant. After SIR treatment, greater decreases in hepcidin levels were consistently observed in pts with vs without BL anemia across studies by Wk 4.

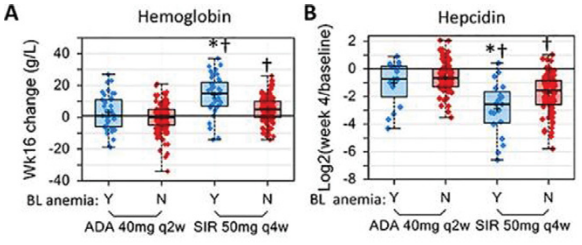


Figure 1. For the SIRROUND-H study, changes in (A) hemoglobin (week 16 change from baseline in g/L) and (B) hepcidin (log_2(week 4/baseline)) are plotted for each available patient, stratified by treatment group and baseline (BL) anemia status (Y, blue; N, red). * p<0.05 for baseline anemia Y vs. N within treatment group; † p<0.05 vs. adalimumab, within baseline anemia group. ADA, adalimumab; SIR, sirukumab.

Conclusions: SIR consistently increased Hb levels in RA pts (DMARD-IR, TNFi-IR, monotherapy), most prominently in pts with BL anemia, resulting in significant reductions in the prevalence of anemia. These effects were independent of the extent of improvement in RA disease activity, suggesting additional benefits of SIR beyond clinical response in RA. By inhibiting IL-6, SIR may decrease key iron-regulatory proteins, such as hepcidin, and shift homeostasis towards an increase in the pool of iron available for red blood cell Hb, thus ameliorating anemia of chronic inflammation associated with RA.

Disclosure of Interest: M. Loza Employee of: Janssen Research & Development, LLC, K. Campbell Employee of: Janssen Research & Development, LLC, K. Sweet Employee of: Janssen Research & Development, LLC, B. Hsu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, S. Daga Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, B. Dasgupta Employee of: Janssen Research & Development, LLC

DOI: 10.1136/annrheumdis-2017-eular.3570

FRI0244 LOW DOSE OF RITUXIMAB IS EFFECTIVE FOR MAINTENANCE OF CLINICAL REMISSION OR LOW DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

N. Avgoustidis, I. Flouri, C. Adamichou, E. Kabouraki, A. Eskitzis, P. Kyfonidou, I. Papalopoulos, A. Fanouriakis, A. Repa, N. Kougkas, G. Bertsias, P. Sidiropoulos. *Department of Rheumatology, Clinical Immunology and Allergy, University Hospital of Heraklion, Crete, Greece, Heraklion, Greece*

Background: Although existing data support the effectiveness of the low dose regimen (LDR, 1gr every 6 months) of rituximab as initial treatment for active rheumatoid arthritis (RA) (2), it is unknown whether this regimen may be used to maintain the therapeutic effect in patients achieved clinical remission or low disease activity (LDA) upon treatment with conventional rituximab regimen (2gr every 6 months)

Objectives: To evaluate the effectiveness of the rituximab LDR for maintenance of clinical remission and/or LDA in patients with RA in clinical practice.

Methods: Long-term prospective study of RA patients who received rituximab in the Rheumatology Department of the University Hospital of Heraklion during 03/2005–07/2016. All patients on clinical remission [DAS 28 (ESR) <2.6] or LDA [DAS28 (ESR) <3.2] for at least 12 months were treated with the LDR after obtaining verbal consent.

Results: We analyzed 247 patients who received conventional rituximab regimen, of median age (IQR) 62 (54.3–70.4)years, females (84%), disease duration 9.6 (5.6–18.3) years,52% seropositive (RF or anti-CCP). Patients have had failed in (median) 3 (2–3) non-biologic (nbDMARDs) and 1 (1–2) biologic DMARDs (bDMARDs) before rituximab initiation. At baseline of rituximab treatment, 58.3% and 91.1% of them were on steroids and (nbDMARDs) respectively, while the disease activity was high [mean DAS28 (ESR): 5.84 (5.20–6.49)] and they had impaired physical functioning [mean HAQ: 1.0 (0.63–1.38)].

Overall, 27/247patients (11%) received the LDR. Before the initiation of LDR, the duration of rituximab treatment was 24 (18–48) months and cumulative rituximab "exposure" was 8 (6–15) gr. At the time of LDR initiation, disease activity [DAS28 (ESR)] was 2.8 (2.2–3.6) and HAQ: 0 (0–0.4), while the time needed for achieving remission or LDA was18 (8–23) months. The median duration of follow-up of patients on LDR was12 (6–20) months. 23 (85%) of patients remained in remission or LDA with median DAS28 (ESR) 2.85 (2.23–3.52) and HAQ 0 (0–0.5) at last follow-up. Only 3 (11%) of the patients experienced an increase of DAS28 (>1.2) and 2 (7%) of patients return to conventional dose.

Conclusions: In clinical practice, RA patients who achieved remission or low disease activity with conventional dose of rituximab may sustain clinical responses if treated with LDR. These preliminary findings support the use of LDR as maintenance treatment regimen and this may allow cost savings. (1)

References:

[1] Gianfranco Ferraccioli et al.Could we use a lower dose of rituximab to treat rheumatoid arthritis in clinical practice: pros and cons? Arthritis Res Ther. 2016; 18: 126.
[2] Chatzidionysiou K, et al. Effectiveness of two different doses of Rituximab for the treatment of rheumatoid arthritis in an international cohort: data from the CERERRA collaboration. Arthritis Res Ther. 2016; 18:50.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4958

FRI0245 ABATACEPT RETENTION RATES AND PROGNOSTIC FACTORS OF RETENTION IN PATIENTS WITH RHEUMATOID ARTHRITIS: 2-YEAR RESULTS FROM THE REAL-WORLD ACTION STUDY

R. Alten[1], H.-M. Lorenz[2], X. Mariette[3], H. Nüßlein[4], M. Galeazzi[5], F. Navarro[6], M. Chartier[7], Y. Elbez[8], C. Rauch[9], M. Le Bars[7]. [1]*Schlosspark-Klinik University Medicine, Berlin;* [2]*University Hospital, Heidelberg, Germany;* [3]*Université Paris-Sud, Paris, France;* [4]*University of Erlangen-Nuremberg, Nuremberg, Germany;* [5]*University of Siena, Siena, Italy;* [6]*Hospital Universitario Virgen Macarena, Seville, Spain;* [7]*Bristol-Myers Squibb, Rueil-Malmaison;* [8]*Excelya, Boulogne-Billancourt, France;* [9]*Bristol-Myers Squibb, Munich, Germany*

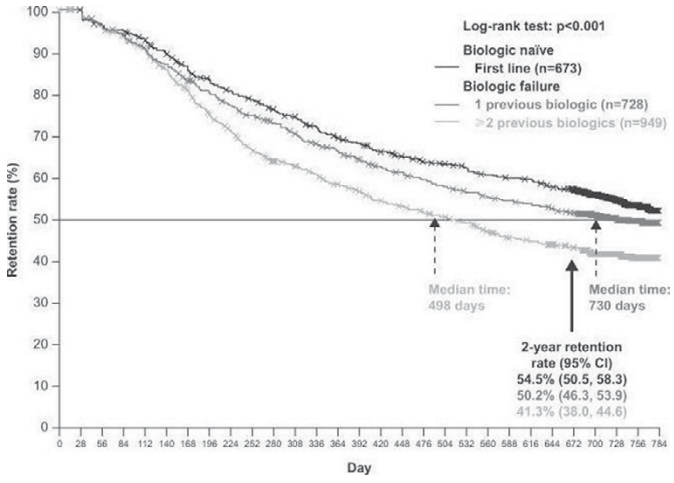
Background: The ACTION (NCT02109666) study was designed to provide

prospective, real-world data on abatacept (ABA) retention in patients (pts) with RA.

Objectives: To assess the retention rate and to identify prognostic factors of ABA retention in the overall ACTION population and by treatment line over 2 yrs.

Methods: ACTION is a 2-yr, international, observational study of pts with RA who initiated IV ABA as first- or as second-/further-line biologic therapy in routine clinical practice. Biologic-naïve and biologic-failure pts were enrolled during three periods between May 2008 and December 2013. The primary endpoint was crude ABA retention rate over 2 yrs (Kaplan–Meier plot). Prognostic factors ($p \leq 0.2$) from univariate analyses with no colinearity, clinically relevant variables and known risk factors were entered into a multivariate model; factors with $p \leq 0.1$ were retained by backward selection. EULAR response was compared by Fisher's exact test.

Results: In the ACTION cohort, 2350/2364 enrolled pts were evaluable for analysis; 673 (28.6%) were biologic naïve and 1677 (71.4%) had failed biologic treatment. Most biologic-failure pts (56.6%) had previously received ≥2 biologics. Some expected differences in baseline characteristics were observed between groups; mean (SD) RA duration was shorter (7.2 [8.2] vs 12.1 [9.1] yrs; $p<0.001$), more pts had RA for ≤2 yrs (35.7 vs 9.0%; $p<0.001$) and fewer pts had radiographic erosions (58.2 vs 71.5%; $p<0.001$) for biologic-naïve vs biologic-failure pts. At Yr 2, the overall retention rate was 47.9% (95% CI 45.7, 50.0). The retention rate was higher in biologic-naïve vs biologic-failure pts (54.5 vs 45.2%; $p<0.001$) and in pts with 1 vs ≥2 previous biologics (Fig). Reasons for discontinuation were comparable between groups; main reasons were lack of efficacy (61.4 vs 67.7%) and safety (21.3 vs 21.2%). RF and anti-citrullinated protein antibody (ACPA) seropositivity were prognostic factors for higher retention in biologic-naïve (p=0.030) and biologic-failure pts (p=0.028); other positively impacting factors were diabetes mellitus (p=0.044; biologic naïve); geographic location ($p<0.001$; biologic naïve) and ABA combination therapy ($p<0.001$; biologic failure). Only Pt Global Assessment (p=0.009; biologic failure) predicted lower retention. Among pts continuing ABA, a greater proportion of biologic-naïve vs biologic-failure pts had a good/moderate EULAR response (90.7 vs 81.6%; p=0.005) and RF/ACPA seropositivity was associated with a better response (p=0.002). There were no new safety signals.



Conclusions: In this first prospective, international, non-interventional research evaluating the long-term IV abatacept retention, RF and ACPA seropositivity were predictors of 2-yr higher retention and better outcomes. Higher retention rates may be achievable with earlier vs later initiation of abatacept treatment, consistent with prior findings from a pooled analysis of EU and Canadian registries.[1]

References:

[1] Iannone F et al. Clin Rheumatol (2016): doi:10.1007/s10067–016–3505–5.

Disclosure of Interest: R. Alten Grant/research support from: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, H.-M. Lorenz Consultant for: AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, X. Mariette Grant/research support from: Biogen, Pfizer, UCB, Consultant for: Bristol-Myers Squibb, LFB, Pfizer, GSK, UCB, H. Nüßlein Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, M. Galeazzi: None declared, F. Navarro Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, Jansen, Lilly, Speakers bureau: Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, M. Chartier Employee of: Bristol-Myers Squibb, Y. Elbez: None declared, C. Rauch Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Le Bars Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.1375

FRI0246 IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE WITH SIRUKUMAB ARE STATISTICALLY SIGNIFICANT, CLINICALLY MEANINGFUL, AND MEET OR EXCEED NORMATIVE VALUES IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO DISEASE-MODIFYING ANTIRHEUMATIC DRUGS: POST HOC ANALYSES OF A PHASE 3 TRIAL

V. Strand[1], K. McQuarrie[2], N. Li[2], R. Ganguly[3]. [1]*Stanford University, Palo Alto, CA;* [2]*Janssen Research & Development, LLC, Spring House, PA;* [3]*GlaxoSmithKline, Collegeville, PA, United States*

Background: Rheumatoid arthritis (RA) is associated with impaired health-related quality of life (HRQoL). Sirukumab (SIR) is an anti–interleukin-6 (IL-6) monoclonal antibody.

Objectives: These post hoc analyses evaluated improvements in HRQoL compared with an age/gender-matched normative population in a phase 3 randomized, controlled trial of SIR in RA pts with inadequate response to conventional disease-modifying antirheumatic drugs (DMARD-IR; SIRROUND-D).

Methods: 1670 pts received SIR 50mg every 4 weeks (q4w), SIR 100mg every 2 weeks (q2w), or placebo (pbo) q2w. Health-related physical/emotional well-being was measured at baseline (BL) and Wk 24 by the 36-item Short Form Questionnaire (SF-36), fatigue by Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue (FACIT-F), and physical function by Health Assessment Questionnaire-Disability Index (HAQ-DI).

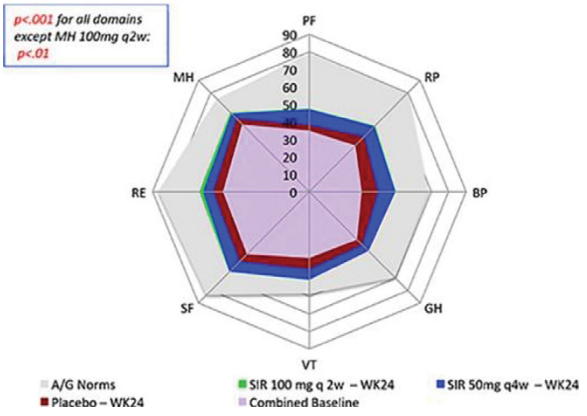
Results: SF-36 physical and mental component summary (PCS and MCS) mean scores at BL were comparable for pbo, SIR 50mg q4w and 100mg q2w (PCS: 33.8, 34.2, and 33.5; MCS: 40.5, 40.5, and 41.8) and indicative of substantial impairment. At Wk 24, treatment with SIR 50mg q4w and 100mg q2w resulted in significantly greater mean improvements from BL vs pbo in SF-36 PCS (5.4 and 5.9 vs 2.3) and MCS (4.9 and 4.2 vs 2.9) scores (all $P<0.001$), exceeding the minimum clinically important difference (MCID) of 2.5. Least squares mean changes in all SF-36 domain raw scores were significantly greater with both doses of SIR than pbo at Wk 24 and all >MCID of 5.0 (Table; Figure). Substantial proportions of pts treated with SIR 50mg q4w or 100mg q2w reported scores ≥normative values in SF-36 domains at Wk 24 (ranges: 20–33% and 21–36%) vs pbo (range: 10–28%). For pbo, SIR 50mg q4w, and SIR 100mg q2w, BL FACIT-F scores were 27.2, 27.1, and 27.5. Significantly greater proportions of pts reported clinically meaningful improvements in FACIT-F (MCID=4) with SIR 50mg q4w and 100mg q2w vs pbo (61.4 and 59.4% vs 43.9%; $P<0.001$). FACIT-F scores ≥normative values were reported by 33% of pts on SIR 50mg q4w and 100mg q2w vs 22% on pbo. HAQ-DI scores at BL were 1.56, 1.50, and 1.52 with pbo, SIR 50mg q4w, and 100mg q2w, with clinically meaningful improvements (MCID= -0.22) reported by 63.0 and 65.4% with SIR 50mg q4w and 100mg q2w vs 46.9% with pbo ($P<0.001$). HAQ-DI scores ≥normative values were reported by numerically more pts receiving SIR 50mg q4w (22%) and 100mg q2w (21%) vs pbo (10%).

Table 1. Improvements in SF-36 Domain Scores at Wk 24 (all $P \leq 0.006$)

Domain	LSM change SIR 50mg q4w	LSM change SIR 100mg q2w	LSM change pbo
Physical function	10.48	12.39	2.85
Role-physical	14.88	16.04	7.96
Bodily pain	19.09	18.98	9.44
General health	8.90	7.53	3.57
Vitality	11.83	11.96	6.37
Social function	13.49	13.25	7.65
Role-emotional	12.50	11.74	6.54
Mental health	9.26	7.97	5.00

LSM, least squares mean.

Figure. SF-36 domains at Wk 24 for SIR 50mg q4w and SIR 100mg q2w



Conclusions: Through 24 wks, SIR treatment resulted in greater improvements in HRQoL than pbo that were clinically meaningful and met or exceeded normative values in DMARD-IR RA pts, with similar effects observed with both doses of SIR.

Disclosure of Interest: V. Strand Consultant for: Abbvie, Amgen, AstraZeneca, BiogenIdec, Boehringer Ingelheim, Celltrion, Crescendo, Genentech/Roche, GSK,

Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi and UCB, K. McQuarrie Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, N. Li Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, R. Ganguly Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline
DOI: 10.1136/annrheumdis-2017-eular.3917

FRI0247 MEDIAN TIME TO LOW DISEASE ACTIVITY IS SHORTER IN TOCILIZUMAB COMBINATION THERAPY WITH CSDMARDS AS COMPARED TO MONOTHERAPY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSES TO CSDMARDS AND/OR TNF INHIBITORS: SUBANALYSIS OF THE SWISS AND AUSTRIAN PATIENTS FROM THE ACT-SURE STUDY

R. Mueller[1], W. Graninger[2], P. Sidiropoulos[3], C. Goger[4], J. von Kempis[1]. *[1]Division of Rheumatology, Kantonsspital St. Gallen, St. Gallen, Switzerland; [2]Division of Rheumatology, Medical University of Graz, Graz, Australia; [3]F. Hoffmann-La Roche Ltd., South San Francisco, United States; [4]Roche Austria GmbH, Vienna, Austria*

Background: To analyze efficacy and safety of tocilizumab in patients with rheumatoid arthritis (RA) and an inadequate response to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) and/or tumour necrosis factor (TNF) inhibitors of the Swiss and Austrian patients from the ACT-SURE study.
Objectives:
Methods: Sub-analysis of RA patients from Switzerland and Austria, who participated in the international phase IIIb, open-label, ACT-SURE study. Patients with an inadequate response to csDMARDs or TNF antagonists were included into the study receiving 8 mg/kg of IV tocilizumab every 4 weeks during a 24 week time period. Therapy with one or more csDMARDs could be continued as combination therapy with tocilizumab (Combo) or stopped, resulting in tocilizumab monotherapy (Mono), at the treating physician's discretion. These two patient groups were analyzed in separate and compared.
Results: Overall, 107 (22 on Mono vs 85 on Combo and) patients were treated with tocilizumab. The percentage of patients with at least one adverse event was significantly lower in the tocilizumab combination (58.8%) as compared to the monotherapy group (81.8%, p=0.0458). No differences in ACR20/50/70/90 response rates were observed between both treatment groups at week 24 (Mono: 63.6%, 40.9%, 22.7%, and 18.2% vs. Combo: 61.2%, 43.5%, 25.9%, and 10.6%). The median time to low disease activity (LDA) was significantly shorter in patients treated with tocilizumab combination therapy Mono: 9.1, Combo 7.9 weeks, Log Rank p=0.038).
Conclusions: In this post hoc regional sub-analysis of the ACT-SURE study no differences for disease activity were found comparing the two patient groups at week 24. However, median time to LDA was statistically shorter in patients treated with tocilizumab combination therapy as compared to tocilizumab monotherapy. Consequently, adding tocilizumab to csDMARD therapy rather than changing to tocilizumab monotherapy may be, in our opinion, the safest strategy to reach maximum effect in RA patients with active disease despite treatment with csDMARD. csDMARDs can be withdrawn either immediately due to adverse events or after at least low disease activity has been reached.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5903

FRI0248 INCIDENCE OF MELANOMA IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB

S. Gale[1], J. Wang[2], J.M. Nebesky[3], A.T. Linke[1], E. Berber[1]. *[1]Genentech, South San Francisco, CA, United States; [2]Roche Products, Welwyn Garden City, United Kingdom; [3]F. Hoffmann-La Roche, Basel, Switzerland*

Background: There have been conflicting reports whether patients with rheumatoid arthritis (RA) receiving conventional or biologic immunosuppressive therapies are at increased risk of specific malignancies. Melanoma is an aggressive malignancy with risk factors including sex, age, fair skin and elevated cumulative UV exposure. Interleukin-6 (IL-6) has a role in pro- and antitumorigenic pathways. Whether tocilizumab (TCZ), a biologic that alters IL-6 signaling, increases the risk of melanoma in patients with RA is unclear.
Objectives: This age- and sex-adjusted standardized incidence ratio (SIR) analysis compared the observed reports of melanoma in patients with RA treated with TCZ in clinical trial and postmarketing settings with the expected number of cases across geographic regions.
Methods: SIRs for melanoma were calculated from the TCZ clinical trials all-exposure population. Postmarketing rates were estimated from the TCZ Global Safety Database population. Both databases were searched cumulatively from 11 April 2005 to 10 October 2015. For clinical trials, observed reports of melanoma in patients with RA treated with TCZ were compared with expected number of cases in the general population based on the 2012 US Surveillance, Epidemiology, and End Results using an age- and sex-adjusted SIR. Postmarketing regional SIRs were calculated based on the estimated commercial exposure in each region and the incidence of melanoma as reported by Globocan by age and sex (2012). Crude postmarketing rates were age- and sex-adjusted according to the clinical trial demographic profile to estimate the expected number of cases of melanoma in each region.
Results: In the clinical trial setting, 4 qualifying cases of melanoma were identified among 7093 patients with RA treated with TCZ (20,828 PY of exposure). The SIR estimate (0.71 [95% CI, 0.19–1.81]) for melanoma incidence in patients with RA treated with TCZ in clinical trials was comparable to that in the general population (Table 1). In the postmarketing setting, the number of observed reports of melanoma was comparable to the expected number of cases in Europe and Japan and fewer than expected in North America (Table 2). The exception is Australia, where SIR estimates indicated more than the expected number of cases in patients with RA receiving TCZ in Australia compared with the general population in that region (SIR 3.71 [95% CI: 2.16, 5.93]).

Table 1. Incidence of melanoma in patients with RA from TCZ clinical trials, stratified by sex

Sex	Observed cases[a]	Exposure (PY)	Expected cases[b]	SIR (95% CI)
Female	3	17,047	4.01	0.75 (0.15, 2.19)
Male	1	3781	1.66	0.60 (0.02, 3.35)
All	4	20,828	5.65	0.71 (0.19, 1.81)

[a] The age range of patients in the study cases was 50-64.
[b] Expected cases are based on Surveillance, Epidemiology, and End Results 2012 age-standardized incidence rates.

Table 2. Incidence of melanoma in patients with RA from TCZ postmarketing reports, stratified by region

Region	Observed cases	Region-Specific Exposure (PY)[c]	Expected cases[d]	SIR (95% CI)
Europe	30	126,683	26.6	1.13 (0.76, 1.61)
North America	17	131,546	36.9	0.46 (0.27, 0.74)
Japan	2	121,732	1.5	1.38 (0.17, 4.98)
Australia	17	6,480	4.6	3.71 (2.16, 5.93)

[c] Combined exposure from Europe, North America, Japan and Australia accounts for 86% of the total cumulative postmarketing exposure and for all cases of melanoma at the data lock point of 10 October 2015.
[d] Expected cases are based on region-specific incidence rates in the general population (Globocan 2012).
PY, patient years; SIR, standardized incidence ratio; TCZ, tocilizumab.

Conclusions: In clinical trials, no evidence was found to suggest there were more cases of melanoma than expected in patients with RA treated with TCZ compared with the general population. Consistent with this, no evidence was found to suggest that patients with RA treated with TCZ in Europe, North America or Japan had more cases of melanoma than expected compared with the general population in each region. In contrast, the estimated SIR of melanoma in patients with RA treated with TCZ in Australia indicated more than the expected number of cases in the general population. This finding is consistent with reports of elevated risk of melanoma in patients with RA in Australia (compared with the general population), where UV exposure is high and methotrexate is a common first-line therapy.[1,2]
References:
[1] Buchbinder et al. Arthritis Rheum. 2008.
[2] Buchbinder et al. BMC Musculoskelet Disord. 2015.
Acknowledgements: Funded by Roche/Genentech.
Disclosure of Interest: S. Gale Employee of: Genentech, J. Wang Employee of: Roche, J. Nebesky Employee of: Roche, A. Linke Employee of: Genentech, E. Berber Employee of: Genentech
DOI: 10.1136/annrheumdis-2017-eular.1314

FRI0249 CIRCULATING FOLLICULAR HELPER-LIKE T CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ABATACEPT

S. Piantoni[1], M. Scarsi[2], F. Regola[1], A. Tincani[1], P. Airò[1]. *[1]Rheumatology and Clinical Immunology Unit, Spedali Civili and University of Brescia, Brescia; [2]Internal Medicine Unit, Esine-Vallecamonica Hospital, Esine, Italy*

Background: Rheumatoid arthritis (RA) is characterized by synovial inflammation and, in most cases, by autoantibodies, including rheumatoid factor (RF) and anti-cyclic citrullinated peptide antigen (ACPA), whose presence is associated to a more severe disease. The capability of producing autoantibodies is acquired by B cells with the "help" of specialized T lymphocytes, known as Follicular helper T (TFH) cells, in the germinal centers (GC) of secondary lymphoid tissues. TFH express the inducible co-stimulator (ICOS), and are characterized by a high expression of CXC-chemokine receptor 5 (CXCR5), which mediate their migration into the GC, where its ligand CXCL13 is expressed. Here, TFH promote the GC development and B cell maturation. These cells are reported to exist in greater quantities in the peripheral blood (circulating TFH-like cells) of RA patients.
Abatacept (ABA) is a fusion protein, which through its CTLA4 portion can bind to CD80 and CD86 on antigen presenting cells, thereby inhibiting CD28 costimulation. Data from animal models and phenotypic analysis of circulating T cells in RA suggest that ABA may act in the secondary lymphoid organ, and not directly on the synovium (1,2). While experimental models show that ABA can block the generation of TFH (3), little is known on the effect of ABA on circulating TFH-like cells of RA patients (4).
Objectives: To analyze the effect of the blockade of costimulation performed by

ABA on the levels of circulating TFH-like cells of RA patients.
Methods: 25 RA patients (F/M=18/7; median age (25th-75th percentile): 57 (44–63) years; ACPA+: 16 (64%); RF+: 17 (68%)), treated for at least 6 consecutive months with ABA were evaluated. Circulating TFH-like cells were identified by flow-cytometry as CD4+ICOS+CXCR5+.The response to treatment was evaluated with the EULAR Criteria.
Results: After 6 months of therapy with ABA the percentage of circulating TFH-like cells among total CD4+ T-cells tended to decrease from a median of 1.8 (0.6–3.8) to 0.8 (0.1–2.3) (p:0.07; Wilcoxon signed rank test). The percentage of circulating TFH-like cells at baseline was higher among patient who did not respond to ABA (n.8; 2.6 (2.0–3.6)) than in those who achieved a moderate or good EULAR response (n:17; 1.0 (0.5–5.4)) ($p<0.01$; Mann-Whitney test), but their trend of reduction was similar in the two groups of patients. No difference in the levels of circulating TFH-like cells was found between ACPA+ and ACPA- RA patients.
Conclusions: ABA tends to reduce the number of circulating TFH-like cells in RA patients, suggesting the relevance of costimulation via CD28 in their generation. A higher percentage of these cells is present in patients not responding to ABA. While this observation suggests their possible use as predictors of clinical response to ABA, further studies are deserved to evaluate whether it reflects different localizations of TFH, or functional variability within this T-cell subset in patients with RA.
References:
[1] Koenders M et al, Arthritis Rheum 2012.
[2] Airo' P et al, Arthritis Rheumatol 2015.
[3] Platt AL et al, J Immunol 2010.
[4] Iwata S et al, Arthritis Rheumatol 2015.
Acknowledgements: Bristol-Myers-Squibb Italy provided an unrestricted research grant for the study conduct and did not interfere with the conception and design of the study, acquisition, analysis, interpretation of data, and manuscript drafting.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4081

FRI0250 SERIOUS ADVERSE EVENTS IN PATIENTS WITH RA TAKING ABATACEPT COMPARED WITH OTHER DMARDS BY LINE OF TREATMENT

S.A. Pedro[1], R. Schumacher[1], K. Michaud[1,2]. *[1]National Data Bank for Rheumatic Diseases, Wichita, KS; [2]University of Nebraska Medical Center, Omaha, NE, United States*

Background: Observational studies are critical in assessing medication safety and effectiveness in the real world. Nonrandom assignment can provide insight to how and when medications are prescribed. Since the US introduction of TNF inhibitors (TNFi) in 1998, several newer biologics with varying mechanisms of action are available to patients and physicians.
Objectives: To compare baseline characteristics and serious adverse events (serious infections (SI), malignancies) of patients who received abatacept (ABA) compared to those who received other comparison cohorts: conventional DMARDs (cD) and biologic DMARDs (bD) by line of treatment.
Methods: Participating patients from 2005–2015 with RA in the National Data Bank for Rheumatic Diseases (NDB) provided treatment and other characteristics through self-reported biannual questionnaires. Initiators of ABA were matched to patients initiating other DMARDs in a 1:3 ratio. All patient-reported outcomes were verified by medical record review. ITT (OT) analyses were performed for malignancies (SI). Incidence rates were calculated using Poisson regression (1000 patients–years (pt-yr)). Marginal structural models were used to estimate the effect of treatment on the outcome by an appropriate control for the effects of time-dependent confounders using stabilized weights and reported as hazard ratios (HR). Variables included sex, employment, smoking, education, income, BMI, insurance, comorbidity index, RA severity, and co-medications.
Results: Overall 1496 ABA patients with 2502 (4896) pt-yr of drug exposure (total follow-up time), 1520 cD treated patients with 4330 pt-yr of drug exposure (4816) and 3490 bD treated patients with 9658 pt-yr of drug exposure (11777) were studied (overall mean age 62 years (83% female)). At baseline, the distribution of first line patients in the several cohorts was: 15.2% ABA, for 23.4% bD and 33.8% cD. Switchers were more likely to have longer duration of RA (mean values (yrs): 11.4 for ABA, 8.3 cD; 14.7 bD first line vs. 17.6 ABA; 17.4 cD; 18.0 bD switchers), higher comorbidities, including prior cancer. ABA patients had worse disease compared to cD or bD, both used as first line or as switchers (mean HAQ any line for ABA 1.3 vs 1.0 (1.2) cD or 1.0 (1.3) bD as first line or as switchers).

Table 1. Incidence rates of malignancies and SI for 3 RA treatment cohorts by line of treatment

	ABA	cD	bD
All malignancies			
0	8.2 (1.7–23.9)	8.2 (4.8–13.1)	5.1 (2.8–8.5)
1	6.3 (2.3–13.7)	11.8 (4.3–25.7)	5.0 (2.2–9.8)
2+	8.3 (4.4–14.3)	4.5 (0.1–25.2)	4.7 (1.5–11.0)
SI			
0	3.0 (0.1–16.6)	15.3 (11.2–20.5)	15.1 (11.4–19.5)
1	17.9 (10.0–29.6)	27.2 (16.9–41.6)	18.6 (13.4–25.1)
2+	19.4 (12.0–29.7)	33.1 (16.5–59.2)	23.9 (16.6–33.2)

Excluding patients with prior events, incidence rates of malignancies tended to be uniform by line of treatment but SI seemed to increase with higher exposure of prior biologics, in all cohorts (Table). HR estimates by MSM did not show an increased risk for ABA in comparison with both cohorts, irrespectively of the line of treatment considered.
Conclusions: Differences in baseline characteristics revealed that channeling bias might be present when comparing ABA with other DMARDs and by line of treatment. After adjustment, no overall risk was found for increased risk of cancer and infections.
Disclosure of Interest: S. Pedro Employee of: National Data Bank for Rheumatic Diseases, R. Schumacher Employee of: National Data Bank for Rheumatic Diseases, K. Michaud Employee of: National Data Bank for Rheumatic Diseases
DOI: 10.1136/annrheumdis-2017-eular.6357

FRI0251 SIRUKUMAB, AN ANTI-IL-6 CYTOKINE MONOCLONAL ANTIBODY, LEADS TO IMPROVEMENTS IN WORK PRODUCTIVITY AND GENERAL HEALTH STATUS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS REFRACTORY TO ANTI-TNF THERAPY: RESULTS FROM THE PHASE 3 SIRROUND-T STUDY

Y. Tanaka[1], D. Aletaha[2], S. Peterson[3], R. Ganguly[4], R. Kurrasch[4], S. Popik[3], P. Agarwal[3], N. Li[3]. *[1]University of Occupational & Environmental Health, Kitakyushu, Japan; [2]Division of Rheumatology, Medical University of Vienna, Vienna, Austria; [3]Janssen Research & Development, LLC, Spring House, PA; [4]GlaxoSmithKline, Collegeville, PA, United States*

Background: Sirukumab is an anti–interleukin-6 (IL-6) monoclonal antibody that selectively binds to the cytokine with high affinity and is in development for rheumatoid arthritis (RA) and other diseases.
Objectives: This study evaluated the effects of sirukumab on work productivity/interference and health status in patients with active RA despite treatment with anti-tumor necrosis factor (TNF) therapy.
Methods: In this randomized, double-blind, phase 3 trial, 878 eligible patients with active RA who were intolerant/refractory to anti-TNFs were randomized 1:1:1 to sirukumab subcutaneous (SC) 50mg every 4 weeks (q4w; n=292), sirukumab SC 100mg every 2 weeks (q2w; n=292), or placebo SC q2w (n=294). At Week 18, placebo patients were re-randomized to 1 of the sirukumab doses if insufficient (<20%) improvement; at Week 24, all patients remaining on placebo crossed over to sirukumab. The Work Limitations Questionnaire (WLQ) evaluated health-related job limitations and productivity loss in 4 domains (mental-interpersonal, output, physical demands, time management); the 3-level EuroQol-5 Dimension (EQ-5D) questionnaire measured 5 dimensions of health status (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).
Results: At Week 24, mean total WLQ scores improved significantly from baseline for sirukumab 50mg q4w and 100mg q2w versus placebo (mean change, –2.2 and –2.3 vs 0.2, respectively; both $p<0.001$), as did all 4 mean WLQ domain scores (all $p\leq0.01$). Improvements from baseline in mean total WLQ and all 4 domain scores were maintained through Week 52 for both sirukumab doses. Mean EQ-5D index and health state visual analog scale (VAS) scores improved significantly from baseline at Week 24 for sirukumab 50mg q4w and 100mg q2w versus placebo (mean index change, 0.2 and 0.2 vs 0.0, respectively; mean VAS change, 13.9 and 15.4 vs 4.8, respectively; all $p<0.001$); improvements from baseline were maintained through Week 52 with both sirukumab doses.
Conclusions: Sirukumab treatment led to significant improvements in work-related productivity and general health status in patients with active RA despite anti-TNF therapy, consistent with demonstrated effects of sirukumab on RA disease improvement.
Disclosure of Interest: Y. Tanaka Grant/research support from: Abbvie, Astellas, Bristol-Myers, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Takeda, Speakers bureau: Abbvie, Asahi Kasei, Astellas, Bristol-Myers, Chugai, Daiichi-Sankyo, Eli Lilly, GlaxoSmithKline, Janssen, Mitsubishi-Tanabe, Pfizer, Sanofi, Takeda, Teijin, YL Biologics, D. Aletaha Grant/research support from: AbbVie, Pfizer, Grünenthal, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, Consultant for: AbbVie, Pfizer, Grünenthal, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, S. Peterson Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, R. Ganguly Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, R. Kurrasch Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, S. Popik Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, P. Agarwal Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, N. Li Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC
DOI: 10.1136/annrheumdis-2017-eular.3597

FRI0252 SUMMARY OF NEUTROPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SIRUKUMAB IN THE SIRROUND PHASE 3 CLINICAL TRIALS

T. Takeuchi[1], Y. Tanaka[2], M. Schiff[3], M. Harigai[4], K. Brown[5], R. Rao[6], K. Fei[7], S. Popik[7], K. Yoshizawa[8], Q. Wang[7], B. Hsu[7]. *[1]Division of Rheumatology, Keio University School of Medicine, Tokyo; [2]University of Occupational and Environmental Health, Kitakyushu, Japan; [3]University of Colorado School of Medicine, Denver, CO, United States; [4]Tokyo Women's Medical University, Shinjuku-ku, Tokyo, Japan; [5]GlaxoSmithKline, Collegeville, PA, United States; [6]GSK Medicines Research Centre, Hertfordshire, United Kingdom; [7]Janssen Research & Development, LLC, Spring House, PA, United States; [8]Janssen Pharm KK Japan, Chiyoda-ku, Tokyo, Japan*

Background: Neutropenia has been reported with interleukin-6 (IL-6) pathway inhibitors and could potentially be associated with increased rates of infection. The reduced neutrophil counts seen with IL-6 inhibitors may be due to effects on margination of circulating neutrophils as opposed to a decrease in bone marrow production or reduced survival. Efficacy of sirukumab (SIR), a human anti-IL-6 cytokine monoclonal antibody, has recently been shown in several phase 3 trials.
Objectives: To assess incidence of neutropenia from completed and ongoing SIRROUND clinical studies.
Methods: Neutrophil counts were compared for SIR 50mg q4w and 100mg q2w doses vs placebo (pbo) in the pbo-controlled period (Wks 0–18) of 2 phase 3 trials and in long-term analysis for the 5-trial, phase 3 program.
Results: 2926 pts received SIR for up to 3.4y with a median duration of 1.46y. For the 18-wk pbo-controlled period, neutropenia was more frequent in both SIR groups compared with pbo. Across all groups, the majority of the decreases in neutrophil counts were National Cancer Institute Common Terminology Criteria for Adverse Events grade 0/1, within the normal range, and the incidence of grade 3/4 decreases was low across groups (Table). Neutropenia began at Wk 2 and persisted through the study period. In long-term analysis, the proportions of pts with grade 1, 2, or 3 neutropenia were slightly higher than in the 18-wk pbo-controlled period, suggesting the majority of events occurred early. No dose relationship was observed in the grade or frequency of neutropenia. Grade 3/4 neutropenia was mostly transient and resolved after interrupting the dose or resolved within the dosing interval such that no change in dose schedule was required. The majority of grade 4 decreases in neutrophils were not correlated with infections; 2 cases of serious infections occurred with grade 4 neutropenia. The distribution of neutropenia by grade was similar in pts who did or did not use disease-modifying antirheumatic drugs (DMARDs) at baseline.

Table 1. Neutropenia by Maximum Toxicity Grade Across Phase 3 Trials (n, %)

Neutrophil count decreased	0–18 wks			Long-term analysis	
	Pbo (N=850)	SIR 50mg q4w (N=848)	SIR 100mg q2w (N=850)	SIR 50mg q4w (N=1454)	SIR 100mg q2w (N=1461)
Grade 0 (≥LLN)	816 (96.9)	576 (68.3)	568 (67.1)	843 (58.0)	806 (55.2)
Grade 1 (3)	19 (2.3)	149 (17.7)	167 (19.7)	313 (21.5)	352 (24.1)
Grade 2 (<1,500–1,000/mm^3)	5 (0.6)	97 (11.5)	94 (11.1)	222 (15.3)	240 (16.4)
Grade 3 (<1,000–500/mm^3)	1 (0.1)	21 (2.5)	16 (1.9)	68 (4.7)	61 (4.2)
Grade 4 (<500/mm^3)	1 (0.1)	0	1 (0.1)	8 (0.6)	2 (0.1)

LLN, lower limit of normal.

Conclusions: Across phase 3 studies, there was no dose effect of SIR on neutropenia, and the use of DMARDs did not have an apparent effect on neutropenia. The majority of grade 4 neutropenia with SIR was not associated with infections.
Disclosure of Interest: T. Takeuchi Grant/research support from: Astellas Pharma, Bristol-Myers K.K., Chugai Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., and SymBio Pharmaceuticals Ltd, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Asahi Kasei Medical K.K., AbbVie GK, Daiichi Sankyo Co., Ltd., Bristol-Myers K.K., and Nipponkayaku Co. Ltd., Speakers bureau: AbbVie GK., Bristol-Myers K.K., Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Janssen Pharmaceutical K.K., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd., Astellas Pharma, Daiichi Sankyo Co., Ltd., Celtrion, and Nipponkayaku Co. Ltd., Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, and Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, and GlaxoSmithKline, M. Schiff Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Johnson & Johnson, UCB, Speakers bureau: AbbVie, M. Harigai Grant/research support from: AbbVie Japan, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Mitsubishi Tanabe Pharma, Ono Pharmaceuticals, Santen Pharmaceutical, Takeda Pharmaceutical, UCB Japan, Teijin Pharma, Consultant for: AbbVie Japan, Janssen Pharma, Chugai Pharmaceutical, Teijin Pharma, Eli Lilly Japan, and Zenyaku Kogyo, K. Brown Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, R. Rao Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, K. Fei Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, S. Popik Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, K. Yoshizawa Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, Q. Wang Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, B. Hsu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC
DOI: 10.1136/annrheumdis-2017-eular.6413

FRI0253 PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB COMPARED WITH PLACEBO OR INTRAVENOUS TOCILIZUMAB IN COMBINATION WITH CSDMARDS

V. Strand[1], K. Lampl[2], C. Birchwood[2], J. Pei[2], K. Tuckwell[3], R. Finch[3], A. Kivitz[4], G. Burmester[5]. *[1]Stanford University School of Medicine, Palo Alto; [2]Genentech, Inc, South San Francisco, United States; [3]Roche, Welwyn Garden City, United Kingdom; [4]Altoona Center for Clinical Research, Duncansville, United States; [5]Charité-Universitätsmedizin Berlin, Free University and Humboldt University of Berlin, Berlin, Germany*

Background: Two previous randomized, controlled trials (RCTs), BREVACTA and SUMMACTA, showed subcutaneous tocilizumab (TCZ-SC) was superior to placebo (PBO) and comparable to intravenous TCZ (TCZ-IV) in combination with csDMARDs for improving RA disease activity.[1,2]
Objectives: To compare the efficacy of TCZ-SC with PBO or TCZ-IV + csDMARDs for improvement in patient-reported outcomes (PROs) in 2 RCT populations.
Methods: Both RCTs enrolled patients (pts) with inadequate responses to DMARDs; up to 20% had inadequate responses to tumor necrosis factor inhibitors. In BREVACTA, pts received blinded TCZ-SC 162 mg or PBO every 2 weeks (q2w) + csDMARDs for 24 weeks. In SUMMACTA, pts received TCZ-SC 162 mg weekly or TCZ-IV 8 mg/kg q4w + csDMARDs for the 24-week double-blind period. PROs, assessed at 12 weeks (prior to rescue) in BREVACTA and 24 weeks in SUMMACTA, included patient global assessment (PtGA; visual analog score [VAS], 0–100 mm), pain (VAS), Health Assessment Questionnaire Disability Index (HAQ-DI, 0–3) and Short Form-36 (SF-36) physical and mental component summary (PCS, MCS: 0–50) and domain (0–100) scores. The proportions of pts reporting scores ≥ minimum clinically important differences (MCID) and ≥ age/gender-matched normative values were assessed for each treatment group.
Results: Baseline PRO scores were mostly comparable between treatment groups in each study and between study populations. In BREVACTA, significantly more pts who received TCZ-SC reported scores ≥ MCID for all PROs at week 12 compared with PBO (54% to 73% vs 42% to 55%, respectively; number needed to treat [NNT], 5.2 to 13.0). Compared with 1% to 20% at baseline, 8% to 34% of pts who received TCZ-SC and 4% to 25% of PBO pts reported scores ≥ normative values in all PROs at week 12 (Table). In SUMMACTA, similar proportions of pts who received TCZ-SC and TCZ-IV reported scores ≥ MCID in all PROs at week 24 (61% to 84% vs 64% to 84%, respectively). The proportion of patients who reported scores ≥ normative values was comparable between the TCZ-SC and TCZ-IV groups across all PROs; compared with 0.2% to 23% at baseline, 14% to 41% of pts who received TCZ-SC and 15% to 42% of pts who received TCZ-IV reported scores ≥ normative values at week 24 (Table).

Table. PROs at 12 weeks in BREVACTA and 24 weeks in SUMMACTA.

	Change From Baseline in PROs								
	BREVACTA†					SUMMACTA†			
	LSM Change From Baseline‡		Week 12 Change ≥ MCID, %		NNT	LSM Change From Baseline‡		Week 24 Change ≥ MCID, %	
	TCZ SC q2w	PBO q2w	TCZ SC q2w	PBO q2w		TCZ SC qw	TCZ IV q4w	TCZ SC qw	TCZ IV q4w
Patient global	−25.5	−13.0	72.4***	53.1	5.2	−35.0	−36.0	83.0	83.6
Patient pain	−20.6	−9.63	63.9***	46.0	5.6	−29.2	−31.1	76.2	80.2
HAQ-DI	−0.4	−0.2	58.2**	46.7	8.7	−0.6	−0.6	73.0	74.6
SF-36 PCS	5.6***	2.9	63.1**	51.7	8.8	8.7	8.9	80.0	79.6
SF-36 MCS	6.1***	1.6	58.5***	44.1	6.9	6.4	6.5	63.0	64.2
Physical functioning	8.9***	2.8	59.2*	50.2	11.1	18.9	19.0	77.2	78.0
Role-physical	14.9***	7.7	64.3*	55.0	10.8	20.9	21.3	77.0	77.7
Bodily pain	17.8***	8.6	72.7***	54.5	5.5	25.5	27.5	84.4	83.9
General health	8.5***	4.2	60.9*	51.2	10.3	13.0	13.3	70.9	73.3
Vitality	12.0***	5.3	66.7**	54.5	8.2	16.1	14.8	74.9	74.7
Social functioning	11.0***	4.8	57.3***	41.7	6.4	20.0	20.4	67.8	70.1
Role-emotional	12.2***	4.6	53.5*	45.5	12.5	15.7	16.9	60.9	64.8
Mental health	9.9***	4.6	61.4**	47.9	7.4	10.7	10.9	67.1	65.1
CDAI	−18.8***	−13.0	–	–	–	−24.8	−25.4	–	–
	Patients Reporting Scores ≥ Normative Values, %								
	BREVACTA†					SUMMACTA†			
	Baseline		Week 12			Baseline		Week 24	
	TCZ SC q2w	PBO q2w	TCZ SC q2w	PBO q2w		TCZ SC qw	TCZ IV q4w	TCZ SC qw	TCZ IV q4w
HAQ-DI	3.9	5.5	15.8	10.8		4.3	3.9	33.3	30.1
SF-36 PCS	1.4	0.9	7.9	3.8		0.2	0.8	14.0	14.7
SF-36 MCS	16.3	19.7	31.6	22.6		19.3	20.3	38.7	39.6
Physical functioning	4.4	5.5	12.0	8.0		2.7	4.9	20.8	21.0
Role-physical	3.4	0.9	13.6	8.0		4.3	3.9	19.1	20.3
Bodily pain	3.2	2.3	20.8	13.2		1.3	2.8	29.8	34.5
General health	7.8	9.6	17.2	11.8		9.2	7.3	21.6	22.4
Vitality	13.1	14.7	32.3	23.6		11.7	12.0	37.9	36.1
Social functioning	9.4	12.4	23.0	16.5		10.2	10.1	29.4	31.9
Role-emotional	10.8	8.7	22.0	13.7		11.9	14.2	25.3	28.5
Mental health	18.6	20.2	33.7	24.5		23.2	21.3	41.4	42.1

LSM, least squares mean; NNT, number needed to treat; PBO, placebo; qw, weekly; q2w, every 2 weeks; q4w, every 4 weeks.
* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.
† Analyses were performed using the intention-to-treat population in BREVACTA (TCZ SC, n = 437; PBO, n = 219) and the per-protocol population in SUMMACTA (TCZ SC, n = 558; TCZ IV, n = 537).
‡ Adjusted for region and body weight category (< 60 kg; 60 to < 100 kg; ≥ 100 kg).

Conclusions: In BREVACTA, TCZ-SC + csDMARDs resulted in significantly greater improvements across all PROs and significantly more pts reporting scores

≥ MCID at week 12 compared with PBO. Similarly, more pts receiving TCZ-SC reported scores ≥ normative values at week 12 compared with PBO, despite few pts with such scores at baseline. Responses were similar between pts treated with TCZ-SC and TCZ-IV + csDMARDs in SUMMACTA at week 24. These data show TCZ treatment resulted in clinically meaningful improvements in PROs and indicate that attainment of normative scores is a realistic goal in treatment of pts with active RA.

References:
[1] Kivitz A, et al. Arthritis Care Res (Hoboken). 2014;66:1653–61.
[2] Burmester G, et al. Ann Rheum Dis. 2014;73:69–74.

Acknowledgements: This study was funded by F. Hoffmann-La Roche/Genentech.

Disclosure of Interest: V. Strand Consultant for: Abbvie; Amgen; AstraZeneca; Biogen Idec; Boehringer Ingelheim; Celltrion; Crescendo; Genentech/Roche; GlaxoSmithKline; Janssen; Lilly; Merck; Novartis; Pfizer; Regeneron; Samsung; Sanofi; UCB, K. Lampl Employee of: Genentech, Inc, C. Birchwood Employee of: Genentech, Inc, J. Pei Employee of: Genentech, Inc, K. Tuckwell Shareholder of: Roche, Employee of: Roche, R. Finch Shareholder of: Roche, Employee of: Roche, A. Kivitz Consultant for: Genentech; Novartis; Pfizer; Sanofi-Regeneron; UCB, G. Burmester Grant/research support from: Roche, Consultant for: Roche

DOI: 10.1136/annrheumdis-2017-eular.3312

FRI0254 EFFICACY OF TOCILIZUMAB FOR SUPPRESSING RADIOGRAPHIC PROGRESSION OF CERVICAL LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARISON WITH METHOTREXATE TREATMENT; TWO YEARS OF FOLLOW-UP ～A MULTICENTER REGISTRY STUDY～

Y. Kanayama[1], T. Kojima[2], Y. Hirano[3], Y. Yabe[4], N. Takahashi[2], Y. Oishi[3], N. Ishiguro[2] on behalf of TBCR study group. *[1]Orthopedic Surgery and Rheumatology, Toyota Kosei Hospital, Toyota; [2]Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya; [3]Rheumatology, Toyohashi Municipal Hospital, Toyohashi; [4]Rheumatology, Japan Community Healthcare Organization Tokyo Shinjuku Medical Center, Tokyo, Japan*

Background: Cervical lesions are known to occur at high frequency as a complication of rheumatoid arthritis (RA). Treatment with biological agents are more clinically effective than the DMARDs that were in use previously, in particular, with their efficacy in suppressing joint destruction having been emphasized. We reported the efficacy of infliximab, anti-tumor necrosis factor antibodies for suppressing the radiographic progression of RA cervical lesions at ACR2009, EULAR2010, 11, 12, 13, 14 and 16. However there is still few studies of efficacy of against RA cervical lesions of Tocilizumab (TCZ), anti-interleukin 6 receptor antibody.

Objectives: To evaluate the efficacy of TCZ for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 2 years.

Methods: We used TCZ or MTX for treating Japanese patients with active RA who fulfilled the ACR criteria in 1987. The final study cohort of each 38 and 71 patients received continuous TCZ and MTX treatment for at least 2 years. For evaluation of cervical lesions, the atlanto-dental interval (ADI), the space available for the spinal cord (SAC), and the Ranawat value were measured by plain lateral radiographs in the flexion position, at initiation and Year 1,2.

Results: In the patients receiving TCZ (n=38) and MTX (n=71), the number of female were each 28 (72%) and 51 (72%) cases (p=0.999). The mean age was 57.3±12.4 and 63.3±10.9 years old (p=0.011); disease duration was 7.0±7.3 and 8.8±9.7 years (p=0.929) and the mean dose of MTX was 9.0±3.4 and 8.3±2.9 mg/w (p=0.335). Clinical findings related to RA were as follows; CRP 3.8±3.1 and 1.5±2.1 mg/dl (p<0.001); ESR 52.7±25.3 and 30.0±20.8mm/h (p<0.001); MMP3 400±300 and 213±356ng/ml (p<0.001); the number of RF-positive 30 (79%) and 58 (82%) cases (p=0.801); DAS28-ESR 5.46±0.92 and 4.24±1.34 (p<0.001); ADI 2.7±1.7 and 2.6±1.6mm (p=0.917); SAC 19.3±2.8 and 20.7±2.5mm (p=0.008) and Ranawat value 15.4±1.6 and 15.9±1.5mm (p=0.073). The respective changes in cervical lesion parameters after 1 year were as follows: ADI: 0.21±0.53 and 0.25±0.44 mm (p=0.327); SAC: –0.16±0.44 and –0.17±0.38 mm (p=0.653); and Ranawat value: –0.13±0.34 and –0.11±0.32 mm (p=0.773). The respective changes in cervical lesion parameters after 2 years were as follows: ADI: 0.32±0.70 and 0.52±0.67 mm (p=0.045); SAC: –0.24±0.49 and –0.45±0.63 mm (p=0.067); and Ranawat value: −0.24±0.49 and –0.35±0.56 mm (p=0.270) in the patients receiving TCZ and MTX (Fig.1). The numbers of patients who did not showed progression in ADI, SAC and Ranawat value were each 30 (79%) and 41 (58%) cases (p=0.035); 30 (79%) and 44 (62%) cases (p=0.087) and 30 (79%) and 49 (69%) cases (p=0.367) after 2 years. Also the number who was able to suppress progression in all three parameters were each 29 cases (76%) receiving TCZ and 41 cases (58%) receiving MTX (p=0.062) after 2 years (Fig.2).

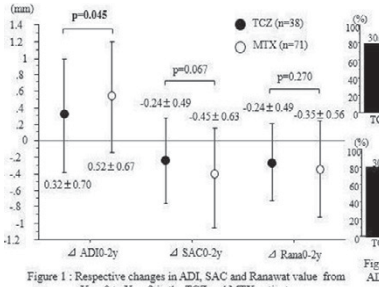


Figure 1 : Respective changes in ADI, SAC and Ranawat value from Year 0 to Year 2 in the TCZ and MTX patients

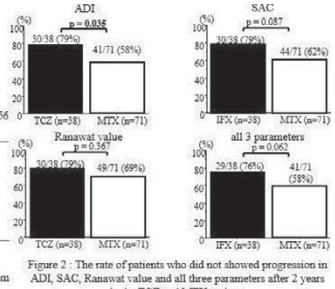


Figure 2 : The rate of patients who did not showed progression in ADI, SAC, Ranawat value and all three parameters after 2 years in the TCZ and MTX patients

Conclusions: This study suggested that TCZ treatment can be used to suppress the progression of RA cervical lesions more than MTX treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4698

FRIDAY, 16 JUNE 2017

SLE, Sjögren's and APS - clinical aspects (other than treatment)

FRI0255 PATTERNS OF DISEASE ACTIVITY IMPACT ON ORGAN DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS

A. Bortoluzzi, M. Padovan, E. Silvagni, C.A. Scirè, M. Govoni. *Department of Medical Sciences, Rheumatology Unit, University of Ferrara and Azienda Ospedaliero-Universitaria Sant'Anna, Cona (Ferrara), Italy*

Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by fluctuating disease activity in which adverse long-term outcomes remain a major challenge. In the face of extreme individual unpredictability of the disease course over time, four different patterns can be defined, as elsewhere described [1], using SLEDAI-2K (Systemic Lupus Erythematosus Disease Activity Index-2K) excluding serology in order to focus on clinical activity. The patterns are clinical quiescent disease (CQD), chronic active disease (CAD), relapsing-remitting disease (RRD) and minimal disease activity (MDA).

Objectives: The aim of our study was to assess the association between different disease activity patterns and damage accrual in SLE patients.

Methods: Patients with SLE registered at our Lupus Clinic at the Rheumatology Unit, between 1 January 2013 and 1 October 2016, were included. Demographic and clinical variables included age, gender, age at SLE onset, major organ involvement. SDI (Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index) was categorized as absent (SDI=0) or present (SDI ≥1), Disease activity patterns (CQD, MDA, RRD, CAD) were retrospectively assessed. Drugs used in the treatment of SLE, including hydroxychloroquine, cumulative dose of glucocorticoid (prednisone equivalent >10 g) and other immunosuppressive drugs, were also collected.
Multivariate logistic regression analyses were performed to identify disease patterns associated with damage accrual. Results are presented as odds ratio (OR) and 95% confidence intervals (CI).

Results: A total of 473 Caucasian patients were observed, mainly female (89.4% F, 10.6% M), mean age 52.6 years (± 14.9 SD). In our cohort, the disease activity pattern distribution was as follows: 65.4% CQD (290 pts), 21.5% RRD (91 pts), 6.1% MDA (28 pts) and CAD in 19.1% of the cases (64 pts). Damage was significantly more frequent in CAD subset (81.2%, 52/64 pts) versus 54.5% in CQD (158/290 pts), 50% in MDA (14/28 pts) and 58.2% in RRD (53/91 pts). Compared to a CQD course, CAD pattern was independently associated with overall damage after controlling for factors including gender, disease duration, cumulative glucocorticoid dosage, major individual organ involvement (neuropsychiatric and renal), positive antiphospholipid antibody profile, exposures to cyclophosphamide and hydroxychloroquine (Table 1).

Table1. Logistic regression analysis of independent factors associated with damage in SLE patients

Factors	Crude odds ratio (95% CI)	*P value*	Adjusted* Odds ratio (95% CI)	*P value*
Disease Activity Pattern				
Clinical quiescent disease	**Reference category**		**Reference category**	
Minimal disease activity	0.84 (0.38 - 1.81)	0.650	0.77 (0.33 - 1.80)	0.541
Relapsing-remitting disease	1.16 (0.73 - 1.87)	0.529	1.03 (0.62 - 1.72)	0.900
Chronic active disease	**3.62 (1.86 - 7.07)**	**<0.0001**	**3.07 (1.49 - 6.34)**	**0.002**
Gender (M)	1.23 (0.68 - 2.22)	0.489	1.29 (0.68 - 2.43)	0.434
Disease duration(yr)	1.05 (1.03 - 1.07)	<0.0001	1.03 (1.01 - 1.06)	0.033
NP involvement	2.86 (1.65 - 4.94)	<0.0001	2.11 (1.17 - 3.80)	0.013
Renal involvement	1.35 (0.76 - 2.41)	0.301	0.95 (0.49 - 1.84)	0.877
aPL positivity	1.68 (1.16 - 2.44)	0.006	1.64 (1.09 - 2.47)	0.017
Cumulative dosage of CS (>10g PDN)	2.50 (1.69 - 3.71)	<0.0001	1.64 (1.03 - 2.61)	0.038
HCQ	0.37 (0.24 - 0.57)	<0.0001	0.41 (0.26 - 0.66)	<0.0001
CYC	2.46 (0.97 - 6.25)	0.058	1.89 (0.66 - 5.46)	0.236

* adjusted for: age, gender, disease duration, NP and renal involvement, cumulative dosage of CS; aPL positivity, HCQ, CYC (*NP, neuropsychiatric; aPL, antiphosphlipid; CYC, cyclophosphamide; HCQ, hydroxychloroquine; M,male; CS,corticosteroid; PDN, prednisone*)

Conclusions: Our results demonstrated that a clinically and persistent CAD triples the risk of damage compared to milder or relapsing courses, while hydroxychloroquine appeared to have a "protective" effect. Identifying the prevailing pattern of disease activity in every patient can be translated into a more effective personalized preventing strategy to reduce damage accrual and improve outcomes.

References:

[1] M. Zen et al. Disease activity patterns in a monocentric cohort of SLE patients: a seven-year follow-up study, Clin. Exp. Rheumatol. 30 (2012) 856–863.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5103

FRI0256 ULTRASOUND CONSENSUS DEFINITIONS ON NORMAL AND ABNORMAL FINDINGS IN SALIVARY GLANDS IN SJÖGREN'S SYNDROME: RESULTS OF AN OMERACT DELPHI PROCESS

S. Jousse-Joulin[1], F. Gandjbakhch[2], S. Ohrndorf[3], M. Backhaus[3], G. Tamborrini[4], I. Chary-Valckenaere[5], L. Terslev[6], A. Iagnocco[7], P. Collado[8], C. Hernandez-Diaz[9], E. Naredo[8], W. Schmidt[3], G. Filippou[10], C. Dejaco[11], M. Mortada[12], A. Hocevar[13], S. Chrysidis[14], G. Mardenly[15], J.J. De Agustin[16], R. Thiele[17], D. Mac Carter[18], S. Finzel[19], P. Hanova[20], C. Glaser[19], D. Hammerfors[21], M.-A. D'Agostino[22], G. Bruyn[23]. *[1]Rheumatology, Hospital, Brest; [2]Rheumatology, Hospital, Paris, France; [3]Rheumatology, Hospital, Berlin, Germany; [4]Rheumatology, Hospital, Basel, Switzerland; [5]Rheumatology, Hospital, Nancy, France; [6]Rheumatology, Hospital, Copenhagen, Denmark; [7]Rheumatology, Hospital, Turin, Italy; [8]Rheumatology, Hospital, Madrid, Spain; [9]Rehabilitation, Hospital, Mexico City, Mexico; [10]Rheumatology, Hospital, Siena, Italy; [11]Rheumatology, Hospital, Bruneck, Austria; [12]Rheumatology & Rehabilitation Department, Hospital, Zagazig, Egypt; [13]Rheumatology, Hospital, Ljubljana, Slovenia; [14]Rheumatology, Hospital, Esbjerg, Denmark; [15]Rheumatology, Hospital, Cairo, Egypt; [16]Rheumatology, Hospital, Barcelona, Spain; [17]Rheumatology, Hospital, Rochester; [18]Rheumatology, Hospital, Whitefish, United States; [19]Rheumatology, Hospital, Freiburg, Germany; [20]Rheumatology, Hospital, Prague, Czech Republic; [21]Rheumatology, Hospital, Bergen, Norway; [22]Rheumatology, Hospital, Boulogne-Billancourt, France; [23]Rheumatology, Hospital, MC Groep Hospitals, Lelystad, Netherlands*

Background: Ultrasonography (US) of salivary glands (USSG) may support diagnosis and evaluation of disease activity in primary Sjögren's syndrome pSS. In order to extent the use of USSG in daily practice, consensus definitions of normal and abnormal USSG findings are needed.

Objectives: To obtain consensual definitions of normal and abnormal USSG findings using a Delphi process.

Methods: Twenty-seven experts participated in the Delphi process. A Likert scale from 1–5 was used in which 1 indicated complete disagreement and 5 complete agreement. Three core items were proposed: 1. Consensus of assessment of SG (parotid gland (PG), submandibular glands (SMG), sublingual glands SLG)). 2. Consensus for elementary lesions of PG, SMG, and SLG changes in PSS patients. 3. Consensus on grading of PG, SM, and SLG in pSS.

Results: The consensus of definitions between experts was reached after three rounds.The results (table 1) showed agreement with more than 75% of agreement in normal and abnormal definitions in SG and concluded to not evaluate SLG in pSS patients as well as to score pSS SG patients with at least two abnormal glands out of 4 (2 PG and 2 SMG) with a scoring system >2 for each abnormal gland.

Conclusions: We developed a consensual US definition of normal and abnormal USGS findings through a Delphi exercise process. This finding will be used as a basis to further proceed with the validation of USGS for clinical application.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4976

FRI0257 URINARY ANGIOSTATIN, CXCL4 AND VCAM-1 AS BIOMARKERS FOR LUPUS NEPHRITIS

C.C. Mok[1], S. Soliman[2], L.Y. Ho[1], F. Mohamed[3], F.I. Mohammed[3], C. Mohan[2]. *[1]Medicine, Tuen Mun Hospital, HK, Hong Kong;[2]Biomedical Engineering, University of Houston, Houston, United States; [3]Rheumatology and Rehabilitation Department, Minya University, Minya, Egypt*

Background: Our preliminary proteomic analysis revealed elevated levels of urinary angiostatin, CXCL4 and VCAM-1 in patients with active lupus nephritis

Objectives: To study the performance of urinary angiostatin, CXCL4 and VCAM-1 in differentiating between active renal and non-renal SLE.

Methods: Patients who fulfilled the ACR classification for SLE with active renal disease, active non-renal disease and inactive disease were randomly recruited, together with a group of healthy controls. Stored urine samples of the participants were assayed for angiostatin, CXCL4 and VCAM-1 and compared among the different groups. ROC analysis was performed to obtain the best cut-off values to calculate the performance of these markers in differentiating among the different groups of patients. SLE disease activity was assessed by the SELENA-SLEDAI and physician's global assessment (PGA). Specificity and sensitivity of these markers in differentiating between active renal and non-renal SLE was determined by 2x2 contingency tables. In patients with active renal disease, correlation between these urinary biomarkers with clinical renal parameters was also performed.

Results: 227 SLE patients (80 inactive SLE; 67 active non-renal disease; 80 active renal disease; 94% women, age 39.2±13.8 years) and 53 controls were studied. Urinary angiostatin, CXCL4 and VCAM-1 levels normalized for creatinine were significantly higher in patients with active renal than non-renal disease (angiostatin 18.4±27.1 vs 1.6±2.91 pg/ng; $p<0.0001$; CXCL 9.11±15.7 vs 5.12±10.4 pg/ng; $p=0.003$; VCAM-1.41±1.31x10^3 vs 0.72±1.10x10^3 pg/ng; $p<0.0001$). The levels of these urinary protein markers were also significantly higher in active SLE patients than inactive SLE patients or healthy controls. Urinary angiostatin, CXCL4 and VCAM-1 correlated significantly with the renal SLEDAI (Rho 0.66, 0.45 and 0.51, respectively; $p<0.001$ in all), total SLEDAI score (Rho 0.60, 0.46 and 0.53, respectively; $p<0.001$ in all) and urine protein-to-creatinine (uPCr) ratio (Rho 0.73, 0.51, 0.59, respectively; $p<0.001$) in all the SLE patients studied. Urinary angiostatin was more specific (specificity 0.82) than elevated anti-dsDNA and low C3 (specificity 0.64 and 0.66) in differentiating active renal SLE from non-renal SLE. In a subset of patients with biopsy proven active lupus nephritis (N=68), these urinary protein markers could not differentiate between proliferative (III/IV) from non-proliferative (I/II/V) types of lupus nephritis. However, urinary CXCL4 (Rho 0.25; $p=0.049$) and VCAM-1 (Rho -0.28; $p=0.02$), but not angiostatin (Rho 0.11; $p=0.39$), correlated significantly with the histologic activity index. There was no significant association between these protein markers and the histologic chronicity index or renal SLEDAI score. On the other hand, urine angiostatin levels (Rho 0.36; $p=0.003$), but not CXCL4 (Rho 0.07; $p=0.59$) or VCAM-1 (Rho -0.11; $p=0.36$), correlated significantly with the uP/Cr ratio in this subgroup of patients.

Conclusions: Urinary angiostatin, CXCL4 and VCAM-1 are potentially useful biomarkers for SLE, in particular lupus nephritis. Further longitudinal studies are necessary to delineate the sensitivity and specificity of these two urinary protein markers in predicting renal flares and prognosis in SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3951

FRI0258 LONG-TERM PROGNOSISOFPATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION: CSTAR-PAH COHORT STUDY

J. Qian[1], M. Li[2], X. Zhang[3], Q. Wang[2], J. Zhao[2], Z. Tian[4], X. Zeng[2] on behalf of CSTAR group. *[1]Internal Medicine; [2]Rheumatology, Peking Union Medical College Hospital, Beijing; [3]Rheumatology, The People's Hospital of Guangdong Province, Guangzhou; [4]Cardiology, Peking Union Medical College Hospital, Beijing, China*

Background: SLE-associated pulmonary arterial hypertension (PAH) is common in Asian countries, and the clinical outcome of patients with SLE-associated PAH is dramatically impaired.

Objectives: This study aimed to identify the long-term clinical outcomes and prognostic factors of patients with SLE-associated PAH confirmed by right heart catheterization (RHC).

Methods: A multicenter cohort of SLE-associated PAH was established. Baseline and follow-up records were collected. The primary endpoint was death from any

Abstract FRI0256 – Table 1

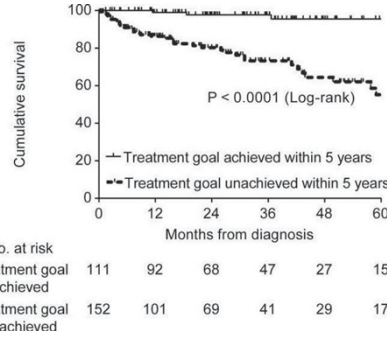
(% of agreement)	Definition of normal US findings	Procedure of scanning	Definition of abnormal US findings	SG to evaluate in pSS	Definition of scoring
Parotid glands	Uniformly echoic texture with a clear delineation from the superficial tissue. Tissue comparable to thyroid parenchyma (81%)	Longitudinal and transverse plane (90%)	Focal or diffuse an/hypoechoic areas (95%)	yes	4-grade semiquantitative scoring system (i.e. grade 0, normal parenchyma; grade 1, minimal change: grade 2, moderate: grade 3, severe: diffuse inhomogeneity occupying all the surface of the gland) (79%)
Submandibular glands	SMG are usually of finer granular echo texture compared to PG or to the normal thyroid parenchyma (89.1%)	Longitudinal and transverse plane (90%)	Idem PG (95%)	yes	Idem PG (79%)
Sublingual glands	SLG has no clear delineation from the superficial tissue because of no true fascial capsule (77%)	longitudinal and transverse plane (77%)	Idem PG (95%)	no	Not useful

cause. The secondary experimental end point was treatment goal achievement (TGA), defined as an integrated outcome.

Results: Among the 310 patients enrolled from 14 PAH centers, the median follow-up was 24.0 months. The 1-, 3- and 5-year survival rates were 92.1%, 84.8% and 72.9%, respectively. The 1-, 3- and 5-year TGA rates were 31.5%, 53.6% and 62.7%, respectively.Serositis, 6MWD >380 m and CI ≥2.5 L/min×m^2 were identified as independent prognostic factors of TGA. TGA within 5 years was identified as a factor associated with survival in patients with SLE-associated PAH (Figure 1).

Table 1. Baseline characteristics of patients with SLE-associated PAH

Characteristics	SLE-associated PAH (n=310)
Age at recruitment, yr	35.0±10.1
Female sex, %	99.4
WHO Fc I-II, %	51.7
6MWD, m	408.6±98.0
NT-proBNP, pg/ml	1660.5±2275.1
SLEDAI	6.1±5.5
mPAP, mmHg	46.5±12.1
CI, L/min × m^2	2.8±0.9
RAP, mmHg	5.8±5.6



Conclusions: TGA was associated with the long-term survival, which supports and provides evidence to the treat-to-target strategy in SLE-associated PAH. Early diagnosis, intervention and heart function preservation are priorities for better long-term outcomes.

References:

[1] Badesch DB, Raskob GE, Elliott CG, Krichman AM, Farber HW, Frost AE, et al. Pulmonary arterial hypertension: baseline characteristics from the REVEAL Registry. Chest. 2010;137:376–87.

[2] Chung L, Liu J, Parsons L, Hassoun PM, McGoon M, Badesch DB, et al. Characterization of connective tissue disease-associated pulmonary arterial hypertension from REVEAL: identifying systemic sclerosis as a unique phenotype. Chest. 2010;138:1383–94.

[3] Condliffe R, Kiely DG, Peacock AJ, Corris PA, Gibbs JS, Vrapi F, et al. Connective tissue disease-associated pulmonary arterial hypertension in the modern treatment era. Am J Respir Crit Care Med. 2009;179:151–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6718

FRI0259 LUPUS LOW DISEASE ACTIVITY STATE (LLDAS) IN PATIENTS WITH LUPUS NEPHRITIS (LN)

D.V. Monova, S. Monov, M. Ivanova, E. Peneva. *Department of Internal Medicine, Medical Institute, Sofia, Bulgaria*

Background: Lupus Low Disease Activity State (LLDAS) is a consensus-based definition of minimally acceptable disease activity in patients with Systemic lupus erythematosus (SLE).

Objectives: The aims of this study were to evaluate what proportion of patients with LN fulfils the definition of LLDAS and to evaluate the effect of LLDAS attainment on damage accrual over a period of 5 years.

Methods: This is a retrospective analysis of data prospectively collected in a longitudinal observational cohort of LN patients. The conceptual definition of LLDAS is a state, which if sustained, is associated with good long-term outcomes. The operational definition of LLDAS is fulfilled when all of the following criteria are met: (1) SLE Disease Activity Index (SLEDAI-2 K) ≤4, with no activity in major organ systems (renal, central nervous system, cardiopulmonary, vasculitis, fever) and no haemolytic anaemia or gastrointestinal activity; (2) no new features of lupus disease activity compared to the previous assessment; (3) a Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI physician global assessment (PGA) (scale 0–3) ≤1; (4) a current prednisolone (or equivalent) dose ≤7,5 mg daily; and (5) well-tolerated standard maintenance doses of immunosuppressive drugs and approved biologic agents, excluding investigational drugs. The definition of LLDAS was applied to each patient for each visit; organ damage was calculated with the SLICC/DI score (SDI) at study entry and at last observation.

Results: 294 patients were eligible for the study (89.79% females, mean age at first visit 31,4±11,9 years, mean disease duration at last visit 19,8±8,7 years). At last observation 219 patients (85,37%) were on treatment with glucocorticoids (GC) and/or immunomodulators. According with all the items of the definition, at last observation LLDAS was present in 146 patients (49,65%); among these, 37 patients (20,8%) maintained a stable LLDAS during the last 5 years of follow-up (LLDAS fulfilled for all visits). 68 patients (23,12%) accrued organ damage during the follow-up; in the cohort as a whole the mean increase in SDI was 0,4±0.67 resulting in a mean final SDI of 1,2±1,8. Patients who maintained LLDAS were younger (p<0,05), had a lower disease activity score at study entry (p<0,001) and were more likely GC-free at last observation (p<0,001). Patients who maintained LLDAS accrued less organ damage but this difference did not reach statistical significance.

Conclusions: High percentage of patients fulfils the proposed definitions for LLDAS at last visit but only a minority maintained this state for all the follow-up period. A minimally acceptable disease activity state is associated with a successful GC tapering and, probably, better long-term outcomes. LLDAS was shown to be associated with protection from damage accrual.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1676

FRI0260 ULTRASOUND STUDY OF PLEURAL PROFILE AND CHEST HIGH-RESOLUTION COMPUTED TOMOGRAPHY (HRCT): DIAGNOSTIC ROLE IN PRIMARY SJÖGREN'S SYNDROME-INDUCED LUNG INVOLVEMENT

F. Ferro [1], A. Bulleri [2], A. Delle Sedie [1], E. Elefante [1], N. Luciano [1], M. Mosca [1], C. Baldini [1]. *[1]Clinical and Experimental Medicine, Rheumatology Unit, University of Pisa; [2]Radiology Unit, University of Pisa, Pisa, Italy*

Background: Ultrasound pleural irregularity (PI-US) is a novel promising tool for non-invasive diagnosis of interstitial lung involvement (ILD) in connective tissue diseases (CTDs). Few data are available on its diagnostic usefulness in primary Sjögren's syndrome (pSS)-induced ILD.

Objectives: a) To assess the accuracy of PI-US to diagnose ILD in pSS when compared to chest tomography (HRCT) (i.e gold standard imaging technique); b) to explore PI-US diagnostic value in early preclinical phases of lung involvement.

Methods: PI-US was performed by a single operator using a MyLab-25 (Esaote), 10 MHz, 5 cm linear probe. PI was defined as the loss of the normal hyperechoic linear pleural contour (score 0–2: normal, minimal and major changes at each intercostal space). Abnormal findings at HRCT were quantified by an expert radiologist according to a semiquantitative score (0–2: absent, moderate, severe). Semi-quantitative scores assigned by PI-US and HRCT to 6 lung fields (2 for the anterior, 2 for postero-superior and 2 for postero-inferior chest surface) were compared. Total and partial scores (for each lung fields) were evaluated. For statistical analysis chi-square, Mann-Whitney test, R-Spearman, and ROC-curve analysis were used.

Results: *Validation study phase (PI-US vs HRCT):* To validate PI-US technique, we enrolled 32 pSS patients [M/F:5/27; median age (IQR): 67 yrs (51.5–71); median disease duration (IQR): 7 (4–11) yrs; anti-Ro/SSA (+) 78.1%]. To be included patients should have performed a HRCT evaluation within 6 months. Thirteen patients (41%) presented HRCT lesions suggestive for ILD. HRCT total scores and PI-US total scores were strongly correlated (r=0.744, p=0.000). Similarly, PI-US and HRCT partial scores related to the postero-inferior fields showed a strong correlation one to each other (r=0.780, p=0.000). ROC-curve analysis identified a total PI-US score of 28.5 (Youden index) as able to predict HRCT-diagnosis of ILD with a sensitivity (SE) of 84.6% and a specificity (SP) of 89.5%. Analogously, a postero-inferior PI-US score of 12.5 demonstrated a SE of 100% and a SP of 89.5% for the ILD diagnosis. *Prospective study phase exploring the usefulness of PI-US for ILD early pre-clinical diagnosis:* We included 24 consecutive pSS patients without overt respiratory symptoms [M/F:1/23; median age (IQR): 55 yrs (47–67); median disease duration (IQR): 4 yrs (1–12); anti-Ro/SSA (+) 60.9%]. Out of them, at the end of the diagnostic work -up, four new cases of HRCT-proven pSS-ILD were diagnosed. Their PI-US mean total score was significantly higher than that observed in non-ILD patients (48±18 vs 16±12, p=0.001) as well as their mean postero-inferior PI-US score (19±9 vs 6±5, p=0.003). The total PI-US and postero-inferior PI-US cut-off retrieved in the first part of the study (i.e. 28.5 and 12.5) allowed us to identify those patients with an HRCT-proven pSS-ILD with a SE of 75% and 100%, a SP of 95% and 89.5%, a PPV of 75% and 57% and a NPV of of 95% and 100%, respectively.

Conclusions: Even if preliminary, this study demonstrated a strong correlation between PI-US and HRCT in the detection of ILD-pSS also in asymptomatic patients, opening new perspectives for the early non-invasive screening of lung involvement in pSS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4368

FRI0261 SKIN CANCER IN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS

M. Taraborelli[1], C. Genitori[2], I. Cavazzana[3], M. Fredi[3], A. Tincani[4], P. Calzavara Pinton[2], F. Franceschini[3]. *[1]Internal Medicine Unit, Mellino Mellini Hospital, Chiari (Brescia); [2]Dermatology Unit and Chair, University and Spedali Civili of Brescia; [3]Rheumatology Unit, Spedali Civili of Brescia; [4]Rheumatology Unit and Chair, University and Spedali Civili of Brescia, Brescia, Italy*

Background: Conflicting results about the prevalence of skin cancer in Systemic Lupus Erythematosus (SLE) have been reported in the literature [1,2].
Objectives: The aim of this study was to retrospectively evaluate the prevalence of malignancies, with a particular focus on skin cancers, in a cohort of SLE patients followed in a single Center.
Methods: All the SLE patients classified according to the ACR and SLICC criteria, attending the Rheumatology and Clinical Immunology Unit of Spedali Civili, Brescia, were retrospectively evaluated. Clinical and laboratory data were obtained from clinical charts. Diagnoses of skin cancers (melanoma and non-melanoma: basalioma, squamous cell carcinoma) and other malignancies were recorded together with the time elapsed from diagnosis of SLE. Univariate analysis was performed to compare characteristics of patients with (K+) and without (K-) cancer. We also compared the prevalence of cancer in our population to that reported in the italian general population (from the Italian National Institute of Statistics, ISTAT, report 2014).
Results: In a cohort of 511 SLE patients (92% females,95% caucasian) regularly followed from 1972 to 2016 (mean age at diagnosis 31 years±13 and median follow-up 12 years, range 1–40) we detected 51 cases (9,9%) with a history of malignancy: melanoma was reported in 3 (0.5%), non melanoma skin cancer (NMSC) in 11 (2%) and other malignancies in 38 cases (7.4%). Table I reports the comparison between patients with and without cancer. Patients with cancer, as well as cases with NMSC and non cutaneous malignancies, showed a higher age at disease onset ($p<0.0001$; $p=0.002$ and $p<0.0001$ respectively) and higher SLE damage ($p<0.0001$; $p=0.019$ and $p<0.0001$ respectively) compared with patients without malignancies. Patients with melanoma showed the same age at SLE onset, but a higher prevalence of discoid lupus ($p<0.0001$) and oral ulcer history ($p=0.02$). No difference in serological SLE features or in disease activity were detected between groups. The prevalence of melanoma in our cohort (0.5%) was only slightly higher than the one reported in the northern Italian general population (0.2%), while the prevalence of NMSC (2%) resulted to be significantly higher than that reported in the same population (prevalence of spinocellular and basocellular cancer 0.1% and 0.5% respectively).

Table I Characteristic of Systemic Lupus Erythematosus patients with and without cancer

Variable	All n.511	K+ n. 51	K- n. 460	melanoma n.3	NMSC n. 11	Other tumors n. 38
Male sex, n (%)	40 (8)	1 (1.9)	39 (8.4)	0 (0)	0	1 (2.6)
Mean age at diagnosis (years), (SD)	31.4 (12.7)	41 (14.48)	32 (12.1)	21 (1.5)	43 (18)	43 (12.6)
Mean disease duration, years (SD)	16.31 (9.53)	18 (22)	16 (9.3)	20 (4.5)	15 (11.7)	18 (11.3)
Mean SLEDAI-2K at inclusion (SD)	11.6 (6.02)	12.18 (5.81)	11.6 (6)	17.33 (8.96)	10.3 (2)	12.2 (6)
Mean last SLICC (SD)	1.5 (1.6)	3 (1.85)	1 (1.5)	3.67 (2.8)	2 (1.5)	3 (1.85)
Discoid lupus (%)	32	3 (5.8)	29 (6.3)	3 (100)	0 (0)	3 (7.8)
Acute cutaneous lupus (%)	270 (53)	24 (47)	246 (53.4)	3 (100)	5 (45.4)	17 (44.7)
Photosensitivity (%)	246/502 (49)	21 (41.1)	225 (48.9)	1 (33.3)	5 (45.4)	16 (42.1)
Glomerulonephritis (%)	160 (31)	13 (25.4)	147 (31.9)	1 (33.3)	2 (18.1)	10 (26.3)
Arthritis (%)	298 (58)	34 (66.6)	264 (57.3)	3 (100)	9 (81.8)	23 (60.5)
Oral ulcers (%)	170 (33)	12 (23.5)	158 (34.3)	3 (100)	0 (0)	9 (23.6)
Chronic alopecia (%)	47 (9.2)	5 (9.8)	39 (8.4)	1 (33.3)	1 (9)	3 (7.8)
Pleurisy (%)	81(16)	10 (19.6)	71 (15.4)	0 (0)	4 (36.3)	6 (15.7)
Pericarditis (%)	63 (12)	5 (9.8)	58 (12.6)	0 (0)	2 (18.1)	3 (7.8)
Leucopenia (%)	134 (26)	14 (27.4)	120 (26)	3 (100)	5 (45.4)	7 (18.4)
Lymphopenia (%)	73 (14)	7 (13.7)	66 (14.3)	1 (33.3)	2 (18.1)	5 (13.1)
Thrombocytopenia (%)	91(18)	9 (17.6)	82 (17.8)	1 (33.3)	1 (9)	7 (18.4)
Deep vein thrombosis/ pulmonary embolism (%)	43 (8.4)	4 (7.8)	37 (8)	0 (0)	1 (9)	4 (10.5)
Anti-dsDNA (%)	439 (86)	43 (84.3)	396 (86)	3 (100)	10 (90.9)	31 (81.5)
Anti-ENA (%)	297 (58)	27 (52.9)	270 (58.6)	2 (66.6)	5 (45.4)	20 (52.6)
Antiphospholipid syndrome (%)	70/509 (13.7)	8 (15.6)	62 (13.4)	0 (0)	2 (18.1)	6 (15.7)
Lupus anticoagulant	115/326 (35.3)	14 (27.4)	136 (29.5)	1 (33.3)	3 (27.2)	10 (26.3)
aCL (IgG and/or IgM)	186/458 (40.6)	26 (50.9)	204 (44.3)	0 (0)	6 (54.5)	19 (50)
anti-B2GPI (IgG and/or IgM)	156/413 (37.8)	25 (49)	222 (48.2)	2 (66.6)	3 (27.2)	20 (52.6)

Conclusions: Non-melanoma was the most common skin cancer observed in our SLE cohort. Its prevalence appeared to be higher than that reported in the general poopulation. SLE patients with melanoma showed a higher frequency of cutaneous lupus history compared with other SLE patients.
References:
[1] Cao L et al PLoS One 2015;10:1–21.
[2] Goobie GC et al. Current Opinion Rheumatology 2015;27:454–60.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4627

FRI0262 CLINICAL, LABORATORY AND IMMUNOLOGICAL CHARACTERISTICS OF 413 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN SOUTH KOREA: A MULTICENTER RETROSPECTIVE COHORT STUDY

E.-K. Park[1], S.-G. Lee[1], J.-H. Park[1], S.-M. Kweon[1], D.H. Sohn[2], Y. Kim[3], G.-T. Kim[3], Y.-S. Suh[4], H.-O. Kim[4], J.-W. Lee[5]. *[1]Internal Medicine, Pusan National University School of Medicine, Pusan National University Hospital, Busan; [2]Microbiology and Immunology, Pusan National University School of Medicine, Yangsan; [3]Internal Medicine, Kosin University College of Medicine, Busan; [4]Internal Medicine, Gyeongsang National University School of Medicine, Gyeongsang National University Changwon Hospital, Changwon; [5]Internal Medicine, Busan St. Mary's Hospital, Busan, Korea, Republic Of*

Background: Epidemiologic studies have described clinical characteristics of patients with systemic lupus erythematosus (SLE) in Middle Eastern Asia and Western countries and marked ethnic and geographic differences in the prevalence, severity and outcome of SLE have been reported. However, data from Northeast Asia countries including South Korea are lacking.
Objectives: To investigate demographic, clinical, laboratory and immunological characteristics and prognosis of patients with SLE in South Korea.
Methods: We retrospectively evaluated 413 SLE patients (380 female, 33 male, mean age 40.6 years) diagnosed at 3 tertiary rheumatology centers in South Korea from 1992 to 2016 by reviewing medical chart. All patients fulfilled 1997 revised American College of Rheumatology classification criteria for SLE and were ethnically Korean.
Results: The mean (±SD) age at disease diagnosis was 30.9 (±12.8) years and the median (IQR) disease duration was 108 (60–168) months. The commonest clinical manifestations in our patients were arthritis (59.1%), fever (49.9%), malar rash (48.4%), alopecia (43.8%) and oral ulcer (35.1%). The frequency of major organ involvement was as follows: biopsy-proven lupus nephritis (40.7%), neuropsychiatric involvement (19.4%), secondary anti-phospholipid antibody syndrome (6.1%) and lupus pneumonitis (1.7%). Class IV (41.1%) was the most common type of lupus nephritis followed by class V (15.5%). Regarding hematologic abnormalities, the cumulative incidence of leucopenia was 74.3%, thrombocytopenia 46.5%, lymphopenia 45.1% and hemolytic anemia 8.7%. Antinuclear antibodies were detected in 97.8%, anti-Sm in 38.4%, anti-dsDNA IgG in 56.5%, anti-cardiolipine IgG in 27.4%, anti-cardiolipine IgM 11.8%, lupus anticoagulant in 23.2%, anti-Ro in 62.3%, anti-La 30.2% and anti-RNP in 47.9%. Twenty (4.8%) patients died during median follow-up of 84 months and the 5-year and 10-year survival rates were 96.9% and 95.5%, respectively (Figure 1). The major causes of death were infection (35%) and diffuse alveolar hemorrhage (20%). In multivariable Cor regression models, male (HR=8.68, $p<0.001$), age at diagnosis ≤16 years (HR=3.33, p=0.033), serositis (HR=3.04, p=0.018) and thrombocytopenia (HR=3.23, p=0.041) were associated with poor survival, while SLE patients with hydroxychloroquine use showed better survival (HR=0.11, p=0.001).

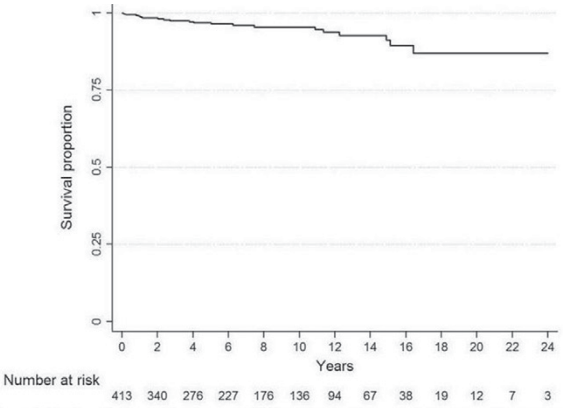


Figure 1. Kaplan-Meier survival curve of 413 patients with systemic lupus erythematosus

Conclusions: Compared with data from other countries, the higher prevalence of hematologic manifestatons and positive anti-Ro antibody were prominent feature of South Korean SLE patients. Overall survival rate in our patients was better than that in other populations.
References:
[1] Khanfir MS et al. TULUP (TUnisian LUPus): a multicentric study of systemic lupus erythematosus in Tunisia. Int J Rheum Dis 2013;16:539–46.
[2] Al Arfaj AS et al. Clinical and immunological manifestations in 624 SLE patients in Saudi Arabia. Lupus 2009;18:465–73.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2284

FRI0263 SYSTEMIC DISEASE ACTIVITY PROGRESSION IN A LARGE COHORT OF PRIMARY SJÖGREN'S SYNDROME: A LONG-TERM FOLLOW-UP DATA BASED ON THE ESSDAI SCORE

L. Quartuccio, S. Zandonella Callegher, S. Gandolfo, C. Fabro, S. De Vita. *Rheumatology Clinic, Udine Hospital Santa Maria della Misericordia, Udine, Italy*

Background: Primary Sjögren's syndrome (pSS) is a chronic slowly progressive

autoimmune disease, which mainly affects the salivary and lachrymal gland function. However, it is an autoimmune systemic disease with a widespread spectrum of systemic manifestations, which are now captured by validated scores (1).

Objectives: The aim of this restrospective study is to evaluate the disease course in a long-term follow-up, by focusing on the accrual of the systemic activity of the disease over time.

Methods: 254 patients suffering from pSS were studied. Mean (standard deviation) age at diagnosis was 52 (13) years. They were 235/254 (92,5%) females. Patients' chart were reviewed in order to compare the baseline ESSDAI score, ie calculated at the diagnosis, with the total ESSDAI accrual, by verifying the new onset ESSDAI domain and/or the worsening in already active ESSDAI domains in the whole available follow-up.

Results: The observation covered 9,1 (6,9) years of follow-up from the diagnosis to the last follow-up visit. The median (range) baseline ESSDAI was 4 (0–31), while the total ESSDAI score accrual up to the last visit was 7 (0–43) ($p<0,0001$, by Wilcoxon). The onset of new ESSDAI domains and/or worsening of already active ESSDAI domains was shown in 136/254 (53,5%) patients, accounting for a total amount of 210 onsets of new domains or worsening in the already active domains [9,1 (95% CI 5,2–27,7) events/100 patients/year]. There was no difference between patients with baseline ESSDAI score <5 and patients with baseline ESSDAI score ≥ 5 (56/103, 54,4% vs 66/121, 54,5%). In only 15/135 (11,1%), the biologic domain was the sole ESSDAI domain, which was worsened or newly recorded. Finally, the ESSDAI domains, which more frequently raised or worsened in the follow-up were haematological (42/210, 20%), biological (37/210, 17,6%), articular (37/210, 17,6%), lymphadenopathy (28/210, 13,3%), and peripheral nervous system (15/210, 7,1%).

Conclusions: Primary Sjögren's syndrome is not a benign disease, a half of patients showing an increasing disease activity, and probably damage, in terms of new onset or worsening of already existing manifestations, even when the disease activity is low at the onset. Importantly, clinically relevant changes over time are much more frequently observed than only biological changes, thus suggesting the need of a careful follow-up by experts, as well as the unmet need of effective treatments, according to disease activity and damage.

References:

[1] Seror R, et al. Outcome measures for primary Sjögren's syndrome: a comprehensive review. J Autoimmun. 2014;51:51–6.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3897

FRI0264 EPIDEMIOLOGIC PROFILE OF ERECTILE DYSFUNCTION IN SLE: A MULTI-CENTER STUDY IN LATIN AMERICAN PATIENTS

J. Merayo-Chalico[1], A. Barrera-Vargas[1], S. Morales-Padilla[1], R. Reyna-De la Garza[1], R. Vázquez-Rodríguez[1], M. Sotomayor[2], D. Gómez-Martín[1], J. Alcocer-Varela[1], C. Abud-Mendoza[3], M. Martínez-Martínez[3], I. Colunga-Pedraza[4], C. Uriarte-Hernández[5], I. Acosta-Hernández[6], D. Fajardo[7], C. García-García[8], D. Padilla-Ortíz[9,10]. *[1]Immunology and Rheumatology; [2]Urology, Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", Mexico City; [3]Rheumatology, Hospital Central "Dr. Ignacio Morones Prieto", San Luis Potosí; [4]Rheumatology, Hospital Universitario "Dr José e González", Monterrey, Mexico; [5]Internal Medicine, Hospital Metropolitano "Vivian Pellas", Managua, Nicaragua; [6]Rheumatology, Instituto Salvadoreño del Seguro Social, San Salvador, El Salvador; [7]Rheumatology, Instituto Mexicano del Seguro Social, Guadalajara; [8]Departamento de Reumatología, Hospital General de México "Dr. Eduardo Liceaga", Mexico City, Mexico; [9]Internal Medicine, Hospital Universitario de la Samaritana; [10]Internal Medicine, Hospital Militar Central, Bogotá, Colombia*

Background: Although systemic lupus erythematosus (SLE) has a higher prevalence in women, the disease usually has a more aggressive course in men. Information regarding erectile function in men with SLE is quite scant.

Objectives: The aim of this study was to describe the prevalence of erectile dysfunction (ED), as well as associated demographic and clinical features, in men with SLE, by means of a systematic, standardized evaluation.

Methods: We performed a transversal study in eight tertiary care centers in Latin America. We included male patients ≥ 16 years who fulfilled ≥ 4 ACR criteria for SLE, and who had regular sexual activity in the previous 6 months. Patients with other rheumatic diseases (except for APS), chronic viral infections and late-onset SLE were excluded. All patients answered the IIEF-5 Questionnaire, which has been validated in Spanish. Other relevant demographic, clinical and serological characteristics were documented. We included two control groups: the first one was made up by healthy men and the second by men with autoimmune diseases different from SLE (non-SLE group).

Results: We included 279 subjects (174 SLE, 55 non-SLE and 50 healthy controls). The prevalence of ED in SLE group 68% (*vs* 22% in healthy group, p=0.001). The mean age of patients with ED in the SLE group was 36.1±1.03, while in patients without ED it was 32.5±1.27 (p=0.022). Whereas there was no difference regarding ED prevalence between SLE patients and the non-SLE group (68 vs 60%, p=0.25), patients with other autoimmune diseases were 10 years older (46.3±1.60 years, p=0.001).

Among SLE patients with and without ED, the presence of persistent lymphopenia ($\leq$1000cells/mcl at three consecutive times, p=0.006), the prednisone dose (9.3±1.2 vs 5.3±1.2mg, p=0.026), as well as the SLICC damage score (1.2±0.1 vs 0.8±0.1 points, p=0.026), were significantly different. Comorbidities and other demographic, serological and treatment variables were not different between those groups. Multivariate analysis showed the following independent risk factors for ED in SLE patients: persistent lymphopenia (OR 2.79 CI95% [2.79–5.70], p=0.001) and corticosteroid use (any dose) in the previous year (OR 2.15 CI95% [1.37–3.37], p=0.001). Only 7% of patients had been questioned about their sexual function in the previous three visits to the rheumatologist; also, 81% of subjects considered it would be appropriate to be asked about their sexual function.

Conclusions: Regardless of comorbidities, treatment (excluding steroids) and type of disease activity, SLE patients have a high prevalence of ED, especially considering most patients are young and sexually active. Rheumatologists should be aware of the relevance of this problem in male SLE patients and should ask about this issues in regular visits.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1653

FRI0265 CYTOKINES AND CORRELATIONS WITH PATIENT REPORTED OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS AND POPULATION CONTROLS

S. Pettersson[1,2], H. Idborg[3], S. Eketjäll[4], I. Gunnarsson[3], E. Svenungsson[3]. *[1]Rheumatology unit, Karolinska University hospital; [2]Department of Neurobiology, Care Sciences and Society, Karolinska Institutet; [3]Rheumatology unit, Department of Medicine, Karolinska Institutet and Karolinska University Hospital, Stockholm; [4]Cardiovascular and Metabolic Diseases, Innovative Medicines and Early Development Biotech Unit, AstraZeneca, Integrated Cardio Metabolic Centre (ICMC), Karolinska Institutet, Huddinge, Sweden*

Background: In open questions patients with systemic lupus erythematosus (SLE) report fatigue as the most distressing symptom. Pro-inflammatory cytokines are generally suggested to contribute to fatigue in chronic diseases, however results are contradictory (1, 2). Patient reported outcome measures (PROMs) quantify patients' experiences of qualities like fatigue and depression, which have great impact on both physical and psychological wellbeing. If PROMs are associated with pro-inflammatory cytokine activity in SLE has not yet been well investigated

Objectives: In this study we explored the relationship between a large set of cytokines and self-assessments of fatigue, anxiety, depression and quality of life in a large group of patients with SLE and in matched controls.

Methods: In a cross-sectional setting, persons with SLE and age- and gender-matched population controls responded to PROMs, assessing fatigue (Multidimensional Assessment of fatigue Scale), depression/anxiety (Hospital Anxiety and Depression Scale) and health related quality of life (Medical Short Form 36 (SF-36)). 30 cytokines were analyzed (MSD 30-plex cytokine assay). Spearman's rank correlation coefficient (r_s) between cytokines and PROMs were calculated.

Results: 423 patients, age 46.6 (±15.3) and 315 controls age 47.5 (±14.6) (p 0.43) were included. Of 30 analyzed cytokines 20 gave reliable results and were correlated to PROMs. Five of the cytokines (IL-6, TNF-alfa, IL-15, MCP-1 and MIP-1-beta) correlated best ($r_s \geq 0.37$) with investigated PROMs (table 1). Fatigue correlated with TNF-α (r_s =0.32), IL-15 (r_s =0.31), and MIP-1-beta (r_s =0.32), $p<0.01$ for all. When summarizing SF-36 results we noted a pattern of stronger correlations between investigated cytokines and the physical component than the mental component. Anxiety and depression correlated, but weakly ($r_s<0.25$).

Table 1. Correlations between cytokines and patient reported outcomes

	IL-6	TNF-α	IL-15	MCP-1	MIP-1β
Fatigue	0.28**	0.32**	0.31**	0.29**	0.32**
Anxiety	0.05	0.12**	0.12**	0.06	0.10**
Depression	0.19**	0.25**	0.21**	0.19**	0.21**
Physical Function§	-0.38**	-0.41**	-0.37**	-0.42**	-0.42**
Role Physical§	-0.29**	-0.38**	-0.32**	-0.35**	-0.34**
Bodily Pain§	-0.24**	-0.29**	-0.28**	-0.27**	-0.30**
General Health§	-0.37**	-0.45**	-0.37**	-0.40**	-0.38**
Vitality§	-0.26**	-0.34**	-0.29**	-0.29**	-0.30**
Social Function§	-0.20**	-0.27**	-0.27**	-0.25**	-0.25**
Role Emotional§	-0.12**	-0.24**	-0.18**	-0.16**	-0.16**
Mental Health§	-0.11**	-0.20**	-0.19**	-0.15**	-0.17**
Physical Component Summary score§	-0.39**	-0.43**	-0.38**	-0.42**	-0.41**
Mental Component Summary score§	-0.07	-0.16**	-0.15**	-0.10**	-0.11**

**Spearman correlation is significant at the 0.01 level (2-tailed). §From SF-36.

Conclusions: Most PROMs were positively associated with pro-inflammatory cytokines. Fatigue and PROMs reflecting physical aspect of disease correlated most convincingly, while correlations with mental aspects were weaker.

References:

[1] Omdal R, et al (2002). Fatigue in patients with systemic lupus erythematosus: lack of associations to serum cytokines, antiphospholipid antibodies, or other disease characteristics. J Rheumatol.

[2] Roerink ME et al (2017). Interleukin-1 as a mediator of fatigue in disease: a narrative review. J Neuroinflammation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2746

FRI0266 **COMPARISON OF CLINICAL AND SEROLOGICAL CHARACTERISTICS BETWEEN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH AND WITHOUT ASSOCIATED JACCOUD ARTHROPATHY**

A. Alía Jiménez, W.A. Sifuentes Giraldo, L. Villalobos Sánchez, M.J. García Villanueva, A. Zea Mendoza. *Rheumatology, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Jaccoud arthropathy (JA) is a chronic non-erosive reversible joint disorder commonly associated with systemic lupus erythematosus (SLE), and occurs in roughly 5% of all cases. Some studies suggest different profiles of clinical and immunological features between SLE patients with or without JA.
Objectives: To compare the profile of clinical and serological manifestations of patients with SLE with and without JA followed in a tertiary care hospital of Madrid.
Methods: We performed a retrospective observational study of a cohort of patients diagnosed with SLE (4 or more ACR criteria) between June 1977 and December 2015. The variables evaluated included demographics, clinical, analytical and radiological manifestations. The definition of JA was based on the presence of clinical criteria (reversible joint deformities) and absence of radiographic erosions typical of rheumatoid arthritis. Statistical analysis was performed using SPSS software version 21.0.
Results: We included 108 patients representing a sample of 24% of the total number of patients with SLE treated at our center during that period. The majority of patients were women (89.8%), mean age at diagnosis was 30±12.29 years (range: 7–75) and duration of disease was 127 months (range: 2–411). Thirteen patients (12.03%) had findings compatible with JA. There were no significant differences in age, sex or race, but the duration of disease was higher in JA patients (190 vs. 118.2 months, p=0.0299). There were significant differences in the presence of malar rash (p=0.0009), photosensitivity (p=0.0050), oral ulcers (p=0.0032) and pericarditis (p=0.000001), which were more frequent in patients without JA, but arthritis, nephritis, pleuritis, seizures, psychosis, Raynaud's phenomenon and antiphospholipid syndrome had a similar distribution between both groups. Among the immunological features, no significant difference was found in relation to hemolytic anemia, lymphopenia, thrombocytopenia, ANA, anti-ENA, anti-DNA, anticardiolipin, anti-β2 glycoprotein I and lupus anticoagulant, but leukopenia was also more frequent in patients without JA (p=0.0041).
Conclusions: In the analyzed sample of patients in our center JA was a relatively frequent finding and was associated with a longer duration of the disease. It was not possible to corroborate other JA associations suggested in previous studies such as a lower frequency of lupus nephritis or major secondary antiphospholipid syndrome, probably due to limited sample size, but there are also other studies that do not demonstrate significant differences in relation to clinical and serological findings in patients with SLE with JA with respect to those who do not present it. Studies involving a larger number of patients with JA associated with SLE are required in order to better identify these differences, so a multicenter initiative could be of great help.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6980

FRI0267 **HEMOPHAGOCYTIC SYNDROME IN PATIENTS FROM SLE REGISTRY FROM THE SPANISH SOCIETY O RHEUMATOLOGY (RELESSER)**

A. Lois-Iglesias[1], I. Rua-Figueroa[2], F. deToro-Santos[1], A. Zea-Mendoza[3], J. López-Longo[4], J. Calvo[5], M. Galindo[6], E. Uriarte-Isacelaya[7], J. Pego-Reigosa[8,9] on behalf of EASSER-RELESSER. *[1]University Hospital A Coruña, A Coruña; [2]Hospital Universitario Dr Negrin, Gran Canaria; [3]University Hospital Ramón y Cajal; [4]HGUGregorio Marañón, Madrid; [5]Hospital, Araba; [6]University Hospital 12 de Octubre, Madrid; [7]University Hospital Donostia, Donostia; [8]Hospital Vigo; [9]IISGS, Vigo, Spain*

Background: Systemic Lupus Erythematosus (SLE) is an autoimmune systemic rheumatic disease that, in our area, presents hematologic manifestations in approximately 70% of cases[1]. Some of them are very rare so there are no large series whose analysis could provide relevant information.
Objectives: To study the characteristics of patients with Hemophagocytic Syndrome (HS) in a large sample of SLE patients.
Methods: SLE patients from RELESSER database were studied. We analysed SLE manifestations present at 12 different domains (mucocutaneous, renal, musculoskeletal, constitutional, hematologic, vascular, cardiac, respiratory, neuropsychiatric, gastrointestinal, ophthalmic and serological) before, during and after HS diagnosis and until the last available assessment. We also studied activity (SELENA-SLEDAI) and damage (SLICC/ACR DI) indices at those moments.We evaluated the treatment received, HS recurrences and the number of deaths by this entity.
Results: 3,656 SLE patients (≥4 ACR criteria) from 45 Rheumatology Units across Spain were studied. Seven patients (<0.5%) with HS were identified. 71.4% were women, with a mean age (± S.D.) at SH diagnosis of 35.1 (± 17.1) years. In 5 of the 7 cases the HS occurred 115.5 (± 162.9) months after SLE diagnosis. In the other 2 cases the diagnosis of both entities was simultaneous. The main triggers of HS were infections, followed by SLE activity flares. At the time of HS diagnosis, they had high SLE activity with a mean SLEDAI score of 13.1 (± 11.3) and 1.4 (± 2.3) SDI score.
Clinically, 100% of the patients presented fever and alterations of the liver profile, 85.8% cytopenias and 71.5% dermatological manifestations. Respiratory manifestations and hemolytic anemia were present in 57.2% of the cases, both; lymph nodes and coagulopathy in 42.9%. Hepatomegaly was detected in 28.6%, as well as neuropsychiatric, digestive and renal manifestations. Splenomegaly was detected in 14.3%. The mean hemoglobin level was 8.6 (± 1.1) g/dl, platelets 85,585 (± 83,390)/mm^3, ferritin 7,410 (± 6,470) ng/ml and triglycerides 404.7 (± 235.6) mg/dl. All patients were admitted and undergonebone marrow study, requiring a mean of 2.2 (± 1.5) treatment lines, using 2.8 (± 1.7) drugs. One patient died during the HS episode by the HS itself and another 2 patients had 2 and 3 recurrences, respectively.
The following table shows the characteristics of each patient.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Number of organ systems affected by SLE before HS diagnosis	9	4	5	5	6	Simultaneous diagnosis of SLE and SH	Simultaneous diagnosis of SLE and SH
Number of organ systems affected by SLE at HS diagnosis	4	1	2	4	2	4	3
Number of organ systems affected by SLE until last assessment	Died	2	2	Follow-up lost	1	5	1
SLEDAI//SLICC-ACR DI at HS diagnosis	4//6	4//0	5//0	29//3	4//1	25//0	21//0
SLEDAI//SLICC-ACR DI 1 year after HS	*	0//0	0//0	*	2//1	0//0	2//13
SLEDAI//SLICC ACR DI at last assessment	*	0//0	0//0	*	0//1	2//0	2//13
Number of treatment lines	1	0	3	2	2	4	3
Number Treatments administered	2 GC and CsA	0	5 GCs, etoposide, iv Ig, CsA, platelets,red cells	3 GC, CYP and iv Ig	2 Amphotericin B, miltefosine	4 GC, iv Ig, CsA, MM	4 GC, Cs A, anakinra and CYP
Relapses	0	2	0	3	0	0	0
Deaths	Yes	No	No	No	No	No	No
Follow-up time (months)	Died	45	80	Follow-up lost	Unknown	26	24

GC:Glucocorticoids, iv Ig: intravenous immunoglobulins,
CYP: Cyclophsphamide, CsA:Ciclosporine A, MM: Mycophenolate mofetil

Conclusions: HS is a rare life-threatening SLE manifestation. It must be suspected in SLE patients with persistent fever who do not respond to antibiotics, cytopenias and evidence of multiorgan involvement. Relapses and death are common in HS associated to SLE.
References:
[1] Pego-Reigosa JM, Rua-Figueroa I, Lopez-Longo FJ, Galindo-Izquierdo M, Calvo-Alen J, Olive-Marques A, et al. Analysis of disease activity and response to treatment in a large Spanish cohort of s with systemic lupus erythematosus. Lupus 2015;24:720–9.
Acknowledgements: Work supported by Spanish Society of Rheumatology, FIS/ISCIII (PI11/02857), BIOCAPS from the European Union 7th Framework Programme/REGPOT-2012–2013.1 (316265), GSK, Roche, Novartis, UCB.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2542

FRI0268 **ULTRASOUND VS. MAGNETIC RESONANCE IMAGING IN DIAGNOSIS OF PRIMARY SJÖGREN'S SYNDROME**

A. Haidmayer[1], M. Magyar[2], M.H. Stradner[1], T. De Zordo[3], A. Lutfi[4], B. Unger[2], W.B. Graninger[1], J. Hermann[1], C. Dejaco[1]. *[1]Department of Internal Medicine; [2]Department of Neuroradiology, Univ. Klinik Graz, Graz; [3]Department of Radiology, Medical University of Innsbruck, Innsbruck; [4]Department of Radiology, Univ. Klinik Graz, Graz, Austria*

Background: Salivary gland (SG) biopsy is the gold standard for the diagnosis of primary Sjögren's syndrome (pSS). Ultrasound (US) and magnetic resonance imaging (MRI) of the SG are emerging techniques. The comparison of both imaging methods for diagnosis and assessment of functional limitation is yet not well investigated.

Objectives: To assess the accuracy of US and MRI and to define possible cutoff values for the diagnosis of pSS.
Methods: Twenty-three patients with pSS according to AECG criteria and typical histology of the SG biopsy and 12 patients with sicca-syndrome and normal SG histology were included in the study. Two experienced ultrasound experts (C.D. 6y, T.D.Z. 5y) did ultrasound of the SG using a B-mode score (0–48 points [1]) and real-time sonoelastography (RTS; 0–16 pts [2]). Morphology of the parotid glands was also assessed by MRI (0–12 pts). We obtained clinical data (C-reactive protein (CRP), antinucleary-antibodies (ANA), Ro-/La-antibodies, Gamma globulins, patient questionaires ESSDAI and SSDI). The statistically analysis was carried out using Kolmogorov-Smirnov-test, student's t-test, or Man-Whitney-U-test. Correlations were performed using Spearman-rang-correlations.
Results: Patients with pSS had significantly higher B-mode- (average =25 [2–44] vs. 9 [1–20], $p<0.001$) and RTS-scores (6.5 [2–13] vs. 4 [1–9], $p<0.001$) than sicca-patients. The same was also found for MRI-assessment (6,96 vs. 2,33, p=0.001). In a Spearman rank correlation, clinical parameters were linked to the imaging techniques The B-mode showed significant inverse correlations with the Saxon-test (r=-0.505, p=0.002) and a positive correlation with MRI (r=0.792, $p<0.0001$). No correlation was found for the activity scores ESSDAI (p=0.221) or SSDI (p=0.219). The MRI score had an inverse correlation with the Saxon-test (r=-0.523, p=0.001). Both imaging techniques showed no relationship with ESR or CRP. We also generated ROC curves of both imaging methods to define possible cutoff values for the diagnosis. For B-Mode we would recommend a value of 12 points (sensitivity 82,6% and specificity 91,7%) and for MRI 3.5 points (78,3% and 91,7%).
Conclusions: Sonography and MRI detected typical morphological changes in the SG of pSS with high sensitivity and specificity. Both methods could become valuable tools for the diagnosis of pSS.
References:
[1] Hocevar, Ambrozic A, Rozman B, Kveder T, Tomsic M. Ultrasonographic changes of major salivary glands in primary Sjogren's syndrome. Diagnostic value of a novel scoring system. Rheumatology (Oxford). 2005;44(6):768–72.
[2] Rubaltelli, Corradin S, Dorigo A, Stabilito M, Tregnaghi A, Borsato S, Stramare R. Differential diagnosis of benign and malignant thyroid nodules at elastosonography. Ultraschall Med. 2009;30(2):175–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6570

FRI0269 "IF IT'S NOT MULTIPLE SCLEROSIS, LOOK FOR A CONNECTIVE TISSUE DISEASE": ATYPICAL DEMYELINATING DISORDERS REFERRED TO A TERTIARY RHEUMATOLOGY CENTRE

A. Fanouriakis[1], K. Voumvourakis[2], M. Papathanasiou[3], T. Doskas[4], T. Karageorgas[1], D. Tseronis[1], D. Kassara[1], A. Erden[5], P. Katsimbri[1], D. Boumpas[1]. *[1]Rheumatology and Clinical Immunology, 4th Department of Internal Medicine; [2]2nd Department of Neurology; [3]2nd Department of Radiology, "Attikon" University Hospital; [4]Department of Neurology, Athens Naval Hospital, Athens, Greece; [5]Department of Rheumatology, Hacettepe University, Faculty of Medicine, Ankara, Turkey*

Background: Central nervous system (CNS) demyelination is the hallmark of multiple sclerosis (MS), but may rarely occur in connective tissue diseases (CTD), mainly systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS).
Objectives: To examine whether patients with demyelinating syndrome and atypical features for MS may exhibit an underlying connective tissue disease.
Methods: Patients referred to the Rheumatology and Clinical Immunology Unit of "Attikon" University Hospital for a demyelinating disorder characterized as "atypical for MS" following neurologic evaluation, were included in the study. All cases were discussed with a neurologist with expertise in MS and CNS magnetic resonance imaging were assessed by an experienced neuroimagist. Cases included either i) a clinical syndrome suggestive of a demyelinating process (demyelinating optic neuropathy, myelopathy, internuclear opthalmoplegia etc.) and/or ii) abnormal imaging of the central nervous system (CNS) with features suggestive of demyelination (ie. presence of supra- and infratentorial lesions, periventricular location, gadolinium enhancement, Dawson's fingers, hypointense T1-lesions ("black holes"), "dirty" white matter). Patients with brain lesions in MRI more compatible with non-specific white matter hyperintensities (WMHI, ie. of possible ischemic/microvascular etiology) were excluded from the study.
Results: 21 patients were included in the study [all women, mean (SD) age at first neurologic manifestation 37.7 (10.6) years]. 17 patients had MRI findings of a demyelinating process in the CNS (brain lesions only in 7, spinal cord lesions only in 4 and both brain and spinal cord lesions in 5 patients); WMHI or normal findings were found in 4 patients with optic neuritis. In this selected group of patients, detailed rheumatologic evaluation revealed clinical and laboratory findings suggestive of a CTD in all patients. The most common findings were: arthritis (80.5%), Raynaud's phenomenon (42.8%), photosensitivity (38.1%), malar rash/erythema (33.3%), livedo reticularis (23.8%) and leukopenia (23.8%). Antinuclear antibodies were positive in two-thirds of patients (66.7%), anti-Ro/La in 19.0% and aPL only in one patient (4.8%). Final diagnoses were undifferentiated CTD, in 10 patients, frank SLE in 9 patients, primary obstetric APS and RA, in one patient each. After a median (range) follow-up of 3 (1–14) years, three patients fulfilled the criteria for MS and received MS-specific therapy, thus were subsequently classified as having an overlap of two diseases.
Conclusions: CNS lesions suggestive of demyelination on MRI must be distinguished from non-specific lesions of microvascular etiology. In cases of demyelinating syndromes not fulfilling criteria for MS, features of an underlying CTD, suggestive of SLE, are frequently found. A small percentage of patients may go on to develop frank MS during follow-up, thus longitudinal monitoring is necessary.
References:
[1] Differential diagnosis of suspected multiple sclerosis: a consensus approach. Miller DH, Weinshenker BG, Filippi M, et al. Multiple Sclerosis 2008; 14: 1157–1174.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6438

FRI0270 URINARY AND SERUM NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS A BIOMARKER IN INDIAN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RELATION TO RENAL INVOLVEMENT AND OVERALL DISEASE ACTIVITY

B. Abujam[1], S. Singh[2]. *[1]Pediatric Allergy Immunology unit, Post Graduate Institute Medical Education Research; [2]PGIMER, Chandigarh, India*

Background: Renal involvement often results in long-term morbidity in childhood Systemic Lupus Erythematosus (cSLE). Neutrophil gelatinase associated lipocalin (NGAL) has been shown to be a reliable structural biomarker for the early diagnosis of kidney injury in many clinical scenarios.
Objectives: This study aimed to detect levels of urinary and serum NGAL and changes in flare and improvement on longitudinal follow up in cSLE in a real world clinical scenario.
Methods: Children <14 years of age attending the Pediatric Rheumatology clinic, fulfilling the 1997 SLE criteria were recruited. Urine and serum samples were collected during routine clinical review and SLE Disease Activity Index (SLEDAI) assessed. Children were divided into 3 categories, active renal, active non-renal and inactive lupus. Active lupus was defined as SLEDAI >4. Urinary and serum levels of NGAL (uNGAL; sNGAL) were assessed by ELISA. Urinary values were normalized for urinary spot creatinine. In addition, some patients were longitudinally followed up and resampled when their disease activity changed.
Results: The study included 122 (F:M =91:31) children, 54 had active renal,14 had active non-renal and 54 had inactive disease. Median (IQR) age was 8.8 (6.5–10.7) years and disease duration was 10 (3–24) months.26 children with nephrotic syndrome and 49 age and gender matched healthy controls were also recruited. Children with active renal lupus had significantly higher uNGAL as compared to other categories.Although sNGAL was significantly higher in active renal as compared to inactive lupus,there was no difference between renal and non-renal active lupus (Table 1). On longitudinal follow up, uNGAL levels increased markedly prior to a flare, significantly higher in renal compared to a non-renal flare ($p<0.05$). On the other hand, active lupus children had a significant fall in their uNGAL on follow up. Their was good correlation between change in SLEDAI and change in absolute uNGAL levels (r =0.84, $p<0.01$). Overall, on ROC analysis, uNGAL classified active renal versus active non-renal and inactive combined with an AUC of 0.986 (95% CI 0.972–1.0). The sensitivity and specificity of a uNGAL cutoff off value of 25750 ng/ml was 96.3 and 91.2% respectively.
Conclusions: Urinary NGAL is a sensitive marker of renal involvement in SLE disease activity and can also be a reliable tool for monitoring renal disease activity changes.

Abstract FRI0270 – Table 1

	Inactive cSLE (n=54)	Active renal cSLE (n=54)	Active non-renal cSLE (n=14)	Healthy controls (n=49)	Nephrotic controls (n=26)
Demographics					
Age (years) (mean±SD)	10.6±3.2	10.9±2.5	10.7±1.9	–	11.0±2.0
Age at onset (years) (mean±SD)	*8.4*± 3.1	*9.4*±2.3	*8.9*±2.4	-	–
Female: male ratio	39:15	41:13	11:3	–	18:8
Disease duration (months) (mean±SD)	23.7±32.4	16.6±23.1	14.5±19.2	–	–
Disease activity					
SLEDAI (mean±SD)	2.1±1.0	20.9±6.6	7.1±2.0	–	–
Renal SLEDAI (mean±SD)	0	12.5±2.7	0	–	–
Serum NGAL (pg/ml) (Median (IQR)*	4400 (2332.5–5400)	18245 (16137.5–21062.5)	18375 (14375.0–26142.5)	–	–
Urine NGAL (pg/ml) Median (IQR)**	14100 (11250–19650)	41875.0 (36243.75–46575)	18475 (15287.5–22500)	1170 (658.5–1714.5)	25040 (19637.5–31762.5)
Urine_NGAL_pg/mg_creatinine Median (IQR)**	14743.7 (10487.7–21051.8)	33288.65 (24610.7–44243.9)	14541.2 (11939.3–22043.08)	1008 (597.7–2042.79)	21874.5 (16328.5–31143.8)

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6970

FRI0271 PREVALENCE AND ASSOCIATED FACTORS OF DEPRESSIVE DISORDERS IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

C.C. Mok[1], L.Y.T. Lo[2], K.S. Poon[2], C.W. Cheng[2]. [1]*Medicine, Tuen Mun Hospital;* [2]*Psychiatry, Castle Peak Hospital, HK, Hong Kong*

Background: Psychiatric symptoms are common in patients with SLE. Most studies utilized self-rated scales of psychiatric symptoms for evaluation. Formal diagnosis of depression was not established by psychiatric interviews.
Objectives: To determine the prevalence of depressive disorders, severity of depressive symptoms and the associated clinical and socioeconomic factors in Chinese patients with SLE.
Methods: Patients who fulfilled ≥4 ACR criteria for SLE were randomly recruited from rheumatology out-patient clinics and hospital admission in a 9-month period. Psychiatric disorders were diagnosed by a direct interview with the psychiatrist using the Chinese-bilingual Structural Clinical Interview for DSM-IV Axis I disorders, patient research version (CB-SCID-I/P). The severity of depressive symptoms was assessed by the validated Chinese Hamilton Depressive Rating Scale (HAM-D). Patients were also asked to complete the Beck Depression Inventory (BDI), Medical Outcomes Study Social Support Survey (MOS-SSS-C) and the WHO Quality of Life Measure-Abbreviated Version (WHOQOL-BREF, BREF (HK)). SLE disease activity (SLEDAI), organ damage (SLICC/SDI) and socio-demographic were collected and correlated with the presence of psychiatric disorders. Logistic regression models were used to study the independent factors associated with depressive disorders and the severity of depressive symptoms.
Results: 175 SLE patients were studied (95%women, age 39.2±12.4 years, SLE duration 10.3±6.7 years). 27 (15%) and 37 (21%) patients were diagnosed with a current depressive (52%major depressive disorder, 22%dysthymia) or anxiety (35%generalized anxiety, 14%panic, 14%phobia, 8%adjustment) disorders, respectively. Patients with depressive disorders, as compared to those without psychiatric disorders, had more active SLE (p=0.03) and were more likely to have a history of psychiatric diagnosis (p<0.001) and financial assistance from Government (p=0.04). Independent factors associated with a depressive disorder were SLEDAI score (1.13 [1.02–1.24];p=0.02), perceived poor social support (p=0.03) and a past history of psychiatric disorders (p=0.003). Age, disease duration and other socio-economic variables such as educational level and marriage status were not correlated with the presence of a depressive disorder. Being separated/divorced (β=0.19;p=0.02), having a higher SLEDAI score (β=0.16;p=0.02), SLE duration (β=-0.18;p=0.02) and a past history of psychiatric disorders (β=0.18;p=0.01) were independently associated with higher HAM-D scores, which reflect more severe depressive symptoms. Depressive disorders and severity of depressive symptoms were significantly associated with poorer quality of life. ROC analysis showed that a cut-off of 14 points of the self-rated BDI had a sensitivity of 89% and a specificity of 83% for differentiating a current depressive disorder from those without.
Conclusions: A diagnosis of depressive disorders is prevalent in Chinese patients with SLE. Independent risk factors are more active disease, perceived poor social support and a past history of psychiatric disorders. Patients with more active SLE, shorter disease duration, a past history of psychiatric disorders and being separated were associated with more serious depressive symptoms. The self-rated BDI provides a good screening tool for identifying depressive disorders in SLE patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3935

FRI0272 EARLY DAMAGE ASSESSMENT AND PREDICTION OF DAMAGE ACCRUAL IN PRIMARY SJÖGREN'S SYNDROME USING SALIVARY GLAND ULTRASONOGRAPHY DURING 2 YEARS OF FOLLOW-UP

C. Baldini[1], N. Luciano[1], C. Seghieri[2], F. Ferro[1], E. Elefante[1], M. Mosca[1]. [1]*Clinical and Experimental Medicine, Rheumatology Unit, University of Pisa;* [2]*Laboratorio Management e Sanità, Scuola Superiore Sant'Anna, Pisa, Italy*

Background: Early detection and prediction of glandular damage in primary Sjögren's syndrome (pSS) is of pivotal importance in patients' stratification and treatment. Recently, ultrasonography (SGUS) has appeared as a promising tool for the assessment of salivary gland involvement in pSS. However, few studies have specifically explored its role in the early identification of salivary gland damage and in monitoring disease progression over the follow-up.
Objectives: a) to explore the contribution of SGUS in the early assessment of pSS-induced glandular damage and in monitoring damage accrual during the follow-up b) to identify predictive factors associated with the development and progression of sonographic changes in salivary glands.
Methods: An inception cohort of 54 pSS (AECG 2002) patients was included in this study at the diagnosis and prospectively followed after 6, 12 and 24 months. Demographic, clinical data and the ESSDAI of the patients were collected at each study visit as well as SGUS score that was calculated every time by the same radiologist. Sonographic assessment of glandular damage was performed by evaluating the size of the parotid and submandibular glands (normal/reduced) and the presence/absence of hyperechoic bands in more than 50% of the glands (i.e fibrosis). Descriptive statistics and logistic regression were used for the data analysis.
Results: We included 54 patients (51F:3 M) with a median duration of symptoms before diagnosis of 11 months (range 36–5 mo) and a median (IQR) ESSDAI at baseline of 5 (1–8). We found that at baseline 13 patients out of 54 (24.1%) already presented one element of damage in their SGUS evaluation, 14/54 (25.9%) more than one element of damage, whereas only 27/54 (50%) of patients did not present any sonographic sign suggestive for damage. In particular, hyperechoic bands were detected in the parotid glands of 12/54 (22%) patients and in the submandibular glands of 21/54 (38.9%); reduced parotid and submandibular gland size were described in 5/54 (9.3%) and in 10/54 (18.5%) of the cases, respectively. Predictive factors associated with sonographic salivary gland damage at the diagnosis were the ESSDAI at baseline (OR =1.13 [95% CI 1.0 to 1.27], p=0.04) and the positivity for Rheumatoid factor (RF) (OR =4.47 [95% CI 1.29 to 15], p=0.02). During the follow-up, 15/54 (27.8%) patients presented a progression of their salivary gland damage. We specifically observed a significant increase in the frequency of reduced parotid (9.3% vs 25.9%, p=0.004) and submandibular gland size (18.5% vs 33.3%, p=0.008) at the end of follow-up. Predictive factors for damage accrual during follow-up were: minor salivary gland focus score (OR =3.5 [95% CI 1.1 to 10.6], p=0.03) and the ESSDAI at baseline (OR =1.64, [95% CI 1.0 to 2.6]p=0.03).
Conclusions: Sonographic assessment of glandular damage apparently revealed a relative high frequency of already established signs of glandular damage in pSS patients at baseline, especially in patients with positive RF and higher ESSDAI. When routinely used, SGUS may accurately allowed to monitor damage accrual over the follow-up, ultimately contributing to a better clinical management of patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4327

FRI0273 ROLE OF PROCALCITONIN AND C-REACTIVE PROTEIN IN SCREENING OF INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C.H. Ho, A.M.H. Leung. *Department of Medicine, Queen Elizabeth Hospital, Kowloon, Hong Kong*

Background: Previous studies revealed conflicting results regarding the role of procalcitonin in predicting infections in patients with systemic lupus erythematosus (SLE).
Objectives: This retrospective study aimed to analyse the role of procalcitonin (PCT) and C-reactive protein (CRP) in predicting infections in SLE patients, and to determine an optimal cut-off value for PCT and CRP for defining sepsis.
Methods: This study was carried out in one single tertiary centre. Adult patients (>18-year-old) with underlying SLE who were admitted to hospital between 1st Jan 2007 and 31st Dec 2015 were included. Demographic data, PCT and CRP upon admission, and other clinical parameters were obtained. Infection was defined by positive culture, or based on clinical and radiological evidence with subsequent response to antimicrobial treatments. Active SLE disease activity was defined by SLEDAI, and also by SLE-related manifestations not included in SLEDAI. Mann-Whitney test was used to test the difference between numerical parameters between patients with and without infection. Spearman's correlation was used to analyse the correlation between PCT and CRP. Receiver operating characteristic (ROC) curves were plotted to define an optimal cut-off values for PCT and CRP in infection.
Results: 33 (27 female & 6 male) SLE patients were included. Both mean and median age were 42-year-old. Among the 21 septic patients, 9 had active lupus and 12 had inactive disease. All but one of the 12 non-septic patients had active lupus. All 4 patients with underlying renal failure belonged to the infection group. There were 13 and 3 patients on immunosuppressive treatments in infection and non-infection groups respectively.
In patients with infection, mean PCT was 5.74ng/ml and mean CRP was 77.22mg/L. In those without, these were 0.29ng/ml and 20.04mg/L respectively. Both PCT (p=0.014) and CRP (p=0.016) levels were significantly higher in patients with infection than those without. There was no significant difference between the PCT and CRP levels in both septic patients (PCT p=0.862, CRP p=0.247) and non-septic patients (PCT p=1.000, CRP p=0.500) regardless of their SLE disease activity.
PCT level correlated positively with CRP level (r=0.456, p=0.008), but it had no correlation with age (p=0.978), gender (p=0.424), underlying renal failure (p=0.304), steroid (p=0.053) or other immunosuppressants (p=0.132) use.
ROC curves of PCT and CRP showed a similar area under curve (AUC) of 0.756 and 0.752 respectively. The cut-off for PCT was 0.78ng/ml (sensitivity 61.9%, specificity 91.7%), giving a positive predictive value (PPV) of 92.9%. The cut-off for CRP was 9.35mg/l (sensitivity 85.7%, specificity 66.7%), giving a PPV of 81.8%. Combining both PCT and CRP above their cut-offs, the specificity of predicting infection improved to 100% but the sensitivity worsened to 52%.
Conclusions: Both PCT and CRP were useful in predicting infection SLE patients regardless of their disease activity. The cut-off of PCT at 0.78ng/ml and CRP at 9.35mg/l gave satisfactory positive predictive value for infection.

References:
[1] Lupus 2011; 20:125–130.
[2] Clin Rheumatol 2014; 33:1209–1215.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5733

FRI0274 MORFOLOGICAL INDEXES IN LUPUS NEPHRITIS – DO THEY HAVE PROGNOSTIC VALUE?

D. Navarro, A.C. Ferreira, H. Viana, F. Carvalho, F. Nolasco. *Nephrology Department, Hospital Curry Cabral, Lisboa, Portugal*

Background: Lupus nephritis (LN) is a serious complication of systemic lupus erythematosus (SLE). With current therapies, a high remission rate is observed, this being the most important prognostic factor. Currently, therapy is guided by findings in the renal biopsy, following the ISN/RPS classification. Although recommended by EULAR, Austin and Hill's morphological indexes are not routinely obtained.
Objectives: To analyze the importance and applicability of the different morphological indexes in predicting response to treatment and prognosis.
Methods: Retrospective single center study of consecutive SLE and biopsy proven LN patients, diagnosed from 2010 to 2016. We evaluated the following outcomes: clinical remission, renal function and proteinuria at end of follow-up (FUP) (g/24h). Complete remission was defined as a reduction of proteinuria to <0,5g/24h, inactive urinary sediment and serum creatinine <115% of baseline; partial remission same parameters, except proteinuria <1g/24h if initial value <3h/24h, or reduction to <3g/24h if initial value >3g/24h. The studied predictors were the INS/RPS LN classification and the morphological indexes described by Austin (Activity and Chronicity) and Hill, obtained after histomorphological review of renal biopsies. Statistical analysis was performed with STATA software.
Results: During 6 years, there were 46 biopsy-proven LN cases, 84,8% (n=39) woman, median 35 years old (27 – 42,5) and 57,6% (n=19) caucasian. 39 patients were already known to have SLE, 7,44 (1,13 – 12,3) years previously.
The median FUP was 31,9 (13,2 – 45,6) months. Based on biopsy findings, 35 patients were started on immunosuppression – induction in 50% of cases with MMF and in 50% with cyclophosphamide; maintenance in 81% with MMF, the remaining with azathioprine. Complete remission was achieved in 58% of patients, 27% achieving partial remission. We observed 4 LN relapses. 96% (n=44) of the patients survived at the end of FUP, with a median serum creatinine of 0,8 mg/dl (0,7 – 0,99), eGFR 99,8 ml/min (71,2 – 116,8) and proteinuria of 0,6 g/24h (0,2 – 1,6).
We observed that Class IV patients had, at presentation, lower eGFR (67,3 vs 94,6 ml/min; p=0,02), higher proteinuria (4,26 vs 2,37; p=0,02) and a tendency towards higher C3 consumption (58,9 vs 77,4; p=0,06). We did not observe correlations between ISN/RNP Classification and the outcomes at the end of FUP. The correlations between clinical findings and morphological indexes (Hill and Austin) are summarized in table 1:

Table 1

	Hill Biopsy Index		Activity Index		Chronicity Index	
	R	*p*	R	*p*	R	*p*
Anti-dsDNA (IU/ml)	0,2	NS	0,3	0,005	-0,07	NS
C3 (mg/dl)	-0,2	NS	-0,3	0,003	0,1	NS
C4 (mg/dl)	-0,2	NS	-0,3	0,004	0,1	NS
Presentation serum creatinine (mg/dl)	0,3	0,03	0,1	NS	0,3	0,03
Presentation eGFR (ml/min)	-0,5	0,01	-0,3	NS	-0,4	0,004
Presentation proteinuria (g/24h)	0,6	0,001	0,4	0,009	-0,3	0,006
End of FUP serum creatinine (mg/dl)	0,3	0,046	0,07	NS	-0,4	0,002
End of FUP eGFR (ml/min)	-0,2	NS	0,09	NS	-0,5	0,002
End of FUP proteinuria (g/24h)	0,4	0,02	0,2	NS	0,3	0,003

Both the Hill biopsy index and the Chronicity index were correlated with renal function and proteinuria at the end of FUP. The Activity index correlated with the immunological findings – C3, C4 and anti-dsDNA.
Conclusions: EULAR guidelines suggest that histomorphological evaluation in LN should go beyond ISN/RNP classification, and our data supports that – we observed a correlation between the renal outcomes and the indexes described by Austin and Hill.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3816

FRI0275 SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH POSITIVES AUTOANTIBODIES WITH REMISSION OR LOW ACTIVITY EXHIBIT BOTH LOWER INTERFERON ALPHA AND INTERLEUKIN-10 LEVELS

E. Grau Garcia[1], F.M. Ortiz-Sanjuan[1], M. Fernandez Matilla[2], C.M. Feced Olmos[1], E. Labrador Sánchez[1], N. Fernández-Llanio[2], I. Chalmeta Verdejo[1], K. Arévalo Ruales[1], R. Negueroles Albuixech[1], J. Ivorra Cortes[1], J.J. Fragio Gil[1], I. Martínez Cordellat[1], R. González Mazarío[1], L. Gonzalez Puig[1], C. Alcañiz Escandell[1], C. Nájera Herranz[1], I. Cánovas Olmos[1], E. Vicens Bernabeu[1], J.E. Oller Rodriguez[1], J.A. Castellano Cuesta[2], V. Fornés Ferrer[3], D. Hervás Marín[3], J.A. Román Ivorra[1]. *[1]Rheumatology Department, HUP la Fe; [2]Rheumatology Section, Hospital Arnau de Vilanova; [3]Biostatistics Unit, IIS la Fe, Valencia, Spain*

Background: Systemic lupus erythematous (SLE) is an autoimmune disease characterized by immune system disruption, including T and B cell activation and upregulation of autoantibody and immunocomplexes production that could damage different organs. Sometimes, patients with positives autoantibodies and serological manifestations show low disease activity or clinical remission. There is not enough information about persistent positive autoantibodies in absence of clinical activity neither the role of proinflamatory cytokines in this context.
Objectives: To assess the clinical and molecular differences in SLE patients with positives autoantibodies and with low clinical activity or in clinical remission compared to the group with clinical activity.
Methods: A cross-sectional, observational study of patients diagnosed of SLE according to SLICC 2012 criteria was performed. In these patients a complete blood-test was made, and clinical data by personal interview was collected. We analyzed the serum concentration of IL10, BLyS and INF1A by colorimetric methods. Biostatistical analysis was performed with R 3.3.2.
Results: We selected 130 SLE patients with serological manifestations (defined by RELESSER study) out of 142 SLE patients. 91 cases showed low activity or remission (SLEDAI<6) and 39 presented moderate or high activity (SLEDAI>6). SLE patients with positives autoantibodies without clinical activity showed significantly lower anti-dsDNA levels (P=0.006), lower complement consumption (P=0.003) and lower accumulated damage evaluated by SLICC score (P=0.041). No differences on time of evolution in both groups were observed. In addition, SLE patients with positives autoantibodies without clinical activity exhibit significantly lower levels of IL10 (P<0.001) and INF1A (P=0.019). No differences on BLyS levels in both groups were observed. Finally, SLE patients with positives autoantibodies with clinical activity present more mucocutaneous lesions (P=0.014), musculoskeletal manifestations (P=0.004), neuropsychiatric manifestations (P=0.002), renal manifestations (P<0.001) and lymphopenia (P=0.008) than patients with positives autoantibodies and without clinical activity.
Conclusions: In our series of SLE patients with both serological manifestations and low clinical activity have lower levels of IL10 and INF1A, compared to patients with high clinical activity. This result would suggest that differences in the cytokine levels are not related to autoantibodies presence but there are other mechanisms involved in cytokine production that would also be involved in maintenance of clinical remission.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5766

FRI0276 PREVALENCE OF DEPRESSION BY BECK II AND IMPORTANCE OF FATIGUE BY FACIT IV QUESTIONNAIRES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS VS CONTROLS IN A SINGLE CENTER OF ARGENTINA

E. Avid, A. Braillard-Poccard, M. Garcia Carrasco, N. Perez, G. Nasswetter, D. Dubinsky. *Rheumatology Division, Hospital de Clinicas Jose de San Martin, Capital Federal, Argentina*

Background: Estimated prevalence of neuropsychiatric symptoms in SLE is among 17 to 71%[1]. Depressive symptoms are around 54%[1,2]. Fatigue is frequently referred, predicts high morbidity and may be influenced by lifestyle and individual psychological characteristics[1].
Objectives: To evaluate the prevalence of depressive symptoms and its association with demographics and clinical variables in patients with SLE. To determine the predictive value of FACIT for fatigue in SLE vs controls.
Methods: Observational, retrospective case- control design. Patients ≥18 years old with SLE (ACR 97) were consecutively evaluated in our centre from January to July 2015. We analyzed age, disease duration, clinical manifestations, antibodies profile, SLEDAI (≥4 scored as active) and SLICC. We recorded familiar psychiatric diseases, educational and socioeconomic level (Graffar Scale), employment and marital status. Beck II and FACIT (IV version) questionnaires were used for evaluate depression and fatigue respectively. We tested two cut points for fatigue:<22 and<40 to determine sensitivity/specificity for this tool in SLE patients vs controls[3]. Continues data were compared using t Student and Mann Whitney. Categorical data: chi-square or Fisher's exact test by SPSS version 20.0. To predic fatigue we calculated the area under the curve by Receiver Operating Characteristic (ROC). Statistical significant= p<0.05.
Results: 77 SLE and 100 controls, all female. *SLE vs control group:* Mean of age ys: 34 (19–49)vs 38 (19–60). Prevalence of depression: 52% (44/77) vs 29% (29/100) (p<0.05). Prevalence of fatigue (FACIT<40): 42% (33/77) and 36% (36/100) (p>0.05). Mean disease duration (months) 48 (24–114). Socio-demographic characteristics, SLICC/SLEDAI, clinical and serological manifestations were not correlated with major depression p>0.05. *FACIT:* Median value: 31 (range 22–40) SLE group. *FACIT<22 total SLE:* 12/77 (15%) and *FACIT<40:* 33/77 (42%). *Cut points FACIT SLE vs controls:* <22: 15% (12/77) vs 1% (1/100) (p<0.05), 30% sensitivity/100% specificity, 100% PPV and 57% NPV. AUC FACIT <22: 0.65 (0.65–0.77). FACIT<40 in SLE vs controls: 42% (33/77) vs 26% (26/100) (p<0.05), 69% sensitivity and 84% specificity, 82% PPV and 70% NPV. AUC FACIT<40: 0.75 (0.64–0.87).
Conclusions: Prevalence of depression was high in our cohort and similar to

previously reported[1]. Our patients showed low levels of SLEDAI/SLICC. There was not relation between activity levels and baseline damage with the presence of depression[4]. FACIT IV scale was a good independent predictor of fatigue in SLE patients with or without depression vs controls.

References:
[1] L Palagini M et al Depression and systemic lupus erythematosus: a systematic review. Lupus 2013.
[2] Hugo FJ et al DSM-III-R classification of psychiatric symptoms in systemic lupus erythematosus. Psychosomatics 1996.
[3] Lai JS et al Validation of the Functional Assessment of Chronic Illness Therapy-Fatigue Scale in Patients with Moderately to Severely Active Systemic Lupus Erythematosus, Participating in a Clinical Trial Journal of Rheumatology 2011.
[4] Segui J et al Psychiatric and psychosocial disorders in patients with systemic lupus erythematosus: A longitudinal study of active and inactive stages of the disease. Lupus 2000.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6198

FRI0277 ANTI-SSA ANTIBODY STATUS IN COMBINATION WITH ULTRASOUND OF MAJOR SALIVARY GLANDS: A SHORTCUT IN THE CLASSIFICATION OF PRIMARY SJÖGREN'S SYNDROME?

E. Mossel[1], K. Delli[2], J.F. Van Nimwegen[1], A.J. Stel[1], F.G.M. Kroese[1], F.K.L. Spijkervet[2], A. Vissink[2], S. Arends[1], H. Bootsma[1] on behalf of EULAR US-pSS Study Group. *[1]Rheumatology and Clinical Immunology; [2]Oral and Maxillofacial Surgery, University Medical Center Groningen, Groningen, Netherlands*

Background: Ultrasound of major salivary glands (sUS) is an upcoming diagnostic method to assess the involvement of major salivary glands in primary Sjögren's syndrome (pSS). In the AECG, ACR and recently published ACR-EULAR criteria, a positive salivary gland biopsy and/or presence of anti-SSA antibodies are necessary to classify a patient as pSS, while sUS is not included as a diagnostic item.
Objectives: To assess whether combining anti-SSA antibody status with sUS outcome can predict classification of patients as pSS in our inception cohort study.
Methods: Consecutive outpatients clinically suspected with pSS underwent sUS of the parotid and submandibular glands. Parenchymal echogenicity, homogeneity, hypoechogenic areas, hyperechogenic reflections and clearness of salivary gland border were scored according to the Hocevar scoring system (total score 0–48).[1] Positive sUS was defined as total score ≥15. Patients underwent a diagnostic work up according to the AECG, ACR and ACR-EULAR criteria. We analyzed the predictive value of the combination of anti-SSA antibody status and sUS outcome for classification as pSS or non-pSS. Separate analyses were done considering either i) parotid gland biopsy or ii) labial gland biopsy as an item, when applying these classification criteria.
Results: Anti-SSA antibody status was positive in 53 (51%) patients and sUS was positive in 40 (39%) patients.
When parotid gland biopsy outcome was considered as an item of the criteria, 45 of 97 patients were classified as pSS according to the AECG, 44 of 97 according to the ACR and 52 of 99 according to the ACR-EULAR criteria. The combination of presence of anti-SSA antibodies with positive sUS showed a very high positive predictive value for classification as pSS (94–97%) and the combination of absence of anti-SSA antibodies with negative sUS highly excludes classification (negative predictive value 98–100%).
When labial gland biopsy outcome was considered as an item of the criteria, 49 of 96 patients were classified as pSS according to the AECG, 43 of 93 according to the ACR and 55 of 97 according to the ACR-EULAR criteria. The combination of presence of anti-SSA antibodies with positive sUS showed a high positive predictive value for classification as pSS (94–97%). However, the combination of absence of anti-SSA antibodies with negative sUS did not per se exclude classification (negative predictive value 89–93%).
Conclusions: In our prospective inception cohort study derived from daily clinical practice, the combination of presence of anti-SSA antibodies and positive sUS outcome highly predicts classification as pSS according to the AECG, ACR and ACR-EULAR classification criteria.

References:
[1] Hocevar et al. Rheumatology (Oxford) 2005;44:768–72.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5938

FRI0278 PREVALENCE OF PRIMARY SJÖGREN'S SYNDROME IN A POPULATION-BASED COHORT IN THE UNITED STATES

G. Maciel[1,2], C. Crowson[3], E. Matteson[2], D. Cornec[4,5]. *[1]Maciel Hospital, Montevideo, Uruguay; [2]Rheumatology; [3]Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester Minnesota, United States; [4]Rheumatology, CHRU Brest, Brest, France; [5]Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester Minnesota, United States*

Background: Different studies worldwide reported highly discrepant estimates for the prevalence of primary Sjögren's syndrome (pSS), ranging from 0.01% of the general population to more than 3%. No previous study reported the prevalence of pSS in the United States.
Objectives: To report the 2015 point prevalence of pSS in the first population-based study performed in the U.S.
Methods: Cases of all potential pSS patients living in Olmsted County, Minnesota on January 1, 2015 were retrieved using the Rochester Epidemiology Project resources, and ascertained by manual medical record review. Definite pSS cases were defined according to physician diagnosis. All patients with doubtful cases and all patients with an associated systemic autoimmune disease were excluded. The use of diagnostic tests was assessed and the performance of classification criteria in this community-based cohort was evaluated. The number of prevalent cases in 2015 was also projected based on 1976–2005 incidence data from the same source population.
Results: A total of 106 patients with pSS were included in the study: 86% were female, with a mean (SD) age of 64.6 (15.2) years and disease duration of 10.5 (8.4) years. A majority were anti-SSA positive (75%) and/or anti-SSB positive (58%), but only 22% met American-European Consensus Group or American College of Rheumatology criteria because the other tests required for disease classification were rarely performed in clinical practice (ocular dryness objective assessment, salivary gland functional or morphologic tests, or salivary gland biopsy). According to the physician diagnosis, age and sex adjusted prevalence of pSS was 10.3/10,000 inhabitants, but according to classification criteria this prevalence would be only 2.2/10,000. The analysis based on previous incidence data projected a similar 2015 prevalence rate of 11.0/10,000. Using figures from the 2015 general U.S. population census, a total of 248,000 patients with pSS (35,000 males and 213,000 females) would currently live in the country. If only cases fulfilling classification criteria are considered, there would be only about 53,000 prevalent cases of pSS in the U.S.
Conclusions: This study reports the first prevalence rate of physician-diagnosed pSS in a well-defined population in the U.S. The estimated prevalence of 10.3/10,000 inhabitants in 2015 is higher than previous results obtained in other geographical areas, probably due to different methodological designs of the studies. Because physicians rarely used tests included in the classification criteria to diagnose the disease in this community setting, current classification criteria do not reflect accurately the diagnosis of pSS in routine clinical practice.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1179

FRI0279 PREVALENCE AND FACTORS ASSOCIATED WITH PRECONCEPTIONAL COUNSELING IN WOMEN WITH AUTOIMMUNE RHEUMATIC DISEASES

G. García-Garza[1], M.A. Saavedra[1], D. Miranda-Hernández[1], A. Sánchez[1], G. García-Collinot[2], R. Bustamante-González[1], L.J. Jara[3]. *[1]Rheumatology; [2]Research Division; [3]Education and Research Direction, Hospital de Especialidades, Cmn la Raza, IMSS, México, Mexico*

Background: Adequate prenatal counseling in women with autoimmune rheumatic diseases (ARDs) may help minimize maternal-fetal complications. However, the available information about the frequency and quality of prenatal counseling given to these patients is limited.
Objectives: To estimate the prevalence of preconceptional counseling and associated factors in women with ARDs.
Methods: A survey was conducted on socio-demographic data, gynecological-obstetric history, and domains related to preconception counseling in women with ARDs at the reproductive stage. It was defined as adequate preconception counseling if the patient knew that the pregnancy should be medically planned, that the complications are associated with severity/activity of the disease, that they should use an effective contraceptive method and that their medications may or may not be used during pregnancy. Descriptive statistics, Student's T test for quantitative variables with normal distribution, Mann-Whitney U test for non-normal and chi-square distribution were used for categorical or ordinal variables.
Results: Of a total of 146 surveys, 131 were analyzed. Only 49 (37.4%) patients received adequate preconception counseling. Two thirds of the patients had systemic lupus erythematosus (Table). The time of evolution of the disease was a factor associated with receiving adequate counseling (5.6 vs 3.6 years, p=0.023). Illness, marital status, and level of education were not factors associated with

	Adequate Counseling (n=49)	Inadequate counseling (n=82)	P value
Age (years) [a]	30.8±7.0	30.5±8.5	0.836
Time of evolution (years)[b]	5.6 (0.25–29)	3.6 (0.25–27)	0.023
Previous pregnancies[b]	1 (0–4)	1 (0–5)	0.192
Rheumatoid arthritis[c]	13 (26.5%)	18 (22%)	0.69
Systemic lupus erythematosus[c]	31 (63.3%)	52 (63.4%)	
Use of contraceptive method[c]	31 (63.3%)	44 (53.7%)	0.282
Use of embryotoxic/teratogenic drugs[c]	39 (79.6%)	34 (41.5%)	0.001
Counseling for a rheumatologist[c]	37 (75.5%)	28 (34.1%)	0.001
Counseling by other doctors[c]	35 (24.5%)	31 (65.9%)	0.197
Professional education[c]	23 (46.9%)	31 (37.8%)	0.616
Married[c]	15 (30.6%)	32 (39%)	0.774

[a]Student's t-test; [b]U of Mann Whitney; [c]Chi square.

adequate counseling. The adoption of a contraceptive method and the number of pregnancies were not different between the two groups. The history of use of embryotoxic/teratogenic drugs was associated with a higher frequency of adequate counseling (79.6% vs 41.5%, p=0.001). According to the patients, adequate counseling was given by the rheumatologist in 75.5% of the cases (p=0.001).
Conclusions: Adequate preconceptional counseling in our patients with ARDs at the reproductive stage is deficient. A multidisciplinary strategy is required to improve the frequency and quality of preconception counseling in patients with ARDs.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6475

FRI0280 ASSOCIATION BETWEEN INSULIN RESISTANCE, SUBCLINICAL ATHEROSCLEROSIS AND ACTIVITY/DAMAGE STATUS IN SLE PATIENTS

H. Sánchez-Pérez[1], B. Tejera Segura[1], M.A. Gonzalez-Gay[2], I. Ferraz-Amaro[1]. *[1]Rheumatology, Hospital Universitario de Canarias, la Laguna; [2]Rheumatology, Hospital Marques de Valdecilla, Santander, Spain*

Background: Insulin resistance (IR) may contribute to an increase in cardiovascular risk in general population as well as in Systemic Lupus Erythematosus (SLE) patients.
Objectives: The aim of this study was to examine the association between IR and disease activity, disease characteristics, drug exposure and subclinical atherosclerosis in patients with SLE.
Methods: Cross-sectional study that encompassed 87 SLE patients and 82 sex-matched controls. IR by homeostatic model assessment (HOMA2), insulin, C-peptide serum levels and lipid profile were assessed in both groups. Activity (SLEDAI), severity (Katz) and damage (SLICC) scores, carotid intima-media thickness (cIMT) and carotid plaques (ultrasound) were assessed in SLE patients. A multivariable regression analysis, adjusted for IR related factors, was performed to evaluate the differences between groups in IR indexes and, in SLE patients, the interrelation between IR and disease activity/characteristics as well as subclinical atherosclerosis.
Results: Median disease duration was 16 years (IQR 9–21). Body mass index, abdominal circumference, hypertension or dyslipidemia did not differ between groups. According to the SLEDAI score, 40% of patients were in no activity, while 32, 21, 18 and 1% were in mild, moderate, high and very high activity respectively. HOMA-IR-C-peptide (beta coefficiente 0.53, [95% CI 0.25–0.82], p=0.00) was increased in SLE patients when compared to controls, as well as HOMA %B C peptide levels (beta coef. 35, 95% CI 18–52, p=0.00). Similarly, insulin sensitivity estimated through HOMA-S% was inferior in SLE patients (-beta coef. -37, 95% CI -63–11, p=0.01).This diferences remained significant even after adjustment for IR related factors.
SLICC damage index was clearly asociated with IR indexes; higher index values were related to higher HOMA-IR-C-peptide (beta coef. 37, [95% CI 16–57], p=0.00) and lower HOMA-S% levels (beta coef. 30%, [95% CI -47–14], p=0.00). Katz severity index showed correlation with HOMA-IR-C-peptide (beta coef.-5, [95% CI -11–0], p=0.04). These associations remained significant after adjustment for age, gender, smoking, hypertension and dyslipidemia, and, in relation with the SLICC index, also after adjustment for prednisone intake. SLEDAI activity index was not related to IR indexes.
The use of prednisone was positively associated with HOMA-IR both when considered binary (beta coef 47, [95% CI 31–63], p=0.00) and continous (beta coef 2 [95% CI 0–5] per mg, p=0.03). Hydroxycloroquine (or other drugs) use was not associated with IR indexes, neither were disease duration, antiDNA titers and complement serum levels.
Carotid plaques were found in 20% of the SLE patients. The presence of carotid plaques was correlated with a higher HOMA-IR-C-peptide (OR 3.15 [95% IC 1.17–8.51], p=0.02), and a higher cIMT value was associated with a lower HOMA-IR-S%>C-peptide (beta coef. 0.98 [95% CI 0.96–0.99], p=0.03). Nevertheless, after adjustment for cardiovascular risk factors this relation was lost.
Conclusions: Activity and damage indexes in SLE patients are independently related to the development of IR. IR is associated with subclinical carotid atherosclerosis in SLE patients on the univariate analysis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2367

FRI0281 UTILITY OF MORNING SAMPLE OF URINE PROTEIN/CREATININE RATIO FOR ASSESSMENT OF PROTEINURIA IN PATIENTS WITH LUPUS NEPHRITIS

H. Zhang, J. Liang, B. Hua, L. Sun. *Department of Rheumatology and Immunology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China*

Background: Proteinuria is the principal urinary biomarker for the screening of Lupus nephritis (LN) and for monitoring disease progression. 24-hour urine collection has been the foundation for monitoring disease activity in patients with LN, but collections are often inaccurate and inconvenient. The European League Against Rheumatism and American College of Rheumatology have recommended the urine protein/creatinine ratio (UPCR) for use in management of LN.
Objectives: We aimed to evaluate the diagnostic accuracy of the morning sample of UPCR compared with 24-hour urine collection for the detection of proteinuria and to determine the UPCR for different proteinuria ranges in patients with LN.
Methods: Three hundred and thirty seven LN patients were enrolled. The correlation between the UPCR in the morning spot urine samples and urinary protein excretion in the 24-hour collections was examined using the Pearson correlation test. The best cutoffs for UPCR predicting a 24-hour protein excretion were determined with the receiver operating characteristic curve (ROC).
Results: It was found a good positive correlation between the UPCR and 24-hour protein excretion, with a correlation coefficient (r) of 0.891 (Fig 1). The best cutoff which gave the maximum area under the curve was 0.44 for 0.5 g, 0.92 for 1.0 g, 2.21 for 2.0 g, 2.70 for 3.0 g, 3.49 for 4.0 g and 4.59 for 5.0g.

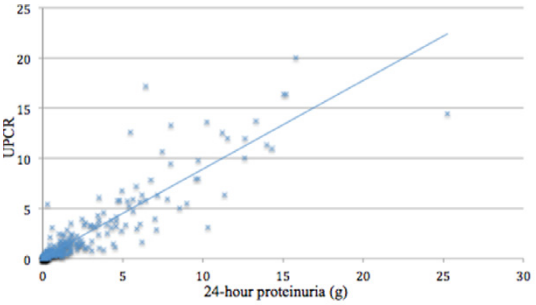


Fig. 1 Scatterplot of correlation between protein content in a 24-hour urine collection sample and morning sample of UPCR

Conclusions: The UPCR can be used as a screening test as a good predictor for proteinuria of LN patients. Also, UPCR is a valuable tool with which to monitor disease progression.
References:
[1] Bertsias GK, Tektonidou M, Amoura Z, et al. Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis. Ann Rheum Dis 2012; 71: 1771–82.
[2] Renal Disease Subcommittee of the American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus Response Criteria. The American College of Rheumatology response criteria for proliferative and membranous renal disease in systemic lupus erythematosus clinical trials. Arthritis Rheum 2006; 54: 421–32.
[3] Medina-Rosas J, Yap KS, Anderson M, et al. Utility of Urinary Protein-Creatinine Ratio and Protein Content in a 24-Hour Urine Collection in Systemic Lupus Erythematosus: A Systematic Review and Meta-Analysis. Arthritis Care Res (Hoboken) 2016; 68: 1310–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5324

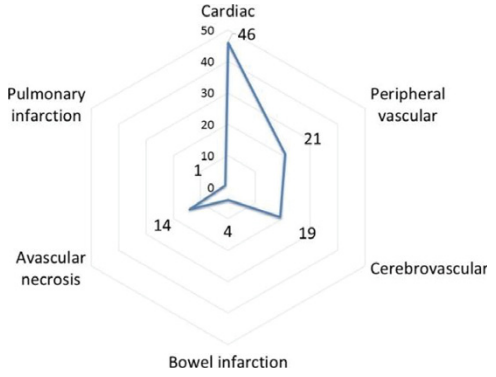
FRI0282 CARDIOVASCULAR DAMAGE IN DECEASED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

I. Padjen[1,2], M. Erceg[3], M. Cerovec[1,2], M. Mayer[1,2], R. Stevanović[3], B. Anić[1,2]. *[1]Department of Internal Medicine, Division of Clinical Immunology and Rheumatology, University Hospital Centre Zagreb; [2]University of Zagreb, School of Medicine; [3]Croatian Institute of Public Health, Zagreb, Croatia*

Background: Cardiovascular comorbidities are a major contributor of damage in patients with SLE. They are driven by classical, as well as SLE-related risk factors, i.e. disease activity and immunosuppressive treatment.
Objectives: We aimed to analyze cardiovascular damage (CVD) in a group of 90 deceased SLE patients regularly followed-up in a routine academic setting at our Department, and to identify features associated with accrual of CVD.
Methods: We retrospectively observed 90 SLE patients (68 females) deceased within the 2002–2011 period. All patients were ≥18 years of age and Croatian residents at the time of death, fulfilling ≥4 classification criteria of the American College of Rheumatology (ACR). We identified patients with CVD, including the following components of the Systemic Lupus International Collaborating Clinics (SLICC)/ACR damage index: cardiovascular damage as defined by the index (cardiac damage), peripheral vascular damage, cerebrovascular accident, pulmonary infarction, bowel infarction and avascular necrosis. An extensive set of variables was compared between patients with and without CVD: demographics, ACR criteria at diagnosis and death, damage (according to the SLICC/ACR index) and its components one year following diagnosis and at the time of death, disease activity at diagnosis (according to the European Consensus Lupus Activity Measurements index, ECLAM), as well as features of the metabolic syndrome, smoking and immunosuppressive treatment. Frequencies were compared using the χ^2 and Fisher's exact test, and continuous variables using the t-test and Mann-Whitney U test. Variables associated with CVD in the univariate analysis were included in a multivariate logistic regression model.
Results: We identified 63/90 patients with CVD, including 46/63 (73%) with cardiac damage, 19/63 (30%) with peripheral vascular damage, 21/63 (33%)

with cerebrovascular accident, 4/63 (6%) with bowel infarction, 14/63 (22%) with avascular necrosis and a single patient with pulmonary infarction (Figure 1). Patients with CVD had a higher disease duration at time of death compared to patients without CVD (12±8 vs. 7±6 years), as well as higher cumulative proportions of hematologic disorder (60/63 vs. 15/27), lymphopenia (48/63 vs. 10/27), pulmonary damage (19/63 vs. 1/27), fractures (25/63 vs. 2/27), higher overall damage (6.0±3.0 vs. 2.4±2.0) and a higher proportion of secondary antiphospholipid syndrome (14/63 vs. 1/27) ($p<0.05$). Conversely, patients with CVD had a lower proportion of discoid lupus at diagnosis (7/49 vs. 9/24) and a lower proportion of skin damage one year following diagnosis (2/63 vs. 5/27) ($p<0.05$). Parameters associated with cardiovascular damage in the multivariate model were cumulative fulfillment of lymphopenia as a classification criterion (odds ratio, OR 4.7 (95% confidence interval, CI 1.3–17.0)) and accrual of pulmonary damage (OR 13.1 (95% CI 2.2–76.3)).

Figure 1. Distribution of cardiovascular damage in the analyzed group (numbers represent frequencies of each subtype of cardiovascular damage)



Conclusions: More than two thirds of deceased patients accrued CVD over the disease course. Lymphopenia and pulmonary damage may be associated with CVD in deceased SLE patients.

References:

[1] Vila LM et al. Arthritis Rheum 2006;55:799–806.
[2] Becker-Merok A and Nossent JC. Lupus 2009;18:508–15.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5197

FRI0283 AN IMMUNOLOGICAL PROFILE COMBINING INNATE AND ADAPTATIVE IMMUNITY BIOMARKERS IDENTIFY RISK FOR EVOLUTION INTO SLE IN WOMEN WITH RECURRENT PREGNANCY LOSS

J. Carbone, E. Sarmiento, J.P. Navarro, E. Fernandez-Cruz. *Clinical Immunology, Hospital General Universitario Gregorio Marañon, Madrid, Spain*

Background: Autoantibodies, low complement levels and higher NK cell counts are present in a subset of women with recurrent pregnancy loss (RPL). The combination of these abnormalities might be a surrogate profile for the presence of a subclinical inflammatory or autoimmune condition.

Objectives: In a cohort of women with unexplained RPL we evaluated if an immunological profile combining innate and adaptive immunity mediators was associated with the presence of distinct clinical characteristics that are commonly observed in autoimmune diseases and if it was a risk factor for developing these diseases. In a small subset of women with the immunological profile we evaluated the activation status of CD4+ and CD8+ cells.

Methods: We evaluated 366 women with RPL defined as 2 or more pregnancy losses and 93 control women. We defined the immune profile as the presence of 2 or more of the following abnormalities: Peripheral blood NK cell percentages >15%, positive antiphospholipid antibodies, positive antinuclear antibodies, positive anti-thyroid antibodies, low complement C3 levels and low C4 complement levels. Evolution to autoimmune diseases was detected during follow-up. Lymphocyte subsets were evaluated by flow-cytometry. Statistics: Chi-square test. Logistic regression.

Results: The prevalence of women with 2 or more immunological abnormalities was 57 out of 366 women (15.6%) and was significantly higher than in control women. Demographic clinical characteristics were similar in women with 2 or more immunological abnormalities as compared with women with only one immunological alteration or no abnormalities. The presence of the immunological profile was significantly associated with the presence of the following clinical characteristics: Leucopenia (p=0.048), lymphopenia (p=0.007), livedo reticularis (p=0.01), cutaneous rash (p=0.009), and arthritis (p=0.001). During follow-up 17 patients (4.6%) developed an inflammatory or autoimmune disease that was not present at the time of the diagnose of RPL including SLE and lupus like disease. Women with the immunological profile were at higher risk for evolution into these diseases: OR 4.19, 95% confidence interval 1.52–11.51, p=0.0055. In 10 women with the immunological profile we observed significantly higher levels of CD4+DR+ and CD8+DR+ T-cells as compared with women without the immune profile.

Conclusions: A subgroup of women with unexplained RPL are at risk of developing clinical characteristics of an inflammatory or autoimmune disease. In this regard, the immunological evaluation of women with RPL might be necessary not only to identify a potential cause of abortion but also to identify women that could require a more careful clinical follow-up. Higher CD4+DR+ and CD8+DR+ T-cells might be a pathogenic pathway leading to development of autoimmune diseases in RPL women.

References:

[1] Viallard JF, Bloch-Michel C, Neau-Cransac M, Taupin JL, Garrigue S, Miossec V, Mercie P, Pellegrin JL, Moreau JF. HLA-DR expression on lymphocyte subsets as a marker of disease activity in patients with systemic lupus erythematosus. Clin Exp Immunol. 2001;125(3):485–91.
[2] CD8+DR+ T-Cells and C3 Complement Serum Concentration as Potential Biomarkers in Thrombotic Antiphospholipid Syndrome. Sarmiento E, Dale J, Arraya M, Gallego A, Lanio N, Navarro J, Carbone J. Autoimmune Dis. 2014.

Acknowledgements: Research Funds. Fundacion Salud 2000. Madrid Spain.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6003

FRI0284 PREDICTORS OF ARTERIAL VASCULAR EVENTS IN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS

J.-G. Erdozain[1], I. Villar[2], J. Nieto[2], I. Ruiz-Arruza[1], J.-I. Pijoan[3], G. Ruiz-Irastorza[1]. *[1]Unidad de Investigacion de Enfermedades Autoinmunes-Servicio de Medicina Interna. BioCruces Health Research Institute. Universidad del País Vasco/Euskal Herriko Unibertsitatea; [2]Servicio de Medicina Interna; [3]Unidad de Investigación. Unidad de Epidemiología Clínica y Soporte Metodológico. BioCruces Health Research Institute., Hospital Universitario de Cruces, Barakaldo-Vizcaya, Spain*

Background: Arterial vascular events (AVE) are among the major causes of morbidity and mortality in patients with Systemic Lupus Erythematosus (SLE). Several studies have been carried out to identify the main factors related to AVE in this population. The ankle brachial index (ABI) is one of the tools currently used to identify patients at greater risk of arterial events in the general population; however it has been scarcely studied in patients with SLE.

Objectives: The objectives of this prospective cohort study were to determine the predictive value of the ABI for occurrence of AVE in patients with SLE and to identify other possible factors associated with an increased risk of AVE.

Methods: 216 patients with SLE were evaluated using an ABI and followed up for 5 years. Pathological ABI is considered an ABI <0.9. Different potential vascular risk factors (traditional, non-traditional and related to SLE and/or the treatments used) were jointly evaluated. AVE: coronary events (angina pectoris, acute myocardial infarction, coronary revascularization by angioplasty or surgery), cerebrovascular events (transient ischemic attack, cerebrovascular accident), peripheral arterial disease (symptomatic intermittent claudication, distal ischemia, revascularization by angioplasty or surgery), and death related to vascular disease. Survival analysis was performed using a competitive risk regression approach, considering non-vascular death as a competitive event, to identify the predictive value of ABI and other factors studied. The Ethical Committee for Clinical Research at Cruces University Hospital approved the study protocol in accordance with the Declaration of Helsinki (CEIC E09/07). All patients signed an informed consent at the time of entry into the study.

Results: During follow-up, 4/216 (1.8%) patients were lost to follow-up. 18 AVE were identified in 17 patients, with one patient having 2 episodes of angina requiring angioplasty (4 coronary events, 11 cerebrovascular events, 2 peripheral arterial disease events and 1 sudden death) and 14 deaths (6 per AVE or their sequelae, 4 due to neoplasias and 4 due to cardio-respiratory pathology). In the competitive risk regression analysis, independent predictors of higher risk of AVE were identified: pathological ABI (subhazard ratio (SHR) 3.51, 95% confidence interval 0.96–12.79, p=0.057), family history of AVE (SHR 6.3, 95% CI 1.97–20.21, p=0.002), cumulative total prednisone (grams) (SHR 1.02, 95% CI 1.01–1.04, p=0.004) and a history of arterial thrombosis (SHR 4.60, 95% CI 1.45–14,59, p=0.010).Female gender was a protective factor for the occurrence of AVE (SHR 0.12, 95% CI 0.04–0.40, $p<0.0001$).

Conclusions: Being male, having a higher cumulative dose of prednisone, having a family history of early vascular disease and having suffered previous arterial thrombosis are independent risk predictors of an AVE in patients with SLE. Having abnormal ABI, even without statistical significance, showed a marked tendency to increase this risk despite the low number of events recorded in the studied cohort.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3013

FRI0285 LUPUS NEPHRITIS IS ASSOCIATED WITH INCREASED RATES OF HOSPITALIZATION AND IN-HOSPITAL MORTALITY COMPARED WITH NON-RENAL LUPUS AND MATCHED CONTROLS: AN ANALYSIS OF INSURANCE CLAIMS DATA

K.A. Belendiuk, H. Trinh, M.D. Cascino, L. Dragone, D. Keebler, J. Garg. *Genentech, Inc., South San Francisco, CA, United States*

Background: Systemic lupus erythematosus (SLE) is heterogeneous in its clinical presentation, course, and prognosis and lupus nephritis (LN) continues

to be a major cause of morbidity and mortality among children and adults with SLE. Up to 60% of adult and 80% of pediatric SLE patients (pts) will eventually develop overt renal disease [1]. To date the excess burden of comorbidities, risk of inpatient hospitalization, and in-hospital death associated with SLE and LN remains incompletely understood.

Objectives: To identify differences in comorbidities, hospitalizations, and in-hospital mortality of SLE and LN cohorts compared to: 1) each other; 2) reference populations of pts without an autoimmune condition (non-AI) matched on gender and age. Reference populations were allowed to have claims for non-autoimmune conditions.

Methods: We conducted a retrospective cohort study using the Truven Healthcare MarketScan® Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefits database, which together comprise 65 million insured US lives between 1999 and 2014. Cohort identification is based on validated algorithms [2, 3] for identification of pts with either LN or SLE without renal involvement using claims data. Pts were matched on age and gender at index date. All eligible participants had 365 days of enrollment prior to and after the index date. End of study for post-index follow-up was captured as whichever of the following occurred first: 1) end of enrollment; 2) end of database; 3) date of death. Results are presented separately for pediatric and adult pts.

Results: 54,813 SLE pts without renal involvement and 8,839 LN pts were identified and matched to reference non AI populations. Compared to the non-renal SLE cohort, pts in the LN cohort were older (49.9±16.6 vs. 48.6±14.3 years) with a higher proportion of males (15.4% vs. 11.2%). Pts with LN had the highest scores on the Charlson Comorbidity Index modified to exclude renal involvement (Table 1). Additionally, adults with LN had higher rates of hospitalizations and longer hospitalizations compared with adults with non-renal SLE, who already had higher rates of hospitalizations and longer hospitalizations than matched controls (Table 2). This pattern of findings was consistent for children. Rates of in-hospital mortality were highest among those with LN but also increased among those with SLE compared with matched controls (Figure 1).

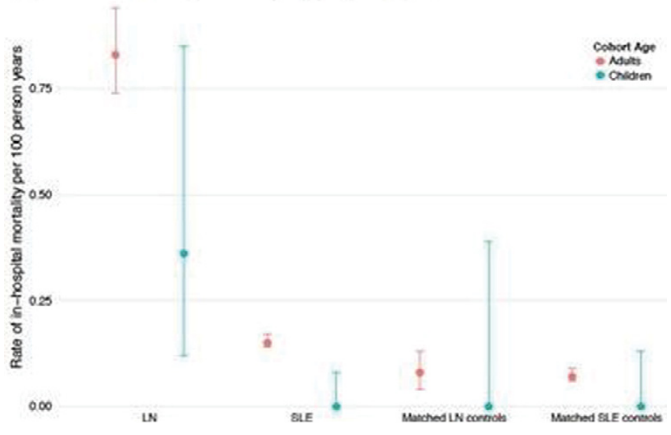
Table 1. Comorbidities on the Charlson Comorbidity Index.

	LN N=8466		non-renal SLE N=53597		non-AI matched controls (LN) N=8466		non-AI matched controls (non-renal SLE) N=53597	
	Mean (Std)	Median (IQR)	Mean (Std)	Median (IQR)	Mean (Std)	Median (IQR)	Mean (Std)	Median (IQR)
Enrollment Duration (days)	1709.5 (887.11)	1442 (1076)	1715.1 (926.53)	1422 (1101)	1195.5 (650.23)	979 (437)	1224.9 (692.48)	988 (464)
Charlson Comorbidity Index								
Baseline	1.5 (1.54)	1 (2)	0.8 (1.24)	0 (1)	0.3 (0.87)	0 (0)	0.3 (0.80)	0 (0)
Follow-Up	5.0 (2.68)	4 (3)	2.6 (2.16)	2 (2)	0.6 (1.34)	0 (1)	0.5 (1.21)	0 (1)
Charlson Comorbidity Index Excluding Renal Diseases								
Baseline	1.3 (1.46)	1 (2)	0.8 (1.19)	0 (1)	0.3 (0.83)	0 (0)	0.3 (0.77)	0 (0)
Follow-Up	3.8 (2.64)	3 (3)	2.5 (2.03)	2 (2)	0.6 (1.27)	0 (0)	0.5 (1.16)	0 (1)

Table 2. Hospitalizations and mortality by age and patient population.

		Children (<18)				Adults (>18)			
		LN N=573	non-renal SLE N=1216	non-AI matched controls (LN) N=573	non-AI matched controls (non-renal SLE) N=1216	LN N=8466	non-renal SLE N=53597	non-AI matched controls (LN) N=8466	non-AI matched controls (non renal SLE) N=53597
Overall risk of hospitalization	Number of patients hospitalized; n(%)	268 (71.85%)	335 (27.55%)	14 (3.75%)	53 (4.36%)	5645 (66.68%)	19172 (35.77%)	1030 (12.17%)	6326 (11.80%)
	Sum of Person-Years for Hospitalization	483.69	3493.28	918.96	2867.38	14761.14	142359.65	17569.43	115370.4
	Incidence Rate (Per 100 Person-Years) for Hospitalization (95% CI)	55.41 (48.97, 62.45)	9.59 (8.69, 10.67)	1.52 (0.83, 2.56)	1.85 (1.39, 2.42)	38.24 (37.25, 39.25)	13.47 (13.28, 13.66)	5.86 (5.51, 6.23)	5.48 (5.35, 5.62)
Total days in hospital	Mean (SD)	19.9 (28.20)	11.1 (18.36)	5.2 (7.24)	5.4 (6.42)	23.0 (35.97)	10.1 (16.15)	5.3 (7.54)	5.0 (6.42)
	Median (IQR)	10 (18)	5 (9)	3 (4)	3 (3)	11 (21)	5 (8)	3 (3)	3 (3)
	Min - Max	1 - 214	1 - 142	1 - 29	1 - 53	1 - 880	1 - 626	1 - 104	1 - 153
Overall risk of mortality	Number of patients with in-hospital mortality; n (%)	5 (1.34%)	0	0	0	260 (3.07%)	304 (0.57%)	15 (0.18%)	88 (0.16%)
	Sum of Person-Years for in-hospital mortality	1380.44	4409.72	942.64	2950.59	31192.18	198473.39	19192.98	126335.39
	Incidence Rate (Per 100 Person-Years) for in- hospital Mortality (95% CI)	0.36 (0.12, 0.85)	0 (, 0.08)	0 (, 0.39)	0 (, 0.13)	0.83 (0.74, 0.94)	0.15 (0.14, 0.17)	0.08 (0.04, 0.13)	0.07 (0.06, 0.09)

Figure 1: Rates of in−hospital mortality by group and age



Conclusions: An SLE diagnosis was associated with a higher burden of comorbidities and higher rates of hospitalizations and in-hospital mortality than non-AI matched controls. Pts with LN had the highest burden of comorbidities and rates of hospitalizations and in-hospital mortality. SLE and LN impose a high burden of morbidity and mortality and the medical need for safe and effective treatments of LN and SLE remains unmet. Clinicians should consider these factors in their assessment and treatment of pts with SLE and LN. The retrospective, claims-based results do not permit pt-level assessment of the relative contributions of disease, treatment, and potential confounders to these findings.

References:

[1] Cameron JS. J Am Soc Nephrol, 1999;10:413–24.
[2] Arkema EV et al. BMJ open, 2016;6:e007769.
[3] Chibnik LB et al. Lupus, 2010;19:741–3.

Disclosure of Interest: K. Belendiuk Employee of: Genentech, Inc., H. Trinh Employee of: Genentech, Inc., M. Cascino Employee of: Genentech, Inc., L. Dragone Employee of: Genentech, Inc., D. Keebler Employee of: Genentech, Inc., J. Garg Employee of: Genentech, Inc.

DOI: 10.1136/annrheumdis-2017-eular.5526

FRI0286 SEROLOGICAL EVOLUTION IN PATIENTS WITH THROMBOTIC ANTIPHOSPHOLIPID SYNDROME

L. Riancho-Zarrabeitia[1], S. García-Canale[1], M. Cubería[1], G. Daroca[1], M. Agudo[1], M. López-Hoyos[2], P. Muñoz[1], V. Martínez-Taboada[3]. *[1]Hospital Universitario Marqués de Valdecilla, Santander, Spain; [2]Immunology; [3]Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain*

Background: Antiphospholipid syndrome (APS) is an autoinmune disease characterized by the presence of antiphospholipid antibodies (aPL) and at least one clinical event (thrombosis and /or pregnancy morbidities). The titers of aPL can fluctuate and eventually become negative. This negativization, particularly if persistent, may be associated with a lower frequency of clinical events.

Objectives: To describe the clinical and serological course of patients with thrombotic APS as well as the factors related with the aPL negativization

Methods: We performed a retrospective study including patients attended at the Rheumatology clinic from a tertiary hospital in Northern Spain. We included 94 patients with thrombotic APS according to Sidney criteria of 2006. They were classified according to the serological evolution as persistently negative aPL, transiently positive, and persistently positive aPL according to previously established criteria.

Results: After a mean follow-up of 145±56 months, 48.9% of patients presented a persistently negative serology, whereas in 12.8% it was transiently positive, and persistently positive in 38.3%. When analyzing potential factors related to the negativization (table 1), we found that patients with positive lupus anticoagulant tended to have a persistently negative serology during follow-up, but it did not reach statistical significance (OR 2.7; 95% CI 0.8–9.4; p=0.145). We found no association between traditional cardiovascular risk factors or previous treatments and the serological evolution.

Variable	Total	Persistently negative (n=46)	Persistently positive and transiently positive (n=48)	P
Age	45±16	44±14	47±17	0.33
Male sex, n (%)	19 (21)	8 (18)	11 (24)	0.61
SLE, n (%)	25 (27)	12 (26)	13 (27)	1
Load of antibodies, n (%)		0.94		
1	29 (31)	15 (33)	14 (29)	
2	40 (43)	19 (41)	21 (44)	
3	25 (27)	12 (26)	13 (27)	
Anticardiolipin antibodies, n (%)	76 (81)	36 (78)	40 (83)	0.60
Antiβ2-GlycoproteinI antibodies, n (%)	59 (63)	27 (59)	32 (67)	0.52
Lupus anticoagulant, n (%)	35 (66)	18 (78)	17 (57)	0.14
Family history of thrombosis, n (%)	17 (31)	10 (40)	7 (24)	0.25
Tobacco use, n (%)	41 (44)	21 (46)	20 (42)	0.83
Hypertension, n (%)	45 (48)	21 (46)	24 (50)	0.69
Dyslipidemia, n (%)	43 (46)	21 (46)	22 (46)	1
Diabetes, n (%)	4 (4)	2 (4)	2 (4)	1
Antimalarials, n (%)	34 (36)	16 (35)	18 (37)	0.83
Heparin, n (%)	34 (36)	16 (35)	18 (37)	0.83
Oral anticoagulants, n (%)	68 (72)	33 (72)	35 (73)	1
Antiplatelets, n (%)	71 (76)	33 (73)	38 (79)	0.63
Corticosteroids, n (%)	5 (5)	2 (4)	3 (6)	1
Immunosuppressants, n (%)	4 (4)	1 (2)	3 (6)	0.36

Conclusions: After a mean follow-up of 12 years, 49% of thrombotic APS patients presented a persistently negative serology. We found no significant association between immunological, traditional cardiovascular risk factors or previous treatments and the persistently negative serology.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5106

FRI0287 INCIDENCE OF LUPUS NEPHRITIS AND 18-MONTH FOLLOW UP IN COLOMBIAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

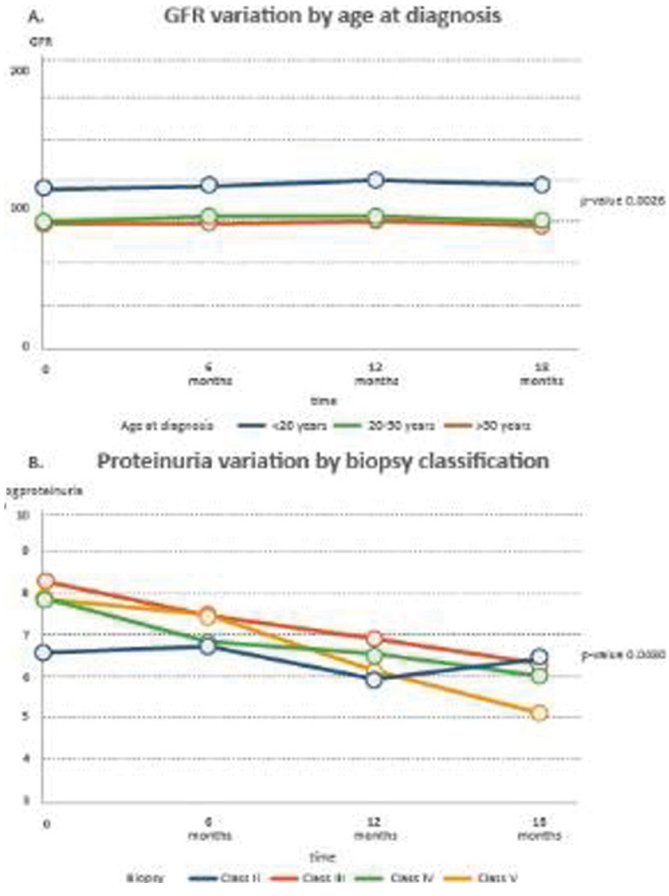
M.A. Alzate[1], D. Hernandez-Parra[1], J.C. Salazar-Uribe[2], P. Ortiz-Salazar[1], R. Pineda[1] on behalf of Artmedica IPS, Medellin, Colombia. *[1]Clinical information group, Artmedica IPS; [2]School of Statistics, Faculty of Sciences, National University of Colombia, Medellin, Colombia*

Background: Lupus nephritis (LN) is one of the major indicators of poor prognosis in patients with systemic lupus erythematosus (SLE). Multiple studies with Latin-

American SLE population have shown a higher prevalence of LN, higher severity, and less favorable outcomes (1).
Objectives: To determine the incidence of lupus nephritis and end-stage renal failure, as well as evaluate progression of renal function and proteinuria during an 18-month follow up in colombian patients with SLE.
Methods: A retrospective cohort study was conducted in 1448 patients with SLE, 41 of which were diagnosed with LN between August/2014 and July/2015. Follow up was made for 18 months, analyzing glomerular filtration rate (GFR) and proteinuria, induction and manteinance therapy, renal relapses, hospitalizations and mortality. Univariate analysis was done to describe sociodemographic and clinical variables. Longitudinal data analysis was performed using linear mixed models with random intercepts. In all cases, a p value <0.05 was considered statistically significant.
Results: Clinical characteristics of patients with LN are shown in table 1. Eighty-five percent of LNs where biopsy-proven. Incidence of LN was 2,83 cases/100 SLE patients/year. The incidence of end-stage renal failure was 7,31 cases/100 LN patients. During the 18-month follow up, 34% of patients had hospitalizations related to SLE activity or complications, 7,3% renal relapse, 2,4% rebiopsy, and no mortality cases. Induction therapy was done with cyclophosphamide in 58,5% and with mycophenolate mofetil in 41,4%, with 30% of the patients requiring re-induction therapy, Ten percent of patients required use of rituximab due to refractory response to multiple treatments. In longitudinal linear analyses, age at diagnosis and anti dsDNA was positively associated to GFR variations (Figure 1,A), while anti Sm, hematologic involvement and biopsy classification were associated to proteinuria variations during time of follow-up (Figure 1,B).
Conclusions: In a real life scenario, anual incidence of lupus nephritis was 2,83 cases/100 SLE patients. A high proportion of patients with refractory response to multiple immunomodulatory treatments for LN were identified.

Table 1. Clinical characteristics of patients with lupus nephritis

Characteristic (N=41)	Mean (SD)
Age	37,2 (11,2)
Age at diagnosis	32,2 (11,1)
Years of evolution	4,6 (4,4)
	N (%)
Female	38 (92,7)
Malar rash	11 (28,2)
Discoid lupus	2 (4,9)
Photosensitivity	18 (46,1)
Oral ulcers	14 (34,1)
Serositis	16 (44,4)
Arthritis	31 (75,6)
Neurological involvement	5 (12,2)
Hematological involvement	32 (78)
ANAs (+)	39/39 (100)
Anti dsDNA (+)	29/41 (70,7)
Anti Sm (+)	17/35 (48,6)
Anti Ro (+)	19/36 (52,7)
Anti La (+)	10/34 (29,4)
Anti RNP (+)	18/36 (50)



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6137

FRI0288 NAILFOLD CAPILLAROSCOPIC PICTURES IN A COHORT OF UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE (UCTD) PATIENTS AND IN THOSE THAT MOVE TO SYSTEMIC LUPUS ERYTHEMATOSUS

M. Meroni[1,2], C. Pizzorni[1], A. Sulli[1], M. Limonta[2], M. Cutolo[1]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Internal Medicine Dept., University of Genova, Genova; [2]Rheumatology Unit, ASST Papa Giovanni XXIII, Bergamo, Italy*

Background: Nailfold capillaroscopy (NVC) is a useful, non-invasive, reproducible and cost-effective diagnostic tool, able to assess the shape of capillaries in the nailfold bed. According to the presence of peculiar abnormalities, it is essential in the early differential diagnosis of connective tissue diseases (CTDs), mainly "scleroderma-spectrum disorders" (SSD). Despite its large diffusion, no univocal NVC patterns have been ascribed to undifferentiated connective tissue disease (UCTD) as well as to systemic lupus erythematosus (SLE).
Objectives: The aim of the study was to evaluate the most common NVC pictures in a population of UCTD patients and if selected NVC pictures might be linked to SLE onset in these patients.
Methods: We evaluated a cohort of 42 UCTD-affected women, diagnosed according to 2014 criteria proposed by Mosca et al. (age, 38 years±46 months; duration of disease, 71±54 months) presenting Raynaud's phenomenon. During the observational period (3 years), all of the UCTD patients were evaluated every 6 months. We considered the following NVC parameters/pictures: presence of ectasic capillary loops (diameter $\geq$20 μm); giant capillaries (diameter $\geq$50 μm); hemosiderin deposits/microhemorrages; capillary number reduction; meandering capillaries (tortuosity); elongated capillaries; ramified/bushy capillaries; micro-vascular array disorganization. SLE diagnosis was posed according to the 2012 SLICC/ACR criteria. Qualitative variables were expressed in frequencies; their association, by non-parametric tests; quantitative variables, by analysis of co-variance.
Results: Non-specific NVC alterations (for instance, not suggestive of SDD) were detected in 40 (98%) of the UCTD patients during the observational period. On the other hands, the presence of hemosiderin deposits, ectasic loops, elongated and ramified capillaries was found associated to the clinical subgroup of UCTD patients that later developed SLE (4/42 subjects, 10%; OR=10.5). In particular, the independent variables "hemosiderin deposits/microhemorrages" (OR=8.32) and "elongated capillaries" (OR 6.28), were found significantly linked to the SLE onset ($p<0.05$), whereas the independent variables "tortuosity" (OR=12.16) and "ramified/bushy capillaries" (OR 9.47) were, at the opposite, predictive for the prosecution of the status of UCTD patient ($p<0.05$).
Conclusions: The present study reports NVC pictures that can be more frequently observed in UCTD patients that include "tortuosity" and "ramified/bushy capillaries". In addition, the NVC analysis suggests the presence of typical capillaroscopic microvascular abnormalities, "hemosiderin deposits/microhemorrages" and "elongated capillaries", that more frequently seem observed in those UCTD patients that move to SLE onset.

References:
[1] Hughes M et al. Best Pract Res Clin Rheumatol. 2016;30:112–32.
[2] Ingegnoli F, et al. J Clin Rheumatol. 2005;11(6):295–8.
[3] Mosca M, et al. J Autoimmun. 2014;48–9:50–2.
[4] Cutolo M et al. Best Pract Res Clin Rheumatol. 2005;19(3):437–52.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5742

FRI0289 CEREBROVASCULAR DISEASE IN THE ANTIPHOSPHOLIPID SYNDROME

M. Estévez, A. Argibay, L. Rodriguez, M. Freire, B. Gimena, J. Fernández-Martín, A. Rivera. *Systemic Autoimmune diseases and Thrombosis Unit, University Hospital Complex of Vigo, Vigo, Spain*

Background: Antiphospholipid syndrome (APS) is a thrombophilic disorder characterized by recurrent arterial and venous thrombosis, and also pregnancy losses associated to antiphospholipid antibodies (APA). Cerebrovascular disease (CVD) is the most common and severe arterial thrombotic manifestation in patients with APS.
Objectives: 1.To determine the prevalence and the type of CVD in patients with APS. 2.To compare the recurrent strokes, affected brain areas, hospitalization, treatment and mortality between patients with CVD, with and without APS.

Abstract FRI0289 – Tabe 1

	Age	OAC	APT	Vascular risk factors	Valvular disease	Brain stem	Frontal lobe	Strokes (≥2)	Mortality	Follow-up
CVD with APS	57,48±21,52	48%	20%	80%	20%	0%	12%	44%	40%	8,64±6,72
CVD without APS	61,16±20,6	0%	72%	68%	0%	20%	36%	16%	44%	2,04±2,99
	p 0,76	p<001	p<001	p 0,33	p 0,02	p0,02	p 0,04	p 0,03	p 0,77	p<001

Methods: Retrospective and, descriptive study of patients with APS (Sidney criteria) and CVD followed for a long period of time in a specific Systemic Autoimmune Diseases and Thrombosis Unit. Subsequently, retrospective case-control study was performed. Case definition: patients with CVD attributable to APS. Control definition: patients with CVD without APS. The controls were matched with cases by sex and age (within the same decade). Chi-square and t-student were used, using the statistical package SPSS22.0.
Results: 25 patients (25/88 28,4%) had CVD, 19 (76%) of primary APS and 6 (21%) of secondary APS. 17 patients (71,6%) were female. The mean age was 57,48±21,52 [range 13–89], with a mean follow-up of 8,64±6,72 years. 24% of patients had atrial fibrillation, 80% had one cardiovascular risk factor and 48% had two or more factors (hypertension 68%, hypercholesterolemia 36%, diabetes 20%, tabaquism 4%). Echocardiographic study was performed in 72% of patients with APS. Mitral valve was mainly involved. Most CVD were ischemic events (92%). The brain areas most involved were the basal ganglia (36%), together with the parietal and temporal lobe (16% respectively). 40% had two or more affected regions. 44% of the patients had two or more episodes of stroke. Lupus anticoagulant was positive in 40%, anticardiolipin antibodies in 76% and anti-β2 glycoproteinI antibodies in 20%.No differences were found with isotypes of APA and recurrent thrombosis or mortality. The treatment applied was oral anticoagulants (OAC) (48%), antiplatelet therapy (APT) (20%) and low molecular weight heparin (20%). In 10 patients (40%) CVD was diagnosed before APS (mean 8.64±6.7 years). The mortality was 44% and 40% of the patients were hospitalized more than once. When we compared the groups: treatment, performed echocardiogram, valvular disease, affected brain areas, recurrent strokes and follow-up time, revealed significant differences (see table 1).OAC were more used in the patients with APS and APT was the most common in control group. Valvular disease was more frequent in case group. The brainstem and the frontal lobe were the areas more affected in patients without APS.The number of strokes was higher in APS group. The patients with CVD and APS had a long-term follow-up.
Conclusions: The prevalence of CVD in our series of APS was 28.4% and most often were ischemic events. Most of the patients were women with high recurrent strokes and mortality. No differences were found with isotypes of APA and recurrent thrombosis or prognosis. CVD with APS patients had more recurrent strokes and longer follow-up.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4509

FRI0290 INTERLEUKIN 10 GENE POLYMORPHISMS IN PRIMARY SJÖGREN SYNDROME IN A TUNISIAN POPULATION

M. Tougorti[1], A. Kallel[2], I. Ben Ghorbel[1], R. Jemaa[2], M.H. Houman[1], N. Kaabachi[2]. *[1]Internal Medicine; [2]Biochemistry, Rabta university hospital, Tunis, Tunisia*

Background: Primary Sjögren syndrome (PSS) is one of the most common auto-immune systemic rheumatic diseases although its prevalence anging between 0.6 and 1.7%. PSS affects exocrine glands and lead to sicca syndrome. Interleukin-10 (IL-10) is a pleiotropic cytokine that is involved in the inflammation process of PSS.
Objectives: The aim of our study was to determine in a Tunisian population, clinical and biological characteristics of patients with primary PSS, allelic and genotypic frequencies of (-1082G/A, -819 C/T and -592 C/A) polymorphisms in IL-10 gene and to evaluate the association of these polymorphism with PSS.
Methods: The population we studied consisted of 242 subjects with female predominance (average age at diagnosis =49 years), divided into 84 PSS patients (fulfilling the revised AECG criteria 2002 and/or ACR proposed criteria 2012),recruited in the internal medicine department of the Rabta hospital and 158 controls recruited in the Greater Tunis. Il 10 level was assessed by ELISA. Polymorphisms genotyping of the IL-10 gene was done using PCR-RFLP technique.
Results: Il10 plasma level was lower in PSS patients (23.71pg/ml, n=73) compared to healthy volunteers (42.27pg/ml, n=60) and the difference was statistically significant (p=0.01).
The genotype frequencies of our population respected Hardy-Weinberg equilibrium distribution both in patients by primary SS than in controls. In PSS patients, the genotype frequencies of -592C/A are 53% for the CC genotype, 41% for the CA and 6% for the AA genotype. In controls these frequencies are respectively 60.3%, 32.9% and 6.8%. The genotype frequencies of -1082 G/A are 29.6% for the AA genotype, 63% for the AG and 7.4% for the GG genotype. In controls these frequencies are respectively 41.5%, 52.1% and 6.3%.
The genotype frequencies of -819 C/T are 47.6% for the CC genotype, 43.9% for the CT and 8.5% for the TT genotype. In controls these frequencies are respectively 41.5%, 52.1% and 6.3%.
No significant differences in genotypic frequencies were observed between cases and controls in the three polymorphisms.
Statistical analysis preformed revealed that there was neither protective nor aggravating hapoltype. However ATC haplotype seems to have a protective impact in controls (p=0.06 and OR=0.20)
Conclusions: IL10 level was significantly higher in PSS patients in precedent studies (1) (2). In our case Il10 level was associated with PSS in Tunisian patients but it was statistically lower than controls. Our results show that the three polymorphisms of gene of IL-10 are not a marker of SGS in the Tunisian population. This result might be explained by allelic variation or ethnic group.
References:
[1] Marka M, Bessenyei B, Zeher M, Semsei I. IL-10 promoter -1082 polymorphism is associated with elevated IL-10 levels in control subjects but does not explain elevated plasma IL-10 observed in Sjogren's syndrome in a Hungarian cohort. Scandinavian journal of immunology. 2005;62(5):474–80.
[2] Vazquez-Villamar M, Palafox-Sanchez CA, Munoz-Valle JF, Valle Y, Orozco-Barocio G, Hernandez-Bello J, et al. Analysis of IL10 haplotypes in primary Sjogren's syndrome patients from Western Mexico: Relationship with mRNA expression, IL-10 soluble levels, and autoantibodies. Human immunology. 2015;76(7):473–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6617

FRI0291 CD4 AND CD8 COUNT IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS – ASSOCIATIONS WITH INFECTION AND DISEASE ACTIVITY

H. Baharuddin[1], N. Zainudin[2], A. Ahmad[2], A. Rosman[2], M. Mohd Zain[2]. *[1]Rheumatology, Universiti Teknologi MARA; [2]Rheumatology, Hospital Selayang, Selangor, Malaysia*

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease driven by the activation of autoreactive T and B cells. Decreased levels of CD4 counts were found in these patients, although there are conflicting data on whether CD4 is associated with SLE disease activity.[1,2,3]
Objectives: To investigate the associations between CD4 and CD8 counts with (1) active SLE and (2) infection in patients with SLE.
Methods: This was a cross-sectional study conducted in a rheumatology referral centre in Malaysia. Inclusion criteria included patients who fulfilled SLICC SLE classification and was admitted to rheumatology ward for active SLE or infection. We excluded patients who had overlap syndrome, retroviral disease or underlying malignancy. SLE Disease Activity Index (SLEDAI) score was assessed by the same rheumatologist.
Statistical analysis was performed using SPSS 20 and a p-value of <0.05 was considered significant. Pearson correlation was used to analyse associations between 2 continuous variables, while comparison between 2 continuous data was performed using student's t test.
Results: Forty-two patients participated in this study. Majority (90.5%) were females with a mean age of 33.05 (±11.42) years and SLE duration of 8.69 (±5.26) years. There were 40 (95.2%) ANA positive, 23 (54.8%) anti-dsDNA positive, 13 (31.0%) anti-smith positive, 24 (57.1%) low C3 and 16 (38.1%) low C4 in this cohort.
There were significant correlations between SLEDAI score and CD4 (r=-0.59, p<0.01) and CD8 counts (r=-0.57, p<0.01). CD4 and CD8 counts were significantly lower in patients with clinically active SLE vs non-active, however, there were no significant differences in CD4 and CD8 counts in patients with infection vs no infection. We also found significantly high anti-dsDNA level and low complement 3, but not complement 4, in active SLE. White cell count was significantly higher in patients with infection. The details are tabulated in Table 1.

Table 1. CD4, CD8 and other parameters in infection and active SLE

Parameters	Infection			Active SLE		
	Yes (±SD), n=21	No (±SD), n=21	p	Yes (±SD), n=26	No (±SD), n=16	p
CD4	566.05 (482.51)	510.43 (479.08)	0.71	*375.58 (348.07)*	*802.56 (544.34)*	*<0.01*
CD8	659.10 (562.91)	456.48 (221.86)	0.13	*406.0 (346.04)*	*804.44 (460.04)*	*<0.01*
SLEDAI	7.14 (7.79)	6.38 (7.13)	0.74	*10.0 (7.54)*	*1.5 (3.30)*	*<0.01*
Anti-dsDNA	110.17 (145.84)	103.14 (186.87)	0.91	*149.01 (193.48)*	*42.47 (53.62)*	*0.05*
C3	0.85 (0.47)	0.93 (0.35)	0.56	*0.78 (0.39)*	*1.06 (0.38)*	*0.03*
C4	0.21 (0.16)	0.19 (0.08)	0.53	0.19 (0.12)	0.21 (0.13)	0.56
WBC	*8.92 (3.98)*	*6.41 (2.52)*	*0.02*	7.52 (3.72)	7.90 (3.30)	0.74

Conclusions: There were significant negative correlations between SLEDAI score and CD4 and CD8 counts, with low CD4 and CD8 counts found in patients with active SLE. There were no significant differences in CD4 and CD8 counts during infection.
References:
[1] Ferreira S, Vasconcelos J, Marinho A et al. CD4 lymphocytopenia in systemic lupus erythematosus. Acta Rheumatol Port 2009; 34: 200–206.
[2] Bonelli M, Savitskaya A, von Dalwigk K et al. Quantitative and qualitative

deficiencies of regulatory T cells in patients with systemic lupus erythematosus (SLE). Int Immunol 2008; 20: 861–868.
[3] Liu MF, Wang CR, Wu CR. Decreased CD4+CD25+ T cells in peripheral blood of patients with systemic lupus erythematosus. Scand J Immunol 2004; 59: 198–202.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6018

FRI0292 ANTI-PHOSPHATIDYLSERINE/PROTHROMBIN (APS/PT) ANTIBODIES IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

P. Bermudez-Bermejo[1], G. Hernandez-Molina[1], D.F. Hernandez-Ramirez[1], V. Zamora-Legoff[1], E. Olivares-Martínez[1], A.R. Cabral[2], C.A. Núñez-Alvarez[1]. *[1]Immunology and Rheumatology, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico; [2]Department of Medicine, The Ottawa Hospital. University of Ottawa, Ottawa, Canada*

Background: Several studies have showed conflicting results regarding the presence and meaning of anti-phosphatidylserine/prothrombin (aPS/PT). However aPS/PT antibodies seem to be a risk factor for thrombosis. Nevertheless, most of the studies have focused on patients with SLE and secondary antiphospholipid syndrome (APS).
Objectives: To assess the prevalence of aPS/PT antibodies, as well as their association with other antiphospholipid (aPL) antibodies (specially lupus anticoagulant [LA]) and thrombosis, in a well-established cohort of primary APS from a single center.
Methods: We included 96 consecutive patients with primary APS according the Sydney classification criteria and/or patients with hematological features (thrombocytopenia and hemolytic anemia) attending a referral center in Mexico City. Patients from both groups fulfilled the Sydney laboratory criteria for APS. We registered demographics, disease duration and type of manifestation. aCL (IgG and IgM), antibodies to purified human anti-β2GP-I (IgG and IgM) and aPS/PT antibodies (IgG and IgM) were assessed by ELISA (INOVA Diagnostics). LA was determined by LA/1 screening reactant and a confirmatory test LA/2 according to published guidelines. We used chi-square ($\chi 2$) test, Spearman correlation analysis and logistic regression.
Results: Most patients were females (69.7%), mean age 44.5±14.6 and median disease duration 7.3 years. The main clinical features were thrombosis (n=74, 77%), hematologic involvement (n=49 patients, 51%) and obstetric events (n=24, 25%) (non-exclusive groups). The prevalence of LA was 69.8%, aCL-IgG 56.8%, anti-β2GP-I IgG 43.1%, aCL-IgM 31.5% and anti-β2GP-I IgM 21%. The frequency of aPS/PT antibodies was 61.2% and 61.6% for IgG and IgM isotype, respectively. When we compared patients with LA+ (n=58) vs. LA- (n=25), the first group had a higher prevalence of aPS/PT-IgG (79.3% vs.16%, p=0.0001) and aPS/PT-IgM antibody (81.5% vs. 31.8%, p=0.001), as well as higher titers (aPS/PT-IgG 130.5 U vs. 8.2 U and aPS/PT-IgM 58.5 U vs. 16.6 U, p=0.0001). aPS/PT-IgG antibodies correlated with aPS/PT-IgM (ρ=0.59, p=0.0001), aCL-IgG (ρ=0.62, p=0.0001), anti-β2GP-I IgG (ρ=0.63, p=0.001) and anti-β2GP-I IgM (ρ=0.35, p=0.001). On the other hand, aPS/PT IgM antibodies correlated with aCL-IgG (ρ=0.57, p=0.0001), aCL-IgM (ρ=0.42, p=0.001), anti-β2GP-I IgG (ρ=0.48, p=0.001) and anti-β2GP-I IgM (ρ =0.59, p=0.0001). We found moderate agreement between the presence of LA and both aPS/PT isotypes (k=0.58 p=0.0001 for IgG, and k=0.47 p=0.001 for IgM). Thrombosis was associated with aPS/PT-IgG antibodies (87.7% vs. 61.1%, p=0.003) but not with aPS/PT IgM (73.6% vs. 81.8%, p=0.37). At the logistic regression analysis, the aPS/PT IgG antibodies remained associated with thrombosis after adjusting by all other aPL antibodies, OR 8.6 95% CI 2.1–33.8, p=0.002.
Conclusions: In this cohort of patients with primary APS, aPS/PT antibodies were highly prevalent, correlated with other aPL antibodies and were associated independently with thrombosis.
References:
[1] Sciascia S, Sanna G, Marru V, et al. Anti-prothrombin (aPT) and anti-phosphatidylserine/prothrombin (aPS/PT) antibodies and the risk of thrombosis in the antiphospholipid syndrome. Thrombosis Haemostasis 2014; 111:354–64.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5578

FRI0293 CHARACTERIZATION AND RISK ESTIMATE OF CANCER IN PRIMARY SJÖGREN SYNDROME: ANALYSIS IN 1300 PATIENTS

P. Brito-Zerón[1,2], B. Kostov[3], G. Fraile[4], D. Caravia-Durán[5], B. Maure[6], F.-J. Rascón[7], M. Zamora[8], A. Casanovas[9], M. Lopez-Dupla[10], M. Ripoll[11], B. Pinilla[12], E. Fonseca[13], M. Akasbi[14], G. de la Red[15], M.-A. Duarte-Millán[16], P. Fanlo[17], P. Guisado-Vasco[18], R. Pérez-Alvarez[19], A.J. Chamorro[20], C. Morcillo[1], I. Jiménez-Heredia[21], I. Sánchez-Berná[2,8], M. Ramos-Casals[2] on behalf of the GEAS-SEMI. *[1]Autoimmune Diseases Unit, Hosp CIMA-Sanitas; [2]Laboratory of Autoimmune Diseases Josep Font, Hosp Clínic; [3]IDIBAPS, Barcelona; [4]Hosp Ramón y Cajal, Madrid; [5]Hosp Universitario Central de Asturias, Oviedo; [6]Complejo Hosp Universitario, Vigo; [7]Hosp Son Espases, Palma de Mallorca; [8]Hosp Virgen de las Nieves, Granada; [9]Hosp Parc Taulí, Sabadell; [10]Hosp Joan XXIII, Tarragona;[11]Hosp Infanta Sofía; [12]Hosp Gregorio Marañón, Madrid; [13]Hosp de Cabueñes, Gijón; [14]Hosp Infanta Leonor, Madrid; [15]Hosp Esperit Sant, Santa Coloma de Gramenet; [16]Hosp de Fuenlabrada, Fuenlabrada; [17]Hosp Virgen del Camino, Pamplona; [18]Complejo Hosp Ruber Juan Bravo, Madrid; [19]Hosp Alvaro Cunqueiro, Vigo; [20]Hosp de Salamanca, Salamanca; [21]Hosp de Sagunto, Valencia, Spain*

Objectives: To characterize the risk of solid and hematological cancer in a large, well-characterized cohort of patients with primary Sjögren syndrome (SjS).
Methods: The GEAS-SS multicenter registry is a network of Spanish reference centers with specific clinical experience in the management of SjS patients. By January 2016, we had analyzed the development of cancer in 1300 consecutive patients fulfilling the 2002 SjS classification criteria. Multivariate Cox proportional-hazards regression analysis allowed adjustment for age at diagnosis, gender and the statistically-significant baseline variables associated with cancer in the univariate analysis. The sex- and age-specific incidence rates (SIR) of cancer were estimated from 2012 Spanish mortality data modeling, using a set of age-, sex- and site-specific incidence:mortality ratios.
Results: After a mean follow-up of 91 months (9922.3 person-years), 127 (9.8%) patients developed 133 cancers. The most frequent type of cancer was B-cell lymphoma (34% of cancers, including 27 MALT and 19 non-MALT B-cell lymphomas). Systemic activity at diagnosis of primary SjS correlated with the risk of hematological neoplasia (HR 1.06, $p<0.001$). Positive cryoglobulins at SjS diagnosis were associated with a high risk of either B-cell or non-B-cell lymphoma subtypes. Patients with cytopenias had a high risk of non-MALT B-cell and non-B-cell cancer, while those with low C3 levels had a high risk of MALT lymphomas and those with monoclonal gammopathy and low C4 levels had a high risk of non-MALT B-cell lymphomas. The estimated SIR for solid cancer was 1.13 (95% CI 0.88–1.46) and 11.02 (95% CI 8.35–14.54) for hematological cancer. SIRs for specific cancers were 36.17 (95% CI 25.44–51.43) for multiple myeloma and immunoproliferative diseases, 19.41 (95% CI 7.29–51.72) for Hodgkin lymphoma, 6.04 (95% CI 3.43–10.64) for other non-Hodgkin lymphomas, 5.17 (95% CI 1.94–13.79) for thyroid cancer, 4.81 (95% CI 1.81–12.83) for cancers of the lip and oral cavity and 2.53 (95% CI 1.05–6.07) for stomach cancer.
Conclusions: One third of cancers developed by patients with primary SjS are B-cell lymphomas. The prognostic factors identified at SjS diagnosis differed according to the subtype of B-cell lymphoma developed. Primary SjS is also associated with an enhanced risk of development of some types of non-hematological cancers (thyroid, oral cavity and stomach).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3391

FRI0294 ULTRASOUND OF THE SALIVARY GLANDS HELPS TO DISTINGUISH BETWEEN PRIMARY AND SECONDARY SJÖGREN SYNDROME

R. Bergner[1], H. Sattler[1], D. Wadsack[1], C. Löffler[1,2]. *[1]Medizinische Klinik A, Klinikum Ludwigshafen, Ludwigshafen; [2]5. Medizinische Klinik, Universitätsklinikum Mannheim, Mannheim, Germany*

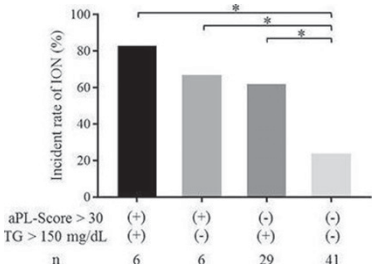
Background: Previous studies have demonstrated typical findings in the ultrasound of salivary glands (USG) in patients with primary Sjögren syndrome (pSS) compared with healthy controls. However, it is unknown, if these findings are only seen in patients with pSS but also in patients with secondary Sjögren syndrome (sSS) or other connective tissue diseases with positive Ro-SSA/La-SSB antibodies.
Methods: We used an ultrasound score developed by Zhang [1] to investigate salivary glands with a score ranging from 0–48. We compared the score from patients with pSS according the criteria of the American-European Consensus Group (group 1) with patients who fulfilled the clinical criteria (1–4), but were Ro-SSA/La-SSB negative (group 2), with patients who had another rheumatic disease, but had sicca symptoms and were Ro-SSA and/or La-SSB positive (sSS) (group 3), with patients with other rheumatic disease without Ro-SSA or La-SSB antibodies (group 4), with patients with other rheumatic disease with Ro-SSA antibodies but no sicca symptoms (group 5) and with patients with no rheumatic disease (group 6), respectively. We investigated the parotid and the submandibular salivary glands bilaterally. The USG was assessed with a score from 0–48 points with a maximum of 12 points for 4 items each (hyoechoic areas, hyperechoic reflexes, inhomogeneity and distinct organ border). If available the score was correlated with the scintigraphically measured function of the salivary glands.
Results: We included USG of 92 patients in our study. Group 1 (n=33) had a score of 16.6±11.6; group 2 (n=7) 2.4±3.5; group 3 (n=16) 8.6±9.5; group 4 (n=16) 5.3±7.8; group 5 (n=11) 4.5±6.7 and group 6 (n=9) 1.5±2.3, respectively. The score between group 1 and all other groups was significantly different ($p<0.01$), with no significant differences between all other groups. In 25 patients a scintigraphy of the salivary glands was available. The excretory function in the scintigraphy highly significantly correlated with the ultrasound score (r=0.53, $p<0.001$).
Conclusions: USG showed significantly higher scores in patients with pSS, than in patients with sSS or other rheumatic disease. USG as a non invasive investigation might be similarly helpful for the diagnosis of pSS like salivary gland functional tests. USG findings can reliable distinguish between pSS and sSS associated with other rheumatic disease, also if they are positive for Ro-SSA/La-SSB.

References:
[1] Zhang X, Zhang S, He J, Hu F, Liu H, Li J, Zhu J, Li Z. Ultrasonographic evaluation of major salivary glands in primary Sjögren's syndrome: comparison of two scoring systems. Rheumatology (Oxford). 2015 Sep;54(9):1680–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6928

FRI0295 HIGH RISK OF IDIOPATHIC OSTEONECROSIS IN SLE PATIENTS WITH HIGH ANTIPHOSPHOLIPID SCORE AND HYPERTRIGLYCERIDEMIA

R. Hisada, M. Kato, N. Ohnishi, M. Kono, S. Tanimura, E. Sugawara, H. Nakamura, K. Ohmura, S. Shimamura, Y. Fujieda, K. Oku, T. Bohgaki, O. Amengual, S. Yasuda, T. Atsumi. *Division of Rheumatology, Endocrinology and Nephrology, Hokkaido University Graduate School of Medicine, Sapporo City, Japan*

Background: Systemic lupus erythematosus (SLE) patients are prone to develop idiopathic osteonecrosis (ION) compared to other connective tissue disease patients or healthy subjects. ION has been shown to occur as a result of ischemia, however, the involvement of antiphospholipid antibodies (aPL) in its pathophysiology remains to be elucidated. In the last years, our group introduced a quantitative marker of aPL "antiphospholipid score (aPL-S)", which well reflected the risk of developing thrombosis [1].
Objectives: We aimed to identify the impact of aPL on the development of ION using aPL-S.
Methods: A single center retrospective study comprising 82 consecutive patients who were diagnosed SLE at the Rheumatology department of Hokkaido University Hospital and underwent magnetic resonance imaging (MRI) of hip joints from January 2000 to December 2016. Among all the enrolled patients, aPL-S, which is calculated from 0 to 86, as well as classical risk factors for ION were evaluated.
Results: All 82 patients (13 males and 69 females) were given glucocorticoids. ION of the femoral head was diagnosed by MRI scan in 37 patients. Male (ION(+): ION(-) 10/37 (27%) vs 3/45 (7%), p=0.016), malar rush (ION(+): ION(-) 22/37 (59%) vs 16/45 (36%), p=0.045), aPL positivity (ION(+): ION(-) 22/37 (59%) vs 15/45 (33%), p=0.026), high aPL-S (>30) (ION(+): ION(-) 9/37 (24%) vs 3/45 (7%), p=0.031), hypertriglyceridemia (fasting triglyceride levels >150 mg/dL) (ION(+): ION(-) 23/37 (62%) vs 12/45 (27%), p=0.002) and high dose of glucocorticoids (equivalent to 0.8mg/kg or more prednisolone) (ION(+): ION(-) 34/37 (92%) vs 21/45 (47%), p<0.001) were identified as risk factors for ION at univariate analysis. Multivariate analysis confirmed high aPL-S (OR 5.27; 95% CI 1.08 to 34.52, p=0.040), hypertriglyceridemia (OR 5.66; 95% CI 1.79 to 20.73, p=0.003) and high dose of glucocorticoids (OR 16.11; 95% CI 4.01 to 92.54, p<0.001) as independent variables. Of note, in 6 patients who had both high aPL-S and hypertriglyceridemia, 83% (5/6) developed ION (Figure 1). Conversely, systemic lupus erythematosus disease activity index and pulsed methylprednisolone therapy were not identified as risk factors for ION.



Conclusions: We newly identified high aPL-S as a risk factor for ION. Furthermore, SLE patients who have both high aPL-S and hypertriglyceridemia are at very high risk of ION. These findings suggest the involvement of microvascular occlusion in the pathophysiology of ION in SLE.
References:
[1] Otomo K, et al. Efficacy of the antiphospholipid score for the diagnosis of antiphospholipid syndrome and its predictive value for thrombotic events. Arthritis Rheum. 2012.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2570

FRI0296 SINGLE CENTER EXPERIENCE WITH 300 SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

S. Tekeoglu, D. Temiz Karadag, O. Ozdemir Isik, A. Yazici, A. Cefle. *Rheumatology, Kocaeli University, Kocaeli, Turkey*

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with diverse clinical manifestations.
Objectives: Here, we present 300 patients with SLE attending our clinic between 2001 and 2017.
Methods: Demographics, clinics, laboratory findings, Systemic Lupus International Clinics (SLICC)/American College of Rheumatology (ACR) damage index scores and treatments were analyzed. Diagnosis was confirmed with 1997 ACR (1) or 2012 SLICC (2) classifications. Descriptive statistical tests were used for analysis.
Results: Demographics and clinical characteristics are presented in Table 1. Anti-dsDNA was positive in 185 (61.6%), anti-Sm was positive in 35 (11.6%), anti-phospholipid antibodies was positive in 67 (22.3%), direct Coombs test was positive in 69 (23%) patients. Complement levels were low in 171 (57%) patients. In patients with renal disease, class IV lupus nephritis was the most common form (37 patients [12%]) followed by class II nephritis (34 patients [11%]). Forty-six patients had antiphospholipid syndrome. Treatments patients ever received are presented in Table 2. Cyclophosphamide treatment was given mostly for renal disease. Within 22 patients receiving rituximab, 2 had thrombocytopenia and 1 had hemolytic anemia unresponsive to other treatments, 1 had protein-losing enteropathy and 1 had lupus enteritis; the rest had lupus nephritis. One patient received intravenous immune globulin (IVIG) for severe neutropenia and 2 patients for severe thrombocytopenia. One patient received plasmapheresis for vasculitis. One patient received IVIG, plasmapheresis, rituximab for severe renal failure, alveolar hemorrhage requiring intensive care unit admission and 1 patient received same treatment for severe unresponsive hemolytic anemia.

Table 1. Demographics, clinical characteristics of patients

Age (years)	46±13 (min-max: 20–83; median: 45)
Duration of follow up (months)	58±52 (min-max: 1–180; median: 48)
Gender (Female/Male)	267 (89%)/33 (11%)
Muco-cutanous (n, %)	214 (71.3%)
Arthritis (n, %)	198 (66%)
Renal disease (n, %)	121 (40.3%)
Leukopenia/lymphopenia (n, %)	200 (66.6%)
Hemolytic anemia (n, %)	19 (6.3%)
Thrombocytopenia (n, %)	58 (19.3%)
Serositis (n, %)	55 (18.3%)
Nervous system disease (n, %)	24 (8%)
Anti-phospholipid Syndrome (n, %)	46 (15.3%)

Table 2. Treatment

Steroid/pulse treatment (n, %)	294 (98%)/65 (21.6%)
Hydroxycholoroquine (n, %)	300 (100%)
Azathioprine (n, %)	196 (65.3%)
Mycophenolate mofetil (n, %)	83 (27.6%)
Cyclophosphamide (iv) (n, %)	78 (26%); 10±4.5 cycles (min-max: 2–17)
Rituximab (n, %)	22 (7.3%)
Intravenous immunglobulin (IVIG) (n, %)	7 (2.3%)
Plasmapheresis (n, %)	4 (1.3%)

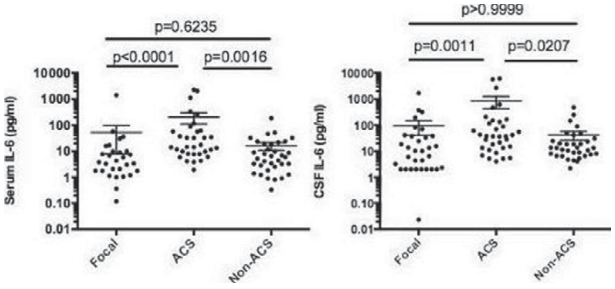
Conclusions: In long term, SLICC/ACR damage index was highest in patients received pulse steroid for renal disease (min:0, max:5). Four (1.3%) patients had pulmonary hypertension, 31 (10.3%) had avascular necrosis, 24 (8%) had viral infections requiring treatment or bacterial infections requiring admission due to immunosuppression, 12 (4%) had malignancy. SLE is an autoimmune disease requiring multi-faceted approach.
References:
[1]) Hochberg MC: Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 40:1725 1997.
[2]) Petri M, Orbai AM, Alarcon GS, et al.: Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum. 64:2677–2686 2012.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3253

FRI0297 ROLE OF SERUM INTERLEUKIN-6 IN BLOOD BRAIN BARRIER DAMAGES IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

S. Hirohata[1], Y. Matsueda[1], T. Yanagida[2], T. Yoshio[3]. *[1]Kitasato University School of Medicine, Kanagawa; [2]Teikyo University School of Medicine, Tokyo; [3]Jichi Medical University, Tochigi, Japan*

Background: Neuropsychiatric manifestation in systemic lupus erythematosus (NPSLE) is one of the most serious complications of the disease. We have recently demonstrated that the breakdown of blood brain barrier (BBB) plays a crucial role in the development of diffuse psychiatric/neuropsychological manifestations (diffuse NPSLE), allowing influx of neuron-reactive autoantibodies from systemic circulation into the brain. However, the mechanism of BBB damages remains unclear. On the other hand, although CSF interleukin-6 (IL-6) has been shown to be elevated in NPSLE, there has been no report on serum IL-6 in NPSLE.
Objectives: The present study was designed in order to elucidate the roles of serum IL-6 in the pathogenesis, especially in development of BBB damages, In NPSLE.
Methods: Paired serum and cerebrospinal fluid (CSF) samples were obtained from 101 SLE patients when they presented active neuropsychiatric manifestations (69 patients with diffuse psychiatric/neuropsychological syndromes [diffuse NPSLE] and 32 patients with neurologic syndromes or peripheral nervous system involvement [focal NPSLE]) and from 22 non-SLE control patients with non-

inflammatory neurological diseases. The levels of albumin and IL-6 in CSF and sera were measured by ELISA.
Results: Serum IL-6 as well as CSF IL-6 was significantly elevated in acute confusional state (ACS) compared with non-ACS diffuse NPSLE (anxiety disorder, cognitive dysfunction, mood disorder and psychosis) or focal NPSLE (figure). Q albumin (CSF/serum albumin quotient) was also significantly higher in ACS than in the other 2 groups of NPSLE. Of note, serum IL-6 (r=0.2801, p=0.0207), but not CSF IL-6 (r=0.1602, p=0.1918), was significantly correlated with Q albumin in patients with diffuse NPSLE, including ACS and non-ACS, although serum IL-6 was significantly correlated with CSF IL-6 in this population (r=0.3205, p=0.082).



Conclusions: These results indicate that serum IL-6 as well as IL-6 is involved in the pathogenesis of NPSLE. The data also confirm that the severity of BBB damages plays a crucial role in the development of ACS, the severest form of diffuse NPSLE. Finally, it is suggested that serum IL-6 might play a most important role in BBB breakdown in NPSLE, whereas CSF IL-6 might be involved in subsequent central nervous system inflammation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2806

FRI0298 APPLICATION OF PROPENSITY SCORE-MATCHING METHODS TO COMPARE DATA FROM LONG-TERM EXTENSION TRIALS WITH DATA FROM AN EXISTING LUPUS REGISTRY

M.B. Urowitz [1], R. Wielage [2], K.A. Kelton [2], R.L. Ohsfeldt [2], Y. Asukai [3], S. Ramachandran [4]. *[1] Centre for Prognosis Studies in Rheumatic Diseases, Toronto Western Hospital, Toronto, Canada; [2] Medical Decision Modeling Inc., Indianapolis, United States; [3] Value Evidence & Outcomes, GSK, Stockley Park, United Kingdom; [4] Value Evidence & Outcomes, GSK, Philadelphia, United States*

Background: Phase III randomised controlled trials (BLISS 52 and 76) in patients with systemic lupus erythematosus (SLE) have established the efficacy and safety of belimumab plus standard SLE therapy (SoC) vs SoC alone. As with many continuation studies, the long-term extensions (LTE) of the BLISS trials (BEL112233/NCT00724867 and BEL112234/NCT00712933) were single-arm, open-label studies; therefore, comparative long-term efficacy of belimumab and SoC vs SoC was not assessed. Existing observational databases could provide a valuable source of comparison data.
Objectives: This study (BEL206347) explores the use of propensity score (PS) adjustment to enable a post-hoc comparison of LTE patients to patients from an existing SLE cohort, assessing long-term efficacy of belimumab plus SoC vs SoC using the SLICC/ACR Damage Index (SDI) as the outcome.
Methods: Potential PS model criteria were identified by a systematic literature review for factors predicting organ damage. PS model criteria were restricted to baseline (at index [first recorded disease activity of SLE Disease Activity Index {SLEDAI} $\geq$6] for SoC cohort) characteristics available for both cohorts, including age, gender, race, disease duration, clinical and laboratory characteristics, SLEDAI over time, baseline SLEDAI and SDI and SoC (e.g. corticosteroid use/dose). Patients with active severe lupus nephritis/central nervous system lupus, those who had received B-cell-targeted therapy or belimumab or those with an index date before 1990 were excluded from the SoC cohort. The primary PS procedure used 1:1 matching with a 20% calliper (PSM); alternatively, inverse PS weighting (IPSW) was used to preserve the LTE sample. The balance in baseline factors across cohorts pre-/post-PS-adjustment was assessed using standardised distance measures.
Results: The literature review identified the Toronto Lupus Cohort (TLC) as an external registry with a comparable patient cohort. Without PS-adjustment, the standardised distance across cohorts exceeded 25% for 13 of 17 baseline factors in the PSM model. After PSM, standardised distance was <10% for all factors, but less than half of the LTE patients were matched. Using IPSW, data from all patients could be used but with a weighted standardised distance of <10% for 8 and <25% for 15 of the 17 PSM model factors.
Conclusions: The TLC was identified as an existing lupus registry with the endpoints of interest and detailed clinical characteristics. PS matching further maximised the comparability of the LTE and TLC cohorts. The final predictors used in the matching will be validated by two SLE clinicians. The preliminary results indicate a statistically adequate balance in clinical characteristics is attainable. PS matching will allow comparison of long-term organ damage in patients with SLE receiving belimumab plus SoC vs SoC alone. This approach can be applied to other extension studies to assess long-term treatment effectiveness.
Acknowledgements: Study funded by GSK. Katie White, PhD, Fishawack Indicia Ltd, provided editorial assistance funded by GSK.
Disclosure of Interest: M. Urowitz Grant/research support from: GSK, UCB and Eli Lilly, Consultant for: GSK, UCB and Eli Lilly, R. Wielage Consultant for: GSK, K. Kelton Consultant for: GSK, R. Ohsfeldt Consultant for: GSK, Amgen and AstraZeneca Hygieia, Y. Asukai Shareholder of: GSK, Employee of: GSK, S. Ramachandran Shareholder of: GSK, Employee of: GSK
DOI: 10.1136/annrheumdis-2017-eular.5071

FRI0299 N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE (NT-PROBNP) LEVEL IN PATIENTS WITH UNTREATED SYSTEMIC LUPUS ERYTHEMATOSUS

T. Panafidina, M. Sokhova, T. Popkova, D. Novikova, E. Alexandrova, E. Nasonov. *V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Objectives: The aim of this study was to determine NT-proBNP serum levels in patients with untreated SLE, thus ruling out any potential effect of SLE therapy: to analyze any possible correlation between NT-proBNP values and traditional risk factors (TRF), inflammatory markers and myocardial function parameters.
Methods: The study included 28 pts (82% females, aged 28,5 [25,0–32,0] years (median [interquartile range 25%>75%]) with untreated SLE (ACR criteria, 1997) and 27 healthy controls (89% females, age 30,0 [23,0–49,0] years). None of SLE pts was treated either with prednisone or cytotoxic drugs at the moment of inclusion, 5 (18%) pts received hydroxychloroquine 200 mg/day. SLE-related factors, including disease duration, clinical features, SLE Disease Activity Index (SLEDAI 2K) and Systemic Lupus International Collaborating Clinics damage index (SLICC/DI) were evaluated in parallel with relevant laboratory findings (blood and urine tests, CRP, IL-6, INF-α, immunoglobulins G, A and M, C3 and C4 complement fragments and others), autoantibodies (ANA, antiDNA, ENA-SSA, -SSB, -Sm, -RNP-70, aPL), echocardiography was performed using standard techniques. Serum levels of NT-proBNP (pg/ml) were measured using electrochemiluminescence method Elecsys proBNP II (Roche Diagnostics, Switzerland). Normal NT-proBNP levels should vary within $\leq$125,0 pg/mL.
Results: Mean SLE duration was 21,0 [5,0–60,0] months, SLEDAI 2K score - 11 [8–9], SLICC/DI score - 0 [0–0]. SLE pts had higher levels of NT-proBNP vs control (160,7 [88,6–335,4] vs 55,2 [36,6–70,3] pg/ml, p<0,001). Elevated levels of NT-proBNP (>125,0 pg/ml) was detected in 18 (64%) SLE pts. In SLE pts NT-proBNP serum levels showed positive correlation with creatinine (r=0,480, p<0,01), uric acid (r=0,427, p<0,05), ACL IgG (r=0,710, p<0,001), antiDNA (r=0,395, p<0,05), ANA levels (r=0,256, p<0,05), left ventricle (LV) end-systolic dimension (r=0,442, p<0,05), mean pulmonary artery pressure (r=0,486, p<0,05); and negative correlation with hemoglobin level (r=-0,493, p<0,01), C4 complement component (r=-0,475, p<0,05), glomerular filtration rate (r=-0,558, p<0,01) and LV ejection fraction (r=-0,505, p<0,01); left ventricular diastolic dysfunction (DDLV) was only in pts with NT-proBNP levels >125,0 pg/ml. Mean NT-proBNP concentration in verified DDLV cases (n=5 (18%)) considerably exceeded normal values, reaching up to 799,2 [276,6–1777,0] pg/ml.
Conclusions: Untreated SLE patients without a history of myocardial infarction, coronary procedure or any evidence of heart failure demonstrated higher NT-proBNP concentration as compared to healthy controls (p<0,001). NT-proBNP levels showed correlation with numerous SLE markers (ACL IgG, ANA, antiDNA, C4 fragment of complement), kidney function (creatinine, uric acid, glomerular filtration rate) and myocardial function (end-systolic dimension of the LV, mean pulmonary artery pressure, LV ejection fraction). No correlation was documented between NT-proBNP concentration and TRF or inflammatory markers (CRP, IL-6, INF-α). All abovementioned data suggest presumable SLE-associated autoimmune damage of cardiomyocytes and/or mediated decrease of myocardial function caused by kidney disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3735

FRI0300 NEUROLOGICAL INVOLVEMENT IN PRIMARY SJÖGREN SYNDROME

T. Ben Salem [1,1,1], I. Naceur, M. Tougorti, M. Lamloum, I. Ben Ghorbel, M.H. Houman. *Internal Medicine, Rabta university hospital, Tunis, Tunisia*

Background: Prevalence of neurological involvements (NI) in primary Sjögren Syndrome (pSS) varies from 10 to 60% and depends on whether they are screened systematically or only when they are symptomatic.
Objectives: The aim of the study was to describe the prevalence, clinical patterns and treatment of NI in pSS.
Methods: We performed a retrospective study of patients with pSS (American-European Consensus Group criteria) and followed in an internal medical department over a period of 15 years. Patients with NI were enrolled after excluding other potential causes. We did investigate neurologic systems only when patients present with symptoms.
Results: Primary Sjögren Syndrome was diagnosed in 155 patients, 41 had neurological manifestations (26.4%). They were 5 male and 36 female. The mean age at disease onset was 49 +/-13 years. The average delay from NI onset to pSS diagnosis was four months for peripheral nervous system (PNS) and 12

months for central nervous system (CNS). NI revealed the disease in 14 cases (34%). CNS and PNS involvements were respectively found in 27 and 19 cases (six patients had both PNS and CNS). In patients with CNS disorders, headache was the most frequent symptom (n=11). Pyramidal syndrome was found in 9 cases and cerebellar syndrome in one patient. Aseptic meningitis was noted in two cases. Brain MRI was performed in 22 cases and showed abnormalities in 82% of cases. T2 and flair weighted hyperintensities were periventricular (n=11), subcortical (n=5), frontal (n=3) and parietal (n=2). Myelitis was found in one patient.

Patients with PNS showed paresthesia (92%), motor deficit (22%) and decreased tendon reflex (18%). Sensory-motor neuropathy was described in 4 cases, pure sensory neuropathy in 6 cases (including one case of small fiber neuropathy) and motor neuropathy in one patient. Mononeuropathy multiplex was found in 4 cases and polyradiculoneuritis in one patient. Neuromuscular biopsy was performed in five patients and showed vasculitis in two cases. Trigeminal nerve and cochlear nerve were respectively involved in four and one patients. Antinuclear antibodies, anti-SSA and anti-SSB antibodies were respectively positive in 71%, 50% and 28% of cases. NI were treated with corticosteroids and immunosuppressive therapy in respectively 56% and 41% of cases. Outcome was good in 48% of the patients. Comparison of clinical and biological features in patients with and without NI showed no significant differences, only fatigue was significantly associated to NI (45.5% vs 12.9%; p=0.005).

Conclusions: In our series, NI prevalence was similar to other groups.

CNS involvements were more frequent than PNS manifestations whereas in other ethnic groups they are less frequent.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2772

FRI0301 CHARACTERIZATION OF FEVER IN HOSPITALIZED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: LESSONS FROM THE JIANGSU COHORT

X. Feng[1], W. Pan[2], L. Liu[3], M. Wu[4], L. Sun[1] on behalf of Jiangsu Lupus Collaborative Group. *[1]Department of Rheumatology, The Affiliated Drum Tower hospital of Nanjing University Medical School, Nanjing; [2]Department of Rheumatology, Huaian First People's Hospital, Huaian; [3]Department of Rheumatology, Xuzhou No. 4 People's Hospital, Xuzhou; [4]Department of Rheumatology, The 3rd Affiliated Hospital of Suzhou University, Changzhou, China*

Background: Fever is one of the main symptoms leading to the admission of patients with systemic lupus erythematosus (SLE) and its causes are usually complicated.

Objectives: To explore the prevalence and clinical characteristics of fever in Chinese SLE patients at the time of their first admission and to find out whether fever is related to a poor prognosis.

Methods: A follow-up study aimed to delineate SLE prognosis had been conducted by our Lupus Collaborative Group under the supervisor of Jiangsu Rheumatology Association to collect the data of patients who had ever recorded first admissions during the 1999–2009 decade (1). Among which, those with admission temperature documented were extracted for the assessment of potential factors associated with fever. The independency of various clinical features linked to fever was established by binary logistic regression analysis, and the relation between fever and patient's survival was determined by Cox regression analysis.

Results: Totally 1,348 patients were enrolled, in which 1,049 (77.8%) had normal temperature, 221 (16.4%) had low and moderate fever and 78 (5.8%) had high fever at the time of their first hospitalization. Compared with those having normal temperature, fever patients were more likely to have short disease duration (RR 0.74), concurrent infection (RR 3.29) and gastrointestinal (RR 1.57) as well as hematological involvements (RR 1.56). High C reactive protein level (RR 2.08) and positive anti-Sm antibody (RR1.55) were the two laboratory factors related to fever at admission. However, age, gender, SLEDAI score or erythrocyte sedimentation rate was not independently associated with fever in this cohort. Cox regression analysis showed that there was no correlation between fever and overall deaths (Figure 1) as well as infection induced deaths.

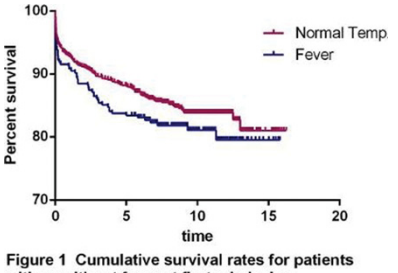


Figure 1 Cumulative survival rates for patients with or without fever at first admission

Conclusions: Both infection and lupus itself (especially gastrointestinal and hematological involvements) contribute to fever in SLE patients. Although the presence of fever increases the complexity of disease treatment, it does not constitute a risk factor for patient's long-term outcome.

References:

[1] Feng X, Pan W, Liu L, et al. Prognosis for hospitalized patients with systemic lupus erythematosus in China: 5-year update of the Jiangsu cohort. PLoS One. 2016;11(12):e0168619.

Acknowledgements: This study was supported by National Natural Science Foundation of China (81373198) and Jiangsu Provincial Special Program of Medical Science (BE2015602).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3140

FRI0302 ELEVATED CYSTEINE-RICH PROTEIN 61 IN SYSTEMIC LUPUS ERYTHEMATOSUS-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

Y. Fan[1], J. Qian[2], Y. Hao[1], M. Li[2], L. Gao[3], X. Zeng[2], Z. Zhang[1]. *[1]Department of Rheumatology and Clinical Immunology, Peking University First Hospital; [2]Department of Rheumatology, Peking Union Medical College Hospital, Peking Union Medical College & Chinese Academy of Medical Sciences, Key Laboratory of Rheumatology and Clinical Immunology, Ministry of Education; [3]Department of Rheumatology, Beijing Shijitan Hospital, Capital Medical University, Beijing, China*

Background: Pulmonary arterial hypertension (PAH) is a complex and devastating complication of connective tissue diseases that leads to severe morbidity and mortality.Unlike in Caucasians, it is systemic lupus erythematosus that recognized as the the major underlying cause of CTD associated PAH in Asian countries, especially in China [1]. Early diagnosis and intervention is vital for better long-term outcome in SLE-PAH patients.Previous study has demonstrated Cysteine-rich protein 61 (Cyr61) was highly expressed in SLE patients [2].However,the role of Cyr61 in pulmonary arterial hypertension (PAH) remains unknown.

Objectives: To explore the value of Cyr61 for PAH in SLE patients by comparing the plasma Cyr61 levels in SLE patients with/without PAH.

Methods: Plasma samples from two tertiary medical centers were obtained from 54 patients with definite SLE-PAH, 52 age,gender and SLEDAI matched SLE patients without PAH, and 54 age and gender matched healthy controls. Plasma Cyr61 concentration was measured by enzyme-linked immunosorbent assay.

Results: Plasma Cyr61 concentration in SLE-PAH patients was significantly higher than the matched SLE patients and healthy controls (median (IQR): 172.5 (143.8, 218.2), 124.9 (104.1, 154.7), 58.17 (28.9, 80.4) respectively, $P<0.001$) (Figure1). The sensitivity and specificity of Cyr61 in predicting the presence of PAH in entire SLE patients were 79.6% and 67.3%. Receiver operating characteristic curve analysis showed the area under the curve was 0.757 (95% CI: 0.662–0.852), with 140.6 pg/ml as the cut off concentration (Figure2). Further multivariate logistic regression analyses revealed high Cyr61 level (>140.6) is an independent risk factor for SLE patients to develop PAH (OR:7.822 (95% CI: 2.224–41.138)) (Table 1). Additionally, weak to moderate positive correlations were observed between Cyr61 concentration and serositis, hematological involvement, red blood cell distribution width, right ventricular systolic pressure and right ventricular diameter measured by echocardiography in entire SLE population.

Figure 1

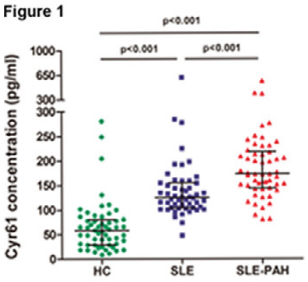


Figure 2

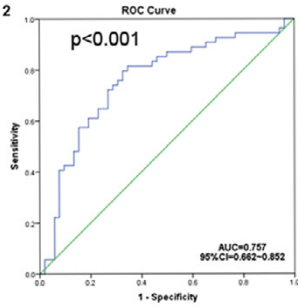


Table 1. Multivariate logistic regression analysis

Variables	OR	95% CI		P value
High Cyr61 level	7.822	2.224	41.138	0.002
Serositis	8.244	1.854	36.663	0.006
Anti-RNP positivity	3.902	1.067	14.267	0.040
Renal disorders	0.174	0.044	0.689	0.013
Anti-dsDNA positivity	0.171	0.046	0.636	0.008

Conclusions: Plasma Cyr61 level was significantly higher in SLE-PAH patients than SLE patients without PAH. Cyr61 may be used as a biomarker for PAH complication in SLE patients.

References:

[1] Hao, Y.J., et al., Connective tissue disease-associated pulmonary arterial hypertension in Chinese patients. European Respiratory Journal, 2014. 44(4): p. 963–972.

[2] Lin, J., et al., Serum Cyr61 is associated with clinical disease activity and inflammation in patients with systemic lupus erythematosus. Medicine (Baltimore), 2015. 94(19): p. e834.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2513

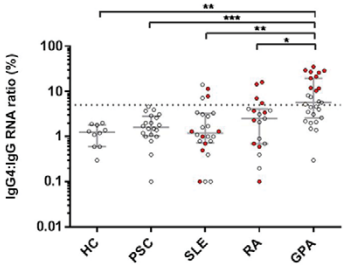
FRIDAY, 16 JUNE 2017

Vasculitis

FRI0303 THE IGG4:IGG RNA RATIO IS A NEW AND PROMISING DISEASE ACTIVITY MARKER IN GRANULOMATOSIS WITH POLYANGIITIS

A. Al-Soudi [1], M. Doorenspleet [1], R. Esveldt [1], S. Tas [1], R. van Vollenhoven [1], P. Klarenbeek [1], N. de Vries [1,2]. *[1]Amsterdam Rheumatology and Immunology Center; [2]Department of Experimental Immunology, Academic Medical Center, Amsterdam, Netherlands*

Background: Granulomatosis with Polyangiitis (GPA) is a form of vasculitis characterized by inflammation of blood vessels in lungs, kidneys and the ear, nose and throat region. Regular monitoring and treatment adjustments are common, as the disease activity tends to fluctuate over time. Unfortunately, good markers for disease activity are lacking. This leads to both over- and undertreatment. Immunoglobulin G4 positive (IgG4+) B-cells and plasma cells are implicated in the pathogenesis of GPA, but the level of serum IgG4 does not seem to be a good disease activity marker. Recently we developed a test that indirectly measures the presence of IgG4+ B-cells/plasma cells by measuring the IgG4:IgG RNA ratio[1]. We hypothesized that this test could be used as disease activity marker.
Objectives: To test the IgG4:IgG RNA ratio in peripheral blood as a disease activity marker in GPA.
Methods: 27 PR3+ ANCA+ positive GPA patients were included in this cross-sectional study. Mean age was 52 years, 56% were female, and 39% had active disease. For each patient the ESR, CRP, BVAS, and ANCA titre were measured and peripheral blood samples were obtained. Patients were defined as having active disease if the BVAS was ≥3. In addition we included 10 healthy controls, and 63 patients with other immune mediated inflammatory diseases (systemic lupus erythematosus (SLE) (n=24), rheumatoid arthritis (RA) (n=19), primary sclerosing cholangitis (PSC) (n=20)). A validated qPCR test was performed in all groups to measure the IgG4:IgG RNA ratio in peripheral blood samples [1]
Results: The median IgG4:IgG RNA ratio was significantly higher in the GPA cohort (5.7, IQR 2.6 – 19.7) compared to all control groups: 1.2 in SLE (0.7 - 3.3; $p<0.01$), 2.5 in RA (0.7 - 4.1; $p<0.05$), 1.6 in PSC (1.0 - 2.8; $p<0.001$) and 1.3 in HC (0.6 - 1.8, $p<0.01$). In addition, the median IgG4:IgG RNA ratio was significantly higher in patients with active disease (23.8; IQR 12.1 – 29.1) compared to patients in remission (3.5; IQR 2.0 – 5.5) ($p<0.0001$). The height of the IgG4:IgG RNA ratio significantly correlated with height of the BVAS (r^2 =0.76, $p<0.0001$), while the ESR, CRP and ANCA titre did not. Interestingly, IgG4/IgG RNA ratios among patients with active disease were consistently above 9.3, and among patients in remission they were below this threshold.



IgG4:IgG RNA ratio (%) in healthy controls (HC), primary sclerosing cholangitis (PSC), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and granulomatosis with polyangiitis (GPA). Red dots represent patients with active disease (resp. SLEDAI, DAS28 and BVAS). * <0.05, **<0.01, *<0.001**

Conclusions: The IgG4:IgG RNA ratio distinguishes active GPA from GPA in remission with excellent specificity and sensitivity. Moreover the ratio shows a significant correlation with disease severity, in contrast to ESR, CRP and ANCA titre. Retesting in another, prospective study is indicated to validate the IgG4:IgG ratio as a novel, highly sensitive and specific marker of disease activity in GPA.
References:
[1] Doorenspleet ME et al. Hepatology 2016; 64(2): 501–7.
Acknowledgements: We thank D. van der Coelen for the technical assistance, the doctors of the vasculitis outpatient clinic, especially Dr. B.J.H. van der Born and Dr. A.E. Hak, for the contribution to patient inclusions, and all the patients that participated in this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5088

FRI0304 THE UTILITY OF 18F FDG-PET/CT IN DISTINGUISHING BENIGN FROM MALIGNANT RETROPERITONEAL FIBROSIS

Y. Wang [1], Z. Guan [2], D. Gao [1], J. Zhu [1], J. Zhang [1], F. Huang [1]. *[1]Rheumatology; [2]Nuclear Medicine, Chinese PLA General Hospital, Beijing, China*

Background: Retroperitoneal fibrosis (RPF) could be idiopathic or secondary to various factors including malignancy. Pathology remains the most reliable diagnostic approach. However, the pathological features have yet been well defined and the feasibility of biopsy procedure depends on several factors such as the proximity of the lesions to abdominal aorta. ^{18}F FDG-PET/CT may help exclude malignancy by assessing FDG-uptake and mapping the whole body, especially when biopsy procedure is inaccessible.
Objectives: To evaluate the utility of PET/CT in distinguishing benign from malignant RPF.
Methods: Patients with benign or malignant RPF diagnosed between September 2011 and June 2016 were included. Morphologic features, FDG-uptake of retroperitoneal lesions and lymph nodes (LNs) were compared. FDG-uptake of retroperitoneal lesions was assessed visually with the referrence of liver and assessed semiquantitatively with SUVmax. LNs were regarded as specific LNs if frequencies of LNs with high FDG-uptake were observed differently between two forms of RPF. ROC analyses were performed to evaluate the diagnostic accuracy.
Results: Seventy-one cases with benign RPF and 21 cases with malignant RPF secondary to lymphoma (15) or metastatic carcinoma (6) with primary sites of pancreas (2), colon (2), stomach (1) and kidney (1) were included. The craniocaudal length, axial width, and distances between anterior or posterior

Table 1. Morphologic features, FDG-uptake of retroperitoneal lesions and lymph nodes (LNs)

Parameters	Benign RPF (71)	Malignant RPF (21)	*p* value
Morphologic features			
Craniocaudal length, median (IQR), mm	107.0 (80.5,136.4)	164.9 (104.7,229.2)	0.001
Axial width, median (IQR), mm	41.0 (32.3,52.0)	85.0 (62.3,98.5)	<0.001
Aorta lumen to anterior limit, median (IQR), mm	8.9 (6.0,12.0)	20.7 (13.9,45.3)	<0.001
Aorta lumen to posterior limit, median (IQR), mm	2.8 (2.2,4.4)	7.4 (4.5,14.5)	<0.001
FDG-uptake of retroperitoneal lesions			
High FDG-uptake, n (%)	55 (77.5)	21 (100.0)	0.017
SUV max, mean (S.D.)	4.8 (1.7)	12.2 (7.1)	<0.001
LNs with high FDG-uptake, n (%)			
Hilar/Mediastinal	27 (38.0)	13 (61.9)	0.054
Cervical	6 (8.5)	5 (23.8)	0.058
Axillary	4 (5.6)	6 (28.6)	0.003
Retroperitoneal	3 (4.2)	16 (76.2)	<0.001
Supraclavicular	2 (2.8)	8 (38.1)	<0.001
Inguinal	1 (1.4)	5 (23.8)	<0.001
Peritoneal	0 (0.0)	10 (47.6)	<0.001
Number of specific LNs, n (%)	0 (0,0)	2 (1,3)	<0.001

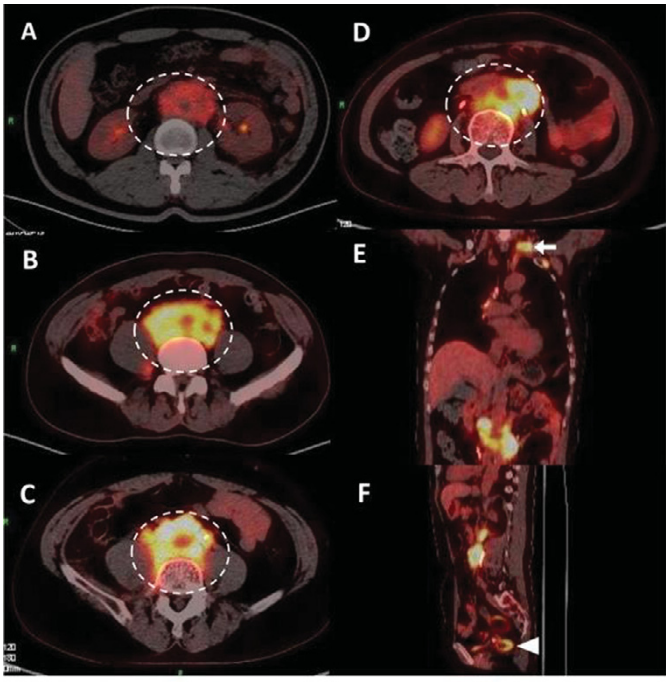


Figure 1. Representative ^{18}F fluorodeoxyglucose positron emission tomograph images for benign retroperitoneal fibrosis (**A**) and malignant retroperitoneal fibrosis secondary to lymphoma (**B, C**) and metastatic carcinoma (**D**). The retroperitoneal process are encircled by circles in the same size with different level of FDG-uptake. **D-F** are images from one patient with histological diagnosis of colon cancer. FDG-uptake is accumulated in left supraclavicular lymph node pointed by the arrow (**E**) and in sigmoid colon pointed by the arrow head (**F**).

limits and aorta were less in benign RPF, however, significant differences were only observed when comparing with lymphoma (p values: all <0.001) but not with metastatic carcinoma (p value: 0.396, 0.181, 0.112 and 0.64). A greater frequency of retroperitoneal lesions with high FDG-uptake (100% vs 77.5%, p value: 0.017) and a higher mean SUVmax (12.2 vs 4.8, p value: <0.001) were observed in malignant RPF. The frequencies of LNs with high FDG-uptake were greater with significance in malignant RPF except for hilar/mediastinal and cervical LNs, hence the rest LNs were regarded as specific LNs. At ROC analyses, the AUCs of SUVmax and specific LNs were 0.893 and 0.947. The sensitivity and specificity were 85.7% and 81.4% when the SUVmax was 6.23. The AUC of logistic regression model combining SUVmax and specific LNs was 0.974 with sensitivity of 90.5% and specificity of 90.1%.

Conclusions: PET/CT could help distinguish benign from malignant RPF, especially when taking into account the FDG-uptake of retroperitoneal process and LNs.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2588

FRI0305 RELATIVE FDG ACCUMULATION OF THE AORTIC WALL LESIONS TO AORTIC BLOOD POOL IN 18F-FDG-PET AND PET/CT COULD BE A USEFUL PARAMETER FOR THE PREDICTION OF DISEASE RELAPSE AFTER SUCCESSFUL TREATMEN IN TAKAYASU ARTERITIS

A. Ihata[1], Y. Kunishita[2], K. Minegishi[2], R. Yoshimi[2], Y. Kirino[2], H. Nakajima[2]. *[1]Department of Rheumatology, Yokohama Medical Center/ National Hospital Organization; [2]Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan*

Background: The assessment of disease activity of Takayasu arteritis (TA) is difficult if symptoms and serum inflammatory marker were not detected. Even in those conditions, relapses were frequently observed during the dose reduction of corticosteroid and immunosuppressant. There is accumulating evidence that 18F-fluolodeoxyglucose-positron emission tomography (FDG-PET) and PET/computed tomography (PET/CT) is useful for monitoring patients with TA when TA was clinically active. However, it is not clear the significance of FDG accumulations when TA was inactive.

Objectives: To investigate a quantitative predictor in FDG-PET or PET/CT scans for the relapse of TA.

Methods: We retrospectively investigated 76 FDG-PET or PET/CT scans and extracted 37 scans which were performed in inactive status. These scans were divided in two groups according to relapse of TA for 5years. The relapse was defined the increase of CRP and steroid dose or addition of immunosuppressant. FDG accumulations in aortic wall lesions of TA was evaluated by semi-quantitative index; the standardized uptake value (SUV). In addition to SUVmax in the aortic wall, we also calculated SUV ratio of maximum aortic wall uptake to mean lung uptake (ratio Lu), SUV ratio of maximum aortic wall uptake to mean liver uptake (ratio Li), and SUV ratio of maximum aortic wall uptake to mean aortic blood pool uptake (ratio BP). We compared groups using these parameters. We also determined the cutoff levels, sensitivity, and specificity of 4 sets of SUVs (SUVmax, ratio Lu, ratio Li, and ratio BP) for the prediction of relapse using Receiver Operating Characteristic (ROC) analysis. Moreover, Kaplan-Mayer analysis for the long-term relapse-free survival was performed to assess the reliability of these cutoff levels.

Results:

Table 1. Characteristics of two groups

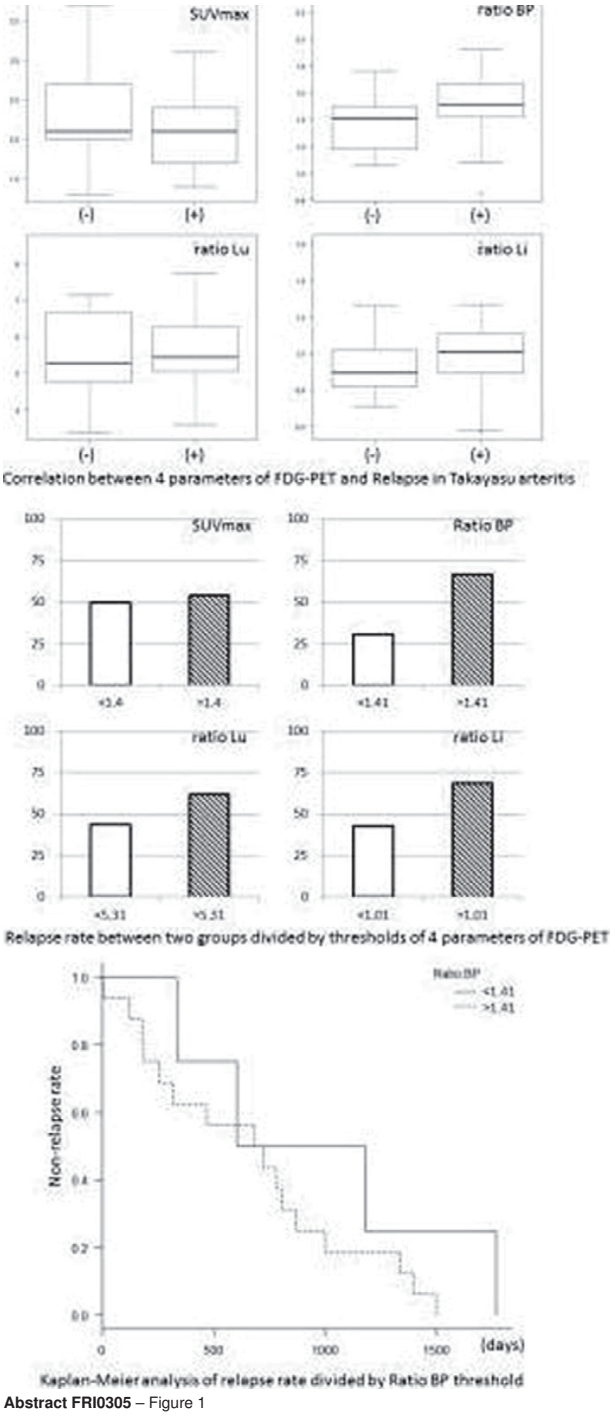
Relapse	(–)	(+)
#	17	20
Age (yr)	47 [30–72]	28.5 [14–68]
CRP (mg/dl)	0.13±0.03	0.13±0.03
Steroid dose (mg/d equivalent to prednisolone)	15.6±2.4	17.7±3.6
Immunosuppressant	2/17	7/35
Duration until relapse (Days)		702.5 [4–1769]

In 37 total PET and PET/CT scan examinations, non-relapse and relapse groups included 17 and 20 scans, respectively. Relapse group had more immunosuppressant users than non-relapse group. Although CRP level and SUVmax were equivalent, ratio of SUV, especially ratio BP of relapse group was higher than that of non-relapse group (p=0.09) (Figure top panel). The cut-off level of these parameters was calculated as follows; SUVmax 1.4, ratio Lu 5.31, ratio Li 1.01, and ratio BP 1.41, respectively. Using these cut-off level, relapse rates of below and over cut-off level were as follows; SUVmax 50% vs 54%, ratio Lu 43% vs 62%, ratio Li 43% vs 69%, and ratio BP 31% vs 67%, respectively (Figure middle panel). Using Kaplan-Mayer analysis, relapse rate of these two groups divided by ratio BP was not significantly different (p=0.268) though these two curves looked different (Figure bottom panel).

Conclusions: Our data suggest that ratio BP at stable condition, which represents relative FDG accumulation of the aortic wall lesions to aortic blood pool, could be a promising predictor to assess the relapse after successful treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6266



Abstract FRI0305 – Figure 1

FRI0306 LONG TERM DRUG-FREE REMISSION IS FEASIBLE IN SEVERE BEHCET'S DISEASE AFTER CESSATION OF SUCCESSFUL ANTI-TNF TREATMENT: A SINGLE CENTER, RETROSPECTIVE LONGITUDINAL OUTCOME STUDY

P.P. Sfikakis, A. Arida, S. Panopoulos, K. Fragiadaki, G. Pentazos, A. Laskari, M. Tektonidou, N. Markomichelakis. *First Department of Propaedeutic and Internal Medicine and Joined Rheumatology Program, National and Kapodistrian University of Athens Medical School, Athens, Greece*

Background: The efficacy of anti-TNF treatment for patients with severe forms of Behcet's disease (BD) is well established (ref), but long term data on the outcome after cessation of such treatment are lacking.

Objectives: To examine whether sustained long term remission of severe BD is feasible after cessation of successful anti-TNF treatment.

Methods: This retrospective longitudinal outcome study was conducted in December 2016 and included all patients with severe BD refractory to conventional immunosuppressive therapy who were considered complete responders to continuous anti-TNF treatment in our center, the first being treated in 2000.

Study's endpoint was the proportion of patients achieving sustained complete remission of BD for at least 3 years after cessation of the anti-TNF agent.
Results: A total of 28 patients in whom infliximab and/or adalimumab treatment was given, always combined with azathioprine unless not tolerated (n=2), and discontinued anytime before December 2013 were eligible for analysis. Following cessation of successful anti-TNF treatment (median duration of 2 years) 13/28 patients achieved the study's end-point. The main reason for anti-TNF administration was sight-threatening ocular disease (n=12) or intestinal disease (n=1). The remaining 15 patients relapsed within 1.5 year (main reason for anti-TNF: ocular disease, n=9; neuro-BD, n=2; severe mucocutaneous disease, n=3; intestinal disease, n=1; median treatment duration of 24 months); 12/15 were successfully re-treated with anti-TNF. So far, 3 of them (ocular disease, n=2; neuro-BD, n=1) have achieved the study's end-point (median re-treatment duration of 2 years). Overall, our 16 patients who achieved the study's end-point (57%) are in complete disease remission ranging from 3 to 12 years (5.7 years, median). Nine patients with severe ocular disease are currently any drug-free (32%), whereas the 7 remaining patients are on low doses of conventional immunosuppressive therapy (25%). Notably, those patients on drug-free remission had shorter median disease duration at initiation of anti-TNF treatment, compared to the remaining patients (1 versus 3 years, respectively).
Conclusions: Sustained drug-free remission for many years after cessation of successful anti-TNF treatment is feasible in some patients with severe BD. Since anti-TNF-induced "cure" can never be differentiated from a spontaneous remission by natural history, further studies should examine whether early anti-TNF treatment must be intended for every patient with severe BD.
References:
[1] Hatemi G, et al. EULAR recommendations for the management of Behçet disease. Ann Rheum Dis. 2008 Dec;67(12):1656–62.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5338

FRI0307 AN OUTCOME SURVEY OF 100 PATIENTS WITH CEREBRAL VENOUS SINUS THROMBOSIS DUE TO BEHÇET'S SYNDROME FOLLOWED UP AT A SINGLE, DEDICATED CENTER

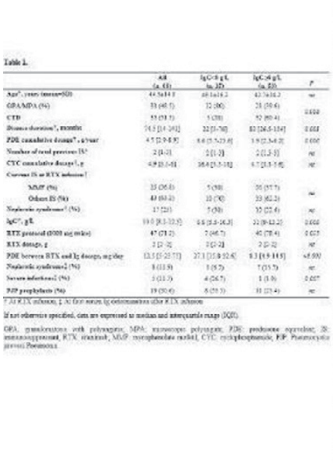
E.A. Kurt[1], Y. Ozguler[1], N. Kocer[2], D. Ucar[3], U. Uygunoglu[4], C. Islak[2], S. Ugurlu[1], G. Hatemi[1], S. Saip[4], M. Melikoglu[1], I. Fresko[1], V. Hamuryudan[1], Y. Ozyazgan[3], S. Yurdakul[1], A. Siva[4], H. Yazici[1], E. Seyahi[1]. [1]*Department of Internal Medicine Division of Rheumatology;* [2]*Department of Radiology;* [3]*Department of Ophthalmology;* [4]*Department of Neurology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey*

Background: Behcet's syndrome (BS) is a well-recognized cause of cerebral venous sinus thrombosis (CVST).
Objectives: We aimed to assess the outcome of a large cohort of patients with CVST due to BS attending a single dedicated center.
Methods: We identified 100 (81 M/19 F) patients with BS who were diagnosed as having CVST. All contacted were called back to the outpatient clinic for clinical and imaging re-evaluation.
Results: The mean age of the patients at the onset of the symptoms was 28±10 years. A total of 48 patients developed CVST before or at the onset of ISG fulfillment, while 52 developed CVST after a median 3 [2–8] years of ISG fulfillment. Superior sagittal (n=47) and transverse sinuses (n=46) were most commonly involved followed by sigmoid sinus (n=26) and jugular vein thrombosis (n=15).
A total of 59 (53 M/ 6 F) patients had vascular involvement in addition to CVST: these were deep vein thrombosis of the lower extremities (n=47), pulmonary artery involvement (n=17), Budd-Chiari syndrome (n=9), vena cava superior thrombosis (n=6) and major arterial disease (n=3). In about half (32/59), CVST preceded any type of additional vascular involvement. Eye involvement was seen in 37, parenchymal CNS involvement in 8 (all later than CVST) and gastrointestinal involvement in 5 patients.
Seven patients had died. By the end of the study, 87 patients were alive and contacted with a median follow-up time of 11 [6–15] years. Only 6 patients had a relapsing CVST course.
Information about medical treatment was present in detail in 87 patients of whom 75 received short courses of glucocorticoids with (n=12) or without anti-coagulants. A total of 81 patients received immunosuppressive agents, most commonly azathioprine. Four patients underwent lumbo-peritoneal shunting surgery (1 was successful) and 1 with arterio-venous fistula underwent vascular embolization.
Fifty patients were re-evaluated at the clinic. None had of symptoms of intracranial hypertension. Ophthalmological examination showed that 17 patients had complications such as bilateral optic atrophy (n=3), bilateral papilledema (n=5), bilateral optic disc pallor (n=4) and fibrotic scars around optic disc (n=5). Sensorineural type hearing loss was detected in 4 patients. Neurological examination was found to be normal in 43 patients with isolated CSVT, whereas abnormal in the remaining 7 patients with concomitant parenchymal CNS involvement.
Cranial MR/MR venographies at the end of follow-up, were abnormal in 36 patients showing occlusion/ irregularity/ hypoplasia or collaterals in the sagittal (n=19) or transverse sinus (n=17). In the remaining 14, MR venographies were normal.
Conclusions: CVST due to BS is closely associated with vascular involvement in the body and may be considered as a risk factor for future vascular involvement. CVST relapses are rare; however, the course is not uneventful: visual acuity or field may be impaired totally or partially because of optic disc atrophy; in addition hearing deficits may occur.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6323

FRI0308 PREDICTORS OF HYPOGAMMAGLOBULINAEMIA IN RITUXIMAB TREATED PATIENTS. A RETROSPECTIVE ANALYSIS ON A MONOCENTRIC COHORT

R. Padoan, M. Felicetti, M. Gatto, P. Polito, F. Ometto, D. Astorri, L. Friso, F. Cozzi, A. Doria, L. Punzi, F. Schiavon. *Operative Unit of Rheumatology, Department of Medicine DIMED, University of Padova, Padova, Italy*

Background: Rituximab (RTX), a chimeric monoclonal antibody against CD20, is increasingly used in the treatment of B-cell lymphomas and autoimmune conditions. It has been shown that some patients develop hypogammaglobulinaemia after treatment.
Objectives: To assess frequency and predictors of hypogammaglobulinaemia after RTX treatment in a monocentric cohort of patients affected with granulomatosis with polyangiitis (GPA), microscopic polyangiits (MPA) and connective tissue diseases (CTD).
Methods: We retrospectively reviewed all patients receiving RTX and concomitant/sequential immunosuppressants between 2007 and 2016 in a single rheumatologic center. Serum levels of total Ig and lymphocyte subsets were recorded at the time of RTX administration and 3–6 months later. We investigated the frequency of hypogammaglobulinaemia (IgG<6 g/L) and its related events.
Results: 72 patients, 30 (41.6%) GPA/MPA, 25 (34.7%) systemic lupus erythematosus, 13 (18.1%) systemic sclerosis and 4 (5.6%) poly-dermatomyositis were treated with RTX. We analyzed 113 RTX infusions, with 41 (36.2%) retreatments (median 2 [2–6]). We excluded 12 patients/18 infusions due to incomplete data.
RTX was administered at the dosage of 1000 mg twice in 68.1% of patients and 375 mg/m^2 weekly in 31.9%. IgG levels after RTX infusion were available in 68 (71.6%) patients. We observed a significant decrease of IgG levels between baseline and 3–6 months after RTX infusion in all patients (0.001). The frequency of patients with IgG<6 g/L was 22.1%, and 8.8% had IgG<4 g/L, significantly higher in GPA/MPA patients (0.008), with short disease duration (0.001), lower IgG levels at baseline (0.008), higher prednisone equivalent (PDE) cumulative dosage per year (0.006) and higher daily PDE dosage after RTX (0.001) (Table 1). After RTX, all patients had complete B-cells depletion.
At univariate analysis, IgG<6 g/L was associated with GPA/MPA diagnosis (0.006, OR 6 [1.5–24.2]), disease duration (<0.001, OR 0.2 [0.1–0.9]), RTX 375 mg/m^2 weekly protocol (p=0.017, OR 4.1 [1.2–13.9]), PDE cumulative dosage per year (<0.001, OR 6.6 [1.3–33.6]), daily PDE intake >15 mg/day after RTX (<0.001, OR 12.7 [3.1–52.5]) and IgG levels before RTX (<0.001, OR 18 [1.8–178]).
At multivariate analysis, daily PDE intake after RTX (>15 mg/day) and GPA/MPA diagnosis resulted independent predictive factors for hypogammaglobulinaemia (p=0.03, OR 9.5, [2.2–41.7] and p=0.43, OR 4.7, [1.1–21.5]).
Patients affected with GPA/MPA were compared to CTD, as reported in Table 2. GPA/MPA patients at infusion were older (0.002), presented shorter disease duration (0.001), lower IgG levels at baseline (<0.001) despite lower rate of nephrotic syndrome (0.003). Moreover they were treated more frequently with Azathioprine (0.007), RTX 375 mg/m^2 weekly protocol (<0.001) and higher PDE cumulative and daily dosage (<0.001, 0.01 respectively).
Only 5 patients (5.2%) experienced severe infections within 12 months, more frequently in IgG<6 g/L patients (0.007).



Conclusions: In autoimmune rheumatic diseases, diagnosis of GPA/MPA and glucocorticoid therapy resulted independent predictors of hypogammagobulinaemia after RTX treatment. Despite low IgG levels were associated with higher infections risk, rare severe infectious events were observed.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6337

FRI0309 CARDIOVASCULAR EVENTS IN ANCA-ASSOCIATED VASCULITIS: A META-ANALYSIS OF OBSERVATIONAL STUDIES

E. Houben[1], E.L. Penne[1], A.E. Voskuyl[2], J.W. van der Heijden[3], M. Boers[2,4], T. Hoekstra[3]. *[1]Internal Medicine, Northwest Clinics, Alkmaar; [2]Amsterdam Rheumatology and Immunology Centre; [3]Nephrology; [4]Epidemiology and Biostatistics, VU University Medical Centre, Amsterdam, Netherlands*

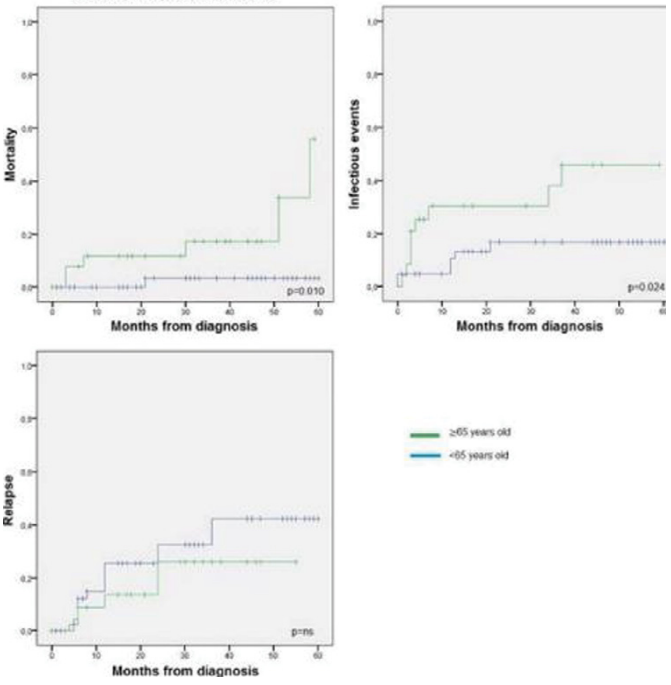
Background: Several chronic inflammatory diseases are associated with cardiovascular disease, but the cardiovascular risk in ANCA-associated vasculitis is poorly quantified.
Objectives: The aim of the present study is to review the evidence for the increased cardiovascular risk in patients with ANCA-associated vasculitis.
Methods: A comprehensive systematic review was conducted in accordance with guidelines of preferred reporting items for systematic reviews and meta-analyses (PRISMA). The databases PubMed, Embase.com and the Cochrane Library (Wiley) were searched for original observational studies reporting an estimate of the association between ANCA-associated vasculitis and cardiovascular events, including ischemic heart disease, cerebrovascular accidents and/or peripheral arterial disease. The quality of the included studies was assessed with the Newcastle–Ottawa Scale. Summary estimates were derived with a random-effects model and reported as relative risks.
Results: 1375 studies were identified and 7 studies were included comprising 14098 ANCA-associated vasculitis patients versus general population controls in 6 studies and chronic kidney disease patients in 1 study. ANCA-associated vasculitis carried a relative risk of 1.65 (95% confidence interval, 1.23–2.22) for all cardiovascular events, 1.60 (1.39–1.84) for ischemic heart disease and 1.20 (0.98–1.48) for cerebrovascular accidents. We did not find studies that addressed the risk for peripheral arterial disease separately. No heterogeneity was seen in the estimates.
Conclusions: This meta-analysis of observational studies supports an increase in cardiovascular risk of about 65% in patients with ANCA-associated vasculitis, similar to that found in other chronic inflammatory diseases. Hence, there is a clear need for active cardiovascular risk management in patients with ANCA-associated vasculitis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1617

FRI0310 LONG-TERM MORTALITY AND COMPLICATIONS IN YOUNG AND ELDERLY PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

A. Berti[1], M. Felicetti[2], R. Padoan[2], G. Brunori[3], F. Schiavon[2], G. Paolazzi[1]. *[1]Rheumatology Unit, S.Chiara Hospital, Trento; [2]Rheumatology Unit, Department of Medicine DIMED, Padua; [3]Nephrology Unit, S.Chiara Hospital, Trento, Italy*

Background: Advancing age is a risk factor for complications and mortality in anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV).[1,2]
Objectives: To analyze differences in infectious, metabolic and cardiovascular complications, renal function, and mortality in patients diagnosed with AAV before or after 65 years of age, and followed for up to 5 years.
Methods: We retrospectively collected long-term clinical and laboratory data of AAV patients of two referral centers in Northern Italy from 2000, and grouped patients in young (YP, <65 years old) and elderly (EP, ≥65 years old).
Results: Of the 114 patients included, 83 had a follow-up of at least 2 years (58 YP vs 25 EP). Median follow-up was 55 [32–100] months in YP and 44 [18–59] months in EP ($p<0.013$). 86.1% (68 patients) and 62.9% (22 patients) were diagnosed with GPA in YP and EP subsets, respectively. At baseline, YP and EP patients were similar in terms of BVAS/WG score, glomerulonephritis and alveolar hemorrhage, whereas creatinine levels (1.1 mg/dL [0.8–2.3] vs 1.82 mg/dL [0.98–3.5], p=0.044), renal insufficiency rate (44.7% vs 67.6%, p=0.026) and ANCA pattern (PR3 67.5% vs 26.5%, MPO 19.5% vs 59.8%; $p<0.001$ for both comparisons) were different in YR and ER, respectively. No significant difference in induction and maintenance regimens was found in the two groups, nor in clinical remission rate after induction treatment (all $p>0.05$).
At 2 year, creatinine levels (YP 1.0 mg/dL [0.85–1.31], EP 1.2 mg/dL [1.1–2.2]) and renal insufficiency rate decreased within each group ($p<0.05$). End-stage renal disease, hypertension rate, cardiac or cerebral ischemic attack rate, diabetes, solid or hematological cancer rate and mean vasculitis damage index were not statistically different in the two groups, whereas heart failure was more represented in EP (0.0% vs 8.3%, p=0.027).
Within the first 5 years of follow-up, severe infection (requiring hospitalization) and mortality rates were significantly higher in EP group when compared with YP group (p=0.024 and p=0.010 by Kaplan-Meier analysis, respectively, Figure 1), mirrored by a higher annual severe infection rate (p=0.041; 0.22±0.69 versus 0.05±0.17) and annual mortality rate (p=0.001; 0.33±1.02 versus 0.01±0.08) in EP group. Relapse rate was similar in YP and EP within 5 years (Figure 1). Lymphopenia rate (at least 1 event, $<1000x10^9$/L) was significantly higher in EP only at 6 month ($p<0.05$), whereas severe lymphopenia ($<500x10^9$/L), leukopenia

Figure 1. Kaplan-Meier curves of mortality, infectious events and relapse within 5 years of follow-up in our cohort of patients with AAV.



($<4000x10^9$/L) or hypogammaglobinemia (Ig<5g/L) rates were similar in both groups during the follow-up. Persistent lymphopenia (≥12months, $<1000x10^9$/L) was detected in 3 patients after cyclophosphamide treatment (2 YP and 1 EP). Only relapse before 2 years of follow-up was associated with infections in YP ($p<0.001$, OR 4.0 [CI 95%, 1.2–13.3]), but not in EP.
Conclusions: Heart failure is more frequent in older patients, which have higher infection and mortality rates. Transient lymphopenia is significantly higher in EP after induction treatment, but is not associated with their increase in infectious events. Despite a similar incidence of relapse in YP and EP, relapsing disease associates with infectious events in YP, but not in EP.
References:
[1] Flossmann O et al. Ann Rheum Dis. 2011 Mar;70(3):488–94.
[2] Timlin H et al. Semin Arthritis Rheum. 2015 Aug;45(1):67–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5595

FRI0311 ENDOVASCULAR INTERVENTION VERSUS SURGERY IN PATIENTS WITH TAKAYASU ARTERITIS: A META-ANALYSIS

J.H. Jung, G.G. Song, S.J. Choi, Y.H. Lee, J.-H. Kim. *Internal Medicine, Korea University Medical Center, Seoul, Korea, Republic Of*

Background: Although medical treatment has advanced, surgical treatment is needed to control the progression and symptoms of Takayau arteritis (TA). Endovascular intervention or surgical revascularization is performed; however, there are few comparative studies of these methods.
Objectives: There are many studies about surgery and endovascular intervention; however, it is still unclear which treatment has better a benefit/risk ratio. Because neither meta-analysis nor large-scale studies are available for surgical treatment of TA, we conducted a meta-analysis to examine the outcome of surgical treatment.
Methods: A meta-analysis comparing endovascular intervention and surgery outcomes was performed using the MEDLINE and Embase databases.
Results: A total of 14 studies of 598 patients and 1,049 lesions were included. Endovascular intervention was performed in 418 lesions and surgery in 631 lesions. Restenosis was more common in endovascular intervention than in surgery (odds ratio [OR] =2.74, 95% confidence interval [CI] =1.75–4.27, $p<0.00001$). Other complications, including stroke, did not differ between endovascular intervention and surgery (OR =0.75, 95% CI =0.49–1.15, $p=0.19$). There was no difference in mortality between the two groups (OR =1.11, 95% CI =0.50–2.46, $p=0.81$).

Table 1. Outcomes of endovascular intervetion compared to sugery in patients with Takayasu artheritis

	Test of association			Test of heterogeneity		
	OR	95% CI	P-value	Model	P-value	I^2(%)
Restenosis	2.74	1.75–4.27	<0.00001	R	0.05	41
Other complications	0.75	0.49–1.15	0.19	F	0.27	18
Stroke	0.5	0.17–1.50	0.22	F	0.98	0
Death	1.11	0.50–2.46	0.81	F	0.67	0

Conclusions: This meta-analysis showed the superiority of surgical revascularization over endovascular intervention.



Figure 1. ORs and 95% CIs of individual studies and pooled data; comparison of endovascular intervention and surgical revascularization for restenosis.

References:

[1] Saadoun D, Lambert M, Mirault T, et al. Retrospective analysis of surgery versus endovascular intervention in Takayasu arteritis a multicenter experience. Circulation 2012;125:813–9.

[2] Nakagomi D, Jayne D. Outcome assessment in Takayasu arteritis. Rheumatology 2016;55:1159–71.

[3] Labarca C, Makol A, Crowson CS, Kermani TA, Matteson EL, Warrington KJ. Retrospective comparison of open versus endovascular procedures for takayasu arteritis. J Rheumatol 2016;43:427–32.

[4] Lee GY, Jeon P, Do YS, et al. Comparison of outcomes between endovascular treatment and bypass surgery in Takayasu arteritis. Scand J Rheumatol 2014;43:153–61.

[5] Kalangos A, Christenson JT, Cikirikcioglu M, et al. Long-term outcome after surgical intervention and interventional procedures for the management of Takayasu's arteritis in children. J Thorac Cardiovasc Surg 2006;132:656–64.

Acknowledgements: No grants or other support were received for this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1953

FRI0312 THE FREQUENCY AND SEVERITY OF PATIENT-REPORTED SYMPTOMS IN GIANT CELL ARTERITIS

S. Monti[1,2], A. Leong[3], J. Robson[4], A. Craven[2], P.A. Merkel[5], R. Watts[6], R. Luqmani[2]. *[1]Rheumatology, University of Pavia, IRCCS Policlinico San Matteo Foundation, Pavia, Italy, Pavia, Italy; [2]NDORMS, Rheumatology Department, Nuffield Orthopaedic Centre, University of Oxford, Oxford, United Kingdom; [3]School of medicine, The University of Queensland, Brisbane, Australia; [4]Rheumatology, Faculty of Health and Applied Sciences, University of the West of England; School of Clinical Sciences at South Bristol, University of Bristol, Bristol, United Kingdom; [5]Division of Rheumatology and Department of Biosatistics and Clincial Epidemiology, University of Pennsylvania, Philadelphia, United States; [6]Rheumatology, Norwich Medical School, Bob Champion Research and Education Building, University of East Anglia, Norwich, Norwich, United Kingdom*

Background: A better understanding of the patients' perspectives is pivotal in the development of patient-reported outcomes (PROs) in vasculitis.
Objectives: To assessed patients' perspective of disease amongst cases with Giant Cell Arteritis (GCA) compared to comparator illnesses mimicking large vessel vasculitis (LVV) included in the Diagnostic and Classification Criteria in Vasculitis Study (DCVAS) database.
Methods: Patient Description of Illness (PDI) forms were circulated amongst Centres participating in the DCVAS study. The PDI form records up to 10 free-text severity ranked symptoms in descending order of severity, a body-map to localise the sites of pain and a free-text short summary of illness description. Free text was reorganized through content and thematic analysis.
Results: PDI forms from 89 patients with GCA and 28 comparators (COM) were analysed. There was no difference in age and sex distribution between groups (mean age 70±8 for GCA and 69±12 for COM). The symptoms description and frequency of the first most severe aspect of disease, including the patient's own words, is presented in Table 1. The symptom regarded as the most severe by both groups was headache. While there were no differences in the frequency of sudden visual loss, visual symptoms were reported more commonly as the most severe feature by COM vs GCA (21% vs 8%, p=0.05). Arthralgia was more frequently reported by COM vs GCA (11% vs 1%, p=0.01). Headache was the most frequently reported symptom in both groups. Patients with GCA reported jaw claudication (37%) as the second most frequently reported symptom, while COM reported arthralgia/arthritis (32%). Shoulder/neck pain was the third most important symptom in GCA (33%), while fatigue was the third most common complaint among COM (21%). Fatigue was reported as the fourth most common feature by 30% of GCA patients.
Conclusions: Headache was the most frequent and most severe symptom reported by patients with GCA and comparators. However, the reported frequencies and severities of other symptoms were significantly different between the two groups.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4051

Abstract FRI0312 – Table 1. Top 10 most recurrent patient-reported symptoms and correspondent severity rank in giant cell arteritis (GCA) and Comparators (COM)

Item	Frequency in GCA	Severity in GCA	Frequency in COM	Severity in COM	Examples of patient's own words
Headache	1	1, 2, 8	1	1, 2, 5	Headaches; Sore head; Thumping headache
Jaw claudication	2	3, 6	6	0	Jaw ache; Pain in jaw and teeth
Shoulder/neck pain	3	3, 4, 5,	0	0	Shoulder upper arm pain
Fatigue	4	5, 6, 10	3	3, 6, 7	Severe tiredness; Fatigue; No energy and exhausted
Myalgia or muscle weakness	5	5, 7, 10	4	3	Aching muscles; Achey limbs; Loss of strength in arms and legs
Blurred vision	6	10	5	4, 8	Blurred vision
Scalp tenderness	7	8	0	4	Irritation to the scalp; Tender scalp
Loss of appetite	8		0	0	Lack of appetite
Flu-like symptoms	9	9	0	0	General ill feeling; Flu-like symptoms; Unwell
Arthralgia or arthritis	10	9	2	3	Hip, knee more on right side; Pain in back of neck, ankles, wrists, and chest
Other ENT	0	0	7	4	Severe sinusitis; sore inside gums
Sudden visual loss	0	0	8		Loss of eyesight to both eyes; Vision loss
Night sweats	0	0	9	4, 8	Night sweats; Night fever sweats
Painful eyes	0	9	10	0	Shooting pain left eye; Pain right eye

FRI0313 THE EFFICACY AND SAFETY OF TOCILIZUMAB THERAPY IN PATIENTS WITH POLYMYALGIA RHEUMATICA WHO WERE RESISTANT OR INTOLERANT TO GLUCOCORTICOIDS AND ADDITIONAL METHOTREXATE

A. Ueno, Y. Yamamura, K. Fujita, N. Shibutou, M. Yamamura. *Center for Rheumatology, Okayama Saiseikai General Hospital, Okayama, Japan*

Background: A recent trial of tocilizumab (TCZ) in patients with newly diagnosed polymyalgia rheumatica (PMR), conducted in Europe and the United States, has shown its efficacy and safety.
Objectives: We examined the efficacy and safety of TCZ for patients with PMR who had been primarily resistant or intolerant to glucocorticoids (GC) and additional methotrexate (MTX).
Methods: Sixty patients had been diagnosed with having PMR since 2011. The patients are all compatible with the 2012 EULAR/ACR provisional classification criteria for PMR, and had been treated first with GC and then, if they were resistant or intolerant to GC, were added MTX, similarly to the 2015 EULAR/ACR recommendations for the management of PMR. The disease activity were measured by PMR-AS.
Results: There were 17 patients with GC/MTX resistant or intolerant PMR (28%). Of them, 9 patients with PMR agreed to the proposal of TCZ addition, and their therapeutic responses to TCZ and its safety were determined. They were at the age of 68.2±10.6, including three males and six females. Before TCZ addition, the patients were treated with prednisolone (PSL) at 7.6±3.0 mg/day plus MTX at 7.1±5.1 mg/week, and serum CRP were at 1.0±1.0 mg/dL. After 8.4±5.7 months of TCZ treatment, PSL and MTX had been reduced to 1.1±1.3 mg/day and 3.3±4.5 mg/week, respectively, with CRP at 0.02±0 mg/dL. GC were able to be withdrawn in 5 patients, and MTX were further withdrawn in 4 patients. Two patients reached drug-free remission (PMR-AS=0.02). During TCZ therapy, each one patient showed the worsening of depression and occlusion of the central retinal vein.
Conclusions: These results indicate that TCZ may provide a therapeutic option for patients with severe PMR who were resistant or intolerant to GC and additional MTX.

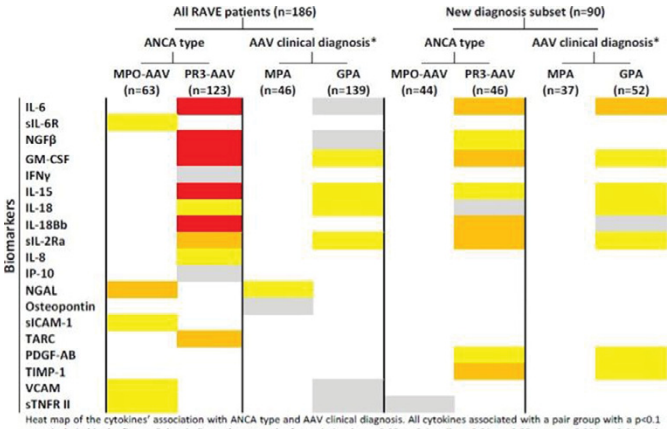
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5945

FRI0314 DIFFERENT SERUM CYTOKINE PROFILES REFLECT ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA) SPECIFICITY IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

A. Berti[1,2], R. Warner[3], K. Johnson[3], D. Cornec[1], D. Schroder[1], B. Kabat[1], P.A. Merkel[4], C.A. Langford[5], G.S. Hoffman[5], C.G. Kallenberg[6], P. Seo[7], R. Spiera[8], E.W. St Clair[9], J.H. Stone[10], U. Specks[1], P.A. Monach[11] on behalf of the RAVE-ITN Research Group. *[1]Mayo Clinic, Rochester, United States; [2]San Raffaele Scientific Institute, Milan, Italy; [3]University of Michigan Medical School, Ann Arbor; [4]University of Pennsylvania, Philadelphia; [5]Cleveland Clinic,*

Cleveland, United States; [6]University Medical Center, Groningen, Netherlands; [7]Johns Hopkins University, Baltimore; [8]Hospital for Special Surgery, New York; [9]Duke University Medical Center, Durham; [10]Massachusetts General Hospital; [11]Boston University, Boston, United States

Background: Evidence supporting the classification of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) based on ANCA type is accumulating.[1]
Objectives: To evaluate serum cytokine profiles in patients with AAV classified by ANCA specificity (proteinase 3 (PR3)-ANCA *versus* myeloperoxidase (MPO)-ANCA) or by clinical diagnosis (granulomatosis with polyangiitis (GPA) *versus* microscopic polyangiitis (MPA)) and clinical phenotypes.
Methods: An antibody array testing 30 soluble mediators, already shown to be implied in the pathogenesis of AAV, was performed in each patient with active AAV at inclusion in the Rituximab in ANCA-Associated Vasculitis (RAVE) trial, as previously described.[2,3] By means of Wilcoxon signed rank test for univariate analyses, we analyzed the association of levels of these cytokines with ANCA specificity, clinical diagnosis, and distinct clinicopathologic phenotype categories derived from the BVAS/WG items recorded at the time of enrollment (capillaritis, granulomatous manifestations, renal involvement, and alveolar hemorrhage; new diagnosis and relapsing disease), as described.[4]
Results: All cytokines tested (see Figure 1 and legend for the complete list), except for RANTES, ACE, bFGF and VCAM-1, were significantly increased in the RAVE cohort when compared to healthy controls ($p<0.05$). Median Birmingham vasculitis activity score and steroid use at screening did not significantly differ between PR3-AAV and MPO-AAV, and between GPA and MPA. Within both ANCA specificities, levels of 9 mediators were significantly higher in PR3-AAV (IL-6, NGFb, GM-CSF, IL-15, IL-18, IL-18Bb, sIL-2Ra, IL-8, TARC; $p<0.05$), compared to 5 different cytokines that were higher in MPO-AAV (sIL6R, NGAL, sICAM-1, VCAM-1, sTNFR II; $p<0.05$). In contrast, only 4 cytokines (GM-CSF, IL-15, IL-18, sIL-2Ra) were higher in GPA than MPA, and 1 (NGAL) was higher in MPA than GPA ($p<0.05$). The association of the majority of cytokines was stronger with ANCA specificity than with the clinical diagnosis (Figure 1). Similarly, the defined clinical phenotypes were also not separated by cytokine signatures as clearly as the ANCA specificity was (*data not shown*). Restricting the analysis to newly-diagnosed patients (n=90) showed the most significant cytokine profile differences associated with PR3-AAV (Figure 1).



Heat map of the cytokines' association with ANCA type and AAV clinical diagnosis. All cytokines associated with a pair group with a $p<0.1$ were included in the figure. Colors indicate the strength of association (grey, $0.05<p\leq0.1$; yellow, $0.01<p\leq0.05$; orange, $0.001<p\leq0.01$; red, $p\leq0.001$). The tested panel of 30 biomarkers also included BAFF, BCA-1, bFGF, G-CSF, PAI-1, KIM-1, MMP-3, RANTES, IL-12(p70), ACE, Clusterin, which showed no association ($p\geq0.1$) and therefore were not included in the figure.

*One patient had an indeterminate type of AAV.

Conclusions: Cytokine profiles separate patients more clearly by ANCA specificity than by clinical diagnosis, suggesting important differences in underlying pathophysiology and validating stratification of patients by ANCA specificity for treatment trials.
References:
[1] Cornec D et al. Nat Rev Rheumatol. 2016 Oct;12(10):570–9.
[2] Monach PA et al. Ann Rheum Dis. 2013 Aug;72(8):1342–50.
[3] Stone J et al. N Engl J Med. 2010 Jul 15;363(3):221–32.
[4] Fussner LA et al. Arthritis Rheumatol. 2016 Jul;68(7):1700–10.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5672

FRI0315 CLINICAL CHARACTERISTICS OF VASCULAR INVOLVEMENT IN BEHCET'S DISEASE

A. Ateş, M. Torgutalp, E. Okatan, E. Uslu, B. Dinçer, E. Yayla, M. Turgay, G. Kınıklı. *Rheumatology, Ankara University School of Medicine, Ankara, Turkey*

Background: Behçet's disease (BD) is a multisystemic inflammatory disorder classified as vasculitis, which can affect all types of vessels. The prevalence of vascular involvement has been reported at rates ranging from 15 to 50%.
Objectives: In this study, we aimed to determine the characteristics of vascular involvement in patients with BD.
Methods: Six hundred and ninety-two patients with BD, who applied to the multidisciplinary BD policlinic between 2006–2016, were retrospectively analyzed. The diagnosis of vascular involvement was made on clinical signs, by Doppler ultrasonography and/or angiography using computed tomographic or magnetic resonance techniques where appropriate.
Results: One hundred and seventy-six patients (%25.4) had vascular involvement. The mean age of patients with vascular involvement (n=176) and non-vascular involvement (n=516) was similar to 42.5±12.3 and 42.2±12.2 years, respectively, while male sex frequency was significantly higher in patients with vascular involvement (72% to %42, $p<0.001$). Uveitis (45%) and erythema nodosum (EN) (47.7%) were significantly higher in patients with vascular involvement than those without vascular involvement (for Uveitis OR: 1.7, p=0.003/for EN: OR: 2.5, $p<0.001$) (Table 1). Deep vein thrombosis was detected in 142 (80.7%) of the patients with vascular involvement and this was the most common type of vascular involvement (Table 2). Arterial involvement was detected in 52 (29.5%) of 176 patients with vascular involvement. Deep venous thrombosis alone was present in 125 (71%) patients, arterial involvement alone in 12 (6.8%) patients, arterial and venous involvement together detected in 40 (22.7%) patients. Arterial involvement was most commonly seen as pulmonary artery involvement in 45 (25.6%) patients [pulmonary artery thrombosis 35 (20%), aneurysm 10 (5.7%) and thrombosis + aneurysm 6 (3.4%) patients]. Twenty (11.3%) patients had other arterial involvement except pulmonary, 8 of them had thrombosis and 12 had aneurysm.

Table 1. Clinical features in patients with and without vascular involvement

	With vascular involvement	Without vascular involvement	OR	95% CI	P value
n (%)	176 (25.4)	516 (74.6)			
Age (year)	42.5±12.3	42,2±12.2			0.762
Male n (%)	127 (72.2)	217 (42.1)	3.57	2.46–5.19	**<0.001**
Genital ulceration n (%)	123 (69.9)	392 (76.1)	0.728	0.498–1.065	0.101
Uveitis n (%)	79 (44.9)	166 (32.4)	1.698	1.196–2.409	**0.003**
Papulopustular erythema or acneiform rash n (%)	101 (51.4)	186 (57.4)	1.274	0.886–1.832	0.190
EN n (%)	84 (47.7)	98 (27.1)	2.460	1.689–3.582	**<0.001**

Table 2. Venous involvement (%)

Deep vein thrombosis	142 (80.7)
Budd-Chiari syndrome	7 (4.0)
Inferior and superior vena cava syndrome	26 (14.7)
Iliac vein thrombosis	18 (10.2)
Safenous vein thrombosis	23 (13.1)
Femoral vein thrombosis	36 (20.5)
Popliteal vein thrombosis	43 (24.4)
Crural vein thrombosis	12 (6.8)
Cerebral sinus thrombosis	20 (12,2)

Conclusions: Vascular involvement in Behçet's disease is commonly seen in males. Deep vein thrombosis is the most common form of vascular involvement. Arterial involvement is important because of its higher risk of mortality (especially pulmonary artery aneurysm). The incidence of EN and uveitis is higher in patients with vascular involvement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4225

FRI0316 FACTORS ASSOCIATED WITH SURGICAL OUTCOMES OF SEVERE AORTIC REGURGITATION IN PATIENTS WITH BEHCET'S DISEASE

B. Ghang[1], D.-H. Lim[2], W.J. Seo[3], Y.-G. Kim[1], B. Yoo[1]. *[1]Rheumatology, Asan medical center, Seoul; [2]Rheumatology, Ulsan University Hospital, Ulsan; [3]Rheumatology, Seoul Veterans Hospital, Seoul, Korea, Republic Of*

Background: In rare cases, Behcet's disease (BD) can cause severe aortic regurgitation (AR) or aortic root destruction that might have lethal outcomes. Conventionally, simple aortic valve replacement (AVR) is performed for the management of severe AR in BD patients; however, the reoperation rate is as high as 78 to 100%, while mortality rate range from 20 to 47%. Recently, several series of case reports showed that compared to AVR, aortic root replacement (ARR) improved the surgical outcomes of AR in BD patients.
Objectives: To identify the factors associated with the long-term surgical outcomes of AR in BD patients.
Methods: We identified 23 patients who had been surgically treated for AR caused by aortic root involvement of BD from January 1996 through December 2013. We evaluated the occurrence of post-surgical adverse events, which were defined as follows: death, aortic valve/graft problem, infective endocarditis, cerebral infarction, and/or re-operation of aortic valve or root. Types of surgery were classified as simple aortic valve replacement (AVR), bioprosthesis aortic root replacement (bARR), and mechanical valved composite graft aortic root replacement (cARR). Clinical parameters including baseline characteristics, C-reactive protein (CRP), erythrocyte sedimentation rate, and medications were extracted from electronic medical records.
Results: Appropriate aortic valve or root surgery cases were 35 in total, with a mean follow up duration of 11±5 years in 23 patients. Out of the 11 cases

that underwent AVR, post-surgical events were observed in 8 (73%) cases. Out of the 12 bARR cases (xenograft in 5 cases and homograft in 7 cases), 9 (75%) cases had post-surgical adverse events. Out of the 12 cARR cases, post-surgical adverse events occurred in 4 (33%) cases. Multivariable cox proportional hazards model indicated that levels of CRP at 1 month after discharge and age at operation were independent prognostic factors associated with event-free probability. Notably, performing cARR was the most significant factor that affected the surgical outcome (HR (95% CI) 0.147 (0.028 – 0.766), p=0.023).

Conclusions: In BD patients with severe AR, the occurrence rate of post-surgical adverse events was associated with the levels of CRP at 1 month after discharge, age at operation, and type of surgery. cARR may be a better surgical option in BD patients with aortic root involvement

References:

[1] Jeong DS, Kim KH, Kim JS, Ahn H. Long-term experience of surgical treatment for aortic regurgitation attributable to Behcet's disease. Ann Thorac Surg. 2009;87(6):1775–82.

[2] Song JK, Kim MJ, Kim DH, Song JM, Kang DH, Lee I, et al. Factors determining outcomes of aortic valve surgery in patients with aortic regurgitation due to Behcet's disease: impact of preoperative echocardiographic features. J Am Soc Echocardiogr. 2011;24(9):995–1003.

[3] Liu Q, Ye W, Liu C, Li Y, Zeng R, Ni L. Outcomes of vascular intervention and use of perioperative medications for nonpulmonary aneurysms in Behcet disease. Surgery. 2016;159(5):1422–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5856

FRI0317 HUMORAL AND CELLULAR IMMUNITY TO VARICELLA-ZOSTER VIRUS IN GIANT CELL ARTERITIS PATIENTS: NO EVIDENCE OF VIRAL REACTIVATION AT ONSET OF DISEASE

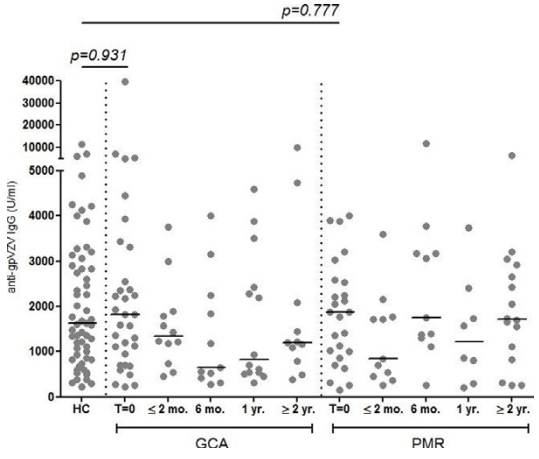
C. Rondaan, K. van der Geest, E. Eelsing, N. Bos, J. Westra, E. Brouwer. *Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen, Netherlands*

Background: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are strongly overlapping diseases that are thought to have a shared etiology [1]. The observation of varicella-zoster virus (VZV) antigen in temporal artery biopsies of GCA patients led to the hypothesis that VZV might be a trigger for the onset of the disease [2]. Herpes zoster occurs when the latently present VZV reactivates. It has been reported that patients with GCA do not appear to be at increased risk of herpes zoster compared with age and sex matched controls, even during treatment with high dose glucocorticoids [3]. Levels of VZV specific immunoglobulin G (VZV-IgG) are known to only slowly decline again after a reactivation [4]. We therefore hypothesized, in line with the proposed etiologic role, to find higher VZV-IgG levels in GCA and PMR patients at disease onset, compared to healthy controls. Furthermore, we expected to find no differences in cell-mediated immunity to the virus between patients and controls assuming that the incidence of herpes zoster is not increased in GCA.

Objectives: To investigate humoral and cellular immunity to VZV in GCA and PMR patients and compare these to results in age-and sex matched healthy controls.

Methods: Antibody responses to VZV glycoprotein were measured in serum samples of 35 GCA patients and 26 PMR patients at baseline (before glucocorticoid treatment) and during follow up, and in 58 healthy controls by an enzyme-linked immunosorbent assay (ELISA). Cell-mediated immunity to VZV was determined by performing interferon-γ (IFNγ) enzyme-linked immunosorbent spot (ELISpot) and intracellular cytokine flow cytometry measurements in 11 GCA patients and 15 PMR patients, and in 26 age and sex matched healthy controls.

Results: Similar levels of VZV-IgG were found in GCA and PMR patients at baseline, and healthy controls. The number of VZV specific IFNγ spot-forming cells was significantly lower in GCA patients than in healthy controls (p=0.029), but not different in PMR patients compared to healthy controls.



Conclusions: Since antibody levels at baseline were not different in GCA and PMR patients compared to healthy controls it seems unlikely that VZV has an important role in the aetiology of GCA or PMR. The finding of a decreased cell-mediated immunity in GCA patients, especially after treatment with high dose corticosteroids may indicate an increased risk of developing herpes zoster.

References:

[1] Buttgereit F, Dejaco C, Matteson EL, Dasgupta B. Polymyalgia Rheumatica and Giant Cell Arteritis: A Systematic Review. Jama 2016 Jun 14;315(22):2442–2458.

[2] Gilden D, Nagel MA. Varicella zoster virus and giant cell arteritis. Current opinion in infectious diseases 2016 Jun;29(3):275–279.

[3] Schafer VS, Kermani TA, Crowson CS, Hunder GG, Gabriel SE, Ytterberg SR, et al. Incidence of herpes zoster in patients with giant cell arteritis: a population-based cohort study. Rheumatology (Oxford, England) 2010 Nov;49(11):2104–2108.

[4] Cradock-Watson JE, Ridehalgh MK, Bourne MS. Specific immunoglobulin responses after varicella and herpes zoster. The Journal of hygiene 1979 Apr;82(2):319–336.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3756

FRI0318 QUALITY OF LIFE IN PATIENTS WITH BEHCET'S DISEASE

D. Santos-Faria, J.L. Silva, M. Cerqueira, J.R. Rodrigues, J. Sousa-Neves, F. Teixeira, D. Peixoto, J. Tavares-Costa, C. Afonso, S. Alcino. *Rheumatoloy, Unidade Local de Saúde do Alto Minho, Ponte de Lima, Portugal*

Background: Behcet's disease (BD) is a chronic and multisystemic inflammatory disorder affecting the skin, mucosa, joints, eyes, arteries, veins and the nervous and gastrointestinal systems. The symptoms may be separated by long or short intervals, occur simultaneously or in sequence, and exhibit a pattern of exacerbation and remission. The disease itself or the impact of the symptoms affect patients physically, mentally and socially with a negative effect in the quality of life (QoL).

Objectives: To determine the health status and quality of life in patients with BD followed in a rheumatology unit and to identify associated demographic and disease-related parameters influencing them.

Methods: Cross-sectional study of 44 BD patients and 39 healthy controls matched for age and sex. All subjects completed the Health Assessment Questionnaire (HAQ) to assess impairment in daily activities due to illness, Short Form-36 (SF-36) and EuroQol Visual Analogic Scale (EQ-VAS) to assess health related quality of life (HRQL). The disease characteristics, including disease duration and clinical involvements were collected. The Birmingham Vasculitis Activity Score (BVAS) was applied for the evaluation of current disease activity among BD patients. P value <0.05 was defined as statistically significant.

Results: Among 44 patients, 35 (79.5%) were female, with a mean age of 40.07 years and mean disease duration of 5.93 years. BD patients had significantly higher HAQ score (p=0.009) and lower levels of SF-36 ($p<0.001$) than the healthy controls. The predominant contributors to this low SF-36 were general health, vitality and role-emotional domains. In comparison with healthy controls, patients with inactive disease (BVAS=0) also had a higher HAQ, but without significant differences (p=0.53). The total SF-36 score also showed lower levels in patients with inactive disease (p=0.04), but when compared the different components, only half of them maintained significant differences, namely role-physical (p=0.03), general health ($p<0.001$), vitality ($p<0,001$) and social functioning (p=0.05). The controls showed a higher EQ-VAS, with a mean of 88.44 comparing to 68.36 in all BD patients ($p<0.001$) and 74.12 in the subgroup with inactive disease (p=0.003). SF-36 score was negatively correlated with HAQ (r=-,553, $p<0.001$) and positively correlated with EQ-VAS (r=.388, $p<0.001$). Longer disease duration correlated with lower levels of only some SF-36 domains, namely physical functioning (r=-.436, p=0.003), role-physical (r=-.533, $p<0.001$) and role-emotional (r=-.465, p=0.001). There was no correlation between disease activity and disease duration (p=0.678) or different scores evaluating QoL (p=0.876). The gender was not associated with statistical differences when compared clinical involvements, disease duration, current disease activity, HAQ, EQ-VAS or SF-36 scores. The heterogeneous nature of the disease expression did not allow the study of the association with the levels of health status and QoL.

Conclusions: Our findings showed lower levels of QoL and global health status in BD compared to healthy controls, mainly in active disease, accordingly with previous studies. The disease itself could be a determinant of disability.

References:

[1] Melikoglu M, Melikoglu MA. What affects the quality of life in patients with Behcet's disease? Acta Reumatol Port. 2014;39(1):46–53.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4147

FRI0319 PREDICTORS OF COMPLETE REMISSION IN POLYMYALGIA RHEUMATICA

D. Birra, A. Zoli, G. Peluso, S.L. Bosello, E. Gremese, G. Ferraccioli.
Dipartimento di Reumatologia e Scienze Affini, Università Cattolica del Sacro Cuore - Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy

Background: Polymyalgia rheumatica (PMR) is an inflammatory rheumatic condition characterized by aching and morning stiffness in the shoulders, hip girdle, and neck that typically occurs in adults over the age of 50. A rapid resolution of symptoms with low-dose glucocorticoids is a feature of PMR although some patients may experience a disease flare-up during steroid tapering.
Objectives: The aim of the study was to investigate possible clinical or laboratory prognostic factors of remission during a 12 month follow up in PMR patients treated with a starting low prednisone dose following the 2015 ACR-EULAR guidelines(1).
Methods: From 86 consecutive outpatients, diagnosed with PMR following ACR/EULAR 2012 provisional clinical criteria for PMR(2), 79 patients (56 women and 23 men), that achieved a complete follow up of at least 12 months, were selected. Clinical evaluation and laboratory tests were performed every 3 months Clinical remission was defined as lack of shoulder and hip girdle pain and as levels of ESR≤40 mm/h and CRP≤0.5 mg/dl.
Results: 37 PMR patients reached a complete remission after twelve months follow-up. We didn't find any significant difference in the mean age and in ESR and CRP values at the beginning of the disease in patients in remission after 12 month of follow up when compared with patients not in remission. Presence of obesity, dyslipidemia, hypertension, diabetes and smoking habits were not significantly different in the two groups of patients. No significant difference in steroid therapy at the beginning and after 6 month of follow up was noted between the two groups of patients. A statistically significant female low clinical remission was seen at the end of 12 month follow up when compared with male complete clinical remission (33.9% versus 78.2%, p=.000) Moreover it was shown that the patients achieving clinical and laboratory remission after six months of therapy were also those who maintained remission at the 12 month. CRP values, instead of ESR ones, were more predictive of remission after one year of therapy. Therefore patients with clinical remission in the absence of normalization of CRP value had greater risk of exacerbation.

Table 1. Demographic and laboratory characteristic of patients

	Remission T12	Non responders T12	p.
Age	75.1±6.7	69.7±5.7	ns
N°	37	42	
Female	19	37	.000
ESR T0 (mm/h)	56±31.6	50.2±29.4	ns
CRP T0 (mg/dL)	3.3±3.3	3.8±4.2	ns
ESR T6 (mm/h)	24.3±16.2	29.9±20.4	ns
CRP T6 (mg/dL)	0.6±0.7	1.5±2.1	.01
ESR T12 (mm/h)	22±15.4	28.7±17.4	ns
CRP T12 (mg/dL)	0.2±0.2	1±0.8	.000
Remission T6	27	7	.000
Prednisone dosage (mg) T0	16.3±8.4	15.5±6.6	ns
Prednisone dosage (mg) T6	5.9±4.8	7.5±5.1	ns
Prednisone dosage (mg) T12	2.3±2.5	4.4±4.7	.04
Dyslipidemia	9	12	ns
Hypertension	21	21	ns
Obesity	9	8	ns
Diabetes	6	8	ns
Smokers	3	3	ns

T0: Baseline; T6: Six months of follow up; T12: One year of follow up; ESR: erythrocyte sedimentation rate; CRP: C-Reactive Protein.

Conclusions: The sixth month of therapy is a crucial target for the management of PMR, because it can help to identify patients at greater risk of exacerbations, which may benefit from a tighter follow-up and a more aggressive therapeutic strategy. Among prognostic factors female sex and high CRP values at sixth months appear to be associated with higher relapse risk and a longer duration of treatment.

References:

[1] Dejaco C, Singh YP, European League Against Rheumatism; American College of Rheumatology, 2015 Recommendations for the management of polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. Ann Rheum Dis. 2015 Oct;74(10):1799–807. doi: 10.1136/annrheumdis-2015-207492.

[2] Dasgupta B, Cimmino MA, Matteson EL. 2012 provisional classification criteria for polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative, Ann Rheum Dis. 2012 Apr;71(4):484–92. doi: 10.1136/annrheumdis-2011-200329.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6262

FRI0320 PREDICTIVE VALUE OF PLATELET TO LYMPHOCYTE RATIO IN RENAL INVOLVEMENT IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS

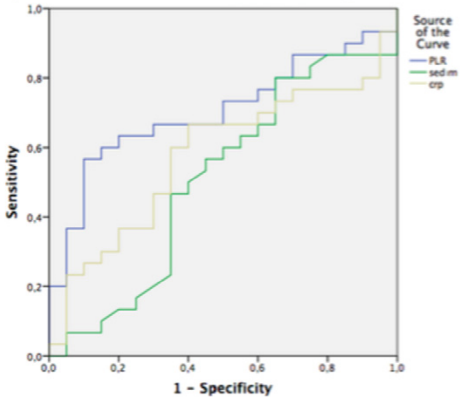
H. Kucuk[1], D. Tecer[2], O. Varan[1], H. Babaoglu[1], S.C. Guven[2], A. Tufan[1], S. Haznedaroglu[1], M.A. Özturk[1], B. Goker[1]. *[1]Department of Internal Medicine, Division of Rheumatology; [2]Department of Physical and Rehabilitation Medicine, Division of Rheumatology, Gazi University Faculty of Medicine, Ankara, Turkey*

Background: Granulomatosis with polyangiitis (GPA) is a granulomatous necrotizing vasculitis with high morbidity and mortality. Anti-neutrophil cytoplasmic antibody (ANCA) is a rvaluable diagnostic marker, however its titer lacks predictive value for the severity of organ involvement. Platelet to lymphocyte ratio (PLR) and mean platelet volume has been regarded as a potential marker in assessing systemic inflammation.
Objectives: We aimed to investigate PLR and MPV as inflammatory marker in patients with GPA.
Methods: GPA patients and age-sex matched healthy controls were included. Demographic, clinical and laboratory information were extracted from medical records. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC), platelets (PLT), lymphocyte and neutrophils counts and glomerular filtration rate (GFR) were recorded. PLR was calculated. Disease activity was assessed with Birmingham Vasculitis Activity Score for WG vasculitis (BVAS/WG).
Results: 56 patients with GPA and 53 healty controls were included. Clinical characteristics and laboratory findings of the study population are shown in Table 1. ESR, CRP, MPV and PLR were significantly higher in patients with GPA than controls. PLR positively correlated with ESR and CRP (r:0.389, p:0.005 and r:0.512 p<0.001, respectively). In contrast, MPV negatively correlated with ESR and CRP (r:-0.308, p:0.028 and r:-0.337 p:0.014, respectively). There were no significant correlation between PLR, MPV and BVAS/WG. Patients with renal involvement had statistically significantly higher PLR than patients without renal involvement (303.01±287.33 vs177.98 + 75.43, p: 0.020 respectively). Moreover PLR negatively correlated with glomerlar filtration rate (r:-0.266 and p:0.009). Receiver operating characteristic curve of PLR, ESR and CRP for differentiating renal involvement is presented in Figure 1. Area Under Curves (AUCs) for PLR, CRP and ESR were 0.703 (95% confidence interval [CI], 0.558–0.849, p=0.016), 0.577 (95% CI: 0.416–0.738, p=0.362), 0.508 (95% CI: 0.337–0.678, p=0.929), respectively. The cutoff level of PLR was 204 (sensitive 65.6%, specifity 62.5%, positive predictive value 70%, negative predictive value 57.7%). Patients with alveolar hemorrhage tended to have higher PLR but this difference did not reach statistically significance (266.60 + 182.90 vs 240.61 + 252.43 p=0.382, respectively).
Conclusions: Results suggest that PLR exhibit favorable diagnostic performance in predicting renal involvement in patients with GPA.

Table 1. Clinical characteristics and laboratory findings of the patients and healthy controls

	GPA patients	Controls	p value
Age (years)	48.14 ± 14.09	46.77 ± 14.14	0.614
Males (n)	33 (58.9%)	26 (49.1%)	0.034
WBC (x 10^3/uL)	12359.96 ± 6604.92	7230.80 ± 1630.33	<0.001
Neutrophils	9267.74 ± 5701.73	4285.73 ± 1597.18	<0.001
Lymphocytes	1805.64 ± 986.24	2311.22 ± 581.93	<0.001
Platelets	343640 ± 174905.10	234939.02 ± 57204.24	<0.001
ESR	54.19 ± 35.42	10.12 ± 7.66	<0.001
CRP	64.18 ± 72.11	3.42 ± 1.59	<0.001
MPV	7.73 ± 0.96	8.76 ± 1.10	
PLR (mean +SD)	253.99 ±	104.79 ± 25.23	<0.001

Figure. ROC curve of PLR, ESR and CRP for differentiating renal involvement

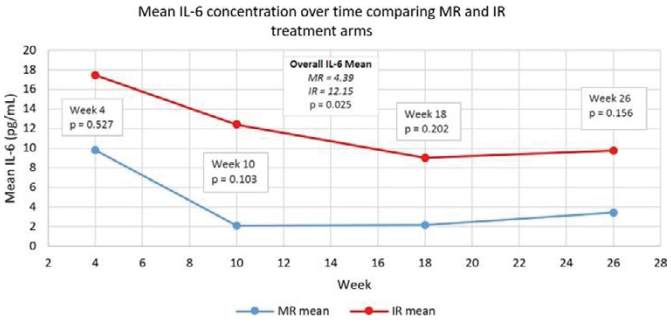


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6473

FRI0321 CIRCULATING IL-6 AND OTHER METABOLIC BIOMARKERS COMPARING EFFECTS OF MODIFIED-RELEASE PREDNISONE (MR) AND IMMEDIATE-RELEASE PREDNISOLONE (IR) IN NEW GCA

E. Miler[1], S. Mapplebeck[1], C. Mackerness[1], L. Wilson[1], T. Aung[1], D. Gayford[1], J.P. Schofield[2], B. Dasgupta[1]. [1]*Southend University Hospital NHS Foundation Trust, Westcliff-on-Sea;* [2]*Napp Pharmaceuticals Limited, Cambridge Science Park, Milton Road, United Kingdom*

Background: GCA may be an interleukin-6 (IL-6) driven disease and IL-6 blockade is emerging as an exciting therapy of IL-6.[1] We measured serial IL-6 levels in new patients with GCA treated in an RCT of modified-release prednisone (MR) versus immediate-release prednisolone (IR) used in a tapering regimen conforming to BSR guidelines.[2,3]
Methods: Patients (n=12) were randomised into two treatment arms (7 MR, 5 IR) and followed up over 26 weeks. IL-6 samples were collected at 9am at weeks 4, 10, 18 and 26 and were measured using Beckman Coulter IL-6 immunoassay, validated in a controlled study according to ACB criteria. We also measured bone markers (CTX, P1NP, vitamin D), HbA1c, cortisol, ACTH and PTH.
Results: Significantly higher overall mean IL-6 levels were seen in the IR arm (n=5) compared to MR (n=7) [unpaired two-tailed Student's t test]. IL-6 levels in both arms were lowest between weeks 4–10 and continued to decrease in the IR arm to week 26, whereas lower but constant levels were seen in the MR arm (Figure)
Mean CTX concentration was significantly higher at week 4 (M =0.29, SE =0.04) compared to Week 26 (M =0.13, SE =0.02) p=0.002. No significant difference was seen between treatment arms.
Patients on MR had complete suppression of ACTH compared to IR ($p<0.05$) without a significant difference between groups in 9 am cortisol levels (p=0.3412). No significant differences were seen in levels of vitamin D, calcium, PTH, ESR, CRP, or HbA1c.



Conclusions: Our study suggests that elevated levels of Il-6 are better suppressed by MR prednisone therapy compared to IR prednisolone in new GCA. Bone resorption marker CTX was significantly reduced in both treatment arms. ACTH suppression with MR prednisone may reflect a greater impact on the HPA axis although cortisol levels were not affected.
Our findings suggest that MR prednisone may warrant further clinical trial investigation in GCA.
References:
[1] Dasgupta, B. and Panayi, G.S., 1990. Interleukin-6 in serum of patients with polymyalgia rheumatica and giant cell arteritis. British journal of rheumatology, 29(6), pp. 456–458.
[2] Spies, C.M., Straub, R.H., Cutolo, M. and Buttgereit, F., 2014. Circadian rhythms in rheumatology–a glucocorticoid perspective. Arthritis research & therapy, 16 Suppl 2, pp. S3.
[3] Dasgupta, B., Borg, F.A., Hassan, N., Alexander, L., Barraclough, K., Bourke, B., Fulcher, J., Hollywood, J., Hutchings, A., James, P., Kyle, V., Nott, J., Power, M., Samanta, A. and BSR and BHPR Standards, Guidelines and Audit Working Group, 2010. BSR and BHPR guidelines for the management of giant cell arteritis. Rheumatology (Oxford, England), 49(8), pp. 1594–1597.
Acknowledgements: Napp Pharmaceuticals Limited, Beckman Coulter, Gabriel Labinjo for technical support.
Disclosure of Interest: E. Miler: None declared, S. Mapplebeck: None declared, C. Mackerness: None declared, L. Wilson: None declared, T. Aung: None declared, D. Gayford: None declared, J. P. Schofield Grant/research support from: Napp Pharmaceuticals Limited and Napp distributes prednisone MR in U.K. (Lodotra), B. Dasgupta: None declared
DOI: 10.1136/annrheumdis-2017-eular.3550

FRI0322 ASSESSMENT OF DAMAGE AND PROGNOSIS IN PATIENTS WITH ADULT IGA VASCULITIS: RETROSPECTIVE MULTICENTERED COHORT STUDY

F. Alibaz-Oner[1], A. Omma[2], A. Sarı[3], O. Karadag[3], D. Uskudar Cansu[4], C. Bes[5], F. Yildiz[6], M.F. Oksuz[7], S. Yilmaz[8], A. Balkarli[9], S. Ureyen[10], H. Direskeneli[1]. [1]*Rheumatology, Marmara University, School of Medicine, Istanbul;* [2]*Rheumatology, Ankara Numune Education and Research Hospital;* [3]*Rheumatology, Hacettepe University, School of Medicine, Ankara;* [4]*Rheumatology, Osmangazi University, School of Medicine, Eskisehir;* [5]*Rheumatology, Bakırkoy Sadi Konuk Education and Research Hospital, Istanbul;* [6]*Rheumatology, Van Education and Research Hospital, Van;* [7]*Rheumatology, Uludag University, School of Medicine, Bursa;* [8]*Rheumatology, Selcuk University, School of Medicine, Konya;* [9]*Rheumatology, Antalya Education and Research Hospital, Antalya;* [10]*Rheumatology, Sakarya Education and Research Hospital, Sakarya, Turkey*

Background: IgA Vasculitis is a leukocytoclastic vasculitis involving small vessels with depositions of immune complexes containing IgA. There is limited data for the prognosis of adult IgA Vasculitis, with also no damage assessment.
Objectives: We aimed to evaluate the clinical characteristics, treatment, outcome and damage of patients with adult IgA Vasculitis.
Methods: We assembled a retrospective cohort of patients with adult IgA Vasculitis, from tertiary Rheumatology Centers in Turkey. All data were abstracted from medical records. Birmingham Vasculitis Activity Score (BVAS),prognostic Five Factor Score (FFS) and vasculitis damage index (VDI) were calculated.
Results: The study included 52 (male/female:40/12) patients with adult IgA Vasculitis. The mean age was 42.2±17 years. Infection history within 6 weeks before presentation was present in 22 (42.3%) patients (18 upper respiratory tract,3 gastrointestinal and 1 urinary tract). Cutaneous manifestations were the most common clinical manifestations (Table 1). All patients were treated with oral glucocorticoids (GC).As additional immunosuppressive agents, azathiopirine was given to 21 (40.4%) and pulse cyclophosphamide to 11 (21.2%) patients. Twenty-eight patients (53.9%) had follow-up of 28.6 months. Five (17.8%) patients relapsed during follow-up. While 3 relapses were major, 2 of them were minor relapses. At the last visit, disease status was evaluated as active or treatment failure by the treating physician in 6 (21.4%) patients. Mortality was 3.6% (n=1) during follow-up, due to pneumonia. The mean VDI score was 0.6 in the last visit. Nine (32.1%) patients had at least one damage item at the end of follow-up period.

Table 1. Clinical characteristics of patients with adult IgA Vasculitis

	Adult IgA Vasculitis (n=52)
Laboratory parameters	
Erythrocyte Sedimentation Rate (mm/hour)*	32.7±22
C-reactive protein (mg/l)†	25.2 (1–94.9)
Proteinuria (>300mg/24 hours)	28 (53.9%)
Creatinine (mg/dl)*	0.9±0.4
Clinical Manifestations, n/52 (%)	
Fever	7 (13.5%)
Weight loss	14 (26.9%)
Myalgia/Weakness/Leg tenderness	24 (46.2%)
Arthritis and/or arthralgia	46 (88.5%)
Neurologic manifestations	1 (1.9%)
Testicular pain or tenderness	3 (5.8%)
Recent onset or severe hypertension	2 (3.8%)
Cutaneous Manifestations	48 (92.3%)
Gastrointestinal manifestations	39 (75%)
FFS=0	29 (55.8%)
FFS=1	15 (28.8%)
FFS≥2	8 (15.4%)
BVAS score at diagnosis*	4.1±1.7

FFS: Five Factor Score, BVAS: Birmingham Vasculitis Activity score. *Mean ± SD; †Median (Minimum–maximum.)

Conclusions: Our results showed that approximately one fifth of patients with adult IgA Vasculitis had relapses during follow-up. At the end of follow-up, one third of patients had at least one damage item. Although, 45% of patients had FFS≥1, the mortality rate was observed to be low in the present study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3865

FRI0323 COMPARISON OF BIOPSY PROVEN GIANT CELL ARTERITIS IN NORTH AMERICA AND SOUTHERN EUROPE: A POPULATION-BASED STUDY

F. Muratore[1], C.S. Crowson[2], L. Boiardi[1], M.J. Koster[2], G. Restuccia[1], T.A. Kermani[3], E.L. Matteson[2], C. Salvarani[1], K.J. Warrington[2]. [1]*Rheumatology Unit, Arcispedale Santa Maria Nuova IRCCS, Reggio Emilia, Italy;* [2]*Division of Rheumatology, Mayo Clinic, Rochester, MN;* [3]*Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, United States*

Objectives: To compare clinical characteristics, treatment, long-term follow-up and prognosis of two population-based cohorts of patients with biopsy-proven giant cell arteritis (GCA) from Olmsted County, Minnesota, USA (Olmsted cohort) and the Reggio Emilia area, Northern Italy (Reggio cohort).
Methods: All patients residing in Olmsted County and the Reggio Emilia area

with a new diagnosis of biopsy-proven GCA in 1986–2007 were retrospectively identified. Patients were followed from GCA diagnosis to death, migration or September 2011. Comparisons were performed using Chi-square and rank sum tests, Kaplan-Meier methods and Cox models.
Results: The study included 110 patients in the Olmsted and 144 in the Reggio cohort. Compared with the Olmsted cohort, patients from the Reggio cohort were younger (mean±SD age 74.6±7.4 years vs 77.8±7.6, p=0.002), more likely to have cranial symptoms (93% vs 86%, p=0.048), temporal artery abnormalities at physical examination (68% vs 42%, p<0.001), partial or complete unilateral or bilateral permanent vision loss (21% vs 6%, p=0.001), systemic symptoms (67% vs 46%, p=0.001) and polymyalgia rheumatica at or before GCA diagnosis (47% vs 26%, p<0.001). Scalp tenderness was less common in the Reggio cohort (36% vs 49%, p=0.033). ESR and CRP were higher (mean 88±29 mm/h vs 73±77, p<0.001 and mean 89.0±60.2 mg/L vs 35.2±43.4, p<0.001 respectively) and hemoglobin lower (mean 11.2±1.4 g/dl vs 11.8±1.4, p=0.004) in Reggio than in the Olmsted cohort. Patients from the Olmsted cohort received a higher initial prednisone dose (mean 53.6±15.3 mg/day vs 49.5±12.8, p=0.001). There were no differences in relapse rates, cumulative glucocorticoid (GC) dosages at 1, 2 and 5 years, and time to first GC discontinuation. However, the Reggio cohort reached a prednisone dose <10 mg/day sooner (median 4.9 months vs 7.9, p=0.012) and had a first relapse later (median 13.6 months vs 7.9, p=0.003) than the Olmsted cohort. Patients from the Reggio cohort had a significantly higher mortality compared to those from the Olmsted cohort (HR 1.72, 95% CI 1.12–2.65 adjusted for age and sex).
Conclusions: Genetic and/or environmental factors may contribute to the differences in clinical characteristics and disease outcomes observed in this study comparing patients with GCA from North America and Southern Europe.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5156

FRI0324 SMALL VESSEL VASCULITIS SURROUNDING A PRESERVED TEMPORAL ARTERY: A DIAGNOSTIC ALGORITHM TO ASSESS CLINICAL SIGNIFICANCE

G. Espigol Frigole[1], M. Terenas[2], S. Prieto-Gonzalez[1], R. Alba[3], J. Hernandez-Rodriguez[1], E. Planas-Rigol[3], M. Corbera-Bellalta[3], N. Terrades[3], M.C. Cid[1]. *[1]Systemic and Autoimmune Diseases Department, Hospital Clinic of Barcelona, Barcelona, Spain; [2]Medicine Department, Hospital de Santa Maria, Lisboa, Portugal; [3]Institut d'Investigacions Biomèdiques Pi i Sunyer (IDIBAPS). CELLEX, Barcelona, Spain*

Background: Systemic vasculitides are complex and heterogeneous diseases with overlapping features that frequently pose a diagnostic challenge to clinicians. The temporal artery biopsy (TAB) is the gold standard for the diagnosis of giant cell arteritis (GCA) but, occasionally, TAB show inflammation of small vessels surrounding a spared temporal artery (SVV) as the only pathologic finding. Ultimate diagnosis and, consequently, optimal treatment remain uncertain in these patient.
Objectives: To analyze the final diagnosis of patients with SVV surrounding a spared temporal artery after a pre-established diagnostic algorithm and to identify clinical and laboratory findings with potential usefulness in predicting the ultimate diagnosis.
Methods: Patients with TAB showing SVV were subjected to the diagnostic algorithm displayed in figure 1, completed by at least 1 year follow-up. Clinical and laboratory features at the time of diagnosis were recorded. The algorithm led to the following final diagnosis: GCA, other systemic vasculitis and undetermined condition. Chi-squared and ANOVA tests were used for statistical comparison using IBM SPSS Statistics 20.
Results: From 1998 to 2007, 380 TAB were performed in our institution. Biopsy disclosing small vessel inflammation surrounding a normal temporal artery (SVV) was described in 47 (12%) patients. In all patients TAB was selected as the first invasive procedure because GCA was initially considered the most likely diagnosis. Accordingly, 24 (51%) fulfilled at least 3 ACR classification criteria for GCA. 7 patients declined to undergo subsequent work-up to complete the diagnostic algorithm, 10 died or were lost to follow –up before completing 1 year. All of them were excluded. The study cohort consisted of 30 patients (19 women and 11 men) aged 77±10.4 years followed for 55.16±55.20 months. In 13 patients the final diagnosis was consistent with GCA based on the absence of SVV in other territories, large-vessel inflammation by imaging or subsequent development of aortic aneurysm; in 12 SVV was subsequently demonstrated in other territories and were diagnosed with other systemic vasculitis (7 AAV, 0 cryo, 3 PAN, 0 vasculitis associated to autoimmune diseases, 2 unclassified small vessel vasculitis), and in 5, diagnosis remained undetermined. No significant differences in clinical or routine laboratory abnormalities were found among patient subgroups stratified according to the final diagnosis.
Conclusions: Inflammation of small vessels surrounding a spared temporal artery in a TAB conveys a substantial diagnostic uncertainly. After a detailed diagnostic work-up most of patients can be diagnosed with GCA. However other systemic vasculitis requiring more aggressive treatment may disclose similar histopathologic findings and are also frequent and diagnosis remains uncertain in a substantial proportion of cases. Search for more accurate molecular biomarkers is necessary for a better interpretation of these findings
Acknowledgements: "Supported by PI15/00092, Plan Estatal de Investigación Científica y Técnica de Innovación 2013–2016 y cofinanciado por el ISCIII-Subdirección General de Evaluación y el Fondo Europeo de Desarrollo Regional (FEDER)"
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5504

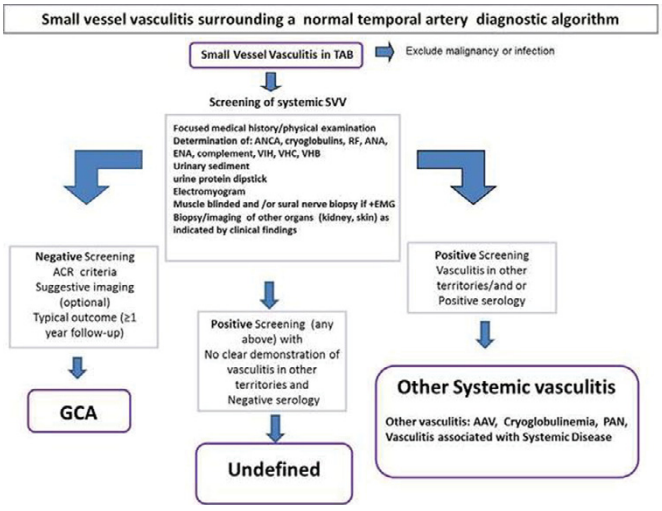


Figure 1

FRI0325 PREVALENCE OF TAKAYASU ARTERITIS IN YOUNG WOMEN WITH ACUTE ISCHEMIC HEART DISEASE

G. Cavalli, A. Tomelleri, E. Baldissera, L. Dagna. *Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UniRAR), Vita-Salute San Raffaele University, Milan, Italy*

Background: Takayasu arteritis (TA), a systemic vasculitis typically occurring in female patients aged ≤40, can affect the coronary arteries and cause ischemic heart disease. The prevalence of TA among young females with acute ischemic heart disease is undetermined.
Objectives: In this study, we investigated the prevalence of TA in young women presenting with ischemic heart disease in the Emergency Department.
Methods: We conducted a retrospective evaluation of the hospital records of 172,790 consecutive female patients aged <45, who accessed the Emergency Department of our institution over 8 consecutive years (2007–2015). The prevalence of TA and of other etiologies of ischemic heart disease was determined. Diagnosis of TA was established based on the 1990 American College of Rheumatology criteria.
Results: Overall, 2,090 women aged <45 presented to the Emergency Department with chest pain, dyspnea, palpitations, angina, heart failure, or cardiac arrest; 40 had confirmed acute ischemic heart disease. The etiology was "classic" atherosclerosis in 24 cases (60%), TA in 4 cases (10%), vasospasm and sympathomimetic drug abuse in 3 cases each (7.5%), coronary artery dissection and microvascular angina in 2 cases each (5%), Takotsubo and radiation-induced cardiomyopathy in 1 case each (2.5%).
Conclusions: Although a diagnosis of TA is likely to be overlooked, TA is not infrequent in younger females presenting with acute ischemic heart disease. Specifically, TA accounted for 10% of cases of acute ischemic heart disease in female patients aged <45, a finding relevant to the diagnosis and management of these young patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2298

FRI0326 RECOMMENDATIONS FOR THE MANAGEMENT OF NEURO-BEHÇET DISEASE BY JAPANESE RESEARCH COMMITTEE FOR BEHÇET DISEASE

H. Kikuchi[1], T. Sawada[2], M. Okada[3], M. Takeno[4], M. Kuwana[4], Y. Ishigatsubo[5], I. Kawachi[6], H. Mochizuki[7], S. Kusunoki[8], S. Hirohata[9]. *[1]Department of Internal Medicine, Teikyo University School of Medicine; [2]Department of Internal Medicine 3, Tokyo Medical University School of Medicine; [3]Immuno-Rheumatology Center, St. Luke's International Hospital; [4]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo; [5]Department of Internal Medicine and Clinical Immunology, Yokohama City University Graduate School of Medicine, Yokohama, Japan, Kanagawa; [6]Department of Neurology, Niigata University Medical and Dental Hospital, Niigata; [7]Department of Neurology, Osaka University Graduate School of Medicine; [8]Department of Neurology, Kinki University School of Medicine, Osaka; [9]Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Kanagawa, Japan*

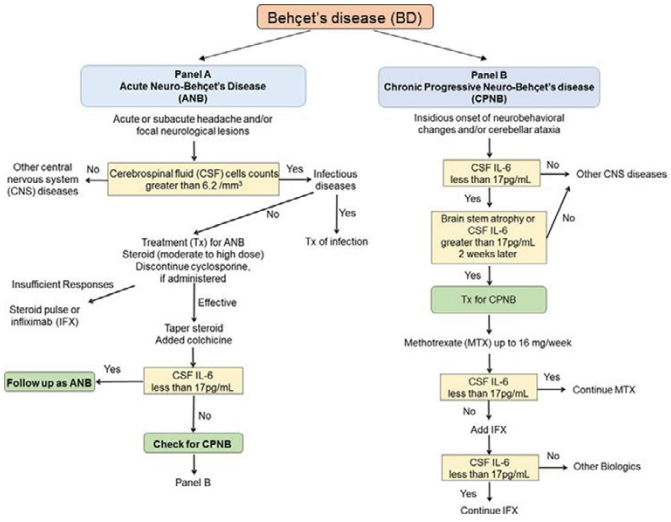
Background: Central nervous system involvement is one of the most serious complications in Behçet's disease (BD). This condition is referred to as neuro-

Behçet's disease (NB) and can be classified into acute type (ANB) and chronic progressive type (CPNB) based upon differences in the clinical course and responses to corticosteroid treatment. Diagnostic criteria were generated in 2013 based on a multicenter clinical survey performed by the Behçet's Disease Research Committee of the Ministry of Health, Labor and Welfare of the Japanese Government. Although "Guidelines for Treatment of NB" was also proposed based on the survey, it is still preliminary.

Objectives: The aim of the current study is to develop evidence-based recommendations for the management of NB supplemented by expert opinions where necessary.

Methods: First, clinical questions (CQs) on NB were extracted from a literature search for problem areas and related keywords, and draft CQs and a flow chart were prepared. The expert committee, a task force of the research subcommittee for NB, consisted of 7 board-certified rheumatologists (one was also a board-certified neurologist) and 3 board-certified neurologists. A systematic literature search was performed using Medline and the Japan Medical Abstract Society databases from 1997 to 2016. A total of 15 initial CQs were generated. These yielded the final recommendations developed from 3 blind Delphi rounds, in which the rate of agreement scores on CQs (range 1 [disagree]–5 [strongly agree]) was determined though voting by the whole committee.

Results: Thirteen recommendations were developed for the management of NB (general 1, ANB 7, CPNB 5). The strength of each recommendation was established based on the evidence level as well as rate of agreement. There was excellent concordance between the level of agreement of rheumatologists and that of neurologists. Based on these recommendations, a flow chart was established for the management for ANB and CPNB (Figure).



Conclusions: The recommendations generated in this study are mainly based not only on expert opinions but on the results of uncontrolled evidence from open trials and retrospective cohort studies. Guidelines that can be used for international studies are needed, for which verification by further properly designed controlled clinical trials is required.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1201

FRI0327 GASTROSCOPIC FEATURES AND CLINICAL CHARACTERISTICS IN 172 CASES OF CHILDREN WITH HENOCH-SCHONLEINPURPURA

H. Zeng. *Department of Pediatric Allergy, Immunology and Rheumatolog, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: To investigate gastroscopic features and explore the relationship between clinical characteristics in children with Henoch-Schonleinpuepura (HSP).

Methods: To take gastroscope in 172 cases of children with HSP in our hospital and summarize the gastroscopic performance.All the case were divided into two groups by gastroduodenal mucosal bleeding or not.It was compared among the total time of abdominal pain, pain relief, hospitalization, fasting and kidney injury case in the groups.

Results: Gastroscope with varying degrees of injury of 172 cases has accounted for 169 cases (98.3%).Gastroscopic mainly revealedgastroduodenal mucosal congestion, edema, rough, erosion, bleeding and ulcer, which involved 148 cases of gastric (86.0%), 158 cases of duodenal involvement (91.9%). Mucosal erosion and bleeding occurs mainly in duodenum,mostly in the descending duodenum. Duodenal bleeding accounted for 36 cases (21.8%) in the bulb and 92 cases (55.8%) in the descendant. Only five cases (2.9%) of ulcer occurred in the duodenum, where four cases of bulbar ulcer, one case of descending ulcer. Esophageal and gastric cardia mucosal just occurred in one case. There were not significant difference ($P>0.05$) among the time of abdominal pain, pain relief, hospitalization and fasting in the group. There was no significant difference ($P>0.05$) in the incidence of kidney injury between two groups of children during hospitalization.

Conclusions: Gastroscopic features of HSP in children is characterized by bleeding, erosion of duodenal mucosa and occasional duodenal ulcer formation, which mostly involve the antral mucosa, rarely involving the esophagus, cardia. There was no significant difference ($P>0.05$) among the severity of gastroscopic performance and the time of abdominal pain, fasting,hospitalization and kidney injury of the cases during hospitalization.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2127

FRI0328 THE DIAGNOSTIC VALUE OF ALPHA-1-ANTITRYPSIN PHENOTYPE IN SYSTEMIC VASCULITIS

I. Belyaeva[1], A. Chudinov[2], M. Pervakova[3], V. Mazurov[1], S. Lapin[3], O. Inamova[2]. *[1]North-West State Medical University named after I.I. Mechnikov, Saint-Petersburg, Russia; [2]Clinical Rheumatological Hospital #25, Saint-Petersburg, RUSSIA; [3]First Pavlov State Medical University of St. Petersburg, Saint-Petersburg, Russian Federation*

Background: Deficiency of alpha-1 protease inhibitor, or alpha-1-antitrypsin (A1AT) is a frequent genetic disorder, which is characterized by low serum level of A1AT and usually manifests as pulmonary emphysema and liver disease. Also the deficiency of A1AT is known to be associated with granulomatosis with polyangiitis (GPA). The influence of A1AT deficiency on GPA clinical course is not clarified.

Objectives: The aim of this study was to estimate the prevalence of pathological A1AT phenotypes in GPA and other systemic vasculitis and to define the influence of A1AT phenotype on clinical course of GPA.

Methods: We enrolled 86 patients with systemic vasculitis, including GPA (N=47), microscopic polyangiitis (MPA, N=16), eosinophilic granulomatosis with polyangiitis (EGPA, N=12), polyarteriitisnodosa (PN, N=11). 46 healthy donors were included in the control group. All blood samples underwent A1AT phenotyping by isoelectrofocusing (IEF) and turbidimetric A1AT measurement. The results of phenotyping were compared to clinical data, such as BVAS activity rate (Birmingham Vasculitis Activity Score), VDI index (vasculitis damage index), organs involvement, inflammatory markers, including antineutrophil cytoplasmic antibodies (ANCA), total IgG concentration and serum levels of C3, C4 complement factors.

Results: Pathological A1AT phenotypes were found in 17% (8/47) of GPA patients, 6,25% (1/16) of MPA patients, 2% (1/46) of healthy donors and were never found in EGPA, PN. The abnormal phenotypes in GPA were 1PiZZ, 4PiMZ, 2PiMF, 1PiMS, and 1PiMS phenotype was identified in MPA patient. Lesion of lung and upper respiratory tract was observed in all patients with pathological phenotypes A1AT (N=8), while in normal phenotype A1AT it was present in 72% and 82% respectively. The mean concentration of A1AT was significantly lower in GPA patients with abnormal A1AT phenotypes, than in patients with normal phenotype A1AT (respectively 1003±148.8 and 1964±127.9 mg/L, $p<0,01$). The average activity by BVAS index in GPA was significantly higher in patients with pathological phenotype A1AT than in patients with normal phenotype A1AT (24,63±2,897 and 18,05±1,444 points, $p<0,05$). Also we revealed excess levels of VDI in cohort of patients with abnormal phenotype A1AT rather, than in cohort of patients with normal phenotype A1AT (6,3±3,1 versus 5,4±2,6, $p<0,05$). The average values concentration of antibodies to proteinase-3 in GPA patients with abnormal phenotype A1AT were significantly higher compared to GPA patients with normal phenotype A1AT (respectively 142,4±25,24 and 86,784±14,98 RU/ml, $p<0,05$). In GPA patients with mutated A1AT phenotypes levels of serum creatinine concentrations ($p<0,01$), levels of total IgG concentration and serum levels of C3 and C4 complement factors ($p<0.05$) also were significantly higher than in group of GPA patients with normal A1AT phenotype.

Conclusions: Pathological A1AT phenotypes are more often observed in GPA patients who have more severe GPA clinical course and higher immunological disease activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4412

FRI0329 EFFICACY AND SAFETY OF INFLIXIMAB ORIGINATOR IN PATIENTS WITH TAKAYASU ARTERITIS WITHIN THE RTU (TEMPORARY RECOMMENDATION OF USE) IN FRANCE

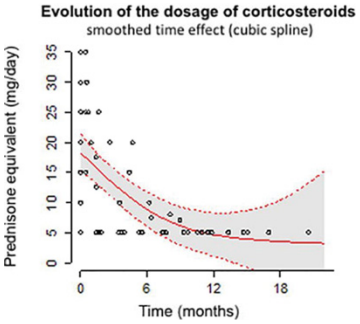
J.-F. Kleinmann[1], L. Arnaud[1], E. Sauleau[2], N. Gouyette[3], R. Tajima[1], J. Sibilia[1] on behalf of CRI (Club Rhumatismes et Inflammation). *[1]Rheumatology; [2]Public Health, Strasbourg's University Hospital, Strasbourg; [3]MSD France, Courbevoie, France*

Background: The benefit/risk ratio of infliximab in refractory patient with Takayasu arteritis (TA) is assumed to be favorable, based on retrospective studies with limited sample size [1, 2] in which infliximab has been prescribed off-label.

Since 2013, the French Temporary Recommendation of Use (RTU) provides a temporary framework allowing the use of infliximab originator in "TA patients refractory to conventional treatment" during a 3-year period.

Objectives: The aim of the study was to evaluate the real-life efficacy and safety of infliximab originator in TA patients initiating or with ongoing infliximab treatment.

Methods: Prospective, multicenter, observational, open-label, study of TA patients treated with infliximab originator.
Results: As of 2016 (2 years of follow-up), the study included 14 patients (13/14 were female; median age 32 [range 12–56] years) with TA (diagnosis according to Ishikawa criteria). At study entry, the median TA duration was 4.7 (0.4–16) years, 12 patients were already treated with infliximab originator (for a median duration of 34 [1–78] months) and 11 patients were receiving corticosteroids (CS).
Infliximab originator was administered at a median dose of 5 (3–6) mg/kg with a median interval of 8 (2–67) weeks between each infusion. Seven patients had an improvement in at least 1 of the NIH disease activity criteria for TA [3] after a median follow-up time of 2 (0.4–11) months), 4 had smoldering disease and 1 patient worsened.
The median daily dose of CS decreased from 13 (5–35) mg/day of prednisone or equivalent at baseline to 7 (5–10) mg/day at 6 months, to 5 (5–6) mg/day at 12 months, and remained stable up to 22 months of follow-up.
Infliximab was discontinued in 6 patients due to inefficacy (n=3), prior to pregnancy (n=2), or remission of TA (n=1). Two adverse events (1 disease flare and 1 spontaneous miscarriage) were reported, without infliximab interruption.



Conclusions: Infliximab originator appears to provide an effective and favourable benefit:risk treatment option to refractory TA patients.
References:
[1] Mekinian et al, Efficacy of Biological-Targeted Treatments in Takayasu Arteritis: Multicenter, Retrospective Study of 49 Patients, Circulation 132(18) (2015) 1693–700.
[2] Mekinian et al, Efficacy and tolerance of infliximab in refractory Takayasu arteritis: French multicentre study, Rheumatology (Oxford) 51(5) (2012) 882–6.
[3] Kerr and al. Takayasu arteritis. Ann Intern Med. 1994; 120: 919–29.
Acknowledgements: The patients were included by AP-HP Cochin (Dr X Puéchal), CHU Angers (Dr C Lavigne), CHU Tours (Pr E Diot), CHU Besançon (Pr N Magy, Dr H Gil), CHU Lille (Pr E Hachulla, Pr M Lambert, Dr H Maillard), AP-HP Kremlin-Bicêtre (Pr I Koné-Paut), AP-HM Marseille (Pr JR Harlé, Dr N Schleinitz), HEGP Pompidou (Dr JE Kahn), CH Royan (Dr A Bonnin), CHU Strasbourg (Pr T Martin, Dr V Poindron), CHU Bordeaux (Pr J Constans).
Disclosure of Interest: J.-F. Kleinmann Consultant for: MSD, L. Arnaud: None declared, E. Sauleau Consultant for: MSD, N. Gouyette Employee of: MSD, R. Tajima: None declared, J. Sibilia Consultant for: MSD
DOI: 10.1136/annrheumdis-2017-eular.1793

FRI0330 FATIGUE AND DEPRESSION IN PATIENTS WITH BEHCET'S DISEASE

J.L. Silva, D. Santos-Faria, J. Sousa-Neves, J. Rodrigues, J. Costa, C. Afonso, D. Peixoto. *Rheumatology, ULSAM, Ponte de Lima, Portugal*

Background: Behcet's disease (BD) is a systemic vasculitis of unknown etiology defined by a classic triad consisting of aphtous ulcers of the mouth and genital and uveitis. In addition to these, BD may involve cardiovascular, pulmonar, neurological, articular and gastrointestinal manifestations. Fatigue, anxiety and depression are important problems in chronic inflammatory diseases. There are few studies on fatigue in BD patients. *Ilhan et al.* [1] reported more fatigue in BD patients than in healthy controls.
Objectives: The objective of this study was to investigate fatigue and depression in patients with BD and to examine the relationship between these symptoms and disease activity and gender.
Methods: Forty four patients with BD and thirty nine healthy controls (HC) were included in this study. Age, gender, disease duration and clinical involvements were recorded. All subjects completed the FACIT Fatigue Scale (FACIT-F), Short Form-36 (SF-36), Hospital Anxiety and Depression Scale (HADS) and Health Assessment Questionnaire (HAQ). Disease activity among BD patients was assessed using the Birmingham Vasculitis Activity Score (BVAS).
Results: The mean age was 40.0 years for BD patients and 38.7 for HC. 77% of BD patients were women. The mean disease duration for BD patients was 6.1 years. All patients had oral ulcers and genital ulceration; 20 had pseudofolliculitis; 9 had uveitis, 9 had erythema nodosum, 12 had articular involvement, 5 patients had vascular involvement, 4 had pathergia, 1 had orchitis and one had gastrointestinal involvement. Thirty two BD patients were taking medication, including colchicine or DMARDs or their combinations. Seventeen patients had inactive disease and twenty seven had BVAS $\geq$1. As shown in Table 1, both the HADS-depression (HADS-D) (4.7 *vs* 2.5) and HADS-anxiety (HADS-A) (8.3 *vs* 5.7) scores were elevated in BD patients compared to healthy controls. FACIT-F was higher in healthy controls in comparison with BD group (44.1 *vs* 36.6), revealing lower levels of fatigue. There were no differences between gender on these scores.

Table 1. Comparison of BD patients and HC

Scales	BD (n=44)	HC (n=39)	P-value
FACIT-F	36.6±7.3	44.1±6.4	**<0.001**
HADS-D	4.7±2.4	2.5±2.4	**0.004**
HADS-A	8.3±4.2	5.7±2.8	**0.03**

There were no significant differences in FACIT-F, HADS-A and HADS-D scores with the disease activity (P=0.952, P=0.391 and P=0.286, respectively).
FACIT-F had a negative correlation with HAQ and HADS and a positive correlation with the different components of SF-36 and age. FACIT-F score was not correlated with disease duration (Table 2).

Table 2. Correlations between FACIT-F and HAQ, HADS-A, HADS-D, SF-36, age, disease duration in BD

	HAQ	HADS-A	HADS-D	SF-36	Age	Disease duration
r-value	-0.670	-0.569	-0.562	0.857	-0.370	0.053
P-value	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.013**	0.103

Conclusions: In our study, fatigue and increased levels of anxiety and depression were more common in BD patients. Contrary to the study of *Ilhan et al* [1], we found that fatigue was not higher in patients with active disease. Similarly, there were no correlation between the assessed scores and gender. In spite of these results, the authors believe that controlling the symptoms may improve the quality of life in BD patients.
References:
[1] Ilhan et al. Fatigue in patients with Behcet's syndrome: relationship with quality of life, depression, anxiety, diability and disease activity. International Journal of Rheumatic Diseases. 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4459

FRI0331 IDENTIFICATION AND VALIDATION OF POTENTIAL METABOLOMIC BIOMARKERS FOR RELIABLE DIAGNOSIS OF BEHCET'S DISEASE USING GAS CHROMATOGRAPHY WITH TIME-OF-FLIGHT MASS SPECTROMETRY

J.K. Ahn[1], J. Hwang[2], H.-S. Cha[3], E.-M. Koh[3]. *[1]Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine; [2]Department of Internal Medicine, Natonal Police Hospital; [3]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic Of*

Background: Although many diagnostic criteria have been developed and revised by experts in the field, diagnosing Behcet's disease (BD) is still complicated and challenging. Metabolomic studies can lead to a better understanding of pathophysiological processes and may uncover new diagnostic markers for classification of disease subgroups and assessment of disease activity in rheumatic diseases. No metabolomic studies on serum have been attempted to improve the diagnosis and to identify potential biomarkers of BD.
Objectives: The purposes of this study were to investigate distinctive metabolic changes in serum samples of BD patients and to identify metabolic candidate biomarkers for reliable diagnosis of BD using the metabolomics platform.
Methods: Metabolomic profiling of 90 serum samples from 45 BD patients and 45 healthy controls (HC) was performed via gas chromatography with time-of-flight mass spectrometry (GC/TOF-MS) with multivariate statistical analyses. Thirty-five patients with BD and age- and sex-matched 35 HCs were randomly selected to form the discovery set, and the validation set is composed of 10 patients with BD and 10 HCs.
Results: We identified a total of 104 metabolites in the serum samples of the discovery set. To maximise the discrimination between groups BD and HCs, we applied supervised partial least squared-discrimination analysis (PLS-DA). A PLS-DA score plot of the discovery set indicated that the cluster of BD patients is well separated from HC clusters in component 1. The variation values of the PLS-DA model are R^2X of 0.246, R^2Y of 0.913, and Q^2 of 0.852, respectively, indicating strong explanation and prediction capabilities of the PLS-DA model. The PLS-DA models did not show clear and consistent discrimination between groups according to drug administration, indicating that drugs used in patients with BD had a negligible effect on the distinct metabolic profiles discriminating BD patients from HCs. A panel of five metabolic biomarkers, namely, decanoic acid, fructose, tagatose, linoleic acid, and oleic acid were selected based on their variable importance on projection values and adequately validated as putative biomarkers of BD (sensitivity 100%, specificity 97.1%, area under the curve 0.993) in the discovery set and validation set. Principal component analysis showed clear discrimination of BD and HC groups by the five metabolic biomarkers in the validation set.
Conclusions: This is the first report on detection of a characteristic metabolic profile of BD and identifying and validating potential metabolite biomarkers in

serum from BD patients using GC/TOF-MS. Further studies including a larger number of patients with BD would be warranted to validate the metabolite profiles for clinical use and to ascertain the feasibility of metabolomic analysis in BD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3104

FRI0332 DIFFERENCES BETWEEN TEMPORAL ARTERY BIOPSY-POSITIVE AND BIOPSY-NEGATIVE GIANT CELL ARTERITIS: A COMPARATIVE COHORT STUDY

K. Yeruva, K.J. Warrington, C.S. Crowson, M.J. Koster. *Rheumatology, Mayo Clinic, Rochester, United States*

Background: Giant cell arteritis (GCA) is the most common systemic vasculitis in patients aged 50 years or older. The presence of cranial features and an abnormal temporal artery biopsy have historically been the primary focus for diagnosis of this condition. A notable percentage of patients with symptoms of GCA have negative temporal artery biopsies, however, few cohort studies exist comparing the presentation and outcome of patients based on temporal artery positivity.
Objectives: To establish a large, single institution cohort of patients with temporal artery biopsy-negative GCA. To identify differences in presentation and outcome among patients with temporal artery biopsy-negative and temporal artery biopsy-positive GCA.
Methods: Patients with temporal artery biopsy-negative GCA diagnosed between 1/1/1998 and 12/31/2013 were identified retrospectively. Final diagnosis was confirmed by consensus among two rheumatologists and a physician abstractor. Baseline characteristics and outcomes were compared to a previously established biopsy-positive GCA cohort (n=286) from the same institution.
Results: 110 patients with temporal artery biopsy-negative GCA were identified. Unilateral biopsies were performed in 73, bilateral-sequential in 10, and bilateral same day in 27 cases. Median duration between steroid initiation and biopsy was 3 days. Median length of first biopsy was 14mm and second biopsy (if performed) was 22mm. Among biopsy-negative patients with advanced imaging within 6-months of diagnosis, 67% (41/61) had evidence of large vessel vasculitis. Patients with biopsy-negative GCA were younger (72.0±9.0 vs 75.0±7.6; p=0.001), met fewer ACR criteria ($\geq$3 criteria 64% vs 95%; p<0.001) and had a shorter time from symptom onset to diagnosis (median 1.1 vs 2.1 months; p<0.001). Vascular risk factors evaluated at diagnosis showed a higher rate of pre-existing hypertension and obesity among patient with biopsy-negative GCA but similar rates of smoking and diabetes mellitus. Frequency of headache and vision loss at time of presentation were similar between groups. However, biopsy-negative GCA patients had more temporal artery tenderness (35% vs 16%; p<0.001) and arm claudication (13% vs 2%; p<0.001) but less frequent jaw claudication (19% vs 52%; p<0.001). Anorexia, fatigue, and arthralgia were also more commonly noted in biopsy-negative patients. Baseline CRP was lower among patients with negative biopsies (44.3±53.6 vs 70.4±63.9 mg/L; p<0.001).
Initial prednisone dose was similar among both cohorts. Although cumulative glucocorticoid (GC) was lower in biopsy-negative patients at 1 year (6.3±2.6 vs 7.2±2.7 g; p=0.004), cumulative GC doses at 2-years and 5-years were equivalent. Biopsy-positive patients (5-years, 56±3%) were able to discontinue GC sooner than biopsy-negative patients (5-years, 30±5%; p<0.001). The number of relapses, time-to-first relapse, annual relapse rate and mortality did not differ based on biopsy positivity.
Conclusions: While similarities are present, notable differences are observed at diagnosis in patients with biopsy-negative GCA. Further research is needed to confirm and understand the variability in GC duration.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1936

FRI0333 OCULAR INVOLVEMENT IN BEHÇET'S DISEASE ABOUT 221 CASES

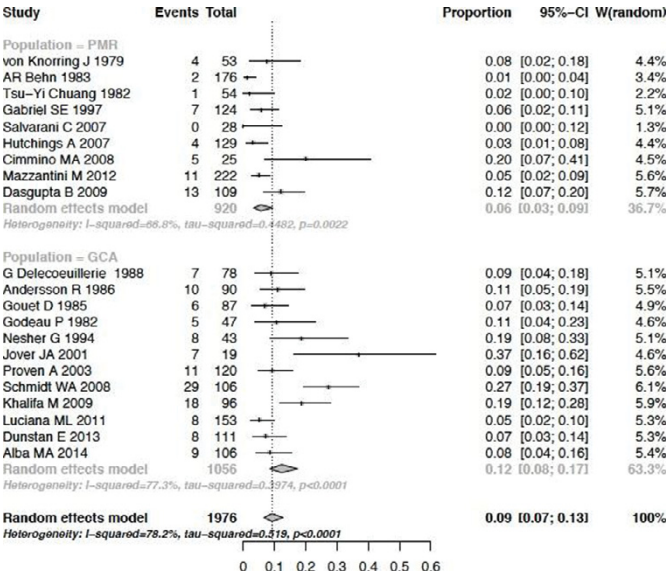
K. Echchilali, W. Bouissar, M. Moudatir, F.-Z. Alaoui, H. Elkabli. *Internal Medicine Department, University Hospital Centre Ibn Rochd, Casablanca, Morocco*

Background: Behçet's disease (BD) is a chronic systemic inflammatory disorder of unknown etiology. It's chracterised by recurrent oral aphtosis and genital ulcer. Ocular involvement has been recognized since the time of Hypocrates. Estamates of the prevalence vary in different countries and may represent differences in the disease, in acces to health care and in availabale treatments.
Objectives: The aim of this study is to describe the epidemiological and clinical characteristics in moroccan patients with ocular BD.
Methods: retrospective study in internal medicine department over 13 years and including 221 patients with ocular BD. The diagnosis was performed by the International Study Group for Behçet's Disease and/or the International Criteria for Behçet's Disease.
Results: 221 (prevalence: 43%) had ocular involvement.154 men and 63 women (sex ratio: 2.5). The mean age at the onset of ocular involvement was 30.5 years. This achievement was inaugural in 18.55% of cases. The average time of diagnosis in other cases was 3.41 years.There was a high prevalence of Uveitis (total: 34%, anterior: 32%, posterior: 31.2). Retinal Vasculitis was noted in 37 eyes and retinal detachment in 17 eyes. Neurological events were associated in 13.57% of cases, joint and vascular events in respectively 18 and 17 cases. The topical corticosteroid therapy was prescribed in 27, 14% of cases, oral in 47, 51% and bolus in 29, 41%. 47, 51% of casers received Cyclophosphamide and 19% received Azathioprine. Cyclosporine was administered in 3 cases, interferon and Infkiximab in 2 cases each. The evolution was good in 111 cases (50.22%), treatment failure was noted in 24% of cases and recidivism in 16.74% of cases.63 patients have evolved into blindness which was bilateral in 51.1% of cases.
Conclusions: Only early diagnosis and appropriate management can improve the prognosis of ocular involvement in BD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5961

FRI0334 WHAT IS THE ABSOLUTE RISK OF DEVELOPING DIABETES MELLITUS IN PATIENTS WITH GLUCOCORTICOID-TREATED POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS? A SYSTEMATIC REVIEW AND META-ANALYSIS

L. Lai[1], E. Harris[1,2], R.M. West[3], S.L. Mackie[1,4]. *[1]Leeds Institute for Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]School of Human and Health Sciences, University of Huddersfield; [3]Leeds Institute of Health Sciences, University of Leeds; [4]NIHR-Leeds Musculoskeletal Biomedical Research Unit, Leeds, United Kingdom*

Background: Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are treated with glucocorticoids (GCs) but long-term GC use is associated with diabetes mellitus (DM). The absolute incidence of this serious complication in this patient group remains unclear.
Objectives: To quantify the absolute risk of GC-induced DM in PMR and GCA in published literature.
Methods: We identified literature from inception to February 2016 reporting diabetes following exposure to oral GC in patients with PMR and/or GCA without pre-existing diabetes. A random-effects meta-analysis was performed to summarise the literature. Risk of bias was assessed using the Cochrane Collaboration tool.
Results: 21 eligible publications were identified. In studies of patients with GCA, mean cumulative GC dose was almost two times higher than in studies of PMR (8.9g vs 5.0g), with slightly longer treatment duration but much longer duration of follow-up (8.8years vs 4.4years). The incidence proportion (cumulative incidence) of patients who developed new-onset DM was 6% (95% CI: 3–9%) for PMR and 12% (95% CI: 8–17%) for GCA. Heterogeneity between studies was high (I^2=78.2%), as there were differences in study designs, patient population, geographical locations and treatment strategies. Based on UK data on incidence rate of DM in the general population[1], the expected background incidence rate of DM over 4.4 years in PMR patients and 8.8 years in GCA patients (the duration of follow-up) would be 4.8% and 9.7%, respectively. Very little information on predictors of DM in PMR or GCA patients was found. The overall risk of bias was high for many of the observational studies, especially relating to definition and recording of outcome and prognostic variables.



Conclusions: Physicians should screen patients treated for PMR/GCA for DM but it remains unclear what is the time-period of greatest risk and the influence of risk factors. Our meta-analysis produced plausible estimates of DM incidence in patients with PMR and GCA but there is insufficient published data to allow precise quantification of the DM risk or, crucially, which patients are at greatest risk.
References:
[1] Sharma M et al. BMJ Open, 2016. 6(1): p.e010210.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4942

FRI0335 EARLIER ONSET AND BRAINSTEM INVOLVEMENT AS KEY FEATURES IN A BRAZILIAN NEURO-BEHÇET'S DISEASE COHORT

L.L. Prado[1], G. Tinone[2], D. Callegaro[2], C.G.S. Saad[1], M. Levy-Neto[1], C. Goncalves[1]. *[1]Rheumatology Division; [2]Neurology Division, Faculdade de Medicina Da Universidade de Sao Paulo, São Paulo, Brazil*

Background: Behçet's disease (BD) is a multisystem disease in which central nervous system involvement – neuro-Behçet's disease (NBD) – may strike young patients with devastating consequences. In this regard, early diagnosis and treatment is essential to prevent injury.
Objectives: This study aimed to analyze NBD clinical features compared to non-neurological BD in order to distinguish disease patterns.
Methods: A retrospective study was performed in 101 BD outpatients from a single tertiary center followed between 2011 and 2016. BD diagnosis was based on the 2014 International Criteria for Behçet's Disease. Demographic, clinical and imaging features of 28 NBD patients were compared to 73 BD patients without neurological involvement.
Results: Earlier disease onset was found in NBD compared to BD (26.0±10.2 vs. 30.2±8.8 years, p=0.04). There were no differences between genders incidences, with a female predominance in both groups (64.3 vs. 72.6%, p>0.05). Over half of patients (53.6%) presented NBD as the first symptom and the mean time between diagnosis and NBD onset was 3.8±5.9 years. Uveitis was less frequent in NBD patients (25% vs. 47.9%, p=0.04), together with cutaneous disease (50% vs. 76.7%, p=0.01) and articular involvement (17.9% vs. 46.5%, p=0.01). Oral ulcers, genital ulcers, intestinal and vascular involvement frequencies were similar in both groups. Regarding NBD presentation, brainstem involvement was the most prevalent (67.9%), followed by central venous thrombosis (32.1%), aseptic meningitis (17.9%), stroke (3.6%) and peripheral neuropathy (3.6%). Most patients (82.1%) had a single neurological attack whereas relapsing disease was found in 18.5%.
Conclusions: Our study found an earlier disease onset in NBD patients and a lower frequency of ocular, cutaneous and articular involvement. Moreover, several patients may unfold the disease as NBD, with lack of other manifestations. In addition, brainstem lesions occurred in most patients. Recognizing these disease patterns might support to expedite NBD diagnosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5514

FRI0336 EFFICACY OF TOCILIZUMAB IN 31 PATIENTS WITH GIANT CELL ARTERITIS

L.C. Domínguez-Casas[1], J. Loricera[1], J.L. Hernández[2], S. Castañeda[3], A. Mera[4], E. Pérez-Pampín[4], E. Peiró[1], A. Humbría[3], J. Calvo-Alén[5], E. Aurrecoechea[5], J. Narváez[6], A. Sánchez-Andrade[7], P. Vela[8], E. Díez[9], C. Moriano[9], P. Lluch[10], C. Moll[10], Í. Hernández[11], V. Calvo-Río[1], J. Ivorra[12], A. Corrales[1], F. Ortiz-Sanjuán[12], C. González-Vela[1], M.Á. González-Gay[1], R. Blanco[1]. *[1]Rheumatology; [2]Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL, Santander; [3]Rheumatology, Hospital Universitario de la Princesa, IIS-IP, Madrid; [4]Rheumatology, Complejo Hospitalario Universitario de Santiago, Santiago de Compostela; [5]Rheumatology, Hospital de Sierrallana, Torrelavega; [6]Rheumatology, Hospital de Bellvitge, Barcelona; [7]Rheumatology, Hospital Universitario Lucus Augusti, Lugo; [8]Rheumatology, Hospital General Universitario de Alicante, Alicante; [9]Rheumatology, Complejo Asistencial Universitario de León, León; [10]Rheumatology, Hospital Mateu Orfila, Menorca; [11]Rheumatology, Complexo Hospitalario Universitario de Vigo, Vigo; [12]Rheumatology, Hospital Universitario y Politécnico la Fe, Valencia, Spain*

Background: Giant cell arteritis (GCA) is often a disease refractory to corticosteroids and, besides, the efficacy of immunosuppressive agents is not well established. In recent years, several case reports and small case series have shown efficacy with the use of tocilizumab (TCZ).
Objectives: Our aim was to assess in a clinical practise setting the short and long-term efficacy of TCZ in GCA patients with refractory disease and/or with unacceptable side effects due to corticosteroids.
Methods: Retrospective multicenter open-label study on 31 GCA patients treated with TCZ [intravenously at standard dose of 8 mg/kg/monthly (n=29), and subcutaneously at a dose of 162 mg/week (n=2)]. We assessed the efficacy on clinical and laboratory parameters, the reduction of the dose of corticosteroids, as well as the short and long-term side effects and the possibility of discontinuation or reduction of the dose of TCZ. Wilcoxon test was used to compare laboratory parameters across time.
Results: We included 31 patients (24 women/ 7 men), with a mean age of 73±9 years. The main clinical features at TCZ onset were: polymyalgia rheumatica (n=21), asthenia (n=8), headache (n=8), constitutional syndrome (n=11), jaw claudication (n=3), and visual loss (n=4). Besides corticosteroids and before TCZ onset, 26 patients had also received several conventional immunosuppressive and/or biologic drugs. Twenty-seven of 31 patients achieved a rapid and maintained clinical improvement after TCZ therapy (Table). After a median follow-up of 18 [interquartile range, 6–30] months we observe a reduction of the median of: a) CRP from 1.9 [1.1–3.7] to 0.1 [0.1–0.7] mg/dL; b) ESR from 44 [17–74] to 12 [4–16] mm/1st hour; and c) the dose of prednisone from 20 [10–45] to 2.5 [0–7.5] mg/day. In this follow-up period, the outcome of patients was as follows: a) discontinuation of TCZ (n=8) due to sustained remission; b) dose reduction due to improvement (n=5) or side effects (n=2); c) withdrawal of TCZ because of side effects (n=7); and d) the same dose that at onset (n=8). The reasons why TCZ had to be discontinued were: severe neutropenia; recurrent pneumonia; colon adenocarcinoma; cytomegalovirus infection; hypertensive crisis during infusion; myelodysplastic syndrome; and overall health deterioration. The latter patient died because of stroke. Another patient also died after the second TCZ infusion due to stroke in the context of an infective endocarditis.

	Baseline	Month 6	Month 12	Month 18	Month 24
Clinical improvement, % (n)		100** (27/27)	95** (20/21)	85** (11/13)	100** (11/11)
Laboratory markers, median [IQR]					
ESR (mm/1st/h)	44 [17-74]** (28)	6 [2-11]** (24)	7.5 [3-23]** (18)	9.5 [2-19]* (12)	6 [2-14]** (10)
CRP (mg/dl)	1.9 [1.1-3.7]** (31)	0.1 [0.1-0.7]** (27)	0.2 [0.1-0.7]** (19)	0.1 [0.1-0.5]* (13)	0.2 [0.1-0.4]** (11)
Dose of corticosteroids, median [IQR]	20 [10-45]** (31)	5 [5-9]** (29)	3.75 [0-5]** (21)	2.5 [0-5]** (13)	2.5 [0-5]** (11)

The number of patients with available data is shown in parentheses
* p <0.05 ** p <0.01 (Wilcoxon test).

Conclusions: TCZ therapy leads to a rapid and maintained improvement in patients with refractory GCA and/or with unacceptable side effects related to corticosteroids. However, the risk of neutropenia and infection should be kept in mind when using this biologic agent in patients with GCA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3262

FRI0337 ANCA PATTERN IN GRANULOMATOSIS WITH POLYANGITIS AND MICROPOLYANGITIS. A RETROSPECTIVE ANALYSIS ON A MULTICENTRIC INCEPTION COHORT

M. Felicetti[1], R. Padoan[1], S. Monti[2], A. Berti[3], G. Paolazzi[3], G. Brunori[4], R. Caporali[2], F. Schiavon[1]. *[1]Department of Medicine DIMED, Operative Unit of Rheumatology, University of Padova, Padova; [2]Department of Rheumatology, IRCCS Policlinico S.Matteo Foundation, University of Pavia, Pavia; [3]Rheumatology Unit; [4]Nephrology Unit, Santa Chiara Hospital, Trento, Italy*

Background: Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are multi-systemic diseases associated with anti-neutrophil cytoplasmic antibody (ANCA) often characterized by overlapping clinical manifestations. Recently ANCA pattern has been reported to define different clinical manifestations and long-term outcomes1.
Objectives: To analyze how ANCA could influence clinical manifestations and long-term outcomes in ANCA-associated vasculitis (AAV) patients, previously classified as GPA or MPA, from three different referral centers of Northern Italy.
Methods: Clinical manifestations and long-term outcomes of GPA and MPA patients were retrospectively collected. We considered clinical (including BVASv3 and VDI), radiological and histological data at diagnosis, relapse and mortality rates at the last follow-up. The complete cohort was splitted into three groups based on ANCA (anti-myeloperoxidase (MPO), anti-proteinase 3 (PR3), and ANCA negative) for statistical analysis.
Results: We included 171 patients, 90 (52.6%) anti-PR3 positive, 52 (30.4%) anti-MPO positive and 25 (14.6%) ANCA negative. Patients were mainly middle aged (52.5±15.9 years), Caucasian (98.2%) and both sexes were equally represented (Female 53.2%).
Anti-MPO positive patients were older (65 [52.5–69.7] years) at disease onset (p<0.001), affected by more comorbidities (p=0.045). They presented more frequently renal involvement (p<0.001) with higher creatinine levels at diagnosis (0.98 [0.75–1.92] mg/dL, p<0.001) (Fig. 1), systemic symptoms (p=0.039) but lower frequency of upper airways involvement (p=0.005).
Anti-PR3 positive scored higher BVASv3 at onset (p<0.001) and presented more upper airways involvement (p=0.033), lung nodules (p=0.002) and skin purpura (p=0.016).
ANCA negative showed a longer diagnostic latency (8.5 [3.5–49] months, p<0.0001), they presented with a higher VDI at diagnosis (1 [0–2.7], p<0.0001)

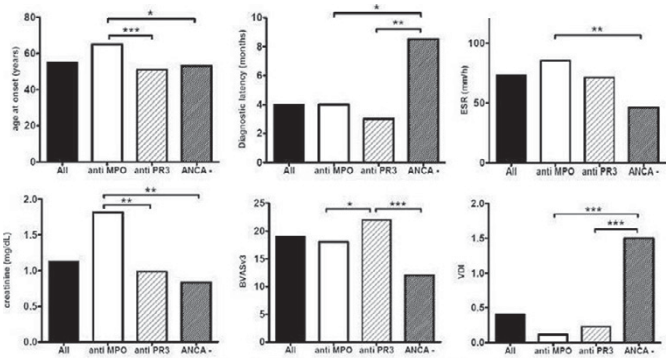


Figure 1: Post hoc analysis results. *Significance level: * p=0,05-0,01; ** p=0,01-0,001; *** p<0,001.*
ESR: erythrocyte sedimentation rate; BVASv3: Birmingham Vasculitis Activity Score version 3; VDI: Vasculitis Damage Index (VDI)

and the highest frequencies of sinuses (p=0.031), laryngeal (p=0.026) and CNS (p=0.020) involvement.
Long-term outcomes were available only in 113 patients. A low long-term mortality rate (8, 7.1% deaths) was noted (mean follow-up of 66.6±30.6 months), significantly higher in anti-MPO positive patients 7 (21.9%) when compared to anti-PR3 positive 1 (1.6%) and ANCA negative 0 (0%) ($p<0.001$). Nevertheless, the highest number of relapses/years were associated with anti-PR3 positivity (0.7±1.3 vs 0.1±0.3 in anti-MPO and 0.4±0.7 in ANCA negative, p=0.012). At multivariate analysis, anti-PR3 pattern resulted an independent predictive factor of relapses (p=0.0036, OR 5.8, IC95%: 1.1–29).
Conclusions: Our study confirms the hypothesis that each ANCA pattern could define a specific disease subset with different clinical manifestations and outcomes in AAV. Furthermore, in our cohort we observed a lower rate of recurrence and a better long term survival (92.9%) than in literature.
References:
[1] Mahr A et al; French Vasculitis Study Group (FVSG) and the European Vasculitis Society (EUVAS): Revisiting the classification of clinical phenotypes of anti-neutrophil cytoplasmic antibody-associated vasculitis: a cluster analysis. Ann Rheum Dis. 2013 Jun;72(6):1003–10.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5606

FRI0338 THERAPEUTIC CONFORMITY TO GUIDELINES AND DRUG-APPROVAL IN ADAMANTIADES-BEHCET'S DISEASE: A RETROSPECTIVE ANALYSIS OF A MIDDLE-EUROPEAN COHORT

T.M. Moosmann[1], C. Veraar[1], A. Frech[2], G. Ratzinger[3], B. Teuchner[4], G. Fraedrich[2], M. Schirmer[1]. *[1]Internal Medicine VI; [2]Vascular Surgery; [3]Dermatology; [4]Ophthalmology, Lkh - Medizinische Universität Innsbruck, Innsbruck, Austria*

Background: Adamantiades-Behcet's disease (ABD) is a chronic systemic vasculitic disease. Because of multiorgan involvement with diagnostic and therapeutic challenges for physicians, treatment decisions can be very difficult.
Objectives: To retrospectively assess the use of medication for ABD-therapy in view of 1.) current guidelines and 2.) approval by authorities in a Middle-European tertiary care center.
Methods: Data between 1997 and 2016 from a Middle-European ABD-cohort were retrospectively analysed. First, medical treatment was evaluated for conformity with the EULAR-recommendations for ABD-management and the anti-TNF therapy recommendations by Sfikakis et al. (1,2). Second, medical treatment was evaluated for use according to indications approved by authorities. Therefore official prescribing informations of the Bundesamt für Sicherheit im Gesundheitswesen (BASG)/European Medicines Agency (EMA), exemplary for Europe, and the Food and Drug Administration (FDA), exemplary for the USA, were screened (3–5). The study was approved by the local ethics committee.
Results: A total of 174 medical interventions were identified in 76 patients. Until 2008, treatment of ABD was based only on few clinical trials. According to EULAR-recommendations 93,7% were considered as being treated appropriately, including 55.2% of therapeutic approaches exactly matching the recommendations. 88.9% of TNF-inhibitors were indicated according to the anti-TNF-therapy recommendations (n=8/9). Out of 27 used drugs only prednisolone was approved by BASG/EMA- and FDA-authorities for a general indication including ABD, and cyclosporin A had the specific BASG/EMA-indication for ABD-uveitis. Another 12 medications had the indications for different symptoms of ABD, and thirteen medications were not authority-approved for any ABD-treatment.
Conclusions: Approvals by BASG/EMA- and FDA-authorities are often missing the indication of ABD. Therefore physicians not only face the complexity of ABD as a rare multiorgan disease, but also have to treat their ABD-patients with unapproved drugs. We propose that medications recommended by international guidelines for the management of rare diseases should be recognized by BASG/EMA- and FDA-authorities, even in case of low evidence.
References:
[1] Hatemi G, Silman A, Bang D, et al. EULAR recommendations for the management of Behçet disease. AnnRheumDis. 2008;67:1656.
[2] Sfikakis PP, Markomichelakis N, Alpsoy E et al. Anti-TNF therapy in the management of Behçet's disease-review and basis for recommendations. Rheumatol. 2007;46:736.
[3] BASG. Arzneispezialitätenregister, 20/09/2016 [Internet]. https://aspregister.basg.gv.at/aspregister/faces/aspregister.jspx?_afrLoop=31622307107626619&_afrWindowMode=0&_adf.ctrl-state=kimc6lskg_4.
[4] EMA. European Medicines Agency - Find medicine - European public assessment reports [Internet] http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp&mid=WC0b01ac058001d124.
[5] FDA. Drugs@FDA: FDA Approved Drug Products, citated 20.09.2016 [Internet]. Available from: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Search_Drug_Name.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5070

FRI0339 B CELL REPOPULATION KINETICS AFTER RITUXIMAB TREATMENT IN ANCA-ASSOCIATED VASCULITIDES COMPARED TO RHEUMATOID ARTHRITIS, AND CONNECTIVE TISSUE DISEASES: A LONGITUDINAL OBSERVATIONAL STUDY ON 120 PATIENTS

J. Thiel, M. Rizzi, A. Troilo, U. Salzer, A. Venhoff, R. Lorenzetti, R. Voll, N. Venhoff. *Department of Rheumatology and Clinical Immunology, University Medical Center Freiburg, Freiburg, Germany*

Background: B cell depletion with rituximab (RTX) is approved for treatment of rheumatoid arthritis (RA) and ANCA-associated vasculitides (AAV). Recently, RTX has been shown to be effective in AAV maintenance therapy, but an optimal RTX treatment schedule is unknown and the time to B cell repopulation after RTX has not been studied.
Objectives: To compare kinetics of B cell repopulation after RTX treatment in AAV, RA and connective tissue diseases (CTD) to improve the design of RTX-retreatment schedules in AAV and other autoimmune diseases.
Methods: Retrospective single-center analysis of patients with AAV, RA or CTD treated with RTX and a follow-up of >9 months were included. B-cell-repopulation was defined as a peripheral B-cell count >0.5% and >5/μl. Prolonged B cell depletion was defined by a B cell repopulation starting later than 12 months after RTX treatment.
Results: 120 patients were included in the study. Sixty-six patients had AAV with 55 classified as granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) and 11 as eosinophilic granulomatosis with polyangiitis (EGPA). Thirty-five patients had RA and 19 were treated with RTX because of CTD. There were no significant differences between the groups regarding age and sex. Most patients were treated with RTX 1000mg twice, two weeks apart. Cumulative CYC doses were higher in patients with AAV or CTD than in RA patients. In RA and CTD we observed a B-cell repopulation in all patients (100%) while only 33 AAV patients (50%) had started B-cell repopulation ($p<0.0001$). 93% of the RA and 88% of the CTD patients showed a normal repopulation within the first 12 months after RTX compared to only 10% in GPA and 0% in EGPA ($p<0.0001$). Mean time to repopulation was significantly longer in GPA/MPA (21 months) and in EGPA (20 months) compared to RA (8.5 months) and CTD (8.7 months). Median time of persistent depletion was 26 months in GPA/MPA, 21 months in EGPA compared to 9 months in RA and 8 months in CTD ($p<0.0001$). In 25 AAV patients B cell depletion persisted longer than 24 months (mean time 4.4±18.1 years). In ten of 55 GPA/MPA patients B-cells were still depleted 4 years, in six patients even after more than 5 years after only one RTX treatment cycle. One patient had a complete B cell depletion even 8 years after the second RTX treatment. Immunoglobulin production was affected by RTX-treatment with a significant decrease in IgG, IgA and IgM compared to baseline values in GPA/MPA, but not in RA or CTD. In EGPA only IgM declined significantly. Significantly more patients with GPA/MPA and EGPA developed a hypogammaglobulinemia (IgG<7g/L, IgM<0.4g/L). In some AAV patients hypogammaglobulinemia became clinically relevant and required IVIG treatment.
Conclusions: In contrast to RA and CTD, in AAV RTX induces long-lasting depletion of B cells that is associated with decreased antibody production. This observation points towards potential defects in the B cell compartment in AAV and has important implications for the design of maintenance treatment schedules using RTX.
Disclosure of Interest: J. Thiel Consultant for: Roche, M. Rizzi: None declared, A. Troilo: None declared, U. Salzer: None declared, A. Venhoff: None declared, R. Lorenzetti: None declared, R. Voll Consultant for: Roche, N. Venhoff Consultant for: Roche
DOI: 10.1136/annrheumdis-2017-eular.4783

FRI0340 B-CELL ACTIVATING FACTOR AS A BIOMARKER OF ACTIVITY OF SYSTEMIC NECROTIZING VASCULITIS (SNV)

L. Petelytska[1], O. Iaremenko[1], K. Iaremenko[2]. *[1]Bogomolets National Medical University; [2]Oleksandrivska City Clinical Hospital, Kyiv, Ukraine*

Background: Non-specific marker of inflammation such as C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) have limited value in assessment of vasculitis activity. Normal ESR values do not exclude the diagnosis of active vasculitis, and its increase may be due to concomitant infection.
Objectives: To evaluate the levels of B-cell activating factor and ESR in pts with different activity of SNV.
Methods: The serum levels of B-cell activating factor (BAFF) and ESR were measured in 48 pts with SNV (granulomatosis with polyangiitis – 22, eosinophilic granulomatosis with polyangiitis – 9, microscopic polyangiitis – 6, polyarteritis nodosa – 11). The 48 pts included 18 male and 30 female with median age 49; 24 were positive for cytoplasmic antineutrophil cytoplasmic antibodies and 11 for perinuclear antineutrophil cytoplasmic antibodies. At screening, 9 pts were without any treatment, 26 pts were receiving glucocorticoids (GCs) and 13 pts were receiving some cytotoxic agents and GCs. Clinical activities of pts were calculated by the Birmingham Vasculitis Activity Score (BVAS). All pts were divided into 3 groups according to the value of BVAS: group 1 (BVAS≤11; n=12), group 2 (BVAS =12–23; n=23) and group 3 (BVAS≥24; n=13). The outcomes of this study were the differences in marker levels between groups estimated by analysis of the absolute changes in marker levels and the areas under receiver operating characteristic (ROC) curves.

Results: The levels of BAFF were significantly higher in group 3 (0.88±0.19 ng/ml) compared with group 1 (0.68±0.13 ng/ml, $p<0.05$), but did not distinguish from the group 2 (0.90±0.35). There were not significant differences in ESR between groups. ROC analysis indicated that the AUC for ESR is 0.63±0.10 ($p=0.17$) and for BAFF – 0.72±0.12 ($p<0.05$), which indicates fair capacity for BAFF differentiate groups of pts with low activity or remission of SNV and pts with severe SNV (sensitivity - 61.5%, specificity - 88.9%), while it was poor for ESR (sensitivity - 85.7%, specificity - 46.4%).
Conclusions: There are significant differences in levels of BAFF between pts with BVAS≥24 and pts with BVAS≤11. According to ROC analysis evaluation of serum BAFF level distinguishes pts with active SNV from pts with low activity or remission better than determination of ESR.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2200

FRI0341 CLINICO-PATHOLOGICAL DISCREPANCIES AND CAUSES OF DEATH IN TAKAYASU ARTERITIS: A RETROSPECTIVE ANALYSIS OF 60 FATAL CASES

O. Zimba[1], M. Bagriy[2]. *[1]the Department of Internal Medicine, Danylo Halytsky Lviv National Medical University, Lviv; [2]Department of Pathological Anatomy, Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine*

Background: Takayasu arteritis (TA) may present with a wide spectrum of symptoms common to other diseases leading to delayed or missed diagnosis.
Objectives: To investigate the rate of undiagnosed clinically cases of TA, and provide a detailed analysis of the wrong diagnoses and the underlying causes of death.
Methods: A retrospective clinicopathological analysis of sixty autopsy cases (52 males and 8 females aged 18 to 45 years) of TA over period of 11 years have been performed. The median age at disease onset was 25, 7 years.
Results: In 33 cases (55%), TA was not diagnosed during the clinical stages but only in autopsy. The most common incorrect clinical diagnosis was atherosclerosis of the aorta and its branches (celiac trunk, renal, mesenteric and iliac arteries) that has misdiagnosed in 14 cases (42.4%) of TA. TA was misdiagnosed as myocardial infarction/ischaemic heart disease in 5 (15.1%), perforated peptic ulcer in 3 (9.1%), polyarteritis nodosa in 3 (9.1%), and infective endocarditis in 2 cases (6.1%). There were other discrepancies in 6 cases (18.2%); in these cases, cerebral haemorrhage, rheumatic heart disease, pulmonary embolism, pheochromocytoma, chronic glomerulonephritis and lung cancer were the wrong clinical diagnoses. The leading position in the mortality structure due to TA belongs to septic shock that observed in 19 cases (31.7%) due to peritonitis/acute abdomen caused by mesenteric artery occlusion with subsequent intestinal necrosis in 12 (63.1%), lower limb gangrene in 6 (31.6%), and prosthetic aortic graft infection in 1 (5.3%). The second-leading cause of death was acute heart failure due to myocardial infarction, and renovascular arterial hypertension (25%). The third common cause of death was haemorrhagic shock in 14 cases (23.3%). The acute bleeding was caused by ruptured aortic aneurysm in abdominal part in 6 cases (42.8%) and ascending aorta with cardiac tamponade in 4 (28.6%). In 2 cases (14.3%), the source of hemorrhage was ulcers of gastrointestinal tract. The surgery has complicated by lethal bleeding in 2 cases (14.3%). In other patients, causes of death were cerebral haemorrhage in 6 (10%), renal failure in 3 (5%), respiratory failure in 1 (1.7%), and revascularization syndrome in 1 (1.7%). In one case, TA coexisted with scleroma of larynx, and asphyxia was direct cause of death.
Conclusions: Our date show a high number of cases of TA (55%) that were identified at autopsy but were not diagnosed clinically. It can be assumed that aortic atherosclerosis, myocardial infarction/ischaemic heart disease were the most common wrong diagnoses in TA. The leading causes of death in TA are septic shock, acute heart failure, and haemorrhagic shock. In addition, it should be noted that in our series of autopsy cases of TA, males (86, 7%) were most frequently affected compared with results other investigations. Interestingly, that the correct diagnosis of TA was established before death in all females' cases. It seems to be a trend to miss the clinical diagnosis of TA in male patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6182

FRI0342 DISTRIBUTION OF VASCULITIDES IN EASTERN MEDITERRANEAN: RESULTS OF A PROSPECTIVE COHORT

O. Karadag, A. Erden, E.D. Batu, E. Bilgin, A.O. Uyaroglu, E. Seyhoglu, E.C. Bolek, E. Firat, H.E. Sonmez, S.Z. Arici, L. Kilic, A. Akdogan, S.A. Bilgen, S. Kiraz, I. Ertenli, S. Ozen. *Hacettepe University Vasculitis Center, Ankara, Turkey*

Background: The ethnic and geographical differences have been commented on, mainly from European data. We lack large data sets from the eastern part of Europe.
Objectives: This study is aimed to present the distribution of vasculitides in the Pediatric and Adult Vasculitis patient groups.
Methods: Hacettepe University is one of the main referral centers in the capital of Turkey, serving approximately 470,000 adult and pediatric patients/a year. Hacettepe University Vasculitis Centre (HUVAC) was established to organize a prospective cohort in 2014. All patients starting from October 2014 have been recorded to the database. Additionally electronic patient recording database between October 2014-December 2016 was searched for the patients having any of the 10th revision of the International Statistical Classification of Diseases (ICD)-10 code for the particular vasculitis. The study group of Hacettepe University Vasculitis Centre (HUVAC) re-evaluated the ascertained patients' hospital records to review their diagnosis according to the 2012 revised Chapel Hill nomenclature criteria.
Results: A total of 1196 patients had been newly followed in this period. 271 (22.7%) of them were pediatric patients and 31.8% of them were newly diagnosed. The leading vasculitis among adult patients was Behcet's Disease whereas in pediatric patients it was HSP/IgA Vasculitis (Table). Granulomatous polyangiitis was the most common small vessel vasculitis in adults. Takayasu arteritis was more frequent than giant cell arteritis among the adult patients. There was a female predominance in patients with large vessel vasculitis.
During prospective follow up, 22 (1.9%) patients deceased; 7 due to the primary disease, 6 due to infections, 7 due to cardio and cerebrovascular diseases.

Table. Distribution and gender of Adult and Paediatric Vasculitides Patients

Adult Patients (n=925)		
Type	Frequency,%	Female, %
Behcet's Disease	50.5	53.7
ANCA Associated Vasculitis	11.9	46.4
• GPA	• 8.9	47.9
• EGPA	• 2.2	52.3
• MPA	• 0.8	57.1
Takayasu's Arteritis	10.7	90
IgA Vasculitis	4.3	47.5
Giant Cell Arteritis	3.8	71.4
Cutaneous Vasculitis	3.2	70
Polyarteritis Nodosa	3.1	44.8
IgG4 Related Disease	2.8	48.2
CTD-Secondary Vasculitis	2.3	71.4
Polimyalgia Rheumatica	2.2	95
Primary CNS Vasculitis	0.8	42.8
Isolated Aortitis	0.8	50
Cryoglobulinemic Vasculitis	0.4	25
Others	3.2	57.3
Paediatric patients (n=271)		
Type	Frequency,%	Female, %
IgA Vasculitis	46.5	45.6
Behcet's Disease	22.5	45.9
Kawasaki Disease	17.3	45.6
Polyarteritis Nodosa	3.7	50.0
Takayasu's Arteritis	2.6	100
ANCA Associated Vasculitis	1.5	75
Vasculopathies (SAVI, DADA2)	1.5	37.5
Others	4.4	52.3

Conclusions: Behcet's Disease is the most frequent vasculitis in Turkey and more than half of the patients had organ/system involvements. GPA is the most common small vessel vasculitis whereas Microscopic polyangiitis is very rare. Among children Kawasaki was less and Behçet's disease markedly more when compared to Western European figures. Even though this study is a single-center one, the number of annual admitted patients of our hospital along with more than 2 years-prospective recruitment, reflects the true burden of vasculitides in Turkey, at the cross-roads between Europe and Middle East.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5322

FRI0343 COGNITIVE DISORDERS IN BEHÇET'S DISEASE: SOME CLINICAL AND PATHOGENESIS RELATIONS

P. Ovcharov[1], T. Lisitsyna[1], D. Veltishchev[2], D. Burenchev[3], D. Ishchenko[2], O. Seravina[2], O. Kovalevskaya[2], Z. Alekberova[1], E. Nasonov[1]. *[1]Nasonova Research Institute of Rheumatology, Moscow, Russia; [2]Moscow Research Institute of Psychiatry; [3]City policlinic No. 12 Moscow Department of Health, Moscow, Russian Federation*

Background: the cognitive disorders (CD) is a special psychopathological problem for Behçet's Disease (BD) patients. The causes of CD aren't enough investigated. Anxiety/depressive disorders and primary neural parenchymal lesions due to BD usually related to CD in these patients.
Objectives: to determine the prevalence of CD in BD patients and its associations with some clinical and magnetic resonance imaging (MRI) scan features.
Methods: the investigation has been realized in accordance with the inter-disciplinary program "Stress factors and mental disorders in immune-mediated inflammatory rheumatic diseases".
106 BD patients were enrolled in the study. The majority of patients were men (72,6%), natives of the North Caucasus (51,9%), with mean age (M±m) 33,3±0,98 years. All the patients met the criteria of the International Study Group for BD (1990) classification. The disease activity was assessed by scoring system BDCAF.
CD were diagnosed with psychology and neuropsychology methods. Mental disorders (MD) were diagnosed by psychiatrist in accordance with the ICD-10 in semi-structured interview. The severity of depression and anxiety was evaluated

by Montgomery–Asberg Depression Rating Scale (MADRS) and Hamilton Anxiety Rating Scale (HAM-A).
Brain MRI including T1- weighted images, T2- weighted images and fluid-attenuated inversion-recovery images (FLAIR) was done in 44 (41,5%) BD patients.
Results: CD of mild to moderate severity were diagnosed in 82 (77,4%) of BD patients. The mechanical memory (50%) and attention deficit (80,5%) were the most frequent manifestations of CD, impairment of associative memory (31,7%) and logical thinking (36,6%) were less frequent. The presence of CD didn't depend on BD activity, severity and duration, as on patient's ethnicity, use of prednisone and immunosupressive agents. The frequency of neurological manifestations (headache, seizures, myelopathy, ataxia) did not differ significantly in patients with and without CD (28% vs 32%, p=0,44). The patients with CD were older (34,3±1,07 vs 29,0±2,14, p=0,006), more often had chronic/recurrent depressive disorders (84,1% vs 50,0%, p=0,001) of moderate severity (MADRS 16,1±0,74 vs 12,2±1,06, p=0,005), chronic stressful life events (91,5% vs 62,5%, p=0,001) and multifocal subcortical parenchymal MRI changes (57,6% vs 9%, p=0,005).
Conclusions: the results have shown high rates of different CD in BD patients. CD were not associated with BD activity and presence of neurological symptoms. CD were related to the diagnoses of stress-related mild to moderate chronic depressive disorders and minor brain multifocal subcortical parenchymal MRI lesions.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3741

FRI0344 NOVEL BIOMARKERS OF SUBCLINICAL ENDOTHELIAL DYSFUNCTION IN BEHÇET'S SYNDROME: EVALUATION OF CROSS-SECTIONAL DISTENSIBILITY AND INTIMA-MEDIA-THICKNESS IN A HOSPITAL-BASED POPULATION

R. Talarico[1], C. Stagnaro[1], S. Barsotti[1], R. Neri[1], C. Tani[1], C. Baldini[1], N. Di Lascio[2], E. Bianchini[2], A. Morales[2], M. Mosca[1]. *[1]Department of Clinical and Experimental Medicine, University of Pisa, Rheumatology Unit; [2]CNR, Institute of Clinical Physiology, Pisa, Italy*

Background: Growing interest exists on the role of markers of subclinical cardiovascular disease as independent predictors of cardiovascular events. Poor data are available on the role of these markers as prognostic factors for Behçet's syndrome (BS).
Objectives: The primary aim was to explore Intima-Media-Thickness (IMT), mean arterial diameter and distensibility (DC) in a group of patients with BS, comparing these data with a healthy control group and a disease control group; the secondary aim was to correlate the vascular parameters with demographic/clinical profile.
Methods: Thirty BS patients (females:12;mean age±SD:43±10.5; mean disease duration±SD:13±5.8) fulfilling the ISG criteria were prospective enrolled. Demographic data, level of disease activity, frequency of smokers, hypertension, family history of cardiovascular risk factors, body mass index (BMI) and current therapies were analysed. For each subject, ultrasound B-mode image sequences of right common carotid arteries were acquired and analysed by an automatic system (Carotid Studio,Quipu) for the measurement of IMT and mean arterial diameter. In addition, carotid pulse pressure (PP) was estimated by tonometry and DC coefficient was obtained. The systolic and diastolic carotid diameters were automatically measured on the distal wall of the common carotid artery, 1–2 cm beneath the bifurcation. Carotid diameter was calculated as the distance between media-adventitia interfaces. Cross-sectional DC was estimated through the variations in arterial cross-sectional area and blood pressure during systole. DC was computed as DC=ΔA/(PP*A) where A is the diastolic lumen area, ΔA is the stroke change in lumen area, and PP is the local pulse pressure.
Results: At time of evaluation, 4/17 patients presented active disease (50% ocular involvement, 25% joint involvement, 25% gastro-enteric involvement; mean BS activity score 5). Mean IMT±SD value resulted of 0.57±0.81, mean arterial diameter±SD value was 6.879±0.81 and mean DC± SD 27.3±14.34. All the vascular parameters considered were significant correlated with BMI, while only IMT and DC were also significant correlated with arterial hypertension. Using a correction analysis for age and sex, we found significant correlations between mean arterial diameter and disease activity and between DC and disease duration. These data resulted significantly different compared to healthy control and a disease control groups, in terms of smaller arterial diameter and higher DC.
Conclusions: Our data have shown that there is a consistent influence of disease activity and duration of disease on mean arterial diameter and DC, respectively. Thus, it is desirable that future pharmacological researches on BS target on this issue.
Acknowledgements:
Seyahi E, Ugurlu S, Cumali R, Balci H, Ozdemir O, Melikoglu M, Hatemi G, Fresko I, Hamuryudan V, Yurdakul S, Yazici H. Atherosclerosis in Behçet's Syndrome. Semin Arthritis Rheum. 2008 Aug;38(1):1–12.
Seyahi E, Ugurlu S, Cumali R, Balci H, Ozdemir O, Melikoglu M, Hatemi G,Fresko I, Hamuryudan V, Yurdakul S, Yazici H. Atherosclerosis in Behçet'sSyndrome. Semin Arthritis Rheum. 2008 Aug;38(1):1–12.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5907

FRI0345 CLINICAL IMPACT OF ALPHA-1-ANTITRYPSIN DEFICIENCY IN GRANULOMATOSIS WITH POLYANGIITIS

S. Deshayes[1], A. Aouba[1], F. Grandhomme[2], K. Kathy[3], D. Mariotte[3], J. Boutemy[1], G. Maigné[1], C. Brière-Bellier[4], C. Delmas[1], B. Bienvenu[1], N. Martin Silva[1]. *[1]Department of Internal Medicine; [2]Department of Biochemistry; [3]Department of Immunology, CHU Côte de Nacre, Caen; [4]Department of Infectious Diseases, CH Mémorial, Saint-Lô, France*

Background: Deficiency in α-1-antitrypsin (AAT), which is the main proteinase 3 (PR3) inhibitor, is now recognized as a pathogenic factor in some cases of anti-PR3 anti-neutrophil cytoplasmic antibodies (ANCA) related granulomatosis with polyangiitis (GPA). However, the clinical impact of AAT deficiency remains poorly established in this setting.
Objectives: The purpose of our study was to describe the clinical phenotypes and outcomes of anti-PR3 GPA patients according to their AAT status.
Methods: A retrospective monocentric study carried out in Caen University Hospital led to identify anti-PR3 GPA patients, from 09/21/2011 to 06/10/2016. AAT dosage and phenotype (isoelectric focusing in agarose gel) were performed for all patients. Categorical variables were reported as percentages and compared using Chi^2 or Fisher's tests according to expected frequencies. Continuous variables were expressed as means and analysed using Student's t-test. Associations between survival, renal survival or relapse-free survival, and AAT phenotype were evaluated by the log-rank test. A p-value <0.05 was considered to be statistically significant.
Results: Among the 72 identified anti-PR3 GPA patients, 40 (56%) were male. Median age at diagnosis was 60.5 years old. Patients mainly had constitutional symptoms (51, 71%), pulmonary (52, 72%), ear, nose or throat (ENT) (49, 68%), rheumatologic (45, 63%), and renal (44, 61%) involvements. Median initial BVAS score was 38 (maximum score: 63). Twelve (17%) deaths and 33 (46%) relapsing patients were noted (median follow-up: 55 months). Forty-eight (67%) patients had MM phenotype, 10 (14%) MZ phenotype, 8 (11%) MS phenotype, 3 (4%) M-variant phenotype, 2 (3%) ZZ phenotype and 1 (1%) ZS phenotype. Allele frequencies of M, Z and S allele were 81, 10 and 6%, respectively. The whole patient cohort had the same immunosuppressant drug regimen.

Tab;e 1

	Z carriers (n=13)	Non-Z carriers (n=59)	p-value	Z or S carriers (n=21)	Non Z or S carriers (n=51)	p-value
Initial BVAS (median)	18	18	0.91	18	18	0.71
Death (%)	15	17	1	14	18	1
Age at diagnosis (years, median)	61	60	0.91	61	59	0.62
Relapse (%)	38	47	0.56	43	47	0.75
Intra-alveolar hemorrhage (%)	47	14	**0.004**	43	12	**0.009**
ENT (%)	92	63	**0.05**	67	69	0.88
AAT level (g/L, median)	1.07	1.65	**<0.001**	1.11	1.65	**<0.001**

Only intra-alveolar hemorrhage (IAH), that was more frequent in Z or S deficient allele patients, and ENT involvement, that was more frequent in those with Z allele, were significantly associated with AAT deficiency. Among the 13 patients carrying Z allele, 9 had normal AAT level, including 6 without any biologic inflammatory parameter at the time of AAT dosage. Global survival, renal survival or relapse-free survival were identical between Z carriers compared to non-Z carriers (respectively 0.77, 0.75 and 1), and between Z or S carriers compared to those without (respectively 0.91, 0.44 and 0.32).
Conclusions: This study confirms the epidemiological association of anti-PR3 GPA with AAT deficiency, and find an interesting higher risk of IAH in this setting. The identical prognosis of both subgroups should be related to other therapeutic added in IAH, including plasma exchanges. Prospective studies are required to specify these data and to assess the need for replacement therapy in AAT deficient patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4500

FRI0346 RENAL INVOLVEMENT IN GRANULOMATOSIS WITH POLYANGIITIS

N. Bulanov[1], E. Makarov[2], E. Kuznetsova[1], M. Bulanova[3], P. Novikov[1], S. Moiseev[1]. *[1]Sechenov First Moscow State Medical University; [2]Lomonosov Moscow State University, Moscow; [3]Vladimir Regional Clinical Hospital, Vladimir, Russian Federation*

Objectives: We assessed the frequency, clinical features and prognosis of renal involvement in granulomatosis with polyangiitis (GPA) and current treatment approaches.
Methods: We performed a retrospective analysis of 234 patients with GPA, diagnosed according to Chapel-Hill Consensus Conference 2012 classification, 81 male and 153 female, aged 53 (41; 62) years. 54 patients (23.1%) had localized GPA. 174 (74.4%) were ANCA positive. Median follow up was 61.5 (32; 105) months. 103 patients (44%) had a history of renal involvement. Frequencies of proteinuria, hematuria, hypertension, rapidly progressive glomerulonephritis (RPGN), acute kidney injury (AKI) and chronic kidney disease (CKD) grades were analyzed.
Results: In 25 patients (24.3% of 103) renal involvement developed at disease

onset, the other 78 patients (75.7%) developed glomerulonephritis after a median of 3 (1; 12) months. Hematuria was present in 94 (91.3%), proteinuria in 85 patients (82.5%), nephrotic syndrome in 11 patients (10.7%), hypertension in 31 patients (30.1%). Rapidly progressive glomerulonephritis (RPGN) defined by the doubling of serum creatinine within ≤3 months developed in 29 patients (28.2% of 103). Myeloperoxidase-ANCA-positive patients (n=12) developed RPGN significantly more often than proteinase-3-ANCA-positive patients (n=78): 7 (58.3%) vs 22 (28.2%) (p=0.0499). 11 (10.7%) patients developed AKI, stage 3 being the most common (in 8 patients). 40 (38.8%) patients exhibited indolent renal disease course, i.e. without worsening of renal function. By the end of the follow-up, 33 (32.0%) patients were diagnosed with CKD grade 3b-5, among them 11 patients (10.7%) developed end-stage renal disease (ESRD). 6 patients (5.8%) died. As the first line induction therapy all patients received corticosteroids in combination with cyclophosphamide in 93 patients (90.3%), rituximab (RTX) in 3 patients (2.9%), mycophenolate mofetil in 7 patients (6.8%). RTX was used for remission induction in 27 (26.2%) patients due to refractory or recurrent disease. During follow-up, 74 patients (71.8%) developed one or more severe relapses with a relapse rate of 0.27 per patient-year. 50 (48.5%) patients had renal relapses (0.096 per patient-year).

Conclusions: Prevalence of renal involvement in the studied group was lower than expected, most likely because of a large proportion of patients with localized GPA. Our study showed that RPGN was not the most common feature of renal involvement. Almost 40% of patients developed indolent course of kidney disease. Nevertheless one third of patients developed CKD G3B or worse by the end of the follow up. Despite effective induction therapy with high-dose corticosteroids, cytotoxic agents and/or RTX relapses, both renal and extrarenal, are frequent.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5104

FRI0347 RHEUMATOID FACTOR IS CORRELATED WITH DISEASE ACTIVITY AND INFLAMMATOTY MARKERS IN ANTINEUTROPHIL CYTOPLASMIC ANTIBOTY-ASSOCIATED VASCULITIS

S. Watanabe, T. Gono, K. Nishina, N. Sugitani, E. Watanabe, H. Yabe, C. Terai.
Rheumatology, Jichi Medical University, Saitama Medical Center, Saitama, Japan

Background: Raised levels of serum rheumatoid factors (RFs) of different immunoglobulin classes had been reported in a high proportion of patients with rheumatoid vasculitis. RF used to be studied and was shown elevated in some forms of vasculitides. Patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) are often positive for RF. However, the clinical significance of RF has been seldom examined in AAV.

Objectives: The aim of this study was to investigate association between the presence of RF and clinical features and outcomes in AAV.

Methods: Eighty-one patients were diagnosed with AAV from 2006 to 2015 in our hospital. Among 81 patients, forty-seven patients (17 males, median age 67 years) who were not complicated with rheumatoid arthritis and in whom RF was measured before the treatment, were studied, retrospectively. Patients were classified using the European Medicines Agency vasculitis classification algorithm. AAV included eosinophilic granulomatosis with polyangitis (n=10), granulomatosis with polyangitis (n=14), microscopic polyangitis (n=16) and unclassifiable vasculitis (UV) (n=7). Patients with UV with MPO-ANCA or PR3-ANCA were included in this study. IgM-RF was measured using a latex agglutination assay. Disease activity was assessed with Birmingham vasculitis activity score (BVAS). IgM-RF, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum ferritin, IgG, IgM, IgA, MPO-ANCA and PR3-ANCA were obtained from hospital records. Clinical manifestations between RF-positive subset (n=29) and RF-negative subset (n=18) were analyzed using Fisher's exact and Wilcoxon rank sum tests. Correlation coefficients were established with Spearman's correlation coefficient. Data were shown as medians (interquartile range).

Results: BVAS was higher (14 (12–22) vs 12 (6–16), P=0.026) in the RF-positive subset than the RF-negative subset. CRP and ESR were higher (P=0.020 and 0.007, respectively) in the RF-positive patients. IgM-RF titers significantly correlated with BVAS (r=0.50, P=0.0004). In addition, CRP, ESR, IgM and IgG also had a significant correlation with IgM-RF titers. The frequency of initiation of dialysis therapy (14% vs 6%), usage of mechanical ventilation (14% vs 0%) and mortality (10% vs 0%) were higher in the RF-positive subset than in the RF-negative subset although no significant differences were shown.

Conclusions: In AAV, IgM-RF titers are significantly correlated with disease activity and inflammatory markers. Presence of RF could be a poor prognostic factor in patients with AAV.

References:

[1] Watts R, Lane S, Hanslik T, et al. Development and validation of a consensus methodology for the classification of the ANCA-associated vasculitides and polyarteritis nodosa for epidemiological studies. Ann Rheum Dis 2007;66:222–227.
[2] Westedt ML, Herbrink P, Molenaar JL, et al., Rheumatoid factors in rheumatoid arthritis and vasculitis. Rheumatol Int 1985;5:209–14.
[3] Kronbichler A, Kerschbaum J, Gründlinger G, et al. Evaluation and validation of biomarkers in granulomatosis with polyangiitis and microscopic polyangiitis. Nephrol Dial Transplant 2016;31(6):930–6.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4555

FRI0348 ASSOCIATED INFLAMMATORY SYNDROMES IN TAKAYASU'S ARTERITIS: MANY FACES OF A DISEASE

S.N. Esatoglu[1], A.M. Celik[2], D. Ucar[3], A.F. Celik[4], S. Ugurlu[1], G. Hatemi[1], M. Melikoglu[1], I. Fresko[1], V. Hamuryudan[1], H. Ozdogan[1], S. Yurdakul[1], H. Yazici[1], E. Seyahi[1]. *[1]Istanbul University, Cerrahpasa Medical School, Department of Internal Medicine, Division of Rheumatology; [2]Istanbul University, Cerrahpasa Medical School, Department of Internal Medicine; [3]Istanbul University, Cerrahpasa Medical School, Department of Ophthalmology; [4]Istanbul University, Cerrahpasa Medical School, Department of Internal Medicine, Division of Gastroenterology, Istanbul, Turkey*

Background: Case reports and series suggest that Takayasu's arteritis (TA) can co-exist with various inflammatory disorders.

Objectives: We conducted a formal study to look specifically at the frequency of inflammatory disorders and symptoms in a large cohort of TA followed by a single tertiary center.

Methods: There were 238 patients registered with a diagnosis of TA. Of these, 19 died, 18 were lost to follow-up and 3 did not wish to response our questionnaire. The remaining 198 patients were called back at the outpatient clinic. A standardized form sought whether the patient was also diagnosed as inflammatory bowel disease (IBD), ankylosing spondylitis (AS), Behçet's syndrome (BS), amyloidosis, uveitis, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (pSS), Sjögren syndrome, psoriatic arthritis, inflammatory myositis, small vessel vasculitis, autoimmune/demyelinating or any other inflammatory disorder.

Results: Overall, 198 (175 F/ 23 M) patients were studied. The mean age at the time of TA diagnosis was 34±12 years. Subclavian artery was the most common involved artery (84%), followed by common carotids (78%) and aorta (65%). Currently, while 25 (16%) patients were off treatment, 72 (47%) patients were using glucocorticoids, 47 (31%) azathioprine, 32 (21%) methotrexate and 44 (29%) biological agents.

We identified in total 37 (19%) patients with inflammatory diseases (IBD: n=12; AS: n=15; and BS: n=10). Table shows their demographic characteristics. Among the remaining 161 patients, the most frequent feature was inflammatory back pain (36%), followed by recurrent oral ulcers (15%), erythema nodosum (11%), arthritis (10%), papulopustular lesions (7%), uveitis (4%), and genital ulcer (1%). It was noted that inflammatory back was mostly located on the dorsal area. Regarding autoimmune diseases, we also observed RA (n=3), psoriasis (n=2), autoimmune hepatitis (n=2), SS (n=1) and SSc (n=1).

Table 1. Demographic features of 37 TA patients with inflammatory bowel disease (IBD), ankylosing spondylitis (AS) or Behçet's syndrome (BS)

Concomitant disease	F/M	Mean age at TA diagnosis (SD)	Mean age at concomitant disease (SD)	Time of TA diagnosis in relation to concomitant disease
AS (n=15)	13/2	31±8	27±11	Simultaneous (n=3) TA preceded (n=7) AS preceded (n=5)
IBD (n=12)	11/1	33±9	31±9	Simultaneous (n=9) TA preceded (n=1) IBD preceded (n=2)
BS (n=10)	7/3	35±13	32±13	Simultaneous (n=5) TA preceded (n=1) BS preceded (n=4)

Conclusions: TA does co-occur with IBD, AS or BS in about 1/5 of the patients, at least in a hospital setting and without a clear temporal pattern. This could be due to the close association of TA with MHC class-1 diseases. In addition, the high prevalence of inflammatory back pain in the dorsal spine in TA needs further scrutiny.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6276

FRI0349 THE SNP RS6871626 LOCATED IN IL12B REGION MAY INFLUENCE ON VASCULAR LESIONS OF TAKAYASU ARTERITIS

T. Nakajima[1], H. Yoshifuji[1], C. Terao[2], K. Murakami[1], R. Nakashima[1], Y. Imura[1], K. Ohmura[1], T. Mimori[1]. *[1]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University; [2]Center for Genomic Medicine, Kyoto University, Kyoto, Japan*

Background: Takayasu arteritis (TAK) is a type of large vessel vasculitis, which affects aorta and its main branches. We previously found a single nucleotide polymorphism (SNP), rs6871626 located in *IL12B* region, as a susceptible gene to TAK and reported that the risk allele at the SNP is associated with the risk of aortic regurgitation (AR)[1)]. However, there have been no studies on the association of the SNP with the organ involvements other than AR in TAK patients.

Objectives: To investigate the association of the SNP with arterial and organ involvements except for AR.

Methods: We examined the medical records of 85 patients with TAK, stratified

Abstract FRI0349 – Table 1. Organ involvements in patients

Organ involvements	AA	AC	CC	p-value	p-values of multiple comparisons†		
					AA vs. AC	AA vs. CC	AC vs. CC
Carotid arterial lesion	78.9% (15/19)	63.9% (23/36)	80.0% (8/10)	0.48*	1.00	1.00	1.00
Descending aortic lesion	75.0% (18/24)	44.2% (19/43)	25.0% (4/16)	0.0048*	0.064	0.0096	0.71
eGFR (ml/min/1.73m^2)	61.3 ± 26.9	72.9 ± 22.8	81.5 ± 28.8	0.011**	0.21	0.042	0.75

Mean ± SD, *Fisher's exact test, **one-way ANOVA, †p-value is corrected by Bonferroni's method.

them into three groups according to the allele at the SNP, AA (n=26), AC (n=43) and CC (n=16) (A is a risk allele), and investigated the association of the SNP and organ involvements.

Results: There were no differences in the complication rates of carotid arterial lesions among the groups (AA 78.9%, AC 63.9% and CC 80.0%). The proportion of patients with lesions in descending aorta (Numano classification[2] IIb∼V) was 75.0% in AA, 44.2% in AC 44.2% and 25.0% in CC and the proportion in AA was significantly higher than in CC (p=0.0096). Moreover, estimated glomerular filtration rate (eGFR) was significantly lower in AA than in CC (61.3±26.9ml/min/1.73m^2 vs. 81.5±28.8 ml/min/1.73m^2, p=0.042).

Conclusions: The SNP rs6871626 located in *IL12B* may influence on the occurrence of descending aortic lesions in TAK patients and this may lead to renal dysfunction.

References:

[1] Terao C et al. Am J Hum Genet. 2013; 93(2): 289–97.
[2] Hata A et al. Int J Cardiol. 1996; 54 Suppl: S155–163.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4548

FRI0350 INVESTIGATING THE LINK BETWEEN ISCHEMIC HEART DISEASE AND BEHCET'S DISEASE: A CROSS-SECTIONAL ANALYSIS

Y. Yavne[1], S. Tiosano[2], A. Watad[2], D. Comaneshter[3], A.D. Cohen[3,4], H. Amital[2]. *[1]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; [2]Department of Medicine 'B', Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Hashomer; [3]Chief Physician's Office, Clalit Health Services, Tel Aviv; [4]Siaal Research Center for Family Medicine and Primary Care, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel*

Background: Behcet's disease (BD) is a multi-systemic chronic inflammatory disorder which involves the vasculature tree of all sizes. Subclinical endothelial injury as a result of chronic inflammation in BD has been associated with thrombosis and arterial stiffness, risk factors for ischemic heart disease (IHD)[1–4]. However, data regarding the association between BD and IHD and the impact of various risk factors on this association, is scarce[3–5].

Objectives: To examine the association between BD and the development of IHD and its potential impact as a cardiovascular risk factor.

Methods: This study was conducted as a case-control study utilizing the database of Clalit Health Services. The proportion of IHD was compared between patients diagnosed with BD and age- and gender-matched controls. Univariate analysis was performed using Chi-square and student *t-test* and a multivariate analysis was performed using a logistic regression model.

Results: 871 BD patients and 4,439 age- and gender-matched controls were included in this study. The proportion of IHD amongst BD patients was increased in comparison with controls (10.9% vs. 7.52% respectively, *p*-value =0.001). After controlling for cofounders, BD was associated with IHD on multivariate analysis (odds ratio 1.485, 95% confidence interval 1.106–1.982, Table 1). When the comparison between BD patients with IHD and controls with IHD was stratified according to risk factors, age younger than 70 and male gender were both found to be significantly elevated in the BD group.

Table 1. Multivariate logistic regression for IHD (*n*=5,220)

Variable	OR	95% CI	*p*-value
Behcet	1.485	1.106–1.982	0.008
Age	1.059	1.047–1.071	<0.001
Male gender	2.929	2.248–3.841	<0.001
BMI	1.010	0.987–1.034	0.388
High SES *vs.* low	0.709	0.503–0.994	0.048
Intermediate SES *vs.* low	0.793	0.600–1.048	0.104
Arab ethnicity	0.872	0.618–1.221	0.430
Hypertension	3.050	2.332–4.010	<0.001
Hyperlipidemia	7.895	5.119–12.781	<0.001
Diabetes	1.624	1.268–2.078	<0.001
Smoking	1.849	1.445–2.371	<0.001

IHD = ischemic heart disease, OR = odds ratio, CI = confidence interval, BMI = body mass index, SES = socioeconomic status.

Conclusions: BD patients have an increased proportion of IHD in comparison with matched controls. The population of BD patients with IHD has a higher proportion of younger males in comparison with controls with IHD. Preemptive screening for IHD may be warranted in this subgroup.

References:

[1] Uyar B, Solak A, Genç B, et al. Evaluation of Arterial Stiffness in Patients with Behçet's Disease by Using Noninvasive Radiological Methods such as Intima-Media Thickness of the Carotid, Ankle-Brachial Pressure Index, Coronary Artery Calcium Scoring, and Their Relation to Serum Fetuin-A Levels: A Case-Control Study. Ann Dermatol. 2015;27:702.
[2] Springer J, Villa-Forte A. Thrombosis in vasculitis: Curr Opin Rheumatol. 2013;25:19–25.
[3] Misra DP, Shenoy SN. Cardiac involvement in primary systemic vasculitis and potential drug therapies to reduce cardiovascular risk. Rheumatol Int. 2016;37.1:151–167.
[4] Pandey A, Garg J, Krishnamoorthy P, et al. Predictors of Coronary Artery Disease in Patients with Behcet's Disease. Cardiology. 2014;129:203–206.
[5] Seyahi E, Memisoglu E, Hamuryudan V, et al. Coronary atherosclerosis in Behçet's syndrome: a pilot study using electron-beam computed tomography. Rheumatology. 2004;43:1448–50.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2936

FRI0351 PAPULOPUSTULAR LESIONS ACCORDING TO AGE, SEX AND LOCALIZATION IN BEHCET'S SYNDROME PATIENTS COMPARED HEALTHY AND DISEASED CONTROLS

Z. Kutlubay[1], Y. Ozguler[2], G. Hatemi[2], K. Tascilar[3], C. Mat[1], H. Yazici[2]. *[1]Department of Dermatology; [2]Department of Internal Medicine Division of Rheumatology, Istanbul University Cerrahpasa Medical Faculty; [3]Department of Internal Medicine, Okmeydani Research and Training Hospital, Istanbul, Turkey*

Background: Papulopustular lesions (PPL) are the most common skin lesions in Behçet's syndrome (BS).

Objectives: To assess whether PPL are different in BS according to localization, age, sex and medications used when compared to rheumatoid arthritis patients (RA) and apparently healthy subjects (HS).

Methods: 209 consecutive BS patients who were routinely followed in our dedicated BS center were studied. Patients with RA (n=146) who were followed up in the rheumatology outpatient clinic of the same unit and HS (n=149) were used as controls. All subjects were clinically evaluated by the same dermatologist and all skin lesions (papules, pustules, comedones, folliculitis, cysts, nodules) on the face, trunk and legs were separately counted. Information regarding the demographic and clinical features of primary disease and medications used were obtained from patients' charts.

Results: Subjects without PPL were excluded before analyses. Demographic features and mean number of PPL according to site of body were summarized in Table-1. Mean number of total PPL were similar between BS and HS and significantly higher than in RA (p<0.001). Mean number of total PPL according to sex were similar in RA and HS but higher in male BS patients compared to female BS patients (p=0.04). When we analyzed the number of PPL according to different body sites, we observed that BS patients had significantly more lesions on the legs when compared to the RA patients and HS (p<0.0001). Number of PPL lesions tend to decrease as the patient ages in BS similar to RA and HS. When leg lesions were analyzed according to age, this difference remained in the age groups 31–50 and >50 but not in the age group ≤30. Corticosteroid use did not impact the results.

Table 1

	BS	RA	HS
N	155 (74%)	57 (39%)*	101 (68%)
F/M	95/60	46/11	52/49
Mean age (SD)	38.6 (10.0)	47.5 (13)†	34.7 (12.0)
N of pts on corticosteroids	24 (15 M/9 F) (15%)	37 (9 M/28F) (65%)	–
Mean n of PPL (SD)	7.8 (8.0)	3.9 (3.8)‡	9.7 (9.5)
Trunk	107 (58F/49M) (70%)	36 (28F/8M) (63%)	81 (37F/44M) (80%)
Face	120 (80F/40M) (77%)	37 (32F/5M) (65%)	84 (50F/34M) (83%)
Legs	48 (21F/27M)§ (31%)	2 (1F/1M) (3.5%)	13 (5F/8M) (13%)

*p<0.001, †p<0.02, ‡p<0.05, §p<0.0001.

Conclusions: BS patients have significantly more PPL on the legs when compared to HS and RA. Number of PPL tend to decrease as the patient ages in BS similar to RA and HS however BS patients still have more PPL on the legs after the age of 50 suggesting that these lesions somehow differ from acne vulgaris, in pathogenesis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6463

FRI0352 **EFFICACY OF BIOLOGICS IN PATIENTS WITH REFRACTORY TAKAYASU ARTERITIS AND ANALYSIS OF THEIR GENETIC BACKGROUNDS**

Y. Gon[1], H. Yoshifuji[1], T. Nakajima[1], K. Murakami[1], R. Nakashima[1], K. Ohmura[1], C. Terao[2], T. Mimori[1]. *[1]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University; [2]Center for Genomic Medicine, Kyoto University, Kyoto, Japan*

Background: Takayasu arteritis (TAK) is a rare disease that mostly affects young females and causes inflammation, stenosis and dilatation of the aorta and its main branches. Although glucocorticoids are effective, relapses occur frequently [1]. Recently, the efficacy of biologics has been reported in refractory TAK. HLA-B*52 is a major genetic risk factor and associated with the severity [2]. Our group reported a SNP in the regions of *IL12B* gene associated with the onset of TAK, and the patients with risk alleles at the SNP showed significantly severer symptoms [3].
Objectives: To evaluate the efficacy and safety of biologics in the treatment of refractory TAK, we analyzed the clinical profiles and genetic information of patients treated with biologics in our institute.
Methods: We searched for TAK patients who used biologics in 163 TAK cases treated in Kyoto University Hospital from 2000 to 2016. From medical records, we extracted information of classifications, symptoms, complications, ESR, CRP, dose of prednisolone (PSL), use of immunosuppressive agents (IS), and adverse events at 0, 1, 6 12 months after the initiation of biologics.
Results: Of 163 cases, 12 (7.4%) were treated with biologics. Two were excluded because biologics were used for coexisting rheumatoid arthritis. Remaining 10 cases were treated with infliximab (IFX, 3–5 mg/kg div. bimonthly, N=4), tocilizumab (TCZ, 8 mg/kg div. monthly, N=3) or ustekinumab (UST, 45 mg s.c. trimonthly, N=3). Sex ratio was 1:9. The age of onset was 29.4±12.2 y.o. (mean±S.D.). According to Hata's classification [4], they were categorized into types I (N=3), IIa (2) and V (5). Three patients had aortic regurgitation. The number of IS used in the past was 1.7±0.8 per patient. B*52 was positive in 7 (70%) patients. All the cases had risk-type alleles (A vs. C) of *IL12B* SNP (AA: AC: CC =4: 6: 0). ESR was significantly decreased (p=0.009) and CRP showed a tendency to decrease after 12 mo. (Table 1). Dose of PSL was significantly decreased from 10.6±1.9 to 7.7±2.4 mg/day after 12 mo. (p=0.018). We could not find significant improvements in imaging modalities such as MR and ultrasonography. Overall duration of treatments with biologics was 39±22 months. Two cases discontinued IFX due to occurrence of breast cancer and infusion reaction, respectively. Chronic heart failure was exacerbated in a case treated with TCZ. Two of 3 patients treated with UST exhibited steroid- sparing effects and none of them discontinued UST in the mean observation period of 31 mo.

Table 1. Changes after the treatment with biologics

	Before	1 mo.	6 mo.	12 mo.	*P* (before vs. 12 mo.)
ESR (mm /h)	31±16	14±9	14±12	12±12	0.009
CRP (mg/L)	15±19	8±13	4±5	2±4	0.075
PSL (mg/day)	10.6±1.9	10.5±2.0	9.0±2.3	7.7±2.4	0.018

Conclusions: Biologics showed steroid-sparing effects in refractory TAK. Besides, there was a tendency that patients who used biologics had B*52 and the risk-type allele of *IL12B* SNP, implicating the refractory courses of them.
References:
[1] Maksimowicz-McKinnon K, Clin Exp Rheumatol 25:S58–9, 2007.
[2] Numano F, Jpn Circ J 46(2):184–9, 1982.
[3] Terao C, Am J Hum Genet 93(2):289–97, 2013.
[4] Hata A, Int J Cardiol 54 Suppl:S155–163, 1996.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4533

FRIDAY, 16 JUNE 2017

Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models

FRI0353 **SERUM PROTEOMICS PROFILE IN SYSTEMIC SCLEROSIS PATIENTS**

M. De Santis[1], E. Generali[1], A. Ceribelli[1], N. Isailovic[1], M. Caprioli[1], G.M. Guidelli[1], C. Selmi[1,2]. *[1]Rheumatology and Clinical Immunology, Humanitas Research Hospital, Rozzano; [2]BIOMETRA Department, University of Milan, Milan, Italy*

Background: Systemic sclerosis (SSc) is characterized in virtually all patients by anti-nuclear antibodies (ANA) with anti-centromere (ACA), anti-topoisomerase I (ant-Scl70), and anti-RNA polymerase III antibodies identifying patient subgroups. However, there are no reliable biomarkers predicting SSc susceptibility and internal organ involvement.
Objectives: We aimed to identify serum protein biomarkers associated with SSc and interstitial lung disease (ILD), using a highly multiplexed proteomic technology.
Methods: We analyzed serum samples of 3 patients with SSc and ILD (2 limited SSc: one ANA positive and one anti-Scl70 positive, and one diffuse SSc anti-Scl70 positive), 3 patients with SSc and no ILD (ACA positive limited SSc), and 4 healthy controls. All subjects were women and age matched. Serum proteomics profiling was performed using the SOMAscan platform (SomaLogic, Inc., Boulder, CO, USA). Statistical analysis included Student's t-test and were performed using the SomaSuite software (SomaLogic, Boulder, CO, USA).
Results: Proteomic analysis identified 33 proteins which differentiate SSc from HC and 9 proteins which differentiate SSc patients with and without ILD. Compared to healthy controls, SSc cases showed an altered expression of proteins involved in extracellular matrix formation and cell-cell adhesion, angiogenesis, and lymphocyte recruitment, activation, and signaling, while an overall inhibition of neutrophil function was noted. An interferon and IL-1 signatures were also found. Patients with SSc and ILD manifested increased protein levels related to intracellular signaling and cell cycle, along with an increase of monocyte chemoattractants and ligands for the leukocyte adhesion compared to SSc without ILD. We further observed a decrease in B cell stimulating factor and IL-22 signaling in SSc with ILD.
Conclusions: Serum proteomic profiles can differentiate SSc from healthy controls and SSc patients with and without ILD; moreover, our results identify biomarkers with a putative pathogenetic significance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5693

FRI0354 **CIRCULATING MICROPARTICLE SUBSETS ARE ASSOCIATED WITH PATIENTS WITH EXTENDED FIBROTIC PHENOTYPE IN SYSTEMIC SCLEROSIS**

K. Sakata[1], H. Yasuoka[1], M. Koseki[1], K. Yoshimoto[1], M. Kuwana[2], T. Takeuchi[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine; [2]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan*

Background: In systemic sclerosis (SSc), systemic remodeling, microvascular injuries and production of autoantibodies are well known as disease hallmarks. However, the master regulator of these characteristics is still unclear. Microparticle (MP) is a small membrane vesicle, released from various kinds of cells, and distributes systemically through circulation[1)]. Recent reports revealed that MP contains various growth factors, proteases and cytokines including TGF-b[2)], suggesting that MP can contribute to immune and mesenchymal responses as a conveyor[3)]. and involve with disease process of SSc. Although, the possible involvement of MPs in the pathogenesis of SSc is indicated, the detailed association of MPs including MP subsets with SSc is not well clarified.
Objectives: To elucidate the association between circulating MP subsets and patients' characteristic of SSc.
Methods: Thirty-six patients with SSc and 13 healthy controls were involved in this study. Platelet-rich plasma containing microparticles was isolated from whole blood using gradient centrifugation and analyzed using flow cytometer. MP was defined as particles smaller than 1.0 μm diameter using Megamix®, and identified each MP subsets based on expression of cell type-specific surface markers; platelet ($CD31^+CD41^+$), endothelial cell ($CD31^+CD41^-$) and monocyte ($CD14^+CD45^+$) using fluorescence-tagged antibodies. Clinical information was retrospectively collected from patients' records, and the correlation with the number of each MP subset was analyzed.
Results: Mean age of 36 patients with SSc was 60.9±1.8 years, 94% was female, and mean disease duration was 11.2±9.5 years. Patients with diffuse cutaneous SSc (dcSSc) was 6 (17%). As for the proportion of MP subsets, platelet-derived MP (PMP) was the largest subset, followed by endothelial cell-derived MP (EMP) and monocyte-derived MP (MoMP) in all samples. In patients with SSc, the number of total MP and all MP subsets were higher than those in healthy controls ($p<0.05$). Also, all MP subsets were significantly higher in patients with dcSSc compared to limited cutaneous SSc ($p<0.001$). We also found that the number of PMP, EMP and MoMP were higher in patients who were positive against anti-topoisomerase I antibody than those negative ($p<0.01$, $p<0.05$ and $p<0.05$, respectively), whereas there were no significant differences in the numbers of each MP subset between the patients positive or negative against other SSc-specific autoantibodies. In addition, the number of PMP and EMP were higher in patients with interstitial lung disease than those without ($p<0.05$). Moreover, all MP subsets were significantly inversely correlated with the percentage of predicted forced vital capacity ($p<0.05$, $p<0.01$, and $p<0.01$, respectively).
Conclusions: These results suggest that MP subsets are associated with extended fibrotic phenotype in patients with SSc, and might be utilized as novel biomarkers.
References:
[1] Bayer C et al. Nat Rev Rheumatol. 6:21–9, 2010.
[2] Antonyak MA et al. Method Mol Biol. 1165:147–73, 2014.
[3] Budoni M et al. Cell Transplant. 22:369–79, 2013.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4275

FRI0355 IL-17A UP-REGULATION IN PERIPHERAL BLOOD MONONUCLEAR CELLS CO-CULTURED WITH AUTOLOGOUS SKIN FIBROBLASTS IS ASSOCIATED WITH DOWN-REGULATION OF PRO-FIBROTIC MEDIATORS AND INCREASED FIBROBLAST APOPTOSIS

S. Vettori[1], G. Barra[2], G. Pasquale[3], L. Pellecchia[1], L. Vicedomini[1], R. De Palma[1], G. Valentini[1]. *[1]Internal and Experimental Medicine "F. Magrassi", University of Campania "Luigi Vanvitelli", Naples; [2]Internal and Experimental Medicine "F. Magrassi", University of Campania "Luigi Vanvitelli", Napoli; [3]Internal and Experimental Medicine "F. Magrassi", University of Campania "Luigi Vanvitelli", Naples, Italy*

Background: IL-17A has been implicated in the pathogenesis of systemic sclerosis (SSc) (1). We previously showed that skewed peripheral blood mononuclear cells (PBMCs) from SSc patients can induce Fas-mediated apoptosis in co-cultured autologous skin fibrobalsts (2).
Objectives: We therefore aimed to investigate IL-17A expression and effects in these co-cultures.
Methods: PBMCs and skin fibroblasts from 5 dcSSc patients with disease duration <3 years were co-cultured up to 10 days in presence of hrIL-2 [20 U/ml] in a 1:10 ratio, as previously described. IL17A, IL17RA, CXCL1, CCL2, CCL3, TGFBR2, SMAD3, CTGF, COL1A1, COL3A1 mRNA expression was assessed by Sybr Green real-time PCR. Chemokine production was further investigated at the protein level by multiple suspension immunoassay. In subset experiments, co-cultures were treated with either IL-17A or IL-17A *plus* anti-IL17 receptor A neutralizing monoclonal antobodies (anti-IL-17RA mAb), then cells were stained with Annexin V, anti-IL17RA, and anti-FAS antibodies and were investigated by flow-citometry.
Results: IL17A mRNA in co-cultured PBMCs was increased by 11.5 fold ($p<0.01$), and IL17RA by 4.3 fold ($p<0.05$) in co-cultured fibroblasts. CXCL-11, CCL2, and CCL3 were also up-regulated at both mRNA (11.9 fold, 773.3 fold, and 29 fold, respectively; $p<0.05$) and protein level (8.9 fold, 11.2 fold, and 252.4 fold, respectively; $p<0.05$). Profibrotic mediators, such as COL1A1, COL3A1, and CTGF mRNA expression in co-cultured fibroblasts was reduced to 0.33 fold, 0.24 fold, and 0.31 fold, respectively ($p<0.05$). This effects were associated with mRNA down-regulation of two key effectors of TGF-β signaling, TGFBR2 and SMAD3 to 0.59 and 0.79 fold, respectively. At flow cytometry analysis, we observed a reduction in co-cultured fibroblasts apoptosis by adding IL-17RA neutralizing mAb to IL-17A treated cells (39% to 16.8%; $p<0.05$), as compared to controls treated with IL-17A and isotype controls. Moreover, IL17RA mAb addition also reduced Fas expression in co-cultured fibroblasts as compared to IL-17A treated cells (47.7% to 10.6%; $p<0.05$).
Conclusions: Our results support the role of IL-17A in the pathogenesis of SSc. Furthermore, here we first show that IL-17A up-regulation in co-cultured PBMCs might play antifibrotic effects in autologous skin fibroblasts and might be implicated in fibroblast apoptosis, interphering with the FAS/FASL pathway.
References:
[1] Brembilla NC, Chizzolini C. T cell abnormalities in systemic sclerosis with a focus on Th17 cells. Eur Cytokine Netw 2012; 23: 128–39.
[2] De Palma R et al. Peripheral T cells from patients with early systemic sclerosis kill autologous fibroblasts in co-culture: is T-cell response aimed to play a protective role? Rheumatology (Oxford) 2010; 49: 1257–66.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6051

FRI0356 ANTISENSE LONG NONCODING RNAS ARE DEREGULATED IN SKIN TISSUE OF SSC PATIENTS

T. Messemaker[1], L. Chadli[2], G. Cai[3], V. Goelela[2], M. Boonstra[1], A. Dorjee[4], S. Andersen[2], H. Mikkers[4], T. Huizinga[4], Z. Li[3], O. Distler[5], M. Whitfield[3], R. Toes[4], J. Aarbiou[2], J. De Groot[2], J. De Vries-Bouwstra[4], F. Kurreeman[4]. *[1]Rheumatology, LUMC; [2]Charles River Lab, Leiden, Netherlands; [3]Geisel School of Medicine at Dartmouth, Hanover, United States; [4]LUMC, Leiden, Netherlands; [5]University Hospital Zurich, Zurich, Switzerland*

Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis of skin and multiple organs of which pathogenesis is poorly understood. Here we studied differentially expressed coding and non-coding genes in relation to SSc pathogenesis with a specific focus on antisense non-coding RNAs.
Objectives: Here we studied differentially expressed coding and non-coding genes in relation to SSc pathogenesis with a specific focus on antisense non-coding RNAs.
Methods: Skin biopsy-derived RNAs from fourteen early SSc patients and six healthy individuals were sequenced with ion-torrent and analysed using DEseq2. Protein-coding and non-coding genes annotated in GENCODEV7 were analysed. Significant long non-coding RNAs were independently replicated in a Northern American dataset.
Results: 4901 genes with a fold change >1.5 and a false discovery rate of less than 5% were detected in patients versus controls. Upregulated coding genes clustered in immunological, cell adhesion and keratin-related processes as previously found by microarray studies. Interestingly, 676 deregulated non-coding genes were detected, 257 of which were classified as antisense genes. 42% of these antisense genes had a concurrent deregulated sense gene. The majority of the sense-antisense genes had a similar effect sizes in an independent North American dataset with three genes (OTUD6B-AS1, CTBP1-AS2 and HMGN3-AS1) exceeding the study-wide Bonferroni-corrected ρ-value ($P_{Bonf}<0.0024$, $P_{combined}=1.6x10^{-9}$, $1.7x10^{-6}$, $2.6xx10^{-6}$, respectively). Intriguingly, the correlation of sense-antisense gene pairs deregulated in SSc is stronger than sense-antisense gene pairs not deregulated in SSc ($p<0.001$).
Conclusions: For the first time we highlight that together with coding genes, (antisense) long noncoding RNAs are deregulated in skin tissue of SSc patients suggesting a novel class of genes involved in pathogenesis of SSc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6165

FRI0357 MICROPARTICLES AS A BIOMARKER AND A REDOX-DEPENDENT REGULATOR OF NEUTROPHIL ACTIVATION AND PROTEOLYTIC ACTIVITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

N. Maugeri, P. Rovere Querini, S. Franchini, E. Tombetti, G. Ramirez, V. D'Alberti, M.G. Sabbadini, M. Bianchi, C. Lunardi, A. Gabrielli, A. Manfredi. *AILS Patient Association on Scleroderma, Milan, Italy*

Background: Persistent oxidative stress and unrelenting vascular inflammation are hallmarks of Systemic Sclerosis (SSc). Platelet-derived microparticles (PD-uP) that express a bioactive redox-dependent moiety, HMGB1 accumulate in the peripheral blood of patients with SSc.
Objectives: To verify whether PD-uP might represent a biomarker of SSc clinical involvement and whether their biological actions is regulated by environmental redox.
Methods: Fifty-four patients with SSc were enrolled so far. Twenty healthy controls (HC) matched for sex and age were studied in parallel. PD-uP were characterized and quantified by flow cytometry. Leukocyte features, including expression and distribution of myeloperoxidase (MPO), were assessed by flow cytometry and confocal microscopy. PD-uP ability to regulate neutrophil activation and proteolytic action was assessed *in vitro* in defined redox conditions and *in vivo* upon intravenous (i.v.) injection in immunocompromised NSG mice, and traced at various times based on recognition of the human platelet antigen CD61. Action on fibroblasts derived from SSc patients and HC are being assessed using biochemical and functional assays.
Results: PD-uP are present in the blood of SSc patients. Their concentration is significantly higher than in the blood of HC ($p<0.0001$). A substantially higher fraction of SSc PD-uP express the prototypic DAMP, HMGB1 (70% SSc vs 5% HC). Among SSc patients, those with pulmonary hypertension had a significantly higher concentration of HMGB1+ PDuP ($p=0.002$). In contrast other disease-associated variables, including the extent of fibrosis and the presence of active SSc pattern at the NVC, were not apparently influent. Neutrophils of SSc patients were activated, as demonstrated by the MPO redistribution from the primary granules to the plasma membrane. Moreover, they had a substantially higher ability to degrade fibrin in vitro, suggesting that enzymes at the plasma membrane are bioactive. Circulating neutrophils appeared to be viable and the fraction of cells undergoing apoptosis was similar in SSc patients and HC. The extent of neutrophil activation was associated with the concentration of HMGB1+ PDuP ($p<0.001$). SSc PDuP but not HC PDuP induced MPO redistribution in vitro. The effect was dependent on HMGB1 and increased by oxidizing moieties. Injection in immunocompromised mice resulted in time-dependent association of SSc PDuP to mouse neutrophils, which contextually redistributed MPO at the plasma membrane.
Conclusions: HMGB1 expression on PD-up of SSc patients could help identify functionally relevant population of microparticles, involved in neutrophil activation/function and possibly valuable as a novel biomarker of vascular remodeling.
References:
[1] Sabbadini MG et al, Lupus, 1999.
[2] Filippi et al., Lancet Neurol 2013.
[3] Rocca MA et al., Brain Struct Funct, 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3980

FRI0358 99MTC-RHANNEXIN V-128 AS A NOVEL EARLY DIAGNOSTIC MARKER FOR INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS

L. Guo[1,2], J. Schniering[1], R. Schibli[3], A. Blanc[3], D. Chicco[4], S. Ye[2], O. Distler[1], M. Béhé[3], B. Maurer[1]. *[1]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [2]Department of Rheumatology, Renji Hospital, Shanghai Jiao Tong University, Shanghai, China; [3]Center for Radiopharmaceutical Sciences, Paul Scherrer Institute, Villigen-PSI, Switzerland; [4]Advanced Accelerator Applications, Colleretto Giacosa, Italy*

Background: Interstitial lung disease (ILD), the primary cause of death in systemic sclerosis (SSc), often occurs early in the disease course, yet only becomes symptomatic when there is already substantial functional impairment and morphologic changes. Thus, there is an unmet need for early diagnosis. Apoptosis is considered the first pathophysiologic event in SSc-ILD. Monitoring of apoptotic processes with nuclear imaging, a sensitive, specific and noninvasive

methodology, might be a promising new approach for the diagnosis of early SSc-ILD.

Objectives: To evaluate the radiotracer ^{99m}Tc-rhAnnexin V-128, which specifically targets a pathophysiologic key molecule of early apoptosis, for the detection of earliest stages of lung involvement in animal models of SSc-ILD with single photon emission computed tomography (SPECT/CT).

Methods: C57BL/6J mice were treated with a single intratracheal injection of bleomycin or saline. Animals were euthanized at days 3, 7, 14 and 21 post-injection (n=6). Lung injury was evaluated by analysis of HE and Sirius red staining. The Ashcroft score was applied for the semi-quantitative evaluation of fibrotic changes. Immunofluorescence using the TUNEL assay and double staining with specific cell markers were performed to determine apoptotic cells. Positive nuclei were quantified by manual and automatic counting with Image J analysis software. Three days after injection with bleomycin or saline, mice were injected with ^{99m}Tc-rhAnnexin V-128 (Advanced Accelerator Applications, Italy). After 1h, images were acquired using small animal SPECT/CT, followed by *ex vivo* autoradiography.

Results: In the model of bleomycin-induced lung fibrosis, inflammatory infiltrates (CD45+) occurred as early as day 3 with peak at day 7, whereas pulmonary fibrosis developed from day 7 as assessed by Sirius red staining and was most pronounced at day 21 (mean Ashcroft score=4.6, p=0.0286). Notably, the number of apoptotic cells evaluated by TUNEL staining, was highest at day 3 (mean ± SE=6.5±1.5positive cells/HPF, p=0.0436) compared with saline controls (mean ± SE=0.7±0.1, p=0.0095) and then decreased over time. To determine the type of apoptotic cells, we performed immunofluorescent co-stainings with different cell markers. Data displayed that endothelial cells (vWF+) and epithelial cells (cytokeratin+), but not inflammatory cells (CD45+) were the primary cells undergoing apoptosis in earliest inflammatory stages of ILD.

In accordance with the findings on tissue level, at day 3 post-injection, we detected *ex vivo* with autoradiography, yet not with *in vivo* SPECT/CT, an increased pulmonary uptake of ^{99m}Tc-rhAnnexin V-128 in the lungs of bleomycin-induced mice compared with saline treated controls.

Conclusions: Apoptosis of epithelial and endothelial cells preceded the development of pulmonary inflammation and fibrosis in the model of bleomycin-induced lung fibrosis. Thus, the use of ^{99m}Tc-rhAnnexin V-128 might be a promising approach for the diagnosis of earliest stages of ILD. However, sensitivity of *in vivo* imaging has to be further improved.

Disclosure of Interest: L. Guo: None declared, J. Schniering Grant/research support from: Swiss National Science Foundation (S-85605–02–01), R. Schibli: None declared, A. Blanc: None declared, D. Chicco Employee of: Advanced Accelarator Applications, S. Ye: None declared, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi;patent licensed mir-29 for the treatment of systemic sclerosis, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha, M. Béhé: None declared, B. Maurer Grant/research support from: AbbVie, Protagen, EMDO, Novartis, Pfizer, Roche, Actelion. Patent licensed: mir-29 for the treatment of systemic sclerosis

DOI: 10.1136/annrheumdis-2017-eular.4945

FRI0359 THE IMPACT OF NARROWBAND ULTRAVIOLET A1 ON PROLIFERATION AND APOPTOSIS MARKERS IN ANIMAL MODEL OF SCLERODERMA

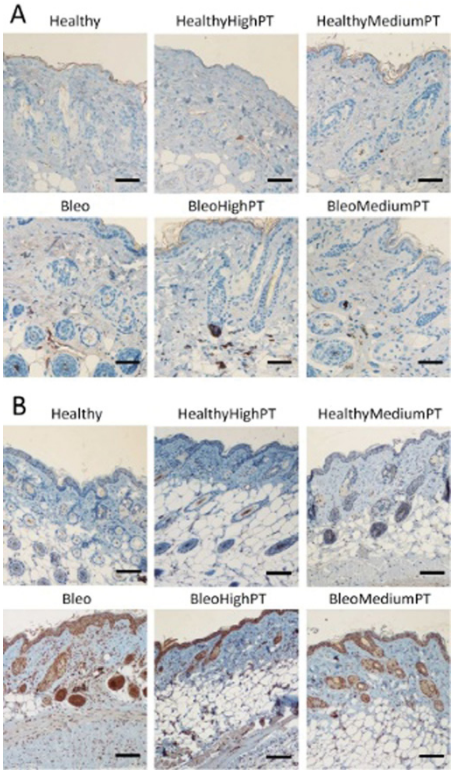
D. Karpec[1,2], R. Rudys[2], L. Leonaviciene[2], Z. Mackiewicz[2], R. Bradunaite[2], G. Kirdaite[2], R. Rugiene[1,2], A. Venalis[1,2]. [1]*Center of Rheumatology, Vilnius University;* [2]*State Research Institute Centre for Innovative Medicine, Vilnius, Lithuania*

Background: Narrowband ultraviolet A1 (UVA1) phototherapy implications for systemic sclerosis still remain the area of research.

Objectives: To define the efficacy and safety of 365±5 nm UVA1 for the dermal fibrosis treatment in bleomycin-induced mouse model of scleroderma.

Methods: DBA/2 strain mice were randomly divided to 6 groups: I – healthy animals; II – control group with bleomycin induced scleroderma, III and IV – mice with established scleroderma, treated with high and medium dose of UVA1, V and VI – healthy mice, treated with high and medium dose of UVA1. Scleroderma model was induced according to the protocol [1]. Light source emitting a narrowband UVA1 of 365±5 nm and of 21 mW/cm^2 power density was used in the study. Phototherapy was performed 3 times weekly for 5 weeks. The average cumulative doses were 1200 J/cm^2 for high and 600 J/cm^2 for medium dose treatments. Histological analysis with hematoxylin-eosin staining for dermal thickness measurement was performed. The immunohistochemical staining for p53, Ki-67 and active caspase-3 proteins was performed using specific antibodies. Statistical significance was expressed by a P value <0.05.

Results: The dermal thickness of mice treated with high and medium dose of UVA1 was significantly reduced to 272.9±113.2 and 394.0±125.9 μm, respectively, in comparison to the control group II (599.0±55.7 μm). The percentage of Ki-67 positive cells in mice with scleroderma after high- and medium-dose of UVA1 did not differ from the control group (II). The expression of p53 was significantly higher in the skin of the control group (II) compared to that of healthy mice skin (group I). After treatment of mice with scleroderma with high- and medium-dose of UVA1, the expression of p53 in the dermal layers did not differ from the control group (II) of non-treated mice. There was no change of p53 nor Ki-67 expressions between healthy (group I) and UVA1-treated healthy mice skin (groups V and VI). The statistically significant increase of active caspase-3 expression in the skin of mice with scleroderma was present after high- and medium-dose of UVA1 (groups III and IV) as compared to that of non-treated mice group (II). The expression profile of active caspase-3 did not differ between healthy (group I) and UVA1-treated healthy mice skin (groups V and VI). Results are summarized in Table 1 (Ki-67) and Figure 1 (A - active caspase-3; B - p53 immunohistochemical analysis).



Conclusions: The cumulative doses of 1200 J/cm^2 and 600 J/cm^2 of narrowband UVA1 effectively reduced the dermal thickness, and the impact was dose-dependent. Phototherapy course did not up-regulate p53 nor Ki-67 proteins in the healthy mice and mice with scleroderma skin. UVA1 radiation caused the increase of the active caspase-3 expression in the skin of mice with scleroderma reflecting the apoptotic feature of narrowband UVA1. The results of this study indicate that 365±5 nm UVA1 phototherapy is safe and effective for the treatment of dermal fibrosis.

References:

[1] Avouac J. Mouse model of experimental dermal fibrosis: the bleomycin-induced dermal fibrosis. Methods Mol Biol 2014; 1142: 91–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2869

FRI0360 ANALYSIS OF ENDOCANNABINOID SYSTEM ELEMENTS AND RELATED INFLAMMATORY MOLECULES IN PERIPHERAL BLOOD LEUKOCYTES OF PATIENTS WITH SYSTEMIC SCLEROSIS

C. Perez-Sanchez, R. Ortega-Castro, C. del Río, M.A. Aguirre, P. Ruiz-Limon, N. Barbarroja, Y. Jimenez-Gomez, I. Arias-de la Rosa, M.C. Abalos-Aguilera, E. Collantes-Estevez, E. Muñoz, C. Lopez-Pedrera. *IMIBIC/Reina Sofia University Hospital/University of Cordoba, Cordoba, Spain*

Background: The Endocannabinoid system (ECS) is a potential target for treatment of systemic sclerosis (SSc). Several cytokines/chemokines have been implicated in the induction of fibrosis in SSc, but their profile in peripheral blood

Abstract FRI0359 – Table 1

Percentage of Ki-67 positive cells	Healthy (I)	Bleo (II)	BleoHighPT (III)	BleoMediumPT (IV)	HealthyHighPT (V)	HealthyMediumPT (VI)
Average (%)	50.4	36.1	35.4	37.2	50.1	49.4
SD	2.6	3.0	3.2	2.8	2.0	1.4

mononuclear cells (PBMCs), and a relationship among specific inflammatory mediators, ECS, and organ involvement has not been established

Objectives: To analyze ECS elements and related inflammatory molecules in PBMCs of SSc patients, and evaluate their relationship with the clinical profile of the disease

Methods: 24 SSc patients [including 5 Pre-SSc, 13 limited cutaneous SSc (lc-SSC) and 6 difusse cutaneous SSc (dc-SSc)] and 24 healthy donors (HD) were included. Purified PBMCs were used for analysis of gene expression of molecules belonging to the ECS: CB1, CB2, GPR55, PPARγ, FAAH, MAGL and TRPV. Inflammatory mediators were evaluated in PBMCs by RT-PCR. Clinical evaluation of patients was performed and correlation/association studies were developed

Results: Cannabinoid type-2 receptor, GPR55 and TRPV1 gene expression were reduced in PBMCs of SSc patients, while FAAH levels were elevated. CB2 levels were lower in lc-SSc in relation to sc-SSc, and related to the presence of auto-antibodies anti-Scl70. Concomitantly, levels of FAAH were higher in dc-SSc in relation to lc-SSc, and associated to the presence of anti-centromere antibodies. A relationship between the low levels of GPR55 and the presence of pulmonary arterial hypertension was further demonstrated. Reduced levels of TRPV were associated to pulmonary involvement.

Analysis of the inflammatory profile showed significantly increased PBMC expression levels of IL-1, IL-8, IL-12, MCP-1, TGFβ, TNFα, and VEGF-A in SSc. In addition, in the patient's group of Pre-SSc, specific elevation in various cytokines was demonstrated (i.e.IL-1,IL-17,VEGF-A), suggesting that these cytokines might act as early biomarkers of disease development. Patient's positive for anti-centromere antibodies showed increased expression of IL-4, IL-17 and MCP-1 in relation to those positive for anti-scl70. PBMCs expression levels of TGFβ, IL-12 and MCP-1 were higher in lc-SSc compared to ds-SSc. Interestingly, we observed a direct relationship between levels of these three cytokines and the occurrence of pulmonary hypertension, a pathology more frequent in lc-SSc, thus suggesting a role for these inflammatory molecules in pulmonary involvement in this form of the disease. Correlation studies demonstrated an interrelation among deregulated expression of various molecules belonging to the ECS (i.e. FAAH, GPR55 and TRPV1) and inflammatory mediators over-expressed in serum and immune cells (i.e. CRP, ESR, MCP-1, TNFα and VEGF-A)

Conclusions: SSc patients show altered gene profile of ECS and inflammatory mediators in PBMCs, which might allow the discrimination between limited and diffuse forms of the disease, and are associated with the presence of specific auto-antibodies and the internal organ involvement. Our overall data suggest an appealing potential target of ECS for treatment of SSc, as it seems to be related to the inflammatory profile

Acknowledgements: CTS-794 and ISCIII (PI15/01333 and RIER RD16/0012/0015

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4946

FRI0361 INTERLEUKIN-4 INDUCES CLASS-SWITCHING TO IGG4 AND SYNERGISTICALLY CONTRIBUTES TO PLASMABLASTS DIFFERENTIATION WITH INTERLEUKIN-21 THROUGH CD40 DEPENDENT MANNER IN IGG4-RELATED DISEASE

M. Akiyama, H. Yasuoka, K. Yoshimoto, T. Takeuchi. *Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan*

Background: IgG4-related disease (IgG4-RD) is a lymphoproliferative disorder characterized by elevated serum levels of IgG4 and increased numbers of circulating plasmablast. We have previously reported that class-switching to IgG4 and plasmablast differentiation are mediated by follicular helper type 2 T cells which are known to secrete interleukin (IL)-4, IL-13, IL-10 and IL-21 (1, 2). However, the cytokines which play a role in the IgG4 class-switching and plasmablast differentiation through cell to cell contact remain unclear in IgG4-RD.

Objectives: The aim of this study was to elucidate the role of follicular helper type 2 T cell cytokines (IL-4, IL-13, IL-10, and IL-21) and cell to cell interaction in the pathogenesis of IgG4-RD.

Methods: Peripheral blood mononuclear cells (PBMCs) were prepared from seven consecutive patients with active, untreated, newly diagnosed IgG4-RD and five healthy controls. To identify the cytokines which induce IgG4 class-switching, the cells were stimulated with IL-4, IL-13 or the combination with other cytokines, such as IL-10 or IL-21. The amounts of IgG4 and IgG in the culture supernatants were measured by cytometric bead arrays. The expression level of activation-induced cytidine deaminase (AID; an enzyme essential for class-switch recombination) was analyzed by quantitative PCR to confirm the induction of class-switching by stimulation with cytokines. The numbers of plasmablasts and plasma cells induced by cytokines stimulation were examined by flow cytometry. Moreover, an anti-CD40 antibody was added to the culture to elucidate the effects of cell to cell interaction on the differentiation of plasmablasts or plasma cells.

Results: IL-4 significantly induced CD40-stimulated PBMCs to undergo IgG4 class-switching in patients with IgG4-RD, while IL-13 did not show any positive effects. Moreover, the IgG4/IgG ratio in culture supernatants was also significantly higher in the stimulation with IL-4 compared to other cytokines in IgG4-RD. In addition, the expression levels of AID mRNA were increased by stimulation with IL-4 compared to that by no stimulation or CD40 stimulation in IgG4-RD. On the other hand, PBMCs from healthy controls showed no significant difference in IgG4 production after stimulation with either IL-4 or IL-13. Furthermore, IgG4 production stimulated with IL-4 was significantly higher in IgG4-RD than that in healthy controls. Assessing additional effects of IL-10 or IL-21 on IL-4, IL-10 and IL-21 did not increase IgG4 production and IgG4/IgG ratio compared to IL-4 alone in IgG4-RD. However, importantly, IL-21 synergistically induced plasmablasts or plasma cells differentiation in combination with IL-4, whereas no obvious change was observed in PBMCs stimulated with IL-4 alone in IgG4-RD. Of note, the differentiation of plasmablasts and plasma cells by IL-4 and IL-21 was markedly abolished in the absence of CD40 stimulation.

Conclusions: Our results strongly suggest that IL-4 plays a pivotal role in IgG4 class-switching, and the effective collaboration between IL-4 and IL-21 contributes to plasmablasts and plasma cells differentiation via CD40 dependent manner in patients with IgG4-RD.

References:

[1] Akiyama M, et al. Arthritis Res Ther. 2016;18:167.

[2] Akiyama M, et al. Arthritis Rheumatol. 2015;67:2476–81.

Acknowledgements: We thank all the physicians and others caring for the patients enrolled in our study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3040

FRI0362 ANGIOGENIC T CELL EXPANSION CORRELATES WITH SEVERITY OF PERIPHERAL VASCULAR DAMAGE IN SYSTEMIC SCLEROSIS

M. Manetti, S. Pratesi, E. Romano, I. Rosa, A. Martiradonna, S. Bellando-Randone, S. Guiducci, L. Ibba-Manneschi, E. Maggi, M. Matucci-Cerinic. *Experimental and Clinical Medicine, University of Florence, Florence, Italy*

Background: The mechanisms underlying endothelial cell injury and defective vascular repair in systemic sclerosis (SSc) remain unclear. Recent studies suggest that a novel T cell subset, the so-called angiogenic T (Tang) cells, may have an important impact on the repair of damaged endothelium. Tang cells are characterised by the co-expression of CD3, CD31 (platelet-endothelial cell adhesion molecule-1) and CXCR4 (or CD184, receptor for the CXC chemokine stromal cell-derived factor-1 (SDF-1)/CXCL12). Tang cells may promote the formation of new blood vessels and endothelial repair by stimulating the function and differentiation of endothelial progenitor cells possibly through the secretion of proangiogenic cytokines, thus fostering postnatal vasculogenesis.

Objectives: This study aimed to analyse the Tang cell population in relation to disease-related peripheral vascular features in SSc patients.

Methods: Tang cells ($CD3^+CD31^+CXCR4^+$) were quantified by flow cytometry in peripheral blood samples from 39 patients with SSc and 18 matched healthy controls (HC). $CD3^+CD31^+CXCR4^+$ Tang cells were expressed as a percentage of total $CD3^+$ T cells. Circulating levels of SDF-1α were assessed in paired serum samples by immunoassay. Skin sections from patients with early diffuse cutaneous SSc (n=7) and HC (n=6) were subjected to CD3/CD31 and CD3/CXCR4 double immunofluorescence staining.

Results: The percentage of circulating Tang cells was not different between the whole SSc patient cohort (median 29.9, interquartile range (IQR) 22.3–36.2) and HC (median 25.2, IQR 23.3–33.5). Subgroup analysis revealed that Tang cells were significantly increased in SSc patients with digital ulcers (DU) (median 35.5, IQR 32.2–42.5) compared either with SSc patients without DU (median 23.3, IQR 18.5–26.6) or with HC ($p<0.0001$ for both). Furthermore, Tang cell percentage was significantly higher in SSc patients with "late" nailfold videocapillaroscopy (NVC) pattern (median 34.9, IQR 25.0–42.0) than in those with "early"/"active" NVC patterns (median 26.5, IQR 20.4–32.9) and in HC ($p=0.01$ and $p=0.04$, respectively). No difference in circulating Tang cell counts was found when comparing either SSc patients without DU or patients with "early"/"active" NVC patterns and HC. In SSc peripheral blood, the percentage of Tang cells was inversely correlated to the levels of SDF-1α (Spearman's rho = -0.59, $p<0.0001$). Immunohistologic assessment of SSc skin sections revealed the presence of Tang cells in perivascular inflammatory infiltrates.

Conclusions: Our findings demonstrate for the first time that Tang cells are expanded in patients with SSc displaying most severe peripheral vascular complications. Such an expansion may be an ineffective attempt to compensate the need for increased angiogenesis and endothelial progenitor cell function. In SSc, Tang cells might represent a potentially useful biomarker reflecting peripheral vascular damage severity. Further studies are required to clarify the function of Tang cells and investigate the mechanisms responsible for their change in SSc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3017

FRIDAY, 16 JUNE 2017

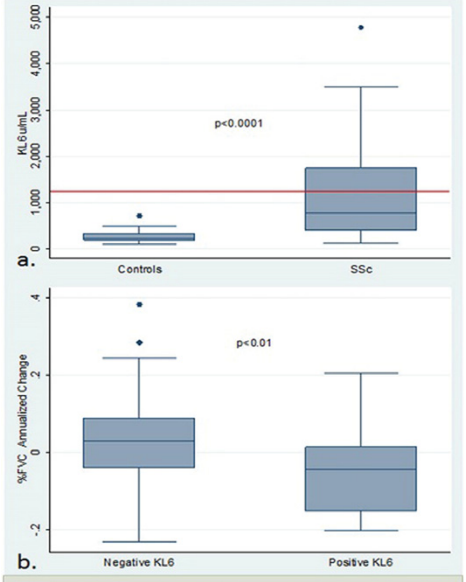
Scleroderma, myositis and related syndromes

FRI0363 KL6 AND NOT CCL-18 IS A PREDICTOR OF EARLY PROGRESSION IN SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE

G. Salazar[1], M. Kuwana[2], M. Wu[1], R.M. Estrada-Y-Martin[3], J. Ying[1], J. Charles[1], C. Bellocchi[4], M. Mayes[4], S. Assassi[4]. *[1]Rheumatology, University of Texas Medical School in Houston/McGovern Medical School, Houston, United States; [2]Department of Allergy and Rheumatology, Nippon Medical Graduate School of Medicine, Tokyo, Japan; [3]Pulmonary and Critical Care, University of Texas Medical School in Houston/McGovern Medical School; [4]Rheumatology, University of Texas Health Science Center at Houston, McGovern Medical School, Houston, United States*

Background: Pneumoproteins are attractive biomarker candidates in systemic sclerosis (SSc) related interstitial lung disease (ILD) because they are easily obtainable and lung-specific. KL-6 and CCL-18 (PARC) have been previously reported as promising predictive biomarkers of lung parenchymal damage in multiple disorders including SSc-ILD.
Objectives: Our goal was to determine the predictive significance of these two pneumoproteins for forced vital capacity % (FVC) decline within the first year of follow-up in patients with early SSc-ILD, in order to inform individualized care in routine clinical practice and facilitate enrichment strategies in clinical trials.
Methods: GENISOS (Genetics versus ENvironment In Scleroderma Outcome Study) cohort patients who had ILD verified by imaging and available pulmonary function tests at enrollment plus 12–18 months thereafter, were included in this study. All patients had disease duration ≤5 years at enrollment. FVC, expressed as percentage of predicted value was used as surrogate for severity of ILD. Annualized percent change in FVC at one year follow up was calculated. Baseline demographic, clinical variables and two pneumo-proteins, KL-6 and CCL-18 were investigated. KL-6 and CCL-18 were measured in the plasma by commercially available, validated ELISA kits. Linear regression with baseline clinical and demographic variables as independent variables was performed in univariable and multivariable models. Only variables that reached p<0.1 were included in the multivariable analyses.
Results: A total of 82 patients with early SSc-ILD were included, 18 were male and 45 had diffuse cutaneous involvement. Mean disease duration was 2.3 years. Rate of FVC% predicted change over time ranged from -0.23 to 0.38, indicating a highly variable course. Baseline KL-6 levels were higher in patients than healthy controls (p<0.0001). Baseline higher KL-6 levels were predictive of faster FVC% decline at the one year follow-up (b=-0.03, *p*=0.04). Upon categorizing KL-6 using a previously determined optimal cut-off of 1273 u/mL (1), its predictive significance remained in the univariate (p=0.01) and multivariable analyses adjusted for Scl-70, disease type and gender (b=-0.03, *p*=0.04). Twenty nine (34.5%) patients had KL6 levels equal or above 1273 u/mL. Although CCL-18 was higher in patients than controls (<0.0001), its levels did not predict rate of FVC decline (provide p-value)

Figure 1. KL-6 levels between patients and controls and %FVC change



a) KL-6 levels (u/mL) in SSc patients versus controls (red line= 1273 cut-off). b) %FVC annualized change in KL-6 positive versus negative patients based on a cut-off of 1273 u/mL. Note: Lower values in %FVC change correspond to a faster FVC decline.

Conclusions: KL-6 but not CCl-18 is predictive of early SSc-ILD progression. In this study, we also validated the previously proposed cut-off of 1273 for KL-6 in an independent cohort. KL-6 is a promising pneumoprotein that can inform individualized clinical care and contribute to enrichment strategies in clinical trials of SSc-ILD.

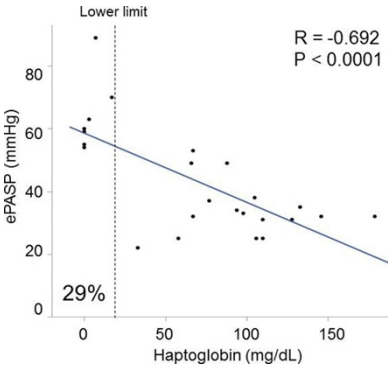
References:
[1] Kuwana M, Shirai Y, Takeuchi T. Elevated Serum Krebs von den Lungen-6 in Early Disease Predicts Subsequent Deterioration of Pulmonary Function in Patients with Systemic Sclerosis and Interstitial Lung Disease. J Rheumatol 2016.

Acknowledgements: This study was funded by the National Institute of Health NIH/NIAMS K23 AR061436 (Assassi); NIH/NIAMS P50-AR05414 and the Department of Defense Congressionally Directed Medical Research Programs (W81XWH-07–01–0111- Mayes).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5145

FRI0364 USEFULNESS OF SERUM HAPTOGLOBIN LEVELS AS A NOVEL MARKER FOR PULMONARY ARTERIAL HYPERTENSION COMPLICATED WITH CONNECTIVE TISSUE DISEASE

H. Nakamura, M. Kato, M. Kono, S. Tanimura, R. Hisada, E. Sugawara, K. Ohmura, S. Shimamura, Y. Fujieda, K. Oku, T. Bohgaki, O. Amengual, S. Yasuda, T. Atsumi. *Division of Rheumatology, Endocrinology and Nephrology, Hokkaido University Graduate School of Medicine, Sapporo, Japan*

Background: Pulmonary arterial hypertension (PAH) is of great clinical significance as a life-threatening complication of connective tissue diseases (CTD). Pulmonary artery thrombotic microangiopathy (PATM) is an important pathophysiology of PAH. The concept of PATM refers to localized thrombotic microangiopathy to be defined histologically and should be discriminated from systemic thrombotic microangiopathy characterized by microangiopathic haemolysis and thrombocytopenia. The degree of PATM has been suggested to be associated with vasodilator response, severity, and prognosis of PAH, and anticoagulation therapy might be effective in PAH patients with features of PATM [1]. Haptoglobin (Hp) is a plasma protein mainly produced by hepatocytes, which binds free haemoglobin released from erythrocytes and protects the kidneys from damage induced by haemoglobin. The Hp is measured in clinical setting as a sensitive marker to detect intravascular haemolysis including thrombotic microangiopathy [2].
Objectives: We hypothesized that serum Hp levels decreased in patients with PAH due to pulmonary microangiopathic haemolysis. The aim of this study was to investigate the association between serum Hp levels and pulmonary artery systolic pressure estimated by echocardiography (ePASP) in patients with CTD.
Methods: This study included CTD patients with suspicion of PAH who were attending Rheumatology Department in Hokkaido University Hospital between August 2015 and August 2016 and underwent echocardiography. PAH was diagnosed based on right heart catheter findings. Serum Hp levels were measured by standardised turbidimetric immunoassay in all patients. Demographic data, laboratory results, and echocardiographic findings were extracted from the medical records. Decreased serum Hp levels were defined as below 19 mg/dL based on the 95th-percentile of healthy controls.
Results: Twenty-four CTD patients with confirmed PAH (CTD-PAH) and 32 CTD patients without PAH (non-PAH) were enrolled. Decreased serum Hp levels were significantly frequent in patients with CTD-PAH compared with non-PAH patients (29% vs 6%, p=0.03). In patients with CTD-PAH, serum Hp levels had a significant negative correlation (r = -0.692, p<0.0001, Figure 1) with ePASP, and serum lactate dehydrogenase (LDH) levels were significantly elevated in patients with decreased Hp levels (233±47 U/L vs 187±42 U/L, p=0.01). Follow up study showed lowering ePASP led to normalizing serum Hp levels.



Conclusions: Serum Hp levels correlated negatively with ePASP in patients with CTD-PAH, and serum LDH levels were higher in CTD-PAH patients with decreased Hp levels. These findings suggest that decreased Hp levels in CTD-PAH patients may reflect PATM and subsequent subclinical haemolysis. Serum Hp levels are a candidate of additional non-invasive marker of CTD-PAH to assess the degree of PATM.

References:
[1] Johnson SR, et al. Thrombotic arteriopathy and anticoagulation in pulmonary hypertension. Chest. 2006.
[2] Barcellini W, et al. Clinical Applications of Hemolytic Markers in the Differential Diagnosis and Management of Hemolytic Anemia. Dis Markers. 2015.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2504

FRI0365 NEW COLLAGEN BIOMARKERS PREDICT PROGRESSION OF FIBROSIS IN SYSTEMIC SCLEROSIS

R. Dobrota[1], S. Jordan[1], P. Juhl[2], B. Maurer[1], L. Wildi[1], A.-C. Bay-Jensen[2], M.A. Karsdal[2], A.S. Siebuhr[2], O. Distler[1]. *[1]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [2]Nordic Bioscience, Herlev, Denmark*

Background: Systemic sclerosis (SSc) is a complex autoimmune disease with extensive fibrosis of the skin and internal organs in which extracellular matrix (ECM) remodeling is a key pathogenic process. Imbalance in the formation and degradation of collagens results in fibrosis. Quantifying the tissue turnover in a highly fibrotic disease such as SSc is very important for the prediction of disease progression and therapeutic efficacy. Given the clinical heterogeneity of SSc patients, biomarkers facilitating personalized medicine approaches are highly needed.
Objectives: To evaluate the potential of selected ECM neo-epitopes as serological biomarkers for diagnosis, prediction of clinical outcomes and disease progression in SSc.
Methods: Healthy controls (HC; n=29), stable SSc (n=149), and progressive SSc patients (n=23, progression defined either as 10% decrease in FVC% predicted or increase in mRSS ≥25% and 5 points on one year clinical follow up), meeting the 2013 ACR/EULAR classification criteria were analyzed. Longitudinal clinical assessment, data recording and sera collection were done according to EUSTAR standards. ECM-degradation (C3M, VICM, C4M2, BGM) and ECM-formation biomarkers (P1NP, P4NP7S, Pro-C3, Pro-C5, Pro-C6) were measured in serum using newly developed ELISA-based assays (Nordic Bioscience). Differences in biomarker levels were analyzed with respect to several fibrosis-related clinical outcomes. Statistical analysis was performed by Man-Whitney U, Kruskal-Wallis and Spearman tests. Biomarkers' sensitivity and specificity was examined by ROC analysis.
Results: Both ECM-degradation and ECM-formation biomarkers differed between SSc patients and HC: The expression of C4M2, Pro-C3, BGM and C3M was significantly increased in SSc patients compared to HC ($p<0.0001$, AUC=0.93; $p<0.0001$, AUC=0.74; $p=0.003$, AUC=0.67; $p<0.0001$; AUC=0.94, respectively), whereas P1NP was significantly lower ($p<0.0001$, AUC=0.78), Figure 1. Furthermore, Pro-C3, VICM and Pro-C6 levels were significantly higher in SSc progressors vs. HC ($p<0.0001$, AUC=0.86; $p=0.003$, AUC=0.75; $p=0.0005$, AUC=0.81, respectively).
Currently, there is no fully validated biomarker predicting worsening of fibrosis. In this regard, most interestingly, the ECM-degradation markers C4M2, BGM, C3M were significantly lower in SSc patients showing progression of fibrosis on follow up versus SSc patients being stable on follow up ($p<0.0001$; $p<0.008$; $p<0.0001$, respectively). Consistently, the formation marker Pro-C6 was significantly increased ($p=0.001$, AUC=0.71) indicating a profound imbalance of ECM turnover in progressors. The strongest difference between progressive and stable SSc patients was seen for the ratio between the formation and degradation biomarkers Pro-C3/C3M which showed an AUC of 0.86 in progressive vs. stable SSc patients ($p<0.0001$).
Conclusions: These data support ECM neo-epitopes as potential new biomarkers of prognostic interest in SSc. This could help identifying patients at risk of progression of their fibrotic disease at one year follow up. The significant decrease in ECM-degradation markers in SSc progressors compared to stable patients suggests an impairment of collagen degradation in this group. The ratio of Pro-C3/C3M is as a new potential predictive index for differentiation of stable vs. progressive patients.
Disclosure of Interest: R. Dobrota: None declared, S. Jordan: None declared, P. Juhl Employee of: Nordic Bioscience, B. Maurer: None declared, L. Wildi: None declared, A.-C. Bay-Jensen Employee of: Nordic Bioscience, M. A. Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, A. S. Siebuhr Employee of: Nordic Bioscience, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche,GSK, Intentiva, Lilly,medac, Mepha, MedImmune, Mitschubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha
DOI: 10.1136/annrheumdis-2017-eular.4909

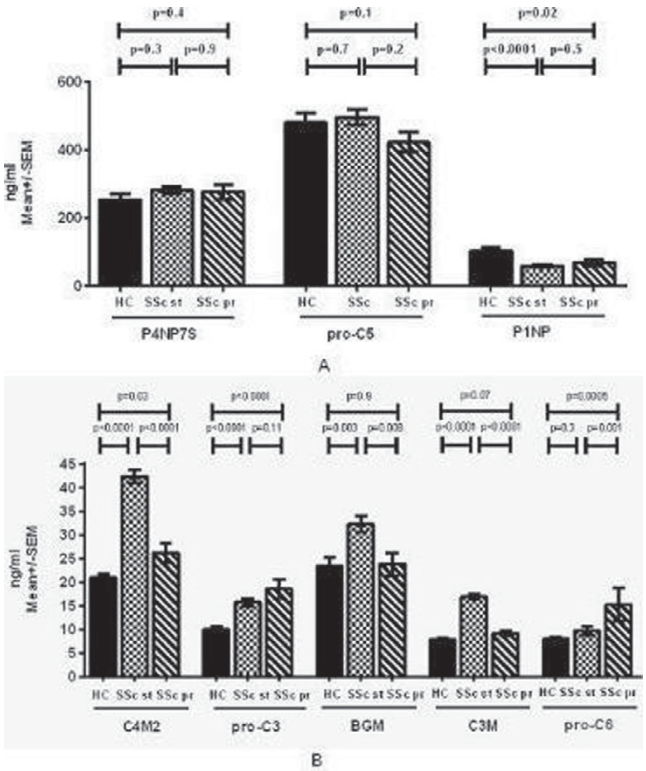


Figure 1: Expression of biomarkers in healthy controls (HC), stable SSc patients (SSc) and progressive SSc patients (SSc pr). A) P4NP7S- amino terminal pro-peptide of procollagen type IV; Pro-C5- formation of collagen type V; P1NP-amino terminal pro-peptide of procollagen type I; B) C4M2-MMP degraded collagen type IV ; Pro-C3- formation of collagen type III ; BGM -biglycan degraded by MMP-2/9; C3M-collagen III degraded by MMP-9; Pro-C6- formation of collagen type VI;

FRI0366 A PILOT STUDY ON ISCHEMIA AND REPERFUSION INJURY DURING A RAYNAUD'S ATTACK: SEQUENTIAL ASSESSMENT OF REDOX STRESS PARAMETERS IN A UNIQUE COOLING AND REWARMING EXPERIMENT

A.M. Van Roon[1], A. Eman Abdulle[1], A.M. van Roon[1], J.D. Lefrandt[1], A.J. Smit[1], H. Bootsma[2], B.O. Fernandez[3], M. Minnion[3], M. Feelisch[3], H. van Goor[4], D.J. Mulder[1]. *[1]Internal Medicine - Vascular Medicine; [2]Rheumatology and Clinical Immunology, University of Groningen - University Medical Center Groningen, Groningen, Netherlands; [3]Clinical and Experimental Sciences, University of Southampton, Southampton, United Kingdom; [4]Pathology, University of Groningen - University Medical Center Groningen, Groningen, Netherlands*

Background: Oxidative stress plays a role in systemic sclerosis (SSc), but the molecular mechanisms involved are incompletely understood. During an attack of Raynaud's phenomenon (RP) a period of ischemia (I), followed by reperfusion (R) occurs frequently, associated with the severity of vasculopathy. [1] Only in secondary RP digital ulcers develop. We hypothesized that I/R injury may play a role in the pathogenesis and could offer new therapeutic targets.
Objectives: To explore the course of oxidative stress in patients with SSc compared with primary RP and healthy controls.
Methods: A total of 30 patients were included: 10 with limited cutaneous SSc (age: 57 (53–61) yr, male/female 5/5), 10 with primary RP (age: 54 (41–58), 2/8), and 10 healthy controls (age: 25 (22–25), 3/7). A standardized cooling experiment was performed and digital perfusion was assessed in all 5 fingers using photo-electric plethysmography: at baseline (T=0) the dominant hand was submerged in water at 33℃, followed by cooling in steps of 3℃ every 4 minutes, until 6℃ or when pain became intolerable (T=1). Recording was continued 10 (T=2) and 30 (T=3) minutes of rewarming to ambient temperature (23℃). Blood was drawn from ipsilateral cubital vein at T0, 1, 2 and 3, markers for tissue injury (lactate, LDH, creatinine phosphokinase (CPK) [routine methods]), redox status (free thiols corrected for total protein) and nitric oxide (NO) activity (NO_2^-, NO_3^-, RXNO) were measured in plasma. [1–3] Numbers are in median (IQR).
Results: Baseline free thiols were significantly decreased in RP vs. controls (5.18 (4.79–5.63) vs 5.87 (5.41–5.99) umol/g, p=0.013), with no differences in lactate, LDH, CPK, and NO activity. Raynaud's attack was induced in all RP patients but not in controls. Median duration of hypoperfusion was greater in SSc vs. PRP (30 (27–35) vs. 12 (9–14) min, p=0.010), with a considerably longer recovery time (8 (4–10) vs. 0 (0–1) min, p=0.006). No changes were observed in lactate, LDH, and CPK levels. A rise in free thiols occurred at recovery (T4) in all 3 groups (figure 1). The concentrations of NO-related products did not change during cooling or recovery. No association was detected between the extent of I/R and plasma parameters.
Conclusions: In patients with RP free thiols were significantly reduced, indicating increased redox stress. During the cooling and rewarming experiment, a clear rise in free thiols was observed during rewarming, irrespective of the underlying disease or finger perfusion. Meanwhile, NO-related products remained stable.

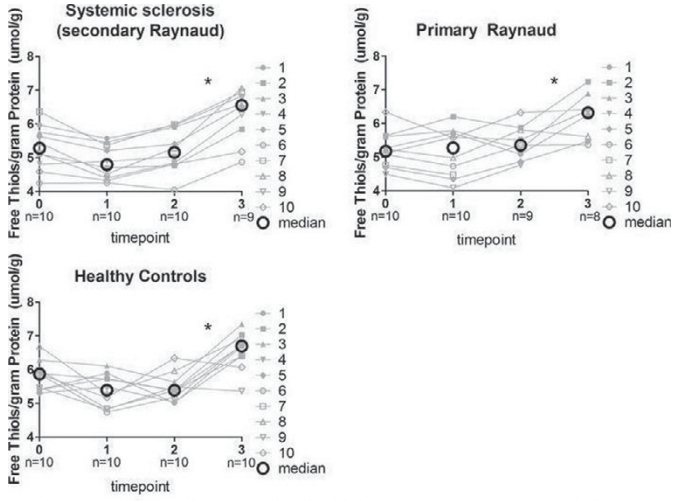


Figure 1. Free thiols per gram protein in all groups * p<0.005 between timepoint 2 and 3

Although these findings need further study, they may suggest activation of ubiquitous antioxidant defense mechanisms during cooling and/or rewarming and should be explored for future use as a potential therapeutic target in RP.

References:
[1] van Roon AM, et. al. Rheumatology (Oxford). 2016 Jun;55(6):1083–90.
[1] 2 Koning AM, et al. Pharmacol Res 2016 Sep;111:452–458.
[2] 3 Umbrello M, et al. J Physiol 2014 Mar 1;592(5):1061–1075.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5972

FRI0367 NEW AUTOIMMUNE TARGETS IN IDIOPATHIC INFLAMMATORY MYOPATHIES - AN ANTIGEN BEAD ARRAY APPROACH

A. Notarnicola[1], C. Hellstrom[2], C. Mattsson[2], E. Andersson[2], H. Idborg[1], E. Jemseby[1], M. Neiman[2], P.-J. Jakobsson[1], P. Nilsson[2], I.E. Lundberg[1].
[1]Department of Medicine, Rheumatology Unit, Karolinska University Hospital and Karolinska Institutet; [2]SciLifeLab, KTH - Royal Institute of Technology, Solna, Stockholm, Sweden

Background: The Idiopathic Inflammatory Myopathies (IIM) is a group of rare systemic inflammatory diseases characterized by severe organ involvement and premature mortality. Several myositis specific auto-antibodies (MSAs) have been recognized and associated with specific clinical manifestations and prognosis, still many patients are autoantibody negative. Identification of new autoimmune targets will be helpful in improving diagnosis, better stratifying into subgroups, prediction of prognosis, tailoring treatment and to understand underlying biological pathways.
Objectives: To identify new autoimmune targets in IIM by antigen bead array (1).
Methods: A bead array with 354 antigens was used to explore the autoimmune reactivity in 881 plasma samples from patients with IIM (N=225), Systemic Lupus Erythematosus (SLE) (N=350) and population controls (N=306). The antigens were selected from initial screenings of 160 SLE-samples on a total of 5760 antigens on planar arrays, and a first verification bead array with 355 antigens. The IIM samples represented three groups of patients with distinct diagnoses: Dermatomyositis (DM, N=83), Polymyositis (PM, N=111) and Inclusion Body Myositis (IBM, N=31), who were regularly followed at the Rheumatology Unit of the Karolinska University Hospital from January 2003 until March 2014. Based on 2 possible levels of cutoff, each sample was classified as reactive to each single antigen (Ag) at low or high cut off or non-reactive.
Results: In general, depending on the cutoff stringency, 86–88% of the 354 selected antigens showed reactivity in at least one sample with no difference between IIM, SLE and controls. Comparing PM, DM, IBM according to the number of samples which showed reactivity towards each single Ag, reactivity at high cut off towards NADH dehydrogenase 1 α subcomplex 11 (NDUFA11), poly(A) RNA polymerase D4 (PAPD4), CD163, l(3)mbt-like 1 (L3MBTL1) and calcium release-activated calcium modulator 2 (ORAI2) was discovered with higher frequencies in the IBM samples compared to PM and DM. In the group of IIM patients testing negative for all the known MSAs increased reactivity at high cut off was observed towards E3 ubiquitin protein ligase 2 (SIAH2), leiomodin 2 (LMO2) and RAD23 homolog A (RAD23A). In the group of IIM patients with history of malignancy and no evidence for anti-p155/140 antibodies the antigens early B-cell factor 2 (EBF2), POU class 6 homebox 1 (POUF61) and growth differentiation factor 7 (GDF7) revealed high serum reactivity. In IIM patients with interstitial lung disease increased reactivity at high cut off was found towards zinc finger protein 688 (ZNF688) and prostaglandin D2 receptor (PTGDR). A high frequency of known target reactivities (MSAs) was also confirmed.
Conclusions: Reactivity towards autoantigens corresponding to human proteins was present in plasma samples from IIM, controls, and SLE. Potentially new autoimmune targets have been discovered in IIM subgroups, although further validation in independent cohorts is needed.

References:
[1] Ayoglu B1 et al. Anoctamin 2 identified as an autoimmune target in multiple sclerosis. Proc Natl Acad Sci U S A. 2016 Feb 23;113(8):2188–93.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5863

FRI0368 NAILFOLD CAPILLAROSCOPY CHANGES REFLECT ENDOTHELIAL ACTIVATION AND INJURY IN PATIENTS WITH SYSTEMIC SCLEROSIS

A.M. Gheorghiu[1], R. Sfrent-Cornateanu[2], D. Marta[3], M. Bojinca[1], S. Magda[4], T. Constantinescu[5], A. Soare[6], R. Dobrota[6], L. Macovei[1], V. Stoica[1], C. Bara[2], C. Mihai[1]. *[1]Internal Medicine and Rheumatology, Cantacuzino Hospital; [2]Immunology and Physiopathology Department, Carol Davila University of Medicine and Pharmacy; [3]Victor Babes National Institute of Research and Development; [4]Cardiology Department, University Emergency Hospital; [5]Marius Nasta National Pneumology Institute, Carol Davila University of Medicine and Pharmacy; [6]Internal Medicine and Rheumatology, Cantacuzino Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

Background: Systemic sclerosis (SSc) is a severe connective tissue disease characterized by vascular and fibrotic changes in the skin and various internal organs. Pathogenesis of SSc includes early-onset vasculopathy with endothelial cell activation, microvascular injury and impaired angiogenesis.
Objectives: We aimed to determine the association of several biological molecules reflecting endothelial cell activation or dysfunction: E- selectin (E-sel), inter-cellular adhesion molecule 1 (ICAM-1), endothelin 1 (ET-1), von Willebrand factor (vWF) and interleukin 6 (IL-6), with distinct capillaroscopic SSc patterns and with more severe disease.
Methods: Forty consecutive SSc patients attending our EUSTAR SSc clinic, aged [median (IQR)] 52 (18) years, male gender 4/40 (10%), diffuse cutaneous subset (dcSSc) 14/40 (35%) were enrolled in this study. Extensive clinical and nailfold capillaroscopy (NFC) pattern assessment, as well as quantification of serum E-sel, ICAM-1, ET-1, vWF, IL-6 and C-reactive protein (CRP) were performed on all patients. Associations between vascular biomarkers and disease characteristics were evaluated by Mann-Whitney U-test and Spearman correlations.
Results: NFC "late" pattern was found in 21 patients, while 6 had "early" and 13 had "active" NFC pattern. All 5 vascular biomarkers correlated with each other good to moderately, with r indices varying between 0.660 and 0.332, the only exception being ET-1 which did not correlate with E-sel. Good correlations (r 0.465 to 0.727) were also found between all 5 biomarkers and CRP. Patients with severe vasculopathy, as reflected by the NFC "late" pattern, had higher levels of IL-6 (median 12.06 vs. 3.08 pg/mL, p=0.001), ET-1 (median 2.06 vs 1.59 pg/mL, p=0.029), vWF (median 3284 vs 2730 IU/mL, p=0.013) and E-sel (median 52.6 vs. 42.3 ng/mL, $p>0.05$), compared to patients with NFC "early" or "active" patterns. There was a significant, negative correlation between lung transfer for carbon monoxide (DLCO) and E-sel, ICAM-1 (both $p<0.001$) and vWF (p=0.013). ET-1 was higher in patients with more severe disease (dcSSc, patients positive for anti-topoisomerase antibodies and patients with a history of digital ulcers – all $p<0.05$).
Conclusions: Serum biomarkers reflecting endothelial cell activation and/or dysfunction are elevated in patients with more severe SSc-associated vasculopathy and correlate with serum CRP. Together with NFC data they might be used for assessing vasculopathy severity in SSc and identifying patients who would benefit from more aggressive vasoactive treatment.
Acknowledgements: *This work was performed as part of the project "Development of a computer-based nailfold videocapillaroscopy (NVC) system for longitudinal evaluation of patients with systemic sclerosis" (QUANTICAP), financed by the UEFISCDI PN-II-PT-PCCA-2013–4-1589 grant.*
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5203

FRI0369 PROSPECTIVE EVALUATION OF THE CAPILLAROSCOPIC SKIN ULCER INDEX (CSURI) IN CLINICAL PRACTICE

U.A. Walker[1], V.K. Jaeger[1], L. Arlettaz[2], M. Banyai[3], J. Beron[4], C. Chizzolini[5], E. Gröchenig[6], R.B. Mueller[7], F. Spertini[8], P. Villiger[9], O. Distler[10]. *[1]University Hospital Basel, Basel; [2]Hôpital du Valais, Sion; [3]Kantonsspital Luzern, Luzern; [4]Actelion Pharma Schweiz AG, Baden; [5]Hôpitaux Universitaires de Genève, Genève; [6]Kantosspital Aarau, Aarau; [7]Kantonsspital St. Gallen, St. Gallen; [8]Centre Hospitalier Universitaire Vaudois, Lausanne; [9]University Hospital Bern, Bern; [10]University Hospital Zurich, Zurich, Switzerland*

Background: Nailfold videocapillaroscopy (NVC) is an imaging technique representing a reliable tool for the classification, diagnosis and monitoring of systemic sclerosis (SSc) patients. The capillaroscopic skin ulcer index (CSURI) was suggested to identify patients at risk of developing digital ulcers (DU) [1].
Objectives: This study aims (1) to describe the practicality of the CSURI in clinical practice, (2) to describe the change of CSURI during follow-up, and (3) to assess associations between the change in CSURI and demographic and disease characteristics.

Methods: This Swiss multicentre, prospective, observational study analysed SSc patients with a history of active DU. Demographic characteristics and routine clinical data were recorded and patients underwent NVC at baseline and at the follow-up visit.

The centres' investigators were trained to perform NVC and, the nailfolds of 8 fingers (digit 2–5 on both hands) were examined if possible. All images were stored centrally and separately analysed by two extensively trained and experienced reviewers (OD & UAW) separately.

In each NVC image the total number of capillaries in the distal row, the number of megacapillaries and the maximum diameter of the megacapillaries were assessed. Based on these 3 characteristics, the CSURI was calculated according to Sebastiani et al. [1] for patients with at least 1 megacapillary present. Data were analysed descriptively.

Results: Between 2011 and 2015, 61 patients fulfilled the eligibility criteria and had at least one follow-up visit (median observation time 1.0 years, interquartile range [IQR] 1.0–1.1). Of these patients, more than a third (reviewer 1: n=24 patients, 39%; reviewer 2: n=26 patients, 43%) had no megacapillaries present on NVC on any assessed finger and hence the CSURI could not be calculated for those either at baseline or follow-up. Therefore, this analysis is based on the remaining 34 patients who had at least one megacapillary present on NVC at baseline and at follow-up by both reviewers (26% male; median age 57 years, IQR 48–65 years).

The median baseline CSURI scores according to reviewer 1 was 5.3 (IQR 2.6–16.3) increasing to a median of 5.9 (1.3–12.0) at follow-up. The CSURI as evaluated by reviewer 2 reduced from baseline (median 6.4, IQR 2.4–12.5) to follow-up (5.0, IQR 1.7–10.0).

None of the assessed demographic or disease characteristics (Box 1) were associated with the changes in the CSURI between baseline and follow-up for the scores obtained by reviewer 1 and reviewer 2 at the same time; although the limited sample size should be kept in mind interpreting this lack of association.

Box 1: Characteristics assessed for associations with the baseline capillaroscopic skin ulcer index (CSURI) as well as the change in CSURI between the baseline and the follow-up visit.

Demographic characteristics
Age
Sex
Smoking habit (Never/previous/current smoker)
Disease characteristics
Time since Raynaud's phenomenon onset
Time since first non-Raynaud's phenomenon manifestation
Time since first digital ulcers
Previous major digital vascular complication (None/soft tissue infection/ auto-amputation/gangrene)
Cutaneous involvement (Diffuse/limited)
Erectile dysfunction
Proteinuria (>300 mg/dl)
Renal crisis
Pulmonary arterial hypertension
Raynaud's phenomenon condition score at baseline
Modified Rodnan skin score at baseline
Number of digital ulcers at baseline
Laboratory parameters
Anti-nuclear antibodies positive
Anti-centromere antibodies positive
Anti-topoisomerase autoantibodies positive

Conclusions: In this study, around 40% of patients could not be evaluated with the CSURI due to the absence of megacapillaries on NVC. Clinical decisions based on the CSURI in routine practice should be made with caution, as it can vary greatly between assessors even if they are extensively trained.

References:

[1] Sebastiani M, et al. Predictive role of capillaroscopic skin ulcer risk index in systemic sclerosis: a multicentre validation study. ARD 2012;71:67–70.

Acknowledgements: This study was supported by Actelion Pharma Schweiz AG.

Disclosure of Interest: U. Walker: None declared, V. Jaeger: None declared, L. Arlettaz: None declared, M. Banyai: None declared, J. Beron Employee of: Actelion Pharma Schweiz AG, C. Chizzolini: None declared, E. Gröchenig: None declared, R. Mueller: None declared, F. Spertini: None declared, P. Villiger: None declared, O. Distler Grant/research support from: 4 D Science, AbbVie, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, iQone Healthcare, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm and Sinoxa, Consultant for: 4 D Science, AbbVie, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, iQone Healthcare, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm and Sinoxa

DOI: 10.1136/annrheumdis-2017-eular.1827

FRI0370 THREE-DIMENSIONAL NAILFOLD CAPILLARY IMAGING BY DYNAMIC OPTICAL COHERENCE TOMOGRAPHY IN SYSTEMIC SCLEROSIS: A VALIDATION STUDY USING NAILFOLD VIDEO-CAPILLAROSCOPY

G. Abignano [1,2], L. Green [1,2], S. Eng [1,2], P. Emery [1,2], F. Del Galdo [1,2]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

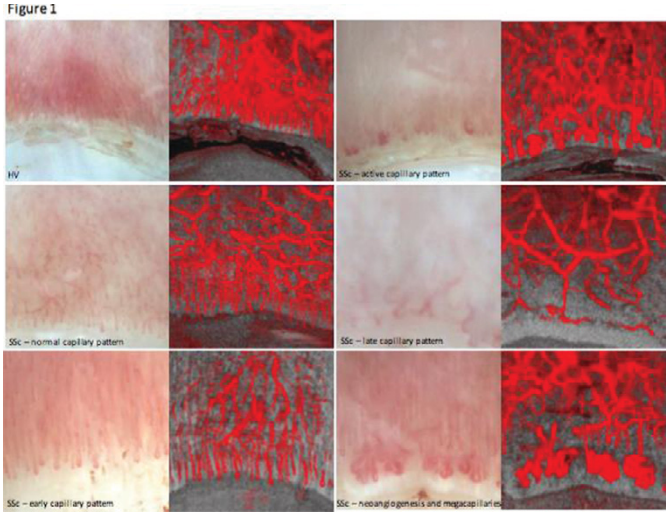
Background: Optical Coherence Tomography (OCT) of the skin has been proposed as imaging biomarker of fibrosis in Systemic Sclerosis (SSc) (1). However, over the past few years, growing efforts have been made to enable OCT to the study of human skin microcirculation including human nailfold (2). Dynamic OCT (D-OCT) is a newly developed OCT technology that allows detection of blood flow in vivo in addition to the images of traditional OCT scans (3).

Objectives: Aims of this study were: 1) to evaluate face/criterion validity and feasibility of nailfold capillary D-OCT imaging as compared with nailfold video-capillaroscopy (NVC) capillary patterns in SSc patients; 2) to investigate whether D-OCT could offer a complementary value to NVC through the 3-dimensional reconstruction and quantification of nailfold capillary abnormalities in SSc patients.

Methods: Fifty subjects including forty SSc patients all fulfilling 2013 EULAR/ACR classification criteria (10 with normal/non-specific, 10 with early, 10 with active, 10 with late capillary pattern respectively) and ten age/gender-matched healthy volunteers (HV) were enrolled in this study. All subjects had NVC done on 8 fingers and classified according to the capillary pattern. Nailfold of the finger with the worst capillary score in SSc patients and the 4th finger (the most affected in the SSc groups) of the dominant hand in subjects with normal capillary pattern was subsequently scanned using Vivosight D-OCT (Michelson Diagnostics Ltd., Kent, UK). D-OCT images were analyzed using the proprietary software tool to extract a quantitative measure of the speckle variance (SV)-signal. Results were expressed as mean±standard error. Statistical analysis was performed using GraphPad Prism software V.7.0.

Results: The finger with the worst capillary score was the 4th (83%) in the SSc patients. The typical nailfold capillary features seen at NVC were visualized at D-OCT images. Representative images are shown in figure 1. Each nailfold D-OCT scan lasted 60 seconds, was well tolerated and did not require use of gel or immersion oil. OCT mean SV-signal measurements were significantly different between HV and SSc patients with any specific capillary pattern (0.16±0.02 vs 0.10±0.01, p=0.0028) and between SSc patients without and with specific capillary pattern (0.14±0.01 vs 0.10±0.01, p=0.02). The mean SV-signal was higher in HV than in SSc patients without specific capillary pattern however the difference was not statistically significant. When analyzing the three specific capillary patterns, SV-signal measurements were not significantly different. Interestingly, within the late capillary pattern, mean SV-signal was significantly lower in patients displaying capillary loss as main feature compared with those with remarkable neoangiogenesis (p=0.03).

Figure 1



Conclusions: D-OCT is a feasible technique able to reproduce the capillary changes seen at NVC in SSc patients. More importantly D-OCT could offer a complementary value to quantify peripheral blood flow at capillary level. Future longitudinal studies are needed to evaluate the sensitivity to change over time and the potential of D-OCT as quantitative outcome measure of microvasculopathy in SSc.

References:

[1] Abignano G et al. Ann Rheum Dis 2013.
[2] An L et al.Opt Express 2010.
[3] Ulrich M et al.Dermatology 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5598

FRI0371 CLINICAL ALGORITHMS FOR THE DIAGNOSIS AND PROGNOSIS OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS

V. Hax[1], M. Bredemeier[2], A.L.D. Moro[1], T.R. Pavan[1], M.V. Vieira[3], E.H. Pitrez[3], R.M.D.S. Chakr[1], R.M. Xavier[1]. *[1]Rheumatology Service, Hospital de Clínicas de Porto Alegre; [2]Rheumatology Service, Hospital Nossa Senhora da Conceição; [3]Radiology Service, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil*

Background: Interstitial lung disease (ILD) is currently the primary cause of death in systemic sclerosis (SSc). Thoracic high-resolution computed tomography (HRCT) is considered the gold standard for diagnosis. Recent studies have proposed several clinical algorithms to predict the diagnosis and prognosis of SSc-ILD.
Objectives: To test the clinical algorithms to predict the presence and prognosis of SSc-ILD, and to evaluate the association of extent of ILD with mortality in a cohort of SSc patients.
Methods: Prospective cohort study, including 177 SSc patients assessed by clinical evaluation, laboratory tests, pulmonary function tests, and HRCT. Three clinical algorithms, combining lung auscultation, chest radiography and % predicted forced vital capacity (FVC)[1], were applied for the diagnosis of different extents of ILD on HRCT. Univariate and multivariate Cox proportional models were used to analyze the association of algorithms [1,2] and the extent of ILD on HRCT with the risk of death using hazard ratios (HR).
Results: The prevalence of ILD on HRCT was 57.1% and 79 patients died (44.6%) in a median follow-up of 11.1 years. For identification of ILD with extent ≥10 and ≥20% on HRCT, all algorithms presented a high sensitivity (>89%) and a very low negative likelihood ratio (<0.16). For prognosis, survival was decreased for all algorithms, especially the algorithm C (HR 3.47, 95% CI 1.62–7.42), which identified the presence of ILD based on crackles on lung auscultation, findings on chest X-ray or FVC <80%. Extensive disease as proposed by Goh and Wells (extent of ILD >20% on HRCT or, in indeterminate cases, FVC <70%) had a significantly higher risk of death (HR 3.42, 95% CI 2.12 to 5.52). Survival was not different between patients with extent of 10 or 20% of ILD on HRCT, and analysis of 10-year mortality suggested that a threshold of 10% may also have a good predictive value for mortality. However, there is no clear cutoff above which mortality is sharply increased.

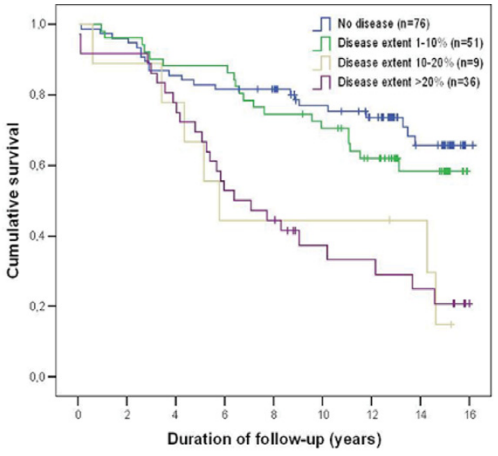


Figure 1. Survival in relation to the extent of lung disease on high-resolution computed tomography ($p<0.0001$ by log rank test).

Conclusions: Clinical algorithms had a good diagnostic performance for extents of SSc-ILD on HRCT with clinical and prognostic relevance (≥10 and ≥20%), and were also strongly related to mortality. Therefore, they probably could be used to obviate the requirement of HRCT in some cases.
References:
[1] Steele R, Hudson M, Lo E, Baron M. Clinical decision rule to predict the presence of interstitial lung disease in systemic sclerosis. Arthritis Care Res (Hoboken) 2012;64:519–24.
[2] Goh NSL, Desai SR, Veeraraghavan S, Hansell DM, Copley SJ, Maher TM, et al. Interstitial lung disease in systemic sclerosis: A simple staging system. Am J Respir Crit Care Med 2008;177:1248–54.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1448

FRI0372 THE DUCAS: PROPOSAL FOR A DIGITAL ULCER ASSESSMENT SCORE IN SCLERODERMA

C. Bruni[1], T. Ngcozana[2], F. Braschi[1], S. Guiducci[1], S. Bellando-Randone[1], Y.A. Suliman[3], J. Grotts[4], C.P. Denton[2], D.E. Furst[5], M. Matucci-Cerinic[1]. *[1]Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Firenze, Italy; [2]Centre for Rheumatology and Connective Tissue Diseases, UCL Division of Medicine, London, United Kingdom; [3]Rheumatology and Rehabilitation Department, Assiut University Hospital, Assiut, Egypt; [4]Department of Biostatistic; [5]Division of Rheumatology, Department of Medicine, University of California at Los Angeles, Los Angeles, United States*

Background: No objective measure is presently available to assess digital ulcer (DU) in SSc patients apart from "healed/non healed" and experience-based clinical judgment.
Objectives: The aim of the current study is to propose a composite DU clinical assessment score (DUCAS) and, to lend it, test its face validity by correlating it with commonly used disease related patient-reported outcomes (PROs) and physician evaluation.
Methods: SSc patients presenting at least one DU and attending the Rheumatology Wound Care Clinic of the Florence University Hospital or the London Royal Free Hospital were enrolled. Patients were assessed with HAQ-DI, Cochin scale, Visual analogic scale (VAS) for DU-related pain (DU_pain, 0–100 mm), patient VAS for global DU status (ptGDU, 0–100mm) and patient global assessment (PtGA, 0–100 mm) as PROs and physician VAS for DU status (phyGDU, 0–100mm). The DUCAS included 7 DU related variables selected by a committee of 8 SSc DU experts - they are outlined in figure 1. Each variable was weighted on a clinical basis and the DUCAS score was the sum of the values for the 7 variables (max=19.5). Spearman's correlation tests were calculated for to examine face validity. A linear regression model with forward and backward stepwise analysis was used to determine the relationship of individual variables with the primary clinical parameter, phyGDU.
Results: 44 SSc patients (9 males, mean age 54,3±15,6 years, mean disease duration 9,9±5,8 years) were enrolled in the study. Mean phyGDU was 44,3±23mm, mean ptGDU was 54±30mm (Wilcoxon p=0.022, phyGDU VAS vs ptGDU) and mean DUCAS score was 4,2±2. Overall DUCAS showed significant positive correlations with all PROs, but when all the individual clinician and patient's variables were modelled, only the overall DUCAS significantly predicted PhyGDU; after backwards stepwise analysis overall DUCAS and ptGDU best predicted PhyGDU, with an adjusted R^2=0,437 and AIC=380,3 (Table 2).

Table 1

A	Linear Regression for DUCAS		B	Linear Model to PhyGDU			Linear Model to PhyGDU after backwards stepwise		
	Spearman Correlation	p		Estimate	SE	p	Estimate	SE	p
PtGA	0,56	<0,001	PtGA	0,011	0,199	0,955			
PtGDU	0,54	<0,001	PtGDU	0,171	0,233	0,467	0,272	0,101	0,01
DU_Pain	0,44	0,003	DU_Pain	0,048	0,182	0,793			
HAQ-DI	0,44	0,003	HAQ-DI	4,58	7,563	0,549			
COCHIN	0,51	<0,001	COCHIN	0,035	0,252	0,891			
PhyGDU	0,63	<0,001	DUCAS	4,636	1,617	0,007	4,841	1,489	0,002

	DUCAS		
1	Number of Digital Ulcers	None	0
		1 DU	1
		2 DUs	2
		More than 3 Dus	3
2	New Digital Ulcers	YES	1
		NO	0
3	Gangrene	YES	3
		NO	0
4	Surgical approch to DU (above standard care)	YES	3
		NO	0
5	Infection of DU	None	0
		Requiring systemic antibiotics	1
		Osteomyelitis	2
		Septicemia	3
6	Unscheduled hospitalisation for DU	YES	3
		NO	0
7	Analgesics to control DU pain	No pain	0
		Non requiried analgesics	0,5
		Non-opioids analgesics	1
		Minor opioids	2
		Major opioids	3
		dose increased since last visit	*+0,5*
		dose decreased since last visit	*-0,5*
	TOTAL SCORE		

Conclusions: DUCAS is a newly proposed clinical score for SSc related DU which has face validity and which may reflect DU status as judged by SSc experts. Further validation of this score will be undertaken.
Acknowledgements: Cosimo Bruni received a EULAR travel bursary to run this project in the UK.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5735

FRI0373 SUBSTANCE P AND VASCULAR ENDOTHELIAL GROWTH FACTOR PRODUCTION BY PERIPHERAL BLOOD MONONUCLEAR CELLS DERIVING FROM PATIENTS WITH SYSTEMIC SCLEROSIS

A. Corrado, E. Sanpaolo, R. Colia, A. Mele, F.P. Cantatore. *Department of Medical and Surgical Sciences - Rheumatology Clinic, University of Foggia, Foggia, Italy*

Background: Many cytokines may potentially play a relevant role in the pathogenesis of different aspects of SSc, particularly fibrosis and endothelial injury. Some data suggest that substance P (SP) may act in an autocrine/paracrine manner to regulate vasoconstriction and/or immunologic and inflammatory responses. VEGF and MCP1, which are produced by inflammatory cells, may be involved in the pathogenesis of vascular changes and accumulation of extracellular matrix in SSc.
Objectives: The aim of this study was to determine the expression of Substance P (SP), Vascular Endothelial Growth Factor (VEGF), Monocyte Chemoattractant Protein-1 (MCP-1) in SSc patients and their relationship with the main clinical manifestations of disease
Methods: 34 SSc patients fulfilling the 2013 ACR/EULAR criteria for SSc and classified according to Leroy as having limited cutaneous (lSSc) or diffuse cutaneous (dSSc) disease were recruited. 28 sex and age matched healthy subjects was used as control. For each recruited patient we analyzed the disease characteristic, including the extent of skin fibrosis, the pattern of internal organ involvement, the presence of digital ulcers (DU) and autoantibody profile. Peripheral Blood Mononuclear Cells (PBMCs) were isolated and cultured from both SSc patients and healthy controls. The expression of SP, VEGF, MCP1 was analyzed by real-time polymerase chain reaction (PCR) and their concentrations where measured in supernatants of cultured PBMCs using enzyme-linked immunosorbent assay (ELISA). The correlation between cytokine expression and clinical manifestations was evaluated
Results: The results showed that the mRNA and the protein levels of SP and VEGF were significantly higher in SSc patients compared to controls (190,55±59,1pg/mL vs 128,85±69,8pg/mL and 422,31±149,4pg/mL vs 309,25pg/mL respectively, $p<0,05$); further, SP and VEGF levels were higher in dSSc compared to lSSc and correlated to disease duration. No difference was detected in MCP1 synthesis and expression between SSc subjects and healthy controls (507,17±153,9pg/mL vs 481,2±118,2 pg/mL) even if in dSSc patients a slight increase was observed. VEGF production negatively correlated with the prevalence of DU. No correlation between cytokines production and heart, lung and gastrointestinal involvement and autoantibody profile was found.
Conclusions: The preliminary data of this study show that SP and VEGF are over-expressed in PBMCs of SSc subjects and are related to the extent of skin involvement, whereas only VEGF production negatively correlates with the prevalence of DU. The exact role played by SP and VEGF in the pathogenesis of vascular injury and fibrosis in SSc and their relationship with the immune abnormalities observed in this disease is not completely clear and the available data are contrasting. Additional *in vitro* and *in vivo* studies are needed to better understand the role of SP and VEGF in the pathogenesis of SSc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6587

FRI0374 BONE MINERAL DENSITY AND TRABECULAR BONE SCORE IN TWO SUBSETS OF SYSTEMIC SCLEROSIS PATIENTS

A. Corrado, A. Mele, A. Trotta, R. Colia, S. Di Bello, F.P. Cantatore. *Department of Medical and Surgical Sciences - Rheumatology Clinic, University of Foggia, Foggia, Italy*

Background: Data concerning the relationship between Systemic Sclerosis (SSc) and alterations of Bone Mineral Density (BMD) are very conflicting. The established standard for measuring BMD is Dual X-ray Absorptiometry (DXA), but it does not provide any informations about the bone microarchitecture, which is a parameter very difficult to evaluate in clinical practice but it is essential to define bone strength. The Trabecular Bone Score (TBS) is a new structural parameter that can be obtained by DXA scanning and it is related to bone microarchitecture and provides data on bone quality irrespective of bone density.
Objectives: The aim of this study is to evaluate the differences in BMD and TBS values in two subsets of patients with SSc (limited and diffuse cutaneous disease – lSSc and dSSc) and to analyse their possible relationship with the parameters of body mass composition and phospho-calcium metabolism.
Methods: 64 post-menopausal patients classified according to Leroy as limited cutaneous (lSSc) or diffuse cutaneous (dSSc) SSc, were recruited. The following clinical parameters were evaluated: internal organ involvement, degree of skin involvement (Rodnan Skin Score), bone mass index (BMI). For each recruited patient, spine and hip BMD, TBS and body mass composition (lean and fat mass, total bone mineral content - BMC) were assessed by DXA. Serum calcium, phosphorus, alkaline phosphatase, intact parathyroid hormone (PTH) and 25-hydroxyvitamin D (25 OHD) were also measured.
Results: BMD at femoral neck and spine was significantly higher in lSSc compared to dSSc patients ($p<0,04$). In lSSc subjects also BMC was significantly higher compared to dSSc ones ($p<0,01$) but, interestingly the TBS was significantly lower ($p<0,03$). lSSc patients presented a higher values of fat mass compared to dSSc ($p<0,05$), with a slightly higher BMI (which did not reach statistical significance). 25OH serum levels were higher in lSSc group, whereas no differences between lSSc and dSSc in serum calcium, phosphorus, alkaline phosphatase were observed.
Conclusions: The presented preliminary data show that in SSc patients with limited cutaneous disease, the BMD values are higher compared to patient with diffuse cutaneous disease; nevertheless in this subset (lSSc) bone quality seem to be reduced, as TBS values are significantly lower. Higher BMC values and serum 25OHD levels observed in lSSc patients could be among the factors that contribute to increasing BMD in this clinical subset. Further analysis should be performed to identify the possible causes of the reduced bone quality in spite of higher BMD in lSSc patients, such as the study of serum adipokines, considering that the presented data show a great fat mass in patients with limited cutaneous disease.
References:
[1] Harvey NC. et al. Trabecular bone score (TBS) as a new complementary approach for osteoporosis evaluation in clinical practice. Bone. 2015 Sep;78:216–24.
[2] Bousson V. et al. Trabecular Bone Score: Where are we now? Joint Bone Spine. 2015 Oct;82(5):320–5.
[3] Corrado A. et al. Relationship between Body Mass Composition, Bone Mineral Density, Skin Fibrosis and 25(OH) Vitamin D Serum Levels in Systemic Sclerosis. PLoS One. 2015 Sep 16;10(9).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5207

FRI0375 REAL-LIFE TREATMENT STRATEGIES FOR SYSTEMIC SCLEROSIS ACCORDING TO EXPERTS

A. Fernández-Codina [1], K.M. Walker [2], J.E. Pope [3] on behalf of the participating members of the Scleroderma Clinical Trials Consortium (SCTC) and Canadian Scleroderma Research Group (CSRG). *[1] Systemic autoimmune diseases unit, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [2] Rheumatology, The Ottawa Hospital, Ottawa; [3] Rheumatology, University of Western Ontario, London, Canada*

Background: Second line treatment options for Systemic Sclerosis (SSc) are limited, and scarce data are available for choosing the order of treatment.
Objectives: The aim of this study is to update the SSc treatment algorithms obtained in 2012[1], based on SSc experts' daily practice.
Methods: An initial survey was designed based on the 2012 algorithms. The survey asked experts whether they agreed with the 2012 algorithms or not, and which changes should be considered. The questionnaire was completed by 62 of 168 surveyed (67% response) between August and October 2016.
Results: For *scleroderma renal crisis* (SRC), there was 65% to 69% agreement with the previous algorithms (1st line angiotensin converting enzyme inhibitors [ACEI], 2nd and 3rd adding: calcium channel blockers [CCB] or angiotensin receptor blockers [ARB], and 4th alpha-blocker). In mild *pulmonary arterial hypertension* (PAH), only 45% of the experts agreed with the old algorithm. The majority suggested first phosphodiesterase 5 inhibitors (PDE5i) or endotelin receptor antagonists (ERA) plus PDE5i, then prostanoids. In severe PAH, 65% agreed with the preexistent scheme (1st prostanoids, 2nd ERA plus PDE5i, 3rd ERA plus prostanoids). For mild *Raynaud's phenomenon* (RP) 66% agreed with the previous algorithm (1st CCB, 2nd adding PDE5i, 3rd ARB or switching to another CCB, 4th prostanoids). Regarding severe RP, 52% agreed with previous (1st CCB, 2nd adding PDE5i, 3rd ERA, 4th prostanoids). Conversely, 60% of the experts did not agree with the prior active *digital ulcer* (DU) treatment, suggesting 1st CCB, 2nd PDE5i, 3rd prostanoids. For *interstitial lung disease* (ILD), for induction only 24% agreed with the older proposal. Experts suggested 1st mofetil mycophenolate (MMF), 2nd intravenous (IV) cyclophosphamide (CYP), 3rd Rituximab. There was a 65% agreement on ILD maintenance (1st MMF, 2nd azathioprine [AZA], 3rd IV CYP, 4th oral CYP). For *skin involvement*, agreement for patients with a modified Rodnan skin score (mRSS) of 10 was 57% (1st methotrexate [MTX]), 2nd MMF); if the mRSS was 24, 32% suggested 1st MMF, 2nd MTX; and mRSS 32, 36% chose 1st MTX, 2nd MMF, 3rd IV CYP, 4th autologous stem cell transplantation (ASCT). In *inflammatory arthritis* 45% agreed with the previous algorithm, whereas others suggested 1st MTX, 2nd low dose steroids, 3rd hydroxychloroquine, 4th rituximab or tocilizumab.
Conclusions: There remains some disagreement for 2nd line treatment of SSc. Combination of PDE5i and ERA are prescribed now in mild *PAH* treatment. Prostanoids have been incorporated as 3rd line agents in active *DU* treatment. MMF is the new 1st line treatment for *ILD* induction and rituximab the 3rd. IV CYA and ASCT were recommended as 3rd and 4th line treatments in patients with severe *skin involvement*. Rituximab and tocilizumab have been incorporated into *inflammatory arthritis* treatment. This can guide therapy in SSc.
References:
[1] Walker KM, Pope J. Treatment of systemic sclerosis complications: what to use when first-line treatment fails–a consensus of systemic sclerosis experts. Semin Arthritis Rheum 2012;42(1):42–55.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1574

FRI0376 DIFFERENCES IN RIGHT VENTRICULAR FUNCTION AND MORPHOLOGY IN SSC-PAH AND IPAH ASSESSED BY RIGHT HEART CATHETERIZATION AND CARDIAC MRI

A.-M. Hoffmann-Vold[1], E. Hopp[2], Ø. Midtvedt[1], T. Garen[1], P. Szodoray[3], Ø. Molberg[1], A.K. Andreassen[4]. *[1]Rheumatology; [2]Radiology; [3]Immunology; [4]Cardiology, Oslo University Hospital, Oslo, Norway*

Background: Systemic sclerosis (SSc) is a serious disorder with high mortality, mainly driven by cardiopulmonary pathologies including *pulmonary arterial hypertension (PAH)*. Patients with SSc-PAH appear to have worse prognosis than idiopathic PAH (iPAH).
Objectives: (A)Compare cardiac magnetic resonance (CMR) of the right ventricle, hemodynamic parameters and immunological markers between patient cohorts with SSc-PAH, iPAH and SSc without PAH, respectively. (B)Evaluate the impact of these variables on PAH-related morbidity and mortality.
Methods: The study cohort included SSc-PAH (n=16), iPAH (n=15) and SSc without PAH (n=20). At baseline, all patients were examined by ventricular volumes by short axis summation of cine CMR, echocardiography and right heart catheterization (RHC). Blood samples were analysed for immune-related factors. At a median follow up of 3 years, clinical data, and new onset of PAH and vital status were registered. A composite outcome for PAH related events was created including: PAH progression, end-stage PAH, hospitalization for PAH worsening and all-cause mortality. Associations between parameters were assessed using ANOVA, Pearson Chi-square, Fishers exact, or independent sample t-test.
Results: Patients with SSc-PAH were significantly older at PAH onset, had lower 6MWD, DLCO% and Hb than the iPAH patients. RHC results are shown in Table 1. CMR showed that SSc-PAH patients had lower right ventricular mass index (RVMI), RV to left ventricular ratio and RV mass to volume ratio (Table 1). Multiplex immune assays demonstrated higher serum levels of IP-10, VEGF and, IL12 in SSc-PAH than in iPAH. At the end of the study, 12/15 SSc-PAH had developed a PAH-related event. Compared to event-free patients, they were marked by significant CMR changes including higher RVM (p=0.006) and RVMI (p=0.005). In the iPAH subgroup, 7/16 patients developed an event. These patients were characterized by younger age at onset (p=0.001), higher NT-proBNP (p=0.017), lower 6MWD (p=0.034), higher RVM (p=0.010), RVMI (p=0.005), RV-to-LV ratio (p=0.001) on CMR.

Table 1. Baseline right ventricle hemodynamic and cardiac magnetic resonance measurements

	SSc-PAH (n=15)	iPAH (n=16)	p-value
RHC			
Cardiac output	6.0 (2.9)	5.4 (1.4)	n.s.
Cardiac index	3.2 (1.5)	2.9 (0.6)	n.s.
RAP, mmHg	4.6 (3.1)	7.2 (3.4)	0.007
sPAP, mmHg	60 (19.8)	88 (23.3)	<0.001
mPAP, mmHg	35.5 (11.7)	55 (17.1)	<0.001
PCV, mmHg	6.2 (2.9)	7.4 (3.1)	n.s.
PA oxygen saturation%	81.3 (33.1)	93.2 (31)	n.s.
PVR (Wood)	5.4 (3.9)	9.7 (4.3)	<0.001
RV MRI			
RVSV index, ml/m^2	40.9 (7.8)	40.4 (7.8)	n.s.
RVESV, ml	144.9 (80.3)	146.8 (46.4)	n.s.
RVEDV, ml	219.5 (84.2)	223.8 (52.8)	n.s.
RVEDV index, ml/m^2	120.8 (50.5)	120.8 (28.3)	n.s.
RVEF, %	37.1 (10.5)	34.5 (10.5)	n.s.
RV mass, g	50.1 (21.3)	72.9 (27.4)	<0.001
RV mass index, g/m^2	26.2 (10.8)	38.2 (14.9)	<0.001
RV-to-LV ratio	0.51 (0.14)	0.82 (0.32)	<0.001
RV mass-to-volume ratio, g/ml	0.22 (0.06)	0.31 (0.08)	<0.001

Conclusions: The CMR measures indicate that the RV adapts differently in iPAH and SSc-PAH; with more pronounced RV hypertrophy in iPAH patients. The mechanisms behind the differences in RV hypertrophy in SSc-PAH and iPAH are not known, but may involve microvascular changes and deregulated inflammatory cascades. This study indicates that CMR may predict PAH progression in SSc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5372

FRI0377 ABNORMAL NAILFOLD CAPILLAROSCOPY PATTERN IS COMMON IN PATIENTS WITH CONNECTIVE TISSUE DISEASE AND ASSOCIATED WITH ORGAN INVOLVEMENT

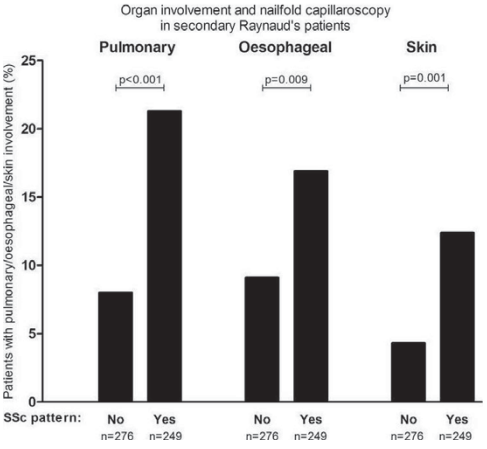
A.M. Van Roon[1], C.C. Huisman[1], A.M. van Roon[1], D. Zhang[2], A.J. Stel[3], A.J. Smit[1], H. Bootsma[3], D.J. Mulder[1]. *[1]Internal Medicine - Vascular Medicine, University of Groningen - University Medical Center Groningen, Groningen; [2]Rheumatology, Medical Center Leeuwarden, Leeuwarden; [3]Rheumatology and Clinical Immunology, University of Groningen - University Medical Center Groningen, Groningen, Netherlands*

Background: Nailfold capillary microscopy (NCM) has been shown to be associated with disease severity and internal organ involvement in non-consecutive systemic sclerosis (SSc) cohorts. NCM may help in early recognition of connective tissue disease (CTD) but it is unclear to which extent NCM abnormalities occur in several CTD and whether these are associated with organ involvement.
Objectives: To assess NCM in consecutive patients with Raynaud's phenomenon (RP) and whether these are associated with signs of organ involvement.
Methods: NCM was assessed in consecutive patients with RP (n=759) by wide-field videocapillaroscopy, according to standardized procedures at a dedicated vascular laboratory by trained and experienced technicians. The pattern was classified as normal (n=325), non-specific (n=188) or SSc pattern (early (n=106), active (n=140) or late (n=0) based on the Cutolo patterns). Potential pulmonary involvement was defined as forced vital capacity or diffusion capacity <70%. Gastro-intestinal involvement as scintigraphically (Tc-99M colloid) oesophagus dysmotility. Skin involvement as puffy fingers or sclerodactyly.
Patients were classified as primary RP (normal NCM and negative serology, n=226) or secondary RP (abnormal NCM and/or serology) groups: early SSc (n=195), SSc (n=40), incomplete Sjögren's syndrome (iSS, n=5), primary SS (pSS, n=30), incomplete systemic lupus erythematodes (iSLE, n=42), SLE (n=30), mixed CTD (MCTD, n=7), rheumatoid arthritis (RA, n=15) or when not meeting criteria as other (n=169). None were diagnosed with polymyositis or dermatomyositis.
Results: SSc pattern was observed in 33% of patients with pSS, 17% SLE, 71% MCTD and 13% RA. Pulmonary, oesophageal and skin involvement was more frequent in secondary RP patients with an SSc pattern, even when analysing only those fulfilling definite criteria for CTD or after exclusion of early SSc and SSc patients. For secondary RP patients, absence of an SSc NCM pattern had a high negative predictive value for pulmonary (92%), oesophageal (91%) and skin (96%) involvement, while positive predictive values were low.

Table 1. Nailfold capillaroscopic pattern per patient diagnosis group in patients with Raynaud's phenomenon

NCM pattern	Primary Raynaud	Secondary Raynaud								
		Definite diagnosis					No classifiable disease			
		SSc	pSS	SLE	MCTD	RA	early SSc	iSS	iSLE	Other
	n=226	n=40	n=30	n=30	n=7	n=15	n=195	n=5	n=42	n=169
Normal	226 (100)	1 (3)	10 (33)	12 (40)	2 (29)	11 (73)	4 (2)	4 (80)	29 (69)	26 (15)
Non-specific	0 (0)	4 (10)	10 (33)	13 (43)	0 (0)	2 (13)	2 (1)	1 (20)	13 (31)	143 (85)
Early	0 (0)	7 (18)	4 (13)	2 (7)	1 (14)	1 (7)	91 (47)	0 (0)	0 (0)	0 (0)
Active	0 (0)	28 (70)	6 (20)	3 (10)	4 (57)	1 (7)	98 (50)	0 (0)	0 (0)	0 (0)

Data in number (percentage).



Conclusions: SSc pattern on NCM is common in CTD patients and is associated with frequent prevalence of organ involvement, even in the absence of (early) SSc. Although this was a retrospective cohort, these data underline the importance of assessing NCM in RP patients to evaluate the risk for organ involvement in CTD other than SSc, already in early disease stages.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1390

FRI0378 CARDIAC INVOLVEMENT IN UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE AT RISK FOR SYSTEMIC SCLEROSIS. A TISSUE DOPPLER IMAGING STUDY

A. Riccardi[1], M. D'Alto[2], P. Argiento[2], E. Romeo[2], I. Di Stefano[1], S. Fasano[1], A. Mattera Iacono[2], A. D'Andrea[2], A. Sanduzzi[3], M. Bocchino[3], L. Docimo[4], S. Tolone[4], M.G. Russo[2], G. Valentini[1]. *[1]Rheumatology Unit; [2]Department of Cardiology, University of Campania "Luigi Vanvitelli"; [3]Department of Clinical Medicine and Surgery, University "Federico II"; [4]Division of General and Bariatric Surgery, University of Campania "Luigi Vanvitelli", Naples, Italy*

Background: Undifferentiated connective tissue disease at risk for Systemic Sclerosis (UCTD-risk-SSc), previously referred to as very early SSc, is a condition characterized by Raynaud's phenomenon (RP) with SSc marker autoantibodies and/or typical capillaroscopic findings and unsatisfying classification criteria for the disease (1). UCTD-risk- SSc patients have been reported to present, in about 40% of the cases, a preclinical vascular internal organ disease as detected by a diffusing lung capacity for CO <80% of the predicted value (lung involvement) and/or a low esophageal sphincter pressure <15 mmHg (oesophageal involvement) and/or a mitral E/A ratio <1 (heart involvement) (2, 3).

Objectives: Aim of the present study was to assess the prevalence of right (RV) or left ventricle (LV) systolic and/or diastolic dysfunction by standard echocardiography and tissue Doppler imaging (TDI).
Methods: Thirty patients with UCTD-risk-SSc (28 female, aged 47±13 years, range 21–70) and 30 age- and sex-matched controls underwent cardiac assessment by standard echocardiography and TDI.
Results: UCTD-risk-SSc patients and controls did not show any difference at standard echocardiographic evaluation. In particular, an inverted E/A ratio was pointed out in 10/30 patients and 7/30 controls (p=ns). TDI showed a mild impairment of LV and RV diastolic (E_m15±4 vs 19±5, $p<0.0001$;E/E_m 6.1±1.7 vs 4.8±1.2, p=0.001; E_t 14±3 vs 16±2, p=0.02; E_t/A_t0.9±0.4 vs 1.3±0.3, $p<0.002$; increased pulmonary artery wedge pressure 9±2 vs 8±1, p=0.001)and systolic function (S_m 13±3 vs 15±2 cm/sec, $p<0.0003$; S_t 14±2 vs 16±3 cm/sec, $p<0.0001$) in UCTD- risk-SSc patients in comparison to controls.
Conclusions: Our study shows that UCTD-risk-SSc patients present a previously unrecognized, mild biventricular systolic and diastolic dysfunction as compared to controls. The pathophysiologic meaning (i.e.intramyocardial artery disease and/or patchy fibrosis) as well the predictive value of developing overt SScin the short time await to be elucidated.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3080

FRI0379 PREVALENCE OF FAM111 B GENE MUTATIONS IN SYSTEMIC SCLEROSIS

A. Gcelu[1], G. Deshpande[2], A.A. Kalla[1], M. Tikly[3], B. Mayosi[2], B. Hodkinson[1]. *[1]Medicine, Division of Rheumatology; [2]Cardiovascular Genetics Laboratory, University of Cape town, Cape Town; [3]Medicine, Division of Rheumatology, University of Witwatersrand, Johannesburg, South Africa*

Background: Systemic sclerosis (SSc) is a prototypic systemic fibrotic disease with unclearly characterized genetic basis. Implicated genes have been associated with autoimmune dysregulation with relatively few variants associated with fibrosis [1]. We have discovered that mutations in *FAM111B* gene cause hereditary fibrosing poikiloderma with tendon contractures, myopathy, and pulmonary fibrosis (POIKTMP)[2], a multisystem fibrotic condition with clinical aspects of SSc [3]. This observation has established *FAM111B* as a candidate gene for SSc.
Objectives:
The objective is to investigate whether *FAM111B* gene mutations are present in SSc patients and further explore relationships between *FAM111B* mutations and clinical expression of SSc.
Methods: Patients with a definite diagnosis of SSc attending the Rheumatology outpatient departments at Groote Schuur Hospital, Cape Town, and Chris Hani Baragwanath Hospital, Johannesburg, were enrolled into the study. Physical examination assessing the extent of disease was done in all patients and the modified Rodnan skin score (mRSS) was used to determine the extent of the skin involvement. Blood samples were collected for DNA extraction and mutation screening using the high-resolution melt technique. Samples with abnormal electropherograms were selected for Sanger sequencing to identify mutations. Public databases were used to verify the frequency of variants in *FAM111B*.
Results: 131 patients were genotyped, 13 men and 118 women, with a mean age of 26.6 years and mean age of symptom onset at 25.3 years. The majority of patients were black (59.5%). 72% of patients had diffuse systemic sclerosis (DSSc) with a median mRSS of 11. Genetic analysis revealed seven rare genetic variants (C832G>A; C855G>T; C917A>G; C937G>A; C988C>T; C995A>C and C1006G>C) in eight patients (five patients from Johannesburg and three patients from Cape Town) [table 1]. These variants were missense mutations of unknown significance with a minor allele frequency <0.01. No *FAM111B* mutations that cause POIKMT were found in patients with SSc.
Conclusions: Rare genetic variants of unknown significance (GVUS) in *FAM111B* gene were found in patients with SSc. It is possible that the GVUS may modify the function of *FAM111B*, and influence the pathogenesis of SSc or are rare polymorphisms with no functional impact.
References:
[1] Romano, E., et al., The genetics of systemic sclerosis: an update. Clin Exp Rheumatol, 2011. 29(2 Suppl 65): p. S75–86.
[2] Mercier, S., et al., Mutations in FAM111B cause hereditary fibrosing poikiloderma with tendon contracture, myopathy, and pulmonary fibrosis. Am J Hum Genet, 2013. 93(6): p. 1100–7.
[3] Khumalo, N.P., et al., Poikiloderma, tendon contracture and pulmonary fibrosis: a new autosomal dominant syndrome? Br J Dermatol, 2006. 155(5): p. 1057–61.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6719

FRI0380 PATIENT PREFERENCES AND DIFFICULTIES CONCERNING THE HOME TREATMENT OPTIONS IN SYSTEMIC SCLEROSIS (SSC)

B. Pagnotelli[1], C. Bruni[1], S. Bellando Randone[1], S. Guiducci[1], G. Lepri[1], J. Blagojevic[1], L. Rasero[2], M. Matucci Cerinic[1], D.E. Furst[1,3]. *[1]Division of Rheumatology; [2]Division of Research & Development Clinical Practice, AOUC, Florence, Italy; [3]Division of Rheumatology, UCLA, Los Angeles, United States*

Background: SSc patients suffer from Raynaud's phenomenon, hand skin hardening and scarring, digital ulcers, esophagus/gastric dysmotility, dysphagia and mucosal dryness. These symptoms significantly reduce patient's life autonomy and impair the capacity to handle their therapy usually made by different modalities of administration: oral, topical, inhalation, intramuscular, subcutaneous, intravenous, and rectal.
Objectives: to investigate the methods of administration used by SSc patients, their preferred methods, their compliance to pharmacological therapy, and the difficulties that are encountered by the patients during pharmacotherapy.
Methods: 2 questionnaires were prepared on an ad hoc basis. The first given to patients, the second to be filled out by the patient's physician. The first questionnaire comprised 25 questions to investigate the problems encountered by patients when taking their medications by correlating these with two validated activities indices: SHAQ-DI (activities of daily living) and the COCHIN scale (hand activities). The second questionnaire collected demographic and important SSc-related clinical information (eg.age, sex, disease duration, symptoms). 80 Ssc patients completed the questionnaires, maintaining anonymity. A "difficulty index" was also filled out, where: 0 = no difficulty to 4 = impossible to use or too difficult to use.
Results:

Table 1. Patient use of pharmacological therapies

	% Using	% Users preferring this method	Difficult index†	Comment
Oral	100	91,25	0,83	Most preferred
Eye drops	52,5	2,5	1,07	Least preferred
Topicals	33,75	3,75	0,77	Cannot open the top (safety lock)
Injections	28,25	2,5	2,17	Cannot apply to skin
Inhaler	16,25	0	1,07	Cannot spray
Vaginal/rectal	6,25	0	1,03	

Table 2. Most frequent problems encountered

	% Using	Most frequent problems	Users have these problems	Difficult index†
Oral	100	Blister: pushing out pills	73,75	2,22
Eye drops	52,5	Open thin stoppers	78,75	1,51
Topicals	33,75	Cannot open the top (safety lock)	70,5	1,4
Inhaler	16,25	Cannot spray/push the inhaler	85	1,71

†4 = most difficult.

In particular, the dimension of the pills is problematic, and has identified a paradoxical situation because large pills are difficult to swallow (41,25% patients who use pills) but at the same time small pills are difficult to pinch with the fingers (62,25% patients who use pills).
Conclusions: SSc patients experience significant problems in maintaining adherence to treatments due to difficulties in the use of blisters and bottles with children proof stoppers. Pills still remain the most preferred method of treatment. In conclusion, patients unanimously wished to avoid the use of blisters, defintively preferring bottles without the children proof stopper to make the treatment easier and provide a more independent life.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4848

FRI0381 INCREASED RISK OF OSTEOPOROTIC FRACTURES IN ADULT PATIENTS WITH POLYMYOSITIS AND DERMATOMYOSITIS: A NATIONWIDE POPULATION-BASED COHORT STUDY

C.-C. Lai[1], W.-S. Chen[1], Y.-P. Tsao[1], Y.-S. Chang[2]. *[1]Division of Allergy, Immunology, and Rheumatology, Taipei Veterans General Hospital, Taipei City; [2]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan, Province of China*

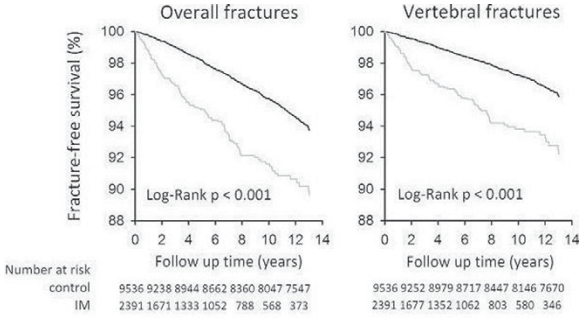
Background: Patients with polymyositis and dermatomyositis (PM/DM) are characterized by chronic muscle weakness due to autoimmune-mediated myositis and are usually treated with corticosteroids initially. PM/DM patients prone to develop osteoporosis and subsequent fractures but are rarely investigated.
Objectives: To explore the incidence rate (IR) and risk factors of osteoporotic fractures (OFs) among adult PM/DM patients.
Methods: We conducted a cohort study by utilizing the Taiwan National Health Insurance database. PM/DM patients and respective age- and gender-matched cohort without PM/DM were enrolled. The primary endpoint was the initial event of OFs. We used the Cox proportional hazard model to study the risk factors of OFs in the PM/DM cohort.
Results: Among 2391 PM/DM patients (67.8% female, mean age: 49.5 years) followed for a mean (SD) of 6.1 (5.0) years, 116 developed vertebral fractures, 32 had hip fractures, and 14 experienced radius fractures (IR: 8.18, 2.20, and 0.96 per 1000 person-years, respectively, Table 1). Compared with the matched cohort, the PM/DM patients had higher IR ratios (IRRs) (95% CIs) of OFs at all age groups at enrollment: 3.27 (2.19 to 4.81, $p<0.0001$) for people <50 years and 2.29 (1.85 to 2.82, $p<0.0001$) for those ≥50 years. The IRRs were 2.39 (1.92

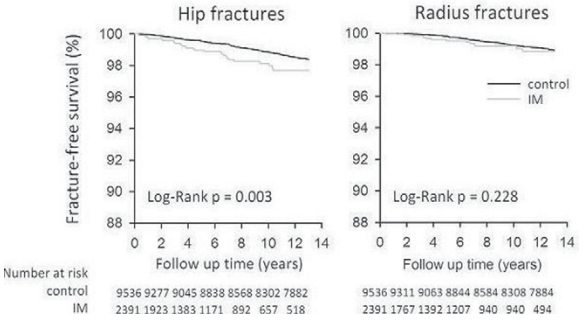
to 2.94, p<0.0001) for vertebral fractures and 1.62 (1.07 to 2.38, p=0.0093) for hip fractures. PM/DM patients experienced vertebral fractures and hip fractures at younger ages (62.2 vs 68.4 and 66.0 vs 75.4 years, respectively; both p<0.001). Multivariable Cox regression analyses showed that being female gender, age ≥50 years, having hypertension, coronary artery disease, asthma, and using daily prednisolone equivalent to >5 mg are associated with OFs.

Table 1. IRs and IRRs of osteoporotic fractures: overall and subgroup analysis

Subgroup	IM IR	Control IR	IRR (95% CI)	p Value
Overall fracture	10.90	5.23	2.08 (1.73 to 2.49)	<0.0001
Age <50 year	4.51	1.38	3.27 (2.19 to 4.81)	<0.0001
Age ≥50 year	22.59	9.85	2.29 (1.85 to 2.82)	<0.0001
Vertebral fracture	8.18	3.43	2.39 (1.92 to 2.94)	<0.0001
Age <50 year	3.39	0.98	3.47 (2.17 to 5.44)	<0.0001
Age ≥50 year	16.82	6.33	2.66 (2.07 to 3.39)	<0.0001
Hip fracture	2.20	1.36	1.62 (1.07 to 2.38)	0.0093
Age <50 year	0.65	0.10	6.56 (1.75 to 24.6)	0.0027
Age ≥50 year	4.87	2.83	1.72 (1.09 to 2.62)	0.0081
Radius fracture	0.96	0.83	1.15 (0.60 to 2.02)	0.3081
Age <50 year	0.43	0.35	1.25 (0.31 to 3.69)	0.3289
Age ≥50 year	1.86	1.40	1.35 (0.62 to 2.63)	0.1857

IR, incidence rate per 1000 person-year; IRR, incidence rate ratio; CI, confidence interval.





Conclusions: Adult PM/DM patients had a high IR of vertebral and hip fractures. Patients who were female, advanced age, having certain comorbidities, and exposed to corticosteroid exhibited a higher risk.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6043

FRI0382 USE OF THE DETECT ALGORITHM FOR EARLY PULMONARY ARTERY HYPERTENSION DIAGNOSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS IN EVERYDAY CLINICAL PRACTICE

C. Koutsianas, S. Subasinghe, K. Douglas. *Department of Rheumatology, The Dudley Group NHS Foundation Trust, Dudley, United Kingdom*

Background: The DETECT algorithm (DA)[1] provides a sensitive tool for early identification of patients with Systemic Sclerosis (SSc) at risk of Pulmonary Arterial Hypertension (PAH) and advocates evaluation with Right Heart Catheterisation (RHC). Few published data look into its implementation in everyday clinical practice and compare it to annual echocardiographic (TTE) screening.
Objectives: To compare DA and TTE screening of SSc patients for RHC referral rates and related patient characteristics.
Methods: Data on 57 consecutive patients with a diagnosis of SSc that had at least one visit to Russells Hall Hospital Scleroderma clinic from February to November 2016 was prospectively collected on Excel (clinical history, physical examination, immunological status, treatment, PFTs, NT-proBNP, urate, ECG, TTE, CXR and HRCT results). DETECT scores were calculated (*www.detect-pah.com*) and compared with the TTE probability for PAH as per the 2015 ESC/ERS Guidelines[2].
Results: 31 patients with a full set of data were included in the final analysis. 93.5% were female with a mean age of 64.4±12.9 years, 87% had limited cutaneous (lc) SSc, 58.1% positive anticentromere antibody and mean time since diagnosis was 6.2±3.2 years. The majority of patients (80%) were asymptomatic for PAH. Mean DLCO was 60.9±18.3% predicted (the DETECT study included on patients with DLCO<60%). We did not exclude patients with renal insufficiency; mean eGFR was 74±17.7ml/min.
The implementation of DA recommended RHC in 18/31 patients (DETECT step 2 score ≥35, 58%, see table 1) compared to just 4/31 (13%) based on TTE by 2015 ESC/ERS guidelines. The additional 14 patients identified by DA were found to have no statistically significant differences in SSc type, dyspnea symptomatology, immunosuppressive treatment, presence of interstitial lung disease (ILD), age, time from diagnosis or symptom onset, eGFR and CRP compared to patients where RHC was not recommended. From the 18 patients identified by DA, only 4 reported shortness of breath. 2/18 had existing cardiac conditions (aortic stenosis, left ventricular hypertrophy), while 9/18 had ILD (5 mild, 2 moderate, 2 severe as per HRCT).

Table 1

	DETECT step 2 score			p
	<35	35–39	>40	
Age, years (median (IQR))	65.8 (26.9)	63.2 (22.3)	72.4 (25.1)	*0.875*
Disease duration, years (median (IQR))	8 (4)	4 (7)	5 (9)	*0.996*
eGFR, ml/min (median (IQR))	80 (28)	83 (17)	54.5 (47)	*0.958*
CRP, mg/L (median (IQR))	3 (5)	3 (3)	3 (2)	*0.636*
DLCO, % (median (IQR))	65 (17)	64 (12)	53 (30)	*0.757*
ILD (no. of patients) No	10	5	3	0.087
Mild	1	3	4	
Moderate	2	1	0	
Severe	0	0	2	

Conclusions: Implementation of DA in a largely asymptomatic non-selected SSc patient population is more sensitive for RHC referral than annual TTE screening. Recommendations for RHC per DETECT score are difficult to predict on symptom and other traditional clinical parameters. The use of DA will lead to increased RHC referrals. Cardiologists may need education on this new method for screening and although the ESC/ERS 2015 guidelines discuss DA, they conclude that its cost-effectiveness has not been clarified as compared with symptom-based detection.
References:
[1] Coghlan JG et al. Evidence-based detection of pulmonary arterial hypertension in systemic sclerosis: the DETECT study. Ann Rheum Dis 2014 Jul;73 (7):1340–9.
[2] Galiè N et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J (2015) 37 (1): 67–119.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5928

FRI0383 DETECT SCREENING FOR PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS: DATA FROM AN EUSTAR COHORT

C. Ancuta[1,2], C. Pomirleanu[1,2], R. Maxim[2], F. Mitu[1,3]. *[1]University of Medicine and Pharmacy Grigore T Popa Iasi; [2]Rheumatology 2; [3]Cardiology, Clinical Rehabilitation Hospital, IASI, Romania*

Background: Early documentation of pulmonary arterial hypertension (PAH) related to systemic sclerosis (SSc) remains a challenge in daily clinical practice, with major prognostic and therapeutic implications. Although several screening algorithms specifically designed to optimize the detection of secondary PAH have already been proposed (e.g., DETECT, REVEAL), no precise approach received complete validation, especially the use of invasive diagnostic right heart catheterization (RHC).
Objectives: Main objective was to assess the risk of PAH in patients with SSc and to compare with PAH screening promoted by European Society of Cardiology/ European Respiratory Society (ESC/ERS) 2009 guidelines, while secondary one to identify predicting factors for developing PAH among clinical and immunological SSc variables.
Methods: Cross-sectional prospective single-center study, applying the DETECT calculator in patients with SSc recruited in EUSTAR 162 center cohort between January 2013- December 2016; all SSc completing at least two monitoring visits at 6 months were considered.
Standard assessments included MEDS (minimal data set EUSTAR), annual echocardiography with systolic pulmonary artery pressure (sPAP), pulmonary function tests with forced vital capacity (FVC), percentage predicted/diffusing capacity for carbon monoxide (DLCO) % predicted, ECG, serum biomarkers (serum urate, NT-proBNP).
PAH risk calculator (http://detect-pah.com/pah-risk-calculator), a tool developed and validated in the DETECT study, is able to identify patients requiring echocardiography (STEP 1) respectively RHC (STEP 2), and was systematically applied in our cohort. All sPAP ≥45 mmHg or between 35–45 mmHg in the presence of dyspnea were proposed for invasive testing.
Statistical analysis was performed in IBM SPSS-19 version, p<0.05.
Results: 41 out 56 SSc in our database were recruited: mainly women (85.36%) with diffuse cutaneous SSc (63.41%), anti-topoisomerase (up to half) and anti-centromere (about one third) positive disease; one out of four 4 SSc presented with digital ulcers and one of three with active capillaroscopic pattern.

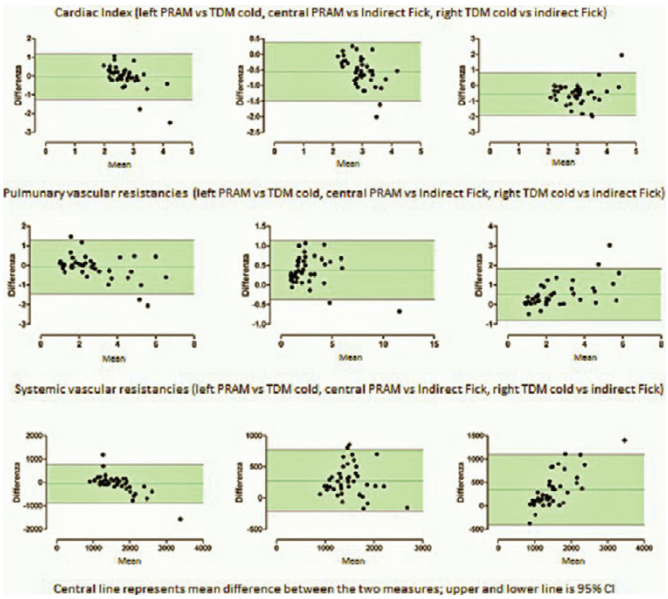
Using the DETECT PAH calculator, 14/ 41 (34.14%) were recommended for RH as follows: an initial value above 300 points in STEP 1 (with further indication of echocardiographic assessment) and subsequent STEP 2 over 35 were recorded. On the other hand, only 9/41 (21.95%) cases met the ultrasound criteria to be addressed to an invasive assessment when applying the ESC/ERS 2009 guidelines, the difference being statistically significant as compared to DETECT ($p<0.05$).
PAH was finally confirmed in 8/41 (19.51%) cases, supporting our preliminary results in a pilot study on a limited number of patients.
Conclusions: DETECT is a reliable algorithm for early detection of PAH in patients with SSc, optimizing PAH screening and prompting the rheumatologist-cardiologist collaboration.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4053

FRI0384 A MINI-INVASIVE TECHNIQUE FOR HAEMODYNAMIC EVALUATION: NEW PERSPECTIVES FOR PULMONARY ARTERIAL HYPERTENSION (PAH) DIAGNOSIS IN SYSTEMIC SCLEROSIS (SSC)

E. Bellucci[1], M.S. Romano[2], M. Chiostri[2], C. Bruni[1], C. Giglioli[2], P. Bernardo[3], M.L. Conforti[1], S. Bellando-Randone[1], S. Guiducci[1], M. Matucci-Cerinic[1].
[1]Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence; [2]Department of Heart and Vessels, Division of Cardiology I; [3]Department of Heart and Vessels, Division of Structural Interventional Cardiology, Azienda Ospedaliera Universitaria Careggi, Firenze, Italy

Background: PAH is one of the most severe complication and cause of mortality in SSc, with frequent late diagnosis as asymptomatic in its early stages. Right Heart catheterization (RHC) is the gold standard for PAH detection, though its invasive nature with high risk of procedure related complications stress the need for developing new screening methods to investigate it in early and possibly reversible stages. Pressure Recording Analytical Method (PRAM) was recently developed to obtain a minimally invasive haemodynamic monitoring, using an arterial line and proximal pulsossimetry. This analyses arterial blood pressure curve and measure both cardiac [Cardiac Index, Cardiac Contractility and Vascular Stiffness ratio (dP/dT)] and vascular [vascular stiffness, elastance], which can be usually obtained only through RHC.
Objectives: to evaluate the clinical usefulness of PRAM method in SSc patients and to identify haemodynamic parameters related to increased risk of developing PAH.
Methods: 40 ssc patients (35 women, mean age 60±9,3 years; mean disease duration 7.5 years) were evaluated with both RHC and PRAM on the same day. Mean pulmonary arterial pressure (mPAP), cardiac index (CI), systemic vascular resistances (SVR), right cardiac power index (RCPI, calculated with $mPAPXCI_{PRAM}/451$) were measured and concordance of the two methods was assessed through Bland-Altmann analysis. Systolic pulmonary arterial pressure and TAPSE from echocardiography, forced vital capacity, total lung capacity, both absolute and alveolar volume adjusted Carbone oxide lung diffusion (DLCO and DLCO/VA) from pulmonary function tests, blood tests parameters, nailfold videocapillaroscopy scleroderma patterns were recorded. Univariate and multivariate logistic regression analysis identified variables correlating with RHC-diagnosed PAH: a scoring system was then created, giving 1 point for value satisfying cut-off level.

Univariate Logistic Regression	Unadjusted OR	95% CI	p value
Dicrote Pressure	1.04	1.00–1.09	0.064
Arterial Elastance	3.16	0.70–14.24	0.134
Right Cardiac Power index	1.11	1.04–1.18	0.002
DLCO	0.94	0.90–0.99	0.021
Multivariate Logistic regression with backward stepwise analysis	Unadjusted OR	95% CI	p value
Right stroke work index	1.12	1.03–1.21	0.007
DLCO	0.94	0.87–1.01	0.072



Results: PRAM showed concordance with RHC estimate of CI and SVR within 95% interval confidence; 14 patients were diagnosed with PAH (mean age 64,4±9,3, mean disease duration 10.5 years, lSSc 61,5%). Multivariate logistic regression analysis showed DLCO (cut off value 47% obtained through ROC curve analysis, p=0.004) and RCPI (cut off value 0.12 Watt obtained through ROC curve analysis, $p<0.001$) as the most highly PAH-associated variables. When combining these two variables in the scoring system, patient with score=0 (DLCO<47% and RCPI<0,12 Watt), score=1 (DLCO<47% or RCPI≥0,12 Watt) and score=2 (DLCO<47% and RCPI≥0,12) were 0%, 21.4% and 78.6% of the PAH population respectively.
Conclusions: PRAM is comparable to RHC in detecting haemodynamic parameters such as SVR and CI. The scoring system combining DLCO and RCPI, obtained with non-invasive tools, could offer the possibility of detecting PAH patients with a high specificity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5817

FRI0385 JOINT MANIFESTATIONS IN PATIENTS DIAGNOSED WITH IDIOPATHIC INFLAMMATORY MYOPATHY: MULTICENTER REGISTRY

D.C. Hernández Flórez[1], L. Valor[1], J. Martinez[1], B. Joven[2], L. Nuno[3], C. Larena[4], I. Llorente[5], C. Barbadillo[6], P. Garcia de la Pena[7], L. Ruiz[8], H. Moruno[9], T. Cobo[10], R. Almodovar[11], L. Lojo[12], M. Garcia[13], F. Lopez-Longo[1]. *[1]H. Gregorio Maranon; [2]H.12 de Octubre; [3]H.La Paz; [4]H.Ramon y cajal; [5]H.La Princesa; [6]H.Puerta de Hierro; [7]H.Norte Sanchinarro; [8]H.Nino Jesus; [9]H.Principe de Asturias, Madrid; [10]H.Infanta Sofia, Asturias; [11]H.F.Alcorcon; [12]H.Infanta Leonor; [13]InMusc, Madrid, Spain*

Background: Idiopathic inflammatory myopathies (IIM) comprise a heterogeneous group of autoimmune conditions. Joint involvement can be considered to be part of the IIM systemic manifestations, together with a possible gastrointestinal, cardiovascular and/ or pulmonary involvement. Although articular involvement in the IIM has been described as variable and non-specific with a chronic course it might be an early symptom of dermatomiositis in up to 30% of cases and in those patients with overlap syndromes.
Objectives: To evaluate and to identify joint manifestations in IIM patients.
Methods: We evaluated a cohort of 479 patients that included 12 hospitals in the Community of Madrid belonging to the IIM registry of the Society of Rheumatology of Madrid (SORCOM-REMICAM) with diagnosis from January 1980 to December 2014. All patients were diagnosed of IIM according to Bohan and Peter criteria (1). The presence of arthralgia and arthritis was considered. IIM were classified as dermatomyositis (primary and secondary dermatomiositis) (DM) and polymyositis (PM) including the rest of the patients (classification I). Also, IIM were classified (II) as primary polimiositis (PPM), primary dermatomyositis (PDM), overlap syndrome (OSd), juvenile myopathies (JM), cancer-associated myopathies (CAM), autoimmune necrotizing myopathy and inclusion body myositis (these were grouped as other myositis; OM).
Results: We found 70 (18%) patients with acute arthritis (<6 weeks), 74 (19%) patients with chronic arthritis (>6 weeks) and 245 (65%) patients without any joint manifestations. Using the Tanimoto et al. criteria (1), the presence of erosive arthritis was observed in 149/479 (38.3%) of the patients. When comparing the joint manifestations in the PM and DM groups (n=250, 52.2% vs. n=229, 47.8%) no statistically significant differences were observed. However, assessing joint manifestations according to classification II, we observed that the highest prevalence was found in the OSd group, followed by the PDM group (p=0.0001). The group with less joint manifestations was JM compared to OSd and PDM (Table 1.

Table 1: Joint manifestations in IIM according to classification II

	Comparison between groups		Frequency	P
Joint manifestations	OSd vs.	PPM	90% vs. 54%	0,0001
		PDM	90% vs. 71%	
		JM	90% vs. 45%	
		CAM	90% vs. 49%	
		OM	90% vs. 58%	
Arthralgias	OSd vs.	PPM	90% vs. 54%	0,0001
		PDM	90% vs. 71%	
		JM	90% vs. 44%	
		CAM	90% vs. 49%	
Arthritis	OSd vs.	PPM	90% vs. 34%	0,0001
		JM	90% vs. 28%	
		CAM	90% vs. 33%	

Conclusions: The presence of joint manifestations associated with IIM in our cohort is higher compared to other studies described in the literature so far and

emphasize the importance of an accurate joint examination in these patients. The OSd group showed more joint manifestations which might be explained by the coexistence of SLE and MCTD patients in this group. Currently, no association between the clinical subtypes of IIM, overall, these results are encouraging and suggest that joint assessment in follow up may be helpful in differentiating subtypes of IIM.

References:
[1] Bohan A, Peter JB. N Engl J Med 1975 Feb 13;292(7):344–7.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7051

FRI0386 THE VALIDATION OF THE SCLERODERMA HEALTH ASSESSMENT QUESTIONNAIRE IN TURKISH SPEAKING PATIENTS WITH SYSTEMIC SCLEROSIS

D. Temiz Karadag [1], F. Karakas [2], S. Tekeoglu [1], O. Ozdemir Işik [1], A. Yazici [1], A. Cefle [1]. *[1] Rheumatology; [2] Internal Medicine, Kocaeli University Medicine School, Kocaeli, Turkey*

Background: The Health Assessment Questionnaire (HAQ) is one of the main instruments for assessing disability in rheumatic diseases.The Scleroderma HAQ (S-HAQ) combines the HAQ with five systemic sclerosis (SSc) related visual analogue scales for Raynaud's phenomenon (RP), digital ulcers, digestive symptoms, pulmonary symptoms, and overall disease severity.
Objectives: To perform cross-cultural adaptation and validation of the S-HAQ in patients with SSc.
Methods: Sixty patients who fulfilled the 2013 ACR/EULAR Classification Criteria for Systemic Sclerosis ACR criteria for SSc were were recruited.Fifty three percent of the patients fulfilled the criteria for limited systemic sclerosis (lcSSc).We evaluated test–retest reliability using the intraclass correlation coefficient (ICC); known-groups construct validity by stratifying patients according to severe organ involvement; and convergent validity using Spearman's correlation with mental and physical components of Short Form 36 version 2 (SF36v2).
Results: Eighty percent of the patients were female and the median age was 56 years old.Finger tip ulcers were observed in 16 patients (26.7%) and severe organ involvements were detected as intersititial lung disease in 32 (53%) and pulmonary hypertension in 5 (8%) of the patients.HAQ Disability Index (HAQ-DI), digestive VAS, pulmonary VAS, digital ulcer VAS, Raynaud's phenomenon VAS and overall disease severity VAS demonstrated high reliability (ICCs=0.819–0.908).The HAQ-DI showed higher correlation coefficients with physical function and role physical components of physical-related scores (r=-0.537 and – 0.453, respectively); social function and role emotional components of mental-related dimensions (r= -0.470 and -0.328, respectively) in the SF-36.Two among five SSc related VAS (VAS digital ulcer and VAS overall disease severity) were highly correlated with HAQ-DI (r=0.527 and 0.481 respectively).The instruments could not discriminate between severe organ involvements and both subsets of SSc.

Table 1. Correlation of HAQ-DI with physical and mental components of SF-36 and, SSc related VAS scores

N=60	Mean±SD and/or %	Correlation Coefficient	*p-value*
Physical function	55.4±23.83	-0.537	0.000
Role physical	33.82±42.67	-0.453	0.001
Body pain	53.82±28.84	-0.290	0.041
General health	39.9±18.43	-0.295	0.037
Vitality	41.08±18.39	-0.286	0.044
Social function	62.25±24.49	-0.470	0.001
Role emotional	49.02±32.9	-0.328	0.02
Mental health	61.12±18.39	-0.295	0.04
VAS digestive	0.39±0.65	0.304	0.028
VAS pulmonary	0.64±0.79	0.380	0.005
VAS RP	0.67±0.74	0.354	0.01
VAS digital ulcer	0.62±0.94	0.527	0.000
VAS overall severity	1.14±0.97	0.481	0.000

Conclusions: The Turkish version of the S-HAQ meet the requirements of reproducibility and validity.More studies are needed to examine the capacity of these instruments to discriminate between severe involvements and disease subsets.This study forms the basis for future studies to evaluate the properties of S-HAQ in Turkish speaking SSc patients more extensively.

References:
[1] R Hesselstrand et al, Psychometric properties of the Swedish version of the Scleroderma Health Assessment Questionnaire and the Cochin Hand Function Scale in patients with systemic sclerosis, Scandjrheumatol Vol. 42, Iss. 4,2013.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3289

FRI0387 ANTI-RNA POLYMERASE III SUBSET OF SCLERODERMA PATIENTS: A MONOCENTRIC STUDY

E. Pigatto, M. Ferranti, M. Favaro, P. Polito, E. Zanatta, P. Galozzi, M. Tonello, L. Punzi, F. Cozzi. *University of Padova, Padova, Italy*

Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by heterogeneous clinical features and variable disease course. Specific antinuclear antibodies (ANA) identify different clinical subsets and are very useful in defining the prognosis of the patients. Recently, the anti-RNA polymerase III antibodies (anti-RNAP) were defined as the third specific ANA of SSc, together with anti-centromere (ACA) and anti-topoisomerase I (anti-Scl70).
Objectives: The aim of this study was to analyze the clinical picture of a group of SSc patients with anti-RNAP in a monocentric cohort of patients and to compare it with other subsets of patients with different specific ANA. In particular, the visceral involvement and the concomitant malignancies were investigated.
Methods: Among the SSc patients referring to the Rheumatology Unit of Padova University, 49 cases with anti-RNAP specific ANA were considered. Patient's demographics data and major clinical manifestations were compared with those of 50 ACA-positive and 52 anti-Scl70-positive patients. The skin score and the presence of digital ulcers, arthritis, interstitial lung disease (ILD), cardiac involvement including pulmonary hypertension, gastrointestinal disease (GI) and scleroderma renal crisis (SRC) were assessed. The presence and type of concomitant malignancies were also evaluated.
Results: 53% of anti-RNAP-positive patients had a diffuse cutaneous form of SSc. The skin score was significantly higher than in ACA-positive patients ($p<0.001$). Digital ulcers were active in 73.5% of cases, without significant difference with the other two subsets. Arthritis was found in 20.4% of cases in comparison to 4% in ACA-positive patients ($p<0.02$). Regarding visceral involvements, GI disease was the most common manifestation in all subsets; SRC was observed in 24.4% of anti-RNAP-positive patients and was significantly more frequent in comparison to ACA-positive ($p<0.005$); ILD showed a prevalence of 42.8% in anti-RNAP subset, lower than in anti-Scl70-positive ($p<0.05$) and higher than in ACA-positive patients ($p<0.01$); cardiac involvement was observed in 32.6% of anti-RNAP-positive patients, without significant difference with the other subsets. Malignancies were found in 33 (67.3%) anti-RNAP-, 18 (36%) anti-Scl70- and 7 (14%) ACA- positive patients. The most common cancer-sites were breast (36%), lung (14%) and colon (10%). The risk of developing cancer was higher in anti-RNAP-positive patients than in other subsets (*OR*:6.35).
Conclusions: Our data demonstrated that anti-RNAP specific antibodies can identify a subset of SSc patients characterized by a severe clinical picture, with a high prevalence of diffuse cutaneous form, SRC, cardiac involvement and ILD. These patients showed also an elevated risk of developing cancer. Our results were consistent with recent published papers on this topic (1,2).

References:
[1] Terras S et al. RNA polymerase III autoantibodies may indicate renal and more severe skin involvement in systemic sclerosis. Int J Dermatol 2016; 55:882–5.
[2] Lazzaroni MG et al. Malignancies in patients with anti-RNA Polymerase III antibodies and Systemic Sclerosis: analysis of the EULAR Scleroderma Trials and Research Cohort and possible recommendations for screening. J Rheumatol 2017; pii: jrheum.160817.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3292

FRI0388 LONG-TERM TREATMENT WITH RITUXIMAB IN SYSTEMIC SCLEROSIS PATIENTS: UPDATE OF OUR CLINICAL EXPERIENCE

F. Lumetti, M. Colaci, C. Esposito, E. Cocchiara, C. Vacchi, A. Spinella, G. Tiengo, D. Giuggioli, C. Ferri. *Scleroderma Unit, Chair of Rheumatology, University of Modena and Reggio Emilia, Policlinico of Modena, Modena, Italy*

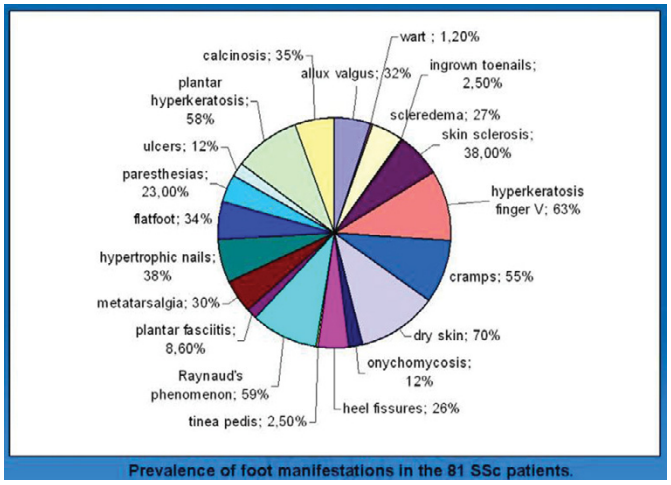
Background: Systemic sclerosis (SSc) is an immune-mediated disorder characterized by abnormal fibrosis and diffuse microangiopathy with skin and internal organ involvement. The treatment of SSc represents a great clinical challenge because of the complex disease pathogenesis including vascular, fibrotic, and immune T- and B-lymphocyte-mediated alterations. Therefore, SSc should be treated by combined or sequential therapies according to prevalent clinico-pathogenetic phenotypes. Some preliminary data suggest that rituximab (RTX) may be usefully employed in SSc patients.
Objectives: The present study aimed to evaluate the efficacy of RTX in our SSc patients' series as well as the long-term effects of this treatment.
Methods: A series of 15 SSc patients (M/F 6/9, mean age 52.7±17.9SD years, mean disease duration 10.3±7.1SD years, L/D cutaneous subsets 5/10) were treated with one or more cycles of RTX (4 weekly infusions of 375 mg/m^2). In all patients RTX was repeated every 6 months for a total of 2–6 cycles. Patients' clinical-serological evaluation, including the self-evaluation of quality of life by means of HAQ and visual analogical scale (VAS) assessment, was performed every 6 months for a mean follow-up period of 42±24SD months.
Results: After the first 6 months following RTX treatment the extent of skin sclerosis measured with modified Rodnan skin score (mRSS) significantly improved (from 17.3±10.4 to 13.4±7.6; $p<.01$), and remained stable at the end of the follow-up (13.3±8.1; p=.009). The usefulness of RTX on skin sclerosis was more evident in patients with diffuse cutaneous SSc (n=10) showing a significant decrease of mRSS after the first 6 months (from 24.2±5.1 to 18.1±4.7; p=.006) and at the end of the follow-up period (18.0±6.0; p=.005). Similarly, a valuable improvement of other cutaneous manifestations, namely hypermelanosis (12/12 pts), pruritus (11/13 pts), and calcinosis (3/6 pts) was observed. Moreover, arthritis revealed particularly responsive to RTX treatment leading to a clear-cut reduction of swollen and tender joints in 12/13 patients; while lung fibrosis detected in

12/15 remained stable during the entire follow-up.These positive clinical changes were mirrored by the subjective improvement of patients' well being in all cases (HAQ from 1.45±0.49 to 0.98±0.38, VAS from 64.5±18.5 to 37.5±8.6). Finally, no significant side effects were observed.
Conclusions: The present study reinforces the previous trials showing the usefulness of RTX in the management of SSc patients, along with its good safety profile. The specific therapeutical activity of RTX, able to down-regulate the B-cell over expression, might explain its beneficial effects on some SSc clinical manifestations; in particular the improvement of both skin sclerosis and articular involvement, along with the possible stabilization of lung fibrosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2235

FRI0389 FOOT INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS: A SINGLE-CENTRE REPORT

G. Cuomo, D. Ruta, E. Frongillo, L. Pirro, A. Del Mastro, C. Romano.
Dipartimento Assistenziale Integrato di Medicina Interna, UOC Medicina Interna - Università degli Studi della Campania - Luigi Vanvitelli, Napoli, Italy

Background: Foot involvement can be a source of morbidity and disability in patients with systemic sclerosis (SSc). Some studies have previously reported severity, echographic and radiographic manifestations of foot involvement in SSc (1,2).
Objectives: The aim of our study was to assess the nature and prevalence of foot problems in patients with SSc reporting a single centre experience.
Methods: A podiatrist and a rheumatologist assessed 81 (76 female) consecutive patients attending our SSc outpatient clinic. The mean age was 50 years (range 21–70). Thirteen (16%) had diffuse cutaneous SSc with a median disease duration from Raynaud's Phenomenon of 5 years (range 3 –19); 68 (84%) had limited cutaneous SSc with a median disease duration of 11.5 years (range 1–41). The overall median disease duration was 11 years (range 1–41). Thirty (37%) were anticentromere antibodies positive, thirty five (43%) anti-scl70 antibodies positive. The two investigators evaluated the presence of the following features: colour changes, pain, previous ulceration, current ulceration, pre-ulceration (discoloration and thinning of the skin), toenail changes, hyperkeratosis, calcinosis, onychomycosis, dry skin, skin sclerosis, warts, scleredema, flatfoot. The presence of paresthesias, cramps, metatarsalgia were also investigated.
Results: The diagram reports the prevalence of foot manifestations in the 81 SSc patients.
Most SSc patients suffer from symptoms related to their feet, particularly dry skin (70%), hyperkeratosis (plantar 58%, finger V 63%), Raynaud's phenomenon (59%), cramps (55%). No statistically significant differences were found between diffuse and limited SSc groups.



Prevalence of foot manifestations in the 81 SSc patients.

Conclusions: Our study suggests that, in patients with SSc, foot problems are common and potentially disabling. A careful assessment of the feet should always be performed in these patients, in order to identify problems at an early stage.
References:
[1] La Montagna G et al. Semin Arthritis Rheum 2002.
[2] Sari-Kouzel H et al. Rheumatology (Oxford) 2001.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6097

FRI0390 EUROPEAN MULTICENTRE STUDY VALIDATES ELF TEST AS BIOMARKER OF FIBROSIS IN SYSTEMIC SCLEROSIS

G. Abignano[1,2], J. Blagojevic[1,2,3], L.-A. Bissell[1,2], R.B. Dumitru[1,2], S. Eng[1,2], Y. Allanore[4], J. Avouac[4], S. Bosello[5], C. Denton[6], O. Distler[7], G. Ferraccioli[5], S. Jordan[7], M. Matucci-Cerinic[3], V. Ong[6], M. Messenger[8], M. Hutchinson[1], M.H. Buch[1,2], P. Emery[1,2], F. Del Galdo[1,2]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; [3]Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Florence, Italy; [4]Department of Rheumatology, University of Paris Descartes, Paris, France; [5]Division of Rheumatology, Fondazione Policlinico Universitario Agostino Gemelli, Rome, Italy; [6]Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom; [7]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [8]NIHR Diagnostic Evidence Co-operative, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: The Enhanced Liver Fibrosis (ELF) test is a serum test including the serum concentrations of amino-terminal pro-peptide of procollagen type III (PIIINP), tissue inhibitor of matrix metalloproteinase-1 (TIMP-1) and hyaluronic acid (HA). A recent single centre study showed that ELF score and its components are markers of overall fibrosis in systemic sclerosis (SSc) mainly reflecting skin and lung involvement (1).
Objectives: To determine the value of ELF score and its single analytes in an independent multicentre cohort of SSc patients.
Methods: 254 SSc patients from 6 European Rheumatology Centres were included in this study. Clinical data were collected at time of sampling. Serum samples were collected and stored according to EUSTAR biobanking recommendations (2). Sera were analysed employing a high-throughput in vitro diagnostic (Siemens Alpha-Centaur). Statistical analysis was performed with SPSS software V.24.
Results: The 254 SSc patients had a mean age 55.8±13.8 years, and included 209 females and 80 patients with diffuse cutaneous SSc (dcSSc). ELF score was overall higher in males than in females (p=0.0236) as well as in dcSSc compared to limited cutaneous SSc patients (p=0.0015). ELF score and the single markers significantly correlated with the degree of skin involvement (mRSS) and inversely correlated with FVC%, TLC% and DLCO%. Concordantly all markers significantly correlated with skin and lung severity as assessed by the Medsger's scale (Table 1). TIMP-1 and PIIINP levels were higher in patients with lung fibrosis assessed by chest HRCT scan (p=0.0126 and p=0.0308 respectively). Significant correlation (p<0.0001) was found between ELF score, TIMP-1, PIIINP, HA and total disease severity and activity. Multivariate analysis indicated that age (p<0.0001), mRSS (p<0.0001) and DLCO% (p=0.005) were independently associated with ELF score.

Table 1. Coefficient correlation (r) between ELF score, PIIINP, TIMP-1, HA serum levels and clinical variables

	ELF score	PIIINP (ng/mL)	TIMP-1 (ng/mL)	HA (ng/mL)
Serum values (median, range)	8.86, 6.22–12.2	6.44, 0.91–34.63	221, 19.09–595.4	36.98, 4.52–355.5
	r	r	r	r
Age	0.41****	0.06	0.26****	0.52****
mRSS	0.36****	0.29****	0.18**	0.16*
FVC%	-0.12	-0.25***	-0.2**	0.02
TLC%	-0.21**	-0.29****	-0.31****	-0.09
DLCO%	-0.25****	-0.39****	-0.30****	-0.18**
Sev_skin	0.28****	0.27****	0.22***	0.17**
Sev_lung	0.25****	0.29****	0.3****	0.18**
Sev_total	0.32****	0.27****	0.33****	0.23***
EScSG-AI	0.30****	0.26****	0.27****	0.22***

*p<0.05; **p<0.01; ***p<0.001; ****p<0.0001.

Conclusions: The value of ELF score as independent marker of skin and lung involvement is confirmed in a second independent multicentre cohort of SSc patients. A longitudinal study paired with analysis of large cohort of healthy controls is currently on going to identify a SSc specific test with the highest predictive value for skin and lung progression independently of age and gender.
References:
[1] Abignano G et al. Ann Rheum Dis. 2014.
[2] Beyer C et al. Ann Rheum Dis. 2011.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3236

FRI0391 A PERFUSION-METABOLIC MISMATCH IN 99MTL AND 123I-BMIPP SCINTIGRAPHY PREDICTS WORSE PROGNOSIS IN SYSTEMIC SCLEROSIS PATIENTS WITH ASYMPTOMATIC CARDIAC INVOLVEMENT

H. Iida, H. Hanaoka, T. Kiyokawa, Y. Takakuwa, T. Okazaki, H. Yamada, S. Ozaki.
Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

Background: Cardiac involvement is a manifestation of systemic sclerosis (SSc) that contributes to significant mortality and morbidity. Since many SSc patients with cardiac involvement are asymptomatic and it may progress silently, early diagnosis is still challenging. The perfusion-metabolic mismatch in cardiac scintigraphy indicates functional abnormality due to myocardial injury and has been expected to detect early cardiac involvement in various diseases. However, its clinical utility has been poorly evaluated in patients with SSc.

Objectives: To evaluate clinical utility of perfusion and myocardial fatty acid metabolism mismatch in SSc patients without cardiac failure.
Methods: All patients who visited St. Marianna University Hospital from 2009 to 2015 and performed cardiac scintigraphy using ^{99m}Tl and ^{123}I-BMIPP were retrospectively evaluated. Patients who fulfilled American Collage of Rheumatology classification criteria of SSc and systemic lupus erythematosus (SLE) were selected. We subtracted %uptake of metabolism (^{123}I-BMIPP) from that of perfusion (^{99m}Tl) on each 17 myocardial segments standardized by American Heart Association. We compared sum of all the scores and each score in 3 coronary artery regions between patients with SSc and SLE. Furthermore, we evaluated incidence of cardiac death or cardiac failure depending on the scores of each coronary artery regions.
Results: Among 177 patients, we analyzed the data in 22 cases with SSc and 23 with SLE. The sum of all mismatch scores was not significantly different between the 2 groups (p=0.37). The mismatch score of left anterior descending coronary artery (LAD) region was significantly higher in SSc than SLE (p=0.05) (Figure 1A). We next divided SSc patients into 2 groups depending on degree of the LAD mismatch score and found the group with low score had higher incidence of cardiac death or cardiac failure (p=0.04) than that with high score (Figure 1B).

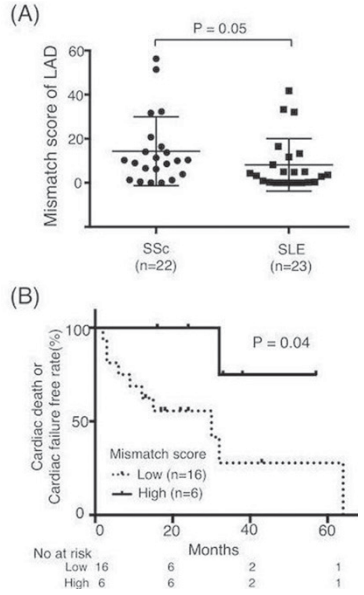


Figure 1

Conclusions: The low mismatch score in LAD region of cardiac scintigraphy could be associated with cardiac death or cardiac failure in SSc patients. Since myocardial fibrosis might replace viable cardiomyocytes leading to loss of ventricular volume, metabolic defect by scintigraphy might be less detectable.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4590

FRI0392 OPPORTUNISTIC INFECTIONS IN PATIENTS WITH MYOSITIS. A RETROSPECTIVE COHORT STUDY

A. Redondo-Benito[1], A. Curran-Fàbregas[2], A. Villar-Gomez[3], E. Trallero-Araguás[4], A. Fernandez-Codina[1], I. Pinal-Fernandez[1], A. Selva-O'Callaghan[5]. *[1]Internal Medicine; [2]Infectious Diseases, Vall d'Hebron General Hospital; [3]Pneumology, Vall d'Hebron General Hospital; [4]Rheumatology Unit. Internal Medicine Dept., Vall d'Hebron General Hospital; [5]Internal Medicine, Vall d'Hebron General Hospital. Universitat Autònoma de Barcelona, Barcelona, Spain*

Background: Idiopathic inflammatory myopathies, also known as myositis, are a heterogeneous group of acquired diseases of probable autoimmune origin, characterized by the presence of inflammatory muscle infiltrates.Infectious complications are not uncommon in myositis, and some predisposing factors, such as upper esophageal involvement, calcinosis cutis, ventilatory insufficiency due to diaphragm involvement, and immunosuppressive drug therapies, seem to be implicated.
Objectives: To describe the prevalence, clinical characteristics, and risk factors for opportunistic infection (OI) in a cohort of patients with inflammatory myopathies, and compare mortality rates between those with and without OIs.
Methods: In total, 204 patients from our myositis cohort were reviewed to identify patients who had experienced an OI during the period 1986–2014. The patients' clinical characteristics, treatment received, and outcome were systematically recorded. Disease activity at the OI diagnosis and cumulative doses of immunosuppressive drugs were analyzed, as well as the specific pathogens involved and affected organs.
Results: The prevalence of OI in the total cohort, was 6.4%: viruses, 44.4% (varicella-zoster virus, cytomegalovirus); bacteria, 22.2% (*Salmonella sp.*, *Mycobacterium tuberculosis*, *M. chelonae);* fungi, 16.7% (*Candida albicans*, *Pneumocystis jirovecii);* and parasites, 16.7% (*Toxoplamosis gondii, Leishmania spp.*) were the pathogens detected. Lung and skin/soft tissues were the organs most commonly affected (27.8%). Overall, 55.6% of OIs developed during the first year after the myositis diagnosis and were significantly associated with administration of high-dose glucocorticoids (p=0.0148). Fever at onset of myositis (p=0.0317), biological therapy (p<0.001) and sequential administration of 4 or more immunosuppressive agents during myositis evolution (p=0.0032) were significantly associated with OI. All-cause mortality in the OI group was 3.69 deaths per 100 patients/year versus 3.40 in the remainder of the cohort (p=0.996).
Conclusions: The prevalence of OI was 6.4% in our myositis cohort. High-dose glucocorticoids at disease onset and severe immunosuppression are implicated in the development of these complications. Mortality did not differ from the remainder of the cohort.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4829

FRI0393 PREVALENCE OF MYOSITIS-SPECIFIC ANTIBODIES IN IDIOPATHIC INFLAMMATORY MYOPATHY COMPARED TO DISEASE AND HEALTHY CONTROLS

J.-B. Vulsteke[1], X. Bossuyt[2,3], D. Dillaerts[3], K. Poesen[4], K. Claeys[5], J. Lenaerts[6], R. Westhovens[6,7], D. Blockmans[1], P. De Haes[8], E. De Langhe[6,7]. *[1]Department of General Internal Medicine; [2]Department of Laboratory Medicine, University Hospitals Leuven; [3]Experimental Laboratory Immunology; [4]Laboratory for Molecular Neurobiomarker Research, KU Leuven; [5]Department of Neurology; [6]Department of Rheumatology, University Hospitals Leuven; [7]Skeletal Biology and Engineering Research Center, Department of Development and Regeneration, KU Leuven; [8]Department of Dermatology, University Hospitals Leuven, Leuven, Belgium*

Background: Myositis-specific autoantibodies (MSA) are increasingly recognized as important diagnostic and prognostic markers in idiopathic inflammatory myopathies (IIM) (polymyositis, dermatomyositis, sporadic inclusion body myositis and necrotizing autoimmune myositis). The prevalence of these MSAs in other systemic autoimmune rheumatic diseases and neuromuscular diseases is unclear.
Objectives: To compare positivity of MSA in a cohort of IIM patients to positivity in healthy controls and different systemic autoimmune rheumatic diseases (SARD) or chronic inflammatory demyelinating polyneuropathy (CIDP).
Methods: A line immunoassay (Myositis 12 IgG DOT for BlueDiver) for IgG autoantibodies against Jo-1, PL-7, PL-12, EJ, SRP, Mi-2, MDA-5, TIF1-γ, HMGCR, SSA/Ro52kD, SAE1/2 and NXP-2 antigens was performed in patients with IIM (n=146), healthy controls (blood donors, n=40) and disease controls (n=200). The disease control group consisted of patients with other SARD (rheumatoid arthritis, RA; systemic sclerosis, Ssc; Sjögren's syndrome, SjS; and systemic lupus erythematosus, SLE) (n=40 for each disease group) and CIDP (n=40). A result >10 arbitrary units was considered significantly positive.
Results: 50% of 146 patients with IIM tested positive for an MSA (table 1), compared to 3,5% of 200 disease controls (table 1). 1 SSc patient was positive for Jo-1, 1 CIDP patient was positive for PL12, 2 SSc patients were positive for TIF1-gamma, 2 patients (1 SSc and 1 SjS patient) were positive for SAE1/2, and 1 SjS patient was positive for NXP2. The prevalence of SAE1/2 and TIF1-gamma positivity was similar in the IIM and disease control group. No healthy control had a significantly positive MSA.

Antibody detected	IIM (n=146)	Disease controls (n=200)	Healthy controls (n=40)
1 positive (>10 AU) MSA detected	68 (47%)	7 (3,5%)	0 (0%)
Jo-1	28 (19%)	1 (0,4%)	0 (0%)
PL12	3 (2%)	1 (0,4%)	0 (0%)
PL7	1 (1%)	0 (0%)	0 (0%)
EJ	2 (1%)	0 (0%)	0 (0%)
Mi-2	7 (5%)	0 (0%)	0 (0%)
MDA-5	7 (5%)	0 (0%)	0 (0%)
SAE1/2	3 (2%)	2 (0,8%)	0 (0%)
TIF1-gamma	2 (1%)	2 (0,8%)	0 (0%)
NXP2	5 (3%)	1 (0,4%)	0 (0%)
SRP	3 (2%)	0 (0%)	0 (0%)
HMGCR	7 (5%)	0 (0%)	0 (0%)
>1 positive (>10 AU) MSA detected	4 (3%)	0 (0%)	0 (0%)
Jo-1 + EJ	1		
Jo-1 + NXP2	1		
SAE1/2 + NXP2	1		
Jo-1 + SAE1/2 + NXP2	1		

Conclusions: MSA positivity in patients with a clinical non-IIM diagnosis (other SARD or CIDP) is infrequent compared to positivity in the IIM group. For TIF1-gamma and SAE1/2 assay performance may need to be optimized. The distribution of subtypes of MSA in this IIM cohort is consistent with data of previous studies.[1]
References:
[1] Allenbach Y, Benveniste O. Diagnostic Utility of Autoantibodies in Inflammatory Muscle Diseases. J Neuromuscul Dis. 2015; 2:13–25.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5143

FRI0394 NEUROPATHIC PAIN IS ASSOCIATED WITH SKIN THICKNESS IN SYSTEMIC SCLEROSIS PATIENTS

J. Sousa-Neves, M. Cerqueira, D. Santos-Faria, J. Leite Silva, C. Afonso, F. Teixeira. *Rheumatology, Hospital Conde de Bertiandos, ULSAM, Ponte de Lima, Portugal*

Background: Systemic Sclerosis (SSc) is a connective tissue disorder characterized by fibrosis of skin and internal organs, vasculopathy and systemic inflammation. To date, few studies assessed pain in SSc patients,(1) namely the neuropathic component. Data is also scarce on defining possible neuropathic pain (NP) predictors in these patients.
Objectives: To determine if patients with SSc have a higher prevalence of NP compared with a group of age and sex matched controls and study possible associations between NP and SSc clinical variables.
Methods: The study evaluated patients diagnosed with SSc fulfilling the SSc classification criteria of the American College of Rheumatology (ACR), older than 18 years old and followed up at our Rheumatology Unit. Forty-eight patients with mean age of 56.98±12.73 years and mean disease duration of 9.77±6.12 years were included. Comparison group comprised 45 age and sex matched controls. Patients and controls were consecutively evaluated at our Unit and NP in 4 questions questionnaire (DN4) was used for assessing the presence of NP. In SSc patients, skin involvement was also evaluated clinically by the modified Rodnan skin thickness score (mRSS) ranging from 0 to 51. Hand mobility (HAMIS) and SSc Severity Scale (SScSS) were also calculated and relevant clinical variables of the disease were collected. Parametric and nonparametric tests were used for comparative analysis. Multivariate logistic regression was used to identify factors associated to NP. Statistical significance was defined as $P<0.05$.
Results: In our study, prevalence of NP assessed by DN4 was significantly higher in SSc patients comparative to controls (56.2% *versus* 13.3%, $p<0.001$). In addition to age and sex, presence of diabetes (p=0.541) was also similar in both groups. In SSc group, patients with and without NP showed some statistically significant differences (table 1).

Table 1. Comparative analysis between SSc patients with and without NP

	NP positive patients (n=27)	No-NP patients (n=21)	P value
Median age, years (IQR)	61 (57–69)	52.38 (42.5–63.5)	0.032
Mean disease duration (years)	11.36±6.55	7.73±4.93	0.04
Diffuse/limited cutaneous subtype (n)	6/21	0/21	0.024
Mean mRSS	22.81±8.74	7.57±3.64	<0.001
Mean HAMIS	10.44±6.16	1.52±2.29	<0.001
Mean SScSS	10.00±4.32	3.90±2.07	<0.001
Digital ulcers n (%)	17 (63.0)	6 (28.6)	0.018
Calcinosis n (%)	15 (55.5)	6 (28.6)	0.062

Multivariate logistic regression revealed that only mean mRSS (odds ratio [OR] =1.90, 95% confidence interval [CI] 1.01 to 3.55, p=0.045) was independently associated with the presence of NP.
Conclusions: To the best of our knowledge, this is the first study evaluating the prevalence of NP in SSc patients in comparison with age and sex matched controls. NP was significantly more prevalent in patients with SSc. Skin thickness assessed by mRSS was independently associated with the presence of NP.
References:
[1] Schiei O et al. Prevalence, severity, and clinical correlates of pain in patients with systemic sclerosis. Arthritis Care Res (Hoboken). 2010 Mar; 62(3):409–17.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5288

FRI0395 INCIDENCE OF MYOSITIS-SPECIFIC AUTOANTIBODY (MSA) SPECIFICITIES IN SERA REFERRED TO NEW ZEALAND (NZ) MEDICAL LABORATORIES

J. O'donnell[1], P. Keating[1], M. van Voorthuizen[1], J. Liu[1], I. Chua[1], A. Soepnel[2], E. Gumbley[2], M. Spellerberg[1]. *[1]Immunology Section, Canterbury Health Labs, New Zealand, Christchurch; [2]Waikato Hospital Laboratory, Waikato Hospital, Hamilton, New Zealand*

Background: Idiopathic inflammatory myopathies can be classified by clinicopathological phenotype into four major groups: overlap myositis (OM), dermatomyositis (DM), immune mediated necrotising myositis (IMMNM) and inclusion body myositis (IBM). The different phenotypes associate with distinct MSA specificities although a variable percentage within each group are seronegative and the majority of IBM patients are seronegative[1]. No commercial assay for the IBM associated specificity, cN1A, is available. In NZ testing for MSA is restricted to two laboratories: Waikato Hospital (WHL) and Canterbury Health Laboratories (CHL). Both laboratories use the commercial Euroimmun Euroline assay. In addition CHL has developed an ELISA for anti HMGCR autoantibodies and receives referrals from throughout NZ.
Objectives: To define the incidence and specificities of MSA in serum samples referred for testing in New Zealand.
Methods: For the period 3 November 2015 to 2 November 2016 each laboratory information system (LIS) was interrogated for requests for MSA. For the purposes of this report positive results were grouped into the specificities associated with each of the defined clinicopathological phenotypes.
DM: Mi2, Tif-γ, MDA 5 NXP2 SAE1
OM: Ku, PM-Scl-100, PL75, Jo1, PL-7, PL-12, EJ, OJ
IMMNM: HMGCR, SRP
Results: Of screened sera (n=793, CHL=622, WHL=171) 11% were positive for MSA (88/793). Positive sera where distributed amongst three clinicopathological associated autoantibody specificities: DM 23% OM 50%,IMMNM 27%. The most common serum specificities were HMGCR (n=24) and Jo-1 (n=13). No serum with specificities to SRP or OJ was detected. 22/24 sera positive for anti HMGCR had an elevated CPK concentration (CPK>2500u/l in 21/24 and CPK=544 in 1/24, reference range =66–220).
Conclusions: In New Zealand 11% of sera referred for MSA testing were positive. As a group the most common specificities were those associated with OM while the most common antigen specificity was to HMGCR. Anti-HMGCR antibodies were almost invariably associated with major elevations in serum CPK.
References:
[1] Beveniste O, Stenzel W, Allenbach Y. Advances in serological diagnostics of inflammatory myopathies. Curr Opin Neurol 2016;29:662–673.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2329

FRI0396 LEVELS PENTRAXIN 3 AND C1Q IN SYSTEMIC SCLEROSIS: ASSOCIATION WITH PULMONARY ARTERIAL HYPERTENSION AND CLINICAL FINDINGS

R. Cevik[1], K. Nas[2], T. Bozan[1], A. Ekinci[3], A. Kamanlı[2], I. Tekeoglu[2], M.O. Ayyildiz[4]. *[1]Physical Medicine and Rehabilitation, Dicle University Hospital, Diyarbakir; [2]Physical Medicine and Rehabilitation, Sakarya University, Faculty of Medicine, Sakarya; [3]Department of Biochemistry; [4]Internal Medicine, Dicle University Hospital, Diyarbakir, Turkey*

Background: Systemic sclerosis (SSc) is an autoimmune rheumatic disease with unknown etiology that characterized fibrosis and vascular endotelial damage with obliteration of the microvasculature caused from exaggerated syntesis of collagen and extracellular matrix deposition in skin and internal organs. Pentraxin 3 (PTX3) accepted as a vascular inflammatory marker which secreted in early stage of endothelial dysfunction.
Objectives: In this study, we aimed to investigate plasma PTX3 and serum complement C1q levels and their relations with cytokines and pulmonary arterial pressure in SSc.
Methods: Fifty nine patients diagnosed SSc and 28 subjects without inflammatory rheumatic disease recruited to the study. Plasma PTX3, and serum TNF-α, IL-1β, IL-4, IL-10, INF-γ, TGF-β and complement C1q measured in both groups. Clinical findings and pulmonary arterial pressure of the SSc patients assessed.
Results: Ages of fifty nine with SSc (54 female and 5 male) and 28 control subjects (23 female and 5 male) were 49,47±12.74 and 43,07±13,71 respectively. PTX3, IL-1β and IL-4 levels found decreased in SSc patients. There were no differentiations between limited and diffuse cutaneous SSc subgroups in terms of PTX3, cytikines and C1q levels. Plasma PTX3 and serum IL-1β concentrations found decreased only limited cutaneous SSc subgroup comparing controls. According to the immunosupressive drugs use; PTX3 levels found decreased in using group and TNF-α ve IL-1β levels found decreased in not using group comparing controls. Significant positive association found between PTX3 and C1q and all cytokines except TGF- β.
Conclusions: PTX3 suggested to be used in the pathogenesis and assessment of disease treatment efficacy of SSc, because of found decreased in SSc patients especially in limited cutaneous and immunosupressive drugs using subgroups. Associations between C1q, and PTX3 and pulmonary artey pressure highlighted possible roles of both parameters in development of pulmonary hypertension. It is possible to develop preventive treatment strategies with better understanding of these associations. Advanced studies should be carried out for clarifying this condition.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6755

FRI0397 EVALUATION OF VITAMIN B12 DEFICIENCY AND ASSOCIATED FACTORS IN PATIENTS WITH SYSTEMIC SCLEROSIS

D. Tas Kilic[1], A. Sari[2], B. Armagan[2], A. Erden[2], L. Kilic[2], M. Kilinckaya[3], T. Turhan[3], A. Akdogan[2], S. Karaahmetoglu[1]. *[1]Department of Internal Medicine, Numune Education and Research Hospital; [2]Department of Internal Medicine Division of Rheumatology, Hacettepe University Faculty of Medicine; [3]Department of Biochemistry, Numune Education and Research Hospital, Ankara, Turkey*

Background: Vitamin B12 (Vit B12) deficiency is a common condition, which can be manifested with non-specific clinical features or with neurological and/or haematological abnormalities in severe cases. In systemic sclerosis (SSc)

gastrointestinal involvement (GI), nutritional status and medications may lead to Vit B12 deficiency.
Objectives: We aimed to investigate the frequency of Vit B12 deficiency and its determinants in SSc patients.
Methods: Sixty-two (90.3% female) SSc patients were enrolled in to the study. The nutritional status of patients was assessed with Malnutrition Universal Screening Tool (MUST). Serum Vitamin B12, homocysteine and Helicobacter Pylori Immunoglobulin G (H. Pylori IgG) levels were measured in all patients. Serum Vit B12 levels of patients were classified as; Low (<200 pg/ml), Borderline (200 - 300 pg/ml) and Normal (>300 pg/ml). Serum homocysteine levels of patients were classified as; Elevated (>9 μmol/L) and hyperhomocysteinemia (>15 μmol/L). H. Pylori IgG antibody level >5 U/ml considered as positive. Serum Vit B12 level <200 pg/ml or being on Vit B12 replacement therapy was considered as B12 deficiency.
Results: The mean age of the patients was 50.2 (12.5) years and mean disease duration was 12.0 (7.5) years. Forty-four (71.0%) patients were limited and 18 (29.0%) patients had diffuse SSc. The mean serum Vit B12 level of the patients was 323.6±291.5 pg/ml. Seventeen (27.4%) patients had normal, 23 (37.1%) patients had borderline and 22 (35.5%) patients had low serum Vit B12 level. Forty-four (71.0%) patients were considered as Vit B12 deficient; 22 had serum Vit B12 level <200 pg/ml (4 of these patients were on vitamin B12 replacement therapy), 22 were already on Vit B12 replacement therapy and Vit B12 level ≥200 pg/ml. The mean homocysteine levels were higher in the group with Vit B12 <200 pg/ml as compared to other groups (p=0.005). In the group with Vit B12 level <200 pg/ml, 33.3% (7/21) of the patients had hyperhomocysteinemia and 76.2% (16/21) had 'elevated homocysteine levels (Table). Fifty-one (82.3%) patients had GIS involvement and 16 (25.8%) patients had medium-high risk MUST score. H. Pylori IgG antibody was positive in 40 (64.5%) patients. There were no statistically significant differences between the patients with and without Vit B12 deficiency regarding to age, mean disease duration, hemoglobin level, GI involvement, medium-high risk MUST score, H. Pylori IgG antibody positivity and other clinical features (p>0.05 for all).

	Vit B12 level			
	>300 pg/ml n=16	200–300 pg/ml n=22	<200 pg/ml n=21	p
Homocysteine μmol/L, mean (SD)	9.1 (3.4)	10.4 (3.0)	14.1 (6.5)	0.005
Homocysteine >9 μmol/L, n (%)	7 (43.8)	16 (72.7)	16 (76.2)	0.084
Homocysteine >15 μmol/L, n (%)	1 (6.3)	0	7 (33.3)	0,004

Homocysteine level was not measured in 3 patients.

Conclusions: SSc patients are at risk for Vit B12 deficiency. Using homocysteine level seems to be unpractical for confirmation of Vit B12 deficiency in a complex disease such as SSc because its level is influenced by many factors. Patients with SSc should be closely monitored for Vit B12 deficiency and replacement therapy should be planned if necessary.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6385

FRI0398 INFLAMMATORY MYOPATHIES WITH CAMPTOCORMIA OR DROPPED HEAD SYNDROME ARE ASSOCIATED SCLEROMYOSITIS WITH LATE ONSET AND DELAYED DIAGNOSIS

L. Pijnenburg[1], F. Maurier[2], N. Poursac[3], M. Couderc[4], N. Vernier[5], I. Guichard[6], J. Sellam[7], J. Sibilia[1], A. Meyer[1] on behalf of French Myositis Network, Club Rhumatisme et Inflammation. *[1]Hôpitaux Universitaires de Strasbourg, Strasbourg; [2]Hôpitaux Privés de Metz, Metz; [3]Hôpitaux Universitaires de Bordeaux, Bordeaux; [4]Hôpitaux Universitaires de Clermont Ferrand, Clermont Ferrand; [5]Hôpitaux Universitaires de Dijon, Dijon; [6]Hôpitaux Universitaires de St Etienne, Saint Etienne; [7]Hôpitaux de Paris, Paris, France*

Background: Severe weakness of axial muscle leads to dropped head syndrome or camptocormia. The signification of these symptoms has not been studied in inflammatory myopathies (IM).
Objectives: To assess the signification of dropped head syndrome and/or camptocormia in patients with IM.
Methods: All practitioners of the French Myositis Network and the Club Rhumatisme et Inflammation (>1000 physicians) were invited to report their patients suffering from IM (myopathy with myositis specific autoantibody and/or typical muscle biopsy according to the ENMC criteria) with camptocormia and/or dropped head syndrome. These axial IM cases were included only if no other explanation of axial weakness was found. IM patients without axial involvement (non-axial IM group), were randomly selected from the participative centers, and included as control patients (ratio 1:2). Clinical, serological, muscle pathological features, management and outcomes were studied using a standardized form.
Results: Twenty patients (sex ratio 2.6) with axial involvement (camptocormia: 60%, dropped head syndrome: 40%) were included. Compared with the control group, these axial IM-patients were older (64.05±11.64 y. vs. 48.22±18.28. p<0.005) and diagnosis of IM was delayed (16.4±4.5 months vs. 8.5±2.7, p<0.05).
All patient except one had also proximal weakness of the limbs. CK blood level was 2794±870 UI/L, which was similar to the controls (2864±559 UI/L). According to the ENMC classification, non-specific myositis was the most frequent finding on muscle biopsy (n=5/15, 30% vs. n=1/24, 4% in the non-axial group, p<0.05) and dermatomyositis (DM) pattern tended to be less frequent in axial-IM patients (3/12 20% vs. 11/24, 46%, p=0.10).
Most of the patients (75%) had also extra muscular involvement including acrosyndrome (45%), interstitial lung disease (35%), sclerodactyly (30%), telangiectasia (25%), digital tip ulcer (10%), sclerodermy (5%). By contrast, no patient had polyarthrithis (vs. 20% in the controls, p<0.05). DM rash was hardly threefold less frequent in axial IM patients (15% vs. 42%, p<0.05).
Auto-antibodies associated with scleromyositis were the most frequent in axial-IM patients (30% vs. 10.3%, p=007, manly anti-PM/Scl). One patient (5%) had cancer within the 3 years before or after IM diagnosis (NS vs. controls).
Thus, most frequent diagnosis in axial IM-patients were scleromyositis (35% vs. 5% in the controls, p<0.05) and inclusion body myositis (20% vs. 2.6% in the controls, p<0.05). DM was twofold less frequent than in control (10% vs 41%, p<0.05). Other IM subtypes were not statistically different from the control groups.
Except patients with diagnosis of sIBM, all axial IM-patients received corticosteroids with another immunomodulatory drugs (median number 2, range 1–5). Half of the axial-IM patients received intravenous immunoglobulin. After a mean follow up of 68.4±3.76 months all patients had improvement, including in axial weakness, except in patients with sIBM. One patient died from ischemic cardiomyopathy.
Conclusions: In IM, camptocormia and dropped head syndrome are associated with late onset scleromyositis and sIBM with delayed diagnosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6564

FRI0399 EFFICACY OF AN INTENSIVE 24-WEEK PHYSIOTHERAPY PROGRAMME IN PATIENTS WITH SYSTEMIC SCLEROSIS - PRELIMINARY DATA FROM A SINGLE-CENTER CONTROLLED STUDY

M. Spiritovic[1,2], H. Smucrova[1], S. Oreska[1], H. Storkanova[1], P. Cesak[2], A. Rathouska[1], O. Ruzickova[1], H. Mann[1], K. Pavelka[1], L. Senolt[1], J. Vencovsky[1], R. Becvar[1], M. Tomcik[1]. *[1]Department of Rheumatology, 1st Medical Faculty, Charles University, Institute of Rheumatology; [2]Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic*

Background: Involvement of skin and musculoskeletal system in systemic sclerosis (SSc) leads to loss of function, disability and reduced quality of life. Data on efficacy of non-pharmacologic care in SSc is very limited due to variety in studied interventions/outcomes.
Objectives: To address the limitations of existing studies, and evaluate the effect of a controlled, long-term (24-week intervention, 24-week follow-up), intensive (1h physiotherapy + 0.5h occupational therapy twice weekly, and home-exercise for 0.5h 5x weekly), tailored physiotherapy programme on function/impairment of hands/face, and quality of life/disability in cohorts with a substantial number of SSc patients.
Methods: All patients fulfilled ACR/EULAR 2013 criteria, had skin involvement of hands/mouth, and were consecutively recruited from 2014 to 2016 at the Institute of Rheumatology in Prague. Both groups received educational materials and instructions for home exercise at baseline, however, only intervention group underwent the intensive physiotherapy programme. At months 0,3,6,12 all patients were assessed by a physician (physical examination, mRSS-Modified Rodnan's skin score, EUSTAR SSc activity score, Medsger SSc severity score), and a physiotherapist blinded to intervention [validated measurements (dFTP-delta finger to palm, inter-incisor/inter-lip distance, grip strength using Baseline dynamometer); tests (HAMIS-Hand Mobility In Scleroderma)], patients filled out patient reported outcomes/questionnaires (CHFS-Cochin Hand Function Scale, MHISS-Mouth Handicap In SSc Scale, HAQ, SHAQ, SF-36) and provided blood for routine laboratory analysis and biobanking. Normality of data was tested, inter-group analysis was performed with 2-way ANOVA, and intra-group analysis by Friedmann's test with Dunn's post hoc test.
Results: 25 SSc patients (22 female/3 male, 14 limited cutaneous (lc)SSc/11 diffuse cutaneous (dc)SSc, median of age 54.0 and disease duration 7.0 years, mRSS 12) were recruited into the intervention group (IG) and 29 patients into the control group (CG) (25 female/4 male, 16 lcSSc/13 dcSSc, median of age 49.0 and disease duration 5.0 years, mRSS 11). Compared to observed statistically significant deterioration in CG over the period of m0-m6, we found statistically significant improvement in dFTP, grip strength, HAMIS, inter-incisor and inter-lip

Parameter (unit)	Intervention group Mean ± SEM	Control group Mean ± SEM	Intra-group analysis (Friedmann+Dunn)		Inter-group analysis (2WA)
			Interevention gr.	Control group	
dFTP (cm)	m0: 5.7 ± 0.5	m0: 6.6 ± 0.5	m0-m3: p<0.001	m0-m3: p<0.01	p<0.0001
	m3: 6.2 ± 0.5	m3: 6.1 ± 0.4	m3-m6: p<0.05	m3-m6: p<0.05	
	m6: 6.8 ± 0.6	m6: 5.8 ± 0.4	m0-m6: p<0.001	m0-m6: p<0.001	
Hand grip strength (kg)	m0: 17.2 ± 1.8	m0: 16.6 ± 1.3	m0-m3: p<0.05	m0-m3: p=NS	p<0.0001
	m3: 19.2 ± 1.9	m3: 14.9 ± 1.4	m3-m6: p=NS	m3-m6: p=NS	
	m6: 19.7 ± 1.9	m6: 13.9 ± 1.9	m0-m6: p<0.001	m0-m6: p<0.01	
HAMIS	m0: 9.8 ± 1.3	m0: 3.9 ± 1.1	m0-m3: p<0.01	m0-m3: p<0.01	p<0.0001
	m3: 7.1 ± 1.2	m3: 6.4 ± 1.2	m3-m6: p<0.01	m3-m6: p<0.001	
	m6: 4.1 ± 0.9	m6: 9.3 ± 1.1	m0-m6: p<0.001	m0-m6: p<0.001	
Inter-incisor distance (mm)	m0: 30.6 ± 1.6	m0: 32.9 ± 1.3	m0-m3: p<0.01	m0-m3: p<0.001	p<0.0001
	m3: 33.3 ± 1.6	m3: 30.2 ± 1.4	m3-m6: p=NS	m3-m6: p=NS	
	m6: 36.2 ± 2.0	m6: 29.8 ± 1.4	m0-m6: p<0.001	m0-m6: p<0.001	
Inter-lip distance (mm)	m0: 39.2 ± 1.6	m0: 41.7 ± 1.1	m0-m3: p<0.01	m0-m3: p<0.05	p<0.0001
	m3: 42.4 ± 1.7	m3: 39.9 ± 1.2	m3-m6: p=NS	m3-m6: p=NS	
	m6: 44.6 ± 1.8	m6: 40.0 ± 1.3	m0-m6: p<0.001	m0-m6: p=NS	

Acronyms: SEM, standard error of the mean; Friedmann, Friedmann's test; Dunn, Dunn's post hoc test; 2WA, two way ANOVA; dFTP, delta finger to palm; HAMIS, Hand Mobility in Scleroderma; m0, month 0 (= at the baseline); m3, month (= in the middle of intervention period); m6, month 6 (= at the end of intervention); p, p-value; NS, not significant

distance (Table 1). Only numerical improvement in IG compared to numerical deterioration in CG, which have not reached statistical significance, were observed in patient reported outcomes (CHFS, MHISS, HAQ, SHAQ, SF-36).

Conclusions: Our physiotherapy program not only prevented the natural course of progressive deterioration of function of hands/mouth (observed in the control group), but led to a significant improvement in monitored parameters, which was clinically meaningful in a substantial proportion of patients.

Acknowledgements: Supported by AZV-16–33574A.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4875

FRI0400 EFFICACY OF INTRAVENOUS IMMUNOGLOBULIN THERAPY IN REFRACTORY DYSPHAGIA IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

M. Giannini[1], M.L. Fiorella[2], D. D'Abbicco[3], A. Amati[4], A. Lia[4], F. Girolamo[4], F. Cacciapaglia[1], F. Iannone[1]. *[1]Dipartimento di Emergenza e Trapianti di Organi - Sezione di Reumatologia; [2]Dipartimento di Scienze mediche di base, neuroscienze ed organi di senso - Clinica Otorinolaringoiatrica; [3]Dipartimento di Emergenza e Trapianti di Organi - Chirurgia Marinaccio; [4]Dipartimento di Scienze mediche di base, neuroscienze ed organi di senso - Sezione di Neurologia, Università degli Studi di Bari, Bari, Italy*

Background: Polymyositis (PM) and Dermatomyositis (DM) are systemic inflammatory diseases affecting skeletal muscles and other organs, particularly hypopharynx and the upper tract of the esophagus, causing motility dysfunction. The current treatment for PM and DM relies on steroids and immunosuppressants, but esophageal involvement is often refractory to standard therapies.

Objectives: To assess the efficacy and safety of intravenous immunoglobulins (Ig-iv) as therapy of refractory dysphagia (1) in patients affected with PM/DM who have received conventional treatments for at least three months. These are the extended data of a previous abstract entitled "Improvement of refractory dysphagia in patients with idiopathic inflammatory myopathies receiving immunoglobulin intravenous therapy" accepted to EULAR 2015 Congress.

Methods: We enrolled 17 patients (15 F), 8 with DM, 9 with PM according to Bohan and Peter criteria, treated with prednisone (mean dose 20 mg/day) ± Methotrexate (15 mg/wk) or Azathioprine (100 mg/day) for at least 3 months, without improvement of dysphagia. All patients received one infusion of Ig at a standard dose (2 g/kg in a day) every two months for 3 cycles. In all patients, at entry and before each infusion, creatine kinase (CK) levels and Manual Muscle strength Test on 12 muscle groups (MMT12) were evaluated. Dysphagia assessment included: Eating Assessment Tool (EAT) impaired for score $\geq$3; Three-oz Swallow Test (3oST) and fibrolaryngoscopy (FEES) for pharyngeal muscle propulsion and stasis of liquid/solid bolus detection. Student T-test and Chi-square test were used to compare baseline and follow-up data.

Results: At entry, all patients had an EAT score $\geq$3 with a mean score of 16.2±9, 3 patients presented a 3oST for solid (STPNS) impaired, and only 1 patient also for liquid (STPNL). CK levels were slightly increased (474±720 UI/L), and MMT12 score was 4.45±0.35. Following Ig-iv therapy we observed a significant improvement of EAT score after the first dose (9±8, p=0.006) with a further reduction after the second dose (7.4±8, p=0.007) and stability after the third one (7.6±8, p=0.008). An improvement of pharyngeal muscle propulsion, with a significant resolution of solid stasis and a partial resolution of liquid stasis were observed. In addition, MMT12 score progressively improved after each dose, increasing at 4.86±0.16 after the third dose (p=0.001). Noteworthy, after the third Ig-iv dose, three patients stopped the steroid and the remaining 12 were treated with a significant lower dose of 5 mg/day of prednisone (p=0.04).

Conclusions: According to literature, our findings provided evidence that Ig-iv induced a meaningful improvement of dysphagia, also having a steroid-sparing effect. An improvement of muscle strength was also detected. Although further studies of larger cohort of patients and a longer follow-up time are needed, our findings corroborate the utility of Ig-iv in the treatment of more resistant idiopathic inflammatory myositis related dysphagia.

References:

[1] Marie I et al. Intravenous immunoglobulins for steroid-refractory esophageal involvement related to polymyositis and dermatomyositis: a series of 73 patients. Arthritis Care Res. 2010;62(12).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5049

FRI0401 INITIAL MANIFESTATION DETERMINES CLINICAL ENTITY AND COURSE IN PATIENTS WITH ANTI-CENTROMERE ANTIBODY: A SINGLE CENTER LONGITUDINAL RETROSPECTIVE COHORT STUDY

M. Tsukamoto[1,2], K. Suzuki[1], N. Seta[2], T. Takeuchi[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo; [2]Department of Internal Medicine, Tokyo Dental College Ichikawa General Hospital, Ichikawa, Japan*

Background: Anti-centromere antibody (ACA) is often detected in sera from autoimmune diseases, such as limited cutaneous systemic sclerosis (SSc) and primary biliary cirrhosis (PBC). ACA-positive Sjögren's syndrome (SjS) is recently considered as a distinct clinical subgroup in SjS [1–2]. The other autoimmune diseases associated with ACA-positive have not fully elucidated and the role of ACA in their pathogenesis still remains unclear. In addition, comprehensive and enough clinical information from the point of view of ACA positive cases has not been accumulated.

Objectives: To clarify clinical features of patients with ACA and their association with autoantibodies.

Methods: Patients with discrete-speckled pattern in anti-nuclear antibody (ANA) test and/or positive ACA, who visited to our department during over 20 years between May 1995 and December 2016, were enrolled. Clinical information and immunological tests including immunoglobulin (Ig) and serum autoantibodies were collected and statistically analyzed.

Results: Discrete-speckled pattern in ANA test and/or positive ACA were identified in 309 patients. There were 292 female and 17 male and the average age was 60 years old. Proportion of concomitant ANA patterns were speckled (16%), homogenous (7%), cytoplasmic (3%) and/or nucleolar (3%) pattern. 186 patients (60%) had Raynaud's phenomenon and 149 patients (48%) had sclerodactyly. 162 patients (52%) had oral and/or ocular dryness symptoms. 21 patients (6%) had interstitial pneumonia and 13 patients (4%) had pulmonary hypertension. 42 patients (13%) had arthritis. 19 patients (6%) had thyroid disease. 214 patients (69%) were classified into 17 autoimmune diseases (including overlap cases) from symptoms at initial visit, while other 95 patients (31%) who did not meet the criteria were not diagnosed. IgG, IgM and IgA in the patients who were classified into autoimmune diseases were higher than that in other patients who were not classified (p=0.0007, p=0.0057 and p=0.0158, respectively). In the 214 patients (69%), there were most of patients who were diagnosed as SSc (n=113, 36%) and/or SjS (n=78, 25%). 25 patients (8%) and 22 patients (7%) were diagnosed with rheumatoid arthritis (RA) and PBC, respectively. On the other hand, the patients who diagnosed as systemic lupus erythematosus were 3 (1%), and nobody was diagnosed as myositis. The mean observation period was 80 months. 2 patients in 95 patients who were unclassified at initial visit were diagnosed as RA or autoimmune hepatitis by developing new symptoms during observation. A patient was newly diagnosed as SSc in addition to SjS because sclerodactyly was newly developed. In other patients, the diagnosis was not changed and added during observation.

Conclusions: Our single center longitudinal retrospective cohort study confirmed that ACA-positive cases were classified into various types of autoimmune disease. Few patients had new symptoms during observation but the initial diagnosis was unchanged. Our data demonstrated that initial manifestation determined clinical entity and course in patients with ACA.

References:

[1] J Rheumatol 2001; 28: 2238.
[2] Int J Rheum Dis 2015; 18: 776.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5692

FRI0402 ONSET CLINICAL INVOLVEMENT AS PROGNOSTIC FACTOR IN SYSTEMIC SCLEROSIS (SSC)

M. Pestaña Fernández[1], M. Rubio Rivas[1], C. Tolosa Vilella[2], A. Guillén del Castillo[3], D. Colunga Argüelles[4], L. Trapiella Martinez[5], V. Fonollosa Pla[3], C.P. Simeón Aznar[3] on behalf of RESCLE. *[1]Internal Medicine Department, Hospital Universitario de Bellvitge, Barcelona; [2]Internal Medicine Department, Corporación Sanitaria Universitaria Parc Taulí, Sabadell; [3]Autoinmune Diseases Unit. Internal Medicine Department, Hospital Vall d'Hebron, Barcelona; [4]Internal Medicine Department, Hospital Universitario Central de Asturias; [5]Internal Medicine Department, Hospital de Cabueñes, Oviedo, Spain*

Background: In most patients with SSc, the onset is in the form of Raynaud's phenomenon (RP), but in a few is in the form of visceral or musculoskeletal involvement or skin sclerosis. Several risk factors are related to poor outcome in patients with SSc, but never before has the mode of onset been described as one of them.

Objectives: To asses the mode of onset as prognostic factor in patients with SSc.

Methods: A retrospective and multicentre cohort study including 1625 patients with SSc, based on the National Spanish Scleroderma Registry (RESCLE) which includes 28 referral centres.

RP, puffy hands, arthralgia/arthritis, skin sclerosis, intersititial lung disease (ILD), pulmonary arterial hypertension (PAH) and esophageal hipomotility where included as clinical modes of onset.

Results: The cohort was split up in two groups: 1342 patients (83%) presented as RP and 283 (17%) presented as non-RP (see graphic below)

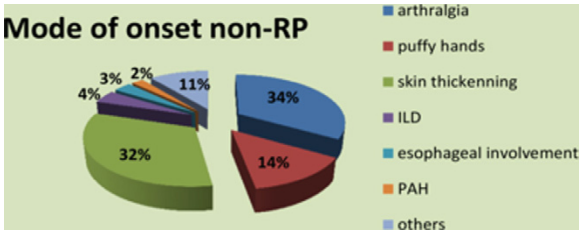
Non-RP patients where younger at onset of disease (44.7±16.5 vs 49±15.6 years, p<0.001), showed higher percentage of diffuse subtipe (36% vs 19%, p<0.001), developed more visceral involvement during the course of the illness and where more frequently anti-RNAp III positive (29 vs 10%, p<0.001).

Overall mortality was 16% in patients presented as RP vs 23% in non-RP patients (p=0.003). Few differences where noted among causes of death related to SSc, but the higher mortality was observed in RP group due to PAH (19% vs 8.1%, p=0.05) and due to ILD in non-RP group (24% vs 8.3%, p=0.002).

Survival of patients with RP at onset was better at anytime than those with a non-RP onset: 0.97 vs. 0.89 at 5 years, 0.93 vs. 0.82 at 10 years, 0.83 vs. 0.63 at 20 years and 0.71 vs. 0.51 at 30 years from onset (p<0.001).

Risk factors for death. Univariate and multivariate analysis

	Univariate analysis HR (95% CI)	p-value	Multivariate analysis HR (95% CI)	p-value
Age at first symptom	1.08 (1.07–1.09)	**<0.001**	1.07 (1.06–1.09)	**<0.001**
Gender (female)	0.40 (0.29–0.54)	**<0.001**	0.55 (0.38–0.78)	**0.001**
Disease subset				
lcSSc	0.57 (0.45–0.72)	**<0.001**	–	–
dcSSc	2.74 (2.14–3.50)	**<0.001**	2.33 (1.74–3.12)	**<0.001**
preSSc	0.05 (0.00–0.62)	**0.020**	–	–
Mode of onset				**<0.001**
RP	0.44 (0.33–0.58)	**<0.001**	1 (ref.)	–
Puffy Hands	2.18 (1.19–4.00)	**0.011**	2.11 (1.07–4.16)	**0.031**
Arthralgia	0.92 (0.53–1.61)	0.779	0.76 (0.40–1.45)	0.407
Skin sclerosis	2.23 (1.45–3.42)	**<0.001**	1.43 (0.88–2.33)	0.150
ILD	11.34 (4.97–25.85)	**<0.001**	3.97 (1.58–9.97)	**0.003**
PAH	31.00 (11.21–85.75)	**<0.001**	13.92 (4.79–40.5)	**<0.001**
Others	2.94 (1.51–5.75)	**0.002**	1.83 (0.85–3.96)	0.123
ILD	2.60 (2.01–3.35)	**<0.001**	1.90 (1.37–2.65)	**<0.001**
PAH	2.60 (2.01–3.35)	**<0.001**	1.64 (1.25–2.15)	**<0.001**
SRC	4.08 (2.64–6.30)	**<0.001**	1.94 (1.14–3.31)	**0.014**
Heart involvement	2.40 (1.89–3.05)	**<0.001**	1.38 (1.05–1.80)	**0.020**



Conclusions: The mode of onset can be considered as independent prognostic factor, and specifically non-RP onset can be considered as a risk factor related to poorer outcome and RP onset and arthralgias can be considered as protector factors.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1675

FRI0403 INCREASED CRP LEVEL IS INTERRELATED WITH CLINICAL AND SEROLOGICAL PHENOTYPES OF SYSTEMIC SCLERODERMA AND ASSOCIATED WITH CRP RS1205 GENE POLYMORPHISM

M. Krylov[1], L. Ananieva[1], O. Koneva[1], M. Starovoytova[1], O. Desinova[1], O. Ovsaynnikova[1], E. Aleksandrova[1], A. Novikov[1], I. Guseva[1], N. Konovalova[2], D. Varlamov[2]. *[1]V. A. Nasonova Research Institute of Rheumatology; [2]All-Russian Research Institute of Agricultural Biotechnology, Moscow, Russian Federation*

Background: Recent studies report on increased serum levels of C-reactive protein (CRP) in systemic scleroderma (SSc) pts.
Objectives: The current study was aimed at identifying potential correlations between CRP levels, immunologic SSc phenotypes and *CRP* rs1205 gene polymorphism in the Russian cohort.
Methods: 92 SSc pts were enrolled in the study. Mean age (± SD) was 49,4±12,6 years, mean (± SD) SSc duration was 11,1±9,0 years, increased CRP levels >5 mg/l were documented in 43% pts. CRP levels were analyzed in the following subgroups: with limited (lcSSc) and diffuse (dcSSC) types, with SSc duration <3 years >3, with or without interstitial lung disease (ILD+) and (ILD-), as well as in subgroups with positive antibody titers to DNA topoisomerase I (ATA+) and antibody to centromeres (ACA+). CRP concentrations were measured with highly sensitive immunoturbidimertry method. Allele-specific real time PCR was used to study *CRP* rs1205 gene polymorphism.
Results: Mean CRP (± SD) level was significantly higher in dcSSc vs lcSSc (11,9±15,5 mg/l; vs 4,7±7,4 mg/l, respectively, *p*=0,006). Pts with disease duration <3 years had higher mean CRP levels as compared to pts with SSc duration >3 years, although the difference was not significant. In pts with disease duration >3 years mean CRP levels were significantly higher among subjects with dcSSc than lcSSc (11,0±15,5 mg/l vs 4,8±7,7 mg/l, respectively, *p*=0,027). Mean CRP level was higher in (ATA+) pts than in (ATA-) pts (11,0±15,4 mg/l vs 5,5±13,7 mg/l, respectively, *p*=0,032). No statistical difference in CRP levels was found between (ILD+) and (ILD-) pts, as well as between (ACA+) and (ACA-) pts.
Carriers of rs1205 CC genotype had higher CRP levels than carriers of rs1205 T allele,*p*=0,087). In pts with SSc duration >3 years and carriers of rs1205 CC genotype mean CRP level was significantly higher than in T-allele carriers (12,0±17,4 mg/l vs 5,4±7,4 mg/l, respectively, *p*=0,021). Similar trends for CRP levels depending on genotypes were established among (ATA+) pts (16,9±20,1 mg/l and 7,3±10,5 mg/l, respectively, *p*=0,031).
Conclusions: Increased CRP levels were found almost in 50% of Russian SSc pts. Higher CRP levels were associated with specific clinical and immunological SSc parameters and *CRP* rs1205 CC genotype, signifying unfavorable prognosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2676

FRI0404 THE EFFECT OF A HOME-BASED OROFACIAL EXERCISE PROGRAM ON ORAL APERTURE OF SYSTEMIC SCLEROSIS PATIENTS

N. Cuzdan Coskun[1], I. Turk[2], V. Ciftci[3], D. Aslan Tas[2], M.C. Dogan[3], I. Unal[4]. *[1]Department of Physical Therapy and Rehabilitation, Division of Rheumatology; [2]Department of Internal Medicine, Division of Rheumatology, Cukurova University Faculty of Medicine; [3]Department of Pediatric Dentistry, Cukurova University Faculty of Dentistry; [4]Department of Biostatistics, Cukurova University Faculty of Medicine, Adana, Turkey*

Background: Microstomia is one of the major problems that causes multiple dysfunctions and affects quality of life in systemic sclerosis (SSc).[1]
Objectives: The purpose of this study is to evaluate the effect of a home-based orofacial exercise program on the oral aperture (OA) of SSc patients.
Methods: SSc patients who fulfilled the *American College of Rheumatology* (ACR) 2013 criteria with an OA of <40mm were included in the study. Patients were randomly divided into two groups. Group 1 was given oral augmentation and mouth stretching exercises with combination of strengthening exercise to masseter muscle twice a day for one month in addition to oral hygiene care advices; followed by no activity but oral hygiene care for the next four weeks. Group 2 received oral hygiene care advices for the first one month followed by the same orofacial exercise program twice a day for the next four weeks. Patients' OA was measured by a dentist at baseline, 1-month, and 2-months.
Results: A total of 52 patients were included in the study. Twenty-seven patients were assigned to group 1 (mean age 53.70±9.79 years; 96.3% female) and twenty-five patients to group 2 (mean age 50.68±11.93 years; 96.0% female). A total of 28 patients (group 1, n=18; group 2, n=10) completed the study. After four weeks period, OA increased in group 1 ($P<0.001$), whereas no change was observed in group 2 ($P=0.906$). At the end of 2 months the intragroup analysis showed no additional increase in group 1 ($P=0.283$), but a statistically significant increase in group 2, regarding the measurement of OA ($P=0.010$). We didn't find any statistically significant difference between OA measurements of the groups 1 and 2 at the end of the trial ($P=0.830$).
Conclusions: The results of this pilot study suggested that an intervention of combined home-based orofacial exercise program might improve oral aperture of SSc patients. Future studies with longer follow-up period and higher number of patients are needed to observe the long-term benefits of the presented home-based exercise program.
References:
[1] Frantz C, Avouac J, Distler O, Amrouche F, Godard D, Kennedy AT, Connolly K, Varga J, Matucci-Cerinic M, Allanore Y. Impaired quality of life in systemic sclerosis and patient perception of the disease: A large international survey. Semin Arthritis Rheum. 2016 Aug;46(1):115–23.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6274

FRI0405 PREVALENCE, CLINICAL CORRELATES AND POSSIBLE CAUSES OF NEUROPATHIC PAIN IN PATIENTS WITH SYSTEMIC SCLEROSIS

P. Ostojic[1], S. Knezevic-Apostolski[2], N. Djurovic[3], B. Stojic[3], D. Bartolovic[4], K. Jankovic[5]. *[1]Institute of Rheumatology, School of Medicine, University of Belgrade; [2]Neurological Outpatient Clinic "Apostolski"; [3]Institute of Rheumatology; [4]Clinic for Medical Biochemistry, Clinical Center of Serbia; [5]School of Medicine, University of Belgrade, Belgrade, Serbia*

Objectives: To assess prevalence, possible causes and clinical correlates of neuropathic pain (NP) in patients with systemic sclerosis (SSc).
Methods: In 42 patients with SSc, presence of NP was assessed using the PainDetect questionnaire and subsequently confirmed by neurological evaluation. Patients with previously diagnosed neurological disorders and diabetes were excluded. Relationship between NP and disease status, symptoms of depression and quality of life was estimated. Index of disease status (IDS) was assessed using the Scleroderma Assessment Questionnaire (SAQ), occurrence of depressive symptoms by the Beck's Depression Inventory (BDI), whilst quality of life was evaluated using the EQ-5D index. In order to evaluate possible causes of NP in SSc, all patients with NP, except one (who did not agree with further assessments) underwent detailed neurological and electroneurography (ENG) examination, as well as $HgbA_1C$ and vitamin B12 level testing.
Results: 12/42 (28.6%) of patients were found to have NP. Patients with and without NP were similar in age and disease duration. NP was found more frequently in patients with lcSSc (32.3%), than in dcSSc (18.2%), as well as in patients with ACA (46.7%) compared to patients with ATA (17.6%) and both ACA and ATA negative patients (20%), but the differences were not statistically significant. Patients with NP had significantly higher mean values of IDS (1.28 vs 0.66) and BDI (18.3 vs 9.9) than patients without NP ($p<0.01$). Mean value of the EQ-5D index was significantly lower in patients with NP (0.39 vs 0.79, $p<0.01$). Patients with NP had significantly higher mean value of Index of vascular status, then patients without NP (2.26 vs 1.36, p=0.02). $HgbA_1C$ and vitamin B12 levels were normal in all SSc patients with NP. Clinical signs of polyneuropathy were noticed in 10 patients by neurological evaluation. Typical symmetric glove-and-stocking hyperesthesia was found in 10/11 (90.9%) of SSc patients with NP, along with symmetric hyporeflexia in 6/11 (54.5%) patients on lower, and 7/11 (63.6%)

on upper extremities. None of patients had allodynia, but impaired vibratory sensibility was found in all patients with NP. Clinical signs of radiculopathy were present in 6 patients. Hypoesthesia was registered in typical dermatomes in 6/11 (54.5%) of patients, with asymmetric hyporeflexia in 2/11 (18.1%) patients on lower, and none of patients on upper extremities. Despite the fact that almost every patient had symptoms and signs suggesting polyneuropathy, in only four of them demyelinating polyneuropathy was detected by ENG.
Conclusions: NP is common in patients with SSc. Presence of NP is associated with more severe SSc, symptoms of depression and worse quality of life. Almost all SSc patients (90.9%) with NP have typical symptoms and signs for polyneuropathy. However, in only few of them polyneuropathy could be detected by ENG. This finding suggests that pure small-fiber polyneuropathy, which is not detectable by ENG, may be the cause of NP in most of patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4492

FRI0406 MORTALITY PROFILE IN SYSTEMIC SCLEROSIS: A LARGE RETROSPECTIVE POPULATION-BASED STUDY FROM BRAZIL

R.P. Rezende[1], R. Gismondi[1], H. Maleh[1], M.L. Rosa[2], R. Ramos[1], L.O. Mocarzel[1]. *[1]Clinical Medicine; [2]Epidemiology and biostatistics, Universidade Federal Fluminense, Niterói-RJ, Brazil*

Background: Systemic sclerosis (SSc) is an uncommon autoimmune multisystem disease associated with reduced life expectancy compared with the general population.[1] In order to prolong survival of this patient population, clear information on the most important death-related conditions is undoubtedly necessary. No mortality data in SSc, however, are available from Latin America, as well as few large series studies have looked at the mortality profile in SSc.
Objectives: We aimed to describe the causes of death in SSc occurred in the state of Rio de Janeiro, Brazil, from 2006–2015, and also to compare the data gathered with the general population mortality.
Methods: All death certificates issued in the state of Rio de Janeiro, Brazil, from 2006–2015 were screened for the code attributed to SSc according to the tenth revision of the International Classification of Diseases (ICD-10), either as an underlying (UD) cause of death (also referred to as basic cause of death) or a non-underlying (non-UD) cause. In addition to compiling the causes of death in both settings, we calculated the non-adjusted as well as the age bracket-adjusted (age at death $<$50 years and $\geq$50 years) mortality ratio against the general population for each cause of death when SSc was listed as a non-UD cause.
Results: Of 1.294.491 fatalities recorded over the study period, ICD-10 code for SSc was listed on 374 (0.02%) death certificates, being a basic cause of death on 223 occasions and a non-UD cause on 151 occasions. The overall mean (SD) age at death in SSc was 58.7 (15.6) years, with men (n=56) having an earlier mean age at death than women (n=318) [53.5 vs 59.6 years, respectively; p=0.004]. For SSc as a basic cause of death, the main non-UD causes were respiratory system diseases (61.4%), in particular pneumonia, followed by septicemia (37.6%), diseases of the circulatory system (34.9%), and renal failure (9.4%). There were no significant differences between the genders for each cause of death. The mean age at death was significantly lower among men vs women for diseases of the respiratory system, respiratory failure, certain infectious and parasitic diseases, and septicemia. For SSc as a non-UD cause of death, the major conditions leading to death were circulatory system diseases (39%), in particular pulmonary arterial hypertension (PAH; 13.2%), followed by certain infections and parasitic diseases (11.9%), malignant neoplasms (10.5%) and diseases of the digestive system (9.9%). Compared with the overall population, patients with SSc had an excess of death (odds ratio [OR] $>$1) due to PAH (OR 138.94), septicemia (OR 1.92), gastrointestinal hemorrhage (OR 2.40), other systemic connective tissue diseases (OR 24.78) and pulmonary fibrosis (OR 11.05), as well as due to heart failure (OR 6.40) for deaths occurred before age 50.
Conclusions: We have shown large data on the mortality profile of patients with SSc, the first from Latin America. Of note, infections and cardiorespiratory diseases had a strong impact on mortality, as evidenced by previous publications.[1] Taking all into account, these data support an increased vigilance for infections, as well as the need to implement effective measures to control modifiable cardiovascular risk factors, including screening for PAH.
References:
[1] Rubio-Rivas M, et al. Semin Arthritis Rheum 2014; 44:208–219.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5366

FRI0407 MACROVASCULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS: IS THERE A RELATIONSHIP WITH MICROVASCULAR PERIPHERAL BLOOD FLOW?

S. Paolino[1], B.M. Colombo[2], B. Ruaro[1], E. Gotelli[1], A. Sulli[1], M. Ghio[1], C. Pizzorni[1], E. Alessandri[1], M. Patanè[1], M. Cutolo[1]. *[1]Department of Internal Medicine, University of Genova, IRCCS AOU San Martino, Genoa, Italy, Research Laboratory and Academic Division of Clinical Rheumatology; [2]IRCCS AOU San Martino, Genoa, Italy, Genoa, Italy*

Background: Raynaud's phenomenon and digital ulcers are common clinical skin manifestations of the microvascular dysfunction in systemic sclerosis (SSc). Although microvascular and macrovascular abnormalities frequently coexist in disease such as diabetes mellitus and other vascular diseases, the possible association between microvascular failure and macrovasculopathy in SSc patients has not been deeply investigated (1).
Objectives: The aim of the study was to estimate in SSc patients the macrovascular function by measuring of the Intima-Media Thickness (IMT) of high-caliber and periferic small-caliber arteries, and to evaluate the possible correlation with microvascular blood perfusion (BP) assessed by Laser Speckle Contrast Analysis (LASCA).
Methods: Twenty-nine female SSc patients (mean age 65.7±12.07 SD years, mean disease duration 97.3±68.01 SD months) were enrolled after informed consent. Carotid IMT was evaluated through B-mode US imaging (Esaote, Genoa) using transducer 18 MHz on both right and left common carotid arteries (CCA) as well as ulnar (UA) and radial arteries (RadA). Therefore, an average IMT score was obtained for any evaluated site. Peripheral BP was assessed by LASCA (Perimed-Sweden) at the level of fingertips, periungueal areas, dorsum and palm of both hands, and face. The BP values were reported as perfusion units (PU) (2). In addition nailfold videocapillaroscopy (NVC) in order to assess the microvascular morphological status was done by nailfold video capillaroscopy (NVC) considering the different progressive SSc patterns and the microangiopathy evolution score (MES) (3–4).
Results: A positive correlation was observed between CCA IMT and age (p=0.004) and disease duration (p=0.02). On the other hand, no significant correlations were observed between IMT of periferic small-caliber arteries (UA and RadA) and age or disease duration. Positive correlations were found between microvascular damage, as assessed by MES and IMT at the level of periferic small-caliber arteries.No significant correlation was observed between macrovascular involvement of high-caliber arteries and peripheral BP as assessed by LASCA. However, at the peripheral site a correlation was observed between RadA IMT and palm (p=0.05), periungueal (p=0.04) and dorsum of hand BP (p=0.0006), as assessed by LASCA. UA IMT showed a correlation limited to the dorsum of the hand (p=0.003).
Conclusions: Significant correlations seem to exist between increased IMT of periferic small-caliber arteries (macrocirculation) and altered peripheral BP (LASCA) at the level of hand microvessels (microcirculation) in SSc patients. These results were found strength by a further correlation with the microvascular damage (MES).
References:
[1] Hettema Me et al. Rheumatology (Oxford) 2008;47:578–83.
[2] Ruaro B et al. Ann Rheum Dis 2014;73:1181–5.
[3] Sulli A, et al. Ann Rheum Dis 2008;67:885–7.
[4] Cutolo et al. J Rheumatol 2000; 27;155.60.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6523

FRI0408 NEOPTERIN AS A SEROLOGICAL MARKER OF DISEASE ACTIVITY IN PATIENTS WITH ANTI-MELANOMA DIFFERENTIATION-ASSOCIATED GENE 5 ANTIBODY POSITIVE CLINICALLY AMYOPATHIC DERMATOMYOSITIS

S. Tsunoda, A. Nishioka, T. Abe, M. Kitano, K. Matsui, H. Sano. *Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, Japan*

Background: Anti-melanoma differentiation-associated gene 5 (MDA5) antibody in clinically amyopathic dermatomyositis (CADM) is associated with rapidly progressive interstitial lung disease (RPILD). RPILD is a rare disorder with a bad outcome, and therefore the intensive treatment with combinational immunosuppressive drugs in addition to steroid need to be initiated. However until now, good serological markers to evaluate disease activity in CADM have not been established. Activated alveolar macrophage is one of the possible candidates worsening the condition of RPILD.
Objectives: To investigate new serological markers of disease activity in anti-MDA5 antibody positive CADM for therapeutic indication.
Methods: Thirteen anti-MDA5 antibody positive CADM patients were enrolled. We serially measured serum anti-MDA5 antibody, and neopterin and IL-18 as markers of activated macrophage by serum enzyme-linked immunosorbent assay. We tracked them at three points in each patients: before treatment, soon after a series of intravenous cyclophosphamide pulse therapy (about 3months later after onset) and the remission status (about one year later after onset).
Results: Four patients died soon after the initial treatment because of the deterioration of RPILD. At onset of the disease, the levels of serum anti-MDA5 antibody and neopterin were extremely high (169.75±24.3 index and 27.6±24.1 nmol/l) in all patients. However serum IL-18 level was almost normal (479.3±301.4 pg/ml). Among the 9 surviving patients, it took about one year for anti-MDA5 antibody level to decrease to the normal range. On the other hand, neopterin level decreased quickly after the initial treatment. The level of anti-MDA5 antibody transitioned from 169.75±24.3 index to 93.1±50.1 index, and then to 44.8±45.4 index (P=0.003). Neopterin level transitioned from 27.6±24.1 nmol/l to 9.1±6.5 nmol/l, and then to 6.4±5.0 nmol/l (P=0.006). IL-18 level transitioned from 479.3±301.4 pg/ml to 246.0±175.8 pg/ml, and then to 233.3±180.1 pg/ml (P=0.02). The level of anti-MDA5 didn't correlate with the level of ferritin (r=0.28), neopterin (r=0.16), IL-18 (r=0.06) and soluble IL-2 receptor (r=0.27), but the level

of neopterin was well correlated with the level of ferritin (r=0.95), IL-18 (r=0.77) and soluble IL-2 receptor (r=0.75).
Conclusions: Anti-MDA5 antibody titer is useful if the patients could reach and maintain the remission or not. Serum neopterin level is useful to predict the clinical status at present for therapeutic indication.
References:
[1] Matsushita, et al. Br J Dermatol. 2016 Jul 25. doi: 10.1111/bjd.14882.
[2] Xu Y, et al. Clin Rheumatol. 2016, 35: 113–6.
[3] Enomoto Y et al. Arthritis Res Ther. 2017,19:9. doi:10.1186/s13075-016-1214-8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4880

FRI0409 OSTEONECROSIS OF THE LUNATE BONE ASSOCIATED TO SYSTEMIC SCLEROSIS

M. Llop Vilaltella, S. Zegarra Mondragón, W.A.A. Sifuentes Giraldo, C. de la Puente Bujidos, M. Vázquez Díaz. *Rheumatology, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Osteonecrosis of the lunate bone (OLB), also known as Kienböck's disease, is a rare disorder that has been recently reported in several patients with systemic sclerosis (SSc)[1], but still it is not clear if this is only a coincidence of 2 rare didsorders or whether OLB is a potentially under-recognized manifestation of SSc.
Objectives: To describe the clinical features of patients with SSc seen in a Spanish tertiary care center, who develop OLB.
Methods: We performed a retrospective observational study that included patients followed in our center between January 2010 and December 2015. Demographic data, clinical and laboratory features, risk factors for osteonecrosis, imaging, treatment and outcome were collected.
Results: A total of 115 SSc patients were identified and 4 of them (3.47%) developed OLB. Mean age of these patients was 59.5 (range: 52–73), being all women. 2 cases were limited cutaneos SSc (lcSSc) and 2 cutaneous diffuse SSc. 3 cases showed anticentromere antibodies and 1 anti-topoisomerase I antibodies, but none presented anticardiolipin antibodies nor had previous thrombotic events. Mean disease duration was 13.5 years (range: 7–17). One patient was ex-smoker, but none had alcohol consumption, and one case was hypertensive. All patients had vascular manifestations (severe Raynaud phenomenon, digital ulcers in treatment with endothelin antagonists and perfusion of iv prostaglandins, and one case had critical digital ischemia); all the patients showed calcinosis in the upper limbs, and they also had joint involvement (50%), gastrointestinal (100%), and pulmonary (50%) manifestations. History of rolonged corticosteroid therapy at low doses (prednisone 5–10 mg/day) was present in all cases and was discontinued one year before the onset of osteonecrosis in one case. OLB was unilateral right in 3 cases and bilateral in one case. The patients presented with clinical pain and/or swelling in the affected wrist in the months prior to diagnosis of OLB, which was evidenced by simple radiography, MRI and bone scintigraphy. One of the cases also showed extensive synovitis in the affected wrist and another one developed collapse of the lunate bone with displaced fragment and edema. Treatment was surgical in 25% of the cases (proximal carpectomy), and conservativein in the rest. Among the total SSc population studied there was another case of lcSSc presenting osteonecrosis of the left tarsal scaphoid bone.
Conclusions: A total of 15 cases of OLB associated to SSc have been reported to date, so it could be an underestimated disease-associated feature of SSc. It has been suggested that its etiology is linked to SSc-related vasculopathy and all our cases had evidence of severe vasculopathy. The location and vascularization of the lunate bone should be taken into account, since no case developed osteonecrosis in other common locations despite corticotherapy, and complete occlusion of the distal ulnar artery has been reported in 3 cases of the literature. The presence of pain, with or without wrist inflammation in SSc patients should make us consider OLB, which is probably more frequent than expected, especially when there is evidence of severe SSc-related vasculopathy.
References:
[1] Frerix M, et al. Is osteonecrosis of the lunate bone an underestimated feature of systemic sclerosis? A case series of nine patients and review of literature. Semin Arthritis Rheum. 2016;45:446–54.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5965

FRI0410 PREDICTORS OF MORBIDITY AND MORTALITY IN PATIENTS WITH EARLY SYSTEMIC SCLEROSIS: LONG-TERM FOLLOW-UP FROM A SINGLE CENTRE INCEPTION COHORT STUDY

S. Panopoulos, V.-K. Bournia, G. Konstantonis, K. Fragiadiaki, P.P. Sfikakis, M.G. Tektonidou. *First Department of Propedeutic and Internal Medicine and Joint Academic Rheumatology Program, National and Kapodistrian University, Medical School, Athens, Greece*

Background: Several studies have investigated the predictors of morbidity and mortality in Systemic sclerosis (SSc). However long-term follow-up data from inception cohorts of early SSc patients are limited.
Objectives: To identify predictors of morbidity and mortality in a single centre inception cohort of early SSc patients at long-term follow-up.
Methods: Our inception cohort comprised SSc patients who fulfilled the American College of Rheumatology criteria, were recruited within 12 months of disease onset and followed prospectively for at least 3 years. Clinical manifestations, laboratory and lung function tests were recorded for each patient at baseline and at 3rd and 6th years of follow up. Multivariate regression analysis and Cox proportional hazard models were used to identify predictors (clinical manifestations, laboratory and lung function tests at baseline) of morbidity and mortality in SSc, respectively.
Results: A total of 114 patients (96 female, mean age at diagnosis 48.1±13.5 years, 53 diffuse SSc subtype) were included in the study, from January 1997 to December 2012. All patients were followed for at least 3 years and 84 patients for at least 6 years. Twenty (17.5%) of 114 patients died during a mean follow up of 101.8±48.5 months. In multivariate regression analysis predictors for major SSc outcomes at 6 years were: diffuse subtype (OR: 6.2, p=0.015), anti-scl-70 positivity (OR: 3.9, p=0.05), esophageal involvement (OR: 6.5, p=0.017) and digital ulcers (OR: 8.6, p=0.003) at baseline for the development of pulmonary fibrosis (PF). The presence of digital ulcers at baseline was a predictor for the development of arrhythmias (OR: 3.7, p=0.05) and the presence of arrhythmias at baseline for the development of pulmonary hypertension (PH) (OR: 5.4, p=0.039). Cox proportional hazard models multivariate analysis revealed that independent predictors of mortality were: male gender (HR: 3.3, p=0.023), diffuse type (HR: 8.7, p=0.004), PF at baseline (HR: 2.7, p=0.05), PH based on echocardiography at baseline (HR: 12.7, p=0.001) FVC <80% (HR: 2.74, p=0.042) and DLCO <60% of predicted value at baseline (HR: 2.97, p=0.019).
Conclusions:
Results from long-term follow-up data from a single centre inception cohort indicate that diffuse SSc subtype, anti-Scl-70 positivity, esophageal involvement and digital ulcers at baseline are independent predictors for the development of PF. Male gender, diffuse subtype, PF, PH and decreased FVC and DLCO at baseline are prognostic factors of mortality.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6656

FRI0411 COADMINISTRATION OF BOSENTAN HAS NO EFFECT ON THE PHARMACOKINETICS OF NINTEDANIB

S. Wind[1], G. Simons[1], J. Bertulis[1], C. Coeck[2]. *[1]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany; [2]SCS Boehringer Ingelheim Comm.V., Brussels, Belgium*

Background: Nintedanib is a potent intracellular inhibitor of tyrosine kinases that has been approved for the treatment of idiopathic pulmonary fibrosis and is being investigated as a treatment for interstitial lung disease associated with systemic sclerosis (SSc-ILD). Bosentan is a dual endothelin receptor antagonist used in the treatment of pulmonary arterial hypertension, which is a common comorbidity of SSc-ILD.
Objectives: To ascertain the effect of bosentan on the pharmacokinetics of nintedanib.
Methods: In an open-label, single-centre study, healthy male subjects aged ≥18 and ≤55 years with a body mass index (BMI) ≥18.5 and ≤29.9 kg/m^2 received a single dose of nintedanib 150 mg alone (period 1) followed by bosentan 125 mg twice daily (bid) for 8 days (bosentan loading dose phase on days 1–6) with a single dose of nintedanib 150 mg on day 7 (period 2). The primary endpoints were the maximum plasma concentration (C_{max}) of nintedanib and the area under the plasma concentration-time curve from time 0 to the last quantifiable concentration ($AUC_{0\text{-}tz}$) of nintedanib. The secondary endpoint was the AUC from time 0 extrapolated to infinity ($AUC_{0-\infty}$) for nintedanib.
Results: Thirteen subjects (12 White; mean [SD] age 35.0 [9.8] years and BMI 24.5 [2.5] kg/m^2) were treated. All subjects completed the planned observation period. Based on C_{max}, $AUC_{0\text{-}tz}$ and $AUC_{0-\infty}$, exposure to nintedanib was similar after a single dose of nintedanib given alone or in combination with multiple doses of bosentan 125 mg bid (Table). Adverse events were reported in 4 subjects (30.8%) on nintedanib alone (period 1), 4 subjects (30.8%) on bosentan 125 mg bid (days 1–6 of period 2) and 2 subjects (15.4%) after administration of bosentan with nintedanib (days 7 and 8 of period 2). All adverse events were mild in intensity.

	Nintedanib 150 mg alone	Nintedanib 150 mg coadministered with multiple doses of bosentan 125 mg bid	Adjusted geometric mean ratio (90% CI)
C_{max} (ng/mL)	21.9	22.7	103.4 (86.1, 124.0)
$AUC_{0\text{-}tz}$ (ng·h/mL)	194.9	192.6	98.9 (91.3, 107.0)
$AUC_{0-\infty}$ (ng·h/mL)	204.3	208.3	102.0 (94.9, 109.6)

Conclusions: Coadministration of bosentan 125 mg bid had no effect on the pharmacokinetics of a single dose of nintedanib 150 mg.

Disclosure of Interest: S. Wind Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG, G. Simons Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG, J. Bertulis Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG, C. Coeck Employee of: Boehringer Ingelheim Pharma GmbH & Co. KG
DOI: 10.1136/annrheumdis-2017-eular.5849

FRI0412 THE POSITIVE EFFECT OF RITUXIMAB IN PULMONARY FIBROSIS OF SYSTEMIC SCLEROSIS

P. Kiryttopoulos[1], T. Michailidis[1], E. Papchianou[1], M. Charalampidis[2], P. Dimitriadis[3], A. Agorastos[4]. [1]*Department of Internal Medicine, General Hospital of Veria, Veria;* [2]*Gastroenterology Department, Theageneio Hospital of Thessaloniki, Thessaloniki;* [3]*Health Center of Alexandria, Alexandria, Greece;* [4]*Oncology Department, St. Thomas Hospital, London, United Kingdom*

Background: Pulmonary fibrosis is one of the gravest manifestations of Systemic Sclerosis (SSc) and conventional DMARDs therapy has not shown any particular positive effect.
Objectives: Our goal was to see whether the elimination pf B - lymphocytes through use of anti – CD20 Mab, Rituximab (RTX) would offer to the improvement of the pulmonary function of SSc patients.
Methods: We studied 23 SSc patients with pulmonary fibrosis, who received treatment with RTX (n=12) or DMARDs treatment (n=11) for 1 to 3 years (1,9 years). Conventional therapy included azathioprine (n=4), mycophenalate (n=6) and methotrexate (n=2). RTX – treated patients were recorded with FVC improvement in the first year of treatment (FVC 81,3 +/- 12,6 vs FVC 87,4 +/- 11,3 out on the onset of the study and at the first year respectively, p=0,02) when on the other hand DMARDs treated patients didn't show any FVC improvement at all.
Results: All RTX – treated patients did not present any lung HRCT deterioration imaging, in contrast to DMARDs – treated patients who were also submitted to lung HRCT each year of the study, all showing signs of CT imaging deterioration. Similar findings, as far as FVC was concerned, were recorded at the 3rd year of the study (RTX patients, n=6 and DMARDs patients, n=11). 3rd year RTX FVC was 92,6 +/-13,2 vs 80,7 +/-11,8 at the onset of the study, p=0,04 when DMARDs treated patients were all presented with worst 3rd year FVC compared to their primary FVC, p<0,01.
Conclusions: Our small cohort of SSc patients with pulmonary fibrosis shows that it is possible that rituximab may be proven helpful to at least prevent the deterioration of the interstitial pulmonary fibrosis of Systemic Sclerosis. The pathophysiology of this particular fibrosis and the possible molecular role of B-lymphocytes in the inversion of this procedure need yet to be furtherly explored.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6398

FRI0413 ACUTE EFFECT OF ILOPROST ON PERIPHERAL CIRCULATION AS ASSESSED BY VIDEOCAPILLAROSCOPY AND 22-MHZ POWER DOPPLER ULTRASONOGRAPHY

T. Schioppo[1,2], A. Orenti[1,3], P. Boracchi[1,3], O. De Lucia[2], A. Murgo[2], P.L. Meroni[1,2], F. Ingegnoli[1,2] on behalf of OPERA study group. [1]*Università degli Studi di Milano;* [2]*ASST Pini-CTO;* [3]*Lab of Medical Statistics, Epidemiology and Biometry GA Maccacaro, Milan, Italy*

Background: Vascular involvement is a hallmark of systemic sclerosis (SSc) and it is responsible for some of the most common complications of the disease such as Raynaud's phenomenon (Rp), digital ulcers (DUs) and pulmonary arterial hypertension. I.V. iloprost (ILO), a prostacyclin analogue, has been shown to be effective in reducing Rp severity, DUs healing and preventing [1].
Objectives: To assess the acute effect of ILO on acral circulation as assessed by nailfold videocapillaroscopy (NVC) and 22-MHz Power Doppler ultrasound (PDUS).
Methods: 44 SSc consecutive patients fulfilling the 2013 EULAR classification criteria were enrolled. Each patient was evaluated before and immediately after I.V. ILO administration (0.5–2.0 ng/Kg/min for 6 consecutive hours). PDUS was performed at the 3rd and 4th finger of the dominant hand after exclusion of ulnar artery occlusion (UAO). In case of UAO non-dominant hand was examined. Ultrasound investigation was performed with Esaote MyLab 70 XVG by means of linear array transducer (10–22 MHz). Power Doppler settings were standardized (Doppler frequency 14.3 MHz, Gain 55%, PRF 750 Hz). PDUS measurements included sagittal scan of nailbed and fingertip qualitatively graded from 1 (no signal) to 4 (marked hyperemia) [2], and resistivity index (RI) of ulnar and radial proper digital arteries. Capillary width (sum of capillary width/mm) was calculated by NVC with magnification 200X performed on two images of the same digits examined by PDUS.
Results: The study population included 44 SSc patients, 40 (90.9%) women, 35 (79.5%) limited cutaneous SSc, median age 60.2 years old and median disease duration 8 years. 19 (43.2%) had history of DUs, among them 15 had experienced more than one DUs and 1 had active DU at the moment of evaluation.
Semiquantitative perfusion score of sagittal scan of nailbed and fingertip pre- and post-therapy are shown in Table 1.
Changes in RI and capillary width pre- and post-infusion are reported in Table 2.
Conclusions: A statistically significant post-infusion rise in RI, fingertip and nailbed PDUS grade were found. Capillary width was also increased, but it was not statistically significant. As such, these novel results indicate that ILO, alongside its clinical effect, is able to enhance vascularization even at the most peripheral levels.

Table 1

	Pre-infusion		Post-infusion		OR (95% CI)
	%	Cumulate %	%	Cumulate %	
Fingertip PDUS					4.21 (2.12–8.35)
Grade 1	29.55	29.55	14.77	14.77	p-value<0.001
Grade 2	22.73	52.28	15.91	30.68	
Grade 3	12.50	64.78	12.50	43.18	
Grade 4	35.23	100	56.82	100	
Nailbed PDUS					8.96 (4.15–19.32)
Grade 1	17.05	17.05	6.82	6.82	p-value<0.001
Grade 2	34.09	51.14	13.64	20.46	
Grade 3	18.18	69.32	14.77	35.23	
Grade 4	30.68	100	64.77	100	

Table 2

	Pre-infusion	Post-infusion	Mean difference (95% CI)
Resistivity index	0.773	0.794	0.021 (0.005, 0.037) p-value=0.0122
Capillary width	247.5	257.9	12.321 (-2.528, 27.171) p-value=0.1077

References:
[1] Pope J et al. Cochrane Database Syst Rev. 2000;(2):CD000953.
[2] Newman JS et al. Radiology. 1996,198:582–584.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3849

FRI0414 CAN ECHOCARDIOGRAPHY REPLACE FOLLOW-UP CARDIAC CATHETERIZATION IN RE-EVALUATION OF PULMONARY ARTERIAL HYPERTENSION? A LONGITUDINAL SINGLE-CENTER STUDY OF 30 CONNECTIVE TISSUE DISEASE PATIENTS

V.-K. Bournia[1], I. Tsangaris[2], L. Rallidis[2], D. Konstantonis[2], A. Anthi[2], S. Orfanos[2], S. Panopoulos[1], P.P. Sfikakis[1]. [1]*First Department of Propedeutic Internal Medicine and Joined Rheumatology Program;* [2]*Pulmonary Hypertension Clinic, Attikon University General Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece*

Background: Transthoracic echocardiography (TTE) is well validated for initial assessment of connective tissue disease patients with suspected pulmonary arterial hypertension (PAH). However, in patients with PAH confirmed by the gold-standard method of right heart catheterization (RHC) the role of TTE in their follow-up is less known.
Objectives: To test the hypothesis that TTE can replace follow-up RHC in connective tissue disease-associated PAH.
Methods: This retrospective study included 30 consecutive patients with systemic sclerosis (n=24) and mixed connective tissue disease (n=6) (mean age±SD: 60±12 years, 87% women), in whom PAH was suggested by TTE and further confirmed by a baseline RHC [pulmonary artery systolic pressure (PASP): 56.8±19.1, range 25–90mmHg; pulmonary vascular resistance (PVR): 5.9±3.8, range 0.7–14.5 Wood units; cardiac output: 4.4±1.3, range 2–7.8 L/min). All 30 patients underwent a second RHC and TTE at follow-up, after 11±6 (range 4–29) months. Ten patients had a 3rd follow-up RHC and TTE 22±7 (range 15–37) months from baseline, thus producing in all 50 pairs of baseline and follow-up measurements. By considering follow-up RHC as the gold-standard, we examined whether clinically meaningful hemodynamic changes (i.e.>15% change from baseline) in either RHC-derived PASP or PVR could be predicted by the corresponding changes from baseline in follow-up TTE. RHC and TTE were always performed, each, by the same examiner.
Results: In 68% of comparisons between baseline and follow-up, the latter TTE measurements could safely replace RHC in terms of PASP estimation. Using Mc Nemars test we confirmed that the two methods did not differ significantly (Table 1). When in addition to changes in PASP, PVR changes were also considered, follow-up TTE could again safely replace the second RHC in 70% patient retests (Table 2). Of note, baseline hemodynamic values or TTE measurements did not differ between patients in whom TTE could replace RHC and those in whom the results of the two methods at follow-up were divergent.

Table 1. McNemars test comparing PASP estimated by repeat TTE to that measured by repeat RHC shows no difference between the two methods

Repeat TTE	Repeat RHC	
	Stable or improved PASP	Deteriorated PASP (>15%)
Stable or improved PASP	25	9
Deteriorated PASP (>15%)	7	9

P=NS (0.8).

Conclusions: In a study where operator-dependent methodological errors are limited we found that the majority of connective tissue disease patients with PAH

Table 2. McNemars test comparing PASP estimated by repeat TTE to hemodynamic parameters measured by repeat RHC when PVR is also considered

Repeat TTE	Repeat RHC	
	Stable or improved PASP and PVR	Deteriorated PASP or PVR (>15%) or PVR (>15%)
Stable or improved PASP	24	10
Deteriorated PASP (>15%)	5	11

P=NS (0.3).

can be safely monitored in the long-term by TTE. Further studies to help identify those patients at need for follow-up RHC are warranted.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2204

FRI0415 CAPILLAROSCOPIC ABNORMALITIES CORRELATE WITH ORGAN DAMAGE IN CHINESE PATIENTS WITH SYSTEMIC SCLEROSIS

W.Y. Yeung[1], C.C. Mok[2], K.L. Lee[1]. *[1]Department of Medicine, Pamela Youde Nethersole Eastern Hospital; [2]Department of Medicine, Tuen Mun Hospital, Hong Kong, -*

Objectives: To study the nailfold capillaroscopic patterns and microangiopathy evolution score (MES) and correlate with the severity of organ damage in Chinese patients with systemic sclerosis (SSc)
Methods: Patients who fulfilled the 2013 ACR criteria for SSc were studied. A full physical examination was performed. Blood was taken for SSc autoantibodies, along with a full lung function test and echocardiogram. The extent of skin involvement was assessed by the modified Rodnan skin score (mRSS). Organ damage of SSc was assessed by the Medsger disease severity scale. A Nailfold capillaroscopic examination was performed by a trained nurse blinded to the medical history of the patients. The following parameters were obtained: (1) capillaroscopy patterns (early, active and late); (2) Degree of enlarged capillaries, giant capillaries, capillary haemorrhages, capillary density, disorganization of vascular array and capillary ramification assessed by a semi-quantitative method; and (3) MES score (sum of capillary density, disorganization of vascular array and capillary ramification). Correlation among the capillaroscopic patterns, individual capillaroscopic parameters and the MES with organ damage was performed by the Spearman's rank correlation test.
Results: A total of 138 Chinese patients were studied (91.3% women; age 56.36±11.81 years). The median disease duration was 8.14±6.21 years. 39 (28.3%) patients had DcSSc and 99 (71.7%) had LcSSc. Anti-centromere, anti-Scl 70 and anti-RNA polymerase III antibodies were present in 28.6%, 28.5% and 5.6% of the patients respectively. Organ damage was present in all patients, most common being skin (84%), lung (79%), peripheral vascular (74%) and GI tract (46%). The median mRSS was 6 (IQR 2–12). A total of 27 patients (19.7%) had early SSc pattern on capillaroscopy, 40 (29.2%) had active pattern and 68 (49.6%) had late pattern. The median MES score was 3.02 (IQR 1.76–5.25). Patients with late SSc pattern on capillaroscopy had significantly longer disease duration and were more likely to have organ damage in the general, peripheral vascular and lung domains compared to those not having late SSc patterns. The total MES score correlated significantly with organ damage scores in the muscle (Rho 0.188; p=0.029), GI tract (Rho 0.169; p=0.048) and lung (Rho 0.265; p=0.006) domains. Regarding individual components of the MES score, capillary density correlated significantly with scores in the peripheral vascular (Rho 0.460; p<0.001), skin (Rho 0.343; p<0.001), joint/tendon (Rho 0.220; p=0.011), muscle (Rho 0.295; p=0.001), GI tract (Rho 0.188; p=0.028) and lung (Rho 0.238; p=0.015) damage domains. Enlarged capillaries correlated significantly with scores in the muscles (Rho -0.205; p=0.017) and lung (Rho -0.213; p=0.029) damage domains. Giant capillaries and microhaemorrhages correlated significantly with scores in the peripheral vascular (Rho 0.239; p=0.005 and Rho 0.228; p=0.007 respectively) damage domains. Disorganization of capillary array correlated significantly with scores in the lung (Rho 0.253; p=0.009) damage domain. Capillary ramifications correlated significantly with the scores in the kidney (Rho 0.171; p=0.048) damage domains.
Conclusions: In Chinese patients with SSc, capillaroscopic patterns and components of the microangiopathy evolution score were associated with severity of organ damage.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2020

FRI0416 CHARACTERISTICS AND CAPILLAROSCOPIC FINDINGS OF SYSTEMIC SCLEROSIS PATIENTS WITH SEVERE PERIPHERAL VASCULAR INVOLVEMENT RECEIVING SPECIFIC VASODILATOR TREATMENT

Y. Yalçınkaya, A.U. Ünal, Z. Ertürk, U. Gazel, S. Kaymaz, A. Aksoy, P. Atagündüz, N. İnanç, H. Direskeneli. *Department of Internal Medicine, Division of Rheumatology, Marmara University, School of Medicine, Istanbul, Turkey*

Background: Severity of peripheral vascular involvement (PVI)is known as an important determinig cause of morbidity in sytemic sclerosis (SSc). Different vasodilating agents have been found to reduce severity and contribute to healing of digital ulcers (DU)in SSc.
Objectives: We aimed to evaluate the characteristics and capillaroscopic patterns of the patients with severe PVI under different vasodilator therapeutic regimens.
Methods: The patients were grouped as "severe PVI" if score of PVI is ≥2 (PVT=2,digital pitting scars; PVT=3, digital tip ulcerations and PVT=4, digital gangrene; Medsger) and "non-severe PVI" if score of PVI is ≤1 (PVI=0,no Raynaud's; PVI=1, Raynaud's requiring vasodilators). We included patients with severe PVI who received cyclic iloprost and bosentan and/or sildenafil and compared to non-severe PVI. Nail fold video-capillaroscopy (NVC)was assessed qualitatively (Cutalo et al., early, active and late patterns).
Results: Severe PVI group more frequently had diffuse cutaneous form, contractures, lung disease, anti-Scl70 positivity and high acute phase response and exposed to immunosuppressives (table-1).

Table 1. Demographics and characteristics of SSc Patients

	Non-severe PVI n=32	Severe PVI group 2 n=22	p
Age (year)/female (%)	44±15/ 88%	48±12/ 87%	NS
Duration of Raynaud's/nonRaynaud's (year)	9±9/5±5	12±10/9±9	NS
Diffuse Cutaneous involvement	5 (16%)	10 (45%)	P=0,039
Anti-Scl70 (+)	7 (22%)	11 (50%)	P=0,024
Interstitial lung disease	7 (22%)	14 (64%)	P=0,001
Flexion contractures	3 (9%)	10 (45%)	P=0,008
Echo PAP>40 mmHg	2 (6%)	4 (18%)	NS
High acute phase response	12 (38%)	18 (82%)	P=0,002
FVC ≤80%/	3 (9%)	12 (55%)	P<0,001
DLCO ≤80%	10 (31%)	14 (64%)	P=0,011
Immunosuppressives- CYC (pulse)	5 (16%)	9 (41%)	P=0,018
– Azathioprin	8 (25%)	10 (46%)	P=0,030
– Mycphenolate mofetil	2 (6%)	10 (46%)	P<0,001
– Rituksimab	1 (3%)	6 (27%)	P=0,027
– Steroids (PRD<10 mg/d)	11 (34%)	17 (77%)	P=0,001

NS = not significant.

Scores of telangiectasia, skin, activity and severity were lower in non-severe group. NVC late pattern was frequent and early pattern was rare in severe PVI groups. Forty-one% (9/22) of patients received second oral agent for PVI. Monotherapy and combination groups had similar scores (table-2).

Table-2: Capillaroscopy Patterns among SSc groups

	non-severe PVI n=32	severe PVI n=22	Cyclic iloprost+ bosentan n=10	Cyclic iloprost+ bosentan+sildenafil n=9
NVC -normal	3(9%)	0	0	0
-early pattern	12(38%)**	2(9%)	1(10%)	1(11%)
-active pattern	10(31%)	2(9%)	2(20%)	0(0%)
-late pattern	8(25%)	18(82%)*	7(70%)	8(89%)
Telangiectasia score (Shah)	3,7±2,5**	6±3,7	4,8±3,2	7,1±4,2
Modified Rodnan skin score	5,8±5*	13,5±8,7	13,6±9,3	13,2±7,6
Activity score (Valentini)	0,9±0,9*	2,1±1,2	2,2±1,3	2,2±1,2
Severity score (Medsger)	3,5±1,7*	7,5±2,4	7,8±2,3	7,4±2,7

**p<0,001, **p<0,05 when severe and non-severe PVI compared*

Conclusions: NVC late pattern was frequent in severe PVI group with long disease duration, exposed to intensive immunosuppresives and received specific vasodilators for PVI. Disease activity and severity were higher in severe PVI group. One third of the severe group required oral combination therapy for PVI. Monotherapy and combination groups were similar in terms of severity. NVC is a useful method to monitor digital ischemia and severe organ involvement in SSc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3584

FRI0417 EXERCISE-INDUCED PULMONARY HYPERTENSION IN SYSTEMIC SCLEROSIS PATIENTS: TRANSCRIPTOME ANALYSIS OF PERIPHERAL BLOOD AT THE EARLY STAGE OF THE DISEASE

Y. Koyama[1], S. Fuke[2], Y. Sato[3], T. Higuchi[1]. *[1]Center for Autoimmune Diseases, Division of Rheumatology; [2]Division of Cardiology, Japanese Red Cross Okayama Hospital, Okayama; [3]DNA Chip Research Inc., Tokyo, Japan*

Background: Pulmonary arterial hypertension (PAH) is prominent as a vascular involvement in systemic sclerosis (SSc), which remains a leading cause of death in spite of current best treatments. As the pulmonary vascular disease (PVD) can be well compensated for, more than a half of the pulmonary circulation is impaired before early PAH is detected. Although recent studies focused on molecular basis of the PVD, the underlying mechanisms have not been fully elucidated, especially at the early stage of the disease.
Objectives: To detect the subclinical PVD, and to explore the changes in transcriptome of peripheral blood at the early stage of SSc associated PAH.
Methods: Total of 74 cases without PAH symptoms (NYHA I) with either Raynaud phenomenon (RP: n=61), skin sclerosis (n=43) or SSc-related autoantibody (anti-RNP: n=10, centromere: n=36, topoisomerase-1: n=2, RNA polymerase III: n=2) were enrolled. To detect the latent PAH, exercise Doppler echocardiography (DE) with Master's two-step stress was carried out. Systolic PAP (sPAP) was determined by maximum velocities of tricuspid regurgitation jets, and exercise induced pulmonary hypertension (exPH) group was segregated from normal response group (exN) with using the definition of a sPAP greater than 40 mm Hg during exercise, or a exercise increase in sPAP by greater than 20 mm

Hg[1)]. For transcriptome analysis, total RNAs from whole peripheral blood cells were extracted with using PAXgene miRNA kit. After constructing single-stranded, strand-specific libraries, multiplex sequencing was done. After quantifying the expressions of transcripts, differentially expressed genes (DEGs) between exPH and exN group were selected by paired T-test ($P<0.05$). And then, hierarchical clustering analysis and pathway enrichment analysis (PathVisio) were performed.
Results: There were no significant differences between exPH and exN group in the result of total skin score, serum BNP, tests of pulmonary function and thermography after 0℃-stress. Positive SSc-related autoantibody was a risk factor for exPH (odds ratio, 1.41); especially, positive anti-RNP seemed to be prominent (odds ratio, 3.21). Based on the 817 DEGs between exPH and exN group, the hierarchical clustering showed major 4 clusters, and one of them consisted of only cases in exPH group. When we focused on 117 genes reported to be directly implicated in the development of PAH[2)], it is noteworthy that 4 of them including TGF-β induced protein were differentially expressed. Pathway analysis of transcriptome revealed that 22 pathways, such as hypertrophy model, lung fibrosis and Wnt/B-catenin signaling, were differently enriched between exPH and exN group.
Conclusions: The paradigm of SSc-PAH management should ideally be aimed at detecting early PVD and starting treatment prior to fulfilling the criteria for PAH. Although detection of early PVD in SSc patients remains a major challenge, exercise DE seemed to be a good, non-invasive method for screening. It is noteworthy that expression changes in some of known PAH-related genes were detected from peripheral blood of exPH patients. It shows the possibility that the therapeutic intervention at early stage of the disease may alter the clinical course.
References:
[1] R. Naeije et al., Am. J Resp. & Critical Care Med. 187, 576–583 (2013). .
[2] Parikh VN et al., Circulation 125, 1520–1532 (2012).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3627

FRI0418 FACTORS ASSOCIATED WITH STEROID-FREE REMISSION IN PATIENTS WITH INFLAMMATORY MYOPATHIES. A RETROSPECTIVE ANALYSIS OF A SINGLE-CENTER COHORT

Y. Sato[1], K. Kobayashi[1], K. Minegishi[1], S. Ohno[1], H. Nakajima[2]. *[1]Center for Rheumatic Diseases, Yokohama City University Medical Center; [2]Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan*

Background: The inflammatory myopathies are a heterogeneous group of connective tissue diseases characterized by muscle weakness and inflammation. Corticosteroids are the standard main treatment for inflammatory myopathies. However, steroid therapy often causes a wide range of side effects. Although immunosuppressive drugs are used as steroid-sparing agents in an effort to prevent disease recurrence, the appropriate duration of steroid use remains unclear.
Objectives: We investigated whether steroid therapy can be safely withdrawn in patients with inflammatory myopathies followed in a single center.
Methods: We retrospectively reviewed clinical charts of 71 consecutive patients (age 51.9±15.7 y.o., female 69%) who met Bohan and Peter criteria for polymyositis (PM)/dermatomyositis (DM) and modified Sontheimer's criteria for clinically amyopathic dermatomyositis (ADM), respectively. Steroid free remission was defined as a 3-month consecutive period of no disease activity without corticosteroid treatment. Factors associated with steroid free remission were examined.
Results: Of 71 identified patients, 29 patients (40%) were DM, 15 patients (21%) were PM, 9 patients (13%) were overlap myositis, and 18 patients (25%) were ADM. Thirty-seven patients (52%) had muscle weakness, 5 patients (7%) had malignancies and 43 patients (61%) had signs of interstitial lung disease. With a mean follow-up of 6.6±5.0 years, 9 patients (13%) died during follow-up period. The remaining 62 patients were treated with corticosteroids alone or in combination with immunosuppressants. Steroid-free remission was achieved in 21 of 62 patients (34%) patients with a mean time to steroid withdrawal of 5.5±4.0 years. Six of 21 patients (29%) relapsed 1.7±1.7 years after steroid withdrawal. There were no differences in onset of age, disease duration, positive ANA, positive Anti Jo-1 antibodies, serum creatine kinase levels, maximum dose of corticosteroids, skin, joint and lung involvement between steroid-free group and non-steroid-free group. Elevated inflammatiory markers were associated with long-term steroid use (p=0.038). Concominant immunosuppressants were more frequently used in non-steroid-free group than steroid-free group (p=0.002).
Conclusions: Steroid-free remission might be achieved in some patients with inflammatory myopathies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4750

FRI0419 THE PREDICTIVE PROGNOSTIC FACTORS FOR CLINICAL COURSE OF POLYMYOSITIS/DERMATOMYOSITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Y. Sugiyama[1], R. Yoshimi[1], M. Tamura[1], N. Hamada[1], H. Nagai[1], N. Tsuchida[1], Y. Soejima[1], Y. Kunishita[1], D. Kishimoto[1], H. Nakano[1], R. Kamiyama[1], K. Minegishi[2], Y. Asami[1], Y. Kirino[1], S. Ohno[2], H. Nakajima[1] on behalf of Y-CURD Study Group. *[1]Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medocine; [2]Center for Rheumatic Diseases, Yokohama City University Medical Center, Yokohama, Japan*

Background: Interstitial lung disease (ILD) and concomitant infectious diseases are the predominant causes of death in polymyositis/dermatomyositis (PM/DM). We have already reported that hypocapnea and ILD lesion in upper lung fields are independent prognostic factors. Micro RNA is a non-coding RNA, which has a certain function such as transcriptional regulation. miR-1 has been reported to be associated with myocyte differentiation and to decrease in muscle tissue from patients with inflammatory myopathies.
Objectives: Here we investigated the association of serum miR-1 level with clinical course of PM/DM-associated ILD (PM/DM-ILD).
Methods: We retrospectively analyzed clinical baseline, serum miR-1 level, initial therapeutic regimens, total amounts of PSL, clinical outcomes, and episode of infection of patient with PM/DM-ILD who had received initial treatment at six hospitals associated with Yokohama City University from 2003 to 2016. The serum miR-1 level was measured by quantitative real-time PCR.
Results: One hundred sixteen (PM 22, DM 51, and clinically amyopathic DM 43) patients were included. The mean age was 56±15 years and 83 were female. As initial therapies, oral PSL, methylprednisolone (mPSL) pulse, intravenous cyclophosphamide (IVCY), and oral calcineurin inhibitor therapies were performed in 113 (97%), 80 (69%), 48 (41%) and 80 (69%), respectively. Forty-one patients had a serious infection at 51±38 days from initiation of immunosuppressants and 10 died of infections. Old age, low $PaCO_2$ and albumin, high LDH and KL-6, high score of ILD, high initial dose of PSL, mPSL pulse, IVCY, calcineurin inhibitor and combination therapy were extracted as risk factors for infection by univariate analyses. A multivariate logistic regression analyses revealed that combination therapy (p=0.012, OR 2.83), old age (p=0.024, OR 2.12), high initial dose of PSL (p=0.024, OR 2.69), low albumin (p=0.031, OR 3.56), and low $PaCO_2$ (p=0.038, OR 2.67) were independent risk factors for infection. Serum samples were obtained from total of 14 patients and 13 healthy controls. Serum miR-1 levels in PM/DM-ILD patients before treatment were significantly higher than those in healthy controls (p=0.047). Also serum miR-1 levels were significantly higher in PM/DM-ILD patients with concomitant infectious diseases as compared to patients without infectious diseases (p=0.043). We further divided the PM/DM-ILD cases into two groups by the serum miR-1 level. The higher miR-1 group showed poorer effectiveness of ILD treatment (p=0.040), and lower lymphocyte count (p=0.013) as compared to the lower miR-1 group.
Conclusions: Appropriate monitoring is important for PM/DM-ILD, especially in older patients with malnutrition or decreased respiratory function. miR-1 can be a new biomarker for predicting treatment response and concomitant infectious diseases during treatment for PM/DM-ILD.
References:
[1] Robert W. Georgantas et al, Inhibition of myogenic microRNAs 1, 133, and 206 by inflammatory cytokines links inflammation and muscle degeneration in adult inflammatory myopathies, Arthritis Rheum, 2014;66:1022–33.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3168

FRIDAY, 16 JUNE 2017

Spondyloarthritis - etiology, pathogenesis and animal models

FRI0420 ASSOCIATION OF SUPRESSOR OF CYTOKINE SIGNALING -3 (SOCS-3) EXPRESSION WITH INTERLEUKIN-23 RECEPTOR (IL-23R) SINGLE NUCLEOTIDE POLYMORPHISMS (SNPS) IN ANKYLOSING SPONDYLITIS (AS)

M.A. Sánchez[1], R. Villares[2], J. Polo y La Borda[3], J. Campos[3], J.M. Rodríguez-Frade[2], J. Sanz[3], B.J. Robles Flores[3], A. Royuela[4], P. Lucas[2], M. Mellado[5], J. Mulero[3]. *[1]Rheumatology, Instituto de Investigación Biomédica Hospital Universitario Puerta de Hierro Majadahonda, Majadahonda (Madrid); [2]Immunology and Oncology Department, Centro Nacional de Biotecnología. CNIC, Madrid; [3]Rheumatology; [4]Clinical Biostatistics Unit, Instituto de Investigación Biomédica Hospital Universitario Puerta de Hierro Majadahonda; [5]Immunology and Oncology Department, Centro Nacional de Biotecnología. CNIC, Majadahonda (Madrid), Spain*

Background: Nowadays genetic-association studies have discovered new genes, other than *HLA-B27*, as *IL-23R* associated with AS. The signalling pathway trough IL-23R is negatively regulated by the SOCS proteins. However, the reports regarding the roles of SOCS in AS are very rare at present.[1,2]
Objectives: The aim of this study is to assess the gene expression of *SOCS-1*,

-2, -3 and *-6* in peripheral blood mononuclear cells (PBMCs) in relation with *IL-23R* SNPs previously associated with AS.
Methods: We studied 74 patients (64,8% males) recruited from the Rheumatology Unit of the Puerta de Hierro Hospital diagnosed of AS following the Modified New York Criteria. The study cohort included patients with a mean age of 55.2±11, 2 years. Total RNA was extracted from PBMCs using the Nucleospin RNA kit (MN) and reverse transcribed into cDNA. mRNA expression was assessed by real-time quantitative RT-PCR using specific primers and Power SYBRGreen PCR Master Mix (Applied Biosystems).SNP genotyping [rs1129026 (G/A), rs10489629 (T/C), rs1343151 (G/A) rs2201841 (C/T), rs1004819 (C/T) y rs11209032 (A/G)] was performed using the Sequenom MassARRAY platform. In 17 cases there were two samples from the same patient. These samples were obtained from two scheduled visits and 99 samples were analyzed so. To determine the effect of independent variables on levels of *SOCS* genes expression, we fitted population-averaged models by generalized linear models, nested by patient, using the *xtgee* command of Stata v.12. *P*-values of <0.05 were considered statistically significant.
Results: Cellular *SOCS-1*,*-2* and *-6* expression did not show significant differences between the risk alleles carriers and the protective alleles carriers in any of the *IL-23R* SNP studied. *SOCS-3* increased significantly in protective alleles carriers of the *IL-23R* intronic SNP rs10489629-C (CC>CT>TT; *P*=0.028), the *IL-23R* non-synonymous SNP (Arg381Gln) rs11209026_A (AG>GG; *P*=0.047) and the *IL-23R* intronic SNP rs1343151-A (AA>AG>GG, *P*=0.005).
Conclusions: Higher *SOCS-3* expression levels for AS patients carriers of protective alleles of the *IL-23R* rs10489629-A, rs11209026-A and rs1343151-A as compared to carriers of risk genotypes could influence the pathogenesis of this disease.
References:
[1] Mol Biol Rep. 2014;41(6):3773–80.
[2] Clin Exp Rheumatol. 2016;34(1):100–5.
Acknowledgements: This work have been supported by Fondo de Investigaciones Sanitarias (PI11/00400) and by RETICS Program, RD08/0075 (RIER) from Instituto de Salud Carlos III (ISCIII), within the VI PN de I+D+I 2008–2011, (FEDER).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3832

FRI0421 DYSREGULATED MIR-125 PROMOTES JOINT ANGIOGENESIS IN PSA THROUGH ALTERED BIOENERGETICS

S. Wade[1], N. Ohnesorge[2], M. Biniecka[3], S. Merrigan[2], T. McGarry[1], M. Canavan[1], D.J. Veale[3], B. Kennedy[2], U. Fearon[1]. *[1]Molecular Rheumatology, Trinity Biomedical Sciences Centre; [2]Conway Insitute, University Collage Dublin; [3]St Vincents University Hospital, Dublin, Ireland*

Background: Psoriatic arthritis (PsA) is characterised by an early vascular phase which is essential in perpetuating pannus growth, immune responses and disease progression. Recently, numerous studies have highlighted the emerging importance of endothelial cell metabolism in controlling angiogenesis. Herein, we propose microRNA, miR-125, modulates EC bioenergetics and orchestrates joint angiogenesis as characterised using *ex-vivo and in-vitro* tissue/cell assays and a novel *in-vivo* zebrafish model.
Objectives: To examine the relationship between miR-125, angiogenesis and cellular metabolism in the PsA synovium.
Methods: Primary PsA synovial fibroblasts (PsA FLS) and microvascular endothelial cells (HMVEC) were transfected with anti-miR-125a. Angiogenic mechanisms were quantified using tube formation assays, invasion by Transwell Matrigel chambers, migration by wound repair and metabolic gene expression by RT-PCR. Real-time analysis of extracellular acidification rates (ECAR) and oxygen consumption rates (OCR) of anti-125 treated HMVEC was assessed using the XF-24 Flux Analyzer (Seahorse Bioscience). To determine if altered metabolism is observed *ex vivo*, glycolysis/oxidative phosphorylation markers (GAPDH/PKM2/GLUT1/ATP), and angiogenic factors (FactorVIII/VEGF/ANG2) were quantified by immunohistology. MiRNA levels were quantified in synovial tissue (ST) and PBMC by RT-PCR and compared to clinical marker and immunohistochemical analysis. The angiogenic effects of miR-125 were assessed *in vivo* using GFP-tagged zebrafish embryos treated with anti-125 morpholinos, or vitamin D3 analog, calcitrol, to monitor vascular development.
Results: An increase in tube formation, cellular invasion and/or migration mechanisms ($p<0.05$) were demonstrated in anti-miR-125a transfected HMVEC and FLS supernatant. Inhibition of miR-125 significantly decreased basal, maximal and spare respiratory capacity ($P<0.009$) with a concurrent decrease in ATP synthesis ($P<0.008$). Increased glycolysis was further confirmed by the observed elevation of glycolytic genes: HK2, GSK3A, PDK1, HP6G (ns) and 3PO target and stimulator of glycolysis, PFKFB3 ($P<0.05$). *In vivo* synovial expression of miR-125 was significantly decreased in PsA versus OA synovial tissue and was associated with increased PsA macroscopic and microscopic vascularity. This was paralleled by a significant increase in the vascular expression of glycolytic markers, PKM2, GLUT1 and ATP5B in PsA compared to OA synovium. Finally, anti-125 morpholinos treated Zebrafish displayed increased vascular sprouting. In contrast, Calcitriol significantly reduced vascular development and increased the expression of miR-125, promoting miR-125 as a potential mechanism for orchestrating angiogenic development *in vivo* and in response to pharmaceutical agents
Conclusions: Our data demonstrates decreased expression of miR-125 in PsA synovium and *in-vivo* models was strongly associated pro-angiogenic mechanisms. Elevated glycolysis following miR-125 inhibition may enables endothelial cells to meet the increased energy and biosynthetic demands for new vessel formation. Correcting these deficiencies and their resulting metabolic shift, either by conventional pharmacological or as novel drug targets, may provide therapeutic benefit, especially in early disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6479

FRI0422 ESTROGEN ATTENUATES THE DISEASE ACTIVITY OF SPONDYLOARTHRITIS IN SKG MICE

H. Jeong[1], E.-K. Bae[2], Y.H. Eun[1], I.Y. Kim[1], E.-J. Park[3], J. Lee[1], E.-M. Koh[1], H.-S. Cha[1]. *[1]Samsung Medical Center; [2]Samsung Biomedical Research Institute, Seoul; [3]Jeju National University Hospital, Jeju, Korea, Republic Of*

Background: Ankylosing spondylitis is a male-predominant disease, and the male gender is also associated with more severe radiographic damage. Estrogen modulates immune-related processes such as T cell differentiation and cytokine production.
Objectives: This study aimed to evaluate the role of estrogen in the disease activity of spondyloarthritis (SpA). The effect of estrogen on the inflammatory cytokines was evaluated.
Methods: The effects of estrogen on the development of arthritis were evaluated by performing an ovariectomy and E2 pellet implantation in the zymosan-treated SKG mouse. Clinical arthritis scores were measured and PET-CT was performed to quantify joint inflammation. Total RNA was extracted from the hindpaws and forepaws and the expression of TNFα, IL-6, IFNγ, IL-4, IL-17A, IL-23, Dkk1, and SOST was measured by QuantiGene 2.0 plex assay.
Results: Zymosan exposure triggered SpA-like diseases in SKG mice, including peripheral arthritis, spondylitis, dactylitis, enteritis, and psoriatic skin lesions. E2-treated mice showed remarkable suppression of arthritis clinically and little infiltration of inflammatory cells in the Achilles tendon and intervertebral disc. ^{18}F-FDG uptake was significantly lower in the E2-treated mice. The expression of TNFα, IFNγ, IL-17A, Dkk1, and SOST was significantly reduced in E2-treated mice compared with sham and ovariectomized mice.
Conclusions: Estrogen suppressed arthritis development in SpA model of SKG mouse. Results of the study suggest that estrogen may have an anti-inflammatory effect on the disease activity of SpA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3341

FRI0423 ANTIBODIES TO TYPE II COLLAGEN: A NOVEL TOOL FOR THE SPONDYLOARTHRITIS DIAGNOSIS?

C. Vinci[1,2], M. Infantino[3], P. Pozzilli[2], V. Grossi[3], M. Manfredi[3], F. Bandinelli[4], F. Li Gobbi[4], A. Damiani[4], R. Strollo[2], M. Benucci[4], A. Nissim[1]. *[1]Biochemical Pharmacology, Queen Mary University of London, London, United Kingdom; [2]Endocrinology and Diabetes, Campus Biomedico, Rome; [3]Immunology and Allergology Laboratory Unit; [4]Rheumatology Unit, San Giovanni di Dio Hospital, Florence, Italy*

Background: Spondyloarthritis (SpA) are an inflammatory joint disease with chronic, progressive, axial inflammation of the spine and the sacroiliac joints. Diagnosis of SpA is done criteria by clinical symptoms, radiology and MRI or ultrasound following ASAS criteria. AS is similar to rheumatoid arthritis (RA) and psoriatic arthritis (PsA) as they are all inflammatory joint disease. Nevertheless they show considerable different pathology. [1]
Objectives: The aim of our study is to test whether a novel assay that we developed for RA can be used for SpA diagnosis. We have previously showed that antibodies to oxidative post-translationally modified collagen type II (oxPTM-CII) are present specifically in RA patients whether ACPA positive or negative. [2]
Our study intends to investigate the reactivity to oxPTM-CII in SpA patients in comparison to early undifferentiated arthritis (EUA) and PsA patients.
Methods: oxPTM-CII were generated using ribose and various reactive oxidants, and then they were analysed by SDS-PAGE. Binding to native and oxPTM-CII was evaluated by ELISA and Western Blotting. We used a cohort of sera from 67 patients with SpA, 54 patients with PsA, 49 patients with EUA. As control we used 19 patients with fibromyalgia (FM) and 70 healthy subjects. The specificity of the binding was further assessed by competitive ELISA and western blot.
Results: We detected stronger reactivity to SpA compared to PsA and even EUA serum samples. Hence specific binding to oxPTM-CII was seen in the 52% of SpA sera compared to 12% in PsA and 10% in EUA. There was no binding in samples from FM and healthy individuals. A group of the most reactive SpA samples was evaluated by western blot confirming a strong binding to several fragments or aggregates of oxPTM-CII.
Conclusions: For the first time we demonstrated that anti-ROS-CII may become a biomarker for SpA diagnosis.
References:
[1] J. Braun and J. Sieper, Ankylosing spondylitis. Lancet, vol. 369, no. 9570, pp. 1379–1390, 2007.
[2] R. Strollo, F. Ponchel, V. Malmström, P. Rizzo, M. Bombardieri, C. Y. Wenham,

R. Landy, D. Perret, F. Watt, V. M. Corrigall, P. G. Winyard, P. Pozzilli, P. G. Conaghan, G. S. Panayi, L. Klareskog, P. Emery, and A. Nissim, Autoantibodies to posttranslationally modified type II collagen as potential biomarkers for rheumatoid arthritis. Arthritis Rheum., vol. 65, no. 7, pp. 1702–12, Jul. 2013.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3498

FRI0424 EQUAL PRESENCE OF CIRCULATING MAIT CELLS IN AXIAL SPA PATIENTS WITH ONLY AXIAL INVOLVEMENT AND AGE- AND SEX-MATCHED HEALTHY CONTROLS

S. Arends, W. Abdulahad, A. Boots, B. Doornbos-van der Meer, E. Brouwer, A. Spoorenberg. *Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen, Netherlands*

Background: Previous studies indicated a potential role for mucosal-associated invariant T (MAIT) cells in the pathogenesis of ankylosing spondylitis (AS).[1,2] Active peripheral arthritis and extra-articular manifestations may influence the presence of circulating MAIT cells in AS.
Objectives: To investigate circulating MAIT cells in a homogenous group of axial spondyloarthritis (SpA) patients with only axial involvement in comparison to age- and sex-matched healthy controls (HC). Secondly, to explore the association of MAIT cells with symptom duration and disease activity.
Methods: Consecutive axial SpA patients from the Groningen Leeuwarden axial SpA (GLAS) cohort without active peripheral arthritis, inflammatory bowel disease, psoriasis or uveitis were included. Patients with active infections or current use of biologics were excluded to rule out possible influence on the presence of circulating MAIT cells. Disease activity was assessed using ASDAS, BASDAI, and serum CRP levels.
The frequencies and absolute numbers of circulating MAIT cells were examined in peripheral blood of all studied samples by 5-color flow cytometry. Immediately after sampling, EDTA-blood was stained with anti-CD3, anti-CD8, anti-TCRVa7.2, anti-CD161, and anti-TCRgd. After staining, the cells were washed, fixed, and analyzed immediately on FACS. MAIT cells were identified phenotypically as $CD3^+CD8^+TCR\gamma\delta^-V\alpha7.2^+CD161^{high}$ cells.
Results: Of the 41 included axial SpA patients, mean age was 46±16 years, 73% were male, mean symptom duration was 23±14 years, and 78% were HLA-B27 positive. Mean ASDAS was 2.6±1.0, mean BASDAI was 4.4±2.5, and median CRP was 3 (range 2–30). 70%, 54% and 37% of axial SpA patients had ASDAS $\geq$2.1, BASDAI$\geq$4 or CRP$\geq$5, respectively. HC had exactly the same age and sex distribution.
Both the percentages and absolute numbers of circulating MAIT cells were comparable between axial SpA patients and HC (Figure 1). In axial SpA patients, absolute numbers of MAIT cells correlated negatively (rho=-0.339) with symptom duration. No significant associations were found between MAIT cells and disease activity, except for a negative correlation (rho=-0.332) between frequency of MAIT cells and BASDAI (Table 1). There were no significant differences in MAIT cells between axial SpA patients with and without active disease according to ASDAS, BASDAI or CRP.

Table 1. Association of percentages and absolute numbers of MAIT cells with symptom duration and assessments of disease activity in axial SpA patients (n=41), Spearman correlation coefficients

	% CD8+ MAIT	nr CD8+ MAIT
Symptom duration (yrs)	-0.248	-0.339*
$ASDAS_{CRP}$	-0.221	0.053
BASDAI (0–10)	-0.332*	-0.126
CRP (mg/l)	-0.137	0.030

*P-value <0.05.

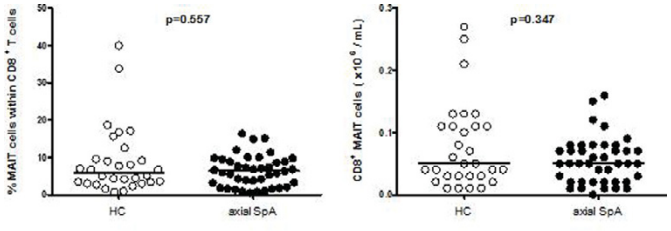


Figure 1. Percentages and absolute numbers of circulating CD8+ MAIT cells in axial SpA patients (n=41) and matched healthy controls (n=30), Mann-Whitney U tests.

Conclusions: In this homogeneous group of axial SpA patients with only axial disease, the presence of circulating MAIT cells did not differ from age- and sex-matched HC. No strong association was found between circulating MAIT cells and symptom duration or disease activity.
References:
[1] Gracey et al. Ann Rheum Dis 2016;75(12):2124–32.
[2] Hayashi et al. J Rheumatol 2016;43(9):1695–703.
Acknowledgements: Funding: This research project was supported by an unrestricted grant from Janssen. Janssen had no role in the design, conduct, interpretation, or publication of this study.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6203

FRI0425 ANALYSIS OF CELLULAR COMPOSITION AND CYTOKINE EXPRESSION IN THE SUBCHONDRAL BONE MARROW IN ANKYLOSING SPONDYLITIS

E.E. Kenngott[1], J. Bleil[1], R. Maier[2], J. Sieper[1], U. Syrbe[1]. *[1]Rheumatology Campus Benjamin Franklin, Charité Universitätsmedizin Berlin; [2]Experimental Rheumatology, Deutsches Rheuma-Forschungszentrum, Berlin, Germany*

Background: Ankylosing spondylitis (AS) is characterized by inflammation within the sacroiliac joints and at the spine including vertebral bodies and facet joints. In AS, bone destruction is followed by new bone formation leading to ankylosis of joints and syndesmophyte development. Histological studies of bone material from AS patients showed subchondral bone marrow changes, namely the transition of the bone marrow into granulation tissue which facilitates subchondral bone destruction but also promotes local bone formation [1, 2]. Currently, it is unclear what promotes the transition of the bone marrow into the granulation tissue.
Objectives: The aim of this study was to look for changes in the subchondral bone marrow in joints from AS patients that may precede and promote transformation into granulation tissue. Therefore, we analyzed the cellular composition of the bone marrow and determined local cytokine expression at subchondral regions of AS facet joints.
Methods: Facet joints were acquired from AS patients undergoing polysegmental correction surgery and compared to joints from autopsy controls. We performed immunohistochemical stainings to determine the number of T cells (CD3) and B cells (CD20), macrophages (CD68, CD163), monocytes (CD14), dendritic cells (DC; CD1a, DCsign) and myelopoietic cells (MPO). To correct for putative differences in fat cell content, software assisted image analysis was used to calculate the area of bone marrow covered by fat cells and the number of nucleated cells (DAPI) as well as myeloid cells. Cytokine expression was determined by mRNA in situ hybridization (TNF, IFNg) or immunohistochemistry (TGFβ, IL-10).
Results: We observed no difference in the number of adaptive immune cells, i.e. CD3+ T and CD20+ B cells, between AS and control joints and found no difference in T/B cell aggregates. Furthermore, no difference in the number of macrophages (CD163+, CD68+) and DCs (CD1a+, DCsign+) was found. The only difference in cellular composition appeared to be a slight trend towards a higher percentage of myelopoietic MPO+ cells/DAPI+ cells in AS joints compared to control joints. The overall number of DAPI+ cells as well as the fat content of the bone marrow was not different between AS and control joints.
Concerning cytokines, TNF mRNA expression was in general low but significantly increased ($p<0.05$) in AS versus control joints. No difference was found for IFNg. The number of TGFβ expressing cells was similar in AS and control joints while the number of IL-10 positive cells was decreased ($p<0.01$) in AS joints.
Conclusions: The results show a shift from pro-inflammatory to anti-inflammatory cytokine expression within subchondral bone marrow sites in AS joints while no major change in the cellular distribution of the major leukocyte subsets is found. The shift in cytokine milieu may contribute to transformation of the bone marrow into granulation tissue. It would be interesting to determine the cellular source of local cytokines, such as of IL-10.
References:
[1] Cruickshank B. Lesions of cartilaginous joints in ankylosing spondylitis. The Journal of pathology and bacteriology 1956;71(1):73–84.
[2] Bleil J, Maier R, Hempfing A, Sieper J, Appel H, Syrbe U. Granulation Tissue Eroding the Subchondral Bone Also Promotes New Bone Formation in Ankylosing Spondylitis. Arthritis Rheumatol 2016;68(10):2456–65.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3173

FRI0426 NO DEMONSTRABLE EFFECT OF IL-23 RECEPTOR VARIANTS ON CLINICAL MEASURES AND IL23/ IL-17 LEVELS IN ANKYLOSING SPONDYLITIS

J. Nossent[1,2], S. Johnsen[3], G. Bakland[2,4]. *[1]School of Medicine, University of Western Australia, Crawley, Australia; [2]Bone and Joint Group, Arctic University, Tromso; [3]Norwegian University of Life Sciences, Ås; [4]Rheumatology, University Hospital North Norway, Tromso, Norway*

Background: IL23 binding to IL23 receptor (IL23R) is necessary for the maturation of Th17 cells and generation of proinflammatory IL17 and TNF in AS. IL23R variants have considerable impact on AS susceptibility in genome-wide association studies.
Objectives: To describe the effect of genotypic IL23R variants on proinflammatory cytokines and disease measures in AS.
Methods: Cross sectional cohort study of patients with established AS (n=334, 90% B27 +, mean age at study 45 years) included in a disease registry. IL23R genotyping for nonsynonymous SNP's (rs11209026 (protective allele A) and rs11209032 (risk allele A) was done by Taqman RT-PCR, while IL23, IL17, IL6 and TNF levels determined by sandwich ELISA and compared with age and gender matched healthy controls (n=72). Genotypic associations with clinical and serological features were analyzed with nonparametric methods.
Results: There was no significant difference between in AS patients and controls

regarding IL23 (276 vs 262 pg/ml, p>0.4) and IL17 levels (184 vs 233 pg/ml, p>0.2). Only 22 (6.6%) AS patients carried the protective rs11209026 A allele, while 206 (61.7%) carried the rs11209032 A risk allele (p=0.03). There was no demonstrable influence of individual genotypes (A vs G, AA vs AG vs GG) or haplotypic combinations on BASFI, spinal function tests, CRP, ESR, IL-23 or IL-17 levels (all p>0.3)

Conclusions: While there is a high prevalence of the IL-23R rs11209032 A risk allele in Caucasian AS patients, this has no demonstrable bearing on clinical disease measures or serum IL-23 and IL-17 levels.

Acknowledgements: The authors wish to acknowledge the technical assistance by mrs K Nilsen and the financial support of the North Norwegian Health Authority Research Fund

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5882

FRI0427 FIRST DESCRIPTION OF GAMMA DELTA T CELLS AT NORMAL HUMAN ENTHESIS

R.J. Cuthbert[1], E. Fragkakis[2], R. Dunsmuir[2], P. Giannoudis[1], E. Jones[1], D. McGonagle[1]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]Department of Spinal surgery, The Leeds teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Recent animal studies have suggested that γδT-cells accumulate at enthesis, secrete IL-17 and are responsible for driving the spondyoarthritis (SpA) phenotype resulting from IL-23 overexpression in mice (1, 2). In humans examination of the immunological profile of enthesis has been hampered by lack of tissue. Recently, we used a novel strategy to show that group 3 innate lymphoid cells are present at the human enthesis (3). Here we extend our methodology to examine the broader immunological profile of human enthesis and to determine if γδT-cells are also present.

Objectives: To characterise γδT-cells at human enthesis and adjacent peri-entheseal bone

Methods: Human etheseal soft tissue (EST) and peri-entheseal bone (PEB) was harvested from normal spinous process in patients undergoing elective spinal orthopaedic procedures. Interspinous EST was dissected from PEB and enzymatically digested, followed by isolation of mononuclear cells. Flow cytometry was then used to determine the proportion of B-cells (CD45+, CD19+) NK cells (CD45+, CD3-, CD56+) and T-cells (CD45+, CD3+). T-cells were then sub divided based on expression of CD4 (T-helper cells), CD8 (Cytotoxic T-cells) and TCRγδ (γδT-cells). All entheseal data was compared to age-matched peripheral blood from healthy controls.

Results: Entheseal digests contained on average a lower proportion of T-cells compared to peripheral blood (p=0.018). However, the proportion of T-cells not expressing either CD4 or CD8 was greater in entheseal tissues (p=0.021), this population was largely composed of γδT-cells. As a proportion of T-cells γδT-cells were 6 fold more numerous in EST compared to peripheral blood (p=0.024), and PEB had 3 fold more. 37% of EST γδT-cells expressed CCR6 this compared to 26% and 34% in PEB and peripheral blood respectively.

Conclusions: γδT-cells are present in normal human enthesis and γδT-cells constitute a greater proportion of the T-cell pool compared to peripheral blood, making it likely that they represent a tissue resident population. Additionally, we observed a very similar proportion γδT-cells that expressed CCR6, a functional marker for IL-17 production, as was observed in mice (2). This is the first description of γδT-cells at the human enthesis and offers tentative confirmation of findings in mouse models where these cells play a key role in SpA pathogenesis.

References:

[1] Sherlock JP, Joyce-Shaikh B, Turner SP, Chao CC, Sathe M, Grein J, et al. IL-23 induces spondyloarthropathy by acting on ROR-gammat+ CD3+CD4-CD8- entheseal resident T cells. Nat Med. 2012 Jul;18(7):1069–76. PubMed PMID: 22772566.

[2] Reinhardt A, Yevsa T, Worbs T, Lienenklaus S, Sandrock I, Oberdörfer L, et al. IL-23-dependent γδT cells produce IL-17 and accumulate in enthesis, aortic valve, and ciliary body. Arthritis & Rheumatology. 2016.

[3] Cuthbert R, Fragkakis E, Dunsmuir R, Millner P, El-Sherbiny Y, McGonagle D. AB0028 Innate Lymphoid Cells Are Present at Normal Human Enthesis Providing A Potential Mechanism for Spondyloarthropathy Pathogenesis. Annals of the Rheumatic Diseases. 2016;75(Suppl 2):906-.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6421

FRI0428 THE JAK1-SELECTIVE INHIBITOR, FILGOTINIB, INHIBITS INFLAMMATION PATHWAYS OBSERVED IN AN IL23-INDUCED PSORIATIC ARTHRITIS MOUSE MODEL

R. Blanqué[1], M. Ongenaert[2], C. David[1], C. Robin-Jagerschmidt[1], A. Cauvin[1], C. Saccomani[1], P. Clement-Lacroix[1], S. Dupont[1], R. Galien[1]. *[1]Galapagos SASU, Romainville, France; [2]Galapagos NV, Mechelen, Belgium*

Background: Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory disease characterized by musculoskeletal involvement and extra-skeletal manifestations such as psoriasis, uveitis and Inflammatory Bowel Disease (IBD). The importance of several pro-inflammatory cytokines, in addition to TNFa, IL-12 and IL-23 which are targets of current treatments, suggests that novel therapies may benefit patients. The JAKs (a family of 4 non-receptor tyrosine kinases) are crucial for the signaling of many pro-inflammatory cytokines. In this regard, the JAK1-selective inhibitor filgotinib (GLPG0634, GS-6034) has shown efficacy in patients with rheumatoid arthritis (RA), a disease that shares some hallmarks with PsA, as well as in Crohn's disease (CD), making this molecule a potential therapy for PsA.

Objectives: To gain insight into filgotinib mode of action using a PsA preclinical model by analysing the gene expression signature of filgotinib in mouse phalanges and colon tissues from an IL23-induced PsA mouse model.

Methods: Spondyloarthopathy was induced by hydrodynamic injection of IL-23 enhanced Episomal Expression Vector (EEV). Animals were treated with filgotinib or vehicle from day 10 (therapeutic mode) and sacrificed after 16 days of treatment. RNAs were extracted from the phalanges and the proximal colon, and transcriptome assays were performed using the Agilent SurePrint G3 mouse chip. Data analysis was performed using empirical Bayes methods and linear models (limma BioConductor package).

Results: In mice, IL-23 induced changes in the transcriptome in both phalanges and colon that were marked by effects on genes related to the IL-23/T_H17 axis. Microarray analysis performed on mouse phalanges and colon revealed that filgotinib partially reversed the impact of IL-23 on gene expression in colon and in phalanges. In both tissues, filgotinib signature was different but some impacted biological programs were similar. A consistent interferon signature was counteracted by filgotinib in both tissues with decreased expression of common genes such as Apobec3, Gbp8, Iigp1 and Oas3. Several markers of inflammation or associated with IL-23 activitywere also decreased with common on Kynu and Cd96 gene expression in both tissues. Of interest, filgotinib repression on inflammatory gene expression was stronger in colon compared to phalanges (Il1b, Clec4e). Moreover expression of some genes involved in gut homeostasis that were induced by IL-23 were decreased by filgotinib in the colon, notably Fpr2 (receptor for formyl peptides) and Mmp7. In phalanges, gene expression associated with IL-23-induced disease was also reversed by filgotinib treatment. Il19, Mtcl1 and Tlr1 which are key mediators in psoriasis, or Rankl that is involved in bone remodeling in PsA were differently regulated by IL-23 and filgotinib.

Conclusions: Systemic expression of IL-23 in mice generated a PsA phenotype that was associated with altered gene expression in diseased tissues. A strong interferon signature was reversed by filgotinib as were several inflammation and disease markers. Together with the previous Phase 2 clinical results in RA and CD, these data support the study of filgotinib for the treatment of PsA patients.

Disclosure of Interest: R. Blanqué Employee of: Galapagos SASU, M. Ongenaert Employee of: Galapagos NV, C. David Employee of: Galapagos SASU, C. Robin-Jagerschmidt Employee of: Galapagos SASU, A. Cauvin Employee of: Galapagos SASU, C. Saccomani Employee of: Galapagos SASU, P. Clement-Lacroix Employee of: Galapagos SASU, S. Dupont Employee of: Galapagos SASU, R. Galien Employee of: Galapagos SASU

DOI: 10.1136/annrheumdis-2017-eular.4911

FRI0429 DYSREGULATION OF THE SPLICING MACHINERY IN LEUKOCYTES FROM ANKYLOSING SPONDYLITIS PATIENTS IS ASSOCIATED TO DISEASE PATHOGENESIS

Y. Jimenez-Gomez[1], C. Lopez-Pedrera[1], S. Pedraza-Arévalo[2], M. del Río-Moreno[2], M.C. Ábalos-Aguilera[1], P. Ruiz-Limon[1], C. Perez-Sanchez[1], M.C. Castro[1], N. Barbarroja[1], I. Arias-de la Rosa[1], P. Font[1], A. Escudero[1], J.P. Castaño[2], R.M. Luque[2], E. Collantes-Estevez[1]. *[1]IMIBIC/Reina Sofia University Hospital/Cordoba University; [2]IMIBIC/Reina Sofia University Hospital/Cordoba University; CIBERobn and ceiA3, Cordoba, Spain*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease, of unknown aetiology, associated to the development of several comorbidities such as atherosclerosis. Splicing is a post-transcriptional process involved in the RNA maturation. Recent studies have revealed that a pathological dysregulation of the splicing machinery or spliceosome is associated to several human diseases. Yet, the spliceosome alterations have not been described in AS.

Objectives: 1) To analyze whether dysregulation of the spliceosome is present in AS. 2) To evaluate the association between the alteration of this process and the clinical, inflammatory, oxidative, and atherogenic profiles present in this pathology.

Methods: Fourteen AS patients and 14 healthy donors (HDs) were included in the study. Disease function and activity status were analyzed using the BASFI and BASDAI. The expression of selected components of the major-(n=12) and minor-spliceosome (n=4), and splicing factors (n=28) was evaluated in purified monocytes, lymphocytes and neutrophils from patients and HDs (n=14 each) by Fluidigm methodology. Oxidative stress, inflammation and atherogenesis were evaluated by flow cytometry and RT-PCR. Endothelial function was determined by the post occlusive hyperaemia test using Laser-Doppler.

Results: Compared to HDs, a significant dysregulation in the expression of relevant splicing factors and spliceosome components was found in all the leukocyte subtypes from AS patients, being neutrophils which displayed higher number of altered molecules. Interestingly, a specific altered profile of major- and minor-spliceosome members, and splicing factors was observed when compared lymphocytes (U4, U6, NOVA1, RMB17), monocytes (PRP8, SF3B TV2, CELF4, ESRP2, RBM3, SAM68 TV1, SRSF10, TIA1) and neutrophils (U11, U2, U2AF2, U11, CA 150, ESRP1, PSF, PTB, SRM160).

Correlation studies revealed that disease activity (CRP, ESR, BASDAI) was associated to the alteration of a vast number of spliceosome components in the three subtypes of analyzed leukocytes. In addition, the BASFI index correlated with the expression of splicing factors ESRP1, SRSF1 and TRA2B in neutrophils. The inflammatory, atherogenic and oxidative profile of AS leukocytes was related to the expression of a number of spliceosome molecules in the three leukocyte subsets, although neutrophils exhibited the highest number of deregulated spliceosome components related to inflammation (STAT3, TNF-α, IL-1α, IL-1β, IL-5) and cell adhesion (ICAM-1, SELL, THBS4, CDH5). Finally, endothelial dysfunction correlated with the expression of several components of the major-spliceosome and splicing factors in monocytes and neutrophils.
Conclusions: 1) AS patients display a dysregulation of the splicing machinery components associated to disease function and activity. 2) The expression of spliceosome members in the different leukocyte subsets is related to the inflammatory, oxidative and proatherogenic profile of AS patients.
Alteration of the spliceosome may provide new biomarkers for diagnosis and clinical monitoring of AS
Acknowledgements: Funding by: JA PI-0314–2012, SER, ISCIII (RIER RD16/0012/0015)
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4845

FRI0431 ALTERED EXPRESSION OF CIRCULATING MICRORNAS IS RELATED TO DISEASE ACTIVITY AND STRUCTURAL DAMAGE IN ANKYLOSING SPONDYLITIS PATIENTS

P. Font, C. Perez-Sanchez, P. Ruiz-Limon, C. Lopez-Pedrera, M.C. Castro-Villegas, M.C. Ábalos-Aguilera, N. Barbarroja, I. Arias-de la Rosa, M.D. Lopez-Montilla, A. Escudero-Contreras, C. Lopez-Medina, E. Collantes-Estevez, Y. Jimenez-Gomez. *Rheumatology Service, IMIBIC/Reina Sofia University Hospital/Cordoba University, Cordoba, Spain*

Background: Ankylosing spondylitis (AS) remains difficult to diagnose before irreversible damage to sacroiliac joint is noticeable. MicroRNAs (miRNAs) are a group of single-stranded non-coding RNAs of 20–25 nucleotides in length that can potentially regulate every aspect of cellular function. Recent studies have demonstrated that miRNAs can be detected in the circulation and serve as potential biomarkers of various inflammatory pathologies.
Objectives: To evaluate whether AS pathogenesis is related to the aberrant expression of plasma miRNAs.
Methods: The expression profile of 800 miRNAs in plasma was determined in pooled samples from AS patients and healthy donors (HDs) (n=3 each) using the nCounter technology. Next, candidate miRNAs were validated by real time RT-PCR in a cohort of AS patients and HDs (n=26 each). In parallel, the expression of validated miRNAs was examined in a cohort of 24 psoriatic arthritis (PsA) patients. To evaluate their relevance in the AS pathogenesis, an analysis was performed by using the web-based bioinformatics tool *Ingenuity Pathways Analysis* (IPA). Association and correlation studies of altered miRNAs with clinical and analytical profile of the AS patients were also performed. AS activity was defined as CRP >5 mg/L and/or BASDAI ≥4 and ESR >20 mm/h. Structural damage was evaluated by mSASSS.
Results: In discovery phase, nine miRNAs were differentially expressed (fold change ≥2) in the plasma of AS patients *vs.* HDs. After validation, higher expression levels of miRNA (miR)-146a-5p, miR-125a-5p, miR-151–3p and miR-22–3p, and lower of miR-150–5p and miR-451a were found in AS *vs.* HDs. Interestingly, higher miR-146a-5p, miR-125a-5p, miR-151–3p and miR-22–3p expression levels in AS than in PsA patients were further observed. The areas under the curve, generated to assess the accuracy of miRNAs as diagnostic biomarkers for AS, ranged from 0.717 to 0.798; the six-miRNAs signature reached 0.947. Bioinformatics analysis revealed that miRNAs targeted inflammatory and bone remodeling genes, underlying their potential role in this pathology. Indeed, correlation studies showed an association between these six miRNAs and potential target proteins associated to AS pathophysiology. In addition, miR-146a-5p, miR-146a-5p, miR-125a-5p and miR-22–3p expression was increased in active *vs.* non-active patients. Moreover, miR-150–5p and miR-451a expression was related to the presence of syndesmophytes in AS patients, underlying their association with structural damage.
Conclusions: 1) Several miRNAs are found differentially expressed in plasma from AS patients vs. HDs and other chronic inflammatory pathologies as PsA, indicating that these miRNAs may be considered potential biomarkers for AS diagnose. 2) The differential expression of certain miRNAs is associated to disease activity and structural damage. Overall, this study identified a six-plasma miRNAs signature that could be attractive candidates as non-invasive biomarkers for the AS diagnosis, and may help to elucidate the disease pathogenesis.
Acknowledgements: Funded by JA PI-0314–2012, SER, and ISCIII (RIER RD16/0012/0015).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4780

FRIDAY, 16 JUNE 2017

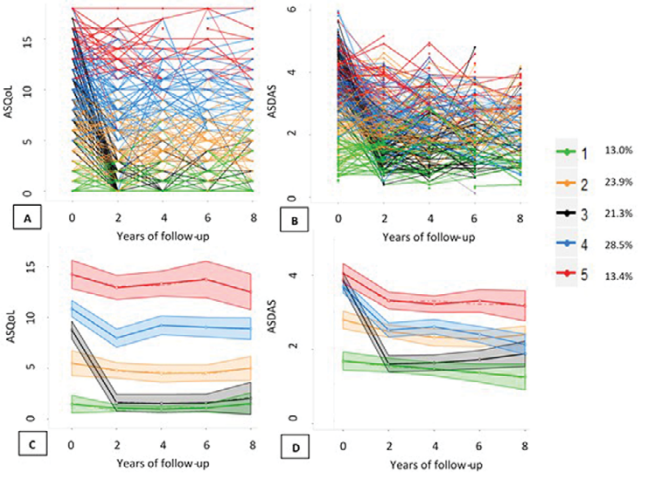
Spondyloarthritis - clinical aspects (other than treatment)

FRI0430 DUAL TRAJECTORIES OF DISEASE ACTIVITY AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

A. van Tubergen[1], M. Imkamp[1,2], A. Boonen[1], S. Arends[3,4], M. Dougados[5], R. Landewé[6], S. Ramiro[7], F. van den Bosch[8], D. van der Heijde[7], F. Wink[4], A. Spoorenberg[3,4], V. Lima Passos[2]. *[1]Maastricht University Medical Center; [2]University Maastricht, Maastricht; [3]University Medical Center Groningen, Groningen; [4]Medical Centre Leeuwarden, Leeuwarden, Netherlands; [5]Hôpital Cochin, Paris, France; [6]Amsterdam Medical Center, Amsterdam; [7]Leiden University Medical Center, Leiden, Netherlands; [8]Ghent University Hospital, Ghent, Belgium*

Background: The ultimate goal of managing Ankylosing Spondylitis (AS) is to improve and maintain the patient's health-related quality of life (HRQoL). To reach this goal, rheumatologists target towards low disease activity, as this is the main modifiable factor. To date, there is insufficient insight into (1) the co-evolution of disease activity and HRQoL, and (2) the heterogeneity in such trajectories among patients.
Objectives: To explore the heterogeneous character of AS by identifying different temporal patterns of co-dependence between disease activity and HRQoL over 8 years follow-up.
Methods: Data from Outcome in AS International Study (OASIS; n=161) and Groningen Leeuwarden AS (GLAS; n=264) cohorts were used. All patients had an established diagnosis of AS. In GLAS, all patients started a biological. HRQoL and disease activity were measured bi-annually using ASQoL and ASDAS-CRP

Figure 1. Joint trajectory latent classes of ASQoL - ASDAS



A-B Spaghetti plots of observed, subject-specific ASQoL and ASDAS lines over a period of 8 years, colored according to their final latent class assignment. Note that each class is represented by both an ASQoL and an ASDAS trajectory.

C-D Estimated average trajectories' lines, corresponding 95% confidence bands and baseline prevalence.

Abstract FRI0430 – Table 1. Baseline characteristics of patients within each ASQoL-ASDAS trajectory

Characteristics	Trajectory 1 (N=55)	Trajectory 2 (N=105)	Trajectory 3 (N=86)	Trajectory 4 (N=124)	Trajectory 5 (N=55)	p-value
Age – yr	43.9±12.4	46.0±12.7	40.9±10.7	47.9±11.3	45.1±13.7	<0.01*
Male sex (%)	46 (83.6)	71 (67.6)	62 (72.1)	83 (66.9)	29 (52.7)	0.01*
Smoking – yes (%)	16/42 (38.1)	23/85 (27.1)	26/74 (35.1)	44/98 (44.9)	20/46 (43.5)	0.13
HLAB27 – positive (%)	50/54 (92.6)	73/103 (70.9)	72/82 (87.8)	94/119 (79.0)	44/55 (80.0)	0.01*
Symptom duration – yr	20.3±10.9	21.4±12.1	17.0±10.9	22.2±13.1	21.3±12.6	0.04*
(Bridging) syndesmophytes present (%)	16/39 (41.0)	45/73 (61.6)	38/70 (54.3)	64/90 (71.1)	18/34 (52.9)	0.02*
Start biological (%)	15/54 (27.8)	41/101 (40.6)	81/86 (94.2)	85/120 (70.8)	35/55 (63.6)	<0.01*

respectively. Patients were classified into latent groups with individuals following a similar course of disease activity and HRQoL. These trajectories were estimated by Group-Based Trajectory Modelling. Next, the trajectories were profiled by comparing the latent groups with respect to baseline factors with ANOVA and Chi-square test.

Results: Five dual trajectories were revealed (Figure): 1. Low impact of AS on patient (13%): stable low ASQoL and ASDAS inactive disease; 2. Moderate impact (24%): stable moderate ASQoL and ASDAS high disease; 3. Improving impact (21%): major improvement in ASQoL and ASDAS; 4. High impact (29%): moderately severe ASQoL with very high but improving ASDAS; 5. Very High Impact (13%): persistently severe ASQoL with high ASDAS. Low impact of AS was mainly characterized by male gender and HLA-B27; improving impact by younger age, short symptom duration, and biological intake; high impact by higher age, long symptom duration, and (bridging) syndesmophytes (Table).

Conclusions: We identified five dual trajectories of disease activity and HRQoL, each demonstrating a clear mutual relationship. These trajectories and their profiles provide insight into the heterogeneity of the impact of AS on patients' health and overall functioning.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3802

FRI0432 CLINICAL WORSENING ACCORDING TO THE PATIENT IS INFREQUENT IN AXIAL SPONDYLOARTHRITIS: RESULTS OF THE ASAS-FLARE STUDY IN 1169 PATIENTS

A. Moltó[1], B. Meghnathi[1], L. Gossec[2], R. Landewé[3], D. van der Heijde[4], M. Dougados[1] on behalf of ASAS-FLARE study group. *[1]Paris Descartes University, Medicine Faculty; APHP, Rheumatology B Department, Cochin Hospital; [2]Sorbonne Universités, UPMC Univ Paris 06; AP-HP, Pitié Salpêtrière Hospital, Department of rheumatology, Paris, France; [3]Department of Clinical Immunology & Rheumatology, Amsterdam Rheumatology Center, Amsterdam and Zuyderland Medical Center, Heerlen; [4]Department of Rheumatology, Leiden University Medical Centre, Leiden, Netherlands*

Background: Prevalence of flares/worsening of the disease in axSpA is not well known, with prevalences ranging from 10 to 40%.

Objectives: To evaluate the prevalence of disease worsening according to the patient's perception in an axSpA population with stable disease and its correlation with disease activity parameters.

Methods: Study: International multicentric (20 countries) longitudinal (2 visits: 1 week – 6 months) observational in 2016, under the guidance of ASAS. Patients: axSpA patients with stable disease according to the rheumatologist. Data on disease characteristics were collected at baseline, and data on disease activity were collected at both visits. Disease worsening was defined at the follow-up visit by the patient using the MCID question ("*Think about all the ways your spondyloarthritis has affected you during the last 48 hours. Compared to the last visit how did you feel during the last 48 hours? Improved/No change/Worse")*. If patients answered "worse", they marked if they considered themselves in an acceptable symptoms state (PASS) and whether they considered treatment intensification was necessary. Analyses were descriptive and changes in disease activity were calculated according to patient-reported worsening.

Results: Among the 1639 patients included, 1169 patients had complete data. Patients were predominantly males (64.8%), had a mean age and disease duration of of 41.7 (SD 12.4) and 12.6 (9.9) years, respectively. History of X-ray sacroiliitis, MRI sacroiliitis and HLAB27+ were present in 944 (80.8%), 471 (40.6%) and 807 (69.0%) patients, respectively. 56% (n=655) patients were receiving a biologic treatment. At the baseline visit, mean BASDAI (0–10) was 3.1 (2.3), mean ASDAS 2.3 (1.0) and mean CRP 8.4mg/L (14.5). Mean interval between both visits was 91.2 (51.0) days. At the follow-up visit, 590 (50.5%), 388 (33.2%) and 191 (16.3%) patients considered their condition had improved, not changed and worsened, respectively. Among the 191 patients reporting a worsening, 123 (64.4%) considered their symptom status unacceptable, and 127 (66.5%) judged their state required treatment intensification. BASDAI, ASDAS and CRP significantly increased in patients considering themselves worsening (Table).

	Worsening	Not worsening**	*p*
Change in BASDAI (0–10)*	1.3 (1.8)	-0.5 (1.5)	<0.005
Change in ASDAS*	0.7 (0.8)	-0.3 (0.8)	<0.005
Change in CRP (mg/l)*	4.5 (14.1)	-2.0 (13.2)	<0.005

*Change is calculated as the absolute change between the visits; ** including improvement and no change in status.

Conclusions: in this real-life study of stable axSpA, worsening, as defined by the patient, was not frequent, but was significantly associated with increase in disease activity measures, including objective parameters such as CRP and not only patient-reported outcomes.

Acknowledgements: This study was supported by ASAS (Assessment in SpondyloArthritis international Society)

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4766

FRI0433 HIGH PREVALENCE OF HIDRADENITIS SUPPURATIVA IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

S. Arends[1,2], A. Rondags[3], F. Wink[2], B. Horváth[3], A. Spoorenberg[1,2]. *[1]Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen; [2]Rheumatology, Medical Center Leeuwarden, Leeuwarden; [3]Dermatology, University Medical Center Groningen, Groningen, Netherlands*

Background: Axial spondyloarthritis (SpA) is associated with several extra-articular manifestations such as the skin disease psoriasis. On the other hand, SpA was found to be more prevalent (3–4%) in patients with another skin disease: hidradenitis suppurativa (HS).[1] HS is a chronic, recurrent, debilitating inflammatory skin disease that involves deep-seated painful nodules in the inverse body regions, with an average prevalence of 1% in the European population and a female predominance (ratio 3:1).[2] Thus far, the prevalence of HS in axial SpA is not exactly known.

Objectives: To investigate the prevalence of HS in patients with axial SpA.

Methods: A self-screening questionnaire with validated questions concerning HS signs and symptoms including prototypical pictures was send to all participating patients from the Groningen Leeuwarden axial SpA (GLAS) cohort in 2016. All patients fulfilled the ASAS axial SpA criteria. Self-reported HS symptoms were verified by checking medical records and/or verification by phone, defined as diagnosis of HS by a dermatologist.

Results: In total, 588 questionnaires were send to the GLAS patients, of which 459 were returned and could be included in the final analysis (response rate 78%). Of the included patients, mean age was 50±13 years, 63% were male, mean symptom duration was 23±13 years, and 78% were HLA-B27 positive.

The questionnaire data showed a high self-reported HS prevalence of 11%. HS symptoms were confirmed by doctor's diagnosis in the large majority of these patients (41/50; 82%), resulting in an estimated HS prevalence of 9%.

The next step will be the comparison of patient characteristics and clinical assessments between axial SpA patients with and without HS.

Conclusions: The present observational cohort study shows that HS is a common skin disease in patients with axial SpA.

References:

[1] Richette et al. J Rheumatol 2014;41(3):490–4.

[2] Zouboulis et al. J Eur Acad Dermatol Venereol 2015;29(4):619–44.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6120

FRI0434 POOR QUALITY OF LIFE IN PATIENTS WITH SPONDYLOARTHRITIS IS NOT EXPLAINED BY STRUCTURAL DAMAGE. DATA FROM REGISPONSER

C. López-Medina, P. Font-Ugalde, J.L. Garrido-Castro, M.C. Castro-Villegas, J. Calvo-Gutiérrez, R. Ortega-Castro, A. Escudero-Contreras, E. Collantes-Estévez on behalf of REGISPONSER working group. *Rheumatology, Hospital Universitario Reina Sofía de Córdoba/ Imibic/ Universidad de Córdoba, Córdoba, Spain*

Background: In recent years it has become increasingly important the evaluation of the global impact of the disease in patients with Spondyloarthritis (SpA) through the use of the Patient-reported Outcomes (PROs) (1). One of the most used PROs is the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire, which refers to Health-Related Quality of Life (HRQoL). Since this is a subjective and multifactorial outcome (2), our goal is to detail the most important factors which are related with the Quality of Life (QoL) in these patients.

Objectives: To evaluate QoL in patients with SpA and to define its association with disease-related factors and patient's features.

Methods: A cross-sectional multicenter study which includes 2229 patients with SpA selected from the national Spondyloarthropaties Spanish Registry (REGISPONSER). The main outcome was the assessment of QoL performed through the ASQoL questionnaire. Subsequently, we studied its relation with different factors organized into 5 groups: sociodemographics, emotional, functionality, disease-related factors and disease activity. Univariate logistic regressions and a multiple linear regression (considering ASQoL as a qualitative dichotomous and quantitative variable respectively) were performed to relate QoL with the studied covariates.

Results: The mean ASQoL score in the entire population studied was 6.09±5.12. The average age was 47.74±13.26 years old and 698 (31.31%) were women.

In univariate logistic regressions, significant differences ($p<0.05$) were seen in many variables included in the 5 groups: poor QoL (ASQoL$\geq$9) is related with gender (female), age, mental and physical component from SF-12 questionnaire, disease duration, inflammatory back pain (IBP), alternating buttock pain, BASRI (Bath Ankylosing Spondylitis Radiographic Index), BASFI (Bath Ankylosing Spondylitis Functional Index), BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), ESR (Erythrocyte Sedimentation Rate) and global patient's VAS (Visual Analogue Scale), among others.

Finally, multivariate linear regression showed that 61.1% of the variability of ASQoL (R^2 =0.611, $p<0.001$) is explained by sex (female), physical component and 2nd item form SF-12 questionnaire (related to functionality), 6th and 7th items form SF-12 (both related to mental status), global patient's VAS, BASFI and BASDAI.

Conclusions: Poor QoL in SpA patients can be explained by high disease activity

and by a deterioration in functionality and mental status. However, clinical form of SpA, disease duration and structural damage in spine do not explain this decrease of QoL.

References:

[1] Machado P, Landewé R, Braun J, Hermann KG, Baraliakos X, Baker D, et al: A stratified model for health outcomes in ankylosing spondylitis. Ann Rheum Dis 2011;70:1758–64.

[2] Fernández-Carbadillo C, Navarro-Compán V, Castillo-Gallego C, Castro-Villegas MC, Collantes-Estévez E, de Miguel E. Disease activity is the major determinant of quality of life and physical function in patients with early axial Spondyloarthritis: Results from the ESPERANZA Cohort. Arthritis Care Res (Hoboken) 2016 Apr 25.1.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2071

FRI0435 COMPARISON BETWEEN CENTRAL AND LOCAL ASSESSMENT OF RADIOGRAPHIC SACROILIITIS IN PATIENTS WITH RECENTLY DIAGNOSED AXIAL SPONDYLOARTHRITIS IN PROOF STUDY

D. Poddubnyy[1], R.D. Inman[2], J. Sieper[1], H. Haibel[1], M. Hojnik[3]. *[1]Charité Universitätsmedizin Berlin, Berlin, Germany; [2]Toronto Western Hospital, Toronto, Canada; [3]AbbVie, Ljubljana, Slovenia*

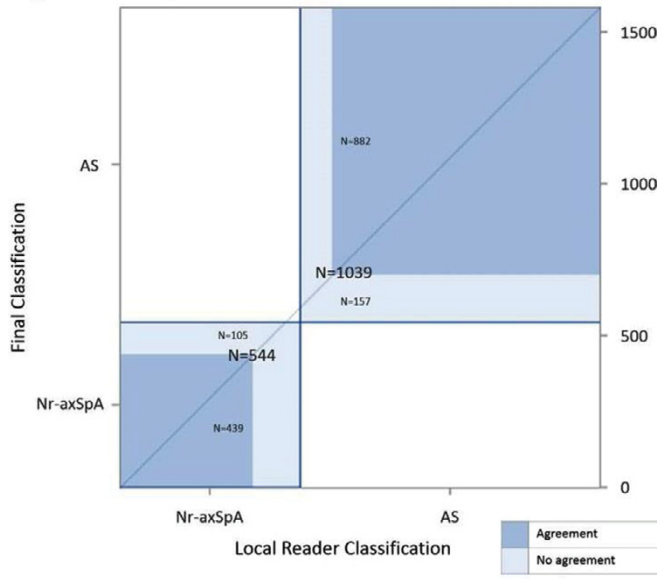
Background: High inter-reader variability of radiographic sacroiliitis assessment has been reported in a number of previous studies, suggesting its low reliability for the diagnosing and classification of axial spondyloarthritis (axSpA).

Objectives: To compare the results of local versus central scoring of radiographic sacroiliitis in a large multinational cohort of patients (pts) with recently diagnosed axSpA.

Methods: PROOF is a prospective observational study evaluating clinical and radiographic outcomes in axSpA pts in rheumatology clinical practice in 29 countries. Pts with axSpA fulfilling ASAS classification criteria were eligible if diagnosed ≤1 year prior to study enrolment. Radiographs of sacroiliac joints (SIJ) collected at baseline were graded according to the modified New York (mNY) criteria (0–4 for each SIJ). Pts with sacroiliitis of grade ≥2 bilaterally or grade ≥3 unilaterally were classified as ankylosing spondylitis (AS); otherwise pts were classified as non-radiographic axSpA (nr-axSpA). All available radiographs were assessed first by a local reader (LR) and then by a central reader (CR1), who was blinded to the results of the LR. In the case of a disagreement in the classification (AS or nr-axSpA), the radiograph was evaluated by the 2nd central reader (CR2), who was blinded to the previous assessments and the final classification was made based on the decision of 2 out of 3 readers.

Results: Of the 2126 pts enrolled in PROOF, 1583 were included in this analysis based on evaluable radiographs of the SIJ. Based on the LR judgment, 987 pts were classified as AS and 596 as nr-axSpA, while 1158 were classified as AS and 425 as nr-axSpA according to CR1. Following CR1 assessment, 1146 (72.4%) pts retained their LR classification, while 437 (27.6%) pts were classified differently. Of the 437 pts with discrepant classification assessed by CR2, 175 (40%) retained their initial LR classification and 265 (60%) were re-classified. The agreement between the CR1 and CR2 (kappa=0.24 [95% CI: 0.17–0.32]) was lower than between LR and CR1 (kappa=0.38 [95% CI: 0.33–0.42]). Finally, 1039 pts were classified as AS and 544 as axSpA; 1321 (83.5%) pts retained their initial classification and 262 (16.5%) were re-classified (157 from nr-axSpA to AS and 105 from AS to nr-axSpA). There was a substantial agreement between local and final central classification (kappa=0.64 [95% CI: 0.60–0.68], Figure). Importantly, pts initially classified by a LR as nr-axSpA (157/596, 26.3%) had significantly higher odds (odds ratio=3.0 (95% CI: 2.3–3.9) of being re-classified compared with pts classified as AS (105/987, 10.6%).

Figure. Final Classification of Patients with axSpA in Relation to Their Initial Local Classification in the PROOF Study Based on the Assessment of the Radiographic Changes in the Sacroiliac Joints.



AS = ankylosing spondylitis; nr-axSpA = non-radiographic axial spondyloarthritis.

Conclusions: In the PROOF study, the agreement between local and central classification of pts with axSpA (nr-axSpA vs AS) based on the grading of SIJ radiographs by mNY criteria was reasonably good. Pts locally classified as nr-axSpA were three times more likely to be re-classified compared with AS pts, which may be related to difficulty in the assessment of less advanced structural changes.

Acknowledgements: AbbVie funded the PROOF study, contributed to its design and participated in data collection, analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.

Disclosure of Interest: D. Poddubnyy Grant/research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, BMS, Boehringer, MSD, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, BMS, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, R. Inman Grant/research support from: AbbVie, Amgen, and Janssen, Consultant for: AbbVie, Amgen, Janssen, Lilly, Novartis, and Pfizer, J. Sieper Grant/research support from: AbbVie, Merck, and Pfizer, Consultant for: AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Janssen, Merck, Novartis, Pfizer, Roche, and UCB, H. Haibel Consultant for: Boehringer, MSD, and Novartis, Speakers bureau: AbbVie, MSD, and Pfizer., M. Hojnik Shareholder of: AbbVie, Employee of: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.1578

FRI0436 CHRONIC PAIN IN PATIENTS WITH ESTABLISHED AXIAL SPONDYLOARTHRITIS AND ASSESSMENT OF PAIN SENSITIVITY BY COMPUTERIZED PNEUMATIC CUFF PRESSURE ALGOMETRY: RESULTS FROM THE SPARTAKUS COHORT

E. Mogard[1], T. Olofsson[1], A. Bremander[2], S. Bergman[3], L.-E. Kristensen[4], J. Kvistgaard Olsen[4], J.K. Wallman[1], E. Lindqvist[1]. *[1]IKVL, Department of Rheumatology, Lund University, Lund; [2]School of Business, Engineering and Science, Halmstad University, Halmstad; [3]Primary health care unit, Department of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [4]The Parker Institute, Department of Rheumatology, Copenhagen University Hospital Fredriksberg and Bispebjerg, Copenhagen, Denmark*

Background: Pain is a common symptom in all arthritides, and remains a problem also with better treatment options. In axial spondyloarthritis (ax-SpA), data on chronic pain remain scarce.

Objectives: To study pain distribution, duration and intensity in ax-SpA, and relate this to disease status and measurement of pressure pain sensitivity.

Methods: Consecutive patients (n=115) with clinical ax-SpA diagnoses (ankylosing spondylitis (AS) or undifferentiated axial spondyloarthritis (USpA)) were examined and answered pain questionnaires. Patients were categorised as having no chronic pain (NCP), chronic regional pain (CRP) or chronic widespread pain (CWP). Pressure pain sensitivity was assessed by computerized pneumatic cuff pressure algometry (CPA) on the dominant lower leg, and pain threshold, pain tolerance and temporal summation (assessed by the temporal summation index, TSI) were recorded. Differences in disease status and pressure pain sensitivity between patients with CWP versus NCP were assessed (Chi-square or Mann-Whitney U-test). Pressure pain sensitivity was also compared between patients with/without unacceptable pain levels (VAS pain >40 versus ≤40; Mann-Whitney U-test).

Results: Fifty percent of patients reported CWP, irrespective of clinical diagnosis (AS 47%, USpA 53%), and more women than men reported CWP (59% versus 37%, p<0.001). Only 18% of all patients reported NCP. Overall, higher disease

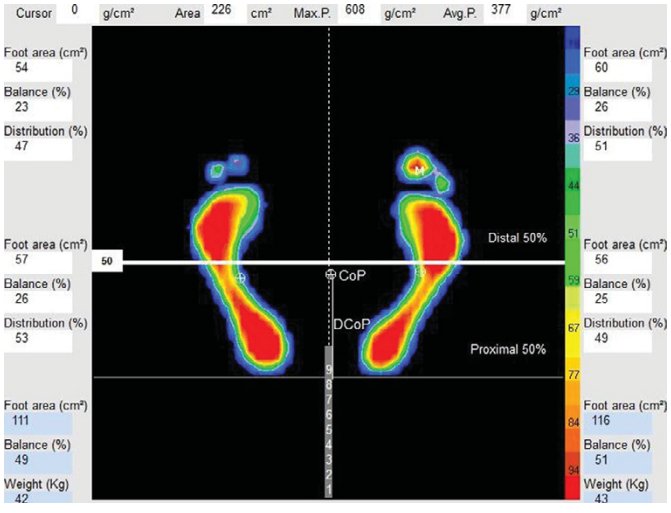
Mean (SD) unless indicated	All cases n=115	Non chronic pain (NCP) n=20	Chronic regional pain (CRP) n=38	Chronic widespread pain (CWP) n=57	NCP vs CWP p value
Female sex, n (%)	66 (57)	6 (30)	21 (55)	39 (68)	0.004
Age, years, years	53 (13)	52 (16)	49 (13)	55 (12)	0.384
Disease duration, years	25 (14)	24 (14)	22 (13)	29 (14)	0.148
HLA-B27 positive, yes (%)	83 (74)	14 (78)	30 (79)	39 (68)	0.560
AS/USpA (ICD-10) n	60/55	13/7	19/19	28/29	0.299
VAS pain, 0–100	37 (27)	15 (18)	32 (26)	49 (24)	<0.001
VAS global	38 (26)	19 (22)	32 (26)	48 (22)	<0.001
VAS fatigue	40 (28)	23 (23)	33 (28)	51 (26)	<0.001
BASDAI	3.5 (2.3)	1.6 (1.6)	3.0 (2.0)	4.9 (2.1)	<0.001
BASFI	2.5 (2.4)	1.1 (1.4)	1.8 (2.3)	3.7 (2.4)	<0.001
BASMI	3.1 (1.6)	2.9 (1.6)	2.9 (1.9)	3.3 (1.4)	0.255
ASDAS-CRP	2.1 (1.0)	1.2 (0.7)	1.8 (0.9)	2.7 (0.8)	<0.001
Pain threshold ,kPa	30.1 (14.4)	33.7 (18.1)	30.7 (11.5)	27.8 (14.8)	0.216
Pain tolerance, kPa	62.1 (26.5)	71.6 (29.5)	63.0 (25.0)	56.8 (25.6)	0.069
TSI	0.60 (0.59)	0.53 (0.46)	0.60 (0.57)	0.63 (0.66)	0.189

activity, pain intensity, worse fatigue, global health and function were observed among patients with CWP compared to those with NCP. There was a trend towards lower pain tolerance in patients with CWP compared to NCP (Table). Lower pain tolerance and higher TSI scores were observed among patients reporting VAS pain >40 versus those with VAS pain scores ≤40 ((mean (SD)) 51.9 (21.2) versus 68.1 (28.1), p=0.007; 0.73 (0.60) versus 0.55 (0.59), p=0.045).
Conclusions: In this population-based, cross-sectional study of established ax-SpA, chronic widespread pain was common, affecting 50% of the patients and generally associated with higher disease activity and worse function. CPA shows promising results regarding assessment of pain sensitivity, although larger studies are needed for more conclusive results.
Acknowledgements: Miriam Walsh-Ingelström performing all CPA assessments
Disclosure of Interest: E. Mogard: None declared, T. Olofsson: None declared, A. Bremander: None declared, S. Bergman: None declared, L.-E. Kristensen Grant/research support from: Oak Foundation, Consultant for: AbbVie, Celgene, BMS, MSD, Novartis, Pfizer, UCB, J. Kvistgaard Olsen: None declared, J. Wallman Consultant for: Celgene, Novartis, UCB, E. Lindqvist: None declared
DOI: 10.1136/annrheumdis-2017-eular.4626

FRI0437 EFFECTS OF ANKYLOSING SPONDYLITIS ON PLANTAR PRESSURE DISTRIBUTION

E. Mesci [1], N. Mesci [2], A. İçağasıoğlu [1]. *[1]Physical Therapy and Rehabilitation, Istanbul Medeniyet University Göztepe Education and Research Hospital; [2]Physical Therapy and Rehabilitation, Haydarpaşa Numune Education and Research Hospital, Istanbul, Turkey*

Background: It is considered that postural changes that occur in patients with ankylosing spondylitis (AS) are biomechanically compensated for by contribution from movements of hip, knee and ankle joints [1]. The effects of this phenomenon on the foot, the most distal segment of the kinetic chain, have not been fully elucidated.
Objectives: In the present study, our aim was to investigate possible changes in plantar load distribution in AS patients.
Methods: The study enrolled 30 AS patients diagnosed as per modified New York criteria and 30 healthy controls matched for age, gender and body mass index. Bath Ankylosing Spondylitis Metrology Index (BASMI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) scores were obtained for all patients. Using a foot pressure platform, the distance from the center of pressure (CoP) to the posterior heel line was measured in centimeters (cm) in both groups (DCoP) (figure 1). Percent total plantar load distribution over the proximal half and distal half of the foot was calculated.
Results: Mean DCoP distance was significantly shorter in AS patients 9.65±0.96 cm) in comparison to that of control group (10.41±0.89 cm) (p=0.011). While the percent total plantar pressure applied on proximal half of the foot was 60.46±7.62% in AS patients, it was only 55.95±6.21% in the control group (p=0.031). However, AS patients had less percent pressure applied on the distal half of the foot (39.53±7.62%) versus control patients (44.04±6.21%) (p=0.031). The mean ratio of the percent pressure distribution over the proximal half of the foot to the percent pressure distribution over the distal half of the foot was significantly greater in AS patients (1.64±0.62) compared to control group (1.31±0.35) (p=0.037).



Conclusions: Plantar pressure distribution seems to be displaced towards the heel in the sagittal plane due to biomechanical changes in patients with ankylosing spondylitis. This points out to the significance of the lower extremities in the compensation of postural changes in AS patients.
References:
[1] Murray HC, Elliott C, Barton SE, Murray A: Do patients with ankylosing spondylitis have poorer balance than normal subjects? Rheumatology 2000, 39:497–500.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6241

FRI0438 RISK FACTORS FOR UVEITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A RETROSPECTIVE COHORT STUDY

E.E. Lee, M.J. Kim, E.Y. Lee, Y.W. Song, E.B. Lee. *Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic Of*

Background: The uveitis is one of the most common extra-articular manifestation of ankylosing spondylitis (AS), occurring in 20–30% of the patients with AS. But it is not clear which factors are associated with the occurrence of uveitis in patients with AS.
Objectives: To evaluate the risk factors for uveitis in patients with AS.
Methods: A total of 1061 Korean patients who were diagnosed with AS at Seoul National University Hospital between January 2004 and December 2015 were evaluated in this study. Using electronic medical record review, the information on the occurrence of uveitis after AS diagnosis and the other demographic and clinical characteristic were obtained, which included age, gender, disease duration, previous history of uveitis, smoking status, Bath ankylosing spondylitis activity index, HLA-B27 positivity and level of serum inflammatory markers. After dividing the patients into those who experienced uveitis after AS diagnosis (uveitis group) and those who did not (non-uveitis group), the potential risk factors for the occurrence of uveitis were evaluated using univariable and multivariable logistic regression analysis. Receiver operating curve analysis was performed.
Results: Among the 1061 patients, 837 (78.9%) were male and their mean (SD) age was 27.9 (6.2) years. During the observation of 4231 patient-year, uveitis occurred in 142 (13.4%) patients (uveitis group). Patients in the uveitis group had longer disease duration than those in the non-uveitis group (10.0±6.6 vs. 8.2±6.2 years, p=0.003). The proportion of the patients with prior uveitis before diagnosis of AS or HLA-B27 positivity were higher in the uveitis group than those in the non-uveitis group. (58.5% vs. 12.1%, 95.7% vs.83.7%, respectively) There were no significant differences in ESR and CRP between the two groups. In the multivariable analysis, two most significant risk factors for new-onset uveitis was the prior uveitis before the diagnosis of AS (OR=11.18 [95% confidence interval (CI): 7.09–17.63]) and HLA-B27 positivity (OR=9.15 [95% CI: 1.23–68.41]). The area under the curve (AUC) of the final multivariable model was 0.809 (95% CI: 0.77–0.85).

Table 1. Risk factors for uveitis in patients with AS (n=1061)

	Uveitis group (n=142)	Non-uveitis group (n=919)	p-value
Males, n (%)	104 (73.2)	733 (79.8)	0.076
Age on symptom onset (years)	28.51±11.56	27.82±11.95	0.541
Disease duration (years)	10.03±6.60	8.22±6.21	*0.003
History of uveitis, n (%)	83 (58.5)	111 (12.1)	*<0.001
Smoking, n (%)	35 (25.0)	184 (20.3)	0.086
ESR (mm/h)	38.84±31.07	28.10±27.33	*0.001
CRP (mg/L)	1.93±2.70	1.60±2.61	0.216
HLA-B27, n (%)	135 (95.7)	764 (83.7)	*<0.001
†BASDAI	6.44±1.71	6.59±1.68	0.500

†BASDAI in AS patients who exposed to TNF inhibitors.

Multivariate analysis showed that history of uveitis and the presence of HLA-B27 as the final risk factors for the occurrence of uveitis.
Conclusions: Prior uveitis before the diagnosis of AS and HLA-B27 positivity were associated with the occurrence of uveitis. These results can be useful to predict occurrence of uveitis in patients with AS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2943

FRI0439 PSYCHIATRIC DISORDERS ASSOCIATED WITH ANKYLOSING SPONDYLITIS

F.G. Yurdakul, Y. Garip, R. Koçak Ulucaköy, E. Almaz, A. Uçkun, H. Bodur. *Physical Medicine and Rehabilitation, Ankara Numune Training and Research Hospital, Ankara, Turkey*

Background: Ankylosing spondylitis (AS) is an inflammatory rheumatic disease characterized by spinal and/or peripheral involvement, enthesitis, dactylitis, and several extra-articular manifestations. Chronic inflammation often leads to reduced spinal mobility and functional disability. The frequency of fatigue, sleep disturbance, and psychological problems has increased in AS patients (1,2).
Objectives: Although there are studies investigating depression and anxiety frequency in AS patients, different psychiatric disorders such as impulsivity, alexithymia and eating disorders have not been evaluated. The aim of this study is to investigate the frequency of different psychiatric disorders in AS patients, and to evaluate the relationship between these disorders with disease activity and functional status.
Methods: Patients with AS (n=70) and healthy controls (n=56) were included in the study. The *Ankylosing Spondylitis Disease Activity Score* (*ASDAS*), Bath Ankylosing Spondylitis Functional Index, Bath Ankylosing Spondylitis Metrology

Index (BASMI), pain visual analog scale, Beck depression scale, Beck anxiety scale, Barrat impulsiveness scale, Toronto alexithymia scale, Eating attitude test, fatigue, Ankylosing spondylitis quality of life, and Nothingam health profile were administered.

Results: The frequency of depression, anxiety and non planning impulsiveness were higher in patients with AS than in healthy controls ($p<0.05$), although no difference was found in terms of alexithymia, fatigue, and eating attitude. Depression and anxiety were correlated with high disease activity, fatigue, impaired physical functioning, and lower quality of life in the patients with AS. Non planning impulsiveness was correlated with fatigue and lower quality of life while there was no correlation with disease activity and functional impairment. BASMI scores were not associated with psychiatric disorders.

Table 1. Demographic characteristics and Psychiatric disorders in Ankylosing spondylitis and healthy controls

	Ankylosing spondylitis patients (n=70)	Healthy controls (n=56)	p
Age (year)	42.85±10.46	44.75±10.04	0.363
Male (%)	57.14%	51.78%	0.548
Beck depression score	13.88±8.99	9.78±8.34	0.006*
Beck anxiety score	14.58±10.02	10.53±8.99	0.014*
Barrat impulsiveness - attentional score	15.68±3.25	15.21±2.72	0.590
Barrat impulsiveness - motor score	19.62±4.28	18.92±4.23	0.301
Barrat impulsiveness - non planning score	26.00±4.57	24.78±3.77	0.021*
Toronto alexithymia score	54.84±12.86	54.32±11.12	0.644
Eating attitude score	21.74±11.18	22.01±13.24	0.488

*$P<0.05$.

Conclusions: Depression and anxiety were associated with disease activation, while impulsivity frequency was increased independently of disease activity. Reducing in the quality of life and functional competence due to the psychiatric disorders indicates that, AS patients may require a psychological care approach during the follow up.

References:

[1] Anxiety and depression correlate with disease and quality-of-life parameters in Chinese patients with ankylosing spondylitis.Xu X, Shen B, Zhang A, Liu J, Da Z, Liu H, Gu Z. Patient Prefer Adherence(2016) 20;10:879–85. doi: 10.2147/PPA.S86612.

[2] Relationship between psychiatric status, self-reported outcome measures, and clinicalparameters in axial spondyloarthritis. Kilic G, Kilic E, Ozgocmen S. Medicine (Baltimore) (2014) doi: 10.1097/MD.0000000000000337.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2629

FRI0440 PRESENCE OF BONE MARROW EDEMA ON MAGNETIC RESONANCE IMAGING OF THE SACROILIAC JOINTS IN MILITARY RECRUITS BEFORE AND AFTER 6 WEEKS OF INTENSIVE PHYSICAL TRAINING

G. Varkas[1,2], M. de Hooge[1], T. Renson[1], P. Carron[1,2], S. De Mits[3], G. Souverijns[4], D. Elewaut[1,2], F. Van den Bosch[1,2]. *[1]Department of Rheumatology, Ghent University Hospital; [2]VIB Inflammation Research Centre; [3]Department of Rehabilitation Sciences and Physical Therapy, Ghent University, Gent; [4]Department of Radiology, Jessa Ziekenhuis, Hasselt, Belgium*

Background: Studies have shown an increase of bone marrow edema (BME) on magnetic resonance imaging (MRI), especially in feet and ankles of professional athletes and in minimally active healthy controls after mechanical stress [1]. Although this has been described for several joints and across different sport activities, information concerning BME in the sacroiliac joints (SIJ) has not been studied. In axial spondyloarthritis (AxSpA), the presence of 1 BME lesion (characteristics typical for AxSpA) on 2 consecutive slices or 2 BME lesions on 1 slice is sufficient to fulfill the definition of a positive MRI as defined by ASAS. Although this definition should only be applied on MRI of symptomatic patients with suspicion of SpA, it is unknown whether BME lesions in healthy controls could meet this definition and therefore incorrectly be interpreted as BME in the context of SpA.

Objectives: Study the effect of intense physical training in healthy subjects on the presence of BME on MRI-SIJ, by investigating whether healthy subjects meet the ASAS definition of a positive MRI and whether this is modulated by mechanical stress.

Methods: Twenty-two military recruits underwent a MRI-SIJ before and after 6 week of intense and uniform physical training. BME lesions were scored by 3 trained readers (MdH, GV and TR) blinded for time sequence and clinical findings. Additionally, the agreement with the definition of a positive MRI defined by ASAS was evaluated. Regarding the number of lesions and fulfillment of the ASAS definition of positive MRI, a consensus was made by agreement of 2 out of 3 readers.

Results: In total, 86.4% (19/22) asymptomatic recruits were male (mean age of 25.0±0.8 years). At baseline, 40.9% (9/22) of recruits presented with at least one BME lesion, whereas this number increased to 50.0% (11/22) at week 6. Indeed, 3 recruits developed BME over time, whereas in one recruit the BME lesions disappeared over time. The mean number of BME lesions was 1.0 (±0.3) at baseline, compared to 1.9 (±0.7) at week 6. Median (25th, 75th percentile) BME lesions were 0.0 (0.0, 2.25) and 0.5 (0.0, 3.0) at respectively baseline and week 6 (P=0.109). Mean change in BME lesions was 0.9 (±0.6). When applying the ASAS definition of a positive MRI, BME was present in 22.7% (5/22) of recruits at baseline, and this increased to 36.4% at follow up, of which an additional 4 initially MRI negative recruits became MRI positive and one recruit no longer fulfilled the definition.

Conclusions: In this small exploratory study we could not find a statistically significant difference in BME on MRI-SIJ after 6 weeks of training. However, over 1/5 of asymptomatic recruits displayed BME lesions, that would meet the ASAS definition of a positive MRI, increasing to more than 1/3 at follow up. Thus, in young active patients, the interpretation of BME lesions should be cautious.

References:

[1] Kornaat PR, Van de Velde SK. Bone marrow edema lesions in the professional runner. The American journal of sports medicine 2014;42(5):1242–6.

Acknowledgements: ASAS research grant 2017.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5947

FRI0441 NECK PAIN IN ANKYLOSING SPONDYLITIS: FOCUS ON ACTIVE INFLAMMATION AT THE CRANIOCERVICAL JUNCTION ON MRI

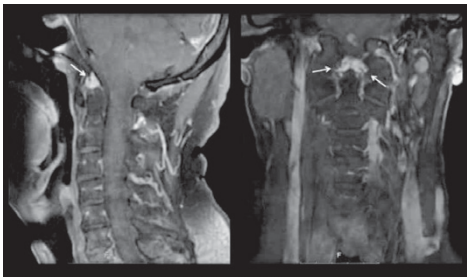
G. Slobodin[1], I. Rosner[1], A. Awisat[1], D. Rimar[1], A. Shpigelman[2], D. Militianu[3]. *[1]Rheumatology; [2]Orthopedic Surgery, Bnai Zion Medical Center; [3]Radiology/Muskulosceletal Imaging, Rambam Medical Center, haifa, Israel*

Background: A wide spectrum of structural changes in the elements of craniocervical junction in patients with ankylosing spondylitis (AS) has been recently described in a retrospective study using computed tomography [1]. The clinical significance of these findings requires further elaboration.

Objectives: To explore and describe inflammatory MR imaging findings in the craniocervical junction in patients with AS and neck pain.

Methods: Eighteen patients with AS and continuing neck pain, as well as 9 patients with fibromyalgia of the same age and similar level of severity of neck pain, who served as a control group, underwent relevant rheumatologic examination, X-ray of cervical spine and MRI study, which included STIR, CUBE T2, FSE and FSE FAT SAT sequences before and after administration of gadolinium.

Results: In the AS group, 12 males and 6 females diagnosed by 1984 New York criteria, of median age 40.5 years (range 31–61 years) and median disease duration of 8 (range 1–35) years, with 13 under treatment with anti-TNF agents were studied. All patients suffered from neck pain, with median VAS of 7 (range 2.5–10). Range of neck spine motion was limited in all but 3 patients. Seven of 18 patients had evidence of cervical syndesmophytes on X-ray. In addition to expected findings of syndesmophytes, active inflammatory lesions were seen in MR imaging in two of 18 patients with AS and in none with fibromyalgia (Fig. 1). Both AS patients with positive MRI were on anti-TNF therapy during the study and did not have syndesmophytes at the cervical spine as also by X-ray films.



Sagittal and coronal FSE T1 FAT SAT images after gadolinium injection showing enhancement of apical and alar ligaments

Conclusions: Active inflammation of both entheses and joints of the craniocervical junction was demonstrated by MRI in some patients with AS and persistent neck pain. Active lesions at the craniocervical junction should be included in the differential diagnosis of neck pain in AS.

References:

[1] Slobodin G, Shpigelman A, Dawood H, Rimar D, Croitoru S, Boulman N, Rozenbaum M, Kaly L, Rosner I, Odeh M. Craniocervical junction involvement in ankylosing spondylitis. Eur Spine J. 2015 Dec;24(12):2986–90.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5818

FRI0442 IDENTIFICATION OF ENTHESITIS AT THE ACHILLES TENDON INSERTION IN PATIENTS WITH ANKYLOSING SPONDYLITIS USING DIGITAL RADIOGRAPHY

I. Sung, S.-J. Kim. *Orthopedic Department, Hanyang University Medical Center, SEOUL, KOREA, Seoul, Korea, Republic Of*

Background: Posterior heel pain is a common symptom in the foot and ankle region, with many different causes that need to be distinguished by differential diagnosis. Among them is ankylosing spondylitis (AS), in which enthesitis of

the heel is common and occasionally is responsible for their initial symptom to seek clinics. An early or timely recognition of active enthesitis of AS from simple radiographs comes to be relevant issue.

Objectives: The purpose of current study is to assess measurement reliability and diagnostic validity for detecting the digital radiographic findings of enthesitis at the Achilles tendon insertion in patients with AS.

Methods: Current study is a blinded, matched, cross-sectional study with 44 patients (65 feet) having clinical enthesitis at the Achilles tendon insertion (Group I), and 44 healthy controls (65 feet) (Group II). Suggested findings of enthesitis including retrocalcaneal recess obliterations from retrocalcaneal bursitis, increased thickness in shadow of the Achilles tendon and posterior soft tissue at its insertion from the swellings of those soft tissues were assessed on digital radiographs of standing hindfoot lateral view, and their measurement reliabilities were determined. To investigate diagnostic validities, diagnostic odds ratio, sensitivity, specificity, positive likelihood ratio (PLR), and negative likelihood ratio (NLR) were estimated for radiographic findings of retrocalcaneal recess obliterations (RRO). For the thickness of the Achilles at its insertion (TAI) and swollen posterior soft tissue, the receiver operating characteristic (ROC) curve analysis was done.

Results: There were no significant differences between two groups in mean age, BMI and sex ratio. Intra- and inter-observer reliability of all measurements showed high degree of agreements (0.786 to 0.941). The diagnostic odds ratio of RRO for detecting enthesitis was 66.0. The sensitivity, specificity were 67.7%, 96.9%, and PLR, NLR were 22.0, 0.33, respectively. The mean TAI of Group I and II were 6.7mm±1.79, 5.01mm±0.81, respectively (p-value$<$0.001). Area under the ROC curve of the TAI was 0.806, and the optimal cut-off value predicting enthesitis was 5.47mm, and its sensitivity and specificity were both 72.3%.

Conclusions: Retrocalcaneal recess obliteration and thickened shadow of Achilles tendon at its insertion and swollen posterior soft tissue on digital radiographs of standing hindfoot lateral view are regarded as the easy and useful findings for enthesitis of the posterior heel. For searching enthesitis at the Achilles insertion in patients with AS, such findings from simple radiographs showed high measurement reliability and validity.

References:

[1] Resnick D, Feingold ML, Curd J, Niwayama G, Goergen TG. Calcaneal abnormalities in articular disorders. Rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and Reiter syndrome. Radiology 1977;125:355–66.
[2] Freedman M, Steller D. Digital radiography of the musculoskeletal system: the optimal image. Journal of digital imaging 1995;8:37–42.
[3] Rudwaleit M, Khan MA, Sieper J. The challenge of diagnosis and classification in early ankylosing spondylitis: do we need new criteria? Arthritis and rheumatism 2005;52(4):1000–1008.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4565

FRI0443 THE EFFECT OF FIBROMYALGIA ON DISEASE ACTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

I. Shapoval, M. Stanislavchuk, K. Zaichko, L. Perebetiuk. *Internal Medicine, National Pirogov Memorial Medical University, Vinnytsya, Ukraine*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that affects the axial skeleton and characterized by pain, stiffness and fatigue [4]. One of the frequent concomitant condition in patients with AS is fibromyalgia (FM). FM shares some common symptoms with AS. According to the many reports concomitant FM in patients with AS has been found in 5.7 - 41.3% cases [1, 2, 3, 5]. Due to the fact that pain is a major component of the disease activity scores of the AS (Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS)), concomitant FM can significantly modify the disease activity in patients with AS.

Objectives: The aim of this study was to evaluate the effect of FM on disease activity in patients with AS.

Methods: Diagnosis of AS was identified according to the modified New York criteria (1984). FM was diagnosed by ACR criteria (1990). Disease activity was assessed by BASDAI and ASDAS.

Results: 80 patients with AS were included into study (15 females and 65 males), age (M ± SD) 41.64±11.4 years. Nineteen patients (23.8%) met the criteria for FM. Patients with AS and AS+FM were representative for age and disease duration. In both groups, ESR (37.7±18.8 and 39.00±19.6 mm/h) was comparable, while ASDAS and BASDAI were significantly different. The disease activity according to both scores was higher in patients with AS+FM. According to the BASDAI in patients with AS disease activity was 5.20±1.4 whereas in patients with AS and FM - 7.14±1.7; according to the ASDAS-ESR difference in disease activity was slightly lower, but remained significant (3.6±0.8 vs 4.2±0.9).

Conclusions: The obtained data indicates that concomitant FM is a frequent condition in patients with AS. Presence of FM in patients with AS significantly modifies the disease activity determined by ASDAS. The ASDAS-ESR is more appropriate for determining the disease activity comparing to BASDAI, because included in calculation ESR diminish the distorting effect of FM.

References:

[1] Fibromyalgia in patients with axial spondyloarthritis: epidemiological profile and effect on measures of disease activity/Fausto Salaffi, Rossella De Angelis, Marina Carottiet al. Rheumatology International 2014;1103–1110.
[2] Occurrence of fibromyalgia in patients with ankylosing spondylitis. /ValderilioFeijó Azevedo, Eduardo dos Santos Paiva, Lúcio Ricardo HiurkoFelippe, Ranieri Amorim Moreira. Bras J Rheumatol 2010;50:646–654.
[3] Ankylosing spondylitis functional and activity indices in clinical practice. Popescu C, Trandafir M, Bădică AM et al. Journal of Medicine and Life 2014:78–83.
[4] Global prevalence of ankylosing spondylitis. Linda E. Dean, Gareth T. Jones, Alan G. MacDonald et al. Rheumatology 2014;53:650–657.
[5] Prevalence of fibromyalgia in patients with ankylosing spondylitis Medical Journal of Dr. D.Y. Patil University 2014:338–341.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3967

FRI0444 INCIDENCE OF INFLAMMATORY BOWEL DISEASE EVENTS IN ADALIMUMAB CLINICAL TRIALS ACROSS INDICATIONS

J.R. Curtis[1], D. Elewaut[2], S. Chen[3], M. Hojnik[4], N. Naveh[5], J.K. Anderson[3]. *[1]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, United States; [2]VIB Inflammation Research Center, University of Gent, Gent, Belgium; [3]AbbVie Inc., North Chicago, United States; [4]AbbVie, Ljubljana, Slovenia; [5]AbbVie, Hod HaSharon, Israel*

Background: Adalimumab (ADA) is approved for treatment of Crohn's disease (CD) and ulcerative colitis (UC); therefore, it is postulated that new onset or flare of inflammatory bowel disease (IBD) is a rare occurrence in ADA clinical trials for non-IBD indications.

Objectives: The purpose of this analysis was to determine the rates of IBD adverse events (AEs) in ADA clinical trials, particularly in spondyloarthritis (SpA) patients (pts) who are at higher risk of IBD as a feature of SpA.

Methods: The rates of IBD AEs in 73 phase 2–4 interventional ADA clinical trials in rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (pJIA), pediatric enthesitis-related arthritis, uveitis (non-infectious intermediate, posterior, or pan-uveitis), hidradenitis suppurativa (HS), adult and pediatric psoriasis (Ps), psoriatic arthritis (PsA), non-PsA peripheral SpA (pSpA), non-radiographic axial spondyloarthritis (nr-axSpA), and ankylosing spondylitis (AS) were analyzed (trials in UC, CD, and intestinal Behcet's disease [BD] were excluded). The search criteria for IBD events included the following standardized MedDRA queries preferred terms: inflammatory bowel disease (IBD), ulcerative colitis (UC), Crohn's disease (CD), IBD-not otherwise specified (NOS), and ulcerative proctitis. The incidence rates (IR) for events of IBD (combined new onset and flare) in interventional clinical trials of ADA are reported as events per 100 pt-years (PY). 95% confidence intervals (CI) were based on exact Poisson confidence limits.

Results: ADA was administered to 23735 pts, representing 36404.6 PY of exposure. Overall, the IR for IBD events in all interventional ADA trials included in this analysis was 0.1/100PY (Table). The rates of IBD events varied across therapeutic indications from $<$0.1 to 0.8/100PY. There were no reports of IBD events in pediatric pts. The IR for IBD events in RA, uveitis, HS, and Ps trials were $<$0.1, 0.2, 0.4, and $<$0.1/100 PY. In SpA, the overall rates of IBD were 0.5/100 PY, while the rates were 0, 0.8, 0.5, and 0.7/100 PY in PsA, non-PsA pSpA, nr-axSpA, and AS, respectively. 2216 pts with axSpA (AS: 2026, nr-axSpA: 190) were exposed to ADA; in AS, 14 IBD events (7 new onset and 7 flares) were reported in 12 pts (7 new onset and 5 flares), while in nr-axSpA, 2 IBD events were reported in 1 pt (2 flares).

Table. Incidence of IBD events in patients from ADA clinical trials.

Indication	N (PYs)	All IBD AEs, n[§]	IR/100 PY (95% CI)
All ADA trials[†]	23735 (36404.6)	40	0.1 (0.1 – 0.2)
Rheumatoid Arthritis	15152 (24813.0)	16	<0.1 (0.0 – 0.1)
Uveitis	387 (538.8)	1	0.2 (0.0 – 1.0)
Hidradenitis suppurativa	733 (836.3)	3	0.4 (0.1 – 1.1)
Psoriasis	3500 (5268.7)	1	<0.1 (0.0 – 0.1)
All SpA[‡]	3218 (3919.9)	19	0.5 (0.3 – 0.8)
PsA	837 (997.5)	0	0.0 (0.0 – 0.4)
Non-PsA pSpA	165 (390.7)	3	0.8 (0.2 – 2.2)
All axSpA[?]	2216 (2531.7)	16	0.6 (0.4 – 1.0)
nr-axSpA	190 (412.2)	2	0.5 (0.1 – 1.8)
AS	2026 (2119.5)	14	0.7 (0.4 – 1.1)

[§]No IBD events were reported in pediatric patients.
[†]All ADA adult and pediatric patients in all interventional studies excluding Crohn's disease, ulcerative colitis, and intestinal Behcet's disease.
[‡]All ADA patients in all interventional studies of PsA, non -PsA pSpA, nr-axSpA, and AS.
[?]All ADA patients in all interventional studies of nr -axSpA and AS.
Abbreviations: IBD = inflammatory bowel disease; ADA = adalimumab; PY = patient years; AEs = adverse events; IR = incidence rates; CI = confidence interval; SpA = spondyloarthritis; PsA = psoriatic arthritis; pSpA = non-PsA peripheral spondyloarthritis; axSpA = axial spondyloarthritis; nr-axSpA = non-radiographic axSpA; AS = ankylosing spondylitis.

Conclusions: The rates of IBD AEs in ADA clinical trials were generally low across all indications, with all events occurring in adult pts. In AS pts, who are at increased risk of manifesting IBD, the rates of IBD for pts treated with ADA (0.7/100 PY [95% CI, 0.4–1.1]) were similar to published placebo rates pooled

across multiple clinical trials (1.3/100 PY [95% CI, 0.2–4.8]).[1] In pts at risk for IBD requiring biologic therapy, ADA is a reasonable therapeutic option based on the observed low IBD event rates in ADA clinical trials and its demonstrated efficacy in treating UC and CD pts.

References:
[1] Braun, J. et al., Arthritis & Rheum, 2007; 57:639–47.

Acknowledgements: AbbVie funded the studies, contributed to their design, and participated in data collection, analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.

Disclosure of Interest: J. R. Curtis Grant/research support from: Amgen, BMS, CORRONA, Crescendo, Janssen, Pfizer, and UCB., Consultant for: Amgen, BMS, CORRONA, Crescendo, Janssen, Pfizer, and UCB., D. Elewaut Grant/research support from: AbbVie, Consultant for: AbbVie, Speakers bureau: AbbVie, S. Chen Shareholder of: AbbVie, Employee of: AbbVie, M. Hojnik Shareholder of: AbbVie, Employee of: AbbVie, N. Naveh Shareholder of: AbbVie, Employee of: AbbVie, J. K. Anderson Shareholder of: AbbVie, Employee of: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.2008

FRI0445 FAECAL CALPROTECTIN, BUT NOT ANTI-SACCHAROMYCES CEREVISIAE ANTIBODIES, IS LINKED TO WORSE DISEASE STATUS IN AXIAL SPONDYLOARTHRITIS PATIENTS WITHOUT INFLAMMATORY BOWEL DISEASE: RESULTS FROM THE SPARTAKUS COHORT

T. Olofsson[1], E. Mogard[1], K. Andréasson[1], J. Marsal[2], M. Geijer[3], L.-E. Kristensen[1,4], E. Lindqvist[1], J.K. Wallman[1]. *[1]Department of clinical sciences Lund, Rheumatology; [2]Department of clinical sciences Lund, Gastroenterology, Lund University, Lund; [3]Department of Radiology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden; [4]The Parker Institute, Department of Rheumatology, Copenhagen University Hospital, Frederiksberg and Bispebjerg, Copenhagen, Denmark*

Background: Inflammatory bowel disease (IBD) is a common comorbidity in axial spondyloarthritis.
Objectives: To study faecal calprotectin (F-calprotectin) levels and anti-*Saccharomyces cerevisiae* antibodies (ASCA) and their associations with disease status and gastrointestinal (GI) symptoms in axial spondyloarthritis.
Methods: Consecutive patients with a clinical axial spondyloarthritis diagnosis were examined and classified as non-radiographic axial spondyloarthritis (nr-axSpA; Assessment of SpondyloArthritis international Society [ASAS] criteria; n=26) or ankylosing spondylitis (AS; modified New York criteria; n=45). Only patients without known IBD were included. F-calprotectin and ASCA IgA and IgG antibodies in serum were measured by commercially available enzyme-linked immunosorbent assay kits (Calpro AS; ORGENTEC Diagnostika).
Results: Elevated levels of F-calprotectin (≥50 mg/kg) were observed in 15% of nr-axSpA and 40% of AS patients (non-significant difference, with reservation for small groups). Overall, worse mean disease activity/disability scores were observed among patients with elevated versus normal F-calprotectin levels (Table), whereas no association was seen between F-calprotectin and GI symptoms. Similar results remained after exclusion of patients with monoclonal antibody type anti-TNF therapy. Elevated levels of ASCA IgA were observed in 8%/2% of nr-axSpA/AS patients, and IgG in 28%/26%. Only 2 subjects were ASCA double positive. Neither disease activity/disability measures nor GI symptoms were associated with ASCA status.

	Nr-axSpA (n=26)	AS (n=45)	F-Calprotectin <50 mg/kg (n=38)	F-Calprotectin ≥50 mg/kg (n=18)	p-value*
Male sex	10 (39%)	26 (59%)	16 (42%)	10 (56%)	0.346
Age, years	45 (10)	58 (13)	54 (13)	55 (14)	0.847
Disease duration, years	18 (10)	32 (14)	26 (14)	31 (15)	0.339
HLA-B27 positive, y/n	24 (92%)	38 (86%)	32 (84%)	17 (100%)	0.083
ASAS 3m NSAID score	25 (37)	31 (36)	21 (33)	37 (40)	0.221
Antibody anti-TNF, y/n	10 (39%)	12 (27%)	14 (36%)	4 (22%)	0.274
VAS global	41 (21)	35 (25)	32 (25)	45 (16)	0.023
VAS pain	40 (23)	37 (28)	34 (26)	42 (23)	0.142
VAS fatigue	41 (28)	39 (27)	34 (28)	46 (21)	0.056
BASDAI	3.5 (1.7)	3.5 (2.6)	3.1 (2.3)	4.2 (2.3)	0.076
BASFI	1.9 (1.4)	3.0 (2.9)	2.2 (2.2)	3.9 (3.1)	0.029
ASDAS-CRP	2.0 (0.8)	2.2 (1.1)	1.8 (0.9)	2.6 (0.9)	0.034
CRP, mg/L	3.1 (3.0)	4.7 (4.6)	3.0 (2.7)	5.7 (5.5)	0.157
F-calprotectin, mg/kg	45 (64)	84 (117)	21 (13)	172 (129)	NA
ASCA IgA, E/ml	3.7 (7.3)	2.1 (1.9)	2.9 (5.8)	3.0 (3.8)	0.175
ASCA IgG, E/ml	10 (20)	6.5 (6.3)	6.9 (6.8)	11 (24)	0.854
Often stomach pain, y/n	17 (65%)	25 (56%)	23 (61%)	11 (61%)	0.967
Frequent defecation, y/n	7 (27%)	9 (20%)	9 (24%)	5 (28%)	0.741
Frequent diarrhoea, y/n	12 (46%)	12 (27%)	12 (32%)	8 (44%)	0.348

N (%) or mean (SD). *Chi^2/Mann-Whitney U-test for comparison of categorical/continuous variables between the F-calprotectin groups. Missing data: ASCA IgA/IgG 4%, F-calprotectin 21%. y/n, yes/no; 3m, 3 months; NA, not applicable.

Conclusions: Elevated levels of F-calprotectin and ASCA IgG antibodies are both common in axial spondyloarthritis patients without IBD, and elevated F-calprotectin may be a marker of more severe spondyloarthritis. Neither F-calprotectin nor ASCA levels were associated with self-reported GI symptoms.

Disclosure of Interest: T. Olofsson: None declared, E. Mogard: None declared, K. Andréasson: None declared, J. Marsal Grant/research support from: AbbVie, Ferring, Hospira, Consultant for: AbbVie, Ferring, Hospira, MSD, Pfizer, Takeda, Tillotts, UCB, M. Geijer: None declared, L.-E. Kristensen Grant/research support from: Oak Foundation, Consultant for: AbbVie, Celgene, BMS, MSD, Novartis, Pfizer, UCB, E. Lindqvist: None declared, J. Wallman Consultant for: Celgene, Novartis, UCB

DOI: 10.1136/annrheumdis-2017-eular.2391

FRI0446 PREVALENCE AND CHARACTERISTICS OF SPONDYLOARTHRITIS ACCORDING TO ASAS CRITERIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE – RESULTS FROM THE SPICE COHORT

J. Haschka[1,2], S. Hirschmann[3], A. Kleyer[1], M. Englbrecht[1], J. Zimmermann[1], F. Faustini[1], D. Simon[1], C.P. Figueiredo[1], A. Cavallaro[1,4], C. Muschitz[2], R. Kocijan[2], H. Resch[2], R. Atreya[3], J. Rech[1], M.F. Neurath[3], G. Schett[1]. *[1]Department of Internal Medicine 3, University of Erlangen-Nuremberg, Erlangen, Germany; [2]Medical Department 2, St. Vincent Hospital, The VINFORCE Study Group, Vienna, Austria; [3]Department of Internal Medicine 1, University of Erlangen-Nuremberg, Erlangen, Germany; [4]Div. of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil*

Background: Musculoskeletal symptoms are considered as one of the most frequent extra-intestinal manifestation in Inflammatory Bowel Disease (IBD) patients with a prevalence of up to 40% involving axial and/or peripheral joints. Data on the prevalence of musculoskeletal disease, in particular of SpA are limited and vary considerably due to different criteria the studies have used to define musculoskeletal disease in IBD patients.
Objectives: To define the prevalence of axial and peripheral spondyloarthritis (SpA) according to Assessment of Spondyloarthritis International Society (ASAS) in patients with Crohn's disease (CD) and ulcerative colitis (UC).
Methods: The SPICE cohort (Spondyloarthritis in Inflammatory Bowel Disease Cohort Erlangen) comprises prospectively recruited colonoscopy- proven Crohn's Disease (CD) or Ulcerative Colitis (UC) patients, who received a pre-defined and standardized musculoskeletal assessment by the rheumatologist. Duration and activity of gastrointestinal and rheumatic disease (axial and peripheral) was documented and fulfillment of ASAS classification criteria for axial and peripheral SpA was tested.
Results: 102 IBD patients (62 with CD and 40 with UC) with a median (IQR) disease of 11.0 (18.0) years were assessed. 38.2% fulfilled ASAS criteria for SpA with no difference between CD and UC. ASAS axial SpA criteria were fulfilled by 12%, ASAS peripheral SpA criteria by 31.4% of the IBD patients. Inflammatory back pain was present in 24.5% with MRI signs of sacroiliitis in 48% of IBD patients with inflammatory back pain. Disease activity according to ASDAS-CRP was moderate to high in 91% of the patients with axial SpA. Peripheral arthralgia was present in 71.6%, while arthritis was found in 18.6% of the IBD patients.
Conclusions: Both major forms of IBD show a similar burden of musculoskeletal disease. More than one third of inflammatory bowel disease patients show axial or peripheral SpA according to ASAS criteria. Peripheral SpA is more commonly found than axial SpA.

References:
[1] Harbord M, Annese V, Vavricka SR, et al. The first European evidence-based consensus on extra-intestinal manifestations in inflammatory bowel disease. J Crohn Colitis 2016; 239–254.
[2] Karreman MC, Luime JJ, Hazes JMW, Weel AEAM. The prevalence and incidence of axial and peripheral spondyloarthritis in inflammatory bowel disease: a systematic literature review and meta-analysis. J Crohn Colitis 2016; 1–12.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2393

FRI0447 SEVERITY OF SACROILIITIS AND ERYTHROCYTE SEDIMENTATION RATE ARE ASSOCIATED WITH A LOW TRABECULAR BONE SCORE IN YOUNG MALE PATIENTS WITH ANKYLOSING SPONDYLITIS

K.Y. Kang. *Division of Rheumatology, Internal Medicine, Catholic University of Korea, Seoul, Korea, Republic Of*

Background: The trabecular bone score (TBS) is a novel method used to evaluate bone microarchitecture. To date, the risk factors associated with a low TBS in AS are unknown and no study has examined the association between TBS and vertebral fracture in ankylosing spondylitis (AS) patients.
Objectives: To examine factors related to a low trabecular bone score (TBS) and the association between TBS and vertebral fracture in patients with (AS).
Methods: One hundred patients (all male, aged <50 years) who fulfilled the modified New York criteria for the classification of AS were enrolled. The TBS and bone mineral density (BMD) were assessed using dual-energy X-ray absorptiometry (DXA). Clinical variables, inflammatory markers, and the presence of vertebral fracture were also assessed. Spinal radiographic progression was measured using the Stokes AS spine score (SASSS). Multivariate linear regression analysis was performed to identify factors associated with TBS.

Results: The mean TBS at the lumbar spine was 1.38±0.13. The TBS showed a negative correlation with disease duration and inflammatory markers, and a positive correlation with BMD at the lumbar spine, femoral neck, and total hip. It also showed a negative correlation with sacroiliitis grade. BMD at the lumbar spine positively correlated with SASSS, whereas TBS showed a negative correlation. A significant decrease in TBS values was observed in patients with spinal radiographic progression (p=0.001). Multivariate analysis showed that ESR and sacroiliitis were independently associated with TBS (p=0.006 and <0.001, respectively). Ten patients had morphometric vertebral fractures. The mean TBS was lower in patients with vertebral fracture than in age-matched patients without fracture (p=0.028).
Conclusions: The TBS in young male patients with AS is associated with the ESR and severity of sacroiliitis. The TBS may be useful as a tool for assessing osteoporosis in AS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1254

FRI0448 EVALUATION OF SUPPURATIVE HIDRADENITIS IN PATIENTS WITH CHRONIC ARTHRITIS TREATED WITH FULL AND TAPERED BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

L. Valor, D. Hernández-Flórez, T. del Río, J.G. Ovalles B, J. Martínez Barrio, I. Janta, B. Serrano, J.C. Nieto, M. Correyero Plaza, L. Garcia Montoya, C. González, F.J. López-Longo, I. Monteagudo. *Hospital General Universitario Gregorio Marañón, Madrid, Spain*

Background: Suppurative Hidradenitis (SH) is an inflammatory skin disease which often responds poorly to treatment. It is a disorder of the apocrine glands (axillary, inguinal and anogenital regions) that can result in infection, inflamed nodules, cysts, abscesses and sinus tracts. There is a 1–4% incidence of SH in patients with spondyloarthropathies and inflammatory bowel disease, possibly due to innate immune system deregulation. The use of biological disease-modifying antirheumatic drugs (bDMARD), specifically tumor necrosis factor inhibitors, has been useful in cases when other therapies fail.
Objectives: To evaluate the prevalence of SH using the SH-questionnaire in bDMARD-treated chronic arthritis patients.
Methods: This cross-sectional study included 325 patients diagnosed with chronic arthritis. Patients were recruited consecutively from the Biological Therapy Unit of the Hospital General Universitario Gregorio Marañón and evaluated from January to March of 2015. All patients had been undergoing full or tapered bDMARD treatment for at least 1 year and none had any history of SH. Those patients deemed to be in clinical remission were on tapered bDMARD dosage. All patients self-completed the validated SH-questionnaire (1) which was considered positive when one answer was affirmative and when lesions presented in >1 anatomical location. Patient pathologies were subclassified into 2 groups: i) peripheral arthritis (PerAR) which includes rheumatoid arthritis (RA), psoriatic arthritis (PsA) and peripheral spondyloarthropathies (PerSpA); ii) axial spondyloarthropathies (AxSpA). Clinical evaluation was performed by the same physician for all patients. Demographic, clinical and laboratory variables were recorded and disease status was assessed through the relevant clinical index, i.e.DAS28-ESR, DAS28-CRP, SDAI, CDAI, BASDAI, BASFI, ASDAS-CRP.
Results: SH-positive was observed in 25/325 (7.7% vs. 92.3%) patients. Of these 25 patients, 12 (48%) were female and 13 (52%) male. Mean age was 52 years (SD±12.9) and mean time since diagnosis was 14 years (SD±9.3). Twenty-four out of 25 patients were undergoing anti-TNF treatment (ETN=10, GOL=7, ADL=6, CTZ=1). Eighty-four per cent of patients were undergoing full bDMARD dosage with the remaining 16% on tapered. By subset pathology, 13 SH positives were PerAR type and 12 were AxSpA (5.8% vs. 11.8%, p=0.062). On analysis of PerAR subtypes, we found 6 patients had PsA and 5 RA. Evaluating clinical disease activity, we found 9/13 patients in the PerAR group to be in clinical remission according to DAS28-ESR and CDAI (p=0.02 for both). Additionally, we found only 4/12 patients in remission in the AxSpA group as defined under BASDAI, BASFI and ASDAS-CRP (p=0.006, p=0.005, p=0.004, respectively).
Conclusions: We found more SH-positives in the AxSpA than in the PerAR group, which is consistent with published data. A bDMARD tapered dosage was related to SH-positivity which might be linked to persistent and undetectable chronic inflammation.
References:
[1] Esmann S, et al. Br J Dermatol. 2010 Jul;163(1):102–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4737

FRI0449 ANALYSIS OF THE CANADIAN ADALIMUMAB POST-MARKETING OBSERVATIONAL EPIDEMIOLOGICAL STUDY ASSESSING EFFECTIVENESS IN ANKYLOSING SPONDYLITIS (COMPLETE-AS): ASSOCIATION BETWEEN BASELINE EXTRA ARTICULAR MANIFESTATIONS AND PATIENT-REPORTED OUTCOMES

L. Bessette[1,2], B. Haraoui[3], M. Khraishi[4], W. Bensen[5], V.P. Remple[6,7]. *[1]Faculty of Medicine, Université Laval; [2]Centre Hospitalier de l'Université Laval, Quebec; [3]Centre Hospitalier de l'Université de Montréal, Montreal; [4]Faculty of Medicine, Memorial University of Newfoundland, St. John's; [5]Division of Rheumatology, McMaster University, Hamilton; [6]School of Population and Public Health, University of British Columbia, Vancouver; [7]AbbVie Corp., Montreal, Canada*

Background: Ankylosing spondylitis (AS) is an immune mediated inflammatory disease. Although characterized by axial and peripheral joint manifestations, extra articular manifestations (EAMs) are a common clinical feature. EAMs have been found to negatively impact health outcomes including quality of life and work capacity.
Objectives: The aim of this analysis was to describe the prevalence of EAMs at baseline and assess their association with patient-reported outcomes (PROs) in a Canadian routine clinical care setting.
Methods: COMPLETE-AS is an ongoing observational study expected to enroll 1120 AS patients from 60–80 sites across Canada. All patients enrolled between June/2011 - October/2015 were included in this analysis. Eligible patients are anti-TNFα naïve adults, with active AS as per the judgment of the treating physician, who require change in current AS treatment. Baseline disease parameters assessed were EAMs (collected from medical chart, physician assessment or patient report), disease activity (BASDAI) and functional status (BASFI); baseline PROs assessed were related to mental health (BDI-II), work limitations (WLQ), and quality of life (QoL; SF-36 Physical (PCS) and Mental (MCS) component summaries). Multivariate linear regression models adjusting for baseline BASDAI and BASFI assessed the impact of EAMs on PROs.
Results: A total of 569 patients were included in the current analysis. Mean (SD) age and duration of disease was 43.3 (13.4) and 5.9 (9.8) years, respectively. The majority of patients enrolled were male (57.1%), Caucasian (86.1%), HLA $B27^+$ (67.0%), and RF^- (93.7%). The most common baseline EAM reported was enthesitis (15.3%), followed by psoriasis (13.0%), inflammatory bowel disease (IBD; 9.1%), and uveitis (3.2%). EAM combination 1 (EAM1: all EAMs) and EAM combination 2 (EAM2: excluding psoriasis), was reported by 33.2%, and 23.7% of patients, respectfully.
Regression analysis adjusting for baseline BASDAI and BASFI, found enthesitis, EAM1, and EAM2 to be significant negative predictors of SF-36 PCS scores ($p<0.05$). Individual EMAs were not found to impact PROs, except for uveitis, found to be a negative predictor of SF-36 PCS scores for which a statistical trend was identified ($p<0.15$). No association between EAMs and SF-36 MCS, BD-II or WLQ scores were found.
Conclusions: In a Canadian routine clinical care setting, a substantial proportion of AS patients requiring a change in treatment report EAMs. Patients with EAMs were found to have significant reduction in baseline QoL specifically related to physical functioning.
Acknowledgements: The authors wish to acknowledge JSS Medical Research, Montreal (QC) Canada for statistical analysis, medical writing and editorial assistance during the preparation of this abstract.
Disclosure of Interest: L. Bessette Consultant for: Janssen, Roche, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, Speakers bureau: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Lilly, Novartis, B. Haraoui Grant/research support from: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, and UCB; Speaking engagements: Amgen, BMS, Janssen, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Pfizer, Roche, and UCB, Speakers bureau: Amgen, BMS, Janssen, Pfizer, and UCB, M. Khraishi Consultant for: AbbVie, Speakers bureau: AbbVie, W. Bensen Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Merck, Pfizer, Roche, and UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Merck, Pfizer, Roche, and UCB, V. Remple Shareholder of: AbbVie Corp., Employee of: AbbVie Corp.
DOI: 10.1136/annrheumdis-2017-eular.3032

FRI0450 COMMONALITIES AND DIFFERENCES IN DATA COLLECTION ACROSS EUROPEAN SPONDYLOARTHRITIS REGISTRIES

M.L. Hetland[1], M. Østergaard[1], J. Askling[2], C. Gabay[3], D. Nordstrom[4], O. FitzGerald[5], M. Hernández Miguel[6], M. Santos[7], Z. Rotar[8], H. Mann[9], F. Iannone[10], M.J. Nissen[3], E. Hauge[1], J. Gomez-Reino[11], F. Díaz-González[12], M. Tomsic[8], K. Pavelka[9], F. O'Shea[5], C. Sullivan[5], M. van de Sande[13], I.E. van der Horst-Bruinsma[13], G.J. Macfarlane[14], G.T. Jones[14], B. Gudbjørnsson[15], T.K. Kvien[16] on behalf of EuroSpA Study Group. *[1]DANBIO, Glostrup, Denmark; [2]ARTIS, Stockholm, Sweden; [3]SCQM, Geneva, Switzerland; [4]ROB-FIN, Helsinki, Finland; [5]ASRI, Dublin, Ireland; [6]Biobadaser, Barcelona, Spain; [7]reuma.pt, Almada, Portugal; [8]biorx.si, Ljubljana, Slovenia; [9]ATTRA, Prague, Czech Republic; [10]GISEA, Bari, Italy; [11]Biobadaser, Santiago; [12]Biobadaser, Santa Cruz de Tenerife, Spain; [13]ARC, Amsterdam, Netherlands; [14]Bsrbr-As, Aberdeen, UK; [15]ICEBIO, Reykjavik, Iceland; [16]Nordmard, Oslo, Norway*

Background: High quality data from prospective, real life patients with spondy-

loarthritis (SpA) is needed to strengthen patient-level research in non-experimental clinical settings. A research network collaboration of registries collecting data on patients with SpA, "EuroSpA" offers opportunities to enhance research capabilities in the real world setting.

Objectives: To assess patient numbers, data extent and completeness in European SpA registries and establish an international research collaboration and common data set to address key data gaps for SpA patients treated in routine clinical practice.

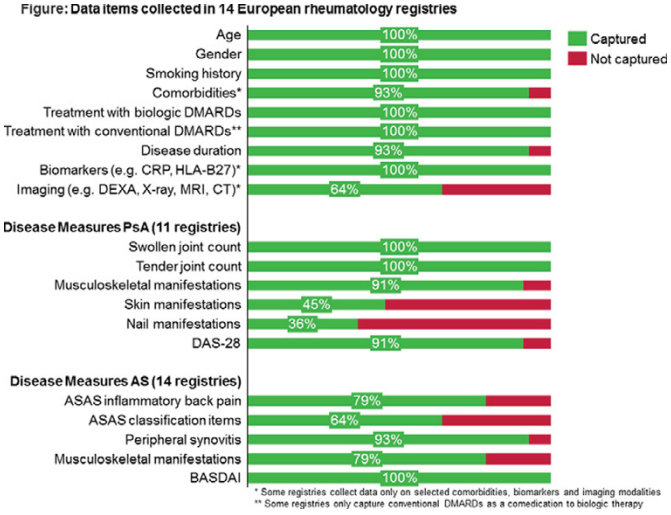
Methods: The "EuroSpA" research network collaboration was established between registries collecting data on SpA patients. A survey was conducted via email and follow-up interviews April-December 2016 to assess patient numbers, data availability and completeness in participating registries. Our survey tool was based on key variables identified through literature review and expert interviews.

Results: 14 European rheumatology registries submitted information on their data covering approximately 63479 SpA patients, including patients with psoriatic arthritis (PsA), ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) (Table).

Table 1. Approximate patient numbers in each SpA registry

Registry	Approximate patient numbers		
	PsA	AS	Nr-axSpA
ARC (Netherlands)		310	80
ARTIS (Sweden)	10000	10000	
ASRI (Ireland)		630	
ATTRA (Czech Republic)	800	2200	150
BIOBADASER (Spain)	500	500	20
Biorx.si (Slovenia)	350	600	
BSRBR-AS (Britain)		1500	650
DANBIO (Denmark)	7800	3900	3400
GISEA (Italy)	2400	1200	600
ICEBIO (Iceland)	376	343	
NOR-DMARD (Norway)	1600	1100	120
Reuma.pt (Portugal)	1600	2700	
ROBFIN (Finland)	1900	1900	400
SCQM (Switzerland)	1900	1400	550
Total	29226	28283	5970

Data coverage was comprehensive for comorbidities, demographic and treatment variables, but limited for imaging and in PsA for skin and nail manifestations (figure).



Conclusions: A European research collaboration network of SpA registries, "EuroSpA", including ≈ 63500 SpA patients enables the collection of key patient variables and strengthens research through increased patient numbers and cross-country comparative research. While core disease activity measures for SpA patients are widely collected, an enhanced standardized core dataset could strengthen future collaboration.

Acknowledgements: The authors acknowledge Craig Richardson from Novartis Pharma AG, Carol Lines and Seline Eisenring from Quintiles IMS for support in survey data collection and editorial assistance, and Novartis Pharma AG, Basel, Switzerland for financial support of the EuroSpA initiative.

Disclosure of Interest: M. L. Hetland Grant/research support from: AbbVie, BMS, MSD, Pfizer, Orion, Novartis, Biogen, Eli Lilly, M. Østergaard Grant/research support from: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, J. Askling: None declared, C. Gabay Grant/research support from: Roche, Pfizer, AB2 Bio, Consultant for: Sanofi, AB2 Bio, AbbVie, Pfizer, BMS, MSD, Roche, Novartis, D. Nordstrom: None declared, O. FitzGerald Grant/research support from: Pfizer, Abbvie, BMS, Novartis, UCB, Janssen, Celgene and Lilly, M. Hernández Miguel: None declared, M. Santos: None declared, Z. Rotar: None declared, H. Mann: None declared, F. Iannone Consultant for: AbbVie, BMS, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Roche, UCB, M. J. Nissen: None declared, E. Hauge: None declared, J. Gomez-Reino: None declared, F. Díaz-González: None declared, M. Tomsic: None declared, K. Pavelka: None declared, F. O'Shea: None declared, C. Sullivan: None declared, M. van de Sande: None declared, I. E. van der Horst-Bruinsma: None declared, G. J. Macfarlane Grant/research support from: Pfizer, AbbVie and UCB, G. T. Jones Grant/research support from: AbbVie, Pfizer, UCB, B. Gudbjørnsson: None declared, T. K. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB

DOI: 10.1136/annrheumdis-2017-eular.3659

FRI0451 SEX DIFFERENCES IN DISEASE ACTIVITY ACCORDING TO COMPOSITE INDICES IN SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Blasco-Blasco[1], I. Castrejón[2], V. Joaní[3], E. Eliseo[4], M. Ruiz-Cantero[1,5].
[1]Public Health, University of Alicante, Alicante, Spain; [2]Rheumatology, Rush University Medical Center, Chicago, United States; [3]Rheumatology, Alicante University General Hospital; [4]Rheumatology, Miguel Hernández University; [5]Ciberesp, Alicante, Spain

Background: The Bath Ankylosing Spondylitis (AS) Disease Activity Index (BASDAI), an index of only patient-self-report measures, and AS Disease Activity Score (ASDAS)[1], which adds patient global estimate and laboratory tests to BASDAI elements are widely used in Spondyloarthritis (SpA). Both indices are specifically designed to evaluate disease activity AS patients. Some studies have shown worse BASDAI in women, but sex-related differences by ASDAS remain unclear [2,3].

Objectives: To analyze reports of sex-stratified disease activity measures -BASDAI and ASDAS- in patients with SpA.

Methods: Data sources included PubMed (1950 to December 2016), Embase, Web Of Science, and manual searches of references lists. We included observational studies and randomized trials comparing disease activity scores, specifically BASDAI and ASDAS, between men and women with SpA. Studies quality was determined in line with the STROBE statement for observational studies and CONSORT statement for RCT, considering <50% positive items as low quality. Randomized effects were performed to report the mean difference (95% confidence interval) by gender, and heterogeneity was measured via I^2 statistic in order to check the results robustness.

Results: From 672 identified studies 18 cross-sectional studies, 3 cohort, 2 case-control studies, and 1 RTC reported sex-stratified BASDAI and ASDAS. ASDAS was evaluated in 3,758 patients (36.5% women) in 9 studies, and BASDAI included 12,329 patients (34.3% women) in 24 studies. In a metanalysis of mean difference BASDAI including 19 studies the mean difference was 0.56 (95% CI: 0.47, 0.66) and I^2=43%, indicating a significantly higher disease activity in women (Figure). In a metanalysis of 7 studies ASDAS the mean difference was 0.06 (95% CI: -0.04, 0.16) and I^2=41%, not showing statistically significant differences.

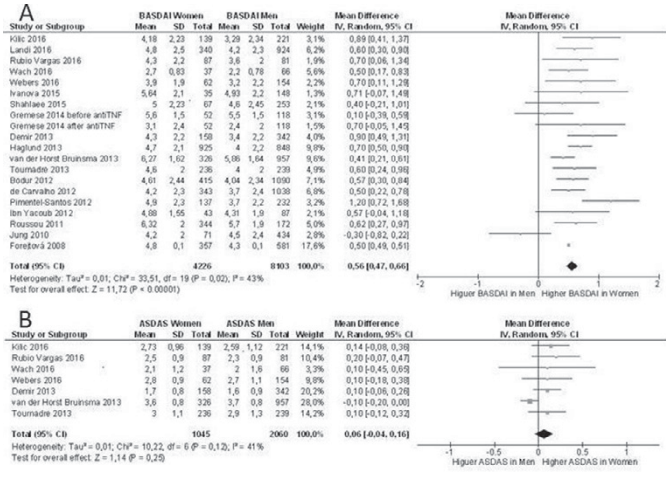


Figure. (A) Mean difference to BASDAI in men vs woman. (B) Mean difference to ASDAS in men vs woman

Conclusions: We identified relevant sex differences in disease activity according to BASDAI with higher disease activity in women, but not according to ASDAS. In SpA, women present more peripheral arthritis and higher pain, which may influence the BASDAI score, mainly based on patient-self-report measures. It is important to recognize these differences that may influence management decisions based on disease activity measures.

References:

[1] van der Heijde D et al. Ann Rheum Dis 2009;68:1811–18.
[2] van der Horst-Bruinsma IE et al. Ann Rheum Dis 2013;72:1221–1224.

[3] Arends S et al. heumatology 2015;54:1333–1335.
Acknowledgements: Faculty of Health Sciences and University Institute for Gender Studies of the University of Alicante supported M. Blasco-Blasco.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4219

FRI0452 IMPACT OF A TRAINING PROGRAM AND EARLY REFERRAL ON DIAGNOSTIC DELAY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE SPANISH ATLAS

M. Garrido-Cumbrera[1], D. Galvez-Ruiz[1], V. Navarro-Compan[2], J. Gratacós-Masmitja[3], C. Blanch Mur[4], E. Collantes-Estevez[5], P. Zarco-Montejo[6], O. Braçe[1]. *[1]Universidad de Sevilla, Seville; [2]H. la Paz, Madrid; [3]H. Parc Tauli, Sabadell; [4]Novartis, Barcelona; [5]Universidad de Córdoba, Cordova; [6]H. Fundación Alarcón, Madrid, Spain*

Background: In patients with axial spondyloarthritis (axSpA), diagnosis delay (DD) postpones the initialisation of the most appropriate treatment with irreversible consequences on physical function, mobility and quality of life of patients. DD is also responsible for increased health costs resulting from incorrect referrals, visits to inappropriate health professionals and poorly planned diagnostic tests. Many initiatives have been undertaken in recent years in an attempt to reduce DD but their influence is still unknown.
Objectives: i) To determine diagnosis delay in patients with ax-SpA in Spain; ii) To assess the pre-diagnosis care process; iii) To analyse the possible beneficial effects on DD of a training programme for primary care physicians and early referral to rheumatology units.
Methods: A sample of 680 patients diagnosed with ax-SpA was interviewed during 2016 as part of the Atlas in Spain. This project aims to improve early diagnosis and to promote the use of effective treatments in ax-SpA patients. Collected data included: socio-demographics, medical visits prior to diagnosis, date for first symptoms and diagnosis and disease characteristics. This information was used to determine the DD and the possible beneficial effects on DD of a training programme for primary care physicians and early referral to rheumatology units. A descriptive analysis was performed, stratifying the results according to the start of the symptoms (before and after 2009). The ESPeranza Program (a Spanish prospective multicentre national health programme aimed at facilitating early diagnosis of patients with ax-SpA) started in 2009.
Results: 53% of the patients included were females. Mean scores (standard deviation) were 45.7 (10.8) years for age and 12.4 (11.2) for disease duration. 77.1% were HLA-B27+. Visits to health professionals prior to diagnosis included: primary care physicians (88.5%), orthopaedic surgeons (71.7%), rheumatologists (70.4%), and physiotherapists (47.6%). The mean number of consultations prior to diagnosis was 2.6; 3.0; 2.0 and 3.4, respectively.
Patients stated the onset of the first ax-SpA symptoms was at mean 24.4 years of age, with diagnosis at mean 32.9 years of age, translating into a mean DD of 8.5 years. For 25% of patients DD was >12 years, whereas a DD of <2 years was found in only 25% of respondents. Mean DD for patients whose first symptoms appeared before 2009 was 9.5 years, whereas for patients whose first symptoms appeared after that date it was significantly reduced to 2.5 years.
Conclusions: The mean delay in diagnosis ax-SpA in Spain is above 8 years. Patients make a large number of visits to a variety of specialist physicians before they are diagnosed, which could point to proof of wrong referrals by primary care. However, DD has fallen drastically (to a mean 2.5 years) since the implementation of the ESPeranza Program in 2009, suggesting that training primary care physicians have substantial beneficial effects on patients with ax-SpA and the care process.
Acknowledgements: This project has been supported by Novartis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6416

FRI0453 CLINICAL AND THERAPEUTIC CHARACTERIZATION OF A COLOMBIAN COHORT WITH SPONDYLOARTHROPATHIES

M.A. Alzate[1], F. Ramirez[2], F. Vargas[2], D. Hernandez-Parra[1], J.C. Salazar-Uribe[3], P. Ortiz-Salazar[1], R. Pineda[1] on behalf of Artmedica IPS, Medellin, Colombia. *[1]Clinical information group; [2]Rheumatology division, Artmedica IPS; [3]School of Statistics, Faculty of Sciences, National University of Colombia, Medellin, Colombia*

Background: Spondyloarthropathies (SpAs) are a group of auto-inflammatory diseases, with overlapping symptoms, that include ankylosing spondylitis (AS), psoriatic arthritis (PsA), undifferentiated spondyloarthritis (Und SpA), enteropathic arthritis, and reactive arthritis (1).
Objectives: To characterize the disease in a large Colombian cohort with SpAs, assessing differences in its classification, clinical manifestations, laboratory results, radiographic changes, and treatment, according to the type of SpA.
Methods: A cross-sectional study was conducted in 621 patients with SpAs, in whom sociodemographic, clinical and therapeutic characteristics were analyzed based on the type of diagnosis. Statistical association was examined by means of Chi-square tests, Fisher's exact test, Mann-Whitney test, and logistic regression analyses. In all cases, a p value <0.05 was considered significant.
Results: Out of the 621 patients included, AS was observed in 54,7%, PsA in 35,7%, and Und SpA in 9,5%. AS was positively associated to male gender (OR 2.05 95%IC 1.5–2.8), younger age at onset, axial involvement (OR 23.2 95%IC 15.2–35.5), uveitis (OR 3.8 95%IC 2.25–6.57), radiographic sacroilitis (OR 6.95 95%IC 3.02–16.02), and HLA-B27 positivity (OR 2.3 95%IC 1.5- 3.5). PsA was associated to female gender, older age at onset, arthritis, and peripheral involvement. According to the therapeutic approach, more use of conventional DMARD therapy was found in PsA and Und SpA, while more use of biology therapy in AS.

Table 1. General characteristics of patients with SpAs

	All N=621		AS N=340		PsA N=222		Und SpA N=59		p-value
	N	%	N	%	N	%	N	%	
Mean (SD)									
Age, year	49.3 (12.4)		45.2 (12.5)		56.7 (11.8)		45.9 (12.9)		**<0.0001**
Age at diagnostic, year	40.1 (12.9)		33.5 (12.6)		46.8 (13.5)		39.9 (12.5)		**<0.0001**
Male	328	52.8	208	61.1	96	43.2	24	40.6	**<0.0001**
Age at onset, <45 years	469	75.5	291	85.5	140	63.1	38	64.4	**<0.0001**
Low back pain	342	55.1	266	78.2	47	21.2	29	49.2	**<0.0001**
Arthritis	411	66.2	152	44.7	213	96	46	78	**<0.0001**
Enthesitis	217	34.9	136	40.	37	16.7	44	74.6	0.38
Dactylitis	116	18.7	49	14.4	45	20.3	22	37.3	**0.0002**
Psoriasis	225	36.2	3	0.88	221	99.6	1	1.7	**<0.0001**
Uveitis	92	14.8	75	22.1	7	3.2	10	16.9	**<0.0001**
Family history	108	17.4	55	16.2	47	21.2	6	10.2	0.09
Sacroilitis (Rx)	70/171	40.9	62/116	53.5	7/37	18.9	1/18	5.6	**<0.0001**
Sacroilitis (MRI)	203/279	72.8	182/212	85.9	21/39	53.9	0/28	0.0	**<0.0001**
HLA-B27	284/438	64.8	229/321	71.3	17/61	27.9	38/56	67.9	**<0.0001**
Axial	397	63.9	328	96.5	37	16.8	32	54.2	**<0.0001**
Peripheral	488	78.6	213	62.6	218	98.2	57	96.6	**<0.0001**
Both	264	42.5	201	59.1	33	14.9	30	50.9	**<0.0001**

SD, standard deviation; Rx, radiography; MRI, Magnetic resonance.

Conclusions: To our knowledge, this is the larger existing cohort with SpAs in Colombia. Understanding the natural history of disease is important to do an early diagnosis and treatment that could prevent irreversible disability.
References:
[1] Ehrenfeld M. Spondyloarthropathies. Best Pract Res Clin Rheumatol. 2012;26(1):135–45.
Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4906

FRI0454 M-SASSS AND CERVICAL SEGMENT C7-D1. SHOULD THE ORIGINAL SCORE BE MODIFIED?

M.J. Moreno-Martinez[1], M.J. Moreno-Ramos[2], L.F. Linares-Ferrando[2]. *[1]Rheumatology, H. Rafael Mendez; [2]Rheumatology, H. U.Virgen de la Arrixaca, MURCIA, Spain*

Background: Ankylosing Spondylitis is characterized by axial involvement. m-SASSS is the radiographic score that is used to evaluate the radiographic progression of the disease. It evaluates different lesions in the lumbar segment and in the cervical segment (from C2-C3 to C7-D1), both with a lateral x-ray.
Theoretically, the C7-D1 intervertebral segment should not be evaluated through a simple lateral radiograph, but with x-rays in special positions.
Objectives: To evaluate the importance of the assessment of the C7-D1 intervertebral segment in patients with Ankylosing Spondylitis.
Methods: The patients come from a Spondyloarthritis Unit (Hospital Virgen of the Arrixaca, Murcia, Spain). All patients are diagnosed with Ankylosing Spondylitis (New York Modified Criteria)
The usual radiographic study was performed to calculate the m-SASSS (lateral cervical and lateral lumbar). We value the alterations found at level C7-D1 of patients and controls.
We compared the alterations found in patients with ankylosing spondylitis with control patients. These came from different rheumatology units, had no inflammatory pathology and had two lateral radiographs at different time periods. We collected demographic data (both from patients and from controls) and from clinical patients (analytical, activity and metrology).
Results: We included 47 patients (81% male and 19% female) with a mean age of 48 (± 8) years and a mean duration of symptoms of 18 (± 8.5) years. The mean time between the two radiographic studies was 3 (± 1.5) years. The control group was made up of 61 people (40, 7% men) with a mean age of 50 years (± 11).
The mean age of the control group was higher than patients (p=0.001).
The C6-C7 intervertebral level could be assessed radiographically with the lateral cervical radiograph in 93,2% of the patients and in 85, 2% of controls, and the C7-D1 level was only assessed in 22, 7% of the patients and 50% of the controls. We analyzed whether the assessment of intervertebral level C7-D1 could be influenced by other variables such as sex, age or duration from the symptoms without finding a statistical result.
The 88, 5% of patients had a lower border of C7 normal or with squaring, erosion or sclerosis. Only 1 patient had syndesmophyte and 2 patients had a bridge between vertebrae. On the upper border of D1, 85, 5% of patients had normal or type-1 lesions (squarin, sclerosis or erosion), there wasn't syndesmophytes and 2 patients had a bridge (Table)

	Injury	Prevalence (%)
Lower border of C7 (n=26)	Normal	65,5%
	Sclerosis, squaring, erosion	23%
	Syndesmophyte	4%
	Bridge	7,5%
Upper border of D1 (n=14)	Normal	57%
	Sclerosis, squaring, erosion	28,5%
	Syndesmophyte	0%
	Bridge	14,5%

Conclusions:
- The cervical segment C7-D1 is not usually valuable through a lateral cervical radiograph.
- Most of our patients with Spondylitis have no significant lesions in this segment.
- It is recommended to modify the m-SASSS index by removing the assessment of the cervical segment C7-D1.

References:
[1] Averns HL, Oxtoby J, Taylor HG, Jones PW, Dziedzic K, Dawes PT. Radiological outcome in ankylosing spondylitis: use of the Stoke Ankylosing Spondylitis Spine Score (SASSS). Rheumatology.1996;35(4):373–376.
[2] Gil JM, Andrades H, Ramos S. Técnico Especialista en Radiodianóstico Del Servicio Gallego de Salud. 1° Ed. Sevilla. MAD; 2006. 674 p.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5239

FRI0455 RADIOGRAPHIC PROGRESSION OF HIP ARTHRITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TNF INHIBITORS

M. Konsta[1,2], M.T. Nurmohamed[2], A. Iliopoulos[1], J,C. van Denderen[2], I. Visman[2], P.P. Sfikakis[1], I.E. van der Horst-Bruinsma[2]. *[1]First Department of Propaedeutic Internal Medicine, Rheumatology Department, Joined Rheumatology Program, National and Kapodistrian University of Athens, Medical School, Athens, Greece; [2]Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands*

Background: Although there is debate whether treatment with TNF inhibitors (TNFi) in AS may not inhibit spinal radiographic progression, the effect on hip involvement may be different (1,2).
Objectives: To estimate the impact of long-term TNFi treatment on radiographic progression of hip arthritis in AS, by adding a quantitative scoring method, previously applied in hip osteoarthritis, to the BASRI-hip score.
Methods: Consecutive TNFi-naïve AS patients (fulfilling the modified New York criteria) who were eligible for TNFi treatment were included. Hip involvement was assessed clinically (pain, reduced range of motion and intermalleolar distance) and radiographically. X-rays of the pelvis and lateral cervical and lumbar spine were obtained at 3 time points: at baseline two and seven years after the start of TNFi. Both hips were scored using: a) BASRI-hip score (BASRI-h score $\geq$2 is classified as definitive hip involvement), b) mean joint space width (MJSW), estimated by measurement of 3 distinct points of interbone distance: 2mm inner of the external end of the acetabulum, vertical line through femoral head center, head-neck center line (1). Spinal X-rays were scored were scored blindly, by 2 independent readers using the mSASSS. The significance of changes was tested by mixed models for longitudinal data.
Results: 262 AS patients (188 men, age: 49.8±12 years, disease duration: 24.4±12 years) under TNFi treatment were included. Definite hip involvement at baseline was detected in 95/262 (36%) patients, who had significantly higher BASRI-hip score [2 (2–2.5) median (IQR) vs. 0.5 (0–1) $p<0.0001$] and lower MJSW (3.6±0.7 vs. 4.5±0.7, $p<0.0001$), compared to those without. In patients with hip arthritis at baseline, both BASRI-h score and MJSW remained unchanged during follow up. In patients without hip arthritis, the BASRI-hip score remained unchanged after 2.5±0.7 years, but increased significantly after 7±2.3 years compared to baseline. In contrast, the MJSW in patients without hip arthritis remained unchanged at the three time points. The mSASSS raised significantly during the follow-up period, regardless of hip involvement (see table).

Variables	Baseline	After 2.5±0.7 years	After 7±2.3 years	P
All pts (n=262)				
BASRI-hip, mean±SD	1.15±1	1.14±1	1.2±1	<0.0001
MJSW (mm), mean±SD	4.17±0.8	4.16±0.8	4.12±0.7	NS
mSASSS, median (IQR)	6 (1–24.5)	8 (1–30)	11 (2–30)	<0.0001
Pts with hip involvement (n=95)				
BASRI-hip, median (IQR)	2 (2–2.5)	2 (2–2.5)	2 (2–2.5)	NS
MJSW (mm), mean±SD	3.59±0.7	3.58±0.7	3.53±0.7	NS
mSASSS, median (IQR)	12 (2.5–36)	17 (3–40.5)	15.5 (3–37.5)	<0.0001
Pts without hip involvement (n=167)				
BASRI-hip, mean±SD	0.49±0.5	0.5±0.53	0.58±0.57	<0.0001
MJSW (mm), mean±SD	4.5±0.7	4.47±0.6	4.44±0.6	NS
mSASSS, median (IQR)	4 (0–18)	7 (1–25)	9 (2–27)	<0.0001

Conclusions: One third of the AS patients suffer from radiographic hip involvement, which seems to stabilize during long-term anti-TNF treatment. Assessment of MJSW may contribute to detect minor changes in contrast to BASRI-hip score' rough estimation.

References:
[1] Konsta M, et. al, Clin Rheumatol. 2013 Aug;32(8):1229–32.
[2] Nystad TW, et. al. Annals of the rheumatic diseases. 2014 Jun;73(6):1194–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6733

FRI0456 AGE AT SPONDYLOARTHRITIS DIAGNOSIS AND RISK OF CARDIOVASCULAR COMORBIDITY: RESULTS FROM THE COMOSPA STUDY

M.H. Derakhshan[1], N.J. Goodson[2], J. Packham[3], R. Sengupta[4], H. Marzo-Ortega[5], A. Molto[6], S. Siebert[1] on behalf of BRITSpA and COMOSPA investigators. *[1]Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow; [2]Academic Rheumatology Department, University of Liverpool, Liverpool; [3]Haywood Rheumatology Centre, Keele University, Keele; [4]Royal National Hospital for Rheumatic Diseases, Bath; [5]NIHR, Leeds Teaching Hospitals Trust and LIRMM, University of Leeds, Leeds, United Kingdom; [6]Paris Descartes University, Hôpital Cochin, Paris, France*

Background: Spondyloarthritis (SpA) and chronic inflammatory diseases are associated with a number of cardiovascular comorbidities. It is unknown whether age at SpA diagnosis is associated with cardiovascular outcomes in later life.
Objectives: To examine the relationship between "younger age at SpA diagnosis" and risk of various cardiovascular comorbidities.
Methods: COMOSPA is a large worldwide cross-sectional study comprising 3984 patients from 23 countries evaluating comorbidities in patients with SpA (1). We evaluated the association between "younger age at SpA diagnosis" (defined in 5-year blocks) and cardiovascular comorbidities using uni-variable and multi-variable binary logistic regression. Each model comprised one cardiovascular co-morbidity as dependent and "age at SpA diagnosis" as predictor adjusted for age, sex, BMI, history of smoking, alcohol, NSAIDs, DMARDs, biologics, steroids and other relevant factors
Results: The data of 3923 patients (64% male) were available for analysis. Current age ranged from 18 to 100 with median (IQR) of 42 (32–53) years. The median (IQR) age at SpA diagnosis was 33 (25–43) years. Main reported cardiovascular-related comorbidities were hypertension (22.4%), ischemic heart disease (IHD) (2.6%), stroke (1.3%) and diabetes mellitus (5.5%).
The risk of hypertension, after adjustment for potential confounding factors was associated with younger age at SpA diagnosis (OR=1.10, 95% CI: 1.05 -1.16), indicating 10% higher risk of hypertension for each 5 year younger age at time of SpA diagnosis (Table). Confounding variables showing significant association with hypertension were current age (OR=1.12, 95% CI: 1.10–1.13, $p<0.001$), male gender (OR=1.47, 95% CI: 1.20–1.80, $p<0.001$), current BMI (OR=1.09, 95% CI: 1.07–1.11, $p<0.001$), ever use of steroids (OR=1.24, 95% CI: 1.03–1.50, $p=0.027$) and ever use of synthetic DMARDs (OR=1.28, 95% CI: 1.05–1.57, $p=0.017$), but not ever use of NSAIDs or biologic DMARDs.
The other cardiovascular comorbidities were not associated with "younger age at SpA diagnosis" after adjustments for relevant confounding factors in multivariable analyses (Table)

Table 1. Association between "younger age at SpA diagnosis" and the risk of cardiovascular disease

	Univariable		Multivariable	
	OR (95% CI)	p value	OR (95% CI)	p value
Hypertension	0.76 (0.74 -0.79)	<0.001	1.10 (1.05 -1.16)	<0.001
IHD	0.74 (0.69 -0.80)	<0.001	0.99 (0.91 -1.086)	0.854
Stroke	0.79 (0.71 -0.87)	<0.001	0.98 (0.86 -1.11)	0.736
Diabetes Mellitus	0.78 (0.74 -0.82)	<0.000	0.95 (0.88 -1.02)	0.172

Conclusions: Younger age of SpA diagnosis is associated with increased risk of developing hypertension but not other cardiovascular comorbidities in this study. The explanation for this association is not clear and does not appear to be due to increased NSAID exposure.
References:
[1] Molto A, et al. Ann Rheum Dis 2016;75:1016–23.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3422

FRI0457 THE ROLE OF SERUM HMGB1 IN BONE REMODELİNG AND OSTEOPOROSIS IN A GROUP OF ANKYLOSING SPONDYLITIS PATIENTS

M. Calis[1], I. Cuce[2], I. Gunturk[3], E. Cuce[1], C. Yazici[4]. *[1]Department of Physical Medicine and Rehabilitation, Erciyes University, Faculty of Medicine, Kayseri; [2]Department of Physical Medicine and Rehabilitation, Adıyaman University Training and Education Hospital, Adıyaman; [3]Institute of Health Sciences, Biochemistry, Erciyes University; [4]Department of Medical Biochemistry, Erciyes University, School of Medicine, Kayseri, Turkey*

Background: Ankylosing spondylitis is characterized by new bone formation and bone loss, associated with inflammation, which are mediated by cytokine-signaling pathways. High mobility group box 1 (HMGB1) protein, is a nonhistone nuclear protein, which is secreted by inflammatory cells, is also defined as a bone-active

cytokine. Recent studies have shown that RANKL induces HMGB1 release and it is required for RANKL-induced osteoclastogenesis in vitro and in vivo.
Objectives: To investigate the relationship of serum HMGB1 levels with RANKL/Osteoprotegerin (OPG) axis and clinical and radiographic parameters in patients with AS.
Methods: In this cross-sectional study, serum samples for total HMGB1, sRANKL and OPG were detected from 54 tumour necrosis factor (TNF) inhibitor naive patients with AS according to the modified New York criteria [mean age 34.9 years (S.D. 7.1); duration of symptoms 8.6 years (S.D. 4.2); male gender 38 patients (70.4%)] and 26 healthy controls. ESR, CRP, Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI) were assessed for each patient. Bone mineral density was measured using dual-energy X-ray absorptiometry (DXA) at lumbar spine (L2–L4) and proximal femur. Lumbar spine radiographs were scored using the modified Stoke AS Spine Score (mSASSS).
Results: Serum HMGB1 levels were relatively higher in patients with AS than HCs however no statistically significant in each other. Serum HMGB1 levels correlated with CRP (rho=0.368 and *P*=0.006), ASDAS-CRP (rho=0.358 and *p*=0.008) and BASDAI (rho=0.334 and *p*=0.014) and BASFI (rho=0.355 and *p*=0.008) in patients with AS. CRP and ASDAS-CRP showed more correlated to HMGB1 serum levels than BASDAI. There was no significant correlation between HMGB1 levels with sRANKL, OPG, mSASSS and spine or femur BMD values. In addition, serum OPG levels and the ratio of sRANKL to OPG from AS patients were significantly higher than those of HCs.

Table 1

	AS patients (n=54)	Healthy controls (n=26)	*p*
Age (yrs)	34.9±7.1	33.3±4.0	N/A
Body mass index (kg/m^2)	26.3±4.7	26.3±2.8	N/A
Disease duration (yrs)	8.6±4.2	–	N/A
ESR (mm/hr)	22.0±8.5	–	N/A
CRP (mg/L)	11.5±8.9	–	N/A
HMGB1 (ng/ml)	337.1±166.1	286.3±126.1	N/A
sRANKL (ng/ml)	148.6±31.4	137.2±46.9	N/A
OPG (ng/ml)	285.5±68.9	317.8±51.8	0.02
sRANKL/OPG	0.6±0.2	0.4±0.1	<0.001

Conclusions: This study showed that levels of HMGB1 in the sera of AS patients, are increased compared to healty controls. Serum HMGB1 levels are related to BASDAI, ASDAS-CRP, BASFI and CRP in patients with AS. Different results in the literature on serum HMGB1 levels as well as our results support the hypothesis that HMGB1 plays a role in the pathogenesis of AS. According to our knowledge, it is the first trial evaluating association between serum HMGB1 levels with sRANKL-OPG axis, bone mineral density and new bone formation in AS patients and it seems not to be related for these conditions.
References:
[1] Zhou Z, Han JY, Xi CX, et al. J Bone Miner Res. HMGB1 regulates RANKL-induced osteoclastogenesis in a manner dependent on RAGE.2008 Jul;23(7):1084–96.
[2] Bidwell JP, Yang J, Robling AG. Is HMGB1 an osteocyte alarmin? J Cell Biochem. 2008 Apr 15;103(6);1671–80.
Acknowledgements: Grant Support: by Erciyes University Council of Scientific Investigations (Project code: TTU-2014–5575).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4303

FRI0458 ASSESSMENT OF BONE MINERAL DENSITY IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS FROM CORSAR COHORT: 2 YEARS FOLLOW UP

O. Rumyantseva, T. Dubinina, A. Demina, D. Rumiantceva, S. Erdes, E. Agafonova, S. Krasnenko, E. Gubar. *Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Bone loss in patients (pts) with early axial spondyloarthritis (axSpA) is insufficiently studied and may be associated with disease activity.
Objectives: To assess the bone mineral density (BMD) in pts with early axSpA base on data from 2 years follow up of CORSAR cohort.
Methods: The research included 65 pts with axSpA (criteria ASAS 2009) with disease duration <5 years and age at onset <45 years. Pts at least 2 years follow up, 32 (49,2%) male, pts mean age was 28,5 (5,8) y., average disease duration 24,1 (15,4) mo, 60 (92,3%) pts were HLA-B27 positive. At baseline all pts were NSAID-naïve, DMARD-naïve, anti-TNF-naïve. For 2 years all pts taking NSAIDs at therapeutic doses, part of the pts received sulfasalazine and anti-TNF. BMD was measured using dual energy x-ray absorptiometry (DXA) of the femoral neck (FN) and lumbar spine (LS) (L2–4) at baseline and after 1 year, and 2 years follow up. BMD reduction was defined as Z score $\leq$ -2 (at least one site).
Results: Low BMD at baseline founded in 9 (13,8%) pts, in 10 (15,3%) pts after 1 year and in 5 (7,7%) pts after 2 years follow up. There were no significantly differences between the mean values of BMD at baseline and after 2 year, data are shown in the Table.

Table 1. BMD at baseline and after 1 and 2 years follow up

	Baseline	1 years after baseline	2 years after baseline	p
BMD LS mean (s.d)	-0,759 (1,13)	-0,679 (1,11)	-0,627 (1,11)	0,541
BMD FN mean (s.d)	-0,527 (0,91)	-0,633 (0,95)	-0,477 (1,00)	0,792

Conclusions: Low BMD was quite rare (14%) in patients with early axSpA. Small frequency of BMD reduction in the Russian cohort of axSpA patients after 2 years of study is probably due to disease activity decrease on anti-inflammatory therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3209

FRI0459 DEVELOPMENT AND VALIDATION OF A SPANISH TOOL FOR SEMI-AUTOMATIC QUANTIFICATION OF SACROILIAC INFLAMMATION BY MAGNETIC RESONANCE IN SPONDYLOARTHRITIS (SCAISS)

P. Zarco[1], R. Almodóvar[1], A. Bueno[2], L.M. Molinero[3]. *[1]Unit Rheumatology; [2]Unit Radiology, Hospital Universitario Fundación Alcorcon; [3]Ingeniera ALCE, Madrid, Spain*

Background: Different systems to quantify inflammatory changes in sacroiliac MRI have been developed.[1, 2] These systems include the Spondyloarthritis Research Consortium of Canada (SPARCC), the Berlin, the Aarhus-Puhakka, and Aarhus-Madsen, the Leeds, the MR Imaging of Seronegative SpA (MISS), Leeds, Sieper/Rudwaleit and Hermann/Bollow scoring systems. In addition, the use of these quantification methods is restricted to clinical trials, since their use in clinical practice is limited due to their complexity, need for trained personal, and prolonged procedural time. The development of computers and data processing software has led to significant advances in methods for image analysis. With the objective to improve interobserver quantification of sacroiliitis while maintaining a practical perspective, our group has developed a semi-automated method to measure bone marrow edema (BME) in MRI images from sacroiliac (SI) joints.
Objectives: The aim of this study is to analyze the validity and reliability of the method.
Methods: The development of the method to quantify inflammation in SI joints involved software selection from a list of potential programs, process-mapping based on discussion, and tuning. Once developed, feasibility (time spent) interobserver reliability (intraclass correlation coefficient), and construct validity (convergent validity) were analysed. Two rheumatologists and a radiologist independently quantified sacroiliitis from SI images from 12 patients with a diagnosis of axial SpA by the new method, and by non-automated methods to rate sacroiliitis (SPARCC* and Berlin). Convergent validity, reliability and feasibility were calculated. (* In the present study, for simplicity reasons and in order to make it closer to the developed technique, the authors modified the SPARCC method by using a single coronal section instead of the standard six consecutive ones).
Results: The interobserver reliability was high, with intraclass correlation coefficients for global score of 0.81 (95% CI: 0.59–0.94). Convergent validity was good, with high correlation with the Berlin (rho between 0.797 and 0.913) and the SPARCC methods (rho between 0.566 and 0.897). Mean time employed in the reading procedure was 30 seconds.
Conclusions: The developed semi-automatic technique permits a fast and valid calculation of overall BME lesion at the SI joint on MRI images.
References:
[1] van der Heijde DM, Landewe RB, Hermann KG, et al. Application of the OMERACT filter to scoring methods for magnetic resonance imaging of the sacroiliac joints and the spine. Recommendations for a research agenda at OMERACT 7. J Rheumatol 2005; 32(10):2042–2047.
[2] Ostergaard M, Poggenborg RP, Axelsen MB, et al. Magnetic resonance imaging in spondyloarthritis–how to quantify findings and measure response. Best Pract Res Clin Rheumatol 2010; 24(5):637–657.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1281

FRI0460 EXTRA-ARTICULAR MANIFESTATIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: A CROSS SECTIONAL STUDY FROM SOUTHERN DENMARK

R.A. Andreasen[1,2], R. Christensen[1], L.E. Kristensen[1], T. Ellingsen[3,4], H.C. Horn[3], I.M.J. Hansen[2,5]. *[1]Rheumatology, The Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen; [2]Rheumatology, OUH, Svendborg Hospital, Svendborg; [3]Rheumatology; [4]Patient data Explorative Network (OPEN), Odense University Hospital; [5]Department of Clinical Research, University of Southern Denmark, Odense, Denmark*

Background: Axial (ax) spondyloarthritis (SpA) is a heterogenous group of chronic rheumatic diseases. Ax-SpA is subdivided into two groups referred to as nonradiographic and radiographic (i.e. AS) respectively. Next to the spinal and articular symptoms, many patients with SpA also have extra-articular manifestations (EAM) which contribute to reduced quality of life [1]. SpA appears to be more frequent in men than woman in its axial presentations, and in reference to the prototype of the disorder, AS, three male cases are documented for every female case. However, since the introduction of the new ASAS criteria for ax-SpA these differences are no longer so apparent[2]. Nevertheless, little is known of the differential clinical expression of SpA between males and females.
Objectives: The objective of this study was to compare patients with AS and

nr-axSpA stratified by gender, using standardized clinical tools (including patient-reported outcomes (P-ROs)) and C-reactive protein (CRP) level as a biomarker for inflammation.
Methods: Ax-SpA patients were included prospectively and underwent an examination program at one visit. We used ASAS criteria and the modified New Yorker criteria for classification. Information on demography and PROs was obtained. A trained physician performed a clinical examination, and BASMI and the The Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC) was used to enthesitis count. Chi-square and t-tests were used for categorical and continuous variables respectively to test the null hypothesis.
Results: Eighty patients with ax-SpA were included. Table 1 shows the results (mean ± SD or relative frequency) for the comparison of demographic and disease characteristics between clinical subgroups.

	Non-radiographic axSpA males n= 20	AS males n=23	*P*-value	Non-radiographic axSpA females n= 29	AS females n= 8	*P*-value
Mean age, years (S.D.)	41.5 ± 15.4	50.6 ± 9.9	0.03	44.0 ± 11.1	47.8 ± 17.3	0.46
HLA-B27 pos. (%)	11 (55)	21 (91)	0.012	13 (45)	8 (100)	0.013
Peripheral arthritis (%)	9 (45)	12 (52)	0.98	14 (48)	7 (88)	0.10
Mean BASDAI (S.D.)	2.5 ± 2.1	2.9 ± 1.9	0.52	4.7 ± 2.2	2.8 ± 2.0	0.043
Mean BASFI (S.D)	2.1 ± 2.2	2.6 ± 2.2	0.53	3.8 ± 2.1	2.4 ± 2.7	0.12
Mean BASMI (S.D)	1.2 ± 1.1	2.7 ± 1.6	0.0012	1.3 ± 1.2	1.5 ± 1.9	0.78
Mean CRP, mg/L (S.D)	6.9 ± 9.6	10.6 ± 17.1	0.20	2.6 ± 2.1	10.6 ± 15.5	<0.001
Mean Pain, VAS 0-100 mm, (S.D)	27.2 ± 23.0	28.6 ± 23.4	0.29	44.9 ± 23.9	25.9 ± 20.1	0.013
Anterior uveitis (%)	3 (15)	10 (43)	0.05	5 (17)	3 (38)	0.33
Psoriasis (%)	8 (40)	9 (39)	0.97	13 (45)	1 (13)	0.12
IBD (%)	3 (15)	3 (13)	0.61	6 (21)	0 (0)	0.31
Mean SPARCC score (entesitis)	1.2 ± 1.3	1.0 ± 1.4	0.63	2.0 ± 1.9	0.8 ± 1.5	0.0092

Conclusions: For the PROs, BASDAI and pain were higher in females diagnosed with nr-axSpA, and the CRP was significantly lower in this group. Peripheral and EAMs were slightly equally prevalent in AS and nr-axSpA in men and women except for uveitis, which is slightly more prevalent in AS. Our data show that AS patients were more frequently male than nr-axSpA patients. These results are in line with previous studies showing that male patients with axial SpA have more structural damage on radiographs than female patients. Among women, this study indicate that pain is more pronounced in non-radiographic axSpA than in AS, potentially revealing that chronic widespread pain (e.g. fibromyalgia) might interfere with the diagnostic accuracy of the non-radiographic axSpA subgroup. However, despite the absence of radiographic changes, patients with nr-axSpA have a burden of illness, with self-reported disease activity and functional impairments comparable with those of patients with structural changes consistent with AS.
References:
[1] Braun J, Kiltz U, Baraliakos X, et al. Optimisation of rheumatology assessments - the actual situation in axial spondyloarthritis including ankylosing spondylitis. Clinical and experimental rheumatology 2014;32(5 Suppl 85):S-96–104.
[2] Gran JT, Ostensen M, Husby G. A clinical comparison between males and females with ankylosing spondylitis. The Journal of rheumatology 1985;12(1):126–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2985

FRI0461 MUSCLE WASTING IN MALE TNF-α BLOCKER NAÏVE ANKYLOSING SPONDYLITIS PATIENTS: A COMPARISON OF GENDER DIFFERENCES IN BODY COMPOSITION WITH DUAL-ENERGY X-RAY ABSORPTIOMETRY

S.E. Ibáñez Vodnizza[1,2], I.M. Visman[3], J.C. van Denderen[3], W.F. Lems[3,4], M.T. Nurmohamed[3,4], I.E. van der horst-Bruinsma[4]. *[1]Rheumatology department, Clínica Alemana de Santiago; [2]Rheumatology department, Hospital Padre Hurtado, Santiago, Chile; [3]Amsterdam Rheumatology and immunology Center, Reade; [4]Amsterdam Rheumatology and immunology Center, VU University Medical Center, Amsterdam, Netherlands*

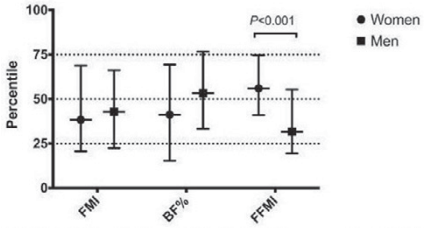
Background: Female Ankylosing Spondylitis (AS) patients have different disease characteristics compared to males. This might be explained by differences in body composition (BC), as women have higher total body fat mass, and adipose tissue can produce adipokines and participate in inflammatory and immunological processes.
Objectives: To assess gender differences in BC measured by Dual-Energy X-ray Absorptiometry (DXA) in a cohort of AS patients naïve to TNF-α blockers, and compare the BC with the reference population.
Methods: AS patients (Modified New York Criteria), 18 years old or older, who had a whole body DXA analysis before TNF-α blockers were included. Demographic information and disease activity measures (ASDAS and BASDAI) were reported. Fat Mass (FM) was reported as total FM (sum of trunk, arms, legs, and head), BF% (ratio FM/Total body mass), and Fat Mass Index (FMI= FM kg/height m^2). Fat Free Mass (FFM), calculated as lean mass + bone mineral content, and its index (FFMI kg/m^2) were reported. BF%, FMI, and FFMI percentiles, according to the reference population tables, stratified by age and gender, were also reported.
Results: Seventy consecutive patients were included, 60% were men. Baseline demographic characteristics were similar in men and women. Women had significantly higher BF% and FMI, and lower FFMI as absolute values (table 1). The FFMI percentile was markedly low in men (31.7%) (Figure 1). After multivariate analysis, an ASDAS-CRP >3.5 was related with lower FFM in the whole group (β-coefficient -5.1, 95% CI -10.2 to -0.1, P=0.047). ASDAS >3.5 was related to lower fat content in men and to higher fat content in women. The same relationships were found for BASDAI ≥4.

Table 1. Body composition characteristics

	All (N=70)	Male (N=42)	Female (N=28)	*P*
Age (median years, IQR)	42 (16)	44.2 (15.2)	40.7 (17.6)	NS
BMI (median, IQR)	25.6 (5)	25.9 (4.8)	24.2 (9)	NS
Underweight (%)	0	0	0	–
Normal (%)	48.6	45.2	53.6	NS
Overweight (%)	35.7	47.6	17.9	0.011
Obese (%)	15.7	7.1	28.6	0.021
Fat Mass, kg (mean, SD)	26 (9.3)	23.9 (8.7)	29.2 (9.6)	0.018
Fat Free Mass, kg (mean, SD)	51.1 (9.9)	56.8 (7)	42.5 (7.1)	<0.001
Body Fat % (mean, SD)	33.3 (8.9)	28.9 (7.3)	40 (6.7)	<0.001
Fat Mass Index (median, IQR)	8.5 (3.6)	8 (4)	9.7 (6)	0.001
Fat Free Mass Index (median, IQR)	17 (2.5)	17.7 (1.8)	15.1 (1.8)	<0.001

BMI = Body Mass Index, NS = not significant.

Figure 1: FMI, BF% and FFMI percentiles according to reference population tables



FMI= Fat Mass Index, BF%= Body fat percentage, FFMI= Fat Free Mass Index. Dot lines represent 25th, 50th and 75th percentile of reference population.

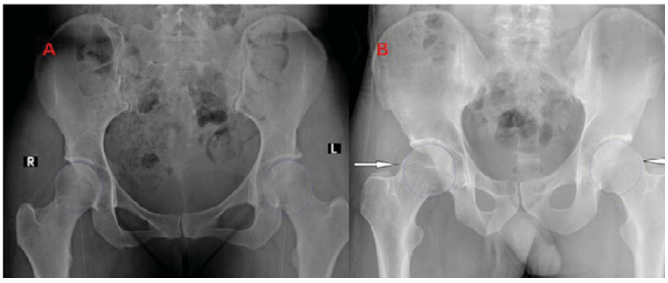
Conclusions: Muscle wasting, measured as low FFMI compared to the reference population, was found in male TNF-α blocker naïve AS patients, especially in those with active disease. Women had higher volumes of body fat than men, but near the median of the reference population. The relationships between fat content and disease activity support the complex association between adipose tissue and inflammation.
Acknowledgements: This study was endorsed by an ASAS (Assessment of SpondyloArthritis international Society) Fellowship.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1180

FRI0462 THE PISTOL-GRIP DEFORMITY IS MORE FREQUENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

O. Tosun[1], D. Solmaz[2], O. Gercik[3], G. Karaca[4], A. Tosun[5], M. Ozmen[3], F.E. Topal[6], S. Akar[3]. *[1]Radilogy, Katip Celebi University Faculty of Medicine, Izmir; [2]Rheumatology, Katip Celebi University Faculty of Medicine, izmir; [3]Rheumatology, Katip Celebi University Faculty of Medicine, Izmir; [4]Radiology; [5]Physical Medicine and Rehabilitation, Katip Celebi University Faculty of Medicine, izmir; [6]Emergency Medicine, Katip Celebi University Faculty of Medicine, Izmir, Turkey*

Background: Femoroacetabular impingement (FAI) is characterized by early pathologic contact of the proximal femur with the acetabulum. Pincer impingement is the acetabular cause of FAI.Whereas cam deformity seen as a flattening of the anterior contour of the head/neck junction or an osseous hump leading a decreased femoral head/neck offset. Patient with FAI presents with a hip or a trochanteric painusually in the sitting position or during or after activity. It might also be an important cause of hip osteoarthritis (OA).
Objectives: Therefore in this study we evaluated the frequency of pistol-grip deformity (PGD), described as the most characteristic feature of cam-type FAI, in axial spondyloarthritis (axSpA) patients as a potential alternative cause of hip or trochanteric pain.
Methods: A total 180 patients (107 [59%] male, mean age 41.9±12.8 years) with axSpA according to ASAS criteria and 198 patients (120 [61%] male, mean age 40.5±14.8 years) admitted to the emergency department (mostly due to trauma) and who had pelvic X-ray were included in the study.Patients with hip OA, hip prosthesis, acetabular protrusion or who have radiographs taken improper technique were excluded. An experienced radiologist assessed all anteroposterior pelvic radiographs. PGD was determined by demonstration of spherical or non spherical shape of femur head on AP pelvic radiography.
Results: The axSpA group consists 135 ankylosing spondylitis and 45 non-radiographic axSpA patients. The mean duration of symptoms was 13.8±11.3

years in axSpA patients. Radiographic findings of cam abnormality (figure) were significantly more frequent in axSpA patients in comparison with control subjects (30/150 [20%] vs 17/193 [9%] and *P*=0.004). Cam-type radiographic abnormality was only present 2 female control subjects and none of female axSpA patients. FAI was significantly correlated with the presence of HLA-B27 (r=0.213 and *P*=0.048), smoking (r=0.194 and *P*=0.018), height (r=0.283 and *P*=0.001) and gender (r=0.443 and *P*<0.001).



Conclusions: Our results showed that radiographic findings compatible with PGD were frequent in axSpA patients. In addition to repetitive injury tothe proximal femoral physis, new bone formation may be responsible for increased FAI in axSpA.In axSpA patients with hip or trochanteric pain, FAI may be kept in mind as an alternative explanation of the symptoms.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3678

FRI0463 OPTIMIZING THE ASSESSMENT OF SPONDYLOARTHROPATHY AMONG OPHTHALMOLOGISTS –A REGIONAL SURVEY

S. Goel[1], P. Kumar[2], A. Moorthy[2]. [1]*Medical student, University of Leicester;* [2]*University Hospitals of Leicester NHS Trust, UK, Leicester, United Kingdom*

Background: Spondyloarthropathy (SpA), is an under diagnosed clinical condition with an average delay in diagnosis of upto 8 years. The delay occurs due to non-specific symptoms which occur in young patients who are unlikely to present to healthcare services as well as presentations to different specialties as a result of extra-articular manifestations.
30% of Ankylosing Spondylitis (AS) patients have acute anterior uveitis (AAU) at some point due to the common link with HLA B-27. Uveitis may precede the diagnosis of Ankylosing Spondylitis (AS) by several years. Previous studies have shown that up to 40% (1) people with AAU have undiagnosed SpA, and are not routinely seen in rheumatology services due to lack of symptom and risk recognition. Early diagnosis in this group is essential to reduce the delay in diagnosis and improve the outcome of SpA.
Objectives: 1.To identify the current assessment of inflammatory back pain, in patients with recurrent AAU, by local ophthalmologists. 2. To identify ways to improve cross specialty referral and reduce delay in the diagnosis of SpA.
Methods: This is a prospective, questionnaire based semi qualitative study. The target population includes specialist ophthalmology trainees, consultants and GPs with a special interest in ophthalmology across the East Midlands. The questionnaire was piloted locally at a regional uveitis meeting. The improved questionnaire was then electronically communicated to ophthalmologists across East Midlands. The data was collated and analyzed using smartsurvey software.
Results: We received 61 responses (response rate =51%), of which 57 (n=57) were analysed. The respondents largely comprised doctors working at university hospitals (74%) and consultants (45%)
17% of the respondents were not confident with taking an inflammatory back pain history. Of the remaining 83%, only 67% respondents would normally think to ask about the main symptoms of back pain related to AS. Thus 44% respondents were not competent in taking an inflammatory back pain history.
With regards to their clinical practice, only 54% of respondents would routinely ask about symptoms of SpA in patients with recurrent AAU, even though 79% would test for HLA-B27. Furthermore, according to 42% of respondents they would never refer a recurrent AAU patient to a rheumatologist.
Most respondents felt that work pressure was the most likely reason for deficit of proper SpA assessment and referrals, followed by lack of support by guidelines
Conclusions: Our survey demonstrates a clear knowledge deficit among ophthalmologists regarding inflammatory back pain and the importance of assessing it in recurrent AAU patients. This can be improved by educating ophthalmologists about SpA in conferences and developing local guidelines about patients with HLA B-27 recurrent AAU related to assessment and referral.
References:
[1] A novel evidence-based detection of undiagnosed spondyloarthritis in patients presenting with acute anterior uveitis: the DUET (Dublin Uveitis Evaluation Tool).
[1] Muhammad Haroon, Michael O'Rourke, Pathma Ramasamy, Conor C Murphy, Oliver FitzGerald.
Acknowledgements: Respondents.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5434

FRI0464 ARTERIAL WALL INFLAMMATION IS NOT AFFECTED BY ANTI-IL17 TREATMENT IN PATIENTS WITH PERIPHERAL SPONDYLOARTHRITIS

L.J.J. Van Mens[1], S.L. Verweij[2], A.W.R. van Kuijk[3], E.S.G. Stroes[2], D.L. Baeten[1,4]. [1]*AMC, Amsterdam Immunology and Rheumatology Center;* [2]*Vascular medicine, Academisch Medisch Centrum;* [3]*Reade, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands;* [4]*UCB, Brussels, Belgium*

Background: Patients with spondyloarthritis (SpA), a chronic inflammatory disease, have an increased cardiovascular risk, which is partly due to increased inflammatory activity in the arterial wall.
IL-17A blockade with secukinumab is an effective treatment for SpA. The role of IL-17A in atherogenesis is controversial, some studies suggest that IL-17A is pro-atherogenic, while others indicate that IL-17A is athero-protective. So, it is not known wat the effect is of treatment with IL-17A blockade on inflammatory activity in the arterial wall.
Objectives: To assess the effect of 3 months treatment with secukinumab on arterial wall inflammation in SpA patients with peripheral disease (pSpA).
Methods: We included 20 patients with clinical pSpA in a 12 week open-label trial. Treatment consisted of 300 mg secukinumab once a week during the first 4 weeks and then every 4 weeks thereafter. EULAR DAS response was used to define a responder/non responder state. To measure arterial wall inflammation we performed a 18-fluorodeoxyglucose positron emission tomography with computed tomography (^{18}F-FDG PET/CT) imaging in 18 patients at baseline and week 12, which is a validated method to quantify arterial wall inflammation. Arterial wall inflammation is measured in both the ascending aorta and carotids, maximal FDG uptake is shown as the maximal target-to-background ratio (TBR_{max}).
Results: 18 patients with pSpA (age 44±12, 72% male) and without a previous cardiovascular event underwent imaging. Overall, three months treatment with secukinumab resulted in a significant improvement of disease activity with 17/18 patients achieving a EULAR DAS response (9 good and 8 moderate responders). Correspondingly, CRP levels decreased significantly (baseline: 3.2 [1.2–12.40] mg/dl vs. wk 12: 2.0 [1.1–5.8] mg/dl, p=0.011). Importantly, treatment with secukinumab did not affect cholesterol levels (total cholesterol baseline: 5.1±1 mmol/l v.s wk 12: 5.5±1 mmol/l, p=0.167; LDL-c baseline: 3.2±0.8 mmol/l v.s wk 12: 3.5±0.9 mmol/l, p=0.219). Additionally, arterial wall inflammation as measured by PET-CT did not change over the course of the 12 weeks treatment with secukinumab (aorta TBR_{max} baseline: 3.3±0.9 vs. wk 12: 3.3±0.7, p=0.861; carotid TBR_{max} baseline: 1.88±0.6 vs. wk 12: 1.76±0.4, p=0.067).
Conclusions: This pilot study in 18 patients with pSpA without any preexisting CV events showed that treatment with secukinumab for 3 months has no effect on arterial wall inflammation as measured by PET-CT. Further research in larger patient groups, over a longer period of treatment, and with different measurements remains warranted to fully elucidate the effect of IL-17A blockade on vascular inflammation.
Acknowledgements: This study was funded by an unrestricted grant from Novartis.
Disclosure of Interest: L. Van Mens: None declared, S. Verweij: None declared, A. van Kuijk Grant/research support from: UCB, Pfizer, MSD, Janssen, Consultant for: Novartis, Celgene, E. Stroes Speakers bureau: Amgen, Sanofi, Merck, D. Baeten Grant/research support from: Pfizer, MSD, AbbVie, Novartis, UCB, Janssen, Boehringer Ingelheim, Consultant for: Pfizer, MSD, AbbVie, Novartis, UCB, Janssen, Boehringer Ingelheim, Eli Lilly, Roche, BMS, Glenmark, Employee of: UCB
DOI: 10.1136/annrheumdis-2017-eular.4709

FRI0465 ANGLES OF SACRUM INCLINATION EFFECT ON RADIOLOGIC IMAGING READING IN SPONDYLOARTHRITIS (THE ANTELOPE-DESIR STUDY)

M. Herbette[1], L. Deloire[2], F. Garrigues[2], L. Gossec[3], A. Simon[4], A. Feydi[5], F. de Bruin[6], M. Reijnierse[6], D. van der Heijde[7], D. Loeuille[8], P. Claudepierre[9], T. Marhadour[1], A. Saraux[1] on behalf of DESIR cohort. [1]*Rheumatology;* [2]*Radiology, CHU Brest and Université Bretagne Occidentale, Brest;* [3]*Rheumatology, Pitié -Salpétriere, Paris;* [4]*Neurosurgery, CHU Brest and Université Bretagne Occidentale, Brest;* [5]*Radiology, CHU Cochin, Paris, France;* [6]*Radiology;* [7]*Rheumatology, Leiden, Leiden, Netherlands;* [8]*Rheumatology, CHU, Nancy;* [9]*Rheumatology, CHU Creteil, Paris, France*

Objectives: To assess the impact of spinal angles on clinical and imaging features of suspicion of axial spondyloarthritis (axSpA).
Methods: The DESIR cohort is a prospective longitudinal cohort study of adults aged 18–50 with inflammatory back pain (IBP) ≥3 months, ≤3 years. Baseline lateral lumbar radiography of patients included in DESIR cohort were read by two central blinded fellow readers (and a rheumatologist spine specialist in case of discrepancy) for Sacral Horizontal Angle (SHA), Lumbosacral angle (LSA) and total Lordotic Angle (TLA) measures. On the basis of literature, patients were classified depending on whether they had TLA more or less than 50°, SHA more or less than 40° or LSA more or less than 15°. Associations between angles and baseline clinical variables, presence of X-Rays (New York) and MRI (ASAS and MORPHO proposal definition) sacroiliitis, presence of spinal signs of spondyloarthritis (mSASSS, BASRI-total, SPARCC scores), presence

of spinal degenerative MRI signs on X-rays (yes or no) and MRI (presence of Modic abnormalities, Pfirrmann score, Canal stenosis, Extrusion, High intensity zone Facet osteoarthritis) according to central reading (two readers) and axSpA diagnostic confidence (according to local clinician's confidence on a 0–10 visual analog scale) were assessed by univariate analysis using the chi-square test (or Fisher's exact test where appropriate) and the Mann-Whitney test. Adjustment for multiple testing was performed according to Bonferroni method.

Results: Of 708 patients, data were available for 677, 675 and 672 for SHA, LSA and TLA, measures with a mean value of 39.2°, 14.5° and 51.5° respectively. Clinical features and diagnostic confidence did not differ between the SHA, LSA and TLA groups. More sacroiliitis imaging, according to ASAS (41.4% versus 32.0%) and MORPHO definition (48.6% versus 39.3%), were reported in TLA<50° group but the differences did not reach statistical significance. Radiological scores were low with a mean value of 0.49 (±1.83), 0.30 (±0.78) and 4.9 (±9.0) for mSASSS, BASRI-total and SPARCC score, respectively, and no inter-group difference was found. In L5S1, more grade 3 and 4 Pfirrmann class and MODIC discopathy (types 1 and 2) were observed for SHA <40°, and TLA <50° (p<0.001) whereas the difference did not reach the significance level for LSA<15° (p=0.05) (table).

Level	L5/S1					
Angles	SHA		LSA		TLA	
	<40	>40	<15	>15	<50	>50
Number of patients	328	300	313	313	270	353
Pfirmann class =3	**99 (30.2)**	**53 (17.7) ****	92 (29.3)	58 (18.5)*	**83 (30.7)**	**68 (19.3) ****
High Intensity Zone	61 (18.6)	35 (11.7)*	60 (19.2)	36 (11.5)*	40 (14.8)	56 (15.9)
Disc protrusion	37 (11.3)	22 (7.3)	27 (8.6)	30 (9.6)	34 (12.6)	24 (6.8)*
Disc extrusion	29 (8.8)	17 (5.7)	28 (8.9)	18 (5.8)	24 (8.9)	22 (6.2)
Canal stenosis	8 (2.4)	2 (0.7)	2 (0.7)	7 (2.2)	7 (2.6)	3 (0.8)
MODIC 1 signal	12 (3.7)	5 (1.7)*	15 (4.8)	2 (0.6)*	13 (4.8)	4 (1.1)*
MODIC 2 signal	7 (2.1)	1 (0. 3)*	2 (0.6)	1 (0.3)*	5 (1.8)	3 (0.4)*
Facet joint osteoarthritis	1 (0.3)	2 (0. 7)	1 (0.3)	2 (0.6)	1 (0.4)	2 (0.6)

Conclusions: Lumbar spine morphology is not associated with any clinical variable, presence on X-Rays or MRI of spinal signs of spondyloarthritis or sacroiliitis. At the L5S1 level, a more horizontal SHA and a reduction of TLA is associated with more degenerative radiological lumbar spine manifestations.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5128

FRI0466 REAL-LIFE PERFORMANCE OF THE ASAS HEALTH INDEX IN ROUTINE CARE OF PATIENTS WITH SPONDYLOARTHRITIS

U. Kiltz, T. Wiatr, X. Baraliakos, K. Fedorov, J. Braun. *Rheumatology, Rheumazentrum Ruhrgebiet, Herne, Germany*

Background: The measurement properties of the ASAS Health Index (ASAS HI) which has been developed to measure health and functioning of patients with spondyloarthritis (SpA) have been evaluated in a cohort study. Its association with structural changes has not been examined to date.

Objectives: To investigate the relationship between clincial data, function and health as assessed by the ASAS HI in patients with axial SpA (axSpA) and to study the influence of structural spinal changes on this instrument.

Methods: Patients fullfilling ASAS classification criteria for axSpA were recruited prospectively. Information was collected on clinical assessments (ASAS HI, NRS pain, BASDAI, ASDAS, BASFI, BASMI), laboratory parameters and spinal x-rays. Images were scored using mSASSS by two independent readers. The relationship between ASAS HI and other health outcomes was evaluated by Spearman correlation.

Results: A total of 150 patients (57 nr-axSpA and 93 AS patients) were included: 68.7% male, mean (SD) age 46.4 (14.1), symptom duration 18.7 (13.5) and diagnosis since 11.4 (11.8) years, and HLA-B27 positive in 82.0%. Values of clinical assessments were ASAS HI 7.4 (4.1), BASDAI 4.7 (2.3), ASDAS 2.7 (1.1), BASMI 3.3 (1.8), pain 5.7 (2.7), and BASFI 4.7 (2.6). Elevated CRP levels were found in 34.8% of the patients. Radiographs of the sacroiliac (SI) joint and the spine were available in 138 patients, 38.0% of which had syndesmophytes and 7.5% had a bamboo spine. The median (IQR) mSASSS value was 4.3 (IQR 1.0–22.1) in AS und 0.2 (IQR 0.0–1.4) in nr-axSpA patients. Patients received a treatment with NSAIDs (62.7%), DMARDs (20.9%) and/or biologics (49.4%). Significant correlation of ASAS HI was found for BASFI (r=0.8), BASDAI (r=0.7), ASDAS (r=0.5) and BASMI (r=0.5, and, all p<0.05). No correlations were found for ASAS HI and radiographic damage (mSASSS r=0.2, occurrence of syndesmophytes r=0.01, occurrence of bamboo spine r=0.2) and CRP levels (r=0.07). Stratifying patients by symptom duration (cut-off 3 years) did not affect these results.

Conclusions: Established measures of function and spinal mobility correlate well with the ASAS HI in patients with axSpA. The influence of structural changes as measured by mSASSS on the ASAS HI was limited in this study, probably due to relatively low mSASSS scores at baseline,. Further study in more and more severe patients is needed to study the association of physical activity, spinal mobility, function and radiographic damage in axSpA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2202

FRI0467 DEVELOPMENT AND PRELIMINARY VALIDATION OF THE COMPUTED TOMOGRAPHY SACROILIAC STRUCTURAL SCORE (CT-SSS) FOR ASSESSMENT OF STRUCTURAL LESIONS IN AXIAL SPONDYLOARTHRITIS

W.P. Maksymowych[1,2], M. Raynal[3], D. Loeuille[3], M.-A. D'Agostino[4], J. Paschke[2], R.G. Lambert[5]. *[1]Medicine, University of Alberta; [2]CaRE Arthritis, Edmonton, Canada; [3]Rheumatology, CHRU de Nancy, Vandœuvre-lès-Nancy; [4]Rheumatology, Université Paris Ouest, Paris, France; [5]Radiology, University of Alberta, Edmonton, Canada*

Background: Computed tomography (CT) is considered the imaging benchmark for the assessment of certain structural lesions in the sacroiliac joints (SIJ) of patients with axial spondyloarthritis (axSpA). Availability of low dose radiation techniques may lead to more widespread use, potentially as a structural endpoint in clinical trials research.

Objectives: We aimed to validate a new CT-based scoring method, the CT Sacroiliac Structural Score (CT-SSS), for assessing structural lesions in the SIJ.

Methods: CT scans of the SIJ from 44 patients (26 females, mean age 49.4 years, mean symptom duration 9.1 years) were reconstructed in the semicoronal plane parallel to the superior border of the sacrum and scoring of lesions was confined to this plane. Structural lesions were scored in consecutive slices in SIJ quadrants (erosion, sclerosis) or SIJ halves (ankylosis) on a dichotomous basis (present/absent) using the same anatomical principles as developed for the SPARCC MRI SIJ inflammation and structural scores. The most anterior slice is defined as visible joint ≥1cm vertical height and when <3 cm is defined as having only upper iliac and sacral quadrants. A visible joint ≥3cm vertical height is defined as having 4 quadrants. At the posterior aspect of the SIJ, there is a natural separation of iliac and sacral cortical bone by structures in the ligamentary portion. Scoring is terminated when <1cm of iliac and sacral bone is appositional. Two readers independently scored CT scans without a prior calibration exercise and using direct online data entry onto a schematic of the SIJ. Reliability was assessed by kappa statistics, intra-class correlation coefficient (ICC), and Bland-Altman limits of agreement.

Results: Scoring was feasible (5–10 minutes per scan) and both ankylosis (ICC=0.95) and erosion (ICC=0.81) were reliably scored (Table). Sclerosis was less reliably scored (ICC=0.39). Presence/absence of ankylosis was reliably detected irrespective of whether this was based on a single slice (κ=0.77) or 3 consecutive slices (κ=0.81). Reliable detection was lower for erosion (κ=0.50 for 1 or 3 slices) and sclerosis (κ=0.44 and 0.48 for 1 and 3 slices, respectively). Bland-Altman graphs illustrate reliability across the range of scores for ankylosis and erosion.

Table 1. Descriptive and Reliability data for CT-SSS score

	Mean (SD) score		Median (IQR) score		ICC	95% L of A
	R1	R2	R1	R2		
Erosion	4.4 (9.7)	6.5 (11.5)	0 (25.5)	0 (21)	0.95	-10.7, 13.5
Ankylosis	7.5 (14.1)	6 (13.6)	0 (12)	0 (12)	0.81	-16.2, 12.2
Sclerosis	6.6 (14.4)	7.4 (18.2)	0 (20)	0 (24.5)	0.39	-34.5, 33.0

IQR interquartile range L of A Limits of Agreement.

Conclusions: The CT-SSS method is feasible and reliable for scoring ankylosis and erosion with minimal calibration. Sclerosis requires further standardization and calibration.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5254

FRI0468 RADIOGRAPHIC HIP INVOLVEMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS. A STUDY OF ITS PREVALENCE AND DETERMINING FACTORS

X. Michelena, M. López de Recalde, H. Borrell, J. Lluch, P. Juárez, I. Morales, M. Pascual, J.-M. Nolla, X. Juanola. *Department of Rheumatology, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*

Background: Hip involvement in Ankylosing Spondylitis (AS) is the most frequent extraspinal manifestation and a common cause of disability and limited mobility, often ending with hip replacement. There are few studies analysing the radiographic changes of the hip and their relationship with other disease variables.

Objectives: To determine the factors associated with radiographic hip involvement and its prevalence.
Methods: A cross-sectional study was performed based on patients with AS, excluding the patients with associated psoriasis or inflammatory bowel disease. To assess radiographic hip involvement, we scored the last anteroposterior pelvic radiograph performed using the *Bath Ankylosing Spondylitis Radiology Index* (BASRI). Demographic, clinical, laboratory and radiographic data were collected and analysed. We considered the presence of hip disease with a BASRI-hip grade of at least 2. Statistical analysis: A descriptive study was performed. To compare differences we used a 1-way ANOVA test and Pearson chi-square. The statistical analyses were done using SPSS 24.0. $p \leq 0.05$ was considered statistically significant.
Results: 215 patients were identified, with a mean age of 52±13.6 years and 76.7% of the patients were male. The age at onset was 25.29±8.22 years. 86.4% of the patients were HLA-B27-positive. Regarding their treatment, 27.9% were under biological therapy. A hip replacement was needed in 14 patients (0.7%), with 6 of them requiring a bilateral hip replacement. The mean BASDAI score, BASFI score and ASDAS CRP index were 4.01±6.31; 4.73±8.8 and 2.17±1.01 respectively.
The table shows the comparison between the two groups based on the presence of hip involvement (BASRI hip $\geq$2). Statistically significant differences were observed in the age, age at onset and presence of peripheral arthritis. Patients with hip involvement had higher scores in BASFI score, ASDAS CRP and ESR. Axial radiographic involvement assessed with axial BASRI score and total SASSSm was associated with hip disease and a significant association was seen between hip involvement and metrological parameters.

	No hip disease n=154 (71.6%)	Hip disease n=61 (29.4%)	P-value
Age* (years)	49.5±13.63	58.16±11.53	<0.001
Age at onset* (years)	26.14±8.4	23.16±7.38	0.017
Male sex, n (%)	113 (73.4)	52 (85.2)	0.063
HLAB27+, n (%)	132 (85.7)	52 (85.2)	0.790
Peripheral arthritis, n (%)	33 (21.4)	25 (41.0)	0.004
Uveitis, n (%)	40 (26.0)	13 (21.3)	0.475
Biological treatment, n (%)	41 (27.0)	19 (31.1)	0.54
BASDAI*	3.84±7.29	4.47±2.14	0.527
BASFI*	3.79±7.15	7.23±11.81	0.012
ASDAS CRP*	2.07±1.01	2.45±0.95	0.014
ASDAS ESR*	1.89±0.90	2.52±1.92	0.002
Schober's index* (cm)	3.61±1.55	2.43±1.69	<0.001
Chest expansion* (cm)	4.97±1.84	3.67±2.02	<0.001
Cervical rotation* (cm)	72.03±19.73	49.18±28.01	<0.001
Lateral flexion* (cm)	12.96±5.18	7.85±4.1	<0.001
Occiput to wall distance* (cm)	2.49±4.36	8.45±8.38	<0.001
Intermalleolar* (cm)	100.22±21.22	82.37±17.91	<0.001
Axial BASRI*	5.31±3.10	8.53±3.38	<0.001
Total SASSSm*	10.24±16.07	30.67±27.31	<0.001

*Mean ± SD.

Conclusions: Radiographic hip involvement assessed with BASRI score is prevalent and it is related with the age at onset, disease activity and the presence of peripheral arthritis. These patients present more disability, less mobility and greater axial radiographic involvement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4375

FRI0469 DIFFERENCES BETWEEN ANKYLOSING SPONDYLITIS PATIENTS WITH AND WITHOUT RADIOGRAPHIC HIP INVOLVEMENT IN CHINA

X. Zheng, Q. Wei, J. Gu. *Department of Rheumatology and Immunology, The Third Affiliated Hospital of Sun Yat-sen Universiy, GuangZhou, China*

Background: Hip involvement, defined by clinical examination or imaging techniques, is a problem of great concern in Ankylosing Spondylitis (AS) patients as it leads to functional impairment and poor outcomes. It has been shown that early age at disease onset, peripheral manifestation and severe axial disease are risk factors, but other characteristics do not show consistency through studies and data is scarce so far.
Objectives: We aim to describe the phenotype differences between AS patients with and without radiographic hip involvement and to identify potential risk factors for hip involvement.
Methods: AS patients fulfilling the Modified New York Criteria and whose pelvic X-rays have been assessed by at least one radiologist and one rheumatologist were included. Radiographic hip involvement was defined by features of osteophytes around the femoral neck, erosions of the acetabulum, axial migration of the femoral head or hip joint space narrowing. The medical records were retrospectively reviewed and collected. Demographic and disease characteristics were compared by descriptive and bivariate statistics using SPSS v19.0 and stata v12.1 package.
Results: Totally 261 AS patients with hip involvement and 429 patients without hip involvement were analyzed. Statistical significance were found between these 2 groups regarding age at disease onset, gender, BMI, disease duration and presence of peripheral arthritis, with all p value$\leq$0.001. Male patients showed strong risk effect on hip involvement with the odds ratio (OR) around 3.27. Meanwhile, the hip-involved group had lower body mass index (BMI), which may relate to long disease duration or high inflammation level. No significant difference of HLA-B27 positivity, family history and other factors were observed (Table 01). Binary logistic regression results showed that age at disease onset, gender, BMI and disease duration were associated with hip involvement in AS ($p<0.001$). As for the symptoms, among 69 hip-involved and 75 non-involved AS with corresponding records, 83% hip-involved and 35% non-hip-involved patients complained of typical inguinal pain (OR=8.95, 95% CI=3.85~21.37, $p<0.001$).

Table 1

	AS with hip involvement (n=261)	AS without hip involvement (n=429)	*p* value
Age, m (SD)	28.57 (8.66)	28.01 (8.53)	0.41
Age at disease onset, m (SD)	18.28 (5.74)	22.31 (6.87)	<0.001
Men, n (%)	240 (91.95)	336 (77.78)	<0.001
BMI, m (SD)	20.35 (3.47)	21.31 (3.30)	<0.001
Disease duration, median (interquartile range)	108.00 (120.00)	48.00 (72.00)	<0.001
HLA-B27 positive, n (%)	230 (90.20)	370 (88.94)	0.61
Family history positive, n (%)	72 (27.80)	100 (23.53)	0.22
Inflammatory low back pain, n (%)	235 (90.38)	381 (88.81)	0.52
Peripheral arthritis, n (%)	118 (45.21)	140 (32.86)	0.001
Dactylitis, n (%)	9 (3.45)	9 (2.10)	0.28
Uveitis, n (%)	28 (10.73)	48 (11.21)	0.84
Enthesitis, n (%)	56 (21.62)	89 (21.04)	0.86
Axial pattern, n (%)	132 (50.57)	249 (58.04)	0.056

Conclusions: Compared to AS patients without hip involvement, the radiographic hip-involved group are younger age at disease onset, more frequently men and complaining of typical inguinal pain, have lower BMI and longer disease duration. AS patients having these concomitant risk factors should undergo further hip assessment in clinical practice.
References:
[1] Jeong H, Eun YH, Kim IY. Characteristics of hip involvement in patients with ankylosing spondylitis in Korea. Korean J Intern Med. 2017 Jan;32(1):158–164.
[2] Vander Cruyssen B, Vastesaeger N, Collantes-Estévez E. Hip disease in ankylosing spondylitis. Curr Opin Rheumatol. 2013 Jul;25(4):448–54.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4159

FRI0470 CIGARETTE SMOKING HAS A DOSE-DEPENDENT RELATIONSHIP WITH DISEASE ACTIVITY AND CORRELATES WITH MORE FUNCTIONAL LIMITATION AND WORSE HEALTH ASSESSMENT IN THE PATIENTS WITH ANKYLOSING SPONDYLITIS

Y. Jiang, Z. Liao, Z. Lin, M. Yang, Y. Zhang, Q. Li, J. Gu. *Rheumatology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease that mainly affects the axial skeleton by causing inflammatory and osteoproliferative changes in the sacroiliac joints and spinal structures [1]. Cigarette smoking is associated with poor outcome in patients with established and early AS [2].
Objectives: Our study was to investigate the relationship between cigarette smoking and pain, disease activity, functional limitation, and health assessment in Chinese patients with AS.
Methods: Patients with AS (n=683) from China took part in a cross-sectional survey. Smoking status was obtained by a standardized questionnaire, involving smoking status (non-smokers, exsmokers, current smokers), the age when starting smoking, cigarette numbers a day and smoking status of family numbers. The Bath AS Disease Activity Index (BASDAI), the Bath AS Functional Index (BASFI), visual Analogue scale of pain, Health Assessment Questionnaire for Spondyloarthropathy (HAQ-S) were analyzed in terms of smoking status and relationship with pack-year history.

Table 1. Demographic features and clinical and laboratory results of the patients with AS and comparison between patients with different smoking status

Variable	All patients N=683	Non-smokers N=407	Ex-smokers N=108	Current smokers N=168	*P*(1:3)	*P*(2:3)	*P*(1:2)
Age (years)	27.33±8.67	26.04±8.65	27.65±8.74	30.24±7.98	0.000	0.001	0.069
Disease duration (years)	6.47±6.47	5.73±6.08	6.81±6.54	8.05±7.05	0.000	0.094	0.071
Morning stiffness (VAS)	3.12±2.86	2.84±2.87	2.87±2.53	3.96±2.89	0.000	0.003	0.739
Overall Pain (VAS)	3.97±2.77	3.78±2.83	3.96±2.70	4.44±2.61	0.005	0.150	0.440
Nocturnal back pain (VAS)	2.93±2.96	2.63±2.90	2.89±2.73	3.68±3.11	0.000	0.049	0.216
ESR (mm/h)	20.94±21.71	20.80±22.61	19.65±20.92	22.11±19.98	0.311	0.150	0.407
CRP (mg/dl)	18.4±26.01	17.33±28.14	18.4±22.76	20.98±22.26	0.001	0.126	0.340
BASDAI	3.36±2.03	3.21±2.05	3.30±1.79	3.76±2.07	0.002	0.065	0.437
BASFI	5.21±9.21	1.47±2.07	1.54±1.98	1.55±1.63	0.018	0.379	0.251
HAQ	0.21±0.33	0.20±0.33	0.19±0.30	0.23±0.33	0.130	0.313	0.213

P(1:3) refers to p value of the The Mann-Whitney U test and t test between non-smokers and current smokers.

Results: Of all the 683 patients, 168 are current smokers, while 108 were ex-smokers and 407 patients never smoked. Mean scores of degree and duration of morning stiffness, overall pain, nocturnal back pain, overall back pain, CRP, BASDAI and BASFI score were all higher in the current smoker group compared to those who had never smoked ($P<0.05$). In Spearman correlation analysis, pack years of smoking in current smokers were significantly associated with disease duration, morning stiffness (VAS) and duration, nocturnal back pain, overall back pain, CRP, and BASDAI ($P<0.01$), and overall pain, BASFI and HAQ-S ($P<0.05$).
Conclusions: Cigarette smoking has a dose-dependent relationship with disease activity and correlates with more functional limitation and worse health assessment in patients with AS.
References:
[1] Braun, J. and J. Sieper, Ankylosing spondylitis. Target treatment criteria. Z Rheumatol, 2009. 68(1): p. 30–6.
[2] Ward, M.M., et al., Risk factors for functional limitations in patients with long-standing ankylosing spondylitis. Arthritis Rheum, 2005. 53(5): p. 710–7.
Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2045

FRI0471 PSYCHOLOGICAL DISORDERS, SLEEP DISTURBANCE AND STRESSFUL LIFE EVENTS IN THE PATIENTS WITH ANKYLOSING SPONDYLITIS

Y. Jiang, M. Yang, Y. Zhang, Z. Liao, Z. Lin, Q. Lv, J. Qi, Q. Wei, S. Cao, J. Gu. *Rheumatology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that may result in pain, functionally limitation and even less life expectancy. Psychological symptoms not only have a substantial negative impact on the quality of life, but also on the course and outcome of the chronic disorder [1]. AS patients may also suffer from various sleep problems, and pain intensity, anxiety, and depression correlated significantly with poorer sleep quality [2]. Stressful life events have a substantial association with psychological disorders, and there is some evidence indicating that even early life stress constitutes a major risk factor for the subsequent development of mental disorder [3].
Objectives: Our study was to investigate psychological disorders, sleep disturbance and stressful life events in Chinese patients with AS, and to assess the correlation between each two disorders.
Methods: AS patients diagnosed with the modified New York criteria for AS were enrolled from several provinces all over China. Participants were required to complete a set of questionnaires and examinations, including demographic and clinical information, Zung self-rating anxiety scale (SAS), Zung self-rating depression scale (SDS), the Social Readjustment Rating Scale (SRRS) and the Pittsburgh Sleep Quality Index questionnaire (PSQI). The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis. The relations between psychological variables, stressful life events, sleep quality and other parameters were examined with Spearman correlation analysis.
Results: Of all the 2772 AS patients, 79.1% were male patients. 79.5% were employed. 48.4% were married. Mean age was 28.99±8.87. Mean disease duration was 6.84±6.78. Mean SAS score was 49.32±18.75. 31.6% of the patients had anxiety, of which 10.8% had severe anxiety. Mean SDS score was 54.97±16.67. 59.3% had suffered from depression, of which 11.3% had severe depression. Mean PSQI score was 6.48±4.32. 31.0% of the patients were poor sleepers. SRRS score was 129.33±145.06. 35.3% had stimulus of psychological and social elements (SPSE), while 14.4% came across severe SPSE. SAS scores were associated with age, age onset, SDS scores, SRRS scores positively and years of education negatively ($P<0.01$). SDS scores were associated with age, SAS scores, SRRS scores positively and years of education negatively ($P<0.01$). SRRS scores also correlated of less sleep efficiency ($P<0.05$).
Conclusions: A large number of AS patients were found to have anxiety, depression, sleep disturbance and stressful life events. These problems correlated with each other. Clinicians should pay more attention to psychological disorders and sleep problems in AS patients.
References:
[1] Gladis MM, Gosch EA, Dishuk NM, Crits-Christoph P (1999) Quality of life: expanding the scope of clinical significance. J Consult Clin Psychol 67: 320–331.
[2] Sayar K, Arikan M, Yontem T (2002) Sleep quality in chronic pain patients. Can J Psychiatry 47: 844–848.
[3] Gourion D (2009) Events of life and links with severe depression at different ages. Encephale 35 Suppl 7: S250-S256.
Acknowledgements: None.
Disclosure of Interest: Y. Jiang: None declared, M. Yang: None declared, Y. Zhang: None declared, Z. Liao: None declared, Z. Lin: None declared, Q. Lv: None declared, J. Qi: None declared, Q. Wei: None declared, S. Cao: None declared, J. Gu Grant/research support from: This project was supported by the National Natural Sciences Foundation of China (31070806), Clinical Subject (2007 and 2010) of Ministry of Public Health of China and from the Foundation of Guangdong province of China (2005A30801005 and 2008B080701086), State Board of Education Fund for the Doctoral (20060558046), Guangzhou Science and Technology Plan Projects (2006Z2-E0221) and 5010 Subject of Sun Yat-sen University (2009–2010)
DOI: 10.1136/annrheumdis-2017-eular.2246

FRI0472 EXTRA-RHEUMATOLOGICAL FEATURES ARE FREQUENTLY ASSOCIATED WITH PERIPHERAL RHEUMATOLOGICAL FEATURES IN AXIAL SPONDYLOARTHRITIS AND INFLUENCE THE CHOICE OF THE ANTI-TNF IN DAILY PRACTICE. AN ANALYSIS OF 519 PATIENTS

A. Moltó, A. Etcheto, L. Gossec, S. Perrot, N. Boudersa, P. Claudepierre, N. Roux, F. Berenbaum, A. Martin, L. Sparsa, P. Coquerelle, M. Soubrier, M. Dougados. *Predict-SpA Study Group, Paris, France*

Background: Axial involvement is the predominant feature of axSpA but both extra-articular (EAM)and peripheral manifestations (including synovitis and dactylitis) can be concomitantly observed.
Objectives: To evaluate whether the EAM are associated with peripheral rheumatological features in axSpA and whether these EAM influence the choice of the anti-TNF.
Methods: *Study design:* Prospective, multicenter, cross-sectional study in France (baseline visit of the Predict-SpA trial). *Patients:* definite axSpA according to the rheumatologist, requiring an anti-TNF. *Data collected:* Past or present signs/symptoms of EAM (psoriasis, uveitis and Inflammatory Bowel disease (IBD)), peripheral (arthritis, enthesitis and dactylitis) SpA features, and the anti-TNF prescribed by the treating rheumatologist (according to usual practice). Statistical analysis: the frequency of peripheral involvement and the type of anti-TNF (e.g. monoclonal antibodies vs soluble receptor) were compared in patients with versus (vs) without EAM.
Results: Of the 519 patients (females: 46%, age: 42±12 years, HLA B27 positive: 65%, X-Ray sacroiliitis: 56%, inflammation on MRI of the sacro Iliac Joint: 56%), 386 were biologic naïve. A past history or current symptoms of psoriasis, uveitis and IBD was observed in 19%, 17% and 5% respectively and a past history or current symptoms of arthritis, enthesitis and dactylitis in 27%, 54%, 11%, respectively
In patients with vs without psoriasis, the % of arthritis, enthesitis and dactylitis were 40% vs 25% (p=0.004), 67% vs 50% (p=0.002) and 18% vs 10% (p=0.026), respectively
In patients with vs without uveitis, the % of arthritis, enthesitis and dactylitis were 31% vs 27% (p=0.445), 57% vs 53% (p=0.200) and 13% vs 11% (p=0.772),respectively
In patients with vs without IBD, the % of arthritis, enthesitis and dactylitis were 36% vs 27% (p=0.440), 68% vs 53% (p=0.180) and 21% vs 11% (p=0. 152), respectively
Monoclonal antibodies were prescribed as the first biologic in 206 out of the 386 patients (53%).This percentage was 56% vs 58% and vs 52% in patients with a current presence of psoriasis vs any history of psoriasis but currently absent and vs without any history of psoriasis, respectively; p=0.785. This percentage was 100% vs nd% (n=0) and vs 53% in patients with a current attack of uveitis vs any history of uveitis but currently inactive and vs without any history of uveitis, respectively; p=0.032. This percentage was 100% vs 50% (n=2) and vs 53% in patients with a current active IBD vs any history of IBD but currently inactive and vs without any history of IBD, respectively; p=0.064.
Conclusions: In this study focused on ax SpA patients, both peripheral rheumatological clinical features and EAM were frequently observed. The peripheral rheumatological manifestations were more frequently observed in case of concomitant psoriasis. Monoclonal antibodies were the preferred anti-TNF in case of a past history (even currently quiescent) of uveitis or IBD in daily practice.
Acknowledgements: This study was conducted thanks to an unrestricted grant from MSD
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4713

FRI0473 PATIENT-PHYSICIAN DISCORDANCE IN GLOBAL ASSESSMENT IN 401 EARLY AXIAL SPONDYLOARTHRITIS (AXSPA) PATIENTS FROM THE DESIR COHORT: WHAT IS THE EFFECT ON OUTCOMES AT 3 YEARS?

C. Desthieux[1], A. Molto[2], A. Saraux[3], B. Fautrel[1], L. Gossec[1]. *[1]Rheumatology, Paris 06 University and Pitié-Salpêtrière Hospital; [2]Rheumatology, Paris Descartes University and Cochin Hospital, Paris; [3]Cavale Blanche University Hospital, Brest, France*

Background: Discordance between patients' and physicians' ratings of disease activity is frequent. We have previously shown this discordance occurs in around 28% of visits in early axSpA though repeated discordance (over several visits) is less frequent (1).
Objectives: To assess in patients with early axSpA, the impact at 3 years of repeated discordance on treatment prescription, functional incapacity and remission.
Methods: DESIR (Devenir des Spondyloarthropathies Indifférenciées Récentes) is a French, multicenter, longitudinal cohort of patients with early inflammatory back pain suggestive of axSpA (2). Patient and physician global assessment

(respectively PGA and PhGA) were rated on a 0–10 numeric scale, every 6 months during 2 years then at 3 years. Only patients with all data available for PGA and PhGA for each of the 6 visits were included. Repeated discordance was defined as an absolute difference |PGA–PhGA|≥3/10 for at least 3 of the 6 visits (i.e., at least half of the visits). Univariable and multivariable logistic models were used to determine if repeated discordance was associated at the 3 years timepoint, with prescription of TNFi, functional incapacity defined as HAQ>0.5, and remission defined as ASDAS-CRP<1.3.

Results: Of 401 patients, mean age 34.6±8.7 years, mean symptoms duration 17.8±10.7 months, 219 (54.6%) were female and mean ASDAS-CRP at baseline 2.7±1.0. At 3 years 140 (34.9%) patients had been prescribed a TNFi, 172 (43.2%) had HAQ>0.5 and 89 (25.1%) were in remission. Over the 6 visits, mean PGA was higher than mean PhGA with a mean absolute difference of 0.8±2.2 points. Discordance concerned 110 (27.4%) patients at baseline and repeated discordance concerned 92 (22.9%) patients. In multivariable logistic regression, after adjusting on the others significant factors (which included MRI sacro-iliitis, HLA-B27 and ASDAS-CRP at baseline), repeated discordance was associated with more functional incapacity (61% vs 38%, odds ratio, OR 2.85 [95% CI 1.49–5.62]) and less remission (10% vs 30%, OR 0.38 [0.15–0.85]) but not more TNFi use (34% vs 35%, 1.39 [0.78–2.54] p=0.27).

Conclusions: In early axSpA, repeated discordance concerned 22.9% of patients confirming the frequency of this situation. Repeated discordance was associated with worse outcomes at 3 years, even after adjustment of other factors including baseline ASDAS, indicating for the first time that discordance may indeed reflect an unsatisfactory management of medical care leading to worse outcomes. Future studies should concentrate on understanding the reasons of patient-physician discordance for disease activity in axSpA.

References:

[1] Desthieux C, Molto A, Granger B, Saraux A, Fautrel B, Gossec L. Patient-physician discordance in global assessment in early spondyloarthritis and its change over time: the DESIR cohort. Ann Rheum Dis. 2015 Oct. 22.

[2] Dougados M, Etcheto A, Molto A, Alonso S, Bouvet S, Daurès J-P, et al. Clinical presentation of patients suffering from recent onset chronic inflammatory back pain suggestive of spondyloarthritis: The DESIR cohort. Joint Bone Spine. 2015 Oct;82(5):345–51.

Acknowledgements: The DESIR cohort is financially supported by unrestricted grants from the French Society of Rheumatology and Pfizer France. These analyses were supported through an unrestricted academic grant from Pfizer France.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4417

FRI0474 DOES AXIAL SPONDYLOARTHRITIS PHENOTYPE CORRELATE WITH IMAGING MORPHOTYPE?

X. Baraliakos[1], A. Szumski[2], H.E. Jones[3], L. Gensler[4]. *[1]Ruhr University, Bochum, Germany; [2]inVentiv Health, Princeton; [3]Pfizer, Collegeville; [4]University of California, San Francisco, United States*

Background: Traditionally, radiographic imaging was used to describe morphological differences between various types of axial SpA (axSpA). The advent of MRI has advanced understanding of disease, enabled earlier diagnosis and visualization of structural changes, and facilitated the identification of non-radiographic axial SpA (nr-axSpA). The magnitude of the pathologic changes in the axial skeleton is used to quantify inflammatory and structural outcomes of clinical trials and treatment of patients with axSpA.

Objectives: To examine the MRI morphology of sacroiliitis (SI) and vertebral corner lesions in patients with primary (1°, no psoriasis) and secondary (2°, with psoriasis) axSpA.

Methods: This posthoc analysis was performed on data from patients with axSpA enrolled in the EMBARK trial (NCT01258738). Only patients with baseline MRI lesions were included. Symmetric and asymmetric SI, structural lesions, and corner inflammatory lesions were analyzed in 1° axSpA vs 2° axSpA patients. Data were analyzed using one-way analysis of variance for continuous parameters, chi-square tests, or Fisher's exact tests for categorical parameters.

Results: The baseline demographics and disease characteristics between the 122 patients with 1° axSpA and 19 with 2° axSpA were similar. Asymmetric sacroiliitis was seen in significantly fewer 1° (43%) vs 2° (68%) axSpA patients. There were no differences in mean SpondyloArthritis Research Consortium of Canada (SPARCC) scores between 1° and 2° axSpA for any of the 4 SI joint (SIJ) quadrants. However, the lower iliac quadrants had the highest SPARCC SIJ score and the upper iliac quadrants had the lowest SPARCC SIJ scores. When analyzing the 4 spine quadrants (lower/upper anterior and lower/upper posterior), 1° patients had higher total SPARCC spine scores than 2° patients for all 4 quadrants at baseline. Collapsing the 4 quadrants shows that 1° axSpA patients had higher SPARCC MRI of the entire spine (23 discovertebral units [DVU]; mean=5.7) compared with 2° axSpA patients (mean=2.7).

Conclusions: We found 1° axSpA patients had more symmetric sacroiliitis and extensive spinal bone marrow edema compared with 2° axSpA patients. In addition, women appeared to have more asymmetric sacroiliitis. These data may help physicians accurately diagnose patients and decide best treatment options.

Disclosure of Interest: X. Baraliakos: None declared, A. Szumski Employee of: inVentiv, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, L. Gensler Consultant for: AbbVie, Janssen, Novartis, Pfizer

DOI: 10.1136/annrheumdis-2017-eular.3681

FRI0475 ANTI-CD74 ANTIBODIES AS DIAGNOSTIC BIOMARKER FOR EARLY AXIAL SPONDYLOARTHRITIS: DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY (SPACE) COHORT STUDY

J.J. de Winter[1], M.G. van de Sande[1], N. Baerlecken[2], I.J. Berg[3], R. Ramonda[4], D. van der Heijde[5], F.A. van Gaalen[5], T. Witte[2], D.L. Baeten[1]. *[1]AMC, Amsterdam, Netherlands; [2]MHH, Hannover, Germany; [3]Diakonhjemmet Hospital, Oslo, Norway; [4]UniPD, Padua, Italy; [5]LUMC, Leiden, Netherlands*

Background: Diagnosis of axSpA is often delayed with 5–10 years. A robust biological disease marker is lacking and could decrease the current diagnostic delay. Two studies showed that serum anti-CD74 IgG antibodies are increased in SpA[1,2].

Objectives: To explore the value of anti-CD74 antibodies as diagnostic biomarker for axSpA in patients with early, chronic back pain.

Methods: We tested the prevalence of anti-CD74 IgG and IgA antibodies in patients from the SPondyloArthritis Caught Early (SPACE) cohort by enzyme-linked immunosorbent assay (ELISA). Patients from the SPACE cohort have chronic back pain for >3 months and ≤2 years with an onset <45 years.

Results: We included 560 patients of the SPACE cohort, of whom 274 patients were diagnosed with axSpA by a rheumatologist at baseline. Anti-CD74 IgG levels did not differ between patients with and without axSpA (p=0.152, Table 1). Median anti-CD74 IgA levels (tested with either casein or BSA as a blocking buffer) were higher in patients with axSpA (both p<0.0001). Despite these differences at the group level, the diagnostic value of the anti-CD74 IgA antibodies was limited as shown by ROC analysis. The optimal cut off according to ROC analysis was an optical density (OD) of 0.875, providing a sensitivity of 38.3% and a specificity of 77.6%. In line with previous reports, further analysis revealed that total IgA levels were elevated in early axSpA patients vs. non-SpA early back pain patients (p=0.008). When correcting the level of anti-CD74 IgA for the level of total IgA, the differentiating capacity of anti-CD74 disappeared for casein but remained intact for BSA (casein: p=0.731, BSA: p=0.038). Additional analyses using the ASAS classification criteria rather than a clinical diagnosis of axSpA, a strict combination of clinical diagnosis and ASAS classification criteria (excluding patients fulfilling the ASAS axSpA criteria without a clinical diagnosis and vice versa) (Table 1) and using the clinical diagnosis at 1 year of follow-up yielded similar results.

	Axial SpA (baseline)			ASAS axSpA criteria (baseline)			Diagnosis and ASAS axSpA positive (baseline)		
	Yes (n=274)	No (n=286)	*P*-value	Yes (n=224)	No (n=351)	*P*-value	Yes (n=108)	No (n=177)	*P*-value
anti-CD74 IgA (casein, OD)	0,73	0,57	**<.0001**	0,74	0,58	**<.0001**	0,78	0,55	**<.0001**
anti-CD74 IgA (BSA, U/mL)	19,92	14,02	**<.0001**	22,55	14,20	**<.0001**	21,82	13,47	**<.0001**
anti-CD74 IgG (OD)	0,50	0,52	0,152	0,49	0,52	.054	0,50	0,52	0,075
anti-CD74 IgA (IC, OD)	0,59	0,6	0,653	0,54	0,62	.112	0,54	0,61	0,383
IgA total (g/dL)	3,94	3,39	**0,008**	3,79	3,51	.084	3,92	3,38	**0,017**
ratio IgA (casein) / IgAtotaal	0,17	0,17	0,731	0,17	0,17	.614	0,18	0,17	0,435
ratio IgA (BSE) / IgAtotaal	4,35	3,56	**0,038**	4,37	3,70	.070	4,37	3,39	**0,036**
ratio IgA IC / IgAtotaal	0,18	0,18	0,387	0,18	0,18	.388	0,17	0,19	0,294

Table 1. Levels of IgG and IgA anti-CD74 antibodies, total IgA and anti-CD74/total IgA ratios in patients from the SPACE cohort. Values are expressed as median and compared using Mann-Whitney U testing. Diagnosis and ASAS axSpA positive: patients diagnosed as axSpA and fulfilling the ASAS axSpA criteria vs. patients not diagnosed as axSpA and not fulfilling the ASAS axSpA criteria.

Conclusions: Serum anti-CD74 IgA antibody levels, but not serum anti-CD74 IgG levels, are elevated in patients with axSpA versus non-SpA with back pain of <2 years duration. However, ROC analyses revealed that these numerical differences are of limited diagnostic value in these patients with early back pain.

Abstract FRI0474 – Table 1

Parameter	Total (n=141)	1° axSpA with			2° axSpA with			P value
		Symmetric SI (n=63)	Asymmetric SI (n=52)	Non-SI (n=7)	Symmetric SI (n=4)	Asymmetric SI (n=13)	Non-SI (n=2)	
Age, y	32.1 (7.4)	30.9 (6.8)	32.5 (7.8)	35.3 (7.3)	29.3 (7.9)	33.5 (6.2)	47.0 (2.8)	0.2132
Male, n (%)	92 (65.3)	46 (73.0)	27 (51.9)	4 (57.1)	4 (100)	9 (69.2)	2 (100)	0.0896
Symptom duration, y	2.6 (1.9)	2.4 (2.2)	2.6 (1.5)	2.7 (1.6)	1.8 (1.5)	3.2 (1.6)	2.9 (1.6)	0.2944
SPARCC MRI SIJ score	10.5 (9.9)	15.9 (10.4)	5.4 (5.1)	2.1 (0.2)	27.5 (10.2)	5.9 (4.1)	2.5 (0.7)	0.0007
Left SPARCC SIJ	5.2 (6.0)	7.9 (6.1)	3.1 (5.3)	0.8 (0.3)	10.4 (7.4)	1.8 (2.1)	1.3 (0.4)	0.0004
Right SPARCC SIJ	5.4 (6.2)	8.0 (7.0)	2.3 (2.5)	1.4 (0.2)	17.1 (6.3)	4.0 (5.0)	1.3 (0.4)	0.0542
SPARCC MRI 6 DVU spinal score	4.7 (6.8)	6.4 (8.5)	3.8 (5.5)	2.4 (2.1)	1.6 (3.3)	2.6 (3.4)	0.8 (1.1)	0.0133
SPARCC MRI 23 DVU spinal score	5.3 (9.3)	7.5 (12.2)	4.0 (6.0)	2.4 (2.1)	1.6 (3.3)	3.4 (5.3)	0.8 (1.1)	0.0335
Fat metaplasia	0.5 (1.6)	0.3 (0.9)	0.9 (2.5)	0 (0)	0.3 (0.5)	0.7 (1.1)	0 (0)	0.6805
Erosions	2.6 (3.5)	4.2 (4.0)	1.1 (2.0)	0.3 (0.4)	3.1 (1.8)	1.0 (1.9)	0 (0)	0.0002

References:
[1] Baraliakos, X. et al. High prevalence of anti-CD74 antibodies specific for the HLA class II-associated invariant chain peptide (CLIP) in patients with axial spondyloarthritis. Ann. Rheum. Dis. 1–5 (2013).
[2] Baerlecken, N. T. et al. Autoantibodies against CD74 in spondyloarthritis. Ann. Rheum. Dis. 73, 1211–4 (2014).
Disclosure of Interest: J. de Winter: None declared, M. van de Sande Grant/research support from: Novartis, Eli Lilly, Boehringer Ingelheim, Benecke, Takeda, Tillotts, MSD, Cellgene, N. Baerlecken: None declared, I. Berg: None declared, R. Ramonda: None declared, D. van der Heijde: None declared, F. van Gaalen: None declared, T. Witte: None declared, D. Baeten Grant/research support from: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim., Consultant for: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim, Eli Lilly, Roche, BMS, Glenmark, Employee of: UCB
DOI: 10.1136/annrheumdis-2017-eular.2271

FRI0476 ANTI-CD74 ANTIBODIES: DIAGNOSTIC PROPERTIES IN LOW HLA-B27 EARLY AXIAL SPONDYLOARTHRITIS

N.R. Ziade[1], F. Fayad[1], I. Mallak[2], G. Merheb[3], T. Witte[4], X. Baraliakos[5].
[1]Rheumatology; [2]Radiology, Hotel Dieu de France, Beirut; [3]Rheumatology, ND Secours, Jbeil, Lebanon; [4]Medicine, Hannover University, Hannover; [5]Rheumatology, Rheumazentrum Ruhrgebiet, Herne, Germany

Background: Axial spondyloarthritis (AxSpA) is a severe and potentially debilitating disease, where earlier diagnosis lead to a better prognosis. Although HLA-B27 antigen is strongly associated with AxSpA, this marker may have a low sensitivity in some Middle-Eastern countries. Recent European studies showed a strong association between antibodies against CD74 and AxSpA with a sensitivity of 85.1%, specificity of 92.2%, and positive likelihood ratio (LR) of 10.8. The diagnostic properties of anti-CD74 may have a particular interest in non-European countries with low HLA-B27 such as Lebanon.
Objectives: In this prospective study, we tested the diagnostic properties of IgG and IgA anti-CD74 as an early diagnostic marker for AxSpA, compared with HLA-B27, in Lebanon, which is known as one of the countries with the lowest HLA-B27 prevalence ever reported.
Methods: Sera of AxSpA patients and healthy blood donors (HBD) were analyzed for HLA-B27 genes (PCR) and for IgG and IgA anti-CD74 (ELISA). The patients were recruited from rheumatology clinics across Lebanon. Clinical assessment and sera sample collection were performed at a center specialized in AxSpA (Hotel-Dieu de France University hospital, Beirut). Inclusion criteria were: age 18–45 years, Lebanese, symptom duration <3 years, AxSpA as per ASAS criteria (imaging arm), no prior biologic therapy. Interpretation of the radiographic images was performed centrally and blindly. Clinical and laboratory assessments of the disease were performed in all AxSpA patients. Comparison between groups was performed with the Fisher exact test and Student's test. For the diagnostic properties of HLA-B27 and anti-CD74, ROC curves were calculated.
Results: 29 AxSpA patients and 75 HBD were tested. AxSpA patients were slightly older (31.3 and 27.4 yo, respectively, p=0.02). Male gender was slightly predominant (51.7% and 53.6%, respectively). 93% had all characteristics of IBP as per ASAS criteria. 62.1% had non radiographic AxSpA. Mean disease duration was 25.2 months (SD 15.9), mean BASDAI 4.5 and mean ASDAS 3.25. 58.6% had extra-articular manifestations (28% enthesitis, 24% psoriasis, 21% peripheral arthritis, 10% IBD and 7% uveitis). 27.6% had familial history of SpA (21%), psoriasis (10%) and Crohn's disease (3.4%). HLA-B27 status was positive in 10 AxSpA patients and in 2 HBD (Sensitivity 34.5%, Specificity 97.2%, Positive LR 12.24). In the ROC analysis, IgG4 anti-CD74 showed the best diagnostic properties for AxSpA (AUC 0.939, cut-off value 0.55). Using this cut-off value, positive values of IgG anti-CD74 were found in 27 axSpA patients and 5 HBD (Sensitivity 93.1%, Specificity 93.3%, positive predictive value 84.4%, negative predictive value 97.2%). Positive LR was 13.97. Anti-CD74 was positive in 58.6% HLA-B27 negative AxSpA (Fig1).

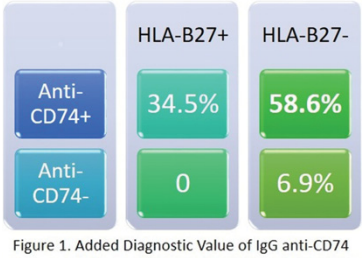


Figure 1. Added Diagnostic Value of IgG anti-CD74 compared to HLA-B27 in Early Axial Spondyloarthritis

Conclusions: In this study in a population with low HLA-B27 prevalence, IgG anti-CD74 antibodies showed higher diagnostic value than HLA-B27 for AxSpA. This is of special interest in populations with low HLA-B27 prevalence, especially on the background of diagnosing AxSpA when using the clinical arm of the ASAS classification criteria.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5208

FRI0477 PROSPECTIVE OBSERVATIONAL STUDY ON THE EVALUATION OF QUALITY OF LIFE IN PATIENTS AFFECTED BY ENTEROPATHIC SPONDYLOARTHRITIS

M.S. Chimenti[1], P. Conigliaro[1], B. Polistena[2], P. Triggianese[1], A. Ruffa[3], C. Canofari[1], F. Cedola[1], S. Onali[3], M. Balan[1], E. Calabrese[1], C. Petruzziello[3], F. Spandonaro[2], G. Monteleone[1], L. Biancone[3], R. Perricone[1]. *[1]Department of system medicine, Rheumatology, Allergology and Clinical Immunology; [2]Department of Economic and Finance; [3]Department of system medicine, Gi Unit, Dpt, University of Rome Tor Vergata, Rome, Italy*

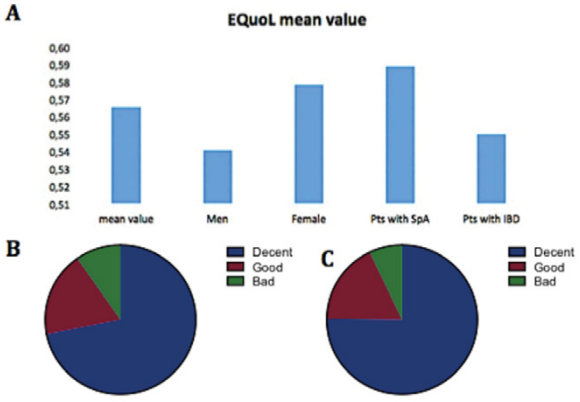
Background: Enteropathic Spondyloarthritis (ESpA) belongs to the group of Spondyloarthritis (SpA) tipically associated with inflammatory bowel disease (IBD) as Crohn's Disease (CD) and Ulcerative Colitis (UC). Joint pain is the most common (22–33%) and significant extra-intestinal manifestation in patients with IBD and its management requires reumatological and gastroenterological competence in collaboration. No data concerning the Health-related quality of life (HRQoL) have been evaluated in patients affected by ESpA.
Objectives: Prospective study was performed in a combined GastroIntestinal and RHEumatologic "GI-Rhe" clinic, in order to evaluate: 1) prevalence and characteristics of articular manifestations in a group of IBD patients; 2) quality of life, state of health and well-being in ESpA patients.
Methods: Patients affected by IBD who presented muscolo-skeletal pain between February 2013 and September 2016 (CD 264 and UC 142) were enrolled. New diagnosis, disease management, adverse events as well as laboratory evaluations were assessed every 3 months during the follow-up. Disease activity, function and quality of life in ESpA patients were assessed by ASDAS-CRP, HAQ-S and EuroQol questionnaire.
Results:

Table 1

	IBD-SpA (N=212)	IBD non-SpA (N=215)
Age (years)	47±13.1	48.3±14.8
Male (n/%)	134/63.2	131/60.9
CD (n/%)	141/66.5	122/56.7
UC (n/%)	71/33.5	93/43.3
SpA disease duration (months)	37±75	NA
IBD disease duration (months)	162.2±115.3	166.6±14.8
CRP (mg/dL)	1.2±8.6	1.2±5.1
CDAI >150 (n/%)	26/18.4*	10/8.2*
Mayo score >3 (n/%)	11/15.5*	0/0*
HAQ-S	0.5±1.3	NA
ASDAS	2.1±1	NA

Data are expressed as mean ± SD. *IBD-SpA versus IBD-non SpA.

A total of 427 patients were evaluated for joint involvement (Table 1). The prevalence of SpA in IBD patients was 49.6% (n=212: UC 71 (43.3%), CD 141 (53.4%)), suggesting that the majority of patients with IBD who complain arthralgia may have a concomitant SpA. Other rheumatologic diseases were detected in the study population in 215 patients defined as IBD non-SpA. There was a significantly higher prevalence of active intestinal disease in patients with SpA with respect to IBD-non SpA (CD: CDAI>150 in 18.4% vs 8.2% p=0.004; UC: Mayo score >3 in 15.5% vs 0%, p=0.0004). The evaluation of the EuroQoL demonstrated a mean value of 0.59 in IBD-SpA patients and of 0.55 in IBD non-SpA (Figure 1A). In IBD-SpA, the health related status was: decent 69.8%, good 17.9% and bad 9.4%. In IBD-non SpA, the health related status was: decent in 74.8%, good in 17.7% and bad in 7% of patients. In both groups, none of the patients had a neither exceptional nor great perception of QoL. No significant differences were observed between the two groups (Figure 1B-C).



Distribution of the health state in the study population

Conclusions: The joint clinic facilitates diagnosis and management of SpA and IBD. Although IBD-SpA patients showed higher IBD disease activity than IBD-non SpA one, both groups of patients have a good health related QL.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4005

FRI0478 SUBCHONDRAL BONE SCLEROSIS ON COMPUTED TOMOGRAPHY – DOES IT HAVE ANY VALUE IN THE DIAGNOSIS OF INFLAMMATORY SACROILIITIS OR IS IT A NON-SPECIFIC FINDING?

O. Azmat[1], R.G. Lambert[1], Z. Jibri[1], W.P. Maksymowych[2]. [1]*Radiology;* [2]*Medicine, University of Alberta, Edmonton, Canada*

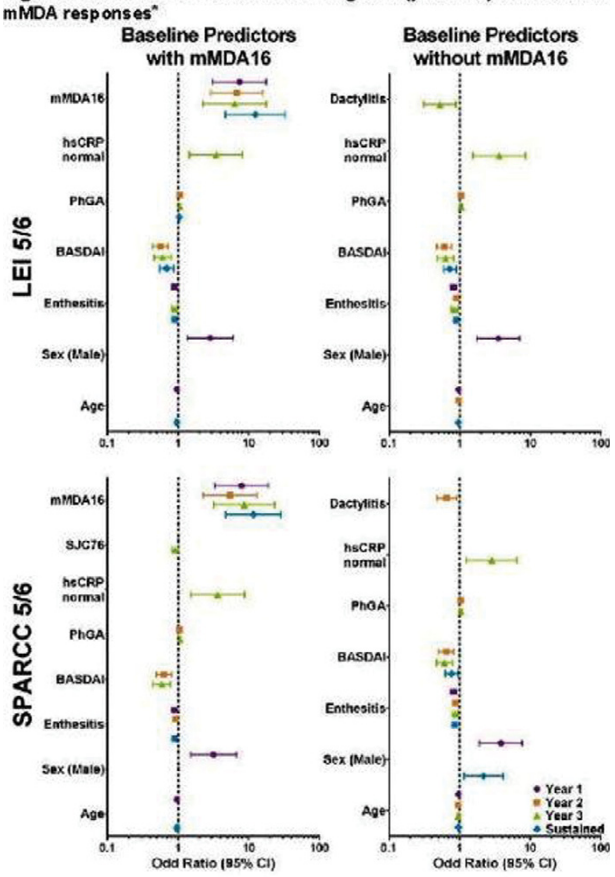
Background: Sclerosis in the sacroiliac joints (SIJ) on radiography and computed tomography (CT) is common but widely considered a non-specific finding of sacroiliitis due to an association with degeneration and osteitis condensans ilii, despite little formal study. Availability of low dose radiation CT may lead to more widespread use for diagnostic evaluation.
Objectives: We standardized the definition of sclerosis on CT and then aimed to determine whether this lesion could be reliably detected and its diagnostic utility.
Methods: 215 CT scans were obtained from patients with a history of low back pain. 107 patients had a clinical diagnosis of spondyloarthritis (SpA) and 108 patients were clinically proven not to have SpA. Groups were age and gender matched (140 males, 75 females, mean age was 45 years). Three musculoskeletal radiologists, blinded to patient demographics and diagnosis, scored the CTs after standardization of lesion definitions and calibration. Erosions, sclerosis, and ankylosis were graded by size and number of articular surfaces/ joints involved. Sclerosis was considered definite if located along the cartilaginous compartment, measured >5mm in all 3 planes, and present >5mm from the joint surface. Discrepant scores were arbitrated and inter-reader reliability calculated by intra-class correlation coefficient (ICC). Diagnostic utility of CT lesions was determined by calculating sensitivity and specificity for the clinical diagnosis and by logistic regression.
Results: ICC for sclerosis and erosion for each articular surface ranged from 0.65–0.76 and 0.71–0.78, respectively. ICC for ankylosis was 0.87–0.89. Sclerosis occurred in 87 (81%) cases with SpA and 25 (23%) controls. For a single articular surface the specificity for sacroiliitis ranged between 88–94%, for any two articular surfaces 95–100%, for all 4 articular surfaces 100%. Sensitivity ranged from 14% (4 articular surfaces) to 55% (either ilium). Erosion and ankylosis had a similar specificity range of 91–100% and 92–93%. The odds ratio was 4.9 for presence of definite sclerosis, and 12.6 for bilateral joint involvement. The odds ratio increased to 84.2 for bilateral erosion and 22.8 for bilateral ankylosis.
Conclusions: When sclerosis measures >5mm in three planes and is located >5mm from a joint perimeter, it has high specificity for sacroiliitis, regardless of how many articular surfaces are involved, with similar specificity to erosion and ankylosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6292

FRI0479 PREDICTORS OF LONG-TERM MODIFIED MINIMAL DISEASE ACTIVITY RESPONSE IN PERIPHERAL SPONDYLOARTHRITIS PATIENTS TREATED WITH ADALIMUMAB

L.C. Coates[1], S. Abraham[2], W. Tillett[3], P.J. Mease[4], S. Ramiro[5], T. Wu[6], X. Wang[6], A.L. Pangan[6], I.-H. Song[6]. [1]*University of Leeds and Leeds Teaching Hospitals NHS Trust, Leeds;* [2]*NIHR/Wellcome CRF, Imperial College Healthcare NHS Trust, London;* [3]*Royal National Hospital for Rheumatic Diseases and University of Bath, Bath, United Kingdom;* [4]*Swedish Medical Center and University of Washington, Seattle, United States;* [5]*Leiden University Medical Center, Leiden, Netherlands;* [6]*AbbVie Inc., N Chicago, United States*

Background: There is a lack of validated outcome measures in non-psoriatic peripheral spondyloarthritis (pSpA). Therefore, a modified version of the minimal disease activity (mMDA)[1] was developed and validated. Identification of factors that predict long-term mMDA response in pSpA patients (pts) can facilitate decisions regarding treatment initiation and maintenance.
Objectives: The purpose of this analysis was to determine predictors of long-term mMDA response following adalimumab (ADA) treatment in pSpA pts from the ABILITY-2 study.
Methods: ABILITY-2[2] was a phase 3 randomized, double-blind trial evaluating the efficacy and safety of 40 mg ADA every other week versus placebo (PBO) over 12 weeks (wks) followed by open-label (OL) ADA for 144 wks in pts with pSpA. This post-hoc analysis included pts who received at least one dose of ADA during the PBO-controlled period or OL extension. The mMDA for pSpA was defined as achieving at least 5 out of the following 6 criteria: 1) TJC78 ≤1; 2) SJC76 ≤1; 3) pt pain visual analog scale (VAS) ≤15 of 100 mm; 4) pt global activity (PtGA) VAS ≤20 of 100 mm; 5) HAQ-DI ≤0.5; and 6) tender entheseal points ≤1 (Leeds Enthesitis Index [LEI] or Spondyloarthritis Research Consortium of Canada [SPARCC] Enthesitis Index). In this post hoc analysis, multiple logistic regression with stepwise variable selection was used to determine predictors of long-term (yrs 1–3) and sustained (defined as mMDA for at least 24 consecutive wks) mMDA responses. Variable selection of baseline (BL) pt demographics and disease characteristics were performed with and without mMDA response at wk 16 (mMDA16) as a candidate. In pts achieving mMDA at wk 16, ADA exposure ranged between 4 and 16 wks.
Results: In pSpA pts treated with ADA, mMDA (5/6 LEI or SPARCC) was achieved by almost 41%, 49%, and 50% of pts at yrs 1, 2, and 3, respectively and sustained mMDA response was achieved by 42% of pts. Regardless of mMDA definition, achieving mMDA response at wk 16 (up to 16 wks of ADA) was a robust positive predictor of attaining both long-term mMDA at yrs 1–3 and sustained mMDA (Figure). In the model examining the BL predictors (model without mMDA16), age, BL enthesitis and BL BASDAI scores were most commonly selected as negative predictors for achieving long-term and sustained mMDA. Other selected predictors included BL dactylitis, physician's global assessment, hsCRP, and male sex; however, these predictors were not consistently selected for all time points or sustained mMDA.
Conclusions: Early mMDA response is a stronger and more consistent predictor of long-term mMDA, whether at 1, 2, or 3 yrs or sustained over time, than BL

Figure. Odds Ratio for Predictors of Long-term (years 1-3) and Sustained mMDA responses*



*Only variables selected by stepwise selection model are shown (model selected variables are significant at P<.05)
mMDA16 = modified minimal disease activity response at week 16; LEI = Leeds enthesitis index; SPARCC = Spondyloarthritis Research Consortium of Canada enthesitis index; hsCRP = high sensitivity C-reactive protein; PhGA = physician's global assessment of disease activity; BASDAI = Bath ankylosing spondylitis disease activity index; SJC76 = swollen joint count (76 joints); CI = confidence interval.

Abstract FRI0478 – Table 1

Sclerosis of articular surface (s) involved	Specificity (95% CI)	Sensitivity (95% CI)
Single articular surface	Either ilium: 87% (82–91) – 91% (87–95)	Either ilium: 46% (39–52) - 51% (44–58)
	Either sacrum: 93% (89–96) – 94% (90 – 97)	Either sacrum: 19% (14–25) - 21% (16–26)
Any 2 articular surfaces	96% (94–99) – 99% (98–100)	10% (6–14) - 41% (35–48)
All 4 articular surfaces	99% (8–100)	14% (9 – 19)
Erosion of articular surface (s) involved	Specificity (95% CI)	Sensitivity (95% CI)
Single articular surface	Either ilium: 90% (85–94)	Either ilium: 77% (71–83)
	Either sacrum: 94% (91–98)	Either sacrum: 65% (58–72)
Any 2 articular surfaces	96% (93–99) – 100% (100–100)	24% (18–31) – 67% (60–74)
All 4 articular surfaces	100% (100–100)	38.1% (31–45)
Ankylosis of articular surface (s) involved	Specificity (95% CI)	Sensitivity (95% CI)
Single joint	92% (88 – 95)	60% (53–66)
Both joints	93% (89 – 96)	58% (51–64)

characteristics. The 5/6 versions of mMDA could be an appropriate treatment target in pSpA pts.

References:
[1] Coates LC, et al., Ann Rheum Dis, 2016; 75:334.
[2] Mease PJ, et al., Arthritis Rheumatol, 2015; 67(4): p.914–23.

Acknowledgements: AbbVie funded the study (NCT01064856), contributed to its design, and participated in data collection, analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.

Disclosure of Interest: L. Coates Grant/research support from: AbbVie, Boehringer-Ingelheim, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Sun Pharma, and UCB, Consultant for: AbbVie, Boehringer-Ingelheim, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Sun Pharma, and UCB, Speakers bureau: AbbVie, Boehringer-Ingelheim, BMS, Celgene, Eli Lilly, Janssen, MSD, Novartis, Pfizer, Sun Pharma, and UCB, S. Abraham Grant/research support from: AbbVie, Celgene, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Celgene, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Celgene, Novartis, Pfizer, and UCB, W. Tillett Grant/research support from: AbbVie, Celgene, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Celgene, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Celgene, Novartis, Pfizer, and UCB, P. Mease Grant/research support from: AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Consultant for: AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Speakers bureau: AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, S. Ramiro: None declared, T. Wu Shareholder of: AbbVie, Employee of: AbbVie, X. Wang Shareholder of: AbbVie, Employee of: AbbVie, A. Pangan Shareholder of: AbbVie, Employee of: AbbVie, I.-H. Song Shareholder of: AbbVie, Employee of: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.1279

FRI0480 SCORING SYNDESMOPHYTES ON CT SPINE IMAGES OF PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS FROM THE SENSITIVE IMAGING OF AXIAL SPONDYLOARTHRITIS (SIAS) COHORT

F. de Bruin[1], R. van den Berg[1], X. Baraliakos[2], J. Braun[2], F. van Gaalen[1], M. Reijniersе[1], D. van der Heijde[1]. *[1]LUMC, Leiden, Netherlands; [2]Rheumazentrum, Herne, Germany*

Background: Low dose Computed Tomography (CT) could potentially be more sensitive than radiographs in the follow up of patients with axial spondyloarthritis (axSpA).

Objectives: Our first goal was to develop a scoring method for the spine and test its interreader variability and frequency of progression in the various parts of the spine.

Methods: Patients (pts) of the Sensitive Imaging of Axial Spondyloarthritis (SIAS) cohort fulfilled the modified New York (mNY) criteria, had ≥1 syndesmophyte in cervical or lumbar spine on radiographs and ≥1 inflammatory lesion on MRI-spine. Baseline and 2 years follow up low-dose CT scans (approximately 2–3 mSV) were performed. Syndesmophytes were scored in the coronal and sagittal planes for all "corners" per view, thus scoring 8 'quadrants' per vertebral unit (VU). Syndesmophytes were scored as absent (score 0), <50% of the intervertebral disc height (IVDH) (score 1), ≥50% of the IVDH but no bridging (score 2) or as "bridging the IDVH" (score 3). Score range 0–552. Two readers, blinded for clinical information and time order, scored the CT scans paired by patient. Scores of the 2 readers were compared using heatmaps. Interreader variability was assessed by (two-way average) ICC and smallest detectable change (SDC) for the whole spine and per segment.

Results: In total, 56 pts (84% male, mean age 48.6) were included. The heatmap (fig 1) presents the similarity in basseline and change scores per reader per VU (VU on the y-axis). Ankylosis (score 3) is most prevalent in the thoracic spine, and syndesmophytes in general are least prevalent in the cervical spine.

Both readers use almost the entire possible range, pick up a similar magnitude of change and have high ICCs. Most change is present in the thoracic spine. A change ≥SDC is seen in 33.9% of the patients.

Conclusions: A fine-grained scoring system for CT spine was developed. Scoring syndesmophytes with good accuracy on CT images was feasible, picking up changes over a 2-year period in a high percentage of patients, especially in the thoracic spine, which is insufficiently visible on radiographs.

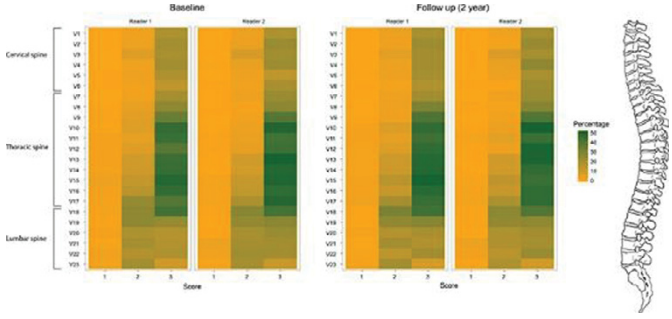


Figure 1

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3533

FRI0481 INTERPLAY BETWEEN PATIENT GLOBAL ASSESSMENT, PAIN AND FATIGUE AND INFLUENCE OF OTHER CLINICAL DISEASE ACTIVITY MEASURES IN PATIENTS WITH ACTIVE SPONDYLOARTHRITIS

O.R. Madsen[1,2], E.L. Egsmose[1,2]. *[1]Department of Rheumatology, Copenhagen University Hospital Rigshospitalet Gentofte, Hellerup; [2]The DANBIO registry, Copenhagen University Hospital Rigshospitalet Glostrup, Glostrup, Denmark*

Background: The Assessment of SpondyloArthritis international Society (ASAS) has selected core sets of variables to include as standardised end points in clinical trials and clinical practice. These core sets include fatigue, pain and patient global assessment (PaGl) as key patient-reported outcome measures (ref.). However, although associations between fatigue, pain and PaGl have been examined to some extent on the group level, studies focusing on the agreement between these patient-reported measures in individual patients are missing. A better understanding of how tight the measures are bounded in individuals may improve our ability to deal with them in the daily clinic.

Objectives: To examine associations on the group level and agreements on the individual patient level between fatigue, pain and PaGl as scored on visual analogue scales (VAS) in the daily clinic by patients with active spondyloarthropathy (SpA).

Methods: Data on 118 SpA patients with active disease planned to initiate treatment with a biological agent were extracted from the Danish registry for biological treatment in rheumatology (DANBIO). Data included fatigue, pain and PaGl, BASDAI and BASFI assessed on VAS-scales (0–100) and age, CRP and physician global assessment. Associations between variables were examined using simple and multiple regression analysis (all mentioned variables including sex was incorporated as independent variables). Agreements between PaGl, pain and fatigue on the individual patient level was examined by Bland-Altman analyses yielding 95% lower and upper limits of agreement (LLoA and ULoA) between intra-individual assessments. The difference between the scores on the group level was expressed as the bias.

Results: Mean age was 42.9±12.6 years, mean BASDAI 56.0±19.0, mean CRP mg/dL12.9 and mean PaGl 65.7±22.6. No significant differences in BASDAI, fatigue, pain, PaGl were demonstrated between men (n=76) and women. Fatigue, pain and PaGl were significantly but only moderately inter-correlated with high standard errors of estimation (SEE): Fatigue vs. PaGl (r =0.57, p<0.0001, SEE =21.4), fatigue vs.pain (r =0.55, p<0.0001, SEE =21.6), and pain vs. PaGl (r =0.81, p<0.0001, SEE =15.1). In multiple regression analyses, pain was independently predicted by PaGl (beta =0.52, p<0.0001) and BASDAI (beta =0.36, p<0.0001) [R =0.82, SEE =14.1, p<0.0001], PaGl by pain (beta =0.54, p<0.0001) and BASDAI (beta =0.33) [R =0.81, SEE =12.7, p<0.0001]), and fatigue by BASDAI (beta =0.44, p<0.0001) and PaGl (beta =0.23, p<0.05) [R =0.63, SEE =20.2, p<0.0001]. Biases between the patient-reported VAS-scores were small but intra-individual differences were substantial: LLoA and ULoA [bias] for fatigue vs. PaGl were -45.5 and 43.5 [-0.97], for fatigue vs. pain -42.3 and 52.9 [5.3], and for

Abstract FRI0480 – Table 1. SDC and interreader variability between readers on timepoint 1, timepoint 2 and for the difference between the timepoints (syndesmophyte growth)

Segment (max score)	Time point	Median and range reader 1	Median and range reader 2	SDC (inter-reader)	No. of patients with growth ≥SDC (%) (n=58)	ICC
Whole spine (552)	Time 1	144 (16–428)	135 (6–447)			0.99 (0.94–1.00)
	Time 2	157 (18–428)	146 (8–461)			0.98 (0.92–0.99)
	Change	9 (-11–96)	8 (-6–93)	12.4	19 (32.8)	0.75 (0.49–0.88)
Cervical (144)	Time 1	8 (0–140)	8 (0–128)			0.96 (0.92–0.98)
	Time 2	8 (0–140)	8 (0–128)			0.98 (0.95–0.99)
	Change	0 (-12–38)	0 (-9–38)	5.41	9 (15.6)	0.85 (0.75–0.91)
Thoracic (264)	Time 1	84 (2–250)	72 (0–264)			0.97 (0.92–0.99)
	Time 2	93 (2–256)	81 (0–264)			0.97 (0.85–0.99)
	Change	6 (-6–94)	6 (-12–93)	12.4	15 (25.9)	0.85 (0.75–0.92)
Lumbar (144)	Time 1	32 (0–140)	36 (0–140)			0.91 (0.79–0.96)
	Time 2	34 (0–144)	39 (0–144)			0.99 (0.98–1.00)
	Change	2 (-10–14)	1 (-4–12)	4.51	14 (24.1)	0.56 (0.26- 0.73)

pain vs. PaGl -35.7 and 23.3 [-6.3]. LLoA and UloA remained constant over the whole range of the VAS-scales.
Conclusions: In patients with SpA, fatigue, pain and PaGl scores were poorly associated and only poorly explained by other potential explanatory variables. On the individual level, disagreements between the scores were substantial. The findings emphasize the complexity of understanding patient-reported outcome measures and their diverging interplay across individuals.
References:
[1] van der Heijde D et al. J Rheumatol 1999; 26: 951–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4117

FRIDAY, 16 JUNE 2017

Psoriatic arthritis

FRI0482 INSULIN RESISTANCE IN PATIENTS WITH PSORIATIC ARTHRITIS

A. Abogamal[1], E. Mahmoud[2], S. Abdulhakiem[1], S. Abdelatif[1], A. Abdelaziz[3]. *[1]Rheumatology; [2]Enocrinology; [3]Clinical Pathology, Alazhar Faculty of Medicine, Cairo, Egypt*

Background: inflammation and, levels of inflammatory markers, CRP and other cytokines are important for enhancing insulin resistance in PsA patients.
Inflammation and, levels of inflammatory markers, CRP and other inflammatory cytokines are important players for enhancement and develpoment of insulin resistance in psoriatic arthritis patients.
Objectives: To investigate the relation between insulin resistance and psoriatic arthritis presence and disease activity.
To investigate the relation between insulin resistance and disease activity in patients with psoriatic arthritis.
Methods: *Patients Inclusion criteria:* all patients in this study had psoriatic arthritis with disease duration 5 years or more. All under conventional DMARDs treatment in the form of methotrexate 12.5 mg/wk, hydroxychloroquine 400mg/day. With no treatment with glucocorticoids, 3 months prior to enrollment in the study and no previous treatment with biologics. All patients were Postmenopausal females with 3 or more years since menopause.
Exclusion Criteria: DM, ischemic heart disease, hypertension, or any other chronic diseases, Smoking, on medications Medications that affect blood lipids, or body composition and metabolic functions. Postmenopausal females who were on hormonal replacement therapy.
Grouping: G I: Included 50 postmenopausal females with psoriatic arthritis. G II: Included 25 normal postmenopausal females, as a control group.
Methods: 1. Full medical history and Complete clinical examination 2. Anthropometric measurements: Body mass index (BMI), Waist-hip ratio (WHR). 3. The following laboratory investigations were done: C-reactive protein (CRP), Fibrinogen, Fasting insulin. 4. Measures of insulin resistance: Homeostasis model assessment of insulin resistance (HOMA-IR): (a) HOMA 1-IR: It is calculated according to the following equation: Fasting insulin (μU/ml) x FBS (mg/dL)/405. (2). Insulin resistance was defined as HOMA-IR >3. 8. (3), (4). (b) HOMA 2-IR: it is the updated (or computer) model with nonlinear solutions, which also uses paired fasting glucose and insulin values, were calculated using the computer model (HOMA calculator version 2.2).
Results: Comparing means of age, BMI, and WHR of both groups' shows no significant difference, which indicates that both groups was matched and valid for comparison. G I have significantly higher values than the control group in the laboratory parameters Insulin, CRP and Fibrinogen as $p>0.05$, and the insulin resistance parameters (HOMA1, HOMA2). G I was significantly higher than the control group as $p>0.05$. Significant positive correlation also found between *Index for Psoriatic Arthritis (DAPSA)* and insulin, HOMA1, and HOMA2.
Conclusions: Psoriatic arthritis is associated with increased risk of insulin resistance. PsA activity is strongly associated with developing insulin resistance in psoriatic arthritis patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5165

FRI0483 WORK CAPACITY AND QUALITY OF LIFE IN A COHORT OF PATIENTS WITH EARLY PSORIATIC ARTHRITIS IN ARGENTINA

F. Colombres[1], H. Berman[2], A. Spindler[2], W. Spindler[2], J.A. Maldonado Cocco[3], M.C. Orozco[4], E. Schneeberger[4], A. Ortiz[5], S. Paira[5], M. Zalazar[6], O. Rillo[6], D. Baenas[7], A. Alvarellos[7], T. Alvarellos[7], M. Garcia[8], A. Salas[8], V. Duarte[9], F. Romanini[9], L. Ferreyra Garrott[10], E. Soriano[10], L. Galindo[11], G. Castelli[12], C. Borlenghi[12], A. Berman[2]. *[1]Hosp. Avellaneda; [2]Centro Medico Privado de Reumatologia, SAN M, de Tucuman; [3]Fundación Reuma, Argentina; [4]Instituto Rehab. Psicofisica, Buenos Aires; [5]Hosp.Cullen, Santa Fe; [6]Hosp. Pirovano, Buenos Aires; [7]Hosp. Privado Cordoba, Cordoba; [8]Hosp. San Martin, la Plata; [9]Hosp. Rivadavia; [10]Hosp. Italiano, Buenos Aires; [11]U.N.T., SAN M, de Tucuman; [12]Pfizer Argentina, Buenos Aires, Argentina*

Objectives: To evaluate work capacity and quality of life in patients with early Psoriatic Arthritis (PsA).
Methods: Multi-center study in which patients with recent onset of PsA (disease duration <3 years) who met the CASPAR criteria established by the Early Spondyloarthritis Committee (CONEART) were enrolled. Work loss and lost workdays within six months prior to the baseline visit attributable to their baseline condition were evaluated, as well as quality of life, measured by PsAQol. Statistical analysis: descriptive statistics, Spearman's correlation, multiple linear regression model.
Results: 108 patients with a PsA diagnosis were enrolled. 53% (57/108) were male, of a mean age of 48.4 (SD 12.5). The mean PsA disease duration was 17.6 (SD 9.8) months. 4/60 patients (6.6%) were positive for HLA-*B27*. BASDAI 4.81±2.66; BASFI 3.75±2.70; PsAQoL 7.24±6.44; HAQ-A 0.72±0.61, physician global activity assessment (by Visual Numeric Scale, VNS) 3.76±2.33, and pain assessment (VNS) 5.22±2.98. The average days lost due to the condition within the past 6 months was 8.6 (SD 32.1), it was significantly associated with the presence of enthesitis, number of swollen joints, worse BASDAI, BASFI, lower level of education, and higher pain and physician global activity assessment ($p<0.0001$). Five patients lost their job due to PsA. 12% of the patients had a disability certificate and the possession of one, according to the logistic regression model, was associated with a longer PsA disease duration (OR 1.09, p=0.02). A poorer quality of life was significantly correlated to the physician assessment of disease activity ($p<0.001$) and pain ($p<0.01$) using a linear regression model.
Conclusions: In this cohort of patients with early PsA, the deterioration of work capacity expressed in lost workdays was associated with disease activity parameters and functional disability. The physician global activity assessment and pain were the main factors associated with the impact on patient's quality of life. Having a disability certificate was associated with longer disease duration. Although this is an early cohort of PsA patients, a worsening in quality of life and work disability was observed.
Disclosure of Interest: F. Colombres: None declared, H. Berman: None declared, A. Spindler: None declared, W. Spindler: None declared, J. Maldonado Cocco Grant/research support from: Pfizer Argentina, M. Orozco: None declared, E. Schneeberger Grant/research support from: Pfizer Argentina, A. Ortiz: None declared, S. Paira Grant/research support from: Pfizer Argentina, M. Zalazar: None declared, O. Rillo Grant/research support from: Pfizer Argentina, D. Baenas: None declared, A. Alvarellos Grant/research support from: Pfizer Argentina, T. Alvarellos: None declared, M. Garcia Grant/research support from: Pfizer Argentina, A. Salas: None declared, V. Duarte: None declared, F. Romanini Grant/research support from: Pfizer Argentina, L. Ferreyra Garrott: None declared, E. Soriano Grant/research support from: Pfizer Argentina, L. Galindo: None declared, G. Castelli: None declared, C. Borlenghi: None declared, A. Berman Grant/research support from: Pfizer Argentina
DOI: 10.1136/annrheumdis-2017-eular.3569

FRI0484 IMPACT OF PSORIATIC ARTHRITIS ON PATIENT-REPORTED OUTCOMES IN 5 EUROPEAN UNION COUNTRIES

A.B. Gottlieb[1], J. Gratacos[2], A. Dikranian[3], L. Fallon[4], B. Emir[5], T. Smith[5], L. Aikman[6], L. Chen[5]. *[1]Department of Dermatology, New York Medical College, Valhalla, NY, United States; [2]University Hospital Parc Tauli Sabadell, Barcelona, Spain; [3]Cabrillo Center for Rheumatic Diseases, San Diego, CA, United States; [4]Pfizer Canada, Montreal, QC, Canada; [5]Pfizer Inc, New York, NY, United States; [6]Pfizer Ltd, Sandwich, United Kingdom*

Objectives: This non-interventional, cross-sectional, descriptive, exploratory analysis aimed to characterise patients (pts) with psoriatic arthritis (PsA) in the 2016 National Health and Wellness Survey (NHWS) and determine the impact of treatment, or no treatment, on pt-reported outcomes.
Methods: The NHWS was a self-administered, web-based, voluntary, confidential questionnaire. Stratified randomised sampling provided a representative sample of EU adults in France, Germany, Italy, Spain and UK. Respondents completing the arthritis module and reporting PsA diagnosis were stratified by: advanced therapies (tumour necrosis factor inhibitors, interleukin antagonists, phosphodiesterase-4 inhibitors) ± other drugs; other therapies (eg conventional synthetic disease-modifying antirheumatic drugs, glucocorticoids, topical medications); or no current treatment. Short Form-36 health survey (SF-36), Work Productivity and Activity Impairment questionnaire and Patient Health Questionnaire-9 (PHQ-9) responses were summarised descriptively.
Results: NHWS was completed by 80,600 adults; 947 completed the arthritis module and self-reported PsA diagnosis. Of these, 65 (7%) reported receiving advanced therapies, 274 (29%) other therapies and 608 (64%) no current treatment. Age and gender were generally balanced between the groups (mean 51–56 years; 51–64% female). More patients on advanced therapies had a body mass index ≥30 (41%) vs other therapies (34%) and no current treatment (26%). Pts on advanced therapies reported more comorbidities (mean 2.2) vs pts on other therapies (mean 1.8) and pts with no current treatment (mean 1.7). More pts on advanced therapies were current smokers (49%) vs pts on other therapies (30%) and pts with no current treatment (32%). Prior to treatment with advanced or other therapies, 94% and 82% self-reported moderate or severe PsA, falling to 58% and 59%, respectively, after treatment, compared with 36% of pts with no current treatment. SF-36 scores and PHQ-9 scores did not widely vary across groups (Table 1). Regardless of treatment groups, pts reported >20% work loss, >45% overall work impairment and >45% activity impairment (Table 1).
Conclusions: More than 60% of pts reporting PsA diagnosis reported no current

Table 1. Mean (SD) outcome scores by treatment type

	Advanced therapies N=65	Other therapies N=274	Not treated N=608
SF-36 MCS	38.0 (11.0)	40.1 (11.6)	39.8 (10.5)
SF-36 PCS	36.0 (9.9)	37.6 (9.6)	43.9 (8.4)
PHQ-9 total score[a]	7.7 (7.0)	9.1 (6.8)	7.8 (7.1)
WPAI domain scores[b]			
% work missed	26.8 (29.7)	27.8 (35.4)	20.8 (27.8)
% impairment at work	55.8 (31.1)	42.8 (29.6)	44.5 (29.3)
% overall work impairment	61.4 (34.2)	49.0 (33.2)	51.1 (32.6)
% activity impairment	62.0 (26.1)	57.8 (26.5)	48.3 (28.9)

[a]N = 22, 45, 137 for advanced therapies, other therapies, not treated, respectively

[b]N for WPAI % work missed = 33, 113, 338, respectively for advanced therapies, other therapies, not treated; N for WPAI % impairment at work and overall work impairment = 33, 99, 328, respectively, for advanced therapies, other therapies and not treated

MCS, mental component summary; PCS, physical component summary; PHQ-9, Patient Health Questionnaire-9; SD, standard deviation; SF-36, Short Form-36 health survey; WPAI, Work Productivity and Activity Impairment questionnaire

treatment. Regardless of treatment group, pts reported >20% work loss and >45% work impairment. Among treated pts, >50% reported moderate or severe PsA, suggesting a need for overall better management of PsA to reduce the disease impact and improve quality of life. Our results are limited by self-reported PsA diagnosis, which may differ from physician-reported PsA diagnosis, and the survey being conducted in the EU only, which may differ from other parts of the world. Further statistical analyses are needed to determine differences between groups and correlation to other health indicators.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by A Pedder of CMC and was funded by Pfizer Inc.

Disclosure of Interest: A. Gottlieb Grant/research support from: Abbott (AbbVie), Amgen, Baxalta, Celgene, Centocor (Janssen), Coronado, Dermira, Eli Lilly, Levia, Merck, Novartis, Pfizer Inc, Xenoport, Consultant for: Abbott (AbbVie), Actelion, Akros, Amgen, Astellas, Baxalta, Beiersdorf, Bristol-Myers Squibb, Canfite, Catabasis, Celgene, Centocor (Janssen), Coronado, CSL Behring Biotherapies for Life, Dermipsor, Eli Lilly, Genentech, GlaxoSmithKline, Incyte, Karyopharm, Meiji Seika Pharma, Mitsubishi Tanabe, Novo Nordisk, Novartis, Pfizer Inc, Takeda, TEVA, UCB, Vertex, Xenoport, J. Gratacos: None declared, A. Dikranian Consultant for: AbbVie, Mallinckrodt, Pfizer Inc, Speakers bureau: AbbVie, Amgen, Celgene, Mallinckrodt, Pfizer Inc, L. Fallon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, B. Emir Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Smith Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Aikman Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Chen Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.2446

FRI0485 IN PERIPHERAL PSORIATIC ARTHRITIS DKK-1 AND PTH ARE LOWER THAN IN RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS

A. Fassio, L. Idolazzi, O. Viapiana, C. Benini, E. Vantaggiato, M. Rossini, D. Gatti. *Rheumatology, Aoui Verona Reumatologia, Verona, Italy*

Background: The recent characterization of the canonical WNT pathway in the regulation of bone modeling and remodeling provided important insights for our understanding of the pathophysiology of bone involvement in chronic arthritis [1]. Dkk-1 and sclerostin are the main regulators of WNT/b-catenin signaling, regulating both bone formation and resorption [2]. In a previous our study we showed that in patients with Rheumatoid Arthritis (RA) Dkk-1 is significantly increased and associated with the presence of typical erosions and lower BMD [3].

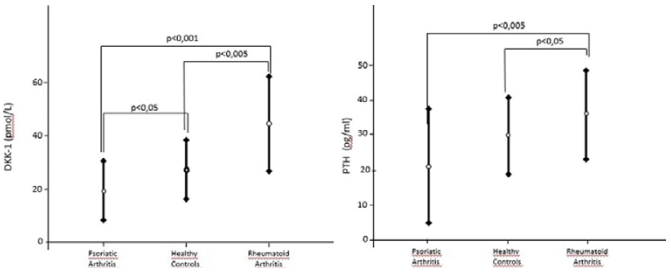
Objectives: we decided to perform this study in order to compare the serum levels of WNT-pathway regulators alongside bone turnover markers (BTM) and Parathyroid Hormone (PTH) between a group of female patients with PsA and healthy controls (HC) or patients with Rheumatoid Arthritis (RA).

Methods: this is a cross-sectional study including 18 patients with PsA classified with the CASPAR criteria, 35 HC, and 28 patients with RA classified with the ACR/EULAR 2010 criteria. Intact N-propeptide of type I collagen (PINP), C-terminal telopeptide of type I collagen (CTX-I), Dickkopf-related-protein 1 (Dkk-1), sclerostin, PTH and 25OH-Vitamin D serum levels were dosed. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Results: the PsA group showed significantly lower Dkk-1 levels when compared to the HC and RA groups. Dkk-1 in the RA group was also significantly higher than in the HC group. A similar trend was documented also for PTH, however a statistically significant difference was observed only when we comparing the PsA vs RA group (table 1, figure 1). No other statistically significant differences in the other markers were found.

Table 1. Values of bone turnover markers (CTX-I, PINP), Dkk-1 and sclerostin of PsA, RA patients and control group (mean ± SD)

	PsA	RA	HC	P (ANOVA)
PINP ng/ml	42,80±16,670	39,19±21,38	42,49±11,52	NS
CTX-I ng/ml	0,21±0 ,17	0,32±0,21	0,28±0,10	NS
Dkk-1 pmol/l	19,45±11,30	44,51±17,81	27,29±11,48	<0,001
Sclerostin pmol/l	30,82±11,25	30,75±10,25	34,23±17,29	NS
PTH pg/ml	21,12±16,63	35,83±13,02	29,69±11,43	<0,005



Conclusions: this study demonstrated for the first time that Dkk-1 levels in PsA are lower than HC, in contrast with RA where they are higher. These results might contribute to explain the different bone involvement of the two different diseases.

References:

[1] Xie W, Zhou L, Li S, et al. Wnt/β-catenin signaling plays a key role in the development of spondyloarthritis. Ann N Y Acad Sci 2016;1364:25–31. doi:10.1111/nyas.12968.

[2] 2 Spencer GJ, Utting JC, Etheridge SL, et al. Wnt signalling in osteoblasts regulates expression of the receptor activator of NFkappaB ligand and inhibits osteoclastogenesis in vitro. J Cell Sci 2006;119:1283–96. doi:10.1242/jcs.02883.

[3] 3 Rossini M, Viapiana O, Adami S, et al. In patients with rheumatoid arthritis, Dickkopf-1 serum levels are correlated with parathyroid hormone, bone erosions and bone mineral density. Clin Exp Rheumatol 2015;33:77–83.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2728

FRI0486 INTRAVENOUS GOLIMUMAB IN ADULT PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: EFFICACY AND SAFETY THROUGH WEEK 24

A. Kavanaugh[1], M.E. Husni[2], D.D. Harrison[3], L. Kim[3], K.H. Lo[3], E.C. Hsia[4]. *[1]University of California, San Diego; [2]Cleveland Clinic, Cleveland; [3]Janssen Research & Development, LLC, Spring House; [4]Janssen Research & Development, LLC/University of Pennsylvania School of Medicine, Spring House/Philadelphia, United States*

Objectives: The GO-VIBRANT study was designed to evaluate the safety and efficacy of intravenous (IV) golimumab (GLM) in adult patients (pts) with active PsA (biologic-naïve).

Methods: GO-VIBRANT is a Phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled trial. Biologic-naïve active PsA pts were randomized (1:1) to IV GLM 2mg/kg at weeks (wk) 0, 4, and every 8 wks thereafter or PBO at wks 0, 4, 12, and 20 with crossover to GLM at wk24. The primary endpoint was ACR20 response at wk14. Multiplicity-controlled endpoints were ACR50, ACR70, PASI 75, change from baseline in HAQ-DI, enthesitis, dactylitis, SF-36 PCS/MCS scores at wk14; and ACR50 and change from baseline in total modified vdH-S (structural damage) score at wk24. Efficacy analyses were based on randomized treatment. Adverse events (AE) through wk24 are reported here. Investigators remain blinded through wk60.

Results: 480 pts were randomized (PBO: 239; GLM: 241). The study met its primary and all controlled secondary endpoints. At wk14, significantly greater proportions of GLM pts vs PBO achieved ACR20 (75.1% vs. 21.8%). Also, GLM treatment resulted in significant change from baseline HAQ-DI score (-0.60 vs. -0.12), ACR50 (43.6% vs. 6.3%), PASI 75 (59.2% vs. 13.6%), ACR70 (24.5% vs. 2.1%), change from baseline in enthesitis and dactylitis scores (-1.8 vs. -0.8 and -7.8 vs. -2.8, respectively), and change from baseline in SF-36 PCS and SF-36 MCS scores (8.65 vs. 2.69 and 5.33 vs. 0.97, respectively) (all p<0.001) at wk14. At wk24, significantly greater proportions of GLM pts vs. PBO pts achieved ACR 50 (53.5% vs. 6.3%, p<0.001). At wk24, there was significantly less progression of structural damage for GLM pts vs PBO as measured by change from baseline in total modified vdH-S score (-0.36 vs. 1.95; p<0.001). ACR20 was significantly higher with GLM than PBO as early as wk2 (45.6% vs. 7.5%; p<0.001). 27.0% of GLM pts (vs. 4.2% PBO) achieved Minimal Disease Activity by wk14. Due to the difference in response rates in GLM vs. PBO treated pts, the number needed to treat for ACR20 at wk14 was 1.9 in a post-hoc analysis (Table). Through wk24,

46.3% of GLM pts and 40.6% of PBO pts had ≥1 AE; 2.9% vs. 3.3% of pts, respectively, had ≥1 serious AE. Two deaths, 2 malignancies, and 1 demyelinating event were reported. The most common treatment-emergent type of AE was infection (20.0% of GLM pts vs. 13.8% of PBO pts). No opportunistic infection or tuberculosis was reported through wk24. The rate of infusion reactions was low at <2%; none was serious or severe.

Table. Clinical Response

	Placebo	Golimumab 2 mg/kg	P-values
Patients randomized, n	239	241	
Clinical efficacy at wk14			
ACR20/50/70, (%)	21.8/6.3/2.1	75.1/43.6/24.5	p<0.001
PASI 75, n (%)*	27/198 (13.6%)	116/196 (59.2%)	p<0.001
Change from BL in HAQ-DI (n) Mean (SD)	222 -0.12 (0.47)	233 -0.60 (0.53)	p<0.001
Change from BL in enthesitis** (n) Mean (SD)	173 -0.8 (1.98)	182 -1.87 (1.75)	p<0.001
Change from BL in dactylitis** (n) Mean (SD)	115 -2.8 (7.03)	130 -7.8 (8.57)	p<0.001
Minimal Disease Activity, n/N (%)	10/239 (4.2%)	65/241 (27.0%)	p<0.001
Number Needed to Treat (95% CI)		1.9 (1.64, 2.18)	
Clinical efficacy at Week 24			
ACR50, n (%)	15 (6.3%)	129 (53.5%)	
Imaging data at Week 24			
Change from BL in vdH-S score (N) Mean (SE)	237 1.95 (0.264)	237 -0.36 (0.144)	p<0.001
HRQoL at wk14			
Change from BL in SF-36 PCS score (n) Mean (SD)	222 2.69 (5.92)	233 8.65 (7.60)	p<0.001
Change from BL in SF-36 MCS score (n) Mean (SD)	222 0.97 (7.64)	233 5.33 (9.95)	p<0.001

*Among pts with ≥3% BSA involvement, **Among pts with finding at baseline, BL:baseline

Conclusions: In pts with active PsA, IV GLM demonstrated significant and clinically meaningful improvements of disease activity and physical function, skin psoriasis clearance, HRQoL, reduction in dactylitis and enthesitis, and inhibition of structural damage progression. GLM was well-tolerated through wk24; the safety profile was consistent with other anti-TNF therapies, including SC GLM.

Disclosure of Interest: A. Kavanaugh Consultant for: Janssen, M. E. Husni Consultant for: Janssen, UCB, Amgen, Novartis, Lilly, Regeneron, D. Harrison Employee of: Janssen Research & Development, LLC, L. Kim Employee of: Janssen Research & Development, LLC, K. H. Lo Employee of: Janssen Research & Development, LLC, E. Hsia Employee of: Janssen Research & Development, LLC

DOI: 10.1136/annrheumdis-2017-eular.1165

FRI0487 APREMILAST IS ASSOCIATED WITH LONG-TERM (4-YEAR) DAS-28 (CRP) REMISSION AND IMPROVEMENTS IN SKIN DISEASE: RESULTS FROM A PHASE III STUDY IN DMARD/BIOLOGIC-EXPERIENCED PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

C.J. Edwards[1], F.J. Blanco[2], J. Crowley[3], M. McIlraith[4], M. Paris[4], N. Delev[4], L. Teng[4], C.A. Birbara[5]. *[1]University Hospital Southampton, Southampton, United Kingdom; [2]INIBIC-Hospital Universitario A Coruña, Galicia, Spain; [3]Bakersfield Dermatology, Bakersfield; [4]Celgene Corporation, Summit; [5]University of Massachusetts Medical School, Worcester, United States*

Background: Treatment goals for long-term control of skin and joint symptoms in active psoriatic arthritis (PsA) include clinically important changes in DAS-28 (CRP), achievement of remission in DAS-28 (CRP), reduction in swollen joint count (SJC), and decrease in skin disease.[1] PALACE 3 included PsA patients with active joint disease and an active skin lesion at the time of enrollment.

Objectives: Report the impact of apremilast (APR) on PsA manifestations over 4 years.

Methods: Patients were stratified by baseline (BL) DMARD use (yes/no) and psoriasis involvement of the body surface area (<3%/≥3%) and randomized (1:1:1) to placebo (PBO), APR 30 mg BID (APR30), or APR 20 mg BID (APR20). After the 24-week PBO-controlled phase, all patients were treated with APR30 or APR20 and could enroll in the long-term extension. Efficacy assessments were conducted through Week 208.

Results: 505 patients were randomized and received ≥1 dose of study medication (PBO: n=169; APR30: n=167; APR20: n=169). A total of 91% (227/249) of patients starting the fourth year of APR therapy completed the Week 208 visit. Patients treated with APR30 demonstrated sustained decreases in disease activity at Week 208, as shown by mean change from BL in DAS-28 (CRP) of –1.66; 80.3% achieved good/moderate EULAR response and 50.4% achieved DAS-28 (CRP) remission. Sustained effect on inflammation at Week 208 was also demonstrated by mean/median percent changes in SJC, a marker of inflammatory activity, of –77.4%/–100.0% (Table); 64.8% of patients had an SJC of 0 or 1. Decreases in disability and maintenance of functionality were shown by sustained improvements in Health Assessment Questionnaire-Disability Index (HAQ-DI) scores (Table). A continued effect on skin disease was shown by decreases in skin involvement, as measured by the Psoriasis Area and Severity Index (PASI); 54.7% of APR30 patients had BL PASI >5 and 27.3% had BL PASI >10; at Week 208, 64.5% had PASI <3 and 77.4% had PASI ≤5. PASI-75 and PASI-50 response rates also demonstrated clinically significant relief (Table). In patients treated with APR20, similar findings were observed at Week 208. No new safety concerns were identified through 208 weeks of APR30 therapy. During Weeks >156 to ≤208 of APR30 exposure, the only adverse event (AE) occurring in ≥5% of patients was nasopharyngitis; most AEs were mild or moderate in severity. Serious AEs occurred in 7.2% of APR30 patients over Weeks >156 to ≤208, similar to rates in earlier study periods. Few discontinuations due to AEs (0.7%) occurred over Weeks >156 to ≤208. The APR20 safety profile was similar to that of APR30.

Outcomes at Week 208	
	APR30 n=129*
DAS-28 (CRP), mean change	−1.66
DAS-28 (CRP) <2.6, n/m (%)	64/127 (50.4)
SJC, mean/median % change	−77.4/−100.0
TJC, mean/median % change	−64.4/−86.6
HAQ-DI (0-3), mean change	−0.42
HAQ-DI MCID ≥0.30/≥0.35, n/m (%)	63/129 (48.8)
ACR20, n/m (%)	85/128 (66.4)
ACR50, n/m (%)	51/128 (39.8)
ACR70, n/m (%)	31/127 (24.4)
PASI-75, n/m (%)§	28/62 (45.2)
PASI-50, n/m (%)§	42/62 (67.7)

Data as observed. *The n reflects the number of patients treated with APR30, regardless of when APR was started (BL, Week 16, or Week 24) and who had data available at Week 208; actual number of patients available for each end point may vary. §Examined among patients with psoriasis involvement of the body surface area ≥3% at BL. APR30=apremilast 30 mg BID; DAS-28=28-joint count Disease Activity Score; CRP=C-reactive protein; SJC=swollen joint count; TJC=tender joint count; HAQ-DI=Health Assessment Questionnaire-Disability Index; MCID=minimal clinically important differences; ACR20/50/70=20%/50%/70% improvement in modified American College of Rheumatology response criteria; n/m=number of responders/number of patients with sufficient data for evaluation; PASI-75/50=≥75%/≥50% reduction from BL Psoriasis Area and Severity Index score; BL=baseline.

Conclusions: Over 208 weeks, APR demonstrated sustained and clinically important improvements in PsA signs and symptoms, including physical function and associated psoriasis, among patients continuing the study. APR was generally well tolerated with an acceptable safety profile.

References:

[1] Gossec L, et al. Ann Rheum Dis. 2016;75:499–510.

Disclosure of Interest: C. Edwards Grant/research support from: Celgene Corporation, Pfizer, Roche, Samsung, Consultant for: Celgene Corporation, Pfizer, Roche, Samsung, Speakers bureau: Abbott, GSK, Pfizer, Roche, F. Blanco Consultant for: Bioibérica, Gebro Pharma, Pfizer, J. Crowley Grant/research support from: AbbVie, Amgen, Celgene Corporation, Janssen, Merck, Pfizer, Consultant for: AbbVie, Amgen, Speakers bureau: AbbVie, M. McIlraith Employee of: Celgene Corporation, M. Paris Employee of: Celgene Corporation, N. Delev Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, C. Birbara Grant/research support from: Amgen, BMS, Incyte, Eli Lilly, Merck, Pfizer

DOI: 10.1136/annrheumdis-2017-eular.3563

FRI0488 PSORIATIC ARTHRITIS IN THE UNITED STATES: INCREASING ALL-CAUSE HOSPITALIZATIONS 1993–2014

G. Singh[1], C. Moise[2], A. Mithal[3], R. Ionescu[2], A. Mithal[4]. *[1]Gastroenterology and Hepatology, Stanford University, Palo Alto, United States; [2]Disciplina Medicina Interna si Reumatologie, Spitalul Clinic "Sf. Maria", Bucharest, Romania; [3]Student; [4]Epidemiology, ICORE, Woodside, United States*

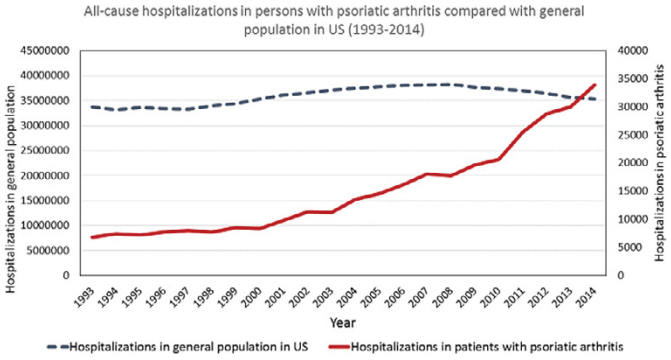
Background: Psoriatic arthritis (PsA) is a rare disease, with an estimated prevalence of 0.02 – 0.42% in Europe and US (1). PsA is often regarded as a mild disease, but recent data suggest an increase in comorbidities and mortality, possibly related to systemic inflammation (1).

Objectives: To study all-cause hospitalizations in patients with PsA in the United States (US) from 1993 to 2014.

Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in NIS from 1993 to 2014 with a primary or secondary diagnosis of PsA, and compared them to total all-cause US hospitalizations during the same period. US population estimates and projections for the resident US population were obtained from the US Census Bureau.

Results: There were 789.8 million all-cause hospitalizations in 6.4 billion person-years of observation from 1993 to 2014 (123.4 hospitalizations per 1,000 person-years). During this time-period, 332,496 hospitalizations occurred in patients with PsA (5.2 per 100,000 person-years). All-cause US hospitalizations increased from 33.7 million in 1993 to 35.4 million in 2014, an increase of 4.8% over 22 years (Figure, dotted blue line). All-cause hospitalizations in PsA patients have increased from 6,866 in 1993 (2.6 per 100,000 person-year) to 33,875 in 2014 (10.6 per 100,000 person-years, a dramatic increase of over 393% (p<0.0001, Figure solid red line). In 2014, hospitalizations in PsA patients accounted for 163,630 hospital days at a total national cost of over US$1.66 billion.

Conclusions: All-cause hospitalizations in patients with PsA in the US have significantly increased by 393% in the last 22 years, almost 80-fold of the 4.8% increase in US population all-cause hospitalization rate in the same time-period. This calls for an increase need for identification and management of serious co-morbid conditions in patients with PsA.



References:
[1] J Gelfand, D Gladman et al. Epidemiology of Psoriatic Arthritis in the Population of the United States. J Am Acad Dermatology, vol 53, p 573–577.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5502

FRI0489 CERTOLIZUMAB PEGOL IS ASSOCIATED WITH LONG-TERM IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES IN PSORIATIC ARTHRITIS: 4-YEAR OUTCOMES FROM THE RAPID-PSA STUDY

D. Gladman [1], R. Fleischmann [2], K. Harris [3], L. Peterson [4], P.J. Mease [5].
[1] University of Toronto and Krembil Research Institute, Toronto Western Hospital, Toronto, Canada; [2] UT Southwestern Medical Center and Dallas Metroplex Clinical Research Center, Dallas, United States; [3] UCB Pharma, Brussels, Belgium; [4] UCB Pharma, Raleigh; [5] Swedish Medical Center and University of Washington, Seattle, United States

Background: Psoriatic arthritis (PsA) is a heterogeneous inflammatory disease that has a substantial impact on patients' (pts) physical and emotional wellbeing.[1] Certolizumab pegol (CZP) is an Fc-free, PEGylated anti-TNF that has been shown to improve patient-reported outcomes (PROs) in pts with PsA over 96 weeks (wks) of treatment in the RAPID-PsA study (NCT01087788).[2]
Objectives: To investigate whether initial improvements in PROs observed with CZP treatment were maintained over 4 years in the RAPID-PsA study.
Methods: RAPID-PsA was double-blind and placebo-controlled to Wk24, dose-blind to Wk48, and open-label to Wk216. Pts were aged ≥18 years, with a diagnosis of active PsA, and had failed treatment with ≥1 DMARD. Pts originally randomized to CZP (400mg at Wks0,2,4 [loading dose] followed by either 200mg every 2 wks [Q2W] or 400mg every 4 wks [Q4W]) continued on their assigned dose during the open-label period. PROs assessed included Patient's Global Assessment of Arthritis Pain (PtAAP; visual analog scale), fatigue (numeric rating scale), Health Assessment Questionnaire-Disability Index (HAQ-DI), Short Form-36 Physical and Mental Component Summary (SF-36 PCS/MCS), Psoriatic Arthritis Quality of Life (PsAQoL), and Dermatology Life Quality Index (DLQI; assessed in the subgroup of pts with ≥3% body surface area affected by psoriasis at baseline [BL]). Data are reported as the mean change from BL (CFB) for pts randomized to CZP at Wk0, with last observation carried forward (LOCF) imputation for Wk24, and LOCF imputation and observed case (OC) values for Wk216.
Results: Of 273 pts randomized to CZP at Wk0, 248 (91%) completed Wk24 and 183 (67%) completed Wk216. Improvements observed to Wk24 of treatment were generally maintained over 4 years (to Wk216) in all PROs assessed, regardless of prior anti-TNF exposure (Table). Similar improvements were observed in both CZP dose regimens for all PROs examined, including PtAAP (CFB at Wk216 in the 200mg Q2W group [with LOCF imputation]: -30.5, in the 400mg Q4W group: -33.8); fatigue (-2.3, -2.3); HAQ-DI (-0.50, -0.49); SF-36 PCS (8.73, 8.77); SF-36 MCS (3.91, 3.28); PsAQoL (-4.6, -4.4); and DLQI (-8.4, -6.8).
Conclusions: Early improvements with CZP treatment were maintained over 4 years in all PROs assessed in the RAPID-PsA study. Similar improvements were observed in pts with and without prior anti-TNF exposure, and in both CZP dose regimens.
References:
[1] Rosen C. Rheumatology 2012;51(3):571–6.
[2] Gladman D. Value in Health 2014;17(7):A386.
Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.
Disclosure of Interest: D. Gladman Grant/research support from: Abbott, Bristol-Myers Squibb, Celgene, Johnson & Johnson, MSD, Novartis, Pfizer, UCB Pharma, Consultant for: Abbott, Bristol-Myers Squibb, Celgene, Johnson & Johnson, MSD, Novartis, Pfizer, UCB Pharma, R. Fleischmann Grant/research support from: Genentech Inc, Roche, Abbott, Amgen, UCB Pharma, Pfizer, Bristol-Myers Squibb, Lilly, Sanofi-Aventis, MSD, Novartis, AstraZeneca, Janssen, Consultant for: Roche, Abbott, Amgen, UCB Pharma, Pfizer, Bristol-Myers Squibb, Lilly, Sanofi-Aventis, Novartis, AstraZeneca, Janssen, K. Harris Employee of: UCB Pharma, L. Peterson Employee of: UCB Pharma, P. Mease Grant/research support from: (Abbott) AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB Pharma, Consultant for: (Abbott) AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Corrona, Dermira, Janssen, Lilly, Merck, Novartis, Pfizer, Sun, UCB Pharma, Zynerba, Speakers bureau: (Abbott) AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Novartis, Pfizer, UCB Pharma
DOI: 10.1136/annrheumdis-2017-eular.1654

Table: Mean change from baseline in patient-reported outcomes at Weeks 24 and 216 in patients with or without prior anti-TNF exposure

	Patients with prior anti-TNF exposure CZP dose combined (n=54)			Patients without prior anti-TNF exposure CZP dose combined (n=219)			Overall CZP dose combined (N=273)		
	Wk24 (LOCF)	Wk216 (LOCF)	Wk216 (OC) [n=34]	Wk24 (LOCF)	Wk216 (LOCF)	Wk216 (OC) [n=151]	Wk24 (LOCF)	Wk216 (LOCF)	Wk216 (OC) [n=185]
Outcome									
Pain (PtAAP) [a]	-33.3	-34.6	-44.2	-27.3	-31.5	-35.9	-28.5	-32.1	-37.4
Fatigue [b]	-2.1	-2.0	-2.5	-2.0	-2.3	-2.8 [n=147]	-2.0	-2.3	-2.7 [n=181]
HAQ-DI [c]	-0.60	-0.59	-0.67	-0.45	-0.47	-0.54	-0.48	-0.50	-0.57
SF-36 PCS [d]	8.37	9.79	11.18 [n=33]	7.92	8.50	9.64 [n=148]	8.01	8.75	9.92 [n=181]
SF-36 MCS [e]	4.57	2.38	5.29 [n=33]	4.49	3.90	5.36 [n=148]	4.50	3.60	5.35 [n=181]
PsAQoL [f]	-4.1	-4.2	-5.1	-3.8	-4.6	-5.1 [n=150]	-3.9	-4.5	-5.1 [n=184]
DLQI [g]	-9.0 [n=36]	-8.1 [n=36]	-10.9 [n=20]	-7.2 [n=130]	-7.5 [n=130]	-7.9 [n=87]	-7.6 [n=166]	-7.6 [n=166]	-6.4 [n=180]

[a] Range: 0–100, where 0=no pain and 100=worst pain (Minimal Clinically Important Difference [MCID]: -10); [b] Range: 0–10, where 0=no fatigue and 10=worst fatigue (MCID: -1); [c] Range: 0–3, where 0=no disability and 3=very severe disability (MCID: -0.3); [d] Range: 1–81, where higher scores indicate better physical status (MCID: +2.5); [e] Range: -9–82, where higher scores indicate better mental status (MCID: +2.5); [f] Range: 0–20, where lower scores indicate better quality of life; [g] Range: 0–30, where lower scores indicate better quality of life (MCID: -5). LOCF: last observation carried forward; OC: observed case.

FRI0490 REAL-LIFE EFFECTIVENESS OF TNF INHIBITORS IN PSORIATIC ARTHRITIS: ARE CHANGING NATIONAL POLICIES ON CHOICE OF TNF INHIBITOR REFLECTED IN RESPONSE TO TREATMENT?

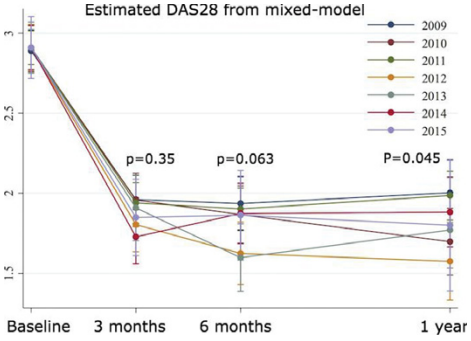
E.K. Kristianslund [1], K.M. Fagerli [1], E. Lie [1], A. Wierød [2], S. Kalstad [3], E. Rødevand [4], F. Krøll [5], P. Mielnik [6], T.K. Kvien [1], I.C. Olsen [1]. *[1] Department of Rheumatology, Diakonhjemmet Hospital, Oslo; [2] Department of Rheumatology, Drammen Hospital, Drammen; [3] Department of Rheumatology, University Hospital of North Norway, Tromsø; [4] Department of Rheumatology, St. Olavs Hospital, Trondheim; [5] Revmatismesykehuset, Lillehammer; [6] Department of Rheumatology, Førde Central Hospital, Førde, Norway*

Background: Tumour necrosis factor inhibitors (TNFi) are essential in the treatment of psoriatic arthritis (PsA). Whether the effectiveness of the five different TNFi differs is not known, as they have not been directly compared. In Norway the national authorities consider the TNFi to be equivalent, and since 2009 the least expensive drug in an annual national tender has been preferred in the publicly funded healthcare system. This has led to substantial year-to-year differences in chioce of first TNFi, the system has acted as an unbiased factor distributing patients between different agents across years.
Objectives: Comparing response to TNFi during the first year of treatment of PsA over years with highly varying uptake of different TNFi.
Methods: From the NOR-DMARD register we included the 715 biologics-naïve patients with PsA who started their first TNFi from 2009 through 2015. The preferred TNFi in national recommendations were: 2009 adalimumab, 2010 golimumab, 2011 and 2012 etanercept, 2013 golimumab, 2014 certolizumab, 2015 certolizumab/biosimilar infliximab (CT-P13). The estimated Disease Activity Score 28 joints (DAS28) at 3, 6 and 12 months after treatment start was compared between treatment years using a mixed-model, adjusted for baseline disease activity, age, sex and treatment centre.
Results: Demographics, choice of TNFi and baseline characteristics are listed for each year 2009–2015 in Table 1. The preferred drug was started in 56–91% of patients. There was a trend towards lower disease activity at baseline over time. There were no significant differences in DAS28 at 3 and 6 months between treatment years, but a difference was found at 1 year (figure).
Conclusions: The results from this innovative analytic approach indicate similar effectiveness of different TNFi in PsA, and consequently supports the practice of selecting agent based on cost and feasibility of use. However, there are potential differences after 1 year. The interpretation of this is challenging, especially as there is a marked difference in outcomes between the years 2011 and 2012, where the distribution of type of TNFi was similar.

Abstract FRI0490 – Table 1

	2009	2010	2011	2012	2013	2014	2015	p-value
N	104	90	162	99	90	108	62	
Age (years), mean (SD)	42.3 (11.2)	40.5 (11.8)	42.5 (12.6)	40.3 (11.1)	42.1 (12.8)	42.9 (11.6)	42.8 (12.4)	0.59
Proportion female	33.0%	36.0%	47.8%	38.4%	40.0%	37.0%	38.7%	0.29
Years since diagnosis, median (IQR)	4.5 (0.8, 14.5)	4.6 (0.7, 15.4)	5.4 (0.7, 16.0)	3.3 (0.6, 13.6)	1.3 (0.4, 8.5)	1.9 (0.2, 7.0)	2.5 (0.2, 10.8)	0.088
Disease Activity Score 28 joints, mean (SD)	3.04 (1.18)	3.09 (1.06)	2.97 (1.04)	2.76 (1.06)	2.78 (0.91)	2.79 (0.94)	2.60 (0.81)	0.051
Clinical Disease Activity Index, mean (SD)	11.02 (5.54)	11.43 (6.92)	10.20 (4.87)	10.08 (4.99)	9.41 (2.83)	10.42 (5.41)	9.08 (4.28)	0.15
Simplified Disease Activity Index, mean (SD)	12.52 (6.11)	12.90 (7.21)	11.34 (5.45)	10.43 (5.27)	10.45 (3.14)	11.41 (5.97)	9.63 (4.49)	0.015
Adalimumab	91.3%	33.3%	22.2%	15.2%	18.9%	13.0%	0.0%	<0.001
Certolizumab	0.0%	2.2%	0.0%	0.0%	11.1%	74.1%	43.5%	
Etanercept	7.7%	7.8%	61.7%	67.7%	5.6%	2.8%	3.2%	
Golimumab	0.0%	55.6%	12.3%	12.1%	63.3%	3.7%	4.8%	
Infliximab	1.0%	1.1%	3.7%	5.1%	1.1%	0.0%	0.0%	
Infliximab biosimilar	0.0%	0.0%	0.0%	0.0%	0.0%	6.5%	48.4%	

p-values for between-year differences.



Disclosure of Interest: E. K. Kristianslund: None declared, K. M. Fagerli: None declared, E. Lie Consultant for: AbbVie, Celgene, Hospira, Pfizer, UCB., A. Wierød: None declared, S. Kalstad: None declared, E. Rødevand: None declared, F. Krøll: None declared, P. Mielnik: None declared, T. K. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, I. C. Olsen: None declared
DOI: 10.1136/annrheumdis-2017-eular.4273

FRI0491 EFFECT OF THE TIGHT CONTROL TREAT-TO-TARGET STRATEGY ON THE DYNAMICS OF ACTIVE MRI SACROILIITIS IN THE RUSSIAN COHORT OF EARLY PERIFERAL PSORIATIC ARTHRITIS PATIENTS (PRELIMINARY RESULTS OF AN ONGOING OPEN-LABEL REMARCA STUDY)

E.E. Gubar, E.Y. Loginova, T.V. Korotaeva, D.E. Karateev. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Axial involvement in early psoriatic arthritis (ePsA) patients (pts) is often poorly diagnosed. Magnetic resonance imaging (MRI) of sacroiliac joints (SIJs) helps to better define spinal involvement and is used as an outcome measure to evaluate treatment of axial disease with TNF blockers. Treat-to-target (T2T) strategy was studied in various manifestations of PsA except axial involvement.
Objectives: to assess the effect of tight control T2T strategy on the 12-months dynamics of active MRI sacroiliitis (MRI-SI) in peripheral ePsA pts.
Methods: 89 treatment-naive pts (M/F–42 /47) with active peripheral ePsA, according to CASPAR criteria were included; mean age 36.5±10.9 yrs., disease duration 12.1±10.1 mo., disease activity index (DAS) 5.2±2.8, C-RP 16.1 [6.6; 31.0] mg/l, ESR 22.5±19.2 mm/h. At baseline and every 3 mo. of therapy all pts underwent standard clinical examination of PsA activity. All patients were evaluated for the presence of inflammatory back pain (IBP) by ASAS criteria. In pts having IBP, disease activity was also measured by BASDAI. At baseline MRI of SIJs was performed in 79 pts, both with and without IBP, on Signa Ovation 0.35T. Bone marrow edema (BME) on MRI (STIR), considered as active MRI sacroiliitis (MRI-SI), was evaluated by an independent reader. MRI of SIJs was repeated after 12 mo. in 20 pts who had completed a year of therapy having MRI-SI at baseline. Positive dynamics was indicated by the disappearance of BME on MRI (STIR). The main goal of T2T strategy was to reach remission or low/minimal disease activity (LDA/MDA). LDA was considered at DAS<1.6 or DAS28<2.6, remission was considered at DAS<1.6 or DAS28<2.6. At baseline all pts were treated with methotrexate (MTX) subcutaneous (s/c). The dose of MTX was escalated by 5 mg eow from 10 mg/wk to 20–25mg/wk. If the patient did not achieve LDA/MDA or remission after 3 mo. of MTX mono-therapy (MoT), combination therapy (CoT) with MTX+ adalimumab (ADA) 40 mg (s/c) eow was started. All pts were treated with NSAIDs: nimesulide 100–200mg or eterikokxib 60–90 mg per day.
Results: IBP was found in 58 out of 89 pts (65.1%). Disease activity by BASDAI in pts with IBP was 4.5±1.6. At baseline MRI-SI was observed in 28 out of 79 (35.4%) pts. Among the group of 20 pts who had completed a year of therapy having MRI-SI at baseline, 16 (80%) pts after 12 mo. of therapy demonstrated positive dynamics. Among these 16 pts, 8 (50%) pts underwent MoT and 8 (50%) pts underwent CoT. In the CoT-group pts received ADA for 6–9 mo. After 12 mo. of therapy, BME of SIJs on MRI still remained in 4 out of 20 (20%) pts. Among these 4 pts 2 pts underwent MoT and 2 pts underwent CoT (both pts received ADA for 3 mo., 9 th-12th mo. of therapy).
Conclusions: tight control T2T strategy in the Russian cohort of peripheral ePsA pts, demonstrated positive dynamics of active MRI-SI in 80% of pts after 12 months of therapy irrespective of the treatment used. These preliminary results demonstrate that tight control T2T strategy is effective not only in peripheral arthritis but also in axial involvement in ePsA. To confirm its effectiveness the strategy still needs to be verified on larger cohorts of pts.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3049

FRI0492 OBESITY IS HIGHLY OVERREPRESENTED AMONG SWEDISH PATIENTS WITH PSORIATIC ARTHRITIS COMPARED WITH THE GENERAL POPULATION

E. Klingberg[1], A. Bilberg[1], B. Eliasson[2], I. Larsson[3]. *[1]Department of Rheumatology and Inflammation Research, Sahlgrenska Academy at University of Gothenburg; [2]Department of Medicine; [3]Department of Gastroenterology and Hepatology, Sahlgrenska University Hospital, Göteborg, Sweden*

Background: Patients with psoriatic arthritis (PsA) are at increased risk of developing cardiovascular disease.
Objectives: To determine the prevalence of cardiovascular risk factors among patients with PsA followed at a Swedish Rheumatology Clinic in comparison with the general population (GP).
Methods: A questionnaire including weight, height, smoking habits, hypertension, diabetes and hyperlipidemia was sent to all PsA patients registered at the Rheumatology Clinic at Sahlgrenska University Hospital, Gothenburg (N=982). Obesity was defined as body mass index (BMI) ≥30 kg/m^{2}and overweight as BMI 25–29.9 kg/m^2. Comparison with the Swedish GP was made using data from the National public health survey, "Health on equal terms", which is sent yearly to 20 000 citizens by the Public Health Agency of Sweden.
Results: 686 (70%) of the PsA patients with mean age 56±11yrs (mean: SD), 52% women, responded.Higher prevalence of self-reported obesity and several cardiovascular risk factors was found in the PsA patients compared with the GP: Obesity 28.7% [GP 15% (95% C.I. 14.5–15.9%)], current smoking 10.5% [GP 9% (8.2–9.3%)], former smoking 43.4% [GP 23% (22.3–24.0%)], never smoking 48.8% [GP 63% (61.9–63.9%)], treatment of hypertension 32.9% [GP 20% (19.6–21.2%)] and diabetes 8.3% [GP 6% (5.4–6.3%)] Treatment of hyperlipidemia was reported by 15.0% [GP no data] and overweight by 36.2% [GP 36% (34.5–36.5%)]. Data stratified by age and sex is shown in the table. (Numbers are % and 95% C.I.)
Conclusions: Obesity was highly overrepresented among the PsA patients. It is imperative to take action against weight gain in overweight patients and promote weight loss in obese patients with PsA, since obesity may be involved in the pathogenesis of the disease and may fuel disease activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3118

Abstract FRI0492 – Table 1

	Obesity		Current smoking		Former smoking		Hypertension		Diabetes	
Sex Age	PsA	GP	PsA	GP	PsA	GP	PsA	GP	PsA	GP
♀ 30–44 (N=58)	27.6	14 (11.5–15.8)	13.8	8 (6.5–9.8)	34.5	19 (16.1–20.9)	3.4	4 (2.9–5.4)	3.4	2 (1.0–2.6)
♀ 45–64 (N=189)	33.9	18 (16.3–19.9)	14.3	13 (11.3–14.4)	49.2	31 (28.7–32.9)	33.9	20 (18.5–22.2)	5.8	5 (4.0–6.0)
♂ 30–44 (N=55)	25.5	12 (9.8–14.4)	7.3	5 (3.9–7.1)	21.8	14 (11.3–16.1)	9.1	7 (4.9–8.4)	1.8	2 (1.0–2.9)
♂ 45–64 (N=202)	26.7	20 (18.3–22.3)	7.4	9 (7.6–10.5)	34.7	25 (23.3–27.7)	31.2	28 (25.9–30.5)	6.4	7 (6.2–8.8)

FRI0493 DISEASE ACTIVITY TOGETHER WITH DEPRESSION CONTRIBUTES TO WORK DISABILITY IN PSORIATIC ARTHRITIS

F. Farkas[1], N. Ikumi[1], A. Szentpetery[1], B. Kirby[2], O. FitzGerald[1]. *[1]Department of Rheumatology; [2]Department of Dermatology, St. Vincent's University Hospital, Dublin, Ireland, Dublin, Ireland*

Background: Work disability (WD) is an important functional outcome measure in inflammatory arthritis, which has been studied comprehensively in rheumatoid arthritis and ankylosing spondylitis, however limited data are available in psoriatic arthritis (PsA)[1]. Depression and anxiety are well known comorbidities in psoriasis and PsA with higher prevalence in PsA[2].
Objectives: The aim of this study was to compare 1) patient-reported outcomes (PROs), including depression/anxiety scores; 2) physician-assessed measures and 3) disease activity using minimal disease activity (MDA) and Composite Psoriatic Disease Activity Index (CPDAI) in PsA patients with and without WD.
Methods: Consecutive patients with PsA fulfilling the CASPAR criteria were enrolled. Patients on disability pension, those with early retirement due to arthritis, those unemployed, away from work due to sick leave were considered as having WD. Patients have completed questionnaires on physical function and health-related quality of life and they were assessed for depression/anxiety using the Hospital Anxiety and Depression Scale (HADS-A and HADS-D) and Penn State Worry Questionnaire (PSWQ). Patients underwent musculoskeletal and skin assessments. Disease activity was compared between work-disabled and employed patients using MDA and CPDAI. Mann-Whitney, Chi-square tests and linear regression model were used to perform statistical analysis.
Results: 100 PsA patients were recruited, 18 were natural retirees, leaving 82 patients available for analysis. Thirty-one (17 male, age 50.9±9.97 years) participants of working age had work disability versus fifty-one (29 male, age 49.1±8.65 years) employed patients. Work-disabled patients had significantly higher HADS-D score (5.07±3.01 vs. 2.57±2.64; p<0.001) and significantly worse PROMs, including HAQ, PsAQoL, EQ-5D, BASDAI, BASFI, ASQoL, BRAF-NRS, pain and general health VAS. HADS-A and PSWQ scores were similar in both groups. Leeds enthesitis index and ESR were significantly higher (p=0.008; p=0.04, respectively) in patients with WD compared to those employed; furthermore the % of patients with CPDAI>4, suggesting moderate to severe disease activity were significantly higher (51.6% vs. 28%; p=0.032) in the WD group. There was no significant difference in MDA status between the two groups. Multiple regression analysis revealed significant relationship between HADS-D scores and CPDAI (B=0.566; p=0.03).
Conclusions: Consistent with previous studies we have observed that the WD rate is high (37.8%) among patients with PsA. This is the first study assessing the relationship between depression and disease activity using CPDAI in PsA patients with work disability. We have found significantly higher HADS-D score and higher % of patients with CPDAI>4 in the WD group compared to those employed. Significant relationship was revealed between depression and CPDAI, which suggests that disease activity together with depression contributes to work disability in PsA.
References:
[1] Tillett W. Rheumatology (Oxford) 2012.
[2] McDonough E. JRheumatol 2014.
Disclosure of Interest: F. Farkas: None declared, N. Ikumi: None declared, A. Szentpetery: None declared, B. Kirby Grant/research support from: Abbvie, O. FitzGerald Grant/research support from: Abbvie, Pfizer, BMS, Consultant for: Abbvie, Pfizer, BMS, Celgene, Janssen, Novartis, UCB, Eli Lilly
DOI: 10.1136/annrheumdis-2017-eular.5311

FRI0494 SECUKINUMAB PROVIDES RAPID AND SUSTAINED PAIN RELIEF IN PSORIATIC ARTHRITIS: 2-YEAR RESULTS FROM THE FUTURE 2 STUDY

I.B. McInnes[1], P.J. Mease[2], G. Schett[3], B. Kirkham[4], V. Strand[5], N. Williams[6], T. Fox[7], L. Pricop[8], S. Jugl[7], K.K. Gandhi[8] on behalf of the FUTURE 2 study group. *[1]University of Glasgow, Glasgow, United Kingdom; [2]Swedish Medical Center and University of Washington, Seattle, United States; [3]University of Erlangen-Nuremberg, Erlangen, Germany; [4]Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom; [5]Stanford University School of Medicine, Palo Alto; [6]RTI Health Solutions, Durham, United States; [7]Novartis Pharma AG, Basel, Switzerland; [8]Novartis Pharmaceuticals Corp., East Hanover, United States*

Background: Pain remains a major clinical challenge in the treatment of psoriatic arthritis (PsA). Secukinumab (SEC) has demonstrated significant efficacy in PsA patients (pts), across a range of quality of life related outcome measures.[1,2]
Objectives: This *post-hoc* analysis evaluated change in pain scores from baseline (BL) to Week (Wk) 104 in PsA pts receiving SEC in the FUTURE 2 study.
Methods: FUTURE 2 study design has been reported.[2] Mean change from BL in pain VAS and SF-36 bodily pain domain scores were evaluated using mixed-effect model for repeated measures (MMRM) through Wk 16 and as observed through Wk 104. Proportion of pts reporting improvements ≥clinically meaningful differences in pain VAS (mean change from BL ≥20%) was assessed. Results are reported for SEC 300 and 150mg in overall population and stratified by prior use of TNF inhibitor (TNFi; TNFi-naïve vs. inadequate responder/intolerant [TNFi-IR]). EQ–5D-3L pain item scores (no-, moderate- or extreme-pain/discomfort) were assessed as proportions.
Results: Mean changes from BL in pain VAS were greater with SEC vs. placebo (PBO) by Wk 3 (least squares mean [LSM]: -16.9, -12.6 with SEC 300 and 150mg, respectively vs. -5.75 with PBO; $P<0.05$), and Wk 16 (LSM: -24.0 and -23.0 for SEC 300 and 150mg, respectively vs. -8.41 with PBO; $P<0.05$). Mean changes were sustained through Wk 104 (-26.1 and -25.9 with SEC 300 and 150mg, respectively). In both SEC groups, >50% pts reported improvements of ≥20% by Wk 3 and this increased through Wk 104. Similarly, SF-36 bodily pain domain scores improved from BL by Wk 4 and 16 with SEC vs. PBO, exceeding minimum clinically important differences of 5.0 (Wk 4: LSM: 16.2 and 16.3 for SEC 300 and 150mg, respectively vs. 5.9 with PBO; $P<0.05$ and Wk 16: LSM: 21.1 and 22.0 for SEC 300 and 150mg, respectively vs. 6.9 with PBO; $P<0.05$). Improvements in pain were consistent in TNFi-naïve and TNFi-IR pts; and of greater magnitude in the naïve subgroup (table). Based on the EQ–5D-3L pain/discomfort item, 99% pts reported moderate to extreme pain or discomfort at BL. At Wk 4, the proportion of pts with no pain or discomfort was greater for the SEC 300mg (15%) and 150mg (10%) vs. PBO (5%) and increased through Wk 104 to 28% and 16% with SEC 300 and 150mg, respectively.

Table 1. Summary of results by TNFi status at baseline

	TNFi-naïve			TNFi-IR		
	SEC 300mg	SEC 150mg	PBO	SEC 300mg	SEC 150mg	PBO
N	67	63	63	33	37	35
Pain VAS						
Wk 16	-27.8*	-25.1†	-11.3	-18.2‡	-21.1§	-4.4
Wk 104	-29.6	-28.3	–	-19.3	-20.4	–
SF-36 bodily pain						
Wk 16	23.8*	25.4*	8.6	18.3§	17.9§	5.2
Wk 104	24.2	22.2	–	24.5	14.0¶	–

*$P<0.0001$; †$P<0.001$; §$P<0.01$; ‡$P<0.05$ vs. PBO. *P*-values and LS mean change at Wk 16 from MMRM analysis. Mean change at Wk 104 from observed data in n=57 (300mg) and 53 (150mg) for TNFi-naïve and n=29 (300mg) and 24 (150mg) for TNFi-IR; ¶n=26.

Conclusions: SEC provides rapid and sustained pain relief through 104 wks in pts with PsA as assessed by multiple clinically relevant patient-reported measures of pain. Improvements were reported by pts regardless of their prior TNFi therapy status.
References:
[1] Strand V, et al. Ann Rheum Dis 2017;76:203–7.
[2] McInnes IB, et al. Lancet 2015;386:1137–46.
Disclosure of Interest: I. McInnes Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, P. Mease Grant/research support from: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Consultant for: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, G. Schett: None declared, B. Kirkham Grant/research support from: AbbVie, Eli Lilly, Novartis, Roche and UCB, Consultant for: Abbott, Eli Lilly and Novartis, Speakers bureau: Abbott, Janssen, Novartis and Pfizer, V. Strand Consultant for: AbbVie, Amgen, BMS, Celgene, Celltrion, Corrona, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi and UCB, N. Williams Consultant for: Novartis through employment at RTI, Employee of: RTI Health Solutions, T. Fox Shareholder of: Novartis, Employee of: Novartis, L. Pricop Shareholder of: Novartis, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.5086

FRI0495 USE OF MELATONIN IN PATIENTS WITH PSORIATIC ARTHRITIS VIOLATIONS OF EMOTIONAL STATUS

I. Blaginina[1], O. Rebrova[1], N. Bludova[1], O. Volman[2]. *[1]Internal Medcine, SI "Lugansk State Medical University"; [2]Lugansk Clinical Regional Hospital, Lugansk, Ukraine*

Background: The ability of melatonin to reduce the activity of the sympathetic nervous system tone and of pituitary-adrenal system ensures its anti-stress properties. It can be used to reduce psycho-emotional manifestations of chronic pain in patients with psoriatic arthritis (PsA).
Objectives: To evaluate the effect of combined therapy with the use of melatonin on the expression of psycho-emotional disorders, and pain in patients with PsA.
Methods: High levels of anxiety and depressive disorders were established in the survey on Spielberger Anxiety Scale and on Hamilton Rating Scale for Depression (HRDS) in 43 patients with PsA (≥5 SJC and ≥5 TJC; CRP ≥0.3 mg/dL). The quality of life was studied by questionnaire Medical Outcomes Study Short Form (SF-36); the severity of morning stiffness, pain, patient's health status (EWS) - using the 100-mm visual analog scale (VAS). All patients were receiving a stable dose of MTX for at least 6 months. They were divided into two groups; 1 group (n=22) additionally received 3 mg of melatonin at bedtime for 2 months of observation
Results: At the end of the observation period the frequency and the level of

severity of depression by HRDS (p=0.0098), and the index of personal anxiety (P=0.009) in group 1 decreased. In the 2nd group above mentioned parameters have not changed. On the 1 group data of SF-36 evaluation: the physical health component has improved - the increase of RP and BP 57.4% and 37.8% from the baseline; vital activity and role functioning due to emotional state, have also increased by 35.6% and 43.5%, respectively. In the 2nd group (n=22) investigated parameters have not undergone significant changes in dynamics. In the 1 receiving melatonin group TJC and SJC have decreased by 15% and 22% (p=0.0079, p=0.0022, respectively) and their dynamics in the 2nd group was less significant (p=0.013 and p=0.017, respectively). Also, patients in group 1 have highly significant (p<0.001) reduction in the severity of morning stiffness and joint pain, and in the 2nd group the changes were less significant (respectively, p=0.043, p=0.016). Positive dynamics of CRP in group 1 was more significant (p=0.003), than it was in 2 patients' group (p=0.033).

Conclusions: In the group of patients treated with melatonin was noted improvement in general condition (a significant improvement in the parameters of the physical components of health, reduction of depressive and psycho-vegetative disorders) and also more significant decrease of the intensity of pain and of morning stiffness duration, of TJC and SJC, than in not treated with melatonin patients. Inclusion of Melatonin in the comprehensive PsA therapy promotes not only reduction of depression symptoms and sleep disorders, but also reduces the severity of the chronic pain manifestations and, consequently, improves the quality of life of patients with this disease

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2378

FRI0496 COMPARING TOFACITINIB SAFETY PROFILE IN PATIENTS WITH PSORIATIC ARTHRITIS IN CLINICAL STUDIES WITH REAL-WORLD DATA

J.R. Curtis[1], H. Yun[1], O. FitzGerald[2], K. Winthrop[3], V.F. Azevedo[4], G. Burmester[5], W.F.C. Rigby[6], K.S. Kanik[7], R. Rojo[7], S. Menon[7], C. Wang[7], P. Biswas[8], T. Hendrikx[9], N. Palmetto[8]. *[1]University of Alabama at Birmingham, Birmingham, AL, United States; [2]Department of Rheumatology, St Vincent's University Hospital, Dublin, Ireland; [3]Oregon Health and Science University, Portland, OR, United States; [4]Universidade Federal do Paraná, Curitiba, Brazil; [5]Charité - University Medicine Berlin, Berlin, Germany; [6]Geisel School of Medicine at Dartmouth, Lebanon, NH; [7]Pfizer Inc, Groton, CT; [8]Pfizer Inc, New York, NY; [9]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of psoriatic arthritis (PsA). Two Phase 3 studies have been completed (NCT01877668; NCT01882439) and a long-term extension (LTE) study is ongoing (database not locked; NCT01976364).

Objectives: To compare incidence rates (IR) for adverse events (AEs) of special interest in a tofacitinib cohort from the Phase 3 PsA trials with real-world experience in a comparison cohort from the US Truven MarketScan database.

Methods: The tofacitinib cohort included adult patients (pts) from 2 Phase 3 studies with ≥6 months PsA diagnosis who met ClASsification of Psoriatic ARthritis (CASPAR) criteria, had active plaque psoriasis, and active arthritis (≥3 swollen and ≥3 tender/painful joints) and who were treated with tofacitinib. Pts were grouped by those who received tofacitinib 5 (N=238) or 10 mg (N=236) twice daily (BID) in the 2 Phase 3 studies, and all pts who received ≥1 dose of tofacitinib in the 2 Phase 3 studies or the LTE (tofacitinib all doses, N=783). The comparison cohort (N=5799) comprised pts with moderate to severe PsA, defined by ≥1 inpatient or ≥2 outpatient 696.0 diagnosis codes on 2 unique calendar days (≥1 by a rheumatologist) between Oct 2010 and Sep 2015, initiating therapy with a systemic agent for PsA. Key Phase 3 study exclusion criteria were applied to the comparison cohort. IRs for serious infection events (SIEs), herpes zoster (HZ), malignancies (excluding non-melanoma skin cancer [NMSC]), NMSC and major adverse cardiovascular events (MACE) were compared.

Results: Mean age, gender and diabetes history were generally similar between the tofacitinib and comparison cohorts (48.7–49.5 years, 42.4–49.2% male, 12.2–15.7% with diabetes history). Overall more pts treated with tofacitinib had prior experience with corticosteroids (15.7–28.2%), conventional synthetic disease-modifying antirheumatic drugs (100%) and tumour necrosis factor inhibitors (48.1–55.9%) vs the comparison cohort (11.9%, 46.6% and 36.6%, respectively). IRs for SIEs were lower for the tofacitinib vs the comparison cohort (Table 1). The tofacitinib cohort had a higher rate of HZ vs the comparison cohort (Table 1). IRs for malignancies and MACE were similar between cohorts (Table 1).

Conclusions: IRs of AEs of special interest reported in tofacitinib PsA Phase 3 studies were generally comparable to those in a general PsA population comprising pts receiving a range of biologic agents, except HZ, which was higher for pts treated with tofacitinb but similar to the incidence observed with tofacitinib treatment in other indications.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by A Pedder of CMC and was funded by Pfizer Inc.

Disclosure of Interest: J. Curtis Grant/research support from: Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer Inc, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer Inc, H. Yun Grant/research support from: Pfizer Inc, O. FitzGerald Grant/research support from: AbbVie, Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer Inc, Speakers bureau: Celgene, Janssen, Novartis, K. Winthrop Grant/research support from: Bristol-Myers Squibb, Pfizer Inc, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Galapagos, Pfizer Inc, UCB, V. Azevedo Grant/research support from: Bristol-Myers Squibb, GSK, Pfizer Inc, UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Serono, Novartis, Pfizer Inc, G. Burmester Grant/research support from: UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Hexal, Janssen, MSD, Medimmune, Novartis, Pfizer Inc, Sanofi, Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Hexal, MSD, Novartis, Pfizer Inc, Roche, W. F. Rigby Grant/research support from: Amgen, Pfizer Inc, Roche, Consultant for: Bristol-Myers Squibb, Eli Lilly, Pfizer Inc, Roche, K. Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Rojo Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Menon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, P. Biswas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Hendrikx Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, N. Palmetto Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.2448

Table 1. Incidence rates (95% CI)[a] [PY exposure] for adverse events of special interest

		SIEs[b]	HZ	Malignancies[c]	NMSC	MACE
Tofacitinib cohort[d]	Tofacitinib 5 mg BID (N=238)	1.30 (0.16, 4.69) [154]	1.96 (0.41, 5.74) [153]	NR	NR	NR
	Tofacitinib 10 mg BID (N=236)	2.00 (0.41, 5.83) [150]	2.66 (0.73, 6.81) [150]	NR	NR	NR
	Tofacitinib all doses (N=783)	NR	NR	0.63 (0.21, 1.48) [791]	0.51 (0.14, 1.30) [789]	0.38 (0.08, 1.11) [791]
Comparison cohort	Any bDMARD (N=5075)	5.02 (4.19, 5.97) [2569]	1.26 (0.91, 1.70) [3343]	0.51 (0.34, 0.74) [5499]	1.40 (1.10, 1.75) [5488]	0.38 (0.22, 0.61) [4468]
	Any bDMARD + csDMARD (N=2542)	5.10 (3.83, 6.66) [1058]	1.53 (0.94, 2.37) [1303]	0.40 (0.16, 0.82) [1751]	1.79 (1.21, 2.53) [1736]	0.25 (0.07, 0.64) [1591]
	Any TNFi (N=4617)	5.13 (4.26, 6.11) [2419]	1.26 (0.90, 1.71) [3181]	0.51 (0.33, 0.74) [5144]	1.39 (1.09, 1.76) [5098]	0.41 (0.24, 0.65) [4183]
	Any TNFi + csDMARD (N=2383)	5.12 (3.83, 6.72) [1015]	1.51 (0.91, 2.36) [1257]	0.42 (0.17, 0.86) [1670]	1.75 (1.17, 2.52) [1656]	0.26 (0.07, 0.67) [1520]
	Adalimumab (N=1934)	4.16 (3.00, 5.63) [1009]	1.16 (0.65, 1.91) [1297]	0.48 (0.23, 0.88) [2095]	1.40 (0.94, 2.01) [2070]	0.41 (0.16, 0.84) [1724]
	Etanercept (N=1412)	4.82 (3.37, 6.67) [747]	1.10 (0.55, 1.97) [1000]	0.41 (0.16, 0.84) [1720]	1.46 (0.95, 2.16) [1709]	0.30 (0.08, 0.76) [1343]
	Infliximab (N=615)	8.91 (6.09, 12.57) [359]	1.94 (0.93, 3.57) [516]	1.21 (0.55, 2.30) [743]	1.35 (0.65, 2.48) [741]	0.47 (0.10, 1.37) [638]
	Golimumab (N=389)	3.49 (1.40, 7.19) [201]	1.16 (0.24, 3.39) [258]	0.00 (0.00, 0.90) [410]	0.99 (0.27, 2.53) [404]	0.91 (0.19, 2.67) [328]
	Certolizumab (N=267)	6.80 (2.74, 14.02) [103]	0.91 (0.02, 5.06) [110]	0.00 (0.00, 2.09) [176]	1.72 (0.35, 5.02) [175]	0.00 (0.00, 2.44) [151]
	Apremilast (N=617)	5.34 (3.56, 9.82) [187]	2.62 (0.85, 6.13) [191]	1.14 (0.24, 3.35) [262]	3.45 (1.58, 6.56) [261]	0.00 (0.00, 1.60) [231]

[a]Patients with event per 100 PY; [b]SIEs: any infection requiring parenteral antimicrobial therapy or hospitalisation or if the infection met criteria for a serious adverse event in the tofacitinib cohort; infections requiring parenteral antimicrobial treatment and hospitalisation in the comparison cohort; [c]All malignancies excluding non-melanoma skin cancer; [d]Tofacitinib 5 and 10 mg BID rows include patients randomised to these doses, respectively, in the two Phase 3 studies (12 or 6 months' duration), tofacitinib all doses row includes patients who received ≥1 dose of tofacitinib in the two Phase 3 studies or the LTE. IR estimates include events occurring ≤28 days after last dose of study drug (or to data cut-off in the LTE). Exposure (PY) is the total follow-up time to the day of the first event within the event-counting period for patients with events, or the last dose day plus a risk period of 28 days after the last dose (or to data cut-off for LTE) for patients without events. bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HZ, herpes zoster; LTE, long-term extension study; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; NR, not reported; PY, patient-years; SIE, serious infection event; TNFi, tumour necrosis factor inhibitor.

FRI0497 WHAT CHOICES DO RHEUMATOLOGIST MAKE IN ESCALATING DMARD THERAPY IN EARLY PSA?

J. Luime[1,2], I. Tchetverikov[3], K. Wervers[1], A. Gerards[4], M. Kok[5], C. Appels[6], H. van Groenendael[7], W. vd Graaff[8], L.-A. Korswagen[9], J. Veris[10], M. Hazes[1], M. Vis[1] on behalf of Cicero. *[1]Rheumatology, ErasmusMC, Rotterdam; [2]Data, Analytics and BI, Maxima Medisch Centrum, Veldhoven; [3]Rheumatology, ASZ, Dordrecht; [4]Rheumatology, Fransciscus - Vlietland, Schiedam; [5]Rheumatology, Maasstadziekenhuis, Rotterdam; [6]Rheumatology, Amphia, Breda; [7]Rheumatology, Reumazorg zuidwest Nederland, Roosendaal; [8]Rheumatology, Beatrix ziekenhuis, Gorinchem; [9]Rheumatology, Franciscus, Rotterdam; [10]Rheumatology, Reumazorg zuidwest Nederland, Goes, Netherlands*

Background: Psoriatic arthritis (PsA) is a multifaceted disease.

Objectives: We aimed to evaluate change in medication over time guided by joints, skin, enthesis, low back pain and dactylitis in newly diagnosed PsA patients

Methods: Newly diagnosed PsA patients were included in the Dutch Early south-west Psoriatic Arthritis cohoRt (DEPAR) study between August 2013 and March 2016. Initial drug treatment and escalation of therapy were described for all patients. Drivers of treatment changes in the first year were evaluated by mixed

Table 1 Multivariable mixed effects ordered ordinal logistic regression of treatment change over time in early PsA

	Odds Ratio	95% CI	
Covariates			
Swollen joint count (per joint)	**1.14**	**1.06**	**1.24**
Tender joint count(per joint)	0.98	0.94	1.02
Tender entheses (per enthesis)	1.06	0.94	1.19
BASDAI (per point)	1.05	0.97	1.15
Dactylitis Index (per point)	**1.05**	**1.00**	**1.09**
timepoints (baseline reference)			
3 months	**1.55**	**1.01**	**2.37**
6 months	1.25	0.78	2.02
9 months	**0.45**	**0.25**	**0.81**
12 months	1.52	0.79	2.91
initial starting values (no dmard reference)			
other sdmards	0.05	-0.52	0.62
methotrexate oral	0.49	-0.08	1.07
methotrexate subcutaneous	4.67	3.95	5.38
leflunomide	5.32	4.57	6.08
biological dmards*	6.23	5.42	7.05
mixed effects parameters			
random slope	0.02	0.01	0.06
random intercept	8.30	6.12	11.25

in bold **p<0.05**; *biological dmards were TNF inhibitors

ordered ordinal regression with outcome treatment change and variables joints (66/68 count), skin (PASI), entheses (LEI and MASES), dactylitis (LDI) and axial disease (BASDAI)

Results: 323 patients had had baseline assessment in March 2016. Their average age was 50.0 years (SD 13.8) and 49% were male. 80% patients had arthritis (19% monoarthritis, 39% oligoarthritis and 23%polyarthritis), 9% had an enthesitis subtype, 2% axial disease and 9% dactylitis. Initial treatment consisted of methotrexate (MTX) (52%), in 7% of other synthetic disease modifying antirheumatic drugs (sDMARDs) and due to treatment of psoriasis 3% biologicals. Within the different phenotypes MTX was most frequently started in polyarthritis (84%) followed by oligoarthritis (63%), monoarthritis (33%) and other phenotypes (5%). At 12 months 70% (n=148) stayed on the initial drug. Of those switched, 9 started MTX, within the initial MTX users (n=74) almost equal percentages stopped, switched to metoject or biological (4%). A smaller percentage (2%) switch to leflunomide. Changes in medication were driven by swollen joint count and the presence of dactylitis (Table 1)

Conclusions: MTX was initiated in about half of the early PsA patients. The majority of patients were kept on the initial treatment strategy in first year. Failure on initial drug led to variation in subsequent drugs with additional start of other sdmards, switch subcutaneuous MTX, to other sdmards or to biological dmards. Treatment change was driven by Swollen Joint Count and presence of Dactylitis. Skin, Enthesis and Axial disease did not play a role in escalating treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5922

FRI0498 OUTCOMES ASSOCIATED WITH ACHIEVEMENT OF VARIOUS TREATMENT TARGETS IN PATIENTS WITH PSORIATIC ARTHRITIS RECEIVING ADALIMUMAB

J. Smolen[1], D. Aletaha[1], D.D. Gladman[2], Y. Zhang[3], F. Ganz[4]. *[1]Medical University of Vienna, Vienna, Austria; [2]University of Toronto, Toronto Western Hospital, Toronto, Canada; [3]AbbVie, Inc., North Chicago, United States; [4]AbbVie, Inc., Baar, Switzerland*

Background: Various instruments are currently used for disease activity and outcome assessment in psoriatic arthritis (PsA). Some measures attempt to incorporate the total spectrum of psoriatic disease manifestations [eg, minimal disease activity (MDA)] while others focus on arthritis assessments [eg, disease activity index for PsA (DAPSA)]. Whether in patients (pts) with PsA it is sufficient to primarily consider joint disease aspects remains unclear.

Objectives: To compare DAPSA remission and low disease activity (LDA) with MDA and very low disease activity (VLDA) for the presence of residual abnormalities of the respective composing variables.

Methods: This post hoc analysis included pts with PsA receiving adalimumab (ADA) in one of two multicenter studies: ADEPT was a 24-week (wk), randomized, double-blind, placebo-controlled trial; ACCLAIM was a 12-wk, open-label study conducted in Canada in care settings that reflected usual practice. Frequencies of DAPSA remission/LDA and MDA/VLDA were summarized, and the individual PsA manifestations within these states were assessed. DAPSA was summed from the following continuous variables: swollen (66) and tender (68) joints, pt global assessment (PtGA, cm), pt pain (PP, cm), and C-reactive protein (CRP, mg/dL). DAPSA remission was defined as $\leq$4 and DAPSA LDA as $>$4 and $\leq$14. MDA criteria were as follows: $\leq$1 tender, $\leq$1 swollen joint, $\leq$1 entheseal point, PP $\leq$15mm, PtGA $\leq$20mm, HAQ $\leq$0.5, and PASI $\leq$3. MDA was calculated as fulfilling 5 of the 7 criteria, and VLDA calculated as fulfilling all 7 criteria. Data were as observed.

Results: Among 151 pts receiving ADA in ADEPT, 33 (22%) each achieved DAPSA remission and LDA at wk 24, and 20 (14%) and 11 (7%) achieved MDA and VLDA, respectively. Pts achieving DAPSA LDA appeared to mirror those in MDA, with the exception of experiencing numerically higher PP, PtGA, and PASI scores at wk 24 (Table). Pts in DAPSA LDA did experience numerically lower SJC when compared with the MDA achievers, and, like MDA achievers, displayed little residual enthesitis. Only VLDA, but not MDA, could match the stringency of DAPSA remission, a finding that was confirmed through analysis of the ACCLAIM cohort.

Table. Mean Values of DAPSA and MDA Components Following 12 or 24 Weeks of Adalimumab in ACCLAIM or ADEPT, Respectively

	DAPSA LDA (>4 – ≤14)		DAPSA Remission (≤4)		MDA (5 of 7 criteria)		VLDA (all 7 criteria)	
Variable	ADEPT n=33	ACCLAIM n=37	ADEPT n=33	ACCLAIM n=7	ADEPT n=20	ACCLAIM n=32	ADEPT n=11	ACCLAIM n=9
TJC, 0–78	3.1 ± 2.96	2.0 ± 1.80	0.3 ± 0.73	0.1 ± 0.38	3.4 ± 5.85	5.1 ± 5.49	0.1 ± 0.30	0.2 ± 0.44
SJC, 0–76	1.7 ± 2.00	2.4 ± 2.53	0.7 ± 1.36	0.3 ± 0.49	4.0 ± 7.97	4.8 ± 4.31	0.1 ± 0.30	0.2 ± 0.44
Pain, 100 mm VAS	17.8 ± 13.28	18.9 ± 16.66	4.1 ± 4.38	3.1 ± 3.89	8.9 ± 7.03	14.3 ± 14.55	4.8 ± 3.92	4.9 ± 4.59
PtGA, 100 mm VAS	17.2 ± 11.92	18.9 ± 18.02	3.7 ± 4.09	1.9 ± 2.67	8.9 ± 7.07	15.6 ± 20.35	4.3 ± 3.64	4.4 ± 4.88
CRP, mg/dL	0.4 ± 0.77	1.0 ± 0.99	0.2 ± 0.18	1.1 ± 0.79	0.3 ± 0.30	1.0 ± 1.27	0.2 ± 0.16	1.6 ± 0.97
PASI	2.5 ± 5.24	1.7 ± 1.47	0.6 ± 1.40	1.3 ± 0.58	0.7 ± 0.59	2.0 ± 3.02	0.3 ± 0.34	1.2 ± 0.55
HAQ-DI	0.4 ± 0.46	0.3 ± 0.47	0.1 ± 0.39	0.2 ± 0.34	0.2 ± 0.40	0.2 ± 0.35	0.0 ± 0.12	0.0 ± 0.09
Enthesitis	0.1 ± 0.40	0.1 ± 0.28	0.1 ± 0.24	0.1 ± 0.38	0.2 ± 0.37	0.2 ± 0.37	0.0 ± 0.00	0.1 ± 0.33
ΔmTSS, 0–570	−0.1 ± 1.30	N/A	−0.2 ± 0.70	N/A	−0.5 ± 2.20	N/A	−0.1 ± 0.51	N/A

All values are mean ± SD, unless otherwise indicated.

DAPSA, disease activity index of psoriatic arthritis; MDA, minimal disease activity; VLDA, very low disease activity; TJC, tender joint count based on 78 joints; SJC, swollen joint count based on 76 joints; mm, millimeter; VAS, visual analog scale; PtGA, patient global assessment of disease activity; CRP, C-reactive protein; mg, milligram; dL, deciliter; PASI, psoriasis activity score index; HAQ-DI, health assessment questionnaire disability index; mTSS, modified total Sharp score.

However, VLDA allowed for numerically higher residual PP and PtGA levels when compared with DAPSA remission. Importantly, residual enthesitis did not differ among pts achieving DAPSA remission or VLDA. Irrespective of disease activity assessment, pts receiving ADA displayed little to no radiographic progression.

Conclusions: In the ADEPT and ACCLAIM cohorts, pts who achieved DAPSA remission or VLDA demonstrated similar outcomes with respect to the individual components of both scores, despite the omission of several of these within the DAPSA. Given the DAPSA's continuous nature, its use may offer a good alternative to fulfillment of the VLDA criteria, but these results require confirmation in different pt populations.

Acknowledgements: AbbVie: study sponsor, contributed to design, data collection, analysis, interpretation, and abstract writing, review, and approval. Medical writing: Ben Wolfe of AbbVie.

Disclosure of Interest: J. Smolen Grant/research support from: AbbVie, Inc., Consultant for: AbbVie, Inc., D. Aletaha Grant/research support from: AbbVie, Inc., Pfizer, Grünenthal, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, Consultant for: AbbVie, Inc., Pfizer, Grünenthal, Merck, Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, D. Gladman Grant/research support from: AbbVie, Inc., Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Pfizer, Novartis, and UCB, Y. Zhang Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., F. Ganz Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc.

DOI: 10.1136/annrheumdis-2017-eular.3762

FRI0499 REAL-WORLD STUDY ON THE PATTERNS AND COST OF TREATMENT FAILURE IN PATIENTS WITH PSORIATIC ARTHRITIS USING US CLAIMS DATA

K. Price[1], E. Alemao[1], L. Burns[1], Z. Guo[1], V. Anupindi[2], S. Goday[3]. *[1]Bristol-Myers Squibb; [2]Mu Sigma, Princeton, United States; [3]Mu Sigma, Bangalore, India*

Background: Current treatments for psoriatic arthritis (PsA) are associated with a range of limitations, e.g. side effects, safety concerns and inadequate efficacy. The economic burden of biologic (b)DMARD failure among patients (pts) with PsA is thought to be substantial,[1] but there is a need to quantify this formally.

Objectives: To evaluate PsA treatment failure (i.e. discontinuation and switching rates) in a US managed care setting and its economic consequences.

Methods: Pts aged $\geq$18 years with 2 diagnosis codes for PsA and 1 claim for a bDMARD from 1 Jan 2007 to 31 Mar 2015 in the Truven Health MarketScan® Database (Commercial and Supplemental Medicare) were eligible for the study. Pts were considered incident if they did not have a PsA diagnosis or a bDMARD prescription during 1 year prior to first PsA diagnosis in the study period, and as prevalent otherwise. Pts had a 1-year follow-up from first PsA diagnosis in the study period. The percentages of pts discontinuing a drug, switching to another drug or continuing on the same drug for 1 year from first date of treatment were reported. Healthcare costs for 1 year from initiation of the first bDMARD, (medical and drug costs associated with treatment failures) were reported as cost per-pt-per-month (PPPM), and a generalized linear model was used to analyse the cost after controlling for various demographic variables.

Results: Of the 18,632 pts treated with a bDMARD, 1298 (6.97%) were incident and 17,334 (93.03%) prevalent. Almost half (n=8994; 48.27%) of the pts continued on the index bDMARD for 1 year. Treatment failed for the remaining pts, with 7852 (42.14%) discontinuing, and 1630 (8.75%; overlap $\leq$30 days between drugs) and 156 (0.84%; overlap $>$30 days) switching. In the prevalent group, 8754 (50.50%) pts continued on the index drug, 7043 (40.63%) discontinued, and 1399 (8.07%; overlap $\leq$30 days) and 138 (0.79%; overlap $>$30 days) switched to another drug. Among incident pts, only 240 (18.49%) continued, 809 (62.33%) discontinued, and 231 (17.80%; overlap $\leq$30 days) and 18 (1.38%; overlap $>$30 days) switched to another drug. Pts with an overlap $>$30 days were excluded from the analysis. Overall, pts who switched had a higher PPPM total cost ($3317) than those who discontinued ($2650; $p<0.0001$) or continued ($2708; $p<0.0001$). Similar results were observed in the prevalent and incident groups, respectively, with pts who switched incurring a higher PPPM total cost ($3241 and $3779) compared with those who discontinued ($2583 and $3237; both $p<0.0001$) or continued ($2700 and $3080; both $p<0.0001$). Increasing age (per year) was associated with a 0.57% higher total cost in the incident group ($p=0.002$) and with a 0.49% higher cost in the prevalent group ($p<0.0001$). Among prevalent pts, females had a 3.08% higher cost than males ($p=0.0069$). The Charlson Co-morbidity Index score predicted a higher cost ($p<0.0001$) among prevalent but not incident pts.

Conclusions: In a US claims study population of pts with PsA, rates of treatment failure as defined by switching or discontinuation were high. Follow-up costs for pts who switched were higher than for pts who continued or discontinued their medication. Baseline age, female sex and co-morbidities were associated with higher treatment costs.

References:

[1] Taylor PC, et al. Rheumatol Int 2016;36:685–95.

Disclosure of Interest: K. Price Employee of: Bristol-Myers Squibb, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, L. Burns Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Z. Guo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, V. Anupindi: None declared, S. Goday: None declared

DOI: 10.1136/annrheumdis-2017-eular.1476

FRI0500 AVOIDANCE OF PHYSICAL ACTIVITY LEADS TO REDUCED INFLAMMATORY ENTHESITIS ON ULTRASOUND

K. Wervers[1], I. Herrings[1], J.J. Luime[1], M. Moed[1], I. Tchetverikov[2], A.H. Gerards[3], J.M.W. Hazes[1], M. Vis[1]. [1]*Rheumatology, Erasmus MC, Rotterdam;* [2]*Rheumatology, Albert Schweitzer Hospital, Dordrecht;* [3]*Rheumatology, Vlietland Hospital, Schiedam, Netherlands*

Background: Enthesitis is one of the manifestations of psoriatic arthritis (PsA), but no clear definition for the diagnosis exists. To further evaluate the added value of sonographic evaluation of entheses in diagnosing enthesitis, more knowledge on factors associated with sonographic enthesitis is needed.
Objectives: We aim to evaluate which clinical characteristics are associated with sonographic enthesitis changes in a cross-sectional PsA population.
Methods: established PsA patients were asked to participate, irrespective of enthesitis complaints. Patients were interviewed on history of musculoskeletal complaints (MSC), more specifically if they had complaints during activities and whether they avoided physical activities (during exercise, work, household tasks, hobbies, chores). Tenderness was determined in the MASEI entheses and those in the Leeds Enthesitis Index (LEI) and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES). Previously we showed that a modified Madrid Sonographic Enthesitis Index (MASEI, i.e. excluding knee enthesis thickness and scoring PD-signal semi-quantitatively) distinguishes entheses of PsA patients from those of healthy volunteers (1). A sonographist unaware of clinical findings scored the modified MASEI. Multivariable linear regressions of structural (erosions, calcifications, structure) and inflammatory (thickness, bursitis and PD) modified MASEI scores were performed (transformed for a better distribution). Variables included age, gender, PsA duration, medication use (non/nsaids vs. sDMARDs vs. bDMARDs), LEI + MASES and avoidance (no vs. yes).
Results: 84 PsA patients participated (45 males, mean age 55, median disease duration 8 years). Median modified MASEI was 12 (IQR 7.25–17), with a structural component score of 7 (3–10) and inflammatory component score of 6 (3.5–8.5). 8 patients used no medication or NSAIDs only, 36 used sDMARDs and 40 used bDMARDs. 45 patients reported avoiding activities. In a multivariable analysis, inflammatory modified MASEI was negatively associated with avoidance (i.e. fewer inflammatory changes in patients reporting avoidance) and positively associated with age, BMI and use of biologics. Structural MASEI was positively associated with age only.

Table 1. Univariable and multivariable linear regression analysis of inflammatory and structural summary scores of MASEI

	inflammatory modified MASEI				structural modified MASEI			
	Univariable		Multivariable		Univariable		Multivariable	
age	**0.018**	[0.005;0.031]	**0.015**	[0.002;0.029]	**0.034**	[0.017;0.051]	**0.032**	[0.013;0.051]
gender (female vs. male)	0.156		0.162		0.122		0.102	
BMI	0.030		**0.031**	[0.002;0.060]	0.041		0.039	
medication use								
none/nsaids vs. sDMARDs	0.365		0.349		0.690		0.463	
none/nsaids vs. bDMARDs	0.484		**0.588**	[0.076;1.100]	0.588		0.462	
sqrt(disease duration)	0.085		-0.021		**0.246**	[0.030-0.462]	0.110	
LEI + MASES	-0.006		-0.005		0.016		-0.005	
avoidance (no vs. Yes)	**-0.415**	[-0.710;-0.119]	**-0.40**	[-0.697;-0.094]	-0.012		0.131	

Data shown as β [95%-CI]

Conclusions: Avoiding physical activities is associated with fewer inflammatory changes of the entheses. More inflammatory changes are seen in older or overweight patients and patients on biologicals, in the latter possibly due to more active disease.
References:
[1] Wervers K, Rasappu N, Vis M, Tchetverikov I, Kok MR, Gerards AH, et al. AB0733 Masei Shows Substantial Changes in The Entheses of Young Healthy Volunteers – Amending Its PD Score and Excluding Knee Entheses Thickness Provides Better Discrimination of Enthesitis in Psoriatic Arthritis Patients. Ann Rheum Dis 2016;75:1155.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3471

FRI0501 REAL-WORLD USE OF SECUKINUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS IN THE UNITED STATES: PATIENT PROFILE AND DOSING REGIMEN USE

K. Oelke[1], G. Chun[2], Y. Li[2], X. Liu[3], J.B. Palmer[2]. [1]*Rheumatic Disease Center, Glendale;* [2]*Novartis Pharmaceuticals Corporation, East Hanover;* [3]*KMK Consulting, Inc, Morristown, United States*

Background: As of January 15, 2016, secukinumab became the first fully human anti–interleukin-17 monoclonal antibody approved for the treatment of patients with psoriatic arthritis (PsA) in the United States. Secukinumab may be administered with or without loading of 150 mg or 300 mg (patients with concomitant moderate to severe psoriasis only) at weeks 0, 1, 2, 3 and 4 followed by maintenance dosing every 4 weeks. The use of a loading regimen of secukinumab in a real-world setting of patients with PsA has not been evaluated since its approval in the United States.
Objectives: To better understand the real-world use of secukinumab by describing the demographic, clinical and treatment characteristics (loading vs no loading) of secukinumab-treated patients with PsA.
Methods: Retrospective data from the Symphony Health Solutions Lx commercial claims database were used to identify patients who had ≥1 secukinumab claim between 01/15/2016 and 06/30/2016. Patients who were included in the analysis were aged ≥18 years, had ≥1 ICD-9 code of 696.0 or ICD-10 code of L40.5 for PsA and had ≥1 pharmacy or medical claim in the 12 months prior to their first secukinumab claim (index date). Patient demographics and secukinumab dosage were examined at the index date. Clinical characteristics, comorbidities and treatment history in the 12 months prior to the index date were identified and presented by use vs no use of loading.
Results: A total of 764 patients met the inclusion criteria. The mean (SD) age was 50.7 (11.6) years, 58.5% of patients were female and 39.8% of patients were from the south. The most common specialties prescribing secukinumab to patients with PsA were rheumatologists (52.1%) and dermatologists (30.0%). A total of 608 patients (79.6%) received loading and 156 (20.4%) did not; at the index date, the majority of patients received secukinumab at the 300-mg dose in the loading (73.2%) and no loading (84.6%) groups. Patient demographics, clinical characteristics and treatment history were generally comparable between groups (Table 1). However, more patients with loading had prior oral corticosteroid (OCS; 30.9% vs 20.5%), targeted synthetic disease-modifying antirheumatic drug (tsDMARD; 24.7% vs 17.3%) and biologic (64.3% vs 59.6%) use compared with those without loading. The most prevalent comorbidities were psoriasis (58.8%), hypertension (34.4%) and hyperlipidemia (26.8%). A higher proportion of patients with loading had hypertension (35.2% vs 31.2%), rheumatoid arthritis (RA; 15.3% vs 10.9%), fatigue (13.5% vs 9.0%) and anxiety (13.3% vs 8.3%) and a lower proportion had psoriasis (57.4% vs 64.1%) compared with those without loading.

Table 1. Demographics, clinical characteristics and treatment history of patients with PsA treated with secukinumab with or without a loading dose of 150 mg

	Overall (n = 764)	Loading (n = 608)	No Loading (n = 156)
Age, mean (SD), years	50.7 (11.6)	50.9 (11.9)	49.9 (10.5)
Female, n (%)	447 (58.5)	358 (58.9)	89 (57.1)
Region, n (%)			
South	304 (39.8)	251 (41.3)	53 (34.0)
Northeast	203 (26.6)	153 (25.2)	50 (32.1)
Midwest	152 (19.9)	118 (19.4)	34 (21.8)
West	104 (13.6)	85 (14.0)	19 (12.2)
Physician specialty, n (%)			
Rheumatology	398 (52.1)	319 (52.5)	79 (50.6)
Dermatology	229 (30.0)	176 (28.9)	53 (34.0)
Index dose, n (%)			
150 mg	187 (24.5)	163 (26.8)	24 (15.3)
300 mg	577 (75.5)	445 (73.2)	132 (84.6)
Treatment history, n (%)			
NSAID	159 (20.8)	124 (20.4)	35 (22.4)
Oral corticosteroid	220 (28.8)	188 (30.9)	32 (20.5)
csDMARD	265 (34.7)	210 (34.5)	55 (35.3)
tsDMARD	177 (23.2)	150 (24.7)	27 (17.3)
Biologic	484 (63.4)	391 (64.3)	93 (59.6)
Adalimumab	167 (21.9)	134 (22.0)	33 (21.2)
Ustekinumab	166 (21.7)	136 (22.4)	30 (19.2)
Etanercept	122 (16.0)	98 (16.1)	24 (15.4)
Certolizumab	65 (8.5)	52 (8.6)	13 (8.3)
Infliximab	55 (7.2)	46 (7.6)	9 (5.8)
Golimumab	38 (5.0)	34 (5.6)	4 (2.6)
Comorbidities, n (%)			
Psoriasis	449 (58.8)	349 (57.4)	100 (64.1)
Hypertension	263 (34.4)	217 (35.2)	49 (31.2)
Hyperlipidemia	205 (26.8)	161 (26.5)	44 (28.2)
Other skin diseases	189 (24.7)	149 (24.5)	40 (25.6)
Cancer	152 (19.9)	118 (19.4)	34 (21.8)
Diabetes	143 (18.7)	113 (18.6)	30 (19.2)
Depression	125 (16.4)	98 (16.1)	27 (17.3)
Obesity	117 (15.3)	96 (15.8)	21 (13.5)
Rheumatoid arthritis	110 (14.4)	93 (15.3)	17 (10.9)
Fatigue	96 (12.6)	82 (13.5)	14 (9.0)
Anxiety	94 (12.3)	81 (13.3)	13 (8.3)

csDMARD, conventional synthetic disease-modifying antirheumatic drug; NSAID, nonsteroidal anti-inflammatory drug; PsA, psoriatic arthritis; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.

Conclusions: This US claims-based study found the majority (≈ 73%) of secukinumab-treated patients with PsA were initiated with a loading regimen. Most patients initiated the 300-mg dose regardless of loading. A higher proportion of patients with loading had prior OCS, tsDMARD and biologic use, as well as hypertension, RA, fatigue and anxiety compared with those without loading, suggesting patients who initiated with loading had more refractory disease. These results provide the first insights into real-world use of secukinumab with and without loading in patients with PsA in the United States.
Acknowledgements: This study was sponsored by Novartis Pharmaceuticals Corporation, East Hanover, NJ.
Disclosure of Interest: K. Oelke Consultant for: Novartis, Speakers bureau: Amgen, AbbVie, Bristol-Meyers Squibb, Pfizer, G. Chun Employee of: Novartis, Y. Li Employee of: Novartis, X. Liu Consultant for: Novartis, Employee of: KMK Consulting, Inc, J. Palmer Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1541

FRI0502 IXEKIZUMAB REDUCES DISEASE ACTIVITY IN ACTIVE PSORIATIC ARTHRITIS PATIENTS WHO HAD PREVIOUS INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR-INHIBITORS

L.C. Coates[1], P. Mease[2], M.E. Husni[3], E. Lespessailles[4,5], D.H. Adams[6], O. Benichou[6], L. Kerr[6], P. Helliwell[1]. *[1]University of Leeds, Leeds, United Kingdom; [2]Swedish Medical Center and University of Washington, Seattle; [3]Cleveland Clinic, Cleveland, United States; [4]Orléans University; [5]Department of Rheumatology, C.H.R. Orléans, Orléans, France; [6]Eli Lilly and Company, Indianapolis, United States*

Background: Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease associated with psoriasis, peripheral arthritis, enthesitis, dactylitis, and spondylitis. Ixekizumab (IXE), a monoclonal high affinity antibody that selectively targets interleukin-17A, has improved disease activity and physical function in bDMARD-naïve patients with active PsA.[1] Herein, results are presented from a phase 3 trial (SPIRIT-P2; NCT02349295) with IXE in patients with active PsA and previous inadequate response to tumour necrosis factor-inhibitors (TNF-i).
Objectives: To explore the impact of IXE, as assessed by composite endpoints that incorporate multiple disease domains including peripheral arthritis, skin disease, enthesitis, dactylitis, spinal disease, functioning, and global disease assessment, up to 24 weeks (wks).
Methods: In this phase 3, multicentre, double-blind study, 363 adult patients with active PsA and a history of inadequate response to TNF-i were randomly assigned at a 1:1:1 ratio to subcutaneous administration of 80-mg IXE either every 4 wks (Q4W; N=122) or every 2 wks (Q2W; N=123) following a 160-mg starting dose at Wk 0 or placebo (PBO; N=118). TNF-i inadequate response was defined as lack of efficacy to one or two TNF-i or intolerance to TNF-i. Response to treatment and disease activity were measured at Wks 12 and 24 by the following composite endpoints: minimal disease activity with skin component measured with the Psoriasis Area and Severity Index (MDA) or the static Physician Global Assessment of psoriasis (mMDA) and Composite Psoriatic Disease Activity Index (CPDAI) as well as traditional measures by Psoriatic Arthritis Response Criteria (PsARC). Treatment comparisons were made by a logistic regression model for categorical data with missing values imputed by nonresponder imputation (NRI); a mixed model for repeated measures analysis was used for continuous data.
Results: At Wks 12 and 24, significantly more patients receiving IXEQ4W or IXEQ2W achieved MDA, mMDA, and PsARC compared with patients receiving PBO (Table). Results for MDA were similar to mMDA results within each treatment group at each time point. CPDAI total scores for patients receiving IXEQ4W or IXEQ2W were significantly improved compared with results for patients receiving PBO.

Table: Summary of Composite Endpoints at Weeks 12 and 24

			PBO (N=118)	IXEQ4W (N=122)	IXEQ2W (N=123)
MDA	Week 12	n (%)	6 (5.1)	31 (25.4)***	21 (17.1)**
	Week 24	n (%)	4 (3.4)	34 (27.9)***	29 (23.6)***
mMDA	Week 12	n (%)	6 (5.1)	31 (25.4)***	23 (18.7)**
	Week 24	n (%)	4 (3.4)	34 (27.9)***	29 (23.6)***
PsARC	Week 12	n (%)	28 (23.7)	61 (50.0)***	64 (52.0)***
	Week 24	n (%)	24 (20.3)	68 (55.7)***	58 (47.2)***
CPDAI	Week 12	Change from baseline	-0.9 (0.4)	-3.0 (0.4)***	-2.8 (0.3)***
		Effect Size	--	-2.1 (-2.8 to -1.5)	-1.9 (-2.6 to -1.3)
	Week 24	Change from baseline	-1.0 (0.4)	-3.7 (0.4)***	-3.4 (0.4)***
		Effect Size	--	-2.7 (-3.5 to -2.0)	-2.4 (-3.2 to -1.7)

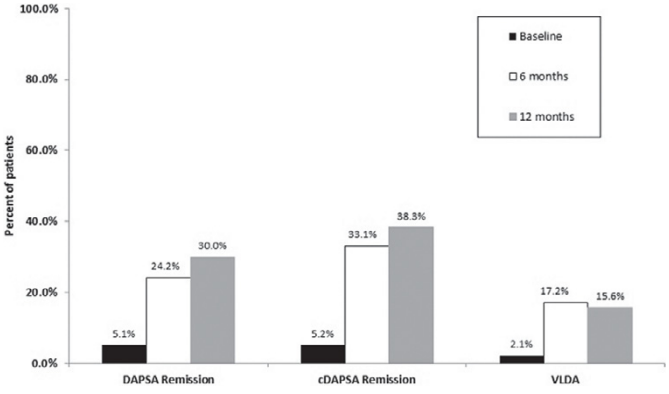
Change from baseline is least square mean (SE); Effect size is least square mean difference versus PBO (95% CI). **p<.01; *** p<.001.

Conclusions: Treatment with either IXEQ2W or IXEQ4W provides improvement in disease activity across multiple symptom domains, as measured by various composite endpoints, in patients with active PsA and who had a previous inadequate response to TNF-i.
References:
[1] Mease P et al. 2017 ARD 76(1):79.
Disclosure of Interest: L. Coates Grant/research support from: Abbvie, Janssen, Consultant for: Abbvie, Celgene, Janssen, Sun Pharma, Pfizer, UCB, MSD, Novartis, Eli Lilly and Company, P. Mease Grant/research support from: Abbvie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Eli Lilly and Company, Merck, Novartis, Phizer, UCB Pharma, Sun, Consultant for: Abbvie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Eli Lilly and Company, Merck, Novartis, Pfizer, UCB Pharma, Sun, Speakers bureau: Abbvie, Amgen, Bristol Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Pfizer, UCB Pharma, M. Husni Consultant for: Eli Lilly and Company, Novartis, Abbvie, Celgene, Bristol Myers Squibb, Amgen, Janssen, and UCB phrama, E. Lespessailles Grant/research support from: Amgen and Eli Lilly and Company, Speakers bureau: Expancience, Novartis and Servier, D. Adams Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, O. Benichou Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, L. Kerr Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Helliwell Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Janssen, Merck, Novartis, and UCB
DOI: 10.1136/annrheumdis-2017-eular.2757

FRI0503 VALIDATION OF NEW POTENTIAL TARGETS FOR REMISSION IN PSORIATIC ARTHRITIS IN PATIENTS TREATED WITH GOLIMUMAB

L.C. Coates[1], P. Rahman[2], E. Psaradellis[3], A. Karellis[3], E. Rampakakis[3], B. Osborne[4], C. Tkaczyk[4], A.J. Lehman[4], F. Nantel[4]. *[1]Leeds University, Leeds, United Kingdom; [2]Memorial University, St-Johns, NL; [3]JSS Medical Research, Montreal, QC; [4]Janssen Inc, Toronto, ON, Canada*

Background: Treat to target recommendations in psoriatic arthritis (PsA) stated that the target of treatment should be remission or inactive disease. At that time, no definitions of remission or inactive disease existed and the only validated target available was the minimal disease activity (MDA) criteria. Since then, other potential targets have been developed including very low disease activity (VLDA) and the Disease Activity in PsA (DAPSA) score remission.
Objectives: Using an existing dataset allowing calculation of DAPSA and clinical cDAPSA scores and the VLDA criteria, the objectives were to calculate the proportion of patients achieving these criteria, their prognostic value and the overall patient impact of these disease states.
Methods: BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients initiating treatment with infliximab, golimumab (GLM) or ustekinumab. PsA patients treated with GLM were included. Data collected at baseline, 6 and 12 months (mts) were used. DAPSA remission was defined as: TJC + SJC + PtGA + Pt pain + CRP $\leq$4. cDAPSA Remission was defined as: TJC + SJC + PtGA+ Pt pain $\leq$4. Very low disease activity (VLDA) was achieved when all 7 MDA criteria were satisfied: TJC28$\leq$1, SJC28$\leq$1, PASI$\leq$1, Pain (VAS) $\leq$15mm, PtGA (VAS) $\leq$20mm, HAQ $\leq$0.5 and tender entheseal points $\leq$1. Correlation between DAPSA, cDAPSA and VLDA were based on tetrachoric analysis.
Results: A total of 188 patients (53.2% female gender) were included with a mean (SD) disease duration of 5.46 (6.91) years. DAPSA remission was achieved in 5.1%, 24.2% and 30.0% of patients at baseline, 6 mts and 12 mts, respectively. Those patients had a significant reduction in the number of TJC, SJC, enthesitis and dactylitis ($p<0.043$). cDAPSA remission was achieved in 5.2%, 33.1% and 38.3% of patients at baseline, 6 mts and 12 mts, respectively. Those patients had a significant reduction in the number of TJC, SJC and enthesitis only ($p<0.002$). VLDA was achieved in 2.1%, 17.2% and 15.6% of patients at baseline, 6 mts and 12 mts, respectively and those patients had a significant reduction in the number of TJC, SJC, enthesitis and PASI ($p<0.002$). The overall correlation for DAPSA or cDAPSA remission vs. VLDA achievement were both at 0.999 (Asymptotic Standard Error <0.027) although this is likely driven by the high number of patients who are not in either state. 75% and 53.3% of patients in DAPSA and cDAPSA remission, respectively, also achieved VLDA ($p<0.001$). In contrast, patients who did not achieve neither cDAPSA nor DAPSA never achieved VLDA. Nonetheless, patients in remission had significantly greater HAQ scores ($p<0.03$) if they had remaining dactylitis or active skin disease (BSA$\leq$10%; cDAPSA only).



Conclusions: DAPSA, cDAPSA and VLDA represent new potential target for remission in PsA with VLDA being the most stringent criteria. There was a high level of correlation between these scores although residual activity in dactylitis and skin despite DAPSA remission has some impact on patients' function.
Disclosure of Interest: L. Coates Grant/research support from: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, UCB, Consultant for: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, UCB, P. Rahman Consultant for: Abbott, AbbVie, Amgen, BMS, Celgene, Janssen, Novartis, Pfizer, Roche, E. Psaradellis Employee of: JSS Medical Research, A. Karellis Employee of: JSS Medical Research, E. Rampakakis Employee of: JSS Medical Research, B. Osborne Employee of: Janssen, C. Tkaczyk Employee of: Janssen, A. Lehman Employee of: Janssen, F. Nantel Shareholder of: Jonhson and Johnson, Employee of: Janssen
DOI: 10.1136/annrheumdis-2017-eular.3855

FRI0504 APREMILAST EXPANDS IL-10-PRODUCING REGULATORY B CELLS, AND DECREASES TH1 AND TH7 CELLS IN PSORIATIC ARTHRITIS AND PSORIASIS

A. Mavropoulos[1], E. Zafiriou[2], A. Varna[1], E. Papadopoulou[2], I. Alexiou[1], A.-V. Roussaki-Schulze[2], D.P. Bogdanos[1], L.I. Sakkas[1]. *[1]Rheumatology and Clinical Immunology; [2]Dermatology, University of Thessaly, School of Health Sciences, LARISSA, Greece*

Background: IL-10-producing regulatory B cells (Bregs), also known as B10 cells, are decreased and inversely correlate with IFN-γ- and IL-17-producing NK and T cells in patients with psoriatic arthritis (PsA) and psoriasis (Ps) (1–3)
Objectives: To assess whether or not apremilast, a PDE4 inhibitor recently approved for the treatment of Ps and PsA, is able to induce IL-10-producing B cells and decrease Th1 cells and Th17 cells in vivo
Methods: PBMCs and magnetically purified B cells were isolated from 21 patients (7 PsA, all responders; 14 Ps, 9 responders) at baseline and post-apremilast treatment (at 3 and 6 months in responders; at 3 months in non–responders, as they switched to biologicals). Phenotypic analysis of CD3, CD19, CD24, CD27, CD38 and intracellular expression of cytoplasmic IL-10, IFN-γ, IL-17 after bacterial CpG (ODN2006) and PMA/ionomycin stimulation was examined by flow cytometry
Results: At 6 months, apremilast significantly increased IL-10-producing Bregs (IL-10+CD19+, B10 cells) compared to baseline and 3 months. B10 cells increase was confined mainly to the transitional Bregs (CD19+CD24highCD38high) rather than memory Bregs (CD19+CD27+CD24high). IFNγ+CD3+ (Th1) and IL-17+CD3+ (Th17) T cells were significantly decreased at 3 and 6 months ($p<0.05$, for both). There was an inverse correlation between percentages of B10 cells and IFN-γ-producing CD3+ cells. The percentage of B10 cells were not changed post-treatemnt in non-responders.
Conclusions: Our data suggest that apremilast may exert its therapeutic effect through the expansion of IL-10-producing Bregs and the decrease of IFN-γ- and/or IL-17-producing T cells
References:
[1] Mavropoulos et al Ann Rheum Dis 2015;74 Suppl 2 423.
[2] Mavropoulos et al Ann Rheum Dis 2016;75 Suppl 2 903.
[3] Mavropoulos et al Arthritis Rheumatol. 2016; 68 (suppl 10).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4665

FRI0505 RESIDUAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS TRIGGERS TREATMENT ADJUSTMENT IN ONLY A QUARTER OF PATIENTS IN DAILY CLINICAL PRACTICE

L.J.J. Van Mens[1], S. Atiqi[1], I.A. Fluri[1], M.G.H. van de Sande[1], A.W.R. van Kuijk[2], D.L. Baeten[1,3]. *[1]AMC; [2]Reade, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands; [3]UCB, Brussels, Belgium*

Background: With expanding therapeutic possibilities for the treatment of psoriatic arthritis (PsA) it will be increasingly important to determine residual disease and define when to adjust treatment. The rationale behind treatment decisions in current daily clinical practice and the relation with residual disease activity has not been reported in literature.
Objectives: To assess the current clinical practice on defining residual disease and the subsequent treatment decisions made in PsA patients.
Methods: This cross sectional study included 142 consecutive PsA patients who visited the outpatient clinic. The treating rheumatologist scored disease activity and his opinion on the presence of residual disease and the subsequent treatment decisions made. Patients scored patient disease activity scores.
Results: Of the 142 patients, 52 patients were considered without residual disease by the treating rheumatologist. These patients indeed show low disease activity on all measured domains, and all patients were considered in remission or low disease activity according to CDAI composite score.
90 of the 142 patients were considered to have residual active disease by their treating rheumatologist. Disease activity was present across all measured domains and 48/90 patients were considered in moderate (39) or high (9) disease activity defined by CDAI. There were no differences between the groups with or without residual disease activity in gender, disease duration, comorbidity, current treatment duration or number of previously used cDMARDS. Residual disease activity was more frequently reported in patients treated with a cDMARD only or a 2nd TNFi.
Of the 90 patients with residual disease, in 21 (23%) treatment adjustment was initiated. Treatment adjustments consisted of: addition or adjustment of analgesic treatment in 6 pts (29%); local or intramuscular corticosteroid therapy in 5 pts (24%); switch of cDMARD to another cDMARD in 4 pts (19%); referral to a paramedic in 2 pts (10%); switch to a 2nd or 3rd TNFi in a patient already using TNFi treatment in 2pts (10%); addition of a cDMARD to current TNFi 1 pt (5%); and start of a TNFi with current use of cDMARD only in 1pt (5%). Treatment changes were considered less frequent in those patients treated with a 2nd TNFi. No differences were seen in disease activity and demographics between those with or without a treatment adjustment.
Reasons not to adjust therapy mostly reported were: complaints were seen as only minor (39/69, 57%). The most frequent other reasons reported were: it was the patients' preference not to adjust medication (10/69, 14%); "we have no other options left" (5/69, 7%); lack of compliance (due to side effects) (5/69, 7%).
Conclusions: Residual disease resulted in treatment adjustment in only a quarter of patients. Not adjusting treatment could not be explained by comorbidities, or a lack of treatment options in a majority of the patients. Our data indicate that future implementation of a treat-to-target approach in PsA does not only require a data-driven consensus on the optimal target to use but also active coaching of physicians and patients to promote treatment adjustments in clinical practice.
Disclosure of Interest: L. Van Mens: None declared, S. Atiqi: None declared, I. Fluri: None declared, M. van de Sande Grant/research support from: Novartis, Eli Lilly, Boehringer Ingelheim; speakersfee: Benecke, Takeda, Tillotts, MSD, Cellgene, A. van Kuijk Grant/research support from: UCB, Pfizer, MSD, Janssen, Consultant for: Novartis, Celgene, D. Baeten Grant/research support from: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim, Consultant for: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim, Eli Lilly, Roche, BMS, Glenmark, Employee of: UCB, This work was financially supported by UCB in the context of an Investigator Initiated Study.
DOI: 10.1136/annrheumdis-2017-eular.3151

FRI0506 HLA PROFILES AND THEIR ASSOCIATIONS WITH DISEASE PHENOTYPES IN A CANADIAN PSORIATIC ARTHRITIS (PSA) COHORT

M. Khraishi[1], C. Molta[2], Z. Khraishi[3], A.M. Lewis[4]. *[1]Rheumatology, Memorial University of Newfoundland, St. John's, Canada; [2]Rheumatology, MainLine Rheumatology Lankenau Medical Center, Philadelphia, United States; [3]University of Western Ontario, London; [4]Epidemiology, Memorial University of Newfoundland, St. John's, Canada*

Background: PSA is a chronic disease with known genetic predisposition that affects 0.3% to 1% of the general population.Certain HLA allelles were reported to be more predominant in PSA and to be associated with certain manifestations.
Objectives: To determine HLA alleles prevalence in PSA patients and their association with clinical features and the severity of PSA in these patients
Methods: Two cohorts of early (established PSA)were followed prospectively.Clinical and laboratory data were collected at 6 months intervals, included PASI scores, nail involvement, joint counts, patient reported outcomes, comorbidities, inflammatory parameters and HLA Class I typing. Statistics utilized IBM SPSS v.23. Frequencies,means,medians and 2-tailed Pearson correlation were calculated.As the majority of our patients have Irish ancestry,we utilized HLA prevalence from an Irish population based data
Results: The cohorts included 265 patients. Of those, one hundred thirty five patients had their HLA analysis done. Fifty one percent of the patients were male, the mean age at onset of PSA 43.07 (19–76) years. Mean age of PSO diagnosis was 33.47 years. Sixty four percent had polyarticular involvement at base line and 17% had documented axial involvement.
Forty two haplotypes were reported in our cohort of those: HLA B27 was present in 33% of the patients (as compared to 6.77% in an Irish control population). HLAA1 was present in 31%, B8 in 21%,B57 in 6.6%B44 in 24.5%, B51 in 10%B58 in 5.6%, HLA B62 in 7%, HLA Bw4 in 43.6%and Bw6 in 46.5%.
The following associations were found to be significant: HLAB49 was negatively associated with age of onset of PSA with a Pearson correlation of -0.610 (P 0.007), also, HLA A23 had a correlation of -0.232 (P 0.016)
B44 was associated with increased total number of comorbidities, Pearson correlation was 0.332 (P 0.0001)
HLA B22 was associated with more severe PASI score with a correlation of 0.488 (P 0.000)
Of note that the only case in the cohort with Crohn's disease had HLA B12 which was previously reported in spondylitis
135 patients were studied,51% were male. The mean age of PSA onset was 43.07 yearsand 33.4 for PSO. 64% had polyarticular disease while 17% had axial involvement. 42 alleles were studied, of those, HLA B27 was present in 33% of patients (vs.6.77% controls) HLAA1 in 31%, B8 in 21%,B57 in 6.6%,B44 in 24.5%,B51 in 10%,B58 in 5.6%, HLA B62 in 7%, HLA Bw4 in43.6%, Bw6 in 46.5%. The following associations were significant: HLAB49& HLA A23 were associated with age of onset of PSA (correlation of -0.610 (P.007) and -0.232 (P.016) respectively. HLA B44 was associated with increased number of comorbidities (correlation 0.332 (P.0001),HLA B22 was associated with severe PASI score (correlation of 0.488 (P.000).The only case in our cohort with Crohn's disease had HLA B12 (previously reported in spondylitis)
Conclusions: The majority of patients had polyarticular involvement.HLABw6 and HLA Bw4 were the most frequent allelles. We found high percentage of patients with HLAB27, HLAA1 vs controls.HLA B27 prevalence was higher in patients with axial involvement but it did not reach significance in our cohort.HLA B44 was strongly associated with increased comorbidities (previous reports suggested protective effect of this allelle).HLA B22 was associated with more severe PASI scores.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1158

FRI0507 THE RELATIONSHIP BETWEEN 10-YEAR CARDIOVASCULAR RISK SCORES AND DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS

N. Ikumi[1], F. Farkas[1], A. Szentpetery[1], B. Kirby[2], O. FitzGerald[1].
[1]Rheumatology; [2]Dermatology, St. Vincent's University Hospital, Dublin, Ireland

Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with an increased prevalence of cardiovascular (CV) disease[1]. This increase may in turn be due to a higher prevalence of traditional CV risk factors as well as to persistent inflammatory musculoskeletal and skin disease[2]. Disease activity in PsA may be assessed by the Composite Psoriatic Disease Activity Index (CPDAI) across 5 domains of involvement: peripheral joints, skin, entheses, dactylitis and spinal manifestations. Long-term CV risk is evaluated using several methods for general population.

Objectives: (1) To describe CV risk factors and 10-year CV risk scores among patients with PsA; and (2) to correlate with baseline CPDAI in this longitudinal study

Methods: PsA patients fulfilling the CASPAR criteria were enrolled consecutively from Rheumatology clinics. Fasting bloods were obtained for glucose, insulin, lipids. Patients underwent thorough physical examination, joint and skin assessments and completed questionnaires on health, depression/anxiety and quality of life. Four different CV risk scores were calculated: (1) Framingham Coronary risk score (FCS); (2) American College of Cardiology and American Heart Association (ACC/AHA) 10-year atherosclerotic cardiovascular disease (ASCVD) algorithm; (3) Systematic Coronary Risk Evaluation (SCORE) algorithm; and (4) QRISK2 (2016). CPDAI was calculated with CPDAI cutoff $\leq$4 representing low/minimal disease activity (LDA) or remission. CPDAI $>$4 represented active disease requiring treatment change.

Results: 100 PsA patients were recruited with mean age 52.4 (±10.5) (male 55%). Mean disease duration for PsA was 17.9 (±10) years. 58 patients (age 52.4±9.6, male 60.3%) had CPDAI$\leq$4 (LDA Gp) and 41 patients (age 52.4±11.9, male 48.8%) had CPDAI$>$4 (active Gp) at baseline. There were significantly more patients with BMI$\geq$35 in active Gp, but mean BMI, waist/hip ratio, blood pressure, fasting glucose, insulin, lipids, and patients taking NSIADs, oral corticosteroid, Methotrexate and/or biologics treatment were otherwise similar compared to LDA Gp. Skin (Psoriasis Area Severity Index (PASI); Dermatology Life Assessment Questionnaire (DLQI)) assessments together with levels of inflammatory markers such as C-reactive protein (CRP) were also similar in both groups. More active Gp had enthesitis (58.5%) and acute dactylitis (14.6%) (P$<$0.01 and 0.02, respectively). The mean FCS, ASCVD, SCORE and QRISK2 were similar in both groups (8.5±7.1% vs. 6.2±6.9%, P=0.11; 8.9±8.5% vs. 7.8±7.9%, P=0.54; 2.2±2.6% vs. 2.0±2.7%, P=0.81; 11.2±9.2% vs. 11.3±11.%, P=0.97, LDA Gp and active Gp respectively). Interestingly, there were more smokers in LDA Gp (60.3% vs 39.0%; p=0.04) and this likely accounts for the higher number of LDA Gp patients with FCS$>$10%.

Conclusions: We found similar prevalence of traditional CV risk factors and similar 10-year CV risk scores in PsA patients regardless of their CPDAI. Further correlation with measures of disease activity over time will be required.

References:

[1] Ogdie A. ARD 2015.
[2] Eder L. ARD 2016.

Disclosure of Interest: N. Ikumi: None declared, F. Farkas: None declared, A. Szentpetery: None declared, B. Kirby Grant/research support from: abbie, O. FitzGerald Grant/research support from: abbie, Pfizer, BMS, Consultant for: abbie, Pfizer, BMS, Celgene, Janssen, Novartis, UCB, Eli Lilly

DOI: 10.1136/annrheumdis-2017-eular.4798

FRI0508 THE EFFECT OF CERTOLIZUMAB PEGOL ON EXTRA-ARTICULAR MANIFESTATIONS OF PSORIATIC ARTHRITIS OVER 4 YEARS OF TREATMENT IN PATIENTS WITH AND WITHOUT PRIOR ANTI-TNF EXPOSURE

O. FitzGerald[1], R. Fleischmann[2], A. Kavanaugh[3], B. Hoepken[4], L. Peterson[5], D. Gladman[6]. *[1]St. Vincent's University Hospital and Conway Institute for Biomolecular Research, University College Dublin, Dublin, Ireland; [2]UT Southwestern Medical Center and Dallas Metroplex Clinical Research Center, Dallas; [3]UC San Diego School of Medicine, la Jolla, United States; [4]UCB Pharma, Monheim, Germany; [5]UCB Pharma, Raleigh, United States; [6]Krembil Research Institute, Toronto Western Hospital, Toronto, Canada*

Background: Extra-articular manifestations (EAMs) of psoriatic arthritis (PsA) include nail psoriasis, dactylitis, and enthesitis, which can significantly impact patients' (pts') quality of life.[1] In the RAPID-PsA trial (NCT01087788), certolizumab pegol (CZP) improved the signs and symptoms of EAMs in pts with PsA over 96 weeks (wks).[2]

Objectives: To report improvements in EAMs of PsA in pts treated with CZP over 4 years, both with and without prior anti-TNF exposure.

Methods: The RAPID-PsA trial was double-blind and placebo-controlled to Wk24, dose-blind to Wk48, and open-label (OL) to Wk216. Pts had active PsA and had failed $\geq$1 DMARD. Pts originally randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wks0, 2, 4) continued their assigned dose in the OL period. We present EAM data for those pts originally randomized to CZP, with involvement of the particular EAM at baseline (BL), and both with and without prior anti-TNF exposure. EAMs assessed include nail psoriasis (modified Nail Psoriasis Severity Index [mNAPSI], BL involvement = BL mNAPSI $>$0), enthesitis (Leeds Enthesitis Index [LEI], BL involvement = BL LEI $>$0), and dactylitis (Leeds Dactylitis Index [LDI], BL involvement = $\geq$1 digit affected with a difference in circumference $\geq$10% compared to the opposite digit). Also presented are the proportions of pts with BL involvement of each EAM who achieved total resolution of the respective EAM on follow-up (a score of 0 for mNAPSI, LEI, or LDI). Observed values are reported, combined for pts receiving either CZP dose regimen.

Results: A total of 409 PsA pts were randomized; 273 received CZP from Wk0. Among CZP-randomized pts, 197 had nail psoriasis at BL (159 without, and 38 with, prior anti-TNF exposure), 172 had enthesitis (133 without, and 39 with, prior anti-TNF exposure), and 73 had dactylitis (56 without, and 17 with, prior anti-TNF exposure). Although relatively few pts were anti-TNF experienced, a large proportion of pts both with and without prior anti-TNF exposure with BL involvement went on to achieve total resolution of the respective EAM following 48 wks of CZP treatment (Table). Among pts completing the study, the proportions achieving total resolution were maintained or further increased from Wk48 to Wk216 (Table). Mean scores of all EAMs assessed showed improvements by Wk48 of CZP treatment in pts both with and without prior anti-TNF exposure, which were maintained to Wk216 in pts completing the study (Table).

Table: Improvements in extra-articular manifestations of PsA over 216 weeks of CZP treatment in patients with and without prior anti-TNF exposure (observed values)

	Week 0 CZP dose combined (N=273)			
	Baseline	Week 48	Week 96	Week 216
Number of patients observed **Mean score (standard deviation)** **Patients with total resolution, n (%)**				
Nail psoriasis (mNAPSI) [a]				
Anti-TNF naïve (n=159)	159 3.4 (2.1) –	139 1.1 (1.5) 71 (51.1)	129 0.7 (1.3) 84 (65.1)	109 0.4 (0.8) 80 (73.4)
Anti-TNF experienced (n=38)	38 2.9 (1.8) –	33 0.9 (2.1) 22 (66.7)	29 0.6 (1.1) 19 (65.5)	23 0.5 (0.7) 14 (60.9)
Enthesitis (LEI) [b]				
Anti-TNF naïve (n=133)	133 3.0 (1.7) –	116 0.8 (1.5) 83 (71.6)	104 0.7 (1.3) 74 (71.2)	85 0.5 (1.0) 65 (76.5)
Anti-TNF experienced (n=39)	39 2.9 (1.6) –	33 1.2 (2.1) 23 (69.7)	27 0.8 (1.4) 19 (70.4)	25 0.5 (1.2) 20 (80.0)
Dactylitis (LDI) [c]				
Anti-TNF naïve (n=56)	56 50.9 (64.7) –	48 0.0 (0.0) 44 (91.7)	46 0.0 (0.0) 42 (91.3)	41 0.3 (2.1) 38 (92.7)
Anti-TNF experienced (n=17)	17 52.5 (42.7) –	14 12.6 (25.3) 11 (78.6)	11 0.0 (0.0) 9 (81.8)	9 4.2 (12.7) 8 (88.9)

EAMs were assessed in patients with involvement of the respective EAM at baseline. [a] Patients with mNAPSI >0 at baseline; [b] Patients with LEI >0 at baseline; [c] Patients with LDI >0 at baseline, defined as having at least 1 digit affected and with a difference in circumference ≥10% compared to the opposite digit.

Conclusions: PsA patients treated with CZP for up to 4 years, both with and without prior anti-TNF exposure, exhibited sustained improvements in the extra-articular manifestations of PsA.

References:

[1] Ritchlin C. Ann Rheum Dis 2009;68:1387–94.
[2] FitzGerald O. Ann Rheum Dis 2015;74(2):349.

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: O. FitzGerald Grant/research support from: AbbVie, Bristol Myers Squibb, Janssen, Novartis, Pfizer, Consultant for: AbbVie, Celgene, Janssen, Pfizer, Roche, UCB Pharma, Speakers bureau: AbbVie, Celgene, Janssen, Pfizer and UCB Pharma, R. Fleischmann Grant/research support from: Abbott, Amgen, AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Genentech, Janssen, MSD Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB Pharma, Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Genentech, GlaxoSmithKline, Janssen, Eli Lilly, Pfizer, Sanofi-Aventis, UCB Pharma, A. Kavanaugh Grant/research support from: Abbott, Amgen, Bristol-Myers Squibb, Janssen, Pfizer, Roche, UCB Pharma, B. Hoepken Employee of: UCB Pharma, L. Peterson Employee of: UCB Pharma, D. Gladman Grant/research support from: Abbott, Bristol-Myers Squibb, Celgene, Johnson & Johnson, MSD Pharmaceuticals, Novartis, Pfizer, and UCB Pharma, Consultant for: Abbott, Bristol-Myers Squibb, Celgene, Johnson & Johnson, MSD Pharmaceuticals, Novartis, Pfizer, and UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.1969

FRI0509 SAFETY AND EFFICACY OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, UP TO 24 MONTHS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: INTERIM DATA FROM OPAL BALANCE, AN OPEN-LABEL, LONG-TERM EXTENSION STUDY

P. Nash[1], L.C. Coates[2], A.J. Kivitz[3], P.J. Mease[4], D.D. Gladman[5], J.A. Covarrubias-Cobos[6], D. Fleishaker[7], C. Wang[7], E. Kudlacz[7], S. Menon[7], T. Hendrikx[8], K.S. Kanik[7]. *[1]Department of Medicine, University of Queensland, St Lucia, Brisbane, Australia; [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom; [3]Department of Rheumatology, Altoona Center for Clinical Research, Duncansville, PA; [4]Swedish Medical Center and University of Washington, Seattle, WA, United States; [5]Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada; [6]Unidad Reumatologica Las Americas S.C.P, Mérida, Yucatán, Mexico; [7]Pfizer Inc, Groton, CT; [8]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for psoriatic arthritis (PsA). Interim data (database not locked) from ≤24 months' participation (3 years' total treatment duration) for patients (pts) with active PsA in an ongoing, open-label, long-term extension study (LTE; NCT01976364 OPAL Balance) is reported.

Objectives: To evaluate the safety, tolerability and efficacy of tofacitinib in pts with active PsA.

Methods: Eligible pts from 2 pivotal Phase 3 tofacitinib PsA studies (NCT01877668 OPAL Broaden, NCT01882439 OPAL Beyond) could enter a 3-year LTE ≤3 months after completing the qualifying study or discontinuing for non study-drug-related reasons. Pts were to receive tofacitinib 5 mg twice daily (BID) for 1 month, after which an increase to 10 mg BID or reduction back to 5 mg BID was permitted at any time for efficacy or safety reasons. Concomitant treatment with a single conventional synthetic disease-modifying antirheumatic drug (csDMARD) was allowed but not required. Primary endpoints were incidence and severity of adverse events (AEs) and change from baseline in laboratory values. Efficacy was a secondary endpoint.

Results: 680/685 enrolled pts were treated. 608 (89.4%) remained at data cut-off. Mean (range) duration of tofacitinib exposure in this LTE was 206 (3–741) days. 661 (97.2%) pts took a csDMARD on Day 1, and 73 (11.0%) later discontinued csDMARD. To Month 24, 860 AEs were reported in 367 (54.0%) pts, 41 (6.0%) pts had serious AEs and 24 (3.5%) pts discontinued due to AEs. Special interest AEs included 6 serious infections (0.9%), 10 herpes zoster events (1.5%) including 1 serious event, 2 major adverse cardiovascular events (0.3%) and 2 malignancies (0.3%). There were 3 deaths (not attributed to treatment, as assessed by the investigator) due to metastatic pancreatic carcinoma, acute cardiac failure and pulmonary embolism. No GI perforation, inflammatory bowel disease or uveitis cases were reported. One AE of latent TB was reported. One pt met discontinuation criteria for laboratory values due to increased serum creatinine >50% and >0.5 mg/dL over the average of screening and baseline creatinine. Small mean decreases in absolute lymphocyte and neutrophil counts, and small mean increases in serum lipid markers, were observed; 18 (2.6%) pts started new lipid-lowering medication during the LTE (80 [11.8%] pts were on lipid-lowering drug at baseline). Efficacy was maintained in the LTE (Table 1).

Table 1. Summary of efficacy through to Month 15[a]

	Tofacitinib (all patients) (N=680)				
	Month 3	Month 6	Month 9	Month 12	Month 15
ACR20, n/N1 (%)	421/606 (69.5)	326/470 (69.4)	219/307 (71.3)	109/154 (70.8)	48/66 (72.7)
ACR50, n/N1 (%)	264/607 (43.5)	217/469 (46.3)	160/308 (52.0)	77/153 (50.3)	31/66 (47.0)
ACR70, n/N1 (%)	154/608 (25.3)	140/471 (29.7)	92/308 (29.9)	48/153 (31.4)	19/67 (28.4)
ΔHAQ-DI, mean (SD) [N1]	-0.5 (0.6) [606]	-0.5 (0.6) [472]	-0.5 (0.6) [308]	-0.5 (0.6) [154]	-0.5 (0.6) [67]
PASI75 response rate, n/N1 (%)[b]	219/387 (56.6)	180/304 (59.2)	113/202 (55.9)	55/100 (55.0)	31/45 (68.9)
ΔLEI, mean (SD)[c] [N1]	-1.6 (1.8) [399]	-1.5 (1.8) [312]	-1.6 (1.8) [204]	-1.4 (2.0) [102]	-1.8 (2.1) [48]
ΔDSS, mean (SD)[c] [N1]	-6.9 (7.8) [330]	-6.8 (8.3) [254]	-6.9 (7.2) [164]	-6.9 (6.6) [83]	-7.3 (7.4) [39]
ΔPain, mean (SD)[d] [N1]	-25.3 (26.8) [604]	-26.3 (28.0) [471]	-28.7 (28.9) [308]	-28.7 (29.2) [154]	-31.4 (29.1) [67]

Baseline values represent those at the start of the qualifying study

Only evaluable pts at a visit of interest were included in the analysis and missing values were not imputed

[a]Efficacy data is reported to Month 15 as sample sizes were too small beyond this time point; [b]Among patients with baseline BSA ≥3% and PASI >0; [c]Among patients with baseline score >0; [d]Patient's assessment of arthritis pain measured using VAS (mm)

Δ, change from baseline; ACR, American College of Rheumatology; ACR20/50/70, ACR20%/50%/70% response rate; BSA body surface area; DSS, Dactylitis Severity Score; HAQ-DI, Health Assessment Questionnaire Disability Index; LEI, Leeds Enthesitis Index; N, number of patients in full analysis set; N1, number of evaluable patients at a visit; n, number of responders; PASI75, Psoriasis Area Severity Index 75% improvement; PsA, psoriatic arthritis; SD, standard deviation; VAS, visual analogue scale

Conclusions: Over 24 months in the LTE, the safety profile of tofacitinib in pts with active PsA was generally similar to that of the pivotal Phase 3 studies. No new safety signals were identified. Efficacy was maintained over time.

Acknowledgements: To be presented at AAD 2017 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by S Morgan of CMC and was funded by Pfizer Inc.

Disclosure of Interest: P. Nash Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer Inc, Roche, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Merck, Novartis, Pfizer Inc, Sanofi, Roche, UCB, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Novartis, Pfizer Inc, Roche, UCB, L. Coates Speakers bureau: Pfizer Inc, A. Kivitz Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Genentech, Pfizer Inc, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Genentech, Pfizer Inc, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Genentech, Pfizer Inc, P. Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer Inc, Sun, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Corrona, Dermira, Janssen, Eli Lilly, Merck, Novartis, Pfizer Inc, Sun, UCB, Zynerba, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Genetech, Janssen, Novartis, Pfizer Inc, UCB, D. Gladman Grant/research support from: Amgen, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer Inc, Novartis, UCB, Consultant for: Amgen, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer Inc, Novartis, UCB, Speakers bureau: Amgen, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer Inc, Novartis, UCB, J. Covarrubias-Cobos Grant/research support from: Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer Inc, D. Fleishaker Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, E. Kudlacz Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Menon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Hendrikx Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.1414

FRI0510 CORRELATION OF THE ROUTINE ASSESSMENT OF PATIENT INDEX DATA (RAPID-3) WITH OTHER PSORIATIC ARTHRITIS COMPOSITE DISEASE ACTIVITY MEASURES IN PATIENTS RECEIVING ADALIMUMAB

P.J. Mease[1], S. Chen[2], F. Ganz[3], W. Tillett[4]. *[1]Swedish Medical Center and University of Washington, Seattle; [2]AbbVie, Inc., North Chicago, United States; [3]AbbVie, Inc., Baar, Switzerland; [4]Royal United Hospitals Bath NHS Foundation Trust, Bath, United Kingdom*

Background: There is increased interest across rheumatologic disease to utilize patient (pt)-reported outcomes (PROs) in disease assessment. Several measures entirely derived from PROs, such as the 3-component routine assessment of pt index data (RAPID-3), have been shown to be closely correlated with physician rheumatoid arthritis assessments using traditional composite scores.[1]

Objectives: To assess the correlation between the RAPID-3 and other psoriatic arthritis (PsA) composite indices [eg, disease activity index for PsA (DAPSA), minimal disease activity (MDA)] in pts with PsA receiving adalimumab (ADA) or placebo (PBO).

Methods: This post hoc analysis used data from the ADEPT trial, which included pts with active PsA despite prior DMARD therapy who were randomized to receive ADA or PBO for 24 weeks (wks). Mean RAPID-3 was summarized by visit for each treatment group. Correlations between RAPID-3 and DAPSA over time were assessed through Pearson and Spearman coefficient. Pts were categorized at wk 24 according to DAPSA [Remission: ≤4; low disease activity (LowDA): >4 – ≤14; moderate disease activity (ModDA): >14 – ≤28; high disease activity (HighDA): >28) and MDA [achievement of 5 of 7 or the more stringent 7 of 7 criteria (very low disease activity [VLDA]): yes, no], and assessed for the numbers of pts in each respective RAPID-3 disease activity state (Remission: ≤3; LowDA: >3 – ≤6; ModDA: >6 – ≤12; HighDA: >12). The Kappa statistic was used to describe the agreement between the numbers of pts in respective disease activity categories by RAPID-3, DAPSA, and MDA. Data were as observed.

Results: Amongst the 151 and 162 pts randomized to receive ADA and PBO, respectively, both groups exhibited HighDA when assessed by RAPID-3 [13.1 for both groups; 55% (ADA) and 54% (PBO) in HighDA]. At wk 24, mean RAPID-3 remained in HighDA for the PBO group (12.6), whereas it decreased to a state of LowDA (6.8) in those receiving ADA. Following 24 wks of treatment, 39% and 24% in the ADA group were in remission by RAPID-3 and DAPSA, respectively. Fewer pts in the PBO group were in remission by either definition at wk 24 (8% and 3%, respectively). At baseline, there was moderate correlation between RAPID-3 and DAPSA in both treatment groups (ADA: 0.512; PBO: 0.510). At wk 24, the correlations in both treatment groups increased, with the correlation observed in the ADA group outpacing the PBO group (ADA: 0.721; PBO: 0.590). Similarly, disease activity categorizations by RAPID-3 correlated with DAPSA and MDA categorizations (Table).

Conclusions: In a PBO-controlled trial of ADA in pts with PsA, there was good correlation between disease activity captured by pt's self-assessment, via the RAPID-3, and physician assessment, underscoring the potential utility of pt-derived measures in assessing disease activity.

References:

[1] Pincus and Sokka. Best Pract Res Clin Rheumatol 2007;21(4):733–53.

Acknowledgements: AbbVie: study (NCT00646386) sponsor, contributed to

Table. Analysis of Categorical RAPID-3 by DAPSA and MDA Categories at Week 24.

	Disease Activity Assessment	RAPID-3 Remission ≤3	LowDA >3–≤6	ModDA >6–≤12	HighDA >12	Kappa
DAPSA						
Adalimumab	Remission	29 (20.9)	3 (2.2)	1 (0.7)	0	
	LowDA	15 (10.8)	11 (7.9)	6 (4.3)	1 (0.7)	0.388[a]
	ModDA	6 (4.3)	8 (5.8)	17 (12.2)	4 (2.9)	0.572[b]
	HighDA	4 (2.9)	4 (2.9)	12 (8.6)	18 (12.9)	
Placebo	Remission	4 (2.8)	0	0	0	
	LowDA	5 (3.4)	3 (2.1)	5 (3.4)	1 (0.7)	0.284[a]
	ModDA	1 (0.7)	7 (4.8)	16 (11)	9 (6.2)	0.484[b]
	HighDA	1 (0.7)	4 (2.8)	29 (20)	60 (41.4)	
Minimal Disease Activity						
Adalimumab	MDA					
	Yes	45 (32.1)	5 (3.6)	1 (0.7)	0	0.574[c]
	No	9 (6.4)	21 (15)	36 (25.7)	23 (16.4)	
	VLDA					
	Yes	11 (15.3)	0	0	0	0.252[c]
	No	17 (23.6)	12 (16.7)	17 (23.6)	15 (20.8)	
Placebo	MDA					
	Yes	7 (4.8)	0	0	0	0.392[c]
	No	4 (2.8)	14 (9.7)	50 (34.5)	70 (48.3)	
	VLDA					
	Yes	1 (1.4)	0	0	0	0.119[c]
	No	7 (10.1)	5 (7.2)	17 (24.6)	39 (56.5)	

All values are n (%), unless otherwise indicated.
[a]Kappa agreement between the numbers of patients across the disease activity categories of the RAPID-3 and the DAPSA.
[b]Kappa agreement between the numbers of patients in the remission + LowDA and ModDA + HighDA disease activity categories of the RAPID-3 and the DAPSA.
[c]Kappa agreement between the numbers of patients in the remission + LowDA and ModDA + HighDA disease activity categories of the RAPID-3 and achievement (yes/no) of 5 (MDA) or 7 of 7 (VLDA) criteria of minimal disease activity.
DAPSA disease activity states: remission, ≤4; LowDA, ≤14; ModDA, ≤28; HighDA, >28.
Minimal disease activity criteria: TJC ≤1; SJC ≤1; PASI ≤1; patient Pain ≤15; patient global ≤20; HAQ-DI ≤0.5; tender entheseal points ≤1.
RAPID-3, routine assessment of patient index data; DAPSA, disease activity index in psoriatic arthritis; MDA, minimal disease activity; LowDA, low disease activity; ModDA, moderate disease activity; HighDA, high disease activity; VLDA, very low disease activity.

design, data collection, analysis, interpretation, and abstract writing, review, and approval. Medical writing: Ben Wolfe of AbbVie.

Disclosure of Interest: P. Mease Grant/research support from: AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Consultant for: AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, Speakers bureau: AbbVie, Amgen, Bristol Myers, Celgene, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB, S. Chen Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., F. Ganz Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., W. Tillett Grant/research support from: AbbVie, Celgene, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Celgene, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Celgene, Novartis, Pfizer, and UCB

DOI: 10.1136/annrheumdis-2017-eular.1952

FRI0511 SECUKINUMAB DEMONSTRATES CONSISTENT SAFETY OVER LONG-TERM EXPOSURE IN PATIENTS WITH PSORIATIC ARTHRITIS AND MODERATE-TO-SEVERE PLAQUE PSORIASIS: UPDATED POOLED SAFETY ANALYSES

P.J. Mease[1], I.B. McInnes[2], K. Reich[3], P. Nash[4], M. Andersson[5], K. Abrams[6], L. Pricorp[6], T. Fox[5]. *[1]Swedish Medical Center and University of Washington, Seattle, United States; [2]University of Glasgow, Glasgow, United Kingdom; [3]Dermatologikum Hamburg and Georg-August-University Göttingen, Hamburg, Germany; [4]University of Queensland, St Lucia, Australia; [5]Novartis Pharma AG, Basel, Switzerland; [6]Novartis Pharmaceuticals Corp., East Hanover, United States*

Background: Pooled safety data from secukinumab psoriasis (PsO) and psoriatic arthritis (PsA) clinical trial programs after ~1 year of exposure have been reported.[1,2]

Objectives: To report updated longer-term secukinumab exposure safety data from PsO and PsA studies (data cut-off: 25 June 2016).

Methods: The PsO data pool consisted of 9 Phase III studies in moderate-to-severe plaque PsO and PsA pool consisted of 3 Phase III studies in active PsA. Secukinumab doses differed in the studies and included intravenous (up to 10 mg/kg) or subcutaneous (s.c.; 75–300 mg) loading, followed by s.c. maintenance dosing (300, 150 or 75 mg). Placebo patients were re-randomised to secukinumab at 12–24 weeks depending on study design. Only data for approved secukinumab 300 and 150mg doses were included in analysis. Exposure adjusted incident rates (EAIR) were used to adjust for differences in exposure.

Results: In both PsO and PsA, the most frequently reported adverse events (AEs) with secukinumab were non-serious infections of the upper respiratory tract, headache and arthralgia (Table). The EAIRs of AEs of special interest with secukinumab including Crohn's disease, *Candida* infections, serious infections, inflammatory bowel disease, major adverse cardiac events and neutropenia (reported in the Table) were similar in both PSO and PsA indications, and comparable to those reported previously.[1,2] No cases of tuberculosis (new onset or reactivation) were reported.

Table 1. Summary of pooled safety of secukinumab in PSO and PsA

	PSO Any secukinumab N=3893	PsA Any secukinumab N=1128
Total exposure, patient-years)	7769.0	1907.0
Min–max exposure (days)	1–1526	16–1464
Death, n (%)	7 (0.2)	4 (0.4)
AE's by EAIR: AE per 100 Pt-years (95% CI)		
Any AE	196.9 (190.3, 203.6)	173.7 (162.5, 185.5)
Any serious AE	7.2 (6.6, 7.8)	8.5 (7.2, 10.0)
Frequent AEs[1]		
Nasopharyngitis	18.2 (17.1, 19.3)	13.7 (12.0, 15.7)
Headache	6.3 (5.7, 6.9)	4.8 (3.9, 5.9)
Upper respiratory tract infections	6.2 (5.6, 6.8)	11.2 (9.6, 12.9)
Arthralgia	5.1 (4.6, 5.6)	4.3 (3.4, 5.3)
AEs of special interest		
Candida infections	2.1 (1.8, 2.4)	2.3 (1.6, 3.1)
Serious infections	1.4 (1.2, 1.7)	1.8 (1.3, 2.5)
Inflammatory Bowel Disease	0.3 (0.2, 0.4)	0.5 (0.2, 0.9)
Crohn's disease	0.1 (0.0, 0.1)	0
Ulcerative colitis	0.2 (0.1, 0.3)	0.1 (0.0, 0.4)
MACE	0.3 (0.2, 0.5)	0.3 (0.1, 0.6)
Neutropenia	0.4 (0.3, 0.5)	0.7 (0.4, 1.2)

[1] Adverse events in the secukinumab group that occurred with an IR >5.0 during the entire safety period in either of the spooled groups; AE, adverse event; EAIR, exposure adjusted incidence rate per 100 patient-years; MACE, major adverse cardiac event; N, number of patients in the analysis.

Conclusions: The safety profile of secukinumab was similar for PsO and PsA patients supporting its long-term use in these chronic conditions. Secukinumab long-term exposure safety data is consistent with that previously reported with shorter-term exposure, including being well tolerated, and without any new safety signals identified.

References:

[1] Van de Kerkhof PC, et al. J Am Acad Dermatol 2016;75:83–98.
[2] Mease PJ, et al. Arthritis Rheumatol 2015; 67:A2886.

Disclosure of Interest: P. Mease Grant/research support from: AbbVie, Amgen, Biogen Idec, BMS, Celgene, Crescendo, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, Biogen Idec, BMS, Celgene, Covagen, Crescendo, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Biogen Idec, BMS, Crescendo, Janssen, Lilly, Pfizer, and UCB, I. McInnes Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB, K. Reich Grant/research support from: AbbVie, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cliag, Leo, Lilly, Medac, Merck Sharp and Dohme Corp., Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB Pharma, Xenoport, Speakers bureau: AbbVie, Amgen, Biogen, Boehringer Ingelheim Pharma, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cliag, Leo, Lilly, Medac, Merck Sharp and Dohme Corp., Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB Pharma, Xenoport, P. Nash Grant/research support from: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Hospira, MSD, Pfizer, Janssen, UCB, Novartis, Roche; Consultancy fees: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Hospira, MSD, Pfizer, Janssen, UCB, Novartis, Roche, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Hospira, MSD, Pfizer, Janssen, UCB, Novartis, Roche, M. Andersson Employee of: Novartis, K. Abrams Shareholder of: Novartis, Employee of: Novartis, L. Pricorp Shareholder of: Novartis, Employee of: Novartis, T. Fox Shareholder of: Novartis, Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.4991

FRI0512 APREMILAST, AN ORAL PHOSPHODIESTERASE 4 INHIBITOR, IS ASSOCIATED WITH LONG-TERM (156-WEEK) IMPROVEMENTS IN BASDAI IN PSORIATIC ARTHRITIS PATIENTS: POOLED RESULTS FROM 3 PHASE III, RANDOMIZED, CONTROLLED TRIALS

P.J. Mease[1], H. Marzo-Ortega[2], A. Poder[3], F. Van den Bosch[4], J. Wollenhaupt[5], E. Lespessailles[6], M. McIlraith[7], L. Teng[7], S. Hall[8]. *[1]Swedish Medical Center and University of Washington School of Medicine, Seattle, United States; [2]NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals and University of Leeds, Leeds, United Kingdom; [3]Clinical Research Centre Ltd, Tartu, Estonia; [4]UZ Gent, Gent, Belgium; [5]Schön Klinik Hamburg Eilbek, Hamburg, Germany; [6]University of Orléans, Orléans, France; [7]Celgene Corporation, Summit, United States; [8]Monash University, CabriniHealth, Melbourne, Australia*

Background: In PALACE psoriatic arthritis (PsA) studies, the Bath Ankylosing Spondylitis Disease Activity Index score (BASDAI) was used as an exploratory measure in a subset of patients (pts) considered by investigators to have axial involvement, although PsA spondylitis was not confirmed by imaging.

Objectives: Report the impact of apremilast 30 mg BID (APR) treatment on BASDAI over 156 wks using pooled PALACE 1–3 data of pts with active PsA despite prior conventional DMARDs and/or biologics.

Methods: APR treatment outcomes were evaluated in a subset of pts with baseline (BL) BASDAI ≥4 ("subset") over 156 wks.
Results: BL BASDAI ≥4 was reported for 454/1493 (30%) pts. Mean PsA duration was similar between the subset and rest of the PALACE 1–3 population (n=1039); mean BL psoriasis body surface area (BSA) and percentage of pts with BSA ≥3% were slightly higher. The subset had higher mean BL values vs the rest of PALACE 1–3 pts for C-reactive protein (1.12 vs 0.93), pain VAS (63.6 vs 53.8 mm), pt's global assessment of disease activity (62.2 vs 53.5 mm), and physician's global assessment of disease activity (PhGA; 59.0 vs 53.0 mm) and markedly worse mean HAQ-DI (1.41 vs 1.08), SF-36v2 Physical Functioning (30.6 vs 35.8), and FACIT-F (25.7 vs 31.8) scores. Despite disease activity differences, BL concomitant oral DMARDs were similar in both groups: 1 DMARD in 61.0% (subset) vs 57.8% (rest of PALACE 1–3 pts); methotrexate was the most common DMARD. In the subset, 73.6% had been treated with only oral DMARDs prestudy (44.9% with only 1); 25.1% had prior biologic use. Mean BL BASDAI in the subset was 6.6 with APR and 6.4 with placebo (PBO). Mean BL BASDAI question 2 score, referring directly to spinal and hip pain, was 6.7. APR resulted in greater mean improvement in BASDAI vs PBO at Wk 16 (–1.53 vs –0.91; *P*=0.0173) and Wk 24 (Table). As early as Wk 16, a 19% mean decrease in the question 2 score was seen with APR vs an increase with PBO. Other disease measures significantly improved early in treatment, including HAQ-DI, fatigue, PhGA, and mPsARC (Table). Long-term improvement was seen across measures, with mean BASDAI reductions of 2.18 at Wk 52 and 2.19 at Wk 156 (Table) and question 2 reductions of 1.94 and 2.28, respectively; treatment resulted in a shift toward lower BASDAI across the subset, with a significant proportion reaching BASDAI <4.

Outcomes at Wk 24, Wk 52, and Wk 156 in Pts With BASDAI ≥4 at BL

	Wk 24		Wk 52	Wk 156
	APR n=156	PBO n=151	APR n=125	APR n=127
BASDAI, mean BL	6.6	6.4	6.6	6.6
BASDAI, mean change from BL	−1.64*	−0.74	−2.18	−2.19
Swollen joint count, mean change	−5.5*	−2.4	−8.5	−10.6
HAQ-DI, mean change	−0.301*	−0.117	−0.464	−0.448
SF-36v2 PF, mean change	4.98*	1.76	7.06	8.21
Pain VAS, mean change, mm	−12.6*	−7.9	−22.1	−21.9
FACIT-F, mean change	4.38*	1.29	6.77	6.31
Pt's global assessment of disease activity, mean change (VAS mm)	−10.9	−5.7	−19.8	−21.2
PhGA, mean change (VAS mm)	−22.1§	−7.4	−34.3	−40.2
Proportion meeting mPsARC, %	46.2§	23.8	77.9	84.1

The n may vary slightly for the end points at each time point. For Wk 24, the n represents the number of pts randomized at BL in the subset; last-observation-carried-forward methodology and non-responder imputation rule were applied to pts who early escaped at Wk 16 or had missing value at Wk 24 for continuous data and binary response, respectively. For Wk 52, the n represents the number of pts randomized to APR at BL in the subset, with an outcome measure at Wk 52. For Wk 156, the n represents the number of pts who were randomized to APR (at BL, Wk 16, or Wk 24), with an outcome measure at Wk 156.
*P<0.05; §P<0.0001 vs PBO, based on an analysis of covariance model for the change from BL, with treatment group, BL DMARD use (yes/no), and study as factors and BL value as the covariate, and the Cochran-Mantel-Haenszel test for binary response, adjusting for BL DMARD use and study. Pt's global assessment of disease activity APR 30 mg BID vs PBO at Wk 24: P=0.0590.
BASDAI=Bath Ankylosing Spondylitis Disease Activity Index score; APR=apremilast 30 mg BID; PBO=placebo; BL=baseline; HAQ-DI=Health Assessment Questionnaire-Disability Index score; SF-36v2 PF=36-item Short-Form Health Survey version 2 Physical Functioning domain score; VAS=visual analog scale; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue score; PhGA=physician's global assessment of disease activity; mPsARC=modified Psoriatic Arthritis Response Criteria; DMARD=disease-modifying anti-rheumatic drug.

Conclusions: In this post hoc analysis of pooled data, pts reporting BASDAI ≥4 at BL appear to experience greater disease burden, including disability, pain, and fatigue; effective treatment strategies may not have been available. APR treatment resulted in long-term improvements in BASDAI and other measures in pts with clinically suspected axial disease.
Disclosure of Interest: P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Consultant for: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Genentech, Janssen, Eli Lilly, Pfizer, UCB, H. Marzo-Ortega: None declared, A. Poder: None declared, F. Van den Bosch Consultant for: AbbVie, Celgene Corporation, Merck, Pfizer, UCB, Janssen, J. Wollenhaupt Grant/research support from: Abbott, BMS, MSD, Pfizer, UCB, Consultant for: Abbott, BMS, MSD, Pfizer, UCB, E. Lespessailles Grant/research support from: Amgen, Eli Lilly, Novartis, Servier, Speakers bureau: Amgen, Eli Lilly, Novartis, Servier, M. McIlraith Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, S. Hall Consultant for: Boehringer Ingelheim, MSD, Roche, Schering-Plough, Servier, Wyeth, Paid instructor for: Amgen, AstraZeneca, Boehringer Ingelheim, Centocor, GSK, MSD, Pfizer, Sanofi Aventis, Sanofi Pasteur, Schering-Plough, Serono, Wyeth, Speakers bureau: Boehringer Ingelheim, GSK, MSD, Pfizer, Roche, Sanofi Aventis, Schering-Plough, Wyeth
DOI: 10.1136/annrheumdis-2017-eular.3299

FRI0513 LONG-TERM (156 WEEKS) IMPROVEMENTS IN PHYSICAL FUNCTION OF DMARD-NAÏVE AND DMARD/BIOLOGIC-EXPERIENCED PSORIATIC ARTHRITIS PATIENTS TREATED WITH APREMILAST: DATA FROM A LARGE DATABASE OF 4 PHASE III CLINICAL TRIALS

P.J. Mease[1], A. Wells[2], J. Wollenhaupt[3], S. Hall[4], F. Van den Bosch[5], E. Lespessailles[6], M. McIlraith[7], D. Nguyen[7], L. Teng[7], C.J. Edwards[8].
[1]Swedish Medical Center and University of Washington School of Medicine, Seattle; [2]Rheumatology and Immunotherapy Center, Franklin, United States; [3]Schön Klinik Hamburg Eilbek, Hamburg, Germany; [4]Monash University, CabriniHealth, Melbourne, Australia; [5]UZ Gent, Gent, Belgium; [6]University of Orléans, Orléans, France; [7]Celgene Corporation, Summit, United States; [8]University Hospital Southampton, Southampton, United Kingdom

Background: Improving and preserving patient (pt) physical function is an important goal for psoriatic arthritis (PsA).
Objectives: To evaluate apremilast's (APR) effects on physical function/functional status for up to 3 yrs in DMARD/biologic-experienced (PALACE 1–3 [PAL1–3] pooled data) and DMARD-naive (PALACE 4 [PAL4]) pts with active PsA.
Methods: Pts were randomized (1:1:1) to placebo (PBO), APR 30 mg BID (APR30), or 20 mg BID (APR20) at baseline (BL). The primary endpoint was at Wk16; a long-term extension is ongoing. A detailed study design has been previously presented. Assessed were mean change from BL HAQ-DI scores and proportions of pts reaching HAQ-DI MCID and reaching scores ≤1.0 (below clinically significant disability), ≤0.5 (minimal disability), and ≤0.25 (general population). Wk16 data were analyzed by LOCF. Wk156 data are as observed. Mean change and MCID outcomes are for all pts receiving APR30 at any time during the study; disability level data are for pts randomized to APR30 at BL.
Results: PAL1–3 (biologic/DMARD-experienced) and PAL4 (DMARD-naïve) pts had similar BL SJC/TJC and DAS-28 (CRP), indicating active PsA. PAL1–3 pts had longer mean duration of PsA and psoriasis, higher PASI scores, and greater corticosteroid use at BL. Despite differences, BL physical disability was clinically significant in both populations (mean HAQ-DI, PAL1–3: 1.2; PAL4: 1.1). Marked disability at BL was seen in some pts randomized to APR30, with HAQ-DI scores up to 2.63–2.88. More PAL1–3 vs PAL4 APR30 pts had BL HAQ-DI >1.0 (60% vs 54%), >1.5 (marked difficulty/need for assistive devices, 31%vs 21%), and >1.75 (major disability, 19% vs 10%), highlighting need for early, effective treatment (tx). Few APR30 pts had BL scores ≤0.5 (18–22%) or ≤0.25 (10–14%). At Wk16, physical function significantly improved with APR30 vs PBO (mean HAQ-DI change, PAL1–3: –0.23 vs –0.08; PAL4: –0.21 vs 0.03; both P<0.0001) and more APR30 vs PBO pts reached HAQ-DI MCID ≥0.30 and ≥0.35. As early as Wk16, overall disability levels also shifted; more APR30 vs PBO pts achieved HAQ-DI ≤1.0 (PAL1–3: 56% vs 48%; PAL4: 60% vs 52%). At Wk156, marked achievement of HAQ-DI ≤1.0, ≤0.5, and ≤0.25 was observed in both populations (Table). LOCF analyses confirmed Wk156 results.

Pts Achieving Improvement in Physical Function by HAQ-DI Level at Wk156*

	PAL1-3	PAL4
Pts Achieving HAQ-DI Disability Threshold, %	**APR30 n=279§**	**APR30 n=94§**
≤1.0[1]	62	65
≤0.5[2]	38	45
≤0.25	28	42
Pts Achieving HAQ-DI MCID Levels, %	**APR30 n=413‡**	**APR30 n=143‡**
≥0.30[3]‖	48	48
≥0.35[4]¶	48	48

HAQ-DI ≤1.0=disability not clinically significant; HAQ-DI ≤0.5=disability remission. HAQ-DI=Health Assessment Questionnaire-Disability Index; MCID=minimal clinically important difference.
*Wk156 data are based on data as observed. §Analysis in pts randomized to APR30 from BL. ‡Analysis in pts randomized to APR30 at any time (BL, Wk16, or Wk24). †Accepted threshold for HAQ-DI MCID in PsA at time of initiation of studies.[3] ¶Currently accepted threshold based on updated research.[4]
1. Sokka T, et al. *Arthritis Rheum.* 2003;48:59-63. 2. Coates LC, et al. *Ann Rheum Dis.* 2010;69:48-53. 3. Mease PJ, et al. *Ann Rheum Dis.* 2004;63(Suppl 1):391. 4. Mease PJ, et al. *J Rheumatol.* 2011;38:2461-2465.

Conclusions: With APR30 tx, physical disability improved early; functionality was maintained for up to 3 yrs. Most pts achieved HAQ-DI ≤1.0; many attained minimal/mild physical impairment. Over 40% of pts receiving APR30 earlier in the tx paradigm had functional ability similar to population norms after 3 yrs; shorter disease duration and no prior DMARD/biologics use in this population suggests that earlier APR tx may increase the likelihood of maximal functionality for some pts.
Disclosure of Interest: P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Consultant for: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Genentech, Janssen, Eli Lilly, Pfizer, UCB, A. Wells Grant/research support from: Celgene Corporation, J. Wollenhaupt Grant/research support from: Abbott, BMS, MSD, Pfizer, UCB, Consultant for: Abbott, BMS, MSD, Pfizer, UCB, S. Hall Consultant for: Boehringer Ingelheim, MSD, Roche, Schering-Plough, Servier, Wyeth, Paid instructor for: Amgen, AstraZeneca, Boehringer Ingelheim, Centocor, GSK, MSD, Pfizer, Sanofi Aventis, Sanofi Pasteur, Schering-Plough, Serono, Wyeth, Speakers bureau: Boehringer Ingelheim, GSK, MSD, Pfizer, Roche, Sanofi Aventis, Schering-Plough, Wyeth,

F. Van den Bosch Consultant for: AbbVie, Celgene Corporation, Merck, Pfizer, UCB, Janssen, E. Lespessailles Grant/research support from: Amgen, Eli Lilly, Novartis, Servier, Speakers bureau: Amgen, Eli Lilly, Novartis, Servier, M. McIlraith Employee of: Celgene Corporation, D. Nguyen Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, C. Edwards Grant/research support from: Celgene Corporation, Pfizer, Roche, Samsung, Consultant for: Celgene Corporation, Pfizer, Roche, Samsung, Speakers bureau: Abbott, GSK, Pfizer, Roche

DOI: 10.1136/annrheumdis-2017-eular.3019

FRI0514 PSORIATIC ARTHRITIS IS ASSOCIATED WITH DIAGNOSTIC DELAY AND WORSE OUTCOME AT THREE MONTHS WHEN COMPARED TO RHEUMATOID ARTHRITIS: RESULTS FROM THE UK NATIONAL AUDIT FOR INFLAMMATORY ARTHRITIS

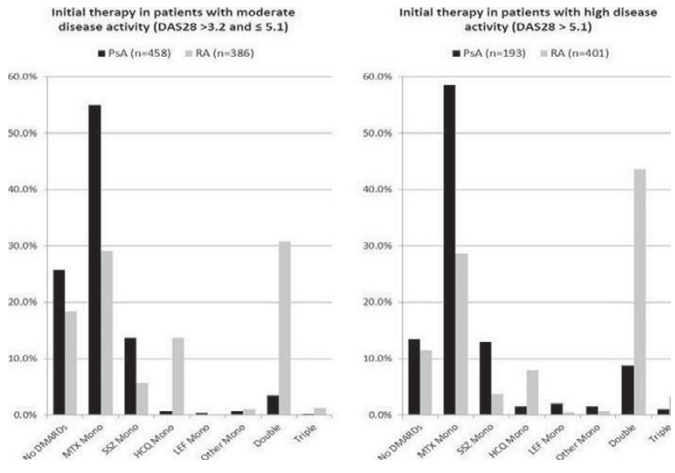
R. Holland[1], A. Davis[2], A. Green[2], A. Nightingale[2], R. Charlton[2], E. Cullen[3], N. McHugh[1]. *[1]Royal National Hospital for Rheumatic Diseases; [2]University of Bath, Bath; [3]Celgene Ltd, London, United Kingdom*

Background: Psoriatic arthritis (PsA) is underdiagnosed in primary care, and can be difficult to distinguish from osteoarthritis. Accumulating evidence suggests that diagnostic delay is associated with poorer functional outcome despite treatment.
Objectives: To develop a better understanding of the diagnostic delay and burden of disease in patients with PsA, and to investigate management within the first three months of diagnosis.
Methods: Data were analysed on all participants with a final diagnosis of PsA from The National Clinical Audit for Rheumatoid and Early Inflammatory Arthritis, undertaken by the British Society for Rheumatology and commissioned by the Healthcare Quality Improvement Programme, recruited between 1/2/2014 and 30/10/2015. Data were collected from patients and clinicians at baseline and three months. 1016 participants with PsA (mean age 49.4±14.5 years; 54% female) were matched 1:1 by age and sex with participants with Rheumatoid Arthritis (RA).
Results: Patients with PsA had a significantly longer delay to presentation and diagnosis than those with RA ($p<0.02$, Table 1), and this remained significant when adjusted for age, sex, ethnicity and social status.
PsA patients had lower median tender (4.0 vs 7.0) and swollen (3.0 vs 5.0) joint counts and lower mean baseline ESR (21.9 vs 27.8 mm/hr) and CRP (16.2 vs 24.2 mg/L) values than patients with RA ($p<0.01$ for all comparisons), and this remained significant when adjusted for potential confounders. Mean baseline scores for the Inflammatory Arthritis Impact of Disease (IAID) questionnaire were lower in patients with PsA (5.34±2.25 vs 5.94±2.35 in RA, lower scores indicating less impact), although this was not statistically significant when adjusted for demographics and disease activity (p=0.36). There was no significant difference between physical function at baseline between the groups (median HAQ 0.88 PsA vs 1.13 RA, p=0.70).
At follow-up, patients with PsA had significantly higher mean IAID scores (4.32±2.60 vs 3.78±2.56, $P<0.05$). In those with paired results, the mean improvement in IAID score was 1.32 (95% CI 0.99–1.65) in PsA vs 2.37 (95% CI 2.07–2.67) in RA. In patients with high disease activity at baseline (DAS28 >5.1) a good EULAR response was seen in only 21.4% in PsA vs 30.3% in RA. There was a marked difference in the DMARDs initially prescribed, and the differences remained significant when only those with a DAS28 score indicating moderate or high disease activity at presentation were analysed, as shown in Figure 1.
Conclusions: This study demonstrates that patients with PsA have a longer delay to diagnosis between both symptom onset and presentation to primary care, and referral to secondary care and diagnosis than those with RA. Despite similar disease impact and physical function at diagnosis, patients with PsA are less likely to receive combination DMARD treatment, and have increased disease burden at three months.

Table 1. Median delay in weeks

	PsA		RA	
	Unadjusted	Adjusted*	Unadjusted	Adjusted*
Symptoms to GP Presentation	8.9	8.9	7.1	6.6
GP Presentation to Referral	5.3	5.4	4.3	4
GP Presentation to Diagnosis	12.4	12.1	9.9	9.7
Symptoms to Diagnosis	29.0	28.6	21.4	21.6

*Adjusted for age, sex, ethnicity and deprivation Index; $p<0.02$ for all between group comparisons.



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5066

FRI0515 CLASSIC CARDIOVASCULAR RISK FACTORS AND MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS: RESULTS OF A SPANISH MULTICENTER STUDY

R. Queiro[1], J.D. Cañete[2], C. Montilla[3], M.A. Abad[3], M. Montoro[3], S. Gómez[3], A. Cábez[3], J.C. Torre Alonso[3], J.A. Román Ivorra[3], J. Sanz[3], J. Salvatierra[3], J. Calvo Alén[3], A. Sellas[3], F.J. Rodriguez[3], A. Bermúdez[3], M. Romero[3], M. Riesco[3], J.C. Cobeta[3], F. Medina[3], A. Aragón[3], M.L. García[3], A. Urruticoechea[3]. *[1]Rheumatology, Hospital Universitario Central de Asturias, Oviedo; [2]Rheumatology, HU, Clinic and IDIBAPS, Barcelona, Spain; [3]Affiliation not provided*

Background: Some cardiovascular risk factors (CVRF) have been related to poorer responses to biological therapy[1]. We aimed to evaluate the potential link between the MDA response and the presence of CVRF in patients treated with traditional and/or biological DMARDs.
Objectives: The objective has been to evaluate the potential association between classic CVRF and the probability of reaching an MDA response in PsA patients.
Methods: Cross-sectional study carried out at 25 rheumatology outpatient clinics in patients who fulfilled the Classification for Psoriatic Arthritis (CASPAR) criteria with at least one year disease duration, and treated with biological or conventional synthetic (cs) DMARDs according to routine clinical practice in Spain. Patients were considered in MDA if they met at least 5/7 of the MDA criteria[2]. The relationship between MDA and CVRF was evaluated by uni and multivariate analyses.
Results: 227 patients were included, 133 (58.6%) were in MDA state (52% on anti-TNFα monotherapy, 24% on csDMARD monotherapy, 24% on anti-TNFα in combination with csDMARD). Among the classic CVRF, tobacco (crude OR: 0.54), sedentary lifestyle (crude OR: 1.95), hyperuricemia (crude OR: 2.01) and obesity (crude OR: 1.54) were related to the likelihood of MDA in the univariate model ($p<0.25$). The only CVRF related to the MDA response in the multivariate analysis was a sedentary lifestyle (OR 3.13, 95% CI: 1.50–6.53; p=0.002). We did not find any association between the number of CVRF and the MDA response.
Conclusions: Contrary to what has been found in other studies, in this cross-sectional multicenter study we could not find any relationship between traditional CVRF (except for sedentary lifestyle) and MDA. In any case, patients with psoriatic disease should be encouraged to maintain healthy lifestyle habits.
References:
[1] Ogdie A, Eder L. Improving cardiovascular health and metabolic comorbidities in patients with psoriatic arthritis. Int J Clin Rheumatol 2015; 10(6):451–459.
[2] Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis 2010; 69(1):48–53.
Acknowledgements: This study was funded by Pfizer.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4083

FRI0516 ASSESSMENT OF DISEASE REMISSION BY POWER DOPPLER ULTRASONOGRAPHY IN PATIENTS WITH PSORIATIC ARTHRITIS

S. Monov[1], R. Shumnalieva[1], D. Monova[2], A. Kopchev[1]. *[1]Department of Internal Medicine, Clinic of rheumatology, Medical University - Sofia; [2]Medical Institute-MVR, Medical University-Sofia, Sofia, Bulgaria*

Background: Treatment strategies nowadays are targeting clinical remission or low disease activity. In some patients with psoriatic arthritis (PsA) clinical findings defer from the ultrasonographic evidence of inflammation which raise the need for revising the remission criteria in the clinical practice.
Objectives: The aim of our study was to estimate the presence of subclinical synovitis by power Doppler ultrasonography (PDUS) in PsA patients, who were considered as being in clinical remission defined by DAS28-ESR (Disease activity score of 28 joints – erythrocyte sedimentation rate) for at least 6 months during the treatment course.
Methods: 64 PsA patients in clinical remission based on DAS28 – ESR <2.6 were included in the study. The patients were examined by two independent rheumatologists. The affected joints were assessed by PDUS (MyLab 60, Esaote) for the presence of synovial hypertrophy (SH) and synovitis scored from 0 to 3 based on the presence and intensity of PD signal. Disease activity was determined by the presence of SH ≥2 degree and a positive PD signal.
Results: We found a persistent synovitis in 23 (35.9%) of the PsA with clinical remission of the peripheral joint involvement. Active synovitis was also found in 7

(10.9%) of the patients with DAS28 <2.6 which were on systemic corticosteroid (CS) treatment regimen.
Conclusions: The presence of active synovitis on PDUS in a significant part of the studied PsA patients (35.9%) which were considered as being in clinical remission for at least 6 months showed that these kind of patients need to be closely followed-up and adequately treated. The systemic CS treatment does not exclude the presence of disease activity in PsA. Further studies for assessment of the synovitis will establish correct criteria for defining and monitoring the disease activity in PsA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6634

FRI0517 QUALITY OF LIFE IN PATIENTS WITH EARLY PSORIATIC ARTHRITIS

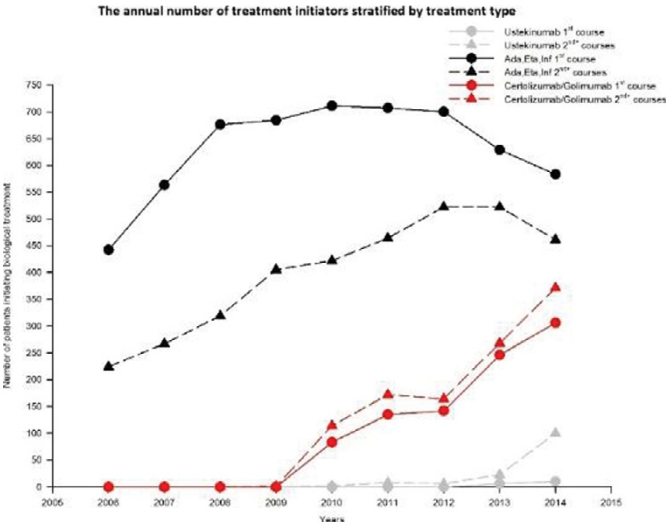
S. Monov, A. Kopchev. *Clinic of Rheumatology, Department of Internal Medicine, Medical University, Sofia, Sofia, Bulgaria*

Background: Psoriatic arthritis (PsA) is a chronic systemic inflammatory disease. Affecting skin, joints, entheses and dactylitis, its impact on health-related quality-of-life (HRQoL) could be substantial.
Objectives: The aim of this study was to describe HRQoL in newly diagnosed PsA patients taking into account skin involvement, swollen joints, tender enthuses and dactylitis.
Methods: HRQoL was assessed by 8 subscales of the Short-Form 36 (SF-36) questionnaire (0–100, higher score represents a better HRQoL). Patients were classified in arthritis subtypes (i.e. mono-, oligo- or polyarthritis) by rheumatologist. Entheses were evaluated using the Leeds Enthesitis Index (LEI) and Maastricht Ankylosing Spondylitis Enthesitis Score (MASES; positive if tender entheses >1). Psoriasis was evaluated using the Psoriasis Area Severity Index (PASI; mild: 0–7; moderate/severe: >7) and dactylitis using the Leeds Dactylitis Index (LDI).
Results: 87 patients (48 male, 39 female, mean age 47,6±15,3) with PsA (21 had monoarthritis, 49 - oligoarthrit and 17 - polyarthritis) completed the SF-36 were included in the study. Psoriasis was mild in 63 (72,41%) patients and moderate/severe in 12 (13,79%) patiients. At least one digit with dactylitis was present in 10 (11,49%) of the patients. A tender enthesis was present in 39 (44,83%) of patients. Mean scores of the subdomains in the SF-36 were similar across the different arthritis groups, with slightly worse scores for polyarthritis compared to mono- and oligoarthritis. However, when stratifying these groups for the presence of a tender enthesis, HRQoL decreased substantially for all groups across all subdomains of the SF-36, with a median difference of 12,9 points. Irrespective of joint involvement, a tender enthesis decreased the mean scores of all subdomains significantly compared to the non-tender enthesis group ($p<0,05$). Severity of psoriasis and presence of dactylitis did not lead to significantly different SF-36 values compared to those not affected.
Conclusions: Having tender entheses impacts HRQoL severly in both its physical and mental dimensions in incident untreated PsA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6603

FRI0518 PRESCRIPTION PATTERNS OF TUMOUR NECROSIS FACTOR INHIBITOR AND USTEKINUMAB IN PSORIATIC ARTHRITIS: A NORDIC POPULATION-BASED COHORT STUDY

T.S. Jørgensen[1], L. Dreyer[1], B. Guðbjörnsson[2], M.L. Hetland[1], B. Glintborg[1], J. Askling[3], K. Chatzidionysiou[3], D. Di Giuseppe[3], L. Jacobsson[3], J.K. Wallman[3], E.K. Kristianslund[4], I.C. Olsen[4], K. Fagerli[4], E. Lie[4], D. Nordström[5], K. Aaltonen[5], J. Joensuu[5], T.J. Love[2], A.J. Geirsson[2], L.E. Kristensen[1]. *[1]On behalf of the DANBIO registry, Copenhagen, Denmark; [2]On behalf of the ICEBIO registry, Reykjavik, Iceland; [3]On behalf of the SRQ registry, Stockholm, Sweden; [4]On behalf of the NOR-DMARD registry, Oslo, Norway; [5]On behalf of the ROB-FIN registry, Helsinki, Finland*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory disorder associated with skin and joint manifestations, several extra-articular symptoms, various comorbidities, and disability. The emergence of tumour necrosis factor inhibitor (TNFi) therapy has dramatically changed the course of disease. Over the past decade new TNFi therapies have emerged (certolizumab pegol and golimumab), and recently ustekinumab and secukinumab have also become available for PsA.
Objectives: The objective of this study was to assess the relative use of biological agents (bDMARDs) in PsA from 2006 through 2014, using data from the Nordic Rheumatology registers.
Methods: Based on data from the observational registers DANBIO, ICEBIO, NOR-DMARD, ROB-FIN, and SRQ registers, PsA patients initiating treatment with bDMARDs as a first or subsequent biological therapy were identified. Adalimumab, etanercept and infliximab were grouped as “first generation TNFi therapies”; certolizumab pegol and golimumab were grouped as “second generation TNFi”. Treatments with ustekinumab during the study period were also identified. Descriptive statistics for prescription patterns of bDMARD therapy were calculated.
Results: A total of 11,458 treatment initiations were identified (DANBIO 3,068, ICEBIO 357, NOR-DMARD 1,113, ROB-FIN 708, SRQ 6,212). 54% of the patients were female. Overall, 5,695 patients initiated a first generation TNFi, 912 a second generation TNFi, and 16 ustekinumab, as their first course of biological treatment. The corresponding numbers for those initiating a second (or more) biological treatment were 3,606, 1,090 and 139 patients, respectively. The figure displays the annual number of treatment initiations stratified by treatment type. The total yearly number of first course biological treatment increased significantly throughout the period ($p<0.001$), and this was also the case for patients switching therapy ($p<0.001$), indicating a previously unmet need for biological therapies in the Nordic population. The annual number of patients initiating first generation TNFi both as first and subsequent course of therapy decreased significantly towards the end of the study period ($p<0.001$). This drop was more than offset by a rapid increase in initiation of second generation TNFi treatments ($p<0.001$). Ustekinumab was primarily used as second or subsequent course of therapy in PsA. The same pattern was seen when stratified for country (data not shown).



Conclusions: Across the Nordic countries the prescription pattern for biological therapies for PsA has changed significantly over time. After 2012 initiation of the first generation TNFi is decreasing both as first and second course therapy, whereas second generation TNFi are increasing both as first and second course of biologic intervention. Collaboration across registers will allow for robust assessment of the uptake of newer biological therapies.
Acknowledgements: This study was partly funded by a grant from NordForsk and Janssen Pharmaceuticals.
Disclosure of Interest: T. S. Jørgensen Speakers bureau: Abbvie, Roche, Novartis, UCB, Biogen, L. Dreyer Speakers bureau: MSD, UCB and Janssen Pharmaceuticals, B. Guðbjörnsson Speakers bureau: Actavis, Celgene, MSD, Pfizer, M. Hetland Speakers bureau: BMS, MSD, AbbVie, Roche, Eli Lilly, Pfizer, Orion, Novartis, B. Glintborg Speakers bureau: Abbvie, J. Askling Grant/research support from: AstraZeneca, UCB, Lilly, Pfizer, Roche, Merck,Samsung, Janssen, K. Chatzidionysiou Speakers bureau: AbbVie, Pfizer, Eli Lilly, UCB, Roche., D. Di Giuseppe: None declared, L. Jacobsson Consultant for: Abbvie, Celegen, MSD, Novartis and UCB, J. Wallman Consultant for: Novartis, Celgene, UCB, E. Kristianslund: None declared, I. Olsen: None declared, K. Fagerli: None declared, E. Lie Speakers bureau: AbbVie, Celgene, Hospira and Pfizer., D. Nordström Speakers bureau: AbbVie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, UCB., K. Aaltonen: None declared, J. Joensuu Speakers bureau: Pfizer., T. J. Love: None declared, A. J. Geirsson: None declared, L. E. Kristensen Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, MSD,
DOI: 10.1136/annrheumdis-2017-eular.4690

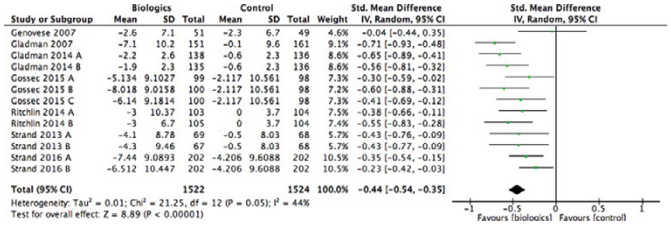
FRI0519 EFFECT OF BIOLOGICS ON FATIGUE IN PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW WITH META-ANALYSIS

T. Reygaerts[1,2], S. Mitrovic[1], B. Fautrel[1], L. Gossec[1]. *[1]Service de Rhumatologie, Pitie-Salpétrière Hospital, Paris, France; [2]Service de Rhumatologie et de Médecine Physique, Erasme Hospital, Bruxelles, Belgium*

Background: Fatigue is an important aspect of disease both in rheumatoid arthritis (RA) and in psoriatic arthritis (PsA) and is of high priority for patients. In RA, a recent Cochrane meta-analysis found a small effect of biologics on fatigue (standardized mean difference, SMD, 0.43; 95% confidence interval, CI: 0.38–0.49).(1) Little is known about this effect in PsA.
Objectives: To assess the effect of biologics on fatigue in PsA randomised controlled trials (RCTs) and to compare this effect with the effect in the same trials, on pain, through a systematic literature review (SLR) and meta-analysis (MA).
Methods: SLR up to January 2017 in PubMed, Embase and Cochrane trials database and in recent congress abstracts, using key words related to PsA and biologics. All RCTs in PsA of any biologic therapy, assessing fatigue (whatever the

score used), with data available for fatigue were included. Data were collected by 2 regarding levels of fatigue (6 trials used FACIT, 1 VAS) and pain (if available) at baseline and at the timepoint closest to 24 weeks after the biologic introduction. A MA was performed using RevMan and SMDs were calculated for each trial and each study dose, for fatigue and for pain. A SMD <0.5 is usually considered small, between 0.5 and 0.8 moderate and >0.8 as important.

Results: After screening 295 publications, 7 RCTs were included in the meta-analysis and assessed TNF blockers (N=3: adalimumab N=2, certolizumab pegol, N=1), secukinumab (N=2), apremilast (N=1) and ustekinumab (N=1) with or without methotrexate, compared to placebo. The studies included 2340 PsA patients: weighted mean age ± standard deviation (SD), 48.7±1.3 years, disease duration 7.7±1.3 years, 53.3% were females. At baseline, joint disease activity was high (weighted mean swollen joint count: 13.0±3.1, HAQ-DI: 1.2±0.1, PASI: 10.4±3.3). Fatigue levels were high at baseline (weighted mean FACIT score: 29.2±1.5). The pooled SMD for fatigue was 0.44 (95% CI -0.35, 0.54) and it ranged 0.04 to 0.71 across drugs and trials with a small to moderate effect (Graph). In 6 of the same studies, the pooled SMD for pain was 0.62 (95% CI 0.52, 0.73) and ranged 0.46 to 0.84.



Conclusions: Biologics had a mild to moderate effect on fatigue at 24 weeks in PsA RCTs. No notable differences across drugs were apparent. Effect sizes were higher on pain with a moderate effect. This effect seems similar to effects noted in RA in the Cochrane meta-analysis (1).These results confirm fatigue may be multifactorial in PsA; biologics bring some improvement at the group level but other treatment modalities should be further explored also.

References:

[1] Almeida C, Choy EHS, He wlett S, Kirwan JR, Cramp F, Chalder T, Pollock J, Christensen R. Biologic interventions for fatigue in rheumatoid arthritis. Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No. CD008334. DOI:10.1002/14651858.CD008334.pub2.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4680

FRI0520 IMPROVED PATIENT-REPORTED OUTCOMES IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH ABATACEPT: RESULTS FROM A PHASE III TRIAL

V. Strand[1], E. Alemao[2], T. Lehman[2], A. Johnsen[2], S. Banerjee[2], H. Ahmad[2], P. Mease[3]. *[1]Stanford University, Stanford; [2]Bristol-Myers Squibb, Princeton; [3]Swedish Medical Center and University of Washington, Seattle, United States*

Background: In the Phase III ASTRAEA study (NCT01860976), abatacept (ABA) significantly increased ACR20 responses, with benefits on other musculoskeletal symptoms in patients (pts) with active psoriatic arthritis (PsA).[1] As PsA impacts HRQoL, assessing treatment (tmt) effect using patient-reported outcomes (PROs) is important.

Objectives: To explore the effect of ABA tmt using PROs in intent-to-treat and *post hoc* analyses of ASTRAEA.

Methods: Pts were randomized (1:1) to SC ABA 125 mg weekly or placebo (PBO) for 24 weeks (W). At W16, pts without ≥20% improvement in joint counts started open-label ABA. Adjusted mean changes from baseline (BL) to W16 (all pts) and W24 (responder analysis) in Short Form-36 (SF-36; physical and mental component summary [PCS, MCS] and individual domains using spydergrams), pain VAS and HAQ-DI scores, Dermatology QoL Index (DLQI) and FACIT-Fatigue scale (FACIT-F) were evaluated in the total population and subgroups stratified by BL CRP level and prior TNFi use. Proportions of pts reporting improvements ≥minimal clinically important difference (MCID) in SF-36 summary (≥2.5) and domain (≥5.0), FACIT-F (≥40) and HAQ-DI (<–0.22) scores and ≥normative values in SF-36 summary (≥50) and domains, FACIT-F (<40) and HAQ-DI (<0.5) at W16 were analysed in the total population.

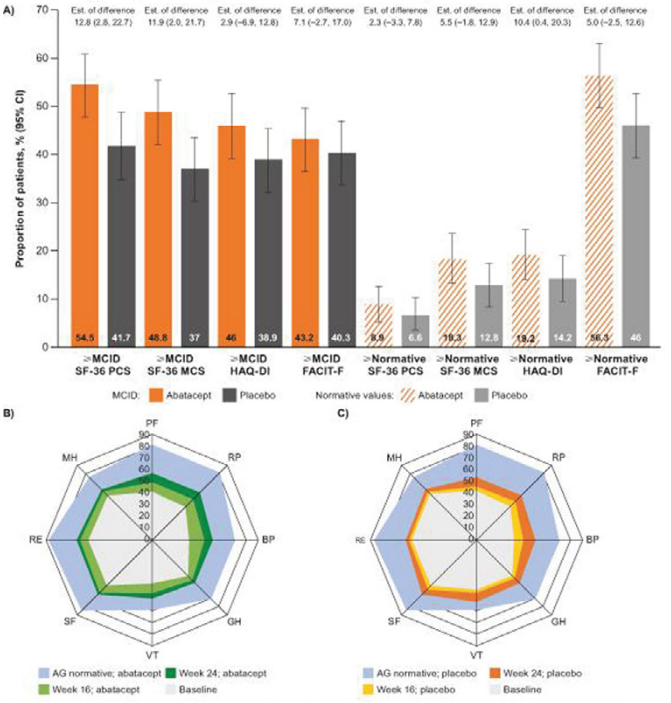
Results: In the total population, improvements in all PROs were numerically greater for ABA (n=213) vs PBO (n=211) at W16 and W24 and significant for SF-36 PCS at W16 and HAQ-DI at W24 (Table). At W16, improvements in all SF-36 domains were numerically greater with ABA, and significant for physical function, bodily pain and vitality. A higher proportion of pts receiving ABA vs PBO reported improvements ≥MCID in SF-36 PCS, MCS, SF-36 domains, FACIT-F, HAQ-DI (Fig) and DLQI (not shown) at W16. The proportion of pts whose scores were ≥normative values at W16 was higher with ABA vs PBO in SF-36 PCS, MCS, FACIT-F and HAQ-DI scores. At W24, improvements in SF-36 domain scores accrued in both groups, with numerical differences in favour of ABA except in social function. Improvements in PROs were greater with ABA tmt in BL CRP>upper limit of normal (ULN) vs CRP≤ULN and in TNFi-naïve vs -exposed subpopulations.

Table 1. Change from Baseline in PROs at 16 and 24 Weeks

PRO	Week 16 (total population)		Week 24 (responder analysis)	
	Abatacept	Placebo	Abatacept	Placebo
SF-36	*n=202*	*n=186*	*n=124*	*n=97*
PCS	3.76 (0.55)*	2.02 (0.57)	5.11 (0.64)	3.69 (0.71)
MCS	2.42 (0.70)	1.15 (0.73)	2.56 (0.83)	2.62 (0.92)
HAQ-DI	*n=202*	*n=187*	*n=124*	*n=98*
	–0.25 (0.04)	–0.15 (0.04)	–0.33 (0.04)*	–0.20 (0.05)
DLQI	*n=212*	*n=189*	*n=126*	*n=98*
	–2.28 (0.34)*	–1.24 (0.35)	–2.49 (0.42)*	–0.71 (0.48)
FACIT-F	*n=202*	*n=189*	*n=126*	*n=99*
	–3.67 (0.65)	–2.61 (0.67)	–4.58 (0.80)	–4.49 (0.89)

Data are adjusted mean change (SE). *95% CI of difference vs placebo did not cross 0.

Figure. Percentage of Patients Reporting Improvements ≥MCID or ≥Normative Values on PROs at Week 16 (A) and SF-36 Domain Scores at Baseline, Week 16 and Week 24 for Abatacept (B) and Placebo (C) Groups Versus Age/Gender Matched Normative Population



AG=age/gender; BP=bodily pain; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue scale; GH=general health; MCID=minimal clinically important difference; MCS=mental component summary; MH=mental health; PCS=physical component summary; PF=physical function; RE=role emotional; RP=role physical; SF=social function; SF-36=Short-Form 36; VT=vitality

Conclusions: Abatacept treatment improved many PROs in pts with active PsA, with larger benefits in the CRP>ULN and TNF-naïve subpopulations.

References:

[1] Mease P, et al. Arthritis Rheumatol 2016;68(suppl 10): [Abstract 1041].

Disclosure of Interest: V. Strand Consultant for: AbbVie, Amgen Corporation, AstraZeneca, Biogen Idec, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Celltrion, Corrona, Crescendo/Myriad Genetics, EMD Serono, Genentech/Roche, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, T. Lehman Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, A. Johnsen Employee of: Bristol-Myers Squibb, S. Banerjee Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, H. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, P. Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo Bioscience, Genentech, Janssen, Novartis, Pfizer, UCB

DOI: 10.1136/annrheumdis-2017-eular.1620

FRI0521 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN WORK PRODUCTIVITY AND HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: 2-YEAR RESULTS FROM FUTURE 1 AND FUTURE 2

V. Strand[1], O. FitzGerald[2], L.C. Coates[3], J.A. Walsh[4], J.D. Cañete[5], V. Bhosekar[6], L. Pricop[7], K. Gandhi[7], S. Jugl[8]. *[1]Stanford University School of Medicine, Palo Alto, CA, United States; [2]St. Vincent's University Hospital, Dublin, Ireland; [3]University of Leeds, Leeds, United Kingdom; [4]University of Utah, Salt Lake City, United States; [5]Hospital Clinic de Barcelona e IDIBAPS, Barcelona, Spain; [6]Novartis Healthcare, Hyderabad, India; [7]Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States; [8]Novartis Pharma AG, Basel, Switzerland*

Background: Patients (pts) with PsA experience significant impairment of work productivity (WP) and health-related QoL (HRQoL). Secukinumab (SEC) has previously been shown to rapidly improve symptoms, physical function and HRQoL in pts with active PsA.[1,2]

Objectives: To assess the impact of SEC on WP and HRQoL through 2 years (yrs) in TNF inhibitor (TNF)-naïve PsA pts and those with an inadequate response or intolerance to TNF inhibitors (TNF-IR).

Methods: 606 and 397 pts were randomized to SEC or placebo (PBO) in FUTURE 1 (10 mg/kg IV followed by 150 or 75 mg SC) and FUTURE 2 (300, 150 or 75 mg SC), respectively. PBO pts were re-randomized to SEC at Wk 16/24. WP was assessed using the WP and Activity Impairment–General Health (WPAI-GH) questionnaire. WPAI-GH includes 6 questions to measure absenteeism, presenteeism, work productivity and impairments in unpaid activity because of health problems during the preceding 7 days. HRQoL was assessed using the PsAQoL questionnaire, encompassing 20 statements that pts rate as true or false on the day of completion. Across both trials, approximately 68% of pts were TNF-naïve and 32% were TNF-IR. Observed data are presented from the full analysis set and in subgroups stratified by prior TNF exposure. Only data with approved doses of SEC (300 and 150 mg) are shown.

Results: In FUTURE 1, 88 of 202 in the SEC 150 mg group were employed and working at baseline (BL); 61 of 100 and 59 of 100 were employed and working at BL in the SEC 300 mg and 150 mg groups of FUTURE 2, respectively. Improvements in all elements of WPAI were reported with SEC 300 and 150 mg in the overall population at Wk 16; responses were sustained through Wk 104 (Table). The greatest improvements were seen in presenteeism (–10.0), work productivity (–10.3) and activity impairment (–14.1), which corresponded to improvements from BL of approximately 29%, 26% and 30%, respectively in the overall population of FUTURE 1 at Wk 104; similar improvements were seen in FUTURE 2 at Wk 104 (300 mg: –14.4 [42%], –11.2 [33%] and –17.7 [38%]; 150 mg: –16.8 [50%], –16.8 [45%] and –18.5 [38%]). Sustained improvements in all elements of WPAI were also evident with SEC in TNF-naïve and TNF-IR pts in both FUTURE 1 and FUTURE 2. Improvements in PsAQoL were reported as early as Wk 4 and sustained through Wk 104. At Wk 104 of FUTURE 2, PsAQoL scores had improved by approximately 46% from BL with SEC 300 mg and 49% with SEC 150 mg in the overall population. Similar improvements were seen in TNF-naïve (47% and 51%, respectively) and TNF-IR pts (45% and 45%, respectively). Consistent results were reported in FUTURE 1. The efficacy of SEC was consistent regardless of concomitant MTX use.

Conclusions: SEC provided sustained improvements in WP and PsAQoL in pts with PsA for up to 104 wks, regardless of prior TNF exposure.

Table. WPAI-GH and PsAQoL outcomes in FUTURE 1 and FUTURE 2 through Week 104

	FUTURE 1			FUTURE 2					
	Overall	TNF-naive	TNF-IR	Overall		TNF-naive		TNF-IR	
	SEC IV-150 mg	SEC IV-150 mg	SEC IV-150 mg	SEC 300 mg	SEC 150 mg	SEC 300 mg	SEC 150 mg	SEC 300 mg	SEC 150 mg
WPAI GH[a] (change from BL)									
Absenteeism (% work time missed due to health)[b]									
Wk 52	–4.0 (n=77)	–5.9 (n=59)	2.3 (n=18)	–2.3 (n=48)	–8.2 (n=51)	–3.4 (n=37)	–7.8 (n=34)	1.3 (n=11)	–8.9 (n=17)
Wk 104	–2.9 (n=58)	–2.4 (n=46)	–4.9 (n=12)	–0.4 (n=45)	–6.8 (n=41)	–1.1 (n=34)	–6.8 (n=30)	1.5 (n=11)	–6.7 (n=11)
Presenteeism (% impairment while working due to health)[b]									
Wk 52	–13.4 (n=73)	–16.2 (n=55)	–5.0 (n=18)	–16.7 (n=49)	–18.2 (n=49)	–18.2 (n=36)	–11.9 (n=32)	–11.8 (n=11)	–30.0 (n=17)
Wk 104	–10.0 (n=55)	–10.7 (n=43)	–7.5 (n=12)	–14.4 (n=46)	–16.8 (n=38)	–16.9 (n=36)	–10.7 (n=27)	–5.0 (n=10)	–31.8 (n=11)
Work Productivity (% overall work impairment due to health)[b]									
Wk 52	–15.8 (n=71)	–18.5 (n=55)	–6.3 (n=16)	–16.3 (n=48)	–18.3 (n=48)	–18.4 (n=37)	–11.5 (n=31)	–9.4 (n=11)	–30.6 (n=17)
Wk 104	–10.3 (n=55)	–11.3 (n=44)	–6.2 (n=11)	–11.2 (n=44)	–16.8 (n=37)	–14.0 (n=34)	–9.4 (n=26)	–1.8 (n=10)	–34.1 (n=11)
Activity Impairment (% activity impairment due to health)[c]									
Wk 52	–14.9 (n=174)	–14.8 (n=126)	–15.2 (n=48)	–20.0 (n=92)	–22.1 (n=89)	–20.7 (n=61)	–23.1 (n=59)	–18.7 (n=31)	–20.3 (n=30)
Wk 104	–14.1 (n=143)	–12.2 (n=107)	–20.0 (n=36)	–17.7 (n=84)	–18.5 (n=78)	–19.7 (n=57)	–19.8 (n=52)	–13.7 (n=27)	–15.8 (n=26)
PsAQoL (change from BL)[c,d]									
Wk 52	–4.0 (n=181)	–4.1 (n=130)	–3.6 (n=51)	–4.1 (n=94)	–5.2 (n=88)	–4.0 (n=62)	–5.6 (n=58)	–4.4 (n=32)	–4.4 (n=30)
Wk 104	–3.8 (n=149)	–3.6 (n=110)	–4.4 (n=39)	–4.6 (n=86)	–5.6 (n=76)	–4.4 (n=57)	–5.6 (n=52)	–4.9 (n=29)	–5.6 (n=24)

[a]In all categories, higher scores indicate higher impact on patients, employers, and society; a decrease from baseline represents improvement; [b]Assessed in 'employed' subjects only; [c]Assessed regardless of subject's employment status; [d]Higher scores represent greater impact on patients' QoL; a decrease from baseline represents improvement

BL, baseline; IV, intravenous; m, number of patients with sufficient data for evaluation; n, number of responders; SEC, secukinumab

References:
[1] McInnes. Lancet 2015;386:1137–46.
[2] Mease. NEJM 2015;373:1329–39.
Disclosure of Interest: V. Strand Consultant for: AbbVie, Amgen, BMS, Celgene, Celltrion, CORRONA, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi, and UCB, O. FitzGerald Grant/research support from: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Sun Pharma, UCB, L. Coates Grant/research support from: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Sun Pharma, UCB, J. Walsh Consultant for: Novartis, J. Cañete Consultant for: AbbVie, Boehringer Ingelheim, Celgene, Janssen, Lilly, Novartis, V. Bhosekar Employee of: Novartis, L. Pricop Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1832

FRI0522 THE ASSOCIATION BETWEEN OCCUPATIONAL-RELATED MECHANICAL STRESS AND RADIOGRAPHIC DAMAGE IN PSORIATIC ARTHRITIS

W. Zhou[1], R. Cook[2], V. Chandran[1,3], D.D. Gladman[1,3], L. Eder[1,4]. *[1]Department of Medicine, University of Toronto, Toronto; [2]Department of Statistics and Actuarial Science, University of Waterloo, Waterloo; [3]Centre for Prognosis Studies in the Rheumatic Diseases, University Health Network; [4]Women's College Research Institute, Women's College Hospital, Toronto, Canada*

Background: Mechanical stress is thought to play a role in the development of psoriatic arthritis (PsA).

Objectives: To determine the association between occupational-related mechanical factors and the severity of radiographic peripheral and axial joint damage in patients with PsA.

Methods: A retrospective cohort study was conducted in patients with long-standing PsA (>10 years duration). Patients were asked to report all paid employment since the age of 18. The key predictor variables included various occupational-related mechanical exposures. For each job, the Occupational Information Network (O*NET) was used to rate the level of exposure to 11 workers abilities and 16 occupational exposures. The outcomes of interest were the extent of radiographic damage in the peripheral and axial joints, as measured by the modified Steinbrocker score (mSS), and the modified Stokes Ankylosing Spondylitis Spine Score (mSASSS). The association between the predictor and outcome variables was assessed by linear multivariable regression models after adjusting for age, sex, PsA duration and lifestyle habits.

Results: 307 eligible patients were analyzed. Univariate analysis identified severeal occupational factors associated with radiographic damage (Table 1–2). In the multivariable regression analysis prolonged repetitive hand movements

Table 1. Linear Regression Analysis – The association between high level of work-related exposure and modified Steinbrocker score

Exposure	Univariate analysis		Multivariable Reduced Model*	
	β (95% CI)	P value	β (95% CI)	P value
Sitting	-15.7 (-29.2, -2.3)	0.02	-11.9 (-25.4, 1.6)	**0.085**
Hands handle	23.1 (4.4, 42)	**0.02**		
Repetitive hands motions	33 (11.7, 54.4)	0.002	29.5 (8.2, 50.8)	**0.007**
Twisting/Bending	18.8 (1.4, 36.2)	0.03		
Minor burns	21.5 (2.7, 40.4)	0.03		
Awkward body position	17.7 (-1.1, 36.5)	0.06		

Table 2. Linear Regression analysis – The association between workers' abilities and modified Steinbrocker score

Exposure	Univariate analysis		Multivariable Reduced Model*	
	β (95% CI)	P value	β (95% CI)	P value
Manual dexterity	2.5 (0.4, 4.6)	0.02		
Arm-hand steadiness	2.7 (0.6, 5.0)	0.01		
Finger dexterity	5.3 (1.4, 9.2)	**0.008**	5.4 (1.6, 9.2)	**0.005**
Trunk strength	2.0 (-0.3, 4.4)	0.09		
Wrist-finger speed	3.2 (-0.4, 6.8)	0.08		
Extent flexibility	1.9 (-0.3, 4.2)	0.10		

*Each model was adjusted for age, sex, duration of PsA, smoking, BMI, Biologics therapy (ever), DMARDs therapy (ever).

was associated with a higher peripheral joint damage score (by mSS, adjusted β=29.5, 95% CI 8.2, 50.8, p=0.007, Table 1), while the association between prolonged time spent sitting and lower mSS was of borderline significance (p=0.085, Table 1). Additionally, occupations that required higher finger dexterity were associated with higher mSS (adjusted β=5.4, 95% CI 1.6, 9.2, p=0.005, Table 2). Regarding axial damage, occupations that involved prolonged walking/running were associated with a higher mSASSS score (adjusted β=4.4, 95% CI 0.1, 8.7, p=0.04). PsA duration was independently associated with both peripheral and axial joint damage (p<0.001).

Conclusions: High level of occupation-related mechanical stress is associated with increased radiographic peripheral joint damage. These findings support the potential role of micro-trauma in the pathogenesis of PsA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4074

FRI0523 SHORT-TERM EFFICACY AND SAFETY OF NEW BIOLOGICAL AGENTS TARGETING THE IL-6, IL-12/23 AND IL-17 PATHWAYS FOR ACTIVE PSORIATIC ARTHRITIS: A NETWORK META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS

W. Dongze, Y. Jiang, L.-S. Tam. *Department of Medicine & Therapeutics, The Prince of Wales Hospital, the Chinese University of Hong Kong, Hong Kong, China*

Background: IL-6, IL-12/23 and IL-17 inhibitors have been found to be highly effective for both skin and joint manifestations of psoriatic arthritis (PsA). Nonetheless, reliable evidence of the comparative benefits and harms for these interventions is absent for treatment selection in daily practice.

Objectives: To investigate the comparative efficacy, safety and tolerability of IL-6, IL-12/23 or IL-17 inhibitors and the proportion attributable to overall treatment for patients with active PsA.

Methods: Randomized controlled trials (RCTs) evaluating the efficacy, safety and tolerability of IL-6, IL12/23 or IL17 inhibitors at weeks 24 were identified by a comprehensive systematic literature review (PROSPERO 2016: CRD42016048166). Quality of evidence was assessed following the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach. Treatment effects were evaluated based on the intention-to treat efficacy rates (ACR20, ACR50), safety parameters (any adverse effect [AE], serious adverse effect [SAE]) and tolerability (discontinuation due to AE [DAE]). Pair-wise meta-analyses and Bayesian network meta-analyses using the random-effects model were performed to estimate pooled odds ratios (ORs) and 95% credible interval (CrI). A subgroup analysis was performed to investigate the effects of prior anti-TNF exposure on the efficacy of ustekinumab and secukinumab.

Results: Six trials were identified which included 2411 participants and 11 treatments. All trials were of generally high quality according to Cochrane compliant rules and GRADEpro assessment. Direct comparisons of each biologic showed that secukinumab, ustekinumab and ixekizumab demonstrated superior efficacy over placebo with respect to all efficacy outcomes (ACR20 and ACR50). Regarding safety and tolerability, ixekizumab has a higher incidence of adverse events while ustekinumab were more tolerable compared with placebo. Mixed treatment comparisons showed that secukinumab (300mg monthly) had the highest efficacy in achieving ACR20 and ACR50; whereas clazakizumab (200mg monthly), ustekinumab (45mg 12 weekly), secukinumab (150mg monthly) had the lowest probability of having AE, SAE, DAE, respectively. Considering the overall risk-benefit profile of IL-6, IL12/23, IL17 inhibitors in the treatment of active PsA, secukinumab (150mg monthly) may offer an optimal balance for active PsA patients (Figure 1). When considering ACR 20 response, subgroup analysis revealed that anti-TNF naïve patient respond significantly better than placebo for all dosages of secukinumab and ustekinumab used. In contrast, only higher dose of secukinumab and ustekinumab were significantly more effective than placebo in anti-TNF failure patient.

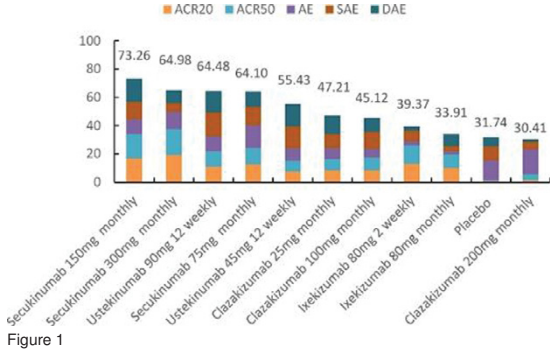


Figure 1

Conclusions: In conclusion, from the available evidence, secukinumab and ustekinumab were found to be the safest and most efficacious short-term treatments for active PsA amongst all the new biologics targeting the IL-6, IL-12.23 and IL-17 pathways.

Acknowledgements: Thank all colleagues working in the Division of Rheumatology, Department of Medicine and Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1469

FRIDAY, 16 JUNE 2017

Osteoporosis

FRI0524 CAROTID ATHEROSCLEROSIS IS ASSOCIATED WITH COMPROMISED VOLUMETRIC BONE MINERAL DENSITY AND MICROSTRUCTURES IN PATIENTS WITH INFLAMMATORY ARTHRITIS

T.H. Cheng[1], Q. Shang[1], E.K.M. Li[1], P.C.H. Wong[1], E.W.L. Kun[2], M. Li[1], T.K.Y. Li[1], T.Y. Zhu[3], A.P.W. Lee[1], L. Qin[3], L.S. Tam[1]. *[1]Department of Medicine and Therapeutics, the Chinese University of Hong Kong; [2]Department of Medicine & Geriatrics, Tai Po Hospital; [3]Department of Orthopaedics and Traumatology, the Chinese University of Hong Kong, Hong Kong, Hong Kong*

Background: Carotid Atherosclerosis is associated with compromised volumetric bone mineral density and microstructures in patients with inflammatory arthritis

Objectives: The aim of this study was to explore the relationship between volumetric bone mineral density (vBMD)/microstructural features and presence of carotid plaque (CP) in patients with inflammatory arthritis.

Methods: 175 inflammatory arthritis patients (81 [46%] PsA, 94 [54%] RA; 70 [40%] males; age: 53±12 years) were recruited into an ongoing prospective study assessing the relationship between inflammation, osteoporosis and carotid atherosclerosis. Carotid plaque and intima-media thickness (IMT) were measured by carotid ultrasound. Areal BMD (aBMD) was measured by dual energy X-ray absorptiometry (DXA). Microstructure features and vBMD of distal radius were measured using high-resolution peripheral quantitative computed tomography (HR-pQCT).

Results: No patients had established cardiovascular disease (CVD). Data from 172 patients at baseline were analyzed for this cross-sectional study. Patients were sub grouped according to the presence or absence of carotid plaque (CP+ group, n=68 [40%]) and CP- group, n=132 [60%]). CP+ group were older (59±10 vs 49±11, $p<0.001$), more likely to be male (54% vs 31%, $p=0.002$), had higher systolic blood pressure (130±19 vs 124±17 mmHg, $p=0.034$) and CVD risk (15.7±14.2 vs 7.9±8.6, $p<0.001$) according to the Framingham Risk Score (FRS) then the CP- group. aBMD, vBMD and microstructure were significantly compromised in the CP+ group. Distal radius aBMD, distal radius total vBMD, trabecular (Tb) vBMD, Tb thickness, cortical (Ct.) vBMD, Ct. thickness and bone volume fraction were 5% ($p=0.004$), 12% ($p<0.001$), 8% ($p=0.007$), 8% ($p=0.004$), 4% ($p=0.007$), 10% ($p=0.001$) and 8% ($p=0.007$) lower in the CP+ group. The differences remained significant after adjustment for gender, disease type and FRS (Table 1).

Table – Distal radius vBMD/microstructure and presence of plaque

	Carotid plaque		*p* value	Adjusted *p* value*
	No (n=104)	Yes (n=68)		
Total radius				
aBMD, g/cm^2	.575 ± .087	.547 ± .091	0.095	0.004
Distal radius				
Total vBMD, mmHA/cm^3	353.8 ± 77.8	315.3 ± 69.7	0.001	<0.001
Trabecular BMD, mmHA/cm^3	141.5 ± 46.2	131.4 ± 38.8	0.138	0.007
Bone volume fraction	.118 ± .039	.110 ± .032	0.142	0.007
Trabecular thickness, mm	.077 ± .017	.071 ± .013	0.019	0.004
Cortical vBMD, mmHA/cm^3	902.6 ± 58.0	870.0 ± 63.5	0.001	0.007
Cortical Thickness, mm	.882 ± .177	.792 ± .211	0.009	0.001

* Adjusted for gender, disease type and Framingham Risk Score

Conclusions: Inflammatory arthritis patients with carotid plaque had lower aBMD, vBMD and compromised bone microstructure in the distal radius even after adjustment for gender, disease type and FRS, suggesting that inflammation may be the common link for both conditions.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3094

FRI0525 ASSOCIATION OF DYSMOBILITY SYNDROME WITH FRACTURE RISK IN THE MROS COHORT

B. Buehring[1,2], B.L. Lewis[1], K.E. Hansen[1], S.R. Cummings[3], N.E. Lane[4], N. Binkley[1], K.E. Ensrud[5], P.M. Cawthon[3]. *[1]Department of Medicine, University of Wisconsin-Madison, Madison, United States; [2]Rheumazentrum Ruhrgebiet, Herne, Germany; [3]California Pacific Medical Center Research Institute, San Francisco; [4]University of California - Davis, Sacramento; [5]University of Minnesota, Minneapolis, United States*

Background: Osteoporosis, obesity and sarcopenia are risk factors for fractures and their combination has a negative effect on musculoskeletal health (MSKH). We proposed a score-based approach to define this combination as "dysmobility syndrome (DS)". DS increases mortality in the NHANES cohort but no data exist on fracture risk. The most widely used fracture risk calculator, the WHO FRAX® tool, does not include several measures of MSKH such as physical function, muscle mass or falls. In this analysis of the Osteoporotic Fractures in Men (MrOS) cohort, we examine whether individuals with impaired MSKH/DS have a higher incidence of fragility fractures and whether this composite score confers additional risk for fracture, beyond risk estimates provided by FRAX®.

Objectives: In this analysis of the Osteoporotic Fractures in Men (MrOS) cohort, we examine whether individuals with impaired MSKH/DS have a higher incidence of fragility fractures and whether this composite score confers additional risk for fracture, beyond risk estimates provided by FRAX®.

Methods: The MrOS cohort was utilized in this study. The score-based approach to define DS includes six factors with one point assigned to each: appendicular lean mass/height2 $<$7.26 kg/m^2, body fat $>$30%, T-score $\leq$-2.5, grip strength $<$30 kg, gait speed $<$1.0 m/s, and falls in last 12 months. A score $\geq$3 indicated DS. We use odds ratios and cox proportional hazard models to analyze risks of major osteoporotic fracture (MOF). Men were censored at the time of fracture or last follow up. We determined the hazards of fracture using presence of dysmobility syndrome, the FRAX® score, and the FRAX® score in quartiles. We used the program R (www.r project.org) to perform all analyses.

Results: 5827 men ages 74±6 years with a mean BMI of 27.4±3.8 kg/m^2 had complete data necessary for this analysis. 391 males (6.7%) met criteria for DS. 571 (10%) experienced a MOF including 245 (4%) hip fractures. DS increased the hazards of major osteoporotic (HR 3.31, 95% CI, 2.58, 4.23) and hip (HR 3.48, 95% CI 2.41, 5.03) fractures. In adjusted models, DS and elevated FRAX® risk each increased the hazards of major osteoporotic and hip fracture. Interaction models showed no significant interaction between the presence of DS and FRAX® score for major osteoporotic (p=0.184) or hip (p=0.177) fractures.

Table 1. Cox Proportional Hazard Models for Fracture

Models	Major Osteoporotic Fracture 571 events Hazard Ratio (95% CI)	Hip Fracture 245 events Hazard Ratio (95% CI)
Dysmobility Index[a]	3.31 (2.59, 4.23)	3.48 (2.41, 5.03)
FRAX Score above treatment threshold	3.56 (2.51, 5.07)	5.52 (4.28, 7.11)
Dysmobility Index *and* FRAX Score	3.14 (2.45, 4.02) 3.17 (2.22, 4.51)	2.21 (1.52, 3.21) 5.14 (3.97, 6.65)

CI, Confidence Interval.

Conclusions: DS was associated with increased MOF fracture incidence even after adjusting for quartiles of FRAX® risk in this cohort of older men. Our study suggests that using a composite assessment of MSKH in addition to already available tools such as FRAX® may improve identification of individuals at high fracture risk. Additional analyses are necessary to examine whether this approach can better distinguish between those who will fracture and who will not and whether the results can be reproduced in women.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2790

FRI0526 ANTI-OSTEOPOROTIC THERAPY DECREASE CANCER RISK IN PATIENTS WITH OSTEOPOROTIC VERTEBRAL FRACTURES

Y.-C. Chen, C.-H. Ko. *Rheumatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, Province of China*

Background: Some studies had looked at the long-term effect of anti-osteoporotic therapy on risks of different cancers in the general population. But epidemiological studies have consistently reported a reduced risk of breast cancer in bisphosphonate users. so there is little data to establish definitive conclusions.

Objectives: This study aimed to determine if anti-osteoporotic therapy can influence cancer risk in patients with osteoporotic vertebral fracture.

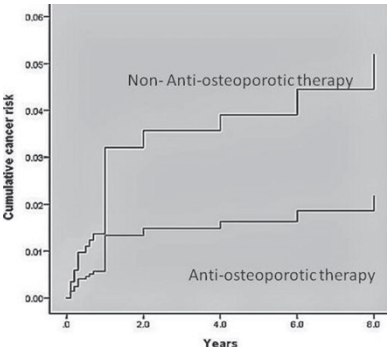
Methods: This retrospective study reviewed of cases of osteoporosis patients with acute vertebral fractures between 2001 and 2015. Anti-osteoporotic therapy were recorded (alendronate, ibandronate, zolendronic acid, raloxifen, teriparatide, denosumab). We followed these patients to develop cancer. All associated co-morbidities were recorded. Cox regression analysis were performed.

Results: There were 1128 patients with acute vertebral fractures were enrolled, among them 693 patients accepted anti-osteoporotic therapy, 432 were not. The mean age of anti-osteoporotic therapy was 73.86±7.52, while the age of nonanti-osteoporotic therapy was 72.82±10.92 (p=0.059). 15 (2.2%) patients of anti-osteoporotic therapy developed cancer, while 24 (5.6%) patients of non-antiosteoporotic therapy developed cancer (p=0.004). After adjusting for potential confounders, patients with antiosteoporotic therapy still had a lower cancer risk (p=0.038; HR: 0.428, 95% CI: 0.192∼0.955). The cancer risk also increased among smokers (p=0.002; HR: 10.505; 95% CI: 2.375∼46.462).

Table 1. Multivariable cox regression analysis of the hazard ratios for cancer

	Regression coefficient	SE	P value	HR (95.CI)
Anti-osteoporosis	-0.848	0.409	0.038	0.428 (0.192–0.955)
Gender	-0.693	0.584	0.236	0.500 (0.159–1.572)
Age	-0.029	0.016	0.071	0.972 (0.942–1.002)
Smmoking	2.352	0.759	0.002	10.505 (2.375–46.462)
liver disease	2.012	0.487	0.001	7.477 (2.880–19.412)
Kidney disease	-0.338	1.224	0.783	0.713 (0.065–7.859)
Cardiovascular disease	0.856	0.677	0.206	2.355 (0.624–8.882)
Pulmonary disease	0.771	0.597	0.197	2.162 (0.671–6.971)

Abbreviations: HR, hazard ratio; SE, standard error.



Conclusions: In this study, anti-osteoporotic therapy decrease cancer risk. So we could safely use these drugs in osteoporotic management.

References:

[1] British Journal of Cancer (2013) 109, 795–806.

Acknowledgements: We thanked Kaohsiung Chang Gang Memorial hospital for data support.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3820

FRI0527 LACUNARITY OF TRABECULAR BONE MICROARCHITECTURE, TBLβ, AS A PREDICTOR OF BONE FRAGILITY FRACTURE AND POTENTIAL INDEX OF OSTEOPOROSIS TREATMENT EFFICACY. THE LOTO STUDY

A. Zaia[1], R. Rossi[2], R. Galeazzi[2], P. Scendoni[3]. *[1]Scientific Direction; [2]Medical Imaging and Services, INRCA Italian National Research Center on Aging, Ancona; [3]Rheumatology Division, INRCA Italian National Research Center on Aging, Fermo, Italy*

Background: Bone mineral density (BMD) by dual-energy X-ray absortiometry (DXA) is still the routinely diagnostic approach for osteoporosis. However, BMD alone is not a good predictor of fracture risk while bone microarchitecture emerges as a determinant of bone fragility independent of BMD. High-resolution magnetic resonance imaging (MRI) represents an effective tool for in vivo characterization of trabecular bone microarchitecture (TBA) by noninvasive/nonionizing methods. Nevertheless, texture analysis is not used in clinical practice because of the large number of parameters to be calculated and analyzed.

We previously developed a MRI method to provide one parameter (TBLβ) sensitive to TBA changes in aging and osteoporosis[1]. Fractal lacunarity was chosen for TBA texture analysis as it is able to describe bone network discontinuity and sizes of bone marrow spaces, whose changes are index of increased fracture risk.

Objectives: Clinical validation of the method as a new tool useful in early diagnosis of osteoporotic fracture risk is the strategic aim of LOTO study. One major objective is to verify the potential of TBLβ in discriminating patients with (VF+) and without (VF-) vertebral fractures. TBLβ as a potential marker of osteoporosis treatment efficacy is also investigated.

Methods: An observational, cross-sectional and prospective study on over50s women at risk for bone fragility fractures was designed to validate the method[2]. Sample size was estimated equal to 280 osteopenic/osteoporotic women with/without prior vertebral bone fragility fractures. The main outcome measure is TBLβ as an index of osteoporotic fracture risk. It is calculated by a software prototype of the gray-scale version of our method on L4 axial images acquired by 1.5T MRI spin-echo multislice technique[3].

Results: A complete set of baseline recording, including DXA-BMD, conventional column Rx morphometry, and lumbar spine MRI-spin echo images for TBA characterization, was obtained for 279 out of 309 subjects eligible for the study. Prevalent VF were found in 31.5% subjects, 47.7% of which defined osteopenic at lumbar spine by DXA-BMD and 67% younger than 65 years. Baseline results from ROC analysis show that the contribution of TBA degeneration (TBLβ=40) to prevalent fractures is statistically higher (p=0.032) than BMD (T-score=-2.5). TBLβ results (Table 1) show that the proposed method is able to discriminate between

VF+ and VF- patients (p=0.001). This result is further stressed in untreated T- subjects (p<0.0001). Treatment, any medication (T+), and drug therapy in particular, significantly counteract the difference between VF+ and VF- within groups (Table 1) and between groups with TBLβ values comparable to untreated VF- patients (p=0.319) and statistically higher than untreated VF+ (p=0.014).

Table 1 Lacunarity of trabecular bone microarchitecture, TBLβ, can assess osteoporosis fracture risk and treatment efficacy

Patients	n VF-/VF+ (%)	TBLβ		p
		VF-	VF+	
Overall	191/88 (100)	66±51	46±42	0.001
T-	121/35 (55.9)	67±51	36±29	0.001
T+, any medication	70/53 (44.1)	65±52	52±48	0.091
VitD/Ca supplements *	25/19 (35.8)	56±49	36±24	0.051
Drug therapy*	45/34 (64.2)	70±54	62±56	0.276
Bisphosphonates**	43/27 (88.6)	70±55	60±54	0.225

VF: prevalent vertebral fractures; **T-** without treatment; **T+** with treatment; * % within T+ patients; ** % within drug therapy group; p: statistical significance from one-tail t-test

Conclusions: These promising results stress the usefulness of the method as a diagnostic tool in the assessment of osteoporotic fracture risk and suggest a potential role of TBLβ as a marker of treatment efficacy. More intriguing results are expected from prospective LOTO data.

References:

[1] Zaia et al. IEEE Trans Inf Technol Biomed 2006; 10:484.
[2] Zaia et al. Osteoporos Int 2016; submitted.
[3] Zaia. World J Orthop 2015; 6:221.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2719

FRI0528 SUCCESSFUL IMPLEMENTATION OF A PHARMACIST-LED FRACTURE LIAISON SERVICE AT A US VETERAN AFFAIRS (VA) HOSPITAL

B. Buehring[1,2,3], T. Holobyn[3], J. Kotek[4], B. Glynn-Servedio[5], S. Wright[6], K. Hansen[1,3], A. Bridges[1,3]. *[1]William S. Middleton Memorial Veterans Hospital, Madison, United States; [2]Rheumazentrum Ruhrgebiet, Herne, Germany; [3]Department of Medicine, University of Wisconsin-Madison, Madison; [4]Milwaukee VA Medical Center, Milwaukee; [5]Durham VA Medical Center, Durham; [6]VA Great Lakes Health Care System, Westchester, United States*

Background: Worldwide, an osteoporosis (OP) care gap exists for individuals with a fragility fracture (FF). Published data shows that US veterans are no exception. To address the OP care gap, fracture liaison services (FLS) are being implemented with the goal to prevent additional FF.

Objectives: Here we report the patient outcomes after initiating a FLS at a US Veterans Affairs (VA) hospital.

Methods: We identified veterans with a pelvic, hip and/or femur shaft fracture by querying a central database. Veterans with traumatic fractures, active OP medication, recent dual-energy X-ray absorptiometry (DXA) and/or hospice status were excluded. The remaining veterans were contacted via letter and the responsible primary health care team was sent a template letter with OP management recommendations via the electronic medical record. Recommendations included DXA, laboratory evaluation, and pharmacologic and non-pharmacologic interventions. In most cases, trained clinical pharmacists serving as FLS coordinators performed all tasks with an expert physician available for questions. Presented data are based on a review 4 months after recommendations were sent.

Results: The initial query revealed 149 veterans with pelvic, femoral, and/or hip fractures without a recent DXA and/or active OP therapy. Of those, 32 (31 males, 1 female) patients suffered a FF and were included in the FLS intervention. Our review showed that 59% of these had a DXA scan, 35% had their calcium/vitamin D intake reviewed, and 40% had started OP therapy or were referred to an OP specialist. When the primary care team's clinical pharmacist instead of the primary care provider implemented the FLS recommendations (10/32), 100% of the recommendations were addressed. Furthermore, 70% of patients had a bisphosphonate ordered, whereas it was 9% when no pharmacist was involved (p=0.0004).

Conclusions: Our study suggests that a pharmacist-led FLS improves post-FF care in US veterans. We found a high percentage of OP care goals met when patients interacted with clinical pharmacists. This observation might be due to the fact that most pharmacists had dedicated training in OP management and their interaction with the patient focused on their FF. In summary, our data suggests that clinical pharmacists trained in OP management can very effectively implement a FLS intervention.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2793

FRI0529 ANALYSIS OF THE EVOLUTION OF CORTICAL AND TRABECULAR BONE COMPARTMENTS IN THE PROXIMAL FEMUR AFTER SPINAL CORD INJURY BY 3D-DXA

L. Gifre[1,2], L. Humbert[3], A. Muxi[4], L. del Rio[5], J. Vidal[6], E. Portell[6], A. Monegal[1], N. Guañabens[1], P. Peris[1]. *[1]Rheumatology, Hospital Clínic of Barcelona, Barcelona; [2]Rheumatology, Hospital Universitari Germans Trias i Pujol, Badalona; [3]Galgo Medical; [4]Nuclear Medicine, Hospital Clínic of Barcelona; [5]CETIR, Barcelona; [6]Spinal Cord Unit, Guttmann Neurorehabilitation Institute, Badalona, Spain*

Background: Spinal cord injury (SCI) is associated with a marked increase in bone loss and risk of osteoporosis development short-term after injury. 3D-DXA is a new imaging analysis providing volumetric measurements of the cortical and trabecular bone from DXA scans.

Objectives: The aim of this study was to assess the evolution of 3D femoral shape, trabecular macrostructure and cortical bone from DXA scans in patients with recent SCI followed over 12 months.

Methods: 16 males with recent SCI (<3 months since injury) were included. Clinical assessment, bone mineral density (BMD) measurements and 3D-DXA evaluation at proximal femur (analyzing the integral, trabecular and cortical volumetric BMD [vBMD] and cortical thickness) were performed at baseline and at 6 and 12 months of follow-up.

Results: vBMD measured by 3D-DXA significantly decreased at integral, trabecular and cortical compartments at 6 months (-31.1 mg/cm^3, -8.8%, p<0.001; -25.4 mg/cm^3, -11.6%, p=0.001; and -20.4 mg/cm^3, -2.4%, p=0.004), with a further decrease at 12 months, resulting in an overall decrease of -58.9 mg/cm^3 (-16.6%, p<0.001), -47.9 mg/cm^3 (-21.9%, p<0.001) and -42.4 mg/cm^3 (-5%, p<0.001), respectively. Cortical thickness also decreased at 6 and 12 months (-8%, p<0.001; and -11.4%, p<0.001), with the maximal decrease being observed during the first 6 months. The mean BMD loss by DXA at femoral neck and total femur were -17.7% (p<0.001) and -21.1% (p<0.001), at 12-months, respectively. Integral vBMD values at baseline were positively correlated with total femur BMD (r=0.874, p<0.001), however no correlation was observed in the changes in these values at 12-months.

Conclusions: 3D-DXA shows the differentiation of the marked bone loss that occurs at both proximal femoral compartments (cortical and trabecular) short-term after SCI. The present data suggest that 3D-DXA could be a useful complementary assessment tool in SCI patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3103

FRI0530 EFECTIVENESS OF AN ORTHOGERIATRIC FRACTURE LIAISON SERVICE COMPARED WITH STANDARD CARE

A. Naranjo[1], S. Fernández Conde[2], S. Ojeda[1], S. Rodríguez[3], L. Torres Hernández[4], I. Bernardos[1], I. Rodríguez[3], V. Kraev[3], C. Hernández Carballo[4], P. Laynez[4]. *[1]Rheumatology, Hospital Univ. Gran Canaria Dr. Negrin, Las Palmas de Gran Canaria; [2]Internam Medicine, Hospital Universitario NS Candelaria, Santa Cruz de Tenerife; [3]Geriatrics, Hospital Univ. Gran Canaria Dr. Negrin, Las Palmas de Gran Canaria; [4]Internal Medicine, Hospital Universitario NS Candelaria, Santa Cruz de Tenerife, Spain*

Background: Our fracture liaison service (FLS) for outpatients has reported to maintain 73% of the patients on antiresorptive 2 years after the fracture. For hip fracture we are concerned about the low capture rate (27%).

Objectives: To analyze the efectiveness of a FLS for inpatients with hip fracture compared with standard care.

Methods: Observational study carried out in two hospitals, one with a FLS (Hospital Negrin) and the other one with standard orthogeriatric care (Hospital Candelaria). The reference population >65 y from H.Negrin and H.Candelaria are 63,382 and 63,249 inhabitants respectively.

We included patient >65 y with fragility hip fracture ocurred between 1th March 2016 and 31th July 2016. Severe dementia, non-fragility fractures and those patients who died during hospital admittance were excluded. All patients underwent hemogram and biochemistry. The densitometry was not performed on any patient. The only difference between hospitals was a dedicated nurse from the FLS H.Negrin who visited inpatients twice a week, interviewed patients, gave education and applied a treatment protocol to be started by Primary Care.

Data recorded were: age, sex, previous fractures and previous treatment for osteoporosis, including calcium, vitamin D, bisphosphonates, denosumab and teriparatide. We also collected the treatment that was included in the discharge report and treatment six month later (checking the electronic prescription).

Results: We included 185 patients (105 from Hospital Candelaria and 80 from Hospital Negrin), mean age 82 y (Table). The percentage of patients receiving a bisphosphonate or equivalent before hospital admittance was similar in both hospitals. However, the percentage after discharge rose by 91% in the hospital with FLS and remain 8% in the hospital with standard care. After six months, 75% of patients from FLS and 15% of patients with standard care had a treatment.

Conclusions: The implementation of an orthogeriatric FLS lead to an increase in treatment for osteoporosis compared with standard care and similar to our outpatient FLS model. The ideal approach to secondary fracture prevention is a FLS model of care in an integrated health care network, overseen by a nurse coordinator.

	Hospital Negrin	Hospital Candelaria	P
Number of patients	80	105	
Age, mean (SD)	82 (7)	82 (8)	0.96
Sex, women n (%)	64 (80)	71 (67)	0.06
Previous fracture, n (%)	13 (16)	12 (11)	0.34
Previous treatment			
Ca and VD, n (%)	26 (32)	13 (12)	<0.001
Bisphosphonate or equivalent, n (%)	8 (10)	9 (8)	0.73
Treatment in the discharge report			
Ca and VD, n (%)	77 (96)	19 (18)	<0.001
Bisphosphonate or equivalent, n (%)	73 (91)	9 (8)	<0.001
Treatment at 6 months			
Ca and VD, n (%)	60 (90)*	27 (29)**	<0.001
Bisphosphonate or equivalent, n (%)	50 (75)*	14 (15)**	<0.001

Ca and VD: calcium and vitamin D. *Data available from 66 patients; 9 not located, 4 deaths, 1 atypical fracture. **Data available from 93 patients; 4 not located, 8 deaths.

References:
[1] Naranjo A et al. Osteoporos Int. 2015;11:2579–85.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1441

FRI0531 DUAL ENERGY X-RAY ABSORPTIOMETRY TESTING IN ELDERLY MEN WITH PROSTATE CANCER INITIATING ANDROGEN DEPRIVATION THERAPY REDUCES SUBSEQUENT FRACTURE RISK

M.E. Suarez-Almazor[1], G.M. Cabanillas Salazar[1], H. Zhao[1], B. Shi[2], J. Kim[3], L. Elting[4]. *[1]General Internal Medicine, MD Anderson Cancer Center; [2]Health Science, The University of Texas School of Public Health; [3]Health Science, University of Texas School of Public Health; [4]Health Science, MD Anderson Cancer Center, Houston, United States*

Background: Androgen deprivation therapy (ADT) is a mainstay therapy for prostate cancer, and a risk factor for bone mineral density (BMD) loss and fractures. Despite this risk, few patients undergo measurement of BMD when initiating ADT. Conceivably, screening for bone loss could lead to identification of patients at risk, and to implementation of bone conserving therapy (BCT), and subsequent decrease in fracture risk.
Objectives: To evaluate the utilization of Dual Energy X-ray Absorptiometry (DXA) testing for measurement of BMD in elderly patients with prostate cancer initiating treatment with ADT, and the effects of testing on subsequent fracture risk.
Methods: We conducted a population-based retrospective cohort study using the Surveillance, Epidemiology, and End Results (SEER) and Texas Cancer Registry (TCR) databases linked to Medicare claims. Medicare is the United States national health insurance program for individuals aged 65 and older. We identified all men over 66 years old with a diagnosis of prostate cancer who received ADT. We identified claims for DXA within 12 months prior, and 12 months after ADT initiation. We assumed that if patients had DXA testing in the year before ADT, this would not be repeated. We then ascertained claims for fractures during follow-up after ADT onset, comparing those who had undergone DXA with those who had not. Statistical analysis included multivariate logistic regression adjusting for demographic and clinical variables.
Results: The cohort included 36,739 men with prostate cancer treated with ADT; 48.3% were over 75 years of age and 75% were white. Only 5.2% of the patients underwent DXA within the window of evaluation. Men were more likely to have DXA id the were white vs. African American, and if the lived in census tracts with higher socio-economic status. When comparing the incidence of fractures, 11.3% of those who underwent DXA had a fracture, compared to 19.4% of those who did not undergo DXA ($p<0.0001$). In the multivariate model an increase in the odds for a fracture was associated with older age, being White, having a prior history of osteoporosis or fracture, were evaluated with DXA.A decrease in the odds for a fracture was associated with having undergone DXA testing (0.70; 95% CI 0.61 – 0.80).
Conclusions: Very few patients with prostate cancer starting ADT undergo DXA despite being at increased risk of fracture. DXA use was associated with socioeconomic status. Our results show that patients who underwent DXA were significantly less likely to have a fracture. Our findings suggest that DXA should be performed in all patients with prostate cancer initiating ADT.
References:
[1] V. B. Shahinian, et al. Risk of Fracture After Androgen Deprivation for Prostate Cancer. N Engl J Med, 352:154–164, 2005.
[2] Philip J. Saylor, Donald S. Kaufman, M. Dror Michaelson, Richard J. Lee, and Matthew R. Smith. Application of a Fracture Risk.
[1] Algorithm to Men Treated With Androgen Deprivation Therapy for Prostate Cancer. J Urol. 2010 June; 183(6): 2200–2205.
Acknowledgements: To our patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6863

FRI0532 DUAL ENERGY X-RAY ABSORPTIOMETRY TESTING IN WOMEN WITH BREAST CANCER INITIATING THERAPY WITH AROMATASE INHIBITORS REDUCES SUBSEQUENT FRACTURE RISK

M.A. Ursani[1], M. Suarez-Almazor[2], M. Yang[2], H.-F. Lu[2], H. Zhao[2], L. Elting[2]. *[1]Medicine, Section of Allergy, Immunology and Rheumatology, Baylor College of Medicine; [2]Internal Medicine, Rheumatology, The University of Texas M.D. Anderson Cancer Institute, Houston, United States*

Background: Estrogen receptor positive breast cancer is commonly treated with aromatase inhibitors (AI). A well-known adverse effect of this therapy is osteoporosis and related bone fractures. National guidelines have promoted the use of dual energy X-ray absorptiometry (DXA) for screening purposes.
Objectives: To evaluate the association between use of DXA among women with breast cancer treated with AI enrolled in Medicare, and subsequent fracture risk.
Methods: Retrospective cohort study using the Texas Cancer Registry (TCR) and the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) data linked with Medicare claims. To help estimate the likelihood of performing a DXA, a multivariable logistic regression model was used. Covariates of age, ethnicity, stage, residence area, and socioeconomic variables were controlled for the analyses. The outcome variable a DXA claim within 12 months after the initiation of the AI therapy. Cox regression model to evaluate time to first fracture after initiation of AI.
Results: The total number of cases within the SEER-Medicare database was 15,350 and in the TCR 4,532. Women aged between 66–74 years and Non-Hispanic white were more likely to get DXA than were Hispanic and Non-Hispanic Black.
In TCR, 2714 patients did not get treatment for osteoporosis in the first 12 months after AI therapy initiation. 2989 patients did not receive treatment for osteoporosis within 12 months of obtaining their first DXA scan. 1330 patients who did not undergo DXA were not treated for osteoporosis; and 1384 patients who underwent DXA got treated for osteoporosis.
The duration of AI treatment was negatively associated with the risk of fracture. Women who received DXA scan showed 11% lower risk of fracture than those who were not scanned (HR 0.89 (0.83, 0.94).
Conclusions: National guidelines suggest to obtain a DXA and start bisphosphonate therapy in female breast cancer patients who are treated with AI therapy. Our data suggests that the majority of women in the TCR and SEER database were not treated for osteoporosis within the first 12 months after initiation of AI therapy. Women who received DXA scan showed a lower risk of fracture than those who were not scanned.
References:
[1] National guidelines suggest to obtain a DXA and start bisphosphonate therapy in female breast cancer patients who are treated with AI therapy. Our data suggests that the majority of women in the TCR and SEER database were not treated for osteoporosis within the first 12 months after initiation of AI therapy. Women who received DXA scan showed a lower risk of fracture than those who were not scanned.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2305

FRI0533 INCIDENCE AND RISK FACTORS OF OSTEOPOROTIC FRACTURE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A MULTICENTER COMPARATIVE STUDY OF THE FRAX CRITERIA AND WHO CRITERIA

S.T. Choi[1], S.-R. Kwon[2], H.-A. Kim[3], J.-Y. Jung[3], S.-S. Kim[4], S.-H. Kim[5], J.-M. Kim[5], J.-H. Park[1], C.-H. Suh[3]. *[1]Internal Medicine, Chung-Ang University College of Medicine, Seoul; [2]Internal Medicine, Inha University College of Medicine, Incheon; [3]Internal Medicine, Ajou University College of Medicine, Suwon; [4]Internal Medicine, Ulsan University College of Medicine, Gangneung Asan Hospital, Gangneung; [5]Internal Medicine, Keimyung University College of Medicine, Daegu, Korea, Republic Of*

Background: The fracture risk assessment tool (FRAX) criteria and the bone mineral density (BMD) criteria of the World Health Organization (WHO) are widely used for the assessment of osteoporotic fracture. Rheumatoid arthritis (RA) is the only disease parameter for the evaluation of osteoporotic fracture in the FRAX model, unlike the WHO criteria. However, the input for RA is just a dichotomous variable in FRAX model.
Objectives: In this study, we evaluated the incidence and risk factors of osteoporotic fracture in patients with RA through the comparison of the FRAX criteria and WHO criteria.
Methods: This study is a multicenter study, including 479 RA patients in 5 hospitals and 384 healthy controls, between January 2012 and December 2016. All of the RA patients fulfilled the 1987 American College of Rheumatology (ACR) criteria or the 2010 ACR/European League Against Rheumatism (EULAR) criteria for RA. The FRAX criteria for high risk of osteoporotic fracture, which is a 10-year probability of $\geq$20% for major osteoporotic fracture or $\geq$3% for hip fracture, were calculated by the FRAX tool including the BMD values. The classification of osteoporosis, according to WHO criteria were based on T-score $\leq$ -2.5. We assessed various demographic factors, clinical and laboratory findings of RA, and

medication use for RA and osteoporosis, and then evaluated the incidence and risk factors for osteoporotic fracture.
Results: The mean age of RA patients was 61.7±11.9 years, and 426 patients were female (88.9%) with 353 postmenopausal women (82.9%). The BMD score of L-spine in RA patients was significantly lower than that in healthy control (-2.21±1.41 vs. 0.97±0.11, $p<0.001$). Osteoporotic fracture was detected in 81 (16.9%) patients with RA. In RA patients, 226 (47.2%) patients met the FRAX criteria for high risk of osteoporotic fracture, and 240 (50.1%) patients satisfied the WHO criteria. The result of the FRAX criteria was affected by the female sex, menopause, smoking, drinking, higher dose of glucocorticoid (≥5mg/day), vitamin D use, calcium use and proton pump inhibitor (PPI) use ($p<0.05$). In multiple linear analysis, the FRAX score to 10-year probability of ≥3% of hip fracture was associated with age (β=0.384, $p<0.001$), body weight (β=-0.110, $p=0.038$), erythrocyte sedimentation rate level (β=0.125, $p=0.010$), glucocorticoid dose (β=0.105, $p=0.024$), and PPI use (β= -0.123, $p=0.010$). The independent risk factors for FRAX criteria were age (OR 1.160, $p<0.001$), female sex (OR 3.942, $p=0.010$), body mass index (BMI) (OR 0.869, $p=0.001$), glucocorticoid dose (OR 1.167, $p=0.025$) and PPI use (OR 2.552, $p=0.019$), and those for WHO criteria were age (OR 1.021, $p=0.040$), glucocorticoid dose (OR 1.109, $p=0.046$) and smoking (OR 2.924, $p=0.031$).
Conclusions: Osteoporotic fractures were found in 16.9% of RA patients. The proportion of patients with high risk of osteoporotic fracture was 47.2% in the FRAX model and 50.1% in the WHO model. Age, female sex, lower BMI, higher dose of glucocorticoid, PPI use and smoking were independent risk factors for osteoporotic fracture in RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4580

FRI0534 REPEATED OSTEOPOROSIS SCREENING IN RHEUMATOID ARTHRITIS: ARE WE COMPLYING WITH GUIDELINES?

A. Gorman[1], V. Sullivan[2], S. Khan[1], A. Mohammed[1], K. O'Rourke[1].
[1]Rheumatology; [2]Midlands Regional Hospital Tullamore, Tullamore, Ireland

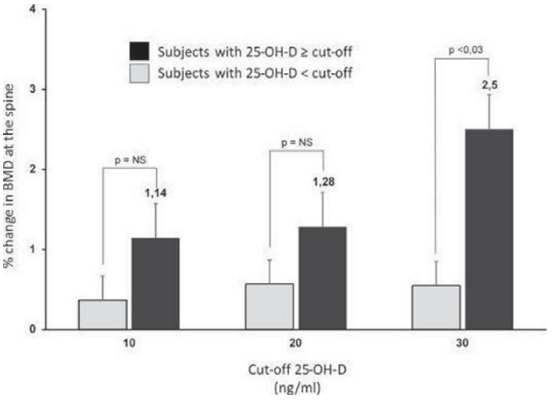
Background: Osteoporosis rates are higher in patients with rheumatoid arthritis (RA). Patients with RA diagnosed with osteoporosis have a 30% increased risk of major fracture [1]. Monitoring response to osteoporosis treatment is recommended however there is no consensus on how frequently this should be performed. The International Society for Clinical Densitometry (ISCD), National Osteoporosis Foundation (NOF) and the American Association of Clinical Endocrinologists (AACE) all recommend repeat Bone Mineral Density (BMD) assessment within two years after initiating osteoporosis treatment to assess response to treatment [2–4]. Furthermore, the NOF and AACE recommend repeat screening every two years after diagnosis [3,4].
Objectives:
- To identify patients with RA and osteoporosis
- To identify if international guidelines are being achieved for reassessment of BMD within two years of treatment commencement in keeping with international guidelines.

Methods: A database of patients with a diagnosis of RA and osteoporosis who attend the Rheumatology department of the Midlands Regional Hospital, Tullamore since January 2013 was reviewed. Outpatient summaries, date of diagnosis, radiology investigations (DEXA scanning), pharmacological treatment and follow up investigations and treatment were documented.
Results: As of August 2016, 770 patients were identified as having RA. 90% of patients had attended the department since 2013. 117 (16.7%) patients were identified as having osteoporosis. Of these, 52.14% of patients were prescribed bisphosphonate therapy, 31.62% denosumab, 9.4% calcium/vitamin D alone, 0.85% other treatment (teriparatide/strontium) and 5.1% were on no treatment. Only 11.9% of these patients had a repeat DEXA scan within two years of starting or changing treatment. 11.1% of patients had repeat DEXA scans booked. The average length of time since a patient's most recent DEXA is 35 months.
Conclusions: Repeat DEXA scanning to assess the response to osteoporosis treatment in people with RA within the timeframe recommended by international guidelines has not been achieved. Patients who fail to respond to osteoporotic treatment are not being identified in a timely manner and therefore are at an increased risk of fractures. The results of this audit will make us more vigilant to identify those patients who are treated for osteoporosis that need repeat DEXA scanning to ensure that treatment is efficacious.
References:
[1] Kanis JA, Johnell O, Oden A, et al. FRAX and the assessment of fracture probability in men and women from the UK. Osteoporos Int 2008; 19:385.
[2] 2013 ISCD Official Postions - Adult http://www.iscd.org/official-positions/2013-iscd-official-positions-adult/ (Accessed on December 02, 2013).
[3] Cosman F1, de Beur SJ, LeBoff MS, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis Osteoporos Int. 2014 Oct;25(10):2359–81.
[4] Watts NB, Bilezikian JP, Camacho PM, Greenspan SL,et al.American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the diagnosis and treatment of postmenopausal osteoporosis. AACE Osteoporosis Task ForceEndocr Pract. 2010 Nov;16 Suppl 3:1–37.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2459

FRI0535 STRONG INFLUENCE OF VITAMIN D STATUS ON BONE MINERAL DENSITY AND BONE TURNOVER MARKERS DURING WEIGHT RESTORATION IN PATIENTS WITH ANOREXIA NERVOSA

A. Giollo[1], L. Idolazzi[1], C. Caimmi[1], A. Fassio[1], F. Bertoldo[2], R. Dalle Grave[3], S. Calugi[3], P.V. Bazzani[3], O. Viapiana[1], M. Rossini[1], D. Gatti[1]. *[1]Rheumatology Unit, Department of Medicine; [2]Internal Medicine Unit, Department of Medicine, University of Verona, Verona; [3]Department of Eating and Weight Disorder, Villa Garda Hospital, Garda, Italy*

Background: Anoressia nervosa (AN) is associated with an increased risk of low bone mineral density (BMD) and fractures as a consequence of an inadequate bone mass peak in adolescence and bone loss in young adulthood. Moreover, recently we have showed that vitamin D (25-OH-D) deficiency is widespread in untreated patients with AN, and there is a strong positive relationship between vitamin D status and BMD in AN. However, if vitamin D status could affect the efficacy of weight restoration in improving bone health in patients with AN is currently unknown.
Objectives: Our aim was to investigate the potential role of vitamin D status in determining the efficacy on bone mineral density (BMD) of weight restoration in AN.
Methods: Bone mineral density assessed by dual-energy x-ray absorptiometry (DXA), vitamin D, N-propeptide of type I collagen (P1NP), C-terminal telopeptide of type I collagen (CTX), intact parathyroid hormone (PTH) were evaluated before and after a 20-weeks intensive weight restoration therapy in patients with anorexia nervosa and secondary amenorrhoea for at least 6-months. The subjects were not receiving medications known to affect bone metabolism.
Results: Ninety-one female patients aged 13–45 years old were evaluated, baseline weight 39.4±5.6 kg and BMI 15.1±1.6 kg/m^2. Weight and BMI were significantly increased in all patients after treatment. The mean BMD values were significantly increased only at the spine (1.0±3.6%, p=0.009). A positive trend was demonstrated between post-treatment 25-OH-D and BMD changes at the spine (p=0.032). However, only the patients with post-treatment 25-OH-D ≥30 ng/ml showed significantly higher increases in BMD at the spine (2.5% vs 0.5% respectively for 25-OH-D ≥30 ng/ml and 25-OH-D <30 ng/ml, p<0.03; Figure 1). Both P1NP and PTH increased, whereas a significant decrease was found in 25-OH-D and CTX ($p<0.05$). Post-treatment CTX levels were inversely correlated with spine BMD. A positive relationship was found between changes in weight and P1NP (R2 =0.27).



Conclusions: In anorexia nervosa, a hypovitaminosis D status counteracts the efficacy of the weight restoration treatment because of an increase in bone resorption mediated by a secondary hyperparathyroidism. Our study strongly support the use of vitamin D supplements for bone health in anorexia nervosa.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3793

FRI0536 THE METHOD OF CALCULATING THE PROBABLE VALUE OF T-SCORE IN PATIENTS WITH MULTIFOCAL ATHEROCALCIFICATION

A.N. Kokov, V. Masenko, S. Semenov, O. Barbarash. *Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation*

Objectives: To determine probable value of T-score for early detection of osteopenic syndrome in patients with multifocal atherosclerosis based on the multislice computed tomography (MSCT) evaluation of vascular calcification.
Methods: 186 male (60±6,7 years) with multifocal atherosclerosis. All the patients underwent the measurement of BMD with X-ray absorptiometry. Moreover, calcium scores (CS) of coronary and brachiocephalic arteries were obtained using Agatston method.
Results: T-score values of lumbar vertebrae -1.07 [-1.54;-0.40], T-score of the proximal femur -2.01 [-2.71;-1.49]. Calcification of the coronary arteries: CS=471.8 [118.2;916,8] and carotid arteries: CS=113.9 [44.5;300.8]. Factors that affect the

probable value of T-score in patients with known rates of calcification of the coronary and carotid arteries were obtained by regression analysis. These factors were equivalent density of coronary calcinoses (p=0,0046), the volume of the carotid calcifications (p=0,0039), the mass of calcifications of the carotid arteries (p=0,0054) and the presence of a stenosis of the carotid arteries (p=0.0001).The predictive model for estimating the probable value of T-score has been is designed using regression coefficients of each of the factors. The value is equal to the Fisher statistic F=9,52, p-value <0.000001, multiple correlation model's coefficient is 0.753.

Conclusions: The results of this study indicate that rates of calcification of the carotid and coronary arteries, resulting in the planned survey on MSCT patients with multifocal atherosclerosis have a high predictive capacity for assessing the probable value of the T-score and early detection of osteopenic syndrome in these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5654

FRI0537 PREVENTION STRATEGY OF OSTEOPOROTIC FRACTURES IN PORTUGAL: AN ANALYSES ON A COHORT OF HIP FRACTURED PATIENTS

A. Daniel[1], M.L. Marques[1], L. Brites[1], C. Torres[2], A. Marques[1], J.A. Pereira da Silva[1]. *[1]Rheumatology Unit, Centro Hospitalar e Universitário de Coimbra; [2]Rheumatology Unit, Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal*

Background: Despite the fact that Portugal has one of the lowest rates of hip fractures in Western Europe, more than 10.000 patients are admitted every year to the Portuguese National Health Service due to hip fragility fractures. The burden of the problem will tend to increase in coming years, unless effective preventive measures are put in place.[1]

Objectives: The aim of our work was to evaluate the percentage of patients under osteoporotic treatment (OT) before and after a hip fracture (HF) and compare these results with the percentage of patients who should be under treatment, according to FRAX model and Portuguese cost-effectiveness guidelines (PG) for OT.[1]

Methods: Patients diagnosed with a HF, between May 1st and October 31st 2013, from a single tertiary hospital, were included in this transversal study. Patients or their primary caregiver were contacted by phone to gather data regarding demographic and clinical features, including risk factors for Osteoporosis (OP) defined by FRAX®. Clinical data was obtained from medical files.

FRAX® without mineral bone density was used to calculate the 10 year fracture risk. For each patient the FRAX® was scored according to data available the day before the present HF (ie the current fracture was not considered as a previous fracture for the purpose of risk prediction). Thresholds for therapeutic intervention were defined according to PG: a 10-year probability of a major osteoporotic fracture (OF) ≥11% and/or a 10 year probability of HF ≥3%[1].

Results: The mean age of the population (n=130) was 81.6±8.6 years, and 69.2% were female. Before the current HF, only 23 (17.7%) of the patients had been prescribed some form of medication for OP: bisphosphonates (n=2), strontium ranelate (n=3) and calcium + vitamin D supplementation (n=13); the other patients or caregivers didn't specify the ongoing medication.

About 65 patients had a previous fracture, of which 8 patients had ≥1 fragility fracture of the hip; 6 had ≥1 symptomatic vertebral fragility fracture and 16 had ≥2 fragility fractures, independently of the site of the fracture. According to PG, all these 30 (26%) patients should be under OT without the need for FRAX® risk calculation.

The mean 10-year major OF probability was 21.2±14% and the mean 10-year HF probability was 13.7±12.9%. According to FRAX®, 104 (80%) of the patients had indication to start OT based on the 10-year risk of major OF and 117 (90%) based on the 10-year risk of HF.

After hospitalization, although all the patients had formal indication for treatment, only 11 (8.5%) patients had received a prescription for OT up to one year after the fracture event.

Conclusions: Similar to other countries, the percentage of patients under OT (before and after HF) in Portugal is extremely low. Risk estimation by FRAX® and application of current PG would allow clinicians to identify these patients and introduce appropriate preventive measures. Continued efforts are needed to promote timely prevention, most especially after the first fragility fracture.

References:

[1] Marques A, Rodrigues AM, Romeu JC et al. Multidisciplinary Portuguese recommendations on DXA request and indication to treat in the prevention of fragility fractures. Acta Reumatol Port 2016;41:305–321.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3277

FRI0538 EVALUATION OF FACTORS THAT INCREASE FRACTURE RISK IN BREAST CANCER

A. Anand[1], M. Ghafouri[2], M. Bukhari[1]. *[1]University Hospitals of Morcambe Bay NHS Foundation Trust; [2]Lancaster University, Lancaster, United Kingdom*

Background: Women with breast cancer are at an increased risk of fractures. This is present in patients with both active and treated disease. In addition to established risk factors of fractures, patients with breast cancer are exposed to additional factors that further compromise bone strength. These factors primarily include: the malignancy interfering with bone metabolism and breast cancer treatments inducing bone loss.

Objectives: To evaluate fracture risk in active and treated breast cancer patients, and to understand the role bone mineral density (BMD) plays in predicting fracture risk.

Methods: The study population included breast cancer patients with active and treated disease referred to dual-energy X-ray absorptiometry (DEXA) scanning at the Royal Lancaster Infirmary between 2004–2015. Patients on aromatase inhibitors were excluded because of its' negative effect on oestrogen.

From this population, we collected BMD measurements of the femur and lumbar vertebra. Alongside information on physical characteristics such as age, height, weight, body mass index (BMI), average tissue thickness, lean and fat mass were measured.

To evaluate other precipitating factors known to increase fracture risk we included: smoking status, steroids use, alcohol, family history of fractures, diagnosis of rheumatoid arthritis and secondary osteoperosis.

Data analysis was done on R 3.3.2 software. Odds ratios were calculated using logistic regression and age adjusted models were compared using the likelihood ratio test. Categorical data was analysed using Chi squared and Fischer's exact test, while continuous data was analyzed using t-test.

Results: The study population was a total of 306 patients with a mean age of 63.6 years. 146 of the study group had active disease, while 160 patient were breast cancer survivors. Of the total population 87 (28%) had sustained at least one fracture.

Active breast cancer insignificantly increased fracture risk in comparison to the cancer survivor population (*OR=1.330, 95% CI=0.801–2.218, p=0.271).*

Physical characteristics that significantly increased fracture risk included increased age and decreased average fat percentage (Table 1). BMD reduction in the femoral neck and all vertebrae significantly increased odds of having a fracture (Table 2). External factors such as smoking status, alcohol consumption, family history and steroid use had no significant effect.

Table 1. Physical Characteristics and Fracture Risk

	Odds Ratio	95% Confidence Interval	*p*-value
Age	1.407	1.106–1.803	0.043
BMI	0.832	0.639–1.074	0.159
Average Tissue Thickness	0.929	0.847–1.016	0.108
Average Fat Percentage	0.069	0.005–0.883	0.040
Fat Mass	0.997	0.994–0.999	0.032
Lean Mass	1.003	1.000–1.006	0.032

Table 2. BMD Results from DEXA Scan

	Odds Ratio	95% Confidence Interval	*p*-value
Left Neck of Femur	0.035	0.035–0.309	0.002
Right Neck of Femur	0.063	0.006–0.561	0.013
Lumber Vertebra Total (L1–4)	0.063	0.013–0.285	0.0002

Conclusions: In conclusion, this study emphasizes DEXA measurements are the best predictive tool for fractures in breast cancer patients. Thus further supporting the need for increased BMD surveillance for those diagnosed with breast cancer who are not on aromatase inhibitors.

References:

[1] Body J: Increased fracture rate in women with breast cancer: a review of the hidden risk. Body BMC Cancer 2011, 11:304.

[2] R Core Team (2016). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3829

FRI0539 IMPACT OF THE IMPLEMENTATION OF A FRACTURE LIAISON SERVICE IN PHARMACEUTICAL EXPENSES FOR OSTEOPOROSIS

A. Naranjo[1], S. Ojeda[1], S. Rodriguez[2], I. Bernardos[1], A. Molina[1], F. de la Nuez[3], M. Negrin[4]. *[1]Rheumatology; [2]Geriatrics, Hospital Univ. Gran Canaria Dr. Negrin; [3]Rational Drug Use Service, Servicio Canario de la Salud; [4]Met. cuantitativos en Economia, Universidad de Las Palmas, Las Palmas de Gran Canaria, Spain*

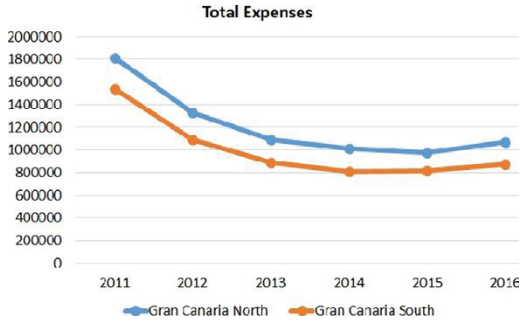
Background: In 2012 a Fracture Liaison Service (FLS) was implemented in Hospital Dr Negrin

Objectives: To analyze the economic impact of the FLS on pharmaceutical expenditure for osteoporosis.

Methods: Expenditure on osteoporosis medication (government inpunt) was collected from January 1th, 2011 to October 1th, 2016. The data distinguish group I (calcium and vitamin D), group II (Bisphosphonates, denosumab, SERM, strontium and teriparatide) and total expenditure (sum of groups I and II). Intravenous bisphosphonates were not included.

Gran Canaria island is organized in two health areas; the North and the South areas. The population aged >65 years in the North and South areas in 2016 were

63.535 and 52.453 people, respectively. In the Gran Canaria South area there is no formal FLS.
An estimate of the number of cases of fracture attended in FLS and that was still under treatment in septiembre 2016 was calculated.
Results: The total expenditure on prescriptions for osteoporosis in 2016 (January to September) in the North area was 1,226,702 €, while in the South area it was 1,069,606 € (a 14% higher in the North area). The expenditure in 2016 for group II (bisphosphonates and equivalents) was 799,840 € and 656,301 € respectively (22% higher in the North area). The evolution of the percentage of total expenditure in osteoporosis for the North area in relation to the total of Gran Canaria was the following: 53.6% in 2011; 54.2% in 2012; 54.4% in 2013; 54.3% in 2014; 53.4% in 2014 and 53.4% in 2016 (Figure). For group II drugs, the percentage of 55% for the North area did not change between 2011 and 2016.
The number of drug prescriptions for group I was 7,551 units in the North area and 7,732 in the South area. For group II, the figures were 3,917 units in the North area and 2,873 units in the South area. That is, the prescription of group I drugs in the January-September 2016 period was similar in both areas (2% higher in the South area), while for Group II it was 36% higher in the North area, being this difference stable between 2011 and 2016.
Between 2012 and 2016, 1,297 patients have been evaluated in the FLS, of which 75% have indication of bisphosphonate or equivalents. The average adherence to treatment at 12 and 24 months is 70% (1). The estimate is that approximately 681 patients (17%) of the 3,917 who receive a drug from group II in the North area in October 2016 derivates from the FLS.



Conclusions: The implantation of a FLS, despite supposing around 16% of the percentage of patients treated with bisphosphonates and equivalents in the health area Gran Canaria North derivates from the FLS has not led to an increase in pharmaceutical expenditure for osteoporosis. We believe that one of the reasons for the non-increase in spending is the rational use of drugs for osteoporosis.
References:
[1] Naranjo A et al. Osteoporos Int. 2015;11:2579.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1485

FRI0540 EVALUATION OF BONE QUALITY USING THE NEW TRABECULAR BONE SCORE (TBS) TOOL IN RHEUMATOID ARTHRITIS PATIENTS

A. Casabella[1], A. Sulli[1], C. Seriolo[2], G. Botticella[2], L. Molfetta[2], M. Cutolo[1], S. Paolino[1], B. Ruaro[1]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS AOU San Martino; [2]Osteoporosis, Bone and Joint Disease Researc Center, CROPO, Di.M.I., University of Genova, Genoa, Italy*

Background: Patients affected by Rheumatoid Arthritis (RA) show an increased risk of low bone mass, as a result of multi-systemic disorders including toxic drug, low vitamin D levels and physical inactivity. Trabecular Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) images, that provides an indirect measurement (Score) of bone axial microarchitecture and allows to get information about bone quality (1,2).
Objectives: The aim of this investigation was to evaluate bone quality in RA patients (high risk population) receiving vitamin D supplementation from at least 3 month, using the TBS.
Methods: 108 female patients (mean age 61±8 years) affected by RA and 60 age- matched controls (CNT) (mean age 64±11 years) were enrolled. Bone Mineral Density (BMD, g/cm^2) of the lumbar spine (L1-L4) was analyzed using a DXA scan (GE,Lunar Prodigy). Lumbar spine TBS (TBS iNsight Medimaps) was derived for each spine DXA examination. All patients were evaluated for serum 25 hydroxyvitamin D (25(OH)D) concentrations.
Results: 78 RA patients (80%) presented a bone loss that was significantly lower when compared with control group ($p<0.001$). Likewise, lumbar spine TBS score was found significantly lower in RA patients compared with CNT ($p<0.001$). Finally, RA patients showed lower 25(OH)D concentrations (18.4±1.3 ng/ml) than CNT (26.2±0.9 ng/ml; $p<0.04$).
Conclusions: This study shows in RA patients a reduction of TBS values that seem placed side by side with reduced BMD values and 25(OH)D serum concentrations. Therefore, TBS could become a new and safe diagnostic tool for the quantification of the bone quality and related osteoporosis, in chronic systemic inflammatory rheumatic diseases, such as RA.
References:
[1] Sinigaglia L, et al. Rheum Dis Clin North Am. 2006;32:631–58.
[2] Avouac J, et al. Arthritis Care Res 2012;64:1871–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6126

FRI0541 RELATIONSHIP BETWEEN CHRONIC PERIODONTITIS AND BONE MINERAL DENSITY IN A CASE-CONTROL STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS AND NON-INFLAMMATORY JOINT DISEASE

J.L. Garnier Rodríguez[1], J. González Febles[2], S. Dadlani[1], M.A. Gómez[3], A. González Díaz[3], L. Expósito Pérez[4], E. Trujillo[4], M. García González[4], B. Rodríguez-Lozano[4]. *[1]Odontology/Periodontology, Dental Clinic Dr Garnier, Santa Cruz de Tenerife; [2]Periodontology, UCM, Madrid; [3]Nuclear Medicine Department; [4]Rheumatology, Hospital Universitario Canarias, Tenerife, Spain*

Background: The association between two chronic inflammatory diseases such as rheumatoid arthritis (RA) and periodontitis (PD) may be explained by causal and noncausal pathways. A possible mechanism in the increased PD observed in patients with RA is systemic bone loss due to the inflammatory process itself among others factors. Several studies have reported associations between OP and PD, not confirmed in other studies.
Objectives: 1.To determine whether OP is associated with PD and with PD severity.
Methods: Observational cross-sectional, case-control study of RA patients ≥18 y.o. meeting ACR/EULAR 2010 criteria for RA in a Rheumatology Dept. and a control group with a non-inflammatory joint disease, with at least 4 teeth, without dental prophylaxis or antibiotic intake 6 months before. Socio-demographic and anthropometric variables with smoking status,Graffar scale, stress level, annual dental prophylaxis, and co-morbidities such as diabetes mellitus (DM), dyslipidemia (DS), ischemic cardiovascular disease (ICD) and history of low-impact fractures. Dual-energy x-ray absorptiometry (DXA) (g/cm^2) was performed with a DXA LUNAR (GE HealthCare) in lumbar spine and femoral neck. Periodontal Variables included plaque index, bleeding on probing, probing pocket depth, recession, clinical attachment level (CAL). Full mouth CAL and periapical x-rays were taken. CAL was classified according to the European Workshop in 2005 (Tonetti), into level 0 (absence), TL1 (mild), TL2 (severe). Statistical Analysis: t-student test, Kruskal Wallis, Chi-square with Stata 13.1.
Results: We studied 344 patients: 187 RA (147 F/40 M) and 157control (101F/56M). Both groups were comparable in age 54.9 (17.9) y.o., body mass index 27.8 (4.6), stress level, DM and ICD. Differences in gender (>no. of males in controls), socioeconomic status (lower level in RA), >no. of current and former smokers RA (19.2%vs 8.9%/24.6%vs 11.5%),OP (23.4% RA vs 7.8%), DS (hipertrygliceridemia 11.2% RA vs 4.4%). PD was found in 97.3% of RA patients vs 66.2% of controls. DEXA was performed in 303 patients: 163 RA/140 controls that showed OP in 38 (23.3%) and 13 (9.3%) of RA and control groups as well as osteopenia in 47 (32.4%) and 16 (11.3%) respectively ($p<0.001$); 81% of these patients presented PD. There was association between PD and OP/osteopenia, so patients with PD had greater abnormal BMD 88% vs 76.3% with normal BMD; patients without PD showed greater normal BMD with statistically significant difference (23.7% vs 11.1%) (p=0.008).
Conclusions: 1. PD was observed in 81% of the patients evaluated with BMD; of these, 89% had OP/ osteopenia, and among the patients without PD a significant normal BMD predominated. 2. PD was found in 97% of RA patients *versus* 66% of controls; similarly OP was present in 23.3% of RA patients *versus* 9.3% of controls, with the diference being significant. 3. There was no association between BMD and PD severity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5485

FRI0542 PREVALENCE OF VERTEBRAL BODY DEFORMITIES RELATED TO OSTEOPOROSIS IN PATIENTS WITH NON-TRAUMATIC LUMBAR OR DORSAL ACUTE PAIN

C.A. Guillen-Astete, C. Pijoán-Moratalla, J.R. Quiñones-Torres. *Rheumatology Department, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Presence of vertebral body deformities is considered a relevant issue in order to chose a particular treatment in patients with osteoporosis. However, only remarcable deformities are properly identified and registred while those, less striking can just be unnoticed in radiological studies not related to osteporosis studies. One of the most usual radiographic study of the axial skeleton is the lumbar and dorsal acute pain. This group of patients is, indeed, suitable stablish proportions of any grade of vertebral body deformities according to the Genant scale.
Objectives: The goal of present study is to determine prevalence of vertebral body deformities in postmenopausial patients radiologically assessed due to lumbar or dorsal non traumatic related pain.
Methods: We performed a simple randomization of the registries of female patients with 65 years old or more who consulted due to dorsal or lumbar

non-traumatic acute pain, between 2014 and 2015. All included registries must had a radiological assessment. The gathering of registries concluded after reach 120% of the estimated sample size for a non finite theoretical population, a precision of 3% and a hypothetical estimated prevalence of 7% based on local previous studies of prevalence of vertebral osteoporotic fractures. Vertebral body measures were performed according to Genant scale recommendations from D7 to L5 as far as possible according to the field of study of the radiological chart plate.

Results: 275 randomized registries of dorsal and lumbar pain were included (total=550). Among patients with dorsal pain we identified 62 (22.5%), 30 (10.9%) and 18 (6.5%) vertebral deformities grade I, II and III respectively. Among patients with lumbar pain we identified 31 (11.2%), 49 (17.8%) and 33 (12%) vertebral deformities grade I, II and III respectively. Prevalence of any grade of dorsal vertebral deformity was 40.00% (CI 34.39 – 45.89) and lumbar was 41.09% (CI 95% 35.44 – 46.99). Lumbar vertebral body deformities grade I and II summed 70.7% while dorsal grade I and II summed 83.6%. From the 93 vertebral body deformities grade I, 6.4% were recognized in their clinical histories, 20.2% of the grade II deformities and 92.1% of the grade III deformities, ($P<0.001$).

Conclusions: Although our population sample is circumscribed to symptomatic patients, our results contribute with prevalence of vertebral body deformities in postmenopausal patients grade I and II and who were mostly unnoticed. Proper identification of vertebral body deformities in patients with osteoporosis is crucial to decide treatment strategies in patients with known osteoporosis. Due to that, prevalence studies of this kind are relevant and useful to avoid diagnostic mistakes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5605

FRI0543 WHICH FACTORS CAN HELP PREDICT FRAGILITY FRACTURES IN PATIENTS DIAGNOSED WITH INFLAMMATORY BOWEL DISEASE? A CASE-CONTROL STUDY

D. Ahmed[1], M. Bukhari[2]. *[1]Lancaster Medical School; [2]Rheumatology, University Hospitals of Morecambe Bay NHS Trust, Lancaster, United Kingdom*

Background: Inflammatory Bowel Disease (IBD) is a known risk factor for developing low bone mineral density (BMD) osteoporosis, due to malabsorption and treatment with steroids. These patients are more susceptible to fragility fractures. Though the percentage of such fractures is low, they can be associated with impaired mortality and morbidity. The difficulty lies in early detection of patients at an increased risk of fractures. Currently the diagnosis of osteoporosis and predictions of fracture risk are calculated assessing patient BMD on dual energy X-ray absorptiometry (DEXA). However, previous studies suggest that despite a decreasing BMD being significantly associated with an increased risk of fracture, its measurement alone is fairly restricted in predicting them; other patient factors must also be brought into consideration (1).

Objectives: To identify specific factors which may assist in the prediction of fragility fractures in a cohort of patients diagnosed with IBD.

Methods: Patients referred to a DEXA scan in the North West of England were identified and those with a referral reason of IBD were studied. Factors measured at BMD scanning include patient age, height, weight, lumbar and femoral head bmd, BMI, smoking history, alcohol use, family history of fractures, steroid exposure, rheumatoid arthritis and secondary osteoporosis. Patients where assorted into cases and controls after adjusting for age and gender. They were then analysed using T tests for continuous variables and Chi squared tests for categorical variables. Univariate and multivariate logical regression models were then utilised to identify factors predicting fractures.

Results: 938 patients were identified of which 721 (76.9%) were female with an average age of 58 as compared to an average age of 53 in men. 274 patients (29%) had fractures of which 238 were females (87%), at an average age of 63 compared to 60 in men. Men were shown to have a greater risk of fractures. Results of the univariate analysis are shown below.

Predictor	All Pts	Pts with Fracture	Pts without Fracture	P-value	Odds ratio (95% CI)
Age at scan	56.8	62.5	54.5	0.00	1.03 (1.03–1.05)
Height	163.7	161.2	164.7	0.21	0.99 (0.96–1.01)
Weight	71.6	70.0	72.2	0.63	0.99 (0.99–1.08)
Alcohol	52	16	36	0.24	1.48 (0.77–2.82)
Smoking	373	109	264	0.69	1.06 (0.79–1.44)
Family History	169	53	116	0.34	1.19 (0.81–1.74)
RA	49	20	29	0.20	1.49 (0.81–2.75)
Secondary op	108	40	78	0.93	1.02 (0.66–1.56)
Left Femoral Neck BMD	0.87	0.82	0.89	0.00	0.11 (0.04–0.31)
Right Femoral Neck BMD	0.92	0.86	0.94	0.00	0.19 (0.62–0.58)
Lumbar Spine BMD	1.22	1.01	1.10	0.00	0.10 (0.44–0.24)
BMI	28.7	26.9	26.6	0.96	0.99 (0.97–1.03)
Steroid	617	134	483	0.00	0.49 (0.36–0.67)

In the multivariate analysis, statistically significant variables were BMI (OR 1.05, 95% CI 1.01–1.08) and steroids (OR 0.49, 95% CI 0.35–0.69) with steroids being protective against fractures.

Conclusions: In the univariate analysis several risk factors are shown to be associated with fractures. These include femoral neck BMD, steroid use, lumbar BMD and the patient age at the time of the scan. The multivariate analysis showed that the biggest predictor after adjusting for age and gender is steroids and BMI with steroids being protective.

References:

[1] Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ. 1996;312(7041):1254–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4013

FRI0544 CLINICAL AND DEMOGRAPHIC PROFILE OF PATIENTS CONSULTING FOR FRAGILITY FRACTURES IN A HOSPITAL IN COLOMBIA DURING THE YEARS 2014-2016: IMAGE OF THE COLOMBIAN HEALTH SYSTEM

D.G. Fernández-Ávila, D.N. Rincón-Riaño, D. Pinzón, J.M. Gutiérrez. *Rheumatology, Hospital Universitario San Ignacio - Pontificia Universidad Javeriana, Bogotá, Colombia*

Background: Osteoporosis represents a major public health problem due to the seriousness of a patient's main complication: fracture. The lack of the Colombian health system for a structured public policy aiming diagnosis and early intervention generates a high volume of patients having fragility fractures.

Objectives: To describe the clinical and demographic characteristics of patients with fragility fractures seen in our hospital. To describe the risk factors for fragility fractures. To inquire about the patient's knowledge about osteoporosis. To follow each case establishing whether after presenting the complication (fracture), the patient would receive an ambulatory treatment covered by the health insurance.

Methods: Cross-sectional descriptive study

Results: 111 patients mean age of 74.4 years (± 11.3 years), 84 (75.6%) were women. All consulted for osteoporotic fracture. The most frequent type of fracture was hip (51.4%), followed by vertebra (23.4%), wrist (22.5%) and humerus (4.5%). 87.4% (n=97) had no personal history of fracture and only 1% had a history of frailty fracture in a first-degree relative. Risk factors: 7.2% (n=8) used glucocorticoids, 3.6% (n=4) antiepileptics and 3.6% (n=4) warfarin. 21.6% (n=24) were smokers. 77.5% (n=86) had never previously undergone a densitometry despite the fact that, because of their age, they had indicated that this study had previously been performed. Knowledge of osteoporosis by patients: 49.5% (n=55) did not know that osteoporosis was present, 58.6% (n=65) did not know that fracture was the main complication of this disease and 62.2% =69) does not relate to fractures with osteoporosis. All patients were educated and sensitized about osteoporosis and the importance of diagnosis and treatment and they were given an order to perform densitometry at discharge, despite the above 24.3% (n=27) densitometry was performed in the next year of the fracture. As for treatment, 33.3% (n=37) received calcium plus vitamin D. Only 9.9% (n=11) received treatment for osteoporosis (7 patients with bisphosphonate and 4 with denosumab), none received teriparatide osteoformer therapy.

Conclusions: The present study demonstrates the lack of understanding by the Colombian patients about osteoporosis. Despite of clear indications described international guidelines, we have found a the lack of densitometry measurements on our follow up patients. More serious, only 10% of the patients received treatment for osteoporosis and none of them used a osteoformer therapy. This proves the suboptimal follow-up made by the health insurance companies of our country. Urgent educational and public health policies are needed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5625

FRI0545 COMPARISON OF MINERAL BONE DENSITY IN HIV-INFECTED PATIENTS FOLLOWED IN A SPANISH TERTIARY HOSPITAL WITH THAT OF NON HIV-INFECTED SPANISH POPULATION

F. López Gutiérrez[1], W.A. Sifuentes Giraldo[1], J.L. Casado Osorio[2], M. Vázquez Díaz[1]. *[1]Rheumatology; [2]Infectious Diseases, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Patients with human immunodeficiency virus (HIV) have a higher prevalence of low bone mineral density (BMD) and fractures than the general population, but there are no comparative studies in Spanish population.

Objectives: To assess the BMD in HIV-infected patients followed in a tertiary hospital of Madrid and compare it with the ESOSVAL cohort, which included 11035 patients and is representative of non-HIV population seen in Spanish tertiary centers.

Methods: We performed a cross-sectional study in which BMD values were determined in a prospective cohort that included HIV-infected patients seen our center during the period 2010–2015. Collected data included demography, comorbidities, treatment and densitometric variables.

Results: 93 patients from a total of a total of 924 with BMD data were eligible for the study after discarding those younger than 55 years, because that group is not included in the ESOSVAL cohort. Mean age of patients of our whole cohort was 43.8 years (range: 17–83), 11% were older than 55 years, of whom 83 were men (83%). Most of them were Caucasians, with a mean body mass index 24.1 (range: 14,7–40.6). Median time of HIV infection was 162,6 months (interquartile range [IQR]: 77.7- 283,3), median CD4+ cells nadir was 224 (IQR: 100–332) and median maximun viral load was 4,9 log (IQR: 4,3–5,4); concomitant hepatitis C

virus infection was present in 29%. 25% were treated with tenofovir plus protease inhibitors, and 47% with tenofovir plus a non-nucleoside reverse transcriptase inhibitor. The mean value of BMD in lumbar spine (LS) was 0.93 g/cm^2 (range: 0.84–1.02) and in femoral neck (FN) 0.78 g/cm^2 (range: 0.69–0.86). For the comparison with the ESOSVAL cohort the worst value of T-score in either LS or FN was chosen and patients were classified according to WHO definitions (osteoporosis ≤ -2.5, osteopenia -1 to -2.5); the results are presented in the table. Only the data for the 50–64 and 65–74 years groups were compared because the number of older HIV patients in our center was small. Significant differences were found between the categories of osteoporosis in men in the 65–74 years old group, and that of osteopenia in women in the 55–64 years old group.

	55–64y		*p*-value	65–74y		*p*-value
	HIV+ n=60	ESOSVAL n=2893		HIV+ n=16	ESOSVAL n=1555	
Males						
T-score ≤ -2,5	20%	12.6%	0.08798	44%	11.2%	0.00005*
T-score -1 to -2,5	61%	48.9%	0.02888*	63%	59.2%	0.79102
Females						
T-score ≤ -2,5	31%	21%	0.38845	50%	29,8%	0.37768
T-score -1 to -2,5	82%	50.1%	0.01296*	50%	49,7%	0.99107

Conclusions: We observed a statistically significant increase in prevalence of osteoporosis in HIV-infected men in the 65–74 years group, and in osteopenia HIV-infected men in the 55–64 years group, in concordance with the presumed greater risk derived from a variety of causes (treatment, chronic inflammatory status, comorbidities, etc.). A non significant trend towards an increased prevalence of osteoporosis in the 55–64 years group, and in osteopenia in the 65–74 years group was seen. As for women, there was a statistically significant increase in osteopenia prevalence in the 55–64 years group with HIV and a non significant trend towards increased prevalence of osteoporosis in that age group, whereas no significant increase was observed in the 65–74 years HIV group, presumably due to the small number of patients included in it.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6877

FRI0546 COMPARISON OF MINERAL BONE DENSITY AND RISK FRACTURE ASSESSED BY THE FRAX TOOL IN HIV-INFECTED PATIENTS FOLLOWED IN A SPANISH TERTIARY HOSPITAL WITH THOSE OF NON HIV-INFECTED SPANISH POPULATION

F. López Gutiérrez [1], W.A. Sifuentes Giraldo [1], M. Vázquez Díaz [1], J.L. Casado Osorio [2]. *[1] Rheumatology; [2] Infectious Diseases, Ramon y Cajal University Hospital, Madrid, Spain*

Background: The Fracture Risk Assessment Tool (FRAX) is a validated clinical fracture risk calculator that estimates 10-year risk of both major osteoporotic and hip fractures in the general population. However, its role in patients with human immunodeficiency virus (HIV) infection is still not clear because may underestimate their risk.
Objectives: To assess the bone mineral density (BMD) and 10-year fracture risk according to FRAX in HIV-infected patients followed in a tertiary hospital of Madrid and compare them with the ESOSVAL cohort, which included 11035 patients and is representative of the non-HIV population seen in Spanish tertiary hospitals.
Methods: We performed a cross-sectional study in which FRAX and BMD values were determined in a prospective cohort that included HIV-infected patients seen our center during the period from 2010 to 2015. Collected data included demography, comorbidities, treatment, risk factors required for the FRAX calculation and densitometric variables.
Results: 97 patients from a total of a total of 311 had bone densitometry data and FRAX assessment available and were included in this study. The mean age of the patients was 55.4 years (range: 50–80), 75 were men (77%), most of them were Caucasians (89%), with a mean body mass index of 24.2 (range: 15–32.7). Median time of HIV infection was 194 months (interquartile range [IQR]: 155.2- 259), median nadir of CD4+ cells was 168 (IQR: 81–308) and concomitant hepatitis C virus infection was present in 40%. Among the risk factors included in FRAX calculation, 44% reported smoking, 10% inadequate alcohol consumption and 3% hyperthyroidism; there was no history of steroid therapy or previous fractures and only one had a family history of hip fracture. The mean value of BMD in lumbar spine (LS) was 0.9 g/cm^2 (range: 0.83–0.99) and in femoral neck (FN) 0.74 g/cm^2 (range: 0.65–0.82). For the comparison with the ESOSVAL cohort the worst value of T-score in either LS or FN was chosen and the patients were classified according to WHO definitions; the results are presented in the table.

	Men 50–64y		*p*	Women 50–64y		*p*
	HIV (n=68)	ESOSVAL (n=2983)		HIV (n=21)	ESOSVAL (n=3043)	
T-score ≤-2,5	14%	12.6%	0.606	33%	21%	0.167
T-score -1 to -2,5	56%	48.9%	0.255	52%	50.1%	0.834
FRAX major fracture ≥10	1.8% (0.4–5.1)	0.1% (0–0.2)	0.002*	2,36% (1.3–4.1)	0.6% (0–1)	0.015
FRAX hip fracture ≥3	0.47% (0–3.5)	0.1% (0.-0.3)	0.002*	0.57% (0–2)	0.7 (0.4–1.1)	0.702

Only the data for the 50–64 years group were compared because the number of older HIV patients in our center was small. No significant differences were found between the categories of osteopenia and osteoporosis in both genders, but there was a significant difference with respect to the risk of both major and hip fractures in males, being higher in patients with HIV infection compared to the population of the ESOSVAL cohort.
Conclusions: HIV-infected patients followed in our center do not show significant differences regarding the prevalence of osteopenia and osteoporosis compared to non-HIV Spanish population represented by the ESOSVAL cohort. However, a trend towards a lesser BMD is seen in all HIV infected groups. The fracture risk estimated by FRAX is significantly higher in HIV-infected men probably due to a higher frequency of associated risk factors.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6954

FRI0547 OSTEOPOROSIS AND BONE METABOLISM IN SYSTEMIC SCLEROSIS

Á. Horváth [1], K. Gulyás [1], H.P. Bhattoa [2], G. Szücs [1], Z. Szekanecz [1], S. Szamosi [1]. *[1] Department of Rheumatology; [2] Department of Laboratory Medicine, University of Debrecen, Faculty of Medicine, Debrecen, Hungary*

Background: Systemic sclerosis (SSc) has been associated with bone loss and increased risk for bone fractures. Disease-related factors, age, corticosteroid therapy may be associated with increased bone turnover and bone loss.
Objectives: Here we performed a detailed study on osteoporosis in SSc. We performed bone density assessment by DXA, as well as peripheral forearm quantitative CT (pQCT). In addition, we assessed bone biomarkers and correlated bone- and disease-associated measures.
Methods: Altogether 44 SSc patients (36 women, 8 men; age: 64.1 years; disease duration: 17.6 years) were randomly recruited for the study. Bone density was assessed by DXA at the lumbar spine and femoral neck. pQCT (Stratec) is able to assess total, trabecular and cortical density. We also determined FRAX, levels of vitamin D, as well as bone markers (Ca, PTH, osteoclacin, P1NP, beta-CTX), markers of autoimmunity (ANA, ACA and anti-Scl70) and clinical manifestations of the disease. Statistical analysis was performed by SPSS v22.0.
Results: Vitamin D levels were lower (53.9 +/- 36.8 nM) than the normal range (>75 nM). 34 out of 44 patients (77%) had D-hypovitaminosis. Abnormally increased PTH, P1NP, OC, CTX levels were observed in 10, 7, 2 and 6 patients, respectively. Previous fractures occurred in 19 patients (43%). The vertebral and hip FRAX values were 13.5% and 4%>respectively. By DXA, osteoporosis of the lumbar spine and hip was detected in 10 and 10 patients, while osteopenia were found in 16 and 20 patients, respectively. With respect to pQCT, total and trabecular bone density in SSc patients (248.4 and 150.9 mg/cm^3) was significantly lower than in healthy controls (354 and 193 mg/cm^3, respectively). Higher OC levels were assocated with the diffuse form of SSc (R=0.330, p=0.035). Longer disease duration correlated with lower pQCT total (R=-0.341, p=0.023) and trabecular density (R=-0.336, p=0.026). Interestingly, most bone markers (P1NP, OC, CTX) positively correlated with gastrointestinal manifestations. Furthermore, pQCT total bone density was siognificantly lower in patients with pulmonary involvement, digital ulcer and anti-Scl70+.
Conclusions: A high proportion of SSc patients have osteopenia or osteoporosis, as well as low vitamin D levels. As determined by pQCT, trabecular loss is more common. Both total and trabecular bone loss, as well as bone markers may be associated with disease duration, anti-Scl70 and some organ manifestations. SSc patients should be screened and treated for osteoporosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3645

FRI0548 INFLUENCE OF HOMOCYSTEINE AND VERTEBRAL FRACTURES ON PREVALENT ABDOMINAL AORTIC CALCIFICATION IN POSTMENOPAUSAL WOMEN: A MULTICENTRIC CROSS-SECTIONAL STUDY

I. Ghozlani [1], A. El Maataoui [2], M. Ghazi [3], A. Kherrab [3], R. Niamane [3]. *[1] Rheumatology Department, Military Hospital; [2] Chemistry-Biochemistry Department, Faculty of Medicine and Pharmacy, Ibn Zohr University, Agadir; [3] Rheumatology Department, Military Hospital Avicenne, Marrakech, Morocco*

Background: Osteoporosis and cardiovascular diseases are two major public health problems. Both are associated with high morbidity, long-term hospitalization, mortality and loss of independence leading to institutionalization. Vertebral morphometry using dual-energy X-ray absorptiometry (DXA) also known as vertebral fracture assessment (VFA) is a fast, low-radiation technique which produces images that are of sufficient quality to be used to diagnose the presence of vertebral deformity consistent with fracture. VFA has demonstrated utility for vertebral visualization and thus is an important tool for fracture detection in women and men. It has been shown also in many populations that this technique can simultaneously identify abdominal aortic calcification (AAC). Hyperhomocysteinemia, a condition that recent epidemiological studies have shown to be associated with increased risk of vascular disease. A potential role of homocysteine in bone fragility has been considered from the observation of a high prevalence of osteoporosis in subjects with homocystinuria.

Objectives: The main of this study was to examine the relationship between plasma homocysteine (Hcy), asymptomatic osteoporotic vertebral fractures (VFs) using vertebral fracture assessment (VFA) and prevalent abdominal aortic calcification (AAC) in Moroccan postmenopausal women.
Methods: The study cohort consisted of 188 consecutive postmenopausal women with no prior known diagnosis of osteoporosis or taking medication interfering with bone metabolism. Mean age, weight, height, body mass index and plasma homocysteine were determined. Lateral VFA images and scans of the lumbar spine and proximal femur were obtained using a Lunar Prodigy Vision densitometer (GE Healthcare Inc., Waukesha, WI). VFs were defined using a combination of Genant's semiquantitative approach and morphometry. VFA images were also scored for prevalent AAC using a validated 24 point scale.
Results: Fifty-eight (30.9%) patients had densitometric osteoporosis. VFs were identified using VFA in 76 (40.4%) patients: 61 women had grade 1 VFs and 15 had grade 2 or 3 VFs. One hundred twenty nine women (68.6%) did not have any detectable AAC, whereas the prevalence of significant atherosclerotic burden defined as AAC score of 5 or higher, was 13.8%. A significant positive correlation between AAC score and homocysteine was observed. Women with extended AAC, were older, had a lower weight, BMI and BMD, higher homocysteine levels and more prevalent VFs than women without extended AAC. Multiple regression analysis showed that the presence of extended AAC was significantly associated with Age and grade 2/3 VFs and not independently associated with homocysteine levels.
Conclusions: This study did not confirm that homocysteine is important determinant of extended AAC in postmenopausal women. However, this significant atherosclerotic marker is independently associated with VFs regardless of age.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1447

FRI0549 IMPACT OF CHEMOTHERAPY ON BONE MINERAL DENSITY IN POSTMENOPATHIC WOMEN WITH BREAST CANCER IN TREATMENT WITH AROMATASE INHIBITORS

J. Loarce-Martos [1], W.A. Sifuentes Giraldo [1], L.V. Maldonado Romero [1], M. Ahijón Lana [1], C. Velázquez Arce [1], N. Martínez Jañez [2], M. Vázquez Díaz [1]. *[1] Rheumatology; [2] Oncology, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Aromatase inhibitors (AI) been related to an increased risk of bone loss and fractures in women receiving these drugs as adjuvant treatment, but few studies have assessed the impact of prior chemotherapy (CT) on bone mineral density (BMD) loss associated to AI.
Objectives: To assess the impact of CT prior to the initiation of AI on BMD in postmenopausal patients with breast cancer (BC) seen at a Spanish tertiary care hospital.
Methods: We perform a longitudinal study in patients who received AI after initial CT (CT group) or as adjuvant therapy without prior CT (non-CT group) followed up for 12 months. BMD was assessed by DXA in lumbar spine (LS) and femoral neck (FN) at baseline and after 12 months of AI treatment following the usual protocol of our center, with in vitro coefficient of variation of 1% in both locations and estimated minimal significant change (MSC) of 0.0223 g/cm^2 in LS and 0.0288 g/cm^2 in FN. Demographics, neoplastic disease data, and osteoporosis risk factors were also collected.
Results: 69 patients (CT group 39, non-CT group 30) attended at our center between August 2011 and December 2014 were included. Mean age at diagnosis was 59.9±7.7 years, most of them have BC stages I-II (84%). Most frequent AI in both groups was letrozole (95%). Baseline characteristics were similar, except for age at diagnosis that was significantly higher in the non-CT group, these data are presented in the table. Mean BMD at the start of AI was significantly lower in LS in the CT group (0.7793 g/cm^2) than in the non-CT group (0.8483 g/cm^2) (p=0.018), but no difference in FN (CT 0.6764 g/cm^2 and non-CT 0.7077 g/cm^2, p=0.123). A significant difference in LS (CT 0.7685 g/cm^2, non-CT 0.8397 g/cm^2, p=0.003) was found in the comparison of BMD means between the two groups at 12 months but not in FN (CT 0.6598 g/cm^2, non-CT 0.6689 g/cm^2, p=0.369). After 12 months of treatment with AI, mean BMD change in the CT group in LS was -0.0107 g/cm^2 (95% confidence interval [CI] -0.0269, +0.0055, p=0.189) and in FN -0.0165 g/cm^2 (95% CI: -0.0339, +0.0009, p=0.063), while in the non-CT group the means changes were in LS -0.0085 g/cm^2 (95% CI -0.0416, +0.0244, p=0.599) and FN -0.0388 g/cm^2 (95% CI -0.0707, -0.0068, p=0.019). During the study period there was a fracture in each group (CT 2.6%, non-CT 3.3%).

	CT group (n=39)	Non-CT group (n=30)	p-value
Age at diagnosis, years (mean ± SD)	58.2±7.3	62±7.9	0.042*
Age of menarche, years (mean ± SD)	12.5±1.2	12.5±1.1	0.980
Age of menopause, years (mean ± SD)	48±4.2	48.9±4.1	0.394
Age >65 years	13 (33%)	9 (30%)	0.284
Body mass index (mean ± SD)	25.8±6	27.6±4.3	0.184
Osteopenia/osteoporosis before AI	35 (89%)	26 (86%)	0.692
Smoking	5 (13%)	2 (6%)	0.401
Previous fracture	2 (5%)	2 (7%)	0.786
Family history of fracture	2 (5%)	2 (7%)	0.786
Calcium + Vitamin D Supplements	26 (67%)	14 (47%)	0.095
Radiotherapy	27 (69%)	23 (77%)	0.493
Prior tamoxifen	5 (13%)	3 (10%)	0.717
Bisphosphonates	2 (5%)	1 (3%)	0,717

Conclusions: Our results do not demonstrate that CT prior to AI treatment significantly decreased BMD during the first year. Mean change in both LS and FN in CT group was not superior to MSC nor to the change in non-CT group, although they had a significantly lower mean BMD in LS than the latter group and this difference was maintained at the end of the study period.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6391

FRI0550 MALE PATIENTS WITH RHEUMATOID ARTHRITIS HAVE AN INCREASED RISK OF OSTEOPOROSIS: FREQUENCY AND RISK FACTORS

J.-H. Park [1], S.-G. Lee [1], E.-K. Park [1], S.-M. Kweon [1], D.H. Sohn [2], Y.-K. Kim [3], H.-S. Tag [3], G.-T. Kim [3], J.-W. Lee [4]. *[1] Internal Medicine, Pusan National University School of Medicine, Pusan National University Hospital; [2] Microbiology and Immunology, Pusan National University School of Medicine; [3] Internal Medicine, Kosin University College of Medicine; [4] Internal Medicine, Busan St. Mary's Hospital, Busan, Korea, Republic Of*

Background: Osteoporosis is a well-known extra-articular manifestation of rheumatoid arthritis (RA) and almost 2 times higher prevalence of osteoporosis was reported in female patients with RA than in healthy subjects. Accordingly, patients with RA are at increased risk of fragility fractures that lead to significant morbidity and mortality and higher healthcare cost. However, most previous epidemiologic studies regarding osteoporosis in RA have focused on female subjects, and little attention has been given to male patients with RA.
Objectives: To compare the prevalence of osteoporosis between male patients with RA and healthy subjects and to identify the risk factors of osteoporosis in male patients with RA.
Methods: By using a cross-sectional design, we recruited 76 male patients with RA aged 50 years and over and 76 sex-matched and age-matched healthy subjects at a university-affiliated rheumatology centre in South Korea from August 2014 to August 2016. We measured bone mineral density (BMD) at L1–4 levels of the lumbar spine and the hip (femoral neck and total hip) in all the subjects by using dual-energy X-ray absorptiometry (DEXA). We assessed the prevalence of osteoporosis defined as a T-score of ≤-2.5 according to the WHO criteria. We also investigated potential risk factors of decreased BMD and the presence of osteoporosis in male patients with RA using linear and logistic regression analyses, respectively.
Results: The mean age and body mass index (BMI) of the male patients with RA were 64.5 years and 22 kg/m^2, respectively, which were comparable with those of the healthy controls. The overall prevalence of osteoporosis at either the spine or the hip in the male patients with RA was significantly higher than that of the healthy controls (22.4% vs 10.5%, respectively; p=0.049). However, no significant differences in the prevalence of osteoporosis at the spine (19.7% vs 10.5%, respectively; p=0.113) and the hip (3.9% vs 0%, respectively; p=0.245) were found between the patients with RA and the controls. For the male patients with RA, the median disease duration was 37 months, the mean 28-joint Disease Activity Score using erythrocyte sedimentation rate (DAS28-ESR) was 3.28 and the median modified total Sharp score was 6. An increased titre of anti-cyclic citrullinated antibody showed a trend toward lower L1–4 BMD (β=-0.0007, p=0.057) in the multivariable linear regression analysis. In addition, DAS28-ESR of >3.2 was independently associated with the presence of osteoporosis (OR=3.85, 95% CI=1.13–13.17, p=0.032) after adjusting for confounding factors. The patients with RA whose BMIs were ≤22 kg/m^2 had a higher risk of osteoporosis (OR=3.43, 95% CI=1.04 -11.33, p=0.043).
Conclusions: Similar to their female counterparts, the frequency of osteoporosis in male patients with RA had an osteoporosis prevalence of about 2.1 times higher than that of the healthy subjects. Increased DAS28-ESR was an independent risk factor of osteoporosis. Our data suggest that appropriate management for osteoporosis in patients with RA is crucial not only for postmenopausal women, but also for men aged 50 years and over.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3061

FRI0551 USE OF GLUCOCORTICOID IS THE RISK FACTOR FOR INADEQUATE RESPONSE TO THE TREATMENT OF OSTEOPOROSIS BY DENOSUMAB

K. Orita [1], T. Koike [2]. *[1] Orthopaedic Surgery, Shirahama Hamayu Hospital, Shirahama Foundation for Health and Welfare; [2] Orthopaedic Surgery, 2. Search Institute for Bone and Arthritis Disease (SINBAD), Shirahama Foundation for Health and Welfare, Shirahama, Japan*

Background: In treating rheumatoid arthritis (RA), T2T (treat-to-Target) is the most reliable treatment strategy. Recent reports have indicated that reaching normal levels of bone mineral density (BMD) might be important for the prevention of fractures in osteoporosis treatment (reference 1 and 2).From this fact, there might be a possibility that T2T targeting BMD might be feasible also in osteoporosis treatment. In doing so, medicines with the ability to sufficiently increase BMD at a fast speed should be needed. Denosumab (DMAb) specifically inhibits the receptor activator for nuclear factor-kappa B ligand (RANKL) improves BMD rapidly at lumbar or hip. Therefore, DMAb is one of candidate drugs for T2T

practice, and it is very important to know risk factors that attenuate its effect in the treatment of osteoporosis.
Objectives: The aim of this study was to identify risk factors for inadequate response to the treatment of osteoporosis by DMAb.
Methods: Sixty-six patients treated with DMAb were observed retrospectively for one year. The mean age was 74 years, women were 91% and 36 patients with RA were included.We measured BMDs at lumbar and hip by dual-energy X-ray absorptiometry (Hologic Discovery) at baseline and one year later. We evaluated the effects of age, body mass index (BMI), use of glucocorticoide (GC), previous treatment for osteoporosis, BMD at baseline, bone metabolic markers (BAP; bone alkaline phosphatase, uNTx; urinary N-telopeptide), serum Ca and P levels and the previous vertebral fractures for inadequate response to DMAb.We defined the cases who could not gain the increase of BMD over 2% at the lumbar vertebrae and 4% at the hip as inadequate responders by taking the measurement error into account.
Results: Dose of PSL was significantly high in non-responder at non-RA trochanter and RA lumbar BMD (p=0.028, 0.006). BAP was higher in non-responder at RA lumbar BMD (p=0.007). Urinary NTX was significantly low in non-responder at non-RA lumbar and RA trochanter BMD (p=0.026, 0.048). Previous treatment for osteoporosis was significantly high in non-responder at non-RA lumbar, total hip and trochanter BMD (p=0.026, 0.022, 0.003).Multivariate logistic analysis including age, BMI, dose of PSL, BMD at baseline, BAP, uNTX, Ca and P level as confounders revealed that dose of PSL was the significant risk factors for no-response at lumbar BMD (OR0.634, 95% CI 0.433–0.93, p=0.02).
Conclusions: Patients receiving GC might not gain an adequate response to the treatment by DMAb for osteoporosis. Reducing dose of GC or altanative treatment regimen might be necessary.
References:
[1] Kuroda T. et al. J Clin Densitom 15: 392–8, 2012.
[2] Bauer D.C. et al. JAMA 174: 1126–34, 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3684

FRI0552 THE CORRELATION BETWEEN EROSION AND BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH DENOSUMAB AND BIOLOGIC DMARDS: A PROSPECTIVE COHORT STUDY

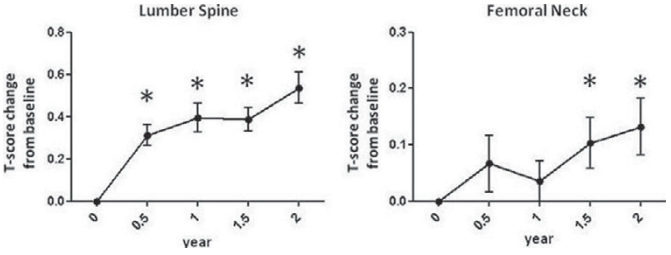
K. Izumi, Y. Kaneko, T. Hasegawa, T. Takeuchi. *Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan*

Background: We have previously reported the efficacy of denosumab combined with biological DMARDs on radiographic progression in rheumatoid arthritis (RA).
Objectives: The aim of this work was to reveal the relationship between the changes in structural joint damage and in bone mineral density (BMD) in patients with RA who were started on denosumab in addition to biologic DMARDs.
Methods: We prospectively evaluated erosion (ERO) and joint space narrowing (JSN) scores by the van der Heijde-modified Sharp method and T-scores of the lumbar spine (LS) and total hip (TH) by dual energy X-ray absorptiometry scans at baseline and 12 months in the RA patients who were started on denosumab (60 mg every 6 months) for osteoporosis in addition to biologic DMARDs. We compared the 12-month change in ERO or JSN scores (∆ERO; ∆JSN) with the change in T-scores of the LS or TH (∆LS; ∆TH).
Results: Twenty-two patients (1 man and 21 women) at the mean±SD age of 74.4±8.1 at baseline were included in this study. The T-scores of the LS and TH at baseline were -1.38±1.57 and -2.53±0.85, respectively. ∆ERO, ∆JSN, ∆LS, and ∆TH were 0.16±0.49, 0.44±0.66, 0.30±0.39, and 0.20±0.42, respectively. BMD was significantly increased from baseline to 12 months. There was a significant inverse correlation between the ∆ERO and the ∆TH (ρ=–0.473, P=0.03), while there was no correlation between the ∆ERO and the ∆LS (P=0.98) nor correlation between the ∆JSN and the ∆LS (P=0.57) or ∆TH (P=0.25).
Conclusions: The change in erosive joint damage of hands and feet showed a significant relationship with the change in femoral BMD in patients with RA treated with denosumab and biologic DMARDs. BMD was ameliorated along with erosion by denosumab combined with biologic DMARDs, and may be an indicator for joint destruction.
References:
[1] Hasegawa T, Kaneko Y, Izumi K, Takeuchi T. Efficacy of denosumab combined withbDMARDs on radiographic progression in rheumatoid arthritis. Joint Bone Spine.2016 Jun 28. pii: S1297–319X(16)30099–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2829

FRI0553 THE EFFICACY OF 2-YEARS DENOSUMAB TREATMENT FOR GLUCOCORTICOID-INDUCED OSTEOPOROSIS (GIOP)

K. Akashi[1], K. Nishimura[2], G. Kageyama[3], S. Ichikawa[1], T. Shirai[1], Y. Yamamoto[1], Y. Ichise[1], H. Yamada[1], I. Naka[1], D. Waki[1], T. Okano[1], S. Takahashi[1], Y. Ueda[1], S. Sendo[1], A. Onishi[1], J. Saegusa[1], A. Morinobu[1]. *[1]Department of Rheumatology and Clinical Immunology, Kobe University Hospital, Kobe,[2]Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, Kurashiki;[3]Department of Rheumatology, Hyogo Prefectual Amagasaki General Medical Center, Amagasaki, Japan*

Background: Osteoporosis is one of the important adverse effects in the glucocorticoids treatment for the patients with rheumatoid arthritis (RA) and connective tissue diseases (CTDs). Although the usefulness of denosmab for primary osteoporosis has been well-established, the efficacy for GIOP remains unclear.
Objectives: This study aimed to clarify the therapeutic effects of denosumab for GIOP.
Methods: We evaluated bone mineral density (BMD) and serum markers of bone metabolism (BAP, NTx, TRACP-5b and P1NP) of patients who had been treated with over 5mg of predonisolone for RA and CTDs, and denosumab for GIOP, for two years in Kobe University Hospital. BMD and serum markers were evaluated every six months for 2 years from the baseline. The changes of those data from baseline were analyzed by Student's t test using GraphPad Prism 5 software and $p<0.05$ was considered statistically significant.
Results: Number of the patients were 53 (male: 4 cases, female: 49 cases), and their characteristics at the beginning of denosumab treatment were as below; age: 64.19±12.0 years old, dose of prednisolon: 10.59±9.97mg/day, BMD of lumber spine: 0.768±0.112g/cm^3, T-score of lumber spine: -2.28±1.01, BMD of femoral neck: 0.540±0.085g/cm^3, T-score of femoral neck: -2.28±0.76. After 2-years denosumab treatment, T-scores of lumber spine (0.54±0.39 gain) and femoral neck (0.13±0.26 gain) were significantly increased from baseline (Figure; mean ± SEM. *:$p<0.05$). In addition, the serum markers of bone metabolism, both absorption and formation, were significantly suppressed with denosumab.



Conclusions: Denosumab can suppress bone metabolic turnover, and increase lumber spine and femoral neck T-scores of GIOP patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3050

FRI0554 NEW BIOMARKER FOR DIAGNOSIS OF OSTEOPOROSIS IN RHEUMATOID ARTHRITIS PATIENTS

Y. Polyakova, L. Sivordova, Y. Akhverdyan, V. Kravtcov, B. Zavodovsky. *Federal State Budgetary Institution "Research Institute of Clinical end Experimental Rheumatology", Volgograd, Russian Federation*

Background: Bone mineral density and proteins/peptides determination in blood and urine as markers of bone resorption and formation are currently used to diagnose osteoporosis (OP) and metabolic bone diseases. However, these methods have some disadvantages for bone turnover evaluation. Recent evidence suggests that in RA changes in the secretion of hormones of white adipose tissue can be revealed [2]. One of them is Adiponectin possessing anti-inflammatory, anti-diabetic and anti-atherogenic properties [1]. Changes in Adiponectin levels may reflect influence of immune inflammation on bone turnover.
Objectives: To study the clinical and diagnostic value of serum Adiponectin determination in RA patients complicated by OP.
Methods: We examined 88 women with documented diagnosis of RA and mean disease duration of 6.56±0.88 years. We used EULAR/ARA 2010 criteria to diagnose the patients. Female patients with II degree of disease activity (DAS28), Steinbrocker stage II (erosive), rheumatoid factor- and anti-cyclic-citrullinated peptide antibody-positive were prevalent. We excluded patients who had surgery or developed an infection within the last 8 weeks, pregnant and breast-feeding women, those with severe heart, liver or kidney disease, immune deficiency, leukopenia or chronic infection.
A control group of 45 healthy females aged of 25 and 59 years were included in the study. There were no reported findings of joint pain and RA symptoms in the group. The groups were adjusted for age ($p>0.05$) and showed no statistically significant differences.
We measured serum Adiponectin levels (μg/ml) using Human Adiponectin ELISA commercial test systems. We plotted a curve using computer software. We diagnosed OP using dual-energy X-ray absorptiometry with LUNAR DPX PRO (GE, USA).
Results: Serum adiponectin levels in the control group were 12.5±0.9 μg/ml (M±m). Adiponectin levels in healthy subjects measured as M ± 2d, ranged between 0.44 and 24.56 μg/ml. Patients with OP and RA had significantly higher levels of serum Adiponectin ($p<0.001$). Mean serum Adiponectin levels in RA patients who had normal bone density and had no OP were 35.21±0.6 μg/ml. Mean serum Adiponectin levels in RA/OP patients with low bone mineral density were 52.42±0.69 μ g/ml. Adiponectin levels of 44 μg/ml and higher were

associated with osteoporosis. Adiponectin levels of 43.9 μg/ml and lower were associated with normal bone density.
Conclusions: Thus, we revealed that Adiponectin levels depend on osteoporosis presence in RA patients. We suppose that Adiponectin determination may be useful laboratory marker for OP diagnosis.
References:
[1] Eliseev M.S. Revmatoidnyj artrit na Kongresse EULAR-2014 v Parizhe: novye zadachi, novye perspektivy. Revmatologija 2014;5(16):2–5.
[2] Polyakova Yu.V., Zavodovsky BV, Sivordova LE, Hakhverdyan Yu.R. Adipokiny with rheumatoid arthritis. International Scientific and Research Journal 2014;12(4):77–78.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2360

FRI0555 LEFT VENTRICULAR EJECTION FRACTION AND BONE MINERAL DENSITY AFTER CARDIAC TRANSPLANTATION

L. Bautista Aguilar, A. Salmoral Chamizo, I. Gomez Gracia, R. Jimenez Gasco, P. Font Ugalde, E.C. Lopez Medina, M.L. Ladehesa Pineda, L. Perez Sanchez, A. Escudero Contreras, E. Collantes Estevez. *Rheumatology, Reina Sofia University Hospital/IMIBIC/ University of Cordoba, Cordoba, Spain*

Background: Left ventricular ejectionfraction (LVEF) has beendirectlyassociatedwith BMD in patientswithheartfailure. Nevertheless, no study has linked yet the left ventricular ejection fraction to bone mineral density and fragility fractures in cardiac transplantation.
Objectives: The main aim of this study was to evaluate the possible relationship between LVEF and BMD in heart transplantation and the association of LVEF with 25 OH vitamin D, paratohormone (PTH) and markers of bone remodeling in patients with heart transplantation (osteocalcin, telopeptide C terminal (CTX).
Methods: Seventy nine patients (66 male) were included in this cross-sectional study with a mean age of 55,75±14,81 years, body mass index (BMI) values of 26,95±5,35 kg/m^2 and an average post-transplantation period of 8,46±8,71 years. Transthoracic doppler echocardiography measuring LVEF (%) was calculated for each of patients, as well as bone mass study that included: bone mineral density scans of lumbar spine and hip, spine radiography, biomarkers of bone metabolism (calcium, phosphorus, osteocalcin,CTX,Parathyroid hormone and vitamin D). The association of LVEF with BMD and biomarkers of bone remodeling was determined by performing multiple linear regression analysis adjusted for variables directly related to BMD (age, sex, BMI, post-transplantation period and pharmacological treatment (daily corticoids dose, immunosuppressive treatment).
Results: A total of 79 patients were included in this present study. BMD in osteoporotic range was found in 31.2% of patients (17.7% in spine,16.52% in femoral neck and 13% in hip). Vitamin D deficiency ($\leq$20ng/d) was detected in 68.4% of patients. Vertebral fracture was found in 30.4% and a 2.6% hip fracture. Bivariate analysis showed that the group of patients with FEVI $\leq$65% had a higher proportion of femoral neck osteoporosis (p=0.04), higher proportion of osteoporosis in total hip (p=0.03) and higher percentage of vertebral fractures (p=0.04) compared with group with LVEF$>$65%.
The multiple linear regression analysis indicated that LVEF was independently associated with osteoporosis in spine (B = -5.225, p=0.011), femoral neck osteoporosis (B = -5.411, p=0.015) and vertebral fractures (B = -5.433, p=0.002). In addition, LVEF was associated with osteocalcin levels (B = -0.105, p=0.002).
Conclusions: These results suggest that post-transplantation LVEF may have an influence on bone remodeling. However, further studies are neededin order to consider LVEF as a risk factor for osteoporosis and fractures due to fragility after heart transplantation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4434

FRI0556 LONG-TERM EFFECTS OF BACK EXTENSOR STRENGTHENING EXERCISES ON QUALITY OF LIFE IN WOMEN WITH OSTEOPOROSIS

S.A. Raeissadat[1], A. Khalili[2], L. Sedighipour[3], M. Heidari Almasi[4]. *[1]Physical Medicine & Rehabilitation Research Center, Modarres hospital; [2]Department of Orthopedic Surgery, Department of Orthopedic Surgery; [3]Physical Medicine & Rehabilitation Research Center, Physical Medicine & Rehabilitation Research Center; [4]Boo-Ali hospital, Tehran, Iran, Islamic Republic Of*

Background: A correlation exists between bone mineral density and physical activity level, suggesting that exercise may increase peak bone mass. Back extensor strength has been of major importance and had a strong effect on quality of life in this population.
Objectives: The aim of the present study was to evaluate the long-term effect of back extensor strengthening exercises on health-related quality of life (QOL) in women with osteoporosis.
Methods: In this randomized clinical trial, 183 women with osteoporosis were treated with pharmacotherapy and weight-bearing and balance-training exercises. The case group additionally performed back extensor exercises at home. Patients filled out the Persian version of the Short Form (SF-36) QOL questionnaire at baseline and 6 months post treatment.
Results: At the end, all physical and mental parameters of the SF-36 questionnaire improved significantly in the case group, except for one subscale of mental health, compared to the control group. In the control group, only some physical health dimensions (bodily pain, role limitation, physical function, vitality), and mental health status as a mental health subscale improved.
Conclusions: considering a major impact of back extensor exercises on improving QOL in women with osteoporosis over the long term, these exercises should be prescribed in routine management of these patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1754

FRI0557 DOES WEIGHTED KYPHO-ORTHOSIS (WKO) REDUCE RISK OF FALL IN WOMEN WITH OSTEOPOROSIS? A PRELIMINARY STUDY

S.A. Raeissadat[1], S.M. Rayegani[2], L. Sedighipour[1], M. Hashemi[2], M.H. Bahrami[2]. *[1]Physical Medicine & Rehabilitation Research Center; [2]Physical Medicine and Rehabilitation research center, Tehran, Iran, Islamic Republic Of*

Background: It was suggested that posture training support with spinal orthosis including weighted kyphorthosis can improve balance in patients with osteoporosis.
Objectives: The aim of the present study was to determine the effects of weighted kyphorthosis on improving dynamic balance tests and consequently reducing risk of fall in women with osteoporosis.
Methods: In this Randomized controlled clinical trial, twenty three patients with osteoporosis were included. The patients were assigned into two groups: 1) control group who received 4-week home-based daily exercise program and 2) intervention group (weighted kyphorthosis) who performed exercises and wore weighted kyphorthosis for one hour twice a day. Patients were assessed using computerized balance tests by Balance Master (NeuroCom) (Limits of Stability, Step Quick Turn, Sit to Stand and Walk across tests) before and 4 weeks after start of treatment.
Results: Speed in walk across test was improved significantly in both groups compared to baseline from (77.6±25 cm/s to 91.57±30 cm/s and from 72.60±20cm/s to 88.73±18 cm/s)in case and control groups respectively. Improvement in right turn time in step quick turn, end point excursion and mean of excursion parameters of Limits of Stability was more significant in orthosis group in comparison with control group ($P<0.05$).
Conclusions: Applying WKO together with exercise program improved some computerized balance tests in women with osteoporosis.WKO can be suggested as an effective intervention in postmenopausal women in order to reduce the risk of falling.
Key words: Osteoporosis, balance tests, Weighted KyphOrthoris, posture training support.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1780

FRI0558 PREDICTORS OF MORTALITY AND RE-FRACTURE AT 1 AND 3YEARS AFTER HIP FRACTURE

L. Brites, M. Marques, A. Daniel, M. Santiago, A. Marques, J. Pereira da Silva. *Rheumatology department, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal*

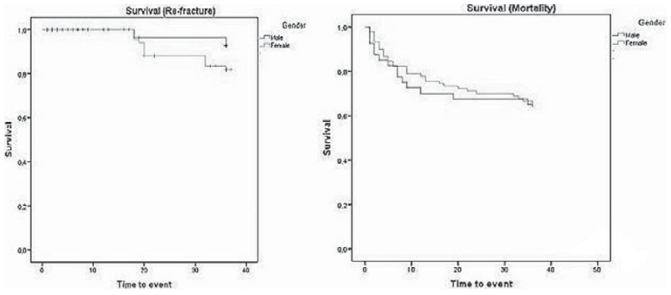
Background: Osteoporosis is a major health problem, particularly in the elderly, because of fragility fractures and their consequences. Hip fractures (HF) are the most ominous in terms of morbi-mortality.
Objectives: The aim of our work was to establish the current mortality and re-fracture rate at 1 and 3 years after HF, as well as their predictors.
Methods: The study included all patients aged $>$40 years, admitted to Coimbra University Hospital between May and October 2013 with the diagnosis of HF. Demographic and clinical data related to the fracture episode was collected from medical files. Patients or the caregiver were contacted to assess potential risk factors at baseline and major post-fracture events at 1 and 3 years after the index HF. The mortality and re-fracture rate 1 and 3 years after fracture were calculated. Possible predictor variables were tested by cox regression analysis: age, gender,

Table 1. Mortality and refracture predictors

	Mortality		Re-fracture	
	p-value	Exp (b)	p-value	Exp (b)
Gender	0,106	2,052	0,265	3,089
Age	0,002	1,075	0,276	0,953
Katz index	0,116	1,154	0,752	0,918
Physiotherapy	0,020	2,167	0,499	0,638
BMI	0,812	0,991	0,142	0,891
Parent hip fracture	0,015	0,355	0,196	0,322
Current smoking	0,453	0,615	0,394	0,417
Corticotherapy	0,013	0,404	0,639	0,637
Rheumatoid arthritis	0,071	2,848	0,798	1,410
Secondary osteoporosis	0,172	0,566	0,154	0,321
Alcohol intake	0,037	0,370	0,980	348544,658
Charlson index	0,000	1,384	0,835	0,941
Number of re-fractures	0,660	0,781		
Anti-osteoporotic treatment			0,430	0,474

physiotherapy, number of re-fractures, BMI, parent hip fracture, current smoking, corticotherapy, rheumatoid arthritis, secondary osteoporosis, alcohol, history of falls, anti-osteoporotic treatment, Katz index of independence in activities of daily living and Charlson comorbidity index. All FRAX® variables were defined as established in this algorithm.

Results: A total of 130 patients satisfied the inclusion criteria, with a mean age of 82±8,7 years, 69% being female). Mortality rates were of 30% and 41% at 1 and 3 years after HF respectively (Fig.1). Age, physiotherapy, parent fractured hip, corticotherapy, alcohol consumption (>3/day) and Charlson índex were statistically significant predictors of mortality at 3 years in multivariable analysis (Tab.1). Re-fracture rates at 1 and 3 years after the index fracture was 3,8% and 11% respectively (Fig.1). We were unable to identify any statistically significant predictors of re-fracture.



Conclusions: We concluded that HF have a great impact on the older population, leading to high morbidity and mortality. In our study, age, physiotherapy, parent hip fracture, corticotherapy, alcohol consumption and Charlson índex are related with increasing mortality in patients who suffered a fagility HF.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4473

FRI0559 CORRELATION OF THE FRACTURE RISK ASSESSMENT TOOL (FRAX) AND ASYMPTOMATIC MORPHOMETRIC VERTEBRAL DEFORMITIES IN HIV-INFECTED PATIENTS

M. Llop Vilatella[1], C. Medina Quiñones[1], C. Macía Villa[1], W.A. Sifuentes Giraldo[1], M. Vázquez Díaz[1], J.L. Casado Osorio[2]. *[1]Rheumatology; [2]Infectious diseases, Hospital Universitario Ramón y Cajal, Madrid, Spain*

Background: Patients infected with the human immunodeficiency virus (HIV) have a high rate of low bone mineral density (BMD) and is thought to be multifactorial. Some instruments have been developed to estimate the risk of osteoporotic fracture in the general population such as the WHO Fracture Risk Assessment Tool (FRAX), which allows calculating the 10-year probability of fractures in men and women from clinical risk factors with or without the measurement of femoral neck BMD. The cut-off values for high risk of hip fracture >3% and for major osteoporotic fracture >20%. Although FRAX has been validated in multiple large cohorts, still there are no clear recommendations of its use in HIV-infected patients older than 50 years.

Objectives: To evaluate the utility of FRAX tool in the prediction of risk of vertebral morphometric deformity (MVD) in HIV-infected patients over 50 years old seen in a Spanish tertiary care center.

Methods: We performed a cross-sectional study in HIV-infected patients with age 50 years treated in our centre during the period 2014–2016. Demographics and risk factors were collected through a specific survey. FRAX was calculated adding HIV as a cause of secondary osteoporosis in all patients with and without BMD measured by dual-energy X-ray absorptiometry scan (DXA). The MVD were assessed using the Genant's semiquantitative method. The sensitivity and specificity of the test were assessed and correlations made with the presence of MVD.

Results: A total of 121 patients were included, 34 women (28%), with a mean age of 54.1 years (range: 50–75). MVD was detected in 25 cases (21%). The patients presented with a mean BMI of 23.7 kg/m^2, 33% were smokers, 7% had a consumption of ≥3 doses of alcohol per day, 9% had a family history of hip fracture but no patient presented with previous history of fracture, corticoid treatment or rheumatoid arthritis. The mean FRAX score for major osteoporotic fracture without BMD was of 2.29 (1.1–8.5), there were 2 patients above 7 and any above 10; the mean FRAX score for hip fracture without BMD was of 0.64 (0.1–3.9), 2 patients were above 3. With DXA, osteoporosis in femoral neck was detected in 8% and in the lumbar spine in 30%, while femoral neck osteopenia was detected in 64% and in the lumbar spine in 45%. Including DXA data, the mean FRAX score for major osteoporotic fracture was 2.52 (0.2–8.2), 2 patients were above 7, and for hip fracture the mean FRAX score was 0.67 (0.01–4.4), with 2 patients above 3. The values of FRAX with DXA or without DXA were very similar, with a variation of -0.4 for the mean value of major osteoporotic fracture and +0.03 for the mean value of hip fracture. In ROC curve, a value above 1 in FRAX for hip fracture with DXA, detected 9 MVD of 29 patients (sensitivity 38%, specificity 80%), a value above 2 detected 4 MVD of 10 patients (sensitivity 17%, specificity 93%) and a value of 3 detected 1 MVD of 2 patients (sensitivity 4%, specificity 99%).

Conclusions: The FRAX tool does not identify properly the HIV-infected patients older than 50 years with MVD as well as the patients who need DXA. An alternative could be to perform X-rays of thoracic and lumbar spine as a screening method in HIV-infected patients with risk factors.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5205

FRI0560 PREDICTORS OF FRACTURES IN FEMALE PATIENTS WITH ANOREXIA

M. Rahm, M. Bukhari. *Rheumatology, Royal Lancaster Hospital, Lancaster, United Kingdom*

Background: Anorexia Nervosa (AN) is an eating disorder characterised by extremely low body weight and body image distortion. It is more common in females and is expected to become increasingly more prevalent. Numerous studies have found AN to have a detrimental effect on bone health. The evidence shows that anorexia is associated with reduced bone mass and strength which increases fracture risk. Few staudes have looked at other predictors of fracture in these patients.

Objectives: The aim of this study was to determine whether further predictors of fracture could be found in female patients suffering from anorexia nervosa (AN).

Methods: Female patients with anorexia refereed for a bone mineral density (BMD) DEXA scan from June 2006 to October 2014 were identified. This cohort of patients was split into two subgroups depending on their fracture status. Demographics collected on scanning and factors such as age at DEXA scan, height, weight, body fat percentage, BMI, lumbar spine L1-L4 BMD and femoral neck BMD were used to compare the fracture group against the controls. Categorical variables such as smoking, comorbidities (Rheumatoid arthritis), alcohol, family history and steroid use were compared using chi squared test and the T test was used tompare continous variables. Logistic regression models were used to model fractures unadjusted and adjusting for age at scan.

Results: A total of 193 female patients with anorexia were included: 45 (23.3%) had sustained a fracture. The results of statistical analysis are shown in Table 1. The data showed there is a significant association with having a low femoral neck BMD and increased fracture risk OR 0.036 (95%, CI 0.003, 0.497). The case group was also significantly taller OR 1.061 (95%, CI 1.009, 1.117) and older P value 0.0027 (95% combined CI 39.193, 42.682). There was no correlation with any of the categorical variables and fracture risk, see Table 2 for results.

Table 1. Results of statistical analysis of continuous variables

Characteristic	Significance (P value)	Cases with fractures	Control group
Age at scan (years)	0.0027	45.71 ±SD10.36	39.49 ± SD12.46
Height (cm)	0.021	165.08 ± SD7.45	162.66 ± SD6.82
Weight (kg)	0.129	58.16 ± SD13.68	53.73 ± SD11.83
Body Fat (%)	0.536	16.36 ± SD11.75	13.62 ± SD10.28
BMI	0.601	21.24 ± SD4.31	20.31 ± SD4.43
Lumbar spine (L1-L4) (g/cm^2)	0.053	0.98 ± SD0.18	1.03 ± SD0.14
Femoral neck BMD (g/cm^2)	0.013	0.81±SD0.15	0.86±SD0.14

Table 2. Results of statistical analysis of categorical variables

Characteristic	Cases with fracture (45)	Control group (148)	Significance (P value)
Smoker	28.9% (13)	34.46% (51)	0.445
RA	2.22% (1)	0.68% (1)	0.349
Alcohol	8.89% (4)	8.78% (13)	0.524
Family history	31.11% (14)	22.97% (34)	0.403
Steroid	15.56% (7)	8.78% (13)	0.197

Conclusions: This study demonstrates that fractures in female patients with anorexia are more likely to occur in those who are taller, older at DEXA scan and in those who have a lower femoral neck BMD. This would inidcate that cortiocal bone loss and taller stature are indepent risks in this cohort. Further work using vitamin D levels as a risk should be performed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3778

FRI0561 SAFETY OF DENOSUMAB IN POST-MENOPAUSAL OSTEOPOROSIS AND IN CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Aubailly[1], T. Barnetche[2], B. Combe[1], C. Gaujoux-viala[3], C. Lukas[1], J. Morel[1], H. Che[1]. *[1]CHU lapeyronie, Montpellier; [2]CHU bordeaux, Bordeaux; [3]CHU Nîmes, Nîmes, France*

Background: Denosumab is a RANK ligand antibody (1) used for the treatment of post-menopausal osteoporosis (OP) and prevention of bone metastases complications (2,3).

Objectives: The aim of this meta-analysis was to assess the safety of Denosumab.

Methods: Data sources included MEDLINE, EMBASE, Cochrane Library, and recent abstracts from ACR and EULAR congresses were searched until March 2016. Randomized controlled trials comparing the safety of Denosumab to placebo or bisphosphonates (BP) in postmenopausal OP and in cancer (either cancer with bone metastases or with hormone therapy) were selected. Data were

extracted by one investigator, confirmed by another, and pooled in meta-analysis using Review Manager software (Cochrane collaboration).
Results: 6136 articles were of potential interest, and 19 met the inclusion criteria. 7 articles compared the safety of Denosumab to BP in post-menopausal OP. There was no significant difference when comparing Denosumab with bisphosphonates in any adverse events (AAE) (RR=0.98, 95% CI=0.95–1.01) serious adverse event (SAE) (RR=1.04, 95% CI=0.81–1.33). Regarding Denosumab versus placebo in post-menopausal OP, 7 studies were included and there was no significant difference in AAE (RR=0.98, 95% CI=0.94–1.01), SAE (RR=1.03, 95% CI=0.96–1.11), however cellulitis was more frequently found with Denosumab (RR=8.03, 95% CI=1.44–44.79). No cases of osteonecrosis of the jaw (ONJ) had been reported. 5 articles were pooled to compare Denosumab with BP in patients with bone metastases and no significant difference was found in AAE (RR=0.99, 95% CI=0.98–1.00), SAE (RR=0.99, 95% CI=0.95–1.03), and ONJ (RR=1.40, 95% CI=0.92–2.13). 4 articles were selected concerning patients treated with placebo or Denosumab in breast and prostate cancer without bone metastases. Although no significant difference was found in AAE (RR 1.01, 95% CI=0.99–1.03), use of Denosumab was associated with a significantly increased risk of hypocalcemia (RR 5.20, 95% CI=1.34–20.13) and of cholecystitis (RR 3.43, 95% CI=1.01–11.69).
Conclusions: In post-menopausal OP, Denosumab had a relatively good safety profile although significantly more cellulitis occurred when compared with placebo. For patient with cancer, Denosumab was associated with more hypocalcemia and cholecystitis than placebo.
References:
[1] Boyle WJ, Simonet WS, Lacey DL. Osteoclast differentiation and activation. Nature. 2003;423(6937):337–42.
[2] Brown JP, Prince RL, Deal C, Recker RR, Kiel DP, de Gregorio LH, et al. Comparison of the effect of denosumab and alendronate on BMD and biochemical markers of bone turnover in postmenopausal women with low bone mass: a randomized, blinded, phase 3 trial. J Bone Miner Res Off J Am Soc Bone Miner Res. 2009;24(1):153–61.
[3] Lipton A, Fizazi K, Stopeck AT, Henry DH, Smith MR, Shore N, et al. Effect of denosumab versus zoledronic acid in preventing skeletal-related events in patients with bone metastases by baseline characteristics. Eur J Cancer Oxf Engl 1990. 2016;53:75–83.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3900

FRI0562 PROPORTION OF HIP AND NON-HIP MAJOR FRACTURES: COSTS AND QUALITY OF LIFE

M.L. Marques, A. Marques, A. Daniel, L. Brites, J.A.P. da Silva. *Rheumatology Department, CHUC, Coimbra, Portugal*

Background: FRAX® country specific risk estimates are a mainstay of current treatment decisions and public health policies in osteoporosis. Because the registries of major non-hip fractures (NHF) is poor in most countries, this estimate is based on the gender- and age-specific ratio of hip fractures (HF) to NHF observed in a prospective population-based study performed in Malmo, Sweden[1]. FRAX® presumes, therefore, that the ratio of incidence and cost of hip/major osteoporotic fractures is similar, in every country, to that observed in Sweden. This major assumption has seldom been questioned.
Objectives: This retrospective single-centre observational study aimed to assess the proportion of HF vs. NHF and the impact of wrist and vertebral fractures, in terms of costs and health-related quality of life (HrQoL), 1 year after the fracture in Portugal.
Methods: We revised the records of all patients observed in an emergency department through a period of 3 months and included those aged 50+ diagnosed with a fragility (low energy) HF or NHF. A telephone interview was conducted in a randomly selected subsample of patients from each type of fracture 1 year after fracture. A questionnaire with socio-demographic data, resource consumption over 1st year and HrQol (EQ-5D) was applied to patients or their caregivers. Direct and indirect costs were estimated from a societal perspective.
Results: In the study period, 1760 patients were observed by the orthopaedics emergency team. Of these, 435 patients had suffered a fracture (129 fragility HF, 152 NHF and 154 fractures that were not considered low-trauma and were therefore excluded). Humerus fractures were also excluded, to mirror the Swedish study. The randomly selected subsample of patients consisted of 66 NHF (55 with wrist and 11 with clinical vertebral fractures). Patients were mostly females in all types of fractures (58% to 82%). The mean age at fracture was higher in HF (81.6±8.59 vs. 69.1±10.06). Falls were the cause of fracture in 97% of cases. Inpatient care was provided to 100% of HF patients vs. 25.8% of NHF patients. The proportion of fractures, average fracture-related costs for the 1st year, and the mean impact upon HrQoL are shown in Table 1.
Conclusions: The proportion HF/NHF observed in Portugal is similar to the Swedish reference values (0.44/0.56). The highest cost were attributed to hip fractures in both countries, followed by vertebral fractures and lastly by wrist fractures. The HrQoL mean loss was higher for vertebral fractures in both countries. The reported costs of vertebral fractures are much higher than in Portugal which may significantly affect the calculation of cost-effectiveness thresholds for intervention.
References:
[1] Borgström F, et al. Osteoporos Int. 2006;17(5):637–50.
[2] Marques A, et al. Osteoporos Int. 2015 Nov;26(11):2623–30.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6942

Abstract FRI0562 – Table 1. Proportion, costs and HrQoL per type of fracture in Portugal and Sweden

	Portugal			Sweden		
Type of fracture	Hip	Wrist	Vertebral	Hip	Wrist	Vertebral
Number (%) of observed fragility fractures	129 (51)	100 (39)	26 (10)	278 (44)	276 (43)	81 (13)
Costs (€) per patient, 1st year (95% CI)	13,434 (12,290; 14,576)*	2220 (1626; 2575)	5390 (1947;6412)	14,221 (12,912; 15,790)	2147 (1923; 2477)	12,544 (10,059; 16,324)
Weighed mean cost (€)	13,434	2867		14,221	4558	
Average loss of HrQoL mean (95% CI)	0.29 (0.22; 0.36)*	0.11 (0.06; 0.15)	0.38 (0.24; 0.52)	0.23 (0.21; 0.26)	0.10 (0.08; 0.12)	0.30 (0.25; 0.36)

*Based on data published elsewhere[2].

FRI0563 USE OF TERIPARATIDE AS A CALLUS ACCELERATOR IN NONUNION OF LOWER LIMB

M. Muratore[1], O.E. Casilli[1], V. Russi[2], P. Pichierri[2], L. Meccariello[2], L. Quarta[1], E. Quarta[1], G. Rollo[2], M. Filipponi[2]. *[1]U.O. Reumatologia- P.O. "V. Fazzi" Lecce; [2]U.O. Ortopedia- P.O. "V. Fazzi" Lecce, LECCE, Italy*

Background: The use of teriparatide in fracture management by high-energy trauma with loss of bone substance and muscle and skin with possible nerve/vascular lesions is poorly documented. The aim of our study is to evaluate how the intermittent administration of teriparatide may affect the bone consolidation newly generated and compression in patients with bone loss and my-skin during treatment reconstruction with the technique of resection Ilizarov-lengthening.
Objectives: In large trauma or in the outcomes of these,in which there is loss of bone substance and muscle and skin the technique of reconstruction of Ilizarov (1 mm/day) is used; the main problem is the long time required to reach complete healing with optimal bone consolidation newly generated and the compression outbreak of ensuring the mechanical strength necessary to be able to remove the external fixator (1). The rationale of this study, therefore, was to evaluate the influence of treatment with teriparatide, administered subcutaneously 1 dose 1 time/day from a pre-filled syringe of 20mcg and for a period of three months, the evolution radiographic, on the healing time and the external fixator removal and on the functional recovery quality in multiple trauma patient.
Methods: In our prospective study, we evaluated two groups of patients: Group 1: 9 patients treated with PTH during bone transport; Control Group 2: 10 patients treated with bone transport.
Results: The group 1 compared to the 2 (control group) showed a bone radiographic progression slower newly-generated in the first month of administration of teriparatide; subsequently it was observed an acceleration of bone maturation but not uniform; after about 3 months, the bone maturation accelerates further also at the level of the compression outbreak if already in compression, allowing the removal of the fixator about 1.5 months earlier than the estimated time. This is due to the reduction of the time allowed for "elongation stage" bone that physiologically is around 1mm/day, thus ensuring an optimal functional recovery.
Conclusions: The action of teriparatide (2) on bone healing is derived from increased differentiation of cells responsible for bone callus formation, chondrocytes and osteoblasts, mediated in part by increased activation of genes that produce the Wnt, Osterix and Runx2, all fundamental elements in the osteoblastogenesis. Although the sample examined is small for the specificity of the described treatment, the data reported showed that the intermittent administration of teriparatide is able to accelerate the timing for the "elongation stage" bone and therefore the bone healing and reconstructive treatment times in serious loss of substance.
References:
[1] Treatment of complex nonunion of the shaft of the tibia using Ilizarov technique and its functional outcome. Sahu RL, Ranjan R. Niger Med J. 2016 Mar-Apr;57(2):129–33.
[2] Stimulation of fracture-healing with systemic intermittent parathyroid hormone treatment. Barnes GL, Kakar S, Vora S, Morgan EF, Gerstenfeld LC, Einhorn TA. J Bone Joint Surg Am. 2008;90(Suppl 1):120–127.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4796

FRI0564 **128 PATIENTS WITH SUBACUTE SYMPTOMATIC FRAGILITY VERTEBRAL COMPRESSION FRACTURES: HIGH INCIDENCE OF MORTALITY, FALLING, MONOCLONAL GAMMOPATHY OF UNCERTAIN SIGNIFICANCE AND MYELOMA, PERNICIOUS ANEMIA AND VITAMIN B-12 DEFICIENCY: IS THIS A PROFILE OF AN OSTEOPOROTIC OR AN AGED POPULATION?**

M. Lovy[1], N. Ben-Shlomo[2], J. Udkoff[3]. *[1]Desert Oasis Healthcare, Palm Springs, California, United States; [2]Ben-Gurion Medical School, Beer Sheva, Israel; [3]University of California, San Diego Medical School, San Diego, California, United States*

Background: Epidemiological studies have identified risk factors for falling and fractures. However there is a paucity of observational studies[1,2] of patients with symptomatic fragility vertebral compression fractures (VCF). These studies were not done in community based populations and did not evaluate the contribution of falling.
Objectives: To study factors contributing to both osteoporosis and falling in a cohort of community based patients with symptomatic subacute fragilty VCF.
Methods: We saw 128 patients with symptomatic subacute fragility VCF in our community based outpatient fracture clinic over a two year period. We performed a complete history and physical, review of past medical records and radiographs, complete blood count, sedimentation rate, chemistry profile, TSH, urinalysis, vitamin B-12, PTH, 25-OH vitamin D, and serum protein electrophoresis (SPE). We performed testosterone level, methylmalonic acid, antiparietal cell antibody and intrinsic factor antibody in select cases. We recorded diseases including diabetes, COPD, cardiac, neurological for each patient.
Results: There were 92 females aged 45–98 years (mean 77.7), 36 males aged 39–94 years (mean 77.6). Factors contributing to falling included peripheral neuropathy-61, use of sedatives-43, blindness-12, foot drop-6, dementia-3, Parkinson's-3, hyponatremia-2. VCF were precipitated by falls in 94 patients, of which 87 occurred at home. VCF occurred with lifting in 8 patients, bending in 3, and were spontaneous in 23. Use of steroids was reported in 18 patients and associated with mulitple ($>$3) fractures ($p<0.0008$). Blindness (p=0.022) and multiple fractures (p=0.049) were found more often among females. Males were more likely to have peripheral neuropathy (p=0.056) and 3 or more medical conditions ($P<0.008$). Age correlated with the number of diseases ($p<0.0001$). Diagnosis based on laboratory studies included vitamin D insufficiency-29, vitamin D deficiency-12, pernicious anemia-6, vitamin B-12 deficiency-8, monoclonal gammopathy of uncertain significance (MGUS)-10, myeloma-2, hypogonadism-12, and iatrogenic hyperthyroidism-3. Ankylosing spondylitis and lymphoma were diagnosed in one patient each. The average age of those that died was 83.9 years compared to 76.8 of the remaining group (p=0.033).
Conclusions: Conditions that increase with age and are associated with an increased risk of falling and fracture include neurological diseases, visual loss, use of steroids and sedatives, MGUS, myeloma, pernicious anemia and vitamin B-12 and vitamin D deficiencies. These were all common in our cohort with subacute symptomatic fragility VCF. Accordingly we recommend vitamin B-12 levels and SPE in the evaluation of all patients with VCF. These findings support the emphasis on interventions to reduce the risk of falling in the elderly and to recognize and treat these age-related conditions in an attempt to mitigate the risk of VCF.
References:
[1] Nola JM, et al, J Rheumatol 2001;28:2289–22–93.
[2] Dumitrescu B, et al, BMC Musculoskeletal Disorders 2008, 9:109.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2171

FRI0565 **FRAGILITY FRACTURES IN PATIENTS ON DEPO-PROVERA ARE NOT ASSOCIATED WITH USUAL RISK FACTORS FOR FRACTURE**

M. Dey, M. Bukhari. *University Hospitals of Morecambe Bay NHS Foundation Trust, Lancaster, United Kingdom*

Background: Depo-Provera is one of the most widely-used contraceptives. The side-effects includes loss in bone mineral density (BMD), increasing fracture risk (1,2). It is not known if conventional fracture risk factors impact fracture risk in these patients.
Objectives: We set out to determine if the usual risk factors for fracture are associated with increased risk of fragility fractures in patients exposed to Depo-Provera.
Methods: Patients referred for bone densitometry at a scanner in North West of England were analysed. Femoral and vertebral BMD, height, weight and body mass index (BMI) were recorded, in addition to: age, diagnosis of rheumatoid arthritis, smoking status, alcohol consumption, family history of fractures, history of secondary osteoporosis, corticosteroid use, total average proportion fat, average tissue thickness, fat mass, and lean mass. Patients with exposure to Depo-Provera were selected for analysis. Initially patients with and without a fracture were compared using Chi-squared test and T-test. Logistic models were fitted univariately and adjusted for age to analyse association between traditional risk factors and fracture.
Results: 304 females (103 currently and 201 previously on Depo-Provera) were included. 62 (20.4%) had sustained had least one fragility fracture. There was no significant difference in fracture risk between those currently and previously on Depo-Provera (p=0.176 95% CI). Decreased left femoral BMD significantly impacted fracture risk (p=0.035 95% CI). All other factors investigated did not significantly increase fracture risk in this cohort.(see table below)

Predictor	All (n=304)	Patients with fracture (n=62)	Patients without fracture (n=242)	*p*-value	Odds ratio (95% CI)
Age at scan (years)	36.7	41.5	39.2	0.083	1.028 [0.10, 1.06]
Height (m)	163.2	163.3	163.2	0.924	1.002 [0.96, 1.04]
Weight (kg)	73.0	76.9	72.1	0.078	1.012 [0.10, 1.03]
Femoral BMD (left) (g/cm^2)	0.966	0.932	0.975	0.035	0.100 [0.01, 0.82]
Femoral BMD (right) (g/cm^2)	0.972	0.945	0.979	0.112	0.177 [0.02, 1.47]
Lumbar spine BMD (L2) (g/cm^2)	1.115	1.099	1.119	0.364	0.432 [0.07, 2.62]
BMI (kg/m^2)	27.4	28.8	27.0	0.068	1.037 [0.10, 1.08]
Average proportion fat	0.274	0.299	0.267	0.069	9.071 [0.86, 101.12]
Average tissue thickness (cm)	17.6	18.3	17.5	0.080	1.076 [0.99, 1.17]
Fat mass (g)	275.2	302.7	268.1	0.053	1.002 [0.10, 1.00]
Lean mass (g)	724.8	697.3	731.9	0.053	0.998 [0.10, 1.00]
Alcohol (no. of patients)	23	8	15	0.102	2.235 [0.78, 5.96]
Smoking (no of patients)	154	31	123	1.000	0.968 [0.53, 1.76]
Family history (no. of patients)	77	17	60	0.744	1.145 [0.57, 2.22]
Rheumatoid arthritis (no. of patients)	11	3	8	0.702	1.485 [0.25, 6.43]
Secondary operation (no. of patients)	48	10	38	1.000	1.032 [0.43, 2.29]
Corticosteroids (no. of patients)	67	18	49	0.169	1.609 [0.80, 3.14]

Conclusions: Our study suggests that fragility fractures in patients taking Depo-Provera are not associated with the usual risk factors for fractures. To our knowledge, this is the first study demonstrating fracture risk in such patients to be independent of conventional risk factors. This therefore indicates an as yet unidentified mechanism of increased fracture risk. Study limitations include the small number of fractures and lack of data on length of treatment with Depo-Provera. Further research is needed into the mechanisms by which the drug gives rise to increased fracture risk, independent of other factors.
References:
[1] Contraception. United States; 2011 Nov;84(5):e31–7.
[2] Obstet Gynecol. United States; 2008 Oct;112(4):788–99.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1539

FRI0566 **TERIPARATIDE AND ALENDRONATE IMPROVED BONE LOSS AND HYPERALGESIA IN A MOUSE MODEL OF OSTEOPOROSIS**

N. Nagao, H. Wakabayashi, S. Kato, G. Miyamura, Y. Naito, A. Sudo. *Department of Orthopaedic Surgery, Mie University Graduate School of Medicine, Mie, Japan, Tsu, Japan*

Background: Osteoporosis may cause not only fractures but also chronic back pain in elderly women. Teriparatide (TPTD) and alendronate (ALN) are widely used in clinical for treatment of osteoporosis. Several studies have demonstrated that TPTD and ALN treatments improved skeletal pain in osteoporosis patients.
Objectives: We investigated the effect of TPTD and ALN on pain-related behavior in ovariectomized (OVX) mice. And we investigated expression of inflammatory cytokines treated OVX mice.
Methods: 8-week-old female ddY mice were OVX and assigned to 4groups; SHAM-operated mice treated with vehicle (SHAM), OVX mice treated with vehicle (OVX), OVX mice treated with TPTD (TPTD) and OVX mice treated with ALN (ALN). Mice were started treatment immediately after surgery. For 4 weeks, mice were injected subcutaneously with vehicle or 40μg/kg ALN twice a week or 40μg/kg TPTD 5 times a week.
The bilateral distal femur metaphyses were analyzed three-dimensionally by μCT 4 weeks after surgery (each group; n=8).
Mechanical sensitivity was tested using von Frey filaments 4 weeks after surgery. To evaluate the 50% withdrawal threshold, seven von Frey filaments with forces of 0.07, 0.16, 0.4, 0.6, 1.0, 1.4 and 2.0 g were applied to the middle of the plantar surface. Data was collected using the up-down method.
To evaluate expression of interleukin-1β (IL-1β), IL-6 and tumor necrosis factor-α (TNF-α), mice were anesthetized and the bilateral hindlimb bone excised. We performed quantitative polymerase chain reaction (q-PCR) from hindlimb bone.
Results: μCT analysis of the distal femur metaphysis showed that bone volume/tissue volume (BV/TV) and trabecular number (Tb.N) were significantly less in the OVX group than in the SHAM group, whereas trabecular separation (Tb.Sp) was significantly greater in the OVX group than in the SHAM group. In the TPTD and ALN group, BV/TV and Tb.N were significantly greater than in the OVX group, whereas Tb.Sp was significantly less than in the OVX group. And in the ALN group, BV/TV and Tb.N were significantly greater than in the TPTD group, but Tb.Sp was no significance.
The 50% withdrawal threshold was significantly lower in the OVX group than in the SHAM group, and it was significantly higher in the TPTD and ALN group than in the OVX group. And the 50% withdrawal threshold was no significance between the TPTD and ALN group.
The expression levels of TNF-α was increased in the OVX group compared with those in the SHAM group. Other cytokines were not increased significantly in the

OVX group. In the TPTD and ALN group, the expression levels of TNF-α was significantly degreased than the OVX group. And the expression levels of TNF-α was no significance between the TPTD and ALN group.
Conclusions: In this study, TPTD and ALN treatments prevented bone loss in OVX mice. Mechanical hyperalgesia in hindlimbs tended to be decreased in the OVX group compared with the TPTD and ALN group. ALN treatment was more effective in bone formation compared with TPTD treatment, whereas pain relief was no significance between TPTD and ALN treatment. These results suggest that TPTD treatment was more effective in osteoporosis patients with skeletal pain.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4628

FRI0567 DIFFERENCES IN ADCHERENCE TO OSTEOPOROSIS MEDICATIONS IN PATIENTS WITH RHEUMATIC DISEASES: A 3-YEAR RETROSPECTIVE COHORT STUDY

O. Nikitinskaya, N. Toroptsova. *Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Patients with rheumatic diseases (RD) have an increased risk of developing osteoporosis (OP) compared with healthy population due to chronic inflammation, low physical activity and using some kind of medications. Persons with RD and OP require prolonged osteoporosis treatment due to increased risk of fracture.
Objectives: To evaluate adherence and persistence with different osteoporosis medications in RD patients with OP during 3 years.
Methods: We conducted a retrospective study of 204 patients (82% women, mean age 54±11 years) with RD (93 – rheumatoid arthritis, 48 – systemic sclerosis, 39 – systemic lupus erythematosus and 24 – ankylosing spondylitis), whom OP was diagnosed in 2013. In 2016 we revised there medical charts for collection information on the osteoporosis treatment and performed telephone contact for patient's self-reporting.
Results: 196 (96%) patients started the OP treatment. Among them 26% - alendronate, 24% received alfacalcidol or supplements of calcium and vitamin D only, 16% - stroncium ranelate, 12% - ibandronate, 9% zoledronic acid, 8% - calcitonin and 5% - denosumab.
8 (4%) patients didn't start the drug treatment at all, 72 (35%) patients were persisted less than 12 months, 47 (23%) – 2 years and 77 (38%) – 3 years. Mean persistence was 2.1, 2.4, 1.6, 1.7, 1.9, 2.0 years for alendronate, alfacalcidol, stroncium ranelate, ibandronate, zoledronic acid, denosumab, respectively. 61 (31%) persons were switched from one antiosteoporotic medication to another due to side effects, inconvenient dose regimen or other reasons. Persistence to oral therapy was better among women than men ($p<0.05$), especially on daily regimen. Discontinuers were less likely than persistent subjects to visit rheumatologist and BMD measurement each year for control of treatment ($p<0.05$). Patients with ankylosing spondylitis were less persistent than persons with other RD. Presence of OP fractures in anamnesis had no significant influence on adherence. 8 (4%) patients had fractures during retrospective period, among them 6 - received only supplements of calcium and vitamin D, 1 - zoledronic acid once and 1 – without OP therapy.
Conclusions: Only 1/3 of patients with RD received antiosteoporotic drugs during 3 years. Visits to rheumatologist and BMD measurements increased subject's persistence. Improving the quality of medical care can be achieved through education and motivation of patients for a long-term treatment of OP.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2422

FRI0568 ECHOSOUND APPROACH FOR SHORT-TERM FOLLOW-UP OF THE DENOSUMAB EFFECT ON BMD RECOVERY AGAINST AROMATASE INHIBITOR IMPACT IN BREAST CANCER PATIENTS

P. Pisani[1], M. Muratore[2], F. Conversano[1], E. Casciaro[1], M. Di Paola[1], R. Forcignanò[3], M. Ciccarese[3], G. Surico[3], L. Quarta[2], E. Quarta[2], D. Costanza[2], R. Franchini[1], R. Tarparelli[4], S. Casciaro[1]. *[1]1National Research Council, Institute of Clinical Physiology; [2]2OU of Rheumatology Galateo Hospital, San Cesario di Lecce, ASL-LE; [3]3OU of Oncology Vito Fazzi Hospital, ASL-LE; [4]4Echolight Spa, LECCE, Italy*

Background: The Aromatase Inhibitors (AIs)-based therapy used in breast cancer patients to profoundly lower estrogen levels seems to enhance the loss of bone mineral density (BMD) and to increase the fragility fracture rate [1]. Several clinical studies demonstrated that, in breast cancer patients that received the adjuvant AIs, the subcutaneous administration of Denosumab-based therapy significantly increased BMD values and reduced the rate of clinical fractures.
Objectives: To monitor the short-term Denosumab and AIs therapeutic effects on BMD in breast cancer patients through an innovative echographic approach, the EchoSound technology [2].
Methods: 154 breast cancer patients selected for receiving the adiuvant AIs therapy were recruited. All the patients underwent spinal and femoral dual X-ray absorptiometry (DXA) examinations before AIs therapy administration starting (time T0). After AIs treatment starting, enrolled patients were divided into 2 groups: 105 patients received only the AIs treatment (Group A), whereas the remaining 49 patients (Group B) received also an additional Denosumab treatment, in order to contrast the BMD reduction induced by AIs administration. Follow-up measurements were conducted at two different time points: 12 (T1) and 18 (T2) months from AIs treatment starting. At time T1, patients underwent both DXA examinations and EchoSound echographic scans, whereas at time T2 only the echographic scans were performed, since DXA cannot be used for short-term follow-ups.
Results: At time T1, the following results were obtained on lumbar spine: Group A showed a BMD decrement, which was equal to -2.07%±1.66% ($p<0.01$) according to DXA and to -2.22%±0.89% ($p<0.01$) according to EchoSound; Group B showed a BMD increase of 4.06%±1.49% ($p<0.01$) and 4.31% ±0.62% ($p<0.01$) as measured by DXA and EchoSound scans, respectively. At time T2, Group A showed a further BMD decrement, resulting in a total decrease of -3.95%±1.09% ($p<0.01$) with respect to T0 values; on the contrary, in Group B Denosumab treatment produced an additional BMD increment, resulting in a total BMD increase of 4.98%±1.03% ($p<0.01$) in the same 18-month period. Similar results were obtained for femoral neck BMD: a total BMD decrease of -2.37%±0.97% ($p<0.01$) during the whole treatment period was observed in Group A, whereas a total BMD increment of 3.53%±0.43% ($p<0.01$) was measured in the same period in Group B.
Conclusions: By using the EchoSound technology the short-term follow-up of the positive Denosumab effects on BMD reduction in patients treated with adjuvant AIs was feasible and accurate. This approach can be also useful to monitor the therapy effectiveness in patients undergoing specific anti-osteoporotic treatments.
References:
[1] J Clin Endocrinol Metab.2011;96:308.
[2] Clin Cases Min Bone Metab 2015;12:142.
Acknowledgements: Work partially funded by FESR PO Apulia Region 2007–13; Action 1.2.4 (grant n. 3Q5AX31: ECHOLIGHT Project).
Disclosure of Interest: P. Pisani: None declared, M. Muratore: None declared, F. Conversano Shareholder of: Echolight spa, a National Research Council spin-off that may or may not benefit from results of this study, E. Casciaro Shareholder of: Echolight spa, a National Research Council spin-off that may or may not benefit from results of this study, M. Di Paola: None declared, R. Forcignanò: None declared, M. Ciccarese: None declared, G. Surico: None declared, L. Quarta: None declared, E. Quarta: None declared, D. Costanza: None declared, R. Franchini: None declared, R. Tarparelli Employee of: Echolight Spa, S. Casciaro Shareholder of: Echolight spa, a National Research Council spin-off that may or may not benefit from results of this study
DOI: 10.1136/annrheumdis-2017-eular.4060

FRI0569 EVALUATION OF BONE MICROARCHITECTURE IN SYSTEMIC SCLEROSIS PATIENTS: RELATIONSHIPS BETWEEN TRABECULAR BONE SCORE (TBS) AND DISEASE SEVERITY

S. Paolino[1], E. Gotelli[1], A. Sulli[1], B. Ruaro[1], M. Ghio[1], C. Pizzorni[1], E. Alessandri[1], V. Tomatis[1], C. Seriolo[2], L. Molfetta[2], M. Cutolo[1], A. Casabella[1]. *[1]Department of Internal Medicine, University of Genova, IRCCS AOU San Martino, Genoa, Italy, Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genoa, Italy; [2]Department of Internal Medicine, University of Genova, Genoa, Italy, Osteoporosis, Bone and Joint Disease Research Center, CROPO, Genoa, Italy*

Background: Systemic sclerosis (SSc) is a rare connective tissue disorder characterized by an increased synthesis and deposition of extracellular matrix in the skin and internal organs (1). Several studies described SSc as potential risk factor for osteoporosis, however, to date the bone quality in SSc is unclear (2). Trabecular bone score (TBS) has been recently proposed as an indirect measure of bone microarchitecture (3).
Objectives: The aim of this study was to assess bone microarchitecture in SSc patients and possible association with disease severity and microangiopathy.
Methods: Twenty-three female SSc patients (mean age 63.2±12.8 SD years, mean disease duration 92.8±66 SD months, mean Raynaud's Phenomenon duration 142.6±126.1 SD months) were enrolled after written informed consent. The assessment of disease severity was performed using the Medsger's severity scale (4). Bone Mineral Density (BMD) measurements at L1-L4, femoral neck and total hip, were performed using DXA Prodigy Densitometer (GE Lunar). TBS was derived for each spine DXA examination using the TBS index (TBS iNsight Medimaps). Nailfold videocapillaroscopy (NVC) was used to assess the microangiopathy based on nailfold video capillaroscopic pattern (NVC) analysis and the microangiopathy evolution score (MES) (5–6). Using the FRAX (Fracture Risk Assessment Tool) we also evaluate the 10-year risk of hip and major joints osteoporotic fracture.
Results: A positive correlation was observed between TBS and Medsger's general organ score (r=0.5; p=0.01); no other correlations were found between TBS and Medsger's score. Interestingly, TBS was positively and significantly correlated with modified Rodnam skin score (mRss) (p=0.01). When the patients were divided in two groups considering skin involvement by mRss, TBS was found significantly higher into the group with mRss >15 compared to the group with mRss <15 (1.255±0.08 vs 1.163±0.03; p=0.01) No correlations were found between NVC patterns/MES and bone quality assessment (TBS) or bone density assessment (BMD), only a significant correlation, as expected, was observed

between MES and skin involvement (mRss) (p=0.05). On the other hands, FRAX, the major osteoporotic fracture risk, positively correlates with Medsger's kidney disease severity (p=0.04) and Medsger's lung disease severity (p=0.04); in addition, FRAX, for hip fracture risk, seems to correlate significantly with Medsger's lung involvement severity (p=0.04).

Conclusions: This study demonstrates in SSc patients a relationship between clinical disease severity (organ fibrosis/failure) and altered bone microarchitecture (TBS). In addition, skin involvement was found significantly correlated with altered quality of the trabecular bone architecture (TBS) and a significant increase of osteoporotic fracture risk (FRAX) was found correlated with kindey and lung involvement.

References:

[1] Varga J, Abraham D. J Clin Invest. 2007 Mar;117(3):557–67.
[2] Loucks J, Pope JE. Semin Arthritis Rheum. 2005 Feb;34(4):678–82.
[3] Silva BC et al. J Bone Miner Res. 2014 Mar;29(3):518–30.
[4] Medsger TA et al. Clin Exp Rheumatol. 2003;21(3 Suppl 29):S42–6.
[5] Sulli A, et al. Ann Rheum Dis 2008;67:885–7.
[6] Cutolo et al. J Rheumatol 2000; 27;155.60.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6415

FRI0570 OSTEOPOROSIS AND BREAST CANCER: OUTCOMES AT A SPECIALIZED OSTEOPOROSIS CLINIC FOLLOWING A STRUCTURED ASSESSMENT

S. Lopez-Salguero[1], J.C. Ordoñez[1], L. Ranieri[1], M. Andrés[1,2], J. Ponce[3], I. Ibero[1]. [1]*Rheumatology, Hospital General Universtiario Alicante;* [2]*Departamento de Medicina Clínica, Universidad Miguel Hernández de Elche;* [3]*Oncology, Hospital General Universtiario Alicante, Alicante, Spain*

Background: Women with breast cáncer (BC) are at risk for the development of bone loss and osteoporosis (OP) mainly due to adjuvant therapies. Aromatase inhibitors (AI) therapy fully suppresses estrogen synthesis, further exacerbating the increased bone resorption and leading to an excess fracture risk. Thus, a close monitoring of bone mineral metabolism is recommended.

Objectives: The aim of the present study was to analyze bone health status and clinical characteristics of women BC referred by oncologist to a specialized clinic and their outcomes during follow-up.

Methods: Retrospective analysis of consecutive female patients with recent BC and low bone mineral density (BMD) referred to the osteoporosis outpatient clinic for assessment, as agreed with oncologists. A descriptive analysis of epidemiological, clinical, laboratory, imaging, and dual energy x-ray absorptiometry (DEXA) data is presented, both at baseline and last visit. 95% confidence intervals (95% CI) were estimated for rate of fragility fractures (FF) at baseline and during follow-up.

Results: A total number of 156 female patients have been assessed up to January 2017; median aged 60.7 (SD±10.6) years old, 89% postmenopausal. BC was mainly non-methastasic (117; 75%), and 110 (70%) patients were on aromatase inhibitors (14 on anastrozole, 89 on letrozole, and 7 on exemestane). 36 patients (23%) were active smokers, and 17 (11%) had stopped smoking. At baseline, 37 patients (24.2%, 95CI% 20–37) had previous FF, mostly vertebral (19) or non-vertebral (13), and three cases had suffered from multiple FF. BMDs were at osteoporotic range at the lumbar spine (median T-score -2.6 p25/75 -2.2, -3.2) and osteopenic at both the femoral neck and hip (mediant T-score -1.9 p25/75 -1.1, -2.3). Regarding antiosteoporotic therapies, bisphosphonates were prescribed in 110 cases (70.5%), denosumab in 24 (15.3%), and raloxifene in two cases (1.2%); in the others (12.8%) only calcium plus vitamin D supplementation was recommended. A total of 107 patients were followed a median of 2.13 years (p25–75 1.23–3.18). During follow-up, new FF occurred in 13 patients (12.1%, 95% CI 6–19), that were vertebral in 8, non-vertebral in 4, both in one case, while no hip FF were detected.

Conclusions: outcomes of a structured assessment of female patients with BC and low BMD are reported here. Despite this, 12% of cases developed a new FF, highlighting the need for special attention to this singular, secondary form of osteoporosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4928

FRI0571 OSTEOPOROSIS AND BREAST CANCER: CAN FRAX-BASED RISK FACTORS ACCURATELY PREDICT FURTHER FRACTURES AT THIS SETTING?

S. Lopez-Salguero[1,1], J.C. Ordoñez[1], L. Ranieri[1], M. Andrés[1,2], J. Ponce[3], I. Ibero[1]. [1]*Rheumatology, Hospital General Universtiario Alicante;* [2]*Departamento de Medicina Clínica, Universidad Miguel Hernández de Elche;* [3]*Oncology, Hospital General Universtiario Alicante, Alicante, Spain*

Background: Women with breast cáncer (BC) are at risk for the development of bone loss and osteoporosis (OP) mainly due to adjuvant therapies, as aromatase inhibitors (AI). Thus, it would be of special interest in this group of patientes, to know at baseline wich factors can predispose to develope fragility fractures (FF) during follow-up, in order to optmize vigilance and treatment.

Objectives: The purpose of this study is to analyze wich risk factors at baseline that can predict the appereance of a new FF in women with BC and OP.

Methods: Retrospective analysis of consecutive female patients with recent breast cancer (BC) and low bone mineral density (BMD) referred to the osteoporosis outpatient clinic for assessment, as agreed with oncologists. Fort he purpose of this anaylisis, only patients with follow-up data (at least six months after baseline visit) were selected. FRAX tool [1]-derived risk factors (age, BMI, DEXA, previous fracture, parent fractured hip, smoking, alcohol, glucocorticoids, rheumatoid arthritis, secondary OP) were taken as explicative variables. Student's t and chi-2 tests were used to perform comparisons base don the appereance of new FF in the study period.

Results: A total number of 156 female patients have been assessed up to January 2017. Of the 107 patients in follow-up (68.5%; median time in follow-up 2.1 years p25–75 1.2–3.2). Median age was 62.07 years old (SD±10,35), being 89% of them postmenopausal. 73 (68,2%) were on AI therapy (10 anastrozole, 59 letrozole and 4 exemestane). At baseline, 29 patients (27.1%) showed a FF (15 vertebral; 10 non vertebral; 2 hip; 2 multiple fracture). Antiosteoporotic treatment was recommended in 95 patients (88.7%). During follow-up, 13 FF were seen (12,1%; CI95% 6–19); being 8 of them vertebral, 4 not vertebral, and one multiple fracture; no new hip FF was seen.

After comparison of the different risk factors according to the development of a new FF, no significant association was found (see table).

Table 1

	New fragility fracture		p
	NO (n=94)	YES (n=13)	
Age (years old), mean ±SD	62.0±10.7	62.1±9.9	0.956
BMI (kg/m^2), mean ±SD	26.5±7.1	23.1±10.0	0.213
Follow-up duration (months) median ±SD	28.6±19,4	30.6±12.8	0.723
DEXA at lumbar spine (T-score) median ±SD	-2.7±0,8	-2.9±0.6	0.256
GFR (ml/min) mean ±SD	91.7±16.0	97.2±11.2	0.282
Menopause (%)	93.4	91.6	0.822
Previous fracture (%)	27.1	38.4	0.512
Parent fractured hip (%)	11.0	25.0	0.125
Smoking (%)	10.0	8.3	0.721
Glucocorticoids (%)	9.9	7.7	1.000
Rheumatoid arthritis (%)	3.2	0	1.000
Aromatase inhibitor (%)	70.9	69.2	0.897
Antiosteoporotic treatment (%)	88.4	92.3	0.676

Conclusions: In this study no relationship between FRAX-based risk factors and the development of new FF in women with OP and BC was found. As new FF occurred in 12% of cases, it highlights the need for special attention to this singular, secondary form of OP.

References:

[1] Kanis JA, Johnell O, Oden A, Jonsson B, Dawson A, Dere W. Risk of hip fracture derived from relative risks: an analysis applied to the population of Sweden. Osteoporosis International 2000; 11: 120–127.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5211

FRI0572 IDENTIFYING WOMEN AND MEN AT HIGH FRACTURE RISK BY LEVERAGING THE ELECTRONIC MEDICAL RECORDS TO ESTIMATE FRAX TREATMENT THRESHOLDS

S. Amin, E. Atkinson, S. Khosla. *Mayo Clinic, Rochester, United States*

Background: In the busy clinic, identifying individuals at high fracture (fx) risk who warrant intervention can be a challenge. There are several medical conditions that increase the risk for bone loss and falls which are recorded in the electronic medical record (EMR).

Objectives: We explored whether we could exploit data available in the EMR to estimate FRAX treatment thresholds to help passively identify patients who would benefit from further bone mineral density screening and management.

Methods: We studied 912 women and men, previously recruited for our bone health studies, in whom FRAX scores (with and without BMD) had been determined and comprehensive medical diagnoses were available through the medical linkage system of the Rochester Epidemiology Project. All diagnoses were categorized by the Clinical Classification Software (CCS) system whereby over 14,000 ICD-9-CM diagnoses are reduced to 568 clinically meaningful categories. If a subject had at least two diagnoses in a CCS category that were at least 30 days apart and within 5 years of their FRAX assessment, the subject was treated as having that CCS code. We used Gradient Boosting Machine (GBM) to create models that would predict the treatment thresholds for the FRAX 10-year risk for major osteoporotic (OP) fx (>20%) and hip fx (>3%), based on available diagnoses. Models were fit using age, sex and CCS category from 80% of the data, retaining 20% for validation.

Results: Of the 564 (62%) women and 348 (38%) men, the mean ± SD age was 61±16 yrs. There were no significant differences in subject characteristics used for FRAX calculation or FRAX scores between the training and validation sets. The c-statistic for GBM models predicting treatment thresholds for FRAX, calculated with BMD, for major OP fx and hip fx were 0.95 and 0.96, respectively, for the training set, and 0.88 and 0.94 for the validation set. Similar results were observed for FRAX scores without BMD.

Conclusions: FRAX treatment thresholds may be reasonably estimated from data available in the EMR to help identify to the clinician those at highest risk

for fracture who would warrant further evaluation. Further work to implement and validate these findings in the EMR system would be necessary.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6572

FRI0573 OSTEOCYTES ARE INVOLVED IN THE PATHOGENESIS OF OSTEOPOROSIS IN CHRONIC CHOLESTASIS. EFFECTS OF BILIRUBIN AND BILE ACIDS ON OSTEOCYTIC CELL LINES

S. Ruiz-Gaspà, A. Parés, A. Combalia, P. Peris, A. Monegal, N. Guañabens. *Liver and Metabolic Bone Diseases Units, CIBERehd-Hospital Clínic, University of Barcelona, Barcelona, Spain*

Background: Mechanisms underlying osteoporosis in chronic cholestasis are complex and poorly understood. In this setting, osteoporosis mainly results from low bone formation, related to the effects of retained substances of cholestasis, such as bilirubin and bile acids. Thus, in "in vitro" studies, unconjugated bilirubin and serum from jaundiced patients decrease osteoblast viability, differentiation and mineralization. However, the influence of cholestasis on osteocytes, the most ubiquitous cells of the skeleton, is unknown.
Objectives: The aim of this study was to analyze the direct effects of increased molecules of cholestasis, such as bilirubin (Bil) and lithocholic acid (LCA), and the potential protective effect of ursodeoxycholic acid (UDCA) on the osteocytes.
Methods: MLO-Y4 and MLO-A5 osteocyte cell lines treated at different times and concentrations with Bil, LCA and UDCA were used to determine: 1) Viability: WST colorimetric method; 2) Differentiation: quantification of alkaline phosphatase (AP) activity; 3) Mineralization: Alizarin red staining quantification; and 4) Apoptosis: quantification of DNA fragmentation and caspase-3 activity.
Results: LCA (100μM) and Bil (50μM) significantly decreased viability in MLO-Y4 from 72 hours (10%) and 48 hours (11%), respectively ($p \leq 0.01$), and Bil decreased viability (49%) in MLO-A5 from 96 hours ($p < 0.01$). Bil decreased AP activity by 47% after 96 hours, under conditions of differentiation in MLO-Y4 ($p \leq 0.01$). There were no effects on AP activity in MLO-A5. After 14 days, Bil was associated with a significant mineralization decrease, as high as 87%, in MLO-A5 ($p \leq 0.02$). Moreover, Bil and LCA increased apoptosis in MLO-Y4, determined by DNA fragmentation (242% and 119%, respectively) and caspase-3 activity (190% and 251%, respectively) ($p \leq 0.01$) after 24 hours. In contrast, UDCA (100 μM) increased viability after 72 hours (11%) and decreased the deleterious effects of LCA or Bil ($p \leq 0.02$). UDCA increased AP activity in MLO-Y4 after 72 hours under growth conditions ($p = 0.018$), and after 24 hours under differentiation conditions ($p \leq 0.01$).
Conclusions: Bilirubin and lithocholic acid have damaging effects on osteocytic cells decreasing viability, differentiation and mineralization, and increasing apoptosis, effects that are neutralized by the UDCA. These results indicate that substances retained in cholestasis impair osteocytic functions, and therefore may be involved in the pathogenesis of osteoporosis in cholestatic diseases.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4711

FRI0574 QUALITY OF LIFE ASSESMENT IN POSTMENOPAUSAL OSTEOPOROSIS

S. Novkovic[1], G. Stanojevic[2]. *[1]Institute of rheumatology; [2]Health Center "Zvezdara", Belgrade, Serbia*

Objectives: To compair two questionaires:a specific one-Osteoporosis Quality of Life Questionnaire (OQLQ) and a general one-Short Form-36 (SF-36),in women with decreased mineral bone density (BMD) and vertebral fractures,and to estimate which one is more useful for everyday work.
Methods: Cross-section study included 50 menopausal women with osteoporosis (OP), who were assessed with the general questionaire,and all known risk factors for osteoporosis were confirmed. Osteodensitometry scan (DXA) was performed on lumbar spine,and based both on T index value and BMD the subjects were divided in two groups:first grour (women with OP, n=25),second group (women with fractures of spinal vertebra due to OP,regardless of BMD, n=25, and with at least 4 months since the last fracture).The quality of life was assessed by two questionaires:a specific one OQLQ- consists of 30 questions divided into 5 areas,which are evaluated from 1 to 7 (the lower the score the more sever function damage and worse quality of life) and the general questionnaire SF-36-containing 36 questions divided into 8 areas (scores from 0 to 100, where the lower value is also a poorer quality of life).Questionnaires were converted to get two summarized scales,so as to obtain the total score for:physical (PCS) and mental functions (MCS).The two questionnaires were compared using appropriate statistical methods in SPSS.
Results: There was no significant differencev between groups regarding: mean age (first=63.3±6.0, second=64.9±7.8),mean age at the start of the menopause (first=46.8±5.3, second=48.2±4.2 years), mean duration of menopause (first=16.4±6.9, second=17.1±6.9 year),but there was statistically significant difference between the number of risk factors for OP (first=1.8±1.2, second=2.8±0.9, $p < 0.01$).Statistically significant between group difference ($p < 0.01$) in mean BMD and T score (first-BMD 0.807±0.057gr/cm^2,T scor -3.12±0.49SD, second- BMD 0.931±0.172 gr/cm^2,T score -2.09±1.45SD).The following DXA values were measured in the second group:8 patients-normal,6-osteopenia,11-osteoporosis,with average number of fractures 2.6±0.8.There was statistically significant between group difference in values of PCS OQLQ questionnaire (first=2.99, 42.7%, second=2.30, 32.8%, $p < 0.01$),as well as in values of MCS OQLQ (first=3.18, 45.4%, second=2.17, 31.0%, $p < 0.01$).Statistically significant difference was also observed regarding values of PCS SF-36 (first=42.2, 42.2%, second=32.5, 32.5%, $p < 0.01$),while regarding MCS SF-36 questionnaire there was no significant between group difference (first=40.2, 40.2%, second=33.3, 33.3%, $p > 0.05$).Mutual comparison of two questionnaires demonstrated correspondence and statistically significant decline in the quality of life in a group with fractures when it comes to PCS and MCS at OQLQ questionnaire and did not record between group difference in MCS SF-36 questionnaire.
Conclusions: It was demonstrated that the specific questionnaire provided more accurate information in all areas of quality of life,with general questionnaire failing to record between group differenc in the field of mental functions.Based on the proven value as an instrument of measurement,its simplicity,accuracy and ease of administration,OQLQ questionnaire is more appropriate for routine use in women with decreasing bone quality and fractures of vertebrae due to osteoporosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3721

FRI0575 SAFETY OF DENOSUMAB IN A MONOCENTRIC COHORT OF KIDNEY TRANSPLANT RECIPIENTS

S. Doddoli, P. Lafforgue, T. Pham. *Bouches Du Rhones, Aix Marseille Unversity, APHM, Marseille, Marseille, France*

Background: The safety of Denosumab, a fully human monoclonal antibody against RANKL, which was developed for treatment of osteoporosis and prevention of fractures, remains unclear in kidney transplanted patients.
Objectives: Our aim was to assess its clinical and biological tolerance in this specific population.
Methods: *Design:* Prospective observational monocentric cohort. *Inclusion criteria:* kidney transplant recipient who received at least one subcutaneous injections of 60 mg denosumab; age $\geq$18 years.
Safety assessment: the following variables were collected every 6 months: infection, reaction at the injection site, plasmatic parameters of renal function and mineral metabolism (estimated glomerular filtration rate, serum creatinine, calcium, 1–25 [OH] vitamin D, PTH).
Results: Patients were recruited from April 2014 to September 2015. All patients received immunosuppression therapy including prednisolone $\geq$5 mg/d. The main baseline characteristics of the 37 kidney transplant recipients were the following [mean]: male: 41%, age: 60.5 years, BMI: 24,1, transplantation duration: 7.1 years, osteopenic patients: 36%, osteoporosis patients: 64%, total lumbar spine T-score: -2.04 SD, total hip T-score: -2.7 SD, T-score femoral neck: 0.676 g/cm^2, serum creatinine: 132.8 mmol/L, calcium: 2.33 mmol/L, 1–25 [OH] vitamin D: 93.5 nmol/L, PTH 95: ng/l. All patients were prescribed vitamin D and calcium supplementation.
During the mean 12-month follow-up period, there were no unexpected adverse event [AE] or severe adverse event, no graft failure and no deaths. No patient experienced fracture. Only one patient presented an infectious AE with recurrent cutaneous abscess. Renal function remained stable with no difference in serum creatinine between baseline and 12 months for the majority of the kidney transplant recipients. However, 9 recipients experienced a decrease in renal function with a mean increased in serum creatinine of 32.5micromol/L between baseline and 12 months. Serum calcium was stable, no hypocalcaemia was observed. Among patients with normal baseline PTH, two presented hyperparathyroidism during the follow-up period. Among the 11 patients with baseline hyperparathyroidism, 7 had an increased PTH level between baseline and 12 months. None were initiated on cinacalcet.
Conclusions: Our results suggest that denosumab is safe in kidney transplant recipients. We did not observe an increase in the infection rates, nor hypocalcemia. However, several patients experienced a decrease in their renal function or an increased hyperparathyroidism.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6899

FRI0576 COMPARING TREATMENT INDICATION BY FRAX AND BMD ALONE IN RHEUMATIC PATIENTS ON LONG-TERM GLUCOCORTICOID IN HONG KONG

S.L. Lau[1], M.L. Yip[2], L.-S. Tam[1], K.L. Lee[3] on behalf of The Hong Kong GIOP Study Group. *[1]Department of Medicine & Therapeutics, The Chinese University of Hong Kong; [2]Department of Medicine and Geriatrics, Kwong Wah Hospital; [3]Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong, Hong Kong*

Background: Bone mineral density (BMD) may underestimate fracture risk since most patients with fracture had osteopenia or normal BMD. The WHO Fracture Risk Assessment Tool (FRAX) incorporated BMD and clinical risk factors (CRF) to estimate the 10-year probability of major osteoporotic fractures (MOF) and hip fracture. FRAX has been adopted by various guidelines to assess the need for therapeutic intervention. Whether FRAX is superior to BMD in identifying high-risk patients in need of anti-osteoporotic treatment is worth exploring.

Objectives: To compare the ability of FRAX and BMD alone in discriminating patients with and without fracture, and their effectiveness in identifying anti-osteoporotic treatment needs

Methods: 1300 rheumatic disease patients on long-term glucocorticoid were screened for vertebral fracture by radiograph from 7 rheumatology clinics. 220 ambulatory patients (110 with vertebral fracture and 110 without vertebral fracture) were recruited and assessed on CRF with FRAX questionnaire, BMD at the lumbar spine, total hip and femoral neck by dual-energy x-ray absorptiometry (DXA). The ten-year probability of MOF and hip fracture (FRAX score) with and without femoral neck BMD were calculated with the WHO FRAX tool.

Results: Both groups of patients were matched in gender, disease type and cumulative glucocorticoid dose ($p>0.1$). Patients in the fracture group were older (63±14 vs 59±12 years, $p<0.01$), of lower body mass index [22.7±3.5vs 24±3.7kg/m^2, $p<0.05$], with a higher prevalence of previous fracture [38 (34.5%) vs 5 (4.5%), $p<0.01$], use of vitamin D [77 (70%)vs 54 (49.1%), $p<0.01$] and bisphosphonates [23 (20.9%) vs 7 (6.4%), $p<0.01$]. A receiver operating characteristic (ROC) curve analysis was performed to determine the ability of FRAX score with or without BMD and BMD alone to discriminate fracture status (Table 1). BMD at the femoral neck and FRAX score with BMD were able to provide adequate discrimination with their area under curve (AUC) >0.70. With regards to treatment indication, only 53/110 (48.2%) of the patients with vertebral fracture were identified as having osteoporosis (T-score ≤ -2.5 at hip/spine) by DXA. In contrast, FRAX with BMD were able to identify 71/110 (64.5%) of the fracture patients whom treatment criteria were met, with a power of 0.97 and effect size of 0.38 (a medium effect) at the 0.05 level.

Table 1. Area under ROC curve on discriminating fracture

		AUC	95% Confidence Interval
BMD at Femoral Neck		0.709	0.640-0.778*
BMD of Total Hip		0.693	0.623-0.763*
BMD of Lumbar Spine		0.654	0.581-0.727*
FRAX with BMD	MOF	0.705	0.635-0.775*
	Hip fracture	0.720	0.651-0.789*
FRAX without	MOF	0.681	0.610-0.752*
BMD	Hip fracture	0.687	0.616-0.758*

*p<0.001

Conclusions: In rheumatic patients on long-term glucocorticoid, FRAX score was more effective in identifying patients with intervention needs than BMD alone. It is suggested that FRAX should be used as a routine assessment to identify patients, even asymptomatic, indicated for anti-osteoporotic treatment.

References:

[1] Aspray, T. J. (2015). Fragility fracture: recent developments in risk assessment. Therapeutic Advances in Musculoskeletal Disease, 7(1), 17–25. http://doi.org/10.1177/1759720X14564562.

[2] Rentero, M. L., Amigo, E., Chozas, N., Fernández Prada, M., Silva-Fernández, L., Abad Hernandez, M. A., ... del Pino-Montes, J. (2015). Prevalence of fractures in women with rheumatoid arthritis and/or systemic lupus erythematosus on chronic glucocorticoid therapy. BMC Musculoskeletal Disorders, 16(1), 300. article. https://doi.org/10.1186/s12891–015–0733–9.

Acknowledgements: We would like to acknowledge the Research Grant Council of Hong Kong for funding support (RGC Ref No.14113714).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3591

FRI0577 CLINICAL CHARACTERISTICS OF SPONTANEUS FRACTURES IN THE BEDRIDDEN PATIENTS UNINTENTIONALLY CAUSED BY CAREGIVERS

T. Kashiwagura[1], Y. Kimura[1], I. Wakabayashi[2], M. Fujii[1], K. Nozaka[3], N. Miyakoshi[3], Y. Shimada[3]. *[1]Department of Orthopedic Surgery; [2]Department of Rehabilitation Medicine, Akita City Hospital; [3]Department of Orthopedic Surgery, Akita University Graduate School of Medicine, Akita, Japan*

Background: The number of bedridden patients in our super-aging society is increasing. We previously studied fractures occurring in bedridden patients during daily activities with caregiver assistance (dry baths, range of motion exercises, transfer to wheelchair, changing diapers, and so forth) and non-traumatic fractures detected by pain, swelling, subcutaneous bleeding, deformity, and so on. These minimal trauma or spontaneous fractures were defined as "*spontaneus fractures in the bedridden patients unintentionally caused by caregivers*". Despite efforts to draw attention to preventing these injuries, the incidence of such fractures has been increasing. Spontaneus fractures caused by caregivers are characterized by the presence of untreated osteoporosis, contracture or spasticity near the lesion, institutionalization or hospitalization, repeated fractures, femur fracture, and other unknown causes.

Objectives: Spontaneus fractures caused by caregivers frequently occur without any noticeable trauma and at present, predicting the risk of occurrence is difficult. This study aimed to explore the usefulness of bone metabolism markers in predicting the risk for spontaneus fractures caused by caregivers.

Methods: Study subjects were selected from a pool of 28 patients (3 men; 25 women) with 33 spontaneus fractures caused by caregivers who were treated in our hospital between April 2006 and July 2016. Patients were selected based on the following inclusion criteria: no renal dysfunction (eGFR ≥60) and those who had undergone measurement of bone metabolism markers. Finally, 12 women with a mean age at onset of 90.6 (76–100) years were enrolled in the study. The following markers were evaluated: the bone formation markers bone type alkaline phosphatase and intact procollagen type 1 amino-terminal propeptide; the bone resorption markers tartrate-resistant acid phosphatase (TRACP)-5b, urinary deoxypyridinoline (DPD), and serum N-telopeptide; and the bone quality markers undercarboxylated osteocalcin (ucOC), urinary pentosidine (Pen), and homocysteine (Hcy).

Results: Low levels of bone metabolism markers were not observed in these subjects. However, TRACP-5b levels were high in six subjects while urinary DPD levels were abnormally high in all subjects with a mean value of 23.3 (9.2–41.4) nmol/mmol creatinine (Cr). With regards to bone quality markers, levels of Hcy and ucOC were high in two and three subjects, respectively; while Pen levels were abnormally high in ten subjects with a mean value of 0.183 (0.0774–0.3115) μg/mg Cr.

Conclusions: The majority of subjects with spontaneus fractures caused by caregivers had untreated osteoporosis and some had repeated fractures, indicating that early treatment of osteoporosis is important. Assessing osteoporosis in bedridden patients is challenging as measurement of bone density is often difficult due to spinal deformity and contracture. Our results suggest that among the bone metabolism markers, DPD and Pen may be useful predictors for the risk of spontaneus fractures caused by caregivers.

References:

[1] T Kashiwagura et al. Clinical results of spontaneous fractures in the bedridden patients unintentionally caused by caregivers. Orthop Surg Traumatol 56:189–193, 2013.

Acknowledgements: The authors would like to thank Y. Sasaki for technical assistance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4531

FRI0578 ODONTOID FRACTURES IN THE ELDERLY: AN UNKNOWN OSTEOPOROTIC FRACTURE?

L.L. Natella[1], N. Bronsard[2], J. Allia[2], L. Hekayem[3], L. Euller-Ziegler[1], F. De Peretti[2], V. Breuil[1]. *[1]Rheumatology/University of Nice, Rheumatology/ University of Nice; [2]Department of Orthopedic Surgery; [3]Emergency Room Department, University of Nice, nice, France*

Background: Current WHO definition of osteoporosis excludes cervical fractures. However, in atraumatic odontoid fractures, mainly reported by orthopedic surgeons, bone status has not been described yet [1].

Objectives: To investigate bone status in elderly patients sustaining a low energy odontoid fracture.

Methods: We conducted a prospective study from January 2016 to January 2017 in patients >65 years old, hospitalized in Nice University hospital for low energy odontoid fracture. An evaluation of bone status was proposed within 3 months after fracture event. Evaluation included demographic data, clinical risk factors of osteoporosis, bone mineral density (BMD) at spine and hip and vertebral fracture assessment (VFA) by dual X-ray absorptiometry and serum analysis to detect secondary osteoporosis.

Results: 38 patients were hospitalized for odontoid fracture: 8 patients <65 years always after a major trauma (mean age 37.1±14.5 y) and 30 patients ≥65 years including 3 after a high energy impact. 27 odontoid fractures followed a low energy impact: 18 women and 9 men, mean age 83.8 y. (±10.7). 8 patients died before bone status assessment (5 men and 3 women), 6 died during hospitalization with a mean delay of 3.5 days (±1.87) and 2 after discharge (1 month and 5 month). 3 patients refused bone status evaluation, 5 were lost to follow-up and 1 is awaiting evaluation. Finally 10 patients had bone status evaluation, all women, mean age 84.2 y. (±8.9). None had parental history of hip fracture, 1 had an early menopause, 1 received aromatase inhibitors for breast cancer and 2 had a history of steroid therapy (>3 months). 3 patients had previously received hormone replacement therapy, 1 received bisphosphonate for 5 years and 4 had calcium + vitamin D supplements. Lumbar spine mean T-score was -1.45 (±1.08), femoral neck: -2.37 (±0.040) and total hip: -1.99 (±0.6). VFA analysis revealed 4 unknown vertebral fractures. The table summarizes population bone status: 8 patients out of 10 fulfilled diagnostic criteria of osteoporosis, including 6 with previous fractures. 2 patients with T-score > -1.DS didn't have hip BMD assessment because of bilateral hip replacement but had previous major osteoporotic fractures. No

Lowest T-score	No fracture (n)	Previous minor osteoporotic fracture (n)	Previous major osteoporotic fracture (n)
T-score > -1 DS	0	0	**2** (1 patient: 2 femoral neck fracture, 1 patient: pelvic and humeral fractures. Both patients had vertebral fracture on VFA)
-1 DS > T-score ≥ -2.5	1	1 (1 wrist)	**2** (1 patient: humeral and vertebral fracture on VFA, 1 patient: 5 ribs fractures)
T-score < -2.5	**2**	**1** (2 wrist fractures)	**1** (vertebral fracture on VFA)

secondary osteoporosis was detected. Serum vitamin D concentration was <30 ng/ml in 5 patients, including 2 with concentration <10 ng/ml.

Conclusions: Our study reveals that odontoid fractures mainly occur in elderly osteoporotic patients after a low energy impact. Although WHO osteoporosis definition excludes cervical fractures, odontoid fracture may be considered as an osteoporotic fracture. Further studies are required to confirm these results.

References:

[1] Watanabe M, et al. Analysis of predisposing factors in elderly people with type II odontoid fracture. Spine J. 2014 Jun 1; 14(6):861–6.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3503

FRI0579 INFLUENCE OF ORAL PREDNISOLONE ON EFFECT OF DENOSUMAB ON OSTEOPOROSIS IN PATIENTS WITH JAPANESE RHEUMATOID ARTHRITIS; 24 MONTHS OF FOLLOW-UP ~A MULTICENTER REGISTRY STUDY~

Y. Kanayama[1], Y. Hirano[2], N. Takahashi[3], S. Asai[3], N. Ishiguro[3], T. Kojima[3] on behalf of TBCR-BONE study group. *[1]Orthopedic Surgery and Rheumatology, Toyota Kosei Hospital, Toyota; [2]Rheumatology, Toyohashi Municipal Hospital, Toyohashi; [3]Orthopedic Surgery, Nagoya University Graduate School of Medicine, Nagoya, Japan*

Background: Denosumab (DMB) is a fully human monoclonal antibody to the RANKL that blocks its binding RANK, inhibiting the development and activity of osteoclasts, decreasing bone resorption, increasing bone density and reducing fracture risk. Osteoporosis (OP) is more frequent in patients with rheumatoid arthritis (RA) than in the general population due to active systemic inflammation as well as the use of glucocorticoid and immobility. However efficacy of DMB is not clear in patirnts with glucocorticoid- induced OP in RA. Therefore we investigated the influence of oral prednisolone on effect of DMB in patients with Japanese RA from initiation to 24 months at this time.

Objectives: This prospective study investigated the efficacy of DMB for 24 months on glucocorticoid- induced OP in RA patients.

Methods: Patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria who had been prescribed DMB from Tsurumai Biologics Communication Registry (TBCR)-BONE between October 2013 and October 2015 were enrolled. The final study cohort of 63 patients received continuous DMB therapy more than 24 months. The DMB dose was 60mg at once every 6 months. In all cases native or activated vitamin D has been used. We reviewed the results for 24 months about the increase and decrease of bone mineral density (BMD) of lumbar spine (LS) and total hip (TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen (PINP) and tartrate-resistant acid phopshatate form 5b (TRACP-5b).

Results: In the patients receiving oral prednisolone group (n=23, GC+) and not receiving group (n=40, GC-), the number of female was each 21 (91%) and 39 (98%) cases (p=0.548). The mean age was 69.8±7.0 and 71.0±7.3 years old (p=0.622); disease duration was 16.0±8.9 and 15.7±12.6 years (p=0.592); the body mass index was 20.7±3.5 and 19.7±3.0 (p=0.335) and the FRAX was 34.2±19.1 and 24.6±13.9 (p=0.040). Clinical findings related to RA and OP at baseline were as follows; CRP 1.2±1.4 and 0.5±1.0 mg/dl (p=0.009); DAS-CRP 3.16±1.17 and 2.50±1.27 (p=0.025); m-HAQ 1.24±0.90 and 0.82±0.82 (p=0.065); P1NP 60.1±38.6 and 56.9±33.5 μg/l (p=0.711); TRACP-5b 513±257 and 505±202 mU/dL (p=0.689); LS-BMD 0.87±0.18 and 0.80±0.14 g/cm^2(p=0.074) and TH-BMD 0.60±0.11 and 0.59±0.08 g/cm^2 (p=0.457). The rate of decreased P1NP from baseline to 6, 12, 18 and 24 months were each -25.6% vs -41.6% (p=0.129) at 6 month, -8.0% vs -42.6% (p=0.031) at 12 month, -19.5% vs -27.5% (p=0.235) at 18 month and -13.8% vs -33.8% (p=0.134) at 24 month and TRAC-5b were -26.5% vs -38.7% (p=0.710) at 6 month, -22.0% vs -35.1% (p=0.229) at 12 month, -25.2% vs -28.1% (p=0.792) at 18 month and -20.6% vs -27.3% (p=0.663) at 24 month in the GS+ vs GS- group. The rate of increased LS-BMD from baseline to 6, 12, 18 and 24 months were each 4.1% vs 4.6% (p=0.671) at 6 month, 5.3% vs 7.0% (p=0.361) at 12 month, 8.1% vs 8.1% (p=0.438) at 18 month and 10.0% vs 7.7% (p=0.104) at 24 month and TH-BMD were 3.3% vs 2.7% (p=0.690) at 6 month, 1.4% vs 3.8% (p=0.804) at 12 month, 6.4% vs 4.0% (p=0.259) at 18 month and 5.7% vs 4.3% (p=0.945) at 24 month in the GS+ vs GS- group (Fig.1,2).

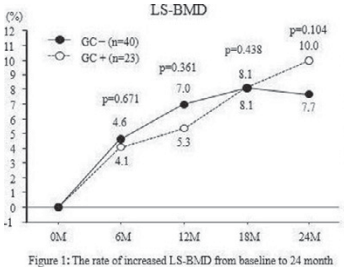


Figure 1: The rate of increased LS-BMD from baseline to 24 month

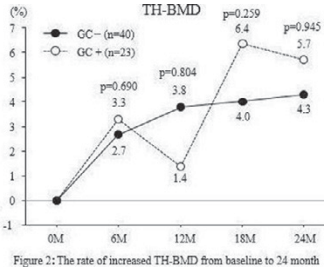


Figure 2: The rate of increased TH-BMD from baseline to 24 month

Conclusions: DMB was effective in OP of RA patients. Oral prednisolone use did not influence the efficacy of DMB for 24 months.

Disclosure of Interest: Y. Kanayama: None declared, Y. Hirano Speakers bureau: Abbvie Japan, Eisai, Mitsubishi Tanabe Pharma, Pfizer, Chugai Pharmaceutical, and Bristol-Myers Squibb, N. Takahashi Speakers bureau: bbvie Japan Co. Ltd, Eisai Co. Ltd, UCB Japan Co. Ltd, Mitsubishi Tanabe Pharma Corporation, Takeda Pharmaceutical Company Ltd, Pfizer Co. Ltd, Chugai Pharmaceutical Co. Ltd, Janssen Pharmaceutical K.K., and Bristol-Myers Squibb Co. Ltd, S. Asai: None declared, N. Ishiguro Grant/research support from: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, Taisho Toyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, ChugaiPharmaceutical, Mitsubishi Tanabe Pharmaceutical,Astellas Pharma and Pfizer Japan, T. Kojima Speakers bureau: Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma,AbbVie, Bristol-Myers Squibb, and Pfizer, Janssenn Pharmaceutical Companies, Astellas Pharma and Chugai Pharma

DOI: 10.1136/annrheumdis-2017-eular.4677

FRI0580 PREDICT SARCOPENIA BY SONOELASTOGRAPHY OF QUADRICEPS MUSCLE IN OSTEOPOROTIC PATIENTS

Y.-C. Chen, C.-H. Ko. *Rheumatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, Province of China*

Background: Reduced muscle mass had associated with high mortality. So it is urgent for simple techniques to early detection sarcopenia. Our objective was to examine the validity of sonoelastography to predict sarcopenia in osteoporotic patients.

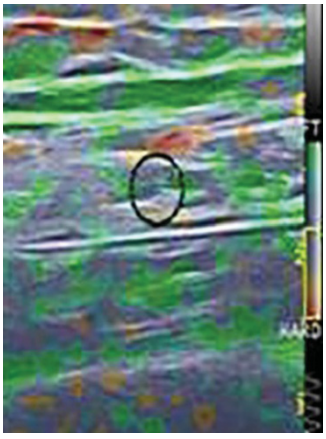
Objectives: To evaluate the association of sonoelastography and dual-energy X-ray absorptiometry in patients with sarcopenia and osteoporosis.

Methods: We conducted an observational study in Kaohsiung Chang Gang Memorial Hospital. Sarcopenia was determined using a dual-energy X-ray absorptiometry. Osteoporosis was defined through estimated bone mass (BM). Sonoelastography was performed over mid thigh over quadriceps muscle. We measure hardness and elastography ratio of quadriceps over subcutaneous fat tissue. ROC analysis was used to find best cut-off point.

Results: A total 47 (23 sarcopenia, 24 non-sarcopenia) osteoporotic patients were enrolled. The mean age was 71.04±9.64 years, and most patients (88.9%) were women. Sonoelastography showed sarcopenia patients had more soft than non-sarcopenia patients, furthermore the elastography ratio of quadriceps over subcutaneous tissue was lower than non-sarcopenia patients. When the cut points determined by receiver operating characteristic (ROC) curve analysis were applied, The best cut-point of hardness was 42.5 (sensitivity, 0.969; 1-specificity, 0.066), while the best cut-point of quadriceps over subcutaneous tissue was 70.5% (sensitivity, 1.00; 1-specificity, 0.079).

Characteristics of study patients

Variables	Sarcopenia (n=23)	Non-sarcopenia (n=24)	*P*-value
Age (years)	71.04 ±9.64	70.82±8.624	0.316
Body mass index (kg/m^2)	23.80±3.45	23.83±4.56	0.977
Gender (Female %)	22 (75.9%)	78 (84.8%)	0.624
EX2/1	0.37±0.15	1.36±0.57	**<0.001**
Hard%	15.44±13.15	76.70±20.12	**<0.001**



Conclusions: Sonoelastography was easily applicable in patients with sarcopenia and osteoporosis. Using hardness content and elastography ratio of quadriceps over subcutaneous ratio render more information of muscle character. Early detection of sarcopenia with sonoelastography in patients with osteoporosis afford future trend of preventive medicine in geriatric patients.

References:

[1] Teber MA, Ogur T, Bozkurt A, Er B, Turan A, Gulbay M, et al. Real-time sonoelastography of the quadriceps tendon in patients undergoing chronic hemodialysis. J Ultrasound Med. 2015;34(4):671–7.

Acknowledgements: This study was supported by Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung (grant CMRPG8F1731).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2709

FRI0581 HEPATITIS B INCREASE MORTALITY IN PATEINTS WITH OSTEOPOROTIC VERTEBRAL FRACTURES

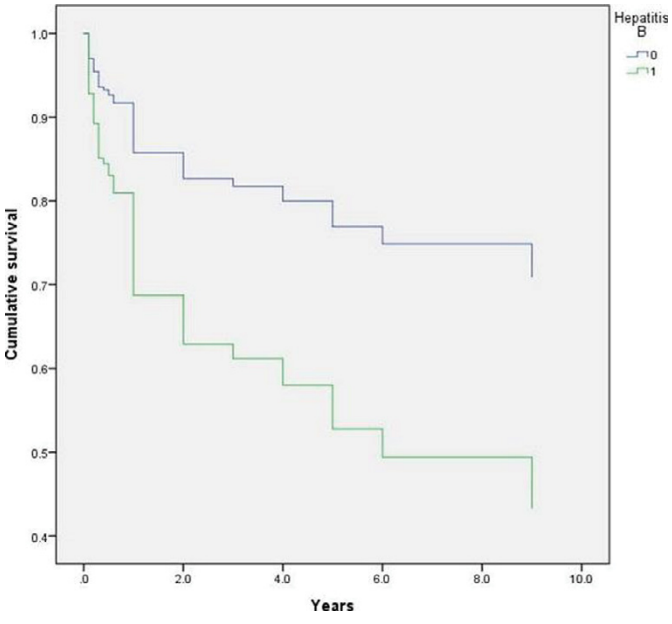
Y.-C. Chen, C.-H. Ko. *Rheumatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, Province of China*

Background: Hepatitis B virus (HBV) is a major cause of chronic liver diseases worldwide, particularly cirrhosis and hepatocellular carcinoma, and the most important liver disease in Taiwan. However, little is known the impact of hepatitis b on osteoporotic patients.
Objectives: This study aimed to determine if hepatitis b can increase the risk of mortality in patients with osteoporotic vertebral fracture.
Methods: This retrospective study reviewed of cases of osteoporosis patients with acute vertebral fractures between 2001 and 2008. All associated co-morbidities were recorded. Kaplan-Meier and cox regression analysis were performed.
Results: There were 432 patients with acute vertebral fractures. The mean age of 72.85±9.28. 31 (7.2%) patients had chronic hepatitis b. Using the Kaplan-Meier curve, hepatitis b had a significant effect on mortality ($p<0.001$, by log rank text). After adjusting for potential confounders, patients with hepatitis b still had a high mortality rate (p=0.019; HR: 2.436∼5.136) 2.137, 95% CI: 1.156∼5.136). The mortality rate also increased among smokers (p=0.026; HR: 3.6043.891; 95% CI: 1.056∼12.301).

Table 1. Multivariable Cox regression analysis of the hazard ratios for adjacent fracture

Variables	Regression coefficient	P value	HR (95CI)
Gender	-0.127	0.764	0.88 (0.383–0.022)
Age	0.004	0.785	1.004 (0.976–1.032)
Smoking	1.282	0.041	3.604 (1.056–12.301)
Alcohol consumption	-0.701	0.396	0.496 (0.098–2.508)
Body mass index (kg/m^2)	0.024	0.446	1.024 (0.964–1.088)
Hepatitis B	0.891	0.019	2.436 (1.156–5.136)
Diabetes	-0.185	0.538	0.831 (0.461–1.498)
Hypertension	-0.271	0.31	0.762 (0.451–1.288)
Stroke	-0.696	0.248	0.499 (0.153–1.625)
Kidney disease	0.809	0.145	2.246 (0.758–6.656)
Cardiovascular disease	0.037	0.946	1.038 (0.351–3.069)
Pulmonary disease	-0.971	0.349	0.379 (0.050–2.883)

Abbreviations: HR, hazard ratio; SE, standard error.



Conclusions: In this study, hepatitis b increase mortality in osteoporotic vertebral fracture patients. So we should pay attention to this group in osteoporotic management.
References:
[1] Chong-Shan Wang et al. Am. J. Trop. Med. Hyg., 66(4), 2002, pp. 389–393.
Acknowledgements: We thank Kaohsiung Chang Gang Memorial Hospital for data support.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3614

FRIDAY, 16 JUNE 2017

Other orphan diseases

FRI0582 OPEN-LABEL, MULTICENTER, DOSE-ESCALATING PHASE II CLINICAL TRIAL ON THE SAFETY AND EFFICACY OF TADEKINIG ALPHA IN ADULT ONSET STILL'S DISEASE

C. Gabay[1], B. Fautrel[2], J. Rech[3], F. Spertini[4], E. Feist[5], I. Koetter[6], E. Hachulla[7], J. Morel[8], T. Schaeverbeke[9], M.A. Hamidou[10], T. Martin[11], B. Hellmich[12], P. Lamprecht[13], H. Schultze-Koops[14], A. Sleight[15], E. Schiffrin[15].
[1]Rheumatology, University Hospitals of Geneva, Geneva, Switzerland; [2]Rheumatology, Pitié Salpetrière University Hospital, Paris, France; [3]Department of Medicine 3, Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany; [4]Division of Immunology and Allergy, CHUV, Lausanne, Switzerland; [5]Rheumatology, Charité Universitatsmedizin, Berlin; [6]Asklepios Klinikum, Hamburg, Germany; [7]CHRU de Lille - Hopital Claude Huriez, Lille; [8]Department of Rheumatology, University and CHU of Montpellier, Montpellier; [9]Rheumatology, Hopital Pellegrin, Bordeaux; [10]CHU de Nantes, Nantes; [11]University Hospital of Strasbourg, Strasbourg, France; [12]Klinik fur Innere Medizin, Rheumatologie und immunologie, Medius Klinik, Kirchheim unter Teck; [13]Rheumatology, University of Lübeck, Lübeck; [14]Medizinische Klinik und Poliklinik IV, LMU, Muenchen, Germany; [15]Ab2 Bio, Lausanne, Switzerland

Background: Adult Onset Still's Disease (AOSD) is a severe systemic autoinflammatory disease. Elevated interleukin (IL)-18 levels correlate with AOSD disease activity, suggesting a central role
Objectives: To examine the safety and efficacy of IL-18 blockade in AOSD with the administration of Tadekinig alpha, a recombinant human IL-18 binding protein
Methods: Patients (Pts) with AOSD according to Yamaguchi criteria were included if they had been previously treated for at least one month with corticosteroids (CS). The pts received either 80 mg (group 1) or 160 mg (group 2) Tadekinig alpha sc three times weekly for 12 weeks. Oral CS and/or conventional DMARDs were allowed at stable dose in combination with Tadekinig alpha. After 3 wks, group 1 pts qualified as non responders (CRP levels did not decrease by ≥50% from baseline values or absence of temperature normalization) could be up-dosed to 160 mg for an additional 12 weeks. The primary endpoint was safety and secondary endpoints included early signs of efficacy
Results: 23 pts were included (10 and 13 in group 1 and group 2, respectively). 6 pts of group 1 were up-dosed to 160 mg. Baseline characteristics and safety and efficacy results are described in Table 1. Most adverse events (AEs) (47) were considered as mild or moderate. Three serious AEs (SAE) were reported including two that were considered not related to the study drug and one possibly related according to the investigator (toxic optic neuropathy). Four premature discontinuations were related to AEs, including 3 cases of injection site reactions and 1 SAE. Systemic response as defined by ≥70% decrease of serum C-reactive protein (CRP) or normalization of CRP and ferritin levels was obtained in 2/10 and 6/13 pts of groups 1 and 2, respectively in the ITT analysis, and in 2/9 and 6/9 pts of groups 1 and 2, respectively, in the PP analysis.

Table 1. Baseline characteristics and safety and efficacy results

	Group 1 (80 mg) (N=10)	Group 2 (160 mg) (N=13)
Age, median (IQR)	49.5 (34.3–58.8)	35 (30–58)
Median disease duration, months (IQR)	25.5 (8.7–44.2)	11.6 (2.1–37.6)
Pts with previous conventional DMARDs	6	7
Pts with previous biological DMARDs	4	5
Pts with SAEs	2	1
Discontinuations due to AEs*	1	3
Discontinuations due to lack of response*	1	2
Arthritis improvement (≥20% reduction in tender and swollen joint count)**	3/9	4/10
Skin rash resolution**	6/7	2/5
CRP level reduction by ≥70%**	2/10	6/13
Normalization of ferritin levels**	0/7	1/5

*Number of Pts, **Denominator corresponds to Pts with clinical manifestations or abnormal values at baseline.

Conclusions: IL-18 blockade by Tadekinig alpha has an acceptable safety profile and is efficacious, in particular at the 160 mg dosage, in patients with refractory AOSD
Disclosure of Interest: C. Gabay Grant/research support from: AB2 Bio, Roche, Pfizer, Consultant for: AB2 Bio, Roche, Pfizer, MSD, BMS, AbbVie, Sanofi, B. Fautrel: None declared, J. Rech: None declared, F. Spertini: None declared, E. Feist: None declared, I. Koetter: None declared, E. Hachulla: None declared, J. Morel: None declared, T. Schaeverbeke: None declared, M. Hamidou: None declared, T. Martin: None declared, B. Hellmich: None declared, P. Lamprecht: None declared, H. Schultze-Koops: None declared, A. Sleight Employee of: Ab2 Bio, E. Schiffrin Employee of: Ab2 Bio
DOI: 10.1136/annrheumdis-2017-eular.2336

FRI0583 IGG4-RELATED DISEASE AMONG PATIENTS PREVIOUSLY DIAGNOSED WITH IDIOPATHIC RETROPERITONEAL FIBROSIS. A NATIONWIDE DANISH STUDY

N. Lomborg[1], M. Jakobsen[2], C.S. Bode[3], P. Junker[4]. *[1]Department of Rheumatology; [2]Department of Pathology, Vejle Hospital, Vejle; [3]Department of Pathology; [4]Department of Rheumatology, Odense University Hospital, Odense, Denmark*

Background: IgG4-related disease (IgG4-RD) is a recently recognized systemic disease of unknown etiology and prevalence [1]. Retrospective single center series have provided evidence that 13–63% of patients with idiopathic retroperitoneal fibrosis (IRPF) could be reclassified as IgG4-RD. Since immunesuppressants or B-cell targeted therapies may halt or reverse progression, early diagnosis and treatment is important to prevent terminal fibrosis.
Objectives: To estimate the occurrence of IgG4 related retroperitoneal fibrosis (RPF) in Danish patients diagnosed with IRPF.
Methods: The National Danish Pathology Register was searched for biopsy codes relating to retroperitoneal tissue and inflammation from 01.01.2004 through 31.12.2013. Patients below 18 years of age, secondary causes, malignancies, infections, and specimens with multinucleated giant cells or granulomas were excluded. Among 724 candidate cases 68 were identified with IRPF. Among these 25 were left out due to small tissue samples, unavailable patient files or lack of consent. Clinical, laboratory data and imagings were reviewed. Paraffin-embedded tissue blocks were retrieved from 18 pathology departments. Four sections were prepared and stained with hematoxylin-eosin, Weigerts elastin and IgG4 immunostaining. Histopathologic features suggesting an IgG4-RD background were recorded (table). Cut-off levels for IgG4 positive cells at $\geq$30 per HPF and IgG4: total IgG ratio at $\geq$40% were applied. Patients were categorized as IRPF, definite or possible IgG4-RD according to international consensus [2]. Intergroup comparisons were done using Mann-Whitney U test or Chi square test.
Results: Forty three patients (29 males), median age 56 years were included among which 19 (44%) met the criteria for IgG4-RD comprising 7 with definite, 12 with possible IgG4-RD and 24 with IRPF. Biopsies were available from all participants. Extraretroperitoneal manifestations, standard laboratory measures and serum IgG4 (in 5 individuals) did not differ significantly between RPF subsets. Patients with an IgG4: total IgG ratio $\geq$40% had significantly more histopathologic features of IgG4-RD compared to a ratio $<$40% (table). Patients with $\geq$30 IgG4 positive cells per HPF had higher numbers of tissue eosinophils than those with lower IgG4+ cell counts.

Table 1. Histopathologic findings in RPF biopsies (N=43) according to IgG4: total IgG ratio

	IgG4/IgG ratio $\geq$40% N=21	IgG4/IgG ratio $<$40% N=22	p-value
Lymphoplasmacytic infiltrate	21	13	0,002
Storiform fibrosis	12	3	0,004
Obliterative phlebitis	5	1	0,078
Phlebitis without obliteration	4	2	0,378
Increased numbers of eosinophils	13	6	0,030

Conclusions: A total of 44% of IRPF patients was diagnosed with IgG4-RD, 16% with definite and 28% with possible IgG4-RD. This estimate may be conservative because specimens with multinucleated giant cells or granulomas were excluded. The closer association of IgG4: total IgG ratio $\geq$40 vs. lower ratios with histopathologic findings supports a direct pathogenic role by IgG4 bearing cells or IgG4 in IgG4 RPF.
References:
[1] Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med 2012;366 6: 539–51.
[2] Deshpande V, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T et al. Consensus statement on the pathology of IgG4-related disease. Mod Pathol 2012;25 9: 1181–92.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2597

FRI0584 RHEUMATIC AND MUSCULOSKELETAL DISORDERS RELATED TO IMMUNE CHECKPOINT INHIBITORS IN CANCER PATIENTS: A PROSPECTIVE SINGLE-INSTITUTION STUDY

K. Marie[1], L. Rouxel[1], R. Veillon[2], F. Martin[2], C. Dutriaux[3], A. Pham-Ledard[3], S. Prey[3], M. Beylot-Barry[3], M. Gross-Goupil[4], B. Bannwarth[1], C. Richez[1], N. Mehsen-Cetre[1], T. Schaeverbeke[1]. *[1]Rheumatology, Hôpital Pellegrin; [2]Pneumology, Hôpital Haut-Lévêque; [3]Onco-dermatology; [4]Medical Oncology, Hôpital Saint-André, Bordeaux, France*

Background: Immune checkpoint inhibitors (ICI) targeting cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) and programmed cell death protein 1 (PD-1) axis have been a major advance in cancer immunotherapy. By enhancing T cell activity, unprecedented long-lasting tumour responses are observed in selected cancers but some patients experience immune related adverse events (irAE).
Objectives: To evaluate the prevalence and type of rheumatic and musculoskeletal disorders in patients receiving ICI at a single institution (University Hospital of Bordeaux, France).
Methods: All cancer patients with musculoskeletal disorders while receiving ICI were referred to our rheumatology department. For each referred patient, an experienced rheumatologist performed a comprehensive clinical evaluation. Blood tests (inflammatory markers, serum creatine kinase, autoantibodies) and imaging (X-rays, ultrasound) were obtained according to clinical findings. HLA-DR phenotyping was also performed for some patients to search for shared epitope.
Results: From September 2015 to December 2016, 329 patients received ICI (anti CTLA-4: n=38; anti PD-1: n=251; anti PD-L1: n=29; combination anti CTLA-4/anti PD-1: n=11) and 21 patients were referred to our rheumatology department (6.4%). Mean age was 65 years and cancer types included melanoma (n=10), non small cell lung cancer (n=9), Merkel carcinoma (n=1) and renal carcinoma (n=1). All musculoskeletal disorders occurred in patients receiving anti PD-1 (nivolumab: n=12; pembrolizumab: n=6) or anti PD-L1 (avelumab: n=2; atezolizumab: n=1), with a median exposure time of 90 days (range: 1–650 days). There were two distinct clinical presentations: 1) inflammatory arthritis (IA) mimicking either rheumatoid arthritis (n=5) or polymyalgia rheumatica (n=8) and, 2) non-inflammatory musculoskeletal conditions (n=8). Of note, one patient was anti-CCP positive but negative for RF. Shared epitope HLA-DRB1 *01:01 was present in 4 patients. Eleven patients required corticosteroid therapy with a median dose of 15mg/day (range: 7–30 mg/day). Non-inflammatory disorders were easily managed with NSAIDs, analgesics and/or physiotherapy. ICI treatment was temporarily discontinued in one patient only, in line with the clinical trial protocol. To date, there was a partial or complete tumour response to ICI in 10 patients whereas 3 had stable disease and 7 had progressive disease. Tumour response or stable disease was observed in 11 of 12 patients with IA but only in 2 of 8 patients with non-inflammatory conditions.
Conclusions: In our series, patients with immune-related IA mimicking rheumatoid arthritis and polymyalgia rheumatica were responsive to low-to-moderate dose of prednisone and did not require ICI discontinuation. Furthermore, tumour response was frequently observed in such patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6703

FRI0585 FREQUENT, UNUSUALLY SEVERE, LONG LASTING, LOCAL AND SYSTEMIC PNEUMOCOCCAL VACCINE REACTIONS IN PATIENTS WITH CRYOPYRIN-ASSOCIATED PERIODIC SYNDROMES (CAPS): RESULTS OF A PROSPECTIVE REGISTRY BASED STUDY

V.K. Jaeger[1], H.M. Hoffmann[2], T. van der Poll[3], H. Tilson[4], J. Seibert[5], A. Speziale[5], G. Junge[5], K. Franke[6], E. Vritzali[5], P.N. Hawkins[7], J. Kuemmerle-Deschner[8], U.A. Walker[1]. *[1]University Hospital Basel, Basel, Switzerland; [2]University of California at San Diego and Rady Children's Hospital, San Diego, United States; [3]University of Amsterdam, Amsterdam, Netherlands; [4]University of North Carolina, Chapel Hill, United States; [5]Novartis Pharma AG, Basel, Switzerland; [6]QuintilesIMS, Real World Insights, NC, United States; [7]University College London, London, United Kingdom; [8]University Hospital Tübingen, Tübingen, Germany*

Background: Pneumococcal, tetanus and influenza vaccinations are recommended for patients with Cryopyrin-Associated Periodic Syndromes (CAPS) when treated with immunosuppressive medication.
Objectives: This study aims to report the safety of pneumococcal and other vaccinations administered to CAPS patients.
Methods: All CAPS patients followed in the β-CONFIDENT (Clinical Outcomes and Safety Registry study of Ilaris® patients) registry between 07/2010 and 12/2015 were analysed if they had received a vaccination. The β-CONFIDENT registry is a global, long-term, prospective, observational registry, capturing and monitoring CAPS patients treated with canakinumab [1].
Results: 68 CAPS patients (56% female, age range 3.5–73 years) had received a total of 159 vaccine injections, 107 injections against influenza, 19 pneumococcal vaccinations (15 pneumococcal polysaccharide vaccines [PPV], 2 pneumococcal conjugate vaccines [PCV], 2 unknown), 12 against tetanus/diphtheria antigens and 21 other vaccinations.
A reaction was observed in 22 vaccine injections (14%) administered to 18 patients. 13 vaccine reactions (68% of all pneumococcal vaccine injections) occurred in 12 patients receiving pneumococcal vaccines. 12 PPV injections (80% of all PPV injections) elicited a vaccine reaction while none was elicited by the PCV injections The high frequency of pneumococcal vaccine reactions contrasted with that of the reactions to other vaccine types: only 17% and 7% of the tetanus/diphtheria and influenza vaccinations, respectively, elicited a vaccine reaction. The odds ratios to react to the pneumococcal vaccines compared to influenza and tetanus/diphtheria vaccines were 31.0 (95% confidence interval (CI) 8–119) and 10.8 (95% CI 2–74).
Vaccine reactions after pneumococcal vaccinations were more severe and lasted significantly longer compared to the reactions after other vaccinations. Fever was elicited by almost half of all PPV injections. All symptoms after pneumococcal vaccination were observed very rapidly, usually within hours. Unlike the symptoms observed after influenza and tetanus/diphtheria vaccination, which resolved rapidly, the symptoms related to PPV were much more prolonged and in some cases lasted more than 3 weeks. In 2 patients, pneumococcal vaccination also elicited symptoms consistent with systemic inflammation due to CAPS reactivation. All 5 vaccine related serious adverse events were associated with pneumococcal vaccination.

Conclusions: Pneumococcal vaccines, unlike other vaccines, frequently trigger severe local and systemic inflammation in CAPS patients. Clinicians must balance potential benefits of pneumococcal immunisation against safety concerns.

References:

[1] Kuemmerle-Deschner JB, et al. Safety and Efficacy of Canakinumab in Patients with CAPS: Interim Results from the Beta-Confident Registry [abstract]. Arthritis Rheumatol. 2015;67(suppl 10).

Acknowledgements: The β-CONFIDENT registry was supported by Novartis Pharma AG, Basel, Switzerland.

Disclosure of Interest: V. Jaeger: None declared, H. Hoffmann Consultant for: the steering committee of the β-CONFIDENT registry and in this function received consulting fees from Novartis., T. van der Poll Consultant for: the steering committee of the β-CONFIDENT registry and in this function received consulting fees from Novartis., H. Tilson Consultant for: the steering committee of the β-CONFIDENT registry and in this function received consulting fees from Novartis., J. Seibert Employee of: Novartis Pharma AG, Basel, Switzerland, A. Speziale Employee of: Novartis Pharma AG, Basel, Switzerland, G. Junge Employee of: Novartis Pharma AG, Basel, Switzerland, K. Franke Employee of: QuintilesIMS who served as the CRO that conducted the β-CONFIDENT registry., E. Vritzali Employee of: Novartis Pharma AG, Basel, Switzerland, P. Hawkins Consultant for: the steering committee of the β-CONFIDENT registry and in this function received consulting fees from Novartis., J. Kuemmerle-Deschner Consultant for: the steering committee of the β-CONFIDENT registry and in this function received consulting fees from Novartis., U. Walker Consultant for: the steering committee of the β-CONFIDENT registry and in this function received consulting fees from Novartis.

DOI: 10.1136/annrheumdis-2017-eular.1513

FRI0586 INTERLEUKIN (IL)-1 INHIBITION WITH ANAKINRA AND CANAKINUMAB IN BEHÇET'S DISEASE RELATED UVEITIS: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

C. Fabiani[1], A. Vitale[2], G. Emmi[3], G. Lopalco[4], L. Vannozzi[3], S. Guerriero[4], S. Gentileschi[2], D. Bacherini[3], R. Franceschini[2], B. Frediani[2], M. Galeazzi[2], F. Iannone[4], G.M. Tosi[2], L. Cantarini[2]. *[1]Humanitas Research Hospital, Rozzano, Milan; [2]University of Siena, Siena; [3]University of Florence, Florence; [4]University of Bari, Bari, Italy*

Objectives: To evaluate the role of interleukin (IL)-1 inhibitors anakinra (ANA) and canakinumab (CAN) in the treatment of Behçet disease (BD)-related uveitis

Methods: multicenter retrospective observational study including 19 consecutive BD patients (31 affected eyes) receiving treatment with anti-IL-1 agents. Data were analyzed at baseline, at 3 and 12 months. Primary end-point: reduction of ocular inflammatory flares (OIF). Secondary end-points: improvement of Best Corrected Visual Acuity (BCVA); reduction of macular thickness defined by optical coherence tomography (OCT) and of vasculitis identified with fluorescein angiography (FA); evaluation of statistically significant differences between patients treated with IL-1 inhibitors as monotherapy, subjects also administered with disease modifying anti-rheumatic drugs (DMARDs) and/or corticosteroids as well as between patients administered with IL-1 inhibitors as first line biologic treatment and those previously treated with TNF-α inhibitors

Results: at 12 months OIF significantly decreased from 200/100 patients/year to 48.87/100 patients/year ($p<0.0001$). The frequency of retinal vasculitis identified by FA significantly decreased between baseline, 3-month and 12-month follow-up visits ($p<0.0001$ and $p=0.001$, respectively). OIF rate was significantly higher in patients co-administered with DMARDs (81.8/100 patients/year) than in patients undergoing IL-1 inhibitors as monotherapy (0.0/100 patients/year) ($p=0.03$). No differences were identified on the basis of corticosteroid use and between patients administered with IL-1 inhibitors as first-line biologic approach or second-line. Steroid dosage was significantly decreased at 12-month visit compared to baseline ($p=0.02$).

Conclusions: treatment with IL-1 inhibitors is effective in the management of BD-related uveitis and provides a long-term control of ocular inflammation in refractory and long-lasting cases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1119

FRI0587 DIFFERENT FACTORS ARE RELATED TO RECURRENCE OF EXISTING ORGAN INVOLVEMENT AND NEW DEVELOPMENT OF ORGAN INVOLVEMENT IN IGG4-RELATED DISEASE

I. Mizushima, S. Tsuge, Y. Fujisawa, S. Hara, F. Suzuki, K. Ito, H. Fujii, K. Yamada, M. Kawano. *Division of Rheumatology, Kanazawa University Hospital, Kanazawa, Kanazawa, Japan*

Background: IgG4-related disease (IgG4-RD) is a recently recognized systemic inflammatory disorder that can affect many organs [1]. In IgG4-RD, relapse including recurrence of existing organ involvement (REOI) and new development of organ involvement (NDOI) easily occurs during the clinical course, and its predictors have been suggested [2, 3]. However, differences between risk factors of REOI and those of NDOI have not been clarified.

Objectives: This study aimed to clarify the respective risk factors of REOI and NDOI in IgG4-RD.

Methods: We retrospectively investigated factors related to REOI and NDOI in 86 IgG4-RD patients whose follow-up period was more than 12 months. For assessment of factors related to REOI and NDOI, we performed uni- and multivariate Cox regression analysis. On stepwise multivariate analysis, we applied the variables with $P<0.1$ in univariate analysis and the predictors of relapse suggested in past reports (age, sex, serum IgG4, IgG, and IgE levels, eosinophil counts, and RF positivity) [2, 3], and used the forward selection method (including factors presenting with $P<0.05$).

Results: The patients comprised 57 men and 29 women (mean age 65.9 years). Mean follow-up period was 63.1 months (range 14–150). At diagnosis, their mean serum IgG4 level was 718 mg/dL (range 10.7–3,610). Seventy-one patients were treated with glucocorticoid (GC). REOI was detected at 52.3 months (range 1.0–120) after the diagnosis in 20 patients, including 4 not receiving GC at that time. On the other hand, NDOI was detected at 37.6 months (range 5.0–120) after the diagnosis in 15 patients, including 8 not receiving GC then. In multivariate Cox regression analysis, blood eosinophil counts [per 100/μL, hazard ratio (HR) 1.072, 95% confidence interval (CI) 1.018–1.129, $P=0.008$] and continuation of GC (vs discontinuation or observation without GC, HR 0.245, 95% CI 0.076–0.793, $P=0.019$) had a significant impact on the time to NDOI, whereas age (per year, HR 0.942, 95% CI 0.899–0.986, $P=0.011$) and ANA positivity (vs negativity, HR 6.632, 95% CI 1.892–23.255, $P=0.003$) had a significant impact on the time to REOI.

Conclusions: The present study suggests that the risk factors of REOI and NDOI in IgG4-RD are different.

References:

[1] Stone JH et al. IgG4-related disease. N Engl J Med. 2012 Feb 9;366(6):539–51.
[2] Yamamoto M et al. Identification of relapse predictors in IgG4-related disease using multivariate analysis of clinical data at the first visit and initial treatment. Rheumatology (Oxford). 2015 Jan;54(1):45–9.
[3] Wallace ZS et al. Predictors of disease relapse in IgG4-related disease following rituximab. Rheumatology (Oxford). 2016 Jun;55(6):1000–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2425

FRI0588 INTERIM RESULTS OF A PHASE 2 STUDY OF XMAB®5871, A REVERSIBLE B CELL INHIBITOR, IN IGG4-RELATED DISEASE

J.H. Stone[1], Z.S. Wallace[1], C.A. Perugino[1], A.D. Fernandes[1], P.S. Patel[1], P.A. Foster[2], D.J. Zack[2]. *[1]Massachusetts General Hospital Rheumatology Unit, Harvard, Boston; [2]Clinical Development, Xencor Inc., Monrovia, United States*

Background: IgG4-related disease (IgG4-RD) is an immune-mediated condition causing fibro-inflammatory lesions that can lead to irreversible organ damage. No approved therapies for IgG4-RD exist. We report the use of a novel monoclonal antibody, XmAb5871, in IgG4-RD. XmAb5871 is a humanized anti-CD19 antibody with an Fc portion engineered for increased affinity (up to 400-fold over native IgG_1) to FcgRIIb, the only Fc receptor on B cells. Co-ligation of CD19 and FcgRIIb leads to inhibition of B lineage cells bearing these targets. Reversible inhibition of B cell function without B cell ablation is one potential advantage of this approach.

Methods: The trial is an open-label investigation of XmAb5871 in active IgG4-RD, defined by an IgG4-RD Responder Index (RI) of ≥3. XmAb5871 (5 mg/kg) is administered IV every 14 days for 12 doses. The primary outcome measure is the proportion of patients on day 169 (2 weeks following the last dose) with a decrease in the IgG4-RD RI of 2 or more points compared to baseline. Glucocorticoids are permitted but not required at entry and must be discontinued by two months. Other immunosuppressive medications are not allowed. Imaging and mechanistic studies are performed at baseline and at selected intervals.

Results: Fifteen patients were enrolled between March 2016 and January 2017. As of October 31, 2016, 12 patients had received at least one infusion of XmAb5871. The median age of the 12 patients is 58 years (range: 43 to 78 years). Two-thirds of the patients are male. Nine of the 12 patients had elevated serum IgG4 concentrations at baseline with a mean serum IgG4 of 499 mg/dL (range: 25–2415; normal <86 mg/dL). The median baseline IgG4-RD RI score was 10 (range: 2–30), with active inflammatory disease in at least one organ system (median 4, range: 1–10). The organs most commonly affected were lymph nodes (75% of patients), submandibular glands (67%), parotid glands (58%), and lacrimal glands (50%). Four patients (33%) had kidney involvement and 3 (25%) had heart/pericardium findings. Nine of 11 patients (82%) have had an initial response to XmAb5871 therapy of at least a three-point reduction in the IgG4-RD RI within two weeks of the first dose. As of Oct 31st, 2016, five patients attained disease remission (an IgG4-RD RI of 0 and no prednisone treatment after 2 months) during the study. Efficacy outcomes will be updated as more patients complete the study. One patient had been on glucocorticoid treatment for 2 years and was on prednisone of 15 mg/day at baseline, but was able to discontinue prednisone by 2 months after starting treatment. Three patients experienced minor, transient gastrointestinal side-effects during the 1st infusion. One patient had infusion-related GI symptoms on the 5thinfusion and subsequently developed rash and arthritis. She was found to have anti-drug antibodies and has discontinued the study. Mechanistic studies show that both peripheral B cells and plasmablasts decrease substantially following therapy in the majority of patients. Studies of the mechanism of this decrease and functional B cell assays are under way.

Conclusions: XmAb5871 is tolerated well in patients with active IgG4-RD and is a promising treatment approach for IgG4-RD.

Disclosure of Interest: J. Stone Grant/research support from: Genetech/Roche, Xencor, Consultant for: Genentech/Roche, Xencor, Z. Wallace: None declared, C. Perugino: None declared, A. Fernandes: None declared, P. Patel: None declared, P. Foster Shareholder of: Full time employee of Xencor, Employee of: Full time employee of Xencor, D. Zack Shareholder of: Full time employee of Xencor, Employee of: Full time employee of Xencor
DOI: 10.1136/annrheumdis-2017-eular.3301

FRI0589 CANCER IS FREQUENT IN PATIENTS WITH ANTICENTROMERE PATTERN

C. Vázquez-Triñanes[1], V. Alende[2], E. González[3], R. Lorenzo[4], T. Caínzos[5], L. González[6], S. Rodríguez[6], B. Sopeña[2] on behalf of Círculo de estudio de las enfermedades autoinmunes de Galicia (CEAG). *[1]Systemic Autoimmune Diseases and Thrombosis Unit, H. Álvaro Cunqueiro, Vigo; [2]Hospital Clínico Universitario de Santiago, Santiago; [3]Complejo Hospitalario de Ourense, Ourense; [4]H. Álvaro Cunqueiro, Vigo; [5]Hospital Arquitecto Marcide, Ferrol; [6]H. Povisa SA, Vigo, Spain*

Background: Anti-centromere pattern (ACA) is infrequently seen among antinuclear antibodies (ANA) detected by indirect immunofluorescence (IFI). ACA is associated with systemic autoimmune diseases (SAD), especially systemic sclerosis (SSc). Some studies had recently related ACA with cancer, mostly with breast and lung cancer [1]. However, most published series of patients with ACA lack information about cancer occurrence. A prevalence of cancer of 11.1% was the only reported data, on a series of 45 unselected patients with ACA [2]
Objectives: Our aim was to study the prevalence of cancer in the largest series of patients with ACA, with a long follow-up. Our second objective was to make a cohort to calculate the incidence of cancer and to try to identify risk markers of cancer in these patients
Methods: We included consecutive patients with at least 2 positive determinations of ANA with ACA by IFI on Hep2 cells between January 1st of 2011 and June 30th of 2015 in 6 Galician hospitals. The authors reviewed each patient's chart to determine the presence of cancer and its type among numerous variables. Then, patients with cancer at the moment of the first positive determination of ANA with ACA were excluded. We checked the presence of any tumour in patients of this cohort at the end of follow-up to calculate the incidence of cancer. Finally, we compared patients with and without cancer by multivariate analysis, with the SPSS 20.0. The ethics committees of each hospital approved the study and patients gave their consent
Results: 369 patients with ACA were studied, of which 333 were women (90.2%), with a mean age of 64.7 years (range: 22–92). The mean follow-up from the first positive ACA determination was 67.6 months. 283 patients (76.7%) had a SAD: 46.3% SSc (79% of whom were lc-SSc), 8.13% primary biliary cholangitis, 7.05% Sjögren's syndrome, 4.6% autoimmune hepatitis and 11 other SAD (polyarthritis, SLE, Raynaud phenomenon, sarcoidosis, mixed connective tissue disease, etc). 45 of these patients (15.9%) had any overlap syndrome. 39 patients had cancer at some time (10.6%), 3 of them with 2 types of cancer. The most frequent were: breast in 9 (23.1%), lung in 5 (11%), NHL in 5 (11%) and colorectal in 4 (10.3%). Cancer preceded the diagnosis of ACA in 19 patients (48.7%), with a mean time to diagnosis of 9.1 years (range 1–18). In the cohort of 350 patients with ACA the incidence was 1.14 per 100 patients per year (n 20). The mean time to diagnosis of cancer was 7.3years (range 1–27). The oldest age was the only risk marker of cancer identified (70.8±13.29 years vs. 63.9±14.32, p 0.005). There were no differences in the other variables analysed including sex, tobacco, diagnosis of SAD, capillaroscopy pattern, ANA titrations and mortality
Conclusions: Cancer was frequent in patients with ACA, with a prevalence of 10.6% and incidence of 1.14 per 100 patients per year. The only risk marker of cancer identified in this population was the oldest age
References:
[1] Briasoulis E, Kamposioras K, Tzovaras V et al. CENP-B specific anti-centromere autoantibodies heralding small-cell lung cancer. A case study and review of the literature. Lung cancer 2008;60:302–306.
[2] Zuber M, Gotzen R, Filler I. Clinical correlation of anticentromere antibodies. Clinical rheumatology 1994;13(3):427–432.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4455

FRI0590 SOLUBLE INTERLEUKIN-2 RECEPTOR LEVELS REFLECT DISEASE ACTIVITY IN IGG4-RELATED DISEASE AND PRIMARY SJÖGREN'S SYNDROME

M. Akiyama, T. Sasaki, Y. Kaneko, H. Yasuoka, K. Suzuki, K. Yamaoka, T. Takeuchi. *Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan*

Background: Soluble interleukin-2 receptor (sIL-2R) is known as an indicator for activation status of lymphocytes and could be a potential biomarker for disease activity of lymphoproliferative disorders and autoimmune diseases.
Objectives: The aim of this study was to examine the association of sIL-2R with disease activity in patients with IgG4-related disease (IgG4-RD) and primary Sjögren's syndrome (pSS).
Methods: Consecutive 45 patients with active, untreated IgG4-RD, 117 patients with pSS, and 10 patients with sicca syndrome (subjects with xerostomia with neither anti-SSA/SSB antibodies nor lymphocytic infiltration by lip biopsy) were enrolled. Disease activity of IgG4-RD and pSS was determined based on the IgG4-RD responder index (IgG4-RD RI) score and the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score, respectively. The association of sIL-2R with disease activity was analyzed.
Results: The levels of sIL-2R and serum IgG were significantly higher in both IgG4-RD (709U/mL, and 1988mg/dL) and pSS (464U/mL, and 1851mg/dL) compared to sicca syndrome (276U/mL, and 1255mg/dL). Serum levels of IgG4, IgE, and circulating eosinophil counts were significantly higher in IgG4-RD (552mg/dL, 732IU/mL, and 366/mm^3) compared to pSS (37mg/dL, 216IU/mL, and 157/mm^3) and sicca syndrome (45mg/dL, 132IU/mL, and 137/mm^3). On the other hand, the levels of serum IgA and IgM were significantly higher in pSS (312mg/dL, and 112mg/dL) compared to IgG4-RD (182mg/dL and 81mg/dL) and sicca syndrome (228mg/dL and 78mg/dL). The levels of serum C-reactive protein, lactate dehydrogenase, CH50, CC chemokine ligand (CCL17)/thymus and activation-regulated chemokines (TARC) were not different among the three groups. In patients with IgG4-RD, the baseline IgG4-RD RI scores significantly correlated with the levels of sIL-2R (ρ=0.715, $p<0.0001$), serum IgG (ρ=0.672, $p<0.0001$) and IgG4 (ρ=0.632, $p<0.0001$), but not serum IgE levels (ρ=0.290, p=0.082) and circulating eosinophil counts (ρ=0.149, p=0.335). In patients with pSS, the ESSDAI scores significantly correlated with the levels of sIL-2R (ρ=0.615, $p<0.0001$) and serum IgG (ρ=0.627, $p<0.0001$), but not the levels of serum IgA (ρ=0.169, p=0.073) and IgM (ρ=0.133, p=0.157). Furthermore, the number of affected organs positively correlated with sIL-2R levels in both IgG4-RD (ρ=0.725, $p<0.0001$) and pSS (ρ=0.559, $p<0.0001$). Receiver operating characteristic curve analysis demonstrated that sIL-2R was the most distinguishable biomarker for the presence of extra-dacryosialadenitis lesions in patients with IgG4-RD, compared to serum IgG and IgG4, with a cut-off value of 424 U/mL (AUC=0.917, $p<0.0001$), and in patients with pSS with 513 U/mL (AUC=0.894, $p<0.0001$). The sIL-2R levels in patients with IgG4-RD decreased significantly after glucocorticoid treatment. Notably, the cases which could be followed up at disease relapse or exacerbation showed the re-elevation of sIL-2R levels.
Conclusions: Soluble IL-2R level is a biomarker for disease activity, in particular for the extent of organ involvements and extra-dacryosialadenitis lesions in patients with IgG4-RD and pSS. Furthermore, sIL-2R level could be useful for longitudinal disease monitoring in patients with IgG4-RD.
Acknowledgements: We sincerely thank all the physicians and others caring for the patients enrolled in this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4220

FRI0591 RISK FACTORS FOR DISEASE RELAPSE IN IGG4-RELATED DISEASE FOLLOWING GLUCOCORTICOIDS TREATMENT

T. Sasaki, M. Akiyama, Y. Kaneko, H. Yasuoka, K. Suzuki, K. Yamaoka, T. Takeuchi. *Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan*

Background: IgG4-related disease (IgG4-RD) is a fibroinflammatory disease characterized by elevated serum IgG4 and infiltration of IgG4$^+$ plasma cells at affected sites. The patients with IgG4-RD respond well to glucocorticoids (GCs), but one-third of the patients experience disease relapse during tapering of GCs (1). The risk factors for disease relapse following treatment are unclear.
Objectives: The aim of this study was to identify the risk factors of disease relapse following reduction of GCs therapy.
Methods: Consecutive, newly diagnosed patients with IgG4-RD who were followed over 6 months after treatment with GCs in our department were enrolled. The patients were divided into two groups according to the presence or absence of disease relapse. Disease relapse was defined as the appearance of new lesions or the re-enlargement of involved organs that required dose-increase of GCs. Patient characteristics and laboratory findings at diagnosis were compared and receiver operating characteristic curve analysis was performed to identify the relevant predictive factors of disease relapse.
Results: A total of 34 patients were included and all patients were treated with GCs alone as initial treatment. Ten patients (29.4%) experienced relapses during GCs dose tapering which was at 16.0 months (median) after GCs initiation. No difference was found in age, sex, body weight, and disease duration between the two groups. The observation periods and the initial/last GCs dose were also not different. However, serum IgG4 (939 vs 450 mg/dl, p=0.008), serum IgG4/IgG ratio (0.35 vs 0.24 p=0.046), soluble IL-2 receptor (907 vs 677 U/ml, p=0.032) and number of organ involvement (4.3 vs 3.0, p=0.028) were significantly higher in patients with relapse than those without, while the level of IgA (135 vs 205 mg/dl, p=0.015) and IgM (60 vs 91 mg/dl, p=0.038) were significantly lower in the patients with relapse. IgG4 decreased to a comparable level in both groups after GCs treatment (200 vs 91 mg/dl, p=0.124), but increased in the relapse group afterward (387 vs 115 mg/dl at last observation, p=0.048). The predictive values (sensitivity, specificity) at IgG4-RD diagnosis for relapse were as follows; serum IgG4 570 mg/dl (90.0%, 75.0%), IgG4/IgG 0.31 (70.0%, 79.2%), soluble IL-2 receptor 470 IU/ml (100.0%, 54.5%), the number of affected organs of four (80.0%, 70.8%), IgA 100 mg/dl (50.0%,100.0%) and IgM 60 mg/dl (80.0%,75.0%) (Figure 1).
Conclusions: Higher serum IgG4, soluble IL-2 receptor, and the number of affected organs and lower levels of serum IgA and IgM at baseline indicate

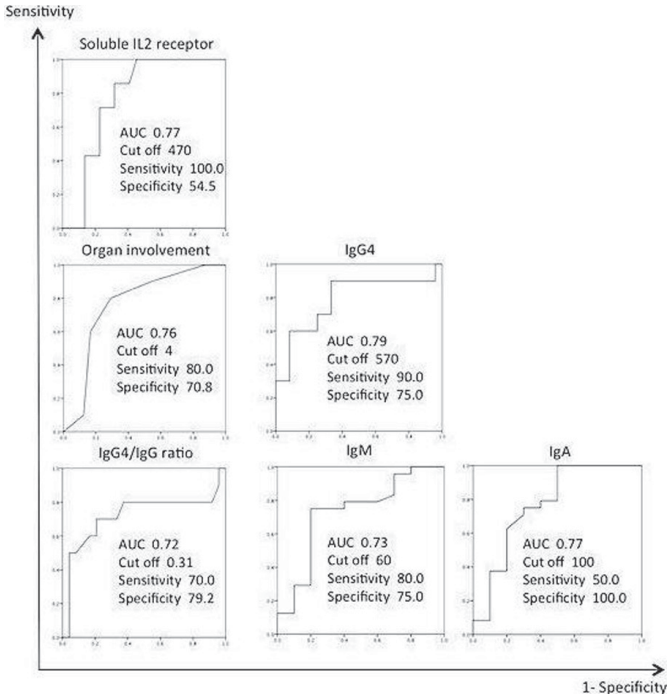


Figure 1

the higher likelihood of disease relapse following GCs therapy in patients with IgG4-RD.

References:

[1] Brito-Zerón P, Kostov B, Bosch X, Acar-Denizli N, Ramos-Casals M, Stone JH. Therapeutic approach to IgG4-related disease: A systematic review. Medicine (Baltimore). 2016;95:e4002.

Acknowledgements: We sincerely thank all the physicians and others caring for the patients enrolled in this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4190

FRI0592 CLINICAL, ANALYTICAL AND RADIOLOGICAL CHARACTERISTICS IN A COHORT OF PATIENTS WITH SARCOIDOSIS

A. Ruiz Román[1], C. Aguilera Cros[1], M. Arcila Durán[1], M. León Luque[1], M. Lisbona Muñoz[1], J.P. Sanchez Serrano[2], J.A. Rodriguez Portal[3], J. Povedano Gomez[1]. *[1]Rheumatology, Hospital Virgen del Rocio, Sevilla; [2]Breeding and Genetics, Irta, Caldas de Montbui; [3]Pneumology, Hospital Virgen del Rocio, Sevilla, Spain*

Background: Sarcoidosis is a systemic granulomatous disease, frequently affecting lungs, eyes and skin, although it may damage other organs, among them the musculoskeletal system

Objectives: To describe the clinical characteristics and radiological pattern in a cohort with predominantly pulmonary sarcoidosis, and to determine the relationship between the levels of angiotensin converting enzyme (ACE), pulmonary radiological stage and sarcoidosis course (chronification or remission)

Methods: Data from 2328 patients in an Interstitial Lung Diseases consultation during the first half of 2016 were analyzed. Out of these, 50 had sarcoidosis.The delay in the diagnosis of sarcoidosis was defined as the difference in years between the diagnostic suspicion and diagnosis of sarcoidosis.

Chi square tests were used, assuming an error of the first species not higher than 0.05, in order to: 1. Study the association between angiotensin converting enzyme (ACE) levels and binary variables (extrapulmonary symptoms, radiological stage and evolution of S) 2. Determine the association between evolution, the radiological stage and the presence of extrapulmonary symptoms.

Results: We included 29 (58%) women and 21 (42%) men, (mean age of 44±11.7 years). Initial diagnosis: 88% S, 8% lymphoma and 4% tuberculosis. Of the 44 diagnosed cases of S, 24 were on the first visit, 11 the following year and 1 seven years later. Of the 4 lymphomas, 2 were diagnosed of S that same year and the other 2 were diagnosed the following year. Of the 2 tuberculosis, one was diagnosed of S in one year and the other at 4 years.

The most frequent extrapulmonary manifestations were cutaneous 24%, followed by the articular, cardiac and ocular in 10%, neurological 8% and renal 4%. In 6% of patients, the first clinical manifestation of the disease was bilateral arthritis of the ankles, The ACE title is increased in 62% of patients, normal in 34%. The mean and standard deviation of the title of patients with an increased ACE value was 150.5 and 53.4 IU/L, respectively. In all patients, x-ray and high resolution tomography were performed, with stage 2 being the most frequent (44%), followed by 3 (20%), 0 and 1 (14%) and 4 (8%). Histological confirmation was obtained by transbronchial biopsy (66%), cutaneous (12%) or lymph node biopsy (12%) in 90% of the patients. 90% of patients have been treated with oral glucocorticoids and 42% associate immunosuppressive therapy.

The ACE levels showed no statistical association with any of the variables studied, although a very clear association (p=0.04754) was observed between the course of the disease and the presence of extrapulmonary symptoms: from the 25 patients without extrapulmonary symptoms, only in 35% of cases the process become chronic.

Conclusions: Our results, in general, coincide with what is published in the literature. In our cohort, initial diagnosis of S was relatively high (28/50 =56%), while misdiagnosis was relatively low (6/50 =12%). The level of ACE does not seem to be clearly associated with the presence of extrapulmonary symptoms, nor with the course of S. However, the presence of extra-pulmonary symptoms seems to lead to a chronification

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5480

FRI0593 ASSOCIATION OF THYMOMA WITH AUTOIMMUNE DISEASES IN A SERIES OF 83 CASES

A. González García[1], W.A. Sifuentes Giraldo[2], J.L. Morell Hita[2], J.L. Patier de la Peña[1]. *[1]Internal Medicine; [2]Rheumatology, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Thymoma is the most common neoplasm originated from the thymus gland and accounting for 50% of anterior mediastinal tumors. Within its clinical manifestations are included the loss of self-tolerance and the development of autoimmunity.

Objectives: To study the frequency of autoimmune diseases (AD) in patients with thymoma and to describe their clinical characteristics and outcome.

Methods: We performed a retrospective observational study of a cohort of patients diagnosed with thymoma and followed-up in our center between January 1985 and September 2016. The variables evaluated included demographics, thymoma characteristics, clinical and analytical manifestations of autoimmunity, treatment and outcome.

Results: A total of 83 patients were included, 56.6% of them women, with a mean age at diagnosis of the thymoma of 58.4±15.8 years (range: 16–94), 31.3% of which corresponded to type I The classification of Masaoka, 39.1% to II, 17.2% to III and 10.9% to IV. There were one or more AD associated in 41 cases (49.4%). The most frequent diagnoses were myasthenia gravis (19), systemic lupus erythematosus (SLE) (4), subacute cutaneous lupus erythematosus (1), Sjögren's syndrome (1), rheumatoid arthritis (1), spondyloarthritis (1), sarcoidosis (1), hemolytic anemia (2), pernicious anemia (1), aplastic anemia (1), cutaneous limited systemic sclerosis (1), urticaria-vasculitis, erythroblastopenia (1), recurrent pericarditis (1), thyroid disease (2) and lichen planus (1). The diagnosis of AD preceded to thymoma in 38.2% of cases and was later in the remaining cases. In 4 cases there was also a concomitant primary immunodeficiency (variable common immunodeficiency 3, CD4 immunodeficiency 1). The most frequently identified autoantibodies were anti-acetylcholine receptor (14/41, 34.1%), anti-striated muscle (3/41, 7.3%), ANA (11/41, 26.8%), (3/41, 7.3%), rheumatoid factor (3/41, 7.3%), anti-thyroid (3/41, 7.3%), antiphospholipids (2/41, 9%) and anticentromere (1/41, 2.4%). In the comparison of patients with and without associated AD, no significant differences were found regarding age, sex or Masaoka classification. There were 6 deaths, 4 in group with associated AD and 2 in the group without AD, but without significant difference (p=0.3797).

Conclusions: In the analyzed population of patients with thymoma of our center, almost half of them developed AD, which in a major group preceded the diagnosis of neoplasia. The spectrum of autoimmunity associated with thymoma was quite broad, including organ-specific AD such as myasthenia gravis (which is most frequently described in the literature) and autoimmune cytopenias, but also to systemic AD, the most common being SLE. The autoimmunity study should be included in the assessment of the patient with thymoma as it could contribute to the early diagnosis of associated AD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6992

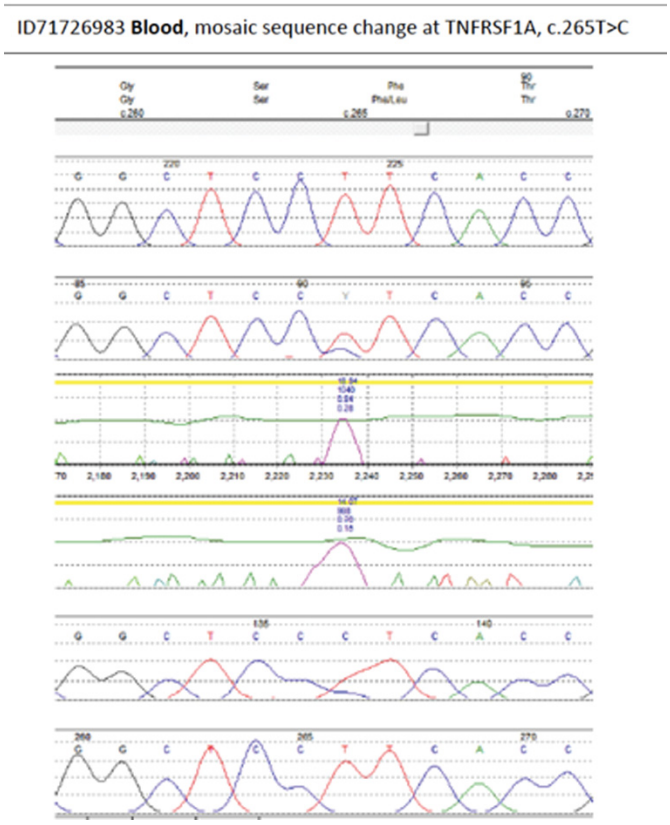
FRI0594 A CASE OF MOSAICISM IN TNF ASSOCIATED PERIODIC SYNDROME (TRAPS)

A. Kontzias[1], C. Calabrese[1], Y.-W. Cheng[2]. *[1]Rheumatology and Immunology; [2]Laboratory Medicine, Cleveland Clinic, Cleveland, United States*

Background: Tumor necrosis factor receptor (TNFR)–associated periodic syndrome (TRAPS) is an autosomal-dominant disease caused by gain-of-function mutations in the TNFRSF1A gene, which encodes the 55-kd TNFR type I (TNFRI) protein. Mosaicism has been recently idenitfied in a single patient.[1] A 60 year old male presented with a 6 year history of intermittent fever as high as 103.5, lasting 3–4 weeks with associated peritoneal symptoms, arthralgias, myalgias, lymphadenopathy, bilateral episcleritis, erythematous rash in his torso. Prednisone up to 60 mg daily only partially alleviated his symptoms and colchicine was ineffective.

Objectives: To explore the role of mosaicism in a patient with adult onset TRAPS phenotype.

Methods: DNA was extracted from the patient's whole blood, saliva and hair root. The TNFRSF1A gene was analyzed by Sanger sequencing in all tissues, and next-generation sequencing in whole blood. In silico molecular modeling was performed to predict the structural and functional consequences of the tumor necrosis factor receptor (TNFR) type I protein mutation.
Results: Sanger sequencing and next-generation sequencing methods revealed differential tissue presence of a misense mutation at c.265 T>C p.Phe89Leu (F89L) Chr12(GRCh37):g.6442960A>G ex3 rs104895245. The mutant allele was present in whole blood and buccal mucosa and absent in hair root, supporting the presence of somatic TNFRSF1A mosaicism. In silico prediction modeling with SIFT and PolyPhen2 suggested that this mutation led to numerous structural rearrangements which resulted in changes in the protein surface profile. The patient had a complete response to treatment with canakinumab an interleukin-1 beta blocker, with resolution of symptoms and normalization of acute-phase protein levels.



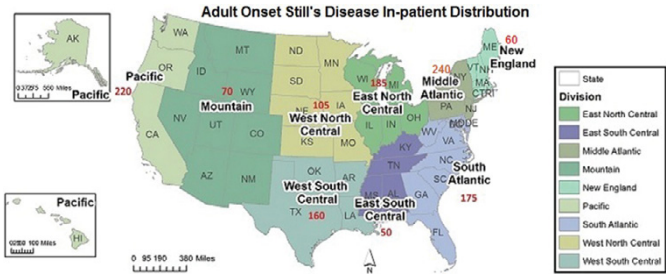
Conclusions: This is the second reported case of TNFRSF1A mosaicism in a patient with TRAPS, which was attributable to a de novo mosaic missense mutation in the TNFRSF1A gene. (c.265 T>C) p.Phe89Leu (F89L) The clinical picture in this patient, including the complete response to IL-1 blockade, was typical of that found in TRAPS. This case suggests that adult onset TRAPS phenocopies may be attributed to somatic (or postzygotic) mutations.
References:
[1] Rowczenio et al Association of Tumor Necrosis Factor Receptor–Associated Periodic Syndrome With Gonosomal Mosaicism of a Novel 24-Nucleotide TNFRSF1A Deletion ARTHRITIS & RHEUMATOLOGY, Vol. 68, No. 8, August 2016, pp 2044–2049.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3485

FRI0595 EPIDEMIOLOGY AND COMPLICATIONS OF HOSPITALIZED PATIENTS WITH ADULT ONSET STILL'S DISEASE IN UNITED STATES: A NATIONWIDE ESTIMATE

B. Mehta[1], W. Briggs[2], P. Efthimiou[3,4]. *[1]Rheumatology, HSS; [2]New York Presbyterian/ Brooklyn Methodist Hospital, New York, United States; [3]Rheumatology, New York Presbyterian/ Brooklyn Methodist Hospital; [4]Medicine, Weill Cornell Medicine, New York, United States*

Background: There is a dearth of epidemiological studies in the US and worldwide on Adult Onset Still's Disease (AOSD). Currently, there is no consensus on its incidence and prevalence in different populations. Most studies report a majority of patients below the age of 35.[1]
Objectives: To describe the demographics, complications and mortality of hospitalized patients with AOSD in United States.
Methods: All adult (>18 years) hospitalized patients in 2013 from a nationwide inpatient sample (NIS) database were captured. AOSD patients were identified using the ICD-9 code 714.2 that was in use in 2013. Patients also coded for Rheumatoid Arthritis, Lupus, Myositis, Polymyalgia Rheumatica, Ankylosing Spondylosis and Psoriatic Arthritis were excluded. This was done in order to truly capture patients with strictly AOSD. NIS is the largest all- payer inpatient care database in the United States with approximately 8 million hospitalizations each year. Discharge weights were used to enable nationwide estimates. Descriptive statistics were represented as means/medians for continuous and as frequencies and percentages for categorical variables.
Results: In 2013, 1410 US patients were coded with the ICD-9 code 714.2 and, after excluding concomitant rheumatic disease diagnoses as per protocol, 1265 AOSD patients were analyzed. AOSD patients had a mean age of 53.8 (SD - 18.1) years and a median age of 54 years. 70.4% were females. The racial/ethnic distribution showed that 61.6% white, 13.9% African American and 17.3% Hispanic patients were affected. 56.9% were hospitalized in urban teaching hospitals. The Mid-Atlantic census division had the highest number of patients – 240 (Figure). 35 (2.8%) of patients developed Macrophage Activating Syndrome (MAS). 30 (2.4%) patients had other severe complications of AOSD like disseminated intravascular coagulation (DIC) and thrombotic thrombocytopenic purpura (TTP). Median length of stay was 4 days and median hospital charges were $31,400 (Table). There were 35 inpatient deaths (mortality 2.8%): 71.4% of deaths were in females, 50% in Asians, and 71.4% were in patients in the 54- 67 age group.

Variables	N=1265	Percentage
Age (mean age in years (standard deviation))	53.9 (18)	
Female Sex	890	70.4%
White	730	61.6%
Black	165	13.9%
Hispanic	205	17.3%
Asian	50	4.2%
Bed Size of the Hospital		
Small	140	13.7%
Medium	270	26.5%
Large	610	59.8%
Location/teaching status of hospital		
Rural	100	9.8%
Urban non-teaching	340	33.3%
Urban teaching	580	56.9%
Macrophage Activating Syndrome	35	2.8%
Other complications - (DIC and TTP)	30	2.4%
In-hospital death	35	2.8%
Length of stay (Median no of days)	4 days	
Total Hospital Charges (Median in dollars)	$ 31,400	



Conclusions: In hospitalized American AOSD patients, the average age was higher than previously thought. This may indicate an aging population with a higher number of comorbidities that justify hospitalization. Mortality increased with age and was higher among women and Asians. To our knowledge, this is the largest epidemiological study of AOSD today in the USA.
References:
[1] Sakata N, Shimizu S, Hirano F, Fushimi K. Epidemiological study of adult-onset Still's disease using a Japanese administrative database. Rheumatol Int 2016;36(10):1399–405 doi: 10.1007/s00296–016–3546–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5490

FRI0596 ANAKINRA TREATMENT IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: A SINGLE-CENTER EXPERIENCE (CASE SERIES)

B. Ergezen, S. Ugurlu, H. Ozdogan. *Division of Rheumatology, Department of Internal Medicine, Cerrahpasa Medical Faculty, University of Istanbul, Istanbul, Turkey*

Background: Approximately in 5 to 10% of FMF patients there is insufficient response and/or intolerance to colchicine treatment. Several reports have pointed out the efficacy of IL-1 blockade in colchicine resistant FMF subgroup.
Objectives: To review the patients followed in our center with FMF who received Anakinra, an anti-IL-1 receptor antagonist, in terms of outcome and side effects.
Methods: 43 FMF patients who were treated with Anakinra were retrospectively

reviewed with regard to indication, effect on disease activity and acute phase response, adverse events and patient global assessment.
Results: There were 43 patients with FMF (20 M/ 23 F) who were treated with Anakinra for various indications (colchicine resistant recurrent febrile attacks in 39, colchicine related side effects in 3, both in 1). The mean age of the patients was 31.73±9.56 years. The mean duration of the disease was 19.90±10.52 years. There were various co-existing pathologies among this study group like Ankylosing Spondylitis (4), Psoriasis (1), Behçet's disease (1), Gout (1), Vasculitis (1), Adult-onset Still's disease (1), Polyarthritis Nodosa (1) and Celiac disease (1). The mean colchicine dose was 1.84±0.31 mg/d. As for the dosage, 35 patients were on 100 mg/day, 6 were 100 mg on alternate days, 2 were on 200 mg/day. The mean duration of anakinra treatment was 10.76±13.64 months. After the initiation of anakinra 29 patients became attack-free, 9 patients reported more than 50% decrease, 3 patients less than 50% decrease, and 2 patients no change in the frequency of the attacks. Mean patient global assessment decreased from 7.55±2.34 to 2.82±2.63 under Anakinra treatment ($p<0.001$).
As for the adverse events, eight patients (%18) had allergic reactions under Anakinra treatment (severe disseminated rash in 1 patient and severe injection site reaction in 4 patients and tolerable injection side reaction in 3) which necessitated termination of treatment in 5 patients. Anakinra was stopped because of genital warts and urinary tract infection in one other patient. Worsening of psoriatic lesions was observed in another patient. There were no adverse events in the remaining 41 patients during the course of treatment. On the other hand, treatment was terminated due to inadequate response in 11 (25%), remission in 2 and patient preference in 3 patients. Nineteen patients are still on Anakinra treatment for 10.09±14.51 months.
Conclusions: Anakinra is an effective and relatively safe alternative treatment in FMF patients with inadequate response or intolerance to colchicine, however approximately one fourth of the patients stop anakinra for insufficient response.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5436

FRI0597 FATIGUE IN FAMILIAL MEDITERRANEAN FEVER (FMF) AND ITS RELATIONS WITH OTHER CLINICAL PARAMETERS

C. Unal Ertekin[1], T. Duruoz[1], D. Karali[2], F. Ulutatar[2]. *[1]PM&R Department, Rheumatology Division; [2]PM&R Department, Marmara University, School of Medicine, Istanbul, Turkey*

Background: Fatigue is a common problem in patients with rheumatic disease. It may cause disability and poor quality of life (1). Although fatigue and its determinants are studied in several rheumatic diseases, there is no study in Familial Mediterranean Fever (FMF).
Objectives: The aim of this study is to investigate fatigue in FMF patients as a disabiling symptom and its associations with clinical and demographic variables.
Methods: FMF patients were recruited into the study according to FMF Tel Hashomer criteria (2). Control group composed of healthy individuals. Patients who were pregnant or who had concomitant medical illnesses such as cancer, fibromyalgia, or psychiatric conditions such as psychosis or bipolar disorder were excluded. Age, gender, disease duration, education, marital status were noted as demographic features. Number of attacks in the last year, type of attack, involvement of joints, dosage of colchicine, genotype, amyloidosis, and severity of FMF was assessed with PRAS score, visual analogue score of pain (VAS-pain) and VAS-fatigue were used as clinical parameters. Pittsburgh Sleep Quality Index (PSQI), Multidimensional Assessment of Fatigue (MAF), Nottingham Health Profile (NHP), Fatigue Severity Scale (FSS), Fatigue Impact Scale (FIS) and Hospital Anxiety and Depression Scale (HADS) were filled out by both control and study group. Assessment of normality was analyzed with Shapiro-Wilk test. Differences in the mean scores of control and study group were compared with independent samples Mann-Whitney U and Kruskal-Wallis test. Relationship between continuous variables was assessed with Spearman's correlation coefficient (rho).
Results: 61 FMF patients and 61 age, gender (44 female, 17 male in each group) matched controls were enrolled into the study. Mean age of FMF and control group were 35.5±11.8 and 35.8±11.7 years, respectively. The mean disease duration was 82.5±81.7 months. Difference between mean of VAS-pain, VAS-fatigue, PSQI total score, MAF, all subsets of NHP, FSS, FIS, HADS scores of FMF patients were significantly higher than control group ($p<0.0001$). The correlations between scales assessing fatigue and other outcome measures in FMF patients was shown in Table.

Spearman'sCorrelation (rho)	VAS.fatigue	MAF	FSS	FIS
PSQI.TotalScore	0.49***	0.53***	0.38**	0.50***
NHP.EnergyLevel	0.43***	0.65***	0.54***	0.55***
NHP.Pain	0.58***	0.66***	0.56***	0.67***
NHP.EmotionalReaction	0.40**	0.54***	0.48***	0.65***
NHP.Sleep	0.32*	0.24	0.12	0.31*
NHP.SocialIsolation	0.27*	0.39**	0.50***	0.54***
NHP.PhysicalAbilities	0.51***	0.64***	0.56***	0.69***
HADS.Anxiety	0.43***	0.55***	0.52***	0.75***
HADS.Depression	0.30*	0.42***	0.42***	0.57***

***=p<0.001; **=p<0.01; *=p<0.05.

Conclusions: This study has shown that fatigue in FMF is associated with a number of psychological, sleep, quality of life and disease related factors. FMF group had increased pain, fatigue, sleep disturbance and decreased quality of life compared to control group. FMF patients with fatigue may benefit from pharmacological and psychological interventions which target these factors.
References:
[1] Nikolaus, Stephanie, et al. Fatigue and factors related to fatigue in rheumatoid arthritis: a systematic review. Arthritis care & research 65.7 (2013): 1128–1146.
[2] Livneh, Avi, et al. Criteria for the diagnosis of familial Mediterranean fever. Arthritis & Rheumatology 40.10 (1997): 1879–1885.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4792

FRI0598 CHARACTERIZATION OF PATIENTS WITH AN INITIAL DIAGNOSIS OF UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE. OBSERVATIONS FROM A LONGSTANDING MONOCENTRIC COHORT

C. Sepúlveda[1,2,3], A.V. Taulaigo[2,3], F. Carreiro[2,3,4], M.F. Moraes-Fontes[2,3]. *[1]Serviço de Medicina, Centro hospitalar Médio Tejo, Abrantes; [2]Unidade de Doenças Auto-imunes/Medicina 7.2, Hospital de Curry Cabral, Centro Hospitalar de Lisboa Central; [3]NEDAI - Núcleo de Estudos de Doenças Autoimunes da Sociedade Portuguesa de Medicina Interna, Lisbon; [4]Serviço de Medicina, Hospital do Divino Espírito Santo, Ponta Delgada, Azores, Portugal*

Background: Evolution from Undifferentiated Connective Tissue Disease (UCTD) to a defined Autoimmune Disease (AID) remains unexplained and usually occurs in the first 3 to 5 years.
Objectives: To determine the frequency and predictors of differentiation from UCTD to AID in a selected cohort of patients originally labelled as UCTD within the first 3 years of follow-up.
Methods: Demographic and clinical features were retrieved: (i) retrospectively, from the AID's Unit current database in December 2016 (n=195), including Systemic Lupus Erythematosus (SLE), incomplete SLE, Sjögren's Syndrome (SS), Systemic Sclerosis (SSc), VEDOSS and Mixed Connective Tissue Disease (MCTD); and (ii) from a prospectively UCTD database created in January 2012 (n=48). Inclusion criteria for the latter pertains to ANA positive patients, not fulfilling any of the existing classification criteria for AID and without severe organ involvement [1]. Patients with cutaneous lesions suggestive of lupus, inflammatory myopathies, erosive arthritis, systemic sclerosis and certain auto-antibody profiles were excluded *a priori* from the definition of UCTD as these are thought to herald defined conditions, as previously defined [2]. Definition of stable UCTD includes patients with at least one clinical manifestation of AID, positive ANA result and disease duration of at least 3 years [3]. Comparisons between stable UCTD and progressing patients were made using Wilcoxon Rank Sum and Chi square tests, p values of <0.05 were considered statistically significant.
Results: Each individual patient was analysed for differentiation into AID at yearly intervals. Overall, the main features of the prospective UCTD cohort were arthralgia (79%), rash (31%), arthritis (19%), sicca symptoms (19%), photosensitivity (17%) and Raynaud (13%). Prospective analysis in the UCTD cohort revealed differentiation in 4/48 patients (8.3%): into rheumatoid arthritis (n=2), psoriatic arthritis (n=1) and SLE (n=1). The main difference between stable UCTD and those that progressed to AID was the presence of arthritis (p=0.003). Median age of onset and symptom duration was similar between both groups. Retrospective analysis yielded very few patients presenting as UCTD (n=5/195): 2/106 SLE; 1/13 incomplete SLE; 1/43 SS; 1/19 SSc; 0/7 VEDOSS and 0/7 MCTD with no distinguishing features.
Conclusions: Very few patients differentiated in the UCTD cohort after 3 years of follow-up and in our retrospectively studied cohort, in accordance to a previous study [4]. Apart from arthritis, there were no other predicting factors for differentiation to AID. UCTD at disease onset seems to be a rare event.
References:
[1] Mosca M, et al. Clin Exp Rheumatol. 1999;17(5):615–20.
[2] Mosca M, et al. Lupus. 2008;17(4):278–80.
[3] Mosca M, at al. J Autoimmun. 2014;48–49:50–2.
[4] Danieli MG, et al. Clin Exp Rheumatol. 1999;17(5):585–91.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5495

FRI0599 A RETROSPECTIVE OVERVIEW OF CLINICAL FEATURES, SEROLOGY AND HISTOLOGY OF IGG4 RELATED DISEASE IN HONG KONG: A DATASET OF 108 PATIENTS FROM FOUR REGIONAL HOSPITALS

C.P. Tang[1], K.L. Lee[1], K.W. Lee[2], W.L. Ng[3], M.C. Wan[4], K.Y. Yuen[5]. *[1]Medicine, PYNEH; [2]Medicine, HKSH; [3]Medicine, UCH; [4]Medicine, RH; [5]Medicine, QMH, HK, Hong Kong*

Background: IgG4 related disease (IgG4RD) is a spectrum of immune mediated disease with multiple organs involvement characterized by organ enlargement, function loss or obstructive symptoms (1, 2).
Objectives: In this retrospective study, clinical, serological and histological features of IgG4RD patients over the past ten years from four regional hopsitals were reviewed.

Methods: Four regional hospitals participated with study period from 1/1/2006 to 30/6/2016. IgG4RD patients were classifed into definite, probable and possible IgG4RD according to Japanese Comprehensive Diagnostic Criteria for IgG4RD (3).
Statistical analysis: Association between the individual categorical covariates and the different organ involvement were analyzed by Fisher's exact test.
Results: 108 patients were included. There were 81 male patients and 27 female patients and the male to female ratio is 3:1. The mean age of diagnosis was 62.8 year old. 57 patients were diagnosed as definite IgG4RD (53%), 14 patients as probable IgG4RD (13%) and 37 patients as possible IgG4RD (34%). Salivary glands involvement was the commonest, (M=45.7% vs F=33.3%), followed by pancreas (M=28.4% vs F=18.5%) and biliary system in male (M=24.7% vs F=11.1%) and orbital in female (M=23.5% vs F=18.5%). 53% patients also had multi organ involvement.
104 patients had serum IgG4 level checked and it was raised in 94 patients (90.4%). 77 patients (74.0%) had IgG4 level above twice upper limit of normal. IgG4 level was normal in 10 patients. 98% and 86.3% patients with multi organ involvement had IgG4 level >135mg/dL (p=0.016) and >270mg/dL (p=0.007) respectively. In the hepatobiliary group (n=36), 30 patients had blood checked for Ca19.9 level and it was raised in 17 patients (56.7%), with the highest level 14127 U/ml.
71 histological reports were available. Lymphoplasmacytic infiltration was a consistent features in all specimens (100%). Eosinophilic infiltration was seen in 19 specimen (27%). Fibrosis was seen in 44 specimens (63%). Sialadenitis and dacryoadenitis were associated with dense fibrosis. Obliterative phlebitis was seen in 7 specimens (10%). IgG4/IgG ratio was reported in 61 specimens. 53 specimens had IgG4/IgG ratio greater than 40% per high power field which accounted for 86.9% of the specimens.
Conclusions: Most patients were male with the peak diagnosis at age 50 to 70. Salivary gland and pancreas were the most common organ involved. Most patients had a raised IgG4 level and most histological specimens showed a raised IgG4/IgG ratio on immunostaining. IgG4 level twice the upper limit of normal was quite specific for the disease and was associated with multi organ involvement.
References:
[1] Pieringer H, et al. IgG4- related disease: an orphan disease with many faces. Orphanet journal of rare diseases. 2014;9:110.
[2] Haitao Du YW et al. IgG4-related disease and the curreny status of diagnostic approaches. EXCLI. 2012;11:651–8.
[3] Umehara H, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. Modern Rheumatology. 2012;22(1):21–30.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2145

FRI0600 THE EFFICACY OF DIFFERENT COLCHICINE DOSES IN TREATMENT OF FAMILIAL MEDITERRANEAN FEVER PATIENTS

E. Uguztemur, S. Çelik, S. Sadri, E. Aşçı, G. Ergun, Ö. Velipaşalar, S. Yılmaz-Öner, C. Bes, N. Alpay-Kanıtez. *Bakırköy Dr.Sadi Konuk Research and Training Hospital, Istanbul, Turkey*

Background: Recommended colchicine dose in familial mediterranean fever (FMF) is 1–1.5 mg/day in adults. If necessary it can be increased up to 3 mg/day by clinical monitoring. In the final FMF recommendation report of the EULAR, it was reported that after 5 years of stable disease, in appropriate patients, the dose of colchicine may be reduced by close follow-up. However, the number of clinical trials supporting this recommendation is not enough.
Objectives: In this study, demographic and clinical characteristics of FMF patients whose disease under control and treated with different doses of colchicine were compared.
Methods: Among the all FMF patients attending to the rheumatology outpatient clinic between April and September 2016, only the patients in non-attacks period at least for the last 1 month were included to the study. Clinical and laboratory findings, MEFV gene mutations, drug compliance of the patients and duration and doses of the colchicine treatment were recorded. The 'international severity scoring system for familial mediterranean fever' (ISSF) score was calculated to determine disease severity. The patients who were under the control (less than 4 attacks per year and ISSF score ≤2) divided to three gruops. These gruops were the patients taking low dose (average daily dose of colchicin <1 mg), median dose>1 mg/day and<1.5 mg/ day and standard dose ≥1.5 mg/colchicine treatment at least for 3 years. Patients treated with DMARDs or biological therapy were excluded from the study.
Results: Of the 162 FMF patients enrolled into the ongoing cohort, 86 patients were excluded from the study due to 57 patients had active disease, 19 had not yet completed 3 years of colchicine treatment and 10 patients received biological or DMARD treatment. The remaining 76 patients (25 male, 51 female) met the study criteria. The mean age was 32±11.5 years and the disease duration was 18.2±10.9 years. Amyloidosis or organ failure was not detected in any of these patients. Because of various reasons (drug side effect, treatment incompatibility, physician advice), 16 patients (21%) were treated with low dose colchicine (group A), 30 patients (39%) with moderate dose of colchicine (group B) and the remaining 30 patients (39%) with standard dose colchicine (group C). There were no statistically significant differences in demographic, clinical or laboratory data among these 3 subgroups.
Conclusions: Disease control in FMF is important to prevent amyloidosis and improve the quality of life. Recent studies contribute to the determination of treatment goals. Reducing the colchicine dose may increase drug compliance in this lifelong treatment. In our study, there was no difference between the treatment groups in amyloidosis, MEFV gene mutation or subclinical inflammation. These findings suggest that the dose of colchicine maybe reduced in inactive patients who determineted by the number of annual episodes and the ISSF score.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6885

FRI0601 HYPERFERRITINEMIC SYNDROME IN A GENERAL UNIVERSITARY HOSPITAL

F. Pierini, I.J. Gandino, J.M. Martinez Perez, S. Ruta, M. Scolnik, E.R. Soriano. *Rheumatology Section, Medical Services, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina*

Background: Hyperferritinemia is associated with severe inflammatory conditions, such as rheumatic diseases with systemic inflammatory responses, and multiorgan dysfunction syndromes.
Objectives: To determine which diseases are associated with hyperferritinemia in a tertiary hospital; to compare ferritin levels between these different entities and to evaluate relationship between levels of ferritin and mortality in these patients.
Methods: A retrospective study was carried out in which all patients over 18 years with at least one determination of serum ferritin equal to or greater than 1000 ng/ml were identified in the laboratory database of our hospital between 1/1/2006 and 6/30/2016. Corresponding electronic medical records were reviewed and demographic data and clinical data were collected. Mortality was assessed at the end of follow-up. Descriptive statistical analysis and logistic regression analysis were performed in order to identify variables associated with mortality.
Results: A total of 1979 patients were included, 1235 men (62.4%) with a mean age of 63.2 years (SD 17.2). Only 36 patients (1.8%) presented a rheumatologic diagnosis as the only cause of high levels of ferritin, with Still's disease (n=8) and systemic Vasculitis (n=9) being the main diagnoses. Table 1 shows patients' characteristics grouped according to whether the elevation of ferritin was associated with a rheumatic disease or not. Median serum ferritin and transferrin saturation in both groups were similar (see Table 1). Mortality was lower for rheumatologic causes (5.9% vs 37.2%, p<0.001). Variables that were associated with mortality in multivariable logistic regression analysis were: maximum ferritin value (OR 1,0004, 95% CI 1,0003–1,0004, p<0.001) and age (OR 1.03, 95% CI 1.02–1.04, p<0.001), whereas the diagnosis of a rheumatic disease was a protective factor (OR 0.11, 95% CI 0.03–0.47, p=0.003). ROC curve for ferritin and mortality showed an area under the curve of 0.59 (95% CI 0.58–0.62). Ferritin levels greater than 3000 ng/ml showed a specificity of 89.2% and a sensitivity of 19.7% for mortality, regardless of cause of ferritin elevation.

Table 1. Patients' characteristics grouped by cause of Hyperferritininemia (Rheumatologic or not)

	Rheumatic disease (n=35)		Other causes of ferritin elevation (n=1944)		p
Female, n (%)	13 (37.1)		731 (37.6)		0.96
Mean age, years (DS)	62.5 (17.1)		52.4 (21.1)		<0.001
Diagnostic	Vasculitis	9	Solid cancer	497	
	Still's disease	8	Infections	336	
	Rheumatoid arthritis	4	Onco-hematologic disease	302	
	SLE	3	Chronic renal insufficiency	236	
	Seronegative arthritis and psoriatic arthritis	3 3	Hepatic disease	188	
	Others	3	Others	152	
	Gout	2	Hematologic disease	128	
	Juvenile idiopathic arthritis	1	Cardiovascular	57	
	Myositis	1	Sepsis	46	
	IgG 4	1	Iron overload	2	
Serum ferritin, median (IQR)	1622 (1264- 3639)		1460 (1200–2140)		0.07
Tranferrin saturation, %, median (IQR)	38 (19–50)		33 (18–55)		0.83
Follow-up time, years, median (IQR)	5.2 (1,2–10.2)		5.7 (1.2–8.9)		0.97
Mortality, n (%)	2 (5.9)		698 (37.2)		<0.001

Conclusions: Rheumatic diseases, represents a very small percentage of the causes of elevation of ferritin above 1000 ng/ml, and were associated with lower mortality than the non-rheumatic causes. Serum ferritin levels were significantly associated with increased mortality regardless of the underlying cause.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2460

FRI0602 NATIONAL RECOMMENDATIONS ON THE USE OF IMMUNOMODULATORY DRUGS IN PATIENTS WITH NON-INFECTIOUS NON-MALIGNANT ANTERIOR UVEITIS

G. Espinosa[1], S. Muñoz-Fernandez[2], J.M. García Ruiz de Morales[3],

J.M. Herreras[4], M. Cordero-Coma[5]. *[1]Department of Autoimmune Diseses, Institut Clinic de Medicina i Dermatologia, Hospital Clinic, Barcelona; [2]Rheumatology, Hospital Universitario Infanta Sofia, Madrid; [3]Immunology, Complejo Asistencial Universitario de León, Leon; [4]Ophtalmology, Hospital Clínico Universitario de Valladolid, Valladolid; [5]Ophtalmology, Complejo Asistencial Universitario de Leon, Leon, Spain*

Background: Anterior uveitis (AU) is the most common pattern of uveitis, that migh lead to important ocular complications including blindness. Immunomodulatory drugs have been used in order to prevent recurrences of uveitis. Nevertheless, it is not clear which drug could be preferred in each patient.
Objectives: To generate recommendations on the use of immunomodulators in adult patients with non-infectious, non-neoplastic anterior uveitis (AU) based on best evidence and experience.
Methods: Delphi methodology was followed. A multidisciplinary panel of 5 experts (2 ophtalmologists, one immunologist, one rheumatologist, one internist) was established, who, in the first nominal group meeting, defined the scope, users, and chapters of the document. A systematic literature review was performed to assess the efficacy and safety of immunomodulators in patients with non-infectious, non-neoplastic AU. All of the exposed above was discussed in a second nominal group meeting and 33 recommendations were generated. Recommendations agreement grade was tested also in 25 additional experts. Recommendations were voted from 1 (total disagreement) to 10 (total agreement). We defined agreement if at least 70% voted $\geq$7. The level of evidence and grade or recommendation was assessed using the Oxford Centre for Evidence-based Medicine Levels of Evidence.
Results: The 33 recommendations were accepted. They include specific recommendations on patients with non-infectious, non-neoplastic UA, as well as different treatment lines. Methotrexate (MTX) or Sulfasalazine were recommended as a first line drugs in refractory cases to topic treatments in patients with AU and spondyloarthritis, inflammatory bowel disease, psoriasis, idiopathic HLA-B27 positive or negative AU. Etanercept was recommended for patients with TRAPS syndrome, and for those with other autoinflammatory syndromes canakinumab o anakinra. In case of bilateral sarcoidosis, relapsing polychondritis or TINU syndrome, MTX was recommended along with systemic steroids. For patients with a flare of AU and Behçet disease, systemic steroids along with azathioprine or a calcineurin inhibitor were recommended. The indication of an immunomodulatory drug in patitnes with multiple sclerosis was considered to be decided with a neurologist. For patients refractory to all exposed above and or intolerant, depending on AU type, a change to another classical immunomodulatory drug or to an anti-TNF was recommended (adalimumab, infliximab, certolizumab or). Except for patients with TINU, etanercept was not recommended because current evidence does not support the use of it to prevent AU flares.
Conclusions: In patients with non-infectious, non-neoplastic AU, these recommendations on the use of immunomodulators might be a guide in order to help in the treatment decision making, due to the lack of robust evidence or other globally accepted algorithms.
Disclosure of Interest: G. Espinosa Grant/research support from: GSK, Actelion, S. Muñoz-Fernandez: None declared, J. García Ruiz de Morales: None declared, J. Herreras Grant/research support from: Allergan and Abbvie, M. Cordero-Coma Grant/research support from: Abbvie, Merck Sharp & Dohme, and Allergan
DOI: 10.1136/annrheumdis-2017-eular.4810

FRI0603 CLINICAL IMPLICATIONS OF ULTRASONOGRAPHY IN MONITORING DISEASE ACTIVITY OF RELAPSING POLYCHONDRITIS: THE ASSESSMENT OF AURICULAR CHONDRITIS IN 3 CASES

H. Nishikawa, Y. Taniguchi, Y. Terada. *Kochi Medical School, Nankoku, Japan*

Background: Relapsing polychondritis (RP) is a rare systemic inflammatory disorder and might often be refractory. Therefore, the discover of imaging modality would be required on diagnosis and treatment of RP.
Objectives: To assess the clinical implications of ultrasonography (US) in monitoring disease activity of relapsing polychondritis (RP).
Methods: Three cases of a 78-year-old man with RP, a 74-year-old woman with RP associated with optic perineuritis and a 42-year-old woman with RP associated with uveitis were assessed by US before and after treatments.
Results: Ultrasonography (US) of the auricle before treatment showed low-echoic swollen auricular cartilage with increased power Doppler signals (PDS) in all cases. US findings corresponded to the above-mentioned biopsy findings. After treatment with prednisolone combined with methotrexate, the auricular swelling completely resolved in all cases. Then, US findings also showed dramatic reductions in swelling of cartilage with the decrease in PDS.
Conclusions: US imaging can be used to differentiate between inflammation, vascular lesions, and tumors in the ear pinna. RP could be differentiated from the damage of repeated trauma (i.e. rugby) with producing subperichondrial serous effusion. As in the present cases, US imaging of the external ear and auricular cartilage in RP also facilitates evaluation of auricular lesions and monitoring of disease activity, especially when we consider the treatment response and the timing of drug tapering.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1769

FRI0604 SUCCESSFUL TREATMENT OF ARTHRITIS INDUCED BY CHECKPOINT INHIBITORS WITH ANTI–INTERLEUKIN-6 RECEPTOR ANTIBODY: A CASE SERIES

S.T. Kim[1], A. Diab[2], M. Uemura[2], S. Garcia[3], P. Hwu[2], J. Tayar[1]. *[1]Rheumatology; [2]Melanoma Medical Oncology, MD Anderson Cancer Center; [3]Rheumatology, Baylor College of Medicine, Houston, United States*

Background: Immune checkpoint inhibitors (CPIs) have significantly improved outcomes for patients with various cancers. However, CPIs are associated with immune-related adverse events (irAEs). Two to three percent of patients receiving a CPI develop arthritis. In general, severe irAEs are treated with a high-dose steroid and a tumor necrosis factor inhibitor (TNFi), usually infliximab; however, TNFi treatment is sometimes contraindicated and, furthermore, entails a theoretical concern of impairing antitumor immunity. Therefore, evidence showing the clinical benefits of non-TNFi biologics in the treatment of irAEs is of immediate interest.
Objectives: We described the effects of anti-IL-6R antibody for the treatment of arthritis-irAE.
Methods: Three patients receiving CPI developed arthritis and were treated with anti-IL-6R antibody. Patients were followed up to 15 months.
Results: All patients had metastatic melanoma (Table 1). No patient had a

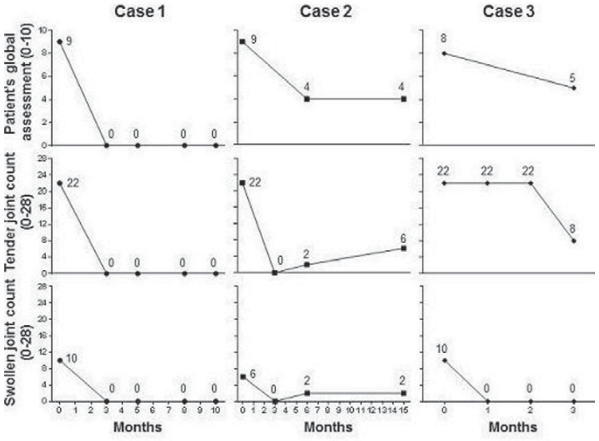


Figure 1. Serial measurement of the patient's global assessment, tender joint count, and swollen joint count before (0 month) and after anti-IL-6R antibody treatment

Abstract FRI0604 – Table 1. Patient demographic and clinical characteristics

Patient	1	2	3
Age, years	71	65	46
Sex	Male	Male	Female
Race	Caucasian	Caucasian	Caucasian
Tumor	Metastatic melanoma	Metastatic melanoma	Metastatic melanoma
CPI	Anti-CTLA4 antibody	Anti-PD-1 antibody	Anti-PD-1 antibody
Onset of arthritis-irAEs (days after initiation of CPI)	100	19	49
Pattern of arthritis	Symmetric polyarthritis involving small joints	Symmetric polyarthritis involving small and large joints	Symmetric polyarthritis involving small joints
History of autoimmune disease prior to CPI treatment	No	No	No, but known positive ANA
Autoantibody results	ANA, CCP neg RF: 27 (UNL: 15.9)	ANA, CCP, RF neg	CCP, RF, Ro, dsDNA neg ANA 1:640 (homogenous) La pos
Discontinuation of CPI treatment due to arthritis-irAE	N/A	No	Yes
Duration of anti-IL-6R antibody therapy, months	12	15	3
Tumor response to CPI as of December 2016 (RECIST 1.1)	Complete remission	Progressive disease	Progressive disease

CPI, immune checkpoint inhibitor; UNL, upper normal limit; ANA, antinuclear antibody; CCP, anti-cyclin citrullinated antibody; RF, rheumatoid factor; Ro, anti-SSA antibody; dsDNA, anti–double-stranded DNA antibody; La, anti-SSB antibody; N/A, not applicable.

history of autoimmune disease at the time of initiation of CPI treatment. One patient developed arthritis 8 weeks after the completion of anti-CTLA-4 antibody treatment. Two patients were receiving anti-PD-1 antibody when they developed arthritis. Patient 2 continued to receive anti-PD-1 antibody despite of arthritis-irAE while patient 3 discontinued anti-PD-1 antibody due to arthritis-irAE. The pattern of arthritis was symmetric polyarthritis involving small and large joints. Patient 1 had a positive rheumatoid factor (unknown baseline) and patient 3 had a positive ANA (known positive prior to CPI treatment). All patients were treated with anti-IL-6R antibody, which was well tolerated. All patients experienced a 40–100% reduction in global assessment, swollen joint count, and tender joint count, and these effects were maintained for up to 15 months of treatment (Figure 1). As of December 2016, all patients were alive; one patient was in complete remission and two patients had experienced progression of their melanoma.

Conclusions: These three cases suggest that anti-IL-6R antibody is an effective alternative to TNFi for the treatment of arthritis-irAE.

Acknowledgements: None

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6504

FRI0605 THE USE OF HAND PERFUSION SCINTIGRAPHY TO ASSESS RAYNAUD'S PHENOMENON ASSOCIATED WITH HAND-ARM VIBRATION SYNDROME

K.A. Lee [1], H.W. Chung [2], S.-H. Lee [1], H.-R. Kim [1]. *[1]Internal Medicine; [2]Nuclear Medicine, Konkuk University Medical Center, Seoul, Korea, Republic Of*

Background: Raynaud's phenomenon (RP) is a prominent manifestation of hand-arm vibration syndrome (HAVS). Previous studies have evaluated the diagnostic validity and characteristics of hand perfusion scintigraphy. However, no study to date has classified or differentiated the findings of this technique based on the aetiology of RP.

Objectives: This study aimed to evaluate the hand perfusion scintigraphic features of hand-arm vibration syndrome (HAVS) and to compare these with the features of primary and secondary Raynaud's phenomenon (RP) associated with connective tissue disease (CTD).

Methods: Hand perfusion scintigraphy was performed in 57 patients with primary RP, 71 patients with HAVS-related RP, and 36 patients with CTD-related RP. We calculated 6 ratios by using the time-activity curve and static blood pool images, the chilled to ambient hand and wrist ratios of the first peak height, initial slope, and blood pool uptake. We analysed 3 morphologic characteristics: slow progress pattern, paradoxically increased uptake pattern in the time-activity curve, and the inhomogeneous radioactivity uptake in the blood pool image.

Results: All of the 71 patients with HAVS-related RP were mine workers. The onset of RP after exposure to vibration was at 21.8±7.3 years, with 26.3±7.0 years of vibration exposure time. The chilled to ambient hand ratios of the first peak height and the initial slope were significantly lower in patients with HAVS-related occupational RP than in patients with primary RP. The presence of a paradoxically increased uptake pattern was significantly lower in HAVS than in primary RP.

Table 1. Comparison of the 6 quantitative variables of patients with Raynaud's phenomenon

Parameter		HAVS	Primary RP	CTD	P value
First peak height ratio	Hand	0.90±0.89[c]	1.50±1.50[c]	1.03±1.12	0.034[a]
	Wrist	0.72±0.31	0.87±0.57	0.80±0.46	0.161[a]
Initial slope ratio	Hand	0.75±0.63[d]	1.43±1.26[d]	1.06±1.29	0.002[a]
	Wrist	0.87±0.83	0.87±0.71	0.84±0.86	0.981[b]
Blood pool uptake ratio	Hand	0.85±0.39	1.10±0.72	0.87±0.67	0.071[a]
	Wrist	0.72±0.18	0.73±0.40	0.73±0.24	0.982[b]

Data are presented as mean ± standard deviation. HAVS: hand-arm vibration syndrome; CTD: connective tissue disease. [a]Significant using analysis of variance (ANOVA). [b]Significant using Welch test. [c]Primary > HAVS (P=0.015 by multiple comparisons), [d]Primary > HAVS (P =0.001 by multiple comparisons).

Table 2. Comparison of presence of the 3 scintigraphic characteristics in the chilled hand of the patients

Characteristics	HAVS (n=71)	Primary RP (n=57)	CTD (n=36)	P value
Slow progression pattern	61 (86.0)	51 (89.5)	32 (88.9)	0.809
Inhomogenous radio-activity uptake pattern	17 (24.0)	18 (31.6)	8 (21.2)	0.513
Paradoxically increased uptake pattern	15 (19.7)[a]	27 (43.9)[a]	10 (27.8)	0.012

Data are presented as number (%). HAVS: hand-arm vibration syndrome; CTD: connective tissue disease. [a]Primary > HAVS (P=0.004) on the basis of Chi-square test.

Conclusions: There were significant differences in hand perfusion scintigraphic features between primary RP and HAVS. These results suggest that the underlying pathophysiology of the two diseases differs; thus, different criteria might be applied for their evaluation

References:

[1] Palmer KT, Bovenzi M. Rheumatic effects of vibration at work. Best Pract Res Clin Rheumatol 2015;29:424–39.

Acknowledgements: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1505

FRI0606 CHARACTERISTICS AND TREATMENT OF NEW ONSET ARTHRITIS AFTER CHECKPOINT INHIBITOR THERAPY

L.A. Christ [1], S. Mönch [1], S. Hasmann [1], I. Goldscheider [2], M. Heppt [2], C. Berking [2], F. Berger [3], C. Dechant [1], A. Skapenko [1], H. Schulze-Koops [1], J. Leipe [1]. *[1]Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, University of Munich; [2]Department of Dermatology and Allergology; [3]Department of Radiology, University of Munich, Munich, Germany*

Background: The recent introduction of biologic agents targeting immunologic checkpoints (immunologic checkpoint inhibitors (ICI)) established immunotherapy as a highly effective cancer therapy. ICI that trigger an anti-tumor response by activation of T cells, may also cause immune-related adverse events (irAEs). Characterization of rheumatic adverse events such as arthritis and data on treatment of irAEs are scarce.

Objectives: To characterize patients with new-onset arthritis under ICI therapy and to assess the efficacy and safety of treatment that aimed to balance anti-tumor and anti-inflammatory therapy.

Methods: In this prospective observational study, patients with melanoma receiving ICI therapy who experienced arthralgias were evaluated for the presence of musculoskeletal inflammation. Data on demographics, ICI regime, time of onset and response to therapy of musculoskeletal irAEs, imaging, joint count, CRP/ESR, and immune serology were collected. Further, response to anti-inflammatory therapies including NSAR, glucocorticoids (GC) and methotrexate was assessed.

Results: Of 7 patients with arthralgias after initiation of ICI therapy, all had objective signs of musculoskeletal inflammation. Arthritis was demonstrated in 6 patients, 3 oligoarthritis (SpA pattern), 2 polyarthritis (RA pattern), 1 monoarthritis. PMR-like disease with typical ultrasound findings was evident in 1 case. The time from start of ICI therapy to onset of synovitis symptoms varied from 1 to 259 days without a timely association to other irAEs. Upon first visit in our clinic, CRP levels were elevated in 6 of the patients (5.5 to 107 mg/l) while immune serology was positive only in one patient (high titer RF and ACPA). Interestingly, in this patient low RF and ACPA titers had been detected when she presented with arthralgias without synovitis five years prior. This patient developed highly active RA one day after the first infusion of nivolumab. Retrospective analysis of cancer staging imaging studies revealed good sensitivity for PET-CT in the detection of synovitis, as opposed to contrast-enhanced CT. The baseline mean overall disease burden (assessed by VAS for pain, 0–10) was 7.6±0.8 and was significantly reduced after 3 months of anti-inflammatory treatment to 1±1.4. Initially, all patients were treated with systemic and four patients also with intraarticular GC. Four of 7 patients flared on GC treatment upon tapering and were given methotrexate. Remission was achieved in all and prednisolone could be tapered. Patients were followed for a median of 152 days, and no safety signal with regard to tumor reappearance was detected.

Conclusions: All patients with arthralgias upon ICI therapy had arthritis or PMR-like disease suggesting a need for increased awareness for musculoskeletal irAE. Inflammatory manifestations were associated with high disease burden and not self-limiting. While GC therapy is effective, flares were frequent after tapering and, thus, potential side-effects including attenuation of the anti-tumor efficacy of ICI are a concern. This is the first report on the efficacy and safety of methotrexate as a GC-sparing agent in ICI-induced arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6532

FRI0607 LONG-TERM AND OPTIMIZATION OF INFLIXIMAB IN REFRACTORY UVEITIS ASSOCIATED TO BEHÇET DISEASE. MULTICENTRE STUDY OF 100 PATIENTS

L.C. Domínguez Casas [1], V. Calvo-Río [1], E. Beltrán [2], J. S-Bursón [3], M. Mesquida [4], A. Adán [4], M. Hernandez [4], F. L-Longo [5], M. H-Grafella [6], E. Valls [7], L. M-Costa [8], A. Sellas [9], J. G-Serrano [10], J. Callejas [10], N. Ortego [10], J. Herreras [11], A. Follonosa [12], O. Maíz [13], A. Blanco [13], I. Torre [14], C. F-Espartero [15], V. Jovani [16], D. Peitado [17], D. Díaz-Valle [18], E. Pato [18], C. F-Cid [19], E. Aurrecoechea [20], M. García [21], M. Caracuel [22], A. Atanes [23], F. Francisco [24], S. Insua [25], S. González-Suárez [26], A. S-Andrade [27], L. Linares [28], F. Romero [29], A. García [30], R. Almodovar [31], E. Minguez [32], C. Carrasco [33], E. Raya [10], M. Alcalde [34], C. F-Carballido [35], F. Pagés [36], M. González-Vela [1], C. Fernández-Díaz [1], N. Vegas-Revenga [1], R. Demetrio-Pablo [1], M. González-Gay [1], R. Blanco [1]. *[1]HUMV, Santander; [2]H Mar, Barcelona; [3]H Valme, Sevilla; [4]H Clinic, Barcelona; [5]H G-Marañón, Madrid; [6]H General; [7]H, Valencia; [8]H Peset, Valencis; [9]H Vall d'Hebron, Barcelona; [10]H S Cecilio, Granada; [11]IOBA, Valladolid; [12]H Cruces, Bilbao; [13]H, Donostia; [14]H Basurto, Bilbao; [15]H Móstoles, Madrid; [16]H General, Alicante; [17]H Paz; [18]H S Carlos, Madrid; [19]H, Pontevedra; [20]H, Torrelavega; [21]H Princesa, Madrid; [22]H, Córdoba; [23]HUAC, A Coruña; [24]H D Negrín, Las Palmas; [25]H, Santiago Compostela; [26]H Cabueñes, Gijón; [27]H L Augusti, Lugo; [28]H Arrixaca, Murcia; [29]F J Díaz; [30]H 12 octubre; [31]F Alcorcón, Madrid; [32]H Clínico, Zaragoza; [33]H, Merida; [34]H S Ochoa, Madrid; [35]H Elda, Alicante; [36]H, Palencia, Spain*

Objectives: To assess the long term efficacy and optimization of Infliximab (IFX) in refractory Uveitis of Behçet Disease (BD)

Methods: Multicentre study of Uveitis associated-BD refractory to conventional immunosupressive drug. Ocular inflammation was evaluated with "SUN criteria" (Am J Ophthalmol 2005;140:509–516) and the macular thickening with OCT. Results are expressed as mean±SD or median [IQR] (comparison, Wilcoxon test)

Results: We studied 100 patients/180 affected eyes (54M/46W), mean age 40.7±10.1. The ocular pattern was panuveitis (n=62), posterior (27) and anterior uveítis (11). Before IFX they received iv MP (28), cyclosporine (75), azathioprine (56), metotrexate (43) and others (33). IFX dose ranged between 3–5mg/kg/4 or 8 weeks. In patients in remission IFX was optimized (n=28) or stopped (n=20).

Table

	Baseline	1st week	1st month	3th month	6th month	1st year	2nd year	3th year	4th year
VA (mean±SD)	0.5±0.35 n= 193	0.5±0.3* n= 189	0.6±0.3* n= 187	0.6±0.3* n= 183	0.6±0.3* n= 176	0.6±0.3* n= 159	0.6±0.3* n= 130	0.6±0.3* n= 88	0.7±0.3* n= 60
Cells in the anterior chamber (median [IQR])	1 [0-2] n= 190	0 [0-1]* n= 187	0 [0-0]* n= 184	0 [0-0]* n= 180	0 [0-0]* n= 171	0 [0-0]* n= 153	0 [0-0]* n= 126	0 [0-0]* n= 82	0 [0-0]* n= 58
Vitritis (median [IQR])	1 [0-2 n= 188	0.5 [0-2]* n= 182	0[0-0]* n= 182	0[0-0]* n= 177	0[0-0]* n= 168	0[0-0]* n= 149	0[0-0]* n= 122	0[0-0]* n= 84	0[0-0]* n= 58
Retinal vasculitis (% affected eyes)	53.4% n= 188	43.1% n= 183	22.2% n= 183	10.9% n= 177	7.4% n= 171	2.4% n= 153	1.9% n= 124	0.4% n= 84	0.4% n= 54
OCT (µ) (mean±SD)	331.5 ± 136.1 n= 59	324± 123.8* n= 53	298.7±101 .8* n= 53	283.2±83. 6* n= 49	265.8±6 6.5* n= 42	264.1 ±61.3* n= 46	263.6 ±65.2* n= 27	239.8± 26.8* n= 14	231.2±3 5.7* n= 8

*p< 0,05. VA=visual acuity. Data are of affected eyes.

Conclusions: IFX is an effective long term-treatment in refractory Uveitis of BD. Optimization and even discontinuation of IFX after remission is possible.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6226

FRI0608 STUDY OF ARTICULAR SARCOIDOSIS IN A TERTIARY CARE HOSPITAL

M. Garijo Bufort[1], E. Vallejo Pascual[2], C. Moriano Morales[1], M. Retuerto Guerrero[1], C. Iñiguez Ubiaga[1], A. Crespo Golmar[1], A. López Robles[1], C. Álvarez Castro[2], E. Diez Álvarez[1], M. Martín Martínez[1], T. Pérez Sandoval[2].
[1]Rheumatology Department of the University Health Care Complex of León; [2]University of Leon, León, Spain

Background: Sarcoidosis is a systemic granulomatous disease, being the joint involvement a poorly studied manifestation.
Objectives: To describe the clinical and demographic characteristics of patients with sarcoidosis, paying particular attention to the joint involvement and its possible relationship with other extra-articular manifestations, as well as the treatment recieved.
Methods: A retrospective, observational study that included 104 patients who were admitted to the Hospital of León between January 2011 and December 2015 with main or secondary diagnosis of sarcoidosis; according to clinical onset, imaging tests and/or anatomopathological study. The variables studied were: age at the time of diagnosis, sex, type of joint involvement, forms of extra-articular involvement, serologic parameters and drugs received. Statistical analysis was performed using SPSSv22.0, $p<0.005$.
Results: 57.7% of the patients included in the study were women with a mean age of 53.42±18.4 years. At the systemic level, 35% of them presented fever, 66.3% lymphadenopathy and 4.8% splenomegaly. 97.1% of the patients presented pulmonary involvement, with stage II being the most common (46.2%). Only 8 patients had cardiac abnormalities. Ocular involvement was observed in 10.6%, predominating uveitis. The most common renal manifestation was hypercalciuria in 6.7%. The presence of neurological involvement was exceptional, detecting 3 cases of neurosarcoidosis. In the cutaneous involvement (2.9%), erythema nodosum predominated (17.3%). The CRP levels were normal in 44.3% (<5mg/dl) and high levels of CRP were found in 25.3% of the sample (>30mg/dl). 62.6% presented pathological figures of ACE. The joint involvement was present in 38.5% of the patients (14.4% in the form of arthralgia, 2.9% as periarthritis, 13.5% as acute arthritis, 4.8% as chronic arthritis and 2.9% as sacroiliitis). The 19,23% debuted as Löefgren syndrome, being seen an association between the presence of acute arthritis and erythema nodosum *(p0,000).* The mean age observed in patients with acute arthritis was lower than the one of the other patients with other joint manifestations (*p0.044)* and a statistically significant relationship was observed between the absence of joint and ocular involvement *(p0,011).* Regarding the treatment of joint manifestations, 30.77% of the cases were resolved with NSAIDs, 46.15% with corticosteroids in a monotherapy and 15.38% required an immunosuppressant. In our study, most patients treated with corticosteroids did not show articular nor ocular involvement *(p0,018),* although when analysing the ocular involvement separately, many received corticoid treatment (42.86%). Only one patient required Adalimumab for refractory uveitis and another presented anti-TNFα-induced sarcoidosis (Infliximab).
Conclusions: The pulmonary involvement is the predominant one in patients with sarcoidosis. The acute arthritis occurs in younger patients and is associated with the onset of erythema nodosum. The joint involvement is usually not severe and, although it has not been demonstrated, it seems that the use of corticosteroids predominates in the extra-articular manifestations. Only 1 in 4 patients showed an increase of acute phase reactants.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6674

FRI0609 USEFULNESS OF FDG-PET/CT IMAGING AND SEROLOGICAL BIOMARKERS TO PREDICT RELAPSE IN IGG4-RELATED DISEASE

M. Kato, H. Ozaki, T. Kameda, M. Izumikawa, S. Nakashima, H. Shimada, R. Wakiya, A. Kondo, N. Kadowaki, H. Dobashi. *Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University, Kita-gun, Japan*

Background: IgG4-RD shows relapses frequently. It is important to search to the factors to predict relapse. Recent research has shown the usefulness of FDG-PET/CT for IgG4-RD because it is more sensitive than conventional imaging to detect organ involvement of the disease. It has been suggested that FDG-PET/CT is also useful for monitoring therapeutic response of IgG4-RD.
Objectives: We investigate the usefulness of FDG-PET/CT imaging and serological biomarkers to predict relapse in IgG4-RD.
Methods: We analyzed 24 patients with IgG4-RD treated for more than 1 year between 2008 and 2016 in our facility. The diagnosis for IgG4-RD was based on comprehensive diagnostic criteria for IgG4-RD. All cases underwent FDG-PET/CT at least once, and laboratory data were collected from their medical records retrospectively. Levels of serum C-reactive protein (CRP), eosinophil/leukocyte ratio, serum IgG, IgG4, IgA, IgM, IgE, sIL2-R and serum compliment were investigated.
Results: The patients had a mean age of 67.9 years (range: 50–87 years). In the cases with high FDG uptake on FDG-PET/CT, they had a greater number of organ involvements, higher serum IgG and sIL-2R levels. Eight patients experienced relapses following treatment. Higher serum IgG predicted relapses of IgG4-RD. FDG-PET/CT findings at baseline were not associated with relapse. FDG-PET/CT was performed in 13 patients after initiation of treatment and 4 patients had a relapse. There were no significant reduction of abnormal FDG uptake in 6 patients, and 4 of 6 patients relapsed.
Conclusions: In this study, we examined the factors to predict relapse in IgG4-RD. Patients with higher serum IgG were regarded as a risk of relapse, but FDG-PET/CT findings at baseline were not associated with relapse. FDG-PET/CT reexamined after initiation of treatment is useful to predict relapse of IgG4-RD.
References:
[1] Umehara H, Okazaki K, Masaki Y, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. Mod Rheumatol. 2012 Feb;22(1):21–30.
[2] Nakatani K. Utility of FDG PET/CT in IgG4-related systemic disease Clin Radiol. 2012 Apr;67(4):297–305.
[3] Zhang J, Chen H, Ma Y, et al. Characterizing IgG4-related disease with 18F-FDG PET/CT: a prospective cohort study. Eur J. Nucl Med Mol Imaging. 2014;41:1624–1634.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5648

FRI0610 PROBLEMS IN THE DIAGNOSIS OF FAMILIAL MEDITERRANEAN FEVER IN TURKEY

M. Erdoğan, Y. Özgüler, G. Karatemiz, S.N. Esatoğlu, G. Güzelant, E. Dinçes, S. Uğurlu, G. Hatemi, H. Özdoğan, E. Seyahi. *Internal Medicine, Division of Rheumatology, Cerrahpaşa Medical Faculty, University of Istanbul, Istanbil, Turkey*

Background: The diagnosis of FMF (Familial Mediterranean Fever) can be missed or delayed even in a country like Turkey, one of the most prevalent places for FMF (1).
Objectives: We compared the duration of delay in diagnosis before and after year 2000, and assessed the problems related with the diagnosis of FMF.
Methods: We studied 143 (102 F, 41 M) consecutive patients with FMF seen at the rheumatology outpatient clinic, between November 2016 and January 2017. Patients completed a self-administered questionnaire that assesses initial symptoms, previous diagnosis and treatments received before the formal diagnosis of FMF. Patients were divided in 2: as Group 1, which includes 70 patients seen for the first time by a physician before 2000 and Group 2, which includes 73 patients seen after 2000.
Results: The median age of the patients was 34 years [IQR:27–45]. The F/M ratio was 2.4. The initial symptom was abdominal pain in the majority (n=134, 89%), followed by fever (n=114, 75%), arthritis (n=66, 44%), pleuritic pain (n=21, 14%), arthralgia (n=11, 7%) and other complaints (n=14, 9%).
The median age at initial symptom was 10 years (IQR:6–23). The median delay in diagnosis was 8 years [IQR:2–15]. This was significantly shorter in Group 2 (median: 4 years [IQR:0–11]) than that observed in Group 1 (median: 10 years [IQR:6–17]), as shown in Table.
A total of 110 patients (73%) were diagnosed with one or more diseases or syndromes other than FMF. These were appendicitis (n=50, 45%), gastrointestinal diseases (n=44, 40%), acute rheumatic fever (n=36, 33%), inflammatory

arthritis (n=18, 16%), gynecological diseases (n=11, 10%) kidney stones (n=9, 8%) and others (n=34, 31%). As shown in Table, the frequency of patients with misdiagnosis, was significantly lower in Group 2 (66%) compared to Group 1 (84%).
A total of 59 patients (39%) received other long-term treatments, mainly monthly penicillin (n=28), prior to colchicine. There were 41 surgical interventions in 36 patients (24%), before the diagnosis of FMF, the most common being appendectomy in 31, gyneacological operations in 5, cholecystectomy in 3 and others in 2 occasions. It was noted that, the frequency of surgical operations was significantly decreased in Group 2 (12%) compared to Group 1 (27%) (Table).
The presence or absence of MEFV mutations was assessed in 69 patients (46%) before the diagnosis or after to reinforce the diagnosis. As expected, this was significantly more frequent in Group 2 (59%) compared to Group 1 (33%) (Table).
Seventy patients (46%) were diagnosed as FMF only after someone else in the family (n=44) or a friend (n=26) had a similar diagnosis. The frequency of these patients was similar when Group 1 and 2 were compared.

Table: Demographic and clinical characteristics of Group 1 (patients seen before 2000) and Group 2 (patients seen after 2000)

	Group 1, (n=70)	Group 2, (n=73)	P
Male/Female, n	22/48	19/54	Non significant
Current age, med [IQR] years	40[31-51.5]	32[24.5-38]	<0.001
Delay in diagnosis, med [IQR] years	10 [6-18]	4 [0-11]	<0.001
Misdiagnosed patients, n (%)	59 (84)	48 (66)	0.011
Surgery before diagnosis, n (%)	19(27)	9(12)	0.026
Assessment of MEFV mutations, n (%)	23 (33)	43 (59)	0.005
Diagnosed as FMF after someone else, n (%)	27(39)	38(52)	0.1

Conclusions: Although there is considerable decrease in delayed diagnosis of FMF, there is still significant amount of misdiagnoses after the year 2000, even in a geography where FMF is highly prevalent.
Table: Demographic and clinical characteristics of Group 1 (patients seen before 2000) and Group 2 (patients seen after 2000)
References:
[1] Tunca M et al; Turkish FMF Study Group.Familial Mediterranean fever (FMF) in Turkey: results of a nationwide multicenter study. Medicine (Baltimore). 2005 Jan;84(1):1–11.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4970

FRI0611 ASSESSMENT OF PANNICULITIS CLINICAL OUTCOMES: RISK FACTORS FOR RECURRENCE AND PREDICTORS OF SLOW REGRESSION OF INDURATIONS

N. Savushkina, O. Egorova, B. Belov. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Currently there's no clear understanding of the clinical course and outcomes of panniculitis with predominant involvement of subcutaneous adipose tissue (SAT), which is often associated with the involvement of locomotor system and viscera. Consistent elaboration of both is of paramount importance, as it may give a deeper insight into clinical and curative factors which may have impact on the disease prognosis.
Objectives: To assess clinical outcomes of panniculitis (risk factors for recurrence and predictors of slow regression of indurations).
Methods: 186 pts (172 females, 14 males) aged 43,5±14,5 years with different types of Pn, who were at the record of V. A. Nasonova Research Institute of Rheumatology during 2009–2015 yy. Disease duration varied from 1 week to 20 years. General clinical examination and lab tests (serum levels of α1-antitrypsin, amylase, lipase, ferritin, creatine phosphokinase (CPK), rheumatoid factor) (RF), ANF, anti-DNA, ANCA), bacteriological and serological tests, radiological examination (chest CT scan), ultrasound examinations of skin and subcutaneous fat (SF) around the nodules, tuberculin skin test and histopathology of nodular skin samples were performed at baseline. Patients were re-tested during the follow up (FUP) when necessary.
Results: Female middle-aged patients prevailed in the study group with the disease duration from 1 week to 25 years. *Saucer*-like depressions as a Pn - specific phenomenon was documented in 28,5% cases. The estimated risk of *saucer*-like depressions was higher in patients who manifested Pn at the age of >40 years (OR 4,9, 95% CI 2,3–10,4; $p<0,0001$); this subgroup also showed lesion proneness to confluence and forming of irregular shape conglomerates (OR 2,9, 95% CI 1,45–5,7; $p=0,002$), tendency to forming large size >3 cm lesions (OR 4,96, 95% CI 2,2–10,97; $p<0,0001$), and the disease lasting over 3 months (OR 24,9, 95% CI 9,2–67,4; $p<0,0001$). All pts were re-examined within 1–6 years. Median time to onset of nodules regression was 2 [1;6] months. Recurrences were documented in 66 (35,5%) pts during the follow up. Logistic regression was used for multivariate statistical analysis in order to identify the potential predictors of delayed (>3 months) nodules regression and recurrence risk factors. Used model identified the following predictors of delayed nodules regression (i.e., disease regression): age >40 years (OR 2,58; CI 1,02–6,5; $p=0,04$), and presence of saucer-like depressions (OR 5,05; CI 1,2–21,7; $p=0,03$). The sensitivity of used statistical model was 70%, specificity – 71%, positive predictive value - 74%. Disease duration >3 months (OR 4,7; CI 2,0–10,6; $p=0,0002$) was identified by our model as the predictor of recurrences with 60% sensitivity, 78% specificity, and 59% positive predictive value.
Conclusions: Pn tends to regress more slowly in pts aged over 40 and in pts having saucer-like depressions. Trend to recurrences is not so evident in Pn, although probability of recurrence increases in pts with longer disease duration at the time of initiation of therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3850

FRI0612 IGG4-RELATED DISEASE IN EASTERN MEDITERRANEAN: CLINICAL FEATURES AND OUTCOMES OF A LARGE COHORT

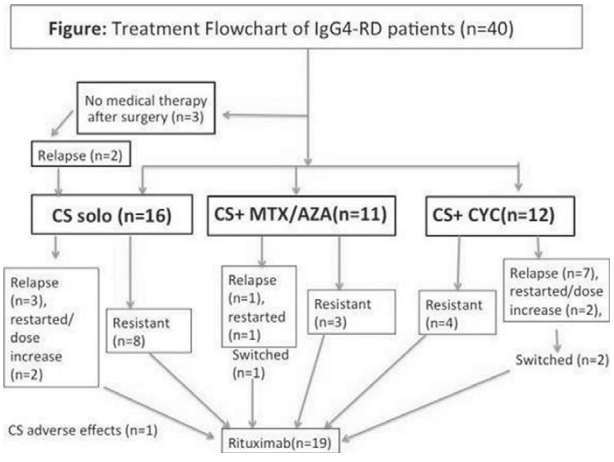
O. Karadag[1], A. Erden[1], A.S. Ayhan[2], E.C. Bolek[3], U. Kalyoncu[1], B. Armagan[1], A. Sari[1], L. Kilic[1], A. Akdogan[1], T. Hazirolan[4], B. Akdogan[5], S.A. Bilgen[1], D.E. Baydar[2], S. Kiraz[1], I. Ertenli[1]. *[1]Department of Rheumatology; [2]Department of Pathology; [3]Department of Internal Medicine; [4]Department of Radiology; [5]Department of Urology, Hacettepe University Faculty of Medicine, Ankara, Turkey*

Background: Since majority of IgG4-related disease (IgG4-RD) patients in the literature are from Far East and United States, there is a lack of large series from other parts of the world.
Objectives: We aimed to identify the clinical characteristics and outcome of Turkish IgG4-RD patients from a tertiary center.
Methods: In step 1, clinical and histopathological features of patients having any disease under the clinical spectrum of IgG4-RD were retrospectively reviewed. For step 2, patients prospectively diagnosed are enrolled into the study. Patients fulfilling the "definite" diagnosis according to comprehensive diagnostic criteria were recruited (enrolled (n=52), excluded (n=47).
Results: Median age was 51.1 years and no gender predominance was observed (Male/female: 26/26). Retroperitoneal fibrosis is the most frequent presentation;

Table 1. Distribution of clinical findings and organ involvement (n=52)

Constitutional symptoms, n (%)	
Fatigue	31 (59.6)
Tiredness	16 (30.7)
Night sweats	15 (28.8)
Weight loss	14 (26.9)
Fever	13 (25)
Retroperitoneal fibrosis, n (%)	23 (44.2)
Lymphadenopathy, n (%)	20 (39.2)
Any cardiovascular involvement, n (%)	15 (28.8)
Periaortitis	12 (23.1)
Pericardium	5 (9.6)
Coronary periarteritis	4 (7.7)
Abdominal aort aneurysm	1 (1.9)
Orbital pseudotumor, n (%)	12 (23.1)
Orbitalmass/proptosis	6 (11.5)
Extraocular muscles	6 (11.5)
Pancreas, n (%)	12 (23.1)
Major salivary glands, n (%)	11 (21.2)
Lacrimal glands, n (%)	9 (17.3)
Mediastinal fibrosis, n (%)	6 (11.5)
Ear, nose, sinuses, n (%)	5 (9.6)
Lung fibrosis, n (%)	5 (9.6)
Skin , n (%)	4 (7.7)
Pleura, n (%)	4 (7.7)
Gall bladder and Biliary ducts, n (%)	4 (7.7)
Thyroid, n (%)	3 (5.8)
Liver, n (%)	3 (5.8)
Kidney (mass) , n (%)	3 (5.8)
Pachymeningitis, n (%)	2 (3.8)

Breast involvement: (n=1), tubulointerstitial nephritis (n=1).



others were lymphadenopathy, orbital pseudotumor, pancreas and salivary glands in decreasing order (Table). Twenty-four (46.1%) of patients had localized involvement. Corticosteroids were mainstay of treatment in 92.5% of patients, and in 57.5% with any immunosuppressive agents as first line treatment. Rituximab has been used for cases resistant to previous treatment or with relapses in 19 (47.5%) of patients. A complete response was achieved in 52.5% of patients and partial response (<50% of regression) in 40%. Two patients deceased due to IgG4-RD attributed problems and no malignancy was observed (median follow up: 18 months).
Conclusions: We observed similar features with previous European cohorts however no male predominance was seen. Even though conventional immunosuppressives were used in more than half of patients, treatment had switched to rituximab ~50% patients owing to resistance or relapses.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4315

FRI0613 H-FERRITIN AND PRO-INFLAMMATORY CYTOKINES ARE INCREASED IN THE BONE MARROW OF ADULT PATIENTS AFFECTED BY MACROPHAGE ACTIVATION SYNDROME

P. Ruscitti[1], P. Cipriani[1], F. Ciccia[2], P. Di Benedetto[1], A.R. Lizzi[3], V. Liakouli[1], O. Berardicurti[1], F. Carubbi[1], G. Guggino[2], G. D'Andrea[3], G. Triolo[2], R. Giacomelli[1]. *[1]Division of Rheumatology, Department of Biotechnological and Applied Clinical Science, School of Medicine, University of L'Aquila, L'Aquila; [2]Division of Rheumatology, Department of Internal Medicine, University of Palermo, Palermo; [3]Department of Biotechnological and Applied Clinical Science, School of Medicine, University of L'Aquila, L'Aquila, Italy*

Background: During macrophage activation syndrome (MAS), an inflammatory life-threatening syndrome, extremely high levels of serum ferritin may be observed [1]. Ferritin is an intracellular iron storage protein comprising 24 subunits that may be divided in heavy (H) subunits and light (L) subunits, based on their molecular weight [2]. The H-/L-subunits ratio may change, depending on the specific tissue and the physiologic status of the cell. In the normal condition, ferritin enriched in L subunits (L-ferritin) has been found in the liver and in the spleen, whereas the ferritin enriched in H subunits (H-ferritin), may be mainly observed in the heart and kidneys [2].
Objectives: We investigated the tissue expression of both H-and L-ferritin as well as the macrophage subsets expressing these molecules, in the inflammatory BM infiltrate of MAS patients. In addition, the co-expression of IL-1β, TNF, IFN-γ and H- or L ferritin, within the inflammatory cells, was assessed. Finally, we explored if the imbalance between H-ferritin and L-ferritin as well as the number of ferritin positive cells may be considered helpful bio-markers to assess the severity of these patients.
Methods: We analysed the bone marrow (BM) biopsies, by immunofluorescence of 10 adult MAS patients affected by rheumatic disease to assess the presence of: i. both H- and L-ferritin; ii. the number of CD68+/H-ferritin+ and CD68+/L-ferritin+; iii. the tissue pro-inflammatory cytokines, IL-1β, TNF, IFN-γ; and we correlated these data with clinical and laboratory data. Furthermore, the presence of ferritins was assessed in the sera of the same patients by western blot analysis.
Results: We observed an increased tissue expression of H-ferritin and of pro-inflammatory cytokines (IL-1β, TNF, IFN-γ). Western blot analysis, in the sera, of H-ferritin mirrored data on the tissue. Furthermore, an increased number of CD68+/H-ferritin+ cells and an infiltrate of cells co-expressing H-ferritin and IL-12, suggesting an infiltrate of M1 macrophages, were observed.
Tissue H-ferritin levels correlated with the decreased counts of WBC (p=0.01) and PLT (p=0.0001); with the increased values of serum ferritin (p=0.012) and C-reactive protein (CRP) (p=0.0058); and with the tissue expression of IL-1β (p=0.006). The number of the CD68+/H-ferritin+ cells correlated with the decreased counts of WBC (p=0.03) and PLT (p=0.0007), and with the increased serum ferritin levels (p=0.0088) and CRP (p=0.049). The analyses concerning tissues L-ferritin as well as the number of CD68+/L-ferritin+ cells and the same parameters failed to show any significant result.
Conclusions: We observed an increased tissue expression of H-ferritin associated with an increased expression of IL-1β. Interestingly, in the BM inflammatory infiltrate an increased number of CD68+/H-ferritin+ cells was shown. Of note, tissue expression of H-ferritin as well as the number of CD68+/H-ferritin+ significantly were associated with the hematological involvement of the disease, suggesting possible bio-markers to assess the severity of these patients.
References:
[1] Ramos-Casals M, et al. Lancet. 2014;383:1503–16.
[2] Rosário C, et al. BMC Med. 2013;11:185.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5420

FRI0614 FREQUENCY OF ORGAN MANIFESTATIONS IN CHRONIC SARCOIDOSIS

R. Bergner[1], K. de Groot[2], G.A. Müller[3], P. Korsten[3]. *[1]Medizinische Klinik A, Klinikum Ludwigshafen, Ludwigshafen; [2]Medizinische Klinik III, Sana Klinikum Offenbach, Offenbach; [3]Klinik für Nephrologie und Rheumatologie, Universitätsmedizin Göttingen, Göttingen, Germany*

Background: Chronic sarcoidosis is a systemic disease of unknown etiology, characterized by the histological finding of granulomas in involved organ systems. The most often affected organ is the lung with approximately 90–95%. Systematic data of organ manifestations other than the lung are scarce and show a wide range from 1–2% up to 50% depending on the series.
Methods: We analyzed data of newly diagnosed chronic sarcoidosis in 3 tertiary hospitals. We analyzed data on organ manifestations (OM), type of OM and laboratory findings. The certainty of OM was classified as grade 0 (not investigated), grade 1 (no sign of OM), grade 2 (clinical sign of OM), grade 3 (signs of OM in laboratory findings or imaging) and grade 4 (histological proven OM), respectively.
Results: We included 151 patients with biopsy-proven chronic sarcoidosis. Mean age was 50.8±15 years with a male predominance (87 [57.2%] vs. 65 [42.8%] patients).
Except for 3 patients, all demonstrated pulmonary involvement. The predominant type of lung involvement was type I (mediastinal lymph node enlargement) in 54.2% and type II (mediastinal lymph node enlargement and interstitial involvement) in 27.7%.
96.5% of patients were investigated for an affection of the kidneys, 97.3% for hepatic, 92.7% for skin involvement, 68.8% for ocular manifestations, 67.5% for ear, nose, throat (ENT) manifestations and 92% for cardiac manifestations, respectively.
Grade 3 (imaging/laboratory) and grade 4 (histology) findings were seen in the kidneys in 7.6/22.8%, in the liver in 13.3/11.9%, in the heart in 10.6/0.7%, in the eyes in 6.6/
Conclusions: OM in chronic sarcoidosis are more frequent than suggested in the current literature, especially renal and hepatic. About 20% of patients with chronic sarcoidosis suffered from moderate to severe CKD due to sarcoidosis, which is a major organ complication contributing to overall morbidity.
We recommend a systematic screening for OM in all patients with chronic sarcoidosis as it is performed in other systemic rheumatic disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6716

FRI0615 SARCOIDOSIS AND CANCER: DIFFERENT PATTERNS OF ASSOCIATION IN A MULTICENTER COHORT FROM SOUTHERN EUROPE

R. Pérez-Alvarez[1], B. Kostov[2], A. González García[3], R. Gómez De La Torre[4], M. Lopez Dupla[5], B. De Escalante[6], A. Alguacil[7], J. Chara[8], J. Velilla[9], J. Rascón[10], J.S. Garcia Morillo[11], C. Tolosa[12], E. Fonseca[13], M. Bonet[14], J.L. Callejas[15], G. de la Red[16], E. Calvo[17], A. Gómez Lozano[18], E. Peral[19], J.F. Gómez Cerezo[20], G. Cruz[21], P. Perez[22], S. Rodríguez Fernández[23], B. Pinilla[24], A. Gato[25], M. Akasbi[26], A. Robles[27], I. Ojeda[28], M.J. Vives[29], C. Morcillo[30], M. Penadés[31], M. De Vicente[32], M. Ramos-Casals[33], L. Pallarés[10], P. Brito-Zerón[30,33] on behalf of the SARCOGEAS-SEMI Registry. *[1]Hosp Alvaro Cunqueiro, Vigo; [2]IDIBAPS, Barcelona; [3]Hosp Ramón y Cajal, Madrid; [4]HUCA, Oviedo; [5]Hosp Joan XXIII, Tarragona; [6]Hosp Clínico, Zaragoza; [7]Hosp Virgen de la Salud, Toledo; [8]Hosp Josep Trueta, Girona; [9]Hosp Miguel Servet, Zaragoza; [10]Hosp Son Espases, Palma de Mallorca; [11]Hosp Virgen del Rocio, Sevilla; [12]Hosp Parc Taulí, Sabadell; [13]Hosp Cabueñes, Gijón; [14]Althaia, Manresa; [15]Hosp San Cecilio, Granada; [16]Hosp Esperit Sant, Santa Coloma; [17]Hosp San Jorge, Huesca; [18]Hosp Sta Caterina, Girona; [19]Hosp Virgen Macarena, Sevilla; [20]Hosp Infanta Sofía, Madrid; [21]Hosp de Poniente, Almería; [22]Hosp Puerta del Mar, Cádiz; [23]Hosp da Barbanza, A Coruña; [24]Hosp Gregorio Marañón, Madrid; [25]CH, Albacete; [26]Hosp Infanta Leonor; [27]Hosp la Paz, Madrid; [28]Hosp Valle del Guadiato, Córdoba; [29]San Joan de Déu, San Boi; [30]Hosp CIMA-Sanitas, Barcelona; [31]Hosp de Manises, Valencia; [32]Hosp Nuestra Señora del Prado, Talavera; [33]Hosp Clínic, Barcelona, Spain*

Objectives: To evaluate the temporal association between the diagnosis of neoplasia and sarcoidosis in a large cohort of Spanish patients with sarcoidosis.
Methods: In January 2016, the Autoimmune Diseases Study Group (GEAS-SEMI) created a national registry (SARCOGEAS) of patients with sarcoidosis. Sarcoidosis was diagnosed with the criteria proposed by the ATS/ERS/WASOG 1999 statement, and extrathoracic disease by the 2014 WASOG instrument. Diagnosis of neoplasia was recorded before and after the diagnosis of sarcoidosis.
Results: The cohort included 1082 patients (82% biopsy-proven, 618 women, mean age 47yrs). Association with neoplasia was detected in 135 (13%) patients who developed 140 neoplasms (110 solid and 30 hematological neoplasia). The neoplasia more frequently reported were breast (n=18), lymphoma (n=16), non-melanoma skin (n=15) and colon (n=15). Association with neoplasia was more frequent in patients born in Spain (97% vs 86%, p<0.001, OR 4.06), older patients (55 vs 46yrs, p<0.001, OR 1.03) and those with bone marrow involvement (14% vs 4%, p<0.001, OR 3.64). Patients in whom cancer preceded the diagnosis of sarcoidosis had a higher frequency of sarcoidosis diagnosed incidentally (20% vs 4%, p=0.011) and a lower frequency of ocular sarcoidosis (3% vs 16%, p=0.016). Patients with associated hematological neoplasia had a higher frequency of ENT (13% vs 1%, p=0.009) and bone marrow (33% vs 9%, p=0.002) involvements in comparison with patients with associated solid neoplasia.
Conclusions: Association between sarcoidosis and cancer was found in 13% of patients (80% solid and 20% hematologic malignancies). Elderly patients and those born in Spain were at high risk of having associated cancer. Asymptomatic

sarcoidosis was more frequently observed in those patients with a previous history of neoplasia, while the association with hematological neoplasms was linked to a higher frequency of sarcoidosis involving ENT and bone marrow.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3700

FRI0616 EYE MANIFESTATIONS OF PATIENTS WITH MUCKLE-WELLS SYNDROME

S. Cekic[1], O. Yalcinbayir[2], S.S. Kilic[1]. [1]*Pediatric Rheumatology;* [2]*Ophtahlmatology, Uludag University Medical Faculty, Bursa, Turkey*

Background: CAPS is a rare autoinflammatory disease associated with mutations in the *CIAS1* gene, encoding for NLRP3 that result in overactivation of the inflammasome and systemic inflammation. Muckle-Wells syndrome (MWS) is a rare autosomal dominant disease which causes episodic fever attacks, sensorineural deafness, recurrent hives, arthritis and eye involvement.
Objectives: Here we present the findings of eye involvement in a family whose 11 members have MWS.
Methods: Clinical data was collected during the course of ongoing patient care.
Results: We evaluated the clinical features of 11 patients who were referred to a tertiary care center. The median age of the patients was 25 years (range: 9–65). The ratio of females /males was 1.2 (6/5). All patients had arthritis with exacerbation on exposure to cold and recurrent episodes of pink eye. The median age of onset of ocular involvement was 8 years (2–45). We observed severe eye involvement in 36% of our cases, including band keratopathy, severe damage of corneal stroma and neovascularization. Corneal involvement and clouding was detected in four patient. Two of those had the diagnosis of keratoconus as well. Patients with keratoconus had corneal scarring due to corneal hydrops verified with corneal topography. The other two patients with corneal clouding had bant keratopathy. One of those patient was a 17 year old girl who had recurrent uveitis with hypopyon which necessiated the use of intravitreal dexamethasone implant. She also had posterior synechia of the iris to the lens. The other eye of that patient had signs of phthisis bulbi. The other patient with bant keraopathy was 46 years old male who had optic atrophy and tractional fibrovascular membranes at the posterior pole of the eye. Anakinra was used for treatment of 5 cases, and canakinumab of 3 cases. It was observed that the frequency of conjunctivitis decreased after anti IL-1 therapy. There was no mutation detected in the study of MEFV (all exons), TNFRSF1A (exons 2 to 7), MVK (all exons), NLRP3 (all exons), NOD2 (exons 4, 8 and 9) and PSTPIP1 (exons 10 and 11) genes.
Conclusions: In this study, it has been shown that eye findings related to MWS can vary from conjunctivitis to severe uveitis. We want to emphasize that ocular involvement in MWS should be carefully assessed, since it can lead to visual impairment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3352

FRI0617 DIAGNOSTIC SENSITIVITY OF CUTOFF VALUES OF IGG4-POSITIVE PLASMA CELL NUMBER AND IGG4-POSITIVE/CD138-POSITIVE CELL RATIO IN TYPICAL MULTIPLE LESIONS OF PATIENTS WITH IGG4-RELATED DISEASE

S. Tsuge, I. Mizushima, Y. Fujisawa, S. Hara, F. Suzuki, K. Ito, H. Fujii, K. Yamada, M. Kawano. *Division of Rheumatology, Department of Cardiovascular and Internal Medicine, Kanazawa University hospital, Kanazawa, Kanazawa, Japan*

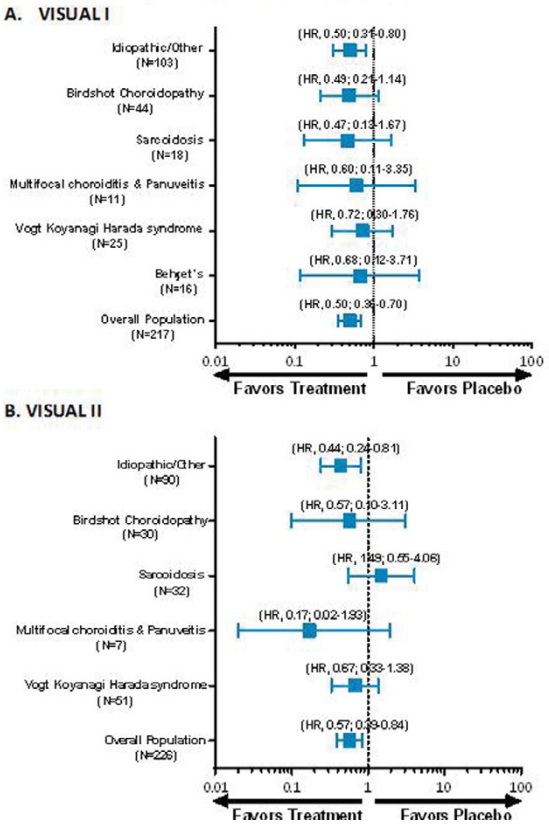
Background: Immunoglobulin G4-related disease (IgG4-RD) is a recently recognized systemic inflammatory disease with multi-organ involvement [1]. Diagnostically, two of the most important hallmarks of IgG4-RD are high IgG4-positive plasma cell (PC) counts and high IgG4/IgG ratios in affected organs. Although the International consensus statement (ICS) on the pathology of IgG4-RD adopted different IgG4-positive PC counts among affected organs for the diagnosis to differentiate IgG4-RD mimickers from IgG4-RD [2], histological and immunohistochemical findings of the specimens from not only one but multiple organs in the same patient has not been evaluated.
Objectives: This study aimed to investigate the diagnostic sensitivity of the cutoff values of IgG4-positive PC number and IgG4-positive/CD138-positive cell ratio proposed by the International consensus statement (ICS) on the pathology of IgG4-RD in typical multiple lesions of patients with IgG4-RD.
Methods: We evaluated IgG4-positive PC number and IgG4-positive/CD138-positive cell ratio in 35 samples from 16 IgG4-RD patients having more than two typical lesions of IgG4-RD.
Results: We evaluated twelve submandibular, eleven ophthalmic, four skin, four kidney, two pancreatic, and one bronchus and prostate lesion each in 16 patients with typical clinical, serological, and radiographic features. Concerning IgG4+ PC number per high power field, most ophthalmic (8/11), kidney (4/4), pancreatic (2/2), and bronchial lesions (1/1) fulfilled the cutoff value of ICS, whereas many of the submandibular (5/12) and skin lesions (0/4) did not. In contrast to the absolute number, almost all lesions fulfilled the cutoff value of IgG4+/CD138+ cell ratio. In five cases, only one or two lesions in the same patient fulfilled the cutoff value of ICS, while the others did not.
Conclusions: These results suggest that ICS criteria have different sensitivities among the affected organs in diagnosing IgG4-RD.
References:
[1] Stone JH, et al. IgG4-related disease. N Engl J Med. 2012;366:539–51.
[2] Deshpande V, et al. Consensus statement on the pathology of IgG4-related disease. Mod Pathol. 2012;25:1181–92.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4170

FRI0618 ADALIMUMAB IN NON-INFECTIOUS UVEITIS – EFFICACY ACROSS DIFFERENT ETIOLOGIES IN THE VISUAL I AND VISUAL II TRIALS

P.T. Merrill[1], A. Vitale[2], M. Zierhut[3], E. Forton[4], H. Goto[5], M. Kron[6], S. Tari[7], S. Pathai[8]. [1]*Rush University Medical Center, Chicago;* [2]*University of Utah, Salt Lake City, United States;* [3]*University of Tuebingen, Center of Ophthalmology, Tuebingen, Germany;* [4]*University of Montreal, Montreal, Canada;* [5]*Tokyo Medical University, Tokyo, Japan;* [6]*AbbVie Deutschland GmbH & Co KG, Ludwigshafen, Germany;* [7]*AbbVie Inc., North Chicago, United States;* [8]*AbbVie Ltd, Maidenhead, United Kingdom*

Background: There is increasing interest in understanding the efficacy of adalimumab across different etiologies of uveitis. No prospective analysis has been conducted to date to determine the efficacy of adalimumab among non-infectious uveitis patients with different etiologies.
Objectives: To assess adalimumab (ADA) efficacy in active and inactive, non-infectious uveitis across different etiologies in patients who were recruited as part of the VISUAL program.
Methods: Exploratory data analyses from two global phase 3, double-masked trials: VISUAL I (patients with active uveitis despite ≥2 weeks of prednisone 10–60 mg/day) and VISUAL II (patients with inactive disease dependent on 10–35 mg/day of prednisone to maintain inactivity) were performed. Patients received placebo (PBO) or ADA subcutaneously (80 mg week 0, followed by 40 mg every other week from week 1 up to 80 weeks). In VISUAL I, all patients received a prednisone burst followed by taper to 0 mg by week 15. In VISUAL II, prednisone taper to 0 mg was mandatory by week 19. The primary endpoint was time to treatment failure (TF) at or after week 6 for VISUAL I; and at or after week 2 for VISUAL II[1,2]. For this analysis, patients were categorized into different uveitis etiologies which they presented at study entry. Hazard ratios (HR) for time to TF were obtained for each uveitis etiology.
Results: The efficacy of ADA was significantly greater than PBO in the largest subgroup of patients with Idiopathic/other uveitis (VISUAL I: 103 and VISUAL II: 90) etiology in both VISUAL I[1] and VISUAL II trials. All other subgroups showed

Figure: Hazard ratios of time to treatment failure by uveitis etiologies.
VISUAL I (A) and VISUAL II* (B) clinical trials.



a trend in favor of ADA, except for Sarcoidosis subgroup in the VISUAL II trial (Figure). Overall safety for both trials has been previously reported [1,2].

Conclusions: These exploratory analyses from the VISUAL I and VISUAL II trials show significantly higher efficacy in ADA-treated patients over PBO in "idiopathic/other" diagnoses of patients with both active and inactive non-infectious uveitis. Furthermore, across different uveitis etiologies, these analyses suggest that ADA-treated patients had a prolonged time to treatment failure compared to PBO.

References:

[1] Jaffe GJ, Dick AD, Brezin AP, et al. N Engl J Med (2016); 375:932–43.
[2] Nguyen QD, Merrill PT, Jaffe GJ, et al. The Lancet (2016); 388(10050): 1183–92.

Acknowledgements: AbbVie funded the VISUAL I and VISUAL II studies and provided writing support. All authors contributed to the development of the content. The authors and AbbVie reviewed and approved the abstract. The authors maintained control over the final content. Medical writing assistance was provided by Gaurav Patki, PhD of AbbVie Inc.

Disclosure of Interest: P. T. Merrill Consultant for: Santen, AbbVie, A. Vitale Consultant for: ACIONT, M. Zierhut Consultant for: AbbVie and Santen, E. Forton Consultant for: AbbVie, Alcon and Allergan, H. Goto Consultant for: AbbVie, M. Kron Shareholder of: AbbVie, Employee of: AbbVie, S. Tari Shareholder of: AbbVie, Employee of: AbbVie, S. Pathai Shareholder of: AbbVie, Employee of: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.2389

FRI0619 COMPARING CANAKIMUMAB AND ANAKINRA IN YOUNG GREEK WOMEN WITH RESISTANT RECURRING PERICARDITIS

P. Kiryttopoulos [1], T. Michailidis [1], E. Papchianou [1], M. Charalampidis [2], P. Dimitriadis [3], A. Agorastos [4], T. Mpektsis [1]. *[1]Department of Internal Medicine, General Hospital of Veria, Veria; [2]Gastroenterology Department, Theageneio Hospital of Thessaloniki, Thessaloniki; [3]Health Center of Alexandria, Alexandria, Greece; [4]Oncology Department, St. Thomas Hospital, London, United Kingdom*

Background: Resistant – recurring pericarditis (RRP) is often associated with autoinflammatory syndromes. Conventional therapy with glucocorticoids and colchicine is often enough unsuccessful, thus nowadays the use of anakinra in such cases is becoming common every – day practice.

Objectives: Our goal was to determine whether RRP was associated with gene mutations relevant with autoinflammatory diseases and then compare the effectiveness of canakimumab and anakinra.

Methods: We studied 18 patients with RRP (all women, from 14 to 36 years old) determing the existence of mutation from the infevers database (25 genes, from MEFV and TNFRSF1A to MVK and SLC 29A3, all related with autoinflammatory diseases). All the patients were proven positive to one of the above mutations (all heterozygous) and then treatment with anakinra (n=9, 100mg sc once daily) and canakimumab (n=9, 150mg sc q4wk) was administered.

Results: During the study (3 years), all anakinra patients stopped receiving per os glucocorticoids and were free of any new pericarditis episodes. 3 of them (33%) stopped any treatment after a year of anakinra therapy and none was presented with any skin reactions.

On the contrary, all canakimumab patients were not able to free themselves of the glucocorticoid treatment, since at least one new episode of pericarditis to each patient was recorded. Two of them were free of pericarditis the last year of the study (though being treated with 2,5mg prednisolone per os daily).

Statistically speaking, the use of IL-1R antagonist in recurrent – resistant pericarditis associated with autoinflammatory mutations was proven much more successful ($p<0,01$) than the use of the IL-1b Mab.

Conclusions: Though the sample of patients (n=18) was too small in order to set us able to reach any safe conclusions, it is quite possible that anakinra may be one effective solution that can prevent the long term administration of corticoids to patients with recurrent pericarditis Canakimumab was not recorded with similar positive results.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6289

FRI0620 MIR-204-3P INHIBITS THE PRODUCTION OF TLR4-RELATED CYTOKINES IN FAMILIAL MEDITERRANEAN FEVER BY TARGETING THE PIK3 SIGNALING PATHWAY

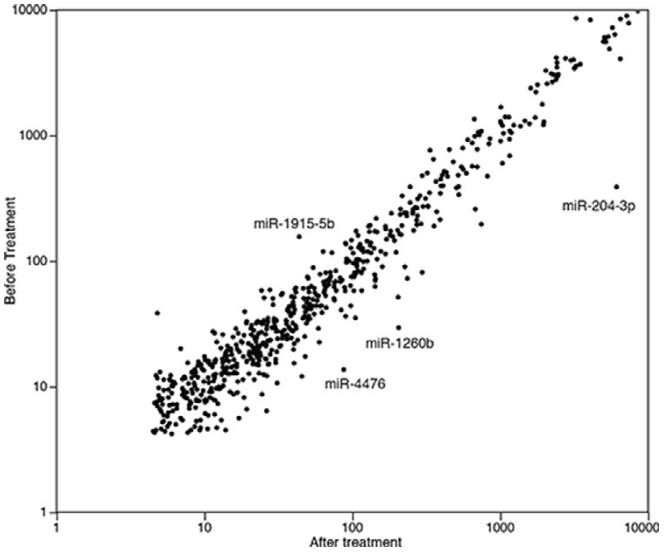
T. Koga [1,2], K. Migita [3], M. Umeda [1], F. Nonaka [4], S.-Y. Kawashiri [1], N. Iwamoto [1], K. Ichinose [1], M. Tamai [1], H. Nakamura [1], T. Origuchi [1], K. Eguchi [5], A. Kawakami [1]. *[1]Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences; [2]Center for Bioinformatics and Molecular Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki; [3]Fukushima Medical University School of Medicine, Fukushima Medical University School of Medicine; [4]Department of Internal Medicine, Sasebo City General Hospital; [5]Center for Rheumatic Disease, Sasebo Chuo Hospital, Sasebo, Japan*

Background: MicroRNAs (miRNAs) are endogenous small RNAs and post-transcriptionally regulate gene expression by pairing with target. There has been emerging evidence showing the association of aberrantly expressed circulating miRNAs in the serum with the pathogenesis or progression of diseases including cancer and autoimmune disease. Although a number of circulating miRNAs associated with inflammation have been identified, the roles of them in patients with FMF and the underlying mechanism remain to be elucidated.

Objectives: The aim of this study was to identify a serum miRNAs profile and potential biomarkers in FMF and clarify their gene targets for understanding the pathogenesis of autoinflammatory diseases.

Methods: We performed miRNA microarray in the serum from FMF in attack and in remission. We subsequently examined the expression of miRNAs that varied before and after the attack in macrophages derived from THP-1 cells stimulated with toll-like receptor (TLR) ligands. Macrophages derived from THP-1 cells transfected with pre-miRNA and anti-miRNA were stimulated with TLR ligands for 24 hours. We collected the supernatants for the quantification of inflammatory cytokine production. To identify the target genes, we overexpressed its miRNA and performed Agilent expression microarray. Transfection with reporter construct and pre-miRNA and anti-miRNA was performed to confirm suppression of target mRNA.

Results: We found that miR-204–3p was greatly decreased in the serum from FMF patients in attack. In vitro study, the expression of miR-204–3p was suppressed by LPS stimulation in macrophages derived from THP-1 cells. Inhibition of miR-204–3p significantly induced the production of TLR4-related cytokines whereas overexpression of miR-204–3p inhibited their production. Bioinformatic analysis showed that miR-204–3p is predicted to target genes implicated in TLR pathway through regulation of PIK3 signaling. Reporter assay revealed that miR-204–3p directly suppressed the luciferase activity of 3'UTR of PIK3CG reporter construct.



Conclusions: These data suggest that serum miR-204–3p has a potential as a useful biomarker among patients with FMF and that miR-204–3p plays a critical role as a suppressor to regulate the production of TLR4 related cytokines by targeting PIK3 signaling pathway.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2813

FRI0621 PREVALENCE OF DIFFERENT ORBITAL ANATOMIC STRUCTURES AFFECTION IN IGG4-RELATED OPHTHALMIC DISEASE: SINGLE CENTER EXPERIENCE

V. Vasilyev [1], E. Sokol [1], T. Safonova [2], S. Palshina [1], N. Kokosadze [3], A. Kovrigina [4]. *[1]Nasonova Research Institute of Rheumatology, Moscow, Russia; [2]Research Institute of Ophthalmic diseases; [3]N.N. Blochin Russian Cancer Research Center; [4]Hematology Research Center, Moscow, Russian Federation*

Background: According to 2009 Japanese nationwide survey of IgG4-related disease (IgG4-RD), orbit is the leading site of affection [1]. However diagnostic criteria and nomenclature of IgG4-RD were developed a few years later [2,3].

Objectives: To evaluate the peculiarities of clinical, laboratory, histological and immunohistochemical presentation of IgG4-related ophthalmic disease (IgG4-ROD).

Methods: During 2004 – 2016, 82 patients were diagnosed with IgG4-RD 53 of whom had IgG4-ROD (men – 17, women - 36). The diagnoses of IgG4-RD and IgG4-ROD were established using comprehensive diagnostic criteria [2,3]. In all patients full clinical, ophtalmological, dental and serological (rheumatoid factor, C-reactive protein, IgG, IgG4, IgM, IgA, ANA, anti-Ro/La, C3/C4 complement) examination was carried. In all cases diagnosis was verified pathomorphologicaly with immunohystochemical staining (anti-CD 138, CD 68, IgG, IgG4, κ-chain, λ-chain), but only in 43 patients the diagnosis of IgG4-RD was established on orbital tissues biopsy. Some patients at baseline were tested on B-cell clonality

in tissue (on frozen tissue section or paraffin embedded) by PCR analysis of immunoglobulin V-D-J genes heavy chain rearrangements (FR1, FR2, FR3); monoclonal secretion was tested in serum protein electrophoresis.

Results: 40 patients with IgG4-ROD had orbital lesions at the onset of the disease and 13 developed them after 2 - 9 years from the onset. The frequency of different orbital anatomic structures involvement see in table 1. 15 (28%) patients had isolated orbital lesions while 38 (72%) had systemic IgG4-RD with simultaneous involvement of 2 - 7 other organs. 6 (14%) patients had unilateral orbital lesions. 23 (53%) patients with IgG4-ROD had associated IgG4-related sialoadenitis and nasal lesions. Most common pathomorphological features of IgG4-ROD see in table 2. The most common laboratory features of IgG4-ROD were elevation of: total serum IgG (44%), serum IgG4 (88%), serum IgE (61%) and monoclonal serum secretion (23%).

Table 1. Prevalence of different orbital anatomic structures affection in IgG4-ROD (n=43)

Anatomicstructure	N,%
Lacrimal gland	93
Extraocular muscules	85,5
Fibroinflammatory lesions of eyelids	32,5
Retrobulbar infiltration	32,5
Optic nerve thickening	32,5
Trigeminal involvement	21
Nasolacrimal duct	4,5

Table 2. Pathomorphological features in IgG4-ROD (n=43)

Pathomorphological feature	N, %
Lymphoplasmatic infiltrate	93
Dense fibrosis	93
Lymphoid follici formation	69
Tissue eosinophilia	32,5
Obliterative phlebitis	14
Vasculitis	7
IgG4/IgG > 40%	90,5
MALT-lymphoma of lacrimal gland	2,3
AL-amyloidosis	2,3

Conclusions: In our cohort of IgG4-RD patients orbit is the leading site of the disease (64.5% of patients) and the disease onset (75% of patients). The majority of patients have bilateral orbital lesions (89%) and systemic course of the disease with other organ involvement (72%). Most often affected orbital anatomicstructures are lacrimal glands, extraocular muscles, retrobulbar infiltration with optic nerve thickening and fibroinflammatory lesions of eyelids. MALT-lymphoma of lacrimal gland and local AL-amyloidosis can complicate the long history of IgG4-ROD. Monoclonal serum secretion and B-cell clonality in the tissue in 23% of patients can potentially act as a background for lymphoma formation.

References:

[1] Uchida K, Masamune A, Shimosegawa T et al. Prevalence of IgG4-related disease in Japan based on nationwide survey in 2009. IntJ.Rheumatol. 2012;2012:358371.
[2] Umehara H, Okazaki K, Masaki Y et al. A novel clinical entity, IgG4-related disease (IgG4RD): general concept and details. ModRheumatol. 2012; 22: 1–14.
[3] Stone JH, Khosroshahi A, Deshpande V et al. Recommendations for the Nomenclature of IgG4-Related Disease and Its Individual Organ System Manifestations. Arth.Rheum. 2012; 64:3061–3067.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4283

FRI0622 A RETROSPECTIVE COHORT STUDY ABOUT THE CLINICAL CHARACTERISTICS OF IGG4-RELATED DISEASES

X. Wu, C. Wang, Y. Miao, Y. Huang, L. Dong. *Department of Rheumatology and Immunology, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China*

Background: Immunoglobulin (Ig) G4-related disease (IgG4-RD) is an increasingly recognized systemic autoimmune disease in the past decade, and encompasses a wide spectrum of disorders previously considered to be unrelated, but with common pathologic, serologic, and clinical features.There have been several hundred literatures on IgG4-RD published in the past few years, however, we still cannot well characterize this complicated disease, including clinical features, treatments as well as mechanisms, which promotesus to further describe this disease.

Objectives: To describe the clinical presentations, laboratory features, imaging manifestations, treatments and evolutions in a cohort of 34 Chinese patients with immunoglobulin G-related diseases (IgG4-RD).

Methods: A retrospective study was performed in Wuhan Tongji Hospital. Electronically stored records of clinical, laboratory, imaging, and histological features were reviewed. The diagnoses were made according to comprehensive diagnostic criteria for IgG4-RD. Disease activity was assessed by IgG4-RD Responder Index (RI).This study was approved by the Ethical Committee of TongjiHospital (TJ-C20150603). All patients were contacted, and consents were obtained from all the participants.

Results: We found that among the whole 34 patients enrolled in this study (median age=51 years, male/female ratio=1.4/1), 65.2% tested patients had a declined HDL level, 82.3% tested patients had an elevated IgG4 level, and lymph node was the most frequently involved organ. 18F-FDG PET/CT had high sensitivity in providing information about the organ distribution of IgG4-RD. The IgG4 level and IgG4-RD RI in the multi-organs affected patients were significantly higher than that in the localized ones. Most patients were prescribed with glucocorticoids (GCs) alone or combined with disease modifying antirheumatic drugs (DMARDs), the majorities responded well, while some relapsed. Patients given rituximab (RTX) obtained good responses.

Table 1. The overall prognosis of 19 patients who were followed up

Prognosis	GCs	GCs + DMARDs	Surgery + GCs	Surgery + DMARDs	Antifungal therapy	MMF	Total, n
Remission, n	5	1	2	0	0	1	9
Recurrence, n	3	4	0	0	0	0	7
Worsen/Persistence, n	0	1	0	1	1	0	3
Total, n	8	6	2	1	1	1	19

Abbreviations: GCs, glucocorticoids; DMARDs, disease-modifying anti-rheumatic drugs; MMF, mycophenolate mofetil.

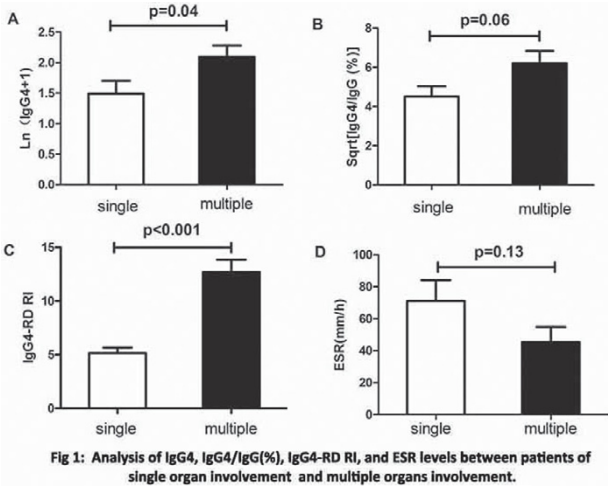


Fig 1: Analysis of IgG4, IgG4/IgG(%), IgG4-RD RI, and ESR levels between patients of single organ involvement and multiple organs involvement.

Conclusions: It was concluded that 18F-FDG PET/CT can be an effective tool to detect involved lesions of IgG4-RD. The addition of DMARDs to the initial GCs therapy in the remission induction stage may not bring much benefit. The most appropriate dosage schedule of RTX needs to be further investigated. Patients with younger age, longer duration of disease, higher IgG4 level and IgG4/IgG ratio may more commonly experience recurrence.

References:

[1] Hamano H, Kawa S, Horiuchi A, et al. High serum IgG4 concentrations in patients with sclerosing pancreatitis. N Engl J Med, 2001,344(10):732–738.
[2] Islam AD, Selmi C, Datta-Mitra A, et al. The changing faces of IgG4-related disease: Clinical manifestations and pathogenesis. Autoimmun Rev, 2015,14(10):914–922.
[3] Martinez-de-Alegria A, Baleato-Gonzalez S, Garcia-Figueiras R, et al. IgG4-related Disease from Head to Toe. Radiographics, 2015,35(7):2007–2025.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3623

FRIDAY, 16 JUNE 2017

Diagnostics and imaging procedures

FRI0623 [18F]FLUORIDE PET-CT IMAGING OF BONE FORMATION IN ANKYLOSING SPONDYLITIS BEFORE AND AFTER 12 WEEKS OF ANTI-TNF TREATMENT

S. Bruijnen[1], N. Verweij[1], L. van Duivenvoorde[1], N. Bravenboer[2], D. Baeten[1], C. van Denderen[1], I. van der Horst-Bruinsma[1], A. Voskuyl[1], P. van de Ven[3], J. Bot[4], B. Boden[4], A. Lammertsma[4], O. Hoekstra[4], P. Raijmakers[4], C. van der Laken[1]. *[1]Rheumatology, Amsterdam Rheumatology and immunology Center; [2]Clinical Chemistry; [3]Epidemiology and Biostatistics; [4]Radiology & Nuclear Medicine, VU University Medical Center, Amsterdam, Netherlands*

Background: Excessive bone formation is an important hallmark of ankylosing spondylitis (AS). Recently, it has been demonstrated that axial bony lesions in AS patients can be visualized using [^{18}F]fluoride PET-CT. This technique may also provide opportunities to monitor changes in bone formation in axial AS lesions during therapy.

Objectives: To assess (1)changes in [^{18}F]fluoride uptake in axial lesions of AS patients before and 12 weeks after treatment with TNF-inhibitors (TNFi) and (2)whether [^{18}F]fluoride uptake on PET is related to focal bone formation in spine biopsies.

Methods: Twelve TNFi naive AS patients (female 7/12; age 39±11years) with high disease activity (BASDAI 5.5±1.1) were included. [^{18}F]fluoride PET-CT scans were performed before initiation of TNFi therapy. In 2 patients, biopsies were obtained from PET identified spine lesions for histologic analysis. Of the remaining 10 patients, a second [^{18}F]fluoride PET-CT scan was performed after 12 weeks of TNFi treatment. PET scans were scored visually for positivity by two blinded expert readers. Subsequently, [^{18}F]fluoride uptake was quantified in PET positive (PET^{+}) lesions using the standardized uptake value corrected for individual integrated whole blood activity concentrations (SUV_{AUC}). Clinical response to TNFi was defined according to ASAS20 at 24 weeks.
Results: At baseline, in all patients at least one axial PET^{+} lesion was found. In spine, 6/10 patients showed 84 lesions (range 2–30;63% thoracic spine, primarily costovertebral joints) and in the SI joints in 9/10 patients were PET^{+} (Fig A). Histological analysis of PET^{+} lesions in the spine confirmed local osteoid formation, which was nearly absent in PET negative lesions. Quantitative PET analysis revealed significantly lower [^{18}F]fluoride uptake in spine lesions at baseline in responders than in non-responders. This difference remained after 12 weeks of treatment (mean difference in SUV_{AUC}: -0.5, 95% CI:[-0.7,-0.2], p=0.001). After 12 weeks of TNFi treatment, [^{18}F]fluoride uptake in clinical responders decreased significantly in the costovertebral (mean difference SUV_{AUC}: -1.0, 95% CI: [-1.3,-0.7]) and SI joints (mean difference in SUV_{AUC}: -1.2, 95% CI: [-2.3,-0.2]) (fig B) in contrast to non-responders (mean difference in SUV_{AUC}: -0.4, 95% CI: [-2.3,1.6] and +0.4, 95% CI: [-0.6, 1.4], respectively). [^{18}F]fluoride uptake in other spinal lesions such as bridging syndesmophytes showed heterogeneous response without a significant decrease in [^{18}F]fluoride accumulation over time at a group level.

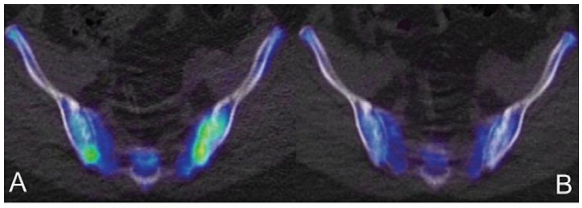


Figure: Example of [^{18}F]fluoride uptake in both SI joints at baseline (A) and a clear decrease of uptake after 12 weeks of TNF-I (B).

Conclusions: [^{18}F]fluoride PET-CT enables non-invasive visualization of (changes in) lesions with bone formation of the whole spine and SI joints in clinically active AS patients, which is confirmed by histological signs of osteoid formation. Part of these lesions, in particular costovertebral lesions in spine and SI joints, decreased in clinical responders to TNFi (and not in non-responders), whereas other spinal lesions remained unchanged at a group level.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2004

FRI0624 STRUCTURAL MRI-BASED CONNECTOMICS IN SLE: A PILOT STUDY

G.A. Ramirez [1,2], E.P. Bozzolo [1], P. Preziosa [3], M.A. Rocca [3], L. Moiola [3], L.A. Coletto [2], E. Tombetti [1,2], P. Rovere-Querini [1,2], M. Filippi [2,3], A.A. Manfredi [1,2]. *[1] Unit of Allergy, Immunology, Rheumatology and Rare Diseases, IRCCS Ospedale San Raffaele; [2] Università Vita-Salute San Raffaele; [3] Institute of Experimental Neurology and Unit of Neurology, IRCCS Ospedale San Raffaele, Milano, Italy*

Background: Neuropsychiatric manifestations are common in patients with systemic lupus erythematosus (SLE). Furthermore, subclinical brain damage occurs in an even higher fraction of patients. However, little is known about the effect of these phenomena on brain connectivity. MRI-based connectomics relies on graph analysis of structural and functional images to detect alterations of the topographic organization of the brain and has been successfully employed to dissect network disassembly in neuroinflammatory diseases such as multiple sclerosis (MS) and Devic's syndrome.
Objectives: To investigate the topographic organization of the brain of patients with SLE with and without neuropsychiatric manifestations.
Methods: Thirty-two patients with SLE (12 with overt neuropsychiatric involvement as per ACR criteria) were enrolled and compared with 32 healthy controls (HC) and 32 patients with relapsing-remitting MS, all matched for sex, age and disease duration (where applicable). Diffusion tensor (DT) and dual-echo MRI scans were obtained. Structural connectivity matrices between 116 cortical and subcortical brain regions were estimated and global and nodal network metrics were calculated.
Results: Conventional MRI revealed that patients with SLE had significantly higher T2-lesional volumes when compared to controls ($p<0.0001$). Patients with definite NPSLE had a higher lesion burden (p=0.006). Network strength, transitivity and global efficiency were all significantly impaired in patients with MS and SLE when compared to HC ($p<0.0001$). MS and SLE were also characterized by higher average path length when compared to HC ($p<0.0001$). Global structural alterations were more significant in MS patients than in patients with SLE (p from 0.005 to 0.01 at multiple comparison). However, antiDNA-positive patients (n=24) showed a more severe phenotype when compared to antiDNA-negative patients (p from 0.026 to 0.041) and did not differ significantly from patients with MS. When regional hubs were analysed, patients with SLE and MS showed a reduced strength compared to HC (p from <0.0001 to 0.001 at multiple comparison). Hub strength impairment was more pronounced in MS when compared to SLE and preferentially involved hubs located in fronto-temporo-parieto-occipital cortices, subcortical nuclei (including the thalamus, caudate nucleus and putamen) and cerebellum (p from 0.001 to 0.05 at multiple comparison). No significant associations were found between global structural parameters, clinical diagnosis of neuropsychiatric SLE, other SLE sub-phenotypes, presence of antiphospholipid antibodies, antiphospholipid syndrome and SLE-related damage burden.
Conclusions: Structural alterations of global and regional brain connectivity occur in patients with SLE, irrespectively of the clinical phenotype. AntiDNA-positive patients are characterized by a more severe phenotype, which is similar to that of patients with relapsing-remitting MS.
References:
[1] Sabbadini MG et al, Lupus, 1999.
[2] Filippi M et al., Lancet Neurol, 2013.
[3] Rocca MA et al., Brain Struct Funct, 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4264

FRI0625 IMPROVEMENT OF JOINT INFLAMMATION AS ASSESSED BY MRI AND POWER DOPPLER ULTRASOUND (PDUS) IN AN OPEN LABEL STUDY IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS TREATED WITH SECUKINUMAB (PSARTROS)

E. Kampylafka, I. D'Oliveira, C. Linz, V. Lerchen, M. Englbrecht, A. Kleyer, J. Rech, G. Schett, A.J. Hueber. *Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nürnberg (FAU) and Universitätsklinikum Erlangen, Ulmenweg 18, 91054 Erlangen, Germany, Erlangen, Germany*

Background: Secukinumab, an anti-interleukin 17A monoclonal antibody, showed significant improvement of signs and symptoms of psoriatic arthritis (PsA) in FUTURE 1 study. Available studies used conventional radiography, not allowing a deeper imaging analysis of the inflammatory changes during application.
Objectives: To assess short term efficacy of secukinumab on inflammation and structural damage according to change in OMERACT-EULAR ultrasound score and the MRI PsAMRIS score in PsA patients.
Methods: PsA patients with active disease (TJC and SJC $\geq$3), were included in the 24 week open label prospective PSARTROS study and treated with subcutaneous secukinumab 300 mg once weekly over 4 weeks, then once every 4 weeks. Baseline 1,5T MRI hand scans and ultrasound imaging of 28 joints were performed at baseline and after 24 weeks of treatment. MRI was scored according to PsAMRIS, ultrasound for synovial hypertrophy and Doppler activity according to OMERACT scores. Statistical significance was set at $p\leq0.05$.
Results: 20 patients, mean age 52±9.9 years, 60% female, mean disease duration 6.7±5.9 years, 50% naïve for biological therapy, were included in the study. Three patients were early discontinued (recurrent pharyngitis, lack of efficacy, withdrawal of consent), and were not included into the longitudinal analysis. Baseline DAS28 was 5.03±0.96, baseline DAPSA was 32.2±12. 1. On baseline MRI, all patients had at least one inflammatory sign (synovitis: 90%, osteitis: 20%, periarticular inflammation: 25%, flexor tenosynovitis: 35%, bone proliferation: 30%, erosions: 60%). Baseline composite PsAMRIS score



A- Baseline coronal T1W fs pos-Gd image shows synovial and periarticular thickness and enhancement (arrow), indicating active synovitis and periarticular inflammation.
B- Follow up image after 24 weeks treatment shows resolution of the periarticular inflammation and only residual synovial enhancement.

was 11.6±12.8 and baseline PsAMRIS synovitis score was 3.7±3.3. Baseline ultrasound synovial hypertrophy and Doppler activity were 6.2±4.5 and 3.5±4.0, respectively. Specific MRI and ultrasound scores were significantly correlated with DAS28 and DAPSA at baseline. Clinical disease activity parameters significantly improved at follow up (DAS28: 2.94±0.95, $p<0.001$; DAPSA: 8.8±5.8, $p<0.001$). PsAMRIS synovitis score (2.5±2.4) as well as composite PsAMRIS score (8.8±10.0) decreased longitudinally with secukinumab treatment (p=0.034 and p=0.039, respectively). There was no progression in erosion or proliferation scores between baseline and follow-up. Synovial hypertrophy and Doppler activity in ultrasound also significantly improved with secukinumab treatment (2.3±3.5; p=0.009 and 1.8±2.7; p=0.003, respectively). A significant percentage of patients reaching minimal disease activity showed residual signs of synovitis in the MRI and US (66% and 50%, respectively).

Conclusions: Secukinumab significantly improves MRI and ultrasound signs of joint inflammation in patients with PsA.

Acknowledgements: This study was supported by an unrestricted grant from Novartis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5094

FRI0626 ANALYSIS OF CORRELATION AND CAUSES FOR DISCREPANCY BETWEEN QUANTITATIVE AND SEMI-QUANTITATIVE DOPPLER SCORES IN SYNOVITIS IN RHEUMATOID ARTHRITIS

H. Rezaei[1], E. af Klint[1], H.B. Hammer[2], L. Terslev[3], M.-A. D'Agostino[4], Y. Kisten[5], L. Arnaud[5]. *[1]Rheumatology department, Institute of Medicine, Karolinska University Hospital, Stockholm, Sweden; [2]Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; [3]Center for Rheumatology and Spine Disease, Rigshospitalet, Copenhagen, Denmark; [4]Rheumatology, APHP, Hôpital Ambroise Paré, Saint-Quentin en Yvelines, Paris, France; [5]Unit of Clinical Therapy Research, Inflammatory Diseases (ClinTRID), Institute of Medicine, Karolinska Institutet, Stockholm, Sweden*

Background: Doppler US is used for the evaluation of synovitis in RA. The amount of Doppler signals are measured in the synovial tissue according to either semi-quantitative (SQS) or quantitative scoring (QS) methods. None of the SQS has been chosen by consensus so far, and this creates some heterogeneity in US in clinical practice and research. Conversely, a major strength of the QS is to allow objective measurement of Doppler pixels using a continuous numeric scale.

Objectives: This study aimed to evaluate the association between $SQS^{1,2}$, and QS^3 in RA patients with active disease. Additionally, to elucidate the reasons for potential discrepancies between SQS and QS assessments, in order to better understand the intrinsic limitations of these methods,

Methods: Adult patients with RA and inadequate clinical response to anti-rheumatic therapy were examined with US. Dorsal US of the wrists, MCP and MTP 2–5 were performed. US images with sign of synovitis were collected and the QS was measured. Five assessors blinded to the QS evaluated the images independently, according to either SQS method. Association between QS and SQS was studied using correlations and multilevel models taking into account the clustering of ratings at the rater, patient and joint levels.

Based on the cut-offs, the discrepant cases were extracted, and each participant was asked to re-grade his/her own discrepant cases, blinded to the initial SQS grading and original QS, and to provide an explanation for the discrepancy. Then, discrepant images and explanations provided were reviewed in consensus and classified into a limited number of categories

Results: Analysis of the 1190 ratings revealed a strong correlation (ρ=0.89, $p<0.0001$) and significant associations ($p<0.0001$) between QS and SQS. Correlations between QS and SQS according to Szkudlarek et al. (ρ=0.87, $p<0.0001$) or Hammer et al. (ρ=0.91, $p<0.0001$) were similar. A total of 239 (20.1%) images were given a SQS grade that did not match that expected based on initial QS, using predefined cutoffs. Main explanations for discrepancies were different perceived ROI (40.7%) and Doppler pixel count near cutoffs between SQS grades (32.3%).

Conclusions: We showed that both SQS methods correlated well with QS to assess synovitis, but SQS methods are intrinsically limited when the Doppler pixel count is close to the cutoffs between the SQS grades. Analysis discrepancies between these methods may help further revision of criteria used to assess disease activity with MSUS in RA.

References:

[1] Szkudlarek M et al. Arthritis Rheum 2003.
[2] Hammer HBet al. Ann Rheum Dis 2011.
[3] Qvistgaard E et al. Ann Rheum Dis 2001.

Acknowledgements: We would like to thank all the participating patients, rheumatologists and nurses who made this study possible.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1149

FRI0627 ULTRASOUND HAND EXAMINATION IS MORE SENSITIVE IN DIAGNOSING HAND OSTEOARTHRITIS THAN CONVENTIONAL RADIOGRAPHY: COMPARISON BETWEEN DIFFERENT ULTRASONOGRAPHIC SCORES

S. Hussain[1,2], P. Sivakumaran[1,2], C. Ciurtin[2]. *[1]University College London Medical School; [2]Department of Rheumatology, University College London Hospitals NHS Foundation Trust, London, United Kingdom*

Background: Hand osteoarthritis (OA) diagnosis is based on a combination of clinical, imaging features and assessment of risk factors, together with clinical associations and outcomes (1). In a real-life context, clinicians face difficulty in differentiating between OA and other hand arthropathies, particularly when the clinical examination is equivocal (e.g. no obvious bony enlargement with the characteristic distribution for hand OA).

Objectives: This is the first study to investigate the usefulness of a standardised ultrasound (US) examination protocol for hand joints in diagnosing hand osteoarthritis (OA) and the correlations between several US scores and clinical, inflammatory and radiographic parameters, aiming to explore which type of investigations are the most useful for diagnosing hand OA.

Methods: We conducted a cross-sectional study including 62 patients, ultimately diagnosed with hand OA based on the ACR diagnosis criteria (2). We compared the 34 joint score of the hand, with smaller, pre-defined joint scores including two scores of 22 and 12 joint each, and another 10 and 6 joint scores for OA. We correlated the US findings with radiographic scores (2108 joints).

Results: Radiographic osteophyte scores correlated very well with the predefined US scores detailed above (R=0.381 to 0.645, $P<0.05$), despite having a low sensitivity for detection of osteophytes (58.6%), and an even lower sensitivity for detection of erosions (38.4%) when compared with the 34 joint US score. There was a good correlation between different US scores (R =0.53 to 0.97, $P<0.05$), apart from the 6 joint score excluding the proximal interphalangeal joints (R= -0181 to 0.207, $P>0.05$).

Conclusions: US examination of the hands can facilitate the diagnosis of hand OA in patients who do not fulfil the ACR criteria, by identifying the presence of osteophytes with the particular distribution and number required for diagnosis in a proportion of patients that was three times higher than that of patients diagnosed based on clinical examination and hand radiography alone.

References:

[1] Zhang W, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW, et al. EULAR evidence-based recommendations for the diagnosis of hand osteoarthritis: report of a task force of ESCISIT. Annals of the rheumatic diseases. 2009 Jan;68(1):8–17. PubMed PMID: 18250111. Epub 2008/02/06. eng.
[2] Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hand. Arthritis and rheumatism. 1990 Nov;33(11):1601–10. PubMed PMID: 2242058. Epub 1990/11/01. eng.

Acknowledgements: S. Hussain and P. Sivakumaran contributed equally to this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2713

FRI0628 ULTRASOUND SHOWS SIGNS OF INFLAMMATION IN MOST PATIENTS WITH RHEUMATOID ARTHRITIS IN LONGSTANDING CLINICAL REMISSION, IRRESPECTIVE OF CONVENTIONAL SYNTHETIC OR BIOLOGIC DMARD THERAPY

U. Møller Døhn, C.H. Brahe, M.L. Hetland, V. Fana, S. Krabbe, M. Ammitzbøll-Danielsen, M. Østergaard, L. Terslev. *Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark*

Background: None of the currently accepted remission criteria in rheumatoid arthritis (RA) incorporate inflammation on imaging. Signs of inflammation on ultrasound (US) and magnetic resonance imaging are frequently seen in RA patients in clinical remission.(1–3) It is not known whether patients in longstanding clinical and radiographic remission obtained through a DAS28 driven treat to target (T2T) strategy by conventional synthetic disease modifying anti-rheumatic drugs (csDMARD) or by biologic (bDMARD) therapy differ with respect to US detected synovitis.

Abstract FRI0626 – Table 1

Cut-offs between grades*	Sensitivity and specificity in the different statistical models							
	Raw data		Model 1		Model 2		Model 3	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Grade 0–1	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Grade 1–2	0.94	0.72	0.99	0.85	0.99	0.82	0.96	0.77
Grade 2–3	0.90	0.84	0.99	0.92	0.99	0.91	0.98	0.92

*Cut-off between grade 0 (G0) and G1: 0%; between G1 and G2: 10%; between G2 and G3: 50%.

Objectives: In RA patients in longstanding clinical and radiographic remission, achieved by a DAS28-driven T2T strategy, to investigate if US signs of inflammation differs between RA patients, treated with csDMARD or bDMARD (+/- csDMARD).
Methods: Eighty-seven patients with RA in longstanding clinical (continuous DAS28<2.6 for the preceding year) and radiographic (no progression for at least 1 year) remission, were included in the study. US of elbows, wrists, MCP2–5, knees, ankles and MTP2–5 were performed using a GE LOGIQE9 US unit. Each joint was scored for grey-scale synovitis (GSS) and synovial color Doppler activity (CDA) by a 0–3 semi-quantitative score. Ultrasound remission was defined in two ways: either no (GSS=0 and CDA=0) or minimal (GSS≤1 and CDA=0) inflammation in any of the 24 assessed joints.
Results: Clinical characteristics and US findings are shown in the table. All 87 patients fulfilled DAS28 remission criteria at entry and CDAI remission was fulfilled in 76% and 79% in the csDMARD and bDMARD group, respectively. Complete absence of any signs of US inflammation (GSS=0 and CDA=0) was seen in 0% and 14% in the csDMARD and bDMARD groups, respectively (p=0.01), while minimal US inflammation (GSS≤1 and CDA=0) was seen in 33% and 40% (NS). CDA in at least one joint was seen in the majority of patients in both groups, 58% and 57% respectively.

Table 1

	csDMARD (n=45)	bDMARD (n=42)	
Females	28 (62%)	28 (67%)	NS
Age (years)	64 (31–82)	57 (25–82)	NS
Disease duration	6 (1–44)	12 (0–54)	p<0.01
IgM-RF/anti-CCP positive	25 (56%)/25 (56%)	28 (67%)/33 (79%)	NS/p<0.05
Erosive disease	23 (51%)	34 (81%)	<0.01
Tender joint count	0 (0–1)	0 (0–1)	NS
Swollen joint count	0 (0–2)	0 (0–2)	NS
C-reactive protein (mg/L)	4 (1–13)	5 (4–26)	p<0.01
DAS28	1.7 (1.1–2.4)	2.0 (1.6–2.5)	p<0.01
CDAI	1.4 (0–5.3)	1.8 (0–7.7)	NS
GSS-score (0–72)	4 (1–18)	6 (0–18)	NS
CDA-score (0–72)	0 (0–12)	0 (0–7)	NS
US minimal inflammation (GSS≤1 & CDA=0)	15 (33%)	17 (40%)	NS
US no inflammation (GSS=0 & CDA=0)	0 (0%)	6 (14%)	p=0.01

Values are given as numbers (percentages) and median (range). Fisher's exact or Mann-Whitney test used for comparisons.

Conclusions: The majority of RA patients, in this cohort of patients in longstanding clinical and radiographic remission obtained through a DAS28 driven T2T strategy, had signs of inflammation as assessed by US, irrespective of receiving biologic treatment or not. For patients in clinical remission, the consequences of sustained US inflammation still have to be investigated.
References:
[1] Brown AK et al.: Arthritis Rheum 2006;54(12):3761–73.
[2] Saleem B et al.: Arthritis Rheum 2009;60(7):1915–22.
[3] Gandjbakhch F et al.: J Rheumatol 2011;38(9):2039–44.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3763

FRI0629 MAGNETIC RESONANCE IMAGING (MRI) INFLAMMATION OF THE FEET DEMONSTRATES SUBCLINICAL INFLAMMATORY DISEASE IN CUTANEOUS PSORIASIS PATIENTS WITHOUT CLINICAL ARTHRITIS

A.J. Mathew[1], P. Bird[2], A. Gupta[3], R.E. George[3], D. Danda[1]. *[1]Clinical Immunology & Rheumatology, Christian Medical College, Vellore, India; [2]University of New South Wales, Sydney, Australia; [3]Dermatology, Christian Medical College, Vellore, India*

Background: Up to 40% of patients with cutaneous psoriasis may develop psoriatic arthritis (PsA). Early detection of PsA by advanced imaging techniques results in better response to therapy. There are very few studies evaluating the MRI appearance in feet of patients with psoriasis and PsA.
Objectives: This study sought to evaluate inflammation at the small joints of feet in a subset of psoriasis patients without clinical arthritis, using an office-based extremity MRI (eMRI) as compared to the findings in overt PsA patients.
Methods: Patients with psoriasis were recruited from Dermatology and Rheumatology clinics of a tertiary care institution in southern India were divided into those without arthritis (PsO) and PsA groups. All consenting patients underwent non-contrast eMRI of the right foot. Demographic and physical examination details were recorded. PsO patients completed the early arthritis in psoriasis (EARP) questionnaire. Two trained readers scored the MRI inflammation (synovitis, tenosynovitis, osteitis) using a modification of the PsAMRI scores (PsAMRIS). [1] Inter-reader agreement was assessed in a random subset of 42 cases using intra-class correlation coefficient (ICC). Proportion of patients with any sign of MRI inflammation was noted. Mann-Whitney U test was used to compare inflammation scores of PsO with PsA patients. Clinical variables were compared with inflammation scores for any association.
Results: A total of 83 patients (30 PsA and 53 PsO) with 75% males and mean age of 42.2±11.6 years were included. ICC for all three variables between the readers was very good (>0.8). There was no statistical difference between the median eMRI inflammatory scores in PsA and PsO patients (p=0.493). Evidence of inflammation was present in 64% and 67% patients in the PsO and PsA groups, respectively (Table 1). Higher NAPSI scores were associated with presence of MRI inflammation (p=0.022).

Table 1. PsAMRIS variables for MRI inflammation of foot in PsO and PsA subgroups

Variable	PsO (n=53)	PsA (n=30)
Synovitis	34 (64%)	19 (63%)
Osteitis	2 (4%)	2 (7%)
Flexor tenosynovitis	9 (17%)	8 (27%)
Inflammation	34 (64%)	20 (67%)

Conclusions: This study corroborates a high proportion of psoriasis patients with subclinical disease of the small joints of foot. Patients with nail involvement had a higher risk of subclinical disease. The cohort is being assessed longitudinally to determine the clinical utility of MRI feet in predicting subsequent development of PsA in patients with psoriasis.
References:
[1] Glinatsi D, Bird P, et al. Validation of the OMERACT psoriatic arthritis magnetic resonance imaging score (PSAMRIS) for the hand and foot in a randomized placebo-controlled trial. J Rheumatol 2015;42:2473–9.
Acknowledgements: This project is being funded by the APLAR and Christian Medical College, Vellore research board.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5705

FRI0630 CAN WHOLE BODY MRI AT BASELINE IDENTIFY DEFINITE INFLAMMATORY ARTHRITIS PATTERNS IN UNDIFFERENTIATED ARTHRITIS?

J.E. Freeston[1,2], K.S. Mankia[1], M.-A. D'Agostino[1,3], R. Hodgson[2], A. Grainger[2,4], I. Matsuura[1], N. Larkman[4], P.G. Conaghan[1], P. Emery[1]. *[1]LIRMM, University of Leeds; [2]NIHR Leeds Musculoskeletal Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; [3]Université Versailles Saint Quentin en Yvelines, APHP Ambroise Paré, Boulogne, France; [4]Radiology, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: When diagnosing inflammatory arthritis (IA) early, focal joint imaging may not reflect the overall inflammatory burden/distribution. Whole body MRI (WBMRI) offers the potential to feasibly scan most joints in a single session.
Objectives: The aims were (i) to describe the WBMRI pattern of disease in early IA (ii) to identify patterns associated with subsequent definite IA.
Methods: Patients were recruited with early inflammatory joint symptoms and/or signs of IA. Clinical data included age, gender, symptom duration, CRP, HLA-B27, RF, CCP Ab and tender/swollen joint counts. Using 3T WBMRI, T2-weighted fat suppressed spine/SIJ images pre contrast and 3D VIBE Dixon images of peripheral joints and entheses post IV contrast were acquired. Images were consensus scored for inflammation/erosion at the spine, SIJ, GHJ, SCJ, wrist, MCP, PIP, hip, knee, ankle, mid/hind foot, MTP and IP joints plus shoulder, ASIS, greater trochanter, knee, Achilles and plantar fascia entheses. Subjects were clinically classified at baseline and 1 year as undifferentiated arthritis (UA), CCP+RA, CCP-RA or Spondyloarthropathy (SpA). Clinicians were unaware of the MRI findings.
Results: 39 patients (23 female) were recruited; mean age 43 years, median symptom duration 18 months (7, 24), TJC 5 (2,11), SJC 1 (0,3) and CRP 2 (2,2). At baseline, 14 were classified as definite disease (RA or SpA) and 25 (14 female) as UA with mean age 40 years, median symptom duration 16.5 months (9.8, 24.3), TJC 3 (1,8), SJC 0 (0,1), CRP 2 (2,2) and 3 (12%) were HLA-B27 positive. The distribution of WBMRI findings in the classified (i.e. definite IA) group was predominantly small joint and tendon-based in the CCP+ RA group, large joint based with 50% having SIJ disease in the CCP- group and similar findings in the SpA group. In the non-classified group (i.e. pUA and rUA), the distribution in pUA was both axial and peripheral, involving joints and entheses, with 25% having SIJ disease. In comparison, findings in the rUA group were similarly distributed but less frequent with no cases of SIJ disease. After 1 year of clinical/laboratory follow-up, 8 were identified as pUA, 6 rUA, 7 CCP+RA, 6 CCP-RA and 12 as SpA. Table 1 shows WBMRI disease distribution by 1 year diagnostic category. The inclusion of affected WBMRI sites in the diagnostic work-up would have appropriately classified 6 further cases of definite SpA, 3 from the pUA and 3 from the CCP-RA groups.

Site of Disease Activity at Baseline on MRI

	Clinical Diagnostic category at 1 year				
	pUA (n=8)	rUA (n=6)	CCP+ RA (n=7)	CCP– RA	SpA (n=12)
Axial	1 (13%)	1 (17%)	0 (0%)	1 (17%)	0 (0%)
SIJ	2 (25%)	0 (0%)	0 (0%)	3 (50%)	4 (33%)
Large Joints	3 (38%)	4 (67%)	4 (57%)	6 (100%)	6 (50%)
Small Joints	6 (75%)	2 (33%)	7 (100%)	5 (83%)	6 (100%)
Tendons	3 (38%)	1 (17%)	5 (71%)	5 (83%)	4 (33%)
Entheses	6 (75%)	3 (50%)	4 (57%)	5 (83%)	8 (67%)

Key: pUA = Persistent UA, rUA = Resolved UA, RA = Rheumatoid arthritis, SpA = Spondyloarthropathy.

Conclusions: In the persistent UA group and CCP-RA group, WBMRI findings at baseline already showed a definite pattern of spinal disease. Therefore the use of WBMRI findings at presentation in addition to clinical assessment would allow clinicians to classify a proportion of patients earlier.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5051

FRI0631 PREDICTIVE VALUE OF POWER DOPPLER ULTRASONOGRAPHY (PDUS) IN THE DIAGNOSIS OF EARLY RHEUMATOID ARTHRITIS

L. Mayordomo[1], C. Jurado[2], M.L. Velloso[1], A. Gutierrez-Leonard[3], P. González-Moreno[4], J.L. Marenco[1], C. Almeida[5]. *[1]Rheumatology Department; [2]Radiology Dp, Hospital Universitario Valme; [3]Physioterapy, HVR; [4]Rheumatology Department, HVM; [5]Research and Statistics Dp, Hospital Universitario Valme, SEVILLA, Spain*

Background: There is a short window of opportunity for early diagnosis and treatment of rheumatoid arthritis, that may be crucial for reaching remission and a low rate of radiographic progression. High resolution power doppler ultrasonography (PDUS) is helpful in early detection of synovitis and allows an accurate classification of patients with joint inflammation.
Objectives: To establish wether the presence of basal power doppler signal in patients with very early arthritis may be helpful in order to establish the risk of final diagnosis of rheumatoid arthritis according ACR criteria 1987 at a year of follow up.
Methods: We studied the presence of ultrasonographic Power Doppler (PD) signal on 28 joints (shoulders, elbows, wrists, MCPs, PIPs, knees) and 44 joints (28 joints and in addition hips, ankles, tarsus, and MTPs), with a mid-range equipment GE L5, in 70 patients with suspected early arthritis The patients were included with at least one of the following inclusion criteria: a) Swelling in 2 or more joints b) pain in MCPs, MTPs and/or the wrists c) morning stiffness of more than 30 minutes with <12 months of duration of the symptoms. Presence or not basal erosions (score ≥2 in at least one joint by modified Sharp method) for each patient were registered (65 patients with basal hands and feet radiology available). Presence of RF and ACPA positive were recorded as well. At one year follow-up was established whether patients met criteria for RA according1987 ACR or not. Statistical study: Chi-square, Fisher exact test, p univariant and Odds Ratio calculation.
Results: The presence of basal power doppler signal in ≥1 joints of 44 (PD44) in baseline visit shows statistically significant association to RA diagnosis at 12 months by ACR 1987 classification criteria, p=0.003, OR=5,43 (1,71–17,24) but the presence of at least one joint with power doppler signal of 28 joints (PD28) did not (p=0.051). Presence hypertrophic synovium with PD44 or not, in at least one joint (HSORPD44) was associated to RA diagnosis as well p=0.024; OR 10,24 (1,12–93,28). RF was positive in 18/70 (25,71%) and was associated to RA diagnosis (p 0.003, OR 8,31 (1,74–39,64), as well as FR/ACPA, positive in 20/70 (28,57%), p=0.001 OR 10 (2,10–47,58). PD44 in addition to positive RF was associated to RA p=0.003, OR 12,93 (1,59–104,94). Presence of basal radiographic erosions (BRE) was associated to RA, p=0.001 OR 7,72 (2,2–26,8). PD44 in addition to BRE was significantly associated to RA p=0.0005, OR 29,33 (3,61–238,37). PD28 in addition to RF or BRE was significantly associated to RA respectively p 0.0005 OR 24,20 (2,98–196.34) and p=0.003 OR 12,93 (1,59–104,94).

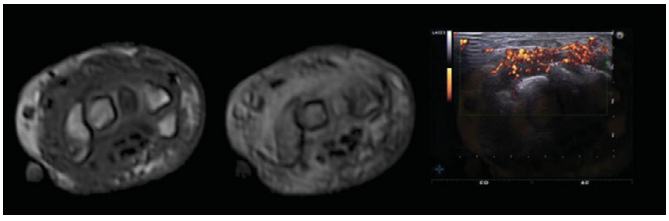
BASAL		RA YES	p (univariate)	OR	CI 95%
PD 44	YES	38/52 (73,1%)	0.003	5,43	(1,71-17,24)
	NO	6/18 (33,3%)			
PD44+FR	YES	15/16 (93,9%)	0.003	12,93	(1,59-104,94)
	NO	29/54 (53,7%)			
PD44+BAS EROS n=65	YES	24/25 (96%)	0.0005	29,33	(3,61-238,37)
	NO	18/40 (45%)			
HSORPD 44	YES	43/64 (67,19%)	0.024	10,24	(1,12-93,28)
	NO	1/6 (16,6%)			
BAS EROS n=65	YES	26/30 (86,7%)	0.001	7,72	(2,2-26,8)
	NO	16/35 (45,7%)			
FR	YES	18/20 (90%)	0.003	8,31	(1,74-39,64)
	NO	26/50 (52%)			
FR/PCC	YES	20/22 (90,9%)	0.001	10	(2,10-47,58)
	NO	24/48 (50%)			

Conclusions: The presence of at least one joint with power doppler signal of 44 joints (PD44) on baseline visit may help to predict the RA diagnosis at 12 months of follow up according to criteria ACR 1987, in patients with early RA. PD 44 in addition to classic RA factors (RF and basal radiographic erosions) increased the risk final of RA, till more than three times in case of concomitant basal PD44 and radiographic erosions.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6282

FRI0632 MRI-US FUSION IMAGES FOR RHEUMATOID ARTHRITIS: CAN DOPPLER SUBSTITUTE FOR GADOLINIUM?

F. Barbieri[1], A. Muda[2], S. Migone[2], V. Prono[2], I. Mussetto[2], N. Romano[2], A. Fischetti[3], V. Tomatis[1], S. Paolino[4], M. Cutolo[4], G. Garlaschi[2], M.A. Cimmino[1]. *[1]Dipartimento di Medicina Interna, Clinica Reumatologica; [2]Sezione di Radiologia; [3]Università di Genova; [4]Clinica Reumatologica, Genova, Italy*

Background: MRI is increasingly used to objectively assess disease activity and damage in patients with rheumatoid arthritis (RA), especially in clinical trials. The preferred scoring method is the RAMRIS, which implies the use of gadolinium, an intravenous contrast agent, to assess synovitis.
Objectives: We evaluated in a small preliminary study if the fusion of MRI and US Power Doppler (PD) images could avoid gadolinium.
Methods: 12 patients (10 women) affected by RA, with at least one involved wrist, were studied. Mean age was 58.8±9.1 years and mean disease duration was 54.5±56.1 months. Disease activity (DAS 28-CRP) was evaluated on the day of the examinations.
MRI was performed on a extremity-dedicated machine (Oscan 0.3 T, Esaote, Genova Italy) and US by MyLab Twice ultrasound scanner with a virtual navigator software (Esaote, Genova, Italy). T3Dt1 sequences were used in the fusion images (parameters: TR/TE/NEX 38/16/1, matrix 192*192*39, FOV 160*160*60, thickness 0.6 mm). US scans were performed sagittally on the radio-lunate joint and axially on the proximal carpal bones of the dorsal wrist with B-mode and PD (PRF 500–750Hz; WF: 3; maximum gain with probe's calibration in air). Magnetic position sensor linked to the US transducer (13 MHz) and low magnetic field transmitters were used to allowed fusion images.
MRI synovitis was scored by the RAMRIS and with the contrast-enhanced dynamic method resulting in rate of early enhancement (REE) and relative enhancement, (RE). The US score was the Global OMERACT-EULAR Synovitis Score (GLOESS) and its individual parts.
Results: Inter-reader agreement for PD by weighted kappa was 0.75 (75%CI 0.53–0.96) for the sagittal and 1 (75%CI 1–1) for the axial view. It was 0.85 (75%CI 0.69–0.98) for MRI synovitis.
There was a correlation between DAS28 and the MRI synovits score (r=0.59, p=0.04), REE (r=0.60, p=0.04), and RE (r=0.58, p=0.05), US Doppler in the long (r=0.75, p=0.005) and in the axial axes (r=0.86, p=0.01), but not with B-mode synovial effusion (r=0.56, p=0.056). The GLOESS correlated with DAS28 (r=0.66, p=0.019), but not with RAMRIS synovitis, erosions or BME nor with REE. The MRI wrist synovitis score did not correlate with the Doppler score on the sagittal and axial views, nor with US B mode score. This was true also for the three individual MRI slices of the wrist, the REE and the RE. The figure shows from the left the pre-contrast axial MRI image, the post-contrast and the fusion images.



Conclusions: Although both MRI and Doppler are good indicators of disease activity in RA, they seem not to be interchangeable. This may be due to the fact that MRI and US show different features of synovitis or, alternatively, that MRI comprised the whole wrist whereas US visualized only its dorsal area. Although our preliminary data do not support the use of fusion images, these should be investigated on larger number of patients with a more extended PD approach.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5433

FRI0633 WHICH ARE THE ULTRASOUND LESIONS UNDERLYING DACTYLITIS?

A. Nzeusseu Toukap[1,2], T. Kirchgesner[3], F. Lecouvet[1,3], P. Navarro[2], B. Vande Berg[1,3], A. Durnez[2], M.S. Stoenoiu[1,2]. *[1]Institut de Recherche Expérimentale et Clinique (IREC), Université catholique de Louvain; [2]Rheumatology department; [3]Radiology department, Cliniques Universitaires Saint-Luc, Brussels, Belgium*

Background: Dactylitis, defined as a diffuse swelling of a digit is a hallmark feature of peripheral spondyloarthritis (SpA), particularly in psoriatic arthritis, with a prevalence between 16% and 48[1].
Objectives: This study aims to assess the frequency of the pathological lesions in dactylitis using ultrasonography (US) and to evaluate their association with patient-reported tenderness.
Methods: Thirty-four dactylitis from 20 consecutive patients suffering from peripheral spondyloarthritis were examined by ultrasound. At US examination, the entire digit was scanned both on dorsal and palmar/plantar sides. The following US pathological lesions were scored: soft tissue thickness, soft tissue edema, soft tissue vascularization, synovitis of metacarpophalangeal (MCP)/metatarsophalangeal (MTP), of proximal interphalangeal (PIP) and of

distal interphalangeal (DIP) joints, inflammatory involvement of both flexor (tenosynovitis) and extensor (paratenonitis) tendons, nail bed vascularization, synovio-entheseal complex at DIP level, enthesitis of flexor tendon, and bone proliferation. Grey-scale (GS) and power-Doppler (PD) synovitis and tenosynovitis were assessed according to OMERACT scores (0–3). Nail bed vascularization was scored 0 to 3. The other US lesions were scored 0 (absent) or 1 (present), both in GS and PD. The standard (HAQ) questionnaire, tender and swollen joint count, patient-reported tenderness, global disease activity scored by physician and by patient were assessed in all patients.

Results: Twelve (60%) patients presented hand and 8 (40%) patients foot dactylitis. Twelve (60%) patients had single dactylitis. Eight patients presented with multiple dactylitis: 4 dactylitis in 1 patient, (5%), 3 dactylitis in 4 patients (20%) patients and 2 dactylitis in 3 (15%) patients. Soft tissue thickening was present in all 34 dactylitis. MCP/MTP joint synovitis was present in 28 digits (82%), PIP joint synovitis in 23 digits (68%) and DIP joint synovitis in 17 digits (50%). Extensor paratenonitis was observed in 21 digits (62%) and flexor tenosynovitis in 20 digits (59%). Enthesitis of extensor tendons was present in 21 digits (62%) and enthesitis of flexor tendon in 5 digits (15%). Osteoproliferation was present in 21 digits (62%). The frequency of synovitis, tenosynovitis and enthesitis did not differ significantly between tender (n=25) and non-tender (n=9) dactylitis. A significant association between tenderness and the presence of power Doppler (χ^2:17.9, $p<0.01$) and of edema in the soft tissue was observed (χ^2:11.5, $p<0.01$).

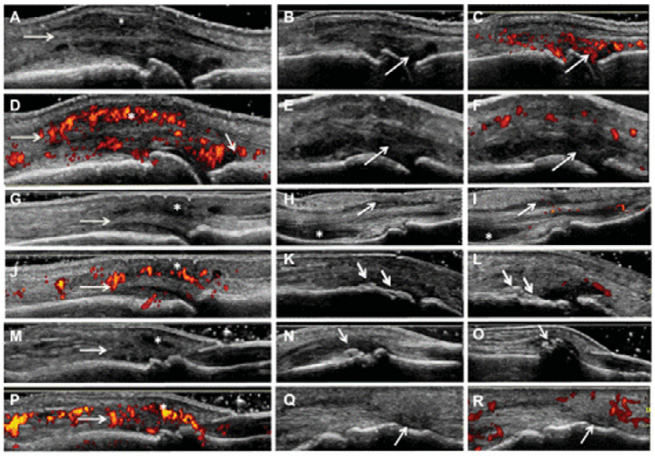


Figure. Ultrasound lesions in dactylitis. Longitudinal scans of digital extensor tendons in GS (A,G,M) and in PD (D, J, P) US showed extensive peritendinous inflammation. Note the tendon thickening (A,G,M), the loss of fibrillar pattern (A,G) and hypoechogenicity (A,M) of the extensor tendon. Digital extensor tendonitis or paratenonitis at the MCP joint (A,D), at the PIP joint (G,J) and at the synovio-entheaseal complex at the DIP joint (M,P) (arrows in panels A,D,G,J,M,P indicate digital extensor tendon and asterisks indicate anechoic or hypoechoic material around the dorsal extensor tendon with PD signals). Longitudinal US scans of MCP and PIP joints in GS (B,E) and PD C,F) mode. PD positive (C) and PD Doppler negative (F) synovitis at the MCP joint (B,C) and at the PIP joint (E,F). Note the pericapsular PD signals in panel F (arrows in panels B,C,E,F indicate synovial hyperthrophy) with (C) or without (F) PD signals. Longitudinal scans of digital flexor tendon (H,I) at the PIP joint. Tenosynovitis of flexor digital tendon is depicted in GS (H) and PD (I) mode. Note the hypoechoic thickened tissue (arrows) with fluid (asterisk) inside the tendon sheath (H) with few synovial and intra-tendinous PD signals (I). Osteoproliferation at the PIP joint (K,L) and at the DIP joint (N,O) depicted in longitudinal scans. Enthesitis of digital flexor tendon is depicted in GS (Q) and PD (R). The latter finding is rare (arrows indicate enthesitis).

Conclusions: Dactylitis is a multi-compartment digit disease, and anatomical lesions are more heterogenous than previously described. A significant amount of joint, tendon and entheseal inflammation persists in non-tender dactylitis. Patient-reported tenderness is associated with the presence of edema and/or power Doppler inside the soft tissue.

References:

[1] Bakewell CJ et al. OMERACT Ultrasound Task Force. Ultrasound and magnetic resonance imaging in the evaluation of psoriatic dactylitis: status and perspectives. J Rheumatol. 2013;40:1951–7.

Acknowledgements: We acknowledge S. Aydin and the OMERACT/EULAR working group for fruitful discussions.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2283

FRI0634 DO ANTHROPOMETRIC FACTORS INFLUENCE MEDIAN NERVE SIZE IN HEALTHY INDIVIDUALS? AN ULTRASOUND AND VOLUMETRY STUDY

A. O'Neill, P. Gardiner, D. McCormick, E. Savage, D. Small. *Rheumatology, Western Health and Social Care Trust, Londonderry, United Kingdom*

Background: Some (but not all) ultrasound studies of median nerve dimensions at the wrist have suggested that anthropometric factors such as height and weight are among the possible sources of variability in the normal population but this has not been systematically studied[1].

Objectives: The purpose of our study was to establish if hand and wrist volume or other standard anthropomorphic factors influenced median nerve size in normal subjects using standard ultrasonographic techniques. If median nerve size is predictably related to anthropomorphic factors, adjusted normal reference ranges would improve the diagnostic precision of the test for carpal tunnel syndrome.

Methods: We studied 30 healthy subjects: 14 females and 16 males. We measured their height, weight, arm span, finger span and wrist circumference. Ultrasonography of the median nerve was carried out at the entrance to the carpal tunnel and at a second level 2 cm proximal to the wrist using an Esaote MyLab Class C ultrasound with a 12–18MHz linear probe. The wrist was marked at the distal wrist crease and 2cm proximally. Hand and wrist volume were measured using water displacement volumetry.

Results: The intra-rater reliability of volumetry measurements was excellent for both hand and wrist volumetry with a Cronbach alpha of 0.99 and 0.88 respectively. The intra-rater reliability for median nerve measurements was excellent with a Cronbach alpha of 0.96. The median nerve dimensions were not significantly different between male and female subjects, nor between the dominant and non-dominant hands. The mean median nerve cross sectional area (CSA) at the distal wrist crease was 10.68 mm^2 and at a point 2cm proximal to this it was 10.18 mm^2. The mean difference in CSA between these two points was 0.5 mm^2. The median nerve CSA was not significantly related to height, weight or hand size. It was not correlated with hand or wrist volume. No significant differences were found in relation to hand dominance or gender.

Spearman's correlation between median nerve CSA (distal, right wrist) and anthropometric factors

	Rho	p
Height	0.063	0.73
Weight	0.290	0.11
BMI	0.094	0.47
Arm Span	0.115	0.38
Finger Span	0.024	0.85
Wrist Circumference	0.095	0.46
Hand Volume	0.102	0.44
Wrist Volume	0.244	0.19

Conclusions: Anthropometric factors including BMI, hand/wrist volume were not found to be closely related to median nerve size in normal individuals.

References:

[1] Cartwright MS et al. Ultrasonographic reference values for assessing the normal median nerve in adults. J Neuroimaging. 2009;19(1):47–51.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3834

FRI0635 DESCRIPTION OF VIDEOCAPILLAROSCOPY OF THE LABIAL MUCOSA IN COMPARISON WITH NAILFOLD VIDEOCAPILLAROSCOPY IN SCLERODERMA

A.M. Beron, S. Sapag duran, H. Laborde, G. Medina, M. Garcia Carrasco, G. Nasswetter, D. Dubinsky. *Rheumatology, Clinical Hospital "Jose de San Martin", University of Buenos Aires., CABA, Argentina*

Background: Capillary bed of labial mucosa may be a potentially useful area for assessing abnormalities on the microcirculation. Videocapilaroscopy of the labial mucosa (LVC) in 12/13 scleroderma (SCL) patients showed capillaries disturbance such as great disorganization and anarchic orientation(1).

Objectives: To describe LVC features in SCL and compare them with healthy controls. (HC). To compare nailfold videocapillaroscopy (NVC) with LVC in HC and SCL patients.

Methods: ≥16 years old patients with SCL (ACR-EULAR 2013) were included consecutively since June to July 2016. Smoking patients were excluded. For the evaluation of the LVC we performed a general displaying and then we studied following areas: a-central (1 cm from the frenulum), b-lateral right and left (both 2 cm from the frenulum) and c-labial border. For evaluation of the NVC, 200x images were obtained from 2nd to 4th fingers both hands and was classified according Cutolo in early, active, late patterns(2). For assesment through LVC: photographs (200x) for each subject were taken. We define quantitative characteristics as means of: capillary diameter, length and density. The average of these parameters was obtained from the evaluation of capillaries included in 1 mm^2 of at least 2 continuous images. In addition, the visibility of the subpapillary venous plexus, architecture, dilatation of capillaries, presence of megacapillaries and avascular areas were qualitatively evaluated (photo 1). Each image was reviewed by two experienced observers. We conducted the same process describe above for each healthy control subject.

Results: Twenty two patients were included (18 female, age 47±11 ys) with SCL (limited 17, diffuse 5); NVC pattern: early 8, active 11, late 3. Healthy subjects 12 (11 female, age: 34±10 years).

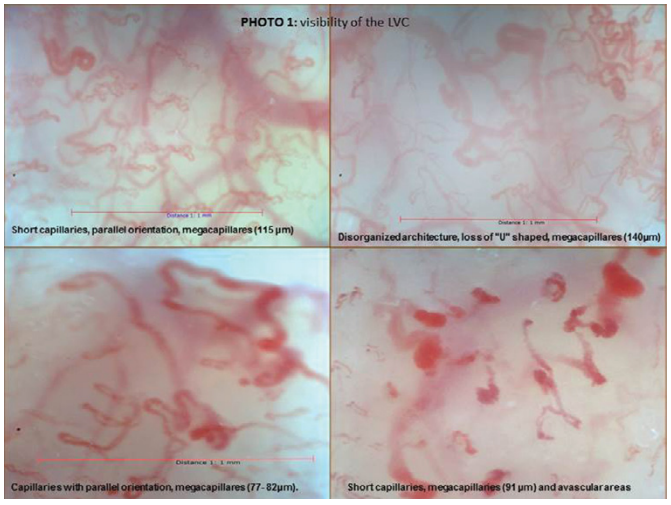
Average capillary density: 17±4.13 (13–26) in SCL vs 21±3.65 (16–28) in HC (p 0.00).

Average capillary diameter: 43±13.54 (17–83) SCL vs 19±1.67 μm (16–21) HC (p 0.02).

Mean capillary length: 185±34 μm (125–248) SCL vs 237±42 μm (178–313) HC (p 0.00).

In 22 SCL patients were observed dilated capillaries in 20 (90%), megacapillaries (≥70 μm) in 10 (45%) and 7 (32%) showed disturbed architecture with lost areas of the normal U-shape and changes in the parallelism of the main axis of the

capillaries. About subpapillary venous plexus in SCL: 7 (32%) were prominent and only one had capillary hemorrhage. In contrast, none of the controls presented these alterations. (p 0.0).
According to the 3 NVC patterns the following averages were observed in the LVC:
Early Pattern (n: 8): diameter 36.93±10.84 μm; Long 191.21±47.58 μm; Density 18.12±5.33 μm.
Active Pattern (n: 11): diameter 48.80±14.80 μm; Length 184.11±29.91 μm; Density 16.72±3.25 μm.
Late Pattern (n: 3): diameter 36.27±10; Long 178.03±28.8 μm, density 19.33±4.16 μm.

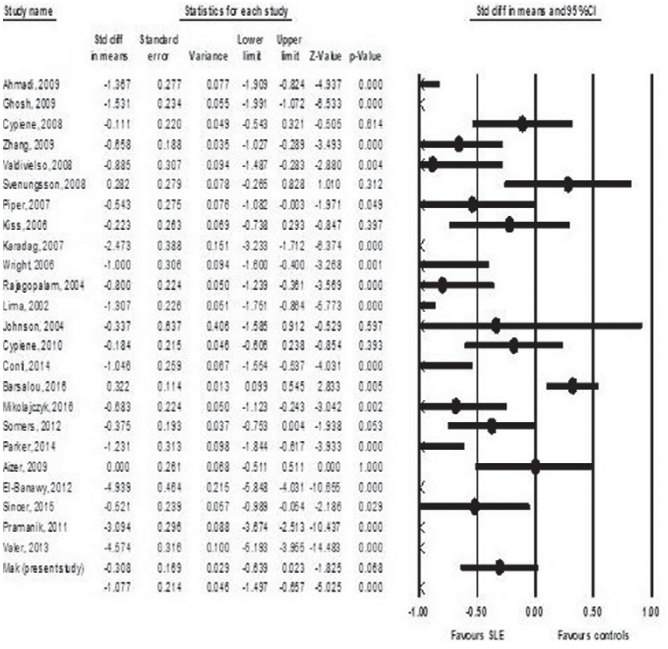


Conclusions: We found that LVC in SCL patients show significant microvascular changes with respect to HC. In addition, all NVC patterns described in SCL showed similar alterations in LVC. Therefore, LVC could be a complementary or alternative method to NVC since it is easily accessible, has good visibility and is not influenced by local mechanical or chemical stimuli that can affect the nail bed.
References:
[1] W Grassi et al. Ann Rheum Dis 1993; 52 (8): 564–569.
[2] M. Cutolo et all. Rheumatology 2006; 45: 43–46.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4329

FRI0636 ENDOTHELIAL DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS – A CASE-CONTROL STUDY AND AN UPDATED META-ANALYSIS AND META-REGRESSION

A. Mak[1], N.Y. Kow[1], H. Schwarz[2], L.L. Gong[3], S.H. Tay[1], L.H. Ling[3]. *[1]Medicine; [2]Physiology; [3]Cardiology, National University of Singapore, Singapore, Singapore*

Background: Endothelium-dependent flow-mediated dilation (ED-FMD), a biophysical marker of endothelial dysfunction, is apparently impaired in patients with systemic lupus erythematosus (SLE). However, such observation is inconsistent because of the lack of standardization of the methodology of ED-FMD measurement and inclusion of patients with different comorbidities amongst different studies.
Objectives: Firstly, we evaluated if ED-FMD is indeed impaired in SLE patients naïve of cardiovascular disease and its traditional risk factors. Secondly, we aimed to determine if the putative contribution of SLE to endothelial dysfunction is in fact confounded by demographic-, disease- and treatment-related factors.
Methods: We assessed and compared the brachial artery ED-FMD (baED-FMD) using the Prosound Alpha-10 ultrasound system® between SLE patients without cardiovascular disease and cardiovascular risk factors and healthy controls (HC) matched for age, gender and body mass index (BMI). Exclusions were pregnancy, a history hypertension, diabetes mellitus, chronic kidney disease, cardiovascular and cerebrovascular diseases, and statin therapy. SLE-related disease activity and organ damage in the SLE patients were assessed using SELENA-SLEDAI and SLICC/ACR DI, respectively. With inclusion of our own data from this case-control study, we performed a comprehensive meta-analysis of case-control studies which compared baED-FMD between SLE patients and HC by determining the effect size of baED-FMD as standard mean difference (SMD). Demographic and clinical factors associated with the effect size were explored by mixed-model meta-regression.
Results: Seventy one SLE patients and 71 HC were studied, and there were 6 men in each group. The mean±SD age and BMI of SLE patients and HC were 39.21±13.4 and 40.37±12.9 years, and 22.54±5.1 and 22.86±4.2 kg/m^2, respectively. In SLE patients, the mean±SD daily prednisolone dose, SELENA-SLEDAI and SLICC/ACR DI were 13.43±14.4mg, 6.52±5.4 and 0.17±0.4, respectively. SLE patients had significantly lower baED-FMD than HC (3.72±2.8% vs 4.63±3.1%, p=0.032). In the SLE group, no association between baED-FMD and age, gender, BMI, blood pressure, duration of SLE, serum C3, C4 and anti-dsDNA levels, SELENA-SLEDAI, SLICC/ACR DI and daily prednisolone dose was found. Similarly, no association was noted between baED-FMD and age, gender and BMI in the HC group. Meta-analysis of 25 case-control studies involving 1,313 SLE patients and 1,012 HC with the random effects model revealed significantly lower baED-FMD in SLE patients compared to HC (SMD -1.077, p<0.001) (see Fig for forest plot). The presence of diabetes mellitus (p=0.04747), higher diastolic blood pressure (p=0.04419) and renal involvement (p=0.02721) were associated with more discrepant baED-FMD between both groups.



Conclusions: SLE patients naïve of cardiovascular disease and its traditional risk factors have impaired endothelial function. While SLE-related disease activity and organ damage are not apparently related to endothelial dysfunction, the presence of diabetes mellitus, renal disease and diastolic hypertension are potential contributors to endothelial dysfunction in SLE patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4350

FRI0637 DIAGNOSTIC PERFORMANCE OF THE NEW OMERACT CRITERIA FOR CPPD IDENTIFICATION BY US: CORRELATION WITH SYNOVIAL FLUID ANALYSIS

A. Adinolfi[1], V. Picerno[1], A. Scanu[2], C. Toscano[1], C.A. Scirè[3], G. Carrara[4], B. Frediani[1], A. Iagnocco[5], N. Damjanov[6], L. Punzi[2], G. Filippou[1]. *[1]University of Siena, Siena; [2]University of Padova, Padova; [3]University of Ferrara, Ferrara; [4]SIR-Epidemiology Unit, Milan; [5]University of Turin, Turin, Italy; [6]University of Belgrade, Belgrade, Serbia*

Background: Ultrasonography (US) has demonstrated to be an accurate tool for the diagnosis of calcium pyrophosphate deposition disease (CPPD) (1). Recently, the OMERACT "US in CPPD" subtask force, has created new definitions for CPPD identification by US, that demonstrated to be reliable at the knee joint, bridging a gap afflicting the old definitions (2). On the other hand, synovial fluid analysis (SFA) is considered to be an accurate and valid method for diagnosing CPPD.
Objectives: The aim of this study wasto evaluate the association between US, using for the first time the new OMERACT US criteria for CPPD, and SFA findings for identifying patients affected by CPPD.
Methods: We enrolled all the consecutive patients, aged more than 60 years old, referred to our outpatient clinic from September 2016 to December 2016, for knee pain and that presented knee effusion of any grade. Patients with suspected chronic inflammatory conditions were excluded.
All the subjects underwent an US exam (EsaoteMyLab 70) of the clinically involved knee, performed by an expert sonographer that applied the new OMERACT criteria for the diagnosis of CPPD at the fibrocartilage (menisci) and hyaline cartilage of the affected knee (2).
Subsequently, a US-guided arthrocentesis was performed, and the synovial fluid was collected and analyzed by a compensated polarized light microscopy (AxioLab A.1 [Zeiss]) by an expert observer in order to assess the presence of CPP crystals. Both observers were blinded to clinical and to each other findings. The Chi-squared test was used to correlate the US and SFA findings.
Results: 49 patients (28 women) were enrolled in the study, with a mean age of 70,29yo (SD±10,93). 28 subjects were affected by CPPD at SFA and 26 patients

were identified as affected by CPPD at US. In 4 patients, the SFA was positive and the US was negative, while in 2 patients the SFA was negative and the US positive. Using the chi-squared test, a very strong association was found between the exams, with a p-value $<$0,0001.

Conclusions: The new OMERACT US criteria for CPPD identification have already demonstrated to be reliable, considering the good to high kappa values yielded in previous multi-observer studies (2). This preliminary study, indicates that the new criteria seem to be also accurate for diagnostic purposes as they strongly correlate with the SFA for the presence of CPPD in knee joints. Further validation studies that will be able to assess the diagnostic accuracy of US are already in the research agenda of the OMERACT group "US in CPPD".

References:

[1] Filippou G, Adinolfi A, Cimmino MA, Scirè CA, Carta S, Lorenzini S, et al. Diagnostic accuracy of ultrasound, conventional radiography and synovial fluid analysis in the diagnosis of calcium pyrophosphate dihydrate crystal deposition disease. ClinExpRheumatol 2016.

[2] Filippou G, Scirè CA, Damjanov N et al. Definition and reliability assessment of elementary ultrasonographic findings in Calcium Pyrophosphate Deposition Disease. Results of an international multi-observer study by the OMERACT "US in CPPD" sub-task force. J Rheumatol, in press.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5164

FRI0638 COMPARISON OF ULTRASOUND AND MRI IN THE DIAGNOSIS OF PROXIMAL AND DISTAL BICEPS TENDON PATHOLOGY

D. Huguet, C. Darrieutort-Laffite, B. Le Goff. *Hopital Hotel Dieu Et Hme, Nantes Cedex 1, France*

Background: Disorders of the long head of the biceps brachii tendon (LHBt) are commonly recognized as a source of shoulder pain. Ultrasound (US) is thought to be of limited value in the diagnosis of partial-thickness tear and non-tear abnormalities of the LHBt because of the difficulty to assess its intra-articular proximal portion. Brasseur recently described that placing the arm in extension/external rotation increased LHBt intra-articular portion visibility.

Objectives: The goal of this study was to determine if the systematic assessment of the intra-articular portion of the tendon, from the rotator interval to its glenoid insertion, with the arm placed in extension/external rotation could increase US sensitivity.

Methods: This was a cross-sectional study. All patients referred for the treatment of a rotator cuff disease (rupture, tendinopathy, calcific deposit) with an available MRI were included. US was performed blinded from the results of the clinical or MRI using a Sonosite Edge with a 6–13 MHz probe. LHBt was studied at different level: in the bicipital groove, at the rotator interval, over the upper pole of the humerus head to its insertion on the superior glenoid tubercule. To increase the visibility of the proximal portion, we placed the arm in extension/external rotation as described by Brasseur [1]. Diagnosis of tendinopathy were tendon enlargement, hypoechogenicity and an increase in the interfibrillar distance. Subluxation or dislocation of the LHBt was defined as a partial or total loss of contact between the tendon and its groove. Tearing of tendon was defined as discontinuity or absence of tendon fibers. Fluid collection was defined as an anechoic ring around the tendon $>$2 mm. Abnormalities of the LBHt on MRI was retrieved from the report. LBHt abnormalities detected on arthroscopy were used as the gold standard.

Results: We included 129 patients, 57 female (44%), and mean age 54 years (33–73). Seventy-five (58%) had a rotator cuff tear and 54 (42%) a tendinopathy. Arthroscopy found LHBt pathological changes in 39% of the case. The summary of the findings obtained with MRI, US (distal and proximal) and arthroscopy are summarised in table 1.

Table 1

LHB	MRI	US distal	US proximal	Arthroscopy
Normal	99	90	111	78
Subluxation	15	6		9
Effusion	12	30		
Tear	3	3	6	6
Flattened			12	2
Thickening				30
Nodular				1
Inflammatory				3

We calculated the sensitivity/specificity of MRI and US (at the proximal and distal level) in the detection of LHBt changes using arthroscopy as gold standard (Table 2).

Table 2

	Sensitivity	Specificity	PPV	PNV
MRI	52%	96%	90%	73%
US proximal	59%	88%	77%	77%
US distal	29%	96%	83%	67%

Conclusions: US has a good specificity but a poor sensitivity in the detection of LHB tendon changes even when a systematic and carreful study of the proximal part of the tendon is undertaken. If detection of distal changes of the tendon in the inter-tubercular groove seems feasible with US, the involvement of the more proximal, intra-articular part of the tendon remains challenging. MRI sensitivity remains also poor. Overall, arthroscopy still remains the gold standard to detect LHB tendon intra-articular pathology.

References:

[1] Brasseur, The biceps tendons: from the top and from the bottom. Journal of ultrasound (2012) 15, 29–38.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4468

FRI0639 COULD BE THE ULTRASOUND STUDY OF PATIENTS WITH TROCHANTERIC PAIN USED TO CHOSE AN SPECIFIC THERAPEUTIC APPROACH?

C.A. Guillen-Astete, M. Teran-Tinedo. *Rheumatology Department, Ramon y Cajal University Hospital, Madrid, Spain*

Background: Previous studies on tendinopathies of the hand (Quervain's tendinitis) and enthesis knee (anserine syndrome) have shown that some sort of ultrasound findings could predict the therapeutic response to specific treatments. Globally, acute inflammatory (power Doppler, synovial effusion) US findings predicts a better response to steroids injection than the chronic US findings (enthesophytosis, bone cortical irregularities).

Objectives: The aim of present study is to determine the probability of therapeutical success of different treatment approaches according to the presence of some specific US findings, in patients with trochanteric pain.

Methods: The image and clinical charts of patients who were assessed due to trochanteric pain between June 2015 and June 2016 in our clinic were reviewed. From those registries, dichotomic data about US findings were collected: Superficial bursitis, deep bursitis, cortical irregularities, enthesophytosis and power Doppler signal. The follow up data were collected from the electronic app or paper control form at day 6 to 9 from the original consultation. Successful treatment was interpreted as at least a reduction of 50% of the basal visual pain scale (rated from 1 to 10). Correlations with US findings were performed using single or composite variables.

Results: One hundred and twenty six registries of patients with trochanteric pain were included. From all of them, 119 belongs to female patients (94.4%). The global US findings were as follows: 43 superficial bursitis, 39 deep bursitis, 47 cortical irregularities, 32 enthesophytosis and 6 power Doppler signal. Thirty seven steroids injection, 64 prescriptions of non steroideal antinflammatory drugs (NSAIDs) and 66 prescriptions of transdermal NSAIDs were performed.

Therapeutic success was achieved in 76.8% of patients who underwent an steroid injection in whom superficial or deep bursitis were identified in the US, and in 79.9% of patients who were treated with transdermal NSAIDs in whom enthesophytosis of cortical irregularities were identified.

By the other hand, patients treated with steroids injections in whom chronic US findings were achieved showed a failure treatment rate of 54.4%. For those in whom any kind of bursitis were identified the failure treatment rate of transdermal NSAIDs was 65.5%. Oral NSAIDs treatments were success in 35% of patients with any kind of bursitis and in 70% of patients with cortical irregularities or enthesophytosis.

Into the composite variables study we find that the treatment with steroid injection in patients with any kind of bursitis with independence of the presence of any chronic US findings had a Relative Risk (RR) of success of 2.66 compared to transdermal NSAID and a RR of 2.26 compared with oral NSAD treatment ($P<0.001$ y $P<0.01$, respectively). The only independent factor that demonstrated a 100% success treatment rate was the presence of power Doppler signal treated using steroid injection.

Conclusions: US findings are useful predictors of therapeutic response in patients with trochanteric pain. In general terms, we found that patients with US acute findings have an increased probability of treatment success when treated with steroid injection while those with US chronic findings have an increased probability of success when treated with NSAIDs (transdermal or systemic).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6556

FRI0640 STRUCTURAL DAMAGE PROGRESSION IN LUPUS ARTHRITIS: A PROSPECTIVE OBSERVATIONAL STUDY

C. Tani [1], A. Delle Sedie [1], D. D'Aniello [2], C. Stagnaro [1], L. Carli [1,3], R. Vagelli [1], F. Balestri [1], S. Accogli [4], D. Caramella [4], M. Mosca [1]. *[1]Rheumatology Unit, University of Pisa; [2]Emergency Department, Azienda Ospedaliero Universitaria Pisana, Pisa; [3]GenOMeC PhD, University of Siena, Siena; [4]Diagnostic and Interventional Radiology, University of Pisa, Pisa, Italy*

Background: Joint involvement is one of the main causes of chronic pain and disability in SLE patients (pts); despite arthritis in SLE is usually considered mild, joint erosions and deformities can be observed with significant impact on patient's quality of life. Imaging techniques are more sensitive than joint count in detecting synovitis and early joint damage.

Objectives: This study was aimed at evaluating the progression of joint damage in SLE and at evaluating predictive factors for damage accrual

Methods: Consecutive SLE pts with active hand-wrists synovitis (detected by joint

count and/or ultrasounds) were enrolled in this 5-years prospective observational study. Clinical assessments as well as joint ultrasound (US) and MRI were performed at baseline and after 5 years. Each patient underwent a non-dominant hand–wrist US examination using a Logiq 9 with a linear probe operating at 14 MHz. Synovitis was defined as the presence of synovial hypertrophy and/or the presence of power Doppler signal (PD). A non-dominant hand–wrist MRI study with a 0.3 T extremity dedicated machine to evaluate the presence of bone erosions (BE) and bone marrow edema (BME) was also performed. Coronal and axial T1-weighted gradient-echo images and coronal STIR images were acquired. The images acquired were scored according to the RAMRIS scoring system for RA by a trained radiologist unaware of the clinical picture and diagnosis.

Results: Fifty-seven pts were enrolled (female 91.2%, mean age 44±12.2 years, mean disease duration 15.9±9 years);43 (75.4%) completed the follow-up, 3 died (5.2%) and 11 (19.4%) were lost to follow-up. At baseline, 7 (12.3%)satisfied criteria for Jaccoud arthropathy (JA) and 7 (12.3%) had a recent onset arthritis (<1 year of duration). 22 pts (28.6%) showed clinical signs of synovitis, 56 (98.2%) presented positive hand-wrists US (synovitis) and in 14 (24.6%) PD signal was also recorded. Six pts (11.76%) already showed erosions at standard X-Ray, while MRI revealed at least one BE in 30 and 54 patients respectively, for a cumulative mean erosive burden of 9.2 erosions (range 1–63). After 5 years of follow-up, 34 pts consented to repeat the assessment; 11 (33%) had JA and 18 (29%) were still presenting clinical signs of synovitis; 28 pts (82.3%) showed synovitis at US with PD in 7 cases (20.5%). The final mean erosive burden resulted 12.3 (range 2–82) with a significant increase from the baseline evaluation (p=0.001). Overall, 16 pts accrued joint damage. Interestingly, erosion progression was observed also in 12 pts with negative joint count but positive US at baseline. The presence of PD at US and BME at baseline was associated with higher erosive burden at follow-up (p=0.03 and p=0.02 respectively)

Conclusions: Arthritis in SLE can be persistent over time and progress to joint damage even in a short tem period despite treatment; normal joint count at physical examination but US findings of synovitis can be associated with erosion progression over time. The presence of PD at US and bone marrow edema at MRI are associated with a more severe damage progression. US and MRI can be a valid help for the clinician to identify patients at higher risk of severe damage to be treated with a more aggressive therapeutic strategy targeting arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6016

FRI0641 WRIST INFLAMMATION AS ASSESSED BY MAGNETIC RESONANCE IMAGING IS ASSOCIATED WITH PATIENT-REPORTED PHYSICAL IMPAIRMENT, GLOBAL DISEASE ACTIVITY AND PAIN IN EARLY RHEUMATOID ARTHRITIS: LONG-TERM RESULTS FROM TWO RANDOMIZED CONTROLLED TRIALS

D. Glinatsi[1], J.F. Baker[2], M.L. Hetland[1,3], K. Hørslev-Petersen[4,5], B.J. Ejbjerg[6], K. Stengaard-Pedersen[7], P. Junker[8], T. Ellingsen[8], H.M. Lindegaard[8], I. Hansen[7], T. Lottenburger[9], J.M. Møller[10], L. Ørnbjerg[1], A. Vestergaard[11], A.G. Jurik[7,12], H.S. Thomsen[3,10], T. Torfing[8], S.M. Bisgaard[1], M.B. Axelsen[1], M. Østergaard[1,3]. *[1]Rigshospitalet, Glostrup, Denmark; [2]Corporal Michael J. Crescenz VA Medical Center, Philadelphia, PA, United States; [3]University of Copenhagen, Copenhagen; [4]King Christian 10th Hospital for Rheumatic Diseases, Gråsten; [5]University of Southern Denmark, Odense; [6]Slagelse Hospital, Slagelse; [7]Aarhus University Hospital, Aarhus; [8]Odense University Hospital, Odense; [9]Vejle Hospital, SLB, Vejle; [10]Copenhagen University Hospital Herlev, Herlev; [11]Hvidovre University Hospital, Hvidovre; [12]Aarhus University, Aarhus, Denmark*

Background: Studies in established rheumatoid arthritis (RA) have shown that radiographic progression is associated with increasing health assessment questionnaire (HAQ) score. However, most studies have failed to demonstrate this association at the early stage of the disease. In addition, little is known about how specific pathologies, e.g. joint inflammation, tenosynovitis and joint damage, contribute to different patient-reported outcomes (PROs).

Objectives: To examine the association between MRI wrist inflammation and damage with PROs in patients with early RA.

Methods: MRIs of the wrist and hand were obtained from 210 early RA patients participating in two investigator-initiated, randomized, controlled studies (CIMESTRA/OPERA), which aimed at achieving inflammatory control by use of conventional and/or biologic drugs combined with intra-articular injection of glucocorticoids. The image-sets were assessed according to the RA MRI scoring system (RAMRIS) for inflammation (synovitis, tenosynovitis, osteitis) and damage (bone erosions, joint space narrowing) at baseline (n=210), 1 (n=206) and 5 (n=113) years follow-up. Data from the two studies were pooled and assessed for associations between MRI features and HAQ, patient global visual analogue scales (VAS-PtGlobal) and VAS pain using Spearman correlation for status and change scores, univariate and multivariable linear regression analyses for change scores and generalized estimating equations for status and change scores. MRI features were further tested for trends against specific hand-related HAQ questions using the Jonckheere trend test.

Results: MRI inflammation, but not damage, showed statistically significant associations with HAQ, VAS-PtGlobal and VAS pain for status and change scores, independently of swollen joint count and level of C-reactive protein. Synovitis and tenosynovitis were the MRI features most consistently associated with PROs, particularly VAS-PtGlobal and VAS pain (Table 1). MRI synovitis and tenosynovitis mean scores increased with the level of difficulty to cut meat and open a milk carton (p<0.01), and similar patterns were seen for other hand-related HAQ items. As an additional analysis, the metacarpophalangeal joints were included in the analyses, but this did not strengthen the associations between MRI pathology and PROs.

Table 1 Univariate and multivariable generalized estimating equations

	Status				Change			
	Univariate		Multivariable		Univariate		Multivariable	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
	HAQ*							
MRI synovitis	0.03 (0.01;0.05)	**0.01**	-0.01 (-0.03;0.01)	0.48	0.08 (0.04;0.12)	**<0.001**	-0.01 (-0.04;0.03)	0.72
MRI tenosynovitis	0.02 (0.00;0.05)	**0.05**	0.02 (0.00;0.03)	**0.04**	0.07 (0.04;0.09)	**<0.001**	0.02 (0.00;0.03)	**0.05**
MRI osteitis	0.01 (0.01;0.02)	**<0.001**	0.01 (0.00;0.02)	**0.01**	0.02 (0.01;0.04)	**0.001**	0.00 (0.00;0.02)	**0.04**
MRI erosion	0.00 (-0.10;0.09)	0.96			0.04 (-0.13;0.21)	0.66		
MRI JSN	0.07 (-0.01;0.15)	0.08			-0.05 (-0.25;0.16)	0.64		
	VAS-PtGlobal*							
MRI synovitis	0.05 (0.01;0.09)	**0.01**	0.00 (-0.04;0.04)	0.89	4.13 (2.55;5.71)	**<0.001**	1.79 (0.34;3.23)	**0.02**
MRI tenosynovitis	0.04 (0.01;0.07)	**0.01**	0.03 (0.00;0.06)	0.06	2.12 (1.14;3.09)	**<0.001**	-0.08 (-1.08;0.92)	0.88
MRI osteitis	0.01 (0.00;0.02)	0.10	0.00 (-0.01;0.01)	0.84	0.90 (0.22;1.58)	**0.01**	0.21 (-0.25;0.66)	0.37
MRI erosion	0.01 (-0.14;0.16)	0.92			-1.55 (-8.80;5.71)	0.68		
MRI JSN	0.09 (-0.07;0.24)	0.27			-2.77 (-10.78;5.24)	0.50		
	VAS pain*							
MRI synovitis	0.05 (0.01;0.08)	**0.01**	0.00 (-0.04;0.04)	0.97	4.84 (3.20;6.08)	**<0.001**	2.20 (0.87;3.53)	**0.001**
MRI tenosynovitis	0.04 (0.01;0.07)	**0.003**	0.03 (0.00;0.06)	**0.02**	2.19 (1.30;3.09)	**<0.001**	-0.02 (-0.91;3.53)	0.96
MRI osteitis	0.01 (0.00;0.02)	0.16			0.89 (0.21;1.57)	**0.01**	0.21 (-0.27;0.68)	0.39
MRI erosion	-0.03 (-0.18;0.12)	0.69			-2.33 (-9.18;4.51)	0.50		
MRI JSN	0.08 (-0.08;0.23)	0.33			-1.24 (-9.09;6.61)	0.76		

Association between magnetic resonance imaging (MRI) parameters and patient-reported outcomes for status scores and change scores. All generalized estimating equations (GEE) were adjusted for age and sex. MRI parameters with a univariate p-value ≤0.10 were included in multivariable GEE analysis where C-reactive protein levels and swollen joint counts were incorporated. *Log-transformed for status scores. Abbreviations: HAQ: Health assessment questionnaire, JSN: Joint space narrowing, VAS: Visual analogue scale, PtGlobal: Patient global.

Conclusions: MRI-assessed inflammation, but not damage, in the early RA wrist is associated with patient-reported physical impairment, global disease activity and pain, and the amount of wrist inflammation influences physical hand function.

Disclosure of Interest: D. Glinatsi: None declared, J. Baker: None declared, M. Hetland Grant/research support from: BMS, AbbVie, Pfizer, UCB-Nordic, MSD, K. Hørslev-Petersen Consultant for: AbbVie and UCB, B. Ejbjerg: None declared, K. Stengaard-Pedersen: None declared, P. Junker: None declared, T. Ellingsen: None declared, H. Lindegaard: None declared, I. Hansen: None declared, T. Lottenburger: None declared, J. Møller: None declared, L. Ørnbjerg: None declared, A. Vestergaard: None declared, A. G. Jurik: None declared, H. Thomsen: None declared, T. Torfing: None declared, S. Bisgaard: None declared, M. Axelsen Grant/research support from: Abbvie, M. Østergaard Grant/research support from: Abbvie, BMS, Janssen and Merck, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, and Wyeth

DOI: 10.1136/annrheumdis-2017-eular.1555

FRI0642 THE POTENTIAL VALUE OF POSITRON EMISSION TOMOGRAPHY (PET)-SCAN IN SYSTEMIC SCLEROSIS FOR THE QUANTITATIVE ASSESSMENT OF INTERSTITIAL LUNG DISEASE

D.M. Peelen[1], B. Zwezerijnen[2], E.J. Nossent[3], L.J. Meijboom[4], O.S. Hoekstra[2], C.J. van der Laken[1], A.E. Voskuyl[1]. *[1]Rheumatology; [2]Nuclear Medicine; [3]Pulmonology; [4]Radiology, VU University Medical Center, Amsterdam, Netherlands*

Background: Interstitial lung disease (ILD) in systemic sclerosis is treated by immunosuppressive drugs (e.g. cyclophosphamide), aimed at reduction of inflammatory response. Differentiation between inflamed and non-inflamed fibrotic tissue might help to develop treatment stratification, with the aim of improving the prognosis of (subgroups of) SSc-ILD patients. ^{18}F-Fluoro-Dexoxyglucose Positron Emission Tomography (^{18}F-FDG PET) scan might be a promising tool to detect inflamed lung areas, as formerly shown in a semi-quantitative setting.[1, 2]

Objectives: This study aims to investigate the potential role of ^{18}F-FDG PET –scan for the quantitative assessment of metabolically active SSc related ILD.

Methods: ^{18}F-FDG PET -scans of 22 patients with systemic auto-immune disease, including 9 with SSc, 9 with systemic lupus erythematosus (SLE) and 4 with primary Sjögren's syndrome (pSS), were retrospectively analyzed. FDG-uptake was quantitatively measured within 2cm-sized Regions of Interest (ROI's) at apical, medial and basal lung levels. A total of 22 ROI's were drawn in each patient. SUVmean values of all ROI's were corrected by the medial SUVmean bloodpool value. Subsequently, the average of 6 posterior basal SUVmean values

was divided by the average of 6 posterior apical SUVmean values (basal/apical ratio). High Resolution Computed tomography (HRCT)-scans and Pulmonary Function Tests (PFT) were examined to confirm the diagnosis of ILD and to specify the pattern of fibrosis.

Results: Mean age of patients was 69.4 (SSc-ILD), 62.5 (SSc without ILD), 38.9 (SLE) and, 49.3 (pSS). In SSc patients, the mean disease duration was 5.0 (SSc-ILD) and 4.4 (SSc without ILD) years. Diffuse cutaneous sclerosis was present in 2 SSc-ILD and 1 SSc without ILD patients, while other SSc patients were diagnosed with limited cutaneous SSc. ILD was present in 5 out of 9 SSc patients as confirmed by HRCT and PFT. ILD was active in 3 out of 5 SSc-ILD patients. Posterior basal/apical SUVmean ratios of SSc-ILD patients were significantly increased compared to SSc patients without ILD (p=0.016), and compared to SLE and pSS patients without ILD (p=0.001 and p=0.016, respectively), which is shown in Figure 1.

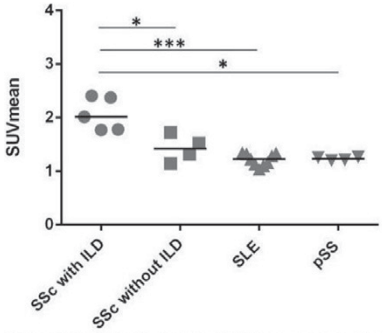


Figure 1: Basal/Apical ratio of SUVmean scores (corrected for bloodpool) in systemic autoimmune patients.
*= p<0.05, ***= p<0.001 (Mann-Whitney test), —— = median

Conclusions: Our findings demonstrate that ^{18}F-FDG PET -scan is potentially useful for the quantitative assessment of active ILD lesions in SSc patients. The technique may therefore provide opportunities to select the patients with inflammatory regions in ILD that are most likely to respond to immunesuppression.

References:

[1] Uehara, T., et al., Deep-inspiration breath-hold 18F-FDG-PET/CT is useful for assessment of connective tissue disease associated interstitial pneumonia. Mod Rheumatol, 2016. 26(1): p. 121–7.
[2] Jacquelin, V., et al., FDG-PET/CT in the prediction of pulmonary function improvement in nonspecific interstitial pneumonia. A Pilot Study. Eur J Radiol, 2016. 85(12): p. 2200–2205.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3677

FRI0643 ENTHESITIS AND FOOT DISABILITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

A. Serce, A. Bal, D. Dulgeroglu, A. Cakci. *Physical Medicine and Rehabilitation, Diskapi YB Education and Resarch Hospital, Ankara, Turkey*

Background: Enthesitis is a primary clinical feature of ankylosing spondylitis (AS). Lower extremity enthesopathy may cause foot pain and functional disability. Detection of enthesitis by using physical examination may be insufficient. Musculoskeletal ultrasonography is a noninvasive and low-cost method for detecting enthesitis readily.

Objectives: The aims of this study were to evaluate enthesitis by using musculoskeletal ultrasonography and foot disability in patients with AS, to compare healthy controls, and to determine the correlation of enthesitis score and foot function with disease activity and functional status.

Methods: In this study, 101 patients with AS and 42 healthy controls were examined for enthesal site abnormalities by using gray-scale ultrasonography. The findings were assessed by using the Glasgow Ultrasound Enthesitis Scoring System (GUESS). The foot function index (FFI), which comprised of pain, disability, and activity limitation subscales, was measured in all the patients with AS and healthy controls for assessment of foot function. Disease activity and functional status were assessed using the Bath AS Disease Activity Index (BASDAI) and Bath AS Functional Index (BASFI), respectively, in patients with AS.

Results: The median GUESS score was 8.00 (1.00–23.00), and, the median total FFI and scores in all the pain, disability, and activity limitation subscales were 14.70 (0.00–75.20), 16.60 (0.00–82.80), 16.10 (0.00–84.40), and 4.00 (0.00–60.00), respectively in patients with AS. The GUESS score, total FFI, and all the subscales scores were significantly higher in the patients with AS than in the controls (p=0.00). GUESS score showed no correlation with BASDAI and BASFI. In patients with AS, total FFI and scores for all subscales showed positive correlations between BASDAI and BASFI, respectively (p=0.00, *r*=0,66; p=0.00, *r*=0,0,50; p=0.00, *r*=0,59; p=0.00, *r*=0,31; p=0.00, *r*=0,60; p=0.00, *r*=0,54; p=0.00, *r*=0.57; p=0.00, *r*=0.50).

Conclusions: The severities of enthesitis and foot disability were higher in patients with AS. Patients with AS may undergo ultrasonographic examination for enthesal foot involvement. Foot disability is related with disease activity and function. Foot involvement and disability should be evaluated comprehensively and managed properly.

References:

[1] Balint PV, Kane D, Wilson H, McInnes IB, Sturrock RD. Ultrasonography of enthesal insertions in the lower limb in spondyloarthropathy. Ann Rheum Dis 202;61:905–910.
[2] Borman P, Koparal S, Babaoğlu S, Bodur H. Ultrasound detection of entheseal insertions in the foot of patients with spondyloarthropathy. Clin Rheumatol 2006;25:373–377.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5112

FRI0644 SUBCLINICAL ULTRASONOGRAPHIC CHANGES OF THE ANTERIOR CHEST WALL JOINTS IN ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS AND THEIR ASSOCIATION WITH CHEST EXPANSION

F.I. Abdelrahman [1], M.A. Mortada [1], A.B. Abdul_Sattar [1], A.A. El Sammak [2]. *[1]Rheumatology and Rehabilitation; [2]Radiology, Zagazig University, Zagazig, Egypt*

Background: Anterior chest wall (ACW) joints can be involved during the course of Rheumatoid arthritis (RA) and ankylosing spondylitis (AS), however, its clinical implications appear to be underestimated by the rheumatology community.

Objectives: To determine the prevelance and types of subclinical ultrasonographic changes in the ACW joints in RA and AS patients and their association with the chest expansion.

Methods: The study was conducted on 132 sternoclavicular joints (SCJ) and 66 manibrusternal joints (MSJ) in 66 subjects (22 AS, 22 RA, and 22 control). Ultrasound (US) assessments were performed to detect synovitis, erosions, ankylosis, osteophytes, or doppler signals. Chest expansion was measured. In RA group, Disease Activity Score (DAS28) and Health Assesment Questionare Disability Index (HAQDI) were recorded. In AS group, Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) were recorded.

Results: US detected subclinical changes of ACW joints in (74.2%) of RA, (77.3%) of AS, and (21.2%) of control groups. There was a highly significant difference between total US changes in RA (74.2%) and control (21.2%) ($p<0.001$) and also between AS (77.3%) and control (21.2%) ($p<0.001$). Non of our control had neither erosions nor ankylosing in MSJ. MSJ ankylosing was signficantly higher in AS (77.3%) than RA (18.2%) ($p<0.001$). MSJ ankylosing was highly associated with limited chest expansion in both RA and AS ($P<0.001$). All patients (100%) in both groups (RA and AS) with MSJ ankylosing by US had limited chest expansion. In RA group, ultrasonographic changes were found to be higher with smoking, longer disease duration and high DAS28. In AS group, ultrasonographic changes were found to be higher with older age, male sex, smoking, longer disease duration and high BASDAI and BASFI.

Table 1. Comparison between RA and AS as regard ultrasonographic changes of anterior chest wall joints

	RA n (%)	AS n (%)	χ^2	p value
SCJ synovitis	34 (77.3)	24 (54.5)	5	**0.02***
SCJ PD activity	14 (31.8)	12 (27.3)	0.2	0.6
SCJ erosion	32 (72.3)	28 (63.6)	0.8	0.4
SCJ osteophyte	4 (4.5)	6 (13.6)	0.4	0.5
MSJ ankylosing	4 (18.2)	14 (63.6)	9.2	**0.002***
MSJ erosion	9 (40.9)	4 (18.2)	2.7	0.09
MSJ osteophyte	1 (0.5)	1 (0. 5)	0	1

*n: number; χ^2: chi-square test; PD: Power Doppler signals.

Conclusions: US detected subclinical changes of ACW joints in a high percentage of RA and AS patients. No erosions or ankylosing in MSJ were Found in the healthy individuals. MSJ ankylosing is more in AS than RA. Relatively, ankylosing of MSJ by US is highly associated with limited chest expansion in RA and AS. Up to the best of our knowledge, our study was the first study that detected subclinical changes of ACW joints in RA and AS by US.

References:

[1] Rodríguez-Henríquez P, Solano C, Peña A, León-Hernández S,Hernández-Díaz C, Gutiérrez M, et al. Sternoclavicular jointinvolvement in rheumatoid arthritis: clinical and ultrasoundfindings of a neglected joint. Arthritis Care Res 2013;65:1177–82.
[2] Frank Verhoeven, Xavier Guillot, Marie Godfrin-Valnet, Clément Prati, et al: Ultrasonographic Evaluation of the Anterior Chest Wall in Spondyloarthritis: A Prospective and Controlled Study; J Rheumatol 2015;42;87–92.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2245

FRI0645 NAILFOLD CAPILLAROSCOPY IN DIABETES MELLITUS TYPE 2

G. Maldonado[1], C. Paredes[2], R. Guerrero[1], C. Ríos[1]. [1]*Universidad Espíritu Santo;* [2]*Universidad Espiritu Santo, Guayaquil, Ecuador*

Background: Diabetes mellitus (DM) is characterized by chronic hyperglycemia states and the development of specific microvascular disorders such as retinopathy and nephropathy. Conventional methods are usually used to study the vascular compromise of this entity, however, the use of capillaroscopy for the evaluation of capillary microarchitecture is not frequently used.
Objectives: The objective of this study was to identify vascular alterations in patients with type II diabetes mellitus and to determine the relationship between capillaroscopic findings and clinical manifestations.
Methods: Observational, descriptive and prospective of patients with diabetes mellitus II selected by inclusion and exclusion criteria. Subjects presenting signs/symptoms or history of any collagen disease, trauma presence in the nailfold due to cosmetic treatment or nail polish, were excluded. The capillaroscopy was performed by an experienced rheumatologist in a room with an ambient temperature of 20–23oC. The fourth and fifth fingers of the nondominant hand were chosen. The capillaries were observed using a 10x magnification capillaroscope (Dino-Lite) and photographs of the last distal row of capillaries were taken. The following capillaroscopic parameters were considered: capillary diameter (ectasia and giant capillaries), crosslinked capillaries, capillary tortuosity, ramified capillaries, avascular zones, hemorrhages, dominant morphology, subpapillar venous plexus visibility, cuticulitis and SD pattern. The images were analyzed by an experienced rheumatologist. Data was analyzed using SPSS. The non-parametric correlations were performed by tau_b Kendall and values were considered statistically significant when $p>0.01$ and they had two tails.
Results: 65 patients were included in the study, with a mean age of 57 years [39–80], of which 75% [49] were women and 25% [16] men. The capillaroscopic findings were evident in 83% of the study population. The most frequent alterations were tortuous capillaries in 63% [41], cross-linked capillary in 59% [38], avascular areas in 48% [34], ectasias in 31% [25]. In smaller frequency, giant capillaries 14% [9], arborified capillaries 11% [7], no haemorrhages, no SD pattern. The capillaroscopic findings representing vascular damage were greater in patients with Diabetes Mellitus than in the control group (Figure 1). Moreover, the capillary morphology in the control group was open versus tortuous in patients with DM. Those patients with capillaroscopic alterations had a longer time of evolution of the disease with an average of 12.8 years, compared to those who did not present alterations that had a mean evolution of the disease of 8.5 years, which shows that those capillaroscopic alterations represent progressive endothelial damage. In addition, an association between the presence of retinopathy and capillary damage at the nail bed level was demonstrated ($p>0.001$).

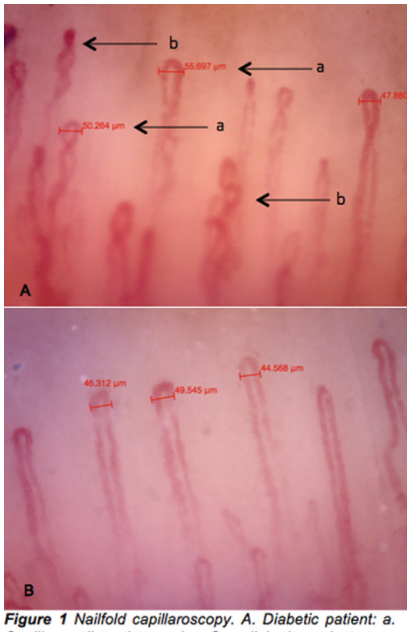


Figure 1 *Nailfold capillaroscopy. A. Diabetic patient: a. Capillary distention b. Crosslinked and tortous capillaries. B. Healthy subject, normal capilaroscopy. Original photos: Génessis Maldonado.*

Conclusions: Capillaroscopy has proven to be a non-invasive, reproducible and reliable technique for the evaluation of vascular microarchitecture within a large group of rheumatic diseases of the scleroderma spectrum. However, it has been shown that it can be used for evaluation other diseases outside the field of Rheumatology such as diabetes, being a tool that should be known by primary care physicians and healthcare workers.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1422

FRI0646 THREE-DIMENSIONAL NAIL IMAGING BY OPTICAL COHERENCE TOMOGRAPHY: A NOVEL BIOMARKER OF RESPONSE TO THERAPY FOR NAIL DISEASE IN PSORIASIS AND PSORIATIC ARTHRITIS

G. Abignano[1,2], P. Laws[3], F. Del Galdo[1,2], H. Marzo-Ortega[1,2], D. McGonagle[1,2]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds;* [2]*NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust;* [3]*Department of Dermatology, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Nail disease is a common feature of psoriasis and psoriatic arthritis (PsA) and can impact quality of life significantly. The assessment of nail disease, unlike skin disease, is challenging with no tissue biomarkers feasible. Commonly used clinical outcomes include the Nail Psoriasis Severity Index (NAPSI) or the modified NAPSI system which are subjective. Optical Coherence Tomography (OCT) can detect changes in psoriatic nails and is a potential tool to assess response to therapy (1).
Objectives: To evaluate OCT imaging changes in cases with nail psoriasis following 6 month-therapy with Apremilast, a PDE4 inhibitor with known efficacy for nail disease in psoriasis and PsA.
Methods: Forty fingernails from four psoriatic patients were imaged at baseline and after 6 month-treatment with Apremilast 30 mg bd using Vivosight OCT scanner (Michelson Diagnostics Ltd., Kent, UK). Three OCT scans were collected from each fingernail (1 transverse and 2 longitudinal – proximal and distal) totalling 240 scans available for analysis. OCT scoring of the forty fingernails, at baseline and six months later, was carried out for changes including: 1. leukonychia/white spots; 2. pitting/localized surface irregularities; 3. diffuse surface waving; 4. onycholysis; 5. subungual hyperkeratosis. OCT score was arbitrarily calculated based on the absence (=0) or presence (=1) of each feature on the three scans of the corresponding fingernail (range 0–15). Macroscopic nail features were scored at baseline and 6 months later using the NAPSI scoring system by a Dermatologist blinded to OCT findings and compared with OCT score. Data were expressed as median (range). Comparison between baseline and follow up measurements was performed using Wilcoxon matched-pairs signed rank test. Difference between two groups and correlation were calculated using Mann-Whitney test and Spearman's test respectively. Statistical analysis was carried out using GraphPad Prism software V.7.0.
Results: Based on NAPSI, twenty-eight/40 fingernails (70%) improved or remained stable after 6 months with the median NAPSI per nail falling from 3.5 (0–7) to 0 (0–6) ($p<0.0001$). The OCT evaluation showed that the entire gamut of nail changes exhibited improvement or stabilization in thirty-three/40 (82.5%) nails after 6 months with median OCT score per nail falling from 8 (3–14) to 4 (1–9) ($p<0.0001$). Difference of the change (Δ) of OCT score between baseline and follow-up significantly correlated with Δ-NAPSI ($r=0.71$, $p<0.0001$).
Conclusions: OCT is able to identify all common psoriasis related nail pathology and changes after treatment. Further studies with larger numbers are needed to validate its potential role as a biomarker for nail disease.
References:
[1] Aydin SZ et al. Dermatology 2013.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4157

FRI0647 COLOR DOPPLER AS A VALUABLE PROCEDURE FOR EARLY DIAGNOSIS OF OCULAR VASCULAR CHANGES IN BEHÇET'S DISEASE

H.H. Al Sherbeni[1], S. Metawie[1], R. Abdel salam[2], H. Azizi[3]. [1]*Rheumatology and Rehabilitation;* [2]*Ophthalmology;* [3]*Radiology, Faculty of Medicine- Cairo University, Cairo, Egypt*

Background: Ocular involvement is a common and serious manifestation of Behçet's disease (BD). It occurs in about 70% of the patients and is associated with a high risk of blindness (Kaçmaz et al., 2008).
Color Doppler is used for imaging retrobulbar vasculature. It measures the peak systolic velocity (PSV) and end diastolic velocity (EDV), from which the resistance index (RI) is calculated in the ophthalmic artery (OA), central retinal artery (CRA), and posterior ciliary artery (PCA) to detect any abnormality in the retrobulbar vessels (Nagaoka, 2006).
Objectives: To determine and compare the orbital Color Doppler haemodynamic parameters of Behçet's patients with those of healthy subjects and to evaluate the OA, CRA, PCA flow velocities and resistance indices (RIs).
Methods: This study included thirty patients suffering from Behçet's disease satisfying at least 3 of the criteria of BD according to the International Study Group for Behçet's disease in 1990. 20 age/sex-matched healthy subjects served as a control group. All patients were subjected to history taking, clinical examination, full ophthalmological examination, routine laboratory investigations and Color Doppler ultrasound (CDU) examination.
Results: The patients' age ranged from 18 to 45 years with a mean of 31.0±7.5. Their disease duration ranged from 0.25 to 20 years with a mean of 5.71±5.84. There were diminished blood flow velocities of the OA, CRA and PCA as the peak systolic velocity (PSV) and end diastolic velocity (EDV) of these arteries were lower than normal while resistance flow indices (RIs) were higher than normal.

Table 1. Results of ocular Doppler ultrasound over right (RT) and left (LT) sided arteries

		RT sided arteries					LT sided arteries			
		Range	Mean	S.D	P-value		Range	Mean	S.D	P-value
OA-PSV	P	6.7–57	27.5	13.5	0.001	P	7.7 - 65	26.37	12.26	0.000
	C	34–40	36.9	2.04		C	32 -43.8	38.73	3.17	
OA-EDV	P	0.0–16.3	6.9	4.06	0.000	P	0.4 -22.4	6.69	4.17	0.002
	C	9–12.3	10.6	1.33		C	7.6 -12.3	10.36	1.52	
OA-RI	P	0.63–1	0.76	0.08	0.020	P	0.62 -0.95	0.75	0.08	0.123
	C	0.67–0.79	0.72	0.72		C	0.67 -0.78	0.73	0.03	
CRA-PSV	P	6.5–37.4	13.2023	6.53	0.288	P	4.3 -37.1	12.61	7.68	0.949
	C	9.4–14.9	11.8467	1.52		C	8.5 -14.9	12.51	1.91	
CRA-EDV	P	1.6–11.8	4.4297	2.13	0.200	P	1.6 -25.8	4.84	4.95	0.466
	C	2.9–14.1	5.5347	3.57		C	2.6 -5.9	4.13	0.913	
CRA-RI	P	0.45–0.79	0.6590	0.07	0.917	P	0.27 -0.80	0.66	0.096	0.883
	C	0.61–0.72	0.6573	0.03		C	0.61 -0.71	0.67	0.037	
PCA-PSV	P	6–45.7	13.82	8.35	0.352	P	6.1 -21.6	13.4	4.22	0.872
	C	9.9–17.3	13.53	2.02		C	10 -15.4	13.5	1.57	
PCA-EDV	P	2.2–11.4	4.96	2.67	0.408	P	1.9 – 7.32	4.7	1.65	0.386
	C	3.5–6.1	5.16	0.99		C	3.2 -6.1	5.04	0.96	
PCA-RI	P	0.49–0.76	0.63	0.06	0.409	P	0.53 -0.68	0.87	1.16	0.435
	C	0.6–0.68	0.63	0.02		C	0.59 -0.69	0.63	0.029	

C = Control, LT = Left, P = Patients, RT = Right, S.D = Standard Deviation.

Conclusions: Behçet's disease patients with ocular involvement have lower CRA, PCA and OA blood flow velocities than healthy control. CDU is helpful in early diagnosis of ocular Behçet's disease activity as it is a widely used, easy-to-perform and accurate method.

References:

[1] Kaçmaz O., Kempen J.H., Newcomb C., Gangaputra S., Daniel E., et al.(2008): The Systemic Immunosuppressive Therapy for Eye Diseases: Cohort Study Group. Am J Ophthalmol; 146(6): 828–836.
[2] Nagaoka T. (2006): Physiological mechanism for the regulation of ocular circulation: Nippon Ganka Gakkai Zasshi. 110 (11): 872–8.
[3] The International Study Group for Behçet's disease (1990): Criteria for diagnosis of Behçet's disease. Lancet; 335:1078–1080.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4113

FRI0648 CONCORDANCE BETWEEN THE TUBERCULIN SKIN TEST AND INTERFERON GAMMA RELEASE ASSAY FOR DIAGNOSING LATENT TUBERCULOSIS INFECTION IN PATIENTS WITH CHRONIC INFLAMMATORY ARTHRITIS

I. Aktas [1], F. Unlu Ozkan [1], T. Nazligul [1], H. Kuzu Okur [2]. *[1]Department of Physical Medicine and Rehabilitation; [2]Department of Chest Disease, Fatih Sultan Mehmet Education and Research Hospital, Istanbul, Turkey*

Background: Biologic therapies have led to a dramatic change in the management of rheumatologic diseases. Although biologic agents provide profound clinical benefits, various adverse events are associated with their use particularly an increased risk of the reactivation of latent tuberculosis. Therefore, screening for latent tuberculosis infection (LTBI) is imperative before initiating biologic agents[1]. Although tuberculin skin test (TST) is the most common test for detecting LTBI, Bacillus Calmette-Gue'rin (BCG) vaccination and non-tuberculosis Mycobacterium infections, can lead to false positive TST results. Interferon-gamma release assay (IGRA) measures the immune response to tuberculosis specific antigens that do not cross react with BCG, and therefore, do not cause false positive reactions in BCG recipients. Its positiveness indicates the presence of tuberculosis infection either latent or active[2].

Objectives: We aimed to prevent the unnecessary anti-tuberculosis prophylaxis in patients whom biologic therapy is planned by evaluating the concordance between the TST and IGRA.

Methods: Patients who have been receiving biologic therapy due to chronic inflammatory arthritis were enrolled in this study. Demographic and clinical data, TST and IGRA results were recorded. The agreement between IGRA and TST results was evaluated by Kappa coefficient.

Results: A total of 35 patients were included; 15 (42.8%) were male and mean age was 43.74±12.72 years. Of the 22 TST positive patients, 13 (37.1%) were IGRA negative. Of the 13 TST negative patients, 3 (8.6%) were IGRA positive. Nine (25.7%) patients were positive for either of the two tests and 10 (28.6%) patients were negative for both tests. There was statistically significant discordance between two tests (p:0.021; $p<0.05$) (Table 1). While positive rate of TST was 62.9%, positive rate of IGRA was 34.3% and Kappa consistency coefficient between two tests was 15.4% (p:0.283; $p>0.05$).

Table 1. Agreement between IGRA and TST results

IGRA	TST		Total	p
	Negative n (%)	Positive n (%)	n (%)	
Negative	10 (28.6)	13 (37.1)	23 (65.7)	**0.021**
Positive	3 (8.6)	9 (25.7)	12 (34.3)	
Total	13 (37.1)	22 (62.9)		

Conclusions: It is very common in rheumatology practice to administer anti-tuberculosis prophylaxis according to the TST. IGRA may reduce the number of patients in whom tuberculostatics are prescribed, especially in BCG recipients in endemic populations, resulting in a benefit of avoiding possible side effects. Furthermore, IGRA is also important for detecting the cases of LTBI that would be missed by TST. Confirmation in larger studies is necessary.

References:

[1] Costantino F, de Carvalho Bittencourt M, Rat AC, et al. Screening for latent tuberculosis infection in patients with chronic inflammatory arthritis: discrepancies between tuberculin skin test and interferon-γ release assay results. J Rheumatol. 2013 Dec;40(12):1986–93.
[2] Ruan Q, Zhang S, Ai J, et al. Screening of latent tuberculosis infection by interferon-γ release assays in rheumatic patients: a systemic review and meta-analysis. Clin Rheumatol. 2016 Feb;35(2):417–25.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5712

FRI0649 STANDARDIZED PROCEDURES FOR ULTRASOUND IMAGING IN PAEDIATRIC RHEUMATOLOGY: PROGRESS OF A EULAR TASK FORCE

I. Janta [1], P. Collado Ramos [2], J. Vojinovic [3], E. Naredo [4], L. Carmona [5]. *[1]Rheumatology, Hospital General Universitario Gregorio Marañón; [2]Rheumatology, Rheum-Pediatric Unit, Hospital Universitario Severo Ochoa, Madrid, Spain; [3]Pediatric Rheumatology, Clinical Center, Faculty of Medicine, University of Nis, Nis, Serbia; [4]Rheumatology, Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz and Autónoma University; [5]Instituto de Salud Musculoesquelética, Madrid, Spain*

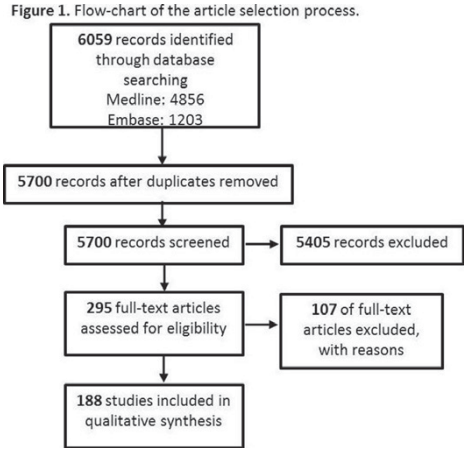
Background: Musculoskeletal ultrasound (MSUS) is a useful imaging technique in paediatric rheumatic diseases (PRD). US has several advantages over other imaging techniques: it is non-invasive, radiation free, rapid, highly accepted by the patients and does not require sedation for scanning in younger children. However, MSUS examination is incriminated to be an operator dependent technique. Moreover, the variability of normal sonoanatomy in children, due to ossification, makes the acquisition and interpretation of MSUS images difficult. The variability in background and experience of ultrasonographers in different countries requires an international multidisciplinary effort for an optimal standardization of MSUS performance in PRD.

Objectives: To perform a systematic literature review on guidelines for MSUS for children published by international societies and articles on how to perform MSUS scanning in children. This represents the first step for an EULAR taskforce, which objective is to develop EULAR Standardized Procedures for Ultrasound Imaging in Pediatric Rheumatology through a consensus process among rheumatologists, paediatric rheumatologists, and radiologists highly experienced in the performance, teaching and research in paediatric MSUS in rheumatologic disease.

Methods: The objective was reformulated according to the PICO-adapted approach, as follows: body parts, ultrasound, and scanning procedures. For each component several synonyms were used. Search limits were applied for animal studies and age. The literature search was performed in Medline and Embase from databases inception to 1st June 2016. References identified were imported into a bibliographic manager and duplicates were removed. To identify eligible studies the remaining articles were assessed by title and abstract. Only articles in English were retained. From the selected studies, data about the examined area, patient position, probe placement, scanning method, landmarks and pathologies using a predefined data collection form.

Results: The literature search resulted in 6059 articles, of which 4856 were captured in Medline and 1203 in Embase. Figure 1 shows the the study flow-chart for article selection. After removing duplicates and scanning titles and abstracts, 295 articles remained for detailed review. After full-text review, 107 articles were excluded. The main reason for article exclusion after full-text review was the lack of standardized examination. Of the remaining articles, 2 described shoulder structures, 14 elbow structures, 5 wrist structures, 9 hand structures, 25 hip

Figure 1. Flow-chart of the article selection process.



structures, 41 knee structures, 14 ankle structures and 2 foot structures. The number of structures described for each joint part was as follows: 3 shoulder, 13 elbow, 2 wrist, 4 hand, 7 hip, 25 knee, 14 ankle, 1 foot.
Conclusions: Several anatomical structures are lacking standardized MSUS examination in children.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5202

FRI0650 NON OMERACT -EXPERT RHEUMATOLOGISTS SONOGRAPHERS AND INTER-ULTRASOUND MACHINE RELIABILITY OF THE OMERACT ULTRASOUND SCORING IN RHEUMATOID ARTHRITIS IN A CLINICAL-BASED SETTING: A BELGIAN STUDY

J.-P. Hauzeur[1], M.-J. Kaiser[2], J. Bentin[3], J.-P. Brasseur[4], B. André[2], P. Carron[5], E. Deflandre[2], C. Naveau[6], C. Ribbens[2], C. Rinkin[2], R. Wittoek[5], M.-A. D'Agostino[7], V. De Maertelaer[8] on behalf of The Belgian Group of Ultrasonography in Rheumatology. *[1]Rheumatology, CHIREC, Braine l'Alleud; [2]Rheumatology, CHU Liège, Liege; [3]Rheumatology, CHU Brugmann, Brussels; [4]Rheumatology, CHU Mont-Godinne, Yvoir; [5]Rheumatology, Ghent University Hospital, Ghent; [6]Rheumatology, GHDC, Charleroi, Belgium; [7]Rheumatology, hôpital Ambroise Paré, Boulogne-Billancourt, France; [8]Biostatistics and Medical Informatics & IRIBHM, School of Medicine, ULB, Brussels, Belgium*

Background: The OMERACT Ultrasound scoring system (USSS) of joint in RA has been shown to be reliable and sensitive to change when used in clinical trial setting. However it is unclear whether this reliability is also achieved in clinical daily practice among Rheumatologists performing US in a non-research setting and using different machines.
Objectives: To assess agreement between non-research sonographers in scoring synovitis using the OMERACT USSS and using the scoring of an OMERACT expert as gold standard. To assess the reliability of the USSS by using different US machines.
Methods: First an OMERACT US expert presented the scoring method and supervised a training session. The wrist, MCP 2 and 3 joints of the left hand (dorsal aspect) of 3 RA patients were then successively evaluated by 9 Rheumatologists with 3 different US machines: Hitachi Arietta = H, GE Logic E9 = G, Esaote MyLab 7= E. The USSS included B-mode acquisition of synovial hypertrophy (SH), joint effusion (JE) and bone erosion (BE), and Power-Doppler (PD) activity. JE, SH and BE were scored binary; SH and PD were score semi quantitatively (0 to 3), by both the 9 participating Rheumatologists and the OMERACT US expert. The agreement between each participant with the scoring of the OMERACT US expert was quantified by proportions. The inter-US machine reproducibility was assessed by kappa statistics for discrete variables and weighted kappa's for ordinate.
Results: The 3 joints of 3 patients each were evaluated on the 4 US items (SH, JF, BE, PD) on a different US machine. So 27 values were obtained for each joint within each item. The percentages of exact agreement (PEA) between these 27 values and the scores of the OMERACT US expert were calculated and ranged between 33% (9/27) for SH-MCP3, 37% for JF-MCP2 and PD-Wrist, 41% for SH-wrist, 48% BE-MCP3, 52% PD-MCP3, 56% PD-MCP3, 59 JF-wrist and BE-MCP2, 63% JF-MCP3, 67% SH-MCP2 and 78% (21/27) for BE-wrist. For the inter-US machines reproducibility, kappa between the 3 machines was calculated on 9 data (3 patients x 3 joints). The reliability was low for detecting JE $\leq$0.211. Acceptable reliability among machines was found for SH, BE and PD (table 1).

Table 1

		H/G	H/E	E/G
Kappa values	JF	0,211	0,143	0,211
	SH	0,529	0,602	0,584
	PD	0,455	0,709	0,434
	BE	0,628	0,615	0,550
Corresponding P-values	JF	0,357	0,588	0,357
	SH	<0,001	<0,001	<0,001
	PD	0,001	<0,001	<0,001
	BE	0,002	0,003	0,004

Conclusions: Non OMERACT-expert Rheumatologists can apply the USSS, and this score works well across different machines. The difference among machines and sonographers is mostly captured by the low reliability of JE. The OMERACT USSS could be used by sonographers in their everyday clinical practice to evaluate the activity of RA patients. Further studies in clinical-based settings will allow to define more precisely the applicability of this scoring system.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5435

FRI0651 OBSERVATIONAL REPRODUCIBILITY STUDY OF UCO-TRACK©, AN AUTOMATIZED MEASUREMENT OF MOBILITY, IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

J. Garrido[1], E. Collantes[2], J. Mulero[3], B. Flores[3], P. Zarco[4], R. Mazzucchelli[4], M. Domínguez-González[4], L. Carmona[5], L. Cea-Calvo[6], M. Arteaga[6], R. Curbelo[5]. *[1]I. Mamónides; [2]H Reina Sofía, Córdoba; [3]H Puerta de Hierro; [4]H Fundación Alcorcón; [5]I. Salud Muscular; [6]Medical Affairs, Merck Sharp & Dohme, Madrid, Spain*

Background: The classical measures of spinal mobility for the assessment of patients with axial spondyloarthritis (SpA), such as BASMI, are subject to inter-observer variability.
Objectives: We assessed the reproducibility of the UCOASMI index (University of Córdoba Ankylosing Spondylitis Metrology Index), a composite index of cervical and spinal mobility obtained with the UCOTrack© motion analysis system (an innovative 3D motion capture system based on video-images) [1], in patients with axial SpA.
Methods: An observational study of repeated measures was carried out in 3 Spanish centers with the technology available (H. Reina Sofía, Córdoba, H. Puerta de Hierro, Madrid and H. Fundación Alcorcón, Madrid). For the assessment of intra-observer reliability, 30 patients (10 per center) were evaluated twice, 3–5 days apart. For the inter-observer reliability, 9 patients were evaluated in the 3 centers by 3 observers (window 3–7 days). The Intraclass Correlation Coefficients (ICC) for UCOASMI and classical metrology measurements were calculated.
Results: We included 30 patients (73% men, mean age 52 [SD 9], mean BASDAI 3.3 [SD 2]). The table shows the intra- and inter-observer reliability values. The reproducibility of UCOASMI was very high, with inter-observer ICC 0.99, and intra-observer ICC 0.97, 0.97 and 0.99, higher than most conventional measurements. The Schober test and cervical rotation showed lower reproducibility (inter-observer ICC between 0.58 and 0.68) and variable intra-observer ICC.
Conclusions: The reproducibility of the UCOASMI, obtained through the UCOTrack© motion analysis system in the 3 centers, was very high, in contrast to the lower reproducibility of the Schobert test and other measures of classical metrology. The reliability of this system opens the door to using this technology to monitor SpA patients and in future research studies.
References:
[1] Garrido-Castro JL, Escudero A, Medina-Carnicer R, et al. Validation of a new objective index to measure spinal mobility: the University of Cordoba Ankylosing Spondylitis Metrology Index (UCOASMI). Rheumatol Int 2014;34:401–6.
Acknowledgements: Funded by MSD, Spain.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3654

FRI0652 MEDIAN NERVE ULTRASOUND FINDINGS AND CLINICAL CORRELATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS: A COMPARATIVE ANALYSIS WITH MATCHED CONTROL SUBJECTS

J. Sousa-Neves[1], M. Cerqueira[1], D. Santos-Faria[1], J. Leite Silva[1], A. Raposo[2], C. Afonso[1], F. Teixeira[1]. *[1]Rheumatology, Hospital Conde de Bertiandos, ULSAM, Ponte de Lima; [2]Rheumatology, Centro Hospitalar Trás-os-Montes e Alto Douro, Vila Real, Portugal*

Background: Median nerve (MN) entrapment in the carpal tunnel seems to be common in patients with Systemic Sclerosis (SSc). Ultrasound (US) evaluation of MN in SSc patients was performed in some previous studies but conclusions were not linear (1).
Objectives: To compare specific MN US parameters of patients with SSc and a group of age and sex matched controls. To understand if specific clinical variables correlate with US parameters assessed in the group of SSc patients.

Abstract FRI0651 – Table 1

	Inter-observer reliability	Intra-observer reliability		
	ICC (95% CI)	Observer 1 ICC (95% CI)	Observer 2 ICC (95% CI)	Observer 3 ICC (95% CI)
UCOASMI	0.99 (0.98–1.00)	0.99 (0.98–1.00)	0.97 (0.94–1.00)	0.97 (0.93–1.00)
Conventional Metrology				
BASMI	0.50 (0.11–0.89)	0.78 (0.54–1.00)	0.61 (0.21–1.00)	0.99 (0.97–1.00)
Right lateral flexion	0.83 (0.64–1.00)	0.94 (0.87–1.00)	0.91 (0.80–1.00)	0.96 (0.91–1.00)
Left lateral flexion	0.88 (0.75–1.00)	0.96 (0.92–1.00)	0.93 (0.85–1.00)	0.97 (0.94–1.00)
Right tragus-wall distance	0.97 (0.95–1.00)	0.96 (0.91–1.00)	0.91 (0.81–1.00)	0.99 (0.98–1.00)
Left tragus-wall distance	0.97 (0.95–1.00)	0.96 (0.91–1.00)	0.90 (0.78–1.00)	0.98 (0.97–1.00)
Schöber test	0.68 (0.39–0.97)	0.64 (0.27–1.00)	0.98 (0.97–1.00)	0.95 (0.89–1.00)
Intermaleolar distance	0.87 (0.73–1.00)	0.93 (0.85–1.00)	0.82 (0.61–1.00)	0.98 (0.97–1.00)
Right cervical rotation	0.65 (0.33–0.96)	0.82 (0.61–1.00)	0.94 (0.87–1.00)	0.98 (0.97–1.00)
Left cervical rotation	0.58 (0.22–0.94)	0.91 (0.81–1.00)	0.75 (0.47–1.00)	0.98 (0.97–1.00)

Methods: We conducted a cross-sectional study comparing MN US parameters of SSc patients followed up at our Rheumatology Unit and control subjects. Exclusion criteria included body mass index (BMI)>30, previous wrist trauma and known diagnosis of carpal tunnel syndrome. Forty-eight out of 62 SSc patients and 45 healthy age and sex matched controls were enrolled. Subjects were consecutively evaluated in our Department. A General Electric LOGIQ S8 US with a 15 MHz linear transducer was used for assessment. MN cross-sectional area (MNA) and perimeter (MNP) of both sides of each person were measured at the level of the carpal tunnel inlet. For comparative analysis, the mean MNA and MNP of combined right and left side were used. Patients' relevant clinical and demographic data were collected. Modified Rodnan skin score (mRSS), hand mobility (HAMIS) and SSc Severity Scale (SScSS) were also assessed. Statistical analysis included Chi-Square test, Mann-Whitney U-test, Kruskal-Wallis and Spearman correlation coefficient. P value <0.05 was defined as statistically significant.

Results: A total of 186 MN were assessed by US. Both groups had the same proportion of diabetes and history of tunnel carpal surgery (p=0.803 and p=0.339, respectively). Median of MNA and MNP were significantly higher in SSc patients (7.5 mm^2 [6.6 to 9.5] and 13.8 mm [12.4 to 15], respectively) (median [interquartile range]) compared with controls (7.0 mm^2 [6 to 8] and 12.9 mm [11.7 to 14], respectively) (p=0.021 and p=0.018, respectively). Higher mRSS correlated with higher MNA (Spearman's rho=0.335, p=0.02) and MNP (rho=0.336, p=0.02). Values of MNA and MNP did not correlate with age, disease duration, HAMIS and SScSS, and were similar according to categories of gender and subset of disease (p>0.05). However, median of MNA and MNP were significantly different between the 3 phases of skin involvement (p=0.007 and p=0.009, respectively), being higher in patients in the oedematous phase (median MNA of 9.25 mm^2 [7.5 to 11.5] and median MNP of 14.5 mm [13.5 to 16.9]).

Conclusions: Our study confirmed an increased MNA and MNP in SSc patients in comparison with healthy age and sex matched controls. Patients in the oedematous phase of skin involvement and patients with higher skin thickness assessed by mRSS showed higher MNA and MNP values.

References:

[1] Bandinelli F et al. Early detection of median nerve syndrome at the carpal tunnel with high-resolution 18 MHz ultrasonography in systemic sclerosis patients. Clin Exp Rheumatol. 2010; 28:15–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4535

FRI0653 SALIVARY GLAND ULTRASOUND IS RELATED TO AUTOIMMUNITY IN PRIMARY SJÖGREN SYNDROME

J.C. Nieto-González[1], F.J. López-Longo[1], E. Estrada[2], E. Naredo[3].
[1]Rheumatology, Hospital G.U. Gregorio Marañón; [2]Psychology, Universidad Camilo José Cela; [3]Rheumatology, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

Background: Primary Sjögren syndrome (pSS) is a systemic autoimmune disease involving exocrine glands, mainly ocular and salivary glands. Salivary gland ultrasound (SGU), of submandibular and parotid glands, in pSS is characterized by hypo/anechoic rounded areas within gland parenchyma, losing the normal homogeneity of the glands (typical SGU)[1]. SGU is a reliable imaging technique for assessing gland echostructure in pSS[2].

Objectives: The aim of our study is to evaluate the relation between typical SGU and clinical and laboratory data in pSS

Methods: We performed SGU to 100 patients with pSS from our rheumatology department selected randomly from a database. We used a semiquantitative score from 0 to 3. Grades 0 and 1 were considered as normal and grades 2 and 3 were considered as typical for pSS. We retrospectively collected demographics (age, gender, disease duration), clinical (extra-glandular manifestations, parotid swelling and lymphoma) and laboratory data (ESR, CRP, rheumatoid factor (RF), antinuclear antibodies (AAN), anti-SSA and anti-SSB antibodies). We divided the patients into 3 groups depending on their autoimmunity profile. Complete seropositive group were patients with RF, AAN and antiSSA or antiSSB positives simultaneously or sequentially. Simple seropositive group were patients with any positive autoantibody (RF/AAN/antiSSA or antiSSB) but not all of them together. Finally, patients without positive autoantibodies were included in the seronegative group

Results: We excluded 7 patients because they were diagnosed with secondary SS. From 93 pSS patients analyzed, 32 (frequency 34.5%) had a typical SGU. Demographics, extra-glandular manifestations and lymphomas were similar between patients with typical SGU and patients with normal SGU. Parotid swelling and longer disease duration were associated with a typical SGU (p<0.05). Patients with positive autoantibodies (AAN, RF, antiSSA and antiSSB) had more frequently a typical SGU. Complete seropositive group had the highest frequency of typical SGU, followed by simple seropositive group. All seronegative patients had a normal SGU. SGU relation with autoimmunity is shown in table 1

	Total	Typical SGU	Normal SGU	*p*
n (%)	*n*=93	*n*=32	*n*=61	
Complete seropositive group	36 (38.7)	25 (78.1)	11 (18.0)	**<0.001**
Simple seropositive group	44 (47.3)	7 (21.9)	37 (60.7)	**<0.001**
Seronegative group	13 (14)	0	13 (21.3)	**<0.001**
AAN + (n:90)	70 (76.9)	31 (96.9)	39 (66.1)	**0.001**
RF + (n:92)	55 (59.1)	28 (87.5)	27 (44.3)	**<0.001**
Anti-Ro + (n:86)	46 (52.9)	27 (84.4)	19 (34.5)	**<0.001**
Anti-La + (n:86)	28 (33.3)	19 (63.3)	9 (16.7)	**<0.001**

Conclusions: Longer disease duration and parotid swelling were associated with typical SGU. Typical SGU was associated with positive autoimmunity, moreover all seronegative patients had a normal SGU

References:

[1] Bialek EJ. US of the major salivary glands: anatomy and spatial relationships, pathologic conditions, and pitfalls. Radiographics 2006.

[2] Damjanov N, Milic V, Nieto-González JC, et al. Multiobserver Reliability of Ultrasound Assessment of Salivary Glands in Patients with Established Primary Sjögren Syndrome. J Rheumatol. 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3571

FRI0654 ULTRASOUND DETECTED PATHOLOGY IN THE ENTHESIS OF THE LOWER LIMB IN AN AGE STRATIFIED COHORT OF ASYMPTOMATIC SUBJECTS -A PROSPECTIVELY DESIGNED DESCRIPTIVE CROSS-SECTIONAL STUDY

J. Guldberg-Møller[1], S.M. Nielsen[1], M.J. Koenig[2], S. Torp-Pedersen[3], L. Terslev[4], A. Torp-Pedersen[1], R. Christensen[1], H. Bliddal[1], K. Ellegaard[1].
[1]The Parker Institute, Frederiksberg; [2]Department of radiology, Herlevand Gentofte Hospital, Gentofte; [3]Department of radiology, Righhospitalet; [4]Rigshospitalet, Glostrup, Denmark

Background: Ultrasound (US) examination of the entheses is increasingly used to document pathological changes in e.g. psoriasis arthritis and spondyloarthritis. Grey-scale (GS) US is used to assess morphological changes and Doppler US to assess increased blood flow.

The OMERACT expert group has agreed on the following elementary components when assessing the entheses on US examination; hypoechogenicity, increased thickness, enthesophytes/ calcifications, erosions, and Doppler activity (1).

Little is known about US assessment of the entheses in asymptomatic persons, thus the frequency and distribution of the above components between genders and age groups is uncertain.

Objectives: To investigate the frequency of enthesitis components in the entheses of the lower limb in a group of healthy subjects.

Methods: We recruited 64 subjects (32 women and 32 men), eight women and eight men in four decades, from 20 to 59 years. None of the subjects had previous or present signs of tendon or joint disease in the lower extremities. None of the participants took any kind of medication.

All subjects were examined by a rheumatologist and blood samples were collected to rule out any clinical signs of tendon or joint disease e.g. swollen and tender

	Age 20-29 (n=8/8)		Age 30-39 (n=8/8)		Age 40-49 (n =8/8)		Age 50-59 (n =8/8)		Total (n=64)
	F	M	F	M	F	M	F	M	
Quadriceps tendon									
Doppler activity		1				1		1	3(5%)
Enthesophyte/ calcifications	1	4	3	2	1	4	2	5	22 (34%)
Increased thickness		1				1			2(3%)
Hypoechogenicity		1				1		1	3(5%)
Patella tendon proximal									0
Doppler activity									
Enthesophyte/ calcifications	1							1	2(3%)
Increased thickness			1				1	1	3(5%)
Hypoechogenicity			1				1	1	3(5%)
Patella tendon distal								1	1(2%)
Doppler activity									
Enthesophyte/ calcifications			1				1	1	3(5%)
Increased thickness			2		1	2	1	3	9(14%)
Hypoechogenicity			1		1	1	1	2	6(9%)
Achilles tendon									0
Doppler activity									
Enthesophyte/ calcifications	3	3	1	6	2	5	2	4	26(41%)
Increased thickness		1		3		1		1	6(9%)
Hypoechogenicity									0
Plantar fascia							1		1(2%)
Enthesophyte/ calcifications									
Increased thickness	1	1		2	1	2	1		8(13%)
Hypoechogenicity	1			1		1			3(5%)

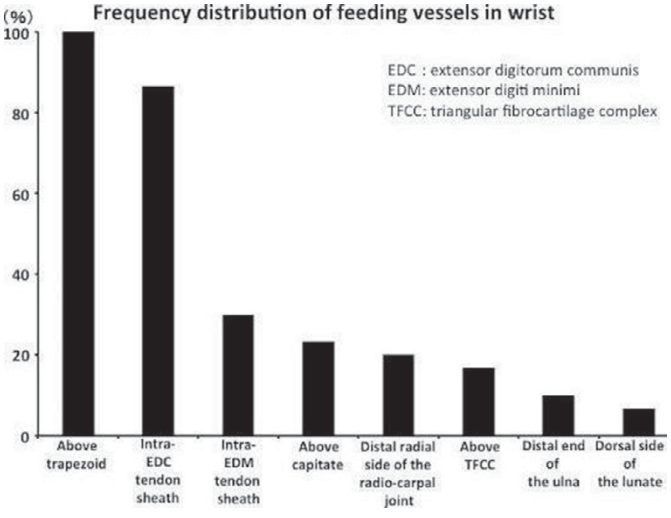
F, female; M, male. All empty fields have the value 0.

entheses or increased inflammatory markers in the blood. The dominant leg was examined with US using a Logiq 9 (GE Medical, Milwaukee, WI, USA) with a ML 6–15 MHz transducer and a fixed pre-set with Doppler settings optimised for inflammatory flow. Both GS and Doppler examination were made.
The entheses were examined for hypoechogenicity, increased thickness, enthesophytes/ calcifications, erosions, and Doppler activity.
Results: No subjects had clinical signs of tendon or joint disease. Seven displayed various degrees of hypermobility and seven had various degrees of flatfoot; some in combination. None of the blood tests indicated any pathology.
On US erosions were only seen in one Achilles insertion (not shown in table). The Doppler activity was not measured in plantar fascia due to attenuation of the heel fad pad. All other US pathology present is seen in the table below.
Conclusions: Only minor pathological findings in the entheses of the lower limb were present in an age stratified cohort of healthy persons. The changes most frequently seen were bony changes in the insertion of the quadriceps and Achilles tendons. A weak tendency toward more pathological findings was seen in this cohort among men, compared to women, and additionally, with increasing age.
The findings suggest that US can be used to diagnose/examine subjects for pathological changes of the entheses although with caution regarding enthesophytes of the quadriceps and Achilles tendon.
References:
[1] Terslev L et al. Defining enthesitis in spondyloarthritis by ultrasound: results of a Delphi process and of a reliability reading exercise. Arthritis Care Res 2014 May;66:741–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3708

FRI0655 ULTRASOUND FINDINGS OF FEEDING VESSELS AND BONE SURFACE IRREGULARITY IN WRIST JOINTS OF HEALTHY CONTROLS

K. Misaki[1], K. Ikeda[2], K. Inoue[1]. *[1]Rheumatology, Kita-Harima Medical Center, Ono; [2]Chiba University, Chiba, Japan*

Background: Musculoskeletal ultrasound (MSKUS) is capable of visualizing synovitis and bone damage such as erosion. In particular, synovial vascularity as measured by power Doppler (PD) is correlated to rheumatoid arthritis disease activity, and PD signal reveals the prevalence of subclinical synovitis overlooked on physical examination. It is frequently difficult to distinguish bone erosion from normal concave surface of the bone. It is necessary for us to know these normal structures well in evaluating disease activity by using MSKUS. Here we examine the normal feeding vessels and bone surface irregularity in wrist joints.
Objectives: To clarify the distribution of feeding vessels in wrist joints and lunate surface irregularity of healthy controls by using MSKUS
Methods: The dorsal side of the bilateral wrists was scanned in 2 perpendicular planes with 2D-probe in healthy volunteers. The distribution and bilaterality of feeding vessels in the capsule and the extensor tendon sheath of wrist joint, and the evaluation of bone surface irregularity at lunate were validated.
Results: The distribution and bilaterality (Blt) of feeding vessels in healthy volunteers (n=30) were as follows:
Above-trapezoid (Rt:100.0%, Lt:100.0%, Blt:100.0%), intra-extensor digitorum tendon sheath (Rt:86.7%, Lt:66.7%, Blt:43.3%), intra-extensor digiti minimi tendon sheath (Rt:30.0%, Lt:30.0%, Blt:10.0%), above-capitate (Rt:23.3%, Lt:30.0%, Blt:10.0%), above-triangular fibrocartilage complex (Rt:16.7%, Lt:30.0%, Blt:6.7%), distal radial side of the radio-carpal joint (Rt:20.0%, Lt:23.3%, Blt:0.0%), distal end of the ulna (Rt:10.0%, Lt:16.7%, Blt:0.0%), dorsal side of the lunate (Rt:6.7%, Lt:0.0%, Blt:0.0%), palmar side of the extensor digitorum tendon sheath (Rt:0.0%, Lt:3.3%, Blt:0.0%). Feeding vessels from vascular channels were depicted at lunate (Rt:53.3%, Lt:46.7%, Blt:43.3%), the distal side of the radius (Rt:20.0%, Lt:16.7%, Blt:3.3%), triquetrum (Rt:10.0%, Lt:16.7%, Blt:0.0%) and capitate (Rt:6.7%, Lt:10.0%, Blt:0.0%). The frequency of the bone surface irregularity at lunate in healthy volunteers (n=47) and the transverse diameter (TD) (Mean±S.D.) of those were Rt longitudinal plane:57.4% (TD1.26±0.33mm), Rt transverse plane: 51.1% (TD1.20±0.31mm), Lt longitudinal plane: 68.1% (TD1.06±0.28mm), and Lt transverse plane: 42.6% (TD1.29±0.31mm). Bilateral evaluation of those was 53.2%.

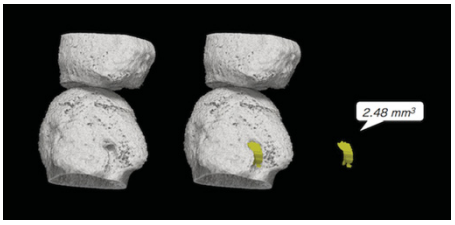


Conclusions: MSKUS evaluation in wrist joints revealed various normal vessels and bone surface irregularity of lunate. It is necessary to distinguish a normal pattern from a pathological pattern in MSKUS examination.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3745

FRI0656 SEMIAUTOMATIC ANALYSIS OF EROSION VOLUME BY HR-PQCT IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Chiba[1], N. Iwamoto[2], M. Osaki[1], A. Kawakami[2]. *[1]Department of Orthopedic Surgery; [2]Department of Rheumatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan*

Background: HR-pQCT is a high resolution CT dedicated to human extremities. It has been used mainly for osteoporosis, while in more recent years it has been applied to research in rheumatoid arthritis (RA).
Objectives: The purpose of this study is to develop a method to quantify the volume of erosions in RA patients semiautomatically using second generation HR-pQCT.
Methods: Twenty patients with RA (70±8 years, 15 female, 5 male) participated in this study. The second and third MCP joints were scanned using HR-pQCT (XtremeCT II, Scanco Medical, Switzerland) at the voxel size of 61μm.
The erosion volume was measured semiautomatically using the dedicated software (TRI/3D-BON, Ratoc System Engineering, Tokyo).
All concave regions on the bone surface around the MCP joints were extracted automatically by subtracting the bone region from the smoothed bone model. Erosions were selected manually by a medical doctor based on certain criteria. The volume of the erosions were measured by voxel counting.
Results: In a total of 37 joints (3 joints were excluded due to severe deformities), 40 erosions were detected by HR-pQCT (phalanx side: 9 erosions, metacarpal side: 31 erosions). The average volume of the erosions was 1.84mm^3, minimum 0.08mm^3, and maximum 16.3mm^3.



Conclusions: The semiautomatic method to quantify the volume of erosions at MCP joints in RA patients by HR-pQCT was developed.
The opinion as to whether concave regions are pathological erosion or physiological concave, vascular channel or recess of osteophyte is occasionally difficult and should be performed by an experienced tester.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4144

FRI0657 COMPARATIVE STUDY OF PAROTID ULTRASONOGRAPHY AND PAROTID GLAND ECT IN PREDICTING THE PATHOLOGICAL BIOPSY OF THE SALIVARY GLAND IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

C. Xiaomei, L. Cong, W. Lijun, L. Cainan, S. Yamei. *Department of Rheumatology and Immunology, People's Hospital of Xinjiang Uyghur Autonomous Region, urumqi, China*

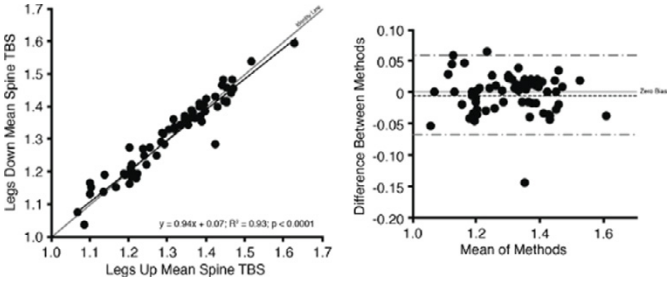
Objectives: To investigate the value of Parotid Ultrasonography and parotid gland radionuclide imaging in predicting salivary gland biopsy of primary Sjögren's syndrome (pSS).
Methods: Sixty - five patients with primary Sjogren 's syndrome and 38 patients with non - Sjogren' s syndrome were enrolled in the Department of Rheumatology and Immunology, Xinjiang Uygur Autonomous Region People 's Hospital from October, 2015 to June, 2016. All patients were accpted the check of Parotid Ultrasonography, Parotid Gland ECT and labial gland biopsy. The data were analyzed statistically.
Results: The sensitivity and specificity of Parotid Ultrasonography in pSS were 65% and 76%, respectively. The area under the ROC curve was 0.936±0.024 for the diagnosis of pSS. The positive predictive rate of parotid gland ultrasonography was 84.0% and the negative predictive rate was 94.4%. Parotid scintigraphy in pSS in the sensitivity of 80.0%, specificity of 69.1%. The positive predictive rate of parotid gland radionuclide imaging for labial gland biopsy was 78.9% and the negative predictive rate was 87.5%. The diagnostic value of Parotid

Ultrasonography in pSS group is superior to that of parotid gland radionuclide imaging, which can effectively reduce the complication of invasive operation.
Conclusions: The diagnosis of pSS by parotid gland ultrasonography is superior to that of parotid gland radionuclide examination. For patients with atypical clinical manifestations who are negative for anti-SSA and/or anti-SSB antibodies, there is no need for a labial biopsy of the labial glands to reduce the number of complications associated with unwanted invasive procedures.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6257

FRI0658 LEG ELEVATION DOES NOT SUBSTANTIALLY AFFECT TBS RESULTS

D. Krueger[1], E. Siglinsky[1], D. Tran[2], L. Del Rio[3], N. Binkley[1]. *[1]Osteoporosis Clinical Research Program, University of Wisconsin, Madison, United States; [2]R&D, Medimaps, Merignac, France; [3]CETIR Grupo Médico, Barcelona, Spain*

Background: Lumbar spine dual energy X-ray absorptiometry (DXA) scans are typically acquired with the patient's legs elevated on a positioning block thereby flattening the normal lumbar lordosis. With GE densitometers it is also possible to acquire lumbar spine scans with the legs down. BMD values obtained with legs down vs. legs elevated does minimally differ, however it is unknown if leg elevation affects trabecular bone score (TBS) results.
Objectives: The purpose of this study is to assess the effect of leg position on TBS.
Methods: Lumbar spine (L1-L4) DXA scans were acquired in legs up and legs down positioning using GE Healthcare Prodigy and iDXA densitometers. The "OneScan" feature mode was not used. These scans were analyzed with enCORE software v 12.3 or 14.1. All scans were re-processed using Medimaps TBS Calculator v2.3 or TBS iNsight v3.0.2 to obtain TBS results. Linear regression and Bland-Altman analyses were performed to compare TBS results in the legs up vs. legs down position.
Results: Sixty-four women, mean age and BMI 65.1 years (range 28.2–86.6) and 26.4 kg/m^2 (range 18.1–34.8) were studied on three Prodigy densitometers. Fifty women, mean age and BMI 68.6 years (range 15.2–92.5) and 26.2 kg/m^2 (range 19.9–35.1) were studied on a iDXA densitometer. With Prodigy and standard legs up positioning, the L1-L4 BMD ranged from 0.738–1.549 g/cm^2 and was highly correlated with legs down positioning, R^2 =0.99. TBS results ranged from 1.072–1.632 and were also highly correlated, R^2 =0.93 with a mean bias of -0.005 TBS units between leg positions (Figure). With iDXA and standard legs up positioning, the L1-L4 BMD ranged from 0.753–1.622 g/cm^2 and was highly correlated with legs down positioning, R^2 =0.97. TBS results ranged from 1.040–1.455 and were also highly correlated, R^2 =0.90 with a mean bias of 0.00 TBS units between leg positions (data not shown).



Conclusions: Leg positioning minimally affects TBS results with GE Healthcare Prodigy and iDXA densitometers but the difference from legs up to legs down is likely of no clinical significance.
Disclosure of Interest: D. Krueger: None declared, E. Siglinsky: None declared, D. Tran Employee of: Medimaps, L. Del Rio: None declared, N. Binkley: None declared
DOI: 10.1136/annrheumdis-2017-eular.3120

FRI0659 INCLUSION OF THE ASSESSMENT OF CERVICAL FACET JOINTS IN THE M-SASSS SCORE IN PATIENTS WITH ANKYLOSING SPONDYLITIS. IMPROVING SENSITIVITY TO CHANGE

M.J. Moreno-Martínez[1], M.J. Moreno-Ramos[2], L.F. Linares-Ferrando[3]. *[1]Rheumatology, H. Rafael Mendez; [2]H. Virgen de la Arrixaca, MURCIA, Spain; [3]Rheumatology, H. Virgen de la Arrixaca, MURCIA, Spain*

Background: Ankylosing Spondylitis is characterized by axial involvement, especially of sacroiliacs and the vertebral bodies, although we also know that other such as facet joints (Fj) are affected. These joints can be seen with a simple x-ray, especially in the cervical spine. Despite their involvement, the different rates of radiographic progression do not assess their alteration.
Objectives: To evaluate the sensitivity to the change of the m-SASSS radiographic score by including the assessment of the cervical Fj.
Methods: The patients come from a Spondyloarthritis Unit (Hospital U. Virgen de la Arrixaca de Murcia, Spain). All patients are diagnosed of Ankylosing Spondylitis (New York Modified Criteria)
The usual radiographic study was performed to calculate the m-SASSS and a lateral cervical radiograph at two different times to calculate the difference between the scores. The score used for Fj (only one score is given for each intervertebral segment) is:
– 0: normal.
– 1: pinching (narrowing of joint space).
– 2: sclerosis in the joint margins.
– 3: joint fusion.
We will analyze the mean of the two m-SASSS radiographic score, with (m-SASSS + Fj) and without the inclusion of the Fj, and the difference between those means. We will also analyze the correlation with the rest of the radiographic scores and with the clinical patient's parameters.
Results: We included 47 patients (81% male and 19% female) with a mean age of 48 (± 8) years and a mean duration of symptoms of 18 (± 8.5) years. The mean time between the two radiographic studies was 3 (± 1.5) years.
In the following table we show the difference of means of the radiographic scores over time:

	First mean (standard deviation)	Last mean (standard deviation)	Significance (p)
Radiographic evaluation of FJ	6±5,2	8,8±6,8	0,0001
m-SASSS	9,3±11,6	10,1±11,7	0,1
m-SASSS+Fj	15,4±13,4	19,3±13,5	0,0001

After comparing Δ mSASSS with Δ mSASSS+Fj, we found significant differences in favor of inclusion: 2.6 (± 2) vs 4.9 (± 4.7), p=0.04.
Conclusions: The inclusion of the evaluation of cervical Fj improves sensitivity to change of m-SASSS.
References:
[1] Averns HL, Oxtoby J, Taylor HG, Jones PW, Dziedzic K, Dawes PT. Radiological outcome in ankylosing spondylitis: use of the Stoke Ankylosing Spondylitis Spine Score (SASSS). Rheumatology.1996;35(4):373–376.
[2] Bleil J, Maier R, Hempfing A, Schlichting U, Appel H, Sieper J, et al. Histomorphologic and Histomorphometric Characteristics of Zygapophyseal Joint Remodeling in Ankylosing Spondylitis: Histomorphometric Characteristics of the Joints of AS Patients. Arthritis Rheumatol.2014;66(7):1745–1754.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5136

FRI0660 IMPACT OF ULTRASOUND IN TREATMENT DECISION OF RHEUMATOID ARTHRITIS

M. Gutierrez[1], C. Pineda[1], R. Espinosa[2], C. Hernandez[1], L. Ventura[1], C. Lozada[1], L.H. Silveira[3], G. Rodriguez[2], E. Cruz[2], A. Vargas[3], C. Bertolazzi[2], A.C. Lozada[1]. *[1]Division of Musculoskeletal and Rheumatic Disorders; [2]Instituto Nacional de Rehabilitacion; [3]Instituto Nacional de Cardiologia, Mexico City, Mexico*

Background: Ultrasound (US) is an important tool to support the clinician in the diagnosis and treatment monitoring of rheumatoid arthritis (RA). The EULAR recommended it for the follow up of RA patients. In spite of the evidence supporting the value of US, the real impact in treatment decisions is not clearly defined.
Objectives: To investigate the impact of US findings in the treatment decisions of rheumatologists in patients with RA in a real-life setting. Additionally, to verify the US findings that play a role in change of treatment, types of changes and their distribution.
Methods: RA patients were included. As a first step, the rheumatologist performed a clinical examination (including DAS28) and recorded the treatment approach suggested according his clinical evaluation (i.e. starting, changing or stopping pharmacological medication as well as local injection). In the same day, after the clinical assessment, the patients were sent for an US examination using the 7-joint score, which was performed by an independent rheumatologist sonographer who reported the US findings to the same rheumatologist that previously evaluated clinically the patient. This last decided, according to the US findings to maintain or change the previous suggested therapy. Additionally, the clinical rheumatologist reported the reasons which induced to change or not the treatment after the US examination
Results: A total of 128 RA patients were included [female 117 (91.4%), male 11 (8.59%)], with mean ± SD disease duration of 9.88±8.22 years. Ninety-four patients (73.4%) had active disease according the DAS 28, whereas 34 (26.5%) were considered in remission.
US findings influenced a change in the treatment in 56 cases (43.7%) (47 with clinical active disease and 9 in remission). Among the main reasons that induced a change in the treatment based on the US examinations were: grade of synovitis (25%), higher number of synovitis than clinical examination (16.6%) and presence of power Doppler (PD) (16.7%). The most frequent treatment changes were increasing dose or start a new combination of DMARDs [39 patients (69.5%)]. The multiple logistic regression analysis showed that synovitis of 2nd metacarpophalangeal joint (MCPj) was the US finding with more influence in the decision to change treatment (p=0.016).

With respect to distribution, 122 patients (95.3%) had al least one joint with US synovitis and 76 patients (59.3%) had at least one joint with PD. The wrist, 2nd MCPj and 2nd metatarsophalangeal joint (MTPj) were the most affected in terms of synovitis whereas the 5th MTPj showed more erosions (37.7%) and the extensor fingers tendons showed more tenosynovitis (23.02%).
Conclusions: US demonstrated to play an important role in the treatment decision of RA patients. The impact was more frequent in patients with active disease but also affected the decision in patients considered in clinical remission.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6689

FRI0661 CAPILLAROSCOPY IN PATIENTS WITH SILICA EXPOSURE. A CASE CONTROL STUDY

M. Freire[1], A. Perez-Gonzalez[1], V. Arnalich[2], D. Boveda-Ruiz[1], A. Salgado[3], J.J. Blanco-Perez[2]. *[1]Unidad de Enfermedades Autoinmunes Sistémicas y Trombosis; [2]Servicio de Neumología, Complejo Hospitalario Universitario de Vigo; [3]Unidad de apoyo a la investigación, Instituto de Investigación Biomedica de Ourense-Pontevedra-Vigo, Vigo, Spain*

Background: Exposure to silica dust has been associated with different autoimmune diseases and immunological abnormalities in which microvascular involvement is very common, as systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis or dermatomyositis.
Objectives: To show capillaroscopic findings in patients exposed and not exposed to silica and to analyze the differences between both groups.
Methods: A case control design was made. Cases (Si+) were subjects exposed to silica (with and without silicosis). Controls (Si-) were healthy subjects not exposed to silica. Capillaroscopy was made with both Zuzi® Optical stereo microscope with Optikam® camera adapted and with USB Digital Microscope Video epiluminiscence Dino-Lite ® in each patient. The capillaroscopic alterations were evaluated according to a semiquantitative method. Background data on CVRF and variables related to capillaroscopy were collected. A comparative study was done.
Results: Capillaroscopy was performed on 61 Si+ and 12 Si- subjects. Mean age of Si+ was 52.6 years (SD: 7.3) and 54 years (SD: 6.6) in Si-. There were no significant differences in CVRF: hypertension (13.1% Si+ and 8.3% Si-), diabetes mellitus (3.3% Si+ and 8.3% Si-) and tobacco exposure (18.0% Si+ and 25.0% Si-). It was observed capillary dilation in 24 (33.9%) Si+ and only in 3 (25.0%) Si-. The dilation score was mild in all Si- while in Si+ was mild in 41.7%, moderate in 37.5% and extreme in 12.5%. 42.7% of Si + had a degree of tortuosity higher than 33% (score 2) whereas in all Si- the degree of tortuosity was <33% (score 1). Capillaroscopic general pattern showed differences between both groups: it was normal in 24 (42.1%) Si+ and 9 (75%) Si-; slightly irregular in 30 (52.6%) Si+ and 3 (25%) Si- and unstructured in 3 Si+ (5.3%) and in none Si-.
Conclusions: The current study shows significant differences between the capillaroscopy of subjects exposed and not exposed to silica, with a trend in more frequency and severity of capillary dilatation, greater frequency of tortuosity in a severe degree and more frequent irregular capillaroscopic pattern in the exposed patients.
References:
[1] Blanc PD, Järvholm B, Torén K. Prospective risk of rheumatologic disease associated with occupational exposure in a cohort of male construction workers. Am J Med 2015;128(10):1094–101.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4132

FRI0662 ASSESSMENT OF BONE DENSITY, STRUCTURE, AND CORTICAL INTERRUPTIONS OF FINGER JOINTS IN PATIENTS WITH RHEUMATOID ARTHRITIS USING HIGH-RESOLUTION PERIPHERAL QUANTITATIVE CT

M. Peters[1], A. Scharmga[1], A. van Tubergen[1], D. Loeffen[1], R. Weijers[1], B. van Rietbergen[1,2], P. Geusens[1], J. van den Bergh[1]. *[1]MUMC, Maastricht; [2]TU/e, Eindhoven, Netherlands*

Background: Rheumatoid arthritis (RA) is characterized by peri-articular bone loss. In patients with RA, lower bone density and structural integrity, and an increased number of erosions compared to healthy controls (HCs) has been demonstrated using High-Resolution peripheral Quantitative CT (HR-pQCT) (1,2). To further characterize RA-related changes, we recently introduced a method for quantifying small cortical interruptions in finger joints (3).
Objectives: To investigate the cortical and trabecular bone density, structure, and cortical interruptions in MCP joints in early and late RA patients compared to HCs using HR-pQCT imaging.
Methods: The 2nd and 3rd MCP joint of 70 subjects (mean age 53.1 (SD 9.2) years) were evaluated by HR-pQCT (82μm isotropic voxel size): 38 HCs, 10 early RA (diagnosis ≤2 years ago) and 22 late RA (diagnosis ≥10 years ago). Images were analyzed for cortical interruptions, and for cortical and trabecular bone density and structure. Descriptives were analyzed per joint by one-way ANOVA with Bonferroni post-hoc testing or Kruskal-Wallis with Mann-Whitney post-hoc testing, as appropriate.
Results: Significant differences with respect to all parameters were found across the groups (Table 1). In early and late RA, the percentage of joints with at least 1 interruption was higher, and number of trabeculae, cortical thickness, total density and cortical density were lower than in HC. In addition, in late RA, number of interruptions, interruption volume and trabecular separation were higher, and trabecular density was lower than in HC. Bone loss at the cortical and trabecular bone was primarily observed at the rim of the joint (Figure 1, arrows).

Table 1. Comparison of cortical interruptions, and bone density and structure parameters across early RA patients, late RA patients and HCs

	HC	Early RA	Late RA	p-value
Cortical interruption parameters	n=82	n=39	n=73	
Percentage of joints ≥1 interruption, %	69.5	89.7 *	82.2	0.025
Number of interruptions	1.50 (1.49)	2.64 (2.95)	5.22* (6.32)	<0.001
Interruption volume, mm^3	1.49 (5.16)	2.05 (6.76)	39.31* (78.51)	<0.001
Bone density parameters	n=50	n=31	n=68	
Total vBMD, mg HA/cm^3	327.3 (35.3)	295.8* (38.9)	286.4* (65.1)	<0.001
Trabecular vBMD, mg HA/cm^3	202.1 (20.6)	185.0 (21.6)	177.3* (42.0)	<0.001
Cortical vBMD, mg HA/cm^3	685.8 (42.8)	643.7* (58.2)	634.0* (73.3)	<0.001
Bone structure parameters	n=50	n=31	n=68	
Trabecular number, mm^1	1.68 (0.31)	1.45* (0.29)	1.52* (0.37)	0.004
Trabecular thickness, μm	102.3 (15.3)	109.1 (17.8)	98.6 (14.7)	0.009
Trabecular separation, μm	513.9 (116.9)	608.4 (132.3)	611.4* (220.6)	0.007
Distribution of trabecular separation, μm	550.6 (287.0)	728.5 (306.1)	689.4 (368.8)	0.029
Cortical thickness, μm	440.0 (99.2)	363.2* (90.2)	357.5* (132.8)	<0.001

Values are displayed as mean (SD) or otherwise described. *Significantly different from HC, $p<0.05$. [1]p-value obtained across the groups. vBMD, volumetric bone mineral density.

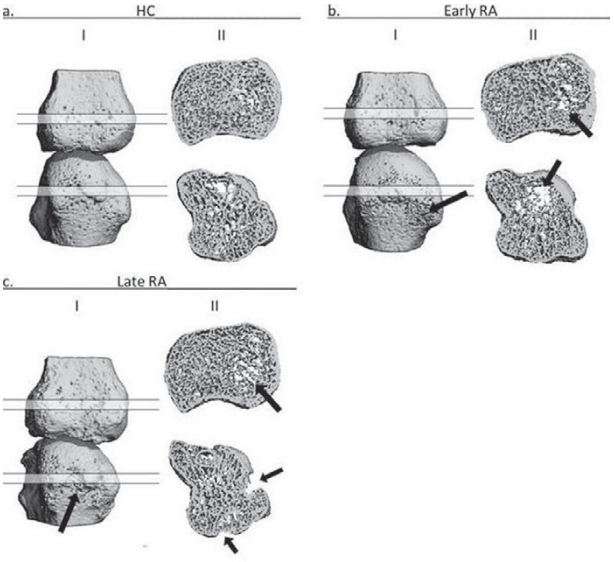


Figure 1. Typical examples of MCP joints; (a) HC, (b) early RA patient, and (c) late RA patient. The total 3D reconstructions are shown (I.) with corresponding 20slices thick axial slices (II). The arrows indicate locations of loss of trabecular and/or cortical structure in the early and late RA patients compared to the HC.

Conclusions: Bone density and structural integrity were impaired in early and late RA patients compared to HCs whereas the number of cortical interruptions is increased. The assessment of such parameters using HR-pQCT is, therefore, a promising tool for the follow-up of bone involvement in MCP joints in patients with RA.
References:
[1] Fouque-Aubert et al., ARD 2010.
[2] Stach et al., A&R 2010.
[3] Peters et al., ACR2016 (abstract).
Disclosure of Interest: M. Peters: None declared, A. Scharmga: None declared, A. van Tubergen: None declared, D. Loeffen: None declared, R. Weijers: None declared, B. van Rietbergen Consultant for: Scanco Medical AG, P. Geusens: None declared, J. van den Bergh: None declared
DOI: 10.1136/annrheumdis-2017-eular.4743

FRI0663 EVALUATION OF A FLUOROENZYME IMMUNOASSAY (ELIA-CTD) IN THE SCREENING OF PATIENTS SUSPECTED FOR AUTOIMMUNE CONNECTIVE TISSUE DISEASES

M. Elkhalifa[1], R. Abdulhadi[1], H. Ramadan[1], S. Barrientos[1], S. Saleh[1], O. Suhial[2], A.W. Al-Allaf[2]. *[1]Laboratory Medicine & Pathology; [2]Medicine, Hamad Medical Corporation, Doha, Qatar*

Background: Detection of auto-antibodies directed against nuclear antigens (antinuclear antibodies or ANA) have important diagnostic and prognostic implications in connective tissue diseases (CTD). The conventional indirect immunofluorescence assay on HEp-2 cell line (ANA-IIF) is the most commonly used method to detect ANA. The ANA-IIF can be labor intensive and suffers from lack of specificity.

Objectives: To evaluate the utility of a new fluoroenzyme Immunoassay "EliA-CTD" as an alternative for screening patients suspected for autoimmune connective tissue diseases.
Methods: Sixteen Hundread (1600) consecutive patients' sera submitted for anti-nuclear antibodies were tested using the ANA-IIF (Diasorin S.P.A, Saluggia, Italy) and the new EliA-CTD screen (Phadia GmbH, Frieiburg, Germany). ANA testing was ordered by both primary and secondary care physicians. The EliA-CTD screening assay is a fluoroenzyme immunoassay which is performed on the Phadia-250 automated platform. The EliA–CTD assay contains ANA-targeted recombinant antigens including dsDNA, Sm-D, Rib-P, PCNA, U1-RNP (70, A, C), SS-A/Ro, SS-B/La, Centromere B, Scl-70, Fibrillarin, RNA Polymerase III, Jo-1, Mi-2, and PM-scl. The test results are expressed as ratio, with >1.0 considered positive. For ANA-IIF, the cut off for positive results was 1:40 or greater. Additionally, further testing for dsDNA and other extractable nuclear antigens (ENA) was undertaken on a subset of sera that were ANA-IIF+ or whenever there was discrepancy between the two methods.
Results: The overall agreement between the two methods was 84.2%. Three hundread and eight (308) out of 1600 (19.3%) samples tested positive by ANA-IIF positive as compared to 101/1600 (6.6%) for the EliA-CTD assay. Additional testing showed that 105 samples were positive for ENA including dsDNA. Of those, 101 were EliA-CTD positive and 81 were ANA-IIF positive. By incorporating the ENA results, the calculated sensitivity and specificity for the EliA-CTD were 97.1% and 99.7% respectively with positive and negative predictive values for the EliA-CTD assay of 96.1% and 99.8%, respectively. The corresponding sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the ANA-IIF assay at different dilutions is shown below:

Titer	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
≥1:40	77.7	84.8	26.0	98.2
≥1:80	60.3	95.3	32.4	98.4
≥1:160	57.4	97.4	41.3	98.4
≥1:320	46.5	98.7	48.8	98.5

Conclusions: The new automated EliA-CTD assay shows superior sensitivity and specificity compared to the conventional labor intensive ANA-IIF. The EliA-CTD can be used as an upfront screening tool for connective tissue diseases. Depending on the clinical details, any EliA-CTD positive results could be reflexly followed by additional testing including ANA-IIF testing to elucidate the titer and pattern.
References:
[1] Hayashi N, Kawamoto T, Mukai M, Morinobu A, Koshiba M, Kondo S, Maekawa S, Kumagai S. Detection of Antinuclear Antibodies by Use of an Enzyme Immunoassay with Nuclear HEp-2 Cell Extract and Recombinant Antigens: Comparison with Immunofluorescence Assay in 307 Patients. Clinical Chemistry 2001; 47(9):1649–1959.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3058

FRI0664 INFLUENCE OF JOINT PATHOLOGY ON OPTICAL SPECTRAL TRANSMISSION IMAGING, ASSESSING INFLAMMATION IN HAND AND WRIST JOINTS OF RHEUMATOID ARTHRITIS PATIENTS

N. Besselink[1], P. van der Meijde[1], A. Marijnissen[1], P. Meijer[2], W. Rensen[2], J. van Laar[1], F. Lafeber[1], J. Jacobs[1]. *[1]Rheumatology and Clinical Immunology, University Medical Centre Utrecht, Utrecht; [2]Hemics BV., Eindhoven, Netherlands*

Background: Rheumatoid arthritis (RA) patients benefit from treat-to-target strategies, aiming for remission or low disease activity[1]. Clinical disease activity measures like the Disease Activity Score (DAS28) have questionable reproducibility and lack sensitivity for low disease activity states; MRI and ultrasound (US) are sensitive, but scanning multiple joints is time-consuming. Optical spectral transmission (OST) is stronger than DAS28 associated with inflammation assessed by both US and MRI[2]. OST measures the blood-specific absorption of light transmitted through tissue, which is reduced in presence of joint inflammation, but also influenced by other joint pathology.
Objectives: Evaluating the influence of joint pathology on the misclassification of joint inflammation, in the hand and wrist joints of RA patients, determined by OST, as compared to US, the reference standard.
Methods: Fifty RA patients with at least one swollen joint, generally with low disease activity were included in this cross-sectional study. Assessments were US, OST, and DAS28, performed according to established guidelines[3] by separate experienced examiners, blinded for other study outcomes. US joint inflammation was defined as a gray-scale score>1 or a power Doppler score>0 (scales 0–3), assessed in MCP, (P)IP, and wrist joints. Using US as reference, diagnostic performance of OST in detecting inflammation at joint level was evaluated using receiver operating characteristic (ROC) analyses; at patient level, DAS28 and OST were correlated to US. Joint pathology potentially influencing misclassification of OST (erosions, osteophytes, tendon (sheet) inflammation, abnormal vasculature, and triangular fibrocartilage complex injuries) were evaluated for significance in a multivariate nominal logistic regression model.
Results: OST performed well at joint level, separately for the MCP (ROC-AUC:0.85), PIP (ROC-AUC:0.79) and wrist (ROC-AUC:0.72) joints and for all joints together (ROC-AUC:0.83). On patient level, DAS28 correlated poorly with US (r=0.29), but OST correlation was good (r=0.72). The presence of joint pathologies per misclassification group is shown in table 1. In the regression model, inflammation in MCP and PIP joints had a higher risk of false negative misclassification in the presence of dorsal bone erosions (OR:3.5, 95% CI:1.7–7.3), volar erosions (OR:5.0, 95% CI:1.8–14.1), flexor tenosynovitis (OR:2.5, 95% CI:1.4–4.5), osteophytes (OR:1.9, 95% CI:1.2–2.8), and extensor tendonitis (OR:3.7, 95% CI:1.6–8.5), and a higher risk of false positive misclassification in the presence of osteophytes (OR:2.3, 95% CI:1.6–3.2).

Table 1: Frequency of joint pathologies, per misclassification group.

Misclassification	Erosions dorsal		Erosions volar		Osteophytes		Flexor tenosynovitis		Extensor tendonitis		Vascular pattern		TFCC	
	Absent	Present	Absent	Present	Absent	Present	Absent	Present	Absent	Present	Absent	Present	Absent	Present
True positives & true negatives	1546 84.4%	34 66.7%	1569 84.2%	12 63.2%	1265 86.6%	315 74.8%	1502 84.3%	79 78.2%	1556 84.3%	25 65.8%	1349 84.6%	231 80.5%	121 65.4%	2 50.0%
False negatives	116 6.3%	13 25.5%	122 6.5%	7 36.8%	85 5.8%	44 10.5%	114 6.4%	15 14.9%	121 6.6%	8 21.1%	109 6.8%	20 7.0%	13 7.0%	1 25.0%
False positives	169 9.2%	4 7.8%	173 9.3%	0 0.0%	111 7.6%	62 14.7%	166 9.3%	7 6.9%	168 9.1%	5 13.2%	137 8.6%	36 12.5%	51 27.6%	1 25.0%
Total	1831	51	1864	19	1461	421	1782	101	1845	38	1595	287	185	4

Conclusions: OST is a sensitive and specific technique to assess inflammation in hand and wrist joints of RA patients with low disease activity, nonetheless, joint pathology like erosions, tendonitis, and osteophytes increase the risk of misclassification of inflammation by OST.
References:
[1] Bijlsma J et al. Early rheumatoid arthritis treated with tocilizumab, methotrexate, or their combination. Lancet 2016;388:343–55.
[2] Van Onna M et al. Assessment of disease activity in patients with rheumatoid arthritis using optical spectral transmission measurements. ARD 2016;75(3):511–518.
[3] Backhaus M et al, Guidelines for musculoskeletal ultrasound in rheumatology. ARD 2001;60(7),641–9.
Disclosure of Interest: N. Besselink: None declared, P. van der Meijde: None declared, A. Marijnissen: None declared, P. Meijer Shareholder of: Hemics, Employee of: Hemics, W. Rensen Shareholder of: Hemics, Employee of: Hemics, J. van Laar: None declared, F. Lafeber: None declared, J. Jacobs: None declared
DOI: 10.1136/annrheumdis-2017-eular.2461

FRI0665 ANTI-HETEROGENOUS NUCLEAR RIBONUCLEOPROTEINS (ANTI- HNRNP) AND OTHER AUTOANTIBODIES FOR DETECTION OF EROSIVE ARTHROPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH JOINT INVOLVEMENT IN COMPARISON BY JOINT X-RAY

S.Y. Hussein[1], N.A. Fathi[1], S.H. Goma[1], N.A. Mohammed[2], E. Mosad[3]. *[1]Physical Medicine, Rheumatology & Rehabilitation, Faculty of Medicine, Assiut university, Egypt; [2]Diagnostic Radiology, Assiut University Hospital; [3]Clinical Pathology, South Egypt Cancer Institute, Assiut, Egypt*

Background: Joint involvement in SLE is very common, affecting 90% of patients at some stage in the course of their disease (1).Arthritis featuring prominent radiological erosion in SLE is less common; however, in a small subset of patients an erosive pattern similar to RA develops (2).
Anti- heterogenous nuclear ribonucleoprotein A2 (anti-hnRNP-A2) occur in about one-third of patients with RA but rarely in other arthritides such as OA, PsA or reactive arthritis. Interestingly, in SLE patients anti-hnRNP-A2 autoantibodies were found to be significantly associated with erosive arthritis (3).
Objectives: To investigate joint involvement in SLE and its relationship with autoantibodies to the hnRNP Ab A1 and A2, rheumatoid factor (R.F), Antinuclear antibody (A.N.A) and Anti-double stranded DNA (Anti-DSDNA) and correlation with articular involvement by joint x-ray.
Methods: Case series study comparing diagnosis of arthritis by hand and wrist x-ray with anti-hnRNP A1 and A2 in Fourty SLE patients aged 17–60 years old with disease duration 1–17 years complaining of arthralgia or arthritis. A controlled group of 21 clinically normal persons, age and sex matched and blood

Table 1. Comparison of serological features in SLE patients with and without erosive arthritis (EA)*

Characteristic	SLE patients with EA	SLE patients without EA	Total	P value
Rheumatoid Factor, N (%)[b]	5 (50)	6 (20)	11 (27.5)	0.079
ANA, N (%)[b]	8 (80)	14 (46.7)	22 (55)	0.069
Anti-double stranded DNA, N (%)[b]	9 (90)	13 (43.3)	22 (55)	0.011*

Table 2. Comparison of radiological findings of hand X-ray in SLE patients with and without erosive arthritis (EA)*

Characteristic	SLE patients with EA	SLE patients without EA	Total	P value
Juxta-articular osteoporosis, N (%)	9 (90)	21 (70)	30 (75)	0.204
Narrowing of joint space, N (%)	9 (90)	9 (30)	18 (45)	0.001*
Subchondral cysts, N (%)	4 (40)	1 (3.3)	5 (12.5)	0.010*
MCP sublaxation, N (%)	7 (70)	3 (10)	10 (25)	0.001*
Interruption of cortical surface, N (%)	7 (70)	1 (3.3)	8 (20)	<0.0001*
New bone formation, N (%)	1 (10)	0	1 (2.5)	0.250
AVN, N (%)	0	1 (3.3)	1 (2.5)	0.750

samples are drawn and centrifuged. RF and auto-antibodies to nuclear antigens anti-nuclear antibodies (ANA) and anti-double stranded DNA were determined in all the patients. All patients underwent X-rays of the hands and wrists.
Results: Anti-hnRNP A1 showed highly significant difference between study and control. Anti-hnRNP A2 showed significant difference between study and control.
Conclusions: This study showed a high frequency of erosive arthropathy and autoantibody to both hnRNP antigens might become useful marker for joint involvement in SLE patients and identify SLE patients prone to develop joint damage
References:
[1] Pipili C, Sfritzeri A, Cholongitas E. Deforming arthropathy in systemic lupus erythematosus. Eur J Intern Med 2008;19(7):482–7.
[2] Pipili C, Sfritzeri A, Cholongitas E. Deforming arthropathy in SLE: review in the literature apropos of one case. Rheumatol Int 2009;29(10):1219–21.
[3] Hassfeld W, Steiner G, Graninger W, Witzmann G, Schweitzer H, Smolen JS. Autoantibody to the nuclear antigen RA33 – a marker for early rheumatoid arthritis.Br J Rheumatol 1993;86:19–203.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4487

FRI0666 INCREASED PREVALENCE OF SUBCLINICAL ATHEROSCLEROSIS IN MODERATE-SEVERE PLAQUE PSORIATIC PATIENTS

N. Vegas-Revenga, J. Martín-Varillas, S. Armesto, M. Drake, V. Portilla, P. Fuentevilla, J. Rueda-Gotor, B. Atienza, L. Domínguez-Casas, C. Fernández-Díaz, R. Blanco, M. González-Gay, A. Corrales. *HUMV, Santander, Spain*

Background: Recent studies suggest that plaque psoriasis may be a risk factor for major adverse cardiac events. This has important therapeutic implications for cardiovascular (CV) risk stratification and prevention in patients with severe psoriasis. For that reason surrogate markers of subclinical atherosclerosis and CV mortality such as carotid plaques (CP) have been studied by carotid US examination.
In most studies of psoriasis done before, the results have shown an increased prevalence of carotid plaques, but it is not always the rule.
Objectives: To compare the prevalence of CP between patients with moderate-severe psoriasis and the general population.
Methods: A cross-sectional study that included 40 patients with moderate-severe psoriasis (PASI>10, BAS>10%), that fulfilled definitions for initiating treatment with a biological agent and 40 age-, sex- and traditional CV risk factors-matched healthy control subjects. Patients with history of CV events, diabetes mellitus, and chronic kidney disease or body max index (BMI)>35 were excluded. Carotid ultrasonography was performed by a MyLab 70 scanner (Esaote; Genoa, Italy), then carotid plaque was defined according to the Manheim Consensus Conference criteria. Statistical analysis: Qualitative data were expressed as number and percentages and quantitative data as mean (SD). Student's t test or Mann-Whitney U were used to compare continuous variables, as appropriate. Chi2 test or Fisher test were used for qualitative variables.
Results: The main data of the patients are summarized in the Table. It is important to highlight that it is based on a young population (mean age<40 years). The two groups did not present significant differences except for high sensitivity C-reactive protein (hsCRP)
As expected given the age of the group, CV risk measured by SCORE was low (0%) with a mean of 0.2 us 0.15. No patient had a high-very high CV risk as measured by SCORE (≥5%).
Patients with psoriasis had a long-standing disease (17.05±11.63 years). The presence of carotid plaques was found in a total of 10 patients with plaque psoriasis (25%), 5 of them had bilateral plaques) and one in the control group (2.5%) without bilateral plaques), p<0.003.

Variable	Plaque Psoriasis (n=40)	Controls (n=40)	P
Age: Mean (SD)	37,68 (11.83)	38.63 (11.83)	0.75
Sex (Male): n (%)	18 (45)	18 (45)	1.0
Psoriasis duration (years): Mean (SD)	17.05 (11.63)	ND	–
Psoriatic Arthritis: n (%)	11 (27.5)	ND	–
HLA-B27 Positive: n (%)	5 (13)	ND	–
BSA: Mean (SD)	38.99 (17.08)	ND	–
PASI: Mean (SD)	19.33 (8.89)	ND	–
hsCRP (mg/L): Mean (SD)	3.26 (3.31)	1.69 (2.62)	**0.001**
ESR (mm/h): Mean (SD)	13.79 (13.23)	8.53 (7.01)	0.17
Systolic hypertension (mmHg): Mean (SD)	121.33 (13.91)	120.08 (11.73)	0.86
Cholesterol (mg/dl): Mean (SD)	196.08 (34.31)	193 (36.42)	0.69
HDL-C (mg/dl): Mean (SD)	55.58 (17.05)	63.88 (20.7)	0.051
Smoking: n (%)	13 (33)	9 (22.5)	0.32
Dyslipidemia: n (%)	21 (53)	17 (42.5)	0.37
Arterial hypertension: n (%)	2 (5)	3 (7.5)	0.99
Obesity (BMI>30) n (%)	7 (18)	3 (7.5)	0.18
SCORE (%): Mean (SD)	0.2 (0.46)	0.15 (0.43)	**0.55**
Carotid plaques			
Yes: n (%)	10 (25)	1 (2.5)	**0.003**
Bilateral: n (%)	5 (13)	0 (0)	**0.02**

Conclusions: Moderate-severe psoriasis is associated with increased prevalence of carotid plaques.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5320

FRI0667 THE RECALL SURVEY: CAN ULTRASOUND AFFECTS CLINICIANS' DECISIONS ABOUT CHANGING TREATMENT IN RA?

O. Epis[1], P. Macchioni[2], A. Delle Sedie[3], M. Canzoni[4], E. Filippucci[5], A. Iagnocco[6], S. Tropea[7], C.F. Bonali[8]. *[1]Rheumatology Unit, Ospedale Niguarda Milano, Milano; [2]Rheumatology Unit, Reggio Emilia Hospital, Reggio Emilia; [3]Rheumatology Unit, Università di Pisa, Pisa; [4]Local Health Unit (ASL) Rome 1, Rome; [5]Rheumatology Department, Università Politecnica delle Marche, Jesi (AN); [6]Academic Rheumatology Unit, Università degli Studi di Torino, Torino; [7]ASP7, Busacca Hospital, Ragusa; [8]Rheumatology Unit, Ospedale San Paolo, Bari, Italy*

Background: In Rheumatoid Arthritis (RA) treatment response is assessed using standard clinical disease activity measure. However ultrasound (US) is able to show subclinical synovitis in patients (pts) with RA who are in clinical remission (CR); further studies are still required to delineate the impact of US findings in the management of RA pts in daily clinical practice.
Objectives: to investigate the influence of US on the clinicians' treatment choices in pts with RA.
Methods: in 2015 an educational event (RECALL Survey) focused on the added value of US in RA pts was held in 22 rheumatology centers in Italy.In every center, the local rheumatologists provided RA pts to be examined by US. Pts signed an informed consent and a brief history of them was collected by the local rheumatologists (previous and current therapy, DAS28, HAQ score). Bilateral US examinations of wrists, metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints were performed by rheumatologists expert in US, to assess synovitis (joint effusion, synovial proliferation, and power Doppler (PD) signal), and bone erosions, using a Logiq E R7, General Electrics, with a 4.2–13 MHz linear probe. All US findings were scored using a 4 degree semiquantitative scoring system.
Results: 465 pts were evaluated. Clinicians, after US evaluations, changed therapy in 23.7% of pts, did not change therapy in 35.5% of pts.In general changes of therapy tended to be made by clinicians when joint effusion or power Doppler signal were present (table 1–2). The presence of erosion did not influence the clinicians' decisions.

Table 1. Changes of therapy and joint effusion

		Joint Effusion		
		Score ≤0	Score >0	Total
Change in therapy	No	86	79	165
	Yes	11	99	110
	Total	97	178	275

Table 2. changes of therapy and Power Doppler

		Power Doppler Signal		
		Score ≤0	Score >0	Total
Change in therapy	No	129	36	165
	Yes	24	86	110
	Total	153	122	275

Conclusions: Ultrasound may be an useful tool in daily rheumatologic practice to help clinicians make decisions about how to treat patients with RA. US results, especially joint effusion and Power Doppler signal, may influence the choice of clinicians to modify a patient's treatment regime.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4090

FRI0668 SONOGRAPHIC AND ANATOMICAL DESCRIPTION OF THE SUBTALAR JOINT

P. Mandl[1], D. Bong[2], P.V. Balint[3], H.B. Hammer[4], M. Miguel[5], E. Naredo[6], I. Möller[2] on behalf of Anatomy for the Image. *[1]Rheumatology, Medical University of Vienna, Vienna, Austria; [2]Rheumatology, Universitat de Barcelona, Instituto Poal de Reumatologia, Barcelona, Spain; [3]Rheumatology, National Institute of Rheumatology and Physiotherapy, Budapest, Hungary; [4]Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; [5]Pathology and Experimental Therapeutics, Universitat de Barcelona, Barcelona; [6]Rheumatology, Joint and Bone Research Unit. Hospital Universitario Fundación Jiménez Díaz and Autónoma University, Madrid, Spain*

Background: The subtalar joint is commonly affected in many rheumatic and musculoskeletal diseases; however, subtalar joint involvement is often neglected or missed during clinical examination due to the fact that the joint is difficult to examine and most clinicians have a limited understanding of its anatomy.
Objectives: To provide a detailed anatomical and US description of the subtalar joint, a single joint that, anatomically, is divided into two separate compartments: the anterior subtalar joint (ASTJ) and the posterior subtalar joint (PSTJ).
Methods: Cadaver specimens of the ankle and foot were examined in detail by ultrasound (US) by rheumatologist experts in musculoskeletal US. The ASTJ of all

the specimens were injected with colored latex while the PSTJs were respectively injected with 1ml of latex of a contrasting color under US guidance. Following the injections, the joints were frozen and cut into 2 centimeter sections from medial to lateral in the sagittal plane. Sections were examined independently by three authors for the presence of latex within the ASTJ, PSTJ and, also, to look for the presence of extra-articular latex extravasation or the spread of latex to adjacent articulations by means of a communication with the ankle joint or the adjacent portion of the subtalar joint.

Results: Six cryopreserved intact ankle-foot specimens from three male and three female cadavers (two right and four left), with a mean age of 74 years (range, 66–80 years) were studied. A recommended list of standardized scanning technique which allows sonographers to evaluate both compartments of the subtalar joint (ASTJ and PSTJ) from the medial, lateral and posterior aspect were developed. All of the specimens (6/6, 100%) contained the appropriate colored latex in the appropriate subtalar joint compartment with minimal leakage into the surrounding soft tissues (Figure 1). Of note, five of the six (5/6, 83%) specimens revealed communication between the PSTJ and the posterior tibiotalar joint. There was no communication between the ASTJ and the tibiotalar joint, nor was there evidence of spread of the latex, i.e. communication, from one subtalar joint compartment to the other.

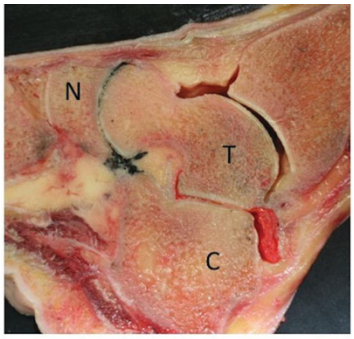


Figure 1. Anatomical specimen showing the anterior subtalar joint (filled with green latex) and the posterior subtalar joint (filled with red latex); C: calcaneus, N: navicular, T: talus

Conclusions: Lack of communication between the ASTJ and the PSTJ and the communication between the PSTJ and the posterior recess of the tibiotalar joint are compatible with other studies. Our study highlights the importance of employing cadaver specimens in musculoskeletal ultrasound, and presents a number of options for US imaging of both the ASTJ and PSTJ that also provide access to these distinct compartments for the purpose of aspiration and injection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2675

FRI0669 VALIDITY OF SEVEN-JOINT VERSUS SIMPLIFIED TWELVE-JOINT ULTRASONOGRAPHY SCORING SYSTEMS IN ASSESSMENT OF RHEUMATOID ARTHRITIS ACTIVITY

R. El-Gohary[1], A. Ahmed[1], A. Khalil[2], H. El-Gendy[1], K. Gado[1]. *[1]Internal Medicine, Rheumatology & Clinical Immunology Subspeciality, Kasr Alainy; [2]New Kasr El-Aini Teaching Hospital, Cairo, Egypt*

Background: Musculoskeletal ultrasonography imposes itself as reliable tool for the disease activity assessment of rheumatoid arthritis (RA) being more sensitive than clinical in detection of synovitis. There is no consensus on the exact joint number should be examined. Naredo et al. developed reduced 12-joint count[1] while Backhaus et al. scored only seven small joints[2]. Although both were found to reflect disease activity it is suitable in a busy clinic to assess the lowest joint count.

Objectives: To investigate the validity of 7-joint ultrasonography (US7) scores in assessment of disease activity in Egyptian RA patients compared with simplified 12-joint ultrasonography (US12) scores and correlate both to composite disease activity indices.

Methods: Fifty Egyptian RA adult patients diagnosed according to the ACR1987 criteria were subjected to detailed history, 28 tender & swollen joint counts (TJC, SJC). The disease activity was assessed by calculating DAS28-CRP, SDAI and CDAI. The Ultrasonographic assessment was performed using a LOGIQP6 with 10–13 MHz broadband linear array transducer by one well-trained blinded rheumatologist. The synovial hypertrophy on GS & PD images were graded using a semi-quantitative 0–3 scale. The simplified US12 was performed as originally described[1]. However the GS & PD synovitis were computed in two separate scores instead of one. The US7 was performed at the clinically dominant side as described by Backhaus et al[2]. Two Sum-US7 scores were added; Sum (GS)-US7 after grading the GS-tenosynovitis and Sum (PD)-US7. Ultrasonography inter/intraobserver reliability was evaluated on 40 stored images using randomization and blinded techniques.The study was approved by the local ethics committee.

Results: The studied population had mean disease duration of 89±60 months. 62% were using more than one DMARD. They showed moderate disease activity as defined by DAS28, SDAI and CDAI (mean 3.7±1.4, 19.9±14.9 & 17.9±13.3 respectively). The GS-scores showed no correlation with disease activity parameters. PD-US12, PD (synovitis)-US7 and Sum (PD)-US7 significantly correlated with the SJC, CRP levels (P values 0.03, 0.04 and 0.01) and DAS28 (P values 0.02, 0.009 and 0.001), furthermore Sum (PD)-US7 correlated with SDAI and CDAI (P values 0.013& 0.042 respectively). Correlation coefficient between the different ultrasonographic scores showed no differance. The ultrasonography reliability showed significant agreement ($P<0.001$). Kappa values were 0.80 & 0.96 for GS & PD interobserver reliability and 0.96 & 1.0 for GS & PD intraobserver reliability.

Conclusions: Our results confirm the validity of PD-scores in assessment of disease activity. However they make the significance of GS questionable. The Sum-(PD) US7 seems to perform better than the original one, it was strongly correlated with CRP and with the three disease composite indices. The studied scores correlated with each other favoring the use of less time consuming US7score.

References:

[1] Naredo E, et al. Validity, reproducibility, and responsiveness of a twelve-joint simplified power Doppler ultrasonographic assessment of joint inflammation in rheumatoid arthritis. Arthritis Care Res. 2008;59(4):515–22.

[2] Backhaus M, et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: A pilot project. Arthritis Care Res. 2009;61(9):1194–201.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3256

FRI0670 THE COURSE OF SUBCLINICAL JOINT INFLAMMATION DURING PROGRESSION FROM ARTHRALGIA TO CLINICALLY DETECTABLE ARTHRITIS, A LONGITUDINAL MRI STUDY

R.M. Ten Brinck, H.W. van Steenbergen, L. Mangnus, A.H. van der Helm-van Mil. *Rheumatology, Leiden University Medical Centre, Leiden, Netherlands*

Background: Subclinical joint inflammation in the phase of arthralgia preceding RA can comprise synovitis, bone marrow edema (BME) and/or tenosynovitis. It is unknown in what time order the different tissues in a joint become inflamed or progress with inflammation. It has been postulated that synovitis is an initial process that is succeeded by bone involvement ("outside-in hypothesis" presuming that synovitis precedes BME and erosions). Alternatively, it is suggested that inflammatory cells in the bone marrow migrate via bone pores to the synovium, promoting synovitis ("inside-out", then BME precedes synovitis). Thirdly, these processes can occur or progress simultaneously. Serial MRI studies can reveal time-relationships. This longitudinal MRI study on patient-level determined the course of joint inflammation during progression from arthralgia to clinical arthritis.

Objectives: To increase the comprehension on the course of MRI-detected subclinical joint inflammation during progression from arthralgia to clinical arthritis, both in ACPA-positive and ACPA-negative arthritis patients.

Methods: We longitudinally followed 29 patients that all progressed from Clinically Suspect Arthralgia to clinical arthritis. 1.5T MRI on hand and foot joints was performed at presentation with arthralgia and subsequently at the development of clinical arthritis. MRIs were evaluated for BME, synovitis and tenosynovitis (summed in the total inflammation score) and erosions by three readers (ICCs 0.98, 0.96 and 0.97) that were blind to clinical data and the order in time. Analyses were repeated in arthritis patients that fulfilled the 2010 criteria for rheumatoid arthritis, and in ACPA-positive and ACPA-negative patients separately.

Results: At presentation with arthralgia the mean age was 43 years, 72% was female, and 28% was ACPA-positive. Median duration to clinical arthritis was 17 weeks. At the time of arthritis development 65% fulfilled the 2010-criteria. During progression from arthralgia to clinical arthritis the median total inflammation score increased from 4.5 (IQR 2.8–7.8) to 6.0 (IQR 2.0–13.5), p=0.01. The BME score increased over time (p=0.04), as did the synovitis score (p=0.002). The tenosynovitis and erosion scores increased as well, though not statistically significant (p=0.10 and p=0.07 respectively). Analyses within the patients that developed 2010-RA revealed that BME (p=0.047), synovitis (p=0.005) and tenosynovitis (p=0.004) all increased significantly, in contrast to the erosion score. At presentation with arthralgia, BME and synovitis scores were higher in ACPA-positive than in ACPA-negative patients; during progression to clinical arthritis the different types of inflammation increased similarly in ACPA-positive and ACPA-negative patients.

Conclusions: During progression from arthralgia to clinically evident rheumatoid arthritis, BME, synovitis as well as tenosynovitis progress simultaneously.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2908

FRI0671 ULTRA-HIGH FIELD MRI AND BIOMECHANICAL INVESTIGATION OF VERTEBRAL BONE MICROARCHITECTURE

S. Guis[1], D. Guenoun[2], A. Fouré[3], M. Pithioux[4], T. Le Corroller[2], J.P. Mattei[1], V. Pauly[5], M. Bernard[3], P. Chabrand[4], P. Champsaur[2], D. Bendahan[3].
[1]Rheumatology 1; [2]Radiology, Aix Marseille Université, AP-HM; [3]CRMBM, UMR 7339; [4]Ism UMR 7287, CNRS; [5]Statistic department, AP-HM, Marseille Cedex 9, France

Background: Fracture risk prediction in patient relies chiefly on bone mineral density (BMD) measurement. However, the decreased bone strength characteristic of osteoporosis is dependent not only on BMD, but also on other factors, most notably bone microarchitecture.
Objectives: The purpose of this study was to investigate bone microarchitecture variables of cadaveric vertebrae using ultra-high field MRI (7 Tesla).
Methods: Twenty four vertebrae (L2, L3, L4) from eight cadavers were studied using 7 Tesla MRI. Their Bone Mineral Density (BMD) were investigated using dual energy X Ray absorptiometry. Then, all specimens underwent mechanical compression tests to failure and the failure load (in Newton) and constraint (in Mpa) were measured. Bone Volume Fraction (BV/TV), Trabecular Thickness (Tb.Th), and Trabecular Spacing (Tb.Sp) were measured in MR images using a Digital topological analysis (Bone J). Measurements were performed by two observators in order to characterize the inter-rater reliability. Statistical analyses were performed using SPSS. Correlations between variables were analyzed using Spearman correlations and Stepwise regression. A p value of 0.05 was considered as significant.
Results: The inter-rater reliability for bone microarchitecture parameters quantification was good. Tb.Th and Tb.Sp measured using high-field MRI were 0.52±0.18 and 0.48±0.10 respectively while the BV/TV fraction was 0.52±0.13. The mean BMD was 0.86±0.20 g/cm^2. The failure load and the constraint measured during the compression tests were 2600±1267N and 1.57±0.81 Mpa respectively. Interestingly, the variables measured during the mechanical tests were significantly
The failure load and constraint measured during the compression tests were significantly correlated with the BMD. Regarding the bone indices quantified using high-field MRI, a significant linear relationship was observed between the trabecular spacing and the BMD (R^2=0.23, p=0.01 and the constraint values to failure (R^2=0.18, p=0.04). A stepwise regression with backward elimination demonstrated that combining BV/TV and BMD improved the relationship with the constraints from an adjusted R^2=0.384 for BMD alone to an adjusted R^2=0.41 for BMD + BV/TV.
Conclusions: In the present study, we demonstrated for the first time that the variables characterizing the vertebral bone microarchitecture quantified using ultra-high field MRI were significantly correlated with biomechanical parameters. In addition, we illustrated that the vertebral bone strength was better described by a variable combining BMD and trabecular bone spacing.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2034

FRI0672 ASSESSMENT OF THE NAIL BED IN PSORIATIC ARTHRITIS (PSA) BY ULTRASOUND (US) AND MRI

S. Paramalingam[1], A. Taylor[2], H. Keen[2,3]. *[1]Rheumatology, Sir Charles Gairdner Hospital; [2]Rheumatology, Fiona Stanley Hospital; [3]School of Medicine, University of Western Australia, Perth, Australia*

Background: PsA can be difficult to distinguish from osteoarthritis (OA) and the treatments vary greatly. Nail involvement can occur in about 15–50% patients with psoriasis[1], which may aid differentiation from OA. If US can reliably detect nail bed changes in early disease then it might be helpful in differentiating PsA from OA
Objectives: This study aims to investigate the nail bed changes seen in patients with PsA and OA using US and MRI, and to determine the impact of nail bed changes on quality of life (QOL).
Methods: Patients who fulfilled the CASPAR PsA or 1990 ACR OA classification criteria were recruited. At baseline, clinical assessment included patient and physician's visual analogue scale (VAS), tender and swollen joints, patient's Leeds Enthesitis Index and quality of life specific to nail psoriasis (NPQ10). Nail abnormalities on the dominant hand such as onycholysis, pitting, nail bed hyperkeratosis and nail bed crumbling were documented. Using US, each nail (1–5) was scored dichotomously for pitting/irregularity, loss of normal trilaminar appearance of the nail. Each nail was scored semi quantitatively for power doppler (PD) signal (0–3) in the nail bed, nail matrix and dermis, and assigned a total PD score. All patients had an MRI of the dominant 2nd to 5th finger.
Results: 14 patients were recruited; demographics, clinical and US detected nail changes are documented in Table 1. Clinical nail changes were not seen in the OA group, but were relatively common in the PsA group. In the PsA group, 54% of nails had US detected structural abnormalities; 12% pitting and 52% loss of trilaminar layer. Only 20% of OA nails had US detected abnormalities. There was a strong relationship between the presence of clinical nail change and US structural changes (chi square 10.769 df 1 p=0.001) but not PD signal score. There was no relationship between clinical or US detected nail scores and NPQ10, patient or physician VAS, swollen joint count or Leeds Enthesitis Index. MRI analysis is pending.

Table 1

	Total (n=14)	PsA (n=10)	OA (n=4)
Age (median (IQR))	56.5 (52.2–63.2)	55.0 (48.0–63.2)	61.0 (55.2–73.5)
Patient VAS (median (IQR))	29.0 (12.5–54.8	39.5 (19.8–54.8)	11.0 (3.8–54.2)
Physician VAS (median (IQR))	35.3 (20.5–57.5)	42.5 (24.5–57.5)	24.0 (4.8–53.8)
NPQ10 (median (IQR))	6.5 (1.8–10.0)	7.0 (5.2–10.2)	1.5 (0.2–5.8)
Swollen joint count (median (IQR))	2.0 (0.0–4.2)	1.5 (0.0–5.2)	2.5 (0.5–5.8)
Leeds Enthesitis index (median (IQR))	1.0 (0.0–2.0)	1.0 (0.0–2.0)	0.5 (0.0–1.8)
Percentage of nails with clinical abnormalities	27.7%	40.0%	0.0%
Percentage of nails with US structural abnormalities	44.3%	54.0%	20.0%
Percentage of nails with PD signal	97.1%	96.0%	95.0%

Conclusions: In this small prospective study, structural abnormalities detected by US appear to correlate well against clinical structural findings, but PD signal does not. No relationship was found between US findings and other clinical parameters. US structural abnormalities may be a better differentiator of PsA and OA than PD signal. MRI validation of these results is pending.
References:
[1] Gisondi P, Idolazzi L, Girolomoni G. Ultrasonography reveals nail thickening in patients with chronic plaque psoriasis. Arch Dermatol Res 304:727–732,2012.
Acknowledgements: This study was funded by a grant from UCB Australia Pty Ltd.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5614

FRI0673 CLINICAL REMISSION IN TOCILIZUMAB-USING RHEUMATOID ARTHRITIS PATIENTS CAN BE OVERESTIMATED: A CROSS SECTIONAL STUDY USING ULTRASOUND SONOGRAPHY

S. Nakabo[1], Y. Tsuji[2], M. Inagaki[2], H. Tsuji[1], T. Nakajima[1], M. Hashimoto[3], M. Furu[3,4], M. Tanaka[3], H. Ito[4], T. Fujii[1,5], Y. Fujii[2], T. Mimori[1]. *[1]Department of Rheumatology and Clinical Immunology; [2]Human Health Sciences Clinical Physiology and Ultrasound Labo; [3]Department of the Control for Rheumatic Diseases; [4]Department of Orthopaedic Surgery, Graduate School of Medicine, Kyoto University, Kyoto; [5]Department of Clinical Immunology and Rheumatology, Wakayama Medical University, Wakayama, Japan*

Background: Several clinical remission (CR) criteria of rheumatoid arthritis (RA) contain acute-phase reactants [C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR)] as their components. However, it is known that they can be underscored by the usage of tocilizumab (TCZ). This may cause overestimation of CR. On the other hand, ultrasound sonography (US) provides objective information independent of acute-phase reactants and assessment by physician and patient, and can detect synovitis in RA patients in CR, which is called sonographic residual synovitis (SRS).
Objectives: To assess whether CR of TCZ-using RA patients are overestimated, by using US.
Methods: We recruited 402 RA patients. Bilateral 2–5 MCP, wrist, ankle, and 2–5MTP joints were scanned by using the Aplio500 (TOSHIBA) with a 12 MHz transducer. Power Doppler (PD) images were obtained by Superb Micro-vascular Imaging (SMI). Gray scale (GS) and PD images were scored using a 0–3 semi-quantitative scale. Clinical information was obtained from the Kyoto University Rheumatoid Arthritis Management Alliance (KURAMA) database, which is based on the assessments by physicians who were blind to the US results. The patients were divided into 4 groups based on their treatment: tumor necrosis factor alpha inhibitors (TNFi), TCZ, abatacept (ABT), and non-biologic (non-Bio) users. Two patients treated by tofacitinib were excluded because the number was too small to analyze. The Boolean (BL)-based, Simplified Disease Activity Index (SDAI)-based, Clinical Disease Activity Index (CDAI)-based, and Disease Activity Score (DAS)28-ESR-based CR criteria were assessed using SRS.
Results: A total of 400 RA patients were analyzed. The number of patients in each treatment group is shown in the Table. When the BL-based, SDAI-based, and DAS28-ESR-based CR criteria were used, SRS in TCZ group was significantly stronger than the other groups (Fig 1–3). On the other hand, when CDAI-based CR criteria was used, the difference was not significant among 4 groups (Fig

	TNFi N=104	TCZ N=35	ABT N=42	Non-Bio N=219	P
Age, years	62.8±13.4	60.0±11.6	64.8±11.1	63.7±13.0	0.28
Sex (M/F)	14/90	8/27	2/40	48/171	0.03
Disease duration, years	12.3±11.6	12.0±11.3	11.5±9.5	13.1±11.2	0.75
Steinbrocker Stage (I/II/III/IV)	28/ 26/17/33	6/9/7/13	10/11/6/15	57/48/49/65	0.73
PhGA, mm	9.9±11.9	9.1±14.2	11.6±15.5	9.2±10.2	0.94
PtGA, mm	26.0±22.5	27.6±23.2	26.9±26.2	25.4±24.6	0.73
CRP, mg/dL	0.4±0.8	0.2±0.6	0.6±1.0	0.5±0.9	<0.01
ESR, mm/hr	22.8±18.6	11.2±11.5	26.7±19.2	22.8±17.6	<0.01
Tender joint count	0.8±1.3	0.7±1.5	1.4±2.9	1.0±1.6	0.27
Swollen joint count	0.8±1.6	0.7±1.1	1.3±2.6	0.9±1.8	0.94
Total GS score	11.1±5.7	14.2±8.1	12.5±5.9	13.9±7.4	<0.01
Total PD score	2.6±3.9	4.6±5.1	3.0±4.0	3.5±4.9	0.04
MTX, mg/week	6.0±4.2	4.2±4.6	3.0±3.6	5.4±4.1	<0.01
Prednisolone dose, mg/day	0.9±2.0	1.3±2.3	1.8±3.4	1.1±2.3	0.19

Mean ± SD.

4). In TCZ group, CRP and ESR were significantly lower than the other groups, although other clinical indicators were comparable (Table).

Fig 1: Boolean-based analysis

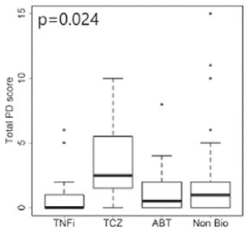


Fig 2: SDAI-based analysis

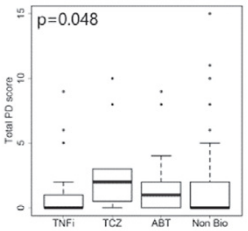


Fig 3: DAS28-ESR-based analysis

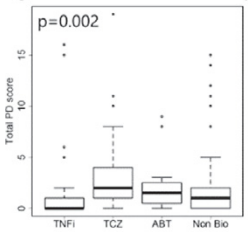
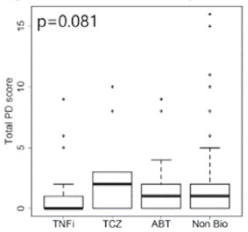


Fig 4: CDAI-based analysis



Kruskal-Wallis rank sum test

Conclusions: US revealed that CR in TCZ-using can be overestimated by BL-based, SDAI-based, and DAS28-ESR-based CR criteria. For TCZ users, CDAI-based CR criteria is more reliable than the other criteria.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1705

FRI0674 USING HIGHER IMAGE RESOLUTION OF MAGNETIC RESONANCE IMAGING OF THE CERVICAL SPINE IDENTIFIES MORE INFLAMMATORY AND STRUCTURAL LESIONS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

S. Krabbe[1], M. Østergaard[1], J. Møller[2], I.J. Sørensen[1], B. Jensen[1], O.R. Madsen[1], S.J. Pedersen[1]. *[1]Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen; [2]Department of Radiology, Herlev Hospital, Herlev, Denmark*

Background: The vertebrae of the cervical spine are rather small and it may be difficult to assess if small areas with signal intensity changes represent the bones, joints or entheses, or derive from the surrounding blood vessels.
Objectives: To investigate if image resolution affects the assessment of inflammatory and structural lesions of the cervical spine.
Methods: Forty-nine patients with axial spondyloarthritis according to the ASAS criteria started anti-TNF treatment and had "standard" resolution (std-res) and "high" resolution (high-res) MRI sequences of the cervical spine performed at baseline and after 48 weeks. 3 patients had follow-up scan already after 6–24 weeks due to study exclusion.
Std-res: STIR sequence: Voxel size 5.0 mm^3 (slice thickness 4.0, spatial resolution 1x1.25); T1W sequence: voxel size 4.5 mm^3 (slice thickness 4.0, spatial resolution 0.9x1.25).
High-res: STIR sequence: Voxel size 3.1 mm^3 (slice thickness 3.5, spatial resolution 0.8x1.11); T1W sequence: voxel size 1.4 mm^3 (slice thickness 3.0, spatial resolution 0.6x0.76).
Images were assessed in known chronology by an experienced axSpA MRI reader (SJP) blinded to clinical data. High-res and std-res were read in random order. MRI lesions of inflammation, fat and new bone formation were defined according to the Canada-Denmark working group [1,2]. Erosions were not assessed.
Results: Inflammatory lesions: In 9 of 43 patients (21%), inflammatory lesions were detected in the cervical spine at baseline at std-res, while this was detected in 14 of 43 patients (33%) at high-res. Using high-res, as compared to std-res, 6 patients were reclassified from negative to positive for inflammation, 1 patient was reclassified from positive to negative, and 8/28 patients remained classified as positive/negative, p=0.13 by Exact McNemar test. The mean inflammation score was significantly higher at high-res compared to std-res (1.7 (SD 4.5) vs. 0.8 (SD 2.7), p=0.04 by paired t-test).
Fat lesions: 11 of 43 patients (26%) had fat lesions in the cervical spine at baseline using std-res, while 10 of 43 patients (23%) had this using high-res. The mean fat score was significantly higher at high-res compared with std-res (1.6 (SD 3.5) vs. 0.8 (SD 1.8), p=0.02 by paired t-test).
Bone spurs/ankylosis: 11 of 43 patients (26%) had bone spurs/ankylosis of the cervical spine at baseline at std-res, while 10 of 43 patients (23%) using high-res. The mean new bone formation score was significantly higher at high-res compared with std-res (2.7 (SD 6.1) vs. 1.4 (SD 3.5), p=0.01 by paired t-test).
Responsiveness: Standardized response mean for inflammation score at std-res was 0.15, and at high-res 0.14. Structural lesions remained largely unchanged in all patients.
Conclusions: More patients were classified as having inflammatory lesions in the cervical spine when using high-res MRI, compared to std-res. Likewise, mean scores of inflammatory lesions, fatty lesions and new bone formation were significantly higher compared with std-res. Further studies are needed to investigate the clinical significance of these findings as well as the frequency of these minor lesions in healthy controls.
ClinicalTrials.gov: NCT01029847.
References:
[1] Lambert RGW, et al. J Rheumatol 2009;S84:3–17.
[2] Østergaard M, et al. J Rheumatol 2009;S84:18–34.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3200

FRI0675 OBTAINING SYNOVIAL BIOPSIES FROM THE WRIST IN PATIENTS WITH NEWLY DIAGNOSED UNTREATED AND LONGSTANDING RHEUMATOID ARTHRITIS FOLLOWED BY INTRAMUSCULAR GLUCOCORTICOID AND METHOTREXATE INITIATION IS SAFE AND THE GLUCOCORTICOID TREATMENT SIGNIFICANTLY REDUCES DISEASE ACTIVITY

S.A. Just[1], C. Nielsen[2], E.K. Hejbøl[3], H.D. Schrøder[3], I.M.J. Hansen[4], T. Barington[2], H.M. Lindegaard[1]. *[1]Rheumatology; [2]Clinical Immunology; [3]Clinical Pathology, Odense University Hospital, Odense; [4]Medicine, Svendborg Hospital, Odense University Hospital, Svendborg, Denmark*

Background: The minimal invasive ultrasound-guided synovial biopsy (USG-SB) method has been shown to be safe and tolerable. The method has accelerated the research field of using synovial biopsies focusing on early diagnosis, disease stratification, biomarker studies and in the future optimal treatment selection for the individual patient. Here synovial biopsies obtained from patients with early arthritis before therapy initiation are essential. A major issue in newly diagnosed RA patients but also in RA patients with longstanding active RA, is to combine an effective fast working treatment with safely obtaining synovial tissue without delaying treatment initiation. In the EULAR early arthritis recommendations, prompt treatment initiation is recommended by combining glucocorticoid bridge therapy with disease-modifying antirheumatic drugs (DMARD). It is therefore essential that accepting synovial biopsy, does not delay start of fast remission-inducing treatment. Especially if synovial biopsies by the USG-SB method in the future shall be used systematically for detailed disease stratification and personalized treatment decisions.
Objectives: Safety of using intramuscular glucocorticoid injection (IGI) immediately after the USG-SB procedure in patients with newly diagnosed untreated RA or longstanding active RA, and the effect of IGI on disease activity after 4 weeks.
Methods: Wrist synovial biopsies were taken) at inclusion and after 6 months from 22 patients with newly diagnosed, untreated RA and 15 with longstanding RA (>5 years). After biopsies patients were offered an IGI of 2 ml of methylprednisolone acetate (Depo Medrol) 40mg/ml. Early RA patients were also started on methotrexate. Disease activity scores in 28 joints (DAS28) were recorded at day of biopsy and again after 4 weeks. Safety data were obtained after 5 days (telephone), 2 weeks (questionnaire) and at first clinical evaluation (4 weeks) after biopsy. Patient-reported outcomes (PRO) with pain, swelling and stiffness of biopsied joint were obtained at day of biopsy and after two weeks.
Results: At present time, all patients have undergone first biopsy and 18/37 second biopsy. At the EULAR congress complete data will be presented. 68% of all patients accepted IGI after first biopsy currently 39% after second procedure. Patients accepting IGI after first biopsy did not have higher DAS-28 (early RA group (p=0.15), longstanding RA (p=0.06)). Time to first follow-up was not significantly different for patients accepting IGI (early RA group (p=0.17), longstanding RA (p=0.05)). Two weeks after biopsy, PRO was not significantly different when comparing IGI vs non-IGI treated. For all patients, DAS-28 was significantly reduced in the group receiving IGI at first clinical evaluation after synovial biopsy (p=0.004, without IGI ΔDAS28: -0.5, with IGI ΔDAS28: -1.7).
Conclusions: Start of treatment with IGI combined with DMARD after obtaining synovial biopsies by the USG-SB procedure from patients with early untreated RA and longstanding RA is safe, and reduces disease activity more than without IGI.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2491

FRI0676 A PROPOSAL FOR A SIMPLE ULTRASOUND METHOD FOR THE DIAGNOSIS OF EARLY RHEUMATOID ARTHRITIS

T. Serban[1,2], I. Satulu[3], O. Vutcanu[1], M. Milicescu[1,2], C.M. Mihai[1,2], M. Bojinca[1,2]. *[1]Internal Medicine and Rheumatology, "Dr. I. Cantacuzino" Clinical Hospital; [2]Internal Medicine and Rheumatology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [3]Rheumatology, Kalmar County Hospital, Kalmar, Sweden*

Background: At this point, the classification criteria for rheumatoid arthritis (RA) are well known and generally applied in clinical practice. (1) Ultrasound (US) assessment can help in distinguishing the patients with early RA (ERA) within the patients with early inflammatory arthritis (EIA).
Objectives: The aim of this study was to develop an US method for the diagnosis

of ERA in a population of EIA patients from an Early Arthritis Research Center (EARC).
Methods: We have assessed all patients with EIA referred to our EARC between 2012–2016. Patients who were diagnosed with other diseases except EIA or ERA, or in whom symptom duration exceeded 12 months, were excluded from the analysis. Every patient underwent clinical, laboratory and ultrasound evaluation. For the proposed US diagnostic method we have evaluated bilaterally 3 joints: wrists, MCP II and III and 2 tendon regions: the extensor ulnaris carpis tendon and the flexor tendons of the fingers. The presence/absence of synovitis/tenosynovitis either in gray-scale or power-Doppler scale was scored in a binary mode as 1/0. In order to simplify the scanning protocol, we considered the flexor tendons of the fingers as a singular structure for each hand which meant that that the presence of US abnormalities in at least one flexor tendon was scored as 1. Thus, the maximum score obtainable in both hands was 10. We analyzed the performance of the proposed US method for the diagnosis of ERA using ROC curve analysis.
Results: Of 253 patients referred to our EARC, 73 satisfied the inclusion criteria; among them, 43 fulfilled the EULAR/ACR criteria for RA (ERA patients), while the other 30 were considered to have undifferentiated EIA. The demographic, clinical and US data of the 73 patients are displayed in the table below. 34/43 ERA patients (76.7%) had a duration of symptoms less or equal to 3 months which classifies them as very ERA (VERA).

Table 1. Demographic, clinical, laboratory and US data of the study patients – data are either n (%), mean ± SD or median (IQR)

Parameters	EIA (n=30)	ERA (n=43)	p
Gender (Female)	17 (56.7%)	27 (62.8%)	0.816
Age	41.70±15.58	55.47±13.71	<0.001
Mean duration of symptoms	3.16±3.22	3.54±3.58	0.556
CRP (mg/l)	7.85 (1.99–26.20)	18.62 (3.57–14.68)	0.848
ESR (mm/h)	26.00 (10.00–44.75)	34.53 (14–51)	0.238
RF (IU/ml)	10.00 (7.85–14.56)	142.75 (35.14–201.74)	<0.001
ACPA (IU/ml)	5.00 (0.5–5.00)	153.96 (46.20–212.00)	<0.001
DAS28	4.00 (3.35–5.05)	4.89 (4.31–5.60)	<0.001
SDAI	17.82 (12.28–26.37)	27.96 (20.92–34.61)	<0.001
US evaluation	0 (0–3)	5 (3–7)	<0.001

In ROC analysis, a cut-off of the US score of 4 had best results for sensitivity and specificity (73.3% and 82.1%, respectively), with an area under the curve of 0.812. The US score correlated with the levels of RF, ACPA, DAS28 and SDAI ($p<0.001$), but not with those of acute phase reactants ($p>0.05$). The time needed for performing the ultrasound examination was less than 10 minutes.
Conclusions: The proposed US method proves to be reliable in identifying patients with ERA. The binary mode of US evaluation allows even persons with little training in US examination to diagnose patients. As the costs and time needed for US evaluation are low, the method is valuable in clinical practice for a rapid assessment of patients with EIA.
References:
[1] Aletaha D et al. Arhritis Rheum. 2010;62:2569–258.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4604

FRI0677 ROLE OF NAILFOLD VIDEOCAPILLAROSCOPY AND 22-MHZ DOPPLER ULTRASOUND IN THE ASSESSMENT OF SYSTEMIC SCLEROSIS-RELATED DIGITAL VASCULOPATHY

T. Schioppo[1,2], A. Orenti[1,3], P. Boracchi[1,3], O. De Lucia[2], A. Murgo[2], P.L. Meroni[1,2], F. Ingegnoli[1,2] on behalf of OPERA study group. *[1]Università degli Studi di Milano; [2]ASST Pini-CTO; [3]Lab of Medical Statistics, Epidemiology and Biometry GA Maccacaro, Milan, Italy*

Background: Microvascular damage plays a critical role in the initiation and perpetuation of systemic sclerosis (SSc). A comprehensive approach should investigate both superficial and deep layers of peripheral microcirculation. In addition to nailfold videocapillaroscopy (NVC), a well-established technique to evaluate outer skin layer vessels, power Doppler ultrasound (PDUS) has been recently used to study microcirculation in the inner levels [1].
Objectives: To study the severity of microvascular involvement in patients with SSc by using both NVC to measure capillary density (outer layer at the nailfold area) and PDUS to detect perfusion (deeper layers at the nailfold and pulp area).
Methods: 100 SSc consecutive patients fulfilling the 2013 EULAR classification criteria were enrolled. PDUS was performed at the 3rd and 4th finger of the dominant hand after exclusion of ulnar artery occlusion (UAO). In case of UAO non-dominant hand was examined. Ultrasound investigation was performed with Esaote MyLab 70 XVG by means of linear array transducer (10–22 MHz). Power Doppler settings were standardized (Doppler frequency 14.3 MHz, Gain 55%, PRF 750 Hz). PDUS measurements included sagittal scan of nailbed and fingertip qualitatively graded from 1 (no signal) to 4 (marked hyperemia) [2], and resistivity index (RI) of ulnar and radial proper digital arteries. Capillary density (number/mm) was calculated by NVC with magnification 200X performed on two images of the same digits examined by PDUS.
Results: 100 SSc patients, 87 (87%) women, 86 (86%) limited cutaneous SSc, median age 62.2 years old, median disease duration 8 years were evaluated. 7 (7%) patients had UAO. Concordance between fingertip and nailbed perfusion as assessed by PDUS is reported in Table 1.

Table 1

		Nailbed PDUS				Sum
		Grade 1	Grade 2	Grade 3	Grade 4	
Fingertip PDUS	Grade 1	15	19	3	1	38
	Grade 2	13	13	6	6	38
	Grade 3	3	5	10	10	28
	Grade 4	2	8	15	71	96
	Sum	33	45	34	88	200

Concordance between fingertip and nailbed perfusion as assessed by PDUS is equal to 0.7398. The lower 97.5% confidence interval limit is 0.6433.
Association between capillary density, and fingertip and nailbed perfusion as assessed by PDUS is shown in Table 2.

Table 2

	Capillary density	p-value of the difference between the mean of the category, with respect to reference (grade 1)
Fingertip PDUS		
Grade 1	2.895	
Grade 2	3.763	0.038
Grade 3	3.500	0.181
Grade 4	3.844	0.007
Nailbed PDUS		
Grade 1	3.212	
Grade 2	3.433	0.597
Grade 3	3.294	0.854
Grade 4	3.949	0.049

Conclusions: To our knowledge, this is the first study to correlate NVC and PDUS finding in SSc patients. Fingertip and nailbed PDUS grade concordance was found to be satisfactory. The mean capillary density tends to be greater with respect to grade 1. This is particularly evident comparing grade 4 and grade 1. As such, these two imaging techniques provide different and potentially complementary information on SSc-related peripheral microvascular involvement. There is potential clinical utility in these observations that has yet to be unlocked fully.
References:
[1] Lescoat A et al. Arthritis Care Res. 2016;Epub ahead of print.
[2] Newman JS et al. Radiology. 1996,198:582–584.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3859

FRI0678 ULTRASOUND-GUIDED SYNOVIAL NEEDLE BIOPSY: SINGLE CENTER EXPERIENCE OF AN EMERGING, MINIMALLY INVASIVE TECHNIQUE IN CLINICAL PRACTICE AND RESEARCH

V.C. Romao[1,2], J. Polido-Pereira[1,2], R. Barros[1], E. Vieira-Sousa[1,2], R. Luís[3], E. Vitorino[3], F. Saraiva[1], J.E. Fonseca[1,2]. *[1]Rheumatology Department, Hospital de Santa Maria, CHLN; [2]Rheumatology Research Unit, Instituto de Medicina Molecular, Faculty of Medicine, University of Lisbon; [3]Pathology Department, Hospital de Santa Maria, CHLN, Lisbon, Portugal*

Background: Synovial biopsy remains an important tool in clinical practice and research for the study of synovitis. Ultrasound-guided needle biopsy (USNB) has recently emerged as a minimally invasive technique, which enables collection of high quality synovial tissue with very good patient tolerance.
Objectives: To report the experience with USNB in our department, since its introduction in late 2013.
Methods: We reviewed the clinical files of all patients who had an USNB in our department. Degree of US joint synovitis was evaluated on a semi-quantitative scale (0–3) in terms of synovial thickness (ST) and power Doppler (PD). Since 2015, we assessed patient tolerance and acceptance of the procedure using a standardized questionnaire, which includes visual analogue scales (VAS) of pain, stiffness and swelling of the biopsied joint. Changes in US and VAS scores were assessed using the Wilcoxon signed-rank test.
Results: Forty-eight patients had 53 USNB, mostly for diagnostic purposes (79%), performed by 4 different operators - Figure 1. All types of joints were biopsied, mostly medium sized (26 wrists, 7 ankles), but also large (3 knees, 4 shoulders, 6 elbows, 3 hips) and small (1 sternoclavicular, 1 naviculocuneiform, 1 metacarpophalangeal and 1 proximal interphalangeal) joints, 2 bursae (subacromial) and 1 tendon sheath. USNB was repeated in the same joint (wrist) twice in 3 patients and three times in one patient. Procedures were well tolerated, with 67% of patients classifying it as easy or very easy, 78% reporting no or only mild discomfort and 77% considering likely/very likely to accept to repeat the biopsy. An increase in analgesic medication in the days following the biopsy was reported by 13 out of 44 questioned patients. After a median of 8 days following the procedure, a significant decrease was observed in VAS scores of pain, stiffness and swelling of the biopsied joint, although 23%, 23% and 31% of the patients reported small increases in these scores (median 9.5, 11 and 10mm, respectively). There was no significant change in US scores pre- and post-biopsy, with only 3 and 2 patients having an increase in ST or PD scores, respectively. Biopsies were overall safe, with 6 minor immediate adverse events (11%). There were no cases of haemartrosis, joint/periarticular

infection or neurovascular damage. Two patients reported transient limitation of the 5th and 1st digit extension following a biopsy of the wrist and 1st extensor compartment tendon sheath, respectively, with no detectable tendinous ruptures on US; 1 patient had a muscular hematoma of the extensor muscles of the forearm following an elbow biopsy.

	Patient & Biopsy characteristics (N=53)		
Age / Female	56 ± 18 years / 34 (64%)		
Diagnosis	21 RA, 13 UA, 8 septic, 5 crystal, 3 PsA, 1SpA, 2 other		
Disease duration	5.3 ± 7.1 years		
DAS28	4.3±1.2		
Clinical indication	42 diagnostic (79%), 11 research (21%)		
Joint size	16 large, 30 medium, 4 small, 2 bursa, 1 tendon sheath		
Infection confirmed	3/42 (7%)		
Immediate tolerance	29% very easy, 38% easy, 24% tolerable, 9% difficult		
Discomfort during procedure	36% no disc., 42% mild disc., 11% moderate disc., 5.5% mild pain, 5.5% intense pain		
Increase pain medication	13 (30%) in days following procedure		
Likelihood to repeat biopsy	41% very likely, 36% likely, 9% maybe, 14% unlikely		
Immediate AE	5 minor local bleeding, 1 transitory forearm extensor paralysis due to anesthesia		
Other AE	2 transient digit extension limitation (D5, D1), 1 muscular hematoma forearm		
	Pre-biopsy	**Post-biopsy**	**p-value**
VAS pain biopsied joint (mm)	62±25	46±29	0.001*
VAS stiffness biopsied joint (mm)	59±30	37±31	0.004*
VAS swelling biopsied joint (mm)	61±26	44±28	0.007*
US synovial thickness score	2.5±0.6	2.2±0.8	0.092
US Power Doppler score	1.0±1.2	1.0±1.1	0.414

*p-value significant at <0.05. AE, adverse events; D1, digit 1; D5, digit 5; DAS28, disease activity score 28 joints; disc., discomfort; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SpA, spondyloarthritis; UA, undifferentiated arthritis; US, ultrasound; VAS, visual analogue scale.

Conclusions: In our center, USNB has proved to be an effective technique for collection of synovial membrane that can be used for diagnostic and research purposes. The vast majority of the procedures were well tolerated, without significant worsening of local joint symptoms or synovitis, and safe, without major adverse events. Importantly, patients' concordance to repeat a USNB was mostly high.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4342

FRI0679 WHOLE SPINE AND SIJ MRI OF PSORIATIC ARTHRITIS PATIENTS: DESCRIPTIVE STUDY OF THE SPINE, AND SACROILIAC JOINTS INVOLVEMENT IN A CROSS SECTIONAL LARGE COHORT

V. Furer[1], M. Stark[2], H. Matz[3], D. Levartovsky[4], J. Wollman[4], I. Wigler[4], H. Sarbagil-Maman[4], D. Paran[1], I. Kaufman[4], M. Anouk[4], S. Borok[4], R. Zemah[4], A. Broyde[4], G. Flusser[5], I. Druckmann[5], O. Elkayam[1], I. Eshed[6]. *[1]Rheumatology, Tel Aviv Medical Center, Sackler School of Medicine; [2]Tel Aviv Medical Center, Tel Aviv, Israel; [3]Dermatology; [4]Rheumatology; [5]Radiology, Tel Aviv Medical Center, Tel Aviv; [6]Radiology, Sheba Medical Center, Sackler School of Medicine, Ramat Gan, Israel*

Background: Detection of axial disease has important implications. Data on the structural changes of the spine and SIJ in PsA is mainly based on plain XR and MRI of SIJ. The prevalence and distribution of spinal changes in PsA as detected by MRI is largely unknown.

Objectives: To evaluate acute and structural changes in spine and SIJ by whole spine MRI performed in a consecutive clinical cohort of PsA.

Methods: Adult PsA (CASPAR criteria) patients were enrolled in the study. All underwent clinical exam, CRP, HLA-B27 tests, and MRI of the entire spine and SIJ. Spinal sagittal T1-W, STIR and semi-coronal T1-W and T2-W with fat saturation sequences of the SIJ were performed. The spine was scored for the presence of syndesmophytes, bone marrow edema (BME)/fatty corners and enthesitis. SIJS were scored (Berlin score) for the presence of BME, fatty replacement, erosions, sclerosis, and ankylosis. Findings were further categorized into active sacroiliitis (ASAS[1]), structural sacroiliitis, and spinal findings compatible with SpA (≥3 BME or ≥4 fatty corners[2]). All MRIs were evaluated by an experienced musculoskeletal radiologist, blinded to clinical data. Data were analyzed by SPSS Version 20.0.

Results: Ninety six patients completed the study.(Table1) Active/structural/total sacroiliitis was detected in 26%/11.5%/37.5% of patients, respectively. Spinal SpA was demonstrated in 15.6%.(Table 2) Isolated spinal changes were detected in 2.1% of the cohort. Presence of inflammatory back pain (IBP) by ASAS correlated with the prevalence of active sacroiliitis (p 0.024) and SpA (axial/SIJ) (p 0.003). The extent of psoriasis severity (PASI) correlated with both SIJ and whole spine SpA changes. (*p 0.02 for both*) Gender differences or biologic therapy did not affect the prevalence of SIJ or spine involvement.

Table 1. Demographic and clinical data

Age (mean, yr)	50±13
Gender M:F	50:46
Psoriasis/PsA duration (mean, yr)	19±13.6/9±8
PASI	3.9±8.9
ASDAS-CRP	2.2±1
Back pain (%)/Inflammatory back pain by ASAS (%)	70%/30%
HLA-B27 (%)	4.4%
Current DMARD Tx (%)/Current biologic Tx (%)	45%/35%

Table 2. Whole spine MRI findings

	N (%) patients
Active Inflammatory Lesions	
≥1 BME corner	22 (23%)
≥1 posterior elements enthesitis	4 (4%)
Structural Lesions	
≥1 corner erosion	10 (10.4%)
≥1 fatty corner	30 (31%)
≥1 syndesmophytes	30 (31%)
Distribution of inflammatory lesions:	
Cervical 2.1%, Thoracic 18.8%, Lumbar 14.6%	
Distribution of structural lesions:	
Cervical 10.4%, Thoracic 32.3%, Lumbar 25%	

Conclusions: In the present PsA cohort, active and structural sacroiliitis was more prevalent vs typical spinal SpA changes. In particular, there was a paucity of SpA changes in the cervical spine. The most prominent axial findings included fatty corners and syndesmophytes. IBP presence and extensive skin disease correlated with SpA axial and SIJ changes.

References:

[1] Lambert RG. Ann Rheum Dis. 2016,75.
[2] Hermann KG. Ann Rheum Dis 2012.71.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4444

FRI0680 SYNOVIAL INTENSITY MEASURED BY ULTRASONOGRAPHY AS AN INDICATOR FOR JOINT INFLAMMATION IN RHEUMATOID ARTHRITIS PATIENTS UNDER TREATMENT

Y. Kondo, K. Suzuki, Y. Inoue, K. Sakata, C. Takahashi, M. Takeshita, Y. Kaneko, K. Yamaoka, T. Takeuchi. *Department of Internal Medicine, Division of Rheumatology, Keio University School of Medicine, Shinjuku, Tokyo, Japan*

Background: Ultrasonography (US) is a useful modality that can directly visualize RA joint inflammation. Recently, brightness of thickened synovium is considered to associate with local synovitis. However the accuracy of US findings with the local pathophysiology remains uncertain since synovial biopsy could be heterogeneous depending on the biopsy site and can be influenced by various medications. On another front, synovial fluid (SF) is homogenous, easy to access and contains abundant inflammatory cytokines and growth factors, which play an important role in the local pathogenesis of RA. However, the association between SF proteins and joint US findings is not clear.

Objectives: To clarify whether synovitis detected by US including synovial hypertrophy, vascularity and brightness reflect local joint molecular pathophysiology.

Methods: Forty-four RA patients were recruited. All patients were performed standardized US examination of knee joint. US images were evaluated by semi-quantitative scoring (synovial hypertrophy; grey scale (GS) US, vascularity; power Doppler (PD) US) and quantitative analysis by using Image J (National Institutes of Health, MD, Maryland USA). The average of the pixels of synovial tissue area (GS quant), PD signal area (PD quant) and mean gray values of synovium (Brightness) in 3 areas of the knee joint were calculated. US guided SF aspiration was performed on the same day and concentrations of cytokines and growth factors were measured by Cytometric Beads Array. (BD Biosciences, NJ, USA)

Results: Median age, disease duration and DAS28-ESR were 64 years, 1.5 years and 5.2 respectively. Mean GSUS and PDUS were 2.3 and 2.0. Nineteen patients were untreated. US inflammatory findings especially PD quant were well correlated with corresponding SF IL-6, IL-8, IL-1β and IL-10.(range of rho;0.40–0.72, $p<0.05$) synovial brightness also inversely correlated with SF VEGF (rho=-0.41, $p<0.05$). When we analyzed untreated and treated RA patients separately, GS quant did not correlate with any SF cytokines in treated group although, PD quant and brightness both significantly correlated with SF IL-6 and VEGF ($p<0.05$). Next, we divided the treated patients into 4 groups according to median of brightness and GS quant to compare the SF IL-6 levels. This analysis showed that SF IL-6 levels were influenced by synovial brightness rather than its hypertrophy. ($p<0.05$)

Conclusions: Our results suggest that not only US PD signals but also synovial brightness is a useful indicator for joint inflammation rather than synovial hypertrophy itself in treated RA patients.

References:

[1] Naredo E et al. Arthritis Rheum 2008; 58: 2248–56.
[2] Kelly S et al. Arthritis Res Ther. 2015 Mar 13;17:58.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4285

FRI0681 **CLINICAL VALIDATION STUDIES OF THE 2012 CLASSIFICATION CRITERIA FOR EARLY RHEUMATOID ARTHRITIS (ERA) IN A DOMESTIC MULTI-CENTER COHORT**

Y. Li[1,2], W. Fan[3], H. Chen[4], P. Yu[5], H. Miao[1], K. Li[3], J. Xu[4], L. Cui[5], G. Zhang[1], K. Xu[1], L. Zhang[1], R. Li[2]. *[1]Shanxi Academy of Medical Sciences Shanxi Dayi Hospital, Taiyuan; [2]Rheumatology and Immunology, Peking University People's Hospital, Beijing; [3]Xinxiang Central Hospital, Xinxiang; [4]the Third Hospital of Hebei Medical University, Shijiazhuang; [5]Kailuan General Hospital, Tangshan, China*

Background: Recently, a new classification criteria for early rheumatoid arthritis (ERA) have been developed.
Objectives: To evaluate the value of 2012 classification criteria for early rheumatoid arthritis (ERA), 2010 ACR/EULAR classification criteria, and 1987 ACR classification criteria in the diagnosis of early RA.
Methods: Early arthritis patients with age more than 16 years, disease duration no more than 1 year, Cat least one joint swelling and tenderness were enrolled in a multicenter, open, cross-sectional study cohort. The patients were diagnosed as RA or other none RA disease by 2 trained experienced rheumatologists. Detailed recorded the clinical and laboratory parameters include disease duration, morning stiffness duration, RF, anti-CCP, ESR, CRP etc.The sensitivity and specificity of three RA classification criteria were compared by McNemar test, The areas under the ROC curve (AUC) of each RA classification criteria were analyzed using MedCalc software.
Results: A total of 310 patients were randomly enrolled in this study, including 182 ERA and 128 non-RA. The sensitivity (88.5%) of ERA criteria were much higher than that of 1987 ACR criteria (45.6%, χ^2=75.013, P<0.0125), and not significantly different with the 2010 ACR/EULAR criteria (91.8%, χ^2=1.042, P>0.05). The specificity of ERA criteria (91.4%) were similar to those of 2010 ACR/EULAR criteria (87.5%, χ^2=1.8, P>0.05) and 1987 ACR criteria (96.1%, χ^2=3.1, P>0.05). The AUC of ERA criteria was 0.962 (95% CI: 0.934, 0.980), which was slightly better than that of the 2010 ACR/EULAR criteria [0.959 (95% CI: 0.931, 0.978), Z=0.380, P=0.7038], and much higher than that of the 1987 ACR criteria [0.885 (95% CI: 0.845, 0.919), Z=4.517, P<0.0001].

Table1. Demographic characteristics of 310 early arthritis

Groups	Cases	Age(year)	Gender		Disease duration (months)	SJC	TJC	Mouning stiffness ≥ 30min	
		$\bar{\chi}\pm s$	Female	%	$\bar{\chi}\pm s$	$\bar{\chi}\pm s$	$\bar{\chi}\pm s$	cases	%
ERA	182	48.2± 14.0	140	76.9	6.7± 3.9	8.6± 7.4	11.4± 7.7	136	74.7
Non-RA	128	42.8± 16.2	49	38.3	4.3± 4.1	2.0± 4.1	3.1± 5.5	17	13.3
P value		0.002	0.000		0.000	0.000	0.000	0.000	

Groups	Cases	ESR(mm/h)	CRP(mg/L)	IgM-RF(+)		抗CCP(+)		HAQ	
		$\bar{\chi}\pm s$	$\bar{\chi}\pm s$	例	%	例	%	M	Q1-Q3
ERA	182	39.7± 25.5	22.0± 28.2	138	75.8	131	72.0	0.7	0.3-1.2
Non-RA	128	32.3± 23.8	28.5± 39.7	8	6.3	2	1.6	0.4	0.2-0.8
P value		0.011	0.099	0.000		0.000		0.001	

SJC：Swollen joint counts；TJC：Tender joint counts

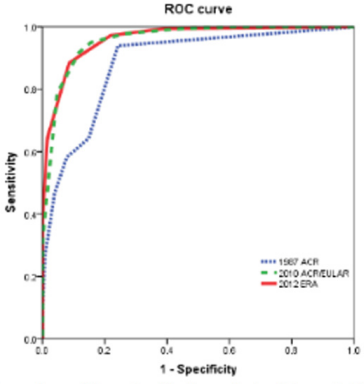


Fig.1 Comparison of three classification criteria of rheumatoid arthritis

Conclusions: Overall evaluation, the diagnostic value of ERA criteria is better than 1987 ACR and 2010 ACR/EULAR criteria in early rheumatoid arthritis. Compared to 2010 ACR/EULAR classification criteria, ERA criteria is obviously more simple and practical.

References:

[1] Li R, Sun J, Ren LM, et al. Epidemiology of eight common rheumatic diseases in China: a large-scale cross-sectional survey in Beijing[J]. Rheumatology, 2012, 51(4): 721–729.
[2] Radner H, Neogi T, Smolen JS, et a1. Performance of the 2010 ACR/EULAR classification criteria for rheumatoid arthritis: a systematic literature review[J]. Ann Rheum Dis, 2014, 73(1): 114–123.
[3] Cader MZ, Filer A, Hazlehurst J, et al. Performance of the 2010 ACR/EULAR criteria for rheumatoid arthritis: comparison with 1987 ACR criteria in a very early synovitis cohort[J]. Ann Rheum Dis, 2011, 70(6): 949–955.
[4] Ye H, Su Y, Li R, et al. Comparison of three classification criteria of rheumatoid arthritis in an inception early arthritis cohort[J]. Clinical Rheumatology, 2016, 35(10): 2397–401.
[5] Zhao JX, Su Y, Liu XY. et al. Classification criteria of early rheumatoid arthritis and validation of its performance in a multi-centre cohort[J]. Clinical and Experimental Rheumatology, 2014, 32(5): 667–673.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3112

FRI0682 **FOLLOW-UP OF TREATMENT RESPONSE WITH DYNAMIC DOPPLER ULTRASOUND IN RAYNAUD'SPHENOMENON**

U. Toprak[1], Z. Ozbalkan[2], M. Edugan[3], S. Parlak[4], S.C. Sandıkci[2], T. Kaya[4], S. Saylisoy[5]. *[1]Department of Radiology, Suleyman demirel University, Isparta; [2]Department of Rheumatology, Ankara Numune Education and Research Hospital, Ankara; [3]Department of Rheumatology, Istanbul University, Capa School of Medicine, Istanbul; [4]Department of Radiology, Ankara Numune Education and Research Hospital, Ankara; [5]Department of Radiology, Eskisehir Osmangazi University, School of Medicine, Eskisehir, Turkey*

Background: This study aims to investigate the role of flow parameters obtained by dynamic Doppler ultrasound in the objective follow-up of treatment response in Raynaud's phenomenon (RP) cases.
Methods: The study included newly diagnosed 33 patients with primary RP (PRP), 31 patients with secondary RP (SRP), and 26 healthy controls. The control group was evaluated with Doppler once, while the patients before treatment and on the third month of thet reatment. Baseline and post-cold provocation diameter (BD, CPD, mm) andflowvolume (BFV, CPFV, mL/min); post-coldprovocationflowstarting time (FST, min), and flowv olume normalizing time (FVNT, min) were recorded. Statistical analysis: for disturubution of thes ex of the groups: chi-square test, for analysing age distrubution among the groups One-way ANNOVA; for analysing the pre and post treatment doppler results: Wilcoxon test and fo rcomparison of the PRP and SRP post treatment values to control group; Krusal Wallis test were used. A p value less than 0,05 was considered statistically significant.
Results: Before-after treatment, there was no significant improvement in the BD in both PRP and SRP groups (0.79±0.17–0.82±0.19 vs. 0.66±0.13–0.68±0.14 PRP vs. SRP, respectively), while FST did not significantly improve in the PRP group (1.15±2.27–0.61±1.41 vs 3.13±4.81–1.58±2.36) (p>0.05). A significant improvement was observed in baseline flow volüme (3.08±2,96 vs 3.91±3.39 (p: 0,002),flow volume normalization time (7.24±7.60 vs 3.84±3.39) (p: 0,0001), after cold provocation flow volume (1.18±1,26 vs 2.17±2.16) (p: 0,0001), after cold provocated diameter (0.63±0.15 vs 0.70±0.16) (p: 0,005) in PRP group after treatment.
In SRP group, only baselined iameter changes were not influenced by the treatment, all other post treatmen tparameters were impoved in all SRP cases including baseline flow volume (2.14±1.94 vs 2.80±2.15) (p:0,009), after cold provocation diameter (0.56±0.15 vs 0.63±0.13) (p: 0.004), after cold provocation flow volume (1.07±1.40 vs 1.46±1.67) (p: 0,004), flow starting time (3.13±4.81 vs 1.58±2.36) (p: 0,021) and flow volume normalisation time (9.58±8.49 vs 4.32±3.56) (p: 0,0001).
There was an improvement in parameters after the treatment in both RP groups comparing by the control groups (p<0.01).
Conclusions: Doppler ultrasound is an objective, cost-effective, safe (does not include radiation), and easy-to-use method in thefollow-up of RP patients on macrovascular level with or without cold provocation before and after treatment.

Acknowledgements:
Keywords: Raynoud Phenomenon, treatment, Doppler ultrasound
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3122

FRIDAY, 16 JUNE 2017

Epidemiology, risk factors for disease or disease progression

FRI0683 **CAUSES OF DEATH IN 350 PATIENTS WITH SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES (SARD)**

J.G. Ovalles-Bonilla[1,2], O. Fernández[3], J. Martínez-Barrio[1], L. Valor[1,2], D. Hernández[1,2], I. Janta[1], B. Serrano[1], C. Sáenz[1], R. González[1], M. Correyero[1], L. García[1], A. López[1], A. Silva[1], J.C. Nieto[1], C. González[1,4], I. Monteagudo[1], F.J. López-Longo[1,4]. *[1]Rheumatology, Hospital General Universitario Gregorio Marañón; [2]Instituto de Investigación Sanitaria Gregorio Marañón, Madrid; [3]Rheumatology, Hospital Universitario de Basurto, Bilbao; [4]Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain*

Background: The major SARD have an increased mortality compared to the general population. It is well known that the main causes of death in Systemic Lupus Erythematosus (SLE) are infections (INF), cardiovascular events (CV), neoplasia

(NEO) and disease activity. However, the compared mortality of Mixed Connective Tissue Disease (MCTD), Systemic Sclerosis (SSc), Poly/Dermatomyositis (PM/DM), overlap syndromes (OS), Sjögren's syndrome (SS), Antiphospholipid syndrome (APS), systemic vasculitis (SV), and undifferentiated or incomplete Connective Tissue Disease (UCTD) is poorly described.
Objectives: To analyze the causes of death and the autoantibodies (AAB) profile among the SARD.
Methods: This was a single center, prospective and observational study. Mortality by all causes and relationship with AAB profile were analyzed in patients diagnosed of SLE, MCTD, SSc, PM/DM, OS (simultaneous or sequential criteria of 2 or more SARD), SS, APS, SV and UCTD or incomplete SARD (at least one clinical criterion of the classification criteria and a related antibody of any of the SARD). Data were obtained from the "Systemic Autoimmune Rheumatic Diseases Registry" of a tertiary referral hospital from 1986 to 2016. Patients with rheumatoid arthritis were excluded. The SARD registry counts with the institutional review board approval.
Results: 1750 patients were included, of whom 1453 (83%) were women. Five hundred fifty six SLE, 125 SSc, 111 PM/DM, 91 OS, 90 MCTD, 250 SS, 71 APS, 211 SV, 117 UCTD and 128 losses to follow-up, the global follow up rate was 92.7%. A global mortality of 350 (20%) cases was observed: 101 INF (28,8%), 89 CV (25,4%), 51 NEO (14,5%), 45 due to disease activity (12,8%), 41 other causes (11,7%) and 23 from unknown causes (6,5%). Table 1 shows detailed mortality causes compared by diseases. A higher mortality was associated ($p<0,05$) with older patients (71 years, 20–96), SV (OR 3,65), male patients (OR 1,95), SSC/PM/DM (OR 1,76), MCTD (OR 1,6) and OS (OR 1,43). AAB to pANCA (OR 4,43), anti-topoisomerase I (OR 3,64), myositis-specific AAB (OR 3.0), cANCA (OR 2,19) and anticardiolipin (OR 1,89) were associated with poorer survival. A higher survival rate was observed in patients with SLE (OR 1,7), SS (OR 1,69) and UCTD (OR 15,57) ($p<0,05$).

CAUSES	SLE, %	SSC, %	MCTD, %	SV, %	PM/DM, %	OS, %	SS, %	APS, %
CV	**30,86**	**27,02**	**42,3**	25,55	18,18	16,12	17,64	21,4
INF	27,16	21,62	3,84	**36,66**	**33,33**	**45,16**	23,52	21,4
NEO	14,81	13,51	15,38	8,88	18,18	9,67	**26,47**	14,28
ACTIVITY	9,87	18,91	19,23	11,11	12,12	19,35	11,76	**28,57**
OTHER	8,64	13,51	11,53	15,55	9,09	3,22	8,82	0.00
UNKNOWN	8,64	5,40	7,69	2,22	9,09	6,45	11,76	14,28

Conclusions: The main causes of death among SARD patients are CV (MCTD, SLE, and SSC), severe infections (OS, SV, and PM/DM), disease activity (APS) and neoplasia (SS). A higher mortality is observed among ANCA positive SV, anti-topoisomerase I positive SSC, MCTD, OS, anticardiolipin and myositis-specific positive patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5564

FRI0684 EARLY TREATMENT WITH METHOTREXATE IMPROVES ALL-CAUSE AND CARDIOVASCULAR SURVIVAL AMONG AN INCEPTION COHORT OF SENIORS WITH RHEUMATOID ARTHRITIS

J. Widdifield[1], J.M. Paterson[2], A. Huang[2], S. Bernatsky[1] on behalf of CANAIM.
[1]Mcgill University, Montreal; [2]Institute for Clinical Evaluative Sciences, Toronto, Canada

Background: We previously observed that incident RA patients have an increased risk of all-cause and cardiovascular disease (CVD) mortality relative to the general population in Ontario.[1]
Objectives: To evaluate the effect of treatment and other factors on all-cause and CVD mortality among incident senior RA patients.
Methods: We studied incident RA patients within the population-based Ontario Rheumatoid Arthritis Database (ORAD) who were diagnosed after their 65th birthdate (ensuring comprehensive drug coverage) between 2000 and 2013. Patients are included in ORAD if they received 3 physician billing RA diagnosis codes (with at least one provided by a MSK specialist) over 2 yrs OR at least 1 hospital RA diagnosis code. All patients were followed from cohort entry (when all case definition criteria were met) until death, out-migration, or end of study period (Dec 2013). Two multivariable Cox regression models were performed to estimate hazard ratios (HRs) for each outcome (all-cause and CVD mortality, separately), exploring the effects of both baseline/early treatment (within the year preceding index date) and time-varying medication exposures over the entire duration of follow-up (for methotrexate, other DMARDs, anti-TNFs, COXIBS, NSAIDs, glucocorticosteroids, statins, antihypertensives), baseline comorbidities (within 3 yrs prior to index date), time-varying development of extra-articular manifestations (as proxy for disease severity), healthcare use, and demographics (age, sex, rurality, SES).
Results: 28,172 incident RA patients were followed for 141,072 person years. During follow-up, 8,848 (31%) patients died with 1,419 (5%) deaths due to CVD, corresponding to an all-cause rate of 62.7 deaths (95% CI 61.4,64.0), and 10.1 deaths due to CVD (95% CI 9.5,10.6) per 1,000 patient-years, respectively. In our multivariable analysis focused on all-cause mortality, early treatment with methotrexate [HR 0.90 (95% CI 0.85,0.96)] and other DMARDs [HR 0.92 (95% CI 0.87,0.97)] were associated with a lower mortality risk. For CVD mortality, early treatment with methotrexate was associated with lower risk estimates [HR 0.71 (95% CI 0.60,0.83)], which was not clearly seen with other DMARDs [HR 0.94 (95% CI 0.82, 1.08)]. Use of COX-II inhibitors and NSAIDs at baseline were associated with lower HR for all-cause and CVD mortality risk, though we were unable to detect clear associations with greater use during follow-up. Greater cumulative exposure to glucocorticosteroids, comorbidities, and extra-articular manifestations of RA were associated with increasing risk of all-cause and CVD mortality.
Conclusions: Patients with early exposure to methotrexate had a lower risk of all-cause and CVD mortality. Our findings support the hypothesis that early treatment, by reducing inflammation, may help improve survival in RA. However, residual confounding cannot be ruled out.
References:
[1] Widdifield J, et al. Risk of Vascular Mortality in Seniors with New-Onset Rheumatoid Arthritis. Arthritis Rheumatol 2016; 68 (suppl 10).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3034

FRI0685 THE PRESENCE OF RHEUMATOID FACTOR IS ASSOCIATED WITH LOWER BONE MASS IN KOREAN HEALTH SCREENING MALE SUBJECTS WITHOUT CLINICALLY APPARENT ARTHRITIS

J. Hwang[1], J.K. Ahn[2], Y.H. Eun[3], E.-J. Park[4], J. Lee[3], E.-M. Koh[3], H.-S. Cha[3].
[1]Department of Internal Medicine, National Police Hospital; [2]Department of Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine; [3]Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul; [4]Department of Medicine, Jeju National University Hospital, Jeju, Korea, Republic Of

Background: Close relationship between the immune and skeletal systems has been recognized through the bone loss in rheumatoid arthritis (RA). Rheumatoid factor (RF) is present in approximately 70–80% of RA patients, which is an autoantibody directed against the Fc component of IgG and associated with osteoporosis and reduced bone mineral density (BMD) in RA. RF is also found nonspecifically in chronic inflammatory condition such as sarcoidosis, hepatitis B or C, and tuberculosis. However, the influence of RF to bone loss is scarcely known in subjects without any specific medical problem.
Objectives: This cross-sectional study aimed to investigate the association between the presence of RF and BMD in Korean healthy male subjects without any history of joint disease.
Methods: Of the 84,344 males who had undergone a comprehensive health checkup program in 2012, 1,390 healthy subjects were recruited, whose BMD and RF results were available. Subjects with history of diabetes, kidney disease, thyroid disease, and malignancy, and taking medicine regarding these diseases, osteoporosis, and arthritis were excluded based on self-reported questionnaire. The RF titer $\geq$20 IU/ml was considered positive. BMD was categorized into 3 groups based on T-score; normal (T-score $\geq$ -1.0), osteopenia (-1.0 $>$ T-score $>$ -2.5) and osteoporosis (T-score $\leq$ -2.5). The association between the presence of RF and BMD was assessed by multiple linear regression analysis.
Results: Of 1,390 males, the mean age was 52.8±10.9 years (range, 22 – 83) and RF was positive in 64 subjects (4.6%). Demographics including smoking history, alcohol consumption, the frequency of vigorous exercise and body mass index (BMI), and laboratory data were not different between RF-positive and –negative subjects except hepatitis B surface antigen, which was more frequently seen in RF-positive subjects (15.6% vs. 4.3%, p =0.001). Low bone mass (osteopenia and osteoporosis) of lumbar spine was more prevalent in subjects aged 50 or more compared with those younger than 50 years (28.0% vs. 10.7%, p $<$0.001) while no differences of femur neck and total hip. RF-positive subjects had significantly lower BMD compared to RF-negative subjects in lumbar spine (1.10±0.18 g/cm^{2}vs. 1.17±0.16 g/cm^2, p =0.002) but neither in femur neck nor total hip. In subjects with higher titer RF ($\geq$40 IU/ml), the mean BMD of lumbar spine was significantly decreased than those with lower titer RF (one-way ANOVA, F(3, 1190) =3.527, p =0.015). After adjusting for multiple confounders such as age, BMI, glomerular filtration rate, serum concentration of calcium, phosphorus, and uric acid, and lifestyle factors (drinking, smoking, and physical exercise), RF positivity was negatively associated with BMD at lumbar spine (B = -0.055 and SE =0.027, p =0.039).
Conclusions: Our results provide epidemiological evidence that the presence of RF could have an unfavorable impact on bone density in apparently healthy male subjects. Additional studies to elucidate the osteoimmunological mechanism of RF are warranted.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2645

FRI0686 NEGATIVE ASSOCIATIONS FOR FASTING BLOOD GLUCOSE, CHOLESTEROL AND TRIGLYCERIDE LEVELS WITH THE DEVELOPMENT OF GIANT CELL ARTERITIS

K. Jakobsson[1,2], L.T. Jacobsson[1,3], A.J. Mohammad[4,5], K.J. Warrington[6], E.L. Matteson[6], C. Turesson[1,2]. *[1]Department of Clinical Sciences, Malmö, Lunds University; [2]Department of Rheumatology, Skåne University Hospital, Malmö; [3]Department of Rheumatology & Inflammation Research, The Sahlgrenska Academy, University of Gothenburg, Institute of Medicine, Gothenburg; [4]Department of Rheumatology, Skåne University Hospital, Lund, Sweden; [5]Vasculitis and Lupus Clinic, Addenbrooke's Hospital, Cambridge, United Kingdom; [6]Division of Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, United States*

Background: Giant cell arteritis (GCA) is the most common vasculitis among patients age >50 years in north European countries. Although ethnic factors and age clearly play a role, the etiology of the disease is largely unknown. Studies of predictors are therefore of major interest. A meta-analysis of observational studies demonstrated that patients with GCA have a significantly reduced prevalence of diabetes at the time of diagnosis (1).
Objectives: To investigate metabolic features prior to diagnosis of GCA in a nested case-control study.
Methods: Individuals who developed GCA after inclusion in a population-based health survey (the Malmö Preventive Medicine Project; N=33346) were identified by linking the health survey database to the local patient administrative register and the national patient register. A structured review of medical records was performed. Four controls for every validated case, matched for sex, year of birth and year of screening, were selected from the database. Fasting blood samples had been obtained and analyzed using standard methods as part of the health survey. Potential predictors of GCA were examined in conditional logistic regression models.
Results: There were 76 cases with a confirmed clinical diagnosis of GCA (61% female; 65% biopsy positive; 95% fulfilled the ACR criteria for GCA). The mean age at diagnosis was 70 years, and the median time from screening to diagnosis was 20 years (range 2–32). The cases had significantly lower fasting blood glucose (fB-glucose) at baseline screening compared to controls [mean 4.7 vs 5.1 mmol/l, odds ratio (OR) 0.49 per mmol/l; 95% confidence interval (CI) 0.30–0.79]. Current smokers had a reduced risk of GCA (OR 0.35; 95% CI 0.18–0.70). The negative association between baseline fB-glucose and GCA remained significant in analysis adjusted for smoking (OR 0.46 per mmol/l; 95% CI 0.28–0.76). Both cholesterol (mean 5.6 vs 6.0 mmol/l) and triglyceride levels (median 1.0 vs 1.2 mmol/l) were lower among the cases at baseline screening, with significant negative associations with subsequent GCA in crude and smoking-adjusted (ORs with 95% CIs 0.66 per mmol/l; 0.46–0.94 for cholesterol, 0.33 per mmol/l; 0.16–0.69 for triglycerides) models. The effect of fB-glucose on the risk of GCA was stronger in men compared to women (smoking-adjusted ORs per mmol/l 0.11; 95% CI 0.03–0.37, and 0.77; 95% CI 0.50–1.18, respectively). Apart from this, results were similar in women and men.
Conclusions: Development of GCA was associated with lower fB-glucose, lower cholesterol and triglyceride levels at baseline, all adjusted for current smoking. These findings are in line with the previous findings of a reduced prevalence of diabetes mellitus at the time of diagnosis of GCA (1). This suggests that metabolic factors influence the development of GCA.
References:
[1] Ungprasert P et al Mod Rheumatol. 2016;26(3):410–414.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4245

FRI0687 BODY MASS INDEX, SMOKING, SOCIOECONOMIC STATUS AND THE RISK OF GIANT CELL ARTERITIS

K. Jakobsson[1,2], L.T. Jacobsson[1,3], A.J. Mohammad[4,5], K.J. Warrington[6], E.L. Matteson[6], C. Turesson[1,2]. *[1]Department of Clinical Sciences, Lunds University; [2]Department of Rheumatology, Skåne University Hospital, Malmö; [3]Department of Rheumatology & Inflammation Research, The Sahlgrenska Academy, University of Gothenburg, Institute of Medicine, Gothenburg; [4]Department of Rheumatology, Skåne University Hospital, Lund, Sweden; [5]Vasculitis and Lupus Clinic, Addenbrooke's Hospital, Cambridge, United Kingdom; [6]Division of Rheumatology, Mayo Clinic College of Medicine and Science, Rochester, Minnesota, United States*

Background: Few studies have examined predictors of giant cell arteritis (GCA). A negative association between body mass index (BMI) and development of GCA has been reported (1, 2). There is limited information on the impact of smoking and socioeconomic factors on the risk of GCA.
Objectives: To further investigate the relation between BMI and GCA, and also assess the role of smoking and socioeconomic factors in this context.
Methods: Two population based health-surveys, The Malmö Preventive Medicine Program (MPMP) and the Malmö Diet Cancer Study (MDCS), performed in the same catchment area between 1974 and 1996. In the MPMP, 33346 subjects (33% women), and in the MDCS, 30447 subjects (60% women) were included. Both surveys included standard physical examinations and self-administered questionnaires. Subjects were classified as blue-collar workers or white-collar workers, using the Socioeconomic Index (SEI) based on self-reported job titles in the Swedish national censuses.
Individuals who developed GCA after inclusion in the two health surveys were identified by linking the health survey databases to local and national patient registers. A structured review of the medical records was performed. Four controls for every validated case, matched for sex, year of birth and year of screening, were selected from the corresponding databases. Potential predictors of GCA were examined in conditional logistic regression models. This is an extension of a previous study, adding more incident cases (2).
Results: A total of 138 cases with a confirmed clinical diagnosis of GCA (median age at diagnosis 71 years; 72% female; 66% biopsy-positive; 94% fulfilled the ACR criteria for GCA) were included. The median time from screening to diagnosis was 15 years (range 0–32).
The cases who subsequently developed GCA had significantly lower BMI at baseline (24.3 vs 25.3 kg/m^2, odds ratio (OR) 0.91 per kg/m^2; 95% confidence interval (CI) 0.86–0.97) and were less likely to be current smokers when entering the health survey (OR 0.56; 95% CI 0.33–0.94). There was no difference in the proportion with low level of formal education between cases and controls (OR 1.27; 95% CI 0.66–2.44). Blue-collar workers tended to be less likely to develop GCA than white-collar workers (OR 0.53; 95% CI 0.28–1.00). This association reached statistical significance in women (OR 0.32; 95% CI 0.13–0.81) but not in men (OR 0.87; 95% CI 0.35–2.16). In multivariate analysis, including both variables and the SEI, the impact of BMI (OR 0.85; 95% CI 0.74–0.96) and smoking (OR 0.26; 95% CI 0.12–0.60) remained significant.
Conclusions: In this study, the negative association between BMI and subsequent GCA was confirmed, and there was an independent protective effect of smoking. Socioeconomic status, reflected by occupation later in life rather than level of formal education, may also influence the risk of developing GCA.
References:
[1] Larsson K et al Ann Rheum Dis 2006; 65:529–532.
[2] Jakobsson K et al Rheumatology 2015; 54:433–440.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4021

FRI0688 PRERA (PREDICTING RHEUMATOID ARTHRITIS): PRELIMINARY FINDINGS FROM AN ON-GOING PROSPECTIVE STUDY OF SEROPOSITIVE AND SERONEGATIVE INDIVIDUALS AND THEIR RISK FOR DEVELOPING RA

M. Mayr[1], M. Hucke[1], V. Nell-Duxneuer[1], T. Stamm[1], G. Steiner[1], T. Perkmann[1], E. Hitzelhammer[2], J. Smolen[1], K. Machold[1], H. Radner[1]. *[1]Rheumatology, Medical University of Vienna; [2]Health Centers of The Vienna General Health Insurance, Wien, Austria*

Background: A characteristic feature of RA is the presence of autoantibodies (AAB), such as rheumatoid factor (RF) and antibodies against citrullinated peptides (ACPA). RF and ACPA are not only diagnostically helpful but are also prognostic indicators for progression of joint destruction.
Objectives: This is an on-going prospective study to investigate the prevalence of AAB in healthy individuals presenting to community health centres and to subsequently determine the incidence of RA in AAB-positive individuals compared to AAB-negative persons over five years considering the presence of certain risk factors.
Methods: Blood drawn at the time of the screening examination was anonymously analyzed for the presence of AAB. AAB positive and age and sex matched AAB negative individuals (2 for each AAB positive subject) were enrolled for further assessment at the central outpatient clinic and examined every 6 months over 5 years. Assessment included laboratory testing (AAB, acute phase parameters), questionnaires on nutrition, lifestyle and general health, 28 joint counts (SJC28, TJC28), the health assessment questionnaire (HAQ), and visual analogue scales for pain and global health. Risk factors were analysed by clusters according to EULAR recommendations for terminology of individuals at risk of RA: hereditary, environmental, systemic autoimmunity and unclassified arthritis and the number of clusters per individual was reported at baseline (1). The primary outcome was the development of RA; individuals lost to follow up were telephone-interviewed for signs and symptoms of RA.
Results: 4858 sera were obtained from which 148 (3%) were seropositive (14 ACPA, 124 RF, 10 both). 113 individuals (2,3%) were followed over 5 years. 37 (32,7%) were seropositive of whom 32 (28,3%) were RF-positive, 2 (5,4%) were ACPA-positive and 3 (8,1%) positive for both. We found no significant differences in demographics and risk factors between seropositive and seronegative individuals at baseline (Table 1). The number of risk clusters per individuals is reported in

Risk Factors		Seronegative (*n*=76)	Seropositive (*n*=37)
Age		54,8 (±12,3)	57,6 (±10,3)
Genetic	Sex (% female)	50 (66%)	23 (62%)
	Family history	11 (14%)	3 (8%)
Environmental	Smoking	20 (26%)	8 (22%)
	BMI >25kg/m^2	37 (49%)	14 (38%)
	Low education	20 (29%)	16 (49%)
Unclassified Arthritis	SJC28	0 (0–2)	0 (0–2)
	TJC28	0 (0–2)	0 (0–3)
	Patient Global	8,9 (±16,8)	5,1 (±10,7)
	HAQ	0,07 (±0,17)	0,05 (±0,15)
	hsCRP	0,29 (±0,46)	0,21 (±0,27)

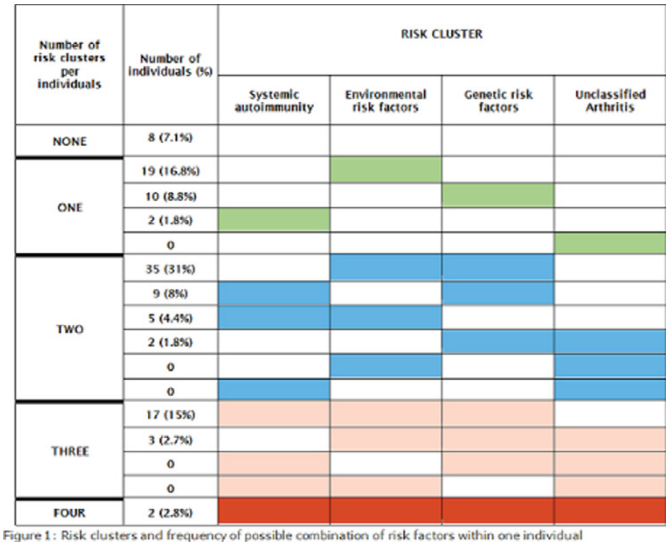


Figure 1: Risk clusters and frequency of possible combination of risk factors within one individual

figure 1. Until now, 43 people were followed for 5 years; additional 52 telephone interviews were conducted. No evidence of RA (clinically or by history) was found.
Conclusions: By now none of the followed individuals had any evidence of inflammatory joint disease based on patient-telephone interviews conducted and completed 5-year follow-up examinations. We were unable to find evidence for practical value of routine AAB screening in healthy individuals without clinical signs of inflammatory joint diseases.
References:
[1] Gerlag et al. (2012) Ann Rheum Dis 2012;71:638–641.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5951

FRI0689 LIPID PEROXIDATION AS RISK FACTOR FOR ENDOTHELIAL DYSFUNCTION IN ANTIPHOSPHOLIPID SYNDROME (APS) PATIENTS

L. Stojanovich, N. Stanisavljevic, A. Djokovic, M. Zdravkovic. *Internal medicine department, University Hospital Center Bezanijska Kosa, Belgrade, Serbia*

Background: APS pathophysiology is not clear enough yet since it has been implicated that aPL can activate cells (endothelial cells, monocytes, platelets), interfere with hemostatic reactions and activate complement reactions [1,2].
Objectives: The aim of this study was to evaluate oxidative stress markers and it relations to endothelial damage as risk factor for thrombosis in patients with primary (PAPS) and secondary (SAPS) antiphospholipid syndrome (APS) in correlation to traditional risk factors.
Methods: Flow mediated (FMD) and nitroglycerine (NMD) induced dilation of the brachial artery were studied in 140 APS patients (90 PAPS, 50 SAPS) and 40 controls matched by age, sex and conventional risk factors for atherosclerosis. Markers of oxidative stress: lipid hydroperoxydes (LOOH), advanced oxidation protein products (AOPP), total sulfhydryl grups (tSHG) and paraoxonase 1 activity (PON1) were determined by spectrophotometric method.
Results: Oxidative stress dominate in APS patients. LOOH and AOPP correlate to lipid fractions ($p<0.05$), unlike PON1, tSHG that correlated to antiphospholipid antibody positivity ($p<0.05$). FMD was lower in APS patients comparing to controls ($p<0.001$). Cholesterol is independent variable for FMD impairment in control group (p=0.011); LOOH in PAPS (p=0.004); LOOH, aCL and triglycerides in SAPS patients (p=0.009, p=0.049 and p=0.012, respectively).Combined predictive of aCL and LOOH is better for FMD impairment than LOOH alone in both PAPS and SAPS patients (AUC 0.727, p=0.001, 95% CI 0.616–0.837 and AUC 0.824, $p<0.001$, 95% CI 0.690–0.957, repectively).
Conclusions: Endothelial dysfunction is doubtlessly present in APS patients with oxidative imbalance as additional risk factor among other risk factors for clinical event. Anticardiolipin antibodies affect endothelial dependent vasodilatation in SAPS patients. We demonstrated synergistic effect of aCL and LOOH as risk for endothelial impairment in both PAPS and SAPS patients.
References:
[1] Foltyn Zadura A, Memon AA, Stojanovich L, Perricone C, Conti F, Valesini G et al (2015) Factor H Autoantibodies in Patients with Antiphospholipid Syndrome and Thrombosis. J Rheumatol 42(10):1786–93.
[2] Stalc M, Poredos P, Peternel P, Tomsic M, Sebestjen M, Kveder T (2006) Endothelial function is impaired in patients with primary antiphospholipid syndrome. Thromb Res 118:455–461.
[3] Becarevic M, Stojanovich L, Ignjatovic S, Dopsaj V. The IgM isotype of anti-annexin A5 antibodies and multiple positivity of conventional antiphospholipid antibodies: increasing the number of clinical manifestations of primary antiphospholipid syndrome. Clinical Rheumatology 03/2016; doi: 10.1007/s10067-016-3230–0.
[4] Ames PR, Batuca JR, Ciampa A, Iannaccone L, Delgado Alves J (2010) Clinical relevance of nitric oxide metabolites and nitrative stress in thrombotic primary antiphospholipid syndrome. J Rheumatol 37:2523–2530.
Acknowledgements: This work was supported by research grant number 175041, and TR 32040 for 2011 - 2017, issued by the Ministry of Science of the Republic of Serbia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2872

FRI0690 RISK OF FRACTURE AMONG PATIENTS WITH GOUT: A POPULATION-BASED COHORT STUDY

A. Abdul Sultan[1], R. Whittle[1], S. Muller[1], E. Roddy[1,2], C. Mallen[1], M. Blagojevic-Bucknall[1], T. Helliwell[1], S. Hider[1,2], Z. Paskins[1,2]. *[1]Research Institute for Primary Care & Health Sciences, Keele University, Staffordshire; [2]Haywood Academic Rheumatology Centre, Staffordshire and Stoke-on-Trent Partnership Trust, Stoke-on-Trent, United Kingdom*

Background: Gout is the most common type of inflammatory arthritis, affecting 2.4% of adults in the UK and is associated with a number of co-morbidities. Our understanding of the association between gout and fracture risk is limited with previous studies offering conflicting results.
Objectives: To determine the risk of fracture among gout patients and assess the potential impact of urate-lowering therapy (ULT) on fracture risk.
Methods: Utilising primary care records from Clinical Practice Research Datalink we identified patients with gout between 1990 and 2004 who were followed up until 2015. Each gout patient was individually matched to 5 individuals without gout based on age, sex, and registered practice. Absolute rate (AR) of fracture and hazard ratios (HR) were calculated using Cox regression models. We further stratified our analysis by age, gender and ULT prescription.
Results: We matched 35,857 patients with incident gout to 148,407 controls. Overall, we found no increased risk of fracture among gout patients compared to controls. However, men with no evidence of ULT had higher absolute risk of fracture compared to controls (AR=39 versus 26 per 10,000 person-years) corresponding to a 23% (HR=1.23; 95% CI 1.12–1.36) increased risk. The risk was particularly high for vertebral (HR=1.50; 95% CI 1.20–1.87) and wrist fracture (HR=1.45; 95% CI 1.21–1.74). Those treated with ULT had a 12% (HR=0.88; 95% CI 0.79–0.98) lower risk of fracture. Similar findings were not observed for women.
Conclusions: We found higher risk of vertebral and wrist fractures among men with gout not prescribed ULT. Those prescribed ULT had lower risk of fracture compared to the general population. Further research is needed to understand the role of ULT in fracture prevention.
Acknowledgements: CDM is funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care West Midlands, the NIHR School for Primary Care Research and a NIHR Research Professorship in General Practice. TH is funded by a NIHR Clinical Lectureship in General Practice and AAS is funded by NIHR Postdoctoral Fellowship. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3761

FRI0691 ASSOCIATION BETWEEN PERIODONTITIS AND THE RISK OF PALINDROMIC RHEUMATISM: A NATIONWIDE, POPULATION-BASED, CASE-CONTROL STUDY

H.-H. Chen[1], W.-C. Chao[1], Y.-M. Chen[1], D.-Y. Chen[2]. *[1]Department of Medical Research; [2]Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, Province of China*

Background: Some patients with palindromic rheumatism (PR) may develop a chronic connective tissue disease, mainly rheumatoid arthritis (RA). About one to two-thirds of PR patients developed RA during a period of follow-up. Periodontitis (PD) has been found to be associated with RA risk. However, the association between PD and PR risk is unknown.
Objectives: To estimate the association between a history of PD and the risk of incident PR.
Methods: This study used a nationwide, administrative database to identify PR cases and non-PR controls. After exclusion of individuals with rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, systemic sclerosis, dermatomyositis or polymyositis before the first PR diagnosis date (index date), we identified 4,421 newly-diagnosed PR cases from 2007 to 2012 and randomly selected 44,210 non-PR controls matched (1:10) for sex, age, and the year of the index date. After adjusting for comorbid diabetes mellitus, we estimated odds ratios (ORs) with 95% confidence intervals (CIs) by conditional logistic regression analysis to quantify the association between a history of PD and the risk of PR. The influences of the lag time and severity of PD were examined by calculating ORs for subgroups of patients based on time interval between the last PD-related visit and the index date and PD-related cumulative cost and visit number.
Results: This study showed an association between a history of PD and newly diagnosed PR (OR, 1.51; 95% CI, 1.41–1.61). The association remained significant after variation of PD definitions. The magnitude of the association was

Table 1. Univariable and multivariable conditional logistic regression analyses for the association between periodontitis defined by various definitions and the risk of palindromic rheumatism

	Univariable OR (95% CI)	Multivariable OR (95% CI)
Various periodontitis exposure definitions		
Periodontitis (ICD9: 523.3–5)	1.50 (1.41–1.60)	1.51 (1.41–1.61)
Chronic periodontitis (ICD9: 523.4)	1.36 (1.20–1.54)	1.37 (1.21–1.55)
Acute or chronic periodontitis (ICD9: 523.3–4)	1.56 (1.46–1.67)	1.57 (1.46–1.68)
Gingival and periodontal diseases (ICD9: 523)	1.56 (1.46–1.66)	1.56 (1.47–1.67)

greater in those who had shorter lag time between the last date of PD diagnosis and PR index date and those who had a higher number of visits for PD or greater cumulative cost of PD-related visits.

Conclusions: This study demonstrated a time- and dose-dependent association between PD exposure and PR risk.

References:

[1] Sanmarti R, Canete JD, Salvador G. Palindromic rheumatism and other relapsing arthritis. Best practice & research. Clin Rheumatol 2004;18(5):647–612.

[2] Chen HH, Huang N, Chen YM, et al. Association between a history of periodontitis and the risk of rheumatoid arthritis: a nationwide, population-based, case-control study. Annals Rheumatic Diseases 2013;72(7):1206–11.

Acknowledgements: The authors would like to thank the Biostatistics Task Force of Taichung Veterans General Hospital, Taichung, Taiwan, ROC for statistical support.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4719

FRI0692 ALLOPURINOL AND THE RISK OF VENTRICULAR ARRHYTHMIAS IN THE ELDERLY: A STUDY USING U.S. MEDICARE DATA

J. Singh, J. Cleveland. *University of Alabama at Birmingham, Birmingham, United States*

Background: Recent studies have shown that hyperuricemia and gout, a condition with hyperuricemia associated with joint inflammation and/or renal manifestations, are associated with a higher risk of coronary artery disease (CAD), acute cardiovascular events including myocardial infarction (MI) and stroke, and cardiovascular mortality. Emerging data suggest that gout and hyperuricemia may also be associated with cardiac arrhythmias such as atrial fibrillation

Objectives: To assess whether allopurinol use is associated with a reduction in the risk of ventricular arrhythmias (VA).

Methods: We used the 5% random sample of Medicare beneficiaries from 2006–2012 to examine new allopurinol use and the risk of incident VA. Multivariable Cox regression analyses were adjusted for demographics (age, race, gender), comorbidity, cardiac medications and conditions associated with VA. We calculated hazard ratios (HR) and 95% confidence intervals (CI).

Results: Of the 28,755 episodes of new allopurinol use, 2,538 were associated with incident VA (8.8%). Among patients with incident VA, 54% were male, 78% were White, and the mean Charlson-Romano comorbidity score was 4.8. The crude incidence of VA per 1,000,000 person-days declined as the duration of allopurinol use increased: 1–180 days, 151; 181 days-2 years, 105; and >2 years, 85. In multivariable-adjusted analyses, compared to non-use, allopurinol use was associated with lower HR of VA of 0.82 (95% CI, 0.76 to 0.90). Compared to allopurinol non-use, longer allopurinol use durations were significantly associated with lower multivariable-adjusted HR for VA: 1–180 days, 0.96 (95% CI, 0.85 to 1.08); 181 days to 2 years, 0.76 (95% CI, 0.68 to 0.85); and >2 years, 0.72 (95% CI, 0.60 to 0.87). Multiple sensitivity analyses adjusting for cardiac conditions, anti-arrhythmic drugs and alternate definitions confirmed our findings with minimal/no attenuation of estimates.

Conclusions: Allopurinol use and use duration >6 months were independently associated with a lower risk of VA. Future studies need to assess the pathophysiology of this potential benefit.

Disclosure of Interest: J. Singh Grant/research support from: Takeda, Savient, Consultant for: from Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology, J. Cleveland: None declared

DOI: 10.1136/annrheumdis-2017-eular.6811

FRI0693 SYNOVIAL CHANGES DETECTED BY ULTRASONOGRAPHY AND THEIR ASSOCIATION WITH OSTEOARTHRITIS-RELATED KNEE PAIN: A 1-YEAR PROSPECTIVE COHORT STUDY

A. Sarmanova[1,2], M. Hall[2,3], G.S. Fernandes[1,4], A.M. Valdes[1,2], D.A. Walsh[1,2], M. Doherty[1,2], W. Zhang[1,2]. *[1]Division of Rheumatology, Orthopaedics and Dermatology, The University of Nottingham; [2]Pain Centre, Arthritis Research UK; [3]School of Health Sciences, The University of Nottingham; [4]Centre for Sports, Exercise and Osteoarthritis, Arthritis Research UK, Nottingham, United Kingdom*

Background: Recently an important role for synovial pathology in the initiation and progression of knee osteoarthritis (OA) has been emphasised. Our previous cross-sectional study showed that synovial changes on US associated with knee pain (KP), but the association was confounded by radiographic severity [1]

Objectives: To examine whether these synovial changes associate with KP changes over 1 year.

Methods: 220 participants with early KP (<3yrs duration) identified from the Knee Pain and Related Health in the Community (KPIC, n=9514) survey in Nottingham, UK formed the cohort for this study. All participants had bilateral US and radiographic examination at baseline, and US was repeated after 1 year. KP was defined as pain in or around the knee on most days for at least a month, and KP severity was measured using a numerical rating scale (NRS 0–10). Change in KP severity was defined according to a Patient Global Impression of Change. Synovial changes (effusion, hypertrophy and Power Doppler (PD) signal) were measured by two observers (inter-observer concordance correlation was 0.8 (0.6 to 0.9) for effusion and 0.7 (0.5 to 0.9) for synovial hypertrophy). Standardised radiographs (semi-flexed weight-bearing and flexed skyline views) were scored using the Nottingham Line Drawing Atlas (NLDA). Radiographic OA was defined as definite joint space narrowing (grade 2) plus definite osteophyte (grade 2) in any compartment. An absolute change in effusion/synovial thickness/pain scores was calculated by subtracting the baseline measure from the follow-up measure within individuals. A correlation analysis was used to examine the association between changes in pain and changes in US values. Potential baseline predictors for KP worsening were examined using multivariate logistic regression analysis.

Results: Of 220 participants in this cohort, 165 (75%) had US measurements at baseline and follow-up (mean age 61yrs; 61% women; 24% ROA). The mean NRS score decreased from 4.44 to 3.01 mm. The mean depth of the effusion and synovial hypertrophy changed from 4.01 mm to 5.37 mm, and from 1.82 to 2.45 mm, respectively. There was no correlation between changes in pain on NRS and changes in US-detected synovial change (Figure 1).

At 1 year follow-up, 58% reported that their KP had improved from baseline, 16% reported worsening, and 27% reported no change in KP. After adjustment for age, gender and BMI baseline US features did not predict worsening pain, whereas ROA did (OR=4.06 95% CI 1.55 to 10.61).

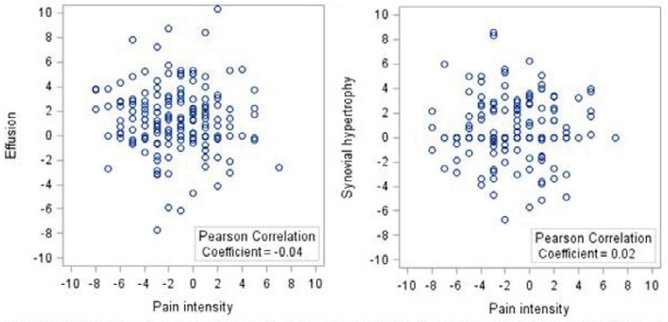


Figure 1. Correlation between changes from baseline in US features (in mm) and knee pain intensity (NRS 0-10)

Conclusions: This cohort study showed that US-detected knee "synovitis" was not a predictor of change in OA symptoms, whereas baseline radiographic OA severity was. It suggests that synovial changes detected by US might reflect aspects of OA pathology discrete from mechanisms driving OA pain change.

References:

[1] Sarmanova A, et al. Arthritis Rheumatol. 2016; 68 (suppl 10). http://acrabstracts.org/abstract/synovial-changes-detected-by-ultrasound-and-its-association-with-knee-pain-a-population-based-case-control-study/.

Acknowledgements: Arthritis Research UK (Grant Refs: 20777 and 20194) and Bolashak PhD Studentship.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5764

FRI0694 PREVALENCE OF RHEUMATIC DISEASE IN AN ADULT POPULATION FROM COLOMBIA. A COPCORD METHODOLOGY STUDY

A.M. Santos[1], J.C. Rueda[1], J.-I. Angarita[1], R. Giraldo[1], E. Forero[2], I. Pelaez-Ballestas[3], J.G. Ballesteros Muñoz[4], E.-L. Saldarriaga[1], J. Ramirez[5], C. Toro[5], J. Londono[6]. *[1]Reumatología, Universidad de la Sabana, Chia; [2]Medicina Interna, Reumatología, Universidad del Norte, Barranquilla, Colombia; [3]Departamento de Reumatología, Hospital General de México, Ciudad de México, Mexico; [4]Departamento de Medicina Interna, Hospital San José; [5]Asociación Colombiana de Reumatología; [6]Reumatología, Universidad de la Sabana-Hospital Militar Central, Bogotá, Colombia*

Background: Rheumatic diseases are the leading cause of permanent disability. In our country are the fourth cause of consultation in health institutions. The COPCORD model constitutes an effective tool in the determination of the prevalence of diseases. Globally, this model has been carried out in Asia, Europe and in some countries of Latin America. In Colombia the epidemiology of rheumatic diseases is not known globally; this would be the first national study that uses the data collection questionnaire using the COPCORD instrument

Objectives: To estimate the prevalence of rheumatic disease and related factors in a Colombian population over 18 years of age in six Colombian cities
Methods: A Cross-sectional analytical study was designed in people older than 18 years. A probabilistic stratified sampling method using three stages. The first stage of sampling was the selection of cartographic sectors in each city. The second stage of sampling was the blocks of each sector. The third stage of sampling was the homes of each block. All household members were surveyed. The sample size was calculated to be 6,528 people (2336 from Bogotá, 1220 from Medellín and Cali each, 746 from Barranquilla, 503 from Bucaramanga and Cúcuta each). The COPCORD questionnaire adapted for Colombia, was applied in the first stage by standardized interviewers. Positive cases were reviewed at home by a first year rheumatology fellow. To assess whether it is a rheumatic disease; the positive cases for a probable rheumatic disease were reviewed by a second year rheumatology fellow and reviewed again with laboratory and image studies by a certified rheumatologist to establish the definitive diagnosis
Results: 3,146 men and 3,547 women were included. Pain in the last 7 days not associated with trauma was reported in 3,213 (48%) participants. The most frequent sites were knees (right 31%, left 29%), hands (right 25%, left 24%), lumbar spine (18%) and shoulders (right 16%, left 14%). Table 1 depicts the prevalence of rheumatic diseases in Colombia

Table 1. Prevalence of Rheumatic Disease in Colombia

	Prevalence (%)	Variation Coefficient	CI 95%
Osteoarthritis	10,81	6	9,68–12,06
Gout	0,56	26	0,33–0,92
Fibromyalgia	0,72	22	0,47–1,11
Soft Tissue Rheumatism	25,82	6	11,60–19,93
Mechanic Low Back Pain	7,24	7	6,28–8,34
Inflammatory Low Back Pain	0,65	28	0,38–1,12
Spondyloarthritis	0,39	51	0,08–0,48
Rheumatoid Arthritis	1,49	15	1,12–1,98
Systemic Lupus Erythematosus	0,05	56	0,02–0,16
Sjögren Syndrome	0,08	61	0,02–0,27
Dermatomyositis	0,03	100	0,00–0,23
Scleroderma	0,02	100	0,00–14
CHIKV infection	6,68	8	5,73–7,78

CI: confidence interval; CHIKV: chikungunya virus.

Conclusions: Our study shows a similar prevalence to those worldwide in scleroderma, dermatomyositis, systemic lupus erythematosus, and spondyloarthritis. A lower prevalence was observed in Sjögren Syndrome, fibromyalgia, gout and osteoarthritis. A slightly higher prevalence of rheumatoid arthritis was observed in our population. The high prevalence of rheumatoid arthritis and soft tissue rheumatism should increase awareness in our governmental health entities given their long term disability risk
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5646

FRI0695 SERIOUS INFECTION ACROSS BIOLOGIC TREATED PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM A NATIONAL REGISTRY

A.I. Rutherford[1], S. Subesinghe[1], R. Byng-Maddick[2], K. Hyrich[3], J.B. Galloway[1]. *[1]Academic Rheumatology Department, King's College London; [2]Rheumatology, Homerton Hospital, London; [3]Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, United Kingdom*

Background: Infection is a complication of biologic therapy in RA.
Objectives: To describe the incidence and pattern of serious infection within the British Society for Rheumatology Biologics Register (BSRBR-RA) by drug.
Methods: The BSRBR-RA is a prospective observational study designed to evaluate the safety of biologics. Adverse events are coded using MedDRA defintitions. This analysis included patients with RA starting a biologic. They were considered at risk from their start date until 3 half-lives after stopping their biologic, death, first serious infection, or completion of three years of therapy, whichever came first. Event rates were compared across biologics using Cox proportional hazards with adjustment for age, gender, disease severity and duration, smoking, seropositivity, polypharmacy and baseline steroid usage.
Results: 19,282 patients were included in the analysis with combined follow-up time of 46,771 years. At baseline the mean age was 57 years, 76% female, mean disease duration 12.3 years and mean DAS28 6.1. 22% were current smokers and 64% had a positive rheumatoid factor. The incidence of serious infection for each biologic and hazard ratios for serious infections including by subclass are tabulated.
A sensitivity analysis limiting to 1st biologic exposure only did not significantly alter the estimates. A second sensitivity analysis limiting to new starters from 2010 found certolizumab still had a lower point estimate but findings were no longer significant (HR 0.79, CI 0.54–1.16).
Conclusions: Although the incidence of serious infection was lowest with certolizumab it is difficult to draw strong conclusions about comparative safety from observational studies due to channelling bias and unmeasured confounding. Rituximab and tocilizumab both had higher unadjusted rates of infection but in the adjusted model the rate was no different suggesting that patient factors as opposed to the drug itself were responsible for the observed difference.
Disclosure of Interest: A. Rutherford: None declared, S. Subesinghe: None declared, R. Byng-Maddick: None declared, K. Hyrich Grant/research support from: Pfizer, Speakers bureau: Abbvie, J. Galloway Consultant for: Roche, BMS, UCB, Pfizer
DOI: 10.1136/annrheumdis-2017-eular.1711

FRI0696 IMPACT OF ADALIMUMAB THERAPY ON BRACHIAL ENDOTHELIAL FUNCTION AND LARGE ARTERY STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

A.L. Demoux[1], K. Aissi[1], B. Chaudier[2], S. Carijn[3], P.-Y. Chouc[3], H. De Baillou[3], P. Rossi[1]. *[1]Internal medicine department, public hospital of Marseille; [2]Internal Medicine Deprtement, Laveran Hospital; [3]CONCERTO Association, Marseille, France*

Background: Anti-TNF alpha treatment may improve endothelial function and mechanical properties of large artery stiffness in patients with inflammatory rheumatic diseases, however studies remain controversial.
Objectives: To study the effect of TNF alpha blockage with adalimumab for 24 weeks on brachial endothelial function and sub-clinical markers of atherosclerosis in patients with inflammatory rheumatic diseases.
Methods: A total of 26 patients (14 males, 12 females; mean age, 47±11 years) with inflammatory rheumatic diseases (16, rheumatoid arthritis; 9, ankylosing spondylitis, 1, psoriasic rheumatism), resistant to disease-modifying antirheumatic drugs, were studied before the first infusion of adalimumab and again after 24 weeks of treatment. Endothelial function was assessed by measuring flow mediated dilatation using an ultrasound Doppler technique on the brachial artery. Other markers of sub clinical atherosclerosis were assessed by arterial stiffness via aortic pulse wave velocity, augmentation index and central blood pressure, and carotid intima-media thickness. Data for body mass index, disease activity using DAS-PCR and BASDAI, C-reactive protein, fasting glycaemia, and lipid profile were collected before treatment and after 24 weeks.
Results: 24 weeks of adalimumab therapy resulted in a reduction of disease activity score and serum levels of C-reactive protein. No significant differences were found in body mass index, total cholesterol, triglycerides and fasting glycaemia. Brachial blood pressure and heart rate remained similar, as well as carotid intima-media thickness. After 24 weeks of treatment with adalimumab, flow mediated dilatation improved significantly; central systolic and diastolic blood pressure decreased significantly; however central pulse pressure, augmentation index and aortic pulse wave velocity remained unchanged.
Conclusions: In patients with inflammatory rheumatic diseases, treatment with adalimumab for 24 weeks resulted in a significant improvement of endothelial function and central arterial pressure.
Disclosure of Interest: A. L. Demoux Grant/research support from: Abbvie, K. aissi: None declared, B. chaudier: None declared, S. carijn: None declared, P.-Y. chouc: None declared, H. de baillou: None declared, P. rossi: None declared
DOI: 10.1136/annrheumdis-2017-eular.6128

Abstract FRI0695 – Table 1

	Etanercept	Infliximab	Adalimumab	Rituximab	Tocilizumab	Certolizumab
Primary Analysis						
Follow-up (yrs)	15314	8829	13071	5910	1963	1685
Infections (single failure)	852	472	709	372	137	64
Incidence per 100 patient years (95% CI)	5.56 (5.20, 5.95)	5.35 (4.89, 5.85)	5.42 (5.04, 5.84)	6.29 (5.69, 6.97)	6.98 (5.90, 8.25)	3.80 (2.97, 4.85)
Serious Infection Hazard Ratio (95% CI)	Ref	0.94 (0.84, 1.06)	0.97 (0.88, 1.07)	**1.15 (1.01, 1.30)**	**1.22 (1.02, 1.47)**	**0.65 (0.51, 0.84)**
Adjusted HR (95% CI)	Ref	0.87 (0.77, 1.00)	0.98 (0.88, 1.08)	0.91 (0.80, 1.04)	1.17 (0.93, 1.47)	**0.69 (0.52, 0.92)**
Adjusted Hazard Ratio By Infection Class (95% CI)						
Sepsis/Bacteraemia	Ref	0.83 (0.41, 1.66)	1.04 (0.57, 1.91)	**2.08 (1.14, 3.80)**	1.83 (0.63, 5.35)	1.03 (0.24, 4.41)
Respiratory Infection	Ref	1.16 (0.96, 1.39)	**1.23 (1.04, 1.45)**	1.03 (0.83, 1.28)	**1.61 (1.15, 2.25)**	0.96 (0.63, 1.46)
Skin Infection	Ref	0.84 (0.66, 1.06)	**0.65 (0.52, 0.82)**	**0.54 (0.39, 0.75)**	0.71 (0.40, 1.24)	**0.27 (0.11, 0.67)**
Gastrointestinal Infection	Ref	0.95 (0.66, 1.38)	0.77 (0.54, 1.11)	0.93 (0.61, 1.42)	1.45 (0.72, 2.90)	0.51 (0.16, 1.63)
Bone/Joint Infection	Ref	**0.56 (0.38, 0.83)**	0.80 (0.58, 1.09)	0.67 (0.43, 1.02)	0.46 (0.17, 1.27)	0.73 (0.32, 1.68)
Genitourinary Infection	Ref	0.74 (0.50, 1.07)	1.18 (0.87, 1.59)	1.15 (0.79, 1.68)	0.67 (0.27, 1.66)	0.55 (0.20, 1.52)
Other	Ref	**0.54 (0.31, 0.91)**	1.08 (0.74, 1.58)	0.72 (0.41, 1.29)	1.15 (0.49, 2.67)	0.50 (0.16, 1.60)

FRI0697 FRENCH NATIONWIDE SURVEY OF CHRONIC PAIN PERCEPTION IN 1739 PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATISM

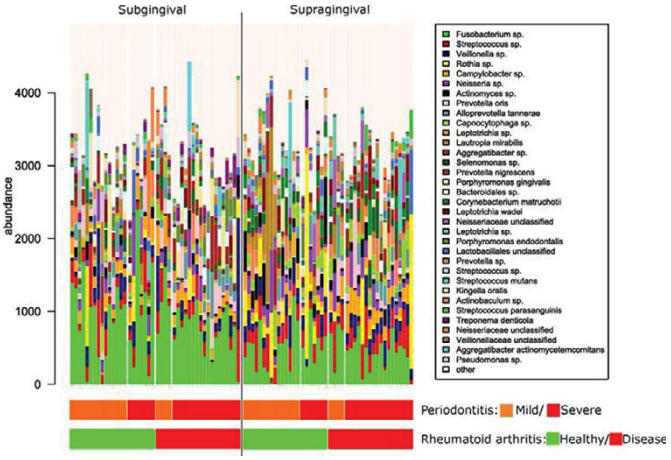
A.-P. Trouvin[1], C. Beller[2], P. Preiss[2], S. Perrot[3]. [1]*Rheumatology, Hopitaux Universitaire Paris Centre - Cochin;* [2]*Association AFPric;* [3]*Pain Center, Hopitaux Universitaire Paris Centre - Cochin, Paris, France*

Background: Pain is a major symptom in chronic inflammatory rheumatism. Pain intensity doesn't always correlate with disease activity and it can persist even when RA seems in clinical and biological remission. Little is known about the patients' perception of their treatment efficacy on pain, of pain influence in their life and their expectations for pain management. A French patients association (AFPric) conducted a national survey to explore patient's point of view on pain in their rheumatism.
Objectives: Describe in patients with chronic inflammatory rheumatism, their perception of treatment efficacy on pain, the impact of pain in their life and their expectations on pain care, in a nationwide survey.
Methods: A nationwide survey with a 20-item questionnaire was conducted. The questions were developed by patients and rheumatologists in focus groups. Questionnaires were e-mailed to every member of the association (9065 members). Answers were collected until the 17th July 2016. Answers were anonymous.
Results: One thousand thirty nine patients (response rate 19.2%) answered the questionnaire with 1510 women (86.8%), mean age was 59 years [18–85 years]. For more than half (58%) of the patients, their rheumatism had more than 10 years of evolution. Rheumatoid arthritis was the main rheumatism with 1377 patients (87%). Among the 1194 patients (76%) under conventional DMARDs 46.4% considered the cDMARDs efficacy on pain was between 70 and 100%, on the other hand for 17.7% of the patients, cDMARDs efficacy on pain was less than 30%. Among the 744 patients (47.6%) receiving a biological DMARD, 66.2% considered bDMARDs efficacy on pain was between 70 and 100% and 10% considered it was 30% or less. Among the 658 patients (42.3%) receiving oral corticosteroids, 56.6% considered corticosteroids' efficacy on pain between 70 and 100% and 12% considered it was less than 30%. Patients were asked to rate the weight of pain among their symptoms, for 38% of the patients pain represents 70 to 100% of the symptoms of their rheumatism, for 31.7% it represents 40 to 60% and for 30.3% 30% or less. The mean weight is 51.55% Almost half of the patients (46.8%) consider that their pain is underestimated by health professionals. For 37.2% of the patients, their current treatments are not appropriate for their current pain intensity. Finally 528 (35.7%) patients are not satisfied with pain management offered by health professionals, 90% of them think that pain management is too standardized and 80% think that functional impact of chronic pain is not taken in consideration. Among the expectations, 95% of the patients wish a tailored pain management by their rheumatologist, 82.9% wish to participate to support groups with health professionals specialized in pain care.
Conclusions: This nationwide survey on pain among chronic inflammatory rheumatism patients shows that even in the biological DMARDs era, pain is the main concerning symptom for the patients. It is striking in this large cohort that almost half of the patients consider their pain insufficiently taken care of.
Acknowledgements: This study received an institutional grant from UCB
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5781

FRI0698 PREVOTELLA AND ALLOPREVOTELLA SPECIES CHARACTERIZE THE ORAL MICROBIOME OF EARLY RHEUMATOID ARTHRITIS

B. Wolff[1], S. Boutin[2], H.-M. Lorenz[3], H. Ueffing[1], A. Dalpke[2], D. Wolff[1]. [1]*Department of Conservative Dentistry, School of Dental Medicine, University Hospital Heidelberg;* [2]*Dept. of Infectious Diseases-Medical Microbiology and Hygiene, University Hospital Heidelberg;* [3]*Division of Rheumatology, Department of Medicine V, Ruprecht Karls University, Heidelberg, Germany*

Background: We previously showed that in this early rheumatoid arthritis (ERA) cohort with a mean disease duration of <6 months, a clinically significant loss of clinical attachment loss as surrogate of alveolar bone loss is detectable compared with a matched healthy control cohort (1). Evidence is accumulating that distinct pathogens residing in reservoirs such as the oral cavity, the lung or the gut may play a role in driving the pathogenesis of RA (2–3).
Objectives: To characterize the oral microbiome associated with ERA.
Methods: 16S amplicon sequencing was used to analyze 88 samples of the supragingival and subgingival microbiome of 22 patients with ERA and 22 matched healthy controls. Oral and periodontal status, clinical activity of ERA and periodontitis, and socio-demographic parameters were used as explanatory variables in the next generation DNA sequencing analysis.
Results: Overall, a total of 4.702.161 16S RNA high-quality sequences were yielded. Using a distance-based similarity of >97% for species-level operational taxonomic unit (OTU) assignment, a total of 1054 OTUs were identified (Fig 1). The oral microbiota was equally rich and diverse in ERA and control group. Subgingivally, *Prevotella oris, Prevotella oralis, Prevotella nigrescens, Alloprevotella rava* and *Alloprevotella tannerae* were associated with early RA independent of severity of periodontitis.



Conclusions: Prevotella and Alloprevotella species were enriched in patients with early RA independent of severity of periodontitis. Further studies are needed to test a causal relationship of these species with onset and/or disease progression of RA.
References:
[1] Oral status in patients with early rheumatoid arthritis: a prospective, case-control study. Wolff B, Berger T, Frese C, Max R, Blank N, Lorenz HM, Wolff D. Rheumatology (Oxford). 2014 Mar;53(3):526–31.
[2] The lung microbiota in early rheumatoid arthritis and autoimmunity. Scher JU, Joshua V, Artacho A, Abdollahi-Roodsaz S, Öckinger J, Kullberg S, Sköld M, Eklund A, Grunewald J, Clemente JC, Ubeda C, Segal LN, Catrina AI. Microbiome. 2016 Nov 17;4(1):60.
[3] Expansion of intestinal Prevotella copri correlates with enhanced susceptibility to arthritis. Scher JU, Sczesnak A, Longman RS, Segata N, Ubeda C, Bielski C, Rostron T, Cerundolo V, Pamer EG, Abramson SB, Huttenhower C, Littman DR. Elife. 2013 Nov 5.
Acknowledgements: Wolff and Boutin contributed equally.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2874

FRI0699 DETERMINANTS OF 12-MONTHS PERSISTENCE IN ANKYLOSING SPONDYLITIS PATIENTS INITIATING SUBCUTANEOUS TNF-ALPHA INHIBITORS

B. Fautrel[1], M. Belhassen[2], C. Hudry[3], M.-C. Woronoff[4], N. Gouyette[5], A. Clément[5], E. Van Ganse[6], F. Tubach[7]. [1]*Sorbonne Universités, UPMC Univ Paris 06; AP-HP, Rheumatology Department, Pitié Salpétrière University Hospital, Paris, France., Paris;* [2]*Hesper 7425, Health Services and Performance Research, University Claude Bernard Lyon 1; PELyon, Pharmacoepidemiologie Lyon, Lyon;* [3]*AP-HP Hôpital Cochin, Paris;* [4]*CHU Besançon, Université Franche-Comté, Comue Ubfc, UMR INSERM 1098, Besançon;* [5]*Merck Sharp & Dohme, Paris;* [6]*Hesper 7425, Health Services and Performance Research, University Claude Bernard Lyon 1, PELyon, Pharmacoepidemiologie Lyon, Lyon;* [7]*APHP, Hôpital Pitié-Salpêtrière, Département de Biostatistiques, Santé publique et Information médicale, APHP, Centre de Pharmacoépidémiologie (Cephepi); INSERM, UMR 1123 ECEVE; Université Pierre et Marie Curie Paris 6, Sorbonne Universités, Paris, France*

Background: Biotherapies such as subcutaneous tumour necrosis factor-alpha inhibitors (SC-TNFis) have transformed the management of inflammatory joint diseases such as ankylosing spondylitis (AS). The assessment of SC- TNFis persistence and its determinants is needed.
Objectives: The objective of this study was to describe treatment persistence in real-world settings, and identify the determinants of persistence among AS patients initiating treatment with an SC-TNFi.
Methods: The French national health insurance scheme database lists all outpatient and inpatient healthcare consumption for individuals covered by the general health insurance scheme. Using French claims data, AS was diagnosed using Long Term Disease status and hospital admission, based on ICD-10 codes. Patients were then identified through prescription filled for adalimumab (ADA), etanercept (ETA), certolizumab pegol (CZP) and golimumab (GLM) between 2012/07/01 and 2013/12/31. A patient was considered as non-persistent in the event of a prolonged interruption of the therapy lasting 91 days or more. Persistence was estimated with Kaplan Meier analysis. Determinants of persistence in the 12 months before initiation were identified using Cox models.
Results: A total of 9,098 patients with AS were identified. In the descriptive analyses of the 12 months persistence, differences were observed for AS patients, with raw/non-adjusted persistence rates of 33.2% for CZP, 49.3% for ETA, 52.4% for ADA and 54.5% for GLM. Results of the Cox model are presented, including hazard ratio for biotherapy, adjusted on sex, age, socio-economic status, and criteria on disease severity. The variables biotherapy, socio-economic status and hospital admission for IRMD did not meet the proportionality hypothesis of risks,

and were corrected by the addition of a variable integrating the interaction with time.

Table 1. Determinants of 12-month non-persistence (Cox model)

	Hazard Ratio	IC 95%		P-value
SC-TNFis				
GLM	1.000	–	–	–
CZP	2.707	2.139	3.426	**<0.0001**
ETA	1.915	1.665	2.203	**<0.0001**
ADA	1.418	1.286	1.565	**<0.0001**
Sex				
Male	1.000	–	–	–
Female	1.377	1.300	1.458	**<0.0001**
Age	0.995	0.993	0.997	**<0.0001**
Deprived socio-economic status: Yes vs No	1.543	1.288	1.849	**<0.0001**
Number of comorbid conditions (per additional condition)	1.150	1.113	1.187	**<0.0001**
Biotherapy line (per additional line)	1.176	1.124	1.231	**<0.0001**
DMARD dispensation: Yes vs No	0.943	0.875	1.015	0.1182
Sulfasalazine dispensation: Yes vs No	0.996	0.915	1.084	0.9257
Long term oral steroids: Yes vs No	0.915	0.806	1.039	0.1719
Hospital admission for IRMD	0.883	0.792	0.984	**0.0249**
Visits to rheumatologist				
0	1.000	–	–	–
1–4	0.925	0.800	1.070	0.2959
>4	0.958	0.829	1.108	0.5645
Interaction with time				
Interaction biotherapy * time	1.001	1.001	1.001	**<0.0001**
Interaction socio-economic status * time	0.999	0.998	1.000	0.0132
Interaction hospital admission for IRMD * time	1.001	1.000	1.001	0.0335

Conclusions: Non-persistent patients were more likely female, with deprived socio-economic status, multiple comorbid conditions, and multiple line of biotherapy. Age, hospital admission for IRMD and treatment with GLM (compared to CZP, ETA and ADA) decreased the risk of non-persistence. Further analyses are needed to assess the impact of non-persistence.

Disclosure of Interest: B. Fautrel Grant/research support from: AbbVie, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgène, Hospira, Janssen, Lilly, MSD, NORDIC Pharma, Pfizer, Roche, SOBI, UCB, M. Belhassen Employee of: PELyon, C. Hudry Consultant for: ABBVIE, MSD, BMS, PFIZER, ROCHE, CELGENE, NOVARTIS, BIOGEN, UCB, SANDOZ, AMGEN., Employee of: COCHIN Hospital, M.-C. Woronoff: None declared, N. Gouyette Employee of: MSD France, A. Clément Employee of: MSD France, E. Van Ganse Consultant for: PELyon; ALK ABELLO; AstraZeneca; Bayer; BMS; BIF; GSK; IMS; LASER; MSD, F. Tubach: None declared

DOI: 10.1136/annrheumdis-2017-eular.5052

FRI0700 PHYSICAL ACTIVITY DECREASED SIGNIFICANTLY BUT MODERATELY DURING WEEKS WHERE PATIENTS REPORTED FLARES: A 3-MONTH STUDY OF 170 RHEUMATOID ARTHRITIS (RA) OR AXIAL SPONDYLOARTHRITIS (AXSPA) PATIENTS WEARING AN ACTIVITY TRACKER

C. Jacquemin[1], H. Servy[2], A. Molto[3], J. Sellam[4], V. Foltz[1], F. Gandjbakhch[1], C. Hudry[5], S. Mitrovic[1], B. Fautrel[1], L. Gossec[1]. *[1]Rheumatology, La Pitié Salpêtrière Hospital, Paris; [2]Sanoia, e-Health services, Gardanne; [3]Rheumatology, Cochin Hospital; [4]Rheumatology, Saint Antoine hospital; [5]Rheumatology, Private practice, Paris, France*

Background: RA and axSpA natural history comprises periods of low disease activity and flares. There is much interest in the concept of flares. Studies have indicated flares may alter patient quality of life, however, there are few data linking flares to quantifiable outcomes.

Objectives: The objective was to assess longitudinally the association between patient-reported flares and physical activity assessed objectively using an activity tracker.

Methods: This prospective multi-center observational study (ActConnect) included patients with definite RA (ACR/EULAR criteria) or axSpA (ASAS criteria) owning a smartphone. Physical activity was assessed continuously over 3 months by the number of steps using an activity tracker, and flares were self-assessed weekly using a specific flare question ("has your disease flared up during the last 7 days?")[1] with a categorical response according to: no flare, 1 to 3 days flare, or >3 days flare. The relationship between flares and physical activity for each week (time point) was assessed by linear mixed models adjusted on rheumatic disease, sex, age, obesity, biologics and employment status.

Results: 170/178 patients (91 RA and 79 axSpA patients; 1553 time points) were analyzed: mean age 45.5±12.4 years, mean disease duration 10.3±8.7 years; 60 (35.3%) were males and 90 (52.9%) received biologics. Disease was well-controlled (mean DAS28: 2.3±1.2; mean BASDAI: 3.3±2.1). Physical activity was moderate (mean steps/day, 7067±2770). Flares were frequent (25.5% of the questionnaires); most (76.8%) were of short duration. Flares, in particular >3 days flares, were independently associated with less weekly physical activity (p=0.02–0.03), leading to a relative decrease of physical activity of 12–21% and an absolute decrease ranging from 836 to 1462 steps/day (Table 1).

Conclusions: Flares were frequent in these low-disease patients, though most flares were of short duration. Flares were related to a moderate decrease in physical activity, confirming objectively the functional impact of patient-reported flares.

References:

[1] VP Bykerk et al, RMD Open, 2016; 2:e000225.doi:10.1136/rmdopen-2015–000225.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1753

FRI0701 DOES PARITY INFLUENCE JOINT DAMAGE PROGRESSION IN WOMEN WITH RHEUMATOID ARTHRITIS?

D. Alpizar-Rodriguez[1], F. Förger[2], D. Courvoisier[1], C. Gabay[1], A. Finckh[1] on behalf of Physicians of the Swiss Clinical Quality Management Program for Rheumatoid Arthritis. *[1]Rheumatology, Department of Medical Specialities, Geneva University Hospitals (HUG), Geneve; [2]Inselspital, Bern, Switzerland*

Background: Disease activity and severity of rheumatoid arthritis (RA) appear to be worse in women than in men [1]. The role of parity on disease activity is controversial, since pregnancy is characterized by a lower disease activity, but the postpartum period by an increase in activity [2]. Radiographic joint damage progression represents the cumulative effect of disease activity and allows us to study the long term effect of parity.

Objectives: To study the impact of parity on radiographic progression in women with RA.

Methods: This is an observational cohort study of RA patients included in the Swiss Clinical Quality Management in Rheumatoid Arthritis (SCQM-RA). Patients enrolled are followed-up yearly and have x-rays assessments at regular intervals. Information about female hormonal factors, such as pregnancies, breastfeeding, menstrual cycles and hormonal treatment were retrospectively retrieved using a questionnaire. For this analysis we included women with at least two x-rays and full information on reproductive factors. The primary outcome was the rate of radiographic progression (Ratingen erosion score) and the secondary outcome was functional disability progression (Health Assessment Questionnaire-Disability Index (HAQ-DI)). We compared the rate of progression between parous and nulliparous women using a multilevel regression model for longitudinal data,

Table 1. Characteristics of women SCQM

General and disease characteristics	Parous n=438	Nulliparous n=288
Age, years, median(IQR)	49 (40-57)*	45 (34-57)
Body mass index, kg/m², median(IQR)	24 (22-28)*	23 (21-27)
Ever smoking, n(%)	281 (64)	163 (57)
Alcohol consumption, n(%)	144 (33)	88 (31)
Disease duration, years, median(IQR)	0.4 (0.1-4.5)	0.4 (0.1-4.7)
ACPA positive, n(%)	294 (67)	201 (70)
Rheumatoid factor, n(%)	295 (67)*	217 (75)
DAS 28, median(IQR)	3.8 (2.8-5.0)	4.0 (2.9-5.1)
HAQ-DI, median(IQR)	0.8 (0.3-1.3)	0.6 (0.3-1.3)
Erosion score, %, median (IQR)	2.0 (0.5-4.9)	1.1 (0.1-4.7)
DMARD treatment, n(%)	332 (77)	223 (77)
Biologic treatment, n(%)	48 (11)	37 (13)
Glucocorticoid use, n(%)	120 (27)	72 (25)
Number of pregnancies, median (IQR)	2 (1-3)	-
Ever breastfeeding, n(%)	303(69)	-

*p-value <0.05, T-student or Kruskal-Wallis test for continuous variables and Chi-squared or Fisher's exact test for categorical variables. ACPA: anticitrullinated protein antibodies; DAS 28: 28-joint Disease Activity Score ESR; HAQ-DI: Health Assessment Questionnaire–Disability Index; DMARD: disease-modifying antirheumatic drugs.

Abstract FRI0700 – Table 1. Physical activity according to flare status in 170 RA and axSpA patients

	No flare (N=1157 assessments)	Flare (N=396 assessments)	p†	Flare ≤3 days (N=304 assessments)	p‡	Flare >3 days (N=92 assessments)	p‡
Number of steps per day	7197 (±2810)	6688 (±2618)	**0.03**	6792 (±2597)	0.17	6347 (±2670)	**0.02**
Range of absolute reduction of steps per day in flare	–	500–3504[a]	–	931–2794[b]	–	836–1462[c]	–
Range of relative reduction of steps per day in flare (%)	–	6.9–48.7[a]	–	13.5–40.6[b]	–	12.2–21.3[c]	–

The mean physical activity levels according to flare status are indicative data from pooled assessments. Results are expressed in mean (±standard deviation). †Linear mixed model with flare yes/no as the explanatory variable. ‡Linear mixed model with no/<3 days/>3 days flares as the explanatory variable. [a]Range considering flare duration from 1 to 7 days. [b]Range considering flare duration from 1 to 3 days. [c]Range considering flare duration from 4 to 7 days.

adjusting for potential confounders, such as age, disease duration, DAS 28 and treatment. In a subanalysis we explored if the x-ray progression was more severe during the active parous period, operationally defined as the 10 years following the first pregnancy or miscarriage.
Results: A total of 726 women were analysed, of which 438 (60%) were parous, with a median number of pregnancies of 2 (IQR: 2–3), a mean of 4.8 x-rays per patient and 10.9 years of follow-up. Baseline patients and disease characteristics were balanced, but parous women were older than nulliparous (median of 49 vs 45 years, p=0.001) (Table 1). During follow-up, erosion progression did not differ significantly between parous and nulliparous women (p=0.94). In a subanalysis, the radiographic progression during the active parous period was not different [0.6% (95% CI: 0.5 to 0.8) vs 0.5% (95% CI: 0.4 to 0.7) by year, respectively, p=0.28]. The decrease of the HAQ-DI score overtime was not different between parous and nulliparous women (p=0.21), and it was not different during the active parous period [-0.02 (95% CI: -0.03 to - 0.01) vs -0.02 (95% CI:- 0.03 to - 0.01) by year, respectively, p=0.67]. We did not find differences in radiographic progression or HAQ-DI score between women with a single pregnancy and multiparous women.
Conclusions: In women with RA, the progression of structural damage and of functional disability did not differ between parous and nulliparous women. Among parous women, the active parous period was not associated with more radiographic damage progression. Although postpartum period is associated with increase in disease activity, our results suggest that parity does not have a negative long term impact on structural damage.
References:
[1] Camacho EM, et al. Ann Rheum Dis. 2010; 69:1834–37.
[2] Pikwer M, et al. Arthritis Res Ther. 2015 Dec 12;17:358.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3915

FRI0702 2-YEAR OUTCOME OF 1077 PATIENTS WITH RECENT-ONSET INFLAMMATORY ARTHRITIS

E.S. Norli[1,2], G. Hetland Brinkmann[2,3], T.K. Kvien[2], O. Bjørneboe[1], A. Julsrud Haugen[3], H. Nygaard[4], C. Thunem[5], E. Lie[2], M.D. Mjaavatten[2].
[1]Rheumatology, Martina Hansens Hospital, Sandvika; [2]Rheumatology, Diakonhjemmet Hospital, Oslo; [3]Rheumatology, Østfold Hospital Trust, Grålum; [4]Rheumatology, Lillehammer Hospital of Rheumatic diseases, Lillehammer; [5]Rheumatology, Betanien Hospital, Skien, Norway

Background: Recent-onset inflammatory arthritis (IA) may represent a broad range of diseases. Few studies have examined the full spectrum of diagnostic outcomes in an unselected cohort of recent-onset IA patients.
Objectives: To describe the disease spectrum and 2-year outcome of recent onset IA in a large multicenter study in Norway.
Methods: Data from the Norwegian Very Early Arthritis Clinic (NOR-VEAC), a 2-year longitudinal observational study of 1118 patients (age 18–75 yrs) with inflammatory arthritis of ≤16 weeks duration, were used. Exclusion criteria were arthritis due to crystal deposits, trauma, osteoarthritis and septic arthritis. Herein we included all patients with follow-up information. Descriptive methods were applied to describe the whole range of diagnostic outcomes (clinical diagnoses made by the treating rheumatologist), as well as disease persistency (defined as disease modifying anti-rheumatic drug (DMARD) use and/or persistent joint swelling) vs resolution of disease for each clinical diagnosis. Patients with temporary DMARD use were classified as no-DMARD users if they were observed for ≥1 year after DMARD cessation. If a patient dropped out of the study before 2 years, the last outcome information was used in a last observation carried forward approach.
Results: 1077 patients (96.3%) were included in the current analyses, of these 64.9% had 2-year follow-up data. Duration of joint swelling before inclusion [median (25–75 perc.)] was 34 (13–66) days, mean (SD) age 46.1 (14.8) years, 54.7% were females, 16.9% anti-CCP positive, and 21.9% anti-CCP and/or RF positive. Presentation as mono-, oligo- (2–4 swollen joints), and polyarthritis (≥5 swollen joints) had approximately the same frequency, 32.5, 35.7 and 31.8%, respectively.
After 2 years 33.0% used DMARDs, and a further 9.3% had joint swelling without DMARD use. The arthritis resolved in the remaining 57.6%. The final clinical diagnoses and their respective outcomes are shown in Figure 1. The most common final diagnoses were undifferentiated arthritis (UA) (39.9%), rheumatoid arthritis (RA) (22.7%), reactive arthritis (17.1%), psoriatic arthritis (6.0%) and sarcoid arthropathy/Löfgren's syndrome (6.2%). A final diagnosis of sarcoid arthropathy, reactive arthritis and UA carried the best prognoses, with resolution of arthritis without DMARDs in 91.0, 85.9 and 73.7%, respectively. Patients presenting with polyarthritis developed persistent disease more often than patients with oligo- or monoarthritis (67.6%, 34.9 and 26.0%, respectively) (p<0.001).
Conclusions: Among 1077 patients with IA of ≤16 weeks duration, UA was the most common diagnosis after 2 years, 22.7% were diagnosed with RA and 6.0% with psoriatic arthritis. The arthritis resolved without DMARDs in the majority of the patients. This is, as far as we know, the first study to describe the whole range of diagnostic outcomes in an unselected cohort of recent-onset arthritis, as well as the persistency of disease according to each diagnosis.
Disclosure of Interest: E. S. Norli: None declared, G. Hetland Brinkmann: None declared, T. K. Kvien Consultant for: Tore K Kvien has received fees for speaking and/or consulting from AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, O. Bjørneboe: None declared, A. Julsrud Haugen: None declared, H. Nygaard: None declared, C. Thunem: None declared, E. Lie: None declared, M. Mjaavatten: None declared
DOI: 10.1136/annrheumdis-2017-eular.1354

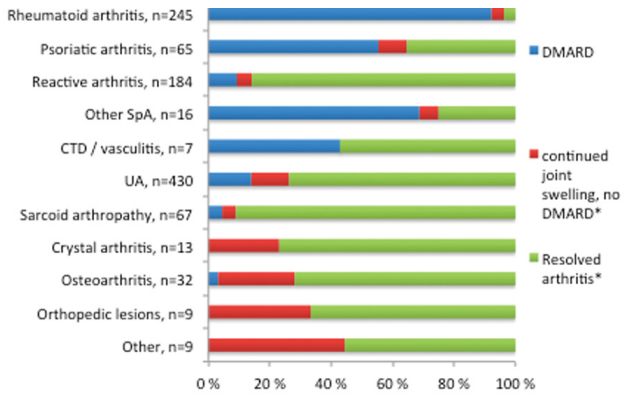


Figure 1. The final clinical diagnoses in 1077 patients with recent-onset inflammatory arthritis, and their respective outcomes
*DMARD use was allowed if the patients were observed ≥1 year after cessation. UA, Undifferentiated arthritis; SpA, Spondyloarthritis; CTD, Connective tissue disease

FRI0703 NEW INCIDENT CASES OF RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND POLYMYALGIA RHEUMATICA IN A CITY OF CENTRAL ITALY: RESULTS OF THE CAMPO-RE STUDY

A. De Socio, F.M. Perrotta, E. Lubrano. *Medicina e scienze della salute, Università degli studi del Molise, Campobasso, Italy*

Background: few studies reported the incidence of rheumatic disease in Italy using the most recent classification criteria.
Objectives: The aim of the CAMPO-RE study was to assess the new incidence cases of Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Polymyalgia Rheumatic (PMR) attending a primary rheumatologic outpatient's clinic of new institution, integrated in the community of Campobasso, a small town in the centre of Italy.
Methods: Campobasso has a population of 49,501 inhabitants (1st January 2016) and Public Health is managed from a single health authority in the entire area. In Italy, all citizens are registered with a National Health System of General Practitioner Physicians (GPP). Between 1st June 2014 to 31st May 2016 all consecutive adult patients, sent by GPP of the municipality of Campobasso with any diagnosis of musculoskeletal symptoms/signs complains were evaluated in a single rheumatology outpatient clinic of our Academic Unit, that represent the first and unique reference for the GPP about rheumatic diseases in the territory. Subjects were classified using the EULAR criteria for RA, the CASPAR criteria for PsA and the 2012 ACR classification criteria for PMR. New incident cases were calculated using the number of cases as the numerator and population based on 1st January census of the municipality of Campobasso as the denominator.
Results: 1003 adult patients, sent by GPP with articular or musculoskeletal complains were visited in our clinic. Of these, 409 patients inhabitants of the municipality of Campobasso were evaluated for the study. During the 2-years study period we diagnosed 18, 19 and 12 new cases of RA, PsA and PMR respectively, with a new incident cases rate of 18.18, 19.19 and 12.12/100,000/year on the whole population of Campobasso municipality. Age-related incident cases were also calculated (table 1).

Table 1. Annual incident cases of rheumatoid arthritis (RA), psoriatic arthritis (PsA) and polymyalgia rheumatica (PMR) trough two-years observation period in the town of Campobasso

Disease	Number of patients	Male/female	Incident cases (number/ 100,000 pt/year), total	Male (number/ 100,000 pt/year)	Female (number/ 100,000 pt/year)
RA	18	4/14	18.18	4.04	15.15
18–29 yr	1	0/1	7.69	–	16.1
30–49 yr	3	1/2	11.08	7.53	15.14
50–65 yr	7	1/6	31.16	9.52	50.15
>65 yr	7	1/6	32.08	10.86	47.56
PsA	19	10/9	19.19	10.1	9.1
18–29 yr	0	–	–	–	–
30–49 yr	6	3/3	22.66	22.61	22.71
50–65 yr	11	5/6	48.97	47.61	50.15
>65 yr	2	2/0	9.17	21.72	–
PMR	12	3/9	12.12	2.02	10.10
18–29 yr	0	–	0	0	0
30–49 yr	0	–	0	0	0
50–65 yr	0	–	0	0	0
>65 yr	12	3/9	54.99	32.58	71.34

Conclusions: The results of our study could contribute to better define the new incident cases of these rheumatic disease classified with the new classification

criteria. The incidences of RA, PsA and PMR seem to be similar to those reported in previous study[1–3].

References:
[1] Alamanos Y, Voulgari PV., Drosos AA. Incidence and Prevalence of Rheumatoid Arthritis, Based on the 1987 American College of Rheumatology Criteria: A Systematic Review. Semin Arthritis Rheum 2006;36:182–8.
[2] Catanoso M, Pipitone N, Salvarani C. Epidemiology of psoriatic arthritis psoriasis. Reumatismo 2012;64:66–70.
[3] Raheel S, Shbeeb I, Crowson CS, Matteson EL. Epidemiology of Polymyalgia Rheumatica 2000–2014 and Examination of Incidence and Survival Trends over 45 Years: A Population Based Study. Arthritis Care Res (Hoboken) 2016; [Epub ahead of print].

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4378

FRI0704 ANALYSIS OF RISK FACTOR FOR PREGNANCY OUTCOMES IN 142 PREGNANCIES COMPLICATED WITH CONNECTIVE TISSUE DISEASE

H. Shimada[1], K. Kanenishi[2], T. Kameda[1], M. Izumikawa[1], S. Nakashima[1], H. Ozaki[1], R. Wakiya[1], A. Kondo[1], N. Kadowaki[1], H. Dobashi[1]. *[1]Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine; [2]Department of Perinatology and Gynecology, Faculty of Medicine, Kagawa University, Kagawa, Japan*

Background: Recently, many connective tissue disease (CTD) patients wish to become a mother because immunosuppressants and biologics enable to improve the outcome of underlying CTD and quality of life respectively. However, Pregnancies in CTD patients often have problems including underlying disease exacerbation, some complications during pregnancy especially in preterm birth, light for date (LFD) and premature rapture of membrane (PROM). Previous study identified that high clinical activities with hypocomplementemia and positive anti-dsDNA antibody were at highest risk for pregnancy loss and preterm delivery in SLE[1)]. It is unclear whether these problems are associated with the activity of underlying CTD or immunosuppressant treatment.
Objectives: We examine the issue of pregnancy and delivery complicated with CTD by the analysis of the cases in our institution.
Methods: We investigated the risk factors of preterm birth, LFD (light for dates) and perinatal complication from exacerbation of underlying disease, anti SS-A antibody, antiphospholipid antibody, doses of corticosteroid, immunosuppressants or biologics before pregnancy in 142 cases which were delivered in our institution.
Results: In 23 among all cases underlying diseases were exacerbated, and these occurred more often in PM/DM (60%), MCTD (33.3%), RA (15.3%) and SLE (13.3%). In SLE, SS, MCTD and PM/DM, preterm births and LFD were closely related to disease exacerbation and dose of corticosteroid, pulse therapy, and these were extracted as risk factors for these perinatal complications. Preterm birth was also associated with low complement (CH50) and high titer of anti-dsDNA antibody, and LFD was associated with high titer of anti-dsDNA antibody before pregnancy. However, there was no significant association with these factors in threatened premature delivery and PROM. In RA, perinatal complications were not influenced by methotrexate and biologics before pregnancy. However, only LFD was related with doses of corticosteroid during pregnancy.
Conclusions: We extracted disease exacerbation and dose of corticosteroid, pulse therapy during pregnancy and also low complement, high titer of anti-double stranded DNA antibody before pregnancy as risk factors of pregnancy outcomes. In pregnancy complicated with CTD, we need to control the disease activity strictly, however, we should consider the increase or pulse therapy of corticosteroid carefully.

References:
[1] Clowse ME, Maqder LS, et al. The clinical utility of measuring complement and anti-dsDNA antibodies during pregnancy in patients with systemic lupus erythematosus. J Rheumatol. 2011 Jun; 38(6):1012–6.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5662

FRI0705 PROGRESSION OF CHRONIC DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AFTER 5-YEAR FOLLOW-UP: DATA FROM A LARGE MONOCENTRIC COHORT

I. Leccese, F. Ceccarelli, C. Perricone, L. Massaro, E. Cipriano, S. Truglia, F. Miranda, F.R. Spinelli, C. Alessandri, G. Valesini, F. Conti. *Lupus Clinic, Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Rome, Italy*

Background: The prevention of chronic damage represents one of the most important target in the management of patients affected by Systemic Lupus Erythematosus (SLE). About 50% of patients develop chronic damage, especially in the early disease phase, due to disease activity, treatment adverse events and comorbidities. Longitudinal studies demonstrated a progressive increase of damage, evaluated by using SLICC Damage Index (SDI).
Objectives: Moving from these evidences, we aimed at evaluating the progression of chronic damage in a monocentric SLE cohort with at least 5-year follow-up and identifying the factors associated with damage progression.
Methods: We analyzed 658 SLE patients diagnosed according to the ACR 1997 revised criteria, referring to a dedicated outpatient clinic. For the present analysis, we evaluated only patients with a minimum follow-up of 5 years and at least one visit per year. Clinical and laboratory data were collected in a standardized, computerized and electronically-filled form, including demographics, past medical history, comorbidities and concomitant treatments. In all patients, chronic damage was determined by using SDI, with the evaluation of 12 organ systems. Disease activity was evaluated by SLEDAI-2K. Furthermore, we calculated the number of flares during the follow-up, defined as an increase in SLEDAI-2K score $\geq$4 from the previous visit, with a minimum interval of 2 months between visits.
Results: According with the inclusion criteria, we analyzed data deriving from 198 SLE patients (17 M/181 F, mean±SD age 46.8±12.1 years, mean±SD disease duration 131±99.7 months). At the first visit 60 patients (30.3%) showed SDI$>$0; in particular SDI=1 was identified in 65%, SDI=2 in 18.3%, SDI=3 in 10%, SDI=4 in 6.7%). At baseline, the presence of chronic damage was significantly associated with age ($P<0.0001$) and disease duration (P=0.001). After 5 years, we registered the progression of chronic damage in 69 patients (34.8%), with a significant increase of SDI values (baseline: median SDI 0.0, IQR 0–1; follow-up SDI: median 0 IQR 0–2, P=0.009). SDI progression resulted significantly more frequent in subjects with damage at baseline (55.0%) in comparison with free-damage patients (26.1%, P=0.0001, Fisher exact test). The progression of chronic damage was significantly associated with neuropsychiatric involvement (P=0.01), disease activity in terms of number of flares during the 5-year follow-up (P=0.001), concomitant anti-phospholipid syndrome (P=0.02) and arterial hypertension (P=0.001).
Conclusions: In our study, we observed a progression of chronic damage in almost 30% of SLE patients after 5 years. In particular, the presence of previous chronic damage seem to be a risk factor for new damage development. Moreover, the lack of disease control and the presence of comorbidities allows damage progression. Taken together, the results of this study underline the need of a better management of SLE patients in order to prevent damage accrual.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6644

FRI0706 HLA-DRB1 ALLELES ARE ASSOCIATED WITH MARKERS OF ENDOTHELIAL INJURY IN FIRST-DEGREE RELATIVES OF RHEUMATOID ARTHRITIS PATIENTS

J.M. Hughes-Austin[1], M. Corr[2], G.S. Firestein[2], V.M. Holers[3], K.D. Deane[3], J.M. Norris[4], J.H. Ix[5,6]. *[1]Orthopaedic Surgery; [2]Rheumatology, Allergy, Immunology, UC San Diego, la Jolla; [3]Rheumatology; [4]Colorado School of Public Health, University of Colorado, Aurora; [5]Medicine, UC San Diego; [6]Nephrology, VA San Diego, la Jolla, United States*

Background: Rheumatoid arthritis (RA) patients experience higher cardiovascular disease (CVD) risk and CVD-related mortality. MHC class II HLA-DRB1 alleles, or the shared epitope (SE), has also been linked to endothelial dysfunction in RA patients. It is not known whether this association exists in individuals who are RA-free, but who are at higher risk due to being a first-degree relative (FDR) of an RA patient.
Objectives: To determine the association between HLA-DRB1 alleles (*0401, *0404, *0405, *0408) and markers of endothelial injury in FDRs of RA patients, a population free of RA and RA-related medications.
Methods: From the Studies of the Etiology of RA, SERA, (a multicenter prospective study of preclinical RA, started in 2002), 113 FDRs who had been positive for any of 5 RA-related autoantibodies (Abs): rheumatoid factor (RF), RF isotypes – IgM, IgG, IgA, or anti-cyclic citrullinated peptide (anti-CCP2) on at least one of their visits, and 100 FDRs who had never been Ab positive were selected, frequency matched on age, sex, and field center site. No FDR met the 1987 ACR Criteria or 2010 EULAR/ACR Criteria for RA. In cross-sectional testing of single samples from baseline, the following were measured: endothelial injury markers: soluble intracellular adhesion molecule-1 (sICAM), soluble vascular cell adhesion molecule-1 (sVCAM) and E-selectin; and high resolution HLA-DRB1 typing for the*0401, *0404, *0405, and *0408 alleles using real-time polymerase chain reaction. ANCOVA was used to evaluate associations between HLA-DRB1 alleles, sVCAM, sICAM, and E-selectin, adjusting for age, sex, race, body mass index (BMI), Ab status, ever smoking, and current statin use.
Results: Among 213 FDRs, age was 50±18 yr, BMI was 27±6, 75% were women, 83% were Caucasian, 35% ever smoked, 11% were currently taking statins, and 38% were SE positive. sVCAM was significantly higher by 135ng/mL in FDRs with the HLA-DRB1*0404 allele (p=0.009) compared to FDRs without the *0404 allele (Table 1). E-selectin was higher by 23ng/mL in FDRs with the HLA-DRB1*0405

Table 1. Differences in levels of endothelial injury markers by HLA-DRB1 alleles in FDRs of RA patients

	n (%)	ICAM (ng/mL)	p-value	VCAM (ng/mL)	p-value	E-selectin (ng/mL)	p-value
SE Positive	81 (38)	11.6 (8.8)	0.19	55.7 (32.5)	0.09	3.7 (2.2)	0.09
401	55 (26)	2.6 (10.0)	0.80	-14.1 (37.0)	0.70	0.4 (2.5)	0.86
404	23 (11)	21.1 (13.9)	0.13	135.4 (50.9)	0.009	6.4 (3.4)	0.06
405	2 (1)	55.1 (44.0)	0.21	186.0 (163.1)	0.26	22.9 (10.8)	0.03
408	6 (3)	-6.6 (25.4)	0.79	7.1 (94.1)	0.94	8.1 (6.2)	0.19

*n=213 (92 Ab+, 121 Ab–).

allele (p=0.03) compared to FDRs without the *0405 allele. Being positive for the SE was not significantly associated with sICAM, sVCAM, or E-selectin levels.
Conclusions: In RA-free FDRs, having an HLA-DRB1*0404 or HLA-DRB1*0405 allele was associated with markers of endothelial injury. Therefore, the genetic predisposition to RA could contribute to parallel development of atherosclerosis during the preclinical period of RA.
References:
[1] Gonzalez-Juanatey C et al., Am J Med 2003; 114:647–52.
[2] Gonzalez-Gay MA et al., Arth Rheum 2007; 57(1):125–132.
[3] Gersuk VH et al., J Immunol Methods. 2006 Dec 20; 317(1–2): 64–70.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4570

FRI0707 DRUG LEVELS AND ANTIDRUG ANTIBODIES IN THE DEVELOPMENT OF PARADOXICAL PSORIASIS AND PALMOPLANTAR PUSTULOSIS

J. Ruwaard[1], E. van der Vlugt[1], P. Brevet[1], L. Berkhout[2], T. Rispens[2], M. Nurmohamed[1], G.J. Wolbink[1,2]. [1]*Amsterdam Rheumatology and immunology Center | Reade;* [2]*Department of Immunopathology, Sanquin Research and Landsteiner Laboratory Academic Medical Centre, Amsterdam, Netherlands*

Background: The pathogenesis of psoriasis and palmoplantar pustulosis induced by Tumor Necrosis Factor inhibitors (TNFi) is largely unknown. Only one study, in 9 inflammatory bowel disease patients, investigated the relation with infliximab drug levels in the development of psoriasis or palmoplantar pustulosis and demonstrated no relation with of trough concentrations in these events (1). However, psoriasis and palmoplantar pustulosis were not studied separately.
Objectives: To study the differences in drug levels and antidrug antibodies (ADA) of TNFi in rheumatoid arthritis (RA) and ankylosing spondylitis (AS) patients who developed de novo psoriasis, palmoplantar pustulosis and those who did not develop skin adverse events.
Methods: In this retrospective study data was collected from the observational cohorts of Reade of consecutive RA and AS patients in whom TNFi was started. At every visit, serum samples were collected. We quantified the samples before/on time of event of the patients who developed psoriasis or palmoplantar pustulosis, for the patients with no skin adverse events (control group) at 24 or 28 weeks. Drug levels and ADA were measured with an Enzyme-linked immunosorbent assay and antibody binding test respectively.
Results: A total of 830 TNFi naive patients with RA and AS were included, of whom 21 developed psoriasis (n=11) or palmoplantar pustulosis (n=10). These patients were only observed in the adalimumab and etanercept cohorts. Sixteen patients with an event and 585 patients in the control group had serum samples available to quantify drug levels and ADA. No statistical significant differences were found in drug levels of adalimumab and etanercept for both RA and AS patients (table 1). Moreover, no statistical significant differences were observed in the detection of ADA between the three groups. However, no ADA were detected in patients who developed psoriasis or palmoplantar pustulosis compared to the overall 13.9% of the RA patients and 25.5% in AS patients.

Table 1. Differences in drug levels and detection of anti-drug antibodies between palmoplantar pustulosis, psoriasis and control group

		Druglevels adalimumab (μg/ml; median (IQR)		Drug levels etanercept (μg/ml); median (IQR)		Anti-drug antibodies adalimumab, no. (%)
RA						
Palmoplantar pustulosis	n=3	7,6 (0,01–12,0)	n=1	4,4	n=3	0 (0)
Psoriasis	n=3	8,5 (6,5–10,0)	n=2	2,3 (1,5–3,1)	n=2	0 (0)
Control group	n=153	7,4 (4,0–10,0)	n=89	2.7 (1.9–3.9)	n=151	21 (13,9)
p-value		0,992		0,380		0,674
AS						
Palmoplantar pustulosis	n=3	9,0 (6,5–10,0)	n=1	1,7	n=3	0 (0)
Psoriasis	n=1	10, 0	n=2	1,3 (0,8–1,7)	n=1	0 (0)
Control group	n=46	8,5 (3,7–11,3)	n=99	2.6 (1.4–4.0)	n=47	12 (25,5)
p-value		0,754		0,406		0,754

RA: rheumatoid arthritis; AS: ankylosing spondylitis; Control group: patients who did not develop skin adverse events; IQR: interquartile range; no. number of patients. p-value <0,05 was considered statistically significant.

Conclusions: Patients who develop paradoxical psoriasis and palmoplantar pustulosis have adequate drug levels and no ADA were detected.
References:
[1] J Crohns Colitis 2015 Nov;9(11):982–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3635

FRI0708 NEUROPATHIC PAIN IS A WEAK PREDICTOR OF NEW ONSET CHRONIC WIDESPREAD PAIN

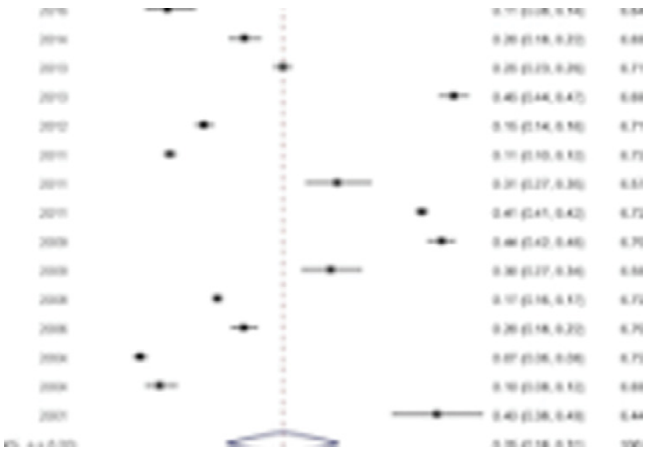
J. McBeth[1], M. Mulvey[2], A. Rashid[1], J. Anderson[1], K. Druce[1]. [1]*Arthritis Research UK Centre for Epidemiology, The University of Manchester, Manchester;* [2]*Leeds University, Leeds, United Kingdom*

Background: Regional pain (e.g. back pain) predicts incident chronic widespread pain (CWP), the clinical hallmark of fibromyalgia. Up to 20% of patients with CWP have neuropathic pain (NP). People with CWP and NP report similar pain characteristics including allodynia (pain in response to normal touch), have common risk factors (age, sex, body mass index, smoking and socioeconomic status) and a shared genetic predisposition. Whether NP is a risk factor for CWP is not known.
Objectives: To test the hypothesis that among persons free of CWP, NP would increase the risk of developing CWP.
Methods: In a population based study participant's pain reports were coded and those free of CWP (ACR criteria: pain lasting ≥3 months in the axial skeleton and contralateral body quadrants) identified. Participants also completed the Douleur Neuropathique 4 (DN4) (which has 7 sensory descriptors of pain (burning, painful cold, electric shocks, tingling, pins and needles, itching, and numbness), scores ≥3 indicating NP); demographics (date of birth, sex, English Index of Multiple Deprivation, occupational status); Hospital Anxiety and Depression (HAD) scale; Estimation of Sleep Problem Scale (ESPS); self-reported pain medications (summed to give a total count); and signed consent. Participants were classified as no pain, having some pain that wasn't neuropathic (NP-; DN4 score <3), or neuropathic pain (NP+; DN4 score ≥3). A follow-up questionnaire mailed 12 months later gathered pain data using the methods in the baseline survey. Based upon their pain reports at follow up participants were classified as "new CWP" for those who reported pain that satisfied the criteria for CWP, or "not CWP". Logistic regression estimated the odds of developing new CWP in the NP-, and NP+ groups compared to the no pain group. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). Population attributable fractions (PAF) estimated the % of new CWP that would be avoided if participants were not exposed to NP- or NP+.
Results: A total of 1162 participants who were free of CWP, completed the DN4 and provided pain data at follow up. Of those 523 (45.0%) had no pain at baseline, 562 (48.4%) had NP- and 77 (6.6%) had NP+. New onset CWP was reported by 153 (13.2%) participants; 19 (3.6%) of the no pain group, 108 (19.2%) of the NP- group, and 26 (33.8%) of the NP+ group. After adjusting for age and sex, compared to the no pain group, the NP- group was 3 times (OR 2.9, 95% CI (2.0, 4.2)) and the NP+ group 4 times (3.9 (2.3, 6.4)) more likely to have new CWP at follow up. These relationships were attenuated but persisted after adjustments for demographics, HAD, ESPS and medication use (NP- (2.9 (1.9, 4.3); NP+ (2.1 (1.1, 4.0)). The PAF was 41.3% (95% CI (25.2, 54.0)) for NP- and 6.0% (0.1, 11.6) for NP+. All of the individual DN4 characteristics except painful cold and itching predicted new CWP with PAF's ranging from 1.6% (0.1, 3.8) for pins and needles to 5.0% (1.1, 8.8) for burning.
Conclusions: NP predicts a small number of new onset CWP cases. CWP is highly prevalent in the general population and effective treatment of pain not of NP origin will have a significant impact on population levels of CWP.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1642

FRI0709 PREVALENCE OF RHEUMATIC DISEASES BASED ON COPCOPRD STUDIES: A SYSTEMATIC REVIEW

J. Moreno-Montoya[1], J. Rodriguez-Amado[2], R. Burgos-Vargas[3], I. Pelaez-Ballestas[3]. [1]*Universidad del Bosque, Bogota, Colombia;* [2]*Research Associate of South Florida, Miami, United States;* [3]*Rheumatology Unit, Hospital General de Mexico, Mexico, Mexico*

Background: Despite many efforts, to date there has been no focused attempt to derive a robust estimate of the prevalence of rheumatic diseases (RDs) to quantify how this is influenced by other factors than them examined in every local study, however, the problems magnitude is rising and due the demographic transition and the increase in the life expectancy
Objectives: To determine, through a systematic review and meta-analysis, the prevalence of RDs in the adult general population and explore its heterogeneity
Methods: MEDLINE, EMBASE, BIREME, LILLACS and Web of Science were searched using a search strategy combining key words and related database-specific subject terms to identify relevant cross-sectional based on COPCORD methodology studies. Also was developed a manual search. Included articles were assessed for risk of bias and quality based on the STROBE statement. Prevalence figures for RDs were analyzed according to female percentage of sampled individuals, mean age and sample size. A mixed effect model was used to obtain the combined prevalence and a meta-regression to estimate the effects of other variables
Results: 44 out from 127 papers were included in English, Spanish or Portuguese. Estimates for any RDs prevalence ranged from 7.2% to 62.3% (26.9%; 95% CI 18.3%>25.6%). For rheumatoid arthritis (RA), the prevalence varied between 0.2% and 6.2% (1.04%; 95% CI 0.4%>1.6%); fibromyalgia (FM) had a mean prevalence of 2.1% (95% CI 1.0%>3.2%) and osteoarthritis: 13.5% (95% CI: 10.6%>16.4%). SLE (systematic lupus erythematosus) was the less frequent condition with average prevalence of 0.14% (95% CI: 0.005%>0.28%). The random-effects pooled prevalence for any RDs was 25% (95% CI: 18.0%, 31.1%). Prevalence was higher in studies with bigger sample size (random effect coefficient: 0.0014, p=002). There was evidence of relevant heterogeneity in the analysis (p<0,001) and for RDs, RA and FM the sample size was positively associated to the perceived heterogeneity. No effects were found for SLE
Conclusions: It was found significant variation among the prevalence across this



review, in particular, related to the sample size used in each study. Two facts must be accounted for, first the statistical difficulties associated to the estimation of small prevalence and the consequent heterogeneity of the estimates, and, second, the limited number of studies included in this meta-analysis. Nonetheless, there is evidence about big heterogeneity what can correspond to non-observed variables, in particular, life-styles, and environmental or genetic traits.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3919

FRI0710 MONOSODIUM URATE CRYSTAL DEPOSITION ASSOCIATED WITH THE CHANGE OF RADIOGRAPHIC GRADE AT THE SACROILIAC JOINT IN AXIAL SPA: A DUAL-ENERGY CT STUDY

J. Zhu[1], A. Aiwu Li[2], E. Jia[2], Y. Zhou[3], J. Xu[2], S. Chen[2], Y. Huang[2], X. Xiao[4], J. Li[2]. *[1]Department of Rheumatology, Nanfang Hospital, Southern Medical University; [2]Department of Internal Medicine of Traditional Chinese Medicine, College of Traditional Chinese Medicine, Southern Medical University; [3]Department of Obstetrics, Guangdong Women and Children Hospital; [4]Department of Radiology, Nanfang Hospital, Southern Medical University, Guangzhou, China*

Background: Previous studies have revealed that ankylosing spondylitis (AS), as the progenitor of axial spondyloarthritis (AxSpA), has been characterized by the insidiously progressive nature of sacroiliitis and spondylitis. Dual-energy computed tomography (DECT) has recently been used to analyse the deposition of monosodium urate (MSU) crystals with higher sensitivity and specificity. However, it remains unclear whether the existence of the MSU crystal deposits detected by DECT at the sacroiliac joint in patients with AxSpA also contributed to the existing structural damage.

Objectives: We performed this study to show the DECT MSU crystal deposits in AxSpA patients without coexisting gout and to ascertain whether the MSU crystal deposits at the sacroiliac joint in those patients increased the risk of the structural joint damage.

Methods: One hundred and eighty-six AxSpA patients without coexisting gout were recruited. The plain radiographs of the sacroiliac joint were obtained, along with the DECT scans at the pelvis and the clinical variables. All statistics based on the left or right sacroiliac joint damage grading (0–4) were calculated independently. Bivariate analysis and ordinal logistic regression was performed between the clinical features and radiographic grades at the sacroiliac joint.

Results: At painful joints or skeleton regions, large quantities of MSU crystal deposits were found in 186 patients with AxSpA, as depicted in green with DECT. The average MSU crystal volume at the left sacroiliac joint, the right sacroiliac joint, and the pelvis were 0.902±1.345, 1.074±1.878, and 5.272±9.044 cm^3, values which were correlated with serum uric acid concentrations (r=0.727, 0.740, 0.896; $p<0.001$). At the left and right sacroiliac joint, the presence of MSU crystal deposits (=11.451, 43.684; $p<0.01$) and the volumes of MSU crystals (Z=9.198, Z=34.607; $p<0.05$) were statistically different among groups divided by the ASDAS scores. In bivariate analysis, wide clinical variables were associated with the changes in sacroiliac joint damage. When others factors were adjusted in the ordinal logistic models, the AxSpA duration, total back pain, BASFI score, and volume of MSU crystallization were the risk factors for the radiographic grade at the left sacroiliac joint (AOR=1.187, 1.428, 3.837, 2.018; $p<0.05$). The same risk factors were obtained for the right sacroiliac joint, except for total back pain. Additionally, the simplified models excluded the repeated variables; the AxSpA duration, BASFI score, and the volume of MSU crystallization at both sides of sacroiliac joint served as risk factors for the radiographic grade (left-AOR=1.180, 3.800, 1.920; right-AOR=1.190, 3.034, 1.418; $p<0.01$).

Conclusions: Large quantities of MSU crystal deposits detected by DECT were found in AxSpA patients without coexisting gout. In addition to AxSpA duration and BASFI score, the MSU crystal deposits at the sacroiliac joint in those patients independently increased the risk of structural joint damage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1417

FRI0711 DISCORDANCE OF THE FRAMINGHAM CARDIOVASCULAR RISK SCORE AND THE 2013 AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION RISK SCORE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

K. Jafri[1], A. Ogdie[2], P. Katz[1], J. Yazdany[1], G. Schmajuk[1,3]. *[1]Rheumatology, University of California, San Francisco, San Francisco; [2]Rheumatology, University of Pennsylvania, Philadelphia; [3]Rheumatology, Veterans Affairs Medical Center, San Francisco, United States*

Background: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are associated with an increased risk of cardiovascular (CV) disease, and multipliers to traditional 10-year CV risk scores, such as a EULAR-recommended 1.5 multiplier in RA, have been proposed to capture this increased CV risk. The discordance between CV risk assessment by the Framingham risk score, a modified Framingham risk score (with a 1.5 multiplier), and the more recent 2013 American College of Cardiology/American Heart Association (ACC/AHA) risk score has not been well-studied in patients with rheumatic diseases.

Objectives: To determine the proportion of discordant 10-year Framingham risk scores and 2013 ACC/AHA risk scores in subjects with SLE and RA, both with and without a 1.5 multiplier to the Framingham risk score, and to assess demographic, CV, and rheumatologic clinical characteristics associated with discordant risk scores.

Methods: A cross-sectional study was conducted using SLE and RA subjects drawn from the University of California, San Francisco, Arthritis, Body Composition, and Disability project. 10-year Framingham risk scores, modified Framingham risk scores (with a 1.5 multiplier), and 2013 ACC/AHA risk scores were calculated. As per Adult Treatment Panel-III (ATP-III) recommendations, a subject with a Framingham risk score (or modified Framingham risk score)$\geq$10% was defined as high-risk by that score, whereas a subject with a Framingham risk score (or modified Framingham risk score)$<$10% was defined as low-risk. A subject with a 2013 ACC/AHA risk score$\geq$7.5% was defined as high-risk by that score, whereas a subject with a 2013 ACC/AHA risk score$<$7.5% was defined as low-risk. A subject with a discordant risk score was defined as one who had a Framingham risk score (or modified Framingham risk score) that characterized him/her as low-risk and a 2013 ACC/AHA risk score that characterized him/her as high risk. Associations of demographic, CV, and rheumatologic characteristics with discordant risk scores were analyzed using chi-squared tests for categorical variables and using independent t-tests for continuous variables.

Results: 11 (7.0%) of the 157 SLE subjects and 11 (11.5%) of the 96 RA subjects had discordant CV risk scores with low Framingham risk scores but high ACC/AHA risk scores. When the 1.5 multiplier was applied to the Framingham risk score, the number of subjects with discordant risk scores did not significantly change. Rheumatologic disease duration, CRP levels, African-American race, diabetes, current use of anti-hypertensive medication, higher age, and higher systolic blood pressure were all significantly associated with discordant risk scores.

Conclusions: Approximately 10% of SLE and RA subjects had discordant 10-year CV risk scores with low Framingham risk scores but high ACC/AHA risk scores, even when a 1.5 multiplier was applied to the Framingham risk score. Prospective studies are needed to address the ability of different CV risk assessment tools, such as the 2013 ACC/AHA risk score, Framingham risk score, and modified risk scores, to predict CV events in rheumatologic patients, especially those with risk factors associated with discordant risk scores.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1171

FRI0712 DRIVERS OF UNREFRESHING SLEEP IN PEOPLE WITH MUSCULOSKELETAL PAIN

K.L. Druce, J. McBeth. *Arthritis Research UK Centre for Epidemiology, The University of Manchester, Manchester, United Kingdom*

Background: Waking feeling unrefreshed is associated with poor health outcomes including an increased risk of cardiovascular death. Pain is a robust predictor of waking feeling unrefreshed. Pain is a complex disorder and it is not clear whether the pain itself, or associated somatic symptoms, mental health conditions and lifestyle factors, predicts waking unrefreshed.

Objectives: To investigate whether reporting pain was an independent predictor of waking unrefreshed among people with musculoskeletal pain.

Methods: Participants in a population study completed the Estimation of Sleep Problems Scale (ESPS), which indicates the number of days in the past month participants have experienced unrefreshing sleep, problems with sleep onset, maintenance and night awakenings. Pain assessments (body map and duration $>$3 months) were used to classify participants as having no pain, acute pain, chronic pain and CWP (ACR criteria: pain lasting $\geq$3 months in the axial skeleton and contralateral body quadrants). Participants also reported demographics (date of birth, sex, English Index of Multiple Deprivation); somatic symptoms (Chalder Fatigue Scale (CFQ 11) and Inflammatory Bowel Syndrome (IBS)); mental health (Hospital Anxiety and Depression (HAD) scale); disability (Stanford Health Assessment Questionnaire (HAQ)) and lifestyle factors (average number

of alcoholic drinks per week, smoking status and Rapid Assessment of Physical Activity (RAPA)). Univariable ordinal logistic regression tested the relationship between pain and waking unrefreshed. The model was then cumulatively adjusted for sleep, somatic symptoms, mental health, disability and lifestyle domains. All models were age, sex and deprivation adjusted. The results of a complete case analysis were comparable to those which used multiple imputation for missing data and the results of the complete case analyses are shown. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI).

Results: Of 1913 people who had complete data, 1376 (72%) woke unrefreshed on at least one day in the past month (41% 1–7 days; 31% ≥8 days). Compared to those with no pain, people with acute pain and chronic pain were two (OR 2.0, 95% CI (1.5–2.6) and 2.2 (1.9–2.7), respectively) times more likely to wake unrefreshed; those with CWP were five (5.0 (4.0–6.3)), times more likely to wake unrefreshed. Following adjustment for all other variables, the relationship between reporting chronic pain (1.5 (1.2–1.8)) or CWP (1.9 (1.4–1.5)) and waking unrefreshed was attenuated, but remained statistically significant. The reporting of acute pain was not an independent predictor of waking unrefreshed (1.4 (0.98–1.9)). Problems with sleep onset (≥8 days vs 0: 2.9 (2.0–4.1)) and maintenance (≥8 days vs 0: 5.9 (4.1–8.4)), night awakenings (≥8 days vs 0: 2.5 (1.7–3.7)), IBS (2.2 (1.2–4.0)), currently smoking (vs never: 1.5 (1.02–2.1)) and engagement in activities such as stretching and yoga (vs none: 0.8 (0.6–0.97)), physical (1.3 (1.2–1.3)) but not mental (0.99 (0.9–1.1)) fatigue, and anxiety (definite vs no: 2.4 (1.8–3.1)), but not depression (definite vs no: 1.5 (0.8–2.6)), were associated with waking unrefreshed.

Conclusions: This study suggests that among people with chronic pain, the risk of waking feeling unrefreshed may be reduced through interventions that target factors such as smoking cessation, IBS management, physical fatigue and anxiety.

Acknowledgements: J. Anderson, M. Mulvey, A. Rashid
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1798

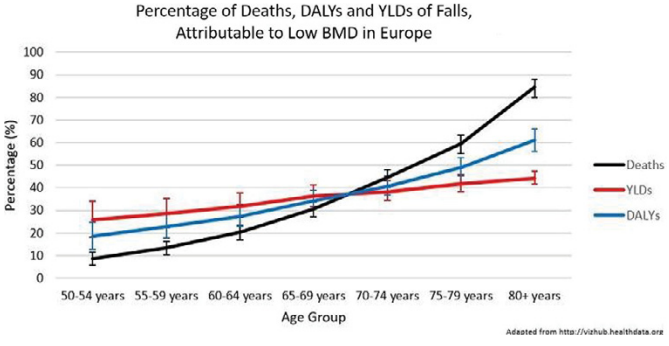
FRI0713 LOW BONE MINERAL DENSITY IS THE MAIN CONTRIBUTOR TO FALLS-RELATED HEALTH BURDEN IN THE EUROPEAN ELDERLY

L. Sanchez-Riera[1], N. Wilson[2], D. Prieto-Alhambra[3], C. Cooper[4], K. Dreinhöfer[5], A. Woolf[6], L. March[2], P. Halbout[7]. *[1]University Hospital Bristol NHS Foundation Trust, Bristol, United Kingdom; [2]Institute of Bone and Joint Research, University of Sydney, Sydney, Australia; [3]Oxford NIHR Musculoskeletal Biomedical Research Unit, University of Oxford, Oxford; [4]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, United Kingdom; [5]Center for Musculoskeletal Surgery, Charité Universitätsmedizin, Berlin, Germany; [6]Institute of Health Research, University of Exeter Medical School, Exeter, United Kingdom; [7]International Osteoporosis Foundation, Nyon, Switzerland*

Background: Falls are the leading injury type in elderly populations and a major health burden and cause of death globally. Most of such burden is due to bone fractures. In the Global Burden of Diseases (GBD) Initiative, the attributable burden of falls due to low bone mineral density (BMD) was analysed through its relationship with fractures.

Objectives: To measure the percentage of disability-adjusted life years (DALYs), years lived with disability (YLDs) and deaths due to falls attributable to low BMD in European population for the year 2015.

Methods: The estimates followed the Counterfactual Risk Assessment Methodology used in the GBD study (1). Systematic review was performed seeking population-based studies with femoral neck (FNBMD) measured by Dual-X-Ray-Absorptiometry in people 50 years and over. Age- and sex- specific levels of mean +/-SD FNBMD (g/cm^2) were extracted from eligible studies, and this was used as the exposure variable. The age and sex-specific 99th percentile from non-Hispanic whites in the National Health and Nutrition Examination Survey (NHANES) 2009–2010 was used as theoretical minimum risk factor exposure distribution, to estimate the potential impact fraction (PIF) of FNBMD for fractures. Relative risks of FNBMD for fractures were obtained from a previous meta-analysis (2). Coded hospital data was used to calculate the fraction of falls-related deaths due to fractures. Disability levels were established by applying disability weights to each type of fracture. Then, PIFs were applied to obtain attributable deaths and disability due to low BMD.



Results: The percentage of falls-related preventable deaths attributable to low BMD is around 9% in the 50–54 age group, increasing to 84% in those aged 80 years and over. Total health burden (DALYs) and disability attribution (YLDs) also increase with age, from 19% and 25% in 50–54 years old, respectively, to 61% and 44% and population aged 80 years and above, respectively. Low BMD constitutes the most important preventable risk factors for falls-related DALYs from 50 years and above, followed by alcohol, occupational risk and smoking.

Conclusions: Low BMD is a major preventable risk factor that explains a very remarkable proportion of falls health burden in Europe, in particular in those aged 70 years and above. This is a growing concern, given the population trajectories, and requires urgent attention.

References:
[1] Forouzanfar M et al, Lancet 2016.
[2] Johnell O et al, JBMR 2015.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6616

FRI0714 LUPUS NEPHRITIS AND PROGNOSIS. EFFECT OF MEMBRANOUS AND OTHER COMPONENTS OF THE HISTOLOGY

M.U. Martinez Martinez[1], C. Vallín-Orozco[1], H.E. Esparza-Holguin[1], G. Aguilera-Barragán Pickens[1], D. Martínez-Galla[2], C. Abud-Mendoza[1]. *[1]Unidad de Investigaciones Reumatológicas; [2]Renal Pathology, Hospital Central "Dr. Ignacio Morones Prieto", Universidad Autónoma de San Luis Potosí, San Luis Potosi, Mexico*

Background: In 1983 Austin et al. informed a series of prognostic factors (including histology) associated with the development of renal failure in patients with lupus nephritis (LN). Differences in actual therapies may have different hazard ratios of renal failure than the described by Austin et al.[1]

Objectives: To evaluate histological factors associated with a decline in kidney function (DKF) in patients with SLE.

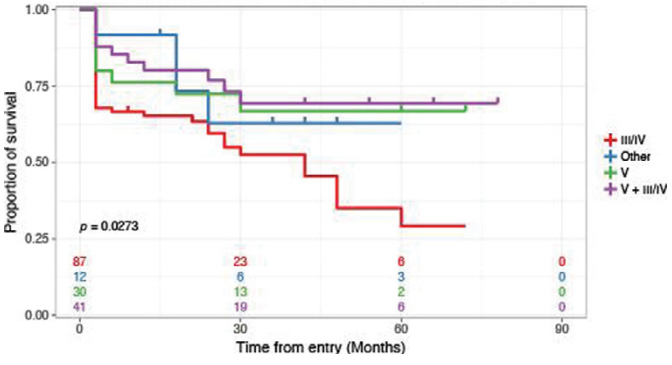
Methods: We evaluated all the patients in whom a kidney biopsy was performed. DKF was defined as a glomerular filtration rate (GFR) of less than 60 ml/min/m^2 in two determinations in the follow-up. Histology was graded according to Austin et al.[1] (activity and chronicity) by a renal pathology specialist. Factors associated with the development of DKF were evaluated through Kaplan-Meier curves and Cox regression analysis (bivariate and multivariate).

Results: At this moment, we have followed 170 patients with LN and kidney biopsy, 130 (76.5%) women, mean age at kidney biopsy was 29.7±13.2 years; classes of LN were: 71 patients (41.8%) class IV, 30 (17.6%) class V, 22 (12.9%) class III/V, 19 (11.2%) class IV/V, 16 (9.4%) class III, and other classes 12 patients; 135 patients (79.5%) have a minimum follow-up of 12 months. There were statistically significant differences in four groups of LN: pure proliferative (classes III or IV), the combination with membranous (III/IV±V), pure membranous (V) or other classes (Figure1).

Table 1. Factors associated with a DKF

Histological feature	Bivariate HR (CI)	Bivariate p-value	Multivariate HR (CI)	Multivariate p-value
Glomerular abnormalities				
Cellular proliferation	1.01 (0.83–1.22)	0.920	NA	NA
Karyorrhexis	0.94 (0.76–1.17)	0.566	NA	NA
Celular crescents	1.09 (0.96–1.22)	0.179	0.95 (0.82–1.10)	0.501484
Hyaline thrombi	0.85 (0.64–1.12)	0.248	0.65 (0.47–0.90)	0.008837
Leukocyte infiltration	1.23 (0.97–1.57)	0.0848	1.03 (0.77–1.40)	0.815447
Glomerular sclerosis	1.79 (1.41–2.26)	<0.001	1.67 (1.23–2.25)	0.000838
Fibrous crescents	1.71 (1.27–2.29)	<0.001	1.55 (1.11–2.16)	0.009917
Membranous	0.50 (0.30–0.85)	0.0105	0.48 (0.27–0.88)	0.017001
Tubulointerstitial abnormalities				
Interstitial cell infiltration	1.31 (1.13–1.56)	<0.001	1.18 (0.95–1.47)	0.126099
Interstitial fibrosis	0.80 (0.92–1.70)	0.162	0.74 (0.47–1.16)	0.194012
Tubular atrophy	1.33 (1.02–1.74)	0.035	1.10 (0.47–1.17)	0.613154

Figure 1. Decline of kidney function according classes of LN



In the bivariate analysis, factors statistically significant associated with the development of DKF were: glomerular sclerosis, fibrous crescents, interstitial cell infiltration and tubular atrophy; having membranous component resulted as a "protector" factor for the development of DKF. The Cox regression model included all the factors with a p-value less than 0.25 in the bivariate analysis; independent factors associated with increased HR of DKF were glomerular sclerosis and fibrous crescents; however, hyaline thrombi and presence of membranous nephritis were associated with a decreased HR of DKF. (Table 1).

Conclusions: We describe factors associated with a DKF. We found that the proliferative LN in combination with membranous have a better prognosis than pure proliferative LN. Our study could help to evaluate the effects of therapies in LN.

References:
[1] Austin HA, et al. Am J Med 1983;75:382–391.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4156

FRI0715 BEING A WOMAN AND HAVING KNEE OSTEOARTHRITIS INCREASES THE LIKELIHOOD OF COMORBIDITIES

M. Herrero Barbero[1], S. Gimenez[2], J. Vergara[3], E. Viles I Lladó[4], H. Martinez[4], G. Rodríguez Roca[5], L. Sánchez[6], J.A. Díaz Muñoz[7], J.F. Frias[8], A. Castaño[9], J.J. Jiménez Díaz[10], Á. Rodríguez de Cossío[11], R. Belenguer[12], J.L. Llisterri[13], J. Vergés Milano[6,14] on behalf of EMARTRO. *[1]Plaça Francesc Macià 7, Bioiberica, Barcelona; [2]Unidad de Gestión Clínica el Limonar, Malaga; [3]Centro de Salud Huercal, Almería; [4]Bioiberica S.A., Barcelona; [5]Centro de Salud la Puebla de Montalbán, Toledo; [6]Bioiberica, Barcelona; [7]Centro de Salud Ávila Rural, Ávila; [8]Hospital Universitario Virgen de las Nieves, Granada; [9]Centro de Salud Corella, Navarra; [10]Centro de Salud Los Cubos, Burgos; [11]Centro de Salud San Martin de la Vega, Madrid; [12]Centro de Salud Algemesí; [13]Centro de Salud Ingeniero Joaquín Belloch, Valencia; [14]Osteoarthritis Fundation International, Barcelona, Spain*

Background: Osteoarthritis (OA) is the most prevalent joint disease and the leading cause of disability from 60 years onwards. In fact, 14,8% of the Spanish population has OA.

Objectives: This study aimed to determine if there is a differential profile and greater comorbidity in women affected by symptomatic knee OA compared to a control group without OA.

Methods: The EMARTRO study was designed as an observational, multicenter, transversal study to compare probability of suffering a comorbidities based on presence of symptomatic knee OA visited by GPs. Sociodemographic, anthropometric, clinical parameters and clinical variables of interest were recorded. The probability of suffering comorbidities in each study group was estimated using the Odds Ratio estimation with conditioned logistic regression models. The HAD scale, the Goldberg health questionnaire were administered to patients and the concomitant medication was also registered. The comparison between groups was done using t-Student, Chi-square and Mann-Whitney.

Results: A total of 897 women were included with a mean (SD) age of 67.4 (6.8) years.

Osteoarthritic women were obese and had a higher BMI compared with control group, 31.2 (5.5) vs 27.5 (4.3) ($p<0.0001$), respectively. Regarding blood pressure, no differences were found in the systolic BP ($p=0.0646$) but in the diastolic, women with OA also had higher values, 77.9 (9.1) vs 75.8 (8.9) mmHg ($p=0.0005$).

In general terms, the presence of OA doubled the probability of having concomitant conditions with respect to controls [OR=2,220 (95% CI: 1,449–3,400) p=0,0002]. Likewise, women with syntomatic knee OA were more likely to have hypertension [OR=1.697 (95% CI 1.299–2.217), $p=0.0001$], venous peripheral vascular disease [OR=2.148 (95% CI 1.547–2.984), $p<0.0001$] and gastroesophageal reflux (OR=1.890 (95% CI 1.297–2.754), $p=0.0009$).

Regarding the mental health of the patients, according to the Goldberg scale, 41% of the patients with OA elicited psychopathology vs 17.8% in controls, $p<0.0001$. As for the HAD scale, there were more cases of anxiety ($p<0.0001$) and depression in the OA women ($p<0.0001$).

The greater burden of physical and mental comorbidity in the OA patients was accompanied by a higher consumption of concomitant medications ($p<0.0001$).

Conclusions: The results of the present study indicate that in patients with knee OA, being female is a risk factor for the development of concomitant pathologies. Also, the increased likelihood of suffering from hypertension, venous peripheral vascular disease and gastroesophageal reflux should determine chronic medications for the treatment of osteoarthritis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3494

FRI0716 RISK STRATIFICATION IN YOUNG PATIENTS WITH ACUTE MYOCARDIAL INFARCTION USING THE ADJUSTED GLOBAL ANTIPHOSPHOLIPID SYNDROME SCORE (AGAPSS)

M. Radin[1], K. Schreiber[2], P. Costanzo[3], I. Cecchi[1], D. Roccatello[1], S. Baldovino[1], M. Bazzan[3], M. Cuadrado[4], S. Sciascia[1]. *[1]Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Torino, Italy; [2]Department of Thrombosis and Haemophilia, Guy's and St Thomas' Hospital, London, United Kingdom; [3]S. Giovanni BoscoHospital, Torino, Italy; [4]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom*

Background: Young adults with acute myocardial infarction are a critical group to examine for the purpose of risk factors stratification and modification [1].

In the setting of underlying systemic autoimmune diseases, premature cardiovascular disease deserves even more attention in these conditions, such as antiphospholipid syndrome (APS), the most common acquired thrombophilia.

Objectives: In this study we aimed to assess the clinical utility of the adjusted Global AntiphosPholipid Syndrome Score (aGAPSS)[2] for the risk stratification of acute myocardial infarction in a cohort of young APS patients with thrombotic events.

Methods: The analysis included 83 consecutive APS patients (≤50 years old) who presented with arterial or venous thromboembolic events. Data on cardiovascular risk factors and antiphospholipid antibodies (aPL) positivity were retrospectively collected. The aGAPSS was calculated for each patient by adding the points corresponding to the risk factors, based on a linear transformation derived from the β regression coefficient as follows: 3 for hyperlipidaemia, 1 for arterial hypertension, 5 for aCL IgG/IgM, 4 for anti-b2 glycoprotein I IgG/IgM and 4 for LA.

Results: Demographic, clinical and laboratory characteristics of the cohort are summarized in Table 1. Higher aGAPSS values were observed in patients with acute myocardial infarction when compared to the others [mean aGAPSS 11.9 (S.D. 4.15, range 4–18) Vs. (mean aGAPSS 9.2, S.D. 5.1, range 1–17); T test: $p<0.05$]. Significantly higher aGAPSS values were also seen in patients with acute coronary syndrome compared to patients with a history of peripheral or cerebrovascular arterial thrombotic events [mean aGAPSS 11.9 (S.D. 4.15, range 4–18) Vs. (mean aGAPSS 6.7, S.D. 5.7, range 1–17); T test: $P<0.005$]. When separating for cardiovascular risk factors and aPL positivity, hypercholesterolemia was significantly higher in the group that developed myocardial infarction compared with patients with a history of any thrombosis and patients with a history of peripheral or cerebrovascular arterial thrombotic events (Chi square test: $p<0.0001$ and $p<0.0001$) and significantly higher rate of multiple positivity

Patients Characteristics	All (n=83)	%
Female sex	75	90
Age, mean (S.D.), years	44,6 (11,3)	
Disease duration, mean (S.D.), years	11,4 (7,8)	
Caucasians, n	82	93
Arterial thrombosis, n	53	60
Venous thrombosis, n	44	50
Acute Myocardial Infarction	13	15
PAPS, n	31	35
SLE and APS, n	44	50
Arterial Hypertension, n	27	31
Hyperlipidemia, n	16	18
LA, n	38	43
aCL IgG/M, n	65	74
IgG	60	68
IgM	35	40
Anti-Beta2GPI IgG/IgM, n	44	50
IgG	39	44
IgM	12	14
Triple aPL positivite	27	31

Table 1. Demographic, clinical and laboratory characteristics of the cohort

	Acute myocardial infarction (13)	Arterial and/or venous thrombosis (70)
Hyperlipidemia	10	9
Arterial Hypertension	4	22
LA	8	31
aCL IgG/M	11/6	51/30
Anti-Beta2GPI IgG/IgM	8/2	31/11
Triple aPL positivite	5	22

Table 2. Patients cardiovascular risk factors and aPL positivity between groups

for LA, aCL (IgG/IgM), anti-β2GPI antibodies (IgG/IgM) were present in the group that developed myocardial infarction (Chi square test: $p<0.05$ for all aPL) (Table 2).

Conclusions: The aGAPSS is based upon a quantitative score and could aid risk stratifying APS patients younger than 50 years for the likelihood of developing coronary thrombotic events and may consequently guide pharmacological treatment for high-risk patients.

References:
[1] Zimmerman FH, Cameron A, Fisher LD, Ng G. Myocardial infarction in young adults: angiographic characterization, risk factors and prognosis (Coronary Artery Surgery Study Registry). J Am Coll Cardiol 1995;26:654–61.
[2] Sciascia S, Sanna G, Murru V, Roccatello D, Khamashta MA, Bertolaccini ML. GAPSS: the Global Anti-Phospholipid Syndrome Score. Rheumatology (Oxford) 2013;52:1397–403. doi:10.1093/rheumatology/kes388.

Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1600

FRI0717 POSITIVE CONVERSION OF TUBERCULOSIS SCREENING RESULTS AND INCIDENCE OF ACTIVE TUBERCULOSIS INFECTION IN PATIENTS RECEIVING BIOLOGIC TREATMENT

M.-C. Park[1], H.W. Kim[1], S.H. Han[2]. *[1]Division of Rheumatology; [2]Division of Infectious Diseases, Yonsei University College of Medicine, Seoul, Korea, Republic Of*

Background: Previous studies reported active tuberculosis infections can occur during biologic treatment in patients with negative baseline LTBI screening. Current recommendations suggesting the annual testing for latent tuberculosis infections are mainly issued for patients with rheumatoid arthritis (RA) receiving anti-TNF inhibitors and there are lacking evidence for patients receiving non-TNF biologic agents and for patients with ankylosing spondylitis (AS) or psoriatic arthritis (PsA).

Objectives: This study was performed to investigate the conversion rate of initially negative tuberculosis screening test results during biologic treatment and the usefulness of repeated screening test for detecting unexpected tuberculosis infection in patients with RA, AS, and PsA.

Methods: A total of 95 patients (43 with RA, 50 with AS, and 2 with PsA) who had negative baseline interferon γ releasing assay (IGRA) results, which were assessed using QuatiFERON-TB Gold in tube (QTF-GIT), prior to initiation of biologic treatment were enrolled in this study. All patients received biologic agents for the treatment of their diseases and rescreening with QTF-GIT were performed in all patients after median 12 months from baseline test. Clinical characteristics were compared between converters and non-converters and incidence of active tuberculosis infection was evaluated.

Results: Patients were treated with different biologics (23 with etanercept, 50 with adalimumab, 5 with infliximab, 4 with golimumab, 1 with certolizumab pegol, 3 with abatacept, and 9 with tocilizumab). Positive conversions of initially negative IGRA were found in 13 (6 patients with etanercept, 4 patients with adalimumab, 2 patients with tocillizumab and 1 patient with abatacept) of 95 patents (13.7%) after initiation of biologic treatment. Age over 50 years and diagnosis of RA were more common in converters. Multivariate analysis showed that age over 50 was an independent risk factor for IGRA conversion with OR 4.36 (95% CI 1.10 - 17.34, p=0.036). During biologic treatments, active tuberculous infections were found in 3 of 13 converters (23.1%)

Conclusions: Although initial screening test showed negative results, the serial follow-up of tuberculosis screening test should be considered during biologic treatment in patients with rheumatic diseases to prevent unexpected tuberculosis infection.

References:
[1] Hatzara C, Hadziyannis E, Kandili A, Koutsianas C, Makris A, Georgiopoulos G, et al. Frequent conversion of tuberculosis screening tests during anti-tumour necrosis factor therapy in patients with rheumatic diseases. Ann Rheum Dis 2015;74:1848–53.
[2] Chen DY, Shen GH, Chen YM, Chen HH, Hsieh CW, Lan JL. Biphasic emergence of active tuberculosis in rheumatoid arthritis patients receiving TNFalpha inhibitors: the utility of IFNgamma assay. Ann Rheum Dis 2012;71:231–7.
[3] Singh JA, Furst DE, Bharat A, Curtis JR, Kavanaugh AF, Kremer JM, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res 2012;64:625–39.

Acknowledgements: This study was supported by a grant of the Korean Health Technology R&D Project, Ministry for Health and Welfare, Republic of Korea (HI14C1774).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1286

FRI0718 PREVALENCE AND PATTERN OF COMORBIDITIES IN CHRONIC RHEUMATIC AND MUSCULOSKELETAL DISEASES: THE COMORD STUDY

N.R. Ziade[1,2], F. Fayad[1,2], B. Khoury[3], M. Zoghbi[4], G. Merheb[5], G. Abi karam[1,2], K. Mroue[6], J. Missaykeh[7]. *[1]Rheumatology, Hotel Dieu de France; [2]Rheumatology; [3]Medicine; [4]Family Medicine, St-Joseph University, Beirut; [5]Medicine, ND des Secours, Jbeil; [6]Rheumatology, Zahra University Hospital, Beirut; [7]Rheumatology, Monla Hospital, Tripoli, Lebanon*

Background: Rheumatic and musculoskeletal diseases (RMD) frequently coexist with other conditions, resulting in multimorbidity, which may compromise arthritis management and lead to diminished quality-of-life and increased mortality. In 2016, EULAR published "Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases", used to guide this study.

Objectives: The primary objective is to evaluate the prevalence and pattern of comorbidities in selected RMD in Lebanese patients. The secondary objective is to evaluate the gap between recommendations and routine comorbidities' screening.

Methods: COMORD is an observational, cross-sectional, multicentric national study. Consecutive RMD patients (Rheumatoid Arthritis (RA), Osteoarthritis (OA), Systemic Lupus Erythematous (SLE), Axial Spondyloarthritis (AxSpA) and Peripheral Spondyloarthritis (pSpA)) as diagnosed by the rheumatologist) were recruited at 6 practices from university hospitals and private clinics in Lebanon. Six axes of comorbidities (Cardiovascular, Malignancies, Infections, Gastrointestinal, Osteoporosis, Depression) were investigated using a case report form (patient interview). Optimal comorbidities screening was defined according to current recommendations and compared with monitoring in practice. Prevalences were presented descriptively. The number of comorbidities was correlated with predictive factors using Poisson Regression. Finally, Latent Class Analysis (LCA) was used to identify patterns of multimorbidity. All analysis were performed on IBM SPSS Statistics 23 and XLSTAT 18.07.

Results: 515 patients were recruited (196 RA, 161 OA, 75 AxSpA, 45 SLE, 40 pSA). Mean age was 56y, 76% were female. There was no difference in the disease distribution between centers. The most common comorbidities were cardiovascular risk factors and diseases, followed by depression and osteoporosis. The number of comorbidities was significantly associated with age ($p<0.001$), obesity ($p<0.001$) and biotherapies (p 0.05). LCA analysis identified 3 main clusters of multimorbidity: OA, RA, AxSPA (Fig 1). The most optimal screening was found for cardiovascular risk factors (84%). DXA was prescribed in 69% of correct indications. As for malignancies, mammograms and pap smears were the most optimally prescribed (36% and 28%). Colonoscopy and dermatology visit were prescribed in 22% and 18%. Correct vaccination (influenza and pneumococcal) was found in 17% and 8%. Predictive factors for optimal screening were age, university setting, social coverage, disease duration and biotherapy.

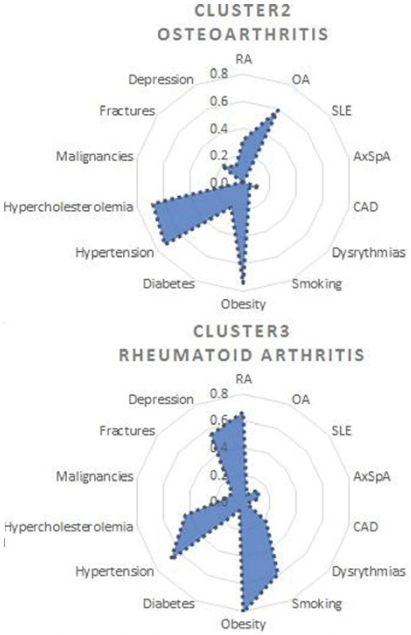


Figure 1. Identified Multimorbidity Clusters by Latent Class Analysis

Conclusions: Comorbidities are prevalent in RMDs and follow specific multimorbidity patterns, with a predominance for cardiovascular, depression and osteoporosis. They are more frequent with age and obesity. Optimal screening needs to be improved.

References:
[1] Baillet et al. Ann Rheum Dis 2016.
[2] Dougados et al. Ann Rheum Dis 2014.

[3] Molto et al. Ann Rheum Dis 2016.
[4] Simoes et al. Arthritis Care & Research 2017.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2186

FRI0719 BURDEN OF HEPATITIS E VIRUS INFECTION IN PATIENTS WITH RHEUMATIC DISEASES

P. Jacques[1,2], E. Padalko[3], E. Verheugen[1,2], L. Cattoir[3], X. Verhelst[4], E. Nys[3], S. Van Gucht[5], V. Hutse[5], V. Suin[5], D. Elewaut[1,2]. *[1]Rheumatology, University Hospital; [2]VIB, Ghent University; [3]Clinical Chemistry, Microbiology and Immunology; [4]Gastroenterology, University Hospital, Ghent; [5]National Reference Centre for Viral Hepatitis, Scientific Institute of Public Health, Brussels, Belgium*

Background: Hepatitis E virus (HEV) is considered an emerging pathogen in developed countries, potentially causing chronic hepatitis.
Objectives: This cross-sectional analysis was undertaken to determine the seroprevalence of HEV in patients with autoimmune or inflammatory arthritis. This subgroup of patients is often treated with immune suppressive drugs, and is generally considered more susceptible to infections.
Methods: Serum samples were obtained from 449 consecutive patients consulting at the department of Rheumatology between October and November 2015. Patient characteristics with respect to diagnosis and treatment were collected. HEV IgM and IgG were measured by ELISA (Wantai Hepatitis E Virus IgG and IgM ELISA, Sanbio BV). Positive or borderline samples were further analyzed for HEV RNA (RealStar® HEV RT-PCR Kit, Altona Diagnostics NRC WIV).
Results: A total of 449 patients were included, 211 men and 238 women. HEV IgG was positive in 82 samples (18.26%), 6 were borderline, and 5 were non-determinable (not enough serum). IgM was positive in only 2 samples (0.45%). These 2 patients had normal liver function tests. Additional PCR was performed on all positive and borderline samples, which turned out negative in all samples. Of the 88 IgG positive and borderline samples, 86 patients had a known diagnosis of chronic inflammatory arthritis, of which 50 patients had previously been diagnosed with rheumatoid arthritis, 18 with spondyloarthritis, 8 with psoriatic arthritis. Fifty patients were treated with biologics (37 TNF inhibitors), 43 patients were treated with methotrexate (mean dose 12.5mg weekly), and 20 were treated with corticosteroids (mean daily dose 5.5mg prednisolone equivalent).
Conclusions: In a consecutive cohort of patients with known diagnosis of autoimmune or inflammatory arthritis, seroprevalence of HEV IgG was 18,2%. No active HEV infection could be detected. We found this to be comparable to a historical cohort of healthy patients from the departments of Orthopedics and obstetrics[1], where prevalence of HEV IgG was 14%.
References:
[1] Van Hoecke F et al. Acta Gastroenterol Belg. 2012 Sep;75(3):322–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5115

FRI0720 CHARACTERISTICS OF PATIENTS WITH GOUT TREATED TO SUA TARGET THAT CONTINUE TO EXPERIENCE FLARES: DATA FROM FRANCE, GERMANY, ITALY, SPAIN, UK AND US

R. Morlock[1], D.C. Taylor[2], S. Baumgartner[3]. *[1]YourCareChoice, Ann Arbor; [2]Health Economics and Outcomes Research, Ironwood Pharmaceuticals, Cambridge; [3]drB Consulting, Spokane, United States*

Background: Gout is a common form of inflammatory arthritis. Treatment guidelines recommend a target serum urate (sUA) ≤6mg/dL. ACR and EULAR treatment guidelines indicate sUA targets may need to be surpassed to achieve treatment benefits in a subset of patient that continue to flare and/or have tophi.
Methods: Data were assessed from a survey of physicians about gout disease management. Patient results were confirmed through in-depth chart audits assessing diagnosis, comorbid conditions, disease severity and laboratory assessments. Disease severity was measured using a physician global assessment, flare counts, joint damage and presence of tophi. Type and dose of XOI, length of current treatment, compliance, physician type and patient socio-demographic factors were identified. Descriptive and multivariate statistics were used to describe patients having ≥2 flares per year (excluding treatment-related flares) in patients achieving target sUA ≤6 mg/dL.
Results: Overall, 251 rheumatologists and 250 primary care physicians were interviewed and provided data from 2505 patients with gout; 82% were male and the average age was 58 years (SD=12). 1823 (73%) patients were treated with an XOI, of these 813 (44%) had a least one assessment of sUA ≤6 mg/dL over a 12-month period. Of the 813 patients reaching sUA target, 307 (37.8%) reported ≥2 flares in the last year. On average, patients at sUA goal with ≥2 flares had been treated over 38.8 months on their current XOI and patients with ≤1 flare had been treated for 40.7 months. Patients at sUA ≤6 mg/dL treated with an XOI and reporting ≥2 flares a year were more likely to have tophi (32.9% vs. 19.2%; p<0.01), alcoholism (22.8 vs. 10.7; p<0.01), CVD (24.8 vs. 17.6%; p=0.014), depression (14.3 vs. 9.3; p=0.027), and diabetes mellitus (23.8 vs. 16.8; p=0.015) compared to patients with ≤1 flare a year. A backward stepwise multivariate model predicting patients classified as controlled (sUA ≤6 mg/dL) and continuing to flare (≥2 flares in the last year) found the physician-reported and chart-documented comorbidities of chronic kidney disease (OR 1.9; p<0.01), alcoholism (OR 2.4; p<0.01), diabetes mellitus (OR 1.5; p<0.05), and have tophi (1.7; p<0.01) to be associated with having higher flare rates despite achieving sUA ≤6 mg/dL. There was no difference by the type of XOI or physician.
Conclusions: Of the patients achieving target sUA level of ≤6 mg/dL, 62% have ≤1 flare; however, over a third reported ≥2 in a 12-month period. Patients with multiple flares were more likely to have higher urate burden in the form of tophi, chronic kidney disease, alcoholism, and diabetes mellitus comorbid conditions. Frequent flares and greater tophaceous burden may require treating more aggressively to an sUA level of 5 mg/dL or lower as recommended by treatment guidelines.
Acknowledgements: This study was funded by Ironwood Pharmaceuticals.
Disclosure of Interest: R. Morlock Consultant for: Ironwood Pharmaceuticals, D. Taylor Employee of: Ironwood Pharmaceuticals, S. Baumgartner Consultant for: Ironwood Pharmaceuticals
DOI: 10.1136/annrheumdis-2017-eular.6142

FRI0721 SLEEP DISORDERS IN PATIENTS AT THE FIRST ACCESS TO A RHEUMATHOLOGY OUTPATIENT CLINIC

R. Tirri, D. Capocotta, R. Ferrara. *Department of internal and experimental Medicine, Unit of Rheumatology of Univerity of study of Campania "Luigi Vanvitelli", Naples, Italy*

Background: Sleep disturbances are frequently found in patients affected by rheumatic conditions (1). Chronic pain, the most common manifestation of these conditions is associated to poor sleep (2).
Objectives: Our primary objective was to evaluate prevalence of excess daytime sleepiness and impaired sleep quality in a patient population at the first access to a Rheumatology outpatient clinic. Secondary objective was evaluation of pain and others factors well known to be associated to sleep disorders.
Methods: 961 out of 1454 (mean age was 52.6 years; 14.3% were male) consecutive patients admitted for the first time to an Italian Rheumatology Outpatient Clinic, between December 2014 and November 2016, accepted to answer a self-administered questionnaire study. We considered the following parameters: pain intensity on visual analogic scale ranging from 0 to 100 according to commonly used classification (3), patient's assessment of General Health (GH), Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Health Assessment Questionnaire (HAQ), and Body Mass Index (BMI). Smoke habits were also considered.
Results: 70 patients showed both sleep disorders (7.3%),624 patients had only impaired sleep quality (64.9%), 25 showed isolated excessive daytime sleepiness (2.6%). 242 patients did not have any sleep disorders (25.2%). We found that the presence of both ESS≥10 and PSQI≥5 was correlated to moderate-severe pain VAS pain≥40, BMI≥35, HAQ≥1 and GH≥50 with a statistical significance (respectively p=0.004; p=0.032; p=0.0004; p=0.0001). A correlation with GH≥50 in the patient group with only PSQI≥5 was detected (p=0.03). Smoke habits did not correlate with sleep disturbance measures investigated. No other correlations were found in the other groups.
Conclusions: Thus excess daytime sleepiness and impaired sleep quality may be a target of therapeutic intervention in the treatment of rheumatic conditions. Further studies are needed to generalize results and suggestions.
References:
[1] Generaal E, Vogelzangs N, Penninx WJH, Dekker J. Insomnia, sleep duration, depressive symptoms, and the onset of chronic multisite musculoskeletal pain. Sleep 2017; 40.
[2] Vivien C Abad, Priscilla S.A. Sarinas, Christian Guilleminault. Sleep and rheumatologic disorders. Sleep Medicine Reviews 2008; 12: 211–228.
[3] Jensen MP, Chen C, Brugger AM. Interpretation of visual analog scale ratings and change scores: a reanalysis of two clinical trials of post-operative pain. J Pain 2003;4:407–14.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6313

FRI0722 CROSS-SECTIONAL ASSOCIATIONS BETWEEN DEMOGRAPHIC, JOB RELATED, HEALTH RELATED AND PSYCHOSOCIAL FACTORS AND THREE DIFFERENT MEASURES OF PRESENTEEISM: RESULTS FROM EULAR-PRO AT-WORK PRODUCTIVITY STUDY

S. Leggett[1], D. Lacaille[2], A. Boonen[3], C. Mihai[4], S. Talli[5], S. Hagel[6], S. Dadoun[7], S. Ramiro[8], A. Bosworth[9], G. Sakellariou[10], S. Verstappen[1,11] on behalf of EULAR-PRO at-work productivity co-investigators. *[1]Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, United Kingdom; [2]University of British Columbia, Vancouver, Canada; [3]Maastricht UMC, Maastricht, Netherlands; [4]Dr. Ion Cantacuzino Hospital, Bucharest, Romania; [5]East Tallinn Central Hospital, Tallinn, Estonia; [6]Lund University and Skane University hospital, Lund, Sweden; [7]APHP Pitie-Salpetriere Hospital, Paris, France; [8]Leiden UMC, Leiden, Netherlands; [9]NRAS, Maidenhead, United Kingdom; [10]IRCCS Policlinico San Matteo Foundation, Pavia, Italy; [11]NIHR Manchester Musculoskeletal BRU, Central Manchester NHS Trusts, Manchester, United Kingdom*

Background: Several measures of at-work productivity loss (i.e. presenteeism)

exist, varying in concept, recall period, and attribution[1]. As a consequence, the contribution of contextual factors may vary which has important implications when considering these factors in studies evaluating the impact of inflammatory arthritis (IA) and osteoarthritis (OA) on presenteeism.

Objectives: To determine demographic, job related and health related factors associated with three different global measures of presenteeism in patients with IA or OA.

Methods: This large cross-sectional international EULAR-PRO study (n=8 countries) includes patients with RA, PsA, AS or OA in paid employment. Data collection included: demographics, job characteristics, health related and psychosocial factors. Patients also completed three global measures of presenteeism, varying in content, attribution and recall period. The Work Productivity Scale–Arthritis (WPS-A) measuring the affect of arthritis on productivity during the last 7 days, the Work Productivity and Activity Impairment Questionnaire (WPAI) measuring interference of arthritis on work productivity in the last month, and the Work Ability Index (WAI) a generic scale measuring current ability to work. For interpretation purposes the scale of the WAI was reversed in this study. Due to skewed data, univariable median regression analyses were performed to assess the association between independent variables with each individual presenteeism instrument.

Results: 503 patients with IA/OA were recruited in this study with a mean age of 47 (SD10) yrs and disease duration of 12.6 (SD10) yrs. Except for male patients reporting a lower WPS-A score, no other demographics were significantly associated with presenteeism (table). Being neutral/unsatisfied about the job, not being able to organize one's own work, reporting higher VAS well-being and disability scores, and experiencing reduced quality of life were all significantly associated with higher presenteeism, a result observed for all three instruments. Furthermore, those with higher anxiety and depression scores also reported having more problems at work due to ill health. Discrepancies between instruments were especially observed between the WPAI (affect of ill health on productivity)/WPS-A (interference ills health on productivity) and WAI (generic scale on ability to work) in relation to job demands, receiving help from colleagues and the option to postpone work.

	WPAI ß (95%CI)	WPS-RA ß (95%CI)	WAI ß (95%CI)
Demographics:			
Age, years	0 (-0.03, 0.03)	0 (-0.03, 0.03)	0 (-0.02, 0.02)
Gender, *female*	0 (-0.51, 0.51)	**-1 (-1.60, 0.40)**	0 (0.51, 0.51)
Job characteristics:			
Job demands:			
not/bit demanding	1	1	1
demanding	0 (-0.72, 0.72)	**1 (0.12, 1.88)**	0 (-0.45, 0.45)
very demanding	**2 (0.25, 1.75)**	**1 (0.09, 1.91)**	0 (-0.47, 0.47)
Job satisfaction:			
very satisfied	1	1	1
neutral	**1 (0.03, 1.97)**	**2 (1.35, 2.46)**	**1 (0.11, 1.89)**
unsatisfied	1 (-0.08, 2.08)	**2 (1.28, 2.72)**	**1 (0.00, 2.00)**
Help colleagues:			
often/always	1	1	1
sometimes	0 (0.49, 0.49)	0 (-0.75, 0.75)	0 (-0.49, 0.49)
never	**-1 (-1.63, -0.37)**	**-1 (-1.95, -0.05)**	0 (-0.63, 0.63)
Able to postpone tasks			
often/always	1	1	1
sometimes	0 (0.60, 0.60)	0 (-0.60, 0.60)	0 (-0.49, 0.49)
Never	**1 (0.30, 1.70)**	**1 (0.30, 1.70)**	0 (-0.57, 0.57)
Able to organise work			
often/always	1	1	1
sometimes	**1 (015, 1.85)**	0 (-0.55, 0.55)	**1 (0.32, 1.68)**
never	**2 (0.55, 3.45)**	**1 (0.06, 1.94)**	**1 (-0.16, 2.16)**
PRO's:			
VAS well-being	**0.07 (0.06, 0.08)**	**0.06 (0.05, 0.07)**	**0.04 (0.03, 0.05)**
HAQ-score	**4 (3.52, 4.47)**	**4 (3.50, 4.50)**	**2.67 (2.15, 3.19)**
EQ-5D	**-6.50 (-7.28, -5.71)**	**-5.82 (-6.67, -4.96)**	**-3.22 (-3.85, -2.58)**
HAD-Anxiety	**0.22 (0.18, 0.27)**	**0.20 (0.16, 0.24)**	**0.11 (0.07, 0.15)**
HAD-Depression	**0.31 (0.24, 0.39)**	**0.33 (0.27, 0.39)**	**0.27 (0.22, 0.33)**

WPAI {0= condition no effect on work–10=condition completely prevented work}; WPS-IA/OA {0=no interference–10=complete interference; WAI $_{rev}$ {0=work ability at its best-10=completely unable to work }; PRO's=patient reported outcomes; VAS well-being = Visual Analogue Scale Well being; EQ-5D = EuroQol 5D measurement; HAQ= health assessment questionnaire; HAD=Hospital Anxiety and Depression scale. **Bold values**=Statistically significant ($p<0.05$).

Conclusions: This is the first study investigating the association of many contextual factors with three commonly used global measures of presenteeism. Overall, job satisfaction and the ability to organize one's own work are the most important job characterises associated with presenteeism and should be considered when measuring presenteeism.

References:

[1] Ref. Leggett et al. Content validity of global measures for at-work productivity. Rheumatology, 2016;55:1364.

Acknowledgements: Funding: EULAR, AbbVie, BMS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5161

FRI0723 TEMPORAL PATTERNS OF SEDENTARY BEHAVIOUR AND PHYSICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

S.A.M. Fenton[1,2], J.L. Duda[1], J.J. Veldhuijzen van Zanten[1,2], G.S. Metsios[3], P.C. Rouse[4], C.-A. Yu[5], G.D. Kitas[2]. *[1]School of Sport Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham; [2]Rheumatology, Russells Hall Hospital, Dudley; [3]Faculty of Education, Health and Wellbeing, Institute of Sport, Wolverhampton; [4]Department for Health, University of Bath, Bath; [5]School of Biomedical Sciences, University of Leeds, Leeds, United Kingdom*

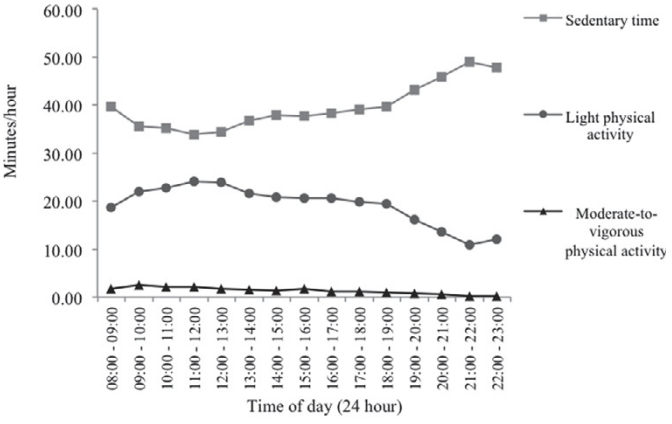
Background: Rheumatoid Arthritis (RA) is associated with increased risk of cardiovascular disease (CVD). Recent evidence suggests sedentary behaviour (waking behaviour ≤1.5 metabolic equivalents whilst sitting/lying) may contribute towards the progression of RA outcomes, including heightened CVD risk (1). Sedentary behaviour occupies the majority of waking hours among people with RA (1). However, the proportion of time spent sedentary is likely to fluctuate over the course of the day, with periods of high sedentarity representing more optimal opportunity for intervention, and thus potentially higher intervention efficacy.

Objectives: The aims of this study were; 1) to explore temporal patterns of sedentary behaviour (and physical activity) among RA patients, and 2) to examine associations between temporal sedentary patterns and predicted 10-year risk of CVD.

Methods: Patients with RA (N=97) wore a GT3X accelerometer for 7 days to assess habitual sedentary time (<100 counts/min) and physical activity (PA; light =100–2019, moderate-to-vigorous = ≥2020 counts/min). Accelerometer data were analysed separately for each hour (valid hour criteria; 60-minutes of data on ≥3 days, including a weekend day). To evaluate 10-year risk of CVD (Q-risk2), patients reported their medical history, provided a fasted blood sample and underwent assessments of blood pressure and body-mass index.

Results: Temporal patterns of sedentary time and PA are reported in Figure 1. Sedentary time declined throughout the morning (08:00–12:00). During the afternoon, sedentary time increased by 4.5 minutes (12:00–18:00; M =34.36±8.86 to M =39.06±7.91). A more marked increase in sedentary time was observed during leisure time (18:00–22:00; M =39.61±7.59 to M =47.90±6.30). Repeated measures analysis of variance (ANOVA) revealed sedentary time was significantly higher during leisure time (M =46.20±5.46) compared to the morning (M =36.88±5.61), and afternoon (M =38.50±6.07) [N =28, $F(2,26)=43.48$, $p=<0.01$]. Significant differences remained after accounting for employment status (i.e., employed vs. unemployed/student, $F(2,23)=1.40$, $p=0.27$). Patients who accumulated M = ≥45.31 sedentary minutes during their leisure time (18:00–23:00, median split), had significantly higher 10-year risk of CVD (M =22.23±13.83) compared to those accruing M=<45.31 sedentary minutes (M=8.09±7.62) [$t(41)=3.92$, $p=<0.01$]. Finally, hourly patterns for light PA were the reverse of those observed for sedentary time. Hourly MVPA engagement was consistently <3 minutes (peak MVPA at 09:00–10:00, M =2.47±4.16).

Figure 1. Temporal patterns of sedentary time, light and moderate-to-vigorous physical activity



Note: Valid data available at each time point ranged from N = 49 (08:00) to N = 71 (13:00). A total of N = 41 participants provided complete data across all hours during the morning (08:00 – 12:00) and leisure time (18:00 – 23:00). N = 64 participants complete data during the afternoon (12:00 – 18:00).

Conclusions: Interventions targeting leisure time sedentary behaviour (18:00–23:00), relative to more occupational sedentary behaviour (08:00–18:00), may offer the greatest potential for sedentary time reduction and associated improvements of CVD risk profile. Due to inverse patterns of engagement, replacing leisure time sedentary behaviour with light PA may offer an effective intervention approach.

References:

[1] Fenton SAM & Kitas GD. Rheumatoid Arthritis: Sedentary behaviour in RA – a new research agenda. Nat Rev Rheumatol 2016;12(12):698–700.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5901

FRI0724 PREDICTORS OF PRESENTEEISM AND ABSENTEEISM IN PATIENTS COMMENCING TREATMENT WITH METHOTREXATE MONOTHERAPY OR BIOLOGIC THERAPY FOR RHEUMATOID ARTHRITIS

S. Leggett[1], M. Lunt[1], A. Barton[2], K. Hyrich[1], K. Walker-Bone[3], S.M. Verstappen[1] on behalf of RAMS and BRAGGSS co-investigators. *[1]Arthritis Research UK Centre for Epidemiology; [2]Arthritis Research UK Centre for Genetics and Genomics, The University of Manchester, Manchester; [3]Arthritis Research UK/MRC Centre for Musculoskeletal Health and Work, The University of Southampton, Southampton, United Kingdom*

Background: The adverse effects of RA on absenteeism (i.e. days absent from work) and presenteeism (at-work productivity loss) are increasingly recognised as an important issue. Research suggests the reasons are multifactorial with many factors such as disease severity, quality of life, and depression possibly contributing to poor work outcomes in patients with RA.
Objectives: To identify predictors of presenteeism and absenteeism over one year in patients with RA commencing treatment with methotrexate (MTX) or biologics for the first time.
Methods: Patients recruited to the Rheumatoid Arthritis Methotrexate Starters study (RAMS) or the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS), and in full or part-time paid employment were included in this analysis. Demographic (e.g., age), clinical (e.g., DAS28), and psychological data (e.g., Hospital Anxiety and Depression scale (HADS)) were collected at baseline. Patients were followed up at six months and one year in both cohorts. Absenteeism in the last month (days missed), and presenteeism (*0 = no interference – 10 = complete interference)*, were measured at all three points using the RA specific Work Productivity Survey (WPS-RA). Patients with at least one follow-up post baseline were included in this analysis. Due to excessive zeros in the WPS-RA, a repeated measure zero inflated negative binomial regression (ZINB) was used to test the association between baseline demographic, clinical and psychological variables and presenteeism and absenteeism over one year.
Results: Data was available for 191 patients in BRAGGSS and 308 in RAMS. In BRAGGSS, the mean age was 51 years (SD 9.5), median symptom duration was 8 years (IQR 5–13); 78% female. In RAMS, the mean age was 52 years (SD 9.6), median symptom duration was 8.5 months (IQR 5–23); 66% female. At baseline, 26% (BRAGGSS) and 27% (RAMS) reported ≥1 days absent from work, and the median presenteeism scores were 5 (IQR 3–7) and 4 (IQR 1–7) for BRAGGSS and RAMS respectively. Presenteeism scores significantly improved over 1 year in both cohorts (BRAGGSS: median 2 [IQR 0–5], RAMS: median 2 (IQR 0–4) Kruskal-Wallis $p<0.001$)), as did absenteeism for both cohorts although non-significant. The ZINB revealed similar predictive patterns in both cohorts for presenteeism and absenteeism (Table 1). For example, for every 0.06 increase in EQ-5D (clinically important difference), the odds of being in the zero presenteeism group (i.e., no at-work productivity loss) over one year increased by a factor of 1.2 in BRAGGSS, and was similar in RAMS. In RAMS, a one unit increase in VAS fatigue decreased the odds of having no absenteeism over one year by a factor of 0.97.

Table 1. Demographic, clinical, and psychological predictors of presenteeism and absenteeism over one year.

	RAMS				BRAGGSS			
	Value	N	Presenteeism ZINB	Absenteeism ZINB	Value	N	Presenteeism ZINB	Absenteeism ZINB
Age, mean (SD)	52.2 (9.6)	308	0.9 (0.9 – 1.0) ¶ 1.0 (1.0 – 1.0)*§	0.9 (0.9 – 1.0)¶ 1.00 (0.9 – 1.0)§	51.4 (9.5)	191	1.0 (0.9 – 1.0)¶ 1.0 (0.9 – 1.0)§	0.9 (0.9 – 1.0)¶ 1.0 (0.9 – 1.0)§
Gender, female n (%)	204 (66)	308	1.1 (0.9 – 1.2)¶ 0.8 (0.5 – 1.3)§	1.0 (0.6 – 1.6)¶ 0.8 (0.5 – 1.5)§	149 (78)	191	1.5 (0.9 – 1.2)¶ 0.6 (0.2 – 1.6)§	2.3 (1.1 – 4.6)*¶ 1.1 (0.3 – 3.7)§
Symptom duration (months), median (IQR)	8.5 (5.0-23.0)	304	0.9 (0.9 – 0.9)*¶ 0.9 (0.9 – 1.0)§	0.9 (0.9 – 0.9)*¶ 1.0 (0.9 – 1.0)§	8 (5-13)	189	1.0 (0.9 – 1.0)*¶ 0.9 (0.9 – 1.0)§	0.9 (0.8 – 1.0)¶ 1.0 (0.9 – 1.1)§
VAS Pain (0-100), mean (SD)	46.0 (26.9)	299	1.0 (1.0 – 1.0)*¶ 0.9 (0.9 – 0.9)*§	1.0 (0.9 – 1.0)¶ 0.9 (0.9 – 0.9)*§	61.3 (22.5)	190	1.0 (1.0 – 1.0)*¶ 0.9 (0.9 – 1.0)§	1.0 (0.9 – 1.0)¶ 0.9 (0.9 – 1.0)§
VAS Fatigue (0-100), mean (SD)	48.7 (29.7)	301	1.0 (1.0 – 1.0)*¶ 0.9 (0.9 – 0.9)*§	1.0 (0.9 – 1.0)¶ 0.9 (0.9 – 0.9)*§	66.9 (23.5)	190	1.0 (1.0 – 1.0)*¶ 0.9 (0.9 – 0.9)*§	1.0 (0.9 – 1.0)¶ 0.9 (0.9 – 1.0)§
HAQ, mean (SD)	0.8 (0.6)	308	1.3 (1.2 – 1.4)*¶ 0.1 (0.0 – 0.2)*§	1.4 (1.1 – 2.0)*¶ 0.4 (0.2 – 0.6)*§	1.3 (0.6)	191	1.4 (1.3 – 1.5)*¶ 0.2 (0.1 – 0.3)*§	1.8 (1.0 – 3.3)*¶ 0.3 (0.1 – 0.6)*§
DAS, mean (SD)	3.9 (1.2)	291	1.1 (1.0 – 1.2)*¶ 0.6 (0.4 – 0.8)*§	1.1 (0.8 – 1.3)¶ 0.7 (0.5 – 0.9)*§	5.2 (0.8)	179	1.0 (0.9 – 1.5)¶ 0.8 (0.5 – 1.5)§	1.4 (0.7 – 2.7)¶ 0.9 (0.4 – 2.0)*§
EQ-5D, mean (SD)≠	0.6 (0.2)	299	0.9 (0.9 – 0.9)*¶ 1.3 (1.1 – 1.6)*§	0.9 (0.9 – 1.0)¶ 1.1 (1.0 – 1.3)*§	0.4 (0.3)	188	0.9 (0.9 – 0.9)*¶ 1.2 (1.1 – 1.3)*§	0.9 (0.9 – 1.0)¶ 1.6 (1.1 – 2.3)*§
HADS anxiety, mean (SD)	6.2 (4.3)	304	1.0 (1.0 – 1.0)*¶ 0.8 (0.7 – 0.9)*§	0.9 (0.9 – 1.0)¶ 0.9 (0.8 – 1.0)§	7.8 (4.0)	191	1.0 (1.0 – 1.0)*¶ 0.8 (0.7 – 0.8)*§	1.1 (1.0 – 1.)*¶ 0.6 (0.4 – 1.1)§
HADS depression, mean (SD)	5.4 (3.9)	305	1.0 (1.0 – 1.0)*¶ 0.7 (0.6 – 0.8)*§	0.9 (0.9 – 1.0)¶ 0.8 (0.7 – 0.9)*§	6.8 (3.8)	191	1.0 (1.0 – 1.0)*¶ 0.7 (0.6 – 0.8)§	1.1 (1.0 – 1.2)*¶ 0.1 (0.0 – 0.9)*§

*Adjusted for age, gender, and disease duration.
*p<0.05.
¶ Relative change in count part of ZINB model, assuming non-zero score.
§ Odds ratio for being in zero scoring group of ZINB model.
≠ A unit increase of 0.06 (a minimal clinically important difference in EQ-5D scores)

Conclusions: The results from this analysis support the notion of a multifactorial relationship between RA and work outcomes. The results suggest that greater quality of life and psychological well-being, amongst other factors, can predict improvements in presenteeism and absenteeism at one year in patients on either MTX or biologics for RA.
Acknowledgements: Funding: Pfzier I-CRP
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5077

FRI0725 PREDICTION OF INTERSTITIAL LUNG DISEASE IN MIXED CONNECTIVE TISSUE DISEASE

S. Reiseter[1], R. Gunnarsson[2], T.M. Aaløkken[3], M.B. Lund[4], J. Corander[5], Ø. Molberg[6]. *[1]Institute of Clinical Medicine, University of Oslo; [2]Dept. of Rheumatology; [3]Dept. of Radiology and Nuclear Medicine; [4]Dept. of Respiratory Medicine, Oslo University Hospital; [5]Institute of Basic Medical Sciences; [6]Institute of Clinical Medicine, University of Oslo, Oslo, Norway*

Background: Mixed Connective Tissue Disease (MCTD) is characterized by high levels of autoantibodies against U1 small nuclear ribonucleoprotein (RNP) and clinical manifestations also found in Systemic Sclerosis, Systemic Lupus Erythematosus, Rheumatoid Arthritis and Polymyositis. Interstitial Lung Disease (ILD) is a severe complication in MCTD and has been reported to affect between 35% and 85% (1) in different cohorts.
Objectives: Here we present a predicting model of ILD in an unselected nationwide MCTD cohort aiming to assist clinicians in identifying MCTD patients with ILD.
Methods: 135 patients with high resolution computed tomography (CT) available for systematic evaluation were included from our nationwide MCTD cohort. Abnormal CT findings of ground glass attenuation and reticular patterns were defined as ILD. Pulmonary function tests were performed within 2 months of the HRCT examination. Serum levels of anti-RNP and Ro-52 autoantibody were determined by line immunoassay (ANA Profile 5 Euroline Blot test kit, Euroimmun, Lübeck, Germany). Logistic regression analyses were used to find the predictive factors of ILD. Variables at a significant level of $P<0.25$ where considered a candidate in the prediction model by manual backward elimination procedure in addition to age and gender.
Results: Results: 52 patients (38%) had evidence of ILD on HRCT. The predictive model is shown in Table 1. $P=0.55$ for goodness of fit test and $P=0.80$ for area under ROC curve.

	Univariable			Multivariable		
	OR	95% CI	P value	OR	95% CI	P value
DLCO <60	5.8	2.3–14.6	<.001	4.6	1.5–13.6	0.006
Anti-RNP antibodies titer >200	3.0	1.5–7.1	0.003	4.9	1.8–13.3	0.003
Never arthritis	5.4	2.1–13.6	<.001	3.3	1.1–9.9	0.033
Age group* at HRCT	1.0	1.0–1.0	0.015	1.6	1.1–2.2	0.012
Anti-Ro52 antibodies present	2.6	1.2–5.9	0.021			
FVC <75	3.0	1.1–8.2	0.040			
ESR >30	2.3	1.0–5.0	0.043			
Sclerodactily	2.0	0.94–4.0	0.071			
Male gender	1.6	0.71–3.5	0.268			

*Patients were divided in 6 age groups (<25 years, 26 to 35 years, 36 to 45 years, 46 to 55 years, 56–65 years and above 65 years). FVC = Forced Vital Capacity % of predicted, DLCO = diffusing capacity of the lung for carbon monoxide % of predicted, RNP = Ribonucleoprotein, ESR = erythrocyte sedimentation rate.

Conclusions: Risk factors of ILD in MCTD are DLCO less than 60% of predicted, high titer RNP antibodies, no previous arthritis and increasing age.
References:
[1] Gunnarsson R, Hetlevik SO, Lilleby V, Molberg O. Mixed connective tissue disease. Best Pract Res Clin Rheumatol. 2016;30(1):95–111.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1841

FRI0726 LONG TERM USE OF ANALGESICS AND NSAIDS IN EARLY RA: LESSONS FROM THE CARERA STUDY

S. Pazmino[1], R. Westhovens[1,2], V. Stouten[1], J. Joly[2], K. Van Der Elst[2,3], P. Verschueren[1,2] on behalf of CareRA study group. *[1]Skeletal Biology and Engineering Research Centre, KU Leuven Department of Development and Regeneration; [2]Rheumatology, University Hospitals Leuven; [3]Skeletal Biology and Engineering Research Centre, KU Leuven Department of Public Health and Primary Care, Leuven, Belgium*

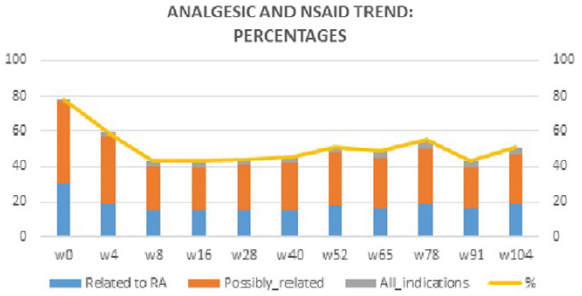
Background: One might consider pain accompanying musculoskeletal conditions as a separate illness entity deserving specific treatment. A subgroup of early Rheumatoid Arthritis (RA) patients has remaining pain despite adequate disease control and this might be reflected in the use of analgesics and NSAIDs.
Objectives: To investigate the usage of analgesics and antiphlogistics prospectively in the pragmatic randomized controlled CareRA trial and describe the users of such drugs taking into account body mass index (BMI), VAS pain and DAS28CRP.
Methods: This study utilized data from the CareRA trial, a 2-year prospective investigator-initiated multicentre pragmatic RCT in patients with early RA (≤1 year) comparing different early intensive treat to target strategies, including glucocorticoid (GC) bridging, aiming for remission in all participants.
All concomitant medication for each patient was recorded, including: name, dose, frequency/timing, continuous/intermittent use, start/end date and indication (possibly/definitely RA-related or other). Meaningful sub-classifications were made (analgesics, cox2-selective and non-selective NSAIDs). We defined two subgroups with prolonged analgesic/NSAID use till w104: the pre-induction group starting before/at baseline (BL) and the post-induction group starting w28-w52, after GC step-down.
Results: From the CareRA cohort (n=379), 90% were on analgesics/NSAIDs at some time during the study and 84% had already started before inclusion (mean 24 weeks). In general, we observed a decreasing trend in the use of analgesics/NSAIDs, with a slight increase after GC step-down. Overall, 266 patients used non-selective and 131 cox2-selective NSAIDs, 154 paracetamol and 85 opioids.
Of the total population, 15, 5% (53 patients) started long-term analgesics/NSAIDs before/at BL (pre-induction group) and 13% (45 patients) from w28-w52 (post-induction group).

A detailed distribution of on-demand/daily analgesic/NSAID use is provided in the table below.

Table 1

Group of long-term users	NSAIDs		Paracetamol	Opioids	Combined therapy
	Non-selective	Selective COX2			
Pre-induction (n=53)	26% (17%/d)	11% (4%/d)	45% (8%/d)	9% (6%/d)	9% (2%/d)
Post-induction (n=45)	33% (16%/d)	20% (7%/d)	33% (4%/d)	13% (7%/d)	0%

Proportionally more patients were using NSAIDs in the post-induction group and paracetamol in the pre-induction group.
Mean DAS28CRP (BL-w104) in the pre-induction group was 3.11 (±0.70) and mean VAS pain 32.7 (±16.3). In this group 62.3% had sustained low disease activity while taking continuous analgesics/NSAIDs. Results in the post-induction group were comparable.
Analgesic/NSAID use was not significantly associated with mean (BL-w104) BMI, DAS28CRP or VAS pain.



Conclusions: Analgesics/NSAID intake in early RA was high (90%) and remarkably about 30% continued using these drugs, despite overall low disease activity. This high consumption might be explained by the ambiguous nature of arthritis-related pain and the lack of differentiation between nociceptive and non-nociceptive pain. Therefore pain management in early RA deserves more attention.

References:

[1] Verschueren, P. et al. ffectiveness of MTX with step-down glucocorticoid remission induction (COBRA Slim) vs other intensive treatment strategies for early RA in a treat-to-target approach: 1-year results of CareRA, a randomised pragmatic open-label superiority trial. Ann Rheum Dis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3399

FRI0727 IMPACT OF MATERNAL SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES ON NEONATAL OUTCOMES: A POPULATION-LEVEL ANALYSIS

S.O. Keeling, A. Savu, P. Kaul. *Department of Medicine, University of Alberta, Edmonton, Canada*

Background: The impact of systemic autoimmune rheumatic diseases (SARDS) on peripartum outcomes is not well described at a population level despite the potential for active disease in this period.
Objectives: We examined the association between SARDs and neonatal outcomes in a contemporary pregnancy cohort in the province of Alberta, Canada.
Methods: The patient population consisted of women giving birth between January 1, 2005 to December 31, 2014 (n=312,081). For women with multiple gestations during the period, one birth event was randomly selected. Women with SARDs included any of the following: systemic lupus erythematosus, systemic sclerosis, myositis and sjogren's syndrome, diagnoses based on the presence of International Classification of Disease version 9/10 codes in outpatient or inpatient records. Baseline characteristics, comorbidities, medication use (available for all births after January 1, 2009), and neonatal outcomes among women with and without SARDs were compared.
Results: Compared to women with no SARDs (n=311,755), women with SARDs (n=326, 0.1%) were slightly older (SARDs 31.3 vs No SARDs 29.3 years ($p<0.01$)) but did not differ in terms of rural residence, ethnicity, median household income or nulliparity. However, rates of pre-term delivery, emergent cesearian section, induction, hypertensive disorders/eclampsia and mortality were higher among women with SARDs than those with no SARDs (Table 1). Offspring of women with SARDs had lower birth weights, were more likely small for gestational age (SGA), and had longer stays in neonatal ICU (Table 1). Among women with SARDs, prescription rates in the 270 days prior to delivery were highest for anti-malarials (Table 2). After multivariable adjustment, both NSAIDS use (OR (95% CI): 5.24 (1.57, 17.52), $p<0.01$) and steroid use (OR (95% CI): 3.15 (1.31, 7.59), $p<0.01$) were significantly associated with a higher risk of preterm delivery.
Conclusions: Women with SARDs are at an increased risk of adverse outcomes during pregnancy. The association between corticosteroid and NSAID use and preterm delivery requires further investigation. Our findings suggest the need for closer monitoring and coordinated care with obstetrics and perinatology in these high risk women.

Table 1. Maternal and Neonatal Outcomes in SARDs vs No SARDs Mothers*

Outcome	No SARDs # (%)	SARDs # (%)	P-value
Pre-term Delivery	22205 (7.1)	58 (17.8)	<0.01
C-section (Emergent)	51132 (16.4)	82 (25.2)	<0.01
Hypertensive disorders	20029 (6.4)	47 (14.4)	<0.01
Small for gestational age	35047 (11.2)	68 (20.9)	<0.01
Congenital Anomaly	5810 (1.9)	11 (3.4)	0.05
Mean days in neonatal ICU	0.8 (5.0)	2.3 (9.6)	<0.01

*Sensitivity analysis utilizing primiparious SARDs vs NonSARDs women confirmed similar results.

Table 2. Unadjusted Effect of Medication Use During Pregnancy on Maternal and Neonatal Outcomes

Outcome	Steroids	NSAIDS	Antimalarials
# (%) SARDS patients on medication	33 (16.3)	13 (6.4)	51 (25.1)
SGA, OR (95% CI)	2.06 (0.91, 4.67)	1.08 (0.29, 4.12)	1.54 (0.74, 3.20)
Gestational Diabetes, OR (95% CI)	1.67 (0.51, 5.47)	n/a	0.91 (0.28, 2.93)
Preterm delivery, OR (95% CI)	3.84 (1.66, 8.89)*	4.96 (1.55, 15.85)*	1.82 (0.83, 4.00)
C-section, OR (95% CI)	0.88 (0.41, 1.90)	0.98 (0.31, 3.11)	0.57 (0.29, 1.13)
Hypertensive disorders of pregnancy, OR (95% CI)	3.67 (1.51, 8.93)*	0.50 (0.06, 4.03)	1.23 (0.51, 2.99)

*$p<0.05$.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4561

FRI0728 OSTEOARTHRITIS AND GOUT: REAL-WORLD EVIDENCE EVALUATING PATIENT CHARACTERISTICS, TREATMENT PATTERNS, AND HEALTHCARE UTILIZATION

S. Krasnokutsky Samuels[1], M. Pillinger[1], S. Kabadi[2], D.C. Taylor[3], R. Morlock[4]. *[1]New York University, New York; [2]AstraZeneca Pharmaceuticals, Gaithersburg; [3]Ironwood Pharmaceuticals, Cambridge; [4]YourCareChoice, Ann Arbor, United States*

Background: Gout and osteoarthritis (OA) are common in the United States, but little is known about potential associations of OA and hyperuricemia/gout with clinical outcomes.
Objectives: This study examined variations in gout severity, management, and healthcare utilization among gout patients with and without OA.
Methods: Data were assessed from a survey of US physicians and patient chart audits. Participating physicians managed the care of ≥50 patients with gout annually; chart audits were of their most recent 5 consecutive adult patients with confirmed gout. Gout severity was measured by physician global assessment, flares, organ/joint damage, and tophi. Treatment characteristics, presence of clinician-confirmed OA, and sociodemographic factors were identified. Descriptive and multivariate (stepwise logistic regression) statistics analyzed the differences among gout patients with and without clinician-confirmed comorbid OA, and assessed urate-lowering therapy (ULT) use and gout control.
Results: Overall, 1159 charts of gout patients were abstracted (230 w/ OA, 929 w/o; 81% male; 71% white); the proportion of patients aged ≥61 was greater for those with gout and OA than those with gout but without OA (63% vs 32%; $P<0.001$). Patients with gout and OA had longer mean duration of gout (63 vs 41 months), were more likely to have tophi (44% vs 19%), joint damage (31% vs 11%), and clinician-rated severe gout (31% vs 12%) than those without OA (all $P<0.01$). Patients with gout and OA were also more likely to receive ULT (89% vs 70%; $P<0.01$), and among those receiving ULT, OA patients treated with allopurinol received a higher average daily dose (325 mg vs 296 mg; $P=0.031$). Gout patients with OA were more likely to have additional comorbidities (cardiovascular disease, kidney disease, COPD, depression, diabetes, hyperlipidemia, hypertension, obesity, prostate problems [men]) and have chronic pain than those without OA (all $P<0.05$). Gout patients with OA reported more office visits (4.0 vs 3.5), were more likely to have an emergency department visit (17% vs 9%), and were more likely to require surgery for gout in the past 12 months (3% vs 0.3%) (all $P<0.01$). In both groups, ULT use was associated with better gout control, but the specific factors predictive of ULT use and disease control varied between those with and without OA.
Conclusions: Gout patients with OA were more likely to have a greater impact on health system spending, with additional comorbidities and more severe gout than those without OA. These data suggest that gout patients with OA constitute a less healthy group in need of more careful monitoring and more aggressive gout management.
Acknowledgements: This study was sponsored by AstraZeneca.
Disclosure of Interest: S. Krasnokutsky Samuels: None declared, M. Pillinger: None declared, S. Kabadi Employee of: AstraZeneca, D. Taylor Employee of: Ironwood, R. Morlock Consultant for: AstraZeneca, Ironwood, Ardea Biosciences
DOI: 10.1136/annrheumdis-2017-eular.5030

FRI0729 **DEFINITION OF REMISSION AND MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW**

T. Gudu[1,1], R. Ionescu. *Rheumatology, Sf Maria Hospital, UMF Carol Davila, Bucharest, Bucharest, Romania*

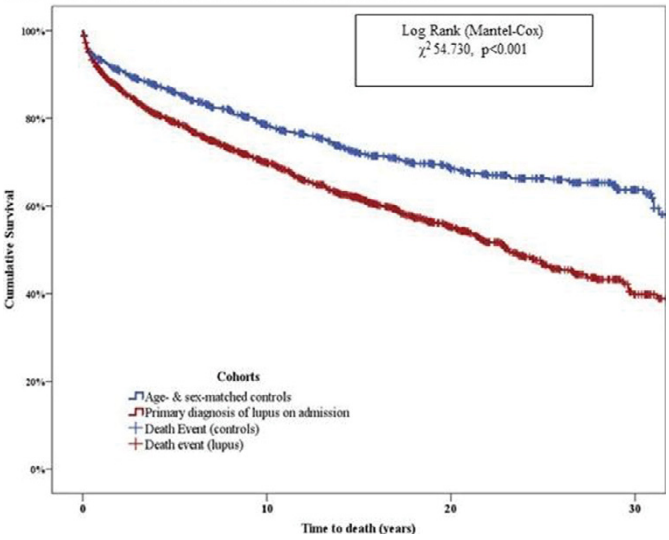
Background: In psoriatic arthritis (PsA) a state of minimal disease activity (MDA) or remission are the target of treatment [1], but due to the heterogeneity of disease manifestations, it is still an unmet need. Coates et al [2] have developed and validated a composite score for MDA that encompasses most disease domains. However, for disease remission there is no accepted definition, with studies "borrowing" measures from rheumatoid arthritis or using their own criteria.
Objectives: The objective of this study was to analyse existing data on the definition of MDA and remission in studies on PsA.
Methods: A systematic literature review was performed. Studies evaluating remission or minimal disease activity in PsA either as a primary or secondary outcome, published between 2007–2017, were identified using the terms ("psoriatic arthritis") AND ("remission" OR "low disease state" OR "low disease activity" OR "minimal disease state" OR "minimal disease activity"). Studies assessing disease activity in general, without specifically mentioning remission or MDA were not included; reviews and case-reports were also excluded.
Results: Two hundred and thirty-five publications were identified, of which 56 were included in the final analysis. The majority were observational studies (85.5%) and there were no qualitative studies identified. In total, 10843 PsA patients were analysed: 8779 in observational studies and 2064 in interventional studies; 4823 patients fulfilled the CASPAR criteria [3] and 6667 (31 studies) were taking a biologic drug at their inclusion. The majority of the studies assessed either MDA (65.5%) or remission (60%), but only 14 studies (25.5%) assessed both of the two outcomes. MDA or remission were mainly used as a secondary outcome (52.7% of the studies).
MDA was assessed mainly in observational studies (61.7%) and in almost all cases (88.9% of the studies) the definition used was the one proposed by Coates et al [2]. Remission was also assessed mainly in observational studies (63.8%). The most used definition (57.6%) was based on the disease activity score (DAS28), with values less than 2.6 considered as "remission". Articular involvement was assessed in all cases, whilst skin psoriasis, dactylitis and enthesites were rarely included in the definition of remission (15.15% each). Physician's assessment was taken into consideration in almost a third of the studies (27.3%), but the patient's assessment (pain or global evaluation) was included in more than half of the studies (69.7%). However, other patient reported outcomes were sparsely used (i.e., fatigue and morning joint stiffness were included in only one study) or not all reported (e.g, social participation, work productivity, depression).
Conclusions: Whilst for MDA there is a standardised definition which is widely used, there is no accepted definition for remission. In defining remission, domains other than articular are seldom used and although patient's opinion is usually evaluated, it rarely includes domains other than pain or global assessment. The concept of remission remains un unmet need in PsA.
References:
[1] Gossec L, Smolen JS, Ramiro S, et al. Ann Rheum Dis 2016;75(3):499–510.
[2] Coates LC, Fransen J, Helliwell PS. Ann Rheum Dis 2010;69(1):48–53.
[3] Taylor W, Gladman D, Helliwell P, et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006;54(8):2665–73.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5813

FRI0730 **THE NEED FOR HOSPITAL ADMISSION FOR SYSTEMIC LUPUS ERYTHEMATOSUS IN WESTERN AUSTRALIA LEADS TO A DOUBLING OF THE ALL-CAUSE MORTALITY RISK AS SEEN IN CONTROLS, ESPECIALLY FOR MEDICARE RELIANT AND MALE PATIENTS**

W.D. Raymond[1], D. Preen[2], C. Inderjeeth[1,3], H. Keen[4,5], J. Nossent[1,6]. *[1]School of Medicine & Pharmacology; [2]School of Population Health, University of Western Australia; [3]Rehabilitation and Aged Care, Sir Charles Gairdner Hospital; [4]Rheumatology, Fiona Stanley Hospital; [5]School of Medicine, Murdoch University; [6]Rheumatology, Sir Charles Gairdner Hospital, Perth, Australia*

Background: Hospitalisation for Systemic Lupus Erythematosus (SLE) is a significant event.
Objectives: We aimed to understand the factors leading to an incident admission and its impact on long term outcome in SLE patients in Western Australia (WA).
Methods: Using whole-population data linkage of hospital admissions, cancer registrations and death records in WA from 1980 to 2015, we performed a retrospective comparative analysis for all patients admitted with a first ever primary diagnosis of SLE (ICD-9-CM 695.4, 710.0, ICD-10-AM L93.0 & M32). For SLE patients, we analysed annual incident hospitalisation rates and compared patient characteristics, all-cause mortality and cancer risk (by Kaplan-Meier and Cox regression) versus age- and gender-matched controls free of rheumatic disease.
Results: The incident hospitalisation rate for SLE (mean 20.9/million/year (CI: 11–35) showed little variation. SLE patients were younger, more likely to be Indigenous, uninsured, have kidney and cardiovascular disorders and to die during their first hospitalisation (Table 1). Cancer risk was equivalent, but a first admission for SLE doubled the risk of subsequent death (OR=1.99, CI: 1.5– 2.7, p<0.001) (Figure 1/Table 2). Medicare reliance (OR 1.7, CI: 1.4 – 1.9, p=0.001) and male gender (OR 1.4, CI: 1.0 – 1.8, p<0.04) were the strongest independent predictors of death.

Figure 1: Kaplan-Meier survival analysis of all-cause mortality for SLE patients and age- and sex-matched controls (free of rheumatic disease) from index hospitalisation.



Conclusions: Hospitalisation rates for SLE in WA have not decreased over 25 years. Once hospital-based management for SLE was required, the risk of all-cause mortality doubled compared to age and gender-matched controls. This risk was greatest in Medicare reliant or male SLE patients and not due to increased cancer risk.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5866

FRI0731 **ASSESSING THE RISK OF RAPID RADIOLOGIC PROGRESSION IN HUNGARIAN RHEUMATOID ARTHRITIS PATIENTS**

G. Szücs[1], J. Gaál[2], P. Géher[3], E. Gömöri[4], A. Kovács[5], L. Kovács[6], K. Nagy[7], E. Posta[8], L. Tamási[9], E. Tóth[10], E. Varga[11], A. Domján[1], Z. Szekanecz[1]. *[1]Department of Rheumatology, University of Debrecen, Faculty of Medicine; [2]Department of Rheumatology, Kenézy County Hospital, Debrecen; [3]Department of Rheumatology, Hospital of Hospitaller Brothers of St. John of God, Budapest; [4]Department of Rheumatology, Pándy Hospital, Gyula; [5]Department of Rheumatology, Hospital of State Railways, Szolnok; [6]Department of Rheumatology, University of Szeged, Szeged; [7]Department of Rheumatology, Ferenc Markhot Hospital, Eger; [8]Department of Rheumatology, András Jósa Hospital, Nyiregyháza; [9]Department of Rheumatology, Semmelweis Teaching Hospital, Miskolc; [10]Department of Rheumatology, Ferenc Flór Hospital, Kistarcsa; [11]Department of Rheumatology, Markusovszky Hospital, Szombathely, Hungary*

Background: Prognosis of rheumatoid arthritis (RA) should be assessed early during the disease course. Rapid radiological progression (RRP) has been defined as a ≥% unit increase in van der Heijde-Sharp score within a year. The matrix risk model has been developed by Vastesaeger et al in 2009. This tool calculates RRP based on non-radiographic indicators such as baseline CRP, RF and swollen joint count.
Objectives: We wished to test the matrix prediction model int he very first Hungarian cohort study.
Methods: In this non-interventional, cross-sectional retrospective study carried out in 11 Hungarian arthritis centres, we assessed high risk (≥40%) of RRP in biologic-naive RA patients with active disease. In order to obtain a representative sample, patients were selected from each centre by a random technique. RRP was calculated according to the matrix model described by Vastesaeger et al. As a secondary endpoint, we compared methotrexate (MTX) responders vs non-responders with respect to RRP.
Results: We screened data of 1843 RA patients. Finally, data obtained from 1356 patients could be used for RRP prediction and MTX responsiveness. The mean age of patients was 55.5 years, 84.7% were women. The mean disease duration was 8.4 years. At the time of the assessment, mean CRP was 17.7 mg/l, RF was 139,3 IU/ml, mean DAS28 was 5.00 and mean swollen joint count was 6.56. High risk ((≥40%) of RRP could be determined in 18.2% of patients. Among continuous variables other than those used for calculation of RRP risk, RA patients with the risk of RRP≥40% (n=247) had significantly lower age than those with RRP<40% (n=1109) (53.33±12.31 vs 56.02±13.50 years; p=0.001). With respect to binary variables, the risk of RRP≥40% was significantly associated

with non-response to MTX (OR: 17.82), male gender (OR: 1.53), ACPA positivity (OR: 2.11), the presence of erosions (OR: 1.37) and current smoking (OR: 1.66). Binary logistic regression analysis revealed that MTX non-response (OR: 16.84), male gender (OR: 1.67) and ACPA positivity (OR: 2.18) were independent predictors of high-risk RRP (≥40%). With regards to MTX responsiveness, binary logistic regression analysis confirmed that both male gender (OR: 5.20) and the presence of erosions (OR: 7.98) were independent predictors of high RRP risk in the MTX responder subpopulation.

Conclusions: In the first bioloigc-naive Hungarian RA cohort assessed for RRP, RRP occurs in almost one-fifth of the patients. These patients differ from others in various clinical and serological parameters. RRP has also been associated with non-response to MTX.

References:

[1] Vastesaeger N, Xu S, Aletaha D, St Clair EW, Smolen JS. A pilot risk model for the prediction of rapid radiographic progression in rheumatoid arthritis. Rheumatology (Oxford). 2009 Sep;48(9):1114–21.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3199

SATURDAY, 17 JUNE 2017

Innate immunity in rheumatic diseases

SAT0001 LACK OF OBESITY-RELATED FEATURES IN ADIPOCYTES AND INFLAMMATORY CELLS IN THE INFRAPATELLAR FAT PAD (IFP)

A. Ioan-Facsinay[1], A. de Jong[1], I. Klein-Wieringa[1], S. Andersen[1], J. Kwekkeboom[1], L. Herb-van Toorn[1], B. de Lange-Brokaar[1], D. van Delft[2], J. Garcia[3], W. Wei[3], H. van der Heide[2], Y. Bastiaansen-Jenniskens[3], G. van Osch[3], A.-M. Zuurmond[4], V. Stojanovic-Susulic[5], R. Nelissen[2], R. Toes[2], M. Kloppenburg[2]. *[1]Rheumatology; [2]Leiden University Medical Center, Leiden; [3]Erasmus MC, University Medical Center, Rotterdam; [4]TNO, Leiden, Netherlands; [5]Janssen, Pharmaceutical Companies Johnson & Johnson, Springhouse, United States*

Background: Obesity is associated with the development and progression of osteoarthritis (OA), both for weight-bearing and non-weight bearing joints. Several lines of research indicate that obesity-related systemic factors, such as adipose tissue-derived factors, could be involved in this association. The infrapatellar fat pad (IFP) is an adipose tissue depot localized in the knee joint. and could mediate obesity-associated effects. However, it is currently unknown whether and how obesity affects IFP.
Objectives: To investigate the presence of obesity-related features in adipocytes and infiltrating immune cells in the IFP of OA patients.
Methods: Knee OA patients (N=155: 68% women, mean age 65 years, mean (SD) BMI 29.9 kg/m^2 (5.7)) were recruited: IFP volume was determined by MRI in 79 knee OA patients, while IFP and subcutaneous adipose tissue (SCAT) were obtained from 106 patients undergoing arthroplasty. Crown-like structures (CLS) were determined using immunohistochemistry. Adipocyte size was determined by light microscopy and histology. Stromal vascular fraction (SVF) cells were characterized by flow cytometry.
Results: IFP volume (mean (SD) 23.6 (5.4) mm^3) was associated with height, but not with BMI or other obesity-related features such as waist circumference, fat percentage and waist to hip ratio. The volume of IFP adipocytes did not correlate with BMI, in contrast to SCAT adipocytes. Few CLS were observed in IFP and their number did not differ between individuals with high and low BMI. Moreover, high BMI was not associated with higher infiltrating immune cell numbers in IFP, nor with changes in immune cell populations. Likewise, no molecular differences were observed in FCM-secreted factors between high and low BMI, except for an increased TNFa secretion in obesity. Since obesity is usually associated with a shift towards pro-inflammatory macrophages in conventional adipose tissue, we have extensively characterized IFP macrophages. Surprisingly, CD206 and CD163, usually associated with an anti-inflammatory phenotype were the most abundantly expressed surface markers on macrophages (81% and 41% respectively). In contrast, cytokine profiles revealed a pro-inflammatory phenotype of the total macrophage population, with cells producing predominantly IL-6 and TNFα, but little IL-10. Interestingly, the CD163+ macrophages were bigger and had a more activated and pro-inflammatory phenotype than their CD163- counterparts. However, no association with BMI could be observed for different macrophage populations or their cytokines.
Conclusions: BMI-related features usually observed in SCAT and visceral adipose tissue could not be detected in IFP of OA patients, a fat depot implicated in OA pathogenesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5728

SAT0002 INNATE LYMPHOID CELLS (ILCS) ARE DIFFERENTIALLY DISTRIBUTED IN INFLAMMATORY AND NON-INFLAMMATORY JOINT DISEASES

I. Meunier[1], I. Marois[2], M. Richter[3], G. Boire[4]. *[1]Meakins-Christie Laboratories, McGill University, Montréal; [2]Université de Sherbrooke, Sherbrooke, Canada; [3]Medicine; [4]Medicine, Division of Rheumatology, Université de Sherbrooke, Sherbrooke, Canada*

Background: Innate lymphoid cells (ILC) are immune cells of the lymphoid lineage not expressing specific antigen receptors.They are classified into three subsets: *ILC1* (including Natural Killer (NK) cells and ILC1) secrete IFN-γ and TNF-α; *ILC2* secrete IL-4, IL-5, IL-9, IL-13, and amphiregulin; *ILC3* (including Lymphoid Tissue Inducer (LTi) and NK cell activating receptor (NCR+ ILC3) secrete IL-17A and IL-22.
Objectives: To enumerate the different subsets of ILCs in peripheral blood and synovial fluids of patients with inflammatory and non-inflammatory joint effusions.
Methods: Patients with confirmed synovial effusion presenting at the Centre hospitalier universitaire de Sherbrooke (CHUS) signed an informed consent form. Cells from joint effusions were separated by Ficoll-density gradient centrifugation, stained for ILC, and analysed using a BD FACS Aria III flow cytometer. For cytokine detection, cells were stimulated for 6h with PMA/ionomycin prior to cell staining. The distribution of ILC subtypes according to various diagnoses is presented in cells/ml and ratios of ILC subtypes per ml of synovial fluid relative to peripheral blood. The protocol was approved by the CRC-CHUS ethics committee.
Results: Synovial fluids and blood from 57 patients with various diagnoses were analyzed. The highest concentrations (cells/mL) of ILC cell subtypes found in the synovial fluids/peripheral blood were: ILC1: 7/4; ILC2: 70/3; LTi: 4x10^4 (in RA)/8x10^4 (in OA); NCR+ ILC3: 1.3x10^5 (in JIA)/5.8x10^4; NK: 5/1.
Synovial fluids relative to peripheral blood frequently presented ratios of ILC cell subtypes $\leq$1, suggesting little preferential homing in the joints. However, synovial fluids (relative to blood) were enriched 45 and 7 times for NCR+ ILC3 in Juvenile Idiopathic Arthritis (JIA) and spondylarthropathy patients, respectively, and 8 and 6 times for LTi in Psoriatic Arthritis and Rheumatoid Arthritis (RA) patients, respectively. We observed marked heterogeneity in ILC numbers within patients with the same inflammatory joint diseases. Part of this heterogeneity was associated with the presence of concomitant joint degenerative disease and low cell numbers in the synovial fluids.
Conclusions: 1. LTi and NCR+ ILC3 subtypes are the ILC most abundant in synovial fluids.
ILC1 and NK cells are rare in synovial fluids and unlikely to be involved in pathogenesis; ILC2 remain infrequent, even when enriched in synovial fluid relative to peripheral blood (e.g. in JIA, RA and gout).
2. Relative to their concentrations in peripheral blood, LTi and NCR+ ILC3 subtypes are markedly enriched in synovial fluids of patients with autoimmune-mediated diseases, notably LTi in RA and Psoriatic Arthritis, and NCR+ ILC3 in spondylarthropathy and JIA. The abundance of these IL-17 secreting cells in synovial fluids from these diseases is especially intriguing.
3. We observed significant heterogeneity within patients with the same clinical diagnosis.
4. The pathophysiological implications of the differential distribution of subtypes of ILC cells across diseases and within clinical diagnoses remain unclear.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4095

SAT0003 SINGLE-NUCLEOTIDE POLYMORPHISMS ASSOCIATED WITH P2X7R FUNCTION REGULATE THE ONSET OF GOUTY ARTHRITIS

J. Tao, M. Cheng. *Department of Rheumatology & Immunology, Anhui Provincial Hospital Affiliated to Anhui Medical University, hefei, China*

Background: Gout is an inflammatory disease, considered to be caused by the increased production of IL-1β stimulated by monosodium urate (MSU) crystals. However, some hyperuricemia patients, even gouty patients with tophi in the joints, never have gout attack, indicating some other pathogenic pathways participating in the secretion of IL-1β rather than MSU in the pathogenesis of acute gouty arthritis. ATP-P2X7R-IL-1β axis may be one of them.
Objectives: The purpose of this study is to explore the role of ATP in the pathogenesis of gout, and the association between ATP receptor (P2X7R) function associated single nucleotide polymorphisms and gout arthritis.
Methods: The non-synonymous SNPs loci of P2X7R in Chinese people were screened, to compare the frequencies of different alleles and genotype distribution of selective SNPs in 117 gouty patients and 95 hyperuricemia patients. Then peripheral white blood cells were purified from the peripheral blood of randomly selected 43 gout patients and 36 hyperuricemia patients from the total. After culturing the cells with MSU or MSU+ATP, supernatants were collected and the concentrations of IL-1β were detected by enzyme linked immunosorbent assay (ELISA).
Results: 1. Eight SNPs loci including rs1653624, rs10160951, rs1718119, rs7958316, rs1621388, rs16950860, rs208294, rs17525809 and rs2230912 were screened and detected, and rs1653624, rs7958316 and rs17525809 were demonstrated associated with gout arthritis. 2. After the stimulation with MSU+ATP, the concentrations of IL-1β in supernatants of gouty patients were significantly higher than that in hyperuricemia groups [(131.08±176.11)pg/ml vs (50.84±86.10)pg/ml]. Furthermore, gouty patients carrying susceptibility genotype AA or AT of rs1653624 had significant higher concentration than that carrying non-susceptibility genotype TT [(104.20±164.25)pg/ml vs (21.90±12.14)pg/ml]. However, no differences were found while stimulated with MSU alone.
Conclusions: ATP promotes the pathogenesis of gouty arthritis by increasing the secretion of IL-1 β, and its receptor (2X7R) function associated single nucleotide polymorphisms may be related to gouty arthritis, which indicates that ATP-P2X7R signaling pathway plays a significant regulatory role in the pathogenesis of gout.
Acknowledgements: This study was sponsored and funded by the Anhui Provincial Natural Science Foundation (1708085MH191) and grants from the National Natural Science Foundation of China (81671601).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5920

SAT0004 NEW AUTOANTIGEN (JKTBP) PART OF STRESS GRANULES CLOSES THE SENSITIVITY GAP IN RHEUMATOID ARTHRITIS

B. Marklein, M. Jenning, K. Muenzer, G. Burmester, K. Skriner. *Department of Rheumatology and Clinical Immunology, Charité University Medicine, Berlin, Germany*

Background: Rheumatoid arthritis triggers the formation of prion-like stress granules. To investigate which members of the heterogeneous nuclear ribonucleoprotein (hnRNP)-family, components of functionally important subcellular

particles are targeted by autoantibodies from RA and other systemic rheumatic diseases.
Methods: Using a protein macroarray we identified JKTBP in humans and animal models of inflammatory rheumatic diseases. Bacterially expressed recombinant JKDBP proteins were used to confirm the obtained data. Epitope, TLR7/9 and MyD88 dependency was determined by ELISA. JKTBP expression in cultivated cells and synovial tissue was analysed by indirect immunofluorescence, immunoblot and immunohistochemistry.
Results: Anti-JKTBP autoantibodies were detected in 46% of the patients with systemic lupus erythematosus (n=103), in 20–30% of the patients with rheumatoid arthritis (n=286), in 10% of the patients with mixed connective tissue disease (n=20) or spondyloathropathy (n=20), and in <10% of patients with other autoimmune disorders (n=382). Sera positive to JKTBP as well as hnRNP-B1, revealed nearly two thirds of the RF IgM/ CCP2-seronegative patients as early RA patients. Combining sensitivities to all autoantigens tested (JKTBP, AUF1, hnRNP-B1), it was possible to identify 92% of the early RA patients (n=91). In the MRL/lpr mouse model of SLE, mice deficient of MyD88 or TLR7/9 lacked anti-JKTBP autoantibodies, whereas mice deficient of SIGIRR/TIR8 showed enhanced anti-JKTBP autoantibody production. These results show that autoantibody generation against JKTBP, AUF1, hnRNP-B1 is dependent on TLR 7 and TLR9 like rheumatoid factor different to TLR 7 dependent generation of snRNPs. For all tested autoantigens either their titter or generation are dependent on the activation of innate immunity genes MyD88 and SIGIRR/TIR8 gene.
In localization, experiments anti-JKTBP autoantibodies specifically stained stress granules (SG) in the cytoplasm. Immunohistochemical studies revealed JKTBP to be highly expressed in SG in the cytoplasm of RA synovial tissue different from OA and normal control tissue
Conclusions: These data identify SG as targeted particle in RA and JKTBP as a novel autoantigen in RA, SLE patients and mouse models of inflammatory rheumatic diseases. In combination with the hnRNPs AUF1 and hnRNP-B1, JKTBP autoantibodies close the sensitivity gap in RA left by rheumatoid factor and anti-CCP2 antibodies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3653

SAT0005 DNA METHYLATION INHIBITORS PRODUCE SUSTAINED REMISSION OF ARTHRITIS IN MICE AND PROMOTE REGULATORY T CELL RESPONSES

W. Tseng[1,2], I.-S. Huang[1], F. Clanchy[1], K. McNamee[1], D. Perocheau[1], P. Ericsson[3], H.-O. Sjogren[3], Z. Xue[3], L. Salford[3], A. Sundstedt[4], R.O. Williams[1]. *[1]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford University, The Kennedy Institute of Rheumatology, Oxford, United Kingdom; [2]Division of Rheumatology, Allergy and Immunology, Chang Gung Memorial Hospital, Keelung, Taiwan, Province of China; [3]Department of Clinical Sciences, Lund University, The Rausing Laboratory; [4]Idogen, Lund, Sweden*

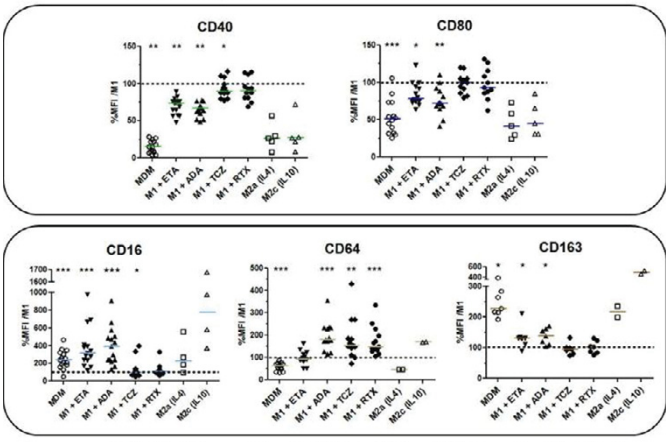
Background: Dysfunction of Tregs results in a breakdown of immunological tolerance and has been implicated in the pathogenesis of autoimmune diseases, including systemic lupus erythematosus, rheumatoid arthritis (RA) and type 1 diabetes. Treg function is regulated by epigenetic factors and we have previously reported the presence of Tregs expressing an aberrant DNA methylation profile in RA.
Objectives: The aim of this study was to assess the potential utility of DNA methylation inhibitors for the treatment of RA, using collagen-induced arthritis (CIA) as an animal model.
Methods: DBA/1 mice were immunised with bovine type II collagen emulsified in complete Freund's adjuvant. The mice were treated with zebularine (400 mg/kg), decitabine (1 mg/kg) or psammaplin A (10 mg/kg) for 4 days, starting on the day of arthritis onset. Treatment was then stopped and the disease was monitored up to day 10 of arthritis. The expression of Treg genes was measured in lymph nodes on day 10 by qPCR. To assess the effect of DNA methylation inhibitors on generation of Tregs, naïve $CD4^+CD25^-$ T cells were cultured with mitomycin C treated APCs plus IL-2, TGFβ and anti-CD3 in the presence or absence of DNA demethylating agents and numbers of $CD4^+FoxP3^+$ Tregs were determined by FACS after 72h.
Results: Treatment with zebularine resulted in a sustained reduction of arthritis severity, accompanied by an increase in the expression of Treg associated genes, *Foxp3, Ctla4 and Tgfb1*, in draining lymph nodes. Treatment with decitabine produced a more profound reduction in disease severity whereas the therapeutic effect of psammaplin A was more transient. All three DNA methylation inhibitors could convert $CD4^+CD25^-$ T cells into $CD4^+FoxP3^+$ Tregs in a dose-dependent manner *in vitro*.
Conclusions: This study has shown that pulse treatment with DNA demethylating drugs produces a sustained reduction in the severity of arthritis and promotes the generation of Tregs. The findings raise the possibility that epigenetic drugs can be used on a short-term basis for re-setting tolerance and boosting Treg responses in human autoimmune disease.
Acknowledgements: This work was supported by grants from Chang Gung Memorial Hospital (Grant Code: CMRPG2D0251) and Idogen.
Disclosure of Interest: W. Tseng: None declared, I.-S. Huang: None declared, F. Clanchy: None declared, K. McNamee: None declared, D. Perocheau: None declared, P. Ericsson: None declared, H.-O. Sjogren Shareholder of: Hans Olov Sjogren is a co-founder of Idogen and a co-inventor of a patent on the use of zeburaline for the treatment of autoimmune diseases., Z. Xue: None declared, L. Salford Shareholder of: Leif Salford is a co-founder of Idogen and member of the board of Idogen and a co-inventor of a patent on the use of zeburaline for the treatment of autoimmune diseases, A. Sundstedt Employee of: Anette Sundstedt is an employee of Idogen, R. Williams Consultant for: Dr. Richard Williams is on scientific board of Idogen
DOI: 10.1136/annrheumdis-2017-eular.3511

SAT0006 ANTI-TNF AGENTS INDUCE MACROPHAGES WITH PRO-RESOLVING PHENOTYPE

Y. Degboe[1,2], B. Rauwel[2], M. Baron[2], J.-F. Boyer[1,2], A. Cantagrel[1,2], A. Constantin[1,2], J.-L. Davignon[1,2]. *[1]Centre de Rhumatologie, CHU Purpan; [2]CPTP, INSERM UMR 1043, Toulouse, France*

Background: Macrophages contribute to the rheumatoid arthritis (RA) pathogenesis. They can display various states of activation or " polarization ", characterized by distinct functions in inflammation, and reversibility depending on their environment [1]. M1 polarization corresponds to the "classical", pro-inflammatory activation as identified in RA. M2 "alternative" polarizations display pro-resolving or wound-healing properties.
Data concerning the effects of RA biological drugs (bDMARDs) on macrophage polarization are scarce.
Objectives: To assess in vitro modulation of macrophage polarization by RA bDMARDs.
Methods: Blood monocytes from 14 healthy donors were positively sorted by CD14+ magnetic selection. Macrophages were Derived from Monocytes (MDM) by 5 days of culture in the presence of MCSF, and activated or not for 24h as M1 pro-inflammatory MDM (by LPS + IFNγ) or as M2 alternative MDM (by IL10 or IL4). MDM were cultured with or without bDMARDs.
We evaluated 2 anti-TNF agents (etanercept (ETA), adalimumab (ADA)), 1 anti-IL6R agent (tocilizumab (TCZ)), and 1 anti-CD20 agent (rituximab (RTX)) used as control monoclonal antibody. bDMARDs effects were assessed separately on differentiation and activation phases by flow cytometric analysis of membrane markers. Functional aspects of polarization were assessed by analysis of cytokine production in supernatants (cytometric bead array) and phagocytosis (flow cytometry).
MDM cultured in the presence of bDMARDs were compared to untreated MDM by a Wilcoxon matched pairs test.
Results: We first validated *membranous polarization markers* in our culture model: CD40 and CD80 as M1 (LPS + IFNγ) markers; CD16, CD163 and CD64 as M2 (IL10) markers, CD206 and CD200R as M2 (IL4) markers.
Anti-TNF significantly modulated surface polarization markers of *MDM* obtained after differentiation. CD40 decreased with both anti-TNFs. CD16 increased with ADA, whereas opposite effects on CD64, decrease with ETA, increase with ADA, were observed. CD206 increased with ADA. CD200R increased with both anti-TNF. We observed a significant increase in CD64 with TCZ. RTX induced no modulation except an increase in CD64.
Concerning the effect of bDMARDs on *M1 activation* (M1 MDM) shown in Figure, anti-TNF agents induced a significant decrease in M1 markers and a significant modulation in M2 (IL10) markers. We observed a decrease in CD40 and CD80, an increase in CD16, CD163, a decrease in CD64 with ETA and an increase with ADA. TCZ induced a slight but significant decrease in CD40 and an increase in CD64. RTX only affected CD64 as observed for differentiation.
In *M2 (IL4) et M2 (IL10) activated MDM*, anti-TNF agents induced a similar trend toward M2 (IL10) phenotype.
Anti-TNF agents led to a significant decrease in *TNFα, IL6, IL12 and IL10 levels* measured in cell culture supernatant after M1 MDM. TCZ mainly affected IL6 and TNFα productions. No significant effect was observed with RTX.

Normalized polarization surface markers on M1 MDM



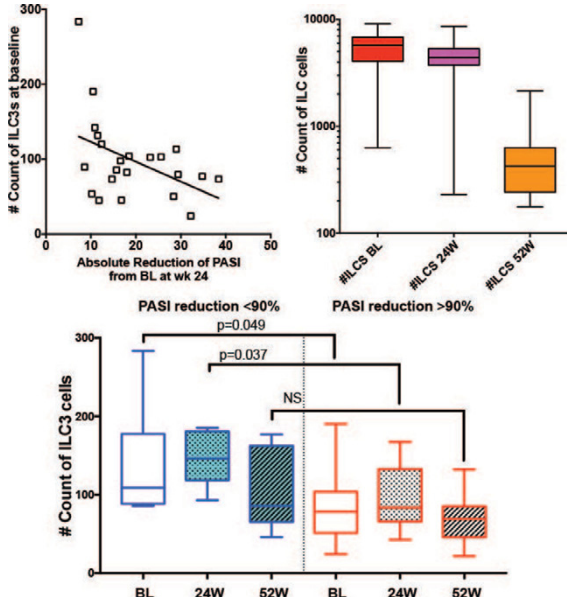
Data were normalized to M1 MDM (represented as a dotted line) for each donor. Statistical comparison of M1 MDM without bDMARD (dotted line) versus M1 MDM with bDMARD, using a Wilcoxon matched pairs test → * p < 0.05 ; ** p<0.005 ; *** p<0.0005

Phagocytosis was superior in M2 (IL10) and M2 (IL4) activated MDM than in M1 MDM. Anti-TNF agents but not TCZ or RTX induced an increase of phagocytosis in M1 MDM.
Conclusions: Anti-TNF agents upregulate M2 alternative pro-resolving markers and downregulate M1 inflammatory markers in macrophages. Our results need to be extended by transcriptional analysis and evaluated in RA patients.
References:
[1] Martinez FO and Gordon S, F1000Prime Reports 2014, 6:13.
Disclosure of Interest: Y. Degboe Grant/research support from: Société Française de Rhumatologie, B. Rauwel: None declared, M. Baron: None declared, J.-F. Boyer: None declared, A. Cantagrel: None declared, A. Constantin: None declared, J.-L. Davignon: None declared
DOI: 10.1136/annrheumdis-2017-eular.1249

SAT0007 GROUP 3 INNATE LYMPHOID CELLS NUMBERS IN PERIPHERAL BLOOD PREDICT USTEKINUMAB (STELARA) THERAPY RESPONSIVENESS IN PSORIATIC DISEASE CASES WITH SUBCLINICAL IMAGING ENTHESOPATHY

Y.M. El-Sherbiny[1,2], L. Savage[1], M. Wittmann[1,2], P. Emery[1,2], M. Goodfield[3], D. McGonagle[1,2]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]National Institute of Health Research Leeds Musculoskeletal Biomedical Research Unit; [3]Department of Dermatology, Leeds Centre for Dermatology, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Ustekinumab[1] targets the common p40 sub-unit of interleukin-12 (IL-12/interleukin-23 (IL-23). In patients treated with Ustekinumab for psoriasis where patients were selected on the basis of subclinical imaging enthesopathy, we have noted an improvement in subclinical imaging enthesopathy (Savage LJ et al submitted), raising the possibility that it may be possible to find a biomarker for predicting response to therapy in psoriatic disease. Innate lymphoid cells may be centrally involved in the pathogenesis of psoriatic skin and joints disease[2], since they express IL-23R receptor and are associated with IL-17/IL-22 production.
Objectives: This work was performed to test the hypothesis that peripheral blood ILC perturbations may be useful in defining response in psoriasis cases with imaging confirmed subclinical enthesopathy.
Methods: Peripheral blood collected at baseline (before therapy, 24weeks, 54 weeks) from patients in the MUSTEK trial (Ustekinumab in psoriasis cases who had ultrasound imaging confirmed subclinical enthesopathy) (n=23). Cellular immunophenotyping was performed density gradient separated PBMCs. Innate lymphoid cells were identified as lineage negative (CD3- TCR$\gamma\delta$- TCR$\alpha\beta$- CD19- CD14- CD11c- CD1a- CD303- FcεRI- CD34- CD123-) with positive expression of CD45, CD127. ILC2 cells were identified as Lineage- CD127+ and CRTH2 positive, while ILC3 were identified as Lineage- CD127+, CRTH2 – and CD117 (c-Kit) positive and further subdivided of NKp44+ and NKp44-. ILC1 were identified as lineage- CD127+ CD117-and CRTH2-. For data analysis we separated cases into PASI>90% or PASI <90% responders. The subclinical enthesopathy scores also fell significantly under therapy (Savage LJ data submitted)
Results: No correlation was found with total ILCs (ILC1,2, AND 3) (R=0.104, p=321, Spearman R) and therapy response. While, The absolute numbers of baseline ILC3s was inversely correlated in with the reduction in the PASI score (R -0.404, p=0308, Spearman R). The ILC3s also fell progressively under therapy. All the patients respond with reduction of PASI score mean 92.6% (range 65.8–100%), Interestingly, those patients with reduction below 90% of PASI score has a significantly higher absolute numbers of ILC3+ cells in peripheral blood at the baseline than PASI (n=6/23) than super-responder group (n=17/23)
Conclusions: Only peripheral blood ILC3s, but not other ILCs changes, correlate with the PASI score (disease activity), Furthermore, excellent responders (PASI reduction >90%) showed strong correlated with higher ILC3 population at the baseline. This may help to use ILC3 enumeration as predictive parameter for ustekinamab clinical therapeutic response and may be relevant to assessing novel biomarkers for subclincal arthropathy in psoriasis.



References:
[1] Kreuger et al. N Engl J Med. 2007 Feb 8; 356(6):580–92.
[2] Vallinova et al. 2014 Apr;134(4):984–91.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5347

SAT0008 DRUG THERAPY ENHANCES TOLEROGENIC PROPERTIES OF DENDRITIC CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Y. Kurochkina[1], M. Tikhonova[2], T. Tyrinova[2], O. Leplina[2], A. Sizikov[1], A. Sulutian[1], L. Konenkova[1], O. Chumasova[1], A. Ostanin[2], E. Chernykh[2]. *[1]Department of Rheumatology; [2]Laboratory of Cellular Immunotherapy, Federal State Budgetary Scientific Institution Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russian Federation*

Background: Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/Th17 responses. Along with stimulating activity, DCs may exhibit suppressive functions via capacity to induce T cell apoptosis/anergy and to generate regulatory T cells. Since these DCs have potential to control autoreactive T-lymphocytes, the enhancing of tolerogenic properties of DCs seems to be a new important strategy in treatment of RA. The experimental research in animals and human in vitro studies revealed the capacity of anti-rheumatic drugs to inhibit stimulating activity and to enhance tolerogenic functions of DCs. However, data concerning the in vivo influences of drug therapies on DC functions in RA patients are not available.
Objectives: The aim of our study is to investigate, whether drug therapies influence the properties of monocyte-derived DCs generated in the presence of IFNα (IFN-DCs) in RA patients, and if the effect of disease-modifying anti-rheumatic drugs differ from that of biological/pulse steroid therapy.
Methods: Thirty nine patients with RA with high and moderate activity of disease were recruited in this study. All patients fullfield ACR/EULAR criteria (2010). Nineteen patients received methotrexate, leflunomide, sulfasalazine or their combination (RA1). Twenty patients were at pulse therapy (methylprednisolone 500mg No. 3) or biological drugs (adalimumab or rituximab) (RA 2). All studies were performed after receiving informed consent. DCs were generated from blood monocytes culturing for 5 days with GM-CSF and IFN-α in the absence and presence dexamethasone, applied on third day. LPS as maturation stimuli was added on fourth day. The expression of CD14, CD83, CD 86, B7H1, HLA-DR, TLR-2 on the surface of DCs was measured by flow cytometry. The functions of DCs were evaluated by measuring cytokine production and DC allostimulatory activity in mixed lymphocyte culture.
Results: Both DC-RA1 and DC-RA2 where shown to display impaired maturation evidenced by elevated expression of CD14 and decreased number of mature (CD14-CD83+) DCs. Wherein, DCs-RA2 demonstrated several additional differences, including increased number of intermediate CD14+CD83+ cells (compared with donors DCs), higher expression of inhibitory molecule B7-H1 (PD-1L) (compare with donors DCs and DCs-RA1) and tendency to lower expression of CD86 and higher expression of TLR-2. Besides, DCs-RA2 produced higher concentrations of IL-6 and had 2-fold lower allostimulatory activity then DCs-RA1. These differences together with phenotypic changes suggested more pronounced tolerogenic properties of DCs-RA2. Despite the revealed DC differences in RA1 and RA2 patients both types of DCs preserved in vitro sensitivity to dexamethasone, that suppressed the production of TNF-α and reduced allostimulatory activity.
Conclusions: The data obtained indicate that, IFN-DCs from RA patients at drug treatments are characterized by tolerogenic properties, which are more pronounced in patients with biological or pulse steroid therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2408

SAT0009 DISTRIBUTION AND INTRACELLULAR SETTITNG OF GRANULYSIN IN WOMEN WITH KNEE OSTEOARTHRITIS

G. Laskarin[1], T. Kehler[2], M. Dominovic[3], V. Persic[4], M. Rogoznica[4], D. Rukavina[1]. *[1]Medicinski fakultet Sveučilišta u Rijeci, Rijeka; [2]Specialized Hospital "Thalassotherapia-Opatija"; [3]Medicinski fakultet Sveučilišta u Rijeci; [4]Tth Opatija, Opatija, Croatia*

Background: The role of the cell-mediated immune response is recently recognized in osteoarthritis (OA) (1). Granulysin (GNLY) is mediator of cellular immunity and cytotoxic molecule expressed in T and NK cells in regulatory (15 kDa) and cytotoxic (9 kDa) forms (2). Cytotoxic 9 kDa form of GNLY mediates apoptosis of eukaryotic cells (3) and might be responsible for silent unscheduled apoptosis of joint tissue cells in patients with OA without clinically recognized

systematic immune reaction, as measured by erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) (4). We investigate GNLY distribution and intracellular setting in peripheral blood lymphocytes of patients with OA.

Objectives: Women with knee OA (17), and age and sex appropriated control (17) were tested. All of them signed informed consent before sampling of peripheral blood (PB).

Methods: Medical history, clinical examination, X-ray and routine laboratory testing (ESR, CRP) were used for diagnosing OA. Peripheral blood mononuclear cells (PBMC) were isolated by gradient density centrifugation and used for multiple, simultaneous intracellular [total GNLY, 9 kDa GNLY, 15 kDa GNLY and Lysosomal-associated membrane protein-1 (LAMP-1)] and surface antigens (CD3 and CD56) detection by immunofluorescence. Data were analyzed by flow cytometry or confocal microscopy.

Results: In OA and control samples the percentage of total GNLY+ cells and GNLY expressing NK and T cells did not significantly differ and correlate with ESR and CRP. The frequency of GNLY+ cells was always higher in natural killer (NK) then in T cells and 9 kDa GNLY dominated over 15 kDa GNLY. However, 9 kDa GNLY co-localized more with the marker of cell degranulation, LAMP-1 in polarized granules of OA patients when compared to the control or to the 15 kDa GNLY.

Conclusions: The increase in the expression of cytotoxic (9 kDa) over regulatory (15 kDa) GNLY form in PBMC and its intracellular setting in polarized exocytic granules suggests the involvement of activated GNLY$^+$ lymphocytes in the immunopathogenesis of knee OA, indispensable of ESR and CRP.

References:

[1] Yamada H, Nakashima Y, Okazaki K, et al. Preferential accumulation of activated Th1 cells not only in rheumatoid arthritis but also in osteoarthritis joints. J Rheumatol 2011;38:1569–75.
[2] Clayberger C, Finn MW, Wang T, et al. 15 kDa granulysin causes differentiation of monocytes to dendritic cells but lacks cytotoxic activity. J Immunol 2012;188:6119–26.
[3] Pardo J, Pérez-Galán P, Gamen S, et al. A role of the mitochondrial apoptosis-inducing factor in granulysin-induced apoptosis. J Immunol 2004;167:1222–9.
[4] Kehler T, Laskarin G, Massari D, et al. Possible role of granulysin in pathogenesis of osteoarthritis. Med Hypotheses 2015;85:850–3.

Acknowledgements: The experiments were financed by the University of Rijeka (No.13.06.1.1.06) and "Thalassotherapia- Opatija", Opatija, Croatia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5499

SAT0010 THE DAMP PROTEIN S100A8/A9 IS CRUCIALLY INVOLVED IN MYELOID-DERIVED SUPPRESSOR CELL (MDSC) DIFFERENTIATION AND FUNCTION IN COLLAGEN-INDUCED ARTHRITIS

M. Kuhlencord, Y. Kusche, S. Zenker, T. Vogl, J. Roth. *Institute of Immunology, Münster, Germany*

Background: Over the last years, the differentiation and activation of MDSC under tumor conditions has been studied extensively. Various tumor-derived factors have been identified in promoting the accumulation of this suppressive cell population. Recent findings determined the two alarmins S100A8 and S100A9 as important factors in the differentiation of MDSC during tumor conditions. However, little is known about the S100A8/A9 driven expansion and activation, as well as the relevance of these cells in autoimmune diseases such as rheumatoid arthritis.

Objectives: We therefore analyzed the mechanisms involved in S100A8/A9 driven MDSC accumulation and their functional importance in a mouse model of rheumatoid arthritis.

Methods: To investigate the effect of S100A8/A9 on MDSC differentiation, bone marrow cells from wild type (wt), S100A9 knockout (A9ko) and S100A9 transgenic (A9tg) mice were analyzed. Accumulation of MDSC and their phenotypical characterization was performed by FACS analysis and functional characterization including arginase activity, NO- and ROS-production and T cell proliferation assays.

The role of S100A8/A9 and MDSC in arthritis was investigated using the collagen-induced arthritis (CIA) mouse model. Accumulation of MDSC in different organs was analyzed by FACS and systemic S100A8/A9 levels were measured by ELISA. Ex vivo functional analysis of purified MDSC was performed to assess the potential of these MDSC to inhibit T cell responses.

Results: Our in vitro studies reveal that, in the presence of S100A8, myeloid progenitor cells differentiate to immature cells that phenotypically as well as functionally resemble MDSC. These cells are characterized by co-expression and up-regulation of arginase activity, NO- and ROS-production, and exhibit strong suppressive effects on the proliferation of both CD4- and CD8-positive T cells. Furthermore, accumulation of MDSC by extracellular S100A8 was found to be mediated via the Toll-like receptor 4 signaling pathway. In addition, lack of intracellular S100A8/A9 results in a decreased number of MDSC as well as a reduced suppressive activity of these cells, implying a dual role of these proteins for MDSC differentiation and function.

Investigating the role of S100A8/A9 and MDSC in a mouse model of CIA, a clear correlation between disease scores, MDSC numbers and systemic S100A8/A9 levels was observed. Furthermore, disease activity was reduced in wt and A9tg mice compared to A9ko mice and was in line with an increased accumulation of MDSC in the lymph nodes. Next to an enhanced suppressive activity of MDSC isolated from lymph nodes of wt and A9tg mice, these MDSC promoted the accumulation of regulatory T cells (Treg) whilst suppressing the differentiation of TH17 cells. In contrast, MDSC isolated from lymph nodes of A9ko mice had no effect on Treg differentiation and did not inhibit TH17 emergence.

Conclusions: Our in vitro results clearly show a S100A8/A9 dependent accumulation of cells that phenotypically as well as functionally resemble MDSC also under non-tumor conditions. In vivo data strongly support the importance of these findings. By influencing MDSC accumulation and function, S100A8/A9 is critically involved in regulating the disease outcome in rheumatoid arthritis, implying an important role of S100A8/A9 derived MDSC in regulating immune reactions during autoimmune diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6683

SAT0011 THE ACTIVATION OF MUSCARINIC ACETYLCHOLINE RECEPTORS INFLUENCES THE ONTOGENY OF NEUTROPHILS

S. Sommerlatte[1], L. Kappes[1], S. Pitann[1], G. Marschner[1], H. Heidecke[2], P. Lamprecht[1], A. Mueller[1], T. Lange[1], O. Cabral-Marques[1], G. Riemekasten[1]. *[1]Rheumatology, University of Lübeck, Lübeck; [2]CellTrend GmbH, Luckenwalde, Germany*

Background: There is growing evidence that nervous and immune system communicate with each other through soluble mediators.[1] Immune cells such as neutrophils express muscarinic acetylcholine receptors (mAChR), which are neuroimmune receptors and highly prevalent in the nervous system.[2] Aberrant neutrophil functioning plays an important role in various autoimmune diseases. Dysregulation of neutrophil immune responses such as oxidative burst and migration is one of the key mechanisms leading to tissue damage in autoimmune diseases.[3] However, the impact of mAChR activation on neutrophils remains contradictory.

Objectives: We aimed to determine effects of muscarinic receptor activation on development and functions of neutrophils.

Methods: Neutrophils were isolated from peripheral blood of healthy donors by dextran sedimentation. After one hour in the absence or presence of the natural ligand acetylcholine (Ach) (10nM-100μM) or the muscarinic agonist oxotremorine-m (oxo-m) (10nM-100μM), neutrophil respiratory burst was analyzed by dihydrorhodamine (DHR) flow cytometry assay and migration assessed by transwell assay in response to N-formylmethionyl-leucyl-phenylalanine (fMLP). Cells that migrated were quantified by flow cytometry. To analyze the effects mAChR activation on the development of neutrophils, HL-60 cells were incubated in the presence of DMSO (1%), oxo-m (100μM) or DMSO plus oxo-m. After 6 days, cells were harvested and expression of maturation markers (CD15, CD63 and CD16) as well as mAChR (M1-M5) were measured by flow cytometry.

Results: We observed no effects of mAChR activation on the respiratory burst of neutrophils. However, both ACh and oxo-m inhibited neutrophil migration in a dose-dependent manner, but with peculiar differences. By increasing acetylcholine concentrations, we observed a reduction of neutrophil migration in a directly proportional manner. On the other hand, while the lowest dose (10nM) of oxo-m inhibited migration most effectively, the increase of oxo-m showed inversely proportional effects on neutrophil migration. Thus, we aimed to investigate, if the highest dose of oxo-m has a different effect on neutrophils ontogeny. In agreement with the results obtained with neutrophils, the incubation of HL-60 cells with the highest dose of oxo-m showed no effect on oxidative burst and migration and induced no changes in the expression of mAChRs (M1-M5), CD16 and CD63 in HL-60 cells. However, we observed that it resulted in significantly increased surface levels of the neutrophilic lineage marker CD15.

Conclusions: Our data indicate a differential activation of mAChR affecting different steps of neutrophil ontogeny. Considering this finding, abnormalities in the activation of muscarinic receptors as have been observed in autoimmune diseases might contribute to neutrophil dysfunction and need further investigation.

References:

[1] Blalock, J. E. The syntax of immune-neuroendocrine communication. Immunol Today 15, 504–511 (1994).
[2] Milara et al. Non-neuronal cholinergic system contributes to corticosteroid resistance in chronic obstructive pulmonary disease patients. Respiratory Research (2016) 17:145.
[3] Wright, H. L. et al. The multifactorial role of neutrophils in rheumatoid arthritis Nat Rev Rheumatol 10 593–601 (2014).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6573

SAT0012 S100A8/A9 INCREASES THE MOBILIZATION OF LY6C HIGH MONOCYTES TO THE SYNOVIUM DURING EXPERIMENTAL OSTEOARTHRITIS

N. Cremers[1], E. Geven[2], A. Blom[2], M. van den Bosch[2], P. van der Kraan[2], P. van Lent[2]. *[1]Experimental Rheumatology; [2]Radboud university medical center, Nijmegen, Netherlands*

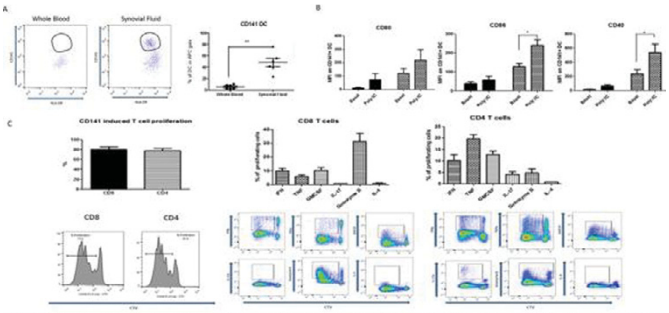
Background: It is increasingly recognized that part of the pathology in osteoarthri-

tis (OA) is driven by a low-grade inflammation in the synovium. Pro-inflammatory cytokines released locally during OA, such as S100A8/A9 which are expressed for prolonged periods when compared to IL-1β, IL-6, and TNF-α, may recruit monocytes from the bone marrow (BM) to the joint. In mice, two functionally distinct monocyte populations are described: (i) pro-inflammatory Ly6C^{high} monocytes; and (ii) patrolling Ly6C^{low} monocytes.
Objectives: The objective of our study is to investigate the role of S100A8/A9 in the recruitment of the different monocyte populations during early collagenase-induced OA (CiOA).
Methods: S100A8 was intra-articularly injected into the knee joint of naïve wild type C57BL/6 (WT) mice to investigate their direct role in recruitment of monocytes. CiOA was induced by unilateral intra-articular collagenase injection in WT, and S100A9KO mice to investigate the role of S100A8/A9 in more detail. At CiOA day 7, WT and S100A9KO mice were sacrificed together with age-matched saline-injected control mice (n=6/group), and expression of several monocyte cell markers, chemokines, and adhesion molecules were measured in the synovium and BM, in which the cells were also analyzed by FACS. Monocytes were identified as (B220/CD90/CD49b/NK1.1/Ly6G)^{low}CD11b^{high}(F4/80/MHCII/CD11c)^{low}, which were further divided into subsets based on their Ly6C expression.
Results: Injection of S100A8 into the knee joints of naïve mice led to a significantly elevated expression of monocyte-related markers (Ly6C, CCR2, and CX3CR1) and monocyte attracting chemokines (MCP-1, CX3CL1, MIP1α, and KC) within the synovium after 1 and 3 days, suggesting that S100A8/A9 is directly involved in the attraction of monocytes. At CiOA day 7 in WT mice, numbers of Ly6C^{high}, but not Ly6C^{low} monocytes, were strongly increased (7.6-fold) in the synovium as compared to saline-injected control joints. In contrast, S100A9KO mice showed a significant increase in Ly6C^{low} monocytes (2-fold), whereas the number of Ly6C^{high} monocytes remained unaffected. Concurrently, a strong upregulation of several chemokines (MCP1, CX3CL1, KC, and MIP1α) was observed locally in the synovium, of which only the Ly6C^{low} mobilization marker CX3CL1 was significantly higher in S100A9KO mice, corresponding with the increased Ly6C^{low} monocytes in the synovium of S100A9KO mice. This could however not explain the local increased number of Ly6C^{high} monocytes at CiOA day 7 in WT mice, and therefore we next investigated the main source of the monocytes, which is the BM. We observed a decrease of 14% of myeloid cells (consisting partly of Ly6C^{high} monocytes) in the BM of WT mice at CiOA day 7, whereas there were no changes in the BM of S100A9KO mice, suggesting that S100A8/A9 affects the release of myeloid populations from the BM. In line with that, expression of adhesion molecules (LFA-1, VCAM, VE-cadherin, PECAM1, and L-selectin) was lower at CiOA day 7 in the BM of S100A9KO mice when compared to WT mice.
Conclusions: Local induction of OA leads to S100A8/A9 production, and subsequently to the mobilization of Ly6C^{high} monocytes into the joint, driving OA pathology.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6181

SAT0013 THE PATHOGENIC ROLE OF MYELOID CD141+ DENDRITIC CELLS IN INFLAMMATORY ARTHRITIS

M. Canavan[1], T. McGarry[1], K. Killick[2], B. Moran[3], D. Cluxton[3], C. Orr[4], H. Convery[4], S. Wade[1], S. Wade[1], R. Mullan[5], J. Fletcher[3], D.J. Veale[4], U. Fearon[1]. *[1]Molecular Rheumatology, Trinity College Dublin, Dublin; [2]Systems Biology Ireland, Conway Institute of Biomolecular and Biomedical Research, UCD, Dublin 4; [3]Immune Regulation in Human Disease, Trinity College Dublin, Dublin; [4]The Centre for Arthritis and Rheumatic Diseases, St Vincents University Hospital, Dublin 4; [5]Rheumatology Department, The Adelaide and Meath Hospital, Dublin, Ireland*

Background: Dendritic cell (DC) are a heterogeneous group of antigen presenting cells that can be subdivided into CD1c$^+$ & CD141$^+$ DC. CD141$^+$ DC are a rare population of DC that were first discovered in 2010 in human peripheral blood. Due to their rarity very little is known about the function of these cells in other tissue in or indeed disease. These newly described DC subset have thus never been described in Inflammatory Arthritis (IA) or any of the rheumatic diseases.
Objectives: To identify CD141 DC in IA synovium and functionally assess if these cells play a pathogenic role in IA.
Methods: CD141$^+$DC were magnetically purified from synovial fluid mononuclear cells (SFMC) and peripheral blood mononuclear cells (PBMC) stimulated and stained with a panel of fluorochrome conjugated antibodies for multicolour flow cytometry. CD141$^+$ DC isolated and purified from IA synovial fluid were subsequently cocultured with allogenic CD3$^+$ T cells for 6d after which intracellular cytokine production was assessed by flow cytometry. Supernatants from this DC-T cell cocultures were used to treat synovial fibroblasts & the expression of adhesion molecules, cytokines & MMPs was measured. Finally using sorted populations of CD141$^+$ DC from SFMC and PBMC, RNA sequencing was performed and differentially expressed genes and interaction network analysis were identified using the DeSeq2 R package, Ingenuity® Pathway Analysis (IPA) and InnateDB and Cytoscape.
Results: Within IA synovial fluid (SF), CD141$^+$ DC are significantly enriched compared to WB & express higher levels of the costimulatory activation markers CD80 CD86 and CD40. Following coculture of these SF CD141$^+$ DC with CD3$^+$ T cells, CD141$^+$ DC induce both CD8$^+$ & CD4$^+$ T cell proliferation. SF CD141$^+$ DC induce Granzyme B production from CD8$^+$ T cells & TNFα, IFNγ & GMCSF from CD4$^+$ T cells. The IA synovium consists of a complex interplay of multiple cell types. Therefore next we examined the effect of this CD141$^+$ DC-T cell interaction on the key invasive cells in the synovium – synovial fibroblasts. Supernatants from CD141 activated T cells were cultured with fibroblasts & induced expression of ICAM-1, IL-6, IL-8, MMP1 & MMP3. SF CD141 expressed significantly higher levels of the the hypoxia marker TREM1, activation of which induces further expression of CD80, CD86 and CD40. Coculture of these TREM1 activated CD141 with CD3$^+$T cells increases IFNγ and IL-17a production. Finally RNASeq analysis revealed that there are 2089 differentially expressed genes between SF CD141$^+$DC & WB CD141$^+$DC. These genes are involved in a number of key pathways such as energy metabolism, chemokine & cytokine signalling. Principal Component Analysis (PCA) revealed that CD141$^+$ DC with the synovium are distinctly different from blood CD141$^+$ DC



A) CD141 DC are enriched in the IA synovium compared to peripheral blood. B) IA CD141 from synovial fluid (SF) express higher expression of activation markers and respond to TLR engagement. C) CD141 DC isolated from IA SF induce CD4+ and CD8+ T cell proliferation and cytokine secretion

Conclusions: CD141$^+$ DC are enriched in the IA joint in an active state. RNASeq analysis revealed they are distinct from blood CD141$^+$DC and our *in vitro* data would support the hypothesis that these CD141$^+$DC contribute to synovial inflammation and joint destruction.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6169

SAT0014 THE MUTATED RNA SPLICING PROTEIN HNRNP-A3 IS A NOVEL AUTOANTIGEN IN SYSTEMIC RHEUMATIC DISEASES A LINK TO WARBURG EFFECT IN RA

B. Marklein[1], M. Hansson[2], G. Steiner[3], G. Burmester[1], K. Skriner[1]. *[1]Department of Rheumatology and Clinical Immunology, Charité University Medicine, Berlin, Germany; [2]Rheumatology Unit, Department of Medicine, Karolinska Institutet, Stockhom, Sweden; [3]2Division of Rheumatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria*

Background: The present study was undertaken to investigate novel anti-hnRNPs autoantibodies in rheumatic diseases.
Objectives: Novel mutated hnRNP A3 was cloned out of RA synovial tissue linking it directly to Warburg effect and lactate production in RA. Increased lactate production in RA synovia and tumors is klinked to alternative splicing process from PKM1 to PKM2 hnRNPs dependent.
Methods: After immunobloting and 2D-gel-eletrophoresis of a semipurified hnRNP fraction two protein spots were sequenced and identified to be highly similar to hnRNPA3. The hnRNP A3 variants were cloned from RA synovial tissue, which identified the isoforms found on protein level. 3700 RA sera were screened for the presence of mutated anti-hnRNP A3 autoantibodies using recombinant proteins and peptides thereof. Binding of RNA to hnRNP A3 (MA3) and mutated citrullinated A3 peptides (MCA3) the epitope recognition was investigated. Expression of hnRNP A3 in synovial tissue was analysed by
Results: Autoantibodies to MA3 protein were detected in 13% of RA (n=215) patients, in 9% SLE (n=154), in 27% of MCTD patients (n=44/10) and in less than 5% of 129 patients with other rheumatic disorders but not at all in healthy controls on immunoblot. When using renaturated MA3 on ELISA 22% of RA patients were detected and 87% of these patients had erosive arthritis. Same modification as in cancer cells were identified in synovial tissue and verified by MS and DNA sequencing. Using 2–3 citrullinated MCA3 peptides up to 81% of patients (n=150) with established and 67% (n=2926) of patients with an early RA with a specificity of 97% were detected. In early RA 27% and 25% in established RA of CCP2 negative and 93% of CCP2 positive patients were identified.
By combining with the already established CCP2 and the new MCA3, 72% of early patients are positive. MCA3 autoantibodies predominantly occur ($p<0.001$) in an erosive, severe course of disease and approximately 60% of these patients receive a TNF alpha blocker within a year. MRL Lpr/lpr sera were hnRNP-A3 reactive and the antibody generation is Toll 7 and 9 dependent. Anti-hnRNP-A3-antibodies are directed to conformational RNA binding epitopes. Expression of hnRNP-A3 revealed the antigen to be overexpressed in RA synovial tissue.
Conclusions: Mutated hnRNP-A3 is as a novel Toll7/9 dependent autoantigen in systemic rheumatic diseases. These mutated proteins are major components of RNA and DNA containing alternative splicing complexes leading to the Warburg effect and and autoantibodies predominantly occurre in an erosive, and severe courses of RA.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3647

SAT0015 ANCA-ASSOCIATED VASCULITIS- AND SYSTEMIC LUPUS ERYTHEMATOSUS-INDUCED NEUTROPHIL EXTRACELLULAR TRAPS HAVE INTRINSICALLY DIFFERENT FEATURES

L.S. Van Dam[1], T. Kraaij[1], S.W. Kamerling[1], M.C. Avramut[2], C.R. Jost[2], A.J. Koster[2], H.U. Scherer[3], C.D. Pusey[4], A.J. Rabelink[1], C. van Kooten[1], Y.K. Teng[1]. *[1]Nephrology; [2]Molecular Cell Biology; [3]Rheumatology, LUMC, Leiden, Netherlands; [4]Renal and Vascular Inflammation, Imperial College, London, United Kingdom*

Background: Neutrophil extracellular traps (NETs) are immunogenic, extracellular DNA structures that harness important autoantigens to be recognized by the adaptive immune system. NETs are thought to play a pivotal role in the pathogenesis of many systemic autoimmune diseases including ANCA-associated vasculitis (AAV) and systemic lupus erytematosus (SLE). However it is still unclear how and if NETs can act as a common pathway in the pathophysiology of these clinically divergent autoimmune diseases.
Objectives: To investigate the characteristics of NETs induced by sera of AAV and SLE patients.
Methods: The present study involved 101 AAV patients, 59 SLE patients and 10 healthy controls. Healthy neutrophils were stimulated with 10% serum of these patients to induce NETs. Quantity of NET induction was measured by a novel, highly-sensitive NET quantification assay using 3D-confocal laser scanning microscopy[1]. Qualitative characteristics of NETs were investigated by immunofluorescence microscopy that detected co-localisation of several established autoantigens and NET-markers on AAV- and SLE-induced NETs, including citrullinated histon-3 (CitH3), neutrophil elastase (NE), high mobility group box-1 (HMGB1), myeloperoxidase (MPO) and proteinase-3 (PR3). Additionally, the morphology and kinetics of AAV- and SLE-induced NETosis were visualized by live imaging and electron microscopy.
Results: Quantifying ex vivo NET induction demonstrated that AAV sera induced significant more NETs (median [Q1 - Q3]: 20.74 [9.56 – 74.14]), compared to SLE sera (5.02 [1.88 – 14.33]). Also qualitatively, NETs induced by AAV or SLE sera were distinct. In both cases, NETs showed co-localisation of MPO and PR3 with extracellular DNA. However, AAV-induced NETs had significantly higher Cith3 expression than SLE-induced NETs. Interestingly, the opposite was observed for other markers as HMGB1 was exclusively expressed on SLE-induced NETs and NE was also higher expressed on SLE-induced NETs compared to AAV-induced NETs. Intriguingly, the distinction between AAV and SLE NETs was further corroborated by live imaging demonstrating differences in morphology and chronology of NET induction: in SLE NET-clusters were induced within the 1st hour while in AAV non-clustered NETs composed of long, thin DNA-fibres were induced in 2–4 hours through lytic expulsion.
Conclusions: The present study demonstrates that NET induction in AAV and SLE results in quantitative and qualitative distinct NETs indicating that NET formation in AAV and SLE is likely based on intrinsically different processes. These data increase our understanding of the pathophysiologic relevance of NETs and how they could be considered as a common pathway underpinning different autoimmune diseases.
References:
[1] Kraaij T, et al, A novel method for high-throughput detection and quantification of neutrophil extracellular traps reveals ROS-independent NET release with immune complexes, Autoimmun Rev (2016).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3804

SAT0016 A NEW SUBSET OF NK CELLS, WITH ENHANCED CYTOTOXIC FUNCTION, IS INCREASED IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

D.D.J. Cruz González[1], L. Baranda-Cándido[2], C. Abud-Mendoza[2], J. Alcocer-Varela[3], R. González-Amaro[1], D. Gómez-Martin[3], A.E. Monsiváis-Urenda[1]. *[1]Medicina Translacional y Molecular. Centro de Investigación en Salud y Biomedicina; [2]Departamento de Reumatología. Hospital Central "Ignacio Morones Prieto", Facultad de Medicina. Universidad Autónoma de San Luis Potosí, San Luis Potosí; [3]Departamento de Reumatología e Inmunología, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Ciudad de México, Mexico*

Background: Natural killer cells (NK cells) are granular lymphocytes that belong to innate immunity, its major function is the lysis of virus-infected or tumoral cells. These functions are regulated by activating (NKG2D, NKp46, NKP30, NKG2C, CD161) and inhibitory receptors like KIRs and NKG2A. The role of NK cells in autoimmunity is poorly understood; it is well known that in systemic lupus erythematosus (SLE) patients there are decreased levels of NK cells. NK cells can modulate the adaptive immunity through its interaction with dendritic cells (DCs); the activation or killing of DC by NK cells depends of the ratio NK:DC. However, the interactions NK:DC in SLE have not been well studied. A new subset of NK cells with DCs characteristics has been reported in a model of lupus mice; however, the possible increment of NK cells with DC like phenotype in SLE has not been reported.
Objectives: To analyze the phenotype of circulating NK cells as well as its function in SLE patients.
Methods: Sixty SLE patients and fifty-five controls were included in this study. Diagnosis was made according to ACR criteria. Activity of disease was measured by SLEDAI index. The expression of NKG2A, ILT2, NKG2D, NKG2C, NKp30, NKp46, CD161, CD134, CD80, CD86, HLA-DR, CD11c+ was evaluated in NK cells (CD3-CD56+) from peripheral mononuclear cells. NK cell function was assessed by the percentage of monocyte-derived DC lysis by NK cells.
Results: Diminished levels of circulating NK cells were found in SLE patients ($p=0.0439$) compared to healthy subjects. NK cells from SLE showed higher levels of the inhibitory receptor ILT2+($p=0.0024$), and the costimulatory molecules CD86+ ($p=0.0136$) and CD134+($p=0.0238$); in addition, SLE patients displayed a higher expression of MHC-class II molecule, HLA-DR+ ($p<0.0001$). Interestingly, higher levels of atypical NK cells CD11c+HLA-DR+ ($p=0.0075$) were found in SLE patients compared with healthy subjects. Furthermore, we found that SLE patients showed a significate increased level of monocyte derived-DC lysis by NK cells.
Conclusions: In this study, we show for the first time that NK cells in SLE have an altered phenotype, expressing receptors, which are characteristic of dendritic cells (CD134, CD86 and HLA-DR). The expression of these receptors may provide NK cells with the ability to activate T cells, which together with their higher capacity to lyse immature or tolerogenic DCs could contribute to SLE pathogenesis. It is known that NK cells could have a dual role in autoimmune diseases, here we propose that the lysis of DC mediated by NK cells could be important to modulate the disease activity in SLE patients. Even more, in this report we identify a new subset of NK cells, CD11c+ HLA-DR+, reported previously in a mouse lupus model. It is essential to highlight that these NK cells with DC-like phenotype could be crucial for the development of SLE.
References:
[1] Caligiuri MA. Bone 2008; 112: 461.
[2] Voynova EN, et al. J Immunol 2015; 194: 1503.
[3] Aranami T, et al. J Immunol 2006;177: 5659.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3565

SATURDAY, 17 JUNE 2017

Adaptive immunity (T cells and B cells) in rheumatic diseases

SAT0017 INVESTIGATING NOVEL AUTOANTIBODIES IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS

M.C. Baker, N. Lingampalli, W. Robinson. *Rheumatology, Stanford University, Palo Alto, United States*

Background: Granulomatosis with polyangiitis (GPA) is a disease characterized by inflammation in small blood vessels, leading to significant organ damage and ultimately great morbidity and mortality. The presence of anti-neutrophil cytoplasmic antibodies (ANCAs) is a hallmark of the disease, and thought to directly play a role in pathogenesis by activating primed neutrophils. The two major antigens that ANCAs are believed to recognize are myeloperoxidase (MPO) and proteinase 3 (PR3). Although anti-MPO antibodies are directly pathogenic when transferred or induced in animal models, the evidence is less clear for PR3. Clinically, it is debated whether levels of anti-PR3 correlate with disease activity. Therefore, we believe that anti-PR3 antibodies are not the primary drivers of disease in patients with PR3+ ANCA-vasculitis (i.e. GPA), and that novel autoantibodies may play a role in disease pathogenesis.
Objectives: The objective of this work is to identify the human autoantigen targets of novel autoantibodies identified in GPA, and to test their association with disease. The goal is to discover novel autoantigens that will ultimately lead to new diagnostics and therapeutics.
Methods: Cell-barcode-enabled antibody repertoire sequencing was performed on blood plasmablasts (antibody-producing cells formed during an immune response) from five PR3+ ANCA-vasculitis patients with GPA treated with rituximab in the RAVE trial. Phylogenetic trees were bioinformatically created in order to identify clonal families of plasmablasts. Antibodies representing clonal families of plasmablasts were recombinantly expressed and are being tested using human protein arrays and ELISAs to determine their antigen specificity.
Results: All five PR3+ ANCA-vasculitis patients sequenced from the RAVE trial achieved complete remission but subsequently flared. Plasmablasts were isolated at the baseline flare, at remission and at the post-rituximab flare. Phylograms of the antibody repertoires revealed clonal families of affinity-matured antibodies that share heavy and light chain VJ usage. A total of 24 representative antibodies were selected for recombinant expression, including representative antibodies derived from clonal families: (1) shared across patients at baseline flare and/or post-rituximab flare (n=5), (2) present at baseline flare and post-rituximab flare (n=7) [persistent clone or same clone came back], (3) present at baseline flare or post-rituximab flare (n=6), (4) present in remission and post-rituximab flare (n=5) [achieves remission despite clone presence], (5) present in remission (but not flare) (n=1) [patient in remission despite clone presence]. None of the 24 antibodies bind PR3 in an ELISA and thus these antibodies do not represent

ANCAs. Antigen discovery to determine the targets of these recombinant plasmablast antibodies is ongoing.
Conclusions: Plasmablasts from patients with GPA in the RAVE trial were sequenced and antibody repertoires were generated. Clonal families of plasmablasts, including those expressing antibodies possessing shared CDR sequences across multiple patients, were identified and recombinantly expressed. None of the 24 antibodies bound to PR3, suggesting these are not ANCAs and are potentially novel autoantibodies. Identification of the antigen targets of these antibodies is ongoing.
Acknowledgements: The Immune Tolerance Network
Training Program in Adult and Pediatric Rheumatology 2T32AR050942–11
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3261

SAT0018 EFFECTS OF ANTI-TNF ALPHA THERAPY ON B CELLS IN RHEUMATOID ARTHRITIS (RA) PATIENTS

O. Pala[1], A. Diaz[2], B. Aubourg[1], E. Greidinger[1], B.B. Blomberg[2], D. Frasca[2]. *[1]Rheumatology; [2]Microbiology&Immunology, University of Miami, Miami, United States*

Background: Our laboratory has previously characterized defects in humoral B cell responses of aged mice and humans. These defects include: the reduction in activation-induced cytidine deaminase (AID), required for the generation of optimal antibody responses, and the reduction in the percentage/number of the subset of switched memory B cells (1). AID and switched memory B cells have been proposed to be effective predictive biomarkers of vaccine responses (2). Moreover, we have shown that aging is characterized by increased systemic inflammation which induces intrinsic B cell inflammation, measured by intracellular (ic) TNF-α, and this significantly decreases the capacity of the same B cells to make protective antibodies in response to vaccination (3). Other marker of B cell intrinsic inflammation is micro-RNA (miR) expression, particularly miR-16 and miR-155, which is increased in elderly B cells and negatively correlated with B cell function (4).
Objectives: Our goal for this study was to evaluate B cell phenotype and function in RA patients treated Methotrexate (MTX), alone or together with anti-TNF-α. We hypothesized that patients treated with anti-TNF-α will show improved B cell function due to reduction in icTNF-α.
Methods: We recruited 9 RA patients, 5 patients on MTX and 4 on MTX/anti-TNF-α. We measured the relevant B cell subsets in blood (Naïve, switched memory, IgM memory and late memory) by flow cytometry. Staining was performed with antibodies specific for CD19, CD27 and IgD. In addition, we isolated blood B cells using magnetic beads, and measured the expression of miR-16 and miR-155 on blood B cells by qPCR.
Results: Preliminary data showed that the percentages of switched memory (IgD-CD27+) B cells are significantly higher ($p<0.003$) in patients undergoing MTX/anti-TNF-α therapy. We also observed a significant decrease in naïve B cell percentages ($p<0.028$). Preliminary results also showed a decrease in the mRNA expression of both miR-16 and miR-155 in patients on combination therapy compared to MTX alone.
Conclusions: These results support the hypothesis that therapy with anti-TNF-α is beneficial for improving B cell function in RA patients, as compared to MTX therapy alone. Future experiments will seek to evaluate intrinsic B cell TNF levels in these patients and correlate them with measurements of B cell function. Treatment with anti-TNF-α may be able to block the excessive amounts of systemic TNF-α and in turn B cell intrinsic TNF-α which could improve the antibody responses and the risk of infections in RA patients undergoing therapy.
References:
[1] Frasca, D., and B. B. Blomberg. 2013. Age effects on mouse and human B cells. Immunol Res. 57(1–3): 354–360.
[2] Frasca, D., A. Diaz, M. Romero, M. Phillips, N. V. Mendez, A. M. Landin, and B. B. Blomberg. 2012. Unique biomarkers for B-cell function predict the serum response to pandemic H1N1 influenza vaccine. Int Immunol. 24(3): 175–182.
[3] Frasca, D., M. Romero, A. Diaz, S. Alter-Wolf, M. Ratliff, A. M. Landin, R. L. Riley, and B. B. Blomberg. 2012. A Molecular Mechanism for TNF-alpha-Mediated Downregulation of B Cell Responses. J Immunol 188: 279–286.
[4] Frasca, D., A. Diaz, M. Romero, F. Ferraci, and B. B. Blomberg. 2015. MicroRNAs miR-155 and miR-16 Decrease AID and E47 in B Cells from Elderly Individuals. J. Immunol.195 (5): 2134–2140.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4331

SAT0019 ESTROGEN INFLUENCES THE SIALYLATION PROFILE AND INFLAMMATORY PROPERTIES OF ANTIBODIES – A POTENTIAL EXPLANATION FOR THE SEX DIFFERENCES AND INCREASED RISK FOR RA IN POSTMENOPAUSAL WOMEN

C. Engdahl[1,2], J. Raufer[1], U. Harre[1], A. Bondt[3], R. Pfeifle[1,4], G. Krönke[4,5], H.U. Scherer[6], H. Forsblad[2,7], G. Schett[1]. *[1]Department of Internal Medicin 3, Clinical Immunolgy, Erlangen, Germany; [2]Department of Rhemtology and Inflammation reserch, CBAR, Institue of Medicine, Gothenburg, Sweden; [3]Department of Rheumatology, Lediden University Medical Center, Leiden, Netherlands; [4]Nikolaus-Fiebiger Center for Molecular Medicine, FAU Erlangen-Nuremberg, Erlangen; [5]Department of Internal Medicin 3, Clinical Immunolgy, Gothenburg, Germany; [6]Department of Rheumatology, Lediden University Medical Center, Leiden, Netherlands; [7]Department of Public Health and Clinical Medicine, Rheumatology, Umeå University, Umeå, Sweden*

Background: Rheumatoid arthritis preferentially affects women. RA has its peak over 50 years coincidencing with the decrease in sex hormones in menopause. Recently, the transition from asymptomatic autoimmunity to RA has been shown to essentially depend on the glycosylation status of antibodies affecting the binding affinity to Fc gamma receptors[1]. Hence a decrease in the sialylation of antibodies resulting from a decrease in the activity of the sialylation enzyme β-galactoside α2,6-sialylltransferase (St6Gal1) was shown to trigger the onset of RA.
Objectives: To test whether estrogen influences the glycosylation status of antibodies and St6Gal1 expression explaining why postmenopausal women are particularly prone to develop RA
Methods: In the experimental part we tested the influence of estrogen on antibody glycosylation and St6Gal1 expression. Ovariectomized mice, which were either left without estrogen supplementation or were supplemented with estrogen (hormone replacement), were immunized with ovalbumin (OVA) to induce antibody production. Immunoglobulin G (IgG) levels were analyzed by ELISA and the glycosylation of the Fc-part of total and OVA-specific IgG was determined by lectin ELISA and MALDI-TOF, respectively. St6Gal1 expression in plasma cells was determined by RT-PCR and FACS. Inhuman part we measured the effects of estrogen treatment on autoantibody levels and IgG glycosylation in a cohort of postmenopausal RA patients over 2 years[2].
Results: Ovariectomy and loss of estrogens was associated with a lower sialylation of OVA-specific IgG. Conversely estrogen treatment significantly increased the sialylation level of newly formed OVA-specific and totals IgG as well as enhanced the expression of St6Gal1 enzyme in plasma cells suggesting a shift towards an anti-inflammatory pattern of IgG. These results were confirmed with estrogen treated postmenopausal RA patients showing that hormone replacement therapy significantly increased antibody glycosylation, while in a control RA population not exposed to estrogens no such increase in sialylation of IgG was found. Estrogens however, did not influence the CCP autoantibody levels.
Conclusions: These findings indicate that estrogen regulates St6Ga1 and increases the glycosylation of IgG. Lack of estrogen decreases IgG glycosylation and results in pro-inflammatory properties of IgG which may explain the increase prevalence of RA in postmenopausal women.
References:
[1] Pfeifle et al. Regulation of autoantibody activity by the IL-23-T_H17 axis determines the onset of autoimmune disease. Nat Immunol. 2017 Jan;18(1):104–113.
[2] D'Elia HF, et al. Influence of hormone replacement therapy on disease progression and bone mineral density in rheumatoid arthritis. J Rheumatol. 2003 Jul;30(7):1456–63.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6287

SAT0020 THE CITRULLINOME IN TISSUE AND BIOFLUIDS OF HUMAN AND MOUSE ORIGIN

T.B.G. Poulsen[1], D. Damgaard[2], T.B. Bennike[1], M.K. Meyer[3], K.J. Elbæk[1], V. Andersen[4], S. Birkelund[1], C.H. Nielsen[2], A. Stensballe[1]. *[1]Department of Health Science and Technology, Aalborg University, Aalborg; [2]Center for Rheumatology and Spine Diseases, Copenhagen University Hospital, Rigshospitalet, Institute for Inflammation Research, Rigshospitalet, Institute for Inflammation Research, Copenhagen; [3]Department of Rheumatology, North Denmark Regional Hospital, Hjørring; [4]IRS-Center Sonderjylland, Hospital of Southern Jutland, Aabenraa, Denmark*

Background: Protein citrullination is fundamental to several essential processes in apoptosis and antimicrobial defense, however, also linked to multiple pathogenic endpoints. This post-translational modification (PTM), by conversion of arginine to citrulline residues, is mediated by peptidylarginine deiminase (PAD) enzymes found in specific cells and tissues. In polymorphonuclear cells (PMNs) these enzymes enable NETosis, a specialized form of programmed necrosis and the formation of NETs (neutrophil extracellular traps). Also, these enzymes are expressed in the synovium of patients with rheumatoid arthritis (RA) thereby triggering the production of autoantibodies against citrullinated proteins (ACPAs).
Objectives: Our objective was to optimize methodology for characterization of this PTM and determine the citrullinome in tissue and biofluids of human and mouse origin in clinical relation to rheumatoid arthritis (RA), osteoarthritis (OA), Spondyloarthritis (SpA) as well as presence of ACAPs and NETs
Methods: Synovial fluid (SF) and plasma was collected from patients diagnosed with RA, OA, SpA (n=120). Inflammation levels patients were characterized with plasma C-reactive protein (CRP), and circulating anti-CCP levels as well as 10 most relevant proinflammatory cytokines. Intestinal tissue (colon mucosa) from RA patients (n=10) and joint lysate from collagen-induced arthritis mouse model (n=24). All samples were analyzed by citrulline specific sample preparation and high-end mass spectrometric analysis [1,2]. Follow-up studies were performed by multiple techniques including confocal microscopy and cell-free DNA measurement.

Results: The proteome analysis of SF allowed deepest proteome analysis so far (Proteoforms >1300) as well as a number of citrullinated sites. The three patient groups could be differentiated by cluster analysis and the occupancy of each modified site calculated. The investigation of the intestinal tissue enabled identification of 223 citrullinated peptides from 121 proteins. Three of the peptides were unique to RA. The list of citrullinated proteins was enriched in extracellular and membrane proteins and included known targets of anticitrullinated protein antibodies (ACPAs). Investigation of collagen-induced arthritis mouse model enabled differential analysis of the proteome as response to treatment and determination of the PTMs associated with this model.
Conclusions: Our deep proteome based analysis of tissue and biofluids have enabled an extended catalogue of citrullinated proteins and sites relevant to improved disease subtyping as well as a source of citrullinated sites for future studies.
References:
[1] Bennike, T.B., Ellingsen, T., Glerup, H., Bonderup, O.K., Carlsen, T.G., Meyer, M.K., Bøgsted, M., Christiansen, G., Birkelund, S., Andersen, V., et al. (2017). Proteome Analysis of Rheumatoid Arthritis Gut Mucosa. J. Proteome Res. 16, 346–354.
[2] Tue Bennike, Kasper B. Lauridsen, Michael Kruse Olesen, Vibeke Andersen, Svend Birkelund and Allan Stensballe (2013). Optimizing the Identification of Citrullinated Peptides by Mass Spectrometry: Utilizing the Inability of Trypsin to Cleave after Citrullinated Amino Acids. Journal of Proteomics & Bioinformatics 06.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6934

SAT0021 HUMAN CD4 T CELLS AND SYNOVIAL FIBROBLASTS COOPERATE TO PROMOTE INFLAMMATION IN THE RA SYNOVIAL JOINT

A. Petrasca[1], G. Jameson[1], T. McGarry[2], D.J. Veale[3], U. Fearon[2,3], J.M. Fletcher[1,2]. *[1]School of Biochemistry and Immunology; [2]School of Medicine, Trinity Biomedical Sciences Institute, Trinity College Dublin; [3]Department of Rheumatology, St. Vincent's University Hospital, Dublin, Ireland*

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterised by synovial tissue proliferation and degradation of articular cartilage. Activated synovial fibroblasts proliferate and express matrix-degrading proteases, adhesion molecules and proinflammatory cytokines, which contribute to cartilage and joint destruction. Moreover, synovial cell activation correlates with infiltration of inflammatory lymphocytes and monocytes which in turn contribute to synoviocyte activation, thus further exacerbating inflammation.
Objectives: The functional relationship linking fibroblasts and T lymphocytes in this complex microenvironment has yet to be characterised. Therefore, we established an *in vitro* model to examine the outcomes of co-culturing activated human CD4 T cells with RA synovial fibroblasts.
Methods: Co-culture assays were carried out using immortalised K4IM RA synovial fibroblasts or synovial fibroblast cells derived from arthroscopy biopsies of RA patients. Human CD4 T cells were stained with a proliferation-tracking dye and co-cultured with pre-seeded synovial fibroblasts for 5 days. The resulting cell cultures and supernatants were examined for proliferation, cytokine production, secretion of matrix metalloproteinases and expression of adhesion molecules.
Results: We found that CD4 T cells and K4IM cells reciprocally induced an increased expression of adhesion molecules ICAM and VCAM. Furthermore, co-culture of CD4 T cells and synovial fibroblasts resulted in proliferation of CD4 T cells expressing increased levels of the proinflammatory cytokines IFN-γ and IL-17a and RANKL after 5 days. Lastly, co-culture of T cells and synovial fibroblasts resulted in secretion of IL-6, IL-8, IFN-γ and IL-17a and matrix metalloproteinases MMP-1 and MMP-3.
Conclusions: These results indicate that CD4 T cells work mutually with synoviocytes to create an inflammatory microenvironment likely to promote joint destruction. Future studies will characterise the role of glucose metabolism in these cells and investigate if metabolism is intrinsically coupled to effector functions in these cells.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6294

SAT0022 EPIGENOME-WIDE ASSOCIATION STUDY OF RHEUMATOID ARTHRITIS IDENTIFIES DIFFERENTIALLY METHYLATED LOCI IN B CELLS

A. Julià[1], D. Absher[2], M. López-Lasanta[1], N. Palau[1], A. Pluma[1], L. Waite Jones[2], J.R. Glossop[3], W.E. Farrell[3], R.M. Myers[2], S. Marsal[4]. *[1]Grup de Recerca de Reumatologia, Vall Hebron Research Institute, Barcelona, Spain; [2]Absher Lab, HudsonAlpha Institute for Biotechnology, Huntsville, United States; [3]Keele University, Institute for Science and Technology in Medicine, Staffordshire, United Kingdom; [4]Grup de Recerca de Reumatologia, Vall Hebron Research Institute, Alabama, Spain*

Background: Epigenetic regulation of immune cell types could be critical for the development and maintenance of autoimmune diseases like Rheumatoid Arthritis (RA). B cells are highly relevant in RA, since patients express autoantibodies and depleting this cell type is a successful therapeutic approach. Epigenetic variation, such as DNA methylation, may mediate the pathogenic activity of B cells.
Objectives: In this study, we performed an epigenome-wide association study (EWAS) for RA with three different replication cohorts, to identify disease-specific alterations in DNA methylation in B cells.
Methods: Genomic methylation in isolated B lymphocytes was assayed on the Illumina HumanMethylation450 BeadChip, assaying >450,000 different CpG sites. Differential methylated positions (DMPs) were identified in a discovery cohort using a single-point analysis using logistic regression, as well as a pathway-level analysis using a newly developed permutation-based method. A discovery cohort of 50 RA patients and 75 healthy controls from Spain was used to identify the most differentially methylated regions after multiple test correction. Using an independent sample of 15 patients and 15 controls from the same population we performed a replication analysis of the most significant CpG sites and pathways. Using an additional case-control sample of 24 individuals from the UK we provided further evidence of association of the DMPs with RA. Finally, in silico datta from a cohort of systemic lupus erythematosus patients (SLE, n=47) and controls (n=56) from the US, we tested the association of the associated DMPs.
Results: A total of 64 CpG sites were found to be differentially methylated in RA patients compared to controls in the discovery stage after multiple test correction ($q<0.05$). Six biological pathways were also differentially methylated in RA B cells. Analysis of these epigenetic changes in the independent Spain cohort replicated the association of 10 CpG sites located on 8 genes and 2 intergenic regions. Differential methylation at the *CBL* signaling pathway was also replicated. Using the UK case-control cohort, association between RA risk and methylation levels at *CD1C* (P=2.26x10^{-9}) and *TNFSF10* (P=1.67x10^{-8}) loci was further validated. Most of the replicated DMPs associated with RA were also found to be associated with differential methylation in SLE B cells.
Conclusions: Our results highlight genes that may drive the pathogenic activity of B cells in RA and suggest shared methylation patterns with SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2338

SAT0023 DIRECT-ACTING ANTIVIRAL-BASED THERAPY RESTORES IMMUNE TOLERANCE IN HEPATITIS C-INDUCED CRYOGLOBULINEMIA VASCULITIS

C. Comarmond[1], M. Garrido[2], A.-C. Desbois[2], M. Costopoulos[3], M. Le Garff-Tavernier[3], S.N. Si Ahmed[4], L. Alric[5], H. Fontaine[6], B. Bellier[7], A. Maciejewski[7], M. Rosenzwajg[7], D. Klatzmann[7], L. Musset[8], T. Poynard[9], P. Cacoub[10], D. Saadoun[10]. *[1]Internal Medicine and Clinical Immunology; [2]INSERM, UMR_s 959, FRE3632, Hôpital Pitié-Salpêtrière; [3]Biological Hematology, Groupe Hospitalier Pitié-Salpêtrière, Paris; [4]Hepatology, Hôpital d'Orléans, Orléans; [5]Internal Medicine, Centre hospitalier universitaire Purpan, Toulouse; [6]Hepatology, CHU Cochin; [7]INSERM, UMR_s 959, FRE3632; [8]Immunology, UF d'Immunochimie et d'autoimmunité; [9]Hepatology; [10]Internal Medicine and Clinical Immunology, CHU Pitié-Salpêtrière, Paris, France*

Objectives: Interferon-free direct-acting antiviral (DAA)-based therapy has proven to be very effective in patients with hepatitis C virus-cryoglobulinemia vasculitis (HCV-CV). However, their mechanisms of action and their effects on cellular immunity remain poorly defined.
Methods: 27 HCV-CV patients treated with DAA therapy, 12 healthy donors (HD) and 12 HCV were included. We investigated the effects of DAA-based therapy on cellular and cytokine abnormalities in HCV-CV patients by flow cytometry, cytokine Multiplex and enzyme-linked immunosorbent assay.
Results: Compared with HD and HCV, pre-DAA abnormalities in HCV-CV patients included a decreased percentage of $CD4^+CD25^{hi}FoxP3^+$ regulatory T cells ($P<0.01$) with increases in $IgM^+CD21^{-/low}$ memory B cells ($P<0.05$), $CD4^+IFN\gamma^+$ ($P<0.01$), $CD4^+IL17A^+$ ($P<0.01$) and $CD4^+CXCR5^+IL21^+$ follicular helper T cells (Tfh) ($P<0.01$). $IgM^+CD21^{-/low}$ memory B cells were negatively correlated with regulatory T cells (Tregs) (P=0.03), and positively correlated with Tfh (P=0.03) and serum cryoglobulin levels (P=0.01). DAA-based therapy was associated with an increase in Tregs frequency (1.5% ± 0.18% versus 2.1% ± 0.18%), and decreased $IgM^+CD21^{-/low}$ memory B cells and Tfh percentage (35.7% ± 6.1% versus 14.9% ± 3.8%, and 12% ± 1.3% versus 8% ± 0.9%, respectively). B lymphocyte stimulator receptor 3 and programmed death-ligand 1 staining expression on B cells increased in HCV-CV after DAA-based therapy (MFI 37±2.4 versus 47±2.6, $P<0.01$; and 29±7.3 versus 48±9.3, $P<0.05$ respectively).
Conclusions: Our results indicate that DAA-based therapy effectively normalizes many of the disturbances in peripheral B and T lymphocyte homeostasis of HCV-CV patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3911

SAT0024 ALTERATIONS OF PERIPHERAL BLOOD B-CELL SUBSETS IN EARLY RHEUMATOID ARTHRITIS

E. Suponitskaya, A. Avdeeva, A.A. Aleksankin, E. Gerasimova, E. Aleksandrova, T. Popkova, A.N. Novikov, D.K. Karateev. *Institute of Rheumatology, Moscow, Russian Federation*

Background: Alterations of B-cell subpopulation have been described in the

peripheral blood of rheumatoid arthritis (RA) patients (pts), but differences between B-cell subsets distributions in early and late onset RA (LORA) are still unclear [1,2].

Objectives: To examine B-cell subsets in peripheral blood of healthy donors, early (disease duration <6 months) RA (ERA) and LORA pts by flow cytometry, and to analyze the association between B-cell subsets and RA activity.

Methods: 24 active ERA pts (20F/4M); median age 54 years (range) (38–64); disease duration 5 months (4–6); DAS28 score 5.2 (4.7–5.9); RF+75%, ACCP+ 87.5% and 20 LORA pts (16F/4M); median age 58 years (range) (44–62); disease duration 12 years (4.5–17.5); DAS28 score 5.3 (4.6–6.2); both RF+ and ACCP+ 80%, were assessed for B-cell subpopulations and laboratory data: ESR, CRP. LORA pts were treated with DMARDs (anti-TNF-α, Methotrexate), glucocorticoids, and NSAIDS; ERA pts received NSAIDS only. CD19+B cells, memory B cells (CD19+CD27-), non-switched memory B cells (CD19+IgD+CD27+), switched memory B cells (CD19+IgD-CD27+), naïve (CD19+IgD+CD27-), double-negative (CD19+IgD-CD27-), transitional (CD19+IgD+CD10+CD38++CD27-) B cells, and plasmablasts (CD19+CD38+++IgD-CD27+CD20-) were analyzed using multicolor flow cytometry.

Results: The median percentages (range) of non-switched memory B cells (CD19+IgD+CD27+) were lower in ERA and LORA RA cohorts compared to donors: 3.0% (1.6–5.5) and 6.2% (2.4–10.2) vs 7.4% (3.7–11.1), respectively, $p<0.05$ for both cases. In LORA pts, the median percentages (range) and absolute numbers of switched memory B cells (CD19+IgD+CD27-) were higher compared to both ERA pts and donors: 24,1% (14,0–42.3) vs 8,3% (4.4–12.9) and 12.8% (9.3–17.0); and 0.03 (0.02–0.05) vs 0.01 (0.006–0.02) and 0.02 (0.01–0.04), respectively; $p<0.05$ for all cases. The median percentages of naïve B cells (CD19+IgD+CD27-) were significantly higher in ERA pts compared to LORA pts and healthy donors: 75.3% (69.7–83.6) vs 54.3% (39.7–69.1) and 64.7% (57.6–72.4), respectively, $p<0.05$ for both cases.

In ERA pts, we found a significant correlation between absolute numbers of non-switched memory B cells (CD19+IgD+CD27+), RF and anti-CCP: r=0.50 and 0.45, respectively, $p<0.05$ for both cases. In LORA pts, the percentage of memory B cells (CD19+CD27+) correlated positively with ESR (r=0.58), $p<0.05$; a positive association was observed between the absolute numbers of switched memory B cells (CD19+IgD-CD27+), CRP (r=0.48) and RF (r=0.49), $p<0.05$ for all cases.

Conclusions: in ERA pts, immunophenotyping showed increased frequencies of naïve B cells and decreased frequencies and absolute numbers of switched memory B cells compared to LORA cohort.

References:

[1] Fedele et al. BMC Immunology 2014, 15:28. doi: 10.1186/s12865-014-0028-1. Memory B cell subsets and plasmablasts are lower in early than in long-standing Rheumatoid Arthritis.

[2] Moura RA et al. Rheumatology 2010 Jun;49(6):1082–92. doi: 10.1093/rheumatology/keq029. Alterations on peripheral blood B-cell subpopulations in very early arthritis patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1533

SAT0025 MIR 106A, MIR 19A-B, MIR 20A AND MIR21A REGULATE Vγ9Vδ2 FUNCTIONS PARTICIPATING IN THE INFLAMMATORY RESPONSES OCCURRING IN RHEUMATOID ARTHRITIS

G. Guggino[1], F. Ciccia[1], V. Orlando[2], L. SAieva[2], P. Ruscitti[3], P. Cipriani[3], I. Chalcarz[4], R. Alessandro[4], R. Giacomelli[3], F. Dieli[4], N. Caccamo[4], G. Triolo[4]. *[1]DIBIMIS; [2]DIBIME, University of Palermo, palermo; [3]University of L'Aquila, L'Aquila; [4]University of Palermo, Palermo, Italy*

Background: miRNAs are non-coding RNAs which have significant roles in regulating gene expression. The miR17-92 cluster appears to be a key factor in the inflammatory pathways activated during RA.

Objectives: In this study we aimed to evaluate miR17–92 expression and functions in γδ T cell subsets in RA patients, γδ T cells, in fact produce pro-inflammatory cytokines such as IFN-g, IL-6 and IL-8 that may contribute to the inflammatory responses in RA.

Methods: Heparinized peripheral blood from 10 early RA untreated patients and 10 healthy donors was obtained for this study. Polyclonal Vγ9Vδ2 T cell lines were generated first by magnetic isolation followed by sorting (FACSAria) and further analysed by flow cytometry to define their phenotype and their pattern of cytokine production. Expression analysis of miRNA17–92 cluster was performerd by RT-PCR and after identification of relevant miRNA involved in RA, mRNA expression of miRNA target genes was studied.

Results: A remarkable change in the distribution of Vγ9Vδ2 T cell functional subsets with an expansion of effector subsets and a reduction of naïve cells, was observed in the peripheral blood of RA patients, as compared to healthy donors, which were accompanied by modifications in proinflammatory cytokine expression. Particularly, $T_{EM\ (effector\ memory)}$ and $T_{EMRA\ (effector\ memory\ terminally\ differentiated)}$ cells resulted the major souce of IL-6 and IL-8. A significant correlation between miRNA expression and levels of IL-6 and IL-8 was found. The comparative analysis of miRNA expression among Vγ9Vδ2 T cell subsets, between RA patients and healthy controls showed a downregulation of miR106a-5p and miR20a-5p and an upregulation of miR 21a-5p among Vγ9Vδ2 T_{EM} cells; a downregulation of miR19–3p among Vγ9Vδ2 T_{EM} and $Tc_{M\ (central\ memory)}$ cells was also found. This miRNA expression regulated IL-8 and IL-6 gene transcription contributing to the survival of the pro-inflammatory pool reducing the expression of the PDCD4 gene.

Conclusions: Our results provide evidence of a role of miR106a, miR19–3p, 20a and 21a in the regulation of Vγ9Vδ2 T cells function in RA patients and suggest the possibility that the miR17–92 family and γδ T cells participate to the pathogenesis of RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5698

SAT0026 SIGNALLING THROUGH INSULIN-LIKE GROWTH FACTOR 1 RECEPTOR CONTRIBUTES TO IL-6 PRODUCTION AND SUPPORTS T CELL DEPENDENT INFLAMMATION IN RHEUMATOID ARTHRITIS

M. Erlandsson[1], M. Nadali[2], S. Töyrä Silfverswärd[2], M.N. Svensson[2], I.-M. Jonsson[2], K.M. Andersson[3], M.I. Bokarewa[2]. *[1]Rheumatology and Inflammation Research; [2]Dept of Rheumatology and Inflammation Research; [3]Dept. of Rheumatology and Inflammation Research, Gothenburg University, Gothenburg, Sweden*

Background: Insulin-like growth factor (IGF) 1 receptor is essential for cell energy metabolism. It plays a key role linking glucose and lipid metabolism of active cells and may turn pathogenic in uncontrolled tissue growth in tumours. In rheumatoid arthritis (RA), the IGF-1R signalling is activated supporting expansion of the inflamed synovia.

Objectives: The aim of the present study was to understand the place of IGF-1R expression and signalling for development of adaptive immune responses in the setting of prospective RA cohort and in experimental arthritis.

Methods: Clinical associations of IGF1R expression in leukocytes of the peripheral blood were studied in 84 female RA patients with mean disease duration 8 years, all treated with methotrexate. Consequences of the IGF1R signalling inhibition for arthritis were studied in mBSA immunised Balb/c mice treated with NT157 compound promoting degradation of the insulin receptor substrates IRS-1/2.

Results: In RA patients, high expression of IGF1R in leukocytes was associated with systemic inflammation as verified by higher transcription factor NF-kB (p=0.033), serum levels of IL-6 (p=0.006) and erythrocyte sedimentation rate (p=0.003), and higher pain perception (VAS, p=0.019). Additionally, women with high IGF1R were often in need of combined DMARD treatment (p=0.045). Phosphorylated IGF1R and STAT3 enrich T cells infiltrate in RA synovia. Treatment with NT157 rendered no metabolic consequences to mouse body weight and serum glucose levels. NT157 inhibited the phosphorylation of IGF1R and STAT3 in synovia, and alleviated arthritis and erosions in mice. It also reduced IGF1R+ T cell population in spleen and despaired ERK and Akt signalling. This limited the ability of mBSA-specific T cells to produce IL-6 (p=0.013), IFNg (p=0.024) and IL-17 (p=0.0097). The reduction of IL-6 and IL-17 levels was associated with changed RoRgt/FoxP3 balance.

Conclusions: IGF1R signalling contributes to severe RA by triggering T cell dependent inflammation in arthritis. Inhibition of IGF1R on the level of insulin receptor substrates alleviates arthritis by restricting IL-6 dependent formation of Th17 cells and may open for new treatment strategies in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6191

SAT0027 IMMUNOMODULATORY EFFECTS OF MGD010, A DART® MOLECULE TARGETING HUMAN B-CELL CD32B AND CD79B

W. Chen, S. Shankar, J. Lohr, X.-T. Yao, H. Li, X. Chen, J. Muth, N. Gal-Edd, E. Bonvini, S. Johnson, N. Pandya, P.A. Moore, J. Wigginton. *Macrogenics, INC., Rockville, United States*

Background: B-cell targeted therapeutics have proven efficacious in the treatment of autoimmune diseases, generating impetus to develop alternate strategies that provide activity with rapid onset and no B-cell depletion. To this end, MGD010, a bispecifc DART® molecule, was designed to exploit the inhibitory function of the checkpoint molecule, CD32B, (FcγRIIb) via its simultaneous co-ligation with the BCR component, CD79B. Initial phase 1 studies performed in healthy subjects demonstrated MGD010 was well tolerated in a single-dose, dose escalation to up to 10 mg/kg, with no evidence of peripheral B-cell activation or depletion. MGD010 exhibited pharmacokinetic properties of an antibody-based molecule, with dose-dependent B-cell occupancy saturating at >1mg/kg and diminished propensity for ex-vivo BCR-induced B-cell activation (1). To further understand the potential for MGD010 to modulate ongoing immune responses, the impact of MGD010 on the immune response to Hepatitis A (HAV) vaccination, a T-cell dependent neo-antigen challenge, was evaluated in normal healthy subjects.

Objectives: To determine effects of MGD010 on humoral and cellular immune responses in normal healthy volunteers.

Methods: This was an open label, placebo controlled cohort-expansion in normal healthy volunteers. Subjects (n=8 per group) were randomly assigned to receive an IV administration of a single dose of 3 or 10 mg/kg MGD010 or placebo. All subjects received a single intramuscular dose of hepatitis A vaccine (HAV) (1.0 mL or ~50U) 24 hours after administration of MGD010 or placebo. Subjects were monitored for adverse events for 56 days after administration of drug or placebo. Analyses included peripheral lymphocyte

counts and immunophenotyping, determination of serum immunoglobulin levels, seroconversion rate of HAV and quantification of serum HAV IgG concentration.
Results: Twenty-four (24) healthy subjects were enrolled for the study and 23 completed the study. One subject discontinued prior to completion due to inability to follow study procedures. There were no severe adverse events in subjects who received 3 or 10 mg/kg MGD010. The only serious adverse event reported in t in a subject who had received placebo and was not drug related. There were no CTCAE grade 3 or higher adverse events related to MGD010. Consistent with prior observations (1), ex vivo flow cytometric analysis confirmed dose-dependent MGD010 binding to peripheral B cells without B-cell depletion, accompanied with decreased surface BCR and CD40 expression as well as a moderate decrease in total serum IgM levels. Reduced HAV seroconversion rates were observed in subjects treated with MGD010 as compared to placebo, with significantly lower HAV-specific IgG levels in subjects treated with MGD010 compared with placebo group ($P < 0.05$).
Conclusions: These studies demonstrate that by pharmacologically exploiting the activity of the checkpoint molecule CD32B in combination with the BCR CD79B component, a single dose administration of either 3 or 10 mg/kg MGD010 delivers an immunomodulatory effect that effectively counters B-cell function. Together with a good safety profile, these data provide compelling rationale for further developing MGD010 as a therapeutic modality for autoimmune diseases.
References:
[1] Pandya, N et al., EULAR16–4079.
Acknowledgements:.
Disclosure of Interest: W. Chen Employee of: MacroGenics, S. Shankar Employee of: MacroGenics, J. Lohr Employee of: MacroGenics, X.-T. Yao Employee of: MacroGenics, H. Li Employee of: MacroGenics, X. Chen Employee of: MacroGenics, J. Muth Employee of: MacroGenics, N. Gal-Edd Employee of: MacroGenics, E. Bonvini Shareholder of: MacroGenics, Employee of: MacroGenics, S. Johnson Shareholder of: MacroGenics, Employee of: MacroGenics, N. Pandya Shareholder of: MacroGenics, Employee of: MacroGenics, P. Moore Shareholder of: MacroGenics, Employee of: MacroGenics, J. Wigginton Shareholder of: MacroGenics, Employee of: MacroGenics
DOI: 10.1136/annrheumdis-2017-eular.6434

SAT0028 AIOLOS OVEREXPRESSION IN SYSTEMIC LUPUS ERYTHEMATOSUS B-CELL SUBTYPES AND BAFF INDUCED MEMORY B-CELL DIFFERENTIATION ARE REDUCED BY CC-220 MODULATION OF CEREBLON ACTIVITY

G.E. Ringheim, J. Kosek, L. Capone, P.H. Schafer, Y. Nakayama. *Inflammation and Immunology, Celgene Corporation, Summit, United States*

Background: Systemic Lupus Erythematosis (SLE) is an autoimmune disease characterized by alterations in B-cells, autoantibody production, and elevations in circulating B-cell activating factor (BAFF). Aiolos single nucleotide polymorphisms and elevations in Aiolos mRNA are associated with SLE susceptibility. CC-220 is a Cullin Ring Ligase 4 Cereblon (CRL4CRBN) E3 Ubiquitin Ligase Modulator that induces ubiquitination and degradation of Aiolos and Ikaros transcription factors. We investigated the effects of CC-220 in B-cells from SLE patients to assess its impact on Aiolos protein levels and B-cell proliferation, differentiation, and antibody production.
Objectives: Determine the protein levels of the B-cell transcription factors Aiolos and Ikaros in B-cell subtypes of SLE patients and assess the impact of the cereblon modulator CC-220 on Aiolos and Ikaros protein degradation, proliferation, and plasmablast differentiation.
Methods: Peripheral blood mononuclear cells (PBMC) were measured for levels of circulating B-cell subtypes, B-cell activation state, and Aiolos and Ikaros protein levels by flow cytometry. Cell types were defined as: $CD27^-IgD^+$ naive, $CD27^+IgD^-$ switched memory, $CD27^+IgD^+$ nonswitched memory, and $CD27^-IgD^-$ double negative B-cells and $CD20^-CD38^+$ plasmablasts. Measurements of BAFF, IL-2 and IL-21 from plasma and IgG and IgM were done by ELISA. Plasmablast differentiation was induced by BAFF, IL-2, and IL-21 co-stimulation of B-cell cultures for 5 days in the absence and presence of CC-220.
Results: Plasma samples from SLE patients were found to have higher circulating BAFF, similar IL-2 levels, and reduced IL-21 levels relative to healthy individuals. Alterations in circulating B-cell subtypes occur in SLE patients including reduction of memory and elevations of naive and double negative B-cells. Alterations in biomarkers associated with chronic B-cell activation, including elevation of CD95 and reduction of CD21 and CD23 were also observed. Assessment of the B-cell differentiation transcription factors Aiolos and Ikaros in SLE B-cells showed that Aiolos, but not Ikaros is elevated in naive, switched memory, nonswitched memory, and double negative B-cells. CC-220 treatment reduced Aiolos and Ikaros protein levels in both SLE and healthy individuals in all four B-cell subtypes measured. CC-220 treatment was associated with reduced B-cell proliferation, plasmablast differentiation, and secretion of IgG and IgM in cells co-stimulated with BAFF, IL-2 and IL-21. Similarly, CC-220 reduced the expression of genes involved in B-cell differentiation including IRF-4, Xbp-1, Blimp-1, and IgJ indicating an early blockade in B-cell differntiation.
Conclusions: Our observations that SLE is associated with alterations of circulating B-cell subtypes and their activation state, Aiolos overexpression in B-cells, and increases in circulating BAFF support the hypothesis that B-cells play a significant role in SLE pathology. Moreover, these observed changes suggest that B-cells may be predisposed towards plasmablast differentiation and antibody production in SLE. CC-220 administration reduced Aiolos and Ikaros protein levels in B-cells and reduced proliferation, plasmablast differentiation and antibody production at clinically obtainable drug concentrations (<10 nM).
Disclosure of Interest: G. Ringheim Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, J. Kosek Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, L. Capone Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, P. Schafer Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, Y. Nakayama Shareholder of: Celgene Corporation, Employee of: Celgene Corporation
DOI: 10.1136/annrheumdis-2017-eular.5294

SAT0029 B CELL DEPLETION AFFECTS CD8 T CELLS IN ANCA-ASSOCIATED VASCULITIS

A. Néel[1,2], M. Bucchia[3], M. Néel[2], M. Rimbert[2,4], C. Agard[1], M. Hourmant[5], G. Tilly[2], M. Yap[6], F. Perrin[1], J. Graveleau[1], P. Godmer[7], S. Brouard[2], C. Bressollette[8], F. Fakhouri[2,5], M. Hamidou[1,2], N. Degauque[2]. *[1]Internal Medicine, Nantes University Hospital; [2]U1064, INSERM; [3]Pediatrics; [4]Immunology; [5]Nephrology, Nantes University Hospital; [6]INSERM, Nantes; [7]Internal Medicine, CH Bretagne Atlantique, Vannes; [8]Virology, Nantes University Hospital, Nantes, France*

Background: In anti-neutrophil cytoplasmic antibodies associated vasculitis (AAV), several clues suggest that the efficacy of B cell depletion therapy lies beyond the suppression of ANCA-producing cells and may involve the suppression of B-T cell crosstalk. However, little if any data are available regarding the impact of rituximab on CD4, regulatory T and CD8 T cells in this setting.
Objectives: To compare the effect of conventional immunosuppressants (CIS) and rituximab (RTX) on 3 T cells compartments in AAV. To assess the impact of patients B cells and that of B cell depletion on CD8 T cell cytokine production.
Methods: Thorough cross-sectionnal immunophenotypic analysis of CD4, regulatory T and CD8 cells of 53 patients with AAV, using polychromatic flow cytometry. A multiplex Luminex immunoassay was used to measure Cytokine/chemokine production of in vitro stimulated CD8 T cells. Active untreated AAV patients' B cells and/or CD8 T cells were cocultures for 72h with Staphylococcal Enterotoxin (Autologous and criss-cross experiments), and CD8 T cells cytokine production was then measured by flow cytometry.
Results: Among CD4 T cells, we found that frequency of naïve and memory subsets and the expression of CCR5, CCR4 and CD161 were not influenced by maintenance treatment type. Similarly, total Treg frequency and Treg subsets including CD161+, Helios+, resting (CD45RA+) and memory (CD45RA-FoxP3hi) Tregs were comparable among RTX and CIS treated patients. By contrast, the type of maintenance treatment markedly influenced the CD8+ T cell compartment. Patient under B cel depletion therapy had less TEMRA (CD45RA+CCR7-) and more TEM cells than those receiving CIS, and ressembled those in long term remission off therapy. CMV seropositivity did not explained the observed diifferences. Longitudinal data confirmed that B cell depletion significantly decreased TEMRA (CD45RA+CCR7-) CD8 T cell frequency ($p<0.001$), whereas CIS had the opposite effect. Furthermore, we found that in vitro stimulated CD8 T cells from B cell depleted patients produced less pro-inflammatory cytokine/chemokine than those from patients treated with CIS. In coculture with B cells and SEB, patients CD8 cells coculture produced higher level of inflammatory cytokines than those from controls, but only when they were stimulated with patients' B cells.
Conclusions: B cell depletion therapy has a significant impact on the CD8 T cell compartment in terms of phenotype and function. B cell can promote pro-inflammtory function of CD8 T cell in vitro. CD8 T cell are found in vasculitis lesions. These observations raise the question whether the disruption of B cell help to CD8 T cells could contribute to the dramatic efficacy of RTX. Further studies are needed to demonstrate the implication of patients' CD8 T cell in tissue damage.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6894

SAT0030 BREACH OF AUTOREACTIVE B-CELL TOLERANCE BY POST-TRANSLATIONALLY MODIFIED FOREIGN PROTEINS

J. Dekkers[1], M. Verheul[1], J. Stoop[1], B. Liu[1], A. Ioan-Facsinay[1], P. van Veelen[1], A. de Ru[1], G. Janssen[1], M. Hegen[2], S. Rapecki[3], T. Huizinga[4], L. Trouw[4], R. Toes[4]. *[1]Rheumatology, LUMC, Leiden, Netherlands; [2]Pfizer, Boston, United States; [3]UCB, Slough, United Kingdom; [4]LUMC, Leiden, Netherlands*

Background: Autoimmunity in Rheumatoid arthritis (RA) patients is characterized by a spectrum of anti-modified protein antibodies (AMPA) directed against post-translationally modified (PTM) proteins. The best-known AMPA in RA are anti-citrullinated protein antibodies (ACPA). Much less is known about the occurrence and aetiology of other AMPA responses in RA such as autoantibodies directed to malondialdehyde-acetaldehyde (MAA) adducts, acetylated antigens, and carbamylated proteins. Anti-carbamylated protein (anti-CarP) autoantibodies recognize carbamylated proteins containing a homocitrulline, a PTM structurally similar to citrulline. With the presence of various AMPA responses in RA, PTM proteins have been implicated in the breach of autoreactive B-cell tolerance

leading to the formation of these autoantibodies. At present it is unkown how AMPA are generated and how autoreactive B-cell responses against PTM proteins are induced.
Objectives: To investigate how PTM proteins, more specifically carbamylated proteins, could contribute to a breach of B-cell tolerance.
Methods: Serum reactivity towards five different carbamylated proteins was determined for 160 RA-patients and 40 healthy individuals. Anti-CarP antibody cross-reactivity was studied by inhibition experiments. Mass spectrometry was performed to identify carbamylated self-proteins in human rheumatic and osteoarthritic joint tissue. Mice were immunized with carbamylated- or non-modified foreign (OVA) and self-antigens (mouse Albumin). Sera of immunized mice and monoclonal antibodies were analyzed for antigen reactivity.
Results: We show that anti-CarP antibodies in RA are highly cross-reactive towards multiple carbamylated proteins, including modified self- as well as modified non-self proteins. Immunization with carbamylated foreign proteins (Ca-OVA) induced a strong anti-CarP response against both carbamylated foreign- and self-proteins. Similar to murine serum anti-CarP antibodies, murine monoclonal anti-CarP antibodies were highly specific and cross-reactive to multiple carbamylated (auto)antigens. Although citrulline greatly resembles homocitrulline residues in structure, murine anti-CarP antibodies differ in antigen recognition profile from ACPA as they are able to discriminate between citrullinated and homocitrullinated forms of the same protein. Interestingly, we were able to identify carbamylated-albumin, in RA synovial tissue, indicating that albumin is present in carbamylated form locally in the inflamed joint.
Conclusions: Self-reactive AMPA-responses can be induced by exposure to foreign proteins containing PTM. Our findings show that autoreactive B-cell responses against PTM self proteins can be induced by exposure to PTM foreign proteins and provide new insights on the breach of autoreactive B-cell tolerance by foreign proteins.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5984

SAT0031 DETECTION AND ISOLATION OF ANTIGEN SPECIFIC B CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS

J. Nilsson[1], M. Bergquist[1], K. Önnheim[1], I.-L. Mårtensson[1], J. Viljanen[2], E. Lönnblom[3], B. Xu[3], O. Sareila[3], J. Kihlberg[2], R. Holmdahl[3], I. Gjertsson[1]. *[1]Rheumatology and Inflammation Research, Gothenburg University, Göteborg; [2]Department of Chemistry, BMC, Uppsala University, Uppsala; [3]Medical Inflammation Research, Dept of medical Biochemistry and biophysics, Karolinska Institute, Stockholm, Sweden*

Background: The majority of autoimmune diseases, e.g. rheumatoid arthritis (RA), are characterized by autoantibodies that are produced by B cells. We have identified several novel post-translationally modified epitopes in collagen type II (CII), a major cartilage constituent that are autoreactive. In mouse models, autoantibodies that bind to these epitopes can either induce or protect against inflammatory arthritis. However, very little is known about the frequencies or phenotype the B cells that produce these autoantibodies in humans.
Objectives: The aim of this project is to study the B cells that produce autoantibodies reactive to CII-epitopes in patients with RA.
Methods: Clinical data and peripheral blood were collected from patients with RA (n=100). Titres of CII-reactive serum-autoantibodies were determined by Luminex. The different subsets of B cells that expressed a CII-reactive B cell receptor (BCR) were analysed and isolated in patients with positive (n=10) or negative (n=5) titres for autoantibodies recognizing the CII-epitopes cyc48 (CII-F4-R-Cit) and cyc49 (CII-F4-Cit-R) as well as in healthy controls (n=3) using flow cytometry.
Results: In patients with detectable autoantibodies to cyc48 and cyc49, their titres were 13761±3815 and 5585±1992 (mean ± SEM), respectively. The corresponding titres in the patients negative for these autoantibodies were 122±55 and 234±75. In autoantibody-positive patients, the frequencies of cells expressing a BCR reactive for cyc48 and cyc49 in different subsets were: transitional cells 0.88±0.18% and 1.33±0.33%; naïve cells 0.09±0.0008% and 0.13±0.06 and memory cells 0.31±0.25 and 0.30±0.12%. All frequencies were well above those detected in patients without cyc48/49 titres and in healthy controls. A higher proportion (p=0.03) of the cyc48/49 positive patients were treated with methotrexate compared to cyc48/49 negative patients, no other clinical differences were recorded. CII-reactive single B cells were isolated in order to clone the BCR
Conclusions: In patients with manifest RA there is a relatively high and detectable frequency of transitional B cells that express a joint-specific BCR, which suggests that the deletion of autoreactive B cells in the bone marrow in RA patients is defective. As there is a decrease in the proportion of naïve CII-specific B cells, a substantial amount of the autoreactive cells are deleted in the periphery. However, peripheral B-cell tolerance is incomplete, as CII-specific B cells are enriched in the pool of memory B cells.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3680

SAT0032 EX VIVO ANALYSIS OF AUTOANTIGEN-SPECIFIC T CELL RESPONSES USING A MULTI HLA-CLASS II TETRAMER APPROACH

C. Gerstner[1], H. Uchtenhagen[1,2], A. Dubnovitsky[3,4], W. Kwok[2], E.A. James[5], V. Malmström[1]. *[1]Rheumatology Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden; [2]Translational Research program, BRI at Virginia Mason, Seattle, United States; [3]Department of Clinical Neurosciences; [4]Science for Life Laboratory, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden; [5]Tetramer Core, BRI at Virginia Mason, Seattle, United States*

Background: HLA class II tetramers allow the direct *ex vivo* enumeration and phenotypic characterization of antigen-specific T cells and have proven a useful tool in different settings, e.g. allergy and vaccination.
In rheumatoid arthritis (RA), many candidate auto-antigens have been characterized and are believed to play a role in the disease.
Objectives: Based on flow cytometry we developed a multi HLA-class II tetramer approach that renders it possible to look at numerous specificities simultaneously and is sufficiently sensitive at the same time as auto-reactive T cells are likely to be rare. We focused on validated citrullinated T cell epitopes previously studied in RA, namely a-enolase, fibrinogen and CILP.
To test the robustness and sensitivity of our multi-tetramer assay, we performed repeated experiments on PBMCs of HLA-DRB1*04:01-positive healthy controls as well as HLA-DRB1*04:01-positive RA patients.
Results: First, we examined the sensitivity of the panel by assessing PBMC from healthy donors and we could detect low frequencies of auto-reactive T cells in these samples (1–10 per million CD4), mostly displaying a naïve phenotype, which was in sharp contrast to influenza-specific T cells in the same donors which were 10–20 fold higher in numbers and of memory phenotype. Next, we tested the robustness of the panel by running technical repeats of all healthy donor samples, which yielded similar frequencies. Thereafter, we focused on RA patient PBMC obtained from repeated blood draws (2–4 weeks apart). Also in these samples, frequencies ranged between 1–10 tetramer-positive cells per million CD4+ T cells, i.e. similar as in healthy controls. Moreover, not all T cell specificities were present in all patients. Still, we found the frequencies to be stable in the repeated blood draws in approximately half of the individuals, implicating that frequencies close to 1 cell per million CD4+ T cells is borderline of what we can stably detect. Importantly, the patient samples utilized were not taken from time points of active disease, where we hypothesize frequencies to be elevated. This may be the case also in synovial fluid and as a proof of principle, we assessed synovial fluid samples of HLA-DRB1*04:01+ RA patients and were able to detect auto-reactive T cells at frequencies comparable to the ones found in peripheral blood.
Conclusions: In conclusion, we developed a sensitive tetramer panel allowing the simultaneous enumeration and phenotypic characterization of antigen-specific T cells in *ex vivo* samples from RA patients that can be used for monitoring and in-depth studying of these cells during the course of disease and treatment in individual patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2796

SAT0033 SMOKING CONTRIBUTES TO EXHAUSTED STATE OF CD4+ T CELLS IN RHEUMATOID ARTHRITIS

C. Wasén, M. Turkkila, M. Erlandsson, K.M. Andersson, M. Brisslert, S. Töyrä Silfverswärd, M.I. Bokarewa. *Department of Rheumatology and Inflammation Research, University of Gothenburg, Gothenburg, Sweden*

Background: Rheumatoid arthritis (RA) has recently been linked to an exhausted state of $CD4^+$ T cells in peripheral blood of patients [1]. Exhaustion of $CD4^+$ T cells limits their proliferation and increases cell death. In $CD8^+$ T cells smoking counteract exhaustion, which may lead to increased cytotoxic activity exemplified by targeting of cells with high expression of the anti-apoptotic protein survivin [2]. Exhaustion of $CD4^+$ T cells coincides with expression of interferon (IFN) response genes [3], referred to as the IFN signature. The development of the IFN signature has been suggested to predate RA [4].
Objectives: We investigated how smoking affect the $CD4^+$ T cell population in peripheral blood of RA patients with focus on the exhaustion marker programmed cell death-1 (PD-1).
Methods: Blood samples were collected from RA patients and healthy women with different smoking status and analysed for PD-1 and survivin expression using flow cytometry and qPCR. Sorted Th17 cells from peripheral blood were analysed for expression of 18 genes up regulated during exhaustion [3], herein referred to as the exhaustion set, and serum levels of survivin were assessed by ELISA. Peripheral blood CD4+ cells were analysed for their expression of seven IFN response genes [4]. The role of survivin in the formation of exhausted $CD4^+$ T cells was studied in collagen-induced arthritis (CIA), where mice were treated with nicotine or vaccinated with survivin peptides.
Results: High frequency of exhausted $PD\text{-}1^+CD4^+$ cells was found in smoking RA patients. The numbers of $PD1^+CD4^+$ cells correlated inversely with the PD-1 expression by cytotoxic $CD8^+CD107^+$ cells (r=-0.62, p=0.01). Additionally, the frequency of $PD\text{-}1^+CD4^+$ cells increased with reduction of the $CD4^+$ population (r=-0.71, p=0.002). The IFN signature was found exclusively among smoking RA patients. The patients with the IFN signature all had $CD4^+$ cells with low survivin

production. Th17 cells from RA patients with high serum survivin were enriched in genes of the exhaustion set. $CD4^+$ cells with high survivin expression were negative for PD-1, while PD-1^{hi} cells had low expression of survivin. In CIA mice the survivin^{hi}PD-1^- $CD4^+$ cells were reduced by nicotine treatment (p=0.03) or survivin vaccination (p=0.009).

Conclusions: Smoking associates with exhaustion of $CD4^+$ T cells in RA by increasing the frequency of PD-1^+CD4^+ cells and supporting the IFN signature. Balancing T cell exhaustion and preventing the IFN signature are potential future treatment strategies for RA.

References:
[1] Frenz T, et al. J Allergy Clin Immunol 2016. 138(2): 586–589.
[2] Wasén C, et al. J Autoimmun 2017. DOI: 10.1016/j.jaut.2016.12.00.
[3] Crawford A, et al. Immunity 2014. 40(2): 289–302.
[4] Lübbers J, et al. Ann Rheum Dis 2013. 72(5): 776–780.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6546

SAT0034 ANALYSIS OF THE T-CELL SUBSET COMPOSITION IN ANKYLOSING SPONDYLITIS PATIENTS WITH LONG-STANDING ANTI-TNF THERAPY

S. Dulic[1], Z. Vásárhelyi[2], A. Bajnok[3], B. Szalay[4], G. Toldi[2], L. Kovács[1], A. Balog[1]. *[1]University of Szeged Departement of Rheumatology, Szeged; [2]First Department of Obstetrics and Gynecology; [3]First Department of Pediatrics; [4]Department of Laboratory Medicine, Semmelweis University, Budapest, Hungary*

Background: Ankylosing spondylitis (AS) is a chronic, progressive, immune-mediated inflammatory disease, driven primarily by Th1 and Th17 cells. Anti-TNF therapies are successfully used in AS to achieve and maintain remission. However, their influence on the composition of the T-cell repertoire is not clear, and, in particular, the few published studies involve mostly patients with anti-TNF treatment of short duration.

Objectives: We aimed to characterize the changes in several T cell subsets after long-term anti-TNF treatment in AS patients.

Methods: Twenty-two AS patients on long-term anti-TNF therapy were evaluated (15 anti-TNF-responders and 7 non-responders). A wide range of cell subtypes were analysed with flow cytometry and compared with therapy-naïve and short-term data.

Results: Key findings include decreased proportions of naive CD4 and CD8 cells, increased frequencies of Th1 and Th17 cells and higher Th1/Th2 and Th17/Treg ratios in the long-term anti-TNF-treated patients (responders, non-responders and total), which was found to be significant not only when compared with healthy controls, but also with therapy-naive and short-term anti-TNF-treated AS patients. We have found several alterations within the various activated T-cell subsets – increase in CD4HLADR cells in responders, in CD8HLADR cells in the whole AS group and in responders, and in CD4CD25 cells in responders, and decrease in CD4CD69 cell percentages in long-term treated patients – becoming evident only after long-term anti-TNF-therapy.

Conclusions: This study provides a comprehensive assessment of the impact of anti-TNF therapy on the T cell repertoire in AS, and indicate that these therapies induce profound changes within T-cells. Changes in T cell phenotype seem to develop progressively during therapy, even in inactive disease, and reflect an ongoing effector T-cell differentiation and activation, and a normalization of Treg development.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6335

SAT0035 INHIBITION OF PROTEIN KINASE C THETA BY THE SELECTIVE INHIBITOR CC-90005 INDUCES T CELL ANERGY

E.M. Hur, L. Capone, J. Kosek, P.H. Schafer, G.E. Ringheim. *Translational Development, Celgene Corp., Summit, United States*

Background: Protein Kinase C theta (PKC-θ), a member of the PKC family of serine/threonine kinases, is essential in T cell receptor (TCR) signaling and T cell activation [1]. Inhibition of PKC-θ activity may provide new therapeutic options for autoimmune diseases with a T effector cell dependent pathology. CC-90005 is a highly selective small molecule inhibitor of PKC-θ.

Objectives: Evaluate the impact of specific PKC-θ inhibition on T-cell activation and anergy using the highly selective inhibitor CC-90005.

Methods: Human peripheral blood mononuclear cell (PBMC) or isolated T cell cultures were pre-treated with CC-90005 (0.1–10 μM) and stimulated for various times up to 24 h with anti-CD3 and anti-CD28 activation of the TCR, followed by a washout incubation period (1 h-24 h). Cells were then re-stimulated in the presence or absence of CC-90005 and cultured a further 24–96 h. T cell activation was assessed by CD25 and CD69 cell surface expression, thymidine incorporation, and cytokine production.

Results: Upon TCR stimulation, CC-90005 significantly inhibited CD25 and CD69 expression and T cell proliferation in PBMC and isolated T cells. Similarly, CC-90005 inhibited the production of Th1, Th2, Th17 and other pro-inflammatory cytokines. Furthermore, the inhibitory effects of CC-90005 on T cell activation persisted after washout in stimulated T cells, indicating an induction of an anergic cell state. CC-90005 anergy induction was shown to require only short initial exposures of as little as 2 h and to maintain anergy for as long as 48–96 h post CC-90005 washout. However, T cells pre-treated with the inhibitor in the absence of concomitant TCR stimulation were able to respond to stimulus after as little as 1 h washout, indicating a rapid recovery of PKC-θ activity and T-cell function. CC-90005 upregulated an anergy-related E3 ubiquitin ligase, Gene related to anergy in lymphocytes (GRAIL) in T cells. Elevated expression level of GRAIL was maintained in unresponsive T cells after washout, suggesting that GRAIL was a possible downstream mediator of CC-90005 effect on T cell anergy.

Conclusions: CC-90005, a specific inhibitor of PKC-θ, significantly inhibits TCR-mediated T cell activation, proliferation, and cytokine production. Moreover, inhibition of these T-cell functions persists after drug withdrawal and restimulus of T-cells, but only if the primary T cell activation event occurrs in the presence of CC-90005. Thus, CC-90005 induces a functional unresponsiveness anergic state in T cells if present during TCR activation, which may have long-term therapeutic benefit in the treatment of T-cell mediated autoimmune and allergic inflammatory conditions.

References:
[1] Zhang EY, Kong K-F, Altman A. The yin and yang of protein kinase C-theta (PKCθ): a novel drug target for selective immunosuppression. Elsevier Inc. 2013. doi:10.1016/B978-0-12-404717-4.00006-8.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5082

SAT0036 IL-17+CD8+ T CELLS ENRICHED IN THE SYNOVIAL FLUID OF PSA/SPA PATIENTS EXHIBIT A PRO-INFLAMMATORY CYTOKINE PHENOTYPE

K.J.A. Steel[1], E. Chan[2], B.W. Kirkham[2], L.S. Taams[1]. *[1]Centre for Inflammation Biology and Cancer Immunology (CIBCI), Division of Immunology, Infection & Inflammatory Disease (DIIID), King's College London; [2]Department of Rheumatology, Guy's & St Thomas' NHS Trust, London, United Kingdom*

Background: Seronegative spondylarthropathies (SpA) share common clinical and immunological characteristics, including a common association with MHC class I, suggesting a role for CD8+ T cells. In contrast, rheumatoid arthritis (RA) is associated with MHC class II. We previously showed that IL-17+CD8+ T cells are increased in the synovial fluid (SF) of patients with psoriatic arthritis (PsA) but not RA, compared to peripheral blood (PB). This study extends this analysis to other SpA types, and phenotypes the SF IL-17+CD8+ T cells to further elucidate their potential pathogenic role.

Methods: Paired PB and SF were collected from patients with RA, PsA and other SpA types (ankylosing spondylitis (AS), reactive arthritis (ReA), enteropathic arthritis (EA) and peripheral SpA (p-SpA)) from Guy's Hospital Rheumatology clinic with informed consent. PB from healthy controls (HC) was collected at King's College London. PBMC and SFMC were isolated and stimulated *ex vivo* with PMA/ionomycin in the presence of golgistop before analysis of surface marker and cytokine expression by flow cytometry.

Results: The percentage of IL-17A+CD8+ T (Tc17) cells was increased in the SF of PsA (median 0.9%, p=0.0012, n=13) as well as other SpA patients (0.34%, p=0.0009, n=14), but not RA patients (0.07%, p=0.3, n=7) compared to matched PB (median 0.10%, no significant differences between disease and control PB). The percentage of SF IL-17A+CD4+ T (Th17) cells was increased in patients with SpA (2.14%, p=0.004, n=14), RA (2.31%, p=0.016, n=7) and to a lesser extent PsA (0.97%, p=0.057, n=13), compared to PB (median 0.61%, no significant differences between disease and control PB).

Phenotypically, most SF IL-17A+CD8+ T cells expressed CCR6 (median 88%, n=7) and CD161 (75%, n=8), known markers of IL-17+CD4+ T cells. A high percentage also expressed CD103 (69%, n=9), which was not observed in the synovial IL-17A+CD4+ T cells (2%, n=10). A high frequency of IL-17A+CD8+ T cells co-expressed a range of pro-inflammatory cytokines including IFN-γ (72%, n=12), GM-CSF (58%, n=7), TNF-α (48%, n=12) and to a lesser extent IL-21 (20%, n=6) and IL-22 (5%, n=6). IL-10 was usually co-expressed at very low levels (1%, n=7), although 2 samples showed co-expression of IL-10 (33%, n=2). CCR6, CD161, GM-CSF and IL-21 were not significantly co-expressed by either IL-17A negative CD8+ or IFNg+CD8+ (Tc1) T cells from the SF, indicating this may be a co-expression profile specific to IL-17 expressing T cells.

Conclusions: These findings confirm the presence of an IL-17A+CD8+ T cell subset in the SF of PsA patients and extend this to other SpA types. The expression of the integrin CD103 by these cells indicates they may represent a tissue resident memory (Trm) population in the synovial joint. In addition to IL-17A, the co-expression of several pro-inflammatory cytokines combined with low expression of IL-10, suggests a pro-inflammatory role for these cells.

Acknowledgements: *This work was funded in part by the King's Health Partners R&D Challenge Fund (R140808) and in part by research support from Novartis.*
Disclosure of Interest: K. Steel: None declared, E. Chan: None declared, B. Kirkham Grant/research support from: Novartis, UCB, Abbvie, Bristol Myer Sqibb, Celgene, Janssen, MSD, Pfizer, Roche, L. Taams Grant/research support from: Novartis and UCB
DOI: 10.1136/annrheumdis-2017-eular.5117

SATURDAY, 17 JUNE 2017

Rheumatoid arthritis - prognosis, predictors and outcome

SAT0037 THE EFFECTS OF B CELL DIRECTED THERAPY ON DISEASE RELEVANT BIOMARKERS IN SUBJECTS AT RISK OF RHEUMATOID ARTHRITIS

D. Gerlag[1], M. Safy[2], K. Maijer[2], T. Ramwadhdoebe[2], S. Tas[2], N. de Vries[2], M. Starmans-Kool[3], A. van Tubergen[4], M. Janssen[5], S. Eyre[6], L. Klareskog[7], K. Zwinderman[2], P.-P. Tak[2]. *[1]Amsterdam Rheumatology and Immunology Center; [2]Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands, Amsterdam; [3]Zuyderland Medical Center, Heerlen; [4]Maastricht Medical Center, Maastricht; [5]Rijnstate Hospital, Arnhem, Netherlands; [6]Arthritis Research UK Centre for Genetics and Genomics, Manchester, United Kingdom; [7]Karolinska Institute, Stockholm, Sweden*

Background: Exploration of the mechanism underlying the delay of development of clinical signs of seropositive rheumatoid arthritis (RA) observed after B cell directed therapy in individuals at risk of developing autoantibody positive RA may offer insights into the mechanism of disease and may assist the development of preventive strategies.
Objectives: To explore the effects of a single infusion of rituximab (anti-CD20 antibody) on the observed delay of the onset of clinically manifest arthritis in individuals at risk of developing autoantibody positive RA.
Methods: In a study of 81 subjects positive for both anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) with arthralgia who never had clinically manifest arthritis and never used disease-modifying antirheumatic drugs, a 55% reduction of the risk of developing arthritis was observed 12 months after receiving a single iv infusion of 1000 mg rituximab when compared to placebo. In this group there was a delay in the development of arthritis of 12.0 months (12 months placebo vs 24 rituximab group) at the 25% quartile (75% free of arthritis) of the cumulative arthritis-free survival. Explorative analysis of disease-related biomarkers was performed in subgroups to better understand the mechanisms of the observed delay of clinical disease onset.
Results: Baseline levels of ESR (mm/h; HR 1.03; p=0.016), the total number of B cells in peripheral blood (HR 1.48; p=0.047), the presence of anti-alpha-enolase 1 (anti-CEP1) antibodies (HR 3.71; p=0.004) and the percentage of regulatory B cells (HR 1.04; p=0.002) were related to arthritis development over time. Importantly, genetic analysis of 100 RA associated SNPs showed that the top SNP associated with arthritis development in the rituximab-treated group (OR=7, MAF in cases 60% compared to 17% in unaffected) was in the PLCL2 gene, described to play a role in B cell signaling[1]. In individuals treated with rituximab, B cell numbers and subtypes mainly of the memory and regulatory compartment as well as serum levels of IgM-RF ($p<0.0001$), IgA-RF (p=0.003), total IgM (p=0.001), and anti-CCP (p=0.035) showed statistically significant changes over time compared to individuals who received placebo. Exploratory analysis showed trends for multiple biomarkers in the B cell compartment that appeared predictive of the development of arthritis.
Conclusions: A single infusion of 1000 mg rituximab significantly affects B cell numbers and subsets of memory and regulatory B cells as well as a reduction of disease-related antibodies and immunoglobulin levels in individuals at risk of RA. The changes coincide with a decrease in risk and a delay in development of arthritis in this population. PLCL2 gene polymorphism was associated with arthritis development in rituximab-treated individuals.
References:
[1] Takenaka K, Fukami K, Otsuki M, Nakamura Y, Kataoka Y, Wada M, Tsuji K, Nishikawa S, Yoshida N, Takenawa T. Role of phospholipase C-L2, a novel phospholipase C-like protein that lacks lipase activity, in B-cell receptor signaling. Mol Cell Biol. 2003 Oct;23(20):7329–38.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5650

SAT0038 SERUM B LYMPHOCYTE CHEMOATTRACTANT PROTEIN 13 (CXCL 13) AND MUSCULOSKELETAL ULTRASONOGRAPHIC FINDINGS IN EARLY RHEUMATOID ARTHRITIS

E. Baraka, S. Egila, G. Hamad, M. Khalil. *Rheumatology, Rehabilitation and Physical medicine, Benha Faculty of Medicine, Benha University., Cairo, Egypt*

Background: Patients in clinical remission may continue to have synovitis detected by the musculo skeletal ultrasonography (MSUS).Recently,B-lymphocyte chemoattractant chemokine (CXCL13) has reported to be upregulated and risen to be a possible new marker of disease inflammation in RA
Objectives: to detect early synovitis by grey scale and power Doppler MSUS, measure serum levels of CXCL13 and to correlate these levels with both clinical and ultrasonographic disease activity in early RA patients
Methods: RA was assessed by the modified disease activity score (DAS28).Hands and feet plain radiography were evaluated by Laresn score. A semi-quantitative score (0–3) was used to score synovial effusion (SE), synovial proliferation (SP) and power Doppler (PD) signals by MSUS in 6 synovial sites in 3 joints bilaterally: wrist (dorsal radiocarpal recess). 2nd MCPJ (dorsal and palmar side) and knee (suprapatellar recess) according to the European Leauge Against Rheumatism guidelines. A total MSUS score is the sum of scores for SE, SP and PD signals of the six joints in each patient (0–54).Quantitative detection of serum (CXCL13) levels of all subjects was done by ELISA.
Results: The mean serum CXCL13 values were highly significantly higher in fifty RA patients than in 30 age and sex matched control subjects with a mean of (388.86±283.63 pg/ml) and (62.96±32.5 pg/ml) respectively ($p<0.001$) and were significantly positively correlated with morning stiffness durations ($p<0.001$), Tender Joint Counts ($p<0.001$), Swollen Joint Counts ($p<0.001$), VASs ($p<0.001$), ESR 1st h values ($p<0.001$) and the platelets count ($p<0.05$), negatively correlated with disease durations ($p<0.05$) and HB concentrations ($p<0.05$) and showed no differences according to presence of extra-articular manifestations or CRP, RF or ACCP seropositivity.($p>0.05$). In our RA patients' group, MSUS detected either synovial effusion and /or synovial hypertrophy with or without PD signal in 132 (65%) joints out of 203 clinically silent joints and and detected erosions in 93/300 joints (31%) compared to 27/300 joints (9%) detected by x ray.the serum CXCL13 levels were highly significantly positively correlated with the total MSUS score for each patient ($p<0.001$),SP and SE gradings ($p<0.001$) and ($p<0.05$) and were significantly higher in RA patients with MSUS detected erosions but were not correlated with either PD gradings (p=0.11) or Larsen scores ($p>0.05$).
Conclusions: MSUS is more sensitive than clinical assessment and conventional radiology in detecting synovitis and erosions in RA. Serum CXCL13 levels correlated with MSUS and DAS 28 scores and can be used as a marker for activity and severity of RA.Screening early RA patients by MSUS for more precise evaluation of synovitis activity, severity and better management of the disease and follow up patients to detect if elevated CXCL13 affect RA disease progression or patient disability are recommended.
References:
[1] Naredo E, Valor L, De la Torre I, Martinez-Barrio J, Hinojosa M, Aramburu F, et al., (2013): Ultrasound joint inflammation in rheumatoid arthritis in clinical remission: how many and which joints should be assessed? Arthritis Care Res.;65.
[2] Perricone C, Ceccarelli F, Modesti M, Vavala C, Di Franco M, Valesini G, et al., (2012): The 6-joint ultrasonographic assessment: a valid, sensitive-to-change and feasible method for evaluating joint inflammation in RA. Rheumatology; 51(5):866–73.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1316

SAT0039 LARGE TENDER JOINTS HAVE THE GREATEST IMPACT ON LONGITUDINAL TRAJECTORIES OF FUNCTION IN EARLY RHEUMATOID ARTHRITIS

S.H.L. Lim[1], O. Schieir[2], S. Bartlett[3], G. Boire[4], B. Haraoui[5], E. Keystone[2], D. Tin[6], C. Thorne[6], J. Pope[7], V. Bykerk[8], C. Hitchon[1] on behalf of Canadian Early Arthritis Cohort Canada (CATCH) Investigators. *[1]University of Manitoba, Winnipeg; [2]University of Toronto, Toronto; [3]McGill University, Montreal; [4]Universite de Sherbrooke, Sherbrooke; [5]Institut de Rhumatologie de Montreal, Montreal; [6]Southlake Regional Health Center, Newmarket; [7]Western University, London, Canada; [8]Hospital for Special Surgery, New York, United States*

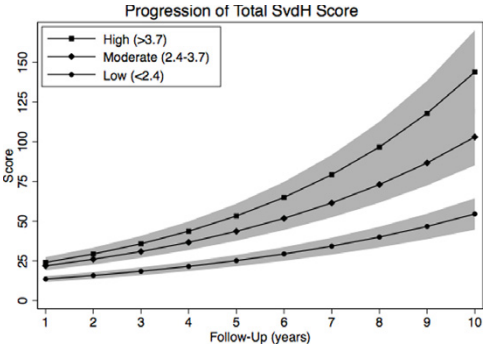
Background: Physical function remains suboptimal in patients with early rheumatoid arthritis (ERA) despite adequate disease control. Hence, factors impacting function need further evaluation. Large weight bearing joints are more likely to impact overall function than small non-weight bearing joints although the magnitude of impact may be task dependent. By weighting large joints more than small joints, the Lansbury Articular Index (LAI) may have stronger associations with function than standard joint counts that give equal weight to small and large joints.
Objectives: 1) To compare the correlations of weighted and non-weighted arthritis joint measures with physical function over time; and 2) to determine the impact of large compared to small joint involvement on the trajectory of HAQ in ERA.
Methods: ERA participants had <1 year symptom duration at enrolment in a multicentre Early Arthritis Cohort and were followed prospectively. Arthritis activity measures (DAS28, tender 28 joint count (TJC28), swollen 28 joint count (SJC28), function (Health Assessment Questionnaire; HAQ) were captured at each visit. The LAI weighted 28 joint count (LT28) and swollen joint count (LS28) were calculated based on the standard 28 joint sites. Correlations of trajectories were calculated using joint modeling for each of the following: DAS28, TJC28,SJC28,LS28 LT28 with the HAQ (2 trajectories/model). Unadjusted effects of large joints (shoulders, elbows, hips knees, ankles) and hand joints (time-varying) on the HAQ trajectory were estimated with a series of generalized estimating equations (GEE). GEE models were adjusted for baseline age, sex and education.
Results: ERA subjects (n=2125, 73% female; baseline mean (SD) age 53 (15) years, DAS28 5.1 (1.4)), were followed for median (IQR) 24 (10,48) months. At their last visit 44% were in remission ($DAS28<2.6$). HAQ over time was highly correlated with the following: DAS28 (r=0.83), LT28 (r=0.83), and TJC28 (r=0.85) and moderately with the LS28 (r=0.59) and SJC28 (r=0.61) trajectories. Each increase in joint involvement was associated with increase in HAQ: large tender joint (0.110 (95% CI 0.102–0.116)); large swollen joint (0.109 (0.099–0.120)); tender hand joint (0.036 (0.032–0.039)); swollen hand joint (0.035 (0.032–0.039)).

In multivariable modeling, after adjusting for age, sex, and education, large joints had greater effects (tender 0.074 (0.065–0.084), swollen 0.027 (0.014–0.04)) on HAQ than hand joints (tender 0.013 (0.009–0.017), swollen 0.008 (0.003–0.013)).
Conclusions: Both Lansbury and standard joint count trajectories correlate similarly with HAQ in ERA. The weighting of large joints in LAI was insufficient to reflect the full impact of large joint involvement in ERA probably because HAQ questions emphasize large joint activities. The effects of large joint swelling may be under recognized due to difficulty in measuring hip, shoulder or elbow swelling. Overall, tender joints had a greater impact on function than swollen joints and large tender joints had the most impact on function.
Disclosure of Interest: S. H. L. Lim: None declared, O. Schieir: None declared, S. Bartlett Consultant for: Pfizer UCB, G. Boire: None declared, B. Haraoui Grant/research support from: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Eli Lilly Janssen, Merck, Pfizer, Roche and UCB, Speakers bureau: Amgen,BMS Janssen, Pfizer and UCB, E. Keystone Grant/research support from: Abbott Laboratories, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb, F.Hoffmann-La Roche Inc, Janssen Inc, Lilly Pharmaceuticals, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, UCB, Consultant for: Abbott Laboratories, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Crescendo Bioscience, F Hoffmann-La Roche Inc, Genentech Inc, Janssen Inc, Lilly Pharmaceuticals,Merck, Pfizer Pharmaceuticals, UCB, Speakers bureau: Abbott Laboratories, AstraZeneca LP, Bristol-Myers Squibb Canada, F Hoffmann-La Roche Inc, Janssen Inc, Pfizer Pharmaceuticals, UCB,Amgen, D. Tin: None declared, C. Thorne Grant/research support from: AbbVie, Amgen, Celgene, CareBiodam, Lilly, Norvartis, Pfizer, Sanofi, UCB, Consultant for: AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, UCB, Speakers bureau: Medexus/MEdac, J. Pope Grant/research support from: Amgen, BMS, Pfizer, Roche, UCB, Consultant for: AbbVie, Actelion, Amgen, Bayer, BMS, Genzyme, Hospira, Lilly, Merck, Norvartis, Pfizer, Regeneron, Roche, Sandofi, UCB, V. Bykerk Shareholder of: Biogen (family), Consultant for: Abbvie, Pfizer, Genenech/Roche, Regeneron, BMS, UCB, Employee of: Biogen (family), C. Hitchon Grant/research support from: UCB
DOI: 10.1136/annrheumdis-2017-eular.3328

SAT0040 ASSESSING 5-YEAR RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS WITH MODERATE DISEASE: FINDINGS FROM A UK MULTI-CENTRE PROSPECTIVE OBSERVATIONAL STUDY

L. Carpenter[1], S. Norton[2], E. Nikiphorou[3], K. Jayakumar[4], D.F. McWilliams[5], J. Dixey[6], P. Kiely[7], D.A. Walsh[5], A. Young[4] on behalf of ERAS and ERAN. *[1]Life and Medical Sciences, University of Hertfordshire; [2]Psychology Department, Institute of Psychiatry; [3]Department of Rheumatology, Whittington Hospital NHS Trust, London; [4]Department of Rheumatology, St Albans City Hospital, St Albans; [5]Arthritis UK Pain Centre, University of Nottingham, Nottingham; [6]Department of Rheumatology, New Cross Hospital, Wolverhampton; [7]Department of Rheumatology, St Georges University Hospitals NHS Foundation Trust, London, United Kingdom*

Background: Early, intensive treatment to achieve remission, or at least low disease target (Treat-to-Target, T2T), is advocated to prevent and/or reduce structural joint damage and disability in early Rheumatoid Arthritis (RA). A recent study shows how patients with moderate disease exhibit similar rates of functional disability and orthopaedic surgical interventions to those patients with high disease[1]. To our knowledge, no study has looked at longitudinal observational data to investigate the progression of structural joint damage in these patient sub-groups.
Objectives: To investigate the long-term progression of radiographic joint damage in patients with sustained moderate disease activity.
Methods: Demographic, clinical, laboratory and radiographic data from the Early Rheumatoid Arthritis Study (ERAS) was available for 1,465 patients. Radiographic damage was scored using the modified Sharp/van der Heijde (SvdH) method. The original three variable 44 joint count Disease Activity Score (DAS-44) was used. Mean DAS-44 over the first 5 years was estimated for patients with at least two DAS-44 scores. Patients were stratified based on EULARs thresholds of low ($<$2.4), moderate (2.4–3.7) and high ($>$3.7) disease. Mixed-effects negative binomial regression modelled patients' radiographic progression over 5 years, whilst controlling for key confounders, including age at onset, sex, rheumatoid factor status and baseline functional disability.
Results: A total of 1,110 patients with 3,751 observations over the 5 year period (mean =3.4 observations per patient) were analysed. 396 (36%), 363 (33%) and 351 (32%) patients were classified in the low, moderate and high DAS-44 groups respectively. The low group had lower SvdH scores at 1 year compared to the moderate group (12.9 vs. 19.2, $p<0.001$). Furthermore, the low group also experienced half the annual rate of change over the 5 years compared to the moderate group (3.6 vs. 7.4, p=0.002). In contrast, the high group had similar SvdH scores at year 1 compared the moderate group (20.4 vs. 19.2, p=0.884), but increased annual progression over the 5 years (10.0 vs. 7.4, p=0.010). Despite the increased annual progression rate, the difference in SvdH scores between the moderate and high groups remained non-significant at 5 years.
Conclusions: Sustained moderate disease over the first five years of RA indicates similar levels of radiographic progression compared to sustained high disease.



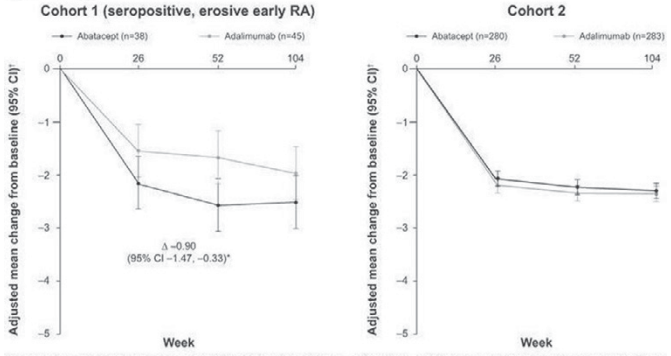
This study provides support on the importance of tight treatment control with early and aggressive therapy according to T2T principles. Preventing sustained moderate disease activity states can help reduce radiographic progression and consequently joint destruction, minimising the risk of disability in the long-term.
References:
[1] Nikiphorou, E. et al. Association between rheumatoid arthritis disease activity, progression of functional limitation and long-term risk of orthopaedic surgery: combined analysis of two prospective cohorts supports EULAR treat to target DAS thresholds. Ann. Rheum. Dis. annrheumdis–2015–208669 (2016).
Disclosure of Interest: L. Carpenter Grant/research support from: NIHR Programme Grant, S. Norton: None declared, E. Nikiphorou: None declared, K. Jayakumar: None declared, D. McWilliams: None declared, J. Dixey: None declared, P. Kiely: None declared, D. Walsh: None declared, A. Young: None declared
DOI: 10.1136/annrheumdis-2017-eular.3893

SAT0041 EFFICACY OF ABATACEPT VERSUS ADALIMUMAB IN PATIENTS WITH SEROPOSITIVE, EROSIVE EARLY RA: ANALYSIS OF A RANDOMIZED CONTROLLED CLINICAL TRIAL (AMPLE)

R. Fleischmann[1], M. Weinblatt[2], H. Ahmad[3], M. Maldonado[3], E. Alemao[3], J. Ye[3], M. Schiff[4]. *[1]University of Texas Southwestern Medical Center, Dallas; [2]Brigham and Women's Hospital, Boston; [3]Bristol-Myers Squibb, Princeton; [4]University of Colorado, Denver, United States*

Background: Patients (pts) who are anti-citrullinated protein antibody (ACPA) positive tend to develop more severe erosive disease than ACPA-negative pts.[1] The presence of seropositivity and erosions have been noted in EULAR treatment guidelines as poor prognostic factors to identify pts with RA who require early and aggressive clinical intervention.[2] Since the disease in pts with seropositive, erosive early RA is mostly driven by immunological features, response to RA therapy may vary based on therapeutic mechanism of action (MOA).
Objectives: To investigate the efficacy of abatacept (ABA) vs adalimumab (ADA) in pts with seropositive, erosive early RA.
Methods: AMPLE (NCT00929864)[3] was a 2-year, Phase IIIb study in which biologic-naïve pts with RA were randomized 1:1 to either SC ABA 125 mg weekly or SC ADA 40 mg biweekly, both with background MTX. This *post hoc* analysis of AMPLE compared clinical outcomes between treatment groups in a subpopulation of pts with specified baseline criteria: disease duration $\leq$6 months, RF or ACPA seropositivity and $>$1 radiographic erosion. Disease activity and patient-reported outcomes were evaluated at Weeks 26, 52 and 104. Endpoints were compared between ABA and ADA groups using chi-square test for categorical variables, analysis of covariance model (ANCOVA) controlling for baseline covariates and DAS28 (CRP) stratification for continuous variables.
Results: Of 318 and 328 pts in the ABA and ADA groups, respectively, 38 and 45 pts had all specified baseline characteristics (Cohort 1) and 280 and 283 pts had an absence of at least 1 of the specified characteristics (Cohort 2). Overall, the baseline characteristics, including anti-cyclic citrullinated peptide titres, were well balanced between the groups, with the exception of weight. For Cohort 1, adjusted mean change (95% CI) from baseline DAS28 (CRP) with ABA vs ADA was –2.18 (–2.61, –1.75) vs –1.56 (–2.01, –1.11) at Week 26, –2.58 (–2.99, –2.17) vs –1.68 (–2.10, –1.25) at Week 52 and –2.50 (–2.97, –2.03) vs –2.0 (–2.49, –1.50) at Week 104. Similar trends of increased efficacy with ABA vs ADA were observed for changes from baseline CDAI, SDAI, HAQ-DI, pain and fatigue; no differences in radiographic progression were observed. For Cohort 2, no differences in clinical outcomes between ABA and ADA groups were observed. Given the differences in baseline weight between ABA and ADA groups in Cohort 1, sensitivity analyses that excluded pts $>$100 kg and adjusted for baseline weight were performed and demonstrated minimal effect of weight on treatment efficacy.
Conclusions: This *post hoc* analysis seems to indicate a trend of increased efficacy for abatacept in pts with seropositive, erosive early RA compared with the TNF inhibitor adalimumab. Given the small sample size, additional pre-specified randomized studies are needed to compare the benefit of biologic DMARDs with different MOAs in pts with early, rapidly progressing RA.
References:
[1] Combe B, et al. Ann Rheum Dis 2016 Dec 15. doi: 10.1136/annrheumdis-2016–210602.

Figure. Adjusted Mean Change from Baseline in DAS28 (CRP) at Weeks 26, 52 and 104 by Patient Type



*Adjusted mean change from baseline at Day 365 (−2.58 [−2.99, −2.17] vs −1.68 [−2.10, −1.25]) for abatacept ERP vs adalimumab ERP patients
†Adjustment based on ANCOVA model with treatment as factor and baseline values, DAS28 (CRP) stratification as covariates
For 95% CI within each group, normal approximation was used if n>5, otherwise exact method was used
ERP=early rapidly progressing

[2] Aletaha D, et al. Arthritis Rheum 2010;62:2569–81.
[3] Weinblatt M, et al. Arthritis Rheum 2013;65:28–38.
Disclosure of Interest: R. Fleischmann Grant/research support from: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Roche, sanofi-aventis, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer, Roche, sanofi-aventis, UCB, M. Weinblatt Grant/research support from: Amgen, Bristol-Myers Squibb, Crescendo Bioscience, UCB, DxTerity, Consultant for: Amgen, Bristol-Myers Squibb, Crescendo Bioscience, UCB, AbbVie, Lilly, Pfizer, Roche, H. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Maldonado Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, J. Ye Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Schiff Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, JNJ, UCB, Speakers bureau: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.3521

SAT0042 SEVERITY OF RADIOGRAPHIC DESTRUCTION ON PERIPHERAL JOINTS IS A STRONG INDEPENDENT RISK FACTOR FOR CAROTID ATHEROSCLEROSIS

J.S. Eun, E.S. Lee, J.W. Kang, J.H. Kim, J.Y. Kang, G.B. Bae, N.R. Kim, S.J. Lee, E.J. Nam, Y.M. Kang. *Kyungpook National University School of Medicine, Daegu, Korea, Republic Of*

Background: In our previous study, we identified that cumulative inflammatory burdern contributes to the development of carotid atherosclerosis through a synergistic interaction with conventional cardiovascular (CV) risk factors in patients with rheumatoid arthritis (RA). However, it is controversial whether the presence of joint destruction which result from inflammatory burden may be a risk factor for carotid atherosclerosis.
Objectives: To investigate whether intima-media thickness (IMT) and plaques of carotid artery are influenced by radiographic joint destruction in patients with RA.
Methods: A total of 186 patients with RA were included in the present study. Plain X-ray of joints were used to assess the severity of joint destruction. We developed a new radiographic scoring system, named Rheumatoid Arthritis-Radiographic Severity Score (RA-RSS), which scores 21 joint groups with the modified Steinbrocker method. The following joint groups were included: 2 proximal interphalangeal (PIP) joint group, 2 metacarpophalangeal (MCP) joint group, 2 wrist joint group, 2 elbow joint group, 2 shoulder joint group, 1 atlantoaxial joint group, 2 hip joint group, 2 knee joint group, 2 ankle joint group, 2 tarsometatarsal (TMT) joint group, and 2 metatarsophalangeal (MTP) joint group. The grade was determined by the worst changes in each joint group of PIP, MCP, TMT, and MTP joints. RA-RSS grades are assigned as follows: 0 = No radiographic changes; 1 = mild destruction of bone and cartilage; 2 = moderate destruction of bone and cartilage or joint deformities; 3 = Severe destruction of bone and cartilage or bony ankylosis (Score ranges from 0–63). We performed carotid ultrasound to detect the presence of carotid atherosclerosis.
Results: Among 186 patients who were graded using RA-RSS, 110 patients had carotid plaques (59.1%). RA-RSS was significantly higher in patients with plaques compared to patients without plaques (11.2±8.79 vs. 7.6±7.72, p=0.004). Patients were divided into two groups by the cut-off value of plaque development as determined using receiver operating characteristic (ROC) curves: 115 (61.8%) patients with RA-RSS $<$10 and 71 (38.2%) with RA-RSS $\geq$10. There was a significant difference between the groups with respect to the presence of plaques (48.7% vs. 76.1%, $p<0.001$), while there was no difference in mean carotid IMT (0.87±0.19 vs. 0.88±0.14, p=0.684). The mean age, the presence of conventional CV risk factors, Korean version of the modified HAQ (mKHAQ), DAS28-ESR, and RA-RSS $\geq$10 were significantly associated with plaque development. Multivariate logistic regression analysis showed that RA-RSS $\geq$10 (OR 2.94 [95% CI 1.48–5.84]) and the presence of conventional CV risk factors (OR 2.30 [95% CI 1.21–4.35]) were independent risk factors for plaque development.
Conclusions: The present study shows that radiographic destruction over peripheral joints, which directly reflects cumulative inflammatory burden, is a strong independent risk factor for plaque development that is associated with CV events and mortality.
References:
[1] Churl Hyun Im, et al. Inflammatory burden interacts with conventional cardiovascular risk factors for carotid plaque formation in rheumatoid arthritis. Rheumatology (Oxford). 2015 May;54(5):808–15.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5985

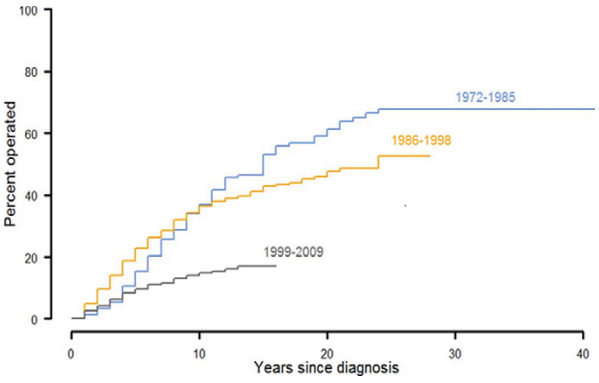
SAT0043 FACTORS AFFECTING THE NEED FOR ORTHOPAEDIC SURGERY IN PATIENTS WITH RHEUMATOID ARTHRITIS. RESULTS FROM 1010 PATIENTS DIAGNOSED WITH RA FROM 1972-2009

B.-T.S. Fevang[1,2], A.M. Fenstad[3], O.N. Furnes[3,4], T.W. Nystad[1,3]. *[1]Dept. of Rheumatology, Haukeland University Hospital; [2]Dept. of Clinical Sciences, University of Bergen; [3]The Norwegian Arthroplasty Register, Haukeland University Hospital; [4]Department of Surgical Sciences, University of Bergen, Bergen, Norway*

Background: Surgery still comprises a necessary part of treating RA patients, when medication fail to prevent joint destruction. Orthopaedic corrective procedures are considered a reliable and objective proxy for a destructed joint, and is an important outcome measure in RA.
Objectives: To investigate how patient characteristics, time of diagnosis and treatment affect the need for orthopaedic surgery in patients with rheumatoid arthritis (RA).
Methods: We reviewed the medical history of 1544 patients diagnosed with RA at Haukeland University Hospital in Bergen, Norway from 1972 to 2009, of which 1010 (mean age 57, 69% women) were included in the study. Relevant orthopaedic procedures were obtained from the Norwegian Arthroplasty Register and the hospital's administrative patient records. 693 procedures (joint synovectomies 22%, arthrodeses 21%, prostheses 41% and forefoot procedures 12%) were performed in 315 patients. Survival analyses were completed to evaluate the impact of age, sex, radiographic changes and year of diagnosis, on the risk of undergoing surgery.
Results: Patients diagnosed in 1972–1985 and 1986–1998 had a relative risk (RR) of 2.4 and 2.2 ($p<0.001$) respectively, of surgery compared to patients diagnosed in 1999–2009. Radiographic changes at diagnosis and female sex were also significant risk factors. Disease activity at baseline did not affect the outcome. Anti-rheumatic medication was significantly different in the three time periods.

Variable category	5 years[a]	10 years[a]	RR	95% CI	p-value
Gender, male	13	22	1		
female	19	30	1.35	1.02–1.77	0.035
Age (years)					
<69	15	27	1		
≥70	22	31	1.04	0.77–1.42	0.78
Radiolographic changes at diagnosis					
No arthritis	12	21	1		
Possible arthritis, or MR findings only	19	26	1.01	0.66–1.57	0.92
Arthritis	23	34	1.46	1.10–1.94	0.008
Osteoarthritis	35	55	2.81	1.94–4.05	<0.001
Time period					
1999–2009	12	18	1		
1986–1998	25	38	2.16	1.62–2.87	<0.001
1972–1985	15	37	2.38	1.71–3.31	<0.001

[a]5- and 10-year survival, in percent.



Conclusions: Patients with early years of diagnosis had greatly increased risk of having an RA related procedure performed. This is probably due to the year of diagnosis being a proxy for the type and intensity of medical treatment.
References:
[1] Goodman SM. Rheumatoid Arthritis Therapy and Joint-replacement Surgery: Are We Making a Difference? J Rheumatol. 2016;43:833–5.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2961

SAT0044 A 10-YEAR FOLLOW UP STUDY OF EARLY SERONEGATIVE ARTHRITIS DIAGNOSED AT AN ADULT AGE

K. Paalanen, J. Asikainen, T. Rannio, P. Hannonen, T. Sokka. *Rheumatology Department, KSSHP, JyväskylÄ, Finland*

Background: Up to 20–30% of patients enrolled into RA cohorts and clinical trials are seronegative. However, in studies examining predictors, prognosis, and response to treatment, seropositive and seronegative groups of patients seem to behave differently. Only a few studies have focused on the long term follow up of seronegative arthritis.
Objectives: To investigate long-term outcomes of patients with seronegative arthritis during a 10-year follow-up period including clinical outcomes and reclassification of diagnosis when applicable.
Methods: A total of 1046 patients were classified as early RA in 1997–2005 at single rheumatology center and scheduled for a ten year follow-up, including 434 seronegative patients who are subjects of the present analysis. Follow-up examinations were carried out for at least 2 years and then at 5 and 10 years by the treating specialist including complete clinical examination and patient reported outcomes. In addition, case –reviews were performed, with re-classification of the cases when applicable
Results: Among the 434 seronegative patients (69,4% women, mean age 58), 271 subjects were seen for the 10 year visit with the mean disease activity DAS28 of 2,3 (SD 1,02) and the mean HAQ of 0,71 (SD 0,72). Out of the remaining 146 patients, 88 had died and 53 did not attend the 10-year visit due to altered diagnosis, refusal or comorbidity. Five patients had dropped out and files of 17 patients were missing. During the follow-up of 10 years, 12/434 (2,7%) patients could be classified as seropositive or erosive RA: 4 turned seropositive (2 for ACPA and 2 for RF [>2x normal level]) and 8 developed erosions typical for RA. Reclassification revealed 70 (16,1%) cases of polymyalgia rheumatica, 47 (10,8%) cases of osteoarthrosis without evidence of inflammatory disease, 47 (10,8%) cases of psoriatic arthritis, 39 (9,0%) cases of spondylarthritis and 16 (3,7%) cases of plausible reactive arthritis. Few cases were reclassified as gout (11 cases (2,5%)) and pseudogout (3 cases (0,7%)). Also paraneoplastic arthritis (6 cases (1,4%)), juvenile arthritis (5 cases (1,2%)), hemochromatosis (2 cases (0,5%)), ankylosing spondylitis (2 cases (0,5%)) and temporal arteritis (2 cases (0,5%)) were revealed during follow up. One case of each reflex sympathetic dystrophy, trauma-induced arthritis, meniscal injury, optional Nasu Hakola disease, microscopic polyangiitis (MPA), granulomatous polyangiitis (GPA), antisynthetase syndrome and colitis ulcerosa were also found. The remaining 147 patient (33,8%) could not be reclassified in any clear cut diagnosis. A total of 44 of these undifferentiated cases had transient arthritis, 43 cases had features of seronegative spondylarthritis and 57 cases remained totally unspecified, while three patients had features of inflammatory connective tissue disease (SLE and Sjögren's syndrome), but they did not meet available classification criteria. In addition, files of 17 (3,9%) patients were missing from the analyses.
Conclusions: Over a 10-year period, 97% of seronegative patients remained seronegative and did not develop RA-like erosions. Reclassification revealed significant heterogeneity in the diagnosis of seronegative RA. Therefore, seronegative arthritis should not be studied as a homogenous disease entity.
References:
[1] Padyukov, Arthritis Rheum 2004, 50: 3085–3092.
[2] van Dongen, Arthritis Rheum 2007, 56: 1424–1432.
[3] Jantti, Clin Rheumatol 2002, 21: 353–356.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2332

SAT0045 11 YEARS' FOLLOW-UP OF A DANISH 2-YEAR TREAT-TO-TARGET RANDOMIZED CONTROLLED TRIAL IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: BASELINE PREDICTORS OF FUNCTIONAL AND RADIOGRAPHIC OUTCOMES

M.L. Hetland[1,2], K. Stengaard-Petersen[3], P. Junker[4], H. Lindegaard[4], T. Ellingsen[4], J. Pødenphant[5], H. Skjødt[6], A. Vestergaard[7], B. Ejbjerg[8], S. Jacobsen[9], N.S. Krogh[10], M. Østergaard[2], K. Hørslev-Petersen[11]. *[1]DANBIO; [2]COPECARE, Rigshospitalet, Glostrup; [3]Department of Rheumatology, University Hospital, Aarhus; [4]Department of Rheumatology, University Hospital, Odense; [5]Department of Rheumatology, Gentofte Hospital, Gentofte; [6]Department of Rheumatology, Rigshospitalet, Glostrup; [7]Department of Radiology, Hvidovre Hospital, Hvidovre; [8]Department of Rheumatology, Slagelse Hospital, Slagelse; [9]Department of Rheumatology, Rigshospitalet; [10]ZiteLab, Copenhagen; [11]Kong Christian X's Gigthospital, Gråsten, Denmark*

Background: Few RCTs have investigated long-term (>10 years (yrs)) outcomes of goal-directed synovitis suppression in early rheumatoid arthritis (RA). The CIMESTRA trial was a 2-year double-blinded Danish multicenter study on aggressive treatment with csDMARDS (methotrexate (MTX) versus MTX and cyclosporine) in combination with intra-articular glucocorticoids (1+2). Disease control after 2 yrs was excellent with ≈50% in remission and halted radiographic progression in both groups. We present 11 yr follow-up data.

Baseline predictors of:			
-Functional status (HAQ_{10}-)*	**Coefficient**	**95% CI**	**p-value**
DAS28 (per unit increase)	0.10	0.02-0.18	0.02
Anti CCP (positive)	0.24	0.02-0.46	0.03
-Radiographic progression (ΔTSS_{0-10}-)*	**Coefficient**	**95% CI**	**p-value**
Anti CCP (positive)	7.69	0.91; 14.47	0.03
MRI bone marrow edema (per unit increase)	0.87	0.19; 1.55	0.01

: Initial baseline variables in the HAQ_{10}- (§) and ΔTSS_{0-10}-(#) multivariable linear models before backward selection were: Total Sharp-van der Heijde-Score (TSS)[§#]; Health Assessment Questionnaire score[§]; Disease Activity Score (28-joint count, 4 variables)[§]; age[§]*; anti CCP[§]*; gender[§]*; MRI erosion score[§]*; MRI synovitis score[§]*; MRI bone marrow edema[§]*. CI, confidence interval; CCP, cyclic citrullinated peptide (dichotomized value); MRI, magnetic resonance imaging.

Objectives: The aims were to 1) investigate the clinical and radiographic status and 2) identify baseline predictors of functional status and erosive progression.
Methods: Of 160 patients (pts) included, 130 pts also had MRI of the wrist performed at baseline. 17 pts had died since baseline. All living pts were contacted and 120 signed informed consent to participate in a 11 yrs' follow-up visit assessing e.g. treatment, disease activity (DAS28, CRP, 4 variables), physical function (HAQ), X-ray of hands and feet. Baseline MRI was scored by OMERACT rheumatoid arthritis MRI scoring (RAMRIS) system, X-rays by Sharp-van der Heijde total Sharp Score (TSS). Multivariable linear regression analyses of a panel of baseline variables (see foot note in table) with backward selection were performed with HAQ at 11 yrs (HAQ_{11}) and radiographic progression since baseline (ΔTSS_{0-11}) as dependent variables.
Results: 120 of 160 pts (75%) completed the 11 yrs visit. 96 pts with available baseline MRI and X-rays of both time points were included in the prediction models. Withdrawal analysis comparing the 160 pts with the 40 and 64 pts who were not included showed similar baseline characteristics except for higher DAS28 and HAQ score for withdrawers. Follow-up was after 11.6 yrs (10.7–12.2) (median (IQR)). Pts were 63 yrs (55–72) and 70% females. 20% received biologics (+/- csDMARD), 53% csDMARD alone, 27% were in drug free remission. DAS28 was 2.0 (1.5–2.6); pain score: 1 cm (0.3–3); pt. global: 1.1 cm (0.2–2.9); swollen joint count (28SJC): 0 (0–0); tender joint count (28TJC): 0 (0–1). 76% of pts were in DAS28 remission; HAQ-score was 0.25 (0–0.75); ΔTSS_{0-11}(median (IQR)):4 (0–13); ΔTSS_{0-11}(mean±SD): 10.9±16.9). The annual progression rate since baseline was median (IQR):0.4 (0–1.1); mean±SD:0.96±1.52. Multivariable linear regression analyses are shown in Table.
Conclusions: 11 years after diagnosis 75% were in DAS28 remission. HAQ-score was low, and mean radiographic progression was <1 TSS unit/year. High DAS28 and positive anti-CCP at baseline were independent predictors of poorer functional status. Baseline MRI bone marrow edema and anti-CCP positivity were independent predictors of radiographic progression.
References:
[1] Arthritis Rheum 2006; 54: 1401–9.
[2] Ann Rheum Dis 2008; 67: 815–22.
Disclosure of Interest: M. L. Hetland Grant/research support from: AbbVie, BMS, MSD, Pfizer, Orion, Novartis, Biogen, Eli Lilly, K. Stengaard-Petersen: None declared, P. Junker: None declared, H. Lindegaard: None declared, T. Ellingsen: None declared, J. Pødenphant: None declared, H. Skjødt: None declared, A. Vestergaard: None declared, B. Ejbjerg: None declared, S. Jacobsen: None declared, N. S. Krogh: None declared, M. Østergaard Grant/research support from: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, K. Hørslev-Petersen: None declared
DOI: 10.1136/annrheumdis-2017-eular.1720

SAT0046 TNF ANTAGONIST DRUG SAFETY ASSESSMENT BY PHARMACOVIGILANCE SIGNALING AND POST-MARKETING ADVERSE EVENT REPORTS

M. Cavaco[1], F. Araujo[2,3], J. Eurico Fonseca[4,5], J. Goncalves[1]. *[1]iMed – Research Institute of Medicines, Faculdade de Farmacia Universidade de Lisboa, Lisboa; [2]Rheumatology Unit, Hospital de Sant'Ana, Cascais; [3]Institute of Microbiology; [4]Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, Lisbon; [5]Rheumatology Department, Centro Hospitalar de Lisboa Norte, EPE, Hospital de Santa Maria, Lisbon Academic Medical Centre, Lisboa, Portugal*

Background: TNF antagonists have been equally effective in the treatment of immunoinflammatory diseases. However, differences in their characteristics and the introduction of biosimilars may be associated with different safety profiles.
Objectives: The main goal of this study is to compare the safety of infliximab (IFX), etanercept (ETN), and adalimumab (ADA), as well as of IFX-biosimilar.
Methods: We assessed the adverse events reported in the EudraVigilance database between 2004 and 2016. The MEdDRA® system was used to classify the adverse events according to the primary system organ class. For a direct

comparison of the data obtained, the adverse events reported for each drug were normalized using the number of treatments for the same period. The reporting odds ratio (ROR) and its 95% confidence intervals (CI) were calculated regarding the different categories of adverse events. The incidence of serious adverse events, serious infections, withdrawals due to adverse events and deaths were also calculated.

Results: The EudraVigilance database contains 851 882 adverse events reported for IFX, ETN, and ADA. During this period, the different TNF antagonists have shown almost the same safety profile. The reported adverse events were classified by systems organ class (SOC) and the most frequent were administration site conditions (28.8%) and infections and infestations (11.2%), Safety was not statistically different. The comparison between IFX originator and its biosimilar did not show statistically significant differences in safety (ROR 1.08 [0.80, 1.46]) during the initial 3-years after launch for both drugs. However, a small non-significant increase in immune reactions during administration was reported for IFX-biosimilar, which might reflect increasing attention for this class of drugs.

Conclusions: The comparison of reference IFX and IFX-biosimilar did not demonstrate statistically significant differences in safety. This pharmacovigilance study provides the first analysis of TNF antagonists from the EudraVigilance database and offers a framework for safety comparison between originators and biosimilar TNF antagonists.

Acknowledgements: We would like to acknowledge Eudravigilance for providing access to the database.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5884

SAT0047 PREDICTING MAINTENANCE OF RESPONSE BASED ON DISEASE CHARACTERISTICS AND EARLY CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS UPON WITHDRAWAL OF ADALIMUMAB

J.S. Smolen[1], P. Emery[2], H. Zhang[3], X. Wang[3], J. Suboticki[3], I. Sainsbury[3], A. Kavanaugh[4]. *[1]Medical Univ of Vienna, Vienna, Austria; [2]Leeds Inst of Rheumatic & Musculoskeletal Medicine, Leeds, United Kingdom; [3]AbbVie, N Chicago, IL; [4]Univ of California, San Diego, CA, United States*

Background: Some patients (pts) with rheumatoid arthritis (RA) achieve low disease activity (LDA) after treatment with adalimumab (ADA) plus methotrexate (MTX) and can maintain LDA after ADA withdrawal[1]. However, others experience a flare in disease activity. The factors associated with loss or maintenance of response are not understood.

Objectives: To identify pt disease characteristics and early clinical responses, which predict maintenance of LDA upon ADA withdrawal in individual RA pts.

Methods: Data from the OPTIMA trial were used in this *post hoc* analysis. In period 1 (P1), pts were treated for 26 weeks (wks) with ADA+MTX or placebo (PBO) +MTX. Pts on ADA+MTX who achieved DAS28-CRP <3.2 at wks 22 and 26 (responders) were randomized to ADA withdrawal, or ADA+MTX continuation up to Wk 78. Responders to PBO+MTX in P1 continued on PBO+MTX up to Wk 78 (PBO continuation). Data from the ADA withdrawal arm were used to predict LDA at Wk 78 by DAS28-CRP (≤3.2) or SDAI (≤11). Potential factors including baseline (BL) disease characteristics and Wk 26 responses, including DAS28-CRP, SDAI, ACR score components, modified total sharp score (mTSS) and joint space narrowing score (JSN), were screened by the LASSO method[2], which performs variable selection by penalizing unduly complicated models, with/without incorporating the speed of DAS28-CRP or SDAI response as an individual predictor. Logistic regression on the LASSO-selected factors yielded coefficients used to derive individual scoring equations and prediction scores for Wk 78 outcomes (fig footnote). Prediction score cutoffs were established by the regression tree method[3]. The results were validated in data from the PBO continuation arm.

Results: For the prediction of DAS28-CRP LDA at Wk 78, BL physician global assessment (PhGA) and health-assessment questionnaire-disability index (HAQ-DI), and Wk 26 DAS28-CRP, HAQ-DI, JSN and CRP were selected by LASSO, and used to calculate the prediction score. Including speed of response did not affect the predictors chosen. Out of 9 pts predicted not to have DAS28-CRP LDA at Wk 78, 0 had LDA (NPV=100%) (fig 1). Out of 66 pts predicted to have DAS28-CRP LDA at Wk 78, 63 predictions were correct (PPV=96.5%). Results were comparable for most cutoff categories in the validation arm (PPV=82%); however, no pts were predicted to have a non-response at Wk 78. For the prediction of SDAI LDA at Wk 78, the NPV was 86% (1/7 predictions incorrect); PPV was 95% (39/41 predictions correct); in the validation arm, the PPV was 82%.

Conclusions: DAS28-CRP LDA at 78 wks could be individually predicted for up to 63% pts in OPTIMA who withdrew ADA/continued PBO+MTX with 96.5% accuracy, based on demographics and clinical outcomes at 6 months. This instrument could help identify pts who may be able to maintain LDA upon ADA withdrawal.

References:

[1] Smolen et al, 2013. Lancet;383.
[2] Tibshirani, R, 1996. J Royal and Stat Society; 58.
[3] Breiman L., et al, 1984. Classification and Regression Trees. Wadsworth.

Acknowledgements: AbbVie: study sponsor, contributed to design, data collection, analysis, interpretation; and writing, reviewing, approval of final version. Medical writing: Naina Barretto of AbbVie.

Disclosure of Interest: J. Smolen Grant/research support from: AbbVie, Consultant for: AbbVie, P. Emery Grant/research support from: from Pfizer, MSD, AbbVie Inc., BMS, UCB, Roche, Novartis, Samsung, Sandoz and Lilly., Consultant for: from Pfizer, MSD, AbbVie Inc., BMS, UCB, Roche, Novartis, Samsung, Sandoz and Lilly., H. Zhang Employee of: AbbVie, X. Wang Employee of: AbbVie, J. Suboticki Employee of: AbbVie, I. Sainsbury Employee of: AbbVie, A. Kavanaugh Grant/research support from: AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB., Consultant for: AbbVie Inc., Amgen, Astra-Zeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB.

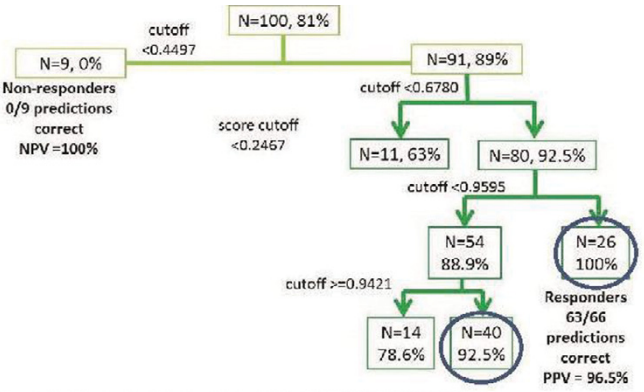


Figure 1: Regression tree to predict Week 78 DAS28-CRP LDA. The percentages of patients with an LDA response at Week 78 are indicated in the boxes. The encircled boxes indicate the patients predicted to have LDA at Week 78.

Individual scoring equation for reaching Week 78 DAS28_LDA: Logit = 6.717 – 0.212*HAQ – 0.039 * PhGA – 0.004 *DAS28_WK26 – 1.393*HAQ_WK26 - 0.027*JSN - 0.292*CRP_WK26

For reaching Week 78 SDAI LDA: Logit = 4.668 – 0.028 * PhGA – 0.161*CRP_WK26 – 1.411*RoW_indicator; RoW = rest of the world, including Argentina, Australia, New Zealand, South Africa

Individual prediction score: $\frac{\exp(logit)}{1+\exp(logit)}$.

DOI: 10.1136/annrheumdis-2017-eular.2503

SAT0048 THE PATTERN OF ACPA REACTIVITIES IN ANTI-CCP POSITIVE INDIVIDUALS WITH NON-SPECIFIC MUSCULOSKELETAL SYMPTOMS AT RISK OF DEVELOPING RA

A. Hensvold[1], Y. Kisten[1,1], V. Joshua[1], M. Hansson[1], L. Mathsson-Alm[2], A. Karlsson[1], H. Rezaei[1], E. af Klint[1], G. Fei[1], A. Catrina[1]. *[1]Karolinska University Hospital and Karolinska Institutet, Stockholm; [2]ThermoFisher Scientific, Uppsala, Sweden*

Background: There is today a paucity of prospective studies to describe the natural longitudinal history of anti-ccp positive individuals developing RA or not developing RA. Further no study to investigate the detailed ACPA reactivities in such a setting is currently available.

Methods: Individuals at risk of developing RA were included in a cohort at Karolinska University Hospital, Stockholm. Examinations of peripheral joints was repeated at one year follow-up visit or at any time the patients experienced worsening of their symptoms. Peripheral blood samples were available at inclusion (n=70). Serum was run on a microarray based on the ImmuoCAP ISAC system testing for ACPA reactivities toward 13 different citrullinated peptides (fillagrin, fibrinogen, alpha-enolase, vimentin, histone) (1).

Results: Individuals referred from primary care with musculoskeletal complaints and positive anti-ccp test were systematically investigated as part of routine care at our rheumatology clinic. Individuals lacking self-reported history of suspect arthritis, clinical arthritis according to rheumatologist and signs of synovitis on ultrasound examination were included in a clinical Risk-RA program with life-style coaching and personalized information on the risk of developing RA. Seventy individuals, with a mean age of 48 years (SD 15) and 86% females, were included in the program. Twenty (29%) individuals developed arthritis during a medium follow up time of 7 months (range 1–25 months).

Number of ACPA reactivities at baseline was significant higher among those developing (in mean 6 reactivities) as compared to those not developing arthritis (in mean 4 reactivities). A increased proportion of individuals were showing reactivity towards citrullinated (cit) vimentin (vim) 60–75, fibrinogen (fib) 573 and enolase (eno) (CEP-1) among those developing arthritis (80% for anti-cit-vim 45% for anti-cit-fib and 60% for anti-cit eno) as compared to those not developing arthritis (41% for anti-cit-vim, 30% for anti-cit-fib and 52% for anti-cit-eno). Increased level of anti-cit-vim and anti-cit-eno antibodies was also observed at inclusion for those individuals developing arthritis as compared to those not developing arthritis.

Conclusions: We describe here the pattern of ACPA reactivities in anti-CCP positive individuals with non-specific musculoskeletal symptoms at risk of developing RA and without clinical and ultrasonograph signs of synovitis and report that 30% of these patients will develop arthritis during a short follow-up. Number, frequency and titers of specific ACPA reactivities appear to be enriched already at inclusion among those patients that developed arthritis during follow-up.

References:

[1] Hansson et al Arthritis Res Ther 2012.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6909

SAT0049 21ST CENTURY STATE OF RHEUMATOID ARTHRITIS MANAGEMENT IN THE UK

A.L. Tan[1], M. Buch[1], D. O'Reilly[2], T. Sheeran[3], A. Bishop-Bailey[4], G. Nock[4], S. Chitale[5], P. Emery[1]. *[1]NIHR Leeds Musculoskeletal Biomedical Research Unit, Chapel Allerton Hospital, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds; [2]West Suffolk NHS Foundation Trust, West Suffolk Hospital, Bury Saint Edmunds; [3]Rheumatology, Cannock Chase Hospital, Royal Wolverhampton Trust, Cannock; [4]pH Associates, pH Associates, Marlow; [5]Rheumatology, Peter Maddison Rheumatology Centre, North Wales, Llandudno, United Kingdom*

Background: The rheumatoid arthritis (RA) Treat to Target (T2T) recommendations[1] defined in 2010 aimed to support clinicians to achieve optimal therapeutic outcomes for their patients.
Objectives: 38 hospitals prospectively audited management of newly diagnosed RA patients to determine compliance with the T2T recommendations and therapeutic outcomes achieved.
Methods: From April 2012 to September 2016 and upon diagnosis of RA, data on disease history, management and clinical outcomes were collected prospectively in a web based tool. Follow up to date provides data for up to 24 months from diagnosis (baseline).
Results: 1571 patients were recruited in 38 centres, with 12 months' follow up for 713 patients and of these 269 also had 24 months' follow up. 1021 (65%) patients were female and 1360 (87%) had a treatment target documented at baseline (1235 [79%] disease activity score 28 (DAS28) remission and 125 [8%] low disease activity state (LDAS)). DAS28 remission is defined as DAS28 <2.6, LDAS is defined as DAS28 ≥2.6<3.2. Median baseline DAS28 scores were 4.9 and 5.3 for patients having a DAS28 remission and LDAS target, respectively. The table shows DAS28 scores at baseline, 12 and 24 months, and disease management received for the subset of patients with available DAS28 scores at the relevant time points, stratified by those who did/did not achieve their remission target and those with/without sustained remission at 24 months. Of the 108 patients eligible to receive biologic therapy, according to NICE guidance, 39 (36%) received a biologic within their first 24 months of treatment.

	Patients with 12 months follow up (n=713)		Patients with 24 months follow up (n=269)	
	In remission at 12 months [n=276]	Not in remission at 12 months [n=239]	Sustained remission at 24 months [n=32]	Remission not sustained at 24 months [n=96]
% patients compliant with TTT standards				
N (%) with baseline target set (remission or LDAS)	244 (88%)	183 (77%)	29 (91%)	76 (79%)
N (%) with >4 visits in the first year of management	207 (75%)	175 (73%)	31 (97%)	81 (84%)
N (%) with >4 DAS scores in the first year of management	180 (65%)	155 (65%)	24 (75%)	48 (50%)
N (%) with dual therapy within 6 months of diagnosis	148 (54%)	154 (64%)	17 (53%)	53 (55%)
Disease scores				
median baseline DAS28 (n with available score)	4.6 [n=226]	5.1 [n=193]	4.5 [n=26]	5.3 [n=67]
median 12 month DAS28 (n with available score)	1.9 [n=276]	3.9 [n=239]	1.9 [n=23]	2.9 [n=63]
median 24 month DAS28 (n with available score)	2.1 [n=43]	3.4 [n=43]	1.6 [n=32]	3.0 [n=96]

Conclusions: The results suggest that more patients with a target set at baseline are in remission at 12 months and at 24 months than those without a target set. Number of visits, number of DAS28 scores and starting dual therapy within 6 months do not appear to affect the proportion of patients in remission at 12 months, but active management in the first 12 months (>4 visits, >4 DAS28 scores) does appear to be associated with more patients in remission at 24 months. Thus we conclude that treating RA early and aggressively, in line with the T2T guidelines, leads to sustained clinical improvement.
References:
[1] Smolen et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis 2010;69:631–637.
Disclosure of Interest: A. L. Tan Consultant for: I have received honoraria from AbbVie Ltd., M. Buch Consultant for: has received previous honorarium/consultancy with Abbvie, Astra Zeneca, Bristol-Myers Squibb, Lilly, Roche-Chugai, Sandoz and research grants from Roche and Pfizer., D. O'Reilly Consultant for: has been paid research/consultancy fees/other honoraria by Amgen, Abbvie, MSD, pH Associates, Roche, UCB and Wyeth., T. Sheeran Consultant for: has been paid consultancy fees by Roche, AbbVie, Novatis and Pfizer., A. Bishop-Bailey Employee of: I am an employee of pH Associates, the company commissioned by Abbvie to design and implement the study, as well as perform analysis and presentation/publication of the study data., G. Nock Employee of: I am an employee of pH Associates, the company commissioned by Abbvie to design and implement the study, as well as perform analysis and presentation/publication of the study data., S. Chitale Consultant for: has been on an advisory board for Abbvie and Pfizer, and has received educational grants from Abbvie, Pfizer and UCB., P. Emery Consultant for: undertaken clinical trials and provided expert advice to Pfizer,MSD,Abbvie,BMS,UCB,Roche,Novartis,Samsung, Sandoz and Lilly
DOI: 10.1136/annrheumdis-2017-eular.4740

SAT0050 EARLY RESPONSE TO CERTOLIZUMAB PEGOL IN RHEUMATOID ARTHRITIS PREDICTS OUTCOME: DATA FROM A PROSPECTIVE OBSERVATIONAL STUDY

A. Saraux[1], R.M. Flipo[2], F. Fagnani[3], J. Massol[4], B. Combe[5], P. Huot-Marchand[6], J.M. Joubert[7], J. Dunkel[8], G. Cukierman[7]. *[1]C.H.U. la Cavale Blanche, Brest; [2]C.H.U. Hôpital Roger Salengro, Lille; [3]Cemka Eval, Bourg-la-Reine; [4]Phisquare, Besançon; [5]C.H.U. Lapeyronie, Montpellier; [6]MAPI, Lyon; [7]UCB Pharma, Colombes, France; [8]UCB Pharma, Monheim, Germany*

Background: Treat-to-target strategies for rheumatoid arthritis (RA) require reliable clinical markers of treatment response in order to adapt therapy. Markers of early treatment failure can be used to ensure that patients (pts) are not unnecessarily exposed to ineffective therapy. Data from interventional clinical trials suggest that early clinical measures of disease activity (such as CDAI, DAS28 or HAQ-DI) after 12 weeks (wks) of treatment can reliably predict treatment failure at 1 year (yr).[1–3] However, it is unknown how such indicators perform in real-world settings.
Objectives: To evaluate the performance of clinical markers of early treatment failure (Wk12) as predictors of treatment failure at 1yr in everyday clinical practice.
Methods: Data from a 1yr interim analysis of the ECLAIR study were used: a longitudinal, prospective, observational, multicentre study of pts with RA starting treatment with certolizumab pegol (CZP) in France. Pts were evaluated at study entry and thereafter at 3-monthly routine consultations. Disease activity was assessed at each visit using CDAI, DAS28 and HAQ-DI. At Wk12, pts with missing data or no longer taking CZP were excluded from the analyses. Linear interpolation, LOCF or NRI were used to impute missing data at 1yr, including data from pts who left the study early. Different definitions for treatment non-response were applied based on CDAI or ΔDAS28 and ΔHAQ-DI relative to pre-treatment values. Non-response at Wk12 was defined as CDAI>10, ΔDAS28<1.2 or ΔHAQ-DI<0.22. Then, failure at 1yr was defined as CDAI>22, DAS28>3.2 and HAQ-DI>0.5. Positive predictive values (PPV; proportion of treatment failures at 1yr in Wk12 non-responders) were used to evaluate the predictive performance of each tool.
Results: Overall, 792 pts were enrolled and data from 730 pts analysed. Performance of CDAI at predicting treatment failure at 1yr was assessed in 532 pts (198 data values missing at Wk12). Response and failure rates at Wk12 and 1yr are presented (see Table). The PPV for CDAI was 88.8%, indicating that almost 9/10 pts identified as non-responders at Wk12 fail to respond at 1yr. Specificity was also high (96.0%), indicating that <5% of pts who achieved CDAI response at 1yr were non-responders at Wk12. Similar analyses performed for DAS28 and HAQ-DI produced PPVs of 69.0% and 75.4%, respectively.

Table: Response and failure rates of CZP-treated patients at Week 12 and 1 year

	CDAI at 1 year		
CDAI at Week 12	**>22 (Failure)**	**≤22 (Response)**	**Total**
>10 (Non-response)	79	10	89
≤10 (Response)	205	238	443
Total	284	248	532
	Sensitivity=27.8%, Specificity=96.0%, PPV=88.8%, NPV=53.7%		
	DAS28 at 1 year		
ΔDAS28 at Week 12	**>3.2 (Failure)**	**≤3.2 (Response)**	**Total**
<1.2 (Non-response)	136	61	197
≥1.2 (Response)	102	135	237
Total	238	196	434
	Sensitivity=57.1%, Specificity=68.9%, PPV=69.0%, NPV=57.0%		
	HAQ-DI at 1 year		
ΔHAQ-DI at Week 12	**>0.5 (Failure)**	**≤0.5 (Response)**	**Total**
<0.22 (Non-response)	175	57	232
≥0.22 (Response)	154	110	264
Total	329	167	496
	Sensitivity=53.2%, Specificity=65.9%, PPV=75.4%, NPV=41.7%		

CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score; HAQ-DI: Health Assessment Questionnaire-Disability Index; NPV: Negative predictive value; PPV: Positive predictive value.

Conclusions: The PPV describing the performance of early CDAI measure as a

predictor of treatment failure at 1yr among CZP-treated RA pts was high; 88.8% of pts identified as non-responders at Wk12 will represent a treatment failure at 1yr. Simple tools such as CDAI, assessed during routine consultations, may be reliable markers to predict treatment failure without need for complementary biological tests.

References:
[1] Keystone EC. J Rheumatol 2011;38:990–6.
[2] Curtis JR. Arth Care Res 2012;64:658–67.
[3] van der Heijde D. J Rheumatol 2012;39:1326–33.

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. We also thank Isabelle Bru (UCB Pharma) who helped conduct the ECLAIR study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: A. Saraux Consultant for: UCB Pharma, R. M. Flipo Consultant for: UCB Pharma, F. Fagnani Consultant for: UCB Pharma, J. Massol: None declared, B. Combe Grant/research support from: Merck Pfizer Inc, Roche-Chugai, Consultant for: Merck, Pfizer, Roche-Chugai, UCB Pharma, Bristol-Myers Squibb, Celgene, Eli Lilly, Speakers bureau: Merck, Pfizer, Roche-Chugai, UCB Pharma, Bristol-Myers Squibb, Celgene, Eli Lilly, Novartis, P. Huot-Marchand: None declared, J. M. Joubert Employee of: UCB Pharma, J. Dunkel Employee of: UCB Pharma, G. Cukierman Employee of: UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.1974

SAT0051 CITRULLINATION OF ADENOSINE DEAMINASE ISOFORMS IN RHEUMATOID ARTHRITIS

S. Sharoyan[1], L. Karapetyan[1], R. Harutyunyan[2], S. Mardanyan[1], A. Antonyan[1]. [1]*H.Ch. Buniatian Institute of Biochemistry of Armenian NAS;* [2]*"Yerevan" Medical Center, Yerevan, Armenia*

Background: One of the most important discoveries in rheumatology is the characterization of citrulline containing auto-antigens [1]. The identification of citrullinated proteins as auto-antigens and the development of new assay based on the detection of anti-citrullinated protein antibodies (ACPAs) become a breakthrough in the diagnosis and treatment of rheumatoid arthritis (RA). Mitsui and coauthors *in vitro* identified adenosine deaminase (ADA) as an ACPA antigen [2]. Earlier we have reported the enhance of ADA activity in synovial fluids (SFs) of RA patients [3].This increasing was in correlation with the ratio of small isoenzyme (SADA) to the large (LADA) [4].The comparison of citrullination states of SADA and LADA can be a clue for understanding the mechanism of SADA/LADA increase in RA, which is important both in diagnosis and treatment of the disease.

Objectives: The objectives of this study were a) to separate SADA and LADA isoforms from SFs of RA patients and b) to compare their citrullination degree.

Methods: The SADA and LADA isoforms from SFs of RA patients were separated and purified using gel-filtration and ion-exchange chromatography [4]. The citrullination degree of the isoforms was measured in the colorimetric assay with diacetylmonoxime (DAMO) [6] using the absorbance at 530 nm and free L-citrulline as a standard.

Results: The SF samples of 20 RA patients with initial ADA activity in the range 35–190 IU/L were used. Earlier we demonstrated a negligible level of SADA at initial ADA lower of this interval. In the samples with medium initial activity (35–55 IU/L), SADA/LADA ratio was $\approx$ 1/2. In those with high ADA activity (100–190 IU/L) this ratio was $\approx$ 4. The separation and purification of LADA from 10 SFs revealed that it is not citrullinated in any case. In SADA from SFs with medium ADA activity, we failed to register the citrullination. In SADA from SFs with the initial ADA activity $\geq$100 IU/L, the significant citrullination ($\approx$ 0.6 μmol/mg of protein) was registered.

Conclusions: The obtained results evidence that SADA from SFs with high ADA activity can serve as new citrulline containing ACPA antigen. This finding can be a base of developing new strategy (e.g. seeking specific inhibitors) for treatment of RA patients because citrullination enhances the ADA activity [2], hampering the increase of adenosine by methotrexate.

References:
[1] vanVenrooij WJ, van Beers JJ, Pruijn GJ. Anti-CCP Antibody, a Marker for the Early Detection of Rheumatoid Arthritis. Ann NY Acad Sci.1143:268–85, 2008.
[2] Mitsui H, Arito M, Sato T, Yokoyama MK, Suematsu N, et al. Novel anti-citrullinated peptide autoantibodies identified by proteomics with in vitro citrullinated proteins in patients with rheumatoid arthritis. Inflammation and Regeneration 33:121–30, 2013.
[3] Antonyan A, Sharoyan S, Haroyan A, Harutyunyan R, Mardanyan S. Adenosine Deaminase activity in synovial fluid at arthritis. Proceedings of YSU. Chemistry and Biology 3:28–32, 2013.
[4] Antonyan A, Sharoyan S, Haroyan A, Harutyunyan R, Mardanyan S. Adenosine Deaminase Isoforms in synovial fluid at Rheumatoid arthritis. Proceedings of YSU. Chemistry and Biology 2:54–57, 2014.
[5] Boyde TR, Rahmatullah M. Optimization of conditions for the colorimetric determination of citrulline, using diacetylmonoxime. Anal Biochem 107:424–431, 1980.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1433

SAT0052 HIGH CHANCE OF COMPREHENSIVE DISEASE CONTROL (CDC) IN VERY EARLY AND NORMAL WEIGHT RHEUMATOID ARTHRITIS PATIENTS TREATED ACCORDING TO THE TREAT TO TARGET STRATEGY

A.L. Fedele, L. Petricca, B. Tolusso, S. Alivernini, C. Di Mario, G. Di Sante, G. Ferraccioli, E. Gremese. *Institute of Rheumatology, Fondazione Policlinico Universitario A. Gemelli, Rome, Italy*

Background: The ultimate goal for Rheumatoid Arthritis (RA) management is the simultaneous achievement of all clinical, functional and structural efficacy, i.e. comprehensive disease control (CDC) [1].

Objectives: To evaluate the effective chance and the consequences of CDC achievement in real world practice of Early Arthritis Clinic (EAC).

Methods: A total of 349 early rheumatoid arthritis (ERA) patients with a disease duration of less than 12 months were enrolled in the study. ERA patients fulfilled the 2010 ACR criteria for RA and were followed according to the treat-to-target strategy. Subjects with symptom duration less than 3 months were defined as having "very early RA" (VERA). The mean follow-up (FU) was 38.2±32.8 months. At baseline, and every three months, the ACR/EULAR core data set variables were recorded. At baseline and every year hand and foot radiographs were examined according to modified Total Sharp score (mTSS). At each visit, clinical improvement and remission were evaluated according to EULAR criteria. The achievement of CDC (28-joint Disease Activity Score using C reactive protein $<$2.6, Health Assessment Questionnaire $<$0.5 and change from baseline in mTSS $\leq$0.5) was assessed every year of follow-up.

Results: At the twelfth month of FU 148 (42.4%) ERA patients achieved CDC, while at the time of last FU 228 (65.3%) subjects reached this target.

Patients achieving CDC at the 12th month of FU were younger (*p=0.05*), in higher percentage male (*p=0.004*), and with a normal weight (body mass index, BMI $<$25) (*p=0.003*) and had a shorter disease duration, comprising a greater number of VERA (*p=0.01*), compared to subjects not achieving disease control. There were no differences concerning autoantibody positivity and presence of erosions at onset between the two analyzed cohorts. Adjusting the analysis for age, the variables that arose as independent predictors of CDC at the 12th month of FU were a disease duration less than 3 months [OR (95% CI): 1.97 (1.23–3.14)] and a normal BMI [OR (95% CI): 2.05 (1.32–3.21)].

In our cohort, 105 (30.1%) ERA patients were treated with biological disease modifying anti-rheumatic drugs (bDMARDs) over time. Biotechnological therapy was less frequently started by subjects in CDC, both after 12 months (*p=0.003*) and at the time of last FU (*p$<$0.0001*). At the multivariate analysis, not achieving CDC at the 12th month of FU [OR (95% CI): 2.69 (1.59–4.57)] and a BMI $\geq$25 [OR (95% CI): 2.05 (1.23–3.42)] were the variables significantly associated to bDMARD therapy over time.

Conclusions: The simultaneous achievement of symptom control, inhibition of radiographic progression and normalization of function, is a feasible target in real word EAC. Having a VERA and a normal weight are associated to a high chance of "deep" remission.

References:
[1] Emery P, et al. Ann Rheum Dis 2015; 74: 2165–2174.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5496

SAT0053 THE INCIDENT IMMUNOLOGICAL STATUS PREDICTS DRUG-FREE DISEASE FLARE IN RHEUMATOID ARTHRITIS PATIENTS ACHIEVING STRINGENT CLINICAL AND ULTRASONOGRAPHIC CONTROL OF THE PERIPHERAL INFLAMMATORY PROCESS

A. Manzo, S. Bugatti, F. Benaglio, B. Vitolo, G. Sakellariou, R. Caporali, C. Montecucco. *Rheumatology and Translational Immunology Research Laboratories (LaRIT), Division of Rheumatology, IRCCS Policlinico San Matteo Foundation/University of Pavia, Pavia, Italy*

Background: The development of predictive tools to evaluate health risks and design personalized health plans in patients with rheumatoid arthritis (RA) achieving remission still represents a major unmet need. In this perspective, the relative weight of clinical, ultrasound and immunological assessment of disease characteristics for predicting recurrence of the inflammatory process under drug-free conditions remains unclear.

Objectives: To investigate the predictive value of baseline clinical remission stringency, synovial power Doppler (PD) ultrasound indices and the incident autoimmune status, as predictors of flare under drug-free conditions after a DAS28-driven treatment strategy with methotrexate (MTX) in early RA.

Methods: 85 RA patients achieving stable remission and candidate to MTX withdrawal were recruited according to the following criteria: 1) introduction of MTX within 12 months from symptoms' onset, 2) at least 24 months of MTX treatment with a DAS28-driven protocol targeting low disease activity (LDA), 3) DAS28$<$2.6 for $\geq$6 months in the absence of corticosteroids. Following treatment suspension, patients were monitored at three months' intervals across 24 months through clinical, ultrasound (hands-feet-axillary lymph nodes), radiographic and immunologic screenings (ACPA-RF status, CXCL13 circulating levels [1–2] and FACS analysis for quantification of Ki67+/regulatory T-B cell subsets). Treatment was re-introduced in case of DAS28$\geq$3.2 or stable LDA.

Results: At baseline, 84% of the patients were in remission according to the SDAI (<3,3) with 44% of the cases showing SDAI remission and absence of PD signal in hands and feet (SDAI<3,3 and PD=0). Despite stringent remission, 48% of the patients showed an episode of flare during follow-up with a peak incidence between 6 and 9 months after drug withdrawal. With the exception of a mild protective role of SDAI remission, none of the investigated clinical and ultrasound parameters (alone or in combination) showed a significant impact on clinical evolution across 24 months. ACPA IgG levels showed instead a strong, inflammation-independent predictive value for disease recurrence, an observation that was confirmed in the overall cohort (HR: 3.39 [1.7–6.64], p=0.0006, Cox regression) and, invariably, across progressive clinical and/or ultrasound remission thresholds (SDAI remission, SDAI remission-PD=0). Sub-analyses focused on short-term events (0–6 months after DMARDs withdrawal), identified the systemic level of CXCL13 at baseline as the strongest predictor of early disease recurrence in ACPA IgG positive individuals.

Conclusions: The systemic immuno-type of patients in remission is the major determinant of drug-free disease recurrence, over and above drug-induced achievement of stringent clinical and ultrasonographic control of the peripheral inflammatory process.

References:

[1] Meeuwisse CM et al. Identification of CXCL13 as a marker for rheumatoid arthritis outcome using an in silico model of the rheumatic joint. Arthritis Rheum 2011; 63: 1265–73.

[2] Havenar-Daughton C et al. CXCL13 is a plasma biomarker of germinal center activity. Proc Natl Acad Sci U S A 2016; 113: 2702–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6958

SAT0054 RISK FACTORS FOR ACUTE EXACERBATION OF RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL PNEUMONIA

A. Yashima, H. Yamashita, R. Kamei, K. Suga, M. Nakano, S. Yamada, Y. Takahashi, H. Kaneko. *Division of Rheumatic Diseases, National Center for Global Health and Medicine, Tokyo, Japan*

Background: Acute exacerbation (AE) is recently recognized as deterioration of respiratory status in idiopathic pulmonary fibrosis. It is reported that AE also occurs in other interstitial lung diseases (ILD) such as collagen vascular diseases associated ILD (CVD-ILD). However, the characteristics and risk factors of AE in CVD-ILD are not clearly identified.

Objectives: To clarify the characteristics of patients with rheumatoid arthritis-associated interstitial pneumonia (RA-IP) and to investigate the risk factors associated with AE and its survival of RA-IP.

Methods: We examined the clinical features of 60 RA-IP patients admitted to our hospital between July 2010 and September 2016. We compared the characteristics between patients who developed AE (AE group) and those who didn't (non-AE group), and between patients who survived after AE (alive group) and those who died after AE (dead group), and identified variables significantly associated with AE occurrence and survival using Cox hazards analyses.

Results: Thirty-six (60%) were female. Twenty-two (36.7%) developed AE and seven of them (11.7%) died with the mean follow-up period of 2.7 years. The mean age at RA diagnosis was 61.1±16.3 years in AE group and 61.5±13.1 years in non-AE group. Sex, smoking habit and high-resolution computed tomography (HRCT) pattern were not significantly different between two groups. Although there was no significant difference, more patients in AE group received methotrexate (MTX) treatment than those in non-AE group (40.9% vs. 18.9%, *p*=0.08), and MTX use was significantly associated with occurrence of AE in a Cox hazard analysis (Hazard ratio [HR] 1.09, 95% confidence interval [CI] 1.01–1.18). Further, age (median 70 vs. 82 years, *p*=0.002) and matrix metalloproteinase-3 (MMP-3) level (median 84.8 vs. 205.6 ng/mL, *p*=0.03) on admission were significantly higher in dead group than in alive group. Univariate analyses revealed that age ≧ 75 years (HR 10.53, 95% CI 1.26–88.15), MMP-3 ≧ 200 ng/mL (HR 15.58, 95% CI 1.38–175.8), and 3L or more oxygen use (HR 8.46, 95% CI 1.02–70.49) on admission were associated with death (Table 1).

Table 1. Risk factors for AE mortality based on univariate Cox hazard analyses

	HR	95% CI	*p* value
Age ≥75 years	1.19	1.05 to 1.36	0.008
Sex, male	1.65	0.37 to 7.41	0.51
HRCT, UIP pattern	3.82	0.74 to 19.8	0.11
KL-6 ≥700 U.mL	1.32	0.24 to 7.22	0.75
LDH ≥400 IU/L	0.40	0.05 to 3.32	0.40
MMP-3 ≥200 ng/mL	15.58	1.38 to 175.80	0.03
O_2 ≥3 L	9.46	1.02 to 70.49	0.05

UIP, usual interstitial pneumonia; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase.

Conclusions: Our data suggest that MTX use relates to the occurrence of AE, and age, MMP-3 level, and oxygen volume on admission relate to AE survival in patients with RA-IP.

References:

[1] Hozumi H, Nakamura Y, Johkoh T, et al. BMJ Open 2013; 3: e003132.

[2] Suda T, Kaida Y, Nakamura Y, et al. Respiratory Medicine 2009; 103: 846–853.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2683

SAT0055 BARICITINIB SHOWED RAPID AND GREATER REDUCTION IN PAIN COMPARED TO ADALIMUMAB OR PLACEBO IN PATIENTS WITH RHEUMATOID ARTHRITIS

P. Taylor[1], B. Zhu[2], C. Gaich[2], X. Zhang[2], A.M. DeLozier[2], D. Schlichting[2], H. Patel[2], F. Durand[2], B. Fautrel[3]. *[1]University of Oxford, Oxford, United Kingdom; [2]Eli Lilly and Company, Indianapolis, United States; [3]University Pierre et Marie Curie, Paris, France*

Background: A rapid and meaningful reduction in pain is important to quality of life in patients (pts) with rheumatoid arthritis (RA). Baricitinib (bari) is a selective inhibitor of Janus kinase (JAK)1/JAK 2 in development for pts with active RA.[1]

Objectives: To evaluate the effect of bari treatment on pain reduction compared to adalimumab (ADA) or placebo (PBO) in pts with inadequate response to methotrexate (MTX) or biologic disease-modifying antirheumatic drugs (bDMARDs).

Methods: In RA-BEAM (NCT01710358), 1305 patients with inadequate response to MTX were randomised 3:3:2 to PBO QD, bari 4 mg once daily (QD), or ADA 40 mg biweekly.[2] In RA-BEACON (NCT01721044), 527 pts with inadequate response or intolerance to bDMARDs were randomised 1:1:1 to PBO or bari (2 or 4 mg) QD.[3] This post-hoc analysis reports the pts' assessment of pain using a visual analogue scale (VAS, range: 0 to 100 mm). The proportion of pts who achieved pain improvement of ≥30%, ≥50%, and ≥70% of their baseline pain at 1, 2, 4, 8, 12, 16, 20, and 24 weeks of treatment were compared between treatment groups using logistic models adjusted for geographic region, baseline pain score, baseline joint erosion status (RA-BEAM only), and history of bDMARD at screening (RA-BEACON only). Missing data were imputed using modified last observation carried forward.

Results: Mean baseline pain scores were 60, 62, and 61 for PBO, bari 4 mg, and ADA, respectively, in RA-BEAM and 65, 62, and 66 for PBO, bari 2 mg, and bari 4 mg, respectively, in RA-BEACON. A significantly greater proportion of pts treated with bari 4 mg achieved ≥30% and ≥50% pain improvement as early as week 1 compared to PBO (both studies) and as early as week 4 compared to ADA (RA-BEAM) (Table). A significant pain improvement of ≥70% was achieved at week 12 for pts treated with bari 4 mg compared to PBO (both studies) and ADA (RA-BEAM). Pain improvement of ≥30%, ≥50%, and ≥70% with bari 2 mg was significant compared to PBO by week 12 (RA-BEACON). Significant improvements in pain for bari vs PBO and bari vs ADA were sustained through week 24.

Table 1. Percent Pain Improvement in RA-BEAM and RA-BEACON

	RA-BEAM			RA-BEACON		
	PBO (N=488)	Bari 4 mg (N=487)	ADA (N=330)	PBO (N=176)	Bari 2 mg (N=174)	Bari 4 mg (N=177)
Pain Improvement ≥30%						
Week 1	27	48***	47***	20	25	32**
Week 4	37	67***†	60***	29	38	50***
Week 12	47	73***†	64***	31	43*	58***
Week 24	49	74***	69***	34	44*	57***
Pain Improvement ≥50%						
Week 1	13	26***	28***	6	9	17**
Week 4	22	48***‡	37***	15	25*	30***
Week 12	31	57***†	49***	17	31**	35***
Week 24	32	61***†	52***	20	32**	45***
Pain Improvement ≥70%						
Week 1	4	12***	11***	2	3	6
Week 4	8	26***	21***	6	11	14*
Week 12	14	37***‡	28***	7	19***	18**
Week 24	16	41***‡	32***	9	22***	29***

*p≤0.05 vs PBO; **p≤0.01 vs PBO; ***p≤0.001 vs PBO; †p≤0.05 vs ADA; ‡p≤0.01 vs ADA; p-values based on logistic regression model. ADA = adalimumab; Bari = baricitinib; PBO = placebo.

Conclusions: Bari-treated pts reported significantly greater and more rapid reductions in pain severity as measured by the pain VAS compared to PBO or ADA; improvements were sustained through 24 weeks. The results were similar regardless of the pt population.

References:

[1] Fridman JS, et al. J Immunol 2010;184:5298–307.

[2] Taylor PC, et al. Arthritis Rheumatol 2015;67 (suppl 10):abstr 2L.

[3] Genovese MC, et al. N Engl J Med 2016;374:1243–52.

Disclosure of Interest: P. Taylor Grant/research support from: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Galapagos, GlaxoSmithKline, Merck, Pfizer, UCB, Biogen, Sandoz and Janssen., Consultant for: AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Galapagos, GlaxoSmithKline, Merck, Pfizer, UCB, Biogen, Sandoz and Janssen., B. Zhu Employee of: Eli Lilly and Company, C. Gaich Employee of: Eli Lilly and Company, X. Zhang Employee of: Eli Lilly and Company, A. DeLozier Employee of: Eli Lilly and Company, D. Schlichting Employee of: Eli Lilly and Company, H. Patel: None declared, F. Durand: None declared, B. Fautrel Consultant for: AbbVIe, Biogen, BMS, Celgene, Hospira, Janssen, Lilly, Novartis, Pfizer, Roche, SOBI pharma, UCB

DOI: 10.1136/annrheumdis-2017-eular.1346

SAT0056 RHEUMATOID ARTHRITIS MAGNETIC RESONANCE IMAGING SCORE (RAMRIS) CAN PREDICT DAS-28 THERAPY RESPONSE AFTER 6 MONTHS: RESULTS OF THE GERMAN ARTHROMARK COHORT

P. Sewerin[1], S. Vordenbäumen[1], C. Schleich[2], R. Sengewein[1], R. Brinks[3], G. Pongratz[3], J. Lesch[1], L. Le[4], U. Mansmann[4], M. Schneider[1], B. Ostendorf[1] on behalf of ArthroMark Studygroup. *[1]Department for Rheumatology; [2]Department for diagnostic and interventional Radiology; [3]Hiller-Research-Center for Rheumatology, University Hospital Duesseldorf, Düsseldorf; [4]Institute for Medical Information Sciences, Biometry and Epidemiology, Ludwig Maximilian University of Munich, Munich, Germany*

Background: Remission is the ultimate goal in rheumatoid arthritis (RA). The absence of rheumatoid factors (RF) and /or anti-citrullinated protein (CCP) antibodies, no bone erosions on conventional x-rays, the presence of low disease activity, and early therapeutic intervention are established good prognostic markers. Magnetic resonance imaging (MRI) is a well evaluated imaging technic and is increasingly used in daily practice. In this study, we prospectively investigated the prognostic performance of high-field MRI and serological biomarkers 6 months after initiation of methotrexate in patients with early RA (eRA)

Objectives: To evaluate the value of high-resolution MRI of the hand as a prognostic marker for EULAR-response and remission after 6 month of MTX therapy in early RA patients

Methods: Prospective cohort study on the ArthroMark cohort using 3T MRI of the hand at baseline (V0) before initiating an MTX-therapy in eRA patients, after 3 months (V3) and after six months (V6). 28 patients (Ø 56.8 years) with RF and/or CCP positive RA and a disease duration <6 months (mean16.3 weeks) fulfilling the 2010 ACR/EULAR criteria were examined. EULAR core set of variables were recorded: patient's global assessment of overall disease activity; number of tender and swollen joints, ESR and CRP. The following biomarkers were assessed by ELISA: Dkk-1, Osteoprotegerin, IL-22, MMP-3, TNF-Alpha and Neuropeptide-Y. Remission was defined as DAS28 <2.6 according to the ACR/EULAR remission criteria. MRI-scans were analysed by using OMERACT RA-MRI scoring system (RAMRIS). To adjust for intrapersonal correlation, we calculated generalized linear mixed models with time being recognized as a confounder in pretests.

Results: A low RAMRIS subscore for erosions (p=0.019) or total RAMRIS score predicted response at V3 (p=0.03). No significant results were found for the other imaging markers assessed for response prediction at either V3 or V6. Concerning remission, low levels of RANKL at baseline were significantly associated with EULAR remission at V6 (p=0.033). The other markers assessed did not show significant results at either V3 or V6.

In multivariate analyses, response was predicted more accurately with the inclusion of either RAMRIS (p value LR-test =0.035), RAMRIS synovitis subscore at MCP-2 (p-value LR-test =0.035) or a combination of the two (p-value LR-test =0.042). Remission was more accurately predicted when RANKL was considered with low RANKL improving the chance of remission. In contrast to response-prediction, MRI did not significantly add to the prediction model for remission.

Conclusions: Low RAMRIS scores or RAMRIS synovitis subscores at MCP-2 were predictive for therapy response after 6 months in our generalized mixed model. Baseline RANKL was able to significantly predict remission. Our data suggests that MRI and/or biomarkers may aid response prediction and facilitate patient selection for intensified therapy in the future.

Acknowledgements: ArthroMark study is funded by the Federal Ministry of Education and Researche (Bundesministerium für Bildung und Forschung, BMBF, FKZ 01EC1009A).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3808

SAT0057 PROSPECTIVE OBSERVATIONAL REAL-LIFE STUDY (STRATEGE) SHOWS THE EFFICACY OF TREAT-TO-TARGET STRATEGY AND METHOTREXATE MONOTHERAPY OPTIMIZATION IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS

R.-M. Flipo[1], C. Gaujoux-Viala[2,3], C. Hudry[4,5], E. Zinovieva[6], H. Herman-Demars[6] on behalf of STRATEGE study observers. *[1]Rheumatology Department, Lille University Hospital Roger Salengro, Lille; [2]Rheumatology Department, Nîmes Hospital, Nîmes; [3]Montpellier University, Montpellier; [4]Rheumatology Institute; [5]Rheumatology Department, Cochin Hospital; [6]Medical Department, Nordic Pharma, Paris, France*

Background: Current guidelines consider MTX as initial gold standard treatment for patients (pts) with RA. They also propose various strategies for MTX inadequate responders, among which the most frequent are optimization of MTX therapy (alone or in combination with csDMARDs or bDMARDs).

Objectives: The objective of the trial was to explore the strategies applied in daily practice in RA pts with inadequate response to MTX.

Methods: STRATEGE was a prospective, observational, multicenter study. Main inclusion criteria were: confirmed RA (ACR 1987 or ACR/EULAR 2010 criteria) and treatment by MTX monotherapy with clinical, structural, functional and/or therapeutic evolution leading to therapeutic management modification. Data were obtained at 2 time-points: baseline and 6-month follow-up.

Results: Between Sept 2014 and July 2015, 176 rheumatologists, at 90% with private practice, included 854 pts, 801 of which composed the analyzable baseline set. Pts baseline characteristics were [mean (SD)]: age: 57.4 (13.7) yrs; RA duration: 5.3 (6.7) yrs; DAS28: 4.0 (1.1), with the following distribution: <2.6 for 10%, >3.2 for 74% and >5.1 for 16%; HAQ: 1.1 (0.84); and extra-articular features and erosive disease for respectively 10.5% and 39.9% of pts. All pts were receiving MTX monotherapy, orally for 67.6% and at mean (SD) dose of 14.2 (4.1) mg/wk for oral and 16.6 (3.8) mg/wk for parenteral administration. Concomitant treatment included corticosteroids for 45.8% of pts, at a mean (SD) dose of 8.2 (6.3) mg/d, and folic acid for 90.0%. After the inclusion visit, MTX prescription has been identically maintained (dose and route) for 28.1% of pts, interrupted for 1.9% and modified for 70.0%. Changes included dose increasing for 50.2%, dose tapering for 1.8% and a route modification for 21.4% (88.2% oral -> parenteral). After inclusion visit, MTX oral versus (vs) parenteral balance was respectively 49.8% at mean (SD) dose 16.2 (4.0) mg/wk vs 45.8%, 18.0 (3.9) mg/wk. Biologic treatment was initiated for 14.6%, in association with MTX for 95.7%. Other csDMARD treatment was initiated for 1.2% in monotherapy and for 3.6% in association with MTX. The reasons for treatment modification were mainly active RA (72.0%), worsening of clinical and biologic parameters (31.4%), radiographic progression (14.5%), remission not achieved (12.4%), steroid dependence (11.3%), and MTX intolerance 5.0%. Six-month follow-up results show that all the active treatment strategies were significantly and equally successful in improving disease activity (Table).

Table 1

	N	DAS28 Baseline	DAS28 (M6)	D DAS28	*p*
MTX unchanged (Ref.)	126	3.4 (1.3)	2.5 (1.0)*	-0.8 (1.2)	–
MTX optimization	519	4.0 (1.0)	2.9 (1.2)*	-1.1 (1.3)	0.10
bDMARDs	117	4.6 (1.1)	3.2 (1.1)*	-1.4 (1.3)	0.22
csDMARDs	39	4.3 (1.2)	3.1 (1.3)*	-1.3 (1.4)	0.37

Data presented: mean (SD). *$p<0.0001$ (M6 *vs* baseline), ANCOVA, adjusted for DAS28 at baseline.

Conclusions: Consistently with all current guidelines, results of the large prospective observational study STRATEGE reveal an important place held by initial MTX treatment optimization before initiation of a biotherapy and emphasize the importance of treat-to-target strategy.

Disclosure of Interest: R.-M. Flipo Consultant for: Nordic Pharma, C. Gaujoux-Viala Consultant for: Nordic Pharma, C. Hudry Consultant for: Nordic Pharma, E. Zinovieva Employee of: Nordic Pharma, H. Herman-Demars Employee of: Nordic Pharma

DOI: 10.1136/annrheumdis-2017-eular.2707

SAT0058 EFFECTS OF BARICITINIB ON PATIENTS WHO STOP METHOTREXATE MONOTHERAPY AND SWITCH TO BARICITINIB MONOTHERAPY

R. Fleischmann[1], T. Takeuchi[2], M. Schiff[3], D. Schlichting[4], L. Xie[4], M. Issa[4], I. Stoykov[4], J.R. Lisse[4], P. Martinez-Osuna[4], T. Rooney[4], C.A. Zerbini[5]. *[1]U Texas SW Medical Center, Dallas, United States; [2]Keio University, Tokyo, Japan; [3]Univ Colorado Hospital Rheum, Colorado; [4]Eli Lilly and Company, Indianapolis, United States; [5]Univ Sao Paolo, Sao Palo, Brazil*

Background: Baricitinib (bari) is a reversible oral Janus kinase (JAK) inhibitor with selectivity for JAK1/JAK2 in development for treatment of patients (pts) with active rheumatoid arthritis (RA). In the 52-week (wk) Phase 3 RA-BEGIN study of MTX-naïve pts, there were 3 arms: bari 4 mg once daily (QD), methotrexate (MTX) up to 20 mg weekly (QW), and the combination of bari plus MTX (bari+MTX). Nonresponders were rescued from week 24 onwards by receiving bari+MTX, regardless of original treatment. Bari monotherapy showed superior efficacy compared to MTX monotherapy and similar clinical efficacy to bari+MTX.

Objectives: Efficacy and safety were evaluated in pts from RA-BEGIN who switched from MTX or bari+MTX therapy to bari monotherapy upon entering the long-term extension (LTE) study (RA-BEYOND).

Methods: In RA-BEGIN, 588 pts were randomised 4:3:4 to MTX, bari monotherapy 4 mg, or bari+MTX. At Wk 52, pts could enter the LTE; all pts received bari 4 mg monotherapy. MTX could be added in the LTE by investigator decision. Seventy-seven percent of pts (451/588) enrolled in the LTE, of whom 423 had not been rescued in RA-BEGIN. This post hoc analysis evaluated clinical efficacy of pts who continued bari monotherapy compared to those in whom MTX was added within the first 24 wks of the LTE.

Results: Of these 423 pts, 200 (47%) remained on monotherapy at Wk 24 of the LTE and 223 pts started on MTX before wk 24. Most (193) had initiated MTX within 4 wks of starting the LTE study, evenly balanced from the 3 original arms of RA-BEGIN. Across study arms, pts who had MTX added in the LTE had worse disease control upon entry and during the LTE. Through 24 wks, statistically significant improvement in disease state was observed in the MTX-to-bari group regardless of whether or not MTX was added back. In the bari-to-bari monotherapy group, the addition of MTX led to lowered disease activity, which was statistically significant. No statistically significant changes in disease activity were observed in the pts who were switched from bari+MTX to bari monotherapy regardless of additional MTX therapy (Table 1). Exposure-adjusted incidence rates for total treatment-emergent adverse events, including non-serious infections, were lowest in the MTX-to-bari group. Clinically significant or consistent differences in SIE,

SAEs, or AEs leading to study drug discontinuation were not seen in any of the arms, whether MTX was added or not.

Table 1. Efficacy through 24 Weeks in the LTE RA-BEYOND Study for Patients Not Rescued in RA-BEGIN

		MTX to Bari (N=69, +MTX); (N=67, -MTX)			Bari to Bari (N=67, +MTX); (N=57, -MTX)			Bari+MTX to Bari (N=87, +MTX); (N=76, -MTX)		
		Wk 52	Wk 64	Wk 76	Wk 52	Wk 64	Wk 76	Wk 52	Wk 64	Wk 76
ACR20[a], %	+MTX	84.1	88.4	94.2	86.6	86.6	86.6	89.7	87.4	87.4
	-MTX	83.6	86.6	82.1	94.7	87.7	87.7	97.4	90.8	86.8
ACR50[a], %	+MTX	53.6	82.6	81.2	64.2	71.6	70.1	77.0	71.3	71.3
	-MTX	61.2	79.1	71.6	77.2	82.5	80.7	85.5	77.6	77.6
ACR70[a], %	+MTX	34.8	65.2	59.4	40.3	49.3	53.7	55.2	51.7	52.9
	-MTX	44.8	62.7	62.7	63.2	66.7	68.4	65.8	55.3	56.6
CDAI[b]	+MTX	12.1	7.6**	6.9**	10.0	6.7**	6.6**	8.5	9.3	8.4
	-MTX	8.9	4.4**	4.9**	5.5	4.5	4.0*	5.2	4.7	5.9
SDAI[b]	+MTX	13.1	8.1**	7.2**	10.7	7.2**	7.2**	9.0	9.8	8.9
	-MTX	9.8	4.8**	5.3**	6.0	4.9	4.5*	5.6	5.3	6.3
HAQ-DI[b]	+MTX	0.79	0.57**	0.56**	0.72	0.61*	0.51**	0.55	0.60	0.59
	-MTX	0.67	0.48**	0.48**	0.46	0.46	0.54	0.45	0.45	0.58

Abbreviations: ACR20/50/70=20, 50, or 70% improvement in American College of Rheumatology criteria; Bari=baricitinib; CDAI=Clinical Disease Activity Index; HAQ-DI=Health Assessment Questionnaire-Disability Index; LTE=long-term extension; MMRM=mixed model for repeated measures; MTX=methotrexate; SDAI=Simplified Disease Activity Index; Wk=week.
Results are subdivided into those patients placed back on MTX (+MTX) and those who remained true Bari monotherapy (-MTX). Wks are based on time since initial randomisation in the 52-wk RA-BEGIN study. Analyses are based on a September 1, 2016 data cutoff.
[a]Using nonresponder imputation and baseline of RA-BEGIN. [b]Data are mean values.
*p≤0.05, **p≤0.01; p-values are based on within-group least squares mean change from LTE baseline (Wk 52) using MMRM.

Table 2. Safety through 24 Weeks in the LTE RA-BEYOND Study for Patients Not Rescued in RA-BEGIN

n (%) [EAIR]		MTX to Bari (N=69, +MTX); (N=67, -MTX)	Bari to Bari (N=67, +MTX); (N=57, -MTX)	Bari+MTX to Bari (N=87, +MTX); (N=76, -MTX)
Patients with ≥1 TEAE	+MTX	26 (37.7) [87.4]	28 (41.8) [108.2]	37 (42.5) [104.0]
	-MTX	19 (28.4) [66.7]	28 (49.1) [120.0]	36 (47.4) [119.2]
Infections	+MTX	11 (15.9) [37.0]	14 (20.9) [54.1]	19 (21.8) [53.4]
	-MTX	7 (10.4) [24.6]	10 (17.5) [42.9]	18 (23.7) [59.6]
AEs that led to study drug discontinuation	+MTX	0	2 (3.0) [7.7]	0
	-MTX	1 (1.5) [3.5]	2 (3.5) [8.6]	2 (2.6) [6.6]
Patients with ≥1 SAE	+MTX	0	6 (9.0) [23.1]	2 (2.3) [5.6]
	-MTX	3 (4.5) [10.4]	2 (3.5) [8.4]	3 (3.9) [9.9]
Serious infections	+MTX	0	2 (3.0) [7.7]	1 (1.1) [2.8]
	-MTX	2 (3.0) [6.9]	1 (1.8) [4.2]	0

Abbreviations: AEs=adverse events; Bari=baricitinib; EAIR=exposure adjusted incidence rate; LTE=long-term extension; MTX=methotrexate; SAE=serious adverse event; TEAE=treatment-emergent adverse event.
Results are subdivided into those patients placed back on MTX (+MTX) and those who remained true Bari monotherapy (-MTX). Analyses are based on a September 1, 2016 data cutoff. Data are n (%) [EAIR].

Conclusions: Switching from MTX to bari monotherapy, maintaining bari monotherapy was associated with improvements in depths of disease control during the initial 24 wks post-switch. Disease control did not significantly change after withdrawal of MTX from combination therapy. Pts who entered the LTE with suboptimal disease control after treatment with bari monotherapy may benefit from the addition of MTX. Discontinuation of MTX in pts treated with combination during the index study was associated with maintenance of response. There were no differences in important measures of safety including events that are serious or led to discontinuation.

Disclosure of Interest: R. Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Genetech, GlaxoSmithKline, Janssen, Eli Lilly and Company, Merck, Pfizer, Regeneron, Roche, Sanofi Aventis, UCB, Consultant for: AbbVie, Akros, Amgen, Bristol-Myers Squibb, Celgene, Genentech, GSK, Janssen, Eli Lilly and Company, Pfizer, Sanofi-Aventis, UCB, T. Takeuchi Consultant for: Pfizer Japan, Astra Zeneca KK, Eli Lilly Japan KK, Novartis Pharma KK, Daiichi Sankyo Co Ltd, Nipponkayaku Ltd, Janssen Pharma KK, Merck Serono Ltd, Takeda Pharma Ltd, Mitsubishi Tanabe Pharma, Astellas Pharm, Abbvie GK, Bristol-Myers KK, Asahi Kasei Medical KK, Speakers bureau: Celtrion, Nipponkayaku Ltd, Pfizer Japan, UCB Japan, Daiichi Sankyo Ltd, Takeda Pharma Ltd, Chugai Pharma Ltd, Abbvie GK, Bristol-Myers KK, Eisai Ltd, Mitsubishi Tanabe Pharma, Janssen Pharma KK, Astellas Pharma, M. Schiff Consultant for: Abbvie, Amgen, Antares, BMS, Eli Lilly and Company, J&J, Novartis, Novo Niordisk, Pfizer, Roche, UCB, Speakers bureau: Abbvie, BMS, D. Schlichting Employee of: Eli Lilly and Company, L. Xie Employee of: Eli Lilly and Company, M. Issa Employee of: Eli Lilly and Company, I. Stoykov Employee of: Eli Lilly and Company, J. Lisse Employee of: Eli Lilly and Company, P. Martinez-Osuna Employee of: Eli Lilly and Company, T. Rooney Employee of: Eli Lilly and Company, C. Zerbini Grant/research support from: Pfizer, Novartis, Eli Lilly and Company, Merck, Sanofi, Amgen, Celtrion, Consultant for: Merck, Pfizer, Sanofi, Eli Lilly and Company

DOI: 10.1136/annrheumdis-2017-eular.1334

SAT0059 HIGH RADIOGRAPHIC PROGRESSION IS RARE AND GETS LESS FREQUENT IN RA PATIENTS OF THE SWISS SCQM COHORT FROM 1998 TO 2015

S. Mueller[1], R. Thalmann[1], H. Schulze-Koops[2], N. Graf[3], J. von Kempis[1].
[1]Division of Rheumatology, Kantonsspital St. Gallen, St. Gallen, Switzerland; [2]Rheumaeinheit, Klinikum der Universität München, Campus Innenstadt, Munich, Germany; [3]Graf Biostatistics, Winterthur, Switzerland

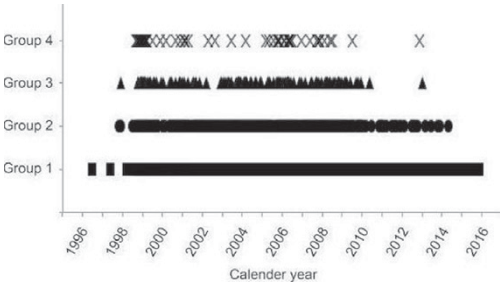
Background: The primary goal of current therapeutic strategies in RA is to control disease activity and at the same time to prevent radiographic progression. A disconnect between a missing radiographic progression and higher disease activity under treatment with biologic agents has been discussed. In general, analyses of radiographic progression in RA rather focus on radiographic non-progression or repair and high radiographic progression in spite of therapy has, to our knowledge not been analysed in detail in the last years, neither in RCTs nor in cohort studies.

Objectives: To analyse the occurrence of high radiographic destruction and it's development in the era of biologic treatment.

Methods: We included all RA patients from the Swiss registry SCQM with at least two subsequently scored radiographs. Radiographic destruction was scored with the Ratingen erosion score and calculated by dividing the change of Ratingen scores by time (>6 months) between two subsequent radiographs. To analyse high radiographic progression we looked for the height and time of the highest (peak) radiographic progression in every individual patient for the analysis. The individual peak radiographic progression was analysed in groups as change of Ratingen scores/year: 0-≤10, 10-≤20, 20-≤30, >30 (groups 1–4). The time point of the individual peak radiographic progression was analysed per group (follow up 1998 – 2015). The baseline disease characteristics were compared using standard descriptive statistics (Kruskal-Wallis or Chi-square tests).

Results: 4'033 patients were included into the analysis. 3'049 patients had a peak radiographic progression between 0 and ≤10/year, 773 between 10 and ≤20, 150 between 20 and ≤30, and 61 of >30. All patient groups were within the same age range (mean: 56.5 – 60.5 years). Rheumatoid factor and ACPA were more frequent in patient groups with higher peak radiographic progression (RF: 73.6, 80.0, 88.9, 90.0; ACPA: 66.8, 73.4, 74.3, 82.1, groups 1–4, respectively). When the rate of radiographic progression before and after peak progression was analysed, 69.7%, 74.7%, 76.9%, and 93.3% of the patients had a radiographic progression of 25% or lower as compared to peak progression before and 76.1%, 81.8%, 91.1%, and 93.8% after this peak progression, respectively for patients in groups 1 to 4 (Figure A).

The disease activity, as assessed by DAS 28, was significantly higher in all patient groups before peak progression and lower thereafter (Figure B, p<0.001). Average HAQ-DI scores increased after peak radiographic progression in group 4 (Figure C, p=0.005) whereas it is stable or even decreases among the patients of the other patient groups.



Conclusions: High peak radiographic progression is a rear phenomenon that gets less frequent in patients over the last years of observation. This may be an effect of modern therapy. Among the patients with high radiographic progression, (1) a greater delay between diagnosis and first symptoms was found and (2) the use of biologic agents was less frequent. These data suggest that the decreasing frequency of very high radiographic peak progression in the Swiss RA patients reflect a more effective therapeutic approach in the last years.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4232

SAT0060 RESPONSE TO CONVENTIONAL SYNTHETIC DMARDS DIFFERS DEPENDING ON RHEUMATOID FACTOR LEVELS IN ANTI-CITRULLINATED POSITIVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

S. Bugatti, A. Manzo, G. Zanframundo, F. Benaglio, G. Sakellariou, C. Montecucco, R. Caporali. *Rheumatology and Translational Immunology Research Laboratories (LaRIT) and Early Arthritis Clinic, Division of Rheumatology, University of Pavia, IRCCS Policlinico San Matteo Foundation, Pavia, Italy*

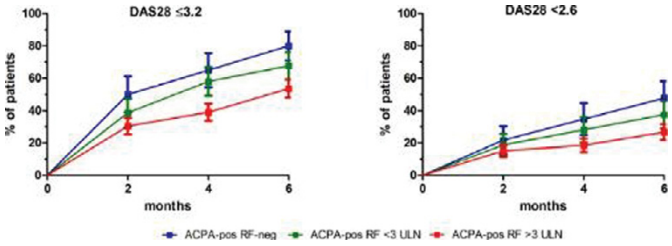
Background: In rheumatoid arthritis (RA), several autoantibody characteristics, including specifities, levels and isotypes, may influence their pathogenic properties and impact on clinical presentation and outcomes of the disease (1, 2). In particular, classical IgM rheumatoid factor (RF) may boost inflammation triggered by anti-citrullinated protein antibodies (ACPA) (3).

Objectives: To investigate whether RF impacts on disease characteristics and response to therapy in ACPA-positive early RA patients treated with conventional synthetic disease modifying drugs (csDMARDs).

Methods: 574 early RA patients consecutively enrolled in our Early Arthritis Clinic between 2005 and 2014 were included. Patients had symptoms' duration <12 months, were glucocorticoid- and DMARD-naïve, and fulfilled RA criteria at inclusion. IgM RF and IgG ACPA were determined in baseline sera by immunonephelometry and a second-generation EliA CCP assay respectively. Autoantibody levels were considered high when >3 times the upper limit of normal (ULN). Patients were treated with incremental doses of methotrexate according to a treat-to-target strategy aiming at low disease activity (LDA, DAS28 ≤3.2). The associations between autoantibody specifities and levels and the achievement of LDA and disease remission (DAS28 <2.6) over 6 months were investigated by Cox regression.

Results: 360 patients tested RF and/or ACPA positive (31.9% single RF-positive, 10.3% single ACPA-positive, 57.8% ACPA and RF double-positive) and were

selected for outcome analyses. Among seropositive patients, both LDA and remission were less frequently achieved in case of RF-positivity. Relevantly, in ACPA-positive patients (n=273), the co-occurrence of RF dose-dependently influenced clinical outcomes. After 6 months of treatment, LDA and disease remission were achieved respectively by 69.6% and 47.8% of single ACPA-positive, 68.8% and 37.5% of ACPA-positive RF-low, and 57% and 27.6% of ACPA-positive RF-high patients (chi-square for trend p=0.18 for LDA, p=0.05 for remission). After adjusting for confounders (age, gender, symptoms' duration, baseline disease activity, use of prednisone, recruitment period), high levels of RF independently predicted failure to achieve LDA with an HR (95% CI) of 0.61 (0.39 to 0.95) and failure to achieve remission with an HR (95% CI) of 0.63 (0.35 to 0.99) (Figure 1). In contrast, ACPA levels did not show any significant predictive value, neither for thresholds of >3 ULN nor of >100 U.



Conclusions: Among ACPA-positive RA patients, disease characteristics may vary in association with the extent of overall humoral autoimmunity. In particular, the concomitant presence of high levels of IgM RF seems associated with lower response rates to csDMARDs. Collectively, these findings highlight the importance of further subclassifying patients with autoantibody-positive RA in order get deeper insights into disease mechanisms and clinical outcomes.

References:

[1] Aletaha D et al. Arthritis Res Ther 2015;17:229.
[2] Derksen VFAM et al. Ann Rheum Dis 2017;doi:10.1136/annrheumdis-2016–209794.
[3] Sokolove J et al. Arthritis Rheumatol 2014;66:813–21.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5778

SAT0061 HAQ SCORE IS AN INDEPENDENT PREDICTOR OF SUSTAINED REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

S.-S. Lee[1,1], J.-H. Kang, J.-E. Kim, K.-E. Lee, D.-J. Park. *Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic Of*

Objectives: We compared remission rates, according to different definitions of remission in rheumatoid arthritis (RA) and investigated the potential predictors of sustained remission at the 2-year follow-up.

Methods: We obtained data on 291 RA outpatients, seen from July 2009 to September 2012. Sociodemographic data and answers to questionnaires were collected in face-to-face interviews. Remission was defined according to the Disease Activity Score in 28 joints (DAS28)-ESR, DAS28-CRP, Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), and ACR/EULAR Boolean definition. Sustained remission was defined as when the patient continued in remission at two consecutive annual assessments. Predictors of sustained remission according to the DAS28-CRP were assessed by univariate and multivariate analyses.

Results: For the 291 RA patients, the remission rates of RA were 17.9% (DAS28-ESR), 54.3% (DAS28-CRP), 10.3% (SDAI), 10.0% (CDAI), and 5.8% (Boolean). On follow-up for 2 years, the sustained remission rates of RA were 46.5% (DAS28), 55.0% (DAS28-CRP), 37.5% (SDAI), 32.0% (CDAI), and 30.8% (Boolean). RA patients who achieve sustained remission according to the DAS28-CRP were younger, and had more education, higher monthly income, lower Health Assessment Questionnaire (HAQ) score, lower physician global assessment, lower patient global assessment, lower patient pain assessment, and higher EQ-5D. In multivariate analysis, only the HAQ score predicted sustained remission according to DAS28-CRP (OR=0.257, 95% CI 0.067–0.980, p =0.047).

Conclusions: The remission rates of RA patients differed according to the definition of remission, and the highest sustained remission rate was classified by the DAS28-CRP. A lower HAQ score was an independent predictor of sustained remission over 2 years, according to the DAS28-CRP.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2363

SAT0062 14-3-3ETA PREDICTS JOINT DAMAGE PROGRESSION AND FLARING AFTER ADALIMUMAB DISCONTINUATION

S. Hirata[1,2], A. Marotta[3], K. Hanami[2], Y. Tanaka[2]. *[1]Hiroshima University Hospital, Hiroshima; [2]University of Occupational and Environmental Health, Kitakyushu, Japan; [3]Augurex Life Sciences Corp, Vancouver, Canada*

Background: The HONOR (humira discontinuation without functional and radiographic damage following sustained remission) study was designed to investigate the possibility of patients discontinuing adalimumab (ADA) therapy for 1 year without flaring (DAS28-ESR ≥3.2). 14–3-3η is a mechanistic serum marker that is modifiable over the disease course, does not correlate with CRP and is a predictor of radiographic progression even in patients who achieve clinical remission. The uncoupling of inflammation and joint damage processes in RA underscores a risk of premature discontinuation of biologic treatment when aiming to achieve sustained remission. Serum markers that could indicate which patients are at risk of flare and continued joint damage despite clinical remission are highly desirable.

Objectives: In this study, serum 14–3-3η was investigated as a predictor of joint damage and flares in the HONOR cohort.

Methods: Serum 14–3-3η levels were measured in 62 Japanese patients, 51 of which were from the HONOR study at baseline, 1-year after treatment initiation, at discontinuation and at the time of flare. Of the 62 patients, 46 (74%) patients achieved sustained drug-free remission up to 1 year following ADA discontinuation. Sharp van der Heidje (SHS) scores were available at therapy initiation, discontinuation, and at 52 weeks following. Relationships between continuous variables were assessed using uni- and multi-variable Gaussian linear regression models and logistic regression.

Results: At baseline and discontinuation, median (QR) 14–3-3η levels were 0.28 ng/ml (0.07–2.11) and 0.22 ng/ml (0.04–1.28) respectively, with 26 (59%) of 44 and 29 (54%) of 54 patients being positive (≥0.19 ng/ml) at the corresponding time-points. Paired t-test revealed that levels of 14–3-3η were significantly different between baseline and discontinuation, p=0.030. Level of 14–3-3η at baseline was positively associated with SHS at 12 months and at the time of flare, p=0.038. Bivariable modeling revealed that baseline 14–3-3η together with the change in 14–3-3η had a significant interacting effect on SHS at 12 months and the time of flare, p=0.02. Higher baseline 14–3-3η levels together with an increase in levels at the time of discontinuation was strongly associated with an increased SHS. Adding CRP, flare, sustained remission through 12 months, MTX dose at initiation and at ADA discontinuation did not improve predictive effects of 14–3-3η with SHS. Baseline 14–3-3η levels alone was not associated with flares at 12 months (p=0.15) however when combined with CRP, a significant interaction was present (p=0.03). Specifically, patients with a low CRP, and a high 14–3-3η level had a higher likelihood of flaring versus those with a low 14–3-3η, 22% versus 12%.

Conclusions: Baseline 14–3-3η and increases in its levels are associated with worse radiographic outcomes in patients who achieve clinical remission and discontinue ADA. To reduce the risk of flare in patients who are candidates for discontinuation of ADA, CRP and 14–3-3η measurements should be considered in combination as markers of flare prediction.

Disclosure of Interest: S. Hirata: None declared, A. Marotta Employee of: Augurex Life Sciences Corp., K. Hanami: None declared, Y. Tanaka: None declared

DOI: 10.1136/annrheumdis-2017-eular.5426

SAT0063 A PROSPECTIVE STUDY ON COMPARISON OF COMPOSITE INDICES WITH ULTRASOUND FOR DETECTING REMISSION AND PREDICTION OF FLARE IN 2 YEARS

M.O. Olmez[1], E.K. Gunal[2], S.B. Ureyen[3], H. Keskin[2], A.B. Ozturk[4], H.G. Yeter[5], E. Cobanoglu[5], S.Z. Aydin[3]. *[1]Internal Medicine; [2]Rheumatology, Istanbul Medeniyet University School of Medicine, Istanbul, Turkey; [3]Rheumatology, University of Ottawa, Faculty of Medicine, Ottawa, Canada; [4]Allergy and Immunology; [5]Koc University, School of Medicine, Istanbul, Turkey*

Background: Treat-to-target (T2T) approach suggests using a composite index when following patients with rheumatoid arthritis (RA) without identifying which one to use.

Objectives: In this prospective study we aimed to compare the accuracy of different indices for RA patients in remission taking Ultrasound Global Synovitis Score (GLOESS) as a gold standard and their predictive value for flares in 2 years.

Methods: RA patients who were considered to be in clinical remission according to the clinician were recruited. Disease activity was assessed using DAS28-CRP, CDAI, SDAI and RAPID-3 and 38 joints per patient were scanned by US and scored according to GLOESS. The total GLOESS scores were calculated for 38 joints and also for 28 joints by excluding the MTP joints. The number of joints with ≥2 GLOESS was calculated. Flare data was collected in 3 subsequent visits in the following 2 years, whenever available.

Results: Ninety-six consecutive patients (80.2% females) were recruited. Patients were more frequently categorized as being in remission using DAS28 (80%) compared to CDAI (50%), SDAI (45.2%) and RAPID 3 (37.5%). Patients that were in remission according to CDAI had lower GLOESS scores on 28 joints (p=0.05) and had less joints with ≥2 signals (p=0.04) (table). For SDAI patients in remission had significantly less number of joints with grade 3 signals (p=0.03) and tend to have lower GLOESS scores on 28 joints as well as lower number of joints with ≥2 signals (p=0.06). None of the US scores were able to differentiate different disease states according to DAS28-CRP or RAPID. Flare data was available in 76 patients, 22 of whom had flares. Patients that had flare had higher GLOESS scores on 28 joints at baseline (p=0.05) and tend to have higher number of joints with grade 3 signals (p=0.06). Although numerically higher, none of the clinical indices were able to predict flares based on remission status (remission vs non remission: CDAI: 22.5% vs 36.1, p=0.2; SDAI: 22.9 vs 36.8, p=0.2; DAS28: 25.4% vs 50%, p=0.1; RAPID3: 20% vs 34.8%, p=0.2).

Table 1. The distribution of US-GLOESS according to different categories by indices

	GLOESS 38 joints mean±SD	GLOESS 28 joints mean±SD	Joint counts ≥ score 2 mean±SD	Joint counts with score 3 mean±SD
DAS-28				
Remission (n=77)	10.9±7.5	7.8±7.2	3.5±3.1	0.7±1.3
LDA (n=11)	14.5±6.6	10.0±5.4	4.9±3.0	0.9±1.4
VMDA (n=5)	9.6±6.2	5.4±3.5	3.0±2.3	0.80±1.7
CDAI				
Remission (n=48)	10.0±6.9	6.9±6.2	3.02±2.7	0.60±1.0
LDA (n=48)	12.7±7.7	9.1±7.2	4.3±3.3	0.94±1.5
SDAI				
Remission (n=42)	9.9±6.6	6.6±5.9	2.9±2.6	0.5±0.9
LDA (n=50)	12.4±7.8	9.1±7.5	4.2±3.3	0.9±1.5
MDA (n=1)	13.0	4.0	5.0	0
RAPID				
Remission (n=36)	10.3±6.2	6.7±4.6	3.1±2.6	0.5±0.8
Low activity (n=28)	9.6±5.8	6.6±4.6	2.7±2.2	0.3±0.7
MDA (n=30)	14.0±9.4	10.7±9.7	5.1±3.9	1.4±1.9
HDA (n=2)	15±1.4	8.5±2.1	5±1.4	0

LDA: Low disease activity MDA: Moderate disease activity HDA: High Disease activity.

Conclusions: Our results show that CDAI is superior then other clinical indices to assess remission in RA. US has the superiority over clinical indices to predict flares and 28 joint GLOESS is superior to 38 joints.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3227

SAT0064 HIGH MMP3 SERUM LEVELS ARE ASSOCIATED WITH EXTENSIVE STRUCTURAL DAMAGE IN PATIENTS WITH EARLY, TREATMENT NAIVE RHEUMATOID ARTHRITIS (RA): TWO YEARS PROSPECTIVE CLINICAL AND ULTRASONOGRAPHIC STUDY

S.Z. Prodanovic[1], G. Radunovic[2], M. Sefik-Bukilica[3], M. Zlatanovic[4], K. Simic-Pasalic[5], S. Seric[6], N. Damjanov[7]. *[1]Clinical IVb; [2]Deputy of head; [3]Clinical IVa; [4]Clinical III; [5]Clinical VI; [6]Radiology Department; [7]Head of Institute, Institute of Rheumatology, Belgrade, Serbia*

Objectives: To investigate the association of high baseline MMP-3 serum levels with hands and feet joints structural damage progression, estimated by ultrasonography (US), in patients with early, treatment "naïve" RA without X-ray visible erosions.
Methods: Sixty-three pts. (9 males and 54 females; mean age 53.4 yrs 21–81±14.1) with early RA (EULAR/ACR 2010 criteria) and symptom duration of ≤12 months (mean duration of 3.8 months) had baseline serum MMP-3 levels tested. Patients had been DMARDs/glucocorticoid naïve, without visible X-ray erosions at the study entry. The subsequent structural joints damages, that were estimated by high frequency linear probe by ESAOTE My Lab 70 machine, as well as clinical markers of disease activity, in the first 2 years were followed. The presence of bone erosion was analyzed at the wrist, MCP2 and MCP5 joints of both hands, as well as at MTP5 joints according to OMERACT US group definition. In order to estimate progression of preexisting erosion the total volume (TV) of bone erosion were calculated by multiplying three diameters (mm): a-the length of erosion; diameter b- the width and diameter c-the depth of erosion. Anova statistical method was performed in data processing.
Results: 46 pts. had basal serum MMP-3 level higher than normal (MMP-3 positive). The 504 joints were assessed summary by US on each visit. The 122 bone erosions in total (1.9 per patient) were depicted at baseline and 213 bone erosions (4.3 per patient) at follow-up visit in whole group. After 24 months MMP3 positive pts. had significantly higher total number of US erosions than MMP-3 negative (3.8 vs. 2.4, p=0.039). The total volume of bone erosion (mm^3) was higher in MMP-3 positive than MMP-3 negative pts. after 24 months of treatment, but without statistical significance (18.6 vs. 8.9, p=0.07). MMP-3 positive pts. had a significantly higher value of ESR, CRP and DAS28 than MMP-3 negative pts. at the baseline visit (53.6 vs.25.9, p=0.002; 36.6 vs. 9.5, p=0.005; 6.0 vs. 4.8, p=0.002, respectively). All of those parameters were significantly decreased after 24 months in a group of MMP-3 positive compared to MMP-3 negative pts. (p=0.009, p=0.021, p=0.028, respectively).
Conclusions: After 2-year of follow-up, US assessment showed a significantly higher number of new bone erosions in patients with early, treatment "naïve" RA and baseline MMP3 levels higher than normal (MMP3 positive) compared to patients with normal baseline levels of MMP3, as well as a biger TV of bone erosions but not statistically significant. The parameters of RA activity (ESR, CRP, DAS28) significantly correlated with baseline MMP-3 levels of higher than normal.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4002

SAT0065 ACPA AGAINST DIFFERENT CITRULLINATED PEPTIDES IDENTIFY SPECIFIC PHENOTYPES OF RHEUMATOID ARTHRITIS

M. Brink[1], M. Hansson[2], L. Mathson-Alm[3], M. Cornillet[4], J. Rönnelid[3], K. Skriner[5], G. Serre[4], R. Holmdahl[6], L. Klareskog[2], S. Rantapää-Dahlqvist[1]. *[1]Public Health and Clinical Medicine, Rheumatology, Umeå University, Umeå; [2]Rheumatology Unit, Dept of Medicine, Karolinska Institute, Stockholm; [3]Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden; [4]U 1056 Inserm, Univeristy de Toulouse, Toulouse, France; [5]Medicine, Charité University, Berlin, Germany; [6]Medical Inflammation Research, Karolinska Institute, Stockholm, Sweden*

Background: Anti-citrullinated protein/peptide antibodies (ACPA) have been suggested to identify a more severe phenotype of rheumatoid arthritis (RA).
Objectives: In this study in an inception cohort of early RA we have analysed a number of antibodies against different citrullinated and/or mutated peptides using a multiplex platform in relation to the patients disease inflammation and radiological destruction
Methods: Patients with early RA (≤12 m of symptoms) fulfilling the 1987 ARA criteria (n=1022, 692f/330m, mean age56.7±14.0 years) were sampled at the time of diagnosis and assessed using disease activity score (DAS28) at baseline, 6, 12, 18 and 24 months. Radiographs were graded using Larsen score (baseline and *at* 24 m). Plasma sampled at baseline was analysed for presence of antibody reactivities against 21 different citrullinated peptides/proteins; Fibrinogen (Fib) α36–50, Fibα573, Fibα591, Fibα621–635, Fibβ36–52, Fibβ60–74, Fibβ62–78 (72), Fibβ62–78 (74), Filaggrin (Fil307–324), α-Enolase peptide 5–21 (CEP-1), Vimentin (Vim) 2–17, Vim60–75, F4-R-Cit, F4-Cit-Cit, F4- Cit-R), or mutated proteins (Bla26, Pept1, Pept5, PeptZ1, PeptZ2) and type II Collagen citrullinated or not using a custom-made microarray assay based on the ImmunoCAP ISAC system (Phadia AB, Sweden). Cut-off levels were at the 98th percentile of controls (n=477). Anti-CCP2 was analysed using ELISA (Euro Diagnostica, Sweden).
Results: The most frequent appearing ACPA were; Fibβ60–74 (63%), Vim60–75 (56.6%), Fibβ36–52 (55.1%), Fil307–324 (54.9%), CEP-1 (53.7%) and Pept5 (52.0%) besides CCP2 (67.5%). Adding all ACPAs gave additional 13.1% of positivity in the anti-CCP2 negative group, yielding a positivity of 77.5%. The median (IQR) number of positive ACPA-peptide was 8 (11). There was a high degree of correlation between the antibodies, e.g., anti-Fibβ60–74 vs. -Vim60–75, -Fibβ36–52 or anti-CCP2 antibodies and also anti-Fil307–324 vs. -Fibβ36–52, -F4 R-Cit or anti-CCP2 antibodies (rs 0.692–0.79). Positivity for all antibodies was associated with higher ESR (baseline and AUC_{24}). A number of antibodies were associated with both high DAS28 (baseline and AUC_{24}) and radiological findings/progression (anti-CCP2, - Fil307–324, -Vim60–75 and Vim 2–17, and -CEP1 antibodies), whilst some others were more associated with inflammation (DAS28, baseline and AUC_{24}) (anti-Fibβ60–74, -Pept5 and -F4R-cit antibodies) and others more with radiological destruction/progression (anti-Fibβ36–52, -Fibβ74, -PeptZ1, -F4 Cit-R antibodies). Partial least squares regression analyses confirmed the results with significant correlation between radiological progression and antibodies against Vim2–17, Fibβ36–52, CEP1, Fibα621–635, and CCP2 and between DAS28AUC_{24} and Vim60–75, Vim2–17, Fibα621–635 and F4-R-Cit. Patients treated with biologics during the first 24 months (11.2%) were significantly more frequent positive for anti-CCP2, -Vim60-75, -Fibα36–50, -PeptZ1 and -PeptZ2 antibodies vs. being negative.
Conclusions: Analyses at baseline, of the ACPA specificity profiles allowed different patterns of disease activity and radiological progression during the first 24 months of the disease to be identified.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5085

SAT0066 HISTOLOGICAL AND ULTRASOUND SYNOVIAL PREDICTORS OF CLINICAL DIFFERENTIATION TO DEFINED ARTHRITIS IN PATIENTS WITH SERONEGATIVE UNDIFFERENTIATED PERIPHERAL INFLAMMATORY ARTHRITIS

S. Alivernini[1], L. Petricca[1], B. Tolusso[1], L. Bui[2], C. Di Mario[1], M.R. Gigante[1], G. Di Sante[1], R. Benvenuto[2], A.L. Fedele[1], F. Federico[2], E. Gremese[1], G. Ferraccioli[1]. *[1]Institute of Rheumatology; [2]Institute of Pathology, Catholic University of the Sacred Heart, Rome, Italy*

Background: Undifferentiated Peripheral Inflammatory Arthritis (UPIA) is a common diagnosis at the first clinical evaluation in rheumatological settings. However, the likelihood of developing a well-defined rheumatic disease in UPIA patients is still matter of debate.
Objectives: To examine the role of ultrasound (US) and histological parameters in the disease outcome of patients with seronegative UPIA.
Methods: Fourty-two patients with IgA/IgM-Rheumatoid Factor and anti-citrullinated peptide antibodies negative UPIA, naïve to any Disease-Modifying Anti-Rheumatic Drugs, underwent Gray Scale (GSUS) and power Doppler (PDUS) evaluation and US guided synovial tissue biopsy. Synovial expression of CD68, CD3, CD21, CD20 and CD31 was evaluated by immunohistochemistry. IL-6, VEGF-A and VEGF-D peripheral blood (PB) and synovial fluid (SF) levels were measured by ELISA. To exclude Reactive Arthritis, each patient underwent genital and throat swabs. Afterwards, each UPIA patient was treated with chloroquine 250 mg/daily and followed every 3 months for 1 year and classified as having

UPIA, Rheumatoid Arthritis (RA), Spondyloarthritis (SpA) or Psoriatic Arthritis (PsA), respectively.

Results: During the follow-up 6 (14.3%) UPIA reached a defined diagnosis (2 RA, 2 SpA and 2 PsA, respectively). At baseline, UPIA who differentiated had higher GSUS (p=0.01) and PDUS scores (p=0.02) compared to patients who remained as UPIA within 1 year. At baseline, UPIA who differentiated towards defined arthritis had higher histological scores for lining and sublining $CD68^+$ (p=0.005 and p=0.04 for lining and sublining, respectively), sublining $CD3^+$ cells (p=0.002) and $CD31^+$ vessels count (p<0.001) than patients who remained as UPIA. In addition, there were direct correlations between baseline GSUS and PDUS scores with lining $CD68^+$ cells scores (p<0.001 for GSUS and p=0.02 for PDUS scores respectively), sublining $CD68^+$ cells scores (p=0.02 for GSUS and p=0.03 for PDUS scores respectively), sublining $CD3^+$ cells score (p=0.002 for GSUS and p=0.002 for PDUS scores respectively) and $CD31^+$ vessels count (p<0.001 for GSUS and p=0.01 for PDUS scores respectively) in UPIA. Finally, the areas under the receiver operating characteristic (ROC) curves $CD31^+$ vessels count (cut-off value: 24.3), GS score (cut-off value: 1.5) and PDUS score (cut-off value: 1.5) were calculated to assess the best cut-off points to identify the differentiation likelihood during the follow-up in UPIA patients. The logistic regression analysis, demonstrated that having baseline GSUS and PDUS scores ≥1.5 [OR:13.64 (95% CI: 0.98–242.59); p=0.05] and $CD31^+$ vessels count ≥24.3 [OR:51.13 (95% CI: 3.15–829.16); p=0.01] were independent factors associated with the achievement of defined arthritis.

Conclusions: Histological and US assessment may help in the identification of patients with seronegative UPIA with high likelihood of clinical differentiation towards defined arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4841

SAT0067 FURTHER TREATMENT INTENSIFICATIONS IN UNDIFFERENTIATED AND RHEUMATOID ARTHRITIS PATIENTS ALREADY IN LOW DISEASE ACTIVITY HAVE LIMITED BENEFIT TOWARDS PHYSICAL FUNCTIONING

S.A. Bergstra[1], O. Olivas[2], G. Akdemir[1], N. Riyazi[3], G. Collee[3], J.H. Van Groenendael[4], R.B. Landewé[5,6], C.F. Allaart[1]. *[1]Rheumatology, LUMC, Leiden, Netherlands; [2]Rheumatology, Hospital Universitario 12 de Octubre, Madrid, Spain; [3]Medical Center Haaglanden, The Hague; [4]Reumazorg Southwest Netherlands, Bergen op Zoom; [5]Amsterdam Rheumatology & Immunology Center, Amsterdam; [6]Zuyderland Medical Center, Heerlen, Netherlands*

Background: It is recommended to optimize treatment as long as a predefined treatment target is not met, but should we aim at remission if patients are in low disease activity (LDA)?

Objectives: To assess if RA or undifferentiated arthritis (UA) patients who achieved LDA benefit with better functional ability from treatment intensification aimed at DAS remission.

Methods: In the IMPROVED study 610 patients with early RA (ACR 2010) or UA were "treated to target" aimed at DAS remission, assessed 4-monthly. Initial treatment was methotrexate (MTX) + tapered high dose prednisone. Patients with DAS≤1.6 tapered treatment. Patients with DAS>1.6 were randomized to MTX + hydroxychloroquine + sulphasalazine + prednisone or to MTX + adalimumab. Over 5 years, patients with DAS>1.6 were required to increase, change or restart medication. HAQ was measured 4-monthly. A linear mixed model analysis with random intercept was performed to test the relationship between changes in therapy and HAQ over time. Patients in LDA with DAS>1.6 with and without (i.e. protocol violation) treatment change were compared. ΔHAQ and ΔDAS at each visit compared to the previous visit were calculated. We tested the interaction effect between change in treatment and follow-up time adjusted for possible confounders.

Results: Overall, over 5 years DAS (baseline mean (SD) 3.2 (1.7)) and HAQ (1.2 (0.7)) showed a statistically significant and clinically relevant decrease (ΔHAQ -0.59, 95% CI -0.61, -0.57; ΔDAS -1.77, 95% CI -1.79; -1.75). The number of patients in LDA per visit ranged from 88 to 146, of which 26% to 73% (increasing over time) had no treatment change due to protocol violations. We found a statistically significant but not clinically relevant effect of treatment change on ΔHAQ, corrected for baseline HAQ, age, gender and treatment arm (model 1, β -0.085, 95% CI -0.13, -0.044). When ΔDAS was added (model 2), the effect of treatment change was partly explained by ΔDAS and no longer statistically significant (β -0.022, 95% CI -0.060; 0.015). The effect of treatment intensification on HAQ improvement became less over time, as demonstrated by a statistically significant interaction between change in HAQ and time in follow-up in model 3 (β 0.0098, 95% CI 0.0010; 0.019) (table 1).

Table 1: Linear Mixed Model analysis to assess the effect of treatment intensification on change in HAQ.

	β	P	95% CI
Model 1 (n patients = 479, n visits = 1528)*			
Treatment intensification	-0.085	<0.001	-0.13; -0.044
Follow-up time[b]	0.0057	0.019	0.00094; 0.010
Model 2 (n patients = 476, n visits = 1509)*			
Treatment intensification	-0.022	0.246	-0.060; 0.016
Follow-up time[b]	0.0022	0.313	-0.0021; 0.0066
DAS change	0.23	<0.001	0.21; 0.26
Model 3 (n patients = 476, n visits = 1509)*			
Treatment intensification * follow-up time	-0.10	0.013	-0.18; -0.021
Follow-up time[b]	-0.0034	0.323	-0.010; 0.0033
Treatment intensification * follow-up time	0.0098	0.029	0.0010; 0.019
DAS change	0.23	<0.001	0.21; 0.26

HAQ = health assessment questionnaire, SE = standard error, CI = confidence interval.
*All models were adjusted for age, gender, treatment arm and baseline HAQ.
[b]Follow-up time is added to the model as visit number, with time between visits being 4 months.

Conclusions: Treatment intensification in early RA or UA patients who have already achieved low disease activity is associated with a statistically significant decrease in HAQ, but not with a clinically meaningful improvement in functional ability. The effect on ΔHAQ decreased with increasing follow-up time. Therefore not remission or low disease activity, but good functional ability may be the optimal treatment target at which to steer treatment adjustments. These results suggest that, whereas remission may be the optimal goal, when patients in low disease activity have acceptably low HAQ, further treatment intensification may only have downsides such as side effects and costs.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1606

SAT0068 THE TIME UNTIL PERFORMING TIGHT CONTROL AS A TREAT-TO-TARGET STRATEGY AND THE TOLERABILITY OF METHOTREXATE STRONGLY INFLUENCE THE ACHIEVEMENT OF CLINICAL REMISSION IN RHEUMATOID ARTHRITIS

T. Hagiwara, K. Kamada, N. Namura. *Rheumatology, Takarazuka City Hospital, Takarazuka, Japan*

Background: Clinical remission (CR) is the first targeted outcome of early treatment for rheumatoid arthritis (RA). Therefore, a consensus is needed for achieving CR by using the treat-to-target (T2T) strategy in RA treatment. However, in patients who received long-term insufficient treatment for RA, achievement of CR becomes increasingly difficult, especially if there is delay in the treatment.

Objectives: We aimed to examine factors that hinder successful RA treatment. We believe that making primary-care physicians aware of treatment results will increase the remission rate of RA.

Methods: We examined 388 patients with RA who were observed between January and October 2016 and who had not received new disease-modifying anti-rheumatic drugs (DMARDs) more than 3 months before the observation day. We investigated their age at RA onset, sex, Steinbrocker radiographic stage and functional class, activity level, rheumatoid factor (RF), the anti-cyclic citrullinated peptide antibody and DMARDs prescribed at the first consultation (Prescribed Before), disease activity, status of methotrexate (MTX), glucocorticoids (GCs), and biologic agent use at the last observational day.

First, we analysed the assumed remissions by using the Boolean-based definition (Boolean remission) as a purpose variable for these factors. Furthermore, we examined the odds ratio (OR) and 95% confidence interval (95% CI) by using a multiple logistic regression analysis for the statistically significantly different factors.

As for the time-related factor, we recognized that each factor had distinct multiplex collinear characteristics. Therefore, we adopted the time required for the first consultation as disease duration with the most effective values as the analysis object. The representative factor for the functional assessment adopted class according to the number of effective analyses.

Results: We recognised the statistically significant differences in disease duration, stage, class at the time of the first medical examination, RF, Prescribed Before, and state of MTX and GCs use at the last observation day for the achievement of Boolean remission.

We examined the multiple logistic regression analysis with the previously mentioned results and obtained the following results.

- Disease duration (per 1 year); OR 1.110, 95% CI 1.048–1.175, p<0.001.
- MTX (state; using vs no using); OR 2.522, 95% CI 1.560–4.076, p<0.001.
- Class at 1st interview; OR 1.512, 95% CI 1.126–2.029, p<0.01.
- GCs (state; no using vs using); OR 1.803, 95% CI 0.912–3.565, p=0.090.
- Disease duration (≤1.605y vs >1.605y); OR 2.233, 95% CI 1.437–3.470, p<0.001.
- MTX (state; using vs no using); OR 2.656, 95% CI 1.644–4.291, p<0.001.
- Class at 1st interview; OR 1.589, 95% CI 1.181–2.136, p<0.01.
- GCs (state; no using vs using); OR 1.883, 95% CI 0.956–3.711, p=0.067.

Conclusions: Our results indicated the importance of the time required for consultation facilities with the T2T strategy treatment, tolerability for MTX use, and mild dysfunction at the first interview.

The window of opportunity to achieve remission for patients with RA has less time than expected. Therefore, we recommend that physicians should introduce patients with RA to a rheumatologist following the T2T strategy promptly when the primary care provided by the family physician is insufficient.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2454

SAT0069 A RAPID3-LIKE INDEX DOCUMENTS SUPERIOR EFFICACY OF BARICITINIB TO ADALIMUMAB AND PLACEBO, SIMILAR TO DAS28 AND CDAI IN THE RA-BEAM CLINICAL TRIAL IN PATIENTS WITH RHEUMATOID ARTHRITIS

T. Pincus[1], B. Zhu[2], C.J. Larmore[2], J.D. Bradley[2], N. Patel[2], C.L. Gaich[2], A.E. Koch[2]. *[1]Rush University Medical Center, Chicago; [2]Eli Lilly and Company, Indianapolis, United States*

Background: RAPID3 (Routine Assessment of Patient Index Data) indicates differences in efficacy of active versus control treatments at levels similar to DAS28-ESR (Disease Activity Score 28-Erythrocyte Sedimentation Rate) and CDAI (Clinical Disease Activity Index) in clinical trials of adalimumab, abatacept, certolizumab.
Objectives: To compare improvement according to RAPID3, DAS 28-ESR, and CDAI in the RA-BEAM trial of baricitinib vs adalimumab and placebo.
Methods: Post-hoc analyses were performed of the RA-BEAM trial, in which patients with moderately to severely active rheumatoid arthritis and an inadequate response to methotrexate (MTX) were randomized to baricitinib, adalimumab, or placebo. All patients were to continue stable background MTX and other DMARDs, as well as stable low-dose prednisone and/or NSAIDs, if indicated. A RAPID3-like index was computed from 3 measures: physical function (FN), pain (PN), and patient global assessment (PATGL). FN on a HAQ (Health Assessment Questionnaire) of 20 items [rather than MDHAQ (multidimensional HAQ) of 10 items] was recalculated from 0–3 to 0–10; PN and PATGL (visual analog scales) were recalculated from 0–100 to 0–10, for a 0–30 total score, hence "RAPID3-like". Mean values at baseline and Week 24 for RAPID3-like, DAS28-ESR, and CDAI, and percent change from baseline were computed in the 3 treatment groups. The proportion of patients with high/moderate activity/severity at Week 24 versus low activity/severity/remission, as well as correlations of the 3 indices at Week 24, were calculated. Statistical significance for percent change was analyzed using Wilcoxon tests, after imputation of missing values using modified last observation carried forward (mLOCF); low activity/severity/remission was compared between groups using a logistic model, adjusting for region and baseline joint erosion status after imputation of missing values using non-responder imputation.
Results: Improvement from baseline to Week 24 ranged from 19.2% to 37.0% in placebo patients, 40.0% to 65.9% in baricitinib-treated patients, and 37.6% to 60.9% in adalimumab-treated patients (Table), least in DAS28-ESR, intermediate in RAPID3-like, and highest in CDAI. Changes according to RAPID3-like, DAS28-ESR and CDAI were similar in the 3 treatment groups; baricitinib and adalimumab were superior to placebo according to all indices, and baricitinib was superior to adalimumab according to RAPID3-like and CDAI (Table). Correlations of RAPID3-like with DAS28-ESR and CDAI ranged from r=0.61 to 0.75 and for DAS28-ESR with CDAI from r=0.86 to 0.91 (all $p<0.001$). The proportion of patients with low activity/severity/remission at Week 24 ranged from 9.6% to 19.7% in placebo patients, 31.6% to 49.9% in baricitinib-treated patients, and 33.6% to 47.6% in adalimumab-treated patients. RAPID3-like results were intermediate between DAS28-ESR and CDAI.

Table. Disease Activity/Severity by 3 Indices through Week 24 in RA-BEAM

		Baseline Mean	Week 24 Mean	Week 24 % Change from Baseline	Correlation with DAS28-ESR	Correlation with CDAI	High or Mod at Week 24 n (%)	Low or Remission at Week 24 n (%)
RAPID3-like	Placebo (N=488)	17.2	12.7	-22.5%	0.69	0.61	399 (81.8%)	89 (18.2%)
	Baricitinib (N=487)	17.7	8.4	-51.0%***‡‡	0.67	0.63	266 (54.6%)	221 (45.4%)***‡‡
	Adalimumab (N=330)	17.8	9.6	-45.6%***	0.75	0.70	217 (65.8%)	113 (34.2%)***
	All (N=1305)				0.73	0.67		
DAS28-ESR	Placebo (N=488)	6.4	5.2	-19.2%	N/A	0.91	441 (90.4%)	47 (9.6%)
	Baricitinib (N=487)	6.5	3.9	-40.0%***	N/A	0.86	333 (68.4%)	154 (31.6%)***
	Adalimumab (N=330)	6.4	4.0	-37.6%***	N/A	0.87	219 (66.4%)	111 (33.6%)***
	All (N=1305)				N/A	0.90		
CDAI	Placebo (N=488)	37.6	23.4	-37.0%	0.91	N/A	392 (80.3%)	96 (19.7%)
	Baricitinib (N=487)	38.1	13.0	-65.9%***‡	0.86	N/A	244 (50.1%)	243 (49.9%)***
	Adalimumab (N=330)	38.0	15.0	-60.9%***	0.87	N/A	173 (52.4%)	157 (47.6%)***
	All (N=1305)				0.90	N/A		

***Significant at 0.001 level, Baricitinib or Adalimumab vs.Placebo.
‡‡, ‡Significant at 0.01 and 0.05 levels respectively, Baricitinib vs. Adalimumab.
Abbreviations: CDAI=Clinical Disease Activity Index; DAS28-ESR=Disease Activity Score 28-erythrocyte sedimentation rate; High=high disease activity/severity; Low=low disease activity/severity; Mod=moderate disease activity/severity; N=number of patients; RAPID3-like=Routine Assessment of Patient Index Data 3-like.

Conclusions: RAPID3-like documented greater efficacy of baricitinib versus adalimumab and placebo in the RA-BEAM trial, with results in similar ranges to DAS28-ESR and CDAI. RAPID3 is feasible to provide quantitative, standard medical history data; almost of the time and effort is by the patient rather than a health professional, assuring quantitative data in the infrastructure of usual clinical care.

Disclosure of Interest: T. Pincus Shareholder of: Health Report Services, B. Zhu Employee of: Eli Lilly and Company, C. Larmore Employee of: Eli Lilly and Company, J. Bradley Employee of: Eli Lilly and Company, N. Patel Employee of: Eli Lilly and Company, C. Gaich Employee of: Eli Lilly and Company, A. Koch Employee of: Eli Lilly and Company
DOI: 10.1136/annrheumdis-2017-eular.1813

SAT0070 BARICITINIB VERSUS ADALIMUMAB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: ANALYSIS OF PATIENTS ACHIEVING A MODERATE EULAR RESPONSE AT WEEK 4

T.K. Kvien[1], P. van Riel[2], A. Rubbert-Roth[3], R. Blanco[4], S.S. Liu-Leage[5], E. Larsson[5], H. Lund[5], P. López-Romero[5], L. Zaremba-Pechmann[5], P. Emery[6]. *[1]Diakonhjemmet Hospital, Oslo, Norway; [2]Bernhoven, Uden, Netherlands; [3]Uniklinik Köln, Köln, Germany; [4]Hospital Universitario Valdecilla, Santander, Cantabria, Spain; [5]Eli Lilly and Company, Indianapolis, United States; [6]Leeds MSK Biomed/Chapel Allerton Hosp, Leeds, United Kingdom*

Background: Baricitinib (BARI) is a selective inhibitor of Janus kinase,[1] improves disease activity in patients (pts) with rheumatoid arthritis (RA), and is associated with inhibition of structural joint damage.[2–4] Response to BARI observed at week (wk) 4 may be useful to predict future response.[5]
Objectives: To characterise pts with RA who achieved moderate EULAR responses (MERs)[6] at wk 4 and to describe the outcomes through wk 52 while continuing the assigned treatment.
Methods: Pts enrolled in the RA-BEAM study with active RA who had an inadequate response to methotrexate (MTX) were randomised 3:3:2 to placebo (PBO), BARI 4 mg once daily, or adalimumab (ADA) 40 mg biweekly.[1] Pts who showed good or no EULAR responses at wk 4 were excluded. For the MER cohort, the cumulative incidence for first transition to good EULAR response and to no EULAR response from wk 4 through wk 52 was estimated in the presence of competing risks events, which either hinder observation of the events of interest or modify the chance that these events occur.[7] Pts who transitioned from MER to no EULAR response or pts who were rescued or discontinued because of an adverse event or lack of efficacy were counted as no EULAR response; pts who discontinued the study for other reasons (eg, lost to follow-up, death) were censored at the time of discontinuation. No formal statistical tests were performed for these post hoc analyses.
Results: Of 1305 pts who received at least 1 dose of study drug, 683 experienced MERs at wk 4, including 37.3% (182/488), 62.0% (302/487), and 60.3% (199/330) of pts on PBO, BARI, and ADA, respectively. Pts who achieved MERs at wk 4 on BARI and ADA had similar baseline disease activity characteristics (Table 1). The mean age of the MER subgroup was 53 years, and the mean disease duration was 8.7 years. The mean MTX dosage was 15 mg/wk, and 59% of pts were taking concomitant oral glucocorticoids. At wk 4, 27% (131/487) and 11% (54/487) of pts on BARI vs 29% (95/330) and 11% (36/330) of pts on ADA experienced no response or good response, respectively. The cumulative incidence for the first transitions to good EULAR response at wks 12, 24, and 52 was higher in pts who reached MERs at wk 4 on BARI than those on ADA. The cumulative incidence for the first transitions to subsequent no EULAR response was higher in pts who achieved MER at wk 4 on ADA (Figures 1A and 1B, Table 2) than those on BARI.
Conclusions: Among pts achieving early MER on BARI and ADA, subsequent loss of response was less common for pts on BARI than for those on ADA. Transitions to good EULAR response were more common for pts who achieved MERs on BARI than for those on ADA. Mechanistic explanations warrant future study.

Table 1: Baseline Characteristics for Patients with Moderate EULAR Response at Week 4

Characteristic	Baricitinib n = 302*	Adalimumab n = 199*
Background therapy (MTX only), no. (%)	259 (85.8)	173 (86.9)
Background therapy (MTX + other cDMARD), no. (%)	43 (14.2)	26 (13.1)
DAS28-ESR, mean (SD)	6.6 (0.9)	6.5 (0.9)
DAS28-ESR category, no. (%)		
>3.2 to ≤5.1	12 (4.0)	8 (4.0)
>5.1	290 (96.0)	191 (96.0)
Baseline mTSS, mean (SD)	42.0 (50.0)	47.1 (51.9)
HAQ-DI total score, mean (SD)	1.6 (0.7)	1.6 (0.7)

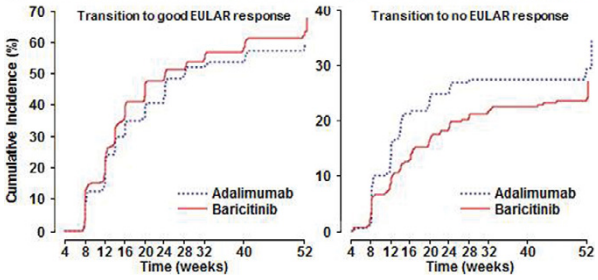
Abbreviations: cDMARD=conventional disease-modifying antirheumatic drug; DAS28-ESR=Disease Activity Score modified to include the 28-joint count based on the erythrocyte sedimentation rate; HAQ-DI=Health Assessment Questionnaire-Disability Index; mTSS=modified Total Sharp Score; MTX=methotrexate.
*501 patients reached moderate EULAR response at week 4: 302/487 (62%) and 199/330 (60%) for BARI and ADA, respectively.

Table 2: Time to First Transition to Good and to No EULAR Response (DAS28-ESR)

	Baricitinib			Adalimumab		
	Cumulative Incidence (%)	95% CI Lower	Upper	Cumulative Incidence (%)	95% CI Lower	Upper
Transition to Good Response						
Week 12	18.3	14.1	22.8	15.2	10.6	20.5
Week 24	49.2	43.4	54.7	42.9	35.9	49.7
Week 52	63.6	57.8	68.8	58.1	50.9	64.7
Transition to No Response						
Week 12	8.6	5.8	12.2	13.2	8.9	18.3
Week 24	18.9	14.7	23.5	25.5	19.6	31.7
Week 52	24.2	19.5	29.2	28.9	22.7	35.4

Abbreviations: CI=confidence interval; DAS28-ESR=Disease Activity Score modified to include the 28-joint count based on the erythrocyte sedimentation rate.

Figure 1: Time until First transition to Good and No EULAR Response (DAS28-ESR)



References:
[1] Taylor et el. 2015 ACR Meeting. Abstract 2L.
[2] Dougados M, et al. Ann Rheum Dis. 29 Sep 2016.
[3] Smolen et al. Ann Rheum Dis. 31 Oct 2016.
[4] Fleischmann R et al. Arthritis Rheumatol. 09 Oct 2016.
[5] Kremer et al. 2015 ACR Meeting. Abstract 1050.
[6] Gestel et al. Arthritis Rheum 1996.
[7] Lin G et al. SAS Global Forum 2012.

Acknowledgements: Inmaculada de la Torre MD, PhD, Senior Medical Advisor, contributed to this abstract.

Disclosure of Interest: T. K. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, and UCB, P. van Riel Consultant for: Eli Lilly and Company, A. Rubbert-Roth Consultant for: Eli Lilly and Company, R. Blanco Consultant for: Eli Lilly and Company, S. S. Liu-Leage Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, E. Larsson Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, H. Lund Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. López-Romero Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, L. Zaremba-Pechmann Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Emery Consultant for: Pfizer, MSD, Abbvie, BMS, UCB, Roche, Novartis, Samsung, Sandoz, Eli Lilly and Company

DOI: 10.1136/annrheumdis-2017-eular.2217

SAT0071 RHEUMATOID ARTHRITIS (RA) REGISTRY IN AKITA PREFECTURE, WHERE AGING IS THE MOST ADVANCED IN JAPAN

T. Aizawa[1], T. Kashiwagura[2], N. MIyakoshi[3], Y. Shimada[3]. *[1]Dept. of Orthopedic Surgery, Kitaakita Municipal Hospital, Kitaakita City; [2]Akita City Hospita; [3]Dept. of Orthopedic Surgery, Akita University Graduate School of Medicine, Akita City, Japan*

Background: The rate of aging (percentage of population aged 65 years and over) in Akita Prefecture is 33.8% (26.6% for the whole of Japan), the highest throughout Japan. The Akita Orthopaedic Group on Rheumatoid Arthritis (AORA) was established in 2010. Since then, patients have been enrolled every year to prepare the registry.
Objectives: To compare patient characteristics as well as clinical effectiveness between the treatments with and without use of methotrexate (MTX) and a biological (BIO) using the data of the AORA registry.
Methods: The subjects were 2,016 patients enrolled in the Akita registry in 2015. The subjects included 403 men and 1,613 women. According to the use of MTX and BIO, 2,016 patients were divided into the group treated with no use of MTX or BIO (group A), that treated with BIO, but no use of MTX (group B), that treated with MTX, but no use of BIO (group C), and that treated with MTX and BIO (group D).
Results: The subjects were grouped into group A (n=673), B (n=153), C (n=805), and D (n=385). MTX was used in 59.0% and BIO was used in 26.7% of all patients. The mean ages were 69.6 years (group A), 65.7 years (group B), 65.6 years (group C), and 62.6 years (group D). The aging rates were 67.9% (group A), 55.6% (group B), 56.8% (group C), and 48.3% (group D), which shows that aging was more advanced in group A.
The rates of patients with a complication of hypertension, diabetes, respiratory disease, cerebrovascular disease, heart disease or malignant tumour were 52.0% (group A), 54.2% (group B), 45.5% (group C), and 40.8% (group D). The incidence of complication was the lowest in group D.
The rates of patients who received one or more of conventional synthetic disease-modifying antirheumatic drugs (cs DMARDs) other than MTX were 79.0% (group A), 42.5% (group B), 39.9% (group C), and 19.2% (group D). Although bucillamine and salazosulfapyridine were frequently used in any group, concomitant use of tacrolimus was remarkable in group A and C, while that of iguratimod was remarkable in groups C and D. The rate of use of a prednisolone (PSL), was significantly higher in group B. The dose of PSL was significantly higher in group A. In regard to BIO, three drugs of etanercept, tocilizumab, and abatacept accounted for 90% in group B. In group D, etanercept and tocilizumab were also frequently used, followed by infliximab, adalimumab, golimumab and abatacept.
In DAS28ESR, the rate of combined low disease activity and remission was significantly higher in group D. The mean values of C-reactive protein (CRP) (mg/dL) were 0.61 (group A), 0.52 (group B), 0.47 (group C), and 0.35 (group D), which shows that the mean value was significantly higher in group A than group D. The mean values of matrix metalloproteinase 3 (MMP3) (ng/dL) were 119.0 (group A), 130.6 (group B), 100.7 (group C), and 88.9 (group D), which shows that the mean value was significantly higher in group A and B than group C and D.
Conclusions: Using the AORA registry, we compared patient characteristics as well as clinical effectiveness between the treatments with and without use of MTX and BIO. Since in group A, neither MTX nor BIO could be used in most patients, one had to practically rely on PSL. The study suggests that remission needs to be achieved prior to increase in complication due to aging.

References:
[1] Population census in Japan, 2015.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2560

SAT0072 DOSE REDUCTION OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS ACHIEVING SUSTAINED DISEASE CONTROL: RESULTS OF A PROSPECTIVE STUDY

T. Takeuchi[1], M. Genovese[2], B. Haraoui[3], L. Xie[4], R. Klar[5], A. Luisa Pinto Correia[4], T. Rooney[4], S. Otawa[4], J.S. Smolen[6]. *[1]Keio University, Tokyo, Japan; [2]Stanford University Medical Center, Palo Alto, United States; [3]Centre Hospitalier de l'Université de Montréal, Montreal, Canada; [4]Eli Lilly and Company, Indianapolis; [5]Quintiles IMS Holdings, Inc, Durham, United States; [6]Medical University of Vienna, Vienna, Austria*

Background: In patients (pts) with active rheumatoid arthritis (RA) and inadequate response (IR) to DMARDs, ph3 studies demonstrated efficacy of baricitinib (bari) (2mg and 4mg). Larger, more rapid treatment effects were observed for bari 4mg.
Objectives: To investigate the effects of bari dose step-down in pts who achieved sustained disease control with bari 4mg.
Methods: Pts with RA who completed a bari ph3 study could enter a long-term extension (LTE) study. In the LTE, pts who received bari 4mg for ≥15 months and who achieved sustained low disease activity ([LDA]-CDAI score ≤10) or remission (CDAI ≤2.8) at 2 consecutive visits ≥3 months apart were re-randomised in a blinded manner to continue bari 4mg or step down to 2mg. Patients could rescue (to bari 4mg) if CDAI >10. Efficacy and safety were assessed through 48 weeks (wks) following re-randomisation.
Results: Among pts who achieved sustained disease control with bari 4mg, dose reduction to 2mg resulted in significant increases in disease activity at 12, 24, and 48 wks; however, the majority of pts in both groups maintained the state of LDA

Abstract SAT0072 – Table 1

	Pts originating from RA-BEAM, RA-BUILD, RA-BEACON Combined†					
	Week 12		Week 24		Week 48	
	Continued bari 4 mg N=396	Stepped down to bari 2 mg N=394	Continued bari 4 mg N=353	Stepped down to bari 2 mg N=358	Continued bari 4 mg N=245	Stepped down to bari 2 mg N=245
Efficacy measure	NRI after rescue or for missing data					
CDAI LDA ≤10	359/396 (90.7)	326/393 (83.0)**	309/353 (87.5)	269/357 (75.4)***	198/245 (80.8)	167/245 (68.2)**
CDAI remission ≤2.8	158/396 (39.9)	143/393 (36.4)	149/353 (42.2)	127/357 (35.6)	99/245 (40.4)	82/245 (33.5)
	NRI only for missing data (observed data used after rescue)					
CDAI LDA ≤10	359/396 (90.7)	326/393 (83.0)**	314/353 (89.0)	289/357 (81.0)**	212/245 (86.5)	196/245 (80.0)
CDAI remission ≤2.8	158/396 (39.9)	143/393 (36.4)	150/353 (42.5)	133/357 (37.3)	103/245 (42.0)	90/245 (36.7)
Safety measure	Wks 0–48					
n [EAIR/100 PYE]	Continued bari 4mg N=396				Stepped down to bari 2mg N=394	
SDEAE	225 [70.5]				196 [65.4]	
Infection	99 [31.0]				70 [23.3]	
SAE	23 [7.2]				23 [7.7]	
Serious infection	8 [2.5]				4 [1.3]	
AE → discontinuation	9 [2.8]				11 [3.6]	

Efficacy and safety data are n/N (%), and n [EAIR/100 PYE], respectively. †RA-BEAM = MTX-IR pts; RA-BUILD = csDMARD-IR pts; RA-BEACON = bDMARD-IR pts; EAIR = exposure-adjusted incidence rate; NRI = nonresponder imputation; PYE = patient-years of exposure; SDEAE = step-down emergent adverse event. **p≤0.01, ***p≤0.001 vs. continued bari 4mg.

or remission. Rescue rates were 7.3% for bari 4mg, 17.1% for bari 2mg. Most rescued patients could regain LDA or remission. Dose reduction was associated with a lower rate of non-serious infections; rates of SAEs and AEs leading to discontinuation were similar across groups.

Conclusions: These data indicate that 4mg once daily was the most efficacious dose of bari for pts with RA; increases in disease activity were consistently seen with dose reduction from 4mg to 2mg in well-controlled pts. However, after step-down most pts could maintain LDA or remission, or recapture control with return to 4mg if needed. Attempted dose taper may be a reasonable consideration for some pts following induction of sustained disease control with bari 4mg.

Disclosure of Interest: T. Takeuchi Consultant for: Pfizer Japan, Astra Zeneca KK, Eli Lilly Japan KK, Novartis Pharma KK, Daiichi Sankyo Ltd, Nipponkayaku Ltd, Janssen Pharma KK, Merck Serono Ltd, Takeda Pharma Ltd, Mitsubishi Tanabe Pharma, Astellas Pharma, Abbvie GK, Bristol-Myers KK, Asahi Kasei Medical KK, Speakers bureau: Celtrion, Nipponkayaku Ltd, Pfizer Japan, UCB Japan, Daiichi Sankyo Ltd, Takeda Pharma Ltd, Chugai Pharma Ltd, Abbvie GK, Bristol-Myers KK, Eisai Co Ltd, Mitsubishi Tanabe Pharma, Janssen Pharma KK, Astellas Pharma, M. Genovese Grant/research support from: Eli Lilly and Company, Abbvie, Astellas, Galapagos, Pfizer, Vertex, Consultant for: Eli Lilly and Company, Abbvie, Astellas, Galapagos, Pfizer, Vertex, B. Haraoui Grant/research support from: Amgen, BMS, UCB, Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Eli Lilly and Company, Pfizer, Roche, UCB, Speakers bureau: Pfizer, UCB, L. Xie Employee of: Eli Lilly and Company, R. Klar Employee of: Quintiles IMS Holdings, Inc., A. Luisa Pinto Correia Employee of: Eli Lilly and Company, T. Rooney Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Otawa Employee of: Eli Lilly and Company, J. Smolen Grant/research support from: from Abbvie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Speakers bureau: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB

DOI: 10.1136/annrheumdis-2017-eular.1073

SAT0073 MIR-186-5P TARGETING IL-33 GENE AS BIOMARKER TO PREDICT SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

T.H. Cheng[1], Q. Shang[1], W.Y. Mak[1], M. Li[1], K.Y. Kwok[2], I.C.W. Yim[3], E.K.M. Li[1], P.C.H. Wong[4], V.W.N. Lao[5], H.T. Pang[5], L.S. Tam[1]. *[1]Department of Medicine and Therapeutics, the Chinese University of Hong Kong; [2]Department of Medicine, Queen Elizabeth Hospital; [3]Department of Medicine, Tseung Kwan O Hospital; [4]Department of Medicine and Therapeutics, Prince of Wales Hospital; [5]Department of Medicine and Geriatrics, Kwong Wah Hosptial, Hong Kong, Hong Kong*

Background: Patients with rheumatoid arthritis (RA) die prematurely compared with the general population, primarily because of cardiovascular diseases (CVD). Interleukin-33 (IL-33) is a member of the IL-1 cytokine family which was important in the pathogenesis of RA and development of CVD. Blood IL-33 protein was not detectable in most subjects, even in RA patients. Thus, the usability of IL-33 as a biomarker for CVD is limited. MicroRNAs (miRNAs) are small non-coding RNAs that function as post-transcriptional regulators of gene expression.

Objectives: This study was to ascertain if dysregulated miRNAs targeting *IL-33* gene in early RA (ERA) patients were associated with subclinical atherosclerosis in ERA patients.

Methods: 76 ERA patients were recruited in this cross-sessional study. Potential miRNAs binding to 3'UTR of the *IL-33* gene were predicted by miRanda (www.microRNA.org). 10 miRNAs with highest possibility targeting functional sites of *IL-33* gene were quantified in cell free plasma samples using a $2^{\Delta Ct}$ method. Caenorhabditis elegans miR-39 (cel-miR-39) was used as spike-in control. The results were then log transferd. Carotid plaque (CP) was measured and identified at bilateral common carotid artery, bulb, and proximal internal carotid artery using a high-resolution B mode ultrasound. Receiver-operating characteristic curve (ROC) analysis was performed to determine the discriminating power of the miRNA for the presence of CP.

Results: CPs were identified in 26/76 (34%) subjects (CP+ group). Subjects in the CP+ group were older [58±10 vs 48±11 years old, p=0.001], predominantly male [48 (42.3%) vs 43 (14.0%), p=0.006], with a higher C-reactive protein (CRP) level [24.9±25.0 vs 11.8±13.7 mg/dL, p=0.018] and higher cardiovascular risk [Framingham risk score (FRS): 12.8±11.6 vs 5.7±6.8, p=0.008] (Table 1). All miRNAs were detected in >80% of subjects in both group. Plasma level of miR-186–5p in the CP+ group was significantly higher than that in the CP- group [log miRNA: 3.28±3.21 vs 2.58±1.13 p=0.008]. It was still significant after adjusting age, sex, plasma CRP and FRS (p=0.030) (Table 1). Using multivariate logistic regression, miRNA-186–5p was an independent predictor of the presence of carotid plaque (OR: 1.919, 95% CI=1.096–3.361, p=0.023) after adjustment of FRS and CRP level. [Area under the ROC (AUC) 0.66, 95% CI: 0.60–0.80 p=0.024].

Conclusions: miR-186–5p was an independent predictor for presence of subclinical atherosclerosis and may serve as a novel biomarker for risk stratification in ERA patients with mild to moderate cardiovascular risk.

Table 1 - Characteristics of patients with and without carotid plaque

	Carotid Plaque						p	p*
	Absence (n=50)			Presence (n=26)				
Age	48	±	11	58	±	10	0.001	
Gender, male	43		14.0%	15		42.3%	0.006	
CRP, mg/dL	11.8	±	13.7	24.9	±	25.0	0.018	
Franmingham Risk Score	5.7	±	6.8	12.8	±	11.6	0.008	
log miRNA								
miR_9_5p	0.39	±	0.99	0.26	±	0.36	0.809	0.225
miR_382_5p	0.87	±	0.88	0.94	±	0.82	0.809	0.730
miR_377_3p	0.69	±	0.61	0.94	±	0.83	0.227	0.550
miR_590_3p	0.10	±	0.20	0.33	±	0.61	0.684	0.222
miR_499a_5p	0.11	±	0.17	0.19	±	0.29	0.809	0.406
miR_145_5p	2.43	±	1.05	3.30	±	1.82	0.227	0.091
miR_542_3p	0.08	±	0.27	0.08	±	0.14	0.373	0.886
miR_186_5p	2.58	±	1.13	3.28	±	1.21	0.008	0.030
miR_214_3p	0.41	±	0.66	0.61	±	0.65	0.091	0.085
miR_496	0.14	±	0.32	0.17	±	0.25	0.809	0.546

**Multivariate analysis adjusted with age, sex, plasma CRP and FRS*

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2840

SAT0074 PERSISTENCE WITH METFORMIN TREATMENT AND ONSET OF RHEUMATOID ARTHRITIS

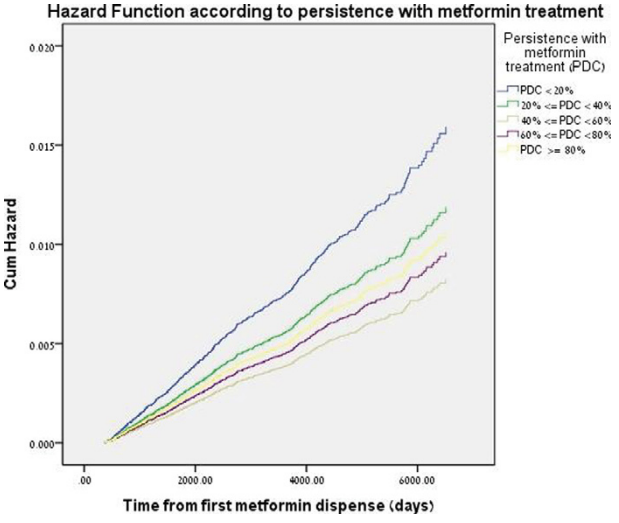
M.E. Naffaa[1], V. Rosenberg[2], G. Chodick[2,3], V. Shalev[2,3], S. Tiosano[3,4], H. Amital[3,4]. *[1]Rheumatology unit, Galilee Medical Center, Nahariya; [2]Maccabi Healthcare Services; [3]Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv; [4]Internal Medicine 'B', Sheba Medical Center, Ramat-Gan, Israel*

Background: Several studies have suggested that metformin, an oral hypoglycemic agent, possess an anti-inflammatory property and may have a role in the treatment of rheumatoid arthritis (RA)[1,2], but little is known on its preventive effects.

Objectives: To examine the association between persistence with metformin and the onset of RA.

Methods: Using the computerized medical database of a large health organization in Israel (Maccabi Healthcare Services, MHS) we have identified incident RA cases among new users of metformin between 1998 and 2014. Included were patients aged 18 or above with one year of follow up before and after the therapy initiation. RA was defined according to physician diagnoses. Participants were followed until the earliest of the following dates: onset of RA, leaving MHS, death, end of follow up (1.1.2016). Persistence with metformin was assessed by calculating the mean proportion of follow-up days covered (PDC) with metformin during the study period.

Results: A total of 113,749 eligible patients were included. During the study follow up period (794,386 person-years) we identified 600 incident cases (incidence rate of 75 cases per 100,000 PY). The incidence of RA in women (111 per 100,000 PY) was higher compared to men (42 per 100,000 PY). In a multivariable model, persistence with metformin (PDC≥80%) was associated with lower risk of RA (hazard ratio (HR) 0.66; 95% confidence interval (CI) 0.53–0.82) compared to non-persistent participants (PDC<20%). Figure 1 shows the hazard function according to persistence with metformin treatment. Similar risk reduction was observed among men but did not reach statistical significance (HR=0.85; 95% CI 0.54–1.32).



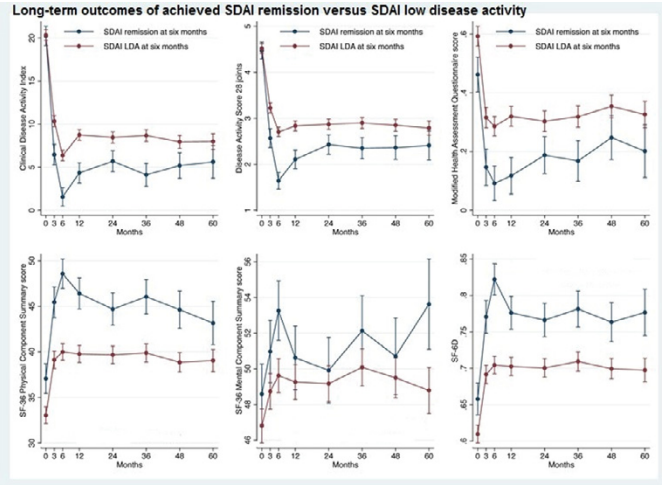
Conclusions: In the present study, we observed an association between high persistence to metformin therapy and reduced risk of developing RA in women.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4226

SAT0075 DOES EARLY REMISSION LEAD TO BETTER 5-YEAR OUTCOMES THAN LOW DISEASE ACTIVITY? RESULTS FROM THE REAL LIFE NOR-DMARD STUDY

V. Norvang, I.C. Olsen, E. Lie, E.K. Kristianslund, T.K. Kvien, E.A. Haavardsholm, T. Uhlig. *Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*

Background: When initiating therapy with synthetic disease-modifying anti-rheumatic drugs (sDMARDs) in patients with rheumatoid arthritis (RA), the recommended target is remission or low disease activity (LDA). Limited data exist on the impacts of reaching remission rather than LDA on long-term outcomes.
Objectives: To compare RA-patients who achieved Simplified Disease Activity Index (SDAI) remission versus LDA 6 months after initiating sDMARD therapy, with regard to physical function, Health Related Quality of Life (HRQoL) and disease activity during 5 years of follow-up in a routine clinical setting.
Methods: Data were provided NOR-DMARD, a prospective multicentre longitudinal observational study. We selected DMARD-naïve patients with RA enrolled between December 2000 and April 2009 who had a registered visit with available SDAI status 6 months after initiating sDMARD therapy. Data on each patient were collected at baseline, after 3, 6 and 12 months, and yearly thereafter, including the modified Health Assessment Questionnaire (MHAQ), the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36) with Physical and Mental Components Summary scores (PCS and MCS, respectively) and SF-6D, and assessments that allowed the calculation of the composite disease activity scores SDAI, Clinical Disease Activity Index (CDAI) and the Disease Activity Score based on 28 joint counts (DAS28). Multivariate linear mixed models were used to explore the effect of SDAI status at 6 months on physical function (MHAQ), HRQoL (SF-36 PCS and MCS, SF-6D) and disease activity (SDAI, CDAI, DAS28) during 5 year follow-up. The statistical models were adjusted for age, gender, disease duration and baseline disease activity. Furthermore, we performed mixed model analyses separately for patients in LDA, MDA and HDA at baseline, exploring the impact of SDAI status at 6 months on long-term disease activity in each sub-group.
Results: Of 1148 eligible patients, 867 patients (75.5%) started with methotrexate in monotherapy and 281 (24.5%) started with another sDMARD or sDMARD combination. Patients in SDAI remission (n=145; 16.6%) rather than LDA (n=454; 39.5%) 6 months after initiating therapy had better physical function (MHAQ, estimated mean difference 0.11–0.20, $p<0.02$), higher SF-36 PCS (4.13–8.16, $p<0.003$) and SF-6D (0.06–0.12, $p<0.0001$), and lower disease activity (SDAI, 2.24–5.15, $p<0.05$) for all visits during 5 years of follow-up. Stratified mixed models analyses of patients in SDAI LDA, MDA and HDA at baseline, resulted in an overall significant long-term beneficial effect of achieving remission rather than LDA at 6 months; however, the differences were less distinct for patients who were already in a state of LDA at baseline.



Conclusions: The achievement of SDAI remission 6 months after initiating DMARD-therapy was associated with favourable long-term outcomes compared with the achievement of SDAI low disease activity. The results from the study support that stringent remission is the optimal treatment target in patients with RA.
Disclosure of Interest: V. Norvang: None declared, I. Olsen: None declared, E. Lie Consultant for: AbbVie, Celgene, Hospira, Pfizer, UCB, E. Kristianslund: None declared, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer, Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz, UCB, E. Haavardsholm Grant/research support from: AbbVie, Pfizer, Roche, MSD, UCB, Consultant for: AbbVie, Pfizer, Roche, Eli Lilly, Celgene, UCB, T. Uhlig: None declared
DOI: 10.1136/annrheumdis-2017-eular.3874

SAT0076 SERUM LEVEL OF SYNDECAN-4 AND ITS CORRELATION WITH CLINICAL PARAMETERS IN RHEUMATOID ARTHRITIS PATIENTS

X. Ye, J. Zhao, Z. Zhang. *Rheumatology and Clinical Immunology Department, Peking University First Hospital, Beijing, China*

Background: Heparan sulfate proteoglycan syndecan-4 plays an important role in inflammation. However, the role of syndecan-4 in rheumatoid arthritis (RA) has not yet been elucidated.
Objectives: To detect serum level of syndecan-4 in RA patients and investigate its correlation with RA clinical parameters.
Methods: The concentration of serum syndecan-4 was assayed by enzyme-linked immunosorbent assay (ELISA). 43 patients' serum samples from our RA cohort study between 2014 and 2016, and 20 age- and gender-matched osteoarthritis (OA) patients' serum samples were collected and analyzed. Compared the serum syndecan-4 levels in RA patients with DAS28$\geq$3.2 and DAS28$<$3.2 by Wilcoxon signed rank test. The relationships between serum syndecan-4 levels and RA clinical parameters (DAS28, rheumatoid factor (RF), erythrocyte sedimentation rate, C-reactive protein, etc.) were analyzed.
Results: Baseline serum syndecan-4 levels of RA patients were significantly higher than the matched OA patients (1101.56 pg/mL vs 281.41 pg/mL, $p<0.001$). In RA patients who had sera both at the point of DAS28$\geq$3.2 and DAS28$<$3.2 (n=13), we found that the former syndecan-4 levels were higher than the latter (1666.22 pg/mL vs 1378.34 pg/mL, p=0.65). The levels of serum syndecan-4 and RF were significantly and positively correlated in RA patients (r=0.696, p=0.008). Furthermore, there is a tendency that serum syndecan-4 levels were higher in the RF-positive (n=31) than in the RF-negative (n=12) RA patients (1344.43 pg/mL vs 971.27 pg/mL, p=0.078).

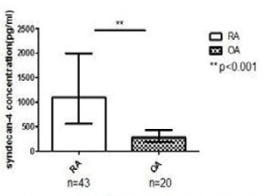


Figure 1. Serum syndecan-4 levels of RA patients and matched OA patients.

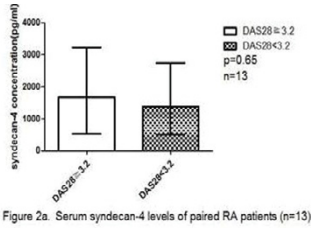


Figure 2a. Serum syndecan-4 levels of paired RA patients (n=13)

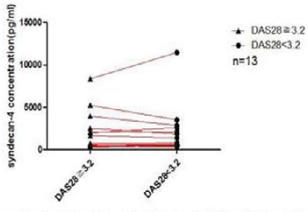


Figure 2b. Serum syndecan-4 levels of paired RA patients (n=13).

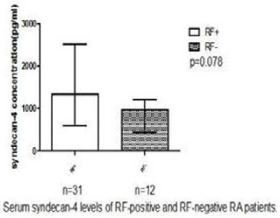


Figure 3. Serum syndecan-4 levels of RF-positive and RF-negative RA patients

Conclusions: Compared with age- and gender- matched OA patients, serum syndecan-4 concentration is significantly higher in RA patients. Serum syndecan-4 level is positively correlated with RF. Syndecan-4 may play an important role in thes pathogenesis of RA. Further investigation is required to study the mechanism of syndecan-4 in RA.
References:
[1] Zhao J, Guo J, Wang L, et al. The role of a proliferation-inducing ligand (APRIL) in the pathogenesis of rheumatoid arthritis. Scand J Rheumatol 2014;43(6):462–9.
[2] Patterson AM, Cartwright A, David G, et al. Differential expression of syndecans and glypicans in chronically inflamed synovium. Ann Rheum Dis 2008 May;67(5):592–601.
[3] Endo T, Ito K, Morimoto J, et al. Syndecan 4 Regulation of the Development of Autoimmune Arthritis in Mice by Modulating B Cell Migration and Germinal Center Formation. Arthritis Rheumatol 2015 Sep;67(9):2512–22.
Acknowledgements: We are indebted to all the patients who kindly participated in this study. This study was partly supported by Peking University Clinical Research Institute.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1091

SAT0077 CLINICAL FEATURES AND PERFORIN A91V GENE ANALYSIS IN SO-JIA CHILDREN WITH MACROPHAGE ACTIVATION SYNDROME

X. Chen[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening syndrome.Here we aim to review the precipitating events,clinical features, treatment, outcome and perforin A91V gene analysis in systemic onset juvenile idiopathic arthritis (SoJIA) children with MAS.

Methods: Retrospective review of cases of MAS from a collected database of fourteen children with SoJIA from 2003 to 2008. Gene-specific polymerase chain reaction (PCR) primers were used to analyze the perforin A91V gene polymorphism.
Results: Fourteen patients (nine boys) were considered to have evidence of MAS, with age ranged from 4 months to 12 years.The primary diagnosis was systemic onset juvenile idiopathic arthritis.No medication was identified as trigger. Eleven had infections prior to MAS,specific infectious agents were identified in four. High fever, new onset hepatosplenomegaly, lymphadenopathy, liver dysfunction,abnormal lipid metabolism and hemophagocytosis were common clinical features.Two cases were with acute respiratory distress syndrome (ARDS),multiple organ failure (MOF) in three and three died. The perforin A91V (NCBI:SNP rs35947132) variant gene was detected in seven systemic onset juvenile idiopathic arthritis compolicated with MAS cases, but no mutation were found. Glucocorticoid, intravenous immunoglobulin, immunoimpressive therapy were effective and HP (Plasmapheresis) used in one serious case was also effective.
Conclusions: MAS is a rare and potentially fatal complication of childhood rheumatoid diseases,especially systemic onset juvenile idiopathic arthritis. Most of our patients were male, and most cases were preceded by infection. Bone marrow studies support the diagnosis. MOF may be a poor prognostic sign.Aggressive early therapy is essential.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1989

SAT0078 MAGNETIC RESONANCE IMAGING OF THE HANDS IN RHEUMATOID ARTHRITIS: UNILATERAL OR BILATERAL?

Y.-Q. Mo[1], Z.-H. Yang[2], H.-N. He[3], J.-D. Ma[1], J.-J. Liang[1], L. Dai[1].
[1]Rheumatology; [2]Radiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University; [3]Zhongshan School of Medicine, Guangzhou, China

Background: MRI had higher sensitivity of detecting inflammation than physical examination and higher sensitivity of detecting bone damage than X-rays. Physical examination and X-rays are usually performed on bilateral hands of RA patients, however, MRI evaluation of unilateral hand was recommended by OMERACT at the very beginning when RA MRI score (RAMRIS) was validated in the databases only consisting of images of dominant wrists and/or metacarpal phalangeal joints (MCPJs). Recently, high performance of whole-body MRI and multi-channel synergic coil enable simultaneous scan of bilateral hands.
Objectives: To explore the advantages of bilateral hands MRI on RA.

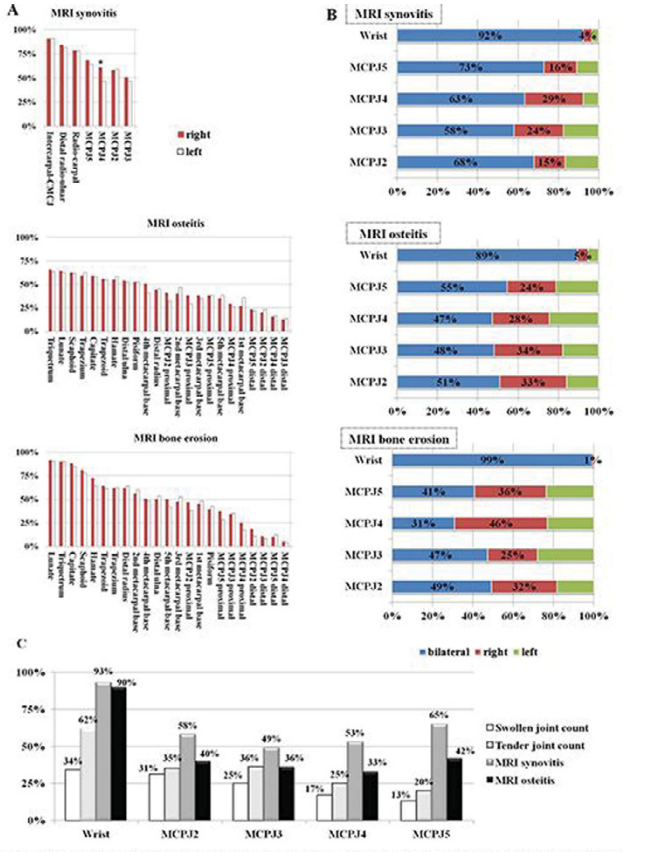


Figure 1 A: The frequencies of MRI synovitis, osteitis and bone erosion per joint or bone in the right and left hands of RA patients separately. B: The percentages of bilateral or unilateral involvement for each joint among patients with MRI synovitis, osteitis and bone erosion. C: The frequencies of joint swelling, tenderness, MRI synovitis and osteitis in wrists and MCPJ2~5 separately among 120 RA patients. MRI synovitis in the wrist included synovitis in distal radio-ulnar joint, radio-carpal joint and intercarpal-CMCJs. MRI osteitis in the wrist included osteitis in eight carpal bones, the distal radius, the distal ulna and five metacarpal bases. MRI osteitis in each MCPJ contained two parts: metacarpal head (proximal) and phalangeal base (distal). * p<0.05.

Methods: Consecutive hospitalized RA patients were recruited from April 2014 to April 2016 at Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University. Together with assessing swelling and tenderness of 28 joints essential for DAS28, bilateral wrists and MCPJ2~5 of each patient were scanned simultaneously on 3.0T MRI system. MRI synovitis, osteitis and bone erosion were scored referred to the definitions and atlas of RAMRIS system.
Results: (1) Among 120 RA patients were included, 79% were female, age (median and IQR, similarly hereinafter) was 52 (44~61) years, disease duration was 48 (12~120) months and DAS28-crp was 5.9 (4.7~6.9). The mean imaging time for the entire MRI examinations including the time of patient positioning and contrast agent injection was 23 minutes. The mean scoring time was 10 minutes for $RAMRIS_{bilateral\ hands}$ and 7 minutes for $RAMRIS_{unilateral\ hand}$. Interreader ICC for $RAMRIS_{bilateral\ hands}$ was 0.852 in synovitis, 0.739 in osteitis and 0.815 in bone erosion.
(2) The frequencies of MRI synovitis, osteitis and bone erosion per joint or bone were shown in figure1A. For MCPJ2~5, 27%~42% of RA patients showed unilateral synovitis, 45%~53% showed unilateral osteitis and 51%~69% showed unilateral bone erosion (Figure1B).
(3) Of wrists with MRI synovitis, 73% were not swollen and 48% were not tender at physical examination. Of wrists with MRI osteitis, 74% were not swollen and 49% were not tender. Similar trend was seen in MCPJ2~5 (Figure1C).
(4) The most clinically involved hands (or dominant hand in case of equally severe involved) were usually chosen for MRI of unilateral hand. Here 70 patients showed more severe involvement in unilateral hand according to patients' complaint and physical examination. However, MRI verified 42%, 40% and 42% of them respectively had more synovits, osteitis and bone erosion in the opposite hand. The other 50 patients had equally severe involvement at physical examination and the dominant hands were chosen. MRI verified 30%, 49% and 33% of them respectively had more synovits, osteitis and bone erosion in the non-dominant hand.
(5) $RAMRIS_{bilateral\ hands}$ was correlated positively with RA disease activity indices, X-ray Sharp/vdH total score and subscores (all $p<0.05$). Moderate correlation was found between $RAMRIS_{bilateral\ hands}$ in synovitis and ESR, CRP, TJC28, SJC28, DAS28, SDAI or CDAI (all $r>0.4$, $p<0.001$). Relatively high correlation was found between $RAMRIS_{bilateral\ hands}$ in bone erosion and X-ray Sharp/vdH total score or erosion subscore (all $r>0.7$, $p<0.001$).
Conclusions: Performing MRI of bilateral hands yields additive information compared with imaging only unilateral hand.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6106

SAT0079 ASSOCIATION OF ALCOHOL CONSUMPTION AND DISEASE ACTIVITY IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: ANALYSIS OF THE IORRA COHORT

Y. Shimizu[1], E. Tanaka[1], E. Inoue[1,2], M. Ochiai[1], R. Yamaguchi[1], N. Sugimoto[1], A. Nakajima[1], K. Ikari[1], A. Taniguchi[1], H. Yamanaka[1]. *[1]Tokyo Women's Medical University Institute of Rheumatology; [2]National Center for Child Health and Development Center for Clinical Research for Development, Tokyo, Japan*

Background: While the results of several observational studies suggest that light-to-moderate alcohol consumption may decrease the risk for susceptibility to or severity of rheumatoid arthritis (RA) (1–3), findings regarding the effect of alcohol consumption on RA disease activity are conflicting. Furthermore, there are few reports of longitudinal studies regarding the effect of alcohol consumption on RA disease activity. In addition, although alcohol consumption in the Japanese general population was lower than that in European countries, according to the 2011 World Health Organization's Global Status Report on Alcohol and Health, there are few reports specifically concerning alcohol consumption in Japanese RA patients.
Objectives: To examine the longitudinal relationship between alcohol consumption and changes in disease activity in patients with RA using the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort database.
Methods: Subjects were RA patients who participated in the IORRA cohort study between October 2014 and October 2015. Patients were assigned to one of 5 groups according to alcohol-drinking status at baseline: the non-drinking group, drinking group 1 (0 g < amount of drinking per day [Alco-drink] ≦14 g), drinking group 2 (14 g < Alco-drink ≦28 g), drinking group 3 (28 g < Alco-drink ≦50 g), and drinking group 4 (50 g < Alco-drink). Multiple regression analyses were used to examine the relationship between alcohol consumption and baseline DAS28, and change in DAS28 between baseline and 1 year.
Results: Data from a total of 4,695 Japanese patients with RA (female: 86.6%, mean age: 61.3 years old, mean disease duration: 15.2 years, and mean DAS28: 2.5) were analyzed. The number of patients and their characteristics (% female, mean age, mean disease duration, mean DAS28 at baseline/after 1 year) in the non-drinking group, and drinking groups 1, 2, 3, and 4 were 2,735 (92.8%, 64.0 years old, 16.1 years, 2.7/2.7); 646 (89.9%, 58.7 years old, 14.8 years, 2.4/2.5), 497 (82.5%, 56.7 years old, 13.8 years, 2.3/2.3), 444 (71.6%, 56.4 years old, 13.0 years, 2.3/2.3), and 373 (58.2%, 57.5 years old, 13.7 years, 2.2/2.3), respectively. Baseline DAS28 in drinking groups 2 (p=0.02), 3 ($p<0.01$), and 4 ($p<0.01$) was significantly lower than that in the nondrinking group. Multivariate regression analysis revealed that there was no association between alcohol-drinking status and the change in DAS28 at 1 year, after adjusting for DAS28 at baseline.

Conclusions: Although moderate-to-heavy alcohol consumption was associated with lower baseline DAS28 in patients, alcohol drinking status was not associated with change in disease activity, as measured by DAS28, at 1-year follow-up.

References:
[1] Di Giuseppe D. BMJ, 2012 Jul 10;345:e4230.
[2] Kallberg H. Ann Rheum Dis, 2009;68:222–7.
[3] Maxwell JR. Rheumatology (Oxford), 2010;49:2140–6.

Disclosure of Interest: Y. Shimizu: None declared, E. Tanaka Consultant for: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical., E. Inoue: None declared, M. Ochiai: None declared, R. Yamaguchi: None declared, N. Sugimoto Speakers bureau: Takeda Pharmaceutical and Bristol Myers Squibb., A. Nakajima Consultant for: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., Speakers bureau: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., K. Ikari Grant/research support from: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., Speakers bureau: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., A. Taniguchi Grant/research support from: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., Speakers bureau: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., H. Yamanaka Grant/research support from: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi- Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Consultant for: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Speakers bureau: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers.
DOI: 10.1136/annrheumdis-2017-eular.2340

SAT0080 CLINICAL SIGNIFICANCE OF SOLUBLE CD163 IN REFRACTORY SYSTEMIC-ONSET IDIOPATHIC ARTHRITIS

Y. Cui[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: The present study explored the correlation of soluble CD163 with refractory systemic-onset juvenile idiopathic arthritis (refractory So-JIA) as well as the clinical significanceof soluble CD163 in (refractory So-JIA).
Methods: A total of 33 young patients diagnosed with So-JIA in the active period and 30 young patients diagnosed with So-JIA in the inactive period at Guangzhou Women and Children's Medical Center (Guangzhou, China) from January 2010 to January 2012 as well as 40 age-matched healthy individuals, who had visited the hospital for medical examination in the same time-period were enrolled in the present study. Flow cytometry was used to determine the lymphocyte count and ELISA was adopted for determining the levels of soluble CD163 in serum
Results: The levels of soluble CD163 and their correlation with indexes of disease activity were observed. In patients with So-JIA in the active period, the levels of soluble CD163 and the Tcell count were significantly higher than those in the inactive So-JIA and healthy individuals ($P<0.05$). Furthermore, the levels of soluble CD163 were positively correlated with C-reactive protein, ferritin, erythrocyte sedimentation rate, white blood cell count and immunoglobulin E as indexes of disease activity ($P<0.05$).
Conclusions: Soluble CD163 is a more valuable index for early recognise refractory active So-JIA, which can provide a basis for active period development and clinical observation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1993

SAT0081 RELATIONSHIP BETWEEN RHEUMATOID FACTOR POSITIVITY AND TREATMENT EFFECT WITH A FIRST BIOLOGIC AGENT IN RHEUMATOID ARTHRITIS: MULTICENTER STUDY USING A MIXED-EFFECT MODEL

Y. Ogawa[1], N. Takahashi[2], N. Ishiguro[2], T. Kojima[2]. *[1]Sakashita Hospital, Nakatsugawa; [2]Nagoya University Graduate School of Medicine, Nagoya, Japan*

Background: Although the presence of rheumatoid factor (RF) may be a risk factor for the onset and progression of rheumatoid arthritis (RA), sufficient literature does not exist to support the clinical relationship between RF positivity and the effects of treatment with biologic disease-modifying antirheumatic drugs (bDMARDS). This multicenter study aimed to explore the association of RF positivity with the effects of bDMARDS treatment in bio-naïve RA patients using a linear mixed-effect model.
Objectives: In a multicenter study, patients are clustered within institutions, therefore results of adjustment models are likely to be biased by random, unobserved between-institution differences. Such bias could lead to inaccurate prediction and interpretation of outcomes. We used a linear mixed-effect model including between-institution variation as a random effect, which would improve the performance of this multicenter study.
Methods: In total, 625 bio-naïve RA patients registered in the Tsurumai Biologics Communication Registry (TBCR), which comprises Nagoya University and 15 affiliated institutions in Japan, who received bDMARDS treatment during the study period (2006–2016) were eligible for inclusion. Demographic information and disease characteristics were assessed at baseline. DAS28 using erythrocyte sedimentation rate was recorded at baseline and following 24 weeks of therapy. In order to predict DAS28 improvement at 24 week, a linear mixed-effect model including between-institution variation as a random effect, controlling for RF positivity, age, sex, stage, methotrexate (MTX) use, prednisolone (PSL) use, tumor necrosis factor inhibitor (TNFi) or non-TNFi, and DAS28 at baseline, was developed.
Results: Of the 625 patients, 513 showed RF positivity and 112 were antibody negative. Mean ± SD age at baseline was 56.9±14.0 years; 509 patients were women (81.4%). The mean ± SD DAS28 score at baseline was 5.19±1.24. Proportion of MTX and PSL use were 79.3% and 58.1%, respectively. Following adjustment for relevant covariates, RF positivity was associated with a decrease biologic treatment effect ($\beta = -0.33\pm0.12$, $p<0.05$). In another model including an additional interaction term of RF status and TNFi or non-TNFi, the influence of RF status on treatment effect was persistent ($\beta = -0.26\pm0.14$, $p<0.1$). These two models had comparable AIC. A model excluding RF positivity term had larger AIC than these two models, suggesting that RF positivity is crucial for predicting the effect of bDMARDS treatment.

Fixed effects

	β coefficient estimate	Std. Error	p value
(Intercept)	0.18	0.42	0.67
RF positivity	-0.33	0.12	<0.05
DAS28 at baseline	0.74	0.041	<0.05
Age	-0.016	0.0037	<0.05
Female gender	-0.35	0.12	<0.05
Non-TNFi use (TNFi as reference)	0.29	0.12	<0.05
Methotrexate use	0.084	0.12	0.51
Prednisolone use	-0.23	0.10	<0.05
Stage	-0.24	0.10	<0.05

Conclusions: In our multicenter study using a linear mixed-effect model including between-institution variation as a random effect, RF positivity, in addition to some well-known variables, was found to be independently associated with decreased effects of bDMARDS treatment in bio-naïve RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1508

SAT0082 THE INVESTIGATION FOR THE INFLUENCE OF SILASTIC ARTHROPLASTY OF METACARPOPHALANGEAL JOINT ON THE ACTIVE EXTENSION RANGE OF PROXIMAL INTERPHALANGEAL JOINT IN THE RHEUMATOID HAND

Y. Sakuma, M. Nakayama, H. Tobimatsu, H. Imamura, K. Yano, K. Ikari. *Orthopedic Surgery, Institute of Rheumatology, Tokyo Women's Medical University, Tokyo, Japan*

Background: The ulnar deviation (Ud) deformity of the metacarpophalangeal (MCP) joints is a typical deformity in the patients of rheumatoid arthritis (RA). Joint replacement arthroplasty can be indicated for the treatment of severe Ud deformity, silastic prosthesis being widely used with generally good results [1]. There are few, however, previous reports focusing on the relationship between the range of motion (ROM) of the MCP and PIP joints after the surgery.
Objectives: The objective of this study was to investigate the influence of silastic replacement arthroplasty of MCP joint replacement on post-operative extension range of PIP joint of the same finger.
Methods: RA patients who underwent silastic replacement arthroplasty of at least 1 MCP joint except for thumb for the treatment of Ud deformity were reviewed. There were 80 hands of 65 patients, average age of whom was 70.1 (32.4 - 86.1) years old, 56 patients being female and 9 being men. The ROM of the PIP joints before and after surgery was collected from the medical records, and the relationship between the post-operative change of ROM in PIP joints and post-operative ROM of in the MCP joint of same finger was examined. Paired-t test and the correlation coefficient were used for statistical analysis.
Results: The mean active extension range of PIP joints in index to little finger changed from -0.68° (-56.0–30.0) to 0.92° (-52.0–30.0)° [P=0.55], -5.64° (-104.0–30.0) to -8.44° (-56.0–30.0) [P=0.03], -3.44° (-112.0–32.0) to -8.91° (-94.0–40.0) [P=0.08], and -9.81° (-96.0–30.0) to -17.2° (-76.0–30.0) [P=0.07], respectively. There was an indication of a decrease in post-operative extension range of PIP joint except for the index finger. The ROM of the PIP joint was reduced only in the little finger, but was significantly increased in the index and middle finger. Correlation coefficients between the active flexion range of the MCP joint and the active extension range of the PIP joint of index to little finger was 0.34, 0.19, 0.08, and 0.33 respectively, no correlation being found.
Conclusions: Post-operative decline in active extension of the PIP joint might be a compensatory change accompanying a shift of the arc of motion of the

replaced MCP joint to a more extended position [2]. However, since the correlation between extension deficit of PIP join and MCP joint flexion range was not actually observed, it is unlikely that a decrease in the extension of the PIP joint is a result of compensation. There is a possibility that the procedure such as intrinsic tendon release, bone shortening by resection of metacarpal head, and centralization of extensor tendon [3], might influence the postoperative PIP joint motion. It is necessary to pay attention to changes in the ROM of the PIP joint after joint replacement arthroplasty of MCP joint.

References:
[1] Escott BG, Ronald K, Judd MG, Bogoch ER. NeuFlex and Swanson metacarpophalangeal implants for rheumatoid arthritis: prospective randomized, controlled clinical trial. J Hand Surg Am. 2010 Jan;35(1):44–51.
[2] Mannerfelt L, Andersson K. Silastic arthroplasty of the metacarpo- phalangeal joints in rheumatoid arthritis. J Bone Joint Surg 1975; 57A:484 – 489.
[3] Swanson AB. Flexible implant arthroplasty for arthritic finger joints: rationale, technique, and results of treatment. J Bone Joint Surg Am. 1972 Apr;54(3):435–55.

Acknowledgements:.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4536

SAT0083 TOCILIZUMAB INDUCED CLINICAL REMISSION IN RHEUMATOID ARTHRITIS HAD MORE RESIDUAL DOPPLER SIGNALS IN COMPARISON WITH OTHER BIOLOGICS

Y. Hara[1], Y. Ishida[1], Y. Yamaguchi[1], Y. Yoshimine[1], T. Wibowo[1], Y. Manabe[1], M. Yaga[2], K. Kawamoto[1], H. Nakahara[1], S. Higa[1], T. Igarashi[1], K. Maeda[1], A. Ogata[1]. *[1]Division of Allergy, Rheumatology and Connective Tissue Diseases, Department of Internal Medicine; [2]Respiratory Medicine, Department of Internal Medicine, Ntt West Osaka Hospital, Osaka, Japan*

Objectives: To study the residual Power Doppler (PD) signals for assessing synovitis in CRP negative patients with rheumatoid arthritis (RA) treated with biologics.
Methods: Biologics treated RA patients who were maintained normal CRP for more than 6months (34 TNF inhibitors, 37 Tocilizumab, 23 Abatacept) were assessed by ultrasonography. Residual PD signals were assessed in MCP, PIP, and wrist joints with both hands. We assumed patients who had any PD signals in assessed joints were “residual PD signals”.
Results: All treated patients with biologics maintained normal CRP for a half year (n=94). 35.1% of patients treated with biologics had positive PD signals. The remission rates of DAS28-ESR, CDAI, and Boolean were 68.7%, 62.8%, and 48.9% respectively. 28.1% of patients who achieved DAS28-ESR remission had residual PD signals, 22.0% in CDAI, and 21.7% in Boolean. 23.8% of patients treated by TNF inhibitors who achieved DAS28-ESR remission had residual PD signals, 34.6% in Tocilizumab, and 20.0% in Abatacept. In case of setting the DAS28-ESR remission less than 3.0, 30.2% of patients who achieved DAS28-ESR remission had residual PD signals, 29.0% in less than 2.0, and 12.5% in less than 1.5. The patients who have no tender or swollen joints and the excellent patient oriented global health assessment (VAS score was zero) had fewer residual PD signals (23.4% vs 58.6% in tender joints, 26.7% vs 66.7% in swollen joints, and 13.3% vs 44.4% in patient VAS).

Table 1. Rate of remission and residual PD signals

	All biologics	TNF inhibitors*	Tocilizumab	Abatacept
Patients number	94	34	37	23
Residual PD signals**	33/94 (35.1%)	9/34 (26.4%)	15/37 (40.5%)	9/23 (39.1%)
DAS28-CRP remission				
Achieved***	78/94 (83.0%)	32/34 (94.1%)	31/37 (83.8%)	15/23 (65.2%)
Residual PD signals	22/78 (28.2%)	8/32 (25.0%)	10/31 (32.3%)	4/15 (26.7%)
DAS28-ESR remission				
Achieved	57/94 (68.7%)	21/34 (72.4%)	26/37 (78.8%)	10/23 (47.6%)
Residual PD signals	16/57 (28.1%)	5/21 (23.8%)	9/26 (34.6%)	2/10 (20.0%)
CDAI remission				
Achieved	59/94 (62.8%)	26/34 (76.5%)	23/37 (62.2%)	10/23 (43.5%)
Residual PD signals	13/59 (22.0%)	5/26 (19.2%)	7/23 (30.4%)	1/10 (10.0%)
Boolean remission				
Achieved	46/94 (48.9%)	21/34 (61.8%)	17/37 (45.9%)	8/23 (34.8%)
Residual PD signals	10/46 (21.7%)	5/21 (23.8%)	4/17 (23.5%)	1/8 (12.5%)

*TNF inhibitors (Infliximab (n=6), Etanercept (n=14), Adalimumab (n=7), Golimumab (n=4), Certolizumab pegol (n=3)). ** Residual PD signals: patients who had any PD signals in asessed joints. ***Achieved: remission rate in biologics treated patients who were maintained normal CRP for a half year.

Conclusions: The patients who achieved clinical remission had residual PD signals. Patients with Tocilizumab induced remission had more residual PD signals compared with TNF inhibitor or Abatacept induced remission. More strict criteria of clinical remission may reduce residual PD signals in patients treated by Tocilizumab.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2417

SAT0084 CHARACTERISTICS OF PATIENTS WHO RESPOND POORLY TO REDUCTION OF BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS; RT-4 STUDY POST HOC ANALYSIS

Y. Urata[1], S. Abe[2], B. Devers[2], Y. Nakamura[3], H. Takemoto[4], K.-I. Furukawa[5]. *[1]Department of Rheumatology, Tsugaru General Hospital, Gosyogawara; [2]Marketing Department, Diagnostics Division, Sekisui Medical Co., Ltd., Tokyo; [3]Department of Orthopedic Surgery; [4]Department of Dermatology, Tsugaru General Hospital, Gosyogawara; [5]Department of Pharmacology, Hirosaki University Graduate School of Medicine, Hirosaki, Japan*

Background: A number of studies have shown that reduction of biological disease-modifying anti-rheumatic drugs (bDMARDs) is possible for rheumatoid arthritis (RA) patients in whom bDMARD treatment has induced clinical remission or low disease activity. However, there have been few studies which have evaluated the background characteristics of patients who have difficulty in reducing bDMARDs despite being in clinical remission or having low disease activity.
Objectives: To clarify the characteristics of RA patients who have difficulty with bDMARD reduction despite maintaining clinical remission in the rT-4 study.
Methods: This study is a post-hoc analysis of the rT-4 study. Briefly introducing the rT-4 study: 209 RA patients demonstrating both SDAI remission and MMP-3 normalization using bDMARDs for $\geq$3months were randomly allocated to one of four strategy groups: Standard care (SC group; n=50); SDAI-driven therapy (n=53); MMP-3-driven therapy (n=55); or both SDAI and MMP-3-driven therapy group (Twin; T group; n=51). Dose reduction methodology (every 3 months): ettanercept (ETN) - period between injections increased by one week; tocilizumab (TCZ) - dose reduced by 80mg or period between injections increased by one week; up to a minimum dose of: ETN - 25 mg every 5 weeks; TCZ - 80 mg every 5 weeks or 162 mg every 5 weeks. The dose was reverted to the previous level in the event that the target scores were exceeded, and the lower dose was eventually reattempted after the target was re-achieved. The primary outcome was the difference in the proportion of patients who maintained remission at 12 months among the four groups, compared against a non-inferiority margin of 10%. The results of the rT-4 study revealed that a twin target strategy can achieve effects non-inferior to standard care with regard to maintaining clinical remission. Specifically, subgroup analysis was carried out between the T and SC groups of the rT-4 study. A factor was defined as significant when the difference in the proportion of patients who maintained remission at 12 months in the two groups across subgroups, exceeded 10%.
Results: The requisite margin was recognized only for rheumatoid factor (RF) negativity (35.2%; 95% CIs of 14.4 to 65.0). Others factor were not identified.
Disease activity is likely to be affected by even a small dose reduction of bDMRADS in RA patients who are RF negative, regardless of the presence or absence of anti-citrulline antibody, and it can probably be explained as a nocebo effect. Nocebo effects occur in studies which investigate the effectiveness of drug reduction, and we believe that the nocebo effect is prone to happen in RF-negative patients.
Conclusions: The twin target strategy can be used to reduce the dose of bDMARDs for RA patients while maintaining the effectiveness of said bDMARDs, with the exception of RF negative patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2498

SAT0085 A STUDY ON CHARACTERISTICS OF RHEUMATOID ARTHRITIS PATIENTS ACHIEVING DEPRESSION REMISSION WITH 6 MONTHS OF BIOLOGIC AGENT TREATMENT

Y. Miwa[1], N. Yajima[1], T. Isozaki[1], R. Takahashi[1], Y. Miura[1], Y. Ikari[1], M. Hatano[1], T. Hayashi[1], T. Kasama[1], K. Sanada[2] on behalf of ASHURA Registry Group. *[1]Division of Rheumatology, Department of Medicine; [2]Department of Psychiatry, Showa University School of Medicine, Tokyo, Japan*

Background: Approximately 15% of RA patients also suffer from depression, with an odds ratio of 1.42 (95% CI 1.3 - 1.5) compared with healthy people. A previous study reported that biological agents can improve the depressed state associated with RA. Although previous studies have been cross-sectional, there were no reports that analyzed factors that led to depression remission.
Objectives: To examine the relationship between baseline factors and depression remission after six-month biologic agent treatment in rheumatoid arthritis (RA) patients.
Methods: The subjects were 384 RA patients treated with biologic agents. The following patient’s characteristics were investigated: age, gender, number of previous drugs, disease duration, type of biologic agents, baseline steroid dosage, methotrexate dosage and serum matrix metalloproteinase-3 (MMP-3) levels. For evaluation, we used the Simplified Disease Activity Index for RA disease activity; the Health Assessment Questionnaire Disability Index (HAQ-DI) score for activities of daily living; the Short Form-36 for nonspecific health-related quality of life; and Hamilton Depression Rating Scale (HAM-D) scores for depression status. Depression remission was defined by HAM-D$\leq$7 after 6 months of treatment. The subjects were divided into two groups according to the presence or absence of depression, and a retrospective study was performed.
Results: We included 152 patients in the analysis. Two hundred thirty-two

patients were excluded due to primary and secondary failure, complications, loss to 6-month follow-up, incomplete data, etc. Compared with a group of RA patients with depression remission (n=124), a group of patients with no depression remission (n=28) had a younger age (p=0.000), female sex (p=0.039), lower serum MMP-3 levels (p=0.021), lower HAQ-DI (p=0.018), lower HAM-D score (p=0.000), and higher Role/Social component summary score of the SF-36 (p=0.009) by univariate analyses. The binominal logistic analyses findings were as follows: younger age (p=0.0045, odd ratio: 0.94, 95% CI: 0.8–0.98), female sex (p=0.021, odd ratio: 0.21, 95% CI: 0.054–0.79), and lower HAM-D scores (p=0.0073, odd ratio: 0.85, 95% CI: 0.76–0.96).

Conclusions: It was suggested that RA patients who are female, younger in age and have lower depression scores at baseline are more likely to achieve depression remission status with the biologic treatment.

Acknowledgements: All Showa University in Rheumatoid Arthritis (ASHURA) group

Disclosure of Interest: Y. Miwa Grant/research support from: Astellas Pharma Inc., Mitsubishi Tanabe Pharma Corporation, Pfizer Japan Inc., Chugai Pharmaceutical Co., Ltd., and Eizai Co., Ltd., Ono Pharma Co., Ltd., N. Yajima: None declared, T. Isozaki: None declared, R. Takahashi: None declared, Y. Miura: None declared, Y. Ikari: None declared, M. Hatano: None declared, T. Hayashi: None declared, T. Kasama Grant/research support from: Mitsubishi Tanabe Pharma Corporation and Pfizer Japan Inc., K. Sanada: None declared

DOI: 10.1136/annrheumdis-2017-eular.1443

SAT0086 THE ASSOCIATION BETWEEN ELDERLY RHEUMATOID ARTHRITIS PATIENTS USING BIOLOGICS AND ADVERSE EVENTS: RETROSPECTIVE COHORT STUDY

Y. Ikari, Y. Miwa, N. Yajima. *Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Hatanodai Shinagawaku Tokyo, Japan*

Background: In Japan, the definition of the elderly was suggested as being over 75 years old by the Japan Geriatric Society. The effectiveness of biologics in elderly rheumatoid arthritis (RA) patients has been demonstrated in several clinical trials and cohort studies[1]. On the other hand, regarding safety, there are reports that the use of biologics in elderly RA patients is a significant risk for severe infections and that they do not increase the risk of serious infection [2,3]. There is little evidence to support the association between age of RA patients and adverse events caused by biologics.

Objectives: We aimed to examine whether the age of RA patients was associated with adverse events caused by biologics.

Methods: RA patients using biologics were eligible. The participants were collected at Showa University Hospital, Showa University Northern Yokohama Hospital and Showa University Koto Toyosu Hospital from 2005 to 2016 in a retrospective cohort study.

RA patients of 75 years and above compared with RA patients under 75 years.

The primary outcome was the rate of discontinuation due to adverse events caused by biologics. Statistical analysis was Pearson's chi-square test. Multivariable analysis was performed by multi linear analysis. Covariates were sex, glucocorticoids dose, csDMARDs, interstitial pneumonia, diabetes mellitus and chronic kidney disease.

Results: In total, 309 patients were enrolled. The mean age standard deviation was 57.1±15.6years, and 83.4% were women. 174 (56.3%) took glucocorticoid, and the mean glucocorticoid dose was 3.13±3.9mg.The patients over 75 years were 42 patients (13.6%), and those under 75 years were 267 patients (86.4%). The rate of discontinuation due to adverse events caused by biologics was 11/42 (26.2%) in the patients over 75 years and over, and 21/267 (7.9%) in the patients under the age of 75 (Relative Risk 1.24; 95% Confidential Interval (CI) 1.04 to 1.50; P 0.0003). Adverse events were bacterial pneumonia, pneumocystis pneumonia, exacerbation of interstitial pneumonia, urinary tract infection, herpes zoster, cytopenia, eruption, congestive heart failure. In the multivariable analysis adjusting for confounders, the rate of discontinuation in the group aged 75 years and older was significantly higher than that in the group under the age of 75 (regression coefficient 1.35; 95% CI 0.39–2.31; p=0.006).

Conclusions: Our results demonstrated that the rate of discontinuation due to adverse events by biologics was high significantly in RA patients over 75 years and above.

References:

[1] Genevay S, Finckh A, Ciurea A et al. Tolerance and effectiveness of anti-tumor cecrosis factor alpha therapies in elderly patients with rheumatoid arthritis:a population-based cohort study.Arthritis Rheum 2007;57(4):679–85.

[2] Galloway JB, Hyrich KL, Mercer LK et al. Anti-TNF therapy is associated with an increased risk of serious infections in patients with rheumatoid arthritis especially in the first 6 month of treatment:updated resurts from the British Society for Rheumatology Biologics Register with special emphasis on risks in the elderly. Rheumatology (Oxford) 2011;50(1):124–31.

[3] Widdifield J, et al. Serious infections in a population-based cohort of 86,039 serious with rheumatoid arthritis. Arthritis Care Res (Hoboken) 2013;65(3):353–61.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5823

SAT0087 THE RELEVANCE OF POOR PROGNOSTIC FACTORS FOR ACHIEVING LOW DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A COLLABORATIVE ANALYSIS OF THREE GERMAN COHORTS

Y. Meissner[1], K. Albrecht[1], A. Richter[1], L. Baganz[1], D. Huscher[1], M. Schneider[2], A. Strangfeld[1], A. Zink[1,3]. *[1]German Rheumatism Research Center, Berlin; [2]Heinrich-Heine University, Duesseldorf; [3]Charité University Medicine, Berlin, Germany*

Background: Poor prognostic factors (PPF) are used as decision-criteria for treatment strategies in patients with rheumatoid arthritis (RA). However, their definition is based on the outcome of rapid radiologic progression.

Objectives: To investigate the impact of PPF in RA on achieving low disease activity (LDA) at follow-up.

Methods: We performed a collaborative analysis of three large German RA cohorts. Patients under routine care were either DMARD-naïve (n=991, early arthritis cohort CAPEA), on 1st conventional synthetic (cs)DMARD (n=2,547, National Database of the German Arthritis Centres (NDB)), or switching to a 2nd (n=1,959) or a 3rd DMARD (n=1,854, both biologics register RABBIT). Disease activity based on DAS28, autoantibody positivity (RF+/ACPA+), erosions, disability (HAQ≥1.2) and intake of glucocorticoids (>5mg/d) were evaluated as PPF at baseline. The outcome was DAS28 at 0, 3, 6 and 12 months. With multinomial logistic regression analyses, predictors of either LDA (DAS28<3.2) at 12 months or treatment escalation (adding or switching to cs/biologic (b)DMARD) were investigated.

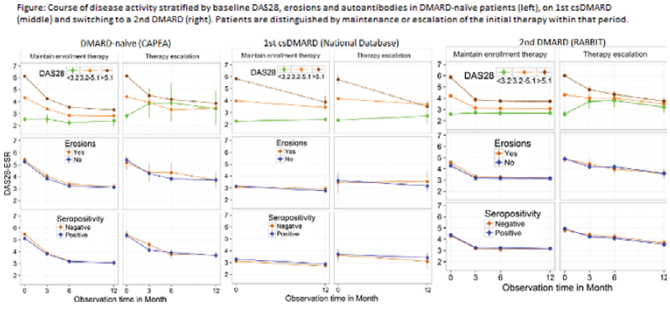
Results: Patients had a mean age of 57 to 60 years; 63% of DMARD-naïve patients and 71–72% of all others were female. Disease duration was 13 weeks in early RA (CAPEA) and 5–8 years in other cohorts. Patients with more treatment failures had more often PPF (not shown).

The figure shows the course of disease activity stratified by baseline DAS28, erosions and RF/ACPA. Values of DAS28 at baseline did not differ depending on presence/absence of erosions and autoantibodies. In all cohorts, irrespective of maintaining or escalating the initial treatment, patients with or without erosions and autoantibodies had similar DAS28 outcomes, whereas patients with moderate or high baseline DAS28 had higher disease activity during follow-up. The proportion of patients that did not achieve LDA at 12 months was 46% in DMARD-naïve, 34% on 1st DMARD, 47% switching to 2nd and 49% switching to 3rd DMARD.

In the multinomial model, a 1-unit increase in DAS28 was associated with a decreased probability to achieve LDA in all cohorts (table). In contrast, autoantibodies (OR from 0.8 to 1.3) and erosions (OR from 0.8 to 1.6) had no impact on achieving LDA at month 12 or on treatment escalation. The latter applied for DAS28 (OR from 0.9 to 1.5) and HAQ (OR from 0.7 to 1.2) regarding only treatment escalation.

Table 1. Selected OR (95% CI) of multinomial logistic regression

	DMARD-naïve	1st DMARD	2nd DMARD	3rd DMARD
Predictiors of LDA				
Age (by 5 yrs)	0.96 (0.9–1.0)	0.9 (0.8–0.99)	0.95 (0.91–0.99)	0.96 (0.9–1.0)
DAS28 (per 1 unit)	0.8 (0.6–0.9)	0.6 (0.4–0.9)	0.7 (0.6–0.8)	0.6 (0.6–0.7)
HAQ ≥1.2	0.9 (0.6–1.3)	1.1 (0.6–1.9)	0.6 (0.5–0.8)	0.6 (0.4–0.7)
GC >5 mg/d	1.6 (1.2–2.3)	0.6 (0.3–1.3)	1.0 (0.8–1.3)	0.99 (0.8–1.3)
b vs. csDMARD	–	–	1.4 (1.0–1.9)	1.4 (1.0–1.8)
Predictors for treatment escalation				
Age (by 5 years)	0.9 (0.9–0.98)	0.8 (0.7–0.9)	0.9 (0.8–0.9)	0.9 (0.9–0.96)
GC >5 mg/d	1.3 (0.8–1.9)	4.2 (1.6–11.0)	1.5 (1.1–2.0)	1.5 (1.2–2.0)



Conclusions: Although autoantibodies and erosions were associated with treatment failure, their absence did not predict LDA. Instead, baseline disease activity, functional status and glucocorticoid use may be more useful to guide treatment strategies when LDA is the target.

Disclosure of Interest: Y. Meissner Grant/research support from: CAPEA: funded by an unconditional grant from Pfizer. NDB: funded by unconditional grants from the German Collaborative Arthritis Centres and from a consortium of 11 pharmaceutical companies to the German Academy for Continuing Medical Education in Rheumatology. RABBIT: supported by a joint, unconditional grant from AbbVie, BMS, Celltrion, MSD, Pfizer, Roche, Samsung and UCB., K. Albrecht: None declared, A. Richter Consultant for: Pfizer, L. Baganz: None declared, D. Huscher: None declared, M. Schneider Grant/research support from: Abbvie, Chugai, UCB, Consultant for: Abbvie, Astra-Zeneca, BMS, Boehringer-

Ingelheim, Chugai, Lilly, MSD, Pfizer, Roche, Sanofi-Aventis, UCB, A. Strangfeld Speakers bureau: BMS, MSD, Pfizer, Roche, Sanofi-Aventis, A. Zink Speakers bureau: AbbVie, BMS, MSD, Pfizer, Roche, UCB
DOI: 10.1136/annrheumdis-2017-eular.4697

SATURDAY, 17 JUNE 2017

Rheumatoid arthritis - comorbidity and clinical aspects

SAT0088 HDL CHOLESTEROL EFFLUX CAPACITY IN RHEUMATOID ARTHRITIS PATIENTS: CONTRIBUTING FACTORS AND RELATIONSHIP WITH SUBCLINICAL ATHEROSCLEROSIS

B. Tejera Segura[1], M. Macía-Díaz[2], J.D.M. Machado[2], A. de Vera-González[3], A. González-Delgado[3], J.M. Olmos[4], J.L. Hernández[4], F. Díaz-González[1], M.A. González-Gay[5], I. Ferraz-Amaro[1]. *[1]Division of Rheumatology; [2]Pharmacology Department; [3]Central Laboratory Division, Hospital Universitario de Canarias, Tenerife; [4]Division of Internal Medicine; [5]Rheumatology Department, Hospital Universitario Marqués de Valdecilla-IDIVAL, Santander, Spain*

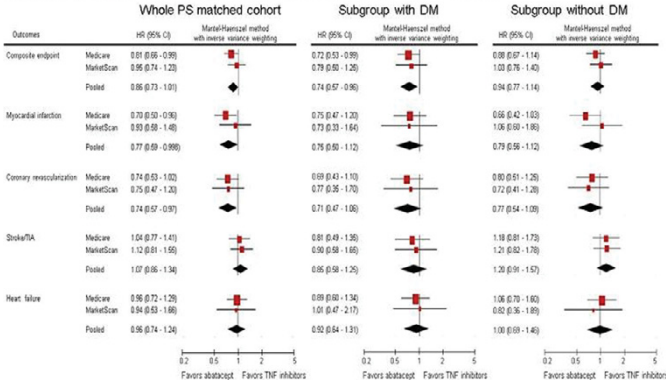
Background: Lipid profiles appear to be altered in rheumatoid arthritis (RA) patients due to disease activity and inflammation. Cholesterol efflux capacity (CEC) has not only been linked to cardiovascular events in the general population, but also to be impaired in RA patients.
Objectives: To analyze whether CEC is related to subclinical atherosclerosis, as determined by the presence of carotid plaque or increased levels of carotid intima-media thickness (cIMT) in RA patients. Secondarily, we aimed to describe the disease-contributing factors that are related to CEC as an expression of the abnormalities in the lipid profile associated with the disease.
Methods: Cross-sectional study that encompassed 401 individuals; 178 patients with RA and 223 sex-matched controls. CEC was measured using an *in vitro* assay, lipoproteins serum concentrations, and standard lipid profile were assessed in patients and controls. Carotid intima-media thickness and carotid plaques were assessed in RA patients. A multivariable analysis was performed to evaluate the relation of CEC with RA-related data, lipid profile and subclinical carotid atherosclerosis.
Results: Mean CEC was not significantly different between RA patients (18.9 ± SD 9.0%) and controls (16.9±10.4%), p=0.11. Demographic variables were not associated with CEC except for a correlation with male gender that was only found in RA patients, but not in controls. Systolic blood pressure inversely correlated with CEC in controls (beta coefficient -0.1 [-0.2–0.0] %, p=0.025). In RA patients, a similar trend was found although a statistically significant difference was not reached. Neither the traditional cardiovascular risk factors nor the cardiovascular co-morbidity-related data were associated with CEC. Similarly, lipid profile did not show any relationship with CEC in patients or controls. ESR tended to be associated with a lower CEC although it did not reach statistical significance. RA patients with low (beta coef. -5.2 [-10.0–0.3] %, p=0.039) and moderate disease activity (beta coef. -4.6 [-8.5–0.7] %, p=0.020) were associated with inferior levels of CEC when compared to patients in remission. CEC was not found to be associated with cIMT in RA patients. However, higher CEC was associated with a protective effect for the presence of carotid plaque in RA patients. This relationship was maintained even after multivariate analysis (OR 0.94 [0.89–0.98], p=0.015).
Conclusions: Our study, which includes the largest series of RA patients ever assessed for CEC, reveals for the first time that CEC is related to subclinical atherosclerosis in RA patients. The fact that CEC is also associated with disease activity reinforces the idea that CEC may be a mediator between disease activity and subclinical atherosclerosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4100

SAT0089 COMPARATIVE CARDIOVASCULAR SAFETY OF ABATACEPT AND TUMOR NECROSIS FACTOR INHIBITORS IN RHEUMATOID ARTHRITIS PATIENTS WITH AND WITHOUT TYPE 2 DIABETES: A POPULATION-BASED COHORT STUDY

E.H. Kang[1,2], Y.P. Jin[1], G. Brill[1], J.P. Lewey[1,3], E.P. Patorno[1], R. Desai[1], S.C. Kim[1]. *[1]Division of Pharmacoepidemiology and Pharmacoeconomics, Harvard Medical School and Brigham and Women's Hospital, Boston, United States; [2]Division of Rheumatology Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea, Republic Of; [3]University of Pennsylvania, Philadelphia, United States*

Background: Patients with rheumatoid arthritis (RA) are at high risk of developing cardiovascular disease (CVD) and may benefit from potent disease-modifying anti-inflammatory drugs such as biologics. Since diabetes mellitus (DM) is a major risk factor for CVD, RA patients with DM constitute a high CVD risk subgroup, calling for particular attention. However, there is a lack of knowledge on the comparative cardiovascular safety of different biologics in RA patients with DM.
Objectives: To examine the comparative cardiovascular safety of abatacept versus TNF inhibitors in RA patients with and without DM.
Methods: RA patients enrolled in both public (Medicare) and commercial (Truven MarketScan) health plans in the U.S. who newly initiated abatacept or TNF inhibitors were eligible. The primary outcome of interest was a composite CVD endpoint of myocardial infarction (MI), stroke/transient ischemic attack (TIA), and coronary revascularization. The secondary outcomes included each component of the composite CVD endpoint and heart failure (HF). After 1:1 propensity score (PS) matching between two exposure groups, Cox proportional hazard model was used to estimate the hazard ratio (HR) and 95% confidence interval (CI) for each outcome, comparing abatacept to TNF inhibitors. PS matching was separately done in subgroups with or without baseline DM in each database. PS-matched HRs from the two databases were pooled using an inverse variance–weighted fixed-effect model.
Results: We identified 31,899 Medicare enrollees (6,107 new users of abatacept and 25,792 new users of TNF inhibitors) and 71,956 commercial enrollees (6,942 new users of abatacept and 65,464 new users of TNF inhibitors) with RA. After PS matching, 2,119 pairs with DM and 3,984 pairs without DM were identified in Medicare and 1,371 pairs with DM and 5565 pairs without DM in MarketScan. The PS matched HR (95% CI) for the composite CVD endpoint in the whole cohort was 0.81 (0.66–0.99) in Medicare and 0.95 (0.74–1.23) in MarketScan with a pooled HR (95% CI) of 0.86 (0.73–1.01). In the subgroup with DM, HR (95% CI) for composite CVD endpoint was 0.72 (0.53–0.99) in Medicare and 0.79 (0.50–1.25) in MarketScan with a pooled HR (95% CI) of 0.74 (0.57–0.96). In the subgroup without DM, HR (95% CI) was 0.88 (0.67–1.14) in Medicare and 1.03 (0.76–1.40) in MarketScan with a pooled HR (95% CI) of 0.94 (0.77–1.14). For secondary outcomes (Figure 1), the pooled HR (95% CI) was 0.77 (0.59–1.00) for MI and 0.74 (0.57–0.97) for coronary revascularization in the whole cohort. There was a trend toward a decreased risk, albeit statistically insignificant, for MI and coronary revascularization in each subgroup. There was no significant difference in the risk for stroke/TIA and HF.

Figure 1. Cardiovascular safety of abatacept compared to TNF inhibitors

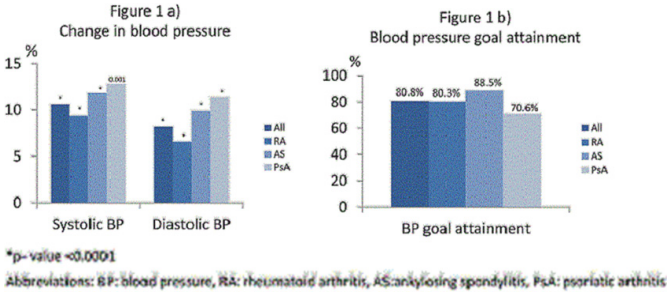


Conclusions: Among RA patients, abatacept may be associated with a reduced risk of coronary events compared to TNF inhibitors, particularly in patients with DM. The risk of HF was not different between these two groups.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2407

SAT0090 SUCCESS RATE OF BLOOD PRESSURE GOAL ACHIEVEMENT IN INFLAMMATORY JOINT DISEASES

S. Rollefstad, P. Norheim, E. Ikdahl, G. Wibetoe, A.G. Semb. *Preventive Cardio-Rheuma Clinic, Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*

Background: The excess risk of cardiovascular disease (CVD) in patients with inflammatory joint diseases (IJD) is attributable to several risk factors, including a high prevalence of hypertension. However, there is limited knowledge on the effect of antihypertensive treatment (a-HTT) in these patients.
Objectives: Our objective was to initiate a-HTT when indicated and treat to guideline recommended blood pressure (BP) goal in IJD patients. We also aimed to evaluate the effect of a-HTT in this patient population, and which factors were associated with BP goal attainment.
Methods: Patients with IJD (n=765) were referred from a rheumatology outpatient clinic or general practitioners to a preventive cardio-rheuma clinic. All patients underwent a CVD risk evaluation, including BP measurements (performed using and Omron M7 apparatus). Antihypertensive treatment was initiated in accordance with guidelines, and the BP treatment goal was <140/90 mmHg.
Results: Of the 765 IJD patients referred (rheumatoid arthritis n=450, ankylosing spondylitis n=210 and psoriatic arthritis n=105), 104 (13.6%) had an indication for BP lowering, while 224 (29.3%) were already using a-HTT at the first consultation. For those where a-HTT was initiated at baseline (n=104), there was a highly significant change in BP from first to final consultation (Fig 1a). BP goal was achieved in 84 (80.8%) patients (Fig 1b), using mean±SD 3.1±1.7 consultations. Dose adjustments was done in 38 (36.5%) of the patients with median (IQR) a-HTT dose adjustments of 1 (1, 1.25). In 9 (8.7%) patients the

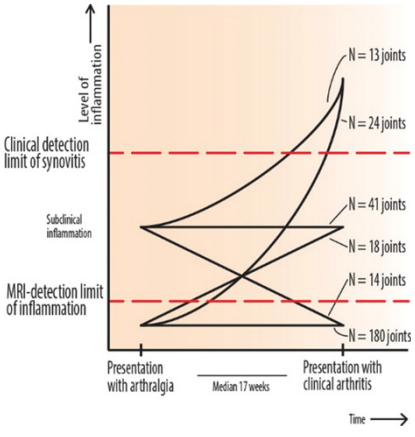


a-HTT was changed. Systolic BP ($p<0.0001$) was significantly associated with BP goal attainment in age- and sex adjusted logistic regression analyses, while the use of anti-rheumatic medication or inflammatory biomarkers at baseline was not. Patients with the lowest systolic BP were more likely to achieve BP goals. For patients already on a-HTT (n=224), only 52.7% had a BP <140/90 mmHg at baseline. After up titration or change of a-HTT, the percentage of patients achieving BP goal in this group increased to 82.6%.
Conclusions: This is to our knowledge the first prospective report on success rate of BP goal achievement in patients with IJD. Approximately 80% reached BP target, which is even a higher proportion than what is shown in the general population. Treatment to BP goal is feasible in patients with IJD, and is not complicated by inflammation or use of anti-rheumatic medication.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6937

SAT0091 IS CLINICAL ARTHRITIS ALWAYS PRECEDED BY SUBCLINICAL INFLAMMATION? A LONGITUDINAL STUDY AT JOINT LEVEL IN PATIENTS WITH ARTHRALGIA THAT DEVELOPED ARTHRITIS

R.M. Ten Brinck, H.W. van Steenbergen, A.H. van der Helm-van Mil.
Rheumatology, Leiden University Medical Centre, Leiden, Netherlands

Background: The clinical phase of Rheumatoid arthritis (RA) is preceded by a phase with subclinical inflammation. MRI can detect subclinical inflammation and, at patient level, this is predictive for the development of clinical arthritis. However, at joint level it is unknown how arthritis develops. It is unknown how frequently joints with subclinical inflammation progress to clinical arthritis, and vice versa, how often joints that developed clinical arthritis had local subclinical inflammation during the preceding phase of arthralgia. A longitudinal MRI study in patients that developed arthritis can unravel if arthritis development is restricted to some locations in which the severity of inflammation increases over time or, alternatively, if the process is more generalized with a weak association between the locations of subclinical inflammation and subsequent clinical arthritis.
Objectives: This longitudinal study at joint level during progression from pre-RA to RA determined the relation between the location of subclinical inflammation and clinical arthritis over time.
Methods: 290 small joints (4 MCPs, 1 wrist, 5 MTPs per person) of 29 patients that presented with arthralgia and developed clinical arthritis were studied with 1.5T MRI at both time-points. MRIs were evaluated for BME, synovitis and tenosynovitis by three readers (ICCs 0.98, 0.96 and 0.97) that were blind to clinical data and the order in time. Subclinical inflammations was defined as presence of BME, synovitis and/or tenosynovitis.
Results: The median time between presentation with arthralgia and clinical arthritis development was 17 weeks. At presentation with arthralgia 68 joints had subclinical inflammation and no significant association was found between joint tenderness and the presence of local MRI-detected subclinical inflammation (OR 0.98; 95% CI 0.48–1.9). Over time, 21% of 68 joints had resolution of subclinical inflammation, 60% had persistent subclinical inflammation and 19% developed clinical arthritis. At arthritis development 37 joints were swollen. Of these, 24 (65%) had no prior subclinical inflammation at the time of presentation with arthralgia (Figure).



Conclusions: This first longitudinal MRI-study on joint level in pre-RA suggested that the majority of joints that developed clinical arthritis had no (long-lasting) preceding phase with subclinical inflammation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4693

SAT0092 PROGRESSION OF ATHEROSCLEROSIS OVER 5 YEARS IN A COHORT OF EARLY INFLAMMATORY ARTHRITIS PATIENTS: RESULTS FROM THE NORFOLK ARTHRITIS REGISTER

S. Skeoch[1], M. O'Sullivan[1], J. Gwinnutt[1], H. Mirjafari[1], J. Chipping[2], H. Edlin[3], A. MacGregor[2], S. Verstappen[1], D. Symmons[1], I. Bruce[1,4]. [1]*Centre for Epidemiology, University of Manchester, Manchester;* [2]*Norwich Medical School, University of East Anglia, Norwich;* [3]*The Department of Radiology;* [4]*Manchester NIHR Musculoskeletal Biomedical Research Unit, Central Manchester University Hospitals NHS Foundation Trust, Manchester, United Kingdom*

Background: Carotid artery intimal medial thickness (IMT) on ultrasound (US) is a validated measure of subclinical cardiovascular (CV) disease. Rates of IMT progression of 0.001cm/year[1] have been observed in the general population and faster progression is associated with increased CV risk.
Objectives: To describe change in IMT over 5 years in a cohort of early inflammatory arthritis (IA) patients and the association of IMT with estimated CV risk and IA related factors.
Methods: Between 2004 and 2010, patients enrolling in the Norfolk Arthritis Register (a UK inception cohort of IA patients) aged from 16 to 65 years with symptom duration less than 2 years, were invited to take part in the NOAR CVD sub-study. In addition to standard IA disease assessments at 0, 2 and 5 years, traditional CV risk factors were measured at baseline and Framingham based 10-year CV risk score was calculated. IMT was measured in the common carotid arteries at baseline and year 5 using a previously validated US protocol. Patient reported clinical CV events at follow up visits which were then verified by a physician. The associations of baseline CV risk and IA characteristics (tender and swollen joint count, rheumatoid factor, CRP, health assessment questionnaire (HAQ), baseline disease modifying anti-rheumatic therapy use) with baseline IMT (IMT_0) and change in IMT at year 5 (IMT_Δ) were tested using non-parametric statistics. The association of IMT_Δ with IA characteristics over time (cumulative joint counts, change in HAQ) and medication use during follow up (statins, biologic therapy) with IMT_Δ were explored using non-parametric statistics.
Results: 201 patients with a median (IQR) age and symptom duration of 51 (42, 58) years and 10.4 (7.7, 14.4) months respectively were studied. 143 (71%) subjects were female. Median IMT_0 was 0.06 (0.05, 0.07) cm and median IMT_Δ at 5-year follow up period was 0.01 (0, 0.01) cm with an estimated median annual IMT_Δ of 0.002cm. IMT had progressed in 104 (51.5%) patients and regressed in 23 (11.4%) patients by year 5. The median CV risk score at baseline was 5.6 (2.6, 10.7)% and was associated with IMT_0 but not IMT_Δ ($r=0.46, p<0.01$; $r=0.03$, $p=0.73$ respectively). There was no association between baseline IA characteristics and IMT_0 or IMT_Δ. There was a trend towards an association between cumulative swollen joint count and IMT_Δ ($r=0.14$, $p=0.057$) but no association with cumulative tender joint count, change in HAQ, statin or biologic use (all $p>0.05$). CV events occurred in 5 patients during follow up. Of these patients, 3 had IMT progression, 1 had no change and 1 had IMT regression.
Conclusions: Overall, patients with early IA had a higher than expected rate of IMT progression; a significant proportion however had regression in IMT over time. Trajectories of CV risk may vary within the IA population and identifying protective factors will help to better target strategies for CVD prevention in IA.
References:
[1] G Howard et al. Carotid artery intimal-medial thickness distribution in general populations as evaluated by B-mode ultrasound. ARIC Investigators. Stroke. 1993;24:1297–1304.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6583

SAT0093 HIGH TRIGLYCERIDES AND LOW HDL LIPID PROFILE AS A SURROGATE MARKER OF HDL DYSFUNCTION IN RA: POTENTIAL LINKS WITH INFLAMMATION AND OXIDATIVE STATUS

J. Rodríguez-Carrio[1], M. Alperi-López[2], P. López[1], R. López-Mejías[3], S. Alonso-Castro[4], F. Abal[5], F.J. Ballina-García[2], M.Á. González-Gay[3,6,7], A. Suárez[1]. [1]*Area of Immunology, University of Oviedo;* [2]*Department of Rheumatology, Hospital Universitario Central de Asturias, Oviedo;* [3]*Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander;* [4]*Department of Rheumatology, Hospital de Cabueñes, Gijón;* [5]*Centro de Salud Sariego, SESPA, Pola de Siero;* [6]*Department of Medicine, University of Cantabria, Santander, Spain;* [7]*Cardiovascular Pathophysiology and Genomics Research Unit, University of the Witwatersrand, Witwatersrand, South Africa*

Background: the interactions between inflammation and lipid profile in RA are

poorly understood. The study of lipid profiles in RA has been biased towards lipoprotein levels, whereas those of triglycerides (TG) and lipoprotein functionality have been neglected.

Objectives: since recent findings point to an emerging role for TG and TG-rich lipoproteins (TRL) on inflammation, we aimed to evaluate a combined lipid profile characterized by high TG and low HDL levels ($TG^{high}HDL^{low}$) in RA.

Methods: lipid profiles were analyzed in 113 RA patients, 113 healthy controls (HC) and 27 dyslipemic subjects (DL). A group of 13 biological-naïve RA patients was prospectively followed for 3 months upon TNFα-blockade. Serum levels of inflammatory mediators were assessed by immunoassays. PON1 activity and Total Antioxidant Capacity (TAC) were quantified in serum. PON1 rs662 status was evaluated by RT-PCR

Results: the prevalence of the $TG^{high}HDL^{low}$ profile was similar among RA patients (29/113), HC (30/113) and DL (11/27), linked to higher TRL levels in all groups. However, this profile was associated with increased CRP (p=0.012), TNFα (p=0.004), MCP-1 (p=0.004), IP-10 (p=0.018) and leptin ($p<0.001$) serum levels in RA, where decreased PON1 activity and TAC were found (both $p<0.001$). TRL serum levels were positively correlated to inflammatory mediators, whereas a negative association was found for PON1 activity (r=-0.203, p=0.036). These findings remain after excluding patients with previous CV events or those under statins. No associations were observed in the HC and DL groups. When RA patients were stratified by PON1 rs662 status, these associations were restricted to the low activity genotype (QQ) (TNFα: p=0.002, MCP-1: p=0.013, EGF: p=0.047, IP-10: p=0.018 and leptin: p=0.002), whereas no effect of the lipid profile was observed in those harboring the QR or RR genotypes (all $p>0.050$). As expected, QQ-patients exhibited a lower PON1 activity compared to the other genetic variants (both $p<0.010$). The $TG^{high}HDL^{low}$ prevalence was related to a decreased anti-TNFα usage in the cross-sectional sample (p=0.004). A poor clinical response upon TNFα-blockade was related to an increasing prevalence of the $TG^{high}HDL^{low}$ profile over treatment (p=0.021) and elevated baseline TRL levels (p=0.042).

Conclusions: the $TG^{high}HDL^{low}$ profile is associated with systemic inflammation, increased TRL levels, decreased PON1 activity and a poor clinical outcome upon TNFα-blockade in RA. Overall, these findings support the link between inflammation and lipid profile, oxidative status and TRL having a pivotal role. The $TG^{high}HDL^{low}$ profile can be proposed as a surrogate marker of HDL dysfunction in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4380

SAT0094 METABOLIC AND CARDIO-VASCULAR BENEFITS OF HYDROXYCHLOROQUINE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

C. Rempenault[1], B. Combe[1], T. Barnetche[2], C. Gaujoux-Viala[3], C. Lukas[1], J. Morel[1], C. Hua[1]. *[1]Rheumatology, University Hospital Lapeyronie, Montpellier; [2]Rheumatology, University Hospital Pellegrin, Bordeaux; [3]Rheumatology, University Hospital Carémeau, Nimes, France*

Background: Cardiovascular disease (CVD) is the leading cause of mortality in rheumatoid arthritis (RA) patients (1). Hydroxychloroquine (HCQ) has been shown to improve major outcomes like survival rates in other inflammatory diseases, like systemic lupus (2).

Objectives: The aim of our study was to assess currently available literature on the cardiovascular impact of hydroxychloroquine (HCQ) in patients with RA.

Methods: We systematically searched literature (via Pubmed, Embase and abstracts from recent ACR and EULAR congresses) for studies evaluating the effects of HCQ, wether in monotherapy or in combination with other conventional synthetic disease modifying antirheumatic drugs (csDMARDs) on cardiovascular outcomes or known risk factors for CVD in RA patients (lipid profiles, diabetes incidence, insulin resistance and incidence of CVD). A meta-analysis was performed with Review Manager Software, with random effects models, whenever methodologically possible and relevant. Data were extracted by one investigator and independently checked by another.

Results: The literature search revealed 185 articles and abstracts of potential interest, and further examination resulted in 16 studies fulfilling required criteria for preplanned analyses regarding the cardiovascular impact of HCQ in RA. For lipid profiles, the mean difference (mg/dL) between HCQ users versus nonusers was -9,82 (95% confidence interval [95% CI] 14.03; 5.60) for total cholesterol, -10.61 [14.17;7.04] for low density lipoprotein, -19.15 [27.20; 11.10] for triglycerides and +4.13 [2.22;6.04] for high density lipoprotein (figure 1); with respectively a decrease (mg/dL) of 13.15 [20.96; 5.34], 12.35 [20.14; 4.36], 12.54 [28.94; 3.86] and an increase of 1.67 [0.96, 4.31] after HCQ initiation. Diabetes incidence was reduced in "HCQ ever users" versus "patients who never used HCQ" with a hazard ratio of 0.59 [0.49; 0.70]. In addition, HCQ seems to decrease insulin resistance and incidence of cardiovascular events but data were too scarce for meta-analysis.

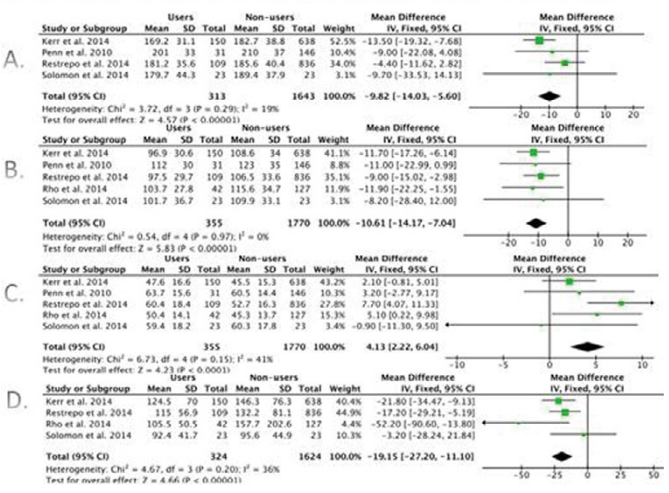
Conclusions: Beside its limited efficacy on disease activity, this study supports the interest of HCQ on lipid profiles, and diabetes incidence, and to a lesser extent on cardio-vascular events and insulin resistance in RA patients. Therefore, this study suggests that HCQ may be of some interest in RA, in combination with other csDMARDS.

References:

[1] Aviña-Zubieta JA, Choi HK, Sadatsafavi M, Etminan M, Esdaile JM, Lacaille D. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. Arthritis Rheum. 2008 Dec 15;59(12):1690–7.

[2] Petri M. Hydroxychloroquine use in the Baltimore Lupus Cohort: effects on lipids, glucose and thrombosis. Lupus. 1996 Jun;5 Suppl 1:S16–22.

Figure 1. Forest plot for the mean difference (mg/dL) between HCQ users and non-users of total-cholesterol (A), low-density-lipoprotein (B), high-density-lipoprotein (C), and triglycerides (D).



Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2048

SAT0095 INCRETINS-INSULIN AXIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

B. Segura[1], A. de Vera-González[2], A. González-Delgado[2], J.M. Olmos[3], J.L. Hernández[3], R. López-Mejías[4], B. Ubilla[4], M.A. González-Gay[5,6], I. Ferraz-Amaro[1]. *[1]Division of Rheumatology; [2]Central Laboratory Division, Hospital Universitario de Canarias, Tenerife; [3]Division of Internal Medicine; [4]Division of Rheumatology; [5]Division of Rheumatology, IDIVAL, Hospital Universitario Marqués de Valdecilla, Santander, Spain; [6]Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, University of the Witwatersrand, Johannesburg, South Africa*

Background: Rheumatoid arthritis (RA) patients have higher levels of resistance to the action of insulin (IR) compared to healthy subjects.The "Incretin effect" consists in a greater release of insulin by the pancreas when there is a gastrointestinal glucose stimulation, compared to an intravenous stimulation. It is known that this effect is altered in patients with IR.

Objectives: To determine if the incretins-insulin axis is altered in patients with RA and if this correlates to IR in patients with RA, as well as if it is explainable by certain features of the disease.

Methods: Cross-sectional study that includes 361 non-diabetic individuals, 151 patients with RA and 210 controls. Serum levels of insulin, C-peptide, Amylin, glucagon-like peptide 1 (GLP-1), gastric inhibitory polypeptide (GIP) and dipeptidyl peptidase 4 (DPP-4) were analyzed in patients and controls. Indexes of resistance and sensitivity to insulin activity were determined by HOMA2.

A "meal test" consisting on the intake of 500 kcal was performed to a subset of 10 patients and 10 controls, in order to determine the postprandial curves of glucose, insulin, C-peptide, GLP-1 and GIP. Differences between patients and controls as well as the relationship of selected characteristics of the disease with the baseline and postprandial levels of incretins were analyzed using multivariate regression. During the meal test, areas under the curve (AUC), maximum concentrations and the minutes of response were compared between patients and controls. This study was approved by the Clinical Trial Committee of the University Hospital of the Canary Islands.

Results: Patients with RA showed, at baseline and after multivariate adjustment, higher levels of insulin (9.8±6.5 vs 13.0±13.4 U/ml, p=0.05), C-peptide (1.53±0.77 vs. 3.37±2.94 ng/ml, p=0.00), GLP-1 (0.49±1.28 vs. 0.71±0.22, p=0.00) and GIP (0.37±0.40 vs. 1.78±0.51, p=0.00). Similarly, IR indexes such as HOMA2-IR and HOMA2%B, built with insulin or Cpeptide, were higher in patients with RA compared to controls. Patients with RA, showed significantly lower levels of DPP-4 (811±459 vs. 696±301 ng/ml,p=0.02) after multivariate analysis. Amylin levels did not differ between patients and controls. Both C-reactive protein (beta coefficient 0.54,95% CI 0.16–0.96, p=0.013) and Erythrocyte Sedimentation Rate (beta coef. 0.01,0.00–0.01, p=0.033) showed a positive relationship with HOMA2%B and GIP levels, respectively. The presence of anti-cyclic citrullinated peptide antibody (beta coef. 157 CI 58–256, p=0.002) and the levels of disease activity measured by DAS28 (beta coef. 46,CI 6–87, p=0.026) and CDAI (beta coef 1.27 (0.28–2.26), p=0.012) showed a positive relationship with the levels of DPP-4. Patients with RA showed Pearson correlation coefficient of incretines, DPP-4 with insulin, C peptide and IR lower compared to control group. After the meal test patients with

RA exhibited an AUC of glucose and GIP greater than controls and a slower C-Peptide response time (75 vs. 30 minutes, p=0.029).
Conclusions: Incretins-insulin axis is altered in patients with RA compared to controls.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5144

SAT0096 MYOCARDIAL FUNCTION IMPROVES IN RHEUMATOID ARTHRITIS PATIENTS TREATED ACTIVELY A MAGNETIC RESONANCE FOLLOW-UP STUDY

R. Koivuniemi[1], A. Kuuliala[2], S. Kivistö[3], M. Holmström[3], M. Leirisalo-Repo[1]. *[1]Rheumatology; [2]Bacteriology and Immunology; [3]Medical Imaging Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland*

Background: Rheumatoid arthritis (RA) patients are susceptible to development of heart failure (HF). Increased HF risk is not explained by increased prevalence of coronary heart disease (CHD) or traditional cardiovascular (CV) risk factors. Chronic inflammation is suggested to play an important role. In parallel with others (1, 2), we observed RA patients with active disease to have myocardial dysfunction and local myocardial late gadolinium enhancement (LGE) indicative of fibrosis or inflammation on cardiac magnetic resonance (cMR) (3).
Objectives: In our patients (3), we here studied the effects of disease modifying anti-rheumatic drugs (DMARDs) on the myocardium over one-year period.
Methods: Fifty-eight female patients with active RA (<70 years) and 22 fibromyalgia (FM) patients underwent cardiac magnetic resonance (cMR). Two RA groups existed: patients with untreated active early RA (ERA) starting conventional synthetic DMARDs (csDMARDs) or biological DMARDs (bDMARDs) and patients with chronic RA (CRA) who had inadequate response to csDMARDs and were candidates for bDMARDs. Patients with CHD, diabetes and smoking were excluded. CMR was performed to analyze LGE and ventricular function before and after one-year DMARD therapy
Results: Of 30 ERA patients, each started csDMARDs (77% as combination), two started also bDMARD. Of 28 CRA patients, each started bDMARD (one monotherapy).

Table 1. Patient charasteristics at baseline

	RA patients	FM patients	p-value
Age, years; mean ± SD	49±14	54±12	0.112
Rheumatoid factor positivity; n (%)	48 (84)		
Anti-citrullinated peptide antibody positivity; n (%)	51 (90)		
Extra-articular features; n (%)	19 (33)		
Erosions on radiographs; n (%)	26 (47)		
Body mass index, kg/m^2; mean±SD	25±4	27±5	0.012
Mean blood pressure, mmHg; mean±SD	113±17	114±15	0.814
Glycosylated hemoglobin A1C, mmol/mol; mean±SD	5.4±0.3	5.6±0.3	0.037
Low density lipoprotein, mmol/l; mean±SD	3.0±0.8	3.4±0.8	0.025

In RA patients, biventricular systo-diastolic function of the heart was impaired compared to FM (Table 2). Over the study-period, myocardial function improved (Table 2) and DAS28-CRP declined (3.5±1.1 vs 2.3±1.0; p<0.001). Only RA patients had LGE, with no improvement over time (67%).

Table 2. Cardiac magnetic resonance findings in RA and FM patients

RA patients	Baseline mean±SD	Follow-up mean±SD	p-value	FM vs RA patients at baseline	p-value
LV EF%	59±4	59±5	0.477	61±7	0.085
LV ESV, ml/m^2	34±6	33±8	0.449	29±8	0.011
LV EDV, ml/m^2	82±11	81±11	0.645	74±11	0.010
LV TPFR, ms	472±99	445±106	0.035	–	–
RV EF%	59±6	60±6	0.065	61±7	0.314
RV ESV, ml/m^2	34±9	32±8	0.009	29±7	0.043
RV EDV, ml/m^2	81±12	79±11	0.034	73±9	0.006

LV = left ventricle, RV = right ventricle, ESV = end-systolic volume, EDV = end-diastolic volume, EF = ejection fraction, TPFR = time to peak filling rate.

Conclusions: Myocardial function was impaired in RA patients with active RA compared to FM controls, although the latter group had worse classical CV risk factor profile. After one-year DMARD-treatment targeting to remission, myocardial function improved in parallel with decreasing RA activity. Inflammation seems to be deleterious to the myocardium. Tight control of RA activity may improve myocardial function.
References:
[1] Ntusi N, JACC Cardiovasc Imaging 2015.
[2] Kobayashi H, Arthritis Care Res 2016.
[3] Holmström M, Clin Exp Rheumatol 2016.
Acknowledgements: Main funding: The Finnish Medical Foundation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4661

SAT0097 FACTORS ASSOCIATED WITH ATHEROSCLEROSIS PROGRESSION IN PATIENTS WITH LOW-ACTIVE RHEUMATOID ARTHRITIS

A. Giollo[1], A. Dalbeni[2], A. Tagetti[2], S. Atanasio[2], G. Orsolini[1], G. Cioffi[3], F. Ognibeni[3], M. Rossini[1], C. Fava[2], O. Viapiana[1]. *[1]Rheumatology Unit, Department of Medicine; [2]General Medicine and Hypertension Unit, Department of Medicine, University of Verona, Verona; [3]Department of Cardiology, Villa Bianca Hospital, Trento, Italy*

Background: Longitudinal studies of the carotid intima-media thickness (IMT) change in RA suggested a role for inflammation in atherosclerosis progression. However, data on well controlled joint disease are scarce since most studies enrolled patients with very high disease activity.
Objectives: To estimate atherosclerosis progression and identify influencing factors in a cohort of longstanding and well controlled RA patients.
Methods: One hundred nine RA patients (females 80%, age 59±12 years, disease duration 15.6±10.6 years, mean Framingham 10-year CV disease risk score 16±12%) without previous cardiovascular (CV) events underwent carotid ultrasound (CUS) examination at baseline and after a mean time of 1.1±0.3 years. Atheromatous plaques and intima-media thickness (IMT) were assessed. Data on CV risk factors, inflammation markers, medications, and RA characteristics were collected.
Results: Overall, we observed a significant increase of IMT (0.03±0.10 mm, p=0.005) and plaques (+ 8%, p=0.035). The IMT progression rate was 0.027 mm/year (95% CI 0.007 - 0.046). Disease activity (DAS28-CRP) remained stable (2.68±1.01 vs 2.79±1.33, p=0.45). Anti-rheumatic, cardiovascular medications and the number of CV risk factors were substantially unchanged. In models of regression analysis sex, age, dyslipidemia, hypertension and use of corticosteroids were independently associated with the increase of IMT, whereas there were no confounding from use of biological therapies, seropositivity or disease duration. Patients with active disease (DAS28-CRP ≥2.6) had a significant increase in IMT (0.04±0.11 mm, p=0.009). Conversely, there was not a significant progression of patients in remission, who had also a lower prevalence of hypertension (40% vs 64%, p=0.027), dyslipidemia (43% vs 58%, p=0.044), and use of corticosteroids (37% vs 63%, p=0.007) and were receiving more frequently methotrexate (60% vs 40%, p=0.027).
Conclusions: In patients with established and controlled RA, the progression of atherosclerosis is mainly driven by traditional CV risk factors than disease activity. In addition, a remission state is associated with a lower prevalence of CV risk factors, which in turn could account for a slower progression of atherosclerosis in these patients. This study provides evidence that even in RA patients who achieve good disease control the treatment of CV risk factors should be optimized.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3789

SAT0098 THE ASSOCIATION BETWEEN WORK DISABILITY AND MENTAL HEALTH IN RHEUMATOID ARTHRITIS

A. Houssien[1], S. Norton[2], E. Nikiphorou[2], F. Matcham[2], J. Galloway[2]. *[1]Academic Rheumatology Department, King's College London; [2]Academic Rheumatology, KCL, London, United Kingdom*

Background: Rheumatoid arthritis (RA) is characterised by joint inflammation, resulting in functional impairment. Consequently, it has long been recognised that work disability is common in RA. However, despite significant pharmacological advances in disease control, little is known about contemporary impact upon work. Depression has emerged in recent years as a key comorbidity in RA. In the general population, depression is strongly correlated with work disability
Objectives: To establish the extent to which depression associates with work ability in RA in a cross sectional study.
Methods: Our hospital routinely collects data via an electronic screening interface, which incorporates a series of validated questionnaires, which patients complete via an iPad while waiting for their appointment. The dataset is linked to the clinical record. For this study, cross sectional data were extracted on adults with RA. Question 2 of the Work and Social Adjustment Scale ("Because of my [RA] my ability to work is impaired") was used as a measure or work disability (scale 0–8). Mental health status was collected using the Patient Health Questionnaire-2 (PHQ), with a score≥3 considered a positive screen for depression.

Table 1

Characteristic	Whole Cohort N=385	PHQ2 score <3 n=263	PHQ2 score ≥3 n=122	p value
Age, mean (SD)	54 (15)	54 (15)	55 (14)	0.768
Female, n (%)	305 (79)	207 (79)	98 (80)	0.681
Seropositive, n (%)	261 (73)*	175 (72)*	86 (76)*	0.705
Disease duration, mean (SD)	6.6 (8.0)	6.0 (7.0)	8.0 (10.0)	0.118
DAS28, mean (SD)	4.0 (1.7)	3.6 (1.6)	4.7 (1.6)	<0.001
HAQ, mean (SD)	1.3 (0.9)	1.0 (0.8)	1.9 (0.7)	<0.001
Work ability, mean (SD)**	3.1 (2.9)	2.1 (2.4)	5.1 (2.6)	<0.001
Univariate regression				
Beta coefficient (95% CI)		Ref	2.94 (2.40 to 3.50)	<0.001
Multivariate regression***			1.40 (0.84 to 1.96)	<0.001

*Missing data on serostatus in 28 subjects. **Work ability on scale 0–8 from WSAS scale. ***Adjusted for age, gender, disease duration, HAQ and DAS score.

Results: Of 385 patients with RA were included in the analysis. Their demographics are shown in the Table.1 Patients scoring 3 or more on the PHQ had more severe RA (higher DAS/HAQ), but there was no significant difference in age, sex or disease duration. 124 (32%) reported no work disability, with the overall mean score 3.0. Patients screening positive for depression had a significantly lower work ability even after adjusting for available confounders.
Conclusions: There is a significant correlation between depression in RA and work ability, which persists even after accounting for disease severity. The magnitude of association observed was even greater than that seen between physical function and work. Although unmeasured confounding remains likely, these data confirm the link between depression and work in RA. It is likely that the relationship is bidirectional, between depression and work in RA. Beyond the importance of addressing work ability in RA, the results highlight the need for screening and targeting depression as part of routine clinical care beside the holistic approach of mangement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6513

SAT0099 POLYPHARMACY IS ASSOCIATED WITH AN INCREASED RISK OF ADVERSE OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS

A.D. Amarilla Vallejo[1], A. Rutherford[1], M. Filkova[2], M. Molokhia[3], E. Nikiphorou[1], S. Norton[1], K. Hyrich[4], J. Galloway[1]. *[1]Academic Department of Rheumatology, King's College London, London, United Kingdom; [2]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic; [3]Primary Care and Public Health Sciences, King's College London, London; [4]Arthritis Research UK. Epidemiology Unit, University of Manchester, Manchester, United Kingdom*

Background: In the general population, polypharmacy (PP) is associated with increased risk of adverse events. The relationship between adverse outcomes and PP in Rheumatoid Arthritis (RA) has not been studied in depth. The mantra of treatment in RA encourages PP through combination Disease Modifying Anti-Rheumatic Drugs (DMARD).
Objectives: To study the relationship between PP and serious adverse events in RA, including the influence of DMARDs within the PP count.
Methods: Data from the British Society for Rheumatology Biologics Register were analysed. PP was defined as number of drugs co-prescribed at baseline, with two models: (1) including DMARDs (2) excluding DMARDs from the medication count. PP was stratified by 0–5, 6–9 and >10. Patients were studied from initiation of 1st biologic until 1st serious adverse event (SAE), 3 years of follow up, or last available visit, whichever came first. A Cox-proportional hazard model was used, with adjustment for a priori selected cofounders.
Results: This study included 15,004 patients commencing biologics. The demographics are shown in table 1. Excluding DMARDs from the PP cohort, 7,115 (47%) of the patients were taking up to 5 drugs; 6,010 (40%) were taking 6 to 9 drugs; 1,870 (12%) were taking 10 or more medications. Higher levels of PP associated with older age, more severe disease, and longer disease duration. PP predictably associated with comorbidities; the relationship was not linear: comorbidity count appeared to show a ceiling effect. The overall incidence of SAEs was 25.5/100 person years (95% CI 24.7–26.3). The rate of SAEs increased across the PP counts (See Table 1). The relationship remained significant after adjusting for comorbidities. Including DMARDs within the PP count attenuated the association.
Conclusions: PP is common in patients with RA and is associated with adverse outcomes especially when patients are on >10 drugs. Including or excluding DMARDs from the PP model had negligible impact on findings. The relationship between PP and comorbidity is worthy of further research, as PP represents a potentially simple but valuable predictor of adverse outcomes, and a suitable surrogate for comorbidity in epidemiological analyses.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2262

Abstract SAT0099 – Table 1

	All Patients	0–5 drugs	6–9 drugs	>10 drugs
		PP count excluding DMARDs		
	N=15,004	n=7,115	n=6,019	n=1,870
Baseline characteristics				
Mean Age in years	56.3	54.0	57.6	61.0
Mean DAS 28 (SD)	4.30 (1.76)	4.17 (1.79)	4.51 (1.67)	4.88 (1.67)
Mean HAQ (SD)	1.93 (0.64)	1.85 (0.65)	2.10 (0.56)	2.15 (0.58)
Mean Disease Duration (SD) in years	12.59 (9.72)	11.96 (9.32)	13.79 (10.26)	14.67 (10.96)
Comorbidity (SD)	1.87 (0.80)	1.65 (0.74)	2.29 (0.73)	2.57 (0.68)
Analysis of Serious Adverse Events				
Exposure time (person-years)	14,200	9,690	3,706	804
Event count (single failure model)	3261	2002	1251	368
Incidence rate (95% CI)	25.5 (24.7–26.3)	20.6 (19.7–21.5)	33.7 (31.9–35.6)	45.7 (41.3–50.7)
Including DMARDs in PP model				
Unadjusted HR (95% CI)	–	Ref	1.20 (1.11–1.29)	1.82 (1.66–1.99)
Adjusted HR (95% CI)	–	Ref	1.05 (0.97–1.13)	1.39 (1.26–1.54)
Excluding DMARDs in PP model				
Unadjusted HR (95% CI)	–	Ref	1.63 (1.52–1.75)	2.21 (1.98–2.47)
Adjusted HR (95% CI)	–	Ref	1.18 (1.09–1.28)	1.35 (1.19–1.53)

Adjusted for age, sex, DAS, HAQ, disease duration and comorbidities.

SAT0100 ACPA AND ABDOMINAL ADIPOSITY ARE INDEPENDENT PREDICTORS OF INCREMENTS IN BASAL INSULIN IN PATIENTS WITH RA

E. Gomez-Bañuelos[1], K. Arrona-Rios[2], S. Duran-Barragan[3], L. Gonzalez-Rosas[2], J. Aguilar-Arreola[2], F.D.J. Perez-Vazquez[1], G.-I. Diaz-Rubio[1], E. Chavarria-Avila[1], F. Corona-Meraz[1], A. Saldaña-Millan[1], R.-E. Navarro-Hernandez[1], M. Vázquez-Del Mercado[1,2]. *[1]Instituto de Invesgitación en Reumatología y del Sistema Musculoesquelético, Universidad de Guadalajara; [2]Servicio de Reumatología, División de Medicina interna, Pnpc 004086, CONACyT; [3]Instituto de Invesgitación en Reumatología y del Sistema Musculoesquelético, Hospital Civil de Guadalajara, "Juan I. Menchaca", Guadalajara, Mexico*

Background: Insulin resistance (IR) is a comorbidity found in about 40%of RA patients. Currently, there is little information regarding the role of antibodies against citrullinated proteins and IR development in RA. Patients positive for ACPA and/or RF may be at higher risk of IR since these group of patients has a higher expression pro-inflammatory citokines like TNFa and IL-6, both implicated in the pathogenesis of IR.
Objectives: To analyze the contribution of autoantibodies positivity (ACPA and/or RF) and their impact in the development of IR in patients with RA.
Methods: We retrospectively analyzed patients classified with RA per ACR 1987 and ACR/EULAR 2010 criteria with at least one year of follow-up in a cohort of RA patients without comorbidities from Hospital Civil "Juan I. Menchaca". DAS-28, basal insulin, HOMA-IR and anthropometric parameters: Body weight, body mass index (BMI), Sum 4 skinfold thicknesses (S4T), Waist to hip ratio (WHR), waist circumference (WC) and total fat mass (FM); were determined at current and baseline. Mean differences between the two time points were calculated. A multiple regression model was constructed considering mean insulin change as dependent variable.
Results: We studied 57 RA patients, 44% (25) with IR and 56% (32) without IR. Of these, 21% (12) developed IR during follow-up. BMI, FM and ST4 were higher at baseline in patients with current IR at baseline. Ptients who developed IR during follow-up had a mean increase of DAS-28 of 1.27 ($P<0.005$ vs. patients who improved or never developed IR). Patients positive for ACPA had a greater increase in IR during follow-up. Multivariate analysis revealed that ACPA, increments in WHR and ST4 were independent predictors of basal insulin increases during follow-up.
Conclusions: ACPA and abdominal adiposity (WHR) are independent predictors of IR development in RA
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6862

SAT0101 POSSIBILITY OF BACTERIAL INFECTION PROPHYLAXIS OF TRIMETHOPRIM-SULFAMETHOXAZOLE IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING TREATMENT WITH BIOLOGICS: A SINGLE-CENTER, RETROSPECTIVE, CASE-CONTROL STUDY

E. Kikuchi, N. Aoki, T. Yoshioka, T. Okai. *Center for Rheumatology and Joint Surgery, Kawakita General Hospital, Tokyo, Japan*

Background: Trimethoprim-sulfamethoxazole (TMP-SMX) is widely used for the prophylaxis of *Pneumocystis jiroveci* pneumonia (PCP) in immunocompromised patients, but data about the prophylactic effect of TMP-SMX against bacterial infections are insufficient.
Objectives: To analyze the prophylactic effect of TMP-SMX against severe bacterial infections in elderly patients with rheumatoid arthritis undergoing treatment with biologics.
Methods: Data were retrospectively collected from the medical records of patients with rheumatoid arthritis at our center. We divided the elderly patients (65 years or above) who took biologic agents into two groups. The first group (TMP-SMX+) comprised patients who previously or concurrently started TMP-SMX with biologic

agents for the purpose of PCP prophylaxis and continued with it throughout the treatment with biologics. The second group (TMP-SMX−) comprised patients who were not prescribed TMP-SMX throughout the treatment with biologics. We analyzed the retention rate of each group by Kaplan-Meier curves and the Wilcoxon test. The primary end point was the 18-month retention rate of biologics without severe infection (defined as hospitalization or multiple days of intravenous antibiotic treatment in the clinic, including suspected cases).

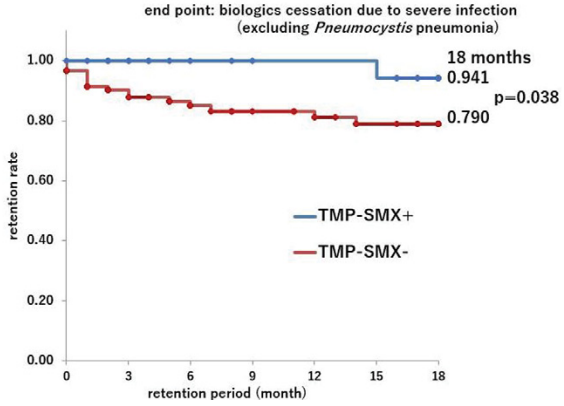
Results: The TMP-SMX+ group included 30 patients with a mean age of 76.7±7.0 years. The rate of ACPA positivity was 80.0%, MTX use was 73.3%, oral steroid use was 43.3%, and bio-naive patients was 73.3%. The number of patients treated with abatacept, certolizumab pegol, etanercept, golimumab, infliximab, and tocilizumab was 13, 1, 7, 7, 1, and 1, respectively. The cumulative retention rates at 12 and 18 months were 1.000 and 0.941, respectively. Prophylactic doses of TMP-SMX were between TMX 20mg/SMX 100mg/day and TMX 91mg/SMX 457mg/day.

The TMP-SMX− group included 113 patients with a mean age of 73.6±5.6 years. The rate of ACPA positivity was 79.3%, MTX use was 70.8%, oral steroid use was 54.9%, and bio-naive patients was 80.5%. The number of patients treated with abatacept, adalimumab, certolizumab pegol, etanercept, golimumab, infliximab, and tocilizumab was 15, 15, 4, 41, 7, 18, and 13, respectively. The cumulative retention rates at 12 and 18 months were 0.812 and 0.790, respectively. There was a significant difference between the retention rates in the two groups (p =0.038, Wilcoxon test). Five patients were enrolled in both groups because another biologic agent was used in different periods.

In the TMP-SMX+ group, only one patient was hospitalized for probable bacterial pneumonia (causative bacteria not detected). In the TMP-SMX− group, nine patients were hospitalized for pneumonia, three for septic arthritis, two for urinary tract infection, and two for soft tissue infection. The causative bacteria were *Escherichia coli*, *Klebsiella oxytoca*, *Enterococcus faecalis* and others.

Furthermore, seven patients in the TMP-SMX− group were treated for PCP, whereas no patients contracted PCP in the TMP-SMX+ group.

The retention rates of biologics for elderly (≧65 years) RA patients



Conclusions: Prophylactic administration of TMP-SMX may reduce the risk of bacterial infection in elderly patients with rheumatoid arthritis undergoing treatment with biologics.

References:

[1] Limper AH et al. Am J Respir Crit Care Med. 2011;183(1):96–128.
[2] Katsuyama et al. Arthritis Res Ther. 2014 Feb 5;16(1):R43. doi: 10.1186/ar4472.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4650

SAT0102 THE EFFECT OF LACTATION ON THE ACTIVITY OF RHEUMATOID ARTHRITIS

E. Matianova, N. Kosheleva. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia, Moscow, Russian Federation*

Background: It has been reported that rheumatoid arthritis (RA) onset in females is often associated with post-partum period and lactation. Moreover, flares of pre-existing RA occur in 33–91% of cases during post-partum and breastfeeding periods.

Objectives: To assess the effect of lactation on RA activity during the post-partum period.

Methods: Prospective study included 32 RA pts (ARA criteria, 1987) who were followed up and assessed at 30–34 weeks of pregnancy, and at 1, 3, 6 and 12 months post-partum. Pts' median age was 29 (20–37) years, disease duration 8 (1–28) years. RF (62,1%) and ACPA (58,6%) seropositive, of radiographic stage 2–3 (72,4%) and functional class 1–2 (86,2%) prevailed. At each control visit DAS28^{CRP} score and the number of between the visits flares were obtained among breastfeeding and non-breastfeeding women. RA flare was documented based on changes in DAS28^{CRP} score values vs the previous visit following EULAR recommendations.

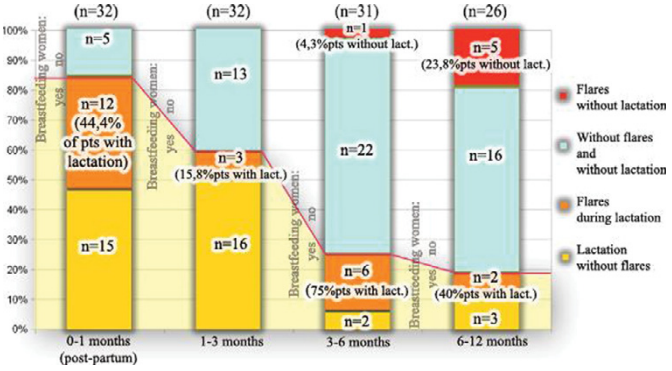
Results: 6 pts were lost for follow up (FUP; the 1 after Mo 3?, 5 after Mo 5–6 post-partum). Lactation immediately after birth was suppressed in 5 (15,6%)pts. 27 (84,4%)pts were breast-feeding their babies for the period from 2 weeks to 16 months (Me=2,5 [1;6] months). All relevant data on the study population during the FUP is summarized in the Table1.

During the whole FUP the DAS28^{CRP} score was higher among breast-feeding females, although the difference was statistically significant only during the first month post-partum (p=0,01). During the first month post-partum, as well as at Mo3 post-partum RA flares were registered only in nursing mothers, i.e. in 12 out of 27, and in 3 out of 19, respectively. The number of nursing mothers after 3d month was reduced to 8. RA flares in these breast-feeding women were more frequent, than in non-breast-feeders during 3 to 6 months period of the FUP: 6 vs 1 (RR=10,3, 95% CI=2,6;40,1; p=0,0002).Only after 6 mo postpartum the rate of RA flares among nursing mothers did not statistically significant exceed the rate among non-feeders (in 2 out of 5 vs 5 out of 21, p>0,05) (Fig.1).

Assessment of RA flares at all 121 points during 12 months post-partum FUP (59 points during lactation, 62 – after termination of lactation) demonstrate that RA flares were documented in 23 (39%) lactating women and in 6 (9,7%) non-lactating women. Therefore, the risk of RA flare in lactating women was 4-fold higher vs the risk in non-lactating women (RR=4; 95% CI=1,8;9,2; p=0,0002).

Increased RA exacerbation rates among nursing mothers is partially explained by postponement of active therapy. The majority of pts refused initiation of therapy for the sake of breastfeeding.

Approaches to breastfeeding practices in RA mothers should be individual. Nursing is acceptable during RA remission or low disease activity given the patient continues on the recommended drugs, compatible with breast-feeding.



Conclusions: Lactation and breastfeeding is associated with 4-fold higher risk of RA exacerbation as compared to non-breastfeeding population (RR=4; 95% CI=1,8;9,2; p=0,0002)

References:

[1] Hazes JM at all. Rheumatoid arthritis and pregnancy: evolution of disease activity and pathophysiological considerations for drug use. Rheumatology. 2011 Nov;50(11):1955–68.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4874

SAT0103 NON-DIPPING STATUS IS ASSOCIATED WITH DIASTOLIC NOCTURNAL HYPERTENSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Troitskaya, S. Velmakin, S. Villevalde, Z. Kobalava. *Propaedeutics of internal disease, RUDN University, Moscow, Russian Federation*

Background: Rheumatoid arthritis is associated with increased cardiovascular risk. Nocturnal hypertension and non-dipping status are important determinants of cardiovascular mortality and morbidity. Little is known about their associations in patients with RA.

Objectives: The aim of the study was to assess the prevalence of nocturnal hypertension and its associations in patients with RA.

Methods: 62 patients with RA (EULAR 2010) without known cardio-vascular disease were examined (73% females, age 58,5±15,4 (M±SD) years, 13%

Abstract SAT0102 – Table 1. The mean DAS28^{CRP} scores in the groups

	III pregn trimester		1 month		3 month		6 month		12 month	
	n	DAS28^{CRP}	n	DAS28^{CRP}	n	DAS28^{CRP}	n	DAS28^{CRP}	n	DAS28^{CRP}
Nursing mothers	–	–	27	3,6±1,2*	19	3,4±1,2	8	3,7±1,1	5	3,2±1,5
Nonnursing mothers	32	3±1,2	5	3,1±1,4*	13	3,3±1,9	23	2,9±1,4	21	2,9±1,1

*p=0,01.

smokers, 61% with AH, 34% with dyslipidemia). Median duration of RA was 8 years (IQR 3–17). Seropositive RA was diagnosed in 69% of patients. Median CRP was 12,1 mg/dl (IQR 2,2–23,4 mg/dl), median rheumatoid factor (RF) was 32,5 IU/ml (IQR 8,3–173 IU/ml). All patients received disease-modifying antirheumatic drugs, 22 (38%) - biological treatment. Median duration of AH was 6,1 years (IQR 0–10 years. All patients with AH received antihypertensive treatment. 24-h peripheral and central BP monitoring was performed (BPLab Vasotens, "Petr Telegin"). Arterial stiffness was assessed by applanation tonometry (Sphygmocor, AtCor, Australia). $P<0.05$ was considered significant.

Results: Mean office BP was 130±15/80±10 mmHg. Mean pulse wave velocity (PWV) was 9,3±3,2 m/s. The dipping states were as follows: non-dipping in 39 (62,9%) patients, dipping – In 7 (11,3%), extreme dipping – in 5 (8,1%) and reverse dipping in 11 (17,7%). Median of nocturnal fall in systolic BP was 3,5% (IQR 0–9%). Isolated nocturnal AH was observed in 12 (19,4%) pts. Patients were divided into 2 groups according to nocturnal fall of BP: G1 (non-dipping - >10%) – 42 (67,7%) pts and G2 (dipping- <10%.) – 16 (32,3%) pts. Non-dippers were older (56,7±16,2 vs 49±12,5 years), more often were smokers (20 vs 0%), had higher BMI (25,4±6,0 vs 22,3±5,1 kg/m^2), median duration of AH (1,5; IQR 0–11 vs 0; min 0, max 1 years), median duration of RA (10; IQR 7–19 vs 2,5; IQR 2–6,5 years), PWV (8,6±2,8 vs 7,2±2,1 m/s), nocturnal BP (120,4±12,7/69,8±10,4 vs 103,8±8,8/59,4±4,4 mmHg), $p<0,05$ for trend. Spearmen analysis revealed significant correlations between nocturnal fall in SBP and RA duration (r=-0,3), central BP (r=0,2 for SBP and DBP), night SBP and DBP (r=-0,3 and -0,5 respectively), $p<0,05$ for trend. Multiple regression analysis showed that elevation of central office DBP and night DBP were significant predictors of non-dipping state (β=-3,7, p=0,008 and -0,7, $p<0,0001$ respectively).

Conclusions: The majority of patients with rheumatoid arthritis are characterized by non-dipping state. Diastolic nocturnal hypertension is a significant predictor of non-dipping in this patient population.

References:

[1] Androulakis E., Papageorgiou A., Chatzistamatiou E. et al. Improving the detection of preclinical organ damage in newly diagnosed hypertension: nocturnal hypertension versus non-dipping pattern J Hum Hypertens 2015;29:689–695.
[2] Redon J., Lurbe E. Nocturnal blood pressure versus nondipping pattern. What do they mean? Hypertension 2008;51:41–42.
[3] Kim B., Kim Y., Lee Y. A Reverse Dipping Pattern Predicts Cardiovascular Mortality In a Clinical Cohort. J Korean Med Sci 2013;28:1468–1473.
[4] Hamamoto K., Yamada S., Yasumoto M. et al. Association of nocturnal hypertension with disease activity in rheumatoid arthritis. Am J Hypertens 2016;29:340–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5319

SAT0104 THE IMPACT OF DISEASE ACTIVITY ON PATIENT REPORTED COGNITIVE DYSFUNCTION ("BRAIN FOG") IN RHEUMATOID ARTHRITIS

G.W. Reed[1], L.R. Harrold[1], O. Pala[2], J.M. Kremer[3]. *[1]University of Massachusetts, Worcester; [2]University of Miami, Miami; [3]Albany Medical College and The Center for Rheumatology, Albany, United States*

Background: Rheumatoid arthritis (RA) is a systemic, inflammatory disease and its burden extends beyond joint disease. In recent years, there has been significant advances in treating joint disease but we need a greater understanding of physical and especially psychosocial comorbities to improve quality of life in RA patients. In particular, patients often report "brain fog" meaning a diminished ability to think, learn, remember and perform other mental tasks. Doctors have long recognized that patients with certain physical conditions can experience cognitive dysfunction. Limited information is available in the literature with regard to the prevalence of cognitive dysfunction and factors associated with the condtion in RA.

Objectives: To characterize the association of disease activity with patient reported cognitive dysfunction in patients with RA overall and stratified by age.

Methods: We identified patients with RA aged ≥18 years who were enrolled in the Corrona registry who were biologic naïve at their last follow-up visit (October 2010–June 2016). We compared those who reported cognitive dysfunction (responded "yes" to the question asking if they had "problems with thinking") to those who did not with respect to disease activity based on the Clinical Disease Activity Index (CDAI). Unadjusted and adjusted logistic regression models controlling for demographic (age, gender, race, education), comorbidity/lifestyle (diabetes, fibromyalgia, body mass index, smoking) and RA disease characteristics (disease duration, disability and prednisone dose) were conducted. We further examined whether the relationship between disease activity and cognitive dysfunction varied based on patients age (<55 vs. >55 years) testing the moderating effect using a likelihood ratio test.

Results: There were 10,401 patients who met inclusion criteria of whom 863 (8%) reported cognitive dysfunction. Those who reported cognitive dysfunction were more likely to be women (83% vs. 73%, $p<0.001$), younger (62 vs. 64 years, $p<0.001$), disabled (24% vs. 8%, $p<0.001$), with moderate/high disease activity based on the CDAI (51% vs. 31%, $p<0.001$). In adjusted models, the likelihood of cognitive dysfunction increased with higher levels of disease activity in the total population (Table). The impact was more pronounced in those age <55 (p=0.007; Table).

	Total population*	Age <55**	Age ≥55**
Disease activity OR (95% CI)*			
Remission	1	1	1
Low	2.70 (2.11–3.45)	3.97 (2.34–6.75)	2.42 (1.84–3.20)
Moderate	3.56 (2.75–4.61)	5.93 (3.45–10.19)	3.01 (2.24–4.05)
High	3.90 (2.92–5.21)	7.92 (4.49–13.98)	2.90 (2.04–4.12)

*Adjusted for age, gender, race, disability, education, smoking status, body mass index, diabetes, fibromyalgia, disease duration and prednisone dose. **Adjusted for gender, race, disability, education, smoking status, body mass index, diabetes, fibromyalgia, disease duration and prednisone dose.

Conclusions: Increasing disease activity is associated with a higher likelihood of reporting cognitive disfunction. The effect was more pronounced in younger as opposed to older RA patients.

Disclosure of Interest: G. Reed Shareholder of: Corrona, LLC, Employee of: Corrona, LLC, L. Harrold Shareholder of: Corrona, LLC, Grant/research support from: Pfizer, Inc., Consultant for: Roche, Employee of: Corrona, LLC, O. Pala: None declared, J. Kremer Shareholder of: Corrona, LLC, Grant/research support from: AbbVie, Genentech, Lilly, Novartis, Pfizer, Consultant for: AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, Employee of: Corrona, LLC

DOI: 10.1136/annrheumdis-2017-eular.5131

SAT0105 SURVIVAL IN FIRST LINE OF BIOLOGIC AGENTS IN AN APULIAN COHORT OF RHEUMATOID ARTHRITIS PATIENTS WITH OCCULT HEPATITIS B VIRUS INFECTION

G. Carlino[1], M. Fornaro[2], F. D'Onofrio[3], N. Maruotti[2], A. Semeraro[4], C. Zuccaro[5], L. Santo[6], A. Marsico[4], R. Bucci[7], L. Quarta[8], O. Casilli[8], P.C.F. Falappone[5], F. Iannone[2]. *[1]Rheumatology Service, ASL LECCE - DSS Casarano and Gallipoli, Casarano; [2]DETO – Rheumatology Unit, University of Bari, Bari; [3]UOC Reumatologia Universitaria, University of Foggia, Foggia; [4]O.U. of Rheumatology, ASL Taranto, Taranto; [5]Ambulatorio di Reumatologia, Ospedale di Brindisi, Brindisi; [6]O.U. of Rheumatology, ASL Barletta, Barletta; [7]Rheumatology Hospital Unit, A.O.U. Foggia, Foggia; [8]O.U. of Rheumatology, "V.Fazzi" Hospital, Lecce, Italy*

Background: The occurrence of hepatitis B virus (HBV) infection may be a concern during the treatment of patients with Rheumatoid Arthritis (RA). We wondered whether a state of HBV occult infection (anti-HBcAg-pos, HBsAg-neg, HBV-DNA-neg) might influence the effectiveness of biological drugs in RA patients in real-world settings.

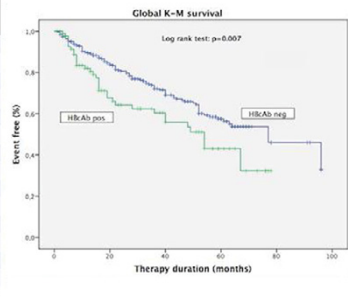
Objectives: We performed a retrospective analysis to evaluate the survival on first line biologic drug of RA Apulian patients with HBV occult infection.

Methods: We analyzed longitudinal data of 384 consecutive RA patients starting a first biological drug in a time frame from 1st January 2008 to 31st December 2014. Demographic and disease related characteristics were collected at baseline and at last observation visit. Baseline serological markers of HBV infection and causes of discontinuation of treatment were also recorded. Primary endpoint was the influence of anti-HBcAg-pos on drug survival, estimated by Kaplan-Meier life table analysis. Estimates hazard ratios (HRs) of drug discontinuation or achievement of Clinical Disease Activity Index (CDAI) based remission at last visit, adjusted for disease characteristics, biological drug class and anti-HBcAg-pos were computed by Cox-regression models.

Results: No baseline demographic and disease characteristics difference between anti-HBcAg-pos and anti-HBcAg-neg RA patients were detected, except for DAS28 that was significantly higher in anti-HBcAg-pos group. Drug survival rate was significantly lower in anti-HBcAg-pos (57.6%, median survival time (95% CI) 54 months (38–69)) than in anti-HBcAg-neg patients (67.8%, median survival time (95% CI) 77 months (59–94)). Median survival time for ineffectiveness was 15 months (12–17) for anti-HBcAg-pos and 24 months (18–30) for anti-HBcAg-neg patients (p=0.04). Cox regression models showed a significant association between anti-HBcAg-neg (HR 0.60, 0.39–0.92) or RF/ACPA-neg (HR 1.69, 1.16–2.46) and drug discontinuation, while co-therapy with MTX (HR 2.14, 1.01–4.58) or with steroids (HR 0.38, 0.16–0.91), and RF/ACPA neg (HR 0.45, 0.21–0.95) were independently associated with the achievement of CDAI based remission.

	All (nr. 384)	Anti-HBc neg (nr. 298)	Anti-HBc pos (nr. 86)	P
Age	59 ±10	59 ±10	57 ±12	ns
Female. nr (%)	290 (75)	229 (77)	61 (72)	ns
Disease duration	41 ±58	38 ±58	51 ± 60	ns
Comorbidities. nr (%)	263 (63)	132 (44)	28 (33)	ns
ESR-DAS28	4.5 ±1.2	4.4 ±1.1	4.8 ± 1.2	0.007
CDAI	20.3 ±11	20 ±10	21 ±11	ns
HAQ-DI	1.4 ±0.7	1.4 ±0.6	1.3 ± 0.7	ns
RF nr (%)	252 (66)	199 (67)	53 (62)	ns
Etanercept nr (%)	135 (35)	112 (38)	23 (27)	ns
TNFa mAb nr (%)	122 (32)	103 (35)	19 (22)	ns
Tocilizumab nr (%)	60 (16)	39 (13)	21 (25)	ns
Abatacept nr (%)	66 (17)	44 (15)	22 (26)	ns
Glucocorticoids nr (%)	304 (80)	235 (79)	69 (80)	ns
MTX nr (%)	323 (84)	262 (88)	61 (71)	ns

Values are the mean ± SD unless otherwise indicated. *28 joints Disease Activity Score; CDAI = Clinical Disease Activity Index; RF =Rheumatoid Factor; MTX =Methotrexate.



Conclusions: HBV occult infection seems to influence negatively the effectiveness

of biological therapies in RA patients. However, being a real-life setting, unknown confounding factors might generate an apparent association or mask a true correlation between the HBcAb status and clinical outcomes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2032

SAT0106 FURTHER "WELLNESS" CAN BE ACHIEVED BY SURGICAL INTERVENTION IN THE IMPAIRED HAND EVEN FOR PATIENTS WITH WELL-CONTROLLED RHEUMATOID ARTHRITIS

H. Ishikawa[1], A. Abe[1], Y. Nomura[1], S. Ito[1], T. Kojima[2], M. Kojima[3], N. Ishiguro[2], A. Murasawa[1]. *[1]Rheumatology, Niigata Rheumatic Center, Shibata; [2]Orthopedic Surgery, Nagoya University Hospital; [3]Medical Education, Nagoya City University Hospital Graduate School of Medicine, Nagoya, Japan*

Background: The hand is the most frequently involved site in rheumatoid arthritis (RA). The treatment aim of RA is achieving and maintaining remission (REM) or low disease activity (LDA) via tight medical control. However, despite remarkable advances in medication, progressive deterioration and/or deformity of the hand, if adequate medication is not administered in the early stage. Surgical reconstruction is still required in hands with functional loss and/or a grotesque appearance caused by joint deterioration or tendon rupture. Recently, patients have expressed a desire to achieve functional REM with a higher quality of life (QOL) and improved mental wellness.

Objectives: The objective of this study was to clarify the systemic effects of surgical intervention in the impaired hand, even in patients with well-controlled disease who have achieved REM or LDA.

Methods: A prospective cohort study was performed in 119 hands of 119 patients with functional loss and/or a grotesque appearance due to RA who underwent primary elective surgery between October 2012 and September 2014. A total of 42 hands in 42 patients (males: 2, females: 40) had a disease activity of REM or LDA just before surgery. In the REM/LDA group, the average (range) age was 61 (29–82) years, and the average (range) disease duration was 15 (2–35) years. The procedures performed included Darrach procedure (ulnar head resection) in 17 hands, radiolunate arthrodesis in 10, extensor tendon reconstruction in 6, thumb/finger metacarpophalangeal joint arthroplasty (Swanson) in 14, proximal interphalangeal (interphalangeal) joint fusion in 4, and thumb CM joint arthroplasty (Thompson) in 4 and so on. The patient-reported outcome (PRO) was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI), EuroQol-5 Dimensions (EQ-5D), Beck Depression Inventory-II (BDI-II), Patient's General Health using visual analogue scale of 100 mm (Pt-GH), and the Disabilities of the Arm, Shoulder and Hand (DASH). The 28-joint Disease Activity Score using C reactive protein (DAS28-CRP) and Grip power (GP) were also examined. All of these items were investigated just before surgery (baseline) and again at 6 and 12 months after surgery.

Results: On the whole, the physical function (HAQ-DI, DASH, GP), QOL (HAQ-DI, EQ-5D, Pt-GH), mental wellness (BDI-II, Pt-GH), and disease activity (DAS28-CRP) were significantly improved at 6 and 12 months after surgery compared to baseline ($p<0.05$)[1)]. In the REM/LDA group, a significant improvement was noted in the upper-extremity function (DASH), QOL (EQ-5D), and disease activity (DAS28-CRP) at 6 and 12 months after surgery; however, we did not observe any significant changes in any other items (Table1).

Table 1: Outcome of surgical intervention in the impaired hand for patients with rheumatoid arthritis

		HAQ-DI	EQ-5D	BDI-II	Pt-GH (mm)	DASH	GP (mmHg)	DAS28-CRP
Total n=119	baseline	1.07 (0.73)	0.72 (0.12)	13.4 (9.4)	35 (23)	42.1 (22.5)	126 (58)	3.1 (0.9)
	PO# 6mos.	0.97* (0.78)	0.76** (0.14)	11.7** (8.6)	24** (21)	36.7** (21.7)	135* (55)	2.4** (2.1)
	PO# 12mos	0.91** (0.78)	0.76** (0.14)	11.9** (9.1)	24** (20)	35.7** (23.0)	139** (60)	2.2** (0.8)
REM+LDA n=42	baseline	0.85 (0.63)	0.75 (0.14)	11.0 (8.1)	15 (13)	34.6 (21.8)	143 (61)	2.1 (0.5)
	PO# 6mos.	0.80 (0.68)	0.80** (0.15)	10.1 (8.1)	16 (18)	30.2** (19.6)	143 (57)	1.8** (0.6)
	PO# 12mos	0.81 (0.760)	0.79** (0.16)	10.8 (8.3)	14 (14)	30.1** (21.0)	151 (66)	1.8** (0.7)

Mean(SD) *: p<0.05 compared to baseline, **: p<0.01 compared to baseline

Conclusions: Achieving REM or LDA is not the ultimate goal of treatment for patients with functional loss and/or a grotesque appearance of their hands. Further "wellness" can be achieved by surgical intervention in the affected hand, even for patients with well-controlled RA. Such intervention can also ameliorate the disease activity.

References:

[1] Ishikawa H, Murasawa A, Nakazono K, et al. The patient-based outcome of upper-extremity surgeries using the DASH questionnaire and the effect of disease activity of the patients with rheumatoid arthritis. Clin Rheumatol. 2008;27:967–973.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2850

SAT0107 FACTORS THAT INFLUENCE ON PAIN CONTROL DURING TREATMENT FOR RHEUMATOID ARTHRITIS PATIENT

I. Yoshii[1], T. Chijiwa[2]. *[1]Rheumatology, Yoshii Hospital, Shimanto City; [2]Rheumatology, Kochi Memorial Hospital, Kochi, Japan*

Background: Pain control is the most important theme for treatment of rheumatoid arthritis (RA) patient. For pain control, it is obviously important key to control disease activity control. However, patient status at start of treatment (BL), can be also important as well as disease activity control. Including these factors, keys that can reduce pain should be clarified.

Objectives: In this study, factors that affect on pain control were evaluated statistically from real clinical data.

Methods: In 685 RA patients who have been treated for more than 1 year, 500 patients were monitored their disease activity with parameters in 28-joints disease activity index with C-reactive protein (DAS28-CRP), pain score with using visual analogue scale (PS-VAS), modified Health Assessment Questionnaire Disability Index (mHAQ). Drugs administered for patient had been checked at the time of consult.

PS-VAS at consult was evaluated, as it demonstrated no more than 15mm, or decrease than last time more than 20mm was evaluated as "Pain Reduced". Patients sex, ACP, Sharp/van der Heijde Score (SHS), patients current age, history length, DAS28-CRP and its components, PS-VAS at BL, and followed consultation, drug usage and its dosage were evaluated for Pain Reduced statistically with Binary Logistic Regression Analysis. Significant level was set within 1%.

Results: 14,005 times from 495 patients were enrolled in this study. At BL, male patient, higher ACPA, younger age at onset and at BL, older age at following consultation, short following term, smaller SvdHS, greater tenderness joint count (TJC), swollen joint count (SJC), smaller patient's global assessment (PGA), evaluator's global assessment (EGA), great CRP, and smaller mHAQ and DAS28-CRP at BL demonstrated significant contribution on Pain Reduce. In following consult, smaller mHAQ, PS-VAS, and DAS28-CRP, in which smaller PGA and EGA, demonstrated significant contribution on Pain Reduce. In drugs, paraetamol/tramadol combination drug use, non-steroid anti-inflammation drug (NSAIDs) use, pregabalin use, tofacitinib use, and opioid use, and methotrexate dose decrease demonstrated significant contribution on Pain Reduce.

Conclusions: These results suggest that pain control for RA patient depends on patient's status at baseline. And followed disease activity control and activity in daily life (ADL) maintenance. In adding with these, drug selection is also important key. It is also suggested specific drugs have higher effect on pain control. Anti-chronic pain agent can be candidate for pain relief for the patient who complains remnant pain even after successful disease activity control and ADL maintenance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4213

SAT0108 CLINICAL SIGNIFICANCE OF ANTI-ACTIN ANTIBODIES IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES

I. Ayadi, L. Laadhar, M. Kallel-Sellami. *Immunology, la Rabta Hospital, Tunis, Tunisia*

Background: Anti-actin antibodies (AAA) are well-described as the major component of smooth muscle autoantibodies (microfilament antibodies). They are specially detected in patients with chronic active hepatitis (CAH) and celiac disease (CD). AAA have also been found less frequently in various other autoimmune disorders including systemic lupus erythematosus (SLE), Sjogren's syndrome, and myasthenia gravis, as well as in primary biliary cirrhosis and alcoholic liver disease.

Objectives: to study clinicobiological characteristics of patients with AAA in autoimmune inflammatory rheumatic diseases (AIRD).

Methods: From January to December 2016, we have collected all cases of patients with AAA presenting for symtomatology of AIRD. The presence of AAA was detected fortuitously by indirect immunofluorescence (IIF) in accordance with its characteristic fluorescence pattern in HEp2 cells (BioRad©). The specificity for F-actin was confirmed by IIF on rat liver-kidney-stomach sections (Biosystem®) and/or Immunodot (Euroimmun®). Coeliac disease related antibodies were performed in all patients with AAA.

Results: Six patients were included: 5 women and a man with a mean age of 43.5 years. AIRD have been suspected in these patients and the mean clinical features were inflammatory polyarthralgia and fever. AIRD was diagnosed in three cases: One patient presented with SLE and two others with rheumatoid arthritis (RA). Hepatic function was disturbed with elevated serum ALT and AST activities in one case higly suspected of CAH. CD was diagnosed in one case. The sixth patient had positive antinuclear antibodies, hypocomplementemia and anti-Ro52, anti-SSB and anti-DFS antibodies associated with FR but didn't

fulfilled SLE criteria. The immunological tests showed anti-nuclear antibodies among all patients with high titre and anti-DNA antibodies in SLE and CAH patients respectively. One RA patient had anti-Ro60 antibodies.

Conclusions: During our study, AAA were found fortuitously in AIRD. This association is rarely described in the literature. Hepatic involvement can be seen during AIRD. Nevertheless, a CAH and CD associated shouldn't be disregarded.

References:

[1] Diagnostic value of anti-actin antibodies in a French multicenter study. P.Chretien-Leprince et al; Ann N Y Acad Sci. 2005;1050:266–73.

[2] Smooth-muscle antibodies in rheumatoid arthritis. I.Andresen et al; Acta Pathol. Microbiol. Scand. 1980;88: 131–135.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6748

SAT0109 QUANTITATIVE ESTIMATES OF DAMAGE AND DISTRESS, IN ADDITION TO INFLAMMATION, AND THE PROPORTION EACH OF THE 3 VARIABLES AFFECTS CLINICAL MANAGEMENT DECISIONS (TOTAL=100%) MAY CLARIFY ASSESSMENT OF CLINICAL STATUS IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

K.A. Gibson[1,2,3], I. Castrejon[4], T. Pincus[4]. *[1]Rheumatology, Liverpool Hospital; [2]ingham Research Institute, Liverpool; [3]University of New South Wales, Sydney, Australia; [4]Rheumatology, Rush University Medical Center, Chicago, United States*

Background: Quantitative assessment in rheumatoid arthritis (RA) is directed to inflammatory activity (INF) and not to joint damage (DAM) and distress (STR - seen as fibromyalgia, depression, etc.). However, DAM and STR may affect clinical management and outcomes of treatment in many RA patients. For example, an RA patient with well-controlled INF who has secondary fibromyalgia may have 0 swollen joints (SJC) and an ESR≥ of 15, but nonetheless have a DAS28 of 5.1, CDAI of ≥22, and RAPID3 of ≥16 (indicating high activity), based on 14/28 tender joints and a patient global assessment of 80/100. Therefore, quantitative estimates of DAM, and STR, as well as INF may clarify patient status and clinical management decisions.

Objectives: To analyze physician quantitative estimates for the proportion of management decisions attributed to INF, DAM, or STR (total=100%) in RA patients seen in routine care.

Methods: At one academic rheumatology center, the rheumatologist completes four 0–10 visual analog scales (VAS) for overall global assessment (DOCGL), INF, DAM, and STR. In patients with DOCGL ≥2, the proportion of management decisions are estimated as %INF+%DAM+%STR=100%. Cross-tabulations were computed for various phenotypes in 5 INF+DAM and INF+STR categories, 0, 1–20%, 21–40%, 42–60%, and 61–100%.

Results: Among the 77 RA patients, >40% of clinical management decisions were attributed to INF in only 31 (40%), versus >40% to DAM in 33 (43%), and >40% to STR in 17 (22%) (Table). No category of INF+DAM or INF+STR included more than 20% of the patients, and patients were found in 17 of 25 possible categories for combinations of INF+DAM and INF+STR. The 13 patients (17%) in whom INF was estimated to contribute 0% to management included 3 of 5 DAM and 5 of 5 STR categories (Table). The 23 patients with 1–20% of management attributed to INF included 4/5 DAM and 5/5 STR categories. The 10 with 21–40% INF included 4/5 DAM and 4 STR categories. The 16 with 41–60% attributed to INF included 3 DAM and 2 STR categories. Only 15 of the 77 patients (19%) had >60% attributed to INF.

Number among 77 RA patients with physician estimates of % inflammation, % damage and % distress (total=100%) in clinical management decisions (% is of all patients)

% Inflammation:	0	1–20%	21–40%	41–60%	61–100%	Total
N	13 (17%)	23 (30%)	10 (13%)	16 (21%)	15 (19%)	77
% Damage:						
0–20%	3 (4%)	8 (10%)	5 (6%)	3 (4%)	14 (18%)	33 (43%)
21–40%	0	0	2 (3%)	8 (10%)	1 (1%)	11 (14%)
41–60%	3 (4%)	4 (5%)	1 (1%)	5 (6%)	0	13 (17%)
61–80%	0	6 (8%)	2 (3%)	0	0	8 (10%)
81–100%	7 (9%)	5 (6%)	0	0	0	12 (16%)
% Distress:						
0–20%	7 (9%)	13 (17%)	3 (4%)	15 (19%)	15 (19%)	53 (69%)
21–40%	1 (1%)	2 (3%)	3 (4%)	1 (1%)	0	7 (9%)
41–60%	2 (3%)	2 (3%)	2 (3%)	0	0	6 (8%)
61–80%	1 (1%)	4 (5%)	2 (3%)	0	0	7 (9%)
81–100%	2 (3%)	2 (3%)	0	0	0	4 (5%)

Conclusions: Quantitative physician estimates of the proportion of clinical management decisions attributed INF, DAM, and STR may help clarify RA patient status and document a basis for clinical decisions. High levels of DAM and/or STR may explain in part why a target of RA remission often is not met in many patients seen in routine clinical care.[1]

References:

[1] Tymms et al, Arth Care & Res 66:190–196, 2014.

Disclosure of Interest: K. Gibson: None declared, I. Castrejon: None declared, T. Pincus Shareholder of: Health Report Services, Inc

DOI: 10.1136/annrheumdis-2017-eular.6239

SAT0110 THE IMPACT OF PUMMONARY INVOLVEMENT TO THE TREATMENT OF REUMATOID ARTHRITIS

K. Setoguchi[1], F.Y. Chen[1], S. Kamei[1], M. Ogawa[1], S. Kobayashi[2]. *[1]Systemic immunological diseases, Tokyo metropolitan Komagome Hospital; [2]Allergy and Rheumatology, Graduate school of medicine, The University of Tokyo, Tokyo, Japan*

Background: Standard treatment of patients with rheumatoid arthritis (RA) complicated with pulmonary involvements has not been clarified.

Objectives: To evaluate the influence of pulmonary involvement on immunological background and treatment of patients with RA.

Methods: A cross-sectional study was conducted, in which medical records of 479 RA patients who visited our hospital during September the first to November 31th, 2016 were reviewed. Pulmonary involvements were diagnosed by imaging including plain chest radiography or chest computed tomography findings. Patients were divided into two groups, with or without pulmonary involvement, and compared with immunological background (serum level of rheumatoid factor (RF), anti-CCP antibody and recent treatment.

Results: Among 479 patients, pulmonary involvements were diagnosed in 158 patients (female =116), mean age was 73.4 (standard deviation (SD) 9.0) year old, and mean disease duration was 143.3 (SD 125.9) months. Pulmonary involvements included interstitial pneumonia (N=52), organizing pneumonia (N=11), airway diseases (N=36), old tuberculosis (N=18), nontuberculous mycobacteria (N=13), pleurisy (N=5). Higher anti-CCP titers were found in RA with pulmonary involvement than RA only (medians 303.9±596.5 versus 163.5±256.1 U/mL, P<0.001), and the same result was found in RF (medians 322.5±437.2 versus 157.9±277.5 IU/mL, P<0.001). Methotrexate (MTX) was less frequently used (N=56, 35.4% versus N=205, 63.9%, P<0.001), but biological agents were more used (N=31, 19.6% versus N=49, 15.3%), especially abatacept (ABT) was highly used (N=15, 9.5% versus N=8, 2.5%).

Conclusions: RA patients with pulmonary involvements had high immunological response and were less prescribed MTX with may injure lungs and more used ABT. Association between pulmonary involvement and high titer of ACPA, and between positivity for RF or ACPA and good response of ABT were reported. ABT may be useful treatment for RA patients with pulmonary involvement.

References:

[1] Gottenberg JE et al.: Arthritis Rheumatol.68 (6):1346–1352.2016.

[2] Rocha-Munoz AD et al.: J immunol Res. Epub 2015 May 19.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3936

SAT0111 CLARA CELL PROTEIN CC16 AND ITS PATHOGENIC ROLE IN BRONCHIAL OBSTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

K.V. Nochevnaya[1], I.I. Nesterovich[2], Y.D. Rabik[2], A.A. Speranskaya[3], V.P. Zolotnitskaya[3], N.A. Amosova[3], V.I. Amosov[3], V.I. Trofimov[2], T.D. Vlasov[4]. *[1]Hospital Therapy Department, Department of Pathophysiology; [2]Hospital Therapy Department; [3]Radiology Department; [4]Department of Pathophysiology, Academician I.P. Pavlov First St. Petersburg State Medical University, Saint Petersburg, Russian Federation*

Background: Bronchial obstruction (BO) is a common manifestation of lung involvement in rheumatoid arthritis (RA) with high incidence from 60 to 80% of all cases. However the pathogenesis of BO in patients with RA remains unknown. Serum level of protein CC16 produced by Clara cells in terminal bronchioles has been reported to decrease in BO associated with bronchial asthma, chronic obstructive pulmonary disease and others. CC16 was considered to demonstrate anti-inflammatory effect via inhibition of interferon-gamma, tumor necrosis factor alpha, interleukin 1 beta, neutrophil elastase and other proinflammatory factors. Also it was shown that CC16 deficiency has a pathogenic effect in BO. In the same time the role of protein CC16 in the pathogenesis of autoimmune diseases (and RA) is not studied.

Objectives: We aimed to evaluate serum level of CC16 in patients with RA in dependence on the presence and severity of BO.

Methods: Serum levels of CC16 in 66 patients with RA and 13 healthy controls were measured by enzyme linked immunoadsorbent assay (ELISA). Patients with RA underwent survey, physical examination and pulmonary function tests (PFTs) including spirometry and bronchodilator test with inhalation of salbutamol (N=41) and body plethysmography (N=11). Statistical processing was carried out using Spearman correlation coefficient and Mann-Whitney test. P value <0.05 was considered as significant.

Results: More than 60% of participants with RA had BO in terminal bronchioles (small airway obstruction), which was revealed with changes of expiratory flows (forced expiratory volume in 1s (FEV1), forced expiratory flow (FEF) between 50% and 75% of forced vital capacity), residual volume (RV) and bronchial resistance (SGaw) in relation to proper values. Depression of post-bronchodilator $FEF_{75\%}$ lower than 70% was adopted as the main criterion of BO. There were no differences (p value >0,05) between serum levels of CC16 in patients with RA (20,14±1,49 ng/ml) and control group (22,70±2,13 ng/ml). However in patient group those with BO had significantly lower levels of CC16 (15,59±1,89 compared with 27,43±2,81 in patients without BO, p value <0,01). Lower CC16 was associated with decreased post-bronchodilator FEV1 and $FEF_{75\%}$ (r =0,345, p

value <0,05 and r =0,486, p value <0,01 respectively), depressed bronchial resistance SGaw (r =0,773, p value <0,01) and increased RV (r = -0,736, p value <0,01), which determined BO severity.

Conclusions: More than half of patients with RA have BO predominantly in terminal bronchioles. Accepting significant decrease of Clara cell protein CC16 in patients with RA having BO we suppose pathogenic relationship between functional depression of Clara cell anti-inflammatory activity and BO in this category of patients.

References:

[1] Park HY. Club cell protein 16 and disease progression in chronic obstructive pulmonary disease (2013).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4585

SAT0112 PREVALENCE AND INCIDENCE OVER 3 YEARS OF DIFFERENT COMORBIDITIES IN RHEUMATOID ARTHRITIS (RA): A 3 YEAR LONGITUDINAL STUDY IN 769 ESTABLISHED RA PATIENTS

L. Gossec, M. Soubrier, F. Foissac, F. Fayet, N. Balandraud, T. Bardin, C. Beauvais, G. Chales, I. Chary-Valckenaere, E. Dernis, L. Euller-Ziegler, R.-M. Flipo, M. Gilson, T. Marhadour, X. Mariette, G. Mouterde, S. Pouplin, P. Richette, A. Ruyssen-Witrand, T. Schaeverbeke, C. Sordet, M. Dougados. *COMEDRA working group, Paris, France*

Background: Comorbidities including cardiovascular (CV) risk, cancer and osteoporosis are frequent in RA.[1]

Objectives: To quantify at baseline and 3 years later, the prevalence (at baseline) and incidence (over 3 years) of some selected comorbidities.

Methods: This was an open long term (3 years) extension of the COMEDRA 6-month randomized controlled trial in which patients with definite, stable RA were visiting a nurse for comorbidity counselling.[2] Comorbidity status was assessed through face-to-face interviews and nurses provided advice on screening and management, at baseline and 3 years later. The frequency of comorbidities was assessed at both timepoints and incidence of new cases was assessed as overall % of patients and as relative increase in the given comorbidity.

Results: Of the 970 recruited patients, 776 (80%) were followed up at 2–4 years (15, 1.5%, had died) and 769 (79%) had available data for comorbidities at both timepoints: at baseline, mean (±SD) age 58 (±11) years, mean disease duration 14 (±10) years; 614 (80%) were women and 538 (70%) were receiving a biologic with a mean DAS28 of 3.1±1.3.

At baseline, the most frequent comorbidities were history of fracture (31.9%) and high blood pressure (30.9%) and at 3 years the comorbidity which had most increased (i.e., incidence) in this population aged around 60 years, was high blood pressure (4%) whereas smoking had decreased (Table).

Table: frequency of comorbidities at baseline and 3 years later

Comorbidity	COMEDRA study baseline (month 0 for group I and month 6 for group II)	Follow-up at 3 years	Absolute increase, % of 769 patients (relative increase, % of baseline prevalence)
Myocardial infarct	13 (1.7)	18 (2.3)	0.6 (38.4)
Angina	9 (1.2)	17 (2.2)	1.0 (88.9)
Stroke	16 (2.1)	29 (3.8)	1.7 (81.2)
Obliterating arteriopathy	8 (1.0)	14 (1.8)	0.8 (75.0)
Diabetes	39 (5.1)	50 (6.5)	1.4 (28.2)
High Blood Pressure	238 (30.9)	270 (35.1)	4.2 (13.4)
Hyperlipidemia	149 (19.4)	170 (22.1)	2.7 (14.1)
Obesity (BMI>=30)	114 (14.8)	124 (16.1)	1.3 (8.8)
Smoking	120 (15.6)	104 (13.5)	-2.1 (-13.3)
Colon cancer	2 (0.3)	2 (0.3)	0 (0)
Breast cancer	23 (3.0)	27 (3.5)	0.5 (17.4)
Lung cancer	1 (0.1)	2 (0.3)	0.2 (100.0)
Prostate cancer	3 (0.4)	4 (0.5)	0.1 (33.3)
Uterus cancer	7 (0.9)	7 (0.9)	0 (0)
Skin cancer (all types)	26 (3.4)	36 (4.7)	1.3 (27.8)
Lymphoma	2 (0.3)	3 (0.4)	0.1 (50.0)
History of fracture	245 (31.9)	256 (33.3)	1.4 (4.5)

Conclusions: Comorbidities are frequent in RA though screening does not always address the most frequent or severe comorbidities. Efforts must be pursued to improve comorbidity screening and prevention.

References:

[1] Ref 1. Baillet A, Gossec L et al. Ann Rheum Dis. 2016;75(6):965–73.

[2] Ref 2. Dougados M, Soubrier M, et al. Ann Rheum Dis. 2015;74(9):1725–33.

Acknowledgements: grant from Roche France and from the French National Research Program (PHRC AOM 12072).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2978

SAT0113 OBESITY AND METABOLIC SYNDROME INFLUENCE ON N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE LEVELS IN RHEUMATOID ARTHRITIS PATIENTS

L. Kondratyeva, T. Popkova, I. Kirillova, D. Novikova, A. Novikov, E. Alexandrova, E. Nasonov. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: N-terminal pro-brain natriuretic peptide (NT-proBNP) is a recognized myocardial injure marker, a known predictor of heart failure and cardiovascular death. Rheumatoid arthritis (RA) patients (pts) were shown to have higher than in general population NT-proBNP concentrations, positively correlating with IL-6 levels. Adipose tissue is considered be one of the sources of this pro-inflammatory cytokine. But on the other hand, metabolic syndrome (MS) and obesity, which also occur in RA pts, are usually associated with lower NT-proBNP levels in general population.

Objectives: To find out whether overweight/obesity or MS may modify NT-proBNP levels in RA pts.

Methods: A total of 68 early RA pts (72% females, 28% males) was enrolled in the study. Mean disease duration was 6 [4;8] months, and RA activity using DAS28 calculator was 5,6 [5,1;6,4] scores. The majority of pts had positive RF (87%) and ACPA (88%). All pts were glucocorticoids and disease-modifying antirheumatic drugs - naïve prior to inclusion. The overweight/obesity was determined by WHO criteria in patients with body mass index (BMI) ≥25 kg/m^2. National Cholesterol Education Program/Adult Treatment Panel III criteria were used to confirm MS. Serum levels of NT-proBNP (pg/mL) were measured using electrochemiluminescence test Elecsys proBNP II (Roche Diagnostics, Switzerland). NT-proBNP levels >125,0 pg/mL were considered as elevated.

Results: Overweight and obesity were established in 54,4% RA pts. Overweight/obese RA pts were older than pts with normal BMI (57 [53;61] years vs 48 [34;61] years, p=0,02), had higher DAS28 scores (5,85 [5,20;6,57] vs 5,28 [4,76;5,69], p<0,01), higher CRP (38,8 [14,3; 47,9] mg/L vs 12,8 [2,2;28,8] mg/L, p<0,01). Elevated NT-proBNP concentrations were found in 62,2% overweight/obese pts vs 29,0% pts with normal weight (p<0,01), median NT-proBNP concentrations were 153,4 [87,3;236,9] pg/mL vs 75,2 [40,2;147,4] pg/mL, respectively (p=0,02). MS was established in 62,2% pts with BMI ≥25kg/m^2 and in 25,8% pts with BMI<25kg/m^2 (p<0,01). Median NT-proBNP concentrations did not vary significantly in pts with and without MS, whether they were overweight/obese (p=0,75), or had normal BMI (p=0,27). Although higher rates of elevated NT-proBNP concentrations were documented in pts with MS (61,3% vs 35,1%, p=0,03). NT-proBNP levels positively correlated with waist circumference (r=0,33, p<0,01), ESR (r=0,25, p=0,04), and CRP (r=0,3, p=0,01).

Conclusions: Overweight and obesity in RA pts were associated with increased NT-proBNP levels. Abdominal obesity was identified as the only MS component, influencing NT-proBNP levels, presumably via up-regulation of the inflammatory process.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3731

SAT0114 POOR CARDIOVASCULAR RISK MANAGEMENT IN RHEUMATOID ARTHRITIS PATIENTS DESPITE AN EXPLICIT CARDIOVASCULAR RISK MANAGEMENT PROGRAM

M. Heslinga[1], I. van den Oever[1], E. Griep[2], H. Griep-Wentink[2], Y. Smulders[3], W. Lems[1,4], M. Boers[1,4], A. Voskuyl[4], M. Peters[3], D. van Schaardenburg[1], M. Nurmohamed[1,4]. *[1]Amsterdam Rheumatology and immunology Center | Reade, Amsterdam; [2]Antonius Hospital Zuidwest Friesland, Sneek; [3]VU University Medical Center; [4]Amsterdam Rheumatology and immunology Center | VU University Medical Center, Amsterdam, Netherlands*

Background: In 2011, we started a cardiovascular (CV) risk management program for rheumatoid arthritis (RA) patients visiting Reade in the Netherlands. We previously reported the presence of under treatment of hypercholesterolemia and hypertension [1].

Objectives: To assess the effectiveness of our CV risk management program after one year.

Methods: CV risk screening was performed at baseline and we informed the general practitioner (GP) about the results, including advices regarding the initiation of cardio preventive drugs. In high risk patients, antihypertensives were recommended when systolic blood pressure >140 mm/Hg and statins were recommended when low-density lipoprotein >2.5 mmol/l. The decision to start preventive medication was left to the GP. CV risk screening was repeated after one year. Patients completed a questionnaire about the actions that were taken following the results of the initial screening.

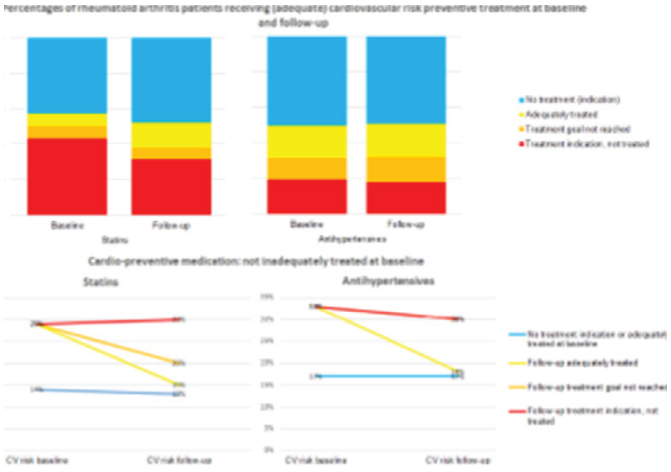
Results: Of the 266 patients 202 (76%) were female, the mean age was 58±11 years. After one year, 88 out of 134 patients who received inadequate or no treatment at baseline were still untreated or undertreated. Of the 188 (71%) patients who were at high CV risk and who did have an indication to start therapy, only 7.5% was contacted by their GP and another 6.8% arranged an appointment themselves. While the 10-year CV risk did not decrease in the group as a whole, a risk reduction was found in the patients that started medication. Remarkably, 42% of patients reported lifestyle changes, including more exercise (20%), diet adaption (16%) and weight loss (9%).

Conclusions: It is striking that one year after the introduction of our CV risk

Table 1. Cardiovascular risk factors at baseline and after one year

	Baseline	Follow-up
CV disease history	20 (7.5)	23 (8.6)
CV risk <10%	43 (16.2)	52 (19.5)*
CV risk 10–20%	60 (22.6)	62 (23.3)
CV risk >20%	143 (53.8)	129 (48.5)*
SBP in mm/Hg	135±17	135±18
Body Mass Index in kg/m^2	26.4±5.0	26.3±4.8
TC in mmol/l	5.5±1.0	5.2±1.0**
Triglycerides in mmol/l	1.4±0.8	1.4±0.8
LDL-cholesterol in mmol/l	3.2±0.9	3.0±0.9**
HDL-cholesterol in mmol/l	1.6±0.5	1.6±0.5
TC/HDL-ratio	3.7±1.2	3.7±1.2**
Current smokers	60 (22.6)	53 (20.1)
Diabetes mellitus	12 (4.5)	12 (4.5)
SBP >140 mm/Hg	95 (35.7)	96 (36.2)
LDL >2,5 mmol/l	208 (78.8)	180 (68.4)**
TC ≥6.5 mmol/l	37 (13.9)	26 (9.8)
Antihypertensives	81 (30.5)	88 (33.1)
Statins	38 (14.3)	57 (21.4)**

CV = Cardiovascular, HDL = high-density lipoprotein, LDL = low-density lipoprotein, TC = total cholesterol, SBP = Systolic blood pressure. Results are presented as mean ± standard deviation or n, (%). *p<0.05, **p<0.01.



management program, only 14,3% patients with an indication for preventive treatment visited their GP and only 14% started with CV risk lowering drugs. This is mainly caused by the small percentage of high risk patients that contacted their GP. On the other hand, a high percentage reported the start of healthy lifestyle. These results underscore the need for a short-term follow-up, in close collaboration with primary care providers to ensure appropriate CV risk management. This is a future implementation project that will be initiated shortly.

References:

[1] Ann Rheum Dis 2015;74:192.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3188

SAT0115 EFFECT OF BIOLOGICAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (BDMARDS) ON CARDIO VASCULAR DISEASE (CVD) RISK IN RA PATIENTS:THREE YEARS RESULTS FROM A CANADIAN COHORT

M. Khraishi[1], C. Molta[2], A. Lewis[3]. *[1]Rheumatology, Memorial University of Newfoundland, St. John's, Canada; [2]Rheumatology, MainLine Rheumatology Lankenau Medical Center, Philadelphia, United States; [3]Epidemiology, Memorial University of Newfoundland, St. John's, Canada*

Background: RA patients have a higher risk for developing CV Diseases (e.g. IHD and stroke) than the general population.We reported previously (ACR, EULAR) the results CV risk in our patients treated with bDMARDs for 1& 2 years.

Objectives: To assess the effect of bDMARDs treatment on 10-year CV disease risk in patients with RA after 36 months and evaluate the impact of their use on the incidence of CV events

Methods: A cohort of RA patients was followed prospectively.Demographics, disease activity parameters, inflammatory markers, CV events, CVD 10 year risk assessment [Framingham Risk Score (FRS)] were ascertained at the baseline and every six months, up to 36 months.Statistical analysis utilized SPSS (IBM version 24) software.

Results: 321 patients were included, of those 270 patients were followed for three years. Eight BDMARDs were included evaluating their effect on disease activity and CV risk in 233 patients who continued on their prospective biologic for the three years.

Significant overall reduction in disease activity in all groups was obtained as compared to baseline. The whole group DAS improved from 3.996 to 3.118. The HAQ also improved significantly (1.201 to 0.857) and the CRP improved significantly (12.91 mg/L to 7.3).

Overall, Total cholesterol (TC) changed from 5.195 mmol/L at baseline to 4.992 (P 0.001). High Density Lipoprotein Cholesterol (HDL-C) increased significantly at 36 months from 1.336 to 1.376. However, the Atherogenic Index (AI) for the whole cohort changed from 3.636 to 3.845. The overall 10 year risk of cardiovascular event increased from 12.878 to 13.8

The cohort included 321 patients. Eight bDMARDs were evaluated to assess their effect on disease activity and CVD risk. The outcomes in 233 patients who continued their prospective biologic for the three years were reported (table). 77% were females, median RA duration was 11 ys. Significant reduction in disease activity in all groups was achieved vs. baseline. The DAS improved from 3.996 to 3.118, the HAQ improved significantly (1.201 to 0.857) and the CRP also improved significantly (12.91 mg/L to7.3). Overall, Total cholesterol (TC) changed from 5.195 mmol/L at baseline to 4.992 (P 0.001). High Density Lipoprotein Cholesterol (HDL-C) increased significantly at 36 months from 1.336 to 1.376. The Atherogenic Index (AI) for the cohort changed from 3.636 to 3.845. The overall 10 year risk of cardiovascular event increased from12.878 to 13.8.

Table 1

	Rituximab n=40	Tocilizumab n=42	Golimumab n=24	Adalimumab n=42	Abatacept n=35	Etanercept n=39
DAS 28	4.3 vs 3.7 P 0.014	4.2 vs 2.8 P<0.001	4.1 vs 3.4 P 0.028	3.4 vs 2.8 P 0.011	4.3 vs 3.1 P<0.001	4.0 vs 2.8 P 0.0015
HAQ	1.3 vs 1.1	1.0 vs 0.9	1.2 vs 1.0	1.7 vs 0.5	1.2 vs 1.0	1.1 vs 0.7 P<0.001
Swollen Joint Count	3.8 vs 2.1 P 0.005	5.0 vs 1.8 P<0.001	5.3 vs 6.7	3.6 vs 1.7 P 0.010	3.7 vs 3.6	3.9 vs 1.7 P<0.001
AI	4.0 vs 3.7 P 0.045	4.7 vs 4.0	3.2 vs 3.94	3.8 vs 3.7	4.1 vs 3.9	4.2 vs 3.7
10 yr CV Risk	15.9 vs 17.9	13.5 vs 14.4	14 vs 15.7	10.1 vs 13.2 P 0.009	13.5 vs 14.1	11.2 vs 12.2

Conclusions: The bDMARDS studied were effective in controlling the disease activity of RA. Although the overall CVD risk was not reduced in the group as a whole at 36 months, bDMARDS may still play a role in reducing the CVD risk in these patients

Disclosure of Interest: M. Khraishi Grant/research support from: Roche Canada, C. Molta: None declared, A. Lewis: None declared

DOI: 10.1136/annrheumdis-2017-eular.1436

SAT0116 PREVALENCE OF UNACCEPTABLE PAIN IN PATIENTS WITH LONG-STANDING RA

M.L. Andersson, K. Forslind, B. Svensson. *Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund and Helsingborg, Sweden*

Background: Pain in patients with rheumatoid arthritis (RA) is the most common and troublesome symptom, occurs frequently in many sites in the muscular-skeletal system, causes fatigue and functional impairment. The origin of pain in RA may be inflammatory and/or other, such as increased sensitivity to pain, fibromyalgia and osteoarthritis.

Objectives: To study unacceptable pain in an inception cohort of patients with RA at 15 years follow-up

Methods: This study concerns 477 patients from the BARFOT inception cohort study, consisting of 839 patients with early RA, who have passed the pre-defined 15 year follow-up visit. Unacceptable pain (UP) was defined as ≥40 mm on a continuous VAS pain scale of 100 mm with the ends "no pain" and "worst possible pain" (1). ADL- function was assessed by the HAQ test, physical function by the SOFI test and joint damage by the van der Heijde modified Sharp method. Remission was defined as DAS28 ≤2.6.

The prevalence of UP over time as well as the relationship of UP with clinical variables were assessed. Baseline predictors of UP after 15 years were evaluated by logistic regression.

Results: The mean baseline VAS pain was 45 mm, decreased after 6 months to 29 and remained after that fairly stable through the years ending in 31 at 15 years. UP followed a similar course with 56% of the patients at baseline, which decreased to 30% after 6 months and then behaved stable until 15 years, 34%. Seventy-seven per cent of the patients with UP were not in remission at 15 years, while 23% had UP in spite of being in remission.

Patients with UP who were in remission at the 15 years visit had higher mean age (p=0.004), ESR (p=0.001) and SOFI (p=0.001) than patients without UP.

Patients with UP who were not in remission at this point in time were more often women (0.008) and had more tender joints (p=0.001) than patients who did not have UP.

In both remission groups the mean DAS28, patient global assessment and HAQ were higher in patients with UP compared with patients without.

The means of the x-ray joint damage scores - total score, erosion and joint space narrowing scores - were very similar among patients with or without UP, statistically not significant.

A logistic regression analysis of the ability of baseline variables to predict UP at 15 years was performed. It was shown that female gender and baseline pain independently predicted unacceptable pain at 15 years in patients not in remission while in patients in remission high age and ESR were independent predictors.

Conclusions: Pain is a frequent and relentless suffering during the long-term course of rheumatoid arthritis. In this study, 34% of the patients had unacceptable pain 15 years after diagnosis indicating unsatisfactory treatment. Unacceptable pain also occurred in patients in remission indicating that pain in RA is multifactorial. Therefore, the cause of pain should be identified and treatment initiated accordingly.

References:
[1] Altawil, R. Pain mechanisms of fatigue and autonomic function in rheumatoid arthritis [dissertation]. Stockholm: Karolinska Institutet; 2016.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3641

SAT0117 RETENTION RATES OF ADALIMUMAB, ETANERCEPT, AND INFLIXIMAB AS 1ST- OR 2ND-LINE BIOTHERAPY FOR RHEUMATOID ARTHRITIS PATIENTS IN DAILY PRACTICE IN AUVERGNE

M. Soubrier[1], B. Pereira[2], T. Frayssac[1], A. Fan[1], M. Couderc[3], S. Malochet-Guinamand[1], S. Mathieu[1], Z. Tatar[1], A. Tournadre[3], J.-J. Dubost[1]. *[1]Rheumatology, C.H.U. HÔPITAL GABRIEL MONTPIED; [2]DRCI, CHU Gabriel Montpied; [3]Rheumatology, CHU Hopital Gabriel Montpied, Clermont-Ferrand, France*

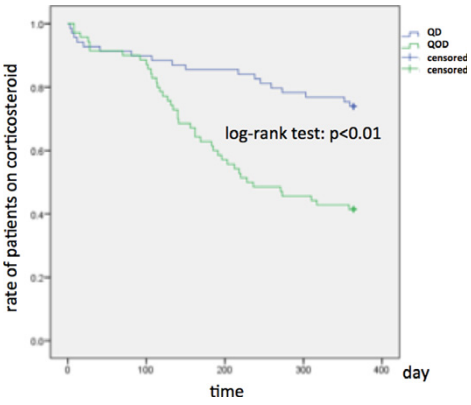
Background: The use of anti-tumor necrosis factor-alpha agents, or anti-TNFs, has greatly improved the treatment of rheumatoid arthritis (RA). The first three anti-TNFs available to us (infliximab, adalimumab, and etanercept) are the most widely used in treating RA. Their efficacy and safety, demonstrated in extensive randomized and controlled trials (RCTs), were not shown to vary significantly when compared indirectly based on randomized studies. Nevertheless, the randomized studies were of short duration and included a selected population that differed from patients treated in daily practice.
Objectives: To compare, in real-life conditions, the retention rates of the initial anti-TNF treatment (etanercept [ETN], adalimumab [ADA], and infliximab [IFX]) initiated as first-line biotherapy for rheumatoid arthritis (RA) and to evaluate, in case of failure, the switch to another anti-TNF or a non-anti-TNF biological.
Methods: Monocentric retrospective cohort including all patients with RA starting a first anti-TNF between 2001 and 2015.
Results: Among the 346 patients analyzed, 201 received ETN, 82 ADA, and 63 IFX. The first anti-TNF was interrupted in 151 cases. The retention rates were 82.8%, 67.6%, 46.5%, 28.1%, and 22.5% at 1, 2, 5, 10, and 15 years, respectively, with a median retention duration of 52.8 [18.9 -136.2] months (ETN: 59.3 [19.1-NA), ADA: 79.9 [19.3–136.2], and IFX: 37.2 [17.5–134.5], p=0.49). The predictive factors of discontinuation were active RA (DAS28-CRP HR: 1.22 [1.03–1.45]), inflammatory syndrome (ESR HR: 1.01 [1.0–1.02]; CRP HR: 1.00 [1.00–1.01]), absence of MTX treatment (HR: 0.60 [0.43–0.83]), and corticosteroid use (HR: 1.91 [1.31–2.78]). The patients who switched to another anti-TNF treatment had an inferior retention than those who switched to a non-anti-TNF treatment (HR: 0.39 [0.17 - 0.87], p: 0.02). p=0.02).
Conclusions: In real life, there was no difference in retention among the three anti-TNF agents, and 25% of patients continued them at 15 years. After failure of an anti-TNF, the switch to a non-anti-TNF biotherapy showed better retention.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3676

SAT0118 SAFETY AND EFFICACY OF ALTERNATE-DAY CORTICOSTEROIDS AS ADJUNCTIVE THERAPY IN RHEUMATOID ARTHRITIS

M. Suda[1], S. Ohde[2], T. Tsuda[1], M. Kishimoto[1], M. Okada[1]. *[1]Immuno-Rheumatology Center, St. Luke's International Hospital; [2]Center for Clinical Epidemiology, St. Luke's International University, Tokyo, Japan*

Background: Corticosteroids are often used for treating rheumatoid arthritis. However, minimizing adverse events while maximizing efficacy remains challenging. An alternate-day corticosteroid dose is known to decrease adverse events.
Objectives: To investigate the safety and efficacy of an alternate-day corticosteroid dose for treating rheumatoid arthritis.
Methods: We have conducted a retrospective cohort study among patients over 18-year-old who started oral corticosteroids (prednisolone and methylprednisolone) as treatment of rheumatoid arthritis from 2005 to 2014 at St. Luke's International Hospital, a tertiary-level community teaching hospital in Tokyo, Japan. Patients were included if they met the American College of Rheumatology/European League Against Rheumatism 2010 classification criteria for rheumatoid arthritis, and had positive anti-cyclic citrullinated peptide antibody. They were excluded for a history of corticosteroid use for other diseases, or if they were lost to follow-up within 1 year after starting corticosteroids. We divided patients into a daily corticosteroid group (QD) and an alternate-day corticosteroid group (QOD). Patients who received both daily and alternate-day corticosteroids were assigned to the daily group. We investigated the percentage of patients without any infection within 1 year after starting corticosteroids. We have conducted multivariate logistic regression model analysis to calculate adjusted odds ratio for QD/QOD to the outcome. We also investigated the mean decrease in C-reactive protein (CRP) at 1 month as a marker of short-term effectiveness, and the percentage of patients free from corticosteroid at one year, using student's t-test.
Results: In total, 139 patients were analysed (69 in the QD group, 70 in the QOD group). The maximum dose of corticosteroid in one year was not significantly different in two groups (11.4±7.7 mg/day VS 10.1±5.3 mg/day; P=0.267), and the mean daily dose of corticosteroid in one year was significantly higher in the QD group (6.1±4.4 mg/day vs 3.9±1.7 mg/day; P<0.01).The percentage of patients without any infection was 49.2% in QD group, and 75.7% in QOD group. Univariate analysis showed QD group is significantly associated with higher incidence of infection (P=0.001). After multivariate analysis adjusted with age, gender, initial CRP value, mean daily dose of corticosteroid in one year, use of biologic DMARDs, and duration of rheumatoid arthritis, the odds ratio of QD for any infection in 1 year was 3.9 (95% confidence interval [CI], 1.7–8.8; P=0.001).The mean decrease of CRP at 1 month was 1.5 mg/dl in QD group, and 1.1 mg/dl in QOD group (P=0.435).The percentage of patients free from corticosteroids at one year was 26.1% in QD group, and 58.6% in QOD group (P<0.01). Kaplan-Meier plot showed that QD group patients are more difficult to become free from corticosteroid (log-rank test: p<0.01).



Conclusions: Alternate-day corticosteroid dose has a lower adverse event rate and is as effective as a daily corticosteroid dose for treating rheumatoid arthritis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4160

SAT0119 PREGNANCY OUTCOMES IN WOMEN WITH AND WITHOUT RHEUMATOID ARTHRITIS

M.E.B. Clowse, G. McDaniel, A.M. Eudy. *Rheumatology, Duke University Medical Center, Durham, United States*

Background: Prior studies have suggested higher rates of preterm birth in pregnancies to women with rheumatoid arthritis.
Objectives: We sought to identify differences in the pregnancy outcomes of women with and without RA, and pregnancies that occurred prior to and following RA diagnosis.
Methods: A cross-sectional survey was completed by 75 women with RA age-matched to 75 women without RA. Information collected about each prior pregnancy included: pregnancy outcome (spontaneous abortion, stillbirth, elective termination, ectopic pregnancy, or live birth); the timing of delivery; infant anomalies; methotrexate exposure in pregnancy; and whether the pregnancy was planned. Simple statistics were used to compare pregnancy outcomes between women with and without RA and pregnancies prior to and following RA diagnosis.
Results: The majority of women with RA (83%) and controls (64%) were white, and 11% of women with RA and 28% of controls were African American. About half of controls and 31% of women with RA had education beyond college. The average age at the time of the survey was 32 years (SD: 5) in both RA patients and controls, and the average age at RA diagnosis was 23 years (SD: 10). There were 76 pregnancies in 40 women with RA and 99 pregnancies in 33 healthy controls (see table). The overall rates of live birth, spontaneous abortion, and ectopic pregnancies were similar between groups; there were no stillbirths.
The rate of elective termination was significantly different, with 9% of RA and 30% of control pregnancies terminated (p=0.005). The large majority of the terminations in women with RA occurred prior to diagnosis. The higher frequency of unplanned pregnancy among the controls (38% unplanned RA vs 67% unplanned controls, p=0.0002) likely contributed to this higher termination rate. Of unplanned pregnancies, 45% were terminated in controls, 33% in pre-RA pregnancies, and 9% in post-RA pregnancies. No planned pregnancies were terminated. Three pregnancies in women with RA were exposed to methotrexate (2 unplanned, 1 planned) resulting in 2 spontaneous abortions and 1 live birth, born at term without any reported abnormalities.
The rates of preterm birth and infant abnormalities did not differ significantly between those with and without RA, though among women with RA, all preterm births and infant abnormalities occurred after RA diagnosis. Each of the RA preterm births was delivered between 31–34 weeks gestation. Preeclampsia

was more common in women with RA, but did not differ significantly between pregnancies prior to and after RA diagnosis.
A total of 41% of the post-RA pregnancies had an adverse pregnancy outcome (miscarriage, preterm delivery, or infant abnormality), compared to 13% of pre-RA pregnancies (p=0.01) and 20% of control pregnancies (p=0.01).

	Pregnancies in Healthy Controls	Pregnancies in women with RA	Pregnancies prior to RA	Pregnancies after RA
Number of Pregnancies	99	76	32	44
Live Births	53 (54%)	51 (67%)	20 (63%)	31 (70%)
Spontaneous Abortion	13 (13%)	15 (20%)	4 (13%)	11 (25%)
Ectopic Pregnancies	3 (3%)	3 (4%)	2 (6%)	1 (2%)
Elective Termination	30 (30%)	7 (9%)†	6 (19%)	1 (2%)
Preterm Birth	6/53 (11%)	5/51 (10%)	0	5/31 (16%)
Preeclampsia	1/53 (2%)	9/51 (18%)†	5/20 (25%)	4/31 (13%)
C-section	14/52 (27%)	15/51 (29%)	7/20 (35%)	8/31 (26%)
Abnormal Infant	3/54 (6%)*	3/51 (6%)	0	3/31 (10%)
Adverse Pregnancy Outcome	20 (20%)	22 (29%)	4 (13%)	18 (41%)‡

*one twin pregnancy in controls
†p<0.05, controls vs. RA pregnancies
‡p<0.05, pre- vs. post-RA pregnancies

Conclusions: Women with RA, overall, had similar rates of miscarriage, stillbirth, and ectopic pregnancy compared to healthy women, but pregnancies that occurred after RA diagnosis had higher rates of these adverse outcomes. More pregnancies in women with RA were planned, leading to a lower rate of elective termination.
Acknowledgements: This study was funded by Pfizer.
Disclosure of Interest: M. Clowse Grant/research support from: Pfizer, Janssen, Consultant for: UCB, G. McDaniel: None declared, A. Eudy: None declared
DOI: 10.1136/annrheumdis-2017-eular.6338

SAT0120 EVALUATION OF THE RISK OF OVERALL MALIGNANCY AND MALIGNANT LYMPHOMA WITH METHOTREXATE AND BIOLOGICAL AGENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON THE IORRA COHORT DURING A 14-YEAR OBSERVATION PERIOD

N. Sugimoto[1], E. Tanaka[1], E. Inoue[1,2], M. Kawano[1], M. Ochiai[1], Y. Shimizu[1], R. Yamaguchi[1], K. Ikari[1], A. Nakajima[1], A. Taniguchi[1], H. Yamanaka[1]. [1]*Institute of Rheumatology, Tokyo Women's Medical University;* [2]*Center for Clinical Research for Development, National Center for Child Health and Development, Tokyo, Japan*

Background: While dramatic progress has been made in this decade with treatments for rheumatoid arthritis (RA), such as methotrexate (MTX) and biological agents, concern about the safety, including the occurrence of malignancy, of these highly effective drugs still exists in daily clinical practice. There has not been an evident association between the use of biological agents and the occurrence of malignancy in most reports from clinical trials[1] and observational studies[2], although MTX use might be associated with the development of malignant lymphoma, called MTX-associated lymphoproliferative disorder[3], in patients with RA. In an analysis of risk factors for overall and site-specific malignancies in Japanese patients with RA, higher disease activity was identified to be a risk factor for overall malignancies (hazard ratio [HR] 1.10, 95% CI 1.02–1.19), suggesting that tight control of RA disease activity would reduce the occurrence of malignancies in patients with RA[4]. However, the risk of malignancies with RA treatments including MTX and biological agents was not assessed in that analysis.
Objectives: We investigated the association between the occurrence of malignancies (overall and malignant lymphoma) and drug use (MTX and biological agents) in a large observational cohort of Japanese patients with RA over a long-term period.
Methods: Among Japanese patients with RA enrolled in the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort from April 2000 to September 2013, data for all malignancies were extracted from patients' self-reports and confirmed by medical records. Data for malignancies occurring in patients who dropped out of the IORRA study during the subsequent three months were also collected from medical information from affiliated hospitals. We analysed whether MTX and biological agents were risk factors for overall malignancy and malignant lymphoma using a marginal structural Cox proportional hazards model[5] adjusted for age, gender, smoking history, body mass index, RA disease duration, rheumatoid factor positivity and disease activity (28-joint disease activity score).
Results: Among 11,106 Japanese patients with RA representing 68,483 person-years, 507 overall malignancies, including 68 malignant lymphomas, were confirmed. Neither MTX nor biological agent use was a significant risk factor for overall malignancy, with an HR (95% CI) of 1.18 (0.77–1.81) and 1.01 (0.65–1.57), respectively, or for malignant lymphoma, with an HR (95% CI) of 1.17 (0.55–2.48) and 1.26 (0.43–3.64), respectively.
Conclusions: The use of MTX and biological agents was not significantly associated with the occurrence of overall malignancy or malignant lymphoma during long-term longitudinal observation of Japanese patients with RA.
References:
[1] Moulis G, et al. PLoS One. 2012;7:e48991.
[2] Mariette X, et al. Ann Rheum Dis. 2011;70:1895–904.
[3] Kameda T, et al. Arthritis Care Res (Hoboken). 2014;66:1302–9.
[4] Sugimoto N, et al. EULAR Congress 2016;FRI0143.
[5] Choi HK, et al. Lancet. 2002;359:1173–7.
Disclosure of Interest: N. Sugimoto Speakers bureau: Takeda Pharmaceutical and Bristol Myers Squibb., E. Tanaka Consultant for: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical., Speakers bureau: Abbvie, Eisai Pharmaceutical, Chugai Pharmaceutical, Bristol Myers Squibb, Astellas Pharmaceutical, Pfizer, Takeda Pharmaceutical, and Ayumi Pharmaceutical., E. Inoue: None declared, M. Kawano: None declared, M. Ochiai: None declared, Y. Shimizu: None declared, R. Yamaguchi: None declared, K. Ikari Grant/research support from: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., Speakers bureau: Astellas, UCB, Bristol-Meyers, Pfizer, Eisai, Tanabe-Mitsubishi, Chugai, AbbVie, Janssen Pharmaceutical, Otsuka, Kaken, Asahi-Kasei, Hisamitsu and Takeda., A. Nakajima Consultant for: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., Speakers bureau: Bristol-Meyers, Mitsubishi Tanabe Pharma, Nippon Kayaku Co. Ltd., Novartis Pharma, Pfizer, Siemens Healthcare Diagnostics K.K. and Takeda Pharmaceutical Company., A. Taniguchi Grant/research support from: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., Speakers bureau: AbbVie, Eisai, Takeda, Tanabe-Mitsubishi, Teijin Pharma, Pfizer., H. Yamanaka Grant/research support from: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Consultant for: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers., Speakers bureau: MSD, Ayumi, AbbVie, Eisai, Ono, Astellas, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, Nippon Shinyaku, Pfizer. UCB. Nippon Kayaku, YL biologics, Bayer and Bristol-Meyers.
DOI: 10.1136/annrheumdis-2017-eular.2663

SAT0121 COMORBITIES AND DISEASE ACTIVITY ARE RELEVANT FOR FUNCTIONAL DISABILITY IN RHEUMATOID ARTHRITIS

N. Andrade[1], A.M. Kakehasi[2], C. Machado[2], K. Gomes[3], M.F. Guimarães[2], S. Krampe[1], C. Rodrigues[3], C. Brenol[1]. [1]*Federal University of Rio Grande do Sul, Porto Alegre;* [2]*Universidade Federal de Minas Gerais, Belo Horizonte;* [3]*University of Fortaleza, Fortaleza, Brazil*

Background: Health status in rheumatoid arthritis (RA), as measured by Health Assessment Questionnaire - Disability Index (HAQ-DI), has been established as a relevant quantitative measure to assess and monitor the disease (1). Current RA therapy has shown improvement in patient-reported outcomes, but more data on specific factors influencing health status are needed (2).
Objectives: To assess the relationship between functional disability and clinical factors in patients with RA, using the HAQ score.
Methods: Cross-sectional study in patients with RA according to the ACR classification criteria from three Brazilian University Hospitals. Demographic and comprehensive clinical data, including components of metabolic profile were collected. Blood pressure, weight and height were determined in the assessment visit and recent laboratory data were assessed from medical records. Disease activity was evaluated by the Disease Activity Score in 28 joints (DAS28) and functional disability was assessed by the HAQ-DI, considering an index>0.5 as disability. All analyses were performed using Stata for MAC 12.0 software. Variables that achieved a p–value<0.3 in the univariate analysis were considered as candidates to take part of a multivariate binomial logistic model, and in this model, variables were considered as statistically significant at the 0.05 significance level (3).
Results: 453 patients were included, 380 (83.9%) women, mean age 55.7 (±12) years, 356 (79.1%) Caucasian, and mean disease duration of 13.3 (±9) years. Methotrexate were used by 73.5% of the sample. Mean DAS28 was 3.9 (±1.4), mean HAQ score was 1.11 (±0.77), and 23.9% of the patients had HAQ score>0.5. Dyslipidemia, diabetes mellitus (DM), high blood pressure (HBP) and family history of premature cardiovascular disease occurred in 28.6%, 12.8%, 51% and 21.4% of the patients, respectively. Mean body mass index (BMI) was 27.1 (±4.9) kg/m^2. In multivariate analysis age, DAS28, tobacco use, and diabetes mellitus were independently associated with HAQ>0.5 (TABLE 1).

Table 1. Association between clinical parameters, disease activity, and functional disability (HAQ >0.5)

Parameters	OR (IC95%)	p
Age	1.01 (1.01;1.03)	<0.001
DAS28	2.74 (1.69;4,45)	<0.001
Tobacco use	1.37 (1.06;1.77)	0.016
Diabetes Mellitus	1.83 (1.82;1.83)	<0.001

DAS28 – disease activity score in 28 joints; BMI – body mass index; OR – odds ratio.

Conclusions: Our results depicted that distinct factors could reflect in the functional status response in RA patients. This is relevant since it may influence the clinicaly important difference when evaluating the HAQ response in populations with diverse cultural features and different comorbidities prevalence.

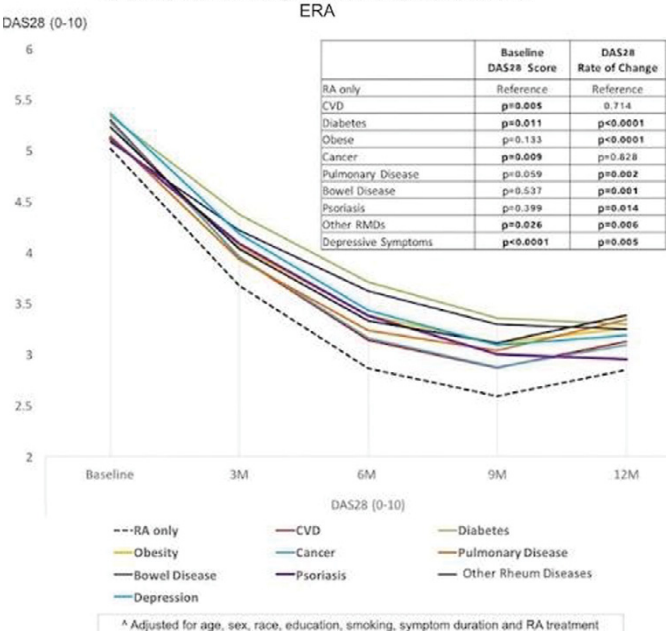
References:
[1] Fries JF, Spitz P, Kraines RG, Holamn HR: Measurement of patient outcome in arthritis. Arthritis Rheum 1980; 23: 137–45.
[2] Pincus T. Are Patient Questionnaire Scores as "Scientific" as Laboratory Tests for Rheumatology Clinical Care? Bull NYU Hosp Jt Dis. 2010;68(2):130–139.
[3] Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. Source Code for Biology and Medicine. 2008;3:17. doi:10.1186/1751–0473–3-17.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5544

SAT0122 WHICH MULTIMORBID CONDITIONS ARE MORE PREVALENT AROUND THE TIME OF EARLY RA DIAGNOSIS AND HAVE THE GREATEST IMPACT ON TRAJECTORIES OF DISEASE ACTIVITY IN THE FIRST YEAR? RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT

O. Schieir[1], S.J. Bartlett[2,3], C. Hitchon[4], J. Pope[5], G. Boire[6], B. Haraoui[7], E. Keystone[1], D. Tin[8], C. Thorne[8], V.P. Bykerk[1,9] on behalf of Canadian Early Arthritis Cohort Canada (CATCH) Investigators. *[1]University of Toronto, Toronto; [2]McGill University, Montreal, Canada; [3]Johns Hopkins University, Baltimore, United States; [4]University of Manitoba, Winnipeg; [5]Western University, London; [6]Universite de Sherbrooke, Sherbrooke; [7]Institut de Rhumatologie de Montreal, Montreal; [8]Southlake Regional Health Center, Newmarket, Canada; [9]Hospital for Special Surgery, New York, United States*

Background: Multimorbidity (MM) is highly prevalent in early RA (ERA), and higher counts of conditions are associated with poorer disease control[1]. It is important to understand the number of, and which specific conditions most affect disease presentation, early therapies and disease activity over time.
Objectives: To estimate the prevalence of MM conditions at the time of ERA diagnosis and associations with ERA clinical characteristics, early treatment, and trajectory of disease activity in the 1st year of follow up.
Methods: Data were from ERA patients (<1-year of symptoms) enrolled in CATCH (Canadian Early Arthritis Cohort) who met 1987 or 2010 RA criteria, and had at least two DAS28 measures in the first year. We examined baseline prevalence of: 1) cardiovascular disease (CVD), 2) diabetes, 3) cancer, 4) pulmonary disease, 5) bowel disease, 6) other rheumatic diseases, and 7) psoriasis, obtained from patient-reports of physician-diagnosed medical conditions, 8) obesity (BMI≥30), and 9) depressive symptoms (RAND-12 <42). We compared baseline demographic and clinical characteristics in ERA + each condition vs. ERA alone. We estimated adjusted effects of each condition on early use of RA therapies with logistic regression and adjusted effects of each condition on DAS28 trajectory over the first year of follow up with linear growth models.
Results: The sample included 1,595 patients, 1153 (72%) were female, with a mean (sd) age of 54 (15) years and 6 (3) months of symptoms. At baseline 1,434 (92%) were treated with conventional DMARDs (mostly methotrexate (76%)) and 33 (2%) with a biologic. More than 70% of ERA patients reported at least one MM, and over 30% reported 2+ MMs. Patients with MM were often older and had higher disease activity at baseline, with variations by condition. Patients with RA+CVD or depressive symptoms had a 60% and 90% higher adjusted odds of baseline steroid use, respectively (p<.001). In fully adjusted growth models, relative to patients with ERA only, patients with: a) diabetes, other rheumatic diseases or depressive symptoms had higher baseline DAS28 scores and less improvement over time, b) pulmonary disease, bowel disease, psoriasis or obesity had similar baseline DAS28 scores but less improvement over time; and c) CVD or cancer had higher baseline DAS28 scores but similar improvement over time (all p<0.05).
Conclusions: Multimorbidity is common in ERA patients seen in routine practice and associated with higher disease activity at baseline, less improvement over time, or both, and a greater likelihood of prescribing steroids for certain conditions. Integrating MM in to current RA care strategies may help achieve better patient outcomes.
References:
[1] Hitchon CA, et al. Self-reported comorbidity is common in early inflammatory arthritis and associated with poorer function and worse arthritis disease outcomes: results from the Canadian Early Arthritis Cohort. Rheumatology. 2016. doi: 10.1093/rheumatology/kew061.
Disclosure of Interest: O. Schieir: None declared, S. Bartlett Consultant for: UCB, Pfizer, C. Hitchon: None declared, J. Pope Grant/research support from: Amgen, BMS, Pfizer, Roche, UCB, Consultant for: AbbVie, Actelion, Amgen, Bayer, BMS, Genzyme, Hospira, Lilly, Merck, Norvartis, Pfizer, Regeneron, Roche, Sanofi, UCB, G. Boire: None declared, B. Haraoui Grant/research support from: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Eli Lilly Janssen, Merck, Pfizer, Roche and UCB, Speakers bureau: Amgen,BMS Janssen, Pfizer and UCB, E. Keystone Grant/research support from: Abbott Laboratories, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb, F.Hoffmann-La Roche Inc, Janssen Inc, Lilly Pharmaceuticals, Novartis Pharmaceuticals, Pfizer Pharmaceuticals, Sanofi-Aventis, UCB, Consultant for: Abbott Laboratories, AstraZeneca Pharma, Biotest, Bristol-Myers Squibb Company, Crescendo Bioscience, F Hoffmann-La Roche Inc, Genentech Inc, Janssen Inc, Lilly Pharmaceuticals,Merck, Pfizer Pharmaceuticals, UCB, Speakers bureau: Abbott Laboratories, AstraZeneca LP, Bristol-Myers Squibb Canada, F Hoffmann-La Roche Inc, Janssen Inc, Pfizer Pharmaceuticals, UCB,Amgen, D. Tin: None declared, C. Thorne: None declared, V. Bykerk: None declared
DOI: 10.1136/annrheumdis-2017-eular.6369

Adjusted^ effects of multimorbid conditions on trajectory of DAS28 over the first year of follow up in patients with ERA



	Baseline DAS28 Score	DAS28 Rate of Change
RA only	Reference	Reference
CVD	p=0.005	0.714
Diabetes	p=0.011	p<0.0001
Obese	p=0.133	p<0.0001
Cancer	p=0.009	p=0.828
Pulmonary Disease	p=0.059	p=0.002
Bowel Disease	p=0.537	p=0.001
Psoriasis	p=0.399	p=0.014
Other RMDs	p=0.026	p=0.006
Depressive Symptoms	p<0.0001	p=0.005

SAT0123 MULTIDIMENSIONAL EVALUATION OF PAIN IN RHEUMATOID ARTHRITIS

P. Vergne-Salle[1], S. Pouplin[2], A. Bera-Louville[3], M. Soubrier[4], C. Richez[5], R.-M. Javier[6], S. Perrot[7], P. Bertin[1]. *[1]Rheumatology, University Hospital, Limoges; [2]Rheumatology, University Hospital, Rouen; [3]Rheumatology, University Hospital, Lille; [4]Rheumatology, University Hospital, Clermont-Ferrand; [5]Rheumatology, University Hospital, Bordeaux; [6]Rheumatology, University Hospital, Strasbourg; [7]Pain center, University Hospital, Paris, France*

Background: Although pain in rheumatoid arthritis (RA) is frequently thought to be inflammatory in nature, some studies reported clinically significant pain despite relatively low rheumatoid arthritis (RA) disease activity. Less than 50% of patients are satisfied by the management of pain.
Objectives: to report a recent multidimensional evaluation of pain in a large RA population.
Methods: Patients with RA were enrolled in 7 French Rheumatology Centers during a visit or a hospitalization in a transversal observational study. Socio-demographic data, previous and prescribed medications, disease duration, immunologic status, DAS28 score were assessed. Patients completed the multidimensional pain questionnaire from french health autority, the health assessment questionnaire (HAQ), the Beck depression scale and the anxiety scale STAI. Joint damage was evaluated by a simple erosion narrowing score.
Results: Of the 299 screened patients, 295 were included with a mean age of 58.4±11.7 years, 80.3% of female, a mean disease duration of 13.2±9.6 years, positivity of rheumatoid factors in 76.4%, anti-citrullin antibodies in 74% of cases. Concerning medications, 42.7% were treated by corticoids (mean dose=6.4 mg/d), 66% by analgesic drugs (64.1% with acetaminophen, 45.6% weak opioids, 7.1% strong opioids) and 24.4% with NSAIDs. The RA treatments were DMARDs in 69.1% and biotherapies in 82.7% of cases. The mean DAS-28 score was 3.1±1.3 with 38.7% of patients in remission and 15.4% in low disease activity. The verbal scale for satisfaction about pain management showed that a third of patients was very satisfied, the half satisfied, 16% weakly or not satisfied. The mean pain visual analogic scale (VAS) for the last 8 days was 33.6 mm ±26.5/100. 39% of patients had a pain VAS >40 mm/100. The Beck scale showed a moderate to severe depression in 34,3% of patients. Anxiety was present in 57.5%. The impacts of pain on daily behaviors were more important on work. The pain VAS for the 8 days was correlated with the score of depression et with the DAS-28 score (p<0.0001). The population with a pain VAS >40 mm had a significant more important Beck score, anxiety score, HAQ, DAS-28 score and had more impacts of pain on daily behaviors There was no association between pain and structural damage and disease duration. There was no difference between the populations with VAS>40 or <40 mm in terms of IL-6, IL-17 and IL-33 serum levels. The multidimensional evaluation of pain wasn't different between treatement groups (DMARDs, biotherapies) and between the different biotherapies. Multivariate analysis with principal component analysis

found statistically significant associations between pain VAS and depression score, impacts of pain on daily behaviors and between pain VAS and DAS-28.
Conclusions: Almost 40% of patients had moderate to severe pain in a population of severe RA followed in hospital centers and treated with biotherapies in more than 80% of cases. Therefore, pain is still a major outcome to consider in RA. But, the proportion of patients with moderate to severe pain is less important than that one published by Taylor et al. Pain is associated with the DAS-28 score, but also with the depression score.
References:
[1] Taylor P et al. J Int Med Res 2010; 38: 1213–24.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3287

SAT0124 HIGHER BMI AND SHORTER DISEASE DURATION ARE ASSOCIATED WITH "FIBROMYALGIC" RHEUMATOID ARTHRITIS – EVALUATION USING POWER DOPPLER ULTRASONOGRAPHY

P. Cheung, M. Lahiri. *Rheumatology, National University Hospital, Singapore, Singapore, Singapore*

Background: Power Doppler ultrasonography (PDUS) can differentiate RA patients who truly have active disease. Patients with persistent joint tenderness may not necessarily have true inflammation; yet composite disease activity indices remain high, leading to treatment escalation. These patients are often referred to having "fibromyalgic RA" where tender joints far exceed that of swollen joints.
Objectives: We evaluated the predictors of "fibromyalgic RA (FMRA)," defined as patient-reported tender joint count (TJC) at least 7 greater than PDUS joint count.
Methods: Consecutive RA patients were recruited in a tertiary rheumatology centre in Singapore. Patients self-assessed 28 joints for tenderness, followed by blinded PDUS assessment of the corresponding joints. Patients were grouped into either, (i) PDUS joint count > patient-reported TJC, (ii) PDUS joint count = patient-reported TJC (iii) patient-reported TJC > PDUS joint count, (difference <7) (iv) patient-reported TJC > PDUS joint count, (difference ≥7). Group (iv) is defined as FMRA. Predictors of FMRA were evaluated by multinomial logistic regression.
Results: Of the 101 patients, 81% were female, 72% Chinese, median age of 53.8 (IQR 48.1;62.4) and disease duration of 6.2 (1.9;8.8) years. Median BMI was 23.6 (20.8;27.0) and DAS28 was 3.2 (2.5;4.2). FMRA patients (15%) had a high median patient-reported TJC of 13 (10;18) but low median PDUS joint count of 1 (0;4). Compared to the other groups, they had higher median DAS28 of 4.6 (3.3;5.2), shorter mean disease duration of 2.3 (0.4;6.8) years, and higher median BMI of 26.9 (23.7;32.2). No differences in mean ESR or proportion of patients with seropositive disease were observed. Using Group (i) as the reference, patients with FMRA were more likely to have a higher BMI (adjusted OR=1.6, 95% CI 1.2; 2.1,p=0.001 for every unit increase) and shorter disease duration (adjusted OR=0.8, 95% CI 0.7;0.98,p=0.03 for every additional year). Age, gender, ethnicity, disease activity (PDUS score) and seropositivity were not significant predictors of FMRA.
Conclusions: Higher BMI and shorter disease duration were independent predictors of FMRA. Use of PDUS would be useful in this group, rather than basing treatment decisions on composite disease activity indices alone.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1598

SAT0125 TENOSYNOVITIS IN RHEUMATOID ARTHRITIS: PREVALENCE AND DETERMINANTS OF TENOSYNOVITIS DETECTED IN THE SONAR-ULTRASOUND EXAMINATION IN THE SCQM COHORT

R. Micheroli[1], A. Scherrer[2], L. Brulhardt[3], H. Ziswiler[4], P. Zufferey[5], B. Möller[6], A. Ciurea[1], G. Tamborrini[7]. *[1]USZ; [2]SCQM, Zurich; [3]Hôpital Neuchâtelois, la Chaux-de-Fonds; [4]OsteoRheuma, Bern; [5]CHUV, Lausanne; [6]Inselspital, Bern; [7]Ultrasound Center Rheumatology, Basel, Switzerland*

Background: Tenosynovitis is one of the common features of rheumatoid arthritis (RA). The diagnosis of tenosynovitis is frequently made clinically but for the detection of tenosynovitis, ultrasound (US) is more sensitive. US and MRI detected tenosynovitis is a predictor for unstable remission and erosive progression in RA.
Objectives: The aim of this study was to assess the prevalence and determinants of TS detected in the SONAR (Swiss Sonography Group in Arthritis and Rheumatism) examinations in patients with Rheumatoid Arthritis in the SCQM Cohort.
Methods: The SONAR ultrasound examination consists of a semi-quantitative score employing both multiplanar gray scale (B-mode) and Doppler-mode (PwD) and a TS composite score (grade 0–3). Pathologic TS was defined as TS grade 2–3. Characteristics of patients with and without TS are shown using standard descriptive methods. In a longitudinal sub-group the change in TS from no TS to pathologic TS or vice versa and DAS28 over time was categorized as "worse" (ΔDAS28 ≥2.1), "same" and "better" (ΔDAS28 ≤-2.1) and the correlation between change DAS28 and in tenosynovitis was evaluated.
Results: 941 RA patients with TS score were available. 20% of included patients showed signs of TS. The presence of TS was associated with male gender and higher values of disease activity and physical function disability. Furthermore, 15% of patients in DAS28 Remission had sonographic TS. TS was less frequently observed in patients on biologic therapies (Table 1). The longitiudinal sub-group consisted of 348 patients. The correlation between change in DAS28 and change in TS was poor (polychoric correlation 0.28 [0.14, 0.43]).

Table 1. Patient Characteristics at first Tenosynovitis measurement

Parameter	Tenosynovitis		OR [95% CI]
	Yes (N=184)	No (N=757)	
Male gender, n (%)	59 (32)*	158 (21)*	1.8 [1.2, 2.5]*
Mean age in years	57	56	1.0 [0.99, 1.02]
Mean disease duration in years	5	3	0.98 [0.96, 1.00]
RF positive, n (%)	123 (68)	511 (70)	0.9 [0.7, 1.3]
Anti-CCP positive, n (%)	109 (65)	477 (70)	1.1 [0.6, 2.1]
DAS28 Remission, n (%)	24 (15)*	232 (38)*	0.3 [0.2, 0.5]*
Mean DAS28	3.9*	3.1*	1.6 [1.4, 1.8]*
Mean B-Mode SONAR Score	12.0*	8.0*	1.1 [1.04, 1.08]*
Mean PD-SONAR Score	2.0*	1.0*	1.0 [1.06, 1.12]*
Mean Physician Global Assessment	4.0*	2.0*	1.4 [1.3, 1.5]*
Mean HAQ Score	0.8*	0.5*	1.6 [1.1, 2.2]*
On biologic, n (%)	61 (33)*	399 (53)*	0.4 [0.3, 0.6]*
On synthethic DMARD, n (%)	110 (60)	500 (66)	0.8 [0.6, 1.1]*

*p<0.05.

Conclusions: In the SCQM RA cohort TS is associated with male gender and an overall higher disease activity. One should actively look for TS even in RA patients in DAS28 remission.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4006

SAT0126 MENTAL HEALTH BENEFITS ASSOCIATED WITH REDUCTION IN DISEASE ACTIVITY AMONG RHEUMATOID ARTHRITIS PATIENTS: A SYSTEMATIC REVIEW OF THE LITERATURE

V. Strand[1], R. Rendas-Baum[2], M. Kosinski[2], D. Brooks[3], R. Ganguly[3]. *[1]Stanford University, Palo Alto, CA; [2]Optum, Inc., Eden Prairie, MN; [3]GlaxoSmithKline, Collegeville, PA, United States*

Background: The association between physical functioning and rheumatoid arthritis (RA) disease activity is well established. In randomized controlled trials (RCTs) of RA treatment, reductions in disease activity result in improved physical functioning. The mental health benefits associated with reductions in disease activity are less well recognized.
Objectives: Investigate the association between reductions in RA disease activity and measures of mental health status.
Methods: A systematic review of the published literature of RCTs in RA was conducted. The search was limited to those published in the last 10 years that included the Short-Form (SF)-36 Health Survey as an outcome measure.
Results: The search strategy yielded 77 articles of which 38 were excluded for the following reasons: not RCT (23); focus exclusively on early RA (9); psychometric evaluation (4); review study (1); and off topic (1). Of the 39 articles reporting mean changes in scores on the SF-36 mental health (MH) and role emotional (RE) domains by treatment group, 3 articles also presented these changes in association with reductions in RA disease activity measures.[1–3] In relation to American College of Rheumatology (ACR) response criteria, small to moderate (0.2–0.5 standard deviation [SD]) effect size changes in RE and MH domain scores were observed among RA patients whose ACR responses ranged from 20–49%. Moderate to large effect sizes (0.5–0.8 SD) were reported in RE and MH domain change scores among ACR50 responders. Similar changes in RE and MH domain scores were reported by patients with reductions in Simplified Disease Activity Index (SDAI) of ≥10 points.
Conclusions: The benefits of clinically meaningful reductions in disease activity among RA patients not only include improved physical functioning but also meaningful improvements in overall mental health status. The improvement in mental health is positively associated with reduction in disease activity, with only small to moderate improvements associated with less than ACR50 responses. Additional work is needed to investigate the incremental effects of RA therapies on mental health beyond the effects related to improvements in disease activity.
References:
[1] Emery P, et al. J Rheumatol. 2006;33(4):681–689.
[2] Russell AS, et al. Ann Rheum Dis. 2007;66(2):189–194.
[3] Strand V, et al. Health Qual Life Outcomes. 2014;12:31.
Disclosure of Interest: V. Strand Consultant for: Abbvie, Amgen, AstraZeneca, BiogenIdec, Boehringer Ingelheim, Celltrion, Crescendo, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi and UCB, R. Rendas-Baum Employee of: Optum, M. Kosinski Employee of: Optum, D. Brooks Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, R. Ganguly Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline
DOI: 10.1136/annrheumdis-2017-eular.3568

SAT0127 UNFAVORABLE BODY COMPOSITION ALREADY AT THE ONSET OF CLINICAL ARTHRITIS

S.A. Turk[1], D. van Schaardenburg[1,2], M. Boers[3], S. de Boer[1], C. Fokker[1], W.F. Lems[1,3], M.T. Nurmohamed[1,3]. *[1]Amsterdam Rheumatology and immunology Center| Reade; [2]Amsterdam Rheumatology and immunology Center| Academic Medical Center; [3]Amsterdam Rheumatology and immunology Center| VU University Medical Center, Amsterdam, Netherlands*

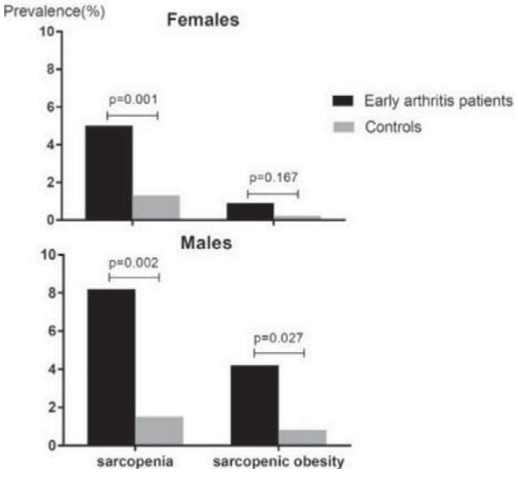
Background: Rheumatoid arthritis is associated with an increased cardiovascular (CV) risk. There is mounting evidence that inflammation is involved in the pathogenesis thereof (1). An unfavorable body composition is, independently, associated with an increased CV risk, and often present in established arthritis patients. This unfavorable composition is a loss of muscle mass (sarcopenia), in the presence of a stable or even increased (abdominal) fat mass (sarcopenic obesity) (2).
Objectives: Currently it is unknown when this unfavorable body composition develops. Therefore, we compared body composition in DMARD-naïve early arthritis patients with non-arthritis controls and explored the association with disease activity and traditional CV risk factors.
Methods: A total of 317 consecutive early arthritis patients and 1268 age, gender and ethnicity matched non-arthritis controls (3) had a Dual-energy X-ray absorptiometry scan to assess lean (muscle) mass index (LMI), fat mass index (FMI), fat mass distribution (arms and legs versus trunk) and android to gynoid fat mass ratio. For the obesity definition, the cut offs of Gallaher et al. were applied. For the sarcopenia definition, cut offs based on the control group were applied (mean minus two times SD). In addition, a disease activity score, erythrocyte sedimentation rate, lipid profile (total cholesterol, HDL, LDL and triglycerides) and blood pressure assessments were done.
Results: Early arthritis patients (84% fulfilling the 2010 ACR/EULAR criteria) had a significantly lower mean LMI ($p<0.01$) compared with controls. Female patients had a higher mean FMI ($p<0.01$) and more fat was distributed to the trunk in patients (females $p<0.01$, males $p=0.07$) (table). The prevalence of an unfavorable body composition (i.e. sarcopenia and sarcopenic obesity) was higher than in controls, for females 5.0% versus 1.3%, OR: 4.2, $p<0.01$ and for males 8.2% versus 1.5%, OR: 5.7, $p<0.01$ (figure). A higher FMI, more android fat and more fat distributed to the trunk were associated with higher blood pressure and lipid levels (and lower HDL levels). There was no clear relationship between body composition parameters and disease activity.

Table 1. Body composition of early arthritis patients and non-arthritis controls

	Arthritis females	Control females	Arthritis males	Control males
Fat mass index (mean, SD)	27.6 (5.3)	26.6 (4.6)*	26.8 (4.4)	27.4 (3.6)
% of fat distributed to the trunk (mean, SD)	52.2 (6.3)	49.4 (6.5)*	58.8 (6.4)	57.6 (5.6)
Android to gynoid fat mass ratio (mean, SD)	0.5 (0.2)	0.5 (0.2)	0.7 (0.2)	0.8 (0.2)*
Lean mass index (mean, SD)	6.6 (0.9)	6.7 (0.8)*	8.0 (1.1)	8.6 (1.0)*
Obese (n,%)	99 (45.2)	334 (38.4)	50 (52.1)	222 (57.7)
Sarcopenic (n,%)	11 (5.0)	11 (1.3)*	8 (8.2)	6 (1.5)*
Sarcopenic obesity (n,%)	2 (0.9)	2 (0.2)	4 (4.2)	3 (0.8)*

n = number, SD = standard deviation, % == percentages *p-value <0.05 between arthritis and non-arthritis controls.

Figure. Prevalence of sarcopenia and sarcopenic obesity in early arthritis patients compared with non-arthritis controls.



Conclusions: Patients at the clinical onset of arthritis more often have an unfavorable body composition (sarcopenia and sarcopenic obesity) than non-arthritis controls. An unfavorable body composition was associated with higher blood pressure and lipid levels (and lower HDL levels).
References:
[1] Curr Vasc Pharmacol 2010; 8(2):285–292.
[2] Age (Dordr) 2015; 37(6):121.
[3] Eur J Epidemiol 2015; 30(8):661–708.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2174

SAT0128 CLINICAL FEATURES AND EVOLUTION OF PULMONARY FUNCTION IN A SINGLE-CENTER COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS RELATED INTERSTITIAL LUNG DISEASE

S.C. Rodriguez-García, R.A. Castellanos-Moreira, M.V. Hernandez-Miguel, J. Ramirez, A. Cuervo, J. Cañete, R. Sanmarti-Sala. *Rheumatology, Hospital Clinic Barcelona, Barcelona, Spain*

Background: Interstitial lung disease (ILD) is an extra-articular manifestation of Rheumatoid Arthritis (RA), has been related with a poor prognosis. However, there is a lack of clinical data regarding its evolution with different treatment approaches.
Objectives: Our aim was to assess clinical features and evolution of ILD in a cohort of RA patients from a tertiary hospital
Methods: Single-centre retrospective observational study including all patients diagnosed with ILD with a previous or posterior diagnosis of RA evaluated from January 2007 to December 2016 in the Rheumatology Department of a university hospital.
Variables analysed: age, sex, smoking status, duration of RA, presence and titers of ACPA (antiCCP2) and rheumatoid factor (RF), presence of erosions, use of glucocorticoids (GC), synthetic and biological DMARDs before and after ILD diagnosis and presence of other extra-articular manifestations.
We also analysed: duration of ILD, HRCT (High Resolution Computed Tomography) patterns and pulmonary function tests (PFT) at baseline and during follow-up to assess the evolution of the disease. The PFT results were evaluated according to the American Thoracic Society/European Respiratory Society definitions (1).
Results: Twenty-one patients (18 women) were included, mean age 68. 4±11.9, mean RA duration 12.3±8.2 years. 9.5% were current smokers and 33.3% former smokers. 61.9% were ACPA + (52.4% with high basal titers, median ACPA titers: 698) and 81% RF+ (47.6% with high basal titers). 71.4% had erosions and 5 patients (23.8%) had extra-articular manifestations, mainly rheumatoid nodules.
RA diagnosis was made after that of ILD in 4 patients; mean elapsed time 1.56±1.26 years. In the other 17 patients, the mean duration of RA until ILD diagnosis was 11.2±7.2 years.
Currently 17 subjects (85%) receive GC; 4 (19%) in monotherapy and 11 (57.9%) synthetic DMARDs (5 methotrexate, 3 leflunomide (LEF), 1 hydroxychloroquine (HCQ) and 2 with double therapy (HCQ/AZA and HCQ/LEF)).
Four patients are currently treated with biological therapy (2 abatacept (ABA), 1 rituximab and 1 etanercept (ETN)), all of them in monotherapy.
Five patients received TNFi prior to ILD diagnosis (3 ETN, 1 infliximab and 1 adalimumab). Biological therapy was withdrawn in 3 cases and switched to ABA in the two remaining ones.
The median duration of EPID was 2.5 (range 0.7–11.9) years. HRCT patterns were: non-specific interstitial pneumonia (NSIP) 52.9%, usual interstitial pneumonia (UIP) 17.6%, cryptogenic organized pneumonia (COP)11. 8%, and other patterns 17.7%.
14 patients had baseline and follow-up PFT: 9 (64.3%) remained stable; 3 (21.4%) improved and 2 (14.3%) worsened (1 had received previous ETN). There was a trend for worsening of PFT in patients with UIP pattern.
No patient died from ILD during this period
Conclusions: In our RA-ILD cohort, NSIP was the most common HRCT pattern and PFT remained stable in most patients during follow-up. Five patients (23.8%) had received TNFi prior to ILD diagnosis and only one of them showed worsening of PFT during ETN treatment, with clinical improvement after withdrawal.
References:
[1] Pellegrino R et al. Eur Respir J. 2005;26:94868.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3284

SAT0129 EXPLORATION OF COMORBIDITY INDICES IN AN ETHNIC RHEUMATOID ARTHRITIS SUBSET

S. Dowell[1], G. Kerr[2], C. Swearingen[3], M. Quinones[1], J. Berrian[1], S. Hochberg[1] on behalf of EMRAC Working Group. *[1]Rheumatology, Howard University Hospital; [2]Rheumatology, Washington VAMC, Washington; [3]NYU, New York, United States*

Background: Comorbidity is common in ethnic patients with rheumatoid arthritis (RA) and often impact choice of DMARD therapy and clinical outcomes. In addition to simple summation of comorbidities, composite indices have been proffered as better predictors of poor clinical outcomes in patients with rheumatoid arthritis[1]. However, their applicability in ethnic RA subsets is unknown.
Objectives: To compare composite to mean comorbidity indices in ethnic subsets with rheumatoid arthritis.
Methods: Patients enrolled in the Ethnic Minority RA Consortium (EMRAC), with at least 6 months of followup data were analyzed. At enrollment, sociodemographic data and RA disease status, rheumatic disease comorbidity index (RCDI)[1] and comorbidity count (COUNT)[1] were analyzed amongst ethnic subsets. Spearman correlation was estimated between RCDI and COUNT while Poisson regression

was used to model the differences in the comorbidity indices between race groups.

Results: 453 EMRAC subjects were analyzed; 342 (81.4%) were female, average age was 58.9 (± 15.1) years, average duration 13.3 (±11.1) years and average follow-up length 2.1 (±1.4) years. Individual comorbid frequencies as well as comorbid indices are summarized in Table 1. Spearman correlation between overall RDCI and COUNT was 0.90 (95% CI [0.88, 0.91], P<0.001). Hispanics, however, had significantly lower comorbidity indices scores than other race groups (RDCI Hispanic vs White P=0.003, Hispanic vs Black P=0.004, Hispanic vs Other P=0.038; COUNT Hispanic vs White P=0.012, Hispanic vs Black P=0.004, Hispanic vs Other P=0.151).

Table 1. Clinical Characteristics of EMRAC study cohort

	White	Black	Hispanic	Other	Total
N	102	195	85	71	453
Hypertension [N (%)]	36 (35.3%)	79 (40.5%)	24 (28.2%)	31 (43.7%)	170 (37.5%)
Coronary Artery Disease [N (%)]	12 (11.8%)	14 (7.2%)	3 (5.9%)	2 (2.8%)	31 (6.8%)
Other Heart Disease [N (%)]	11 (10.8%)	6 (3.1%)	2 (2.4%)	2 (2.8%)	21 (4.6%)
Fracture [N (%)]	11 (10.8%)	8 (4.1%)	2 (2.4%)	2 (2.8%)	23 (5.1%)
Psychiatric Disease [N (%)]	5 (4.9%)	10 (5.1%)	1 (1.2%)	0 (0.0%)	16 (3.5%)
Diabetes [N (%)]	11 (10.8%)	33 (16.9%)	9 (10.6%)	8 (11.3%)	61 (13.5%)
Cancer [N (%)]	9 (8.8%)	8 (4.1%)	5 (5.9%)	3 (4.2%)	25 (5.5%)
Stomach [N (%)]	8 (7.8%)	9 (4.6%)	8 (9.4%)	7 (9.9%)	32 (7.1%)
Stroke [N (%)]	4 (3.9%)	6 (3.1%)	2 (2.4%)	2 (2.8%)	14 (3.1%)
Hyperlipidemia [N (%)]	19 (18.6%)	29 (14.9%)	9 (10.6%)	12 (16.9%)	69 (15.2%)
Chronic Bronchitis [N (%)]	10 (9.8%)	17 (8.7%)	5 (5.9%)	5 (7.0%)	37 (8.2%)
Pulmonary Fibrosis [N (%)]	2 (2.0%)	5 (2.6%)	4 (4.7%)	0 (0.0%)	11 (2.4%)
Kidney Disease [N (%)]	3 (2.9%)	5 (2.6%)	0 (0.0%)	2 (2.8%)	10 (2.2%)
RAPID3	13.1 (6.8)	12.5 (7.4)	14.8 (6.9)	13.7 (7.2)	13.3 (7.1)
Enrollment					
RDCI	1.8 (2.1)	1.7 (2.0)	1.2 (1.7)	1.6 (1.8)	1.6 (1.9)
COUNT	1.0 (1.3)	1.0 (1.3)	0.7 (0.9)	0.9 (1.1)	0.9 (1.2)

Mean (SD) reported unless otherwise noted.

Conclusions: In an ethnic RA subset, the RCDI and COUNT correlated well across ethnic groups. The comorbidity indices were not associated with RA disease activity at enrollment as assessed by the RAPID3. Hispanics had lower RCDI and COUNT scores compared to other race groups but also presented at a younger age which could account for this difference. More studies are needed to determine the predictive value of these indices in determining poor outcomes and mortality in this ethnic subset.

References:

[1] England, BR et al. Arthritis Care Res. 2015 Jun; 67(6): 885–872.

Disclosure of Interest: S. Dowell Grant/research support from: Bristol Myers Squibb, Pfizer, Genentech, Speakers bureau: Horizon Pharma, G. Kerr Grant/research support from: Bristol Myers Squibb, Pfizer, Genentech, C. Swearingen Grant/research support from: Bristol Myers Squibb, Pfizer, Genentech, M. Quinones Grant/research support from: Bristol Myers Squibb, Pfizer, Genentech, J. Berrian Grant/research support from: Bristol Myers Squibb, Pfizer, Genentech, S. Hochberg Grant/research support from: Bristol Myers Squibb, Pfizer, Genentech

DOI: 10.1136/annrheumdis-2017-eular.5842

SAT0130 EVALUATION OF THE FACTORS RELATED WITH RISK OF FALLING AND FEAR OF FALLING IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Unsal Delialioglu[1], G. Kilinc Kamaci[1], S. Ozel[1], F. Yurdakul[2], H. Bodur[2]. *[1]Ankara Physical Therapy and Rehabilitation Training and Research Hospital; [2]Ankara Numune Training and Research Hospital, Ankara, Turkey*

Background: People with rheumatoid arthritis (RA) have an increased risk of falls (1,2). The identification of predictive and potentially modifiable risk factors is essential for the development of effective falls prevention strategies (3).

Objectives: The aim of the study is to determine the relationship between falling risk and falling fear with balance, lower extremity muscle strength, functional status, disease activity and pain in patients with Rheumatoid Arthritis (RA)

Methods: A total of 124 patients (92 females, 32 males) who were diagnosed with RA according to the American College of Rheumatology (ACR) diagnostic criteria were included in the study. The fear of falling was assessed by the Fall Efficacy Scale (FES-I) and the shortened form (Short FES-I). Disease activity was assessed using the Disease Activity Score-28 (DAS28), the functional status was assessed with Health Assessment Questionnaire (HAQ). While lower extremity muscule strenght was determined using Chair Stand Test, Four Balance Test was used to determine the balance. The pain intensity was determined using 10 cm Visual Analogue Scale-Pain (VAS-pain).

Results: The mean age of the patients is 54.75±10.96 years, the mean duration of illness is 14.10±10.99 years. A statistically significant relationship was found between FES-I, Short FES-I scores and HAQ (respectively r:0,776, p:0,000; r:0,783, p:0,000), VAS rest (r:0.397, p:0,000; r:0,405, p:0,000), VAS motion (r:0.542, p:0,000; r:0,519, p:0,000), DAS28 values (r:0.216, r:0.181; r:0,260, p:0,004). There was a significant negative correlation between FES-I, Short FES-I scores and Chair Stand Test (respectively r:-0.644, p:0,000; r:-0.652, p:0,00), Four Balance Test (r:-0.597, p:0,000; r:-0.611, p:0,00). There was a statistically significant correlation between the number of falls in the last year and age, duration of illness, HAQ, DAS28, VAS scores (p<0,05)

Conclusions: The risk of falling and fear of falling is associated with balance, lower extremity muscle strength, disease activity, functional status, and pain in patients with RA. Therefore; the risk of falling and fear of falling should be determined and necessary measures must be taken in patients with RA.

References:

[1] Böhler C, Radner H, Ernst M, Binder A, Stamm T, Aletaha D, Smolen JS, Köller M. Rheumatoid arthritis and falls: the influence of disease activity. Rheumatology (Oxford). 2012 Nov;51(11):2051–7.
[2] Armstrong C, Swarbrick CM, Pye SR, O'Neill TW. Occurrence and risk factors for falls in rheumatoid arthritis Ann Rheum Dis. 2005 Nov;64(11):1602–4.
[3] Stanmore EK, Oldham J, Skelton DA, O'Neill T, Pilling M, Campbell AJ, Todd C. Risk factors for falls in adults with rheumatoid arthritis: a prospective study. Arthritis Care Res (Hoboken). 2013 Aug;65(8):1251–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2022

SAT0131 MEDIAN NERVE THICKNESS RELATED TO RENAL IMPAIRMENT IN RHEUMATOID ARTHRITIS

S. Hannawi[1], I. AlSalmi[2]. *[1]Rheumatology, Ministry of Health and Prevention of UAE, Dubai, United Arab Emirates; [2]Nephrology, Royal Hospital, Muscat, Oman*

Background: Autoimmune processes, contribute to the burden of kidney disease. The reported kidney disease prevalence in patients with rheumatoid arthritis (RA) ranges from 5%>50% based on studies of different designs. Historically, patients with RA-associated renal amyloidosis had higher mortality rates relative to the general population. The occurrence of haematuria, proteinuria, or CKD has been reported to be associated with a 3- to 4-fold increased risk of death. Subclinical decreased kidney function has been identified as an independent risk factor for cardiovascular (CV) events with increase mortality in patients with RA. On the other hand, both rheumatoid arthritis and renal impairment have been reported to be associated with increase prevalence of carpal tunnel syndrome.

Objectives: To establish the median nerve thickness (measured by ultrasound) in RA and its relation to renal function.

Methods: 120 RA patients were recruited through a specialized rheumatology clinic. The US measurements were performed by the same person. Patients were sitting with their forearm resting in a supinated position on a small table. The US probe (an 8–16 MHz linear array transducer) was held as lightly as possible to avoid disturbing the anatomy of the nerve. The median nerve was examined at the entrance of the carpal tunnel, between the pisiform bone and the tubercle of the scaphoid bone, where the distal volar crease is an external pisiform landmark. A continuous trace was made just within the hyperechogenic boundary of the nerve. The cross-sectional area of the median nerve was calculated directly by the software of the US equipment. Each median nerve was measured three times, and the mean value was used for further analyses. Modification of Diet in Renal Disease (MDRD) equation used to estimate the Glomerualr Filatration Rate (GFR). The average of the right and the left areas of the median nerve were used when exploring bivariate correlations to the renal variables (Pearson's correlation coefficients). All statistics were performed using STATA programe.

Results: the average median nerve thickness was 9.79±2.6 mm^2 (Range 1.5 -22.25). The average GFR was 122±20 ml/min (59.6–286). Thickness of the median nerve was positively associated with the age of the participants (p=0.03, CI: 0.00, 0.08), body mass index (p=0.04, CI: 0.00, 0.21), uric acid level (p=0.033, CI: 0.00, 0.01), and urine microalbumin (p=0.04, CI 0.00, 0.01). GFR showed no significant relation the thickness of the median nerve.

Conclusions: RA patients without symptoms or clinical signs have a median nerve thickness that is positively correlated to the level of microalbumin and uric acid. Whether sosnographic examination of the median nerve would be helpful in predicting who is going to have a deteriorated renal function need to be explored in a larger study.

References:

[1] Boers, M., et al., Subclinical renal dysfunction in rheumatoid arthritis. Arthritis Rheum, 1990 33(1): p. 95–101.
[2] Daoussis, D., et al., Cardiovascular risk factors and not disease activity, severity or therapy associate with renal dysfunction in patients with rheumatoid arthritis. Ann Rheum Dis, 2010. 69(3): p. 517–21.
[3] Pathan, E. and V.R. Joshi, Rheumatoid arthritis and the kidney. J Assoc Physicians India, 2004 52: p. 488–94.

Disclosure of Interest: None declared

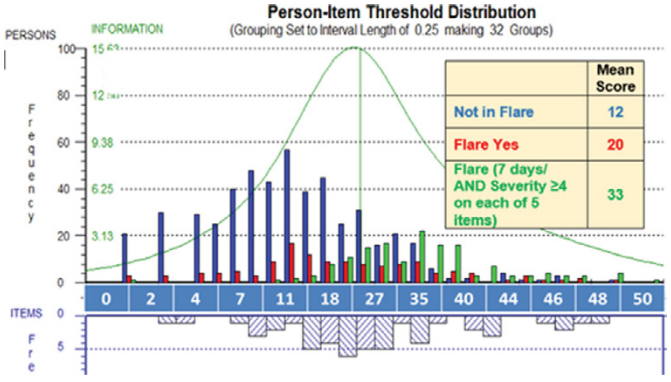
DOI: 10.1136/annrheumdis-2017-eular.1660

SAT0132 THE RHEUMATOID ARTHRITIS FLARE QUESTIONNAIRE (RA-FQ): RESULTS OF RASCH ANALYSIS AND FEEDBACK ON REAL-WORLD APPLICATIONS FROM INTERNATIONAL RA PATIENTS AND CLINICIANS

S.J. Bartlett[1,2], S.P. Barbic[3], V.P. Bykerk[4], B. Fautrel[5], F. Guillemin[6], A. den Broeder[7], R. Alten[8], R. Christensen[9], E. Choy[10], D. Furst[11], S. Hewlett[12], A. Leong[13], L. March[14], T. Woodworth[11], B.I.O. Clifton[2] on behalf of CATCH, STPR, & DRESS Investigators. *[1]McGill University, Montreal, Canada; [2]Johns Hopkins, Baltimore, United States; [3]University of British Columbia, Vancouver, Canada; [4]HSS, New York, United States; [5]Pierre & Marie Curie Universite, Paris;*

[6]Universite de Lorraine, Nancy, France; [7]Maartens Kliniek, Nijmegen, Netherlands; [8]Schlosspark Klinik, Berlin, Germany; [9]Parker Institute, Copenhagen, Denmark; [10]Cardiff University, Cardiff, United Kingdom; [11]UCLA, Los Angeles, United States; [12]University of the West of England, Bristol, United Kingdom; [13]Healthy Motivation, Santa Barbara, United States; [14]University of Sydney, Sydney, Australia

Background: Disease flares in RA are common. The RA Flare Questionnaire (RA-FQ) can be used to identify and quantify flares in rheumatoid arthritis (RA).
Objectives: To further explore the psychometric properties RA-FQ, we used Rasch analysis and reviewed results with RA patients research partners (PRPs) and clinicians to gain additional insight into the interpretability, meaningfulness, and utility of results.
Methods: People with RA in observational trials in Canada (CATCH; n=896) and France (STPR; n=138), and an RCT in the Netherlands (n=178) completed the RA-FQ. RUMM2030 was used to evaluate unidimensionality, targeting of items to people, reliability, response options, redundancy, local dependence, and response bias by sex, across age categories, and by country/language. ROC curves were used to identify sensitivity and specificity across potential threshold values to identify flares in different contexts of use. We reviewed results with RA patients research partners (PRPs) to gain additional insight into the interpretability, meaningfulness, and utility of results. Ten PRPs first completed the questionnaire then reviewed individual and group findings to provide feedback. RA clinicians provided feedback on utility and relevance of proposed cut points to identify flares.
Results: Rasch results supported the simple summation of items for a total score ranging from 0–50. Each item had ordered thresholds and acceptable fit. Reliability, was high (PSI =.91). Items and people covered a continuum ranging from -3.2 to +3.4 logits, and items were well-targeted to respondents. Overall model fit was excellent (χ^2 =31.6, df=45; p=0.935). There was little evidence of differential item functioning by sex, age, or country/language. Items suggest flare symptoms and impacts increased together showing a consistent story of how individuals experience worsening RA disease activity. Among PRPs, scores ranged from 10 to 41. There was unanimous agreement from the patients that the story depicted and individual results obtained were easily understood, meaningful, and very reflective of their current state. Many patients noted that beyond clinical trials, the RA-FQ could also enhance communication between doctors and patients at routine visits. Several noted potential applicability in monitoring day-to-day status and with self management. Thresholds for clinically important worsening to identify flare varied by setting, patient population, and context of use.



Conclusions: Taken together, results from classical and Rasch analyses support for the robust psychometric properties of the RA-FQ. The 5-item measure is easy to complete and simple to score. Feedback from RA PRPs and clinicians increase confidence in the relevance, meaningfulness, and easy interpretation of RA-FQ results for clinicians, researchers, and patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5593

SAT0133 SUDOMOTOR DYSFUNCTION IN RHEUMATOID ARTHRITIS PATIENTS IN THE ABSENCE OF TRADITIONAL CARDIOVASCULAR RISK

T. Syngle[1], S. Kaur[2], I. Verma[3], A. Syngle[4]. *[1]#547, Sector 16D, Chandigarh, India, Healing Touch Foundation, Chandigarh, India; [2]Cardio-Rheuma & Healing Touch City Clinic, Chandigarh; [3]Maharishi Markandeshwar College of Pharmacy, M.M University, mullana; [4]Cardio-Rheuma & Healing Touch City Clinic and Fortis Multi Specialty Hospital, Chandigarh, India*

Background: Rheumatoid arthritis (RA) is an autoimmune chronic inflammatory disease associated with cardiovascular autonomic neuropathy. Cardiovascular autonomic neuropathy is a significant risk predictor for sudden cardiac death in rheumatoid arthritis.[1] Sudomotor dysfunction reflects small fibre neuropathy, cardiovascular autonomic neuropathy and peripheral sympathetic autonomic neuropathy.[2] However, sudomotor dysfunction and its relationship with inflammatory measures remain unexplored in RA patients in the absence of traditional cardiovascular (CV) risk factors.
Objectives: The aim of present study was to assess the sudomotor function and its association with disease specific measures: ESR, CRP and DAS-28 in RA patients with no apparent conventional cardiovascular risk factor.
Methods: In this cross-sectional study, 60 RA patients fulfilling 2010 Rheumatoid Arthritis Classification Criteria[3] and 40 age and sex-matched healthy controls were recruited. Sudomotor function was assessed using Sudoscan (Impeto Medical, Paris, France) through measurement of electrochemical skin conductance of hands and feet.[2] Sudoscan investigates the sweat gland activity and used as a surrogate to study the damage of sympathetic sudomotor nerves in neuropathy. It is an indirect assessment tool of sudomotor function. Inflammatory measures such as ESR and CRP and DAS-28 (disease activity score in 28 joints) were determined.
Results: Rheumatoid arthritis patients had significantly impaired sudomotor function (56.90±12.95 vs. 76.15±8.45 μs, p<0.00, Figure 1A), elevated ESR (31.30±12.34 vs. 16.72±4.46, p<0.001) and CRP (10.55±3.81 vs. 3.81±1.03, p=0.002) as compared to healthy controls, respectively. The mean disease duration of RA patients was 9.15±5.76 and they had high disease activity (mean DAS-28, 4.60±1.72). Sudomotor function was found to be inversely correlated with ESR (r =0.42, p=0.001, Figure 1B), CRP (r =0.60, p<0.001, Figure 1C) and DAS-28 (r =0.38, p=0.003, Figure 1D).

Fig. 1A. Comparison between sudomotor function RA patients and healthy controls

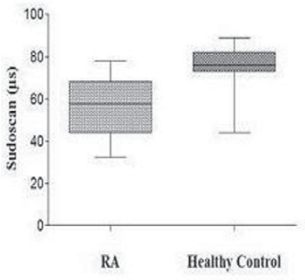


Fig. 1B. Inverse correlation between sudomotor function and ESR

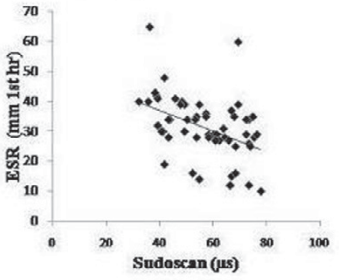


Fig. 1C. Inverse correlation between sudomotor function and CRP

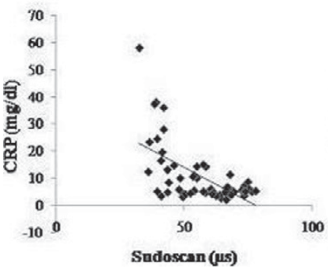
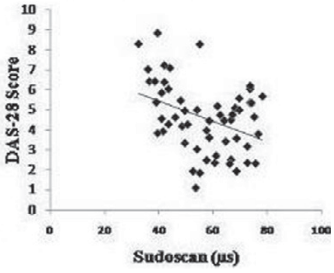


Fig. 1D. Inverse correlation between sudomotor function and DAS-28 score



Conclusions: Cardiovascular autonomic neuropathy occurs in RA in the absence of traditional CV risk factors. Sudomotor dysfunction is significantly associated with increased level of ESR, CRP and disease activity suggesting that increased inflammation may cause sudomotor dysfunction.
References:
[1] Milovanovic B et al. Srp Arh Celok Lek 138:26–32.
[2] Mayaudon H et al. Diabetes Metab. 2010;36:450–54.
[3] Aletaha D et al. Arthritis Rheum. 2010;62:2569–81.
Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4382

SAT0134 DAILY MONITORING OF ARTERIAL STIFFNESS IN WOMEN WITH RHEUMATOID ARTHRITIS

T.A. Romanova, N.M. Nikitina, A.P. Rebrov. *Hospital Therapy Department, State Medical University of Saratov, Saratov, Russian Federation*

Background: Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular (CV) disease. Monitoring of arterial stiffness could be used as an additional tool of cardiovascular risk assessment.
Objectives: of the study is to evaluate the main parameters daily monitoring of arterial stiffness (DMAS) in women with rheumatoid arthritis with or without arterial hypertension (AH).
Methods: DMAS was measured in 63 women with RA (ACR 1987 and/or EULAR/ACR 2010 criteria). The first group involved 39 RA female patients with AH (mean age – 58.3±6.08 years; median of RA duration - 8 [4; 14] years, median of DAS 28- 5.08 [4.04; 5.85]), the second group included 24 women with RA without AH (mean age 55±7.15 years; duration of RA is 10 [3; 17] years, mean DAS 28 – 5.25 [4.6; 5.7]).
30 women with AH without RA and other joint diseases and 22 healthy females were involved as a controls. Persons with and without RA were comparable

inconventional cardiovascular risk factors. Exclusion criteria were smoking, diabetes mellitus, symptomatic AH, cardiovascular diseases (except AH).
DMAS was measured by using the BPlab with technology VASOTENSE (Russian).An index of arterial stiffness (ASI), a daily index of arterial stiffness (AASI), an aortic pulse wave velocity (PWVao), augmentation index (AIx) were measured. All indexes were estimated at day and night hours.
Statistics was performed with STATISTICA 7.0 (StatSoft, USA).
Results: Hypertensive RA patients and AH patients without RA had comparable DMAS parameters (ASI, PWVao, AIx). The AASI index was higher in RA patients without AH versus controls (0.48±0.2 and 0.29±0.17, respectively, p=0.00001) and the AASI index was higher in hypertensive RA patients versus AH patients (0.5±0.2 and 0.38±0.15, respectively, p=0.01). AASI >0.07 revealed at RA patients more often than in controls: at 13.15% of hypertensive RA patients and at 16.6% of RA patients without AH, respectively, $p<0.05$. The increase of PWVao observed at RA patients frequently than in controls ($p<0.05$).
Daily index ASI100 was higher in RA patients without AH than in healthy controls (121 [109.5; 139] mmHg vs. 107 [103; 115] mmHg, p=0.014).
The increased of AIx75 was registered in 25% of RA patients without AH and in 9.09% of controls (p=0.08). PWVao and average Aix75 correlates with ESR (r =0.38 and r =0.36, respectively, $p<0.05$) in RA patients with AH; AASI correlates with level C-reactive protein (r=0.36, $p<0.05$).
ASI and AASI in RA patients with AH correlates with age (Spearmen's r =0.41 and r =0.36, respectively, $p<0.05$), systolic blood pressure (r =0.76 and r =0.65, respectively, $p<0.05$); pulse blood pressure (r=0.77 and r =0.43, respectively, $p<0,05$).
Conclusions: Arterial stiffness, according to daily monitoring, in RA patients is higher than in hypertensive patients without RA and healthy controls. Arterial stiffness in patients with RA and AH is higher than in patients with RA without AH or AH without RA. Age, systolic blood pressure, pulse blood pressure, high levels of ESR and C-reactive protein associated with increased arterial stiffness in RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5683

SAT0135 CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS PATIENTS FROM SOUTHERN BRAZIL AND ITS ASSOCIATION WITH SERUM LEVELS AND GENOTYPIC VARIATION OF MANNOSE BINDING LECTIN

B. Stadler[1], T.A.F.G. Dos Santos[1], T. Skare[1], R. Nisihara[1,2], R. Petisco[3], I. Goeldner[2], S. Utiyama[4], I.J.T. Messias-Reason[2]. *[1]Rheumatology Unit, Hospital Universitário Evangelico de Curitiba; [2]Department of Medical Pathology, Federal University of Paraná; [3]Evangelic School of Medicine; [4]Department of Clinical Analysis, Federal University of Paraná, Curitiba, Brazil*

Background: The binding lectin mannose (MBL) is a serum protein of collectin family that appears to be involved in the inflammatory process and in the genesis of atherosclerotic disease.
Objectives: To study the association of serum levels of MBL and its genotypic variation with carotid arteries intimal thickness (IMT) in rheumatoid arthritis (RA) patients from Southern Brazil.
Methods: Serum level, MBL genotyping and IMT were studied in 90 RA patients along with their demographic, clinical and laboratory profile. MBL levels were measured in 90 healthy controls.
Results: There was significant difference between mean serum levels of MBL in patients with RA and controls (528 ng/mL vs 937.5 ng/mL, p=0.05, respectively). The median IMT in RA patients was 0.59 mm (0.51 to 0.85 mm). There was no correlation between levels of MBL with disease activity measured by DAS-28 (disease activity score-28), erythrocyte sedimentation rate (ESR), autoantibodies presence or IMT (p=NS). A negative correlation was found between MBL levels with CRP levels (p=0.02). The mutation vat codon 54 (variant B) and HYPA haplotype were the most frequent (67.5% and 31.7%, respectively) in the RA sample. Dominant genotypes (A/A) are associated with lower IMT when compared with heterozygotes (A/O; p=0.04) and homozygous recessive (O/O; p=0.05). Also dominant genotypes had lower CRP when compared with heterozygous (p=0.04) or with recessive genotypes (p=0.05).

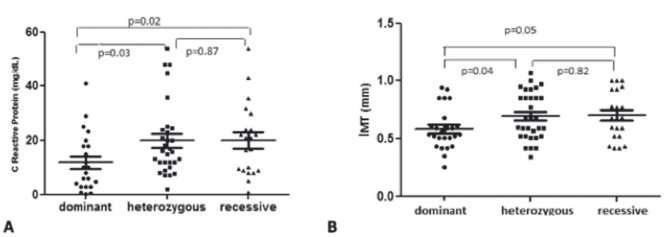


FIGURE 1: MBL GENOTYPING, C REACTIVE PROTEIN (CRP) AND CAROTID INTIMA MEDIA THICKNESS (IMT)

Conclusions: RA patients had lower MBL levels than controls. MBL serum levels are negatively associated with CRP; low producers of MBL had increased thickness of the IMT than high producers.

References:
[1] Scarno A, Perrotta FM, Cardini F, Carboni A, Annibali G, Lubrano E, et al. Beyond the joint: Subclinical atherosclerosis in rheumatoid arthritis. World J Orthop [Internet]. 2014;5(3):328–35. Available from: http://www.wjgnet.com/2218-5836/full/v5/.
[2] Ip WK, Lau YL, Chan SY, Mok CC, Chan D, Tong KK, et al. Mannose-binding lectin and rheumatoid arthritis in southern Chinese. Arthritis Rheum. 2000;43(8):1679–87.
[3] J Maury CP, Aittoniemi J, Tiitinen S, Laiho K, Kaarela K, Hurme M, et al. Variant mannose-binding lectin 2 genotype is a risk factor for reactive systemic amyloidosis in rheumatoid arthritis. Jounal Intern Med. 2007;262:466–9.
[4] Graudal NA, Homann C, Madsen HO, Svejgaard A, Jurik AG, Graudal HK, et al. Mannan Binding Lectin in Rheumatoid Arthritis. A Longitudinal Study. J Rheumatol. 1998;25(4):629–35.
[5] Carvalho EG, Utiyama SRR, Kotze LMS, Reason ITM. Lectina ligante de manose (MBL): características biológicas e associação com doenças. Res bras alerg imunopatol. 2007;30(5):187–93.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6998

SAT0136 ASSOCIATION OF GENOTYPES FOR BCL1 POLYMORPHISM IN THE GLUCOCORTICOID RECEPTOR GENE WITH ISCHEMIC HEART DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

V.S.S.U. Kmyta, O. Savchenko, L. Prystupa. *Internal Medicine Department, 4682, Sumy, Ukraine*

Objectives: The objective is to study association of genotypes for Bcl1 polymorphism in the glucocorticoid receptor (GR) gene with ischemic heart disease (IHD) in patients with rheumatoid arthritis (RA).
Methods: 161 subjects with rheumatoid arthritis aged 40 years and older were examined by means of instrumental, clinical and laboratory examinations. Rheumatoid arthritis was diagnosed according to ACR/EULAR Classification Criteria (2010). The IHD diagnosis was verified by means of AHA/ACC guidelines (2012). BCL1 polymorphism in exon 2 was identified using polymerase chain reaction with subsequent analysis of restriction fragment length polymorphism by Fleury I. et al. (venous blood was used as the material for the study). Statistical analysis was performed using SPSS–17 program.
Results: It was revealed that 76 (47.2%) patients had isolated RA (group I), while 85 (52.8%) individuals had RA with concomitant IHD (group II). In group I, there were 29 (38.2%) patients with C/C genotype, 39 (51.3%) – with C/G genotype, and 8 (10.5%) – with G/G genotype. The distribution in group I was as following: 16 were homozygous for the C allele (18.8%), 40 were heterozygous (47.1%) and 29 were homozygous for the G allele (34.1%) (χ^2=15.23; p=0.02). It was established that the risk of ischemic heart disease was 6.57 times higher in homozygotes for the G allele (OR=6.57; 95% CI=2.44−17.73; p=0.001) as compared with homozygotes for the C allele.
Conclusions: It was established that G/G genotype prevailed in RA patients with ischemic heart disease, while C/C genotype prevailed in patients with isolated RA. The risk of IHD development in patients with RA was associated with G/G genotype for Bcl1 polymorphism in the GR gene.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3998

SAT0137 BONE MINERAL DENSITY MEASUREMENT INTERVALS FOR SEROPOSITIVE RHEUMATOID ARTHRITIS PATIENTS NOT TREATED FOR OSTEOPOROSIS

W. Park, K.-H. Jung, S.-R. Kwon, M.-J. Lim, S.-G. Park, M.-J. Jo. *In-Ha University Hospital, Incheon, Korea, Republic Of*

Background: Osteoporosis occurs more frequently in rheumatoid arthritis (RA) patients than in healthy individuals. However the appropriate interval for the bone mineral density (BMD) measurement in RA patients is not well established.
Objectives: This study investigated the effective BMD measurement interval and the risk factors associated with the development of osteoporosis for RA patients.
Methods: A retrospective study was performed on 511 RA patients aged more than 40 years old who had undergone BMD (DXA, GE LUNAR PRODIGY ADVANCE) testing more than once and who had normal BMD or osteopenia at the baseline BMD test and no history of any fracture of the spine or femur. The subjects were categorized into four subgroups: normal BMD (T-score > -1), mild (-1 ≥ T-score > -1.5), moderate (-1.5 ≥ T-score > -2), and advanced (-2 ≥ T-score > -2.5) osteopenia. The BMD testing interval was defined as the estimated time for 10% of the RA patients to make the transition into osteoporosis without osteoporotic fracture or the administration of any osteoporosis drug.
Results: The observation period was 2,214 patient-years, with an average of 4.3 years. The estimated BMD testing interval was more than 10 years for normal, 4.3 years for mild, 2.5 years for moderate, and 1.5 years for advanced osteopenia in each of the RA patient groups.
Conclusions: Our study indicated that in normal or osteopenic RA groups, a baseline BMD T-score is the most important factor in estimating the interval in which osteoporosis is predicted to occur. In addition, we recommend that the BMD measuring interval should be greater than 10 years in normal BMD RA

Table 1. Interval between baseline BMD testing and the development of osteoporosis

Baseline BMD	Mean interval to develop osteoporosis (year)		Mean interval to develop osteoporosis in 10% of each group (year)	
	Lumbar spine	Femur neck	Lumbar spine	Femur neck
Normal	9.4 (9.29–9.49)[a]	9.4 (9.25–9.53)[a]	>10	>10
Mild osteopenia	9.2 (8.58–9.71)[a]	9.1 (8.94–9.22)[a]	4.3	>10
Moderate osteopenia	7.9 (6.94–8.76)[a]	9.4 (8.93–9.87)[a]	2.5	7.5
Advanced osteopenia	5.4 (4.61–6.21)[a]	8.6 (7.68–9.50)[a]	1.5	2.2

BMD, bone mineral density. [a]Mean (95% confidence interval).

patients, 4 years in mild, 2 years in moderate, and 1 year in advanced osteopenic RA patients on the basis of L-spine BMD.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4638

SAT0138 OPTIMIZING TARGETED THERAPY: CAN PROMS FILL THE GAP BETWEEN PATIENTS- AND PHYSICIAN- PERCEIVED REMISSION IN RHEUMATOID ARTHRITIS

Y. El Miedany[1], M. El Gaafary[2], N. El Arousi[3], S.S. Youssef[3], D. Palmer[4].
[1]Rheumatology, Darent Valley Hospital, Dartford, United Kingdom; [2]Community and Public health; [3]Rheumatology and Rehabilitation, Ain Shams University, Cairo, Egypt; [4]Rheumatology, North Middlesex University Hospital, London, United Kingdom

Objectives: 1. To compare the patient perspective on remission in RA in comparison to the rheumatologist perceived remission perspectives.
2. To determine the value of Patient Reported outcomes in identifying specific symptoms and aspects of disease able to define remission in RA from the patient perspective.
Methods: RA patients diagnosed according to ACR/EULAR criteria were treated according to treat-to-target regime with regular disease activity monitoring (every 1–3months). Remission was measured in two ways: 1) patient perceived remission using the question "Would you say that, at this moment, your disease activity is as good as gone? (yes/no)"; and 2) Physician perceived remission was defined as a physician global assessment ≤1 on a 0–10 VAS, phrased: "How active do you think the rheumatoid arthritis of your patient is today?" The study included 188 RA patients (76 males, 112 females; mean age 52.4±11 years) and 87 rheumatologists (30 males, 57 females; mean age 48.7±11.7 years). All participants were asked to complete a questionnaire which was composed of all domains identified in relation to the disease remission. 10 cm visual analogue scale (scored 0–10) was used to illustrate the importance of each factor in an individual opinion. The list included joint pain, functional ability, quality of life, absence of morning stiffness, absence of fatigue, normal laboratory tests, no comorbidity risk, radiologic remission, Disease Activity score and ability to work. In addition, patients were asked to complete a copy of the PROMs [1]. One-way analysis of variance was used for the comparison of independent variables. Spearman correlation coefficient was used to assess the correlation between variables.
Results: There were no significant differences in questionnaire answers in relation to patients' demographics and present disease activity. Regarding the patient perceived remission, the top 4 were: pain (76%), functional ability (71%), quality of life (69%) and fatigue (43%). Regarding the physician perceived remission, the following factors were rated more relevant by rheumatologists than the patients ($p<0.001$): low disease activity score (88%), radiologic remission and progression of erosions (76%), lab measures (ESR/CRP) (57%) followed by difficulties in performing paid work (49%).
Functional ability was scored significantly higher in patients >65 as compared with patients <65 years of age (9.6 vs 8.1 on VAS, p=0.03). In contrast the patient's cohort <65 years of age, rated quality of life at a higher level (9.7) than those below 65 (8.4). Functional ability was scored higher in patients with longer-standing disease as compared to patients with shorter disease duration ($p<0.05$). PROMs enabled the patient and the treating physician identify the aspects of relevance necessary for optimal clinical management.
Conclusions: Different factors are important for rheumatologists and RA patients regarding disease remission. Treatment satisfaction is determined not only by disease activity indices but also by other patient-oriented factors. PROMs could optimise targeted therapy as it can play a significant role in identifying disease activity parameters relevant to both the treating rheumatologist as well as the patient.

References:

[1] El Miedany et al. Clin Exp Rheumatol 2010; 28(5):734–44.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4491

SAT0139 ASSESSING ENTHESITIS BY ULTRASONOGRAPHY IN PATIENTS WITH SERONEGATIVE RHEUMATOID ARTHRITIS

Z. Erturk[1], T. Özsoy[2], I. Yağcı[2], Y. Yalçınkaya[1], Ü. Gazel[1], P. Atagündüz[1], H. Direskeneli[1], N. İnanç[1]. *[1]Rheumatology; [2]Physical Therapy and Rehabilitation, Marmara University, Istanbul, Turkey*

Background: In patients with seronegative rheumatoid arthritis (RA) there is a difficulty to make the differential diagnosis with the spondyloarthropathies.
Objectives: To assess the presence of enthesitis in patients with seronegative rheumatoid arthritis in comparison with the healthy controls, patients with seropositive rheumatoid arthritis and ankylosing spondylitis.
Methods: In this cross-sectional study, seronegative and seropositive rheumatoid arthritis patients, who fulfilled the 2010 ACR/EULAR criteria, patients with ankylosing spondylitis and healthy controls have been assessed by grey scale and power doppler ultrasonography for the presence of enthesopathy at the achilles, plantar fascia, proximal patella, distal patella, quadriceps, tibialis anterior, triceps, common flexor and extensor tendons. Clinical assessment of the patient groups included demographic findings, health assessment questionnaire and disease activity score.
Results: In our study, we recruited age and sex matched 27 seronegative RA, 17 healthy controls, 20 seropositive RA and 12 ankylosing spondylitis patients. We evaluated and analysed both right and left sides of the enthesis regions separately which have been indicated in the methods section. The mean DAS28, mean ESR and mean CRP of the patients with seronegative RA were 3.6±1.28, 32.2±21.2 and 12.37±27.77 respectively (Table 1).
Median of Madrid sonographic enthesitis index (MASEI) was 5 in patients with seronegative RA. 4 patients have severe scores. There were significant differences between seronegative RA and healthy controls (3, p=0.014) but no differences has been observed between seronegative RA with seropositive RA (6) and anklosing spondylitis (7) in MASEI scores.
In comparison, hypoechogenicity of quadriceps tendon (16 (29.6%) vs 1 (2.5%), p=0.001), bone erosion at the quadriceps tendon attachment (9 (16.6%) vs 0, p=0.007), hypoechogenicity of triseps (13 (24%) vs 7 (17.5%), p=0.049) have been observed more frequently in patients with seronegative RA than seropositive RA. Significantly higher number of patients with bone erosion at the distal patella (10 (41.6%) v 3 (5.5%), p= <0.001), enthesophyte of achilles tendon (7 (29.1%) vs 2 (3.7%), p=0.001) have been detected enthesophyte of proximal patella (7 (29.1%) vs 0, p≤0.001) in patients with ankylosing spondylitis than seronegative RA.

Table 1

	Seronegative RA	Healthy controls	Seropositive RA	Ankylosing spondylitis
Age, years	51,85±11,49	44,42±7,6	52,05±11,26	41,75±5,1
Women, n (%)	48 (88,9)	34 (100)	36 (90)	20 (83)
RA duration, year	9,8±6,75		11,25±9,1	
RF titre (median)	10,77±3,21		345,88±405,32	12,1±3,23
Anti-CCP titre, median	3,99±4,13		326, 81±286, 2	4,32±3,7
DAS28, median	3,6±1,28		3,73±1,45	
ESR, median	32,2±21,2	23,3±11,8	41,63±28,07	19,83±9,38
CRP, median	12,37±27,77	3,14±3,87	14,34±19,97	6,61±5,6

Conclusions: We observed that enthesis involvement was not seldom in patients with seronegative RA. Furthermore there were also similar frequency of entesis involvement in seropositive patients with RA. The value of enthesis sites evaluationfor the differential diagnosis of patients with seronegative RA should be further investigated and the assessment of enthesis sites in seronegative and seropositive RA patients can be important to detect active and chronic changes at the enthesis region.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4457

SATURDAY, 17 JUNE 2017

Rheumatoid arthritis - anti-TNF therapy

SAT0140 EFFECT OF OBESITY IN RESPONSE TO BIOLOGICS IN RHEUMATOID ARTHRITIS

A. Khan[1], S. Sukumaran[2], M. Kanitkar[1], A.-S. Zafar[2], S. Shah[2], S. Adnan[2].
[1]Department of Rheumatology, Queen Elizabeth Queen Mother Hospital, Margate; [2]Department of Rheumatology, William Harvey Hospital, Ashford, United Kingdom

Background: Obesity epidemic has impacted practically every area of health including care of patients with RA. Adipose tissue is an active organ that produces pro-inflammatory molecules. A significant treatment challenge remains is the standard dose of RA medications may not attain same concentrations at sites of inflammation in obese vs non-obese patients thus making them less effective.
Objectives: The study aim was to determine whether obesity represents a risk factor for a poor remission in RA requiring biologic therapies. Obesity may be associated with more severe and refractory inflammation through increased levels of inflammatory adipocytokines leptin, resistin or visfatin or decreased levels of the anti-inflammatory adipocytokine adiponectin. We retrospectively analysed 178 patients diagnosed with RA at East Kent University Hospitals.
Methods: Data analysed for age, sex, disease duration, prior DMARD, positivity RF and anti-CCP antibodies and response to biologics DAS28 score pre-treatment and at 6 months were analysed.Main aim was to analyse any difference between obese and non-obese patients in terms of their response to treatment. Obese patients were defined with a BMI of 30 or above.
Results: See Table 1.

Table 1. Demographics and Baseline Characteristics

Variable	Category	Non-Obese (n=95)	Obese (n=83)	P-value
Sex	Female	61 (64%)	66 (80%)	**0.02**
	Male	34 (36%)	17 (20%)	
Age		53±12	50±13	0.08
Duration disease		8 [6, 11]	12 [7, 14]	**<0.001**
Rheumatoid factor	Negative	20 (21%)	60 (72%)	**<0.001**
	RF	12 (13%)	8 (10%)	
	CCP	17 (18%)	0 (0%)	
	RF/CCP	46 (48%)	15 (18%)	
CRP		35 [10, 51]	24 [7, 40]	**0.02**
ESR		37 [14, 59]	28 [17, 45]	0.57
MTX		15.5±9.2	13.5±9.6	0.15
Administration	Infusion	4 (4%)	5 (6%)	0.74
	Subcutaneous	91 (96%)	78 (94%)	
DAS pre-treatment		5.6±0.7	5.4±0.8	0.06

Results suggested that there were significant differences between two groups for sex, duration of disease, RF and CRP. There was also some evidence of difference between groups in terms of their age and pre-treatment DAS28 score but these differences were only of borderline statistical significance. There was smaller proportion of males in the obese group with 20% male compared to 36% of non-obese patients. Obese patients had on average a longer disease duration with a median of 12 years compared to a median of 8 years for the non-obese group. The RF status also varied between groups with a much higher proportion of patients in the negative category for the obese group. CRP values were significantly lower in the obese group with a median of 24 compared to 35 in the non-obese group.

Table 2. EULAR response between obese and non-obese patients

EULAR response	Non-Obese N (%)	Obese N (%)	P-value
No response	9 (9%)	32 (39%)	<0.001
Moderate response	40 (42%)	36 (43%)	
Good response	46 (48%)	15 (18%)	<0.001
	Non-Obese (n=95), Mean ± SD	Obese (n=83), Mean ± SD	
DAS28 post-treatment	3.2±1.0	4.2±1.3	
DAS28 reduction	2.4±1.3	1.1±1.3	

Non-obese had the best response with 48% good response compared to18% of the non-obese group with post treatment mean DAS28 score of 3.2 and mean reduction of 2.4.

Conclusions: Obesity is important factor that impacts treatment and outcome in RA. Future clinical studies to elucidate the pharmacokinetics of specific biologic agents in relation to BMI should provide further clinical guidance.

References:

[1] Gómez et al.What's new in our understanding of the role of adipokines in rheumatic diseases? Nat Rev Rheumatol.2011.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2526

SAT0141 OPTIMAL CIRCULATING ADALIMUMAB LEVELS RANGE ASSOCIATED WITH GOOD CLINICAL RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

A. Jochems[1], A. Martinez-Feito[1], C. Plasencia[1], B. Hernández-Breijo[1], A. Mezcúa[2], A. Villalba[1], I. Monjo[1], P. Nozal[2], A. Balsa[1], M.D. Pascual-Salcedo[1]. *[1]Immuno-Rheumatology Research Group; [2]Immunology Unit, University Hospital la Paz, Madrid, Spain*

Background: TNF inhibitors have become an important part of healthcare worldwide for inflammatory diseases such as RA[1]. Many publications show that responding patients have higher Adalimumab (Ada) serum trough levels (ATL) than non-responders. These factors are influenced by age, weight, gender or pharmacokinetics, which in turn depend on immunogenicity. Concomitant use of immunomodulators such as methotrexate (MTX) reduces immunogenicity and enhances therapy benefits[1,3].Increasing drug dosage in patients with less response is the standard practice, while lowering dosage is advisable in patients achieving remission. Many recent publications[2] assess serum trough levels that reflect optimal response and which could be used as benchmark for guidance to implement the Therapeutic Drug Monitoring.

Objectives: To establish an optimal Ada serum trough level (ATL) range in RA patients associated with good clinical response.

Methods: A prospective observational study with 40 RA patients under Ada treatment recruited in the Rheumatology Unit of Universitary Hospital La Paz was conducted. Demographic data, ATL and clinical activity of patients treated with 40 mg/kg every other week from 4 months up to 12 years of treatment were collected. A total of 206 samples were analyzed [χ=5 (3–13) samples/patient]. Disease activity was assessed using the DAS28 index and clinical improvement with $\triangle$DAS28. ATL were measured with a capture ELISA[3] [correlation with Promonitor (Derio, Vizcaya, Spain) k=1, r=0.91; and with Sanquin (Amsterdam, The Netherlands) k=1, r=0.86] and statistical analysis were performed with GraphPadPrism 5.0 software.

Results: Demographic data of our cohort were: mean age (±SD) 56.75±16.06, with 82.5% of females and 45% of patients treated with concomitant MTX. Sixty-five and 72% of patients were RF and ACPA positive, respectively. ATL were similar in patients treated with concomitant MTX (χ=3.82±2.42 μg/ml) or Ada monotherapy (χ=3.54±2.43 μg/ml) p=0.81.

Consistent with previous studies[1,2], low-disease activity patients (DAS28$\leq$3.2) presented higher Ada circulating levels than patients with high-disease activity [3.7 μg/ml (IQR 2.97–5.48) vs. 1.71 μg/ml (IQR 0.23–4.51), p=0.01]. The median of Ada levels excluding the values (n=6) that showed immunogenicity was 3.42 μg/ml (IQR 1.55–5.03) where 3.50 μg/ml represented the most frequent value (15% of patients). Lack of clinical improvement ($\triangle$DAS$<$1.2) was linked to drug levels below percentile 25 (p=0.04) whilst Ada levels above percentile 75 did not ensure more clinical improvement (p=0.7) than the values around the median.

Conclusions: ATL correlate with the disease activity and with the clinical improvement. The optimal range associated with good therapeutic response after the standard dose is *1.5–5 μg/ml*. Higher circulating drug levels do not entail better response, which indicates they could be unnecessary. The knowledge of the optimal drug ranges can guide the Personalized Drug Therapy in order to maximise effectiveness and minimise costs.

References:

[1] Pouw, M.F., et al. ARD, 2013.
[2] Chen, D., et al. ARD, 2014.
[3] Pascual- Salcedo, D. Rheumatology (Oxford), 2011.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4861

SAT0142 PREDICTORS OF INADEQUATE RESPONSE AND RAPID RADIOGRAPHIC PROGRESSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS RECEIVING METHOTREXATE: A POST HOC ANALYSIS OF 2 RANDOMIZED, CONTROLLED TRIALS OF ADALIMUMAB

A. Kavanaugh[1], R.F. van Vollenhoven[2], B.A. Wolfe[3], S. Florentinus[3], S. Chen[3], J.L. Subotícki[3], J.S. Smolen[4]. *[1]Division of Rheumatology, Allergy, and Immunology, University of California, San Diego, la Jolla, United States; [2]Amsterdam Rheumatology and Immunology Center ARC, Amsterdam, Netherlands; [3]AbbVie Inc., North Chicago, United States; [4]Medical University of Vienna, Vienna, Austria*

Background: Methotrexate (MTX) is recommended as first-line therapy in patients (pts) with rheumatoid arthritis (RA).[1] However, information is limited regarding factors that may predict a poor response to MTX.

Objectives: To identify predictors of MTX insufficient response (IR) and rapid radiographic progression (RRP) among pts with early RA receiving 6 months (mos) of MTX therapy.

Methods: In OPTIMA, pts with RA $<$1 year were randomized to receive either adalimumab (ADA) 40 mg every other wk (EOW) + MTX weekly (wkly) or placebo (PBO) EOW + MTX wkly for 26 wks. In PREMIER, pts with RA $<$3 years were randomized to receive ADA 40 mg EOW + MTX wkly, ADA 40 mg EOW + PBO wkly, or PBO EOW + MTX wkly for 2 years. This post hoc analysis compared MTX-IR pts, defined as not reaching stable low disease activity at wks 22 and 26 in OPTIMA and wks 20 and 24 in PREMIER, with pts who responded to initial MTX monotherapy. Comparisons were also made between pts who did and did not have RRP, assessed by an increase in modified Total Sharp Score (mTSS) of $>$1.5 from baseline (BL) to 6 mos. In pts with available data, backward logistic regression was used to identify potential predictors of MTX-IR and RRP. Candidate predictors included BL demographics, time-averaged disease parameters for 3 time intervals (through 4 wks, 8 wks, and 12 wks of MTX exposure), and BL disease characteristics for the 12-wk interval. Time-averaged variables were calculated as area under the curve standardized for length of time interval.

Results: This analysis included 525 MTX-IR and 162 MTX responders. Mean disease duration at BL was 6 mo for both groups. The mean Disease Activity Score 28 (C-reactive protein; DAS28[CRP]) was 6.2 vs 5.6, Health Assessment Questionnaire Disability Index (HAQ-DI) was 1.6 vs 1.3, and mTSS was 15.5 vs 12.2 for MTX-IR vs MTX responders, respectively. 171 pts experienced RRP, while 499 pts had no RRP; the mean disease duration at BL was 6 mo for both groups. The mean DAS28(CRP) was 6.4 vs 6.0 and HAQ-DI was 1.6 vs 1.5 for pts experiencing RRP vs pts who did not experience RRP, respectively. Mean mTSS at BL was higher for pts who experienced RRP (20.7) vs those who did not (12.4). Predictors of MTX-IR and RRP at 6 mos are shown in the Figure. Time-averaged HAQ-DI and DAS28(CRP) through 12 wks were the strongest predictors of both MTX-IR and RRP. Additionally, early clinical response (time-averaged DAS28[CRP]) at both 4 and 8 wks was predictive of both MTX-IR and RRP; however, time-averaged HAQ-DI was not predictive until wk 12.

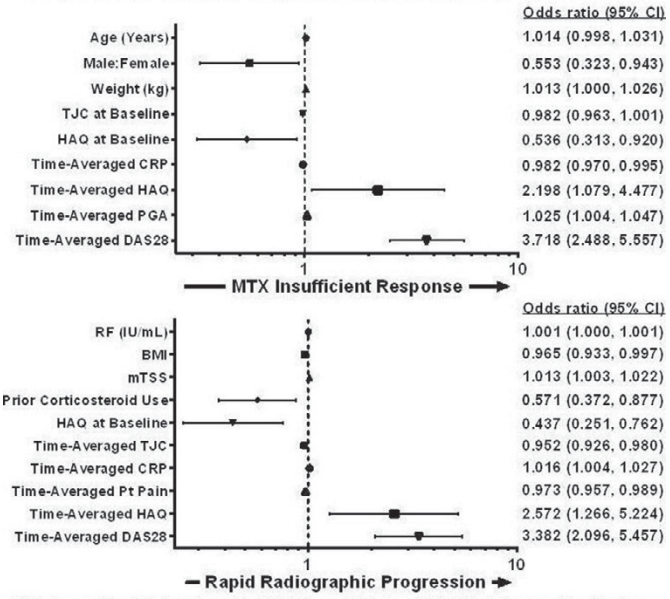
Conclusions: In the OPTIMA and PREMIER trials, post-BL measures of RA activity appeared to be the strongest predictors of subsequent MTX-IR and of RRP. Pts who are likely to progress on MTX or have RRP may be good candidates for switching to earlier step-up therapy to reduce the likelihood of permanent bone damage.

References:

[1] Singh JA, et al. Arthritis Care Res (Hoboken). 2016;68(1):1–25.

Acknowledgements: AbbVie: study sponsor, contributed to design, data collection, analysis, interpretation; and (funded) writing, reviewing, approval of final version. Medical writing: Y.E. Yarker, M.J. Theisen, Complete Publication Solutions, LLC.

Figure. Predictors of Methotrexate Insufficient Response or Rapid Radiographic Progression in Patients with Early Rheumatoid Arthritis Receiving Methotrexate[A]



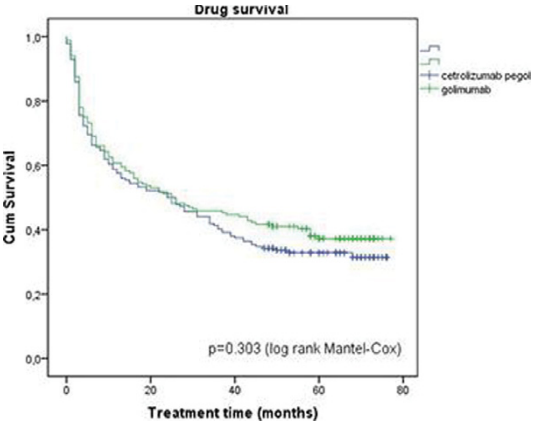
BMI, body mass index; CRP, C-reactive protein; DAS28, Disease Activity Score 28; HAQ, Health Assessment Questionnaire; mTSS, modified Total Sharp Score; MTX, methotrexate; PGA, Physician Global Assessment of disease activity; Pt pain, patient's assessment of pain; RF, rheumatoid factor; TJC, tender joint count.
[A]Time-averaged value through week 12 are shown.

Disclosure of Interest: A. Kavanaugh Grant/research support from: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Consultant for: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Centocor-Janssen, Pfizer, Roche, and UCB, R. F. van Vollenhoven Grant/research support from: AbbVie, Amgen, BMS, GSK, Pfizer, Roche, and UCB, Consultant for: AbbVie, Biotest, BMS, Crescendo, GSK, Centocor-Janssen, Lilly, Merck, Pfizer, Roche, UCB, and Vertex, B. A. Wolfe Shareholder of: AbbVie, Employee of: AbbVie, S. Florentinus Shareholder of: AbbVie, Employee of: AbbVie, S. Chen Shareholder of: AbbVie, Employee of: AbbVie, J. L. Suboticki Shareholder of: AbbVie, Employee of: AbbVie, J. S. Smolen Grant/research support from: AbbVie, Consultant for: AbbVie, Speakers bureau: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.1892

SAT0143 COMPARISON OF TREATMENT WITH GOLIMUMAB AND CERTOLIZUMAB-PEGOL IN ARTHRITIS- RESULTS FROM THE SOUTH SWEDISH ARTHRITIS TREATMENT GROUP (SSATG) REGISTER

C. Roseman, E. Lindqvist, P. Geborek, M. Crnkic Kapetanovic. *Section of Rheumatology, Lund University, Department of Clinical Sciences Lund, Skåne University Hospital, Lund, Sweden*

Background: "Head to head" studies comparing the efficacy and tolerability of different TNF inhibitors are scarce, in particular the comparison between certolizumab pegol and golimumab.
Objectives: To compare the efficaciousness, drug survival and tolerability of certolizumab-pegol and golimumab in adult patients with establish arthritis (RA, JIA, SpA or unspecified polyarthritis) starting these treatments between February 2010 and December 2013 at out-patient unit at the Skåne University Hospital, Department of Rheumatology Lund/Malmö and two associated private rheumatology units.
Methods: All patients starting treatment with biologics were consecutively included in the South Swedish Arthritis Treatment Group (SSATG) register and regularly followed up according the standard protocol including: SJC/TJC, CRP, ESR, physicians global assessment of disease activity, patients' assessment of disease activity and pain (VAS global and VAS pain) and HAQ. Last follow up date was October 17th 2016. Kaplan-Meier survival analysis was used to estimate the drug survival. Possible predictors of drug survival were analysed using Cox regression model.
Results: In total, 352 patients (71% women, mean age 51 years, mean disease duration 12 years, started these treatments during study period. Of these, 168 received golimumab and 184 certulizumab-pegol. Mean treatment time was 31 months (range 0–77). Percentage of patients with RA, SpA, JIA and unspecified arthritis were 58,4%, 16,4%, 5,7%, and 19,5% respectively. Certolizumab-pegol was more used in RA (67% vs 49%) and JIA (8% vs 2%) while golimumab was more frequent among patients with SpA (21% and 12%) or PsA (23% and 10, respectively). Only 7% of golimumab and 10% of certulizumab-pegol patients received these drugs as first biologic treatment and approximately 50% of patients received these drugs as $\geq$3. biological treatment.
In golimumab treated patients mean DAS28 decreased from 4,3 (baseline) to 3,3 (3 months); 2,8 (6 months) and 2,7 (12 months) but levelled off at 36 months follow up. Corresponding mean DAS28 levels in certulizumab-pegol treated patients were 4,6 (baseline); 3,2 (3 months); 2,8 (6 months) and 2,6 (12 months). The similar pattern was seen in changes in HAQ and CDAI over the study time. There were no statistically significant differences in DAS, HAQ or CDAI between treatments at any follow up visit. At the end of follow up 64 (38%) of golimumab and 60 (32%) of certulizumab-pegol patients remained on their treatment. No significant difference in drug survival was seen between the treatments (Figure). Patients with spondylartropathy had significantly better survival on golimumab compared to RA patients (p=0,005)whicih remained after adjustment for age, gender, CRP, number of previous biologics and concomitnt methotrexate at baseline.



Conclusions: Spondylarthropathy including psoriatic arthritis was associated with better drug survival on golimunab compared to certolizumab pegol. No other significant differences in efficacy, tolerability or drug survival were seen between golimumab and certolizumab pegol in patients with established arthritis in daily clinical practice. Approximately one third of patients starting these treatments remained on treatment after 3 years.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4818

SAT0144 TUMOR NECROSIS FACTOR-ALPHA INHIBITORS AND PSYCHIATRIC SIDE EFFECTS: RESULTS FROM THE FRENCH PHARMACOVIGILANCE DATABASE

C.M. Yelnik[1], L. Gaboriau[2], N. Petitpain[3], H. Théophile[4], C. Scalbert[5], E. Delaporte[5], S. Gautier[2], M. Lambert[1]. *[1]Internal Medicine Department, University of Lille, UFR Medicine, Universitary Hospital Center of Lille; [2]Regional Pharmacovigilance center of Hauts-de-France, Lille; [3]Regional Pharmacovigilance center of Lorraine, Nancy; [4]Universitary Hospital Center of Bordeaux, Regional pharmacovigilance center of Bordeaux, Bordeaux; [5]Dermatology department, University of Lille, UFR Medicine, Universitary Hospital Center of Lille, Lille, France*

Background: Although Tumor Necosis Factor alpha (TNF-α) is a major proinflammatory cytokine in the brain, potential psychiatric side effects of TNF-α inhibitors have been little investigated. Manic and psychotic disorders are not recognized as TNF-α inhibitors' side effects even though few reports of such complications have been reported.
Objectives: This study reports cases with psychiatric symptoms (in the spectrum of psychotic and manic disorders) that occur during treatment with tumor necrosis factor alpha (TNF-α) inhibitors and aims to evaluate the role of these agents as causative factors.
Methods: We searched the French Pharmocovigilance Database for consecutive cases of positive psychiatric side effects reported during treatment with TNF-α inhibitors. Major psychiatric symptoms were defined, according to DSM-V, as mania and psychosis, and minor psychiatric symptoms as psychomotor agitation, euphoria, hallucinations, personality distortion, and increased libido. Each case had one major symptom or at least one minor symptom.
Results: Among 7912 consecutive cases of side effects registered in the database for TNF-α inhibitors, 184 reported psychiatric symptoms, and of these, 71 met inclusion criteria, whereas 113 met an exclusion criterion. Depression was the most frequent cause for exclusion. TNF-α inhibitors were the only medication suspected in 56 cases (79%). The time between beginning TNF-α inhibitors and onset of symptoms varied from hours to months with a median time of 49 days (IQR=156); initial symptoms mostly worsened under treatment. TNF-α inhibitors were withdrawn in 42 (61%) cases. The improvement of symptoms was significantly associated with treatment withdrawal (78% versus 22%, *p=0.01*). Relapses occurred after rechallenge of TNF-α inhibitors in three of four patients.
Conclusions: We report the first cohort of 71 cases with psychiatric symptoms in the spectrum of manic and psychotic disorders during treatment with TNF-α inhibitors. Our experience suggests that anti-TNFα therapy may cause manic or psychotic side effects.
Disclosure of Interest: None declared

Table 1. Description of psychiatric symptoms registered in the database for TNF-α inhibitors

Characteristics	Patients (Total = 71)
Major psychiatric symptoms:	11 (15%)
– Manic episode	8 (11%)
– Acute psychosis	3 (4%)
Minor psychiatric symptoms:	60 (85%)
– Anxiety/Nervousness	10 (14%)/6 (8%)
– Insomnia or decreased need for sleep	31 (44%)
– Psychomotor agitation/Aggressiveness	6 (8%)/8 (11%)
– Hallucinations	7 (10%)
– Libido exacerbation	2 (3%)
– Euphoria, grandiosity	4 (6%)
– Derealization, depersonalization	3 (4%)
Psychiatric side effect improved:	45 (63%)
– TNF-α Inhibitors withdrawn	32 (45%)
– TNF-α Inhibitors not withdrawn	9 (13%)
– Missing data	4 (6%)
Psychiatric side effect did not improved:	16 (22%)
– TNF-α Inhibitors withdrawn	8 (11%)
– TNF-α Inhibitors not withdrawn	4 (6%)
– Missing data	3 (4%)
Missing data improved/not improved	10 (14%)

DOI: 10.1136/annrheumdis-2017-eular.1610

SAT0145 INFLUENCE OF BODY MASS INDEX (BMI) ON THE DISEASE INFLAMMATORY ACTIVITY AND TREATMENT REPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Villalba Yllan[1], V. Navarro Compan[1], C. Plasencia Rodriguez[1], D. Peiteado Lopez[1], G. Bonilla Hernan[1], L. Nuño Nuño[1], A. Martinez Feito[2], D. Pascual-Salcedo[2], C. Diego[2], A. Balsa Criado[1]. *[1]Rheumatology; [2]Immunology, Hospital Universitario la Paz, Madrid, Spain*

Background: The use of biological therapy (BT) in rheumatoid arthritis (RA) has supposes a very important change in the disease's treatment and prognosis. Drugs like Anti-TNFα have proven unquestionable effectiveness. However, the lack or loss of such effectiveness over time raises the dilemma of what factors may influence it. There are studies that suggest the influence of BMI on the efficacy of these drugs and therefore on the control of the disease.
Objectives: To determine the influence of BMI on disease activity and response to treatment with infliximab (ifx) in patients with RA.
Methods: A retrospective observational study of a population of 76 patients with RA who received infliximab treatment, in a standard guideline of 3 mg/kg, in our service between 2000 and 2016 inclusive. The BMI was classified for some sub-studies in four categories: low (<18.5), normal (=18.5- <25), overweight (=25- <30) and obesity (=30). Disease activity was determined by DAS28 at three times: at baseline, at 6 months and at the year of infliximab treatment; Response to treatment was assessed by deltaDAS28 and EULAR response at 6 months and 1 year of treatment. The EULAR response was classified into two categories: "yes" (DeltaDAS28>1.2, or>0.6 and DAS28 <5.1) and "no" (DeltaDAS28 <.6, or <5.1). First, activity and response rates to treatment were compared in these four groups over the three periods. A regression analysis was then performed for BMI and both activity and response to treatment.
Results: Characteristics of the 76 patients included in the study when initiating IFX therapy were: 66 (86.8%) were women, median (range) age 54 (21–83) years, 77,% RF+, 81% ACPA+, disease duration 10,8 (1,0–39,0) years, 59% with concomitant methotrexate and 55% with other DMARDs. Median (range) BMI was 25,5 (16,7–40,2) kg/m^2. According to BMI, patients with underweight, normal, overweight and obesity were 0 (0,0%), 41 (53,9%), 22 (28,9%) and 13 (17,2%), respectively. The association between BMI and disease activity (median DAS28 (p25-p75)) is shown in Table 1:

Table 1

	Normal	Overweight	Obesity
DAS28 bas	5,63 (4–84–6,30)	5,44 (4,45–6,73)	6,25 (4,42–7,07)
DAS28 6m	3,90 (2,89–5-12)	3,97 (3,32–5,43)	4,80 (3,35–5,72)
DAS28 1y	3,91 (2,89–5,01)	3,69 (2,97–5,29)	4,48 (2,70–5,87)

The association between BMI and treatment response (median deltaDAS28 (p25-p75) and EULAR response (%)) is shown in Table 2:

Table 2

	Normal	Overweight	Obesity	*p*
ΔDAS28				
ΔDAS28 0–6m	1,72 (0,84–2,77)	1,39 (0,38–2,49)	0,77 (0,40–1,59)	*0,2*
ΔDAS28 0–1y	1,56 (0,81–2,74)	1,77 (,092–2,92)	1,20 (0,73–1,90)	*0,2*
EULAR response 6m	70,7	68,2	30,8	*0,065*
EULAR response 1y	61,0	54,5	61,5	*0,065*

In the longitudinal analysis, a trending but not statistically significant relationship between adjusted BMI and DAS28 was observed at six month and at one year of treatment onset: β: 0,051; 95% CI (-0,06 to 0,109) and β: 0,037; 95% CI (-0,022 to 0,097)

Conclusions: BMI seems to influence, in a non significantly manner, in disease activity and in treatment response in RA treated with infliximab. Obesity BMI values are associated with increased activity and a lower response to this treatment than lower BMI values.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4449

SAT0146 RANDOMISED DOUBLE-BLIND STUDY SHOWS COMPARABLE LONG-TERM EFFICACY AND SAFETY BETWEEN RITUXIMAB BIOSIMILAR CT-P10 AND INNOVATOR RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: 48-WEEK RESULTS

C.-H. Suh[1], E. Chalouhi El Khouri[2], P. Miranda[3], F. F Cons Molina[4], P. Shesternya[5], F. Medina-Rodriguez[6], P. Wiland[7], S. Jeka[8], J. Chavez-Corrales[9], T. Linde[10], P. Hrycaj[11], I. Hospodarskyy[12], M. Abello-Banfi[13], J. Jaworski[14], M. Piotrowski[15], W. Park[16], S.C. Shim[17], S.J. Lee[18], S.Y. Lee[18], D.H. Yoo[19]. *[1]Ajou University School of Medicine, Suwon, Korea, Republic Of; [2]Clinica Internacional, Lima, Peru; [3]Centro de Estudios Reumatológicos, Santiago, Chile; [4]Centro de Investigacion en Artritis y Osteoporosis, Mexicali, Mexico; [5]KrasSMU, Krasnoyarsk, Russian Federation; [6]Biologics Especializados SA, Mexico City, Mexico; [7]Medical University, Wroclaw; [8]2nd University Hospital, CM UMK, Bydgoszcz, Poland; [9]Clinica San Borja, Lima, Peru; [10]Rheumatology Medical Center, Halle/Saale, Germany; [11]Poznañ University of Medical Sciences, Poznañ, Poland; [12]Ternopil Medical University, Ternopil, Ukraine; [13]Centro Integral de Reumatologia del Caribe, Barranquilla, Colombia; [14]Reumatika - Centrum Reumatologii, Warszawa; [15]Medical University of Lublin, Lublin, Poland; [16]IN-HA University, School of Medicine, Incheon; [17]Chungnam National University Hospital, Daejeon; [18]Celltrion, Inc., Incheon; [19]Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic Of*

Background: In phase 1 trials (NCT01534884 and NCT01873443), pharmacokinetic equivalence of CT-P10, biosimilar of rituximab, to innovator rituximab (RTX) was demonstrated. In the phase 3 study, equivalence of PK and efficacy up to week 24 were achieved between CT-P10 and RTX (US and EU sourced)[1,2].
Objectives: To investigate the long-term efficacy, pharmacodynamics, immunogenicity and safety of CT-P10 up to week 48.
Methods: Patients with rheumatoid arthritis were randomly assigned to CT-P10, US-RTX or EU-RTX, in combination with MTX. The patients received 2 treatment courses at Week 0 and 24, each consisting of 2 infusions of 1000mg study drug at 2-week interval.
Results: A total of 372 patients were randomised, and 330 patients completed the 2nd course treatment. DAS28 scores through Week 48 were comparable between CT-P10 and US/EU-RTX (Figure), as well as the proportion of ACR responses at Week 48 between the CT-P10 and combined rituximab groups; 81.3% and 79.8% for ACR 20, 55.4% and 53.9% for ACR50, and 31.7% and 33.7% for ACR 70, respectively.

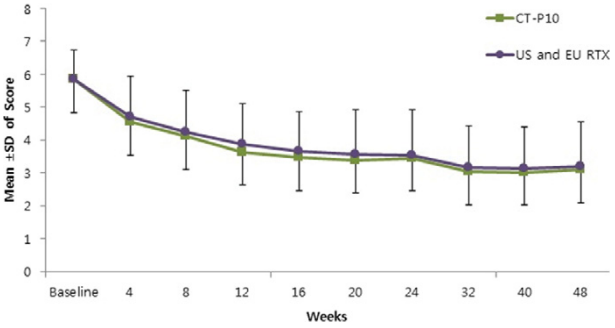


Figure 1. Efficacy Results – DAS28.

B-cell depletion was comparable from after the 1st infusion and up to Week 48. Number (%) of patients with positive anti-drug antibodies in the CT-P10, US-RTX, and EU-RTX was 7 (4.9), 13 (9.4), and 5 (8.6), respectively at Week 48.
The safety profile was also similar across groups (Table).

Table 1. Summary of Safety Profile [n (%)]

	CT-P10 (N=161)	US-RTX (N=151)	EU-RTX (N=60)	Reference Products (US-RTX + EU-RTX) (N=211)
AE	122 (75.8)	96 (63.6)	37 (61.7)	133 (63.0)
Serious Adverse Event	13 (8.1)	14 (9.3)	2 (3.3)	16 (7.6)
Infection	61 (37.9)	53 (35.1)	17 (28.3)	70 (33.2)
Serious infection	2 (1.2)	3 (2.0)	0	3 (1.4)
Infusion related reaction (IRR)*	33 (20.5)	12 (7.9)	13 (21.7)	25 (11.8)
Malignancy	0	2 (1.3)	1 (1.7)	3 (1.4)
Progressive multifocal leukoencephalopathy	0	0	0	0

*None of IRR were serious or led to study drug discontinuation.

Conclusions: This phase 3 randomised controlled trial demonstrated the comparability of CT-P10 with two rituximab in terms of efficacy, pharmacodynamics, immunogenicity and safety for 1 year.

References:
[1] Suh CH, et al. 2016 ACR Abstract No. 1634.
[2] Yoo DH, et al. 2016 ACR Abstract No. 1635.

Disclosure of Interest: C.-H. Suh Consultant for: Celltrion, Inc., E. Chalouhi El Khouri Grant/research support from: Celltrion, Inc., P. Miranda Grant/research support from: Celltrion, Inc., F. F Cons Molina Grant/research support from: Celltrion, Inc., P. Shesternya Grant/research support from: Celltrion, Inc., F. Medina-Rodriguez Grant/research support from: Celltrion, Inc., P. Wiland Grant/research support from: Celltrion, Inc., S. Jeka Grant/research support from: Celltrion, Inc., J. Chavez-Corrales Grant/research support from: Celltrion, Inc., T. Linde Grant/research support from: Celltrion, Inc., P. Hrycaj Grant/research support from: Celltrion, Inc., I. Hospodarskyy Grant/research support from: Celltrion, Inc., M. Abello-Banfi Grant/research support from: Celltrion, Inc., J. Jaworski Grant/research support from: Celltrion, Inc., M. Piotrowski Grant/research support from: Celltrion, Inc., W. Park Consultant for: Celltrion, Inc., S. C. Shim Consultant for: Celltrion, Inc., S. J. Lee Employee of: Celltrion, Inc., S. Y. Lee Employee of: Celltrion, Inc., D. H. Yoo Consultant for: Celltrion, Inc.

DOI: 10.1136/annrheumdis-2017-eular.6553

SAT0147 SERUM LEVELS OF THE ANTI-TNF BIOLOGICS CORRELATE WITH CLINICAL EFFICACY IN PATIENTS WITH INFLAMMATORY ARTHRITIS

C.C. Mok[1], B. Fong[1], L.Y. Ho[1], C.H. To[2]. [1]*Medicine, Tuen Mun Hospital;* [2]*Medicine, Pok Oi Hospital, HK, Hong Kong*

Objectives: To study the correlation between levels of the anti-TNF biologics and clinical efficacy in patients with inflammatory arthritis

Methods: Adult patients who fulfilled the criteria for rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PSA) and were commenced on standard doses of the anti-TNF biologics were recruited. Serum samples saved at baseline, month 6 and 12 were assayed for the trough levels of the biologics (± anti-drug antibodies) retrospectively. Patients were followed longitudinally and efficacy analyses were conducted at 3-month intervals without the knowledge of the drug levels. Biologics would be discontinued from 6 months onwards according to protocol-based improvement criteria for each disease. Clinical efficacy of the anti-TNF biologics was compared among patients with different levels of the drug by statistical methods.

Results: 112 patients were studied (58 RA, age 51.2±10.9 years, disease duration 72.9±67 months; 41 SpA, age 39.1±9.9 years, disease duration 74.3±81.6 months; 13 PSA, age 53.5±10.7 years, disease duration 44.3±35.4 years). The number of patients treated with infliximab (IFX), adalimumab (ADM), golimumab (GLM) and etanercept was 3, 31, 36 and 42, respectively. At month 12, neutralizing antibodies against IFX, ADM and GLM were present in 2 (67%), 14 (45%) and 1 (3%) of the patients, respectively. In ADM users, the drug level was significantly lower in those with antibodies than those without (1.81±2.63 vs 8.02±4.14 ug/ml; $p<0.001$). Antibody titer against ADM correlated negatively with the levels of ADM (Rho -0.72; $p<0.001$). Patients were stratified arbitrarily into 3 groups for each biologic according to the trough levels of the drugs. Low drug concentrations were defined as levels $\leq$1.30 ug/ml, 0.05 ug/ml and 0.60 ug/ml in ADM, ETN and GLM users, respectively. In patients with RA/PSA (N=71), patients with the lowest anti-TNF drug level group (N=30) had a non-significant trend of less improvement in DAS28, CDAI scores at month 12 when compared to others (N=41). However, significantly more patients withdrew treatment due to inefficacy at month 12 in this group compared to others (67% vs 7.3%, $p<0.001$). In patients with SpA (N=41), patients with lowest anti-TNF drug levels stratum (N=9) had significantly less improvement in ASDAS compared with others at month 12 (N=32) (-0.57±0.63 vs -1.93±1.28; p=0.003). The proportion of patients who achieved an ASAS20 response was also significantly lower in this group of patients (33% vs 75%; p=0.04). In all the 112 patients studied, the cumulative withdrawal rate of the anti-TNF biologics at month 12 (by Kaplan-Meier's analysis) was significantly higher in those with low drug levels when compared to others (26.1% vs 54.6%; $p<0.001$ by log rank test).

Conclusions: The presence of neutralizing antibodies to the anti-TNF monoclonals is associated with lower trough levels of the drugs. Trough level of the anti-TNF biologics is useful for optimizing the clinical efficacy of the drugs in patients with inflammatory arthritis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5681

SAT0148 RABBIT RISK SCORE FOR SERIOUS INFECTIONS IN A ROMANIAN COHORT OF RHEUMATOID ATHRITIS TREATED WITH BIOLOGICS

C. Ancuta[1,2], C. Pomirleanu[1,2], R. Maxim[2], L. Petrariu[2], G. Strugariu[2], E. Ancuta[3], R. Chirieac[4]. [1]*University of Medicine and Pharmacy Grigore T Popa Iasi;* [2]*Rheumatology 2, Clinical Rehabilitation Hospital;* [3]*Research Dept., Elena Doamna Clinical Hospital;* [4]*Sanocare Medical & Research Center, IASI, Romania*

Background: The risk of infections, especially severe infections (SI), remains of particular interest in rheumatoid arthritis (RA), both defective immune response and therapeutic immunosuppression being responsible.

The RABBIT Risk Score (RRS), an instrument developed and validated for RA in the German Biologics Register RABBIT and replicated in other RA settings (British Register), allows the estimation of SI occurring during 12 months according to patient characteristics, based on data from similar risk profiles.

Objectives: To evaluate the RSS reliability in a Romanian RA cohort under different biologics, considering the agreement between observed and expected rates of SI at 12 months.

Methods: Longitudinal study on 272 consecutive RA with moderate-to-severe active disease, starting their biologic according to local guidelines, enrolled between 2008 and 2016 in a single academic center.

Along with disease activity and therapeutic response, baseline RRS (http://www.biologika-register.de/en/home/risk-score/) was applied for each case, based on multiple risk factors for infections including age, functional status, chronic lung and renal comorbidities, previous SI, number of treatment failures, current biologic (TNF or non-TNF inhibitors), mean corticosteroid dose.

The predictive value of RRS was considered by comparing the number and rate of expected versus reported SI in the first year of biologics (ROC curve, $p<0.05$), assessing the number of adverse events per year and per 100 patient-years, cases with at least one infection.

Statistical analysis (univariate, multivariate) was stratified according to different predictors of infection, patients being classified in two groups based on their recruitment before (2008–2012) and after (2013 up to date) implementation of national biologic register RRBR.

Results: The performance of RSS was previously established in a pilot study on 181 RA. Currently, the RSS was considered in 144 RA recruited to the first group and 128 to the second. The prescription pattern significantly changed ($p<0.05$) for patients enrolled in last years: RA were more likely to receive earlier bDMARD, for lower activity and functional status; moreover, lower corticosteroids (dose, duration) and fewer synthetic DMARDs before starting biologics were reported ($p<0.05$).

24.63% RA developed SI (a total of 67 episodes, 1.47% fatal outcomes). Irrespective of RA settings and scenarios, history of biologics, specific drug administered (TNF or non-TNF), RRS indicated an outstanding agreement between the observed and expected SI rates ($p>0.05$).

In addition, the rate of SI was lower in RA recruited after 2013 ($p<0.05$), while RRS has better predictive significance in the second cohort ($p<0.05$).

Conclusions: The RABBIT Risk Score is a consistent tool, able to predict serious infections in Romanian RA receiving biological therapy (TNF and non-TNF drugs), optimizing the selection of appropriate medication based of individual infectious risk profile in routine practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2774

SAT0149 COMPARATIVE EFFECTIVENESS OF TOFACITINIB, BIOLOGIC DRUGS AND TRADITIONAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS

C.S. Moura[1], M.A. Machado[1], H. Behlouli[1], J.R. Curtis[2], M. Abrahamowicz[1], S. Bernatsky[1]. [1]*Division of Clinical Epidemiology, McGill University, Montreal, Canada;* [2]*Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, United States*

Background: Most rheumatoid arthritis (RA) patients initiate therapy with methotrexate (MTX), but only 1/3 will have low disease activity with this agent alone. Several therapeutic options are available for patients with MTX-resistant RA, including new Janus kinase (JAK) inhibitors (eg.: tofacitinib).

Objectives: To compare the effectiveness of traditional disease-modifying antirheumatic drugs (DMARDs), biologic DMARDs and tofacitinib for RA patients with inadequate response to MTX.

Methods: We used MarketScan® databases (2011–2014) to study adult RA individuals previously treated with methotrexate (oral or SQ) and newly prescribed one of the medications under study. The date of first filled prescription or infusion drug was defined as the cohort entry and a 12-month pre-period was used to exclude prior users of biologics or tofacitinib. We required subjects to be continuously enrolled in the medical and pharmacy plan 12 months before and after the cohort entry. Effectiveness was access through an algorithm previously validated[1], based on the following criteria: 1) non-adherence; 2) switching/adding a new biologic or tofacitinib; 3) switching/adding a new DMARD; 4) increasing of the dose of the starting therapy; 5) use of glucocorticoid joint injections; and 6) increasing the dose of oral glucocorticoid. A patient's therapy was defined as not effective if at least one of the criterion occurred during the first year of follow-up.

Results: 16,305 RA patients were included; 2,879 began therapy with DMARD, 13,345 with biologics and 81 with tofacitinib. Among all patients, 77.5% were female and the mean age was 56.2 years (standard deviation 12.6). Table 1 shows the proportion of patients that meet the individual criterion and that achieved effectiveness at the end of one-year follow-up.

Conclusions: Similar rates of therapy effectiveness were observed among groups, although the rates for the individual criteria differed. Fewer patients initiating biologic agents were non-adherent compared to DMARD and tofacitinib therapy, but switch/adding and injections tended to be higher in this group.

Table 1. Proportion and 95% confidence interval (CI) of patients who achieved therapy effectiveness and the individual criteria

Effectiveness criteria	DMARD		Biologics		Tofacitinib	
	%	95% CI	%	95% CI	%	95% CI
Non-adherence	75.1	73.5; 76.7	54.5	53.6; 55.3	69.1	59.1; 79.2
Switch/add biologic or tofacitinib	16.1	14.8; 17.5	34.6	33.8; 35.4	18.5	10.1; 27.0
Switch/add DMARD	13.0	11.7; 14.2	16.6	16.0; 17.3	16.0	8.1; 24.0
Increase in dose or frequency	8.6	7.6;9.7	6.9	6.5; 7.3	0	0
Glucocorticoid joint injection	7.8	6.9; 8.9	14.0	13.4; 14.6	9.6	3.4; 16.4
Increase in dose of oral glucocorticoid	19.0	17.6;20.5	17.6	17.0;18.2	22.2	13.2;31.3
Effective therapy (none of the criteria)	15.5	14.2; 16.8	17.9	17.2; 18.5	14.8	7.1; 22.6

References:
[1] Curtis JR et al. Derivation and preliminary validation of an administrative claims-based algorithm for the effectiveness of medications for rheumatoid arthritis. Arthritis Res Ther. 2011;13(5).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4992

SAT0150 PROSPECTIVE, INTERVENTION, MULTICENTER STUDY OF UTILITY OF BIOLOGIC DRUG MONITORING WITH RESPECT TO THE EFFICACY AND COST OF ADALIMUMAB TAPERING IN PATIENTS WITH RHEUMATIC DISEASES: PRELIMINARY RESULTS OF INGEBIO STUDY

E. Ucar[1], Í. Gorostiza[2], C. Gómez[1], C.E. Pérez[1], J.R. De Dios[3], B. Alvárez[3], A. Ruibal[3], C. Stoye[3], M. Vasques[3], J. Belzunegui[4], A. Escobar[2], Z. Trancho[2], A. Ruiz del Agua[5], A. Martínez[5], C. Jorquera[2], D. Nagore[5]. *[1]Rheumatology; [2]Research Unit, Basurto University Hospital, Bilbao; [3]Rheumatology, Hospital Univeristario Araba, Vitoria; [4]Rheumatology, Donostia University Hospital, San Sebastian; [5]R&D, Progenika-Grifols, Derio, Spain*

Background: Adalimumab (ADL) tapering based on clinical assessment is a usual practice especially in patients who have achieved clinical remission.
Objectives: To analyze how personalized management guided by biological drug monitoring (BDM) in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) patients impacts the annual direct costs to the Health System and the quality-adjusted life year with respect to conventional practice in Spain. To evaluate the effectiveness of BDM in the reduction of the number of days with high disease activity compared with conventional practice.
Methods: In a pragmatic, non-randomized, non-inferiority clinical study, adult patients treated with ADL (40 mg sc) who remained clinically stable for at least 6 months were recruited in 3 sites. Patients were grouped in Control (CG) and Intervention groups (IG) according to the site. ADL frequency was adjusted based on physician criteria. Patients are assessed at 8 timepoints (8 visits) for up to 18 months. Trough ADL and anti-ADL antibodies levels are measured with Promonitor-ADL and Promonitor-ANTI-ADL (Progenika, SA). BDM data were released only to the IG, and blinded to the CG (managed according to clinical assessment only). Physicians in the IG were not obliged to follow any therapeutic algorithm based on BDM results but could use tests to alter doses based on their judgement. Endpoints include DAS28, BASDAI, BASFI and HAQ-DI scores at every timepoint. Cost-effectiveness will be evaluated according to associated costs and QALY.
Results: A total of 169 patients were recruited (disease, N IG, N CG, %) (RA, 30, 33, 37.3%; PsA, 33, 21, 32%; and AS, 46, 6, 30.8%). Median disease duration was 117, 98.5 and 101.5 months for RA, PsA and AS, respectively. At baseline, 10 (16.7%) and 29 (26.6%) patients had low disease activity, 50 (83.3%) and 80 (73.4%) patients were in remission, and median trough ADL levels were 5,5 and 5,3 mg/L in the CG and IG, respectively. Mean follow-up (FU) was 505 and 499 days in the CG and IG, respectively. ADL doses were tapered in 22/60 (36,7%) and 39/109 (35,8%) patients in the CG and IG, respectively. Patients were in remission an average of 329 vs 344 days in the CG and IG, respectively. The number of flares in the CG and IG was 53 and 69, respectively. The rate of flares per patient-year of FU is 0,639 vs 0,463 in the CG and IG, respectively (difference of -0,176; CI95%: -0,379 to 0,0289). The risk of flare is 27,5% lower in the IG (IRR=0,7252; CI95%: 0,4997 to 1,0578). Quality of life (EQ-5D-5L) was significantly better in the IG at visits 2 (p=0,001) and 3 (p=0,035); EQ-5D-5L was higher (although not statistically significant) in the IG in the remaining visits. Average cost of ADL per patient-year was 11.898,60€ vs 11.240,81€ (-657.78€) in the CG and IG, respectively.
Conclusions: Preliminary results show that rheumatic patients have better quality of life, lower risk of flares and incur in lower treatment costs if patient management is complemented with BDM data.
Disclosure of Interest: E. Ucar: None declared, Í. Gorostiza: None declared, C. Gómez: None declared, C. Pérez: None declared, J. De Dios: None declared, B. Alvárez: None declared, A. Ruibal: None declared, C. Stoye: None declared, M. Vasques: None declared, J. Belzunegui: None declared, A. Escobar: None declared, Z. Trancho: None declared, A. Ruiz del Agua Employee of: Employee of Progenika Grifols, A. Martínez Employee of: Employee of Progenika Grifols, C. Jorquera: None declared, D. Nagore Employee of: Employee of Progenika Grifols
DOI: 10.1136/annrheumdis-2017-eular.4785

SAT0151 EFFICACY AND SAFETY OF BIOLOGIC THERAPY IN ELDERLY RHEUMATOID ARTHRITIS PATIENTS COMPARED TO YOUNG - A SYSTEMATIC REVIEW

D. Dalal[1], J. Duran[2], T. Brar[1], R. Alqadi[3], C. Halladay[4], A. Lakhani[1], J. Rudolph[4]. *[1]Medicine, Brown University School of Medicine, Providence, United States; [2]Medicine, Pontificia UniversidadCatolica de Chile, Santiago, Chile; [3]Medicine, Roger William Medical Center; [4]Medicine, VA Medical Center, Providence, United States*

Background: Rheumatoid arthritis (RA) patients are disproportionately older (33% >60 years). With improved biologic therapy for RA, there is a need to understand the efficacy and safety of biologic therapies in older RA (oRA) patients.
Objectives: To systematically review published literature to summarize the available evidence of efficacy and safety of biologic agents in oRA compared to young RA (yRA) patients.
Methods: A search in EMBASE, MedLine, Toxline, clinicaltrials.gov and Cochrane database was performed to identify clinical trials (RCT) and observational (OBS) studies of >6 months comparing the efficacy and safety of biologic agents in oRA relative to yRA. The biologics of interest were all anti-TNF agents, abatacept (ABA), tocilizumab (TCZ), rituximab (RTX) and tofacitinib (TOF). English language studies conducted in adult RA that reported age-associated outcomes were included. Studies assessing juveniles, inflammatory arthritis or not reporting older age outcomes were excluded. Safety outcomes included infections, adverse drug reactions (ADR), and malignancy. 2 independent rheumatologists reviewed abstracts, full text articles, and abstracted data from included articles. Conflicts were resolved by a 3rd reviewer. Abstracted data was summarized and evaluated for use within a meta-analysis
Results: Of 5353 abstracts, 187 were identified for full text review and 32 articles were included in this review. Articles were focused on efficacy (n=9), safety (n=15), or both (n=8). Most articles (n=22; 69%) focused on anti-TNF agents, then TCZ (n=4), ABA (n=2), TOF (n=2), RTX (n=1) and all biologics (n=1). Most studies were OBS studies (n=28, 88%) and fewer (n=4) were post-hoc analyses of RCT. In total, 99947 unique patients were identified, of which ~24% were older. Most studies used valid definitions of RA and outcomes; only 25% of the studies have <20% loss to follow up. There was heterogeneity in reporting outcomes and time of follow up.
Out of the 12 efficacy studies focusing on anti-TNF agents, 9 (75%) showed a reduced efficacy in oRA on DAS28, HAQ, CDAI, SDAI, EULAR or ACR response scales relative to yRA. Studies focusing on TCZ (n=2) and RTX (n=1) also showed a reduced efficacy in oRA. OBS studies in ABA (n=2) showed comparable efficacy in oRA and yRA. Meta-analysis was limited by heterogeneity.
Safety was the focus of anti-TNF (n=15), TCZ (n=3), 2 on TOF (n=2), 1 on ABA (n=1), RTX and all biologics (n=1) studies. Among these 23 safety studies, 74% (n=17) demonstrated worse safety outcomes in oRA. like in oRA. Of studies focusing on infection in anti-TNF agents, 82% (9 of 11) reported increased risk in oRA. Among the anti-TNF studies, 2 out of the 4 (50%) measured more ADR in oRA. A meta analysis of 4 studies reporting infectious outcomes in anti-TNF agents at >1 year found a pooled risk estimate was 1.59 (95% CI 1.45–1.76).

Figure 1: Forest plot of studies of anti-TNF agents measuring risk ratio of efficacy on EULAR or DAS28 response scale

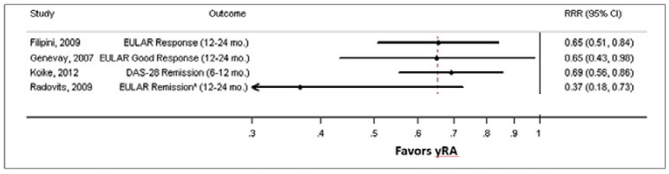
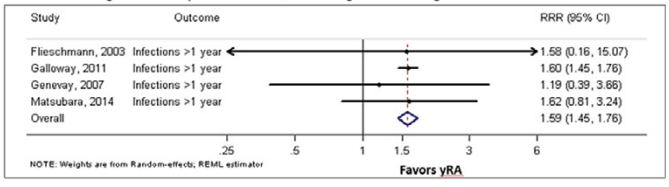


Figure 2: Forest plot of studies of anti-TNF agents measuring risk ratio of infections



Conclusions: There is heterogeneity within the literature of biological agents in RA, particularly when age is considered. Given the anticipated population increase in the oRA, there is an urgent need for analysis of these medications in oRA patients for both safety and efficacy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1493

SAT0152 REAL-LIFE INFLIXIMAB AND ADALIMUMAB TROUGH LEVEL AND ANTI-DRUG ANTIBODY MEASUREMENTS IN RHEUMATOLOGY: THE FINNISH EXPERIENCE

D. Ho[1], S. Valtanen[2], M. Havana[2], L. Kröger[3], K. Eklund[4], S. Jokiranta[1,2].
[1]Research Programs Unit, Immunobiology, University of Helsinki; [2]United Medix Laboratories Ltd, Helsinki; [3]Pediatric Rheumatology, Kuopio University Hospital, Kuopio; [4]Rheumatology, Helsinki University and Helsinki University Hospital, Helsinki, Finland

Background: Therapeutic drug monitoring of TNF inhibitors (TNFi) may optimize clinical benefits while at the same time reducing financial costs and risk of adverse events[1,2]. Monitoring the TNFi trough levels (TLs) and the anti-drug antibodies (ADAbs) can provide relevant information to make rational adjustments to therapy if indicated.
Objectives: To identify distributions and trends in infliximab (IFX) and adalimumab (ADL) TLs and ADAbs from clinically requested, real-life samples from Finnish patients with rheumatoid arthritis (RA), spondyloarthropathies (SpA), or juvenile idiopathic arthritis (JIA).
Methods: Samples for TL and ADAbs were taken on a clinical basis in daily practice from four university hospitals and 15 central hospitals in Finland and sent for analysis to United Medix Laboratories. Samples were collected and analyzed from January 2012 to February 2016. TL measurements were performed by enzyme-linked immunosorbent assay (either at Sanquin laboratories, Amsterdam, The Netherlands, or in Helsinki, Finland using Promonitor ELISA, Progenika Biopharma). TLs from 2–10 μg/ml (IFX) or 5–10 μg/ml (ADL) were considered as general target ranges. ADAb measurements were performed by radioimmunoassay (Sanquin). 1762 TL (1241 patients), 1598 ADAb (1203 patients), and 860 combined TL and ADAb samples (718 patients) were analyzed. Statistical analyses were performed by SPSS (IBM, Armonk, NY). $p<0.05$ was considered statistically significant.
Results: The highest proportions of samples with very low TLs (<0.1 μg/ml) were seen in IFX-treated RA patients (14.5%) and ADL-treated SpA patients (12.6%). The proportion of all samples in the general target range was 51.3% (IFX) and 33.4% (ADL). A greater proportion of ADL RA and SpA samples had possibly supratherapeutic (>10 μg/ml) TLs (RA: ADL, 22.9% vs IFX, 10.4%, $p<0.01$ and SpA: ADL, 21.4% vs IFX, 15.0%, p=0.05). A greater proportion of ADL JIA samples had TLs >10 μg/ml (ADL, 54.5% vs IFX, 36.3%, $p<0.01$). Proportions of samples with ADAbs (>12 AU/ml) ranged from 18.0% (IFX RA) to 28.6% (ADL SpA). A greater proportion of ADL samples with TLs of 2–5 μg/ml and detectable ADAbs (>12 AU/ml) (RA: ADL, 3.3% vs IFX, 0%; SpA: ADL, 5.6% vs IFX, 0%; JIA: ADL, 3.4% vs IFX, 0.9%) was observed.
Conclusions: IFX RA and ADL SpA samples had the highest proportions of very low TLs. Compared to IFX, greater proportions of ADL samples (all indications, particularly JIA) had TLs >10μg/ml. Proportions of samples with ADAbs >12 AU/ml ranged from 18.0% to 28.6%. Compared to IFX, a greater proportion of ADL samples with possibly therapeutic TLs had detectable ADAbs.
References:
[1] Bendtzen K. Anti-TNF-alpha biotherapies: perspectives for evidence-based personalized medicine. Immunotherapy 2012;4:1167–1179.
[2] Laine J, Jokiranta TS, Eklund KK, Väkeväinen M, Puolakka K. Cost-effectiveness of routine measuring of serum drug concentrations and anti-drug antibodies in treatment of rheumatoid arthritis patients with TNF-α blockers. Biologics 2016;10:67–73.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5943

SAT0153 EFFECTIVENESS OF LOW AND HIGH DOSE METHOTREXATE IN COMBINATION WITH ADALIMUMAB IN A REAL WORLD SETTING: RESULTS FROM THE CORRONA RHEUMATOID ARTHRITIS REGISTRY

D. Pappas[1,2], J. Griffith[3], C.A. Schlacher[3], Y. Shan[2], C. Karki[2], J.M. Kremer[4].
[1]Columbia University, New York; [2]Corrona, LLC, Southborough; [3]AbbVie, Inc., Abbott Park; [4]Albany School of Medicine, Albany, United States

Background: Combination therapy of methotrexate (MTX) with biologics results in superior outcomes vs. monotherapy. Recent clinical trials have shown that lower MTX doses may be sufficient in patients with rheumatoid arthritis (RA) to achieve similar clinical and patient reported outcomes (PROs)[1,2].
Objectives: To evaluate whether high MTX dose in combination with adalimumab (ADA) results in improved clinical and PROs compared with low MTX dose.
Methods: Adult RA subjects naïve to other monoclonal antibodies, initiating standard dose ADA (40mg q2w) in combination with oral MTX (low dose: ≤12.5 mgs and high dose: ≥15 mgs) during 2003–2016 and had a 6 month follow-up visit were included. The primary outcomes were mean change in clinical disease activity index (CDAI), and PROs (mHAQ, pain, fatigue, morning stiffness) from baseline to 6 months. Secondary outcomes included achievement of remission (CDAI≤2.8)/low disease activity (CDAI≤10). Outcomes were evaluated adjusting for covariates that differed at baseline using mixed model linear regression. Persistency of ADA between the two groups was examined using Kaplan-Meier survival analysis.
Results: A total of 519 patients were included: N=101 and N=418 initiated ADA with low and high dose MTX respectively. Patients on high dose MTX were significantly younger (53.3 vs 59.7 years), with lower disease duration of RA (8.8 vs 11.2 years) compared to low dose MTX group. Patients in the high dose group also had higher disease activity (mean CDAI: 20.8 vs 15.4) and more likely to be biologic-naïve (71.3% vs 55.4%), compared to the low dose group (all $p<0.05$). Unadjusted and adjusted analyses found no sufficient evidence that patients on high dose MTX had a better improvement in the outcomes selected (table). Persistency of ADA did not differ between the two groups.

Table: Outcomes at 6 months among ADA plus low (≤12 mg) vs. high dose (≥15 mg) combination MTX therapy

	ADA + ≤12.5 mg (low dose)	ADA + ≥15 mg (high dose)	Unadjusted†	Adjusted†*
6 month outcomes	**Mean (SD)**	**Mean (SD)**	**β (95% CI)**	**β (95% CI)**
Change in CDAI	-5.1 (13.1)	-8.0 (14.2)	-2.65 (-5.68, 0.38)	2.70 (0.27, 5.12)
Change in mHAQ	-0.04 (0.30)	-0.09 (0.43)	-0.05 (-0.14, 0.04)	0.03 (-0.06, 0.13)
Change in pain	-3.3 (26.9)	-9.0 (28.1)	-5.59 (-11.65, 0.46)	2.25 (-3.21, 7.72)
Change in fatigue	1.8 (23.3)	-3 (27.6)	-4.81 (-12.54, 2.92)	-1.99 (-9.96, 5.98)
	Response rate n (%)	**Response rate n (%)**	**Odds Ratio† (95% CI)**	**Odds Ratio†* (95% CI)**
Achievement of Remission (CDAI≤2.8)	7 (11.7%)	47 (15.1%)	1.17 (0.47, 2.88)	0.92 (0.36, 2.4)
Achievement of LDA (CDAI≤10)	28 (46.7%)	135 (43.3%)	0.841 (0.47, 1.49)	0.63 (0.31, 1.26)

mHAQ: modified Health Assessment Questionnaire; LDA: Low Disease Activity; † Compared with low dose MTX group as a reference; *Adjusted for age, duration of RA, work status, insurance status, prior biologic count, MTX continuation, baseline CDAI and patient pain.

Conclusions: In this real world study, improvements in PROs and achievement of LDA/remission at 6 months were similar in the groups initiating ADA in combination with either low dose or high dose MTX.
References:
[1] Gurjit S. et al. doi:10.3899/jrheum.151009.
[2] Gerd-Rudiger Burmester. et al. doi:10.1136/annrheumdis-2013–204769.
Acknowledgements: This study is sponsored by Corrona, LLC. Corrona, LLC has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB. The design, study conduct, and financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.
Disclosure of Interest: D. Pappas Grant/research support from: AbbVie, Inc, Consultant for: AbbVie, Inc, Employee of: Corrona, LLC, J. Griffith Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc, C. Schlacher Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc, Y. Shan Employee of: Corrona, LLC, C. Karki Employee of: Corrona, LLC, J. Kremer Shareholder of: Corrona, LLC, Grant/research support from: AbbVie, Genentech, Lilly, Novartis, Pfizer, Consultant for: AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, Employee of: Corrona, LLC
DOI: 10.1136/annrheumdis-2017-eular.1525

SAT0154 EFFECTIVENESS AND SAFETY OF CT-P13 IN PATIENTS WITH RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS, PSORIATIC ARTHRITIS AND PLAQUE PSORIASIS: OBSERVATIONAL STUDY IN REPUBLIC OF KOREA

D.-W. Kim[1], T.-H. Kim[2], S.R. Kwon[3], E.Y. Lee[4], C.-N. Son[5], Y.S. Kim[6], S.H. Kim[7], Y.-B. Park[8], J.-W. Hur[9], H.-S. Lee[10], S.J. Lee[11], S.H. Lee[11]. *[1]Inje University Busan Paik Hospital, Busan; [2]Hanyang University Hospital for Rheumatic Diseases, Seoul; [3]Inha University Hospital, Incheon; [4]Seoul National University College of Medicine, Seoul; [5]Keimyung University Dongsan Medical Center, Daegu; [6]Chosun University Hospital, Gwangju; [7]Gwangmyeong Saeum Hospital, Gyeonggi-do; [8]Yonsei University Severance Hospital; [9]Eulji University Seoul Hospital, Seoul; [10]Hanyang University Guri Hospital, Gyeonggi-do; [11]Celltrion, Inc., Incheon, Korea, Republic Of*

Background: CT-P13 is approved as a biosimilar of innovator infliximab for marketing in 79 countries around the world. After approval, observational study has been conducted in Republic of Korea in patients with Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA) and Plaque Psoriasis (PS).
Objectives: To evaluate the effectiveness and safety of CT-P13 under routine care in Republic of Korea.
Methods: This observational study included both biologic naïve patients (Naïve group) and patients who switched from other anti-tumor necrosis factor (TNF)s to CT-P13 (Switch group). Effectiveness were evaluated based on remission (DAS28≤2.6 in RA, BASDAI<3 in AS and absence of swollen and tender joint counts in PsA), and response (BASDAI 20/50/70 in AS and PASI 50/75 in PS). Adverse events (AEs) were collected over 6 month period.
Results: Total 940 patients (400 with RA, 531 with AS, 3 with PsA and 6 with PS) were registered and 338 (36.0%) patients (108 with RA, 228 with AS, 2 with PS) who switched to CT-P13 were included.
The proportion of patients achieving remission was similar between Naïve and Switch groups in both RA and AS during post-baseline visits (Table 1). In RA, the proportion of patients achieving each disease activity category by DAS28 was similar between Naïve and Switch groups (Figure 1). The proportion of patients

who achieved BASDAI 20/50/70 response gradually increased from week 6 to week 24 or 30 in Naïve group with AS (Figure 1).
Fifty percent of naïve patients with PsA achieved clinical remission. The proportions of both PASI 50 and 75 responses were 50% at Week 22 in Naïve group and were 100% and 50% in Switch group, respectively during post-baseline visits in PS patients.
Throughout this study, treatment-emergent adverse events (TEAE) and treatment-emergent serious adverse events (TESAE) were reported as Table 2. Only 11% of patients experienced infection.

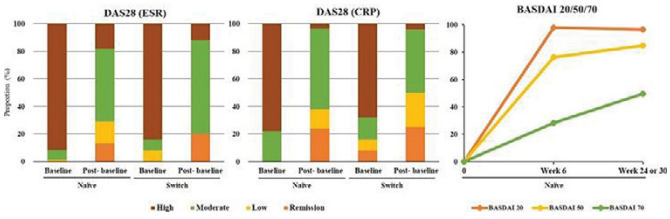
Table 1. Clinical remission in RA and AS

		Naïve		Switch	
		Baseline	Post-baseline	Baseline	Post-baseline
RA	DAS28 (ESR)	0/181 (0.0%)	24/182 (13.1%)	0/25 (0.0%)	5/25 (20.0%)
	DAS28 (CRP)	0/180 (0.0%)	43/179 (24.0%)	2/25 (8.0%)	6/24 (25.0%)
AS	BASDAI	2/292 (0.7%)	199/292 (68.2%)	112/209 (53.6%)	150/210 (71.4%)

Table 2. Summary of safety results

n/N (%)	RA	AS	PsA	PS
TEAE	198/400 (49.5)	183/531 (34.5)	1/3 (33.3)	3/6 (50.0)
TEAE related with CT-P13	73/400 (18.3)	64/531 (12.1)	0/3 (0.0)	2/6 (33.3)
TESAE	52/400 (13.0)	14/531 (2.6)	0/3 (0.0)	1/6 (16.7)
TESAE related with CT-P13	15/400 (3.8)	6/531 (1.1)	0/3 (0.0)	0/6 (0.0)
Infusion-related reactions	28/400 (7.0)	11/531 (2.1)	0/3 (0.0)	0/6 (0.0)

Figure 1. Clinical response of RA and AS



Conclusions: CT-P13 is efficacious and well-tolerated in RA/AS/PsA/PS patients. Efficacy and safety results in patients treated with CT-P13 were clinically consistent to historical data [1,2,3]. Especially, Switch group results showed that CT-P13 provides a useful alternative to other anti-TNFs.
References:
[1] Kobayashi et al (2016).
[2] Hetland et al (2005).
[3] Hetland et al (2010).
Disclosure of Interest: D.-W. Kim: None declared, T.-H. Kim: None declared, S. R. Kwon: None declared, E. Y. Lee: None declared, C.-N. Son: None declared, Y. S. Kim: None declared, S. H. Kim: None declared, Y.-B. Park: None declared, J.-W. Hur: None declared, H.-S. Lee: None declared, S. J. Lee Employee of: CELLTRION,Inc., S. H. Lee Employee of: CELLTRION,Inc.
DOI: 10.1136/annrheumdis-2017-eular.1597

SAT0155 ADALIMUMAB IN COMBINATION WITH NON-METHOTREXATE CONVENTIONAL SYNTHETIC DISEASE MODIFYING RHEUMATIC DRUGS IN A CLINICAL TRIAL SETTING

E.C. Keystone[1], J. Suboticki[2], J. Griffith[2], Y. Zhang[2], J.M. Kremer[3]. *[1]Mount Sinai Hospital, University of Toronto, Toronto, Canada; [2]AbbVie, Inc., North Chicago; [3]Albany School of Medicine, Albany, United States*

Background: Biologics in combination with methotrexate (MTX) are associated with improved outcomes versus monotherapy. However, few data exist regarding the use of non-MTX conventional synthetic disease modifying rheumatic drugs (csDMARDs) with biologics.
Objectives: To assess the effectiveness and safety of adalimumab (ADA) in combination with MTX and non-MTX csDMARDs through 6 months.
Methods: This post hoc analysis used data from the 24-week (wk) placebo-controlled trial of ADA (STAR), assessing safety and efficacy of ADA+csDMARDs in patients (pts) with moderate to severe RA.[1] For those pts receiving 1 csDMARD, pts were subgrouped according to csDMARD. The most frequently used csDMARDs assessed were MTX, sulfasalazine (SSZ), hydroxychloroquine (HCQ), and leflunomide (LEF). Nineteen pts who received parenteral gold in combination with ADA were excluded from this analysis. Baseline demographics and disease characteristics were summarized across csDMARD groups. 20/50/70% improvement in American College of Rheumatology (ACR) response criteria were assessed for each subgroup. Other clinical and functional endpoints were assessed using ANCOVA within subgroups as the least square (LS) means of the mean change from baseline to wk 24. Adverse events (AEs) were monitored throughout.
Results: Of the 290 pts randomized to receive ADA, 237 (82%) received ≥1 csDMARD [174 (60%) and 63 (22%) received ADA in combination with 1 and ≥2 csDMARDs, respectively]. Of the 63 pts who received ≥2 csDMARDs in combination with ADA, 55 (87%) received concomitant MTX therapy. Similarly, most of the pts receiving ADA in combination with a single csDMARD received MTX [114 (66%)], while 60 pts received ADA in combination with a single non-MTX csDMARD. Pts receiving non-MTX csDMARDs were slightly younger, on average, than those receiving MTX (mean age: 51.4 vs 56.4 years), but demonstrated slightly higher mean HAQ-DI (1.37 vs 1.26) and CRP (2.4 vs 1.3) at baseline. Following 6 months of combination therapy, pts receiving ADA+MTX experienced numerically better clinical and functional outcomes to pts receiving ADA+non-MTX csDMARDs (Table). The lower response in the non-MTX DMARD group appeared to be driven by pts receiving LEF, who tended to experience lower levels of response in combination with ADA. Overall, frequencies of AEs were similar between combination therapy with MTX and non-MTX csDMARDs (~90% in both groups). Serious AEs were observed in 10% of pts receiving non-MTX csDMARDs and 5% of pts receiving MTX. A total of 42% in the non-MTX csDMARD and 60% in the MTX group experienced infections during the course of the study. There were 3 serious infections, all occurring in the MTX group.

Table. Week 24 Clinical and Functional Outcomes Among Patients Receiving Adalimumab in Combination With a Single csDMARD

		ADA+non-MTX csDMARD n=60			
Variable	ADA+MTX n=114	Pooled n=60	LEF n=25	SSZ n=12	HCQ n=23
ACR20	69 (61)	27 (45)	8 (32)	7 (58)	12 (52)
ACR 50	40 (35)	14 (23)	3 (12)	4 (33)	7 (30)
ACR70	22 (19)	7 (12)	0 (0)	3 (25)	4 (17)
DAS28(CRP)	-1.912[a]	-1.923[b]	-1.516[c]	-1.979[d]	-2.206[e]
SDAI	-22.60[a]	-22.21[b]	-18.41[c]	-23.80[d]	-24.61[e]
CDAI	-21.90[f]	-20.95[g]	-18.05[c]	-23.79[d]	-22.02[h]
HAQ-DI	-0.509[f]	-0.435[i]	-0.251[e]	-0.595[d]	-0.524[h]

Discrete variables are summarized as n (%).
All continuous variables are within group LS means in mean change from baseline to week 24 using ANCOVA, with csDMARD subgroup as a factor and baseline value as covariate, with the exception of the pooled group, which is mean change from baseline.
[a]n=105; [b]n=52; [c]n=20; [d]n=11; [e]n=21 ; [f]n=106; [g]n=53; [h]n=22; [i]n=54.
csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; ADA, adalimumab; MTX, methotrexate; LEF, leflunomide; SSZ, sulfasalazine; HCQ, hydroxychloroquine; ACR, American College of Rheumatology; DAS28(CRP), 28-joint disease activity score based on C-reactive protein; SDAI, simplified disease activity index; CDAI, composite disease activity index; HAQ-DI, health assessment questionnaire disability index.

Conclusions: MTX administered in combination with biologics, like ADA, leads to superior outcomes vs monotherapy. For pts who can't tolerate MTX, non-MTX csDMARDs, specifically HCQ and SSZ but not LEF, may be good alternatives, as outcomes were largely comparable with those of pts receiving MTX when combined with ADA. The limited sample size examined in this analysis should be confirmed in a larger pt population.
References:
[1] Furst DE, et al. J Rheum 2003;30(12):2563–71.
Acknowledgements: AbbVie: study sponsor, contributed to design, data collection, analysis, interpretation, and abstract writing, review, and approval. Medical writing: Ben Wolfe of AbbVie.
Disclosure of Interest: E. Keystone Grant/research support from: AbbVie, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Centocor, F Hoffmann-LaRoche, Genentech, Genzyme, Merck, Novartis, Nycomed, Pfizer, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Centocor, F Hoffmann-LaRoche, Genentech, Genzyme, Merck, Novartis, Nycomed, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Biotest, Bristol-Myers Squibb, Centocor, F Hoffmann-LaRoche, Genentech, Genzyme, Merck, Novartis, Nycomed, Pfizer, UCB, J. Suboticki Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., J. Griffith Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., Y. Zhang Shareholder of: AbbVie, Inc., Employee of: AbbVie, Inc., J. Kremer Shareholder of: Corrona, LLC, Consultant for: AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, Employee of: Corrona, LLC
DOI: 10.1136/annrheumdis-2017-eular.2736

SAT0156 EXPOSITION TO BIOLOGICAL THERAPY DURING PREGNANCY: A SINGLE-CENTRE STUDY OF PREGNANCY OUTCOME IN MOTHERS WITH RHEUMATIC DISEASES

E. De Stefani[1], M. Padovan[1], A. Bortoluzzi[1], R. Capucci[2], M. Govoni[1]. *[1]Department of Medical Sciences, Section of Rheumatology, University of Ferrara and Azienda Ospedaliero-Universitaria di Ferrara; [2]Department of Obstetrics and Gynecology, Azienda Ospedaliero Universitaria S.Anna, Ferrara, Italy*

Background: Biologic DMARDs fall within the FDA category B or C. However many case series and registry data are available about women exposed during pregnancy.
Objectives: to extend information on this topic by the contribution of a tertiary single centre case series
Methods: Data were collected from a single-centre cohort of outpatients followed between 2006 and 2016. Women with rheumatic diseases (RD) exposed to biological (BE) agent during pregnancy or in the 3 months before conception were included. Outcomes in the BE group were compared with an age-matched group of pregnant women with RD non-exposed to biological agent (NE). Demographic and clinical data,obstetric outcome and neonatal complications were recorded.
Results: 34 pregnancies in 28 patients were included: 14 Rheumatoid Arthritis (RA), 6 ankylosing spondylitis (AS), 2 Psoriatic arthritis (PsA), 4 Undifferentiated spondyloarthritis (uSpA), 1 Dermatomyositis (DM), 1 Adult Onset Still's disease

(AOSD); all were exposed to a biologic agent: 16 Etanercept (ETA), 7 Adalimumab (ADA), 4 Infliximab (IFX), 1 Certolizumab (CTZ), 5 Rituximab (RTX), 1 Anakinra (ANK). Median age was 34 yrs (range 24–50). All patients treated with TNFi and ANK withdrew therapy in early pregnancy (<10 weeks gestational age). 2 RA patients had 2 pregnancies each, during ETA treatment. A RA woman became pregnant 4 times during RTX therapy. 10 patients were also on csDMARDs therapy at the time of conceptions: 7 Hydroxycloroquine (HCQ),1 HCQ + Sulphasalazine (SSZ), 1 Cyclosporine A (CYA), which was continued, and 1 with Methotrexate which was immediately withdrawn. 1 RA patient started SSZ from the 24th week. 15 patients (7 RA, 2 PsA, 2 AS, 2 uSpA, 1 DM) started or increased oral and/or intra-articular steroids because of disease flare. A control group of 45 pregnancies observed in 42 patients not exposed to biologics was selected="selected" (19 RA, 12 uSpA, 3 Juvenile Idiopatic Arthritis (JIA), 5 PsA, 1 AS, 1 DM, 1 AOSD), median age 35 (range 22–42). 18 patients were treated with csDMARDs during pregnancy (8 HCQ; 4 SSZ; 2 CYA+HCQ; 4 SSZ+HCQ). No other drugs were taken at the time of conception, apart from low dose of steroids in 24 cases; in 1 case intra-articular steroids were given because of disease flare.

Pregnancy outcomes are summarized in tab.1: therapeutic abortions were performed for an extrauterine pregnancy occurred twice in the patient with RA who became pregnant 4 times during RTX treatment, after the 5th and the 6th retreatment. After the 4th retreatment she had an early spontaneous abortion. Previously, she delivered 2 healthy children after exposure to ETA and 3 treatment cycles of RTX. No serious perinatal complication occurred, excluding very preterm baby delivery at 28th weeks, who needed neonatal intensive care. No congenital malformations were observed. Klinefelter syndrome was diagnosed in 1 case.

Tab. 1: Pregnancy outcomes of women with RD exposed to biological (BE) compared with pregnant women with RD non-exposed to biological agent (NE).

	BE group (34)	NE group (45)	p
Live births	29 (85,3%)	43 (95,5%)	ns
Spontaneous abortion	2 (5,9%)	2 (4,4%)	ns
Therapeutic abortion	2 (5,9%)	0	ns
Voluntary interruption of pregnancy	1 (2,9%)	0	ns
Pre-term delivery	5 (14,7%)	6 (13,3%)	ns
Preterm rupture of membrane	3 (8,8%)	4 (8,9%)	ns
Intra-uterine growth restriction	1 (2,9%)	1 (2,2%)	ns
Average birth weight	2875 g (720-4234)	3140 (1880-4200)	ns
Low birth weight (<2500 g)	6 (17,6%)	5 (11,1%)	ns

Conclusions: In our case series no significant differences did occur in pregnancy outcome between BE and NE group, according to the most recent data published in literature. Additional data from larger numbers of pregnacy exposed to biological agents are required.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4929

SAT0157 MYCOBACTERIUM TUBERCULOSIS SPECIFIC RESPONSES FROM CD8+ AND CD4+ T CELLS IN PATIENTS WITH LATENT AND ACTIVE FORM OF TUBERCULOSIS

E. Zanova[1], D. Kozakova[1], M. Polanova[2], I. Solovic[2], I. Rybar[3]. *[1]National Institute of Rheumatic Diseases, Piešťany; [2]National Institute of Tuberculosis, Pulmonary Diseases and Thorax Surgery, Vysne Hagy; [3]Slovak Health University, Bratislava, Slovakia*

Background: Testing the presence of latent or active tuberculosis using IGRA tests is necessary part of the diagnostic screening at risk individuals. QuantiFERON-TB Gold Plus (QFT-Plus) is a test for cell-mediated immune (CMI) responses to peptide antigens that simulate mycobacterial proteins. Peptide antigens in TB1 tube elicit CMI responses from CD4+ T-helper lymphocytes, in TB2 tube from CD8+ T-cytotoxic lymphocytes. Test is based on the ability of effector T lymphocytes to produce the cytokine interferon gamma (IFN-γ).

Objectives: To compare and evaluate levels of IFN-γ produced by CD4+ and CD8+ cells in TB1 and TB2 tubes.

Methods: It was studied 33 subjects with latent form of tuberculosis (LTBI) and 33 subjects with active TB. QFT-Plus was used to detect in vitro responses to peptide antigens associated with *Mycobacterium tuberculosis* infection (ELISA, QIAGEN). Results were obtained by calculation of INF-γ levels in Mitogen, TB antigen (TB1, TB2) and Negative control tubes using QFT analysis software.

Results: QFT-Plus positive results were observed in both groups of people. Increased levels of IFN-γ produced by CD4+ cells (TB1) has been detected in 21 subjects with LTBI (63,64%) and in all 33 subjects with active TB (100,0%). Increased levels of IFN-γ produced by CD8+ cells (TB2) has been detected in 27 people with LTBI (81,82%) and in all 33 people with active TB (100,0%). Joint increase levels of IFN-γ in the tubes TB1 and TB2 was observed in 16 individuals with LTBI (48,48%) and in all 33 individuals with active TB (100,0%). In the group of patients with a negative QFT-Plus it was not observed increased levels of IFN in tubes TB1 and TB2.

Conclusions: Our findings confirm specific CD4+ and CD8+ T cell response to mycobacterial protein antigens in individuals with LTBI and also in active TB subjects, in which INF-γ was frequently found. The immunological response represented by CD4+ and CD8+ T cells was not detected in subjects with QFT-Plus negative.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5611

SAT0158 EFFICACY OF SWITCHING FROM ETANERCEPT TO ADALIMUMAB IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS PATIENTS WHO EXPERIENCED A FIRST-LINE BIOLOGIC THERAPY FAILURE: THE FEARLESS STUDY

E.G. Favalli[1], A. Becciolini[1], A. Carletto[2], F. Conti[3], G. Amato[4], E. Fusaro[5], L. Quartuccio[6], A. Lo Monaco[7], M. Benucci[8], F. Salaffi[9], A. Semeraro[10], M. Biggioggero[11], S. Parisi[5], F. Ceccarelli[3], I. Piazza[2], R. Foti[4]. *[1]Department of Rheumatology, Gaetano Pini Institute, Milano; [2]Rheumatology Unit, AOUI, Verona; [3]Dipartimento di Medicina Interna e Specialità Mediche, Reumatologia, Sapienza Università di Roma, Roma; [4]Rheumatology Unit, A.O.U. Policlinico Vittorio Emanuele, Catania; [5]Rheumatology, Azienda Ospedaliera Universitaria Città della Salute e della Scienza, Torino; [6]Clinica di reumatologia, Dipartimento di scienze mediche e biologiche, ASUIUD, Udine; [7]UOC di Reumatologia, Azienda Ospedaliero-Universitaria Sant'Anna Cona-Ferrara, Ferrara; [8]SOS Reumatologia, Ospedale S. Giovanni di Dio, Firenze; [9]Clinica Reumatologica, Università Politecnica delle Marche, Ancona; [10]U.O.Reumatologia, ASL Taranto-PP.OO.SS. Annunziata Taranto e Valle d'Itria, Taranto; [11]Department of Clinical Sciences and Community Health, Division of Rheumatology, University of Milan and Gaetano Pini Institute, Milano, Italy*

Background: The strategy for the choice of the second biologic agent after the failure of the first TNF inhibitor (TNFi) is still an unclear aspect in the treatment of both rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Switching between structurally different TNFis (from etanercept [ETN] to monoclonal antibody [mAb] or vice versa) has been proposed as a more effective procedure than switching among different mAbs, but to date no study has been specifically focused on exploring this topic.

Objectives: To evaluate the comparative 2-year retention rate and the 12-month efficacy of adalimumab (ADA) as second biologic agent in etanercept (ETN) non-responder RA and PsA patients in a multicentre retrospective study.

Methods: All RA and PsA patients from 11 Italian Rheumatology Units treated with ADA after a first-course ETN failure and with at least 12-month follow-up were retrospectively collected in a multicentre registry. Data analysis was limited to the period from January 2002 to May 2016. Two-year ADA retention rate was calculated by Kaplan-Meier method. 12-month ADA response was defined as achievement of disease activity score 28 calculated by using erythrosedimentation (DAS28-ESR) <2.6 (remission) or >2.6 and <3.2 (low disease activity, LDA). Sub-analyses according to reason for ETN discontinuation and concomitant methotrexate in RA and PsA patients have been performed.

Results: The study population (219 patients) included 117 RA (female 85.5%, mean [± standard deviation, SD] age 53.2±13.5 years, mean [±SD] disease duration 10.1±7.7; positive rheumatoid factor 70.2%; positive anti-citrullinated peptide antibodies [ACPA] 59.6%; mean [±SD] baseline DAS28-ESR 4.97±1.3; MTX users 64.9%) and 102 PsA (female 63.7%; mean [±SD] age 51.7±10.6; mean [±SD] disease duration 7.1±5.1; mean [±SD] baseline DAS28-ESR 4.4±1.1; MTX users 50%). The 2-year retention rate was 48.2% in RA and 56.5% in PsA patients, irrespective of reason for ETN discontinuation. Similarly, concomitant MTX was not associated with an increased drug survival in both RA (p=0.09) and PsA (p=0.969) subgroup. 12-month clinical remission and LDA were achieved respectively in 27.3% and 23.9% RA patients, and 27.4% and 23.5% PsA patients.

Conclusions: In our large real-life cohort, the use of ADA in primary and secondary ETN failures was highly effective in both RA and PsA patients, with more than 50% of ADA treated patients achieving remission or LDA. Reasons for ETN discontinuation were not associated with different ADA clinical response, as well as concomitant MTX.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3747

SAT0159 IMPACT OF PARTICIPATION IN THE ADALIMUMAB PATIENT SUPPORT PROGRAM ON FUNCTIONAL AND CLINICAL OUTCOMES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: PASSION STUDY

F. Van den Bosch[1], A. Ostor[2], S. Wassenberg[3], J.K. Anderson[4], N. Chen[4], C. Wang[4], V. Garg[4], J. Kalabic[5]. *[1]Ghent University Hospital, Ghent, Belgium; [2]Addenbrooke's Hospital, Cambridge, United Kingdom; [3]Rheumazentrum, Ratingen, Germany; [4]AbbVie Inc., North Chicago, United States; [5]AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany*

Background: Patients (pt) with Rheumatoid arthritis (RA) who are treated with adalimumab (ADA) are offered a Patient Support Program (PSP) with variety of services. To date, no prospective study has been conducted to analyze the acceptance and the impact of these PSPs on treatment effectiveness and pt satisfaction.

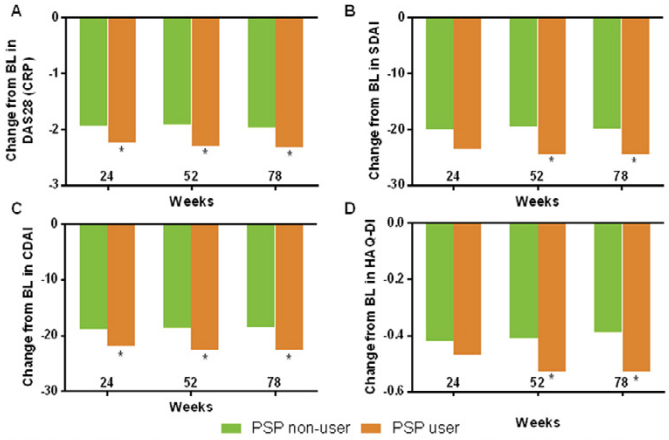
Objectives: The purpose of this study was to examine the effectiveness of ADA on rheumatoid arthritis (RA) treatment course in the context of PSP participation.

Methods: PASSION (NCT01383421) was a 78-week (wk) post-marketing observational study of pts with RA receiving ADA in routine clinical care. Pts from the EU, Israel, Mexico, Puerto Rico, and Australia with an insufficient response to ≥1 disease-modifying antirheumatic drug (DMARD) newly initiating ADA (1 prior

biologic DMARD was allowed) were enrolled. The primary endpoint was the % of pts achieving the minimal clinically important difference (MCID; improvement of ≥0.22 compared to baseline [BL]) in the Health Assessment Questionnaire Disability Index (HAQ-DI) at wk 78. Non-responder imputation (NRI) was used to account for the missing values. Secondary clinical parameters included % of pts achieving MCID in HAQ-DI at wks 24 and 52 and changes in the 28-joint DAS based on CRP (DAS28(CRP)), Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI) at wks 24, 52, and 78 vs BL. Pts were categorized based on their participation in the PSP: ever (PSP users) vs never (PSP non-users) and outcomes were compared after adjusting for corresponding BL values.

Results: Overall, the primary endpoint, percentage of pts achieving the MCID for HAQ-DI, was achieved by 72.1% (as observed) and 42.8% (NRI) of pts at week 78 with the percentage of pts achieving the MCID for HAQ-DI significantly higher in PSP users vs PSP non-users (48.1% vs 37.8% [NRI]; $P<0.001$). From 1,025 pts, 48.7% pts were PSP users (BL: mean age, 54.3 years (y); % female, 77.1%; mean RA duration, 7.8 y; mean HAQ-DI, 1.5; mean DAS28(CRP), 5.3; mean SDAI, 35.6; mean CDAI, 33.3; 17.8% pts had received prior biologic DMARD. Significant changes ($P\leq0.05$) from BL to wk 78 were observed for pts using the PSP vs PSP non-users in HAQ-DI (0.53 vs 0.39), DAS28(CRP) (−2.33 vs −1.97), SDAI (−24.5 vs −19.8), and CDAI (−22.66 vs −18.55) scores (Figure). Study discontinuation rates were significantly ($P<0.001$) lower among PSP-users vs PSP non- users (25.5% vs 41.6%). Reasons for discontinuations are listed in the Table.

Figure: Changes from baseline in DAS28 (CRP) (A), SDAI (B), CDAI (C), and HAQ-DI (D) over time between PSP users and PSP non-users.



*significantly different between PSP users and PSP non-users ($P<0.05$). Data represented by LOCF imputation for intent-to-treat population. Results are adjusted for BL DAS28(CRP), SDAI, CDAI, and HAQ-DI. LOCF=Last Observation Carried Forward

Table: All reasons for study discontinuation by PSP utilization category

Subject Disposition	All Patients N=1025	PSP user N=499	PSP non-user N=526
Discontinued (%)* **	**346 (33.8)**	**127 (25.5)**	**219 (41.9)**
Adverse event	52 (5.1)	22 (4.4)	30 (5.7)
Withdrew consent	37 (3.6)	13 (2.6)	24 (4.6)
Lost to follow-up	46 (4.5)	17 (3.4)	29 (5.5)
Serious adverse events	24 (2.3)	10 (2.0)	14 (2.7)
Lack of efficacy	168 (16.4)	66 (13.2)	102 (19.4)
Other	51 (5.0)	16 (3.2)	35 (6.7)

***Statistically significant at $P<0.001$

Conclusions: The final study results showed that, in pts with moderate to severe RA who initiated ADA, significantly better improvement in functional and clinical outcomes was achieved in the PSP users vs the PSP non-users. Improvements were achieved at early timepoints and continued to increase throughout the study.

Acknowledgements: AbbVie funded the study and the analysis, and approved the abstract for submission. Medical writing assistance was provided by Gaurav Patki, PhD and Benjamin Wolfe, PhD from AbbVie.

Disclosure of Interest: F. Van den Bosch Consultant for: AbbVie, Celgene, Janssen, Pfizer, and UCB, Speakers bureau: AbbVie, Celgene, Janssen, Pfizer, and UCB, A. Ostor Consultant for: Roche, Chugai, MSD, AbbVie, Pfizer, Novartis, Napp, and BMS, S. Wassenberg Consultant for: AbbVie, Celgene, Novartis, Pfizer, MSD, Lilly, Janssen and UCB, Speakers bureau: AbbVie, Celgene, Novartis, Pfizer, MSD, Lilly, Janssen and UCB, J. K. Anderson Shareholder of: AbbVie, Employee of: AbbVie, N. Chen Shareholder of: AbbVie, Employee of: AbbVie, C. Wang Shareholder of: AbbVie, Employee of: AbbVie, V. Garg Shareholder of: AbbVie, Employee of: AbbVie, J. Kalabic Shareholder of: AbbVie, Employee of: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.1876

SAT0160 IMMUNOGENICITY OF BIOSIMILARS FOR THE TREATMENT OF INFLAMMATORY RHEUMATIC DISEASES: A REVIEW FROM CONFIRMATORY CLINICAL TRIALS

F. Araújo [1,2], J. Gonçalves [3], J.E. Fonseca [4,5]. *[1] Rheumatology, Hospital de Sant'Ana, SCML, Cascais; [2] Institute of Microbiology, Faculdade de Medicina da Universidade de Lisboa, Lisboa; [3] iMed-Research Institute of Medicines, Faculdade de Farmácia da Universidade de Lisboa; [4] Rheumatology, Hospital de Santa Maria, Lisbon Academic Medical Centre, Lisbon; [5] Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal*

Background: The assessment of immunogenicity is mandatory during the comparability exercise of biosimilar candidate drugs, as even small structural differences can potentially elicit antidrug antibodies (ADA) and affect efficacy and safety.

Objectives: To review the incidence of ADA and neutralizing ADA (nADA) in confirmatory clinical trials of biosimilar drugs approved for the treatment of inflammatory rheumatic conditions in the European and North-American markets; to review the type of assays used for this purpose; to compare the incidence of ADA with historical data from reference biotechnological drugs.

Methods: We performed a literature search in the Medline database and hand searched EULAR and ACR meeting abstracts to identify phase I and III confirmatory clinical trials of biosimilar drugs for the treatment of rheumatic conditions approved in the European and North-American markets. Open-label extensions involving biological switch were not included. All outcomes regarding immunogenicity were extracted (ADA, nADA and type of immunogenicity assays).

Results: We screened 255 articles by title and abstract and 7 publications fulfilled our inclusion criteria. Three meeting abstracts were also included. Six studies assessed infliximab biosimilars (CT-P13 and SB2), three studies assessed etanercept biosimilars (SB4 and GP2015) and one study assessed an adalimumab biosimilar (ABP 501). All but two concerned phase III trials and seven were performed on rheumatoid arthritis patients. All biosimilars had comparable immunogenicity profiles in respect to their reference drugs, except for the etanercept biosimilar SB4, which presented significantly less ADA when compared to reference etanercept (0.7% vs 13.1% at 24 weeks and 1.0% vs 13.2% at 52 weeks, $p<0.001$ for both). As expected, infliximab had the highest incidence of ADA; the proportion of ADA in studies of infliximab and adalimumab was higher when compared to historical data. Only 4 studies reported nADA, which were highest in the infliximab biosimilar CT-P13 54-week study in ankylosing spondylitis patients. Electrochemiluminescence immunoassay was the preferred method to measure ADA. Table 1 summarizes the main findings in the included studies.

Table 1. Immunogenicity of biosimilars approved for the treatment of inflammatory rheumatic diseases. ADA: antidrug antibody, NA: not available, nADA: neutralizing antidrug antibody. *The EGALITY study presented a four-arm design in which two arms were continuously treated with either reference etanercept or GP2015 and the other two arms were systematically switched. The results presented in this table concern the groups continuously treated with reference etanercept or GP2015

Study population		Reference drug ADA (%)	Reference drug nADA (%)	Biosimilar ADA	Biosimilar nADA (%)	ADA/nADA assay
Rheumatoid arthritis	**CT-P13 (infliximab)**					
	Yoo 2013 (PLANETRA, 30 w)	48.2	NA	48.4	NA	Electrochemiluminescence immunoassay/NA
	Yoo 2016 (PLANETRA, 54 w)	36.0	NA	41.1	NA	Electrochemiluminescence immunoassay/ flow-through immunoassay
	SB2 (infliximab)					
	Choe 2015 (30 w)	49.7	NA	55.1	NA	Electrochemiluminescence immunoassay/ competitive ligand-binding assay
	Choe 2015 (54 w)	57.5	NA	62.4	NA	NA
	SB4 (etanercept)					
	Emery 2015 (24 w)	13.1	3	0.7	0	Electrochemiluminescence immunoassay/ competitive ligand-binding assay
	Vencovsky 2015 (52 w)	13.2	NA	1.0	NA	NA
	ABP 501 (adalimumab)					
	Cohen 2015 (24 w)	38.2	11.1	38.3	9.1	NA
Ankylosing spondylitis	**CT-P13 (infliximab)**					
	Park 2013 (PLANETAS, 30 w)	22.5	NA	27.4	NA	Electrochemiluminescence immunoassay/NA
	Park 2016 (PLANETAS, 54 w)	23.0	100	19.5	100	Electrochemiluminescence immunoassay/ flow-through immunoassay
Psoriasis	**GP2015 (etanercept)**					
	Griffiths 2016 (EGALITY, 52 w)*	1.9	0	0	0	Electrochemiluminescence immunoassay/ competitive ligand-binding assay

Conclusions: Currently approved biosimilars for the treatment of rheumatic diseases have comparable immunogenicity profiles in respect to their reference drugs. The discrepancy in ADA between SB4 and reference etanercept did not correlate with efficacy or safety and did not preclude biosimilarity, according to the regulatory agencies. The higher proportion of ADA compared to historical data may be explained by the greater sensitivity of current immunogenicity assays, such as electrochemiluminescence.

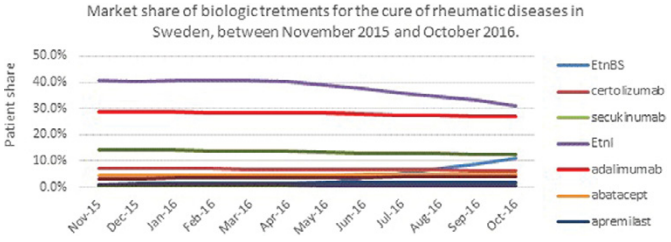
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2486

SAT0161 PRELIMINARY REAL WORLD DATA ON SWITCHING PATTERNS BETWEEN ETANERCEPT, ITS RECENTLY MARKETED BIOSIMILAR COUNTERPART AND ITS COMPETITOR ADALIMUMAB, USING SWEDISH PRESCRIPTION REGISTRY

R. Alten[1], P. Neregård[2], H. Jones[3], E. Singh[3], C. Curiale[4], T. Meng[5], L. Lucchese[6], C. Miglio[6], J. Young[7], G.J. Bergman[7]. [1]*Schlosspark-Klinik, Berlin, Germany;* [2]*Pfizer, Stockholm, Sweden;* [3]*Pfizer, Collegeville, United States;* [4]*Pfizer, Rome, Italy;* [5]*Pfizer, Berlin, Germany;* [6]*QuintilesIMS, London, United Kingdom;* [7]*QuintilesIMS, Solna, Sweden*

Background: The increasing availability of biologic treatments over the past 10 years has revolutionized the management of chronic inflammatory autoimmune diseases such as rheumatic diseases. In April 2016, the first etanercept biosimilar (EtnBS) was launched in Sweden, which may represent a cheaper option to its innovator counterpart and other anti-TNF agents.
Objectives: The objective of this study was to describe the position of etanercept innovator (EtnI) within the Swedish biologic market for rheumatic diseases, before and after the launch of its biosimilar. The study also provides early real-world data on the market penetration of EtnBS by evaluating switching dynamics to and from this drug since the date of launch.
Methods: The overall biologic market share across all type of rheumatic diseases was monthly tracked over the last year of available data in the Swedish Prescription Registry (100% coverage). The proportion of patients receiving a rheumatologists' prescription for any biologic in each month, from November 2015 to October 2016, was recorded. In addition, switching dynamics of patients initiating EtnBS treatment between April 2016 and October 2016 were studied. The proportion of patients receiving no biologic treatment (naïve) and of those on treatment with EtnI, adalimumab and other biologic agents in the 12 months prior to initiate EtnBS was reported. Further, the proportion of patients who switched from EtnBS back to EtnI or adalimumab and the mean time to this second switch were also evaluated.
Results: EtnI and adalimumab dominate the biologic market for rheumatic diseases in Sweden, holding the 40% and 28% of market share, respectively, up to April 2016. However, in the 6 months after EtnBS was launched, the share of EtnI decreased constantly, dropping to 31% in October 2016 (Figure 1). Since April 2016, we identified in total 2,439 patients receiving first prescription of EtnBS by a rheumatologist. Of these, 977 (40.1%) were naïve to biologic, 1,179 (48.3%) had prior treatment with EtnI, 107 (4.4%) with adalimumab, 176 (7.2%) with other biologics. Among the patients who changed to EtnBS from prior EtnI, the 7% switched back to EtnI after an average time of 43 days. Similarly, of those who were on previous adalimumab treatment, 6% switched back to adalimumab after, on average, 57 days.



Conclusions: Many patients changed from EtnI to its biosimilar treatment since its launch in Sweden. However, this study showed that 7% of these patients switch back to their original treatment after short time. Despite the change from a brand biologic to the biosimilar is very likely made for economic reasons, the reasons for switching back to the innovator are not clear and may imply patients' preference or clinical reasons. Interestingly, the same pattern is observed for patients changing from adalimumab to EtnBS. Longer-term studies are required to confirm these early observations and investigate the reasons for switching back.
Disclosure of Interest: R. Alten Grant/research support from: The study was sponsored by Pfizer, P. Neregård Employee of: Pfizer, H. Jones Employee of: Pfizer, E. Singh Employee of: Pfizer, C. Curiale Employee of: Pfizer, T. Meng Employee of: Pfizer, L. Lucchese Grant/research support from: The study was sponsored by Pfizer, C. Miglio Grant/research support from: The study was sponsored by Pfizer, J. Young Grant/research support from: The study was sponsored by Pfizer, G. J. Bergman Grant/research support from: The study was sponsored by Pfizer
DOI: 10.1136/annrheumdis-2017-eular.3585

SAT0162 SWITCHING FROM ETANERCEPT TO CHS-0214: A ONE YEAR, RANDOMIZED, DOUBLE-BLIND STUDY IN PATIENTS WITH RHEUMATOID ARTHRITIS

J. O'Dell[1], A. Kivitz[2], T. Takeuchi[3], Y. Tanaka[4], I. Louw[5], T. Tiabut[6], S. Nakashima[7], J. Hodge[8], H. Tang[8], B. Finck[8] on behalf of The RApsody Study Group. [1]*University of Nebraska Medical Center, Omaha, NE;* [2]*Altoona Center for Clinical Research, Duncansville, PA, United States;* [3]*Keio University School of Medicine, Tokyo;* [4]*School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan;*[5]*Panorama Medical Center, Cape Town, South Africa;* [6]*City Clinical Hospital No. 1 of Minsk, Minsk, Belarus;* [7]*Daiichi-Sankyo, Tokyo, Japan;* [8]*Coherus BioSciences, Redwood City, United States*

Background: CHS-0214 is in development as a proposed biosimilar of etanercept for the treatment of rheumatoid arthritis (RA) and other auto-immune diseases.
Objectives: Equivalence of CHS-0214 to etanercept was demonstrated at 24 weeks in a global confirmatory, safety and efficacy study in patients with RA. This update provides efficacy results at 48 weeks and safety results over 52 weeks (or over 48 weeks for subjects who continued to the open-label safety extension study).
Methods: Patients had moderate/severe RA and an inadequate response to methotrexate (MTX). Patients were randomized to CHS-0214 or etanercept (commercial European-sourced) at 50 mg SC QW for 24 weeks (Part 1). Patients achieving ACR20 at Week 24 with no safety concerns then received CHS-0214 50 mg SC QW open-label for 24 weeks (Part 2). Patients continued their stable dose of MTX throughout the study.
Results: At Week 24, the response rates were 91.0% vs. 90.6% for ACR20, 67.6% vs. 63.7% for ACR50, and 38.3% vs. 37.9% for ACR70, in the CHS-0214 group (n=256) vs. etanercept group (n=256), respectively. At Week 48, the response rates were 93.8% vs. 92.7% for ACR20, 75.0% vs. 73.6% for ACR50, and 49.6% vs. 51.4% for ACR70, in patients who received CHS-0214 for 48 weeks (n=224) vs. patients who received etanercept for 24 weeks and then switched to CHS-0214 for 24 weeks (n=220), respectively. Thus, response rates were maintained both in patients who were switched at Week 24 from etanercept to CHS-0214 and in patients who received CHS-0214 for 48 weeks.
Over the 52-week study, adverse events (AE) were reported in 74.4% of patients who received CHS-0214 for 48 weeks and 76.6% who received etanercept for 24 weeks and were switched to CHS-0214 for 24 weeks. The majority of adverse events were mild or moderate in severity. No deaths were reported. Serious AEs were reported in 4.6% and 7.5% of patients, and serious AEs related to study drug per the investigator were reported in 0.9% and 1.9% of patients in the CHS-0214 and etanercept/CHS-0214 groups. Binding anti-drug antibodies (ADA) occurred in 1.3% and 4.7% of patients receiving CHS-0214 and etanercept during Part 1. In Part 2, treatment-emergent binding ADA occurred in 1.4% of patients receiving CHS-0214 and 0.7% of patients who switched from etanercept to CHS-0214.
Conclusions: This randomized, double-blind, active-control, global study demonstrated equivalence of CHS-0214 to etanercept based on the primary endpoint (ACR20 at Week 24) and maintenance of the efficacy response through Week 48. CHS-0214 was well tolerated and effective in patients with rheumatoid arthritis with no clinically meaningful differences to etanercept with regard to safety and immunogenicity. Over the 52-week study, no clinically meaningful differences in safety, immunogenicity, or efficacy were observed in patients who were switched from etanercept to CHS-0214 in comparison with those who only received CHS-0214.
Disclosure of Interest: J. O'Dell Consultant for: Coherus BioSciences, A. Kivitz: None declared, T. Takeuchi Consultant for: AbbVie, Asahi Kasei Pharma, Astellas, Astra Zeneca, BMS, Celtrion, Chugai, Daiichi-Sankyo, Eisai, Eli-Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer, Sanofi-Aventis, Santen, Taisho Toyama, Takeda, Teijin Pharma, Y. Tanaka Consultant for: Abbvie, Astellas, BMS, Chugai, Daiichi-Sankyo, Eisai, GSK, Janssen, Mitsubishi-Tanabe, MSD, Novartis, Pfizer, Santen, Takeda, UCB, I. Louw: None declared, T. Tiabut Grant/research support from: Coherus BioSciences, S. Nakashima Employee of: Daiichi-Sankyo, J. Hodge Shareholder of: Coherus BioSciences, Employee of: Coherus BioSciences, H. Tang Shareholder of: Coherus BioSciences, Employee of: Coherus BioSciences, B. Finck Shareholder of: Coherus BioSciences, Employee of: Coherus BioSciences
DOI: 10.1136/annrheumdis-2017-eular.2480

SAT0163 SYSTEMATIC SWITCH FROM INNOVATOR INFLIXIMAB TO BIOSIMILAR INFLIXIMAB IN INFLAMMATORY RHEUMATIC DISEASES IN DAILY CLINICAL PRACTICE: THE EXPERIENCE OF COCHIN HOSPITAL, PARIS, FRANCE

J. Avouac[1], A. Molto[1], V. Abitbol[2], A. Salcion[1], L. Gutermann[3], O. Conort[3], F. Chast[3], C. Le Jeunne[4], C. Goulvestre[3], S. Chaussade[2], A. Kahan[1], C. Roux[1], Y. Allanore[1], M. Dougados[1]. [1]*Rheumatology;* [2]*Gastroenterology;* [3]*Paris Descartes University, Cochin Hospital, Paris, France;* [4]*Internal Medicine, Paris Descartes University, Cochin Hospital, Paris, France*

Background: Biosimilars of originator biologic therapeutics are going to change medical practices. In October 2015, the medical community of Cochin Hospital decided to systematically propose the switch from innovator infliximab to biosimilar infliximab to all treated patients.
Objectives: To investigate efficacy and safety of switching treatment from innovator infliximab to biosimilar infliximab.
Methods: This is a usual care study conducted in patients aged >18 years who agreed to switch to biosimilar infliximab, and who received at least 3 infusions of innovator infliximab prior to the switch.
The primary outcome of the study was the retention rate of biosimilar infliximab at the time of the third infusion. Secondary outcomes included the factors associated with biosimilar discontinuation, the change between baseline and the last visit (July 2016) in DAS28-CRP (rheumatoid arthritis, RA), BASDAI/ASDAS (axial

spondyloarthritis, axSPA) and infliximab trough levels, and the occurrence of adverse events.
Results: 260 patients fulfilled the inclusion criteria: 182 patients followed-up in Rheumatology (131 with axSPA, 31 with RA, and 20 with other inflammatory rheumatic diseases), 64 in Gastroenterology and 14 in Internal Medicine.
The retention rate at the time of the third biosimilar infusion was 82% (149/182 patients), which was lower than the rate observed in patients with inflammatory bowel diseases or uveitis followed-up in Gastroenterology and Internal Medicine, respectively (71/78 patients, 91%).
Between baseline and the last visit (mean follow-up: 34±4.5 weeks), 48/182 (26%) patients, including 36 patients with axSPA, discontinued biosimilar infliximab, mainly due to experienced inefficacy (n=47). No clinical or biological factors were associated with biosimilar discontinuation.
One infusion reaction led to treatment discontinuation. No serious adverse events occurred. 43 patients restarted innovator infliximab, 2 patients switched to etanercept, 1 to abatacept and 2 maintained biological-free.
In RA patients, the mean DAS28-CRP remained stable from baseline to the last visit: 3.38±1.16 to 3.08±1.08 (p=0.217). In axSpA patients, the mean BASDAI increased from 2.94±2.20 to 3.18±2.21 (p=0.046) and the mean ASDAS increased from 1.79±0.90 to 1.99±1.08 (p=0.022). In RA and axSPA, mean CRP levels at baseline (5.95±6.06 and 5.98±11.14 mg/l respectively) and the last visit (6.52±11.32 and 5.03±8.26 mg/l respectively) were not statistically different (p=0.289 and p=0.271, respectively).
Mean infliximab trough levels were similar in patients with RA (3.70±5.36 vs. 3.21±4.35 μg/ml, p=0.551) and AxSPA (5.88±5.82 vs. 5.70±5.42 μg/ml, p=0.617) during follow-up.
Conclusions: In the majority of patients, innovator infliximab can be switched to biosimilar infliximab without changes in efficacy and safety during 34 weeks follow-up. However, 26% of patients discontinued biosimilar infliximab, mainly those with AxSPA due to a subjective increase in BASDAI or ASDAS scores, possibly explained by suggestion or attribution effects rather than pharmacological differences.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3791

SAT0164 ASSOCIATION BETWEEN FLARE AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

J.S. Smolen[1], H. Jones[2], E. Mahgoub[2], R. Pedersen[2], L. Marshall[2]. *[1]Medical University of Vienna, Vienna, Austria; [2]Pfizer, Collegeville, United States*

Background: Biologic therapy has improved RA management, enabling some patients to achieve remission. Many clinicians decrease the biologic dose for patients in low disease activity (LDA) or remission. However, it is unclear which patients may flare and if flare contributes to radiographic progression.
Objectives: To assess whether patients who flared had a higher incidence of radiographic progression, and to compare patients with and without flares.
Methods: PRESERVE (ClinicalTrials.gov: NCT00565409) was a 2-period trial in patients with moderate RA despite MTX. Period 1 was open-label, single treatment induction with etanercept (ETN) 50mg+MTX weekly (QW) for 36 wks. Patients in LDA or remission (disease activity score for 28 joints [DAS28] $\leq$3.2) during wks 12 to 36 continued to Period 2, the randomized, double-blind phase to evaluate maintenance of LDA/remission. Patients were randomized to ETN 50mg+MTX QW, ETN 25mg+MTX QW, or placebo+MTX QW to wk 88. This post hoc analysis evaluated flare and radiographic progression at wk 88. Flare was defined 2 ways: 1) loss of LDA with/without DAS28 change of 0.6; and 2) relapse (DAS28$>$5.1 or DAS28$>$3.2 at $\geq$2 time points). Radiographic progression was evaluated according to 4 levels of stringency: 1) minimally clinically important difference (modified total Sharp score [mTSS] change $\geq$5); 2) smallest detectable difference (mTSS change $\geq$2.3); 3) mTSS change $\geq$0.5; and 4) mTSS change $>$0. Baseline (BL) characteristics were compared for patients with vs without flare, defined as loss of LDA and DAS28 change of 0.6. Analysis of covariance and chi-square test compared continuous and categorical outcomes, respectively.
Results: Age, race, BMI, and disease duration did not differ significantly for flare vs non-flare, total N=531. BL DAS28 was higher for flare vs non-flare: mean (SD) 4.37 (0.45) vs 4.27 (0.45), p=0.046. Other BL disease characteristics were similar between groups. With flare defined as relapse, significantly more flare than non-flare patients showed all 4 degrees of radiographic progression (table). With flare defined as LDA loss with/without DAS28 change of 0.6, radiographic progression did not differ significantly between groups, but numerically more patients with flare progressed. This was the trend for all treatments; the numbers were too small to analyze. Numerically more placebo patients progressed, regardless of flare status or progression category (data not shown).

Table. Radiographic progression at week 88

Outcome	Flare Patients	Non-flare Patients	P-value*
Flare defined as loss of LDA and DAS28 change of 0.6			
mTSS $>$0	43/271 (15.9)	31/260 (11.9)	0.2109
mTSS $\geq$0.5	38/271 (14.0)	24/260 (9.2)	0.1045
mTSS $\geq$2.3	20/271 (7.4)	10/260 (3.8)	0.0914
mTSS $\geq$5.0	9/271 (3.3)	2/260 (0.8)	0.0633
Flare defined as loss of LDA			
mTSS $>$0	44/280 (15.7)	30/251 (12.0)	0.2586
mTSS $\geq$0.5	39/280 (13.9)	23/251 (9.2)	0.1043
mTSS $\geq$2.3	20/280 (7.1)	10/251 (4.0)	0.1338
mTSS $\geq$5.0	9/280 (3.2)	2/251 (0.8)	0.0670
Flare defined as relapse			
mTSS $>$0	35/181 (19.3)	39/350 (11.1)	0.0119
mTSS $\geq$0.5	31/181 (17.1)	31/350 (8.9)	0.0065
mTSS $\geq$2.3	19/181 (10.5)	11/350 (3.1)	0.0011
mTSS $\geq$5.0	9/181 (5.0)	2/350 (0.6)	0.0015

*Fisher's exact test. Overall treatment group. Values are n/N (%).

Conclusions: Using relapse as a rigorous definition of flare, radiographic progression occurs in significantly more flare than non-flare patients, demonstrating that it is a consequence of flare following biologic withdrawal.
Disclosure of Interest: J. Smolen Grant/research support from: Abbvie, Janssen, Lilly, MSD, Pfizer, Roche, Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, Celgene, Celtrion, Glaxo, ILTOO, Janssen, Lilly, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, Speakers bureau: Abbvie, Amgen, Astra-Zeneca, Astro, Celgene, Celtrion, Glaxo, ILTOO, Janssen, Lilly, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, UCB, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, E. Mahgoub Shareholder of: Pfizer, Employee of: Pfizer, R. Pedersen Shareholder of: Pfizer, Employee of: Pfizer, L. Marshall Shareholder of: Pfizer, Employee of: Pfizer
DOI: 10.1136/annrheumdis-2017-eular.1854

SAT0165 REAL-WORLD UTILIZATION OF CONCOMITANT MEDICATIONS IN PATIENTS INITIATING ETANERCEPT: A RETROSPECTIVE COHORT STUDY OF CANADIAN CLAIMS-LEVEL DATA

M. Khraishi[1], Y. Zhang[2], J. Ivanovic[2], B. Millson[2], M.-J. Brabant[2], E. Singh[3], J. Woolcott[4], H. Jones[3]. *[1]Faculty of Medicine, Memorial University of Newfoundland, St. Johns; [2]Health Access & Outcomes, QuintilesIMS, Kanata, Canada; [3]Inflammation and Immunology, Global Medical Affairs, Pfizer Inc., Collegeville, United States; [4]Health Economics and Outcomes Research, Pfizer Inc., Kirkland, Canada*

Background: Methotrexate (MTX) and prednisone (pred) are immune suppressants frequently used to treat immune-mediated inflammatory diseases (IMIDs). Etanercept is a soluble TNF receptor (humanized protein) indicated for the treatment of IMIDs, including rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis (PsO), and ankylosing spondylitis (AS). Limited information exists on how MTX or pred use changes in patients who initiate etanercept in real-world settings.
Objectives: To evaluate whether initiation of etanercept impacts use of co-therapy with MTX or pred in Canadian patients with IMIDs.
Methods: A retrospective cohort study was conducted using claims-level data from QuintilesIMS Private Drug Plan database, Ontario Public Drug Plan database, and Quebec Public Drug Plan database. Bio-naïve patients initiating etanercept between 07/2013 and 06/2015, were identified and their claims made for MTX or pred were analyzed. Patients' utilization of MTX or pred was calculated as average weekly dose in mg, and then compared in the 6-months pre versus 12-months post initiation of etanercept using a paired t-test. Differences in the presence of concomitant medications pre and post-etanercept were also examined using a paired t-test.
Results: The study captured 3,745 etanercept patients (61% female, 77% aged between 18 and 65, 84% rheumatic diseases, and 15% PsO) across Canada in the selection period. Of selected patients, 33% used MTX (n=1,244) and 14% (n=523) used pred pre and post initiation of etanercept. In concomitant MTX patients, the average weekly dose dispensed was 25.2mg in the 6 months prior to initiation of etanercept, and 25.0mg in the 12 months following the first claim of etanercept (p=0.7493). In concomitant prednisone patients, the average weekly dose dispensed reduced from 123mg pre-etanercept to 108mg post-etanercept initiation (p=0.2316). 19% of patients stopped MTX (n=287) use post-etanercept initiation, compared to 36% who stopped pred use (n=289).
Conclusions: In this real-world setting, approximately 1/5 of patients stopped or reduced co-therapy of MTX; and 1/3 of patients stopped or reduced co-therapy of pred following initiation of etanercept; however, those patients who remained on co-therapy showed non-significant changes in their average consumption. Further research is needed to understand the impact on overall patient outcomes and safety.
Disclosure of Interest: M. Khraishi Consultant for: Pfizer Canada and Amgen Canada, Y. Zhang: None declared, J. Ivanovic: None declared, B. Millson: None declared, M.-J. Brabant: None declared, E. Singh: None declared, J. Woolcott: None declared, H. Jones: None declared
DOI: 10.1136/annrheumdis-2017-eular.6947

SAT0166 MARKERS OF RESPONSE TO INFLIXIMAB IN RHEUMATOID ARTHRITIS – THE PLACE OF ANTINUCLEAR ANTIBODY AND NUCLEASE SERUM ACTIVITY

M. Volkava[1], A. Kundzer[1], I. Generalov[2], D. Petrovich[1]. *[1]Cardiology and Rheumatology, BelMAPGE, Minsk; [2]Clinical Microbiology, VSMU, Vitebsk, Belarus*

Background: It is important to study new potential markers of response to treatment in rheumatoid arthritis (RA), because up to 40% patients don't achieve

remission even using biological therapy. DNAse activity of the blood serum and antinuclear antibody may be useful in this context. Changes of serum DNase activity in the RA treatment by biological agents previously have been not investigated.

Objectives: The aim of this work is to study the dynamics clinical and laboratory parameters, DNAse serum activity and ANA during the RA treatment by infliximab (INF) and assess the prognostic potential of them in prediction of response to INF.

Methods: 24 RA patients were involved in the study. All patients fulfilled the EULAR/ACR 2010 RA criteria. 22/24 patients received 6 infusions of INF at a dose of 3 mg/kg according to standard protocol: at 0th, 2th, 6th and then every 8 week. 2/24 patient received 4 infusions of INF. All patients received synthetic DMARDs therapy by metotrexate (10–17,5 mg weekly), 18/24 patients received glucocorticoids (methylprednisolone 4–8 mg daily) and non-steroidal anti-inflammatory drugs. Prior to treatment by INF patients did not receive any biological agents. All patients had high disease activity before INF treatment (DAS28<5,1).

ANA determination was performed by indirect immunofluorescence on Hep-2 cells using digital system AKLIDES. ANA was measured in serum samples before 1st INF administration, at 22–30 weeks after the 1st INF administration.

To determine the DNAse activity of serum the method of rivanol clot was used. DNase activity was measured in serum samples before 1st INF administration, at 6 weeks after the 1st INF administration, at 30 week of treatment.

Results: At week 30, ACR70 improvement reached 5/22 of the patients, ACR50 - 10/22 of the patients, ACR20 – 4/24 of patients.

At 30 weeks of treatment by INF 2/22 of patients achieved remission (SDAI<3,3), 10/22 - a low disease activity (3,3 <SDAI ≤11).

13/24 patients were ANA-positive before INF treatment, 12/22 - after 24 weeks of treatment.

Levels of serum DNase activity did not differ before and during the INF treatment (p>0,05).

For assessment prognostic value of laboratory signs for INF response prediction logistic regression was used. Prognostic model, which included changes in ANA (Δ ANA) and DNAse serum activity level (Δ DNAse serum activity), anti-CCP- and RF-negativity was better (p=0,02) (area under ROC-curve =1,0; 95% CI 0,844–1,00 p=0,0001) than the model, which included only anti-CCP- and RF-negativity (area under ROC-curve =0,795; 95% CI 0,597–0,924, p=0,0141).

Conclusions: The study confirmed the efficacy of RA treatment by INF for anti-CCP and RF negative patients. DNAse serum activity and ANA may be used as additional prognostic biomarker of INF response. For the assessment DNAse activity as marker of response to therapy is needed futher investigations with more number of patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6941

SAT0167 CAN INFLIXIMAB EFFICACY BE PREDICTED BASED ON BLOOD CONCENTRATION AT THE FOURTH DOSE?

M. Sato[1], M. Takemura[2], T. Tani[1], T. Ohashi[1]. *[1]Rheumatology, Ohashi and Tani Orthopedics, Gifu; [2]Advanced Diagnostic System Research Laboratory, Fujita Health University Graduate School of Health Sciences, Toyoake, Japan*

Background: Biological drugs exhibit excellent efficacy and continuity in the treatment of rheumatoid arthritis (RA) and play an important role in RA treatment. Blood concentration is an important factor in the efficacy of biological drugs, particularly antibody drugs. Infliximab (IFX) is an antibody drug against TNF-α and is reported to require a blood concentration of ≥1 μg/mL to be effective.

Objectives: To investigate whether clinical efficacy can be predicted based on blood concentrations at the fourth dose of IFX in patients with RA.

Methods: This study included 56 patients with RA who were treated with IFX. Patients included 13 men and 43 women aged from 26 to 81 years (mean, 60.3 years). The IFX concentration was measured immediately before administering the fourth IFX dose (8 weeks after administering the third dose). We then investigated the relationship between subsequent IFX efficacy and IFX concentration immediately before the fourth dose of IFX in these patients with RA. Concentrations were measured in stored frozen serum by using the ELISA method.

Results: The IFX concentration immediately before the fourth dose was ≥1 μg/mL in 32 patients (≥1 μg/mL group) and <1 μg/mL in 24 patients (<1 μg/mL group). At the fourth dose, IFX was effective in 30 patients (93.8%) in the ≥1 μg/mL group, at a mean concentration of 5.18 μg/mL, while the mean concentration was 5.69 μg/mL for the remaining 2 non-responders. IFX was also effective in 21 patients (87.5%) in the <1 μg/mL group but did not elicit any response in the other 3 patients. At this point, all 5 non-responsive patients were primary non-responders. Of all 51 responders, 58.8% were in the ≥1 μg/mL group and 41.2% were in the <1 μg/mL group. Based on the data, we observed no relationship between efficacy and IFX concentration. After 1 year of IFX treatment, 36 of the 56 patients were responsive and 20 were non-responsive. In the 2 groups, 26 responsive patients (63.9%) and 9 non-responsive patients (45.0%) had an IFX concentration of ≥1 μg/mL immediately before the fourth dose.

Conclusions: At the fourth dose, many of the patients with an IFX concentration of <1 μg/mL were also responsive to the treatment, so future efficacy was difficult to predict based on IFX concentration. In other words, during clinical evaluation, measurement of IFX concentrations is not necessary in responsive patients. However, IFX concentrations should be measured in non-responsive patients or patients with a diminished response. If the concentration is <1 μg/mL, IFX efficacy should be restored by increasing the dose or shortening the administration interval.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6072

SAT0168 DISCONTINUATION OF FIRST BIOLOGIC THERAPY IN RHEUMATOID ARTHRITIS: MAIN CAUSES AND CORRELATION BETWEEN SECONDARY INEFFICACY AND DEVELOPMENT OF IMMUNOGENICITY

P. Bogas[1], C. Plasencia[1], D. Pascual-Salcedo[2], G. Bonilla[1], E. Moral[1], C. Tornero[1], L. Nuño[1], A. Villalba[1], D. Peiteado[1], A. Martinez[2], B. Hernandez[2], A. Balsa[1]. *[1]Rheumatology; [2]Immunology, Hospital Universitario la Paz, Madrid, Spain*

Background: Biologic therapy has been a major change in Rheumatoid Arthritis (RA) prognosis, but around 40% of patients (pts) fail to respond. Part of this treatment failure can be explained by the development of anti-drug antibodies (ADA), but the ADA-associated secondary inefficacies rate is currently unclear

Objectives: To assess in our AR cohort treated with Adalimumab (Ada), Infliximab (Ifx), etanercept (Etn), certolizumab (Czp), Tocilizumab (Tcz) and Abatacept (Abt) as 1st biologic agent, the frequency of drug suspension as well as the main causes for discontinuation and the secondary inefficacy rate associated with the development of immunogenicity

Methods: From the RA cohort that initiated their 1st biologic agent at Hospital La Paz between 2005 and 2016, only those who had suspended those drugs were included, and causes for suspension were collected. Clinical activity was measured by DAS28 and Delta-DAS28 at 6 months of treatment to classify discontinuation by primary or secondary inefficacy. Drug levels (DL) and/or ADA were also measured by ELISA at 6 months since initiating the biologic agent in 43 pts and at drug discontinuation in 59 pts. Primary inefficacy was defined as DAS28>3.2 and delta-DAS28 <1.2 at 6 months with DL present. Secondary inefficacy was defined both as DAS28>3.2 plus delta-DAS28 <1.2 at 6 months with ADA+ and Delta-DAS28>1.2 or DAS28 <3.2 at 6 months with subsequent loss of efficacy. Statistical analysis was performed using SPSS version 20.0

Results: From the 246 pts who started their first biologic therapy, 144 (58%) pts who had definitively discontinued were included. [Ifx (n 35, 24%), Ada (n 40, 28%), Etn (n 30, 21%), Czp (n 23, 16%), Tcz (n 10, 7%) y Abt (n 6, 4%)]. 116 (80,6%) were women. The mean age was 56.3±14.7 years. The mean time of biologic was 2.23±1.96 years. From the global cohort, 18 (12.5%) drop out the treatment due to primary inefficacy, 41 (28.5%) to secondary inefficacy, 57 (39.6%) to adverse effects (AE), 11 (7.6%) to remission and 17 (11.8%) to other causes (surgery, pregnancy, etc.). 12.5% pts who discontinued due to AE or other causes had also a primary or secondary inefficacy; by including those pts in these last causes for suspension, a total of 20 pts (14%) failed due to primary inefficacy and 57 pts (39.6%) to secondary inefficacy. The most frequent AEs were: infections (35%), cutaneous AEs (psoriasis, rash, etc. (10.5%), infusion reactions (9%) and neoplasia (9%). Of the 59 pts who had DL/ADA measured at drug discontinuation, 42.4% were ADA +. Within the group that failed due to secondary inefficacy and had DL/ADA determined, 50% were ADA+; nevertheless this rate was smaller in suspensions due to other causes. Likewise, in the ADA+ pts, 73% suspended due to secondary inefficacy

Demographic Characteristics	
Age (years)	64±15,4
Sex (Female)	116 (80,6%)
Smokers	25 (17,6%)
BMC	27,79±8,87
Disease duration	16,7±8,04
RF +	117 (81,3%)
Anti-CCP +	119 (85,6%)
Duration of treatment (years)	2,23±1,96
Basal DMARDs	127 (89%)
Basal Methotrexate	82 (57,3%)
Basal Leflunomide	57 (39,6%)
Basal Salazopyrine	13 (9,1%)
Basal CPR	15,14±19,4
Basal ESR	34,2±23,4
Basal DAS	5,24±1,32

Conclusions: In our RA cohort, adverse effects were the main cause for discontinuation, with infections at 1st place. The 2nd cause conditioning interruption was the secondary inefficacy, in which 50% of our pts were ADA+ at drug

discontinuation. These data suggest that the development of ADA is a frequent cause of secondary inefficacy in our RA pts
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6371

SAT0169 MAINTENANCE AND IMPROVEMENT IN CLINICAL EFFICACY BETWEEN WEEK 12 AND 24 IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SB4 OR REFERENCE ETANERCEPT

P. Emery[1], J. Vencovsky[2], E. Keystone[3], J. Ghil[4], S.Y. Cheong[4], E.E. Hong[4]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; [2]Institute of Rheumatology, Prague, Czech Republic; [3]Mount Sinai Hospital, Toronto, Canada; [4]Samsung Bioepis Co., Ltd., Incheon, Korea, Republic Of*

Background: SB4 is approved by the European Commission as a biosimilar of the reference etanercept (ETN).
Objectives: To evaluate the maintenance and improvement in clinical efficacy between week 12 and 24 in patients with rheumatoid arthritis (RA) treated with SB4 or ETN from a post-hoc analysis of phase III results.
Methods: Patients with RA were randomised to receive 50 mg/week of either SB4 or ETN with background methotrexate. American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) responses were compared at week 12 and week 24. At week 12, patients with available assessment results were categorised as ACR responders or ACR non-responders and EULAR responders (patients with moderate or good EULAR response) or EULAR non-responders. The same was assessed for week 24 and patients with missing data at week 24 were regarded as non-responders.
Results: A total of 551 patients (283 patients from SB4 and 268 patients from ETN) completed 24 weeks of the study. In both treatment groups, efficacy was well maintained between week 12 and week 24. Among patients who were ACR20, 50, or 70 responders at week 12, 90.8% vs. 91.4%, 80.5% vs. 80.6%, and 74.5 vs. 77.5% of patients from SB4 and ETN, respectively, maintained their responses at week 24. Likewise, EULAR response was maintained by 93.1% vs. 92.6% of patients who had a good or moderate response at week 12. (Table).
The improvement in ACR responses between week 12 and 24 was comparable between SB4 and ETN group (Table). In SB4 and ETN, respectively, 42.1% vs. 50.5% of 12-week ACR20 non-responders became ACR20 responders at week 24. Similarly, 20.9% vs. 21.9% of 12-week ACR50 non-responders became ACR50 responders and 13.0% vs. 11.4% of 12-week ACR70 non-responders became ACR70 responders. The improvement in EULAR responses was also comparable between SB4 and ETN. 43.2% vs. 52.2% of 12-week EULAR non-responders in SB4 and ETN, respectively, became EULAR responders at week 24.

Table. Maintenance and improvement of efficacy between week 12 and week 24

		Week 24 responders	
		SB4 50 mg n/n' (%)	ETN 50 mg n/n' (%)
ACR20	Responder at week 12	179/196 (91.3%)	162/175 (92.6%)
	Non-responder at week 12	41/97 (42.3%)	51/105 (48.6%)
ACR50	Responder at week 12	91/114 (79.8%)	75/93 (80.6%)
	Non-responder at week 12	37/179 (20.7%)	41/187 (21.9%)
ACR70	Responder at week 12	38/51 (74.5%)	31/40 (77.5%)
	Non-responder at week 12	31/242 (12.8%)	28/240 (11.7%)
EULAR response*	Responder at week 12	231/246 (93.9%)	215/231 (93.1%)
	Non-responder at week 12	19/46 (41.3%)	24/49 (49.0%)

n, number of responders; n', number of responders or non-responders at week 12
*Patients with moderate or good EULAR response were regarded as responders.

Conclusions: Efficacy of SB4 and ETN was well maintained and the maintenance rate was comparable between week 12 and week 24. In addition, a similar and considerable proportion of patients in SB4 and ETN who did not achieve a clinical response at week 12 reached clinical response at week 24. These results suggest that etanercept non-responders at week 12 may benefit from continuing treatment up to 24 weeks.
Disclosure of Interest: P. Emery Grant/research support from: Abbvie, BMS, Pifzer, USB, MSD, Novartis, Lilly, Consultant for: Samsung Bioepis Co., Ltd., J. Vencovsky Consultant for: Samsung Bioepis Co., Ltd., Biogen, E. Keystone Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Janssen, Lilly, Novartis, Pfizer, Consultant for: Abbott, AstraZeneca, Biotest, BMS, Genentech, Janssen, Lilly, Merck, Pfizer, Samsung Bioepis, Speakers bureau: Abbott, AstraZeneca, BMS Canada, Janssen, J. Ghil Employee of: Samsung Bioepis Co., Ltd., S. Y. Cheong Employee of: Samsung Bioepis Co., Ltd., E. Hong Employee of: Samsung Bioepis Co., Ltd.
DOI: 10.1136/annrheumdis-2017-eular.3344

SAT0170 B-CELL PHENOTYPE AND IGD-CD27- MEMORY B CELLS ARE AFFECTED BY TNF-INHIBITORS AND TOCILIZUMAB TREATMENT IN RHEUMATOID ARTHRITIS

R.A. Moura[1], C. Quaresma[1], A.R. Vieira[1], M.J. Gonçalves[1,2], J. Polido-Pereira[1,2], V.C. Romão[1,2], N. Martins[2], H. Canhão[1,2], J.E. Fonseca[1,2]. *[1]Rheumatology Research Unit, Instituto de Medicina Molecular; [2]Rheumatology Department, Centro Hospitalar de Lisboa Norte, EPE, Hospital de Santa Maria, Lisbon, Portugal*

Background: The use of TNF-inhibitors and/or the IL-6 receptor antagonist, tocilizumab, in rheumatoid arthritis (RA) have pleiotropic effects that also involve circulating B-cells.
Objectives: The main goal of this study was to assess the effect of TNF-inhibitors and tocilizumab on B-cell phenotype and gene expression in RA.
Methods: Blood samples were collected from untreated early RA (ERA) patients (<1 year of disease duration), established RA patients under methotrexate treatment, established RA patients before and after treatment with TNF-inhibitors and tocilizumab, and healthy donors. B-cell subpopulations were characterized by flow cytometry and B-cell gene expression was analyzed by real-time PCR on isolated B-cells. Serum levels of BAFF, CXCL13 and sCD23 were determined by ELISA.
Results: The frequency of total CD19+ B-cells in circulation was similar between controls and all RA groups, irrespective of treatment, but double negative (DN) IgD-CD27- memory B-cells were significantly increased in ERA and established RA when compared to controls. Treatment with TNF-inhibitors and tocilizumab restored the frequency of IgD-CD27- B-cells to normal levels, but did not affect other B-cell subpopulations. TACI, CD95, CD5, HLA-DR and TLR9 expression on B-cells significantly increased after treatment with either TNF-inhibitors and/ or tocilizumab, but no significant changes were observed in BAFF-R, BCMA, CD69, CD86, CXCR5, CD23, CD38 and IgM expression on B-cells when comparing baseline with post-treatment follow-ups. Alterations in B-cell gene expression of BAFF-R, TACI, TLR9, FcγRIIB, BCL-2, BLIMP-1 and β2M were found in ERA and established RA patients, but no significant differences were observed after TNF-inhibitors and tocilizumab treatment when comparing baseline and follow-ups. Serum levels of CXCL13, sCD23 and BAFF were not significantly affected by treatment with TNF-inhibitors and tocilizumab.
Conclusions: In RA, treatment with either TNF-inhibitors or tocilizumab affects B-cell phenotype and the frequency of memory B-cell subpopulations in peripheral blood, particularly DN (IgD-CD27-) B-cells, but not B-cell gene expression or serum levels of CXCL13, sCD23 and BAFF, when comparing baseline with post-treatment follow up. Overall, our results may suggest that TNF-inhibitors and tocilizumab inhibit B-cell trafficking towards inflammatory sites, thus supporting activated B-cell recirculation from tissues through blood and lymphatic systems.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3011

SAT0171 ABP 501 BIOSMILAR TO ADALIMUMAB: FINAL SAFETY, IMMUNOGENICITY, AND EFFICACY RESULTS FROM AN OPEN-LABEL EXTENSION STUDY

S. Cohen[1], J.L. Pablos[2], H. Wang[3], G.A. Müller[4], A. Kivitz[5], A. Matsumoto[6], E. Krishnan[3]. *[1]Metroplex Clinical Research Center, Dallas, United States; [2]Instituto de Investigación Hospital, Madrid, Spain; [3]Amgen, Thousand Oaks, United States; [4]Abteilung für Nephrologie und Rheumatologie, Göttingen, Germany; [5]Altoona Center for Clinical Research, Duncansville; [6]Arthritis and Rheumatism Associates, Wheaton, United States*

Background: ABP 501 has been approved by the US FDA as the first biosimilar to the fully human recombinant monoclonal antibody, adalimumab. Totality of evidence to date suggests that ABP 501 is highly similar to adalimumab. Subjects receiving either ABP 501 or adalimumab in the active-controlled, comparative, pivotal phase 3 study in rheumatoid arthritis (parent study) continued on to this open-label extension (OLE) study if they had completed the final week 26 visit of that study.
Objectives: To describe the safety, immunogenicity, and efficacy outcomes of ABP 501 in the OLE study.
Methods: Subjects who completed the parent study were screened and were included if they met the eligibility requirements. All subjects included in the OLE were treated with ABP 501 40 mg subcutaneously every other week for 68 weeks followed by disease assessments at week 70 and the follow-up safety assessment at week 72 (or early termination). Data were summarized descriptively and no inferential analyses were performed.
Results: Of the 467 subjects enrolled in the OLE study, 466 were treated with ABP 501. Of these, 237 transitioned from the adalimumab arm of the parent study; 412/467 completed the study. Demographics and disease characteristics were balanced between subjects who transitioned from adalimumab and those who continued on ABP 501 from the parent study. Overall, the incidence of treatment-emergent adverse events (TEAEs) was 63.7% (297/466) and that of grade ≥3 TEAEs was 9.0% (42/466); incidence of TEAEs leading to discontinuation of investigational product was 3.6% (17/466). TEAEs with incidence ≥5% were nasopharyngitis (9.2%), upper respiratory tract infection (8.6%), bronchitis (6.4%), rheumatoid arthritis (6.2%), hypertension (4.7%), and pharyngitis (4.1%). The incidence of serious adverse events was 9.9% (46/466). Most common

TEAEs of interest were infections (40.8%), liver enzyme elevations (5.4%), and hypersensitivity (4.3%).
Overall, 18.2% (85/466) of subjects developed binding antidrug antibodies (ADAs) and 6.9% (32/466) developed neutralizing ADAs in the OLE study. The rates of ADA formation were similar between subjects who transitioned from adalimumab and those who continued on ABP 501.
The ACR20 response rate (using the parent study baseline) was 73.3% (340/464) at the OLE study baseline, 77.6% (361/465) at week 4, 74.2% (336/453) at week 24, 77.6% (337/434) at week 48, and 78.8% (327/415) at week 70. The overall mean DAS28-CRP change from parent study baseline was −2.25 (n=440) at the OLE study baseline, −2.36 (n=463) at week 4, −2.41 (n=450) at week 24, −2.55 at week 48 (n=433), and –2.60 at week 70 (n=412).
Conclusions: In this OLE study of ABP 501, efficacy documented in the parent study was maintained with no new safety findings. Long-term safety, immunogenicity, and efficacy results were similar between subjects who transitioned from adalimumab and those who continued on ABP 501 from the parent study.
Disclosure of Interest: S. Cohen Consultant for: Amgen Inc, J. L. Pablos Consultant for: Amgen Inc, H. Wang Shareholder of: Amgen Inc, Employee of: Amgen Inc, G. Müller Consultant for: Amgen Inc, A. Kivitz Consultant for: Amgen Inc, A. Matsumoto Consultant for: Amgen Inc, E. Krishnan Shareholder of: Amgen Inc, Employee of: Amgen Inc
DOI: 10.1136/annrheumdis-2017-eular.3288

SAT0172 ECONOMIC OUTCOMES, TREATMENT PATTERNS, AND ADVERSE EVENTS AND REACTIONS FOR PATIENTS PRESCRIBED INFLIXIMAB OR CT-P13 IN THE TURKISH POPULATION

K. Phillips[1], T. Juday[2], Q. Zhang[3], A. Keshishian[3]. *[1]Vanderbilt University Medical Center, Nashville; [2]AbbVie Inc., North Chicago; [3]STATinMED Research, Ann Arbor, United States*

Background: CT-P13, a biosimilar drug product to infliximab, was approved and marketed in July 2014 in Turkey. There is little information on the costs, treatment discontinuation and adverse events and reactions between patients who switched from infliximab to CT-P13 and patients who continued infliximab.
Objectives: The study objective was to evaluate health care costs, treatment discontinuation, and adverse events and reactions between patients who switched from infliximab to CT-P13 and patients who continued infliximab in the Turkish population.
Methods: Adult patients with ≥1 claim for infliximab or CT-P13 were identified in a Turkish healthcare administrative database representing 80% of the Turkish population during the identification period (16 July 2014–31 Aug 2015). Patients were required to continuously use infliximab for ≥6 months with no hospitalizations. Eligible patients either continued on infliximab (index date: date of first infliximab prescription), or switched from infliximab to CT-P13 (index date: switch date). Patients were excluded if they had ≥1 condition with an indication for infliximab during the baseline period. Patients who switched to CT-P13 were 1:10 matched to patients who continued infliximab based on the length of infliximab use prior to the index date. Demographics and clinical characteristics were measured 12 months pre-index date. Generalized linear models were used to compare adjusted health care costs, Cox regression was used to evaluate the adjusted risk of discontinuation, and Poisson regression was used to evaluate the adjusted risk of adverse events and reactions.
Results: The study included 1,524 patients, of whom 1,388 were continuous infliximab users and 136 switched to CT-P13. Ankylosing spondylitis and rheumatoid arthritis were the most common conditions indicated for infliximab and CT-P13; however, patients were much less likely to be switched to CT-P13 for other conditions. After adjusting for demographics and clinical characteristics, patients who switched to CT-P13 had higher outpatient ([Turkish lira] TL 269 vs TL 181; p=0.005), inpatient (TL 64 vs TL 29; p=0.313), and pharmacy costs (TL 1,473 vs TL 1,329; p=0.371), which resulted in significantly higher total health care costs (TL 2,009 vs TL 1,640; p=0.046) compared to patients who continued infliximab. Additionally, patients who switched to CT-P13 were more likely to discontinue treatment (13.2 vs 1.52 per 1000 person-years) compared to those who continued infliximab. Of patients who discontinued CT-P13, 79% switched back to infliximab. After adjusting for baseline characteristics, patients who switched to CT-P13 were significantly more likely to discontinue treatment compared to those who continued infliximab (HR=5.53; 95% CI: 4.01–7.63). There was no difference in the adjusted incidence rate ratio (IRR) between the cohorts for adverse events (IRR=0.67; 95% CI: 0.19–2.30) and reactions (IRR=0.84; 95% CI: 0.55–1.27).
Conclusions: Patients who switched to CT-P13 had significantly higher health care costs and were also more likely to discontinue treatment compared to those who continued infliximab. However, there was no difference in the rate of adverse events and reactions.
Disclosure of Interest: K. Phillips Consultant for: AbbVie Inc., T. Juday Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Q. Zhang Employee of: STATinMED Research, A. Keshishian Employee of: STATinMED Research
DOI: 10.1136/annrheumdis-2017-eular.2933

SAT0173 SWITCHING FROM REFERENCE PRODUCT ETANERCEPT TO THE BIOSIMILAR SB4 IN A REAL-LIFE SETTING: FOLLOW-UP OF 147 PATIENTS

V. Sigurdardottir[1,2], T. Husmark[1], A. Svärd[1,2]. *[1]Reumatologkliniken, Falu lasarett; [2]Centre of Clinical Research Dalarna, Falun, Sweden*

Background: The etanercept biosimilar SB4 was introduced in Sweden in early 2016. SB4 has been shown in a randomized controlled trial to be equivalent to its etanercept reference product (ERP) in terms of efficacy and safety in subjects with active rheumatoid arthritis (RA) (1). In light of this, and the fact that biosimilars offer considerable cost savings, all patients being treated with ERP at our clinic were switched to treatment with SB4 in april 2016.
Objectives: To describe the clinical experiences of switching patients on treatment with ERP to SB4 at our clinic.
Methods: All patients using ERP 50 mg at our clinic were identified using the Swedish Rheumatology Quality Register (SRQ). The patients were issued prescriptions for SB4 50 mg and were sent a letter encouraging them to switch to SB4 when they ran out of ERP. The process of switching was started 21st. However, the actual date of starting treatment with SB4 might have been 0–90 days from April 20th for individual patients, as prescriptions are written in 3 month increments.
Patients were followed up clinically and in the SRQ as planned at the last visit before switching.
For RA and psoriatic arthritis (PsA) patients DAS28 values from the last visit preceding the switch and the last visit after the switch registered up to January 2017 were collected from the SRQ. The paired T-test was used to compare mean DAS28 before and after switching.
Results: Before the switch, 147 patients were on treatment with ERP. Indications for treatment were RA (N=76), PsA (N=28), other spondyloarthritis (N=13), ankylosing spondylitis (N=12), unspecified arthritis (N=10) and juvenile arthritis (N=8).
At the end of January 2017, 126 patients (86%) were still on SB4.
Since the switch, 9 patients have requested to be switched back to ERP, 2 made the request before initiating therapy with SB4. No objective evidence for lack of efficacy was seen in these 9 patients. Seven patients have stopped treatment with SB4 because of inactive disease. Five patients have been switched to a non-etanercept biologic because of lack of efficacy, these patients also had lack of efficacy when on ERP.
The 76 RA patients had a mean disease duration of 17 years and had been on ERP for a mean duration of 4.7 years. As of January 2017, 60 of the RA patients have been on a follow-up visit and 54 of these had available DAS28 data from both the last visit before and after switching. For the RA patients DAS28 was 2.80 before and 2.79 after switching, p=0.960. Complete DAS28 data was available for 23 of the 28 PsA patients, mean DAS28 was 2.54 before switching and 2.06 after, p=0.161. The mean duration since switching at follow-up was 22 weeks for the RA and PsA patients.
Conclusions: Switching from the etanercept reference product to the biosimilar SB4 was acceptable to most of our patients. Low mean disease activity has been maintained in the RA and PsA group after the switch.
References:
[1] Emery P, Vencovsky J, Sylwestrzak A, Leszczynski P, Porawska W, Baranauskaite A, et al. A phase III randomised, double-blind, parallel-group study comparing SB4 with etanercept reference product in patients with active rheumatoid arthritis despite methotrexate therapy. Annals of the Rheumatic Diseases. 2017;76(1):51–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4391

SAT0174 USE OF A 8-WEEK OBSERVATIONAL PERIOD FOR PREDICTING REMISSION AND LOW DISEASE ACTIVITY AT 52 WEEKS IN RA PATIENTS TREATED WITH CERTOLIZUMAB PEGOL – A MULTICENTER STUDY

Y. Kanayama[1], A. Kaneko[2], N. Takahashi[3], T. Kato[4], M. Hayashi[5], Y. Hattori[2], N. Asai[3], N. Ishiguro[3], T. Kojima[3] on behalf of TBCR study group. *[1]Orthopedic Surgery and Rheumatology, Toyota Kosei Hospital, Toyota; [2]Orthopedic Surgery and Rheumatology, Nagoya Medial Center; [3]Orthopedic Surgery, Nagoya University Graduate school of Medicine, Nagoya; [4]Orthopedic Surgery, Kato clinic, Okazaki; [5]Orthopedic Surgery and Rheumatology, Nagano Red Cross Hospital, Nagano, Japan*

Background: Certolizumab pegol (CZP) is a polyethylene glycol (PEG)ylated Fc-free new anti-TNF α agent. However few data still reported clinical efficacy of CZP treatment in the routine practice.
Objectives: This study aimed to provide clinical evidence of an adequate observational period for predicting remission and low disease activity (LDA) achievement at 52 weeks in RA patients treated with Certolizumab pegol (CZP).
Methods: Patients with a diagnosis of RA according to the 2010 ACR/EULAR criteria who had been prescribed CZP from Tsurumai Biologics Communication Registry (TBCR) between May 2013 and October 2015 were enrolled.The final study cohort of 98 Japanese RA patients. We reviewed the methods about the improvement of DAS28-ESR and SDAI which was an index of disease activity of RA using Wilcoxon signed-rank test and the rate of remission and LDA patients at

Week4, 8, 12, 24 and 52 by LOCF method. Also we used ROC analysis in order to determine the optimal period to achieve remission for the DAS-ESR and SDAI at Week52.

Results: The group of patients included 16 males and 82 females. The mean age was 59.5±14.7 years old; the disease duration was 9.4±8.8 years; the patients of receiving methotrexate (MTX) was 73 cases (74%); the MTX dose was 11.2±3.6 mg/week and b-DMARD naïve patients was 57 cases (61%). Clinical findings related to RA were as follows: mean tender joint count, 5.2±4.7; swollen joint count, 5.0±4.0; patient's and physician's global assessment of disease activity, 48.9±27.4 and 42.3±23.2mm; CRP, 1.9±2.2 mg/dL; ESR, 47.4±34.0 mm/h; MMP3, 233±186 ng/ml; the rate of rheumatoid factor positive patients was 78%; DAS28 (ESR), 4.84±1.36; and SDAI, 21.2±11.3. The mean DAS-ESR improved to 3.54±1.35, 3.31±1.46, 3.37±1.47 and 3.31±1.43 at Week 4, 12, 24 and 52 ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$) and the mean SDAI improved to 11.4±9.0, 9.7±9.0, 9.8±9.1 and 9.4±9.1 at Week 4, 12, 24 and 52 ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$) significantly (Fig.1). At Week 4, 12, 24 and 52 the rate of patients who achieved remission were each 28.8, 37.2, 32.9, 33.7% and 11.7, 29.3, 30.5, 28.8% in DAS-ESR and SDAI criteria (Fig.2). Also at Week 4, 12, 24 and 52 the rate of patients who achieved low disease activity (LDA) were each 46.6, 53.2, 51.2, 55.8% and 58.8, 64.1, 65.9, 71.3% in DAS-ESR and SDAI criteria. Areas under the receiver operating characteristic curves for the DAS28-ESR and SDAI at each time point for remision achievement at 52 weeks were each 0.578 and 0.702 at baseline, 0.755 and 0.822 at week4, 0.821 (cut-off index 2.73, odds ratio 16.7, sensitivity 0.75, specificity, 0.85) and 0.856 (cut-off index 5.30, odds ratio 29.6, sensitivity 0.86, specificity, 0.82) at week8, and 0.820 and 0.809 at week12.

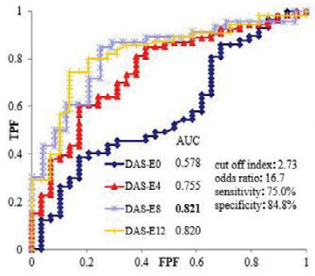


Figure 1 : ROC curves of the DAS28-ESR at each time point for predicting the achievement of remission at week 52 after starting CZP treatment

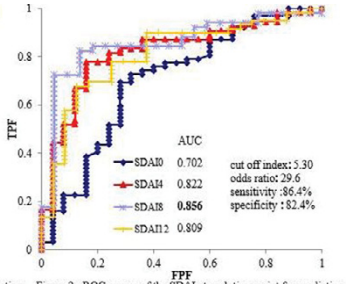


Figure 2 : ROC curves of the SDAI at each time point for predicting the achievement of remission at week 52 after starting CZP treatment

Conclusions: The new TNF-antagonist therapy of CZP was effective early and rapidly in patients with active Japanese RA. This study suggested that eight weeks is an adequate optimal period to judge whether the achieved remission or not at Week 52.

Disclosure of Interest: Y. Kanayama: None declared, A. Kaneko Speakers bureau: Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma, Chugai Pharma, Abbott, Bristol-Myers Squibb, UCB, Janssen, and Pfizer, N. Takahashi Speakers bureau: Abbvie Japan Co. Ltd, Eisai Co. Ltd, UCB Japan Co. Ltd, MitsubishiTanabe Pharma Corporation, Takeda Pharmaceutical Company Ltd, Pfizer Co. Ltd, Chugai Pharmaceutical Co. Ltd, Janssen Pharmaceutical K.K., and, T. Kato: None declared, M. Hayashi: None declared, Y. Hattori: None declared, N. Asai: None declared, N. Ishiguro Grant/research support from: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, Taisho Toyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol- Myers Squibb, AbbVie, Chugai Pharmaceutical, Mitsubishi Tanabe Pharmaceutical, Astellas Pharma, and Pfizer Japan, Speakers bureau: Daiichi Sankyo, Takeda Pharmaceutical, Hisamitsu Pharmaceutical, Otsuka Pharmaceutical, Taisho Toyama Pharmaceutical, Kaken Pharmaceutical, Eisai, Janssen Pharmaceutical, Bristol-Myers Squibb, AbbVie, Chugai, T. Kojima Speakers bureau: Mitsubishi Tanabe Pharma, Takeda Pharma, Eisai Pharma, AbbVie, Bristol-Myers Squibb, and Pfizer, Janssenn Pharmaceutical Companies, Astellas Pharma and Chugai Pharma

DOI: 10.1136/annrheumdis-2017-eular.4653

SAT0175 A DESCRIPTIVE ANALYSIS OF REAL-WORLD TREATMENT PATTERNS IN A TURKISH RHEUMATOLOGY POPULATION THAT CONTINUED INNOVATOR INFLIXIMAB (REMICADE) THERAPY OR SWITCHED TO BIOSIMILAR INFLIXIMAB

Y. Yazici[1], L. Xie[2], A. Ogbomo[2], D. Parenti[3], K. Goyal[3], A. Teeple[3], L. Ellis[3], I. Simsek[4]. *[1]New York University Hospital for Joint Diseases, New York; [2]STATinMED Research Inc, Ann Arbor; [3]Janssen Scientific Affairs, LLC, Horsham, United States; [4]Guven Hospital, Ankara, Turkey*

Objectives: This study examined treatment patterns in a rheumatology patient (pt) population initially prescribed innovator infliximab (IFX) that either switched to biosimilar infliximab (CT-P13) or continued on IFX following availability of CT-P13 in the Turkish healthcare system.

Methods: Adult pts with ≥1 diagnosis code (ICD-10-CM M05.X; M06.X) for rheumatoid arthritis (RA) and a prescription for IFX were identified in a national Turkish health care database during the study period (01DEC2010–01DEC2015). Eligible pts were those who continued on IFX (Continuers cohort; CC) or switched from IFX to CT-P13 (Switchers cohort; SC) during the identification period; had continuous medical/pharmacy benefit enrollment ≥12 months before and ≥6 months after the index date (date of switch for SC and a random IFX prescription date for CC); had a prescription claim for IFX within 16 weeks of the index date during the baseline period. Demographics, concomitant disease, medications, and treatment patterns (dose, refill interval, discontinuation, and switch) were summarized. A confirmed discontinuation was defined as a switch to another biologic medication or the absence of an index biologic claim for ≥120 days without censoring. Patient weight was unavailable in the dataset.

Results: Key results are shown in the Table. A total of 3018 pts met study criteria. The majority (95%; n=2870; CC) continued on IFX and had a mean age of 44 years; 46% were female and mean follow up of 12 months. A total of 148 pts (5%) switched to CT-P13 (SC) and had mean age of 44 years; 51% female and mean follow up of 9 months. Approximately 40% of pts in each cohort had a concomitant diagnosis for ankylosing spondylitis (AS; Table). Other concomitant diseases and medications appeared balanced between cohorts. In the CC, pts had an average of 4.7 infusions at a mean dose of 4.4 vials approximately every 10 weeks. In the SC, pts had an average of 2.6 infusions at a mean dose of 3.6 vials approximately every 10 weeks. Therapy discontinuation occurred in 38% in the CC; average time to any discontinuation or censoring of IFX was 256 days (Table). In the SC, CT-P13 discontinuation was observed in 82%; average time to any discontinuation or censoring of CT-P13 was 124 days; 74% of SC switched to another biologic with 94% of these returning to IFX.

	Switchers Cohort (N=148)		Continuers Cohort (N=2870)	
	N/Mean	%/SD	N/Mean	%/SD
Age (Mean) (years)	44	13	44	12
Gender				
Female	75	51%	1,332	46 %
Average Length of Follow up Period (in Months)	9	2	12	3
Concomitant Disease During Baseline Period				
Ankylosing Spondylitis	73	49%	1,214	42%
Psoriatic Arthritis or Psoriasis	19	13%	582	20%
Crohn's Disease	6	4%	191	7%
Ulcerative Colitis	8	5%	157	5%
Concomitant RA-Medications During Follow-Up Period				
Methotrexate	31	21%	652	23%
Sulfasalazine	21	14%	340	12%
Dosing Characteristics				
Average # of doses within follow up period	2.6	1.6	4.7	2.4
Mean # of weeks between doses	10.1	5.1	9.9	3.8
Mean # of days between 1st and 2nd dose	75	48	70	34
Mean # of days between 2nd and 3rd dose	72	38	70	29
Mean # of days between 3rd and 4th dose	65	31	67	26
Mean # of vials per Infusion	3.6	1.6	4.4	1.9
Switching				
# and % of patients with ≥1 switch	110	74%	471	16%
% of Primary Switches from CT-P13 to IFX	103	94%	NA	NA
Discontinuation				
# of Patients Confirmed to Have Discontinued	121	82%	1,089	38%
Time to confirmed discontinuation (days)	94	58	126	91
Time to any discontinuation or censoring (days):	124	87	256	138

Conclusions: This study shows switching from IFX to CT-P13 was infrequent. However, in those switching to CT-P13, a high percentage (82%) of CT-P13 discontinuation was observed and the majority returned to IFX. Further studies are needed to understand the reasons for these observations.

Disclosure of Interest: Y. Yazici Grant/research support from: Janssen Scientific Affairs, LLC, L. Xie Consultant for: Janssen Scientific Affairs, LLC, A. Ogbomo Consultant for: Janssen Scientific Affairs, LLC, D. Parenti Employee of: Janssen Scientific Affairs, LLC, K. Goyal Employee of: Janssen Scientific Affairs, LLC, A. Teeple Employee of: Janssen Scientific Affairs, LLC, L. Ellis Employee of: Janssen Scientific Affairs, LLC, I. Simsek Grant/research support from: Janssen Scientific Affairs, LLC

DOI: 10.1136/annrheumdis-2017-eular.1128

SATURDAY, 17 JUNE 2017

Rheumatoid arthritis - other biologic treatment

SAT0176 PATTERNS OF BIOLOGIC DMARD MONOTHERAPY IN A LARGE NATIONWIDE RHEUMATOID ARTHRITIS COHORT: DATA FROM 1036 PATIENTS

K. Thomas[1], E. Kaltsonoudis[2], A. Drosos[2], I. Papalopoulos[3], P. Sidiropoulos[3], P. Katsimbri[1], D. Boumpas[1], P. Tsatsani[4], S. Gazi[4], E.P. Grika[1], P.G. Vlachoyiannopoulos[1], K. Fragiadaki[1], M. Tektonidou[1], P.P. Sfikakis[1], K. Karagianni[1], L.I. Sakkas[5], L. Pantazi[6], K. Boki[6], T. Dimitroulas[7], A. Garyfallos[7], D. Kasimos[8], G. Evangelatos[9], A. Iliopoulos[9], C. Georganas[10], P. Vounotrypidis[10], M. Areti[10], P. Georgiou[11], K. Delis[10], K. Mavragani[1], I. Bournazos[10], G. Katsifis[12], C. Mavromatis[10], G.D. Kitas[13], D. Vassilopoulos[1].

[1]Joint Rheumatology Program, University of Athens, Athens; [2]University of Ioannina, Ioannina; [3]University of Crete, Heraklion; [4]KAT Hospital, Athens; [5]University of Thessaly, Larissa; [6]Sismanoglio Hospital, Athens; [7]Aristotle University, Thessaloniki; [8]401 General Military Hospital; [9]NIMTS Hospital; [10]Private practice, Athens; [11]Agios Andreas Hospital, Patras; [12]Rheumatology Unit, Naval Hospital; [13]Hygeia Hospital, Athens, Greece

Background: There are limited literature data regarding the characteristics of rheumatoid arthritis (RA) patients treated with biologic DMARD (bDMARD) monotherapy.
Objectives: To evaluate the disease and treatment characteristics of RA patients treated with bDMARD monotherapy.
Methods: Multicenter, cross-sectional RA epidemiological study in Greece (06/2015–05/2016, ERE RA Study Group). Demographics, disease characteristics, treatment and co-morbidity data were collected via a web-based platform
Results: 1036 RA patients treated with bDMARDs were identified during the one year recruitment period (female: 82%, mean age: 61.5±13 years, mean disease duration: 12.5±8.9 years, mean DAS28-ESR: 3.4±3.3). Among them, 26% (n=273) were receiving bDMARDs as monotherapy and 8% (n=23) of them had never tried conventional synthetic DMARDs (csDMARDs) before; The latter group (n=23) compared to the csDMARD-exposed (92%, n=250) group, had more often co-morbidities [cardiovascular disease (22% vs. 8%, p=0.029), chronic hepatitis (13% vs. 3%, p=0.02), hypertension (57% vs. 38%, p=0.08), COPD (13% vs. 4.4%, p=0.07)] or were active smokers (41% vs. 14%, p=0.001). csDMARD discontinuation was mainly due to adverse events (AEs, 58%) followed by inadequate response (IR, 44%). Compared to the cs- and b-DMARD combination therapy group, monotherapy treated patients were more frequently seropositive (64% vs. 57%, p=0.003), had lower DAS28-ESR (3.2 vs 3.5, p=0.009) and were more likely to have discontinued csDMARDs for AEs (58% vs. 21%, $p<0.001$) or IR (44% vs. 27%, $p<0.001$). Tocilizumab (22.3% vs. 12.7%, $p<0.001$) and rituximab (19.8% vs. 13.5%, p=0.013) were utilized more often, whereas adalimumab less often (8.8% vs. 14.8%, p=0.012) as monotherapy compared to as part of combination therapy.
Conclusions: In our large RA cohort, one out of four bDMARD treated patients, were receiving bDMARDs as monotherapy. Co-morbidities rather than RA characteristics influence the initial decision for bDMARD monotherapy whereas among those starting combination cs- and b-DMARD therapy, the majority discontinue csDMARDs due to AEs.
Acknowledgements: Grant support from the Hellenic Rheumatology Society and Professional Association of Rheumatologists.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4390

SAT0177 SAFETY EVENTS ARE SIMILAR WITH ABATACEPT VS PLACEBO TREATMENT IN RA: RESULTS FROM INTEGRATED DATA ANALYSIS FROM NINE CLINICAL TRIALS

B. Soule[1], M. Hochberg[2], D. Fleming[1], A. Torbeyns[1], T. Simon[1], S. Banerjee[1], M. Boers[3]. *[1]Bristol-Myers Squibb, Princeton; [2]University of Maryland, Baltimore, United States; [3]VU University Medical Center, Amsterdam, Netherlands*

Background: Abatacept is a selective co-stimulation modulator that consists of the extracellular domain of human cytotoxic T lymphocyte-associated antigen-4 linked to the modified Fc portion of human immunoglobulin and was approved initially for the treatment of RA in 2005. The integrated safety database for abatacept in adult RA comprises data from short- and long-term periods of 16 open-label and double-blind RA clinical trials, and combines studies of both IV and SC abatacept involving 7044 total patients. Of these, data from the 9 double-blind, placebo-controlled studies involving 4138 total patients were included in this analysis. The most recent overall safety analysis was performed in 2012 and reported IV and SC results separately.
Objectives: To provide an update of the overall abatacept safety profile based on data analysis from both IV and SC trials.
Methods: This evaluation included all patients with RA enrolled in 9 key double-blind, placebo-controlled clinical trials of IV and/or SC abatacept. The safety analysis includes all serious adverse events (SAEs), as well as AEs of interest including infections, malignancies and autoimmune diseases.
Results: In total, 2653 patients were exposed to abatacept and 1485 received placebo. During the double-blind, controlled period, the mean (SD) duration of exposure was 10.3 (3.5) months for the placebo group and 10.8 (3.3) months for the abatacept group for a total exposure of 2357 and 1254 patient years, respectively (Table 1). The proportion of patients as well as incidence rates for death, SAEs, infections, malignancy and autoimmune diseases were similar between those treated with abatacept and placebo (Table 2).
Conclusions: In a large RA clinical trial database, safety events including deaths, serious infections, opportunistic infections, malignancies and autoimmune diseases occurred at similar frequencies and rates in the abatacept and placebo treatment groups.
Disclosure of Interest: B. Soule Employee of: Bristol-Myers Squibb, M. Hochberg Shareholder of: Theralogix LLC, Grant/research support from: NIH, Consultant for: Bristol-Myers Squibb, EMD Serono Inc., Genentech/Roche, Novartis Pharma AG, Pfizer Inc, UCB Inc., D. Fleming Employee of: Bristol-Myers Squibb, A. Torbeyns Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, T. Simon Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Banerjee Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Boers Consultant for: Bristol-Myers Squibb
DOI: 10.1136/annrheumdis-2017-eular.2383

Table 1. Demographic Data

	Abatacept (N=2653)	Placebo (N=1485)
Mean age, yr (SD)	51.7 (12.4)	51.4 (12.3)
Female, %	79.1	79.7
White, %	86.1	86.5
NSAIDs, %	79.0	79.6
Glucocorticoids, %	51.6	49.4
Mean oral dose, mg (SD)	*7.5 (8.1)*	*9.1 (9.1)*
MTX, %	68.2	63.8
Anti-TNF, %	6.4	5.5

Table 2. Events During the Double-Blind, Placebo-Controlled Period

	Abatacept (N=2653)		Placebo (N=1485)	
Outcome	N (%)	IR (95% CI)	N (%)	IR (95% CI)
Deaths	12 (0.5)	0.5 (0.3, 0.9)	12 (0.8)	1.0 (0.5, 1.7)
SAEs	331 (12.5)	14.8 (13.3, 16.5)	174 (11.7)	14.6 (12.5, 17.0)
Discontinued due to SAEs	68 (2.6)		22 (1.5)	
Infections	1440 (54.3)	91.3 (86.7, 96.2)	761 (51.6)	90.8 (84.4, 97.4)
Serious infections	41 (1.5)	1.7 (1.2, 2.3)	16 (1.1)	1.2 (0.7, 2.0)
Solid organ malignancies	26 (1.0)	1.11 (0.7, 1.6)	12 (0.8)	1.0 (0.5, 1.7)
NMSC (combined)	14 (0.5)	0.6 (0.3, 1.0)	5 (0.3)	0.4 (0.1, 0.9)
Autoimmune diseases	198 (7.5)	8.5 (7.3, 9.8)	115 (7.7)	9.2 (7.6, 11.1)
COPD	13 (0.5)	0.6 (0.3, 1.0)	2 (0.1)	0.2 (0.0, 0.6)

SAT0178 PULMONARY INVOLVEMENT IN RHEUMATOID ARTHRITIS TREATED WITH BIOLOGIC

E. Guerrero[1], M.L. García[1], E. Galindez[1], E. Ruíz[1], I. Torre[1], L. Estopiñan[1], O. Fernández[1], A. Inchaurbe[1], C. Perez[1], J. Blanco[1], I. Calvo[1], O. Ibarguengoitia[1], N. Rivera[1], I. Gorostiza[2] on behalf of Rheumatology Service. *[1]Rheumatology Service; [2]Research Unit, Basurto Hospital, Bilbao, Spain*

Background: Use of biologic therapy (BT) has been determinant in Rheumatoid Arthritis' (RA) change of management and outcomes improvement for the last decade. Classic extraarticular manifestations are now uncommon, except for the pulmonary involvement, which can occur due to different causes and can complicate our patients' treatment and prognosis.
Objectives: The aim of this study is to evaluate the presence of pulmonary complication in RA patients under BT in our hospital, and assess its severity and the modifications required.
Methods: Review of clinical records of 208 RA patients receiving BT in the last 5 years (January 2012 to December 2016). 23 cases of preexisting lung disease for other causes have been excluded and finally 26 patients have been finally included. Demographic data, characteristics of RA, types of pulmonary involvement, evolution and changes in treatment have been collected. Statistical analysis were performed using SPSS v22.
Results: 73.1% are women, mean aged 59 years (31–80); 53.8% never smokers. They suffer from long term RA (median 176.92 months, SD 199.34); only 2 patientes have been recently diagnosed (less than a year). They are mainly seropositive (85% RF positive) with positive CCP antibodies in 69.2%, and with erosive disease in 70%. 25% have other extraarticular manifestations (3 rheumatoid nodules, 4 cardiac involvement).
Half of the patients were in remission or low activity (DAS 28) at the time of pulmonary disease diagnosis, and the median of CRP was 0.52 mg/dL (SD 1.72). 90% had received Methotrexate and almost half of them Leflunomide; 30% had been treated with BT (50% TNF alpha inhibitors).
Intersticial lung disease (ILD) was the most frequent pulmonary involvement (57.7%) and non-specific interstitial pheumonia (NSIP) the most prevalent pattern (>60%). We also found obstructive pulmonary disease (11.5%) and vascular involvement (7.7%). 40% of the patients had a normal radiograph (all of them a pathological CT).
Treatment was modified in 53.8% of the cases (synthetic DMARD was kept in 68% and BT in 64%).
The average time of evolution of pulmonary involvement is 37.85 months (1–156). 80% of the patients kept stable or improved from their arthritis and also from respiratory disease. Only one received a lung trasplant and another one died.
We haven't found an association between different types of pulmonary involvement and the different variables analyzed in the study. We didn't show significant differences in prognosis related to pulmonary disease distinct patterns; up to 80% of patients with ILD stabilize or improve.
Conclusions: Prevalence of pulmonary disease in our experience in RA patients under BT is similar to prevalence in other observational studies (10–20%), because diagnosis here is due to casual detection in a routine chest X-ray or for clinical suspicion for respiratory symptoms (cough, dyspnea, ...). The evolution has been good perhaps for the high prevalence of NSIP, which requires less therapeutic intervention. Protocols for systematic search of lung disease in RA patients seem essential for its proper diagnosis, and there is a need for further research in pathogenesis and management of this complication.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4252

SAT0179 THE ASP358ALA VARIANT IN THE IL6R GENE IS SIGNIFICANTLY ASSOCIATED WITH DIFFERENCES IN SOLUBLE IL-6R PROTEIN LEVELS BUT NOT WITH DIFFERENCES IN SARILUMAB RESPONSE IN RHEUMATOID ARTHRITIS (RA) PATIENTS

A. Damask[1], A. Boyapati[1], J.D. Hamilton[1], S. Hamon[1], C. Paccard[2], J. Parrino[1], J. van Adelsberg[1], N.M. Graham[1], J. Penn[1], A. Lopez[1], J. Reid[1], J. Overton[1], A. Baras[1], A.R. Shuldiner[1], C. Paulding[1]. *[1]Regeneron Pharmaceuticals, Inc, Tarrytown, United States; [2]Sanofi R&D, Chilly-Mazarin, France*

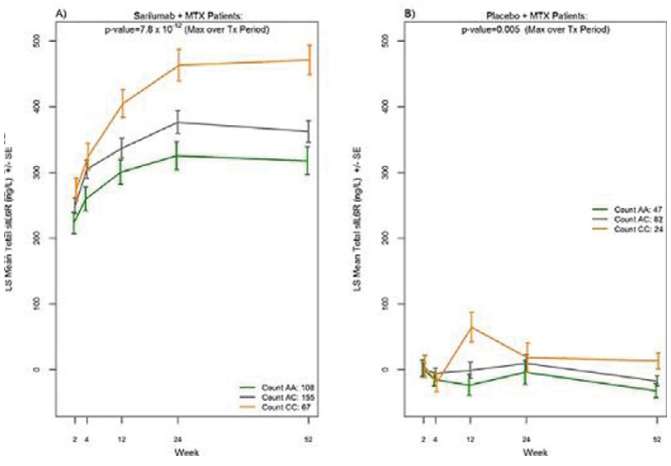
Background: Sarilumab is a human mAb that blocks IL-6 from binding to both membrane-bound and soluble IL-6Rα (sIL-6R). A missense variant in the *IL6R* gene, Asp358Ala (rs2228145), falls within a proteolytic cleavage site and individuals with an alanine at this position have increased sIL-6R in circulation.[1] In addition, this variant has been associated with several diseases including RA.[2]
Objectives: To determine the impact of the Asp358Ala variant on sIL-6R concentrations and response of RA patients to sarilumab.
Methods: DNA was collected from patients enrolled in the MOBILITY study (NCT01061736) that evaluated the efficacy and safety of sarilumab + methotrexate (MTX) in RA patients with inadequate response to MTX. The pharmacogenetic analysis was conducted on 599 Caucasian patients (396 sarilumab 150 or 200 mg q2w + MTX, 203 placebo + MTX).
Results: Concentrations of sIL-6R were strongly associated with the Asp358Ala genotypes at baseline (p=4.2 × 10^{-11}). The difference in sIL-6R concentrations between genotype groups continued to increase in sarilumab-treated patients through the end of treatment, particularly for the CC genotype (Figure; p=7.8 × 10^{-12}). There was a modest association for change in sIL-6R in placebo + MTX–treated patients (p=0.0052). Variation in Asp358Ala was not associated with sarilumab efficacy, including mTSS at week 52 and ACR scores (Table).

Table 1. Efficacy Endpoints[1] and sIL-6R Levels by Asp358Ala Genotypes in Sarilumab-Treated Patients[2]

Genotype	sIL-6R	mTSS[3]	ACR20	ACR50	ACR70	MCR[4]	SJC[5]	TJC[6]
AA (n=129)	317.7 (21.0)	1.4 (0.5)	59	40	22	13	-10.9 (0.8)	-16.5 (1.2)
AC (n=190)	362.3 (16.4)	0.7 (0.3)	65	43	22	12	-11.1 (0.6)	-18.3 (1.0)
CC (n=77)	470.8 (22.8)	0.9 (0.5)	75	48	31	17	-11.6 (1.0)	-19.1 (1.5)
p value	7.8×10^{-12}	0.89	0.06	0.67	0.57	0.71	0.25	0.20

[1]sIL-6R, mTSS, SJC, TJC show LS mean (SE). Wk 24 ACR20, ACR50, ACR70, and MCR show % achieving endpoint. [2]150 or 200 mg q2w doses combined. [3]van der Heijde modified total Sharp score at wk 52. [4]Major clinical response is defined as achieving and maintaining ACR70 for ≥24 consecutive weeks during the 52-wk period. [5]Swollen joint count. [6]Tender joint count.

Figure 1. Total sIL-6R by Asp358Ala genotype in patients treated with A) Sarilumab + MTX and B) Placebo + MTX



Conclusions: The Asp358Ala variant in the *IL6R* gene is significantly associated with differences in sIL-6R levels at baseline and after sarilumab treatment. The differences across genotypes may be due to increases in sIL-6R production. Importantly, this variant was not associated with differences in sarilumab treatment response. These data suggest that the sarilumab doses used for this clinical study saturate both the membrane and soluble forms of IL-6R and effectively block IL-6 signaling. Sarilumab provides therapeutic benefit for RA patients irrespective of their Asp358Ala genotype status.

References:
[1] Garbers et al. Biochim Biophys Acta. 2014;1842:1485–1494.
[2] Okada et al. Nature. 2014;506:376–381.

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.
Disclosure of Interest: A. Damask Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Boyapati Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Hamilton Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, S. Hamon Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, C. Paccard Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, J. Parrino Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. van Adelsberg Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, N. Graham Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Penn Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Lopez Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Reid Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Overton Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Baras Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, A. Shuldiner Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, C. Paulding Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc
DOI: 10.1136/annrheumdis-2017-eular.4983

SAT0180 EFFICACY AND SAFETY OF SARILUMAB 200 MG Q2W ADMINISTERED AS COMBINATION THERAPY OR MONOTHERAPY IN DIFFERENT PATIENT POPULATIONS WITH ACTIVE RA

M.C. Genovese[1], R. Fleischmann[2], H. van Hoogstraten[3], E.K. Mangan[4], S. Jayawardena[3], G.R. Burmester[5]. *[1]Stanford University Medical Center, Palo Alto; [2]Metroplex Clinical Research Center, University of Texas Southwestern Medical Center, Dallas; [3]Sanofi Genzyme, Bridgewater; [4]Regeneron Pharmaceuticals, Inc, Tarrytown, United States; [5]Charité - University Medicine Berlin, Free University and Humboldt University of Berlin, Berlin, Germany*

Background: Sarilumab, a human mAb blocking the IL-6Rα, was evaluated in 3 pivotal clinical trials.
Objectives: To assess efficacy and safety of sarilumab 200 mg q2w + csDMARDs or as monotherapy (MONARCH) in adults with active RA and inadequate response or intolerance to MTX (MOBILITY/MONARCH) or TNFi (TARGET).
Methods: MOBILITY (NCT01061736) was a 52-wk study; TARGET (NCT01709578) and MONARCH (NCT02332590) were 24-wk studies. Patients were randomized to placebo (Pbo) or SC sarilumab 150 or 200 mg q2w + MTX (MOBILITY) or csDMARDs (TARGET). MONARCH patients were randomized to SC monotherapy with adalimumab 40 mg q2w or sarilumab 200 mg q2w. Efficacy endpoints assessed in all 3 studies will be presented.
Results: Within studies, baseline demographic and disease characteristics were similar among treatment groups. Sarilumab 200 mg q2w improved ACR responses, HAQ-DI, DAS28-CRP, and CDAI (Table). Treatment response with sarilumab + csDMARDs was similar in MTX-IR and TNF-IR patients and with sarilumab monotherapy. Incidence of TEAEs and SAEs with sarilumab was more frequent vs Pbo (MOBILITY, TARGET) and similar to adalimumab (MONARCH). The most common TEAEs included infections, neutropenia, and injection site reactions and occurred more often with sarilumab vs Pbo (MOBILITY, TARGET). In MONARCH, rates of infection were similar with sarilumab and adalimumab,

Abstract SAT0180 – Table 1. Sarilumab Efficacy in 3 Phase 3 Studies

	MOBILITY		TARGET		MONARCH	
	Pbo + MTX (N=398)	Sarilumab 00 mg q2w + MTX (N=399)	Pbo + csDMARDs (N=181)	Sarilumab 200 mg q2w + csDMARDs (N=184)	Adalimumab 40mg q2w (N=185)	Sarilumab 200 mg q2w (N=184)
ACR20, wk 24, %	33.4	66.4*	33.7	60.9*	58.4	71.7†
ACR50, wk 24, %	16.6	45.6*	18.2	40.8*	29.7	45.7†
ACR70, wk 24, %	7.3	24.8*	7.2	16.3*	11.9	23.4†
HAQ-DI, mean change from baseline ± SD						
Wk 16/12/24	-0.3±0.6	-0.6±0.6*	-0.3±0.5	-0.5±0.6*	-0.4±0.6	-0.6±0.7†
DAS28-CRP, mean change from baseline ± SD						
Wk 24	-1.6±1.4	-3.0±1.3*	-2.0±1.2	-3.2±1.3*	-2.1±1.2	-2.9±1.3‡
CDAI, mean change from baseline ± SD						
Wk 24	-20.3±15.8	-27.9±13.2*	-23.9±12.9	-30.4±14.5*	-25.5±12.9	-29.7±12.7‡

*P<0.01 vs Pbo. †P<0.01 vs adalimumab. ‡Nominal P<0.01 vs adalimumab.

although neutropenia was more frequent with sarilumab. Safety of sarilumab was generally comparable in monotherapy and combination studies; monotherapy was associated with fewer ALT elevations >3 × ULN compared with combination therapy: MONARCH, 3%; MOBILITY, 8%; TARGET, 4%.
Conclusions: Sarilumab 200 mg q2w + csDMARDs significantly reduced disease activity and improved physical function to a similar extent regardless of population (MTX-IR or TNF-IR) and as monotherapy. Safety profile of sarilumab was generally comparable across all 3 trials, with monotherapy resulting in fewer ALT elevations.
Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial assistance was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.
Disclosure of Interest: M. Genovese Grant/research support from: Roche, Sanofi, GlaxoSmithKline, R-Pharma, RuiYi, and Bristol-Myers Squibb, Consultant for: Roche, Sanofi, GlaxoSmithKline, R-Pharma, RuiYi, and Bristol-Myers Squibb, R. Fleischmann Grant/research support from: AbbVie, Amgen, Ardea, AstraZeneca, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Janssen, Eli Lilly, Merck, Pfizer, Roche, Sanofi, and UCB, Consultant for: AbbVie, Akros, Amgen, AstraZeneca, Bristol-Myers Squibb, Janssen, Eli Lilly, Pfizer, Roche, and UCB, H. van Hoogstraten Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, E. Mangan Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, S. Jayawardena Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, G. Burmester Grant/research support from: AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, and UCB
DOI: 10.1136/annrheumdis-2017-eular.1275

SAT0181 LOW DOSE INTERLEUKIN-2 COMBINED WITH TOCILIZUMAB SELECTIVELY INCREASES REGULATORY T CELLS HELPING REFRACTORY RHEUMATOID ARTHRITIS PATIENTS ACHIEVE REMISSION MORE RAPIDLY

Z. Sheng-Xiao[1], M. Xiao-Wen[2], L. Xiao-Qing[1], M. Miao[1], W. Xiao-Yan[1], N. Hong-Qing[2], W. Cai-Hong[2], L. Xiao-Feng[1]. *[1]Rheumatology; [2]The Second Hospital of Shanxi Medical University, Taiyuan, China*

Background: Rheumatoid arthritis (RA) is a prevalent chronic autoimmune inflammatory disease. Its pathogenesis is closely associated with a failure of endogenous immune tolerance that caused by the imbalance of pro-inflammatory T helper 17 (Th17) cells and anti-inflammatory regulatory T (Treg) cells. Low-dose Interleukin-2 (IL-2) has been showed to induce both Th17 and Treg cells' expansion and activation while IL-6 antagonist Tocilizumab suppresses the differentiation of Th17, which is expected to control the development of RA.
Objectives: To study the influence of the combination of IL-2 and Tocilizumab on T cells subgroups and its clinical efficacy and safety on refractory RA.
Methods: Total 50 RA patients with low Treg cells, who had been treated with glucocorticoids and DMARDs for over 6 months, were divided into three groups randomly. Patients in non-IL-2 group (n=15) were still given conventional glucocorticoids and DMARDs. Patients in IL-2 group (n=26) were not only given those treatments, but injected subcutaneously human IL-2 (aldesleukin) at 50 WIU per day for a 5 day course. Patients in IL-2 and Tocilizumab group (n=9) were not only received the treatment like IL-2 group, but also treated with Tocilizumab at the dosage of 160mg during the day 1 and day 3. The demographic features, clinical manifestations and laboratory indicators were compared before and after the treatment.
Results: There was no difference among all groups in gender, age and course of the disease (p >0.05). The ratios of Th1/Th2 and Th17/Treg were significant correlated with ESR, the number of tender or swollen joints and DAS28-ESR (p<0.05) in all three groups of patients. After treatment, the number of Th17 cells and Treg cells was significantly increased in IL-2 group (p<0.01). In IL-2/Tocilizumab group after the treatment, the number of Treg cells were also significantly increased (p<0.05), but not the Th17 cells (p>0.05), leading to a quickly decrease in their ratio (p<0.05). Before the treatment, there was no difference in clinical manifestations among all three groups (p>0.05), but compared with non-IL-2 group, there was a significantly decrease in the number of tender joints (p<0.01) or swollen joints (p<0.05) and DAS28-ESR (p<0.01) in IL-2 group and IL-2/Tocilizumab group after the treatment. Patients in IL-2/Tocilizumab group had better clinical manifestations' remission although no significant difference compared with IL-2 group (p>0.05). There was no difference in blood routine, liver and renal functions both before and after the treatment among all groups (p>0.05).
Conclusions: IL-2 can effectively increase the level of Treg cells as well as that of Th17 to some degree; while IL-2 combined with Tocilizumab only effectively expand Treg cell number without Th17 increasing, thereby quickly recovers the balance of Th17 and Treg cells. This combination selectively stimulate Treg Cells leading to induce autoimmune tolerance, and seems to help RA patients achieve remission in a rapid way without over-treatment and evaluated side effect, though the long term benefits of this therapy are required to further study in more patients.
Acknowledgements: The authors thank Chong Gao for the assistance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3611

SAT0182 SIRUKUMAB LEADS TO SIGNIFICANT AND CLINICALLY MEANINGFUL IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE THAT MEET OR EXCEED NORMATIVE VALUES IN PATIENTS WITH RHEUMATOID ARTHRITIS REFRACTORY TO TNF INHIBITORS IN POST HOC ANALYSES OF A PHASE 3 TRIAL

V. Strand[1], R. Ganguly[2], N. Li[3], K. McQuarrie[3]. *[1]Stanford University, Palo Alto, CA; [2]GlaxoSmithKline, Collegeville, PA; [3]Janssen Research & Development, LLC, Spring House, PA, United States*

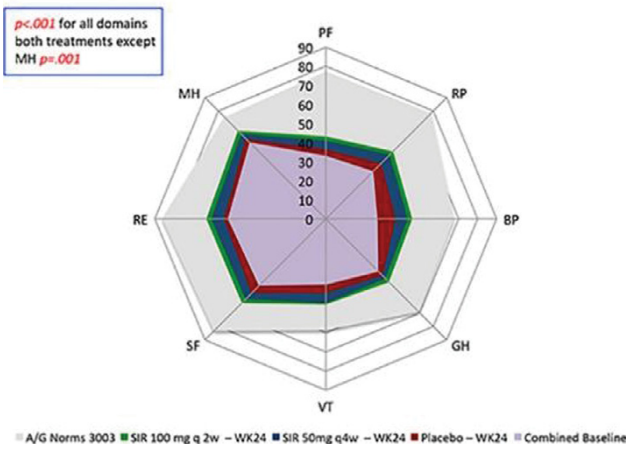
Background: Patients (pts) with rheumatoid arthritis (RA) experience reduced health-related quality of life (HRQoL). Sirukumab (SIR) is an anti–interleukin-6 (IL-6) monoclonal antibody.
Objectives: These post hoc analyses evaluated improvements over time in HRQoL relative to an age/gender-matched normative population in RA pts with inadequate responses to tumor necrosis factor inhibitors (TNF-IR) from the phase 3 SIRROUND-T trial.
Methods: 878 pts received SIR 50mg every 4 weeks (q4w), SIR 100mg every 2 weeks (q2w), or placebo (pbo) q2w. Health-related physical/emotional well-being were measured at baseline (BL) and Wk 24 by the 36-item Short Form Questionnaire (SF-36), fatigue by Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue (FACIT-F), and physical function by Health Assessment Questionnaire-Disability Index (HAQ-DI).
Results: SF-36 physical and mental component summary (PCS and MCS) mean scores at BL for pbo, SIR 50mg q4w, and 100mg q2w indicated substantial impairment (PCS: 33.2, 31.8, and 32.4; MCS: 41.9, 41.2, and 42.1). Significantly greater improvements from BL were reported at Wk 24 with SIR 50mg q4w and 100mg q2w vs pbo in PCS (4.8 and 5.1 vs 1.7) and MCS (3.9 and 4.0 vs 1.1) mean scores (all P<0.001), exceeding the minimum clinically important difference (MCID) of 2.5. Significantly greater least squares mean changes in the 8 SF-36 domain raw scores were reported with both doses of SIR vs pbo at Wk 24; all were >MCID of 5.0 (Table; Figure). More pts receiving SIR 50mg q4w or 100mg q2w reported SF-36 domain scores ≥normative values (ranges: 11–34% and 13–42%) vs pbo (range: 6–29%). For pbo, SIR 50mg q4w, and SIR 100mg q2w, BL FACIT-F scores were 26.0, 24.2, and 25.2; clinically meaningful improvements ≥MCID (4 points) were reported by 54.3 and 51.4% of pts receiving SIR 50mg q4w and 100mg q2w vs 33.7% with pbo (P<0.001). Numerically greater percentages of pts reported scores ≥normative values with both doses of SIR vs pbo (27 and 28% vs 16%). BL HAQ-DI scores were 1.57, 1.65, and 1.61 with pbo, SIR 50mg q4w, and 100mg q2w. Clinically meaningful improvements (change of ≤-0.22) were reported by significantly higher proportions of pts receiving SIR 50mg q4w (52.2%) or 100mg q2w (54.8%) vs pbo (37.4%; P<0.001). Numerically more pts reported HAQ-DI scores ≥normative values with SIR 50mg q4w and 100mg q2w vs pbo (13 and 16% vs 9%).

Table 1. Improvements in SF-36 Domain Scores at Wk 24 (all P<0.001)

Domain	LSM change SIR 50mg q4w	LSM change SIR 100mg q2w	LSM change pbo
Physical function	9.38	10.75	0.47
Role-physical	12.85	13.52	5.03
Bodily pain	17.66	17.51	7.46
General health	6.81	7.76	1.57
Vitality	10.10	9.68	4.14
Social function	12.40	11.75	3.68
Role-emotional	9.29	9.86	0.42
Mental health	6.73	7.96	2.10

LSM, least squares mean.

Figure. SF-36 domains at Wk 24 for SIR 50mg q4w and SIR 100mg q2w



Conclusions: In TNF-IR RA pts, SIR treatment resulted in greater and clinically meaningful improvements in HRQoL vs pbo that met or exceeded population normative values, with similar results for SIR 50mg q4w and 100mg q2w.
Disclosure of Interest: V. Strand Consultant for: Abbvie, Amgen, AstraZeneca, BiogenIdec, Boehringer Ingelheim, Celltrion, Crescendo, Genentech/Roche, GSK,

Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi and UCB, R. Ganguly Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, N. Li Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, K. McQuarrie Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC
DOI: 10.1136/annrheumdis-2017-eular.3904

SAT0183 CLINICAL REMISSION IN SUBJECTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB AS MONOTHERAPY OR IN COMBINATION WITH METHOTREXATE OR OTHER SYNTHETIC DMARDS: A REAL-WORLD CLINICAL TRIAL (TOSPACE)

R. Sanmarti[1], E. Martín Mola[2], J.E. Fonseca[3], D.J. Veale[4], A. Escudero[5], C. González[6] on behalf of ToSpace Study group. *[1]Hospital Clinic, Barcelona; [2]Hospital la Paz, Madrid, Spain; [3]Hospital de Santa Maria, Lisboa, Portugal; [4]St.Vincent's University Hospital, Dublin, Ireland; [5]Hospital Reina Sofía, Córdoba; [6]Hospital Gregorio Marañón, Madrid, Spain*

Background: Subcutaneous tocilizumab (TCZ-SC) has demonstrated non-inferiority to TCZ-IV and superiority to placebo
Objectives: The primary objective of this study was to assess the 24-week efficacy and safety of subcutaneous (SC) tocilizumab (TCZ) 162 mg weekly (qw) as monotherapy or in combination with methotrexate (MTX) or other synthetic (s) DMARDs in patients with active rheumatoid arthritis (RA) in the real world setting
Methods: This multinational (Spain, Ireland, Portugal), multicenter, phase IIIb study. Subjects ≥18 years of age with active RA (DAS 28-ESR >3.2) who have had inadequate response or intolerance to sDMARDs or to a first anti-TNF drug. The study comprised a phase 1 with open-label design in which patients received TCZ-SC 162 mg qw (+/- oral/SC MTX or other sDMARDs) for 24-weeks and the main outcome was the percentage of patients achieving sustained clinical remission (DAS 28-ESR <2.6) at Week 20 and Week 24 (primary outcome of the study); and a phase 2 where patients achieving sustained clinical remission during the phase 1 were randomized to receive TCZ-SC 162 mg qw or TCZ-SC 162 mg q2w (+/- oral/SC MTX or other sDMARDs) for an additional 24 weeks; the main outcome of the phase 2 was the percentage of patients who maintained the remission at week 48 (i.e. DAS 28-ESR<2.6)
Results: 401 patients were included in the phase 1, 74 patients received TCZ-SC monotherapy and 327 patients received TCZ-SC in combination with oral/SC MTX or other sDMARDs. Sustained clinical remission rates were comparable between the mono- and combination-therapy groups at 24 week (48.4% vs. 52.9%, p=0.523). Of the 179 patients who achieved sustained clinical remission during the phase 1, 89 were randomly assigned to receive TCZ-SC 162 mg qw and 90 to receive TCZ-SC 162 mg q2w. At the end of phase 2, the percentage of patients who maintained the remission at week 48 was 91.5% with TCZ-SC qw and 73.9% with TCZ-SC q2w (p=0.002). Main efficacy outcomes for both phases of the study are presented in the table. Rates of serious adverse events (AEs) and rates of AEs leading to drug discontinuation were similar in patients treated with mono or combination therapy, and in patients treated with TCZ-SC qw or TCZ-SC q2w.

Phase 1 – Outcome	TCZ-SC monotherapy N=74	TCZ-SC Combination N=327	p-value
Sustained clinical remission, %	48.4	52.9	0.523
ACR20, %	79.7	83.3	0.495
ACR50, %	59.4	58.7	0.923
ACR70, %	40.6	37.7	0.666
ACR90, %	23.4	16.7	0.207
HAQ-DI (baseline/24 weeks), mean	1.49/0.85	1.36/0.82	NS
Phase 2 – Outcome	**TCZ-SC 162 mg qw N=89**	**TCZ-SC 162 mg q2w N=90**	**p-value**
Clinical remission, %	91.5	73.9	0.002
ACR20, %	96.4	88.8	0.056
ACR50, %	88.1	79.8	0.766
ACR70, %	71.4	65.2	0.377
ACR90, %	45.2	32.6	0.088
Mean change in DAS28	-0.02	0.35	0.037

Conclusions: In the real world setting, treatment with TCZ-SC 162 mg weekly in patients with active RA is associated with rate of sustained clinical remission of approximately 50% regardless it is administered as monotherapy or in combination with a sDMARD. The proportion of patients who remained in clinical remission at week 48 was significantly higher with TCZ-SC qw than with TCZ-SC q2w. The safety profile of TCZ-SC was consistent with previous studies of TCZ-SC and TCZ-IV
Disclosure of Interest: R. Sanmarti Grant/research support from: Roche, E. Martín Mola Grant/research support from: Roche, J. Fonseca Grant/research support from: Roche, D. Veale Grant/research support from: Roche, A. Escudero Grant/research support from: Roche, C. González Grant/research support from: Roche
DOI: 10.1136/annrheumdis-2017-eular.4951

SAT0184 THERAPEUTIC DRUG MONITORING ON RHEUMATOID ARTHRITIS PATIENTS WITH REDUCED DOSES OF INTRAVENOUS TOCILIZUMAB

V. Ruiz-Esquide[1], C. Bastida[2], M. Pascal[2], J. Yagüe[3], D. Soy[2], R. Sanmartí[1]. *[1]Rheumatology; [2]Pharmacy; [3]Immunology, Hospital Clínic de Barcelona, Barcelona, Spain*

Background: Tocilizumab (TCZ) is an effective treatment for rheumatoid arthritis (RA). Literature suggests there is great variability in intravenous (iv) TCZ serum concentrations among individuals. Moreover, optimal drug dosage does not seem to be clear since Regulatory Agencies (FDA and EMA) approved the drug with a different initial posology. Empirical dose de-escalation strategies are being fostered in patients with disease remission.
Objectives: The purpose of the study was to examine TCZ serum concentrations at the different prescribed doses in RA. Secondary objectives were to evaluate the relationship between drug serum concentrations and laboratory parameters of disease activity.
Methods: Prospective, observational, single-center study conducted in a university tertiary hospital. Enrolled RA patients received iv TCZ at a dose range from 4 to 8 mg/kg every 28 days. Demographic characteristics and clinical laboratory data were obtained at study entry. Blood samples for drug concentration testing were collected from the third TCZ dose onwards, just before TZC infusion and, when possible, once a week until the next drug administration.
Results: 35 patients (88.6% women, 80% Caucasian) were included. Mean age ±SD was 54.1±12.3 and the median [range] of disease duration was 11.1 [2.9–48.5] years. Median treatment duration with iv TCZ was 36.5 [3–68] months. 54% of patients received the standard dose of 8mg/kg whereas the rest received reduced doses (23% were on 6mg/kg and 23% on 4mg/kg) due to persistent remission/low disease activity. 20 patients (57.1%) were being treated with low steroid dose and 24 (68.6%) were on concomitant DMARD, mainly methotrexate. Regarding drug concentration testing, a total of 109 samples were obtained. 19 patients participated to multiple drug sampling between two drug administrations and in the 17 remaining patients, a pre-dose sample was drawn. Mean TCZ concentrations are displayed in table 1 and showed in figure 1. No significant differences were observed in median pre-dose TCZ concentration values (54 samples) between patients on 8 and 6 mg/kg whereas significant lower drug levels were observed in those taking 4 mg/kg.
According to inflammatory parameters, mean C-reactive protein (CRP) concentration was significantly lower in those patients with trough TCZ concentrations >1μg/mL compared to those <1μg/mL (0.066mg/dL vs 0.689mg/dL, respectively; p<0.001). This difference was not observed with calprotectin serum concentrations (2.260μg/mL vs 2.143μg/mL).

Table 1. Mean (±sd) iv TCZ serum concentrations at different prescribed doses within time

Time (days)	TCZ 8 mg/kg	TCZ 6 mg/kg	TCZ 4 mg/kg
Pre-infusion (Ctrough)	8.9±6.1	5.7±9.1	0.8±1.2
T7	84.8±33.9	48.8±18.6	26.1±6.4
T14	46.4±19.8	31±11.4	15.2±5.6
T21	21.6±9.5	19.7±10.5	7.1±4.4
T28 (Ctrough)	10.6±7.3	10.3±10.8	1.3±2.3

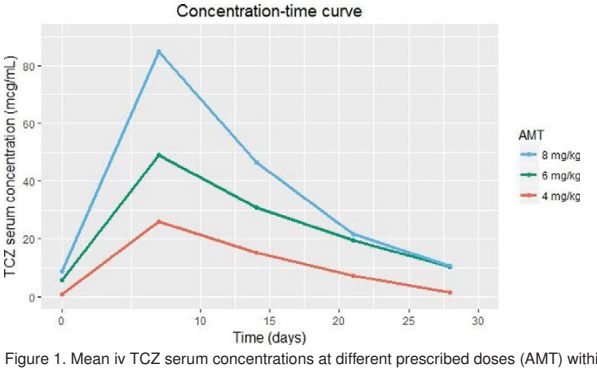


Figure 1. Mean iv TCZ serum concentrations at different prescribed doses (AMT) within time.

Conclusions: Trough TCZ serum concentrations do not differ between patients on an 8 and 6 mg/kg regimen. Therefore, according to the pharmacokinetics observed in our study, a maintenance dose of iv TCZ 6mg/kg would be appropriate for most RA patients. Although CRP levels are significantly higher in patients with trough iv TCZ concentrations <1μg/mL, serum calprotectin did not show the same tendency.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4518

SAT0185 **BIO-HOLIDAY THERAPY WITH A TIGHT CONTROL STRATEGY IN RHEUMATOID ARTHRITIS PATIENTS WITH CLINICAL DISEASE ACTIVITY INDEX REMISSION ENABLES MAINTENANCE OF BONE METABOLISM STATUS**

E. Torikai, M. Suzuki, Y. Matsuyama. *Orthopaedic Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan*

Background: The cost of Bio therapy has become a major problem in health economics and is unaffordable for some patients. Thus, it is important to consider whether we should discontinue or extend the interval of Bio. At EULAR 2016, we reported that maintaining disease activity, radiographic progression, and physical function via Bio-holiday therapy in rheumatoid arthritis (RA) patients with clinical disease activity index (CDAI) remission under a tight control strategy is possible. Osteoporosis is another issue for RA patients. RA patients generally develop osteoporosis more frequently than healthy individuals because of increased bone resorption and inhibited bone formation.
Objectives: To investigate bone metabolism markers and bone mass index of RA patients with CDAI remission who underwent Bio-holiday therapy.
Methods: Sixty-four RA patients with CDAI remission were included and were classified into two groups. Bio-holiday group (group H) comprised 34 patients [golimumab (GLM) and tocilizumab (TCZ), 18 and 16 patients, respectively] and in which patients were taken off Bio if they achieved CDAI remission. Patients visited our clinic at least once every 2 months and were treated with Bio within 3 months after falling out of CDAI remission. They could be taken off Bio again when they reached CDAI remission. The Bio group (group C) comprised 30 patients (GLM and TCZ, 16 and 14 patients, respectively). The mean ages of groups H and C were 52.9 and 55.6 years, respectively, and the mean disease durations were 3.98 and 4.13 years, respectively. There were no statistical differences between the backgrounds of the two groups. We compared the change in bone metabolism makers [urine type I collagen cross-linked N-telopeptide (NTX), serum tartrate-resistant acid phosphatase 5b (TRACP5b), serum bone-specific alkaline phosphatase (BAP), and serum osteocalcin (OC)] and bone mineral density (BMD) of lumber spine (L-spine) and femoral neck (FN) between both groups for 2 years.
Results: The mean withdrawal periods were 12.1 and 8.8 months with GLM and TCZ, respectively. Three and four patients dropped out because of financial constraints in the in the groups H and C, respectively. One patient in each group dropped out because of RA flare-up. No patients in either group discontinued their therapy because of adverse events. Besides one patient who dropped out because of RA flare-up, all remaining patients in the group H were able to achieve CDAI remission without delay. There were no statistical differences in CDAI throughout the study period (Fig.1). There were no statistical differences in any of the bone metabolism makers throughout the study period (Table.1) and BMD of L-spine (Fig. 2(a)) and FN (Fig. 2(b)) at baseline and last evaluation.

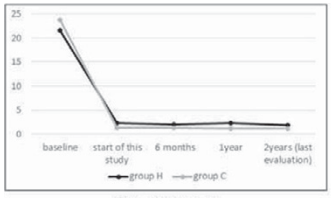


Fig.1 CDAI score

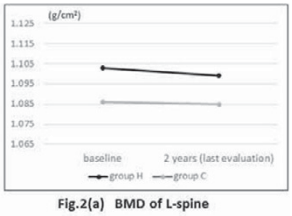


Fig.2(a) BMD of L-spine

[group H]	Start of this study	1 year	2 years
NTX(nmolBCE/mmolCr)	42.6± 24.7	44.3± 27.3	42.1± 26.6
TRCP5b (mU/dL)	355± 170	347± 156	364± 183
BAP (μg/L)	15.5± 6.1	16.5± 6.3	15.9± 6.0
OC (ng/mL)	11.9± 6.5	10.8± 6.2	11.3± 6.6
[group C]	Start of this study	1 year	2 years
NTX (nmolBCE/mmolCr)	40.3± 25.1	44.1± 28.4	43.5± 28.0
TRCP5b (mU/dL)	349± 169	352± 176	358± 165
BAP (μg/L)	15.9± 5.9	16.2± 6.1	16.4± 6.3
OC (ng/mL)	10.6± 5.9	10.9± 5.8	10.8± 6.2

Table.1 bone metabolism makers

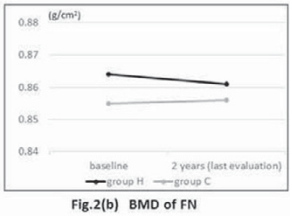


Fig.2(b) BMD of FN

Conclusions: We conclude that maintaining disease activity bone metabolism status via Bio-holiday therapy for RA patients with CDAI remission under a tight control strategy is possible. Given that the flare-up rate in RA patients with deep remission is not high, it is not difficult to resume Bio therapy and gain CDAI remission. Furthermore, this treatment is financially durable. Therefore, we recommend Bio-holiday therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2088

SAT0186 **EFFECTS OF DENOSUMAB, A SUBCUTANEOUS RANKL INHIBITOR, ON THE PROGRESSION OF STRUCTURAL DAMAGE IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH CSDMARDS: RESULTS FROM THE 12-MONTH DOUBLE BLIND PHASE 3, DESIRABLE STUDY**

T. Takeuchi[1], Y. Tanaka[2], S. Soen[3], H. Yamanaka[4], T. Yoneda[5], S. Tanaka[6], T. Nitta[7], N. Okubo[7], H.K. Genant[8], D. van der Heijde[9]. *[1]Keio University School of Medicine, Tokyo; [2]University of Occupational and Environmental Health, Kitakyushu; [3]Kindai University Nara Hospital, Ikoma; [4]Institute of Rheumatology Tokyo Women's Medical University, Tokyo, Japan; [5]Indiana University School of Medicine, Indianapolis, United States; [6]The University of Tokyo; [7]Daiichi Sankyo Co. Ltd, Tokyo, Japan; [8]University of California, San Francisco, United States; [9]Leiden University Medical Center, Leiden, Netherlands*

Background: Denosumab is a fully human monoclonal antibody (IgG_2 subclass) that inhibits bone resorption by inhibiting RANKL, a key mediator of osteoclast formation, function, and survival.
Objectives: To evaluate the effect of denosumab 60 mg every 6 months (Q6M) or every 3 months (Q3M) on the progression of joint damage in Japanese patients with RA on csDMARD background treatment.
Methods: DESIRABLE is a 12-month randomized, double-blind, placebo-controlled, parallel-group study in patients with RA receiving csDMARD treatment. Subjects fulfilling the 1987 ACR criteria or 2010 ACR-EULAR criteria were randomized (1:1:1) to denosumab 60 mg Q6M, denosumab 60 mg Q3M, or placebo. The primary endpoint is the change from baseline to 12 months in the van der Heijde modified total Sharp score (mTSS). Radiographs of hands and feet at baseline, 6 months and 12 months were scored with blinded time order by 2 readers independently. Average score of the 2 readers is used for the analysis. Comparisons of each denosumab group with placebo for the change from baseline were performed using van Elteren stratified rank test adjusting for baseline glucocorticoid use. Missing scores were imputed using linear extrapolation/interpolation.
Results: Among 679 patients randomized, 667 (placebo, n=223; Q6M, n=222; Q3M, n=222) received at least one dose of study drug, and 60 (placebo n=15; Q6M, n=23; Q3M, n=22) were discontinued during the study. Demographic and baseline characteristics were similar across the groups (Table 1). Mean change from baseline in mTSS and erosion score (ES) at 12 months was significantly lower with both denosumab 60 mg Q6M and Q3M compared with placebo, with no obvious evidence of an effect on joint space narrowing (JSN) score for denosumab. (Table 2).
Consistently, the percent of nonprogressors (ie, mTSS change $\leq$0.5) at 12 months was significantly greater with denosumab 60 mg Q6M (75.6%, p=0.010) and Q3M (78.1%, p=0.001) compared with placebo (64.2%).
Incidence of adverse events (AEs), serious AEs, and AEs leading to discontinuation of study drug were similar across treatment groups. No events of osteonecrosis of the jaw or atypical femoral fracture were observed.

Table 1. Baseline demographics and characteristics

Characteristic	Placebo N = 218	Denosumab 60 mg Q6M N = 217	Denosumab 60 mg Q3M N = 219
Female	167 (76.6)	168 (77.4)	154 (70.3)
Age (years)	55.8 ± 11.7	58.1 ± 12.3	58.2 ± 12.0
Disease duration (years)	2.1 ± 1.3	2.2 ± 1.3	2.2 ± 1.3
Rheumatoid factor positive	137 (62.8)	140 (64.5)	128 (58.4)
MTX use	190 (87.2)	176 (81.1)	189 (86.3)
Glucocorticoid use	69 (31.7)	73 (33.6)	68 (31.1)
DAS28-CRP	3.4 ± 1.0	3.6 ± 1.1	3.5 ± 1.0
mTSS	13.1 ± 21.4	15.9 ± 22.2	15.2 ± 19.0

Data presented are Mean ± SD or n (%).

Table 2. Change from baseline in mTSS, ES and JSN at 12 months

Characteristic	Placebo N = 218	Denosumab 60 mg Q6M N = 217	Denosumab 60 mg Q3M N = 219
mTSS	1.49 ± 3.76	0.99 ± 3.77 (p = 0.024)	0.72 ± 2.32 (p = 0.006)
Erosion score	0.98 ± 2.48	0.51 ± 2.15 (p = 0.010)	0.22 ± 0.95 (p < 0.001)
JSN score	0.51 ± 1.72	0.48 ± 2.08 (p = 0.257)	0.50 ± 1.76 (p = 0.533)

Data presented are Mean ± SD

Conclusions: Denosumab inhibited the progression of joint destruction significantly more than placebo and was generally well tolerated in Japanese patients with RA on csDMARDs. Denosumab has potential to be a new therapeutic option to inhibit structural progression for patients with RA.
Disclosure of Interest: T. Takeuchi Grant/research support from: Astellas, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, AYUMI Pharmaceutical, Takeda, Teijin Pharma, AbbVie, Asahi Kasei Pharma, and Taisho Toyama, Consultant for: AstraZeneca, Eli Lilly, Novartis, Mitsubishi Tanabe, Asahi Kasei Pharma, AbbVie, Daiichi Sankyo, Bristol-Myers Squibb, Nipponkayaku, Janssen, Merck Serono, Takeda, Astellas, and Pfizer, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi Tanabe, Pfizer, Takeda, Astellas, Daiichi Sankyo, Celtrion, and Nipponkayaku, Y. Tanaka Grant/research support from: BMS, MSD, Chugai, Mitsubishi Tanabe, Astellas, AbbVie, and Daiichi Sankyo, Speakers bureau: UCB Pharma, Mitsubishi Tanabe, Abbott, AbbVie, Eisai, Chugai, Janssen, Pfizer, Takeda, Astellas, Daiichi Sankyo, GSK, AstraZeneca, Eli Lilly, Quintiles, MSD, and Asahi Kasei Pharma, S. Soen Grant/research support from: Eisai, Daiichi Sankyo, and Takeda, Speakers bureau: Asahi Kasei Pharma, Astellas, Eisai, MSD, Ono Pharmaceutical, Daiichi Sankyo, Takeda, Chugai, Teijin

Pharma, and Pfizer, H. Yamanaka Grant/research support from: UCB Pharma, AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda, Consultant for: UCB Pharma, AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi Tanabe, Pfizer, and Takeda, T. Yoneda Consultant for: Daiichi Sankyo, S. Tanaka Consultant for: Amgen inc, Amgen Astellas, KYOCERA Medical, Daiichi Sankyo, Teijin Pharma, Asahi Kasei Pharma, Ono Pharmaceutical, Eli Lilly, and Pfizer, T. Nitta Employee of: Daiichi Sankyo, N. Okubo Shareholder of: Daiichi Sankyo, Employee of: Daiichi Sankyo, H. K. Genant Consultant for: Daiichi Sankyo, Pfizer, Amgen, BioClinica, Eli-Lilly, Janssen, Servier, Novartis, Takeda, Merck, Biomarin, Clemencia, Agnovos, and Regeneron, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi Sankyo, Eli-Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, and UCB Pharma, Employee of: Imaging Rheumatology bv

DOI: 10.1136/annrheumdis-2017-eular.1081

SAT0187 SAFETY, PHARMACOKINETICS AND EFFICACY OF E6011, AN ANTI-FRACTALKINE MONOCLONAL ANTIBODY, IN A FIRST-IN-PATIENT PHASE 1/2 STUDY IN RHEUMATOID ARTHRITIS; ADDTIONAL DATA OF 400 MG COHORT

Y. Tanaka[1], T. Takeuchi[2], H. Umehara[3], T. Nanki[4], N. Yasuda[5], F. Tago[6], Y. Kitahara[6], M. Kawakubo[6], S. Hojo[6], T. Kawano[5], T. Imai[5]. *[1]University of Occupational and Environmental Health, Japan, Kitakyushu; [2]Keio University, Tokyo; [3]Division of Rheumatology and Immunology, Nagahama City Hospital, Shiga; [4]School of Medicine, Faculty of Medicine, Toho University, Tokyo; [5]KAN Research Institute, Inc., Kobe; [6]EISAI Co. Ltd., Tokyo, Japan*

Background: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. Accumulating evidence is telling that FKN-CX3CR1 axis plays a pivotal role in leukocyte/lymphocyte accumulation in inflamed tissues in RA[1]. Last year, we presented an interim report (up to 200 mg cohort) of Phase 1/2 study of E6011, a novel humanized anti-FKN monoclonal antibody, for active Japanese RA patients[2].

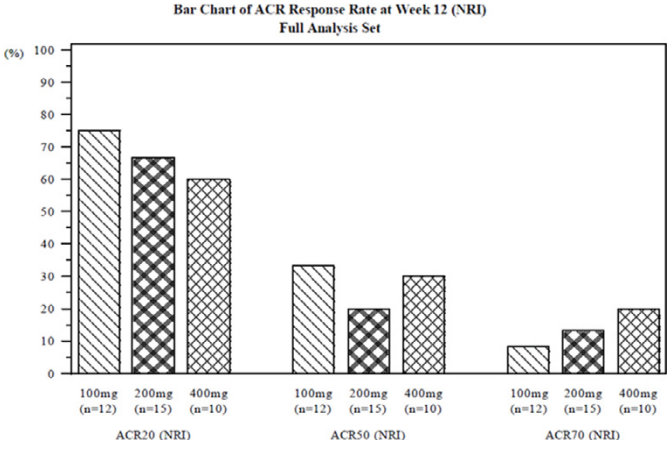
Objectives: To evaluate safety, pharmacokinetics and efficacy of E6011 with the dosage up to 400 mg in a Phase 1/2, open-label, multiple ascending dose study in RA patients (NCT02196558).

Methods: Active RA patients with inadequate response (IR) to MTX or TNF inhibitors (TNFi) were received 7 consecutive doses (subcutaneous) of E6011 at week 0, 1, 2 and thereafter every 2 weeks up to week 10. The safety, pharmacokinetics and efficacy up to week 12 were evaluated.

Results: Twelve, 15 and 10 subjects were enrolled in the cohort of 100, 200 and 400 mg dosage, respectively, in total 37 subjects received repeated subcutaneous (SC) administrations of E6011. As a result, repeated dose of E6011 was found safe and well tolerated. The incidence of adverse event (AE), treatment-related AE and serious AE were 56.8%, 29.7% and 5.4%, respectively. AEs occurring in ≥2 subjects were nasopharyngitis, Injection site erythema, headache and oropharyngeal pain, among which there were no severe AEs, serious infections and deaths. No significant differences were observed in the incidence or severity of AEs across the cohorts.

After starting multiple SC injection of E6011, serum E6011 concentration reached steady-state at week 2, and its level was maintained up to week 12 in all cohorts. Clinical outcome was also available in the study in which response rates of ACR20, 50 and 70 at week 12 calculated using the non-responder imputation (NRI) were 75.0%, 33.3%, 8.3% in 100 mg cohort, 66.7%, 20.0%, 13.3% in 200 mg cohort and 60.0%, 30.0%, 20.0% in 400 mg cohort, respectively. The percentage of patients categorized "good response" with the EULAR response criteria at week 12 (NRI) were 16.7% in 100 mg cohort, 20% in 200 mg cohort and 40% in 400 mg cohort.

Conclusions: E6011 was safe and well tolerated, and the study demonstrated a promising efficacy of E6011 in active RA patients with MTX- or TNFi-IR. The results obtained suggest that a novel approach to target FKN/CX3CR1 interaction will be clinically beneficial for RA, and support to conduct phase 2 clinical trials in which the efficacy and safety should be confirmed in a placebo controled double-blind manner.



References:

[1] Nanki T. Arthritis Rheum. 2002; 46(11):2878–83.
[2] Tanaka Y, et al., EULAR Congress 2016, Poster Number FRI0236.

Acknowledgements: The authors wish to thank the study investigators.

Disclosure of Interest: Y. Tanaka Grant/research support from: Mitsubishi-Tanabe, Takeda, Daiichi-Sankyo, Chugai, Bristol-Myers, MSD, Astellas, Abbvie, Eisai, Speakers bureau: Abbvie, Chugai, Daiichi-Sankyo, Bristol-Myers, Mitsubishi-Tanabe, Astellas, Takeda, Pfizer, Teijin, Asahi-kasei, YL Biologics, Sanofi, Janssen, Eli Lilly, GlaxoSmithKline, T. Takeuchi Grant/research support from: Astellas, Bristol-Myers, Chugai, Daiichi-Sankyo, Eisai, AYUMI, Takeda, Teijin, AbbVie, Asahikasei, Taisho-Toyama, Consultant for: Astra Zeneca, Eli Lilly, Novartis, Mitsubishi-Tanabe, Asahi-Kasei, AbbVie, Daiichi-Sankyo, Bristol-Myers, Nipponkayaku, Janssen, Merck Serono, Takeda, Astellas, Pfizer, Speakers bureau: AbbVie, Bristol-Myers, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Pfizer, Takeda, Astellas, Daiichi-Sankyo, Celtrion, Nipponkayaku, H. Umehara: None declared, T. Nanki Grant/research support from: Chugai, Eisai, Takeda, Teijin, Eli Lilly, Bristol-Myers, AbbVie, Ono, Novartis, Asahi-Kasei, Consultant for: UCB, Eisai, Chugai, Speakers bureau: Mitsubishi-Tanabe, Chugai, Eisai, Takeda, Astellas, Janssen, Eli Lilly, Ayumi, Pfizer, Ono, AbbVie, N. Yasuda Shareholder of: EISAI, Employee of: EISAI, F. Tago Employee of: EISAI, Y. Kitahara Shareholder of: EISAI, Employee of: EISAI, M. Kawakubo Shareholder of: EISAI, Employee of: EISAI, S. Hojo Employee of: EISAI, T. Kawano Employee of: KAN Research Institute, T. Imai Employee of: KAN Research Institute

DOI: 10.1136/annrheumdis-2017-eular.1401

SAT0188 FIRST-LINE TREATMENT PATTERNS OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY POSITIVE VERSUS NEGATIVE

K. Price[1], Y. Doleh[1], M. Eaddy[2], A. Ogbonnaya[2], H.-C. Shih[2], H. Ahmad[1], L. Lamerato[3], A. Szymialis[1]. *[1]Bristol-Myers Squibb, Princeton; [2]Xcenda, LLC, Palm Harbor; [3]Henry Ford Health System, Detroit, United States*

Background: Patients with RA who are at a higher risk for progressive and destructive arthritis could be identified using anti-cyclic citrullinated peptide (anti-CCP) levels.[1] Treatment guidelines recommend the use of non-biologic DMARDs as initial treatment in RA; but, if warranted, biologic (b)DMARDs could be considered in early treatment of RA.[2] Real-world data describing treatment patterns based on anti-CCP designations are limited.

Objectives: This study evaluated treatment patterns of patients with RA who are anti-CCP positive (+) or negative (–).

Methods: This retrospective study was based on electronic medical record (EMR) data with a supplemental chart review from a large integrated delivery system. Patients newly diagnosed with RA (International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis code 714.0x) were identified between 1 January 2009 and 31 December 2014. The first RA diagnosis date was designated as the index date. Patients were required to have 12 months of continuous activity in the EMR (6 months pre- and 6 months post-index). Based on the baseline anti-CCP test results, patients were categorized as anti-CCP+ (≥7.0 U) or anti-CCP– (<7.0 U). First-line therapy (time to treatment initiation, treatment regimen, treatment changes and response to treatment) was evaluated in the post-index period. Response to treatment was determined based on physicians' notes.

Results: Overall, 217 anti-CCP+ and 191 anti-CCP– patients with RA were included in this study. A higher proportion of anti-CCP+ (153, 70.5%) than anti-CCP– patients (44, 23.0%; p<0.0001) initiated treatment, generally within 1 month after diagnosis (anti-CCP+, mean [SD]: 31.1 [42.1] days and anti-CCP–, 28.1 [37.4] days; p=0.6538). MTX was most commonly used as first-line therapy. More anti-CCP+ than anti-CCP– patients received MTX (73.2 vs 56.8%; p=0.0374), while more anti-CCP– than anti-CCP+ patients received hydroxychloroquine (31.8 vs 13.1%; p=0.0037). Only three anti-CCP+ and no anti-CCP– patients were treated with a bDMARD. Response to treatment was similar between the cohorts (p=0.2444); 22.9% of anti-CCP+ and 18.2% of anti-CCP– patients had a complete response to the first-line therapy, and 33.3% of anti-CCP+ and 25.0% of anti-CCP– patients had a partial response to the first-line therapy. Treatment change, however, significantly differed between the two cohorts (p=0.0058); 11.1 and 9.1% of patients discontinued, 9.8 and 9.1% of patients switched, and 3.9 and 9.1% of patients augmented in the anti-CCP+ and anti-CCP– cohorts, respectively. Treatment changes occurred approximately 3 months after treatment initiation (anti-CCP+, 82.0 [49.7] days and anti-CCP–, 83.8 [52.7] days; p=0.9178).

Conclusions: After diagnosis of RA, patients who are anti-CCP+ were more likely to start therapy, indicating that physicians were more aggressive in treating this cohort. Patients were treated according to guidelines with non-biologic DMARDs, predominantly MTX. Patterns of treatment change differed between the cohorts; however, treatment response was similar with a complete response rate of 20%.

References:

[1] Singh JA, et al. Arthritis Rheumatol 2016;68:1–26.
[2] Niewold TB, et al. QJM 2007;100:193–201.

Disclosure of Interest: K. Price Employee of: Bristol-Myers Squibb, Y. Doleh Employee of: Bristol-Myers Squibb, M. Eaddy Consultant for: Xcenda, A. Ogbonnaya Employee of: Xcenda, H.-C. Shih Employee of: Xcenda, H. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, L. Lamerato Grant/research support from: Centers for Disease Control, National Cancer Institute, Policy Analysis, Inc, Outcomes Research Solutions, Xcenda, eMAXHealth, Merck Pharmaceuticals, Pfizer Pharmaceuticals, Reagan Udall Foundation, AstraZeneca, Employee of: Henry Ford Health System, University of Michigan-Dearborn, A. Szymialis Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb
DOI: 10.1136/annrheumdis-2017-eular.1794

SAT0189 FACTORS INFLUENCING THE PRESCRIPTION OF TOCILIZUMAB ALONE OR IN COMBINATION WITH DMARDS IN RHEUMATOID ARTHRITIS PATIENTS IN A REAL LIFE SETTING. POOLED ANALYSIS OF 3 OBSERVATIONAL STUDIES

A. Saraux[1], A. Cantagrel[2], B. Combe[3], R.-M. Flipo[4], I. Idier[5], C. Baffie[6], J. Tebib[7]. *[1]Rheumatology, University Hospital, Brest; [2]Rheumatology, University Hospital, Toulouse; [3]Rheumatology, University Hospital, Montpellier; [4]Rheumatology, University Hospital, Lille; [5]Medical, Chugai Pharma France, Paris la Defense; [6]Statistics, Roche SAS, Boulogne; [7]Rheumatology, University Hospital, Lyon, France*

Background: Tocilizumab (TCZ) as monotherapy (Mono) is nowadays a standard treatment in rheumatoid arthritis (RA) for patients in whom methotrexate (MTX) is inappropriate[1].
Objectives: To describe factors influencing the use of TCZ in Mono or in combination with DMARDs (Combo) in real-life practice in RA patients (pts).
Methods: *Analysis:* pooled data of 3 prospective, multicentre, observational studies (PEPS n=610, Spare-1 n=307, Act-solo n=577). *Patients:* RA pts requiring TCZ treatment according to their physician. *Treatment:* TCZ as prescribed in real life. *Endpoint:* Evaluation of factors influencing the use of TCZ in Mono or in Combo. *Data collected:* demographic characteristics, past medical history, RA characteristics and history including previous RA treatments, TCZ treatment strategy (Mono or Combo). *Statistical analysis:* Pts fulfilling inclusion and non-inclusion criteria and with ≥1 TCZ infusion were analyzed. 1- descriptive analysis 2- Univariate and multivariate analysis to determine factors influencing the use of TCZ in Mono. Variables with more than 20% of missing data were excluded from the multivariate model.
Results: 1494 pts (3 studies) were analysed at inclusion. Pts' characteristics: 56% of the pts were >55 years old, 79.6% female, mean RA duration 11.1±9.3 years, 83.0% positive for rheumatoid factors and/or ACPA, 77.3% with erosive disease on X-rays, mean ESR 29.9±23.1mm, mean CRP 19.9±26.2 mg/l mean DAS 28-ESR 5.21±1.22, mean HAQ-DI 1.56±0.68, and mean pain VAS 61.5±23.2. Past RA treatment included csDMARDs in 98.5% and biologics in 77.8% (median=2 [1–6]). TCZ was initiated as Mono in 36.4% of pts and in Combo in 63.6%, with MTX in 83.3% of Combo pts (mean dose 15.7±4.4mg/week). Corticosteroids were used in 74% of pts (mean dose 10±7mg/day). Variables associated with a TCZ prescription in Mono were age (≥65 years), number of previous bDMARD, use/dose of steroids, ESR/CRP values, VAS global activity (physician and pt), pain VAS and HAQ-DI. In the multivariate analysis, variables associated with a TCZ prescription in Mono were age ≥65 years (OR=1.71 [1.30 - 2.24], p<0.001), number of previous bDMARD (1 bDMARD, OR=1.35 [0.94 - 1.92], 2 bDMARD OR=1.82 [1.28 - 2.60], ≥2 bDMARD, OR=1.19 [0.82 - 1.71] p=0.006), higher pain VAS (OR=1.09 [1.04 - 1.15], p=0.001), higher ESR value (OR=1.07 [1.02 - 1.12], p=0.013).
Conclusions: This pooled analysis suggests that physicians preferably prescribe TCZ alone in older patients, heavily treated before, with higher inflammatory markers and higher pain VAS. This use might be explained by physicians' reluctance to prescribe the association in frailer patients and complementary data on comorbidity factors will be analysed to support this hypothesis.
References:
[1] JS. Smolen et al, Ann Rheum Dis doi:10.1136/annrheumdis-2013–204573.
Disclosure of Interest: A. Saraux: None declared, A. Cantagrel: None declared, B. Combe Consultant for: Chugai Pharma France, R.-M. Flipo Consultant for: Chugai Pharma France, I. Idier Employee of: Chugai Pharma France, C. Baffie Employee of: Altizem for Roche SAS, J. Tebib: None declared
DOI: 10.1136/annrheumdis-2017-eular.2916

SAT0190 ESTIMATE OF CLINICAL AND ANTIDESTRUCTIVE EFFECTS OF RITUXIMAB IN RHEUMATOID ARTHRITIS

A.V. Pivanova, G. Lukina, Y. Sigidin, A. Smirnov, K. Kuzikyants, A. Kuznetsova. *Nasonova Research Institute of Rheumatology, MOSCOW, RUSSIA, Moscow, Russian Federation*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by synovial hyperplasia, mononuclear cell infiltration, bone erosion and joint destruction. Antirheumatic treatment plays a important role in controlling the inflammation of rheumatoid arthritis and in minimizing joint damage. Rituximab - it is a chimeric monoclonal antibody that targets the CD20 molecule expressed on the surface of B cells. It has been successfully used to treat rheumatoid arthritis, and it is worth noting that his antidestructive effect sometimes does not meet the clinical.
Objectives: to assess clinical and antidestructive effect of Rituximab (RTX) in patients with rheumatoid arthritis (RA).
Methods: 108 patients (pts) with RA, most of them were middle-age women with high disease activity (mean DAS28 6,1±1,04, RF-positive 77%, ACCP-positive 83%) treated with RTX (1000 mgx2 or 500 mgx2). Clinical effect was evaluated by EULAR criteria; radiological progression by SVH method.
Results: 104 patients were treated by RTX (500 x2 or 1000 x2), had good response: after 48 week of treatment clinical improvement was achieved in 65% pts, good and moderate response by EULAR criteria in 23% and 42% pts accordingly. Noteworthy, after 12 months of treatment RTX radiological progression was absent in 50% pts with high disease activity.
Conclusions: RTX treatment slowed joint damage without clinical improvement. Clinical and antidestructive results did not always coincide which suggests different mechanisms of clinical and antidestructive effects of anti-B-cell therapy
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6524

SAT0191 PATTERNS OF INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS AND ABATACEPT. MULTICENTER STUDY OF 63 PATIENTS

C. Fernández-Díaz[1], S. Castañeda[2], C. Ojeda[3], A. Olivé[4], P. Carreira[5], T. Perez-Sandoval[6], M. Retuerto[7], E. Cervantes[8], S. Rodriguez[4], B. Robles[9], B. Hernandez[3], A. Urruticoechea[10], O. Maiz[11], D. Palma[12], L. Arboleya[13], G. Bonilla[14], I. Rodriguez[15], C. Delgado[16], R. Exposito[17], A. Ruibal[18], J. Blanco[19], M. Rodriguez[20], J. Bernal[21], P. Vela[21], B. Alvarez[22], C. Fito[23], J. Narvaez[24], M. Moreno[25], M. Lopez[26], N. Mena[27], S. Romero[28], C. Aguilera[29], S. Ordoñez[30], I. Villa[31], V. Mora[1], M. Gonzalez-Gay[1], J. Hernandez[1], R. Blanco[1]. *[1]HUMV, Santander; [2]H.Princesa, Madrid; [3]H Macarena, Sevilla; [4]H Trias, Barcelona; [5]H 12 Octubre, Madrid; [6]H; [7]H., Leon; [8]H, Santiago; [9]H. P Hierro, Madrid; [10]H, Ibiza; [11]H, Donostia; [12]H, Lorca; [13]H, Oviedo; [14]H. Paz, Madrid; [15]H, Vigo; [16]H., Zaragoza; [17]H., Laredo; [18]H., Araba; [19]H.Basurto, Bilbao; [20]H., Ourense; [21]H., Alicante; [22]H, Araba; [23]H, Pamplona; [24]H.Bellvitge, Barcelona; [25]H.Arrixaca, Murcia; [26]HVHebron, Barcelona; [27]H, Malaga; [28]H, Pontevedra; [29]H, Sevilla; [30]H, Lleida; [31]H, Sierrallana, Spain*

Background: Disease modifying antirheumatic drugs (DMARDs) such as methotrexate (MTX), leflunomide (LFN) or antiTNFα have been implicated in development/exacerbation of Interstitial lung disease (ILD)of rheumatoid arthritis (RA). Several radiological patterns of ILD have been described: i) usual interstitial pneumonia (UIP), ii) nonspecific interstitial pneumonia (NSIP), iii) obliterating bronchitis (OB), and iv) Organized pneumonia (OP)
Objectives: To assess the response to Abatacept (ABA) in these patterns of ILD
Methods: Multicenter study of RA-ILD treated with ABA. ILD was diagnosed by high-resolution CT scan (HRCT) and classified in radiological patterns (Travis et al). We consider 3 subgroups: a) UIP, b) NSIP and c) "other" (OB, OP or mixed). ABA was used at iv or sc standard dose. We assessed: a) Dyspnea (Medical Research Council-modified scale; significant variations≥1); B) Respiratory function tests; significant changes≥10% in forced vital capacity (FVC) and DLCO≤10%, c) HRCT, d) DAS28. A comparative study was performed for the quantitative (U-Mann-Whitney) and qualitative variables (Fisher test) between the baseline and 3, 6 and 12 months.
Results: We included 63 patients (27 women/36 men), mean age; 63.1±9.6 years. At ABA onset the RA had a median evolution of 6.8 [2–13.6] years and the ILD of 1 [0.3–3.03]. RA was seropositive in 85.7%. The diagnosis of ILD was confirmed by biopsy (n=18). The ILD was related to DMARDs: MTX (4), etanercept (3), adalimumab (3), certolizumab (2), Infliximab (1). ABA was used in monotherapy (26) or combined with other DMARDs (37); LFN (15), Cyclosporin (1), sulfasalazine (4), MTX (6), hydroxychloroquine (10), azathioprine (4), chloroquine (1). Table 1 shows the evolution in the available cases. A significant improvement in dyspnea and HRCT was observed in the NIU type. DLCO remained stable in most patients regardless of the radiological pattern. The activity of RA (DAS28) also improved.

Table 1

	Baseline			3month			6month			12month		
	UIP	NSIP	Others	UIP	NSIP	Other	UIP	NSIP	Other	UIP	NSIP	Other
MMRC. n(%)				n=26	n=16	n=16	n=24	n=16	n=15	n=13	n=10	n=8
No changes	n=29	n=17	n=17	18 (65.4)	12 (75)	13 (81.3)	17 (70.8)	12 (75.9)	11(73.3)	7 (53.8)	7 (70)	6 (75)
Improvement				**9(34.6)****	3 (18.8)	3 (18.7)	**5(20.8)***	3 (23.1)	4 (26.7)	**3 (23.1)***	3 (30)	2 (25)
Worsening				0	1 (6.2)	0	2(8.4)	0	0	3 (23.1)	0	0
CVF. n (%)				n=12	n=4	n=2	n=6	n=7	n=3	n=10	n=5	n=7
No changes	n=27	n=17	n=16	10 (83)	3 (75)	2 (100)	5 (83.3)	1 (14.3)	3 (100)	10(100)	3 (60)	2 (28.6)
Improvement				2 (16.7)	0	0	1 (16.7)	**4 (57.1)****	0	0	2 (40)	**3 (28.6)***
Worsening				0	1(25)	0	0	2 (28.6)	0	0	0	2 (28.6)
DLCO. n (%)				n=7	n=4	n=2	n=5	n=3	n=3	n=7	n=3	n=6
No changes	n=23	n=12	n=13	5 (71.4)	4 (100)	1 (50)	3 (60)	2 (66.7)	2 (66.7)	5 (71.6)	2 (66.7)	3 (33.3)
Improvement				2 (28.6)	0	1 (50)	1 (20)	0	0	2 (28.6)	0	2 (5)
Worsening				0	0	0	1 (20)	1 (33.3)	1 (33.3)	0	1 (33.3)	1 (16.7)
HRTC. n (%)				n=6	n=3	n=1	n=6	n=5	n=5	n=9	n=5	n=3
No changes	n=29	n=17	n=17	3 (50)	2 (66.7)	0	3 (50)	2 (40)	2 (40)	4 (44.4)	2 (40)	1 (33.3)
Improvement				**2 (33.3)***	1 (33.3)	1 (100)	1 (16.7)	2 (40)	**3 (60)***	**3 (33.3)***	2 (40)	**2 (66.7)***
worsening				1 (16.7)	0	0	2 (33.3)	1 (20)	0	2 (22.2)	1 (20)	0
DAS28	n=29	n=16	n=16	n=17	n=8	n=8	n=14	n=13	n=9	n=14	n=10	n=9
median[IQR]	5.3 [4.4-6.3]	5.17[3.5-5.9]	5.21[3.8-5.9]	3.0 [2.24.8]	3.1[2.24.8]	**2.3[1.9.4.4]***	3.7[2.24.9]	**3.1[2.6.4.6]***	**2.8[1.3.3.7]***	**3.8[2.5.5.1]***	3.1[2.3-3.9]	**3.1[2.3.4.5]***
CRP (mg/dl),	n=29	n=14	n=16	n=17	n=5	n=9	n=14	n=12	n=10	n=14	n=9	n=9
median[IQR]	3.1 [0.8-8.7]	1.7 [0.9-4.9]	1.7 [1.0-4.8]	1.2 [0.3-5.4]	3.3[0.9-7.0]	1.5[0.6-3.9]	1.9[0.4-10.1]	**0.8 [0.4-2.1]***	**0.6 [0.5-1.9]***	4.2[0.8-13.0]	1.5 [0.4-7.6]	1.5[0.7-4.6]
ESR (mm/1st h),	n=29	n=15	n=16	n=20	n=5	n=9	n=16	n=12	n=10	n=13	n=10	n=10
median[IQR]	32[11.5-49.0]	41.0[30.0-63.0]	26.5[16.8-51.3]	16.5[10-40.8]	52.0[25.5-71.5]	19[10.5-29.5]	43[10.5-66.5]	**18.5 [8.0-29.8]***	18.5[9.0-44.5]	43.0[10.5-63.5]	**31.0 [18.0-54.0]***	27.0[14.3-38.0]
Prednisone mg	n=26	n=17	n=14	n=18	n=11	n=8	n=5	n=12	n=9	n=9	n=8	n=8
median[IQR]	7.5[5.0-11.3]	10.0[5.0-25.0]	7.8[4.4-15.0]	5.0[5.0-10.0]	7.5[5.0-25.0]	7.5[5.0-13.8]	5.0[5.0-10.0]	**5.0[2.5-7.5]***	**5.0 [3.8-7.8]***	5.0[2.5-18.8]	**5.0 [3.1-7.5]***	3.8 [2.5-6.9]

The comparisons are with respect to the baseline visit. * p <0.05; ** p <0.01.For the qualitative variables only the variable "improvement" is calculated.

Conclusions: ABA appears to be effective in ILD associated-RA, including the pattern of poor prognosis (UIP).

References:
[1] Travis WD et al. J Respir Crit Care Med 2013 188:733–748.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3492

SAT0192 SARILUMAB SUPPRESSES THROMBOSIS-RELATED GENE EXPRESSION IN CIRCULATING BLOOD CELLS IN MTX-IR AND TNF-IR PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

C. Paccard[1], J. Msihid[1], A. Brisacier[1], A. Damask[2], C. Paulding[2], M. Zilberstein[3], A. Boyapati[2]. *[1]Sanofi R&D, Chilly-Mazarin, France; [2]Regeneron Pharmaceuticals, Inc, Tarrytown; [3]Sanofi R&D, Bridgewater, United States*

Background: Bone and joint damage due to chronic inflammation in the synovium of patients with RA is mediated by IL-6 and other cytokines. IL-6 mediates effects inside the joint and systemically and is blocked by sarilumab, a human mAb blocking the IL-6R?. Safety and efficacy of SC sarilumab (150 or 200 mg q2w) was evaluated in combination with MTX in patients with RA and inadequate response (IR) to MTX (MOBILITY; NCT01061736) or csDMARDs in patients with RA and IR or intolerance to ≥1 TNFi (TARGET; NCT01709578).

Objectives: To compare gene expression patterns in circulating blood cells after treatment with sarilumab vs placebo in patients from MOBILITY and TARGET.

Methods: Total RNA was isolated from whole blood collected at baseline (predose) and wk 2 posttreatment in patients from MOBILITY (placebo, n=58; sarilumab 150 mg q2w, n=60; sarilumab 200 mg q2w, n=46) and TARGET (placebo, n=19; sarilumab 150 mg q2w, n=27; sarilumab 200 mg q2w, n=16). Gene expression data were generated using microarray analyses (Agilent 8 × 60k platform). Data were processed using the limma package (R Bioconductor). Background correction and quantile normalization were performed and probes with low expression were filtered; 48,109 probes were analyzed. Effect of sarilumab vs placebo on gene expression was assessed in each study using linear mixed models. *P* values were adjusted using the Benjamini-Hochberg procedure to control false discovery rate (FDR; 5% threshold).

Results: After *P* value adjustment to control FDR at 5%, 2 genes implicated in thrombosis and atherosclerosis (thrombomodulin [THBD] and platelet endothelial cell adhesion molecule 1 [PECAM-1]) were downregulated after treatment with sarilumab 200 mg q2w vs placebo in both studies (Table). These genes decreased with a fold-change (FC) ≤0.8 in both studies ($P<0.001$). An additional gene associated with coagulation, von Willebrand factor (vWF), was significantly decreased in MTX-IR but not TNF-IR patients. Numerical decreases in gene expression between sarilumab 150 mg q2w and placebo did not reach significance.

Table 1. Select Genes Regulated by Sarilumab 200 mg q2w at Week 2

	MOBILITY Sarilumab 200 mg q2w + MTX		TARGET Sarilumab 200 mg q2w + csDMARDs	
Gene	*P* value	Fold reduction[a]	*P* value	Fold reduction[a]
THBD	6.3×10^{-7}	0.67	3.9×10^{-6}	0.58
PECAM-1	1.6×10^{-9}	0.78	2.1×10^{-4}	0.78
vWF	1.3×10^{-10}	0.58	0.55	0.91

[a]Fold reduction vs placebo.

Conclusions: In patients with active RA, sarilumab may decrease thrombosis-related gene expression in circulating immune cells. Additional analysis of the serum levels of thrombosis risk proteins is needed to test the hypothesis that sarilumab treatment decreases levels of thrombosis risk factors.

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: C. Paccard Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, J. Msihid Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, A. Brisacier Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, A. Damask Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, C. Paulding Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, M. Zilberstein Shareholder of: Sanofi R&D, Employee of: Sanofi R&D, A. Boyapati Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc

DOI: 10.1136/annrheumdis-2017-eular.5183

SAT0193 RA PATIENTS WITH INFLAMMATORY ANEMIA BENEFIT FROM INCREASED HEMOGLOBIN AND DECREASED FATIGUE UNDER TOCILIZUMAB THERAPY

C. Specker[1], H. Kellner[2], P. Kästner[3], C. Volberg[4], V. Braunewell[5], I. Schwarze[6], M. Aringer[7], M. Sieburg[8], M.W. Hofmann[9], J.P. Flacke[10], H.-P. Tony[11], G. Fliedner[12]. *[1]Kliniken Essen Süd, Essen; [2]Schwerpunktpraxis für Rheumatologie und Gastroenterologie, München; [3]MVZ Ambulantes Rheumazentrum Erfurt, Erfurt; [4]Rheumazentrum Neuss, Neuss; [5]Schwerpunktpraxis Rheumatologie, Mönchengladbach; [6]Praxis für Internistische Rheumatologie, Leipzig; [7]Medizinische Klinik III, Rheumatologie, Technischen Universität Dresden, Dresden; [8]Rheumatologische Gemeinschaftspraxis, Magdeburg; [9]Rheumatologie, Chugai Pharma Europe Ltd., Frankfurt; [10]Rheumatologie, Roche Pharma AG, Grenzach-Wyhlen; [11]Rheumatologie/Immunologie der Medizinischen Klinik und Poliklinik II, Universitaetsklinikum Wuerzburg, Wuerzburg; [12]Rheumapraxis, Osnabrueck, Germany*

Background: According to WHO definition approximately 15% of all patients with rheumatoid arthritis (RA) suffer from anemia (hemoglobin <13 g/dl for men and <12 g/dl for women). Interleukin 6 (IL-6) takes an active part in the pathogenesis of this inflammatory anemia.

Objectives: The 6th interim analysis of the non-interventional ICHIBAN study (NCT01194401) evaluated the occurrence of inflammatory anemia, characterized the patient population with anemia, and observed the response during intravenous Tocilizumab therapy (TCZ i.v.). Patients were subgrouped according to their anemic/non-anemic status at baseline.

Methods: Since 2010 the ICHIBAN study collects clinical data of the routine use of TCZ i.v. in RA patients. The observation period for each patient is up to two years. At the due date of the current interim analysis (Dec 10, 2015) 2999 patients were enrolled. 902 patients have completed the maximal 104 weeks observation period (Group W104).

Results: At baseline, the proportion of patients with anemia (acc. to WHO definition) was 21.4% (men) and 22.0% (women) in the group W104.

On comparison, RA patients with anemia showed, amongst others, increased inflammation parameters, a higher disease activity and higher rates of comorbidities. Already after 4 weeks with TCZ i.v. the proportion of patients with anemia improved to 12.1% (men) and 12.7% (women). After 104 weeks therapy the proportion of patients with anemia reduced further to 7.4% (men) and 8.4% (women). The relevant response parameters and laboratory values are shown in Table 1.

Despite the higher disease activity at baseline for anemic patients, the benefit was comparable for patients with and without anemia. DAS28-ESR values decreased on average by 2.9 (women) and 3.1 (men) in RA patients with anemia and by 2.7 (women) and 2.8 (men) in RA patients without, resulting in similar disease scores at the end of the observational period.

The effectiveness of TCZ i.v. was also confirmed by patient reported outcomes (PROs) via visual analogue scales (VAS). In particular, a reduction of the intensity of pain (>50%) and a reduction of fatigue (>38%) was observed (Table 1).

Table 1 Treatment response to TCZ in anemic patients (at baseline)

		Week 0 (Baseline)	Last visit with TCZ
% Anemia	male	21.4% (46/215)	7.4% (16/215)
	female	22.0% (151/687)	8.4% (58/687)
Hemoglobin [g/dl]	male	12.2 (11.8, 12.7)	13.8 (13.2, 14.7)
Median (Q1, Q3)	female	11.1 (10.3, 11.6)	12.7 (11.9, 13.4)
Erythrocytes [10^{12}/l]	male	4.5 (4.0, 4.7)	4.7 (4.3, 5.0)
Median (Q1, Q3)	female	4.1 (3.8, 4.4)	4.2 (4.0, 4.5)
CRP [mg/l]	male	42.1 (27.3, 71.2)	7.3 (1.5, 25.4)
Median (Q1, Q3)	female	30.0 (11.1, 61.0)	3.1 (1.0, 11.9)
ESR [mm/h]	male	46.5 (30.0, 68.0)	4.5 (2.0, 13.0)
Median (Q1, Q3)	female	42.0 (28.0, 74.0)	8.0 (4.0, 16.0)
DAS28-ESR			
Change from baseline	male		-3.1 ± 2.1
Mean ± SD	female		-2.9 ± 1.5
% Remission (< 2.6)	male	0.0% (0/46)	52.2% (24/46)
	female	0.0% (0/151)	45.0% (68/151)
Visual analogue scales			
Fatigue	male	62.0 (40.0, 79.0)	30.0 (10.0, 52.0)
Median (Q1, Q3)	female	65.0 (35.0, 85.0)	40.0 (15.0, 63.0)
Intensity of pain	male	70.0 (45.0, 83.0)	32.0 (10.0, 61.0)
Median (Q1, Q3)	female	65.0 (43.0, 86.0)	30.0 (12.0, 56.0)
Sleep disturbances	male	48.0 (19.0, 67.0)	12.0 (5.0, 50.0)
Median (Q1, Q3)	female	52.0 (21.0, 80.0)	38.0 (12.0, 66.0)

(CRP = C-Reactive Protein; ESR = Erythrocyte Sedimentation Rate; Q1, Q3 = 1st / 3rd quartile; SD = standard deviation)

Conclusions: At start of therapy, approximately one out of five patients documented in ICHIBAN showed anemia according to the WHO definition. During TCZ i.v. therapy a noticeable decrease in the rate of anemia and improved hemoglobin values were observed. These effects can already be seen after four weeks of treatment and continue up to the end of this study (i.e. 2 years). Despite the higher burden of disease at baseline in RA patients with anemia, TCZ i.v. therapy resulted in good clinical response rates and PROs.

Acknowledgements: We would like to thank all patients, their families, the investigators and the nurses who participated in this trial. This research was funded by Roche Pharma AG, Germany, and Chugai Pharma Europe Ltd., Germany. Support for third-party writing assistance for this abstract presentation

was provided by Roche and Chugai and performed by Ecron Acunova GmbH, Germany.

Disclosure of Interest: C. Specker Grant/research support from: Chugai, DRFZ, Consultant for: Abbvie, Janssen, Chugai, MSD, Novartis, UCB, Lilly, Boehringer, Speakers bureau: Abbvie, Celgene, Chugai, Euroimmun, MSD, Pfizer, UCB, H. Kellner: None declared, P. Kästner: None declared, C. Volberg: None declared, V. Braunewell: None declared, I. Schwarze: None declared, M. Aringer: None declared, M. Sieburg: None declared, M. Hofmann Employee of: Chugai Pharma Europe Ltd., Zweigniederlassung Deutschland, J. Flacke Employee of: Roche Pharma AG, Germany, H.-P. Tony Consultant for: Roche Pharma, Abbvie, BMS, Chugai, Janssen, Novartis, Pfizer, Sanofi, Lilly, MSD, Astra-Zeneca, G. Fliedner: None declared

DOI: 10.1136/annrheumdis-2017-eular.5876

SAT0194 SIRUKUMAB INTEGRATED SAFETY IN RHEUMATOID ARTHRITIS PATIENTS: ANALYSIS OF THE SIRROUND PHASE 3 DATA

D. Aletaha[1], C. Thorne[2], M. Schiff[3], M. Harigai[4], R. Rao[5], N. Goldstein[6], B. Cheng[6], C. Cohen[7], B. Hsu[6], K. Brown[7]. *[1]Medical University of Vienna, Vienna, Austria; [2]University of Toronto and Southlake Regional Health Centre, Newmarket, ON, Canada; [3]University of Colorado School of Medicine, Denver, CO, United States; [4]Tokyo Women's Medical University, Tokyo, Japan; [5]GSK Medicines Research Centre, Hertfordshire, United Kingdom; [6]Janssen Research & Development, LLC, Spring House, PA; [7]GlaxoSmithKline, Collegeville, PA, United States*

Background: Sirukumab (SIR), a human monoclonal antibody that selectively binds the IL-6 cytokine, is in development for the treatment of rheumatoid arthritis (RA). Efficacy of SIR was shown in several phase 3 trials in RA patients (pts; SIRROUND program).

Objectives: To analyze safety data from completed/ongoing studies in the SIRROUND program.

Methods: Safety comparisons included SIR 50mg q4w and 100mg q2w doses vs placebo (pbo) in the pbo-controlled period (Wk 0–18) of 2 phase 3 studies. A long-term comparison of the safety of SIR 50mg q4w and 100mg q2w for the entire program was also performed.

Results: In phase 3 studies, 2926 pts received SIR for up to 3.4y (median duration, 1.46y). During Wk 0–18, there were more adverse events (AEs), AEs leading to discontinuation, and serious AEs (SAEs) with SIR vs pbo, with cumulative rates of SAEs remaining constant over time (Table). In general, no dose effect with SIR was observed in the 18-wk or long-term analysis. Mortality rates were similar across treatment groups through 18 wks and remained stable in long-term analysis. Serious infections were more frequent in SIR-treated pts vs pbo during Wk 0–18, with similar rates through long-term analysis. Rates of gastrointestinal (GI) perforations and malignancies were low and similar across groups during the 18-wk and long-term analysis; major adverse cardiovascular event (MACE) rates were similar through 18 wks and numerically higher with SIR 50mg q4w vs 100mg q2w in long-term analysis.

Conclusions: SIR is well tolerated in pts with moderately to severely active RA. Overall, no dose relationship was observed between SIR 50mg q4w and 100mg q2w for types or frequencies of AEs.

Disclosure of Interest: D. Aletaha Grant/research support from: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, Consultant for: AbbVie, Pfizer, Grünenthal, Merck Medac, UCB, Mitsubishi/Tanabe, Janssen, and Roche, C. Thorne Grant/research support from: AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Amgen, Celgene, Centocor, Genzyme, Hospira, Janssen, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, Sanofi, and UCB, Speakers bureau: Medexus/Medac, M. Schiff Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Johnson & Johnson, UCB, Speakers bureau: AbbVie, M. Harigai Grant/research support from: AbbVie Japan, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Mitsubishi Tanabe Pharma, Ono Pharmaceuticals, Santen Pharmaceutical, Takeda Pharmaceutical, UCB Japan, Teijin Pharma, Consultant for: AbbVie Japan, Janssen Pharma, Chugai Pharmaceutical, Teijin Pharma, Eli Lilly Japan, and Zenyaku Kogyo, R. Rao Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline, N. Goldstein Employee of: Janssen Research & Development, LLC, B. Cheng Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, C. Cohen Employee of: GlaxoSmithKline, B. Hsu Shareholder of: Janssen Research & Development, LLC, Employee of: Janssen Research & Development, LLC, K. Brown Shareholder of: GlaxoSmithKline, Employee of: GlaxoSmithKline

DOI: 10.1136/annrheumdis-2017-eular.5176

SAT0195 RITUXIMAB SHOWS BETTER SUSTAINABILITY THAN TNF INHIBITORS WHEN USED FOLLOWING INITIAL BIOLOGIC DMARD FAILURE IN THE TREATMENT OF RHEUMATOID ARTHRITIS: 8 YEARS OF REAL-WORLD OBSERVATIONS FROM THE RHUMADATA® CLINICAL DATABASE AND REGISTRY

D. Choquette[1], L. Bessette[2], B. Haraoui[1], F. Massicotte[1], J.-P. Pelletier[1], J.-P. Raynauld[1], M.-A. Rémillard[1], D. Sauvageau[1], A. Turcotte[2], É. Villeneuve[1], L. Coupal[1]. *[1]Rheumatology, Institut de recherche en rhumatologie de Montréal (IRRM), Montréal; [2]Rheumatology, Centre d'ostéoporose et de rhumatologie de Québec (CORQ), Québec, Canada*

Background: In the absence of biomarkers predicting response to a specific therapy, the choice of second biologic is based mostly on habit and availability of an alternative agent. Traditionally, a second anti-TNF was the preferred option,

Abstract SAT0194 – Table 1. Treatment-emergent AEs in Phase 3 Studies

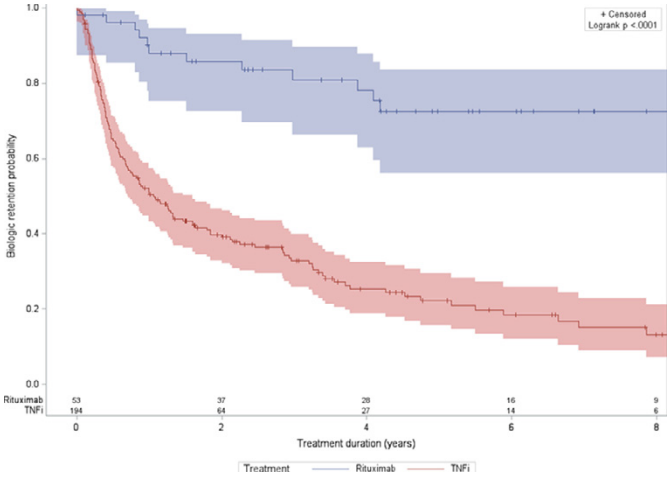
	Wk 0–18			Long-term analysis (Wk 0-safety cutoff)	
Ine	Pbo (N=850)	SIR 50mg q4w (N=848)	SIR 100mg q2w (N=850)	SIR 50mg q4w (N=1461)	SIR 100mg q2w (N=1465)
AEs, n (%)	444 (52.2)	515 (60.7)	548 (64.5)	1207 (82.6)	1237 (84.4)
AEs leading to discontinuation, n (%)	22 (2.6)	34 (4.0)	45 (5.3)	174 (11.9)	196 (13.4)
SAEs, n (%)	27 (3.2)	41 (4.8)	46 (5.4)	265 (18.1)	268 (18.3)
Incidence*	9.36 (6.17–13.61)	14.36 (10.30–19.48)	16.14 (11.82–21.53)	13.12 (11.58–14.79)	13.12 (11.60–14.79)
Serious infection, n (%)	7 (0.8)	16 (1.9)	14 (1.6)	102 (7.0)	101 (6.9)
Incidence*	2.40 (0.97–4.95)	5.52 (3.15–8.96)	4.81 (2.63–8.07)	4.76 (3.88–5.77)	4.67 (3.81–5.68)
GI perforation, n (%)	0	1 (0.1)	3 (0.4)	5 (0.3)	9 (0.6)
Incidence*	0 (0–1.02)	0.34 (0.01–1.91)	1.02 (0.21–2.99)	0.23 (0.07–0.53)	0.41 (0.19–0.77)
MACE, n (%)	2 (0.2)	3 (0.4)	2 (0.2)	20 (1.4)	9 (0.6)
Incidence*	0.68 (0.08–2.47)	1.03 (0.21–3.00)	0.68 (0.08–2.46)	0.92 (0.56–1.42)	0.41 (0.19–0.77)
Malignancy, n (%)	2 (0.2)	1 (0.1)	1 (0.1)	23 (1.6)	19 (1.3)
Incidence*	0.68 (0.08–2.47)	0.34 (0.01–1.91)	0.34 (0.01–1.91)	1.05 (0.67–1.58)	0.86 (0.52–1.35)
Death, n (%)	1 (0.1)	1 (0.1)	1 (0.1)	15 (1.0)	14 (1.0)
Incidence*	0.34 (0.01–1.91)	0.34 (0.01–1.91)	0.34 (0.01–1.90)	0.68 (0.38–1.13)	r 0.63 (0.35–1.06)

*Incidence per 100 pt-years (95% CI).

Abstract SAT0195 – Table 1. First bDMARD history and Retention Characteristics of Second bDMARD used

	Second bDMARD					
	TNFi			Rituximab		
First bDMARD Failed	Failure type		All	Failure type		All
	Primary	Secondary		Primary	Secondary	
TNF inhibitor	41 (25.5%)	120 (74.5%)	161 (100.0%)	17 (28.8%)	42 (71.2%)	59 (100.0%)
Other mode of action	6 (18.2%)	27 (81.8%)	33 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	47 (24.2%)	147 (75.8%)	194 (100.0%)	17 (28.8%)	42 (71.2%)	59 (100.0%)
Second bDMARD Retention Probability at:						
6 Months		64.68% (3.45%)			96.15% (2.67%)	
12 Months		50.54% (3.61%)			88.05% (4.59%)	
24 Months		39.77% (3.59%)			85.84% (4.97%)	
60 Months		22.26% (3.53%)			72.44% (6.95%)	
96 Months		13.22% (3.62%)			72.44% (6.95%)	
Biologic Retention Time (years)						
Mean, mean (SE)		2.71 (0.25)			6.73 (0.46)	
Lower Quartile, (95% CI)		0.36 (0.28–0.44)			4.18 (1.51–8.48)	
Median, (95% CI)		1.08 (0.71–1.60)			– (8.42 –)	
Upper Quartile, (95% CI)		4.26 (3.25–6.64)			– (–)	

but recent registry data point to better responses and retention if a drug with a different mode of action is prescribed.
Objectives: Assess the long-term retention of rituximab (RTX) and TNFi following first biologic (b)DMARD inadequate response in RHUMADATA® registry patients (pts) with RA.
Methods: Data from RHUMADATA® pts with RA prescribed either RTX or TNFi as the second bDMARD after 1 January 2006 were analysed. Pts were followed until treatment discontinuation or 9 January 2017 cut-off. Pt characteristics were compared using descriptive statistics, bDMARD discontinuation rates using Kaplan-Meier methods, and proportional hazard models were used to identify predictors of treatment discontinuation.
Results: Data for 53 and 194 pts prescribed RTX or a TNFi, respectively, as second-line treatment were extracted. No clinically significant differences in baseline characteristics were noted between treatment groups. Most pts were women (74.9%), average age (SD) was 45.2 (12.9) years at diagnosis and disease duration 10.5 (8.7) years. Most pts were stopping an anti-TNF agent: 100% of those who were switched to RTX and 83% of those who were prescribed a second anti-TNF. Overall, 77.3% of pts stopped their first bDMARD after >6 months of treatment (secondary failure). Significant differences in retention between RTX and TNFi groups (log-rank p≤.0001) were observed (Table, Figure). Results remained unchanged for pts treated with TNFi only in first line, and primary/secondary failure of the first bDMARD did not affect sustainability of the second agent. Lack of efficacy (54.4%) and AEs (16.5%) were the most commonly cited reasons for treatment discontinuation.

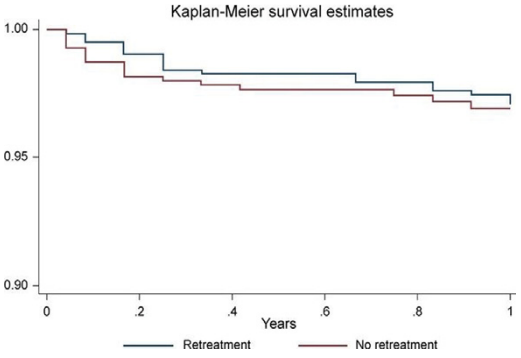


Conclusions: Rituximab has better sustainability over a second line TNFi in RA patients having failed one prior bDMARD.
Disclosure of Interest: D. Choquette Grant/research support from: Roche, Consultant for: Roche, L. Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant for: BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, B. Haraoui Grant/research support from: BMS, Janssen, Roche, Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Merck, Pfizer, Roche, Sandoz, UCB, Speakers bureau: Pfizer, UCB, F. Massicotte: None declared, J.-P. Pelletier: None declared, J.-P. Raynauld Speakers bureau: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, Sanofi, Novartis, UCB, M.-A. Rémillard: None declared, D. Sauvageau: None declared, A. Turcotte Consultant for: Amgen, Abbvie, BMS, Celegene, Janssen, Roche, Pfizer, Lilly, Novartis, Merck, Sanofi, UCB, Speakers bureau: Amgen, Abbvie, BMS, Celegene, Janssen, Roche, Pfizer, Lilly, Novartis, Merck, É. Villeneuve Consultant for: Celgene, Cimzia, Pfizer, Speakers bureau: Abbvie, Roche, BMS, L. Coupal: None declared
DOI: 10.1136/annrheumdis-2017-eular.6361

SAT0196 REPEATED RITUXIMAB INFUSIONS FOR THE THERAPY OF RHEUMATOID ARTHRITIS IS NOT ASSOCIATED WITH INCREASED RATES OF SERIOUS INFECTIONS

D.A. Pappas[1,2], G.W. Reed[2,3], S. Zlotnick[4], J. Best[4], R. Magner[3], G. Persuitte[2], J. Greenberg[2,5]. *[1]Columbia University, New York, NY; [2]Corrona, LLC, Southborough, MA; [3]University of Massachusetts Medical School, Worcester, MA; [4]Genentech, Inc., South San Francisco, CA; [5]New York University School of Medicine, New York, NY, United States*

Background: Extended observations in clinical trials have not demonstrated an increased risk of serious infection events (SIE) in patients with rheumatoid arthritis (RA) treated with rituximab.[1] However, continuous surveillance using large-scale observational data is of importance.
Objectives: To evaluate the rate of SIEs among patients with RA who received only an initial rituximab infusion vs those retreated with ≥1 rituximab infusion during the first year of therapy, and also to describe characteristics of rituximab-treated patients who experienced an SIE vs those who did not.
Methods: Patients with RA enrolled in the Corrona registry and treated with rituximab were followed until their most recent Corrona registry visit, first SIE, switch to another biologic or targeted synthetic disease-modifying antirheumatic drug, or 12 months after the most recent infusion with no further retreatment – whichever occurred first. The rate of SIEs was estimated in the overall population as well as in patients retreated with ≥1 infusion every 12 months after rituximab initiation and in those who did not receive a repeat infusion in the first 12 months. Patient characteristics were compared between those who experienced an SIE and those who did not.
Results: A total of 1361 patients with 1821 patient-years (PY) of follow-up were included; there were 59 SIEs for a rate of 3.24 SIE/100 PYs. 637 patients (46.8%) received ≥1 rituximab retreatment during the first 12 months and 724 (53.2%) received only the initial infusion. In the retreatment population there were 40 SIEs per 1312.8 PY for a rate (95% CI) of 3.05/100 PY (2.18–4.15), and in the no retreatment population there were 19 SIEs per 508.71 PY for a rate (95% CI) of 3.73/100 PY (2.25–5.83). The Kaplan-Meier curve depicting the occurrence of SIEs in the 2 cohorts during the first year of follow-up is shown (Figure). In the 59 patients (4.3%) who experienced an SIE, the mean (SD) number of rituximab infusions was 1.88 (1.18), compared with 2.07 (1.70) in the 1302 patients (95.7%) who did not experience an SIE. Patients who experienced an SIE vs those who did not were older (mean age [SD]: 62.9 [9.9] vs 58.1 [12.55] years), had longer disease duration (19.1 [13.1] vs 13.6 [10.4] years), were more frequently diabetic (16.9% vs 8.3%) and more frequently had cardiovascular disease (25.4% vs 12.8%), prior history of SIEs (18.6% vs 5.8%) and pulmonary disease (10.2% vs 4.8%). There were no differences in other clinical, demographic and medication history characteristics; steroid therapy was similar between the groups.



Conclusions: Retreatment with rituximab infusions was not associated with a higher rate of SIEs in this study. Patients who experienced an SIE had a higher prevalence of risk factors for infections.
References:
[1] Van Vollenhoven RF et al. J Rheumatol. 2015;42:1791–6.
Acknowledgements: This study is sponsored by Corrona, LLC. Corrona, LLC has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.
Disclosure of Interest: D. Pappas Grant/research support from: AbbVie, Consultant for: AbbVie, Employee of: Corrona, LLC, G. Reed Shareholder of: Corrona, LLC, Employee of: Corrona, LLC, S. Zlotnick Employee of: Genentech, Inc., J. Best Employee of: Genentech, Inc., R. Magner: None declared, G. Persuitte Employee of: Corrona, LLC, J. Greenberg Shareholder of: Corrona, LLC, Consultant for: Genentech; Janssen; Novartis; Pfizer; Eli Lilly, Employee of: Corrona, LLC
DOI: 10.1136/annrheumdis-2017-eular.1752

SAT0197 TREATMENT OUTCOMES WITH ANTI-TNF AND NON-ANTI-TNF DISEASE-MODIFYING THERAPY BY BASELINE BODY MASS INDEX

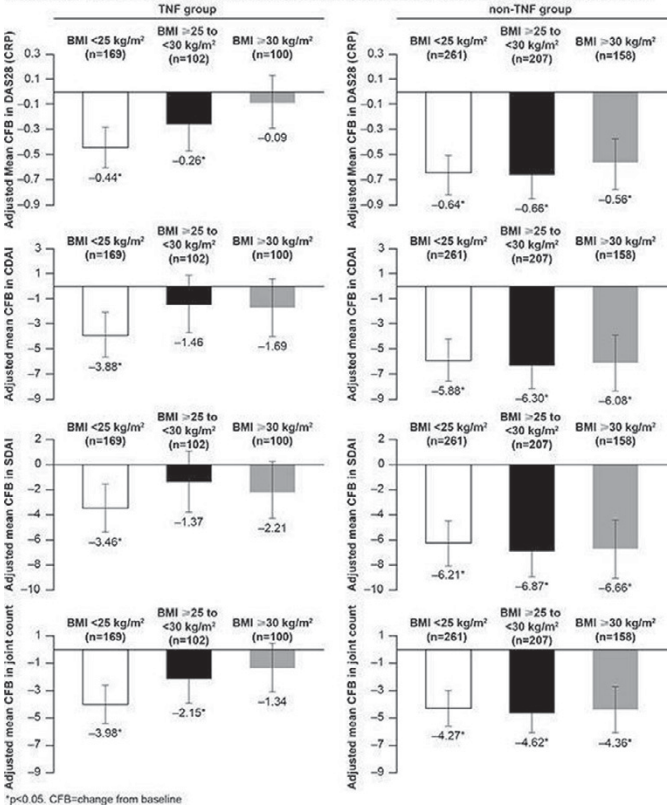
E. Alemao[1], Z. Guo[1], C. Iannaccone[2], M. Frits[2], M. Weinblatt[2], N. Shadick[2]. *[1]Bristol-Myers Squibb, Princeton; [2]Brigham and Women's Hospital, Boston, United States*

Background: Recent studies have indicated that being overweight or obese could reduce the effect of anti-TNF treatment in patients (pts) with RA.[1,2] Other data show that certain biologic (b)DMARDs, such as abatacept, work independently of BMI.[3,4] Additional data on the role of BMI on treatment outcomes in clinical practice settings is required to inform clinical practice.
Objectives: To evaluate the impact of BMI on outcomes of disease activity in pts with RA treated with TNF and non-TNF agents (conventional or other bDMARDs).
Methods: Pts enrolled in a tertiary care centre RA registry, established in 2003, were analysed. The registry mostly comprises pts with established RA who were evaluated semi-annually for multiple clinical patient-reported outcomes and resource utilization parameters, and annually for composite disease activity measures such as DAS28 (CRP), CDAI and SDAI. The current analysis is based on pts enrolled in the RA registry with BMI values at time of enrolment. Pts were classified into groups based on BMI: normal (BMI <25 kg/m^2), overweight (BMI ≥25 to <30 kg/m^2) and obese (BMI ≥30 kg/m^2). Outcomes evaluated included change from baseline in DAS28 (CRP), CDAI, SDAI and joint counts at 12 months

from treatment exposure. Treatments were categorized into TNF and non-TNF, which included conventional DMARDs and other non-TNF biologics. Multivariate linear regression analyses were used to evaluate impact of BMI on treatment outcomes controlling for baseline covariates of age, sex, disease duration, co-morbidities, baseline disease activity and serostatus. Separate models were run for the TNF and non-TNF groups.

Results: A total of 997 (78%) pts in the registry had baseline BMI values and were included in the analysis. Around 37% (n=371) had TNF exposure and were included in the TNF cohort; the remainder (63%; n=626) were included in the non-TNF cohort. Proportions of pts in the normal, overweight and obese groups for the TNF cohort were 45.5% (n=169), 27.5% (n=102) and 27.0% (n=100), respectively. For the non-TNF cohort, these were 41.7% (n=261), 33.1% (n=207) and 25.2% (n=158), respectively. In both cohorts, pts with normal BMIs were younger vs the overweight and obese BMI groups. However, obese BMI pts had higher disease activity measures at baseline (mean [SD] CDAI: 22.8 [17.8] for TNF and 24.9 [17.3] for non-TNF) vs the normal BMI pts (17.5 [15.9] for TNF and 19.9 [16.7] for non-TNF) and overweight BMI pts (20.9 [16.5] for TNF and 20.5 [15.0] for non-TNF). Adjusted mean change from baseline in disease activity in the TNF cohort was significantly reduced across all disease activity measures for the normal BMI group ($p<0.05$), but not for the overweight and obese groups (Fig). There were significant reductions in disease activity measures for all BMI groups (all $p<0.05$) in the non-TNF cohort (Fig).

Figure. Association between BMI and Treatment Outcomes DAS28 (CRP), CDAI, SDAI and Joint Count



*p<0.05. CFB=change from baseline

Conclusions: Independent of BMI, non-anti-TNF therapy demonstrated similar outcomes in pts with RA. However, obese and overweight pts with RA (vs normal weight) had less improvement in disease activity (as measured by DAS28 [CRP]) with anti-TNF therapy.

References:

[1] Gremese E, et al. Arthritis Care Res 2013;65:94–100.
[2] Klaasen R, et al. Arthritis Rheum 2011;63:359–64.
[3] Gardette A, et al. Ann Rheum Dis 2015;74:1041.

Disclosure of Interest: E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Z. Guo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, C. Iannaccone: None declared, M. Frits: None declared, M. Weinblatt Grant/research support from: Amgen, Bristol-Myers Squibb, Crescendo Biosciences, UCB, DxTerity, Consultant for: Amgen, Bristol-Myers Squibb, Crescendo Biosciences, UCB, AbbVie, Lilly, Pfizer, Roche, N. Shadick Grant/research support from: Bristol-Myers Squibb, UCB, Mallinckrodt, Amgen, Brescendo Biosciences, Consultant for: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.1566

SAT0198 TOCILIZUMAB FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS: DISCONTINUATION DUE TO INEFFICACY AND TOXICITY – EXPERIENCE FROM A LARGE TEACHING HOSPITAL

E. Byrne, P. Mark, S. Khalid, K.-P. Kuet, R. Kilding, K. Graves, J. Maxwell, M. Akil. *Rheumatology, Sheffield Teaching Hospitals, Sheffield, United Kingdom*

Background: Tocilizumab (TCZ) is a humanised anti interleukin-6 receptor antibody licensed for use for the treatment of moderate to severe Rheumatoid Arthritis (RA) as monotherapy or in combination with methotrexate (MTX).

Objectives: To describe the use of TCZ for RA in a large UK teaching centre and examine reasons for treatment discontinuation.

Methods: A retrospective case note review of all adult patients receiving TCZ either alone or in combination with DMARDS, for the treatment of RA between April 2009 and January 2017 in Sheffield, UK.

Results: 132 patients received TCZ for RA. 71% were female. 61% were CCP positive. Mean disease duration was 15.6 years (range 1.5–43). 46 (34.6%) received TCZ as monotherapy, 55 (42.1%) in combination with MTX and 31 (23.3%) other DMARDS. 23% of patients received concomitant oral prednisolone. Median duration of TCZ treatment was 27 months across the whole cohort, and 19 months in those who discontinued treatment.

Overall 44 (33%) patients discontinued TCZ; 5 due to primary and 10 secondary inefficacy, 27 patients due to adverse events (8 recurrent infection, 5 abnormal LFT, 4 malignancy, 3 rash, 7 other including 1 death whilst on treatment). A logistic regression model, including gender, smoking status, disease duration, DMARD use, steroid treatment and number of prior biologics was constructed to examine association with treatment discontinuation. Of these factors, disease duration ($p=0.05$) and number of previous biologics ($p=0.09$) were weakly associated with persistence of TCZ and in particular there was no association of concomitant DMARD or steroid treatment with discontinuation either due to lack of efficacy or adverse events. Table 1 demonstrates the proportion of patients stopping treatment, and treatment duration according to previous biologic treatment received. We have not seen any cases of infusion reaction, diverticular perforation or reactivation of tuberculosis.

Table 1. Proportion of Patients Continuing TCZ and Treatment Duration According to Previous Biologic Treatment

		Previous Biologics Received			
		0	1	2	3 or more
Continued	N (%)	15 (83%)	31 (66%)	24 (51%)	12 (60%)
	Treatment Duration (Mths)*	46	27	26	58
Discontinued	N (%)	3 (17%)	16 (34%)	23 (49%)	8 (40%)
	Treatment Duration (Mths)	4.5	14	24	18
	Lack of Efficacy/Toxicity	2/1	7/9	9/14	3/5

*To date.

Conclusions: Our real world data on the use of TCZ in the treatment of adult patients with RA is consistent with clinical trial data for efficacy and safety and is similar to other biological drugs used in the treatment of RA. We have seen a relatively low rate of withdrawal due to primary and secondary treatment failure.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5105

SAT0199 SUBCUTANEOUS TOCILIZUMAB MONOTHERAPY OR COMBINED WITH A CSDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS: TOZURA, A POOLED ANALYSIS OF PHASE IV STUDIES IN 22 COUNTRIES

E. Choy[1], R. Caporali[2], R. Xavier[3], B. Fautrel[4], R. Sanmarti[5], C. Bernasconi[6], A. Pethö-Schramm[6]. *[1]Cardiff University, Cardiff, United Kingdom; [2]University of Pavia, Pavia, Italy; [3]Universidade Federal do Rio Grande do Sul Porto Alegre, Rio Grande do Sul, Brazil; [4]Pierre and Marie Curie University, Paris, France; [5]Universitat de Barcelona, Barcelona, Spain; [6]F. Hoffmann-La Roche AG, Basel, Switzerland*

Background: Tocilizumab administered subcutaneously (TCZ-SC) has been approved for the treatment of rheumatoid arthritis (RA) both as mono- and combination therapy.

Objectives: To evaluate the efficacy and safety of TCZ-SC 162 mg once weekly (qw) as monotherapy or in combination with conventional synthetic DMARDs (csDMARDs) over 24 weeks in adult patients (pts) with moderate to severe RA.

Methods: TOZURA is a multinational, open-label, single-arm umbrella program comprising 7 single-country and 4 regional multicountry protocols (total 22 countries). Pts enrolled were inadequate responders to DMARD, and previous biologic DMARDs were allowed in 8 of 11 protocols. Pts received TCZ-SC 162 mg qw for 24 weeks administered at the investigator's discretion as monotherapy or in combination with a csDMARD. Stable oral NSAIDs and corticosteroids (CS), ≤10 mg/day prednisone or equivalent, were allowed. Efficacy and safety were evaluated at weeks 1, 2, 4 and every 4 weeks for 24 weeks (plus 8 weeks for safety). Propensity score-based matching was used for between-group tests.

Results: Of 1804 pts treated, 353 (19.6%) received monotherapy (mono) and 1451 (80.4%) combination therapy (combo); 349 pts (19.3%) had received a prior biologic DMARD. Background characteristics: 81.6% female; mean age, 54.1

years; mean RA duration, 7.7 years; and 82.7% seropositive –similar between treatment groups. Baseline CS was less frequent in the mono vs combo group (41.1% vs 51.2%); however, the mean prednisone equivalent daily dose was similar (6.6 vs 6.5 mg/day, respectively). Pts who continued TCZ to week 24 based on Kaplan-Meier estimates (95% CI) were 79.3% (74.7%>83.2%) for mono and 85.6% (83.7%>87.3%) for combo. DAS28 scores decreased comparably from baseline to week 24 in both groups (mean change: mono −3.40 and combo −3.46), with no significant difference between groups (P =0.61). Results were similar for the Clinical Disease Activity Index (CDAI, mean change by week 24: −23.5 and −23.8, with no significant difference between groups: P=0.42). The proportion of pts who achieved DAS28 or CDAI-based remission, low disease activity or ACR20/50/70/90 responses was similar between groups (Figure 1). In all, 18.2% of pts withdrew; 6.4% did so for safety reasons (mono 9.1%, combo 5.8%). AE rates were similar between groups (Table). Serious AE (SAE) rates were 14.6/100 PY (mono: 22.8/100 PY, combo: 12.8/100 PY). Serious infection and infestation rates were 3.6/100 PY (mono: 4.0/100 PY, combo: 3.5/100 PY) – similar between groups. Six deaths occurred (0.64/100 PY), 1 in the monotherapy group (0.57/100 PY) and 5 in the combination (0.65/100 PY) group.

Figure 1: DAS28 and CDAI Disease Activity and ACR Responses*

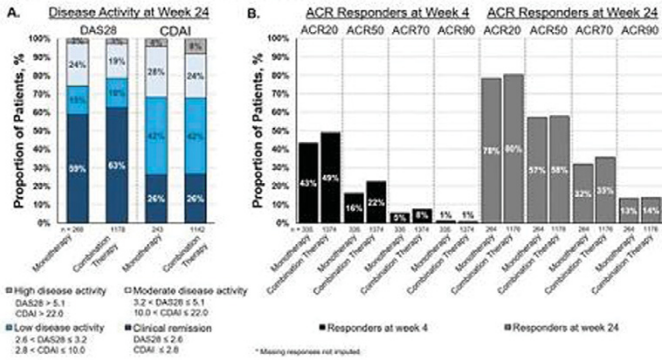


Table: Summary of Relevant Adverse Events

		Total Population (N = 1804; 943.3 PY)	Monotherapy (n = 353; 175.7 PY)	Combination Therapy (n = 1451; 767.6 PY)
Adverse events	Total patients with ≥ 1 AE, n (%)	1508 (83.6%)	282 (79.9%)	1226 (84.5%)
	Rate of AEs per 100 PY	622.4	622.1	622.5
Serious adverse events	Total patients with ≥ 1 SAE, n (%)	105 (5.8%)	29 (8.2%)	76 (5.2%)
	Rate of SAEs per 100 PY	14.6	22.8	12.8
Serious infections and infestations	Total patients with ≥ 1 SAE, n (%)	27 (1.5%)	6 (1.7%)	21 (1.4%)
	Rate of SAEs per 100 PY	3.6	4.0	3.5
Withdrawals due to insufficient therapeutic response	Total patients with ≥ 1 reason, n (%)	40 (2.2%)	9 (2.5%)	31 (2.1%)
Withdrawals due to safety reasons*	Patients, n (%)	116 (6.4%)	32 (9.1%)	84 (5.8%)
Deaths	Number of deaths, n (%)	6 (0.3%)	1 (0.3%)†	5 (0.3%)‡
	Rate of deaths per 100 PY	0.64	0.57	0.65

AE, adverse events; SAE, serious adverse events; PY, patient-year.
* Deaths, anaphylaxis and hypersensitivity reactions not included.
† Coronary artery disease.
‡ Myocardial infarction, pneumonia, pulmonary fibrosis, sepsis, septic shock.
Note: TOZURA trial numbers: NCT01995201, NCT02046603, NCT02011334, NCT02031471, NCT02001987, NCT01941095, NCT01941940, NCT02046616, NCT01988012, NCT01987479, NCT01951170.

Conclusions: TCZ-SC demonstrated convincing and comparable efficacy as mono- and combination therapy in pts with RA as was previously observed with TCZ-IV. The safety profile of TCZ-SC is consistent with the known safety profile of TCZ as monotherapy and in combination with csDMARDs.

Acknowledgements: Funded by F. Hoffmann-La. Roche, Ltd.

Disclosure of Interest: E. Choy Grant/research support from: F. Hoffmann-La Roche, Chugai Pharmaceutical, Consultant for: F. Hoffmann-La Roche, Chugai Pharmaceutical, Speakers bureau: F. Hoffmann-La Roche, Chugai Pharmaceutical, R. Caporali Consultant for: AbbVie, Bristol-Myers Squibb, F. Hoffmann-La Roche, UCB and MSD Pharmaceuticals, R. Xavier Consultant for: F. Hoffmann-La Roche, Pfizer, Janssen Pharmaceuticals, AbbVie, Eli Lilly and Company, Speakers bureau: F. Hoffmann-La Roche, Pfizer, Janssen Pharmaceuticals, Abbvie, Eli Lilly and Company, B. Fautrel: None declared, R. Sanmarti: None declared, C. Bernasconi Employee of: F. Hoffmann-La Roche (contractor), A. Pethö-Schramm Employee of: F. Hoffmann-La Roche

DOI: 10.1136/annrheumdis-2017-eular.1615

SAT0200 BIOLOGIC THERAPY RETENTION IN RHEUMATOID ARTHRITIS (RA) PATIENTS (PTS) ACCORDING TO THE MOSCOW ARTHRITIS REGISTRY (MAR)

G. Lukina[1], E. Koltsova[2], E. Schmidt[3], E. Zhilyaev[4]. *[1]V.A. Nasonova Research Institute of Rheumatology, Moscow Clinical Scientific Center; [2]Research Institute of the Organization of health and healthcare management; [3]City Clinical Hospital 1 named after N.I. Pirogov; [4]Russian Medical Academy of continuing professional education, CJSC "European Medical Center", Moscow, Russian Federation*

Background: The use of biologics significantly improved results of the therapy of RA pts who did not achieve the target disease activity level on traditional DMARDS treatment. However the biologic therapy is in many cases withdrawn due to inefficacy or side effects (seldom because of sustained remission). Retention on treatment is a good integral index of efficacy and safety of biologics used in the real clinical practice.

Objectives: To assess the treatment survival of various biologics in RA pts in the real clinical practice.

Methods: Patients from MAR with RA receiving biologics were enrolled. Cases with missed results were excluded. A Cox proportional hazards regression model was used to determinethe predictors of the treatment discontinuation risk. Comparison of biologics retention rates for different biologicswas performed by means of Kaplan-Meier survival curves. Bonferroniadjustment was applied because of multiplicity of comparisons.

Results: 306 RA pts (mean age 54,5 years, mean age of disease onset 39,6 years, 86,5% women, 18% smokers, RF-positive 83,7%) were included in the study and 394 treatment courses (263 retrospective and 131 prospective) were analyzed. It was shown that significant independent predictors of discontinuation risk were: the biologic drug, the sequence number of the biologic drug in the patient and the age of RA onset. Risk of withdrawal was minimal by the use of the first biologic and increased by administration of the next ones. It also increased in pts with late onset of RA. Mass body index, age of the patient and the dose of methotrexate did not show significant correlations. Abatacept (ABA) demonstrated significant superiority over adalimumab (ADA) ($p<0.001$), infliximab (INF) ($p<0.001$), rituximab (RTM) (p=0.004) and etanercept (ETA) (p=0.035) when they was used as the first biologic drug. The treatment survival of tocilizumab was significantly higher compared to INF (p=0.02). As a second-line biological therapy ADA was maintained significantly longer than the INF (p=0.048).

Conclusions: Results of the real clinical practice trial show the significant differences in the retention rates of some biologics. It is reasonable to take these differences into consideration by the planning of the biologic treatment of RA pts.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3657

SAT0201 ABATACEPT BUT NOT TNF INHIBITORS BLOCK AUTOANTIBODY-MEDIATED CYTOKINE PRODUCTION BY MONOCYTES

A. Bozec[1], Y. Luo[2], C. Engdahl[1], C. Figueiredo[3], H. Bang[4], G. Schett[1]. *[1]University of Erlangen-Nuremberg, Erlangen, Germany; [2]University of Chengdu, Chengdu, China; [3]Universidade de São Paulo, Sao Paulo, Brazil; [4]Orgentec Inc., Mainz, Germany*

Background: The anti-inflammatory effect of abatacept (CTLA4-Ig) is most pronounced in patients with high-titer autoantibodies (including anti-citrullinated protein antibodies, ACPA, and rheumatoid factor, RF) even exceeding the effect of TNF inhibitors (TNFi)[1]. Considering that autoantibodies trigger inflammatory cytokine production by monocytes[2] and that abatacept bind to monocytes influencing their functional state[3] we hypothesized that abatacept, in contrast to TNFi, may effectively inhibit the production of several different cytokines by ACPA-or RF-challenged monocytes.

Objectives: (i) To test whether abatacept inhibits the production of TNFa, IL-1b, IL-6 and IL-8 by monocytes exposed to ACPA or RF, (ii) to compare these effects of abatacept with those of TNFi and (iii) to investigate whether the effect of abatacept on cytokine production is based on IDO induction in monocytes.

Methods: CD68+ monocytes were isolated from peripheral blood and stimulated with MCSF for 24 hours before exposing them to random IgG alone (negative control), 10mg/mL purified anti-citrullinated vimentin antibodies (ACPA), 10mg/mL RF or LPS (positive control) in cell culture plates coated with citrullinated vimentin (to allow ACPA immune complex formation). ACPA and RF stimulation was done in the presence or absence of abatacept or TNF-antibody (adalimumab) with or without IDO inhibitor 1-MT. Supernatants were analyzed for four key pro-inflammatory cytokines TNFa, IL-1b, IL-6 and IL-8 by cytokine array (R&D Proteome Profiler) after 24h.

Results: Exposure to ACPA or RF dramatically induced the production of TNFa (20 fold and 27-fold, respectively) IL-1b (each 4-fold), IL-6 (12-fold and 11-fold, respectively) IL-8 (43-fold and 30-fold, respectively) in human monocytes. Abatacept significantly inhibited this up-regulation of inflammatory cytokine production with TNFa reduced by 79%, IL-1b by 74%, IL-6 by 88% and IL-8 by 83%. In contrast, TNFi did not influence autoantibody-induced production of IL-1b, IL-6 and IL-8. Inhibition of IDO by 1-MT reversed the effect of abatacept and unlocked cytokine production in the presence of ACPA and RF.

Conclusions: These data show that abatacept interferes with autoantibody mediated cytokine production by induction of IDO. The fact that several different

effector cytokines are inhibited simultaneously may explain the strong anti-inflammatory effect of abatacept in RA patients with high-titer ACPA and RF.

References:
[1] Sokolove J, et al. Impact of baseline anti-cyclic citrullinated peptide-2 antibody concentration on efficacy outcomes following treatment with subcutaneous abatacept or adalimumab: 2-year results from the AMPLE trial. Ann Rheum Dis. 2016;75:709–14.
[2] Clavel C, et al Among human macrophages polarised to different phenotypes, the M-CSF-oriented cells present the highest pro-inflammatory response to the rheumatoid arthritis-specific immune complexes containing ACPA. Ann Rheum Dis. 2016;75:2184–2191.
[3] Bozec A, et al. T cell costimulation molecules CD80/86 inhibit osteoclast differentiation by inducing the IDO/tryptophan pathway. Sci Transl Med. 2014;6:235ra60.

Acknowledgements: This project was supported by an unrestricted research grant from BMS and the IMI project BTCure.

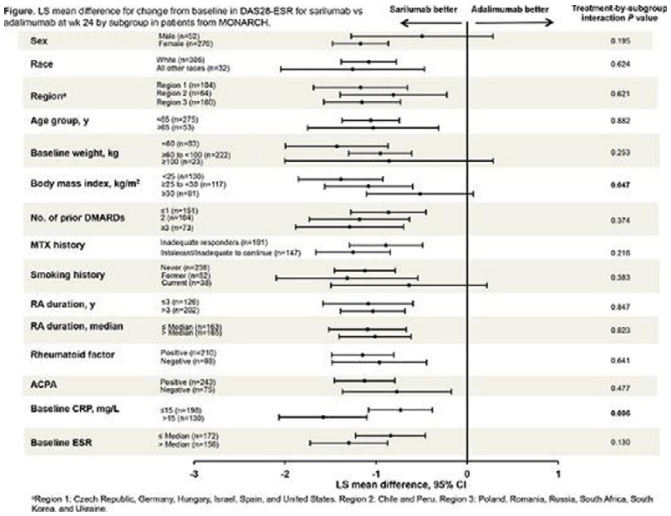
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4363

SAT0202 EFFICACY AND SAFETY OF SARILUMAB MONOTHERAPY VERSUS ADALIMUMAB MONOTHERAPY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS IN THE PHASE 3 MONARCH STUDY, INCLUDING SUBPOPULATIONS

G.R. Burmester[1], Y. Lin[2], E.K. Mangan[3], H. van Hoogstraten[2], T. Kimura[3], J.I. Vargas[4], E.B. Lee[5]. *[1]Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany; [2]Sanofi Genzyme, Bridgewater; [3]Regeneron Pharmaceuticals, Inc, Tarrytown, United States; [4]Quantum Research, Puerto Varas, Chile; [5]Seoul National University College of Medicine, Seoul, Korea, Republic Of*

Background: Efficacy and safety of sarilumab + csDMARDs in RA patients have been demonstrated.
Objectives: To compare sarilumab monotherapy with adalimumab monotherapy in the ITT population of adults with active RA from MONARCH (NCT02332590) and across predefined subgroups.
Methods: Adults (N=369) intolerant of, inappropriate for, or inadequate responders (IR) to MTX (per investigator judgment) received SC sarilumab 200 mg q2w or adalimumab 40 mg q2w monotherapy. The primary endpoint was change from baseline in DAS28-ESR at wk 24. Consistency of treatment response (sarilumab vs adalimumab) for this endpoint was assessed in prespecified subpopulations.
Results: At wk 24, sarilumab was superior to adalimumab in change from baseline (BL) in DAS28-ESR (-3.3 vs -2.2; $P<0.0001$). Sarilumab-treated patients achieved significantly higher rates of ACR20 response (71.7% vs 58.4%; $P=0.0074$) and greater improvement in HAQ-DI (-0.6 vs -0.4; $P=0.0037$) and CDAI (-28.9 vs -25.2; nominal $P=0.0013$) vs adalimumab-treated patients. Extent of treatment effect with sarilumab vs adalimumab in change from baseline in DAS28-ESR at wk 24 was generally consistent ($P>0.05$) across subgroups; significant treatment-by-subgroup interactions were observed for body mass index ($P=0.047$) and baseline CRP ($P=0.006$) (Figure). The magnitude of treatment effect for DAS28-ESR was greater in patients with lower BMI and higher baseline CRP. Treatment effect was generally similar for other efficacy endpoints assessed, including ACR20, HAQ-DI, and CDAI. Clinical and functional responses in RF+/ACPA+, RF+/ACPA-, RF-/ACPA+, and RF-/ACPA- patients were similar to overall study results. Incidence of AEs was similar in both groups, including incidences of infections and serious infections. The most common AEs were neutropenia and injection site erythema (sarilumab) and headache and worsening of RA (adalimumab).



Conclusions: Sarilumab monotherapy demonstrated superiority to adalimumab monotherapy in the ITT population in change from baseline in DAS28-ESR. The extent of treatment effect with sarilumab vs adalimumab was generally consistent across subpopulations. Overall incidences of AEs and serious AEs and rates of infection and serious infection were similar between groups.

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Medical writing support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: G. Burmester Grant/research support from: AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, and UCB, Y. Lin Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, E. Mangan Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, H. van Hoogstraten Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, T. Kimura Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, J. Vargas Grant/research support from: Roche, Bristol-Myers Squibb, and Pfizer, Speakers bureau: Bristol-Myers Squibb, E. Lee Consultant for: Pfizer

DOI: 10.1136/annrheumdis-2017-eular.4540

SAT0203 SIGNIFICANCE OF EXTENSION OF TOCILIZUMAB INFUSION INTERVALS FROM 4 WEEKS TO 6 WEEKS IN RA PATIENTS WHO HAD SHOWN GOOD RESPONSE TO 4 WEEK INTERVALS

H. Uda[1], K. Shigematsu[2], O. Saiki[1,3]. *[1]Rheumatology; [2]Orthopedics, Higashiosaka City Medical Center, Higashiosaka; [3]Internal Medicine, Shiraishi Hospital, Imabari, Japan*

Background: A period of 4 weeks (w) has been recommended as tocilizumab (TCZ, 8mg/kg) infusions. However, we found that 5 or 6w intervals were also effective in more than 90% of RA patients with low disease activity (LDA) at 4w intervals (1).
Objectives: We conducted the study to investigate the significance of extension of intervals from 4w to 6w. We compared, in the same patients, the clinical features such as diseases activity, major and minor side reactions between at 4w and at 6w. Moreover, we also considered the mechanisms.
Methods: This was a retrospective observational study. Among RA patients who had shown LDA with TCZ infusions at 4w intervals, the patients who could extend the intervals from 4w to 6w with LDA for more than 2 years without changing the doses of oral medicines were enrolled. In the same patients, we compared the events of serious and common side reactions between at 4w and 6w intervals. We examined the course of the levels of total cholesterol (TCHO), triglyceride (TG), and platelet (PLT) counts. We also examined the levels of serum trough TCZ and IL-6.
Results: Among 120 patients who maintained LDA at 4w intervals, more than 60% of patients maintained LDA at 6w intervals. When we compared the disease activity of 6w-responders between at 4w and 6w-intervals, all parameters reflecting the disease activities such as CRP and DAS28CRP score at 6w intervals were elevated significantly, but were still within LDA. At 4w intervals, serious adverse events were occurred as much as 11 cases during 2 years. At 6w intervals, however, they were decreased to 3 cases only in the same period. The common adverse events such as general fatigue, nausea, and dizziness occurred frequently at 4w intervals in most of the patients. At 6w intervals, these common adverse events were decreased significantly. At 4w intervals, the levels of TCHO and TG were elevated significantly. At 5w and 6w intervals, however, they were decreased accordingly. At 6w intervals, they were within normal limits. In most of patients, the levels of PLT counts were decreased significantly at 4w intervals. At 5w and 6w intervals, however, they were increased gradually. When TCZ were infused at 4w intervals, the serum trough TCZ levels were around 10 μg/mL. In contrast, they became undetectable when extended to 5w, and it is obvious that the trough TCZ levels of 6w were lower than 5w. The levels of IL-6 were significantly high at 4w-intervals, but the levels of IL-6 were decreased to less than 10 pg/mL at 5w-intervals.
Conclusions: The present study provide evidence that more than half of RA patients who showed good response to TCZ infusions at 4w could extend the intervals to 6w. By extension of intervals to 6w, major and minor side reactions were reduced significantly, and the levels of TG, TCHO and PLT were also normalized with sustaining LDA, suggesting that the dose of TCZ (8mg/kg) at 4w intervals might be excessive in some patients. Taken together, we should be careful for deciding the intervals of TCZ infusion in each patient.

References:
[1] Saiki O, Uda H. Successful extension of tocilizumab infusion intervals from 4 weeks to 6 or 5 weeks in 90% of RA patients with good response to 4 weeks intervals. Clin Exp Rheumatol (2017 in press).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3602

SAT0204 ABATACEPT SURVIVAL IN RHEUMATOID ARTHRITIS PATIENTS AT 2 YEARS IS 59%; ITS USE AS A 2ND LINE BIOLOGIC AGENT AND LOWER BASELINE HAQ PREDICT BETTER SURVIVAL IN CLINICAL PRACTICE: A PROSPECTIVE, OBSERVATIONAL SINGLE CENTER STUDY

I.D. Flouri[1,1], A. Repa[1], N. Avgoustidis[1], N. Kougas[1], A. Fanouriakis[1], I. Papalopoulos[1], C. Adamichou[1], P. Kyfonidou[1], E. Kampouraki[1], M. Terizaki[1], D.T. Boumpas[2], G. Bertsias[1], P. Sidiropoulos[1]. *[1]Rheumatology, Clinical Immunology and Allergy, Faculty of Medicine-University of Crete, Heraklion-Crete; [2]4th Internal Medicine Department, Attikon University Hospital, Athens, Greece*

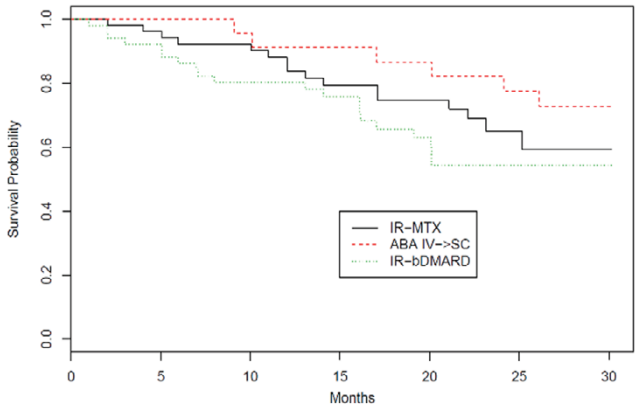
Background: Long-term prospective observational studies are complementary to controlled clinical trials to explore effectiveness and safety of biological therapies in clinical practice.
Objectives: To study abatacept survival, reasons of discontinuation and clinical responses in everyday clinical practice of patients with rheumatoid arthritis (RA).
Methods: Prospective, observational single center study at the Rheumatology Clinic, University Hospital of Heraklion, Crete. At baseline, patient demographics, co-morbidities and disease characteristics are being recorded, while during follow-up, discontinuations, disease activity and adverse events are collected. For this analysis, all patients who received Abatacept intravenously from 6/2007 till 6/2016 were included. Kaplan-Meier curves and Cox regression analysis were used to determine drug survival and predictors thereof. Linear regression was used to compare DAS difference at 12 months between different lines of bDMARD therapy.
Results: A total of 224 patients (women: 87%, seropositive: 34%) were included. Median (IQR) age was 63 (56–70) years, disease duration 7.4 (4–13.4) years and baseline DAS28 5.9 (5.2–6.5). Abatacept was the 1st bDMARD in 59 (26%), 2nd in 71 (32%) and ≥3rd in 94 (42%) patients. During follow-up [total: 508 patient-years, median (IQR): 1.7 (0.7–3.3) years], 54% patients discontinued therapy (87% for treatment failure, 10% for adverse events). Two-year treatment persistence was 59%. In multivariable regression analysis, predictors of longer Abatacept survival were lower baseline HAQ [HR (95% CI) for unit increase =2.29 (1.5–3.48), p<0.001], longer disease duration [HR (95% CI) for ≥8 vs.<8 years=0.51 (0.30–0.88), p=0.016], Abatacept as 2nd vs 1st or ≥3rd bDMARD [HR =0.52 (0.30–0.91), p=0.022] and a more recent year of therapy start [HR=0.39 (0.16–0.95), p=0.022].
DAS28<3.2 and remission at 6 (12) months were achieved by 12% (18%) and 5% (7%) of patients respectively. DAS28 difference at 12 months was greater in patients who received Abatacept as the ≤2nd than those on ≥3rd bDMARD (p=0.009).
A total of 312 adverse events were registered, of which 65 were serious (SAE). Incidence of total (serious) adverse events was 61 (13) /100 patients/year. SAE included 5 cases of cancer, 10 cardiovascular events and 24 infections, mainly of the respiratory tract.
Conclusions: In the present study, Abatacept survival at 2 years was 59%. The majority of patients discontinued therapy due to inadequate response. Use as a 2nd line biologic agent and lower baseline HAQ predicted better survival. Improvement in DAS was higher when Abatacept was used as the ≤2nd bDMARD. Rates of remission or low disease activity in clinical practice are rather low, while the safety profile was excellent.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6931

SAT0205 LONG-TERM DRUG SURVIVAL AND CAUSES OF DISCONTINUATION OF SUBCUTANEOUS ABATACEPT IN RHEUMATOID ARTHRITIS: 32-MONTH RESULTS FROM A PROSPECTIVE COHORT STUDY

J.C. Sarmiento-Monroy[1,2], N. Molano-Gonzàlez[2], M. Rodríguez-Jiménez[2], R.D. Mantilla[1,2]. *[1]Rheumatology, Center of Dermatology and Rheumatology (FUNINDERMA); [2]Center for Autoimmune Diseases Research (CREA), Universidad del Rosario, Bogotá D.C., Colombia*

Background: Survival time or time to discontinuation of medication is a surrogate of the long-term impact on the course of disease in real life. It reflects clinical effectiveness in the absence of significant adverse events [1]. Treatment discontinuation can result from loss of efficacy or safety concerns, but prognostic factors for patient retention have not been explored thoroughly despite data for abatacept and other biologics being available from national registries [2].
Objectives: To assess drug survival of subcutaneous (SC) abatacept among patients with rheumatoid arthritis (RA) according to treatment background.
Methods: This was a prospective study in which well-characterized patients with RA (by 1987 ACR criteria) were assessed from April 2014 to December 2016. Each patient was evaluated by a rheumatologist in a single rheumatology outpatient private center in Bogotá, Colombia. Patients were stratified by treatment background: (n=54) biologic-naïve, (n=24) switched from IV to SC abatacept administration, and (n=51) inadequate response to at least 1 biologic disease-modifying antirheumatic drug. The Mantel-Haenszel test was used to test if there were any differences in the survival curves among groups. The test was performed by the survdiff function of the "survival" R package [3].
Results: A total of 129 patients were included. Baseline characteristics of patients were as follows: female gender 86%, mean age 52±13 years, median disease duration 10 (IQR 11) years, Rheumatoid Factor positive 94%, Anti-Cyclic Citrullinated Peptide Antibodies 89%, and erosive phenotype 35%. At baseline, mean DAS28 and RAPID3 were 5.4±1.3 and 16.6±6.8, respectively. SC abatacept monotherapy was reported in 27%. Demographics and disease characteristics were similar in all groups, except for baseline DAS28 and RAPID3 in switch group (p<0.0001). According to the Mantel-Haenszel test (Fig.1), there were not significant differences between survival curves (p=0.158). Forty-three patients (33%) discontinued treatment. The most frequent reasons for drug suspension were loss of efficacy in 25%, insurance-related problems (i.e., access to medication/specialist) and adverse drug reactions in 16%. Other causes include lack of efficacy, surgeries (i.e., articular replacement), patient preference, and pregnancy.

Figure 1. Subcutaneous abatacept survival by treatment background.



IR-MTX: inadequate response to methotrexate (biologic-naïve); ABA IV→SC: switched from intravenous to subcutaneous abatacept administration (125mg-wk); IR-bDMARD: inadequate response to biologic Disease-Modifying AntiRheumatic Drugs.

Conclusions: Our results disclose a similar drug survival of SC abatacept regardless of treatment background. Patients switching from IV to SC formulation of abatacept had lower activity and functional impairment at baseline, and survival tends to be higher through follow-up. The insurance-related limitations is a reality in Latin American countries, and could have a negatively impact on survival time of several drugs.
References:
[1] Nüßlein HG, et al. BMC Musculoskelet Disord. 2015;16:176.
[2] Souto A, et al. Rheumatology (Oxford). 2016;55(3):523–34.
[3] Therneau, T. and Grambsch, P.M. 2000.
Acknowledgements: The authors are grateful to all the members of the Center of Dermatology and Rheumatology (FUNINDERMA) for their contribution to this work.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4348

SAT0206 RETENTION OF TOCILIZUMAB AS MONOTHERAPY VERSUS TNF INHIBITORS WITH CONVENTIONAL SYNTHETIC DMARDS IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO TNF INHIBITORS: A STUDY FROM THE TOCERRA COLLABORATION

K. Lauper[1,2], D.C. Nordström[3], K. Pavelka[4], V. Hernandez[5], M.J. Santos[6], Z. Rotar[7], F. Iannone[8], C. Codreanu[9], G. Lukina[10], S.L. Gale[11], K. Sarsour[11], A. Pethoe-Schramm[12], D.S. Courvoisier[1], C. Gabay[1,2]. *[1]Univ Hosp of Geneva, Geneva; [2]SCQM Registry, Zurich, Switzerland; [3]ROB-FIN Helsinki Univ Central Hosp, Helsinki, Finland; [4]Charles Univ, Prague, Czech Republic; [5]Rheumatology Department, Hospital Clinic Barcelona, Barcelona, Spain; [6]Rheumatology Unit, Hospital Garcia de Orta, Almada, Portugal; [7]BioRx.si, Univ Med Center, Ljubljana, Slovenia; [8]GISEA, Univ Hospital of Bari, Bari, Italy; [9]Univ of Medicine and Pharmacy, Bucharest, Romania; [10]ARBITER, Inst of Rheumatology, Moscow, Russian Federation; [11]Genentech, South San Francisco, CA, United States; [12]F. Hoffmann-La Roche, Basel, Switzerland*

Background: Tocilizumab (TCZ) as monotherapy has been shown to be more efficacious than the TNF inhibitor (TNFi) adalimumab as monotherapy in patients with rheumatoid arthritis (RA). However, effectiveness data comparing TCZ as monotherapy versus TNF inhibitors in combination with csDMARDs are limited.
Objectives: To examine retention of TCZ administered alone (TCZ mono) versus TNFi in combination with csDMARDs (TNFi combo) in patients with RA who had an inadequate response to ≥1 TNFi (TNFi-IR).
Methods: Patients with RA who were TNFi-IR and treated with TCZ mono or TNFi combo with baseline (BL) data, not immediately lost to follow-up and started treatment after TCZ was available across 9 European registries in TOCERRA from 2009 to 2016 were included. The hazard for TCZ discontinuation was modeled using a country-stratified Cox proportional hazards model, adjusting for

age, gender, disease duration, seropositivity, HAQ and CDAI at BL, number of previous csDMARD and biologic DMARD (bDMARD), glucocorticosteroid and calendar year of treatment initiation. Missing data on covariates were imputed using multiple imputation with chained equations.
Results: A total of 4748 patients were eligible, including 585 who received TCZ mono and 4163 who received TNFi combo. Patients who received TCZ mono were older with a longer disease duration, more previous bDMARDs and less glucocorticosteroids at baseline (Table 1) compared with patients who received TNFi combo. The crude median retention for TCZ mono was 1.82 years (95% CI: 1.59–2.09) and 1.54 years (95% CI: 1.43–1.64) for TNFi combo, (P=0.65). Causes of discontinuation differed between TCZ mono and TNFi combo (P<0.001): TCZ mono stopped more frequently for ineffectiveness (25.7% vs. 13.8%) and TNFi combo stopped more frequently for safety issues (18.3% vs. 12.8%). In a country-stratified, covariate-adjusted analysis, we found that hazards of discontinuation were significantly lower among patients who received TCZ mono (HR: 0.71, P<0.001). More previous treatment with bDMARDs and a greater HAQ and CDAI at BL were significantly associated with greater risk of discontinuation.

Table 1. Baseline characteristics.

	TCZ mono (N = 585)	TNFi combo (N = 4163)	*P*
Age, yr, median [IQR]	57.8 [44.2-65.5], n = 585	54.3 [44.2-61.7], n = 4161	< 0.001
Female gender, N (%)	485 (82.9%), n = 585	3333 (80.1%), n = 4161	0.12
Disease duration, yr, median [IQR]	9.7 [4.5-16.7], n = 569	7.8 [3.3-14.3], n = 3575	< 0.001
Seropositivity (RF and/or ACPA), N (%)	445 (83.6%), n = 532	2573 (81.0%), n = 3175	0.17
N previous bDMARDs, N (%)			< 0.001
1	250 (42.7%)	2882 (69.2%)	
2	206 (35.2%)	526 (12.6%)	
≥ 3	129 (22.1%)	755 (18.1%)	
Glucocorticosteroids, N (%)	193 (33.0%), n = 585	2487 (59.7%), n = 4163	< 0.001
Concomitant csDMARD, N (%)			--
MTX	--	1766 (42.4%)	
MTX + other	--	1291 (31.0%)	
Other	--	1106 (26.6%)	
CDAI, mean (SD)	23.2 (16.1), n = 322	21.9 (14.7), n = 3021	0.25
HAQ, mean (SD)	1.4 (0.7), n = 226	1.1 (0.7), n = 2429	< 0.001

Conclusions: In routine care across 9 European countries, TCZ mono retention is better than TNFi combo in patients with RA who were TNFi-IR.
Acknowledgements: Funding by F. Hoffmann-La Roche/Genentech.
Disclosure of Interest: K. Lauper: None declared, D. Nordström Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB, Consultant for: AbbVie, BMS, MSD, Roche, UCB and Pfizer, K. Pavelka Grant/research support from: AbbVie, Roche, Medis, MSD and Pfizer, Consultant for: AbbVie, Roche, Amgen, MSD, BMS, UCB and Egis, V. Hernandez: None declared, M. J. Santos: None declared, Z. Rotar: None declared, F. Iannone: None declared, C. Codreanu: None declared, G. Lukina Consultant for: BMS, Roche, MSD, AbbVie and Pfizer, S. Gale Employee of: Genentech, K. Sarsour Employee of: Genentech, A. Pethoe-Schramm Employee of: F. Hoffmann-La Roche, D. Courvoisier: None declared, C. Gabay Grant/research support from: AB2 Bio, AbbVie, Actelion, BMS, Debiopharm, MSD, Novartis, Pfizer, Regeneron, Roche, Sanofi and UCB, Consultant for: AB2 Bio, AbbVie, Actelion, BMS, Debiopharm, MSD, Novartis, Pfizer, Regeneron, Roche, Sanofi and UCB
DOI: 10.1136/annrheumdis-2017-eular.6503

SAT0207 LONG-TERM EFFECT OF BIOLOGICAL THERAPIES ON BONE MINERAL DENSITY (BMD) FOR RA PATIENTS COMPARED TO PATIENTS TREATED BY SYNTHETIC DMARD OVER AN 8-YEAR FOLLOW-UP

L. Bustamente[1], V. Breuil[2], R. Fabre[3], L. Euller-Ziegler[2], C. Pradier[3], C. Roux[1]. *[1]Rheumatology, University Nice, Sofia Antipolis, Nice; [2]Rheumatology; [3]Santé publique, University Nice, Sofia Antipolis, Nice Cedex 1, France*

Background: Secondary osteoporosis is a comorbidity of Rheumatoid Arthritis (RA). Previous studies have suggested that biological therapies may reduce the rate of generalized bone loss in RA. Most of them focus on the short-term effect of Tumor Necrosis factor alpha (TNFα) inhibitors while the long-term effect of biological therapies is rarely studied.
Objectives: Our primary aim was to analyze the long-term effect of biological therapies on bone mineral density (BMD) for RA patients compared to patients treated by synthetic DMARD over an 8-year follow-up.
Methods: Patients were selected from a prospective, observational cohort of RA patients meeting the ACR/EULAR 2010 settings in Nice University Hospital between 2001 and 2016. BMD was assessed before the introduction of the biological therapy and during the follow-up. Two groups were studied: patients treated by biological therapies (TNFα inhibitors, Tocilizumab, Abatacept, Rituximab or Anakinra) and patients treated by synthetic DMARD only. Demographic, disease and treatment data were collected at each visit and BMD of the lumbar spine, femoral neck and total hip were assessed using dual energy X-ray absorptiometry (DXA) at baseline and after 1, 2, 3, 5 and 8 years.
Results: A total of 181 patients with active RA starting a biological therapy were included versus 131 patients treated by synthetic DMARD. In both groups, the BMD of the lumbar spine, femoral neck and total hip remained stable after a 2-year follow-up (respectively -0.37%, p=0.66 versus +0.02%, p=0.83, -3.70%, p=0.77 versus -5.35%, p=0.74 and -3.31%, p=0.45 versus -4.84%, p=0.16), while a significant bone loss was found between initial measurement and 3, 5 and 8 -year-follow-up at femoral neck and total hip level. There was no significant difference between patients whether treated by biological or non-biological DMARD neither over the 0–1-year period nor over the 0–2, 0–3, 0–5 and 0–8-periods. Bone loss in patients treated by Tocilizumab were statistically lower at femoral neck level compared with TNFα inhibitors (p=0.02), Abatacept (p=0.02) and Rituximab (p=0.02), but also at total hip level, in comparison with TNF α inhibitors (p=0.05) and Abatacept (p=0.05).
Conclusions: This study is the first to assess the effects of biological RA therapies as compared to synthetic DMARD ones. It highlights the protective effect of both biological and non-biological DMARD on bone loss during the first two years of treatment with no significant difference between them. Our results suggest that the effects of RA treatments depend on the inflammatory and disease activity which must be monitored clearly. Tocilizumab seems to be more effective than the other biological therapies, but further studies are necessary to confirm or infirm this tendency.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2851

SAT0208 CYCLING VERSUS SWAPPING IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH AN INADEQUATE RESPONSE TO AT LEAST ONE TUMOR NECROSIS FACTOR ALPHA INHIBITOR: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

M.A. Lopez-Olivo[1], A. Matusevich[2], M.E. Suarez-Almazor[1]. *[1]General Internal Medicine, The University of Texas, MD Anderson Cancer Center; [2]School of Public Health, The University of Texas, Health Science Center at Houston, Houston, United States*

Background: In patients with rheumatoid arthritis (RA) who do not respond or lose response, opinions are divided on whether it is better to try an alternative TNFi (cycling) or switch to a therapy with a different mode of action (swapping).
Objectives: To compare the efficacy and safety of the cycling versus the swapping strategies.
Methods: We searched 4 electronic databases, sources of gray literature, and bibliographic references of relevant articles for observational studies evaluating the efficacy and safety of targeted therapies in adult RA patients who failed to respond to at least one TNFi. Studies were excluded if they were single-arm or had insufficient data to evaluate the outcomes of interest. Two independent reviewers selected studies, extracted data and evaluated study quality using the Newcastle-Ottawa Scale (NOS). Our primary outcome measure was change in Disease Activity Score of 28 joints (DAS28). We also evaluated the modified American College of Rheumatology 20%, 50% and 70% response criteria (mACR which excludes acute phase reactants) and total serious adverse events. All analyses were based on the random-effects model.
Results: Of 33,716 citations, 24 observational studies (n=10,074 patients) representing 14 countries, met the inclusion criteria. Eight were conference abstracts. Most publications (13 of 24) were based on registries. Most studies had a NOS score equal to or greater than 7 (out of 9) with comparability being the weakest domain. The mean age of patients was 48.7–62.8 years, the majority were females (78%) with a disease duration of 6–17.3 years and a baseline disability score 0.6–2.0. Sixteen studies evaluated cycling versus swapping directly of which 13 were suitable for analysis. Most compared TNFi to rituximab (10 of 13) with two studies investigating tocilizumab or abatacept and one comparing non-TNFi as a group. Other comparisons reported were: (i) cycling vs. conventional disease modifying antirheumatic drugs (cDMARDs), (ii) swapping vs. cDMARDs, (iii) cycling vs. another cycling alternative, (iv) swapping vs. another swapping alternative, (v) swapping monotherapy vs. swapping combined with cDMARDs, and (vi) combination of TNFi and non-TNFi vs. TNFi alone. At 12 and 24 weeks, DAS28 score improved significantly in those swapping compared to those cycling (mean difference (MD) 0.89, 95% confidence interval (CI) 0.05 to 1.74 and MD 0.34 95% CI: 0.2, 0.48; respectively). Similar results were observed for the mACR50 favoring the swapping strategy at 24 weeks (OR =1.45 95% CI: 1.06, 1.98). At 52 weeks no difference was observed. No statistically significant differences were observed between groups in the odds of achieving DAS28 remission, mACR20 or mACR70, or experiencing a serious adverse event.
Conclusions: Current evidence from observational studies shows greater improvements with the swapping strategy compared with the cycling strategy in terms of efficacy for RA patients failing their first TNFi. No differences were observed regarding safety. Data were not available for anakinra, certolizumab pegol, golimumab, or tofacitinib.
Acknowledgements: Funding for this project was provided by the Rheumatology Research Foundation Investigator Award.
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6490

SAT0209 OBSERVATIONAL STUDY ON THE EFFECTS OF IL-6 INHIBITOR THERAPY ON MYOSTATIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

M.J. Chapman[1], R.P. Narayanan[2], A. Cross[3], R. Moots[3], J. Wilding[2], N. Goodson[3]. *[1]Department of Rheumatology, Aintree University Hospital; [2]Department of Obesity and Endocrinology; [3]Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, United Kingdom*

Background: Rheumatoid cachexia (RC), a phenotype of increased adiposity, reduced lean mass and insulin resistance can occur in rheumatoid arthritis (RA). It is most prevalent in those with high disease activity and is associated with increased cardiovascular morbidity and mortality. Tocilizumab (TCZ), a monoclonal anti-IL-6 antibody, successfully reduces disease activity in RA. It has also been associated with improved insulin sensitivity, increased lean mass and hyperlipidaemia. The serum concentration of myostatin, a myokine released by skeletal muscle, is increased in most disease states associated with cachexia. Moreover, its knockout and inhibition increase lean mass. However, its role in RA has not been fully elucidated.
Objectives: To investigate the effect of tocilizumab treatment on serum myostatin in patients with RA.
Methods: 19 patients with RA (16 female, 3 male) mean age 49.6yrs, mean DAS28 6.1, median disease duration 10yrs (range 0 to 30), mean BMI 27.4, received 13 IV infusions of TCZ 8mg/kg every four weeks as part of a 52 week, single-centre, open-label study (ACT-NEUT [1]). 8 had previously been exposed to a biological agent, 4 were on regular steroids, and all patients received concurrent methotrexate. Serum myostatin was measured at 0, 1, 3 and 6months of treatment using ELISA. BMI, serum lipid profile, CRP, ESR and DAS28 were measured at each visit (0, 1, 3 and 6months). Data were analysed using STATA 14. Change between 0, 3 and 6months was analysed using Wilcoxon signed rank test, statistical significance was confirmed using mixed model analysis adjusting for BMI, age and gender. Linear regression with adjustment for age, BMI and gender assessed correlation at baseline.
Results: DAS28, CRP and ESR all significantly decreased with TCZ treatment. A significant increase in BMI (25.5 (IQR 21.6–31.7) vs 26.0 (IQR 21.4–32.5) p=0.0052) between baseline and 6months and serum triglycerides between baseline and 3 months (1.3 (IQR 1.3–2.2) vs 1.6 (IQR 1.3–2.6) p=0.028) was seen with TCZ. Baseline serum myostatin concentrations were negatively correlated with baseline DAS28 (r^2=0.39 p=0.038). Treatment with tocilizumab for 6months resulted in a significant increase in serum myostatin from baseline (2.7ng/mL (IQR 2.0–3.1) vs 3.3ng/mL (IQR 3.0–5.0) p<0.001) [Fig. 1]. Moreover, a significant association was seen between baseline myostatin and change in cholesterol at 3 months (r^2=0.51 p=0.029), when adjusting for baseline cholesterol, age, gender, BMI and change in BMI.

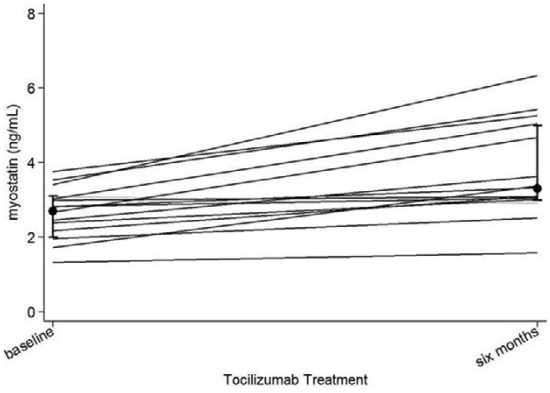


Fig 1. Serum myostatin levels significantly increase after six months of tocilizumab in patients with rheumatoid arthritis. Values shown are actual serum values for individual patients (n=19 at baseline n=15 at 6months). Black lines represent increasing serum values, grey lines decreasing values with treatment. Circles represent median±IQR. Change evaluated by Wilcoxon signed rank test p<0.001

Conclusions: We have demonstrated a significant correlation between myostatin and DAS28 and a significant change in myostatin with tocilizumab treatment. It is possible that IL-6 blockade results in a rise in myostatin. This might attenuate any improvement in muscle wasting. Future studies should measure body composition and muscle function to help understand the changes we have observed.
References:
[1] Wright HL, Cross AL, Edwards SW, Moots RJ. Effects of IL-6 and IL-6 blockade on neutrophil function in vitro and in vivo. Rheumatology. 2014 Jul;53(7):1321–31.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5831

SAT0210 IMPROVEMENT OF DISEASE ACTIVITY IN A 5-YEAR COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED UNDER TREAT TO TARGET RECOMMENDATIONS RECEIVING BIOLOGICAL THERAPY

P. Santos-Moreno[1], D. Gomez[1], E. Castillo[1], R. Giraldo[1], G. Ballesteros[1], L. Villarreal[2], J. Bello[3], D. Buitrago-Garcia[3]. *[1]Rheumatology; [2]Psychology and processes; [3]Epidemiology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: Treat to Target (T2T) strategy becomes from the need to develop therapeutic targets and tools to achieve defined outcomes in rheumatoid arthritis (RA), this strategy has become recognized as a standard of good practice embodying the principle that rapid attainment of remission, or low disease activity, can halt joint damage and maintain good quality of life. However, there is no direct comparison between biologics in cohorts of patients with long-standing RA using T2T approach in real-life settings, which could have implications in treatment decisions and health economics.
Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy for a 5 year period in patients with biological therapy in a large cohort of patients from a Colombian specialized in RA center with multidisciplinary approach.
Methods: A descriptive dynamic cohort study was performed. Records of patients using biological DMARD treatment (Anti-TNF and others) from specialized in RA center were reviewed; those patients were followed-up under T2T standards. Clinical follow-up was according to DAS28 as follows: every 3–5 weeks (DAS28 >5.1), every 7–9 weeks (DAS28 ≥3.1 and ≤5.1), and every 11–13 weeks (DAS28 <3.1). Therapy had to be adjusted with DAS28 >3.2 unless patient's conditions don't permit it. We divided patients in three groups: low disease activity (LDA), moderate disease activity (MDA) and severe disease activity (SDA) patients. Descriptive epidemiology was done, percentages and averages were calculated; the median of each variable was analyzed using t-Student assuming normality for DAS28 distribution and the level activity disease was analyzed using Pearson's statistics.
Results: During 60 month period we included 695 patients with biological therapy, 85% were female and 15% male. Mean age was 58 years ± 11. At beginning mean DAS28 was 4.1±1.1 and 20% of patients were in SDA, and 55% in MDA. At the end of 5 year period mean DAS was 3.2±0.89 and only 7% of patients were in SDA and 33% in MDA. The median was analyzed using t-Student assuming normality for DAS28 distribution. It showed statistical significant improvement (p<0.00).

ACTIVITY LEVEL	TIME 0 n(%)	2011-2012 n(%)	2013-2014(%)	2015-2016(%)
REM	-	50 (7)	166 (24)	217 (31)
LDA	178(26)	236 (34)	181(26)	198(28)
MDA	382 (55)	361(52)	278 (40)	234(74)
SDA	135 (19)	98(14)	70(10)	46(7)

Conclusions: There was a global improvement of DAS28 in a cohort of RA patients receiving biological therapy followed and treated under recommendations of T2T approach demonstrating that with the strategies mentioned above it is possible to obtain a good control of the activity of the disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5579

SAT0211 REAL WORLD DATA OF RITUXIMAB EFFECTIVENESS IN RHEUMATOID ARTHRITIS: DIFFERENCES BETWEEN BIOLOGIC-NAIVE PATIENTS AND PREVIOUSLY EXPOSED TO BIOLOGICS

R.M. Ferreira, R. Fonseca, D.R. Gonçalves, F. Aguiar, T.M. Rocha, A. Bernardo, S. Pimenta, M. Bernardes, L. Costa. *São João Hospital Centre, Porto, Portugal*

Background: Rituximab is only approved for rheumatoid arthritis (RA) treatment in patients with an incomplete response or intolerance to others DMARDs, including TNF alfa inhibitors. It represents a significant advance in RA biologics arsenal due to its safety and efficacy profiles.
Objectives: To evaluate the effectiveness of rituximab in RA patients and to compare the response between first-line rituximab patients and those previously exposed to other biologics.
Methods: An observational retrospective study was conducted, including all the consecutive patients with diagnosis of RA under rituximab, followed at our Rheumatology department until December 2016. Demographic and clinical data were obtained by consulting the national database (Reuma.pt). DAS28 variations and EULAR response were measured at 6, 12 and 18 months. Parametric and non parametric tests were used for statistics (SPSS 20.0).
Results: We included 63 RA patients (81% of women), with a mean (SD) age of 61 (10) years and a mean disease duration of 19 (10) years; 86% rheumatoid factor positive and 87% anti- citrullinated peptide antibody (ACPA) positive. Bone erosions and extra-articular manifestations were present in 85,7% and 58,7% of the patients, respectively. At baseline, the mean DAS28 was 5.79 (65% and 29% of patients with severe and moderate disease activity, respectively, and 6% in clinical remission). Thirty patients were treated with rituximab as first-line therapy and 33 patients were previously exposed to other biologics. Combination therapy

with methotrexate (MTX) was observed in 48% and with others classic DMARDs in 30%, while 22,3% received rituximab monotherapy. First-line rituximab option was justified by lung involvement in 21%, past malignancy in 13%, recurrent infections in 5%, congestive cardiac failure in 3%, vascular involvement in 3% and untreated latent tuberculosis in 3%. In the group previously exposed to biologics, 13% switched therapy due to ineffectiveness and 87% due to adverse events. No significant differences were found between the 2 groups in terms of age, gender, concomitant use of MTX and baseline DAS28. The group previously exposed to biologics had a longer disease duration (mean 23 vs 15 years, p=0.001) and fewer patients with ACPA seropositivity (79% vs 97%, p=0.035). There was a significant reduction of DAS28 at 6, 12 and 18 months ($p<0.001$ for all). Fifty six percent of the patients achieved a EULAR response at 6 months, 46% at 12 months and 59% at 18 months. DAS28 variation at 6 months differed significantly between groups, with a better clinical response in naive biological patients comparing to those previously exposed to biologics (median 1.173 vs 0.477; p=0.038). There were no differences in terms of DAS28 variation at 12 and 18 months (p=0.642 and p=0.135, respectively) and in EULAR responses at 6, 12 and 18 months between the groups (p=0.289, p=0.523 and p=1.000, respectively).

Conclusions: Our study confirms the effectiveness of rituximab in RA patients and suggests a higher magnitude of response in naive biological patients at 6 months of RTX therapy. These findings put in perspective an extension of rituximab as a first-line biologic for RA treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4494

SAT0212 SARILUMAB DOSE REDUCTION IN AN OPEN-LABEL EXTENSION STUDY IN RA PATIENTS WITH INADEQUATE RESPONSE TO TNF INHIBITORS

R. Fleischmann[1], P. Hrycaj[2], H. van Hoogstraten[3], E.K. Mangan[4], Y. Lin[3], S. Jayawardena[3], G.R. Burmester[5]. *[1]Metroplex Clinical Research Center, University of Texas Southwestern Medical Center, Dallas, United States; [2]Department of Rheumatology and Clinical Immunology, Poznań University of Medical Sciences, Poznań, Poland; [3]Sanofi Genzyme, Bridgewater; [4]Regeneron Pharmaceuticals, Inc, Tarrytown, United States; [5]Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin, Germany*

Background: Sarilumab is a human mAb blocking the IL-6Rα. In the phase 3 TARGET study (NCT01709578), sarilumab (150 or 200 mg SC q2w) + csDMARDs demonstrated efficacy in adults with active, moderate-to-severe RA and inadequate response or intolerance to ≥1 TNFi. Infections, neutropenia, injection site reactions, increased lipids, and increased transaminases were among the most common TEAEs. EXTEND (NCT01146652) is an open-label extension study evaluating long-term safety and efficacy of sarilumab in patients from the sarilumab clinical development program.

Objectives: To examine the effects of dose reduction of sarilumab 200 mg q2w to 150 mg q2w in patients from TARGET that occurred in EXTEND primarily for protocol-specified laboratory abnormalities.

Methods: Patients were switched to or initiated on sarilumab 200 mg q2w after enrolling in EXTEND. Per protocol, investigators could reduce the sarilumab dose from 200 mg q2w to 150 mg q2w for ANC ≥0.5 to 1.0 Giga/L, platelet count ≥50 to 100 Giga/L, or ALT ≥3 to 5×ULN. Dose reductions were also performed at the investigator's discretion. Efficacy data from EXTEND were analyzed before and 24 weeks after dose reduction.

Results: As of the July 2016 interim analysis (N=452), dose reduction from sarilumab 200 mg q2w to 150 mg q2w had occurred in 14.6% of patients (n=66) from TARGET. The most common reasons for dose reduction were decreased ANC (8.8%; n=40) and increased ALT (3.3%; n=15). At the time of analysis, 80.3% of patients (n=53) whose dose was reduced were continuing treatment, with a median treatment duration of 1.6 years after dose reduction. Improvements in ANC and ALT were observed over the 6 months after dose reduction (Table 1). Efficacy was maintained 24 weeks after dose reduction (Table 2).

Table 1. ANC and ALT After Dose Reduction[a]

	Before dose reduction n (%)	6 months after dose reduction n (%)
ANC		
≥0.5 to <1.0 Giga/L	25/40 (62.5)	5/39 (12.8)
<0.5 Giga/L	0	0
ALT		
>3 to ≤5×ULN	13/15 (86.7)	1/13 (7.7)
>5 to ≤10×ULN	1/15 (6.7)	0

[a]Denominator represents patients who dose reduced because of decreased ANC or increased ALT who had ANC/ALT measured within specified time point.

Table 2. Efficacy After Dose Reduction

	Before dose reduction (N=60)	6 months after dose reduction (N=53)
ACR20 response rate, n (%)	49 (81.7)	43 (81.1)
ΔHAQ-DI, mean (SD)	-0.7 (0.6)	-0.8 (0.7)
ΔDAS28-CRP, mean (SD)	-3.0 (1.2)	-3.0 (1.3)
ΔCDAI, mean (SD)	-28.4 (12.5)	-28.6 (14.6)

Conclusions: In patients from TARGET whose sarilumab dose was reduced from 200 mg q2w to 150 mg q2w during EXTEND, there was an improvement in laboratory abnormalities and continuation of treatment for the majority of patients. Improvements in signs and symptoms of RA and physical function were maintained after dose reduction.

Acknowledgements: This study was sponsored by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Editorial support was provided by MedThink SciCom and funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Disclosure of Interest: R. Fleischmann Grant/research support from: AbbVie, Amgen, Ardea Biosciences, Bristol-Myers Squibb, Celgene, GlaxoSmithKline, Eli Lilly, Pfizer, Roche, Sanofi, and UCB, Consultant for: AbbVie, Akros Pharma, Amgen, AstraZeneca, Bristol-Myers Squibb, Janssen, Eli Lilly, Pfizer, Roche, and UCB, P. Hrycaj Consultant for: Pfizer, Celltrion, and Egis, H. van Hoogstraten Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, E. Mangan Shareholder of: Regeneron Pharmaceuticals, Inc, Employee of: Regeneron Pharmaceuticals, Inc, Y. Lin Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, S. Jayawardena Shareholder of: Sanofi Genzyme, Employee of: Sanofi Genzyme, G. Burmester Grant/research support from: AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, MedImmune, Merck, Pfizer, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, and UCB

DOI: 10.1136/annrheumdis-2017-eular.5155

SAT0213 LOW DOSE IL-2 RESTORES DECREASED ABSOLUTE NUMBER OF REGULATORY T CELLS AND IMBALANCE BETWEEN TH17 AND REGULATORY T CELLS IN PATIENTS WITH RHEUMATOID ARTHRITIS

R. Jia[1], X. Li[1], C. Wang[1], C. Gao[2]. *[1]The Department of Rheumatology, the Second Hospital of Shanxi Medical University, Taiyuan, China; [2]Pathology, Joint Program in Transfusion Medicine, Brigham and Women's Hospital/Children's Hospital Boston, Harvard Medical School, Boston, United States*

Background: A therapeutic revolution in the past decade is still a considerable unmet need in the treatment of rheumatoid arthritis (RA). On the other hand, dysfunction of regulatory T cells (Tregs) has been considered to be a pivotal cause of RA and correction of this dysfunction to be a potential RA therapy[1]. However, abnormalities of Tregs in patients with RA were reported controversially in previous studies[2], in which only proportion was measured and Tregs were defined using different protein markers.

Objectives: In this study, we measured both absolute numbers and proportions of CD4+CD25+Foxp3+ Tregs in peripheral blood of RA patients and investigated the effects of low-dose recombinant human IL-2 (rhIL-2) on Tregs and CD4+ effector T cell subsets in patients with RA.

Methods: Both absolute numbers and proportions of Treg and Th17 cells in peripheral blood, defined as the CD4+CD25+FOXp3+T or CD4+IL-17 + T cell population, were examined by flow cytometry in 342 patients with RA with different 28-joint Disease Activities (DAS28), including 75 who had never received disease-modifying antirheumatic drugs (DMARD) and 151 who were receiving or had received DMARD. Among these patients, 112 consented at enrollment to receive rhIL-2 treatment. Before and after treatment, the Th17 and Treg cells in peripheral blood were analyzed by flow cytometry.

Results: The absolute count of Treg cells in patients with RA was significantly low compared with that of healthy controls ($P<0.05$), but the absolute count of Th17 cell was no different between RA and healthy controls. After the course of rhIL-2 treatment, there was a significant increase in the absolute count of Th17 and Treg cells in the CD4+ T cell population ($P<0.01$), but Th17/Treg was significantly low after the treatment.

Conclusions: The data suggest that, besides propotion, the decrease of Treg cell number, defined as the CD4+CD25+FOXp3+population, may contribute to the pathogenesis of RA. Over the treatment of rhIL-2, there was a more significant increase in the absolute count of Treg cells than that of Th17, and consequently restore the balance of Th17/Treg.

References:

[1] Miyara M, Ito Y, Sakaguchi S. TREG-cell therapies for autoimmune rheumatic diseases. Nature reviews Rheumatology 2014;10:543–51.

[2] Morita T, Shima Y, Wing JB, Sakaguchi S, Ogata A, Kumanogoh A. The Proportion of Regulatory T Cells in Patients with Rheumatoid Arthritis: A Meta-Analysis. PloS one 2016;11:e0162306.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2808

SAT0214 AN ANALYSIS OF INCREASING SPACING TIME FOR THE INTRAVENOUS ADMINISTRATION OF TOCILIZUMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Ito[1], D. Kobayashi[1], C. Takai[1], Y. Nomura[1], A. Abe[1], H. Otani[1], H. Ishikawa[1], A. Murasawa[1], I. Narita[2], K. Nakazono[1]. *[1]Niigata Rheumatic Center, Shibata; [2]Division of Clinical Nephrology and Rheumatology Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan*

Background: Although the biological disease-modifying antirheumatic drugs (bDMARDs) are the most effective treatment for rheumatoid arthritis (RA), the costs are much higher than those of conventional synthetic DMARDs. A number

of studies on discontinuation, dose reduction and/or spacing of bDMARDs have been performed, but there have been few reports on increased spacing time between tocilizumab (TCZ) administrations so far.
Objectives: To analyze the efficacy of spacing of the intravenous (IV) administration of TCZ in patients with RA.
Methods: 63 patients (11 M, 52 F) who were administered IV TCZ for more than 1 year were enrolled. Eleven patients had shifted to subcutaneous injection and the data at the last IV infusion were analyzed.
Results: Mean age was 57.4 years old (30–78), mean body weight was 55.5kg (37–85.5), mean duration of illness was 10.7yrs (0–32), The number of the bDMARDs previously administered were 0.9 (0–3), and duration of TCZ treatment was 46.9 months (13–83). The intervals between administrations were 4 weeks: 28.6%, 5 weeks: 38.1%, 6 weeks: 17.5%, 7 weeks: 6.0%, 8 weeks: 7.9%, and 10 weeks: 1.6%. Tender joint count, swollen joint count, erythrocyte sedimentation rate (ESR), C-reactive protein, matrix metalloproteinase-3 (MMP-3), patient's visual analogue scale (VAS), doctor's VAS, disease activity score (DAS) 28-ESR, simplified disease activity index (SDAI), clinical DAI (CDAI) were significantly improved. All of patients remission rates were 90.5% for DAS28-ESR, 44.4% for CDAI, and 42.9% for SDAI. Patients with prednisolone (PSL) decreased from 50 to 38 (p=0.031), at doses of 5.3 (2–10) to 2.7 (0.5–5) mg/day (p<0.0001). Patients with methotrexate (MTX) decreased from 46 to 32 patients (p=0.017), at doses of 8.1 (2–18) to 6.6 (2–14) mg/weeks (p<0.0001). There were no changes in the usage of other csDMARDs. The remission rates of the patients with increased spacing (n=45) were 75.6% for DAS28-ESR, 28.9% for CDAI, and 35.6% for SDAI. In 45 patients with increased spacing, both PSL and MTX were significantly reduced even after spacing (2.9: 0.5–5.5 to 2.6: 1–7.0) mg/day, and (6.45: 2–10 to 5.2: 2 -12) mg/ weeks, respectively (p=0.0013, p=0.0085). At the introduction of TCZ, there was no difference in the serum levels of MMP-3 in patients with increased spacing and without spacing 274.8 (24–1310) ng/ml vs 283.3 (32–626) ng/ml p=0.692). Serum revels of MMP-3 at the first time of increased spacing were significantly lower in the patients with increased spacing than those at the final point of patients without spacing 72.0 (22.2–236.0) ng/ml vs 165.8 (35.8 -619.0) ng/ml, p=0.000752. The number of patients with normal levels of MMP-3 among the patients with increased spacing were 25/45 (55.6%) with significantly higher levels for those patients who had no spacing 3 /18 (16.7%, p=0.00567).
Conclusions: TCZ treatment was associated with significantly reduced disease activity and reduced use of PSL and MTX. Increased spacing between administrations was used in 71.4% of the patients. TCZ was able to reduce PSL and MTX even after spacing. MMP-3 might be a useful marker to decide the spacing period. TCZ is the most inexpensive bDMARD in Japan, but with increased spacing, it is possible to reduce the cost even further with acceptable control of RA symptoms.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2335

SAT0215 CHARACTERISTICS OF PATIENTS WITH ANKYLOSING SPONDYLITIS, RHEUMATOID AND PSORIATIC ARTHRITIS IN TREATMENT WITH BIOLOGICS IN VERONA'S COHORT: RESULTS FROM VENETO'S REGION BIOLOGICS REGISTER

S. Troplini, O. Viapiana, E. Fracassi, A. Carletto, L. Idolazzi, G. Orsolini, A. Giollo, M. Rossini. *Rheumatology Unit, University of Verona, Verona, Italy*

Background: Since 2013, in Veneto's Region, data registration is mandatory for all patients affected by Rheumatoid arthritis (RA), Psoriatic Arthritis (PA), Ankylosing Spondylitis (AS) in treatment with biologic agents. The biologic DMARDs currently marketed in Italy are: anti-TNF (originator and biosimilar infliximab, etanercept, adalimumab, certolizumab and golimumab), anti-IL6 (tocilizumab), anti-CD20 (rituximab), CTLA-4 like (abatacept) and anti IL-12/23 (ustekinumab).
Objectives: The aim of this study was first to describe the characteristics of patients with RA, PA, AS under biologics and then, to extract and analyze real-life data regarding rheumatic treatments in Verona's cohort.
Methods: The study has been carried out on behalf of Regione del Veneto, Giunta regionale- Ricerca Sanitaria Finalizzata-Venezia-Italy. Data used for analysis were retrieved from Veneto's Region Biologics Register (VRBR). VRBR provides that core variables such as onset and type of disease, anthropometric characteristics (age, sex, body weight, height) are registered at the beginning. Furthermore, prior and concomitant rheumatic treatment (conventional and biologic DMARDs, corticosteroids, NSAIDs), disease activity indicators (DAS 28-PCR, ASDAS-PCR, pain-NRS), prognostic factors (positivity for rheumatoid factor and/ or anti-citrulline antibodies in AR, presence of radiological erosions) were assembled at baseline, every 6 months and at the time of biologic's switch or swap.
Results: A total of 983 patients under biologics were examined; 543 (55,2%) with AR, 272 (27,7%) with AP and 168 (17,1%). Between these, 262 (27,2%) patients were naïve to biologics, 128 with AR, 84 with AP, 50 with SA. Mean duration of disease was of 15,3, 10,7 and 12,6 years respectively for RA, PA and AS. Radiological erosions were present in 73% of RA-patients and the percentage was higher in those with positivity for rheumatoid factor and/ or anti-citrulline antibodies (84,4% versus 56,2%). More than half of the patients in this cohort were treated at least with one biologic agent; anti-TNFs were the main biologic used (RA:54,8%, PA:92,7%, AS: 100%) followed by Abatacept (25,4%), tocilizumab (12,3%) and rituximab (5,9%) in patients with RA. Methotrexate (MTX) was the prevalent associated c-DMARDs (41,8% in RA and 34,2% in PA) with mean dose of 11,9 mg/week in RA and 12,1 mg/week in PA. The optimal dose of methotrexate was not achieved prevalently because of drug intolerance.
Conclusions: Profile of both conventional and biological DMARDs looks very different according to the type of rheumatic disease. The first data show an underuse of MTX in patients with RA and PA under biologics with a low mean dosage due to intolerance. Next step is to evaluate long-term outcomes in clinical practice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5718

SAT0216 ABATACEPT EXPERIENCE IN BIOLOGIC NAIVE RHEUMATOID ARTHRITIS PATIENTS: HUR-BIO REAL LIFE RESULTS

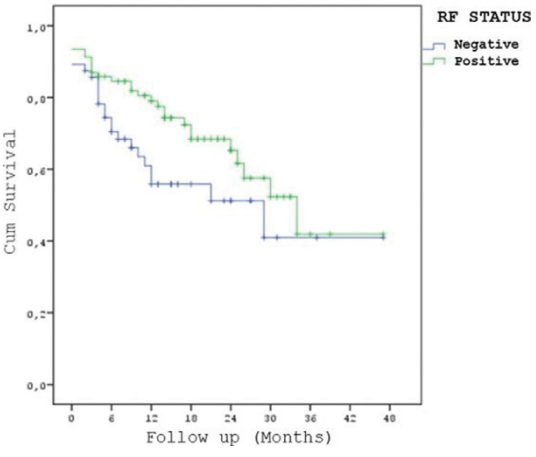
A. Sari, B. Armagan, L. Kilic, A. Erden, O. Karadag, A. Akdogan, S. Apras Bilgen, S. Kiraz, U. Kalyoncu, I. Ertenli. *Rheumatology, Hacettepe University School of Medicine, Ankara, Turkey*

Background: Abatacept (ABA), a T lymphocyte blocker, is one of the treatment options in rheumatoid arthritis (RA) patients who are resistant to initial therapy with non-biologic disease modifying drugs (DMARDs).
Objectives: Aim of this study was to evaluate the effectiveness, safety and drug survival rates of ABA in RA patients registered in HUR-BIO (Hacettepe University Rheumatology Biologic Registry) database.
Methods: HUR-BIO is a prospective,single center database of biological treatments including 1229 RA patients by August 2016. In total, 247 of patients had received ABA and in 175 (71%) of them ABA was the first biological agent. In this analysis, 158 patients were evaluated due to lack of first follow-up visit in 17 patients. Demographics, clinical and serological data were evaluated. DAS-28 and HAQ-DI scores before ABA and last follow-up visit were also assesed. Kaplan-Meier analysis was used to estimate drug survival rates.
Results: Among 175 (82% female) patients, mean age was 53.6±11.3 and mean disease duration was 10.3±7.3. Seropositivity for RF and/or ACPA was present in 74.8% of patients. Table 1 represents DAS-28 scores of patients before ABA and last follow-up visit. Mean duration from ABA initation to first and last follow-up visit was 4.5±3.1 and 15.1±10.2 months, respectively. Female gender was found as a risk factor in terms of remaining of DAS-28 above 3.2 at first control [OR 5,63 (%95 CI 1,72–18,41)]. In first follow-up visit, improvement in DAS-28 score of ≥1,2 from baseline was more frequent in ACPA positive patients (48/62 (77.4%) vs 17/33 (51.5%), p=0.01). HAQ score of >1.0 was observed in 57.8%, 36.3%and 26.1% of patients at baseline, first follow-up visit and last follow-up visit, respectively. ABA had been cessated in 60 (38.0%) patients during follow-up. The reason for ABA withdrawal was primary unresponsiveness in 22 (36.6%) patients and infection in 2 (3.3%) patients. Drug survival for ABA was shown in Figure 1. Log-rank between RF positive and negative patients was found as 0.067.

Table 1. DAS-28 scores at first and last follow-up visits

	First control visit (n=136)	Last control visit (n=136)
Follow up duration, mean (SD)	4.5 (3.1)	12,3 (10.9)
DAS-28 >5.1,n (%)	11 (8.2)	16 (11.8)
DAS-28=3.2–5.1,n (%)	56 (41.8)	46 (33.8)
DAS-28=2.6–3.2,n (%)	23 (17.2)	23 (16.9)
DAS-28 <2.6,n (%)	44 (32.8)	51 (37.5)
Remission or low disease activity among patients with at least one follow-up visit, n (%)	67 (50.0)	74 (54.4)
Remission or low disease activity among all patients, n (%) (The worst scenario)	67/158 (42.4)	74/158 (46.8)

Figure 1. ABA survival rates in RF positive and negative patients



Conclusions: In our database, 70% of RA patients received ABA were biologic naive. Remission or low-disease activity was achieved approximately 50% of patients in first follow-up visit with an average of 4.5 months after begining of the treatment. Functional improvement was observed in two thirds of patients.

Death or life threatening side effects were not seen during follow-up. ABA is an acceptable treatment option in DMARD resistant biologic naive RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4082

SAT0217 EARLY PATIENT-REPORTED OUTCOMES AND CLINICAL OUTCOMES WITH ABT-494 IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS WHO ARE INADEQUATE RESPONDERS TO METHOTREXATE OR TUMOR NECROSIS FACTOR INHIBITORS: POST-HOC ANALYSIS OF PHASE 2 RANDOMIZED CONTROLLED TRIALS

V. Strand[1], N. Tundia[2], I.H. Song[2], S. Meerwein[2], J. Lin[2], N. Chen[2], A. Friedman[2]. *[1]Stanford University, Palo Alto; [2]AbbVie Inc., North Chicago, United States*

Background: Janus kinase (JAK) inhibitors are being evaluated for treatment of active rheumatoid arthritis (RA). Understanding their onset of action on patient reported outcomes (PROs) and clinical endpoints in RA patients (pts) is limited.
Objectives: To assess onset of benefit with ABT-494, a selective JAK1 inhibitor vs placebo (PBO) in RA pts with active disease ≥3 months in 2 randomized controlled trials (RCTs) evaluating safety and efficacy of ABT-494. M13–537 (NCT02066389) included pts who were inadequate responders to methotrexate (MTX-IR) and M13–550 (NCT01960855) to tumor necrosis factor inhibitors (TNF-IR).
Methods: Data were analyzed separately for each RCT in pts who received 6mg or 12mg bid ABT-494 or PBO. Analyses included cumulative assessment of PROs such as patient global assessment of disease activity (PtGA), pain Visual Analogue Scale (VAS) and Health Assessment Questionnaire Disability Index (HAQ-DI) in terms of Routine Assessment of Patient Index Data 3 (RAPID3) scores, and clinical outcomes such as DAS28 (CRP) and CDAI. To assess onset and maintenance of effect, the number of pts whose improvements met or exceeded minimal important differences (MID) RAPID3: reduction ≥3.6; DAS28: reduction ≥1.2; CDAI: reduction ≥11.0 and were calculated at weeks 2 and 12. Additionally, Kaplan-Meier (KM) analysis estimated mean time to achievement of RAPID3, DAS28 and CDAI MID. Non-responder imputation accounted for missing data.
Results: In M13–537 (N=150 pts) and M13–550 (N=166 pts) RCTs, significantly more pts in ABT-494 12mg groups reported improvements ≥MID in RAPID3 vs PBO at Wk 2: 68% vs 30% and 73% vs 38%, respectively (Table). In M13–537, significantly more pts receiving ABT-494 6mg BID vs PBO (54% vs 30%) had improvements ≥MID in RAPID3. These responses were sustained throughout both trials in pts receiving 12mg ABT-494 (M13–537: 80%; M13–550: 71%). Significantly more pts achieved and maintained changes ≥MID in DAS28 in both RCTs and in CDAI in M13–550. Based on KM analyses, in M13–537, estimated mean time (±SE) to achievement of RAPID3 MID was shorter for both ABT-494 doses vs PBO (12mg: 3.9±0.5 weeks; 6mg: 3.9±0.4 weeks; PBO 6.0±0.6 weeks). Similarly, estimated mean time to these responses was shorter with both ABT-494 doses vs PBO (12mg: 3.6±0.4 weeks; 6mg: 4.9±0.6 weeks; PBO: 6.6±0.6 weeks) in M13–550, although it was underestimated due to censoring.

Table. Number of patients reporting clinically meaningful improvements over study period.

	M13-537			M13-550		
n (%)	ABT-494 6mg N=50	ABT-494 12mg N=50	PBO N=50	ABT-494 6mg N=55	ABT-494 12mg N=55	PBO N=56
RAPID3: ≥MID						
Week 2	27 (54)[a]	34 (68)[b]	15 (30)	25 (45)	40 (73)[b]	21 (38)
Week 12	32 (64)	40 (80)[b]	24 (48)	35 (64)[a]	39 (71)[b]	23 (41)
DAS28: ≥MID						
Week 2	26 (52)[a]	27 (54)[b]	9 (18)	27 (49)[a]	36 (65)[b]	14 (25)
Week 12	37 (74)[a]	44 (88)[b]	22 (44)	32 (58)	38 (69)[b]	23 (41)
CDAI: ≥MID						
Week 2	25 (50)	25 (50)	17 (34)	33 (60)[a]	33 (60)[b]	21 (38)
Week 12	36 (72)[a]	42 (84)[b]	26 (52)	39 (71)	42 (76)[b]	29 (52)

[a]P<.05 for ABT-494 6mg vs PBO (chi-square test).
[b]P<.05 for ABT-494 12mg vs PBO (chi-square test).

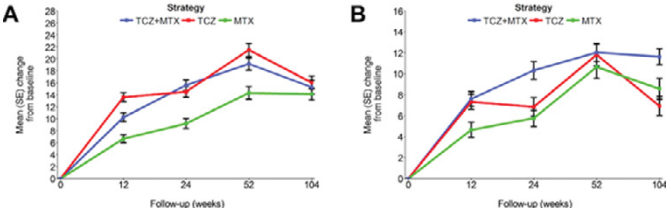
Conclusions: Patients treated with ABT-494 showed fast clinically meaningful improvements in patient reported disease activity, pain, physical function cumulatively assessed as RAPID3, as well as clinical outcomes DAS28 and CDAI, as early as week 2 and sustained through week 12 in both MTX-IR and TNF-IR populations.
Acknowledgements: Financial support for the study and medical writing support (Joann Hettasch, Fishawack Group, Conshohocken, PA) was provided by AbbVie. AbbVie participated in interpretation of data, review, and approval of the abstract. All authors contributed to development of the abstract and maintained control over final content.
Disclosure of Interest: V. Strand Consultant for: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB; Ad boards: AbbVie, Amgen, AstraZeneca, BMS, Celgene, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB, N. Tundia Shareholder of: AbbVie, Employee of: AbbVie, I. H. Song Shareholder of: AbbVie, Employee of: AbbVie, S. Meerwein Shareholder of: AbbVie, Employee of: AbbVie, J. Lin Shareholder of: AbbVie, Employee of: AbbVie, N. Chen Shareholder of: AbbVie, Employee of: AbbVie, A. Friedman Shareholder of: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.1143

SAT0218 EFFECT OF TOCILIZUMAB IN DMARD-NAÏVE EARLY RHEUMATOID ARTHRITIS PATIENTS ON HEALTH-RELATED QUALITY OF LIFE: RESULTS OF THE U-ACT-EARLY TRIAL

X.M. Teitsma[1], J.W. Jacobs[2], P.M. Welsing[2], A. Pethö-Schramm[3], M.E. Borm[4], J.M. van Laar[1], F.P. Lafeber[1], J.W. Bijlsma[1]. *[1]Rheumatology and Clinical Immunology; [2]UMC Utrecht, Utrecht, Netherlands; [3]F. Hoffmann-La Roche, Basel, Switzerland; [4]Roche Nederland B.V., Woerden, Netherlands*

Background: Tocilizumab (TCZ), a humanized interleukin-6 receptor inhibitor, has been shown effective in suppressing symptoms of rheumatoid arthritis (RA). In U-Act-Early, a significantly greater proportion of patients with early RA who initiated TCZ (84%) or TCZ plus MTX therapy (86%) achieved sustained remission (Disease Activity Score assessing 28 joints (DAS28) <2.6 with ≤4 swollen joints for ≥24 weeks), when compared to those initiating MTX (44%).[1]
Objectives: To determine the effect of treat-to-target TCZ therapy, with or without MTX, on health-related quality of life (HRQoL) in disease modifying anti-rheumatic drugs (DMARD)-naïve patients with early RA.
Methods: Patients (n=317) were randomized to initiate TZC, TCZ+MTX or MTX therapy and treated according to a step-up strategy. TCZ was given (8 mg/kg) every 4 weeks and MTX (oral) was started at 10 mg/week and increased with steps of 5 mg steps 4 weekly up to 30 mg/week (or maximum tolerable dose) until remission. If after 20 weeks remission was not achieved, hydroxychloroquine was added and discontinued 12 weeks thereafter if the target still was not achieved. Patients who originally initiated monotherapy then switched to TCZ+MTX therapy and those already on this combination therapy switched to a tumour necrosis factor inhibitor. To evaluate the effect of TCZ on HRQoL, we used the 36-item Short-Form (SF-36), which can be summarized into a physical (PCS) and mental (MCS) component score. HRQoL was measured at baseline and after 12, 24, 52, and 104 weeks. A linear mixed effect model with a random intercept was used to evaluate differences between treatment strategies over time with visit (time), strategy, baseline SF-36 score, baseline DAS28 level (i.e., DAS28 <5.1 or ≥5.1) and centre as fixed effects. The proportions of patients exceeding the minimum clinically important differences (MCID, ≥2.5-point increase from baseline) were tested for significance using the two-sided Pearson's chi-squared test.
Results: We found significantly greater improvements over time in the SF-36 PCS in patients initiating treatment with TCZ (TCZ *vs* MTX; p=0.041, TCZ+MTX *vs* MTX; p=0.011, Fig. 1). For the SF-36 MCS, no significant differences over time were noted between the treatment arms (p≥0.11). A significantly higher proportion of patients initiating treatment with TCZ (76%; p=0.016, 89%; p=0.030) or TCZ+MTX (73%; p=0.049, 89%; p=0.027) achieved MCID in the SF-36 PCS at week 12 and week 52, when compared to those initiating treatment with MTX (59% and 73%, respectively). Although the proportions of patients achieving MCID in the SF-36 MCS were numerically higher in the TCZ arms, no significant differences were found (p≥0.06).

Fig. 1: Mean (SE) change from baseline in SF-36 PCS (**A**) and SF-36 MCS (**B**).



Conclusions: Initiation of TCZ, with or without MTX, at start of therapy resulted in statistically significant and clinically relevant improvements in the HRQoL when compared to initiation of MTX alone and may be considered as a valuable treatment strategy in DMARD-naïve patients with early RA.
References:
[1] Bijlsma JW, Welsing PM, Woodworth TG, et al. Early rheumatoid arthritis treated with tocilizumab, methotrexate, or their combination (U-Act-Early): a multicentre, randomised, double-blind, double-dummy, strategy trial. Lancet 2016; 388:343–55.
Disclosure of Interest: X. Teitsma: None declared, J. Jacobs: None declared, P. Welsing: None declared, A. Pethö-Schramm Employee of: Employee of F.Hoffmann-La Roche, M. Borm Employee of: Roche Nederland B.V., J. van Laar Consultant for: Received fees from MSD, Pfizer, Roche, Eli Lilly and BMS, F. Lafeber: None declared, J. Bijlsma Grant/research support from: Received research grants (to his department) and consultancy fees from AbbVie, BMS, Crescendo, MSD, Mundipharma, Pfizer, Roche, Sun and UCB
DOI: 10.1136/annrheumdis-2017-eular.2190

SATURDAY, 17 JUNE 2017

SLE, Sjögren's and APS - treatment

SAT0219 EFFICACY AND SAFETY OF ATACICEPT IN PATIENTS WITH HIGH DISEASE ACTIVITY IN A 24-WEEK, RANDOMIZED, PLACEBO-CONTROLLED, PHASE IIB STUDY (ADDRESS II)

J.T. Merrill[1], D.J. Wallace[2], A. Kao[3], C. Vazquez Mateo[3], P.A. Fraser[3], P. Chang[3], D. Isenberg[4]. *[1]Oklahoma Medical Research Foundation, Oklahoma City; [2]Cedars-Sinai Medical Center, University of California Los Angeles, Los Angeles; [3]EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, United States; [4]University College London, London, United Kingdom*

Background: Atacicept targets B-cell stimulating factors BLyS and APRIL, and has shown evidence of clinical response in SLE.
Objectives: Exploration of atacicept efficacy and safety in a pre-defined subpopulation of SLE patients with high disease activity (HDA, SLEDAI-2K $\geq$10 at Screening) in the phase IIb ADDRESS II study (NCT01972568).
Methods: Autoantibody positive patients on standard of care therapy were randomized 1:1:1 to double-blind weekly SC injections of atacicept 75 or 150 mg or placebo (PBO) for 24 weeks. Analyses of the HDA subpopulation are now reported.
Results: 52% of the ITT population had HDA (n=158: 52 PBO; 55 atacicept 75 mg; 51 atacicept 150 mg). 92% were female, 67% were white, and baseline characteristics were balanced between groups. At week 24 (Table 1; Figure 1), the proportion of SLE Responder Index (SRI)-4 ($p<0.05$) and SRI-6 ($p<0.005$) responses was greater with atacicept 150 mg vs PBO. BICLA response rate was higher with both doses ($p<0.05$). More patients achieved SLEDAI-2K $\leq$2 with atacicept 150 mg vs PBO ($p<0.01$). Time to severe and moderate-severe flare was significantly reduced at both atacicept doses vs PBO ($p<0.05$). Patients in the quartile with the largest decline in serum IgG had the highest SRI-6 response rates (Table 2). Treatment-emergent adverse event (TEAE) rates were similar between groups (PBO 71.2%; 75 mg 78.2%; 150 mg 74.5%). Serious/severe infections were not increased with atacicept 150 mg (PBO 9.6%; 75 mg 10.9%; 150 mg 0%). There were no patient deaths.
Conclusions: In SLE patients with HDA, Atacicept 150 mg demonstrated significant clinical responses and an acceptable safety profile.
Acknowledgements: The study was sponsored by EMD Serono Research & Development Institute Inc., USA (a business of Merck KGaA, Germany). Medical writing support was provided by Bioscript Science, UK, and funded by Merck KGaA.
Disclosure of Interest: J. Merrill Consultant for: received consulting fees from Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen, D. Wallace Consultant for: received consulting fees from EMD Serono, A. Kao Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, C. Vazquez Mateo Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, P. Fraser Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, P. Chang Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, D. Isenberg Consultant for: received consulting fees from EMD Serono
DOI: 10.1136/annrheumdis-2017-eular.1512

Table 1. Disease activity endpoints at week 24

	Placebo n=52	Atacicept 75 mg n=55	Atacicept 150 mg n=51
SRI-4 response, n (%)	22 (42.3)	32 (58.2)	32 (62.7)*
SRI-6 response, n (%)	15 (28.8)	23 (41.8)	28 (54.9)†
BICLA response¶, n (%)	14 (29.2)	26 (50.0)*	25 (49.0)*
SLEDAI-2K $\leq$2¶, n (%)	7 (13.7)	11 (20.0)	20 (39.2)†
Clinical SLEDAI-2K $\leq$2‡, n (%)	15 (28.9)	24 (43.6)	25 (49.0)*
Severe flare by SFI, n (%)	13 (25.0)	5 (9.1)	3 (5.9)
Time to severe flare by SFI, HR (95% CI)		0.33 (0.12, 0.94)*	0.19 (0.05, 0.68)†
Severe flare by BILAG A, n (%)	12 (23.1)	1 (1.8)	4 (7.8)
Time to severe flare by BILAG A, HR (95% CI)		0.08 (0.01, 0.59)†	0.32 (0.10, 0.99)*
Moderate/severe flare by BILAG A/2B, n (%)	13 (25.0)	5 (9.1)	5 (9.8)
Time to moderate/severe flare by BILAG A/2B, HR (95% CI)		0.33 (0.12, 0.95)*	0.34 (0.12, 0.95)*
Any flare by BILAG A/B, n (%)	31 (59.6)	23 (41.8)	17 (33.3)
Time to any flare by BILAG A/B, HR (95% CI)		0.67 (0.38, 1.17)	0.47 (0.26, 0.86)*

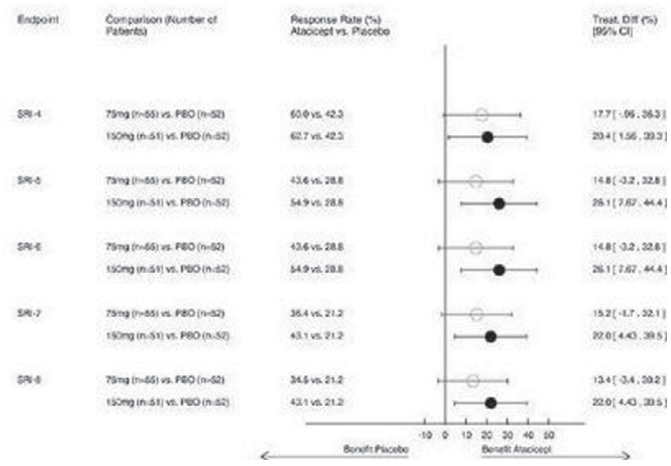
*$p<0.05$; †$p<0.01$; ‡excluding anti-dsDNA and complement parameters; HR, hazard ratio, SRI, SLE responder index; ¶patients with baseline data used for % calculation.

Table 2. Serum IgG reduction by quartile and SRI-6 response at week 24

IgG reduction (by quartile), g/L	Q1 (0–2.97) (n=21)	Q2 (2.98–4.30) (n=26)	Q3 (4.31–5.56) (n=26)	Q4 (5.57–14.73) (n=33)
SRI-6 response rate (%)	38.1	30.8	53.8	63.6
Δ vs Q1 (%)	[Referent]	-7.3	15.7	25.5

SRI, SLE Responder Index.

Figure 1. Forest Plot for SRI Response at Week 24 with Screening Visit as baseline HDA Population



SAT0220 EFFECTS OF TYPE I INTERFERON INHIBITION ON BLOOD LEUKOCYTE SUBSETS IN PATIENTS TREATED IN A PHASE IIB CLINICAL STUDY OF ANIFROLUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

W. White, K.A. Casey, M.A. Smith, L. Wang, D. Sinbaldi, M.A. Sanjuan, G. Illei. *MedImmune LLC, Gaithersburg, United States*

Background: A Phase IIb randomized controlled study (NCT01753193) was conducted with anifrolumab, a fully human, anti-interferon (IFN)–α receptor (IFNAR) specific antibody in adults with moderate to severe SLE. Anifrolumab binds to subunit 1 of the IFNAR and inhibits the activity of all type I IFNs. A complete blood count analysis demonstrated that anifrolumab reversed leukopenia. However, the types of peripheral immune cells affected following treatment have not been reported.
Objectives: To better understand how changes in the immune cell repertoire may be associated with SLE severity, type I IFN test status (high vs. low), and treatment with anifrolumab, we performed flow cytometry to assess peripheral blood cell types: dendritic cells (myeloid and plasmacytoid), B cells (naïve, memory, and plasma cells), neutrophils, and T cells (CD4, CD8, naïve, memory, central memory, and effector).
Methods: Patients were randomized 1:1:1 to anifrolumab 300 mg, or 1,000 mg, or placebo (PBO) every 4 weeks for 48 weeks. Peripheral blood was collected from a subset of patients (91 total) on Days 1 (prior to first dose), 85, 141, 169, 253, 337, and 365. Patients were approximately evenly distributed between treatment arms. Baseline absolute immune cell numbers were compared over treatment course in the context of SLE Disease Activity Index (SLEDAI)–2K scores, type I IFN test, and therapy response. Statistics were calculated using the Student's *t*-test; p-values $\leq$0.05 were considered statistically significant.
Results: At baseline, several blood cell types were lower for patients with SLEDAI $\geq$10, including naïve B cells, and memory T and B cells. In IFN-high patients, neutrophils, memory T cells, and plasmacytoid dendritic cells (pDCs) were significantly decreased. Anifrolumab led to significant increases in absolute numbers of T-cell subsets in the blood of IFN-high patients. In contrast, no significant changes were observed for IFN-low patients. Observed increases were within normal reference ranges. The alterations did not appear to be secondary to tapering of oral corticosteroids, as these cell types were not significantly different in PBO groups, regardless of tapering. Patients with $\geq$6-point SLEDAI reductions following anifrolumab demonstrated significant increases in total CD4 and CD8 T cells, and nonsignificant decreases in memory B cells. Significant increases in pDCs were also evident. Anifrolumab did not cause significant differences in other cell types measured.
Conclusions: Memory T cell numbers, among other cell types, were significantly reduced in patients with SLEDAI $\geq$10 and those classified as IFN high at baseline. This suggests that, for patients with more severe disease, type I IFN may be involved in cell migration into the peripheral tissues from the blood. Consistent with this, we found that neutralization of type I IFN with anifrolumab promoted immigration and/or prevented emigration of potentially pathologic immune cells between the tissues and the blood. These data suggest that some effects observed following anifrolumab treatment might be a result of altering the migration patterns of T and other immune cells, which may partially explain its biological activity.
Acknowledgements: Funded by MedImmune. Medical writing support: R Plant, QXV Comms, an Ashfield company, funded by MedImmune.
Disclosure of Interest: W. White Shareholder of: AstraZeneca, Employee of: MedImmune LLC, K. Casey Shareholder of: AstraZeneca, Employee of: MedImmune LLC, M. Smith Shareholder of: AstraZeneca, Employee of: MedImmune LLC, L. Wang Employee of: MedImmune LLC, D. Sinbaldi Shareholder of: AstraZeneca, Employee of: MedImmune LLC, M. Sanjuan Employee of: MedImmune LLC, G. Illei Shareholder of: AstraZeneca, Employee of: MedImmune LLC

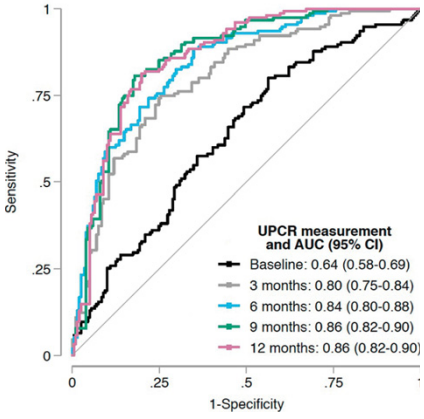
DOI: 10.1136/annrheumdis-2017-eular.3833

SAT0221 SIX-MONTH PROTEINURIA MEASUREMENT PREDICTS RENAL RESPONSE AT 18 MONTHS IN LUPUS NEPHRITIS: ANALYSIS OF TWO PHASE III RANDOMIZED CLINICAL TRIALS

M.D. Cascino[1,2], T. Schindler[3], L.M. Gomez Mendez[2], P. Brunetta[1], L. Dragone[1], M. Dall'Era[2], J. Garg[1]. *[1]Genentech, Inc., South San Francisco; [2]University of California – San Francisco, San Francisco, United States; [3]F. Hoffmann-La Roche, Basel, Switzerland*

Background: Early identification of patients with lupus nephritis (LN) likely to achieve complete renal response (CRR) may expedite the evaluation of new therapies and guide clinical care. Prior analyses have shown that early improvement in proteinuria is associated with subsequent renal response.[1,2] Several ongoing LN trials including NOBILITY, an assessment of the efficacy of the anti-CD20 monoclonal antibody obinutuzumab in combination with standard of care immunosuppression, will evaluate proteinuric response at 6 months as a key secondary endpoint.[3] Whether short-term response accurately predicts future CRR, however, is uncertain.
Objectives: To assess the predictive value of early measurements of the level of proteinuria and to identify proteinuria cutoffs that best identify patients who will achieve CRR at 18 months.
Methods: LUNAR and BELONG were multicenter, double-blinded studies that in total randomized 522 patients with ISN/RPS class III or class IV LN to blinded investigational infusions or placebo in combination with standard of care immunosuppression.[4,5] CRR was assessed at 18 months and defined for this analysis as achievement of urine protein to creatinine ratio (UPCR) <0.5 with normal serum creatinine that was not increased from baseline by $>25\%$. Bootstrapping was used to generate nonparametric receiver operating characteristic (ROC) curves and estimate area under the curve (AUC). The Youden index was used to identify UPCR cutoff values that maximize sensitivity and specificity. Positive predictive value (PPV) and negative predictive value (NPV) were calculated.
Results: ROC curves were constructed for proteinuria measurements at baseline and 3, 6, 9, and 12 months after randomization (Figure 1). AUC increased from baseline to month 3 (0.64 vs. 0.80, $P<0.001$) and from month 3 to month 6 (0.80 vs. 0.84, $P<0.01$) but did not increase beyond month 6 ($P>0.05$ for each pairwise comparison). Achievement of 6-month UPCR <1 was 83.8% sensitive and 71.0% specific for CRR at 18 months and had PPV and NPV of 64.9% and 87.2%, respectively. Evaluation of lower 6-month UPCR cutoff values yielded improvements in specificity and PPV but marked decreases in sensitivity and NPV. In multivariate analysis, the addition of 6-month serum creatinine and percent change in UPCR from baseline did not result in meaningful increases in AUC compared with 6-month proteinuria measurement alone.

Figure: Receiver operating characteristic curves for CRR at 18 months



Conclusions: Level of proteinuria at 6 months alone was predictive of CRR at 18 months in aggregated data from two phase III LN clinical trials. After 6 months of treatment, UPCR <1 had high sensitivity and NPV for CRR at 18 months. This cutoff might be used to prospectively identify patients who are unlikely to achieve complete response within 18 months on the initial therapy for LN. The impact of these findings on guiding treatment decisions outside the setting of randomized clinical trials requires further investigation.
References:
[1] Tamirou Lupus Sci & Med 2015.
[2] Dall'Era Arthritis Rheumatol 2015.
[3] Schindler Ann Rheum Dis 2016.
[4] Rovin B Arthritis Rheumatol 2012.
[5] Mysler E Arthritis Rheumatol 2013.
[1] Trial registry numbers: NCT00282347 (LUNAR) and NCT00626197 (BELONG).
Disclosure of Interest: M. Cascino Employee of: Roche/Genentech, T. Schindler Employee of: Roche/Genentech, L. Gomez Mendez Grant/research support from: Roche/Genentech, P. Brunetta Employee of: Roche/Genentech, L. Dragone Employee of: Roche/Genentech, M. Dall'Era: None declared, J. Garg Employee of: Roche/Genentech
DOI: 10.1136/annrheumdis-2017-eular.5414

SAT0222 BIIB059, A MONOCLONAL ANTIBODY TARGETING BDCA2, SHOWS EVIDENCE OF BIOLOGICAL ACTIVITY AND EARLY CLINICAL PROOF OF CONCEPT IN SUBJECTS WITH ACTIVE CUTANEOUS LE

R. Furie[1], V.P. Werth[2], J.F. Merola[3], T.L. Reynolds[4], L. Stevenson[4], W. Wang[4], K. Smirnakis[4], C. Barbey[5], C. Musselli[4,4], B. Werneburg[4], D. Rabah[4], N. Franchimont[4]. *[1]Northwell Health, Great Neck; [2]Hospital of the University of Pennsylvania and the Veteran's Administration Medical Center, Philadelphia; [3]Brigham and Women's Hospital, Harvard Medical School, Boston; [4]Biogen, Cambridge, United States; [5]Biogen, Zug, Switzerland*

Background: Type I interferons (IFN-I) are central to the pathogenesis of systemic lupus erythematosus (SLE). BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, upon engagement, inhibits the production of IFN-I and other inflammatory mediators. Targeting BDCA2, therefore, represents an attractive therapeutic strategy for inhibiting pDC-driven inflammation that is such a key feature of SLE pathogenesis. BIIB059, an investigational anti-BDCA2 humanized monoclonal antibody, has been shown to engage BDCA2, and this interaction leads to BDCA2 internalization and the consequent in vitro inhibition of TLR-induced IFN-I production by pDCs (Pellerin 2015).
Objectives: This first-in-patient study aimed to assess safety, tolerability, pharmacokinetic (PK) and pharmacodynamic (PD) effects and clinical activity of BIIB059 in adult SLE patients with active cutaneous lupus (CLE) following administration of a single BIIB059 dose.
Methods: A Phase 1b randomized, double-blinded, placebo controlled, multicenter clinical trial was conducted in 12 adult SLE subjects (meeting 1997 ACR criteria) with active cutaneous manifestations (including acute, sub-acute and/or chronic cutaneous forms of cutaneous lupus erythematosus (CLE)). Subjects received a single IV administration of either BIIB059 20mg/kg (n=8) or placebo (n=4). A panel of IFN-responsive genes (IRG) was assessed from whole blood by qPCR at baseline and several post-dose time points. Skin biopsies from active lesions were obtained and evaluated at baseline and week 4 for IFN-regulated proteins, including MxA and IFITM3 using quantitative immunohistochemistry. CLE disease activity was assessed using the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), and safety data, including adverse events (AEs) and laboratory tests, were also collected.
Results: Most SLE subjects had high IRG signatures in the blood. Skin biopsies demonstrated features of inflammation consistent with active CLE, including elevated expression of MxA and other IFN-regulated proteins. A single dose of BIIB059 decreased the expression of IRG in blood and MxA and IFITM3 proteins in the skin in most patients. CD45+ cells were reduced in skin biopsies of BIIB059-treated patients. The reduction in inflammatory cells as well as MxA and IFITM3 expression at week 4 correlated with improvement in CLASI activity score at multiple timepoints post-dose. BIIB059 was generally well tolerated with no discontinuations due to AEs. The incidence of AEs was similar between BIIB059- and placebo-treated SLE subjects, and most AEs were mild or moderate in severity.
Conclusions: A single dose of BIIB059 resulted in inhibition of the IRG in peripheral blood and MxA and IFITM3 expression in lesional skin of SLE subjects, consistent with BIIB059's proposed mechanism of action. The clinical and biomarker data together confirm the role of human pDCs in the pathogenesis of SLE, and support further development of BIB059 in SLE.
Disclosure of Interest: R. Furie Consultant for: Biogen, V. Werth Grant/research support from: Biogen, Consultant for: Biogen, J. Merola Grant/research support from: Biogen, Consultant for: Biogen, AbbVie, Amgen, Eli Lilly, Novartis, Pfizer, Janssen, Mallinckrodt, Momenta, Speakers bureau: AbbVie, Eli Lilly, T. Reynolds Shareholder of: Biogen, Employee of: Biogen, L. Stevenson Shareholder of: Biogen, Employee of: Biogen, W. Wang Shareholder of: Biogen, Employee of: Biogen, K. Smirnakis Shareholder of: Biogen, Employee of: Biogen, C. Barbey Shareholder of: Biogen, Employee of: Biogen, C. Musselli Shareholder of: Biogen, Employee of: Biogen, B. Werneburg Shareholder of: Biogen, Employee of: Biogen, D. Rabah Shareholder of: Biogen, Employee of: Biogen, N. Franchimont Shareholder of: Biogen, Employee of: Biogen
DOI: 10.1136/annrheumdis-2017-eular.6259

SAT0223 INDIRECT COMPARATIVE CLINICAL EFFECTIVENESS OF INTRAVENOUS AND SUBCUTANEOUS FORMULATIONS OF BELIMUMAB FOR THE TREATMENT OF ADULT PATIENTS WITH ACTIVE, AUTOANTIBODY-POSITIVE SYSTEMIC LUPUS ERYTHEMATOSUS WITH HIGH DISEASE ACTIVITY

D. Parks[1], S. Ramachandran[1], M. Kurtinecz[1], Y. Asukai[2], R. Alfonso-Cristancho[1]. *[1]GSK, Collegeville, United States; [2]GSK, Uxbridge, United Kingdom*

Background: The efficacy of belimumab (BEL) vs placebo (PBO), in adult

Abstract SAT0223 – Table 1

	BLISS-52 IV (10 mg/kg)		BLISS-76 IV (10 mg/kg)		North East Asia IV (10 mg/kg)		BEL112341 SC (200 mg)	
	BEL	PBO	BEL	PBO	BEL	PBO	BEL	PBO
Baseline characteristics				*HDA subgroup/original RCT (n/N)*				
	134/273	131/275	171/290	156/287	292/451	135/226	248/556	108/280
SELENA-SLEDAI score, mean (SD)	10.3 (3.4)	11.4 (4.1)	10.8 (4.0)	10.8 (3.7)	10.4 (3.8)	11.3 (4.0)	11.5 (3.3)	11.7 (3.1)
SRI response at 52 weeks, %	45.5	28.2	56.1	34.6	54.0	34.1	64.6	47.2
Outcome at 52 weeks				*Odds ratio SC/IV (95% credibility interval)*				
HDA criteria		1				2		
SRI response		0.90 (0.53, 1.52)				0.88 (0.58, 1.33)		
4-point reduction in SELENA-SLEDAI		0.99 (0.58, 1.68)				0.95 (0.63, 1.43)		
Rate of severe flares		0.69 (0.37, 1.28)				0.89 (0.53, 1.50)		

patients with active, autoantibody-positive systemic lupus erythematosus (SLE) who are receiving standard SLE therapy has been demonstrated. To date, no direct comparison of intravenous (IV) BEL vs subcutaneous (SC) BEL has been performed, hence the importance of an indirect treatment comparison (ITC).

Objectives: To indirectly compare the clinical effectiveness of BEL IV and SC formulations in patients with SLE high disease activity (HDA) via an ITC.

Methods: Three BEL IV Phase lll randomised controlled trials (RCTs; HDA/BLISS-52, 327/577; HDA/BLISS-76, 265/548; HDA/North East Asia study [BEL113750], 427/677) and one BEL SC RCT (HDA/BEL112341; 356/836) were compared via a Bayesian ITC (BEL207255). We evaluated the relative efficacy of the formulations in patients meeting three measures of HDA at baseline (1. BLISS-52 and BLISS-76, C3 <0.9 g/L or C4 <0.16 g/L; BEL112341 and BEL113750, C3 <0.9 g/L or C4 <0.10 g/L; and 2. anti-dsDNA positive [≥30 IU/mL] or 3. Safety of Estrogen in Lupus Erythematosus National Assessment-SLE Disease Activity Index [SELENA-SLEDAI] scores ≥10). Analyses were conducted in patients meeting Criteria 1: low C3/C4 and high anti-dsDNA; and Criteria 2: low C3/C4 and high anti-dsDNA or SELENA-SLEDAI ≥10 or low C3/C4. The primary endpoint was SLE Responder Index (SRI) response (≥4-point reduction in SELENA-SLEDAI, no worsening in Physician's Global Assessment, no new 1A/2B British Isles Lupus Assessment Group domain scores) at Week 52. Secondary endpoints included ≥4-point reduction in SELENA-SLEDAI and SLE Flare Index rate. Safety endpoints were not assessed.

Results: Baseline characteristics were relatively similar between RCTs and a fixed effects model binomial distribution with logit link was used for all efficacy endpoints (Table). In this indirect comparison, no differences were identified between BEL IV and BEL SC for the efficacy endpoints.

Conclusions: In this indirect comparison, BEL IV and BEL SC were similar for SRI response, ≥4-point reduction in SELENA-SLEDAI, or rate of severe flare at Week 52 in patients with SLE. Outcomes were consistent irrespective of the criteria applied.

Acknowledgements: Study funded by GSK. Katie White, PhD, Fishawack Indicia Ltd, UK, provided editorial assistance funded by GSK.

Disclosure of Interest: D. Parks Shareholder of: GSK, Employee of: GSK, S. Ramachandran Shareholder of: GSK, Employee of: GSK, M. Kurtinecz Employee of: GSK, Y. Asukai Shareholder of: GSK, Employee of: GSK, R. Alfonso-Cristancho Shareholder of: GSK, Employee of: GSK

DOI: 10.1136/annrheumdis-2017-eular.4701

SAT0224 THE ROLE OF INTENSIVE IMMUNOSUPPRESSIVE THERAPY IN THE MANAGEMENT OF SLE-ASSOCIATED PULMONARY ARTERIAL HYPERTENSION: A SINGLE-CENTER COHORT STUDY

Q. Wang [1], J. Zhao [1], J. Qian [2], Z. Tian [3], M. Li [1], X. Zeng [1]. *[1]Rheumatology; [2]Internal Medicine; [3]Cardiology, Peking Union Medical College Hospital, Beijing, China*

Background: Autoimmune and inflammatory mechanisms could play a significant role in the pathogenesis of pulmonary arterial hypertension (PAH), especially in patients with systemic lupus erythematosus (SLE). The effect of immunosuppressive therapy in the treatment of SLE-associated PAH (SLE-PAH) has not been fully investigated in a large cohort previously.

Objectives: We aimed to review the clinical outcomes in patients with SLE-PAH cohort treated with intensive immunosuppressive therapy with or without PAH-targeted therapy.

Methods: In this single-center cohort study, 126 patients with SLE-PAH were consecutively enrolled between May 2006 through December 2015. All patients were performed right heart catheriazation to confirm the diagnosis of PAH, and all received intensive immunosuppressive therapy including combination of high-dose glucocorticosteroids and immunosuppressants, such as cyclophosphamide, mycophenolate and calcineurin inhibitors. Baseline demographics, clinical features, laboratory findings, hemodynamic measurements and treatment were analyzed. Kaplan-Meier curves and Cox proportional hazards regression analysis were used to evaluate the role of intensive immunosuppressive therapy.

Results: Of the 126 SLE-PAH patients, eighty-two (65.1%) patients received PAH-targeted therapy at baseline. Demographic and clinical characteristics were shown in Table 1. Survival analysis indicated that responders had a better survival than nonresponders in both with and without PAH-targeted therapy groupPatients with a shorter SLE disease duration (p=0.009) and better baseline pulmonary hemodynamics (mean pulmonary arterial pressure, pulmonary vascular resistance and Cardiac index, p<0.001) were more likely to benefit from immunosuppressive therapy (Table 1).

Table1.Comparison of clinical characteristics in responders and nonresponders to immunosuppressive therapy

	SLE-PAH without target therapy			SLE-PAH with target therapy		
	Responder N=29	Nonresponder N=15	*p-value*	Responder N=44	Nonresponder N=38	*p-value*
Female, n, (%)	29(100)	15(100)	*1.000*	43(100)	37(97.4)	*1.000*
Age, years	33.8±9.2	37.0±10.0	*0.293*	32.1±7.2	35.3±8.3	*0.066*
SLE Disease duration, months	3.5(0,23.7)	6.4(1.0,33.1)	*0.090*	4.8(0,18.9)	6.3(0.7,23.1)	*0.427*
RP,n(%)	19(65.5)	9(60.0)	*0.718*	24(54.5)	24(63.2)	*0.430*
Anti-u1RNP, n (%)	21(72.4)	10(66.7)	*0.676*	25(61.0)	19(50.0)	*0.326*
SLEDAI-2000	7.0±6.2	5.1±4.5	*0.296*	3.0±2.9	3.5±2.6	*0.420*
WHO functional classification						
I-II, n(%)	17(58.6)	5(33.3)	*0.013*	21(47.7)	18(47.6)	*0.292*
III-IV, n(%)	12(41.4)	10(66.7)		23(52.3)	20(52.6)	
6MWD, meter	465.3±77.4	424.0±97.9	*0.180*	417.8±99.4	398.2±92.9	*0.409*
Mean RAP, mmHg	4.2±3.0	2.8±2.8	*0.201*	3.9±4.3	4.3±4.0	*0.706*
Mean PAP, mmHg	37.9±8.2	45.7±7.9	*0.005*	45.1±10.3	53.2±11.0	*0.001*
CI, $l.min^{-1}.m^{-2}$	3.2±0.7	2.5±0.6	*0.003*	2.8±0.6	2.4±0.8	*0.018*
PVR, WU	6.6±2.4	10.5±3.0	*0.001*	9.2±3.6	12.7±4.5	*0.000*

Conclusions: Intensive immunosuppressive therapy markedly improved the long-term outcomes of SLE patients with PAH, especially in the early stage of PAH.

References:

[1] Chung L, Liu J, Parsons L, et al. Characterization of connective tissue disease-associated pulmonary arterial hypertension from REVEAL: identifying systemic sclerosis as a unique phenotype. Chest, 2010; 138:1383–94.

[2] Shirai Y, Yasuoka H, Okano Y, Takeuchi T, Satoh T and Kuwana M Clinical characteristics and survival of Japanese patients with connective tissue disease and pulmonary arterial hypertension: a single-centre cohort. Rheumatology (Oxford), 2012; 51:1846–54.

[3] Kang KY, Jeon CH, Choi SJ, et al. Survival and prognostic factors in patients with connective tissue disease-associated pulmonary hypertension by echocardiography: results from a Korean nationwide registry. Int J Rheum Dis, 2015.

[4] Miyamichi-Yamamoto S, Fukumoto Y, Sugimura K, et al. Intensive immunosuppressive therapy improves pulmonary hemodynamics and long-term prognosis in patients with pulmonary arterial hypertension associated with connective tissue disease. Circ J, 2011; 75:2668–74.

[5] Price LC, Wort SJ, Perros F, et al. Inflammation in pulmonary arterial hypertension. Chest, 2012; 141:210–21.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6594

SAT0225 CEREBLON MODULATOR CC-220 DECREASES NAÏVE AND MEMORY B CELLS AND PLASMACYTOID DENDRITIC CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS: EXPOSURE-RESPONSE RESULTS FROM A PHASE 2A PROOF OF CONCEPT STUDY

A. Gaudy [1], Y. Ye [1], S. Korish [1], D. Hough [1], M. Weiswasser [1], S. Choi [1], R. Furie [2], V. Werth [3], P. Schafer [1]. *[1]Celgene Corporation, Summit, NJ; [2]Northwell Health, Great Neck, NY; [3]University of Pennsylvania and the VA Medical Center, Philadelphia, PA, United States*

Background: CC-220 is a cereblon E3 ligase modulatory compound currently in development for the treatment of Systemic Lupus Erythematosus as well as other autoimmune conditions and multiple myeloma. As a high affinity ligand for cereblon, CC-220 administration results in significant reductions in ikaros (IKZF1) and aiolos (IKZF3), transcription factors which are genetically linked to SLE risk, and are overexpressed in the peripheral blood of SLE patients compared to healthy controls.

Objectives: To describe the pharmacokinetics (PK), pharmacodynamics (PD), and the PK-PD relationship of CC-220 in subjects with SLE.

Methods: CC-220-SLE-001 is a randomized, double-blinded, placebo-controlled,

phase 2a dose escalation study to investigate the safety, PK, PD, and efficacy of CC-220 in patients with SLE. Forty-two (42) adult SLE subjects fulfilling SLE ACR criteria, having a history of SLE for ≥6 months and a baseline Safety of Estrogens in Lupus Erythematosus National Assessment–Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score ≥4 were randomized to placebo or 1 of 4 escalating doses of CC-220 (0.3 mg QOD, 0.3 mg QD, 0.6/0.3 mg alternating QD, or 0.6 mg QD).

Results: CC-220 concentration-time profiles demonstrated dose proportionality between cohorts, with moderate accumulation in the non-alternating dose cohort. CC-220 significantly reduced total CD20+ B cells by as much as 96%, immature B cells by as much as 91.2%, switched memory B cells by as much as 81.4%, BAFFR+ B cells by as much as 67.5%, and plasmacytoid dendritic cells (pDCs) by as much as 86.5% (Day 85 median percent change from baseline). Whereas reductions in B cells were observed, CD4+ as well as CD8+ T cells increased, and the rise in T cells paralleled the observed increase in plasma cells in those subjects who received the highest dose (0.6 mg). An exposure-response analysis demonstrated decreasing B cells, pDCs and neutrophils with increased exposure to CC-220.

Conclusions: It was determined that 0.3 mg QD to 0.6/0.3 mg alternating QD reduced concentrations of B cells and pDC's while avoiding neutropenia. These findings, in combination with the PK, safety, and exploratory efficacy data, support continued development of CC-220 in SLE.

Disclosure of Interest: A. Gaudy Shareholder of: Celgene, Employee of: Celgene, Y. Ye Shareholder of: Celgene, Employee of: Celgene, S. Korish Shareholder of: Celgene, Employee of: Celgene, D. Hough Shareholder of: Celgene, Employee of: Celgene, M. Weiswasser Shareholder of: Celgene, Employee of: Celgene, S. Choi Shareholder of: Celgene, Employee of: Celgene, R. Furie Consultant for: Celgene, V. Werth Grant/research support from: Celgene, Consultant for: Celgene, P. Schafer Shareholder of: Celgene, Employee of: Celgene

DOI: 10.1136/annrheumdis-2017-eular.3036

SAT0226 A FIRST-IN-HUMAN, STUDY OF BMS-986165, A SELECTIVE, POTENT, ALLOSTERIC SMALL MOLECULE INHIBITOR OF TYROSINE KINASE 2

I. Catlett[1], U. Aras[2], Y. Liu[3], D. Bei[2], I. Girgis[2], B. Murthy[2], M. Honczarenko[1], S. Rose[1]. *[1]Innovative Clinical Development; [2]Clinical Pharmacology; [3]Global Biometric Sciences, Bristol-Myers Squibb, Princeton, United States*

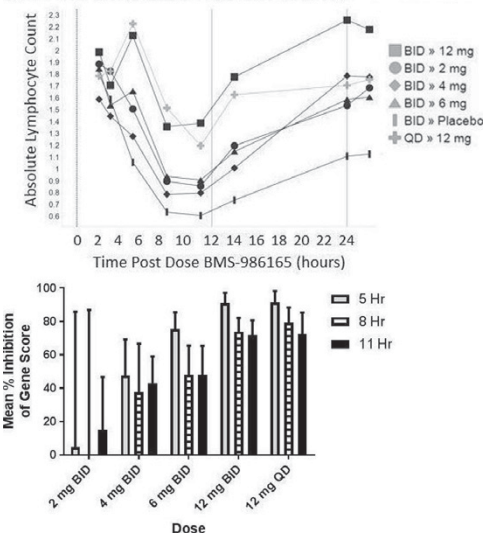
Background: Tyrosine kinase 2 (Tyk2) is a member of the JAK family that phosphorylates STAT proteins downstream of the IL-12, IL-23 and the Type I interferon receptor. Tyk2 genetic variants have been linked to multiple autoimmune diseases,[1] with a deactivating coding variant conferring significant protection against multiple immune-mediated disorders including systemic lupus erythematosus (SLE).[2] Selective pharmacologic inhibition of Tyk2 has proven daunting, given the high degree of similarity among JAK catalytic domains. Using a novel approach, we have developed BMS-986165, a highly selective and potent small molecule inhibitor, which blocks receptor-mediated Tyk2 activation by stabilizing the regulatory pseudokinase domain of the protein. Lupus-like disease is strongly inhibited in NZB/W mice treated with BMS-986165. Together, these data establish Tyk2 as a highly promising therapeutic target for SLE.

Objectives: We report the first evidence of safety, pharmacokinetics (PK), target engagement (TE), and pharmacodynamic activity (PD) of BMS-986165, a novel inhibitor of Tyk2.

Methods: Safety, PK, TE, and PD were assessed in a randomized, double-blind, single and multiple ascending dose study of 108 (83 active: 25 placebo) healthy participants (NCT02534636). Target engagement was assessed by an ex vivo assay, IL-12 and IL-18 induced IFNγ production. Roferon-A was administered to assess in vivo pharmacodynamic effects of BMS-986165 on physiological manifestations of IFN exposure and on IFN-regulated gene (IRG) expression.

Results: BMS-986165 was safe and overall well-tolerated. There were no serious adverse events and the frequency of non-serious adverse events were similar in the active (75%) and placebo (76%) groups. The most frequently reported adverse events by preferred term were headache (23% active versus 28% placebo), nausea (12% active versus 8% placebo), rash (12% active versus 8% placebo), and upper respiratory tract infection (11% active versus 12% placebo). After oral administration, BMS-986165 was rapidly absorbed and exhibited an apparent elimination half-life of 8–15 hours. Modest accumulation (1.4x-1.9x) was observed after multiple dosing. BMS-986165 inhibited IL-12/IL-18-induced IFNγ production in *ex vivo* assays in a dose and concentration dependent manner. Following an *in vivo* challenge with a clinical dose of Interferon-alfa-2A, BMS-986165 demonstrated dose-dependent inhibition of lymphocyte count decreases and expression of 53 IRGs in blood (Figure 1).

Figure 1: *In vivo* pharmacodynamic challenge



Conclusions: BMS-986165 is a safe and potent Tyk2 inhibitor with clear evidence of *ex vivo* and *in vivo* biologic activity in healthy participants, and the potential for once daily dosing. Overall, Inhibition of IL-12/23 and type I IFN pathways support further testing of BMS-986165 in diseases such as lupus and psoriasis. A Phase 2 study in patients with moderate-to-severe psoriasis is ongoing (NCT02931838).

References:

[1] Liang Y, Zhu Y, Xia Y, Peng H, Yang XK, et al. Therapeutic potential of tyrosine kinase 2 in autoimmunity. Expert Opin Ther Targets. 2014 May;18(5):571–80.

[2] Dendrou CA, Cortes A, Shipman L, Evans HG, Attfield KE, et al. Resolving TYK2 locus genotype-to-phenotype differences in autoimmunity. Sci Transl Med. 2016 Nov 2;8(363):363ra149.

Disclosure of Interest: I. Catlett Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, U. Aras Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Y. Liu Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, D. Bei Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, I. Girgis Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, B. Murthy Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Honczarenko Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Rose Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.3809

SAT0227 HEALTH CARE UTILIZATION AND COSTS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN THE UNITED STATES: SYSTEMATIC REVIEW

E. Hammond[1], I.B. Murimi[2], D.H. Lin[2], H. Kan[2], J. Tierce[2], X. Wang[1], H. Nab[3], B. Desta[1], G.C. Alexander[2]. *[1]AstraZeneca, Gaithersburg, MD; [2]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States; [3]AstraZeneca, Cambridge, United Kingdom*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects as many as 518 persons per 100,000 people in the United States and Europe.

However, much of our current knowledge on SLE health care utilization and costs is based on analyses conducted prior to 2011, after which important treatment innovations (e.g., belimumab and, to some extent, rituximab) and health care marketplace changes occurred in the United States.

Objectives: The objectives of this systematic review were to summarize the patterns of health care utilization for patients with SLE and to characterize the direct and indirect costs of SLE by disease severity in the United States.

Methods: We conducted a systematic literature review of adult patients with SLE in the United States by searching PubMed and Embase for relevant articles written in English and published during January 2000–April 2016. We examined health care utilization measures including emergency department (ED) visits, hospitalizations, outpatient visits, medication use, and adherence. We restricted the analysis to observational studies, excluding case reports and commentaries. All monetary costs were converted to US 2016 $.

Results: In total, 4,700 articles were screened, 388 articles were retained for full-text review, and 38 articles were selected for inclusion in this report. Across these 38 studies, mean patient ED utilization rates were 0.9–2.1 visits/year. Mean hospitalization rates were 0.4–2.6 inpatient stays/year, with 5–6 days/stay on average. Patients averaged 10–19 total physician visits/year. More than 90% of patients with SLE had ≥1 visit to a primary care provider annually. In addition, 51–71% visited rheumatologists, and 6–7% visited nephrologists. Health care resource use with respect to ED visits, hospitalization rates, inpatient length of stay, and ambulatory care was greater for patients with lupus nephritis than for patients with SLE without nephritis. Mean annual direct costs from various studies ranged between $15,171–88,445 for patients with SLE regardless of the presence of nephritis. Nearly all studies indicated that mean direct medical costs were greater for patients with moderate or severe disease ($22,300–83,000) than those with mild disease ($8,900–15,000). Mean annual pharmacy costs ranged between $1,572–13,138, accounting for 19–23% of total direct costs, and medical costs ranged between $21,290–82,854. On average, 12–49% of patients were unemployed, and the mean number of sick days/month was 2.3 days. The range of estimates of mean total direct costs for patients with SLE overall were often

larger when derived from commercial claims ($21,600–55,400) than from public payers (Medicare and Medicaid, $16,000–23,000).
Conclusions: Our findings suggest that patients with SLE, especially those with moderate or severe disease, use considerably more health care services and incur greater direct and indirect costs relative to those with mild disease. Thus, SLE remains a significant driver of health care resource utilization and costs.
Disclosure of Interest: E. Hammond Employee of: AstraZeneca, I. Murimi: None declared, D. Lin: None declared, H. Kan Shareholder of: GSK, J. Tierce: None declared, X. Wang Employee of: AstraZeneca, H. Nab Employee of: AstraZeneca, B. Desta Employee of: AstraZeneca, G. C. Alexander: None declared
DOI: 10.1136/annrheumdis-2017-eular.5224

SAT0228 APOPTOTIC EFFECT OF BLYS ON ENDOTHELIAL CELLS AND ENDOTHELIAL PROGENITOR CELLS IS MEDIATED BY BLYS RECEPTROS AND IS REVERTED BY BELIMUMAB

F.R. Spinelli, C. Barbati, F. Ceccarelli, T. Colasanti, F. Morello, L. Massaro, V. Orefice, C. Alessandri, F. Conti, G. Valesini. *Dipartimento di Medicina Interna e Specialità Mediche - Reumatologia, Sapienza Università di Roma, Rome, Italy*

Background: Circulating endothelial progenitor cells (EPCs) are surrogate markers of endothelial function. Several studies demonstrated a reduction and functional impairment of EPCs in patients with Systemic Lupus Erythematosus (SLE), partially accounting for endothelial dysfunction. In murine models of atherosclerosis, treatment with a B Lymphocyte Stimulator (BLyS) inhibitor slowed the progression and reduced the size of atherosclerotic plaque. Belimumab (BLM) is a human anti-BLyS monoclonal antibody approved for the treatment of SLE.
Objectives: We aimed at evaluating the effect of BLyS inhibition on EPCs and endothelial cells both *ex vivo* – in SLE patients receiving BLM– and *in vitro*. Moreover we investigated the expression of receptors for BLyS on EPC and mature endothelial cell surface.
Methods: We enrolled consecutive patients with SLE who were due to start BLM, without known cardiovascular disease and age and sex-matched healthy subjects. Peripheral blood mononuclear cells (PBMC) were isolated by Ficoll density-gradient centrifugation. Cells were incubated with anti-CD34 and anti-VEGF-R2/KDR monoclonal antibodies; acquisition was performed by flow cytometry: EPCs were defined as CD34/KDR double-positive cells. Recovered EPC isolated from healthy donors' PBMC were plated on dishes coated with human fibronectin. Apoptosis was investigated after 6, 12 and 24 hours of incubation with BLyS at different concentrations – 5, 20 and 100 ng/ml – and re-evaluated after 6 hours of co-incubation with BLM at 173 and 300 μg/ml. The same experiments were repeated with the human endothelial cell line EA.hy926. Finally, EPCs and EA.hy926 were incubated with monoclonal antibodies anti-B Activating Factor-Receptor (BAFF-R), B-cell maturation antigen (BCMA) and transmembrane activator and calcium modulator and cyclophilin ligand (CAML) interactor (TACI) and analysed by flow cytometry; the results were expressed as mean fluorescence intensity (MFI).
Results: We treated with BLM 10 female patients (mean age 45.6±10.2 yrs, mean disease duration 17.8±10.8 yrs) with active disease (mean baseline SLEDAI 8.4±2.6). Number of EPCs was significantly lower in SLE patients than in NHS (p=0.005). After 4 weeks of BLM, mean EPC number increased from 0.013±0.016 to 0.021±0.016 (p=0.012 vs baseline; p=n.s. vs NHS). At week 12, EPC number did not significantly differ compared to week 4 nor to baseline.
In vitro studies demonstrated that 20 ng/ml of BLyS induced apoptosis of EPC after 6 hours of incubation; this effect was reverted by the addiction of BLM. Similarly, after 6 hours of incubation with 20 ng/ml of BLyS we detected an increase in EA.hy926 apoptosis that was reverted by co-incubation BLM. Both EPCs and EA.hy926 expressed on their surface BAFF-R (MFI =3.8 and 1.5, respectively) and BCMA (MFI =1.25 and 1.15, respectively); EPCs also expressed TACI (MFI =1.4).
Conclusions: The results of this study demonstrated that the reduction of EPCs number detected in SLE patients was restored by BLM. *In vitro* results support a direct pro-apoptotic effect of BLyS that was reverted by the addition of BLM both in EPCs and EA.hy926 culture. The apoptotic effect of BLyS seems to be mediated by the three receptors (BAFF-R, BCMA and TACI) that are expressed on EPCs and mature endothelial cells surface.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6174

SAT0229 THE USE OF ANTIMALARIAL DRUGS DURING PREGNANCY CAN PREVENT THE DEVELOPMENT OF PREECLAMPSIA IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

M.A. Saavedra[1], D. Miranda-Hernández[1], A. Lara-Mejía[1], A. Sánchez[1], C.V. Cruz-Reyes[1], U. Angeles[2], L.J. Jara[3]. *[1]Rheumatology; [2]Epidemiology Direction; [3]Education and Research Direction, Hospital de Especialidades, Cmn la Raza, IMSS, México, Mexico*

Background: The antimalarial drugs decrease the risk of lupus activity during gestation, but the beneficial effect on other maternal-fetal complications is controversial.
Objectives: To analyze the beneficial effect of antimalarial drugs on maternal-fetal complications in pregnant women with systemic lupus erythematosus (SLE).
Methods: A prospective cohort of pregnant women with SLE (ACR 1997) from January 2009 to June 2015 was studied. The patients were assessed every 4 to 6 weeks and postpartum both, by a rheumatologist and a gynecologist. Clinical, biochemical, and immunological characteristics, along with maternal and fetal complications were registered. For analysis, the patients were allocated to one of two groups: pregnancies exposed to antimalarial drugs in comparison to those not exposed. A logistic regression analysis including variables such as smoking, obesity, infections, first pregnancy, age, SLE flare, drugs (prednisone, antimalarials, aspirin, and azathioprine), anti-DNA antibodies, anticardiolipin antibodies, and antiphospholipid syndrome was performed.
Results: We studied 197 lupus pregnancies, 154 expose to antimalarial drugs and 47 unexposed. We found no differences between groups in age, years of evolution of SLE, first pregnancy, childhood-onset SLE, lupus nephritis, and use of prednisone, aspirin and azathioprine. The rate of most maternal and fetal complications was also similar in both groups (Table). A lower incidence of preeclampsia was observed in patients exposed to antimalarial drugs compared to those not exposed (9% vs 23%, p=0.01). Additionally, 2 maternal deaths in patients not exposed to antimalarial drugs. The logistic regression analysis showed that the use of antimalarial drugs during pregnancy is a protective factor for the development of preeclampsia (RR 0.1, 95% CI 0.05–0.58, p=0.004); on the other hand, active SLE before pregnancy (RR 4.8, 95% CI 1.3–17.8, p=0.01) and lupus nephritis (RR 2.9, 95% CI 0.9–8.8, p=0.05) were associated factors with the development of preeclampsia.

Table 1. Maternal and fetal outcomes

	Antimalarial drugs (n=154)	No antimalarial drugs (n=43)	P value
Maternal complications	74 (48.0)	18 (41.8)	0.47
Preeclampsia	14 (9.0)	10 (23.2)	0.01
PROM	15 (9.7)	1 (2.3)	0.12
Cesarean section	99 (64.2)	29 (67.4)	0.53
Maternal death	0 (0)	2 (4.6)	0.007
SLE flare	60 (38.9)	8 (18.6)	0.01
Renal flare	23 (14.9)	5 (11.6)	0.58
Infection	21 (13.6)	5 (11.6)	0.73
Fetal complications a	71 (46.1)	22 (51.1)	0.56 b
Live births a	137 (88.9)	38 (88.3)	0.98 b
Prematurity a	40 (25.9)	13 (30.2)	0.58 b
Miscarriage a	13 (8.4)	5 (11.6)	0.52 b
Stillbirth a	4 (2.5)	0 (0)	0.28 b
Weeks' gestation c	35.1±5.9	35.0±6.3	0.89 d
Birth weight (g) c	2,534±651	2,444±827	0.5 d
Apgar score 1 c	7.4±1.6	7.2±1.6	0.41 d
Apgar score 2 c	8.6±1.4	8.3±1.3	0.37 d

[a]Results expressed in mean (SD). [b]Student's t-test. [c]Results expressed in numbers and percentages. [d]Chi-square test.

Conclusions: Our study suggests that the use of antimalarial drugs during pregnancy can prevent the development of preeclampsia in women with SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6035

SAT0230 NEW ORAL ANICOAGULANTS IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

M.A. Satybaldyeva, N. Seredavkina, L. Kashnikova, E. Nasonov, T. Reshetnyak. *Nasonova Research Institute of Rheumatology, MOSCOW, RUSSIA, Moscow, Russian Federation*

Background: Antiphospholipid syndrome (APS) is an acquired thrombophilia characterized by reccurent venous and arterial thrombosis, obstetric pathology (fetal loss), and synthesis of antiphospholipid antibodies. Warfarin is a "golden" standard of APS therapy. However it has number of disadvantages. Dabigatran etexilate is a direct thrombin inhibitor and its main differences from warfarin are fixed dose, no need of regular INR monitoring,less elimination half-life.
Objectives: To evaluate efficacy and safety of dabigatran etexilate in patients with APS.
Methods: 38 patients (pts) (F:26, M:12) with primary and secondary APS, 37,2±9,9 years old. 24 pts with primary APS, 14 pts with secondary APS: 13 had systemic lupus erythematosus (SLE) + APS, 1 rheumathoid arthritis (RA) + APS. The diagnosis of APS was established due to international APS criteria (Sydney), SLE – SLICC 2012, RA - ACR/EULAR 2010. The majority number of pts (n=28) received warfarin, others – sulodexide (n=1), low molecular heparin (n=1), had no anticoagulant therapy (n=3), 5 pts received dabigatran etexilate before inclusion to trial. The control of coagulogram was done 3 times: before inclusion to trial, in 24 weeks and in 48 weeks after inclusion. Trial assays were performed in the laboratory in V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation. APPT and thrombin time tests were done with the automated coagulometer Coalysys Plus C (Behnk Electronic, Germany); thrombin time test was done with STA-thrombin reagent (Diagnostica Stago, France), APPT with STA-Cephascreen reagent (Diagnostica Stago, France). Lupus anticoagulant was assessed by the dilute Russell's viper venom time, using Siemens Healthcare (Germany) LA1 (screening) and LA2 (confirmation). IgG or IgM antibodies against cardiolipin and β2 glycoprotein I (β2GPI) were measured with automated enzyme-immunoassay analyzer Alegria with Anti-Cardiolipin IgG/IgM and Anti-beta-2-Glycoprotein I IgG/IgM reagents (Orgentec Diagnostika GmbH, Germany).

Triple positivity was defined as positive antibodies against cardiolipin and β2GPI and a positive test for lupus anticoagulant.
Results: 32 pts had high or medium level of aPL (anticardiolipin antibodies IgG,IgM, anti-β2glycoprotein antibodies IgG,IgM), 6 had low or normal level of aPL. 12 pts were triple positive. APPT and thrombin time before inclusion to trial were 44,2 [36,5;53,5] and 16,1 [14,9;17,0], on 24 week after dabigatran etexilate start 51,0 [40,5;65,7] and 163,5 [108,7;240,0] and on 48 week 58,7 [45,6;63,2] and 194,1 [152,6;255,2] respectively.1 patient was excluded due to non-compliance. During follow-up period from 1,5 to 12 (10,6±3,2) months 7 pts (22,6%, 20,7 per 100 patient-years) experienced reccurent thrombosis including superficial vein thrombosis (n=2; 6,5%, 5,9 per 100 patient-years), thrombosis of paranephric veins (n=1; 3,2%, 2,9 per 100 patient-years), acute cerebrovascular disorders (n=4; 12,9%, 11,8 per 100 patient-years). All pts with reccurent thrombosis had high or medium level of aPL; 2/7 were triple positive, both had acute cerebrovascular disorders. 5 pts (16,1%, 14,8 per 100 patient-years) experienced bleeding: 2 hemorrhoidal bleedings, 1 uterine bleeding, 2 nasal bleedings. There was no case of severe bleeding.
Conclusions: Dabigatran etexilate could be used in patients with APS in the case of warfarin non-effectiveness. These findings need to be confirmed in larger studies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6972

SAT0231 SAFETY OF SUBCUTANEOUS BELIMUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A 6-MONTH OPEN-LABEL EXTENSION STUDY

A. Doria[1], W. Stohl[2], A. Schwarting[3], M. Scheinberg[4], A. Hammer[5], C. Kleoudis[6], J. Groark[5], N.L. Fox[7], D. Roth[5], D. Bass[5], D. Gordon[5].
[1]University of Padua, Padua, Italy; [2]University of Southern California, Los Angeles, United States; [3]ACURA Kliniken, Bad Kreuznach, Germany; [4]Hospital Abreu Sodré, São Paulo, Brazil; [5]GSK, Philadelphia; [6]GSK, Research Triangle Park; [7]GSK (former employee), Rockville, United States

Background: Intravenous belimumab (BEL) 10 mg/kg is approved in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE), on standard SLE therapy (SoC). A Phase III, double-blind (DB), study of subcutaneous (SC) BEL 200 mg weekly plus SoC showed efficacy and safety in patients with SLE.
Objectives: The ongoing safety and efficacy of BEL 200 mg SC weekly were assessed in a 6-month open-label extension (OLE) study.
Methods: Patients with SLE who completed BLISS-SC (BEL112341; NCT01484496), a Phase III, randomised (2:1), DB, placebo (PBO)-controlled, 52-week trial of BEL 200 mg SC, were eligible to enter a 6-month OLE; the outcomes are reported here. Patients were maintained on weekly BEL (BEL group) or switched from PBO to BEL (PBO to BEL group). Baseline differed according to study treatment (Day 0 of the DB phase for BEL; Week 52 of the DB phase for PBO to BEL). The primary focus was safety, evaluated by adverse event (AE) reporting, laboratory tests and immunogenicity. OLE AEs were those occurring on or after the first OL dose. Efficacy evaluations were conducted, at reduced frequency, as per the DB phase[1].
Results: Overall, 677 patients completed the DB phase, 662 entered the OLE; 625 completed. Mean baseline Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index scores were 10.4 (BEL group) and 5.8 (PBO to BEL group, implying better SoC in the DB phase); Systemic Lupus International Collaborating Clinics/ACR Damage Index scores were similar (0.7 and 0.6, respectively). Most OLE AEs were mild/moderate in severity. Despite differences in BEL exposure (BEL: 1 year [DB]; 6-month OLE, and PBO to BEL: 6-month OLE), OLE AE rates were similar (table). Infections and infestations were the most frequent AEs (190/662, 28.7%; drug-related, 55/662, 8.3%; serious AEs [SAEs]; 17/662, 2.6%). AEs of depression/suicide/self-injury (12/662, 1.8%), infections of special interest (17/662, 2.6%), post-injection systemic reactions (21/662, 3.2%) and local injection site reactions (4/662, 0.6%), were low. Two deaths occurred (metabolic acidosis; pneumonia and acute respiratory failure); unrelated to study drug. The percentage of patients worsening (≥2 grade) from baseline was low for all clinical laboratory parameters. Three patients had anti-BEL immune responses during the OLE or follow-up; this resolved on subsequent testing. Efficacy was maintained across the OLE.

Patients, n (%)	PBO to BEL 200 mg SC (n=206)	BEL 200 mg SC (n=456)	Total (N=662)
AE	106 (51.5)	220 (48.2)	326 (49.2)
Treatment-related AE	26 (12.6)	58 (12.7)	84 (12.7)
SAE	14 (6.8)	25 (5.5)	39 (5.9)
Severe AE	9 (4.4)	17 (3.7)	26 (3.9)
AE leading to study drug discontinuation	5 (2.4)	12 (2.6)	17 (2.6)
Death	1 (0.5)	1 (0.2)	2 (0.3)

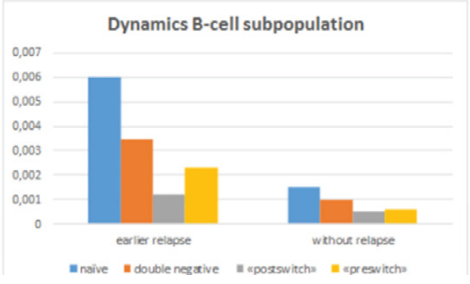
Conclusions: No new differences in safety and efficacy of BEL 200 mg SC plus SoC were seen in this 6-month OLE study compared with the DB phase.
References:
[1] Stohl W et al. Arthritis Rheumatol 2017;doi:10.1002/art.40049.
Acknowledgements: Study funded by GSK. Sam Halliwell, PhD, Fishawack Indicia Ltd, UK, provided editorial assistance funded by GSK.
Disclosure of Interest: A. Doria Speakers bureau: GSK, Pfizer, AstraZeneca, Celgene, Eli Lilly, Baxalta, W. Stohl Grant/research support from: GSK, Celgene, Janssen Research & Development, Pfizer and Sanofi-Aventis Pharmaceutical, Consultant for: GSK, Celgene, Janssen Research & Development, Pfizer and Sanofi-Aventis Pharmaceutical, A. Schwarting Consultant for: GSK, M. Scheinberg Consultant for: Pfizer, GSK, Epirus, Samsung Bioepis, Janssen Pharmaceutica Products, L.P., A. Hammer Shareholder of: GSK, Employee of: GSK, C. Kleoudis Shareholder of: GSK, Employee of: Parexel, J. Groark Shareholder of: GSK, Employee of: GSK, N. L. Fox Employee of: GSK (former employee), D. Roth Shareholder of: GSK, Employee of: GSK, D. Bass Shareholder of: GSK, Employee of: GSK, D. Gordon Shareholder of: GSK, Employee of: GSK
DOI: 10.1136/annrheumdis-2017-eular.5235

SAT0232 B-CELL SUBPOPULATION DYNAMICS IN SLE PATIENTS FOLLOWING RITUXIMAB THERAPY

A.A. Mesnyankina, E.N. Aleksandrova, S.K. Soloviev, E.V. Suponitskaya, A.P. Aleksankin, A.A. Novikov, E.A. Aseeva, E.L. Nasonov. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Objectives: To study B-cell subpopulation dynamics in SLE patients following Rituximab (RTX) therapy.
Methods: The study included 31 SLE pts (3m/28f) with high (SLEDAI2K≥10–28 pts.) and moderate (SLEDAI2K<10–3 pts.) disease activity; out of them 12 pts with SLE nephritis, 5 pts with neurolupus and 8 with vasculitis. RTX was administered to pts who failed to respond to glucocorticoids (GCs) and cytostatics (CTs). B-cells subpopulations were assessed before RTX administration (Mo0), and at Mo3 and Mo6 of RTX therapy. RTX was administered at 500 to 2000 mg doses depending on disease activity. The absolute counts of CD19+ B-cells, the total population of memory B-cells (CD19+CD27+), "preswitch" (CD19+IgD+CD27+) and "postswitch" (CD19+IgD-CD27+) memory B-cells, "naive" (CD19+IgD+CD27-), plasma cells (CD19+CD38+) and double negative B-cells (CD19+CD27-IgD) were measured. All B cell subsets were analyzed with multicolor flow cytometry using a panel of monoclonal antibodies to B-lymphocytes' surface membrane markers.
Results: Following initiation of RTX SLE clinical and lab activity indices have decreased in all 31 pts by Mo3 and Mo6 of follow up (SLEDAI-2K Mo0–Me 15 [12;18], Mo3-Me 6 [4;10], Mo6–Me 4 [2;8]), as well as absolute count CD19+ B-cell population (Mo0–Me 0,119x10^9/l [0,05;0,26], Mo3–Me 0x10^9/l [0;0,003], Mo6-Me 0,004x10^9/l [0;0,02]). B-cell repopulation by Mo6 in 15 out of 31 pts without signs of relapse and 4 pts with earlier relapse SLE was dependent on "naïve" B-cells (Me 0,0015x10^9/l [0,0002;0,01] vs Me 0,006x10^9/l [0,0033;0,008]), double negative (Me 0,001x10^9/l [0,0002;0,002] vs Me 0,0035x10^9/l [0,0018;0,005]) "postswitch" (Me 0,0005x10^9/l [0,00008;0,003] vs Me 0,0012x10^9/l [0,0003;0,0035]) and "preswitch" memory B-cells (Me 0,0006x10^9/l [0,00007;0,001] vs Me 0,0023x10^9/l [0,0005;0,005]).

Figure: dynamics of lymphocyte subpopulations in patients with early relapse and without relapse SLE/



Conclusions: Decrease in clinical and lab SLE activity was documented in all 31 pts by Mo3 after one course of RTX therapy. In 4 pts with earlier relapse SLE at Mo6 B-cell was found repopulation and significant increase "naïve" B-cells, double negative, "postswitch" and "preswitch" memory B-cells compared with the group without relapse.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1704

SAT0233 HIGH ANTI-DSDNA CONTENT IN SLE IMMUNE COMPLEXES IS ASSOCIATED WITH CLINICAL REMISSION FOLLOWING BELIMUMAB TREATMENT

A. Sohrabian[1], I. Parodis[2], N. Carlströmer-Berthén[1], C. Sjöwall[3], A. Jönsen[4], A. Zickert[2], M. Frodlund[3], A. Bengtsson[4], I. Gunnarsson[2], J. Rönnelid[1].
[1]Department of immunology, Genetics and Pathology, Uppsala University, Uppsala; [2]Rheumatology Unit, Department of Medicine, Karolinska Institutet, Stockholm; [3]Rheumatology/AIR, Department of Clinical and Experimental Medicine, Linköping University, Linköping; [4]Section of Rheumatology, Department of Clinical Sciences Lund, Lund University, Lund, Sweden

Background: Systemic lupus erythematosus (SLE) is considered driven by

immune complexes (IC), and autoantibodies are supposed to participate in IC formation. Thus, the fraction of autoantibodies participating in IC formation merits interest as a diagnostic and/or prognostic marker. We have developed a technique to quantify autoantibody content in IC (Sohrabian et al. Ann Rheum Dis 2015;74(Suppl 1):A74).

Objectives: To evaluate quantification of autoantibodies in IC as a measure of disease activity and prognosis for response in belimumab-treated SLE patients.

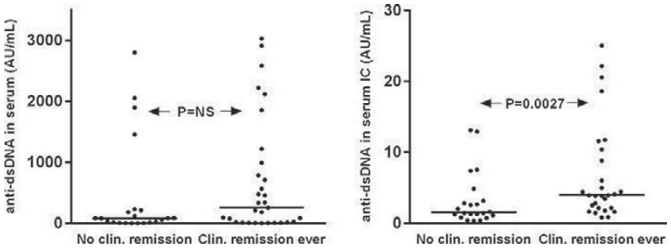
Methods: Fifty-five SLE cases classified according to the ACR criteria were treated with belimumab and followed for one year. High disease activity was defined as SLE Disease Activity Index 2000 (SLEDAI-2K) $\geq$10, or as low levels of complement factors C3 and/or C4. Treatment responses were recorded using the SLE Responder Index (SRI), or as a value 0 for modified SLEDAI-2K with suppression of autoantibody and complement data (clinical remission). Low disease activity was also recorded as Lupus Low Disease Activity State (LLDAS). Response data were recorded at 3, 6 and 12 months.

IC were purified from sera by binding to C1q-coated beads, and thereafter eluted. Autoantibody levels were determined in unmodified serum and in solubilised IC with addressable laser bead immunoassay (FIDIS Connective, Theradiag, Paris) for autoantibodies against dsDNA, histones, ribosomal P antigen, proliferating cell nuclear antigen (PCNA), SSA/Ro60, SSA/Ro52, SSB, Sm, U1RNP and the Sm/RNP complex. Autoantibody levels in serum and in IC were compared with Mann-Whitney's U test between patients with high and low disease activity at baseline and between patients with and without treatment response during the follow-up period.

Results: Antibodies against dsDNA, SSA/Ro60 and Sm/RNP were found in 65%, 54% and 43%, other antibodies with lower percentages. Low complement levels were associated with high serum anti-dsDNA (p=0.003) and anti-ribosomal P antigen (p=0.008) levels, whereas high SLEDAI-2K associated with high anti-dsDNA (p=0.02) and anti-Sm/RNP (p=0.047) levels. Serum levels of antibodies against SSA/Ro60, SSB and SSA/Ro52 were lower in patients attaining LLDAS after 6 months (p=0.02, 0.051 [trend] and 0.04, respectively); these associations were stronger for corresponding IC fractions (p=0.01, 0.005, and 0.002, respectively).

Baseline levels of anti-dsDNA and anti-histones in IC associated with clinical remission ever during the follow-up period (p=0.003 and p=0.05). Low levels of anti-Sm and anti-Sm/RNP in serum but not in IC associated with clinical remission at month 6 (p=0.02 and 0.04 respectively), and for Sm/RNP also at month 3 (p=0.04).

Serum levels of all antibodies except SSA/Ro52 declined during the first 6 months, most prominently for dsDNA, histones ribosomal P, PCNA and Sm/RNP ($p<0.0001$ for all). Levels of antibodies in IC declined only for dsDNA (p=0.048).



Conclusions: Autoantibody levels in serum and in IC show different associations to disease activity and to treatment response. High baseline anti-dsDNA levels in IC were most strongly associated with clinical remission, and decreased during belimumab treatment. Belimumab effect might primarily relate to autoantibodies in IC.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5054

SAT0234 PROSPECTIVE SINGLE CENTRE STUDY OF EFFECTIVENESS OF UPFRONT RITUXIMAB AND MYCOPHENOLATE WITH MINIMUM STEROID IN SLE

B.G. Dharmanand. *Rheumatology, Sakra World Hospital, Sy No.52/2 & 52/3, Devarabeesanahalli, Oppsite Intel, Varthur Hobli, Bengaluru, Karnataka 560103, Bangalore, India*

Background: Treatment options for SLE have significant morbidity and mortality. Side effects from corticosteroid usage limit patient adherence and treatment efficacy. B cell depletion appears to target a critical pathophysiological pathway in SLE. Trails with rituximab have shown mixed results. Rituxilup study demonstrated efficacy and steroid sparing action of rituximab and mycophenolate (1)

Objectives: We aim to analyse our experience of using rituximab and mycophenolate upfront on presentation with minimum oral steroids.

Methods: 12 patients with SLE, seen between Jan 2015 to march 2016, were included in the study. All patients completed 6 months of follow-up. Patients were treated with 2 doses of rituximab (1 g) and methyl prednisolone (500 mg) on days 1 and 15, and maintenance treatment of mycophenolate mofetil (2000mg) and low dose prednisolone ($<$7.5 mg) which was tapered off.

Results: 10 were females and 2 males. Mean age of the patients is 24.5. 9 had lupus nephritis, 1 mesenteric vasculitis, 1 CNS vasculitis and 1 severe cutaneous vasculitis with pancytopenia. Average SLEDAI improved from 14 to 4. 6/9 LN attained complete renal remission and 2 partial remission. one patient died due to infection and renal disease 15 days after infusion. 2 vasculitis and one NPSLE patient improved completely. Two patients had infection requiring hospitalization with in 8 weeks of infusion and one patient had severe bradycardia during the infusion and received only 1000mg rituximab. Steroid was stopped by 6 months in 6 patients and in the dose was below 5 mg in rest.

Conclusions: Early Rituximab and mycophenolate is an effective option for treating severe lupus and has steroid sparing property.

References:

[1] Condon MB, Ashby D, Pepper RJ, et al. Prospective observational single-centre cohort study to evaluate the effectiveness of treating lupus nephritis with rituximab and mycophenolate mofetil but no oral steroids. Ann Rheum Dis (2013) 72:1280–1286.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2902

SAT0235 BIIB059, A MONOCLONAL ANTIBODY TARGETING BCDA2 SHOWS SAFETY, TOLERABILITY, PHARMACOKINETICS, PHARMACODYNAMICS IN HEALTHY VOLUNTEER SUBJECTS

D. Martin[1], L. Stevenson[1], P. Prasad[1], K. Smirnakis[1], A. Kao[1], D. Rabah[1], W. Wang[1], C. Barbey[2], C. Musselli[1], N. Franchimont[1]. *[1]Biogen, Cambridge, United States; [2]Biogen, Zug, Switzerland*

Background: Type I interferons (IFN-I) are central to the pathogenesis of systemic lupus erythematosus (SLE). BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, upon engagement, inhibits the production of IFN-I and other inflammatory mediators. Targeting BDCA2 therefore represents an attractive therapeutic strategy for inhibiting pDC-derived IFN-I and may be an effective therapy for the treatment of SLE. BIIB059, an investigational anti-BDCA2 humanized monoclonal antibody, has been shown to engage BDCA2, and this interaction leads to BDCA2 internalization and the consequent in vitro inhibition of TLR-induced IFN-I by pDCs (Pellerin 2015).

Objectives: This study is a first-in-human study that aimed to assess safety, tolerability, PK and PD of BIIB059 in HV subjects following administration of single ascending doses of BIIB059.

Methods: A randomized, double-blinded, placebo controlled, single ascending dose-escalation was conducted in adult HV. Subjects received a single administration of either BIIB059 or placebo. BIIB059 was administered IV at 0.05, 0.3, 1, 3, 10 or 20mg/kg or SC at 50mg at ratio of 2:1 or 3:1. Blood samples were obtained before and after dose administration up to week 16. Target modulation of BDCA2 and serum BDCA2 concentration were measured using flow cytometry, and an enzyme-linked immunosorbent assay (ELISA), respectively, and anti-drug antibodies (ADA) were measured using a bridging ELISA.

Results: 54 HV (38 BIIB059; 16 placebo) were assigned to cohort 1–7. BIIB059 demonstrated non-linear PK consistent with target mediated drug disposition. Bioavailability of SC administration was $\sim$50%. Treatment with BIIB059 led to rapid and complete down-modulation of BDCA2 on the surface of pDCs at all dose levels. Time to reappearance of BDCA2 on pDC cell surface correlated with circulating levels of BIIB059, establishing an in vivo pharmacokinetic/pharmacodynamics (PK/PD) relationship. Single dose administration of BIIB059 was well tolerated across all dose levels. All AEs were mild to moderate in severity with no serious AEs. There were no clinically significant changes in laboratory assessments, physical examinations, or electrocardiogram (ECG) values. Anti-drug antibodies were detected at low levels in a small number of BIIB059-treated subjects. Responses were largely transient and demonstrated no impact on BIIB059 exposure or association with any safety event.

Conclusions: The first-in-human study in HV demonstrated acceptable safety/tolerability and PK profile in healthy subjects and supports further multiple-dose studies with BIIB059. BIIB059 treatment showed dose dependent target engagement and internalization of BDCA2 establishing a PK/PD correlation *in vivo* on circulating pDC. These data support further evaluation of clinical efficacy and safety of BIIB059 as a potential novel therapy in SLE patients.

Acknowledgements: None

Disclosure of Interest: D. Martin Shareholder of: Biogen, Employee of: Biogen at the time this abstract was written, L. Stevenson Shareholder of: Biogen, Employee of: Biogen, P. Prasad Shareholder of: Biogen, Employee of: Biogen at the time this abstract was written, K. Smirnakis Shareholder of: Biogen, Employee of: Biogen, A. Kao Shareholder of: Biogen, Employee of: Biogen at the time this abstract was written, D. Rabah Shareholder of: Biogen, Employee of: Biogen, W. Wang Shareholder of: Biogen, Employee of: Biogen, C. Barbey Shareholder of: Biogen, Employee of: Biogen, C. Musselli Shareholder of: Biogen, Employee of: Biogen, N. Franchimont Shareholder of: Biogen, Employee of: Biogen

DOI: 10.1136/annrheumdis-2017-eular.6109

SAT0236 SAFETY AND DISEASE ACTIVITY CHANGES IN AN EXTENSION OF A PHASE IIB STUDY OF ATACICEPT IN PATIENTS WITH SLE (ADDRESS II)

D.J. Wallace[1], D. Isenberg[2], S. Wax[3], A. Kao[3], P. Chang[3], P.A. Fraser[3], J.T. Merrill[4]. *[1]Cedars-Sinai Medical Center, University of California Los Angeles, Los Angeles, United States; [2]University College London, London, United Kingdom; [3]EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica; [4]Oklahoma Medical Research Foundation, Oklahoma City, United States*

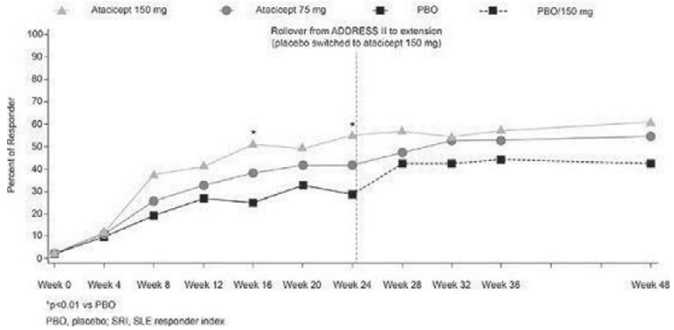
Background: We previously reported results of the 24-week phase IIb ADDRESS II study of atacicept, which demonstrated clinical response in patients with autoantibody-positive SLE, particularly those with high disease activity (HDA; SLEDAI 2K ≥10 at screening).
Objectives: This extension study of ADDRESS II evaluated safety and disease activity in patients with SLE given continued atacicept treatment to week 48 (NCT01972568).
Methods: Atacicept was given as weekly subcutaneous injection to completers of ADDRESS II on average for an additional ≥24 weeks (i.e. ≥48 weeks total from Day 1 of ADDRESS II). Patients already receiving atacicept continued on the same dose (75 mg or 150 mg); those receiving placebo (PBO) switched to atacicept 150 mg (PBO/150 mg).
Results: Of 262 patients completing ADDRESS II, 253 (95%) entered the extension (PBO/150 mg n=83; 75 mg n=82; 150 mg n=88). Demographics were balanced between groups, and most patients were female (91.3%) and white (70%). All three treatment groups had similar rates of treatment-emergent adverse events (TEAEs), TEAEs leading to treatment discontinuation, serious TEAEs, and serious/severe infection (Table 1). Two deaths occurred in the 150 mg arm, considered unrelated to treatment (reported events of stroke and abdominal pain with hematemesis). In the ITT population (n=253), SLE responder index (SRI)-4 rates were maintained between weeks 24 and 48 in the original atacicept groups (75 mg 56.9 vs 55.9%; 150 mg 53.8 vs 56.7%) and moderately increased in the PBO/150 mg group (44.0 vs 48.0%). This improvement was greater for SRI-6 in the HDA subpopulation (PBO/150 mg 28.8% at week 24 vs 42.3% at week 48; 75 mg 41.8 vs 54.5%; 150 mg 54.9 vs 60.8%; Figure 1). The proportion of HDA patients achieving SLEDAI scores ≤2 was also maintained in the atacicept groups (75 mg 20.0 vs 21.8%; 150 mg 37.3 vs 39.2%) and increased in the PBO/150 mg group (13.5 vs 19.2%). In the ITT and HDA populations, most flares occurred before week 24, with reduced risk of severe (BILAG A) and moderate/severe (BILAG A/2B) flares afterwards. Some increase in complement C3 and C4, and decrease in anti-dsDNA antibodies occurred after week 24. Serum IgG decreased moderately, without severe hypogammaglobulinemia (IgG <3 g/L) in any patients.

Table 1. Summary of adverse events

Adverse events, n (%)	PBO/150 mg* (n=83)	Atacicept 75 mg (n=82)	Atacicept 150 mg (n=88)
Any TEAEs	62 (74.7)	63 (76.8)	65 (73.9)
TEAEs leading to treatment discontinuation	6 (7.0)	4 (4.9)	5 (5.7)
Infections and infestations	27 (32.5)	35 (42.7)	43 (48.9)
Herpes zoster	1 (1.2)	0	1 (1.2)
Influenza	1 (1.2)	1 (1.2)	2 (2.3)
Serious TEAEs	15 (18.1)	10 (12.2)	10 (11.4)
Serious/severe infections	4 (4.8)	4 (4.9)	5 (5.7)
Death	0	0	2 (2.3%)†

PBO, placebo; TEAE, treatment-emergent adverse event. *Patients receiving PBO in ADDRESS II who switched to atacicept 150 mg. †Due to 1) stroke and 2) hematemesis.

Figure 1. SRI-6 response rates over time up to week 48 in the HDA population



Conclusions: There were no new safety signals with atacicept between week 24 and 48, and clinical responses achieved during the first 24 weeks were maintained.
Acknowledgements: The study was sponsored by EMD Serono Research & Development Institute Inc., USA (a business of Merck KGaA, Germany). Medical writing support was provided by Bioscript Science, UK, and funded by Merck KGaA, Germany.
Disclosure of Interest: D. Wallace Consultant for: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, D. Isenberg Consultant for: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, S. Wax Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, A. Kao Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, P. Chang Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, P. Fraser Employee of: EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA, USA, J. Merrill Consultant for: Anthera Pharmaceuticals, Lilly, EMD Serono, GlaxoSmithKline and Biogen
DOI: 10.1136/annrheumdis-2017-eular.3665

SAT0237 BONE MARROW AS A TARGET ORGAN OF SYSTEMIC LUPUS ERYTHEMATOSUS: ANALYSIS OF CASES WITH AUTOIMMUNE MYELOFIBROSIS

D. Üsküdar Cansu[1], H. Üsküdar Teke[2], S. Işıksoy[3], C. Korkmaz[1]. *[1]Eskişehir Osmangazi University, School of Medicine, Rheumatology; [2]Eskişehir Osmangazi University, School of Medicine, Hematology; [3]Eskişehir Osmangazi University, School of Medicine, Pathology, Eskişehir, Turkey*

Background: Cytopenia in the course of systemic lupus erythematosus (SLE) may be due to multiple factors. One of these factors can be SLE-associated autoimmune myelofibrosis (AIMF). However, the frequency of SLE-associated AIMF is not well known and the role of clinical and laboratory parameters in the development of AIMF is not clear.
Objectives: Our aim was to identify the frequency of SLE-associated AIMF and compared SLE-associated AIMF group with non-AIMF group in terms of clinical findings and morphological properties of the bone marrow (BM) in cytopenic SLE patients.
Methods: We retrospectively analyzed 224 SLE patients' files who met 1997 revised Classification criteria for SLE. BM aspirates and trephine biopsies were re-examinded. Patients were divided into two groups according to whether they had myelofibrosis or not (AIMF and non-AIMF groups). Concurrent SLE organ involvements, and drugs given pre- and post-AIMF were recorded. BM cellularity, the presence of fibrosis (reticulin or collagen) and grade of fibrosis, the presence of dysplasia, and lymphoid infiltration were recorded.
Results: 45 (20%) of 224 SLE patients were found to experienced BM biopsy due to cytopenia. Four patients were excluded from analyses (2 drug-induced cytopenia, 1 lymphoma, 1 insufficient BM biopsy samples). While AIMF was detected in 29 (70.7%) of the 41 patients, 12 patients did not have AIMF. All patients with AIMF had reticulin fibrosis, 2 patients (6.9%) had also collagen fibrosis. Between the AIMF and non-AIMF groups, no differences were identified in terms of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), SLEDAI, BM cellularity, or BM dysplastic changes (p=0.989, p=0.387, p=0.788, p=0.672, and p=0.494, respectively). In the AIMF group, 27 patients responded to immunosuppressive therapy and corticosteroids, but 2 patients were unresponsive. The response time was longer for the AIMF group compared to the non-AIMF group (3.3±3.1 months vs 1.7±1.2 months, p=0.091). Correlation analysis revealed that higher the grade of BM fibrosis, longer the response time (r=0.471, p=0.002).
Conclusions: AIMF may be underestimated in SLE patients. AIMF as an additional factor for cytopenia in SLE patients may lead to delayed response to appropriate therapy, which was dependent on the presence of high grade fibrosis.
Acknowledgements: None declared
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4330

SAT0238 GLUCOCORTICOID WITHDRAWAL IN AN INCEPTION COHORT OF LUPUS NEPHRITIS PATIENTS

S. Wautier, F. Tamirou, S. Nieuwland-Husson, F.A. Houssiau. *Rheumatology Department, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium*

Background: Few studies have addressed glucocorticoid (GC) withdrawal in lupus nephritis (LN). Yet, this remains a pivotal issue due to GC-induced side effects on the one hand, and to the risk of relapse on the other hand.
Objectives: We reviewed the data of the Louvain Lupus Nephritis Inception Cohort (LOULUNIC) i): to determine the percentage of patients able to permanently or transiently stop GC; ii): to compare their baseline and follow-up characteristics to patients who never stopped; and iii): to assess the consequences of GC withdrawal.
Methods: Ninety patients with new-onset biopsy-proven LN were included. All were under the care of the same senior physician (FAH) during follow-up. Clinical, pathological and biological data were extracted from our data base. The SLICC/ACR-DI was assessed at last visit. Unpaired t-tests, Mann-Whitney tests and ANOVA were used, as appropriate.
Results: Out of 90 patients with incident LN, 43 (48%) ever stopped GC (group E), of which 32 permanently (group P). Median time to stop GC was 37 months. 47 patients (52%) never stopped GC (group N).
At *baseline*, serum creatinine, uP/C ratio, ISN/RPS classes, activity and chronicity indices did not differ between groups, nor did the mean initial dose of methylprednisolone (MP) (N: 28 mg/d; E: 32 mg/d; P: 31 mg/d), the use of IV MP pulses (82

and 77% in N and E groups, respectively) and of IV cyclophosphamide (81 and 77%, respectively).
During the *first year*, mean (SD) uP/C decreased statistically more in group E compared to group N (p=0.028 by ANOVA), with striking differences at month 3 (N: 1.73±1.87; E: 0.96±1.34; p=0.038 by unpaired t-test). This difference at month 3 was also noticed for group P patients (0.85±0.76; p=0.02 by unpaired t-test). Interestingly, the mean MP dose at month 3 was statistically higher in group E (19±8) and P (20±9) compared to group N (15±6) (p=0.005 by unpaired t-test).
At *last follow-up*, serum creatinine was statistically lower in E and P patients compared to N patients. Eight of the 11 patients from the T group suffered form a renal relapse, justifying restart of GC, after a median time of 30 months. Importantly, SLICC/ACR-DI was significantly lower in E and P patients, compared to N patients (p=0.0068 and 0.0027, respectively).
Conclusions: In half of LN patients, complete GC withdrawal is achievable and in one third it can be maintained long term. As expected, patients able to stop GC display less damage at last followup. Patients who were able to stop GC decreased their proteinuria much more promptly during the first year of treatment. Interestingly, they received more GC within the first 3 months of therapy, thereby suggesting that a higher dose of GC during the first 3 months of treatment might be associated with a higher probability of later GC withdrawal.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3132

SAT0239 LATE-ONSET NEUTROPENIA FOLLOWING RITUXIMAB TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS – A ROLE OF THE BAFF/APRIL PATHWAY

I. Parodis, F. Söder, F. Faustini, F. Wermeling, R.F. van Vollenhoven, E. Svenungsson, I. Gunnarsson. *Department of Medicine, Rheumatology Unit, Karolinska Institutet, Stockholm, Sweden*

Background: Rituximab-mediated late-onset neutropenia (LON) has been studied in various diseases, but data from systemic lupus erythematosus (SLE) are limited.
Objectives: To study the prevalence and contributing factors for LON following treatment with rituximab in patients with SLE, including B cell related cytokines and growth factors of the myeloid lineage.
Methods: Patients from the Karolinska SLE cohort treated with rituximab (n=107) were enrolled in this observational study. Rituximab was given according to the lymphoma course (weekly for four weeks), the arthritis course (at week 0 and 2), or as a single infusion, with or without concomitant pulses of cyclophosphamide. LON was defined as an absolute neutrophil count $<$1,500 cells/μL, occurring four weeks to two years after initiation of rituximab treatment, provided that other apparent causes were excluded. Neutropenia occurring later than two years after treatment initiation but during sustained B cell depletion were also considered LON. B lymphocyte stimulator (BLyS/BAFF), a proliferation-inducing ligand (APRIL), interleukin 6 (IL-6), granulocyte colony stimulating factor (G-CSF) and granulocyte-macrophage colony stimulating factor (GM-CSF) were measured by ELISA prior to treatment (n=70) and either at the incidence of LON in patients who developed LON or after approximately the same median time following rituximab treatment in patients who did not develop LON (n=52).
Results: Thirty-four of 107 patients developed LON after a median time of 222 days (IQR: 105–355 days). BLyS levels increased from baseline (median: 0.62 ng/mL; IQR: 0.42–1.07 ng/mL) through the post-treatment measurement, both in patients who developed LON (median: 1.73 ng/mL; IQR: 1.03–2.13 ng/mL; P=0.005) and patients who did not (median: 1.03; IQR: 0.67–1.56 ng/mL; P$<$0.001), but the increase was greater in patients who developed LON, resulting in significantly higher post-treatment BLyS levels (P=0.029). BLyS levels did not differ between the two groups at baseline (P=0.745). We observed a numerical increase in APRIL levels from baseline (median: 1.29 ng/mL; IQR: 0.85–2.3 ng/mL) through the post-treatment measurement in patients who developed LON (median: 2.39; IQR: 1.08–5.16 ng/mL; P=0.074) and a numerical decrease in patients who did not (median: 1.11 ng/mL; IQR: 0.77–1.64 ng/mL; P=0.064), resulting in significantly higher post-treatment APRIL levels in the LON group (P=0.032), from being similar at baseline (P=0.125). We found no difference in levels of G-CSF, GM-CSF or IL-6 between patients who developed LON and patients who did not, either at baseline or at the post-treatment measurement. Higher prednisone dose administered concomitantly to rituximab (P=0.003) and younger age (P=0.001) were found to be associated with the development of LON, whereas neither the use nor the doses of cyclophosphamide were found to have any impact.
Conclusions: The prevalence of rituximab-mediated LON within the SLE patients of the current study (31.8%) was higher compared to previous reports on patients with lymphoma (3–27%), ANCA-associated vasculitis (11.9%) and rheumatoid arthritis (3%). Our results imply a role of the BAFF/APRIL pathway in the immunologic mechanisms underlying this phenomenon and demonstrate that LON following rituximab treatment is a common complication in SLE patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6160

SAT0240 PHASE 3 TRIAL RESULTS WITH BLISIBIMOD, A SELECTIVE INHIBITOR OF B-CELL ACTIVATING FACTOR, IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

J. Merrill[1], R.S. Martin[2], W.R. Shanahan[2], M. Scheinberg[3], K. Kalunian[4], D. Wofsy[5]. *[1]OMRF, Oklahoma; [2]ANTHERA, Hayward, United States; [3]Hospital Abreu Sodré, Sao Paolo, Brazil; [4]UCSD, San Diego; [5]UCSF, San Francisco, United States*

Background: Targeted, biologic inhibitors of B-cell Activating Factor (BAFF) have been evaluated in Phase 3 trials in over 5000 patients with SLE. Post hoc analyses of these studies identify lower placebo response and greater treatment effect using more stringent endpoints in patients entering with higher disease activity, greater corticosteroid doses, and/or anti-double-stranded DNA (dsDNA) and low complement C3 or C4[1,2].
Objectives: The Phase 3 CHABLIS-SC1 trial evaluated blisibimod, an inhibitor of B-cell activating factor (BAFF), in a "responder population" identified from prior studies with this drug class.
Methods: 442 SLE patients with anti-nuclear antibodies or anti-dsDNA, SELENA-SLEDAI score $\geq$10 on standard of care medications were randomized to receive weekly subcutaneous blisibimod (200 mg) or placebo. Corticosteroid taper was encouraged from Week 8 with the goal to reach $\leq$7.5 mg prednisone/day. The primary endpoint at Week 52 was the SLE Responder Index-6 (SRI-6): $\geq$6-point improvement in SELENA-SLEDAI, no new BILAG 1A or 2B domain scores, and $<$0.3-point increase in Physician's Global Assessment.
Results: This study did not meet its primary endpoint at Week 52. Response rates to blisibimod were equivalent to past trials of BAFF inhibitors, but the placebo response was greater. A slightly higher proportion of subjects on blisibimod met the SRI-6 and SRI-4 criteria at most timepoints and more blisibimod-treated subjects achieved corticosteroid taper to prednisone $\leq$7.5 mg/day from Week 40 through Week 52 (p=0.04 at Week 44). Reductions in peripheral B cell lineages, anti-dsDNA, anti-phospholipid antibodies, and serum immunoglobulins, and increases in complement C3 and C4 were observed with blisibimod (see Table).
Blisibimod was well-tolerated. The most common adverse events were upper respiratory tract infection (10.6% vs 14.3% on placebo), urinary tract infection (6.9% vs 10.7%), injection site erythema (7.8% vs 2.0%), injection site reaction (7.3% vs 2.6%), and diarrhea (7.3% vs 2.6%).

Table of Results

	Blisibimod (N=245)	Placebo (N=197)
Disease characteristics at baseline		
SELENA-SLEDAI mean score	13.4	13.5
Low C3/C4 & anti-dsDNA, %	62.4	61.7
Proteinuria $\geq$0.5 g/g, %	32.7	27.9
Mean prednisone dose, mg	15.6	15.6
Oral immunosuppressant use, %	42.4	41.6
Antimalarial use, %	61.2	62.2
Results at Week 52 (*p$<$0.05, **p$<$0.01)		
SRI-6 (primary), %	46.9	42.3
SRI-4, %	56.7	52.0
Taper to $\leq$7.5 mg prednisone/day, %	23.3	16.9
Total B cell change from baseline, counts	-3.30**	-1.58
Anti-dsDNA change from baseline, IU	-134.8	-75.5
C3 and C4 change from baseline, mg/dL	0.11**, 0.03**	0.03, -0.002
Anticardiolipin IgG % change from baseline	-12.7*	9.3

Conclusions: With a deliberate focus on a "responder population" for whom lower placebo rates were observed in previous trials, much higher placebo response rates were observed in the CHABLIS-SC1 trial. Modest benefits of blisibimod were observed on serological effects and corticosteroid tapering.
References:
[1] van Vollenhoven RF et al. Ann Rheum Dis. 2012;71:1343.
[2] Merrill JT et al. Ann Rheum Dis. 2016;75(2):332–40.
Disclosure of Interest: J. Merrill Grant/research support from: BMS, GSK, Consultant for: Anthera, GSK, EMD Serono, Lilly, Astra Zeneca, BMS, UCB, Celgene, Biogen, R. Martin Shareholder of: Anthera, Employee of: Anthera, W. Shanahan Shareholder of: Anthera, Employee of: Anthera, M. Scheinberg Consultant for: GSK,Pfizer, Janssen, Genzyme,Anthera, Novartis, Speakers bureau: GSK,Pfizer, Janssen, Genzyme,Anthera, Novartis, K. Kalunian Grant/research support from: GSK, Celgene, UCB, Consultant for: Anthera, Genentech, BMS, Lilly, Biogen, Shire, Exagen, D. Wofsy Consultant for: Anthera, Genentech, Amgen, GSK
DOI: 10.1136/annrheumdis-2017-eular.2400

SAT0241 EARLY RESPONSE TO BELIMUMAB IN SLE-RELATED JOINT INVOLVEMENT EVALUATED BY ULTRASONOGRAPHIC ASSESSMENT

L. Massaro, F. Ceccarelli, F.R. Spinelli, F. Morello, C. Perricone, F. Miranda, S. Truglia, V. Orefice, I.M. Rutigliano, C. Alessandri, G. Valesini, F. Conti. *Medicina Interna e Specilità Mediche, Reumatologia, Sapienza Università di Roma, Roma, Italy*

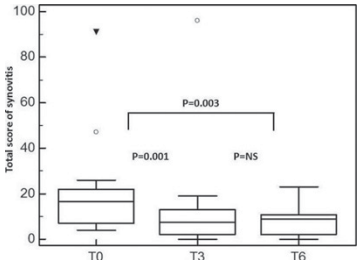
Background: Belimumab (BLM), a fully human monoclonal antibody directed against B lymphocyte stimulator (BLyS), is currently the only biological drug

approved for the treatment of active Systemic Lupus erythematosus (SLE) patients not responding to standard of care. Data from RCTs and observational studies have demonstrated its efficacy, especially in patients with joint involvement. Focusing on this specific manifestation, the response has been also demonstrated by using Disease Activity Score on 28 joints (DAS28) (1). No data are available about the response to BLM in terms of synovitis, assessed by ultrasonography (US).

Objectives: In the present 6-months longitudinal study, we evaluated the response to BLM in SLE patients treated for joint involvement, by using clinimetric indices and US assessment.

Methods: SLE patients starting BLM in the period between August 2013 and December 2016 were prospectively examined. The present analysis was restricted to patients requiring BLM for joint involvement. A complete physical examination and US assessment were performed at baseline (T0) and after 3 (T3) and 6 months (T6). At each time, we assessed the global disease activity by Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K) and the joint involvement activity by DAS28. US evaluation of 12 joints (I-V metacarpophalangeal, I-V proximal interphalangeal, wrist and knee bilateral) was performed to identify inflammatory features (synovial effusion and hypertrophy, power Doppler) according to the OMERACT definitions. These elementary lesions were scored according to a semi-quantitative scale (0=absent, 1=mild, 2=moderate and 3=severe) and a total score, corresponding to the patient's inflammatory status (0–216) was obtained by their sum.

Results: Moving from 35 SLE patients starting BLM, 14 (14 female; mean age±SD 48.4±8.6 years; mean disease duration±SD 255.4±124.2 months) were treated for prevalent joint involvement. At baseline, the mean DAS28±SD was 4.5±1.1, the mean SLEDAI-2K±SD was 6.1±1.5 and the mean daily prednisone±SD was 7.8±3.5 mg. After 3 months of treatment we observed a significant reduction in mean DAS28 (3.1±0.8 *vs* 4.5±1.1, P=0.007) and in mean SLEDAI-2K (3.5±2.1 *vs* 6.1±1.5, P=0.003) compared to baseline. The mean daily prednisone significantly decreased at T6 (4.7±1.4 *vs* 7.8±3.5 mg, P=0.03) while the rest of the therapy remained stable for 6 months. Of note, the mean total US score significantly decreased at T3 compared to T0 (13.7±24.4 *vs* 22.2±22.6, P=0.001). This result was maintained in 12 patients (85.7%) after 6 months with a statistically significant difference compared to T0 (7.9±6.6 *vs* 22.2±22.6, P=0.003) (Figure 1).



Conclusions: The results of the present study demonstrated the efficacy of BLM in SLE-related joint involvement, evaluated by SLEDAI-2K and DAS28, confirming previous data reported in the scientific literature. For the first time, we demonstrated an early response to BLM as proved by the reduction of the total US synovitis score after 3 months, reflecting the improvement of the joint inflammatory status.

References:

[1] Iaccarino L et al. Effects of Belimumab on Flare Rate and Expected Damage Progression in Patients With Active Systemic Lupus Erythematosus. Arthritis Care Res. 2017; 69:115–123.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4238

SAT0242 MEASURES OF PERIPHERAL BLOOD B-CELL DEPLETION PREDICT RENAL RESPONSE IN PATIENTS WITH LUPUS NEPHRITIS TREATED WITH RITUXIMAB

L.M. Gomez Mendez[1], M.D. Cascino[2], J. Garg[2], P. Brunetta[2], M. Dall'Era[1], L. Dragone[2]. *[1]UCSF; [2]Genentech, San Francisco, United States*

Background: LUNAR, a randomized controlled trial, investigated the addition of rituximab (RTX) to standard of care for the treatment of lupus nephritis (LN). While this study did not meet its primary endpoint, there was an increase in partial renal response associated with RTX. Subsequent observational studies have suggested that there is variability in the degree of peripheral blood B-cell depletion in patients with SLE following treatment with RTX and that greater B-cell depletion may result in increased therapeutic efficacy.

Objectives: To assess the relationship between parameters of B-cell depletion and measures of renal response in patients treated with RTX.

Methods: We analyzed data from the LUNAR trial (registry number NCT00282347) who were treated with RTX and for whom complete CD19 measurements and renal endpoints were available (n=70). We developed several parameters to assess the degree, duration and rate of depletion of CD19 counts from randomization through day 364. Complete renal response (CRR) was defined as urine protein to creatinine ratio (UPCR) <0.5, normal serum creatinine or, if normal at baseline, not increased by ≥15%, and inactive urinary sediment. Spearman's correlation was used to identify associations between baseline characteristics and measures of B-cell depletion. The association between measures of B-cell depletion and CRR (at weeks 52 and 78) was examined using logistic regression adjusted for baseline UPCR. Separately, analyses were stratified by baseline anti-double stranded DNA antibody titer status (anti-dsDNA).

Results: Baseline UPCR correlated with the degree of B-cell depletion following RTX treatment by several measures (time spent at CD19 =0 cells/ml [r = -0.32]; CD19 nadir [r =0.33]; percent change from baseline to nadir [r =0.3]). Measures of B-cell depletion were associated with CRR and percent change in UPCR at week 78 (Table 1). Achievement of a nadir of CD19 =0 cells/ml had an odds ratio (OR) =5.18 (95% CI: 1.03–26.1); patients who spent greater than the median percent of time at CD19 =0 cells/ml had OR =3.3 (95% CI: 1.14–9.62) for CRR at week 78. In subgroup analyses, associations between these measures of peripheral blood B-cell depletion and renal response were strongest among patients with high baseline anti-dsDNA titer. No measures of B-cell depletion were associated with CRR at week 52.

Table 1. Adjusted multivariate measures of B-cell depletion and their associations with complete renal response and percent change from baseline UPCR.

	OR of Complete Renal Response (95% CI)		Percent change in UPCR (95% CI)	
	Week 52	Week 78	Week 52	Week 78
CD19 reaches 0 cells/μl at any time point	2.12 (0.49, 9.07)	5.18 (1.03, 26.08)	-18.9% (−42.7, 4.88)	−31.8% (−70.7, 7.01)
Above median percent of time at 0 cells/μl	1.23 (0.41, 3.67)	3.32 (1.14, 9.62)	−11.28% (−31, 8.5)	−39.5% (−68.2, −10.8)
Area under the curve for all B cell measurements in one year	0.78 (0.38, 1.59)	1.88 (0.90, 3.94)	-1.87% (−15.4, 11.6)	1.15% (−19.6, 22.6)
For every 30 of days spent at 0 cells/μl	1.11 (0.89, 1.38)	1.16 (0.95, 1.45)	−2.7% (−6.9, 1.38)	−6.18% (−12.3, 0.06)
Percent of visits at 0 cells/μl	1.01 (0.98, 1.05)	1.03 (1.00, 1.06)	−0.45% (-1.06, 0.15)	−1.05% (-1.93, −0.17)
Every increment of 30 days to nadir	1.06 (0.9, 1.25)	0.92 (0.78, 1.08)	-0.72% (−3.81, 2.34)	1.05% (−3.6, 5.7)
Percent change in CD19 from baseline to nadir	0.74 (0.36, 1.53)	0.56 (0.25, 1.28)	0.01% (−11.4, 11.4)	23% (−0.84, 46.9)
CD19 nadir	0.49 (0.12, 1.94)	0.22 (0.04, 1.12)	19.5% (−2.33, 41.4)	28.4% (−7.06, 63.8)

OR, odds ratio; UPCR, urine protein to creatinine ratio.

Conclusions: Baseline UPCR was inversely correlated with the degree of peripheral B-cell depletion. B-cell depletion measures were associated with increased odds of achieving CRR and decreased UPCR at week 78 and these associations were strongest among patients with high baseline anti-dsDNA titer. These data support the exploration of high-sensitivity B-cell measurements in future studies of B-cell depleting treatments in LN and suggest that longer duration of follow up may better demonstrate efficacy with B-cell depleting agents.

References:

[1] Rovin Arthritis Rheum 2012.
[2] Vital Arthritis Rheum 2011.

Disclosure of Interest: L. Gomez Mendez Grant/research support from: Genentech/Roche, M. Cascino Employee of: Genentech/Roche, J. Garg Employee of: Genentech/Roche, P. Brunetta Employee of: Genentech/Roche, M. Dall'Era: None declared, L. Dragone Employee of: Genentech/Roche

DOI: 10.1136/annrheumdis-2017-eular.5412

SAT0243 EXPOSURE-RESPONSE (E-R) ANALYSIS FOR SELECTION OF OPTIMAL DOSAGE REGIMEN OF ANIFROLUMAB IN PATIENTS (PTS) WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

L.C. Santiago[1], B. Wang[1], P. Brohawn[2], L. Wang[2], G. Illei[2], L. Roskos[2]. *[1]MedImmune LLC, Mountain View; [2]MedImmune LLC, Gaithersburg, United States*

Background: Anifrolumab is a fully human IgG_1 monoclonal antibody directed against subunit 1 of the type I interferon–α receptor (IFNAR1). It is in development for treatment of SLE.

Objectives: To support dosage selection for pivotal anifrolumab studies, using an E−R model.

Methods: In the Phase IIb MUSE study (NCT01438489),[1] adult pts with moderate to severe SLE, who had inadequate responses to standard-of-care (SOC) medications, were randomized 1:1:1 to intravenous anifrolumab 300 or 1,000 mg or placebo every 4 weeks (Q4W), in addition to SOC medications, for 48 weeks. Pts were stratified by type I interferon gene signature (IFNGS) test status (high or low) using a validated 4-gene expression assay, oral corticosteroid dosage (<10 or ≥10 mg/day of prednisone or equivalent), and SLE disease activity index−2K score (<10 or ≥10) at screening. A mechanistic target-mediated drug disposition model[2] was used to describe the pharmacokinetics (PK) of anifrolumab. The dichotomous efficacy endpoint, SLE responder index [SRI (4)], was modeled using logistic regression. A dropout hazard function was used to describe voluntary withdrawals during treatment. Clinical simulations were conducted to assess dosing scenarios in virtual SLE pts.

Results: There was no PK difference between type I IFNGS test–high or –low pts (mean [standard deviation] C_{trough} (Day 169): 17.0 [11.5] μg/mL and 23.3 [16.0] μg/mL, respectively). SRI (4) modeling demonstrated no anifrolumab treatment effect in type I IFNGS test–low pts compared with placebo; interpretation of this

result may be limited by small sample size. In type I IFNGS test–high pts, a log-linear logistic model was used to describe the treatment effect of anifrolumab. Pt dropouts were more likely in nonresponders. Clinical simulations demonstrated dosages <300 mg would result in inadequate PK exposure and suboptimal efficacy in some pts with SLE. In contrast, simulations indicated minimal efficacy improvement for dosages >300 mg, consistent with the Phase IIb MUSE study outcomes.

Conclusions: Based on E–R analyses and overall risk assessment, a 300 mg Q4W, intravenous dosage regimen is recommended for pivotal anifrolumab studies in pts with SLE.

References:
[1] Furie R, et al. Arthritis Rheumatol. 2017;69:376–86.
[2] Wang B, et al. Clin Pharmacol Ther. 2013;93:483–92.

Acknowledgements: Funded by MedImmune. Medical writing support: R. Plant, QXV Comms, an Ashfield company, funded by MedImmune.

Disclosure of Interest: L. Santiago Shareholder of: AstraZeneca, Employee of: MedImmune LLC, B. Wang Shareholder of: AstraZeneca, Employee of: MedImmune LLC, P. Brohawn Shareholder of: AstraZeneca, Employee of: MedImmune LLC, L. Wang Employee of: MedImmune LLC, G. Illei Shareholder of: AstraZeneca, Employee of: MedImmune LLC, L. Roskos Shareholder of: AstraZeneca, Employee of: AstraZeneca

DOI: 10.1136/annrheumdis-2017-eular.3517

SAT0244 A LONG-TERM FOLLOW-UP STUDY OF ALLOGENEIC MESENCHYMAL STEM CELLS TRANSPLANTATION IN PATIENTS WITH DRUG-RESISTANT SYSTEMIC LUPUS ERYTHEMATOSUS

D. Wang [1], L. Sun [2]. [1] *Department of Rheumatology and Immunology;* [2] *Department of Rheumatology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China*

Background: Allogeneic mesenchymal stem cells (MSC) transplantation showed therapeutic effect in active and refractory systemic lupus erythematosus (SLE).

Objectives: To determine the long-term safety and efficacy of allogeneic MSC transplantation (allo-MSCT) in severe SLE patients refractory to previous therapies.

Methods: All consecutive SLE patients who received at least one allo-MSCT were analyzed. SLEDAI score of more than or equal to 8 or with at least one BILAG grade A or at least two BILAG grade B manifestations. All the patients were refractory to corticosteroid and/or immunosuppressive drugs treatment. Allogeneic bone marrow and/or umbilical cord derived MSCs were infused intravenously, with one million cells per kilogram of bodyweight for each infusion. The primary end point was 5-year overall survival. Secondary end points included complete clinical remission, partial clinical remission and relapse.

Results: Eighty-one patients were enrolled and underwent allo-MSCT. Thirteen patients died within 5 years post-MSCT and the 5-year overall survival rate was 84% (68/81). At 5-year follow-up, 22 patients (22/68, 32%) were in complete clinical remission and another 6 patients (6/68, 9%) were in partial clinical remission, and the 5-year disease remission was 41% (28/68). In total, 37 patients had achieved clinical remission (27 in complete remission and 10 in partial remission) at the 5 years visit and then 9 patients subsequently relapsed. The 5-year overall rate of relapse was 24% (9/37). SLEDAI scores, levels of serum albumin and complement C3, peripheral white blood cell and platelet numbers, as well as proteinuria levels continued to improve during the follow-up.

Conclusions: Allogeneic MSCT is safe and resulted in long-term clinical remission in severe and drug-resistant SLE patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2656

SAT0245 SERUM IFN GAMA MAY PREDICT THERAPEUTIC EFFECT OF MESENCHYMAL STEM CELLS TRANSPLANTATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

D. Wang, L. Sun. *Department of Rheumatology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China*

Background: Umbilical cord (UC) derived mesenchymal stem cells (MSCs) show immunoregulatory properties on various immune cells and display clinical effect on lots of autoimmune disease like systemic lupus erythematosus (SLE).

Objectives: The aim of this study is to investigate the effect of SLE environment on UC MSCs and to observe the possible serum biomarker to predict the therapeutic effect.

Methods: UC MSCs were co-cultured with peripheral blood mononuclear cells (PBMC) from active lupus patients at a ratio of 1:4. The proliferation, apoptosis and surface markers of UC MSCs were observed. UC MSCs functional molecules were assessed by real-time PCR and the signaling pathways were analyzed by western blot. Different recombinant cytokines were used to stimulate UC MSCs *in vitro* and the functional factors were determined by real-time PCR. In the last, twenty-six patients with SLE, refractory to conventional therapies, were given UC MSCs transplantation. The clinical effect was followed-up for one year to classify responder and non-responder groups, and baseline serum cytokines were analyzed by ELISA.

Results: The co-culture of lupus patients PBMC had no effect on UC MSCs surface markers and apoptosis, but promoted MSCs proliferation. Lupus PBMC were more prone to stimulate UC MSCs to secret VEGF as well as CXCL-12, compared to PBMC from normal controls. Furthermore, lupus PBMC activated Akt, IκB and Stat5 signaling pathways in UC MSCs but not affect Erk1/2 and Smad1/5/8 pathways. When stimulated by different cytokines, we found that interferon γ (IFN-γ) was still the most important cytokine to induce IDO1 as well as IDO2 productions in UC MSCs; both had dose-dependent manners. Moreover, our clinical study showed that baseline higher levels IFN-γ might predict a good response to MSCs transplantation in active lupus patients.

Conclusions: Baseline IFN-γ levels may predict clinical response to MSCs therapy for active lupus patients, which will help us to choose appropriate patient for clinical transplantation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2661

SAT0246 EXPLORER STUDY: RITUXIMAB USE IN SYSTEMIC LUPUS ERYTHEMATOSUS, A NEW LOOK ON OLD DATA

M. Scherlinger, C. Carcaud, M.E. Truchetet, P. Dufau, L. Couzy, J. Seneschal, T. Barnetche, E. Lazaro, C. Richez. *Fhu Acronym, CHU de Bordeaux, Bordeaux, France*

Background: Even if randomized trials EXPLORER and LUNAR failed to prove the superiority of rituximab versus placebo in patients with systemic lupus erythematosus, several encouraging indications as refractory lupus nephritis and new clinical trials renewed interest for this molecule.

We hypothetized that SLE response criteria used in EXPLORER were not sensible enough to show rituximab efficacy and that new response criteria could show a significant difference.

Objectives: Our objective was to reanalyze EXPLORER trial's raw data using the newly described SLE response criteria.

Methods: We proceeded to a pre-specified re-analyze of EXPLORER trial's raw data. The patients included in EXPLORER study had active SLE disease defined by a British Isles Lupus Assessment Group (BILAG) score A or 2 BILAG B despite immunosuppressive regimen. Renal and neurological SLE were excluded. Patients were randomized through a 2/1 ratio to receive either two 1gr rituximab infusions (day 0 and 15) repeated at month 6 or a placebo. Standard SLE treatment and other immunosuppressant were continued. Patients received in a stratified manner prednisone ranging from 0.5 to 1.0 mg/kg depending on disease severity at inclusion. The original efficacy criterion was a composite clinical score using BILAG at week 52.

In our new analysis, rituximab efficacy was assessed at week 52 using 4 criteria: SRI-4 (Systemic lupus erythematosus Responder Index) with and without a concomitant oral prednisone (OP) tapering objective of <10mg at month 6 (SRI-4 with and without OP tapering), Lupus Low Disease Activity Score (LLDAS) and BILAG-based Combined Lupus Assessment (BICLA).

Results: Data from all 257 patients were available. There was 234 women (91%) with a mean age of 40,3 years among which 177 (69%) received hydroxychloroquine.

At week 52, SRI-4 response rate was 27,2% in the rituximab group vs 22,7% in the placebo group (p=0.43); SRI-4 with OP tapering was 16% in the rituximab group vs 13.6% in the placebo group (p=0.62); LLDAS was 16% in the rituximab group vs 12.5% in the placebo group (p=0.46) and BICLA was 15.4% in the rituximab group vs 15.9% in the placebo group (p=0.91).

Subgroup analyses demonstrated a trend for better efficacy of rituximab compared to placebo in the subgroup of patients co-treated with methotrexate: SRI-4 of 30.6% in the rituximab group vs 12% in the placebo group (n=74, p=0.08). This trend was not found in the subgroup co-treated with azathioprine: SRI-4 of 26.7% in the rituximab group vs 30.6% in the placebo group (p=0.68), nor in the subgroup co-treated with mycophenolic acid: SRI-4 of 23.1% in the rituximab group vs 21.6% in the placebo group (p=0.86). In the subgroup of patients with a BILAG A/B in hematological system or vasculitis at baseline, there was a significantly higher SRI-4 response rate with rituximab: 28,6% vs 5,3% in the hematological group (n=61, p=0,047) and 39,3% vs 0% in the vasculitis group (n=38, p=0,037). Cumulative dose of steroids at week 52 were not statistically different: 4223mg in the rituximab group vs 4390mg in the placebo group (p=0,65).

Conclusions: Our study confirms the results from the original EXPLORER study. These results might be partly related to the study's design, notably the high daily oral prednisone used. Our work suggests efficacy in subgroups with vasculitis and hematological involvement.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1785

SAT0247 EFFICACY AND SAFETY OF MODIFIED-RELEASE PREDNISONE IN MANAGING MODERATE ACTIVITY SYSTEMIC LUPUS ERYTHEMATOUS DURING PREGNANCY: AN IMPLEMENTED CASE-CONTROL STUDY

M. Meroni[1,2], V. Ramoni[3], M. Limonta[2], M. Cutolo[1]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Internal Medicine Dept., University of Genova, Genova; [2]Rheumatology Unit, ASST Papa Giovanni XXIII, Bergamo; [3]Division of Rheumatology, IRCCS San Matteo Hospital Foundation, University of Pavia, Pavia, Italy*

Background: Systemic lupus erythematosus (SLE) primarily affects women of childbearing age. Despite the overall favorable outcome, pregnancy represents a challenge for both patients and clinicians. Since the complications rate is linked to the disease activity, the achievement of remission is recommended before pregnancy. Prednisone represents a cornerstone in SLE management and is safely used, at low doses (<7.5 mg daily), during pregnancy. Modified-release prednisone (MRP) optimize corticosteroid treatment strategy in rheumatic diseases, thanks to its capability of respect the physiological cortisol circadian secretion. MRP has been approved from FDA in SLE treatment, but no data are available regarding its administration during pregnancy.
Objectives: We aimed to investigate whether this drug is safe and effective as the immediate release prednisone (IRP) in SLE pregnant patients.
Methods: We retrospectively evaluated 9 female patients, fulfilling the ACR criteria for SLE, consulting our Centers in a 4-years observational range. All of them, thanks to a stable disease (not requiring treatment regimen modifications within 12 months), experienced a successful pregnancy during the observation. All the cases were taking low-dose MRP (5 to 7.5 mg/daily) as a baseline treatment, from at least 6 months. They were matched to 9 controls, defined as SLE patients with the same age and duration of disease, taking the same prednisone dose, from at least 6 months, in the IR formulation. Overall pregnancy outcome features; SLE disease activity (calculated at least once during pregnancy, SLEPDAI) and at baseline/post-partum (SLEDAI) score; patient's global assessment (VAS) at baseline, during pregnancy and in postpartum (mm); need of treatment changes throughout pregnancy and at postpartum (%) were assessed. Homogeneity tests, percentages and scores comparison were run out by non-parametric statistical analysis.
Results: Mean MRP age group was 26±7; disease duration, 4±8 years; IR one, respectively, 28±6 and 3±9 (both, p=ns). SLEDAI at baseline was 1±0.1 among MPR and 1±0.3 among IR women; SLEPDAI, 1±0.9 and 2±0.2 (both, p=ns). No major perinatal complications were detected. Preterm births, cesarean section rates, newborns weight and APGAR scores did not differ between the two subpopulations (all, p=ns). SLEDAI assessed at postpartum was 2.8±0.6 in MRP subjects and 3.4±0.4 in IR (p<0.05). Patients VAS (MRP *vs* IR) was 3±0.4 and 2±09 at baseline (p=ns); 2±0.6 and 4±0.7 during pregnancy (p<0.05) and 3±0.3 and 4±0.9 at postpartum (p<0.05). Regarding treatment regimen changes (add-on strategy), the observed rates involved 1/9 (MRP) and 5/9 (IR) women during the observational gap (pregnancy+postpartum) (p<0.001). Results synthesis is reported in Table I.

	Cases MRP	P value	Controls IRP
Age (years±months)	26±52	ns	28±43
Disease duration (years±months)	4±8	ns	3±9
PDN dose baseline (mg)	5±2.5	ns	5±2.5
SLEDAI baseline	1±0.1	ns	1±0.3
VAS baseline (mm)	20±6	ns	21±5
PDN dose pregnancy (mg)	5±2.5	p<0.05	7.5±2.5
SLEPDAI	1±0.9	p<0.05	3±0.2
VAS pregnancy (mm)	41±8	p<0.05	23±7
Gestation (weeks±days)	38±5	ns	37±6
Child weight (g)	3230±420	ns	3120±390
APGAR	9±1	ns	9±0
PDN dose postpartum (mg)	2.5±2.5	p<0.05	5±2.5
PDN need to change (%)	11	p<0.001	56
SLEDAI postpartum	2.8±0.6	p<0.05	3.4±0.4
VAS postpartum (mm)	50±4	p<0.05	71±6

Conclusions: Activity (SLEDAI) score was significantly higher at postpartum and treatment had to be increased in IR patients, in comparison to the MRP, to manage SLE. VAS, conversely, was significantly higher among IR, both during pregnancy and postpartum. No major perinatal side effects were observed during the study; minor and expected complications rates did not differ between the two subpopulations. Despite the limited number of subjects, MRP treatment seems to be as safe, but more effective, in comparison to the standard IR one, during pregnancy of SLE-affected women.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3135

SAT0248 BASELINE CLASI-DAMAGE IS A MAJOR PREDICTOR OF SKIN RESPONSE TO BELIMUMAB IN A MULTICENTRIC COHORT OF SLE PATIENTS

M. Gatto[1], L. Iaccarino[1], L. Andreoli[2], F. Conti[3], R. De Angelis[4], S. De Vita[5], L. Emmi[6], R. Gerli[7], M. Govoni[8], M. Mosca[9], C. Salvarani[10], A. Tincani[2], A. Doria[1]. *[1]Unit of Rheumatology, University of Padova, Padova; [2]Rheumatology and Clinical Immunology Unit, Spedali Civili and University of Brescia, Brescia; [3]University LA Sapienza, Rome; [4]Rheumatology Unit, Univerisity of Marche, Iesi; [5]University of Udine, Udine; [6]AOU Careggi, Florence; [7]Rheumatology Unit, University of Perugia, Perugia; [8]Unit of Rheumatology, University of Ferrara, Ferrara; [9]Unit of Rheumatology, University of Pisa, Pisa; [10]Rheumatology Unit, Arcispedale S Maria Nuova - IRCCS, Reggio Emilia, Italy*

Background: Belimumab is used to treat several systemic lupus erythematosus (SLE) manifestations and predictors of response are advisable in clinical practice.
Objectives: To explore the effects of belimumab treatment on skin involvement in SLE patients in a real-life setting.
Methods: SLE patients treated with belimumab (10 mg/kg day 0, 14, 28 and then every 28 days), as add-on therapy in 11 Italian cohorts were prospectively followed-up for 24 months. Skin involvement was measured by the CLASIa score (Cutaneous Cutaneous LE Disease Area and Severity Index Activity) at baseline and every six months until month 24. Damage was measured by CLASI-Damage (CLASId). Response was defined as CLASIa <2 at measured timepoints.
The following variables were tested to determine baseline predictors of response at 12, 18 and 24 months: gender, age, disease duration, SLE activity index 2000 (SLEDAI-2K) ≥10, prednisone dose >7.5 mg/day, baseline CLASIa and CLASId, concomitant immunesuppressants (yes/no) and number of previous immunesuppressants. Statistical analysis was performed with SPSS 22.0 software.
Results: 188 patients were studied, among whom 48 (25.5%) had skin involvement as the leading feature for belimumab therapy. Mean follow-up period was 17.5±10.96 months. Thirty-eight patients completed a 6-month follow-up; 27 completed a 12-month follow-up; 19 completed a 18-month follow-up and 15 completed a 24-month follow-up. Fourteen patients discontinued due to adverse events (7/14, 50%), lack of efficacy (4/14, 28.5%) or other causes (3/14, 21.4%). CLASIa, daily prednisone dosage and SLEDAI-2K significantly decreased during the follow-up (p<0.001). CLASIa<2 was achieved by 25/38 patients (65.7%) at 6 months, 19/27 (70%) at 12 months, 11/19 (58%) at 18 months and 10/15 (67%) at 24 months. A lower baseline CLASIa was associated with CLASIa response at 18 and 24 months (responders vs. non-responders: 3.4±2.4 vs. 9.5±5.6; 3.5±2.5 vs. 11.2±6.5; p<0.005 for both), while a lower baseline CLASId was associated with CLASIa response at each timepoint (responders vs. non-responders: at 12 months: 0.6±0.9 vs. 2.4±2.5; at 18 months: 0.5±0.8 vs. 2.5±2.3; at 24 months: 0.6±0.8 vs. 3.25±2.7; p=0.01 for all). Multivariate analysis was only performed at 12 months due to low patient number at 24 months. CLASId was the only independent negative predictor of response (OR 0.52, p=0.05). Notably, CLASId remained stable during the follow-up.
Conclusions: Belimumab use in cutaneous involvement is associated with reduced activity in skin lesions and hindrance of skin damage. Early use of belimumab before damage is established is likely to be associated with a better response.
Acknowledgements: dr. Margherita Zen, dr. Maddalena Larosa, dr. Francesca Ometto, dr. Mara Felicetti for helping in data collection and statistical analysis
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6461

SAT0249 SAFETY, PHARMACOKINETICS, PHARMACODYNAMICS AND INHIBITION OF T-CELL DEPENDENT ANTIBODY RESPONSE (TDAR) WITH MEDI4920, A NOVEL, ENGINEERED CD40 LIGAND (CD40L) ANTAGONIST: RESULTS OF A FIRST-TIME-IN-HUMAN STUDY

M.G. Albulescu[1], M. Gunsior[2], J. Li[3], J. Bush[4], A. Godwood[1], R. Miday[2], E. Grant[5], D. Howe[1], R. Faggioni[3], L. Roskos[2]. *[1]MedImmune, Cambridge, United Kingdom; [2]MedImmune, Gaithersburg; [3]MedImmune, Mountain View, United States; [4]Covance Clinical Research Unit Ltd, Leeds, United Kingdom; [5]Gilead Sciences Inc, Foster City, United States*

Background: The CD40/CD40L pathway is involved in the T-cell-dependent activation of B cells, which subsequently produce autoantibodies and inflammatory mediators that contribute to autoimmune disease pathology. MEDI4920 is an engineered fusion protein and antagonist of CD40L that lacks the fragment crystallisable (Fc) domain thought to be involved in thromboembolic events (TEs) previously reported with anti-CD40L agents containing an Fc domain.
Objectives: The primary objective of this Phase I, randomised, double-blind, placebo-controlled, single-ascending dose study was to evaluate the safety and tolerability of MEDI4920 in healthy subjects. Secondary objectives were to characterize T-cell-dependent antibody response (TDAR) to keyhole limpet hemocyanin (KLH) neoantigen, pharmacokinetics (PK), and anti-drug antibodies (ADAs) to MEDI4920.
Methods: Fifty-six healthy adult male subjects, aged 19–49 years, received a single intravenous dose of either MEDI4920 (3, 10, 30, 100, 300, 1000 or 3000 mg) or placebo. TDAR inhibition was analysed by measuring serum concentrations of

IgG and IgM antibodies to KLH over time. A dose–response model was generated for TDAR inhibition. Blood samples were collected to evaluate PK, total soluble CD40L (sCD40L) and ADA concentrations.

Results: No deaths, TEs, severe or serious hypersensitivity reactions or infections or infusion-related reactions were observed in the study. One serious adverse event (fractured tibia) was reported in the placebo arm. MEDI4920 showed inhibition of the TDAR IgG response after the second administration of KLH on Day 15 at higher doses (≥300 mg; Figure 1A). An E_{max} model adequately characterised the TDAR dose–response at Day 43 ($p<0.001$; ED_{50}=491 mg), with the 3000 mg dose showing 86% inhibition of the TDAR (95% CI: 68–94%; Figure 1B). MEDI4920 exhibited linear PK. MEDI4920 produced a dose-dependent increase in total sCD40L concentrations. A high ADA incidence (90%) was observed in dose cohorts ≤100 mg; however, ADA incidence (29%) and ADA titres decreased with ≥300 mg doses of MEDI4920. ADA-high subjects had reduced MEDI4920 and total sCD40L concentrations compared with ADA-negative subjects or those with low ADA titres. ADA incidence did not correlate with any clinical events.

Figure 1A: Plot of mean anti-KLH IgG concentrations over time

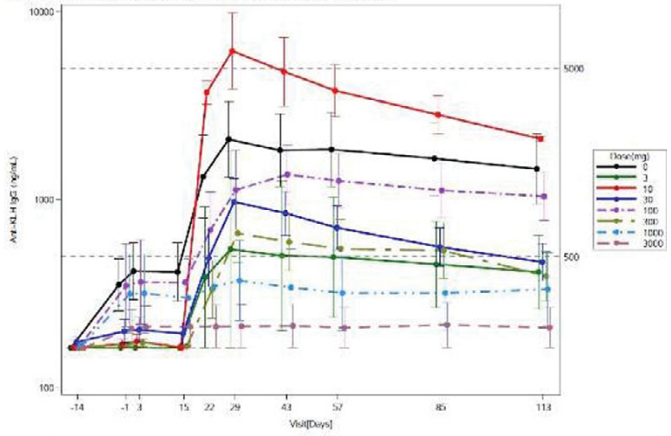
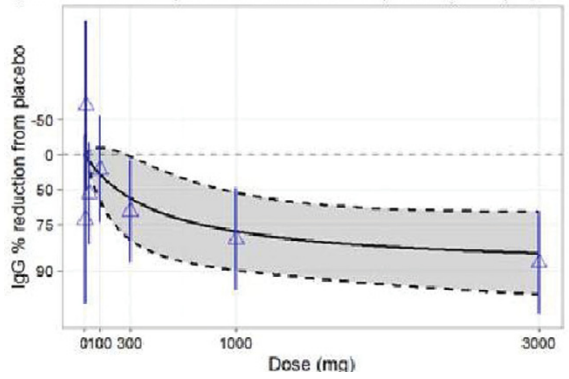


Figure 1B: Plot of dose–response model for TDAR inhibition (anti-KLH IgG at Day 43)



Conclusions: MEDI4920 demonstrated an acceptable safety and tolerability profile, and dose-dependent inhibition of TDAR. The dose-dependent increase in total sCD40L concentrations indicates binding of MEDI4920 to sCD40L and target engagement. The decreases in ADA incidence and ADA titres correlate with increasing MEDI4920 dose, consistent with the immunosuppressive mechanism of action of this molecule. These results support further exploration of MEDI4920 administration in subjects with autoimmune diseases where the CD40/CD40L pathway is activated.

Acknowledgements: Funded by MedImmune. Medical writing support: D. Trivedi, MedImmune LLC, Gaithersburg, MD, USA. Technical editing support: R. Plant, QXV Comms, an Ashfield company, which was funded by MedImmune.

Disclosure of Interest: M. Albulescu Shareholder of: MedImmune, Employee of: MedImmune, M. Gunsior Employee of: MedImmune, J. Li Employee of: MedImmune, J. Bush Employee of: Covance Clinical Research Unit Ltd (Co. contracted [and paid] by the sponsor to conduct the study), A. Godwood Shareholder of: AstraZeneca, Employee of: MedImmune, R. Miday Employee of: MedImmune, E. Grant Shareholder of: AstraZeneca, Employee of: MedImmune, D. Howe Employee of: MedImmune, R. Faggioni Shareholder of: AstraZeneca, Employee of: MedImmune, L. Roskos Shareholder of: AstraZeneca, Employee of: AstraZeneca

DOI: 10.1136/annrheumdis-2017-eular.3468

SAT0250 BODY MASS INDEX IS INVERSELY ASSOCIATED WITH RESPONSE TO RITUXIMAB IN LUPUS NEPHRITIS: ANALYSIS OF THE LUNAR TRIAL

M.D. Cascino[1,2], L.M. Gomez Mendez[1], J. Garg[2], L. Dragone[2], M. Dall'Era[1], P. Brunetta[2]. [1]*University of California – San Francisco, San Francisco;* [2]*Genentech, Inc., South San Francisco, United States*

Background: Increased body mass index (BMI) has been associated with poor functional capacity and systemic inflammation in lupus,[1] alterations in rituximab (RTX) pharmacokinetics,[2] and failure to achieve trial endpoints among patients treated with RTX for ANCA-associated vasculitis.[3] Although RTX is not approved for the treatment of lupus nephritis (LN), current EULAR/ERA-EDTA guidelines include RTX for use in refractory cases.[4] The effect of BMI on outcomes of patients treated with RTX for LN is unknown.

Objectives: To assess the association between pre-treatment BMI and renal response using data from the LUNAR trial.

Methods: LUNAR randomized 144 patients with ISN/RPS class III or IV LN to RTX (2 doses of 1000 mg at baseline and month 6) or placebo in combination with mycophenolate and a steroid taper.[5] BMI was measured at the screening visit. Complete renal response (CRR) was defined as achievement of UPCR <0.5, normal serum creatinine not increased from baseline by >15%, and inactive urinary sediment at week 52. Alternative definitions of response and achievement of CRR at week 78 were also considered. Logistic regression was used to model interactions and to calculate odds ratios (OR) and 95% CI. Peripheral $CD19^+$ B cell measurements were examined.

Results: We identified qualitative interactions between BMI and treatment for CRR and alternative response measures. In unadjusted analysis, each 5 kg/m^2 increase in pre-treatment BMI was associated with OR =0.47 (95% CI 0.24–0.92) in the RTX group and OR =1.44 (95% CI 0.93–2.23) in the placebo group for achievement of CRR (*P* value for interaction =0.006). The results of analysis adjusted for baseline UPCR and serum creatinine are presented in the Table. A sensitivity analysis identified consistent associations between BMI and response in the RTX group only. Among patients in the RTX group, increased BMI was associated with increased time to peripheral $CD19^+$ count <5 cells/μL (Figure).

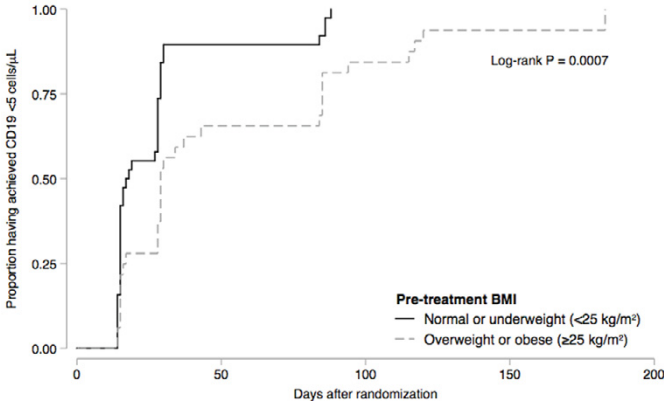
Table 1

	Adjusted OR (95% CI) per 5 kg/m^2 increase in pre-treatment BMI		*P* value for interaction
Response measure	Rituximab (n=72)	Placebo (n=72)	
CRR	0.48* (0.23–0.97)	1.60* (1.01–2.55)	0.005
Overall renal response	0.78 (0.51–1.19)	1.42 (0.94–2.16)	0.045
UPCR <0.5	0.61* (0.38–0.97)	1.37 (0.91–2.07)	0.010
UPCR <0.7	0.58* (0.37–0.92)	1.33 (0.87–2.02)	0.010
CRR at week 78	0.53* (0.29–0.99)	1.58 (0.99–2.52)	0.006

*P <0.05.

All endpoints were measured at week 52 except where specified.

Figure. Kaplan-Meier estimates: Time to peripheral $CD19^+$ count <5 cells/μL



Conclusions: In this exploratory analysis of the LUNAR trial, BMI was inversely associated with renal response among patients treated with RTX. We did not observe this same relationship between BMI and response among patients in the placebo group, and in fact found evidence of a positive correlation between BMI and one measure of response in this group. Among patients treated with RTX, BMI was associated with time to B cell depletion, generating the hypothesis that the observed differences in response are mediated by differences in the timing and/or degree of B cell depletion. These findings warrant additional analyses to better understand the relationships between patient characteristics, pharmacokinetics, B cell depletion, and treatment response in the LN population.

References:

[1] Oeser Arthritis Rheumatol 2005.
[2] Müller Blood 2012.
[3] Bertsias Ann Rheum Dis 2012.
[4] Rovin Arthritis Rheumatol 2012.
LUNAR trial NCT00282347.

Disclosure of Interest: M. Cascino Employee of: Roche/Genentech, L. Gomez Mendez Grant/research support from: Roche/Genentech, J. Garg Employee of: Roche/Genentech, L. Dragone Employee of: Roche/Genentech, M. Dall'Era: None declared, P. Brunetta Employee of: Roche/Genentech
DOI: 10.1136/annrheumdis-2017-eular.5535

SAT0251 PREDICTING AND MANAGING PRIMARY AND SECONDARY NON-RESPONSE TO RITUXIMAB USING B-CELL BIOMARKERS IN SYSTEMIC LUPUS ERYTHEMATOSUS

M.Y. Md Yusof[1,2], D. Shaw[1], Y.M. El-Sherbiny[1,2], A.C. Rawstron[3], P. Emery[1,2], E.M. Vital[1,2]. *[1]Rheumatology, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]NIHR Leeds Musculoskeletal Biomedical Research Unit; [3]Haematological Malignancy Diagnostic Service, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Rituximab (RTX) is the most commonly used biologic for the treatment of SLE. However, there is are no clinically applicable predictors of response, which is of particular importance in this heterogeneous disease with other biologics being restricted to certain subgroups.
Objectives: To assess factors associated with primary and secondary non-response to RTX in SLE in order to develop more targeted and effective B-cell therapy.
Methods: A prospective observational study was conducted in 125 SLE patients treated with RTX in Leeds for over 12 years. A major clinical response was defined as improvement of all active BILAG-2004 domains to grade C/better and no A/B flare. Partial responders were defined by 1 persistent BILAG B. B-cell subsets were measured using highly sensitive flow cytometry. Predictors of response were analysed using logistic regression analysis.
Results: 117 patients had evaluable data. In cycle 1 (C1), 96/117 (82%) achieved BILAG response [major=50%,partial=32%]. In MVA, younger age & B-cell depletion at 6 weeks increased the odds of major response (Table 1). Complete depletion was predicted by normal complement & lower pre-RTX plasmablasts. 77 (with data on 72) C1 responders were retreated on clinical relapse. Of these, 61/72 (85%) responded in C2. Of 11 C2 non-responders, 9 met secondary non-depletion non response (2NDNR) criteria, as defined by *infusion reaction & defective depletion (*incidence=12%) and tested positive for anti-RTX antibodies. Lack of concomitant immunosuppressant & higher pre-RTX plasmablasts predicted 2NDNR.
Conclusions: B-cell subsets should be monitored in the routine care of SLE patients receiving RTX and should aim to achieve complete depletion. About 1 in 8 SLE patients lose depletion on repeat cycles and this is associated with anti-RTX antibodies. Clinical trials using more intensive RTX treatment regimens in those predicted not to completely deplete, or alternatively use of humanised anti-CD20mAbs are likely to increase clinical response rates to B-cell depleting agents.
Acknowledgements: This research was funded/supported by NIHR (DRF-2014–07–155) and (CS-2013–13–032). The views expressed are those of the author(s) & not necessarily those of the NHS, NIHR or the Dept of Health
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6943

SAT0252 THE NUMBER OF TREG CELLS IN PERIPHERAL BLOOD IN PSS PATIENTS IS DECREASED AND LOW DOSE IL-2 CAN PROMOTE ITS PROLIFERATION

M. Miao[1], Z. Hao[1], Y. Guo[1], X. Zhang[2], S. Zhang[1], X. Wu[2], D. Xu[1], C. Gao[3], X. Li[2]. *[1]The Second Hospital of Shanxi Medical University; [2]Department of Rheumatology, the Second Hospital of Shanxi Medical University, Taiyuan, China; [3]Department of Pathology, Joint Program in Transfusion Medicine, Brigham and Women's Hospital/Children's Hospital Boston, Boston, United States*

Background: PSS is a kind of autoimmune disease without clear pathogenesis. Treg cell plays an important role in autoimmune disease. However, opinions about change of amount of Treg cells in peripheral blood in autoimmune disease are various. Besides, the researches mainly focus on RA and SLE but not PSS.
Objectives: To explore the change of the number of Th17 and Treg (CD4+CD25+Foxp3+T cells) cells in peripheral blood in PSS and the effects of low dose IL-2 therapy on the balance of Treg and Th17 cells.
Methods: One hundred and ninety two PSS patients in our department, and 30 healthy controls were put in the research. The amount of Th17 cells and Treg cells were calculated by flow cytometry. Eighty eight in 192 were given low-dose IL-2 (50 WIU/day for 5 days) by hypodermic injection combined with standard therapy which includes glucocorticoid, immune-suppressants, biological agents or combination of them, while others (12 in 69) were given standard therapy only. The amount of these cells were calculated again after therapy.
Results: There was significant decrease in the absolute number of Treg cells and significant increase of the ratio of Th17/Treg cells in PSS patients when compared with healthy controls. There was no significant difference in absolute number of Th17 cells between PSS patients and healthy controls. Further, the number of Treg cells were negatively relative to ESSDAI. Traditional DMARDs had no obvious impact on Treg and Th17 cells. The amount of Treg cells significantly increased after the treatment of IL-2 by 1 week. But there was no significant improvement in clinical manifestations in the short time when comparing combinational treatment of IL-2 and classical drugs with classical therapy. No obvious adverse reactions were observed.

Table 1. Absolute number and percentage of CD4+T subsets in peripheral blood in PSS patients and Healthy controls.

Study Participants	Health	PSS	Untreated PSS
Th17	6.44 (5.10, 8.55)	7.09 (4.05, 11.48)	6.08 (4.30, 12.60)
Treg	36.20 (27.82, 47.02)	28.24 (15.89, 41.36)*	27.30 (17.43, 39.87)*
Th17%	0.96 (0.67, 1.33)	1.26 (0.77, 1.95)*	1.26 (0.86, 1.92)^
Treg%	4.80 (4.19, 6.37)	4.64 (3.10, 6.44)	4.70 (2.52, 6.91)
Th17/Treg	0.18 (0.14, 0.29)	0.27 (0.15, 0.43)*	0.28 (0.15, 0.47)^

Median (range, cells/μl). ^P<0.1, *p<0.05, **p<0.01, ***p<0.0001 vs Healthy controls.

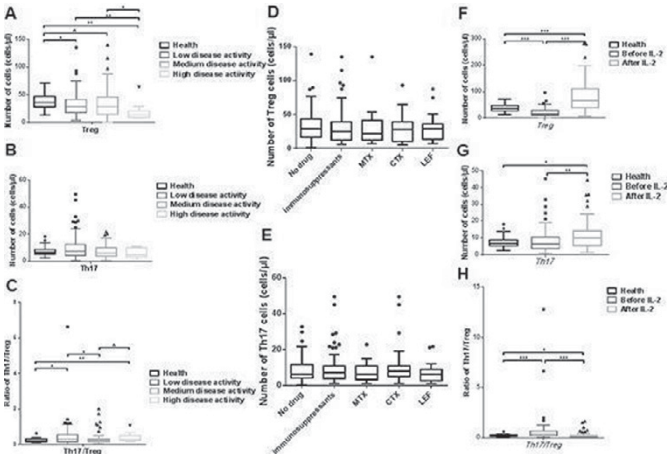


Figure 1

Conclusions: The number of CD4+CD25+Foxp3+T cells in peripheral blood was decreased obviously and was inversely related to ESSDAI. While there was no significant difference of Th17 cells between PSS patients and healthy controls. And there was no correlation between the number of Th17 cells and ESSDAI. So the imbalance of Th17/Treg is due to the decrease of Treg cells not increase of Th17 cell which indicates that the pathogenesis of PSS maybe mainly because of shortage of autoimmune tolerance. Low dose IL-2 therapy can effectively promote proliferation of Treg cells by which low dose IL-2 may induce and restore autoimmune tolerance to benefit disease control.
References:
[1] Takayoshi Morita et al. The Proportion of Regulatory T Cells in Patients with Rheumatoid Arthritis: A Meta-Analysis. PLoS One. 2016 Sep 13.
[2] Noack, M. & Miossec, P. Th17 and regulatory T cell balance in autoimmune and inflammatory diseases. Autoimmun Rev. 13, 668–677 (2014).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6366

Abstract SAT0251 – Table 1

	Non/Partial Response (n=59)	Major Clinical Response (n=58)	UVA OR (95% CI), P-value	MVA OR (95% CI), P-value
Age, mean (SD) years	43 (17)	37 (14)	0.97 (0.95–0.99), p=0.031 per year	0.97 (0.94–0.99), **p=0.037**
White, N (%)	43 (73)	37 (64)	1.53 (0.70–3.34), p=0.292	0.93 (0.34–2.54), p=0.882
Anti-dsDNA, mean (SD) IU/ml	147 (230)	142 (230)	1.00 (0.99–1.00), p=0.913 per unit	1.00 (0.99–1.00), p=0.518
Anti-ENA positivity, N (%)	40 (68)	38 (66)	0.93 (0.42–2.06), p=0.860	1.00 (0.39–2.57), p=1.00
Low C3 and/or C4, N (%)	25 (42)	24 (41)	0.97 (0.46–2.06), p=0.945	1.33 (0.46–3.80), p=0.599
ESR, mean (SD) mm	40 (32)	41 (36)	1.00, (0.99–1.01), p=0.901 per unit	1.00 (0.97–1.00), p=0.349
Concomitant DMARDs,N (%)	41 (69)	35 (60)	0.67 (0.31–1.43), p=0.301	0.39 (0.16–1.00), p=0.051
Global BILAG, mean (IQR)	21 (8)	24 (13)	1.03 (0.99–1.07), p=0.093 per point	1.03 (0.98–1.08), p=0.191
Total B-cell counts x 1000 mean (IQR)	101 (95)	138 (150)	1.00 (1.00–1.01), p=0.169 per unit	1.00 (1.00–1.01), p=0.103
B-cell depletion at 6 weeks, N (%)	29 (49)	39 (68)	2.15 (0.98–4.71), p=0.056	3.44 (1.25–9.48), **p=0.017**

SAT0253 EFFICACY AND SAFETY OF LEFLUNOMIDE THERAPY IN LUPUS NEPHRITIS:A META-ANALYSIS

Q. Ren[1], H. Zeng[2]. [1]*Department of Pediatric Allergy, Immunology and Rheumatolog;* [2]*Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: To evaluate the efficacy and safety of leflunomide in treating lupus nephritis (LN).
Methods: According to the requirements of meta-analysis, a literature search about efficacy and safety of leflunomide therapy in LN was performed among Cochrane clinical controlled trials database, PubMed, BMJ-Clinical Evidence, CNKI, VIP and Wanfang data from the establishment of the database till December 2010.All included RCTs were graded in term of randomization, allocation concealment and blinding and non-RCTs were graded in term of grouping method, blinding, withdrawal and loss of follow-up, baseline comparability, diagnostic criteria and bias control. RevMan 5.0 software was used for meta-analysis.
Results: A total of 828 literatures were included. Five RCTs and 2 non-RCTs were enrolled for meta-analysis.Leflunomide group was treated with leflunomide and glucocorticoid, while control group was given cyclophosphamide and glucocorticoid or placebo. The 24 h urine protein, SCr and SLEDAI scores of leflunomide group were significantly lower than that of cyclophosphamide group. There was no significant difference in C3,positive rate of anti-ds DNA between leflunomide group and cyclophosphamide group. There was no significant difference in infection, herpes zoster,hypertension, palpitations, leukopenia, alopecial, elevation in ALT, memoxenia, rashes, or the incidence of gastrointestinal reactions between the two groups.
Conclusions: Based on the current evidence, the efficacy and safety of leflunomide for treatment of LN are close to cyclophosphamide. Further evidence from RCT studies is needed to elucidate the efficacy and safety of leflunomide for LN.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2051

SAT0254 SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF SUBCUTANEOUS AND INTRAVENOUS ANIFROLUMAB IN HEALTHY VOLUNTEERS

R. Tummala[1], T. Rouse[2], A. Berglind[2], L. Santiago[3]. [1]*AstraZeneca, Gaithersburg, MD, United States;* [2]*AstraZeneca, Gothenburg, Sweden;* [3]*MedImmune, Mountain View, CA, United States*

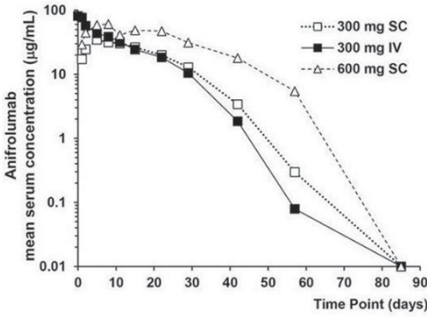
Background: Anifrolumab is a fully human anti–interferon-α receptor monoclonal antibody in Phase III development for systemic lupus erythematosus (SLE). In Phase IIb trials, intravenous (IV) anifrolumab (300 mg every 4 weeks) significantly decreased SLE disease activity with safety and tolerability comparable to placebo.[1]
Objectives: The primary objective of this Phase I, double-blind, randomized, controlled study (NCT02601625) was to characterize the pharmacokinetics (PK), safety, and tolerability of anifrolumab administered subcutaneously (SC) and intravenously to healthy volunteers.
Methods: Thirty male and female adults were assigned to three sequential treatment cohorts of equal size (anifrolumab 300 mg SC injection; anifrolumab 300 mg IV; anifrolumab 600 mg SC by infusion). Individuals were randomized within each cohort to receive a single dose of either anifrolumab (n=6/cohort) or placebo (PBO) (n=4/cohort). Serial blood samples were collected up to Day 85. Serum anifrolumab concentrations were analyzed with a validated assay. PK parameters were estimated by noncompartmental analysis. Immunogenicity of anifrolumab was assessed by measuring serum anti-drug antibodies (ADAs).
Results: Anifrolumab serum concentration-time profiles and primary PK parameters in healthy volunteers are presented in the figure and table, respectively. Anifrolumab serum concentrations were below the limit of detection in all individuals by 85 days post dose. Maximum serum concentrations in the SC cohorts occurred after 4 to 7 days. Exposure to SC anifrolumab increased approximately dose proportionally from 300 mg to 600 mg based on AUC. At the 300-mg dose, anifrolumab exposure after SC administration reached approximately 86% of the IV administration exposure. SC administration of anifrolumab 300 mg and PBO elicited minimal injection-site reactions. Transient injection-site induration occurred in five of six individuals in the anifrolumab 600-mg group and two of four in the PBO group. Transient, mild to moderate injection-site induration and pruritus occurred simultaneously in two of six individuals in the anifrolumab 600-mg group, but not those in the PBO group. Adverse events were reported by 50% (n=9) of anifrolumab-treated and 33% (n=4) of PBO-treated individuals. No serious adverse events were observed. ADAs were detected in only one individual in the anifrolumab 300-mg IV group at the Day-85 assessment.

Anifrolumab Serum PK Parameters

	Anifrolumab		
	300 mg SC (N=6)	300 mg IV (N=6)	600 mg SC (N=6)
C_{max} (μg/mL)			
Mean ± SD	36.2±11.6	82.4±13.2	63.9±20.5
CV (%)	32.1	16.0	32.0
AUC (day.μg/mL)			
Mean ± SD	785±331	907±175	1,828±680[a]
CV (%)	42.1	19.3	37.2
t_{max} (day)			
Median	4.13	0.03	7.00
Minimum–maximum	4.02–7.00	0.03?1.03	3.96?8.95

[a]N=5 because 1 individual was lost to follow-up at 1 month post dose. AUC = area under serum concentration-time curve from time zero extrapolated to infinity; C_{max} = observed maximum serum concentration; CV = coefficient of variation; t_{max} = time to reach maximum serum concentration.

Serum Concentration–Time Profiles



Mean data below limits of detection are plotted as 1/2 of the lower limits of quantification (0.02 μg/mL).

Conclusions: Exposure of anifrolumab 300 mg SC was approximately 86% of IV administration, with single SC administrations of anifrolumab being generally well-tolerated in healthy volunteers.
References:
[1] Furie R, et al. Arthritis Rheumatol. 2017;69:376–86.
Disclosure of Interest: R. Tummala Employee of: AstraZeneca, T. Rouse Employee of: AstraZeneca, A. Berglind Shareholder of: AstraZeneca, BMS, Employee of: AstraZeneca, L. Santiago Shareholder of: AstraZeneca, Employee of: MedImmune
DOI: 10.1136/annrheumdis-2017-eular.2149

SAT0255 A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, ASCENDING-DOSE, SAFETY STUDY OF CC-220 IN SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

V.P. Werth[1], R. Furie[2], S. Korish[3], M. Weiswasser[3], A. Azaryan[3], P.H. Schafer[3], N. Delev[3], S. Choi[3], D. Hough[3]. [1]*University of Pennsylvania School of Medicine, Philadelphia;* [2]*Northwell Health, Great Neck;* [3]*Celgene Corporation, Summit, United States*

Background: CC-220 is a CUL4CRBN E3 ubiquitin ligase modulator that binds to cereblon and leads to potent and deep reduction of the transcription factors Ikaros (IKZF1) and Aiolos (IKZF3), which are overexpressed in the peripheral blood of Systemic Lupus Erythematosus (SLE) subjects. This study evaluated the safety, and tolerability of CC-220 in subjects with SLE. Exploratory efficacy assessments were included.
Methods: Subjects with history of SLE ≥6 months and a baseline of hybrid SELENA-SLEDAI (hSS) score ≥4 were randomized to 1 of 4 escalating doses of CC-220 or matching placebo (PBO). The 4 active treatments were CC-220 0.3 mg QOD, 0.3 mg QD, 0.3 mg alternating with 0.6 mg QD, and 0.6 mg QD; subjects were randomized 4:1 active to PBO in each group for 12 weeks of treatment, followed by 12 weeks of observational follow-up and/or long-term extension. Stable doses of corticosteroids (≤10 mg prednisone or equivalent daily), non-steroidal anti-inflammatory drugs, and antimalarials were permitted. Safety assessments included clinical evaluation of adverse events (AEs), laboratory parameters, electrocardiograms, physical examinations, and overall tolerability. Exploratory efficacy assessments included hSS, Cutaneous Lupus Area and Severity Index (CLASI) skin scores, Physician Global Assessment (PGA), swollen joint counts (SJC), and tender joint counts (TJC).
Results: A total of 42 adult subjects were randomized; 39 subjects were female (93%); Mean age was 47.2 years; 64% were White and 31% were Black or African-American. Mean SLE duration was 9.4 years, with a mean baseline hSS score of 6.6, CLASI activity score of 9.8, and PGA score of 1.3. Seventy-nine percent of subjects completed the study; 9 of 42 subjects discontinued, of which 6 subjects discontinued due to an adverse event (AE): 1 in the placebo group and 5 in the 2 highest CC-220 groups combined. No discontinuations were due to lack of efficacy. Four subjects had serious AEs (highest CC-220 doses: n=2 [pneumonia]; PBO: n=2). Three subjects had neutropenia (grade 3: n=2; grade 1: n=1); 2 subjects in the highest CC-220 dose group had dermatitis, and 1 subject in the 0.3 mg QD and 1 in the 0.6 mg QD dose groups had urticaria. Mean reductions in the CLASI activity score at day 85 ranged from 4.3 to 7.8 in the CC-220 treatment groups compared to an increase of 0.4 in the placebo group. More subjects receiving CC-220 had a ≥4-point reduction in hSS score vs PBO by Day 85 (22.2%>50.0% vs 12.5%).
Conclusions: CC-220 was generally well tolerated in this SLE population over 12 weeks of treatment, with neutropenia and dermatitis observed at the highest doses studied. Treatment with CC-220 resulted in a trend toward greater improvement

in multiple measures of SLE disease activity compared with PBO. These results support further development of CC-220 in SLE patient population.
Disclosure of Interest: V. Werth Grant/research support from: Celgene Corporation, Consultant for: Celgene Corporation, R. Furie Consultant for: Celgene Corporation, S. Korish Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, M. Weiswasser Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, A. Azaryan Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, P. Schafer Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, N. Delev Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, S. Choi Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, D. Hough Shareholder of: Celgene Corporation, Employee of: Celgene Corporation
DOI: 10.1136/annrheumdis-2017-eular.3546

SAT0256 MULTI-TARGET THERAPY WITH MIZORIBINE, TACROLIMUS, AND PREDNISOLONE IN LUPUS NEPHRITIS: ANALYSIS OF 47 CASES

R. Kawato, R. Rokutanda, M. Kishimoto, M. Okada. *Immune-rheumatology center, St.luke hospital, Tokyo, Japan*

Background: Mizoribine (MZB), an inosine monophosphate dehydrogenase inhibitor, is an effective glucocorticoid-sparing agent for gromerulonephritis and variety of rheumatic diseases. However, its clinical usefulness as multi-target therapy in patients of lupus nephritis has been unclear.
Objectives: To evaluate efficacy of multi-target therapy with MZB, tacrolimus (TAC) and prednisolone (PSL) for lupus nephritis.
Methods: We extracted all the cases with lupus nephritis treated with PSL, MZB, and TAC during period from 2008/1 to 2016/10. Retrospective medical chart review was performed to collect following data; baseline patient characteristics, dose of PSL, serum creatinine, urine protein, compliment, anti-DNA ab, remission rates, and safety profiles. We define complete remission as urine protein $<$0.5 g/gCre and normal serum creatinine, partial remission as urine protein decreasing more than 50% at baseline, and $<$3g/day, and normal serum creatinine or increasing within 15%. Patents' records were followed from the beginning of multi-target treatment to 12 months after.
Results: 43 cases (female; n=37, male; n=6, mean age; 37.4 years old) were included for analysis. Of 30 cases who underwent renal biopsy, 10 cases were classified as class IV nephritis, and 7 cases were classified as class III nephritis. Mean urine protein (g/gCr) at baseline, at 3 months, and at 6 months are 1.9, 0.4, and 0.4, respectively. Mean dose of steroid was 32.8 mg/day at baseline, 9.8 mg/day at 3 months, and 8.7 mg/day at 6 month. 79.1% of the patients achieved complete remission at 3 months, and the remission rate was more than 80% at 6 months and later. As for adverse events, 14 cases had some Infection, 3 out of 14 needed antibiotics treatment. Four cases had renal impairment after starting TAC, all of them recovered after stopping or decreasing dose of TAC.
Conclusions: Multi-target therapy with MZB, TAC and PSL showed good remission rate, and few severe adverse events. We need the further evaluation of long-term efficacy of the therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3374

SAT0257 "AIMING FOR THE BULLSEYE": RETINAL TOXICITY SCREENING FOR HYDROXYCHLOROQUINE THERAPY – ARE WE HITTING THE TARGET?

S. Gubbins, J. Steen, A. Gorman, S. Khan, A. Mohammad, K. O'Rourke. *Rheumatology, Midlands Regional Hospital Tullamore, Tullamore, Ireland*

Background: Hydroxychloroquine (HCQ) is commonly used to treat a variety of rheumatological and inflammatory conditions such as RA, SLE and Sjogrens. Retinal toxicity is a well known complication of HCQ therapy. Initially, the incidence of retinal toxicity was believed to be quite minimal1. However, subsequent large epidemiological studies have highlighted its much greater prevalence-up to 7.5% in certain populations2,3. Furthermore, the visual toxicity is typically permanent with possible progression up to years after drug cessation and with no current treatment4. Detection at an early stage has been shown to be crucial in preserving central vision and foveal architecture5. As a result ophthalmological screening is an essential consideration for any patient on HCQ therapy.
In view of the updated scientific data available on toxicity prevalence and the benefits of screening, the American Academy of Ophthalmology (AAO) have updated their screening recommendations for 20166. This includes baseline fundus examination to rule out pre-existing maculopathy and annual screening after 5 years of treatment.
Objectives: To investigate compliance with the AAO Recommendation on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016)6 in a regional rheumatology centre.
Methods: A retrospective analysis was undertaken of the electronic patient records of 161 patients with a diagnosis of connective tissue disease at a single regional centre assessing level of antimalarial usage, adherence to screening guidelines and level of documented toxicity.
Results: Of our cohort, 91 (56%) were on regular HCQ. Of these, 12 had received routine ophthalmology screening and 4 developed documented ocular toxicity. 15 suffered non-ophthalmic toxicity requiring therapy cessation. 46 had been on therapy greater than 5 years and of these 9 (21.5%) had been screened.
Conclusions: Our analysis revealed significant deficiencies in routine screening and demonstrated a high level of toxicity in patients who were routinely screened. This indicates that there may be a significant number of patients with toxicity that is not being picked up and reinforces the importance of screening. We would recommend a more streamlined referral pathway for rheumatology patients on HCQ and hypothesise that this would lead to greater and earlier pick-up of ocular toxicity in this population, ultimately reducing morbidity in this population.
References:
[1] Elman A, Gullberg R Nilsson E, et al. Chloroquine retinopathy in patients with rheumatoid arthritis. Scand J Rheumatol. 1976;5(3):161–66.
[2] Melles RB, Marmor MF. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. JAMA Ophthalmol 2014;132:1453–60.
[3] Levy GD, Munz SJ, Paschal J, et al. Incidence of hydroxychloroquine retinopathy in a large multicentered outpatient practice. Arthritis Rheum. 1997 Aug;40(8):1482–6.
[4] Marmor MF, Hu J. Effect of disease stage on progression of hydroxychloroquine retinopathy. JAMA Ophthalmol 2014;132:1105–12.
[5] Marmor MF, Hu J. Effect of disease stage on progression of hydroxychloroquine retinopathy. JAMA Ophthalmic 2014;132:1105–12.
[6] Michael F, Marmor MD et al, Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision) Ophthalmology Volume 123, Number 6, June 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6547

SAT0258 SYNERGETIC B-CELL IMMUNOMODULATION WITH RITUXIMAB AND BELIMUMAB IS CLINICALLY EFFECTIVE IN SEVERE AND REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS – THE SYNBIOSE PROOF-OF-CONCEPT STUDY

T. Kraaij[1], S.W. Kamerling[1], E. de Rooij[1], P.L. van Daele[2], I. Bajema[3], O.W. Bredewold[1], T.W. Huizinga[4], T.J. Rabelink[1], C. van Kooten[1], Y.K. Teng[1]. *[1]Nephrology, LUMC, Leiden; [2]Immunology, Erasmus MC, Rotterdam; [3]Pathology; [4]Rheumatology, LUMC, Leiden, Netherlands*

Background: The pathogenesis of systemic lupus erythematosus (SLE) is characterized by B-cell hyperactivity leading to autoreactive plasma cells (PCs) that produce pathogenic autoantibodies and contribute to onset and maintenance of SLE. Therefore, novel treatment strategies in SLE are aimed at targeting autoreactive PCs. Rituximab (RTX) is used as off-label treatment in SLE and depletes CD20+ B-cells effectively, but is unable to deplete CD20- PCs. Belimumab (BLM), an anti-BAFF (B-cell activating factor) antibody, demonstrated efficacy in SLE as add-on therapy and resulted in reduction of B-cells and PCs.
Objectives: Because RTX+BLM has potential to target autoreactive PCs, we designed an open-label, proof-of-concept study to assess the clinical efficacy and safety of RTX+BLM in severe, refractory SLE patients.
Methods: A phase 2 proof-of-concept study, the SynBioSe study, was set up to treat severe, serologically active and refractory SLE patients with RTX following BLM. The following endpoints were assessed at 24 weeks: a) clinical efficacy by SLEDAI; b) immunological effects on B-cells and PCs by high sensitivity flow cytometry, immunoglobulins and autoantibody levels, and c) safety parameters.
Results: The study included 11 severe, refractory SLE patients of which 10 had lupus nephritis and 1 patient had neuropsychiatric lupus with a median SLEDAI of 18 [range 8–29]. Treatment with RTX+BLM led to clinically significant improvement to a median SLEDAI score of 2 [0–13] (p=0.002). Low disease activity (SLEDAI $<$4) was achieved in 80%. Clinical response was achieved while tapering steroids from a median dose of 60 [0–60] to 7.5 mg [0–12.5] and concomitant mycophenolate (MMF) was tapered to zero in all patients. With respect to safety, 23 adverse events (AEs) were reported of which none were serious AEs, 8 mild infections and 2 hypogammaglobulinemia. Complement usage was restored in all patients with a median increase in C3 of 33% [range 8–133] and in C4 levels of 39% [9–266]. RTX+BLM led to reduction of anti-dsDNA antibodies, from median 120 IU/ml [18–505] to 35 IU/ml [10–374] (p=0.012). CD19+ B-cells were depleted throughout the complete follow up (from median $206*10^6$ cells/L [range $21*10^6$-$511x10^6$] at screening to $5x10^6$ [0–$24x10^6$] at 24 weeks, p=0.004), including transitional B-cells (from median $1.3x10^3$ cells/L [1–$1.3x10^4$] at screening to 98.5 [0–$3.4x10^3$] at 24 weeks, p=NS). Importantly, total immunoglobulin levels only declined temporarily. The latter was further corroborated by transient reductions in CD3-CD38brCD27brCD20- PCs from median $1.6x10^6$ cells/L [$5.6x10^3$–$1.1x10^7$] to $1.5x10^5$ cells/L [$5.3x10^4$–$1.3x10^7$] at 12 weeks (p=NS). At 24 weeks, these PCs were restored to baseline levels ($1.4x10^6$ cells/L [$9.2x10^4$–$3x10^7$]).
Conclusions: This is the first study to demonstrate that RTX+BLM effectively reduced disease activity in severe, refractory SLE without raising major safety issues, while reducing other immunosuppressant drugs. Autoreactive PCs were specifically targeted by RTX+BLM. Therefore, combination therapy of RTX+BLM is a promising strategy in severe SLE.
Trial registration:ClinicalTrials.gov NCT02284984
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2364

SAT0259 HIGH PLASMA CONCENTRATION OF MYCOPHENOLATE ACID IN EARLY PHASE OF INDUCTION THERAPY PREDICTS GOOD RENAL OUTCOME IN LUPUS NEPHRITIS CLASS III OR IV

T. Kiyokawa, H. Hanaoka, H. Iida, K. Ishimori, Y. Takakuwa, T. Okazaki, S. Ozaki.
Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

Background: Mychophenolate mofetil (MMF) is recommended as initial induction treatment for most cases of lupus nephritis (LN) class III-IV. Although the association between area under the concentration-versus-time curve (AUC) of myochophenolate acid (MPA) and therapeutic efficacy has been well shown in renal transplantation, it has been poorly investigated in LN. Furthermore, MMF interacts with multiple factors and its concentration may be decreased by high prednisolone (PSL) dose, low serum albumin level and low creatinine clearance. Since these factors dramatically change in induction phase of LN, the plasma concentration of MPA may also change by fixed dose of MMF administration. Here, we measured AUC_{0-12} of MPA at different phases of induction treatment, early and middle, and prospectively investigated which concentration predicted future renal response in LN class III-IV.
Objectives: To investigate the relationship between the plasma concentration of MPA in early or middle phase of induction therapy and future renal response.
Methods: We prospectively enrolled patients with biopsy proven LN class III or IV who hospitalized from Apr to Oct 2016. As induction therapy, PSL was started at dose of 1mg/kg/day and tapered to 10mg/day by 12 weeks. Fixed dose of MMF at 2,000mg/day was continuously introduced. We measured 2 points of MPA plasma concentration depending on the phase of induction therapy, at early (week 2) and middle (week 12). We evaluated the association between these concentration and complete renal response (CR) rate at week 12.
Results: Six patients were enrolled. AUC_{0-12} between the early and the middle phase was not correlated (R^2=0.17, p=0.7), but that of the early phase tended to be lower (47.4±25.6 vs 58.9±19.1 mgh/L). All the patients with high AUC_{0-12} (over 40mgh/L) at the early phase achieved CR at week 12 (Figure 1). But we could not find any association between AUC_{0-12} at middle phase and CR rate at week 12.

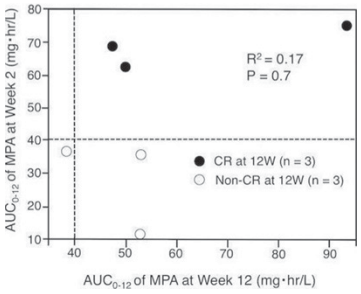


Figure 1

Conclusions: High AUC_{0-12} of MPA at the early phase of induction therapy might predict good renal response.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4622

SAT0260 OVARIAN FUNCTION PRESERVATION WITH GONADOTROPIN-RELEASING HORMONE ANALOGUES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH CYCLOPHOSPHAMIDE

V.A. Pacucci[1], F. Ceccarelli[1], G. Perrone[2], I. Zannini[2], M. Candelieri[2], I. Leccese[1], C. Perricone[1], F. Miranda[1], S. Truglia[1], F.R. Spinelli[1], C. Alessandri[1], G. Valesini[1], F. Conti[1]. *[1]Lupus Clinic, Rheumatology, Dipartimento di Medicina Interna e Specialità Mediche; [2]Gynecology, Dipartimento di Scienze Ginecologico-Ostetriche e Scienze Urologiche, Policlinico Umberto I Sapienza University of Rome, rome, Italy*

Background: The fertility in childbearing Systemic Lupus Erythematosus (SLE) patients can be impaired due to several conditions. In particular, treatment with alkylating agents, as cyclophosphamide (CYC), could determine menstrual irregularities and premature ovarian failure (POF). Gonadotropin-releasing hormone analogues (GnRH-a) is one of the preventive strategy suggested by the recently published EULAR recommendations (1). They are characterized by good safety profile and effectiveness in reducing POF rate in patients with malignancies and autoimmune diseases. So far, only few studies have been published focusing on the use of GnRH-a to prevent POF in SLE women receiving CYC treatment.
Objectives: In the present case-control study, we aimed at evaluating the efficacy of GnRH-a on the ovarian function preservation in SLE patients treated with CYC.
Methods: We enrolled consecutive SLE patients, fulfilled the 1997 ACR revised criteria treated with CYC in the period between 2005 and 2012, receiving GnRH-a (GnRH-a+). As control, SLE patients treated with CYC not receiving GnRH-a (GnRH-a-) were assessed. Clinical and laboratory data were collected in a standardized, computerized and electronically filled form. Ovarian function was assessed by the evaluation of FSH and estradiol level (E2). GnRH-a (triptorelin 3.75 mg/monthly intramuscularly) was prescribed. SLE patients treated with CYC were followed after the treatment every six months during the first year and then annually.
Results: Thirty-tree SLE patients treated by CYC were evaluated in the present analysis: 75.7% of patients were treated for lupus nephritis. Among [FC1] these, 18 GnRH-a+ (mean±SD age 29.3±7.6 years; mean±SD disease duration 7.2±4.2 years) and 15 GnRH-a- (mean±SD age 31.0±10.5 years; mean±SD disease duration 6.3±7.4 years). The mean±SD SLEDAI-2K score in GnRH-a+ patients was 10.1±3.7, in GnRH-a- patients 8.3±3.3 (p=NS). Moreover, no differences were identified concerning the duration of CYC treatment (GnRH-a+: 6.1±2.8 months *versus* GnRH-a- 6.1±2.2 months, p=NS) and follow-up (GnRH-a+: 8.11±2.2 years versus GnRH-a- 9.3±7.2 years, p=NS). The prevalence of POF was significantly higher in GnRH-a- (5 patients, 33.3%) in comparison with GnRH-a+ (2 patients, 11.1%, P=0.0002). A significantly higher mean age at the time of CYC treatment was observed in patients developing POF (37.7±5.9 years) in comparison with those not developing this complication (28.0±8.5 years, p=0.008). Moreover, the use of GnRH-a seems to be protective also in terms of menstrual cycle regularity: the cycle remained regular during treatment in 83.3% of GnRH-a+ and only in 33.3% of GnRH-a- (p=0.003). During the follow-up, 3 patients in the GnRH-a+ group underwent pregnancy, with a good outcome.
Conclusions: The results of the present study showed the protective role of GnRH-a for the preservation of ovarian function in SLE patients treated by CYC. Furthermore, the age resulted the only risk factor associated with POF development.
References:
[1] Andreoli L. et al. Ann Rheum Dis. 2016 Jul 25.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6381

SAT0261 REFRACTORY SYSTEMIC LUPUS ERYTHEMATOSUS IS MAINLY ASSOCIATED WITH THE DECREASED NUMBER OF REGULATORY T CELLS AND LOW-DOSE IL-2 COMBINED WITH RAPAMYCIN CAN EFFICIENTLY RECOVERY THE BALANCE OF TH17/REGULATORY T CELLS

X. Jing[1], X. Liu[1], J. Wang[1], Y. Qiao[1], Z. Liang[1], M. Hao[1], J. Chen[1], C. Gao[2], X. Li[1]. *[1]Department of Rheumatology, The Second Hospital of Shanxi Medical University, Taiyuan, China; [2]Department of Pathology, Joint Program in Transfusion Medicine, Brigham and Women's Hospital/Children's Hospital Boston, Harvard Medical School, Boston, United States*

Background: Refractory system lupus erythematosus (SLE) still relies on aggressive treatment with high-dose glucocorticoids and immunosuppressive agents,but a significant proportion of patients persist with activity or relapse and show serious side-effects by the treatment.However, the imbalance of Th17 cells and regulatory T (Treg) cells in peripheral blood of patients with SLE may be an important factor in the pathogenesis of SLE.Because low-dose IL-2 can selectively enhance Treg function while avoiding the activation of effector T cells and rapamycin can promote the proliferation of Treg cells[1–2],the combination of the low-dose IL-2 and rapamycin has been considered to treat refractory SLE for the purpose of remission.
Objectives: To observe the effect of low-dose IL-2 combined with rapamycin on the balance of Th17/Treg cells in patients with refractory SLE.
Methods: Eighty-two refractory SLE patients (80 women and 2 men),with a mean duration of 72.41±37.52 months and mean age of 36.22±12.48 years, were enrolled.They are in line with the standard of ACR in 1997,who are treated with glucocorticoid and immunosuppressant for more than one year, but the subjects continues to rise to a peak.After the eligible patients are given IL-2 and rapamycin in combination therapy with conventional therapy at 0, 6, 12, 24 week respectively after medication.The clinical symptoms, blood routine, urine routine, ESR, Th17 cells, Treg cells, Th17/Treg cells and the dosage of corticosteroids and immunosuppressant are registered one by one.
Results: At 24 week after treatment,28.9% patients with refractory SLE were relieved.Low-dose IL-2 combined with rapamycin leaded to an increase in the absolute counts of Treg cells in refractory SLE patients,from a median of 12.98 cells/ul (at week 0) to 22.1 cells/ul (at week 24) (P=0.002).The ratio of Th17/Treg cells shows a reduction from a median of 0.44 at week 0 to 0.29 at week 24 (P=0.029).No significant difference was observed in the absolute counts of Th17 after combined treatment.At week 24, the mean dosage of prednisone which refractory SLE patients were receiving decreased from 17.20 mg/d to 8.87 mg/d.And the categories of DMARDs use were also reduced ($P<0.05$).
Conclusions: Our results suggest that refractory SLE is major associated with the decreased number of Treg but not that of Th17.The Th17 and Treg cells in the peripheral blood of patients with refractory SLE tends to balance due to the significantly increase the number of Treg cells after low-dose IL-2 combined with rapamycin treatment.Low-dose IL-2 combined with rapamycin treatment can reduce the dosage of glucocorticoid and DMARDs.
References:
[1] Liao, W.,Lin, J. X. & Leonard,W. J.Interleukin-2 at the crossroads of effector responses,tolerance,and immunotherapy.Immunity 38,13–25 (2013).
[2] Tomasoni R, Basso V, Pilipow K, etal.Rapamycin-sensitive signals control RCR/CD28-driven Ifng,I14and Foxp3 transcription and promoter region methylation.Eur J Immunol,2011,41:2086–2096.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4552

SATURDAY, 17 JUNE 2017

SLE, Sjögren's and APS - clinical aspects (other than treatment)

SAT0262 BCL2-ASSOCIATED ATHANOGENE 3 PROTEIN IS ASSOCIATED WITH B-CELL HYPERACTIVITY INCLUDING LYMPHOMA IN PRIMARY SJÖGREN'S SYNDROME

A. Alunno[1], F. Carubbi[2,3], A. Falco[4], O. Bistoni[1], V. Valentini[1], G. Cafaro[1], R. Giacomelli[2], M. Pascale[4], R. Gerli[1]. *[1]Department of Medicine, Rheumatology Unit, University of Perugia, Perugia; [2]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila; [3]Department of Medicine, ASL 1 Avezzano-L'Aquila-Sulmona, L'Aquila; [4]Department of Pharmacy, University of Salerno, Salerno, Italy*

Background: Bcl2-associated athanogene 3 (BAG-3) is a co-chaperone protein that interacts with the ATPase domain on heat-shock protein 70. BAG-3 is involved is several biologic processes including apoptosis, cytoskeleton organization and autophagy and, therefore, it has been extensively investigated in the field of tumorigenesis (1). In particular, BAG-3 expression is constitutive in human primary tumors including leukemias and lymphomas and it is induced in different normal cell types, including leukocytes, by a variety of stimuli. BAG-3 is able to induce and maintain cell proliferation, resistance to therapy and cell motility, namely metastatization. On this basis, a role of BAG-3 in chronic inflammatory diseases may be postulated, but data on this topic are not available.
Objectives: The purpose of our study was to investigate the expression of BAG-3 in primary Sjogren's syndrome (pSS) and the relationship with clinical and serological features.
Methods: BAG-3 concentration was assessed in the serum of 103 patients with pSS according to the 2002 American-European classification criteria and in 40 sex and age matched healthy donors (HD). Clinical and serological records were collected and statistical analysis was performed with SPSS 21.0.
Results: Twenty-six pSS patients were positive for BAG-3 (BAG-3+), with serum levels ranging from 32.1 to 950 pg/ml. When setting the cut-off value according to the highest value found in HD (300 pg/ml), we identified 13 pSS patients displaying a peculiar clinical serological phenotype. In detail, in this subgroup of pSS patients the prevalence of purpura, low C4, both anti-Ro and anti-La autontibodies, rheumatoid factor and lymphoma was higher, when compared to pSS patients with BAG-3 levels $<$300 pg/ml or BAG-3- (all $p<0.05$). Furthermore, they displayed less frequently sicca symptoms such as xerostomia and xerophtalmia (both $p<0.05$). Binary logistic regression analysis revealed that pSS patients with BAG-3 levels $>$300 pg/ml had on odds ratio (OR) of 12 (95% CI 1.9–86, p=0.009) for lymphoma and this association was independent of the presence of purpura, a well know marker of lymphoma in pSS. When including low complement, another feature associated with lymphoma, in the multivariable analysis, both low C4 and BAG-3 levels $>$300 pg/ml resulted independently associated to lymphoma (OR=24 and 12.4 respectively).
Conclusions: Our study assessed for the first time serum BAG-3 levels in a large cohort of pSS patients. The results showed that the highest levels of BAG-3 identify a peculiar clinical and serological pSS phenotype, as consequence of a B-cell hyperactivity. Since it is known that BAG-3 is an anti-apoptotic protein playing a pivotal role in cell survival, and that B-cell hyperactivity in pSS is the consequence of coordinated and integrated actions of several stimuli and appropriate cytokines, our results may suggest that BAG-3 overexpression is involved in B-cell proliferation and activity, as well as in oligoclonal and monoclonal expansion in pSS.
References:
[1] Rosati A et al. Cell Death Dis 2011;2:e141.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3587

SAT0263 NEOPLASIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN SPAIN: RELESSER REGISTRY DATA

A. Urruticoechea-Arana[1], I. Rua-Figueroa[2], M.A. Martín-Martínez[3], F. Alonso[4], J. López-Longo[5], M. Galindo-Izquierdo[6], A. Olivé[7], J. Calvo[8], A. Fernández-Nebro[9], J.M. Pego-Reigosa[10] on behalf of Group of relesSER. *[1]Rheumatology, Can Misses Hospital, Ibiza; [2]Rheumatology, Doctor Negrín Hospital, Las Palmas de GC; [3]Rheumatology, Research Unit of the Spanish Society of Rheumatology; [4]Research Unit, Spanish Society of Rheumatology; [5]Rheumatology, Gregorio Marañón Hospital; [6]Research Unit, 12 de Octubre Hospital; [7]Rheumatology, Germans Trias and Pujol hospital, Madrid; [8]Rheumatology, Araba Hospital, Vitoria; [9]Rheumatology, Regional of Málaga Hospital, Málaga; [10]Rheumatology, Meixoeiro of Vigo. "Institute of Sanitary Research South Galicia (IISGS)", Vigo, Spain*

Background: There is limited evidence on the risk of neoplasia in autoimmune diseases such as systemic lupus erythematosus.
Objectives: The objective of this study is to analyze the incidence of cancer in the Spanish population with SLE and the factors associated in its development: RelesSER Registry Data.
Methods: We calculated the incidence density of malignant neoplasms, the standardized incidence ratio and the average time to develop the first neoplasm after diagnosis of SLE in patients of the SLE registry of the Spanish Rheumatology Society (RelesSER) fulfilling ACR97 criteria. We carried out a bivariate analysis of the associated factors to neoplasms and multivariate by logistic regression.
Results: A total of 3607 patients (90.4% female) were included. We registered 140 neoplasms in women (4.3%) and 14 in men (4%) ($p<0.821$). Incidence density 7.3/1000 patient-years (95% CI:4.85–10.98) (7.39 in patient-years women and 6.93 in men) without significant differences. After stratification by gender and age, cancer appeared in 3.2% of the women aged under 45 versus 3.8% of the men; 4.1% of women aged 45–65 years versus 5.9% of men and a 5.3% of women 65 and older versus 2.5% of men the same age. The standardized incidence ratio (SIR) was 2.16; 1.51 in men and 2.38 in women, highest for women under 65 years old. The SIR for $>$65 years was 0.98; 0.59 in men and 1.55 in women.
The average time until de development of the first malignant neoplasm was 10 years (RI:5.75–17.00), being lower in women [9.5 (RI: 5.00–17.0) years] than in men [12.5 (8.75–17.5)] and in patients under 45 years versus over 45 years [8.0 (RI: 5.00–16.00)].
Malignant neoplasms were the cause of death in 10% of the patients (15/154), predominantly hematological and breast cancers, both at 19% followed by lung cancer in 14.3%.
Factors associated to malignant neoplasms in the bivariate analysis are shown in (table 1). No immunosuppressive therapy was associated with the development of neoplasms. In the multivariate model, adjusted for age and time of disease duration, age was the only significant variable (OR:1.030; 95% CI: 1.003–1.059; p=0.029) with a trend for ACE inhibitors use (OR:1.866; 95% CI: 0.808–4.306; p=0.144), SLEDAI (last visit) (OR: 0.904; 95% CI: 0.806–1.015; p=0.089, SLICC/ACR DI) (without neoplasias) (OR: 1.160; 95% CI: 0.961- 1.401; p=0.123), and duration of the disease in months (OR: 1.003; 95% CI: 1.000–1.006; p=0.068).

Table 1

	Cáncer	Control	*p*
Gender, men %	4	96	0.821
Gender, women %	4.3	95.7	0.821
Mean age at first criterion, years (DS)	38.35 (16.01)	32.72(14.29)	<0.001
Diagnostic age SLE, years (DS)	40.37 (15.68)	34.75 (14.46)	<0.001
Age at last evaluation, years, mean (DS)	57.74 (14.38)	46.17 (14.58)	<0.001
Disease duration (months), mean (DS)	208.71 (102.95)	140.1 (99.69)	<0.001
Follow-up in Rheumatology (months), mean (DS)	170. 1 (90.75)	118.12 (86.90)	<0.001
Sjogren´s syndrome, %	20.5	14.1	0.029
SLEDAI, median [p25-p75]	1.00 [0.00-3.25]	2.0 [0.00-4.00]	0.026
KATZ, median [p25-p75]	3 [2-4]	2 [1-3]	0.001
SLICC*, median [p25-p75]	1.00 [0.00-3.00]	0.00 [0.00-1.00]	<0.001
CHARLSON*, median [p25-p75]	3 [2.00-4.00]	1 [1.00-3.00]	<0.001
Time on antimalarals (months) median [p25-p75]	78.00 (27.75-136.50)	60.00 (24.00-119.00)	0.099

Conclusions: The incidence of neoplasia in Spanish women with SLE is higher than expected for age and gender. Malignant neoplasms were the cause of death in 10% of the patients, predominating hematological and breast cancers followed by lung cancer.
Acknowledgements: The RelesSER registry has been supported by the FIS (ISCIII) - European Regional Development Fund (FEDER), fellowship PI11/02857. It has also been partially funded by: GSK, UCB, Roche and Novartis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4474

SAT0264 VALVULOPATHY AND PULMONARY HYPERTENSION IN A SERIES OF PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

A. Robles, M.J. Núñez, E. Rodríguez-Castellano, C. Busca, J.J. Ríos, A. Noblejas, F. Arnalich, E. Martínez. *Internal Medicine, Hospital Universitario la Paz, Madrid, Spain*

Objectives: To evaluate the prevalence of cardiac valvular involvement and

pulmonary arterial hypertension (PAH) and predictive risk factors in a cohort of patients with antiphospholipid antibodies.
Methods: We included 232 patients from our cohort who underwent an echocardiogram. A total of 84 (36%) patients with primary antiphospholipid syndrome (PFS), 47 (20%) with APS secondary to systemic lupus erythematosus (SLE), 47 (20%) patients with antiphospholipid antibodies 23%) with SLE without AAF.
The determinations of AAF and lupus anticoagulant were performed according to the indications of the international thrombosis society.
Statistical analysis was performed with SPSS 18; using the Chi square test and the Fisher exact test.
Results: In patients with AAF, the echocardiogram was pathological in 88 patients (52%) (p=0.023). Valvular affectation was evidenced in 64 (38%) (p=0.005) and PAH in 16 (p = ns). Seventeen patients (35%), SAF (48%), SAFS (26%), AIF silent (14%) and 9 patients in the non-AAF group (12%) presented with valvular affectation (p=0.002). PAH presented 19 patients, 9 with SAFP (47%), 6 in the SAFS group (32%), 1 in the silent AAF group (5%) and 3 in the non-AAF group (16%) (p=). Both PAH and valvular involvement were asymptomatic in most cases, although two patients required valvular replacement. The most frequently affected valve in all groups was mitral valve (84%), except in patients with PAH where the most prevalent valvular pathology was tricuspid insufficiency. Patients with valvulopathy and APS had a higher prevalence of total thrombosis than SAF without valvulopathy (p=0.05). Patients with valvulopathy also significantly increased stroke and thrombocytopenia (p=0.04). Patients with valvulopathy had lupus anticoagulant more frequently (p=0.04), with no difference for the rest of AAF.
Conclusions: Subclinical valvular involvement is very common in patients with AAF. Every patient with AAA should be given an echocardiogram in the initial protocol of their study in order to rule out both significant valvulopathy and PAH that can modify the management of the condition.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2548

SAT0265 CLINICAL CHARACTERISTICS OF SYSTEMIC LUPUS ERYTHREMATOSUS IN AN EGYPTIAN POPULATION: A RETROSPECTIVE COHORT

B. Medhat[1], T. El Hadidi[2], K. El Hadidi[1], A. Yousri[1], D. Hassan[1], F. Talaat[1], L. Maged[1], M. Shabaan[3], M. Eissa[1], N. Hamdy El Gobashy[1], N. Sobhy[1], N. Abd El Baki[1], R. El Refai[1], S. Ghoneim[1], W. AbdRahman[1]. *[1]Rheumatology and Rehabilitation, Faculty of Medicine-Cairo University; [2]Rheumatology and Rehabilitation, Armed forced hospital; [3]Rheumatology and Rehabilitation, Helwan hospital, Cairo, Egypt*

Background: Systemic lupus erythrematosus (SLE) is an autoimmune disease with a myriad of manifestations, that could vary among different ethnic and racial groups.
Objectives: To study the prevalence of various manifestations of SLE in an Egyptian population.
Methods: Information in this study was derived from the medical records of SLE patients who followed up in a private clinic in Cairo from January 1980 to June 2016.
Results: This descriptive retrospective case series included 1109 juvenile (19.4%) and adult (80.6%) patients, of which 114 (10.3%) were males and 995 were females (89.7%). Age of onset showed a mean of 26±11.19 years, and the mean of disease duration was 48.78±58.46 months (median: 26 years). The most common manifestations were synovitis (76.7%), malar rash (48.5%), leukopenia (45.7%), and photosensitivity (45.6%). At least one of the antiphospholipid antibodies was present in 41.8% of the patients tested for APL (636 patients). However thromboembolic manifestations and/or recurrent fetal loss occured in 11.5% of the patients. Neuropsychiatric manifestations were evident only in 6.4% of the patients, with seizures being the most common neuropsychiatric manifestation, present in 4% of the patients. 33.1% of the patients had nephritis, which followed the onset of the disease by a mean duration of 20±21.3 months (median=12 months). There were gender differences in the disease characteristics. Cutaneous vasculitis, nephritis, and hypocomplementemia were statistically higher in males (p=0.012, p=0.01, and p=0.041 respectively). Whereas, synovitis, and alopecia were statistically higher in females (p=0.012 and p=0.006 respectively). Patients with juvenile onset had a statisticaly higher frequency of nephritis (0=0.01), seizures (p=0.012) haemolytic anemia (p=0.001), and hypocomplementinemia (p=0.02).
Conclusions: Synovitis and malar rash were the most common manifestations in our study. Secondary antiphospholipid was present in 11.5% of the patients. Male patients and juvenile patients showed a tendency towards a more severe disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2151

SAT0266 EFFECT OF THE METABOLIC SYNDROME ON ORGAN DAMAGE AND MORTALITY IN CHINESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL ANALYSIS

C.C. Mok, S.M. Tse, L.Y. Ho. *Medicine, Tuen Mun Hospital, HK, Hong Kong*

Objectives: To study the effect of the metabolic syndrome (MetS) on organ damage and mortality in patients with SLE.
Methods: Consecutive patients who fulfilled ≥4 ACR criteria for SLE and were assessed for the presence of the MetS between 2010 and 2011 were included. Those patients who did not have MetS assessment or succumbed before 2010 were excluded. The MetS was defined by the updated joint consensus criteria, using the Asian criteria for central obesity, when ≥3 of the following components were present: (1) Increased waist circumference to ≥90cm in men or ≥80cm in women; (2) Elevated blood pressure to ≥130/85mmHg or requiring drug therapy; (3) Elevated serum triglyceride level to ≥1.7mmol/L; (4) Reduced serum high density lipoprotein (HDL)-cholesterol to ≤1.0mmol/L in men and ≤1.3mmol/L in women; and (5) Elevated fasting glucose level to ≥5.6mmol/L. Longitudinal data regarding new organ damage, vascular events and mortality on follow-up were retrieved from our cohort database. The association of the MetS with new organ damage and mortality was studied by logistic regression analyses.
Results: 577 SLE patients were studied (93% women; age at entry 41.2±13.4 years; SLE duration 9.3±7.2 years). The mean follow-up time of the patients since entry was 66.3±1.8 months. The mean body mass index (BMI) of the patients was 22.3±3.9kg/m^2 (11% >27kg/m^2). A total of 85 (14.7%) patients qualified the MetS (28% fulfilling waist; 20% fulfilling blood pressure; 25% fulfilling triglyceride; 33% fulfilling HDL and 9.2% fulfilling glucose criteria). New organ damage and vascular (coronary, cerebrovascular and peripheral vascular) events developed in 128 (22%) and 23 (4.0%) patients, respectively. The most common new arterial events were stroke (50%), acute coronary syndrome (33%) and peripheral vascular disease (17%). Thirty-nine (6.8%) patients died (infection 36%; vascular causes 18%; cancer 15%; lung fibrosis 8%; suicide 3%). Patients with the MetS (N=85), when compared to those without (N=492), had significantly higher SDI accrual at their last clinic visits (0.70±1.0 vs 0.26±0.6; p<0.001). Regarding individual systems, the increase in SDI scores in the ocular, renal, cardiovascular, musculoskeletal and endocrine (new diabetes mellitus) systems were significantly higher in the MetS group of patients. New vascular events (11% vs 2.8%; p=0.001), all-cause mortality (14% vs 5.5%; p=0.003), death due to vascular complications (7.1% vs 0.2%; p<0.001) were significantly more common in patients with MetS than those without. Logistic regression revealed that the MetS was significantly associated with new damage in the ocular (OR 2.77 [1.05–7.34]; p=0.04, renal (OR 4.72 [1.86–12.0]; p=0.001), cardiovascular (OR 3.66 [1.03–12.9]; p=0.04] and endocrine system (OR 41.9 [4.93–357]; p=0.001), adjusted for age, sex, SLE duration and the antiphospholipid antibodies (IgG-anticardiolipin or the lupus anticoagulant). The presence of the MetS increased the risk of new vascular events (OR 2.94 [1.18–7.31]; p=0.02), all-cause mortality (OR 1.60 [0.73–3.47]; p=0.24) and vascular mortality (OR 30.3 [3.42–268]; p=0.002) after adjustment for the same covariates.
Conclusions: In this 5-year longitudinal study, the MetS is significantly associated with new organ damage, vascular events and mortality in patients with SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3939

SAT0267 SERUM 25-HYDROXYVITAMIN D3 LEVELS AND FLARES OF SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL COHORT ANALYSIS

C.C. Mok[1], R. Singh[2], L.Y. Ho[1], P. Jannetto[2]. *[1]Medicine, Tuen Mun Hospital, HK, Hong Kong; [2]Laboratory Medicine and Pathology, Mayo Clinic, Rochester, United States*

Objectives: To study the relationship between serum 25-hydroxyvitamin D3 levels and flares of systemic lupus erythematosus (SLE) in a longitudinal cohort of Chinese patients.
Methods: Patients who fulfilled ≥4 of the ACR criteria for SLE were recruited from our rheumatology out-patient clinics in November 2011. Blood was taken at 10 AM and was assayed for the serum levels of 25-hydroxyvitamin D3 by liquid chromatography tandem mass spectrometry (LC-MS/MS). Patients were stratified according to the 25-hydroxyvitamin D3 levels; group 1 (<15ng/ml, deficiency); group 2 (15–30ng/ml, insufficiency); and group 3 (>30ng/ml, adequate); and were followed longitudinally every 2–4 months for serial assessment of disease activity (by SELENA-SLEDAI) and the occurrence of mild/moderate or severe SLE flares (by SELENA flare instrument). Comparison was made among these groups in the baseline and mean summated SLEDAI over time (area under the curve), and the annual incidence of mild/moderate and severe flares by the one-way ANOVA test.
Results: 276 SLE patients were studied (94% women; age 41.0±13.8 years; SLE duration 8.7±6.6 years). 25 (9.1%) patients had eGFR ≤60ml/min. The proportion of patients with 25-hydroxyvitamin D3 levels of <15, 15–30, >30ng/ml was 26%, 54% and 20%, respectively. Patients with vitamin D deficiency (group 1) were significantly younger, had lower body mass index (BMI) but higher baseline eGFR and SLEDAI scores when compared with the other groups. No significant differences in the clinical manifestations were observed among the three groups of patients except for lower prevalence of facial rash in group 3 (p=0.02). After a mean follow-up of 32.5±5.5 months, 153 mild flares and 91 severe flares developed in our patients. The mean summated SLEDAI score over time was: 3.2±2.0 (group 1); 2.4±1.9 (group 2); and 2.7±2.1 (group 3), respectively (p=0.02). The annual incidence of mild/moderate and severe flares was: 0.26±0.39 and 0.20±0.45 (group 1); 0.20±0.33 and 0.09±0.22 (group 2); and 0.20±0.32 and 0.14±0.46 (group 3), respectively (p=NS in all). In a subgroup of 73 patients who did not have clinical or serological SLE activity at baseline (SLEDAI=0), a similar

but non-significant trend of higher annual rates of mild/moderate and severe flares over time was also observed in patients with vitamin D deficiency. At the last visit, 27 (10%) patients had new damage scores; 5 patients had new vascular events; and 4 patients had new onset diabetes mellitus. There were no significant differences among the three groups of patients with regard to the incidence of new damage or vascular events over time.

Conclusions: Vitamin D insufficiency and deficiency was frequent in our cohort of SLE patients. Patients with vitamin D deficiency were associated with higher baseline and mean disease activity scores, as well as a tendency of more severe lupus flares over time.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3945

SAT0268 CLINICAL PRESENTATION OF NASAL INVOLVEMENT IN PRIMARY SJÖGREN'S SYNDROME: A MULTIDISCIPLINARY TEAM APPROACH TO A NEGLECTED AND DISABLING CONDITION

C. Baldini[1], V. Seccia[2], E. Elefante[1], M. Scarano[2], L. Cristofani[2], F. Ferro[1], N. Luciano[1], M. Mosca[1]. *[1]Clinical and Experimental Medicine, Rheumatology Unit, University of Pisa; [2]Otorhinolaryngology Unit, University of Pisa, Pisa, Italy*

Background: Dry nose is reported quite frequently by patients affected by primary Sjögren's syndrome (pSS) in daily practice. However, a clear definition of nasal involvement in pSS is not available.

Objectives: a) to explore clinical presentation of nasal involvement in pSS analyzing key symptoms, objective findings at the inspection of the external and inner nose and nasal cytology b) to investigate any associations/correlation between nasal involvement and other clinical-serological disease manifestations c) to assess the overall impact of nasal involvement on patients reported outcomes (PROs).

Methods: Consecutive pSS patients (AECG 2002) were seen by a team of rheumatologists and ENT specialists. In addition to a standard rheumatologic evaluation, all the patients underwent a complete ENT evaluation. Nasal symptoms (i.e dry nose, nasal stuffiness, crusting, hyposmia) were collected by an "ad hoc questionnaire" and scored by the patients on visual analogique scales. Inspection of the external and inner nose, endoscopy of the nasal cavity and nasal cytology were performed as well. Allergy testing were also carried out when indicated. The following tools were used to assess PROs: ESSPRI, SF-36 and SNOT-22.

Results: Forty-six pSS patients were included in the study [M:F =45:1; median age (IQR):64 (53–70); median disease duration (IQR): 66 months (24–120)]. Nasal symptoms ranged from: dryness in the nose (56.5%), crusting 10/46 (21.7%), nasal stuffiness 20/46 (45.5%) and hyposmia 7/46 (15.2%). Thirteen patients did not present signs of nasal involvement, whereas 21 patients (45.7%) presented rhinitis sicca (RS), 6 (13%) allergic rhinitis (AR), 4 (8.7%) chronic rhinosinusitis (CRS) and 2 (4.3%) non-allergic rhinitis (NAR). Patients with nasal involvement were more frequently seronegative (p=0.04) and presented significantly higher SNOT-22 scores (p=0.008) when compared to patients without nasal involvement; no additional demographic or clinical differences between the two groups. Allergy testing were more frequently positive in patients with RS and AR. Nasal cytology showed that the rates of the cells (eosinophils and neutrophils) in patients without nasal involvement were negligible whereas they were significantly increasead in pSS patients with RS and AR. The SNOT-22 (r=-.433, p=0.02) and the scores assigned to the VAS of nasal dryness (r=-.755, p=0.003) and crusting (r=-.794, p=0.001) strongly correlated with SF-36 questionnaire. SNOT-22 also correlated with the ESSPRI (r=.399, p=0.04), whereas we did not find a correlation between VAS scores assigned to nasal dryness and VAS scores of oral and ocular dryness. PROs related to nasal symptoms were significantly influenced by a concomitant diagnosis of fibromyalgia.

Conclusions: Rhinitis sicca was the most common clinical presentation of nasal involvement in pSS patients, especially in seronegative patients. Apparently, nasal symptoms correlated weakly with ocular and oral dryness. PROs exploring nasal symptoms revealed that nasal involvement impact significantly on patients quality of life.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4349

SAT0269 RDW LEVELS ARE ASSOCIATED WITH DAMAGE ACCRUAL IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

C. Reategui-Sokolova[1], M. Ugarte-Gil[1], R. Gamboa-Cárdenas[1], F. Zevallos[1], J. Cucho-Venegas[1], J. Alfaro-Lozano[1], M. Medina[1], Z. Rodríguez-Bellido[1], C. Pastor-Asurza[1], G. Alarcón[2], R. Perich-Campos[1]. *[1]Rheumatology, Hospital Guillermo Almenara Irigoyen, Lima, Peru; [2]School of Medicine, The University of Alabama, Birmingham, United States*

Background: Systemic Lupus Erythematosus (SLE) patients show higher Red blood cells Distribution Width (RDW) regardless of anaemia status[1]. RDW has been found to positively correlate with serum IgM, CRP, ESR, and SLE Disease Activity Index 2000 (SLEDAI-2K), and glucocorticoid treatment decreased both SLEDAI-2K and RDW[2].

Objectives: To determine whether RDW levels in SLE are associated with damage accrual.

Methods: This cross-sectional study was conducted in 276 SLE patients, 257 females and 19 males. Evaluations included interview, medical records review, physical examination and laboratory tests. Disease activity was measured with the SLEDAI. Damage accrual was ascertained with the SLICC/ACR damage index (SDI). Univariable and multivariable Poisson regression models were performed to determine if RDW levels were associated with damage accrual. These models were stratified by tertiles of RDW. The multivariable model was adjusted for variables known to be associated with this outcome [age at diagnosis, gender, socioeconomic status, ethnicity, tobacco use, disease duration, SLEDAI, anemia, antimalarials and immunosuppressive drugs use, average daily dose and time of exposure to prednisone (PDN)].

Results: The patients mean (SD) age at diagnosis was 34.38 (13.33) years; nearly all patients were mestizo. Disease duration was 7.04 (6.16) years. The SLEDAI was 5.24 (4.67) and the SDI 0.92 (1.28). The average daily dose of PDN was 6.90 (6.07) mg/d and the time of exposure to PDN was 6.58 (9.59) years. RDW levels were 14.57 (1.52)%. Hemoglobin levels were 12.4 (1.7) g/dl. We divided the RDW levels into tertiles with cut points in 13.8 and 14.0; the highest tertiles were associated with disease damage; with a Rate Ratio (RR) 1.57 (1.07–2.28; p: 0.020 for the highest tertile, and 1.67 (1.15–2.42; p: 0.007) for the medium tertile.

Conclusions: Higher RDW levels are associated with damage accrual in SLE patients independent of other well-known risk factors for such occurrence.

References:

[1] Vayá A, Alis R, Hernández J-L, et al. RDW in patients with systemic lupus erythematosus. Influence of anaemia and inflammatory markers. Clin Hemorheol Microcirc 2013; 54: 333–9.

[2] Hu Z-D, Chen Y, Zhang L, et al. Red blood cell distribution width is a potential index to assess the disease activity of systemic lupus erythematosus. Clin Chim Acta 2013; 425: 202–205.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6368

SAT0270 ULTRASONOGRAPHY OF MAJOR SALIVARY GLANDS IN JUVENILE SJÖGREN'S SYNDROME – PRELIMINARY FINDINGS IN A MULTI-CENTER STUDY

D.S. Hammenfors[1], V. Valim[2], B. Bica[3], S.G. Pasoto[4], V. Lilleby[5], J.C. Nieto-González[6], C.A. Silva[7], E. Mossel[8], R.M. Pereira[9], H. Bootsma[10], J.G. Brun[11], R. Jonsson[12], M.V. Jonsson[13]. *[1]Department of Rheumatology, Haukeland university hospital, Bergen, Norway; [2]Department of Rheumatology/Medical Clinic, Federal University of Espírito Santo, Vitoria; [3]Department of Rheumatology, Federal University of Rio de Janeiro, Rio de Janeiro; [4]Sjögren's syndrome outpatient/Hospital das Clinicas HCFMUSP, University of São Paulo, São Paulo, Brazil; [5]Department of Rheumatology, Oslo University Hospital, Oslo, Norway; [6]Department of Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [7]Department of Pediatric Rheumatology, Federal University of São Paulo, São Paulo, Brazil; [8]Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen, Netherlands; [9]Rheumatology Division - School of Medicine, University of São Paulo, São Paulo, Brazil; [10]Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, University of Groningen, Groningen, Netherlands; [11]Department of Clinical Science – Section for Rheumatology; [12]Broegelmann Research Laboratory, Department of Clinical Science; [13]Department of Clinical Dentistry – Section for Oral and Maxillofacial Radiology, University of Bergen, Bergen, Norway*

Background: Juvenile Sjögren's syndrome (jSS) is a rare, poorly defined and possibly underdiagnosed condition. There is little information on the use of major salivary gland ultrasonography (SGUS) in this patient-group.

Objectives: To characterize symptoms and clinical findings of jSS and to investigate SGUS as a diagnostic tool.

Methods: Sixty-four patients were recruited from Brazil (n=40), Norway (n=11), the Netherlands (n=8) and Spain (n=5). All patients had disease onset at the age of 18 or younger. Clinical examination and sialometry was performed in 60/64 patients. Additional clinical information was obtained from the medical records and through patient interview. SGUS of the parotid and submandibular glands was performed in all patients using linear high-frequency transducers (6–15 MHz), by an expert in SGUS. Glandular homogeneity and presence of hypoechogenic areas were evaluated and glands characterized as normal or SS-like.

Results: The female:male ratio was 6:1. Mean age at diagnosis was 12.1 years (range 4–18), with first symptoms occurring at 10.3 years (range 1–17). Time from onset of symptoms until diagnosis was 1.6 years (range -2–8 years). Subjective oral and ocular symptoms were reported in 70% and 64% patients, respectively. Reduced secretion of tears was detected in 41% patients, and hyposalivation in 31% patients. Minor salivary gland lip biopsy had been performed and focus score determined in 34 patients; 28 biopsies (82%) had focus score $\geq$1. Serologically, 92% were positive for ANA, 73% were anti-Ro/SSA+, 38% were anti-La/SSB+, and 41% were RF+. Salivary gland enlargement had been experienced by 53% of the patients; one patient had also experienced lacrimal gland enlargement. Systemic manifestations at some time-point, was registered in 66% of the patients. Systemic treatment at inclusion was registered in 67% of the patients; previous systemic treatment was registered in 83%. Diagnostic criteria for primary Sjögren's syndrome (pSS) was fulfilled by 34/64 patients (53%) and 39/64 patients (61%),

AECG criteria and ACR/EULAR criteria, respectively. SGUS revealed SS-like changes in 37/64 patients (59%); interestingly, SS-like findings were observed in 22/23 patients in the European cohort, compared to 15/40 patients in the Brazilian cohort.

Conclusions: Common symptoms and findings in jSS include dry mouth, systemic manifestations and salivary gland enlargement, followed by reduced tear secretion and hyposalivation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5804

SAT0271 IS THERE A NEED TO INCLUDE SEROLOGICAL PATTERN TO PREDICT DAMAGE IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: DIAPS APPLICATION

D. Mazilu[1], D. Potarniche[2], I. Saulescu[1], A. Borangiu[1], L. Groseanu[1], C. Constantinescu[1], V. Vlad[2], D. Opris[3], A. Balanescu[1], D. Predeteanu[1], R. Ionescu[1]. *[1]"Sfanta Maria" Clinical Hospital, "Carol Davila" University of Medicine; [2]"Sfanta Maria" Clinical Hospital; [3]"Sfanta Maria" Clinical Hospital, "Carol Davila" Univeristy of Medicine, Bucharest, Romania*

Background: Antiphospholipid syndrome (APS) is an autoimmune disease defined as the presence of antiphospholipid antibodies (aPL), at least a clinical thrombotic event and is associated with an important risk of organ damage. The new index proposed, Damage Index in patients with Thrombotic Antiphospholipid Syndrome (DIAPS) may be an useful tool to estimate cumulative damage in patients with primary and secondary APS. It includes 38 clinical items expanded to show the complexity of clinical manifestations in APS patients.

Objectives: The aim of this study is to analyze the serological pattern as potential predictive factor for an increased DIAPS.

Methods: All consecutive patients known with APS according to the Sapporo and/or Sydney classification criteria were included in our monocentric cohort. Data on medical history, clinical manifestations, aPL profile and medication were collected. DIAPS score was used to measure damage in each patient. The relationship between aPL profile and DIAPS score was analysed.

Results: Seventy six patients with APS were included: 11 patients with primary APS, 65 patients with secondary APS. Their mean disease duration was 9.59±7.39years. The most frequent clinical manifestation from DIAPS was the peripheral vascular (deep vein thrombosis, intermittent claudication, tissue loss, vascular venous insufficiency) found in 61.8% of patients, followed by the neuropsychiatric manifestations (46.1%). The mean DIAPS score in our cohort was 4.25±3.51, not significantly different between patients with primary vs secondary APS (4.72 vs 4.16, p=0.629). Lupus anticoagulant (LA) was found in 25 patiens (32.9%), anti cardiolipin antibodies (aCL) in 49 patients (64.5%) and antibodies to β2-glycoprotein I (β2GPI) in 23 patients (30.3%). There were 36 patients known with a single positive aPL (47.4%), 27 patients (35.5%)with 2 positive aPL and only 2 patients with triple positivity. There were no significant differences regarding antibody profile between patients with primary and secondary APS. Higher values of DIAPS were seen in patients with β2GPI (p=0.042) and with positivity for 2 aPL (p=0.003). DIAPS value correlated to the presence of β 2GPI (p=0.042, R=0.233) and to positivity for two aPL (p=0.003, R=0.341).

Conclusions: Our study suggests that double positivity for aPL, especially the presence of β2GPI confers an increased value of DIAPS in patients with primary and secondary APS.

References:

[1] M-C Amigo et al. Development and initial validation of a damage index (DIAPS) in patients with thrombotic antiphospholipid syndrome (APS). Lupus (2015) 24, 927–934.

[2] LM Amezcua-Guerra. Improving definitions for an index of cumulative organ damage in patients with the antiphospholipid syndrome (DIAPS). Lupus (2016) 25, 671–672.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4105

SAT0272 LACK OF ASSOCIATION OF GLUCOCORTICOID EXPOSURE AND METABOLIC SYNDROME IN SLE

D. Apostolopoulos, A. Hoi, E. Morand. *Monash Health, Melbourne, Australia*

Background: The Metabolic Syndrome (MetS) is a disorder of energy utilisation and storage, associated with an increased risk of cardiovascular (CV) disease. MetS may contribute to the increased CV disease in SLE, but the prevalence, cause, and impact of MetS in SLE is poorly understood, as are the effects of glucocorticoid (GC) exposure.

Objectives: To characterise the prevalence of the features of MetS in a well-characterised cohort of SLE patients, and determine the effect of GC use on these parameters.

Methods: SLE patients studied as part of a single centre prospective longitudinal cohort. Disease activity (SLEDAI-2K), treatment and laboratory details were recorded at each visit. Other investigation results were collected from institution databases. MetS defined as ≥3 criteria[1]: BMI >30kg/m^2; triglycerides>1.7mmol/L; HDL-cholesterol <1.3mmol/L; blood pressure >130/85mmHg or treatment for hypertension; fasting glucose >5.6mmol/L or treatment for hyperglycaemia. Continuous variables were described as median (IQR), and compared using Kruskal-Wallis tests. Categorical variables were described as frequency and compared using Chi-squared tests.

Results:

	Total (289)	GC exposed (211)	GC not –exposed (78)	p-value
BMI >30kg/m^2	50 (17%)	33 (24%)	17 (22%)	0.22
éTriglycerides	80 (28%)	69 (33%)	11 (14%)	0.002
êHDL-cholesterol	95 (33%)	73 (35%)	22 (28%)	0.33
é Fasting glucose	32 (11%)	24 (11%)	8 (10%)	1.00
Hypertension	137 (47%)	110 (52%)	27 (35%)	0.01
Metabolic Syndrome	*49 (17%)*	*36 (17%)*	*13 (17%)*	*1.00*

289 patients were included (87% female; 51% Caucasian, 29% Asian), and median age at enrolment of 37.7y. Median follow-up was 3.43y (med 15 visits). Time adjusted-mean SLEDAI (AMS) over the study period was 3.67. 81% (211) patients received GC (time-adjusted mean 4.25mg prednisolone/d) and AMS was significantly higher in GC-exposed patients (4.19 vs 1.97 [EM1], p<0.01). MetS criteria were met by 49 (17%) of patients (Table 1). Hypertriglyceridaemia and hypertension were significantly more frequent in GC-treated patients, but the prevalence of obesity and other MetS domains, or MetS overall, were not. There were significantly more patients with MetS score =0 in the GC-exposed subset (43/78 vs 76/211 p<0.01).

The prevalence of obesity of 17% is lower than in the general population. There was no significant change in BMI across the period of observation and surprisingly, no association between GC exposure and change in BMI.

Conclusions: The prevalence of MetS in SLE was lower than previously reported in other, smaller, lupus cohorts [2,3]. This study suggests GC exposure was associated with hypertriglyceridaemia and hypertension in SLE. Potential negative effects of active disease on MetS domains require further investigation.

References:

[1] Alberti KGMM, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood; AHA; WHF; International Atherosclerosis Society; International Association for the Study of Obesity. Circ 2009;120(16):1640–45.

[2] Parker B, Ahmad Y, Shelmerdine J, et al. An analysis of the metabolic syndrome phenotype in systemic lupus erythematosus. Lupus 2011;20(14):1459–65.

[3] Chung CP, Avalos I, Oeser A, et al. High prevalence of the metabolic syndrome in patients with systemic lupus erythematosus: association with disease characteristics and cardiovascular risk factors. ARD 2007;66(2):208–14.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6764

SAT0273 FACTORS RELATED TO ALEXITHYMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS

D.P.E. Margiotta, F. Basta, M. Vadacca, G. Dolcini, M. Lo Vullo, A. Rigon, A. Afeltra. *Unit of Allergology, Immunology and Rheumatology, Università Campus Bio-Medico di Roma, Rome, Italy, Rome, Italy*

Background: Several evidences described a considerable prevalence of alexithymia among patients with chronic diseases, such as systemic autoimmune diseases. In patients affected by Systemic Lupus Erythematosus (SLE), alexithymia seems to be related to mood disorders and personality.

Objectives: In this study we evaluated alexithymia in relation to HR-QoL (Health related Quality of Life) and to factor associated to HR-QoL, such as mood disorders, fatigue, work ability, sleep quality and physical activity.

Methods: We consecutively enrolled SLE patients and healthy controls in a cross sectional study with a retrospective design. We wvaluated alexithymia by the Toronto Alexithymia Scale 20 (TAS-20). AHR-QoL was expressed by MOS-SF-36. Mood disorders was assessed by BDI and HAM-H. Fatigue was evaluated by Facit-Fatigue. Physical activity was quantified using International Physical Activity Questionnaire (IPAQ) and the sleep quality using the Pittsburgh Sleep Quality Index (PSQI). Work ability was assessed by Work Productivity and Activity Impairment (WPAI). Cognitive impairment was defined according to MOCA screening test.

Results: Fifty-two SLE patients and 50 age-matched healthy subjects were enrolled in the study. Mean TAS-20 score was significantly higher in SLE compared to controls (p<0.01). Alexithymic patients presented increased values of BDI score and HAM-H score (p<0.01 and p<0.05) and reduced Facit-Fatigue score (p<0.05). We found increased values of Work missed due to health problems and Activity impairment in alexithymic SLE subjects (p<0.05). SF-36 summary components PCS and MCS and SF-36 individual components did not significantly differ between alexithymic and non-alexithymic SLE. A greater proportion of alexithymic SLE patients presented fibromyalgia (p<0.05), low scholastic education (p<0.01), cognitive impairment according to MOCA test (p<0.01) and mild-to-severe depression according to BDI (p<0.01). We did not find differences among alexithymic and non alexithymic in MeS, obesity and physical inactivity prevalence. TAS-20 values positively correlated with BDI score (p<0.001), HAM-H score (p<0.01) and activity impairment score (p<0.01) and negatively with Facit-Fatigue score (p<0.01). In multiple linear regression,

predictors of TAS-20 values were to be fibromyalgic and to have mild-to-severe depression according to BDI. In multiple logistic regression, alexithymia was significantly associated to BDI score (OR 1.2, 95% CI 1.0–1.4) and inversely associated to cognitive impairment (OR 0.1, 95% CI 0.02–0.8).
Conclusions: SLE patients frequently present alexithymic tract. Alexithymia seems to be associated neither to disease feature, to disease course (activity and damage) and to SLE therapy, nor to HR-QoL expressed by SF-36. Nevertheless, alexithymia could be tightly related to QoL-associated factors as depression and fibromyalgia
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6679

SAT0274 URINARY VITAMIN D-BINDING PROTEIN AS A BIOMARKER FOR LUPUS NEPHRITIS

D.J. Go[1,2], J.Y. Lee[2], M.J. Kang[2], I.A. Choi[3], E.Y. Lee[1], E.B. Lee[1], E. Yi[2], Y.W. Song[1,2]. *[1]Department of Internal Medicine, Seoul National University Hospital; [2]Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Medicine, Medical Research Institute, Seoul National University, Seoul; [3]Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, Korea, Republic Of*

Background: Lupus nephritis (LN) is a major complication of systemic lupus erythematosus (SLE). However, conventional biomarkers for assessing renal disease activity are imperfect in predicting clinical outcomes associated with LN.
Objectives: The aim of this study is to identify urinary protein biomarkers that reliably reflect the disease activity or predict clinical outcomes.
Methods: A quantitative proteomic analysis, using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS), was performed to identify protein biomarker candidates that can differentiate between SLE patients with and without LN. Selected biomarker candidates were further verified using urine samples from a larger cohort of SLE patients (n=121) by enzyme-linked immunosorbent assay (ELISA) to investigate their predictive values for LN activity measure. Furthermore, association between urinary level of selected panel of potential biomarkers and prognosis of LN was assessed with a 4-year follow-up study of renal outcomes.
Results: From proteomic assay, vitamin D binding protein (VDBP), transthyretin (TTR), retinol binding protein 4 (RBP4) and prostaglandin D synthase (PTGDS) were selected as candidates for quantification. These proteins were significantly elevated in SLE patients with LN, especially in patients with active LN (n=21). Among them, VDBP well correlated with severity of proteinuria (rho =0.661, $P<0.001$) and renal SLE disease activity index (renal SLEDAI) (rho =0.520, $P<0.001$). In the 4-year follow-up, VDBP was a significant risk factor (hazard ratio 9.627, 95% CI 1.698 to 54.571, P=0.011) for the development of proteinuric flare (randum urine protein/creatinine ratio >1.0) in SLE patients without proteinuria (random urine protein/creatinine ratio <0.5) (n=100) after adjustments of multiple confounders.
Conclusions: Urinary VDBP correlated with proteinuria and renal SLEDAI, and predicted the development of proteinuria.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4356

SAT0275 COMPARISON OF CLINICAL AND SEROLOGICAL DIFFERENCES ACCORDING TO THE AUTOANTIBODY CLUSTER IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE KOREAN LUPUS NETWORK (KORNET) REGISTRY

D.-J. Park, J.-H. Kang, J.-E. Kim, K.-E. Lee, S.-S. Lee. *Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic Of*

Objectives: Individual autoantibodies are associated with the clinical features in patients with systemic lupus erythematosus (SLE). However, few studies have investigated differences in disease presentation based on autoantibody profiles in Asian patients with SLE. This study evaluated autoantibody clusters and compared the clinical and serological presentation and clinical outcome in Korean SLE patients.
Methods: The Korean Lupus Network (KORNET) is a nationwide multicenter, hospital-based registry, set up to prospectively assess outcomes in Korean SLE patients. Of the 505 SLE patients enrolled in the KORNET registry from July 2014 to November 2015, the study group comprised 339 consecutive female SLE patients. Seven autoantibodies (anti-dsDNA, anti-Sm, anti-RNP, anti-Ro, anti-La, lupus anticoagulant (LAC), and anti-cardiolipin antibody [aCL]) were selected for cluster analysis using the K-means cluster analysis procedure.
Results: Three distinct autoantibody clusters were identified: cluster 1, anti-dsDNA and anti-Ro; cluster 2, anti-RNP; and cluster 3, anti-RNP, anti-Ro, and anti-La. Compared with patients in clusters 2 (n=99) and 3 (n=85), patients in cluster 1 (n=155) had a shorter symptom duration before SLE diagnosis and higher incidence of biopsy-proven lupus nephritis. Patients in cluster 3 had a higher incidence of discoid rash, central nervous system involvement, lupus pancreatitis, pulmonary arterial hypertension, Raynaud's phenomenon, and premature gonadal failure. In addition, patients in cluster 3 had the lowest proportion of mean prednisolone >7.5 mg/day in the medication history.
Conclusions: Autoantibody clusters were associated with the clinical features in women with SLE. Clustering autoantibodies could be a valuable approach for differentiating between various clinical subsets of SLE, and may help to guide prediction of the subsequent clinical course and organ damage in these patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2361

SAT0276 EYE TOXICITY IN PATIENTS WITH SYSTEMIC LUPUS ERITHEMATOSUS TREATED WITH ANTIMALARICS IN DOMINICAN REPUBLIC

E. Rodríguez-Bautista[1], Y. Cruz-Rojas[1], I. Mercedes-Núñez[1], E. Tejada-Reyes[1], N. Abreu-Arbaje[2], M. Arbaje-Khoury[2], V. Rosario[1], R. Munoz-Louis[1], R. Peña-Blanco[3], T. Valdez-Lorie[3], R. Alba-Fériz[1]. *[1]Rheumatology, Hospital Docente Padre Billini; [2]Ophthalmology, Centro de Oftalmología y Glaucoma; [3]Rheumatology, Hospital Docente Universitario Francisco Moscoso Puello, Santo Domingo, Dominican Republic*

Background: Antimalarics are derivatives of quinine indicated in the treatment of autoimmune inflammatory diseases. The mechanism of antimalarial toxicity is unclear. It is hypothesized that toxicity is a result of drug binding to retinal pigmentary epithelium, damaging photoreceptors resulting in vision loss. Early retinal toxicity is asymptomatic with subtle alterations in foveal pigmentation generally not evident at routine ophthalmologic examination, progressively producing classic "bull's-eye" maculopathy, manifested as a decrease in central, color and night vision, and central scotoma. To prevent the sequelae of antimalarial use, sensitive tools are used to detect toxic maculopathy such as: campimetry, optical coherence tomography (OCT) and eye fundus.
Objectives: To evaluate ocular toxicity in patients with systemic lupus erythematosus treated with antimalarics.
Methods: Multicenter cross-sectional study, two rheumatology departments clinical records were analyzed from January 2016 to January 2017, with diagnosis of systemic lupus erythematosus according to ACR 1997 criteria, with $\geq$4 years using antimalarial drugs. 298 patients were identified, 93 of them fulfilled inclusion criteria, and were evaluated by two retinologists performing OCT on each patient. Accumulated antimalarial doses were calculated and all variables were analyzed with SPSS software V.22.
Results: 97.8% were females, the mean age was 37.4±13 years, 78.5% of the patients used 4mg/kg of chloroquine (CQ) versus 21.5% took 6mg/kg of hydroxychloroquine (HCQ), the mean use duration was 5.1±2 years, 19.4% of patients had retinal pigment epithelium (RPE) changes suggesting maculopathy, of which, 15% used CQ versus 4.35% with HCQ, 54.50% using CQ had a cumulative dose of 365 grams, 10.75% with HCQ had cumulative doses of 292 grams, and the mean for the cumulative dose of both antimalarials was 485 grams.
Conclusions: Previous studies have shown that the antimalarial toxicity rate are between 7.5%>13.1%, in our population we observed that our patients had a higher toxicity rate associated with the use of CQ compared to HCQ, and no association was found relevant with other variables. We understand that both, patients and physicians who manage this drug, should be educated about the need to maintain an adequate ophthalmologic control, due to the progression of retinopathy from 1 to 3 years after discontinuation of treatment. It is necessary to carry out prospective studies with a greater number of patients.
References:
[1] Block, J.A. (1998) Hydroxychloroquine and retinal safety. The Lancet 351(9105), 771–771.
[2] Battagliotti, C., Gentiletti, A., Pons-Estel, B. Lupus Eritematoso Sistémico, Aspectos Clínicos y Terapéuticos. 1°. Edición, 42, 515–531.
[3] Rosenbaum, J.T., Mount, G.R., et al. (2016). Avoiding Antimalarial Toxicity.Arthritis & Rheumatology.
[4] Marmor MF, Melles RB. Hydroxychloroquine and the retina. JAMA 2015;313:847–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4142

SAT0277 COGNITIVE DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN DOMINICAN REPUBLIC

E. Tejada-Reyes[1], I. Mercedes-Nuñez[1], Y. Cruz-Rojas[1], E. Rodríguez–Bautista[1], K. Polanco-Soriano[2], M. Perdomo-Ramirez[2], V. Rosario[1], R. Muñoz-Louis[1], R. Peña-Blanco[3], T. Valdez-Lorie[3], R. Alba-Fériz[1]. *[1]Rheumatology; [2]Psychology, Hospital Docente Padre Billini; [3]Rheumatology, Hospital Docente Universitario Dr. Francisco E. Moscoso Puello, Santo Domingo, Dominican Republic*

Background: Cognitive dysfunction (CD) is a deficit of cognitive faculties including attention, memory, language, executive function and visuospatial processing. CD is the most frequent neuropsychiatric manifestation of SLE (55–80%) 1 and this is 3 times higher in patients with Systemic Lupus Erythematosus (SLE) than in healthy subjects.2 This is not routinely evaluated because it requires a lot of time. Brief and simple questionnaires are needed to identify CD.
A study carried out by D'Amico et al. evaluated 21 SLE patients and all of them had CD.3 Pedraza et al. analyzed the MMSE score and Montreal Cognitive

Assessment (MOCA) and concluded that MOCA performs much better than MMSE for cognitive impairment correct diagnosis.4

Objectives: To determine the prevalence of CD in SLE patients and compare MMSE and MOCA diagnosis effectiveness.

Methods: All patients with at least 18 years old that met ACR/EULAR 2012 SLE classification criteria were included. Patients with associated comorbidity, not SLE related, that could alter cognitive functions, were excluded. 55 patients that fulfilled the inclusion criteria were admitted to Hospital Docente Padre Billini's rheumatology department from March to April 2016. After obtaining written consent, the psychology department applied both tests, MMSE and MOCA. A standardized form registered demographic variables. Data was analyzed using Microsoft Excel 2013.

Results: 94.5% of the patients were women, 53% were between 31–45 years old, 52.7% were mulatto ethnic, 34.5% had at least a high school degree, 27.2% were diagnosed 1 year before enrollment, 60% had a low activity score using SLEDAI (<4), hypertension was the most common comorbidity with a 38.1%, 90.9% were taking corticoids, 80% were on antimalarial drugs (6 abandoned treatment, 2 by eye involvement, 1 allergic reaction, 2 were diagnosed with SLE the interview day), the most frequent neuropsychiatric symptom ever presented was convulsion (7.2%). Using MMSE 25.4% of the patients showed CD, however after adjusting the results according to the educational level, the percentage increased to 41.8%. MOCA classified that 67.2% of the patients had CD, of which 13 patients were MMSS positive, and finally, 22 classified after the score adjustment.

Conclusions: MOCA is more effective than MMSE to detect CD. Nonetheless the MMSE should be considered as an option for patients with low levels of education.

References:

[1] Nasswetter, G. Tratado de reumatología. AKADIA. 2014. Page 323.
[2] Díaz-Cortés, D. Correa-González, N. Díaz, M. et al. Compromiso del sistema nervioso central en el lupus eritematoso sistémico. Rev colomb reumatol. 2015; 22 (1): 16–30.
[3] D'Amico et al. Estudio multicéntrico de deterioro cognitivo en lupus eritematoso sistémico: ECLES. Rev Arg Reumatol. 2015; 26 (2): 28–32.
[4] Pedraza L.O. Sánchez, E. Plata, S. Montalvo, C. et al. Puntuaciones del MOCA y el MMSE en pacientes con deterioro cognitivo leve y demencia en una clínica de memoria en Bogotá. Acta Neurol Colomb. (Bog) 2014.

Acknowledgements:.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4279

SAT0278 INCREASED FREQUENCY OF NAILFOLD VIDEOCAPILLAROSCOPY ABNORMALITIES IN PRIMARY ANTIPHOSPOLIPID (PAPS) PATIENTS

E. Martin-Nares, G. Hernandez-Molina, P. Bermudez-Bermejo, V. Zamora-Legoff, T.S. Rodriguez-Reyna. *Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico*

Background: Primary antiphospholipid syndrome (PAPS) is characterized by venous and arterial thrombosis, obstetric morbidity and the presence of antiphospholipid antibodies. The utility of nailfold videocapillaroscopy in conditions such as scleroderma (SSc) and primary Raynaud's phenomenon is well known. Whether patients with PAPS have specific findings in nailfold videocapillaroscopy is not well stablished.

Objectives: To evaluate findings on nailfold videocapillaroscopy in patients with PAPS and their association with clinical and serological features.

Methods: We prospectively included 26 PAPS patients according to the modified Sidney criteria and the Alarcón-Segovia criteria for haematologic antiphospholipid syndrome, who regularly attend a tertiary referral center in Mexico City, and 15 healthy controls. We performed nailfold videocapillaroscopy according to the Cutolo technique (Optilia 200x) and obtained: capillary morphology, nonspecific abnormalities (tortuosity, crossed and dilated capillaries, capillary haemorrhages, neo-angiogenesis) and mean vascular density on 32 images per patient. We collected demographic, clinical (thrombosis, obstetric morbidity, non-criteria manifestations and comorbidities), serological (anticardiolipin antibodies, anti-β2 glycoprotein 1 antibodies and lupus anticoagulant) and treatment information. Analysis was performed used SSPS v.22, Chi square test was used to compare frequencies and Student's t test was used to compare means.

Results: PAPS patients had higher frequency of at least 1 abnormal finding on videocapillaroscopy (77% vs 12%, p<0.009, OR=23, 95% CI=4–132), higher frequency of enlarged capillaries (69% vs 0%, p=0.0001, OR=33, 95% CI=3.8–295), lower frequency of "perfect normal" pattern (11.5% vs 56%, p=0.004, OR=0.1, 95% CI=0.02–0.48) than controls, and 8 patients (31%) showed changes compatible with the "early" SSc Cutolo pattern (<4 dilated capillaries/mm, <4 haemorrhages/mm, preserved architecture and no avascular areas). In PAPS patients, capillary haemorrhages were associated to neurologic manifestations (75% vs 14%, p=0.02, OR=19, 95% CI=1.4–248) and to comorbidity with hypertension (75% vs 14%, p=0.02, OR=19, 95% CI=1.4–248).

Conclusions: PAPS patients frequently show at least one abnormality on videocapillaroscopy. The most frequent abnormalities are enlarged capillaries, microhaemorrhages and the presence of an "atypical normal" pattern. Capillary haemorrages are frequently found in patients with neurologic involvement of PAPS. The coexistence of hypertension or other comorbidities may contribute to the development of capillary abnormalities in PAPS patients.

References:

[1] Cutolo M, Pizzorni C, Tuccio M et al. Rheumatology 2004;43:719–726.
[2] Ingegnoli F, Gualtierotti R Lubatti C, et al. Microvasc Res 2013; 90:90–95.
[3] Vaz JL, Dancour MA, Bottio DA et al. Rheumatology 2004;43:1025–7.

Acknowledgements: We wish to thank the Mexican College of Rheumatology for their support in the acquisition of the equipment used to perform this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5663

SAT0279 ANTI-RO52 KDA AND ANTI-RO60 KDA ANALYSIS IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS TO DETECT ANTI-RO FALSE-NEGATIVES

E. Grau Garcia[1], I. Chalmeta Verdejo[1], E. Labrador Sánchez[1], M. Fernandez Matilla[2], F.M. Ortiz-Sanjuan[1], C.M. Feced Olmos[1], N. Fernandez-Llanio[2], K. Arévalo Ruales[1], R. Negueroles Albuixech[1], J. Ivorra Cortes[1], J.J. Fragio Gil[1], I. Martínez Cordellat[1], R. González Mazarío[1], L. Gonzalez Puig[1], C. Alcañiz Escandell[1], C. Nájera Herranz[1], I. Cánovas Olmos[1], E. Vicens Bernabeu[1], J.E. Oller Rodriguez[1], J.A. Castellano Cuesta[2], V. Fornés Ferrer[3], D. Hervás Marín[3], D. Gimenez Romero[4], J.A. Román Ivorra[1]. *[1]Rheumatology Department, HUP la Fe; [2]Rheumatology Section, Hospital Arnau de Vilanova; [3]Biostatistics Unit, IIS la Fe; [4]Physical-Chemistry Department, UV, Valencia, Spain*

Background: Systemic lupus erythematous (SLE) is an autoimmune disease characterized by immune system disruption with autoantibodies production. One of the upregulated autoantibodies is the specific to the Ro antigen, a ribonucleoprotein associated to a small RNA, constituted by the 52KDa and 60 KDa polypeptides, whose epitopes are mainly conformational. The routine detection method for anti-Ro is an enzyme immunoassay, however, is possible to obtain false-negatives for anti-Ro and this could be avoided by analyzing both subunits separately.

Objectives: To identify false-negatives for anti-Ro by analyzing both 52KDa and 60 KDa subunits separately, as well as to characterize if there are clinical or molecular differences in this subgroup of patients compared to anti-Ro negative cases.

Methods: A cross-sectional, observational study of patients diagnosed of SLE according to SLICC 2012 criteria was performed. In these patients a complete blood-test was made, and clinical data by personal interview was collected. INF1A, Anti-Ro, anti-Ro52KDa and anti-Ro60KDa levels where measured by colorimetric methods. Biostatistical analysis was performed with R 3.3.2.

Results: We selected 69 SLE patients with negative results for anti-Ro (2.34±4.17 U/mL) out of 142 total SLE patients. A total of 51 patients were negative for both anti-Ro subunits and 18 cases presented positive results (up to 20 pg/mL) for at least one of them. The subgroup of patients that exhibit simultaneously high levels of anti-Ro52KDa and anti-Ro60KDa have higher clinical activity compared to negative anti-Ro cases (75% of active patients against 41.2% in anti-Ro negative patients). However, no differences in the accumulated damage evaluated by SLICC score between negative anti-Ro cases and patients with at least one positive subunit were observed. We analyze serum levels of INF1A cytokine in the four groups of patients, and anti-Ro and subunits negative cases showed significant lower INF1A levels than the other patients (8.26±14.87 pg/mL and 26.62±40.71 pg/mL respectively; P=0.04). In addition, patients with high levels of anti-Ro52KDa subunit are those with the highest INF1A levels (anti-Ro 52+/anti-Ro60- 23.5±47.6pg/mL of INF1A; anti-Ro 52+/anti-Ro60+ 36.4±37.9pg/mL of INF1A).

Conclusions: In our anti-Ro seronegative patients, a 26% of false-negative cases were detected. These cases with high levels of almost one anti-Ro subunit showed significantly higher levels of INF1A in contrast to negative cases, supporting the fact that they are indeed a different group from the negative cases. Moreover, the high INF1A levels could be the reason of the observed differences in the clinical activity measured by SLEDAI score in both groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5758

SAT0280 A TEN-YEAR SURVIVAL ANALYSIS OF FILIPINO PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT THE NATIONAL KIDNEY AND TRANSPLANT INSTITUTE (PHILIPPINES)

E.M.L. Yap, C.C. Bermudez. *Internal Medicine, National Kidney and Transplant Institute, Quezon City, Philippines*

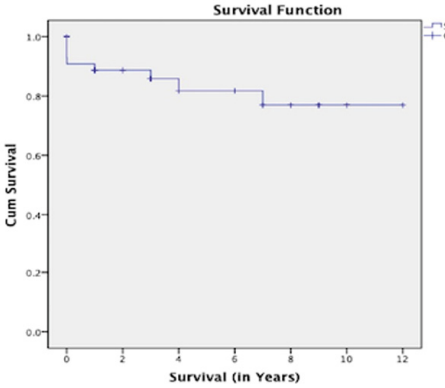
Background: Systemic lupus erythematosus (SLE) is increasingly being diagnosed in our country. Despite the increasing number of patients, there are no studies describing their clinical profile at the time of diagnosis at the National Kidney and Transplant Institute (NKTI). This study aims to describe patients' initial clinical presentations, outcomes, and their survival rate within ten years.

Objectives: To determine the ten-year survival rate and presenting clinical manifestations of Filipino patients first diagnosed with SLE at the National Kidney and Transplant Institute (NKTI)

Methods: This is a retrospective cohort study using chart review of patients first diagnosed with SLE in 2004 followed up in the next ten years.

Results: Eighty-five patients were first diagnosed with SLE wherein their average age was 28.10 years old ±12.03, 34.12% had hypertension, and 74.12% with renal involvement. The patients' cumulative 10-year survival was 75% with average survival time of 9.84 years. Moreover, biopsy- proven lupus nephritis had significantly longer survival time (mean=10.57 years, p=0.006) while those with cardiopulmonary manifestations had shorter survival (mean=0.71 years, p=0.030) as well as those on hemodialysis (mean=8.82 years, p=0.040). Lastly, eleven patients (12.94%) expired during the study period with active diseases and infections as the common causes of mortality.

Figure 1. Kaplan-Meier Curve showing the survival of patients with SLE from 2004 to 2014 ***(Mean=9.842, Median=8.625)***



Interval in years	Estimated Cumulative Survival Rate
1	87%
2	87%
3	84%
4	80%
5	80%
6	80%
7	75%
8	75%
9	75%
10	75%

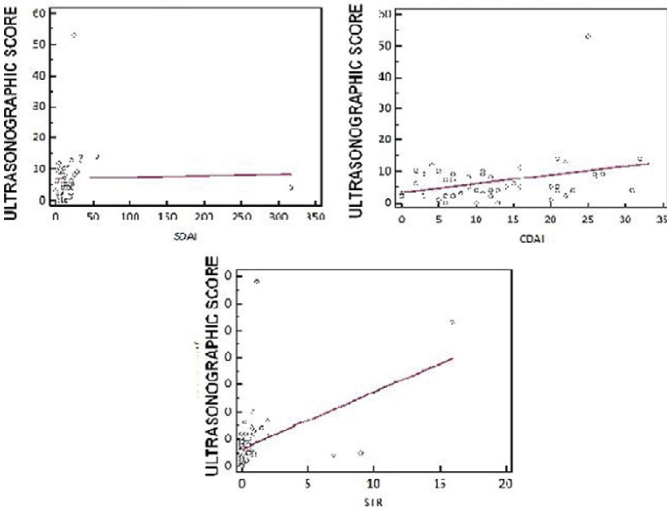
Conclusions: The 10-year survival rate of patients with systemic lupus erythematosus was 75% which was comparable to the findings from several countries. Although renal involvement was the most common initial manifestation, it did not significantly affect survival similar to prominent studies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1303

SAT0281 JOINT ACTIVITY INDICES CORRELATES WITH ULTRASONOGRAPHIC SCORE IN SLE PATIENTS WITH MUSCULO-SKELETAL INVOLVEMENT

E. Cipriano, F. Ceccarelli, C. Perricone, L. Massaro, G. Capalbo, F. Natalucci, F.R. Spinelli, F. Miranda, S. Truglia, C. Alessandri, G. Valesini, F. Conti. *Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Roma, Italy*

Background: Joint involvement represents one of the most frequent manifestations in Systemic Lupus Erythematosus (SLE) patients (incidence 69–95%), with different degrees of severity. Currently, there are no validated indices to evaluate joint involvement in SLE. Musculo-skeletal ultrasonography (US) has been widely applied in patients affected by different arthropathies. US-detected synovitis reflects the inflammatory state at the joint level, as demonstrated by the correlation with histological modifications. Furthermore, US-synovitis significantly correlated with disease activity indices, such as DAS28.
Objectives: In the present study, we aimed at assessing a correlation between the composite indices DAS28 (Disease Activity Score 28), CDAI (Clinical Disease Activity Index), SDAI (Simplified Disease Activity Index), STR (Swollen to Tender Ratio) and the US-detected synovitis in a cohort of SLE patients with joint involvement.
Methods: One hundred seven patients (M/F 7/100, mean age ±SD 48.4±13.8 years, mean disease duration ±SD 156.0±129.6 months) with at least one tender joint were enrolled. We registered the number of swollen and tender joint count (0–28) and the patient's/physician's disease activity on visual analogue scale (0–100). DAS28-ESR, CDAI, SDAI and STR were calculated. The US evaluation of 12 joints (I-V metacarpophalangeal, I-V proximal interphalangeal, wrist and knee bilateral) was performed to identify inflammatory features (synovial effusion, synovial hypertrophy and power Doppler) according with OMERACT definitions. These elementary lesions were scored according to a semi-quantitative scale (0 = absent, 1 = mild, 2 = moderate and 3 = severe). The sum of the semi-quantitative scores allows obtaining a total score of the patient's inflammatory state (0–216).
Results: As reported in Figure 1, by using the Spearman analysis, a positive correlation between US-score and SDAI (r=0.33, P=0.02), CDAI (r=0.29, P=0.03) and STR (r=0.42, P=0.0005) was identified. In particular, SLE patients with high disease activity according with STR value (>1) showed a higher US score (16.3±19.3) in comparison with moderate (7.7±4.5, P=NS) or low disease activity (7.1±7.9, P=0.02). Moreover, US score resulted significantly lower in patients with DAS28 remission compared to those with an active disease (4.5±4.4 *versus* 7.05±5.1, P=0.03; Mann-Whitney test).
Conclusions: We analyzed a large SLE cohort with articular involvement identifying a significant correlation between US scoreand the composite indices CDAI, SDAI and STR. Furthermore, US-score may be able to discriminate DAS28-remission patients. Taken together, these results suggest the ability of composite indices in detecting the joint activity in SLE patients and the possibility

Figure 1: correlation between US score and SDA, CDAI, STR



to use them in clinical practice to assess this frequent and potentially disabling manifestation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5231

SAT0282 AUTOIMMUNITY AND PREGNANCY: EVIDENCE FROM AN OBSERVATIONAL STUDY

F. Del Porto[1], S. Ferrero[2], M. Proietta[3], N. Cifani[3], M. Catoni[1], F.M. Ubaldi[2], L. Rienzi[2], L. Ferri[1], R. Di Rosa[3]. *[1]SApienza University; [2]Genera Valle Giulia, Roma; [3]SApienza University, Rome, Italy*

Background: Obstetrical APS is defined by positive aPLs and a history of one or more unexplained deaths of morphologically normal fetus at or beyond the 10th week of gestation (WG) or one or more consecutive spontaneous abortions before the 10th WG. Also one or more premature birth before 34 WG because of eclampsia, severe pre-eclampsia, or recognized features of placental insufficiency represent one of the diagnostic criteria (1). Infertility is defined as the inability of a couple practicing frequent intercourse and not using contraception to conceive a child after 12 months. Autoimmune diseases are not inclued among major causes of infertility, despite defective embryonic implantation could be considered an aspect of recurrent fetal losses in patients with positive antiphospholipid antibodies, due to their capabilities to reduce trophoblast prolipheration and growth (2).
Objectives: The aim of our study was to evaluate the prevalence of aPLs and pregnancy outcome in a population of women undergoing in vitro fertilization.
Methods: from December 2012 to December 2016, we selected 75 consecutive patients undergoing in vitro fertilization and evidence positive autoantibodies. Each of them was evaluated for genetic, anatomic, hormonal and infective causes of infertility. Moreover antinuclear antibodies (ANA), anticardiolipin antibodies (aCL), anti-β2-glycoprotein I (GP1), lupus anticoagulant (LA) and extractable nuclear antigens (ENA) profile were assessed.
Results: patients mean age was 41.38±4.87 years, ranging from 31 to 53 years. Prevalence of aPLs in our population was 68%. All women showed at least twice positive aPLs. aCL IgM and LA were the main antibody populations observed. ANA were positive in 50% of women, whereas SSA or SSB were positive in 4.17%. In 22.9% of patients a systemic autoimmune disease was newly diagnosed, mainly systemic lupus erythematosus. All patients with hystory of recurrent miscarriages and positive aPL were treated with subcutaneous low weight heparin plus daily oral acetylsalicylic acid (ASA 100 mg) (3). Full term pregnancy was obtained in 45.8% of patients.
Conclusions: Prevalence of aPLs in the general population is 1–5%, whereas in our selected series positive aPLs were detected in 68% of the patients, suggesting that prevalence of aPLs may be increased in infertile patients (4). Moreover, a systemic autoimmune disease was newly diagnosed in 22.9% of patients suggesting that paucisimptomatic disease can be underestimated. Finally we would suggest that treating autoimmune co-morbidities ameliorates implantation rates in women undergoing in vitro fertilization (5).
References:
[1] Miyakis S, Lockshin MD, Atsumi T, et al. J Thromb Haemost 2006; 4:295–306.
[2] Chinhizola CB, de Jesus GR.A. Lupus 2014; 23:1232–1238.
[3] Proietta M, Ferrero S, Del Porto F. Lupus 2014;23:724–725.
[4] AndreoliL, Bertsias GK, Agmon-Levin N et al. Ann Rheum Dis. 2016;30:133–148.
[5] Kocku A, Yavuz E, CeliK H,Bildircin D. Arch Gynecol Obstet 2012;286:1283–1289.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6425

SAT0283 ANTIBODIES TO CARBAMYLATED VIMENTIN IN PATIENTS WITH SYSTEMC LUPUS ERYTHEMATOSUS ARE ASSOCIATED WITH RENAL INVOLVENMENT

F.R. Spinelli, S. Truglia, T. Colasanti, A. Pecani, F. Ceccarelli, F. Miranda, R. Mancini, C. Perricone, M. Pendolino, C. Alessandri, G. Valesini, F. Conti.
Dipartimento di Medicina Interna e Specialità Mediche - Reumatologia, Sapienza Università di Roma, Rome, Italy

Background: Vimentin is a cytoskeleton protein of the intermediate filaments family, expressed by mesenchymal cells including vascular endothelial cells and renal tubular cells. Vimentin has been recently proposed as a target of the in situ immune response in lupus nephritis. Antibodies to vimentin have been described in 10–53% of patients with Systemic Lupus Erythematosus (SLE) and account for a fibrous pattern of cytoplasmic immunofluorescence. Post-translational modifications increase the immunogenicity of vimentin, as demonstrated by the detection of anti-modified vimentin antibodies in patients with rheumatoid arthritis. Carbamylation is a non-enzymatic post-translational modification consisting in the addition of a cyanate group on lysine and arginine residues; since carbamylation is time dependent, structural proteins with a slow turnover are more likely to be carbamylated. The role of carbamylated vimentin as an antigenic target in SLE has not been yet evaluated.
Objectives: Aims of the study were to assess the prevalence of anti-carbamylated vimentin in a cohort of SLE patients and to evaluate the possible associations with clinical and serological feature of the disease.
Methods: Patients with SLE classified according to 1987 ACR criteria were enrolled. Clinical features, autoantibodies profile and disease activity – as measured by SLE Disease Activity Index 2000 (SLEDAI 2K) - were collected. Sera obtained from each patient were tested for anti-carbamylated vimentin by a home-made enzyme-linked immunoassay. Data were expressed as mean±standard deviation or median (interquartile range) when appropriate. To investigate difference in anti-carbamylated vimentin prevalence and anti-carbamylated vimentin serum levels Mann-Whitney and Chi square test were applied. P value <0.05 was considered statistically significant.
Results: We enrolled 109 SLE patients (102F:7M, mean age 39.4±12.6 years, mean disease duration 10.5±9.5 years, mean SLEDAI 2K 5±5.5).
Overall, 30 out of 109 patients (27.5%) were positive for anti-carbamylated vimentin. According to the clinical features, the prevalence of anti-carbamylated vimentin was significantly higher in patients with lupus nephritis (18/44) compared to those without renal involvement (12/66) (41.8% vs 18.2%, p=0.006); moreover, anti-carbamylated vimentin serum levels were significantly higher in patients with lupus nephritis [2561 (1783) OD] compared to those without [1970 (1123) OD; p=0.0178]. We didn't find any difference in prevalence or titre of anti-carbamylated vimentin according to presence/absence of other clinical manifestations (musculoskeletal, muco-cutaneous, hematologic, neuropsychiatric) or serology (low complement, anti-dsDNA). Moreover, we did not find any correlation between anti-carbamylated vimentin serum levels and SLEDAI 2K.
Conclusions: Higher prevalence and serum levels of anti-carbamylated vimentin antibodies in patients with lupus nephritis confirm the role of vimentin as a target of the immune response in patients with glomerulonephritis and suggest their possible role as a biomarker of kidney involvement in SLE patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5819

SAT0284 ASSOCIATION OF PATHOGENIC AND REGULATORY B-CELL SUBSETS WITH CLINICAL AND HISTOLOGICAL FEATURES IN PRIMARY SJÖGREN'S SYNDROME

F. Carubbi[1,2], A. Alunno[3], P. Cipriani[1], P. Di Benedetto[1], V. Liakouli[1], P. Ruscitti[1], O. Berardicurti[1], S. Di Bartolomeo[1], R. Gerli[3], R. Giacomelli[1].
[1]Department of Biotechnological and Applied Clinical Science, Rheumatology Unit, School of Medicine, University of L'Aquila; [2]Department of Medicine, ASL1 Avezzano-Sulmona-L'Aquila, L'Aquila; [3]Department of Medicine, Rheumatology Unit, University of Perugia, Perugia, Italy

Background: Several data pointed out that B-cells play a central role in the development, maintenance and progression of primary Sjögren's syndrome (pSS). B-lymphocyte hyperactivity, salivary gland (SG) infiltration, and the development of B-cell follicles containing germinal center (GC)-like structures, represent hallmarks of the disease. On this basis, B-cell depleting therapy with anti-CD20 monoclonal antibody rituximab (RTX) has been employed in pSS showing promising results. However, currently available data do not allow to draw definitive conclusion on its efficacy.
Objectives: Aim of the study was to assess mature and regulatory B cell subsets in patients with pSS and explore possible associations with clinical and histological features and their possible modulation by RTX treatment.
Methods: We evaluated by flow cytometry peripheral blood (PB) B-cell subsets (mature B cells: Bm1, Bm2, Bm2', Bm3, Bm4, early(e)Bm5, Bm5; IL-10-producing B-cells), in 17 pSS patients and in 10 healthy donors (HD). Nine pSS patients received a course of RTX (1000 mg at days 1 and 15) and PB B-cell subsets were also evaluated after 3 (T3) and 6 (T6) months and compared to baseline values (T0).
Results: We confirmed that the percentage of Bm1, eBm5 and Bm5 was lower and that of Bm2, Bm2' and Bm3+Bm4 was higher in pSS patients compared to HD (all $p<0.05$). When we divided patients according to the ESSDAI score (<5 or ≥ 5) or to SG-GC (presence/absence), we observed for the first time that the percentage of Bm2' cells, also called GC founders, was higher in patients with ESSDAI≥ 5 ($p=0.02$) compared to those with lower ESSDAI score and in pSS patients with GC ($p=0.02$) compared to those without GC. Although we observed a reduction of all B-cells subsets at T3 and T6 after RTX treatment, the proportion of Bm1, Bm3+Bm4, eBm5 and Bm5 persisted lower and the percentage of Bm2 and Bm2' persisted higher in pSS patients ($p<0.05$) compared to HD. No differences regarding IL-10-producing B-cells was obeserved between pSS patients and HD. However, the percentage of IL-10-producing B-cells was higher in patients with ESSDAI≥ 5 compared to patients with ESSDAI<5 ($p=0.02$).
Conclusions: We demonstrated for the first time that a subset of circulating mature B-cells, Bm2', also called GC founders, is strongly associated with higher disease activity and with the presence of SG-GC. Moreover, a higher ESSDAI is associated with higher percentage of circulating IL-10-producing B-cells. Pathogenic B-cell hyperactivity is a hallmark of pSS, however B-cells are also a source of inhibitory cytokines such as IL-10 and TGF-beta and the increase of IL-10 producing B cells that we observed in active pSS patients may suggest an ongoing compensatory mechanism to counteract chronic inflammation. Therefore, the design of novel B cell targeted therapies should ensure that only pathogenic B cells are depleted and regulatory B cell subsets are not hampered while, ideally, potentiated.
References:
[1] Binard A et al. Ann Rheum Dis 2009;68:1447–1452.
[2] Carubbi F et al. Arthritis Res Ther 2013;15:R172.
[3] Carubbi F et al. Lupus 2014; 23:1337–49.
[4] Kroese FG, et al. B-cell hyperactivity in primary Sjögren's syndrome. Expert Rev Clin Immunol. 2014;10:483–99.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4407

SAT0285 THE PHYSICAL PERFORMANCE OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH LOW DISEASE ACTIVITY: COULD THE CARDIOPULMONARY EXERCISE TESTING REFINE ITS ASSESSMENT?

G. Gusetu[1], A. Mociran[2], C. Pamfil[3], L. Damian[2], D. Pop[1], D. Zdrenghea[1], S. Rednic[3]. *[1]Cardiology, University of Medicine and Pharmacy; [2]Rheumatology, County Emergency Hospital; [3]Rheumatology, University of Medicine and Pharmacy, Cluj-Napoca, Romania*

Background: Even during remission, the systemic lupus erythematosus (SLE) patients have reduced exercise performance and this contributes to impairment of their quality of life[1]. Several causes as depression and deconditioning, arthritis, anemia, cardiovascular and respiratory involvement are widely accepted; however the weight of each factor is less known in particular individuals.
Objectives: Our study aimed to assess through cardiopulmonary exercise testing (CPX) the exercise performance of a SLE cohort and to establish its main determinants.
Methods: Thirty-one SLE patients with low disease activity underwent a CPX on cycle ergometer; the main metabolic parameters and standard 12-leads ECG were recorded; before exercise testing, a cardiac Doppler ultrasound was performed. The patient's characteristics, cumulative organ damage and laboratory data were retrieved by medical chart review. The control group consisted of 25 age and sex-matched healthy, non-trained individuals.
Results: Within the study group, 28 (90.3%) were female, the mean age was 42.7±10.6 years and disease median duration 7.9 years. The aerobic performance was decreased by 16.2% (17.6 vs 21.36 ml/kg/min, p=0.022); the main disease characteristics which correlated with maximum oxygen uptake (VO2Mx) were anemia (p=0.035), renal involvement (p=0.05) and antiphospholipid syndrome (APS) (p=0.042) but not disease duration, cumulative damage or the immunological tests (hypocomplementemia, anti-Ro, anti-Sm, anti-dsDNA, AAN or APL antibodies).
One quarter of patients did not reach the ventilatory anaerobic threshold (VAT, expressed as a percentage of calculated VO2Mx), mainly due to musculoskeletal pain (5 patients), dyspnea (2 patients with history of pulmonary embolism) and sudden rise in blood pressure (1 patient). Among the rest of them (23 patients, 74%), the VAT was at the lower limit of normal range (41.03% vs 54.0% for controls, p=0.014) corresponding to a "training reserve" of 31%. Of particular importance from this point of view were the criteria for test termination: dyspnea in 4 patients (1 with anemia, 1 with pulmonary fibrosis and 2 by hyperventilation proved by mean VE/VCO2 =41.5), fatigue (9 patients) and arthralgia (7 patients). Notably, among patients with established diagnosis of mild pulmonary fibrosis, COPD, ischemic or valvular heart disease, not dyspnea but arthralgia or fatigue was the reason for test termination, even if the VO2Mx was lower than recorded in the rest of the group (15.8 vs 19.2 ml/kg/min, p=0.037).
Conclusions: The exercise aerobic capacity of SLE patients is diminished and correlates with anemia, renal involvement and with hystory of pulmonary embolism. Surprisingly, even in patients with mild cardiovascular or respiratory involvement, the decreasing of exercise performance is limited mainly from musculoskeletal symptoms and from deconditioning.
References:
[1] Carvalho MR, Sato EI, Tebexreni AS, et al. Effects of supervised cardiovascular

training program on exercise tolerance, aerobic capacity, and quality of life in patients with systemic lupus erythematosus. Arthritis Rheum 2005;53(6):838–44.

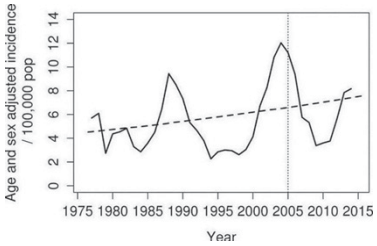
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6619

SAT0286 INCIDENCE AND MORTALITY OF PRIMARY SJÖGREN'S SYNDROME: TIME TRENDS OVER A 40-YEAR PERIOD IN A POPULATION-BASED COHORT IN THE UNITED STATES

G. Maciel[1,2], C. Crowson[3], E. Matteson[1], D. Cornec[4,5]. *[1]Rheumatology, Mayo Clinic, Rochester Minnesota, United States; [2]Hospital Maciel, Montevideo, Uruguay; [3]Division of Biomedical Statistics and Informatics, Department of Health Sciences Research; [4]Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester Minnesota, United States; [5]Rheumatology, CHRU Brest, Brest, France*

Background:
Few studies have reported the incidence of primary Sjögren's syndrome (pSS) in well-defined populations worldwide, and none of them covered a period of time long-enough to analyze potential time trends in incidence rates. Whether pSS is associated with a higher mortality rate compared to the general population is also unclear from previously published studies.
Objectives: To estimate the incidence and mortality rates of pSS among residents of Olmsted County, Minnesota, and their evolution over time.
Methods: All medical records of patients with a diagnosis or suspicion of SS in Olmsted County, MN, from January 1, 2006 to December 31, 2015 were reviewed to identify incident cases of pSS (defined according to physician diagnosis). All patients with doubtful cases and all patients with an associated systemic autoimmune disease were excluded. These cases were combined with a previous 1976–2005 incident cohort from the same population (reference). Incidence rates were age and sex adjusted to the US white 2010 population. Survival rates were compared with the expected rates in the general population of Minnesota.
Results: With 61 incident cases of pSS diagnosed in Olmsted County in 2006–2015, the total cohort included 172 patients with incident pSS in 1976–2015. Of the 172 patients, 151 (88%) were women and 161 (94%) were white, with a mean (SD) age at diagnosis of 58.3 (16.7) years. The average age- and sex- adjusted annual incidence for 2006–2015 was 5.9 per 100,000 population (95% CI 4.4–7.4), and overall incidence for the entire period was 5.8 (95% CI: 4.9–6.6) per 100,000. Incidence was 2 to 7 times higher in females compared to males in the different age classes (5.9 times higher on average), and increased progressively with age, culminating at 19.6 per 100,000 in females aged 65–74 years, with a slight decline thereafter to 15.9 per 100,000 among females aged 75 years and older. The incidence increased with calendar time over the 40-year period (p=0.005, figure). There was no apparent seasonality in the incidence of pSS, with similar number of cases diagnosed during all four seasons. There was no difference in mortality in the pSS cohort compared to expected (standardized mortality ratio 1.15, 95% CI 0.86–1.50).



Conclusions: The average annual incidence of pSS in this population based-cohort was 5.8/100,000, with a progressive increase over the 40 years of the study. Overall survival of pSS patients was not different from the general population.
References:
[1] Nannini C et al. BMJ Open. 2013;3:e003569.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1178

SAT0287 TH1, TH2 AND TH17 LYMPHOID SUBPOPULATIONS IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

G. Medina[1], O.I. Florez-Durante[2], L. Montiel Cervantes[3], R. Molina-Aguilar[3], E. Reyes-Maldonado[2], L.J. Jara[4]. *[1]Clinical Research Unit, Instituto Mexicano del Seguro Social, Hospital de Especialidades Centro Médico la Raza; [2]Escuela Nacional de Ciencias Biológicas, Instituto Politécnico Nacional; [3]Hematology Laboratory; [4]Direction of Education and Research, Instituto Mexicano del Seguro Social, Hospital de Especialidades Centro Médico la Raza, Mexico City, Mexico*

Background: Primary antiphospholipid antibody syndrome (PAPS) is characterized by thrombosis at different levels and maternal fetal complications in the presence of antiphospholipid antibodies (aPL). Lymphoid subpopulations and cellular immune responses have not been fully studied.
Objectives: To analyze the lymphoid subpopulations, Th1, Th2 and Th17 immune response in patients with PAPS and long term evolution.
Methods: Patients with PAPS,>18 years of age, of both sexes and a group of healthy blood donors matched for age and sex were included. All patients were receiving oral anticoagulants (Coumadin type). No patient had a recent episode of thrombosis or other manifestation of APS at the time of the study. Peripheral blood was obtained and lymphoid subpopulations were determined by flow cytometry in order to identified with specific immunological markers for Treg cells: CD4+/CD25+/FoxP3+ and CD8+/CD25+/FoxP3+. The dendritic cells analyzed were: Type 1: Lin1- HLA-DR+/CD11c+; Type 2: Lin-HLA-DR+/CD123+; B lymphocytes with antiCD19-APC; Monocytes with anti-CD14-PE; NK: CD3-/CD16+56+ and NKT: CD3+/CD16+56+ lymphocytes. Th1 cells were identified by IFN-g$^+$ positivity; Th2: positivity for IL-4+; Th17: positivity for IL-17+. Parametric statistics and Mann-Whitney U-test were used.
Results:

	PAPS (cells/μL)	Healthy controls (cells/μL)	p
Total leukocytes	5655	7000	<0.05*
Lymphocites	1800	2085	NS
Total CD3	1033	1338	NS
Total CD4	701	775	NS
Total CD8	258	441	<0.05*
Monocytes	213	219	NS
B lymphocites	41	86	NS
NK	118	177	NS
NKT	33	45	NS
iNKT	9	20	<0.005**
Tγδ Lymphocites	34	45	NS
LTreg 4 Lymphocites	23	13	NS
Treg 8 Lymphocytes	26	13	NS
DC1	2	4	<0.005**
DC2	1	5	<0.0005***

A total of 39 patients with PAPS were included, age: 51.9±12.8, evolution time: 12.8±8.9 years and 35 healthy controls. In patients with PAPS there was a decrease in the total CD8 count ($p<0.05$) in iNKT ($p<0.005$), DC1 ($p<0.005$) and DC2 ($p<0.0005$) cells compared to the control group (Table 1).We found significant decrease in Th1, Th2 and Th17 cytokines basal and after activation compared to healthy controls.
Conclusions: This study shows profound alterations in innate and adaptive immunity in patients with long-term PAPS, characterized by a decrease in certain lymphocyte subpopulations, with consequent functional alteration. These abnormalities can become new therapeutic targets in order to restore immune imbalance. Our findings may explain in part, the development of thrombosis and other complications, despite treatment with oral anticoagulants in PAPS patients with long term disease evolution.
References:
[1] Dal Ben ER, do Prado CH, Baptista TS, Bauer ME, Staub HL. Decreased levels of circulating CD4+CD25+Foxp3+regulatory T cells in patients with primary antiphospholipid syndrome. J Clin Immunol 2013; 33: 876–879.
[2] Xiao J, Zhu F, Liu X, Xiong J.Th1/Th2/Th17/Treg expression in cultured PBMCs with antiphospholipid antibodies.Mol Med Rep. 2012;6(5):1035–9.
[3] Jakiela B, Iwaniec T, Plutecka H, Celinska-Lowenhoff M, Dziedzina S, Musial J. Signs of impaired immunoregulation and enhanced effector T-cell responses in the primary antiphospholipid syndrome. Lupus. 2016; 25(4):389–98.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6222

SAT0288 QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERIYTHEMATOSUS

G. Voicu[1], L. Groseanu[1], M. Abobului[1], V. Vlad[1], F. Berghea[1], D. Predeteanu[1], V. Bojinca[2], I. Saulescu[2], A. Borangiu[2], S. Daia[2], D. Mazilu[2], A. Balanescu[2], C. Constantinescu[2], D. Opris[2], R. Ionescu[2]. *[1]Rheumatolgy; [2]internal medicine and Rheumatolgy, Sfanta Maria Clinic Hospital, Bucharest, Romania*

Background: The Quality of life (QoL) in patients with SLE is deeply affected by multiple factors including psychological and physical factors, the functional status and the general perception over health.
Objectives: Evaluation of Quality of life and the perceptions over the disease in patients with SLE.functional status and the general perception over health.
Methods: This is a 10 month prospective, cross-sectional study performed on 52 patients hospitalized diagnosed with SLE according to SLICC 2012 criteria. There were evaluated demographic data, organs manifestations, disease activity scores (SLEDAI, SLICC) and treatment. To evaluate the QoL several questionnaires were performed: Health Assessment Questionnaire (HAQ), EuroQol five dimensions questionnaire (EQ5d), Illness Perception Questionnaire and SF-36.
Results: All patients were women with the mean age 49 years with a mean durations of illness 136 month (14). The mean SLEDAI – 5,52 (5,37) and SLICC – 2,25 (1,71).
The mean HAQ value was 0,83 (0,81). The HAQ score doesn't correlate with SLICC (p=0,461) and with SLEDAI (p=0,172), but it was correlated with the neuropsychiatric manifestations. So the psychiatric affectation influences performing the usually daily activities (p=0,005).
When assessing Illness Perception Questionnaire, patients considered their life seriously affected by pain, mean value 6,3 (2,6), 72% consider the illness will be

present for the rest of their lives, 90% appreciate that treatment is improving the QoL mean 9,3 (1,3), 68% consider to have many severe symptoms, more than 80% patients consider themselves preoccupied for their illness, more than 70% are emotionally affected by their illness and 48% consider stress being the main determinant factor of their illness.
Questionnaire EQ-5d: 10% must stay in bed due to the disease, 8,33% can not wash or dress themselves, 12,5% are unable to perform usual daily activities, 62% experience pain or a moderate uncomfortable state and 65% are worried and or depressed. Cardio-vascular manifestations are correlated with diminished mobility (p=0,002) leading to deficiency in self care (p=0,002)also correlated with renal (p=0,034) and psychiatric (p=0,022) manifestations. Psychiatric manifestations also affect usual daily activities (p=0,05). Age is correlated with pain and uncomfortable state (p=0,004) but the responses to this item of EQ5D are not correlated with organ affectation, biological modification or disease activity scores. The presence of cutaneous manifestations is correlated with anxiety and depression (p=0,02).
Based on SF36 when calculating the mean value on each category was observed all the 8 categories affected - smallest values at physical role (37,32) and general health (34,21), less influenced part being the social function (51,32).None of this items of SF 36 is correlated with SLICC or SLEDAI.
Conclusions: SLEDAI as well as SLICC or specific organ involvement give no indications over the patients QoL, which must be assessed by performing HAQ and SF 36.
References:
[1] Lupus. 2016 Mar 16. pii: 0961203316638934. [Epub ahead of print]Gender differences in systemic lupus erythematosus concerning anxiety, depression and quality of life.Macêdo EA1, Appenzeller S2, Costallat LT2.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5316

SAT0289 CARDIOVASCULAR RISK STATUS MODIFICATION IN SLE PATIENTS BY MEANS OF CAROTID ULTRASOUND EXAMINATION

H. Sánchez-Pérez, B. Tejera-Segura, I. Ferraz-Amaro. *Rheumatology, Hospital Universitario de Canarias, la Laguna, Spain*

Background: Systemic lupus erythematosus (SLE) is associated with a higher cardiovascular risk (CVR), at least doubled when compared with the general population, as well as an increased prevalence of atherosclerosis,which occurs prematurely and independently of traditional CVR factors. The presence of atheromatous plaques documented with carotid ultrasound (US) examination implies a change in the patient's CVR category to "very high risk",according to the "European Guidelines on cardiovascular disease prevention in clinical practice, 2016". General guidelines do not take into account the specific increase in CVR risk that it's present in patients with autoimmune diseases.
Objectives: To examine if the use of carotid US leads to a more accurate CVR classification in SLE patients, and in that way to a better CVR management.
Methods: Cross-sectional study that emcompassed 102 SLE patients currently being followed in our Rheumatology Department. Demographic variables, the presence of CVR factors and previous/current CV events, disease duration and drug use were analysed; lipid profile was assessed using blood tests, as well as carotid intima media thickness and the presence of carotid plaques using US scan. The current CVR status was calculated using the SCORE classification (low risk $<$1%, moderate risk $<$5%, high risk $<$10% and very high risk $>$10%).
Results: 95% of our patients were women,mean age was 51.6+/- years,median disease duration was 16 years (IQR 9–28). 35.29% of patients presented with at least one CVR factor before the SLE diagnosis,and 61.76% at the time of the research (19.60% current smokers, 39.21% high blood pressure (HBP),33.33% dyslipidemia, 7.84% type II diabetes. A CV event was diagnosed in 11.76% of our patients throughout their SLE disease. According to the SCORE classification,55 of them had a low CVR (53.92%),26 moderate CVR (25.49%),6 high CVR (5.88%) and 15 of them very highCVR (14.70%). Carotid plaques were found in 28 patients (27.45%): 23 of them had never had a CV event (22.54%),21.42% of them were current smokers,64.28% had HBP,53.57% dyslipidemia and 17.86% type II diabetes. After adjustment of the SCORE classification with the presence of carotid plaques,16.36% of patients from the "low CVR" category would be re-classified has having "very high CVR", as well as 30.76% from the "moderate CVR" category and 50% from the "high CVR" category. Of note,8 patients within the "very high CVR" category also presented carotid plaques. Out of this patients with atheroma plaque,13 were not using statins,and in 2 of them it would have been mandatory in order to achieve the LDL $<$70mg/dl target. In 2 of the 15 patients that were indeed under statins this target was not achieved. 60.71% of the atheromatous patients were under hydroxicloroquine use and 17.64% of them used steroids as a regular basis (33.33% of them within the medium range dose)
Conclusions: More than half of our SLE patients presented with at least 1 CVR factor. Around 15% of patients were categorised as "very high CVR" according to the SCORE classification.The presence of carotid plaque was found in 27.45% of our patients,and 82% of them hadn't suffered any CV event. The use of carotid US examination allowed us to re-classify 20 patients (19.60%)in the "very high risk" category according to the SCORE classification. The need for a change in CVR management (ie., change in statin regime)was demonstrated in 4 of this 20 "re-classified" patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6632

SAT0290 OSTEONECROSIS IS THE MOST COMMON ORGAN DAMAGE AND IS ASSOCIATED WITH CUMULATIVE STEROID DOSAGE AS WELL AS LUPUS NEPHRITIS ITSELF IN PATIENTS WITH SLE

H.H. Kwon[1], S. Won[2], Y.B. Joo[3], M.J. Kim[1], H.Y. Kim[1], G.Y. Ahn[1], S.-C. Bae[1]. *[1]Hanyang University Hospital for Rheumatic Diseases; [2]Clinical Research Center for Rheumatoid Arthritis (CRCRA), Seoul; [3]St Vincent's Hospital, Suwon, Korea, Republic Of*

Background: In patients with SLE, musculoskeletal system is common organ system involved cumulatively over time. Osteonecrosis (ON) is common in musculoskeletal damage accrual and often disabling. Steroid use has been a risk factor in the development of ON, but SLE itself has also been suggested to have a role. It is important to understand factors related to the development of ON.
Objectives: We investigated the overall profile of organ damage accrual, particularly musculoskeletal damage and focused on factors associated with ON in a single Asian cohort.
Methods: Patients with SLE who met American College of Rheumatology (ACR) criteria were enrolled and followed from 1998 to 2014 in the Hanyang BAE Lupus cohort. Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) was measured annually. ON was confirmed by X-ray, bone scan or MRI. Patients with ON was compared to controls without ON from the same cohort for clinical, laboratory, and therapeutic factors. Univariate logistic regression followed by multivariate logistic regression were used to determine risk factors for ON.
Results: We recruited 1,219 SLE patients. The most common type of organ damage was musculoskeletal (205 patients, 16.8%). ON was the most common subtype (133 patients, 10.9%) of the musculoskeletal damage. The mean time from diagnosis of SLE to development of ON was 4.97±4.15 (0.17∼20.25) years. One hundred twenty-six patients were eligible for identifying distribution of ON. Overall, 291 joints were affected by ON and mean number of ON joint per patients with ON was 2.3±1.23 (1∼9). The percentage of $>$2 joint involvement was 24.6%. The hip (femoral head) was the most frequently involved joint (65.6%), followed by the knee (distal femur, proximal tibia, proximal fibula, patella: 20.6%), shoulder (humeral head: 5.2%) and ankle (distal tibia, distal fibula, talus: 5.2%).
In univariate analysis, age at diagnosis, follow up duration, accumulative number of ACR criteria, serositis, renal disorder & neurologic disorder (based on ACR criteria), cyclophosphamide & mycophenolate use, and cumulative steroid dosage were significantly associated with ON. In multivariate analysis, renal disorder (p=0.0109), and cumulative steroid usage (p=0.0131) were significantly associated with ON.
To evaluate the effect of cumulative steroid usage on ON, age, sex and disease duration matched ON cases and controls (1:4, a total of 665 patients) were selected from the same cohort. Total cumulative steroid dosage was divided into 4 groups by grams ($>$0 & $\leq$5g, $>$5g & $\leq$10g, $>$10g & $\leq$20g, and $>$20g). More than 10g group of cumulative steroid use was significantly associated with ON. And then we stratified 530 patients according to biopsy proven lupus nephritis (class III to V) and cumulative steroid dose (10g cut-off), and tested by Chi-square test and logistic regression. ON was significantly higher in the group with lupus nephritis within $>$10g group of total cumulative steroid.

Table 1. Total cumulative steroid dose as risk factor for ON

Total cumulative steroid dose(g)	OR (95% CI)	p-value
>0 & ≤5	1.00	
>5 & ≤10	2.00 (0.91-4.39)	0.0844
>10 & ≤20	2.34 (1.19-4.58)	0.0133
>20	2.96 (1.60-5.47)	0.0005

Table 2-1. Association between Osteonecrosis and lupus nephritis based on total cumulative steroid 10g

Total cumulative steroid dose >10g (371 patients)				
	Total	ON(+)	ON(-)	p-value
Lupus nephritis(+)	196	58(29.59)	138(70.41)	0.0018
Lupus nephritis(-)	175	27(15.43)	148(51.75)	

Table 2-2. Association between Osteonecrosis and lupus nephritis based on total cumulative steroid 10g

	OR (95% CI)	p-value
Steroid dose≤10 & Lupus nephritis(-)	1.00	
Steroid dose>10 & Lupus nephritis(-)	1.58 (0.81-3.10)	0.1826
Steroid dose≤10 & Lupus nephritis(+)	2.48 (1.02-5.99)	0.0441
Steroid dose>10 & Lupus nephritis(+)	3.64 (1.97-6.75)	<0.0001

Conclusions: ON was the most frequent damage in lupus patients. We confirmed again cumulative steroid dosage as a risk factor for the development of ON. In addition, lupus nephritis itself was suggested as an independent risk factor for ON.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4547

SAT0291 NON-REPORTING OF SYSTEMIC LUPUS ERYTHEMATOSUS IN DEATH CERTIFICATES OF LUPUS PATIENTS: ITS EXTENT AND PREDICTORS

I. Padjen[1,2], M. Erceg[3], M. Cerovec[1,2], M. Mayer[1,2], R. Stevanović[3], B. Anić[1,2]. *[1]Department of Internal Medicine, Division of Clinical Immunology and Rheumatology, University Hospital Centre Zagreb; [2]University of Zagreb, School of Medicine; [3]Croatian Institute of Public Health, Zagreb, Croatia*

Background: Systemic lupus erythematosus (SLE) is frequently not reported in death certificates of lupus patients, despite its known role as an underlying and/or immediate cause of death. Possible reasons may be insufficient access to patients' medical records at time of death (including details on their medical history) and/or physicians' unawareness of the contribution of SLE to death.
Objectives: We aimed to analyze the extent and predictors of non-reporting of SLE in death certificates of 90 deceased SLE patients regularly followed-up in a routine academic setting at our Department.
Methods: We retrospectively observed 90 SLE patients (68 females) deceased within the 2002–2011 period. All patients were ≥18 years of age and Croatian residents at the time of death, fulfilling ≥4 classification criteria of the American College of Rheumatology (ACR). We identified patients with SLE listed as a cause of death in the death certificate. An extensive set of variables was compared between patients with and without SLE reported in the certificate: demographics, ACR criteria at time of death and damage according to the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC)/ACR index and its components at the time of death. We also compared the proportion of in-hospital deaths and autopsies performed. Frequencies were compared using the χ^2 and Fisher's exact test, and continuous variables using the t-test and Mann-Whitney U test. Variables associated with reporting of SLE in the death certificate in the univariate analysis were included in a multivariate logistic regression model.
Results: SLE was reported in death certificates of 41/90 (46%) patients. Patients with SLE not reported in their death certificates were older at death (62±14 vs. 53±15 years) and diagnosis (53±14 vs 42±18 years) and had a longer time from their last visit at our Department to death (0.80±1.00 vs. 0.34±0.66 years), compared to patients with SLE listed in the death certificate ($p<0.05$). They also had a lower proportion of renal disorder (20/49 vs. 29/41), cardiovascular and pulmonary damage (18/49 vs. 28/41 and 7/49 vs. 13/41, respectively), and died less frequently in hospital (28/49 vs. 35/41) and due to infections (4/49 vs. 26/41) ($p<0.05$). Conversely, these patients had a higher frequency of malignancy as a feature of damage (17/49 vs. 6/41) and a cause of death (14/49 vs. 1/41) ($p<0.05$). Only patients without SLE listed in their death certificate accrued gastrointestinal damage (7/49 vs. 0/41, p=0.015), hence this type of damage could not be included in the multivariate logistic model. In the multivariate model, the presence of infection as a cause of death was the single variable related to (non-)reporting of SLE (OR 0.053; 95% CI 0.012–0.237) (Table 1).

Table 1. Predictors of non-reporting of SLE in death certificates (OR: odds ratio; CI: confidence interval)

Variable	OR	95% CI	p
Age at diagnosis (years)	1.050	0.961-1.148	0.280
Age at death (years)	0.996	0.906-1.096	0.938
Time from last visit to death (years)	1.122	0.496-2.542	0.782
Renal disorder (yes/no)	0.434	0.126-1.499	0.187
Pulmonary damage (yes/no)	0.536	0.119-2.406	0.416
Cardiovascular damage (yes/no)	0.412	0.102-1.666	0.214
Malignancy (feature of damage) (yes/no)	2.934	0.597-14.423	0.185
Infection as cause of death (yes/no)	0.053	0.012-0.237	<0.001
In-hospital death (yes/no)	1.012	0.223-4.592	0.987

Conclusions: Non-reporting of SLE in death certificates of lupus patients may be an obstacle towards assessing the true extent of SLE-related mortality, calling into question the reliability of vital statistics data extracted only from death certificates. Infections as causes of death and gastrointestinal damage may influence reporting of SLE in death certificates.
References:
[1] Calvo-Alen J et al. Rheumatology 2005;44:1186–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2825

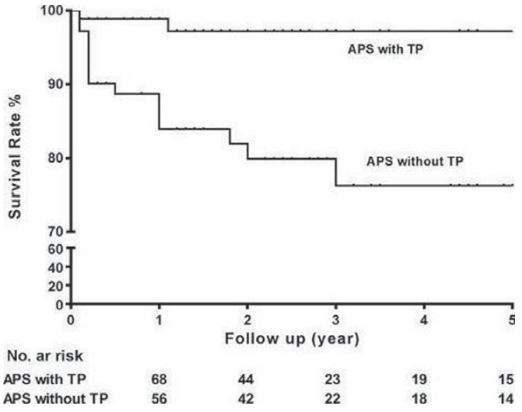
SAT0292 LONG-TERM PROGNOSIS AND PREDICTING FACTORS OF CHINESE PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

J. Zhao, Y. Sun, P. Zhang, Q. Wang, M. Li, X. Zeng. *Peking Union Medical College Hospital, Beijing, China*

Background: Antiphospholipid syndrome (APS) is an acquired autoimmune prothrombotic condition characterized by persistent circulating antiphospholipid antibodies (APL). The pathogenic mechanisms that lead to clinical manifestations associated with APL are only partially understood. And to date, long-term anticoagulation has been the only treatment shown to reduce vascular complications.
Objectives: The aims of the present study were to assess and identify the prognostic factors of the long-term outcomes and mortality of antiphospholipid syndrome (APS) in Chinese patients.
Methods: Records of 160 patients with APS admitted to Peking Union Medical College Hospital in Beijing between 2005 and 2015 were investigated. Demographic characteristics, cumulative clinical and laboratory features, autoantibody profiles were retrieved from the database. Survival rates were studied by Kaplan-Meier method, and COX proportional hazard model was adopted to perform the analysis of predicting factors for mortality.
Results: The entire cohort consisted of 110 (68.8%) female and 50 (31.3%) male patients. Mean (SD) age at study entry was 36.5±14.9 years. The most prevalent thrombotic risk factors were hypertension, dyslipidemia, and smoking, present in 5–15% of the total cohort. In total, 50.6% of the patients had primary APS, 45.9% had APS associated with SLE, 2.0% APS associated with other connective tissue diseases. The most prevalent immunological features at baseline were LA (71.3%), aCL (55.0%), and β2GPI (49.4%). No significant statistical differences were found in the clinical presentation of the APS according to the presence or absence of any of these antibodies. During the 10-year period, 16 (10.0%) patients (8 female and 8 male) died. The overall 1, 3, and 5-year survival rate was 92.6%, 89.1% and 87.1%, respectively. The most common causes of death were severe thrombotic events, including pulmonary embolism, strokes and myocardial infarction (43.8% of total deaths), infections (18.8%). COX proportional hazard model show thrombocytopenia is the independent prognostic factor of mortality (HR 8.228, 95% CI 1.866–36.282).

Table 1. Baseline characteristics of APS patients

Clinical characteristics	Prevalence	Thrombotic event	
		No (N=51)	Yes (N=109)
Female, n/%	110 (68.8%)	42 (82.4%)	68 (62.4%)
Age, year, mean+SD	36.5±14.9	34.2±14.9	37.4±14.9
Thrombotic events			
Arterial thrombosis	59 (36.9%)	–	59 (54.1%)
Venous thrombosis	72 (45.0%)	–	72 (66.1%)
Coexist of arterial and venous thrombosis	22 (13.8)	–	22 (20.2%)
Systemic autoimmune diseases	79 (49.4%)	33 (64.7%)	46 (42.2%)
Thrombophylic risk factors			
Smoking	8 (5.0%)	2 (3.9%)	5 (5.5%)
Dyslipidemia	20 (12.5%)	6 (11.8%)	14 (12.8%)
HTN (systolic>140)	24 (15.0%)	7 (13.7%)	17 (15.6%)
ACL	88 (55.0%)	32 (62.7%)	56 (51.4%)
β2GP1	79 (49.4%)	31 (60.8%)	48 (44.0%)
Lupus anticoagulants	114 (71.3%)	39 (76.5%)	75 (68.8%)
Tri-positive	41 (25.6%)	21 (41.2%)	20 (18.3%)
Thrombocytopenia	71 (44.4%)	23 (45.1%)	48 (44.0%)
Hypocomplementaemia	59 (36.9%)	25 (49.0%)	34 (31.2%)



Conclusions: patients with APS develop significant morbidity and mortality despite current treatment. More attention should be devoted to APS patients with thrombocytopenia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5580

SAT0293 PNEUMOCOCCAL INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

J. Schurder, T. Goulenok, R. Jouenne, A. Dossier, D. van Gysel, T. Papo, K. Sacre. *Paris-7 University, APHP, Bichat Hospital, Paris, France*

Background: A 5-fold increase in the risk of death is due to infection in systemic lupus erythematosus (SLE) patients when compared to age- and sex-matched controls Pneumococcal infection (PI) has been reported to be more frequent and severe in SLE
Objectives: Our study aimed to analyze the risk factors associated with the occurrence and severity of PI in SLE patients
Methods: Medical records of all SLE patients and all patients admitted with PI in the Department of Internal Medicine (Bichat Hospital, Paris, France) from January 2005 to December 2014 were retrospectively reviewed. Clinical characteristics associated with PI occurrence and severity were analyzed, both in SLE and non SLE patients.
Results: One hundred and ninety SLE patients (42.2+14.9 years; 87.4% females) were hospitalized over a 10-year period. PI was the reason for admission in 6 (3.2%) patients, including 5 cases of invasive infection. With a follow-up of 2112.8

years for the total cohort, incidence of invasive PI in SLE was of 236/100.000 patient-years. As compared to the incidence in general French population, invasive PI was 26 times more frequent in SLE patients. PI occurred at a younger age (43.5+14.9 versus 65.3+18.7 years, p=0.009) and was more severe, with a higher frequency of invasive infection (p<0.001) and higher need for ICU admission (p=0.015) in SLE as compared to non SLE patients. Of note, unusual PI sites, including pneumococcal endocarditis (n=1), arthritis (n=1) and peritonitis (n=1) were observed in SLE patients only. Risk factors associated with PI in SLE patients were a serum gammaglobulin level <5g/L (p=0.003) and a past history of lupus nephritis (p=0.047), only. Steroids (p<0.001) and immunosuppressive drugs (p=0.027) were associated with infection severity.

Conclusions: Pneumococcal infections occur at a younger age, are more frequent and severe in SLE patients. Hypogammaglobulinemia and lupus nephritis increased the risk for PI, whereas steroids and immunosuppressive drugs were associated with infection severity only. Our study shows that SLE patients have an increased risk for invasive PI and points to the need for vaccination against *streptococcus pneumoniae* in SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1016

SAT0294 COMPARISON OF CLINICAL CARE BETWEEN CHINESE AND AMERICAN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

J. Dong[1], H. Ma[1], W.N. Roberts[2], L. Wang[1], F. Khan[3], K.A. Lyn Shue[2], L. Zhao[1], L. Pan[1]. *[1]Rheumatology and Clinical Immunology, Affiliated Hospital of Qingdao University, Qingdao, China; [2]Rheumatology; [3]Internal Medicine, University of Louisville, Louisville, KY, United States*

Background: In addition to gender and ethnicity, modifiable variables like geography, socioeconomic status, health system structure, education, and physician expertise may influence outcomes in systemic lupus erythematosus (SLE).

Objectives: To compare characteristics of and treatment options for subsets of Chinese and American patients with SLE to elucidate factors that contribute to disease activity and damage.

Methods: Chart review of 77 Chinese (Qingdao) and 48 Midwestern American (Louisville, Kentucky) patients meeting American College of Rheumatology (ACR) criteria for a diagnosis of SLE followed up for four years were analyzed retrospectively. Organ damage was assessed using the Systemic Lupus International Collaborating Clinics (SLICC)/ACR Damage Index (SDI), and disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). Statistics were parametric exploratory tests of significance and multiple regression analyses in this hypothesis-generating effort.

Results: The interval between the time of onset and diagnosis was 44 months shorter in the Chinese arm (p=0.001), and Chinese patients followed up at six times greater frequency than American patients (p<0.001). Despite the lack of formal matching, the two cohorts featured similar disease activity according to the SLEDAI. Based on the SDI, rates of organ damage were higher in the American group. Chinese patients received more steroids, cyclophosphamide, hydroxychloroquine, intravenous immune globulin, and cyclosporine than the Louisville group, while the Louisville patients received more mycophenolate mofetil and azathioprine (p=0.001).

Table 1

Variable	Qingdao (*n*=77), mean ± SD	Louisville (*n*=48), mean ± SD	*p*-value
Onset age (years)	30.24±11.95	30.21±12.21	0.989
Age at diagnosis (years)	30.89±11.92	34.5±12.99	0.114
Duration between SLE onset and diagnosis (months)	7.94±18.46	52.30±89.90	0.001
Clinic visits per year	10.93±7.09	3.02±1.91	<0.001
Interval between the last two times of follow up (months)	1.89±1.31	12.32±28.32	0.014
Disease duration (years)	5.97±5.72	5.22±5.53	0.466
SLEDAI	5.81±4.32	4.63±4.77	0.156
SDI	0.44±0.64	1.23±1.057	<0.001

Table 2

Medication	Qingdao (*n*=77)	Louisville (*n*=48)	*p*-value
Prednisone	77 (100%)	29 (60.42%)	<0.0001
Cyclophosphamide	34 (44.16%)	6 (12.50%)	<0.0001
Hydroxychloroquine	72 (93.51%)	32 (66.67%)	<0.0001
Methotrexate	9 (11.69%)	3 (6.25%)	0.489
Mycophenolate mofetil	10 (12.99%)	18 (37.50%)	0.001
Azathioprine	2 (2.60%)	5 (10.42%)	0.147
Intravenous immune globulin	12 (15.58%)	1 (2.08%)	0.035
Cyclosporine	17 (22.08%)	1 (2.08%)	0.005

Conclusions: The establishment of follow-up and treatment of SLE differs in specific, identifiable ways between these subsets of Chinese and midwestern American patients. Greater access to and increased frequency of follow-up appears associated with a lesser degree of organ damage, supporting the treat-to-target concept as applied to SLE. Complete, controlled trials in both settings are necessary, and further detailed comparison of larger cohorts may inform conclusions about the likelihood of generalizability of trial results from one setting to another.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5561

SAT0295 ANTI-RO52/TRIM21 ANTIBODIES ARE ASSOCIATED WITH QT INTERVAL PROLONGATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

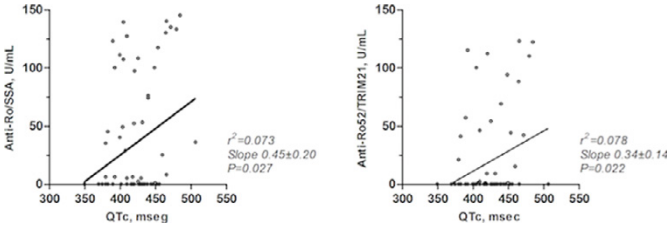
L.F. Perez, L.H. Silveira, L. Amezcua, O. Estevez, M. Moreno. *Reumatologia, Instituto Nacional de Cardiologia Ignacio Chavez, Mexico City, Mexico*

Background: Long QT syndrome (LQTS) is characterized by an abnormal QT corrected (QTc) interval prolongation that is associated with increased risk of sudden death. Studies have associated LQTS with several rheumatic conditions, and evidence points towards a link between the degree of systemic inflammation and the duration of QTc interval. Moreover, recent evidence suggests that anti-Ro antibodies may play a role in the QTc prolongation by mechanisms not fully understood, thus constituting a novel autoimmune-mediated LQTS.

Objectives: This study was aimed to assess whether QTc interval prolongation is associated with the presence of anti-Ro antibodies in SLE, particularly with reactivities against Ro52/TRIM21 antigens.

Methods: Consecutive patients fulfilling the 1997 ACR criteria for SLE were included. Patients with history of ischemic heart disease, with implantable pacemakers, and those taking drugs that potentially could affect QT interval (except for antimalarials) were excluded. Patients underwent a resting 12-lead electrocardiogram recording to measure QT interval corrected by BazzetÕs formula. A QTc interval duration greater than 460 msec in women and 440 msec in men was set to be abnormal. Serum anti-Ro and anti-Ro52/TRIM21 antibody levels were measured by ELISA. Data were expressed as frequencies and means (± standard deviation), and differences were tested by YatesÕ continuity corrected chi square or Mann-Whitney tests, while linear regressions were performed to assess linearity between autoantibody levels and QTc duration. The GraphPad Prism 4.02 software was used for calculations.

Results: Sixty-six patients with mean age of 39±13 years (57 female gender) were included. A QTc prolongation was found in 10 patients (15%), with mean QTc interval of 470±18 msec as compared to 414±23 msec in those with no LQTS. Main clinical and demographic characteristics were similar for both groups, except for a lesser use of antimalarials and higher serum creatinine levels in patients with LQTS. Disease activity was similar between groups.Anti-Ro antibody levels were significantly higher in patients with prolonged QT interval (75±66 U/mL versus 29±44 U/mL; P=0.005); similarly, anti-Ro52/TRIM21 levels were higher in those with LQTS (50±55 U/mL versus 14±30 U/mL; P=0.01). Notably, a linear association (see the Figure) between the QTc intervals and levels of anti-Ro antibodies (r2=0.073; P=0.02) and anti-Ro52/TRIM21antibodies (r2=0.078; P=0.02) was observed.



Conclusions: Our results strengthen the hypothesis that a specific autoantibody-mediated LQTS occur in SLE patients positive to anti-Ro antibodies. This interference in the ventricular repolarization appears to be associated with increased levels of antibodies against Ro52/TRIM21 antigens, and supports the realization of an electrocardiogram as part of the routinely evaluation in SLE patient with circulating anti-Ro antibodies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6695

SAT0296 RELATIONSHIP BETWEEN DISEASE ACTIVITY INDEX SCORES AND SUBJECTIVE ASSESSMENTS IN EARLY SYSTEMIC LUPUS ERYTHEMATOSUS

M. Garabajiu[1], V. Sadovici-Bobeica[1], L. Mazur-Nicorici[1], M. Cebanu[1], V. Salaru[2], M. Mazur[1]. *[1]Rheumatology; [2]Family Medicine, State University of Medicine and Pharmacy "Nicolae Testemitanu", Chisinau, Moldova, Republic of*

Objectives: To evaluate the disease activity in patients with early systemic lupus erythematosus (early SLE) and to compare it to patient's and physician's global assessment.

Methods: Cross-sectional study including 41 early SLE patients that fulfilled SLICC classification criteria, 2012. The early disease was defined one with the duration 2 years from the diagnosis. The disease activity was assessed by SLEDAI-2K and SLAM. Global indices were appreciated by patient and physician global assessments (PGA and MDGA), rated by 0–100 numeric score. We correlated disease activity indices with global assessments by Pearson coefficient.

Results: There were 41 SLE patients integrated in the study, female:male ratio 9,25:1, mean age (SD) 39 (12.35) years (range 20–67 years), disease duration (SD) was 9.92 (9.18) month (range 1–24). The mean disease activity by SLEDAI was 11.2±7.84 (range 2–34) and SLAM – 8.83±4.41 (range 3–22) points, both indices denoted high disease activity level. Mean PGA values were 48.93 (19.13) (range 10–80), and mean MDGA values 45 (19.04) (range 10–80). Also, PGA and MDGA didn't correlate with SLEDAI (r=0,25, p>0,05; r=0,27, p>0,05), while a statistically significant correlation was determined with SLAM index (r=0,85, p<0.001; r=0,46, p=0.002). A subclass analysis of SLAM components showed that cortical dysfunction (depression, psychosis) and the presence of headache correlated with PGA (r=0,36, p<0,05; r=0,4, p<0,05), so we can establish that the difference in correlation between SLAM and SLEDAI with PGA and MDGA is explained by a more accurate disease assessment by SLAM, including also subjective complaints that influences the global patient's status.
Conclusions: The use of SLAM for disease activity assessment in early SLE patients is more sensible than SLEDAI and its results correlates with PGA and MDGA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3710

SAT0297 SLE PATIENTS WITH SECONDARY SJÖGREN'S SYNDROME ARE CHARACTERIZED BY TYPICAL AUTOANTIBODIES AND A PRO-INFLAMMATORY STATE

M. Kvarnström[1], G. Ruacho[2], J.T. Gustafsson[3], A. Zickert[3], V. Oke[3], J. Rönnelid[4], K. Elvin[5], I. Gunnarsson[3], E. Svenungsson[3]. *[1]Dep. of Medicine, Unit of Experimental Rheumatology, Karolinska Institutet, Karolinska Uniververity Hospital, Stockholm; [2]Centre for Clinical Research Sörmland, Uppsala Univerity, Sörmland; [3]Dep. of Medicine, Unit of Rheumatology, Karolinska Institutet, Karolinska Uniververity Hospital, Stockholm; [4]Department of Immunology, Genetics and Pathology, Uppsala Univerity, Uppsala; [5]Unit of Clinical Immunology, Department of Clinical Immunology and Transfusion Medicine, Karolinska Institutet, Karolinska Uniververity Hospital, Stockholm, Sweden*

Background: Sjögren's syndrome occurs in isolation (primary Sjögren's syndrome, pSS), but it is also often secondary (sSS) to, and sometimes difficult to delineate from, other rheumatic diseases, in particular from systemic lupus erythematosus (SLE). Consequently there is a need to investigate similarities and differences between SLE patients with (SLE-sSS) and without sSS (SLE-noSS).
Objectives: To investigate the occurrence of sSS in a large cohort of SLE patients and to explore clinical and laboratory characteristics associated with SLE-sSS as compared to SLE-noSS and controls.
Methods: We included 504 consecutive SLE patients and 322 population controls, individually matched for age and gender to the first patients. All patients fulfilled the 1982 revised ACR criteria for SLE. SLE-sSS was defined according to the American-European consensus criteria (AECC). Accordingly, subjective and objective quantifications of sicca symptoms were recorded on all subjects. All underwent a thorough clinical investigation. SLE-associated autoantibodies, (ANA screening by BioPlex 2200 system, Bio-Rad) and Rheumatoid factor (RF, Phadia Immunocap 250) were determined with standardized methods for all subjects, Routine laboratory workup and a panel of cytokines (MSD 30-plex cytokine assays, performed on samples from 433 consecutive SLE patients and 319 controls) were measured on fasting blood samples.

Immunoglobulins, autoantibodies and pro-inflammatory cytokines in SLE-SS, SLE-noSS and population controls

	Controls N=322 median (IQR) or N(%)	SLE-SS N= 117 median (IQR) or N(%)	SLE-noSS N=387 median (IQR) or N(%)	p-value SLE-SS vs. SLE-noSS
IgA total g/L	2.1 (1.5-2.8)	2.9 (1.8-4.3)	2.7 (1.9-3.6)	0.38
IgG total g/L	10.9 (9.5-12.2)	14.5 (10.4-18.3)	12.4(9.8-15.8)	0.009
IgM total g/L	1.1 (0.8-1.6)	1.0 (0.5-1.6)	0.9 (0.6-1.5)	0.89
anti-dsDNA % positive (+)	5(1.6)	36(31.3)	154(41)	0.06
anti-Ro52 % +	3 (0.9)	56(47.9)	84(21.8)	<0.0001
anti-Ro60 % +	5 (1.6)	69(59)	137(35.9)	<0.0001
anti-La/SSB % +	10 (3.1)	44(37.6)	69(18)	<0.0001
anti-Sm % +	1 (0.3)	19(16.2)	75(19.5)	0.42
anti-RNP 68 % +	0 (0)	11(9.4)	40(10.4)	0.74
Rf IgG % +	10/261(3.8)	17/80(21.2)	35/259(13.5)	0.09
Rf IgM % +	14/283(4.9)	32/83(38.6)	56/281(19.9)	0.0005
Rf IgA % +	12/282(12.4)	34/74(45.9)	75/267(28.0)	0.004
TNF-α pg/mL	2.3(2.0-2.8)	4.9 (3.6-7.1)	4.4 (3.0-6.0)	0.008
IL-6 pg/mL	0.5 (0.4-0.7)	1.5 (0.8-3.0)	1.1 (0.6-2.0)	0.009
MCP-4 pg/mL	55.8 (40.8-80.5)	94.9 (66.9-131.3)	74.7 (52.4-120.0)	0.019
MIP-1 β pg/mL	43.7 (33.4-56.4)	81.1 ((54.8-123.6)	68.9 (50.3-105.1)	0.021
IL12/IL-23p40 pg/mL	131.2 (99.8-179.5)	211.3 (141.4-363.8)	177.1 (119.6274.5)	0.032
IP-10 pg/mL	351.9 (259.2 -476.4)	808 (536-1911)	726 (440-1471)	0.036

Results: SLE-sSS, as defined by AECC, occurred in 23% of the SLE patients. Compared to SLE-noSS the SLE-sSS group was older, both at inclusion (55 vs 43yrs, p<0.0001) and at disease onset (40 vs. 32 yrs p<0.0001), and with a greater number of females (96 vs. 83%, p=0.0007), higher occurrence of leucopenia (57 vs. 45%, p=0.02) and peripheral neuropathy (15 vs 7%, p=0.01). Nephritis was less common in SLE-sSS (32 vs 43%, p=0.03). Higher levels of total IgG, positivity for anti-SSA/Ro52, anti-SSA/Ro60, anti-SSB antibodies, RF IgM and RF IgA further characterized the SLE-sSS group. 20/30 investigated cytokines were detectable, of these 19/20 were higher in SLE than in controls. 6/20 cytokines (TNF-a, IL-6, MCP-4, MIP-1β, IL12/IL-23p40 and IP-10) were upregulated in SLE-sSS vs. SLE-noSS (see table for figures).
Conclusions: Through strictly applying the AECC criteria we report that the frequency of SLE-sSS increases with age and affects roughly ¼ of SLE patients. Nephritis was less common while leucopenia and peripheral neuropathy were more common among SLE-sSS patients. In addition to excess of well-known SS-associated autoantibodies we report higher levels of six pro-inflammatory cytokines in SLE-sSS as compared to SLE-noSS. These findings demonstrate that, though often regarded as a milder version of SLE, patients with SLE-sSS are characterized by a state of chronic systemic inflammation.
Acknowledgements: Susanna Eketjäll at Cardiovascular and Metabolic Diseases, Innovative Medicines and Early Development Biotech Unit, AstraZeneca, Integrated Cardio Metabolic Centre (ICMC), Karolinska Institutet, Huddinge, Sweden
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5449

SAT0298 INFLUENCE OF AGE ONSET IN CLINICAL AND BIOLOGICAL SPECTRUM OF SYSTEMIC LUPUS ERYTHEMATOSUS

M. Kechida[1], N. Lorenzo[2], I. Ben Chaaben[1], R. Klii[1], S. Hammami[1], I. Khochtali[1]. *[1]Internal Medicine and Endocrinology Department, Fattouma Bourguiba Hospital, Monastir, Tunisia; [2]Internal Medicine and cancerology Department, Saint-Cyr Hospital, Lyon, France*

Background: Systemic lupus erythematosus (SLE) is a multi systemic auto immune disease which can affect patients at any age.
Objectives: We aimed to study influence of age onset in clinical and biological spectrum of SLE
Methods: medical records of 89 patients diagnosed as SLE according to the ACR criteria of 1997, between January 2004 and December 2016, were retrospectively analyzed. Patients were divided into 3 groups according to the age of onset: Juvenile onset patients (group 1) (G1) (≤16 years), Adult onset patients (group 2) (G2) (>16 and <50 years), Late onset patients (group 3) (G3) (≥50 years). Clinical and biological comparative study was conducted between the 3 groups. Data were analyzed by chi-square test and potentially associated factors were tested by binary logistic regression.
Results: among the patients 11.2% are in G1, 75.3% in G2 and 13.5% in G3. Prevalence of SLE was higher in female than male (F/M=9/1) but predominance of women was lower in G1 (F/M=4/1) compared to G2 (F/M=10/1) and G3 (F/M=11/1). Patients in G3 had more hypertension (41.7%) compared to G2 (6%) (p=0.5) and G1 (0%) (p=0.04). Vespertilio erythema was less frequently found in G3 (33.3%) compared to G2 (64.2%) (p=0.045) and G1 (80%) (p=0.04). Anti Sm antibodies were more frequent in G1 (87.5%) compared to G2 (38.5%) (p=0.009) and G3 (18.2%) (p=0.003). Multivariate analysis showed that hypertension is significantly associated to late onset lupus (OR=29, 95% IC= [2.77 – 320], p=0.05) and anti Sm antibody is more frequent in juvenile onset patients (OR=12, 95% IC= [1.4- 117], p=0.024).
Conclusions: according to our study, prevalence of lupus is higher in female regardless of age onset. Late onset lupus is associated to a high frequency of co morbidity while anti Sm antibody seems to be a hallmark of juvenile onset.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3003

SAT0299 ATYPICAL ANTIBODIES IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

M. Fernandez Castro[1], J.L. Andreu[2], C. Sanchez-Piedra[3], V. Martínez Taboada[4], A. Olive[5], J. Rosas[6] on behalf of SJOGRENSER group, part of the Spanish Society of Rheumatology Systemic Autoimmune Diseases Study Group (EASSER). *[1]Rheumatology, Hospital Infanta Sofía; [2]Rheumatology, Hospital Puerta de Hierro Majadahonda; [3]Research unit, Spanish Society of Rheumatology, Madrid; [4]Rheumatology, Hospital Marque's de Valdecilla, Santander; [5]Rheumatology, Hospital Hospital Germans Trias i Pujol, Barcelona; [6]Rheumatology, Hospital Hospital Marina Baixa, Alicante, Spain*

Background: One of the main features of primary Sjögren's syndrome (pSS) is

the polyclonal activation of B cells, leading to the synthesis of a large variety of autoantibodies.
Objectives: The aim of this study is to describe the prevalence of atypical autoantibodies in patients with pSS from the SjogrenSER registry.
Methods: SjogrenSER registry is a multicenter transversal study of pSS patients fulfilling European/American consensus criteria 2002. Patients were included by randomization from thirty-three Rheumatology Spanish departments. Data were collected by reviewing clinical records and interviewing the patients. Informed consent was obtained and local ethics committees approved the study. Variables were analysed by descriptive statistical methods, using means, medians, and rates. Chi-square was used to establish the statistical associations, being considered a $p<0,05$ as significant.
Results: Four hundred and thirty-seven patients were included. Ninety-five percent of them were women. The median age of the cohort was 58 years. Twenty-three patients had AntiDNA (5.26%), 10 patients AntiSm (2.29%), 23 patients AntiRNP (5.26%) and 26 patients antiphospholipid antibodies (5.95%). Regarding AntiDNA+ patients, there were minimal non-significant differences in age at diagnosis and age at onset of symptoms compared to AntiDNA- patients (47 vs 50.5 years and 43.5 vs 46.5 years, respectively). The association with some systemic manifestation was only observed with joint involvement, which was significantly more frequent in AntiDNA+ patients (56.5% vs 34.2%, p=0.031). Regarding AntiSm+ patients, a significant negative association with AntiDNA antibodies was observed, being 70% of patients AntiDNA-; we also found a significant positive association with AntiRo and AntiLa, being 100% and 68% of patients AntiRo+ and AntiLa+ respectively. A significant negative association with lymphopenia was observed (no AntiSm+ patient had lymphopenia). AntiRNP+ patients showed a significant negative association with AntiDNA antibodies, being 80% of patients AntiDNA-, and a significant positive association with AntiRo, being 96% patients AntiRo+. A significant positive association was also observed with decreased C4 compared to AntiRNP- patients (28% vs 13.38%, p=0.025). Regarding patients with antiphospholipid antibodies, a significant negative association was observed with antiDNA antibodies, being 93% of patients AntiDNA-. A significant positive association with some systemic manifestation was only observed with the presence of anemia (44% vs 17.7%). A significant positive association with decreased C3 and C4 was also observed, compared with the AntiRNP- patients (C3 20% vs 13.67% and C4 33% vs 12.67%).
Conclusions: More than 5% of pSS patients had antibodies characteristic of other autoimmune diseases. These atypical autoantibodies were significantly related to some pSS characteristic: antiSm, antiRNP and antiphospholipid antibodies were significantly related to the presence of antiRo, antiDNA antibodies were significantly related to joint involvement, antiphospholipid antibodies were significantly related to anemia, and antiRNP and antiphospholipid antibodies were significantly related to hypocomplementemia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2600

SAT0300 HIGH PROPORTIONS OF DEMENTIA AMONG SLE PATIENTS: A BIG DATA ANALYSIS

O. Gendelman[1,2], S. Tiosano[1,2], D. Comaneshter[3], A. Cohen[3,4], Y. Shoenfeld[1,2], H. Amital[1,2]. *[1]Internal Medicine 'B', Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Ramat-Gan; [2]Sackler School of Medicine, Tel-Aviv University; [3]Chief physician's office, Clalit Health Services, Tel-Aviv; [4]Siaal Research Center for Family Medicine and Primary Care, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease affecting wide range of systems including the peripheral and central nervous system[1]. Cognitive impairment leading to dementia is one of the harmful central nervous system manifestations of SLE[2].
Objectives: The aim of this study was to investigate the association of SLE and dementia.
Methods: A cross-sectional study was performed utilizing Clalit Health Care database, the largest HMO in Israel with more than 4.4 million enrollees. SLE patients were compared in a 1:5 ratio to age and sex matched controls. Chi-square and *t* tests were used for univariate analysis, and a logistic regression model was used for multivariate analysis.
Results: The study included 4886 SLE patients and 24,430 age and sex frequency matched controls without SLE. The proportion of dementia was higher among SLE patients compared to controls (1.56% and 0.51% respectively; $p<0.001$).
This finding was consistent across all age groups by univariate analysis.
In a multivariate logistic regression analysis, SLE was significantly associated with dementia (OR =2.039, 95% CI =1.110–2.039).
Conclusions: SLE is significantly associated with dementia. This finding should give rise to search for SLE in patients with an ambiguous cause for dementia, especially those with an early onset cognitive decline.
References:
[1] Tsokos GC. Systemic Lupus Erythematosus. N Engl J Med. 2011;365(22): 2110–2121.
[2] Liang MH, Corzillius M, Bae SC, et al. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum. 1999;42(4):599–608.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5245

SAT0301 SERUM AUTOANTIBODY PROFILING OF PRIMARY SJÖGREN'S SYNDROME PATIENTS REVEALS NOVEL BIOMARKERS ASSOCIATED WITH THE DISEASE, DISEASE ACTIVITY, AND CLINICAL RESPONSE TO VAY736

P. Budde[1], J. Doucet[2], H.-D. Zucht[1], R. Kazma[2], P. Maguire[2], A. Avrameas[2], M.-A. Valentin[2], S. Oliver[3], P. Schulz-Knappe[1], A. Vitaliti[2]. *[1]Medical Research, Protagen, Dortmund, Germany; [2]Translational Medicine/Biomarker Development; [3]Translational Medicine, Novartis Institutes for Biomedical Research, Basel, Switzerland*

Background: Overexpression of B cell activating factor (BAFF) in salivary glands contributes to the pathogenesis of primary Sjögren's syndrome (pSS) by promoting autoantibody (AAB) production. Treatment of pSS patients with VAY736, an anti-BAFF receptor mAb, appears promising and was associated with a depletion of circulating B cells and a positive therapeutic effect [1]. In addition to the classical anti-SS-A/Ro and anti-SS-B/La, a broader set of AABs may reflect B cell disturbances in pSS and could serve as markers during clinical development of novel pSS therapeutics.
Objectives: In this study, we explored novel AABs in pSS patients and healthy controls (HCs) and we tested their associations with the disease, disease activity, and clinical response to VAY736.
Methods: Reactivity of AABs to 1,596 antigens was measured in serum samples from 27 pSS patients from a placebo-controlled trial at baseline and post-treatment week 12 and from 50 age and gender-matched HCs. Patients were treated at baseline with a single dose of VAY736 at 10 mg/kg (n=12), 3 mg/kg (n=6), or placebo (n=9). First, to identify AABs associated with pSS, 3 different methods compared AAB levels at baseline between pSS patients and HCs: Wilcoxon rank sum test, significance analysis of microarrays, and comparison of the 90th quantiles between groups. Second, to identify AABs associated with pSS activity, Pearson correlation of AABs with EULAR Sjögren's Syndrome Disease Activity Index, secondary outcomes, and salivary and serum BAFF were tested, using baseline and week 12 levels as well as relative changes. Third, VAY736 treatment-specific changes in AAB levels were investigated using linear mixed-effects models adjusting for dosage, age, and gender effects.
Results: Of 1,596 antigens, 36 were statistically different between pSS patients and HCs for at least one of the 3 tests, including the known SS-A/Ro and SS-B/La (significant for all 3 tests) as well as novel antigens. SS-A/Ro and SS-B/La AABs were not associated with disease activity or response to treatment. However, 48 AABs were significantly correlated with pSS activity combining all treatment arms, and 12 AABs had baseline values that correlated with change in pSS activity upon VAY736 treatment (unadjusted $p<0.05$). Interestingly, 51 serum AABs correlated with BAFF saliva levels ($|r|>0.55$), but not with BAFF serum levels. The genes encoding novel antigens are involved in apoptotic, anti-viral, metabolic, inflammatory, blood coagulation and B-cell processes, suggesting a possible link to the disease pathology.
Finally, there was no reduction in AABs levels in response to VAY736, possibly because the 12 weeks post-treatment analysis was too short to identify large effects.
Conclusions: In conclusion, we identified new AABs in pSS patients that have the potential to serve as markers of diagnosis, pSS activity, or as predictors of clinical outcome measures. Further large-scale studies are needed to confirm the value of these markers.
References:
[1] Dörner T et al. Arthritis Rheum 2016; 68(suppl S10):4051.
Disclosure of Interest: P. Budde Employee of: Protagen AG, J. Doucet Employee of: Novartis AG, H.-D. Zucht Employee of: Protagen AG, R. Kazma Employee of: Novartis AG, P. Maguire Employee of: Novartis AG, A. Avrameas Employee of: Novartis AG, M.-A. Valentin Employee of: Novartis AG, S. Oliver Employee of: Novartis AG, P. Schulz-Knappe Employee of: Protagen AG, A. Vitaliti Employee of: Novartis AG
DOI: 10.1136/annrheumdis-2017-eular.1905

SAT0302 ANALYSIS OF 9302 PATIENTS FROM THE BIG DATA INTERNATIONAL PRIMARY SJÖGREN SYNDROME COHORT: CLINICAL PRESENTATION AT DIAGNOSIS OF EUROPEAN VS NON-EUROPEAN PATIENTS

P. Brito-Zerón[1,2], N. Acar-Denizli[3], M. Zeher[4], A. Rasmussen[5], R. Seror[6], T. Mandl[7], X. Li[8], C. Baldini[9], J.-E. Gottenberg[10], D. Danda[11], R. Priori[12], L. Quartuccio[13], G. Hernandez-Molina[14], A.A. Kruize[15], S.-H. Park[16], M. Kvarnström[17], S. Praprotnik[18], D. Sene[19], E. Bartoloni[20], R. Solans[21], Y. Suzuki[22], D. Isenberg[23], M. Rischmueller[24], G. Nordmark[25], G. Fraile[26], A. Sebastian[27], A. Vissink[28], T. Nakamura[29], V. Valim[30], R. Giacomelli[31], V. Devauchelle-Pensec[32], B. Hofauer[33], M. Bombardieri[34], V. Trevisani[35], D. Hammenfors[36], S.E. Carsons[37], S.G. Pasoto[38], J. Morel[39], S. Retamozo[40], T.A. Gheita[41], F. Atzeni[42], C. Vollenveider[43], X. Mariette[6], M. Ramos-Casals[2] on behalf of the EULAR-SS Task Force Big Data Consortium. *[1]Hosp CIMA-Sanitas; [2]Hosp Clínic, Barcelona, Spain; [3]Msgsü, Istanbul, Turkey; [4]Univ, Debrecen, Hungary; [5]OMRF, Oklahoma, United States; [6]Univ Paris Sud, Paris, France; [7]Lund Univ, Malmö, Sweden;[8]Anhui Hosp, Hefei, China; [9]Univ, Pisa,*

Italy; [10] Univ, Strasbourg, France; [11] CMC, Vellore, India; [12] Sapienza Univ, Rome; [13] Santa Maria, Udine, Italy; [14] INCMNSZ, México City, Mexico; [15] UMC, Utrecht, Netherlands; [16] Catholic Univ Korea, Seoul, Korea, Republic Of; [17] Karolinska Instit, Stockholm, Sweden; [18] UMCL, Ljubljana, Slovenia; [19] Lariboisière Hosp, Paris, France; [20] Univ, Perugia, Italy; [21] Hosp Vall d'Hebron, Barcelona, Spain; [22] Univ Hosp, Kanazawa, Japan; [23] UCL, London, United Kingdom; [24] TQEH, Adelaide, Australia; [25] Univ, Uppsala, Sweden; [26] Hosp Ramón y Cajal, Madrid, Spain; [27] Med Hosp, Wroclaw, Poland; [28] Univ, Groningen, Netherlands; [29] Univ, Nagasaki, Japan; [30] UFES, Vitória, Brazil; [31] Univ, L'Aquila, Italy; [32] Univ, Brest, France; [33] TUM, München, Germany; [34] QMUL, London, United Kingdom; [35] UNIFESP, Sao Paulo, Brazil; [36] Haukeland Hosp, Bergen, Norway; [37] School Med SBU, Mineola, United States; [38] USP, Sao Paulo, Brazil; [39] Univ, Montpellier, France; [40] INICSA, Cordoba, Argentina; [41] Univ, Cairo, Egypt; [42] L.Sacco Univ, Milan, Italy; [43] German Hosp, Buenos Aires, Argentina

Objectives: Baseline characterization of European patients diagnosed with primary Sjögren syndrome (SS) according to the 2002 AE criteria.
Methods: The Big Data Sjögren Project was formed in 2014 to take a "high-definition" picture of the main features of primary SS by merging international SS databases. International experts of the EULAR-SS Task Force were invited to participate. By January 2017, the database included 9302 consecutive patients recruited from 21 countries of the 5 continents.
Results: A total of 6586 (71%) patients were included from European countries. In comparison with non-European countries, European patients had a higher mean age (54 v 51yrs, p<0.001), higher frequency of men (7% v 5%, p=0.001), dry eyes (94% vs 88%, p<0.001), dry mouth (94% vs 91%, p<0.001), and lower frequency of abnormal ocular (84 vs 86%, p=0.049) and oral (75 vs 81%, p<0.001) tests. Immunologically, European patients had a lower frequency of anti-Ro/La antibodies (69 vs 78%, p<0.001) and a higher frequency of RF (50 vs 47%, p=0.01), low C4 (14 vs 9%, p<0.001) and cryoglobulins (8% vs 3%, p<0.001). Logistic regression identified as independent variables older age (OR 1.02), male gender (OR 2.62), abnormal oral tests (OR 0.26), anti-Ro/La antibodies (OR 0.69), RF (OR 1.76), low C4 (OR 1.97) and cryoglobulins (OR 3.85).
Conclusions: European patients are diagnosed at older age, are more frequently men, and presented a lower frequency of anti-Ro/La antibodies and a higher frequency of immunological markers related to mixed cryoglobulinemia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3502

SAT0303 CLINICAL DIFFERENCES BETWEEN DEFINITE AND PROBABLE ANTIPHOSPHOLIPID (APS) PATIENTS: SHOULD THEY BE TREATED THE SAME?

F. Signorelli, G. Balbi, R.A. Levy. *Rheumatology, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil*

Background: The management of patients with recurrent thromboses/pregnancy morbidity and transient detection of antiphospholipids antibodies (aPL) can be a medical challenge. Although these patients are commonly seen in practice, there are no specific guidelines for the treatment in this situations.
Objectives: To investigate the clinical differences between definite and probable APS patients.
Methods: We performed a cross-sectional study in a group of 90 outpatients seen in our department. Seventy-seven of them met the Sydney classficiation criteria for definte APS, and thirteen had thrombosis or gestational morbidity, but no definite serological criteria for the diagnosis of APS. Clinical and serological features were collected during visits and by chart review, and the two groups were compared. Transient aPL was defined as only one detection of aPL (lupus anticoagulant, anticardiolipin IgM/IgG and/or anti-beta-2-glycoprotein 1 IgM/IgG) after 2 or more assays, at least 12 weeks apart.
Results: Demographic and clinical characteristics are shown in Table 1. In a bivariate analysis, there was no difference between groups regarding the criteria and non-criteria manifestations of APS, except for the presence of livedo (p=0.033). In a multivariate regression analysis, the model was adjusted to age, sex, and variables with p<0.10 in the bivariate analysis (age, sex, race, livedo, Raynaud's phenomenon). No difference between groups was found after the analysis.
Conclusions: This study suggests patients with transient detection of aPL have the same clinical characteristics of patients with definite APS, including thrombotic features, pregnancy morbidity, and non-criteria manifestations. In this context, our data suggests that both groups should be treated according to the current treatment guidelines for APS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6987

Table 1. Demographic and clinical characteristics (N=90)

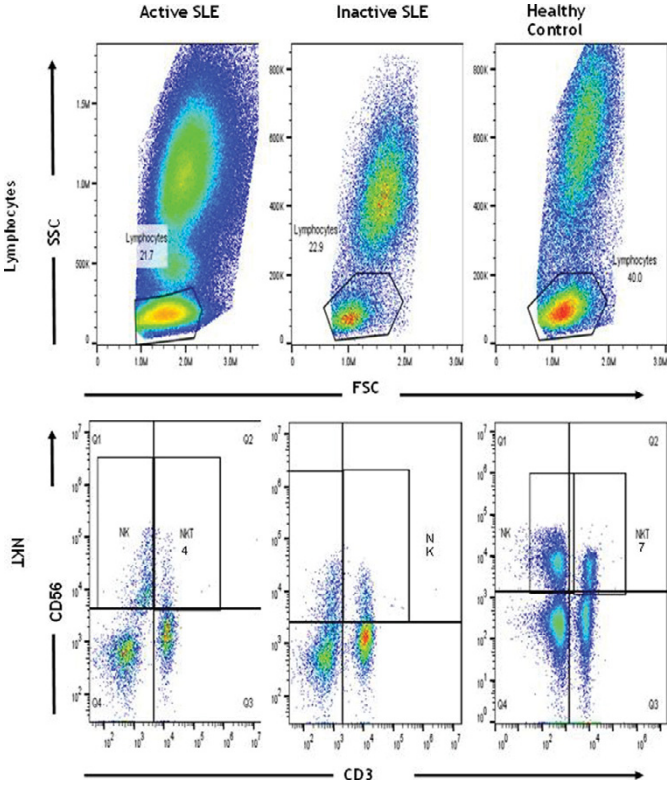
Variable	Definite APS (N=77)	Probable APS (N=13)	P value
Age	42.0±12	40.5±10.3	NS
Female gender	64 (83.1)	12 (92.3)	NS
Caucasian	50 (64.9)	8 (61.5)	NS
Time first manifestation (mo)	120 (33.3–50)	174 (81–202)	NS
	Criteria manifestations		
Thrombotic	72 (93.5)	13 (100)	NS
Obstetric	28 (43.8)*	1 (8.3)**	NS
	Non criteria		
Livedo	20 (26)	0 (0)	p=0.033
Thrombocytopenia	11 (14.3)	0 (0)	NS
Valvulopathy**	7 (11.7)‡	1 (11.1)‡‡	NS
Raynaud phenomenon	21 (27.3)	1 (7.7)	NS
Migraine	36 (46.8)	8 (61.5)	NS

*N=64; **N=12, ‡N=60, ‡‡N=9. Mo = months. CVD = cardiovascular disease. Values showed as N (%) for categorical variables, mean ± SD for normal distribution and Median (interquartil range) for asymmetric distribution.

SAT0304 STIMULATORY AND INHIBITORY KILLER IMMUNOGLOBULIN-LIKE RECEPTORS ON NATURAL KILLER T (NKT) CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): RELATION TO DISEASE ACTIVITY

S.I. Nasef [1], A.M. Asker [2], H.H. Omar [2], H.M. Hassoba [2]. *[1] Physical Medicine, Rheumatology and Rehabilitation; [2] Clinical Pathology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt*

Background: Natural killer T (NKT) cells are a unique subgroup of T cells that represents a bridge between innate and adaptive immunity. The functions of NKT-cells are regulated by the balance between activating and inhibitory Killer cell immunoglobulin-like receptors (KIRs). Systemic lupus erythematosus (SLE) patients showed aberrant expression of KIRs on NKT-cells. Whether the expression pattern of KIRs on NKT-cells is associated with disease activity in SLE is still unknown.
Objectives: Assessment of expression of stimulatory and inhibitory KIRs on NKT-cells in SLE patients and its relation to disease activity.
Methods: We recruited 40 SLE patients and 20 age and gender matched healthy controls. According to SLE disease activity index (SLEDAI), patients were divided into two groups; active SLE (n=20) and inactive SLE (n=20). SLE was active when SLEDAI was ≥4. Immuno-phenotyping by flow cytometry was done using markers for NKT-cells (CD3 and CD56), stimulatory KIRs (KIR2DL4, CD158D) and inhibitory KIRs (KIR3DL1, CD158E1). Absolute counts and percentage of NKT cells expressing CD158D and CD158E1 together with their mean fluorescence intensity (MFI) were measured. The histogram of CD158 expression was used to assess KIRs on NKT cells.
Flow cytometry charts of lymphocytes and NKT cells in SLE patients (active and inactive) and controls are shown in (Figure 1).
Laboratory work included ANA, anti-dsDNA, Anti-smith, C3, C4, CRP and ESR.
Results: Mean age of patients was 29.9±10.8 years. Females constituted 95% (n=38) of patients. Mean disease duration was 4.4±4.5 years. Mean SLEDAI was 11.75±7.43.
NKT-cells absolute number (cell/mm^3) was significantly decreased in SLE patients (89±135) compared to controls (287±133), (*P*=0.001). Likewise, the absolute number of NKT-cells (cell/mm^3) was significantly lower in active SLE patients (65.2±57.8) compared to inactive ones (114.5±181.1), (*P*=0.001).



The expression of inhibitory KIRs was significantly lower in SLE patients (2.83±2.8%) compared to controls (5.54±2.01%) *(P*=0.001) While, stimulatory KIRs were significantly higher in SLE patients (3.2±3.7%) than controls (1.02±0.5%), (*P*=0.001). Active SLE patients showed significantly increased expression of stimulatory KIRs (5.29±4.29%) than inactive patients (1.13±0.89%), (*P*=0.004). However, inhibitory KIRs were significantly decreased in active (1.28±1.32%) than inactive SLE patients (4.38±3.05%), (*p*=0.003).
Expression of stimulatory KIRs correlated positively with ESR (*r*=0.3, *P*=0.04) and negatively with C4 (*r*=-0.4, *P*=0.01). In contrast, inhibitory KIRs correlated negatively with ESR (*r*=-0.5, *P*=0.003) and positively with C4 (*r*=0.4, *P*=0.02).
Using Receiver operating characteristic (ROC) curve analysis, expression of inhibitory KIRs on NKT-cells predicted disease activity at a cut-off value of ≤1.7% with 80% sensitivity and 80% specificity *(P*=0.001). While, expression of stimulatory KIRs on NKT-cells predicted active disease at a cut-off value of >1.4%, sensitivity (85%), and specificity (80%) *(P*=0.001*)*.
Conclusions: SLE activity is associated with an increased expression of stimulatory KIRs as well as a decreased expression of inhibitory KIRs on NKT cells. This may play a role in the pathogenesis of flares and acceleration of disease activity in SLE and could be a therapeutic target for SLE patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3920

SAT0305 HISTOLOGY OF MINOR SALIVARY GLANDS IN PATIENTS WITH SJÖGREN'S SYNDROME, ASSOCIATION WITH CLINICAL AND LABORATORY ASPECTS

S. Colafrancesco[1], F. Arienzo[1], B. Cerbelli[2], A. Gattamelata[1], A. Minniti[1], G. Picarelli[1], C. Giordano[2], G. D'Amati[2], R. Priori[1], G. Valesini[1]. *[1]Dipartimento di medicina interna e specialità mediche; [2]Dipartimento di radiologia, Oncologia e Scienze Radiologiche, Sapienza University of Rome, Rome, Italy*

Background: Minor salivary gland (MSG) biopsy represents an useful tool not only for the diagnosis of primary Sjogren's Syndrome (pSS) but also to evaluate patients prognosis. Recognition of germinal centers (GCs) by hematoxilin eosin (HE) and/or IHC staining for follicular dendritic cells (FDC) detection is mandatory, representing a risk factor for lymphoma development. Focus score (FS) is one of the main instrument to quantify MSG impairment, nonetheless quality information regarding the type of infiltrate such as the entity, structure and localization, are lacking.
Objectives: Aim of this study is to find any association of specific histological features of MSG from patients with pSS with the principal clinical and laboratory features. Moreover, to investigate the utility of histological parameters, other than FS or GCs, for characterizing patients.
Methods: Patients with pSS were enrolled in our SS clinic, and clinical/laboratory data (table) referring to the time of MSG biopsy, gathered on a dedicated database. MSG, removed for diagnostic purposes, were preserved as paraffin embedded tissue, then cut and sequentially stained by H&E and IHC [polyclonal rabbit anti-CD3 (lymphocytes T); monoclonal mouse anti-CD20 (lymphocytes B); monoclonal mouse anti-CD21 (FDC)]. Images were collected by Zeiss Axio Scan and analysed (ZEN software) as follows: FS calculation, mean foci area, percentage of infiltration, presence of segregated foci (SF) (specifically, clear evidence of T and B cells area by CD3-CD20 double staining), GCs and lymphoepithelial lesions (LELs) detection.
Results: 53 MSG from patients with pSS were collected and analysed. Patients clinical and laboratory data are reported in table. FS positively correlated with the percentage of infiltration (p<0.001) as well as with the presence of SF (p=0.005), GCs (p=0.02) and LELs (P=0.005). Mean foci area and percentage of infiltration correlated with SF (p=0.0002 and p<0.001, respectively), GCs (p=0.0004 and p<0.001, respectively) and LELs (both p<0.001). SF correlated with GCs and LEL (p<0.001). Anti nuclear antibodies (ANA) were associated with the presence of SF (p=0.029, OR=5.7 CI=1.1–28.8) while gland swelling was associated with the presence of GCs (p=0.043, OR=4, CI=1.1–15).

Clinical features	Number (%)
Sex (M/F)	4/49
Mean age at diagnosis (mean±SD, years)	54.9±12.1
Xerophtalmia	47/53 (88.6)
Xerostomia	47/53 (88.6)
Salivary gland swelling	16/53 (30.1)
Arthritis	8/53 (15)
Lymphoma	0/53 (0)
Purpura	2/53 (3.7)
PNS and/or CNS involvement	1/53 (1.8)
Pancreatitis	1/53 (1.8)
Laboratory features	
ANA	39/53 (73.6)
Anti-Ro/SSA	17/53 (32.1)
Anti-La/SSB	14/53 (26.4)
Hypergammaglobulinaemia	18/53 (33.9)
Rheumatoid factor	10/53 (19)
Leukopenia	8/53 (15)
Hypocomplementemia	6/53 (11.3)
Monoclonal component	8/53 (15)
Cryoglobulinaemia	2/53 (3.7)

Conclusions: The FS was associated with the presence of GCs and LELs, as well as with more organized infiltrates characterized by segregation in T and B areas (SF), thus representing an useful tool which mirrors the risk of lymphoma. From our study, the qualitative characteristics of the biopsy, including SF, percentage of infiltration or the mean foci area, appear to be strictly linked. Moreover, their association with the presence of GCs and LELs supports the importance to consider also these features during histological examination. The lack of correlation between histological parameters and clinical/laboratory features might reveal a weaker connection between histological findings and specific SS phenotypes except for the relationship between glandular swelling and GCs which confirms how this clinical aspect should be considered as a risk factor for lymphoma development.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5862

SAT0306 ASSOCIATION BETWEEN QUALITY OF SLEEP, QUALITY OF LIFE AND DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

S. Monov[1], D. Monova[2], M. Ivanova[3]. *[1]Department of Rheumatology, Medical University - Sofia; [2]Department of Internal Diseases, Medical University - Sofia, Medical Institute; [3]Department of Internal Diseases, Medical Institute, Sofia, Bulgaria*

Background: Systemic Lupus Erythematosus (SLE) patients are known to have sleep disturbances. Quality of sleep may affect quality of life, but this association has not been systematically evaluated.
Objectives: The aim of this study was to examine the association of quality of sleep, quality of life and SLE disease activity in patients diagnosed with SLE.
Methods: 132 SLE patients with a confirmed diagnosis of SLE according to the ACR classification criteria were enrolled in this study. The patients completed the following questionnaires: the Pittsburgh Sleep Quality Index (PSQI), the 12 item Short Form Health Survey (SF-12), the Lupus Patient-Reported Outcome tool (LupusPRO), SLE Quality of Life Questionnaire (SLE - QoL). Clinical information, including the SLE Disease Activity Index (SLEDAI), was obtained from medical records. Student's t-test, ANOVA, Pearson correlation measured were used in statistical analysis.
Results: The majority of the participants (84,4%) had sleep disturbances (PSQI >5). Total PSQI score was weakly associated with all of the SF-12 subcategories and showed weak to moderate associations with the LupusPRO subcategories (r <0,05), except for "medication" (r <0,20). "Sleep duration" was not associated with any of the SF-12 or LupusPRO subcategories. "Sleep efficiency" was weakly associated with "physical health", "physical function", and "pain" in the SF-12 and LupusPRO. "Sleep quality" and "sleep disturbances" were weakly associated with "pain" and the "emotional" and "mental" subcategories in the SF-12 and LupusPRO. SLE - QoL was significantly higher in patients with good sleep.
Conclusions: We found that quality of sleep, especially "sleep efficiency", was poor for the majority of patients with SLE. Quality of sleep was associated with various aspects of quality of life, especially pain, vitality, and emotional health. Management of pain and emotional health may be important for improving quality of sleep in SLE patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1450

SAT0307 RECURRENCE RATE OF THROMBOSIS FOR PATIENTS WITH ANTI-PHOSPHOLIPID ANTIBODIES INITIALLY AND DISAPPEARED LATER AFTER THROMBOSIS

S.M. Kim[1], J. Kim[2], Y. Kim[3], S.W. Kang[2], S.-C. Shim[2], S.-J. Yoo[3]. *[1]Internal Medicine, Chungbuk National University Hospital, Cheong-ju; [2]Internal Medicine, School of Medicine Chungnam National University; [3]Internal Medicine, Chungnam National University Hospital, Daejeon, Korea, Republic Of*

Background: In case of anti-phospholipid syndrome, anticoagulants are recommended. However, there were no data about recurrence rate for thrombosis in patients with anti-phospholipid antibodies (APS) initially which disappeared later.
Objectives: We compared recurrence rate of thrombosis between negative conversion group and control group.
Methods: We reviewed the medical records of patients diagnosed with thrombosis such as cerebral infarct, myocardial infarct, deep vein thrombosis, or thrombosis of other vessels at a tertiary medical center from 2000 to October 2016. Of these, 14 patients whose APA status was converted from positive to negative after more than 12 weeks were enrolled as negative conversion group. Forty-six patients without APA were matched with the ratio of 1:3∼1:4 according to age, sex, thrombosis type (arterial or venous) and therapeutic agents as control group.
Results: There was no difference between negative conversion group and control group in smoking status, presence of diabetes or hypertension, duration from the thrombosis to last visits or to recurrence, the proportion of patients taking glucocorticoids. There was no difference in the overall recurrence of thrombosis between two groups [negative conversion group, 3/14 (21%) vs. control group,

6/46 (13%), p=0.423]. In the negative conversion group, the number of patients diagnosed with SLE was significantly higher than the control group [SLE, 3/14 (21%) vs. 1/46 (2%), p=0.036]. However, thrombosis had recurred in one out of three patients with SLE.
Conclusions: The cumulative incidence of thrombotic events was not significantly different between negative conversion group and control group.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5787

SAT0308 CLINICAL, BIOLOGICAL AND IMMUNOLOGICAL FEATURES OF SJÖGREN SYNDROME: A STUDY OF 270 TUNISIAN PATIENTS

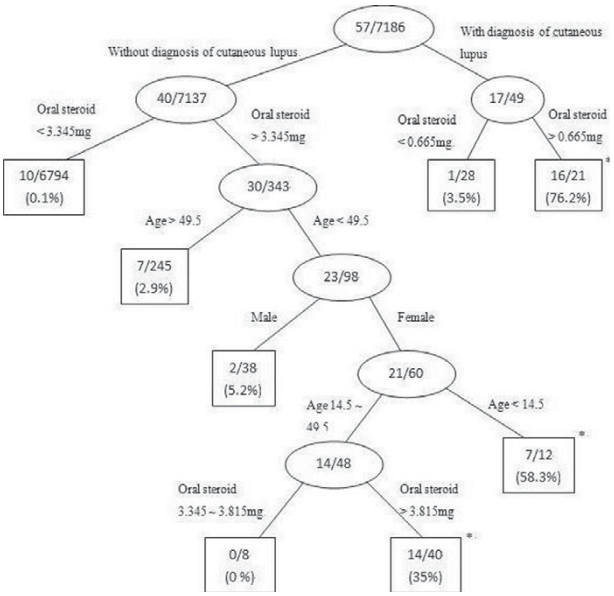
T. Ben Salem, I. Naceur, M. Lamloum, I. Ben Ghorbel, M.H. Houman. *Internal Medicine, Rabta university hospital, Tunis, Tunisia*

Background: Sjögren syndrome (SS) is a chronic autoimmune disease characterized by a sicca syndrome and a wild spectrum of extra-glandular manifestations.
Objectives: The aim of this study was to describe clinical, biological and immunological characteristics of patients with SS and to compare them in primary and associated SS.
Methods: We conducted a monocentric, retrospective study over a period of 15 years. Patients who fulfilled the American European Consensus Group criteria for Sjögren syndrome were enrolled.
Results: SS was diagnosed in 270 patients. The sex-ratio female/male was 10.73. The mean age at disease onset was 45 years +/- 13 years (range 15–74 years) and at diagnosis was 47 years +/- 13 years (range 15–76) with a mean delay of 3 years (range 0–25 years). Sicca syndrome revealed the disease in most cases; both ocular and buccal dryness (n=48), xerophtalmia (n=21), xerostomia (n=21) or parotid gland swelling (n=17). SS was also revealed by joint involvement (n=39), neurological manifestations (n=26) or interstitial lung disease (n=14). SS was systematically screened in 27 patients with another autoimmune disease and was found in 3 mothers who had a child with congenital atrio-ventricular bloc. Patients complained of xerophtalmia and xerostomia in respectively 95.2% and 95% of cases. Minor salivary biopsy was positive in 92.6% of cases. Parotid gland swelling was noted in 40 cases. Arthralgia and arthritis were respectively noted 77% and 18% of cases whereas myalgia and myositis were found in 11% and 5% of patients. Patients had pulmonary involvements in 27% of cases. Peripheral and central nervous system involvements were confirmed in 22% and 13% of cases and 12 patients presented with psychiatric disorders. Raynaud's phenomenon and purpura were noted in 48 and 17 patients. Biological data showed lymphopenia (n=115), anemia (n=83), thrombocytopenia (n=25) and hypergammaglobulinemia (n=151). Antinuclear antibodies were positive in 210 cases; anti-SSA and anti-SSB were present in respectively 57% and 37% of patients. SS was primary in 155 patients and was associated to another autoimmune disease in 113 patients; systemic lupus erythematosus (n=48), rheumatoid arthritis (n=20), systemic sclerosis (n=19), autoimmune liver disease (n=13) and auto-immune thyroiditis (n=9). Arthralgia (91.2% vs 66.2; $p<0.0001$), arthritis (35.7% vs 5.2%; $p<0.0001$), myalgia (17% vs 7.1%; p=0.012) and Raynaud's phenomenon (33.3% vs 7.7%; $p\leq0.0001$) were significantly less frequent in primary SS. Lymphopenia (61.1% vs 32.9%; $p<0.0001$), anemia (48.6% vs 19.5%; $p<0.0001$), inflammatory syndrome (35.8% vs 17.9; p=0.002) and ANA (92% vs 70.9%; $p<0.0001$) were significantly more frequent in associated SS. Corticosteroids and immunosuppressive therapy were used in respectively 141 and 90 patients because of severe complications. Only 3 case of lymphoma were observed and 3 patients died. The mean duration of follow up was 50 months.
Conclusions: Sicca syndrome is the major symptom of SS but extra-glandular manifestations are less frequent and can be serious causing disability specially neurologic and pulmonary involvements. Some manifestations are significantly more frequent in patients with associated autoimmune diseases like joint involvements, Raynaud's phenomenon, anemia and lymphopenia. These manifestations are mainly related to SLE, rheumatoid arthritis and systemic sclerosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3589

SAT0309 CAN WE FORESEE SLE IN ITP PATIENTS? TO DISTINGUISH ITP PATIENTS WITH HIGH RISK OF SLE BY A NATIONWIDE COHORT STUDY-BASED DECISION TREE

T.-H. Li[1], Y.-S. Chang[2], C.-Y. Tsai[3]. *[1]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Chiayi Branch, Taichung Veteran General Hospital, Chiayi City; [2]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Taipei Hospital, Ministry of Health and Welfare, New Taipei City; [3]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Taipei Veteran General Hospital, Taipei City, Taiwan, Province of China*

Background: Immune thrombocytopenic purpura (ITP) is an autoimmune-associated thrombocytopenia which is occasionally the initial presentation of systemic lupus erythematosus (SLE), and thus periodical following up has been suggested. Whereas long-term surveillance on all ITP patients would be time and cost-consuming, and thus to distinguish those with high probability of SLE development among ITP patients should be more practical.
Objectives: To distinguish ITP patients with high risk of SLE development by a decision tree model.
Methods: We enrolled ITP patients without previous SLE diagnosis from the National Health Insurance research database between 1997 and 2012 and identified those certificated with catastrophic illness of SLE during follow up, by which the diagnosis was reconfirmed by another rheumatologists. We also analyzed the symptoms and comorbidities as well as the dose of average oral steroid to derive the decision trees, which classified the ITP patients with different probability of development of SLE.
Results: A total of 10,265 ITP patients were enrolled, among whom 80 patients developed SLE while following-up. The whole ITP patients were allocated to training group (7,186 patients including 57 with SLE) and testing group (3,079 patients including 23 with SLE); the former was used for derivation of the decision-tree based model and the latter for validation of the previously mentioned model, and provided high sensitivity (78.2%), specificity (99.2%) and negative prediction value (99.8%, Fig.). To reduce the complexity, we also pruned our decision tree to propose less-complicated models.



Conclusions: We derived classification decision tree suitable for various clinical scenarios of ITP patients, among whom those with high probability of development of SLE would be distinguished.
References:
[1] Balsalobre Aznar J, Herráez Herrera P, Porta Etessam J, Torres Martín C, Bermell Serrano JC, Núñez López R, et al. Idiopathic thrombocytopenic purpura as first manifestation of systemic lupus erythematosus lupus. An Med Interna. 1999;16:611–4.
[2] Risk factors for future development of systemic lupus erythematosus in children with idiopathic thrombocytopenic purpura. Pediatr Blood Cancer. 2006;47(5 Suppl):657–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1359

SAT0310 ULTRASONOGRAPHIC SCORING OF THE MAJOR SALIVARY GLANDS IN SJOGREN'S SYNDROME: A COMPARATIVE STUDY WITH DISEASE ACTIVITY INDEXES

N. İnanç[1], Y. Yalçınkaya[1], G. Mumcu[2], Z. Ertürk[1], A.U. Unal[1], P. Atagündüz[1], H. Direskeneli[1]. *[1]Department of Internal Medicine, Division of Rheumatology, Marmara University, School of Medicine; [2]Marmara University, Faculty of Dentistry, Istanbul, Turkey*

Background: Sjogren's syndrome (SjS) is characterised by chronic autoimmune inflammation primarily affects the salivary and lacrimal glands. Recently, ultrasonography (USG) of major salivary glands (SG-USG) has been used to evaluate salivary glands in primary and secondary SjS.
Objectives: We aimed to investigate the association between the ultrasonographic scoring of major salivary glands and disease activity indexes in patientswith primary SjS.
Methods: Forty-two primary SjS patients fulfilling ACR-EULAR classification criteria (2002) were included. Disease activity indexes (Sjögren's Syndrome Patients Reported Index (ESSPRI), Visual Analogue Scale (VAS), EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI)] were recorded. Major salivary glands (bilateral parotis and submandibular glands) were scored according to two different scoring system [Hocevar A. (0–48) ve Milic VD. (0–12)].
Results: Demographics, clinical characteristics, disease activity indexes and SG-USG scores were summarised in table 1 and table 2.

Table 1. Demographics and Clinical Characteristics of SjS patients (n=42)

Age (year)	54±11
Gender (F/M)	41/1
Duration of follow-up (month)	55±51
Siccasymptoms	39 (93%)
Arthralgia/arthritis	37 (88%)
Parotitis	9 (21%)
RaynaudPhenomenon	5 (12%)
Leucocytoclasticvasculitis	5 (12%)
Peripheralneuropathy	2 (5%)
Interstitiallungdisease	2 (5%)
Lymphadenopathy	6 (14%)
ANA	34 (81%)
Anti-Ro/La	19 (45%)

Tablo-2: Disease Activity Indexes and SG-USG Scores of SjS Patients

	n=42
ESSPRI-total	15,4±5,4
-dryness	5,7±2,2
-fatigue	5,2±2,6
-pain	5,4±2,6
VAS	55±20
ESSDAI-total	1±1
Hocevar-USG Score	20±10
Milic-USG Score	6±3

Twenty-four (57%) and25 (60%) patients had the cut-offvalues of ≥17 (Hocevar) and ≥6 (Milic USG).The patients with the scores of ≥17 (Hocevar)were found to have higher scores of ESSPRI-total (18±5 vs 14±5, p=0,01). Hocevar and Milic USG scores were shown to be higher in anti-Ro(+) SjS patients (25±10vs14±7and7±3vs4±2, p=0,01).USG scores were not found to be associated with the scores of ESSDAI, VAS and ESSPRI items.

Conclusions: Hocevar scoring system of major salivary glands was found to be related to patient reported activity in SjS. USG scores were associated with anti-Ro positivity. Evaluation of SG-USG might promote the diagnosis and follow-up of the SjS patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6196

SAT0311 PROLONGED EXPOSURE TO ANTIPHOSPHOLIPID ANTIBODIES IS ASSOCIATED WITH ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Y.-J. Park[1], I.-W. Baek[2], K.-J. Kim[1], W.-U. Kim[3], C.-S. Cho[4]. *[1]Division of Rheumatology, St. Vincent Hospital, The Catholic University of Korea, Suwon; [2]Division of Rheumatolgy, Yeouido St. Mary's Hospital, The Catholic University of Korea; [3]Division of Rheumatology, Seoul St. Mary's Hospital, The Catholic University of Korea; [4]Division of Rheumatology, Yeouido St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea, Republic Of*

Background: Antiphospholipid syndrome has been shown to be associated with increased cardiovascular mortality, but the role of antiphospholipid antibodies (aPL) on endothelial dysfunction remains elusive.

Objectives: We investigated the association between endothelial dysfunction and aPL in systemic lupus erythematosus (SLE) patients.

Methods: 188 SLE patients and 62 controls were enrolled. Endothelial function was measured by flow-mediated dilatation (FMD). Cardiovascular risk factors were assessed and quarterly measurement of anti-cardiolipin (aCL) and anti-β_2 glycoprotein I Ab were used to calculate time-integrated values throughout disease duration. Circulating endothelial progenitor cell (EPC), defined by CD34+/KDR+ mononuclear cells, was quantified by flow cytometry.

Results: Median FMD was significantly lower in SLE patient than in controls (6.9 versus 9.3%, $P<0.001$). In univariate analysis, older age, hypertension, thrombocytopenia, and persistent positive lupus anticoagulant (LAC) were associated with decreased FMD in SLE patients ($P=0.021$, $P=0.011$, $P=0.004$, and $P=0.028$). Time-integrated aCL value (TI-aCL), but not a single value, was correlated with decreased FMD ($P=0.001$). Multivariate analysis showed that hypertension and TI-aCL were independent factors for decreased FMD ($P=0.027$, $P=0.008$); addition of positive LAC increased the adjusted probability of decreased FMD ($P=0.023$). FMD was correlated with EPC number ($\gamma=0.342$, $P=0.005$) and TI-aCL was also an independent factor of reduced EPC after multiple adjustment ($P=0.019$). The predicted probability of endothelial dysfunction at median EPC level was higher in group with high TI-aCL than in group with low TI-aCL ($P=0.004$).

Conclusions: Cumulative burden of aPL was closely associated with endothelial dysfunction in SLE patients, which was mediated in part by reduction of EPC.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3063

SATURDAY, 17 JUNE 2017

Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models

SAT0312 MICRORNA-125B AS A POTENTIAL FIBROTIC AND APOPTOTIC REGULATOR IN SYSTEMIC SCLEROSIS

A. Kozlova[1], E. Pachera[1], F. Renoux[1], M. Rudnik[1], B. Maurer[1], A. Jüngel[1], J.H. Distler[2], G. Kania[1], O. Distler[1]. *[1]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [2]Department of Internal Medicine 3, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen-Nuremberg, Germany*

Background: MicroRNAs (miRs) are a class of small, noncoding RNAs that regulate many biological processes. Some microRNAs are involved in skin fibrosis.

Objectives: To analyze the differential expression, regulation and the pathophysiological role of miR-125b in systemic sclerosis (SSc).

Methods: For screening a low density array was run on pooled RNA from fibroblasts derived from 3 SSc patients vs. 3 healthy controls (HC). For further validation we performed qPCR on RNA derived from cultured fibroblasts, whole skin biopsies as well as on paraffin fixed dermis and epidermis. Next, fibroblasts were stimulated with pro-inflammatory and/or pro-fibrotic cytokines such as TGFβ, IL-1β, -4, -13, -17A, TNFα and PDGF. In order to identify downstream effects of miR-125b, knockdown with anti-miR-125b (or scrambled controls) in HC fibroblasts was performed. RNA was isolated from healthy fibroblasts (n=4) after knockdown and was proceeded to deep sequencing using Illumina HiSeq2000. Sequencing data were validated using qPCR on HC as well as SSc fibroblasts. Apoptosis was assessed by Caspase-Glo 3/7 assay and immunofluorescence of cleaved caspase 3 on cultured fibroblasts.

Results: Screening identified miR-125b as one of the candidate miRs differentially expressed in SSc. MiR-125b was confirmed by qPCR in primary dermal fibroblasts (SSc =11, HC =8), where it was downregulated by 47% (median expression 53%, $Q_{1,3}$ 33%, 70%; $p<0.01$). MiR-125b expression appeared to be independent from main cytokines operative in SSc. Additionally, the expression of miR-125b was assessed in skin biopsies of both SSc patients (n=4) and HC (n=5). In SSc, miR-125b was downregulated by 35% (median expression 65%, $Q_{1,3}$ 61%, 78%; $p<0.05$). To localize its expression in the skin, we separately analyzed miR-125b expression in dermis and epidermis of paraffin fixed skin. In both cases, expression of miR-125b was downregulated.

RNA sequencing identified >3500 differentially expressed genes with $p<0.05$. More than half of the differently expressed genes with at least 15% change were predicted targets of miR-125b by TargetScan and MiRWalk, indicating successful functional inhibition of miR-125b. Gene ontology revealed extracellular matrix organization and apoptosis regulation as the two main clusters of differentially expressed genes. Among them, BAK1, BMF and BBC3 are participants of the BCL2 apoptosis pathway and predicted targets of miR-125b. Consistent with the sequencing results, qPCR showed that knockdown of miR-125b upregulates these genes 24, 48 and 72 hours after transfection ($p<0.05$ for each). That was confirmed also on protein level by Western blot. Accordingly, miR-125b knockdown resulted in a higher rate of apoptosis (mean±SD: 60% ± 29%, $p<0.01$) compared to scrambled controls, measured by Caspase-Glo 3/7 assay.

Moreover, miR-125b knockdown reduced TGFβ-induced αSMA expression both on RNA and protein levels, suggesting that miR-125b might play an additional role in the cytoskeletal reorganization of fibroblasts during fibrosis.

Conclusions: MiR-125b is differentially expressed in SSc skin and primary dermal fibroblasts. MiR-125b downregulation increases apoptosis, inhibits cytoskeletal reorganization and therefore might become a potential anti-fibrotic therapeutic strategy.

Disclosure of Interest: A. Kozlova: None declared, E. Pachera: None declared, F. Renoux Grant/research support from: Swisslife, M. Rudnik: None declared, B. Maurer Shareholder of: Patent licensed: mir-29 for the treatment of systemic sclerosis, Grant/research support from: AbbVie, Protagen, EMDO, Novartis, Pfizer, Roche, Actelion, A. Jüngel: None declared, J. Distler Shareholder of: 4D Science, Grant/research support from: Anamar, Active Biotech, Array Biopharma, BMS, Bayer Pharma, Boehringer Ingelheim, Celgene, GSK, Novartis, Sanofi-Aventis, UCB, Consultant for: Actelion, Active Biotech, Anamar, Bayer Pharma, Boehringer Ingelheim, Celgene, Galapagos, GSK, Inventiva, JB Therapeutics, Medac, Pfizer, RuiYi, UCB, G. Kania Grant/research support from: Bayer, O. Distler Shareholder of: Patent licensed: mir-29 for the treatment of systemic sclerosis, Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha

DOI: 10.1136/annrheumdis-2017-eular.3806

SAT0313 **ROLE OF CD248 MOLECULE AS POTENTIAL REGULATOR OF TRANS-DIFFERENTIATION TOWARD MYOFIBROBLASTS OF PERIVASCULAR STROMAL CELLS IN SYSTEMIC SCLEROSIS PATIENTS**

P. Di Benedetto[1], P. Ruscitti[1], V. Liakouli[1], F. Carubbi[1], O. Berardicurti[1], A. Lizzi[2], S. Di Bartolomeo[1], G. D'Andrea[2], R. Giacomelli[1], P. Cipriani[1]. *[1]Department of Applied Clinical Sciences and Biotechnology, Rheumatology Unit, School of Medicine; [2]Department of Applied Clinical Sciences and Biotechnology, University of L'aquila, L'Aquila, Italy*

Background: The microvascular damage is a pivotal event in the pathogenesis of Systemic Sclerosis (SSc) and, after injury, both endothelial cells (ECs) and pericytes might trans-differentiate toward myofibroblast, responsible of fibrosis. Platelet-derived growth factor B (PDGFB) and transforming growth factorβ (TGFβ) play a key role in SSc pathogenesis. PDGFB is a potent mitogen for myofibroblasts, while TGFβ stimulate myofibroblast activation, including alpha smooth muscle actin (αSMA) expression. A key regulator of PDGFB and TGFβ signaling may be the CD248, a trans-membrane receptor required for proliferation and migration of pericytes and fibroblasts. It has been showed that, in an animal model of kidney fibrosis, the genetic deletion of CD248 modulates the response of renal pericytes to injury, by reducing the differentiation of myofibroblasts. The expression of CD248 is required for TGFβ-induced αSMA expression in pericytes and CD248 enhances the PDGFB pathway, mediating the proliferation and migration of perivascular cells.
Objectives: The aim of this work was to evaluate the expression of CD248, in SSc skin biopsies and its possible role in perivascular stromal cells proliferation, responsible to myofibroblast trans-differentiation, during SSc.
Methods: After ethical approval, skin biopsies and bone marrow mesenchymal stem cells (MSCs) were collected from 20 diffuse SSc patients and 10 healthy control (HC). CD248 expression was investigated in the skin, and in isolated MSCs treated with TGFβ or PDGFB, by immunofluorescence, qRT-PCR and western. Furthermore, we silenced CD248 in SSc-MSCs, to confirm the role of this molecule in TGFβ- or PDGFB-signaling modulation.
Results: CD248 expression in SSc skin was significantly higher when compared with HC skin. In particular, an increased expression of CD248 was found in ECs, stromal fibroblast and perivascular like stromal cells, co-expressing CD90, a marker of un-differentiated MSCs. Furthermore, in both, HC- and SSc-MSCs, TGFβ treatment induced a significant reduction of CD248 mRNA expression, in parallel with a significant increase of αSMA and a decrease of proliferation (ki67), when compared with untreated- (UT-) cells. Interestingly, the ability of TGFβ to inhibit CD248 expression in HC-MSCs was significantly higher than SSc-MSCs, suggesting that local environment in SSc patients affect TGFβ ability to suppress CD248 expression in SSc-MSCs. After treatment with PDGFB in both SSc- and HC-MSCs, CD248 expression was not affected, while significant reduction of αSMA and an increased expression of Ki67 was observed compared with UT-cells. After silencing of CD248 in SSc-MSCs, both TGFβ and PDGFB signaling were inhibited.
Conclusions: CD248 over-expression may play an important role in tissue fibrosis by modulating the pericytes to myofibroblast trans-differentiation, via regulation of both PDGFB and TGFβ signaling, during SSc.
References:
[1] Cipriani P et al, J Rheumatol 2016.
[2] Smith SW et al, Nephron 2015.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2686

SAT0314 **A NOVEL HIGHLY SELECTIVE 5-HYDROXYTRYPTAMINE 2B (5-HT2B) RECEPTOR ANTAGONIST AMELIORATING FIBROSIS IN PRECLINICAL MODELS OF SYSTEMIC SCLEROSIS**

C. Wenglén, L. Pettersson, H. Arozenius, G. Ekström. *ANAMAR, Lund, Sweden*

Background: Microvascular injury is one of the first pathological events in systemic sclerosis, and precedes the fibrosis. A consequence of vascular damage is the exposure of subendothelial connective tissue that causes activation of platelets and local serotonin (5-hydroxytryptamine, 5-HT) release. Binding of 5-HT to 5-HT_{2B} receptors on *e.g.* fibroblasts results in increased myofibroblast differentiation and release of excessive amounts of matrix proteins subsequently leading to fibrosis. Thus, pharmacologic inhibition of 5-HT_{2B} receptor signalling may represent a new treatment opportunity for systemic sclerosis.
Objectives: The objective of the present study was to evaluate a novel highly selective 5-HT_{2B} receptor antagonist for its ability to reduce the production of matrix proteins in human dermal fibroblasts and to ameliorate fibrosis in the tight-skin-1 model of systemic sclerosis.
Methods: Dermal fibroblasts isolated from patients with systemic sclerosis were cultured with different concentrations of the 5-HT_{2B} receptor antagonist AM1125 with or without 1 μM 5-HT. Anti-fibrotic effects were evaluated by measuring matrix production, myofibroblast differentiation and TGF-β production. The tight-skin-1 model was used to evaluate anti-fibrotic effects *in vivo* using a therapeutic treatment approach. AM1125 was administered at 10 and 50 mg/kg orally, b.i.d. from week 5 to week 10. Hypodermal thickening, myofibroblast counts and collagen production (hydroxyproline) were evaluated at the end of the treatment period.
Results: *In vitro* the 5-HT_{2B} receptor antagonist AM1125 dose-dependently reduced TGF-β, PAI, nuclear SMAD2/3 and collagens in human dermal fibroblasts. In addition, stress fiber formation and α-SMA mRNA were reduced indicating decreased myofibroblast differentiation. Therapeutic treatment with AM1125 at 50 mg/kg reduced hypodermal thickness ($p<0.001$), myofibroblast counts ($p<0.05$) and hydroxyproline content ($p<0.01$) in the tight-skin-1 model. In addition, the lower dose (10 mg/kg) reduced hypodermal thickness ($p<0.001$).
Conclusions: The results demonstrate that the 5-HT_{2B} receptor antagonist AM1125 prevents pro-fibrotic events in human dermal fibroblasts and attenuates dermal fibrosis using a therapeutic treatment approach in the tight-skin-1 model. Thus, 5-HT_{2B} receptor antagonists, exemplified by the novel compound AM1125, could represent a new treatment opportunity for systemic sclerosis.
Disclosure of Interest: C. Wenglén Employee of: AnaMar, L. Pettersson Employee of: AnaMar, H. Arozenius Employee of: AnaMar, G. Ekström Employee of: AnaMar
DOI: 10.1136/annrheumdis-2017-eular.3750

SAT0315 **IMATINIB-LOADED TARGETED GOLD NANOPARTICLES AMELIORATE EXPERIMENTAL LUNG FIBROSIS INDUCED BY BLEOMYCIN**

V. Codullo[1], S. Breda[1], F. Meloni[1], E. Cova[1], S. Inghilleri[1], M. Colombo[2], D. Prosperi[2], M. Malatesta[3], L. Calderan[3], C. Montecucco[1], J. Distler[4]. *[1]IRCCS policlinico San Matteo Foundation, Pavia; [2]University of Milan - Bicocca, Milan; [3]University of Verona, Verona, Italy; [4]Department of Internal Medicine 3, University of Erlangen-Nuremberg, Erlangen, Germany*

Background: Systemic Sclerosis (SSc) is an autoimmune disorder frequently affected by an interstitial lung involvement (ILD) that significantly deteriorates long term outcomes. In previous experiments we proved that specifically engineered gold-nanoparticles (GNP) loaded with imatinib and targeted with an anti CD44 Ab (GNP-HCim) significantly inhibited proliferation and induced apoptosis of fibroblast-like cells derived from ILD-SSc patients [1]. *In vitro*, GNP-HCim showed higher efficacy compared to the drug alone.
Objectives: To demonstrate in vivo the efficacy of GNP-HCim in ameliorating bleomycin-induced lung fibrosis
Methods: Eight-week-old C57BL6 male mice (n=8/group) were assigned to either: (1) controls receiving intratracheal aereosolization of saline solution and unloaded functionalised GNP (GNP-HC); (2) mice treated with intratracheal instillation of bleomycin (50 uL) on day 0 and GNP-HC; (3) mice treated with bleomycin on day 0 plus GNP-HCim; (4) mice treated with bleomycin plus intraperitoneal (i.p.) Imatinib (50 mg/kg, once daily). GNP-HC or GNP-HCim were administered by intratracheal instillation on day 10–15–20–25 and 3 h before culling. All mice were sacrificed on day 28. Lung specimens were analysed by electron microscopy, immunohistochemistry and immunofluorescence (IF). Data were evaluated by 2 blind observers and analysed with GraphPrism software for statistics.
Results: The administration of imatinib i.p or via GNP-HC reduced pathologic changes of the lungs as evaluated by the Lung Injury score and the Ashcroft score ($p<0.05$ for both). Collagen quantification by Picro Sirius Red revealed a significantly reduced staining only in the GNP-HCim group (p=0.0135 vs controls). IF revealed a significant reduction in αSMA+ myofibroblast counts when mice were inhaled with GNP-HCim (14.36±1.69/hpf) or injected i.p with imatinib (7.64±1.17/hpf) as compared to the controls (24.01±3.58/hpf, p=0.003 and p=0.0013 respectively). IF also showed significantly reduced counts of CD45+ (15.21±1.87/hpf vs 29±2.247/hpf in controls, p=0.0006) and CD44+ cells in groups treated with GNP-HCim (18.61±1.495) or imatinib i.p. (13.57±0.864), versus controls (28.56±2.854, p=0.0111 and p=0.0004 respectively). In imatinib i.p. and GNP-HCim-treated groups there was a significant reduction of phosphorylated c-Abl and PDGF-R, two downstream targets of imatinib, to levels comparable to group 1 controls with respect to the bleomycin group ($p<0.05$ for both). Finally, electron microscopy revealed accumulation of GNP-HCim and GNP in alveolar macrophages.
Conclusions: In the experimental model of bleomycin-induced lung fibrosis imatinib delivered to lungs through inhalation of anti CD44 targeted GNP was as effective as imatinib administered by i.p. route. These data favour the use of GNP in the development of new therapeutic approaches to SSc-ILD, which might be associated to a lower toxicity and side effects of systemic treatment.
References:
[1] Cova E, Ann rheum Dis 2016, 75(Suppl2): 61.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5108

SAT0316 ANGII INVOLVEMENT IN LUNG ENDOTHELIAL DYSFUNCTION AND PAH DEVELOPMENT IN PSGL-1 DEFICIENT FEMALE MICE

R. González-Tajuelo[1], M. de la Fuente-Fernández[1], D. Morales-Cano[2], B. Barreira[2], J. Silván[1], C. Gamallo[1], S. Castañeda[3], E. Vicente-Rabaneda[3], F. Pérez-Vizcaíno[2], Á. Cogolludo[2], L.J. Jiménez-Borreguero[4], A. Urzainqui[1]. *[1]Servicio de Inmunología, Fundación de Investigación Biomédica, Instituto de Investigación Sanitaria-Princesa, Hospital de la Princesa; [2]Departamento de Farmacología, Facultad de Medicina, Universidad Compluentense de Madrid; [3]Servicio de Reumatología, Fundación de Investigación Biomédica, Instituto de Investigación Sanitaria-Princesa, Hospital de la Princesa; [4]Servicio de Cardiología, Hospital de la Princesa, Madrid, Spain*

Background: Pulmonary arterial hypertension (PAH) is a rare disease whose etiopathogenesis is poorly understood, and existing treatments are neither curative nor sufficient for stopping disease progression [1]. PAH is one of the major complications of connective tissue diseases, and 7–15% of patients with systemic sclerosis (SSc) develop PAH [2]. Mice deficient for the leukocytic receptor P-selectin glycoprotein ligand-1 (*PSGL-1*$^{-/-}$) spontaneously develop a SSc-like autoimmune syndrome with ageing [3].
Objectives: To check whether *PSGL*$^{-/-}$ mice may develop PAH and which mechanisms might be implicated in the initiation and progression of the disease.
Methods: Vascular remodeling was assessed by immunohistochemistry on lung sections of WT and *PSGL-1*$^{-/-}$ C57BL/6 mice. Doppler pulse echochardiography was used to evaluate pulmonary artery flow acceleration time/ ejection time (TPV/ET) ratio. Isolated pulmonary artery rings were incubated with KCL, serotonin or acetylcholine and responses were registrated with a wire myograph coupled to an isometric force transducer. Angiotensin II lung concentration was quantified by ELISA. ACE, ACE2, AT1R and AT2R expression was evaluated by western blot. Expression levels of the NO-sensing probe DAR-4M AM and IFN-γ were measured by flow cytometry.
Results: *PSGL-1*$^{-/-}$ mice presented vascular remodeling of distal lung blood vessels. Aged *PSGL-1*$^{-/-}$ females showed reduced flow TPV/ET ratio in the pulmonary artery and RV remodeling, indicating PAH. Moreover, pulmonary arterial rings from aged *PSGL-1*$^{-/-}$ females presented increased vasoconstriction response to KCL and reduced vasodilation response to acetylcholine. Importantly, NO production by lung EC was reduced in aged *PSGL-1*$^{-/-}$ females. Expression of AT2R was reduced in lungs of *PSGL-1*$^{-/-}$ females from a young age. With ageing, the levels of angiotensin II and the percentages of IFN-γ-producing interstitial macrophages, T and B lymphocytes were increased in PSGL-1$^{-/-}$ females.
Conclusions: Together, these studies implicate leukocyte-endothelium interactions for the maintenance of vascular homeostasis and protection against PAH in PSGL-1 deficient female mice.
References:
[1] Montani et al. Orphanet Journal of Rare Diseases. 2013;8(97).
[2] Tedford et al. Circ Heart Fail. 2013;6(5)953–63.
[3] Pérez-Frías et al. Arthritis Rheumatol. 2014;66(11):3178–89.
Acknowledgements: We want to thank Ana Vanesa Alonso and Lorena Flores from the Unit of Advanced Imaging of the CNIC for their crucial support in echocardiography performance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5014

SAT0317 TYPE VI COLLAGEN FORMATION: A NEW OBJECTIVE BLOOD-BASED MARKER REFLECTING FIBROSIS OF THE SKIN IN SYSTEMIC SCLEROSIS

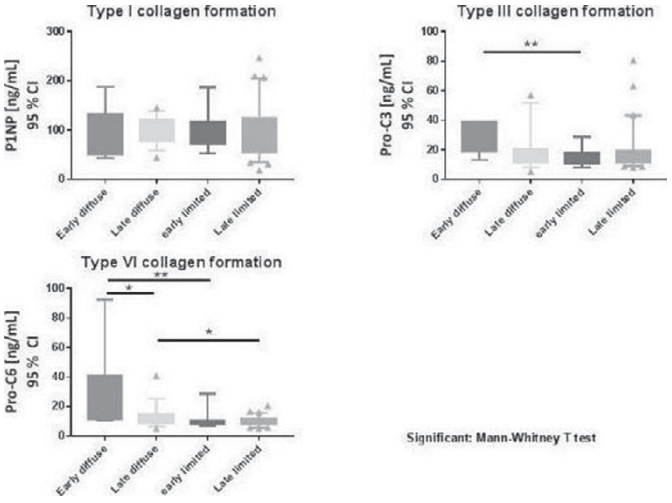
P. Juhl[1], L. Iversen[2], T. Karlsmark[2], M. Karsdal[1], A.-C. Bay-Jensen[1], M. Mogensen[2], A.S. Siebuhr[2]. *[1]Nordic Bioscience, Herlev; [2]Department of dermatology, Bispebjerg Hospital, Copenhagen, Denmark*

Background: Systemic sclerosis (SSc) is characterized by fibrosis of the skin. The dermis of the skin is rich in type I and III collagen, but other collagens as type VI collagen are present in the skin and play a key role in the organization of type I and III collagen. There is a lack of objective disease activity markers in SSc for frequent assessment of patients. The only measurement of disease activity currently is the subjective modified Rodnan skin score (mRSS).
Objectives: The objective is to examine blood-based markers of type I, III, and VI collagen formation as surrogates of disease activity and fibrosis in SSc.
Methods: SSc patients fulfilling the ACR criteria (n=121) were included. The study included both limited SSc (lSSc, n=79) and diffuse SSc (dSSc, n=42) (approval number H-B-2008–131). Markers of type I, III and VI collagen formation (P1NP, PRO-C3 and PRO-C6, respectively) were measured in serum by ELISA. Difference in the markers between groups were tested by Mann-Whitney T test and correlations were assessed by multiple linear regression adjusting for age, gender and BMI. Discriminative power of the markers was analyzed by ROC AUC on tertiles of mRSS.
Results: There were no significant difference in gender, BMI or disease duration between lSSc and dSSc. The mean age of the population was 57.4 (SD 11.6) years, 84% were female, mean disease duration was 11.7 (SD 8.9) years and mean mRSS was 11.2 (SD 8.6).
PRO-C3 and PRO-C6 were significantly higher early (<4 years) dSSc compared to early lSSc patients (both p=0.006). PRO-C6 was significantly elevated in early dSSc compared to late dSSc (p=0.04) and increased in late dSSc compared to late lSSc (p=0.02; Figure). Both PRO-C3 and PRO-C6 correlated with mRSS when adjusted for age, gender, and BMI with R-partial of 0.36 (p=0.0001) and 0.29 (p=0.002), respectively.
Both PRO-C3, and PRO-C6 could separate the patient group having the highest tertile of mRSS from the rest with an AUC (95% CI) of 0.73 (0.62–0.82), and 0.74 (0.63–0.83), respectively. Together, PRO-C3 and PRO-C6 could separate the groups with an AUC (95% CI) of 0.77 (0.67–0.86) (Table 1).
PRO-C3 and PRO-C6 performed equally well for identification of patients with the highest skin score (highest tertile vs. the middle and lower tertile) with a relative risk of 2.3 (1.4–3.8) (Table 2). The risk of being in the highest tertile of mRSS compared to the lowest were significantly higher with a high PRO-C6 (relative risk 2.6, 95% CI: 1.3–5.2) compared to PRO-C3 (relative risk: 2.2, 95% CI: 1.2–3.8) (Table 2).

Table 1

Skin (highest vs lowest tertile)	AUC (95% CI)	P-value
P1NP	0.56 (0.44–0.67)	
PRO-C3	0.73 (0.62–0.82)	<0.0001
PRO-C6	0.74 (0.63–0.83)	<0.0001
PRO-C3, PRO-C6	0.77 (0.67–0.86)	<0.0001

Analyzed by ROC curve.



Conclusions: Markers reflecting fibrosis (measures of type III and VI collagen formation) could be novel objective, and potentially predictive, biomarkers of disease activity and severity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3788

SAT0318 EPIGENETIC REGULATION OF FRA2 BY JMJD3 REGULATES FIBROBLAST ACTIVATION IN SYSTEMIC SCLEROSIS

C. Bergmann[1], A. Brandt[1], C. Dees[1], T. Wohlfahrt[1], Y. Zhang[2], C.-W. Chen[1], T. Mallano[1], R. Liang[1], R. Kagwiria[1], P.-S. Kam[1], A. Bozec[1], D. Abraham[3], R. Rieker[4], A. Ramming[5], O. Distler[6], G. Schett[1], J. Distler[1]. *[1]Internal Medicine III-Rheumatology; [2]University Clinic Erlangen-Nuremberg, Erlangen, Germany; [3]Centre for Rheumatology and Connective Tissue, UCL School of Life and Medical Sciences, London, United Kingdom; [4]Department of Pathology; [5]Centre for Rheumatology and Connective Tissue, University Clinic Erlangen-Nuremberg, Erlangen, Germany; [6]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland*

Background: Chronic and exaggerated fibroblast activation is a central hallmark of Systemic Sclerosis (SSc) fibrotic disease and results in a high morbidity and

Abstract SAT0317 – Table 2

	Highest tertile of skin score vs rest				Highest vs low tertile of skin score			
	OR (95% CI)	P-value	RR (95% CI)	P-value	OR (95% CI)	P-value	RR (95% CI)	P-value
P1NP	1.1 (0.5–2.6)		1.1 (0.6–1.9)		2.3 (0.7–6.9)		1.6 (0.8–3.2)	
PRO-C3	3.7 (1.6–8.3)	p=0.002	2.3 (1.4–3.8)	p=0.001	5.7 (1.7–18.4)	p=0.004	2.2 (1.2–3.8)	p=0.008
PRO-C6	3.7 (1.6–8.3)	p=0.002	2.3 (1.4–3.8)	p=0.001	6.0 (1.9–18.8)	p=0.002	2.6 (1.3–5.2)	p=0.006

OR: odds ratio, RR: relative risk.

mortality. Epigenetic changes might play important roles in mediating chronic fibroblast activation. Trimethylation of H3 at lysine residue K27 (H3K27me3) is a repressive epigenetic mark that was recently identified as an important negative regulator of fibroblast activation [1]. Jumonji domain containing protein 3 (JMJD3) mediates H3K27me3–demethylation. JMJD3 inhibitors are being tested as therapeutic strategies in malignant diseases.

Objectives: The aim of this study was to characterize the role of JMJD3 in fibrotic disease and to explore JMJD3 as a potential drug target in SSc.

Methods: Expression analyses of JMJD3 were performed using qPCR, IF and Western blot. siRNA mediated knockdown and the pharmacologic H3K27me3-demethylase inhibitor GSKJ4 were used to target JMJD3. *In vivo,* we analyzed the effects of GSKJ4 in bleomycin-induced dermal fibrosis and in Topoisomerase-I-induced (TopoI) fibrosis. H3K27me3 levels at the Fra2 promotor were analyzed by CHIP.

Results: We observed increased expression of JMJD3 in SSc skin compared to healthy controls. Fibroblast-specific overexpression of JMJD3 was also reflected in experimental fibrosis models. TGFβ upregulated JMJD3. Inhibition of JMJD3 increased H3K27me3 *in vitro* and *in vivo*. Inhibition of JMJD3 reverted the activated fibroblast phenotype in SSc fibroblasts and decreased the expression of contractile fibers and of α-smooth muscle actin. In addition, JMJD3 inhibition reduced the basal and TGFβ induced collagen secretion of SSc fibroblasts. JMJD3 regulated the TGFβ induced expression of Fra2. GSKJ4 reverted the TGFβ induced reduction of H3K27me3 at the Fra2 promotor. Moreover, the anti-fibrotic effects of JMJD3 inhibition were evened in Fra2 knockout fibroblasts. Overexpression of Fra2 in JMJD3-knockdown fibroblasts restored the profibrotic effect of JMJD3. *In vivo*, inhibition of JMJD3 ameliorated fibrosis in bleomycin- and TopoI- induced experimental fibrosis and reduced dermal thickening, hydroxyproline content and myofibroblast differentiation.

Conclusions: We present first evidence that JMJD3 contributes to the activated phenotype of SSc fibroblasts. TGFβ upregulated JMJD3. Inhibition of JMJD3 prevented the aberrant activation of fibroblasts *in vitro* and ameliorated dermal fibrosis in several mouse models *in vivo*. The profibrotic effects of JMJD3 might be mediated by reducing the H3K27me3 at the Fra2 promotor and consecutive overexpression of Fra2.

References:

[1] Kramer, M., et al., Inhibition of H3K27 histone trimethylation activates fibroblasts and induces fibrosis. Ann Rheum Dis, 2013. 72(4): p. 614–20.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3792

SAT0319 MULTIPARAMETRIC DETECTION OF AUTOANTIBODIES TO INVESTIGATE RELATIONSHIPS BETWEEN SEROLOGICAL AND CLINICAL SUBSETS OF SYSTEMIC SCLEROSIS PATIENTS

P. Budde[1], H.-D. Zucht[1], D.S. Wirtz[1], K. Marquart[1], M. Schneider[2], P. Schulz-Knappe[1], N. Hunzelmann[3]. *[1]Protagen Ag, Dortmund; [2]Rheumatology & Hiller-Forschungszentrum, Heinrich-Heine-University, Düsseldorf; [3]Dermatology, University of Cologne, Cologne, Germany*

Background: Systemic sclerosis (SSc) is a largely heterogeneous autoimmune disease, with patients exhibiting an extensive range of clinical presentations and various disease course. The most widely used classification divides SSc into two major subsets diffuse cutaneous (dcSSc) and limited (lcSSc) SSc by the extent and severity of skin fibrosis. However, not all patients fit into these subsets. This has created great interest to examine disease heterogeneity at the molecular level to uncover unrecognized SSc subtypes that may differ with regard to clinical manifestations, prognosis or therapy response.

Objectives: In large-scale "omics"-type autoantibody (AAB) profiling studies we have recently identified novel SSc-associated autoantigens. Here, we describe the development of a 20 marker multiplexed AAB assay to facilitate the discovery and validation of AAB-based patient subgroups.

Methods: A Luminex bead-based AAB assay was designed by combining 8 connective tissue disease (anti-centromere, anti-Scl70, U1-snRNP, SSB, Ro52, Ro60, SmB, anti-ribosomal P) antigens with 12 novel antigens (including BICD2, JMJD3/KDM6B, and PPP1R2). Novel AAB targets were previously detected in SSc patients with a p-value <0.05 (Mann-Whitney-U-test) and frequency$>15\%$. AAB reactivity was analysed in 92 SSc patients (dcSSc: n=32, lcSSc: n=50, SSc overlap: n=9). The mean modified Rodnan skin score (MRSS), mean disease duration (month), and mean age (years) of the SSc cohort was 10.51, 162.5 and 56.94, respectively. To analyze the individual-level patient similarity of AAB reactivity, the total number of AABs reactive in each patient was calculated and referenced to the number of all available antigens in percent. Patient's demographics and clinical data were dichotomized into patients with mRSS higher or lower than the mean value. Hierarchical cluster analysis was performed to investigate the relationship between AAB patient signatures and clinical and demographic features.

Results: Based on their AAB reactivity pattern, the SSc sample cohort can be decomposed into four apparent clusters and additional fine-level clusters. LcSSc patients were spread over three clusters, each with clearly distinct AAB profile. Compared to dcSSc patients, lcSSc patients were more heterogeneous in their AAB profile. The percentage of lcSSc patients in clusters 1–3 was 70%, 90% and 53%, respectively. Patients in cluster 2 had an extended AAB repertoire that is anti-centromere, KDM6B, SSA, BICD2 and PPP1R2. 63% of all patients in cluster 4 were dcSSc and anti-Scl70 positive, who were most afflicted of the disease. AAB signatures of patients were mapped against dichotomized demographic and clinical features. Moving from cluster 1 to 4 the number of patients with shorter disease duration, lower age, higher mRSS and higher frequency of lung involvement increased.

Conclusions: The multiplexed analysis of AABs in SSc enables defining an AAB reactivity score and patient clusters. This might support to subclassify SSc beyond lcSSc and dSSc.

Disclosure of Interest: P. Budde Employee of: Protagen AG, H.-D. Zucht Employee of: Protagen AG, D. Wirtz Employee of: Protagen AG, K. Marquart Employee of: Protagen AG, M. Schneider Consultant for: Protagen AG, P. Schulz-Knappe Employee of: Protagen AG, N. Hunzelmann: None declared

DOI: 10.1136/annrheumdis-2017-eular.1982

SAT0320 SSC- IGG EFFECTS ARE MEDIATED THROUGH DISTINCT PATHWAYS IN THP-1 CELLS

G. Eleftheriadis[1], M. Wannick[1], C. Sadik[1], G. Riemekasten[2]. *[1]Institute of Experimental Dermatology; [2]Department of Rheumatology, University of Lübeck, Lübeck, Germany*

Background: Peripheral blood mononuclear cells (PBMCs) are thought to play a key role in the pathogenesis and progress of systemic scleroderma (SSc) with patients displaying distinct shifts in count, receptor expression profile and cytokine secretion patterns. SSc-IgG with elevated anti-AT_1R (angiotensin II type 1 receptor)/ET_AR (endothelin-1 type A receptor) -AAb (autoantibody) titers have been correlated to disease severity and progression[1]. It remains poorly understood through which pathways SSc- IgG mediates its effects.

Objectives: In this study we sought to analyze the expression patterns of THP-1 cells (a monocytic cell line) after SSc-IgG application and their reversibility through application of numerous pharmacological inhibitors.

Methods: Transcription of IL-8- and CCL-18 in THP-1-cells after SSc-IgG and normal IgG stimulation was quantified by qPCR. Stimulations of THP-1 cells with total IgG of phenotypically different groups of SSc patients as well as ET-1 and AT-2 were carried out. In addition, stimulation with pharmacological inhibitors was conducted in a dose-dependent-manner. The results were quantified by IL-8- and CCL18-ELISA of the supernatants.

Results: Expression of IL-8 and CCL-18 is induced by SSc-IgG treatment in comparison to normal IgG which does not follow this trend. IL-8 secretion of THP-1 cells upon SSc-IgG stimulation is mediated through specific autoantibody effects and transduced through NF-κB, ERK-, and AP-1 pathways. CCL-18 secretion of THP-1 cells upon SSc-IgG stimulation is not mediated through aforementioned pathways.

Conclusions: A stable cell culture system able to reproduce previous PBMC data on IL-8 and CCL-18 induction upon SSc-IgG-treatment could be established and insight was gained regarding key pathways which are involved in the transduction leading to IL-8 secretion. The effects of specific surface receptor expression profiles on transduction remain to be elucidated.

References:

[1] Günther, J., Rademacher, J., van Laar, J.M. et al. Semin Immunopathol (2015) 37: 529.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5314

SAT0321 MKP-1 AS A PROTECTIVE FACTOR AND NOVEL DRUG TARGET IN SCLERODERMA: MKP-1 DEFICIENT MICE DEVELOP MORE SEVERE DERMAL FIBROSIS IN A WIDELY USED EXPERIMENTAL MODEL OF SCLERODERMA

M. Scotece, M. Hämäläinen, T. Leppänen, E. Moilanen. *The Immunopharmacology Research Group, Faculty of Medicine and Life Sciences, University of Tampere and Tampere University Hospital, Tampere, Finland*

Background: Scleroderma is a chronic connective tissue disease of unknown aetiology. In early stages, vascular injury and inflammation lead to fibrosis, resulting in irreversible damage in various organs. Inflammation is believed to be necessary in order to activate fibroblasts to over-produce extracellular matrix components. At the present, there is no effective standard treatment to reverse or slow down the progression of scleroderma but one of the feasible approaches is to target key inflammatory pathways that are involved in the pathogenesis of the disease.

MKP-1 (Mitogen-Activated Protein Kinase Phosphatase-1) is a nuclear phosphatase present in most cell types and tissues. Studies with MKP-1 deficient mice have undoubtedly shown that MKP-1 is an important regulator of innate and adaptive immune responses to limit and suppress inflammation (1) but its role in fibrosing diseases has not been studied.

Objectives: In the present study, we aimed to investigate the potential protective role of MKP-1 in the pathogenesis of scleroderma by using MKP-1 deficient mice and a widely studied experimental model of scleroderma.

Methods: We used bleomycin-induced dermal fibrosis in the mouse as an experimental model of scleroderma (2). Wild type (WT) and MKP-1 deficient mice were injected subcutaneously with bleomycin every other day for 28 days. Dermal

thickness and collagen accumulation were determined by histological analyses. The expression of several inflammatory and pro-fibrotic mediators were measured by quantitative RT-PCR.
Results: We found that bleomycin-induced dermal thickness and lipodystrophy were increased in MKP-1 deficient mice. Collagen accumulation in the dermis and mRNA expression of collagens 1A1 and 3A1 were enhanced in the skin from MKP-1 deficient mice as compared to the skin from WT animals. Affected skin from MKP-1 deficient mice presented increased expression of factors related to inflammation and fibrosis, namely IL-6, TGF-β1, fibronectin-1 and YKL-40 as well as chemokines MCP-1, MIP-1α and MIP-2.
Conclusions: This study demonstrates, for the first time, that MKP-1 deficient mice develop more severe bleomycin-induced dermal fibrosis than their WT counterparts, indicating that MKP-1 regulates the inflammatory and fibrotic processes typical for experimentally-induced scleroderma. These findings suggest that compounds which enhance expression/activity of MKP-1 have potential as novel drugs for the stage-specific modulation of the pathogenesis of scleroderma.
References:
[1] Korhonen R, Moilanen E. Mitogen-activated protein kinase phosphatase 1 as an inflammatory factor and drug target. Basic Clin Pharmacol Toxicol. 2014; 114:24–36.
[2] Yamamoto T et al. Animal model of sclerotic skin. I: Local injections of bleomycin induce sclerotic skin mimicking scleroderma. J Invest Dermatol. 1999; 112:456–62.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4816

SAT0322 ADAM-17 IS EXPRESSED IN THE INFLAMMATORY MYOPATHY, AND IS INVOLVED WITH INTERSTITIAL LUNG DISEASE (ILD)

A. Nishimi, T. Isozaki, S. Nishimi, S. Ishii, T. Tokunaga, H. Furuya, K. Wakabayashi, T. Kasama. *Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan*

Background: A disintegrin and metalloprotesase (ADAM) family is protease that is thought to have an important role in tissue destruction and inflammatory reaction. ADAMs are also involved in the amputation from the cell surface of inflammatory cytokines. ADAM-17 is one of the ADAM family, and is first described as the protease responsible for tumor necrosis factor (TNF)-α shedding. The implication of ADAM-17 substrates in immunoregulation has made this enzyme an efficient therapeutic target in the treatment of a number of pathological conditions including airway inflammation and arthritis.
Objectives: The function of ADAM-17 in myositis is unclear. Therefore, we clarify the expression of ADAM-17 in inflammatory myopathy and the role of inflammation in interstitial lung diseases (ILD).
Methods: The serum were collected from the patients who were diagnosed with inflammatory myopathy in Showa University Hospital from 2003 to 2015. Twenty-six patients were diagnosed with polymyositis (PM), 34 patients were diagnosed with dermatomyositis (DM), and 10 patients were diagnosed clinically amyopathic dermatomyositis (CADM). Clinical manifestations and clinical data were also collected. The levels of ADAM-17 in the serum samples were measured using enzyme-linked immunosorbent assay (ELISA). ADAM-17 expression was determined in muscle tissues from DM using immunohistological staining. To determine that the role of lung fibrosis in inflammatory myopathy with ILD, we used human lung fibroblasts (HLF). ADAM-17 expression on HLF was also demonstrated by immunohistrogical staining. ADAM-17 expression in interleukine (IL)-6 and IL-6 receptor (IL-6R) stimulated HLF was performed by ELISA.
Results: ADAM-17 in inflammatory myopathy was significantly higher than in healthy control (n=19) (mean ± SEM; 1048±312 pg/ml and 36±18 pg/ml, respectively, $p<0.05$). ADAM-17 in corticosteroid and/or immunosuppressant treatment patient serum was also significantly decreased compared with in pre treatment patient serum (1465±562 pg/ml and 1059±503 pg/ml, respectively, $p<0.01$). In addition, ADAM-17 in inflammatory myopathy with ILD patients (n=46) was significantly higher than in non-ILD patients (n=24) (1379±454 pg/ml and 413±226 pg/ml, respectively, $p<0.05$), while ADAM-15 did not have the differences between ILD and non-ILD group. Finally, we found the expression of ADAM-17 in muscle biopsy tissue. Hence, ADAM-17 on HLF was expressed by immunohistochemistry. ADAM-17 in IL-6 and IL-6R stimulated HLF was significantly higher compared with non-stimulated HLF (48±6 pg/ml and 0±0 pg/ml, respectively, $p<0.05$).
Conclusions: ADAM-17 is expressed in inflammatory myopathies especially with ILD and expressed on HLF, suggesting that ADAM-17 may play the role in lung fibrosis. ADAM-17 may be a potential target in inflammatory myopathies with ILD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3402

SAT0323 THE ENDOTHELIAL-TO-MESENCHYMAL TRANSITION (ENDOMT) IN SCLERODERMA CAN BE PREVENTED BY THE USE OF DUAL ENDOTHELIN RECEPTOR ANTAGONISTS BOSENTAN AND MACITENTAN

C. Corallo[1], M. Cutolo[2], S. Soldano[2], A. Montella[1], C. Chirico[1], R. Nuti[1], N. Giordano[1]. *[1]Medicine, Surgery and Neurosciences, University of Siena, Siena; [2]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, Institute for Research and Health Care (IRCCS), University of Genoa, Genoa, Italy*

Background: Systemic sclerosis (SSc) is characterized by early vascular abnormalities and subsequent fibroblast activation and differentiation into myofibroblasts, leading to fibrosis. Recently, endothelial-to-mesenchymal transition (EndoMT), a complex biological process in which endothelial cells lose their specific markers and acquire a mesenchymal or myofibroblastic phenotype, has been reported in SSc.
Objectives: The goal of the study was to evaluate the potential of endothelin-1 (ET-1) dual receptor antagonists bosentan (BOS) and macitentan (MAC) to antagonize EndoMT *in vitro*.
Methods: 20 patients with limited SSc were enrolled and underwent double skin biopsy (affected and nonaffected skin). Fibroblasts and microvascular endothelial cells (MVECs) were isolated from biopsies. Mono- or coculture of MVECs (isolated from nonaffected skin) with fibroblasts (isolated from affected skin and stimulated with ET-1 and transforming growth factor beta [TGF-β]) were performed. In cocultures, the MVEC layer was left undisturbed or was preincubated with either BOS or MAC. After 48 h of coculture, MVECs were analyzed for their capillary formation ability and for messenger RNA and protein expression of different vascular (CD31, vascular endothelial growth factor-A [VEGF-A], VEGF-A165b) and profibrotic (alpha-smooth muscle actin [α-SMA], collagen type I [Col I], TGF-β) molecules.
Results: MVECs showed a reduced capillary formation ability when cocultured with SSc fibroblasts with respect to mono cultures. CD31 and VEGF-A resulted in downregulation, while VEGF-A165b, the antiangiogenic isoform, resulted in upregulation. At the same time, mesenchymal markers α-SMA, Col I, and TGF-β resulted in overexpression in MVECs. Capillary formation ability was restored when MVECs were preincubated with BOS or MAC, also reducing the expression of mesenchymal markers and restoring CD31 expression as well as the imbalance between VEGF-A and VEGF-A165b.
Conclusions: BOS and MAC seem able to antagonize EndoMT phenomenon in MVECs *in vitro*. Blocking EndoMT is important for two reasons: first, because capillary formation ability in MVECs can be restored; second, because the endothelium-derived fibrotic development in SSc can be counteracted.
Acknowledgements: Thanks to Prof. Bashar Kahaleh and to Dr. Yongqing Wang from University of Toledo Medical Center, Division of Rheumatology and Immunology, OH, USA, for providing SSc microvascular endothelial cells.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5173

SAT0324 INCREASED FREQUENCIES OF CIRCULATING CXCL10-, CXCL8- AND CCL4-PRODUCING MONOCYTES AND SIGLEC-3-EXPRESSING MYELOID DENDRITIC CELLS IN SYSTEMIC SCLEROSIS PATIENTS

T. Carvalheiro[1,2,3], S. Horta[1,4], J.A. van Roon[2,3], M. Santiago[5], M.J. Salvador[5], T.R. Radstake[2,3], H. Trindade[1], J.A. da Silva[5,6], A. Paiva[1,7]. *[1]Blood and Transplantation Center of Coimbra, Portuguese Institute of Blood and Transplantation, Coimbra, Portugal; [2]Department of Rheumatology & Clinical Immunology; [3]Laboratory of Translational Immunology, University Medical Center Utrecht, Utrecht, Netherlands; [4]Department of Chemistry, University of Aveiro, Aveiro; [5]Department of Rheumatology, Coimbra University Hospital Center; [6]Faculty of Medicine, University of Coimbra; [7]Flow Cytometry Unit, Clinical Pathology Service, Coimbra University Hospital Center, Coimbra, Portugal*

Background: Systemic sclerosis (SSc) is an inflammatory and fibrotic disease characterized by vascular dysfunction, excessive extracellular matrix deposition and immune dysregulation. Recent observations suggest that monocytes and dendritic cells (DCs) might be involved in SSc; including cell recruitment, trafficking, activation and an enhanced pro-fibrotic phenotype. Hence these cells might be important contributors to the disease pathogenesis. However, detailed analysis of circulating monocytes and DCs in SSc in relationship to disease activity has not been performed so far.
Objectives: To investigate the *ex vivo* pro-inflammatory properties of classical and non-classical monocytes as well as myeloid dendritic cells (mDCs) in SSc patients in relationship to disease activity.
Methods: This study enrolled 43 SSc patients, 30 classified as limited cutaneous SSc (lcSSc) and 13 as diffuse cutaneous (dcSSc). The healthy control group (HC) included 20 age- and gender- matched individuals. The Spontaneous production of CXCL10, CCL4, CXCL4 and IL-6 was intracellularly evaluated in classical and non-classical monocytes and Siglec-3-expressing mDCs from peripheral blood using flow cytometry. In addition, the production of these cytokines was determined upon toll like receptor 4 (TLR4) plus Interferon-γ (IFN-γ) *in vitro* stimulation.
Results: The frequency of non-classical monocytes spontaneously producing CXCL10 was increased in both lcSSc and dcSSC subsets of SSc patients ($p<0.05$) and CCL4 was augmented in the dcSSc patient subset ($p<0.05$). The proportion of CCL4 producing- mDCs were also elevated in dcSSc patients ($p<0.01$) and the percentage of mDCS producing CXCL10 only in lcSSc patients ($p<0.05$ compared to HC, but $p<0.01$ comparing to dcSSc). Upon *in vitro* stimulation the frequency of non-classical monocytes expressing CXCL8 was

increased in both patient groups ($p<0.01$) and mDCs expressing CXCL8 only in lcSSc ($p<0.01$). SSc patients characterized by the presence or history of lung fibrosis, displayed a higher frequency of non-classical monocytes expressing CCL4 and CXCL10 in dcSSc patients as compared to those without this clinical manifestation ($p<0.01$ and $p<0.05$ respectively). Strikingly, the percentage of classical monocytes producing CXCL8 was augmented upon *in vitro* stimulation in lcSSc patients with lung fibrosis as compared to those without ($p<0.01$). No differences were found in the percentage of IL-6 producing cells.

Conclusions: These data point towards a role of activated non-classical monocytes and mDCs producing enhanced levels of proinflammatory cytokines in SSc, potentially contributing to lung fibrosis.

Acknowledgements: TC is supported by a grant from the Portuguese national funding agency for science, research and technology: Fundação para a Ciência e a Tecnologia [SFRH/BD/93526/2013].

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5050

SATURDAY, 17 JUNE 2017

Scleroderma, myositis and related syndromes

SAT0325 NAILFOLD CAPILLAROSCOPIC CHANGES IN PATIENTS WITH IDIOPATHIC AND SYSTEMIC SCLEROSIS-RELATED PULMONARY ARTERIAL IPERTENSION

A. Corrado[1], M. Correale[2], N. Mansueto[1], A. Mele[1], A. Carriero[1], R. Colia[1], M. Di Biase[3], F.P. Cantatore[1]. *[1]Department of Medical and Surgical Sciences - Rheumatology Clinic; [2]Department of Medical and Surgical Sciences - Cardiology Clinic; [3]Department of Medical and Surgical Sciences - Cardiology Clinic, University of Foggia, Foggia, Italy*

Background: Pulmonary arterial hypertension (PAH) represents one of the main clinical expression of the vascular changes in Systemic Sclerosis (SSc). Many clinical and experimental evidences suggest that lung microvascular changes play a role in the pathogenesis of idiopathic PAH (IPAH) also.

Objectives: The aim of this study is to investigate the presence of capillaroscopic abnormalities in patients with idiopathic PAH and to evaluate the differences in capillary naifold changes between patients with IPAH and SSc patients with and without PAH.

Methods: 37 subjects with SSc (of whom 17 with PAH), 21 subjects with IPAH and 20 healthy subjects were recruited. PAH was diagnosed by right heart chateterization. Periungual capillaroscopy was performed in all recruited subjects, considering the following parameters: loops length and width, capillary density, microhemorrhages, avascular areas, neoangiogenesis. To define the pattern of capillary changes in IPAH and healthy subjects a semiquantitative scoring (normal, minor abnormalities, major abnormalities) was used, whereas in SSc subjects the capillary changes were defined as early, active and late pattern.

Results: In all SSc subjects a capillaroscopic scleroderma pattern was found. Particularly, comparing SSc-PAH vs SSc-nonPAH we found an early pattern in 26,7% vs 50%, an active pattern in 66,6% vs 33,3% and a late pattern in a 6,6 vs 16,7% of subjects. None of IPAH subject presented a capillaroscopic scleroderma pattern, but interestingly in 36,4% of minor or major capillaroscopic changes were found. Analysing the single capillarocopic parameters, capillary density was lower in SSc subjects compared to the other groups; in SSc-PAH was lower than in SSc-nonPAH; in IPAH capillary density was lower compared to healthy control. Capillary width was higher in SSc patients compared to healthy and IPAH subjects, being higher in SSc-PAH compared to SSc-nonPAH. The number of megacapillaries, bushy capillaries and microhemorrages was significantly higher in patients with SSc-PAH compared to SSc-nonPAH patients. Interestingly, compared to healthy controls, the IPAH subjects presented a significantly lower capillary density and a significantly higher mean capillary width. Further, IPAH subjects presented a significant increase of number of microhemorrages and ectasic capillaries compared to healthy controls.

Conclusions: Microcirculation alterations, and particularly the reduction of capillary density and the increase od capillary width appears to be more severe in SSc subjects with PAH compared to SSc subjects without PAH. Capillaroscopic changes can be present in IPAH subjects also. These data support the hypothesis that in SSc peripheral microcirculation changes can be related to the entity of pulmonary microcirculation changes and that an altered vascular lung remodelling could play a role in IPAH also.

References:

[1] Cutolo M et al. The contribution ofcapillaroscopy to the differential diagnosis of connective autoimmune diseases. Best Pract Res Clin Rheumatol. 2007 Dec;21(6):1093–108.

[2] Riccieri V. Systemic sclerosis patients with and without pulmonary arterial hypertension: a nailfoldcapillaroscopy study. Rheumatology (Oxford). 2013 Aug;52(8):1525–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5091

SAT0326 THE ASSCOCIATION OF SERUM TYPE 1 INTERFERON ACTIVITY AND AUTOANTIBODIES IN INFLAMMATORY MYOSITIS

A. Maruyama, N. Ono, M. Sakai, Y. Sadanaga, S. Koarada, Y. Tada. *Rheumatology, Saga universitiy, Saga, Japan*

Background: Recent reports had shown that most of clinically amyopathic dermatomyositis (CADM), which showed poor prognosis, was positive for anti-Melanoma differentiation-associated gene 5 (MDA5) antibody (Ab). It had been shown that patients not only with lupus but with dermatomyositis (DM) also showed increased type 1 interferon (IFN) signature. MDA5 acts as a cytosolic RNA sensor, which drives type 1 IFN production. These facts suggested that type 1 IFN might have some roles in anti-MDA5 Ab positive patients.

Objectives: We evaluated the association of serum type 1 IFN signature and autoantibodies in patients with inflammatory myositis, in particular anti-MDA5 Ab positive patients and anti-aminoacyl-tRNA synthetases (ARS) Ab positive patients.

Methods: Sera from 33 inflammatory myositis patients (13 DM, 10 PM and 10 CADM) were studied for type 1 IFN activity, using a functional reporter cell assay. Briefly WISH cells were incubated with serum containing media for 6 hours. Serum IFN signature scores of the incubated cells were evaluated by the sums of gene expressions of Mx1, IFIT3, IFI44L and IFI44 by real time PCR (Reference). Anti-MDA5 Ab and Anti-ARS Ab were measured by ELISA. We divided these patients into three groups, anti-MDA5 Ab positive group (MDA5 group), anti-ARS Ab positive group (ARS group) and double negative group (DN group). We included double positive patients into MDA5 group. The presence of interstitial lung disease (ILD) and the prognosis were also investigated.

Results: MDA5 group had 12 patients (8 CADM and 4 DM), ARS group had 8 patients (4 DM, 1 CADM and 3 PM), and DN group had 13 patients (5 DM, 1 CADM and 7 PM). 9 of MDA5 group, 5 of ARS group, and 1 of DN group were complicated with ILD. Serum IFN signature scores of MDA5 group were significant higher than those of ARS group and DN group (12.43 1.406, 2.407, p=0.0005). The most of ARS group showed low serum IFN signature activities. The overall survivals of ARS group were fairer than MDA5 group, but not significantly. The deceased cases of MDA5 group showed especially high serum IFN signature activities.

Conclusions: We characterized two major groups in inflammatory myositis patients. ARS group was characterized by low IFN signature with the susceptibility to DM and ILD. MDA5 group was characterized by high serum IFN signature with the high susceptibility to CADM. Our results suggest that these two entities may have different onset mechanisms, leading to different outcomes.

References:

[1] Niewold TB, Rivera TL, Buyon JP, Crow MK. Serum type I interferon activity is dependent on maternal diagnosis in anti-SSA/Ro-positive mothers of children with neonatal lupus. Arthritis Rheum. 2008 Feb;58(2):541–6.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4900

SAT0327 NUTRITIONAL STATUS IN PATIENTS WITH SYSTEMIC SCLEROSIS

A. Wojteczek[1], M. Ziętkiewicz[1], S. Małgorzewicz[2], Z. Zdrojewski[1]. *[1]Department of Internal Medicine, Connective Tissue Diseases and Geriatrics; [2]Department of Clinical Nutrition, Medical University of Gdańsk, Gdańsk, Poland*

Background: Systemic sclerosis (SSc) is a chronic connective tissue disease characterized by involvement of multiple organs. Many clinical aspects, such as gastrointestinal involvement, mood disturbances, functional status, and inflammation, may lead to disease-related malnutrition [1]. The connection between inadequate nutritional status and systemic sclerosis is still not well established. It is important to identify the symptoms of malnutrition, because it is known as a predictor of poor clinical outcome [2].

Objectives: To assess nutritional status in patients with systemic sclerosis.

Methods: The study involved fifty-two patients with SSc (44 women and 8 men, mean age 54,3±11,7 year) who were diagnosed according to ACR/EULAR criteria. The assessment of nutritional status was determined by subjective global assessment (SGA), body mass index (BMI) and level of serum albumin. Appetite was assessed by simplified nutritional appetite questionnaire (SNAQ). In all patients hand grip strength and triceps skinfold were established. The C-reactive protein (CRP), lipid profile, and level of haemoglobin/lymphocytes were measured in serum.

Results: Inadequate nutritional status was diagnosed in 14 patients (26,9%) with SSc. According to SGA 11 (21,15%) patients had signs of mild malnutrition, while 41 (78,85%) were well-nourished. Considering BMI, 1 patient (1,92%) was underweight, 24 (46,15%) were eutrophic, 21 (40,38%) overweight and 6 (11,54%) obese. Significantly lower BMI had patients with inadequate nutritional status (23,17±4,47 vs. 25,98±3,34; p=0,009). Low level of serum albumin was detected in 5 patients (9,6%) with SSc. Level of serum albumin and appetite were significantly decreased in patients with inadequate nutritional status (p=0,009; p=0,003). No statistical differences were noticed in hand grip strength, triceps skinfold, lipid profile, levels of CRP and haemoglobin/lymphocytes.

Conclusions: Malnutrition in systemic sclerosis is still underestimated clinical issue. This study provides useful data about nutritional status of patients with

systemic sclerosis. Altered level of albumin and decreased appetite may lead to worsening in nutritional status. Assessment of nutritional status in this group of patients should be performed regularly, because it can be potentially modified.

References:
[1] Harrison E, Herrick AL, McLaughlin JT, Lal S. Malnutrition in systemic sclerosis. Rheumatology 2012;51:1747–1756.
[2] Krause L, et al. Nutritional status as marker for disease activity and severity predicting mortality in patients with systemic sclerosis. Ann Rheum Dis 2010;69:1951–1957.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6032

SAT0328 AN OPEN-LABEL STUDY OF AMBRISENTAN WITH ANTI-FIBROTIC AGENT COMBINATION THERAPY IN THE TREATMENT OF DIFFUSE SYSTEMIC SCLEROSIS

A. Schorpion[1], M. Shenin[2], R. Neubauer[1], C.T. Derk[1]. *[1]Division of Rheumatology, Hospital of the University of Pennsylvania; [2]Division of Rheumatology, Thomas Jefferson University Hospital, Philadelphia, United States*

Background: Systemic sclerosis (SSc) is marked by immune dysregulation, inappropriate fibrosis and a vasculopathy for which there is currently no universally accepted disease modifying regimen. Ambrisentan, a selective type A endothelin receptor antagonist (ERA) has known benefits in the treatment of the vasculopathy related to pulmonary arterial hypertension and has been postulated to have anti-fibrotic effects. The additive effect of an ERA in combination with an anti-fibrotic agent has not previously been studied in SSc.
Objectives: To determine the safety and efficacy of ambrisentan in combination with an anti-fibrotic agent in early diffuse cutaneous systemic sclerosis (dcSSc).
Methods: Patients already on anti-fibrotic therapy for early dcSSc with onset of skin sclerosis less than 48 months before study entry were placed on ambrisentan 5mg daily for 12 months in an open-label study. Laboratory and clinical parameters to assess safety, as well as severity and progression of SSc were obtained at specified intervals. The primary outcome measure was the modified Rodnan skin score (mRSS), and secondary outcomes were the Medsger severity score, the Short Form Health Survey (SF)-36 questionnaire, pulmonary function tests (PFTs), and 2D echocardiograms (echo).
Results: A total of 15 patients were recruited who were on anti-fibrotic therapy upon entry of the study, most commonly mycophenolate (14 patients) and 1 patient on methotrexate. Of the patients entering the study, 10 patients (66.7%) completed 12 months of treatment with the study drug. Using intention-to-treat analysis, the mRSS improved significantly with a mean difference in mRSS of -8 from study entry to study end (p=0.000167). Among study completers (n=10), there was a trend for improvement in all but one category of the SF-36 while only the physical health component was of statistical significance (p=0.025). The median Medsger severity scores remained unchanged except for a change in median skin score. No statistically significant change was observed in PFTs and in mean estimated pulmonary arterial pressure by echo for those patients in whom data was obtained at baseline and at 12 months (n=12 and n=5, respectively). The most common adverse events included peripheral edema and dizziness. Two patients withdrew from the study due to intolerance of the study drug. Serious adverse events (SAE's) occurred in 4 study subjects and included scleroderma renal crisis (n=1), upper gastrointestinal bleeding (n=1) and infections (n=2). None of the SAEs were deemed to be related to the study drug.
Conclusions: In this prospective open-label study of ambrisentan and anti-fibrotic combination therapy in early dcSSc, we observed significant improvements in the mRSS and patient-perceived physical health status on the SF-36. There was no observed change in peripheral vascular involvement and no consistent trend in PFTs. Combination ambrisentan and anti-fibrotic therapy appears relatively safe in this 12-month study. Larger, controlled trials are needed to further investigate the safety and efficacy of combination therapy.
Acknowledgements: [C.T. Derk received funding support for this study by Gilead Pharmaceuticals]
Disclosure of Interest: A. Schorpion: None declared, M. Shenin: None declared, R. Neubauer: None declared, C. Derk Grant/research support from: Gilead Pharmaceuticals
DOI: 10.1136/annrheumdis-2017-eular.3932

SAT0329 INTRAVENOUS CYCLOPHOSPHAMIDE ACCORDING TO THE EURO-LUPUS NEPHRITIS PROTOCOL FOR PROGRESSIVE INTERSTITIAL LUNG DISEASE IN PATIENTS WITH POLYMYOSITIS/DERMATOMYOSITIS

A. Notarnicola[1], M. Dastmalchi[1], S. Nyren[2], K. Gunnarsson[1], L. Dani[1], I.E. Lundberg[1]. *[1]Department of Medicine, Rheumatology Unit, Karolinska University Hospital and Karolinska Institutet; [2]Department of Molecular Medicine and Surgery (MMK), K1, Diagnostic Radiology, Karolinska University Hospital and Karolinska Institutet, Solna, Stockholm, Sweden*

Background: Interstitial lung disease (ILD) affects 30–70% of patients with Polymyositis (PM) and Dermatomyositis (DM) and is one of the major contributors of morbidity and mortality.
Objectives: To study the efficacy and the safety of intravenous cyclophosphamide (IVCYC) according to the Euro-Lupus nephritis protocol for ILD in PM/DM patients.
Methods: Twelve patients with PM/DM (mean age 54± SD 8), who received, 500 mg IVCYC every other week, up to 12 times, according to the treating physician, as first line treatment, were retrospectively studied. Six patients had anti-Jo1, 4 anti-PL7, 1 anti-PL12, and 1 anti-MDA5 auto-antibodies. The median (IQR) disease duration before IVCYC was 4 (10,8) months. High doses of prednisolone were given for the first month and then gradually tapered. Response to treatment after a median (IQR) follow-up of 5 (2,8) months was based on pulmonary function tests (PFT) and HRCT). The extent of pure ground-glass opacity (pGGO), pulmonary fibrosis (PF), honeycomb cysts (HCs) and emphysema was scored (0=0%, 1=1–5%, 2=6–15%, 3=16–20%, 4=21–25%, 5=26–50%, 6=51–75%, 7= >75%) in the upper, middle and lower lung zones before and after therapy. The total score for each finding was calculated as the sum of the scores of the 3 zones (1).
Results: The mean IVCYC total amount was 4.75 ± SD 1.4 gr. Before IVCYC, the median (IQR) values of forced vital capacity (FVC)%, forced expiratory volume in 1 second (FEV1)%, vital capacity (VC)%, total lung capacity (TLC)% and diffusion capacity of the lung for carbon monoxide (DLCO)% were 67 (26), 60 (14), 63 (11), 63 (12) and 57 (25), respectively. After therapy, the median (IQR) values became 74 (29), 80 (18), 80 (24), 77 (19) and 68 (27), respectively. The difference between baseline and follow-up TLC%, FVC% (fig.1) and VC% median values was statistically significant ($p<0,05$). FVC% and TLC% improved >10% in 6 and 5 patients, respectively; DLCO% improved >15% in 3 patients. Before IVCYC, the median (IQR) scores of pGGO and PF were 12,5 (9) and 12 (7), respectively. After IVCYC, they decreased (7 (6) and 9 (12), respectively). In the group of anti-Jo-1 positive patients, the difference was close to the statistically significant (from 13,5 (10) to 7,5 (15), p=0,06 and from 9,5 (10) to 4,5 (16), p=0,07, respectively). The median (IQR) pGCO scores of anti-Jo-1 negative patients improved (from 11,5 (11) to 8,50 (17)), while the median (IQR) PF scores were unchanged (from 13,5 (4) to 14 (10)). At baseline and follow up, the median scores of HCs and emphysema were 0. No statistically significant correlations were found between PFT values and HRCT scores. The difference of PF extent was negatively correlated with the disease duration before the first IVCYC (r=-0,56, p=0,056, fig 1). No adverse events or drug toxicity were observed.
Conclusions: After IVCYC according to the Euro-Lupus nephritis protocol PFT and HRCT findings improved in PM/DM patients with ILD without any adverse events or drug toxicity. Longitudinal controlled studies are needed to confirm the efficacy and the safety of this treatment protocol.

References:
[1] Goldin JG, et al.High-resolution CT scan findings in patients with symptomatic scleroderma-related interstitial lung disease.Chest. 2008 Aug;134(2):358–67.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5878

SAT0330 LOWER PREVALENCE BUT COMPARABLE CLINICAL CHARACTERISTICS AND PROGNOSIS OF SYSTEMIC SCLEROSIS IN CRETE-GREECE AS COMPARED TO OTHER EUROPEAN COUNTRIES: A SINGLE CENTER EXPERIENCE

A. Repa, I. Gergianaki, G. Spyrou, N. Kougkas, A. Kountouri, N. Avgoustidis, G. Bertsias, P. Sidiropoulos. *Rheumatology, University of Crete, Heraklion Crete, Greece*

Background: Systemic Sclerosis (SSc) is a rare, multisystemic connective tissue disease with significant morbidity. Prevalence and incidence of SSc varies worldwide (0.7–265 cases per 100,000/y[1,2] and 0.06–12.2 cases per 100,000/y[1] respectively). Mortality in SSc patients remains 3.5 times higher than the general population[3]. We sought to generate updated data on the epidemiology and burden of SSc in the Greek population.
Objectives: To study the prevalence and incidence of SSc, describe the clinical characteristics and assess mortality and main causes of death in Crete (Greece) over a 5-year period (2010–2015).
Methods: We conducted a cohort Study in defined geographic area (6,5% of Greek population). We reviewed demographics, clinical features, autoantibodies status and the causes of death from the Scleroderma cohort followed at the Rheumatology clinic of the University Hospital, Heraklion. The cause of death was categorized as related or not to scleroderma. Incidence and prevalence were estimated including patients living permanently in Crete who fulfilled SSc 2013 ACR/EULAR Classification Criteria for Scleroderma.
Results: 72 patients (88% women, mean±SD age at diagnosis 48.5±16.7 years [range 15–87]) were identified, corresponding to a crude point prevalence of $13.8/10^5$ (CI 95% 11–17/10^5) (December 2015). The Incidence rate was estimated at $0.05/10^5$ per year (period 2010–2015). Diffuse SSc (dSSc) was present in 27.7%, limited SSc (lSSc) in 72.2%, while an overlap syndrome in 19.4% (9.7% with systemic lupus erythematosus). Frequencies of anti-Scl70 and anti-cectromere antibodies were 59.7% and 9.7%, respectively. Arthritis was present in 69.5%, lung involvement in 61% (9.7% pulmonary arterial hypertension [PAH]), whereas only a single patient developed renal crisis. 8.3% developed cancer. Case fatality rate during 2010–2015 was 9.7% (CI 95% 7.4–11.9) with an average (±SD) age of death at 65.2 (± 17.6) years. Mortality cases were related to SSc in 30.7%. The main cause of death was sepsis (30.8%) followed by PAH and cardiac arrest (15.4% each). Male gender ($p<0.001$) and presence of PAH (p=0.001) were related to mortality. Mean disease duration until death was 5.3

(±3.2) years in cases of SSc-related death, as compared to 18.3 (±11.0) years in deaths not related to SSc.
Conclusions: SSc prevalence (13,8/10^5) in Crete is consistent with previous (2002) Greek studies (15,4/10^5)[4] albeit lower compared to other European countries and USA[5]. Despite its rarity, the disease has significant burden. The SSc-related mortality occurs early in the disease course. Early recognition and treatment may decrease disease burden and improve the outcomes.
References:
[1] Chifflot H, et al Semin Arthritis Rheum. 2008 Feb;37(4):223–35.
[2] Maricq HR, et al Arthritis Rheum. 1989 Aug;32(8):998–1006.
[3] M. Elhai, C. et al Rheumatology (2012); 51(6):1017–1026.
[4] Alamanos et al Semin Arthritis Rheum. 2005 Apr;34(5):714–20.
[5] Mayes MD, Rheum Dis Clin North Am. 2003 May;29(2):239–54.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2847

SAT0331 AMINAPHTONE INCREASES SKIN BLOOD PERFUSION AND IMPROVES CLINICAL SYMPTOMS IN PATIENTS WITH BOTH PRIMARY AND SECONDARY RAYNAUD'S PHENOMENON: AN OPEN SIX MONTH PILOT STUDY

B. Ruaro, S. Paolino, C. Pizzorni, E. Alessandri, E. Gotelli, M. Cutolo, A. Sulli.
Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS AOU San Martino, Genoa, Italy

Background: Aminaphtone (1,4-Dihydroxy-3-methyl-2-naphthyl-4-aminobenzoate) is a vasoactive drug that was recently demonstrated to improve the symptoms of Raynaud's phenomenon (RP) and to down-regulate endothelin-1 production by endothelial cells (1–3).
Objectives: To evaluate skin blood perfusion and clinical symptom changes during aminaphtone treatment in patients with both primary and secondary RP, during a six-month follow-up.
Methods: Forty-six patients with active RP were enrolled during routine clinical assessment in November 2015 (11 primary RP, mean age 49±19SD years, mean RP duration 6±3 years; 35 secondary RP to systemic sclerosis, mean age 61±17 years, mean RP duration 11±9 years), after informed consent. Aminaphtone was administered 75 mg twice daily (off label) in addition to current treatments (the patients were on a stable drug regimen for at least two months before, which remained unmodified during the follow-up). Blood perfusion was measured by Laser Speckle Contrast Analysis (LASCA) and values recorded as perfusion units (PU) (4), at the level of fingertips, periungual areas, dorsum and palm of hands, and face, at baseline (T0), after one (T1), four (T4), twelve (T12) and twenty-four (T24) weeks of treatment. Raynaud's condition score (RCS) and both frequency and duration of Raynaud's attacks were assessed at the same time. Forty-six patients with RP (9 primary RP and 37 secondary RP to systemic sclerosis) not treated with aminaphtone were also enrolled as a control group and evaluated at T0 and T24.
Results: A progressive statistically significant increase of blood perfusion was observed from T0 to T12 in all skin areas analyzed (median PU at T0, T1, T4, T12, T24 respectively: fingertips 55, 88, 101, 107, 98 periungual areas 44, 88, 91, 92, 92; dorsum of hands 38, 61, 71, 75, 75; palm of hands 56, 85, 89, 94, 82; whole face 127, 138, 144, 159, 129; $p<0.001$ for all areas). From T12 to T24 was not observed any further increase of blood perfusion. A progressive statistically significant decrease of RCS (median at T0, T1, T4, T12, T24: 7, 6, 4, 4, 4; $p<0.0001$), frequency of Raynaud attacks/day (median: 2, 2, 1, 1, 1; $p<0.0001$) and Raynaud duration (median: 20, 20, 10, 4, 4 minutes; $p<0.0001$) was also recorded from T0 to T12. The results were similar in both primary and secondary RP patients (p=0.40). Aminaphtone administration had to be stopped in 2 patients due to headache, and one patient was lost during follow-up. Any statistically significant variation of blood perfusion was not observed in the control group (median PU at T0 and T24 respectively: fingertips 70, 71; periungual areas 68, 70; dorsum of hands 57, 57; palm of hands 59, 59; whole face 132, 130; p=n.s. for all areas).
Conclusions: This study demonstrates that aminaphtone treatment seems able to increase skin blood perfusion and to improve RP symptoms, even in patients affected by systemic sclerosis. These preliminary results should be further confirmed by a randomized clinical trial, also to assess the role that aminaphtone plays in the treatment/prevention of disease clinical complications.
References:
[1] Parisi S, et al. Am J Int Med 2015;3;204–9.
[2] Scorza R, et al. Drugs R D 2008;9:251–7.
[3] Salazar G, et al. Eur J Pharmacol. 2016;782:59–69.
[4] Ruaro B, et al. Ann Rheum Dis. 2014;73:1181–5.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4470

SAT0332 HEPATOBILIARY INVOLVEMENT IN SYSTEMIC SCLEROSIS AND THE CUTANEOUS SUBSETS. CHARACTERISTICS AND SURVIVAL OF PATIENTS FROM THE SPANISH RESCLE REGISTRY

B. Marí Alfonso[1], C. Tolosa-Vilella[2], L. Morera-Morales[2], A. Marín-Ballvé[3], J. Chamorro Fernández[4], X. Pla Salas[5], B. Madroñero-Vuelta:[6], C. Simeón Aznar[7] on behalf of RESCLE Investigators of the Autoimmune Diseases Study Group (GEAS). *[1]Internal Medicine, Corporació Sanitària Parc Tauli; [2]Internal Medicine, Corporació Sanitària Parc Tauli. Sabadell. Barcelona, Sabadell; [3]Internal Medicine, Hospital Clínico Universitario Lozano Blesa, Zaragoza; [4]Internal Medicine, Complejo Asistencial Universitario de Salamanca, Salamanca; [5]Internal Medicine, Consorci Hospitalari de Vic, Barcelona; [6]Internal Medicine, Hospital General San Jorge, Huesca; [7]Internal Medicine, Hospital Universitario Vall d'Hebron, Barcelona, Spain*

Background: Hepatobiliary involvement (HBI) has been associated to systemic sclerosis (SSc). However, it is not considered as characteristic clinical manifestation of that autoimmune disease
Objectives: To assess the prevalence and causes of HBI in SSc and to investigate the clinical characteristics and prognosis of SSc patients with HBI (SSc-HBI) and without HBI (SSc-non HBI).
Methods: Up to January 2015, 1572 SSc patients were collected in the Registro de ESCLErodermia (RESCLE) and causes of hepatobiliary disturbances were recorded. We investigated the HBI related characteristics and survival from the entire cohort and according to the following cutaneous subsets: dcSSc, lcSSc, and SSc sine scleroderma (ssSSc).
Results: Out of 1572, 118 (7.5%) patients had HBI, and primary biliary cholangitis (PBC) was largely the main cause (n=67, 4.3%), followed by autoimmune hepatitis (n=19, 1.2%), and anti-mitochondrial negative PBC (n=6, 0.4%). Other causes of HBI were: secondary liver diseases (n=11, 0.7%), SSc-related HBI (n=7, 0.4%), nodular regenerative hyperplasia (n=3, 0.2%), liver cirrhosis (n=3, 0.2%), and unknown origin (n=2, 0.1%). In multivariate analysis, HBI was independently associated to lesser risk of dcSSc (5.1% vs 24.4%, OR: 0.18, p=0.005%), and higher frequency of calcinosis (26% vs 18%, OR: 1.80; p=0.028), left ventricular diastolic dysfunction (46% vs 27%, OR: 1.73; p=0.027), sicca syndrome (51% vs 29%, OR: 2.03; p=0.003), and anti-centromere antibodies (ACA, 73% vs 44%, OR: 1.86; p=0.023). According to the cutaneous subsets, HBI was associated: (1) in lcSSc subset, to longer time from SSc onset to diagnosis (10.8±12.5 vs 7.2±9.3, OR: 1.03; p=0.012), sicca syndrome (54% vs 33%, OR: 1.96; $p<0.001$), and ACA (80% vs 56%, OR: 2.64; $p<0.001$); and (2) in ssSSc subset, to sicca syndrome (44% vs 19%, OR: 3.43; p=0.018). No associations were found in dcSSc subset. HBI was the cause of death in 2.3% patients. Kaplan–Meier cumulative survival for the SSc cohort and the cutaneous subsets, according to the presence or absence of HBI showed no differences.
Conclusions: The prevalence of HBI in SSc was 7.5%. Primary autoimmune liver diseases accounted for 77% of all conditions. PBC was the main cause of HBI reaching 4.6% of the overall SSc cohort. Patients with HBI were rarely classified as dcSSc subset and the elapsed time from the first SSc symptom to SSc diagnosis was longer. Calcinosis cutis, diastolic dysfunction, sicca syndrome, and the presence of ACA were all independently associated to HBI. In lcSSc subset, HBI was associated to sicca syndrome and ACA but in ssSSc only sicca syndrome was more prevalent. HBI was the cause of death in 2.3%
References:
[1] Assassi S., Fritzler MJ, Arnett FC, et al., Primary biliary cirrhosis (PBC), PBC autoantibodies, and hepatic parameter abnormalities in a large population of systemic sclerosis patients. J Rheum 2009; 36: 2250–2256.
[2] Rigamonti C, Shand LM, Feudjo M, et al. Clinical features and prognosis of primary biliary cirrhosis associated with systemic sclerosis. Gut 2006; 55; 388–394.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5745

SAT0333 PREVALENCE OF SARCOPENIA IN PATIENTS WITH SYSTEMIC SCLEROSIS ACCORDING TO THE REVISED CRITERIA OF THE EUROPEAN WORKING GROUP ON SARCOPENIA IN OLDER PEOPLE

C. March[1], E. Siegert[1], E. Preis[1], A. Makowka[1], F. Buttgereit[1], G. Riemekasten[2], K. Norman[3]. *[1]Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin Berlin, Berlin; [2]Department of Rheumatology, University of Luebeck, Luebeck; [3]Research Group on Geriatrics, Charité-Universitätsmedizin Berlin, Berlin, Germany*

Background: Systemic Sclerosis (SSc) is a chronic inflammatory connective tissue disease that is often associated with gastrointestinal involvement and myopathy. Sarcopenia is defined as age-associated loss of muscle mass, strength and function with profound impact on functionality as well as on mortality (1). "Secondary sarcopenia" has now been described in the context of severe and chronic disease such as malignant disease or inflammatory disorders (2) and been linked to poor clinical outcome.
Objectives: Analysis of the prevalence of sarcopenia in patients with SSc with respect to clinical characteristics, quality of life and severity of physical impairment.
Methods: 129 patients were included. Sarcopenia was defined according to the

criteria of the European Working Group on Sarcopenia in Older People (3) using appendicular lean mass assessed by bioelectric impedance analysis and grip strength - stratifying both by body mass index. We also used the 2016 formula by Scafoglieri et.al to calculate appendicular lean mass (4). This approach is different from previous studies because we combined the new formula with established cut-off values, which incorporate a functional parameter. Muscle function was assessed by hand grip, knee extension strength and peak expiratory flow. Impairment and quality of life were evaluated using the Scleroderma Health Assessment Questionnaire (SHAQ) and Short-Form 36 Health Survey (SF-36®). Clinical data were assessed according to standardised procedures.

Results: The prevalence of sarcopenia in our study group was 27.1%.There were no significant differences between patients with and without sarcopenia regarding age (p=0.838) and disease duration (p=0.832). There were significant differences regarding grip strength (p<0.001), knee extension strength (p=0.003), peak flow (p=0.042), SF-36® Physical Function (p=0.009) and the number of immunosuppressive (p=0.048) and other drugs taken (p=0.037). See Table 1.

Table 1 Comparing analysis between two patient groups (Sarcopenia/ No Sarcopenia)

Variable	Sarcopenia, n = 35	No Sarcopenia, n = 94	p
Women	32 (91.4)	85 (90.4)	0.862
Age (years)	59.5 ± 14.8	59.0 ± 13.5	0.838
Disease duration (years)	8.6 ± 6.0	8.9 ± 6.9	0.832
Body Mass Index (kg/m²)	20.6 ± 2.7	25.5 ± 5.2	< 0.001
Hand grip strength (kgF)	10.3 ± 6.1	18.7 ± 8.0	< 0.001
Knee extension strength (kgF)	13.6 ± 7.2	22.3 ± 16.3	0.003
Peak flow (l/min)	305.8 ± 102.0	348.3 ± 101.9	0.042
SF-36® Physical Health SUM	40.5 ± 18.1	48.5 ± 19.6	0.043
SF-36® Physical Function	41.7 ± 27.1	54.3 ± 27.4	0.026
SHAQ score	0.66 ± 0.12	0.64 ± 0.07	0.010
IPAQ (level of activity – high)	5 (14.3)	28 (29.8)	0.073
Number of medication	6.2 ± 3.8	4.8 ± 3.2	0.037
Number of immunosuppressive medication	1.4 ± 1.1	1.0 ± 1.0	0.048

Data are given in mean ± SD or n (%)
SSc – Systemic Sclerosis; SF-36® - Short Form 36; SHAQ – Scleroderma Health Assessment Questionnaire; IPAQ – International Physical Activity Questionnaire; CRP – C-reactive protein

Conclusions: There is a high prevalence of sarcopenia in patients with SSc even among younger patients. Sarcopenic patients have a significant increase in physical impairment and a decreased quality of life regarding their physical health. Taking a higher number of immunosuppressive or other drugs was identified as a risk factor for sarcopenia. This could be due to severe organ involvement being a confounder or an indication for the immunological component in the pathophysiology of secondary sarcopenia. This suggests that sarcopenia might be linked to severe disease or multimorbiditiy in SSc patients.

References:

[1] Wang C, Bai L. Sarcopenia in the elderly: basic and clinical issues. Geriatrics & gerontology international. 2012 Jul;12(3):388–96.
[2] Dogan SC, Hizmetli S, Hayta E et.al. Sarcopenia in women with rheumatoid arthritis. European journal of rheumatology. 2015 Jun;2(2):57–61.
[3] Cruz-Jentoft AJ, Baeyens JP, Bauer JM et.al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age and ageing. 2010 Jul;39(4):412–23.
[4] Scafoglieri A, Clarys JP, Bauer JM et.al. Predicting appendicular lean and fat mass with bioelectrical impedance analysis in older adults with physical function decline - The PROVIDE study. Clinical nutrition (Edinburgh, Scotland). 2016 Apr 28.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5532

SAT0334 CORRELATING MULIPLEX PLASMA CYTOKINE ANALYSIS WITH RIGHT HEART CATHETERISATION FINDINGS IN SCLERODERMA ASSOCIATED PULMONARY ARTERIAL HYPERTENSION

C.H. Ho[1], S. Nihtyanova[2], B. Ahmed Abdi[2], G. Coghlan[3], C. Denton[2], B. Schreiber[4], V.H. Ong[2]. *[1]Department of Medicine, Queen Elizabeth Hospital, Kowloon, Hong Kong; [2]Centre for Rheumatology and Connective Tissue Diseases, University College London Medical School, Royal Free Hospital; [3]Department of Cardiology; [4]Department of Rheumatology, Royal Free Hospital, London, United Kingdom*

Background: Right heart catheterisation (RHC) is an important test for the diagnosis and subclassification of pulmonary hypertension (PH), one of the serious manifestations of systemic sclerosis (SSc). It provides haemodynamic information for diagnosis and management. Routine RHC in SSc cases with suspected PH permits blood sampling to explore plasma levels of key cytokines that may be markers of mediators of pulmonary arterial hypertension (PAH) pathogenesis.

Objectives: This is an exploratory study to assess for associations between plasma cytokine levels and haemodynamic assessment from RHC in SSc patients.

Methods: SSc patients undergoing routine RHC were recruited. Indications for referral included suspected PH, or those on treatment for established PH for assessment of response to therapy. Blood samples were collected during RHC in consented patients. Demographic and clinical data were obtained. Haemodynamic data from RHC including mean right atrial pressure (mRAP), mean pulmonary arterial pressure (mPAP), pulmonary capillary wedge pressure (PCWP), pulmonary vascular resistance (PVR), cardiac output (CO) and cardiac index (CI) were recorded. Plasma samples were analysed using a bead-based multiplex platform for IL1b, IL4, IL6, IL10, IL17A, IL17F, IL21, IL22, IL23, IL25, IL31, IL33, IFNg, sCD40L and TNFa (Bio-Rad Pro Assays). Plasma from a small group of healthy controls were also analysed for comparison. For analytes found to be below the lower limit of detection of the assays, they were assumed to be equal to the lower limit of the detection as per the assay's protocol.

Results: 32 SSc patients were recruited. Their mean age was 59.4-year-old, and 31 of them (97%) were female. Most (n=29, 91%) had limited cutaneous SSc. The commonest antibody was anti-centromere antibody (n=16, 55%), followed by anti-U3RNP antibody (n=4, 14%). None of these patients had significant pulmonary fibrosis (≥20% involvement on HRCT thorax scan). PAH, defined as mPAP ≥25mmHg & PCWP ≤15mmHg, was diagnosed at RHC in 26 patients (81%).

Among the proteins tested, only the level of sCD40L was significantly different among the three groups, namely SSc with PH, SSc without PH and healthy controls (p=0.008). sCD40L was also the only biomarker which was significant higher among patients with SSc (with and without PH) than healthy controls (p=0.0284).

Interestingly, there was a weak negative correlation between sCD40L and mPAP (correlation coefficient=-0.35, p=0.0486). There was a moderately strong positive correlation between mRAP and IL4 (correlation coefficient=0.57, p=0.0006) and IL10 (correlation coefficient=0.51, p=0.0028). We found no evidence for association between any of the biomarkers and cardiac output, cardiac index, PCWP or PVR.

Conclusions: Our data suggest that some individual plasma proteins may correlate with specific RHC haemodynamic parameters. Future studies will extend these findings and explore whether combining multiple analytes may give stronger non-invasive prediction of relevant haemodynamic variables and could be used in detection or monitoring of PAH in SSc.

References:

[1] Proc Natl Acad Sci USA. 2015 May19;122(20):E2677–86.
[2] Ann Am Thorac Soc. 2016 Jan;13(1)25–30.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5798

SAT0335 SERUM KYNURENINE/TRYPTOPHAN (KYN/TRP) RATIO AND NEOPTERIN (NEO) LEVELS ARE RAISED IN SYSTEMIC SCLEROSIS (SSC) AND ASSOCIATE WITH SPECIFIC CLINICAL AND AETIO-PATHOGENETIC FEATURES

C. Campochiaro[1], S.D. Lytton[2], B. Ahmed Abdi[1], V.H. Ong[1], C.P. Denton[1]. *[1]Centre for Rheumatology and Connective Tissue Diseases, Royal Free Hospital and UCL Division of Medicine, London, United Kingdom; [2]SeraDiaLogistics Benediktenwandstr 7, 81545, München, Germany*

Background: The enzymes IDO degrades Trp into Kyn and is induced by IFN-gamma/IL-1. Neo is produced by monocytes/macrophages after IFN-gamma stimulation through the enzyme GTPCH and is a biomarker for monitoring immune activation in several diseases [1]. The activity of GTPCH is induced in parallel to IDO and the Kyn/Trp ratio has been suggested to be a direct measure of IDO activity [2].

Objectives: To assess serum level of Kyn, Trp, Neo and Kyn/Trp ratio in SSc and potential associations with specific disease features.

Methods: 60 SSc pts and 10 healthy controls (HC) were recruited and serum levels of Kyn, Trp and Neo were measured. Kyn/Trp ratio was calculated. The results were then correlated with specific disease features: disease duration, limited or diffuse disease, autoantibody profile (anti-RNA pol III (ARA), anti-topoisomerase (ATA) and anti-centromere (ACA)), inflammatory markers, Hb level, concurrent modified Rodnan skin score (mRSS), peak mRSS, pulmonary fibrosis (PF), pulmonary arterial hypertension (PAH), history of scleroderma renal crisis (SRC), GI involvement, vasculopathy, environmental exposure, oncology history, smoking status, immunosuppressive treatment, NT-proBNP and urate levels. Non-parametric statistical tests were used.

Results: Kyn/Trp ratio was higher in SSc compared to HC (mean 49.97±32.77 [41.50 – 58.43] vs 22.5±6.3 [13.5 – 32.5] μmol/mmol, p<0.05) and, more specifically, dcSSc showed higher ratio compared to lcSSc that had higher ratio than HC (mean 56.58±39.62 [43.18 – 69.99] vs 40.05±13.93 [34.16 – 45.93] vs 22.5±6.3 [17.99 – 27.01] μmol/mmol respectively, p<0.05). Moreover,

ARA+SSc had a significantly higher ratio compared to ATA+ and ACA+pts (mean 61.24±41.40 [45.78 – 76.70] vs 39.62±17.99 [29.66 – 49.58] and 37.77±10.20 [32.12 – 43.42] μmol/mmol respectively, $p<0.05$). Kyn/Trp ratio was significantly correlated with SRC ($p<0.05$). We found a direct correlation with mRSS (r=0.269, $p<0.05$), peak mRSS (r=0.276), urate level (r=0.376), CRP (r=0.285) and ESR (r=0.320). Conversely, Neo levels, although significantly higher in SSc compared to HC (mean 12.63±9.30 [10.21 – 15.06] vs 7.11±3.31 [4.74 – 9.48] nmol/L, $p<0.05$), were not significantly different in diffuse compared to limited SSc, but were higher in ARA+ compared to ACA+ and ATA+ patients (mean 14.93±11.52 [10.54 – 19.31] vs 10.81±4.95 [8.07 – 13.56] vs 10.02±6.83 [6.24 – 13.80] respectively, $p<0.05$). Neo levels significantly correlated with PAH. A direct correlation (p=0.05) was found with CRP (r=0.471) and ESR (r=0.430).

Conclusions: These data suggest that Kyn/Trp ratio and Neo levels may reflect aetio-pathogenetic mechanisms in SSc and be elevated in the subgroup of dcSSc that are ARA+, or those manifesting SSc complications associated with ARA+. A specific IFN-gamma signature could be thought to be responsible for the higher levels found in patients although larger studies are required.

References:

[1] Ozkan Y et al. Correlation between DAS-28 and neopterin in early rheumatoid arthritis. Clin Rheum. 2012.
[2] Krcmova KJ at al. Fast and sensitive HPLC method for the determination of neopterin, kynurenine and tryptophan in amniotic fluid, malignant effusions and wound exudates. Bioanalysis. 2015.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3786

SAT0336 MALNUTRITION AND SARCOPENIA IN A LARGE COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS

C. Caimmi[1], P. Caramaschi[1], A. Venturini[1], E. Bertoldo[1], M. Ferrari[2], M. Rossini[1]. *[1]Rheumatology Unit; [2]Internal Medicine, University of Verona, Verona, Italy*

Background: Systemic sclerosis (SSc) is an autoimmune disease that may affect gastrointestinal tract, leading to malabsorption and malnutrition. Previous studies defined this complication with no widely accepted criteria. No thorough evaluations of sarcopenia are available.

Methods: 141 SSc consecutive outpatients have been enrolled. A thorough history, blood samples and body composition by densitometry were collected. Malnutrition was defined accordingly to recently published and widely accepted ESPEN criteria (1); sarcopenia was diagnosed in patients with a reduced skeletal muscle index (2).

Results: The table summarizes cohort's characteristics. Malnutrition was diagnosed in 9.2% (CI95%: 4.4–14.0%). Malnourished patients were more often treated with steroids (p=0.039), had worse gastrointestinal symptoms accordingly to UCLA questionnaire (p=0.007), lower physical activity accordingly to International physical activity questionnaire (p=0.028), longer disease duration (p=0.019), worse predicted DLCO/VA and FVC (p=0.009, respectively) and worse disease severity accordingly to Medsger severity score (DSS) ($p<0.001$ for total, p=0.001 for lung and $p<0.001$ for gastrointestinal tract). In multivariate analysis only FVC (p=0.006) and disease severity (p=0.003), in particular lung involvement as defined by DSS (p=0.013), were confirmed to be worse in malnourished patients. Z-scores were significantly lower in malnourished patients at lumbar site p=0.033), even after correcting for possible confounders. Sarcopenia was diagnosed in 20.7% (CI95% 14.0–27.4%); 11/29 sarcopenic patients were also malnourished and 6/29 were cachectic (i.e. sarcopenia + systemic inflammation). Sarcopenic patients had worse DLCO/VA (p=0.003) and lung (p=0.005) involvement accordingly to DSS than non-sarcopenic ones; cachectic had even lower value (p=0.016 for both). Sarcopenic patients had also longer disease duration (p=0.033).

Table 1. Patients' characteristics

Age	63 (13)
Sex (female)§	119 (84.4)
Diffuse disease subset§	44 (31.2)
Disease duration (year)	13.3 (7.2)
Interstitial lung disease§	39 (27.7)
Pulmonary arterial hypertension§	12 (8.5)
Active disease accordingly to Valentini§	27 (19.1)
FVC predicted (%)	103 (23)
DLCO/VA predicted (%)	75 (21)
mRSS*	8 (7)
Medsger severity score*	5 (3)
Erythrocyte sedimentation rate (mm/h)	26 (16)
C-reactive protein (mg/l)*	3 (0)
Endothelin receptor antagonists§	16 (11.3)
Prostanoids (any)§	130 (92.2)
Steroids§	23 (16.3)
Immunosuppressive treatment§	35 (24.8)

*Expressed as media (IQR); §Expressed as absolute valute (%).

Conclusions: Malnutrition defined with widely accepted diagnostic criteria was found to be lower than previously reported (3–7) using screening tool or non-validated criteria. Sarcopenia was found to be somewhat common, although no previous study on comparable cohorts are available. Lung involvement and function was shown to be significantly linked with nutritional status and may not be explained only by muscle weakness given the absence of correlation between muscle weakness and FVC but only with DLCO/VA.

References:

[1] Cederholm et al. Clinical Nutrition 2015;34;335.
[2] Baumgartner et al. Am J Epidemiol 1998; 147:755.
[3] Baron et al. J Rheumatol 2009;36:2737.
[4] Krause et al. Ann Rheum Dis 2010;69:1951.
[5] Murtaugh et al. Clin Nutr 2013;32:130.
[6] Caporali et al. Clin Nutr 2012;31:666.
[7] Rosato et al. Nutrition 2014;30:204.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3420

SAT0337 IMPACT OF ORGAN INVOLVEMENT ON PATIENT-REPORTED OUTCOMES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

D. Huscher[1], K. Albrecht[1], J. Richter[2], J. Henes[3], T. Alexander[4], A. Zink[1,4]. *[1]Epidemiology, German Rheumatism Research Centre, Berlin; [2]Policlinic & Hiller Research Unit for Rheumatology, Medical Faculty, Heinrich-Heine-University Duesseldorf, University Clinic, Duesseldorf; [3]Department of Rheumatology and Clinical Immunology, Eberhard Karls-University of Tuebingen, Tuebingen; [4]Department of Rheumatology and Clinical Immunology, Charité University Hospital, Berlin, Germany*

Background: Idiopathic inflammatory myopathies (IIM) are associated with considerable morbidity, primarily related to severe muscle weakness and visceral involvement, resulting in disability and impaired quality of life[1]. Results from the OMERACT Myositis Special Interest Group indicate that there is insufficient knowledge on patient-reported outcomes (PROs) in IIM[2].

Objectives: To analyse the association between organ involvement and PROs in IIM patients, taking the presence of autoantibodies into account.

Methods: Data of IIM patients, recorded in the National Database of the German collaborative arthritis centres between 2007 and 2014, were analysed. Physician-reported data on myositis disease phenotypes, organ involvement and antibody status were linked with PROs on functional status (FFbH, range 0–100, 100 indicating full capability), and numerical rating scales (0–10) for pain, fatigue, general health, physical and emotional well-being and coping. Multivariable linear regression analysis was used to investigate the impact of phenotype, organ involvement and autoantibodies on PROs, adjusted for sex, age and disease duration.

Results: A total of 142 IIM patients - 60 polymyositis (PM), 46 dermatomyositis (DM), 15 antisynthetase syndrome (ASS), 12 overlap (OL), 9 others - with mean disease duration of 7.4 years were included. 85% showed muscular, 36% skin involvement, 22% arthritis, 28% interstitial lung disease, 17% dysphagia and 9% cardiomyopathy. Visceral (lung, cardiac or gastrointestinal) manifestation was present in 46% (PM), 54% (DM), 100% (ASS), and 80% (overlap). While moderate to severe (4–10) fatigue was predominately reported in overlap (64%) and ASS (70%), pain was more frequent in overlap (55%) and emotional discomfort was reported most frequently in ASS (57%). For all PROs, worse outcomes were documented in patients with visceral manifestation. Myositis-specific autoantibodies, predominantly Anti-Jo1, were present in 63% of the patients, and were associated with more frequent visceral manifestation (73% vs. 46%), especially interstitial lung disease (50% vs. 15%), and arthritis (32% vs. 13%), but less skin involvement (26% vs. 49%). DM and PM subtypes showed almost identical coefficients for fatigue, physical well-being, general health and coping, while PM was associated with higher emotional strain. Pulmonary hypertension had a severe impact on pain, functional status and daily activities. Cardiomyopathy was associated with impaired general health, arthritis with poorer scores for coping, physical and emotional well-being.

Conclusions: IIM patients with distinct subtypes differ considerably regarding the frequency of organ involvement and self-reported dimensions of disease burden. Anti-Jo1 positivity is associated with higher visceral organ involvement and arthritic manifestations and may therefore also indicate a higher patient-reported disease burden.

References:

[1] Marie I. Curr Rheumatol Rep 2012;14:275–85.
[2] Regardt M et al. Report from OMERACT 12. J Rheumatol. 2015;42:2492–5.

Acknowledgements: The database is funded by unconditional grants from the German Collaborative Arthritis Centres and from a consortium of 11 pharmaceutical companies to the German Academy for Continuing Medical Education in Rheumatology.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3822

SAT0338 SURVIVAL IN A TURKISH INFLAMMATORY MYOSITIS COHORT: A SINGLE-CENTRE STUDY

E. Er Gülbezer, F. Yargucu Zihni, G. Karabulut, G. Keser, Y. Kabasakal. *Rheumatology, Ege University Medical Faculty Internal Medicine, Izmir, Turkey*

Background: Inflammatory myositis is an uncommon group of diseases that

can be associated with significant morbidity and mortality related to systemic involvement or treatment-related complications.
Objectives: This study aimed to describe the clinical features and survival of patients with inflammatory myositis in our centre.
Methods: We performed a single-centre, retrospective study on patients with inflammatory myositis (polymyositis [PM], dermatomyositis [DM], or Anti-Jo1 syndrome) seen from 2000 to 2014, noting their demographic data, clinical features and outcome until December 2016. The primary outcome assessed was all-cause mortality. Cumulative mortality rates were estimated using the Kaplan-Meier test; the Log Rank (Mantle-Cox) test was used to compare subgroup differences in survival.
Results: Seventy-four patients (19 PM, 28 DM, 27 Anti-Jo1 syndrome) were available for the study. Median age at diagnosis was 47 years (min 17, max 75) and median follow-up time was 93 months (min 4, max 311). Sixty-one patients (82, 4%) were female and 13 (17, 6%) were male. Malignancy was found in 4 patients (2 invasive ductal adenocancer of breast, 1 over cancer and 1 non-small cell lung cancer) and they were all female DM patients. Nineteen patients (25,7%) died at the end of the follow-up.
The 19 patients with PM consisted of 15 female and 6 male, with a median age at diagnosis of 45 years (min 22, max 74) and median follow-up time of 88 months (min 5, max 204). The 28 patients with DM consisted of 24 female and 4 male, with a median age at diagnosis of 52 years (min 17, max 75) and median follow-up time of 80 months (min 4, max 288). The 27 patients with Anti-Jo1 syndrome consisted of 22 female and 5 male, with a median age at diagnosis of 50 years (min 22, max 63) and median follow-up time of 117 months (min 5, max 311).
Overall survival rates of the whole group were 91%, 83%, and 76% for 1, 5, and 10 years, respectively. The survival rates at 1, 5 and 10 years from the diagnosis were respectively 88%, 82%, %82 for PM, %88, 80%, %80 for DM and 96%, 88%, 74,5% for Anti-Jo1 syndrome. But there was no significant difference between the survival rates of the diagnose groups (p=0,734). Also there wasn't a significant difference between the survival rates of sex and age groups (p=0,503), (p=0,112). But the survival rates were significantly lower in patients with the time from diagnose less than 8 years (p=0,000).

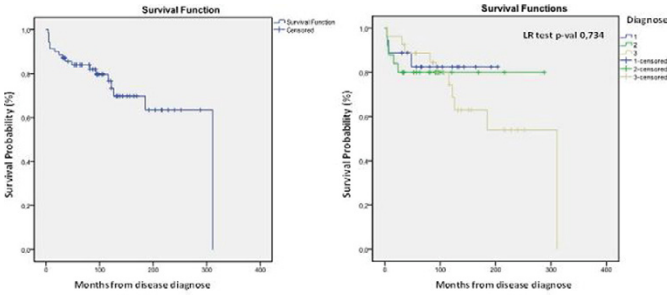


Figure 1. Survival probability of all patients with inflammatory myositis (Graph A) and according to the diagnose* (Graph B).
*1, Polymyositis; 2, Dermatomyositis; 3, Anti-Jo1 syndrome

Conclusions: Our study involved 74 patients followed up for a median of 7, 7 years and is one of the largest cohorts of patients with inflammatory myositis in Turkey. Survival was quite similar with the literature. Usually mortality has been expected in the first years after the diagnosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5956

SAT0339 LUNG TRANSPLANTATION IN PATIENTS WITH INTERSTITIAL LUNG DISEASE ASSOCIATED WITH ANTISYNTHETASE AND ANTI-MDA5 SYNDROMES. EXPERIENCE FROM A REFERENCE SPANISH HOSPITAL

E. Trallero-Araguás[1], C. Berastegui[2], M. López-Corbeto[1], I. Bello[3], A. Román[2], A. Selva-O'Callaghan[4]. *[1]Rheumatology Unit; [2]Pneumology Department; [3]Thoracic Surgery Department; [4]Internal Medicine Department, Hospital Vall d'Hebron, Barcelona, Spain*

Background: Interstitial lung disease (ILD) is the most characteristic feature and prognosis determinant of patients with antisynthetase (AS) and anti-MDA5 syndromes. Despite immunosuppressive treatment, ILD sometimes progresses to an end-stage lung disease, for which lung transplantation (LT) is the only therapeutic option. There is scarce data about post-LT outcome in this group of patients.
Objectives: To describe clinical characteristics and post-LT outcome of patients with ILD associated to AS and anti-MDA5 syndromes included in the LT program of the Vall d'Hebron Hospital of Barcelona.
Methods: We performed a review of patient records listed in the LT program.
Results: From 1990 to 2016 ten patients (5 women) with ILD related to AS or anti-MDA5 syndromes were included in the LT program (3% of patients with ILD accepted for LT). Nine patients (2 anti-MDA5, 4 anti-Jo1, 2 anti-PL12 and 1 anti-PL7) received LT while 1 patient (anti-Jo1) was still in list at the end of this study. Median age (range) of disease diagnosis was 39 years (25–55). Six patients had clinical myopathy [2 dermatomyositis (DM) and 4 polymyositis] whereas 1 patient was diagnosed with amyopathic DM. Four patients had associated pulmonary hypertension. Time between disease diagnosis and patient inclusion in LT list was higher in anti-Jo1 patients [median (range) 8.8 years (8.3–17.6)] than in the rest of the cohort [anti-MDA5 <1 year; antiPL12 0.7 and 3.9 years; anti-PL7 1.3 years] ($p<0.05$). Four patients underwent bilateral LT and 5 unilateral LT. Three patients received an urgent LT (2 anti-MDA5 and 1 anti-Jo1). Six patients presented an histologic pattern of UIP and 3 of NSIP. Early complications (<45 days) included: primary graft disfunction in 3 patients; phrenic paresis in 2 patients and infection in 6 patients. One patient suffered an acute rejection (AR). Six patients presented late complications (>45 days): one patient developed an acute cellular rejection (ACR) and an autoantibody mediated rejection 8 and 10 months from LT respectively; 4 patients suffered chronic lung allograft dysfunction (CLAD), 2 of whom are still alive; Infection was diagnosed in 6 patients. One patient developed a squamous skin carcinoma. No flare of myopathic or lung disease was observed after LT in any case. Four patients (44%) died: 2 of an acute respiratory failure in the immediate postoperatory period (1 caused by suture dehiscence and 1 by refractory ACR); 1 of an invasive aspergillosis, 17 months after LT; and 1 of CLAD after 54 months. Median follow-up (range) of the rest of the cohort was 35 months (8–70). All patients who survived more than 45 days recovered an optimal functional capacity for daily activities with no request for long-term oxygen therapy.
Conclusions: LT should be considered a valid option to treat patients with end-stage or severe and rapidly progressive ILD associated to AS and anti-MDA5 syndromes. An early remission to LT referral centers for evaluation should be considered especially in non-Jo1 patients. No relapse of myositis or ILD was observed after LT. Mortality could not be attributed to the primary disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6320

SAT0340 SUBCLINICAL CARDIOVASCULAR DISEASE IN SCLERODERMA: A STUDY WITH CARDIOVASCULAR RISK CHARTS, CT CORONARY CALCIUM SCORE AND CAROTID ULTRASONOGRAPHY

I. Sanz Pérez[1], F. Martínez Valle[1], A. Guillén del Castillo[1], N. Pizzi[2], A. Roque Pérez[3], H. Cuéllar Calàbria[3], A. Fernández Codina[1], E. Callejas Moragas[1], V. Fonollosa Pla[1], C.P. Simeón Aznar[1]. *[1]Internal Medicine; [2]Nuclear cardiology; [3]Radiology, Hospital Universitari Vall d'Hebron, Barcelona, Spain*

Background: Recently published population-based cohort studies had shown a high prevalence of cardiovascular (CV) disease in Systemic Sclerosis (SSc) patients.
Objectives: The aim of this study is to compare three different methods to measure CV risk in patients with scleroderma.
Methods: We conducted a cross-sectional study in a single center that included 43 SSc patients without CV events. We used both CV risk assessment charts SCORE for populations with low CV risk and REGICOR algorithm adjusted to Spanish subjects. Coronary Compute Tomography (CT) with coronary arterial calcium score (CACscore) was performed considering several cut-off points as predictors of CV risk. Carotid doppler ultrasound was performed to measure the Carotid Intima Media Thickness (CIMT) and for the detection of cholesterol plaques, according to Mannheim consensus criteria.
Results: Risk factors and SSc related features are described in table 1. None of the patients were catalogued as high risk according to SCORE chart (>5%). According to REGICOR chart, 17 patients (39,5%) were catalogued as intermediate risk and none as high risk. Twenty-two patients (51,2%) had carotid plaques (CP) and the CACscore of these patients was 283.4. In patients without CP CACscore was 53,2 ($p<0.05$).
Based on the presence of CP we performed ROC curve with CACscore. The AUC was 0.778. The best cut off point was 28 with a sensibility of 71% and a specifity of 82%. Kappa's coefficient was 0.54. Twenty patients (46.5%) had CACscore>28. Compared to patients with CACscore<28 statistical significance was found on CIMTmax (0.93 vs 0.80mm; $p<0.01$), presence of CP (79% vs 25%, $p<0.01$) and number of CP (2.55 vs 0.43, $p<0.01$). There was no statistical significance on CIMTm (0.71 vs 0.64mm p: 0.11).

Female	37 (82%)
Age	59 (33–83)
Disease duration	19 (3–57)
Limited cutaneous SSc	32 (74,4%)
Diffuse cutaneous SSc	10 (23,3%)
Sine Scleroderma SSc	1 (2,3%)
Arterial Hypertension	26 (60,5%)
Diabetes mellitus	5 (11,6%)
Statin treatment	22 (51,2%)
Smokers	5 (11.6%)
Digital ulcers	24 (55,8%)
Pulmonary Hypertension*	6 (14%)
Interstitial lung disease	20 (46.5%)
Altered conduction in Electrocardiogram	15 (34,9%)
Left Ventricular diastolic dysfunction**	32 (74,4%)
Left ventricular systolic dysfunction**	3 (7%)

*Mean pulmonary artery pressure >25 mm Hg at right heart catheterization. **Measured by echocardiography.

If the presence of CP or CAC score>28 were considered as subclinical atheromatosis disease (SAD), a total of 26 patients (60.5%) were diagnosed. We performed multivariate regression analysis, CIMTm, CIMTmax, low High Density Lipid (HDL), high erythrocyte sedimentation rate (ESR) and age were independent factors for the presence of SAD.
Conclusions: SSc patients often have SAD which is misdiagnosed by CV risk charts. Plaque detection by carotid ultrasonography and CT CACscore are useful to detect SAD. The optimal cut-off point of CACscore in this study is 28. SAD detection would be indicated in elderly, patients with low HDL or high ESR. The measure of CIMT could be useful in some cases.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1515

SAT0341 PILOT STUDY: HOME MANAGEMENT OF ILOPROST IN THE MICROPUMP/24 HOURS, IN PATIENTS SUFFERING FROM SCLERODERMA, FOLLOWED FOR 12 MONTHS

G. Pistone, R. Daita, C. Arcuri, N. Catalano, S. Liuzza, C. Rinollo, G. D'Aguanno, A. Allotta, M. Lo Monaco, R. Mallaci Bocchio, G. Natoli, S. Corrao.
AZ.OSP.ARNAS Civico, PALERMO, Italy

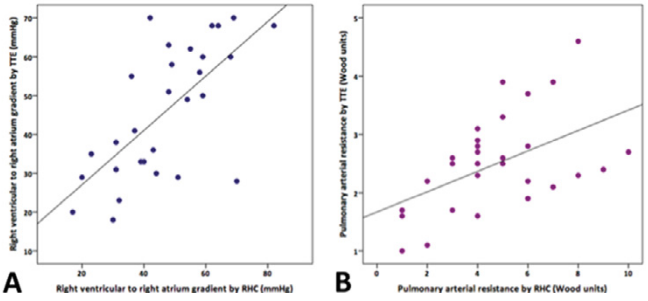
Background: evaluate the effectiveness on Raynaud's phenomenon and on digital ulcers, safety and side effects, during intravenous infusion of iloprost therapy in patients with diffuse and limited scleroderma
Objectives: the effectiveness of the therapy was assessed at 0 and 12 months, on the basis of daily number of episodes of Raynaud's phenomenon, evaluation of digital ulcers changes of the vascular nail bed to capillaroscopio, evaluation of pulmonary hypertension.
Security according to the appearance of adverse events.
Methods: They were enrolled consecutively, for a period of 12 months, 12 patients, 9 women and 2 men, 9 suffering from diffuse scleroderma (positive Scl70) and 3 suffering from limited scleroderma (positive anticentromere), middle age 52,91 years, mean age of disease 7,8 years, 11 non-smoking. They were subjected to infusion of iloprost 1/2 vial diluted in 25 cc of saline solution to 0,6 ml/h, in micropump Infonde for 24 consecutive hours, for 4 days a month for 12 months, 10 patients with peripheral lines and 2 with central venous access.
Results: of 12 patients with the Raynaud's phenomenon, there was a reduction in the daily number in 4 patients, unchanged in 8 patients. Digital ulcers disappeared in 6 patients, they were unchanged in 5 patients, improved although present in 1 patient. In 7 patients capillaroscopic framework remained unchanged, in 5 patients improved capillary density. 10 patients had no pulmonary hypertension, 2 patients had pulmonary hypertension, no change in the two groups at T0 and T 12. None of the patients experienced side effects during the infusion.
Conclusions: the cyclical infusion therapy iloprost prevented the onset of ulcers in patients at T0 not presented or the appearance of new ulcers; it has contributed to the reduction in the daily number of Raynaud's phenomenon and also allowed to reach the same effective dose of a vial of iloprost to dilute in 50 cc of saline solution, allowing the patient to perform at home therapy with greater compliance. In terms of safety none of the patients experienced side effects or adverse effects
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5990

SAT0342 TRANSTHORACIC ECHOCARDIOGRAPHY TO QUANTIFY PULMONARY VASCULAR RESISTANCE IN PATIENTS WITH SYSTEMIC SCLEROSIS

S. Billet[1], T. Chollet[1], P. Fournier[1], L. Tetu[2], G. Prévot[2], M. Galinier[1], D. Carrié[1], O. Lairez[1], G. Pugnet[3]. *[1]Service de Cardiologie, CHU Rangueil; [2]Service de Pneumologie, CHU Larrey; [3]Service de Médecine Interne, CHU Toulouse Purpan, Toulouse, France*

Background: One of the major causes of systemic sclerosis (SSc)-related death is pulmonary arterial hypertension, which develops in 12–15% of patients with SSc and accounts for 30–40% of deaths. Consequently, monitoring of pulmonary arterial pressure (PAP) and resistances is essential in patients with SSc. Abbas formula performed by transthoracic echocardiography (TTE) was reported as a good tool to quantify pulmonary vascular resistances (PVR).
Objectives: Explore the accuracy of TTE and Abbas formula to quantify PVR in patients with SSc.
Methods: All consecutive patients with SSc, diagnosed according to the 2013 ACR/EULAR criteria, or the LeRoy and Medsger criteria for diffuse or limited subsets classification, had within 24H a Doppler echocardiographic examination and right-heart catheterization were performed. The ratio of peak tricuspid regurgitant velocity (TRV, *ms*) to the right ventricular outflow tract time-velocity integral (TVI_{RVOT}, *cm*) obtained by Doppler echocardiography (TRV/TVI_{RVOT}) was then correlated with invasive PVR measurements using regression analysis. An equation was modeled to calculate PVR in Wood units (WU) using echocardiography, and the results were compared with invasive PVR measurements [1].
Results: Thirty-three consecutive patients were included, 13 (39.4%) were male and the mean age was 64.6±12.1 years. Most were classified as limited cutaneous SSc (lcSSc; n=29, 87.9%). All patients tested positive for antinuclear antibodies, 18 (21.2%) for anti-scleroderma-70, 7 (54.5%) for anticentromere antibodies and 2 (6.1%) for anti-RNA polymerase III antibodies. Mean and systolic PAP were 31±9 and 53±16 mmHg respectively. There was a good correlation between right ventricle to right atrium gradient pressure assessed by TTE and RHC (R=0.620, P<0.001). RVP assessed by Abbas formula (2.6±1.0 wood units) were well correlated with RVP assessed by RHC (4.8±2.3; R=0.446, P=0.013).

Figure. Correlations between right ventricular to right atrium gradient and pulmonary arterial resistances assessed by transthoracic echocardiography and right heart catheterization



Conclusions: Doppler echocardiography using Abbas formula may provide a reliable, noninvasive method to determine PVR in SSc patients.
References:
[1] Abbas AE, Fortuin FD, Schiller NB, Appleton CP, Moreno CA, Lester SJ. A simple method for noninvasive estimation of pulmonary vascular resistance. J Am Coll Cardiol. 2003 Mar 19;41(6):1021–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2081

SAT0343 SCREENING OF PULMONARY ARTERIAL HYPERTENSION IN PATIENTS WITH SYSTEMIC SCLEROSIS USING DETECT ALGORITHM – VALIDATION IN THE COHORT OF JAPANESE SINGLE CENTER

H. Yasuoka[1], Y. Shirai[2], Y. Tamura[3], T. Takeuchi[1], M. Kuwana[2]. *[1]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine; [2]Departmenrt of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine; [3]International University of Health and Welfare Mita Hospital, Tokyo, Japan*

Background: Pulmonary arterial hypertension (PAH) complicated with systemic sclerosis (SSc) has the worst prognosis in PAH associated with other connective tissue diseases (1) and is one of leading cause of death in patients with SSc (2). To improve prognosis in SSc patients, earlier detection and diagnosis of PAH by annual screening is recommended even in asymptomatic patients (3). To effectively detect PAH in patients with SSc at earlier phase, DETECT algorithm is reported as a good tool to identify candidates who need right heart catheterization (RHC), with high sensitivity (4). However, its usefulness has not been validated in Japanese cohorts.
Objectives: To validate the effectiveness of DETECT algorithm in the Japanese single center cohort.
Methods: Patients with SSc who visited Keio University Hospital between 2005 and 2016 were included in the study. Patients over 18 years old, disease duration more than 3 years, and DLCO predicted less than 60% were selected and clinical information was retrospectively collected from records. The sensitivity, specificity, and negative and positive predictive values of the algorithm based on the result of RHC evaluation were calculated in a cohort of PAH patients and non-PAH patients, in whom RHC data were available. Validation with patients with data minimally-required for algorithm were also examined.
Results: Three hundred four cases were visited our hospital during from 2005 to 2016. Patients who fulfilled criteria and had data minimally-required for algorithm were 126 cases. Of 126 patients, 50 were examined RHC evaluation and patients diagnosed as pulmonary hypertension were 26 (21%) and 21 (15%) were PAH. When a cohort of PAH patients and non-PAH patients with RHC data was applied to DETECT algorithm, referral rate to RHC evaluation was 78%, missed diagnosis of PAH was 0%. Sensitivity/specificity for detecting PAH patients were 100%/42%, and positive/negative predictive values were 60%/100%, respectively. Evaluation of 126 patients with data minimally-required for algorithm was also examined. Referral rate to RHC evaluation was 43%, missed diagnosis of PAH was 0%, and sensitivity/specificity and positive/negative predictive values for detecting PAH patients were 100%/72%, 43%/100%, respectively. However, there was a patient who was initially excluded at Step 1, but developed PAH one year later.
Conclusions: The DETECT algorithm was reassured as a good tool to effectively screening tool for PAH in SSc patients. However, we have to keep in mind that unnecessity of RHC referral judged by this algorithm does not guarantee the patient to be free from future development of PAH.
References:
[1] Condliffe R et al. Am J Respir Crit Care Med 179:151–157, 2009.
[2] Steen VD et al. Ann Rheum Dis 66:940–944, 2007.

[3] Galiè N et al. Eur Heart J 37:67–119, 2016.
[4] Coghlan JG et al. Ann Rheum Dis 73:1340–1349, 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4608

SAT0344 DISEASE RELATED MALNUTRITION IN SYSTEMIC SCLEROSIS AND ASSOCIATED FACTORS: A CROSS-SECTIONAL STUDY

I. Türk[1], N. Cuzdan Coskun[2], V. Ciftci[3], D. Arslan Taş[1], M.C. Doğan[4], I. Unal[5]. *[1]Department of Internal Medicine, Division of Rheumatology; [2]Department of Physical Medicine and Rehabilitation, Division of Rheumatology; [3]Faculty of Dentistry, Department of Pediatric Dentistry; [4]Department of Pediatric Dentistry; [5]Department of Biostatistics, Çukurova University, Adana, Turkey*

Background: The risk of malnutrition increases in patients with systemic sclerosis (SSc) which has a negative prognostic effect. Additionally malnutrition is a significant cause of morbidity and mortality.
Objectives: The aim of this study was to evaluate the associations between malnutrition and clinical features of the disease, depression in SSc patients.
Methods: Concomitant SSc patients followed in our outpatient and inpatient clinics were enrolled in the study. Skin involvement was assessed with modified Rodnan skin score (mRSS), joint/tendon involvement with finger-tip to palm distance (FTP). İnterstitial lung disease (ILD) and heart involvement were evaluated with clinical and radiological methods. Patients were questioned for dysphagia and gastroesofageal reflux as an indicator of esophageal involvement, early satiety and vomiting as gastric involvement, and diarrhea, constipation and bloating as bowel involvement.[1] Interincisal distance measurement was used to assess the maximal mouth opening capacity. Malnutrition risk was assessed by the Malnutrition universal screening tool (MUST). The Beck Depression Inventory (BDI) was used for measuring the severity of depression. sWe examined associations between malnutrition risk and clinical features of the disease, depression in SSc patients.
Results: Ninety eight SSc patients with 69 diffuse and 29 limited type of the disease were enrolled in the study. 84.7% of the patients were female and the mean age was 52.67±11.28 years. According to MUST scores 61.2% of patients have low, 15.3% medium and 23.5% high risk for malnutrition. We found no difference between the malnutrition risk among genders (p=0.065). mRSS and FTP were significantly different between malnutrition risk groups (p=0.005, 0.050 respectively). Malnutrition risk was higher with patients with ILD than the patients without ILD (p=0.044). Malnutrition risk was higher with patients with bowel involvement than the patients without bowel involvement. (p=0.021).
Interincisal distance was significantly different between malnutrition risk groups (p=0.003). 78.7% of SSc patients have BDI scores $\geq$10, 54.3% of SSc patients have BDI scores $\geq$17. BDI scores were significantly different between malnutrition risk groups ($p<0.001$). Factors affecting malnutrition risk were evaluated with logistic regression analysis. Interincisal distance and bowel involvement were found to be the most relevant factors for malnutrition risk. SSc patients with bowel involvement have 2.519-fold increased risk of malnutrition compared to patients without bowel involvement (95% CI 1.039–6.105). Every 1 mm decrement in interincisal distance was associated with 1.101 fold increase in malnutrititon risk of SSc patients (95% CI 1.032–1.176).
Conclusions: Malnutrition is common in SSc patients. Malnutrition risk is associated with skin, tendon/joint involvement, DU count, ILD, bowel involvement, microstomia and depression severity.
References:
[1] Walker UA, Tyndall A, Czirják L et al. Clinical risk assessment of organ manifestations in systemic sclerosis: a report from the EULAR Scleroderma Trials And Research group database. Ann Rheum Dis. 2007;66:754–63.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6162

SAT0345 THE IMPACT OF GASTROINTESTINAL INVOLVEMENT IN HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS

J. Caetano[1], J. Branco[2], S. Oliveira[1], J. Delgado Alves[1,3]. *[1]Systemic Autoimmune Diseases Unit, Department of Medicine IV; [2]Department of Gastroenterology, Fernando Fonseca Hospital, Amadora; [3]CEDOC, NOVA Medical School, Lisbon, Portugal*

Background: Apart from skin involvement, the gastrointestinal (GI) system is the second most commonly involved organ in systemic sclerosis (SSc), affecting over 80% of the patients. Although rarely being a direct cause of death, it is associated to a high morbidity and to a significant impairment in health-related quality of life (HRQoL). Few data are published considering the influence of GI manifestations in the quality of life of SSc patients.
Objectives: The purpose of this study is to characterize the impact of GI involvement in HRQoL in SSc, and to compare it with that in patients with inflammatory bowel disease (IBD).
Methods: 29 consecutive SSc patients with GI involvement were selected from a cohort of 44 SSc patients, followed in a single referral centre and classified according to 2013 ACR/EULAR criteria. Comparative analysis was made with 24 consecutive patients with IBD without arthritis (14 Crohn's disease; 10 - ulcerative colitis). Health Assessment Questionnaire (HAQ-DI) and Short Form 36 (SF36), physical component summary (PCS) and mental component summary (MCS) scales, were used to assess HRQoL in both groups. The UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract 2.0 (UCLA SCTG GIT 2.0) was performed in SSc patients to assess the severity of GI involvement. Clinical data were obtained by medical records review. T-test and Fisher's exact test were used to compare binary variables. Pearson's correlation was used for continuous variables.
Results: The most common GI segments involved in SSc patients were the esophagus in 90%, the stomach in 60% and the bowel in 48%, while the anorectum was involved in a smaller percentage (10.3%). The mean UCLA SCTG GIT 2.0 score was 0.64±0.51, compatible with a moderate severity, with higher scores obtained for reflux, distention and emotional wellbeing. The mean HAQ-DI score was 1.13±0.57 (0-best health), and the mean PCS and MCS scores were 35.2±9.4 and 35.3±11.4 (100-best health), respectively. These scores were significantly worse than in SSc patients without GI involvement (HAQ-DI - p=0.001; PCS - p=0.04 and MCS - p=0.005). There was a significant correlation between higher UCLA SCTG GIT 2.0 scores and worse quality of life evaluated by HAQ-DI (r=0.42, p=0.03), but the same correlation was not found for the SF36 components. Comparing with IBD patients, SSc patients with GI involvement had worse life quality, with statistical significantly higher HAQ-DI ($p<0.001$) and lower PCS ($p<0.001$) and MCS (p=0.01) scores.
Conclusions: GI involvement in SSc significantly impaired patient's quality of life. The impact of GI involvement in HRQoL of SSc patients was more severe than in IBD patients. Although physical components were relevant, with esophagus being most frequently involved, mental components associated with GI involvement significantly compromised HRQoL in SSc. Therefore, the assessment of SSc patients using clinical severity measure tools, similar to UCLA SCTG GIT 2.0 score, is crucial for a better characterization of the disease and to an optimized clinical approach.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2496

SAT0346 SYSTEMIC SCLEROSIS'S EARLY STAGES AND ITS SIGNIFICANCE IN DAILY PRACTICE

J.P. Abreu, I. Almeida, A. Marinho, C. Vasconcelos. *Unidade de Imunologia Clínica, Centro Hospitalar do Porto, Porto, Portugal*

Background: Systemic Sclerosis (SSc) is an autoimmune disease, characterized by skin and internal organs fibrosis. Its clinical manifestations are heterogeneous, hence, the definitive diagnosis of SSc rely on scores, such as American College of Rheumatology (ACR) for SSc. Leroy and Medsger, proposed the potential criteria for the classification of early stages of SSc, due to the insufficient sensitivity previous methods. Lately EUSTAR proposed the concept of Very Early SSc, defined by the presence of 3 red flag – RF, Puffy Fingers and ANA; if 2 of these are present, capilaroscopy and specific antibody must be accessed; if one of the last positive, further search for Systemic involvement must be taken in account.
Objectives: We propose to: analyse a group of patients that had been diagnosed with early stages of SSc; study the presence of systemic involvement (at the time of diagnosis and throughout the follow-up), and the possible predictors for progression to definitive SSc.
Methods: The patients were selected by consulting the clinical data from patients followed in our hospital with diagnose of early stages of SSc. Very Early SSc criteria were used to define early stage SSc. The data concerning red flags, capilaroscopy, specific auto-antibodies, systemic involvement (Gastrointestinal, Pulmonary, Cardiac, Kidney, Muscoloskeletal).
Results: We obtained a sample of 70 patients, 65 being female subjects (92,9%), with mean age of diagnosis 47,9 years (SD 13,6). 16 patients (22,9%) were classified as Pre-scleroderma at the admission, 16 as Early SSc (22,9%), 15 (21,4%) as Very Early SSc, 16 (22,9%) as possible SSc, 6 (8,6%) as Limited SSc (despite not scoring to ACR criteria) and 1 (1,4%) as Sin Scleroderma SSc. 63 patients (90%) had RP, 15 (21,4%) had puffy fingers, 63 (90%) ANA positivity – 11 patients (15,7%) had 1 red flag, 45 (64,3%) had 2 red flags and 13 (18,6%) had 3 red flags.
54 patients (78.3%) were positive to specific SSc autoantibodies; 47 patients (71.2%) had capiloroscopy compatible with SSc in different stages (17.1% Early, 12,9% Active, 4,3% Late and 32,9% compatible). 54 patients (77,1%) scored for Very Early SSc.
At the moment of the diagnosis, 56 patient (81,2%) had systemic involvement.
34 patients (48,6%) scored to the definitive diagnosis by ACR 2013 criteria, after 2,56 years in mean (SD 2.51) of first diagnosis.
No correlation was found in what concerns to predictors of progression to SSc or systemic involvement.
Conclusions: This study shed a light on the importance of the recognition of SSc's early stages, since a significant part of these patients have systemic involvement at the moment of diagnosis, yet not scoring to ACR 2013 criteria. Almost half of the patients scored to definite diagnosis of SSc at the moment of the last appointment. The importance of these findings rely on the possibility to identify systemic involvement and address it in time to prevent/delay further disease progression.
References:
[1] Avouac J, Matucci-Cerinic M, Miniati I, Denton CP. Systemic Sclerosis. EULAR Online Course on Rheumatic Disease 2016

[2] Varga J. Overview of the clinical manifestations of systemic sclerosis (scleroderma) in adults. UpToDate Jun 2016.
[3] LeRoy EC, Medsger TA Jr. Criteria for the classification of early systemic sclerosis. J Rheumatol 2001;28:1573–6..
[4] Amato L, Gallerani I, Berti S, Fabbri P. Prescleroderma: A Distinct Stage of Systemic Sclerosis. Skinmed. 2003; 2(1).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6927

SAT0347 DISEASE MODIFYING EFFECT OF ILOPROST IN PATIENTS WITH SYSTEMIC SCLEROSIS AND POSSIBLE ROLE OF CXCL4 CHEMOKINE

K. Stefanantoni[1], I. Sciarra[1], M. Vasile[1], R. Palazzo[2], L. Frasca[2], G. Valesini[1], V. Riccieri[1]. *[1]Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma; [2]National center for research and pre-clinical and clinical evaluation of drugs- Immune-mediated diseases UNIT, Istituto Superiore di Sanità (Nat. Inst. of Health), Rome, Italy*

Background: Iloprost is a synthetic prostaglandine used for vascular manifestation of Systemic Sclerosis (SSc), in particular it is indicated for active digital ulcers (DU) and severe Raynaud Phenomenon (RP) (1). It acts on several receptors such as IP and EP receptors and PPRs. Iloprost is also involved in the regulation of gene expression, fibrosis and inflammation (2,3,4). CXCL4 o Platelet Factor 4, is a 70KDa CXC-chemokine synthesized in megakaryocytes and plasmacytoid dendritic cells, released after platelet activation. In SSc, it seems to be higher in patients with early diffuse SSc and it correlates with mRSS and presence of PAH (5).
Objectives: To evaluate the effect of Iloprost on vascular manifestations, on disease activity and on serum levels of CXCL4 at baseline (T0) and after 1 month (T1), 3 months (T3) and 6 months (T6) of therapy.
Methods: 30 patients (M/F =1/29; mean age =58.2 yrs; mean disease duration =12.8 yrs) with established SSc according to ACR criteria, were enrolled. At T0, T1, T3 and T6 treatment with Iloprost at standard dosage we determined RP VAS, number of DU, European Scleroderma Study Group Activity Index (EScSGAI) and serum levels of CXCL4, measured using commercially available immunoassay kit (Human CXCL4/PF4 R&D SYSTEMS®). All patients underwent to a complete clinical, instrumental and laboratory evaluation.
Results: Regarding RP VAS, we found a statistically significant increase (p=0.04) at T3, corresponding to the colder winter period, while it decreased, although not significantly at T1 and at T6, where this reduction was significant compared to T3 values (p=0.0008). Considering the number of active DU, we have highlighted the same trend of the RP VAS. EScSGAI values showed a statistically significant reduction (p=0.03) comparing T3 to T6. Regarding CXCL4, we found significantly higher levels in SSc patients respect to a group of healthy controls (HC) (p=0.047). No significant difference was found in serum levels of CXCL4 at T0, T1,T3 and T6. Evaluating patients with higher levels of CXCL4 at baseline, respect to the average of HC values (CXCL4>25,000 pg/ml) (11/30 patients), we found that 7 subjects had a significant improvement in disease activity at T6 evaluated by EScSGAI (p=0.015). In these patients we also detected a significant reduction in T3 CXCL4 values (p=0.043) persisting and at T6, although not reaching statistical significance. Moreover higher basal levels of CXCL4 in patients with disease duration less of 60 months (p=0.05) and in patients with pericardial effusion (p=0.037) were detected. Besides we found significantly lower levels of CXCL4 in patients with DU history (p=0.049) and esophageal involvement (p=0.008).
Conclusions: Our study confirms the efficacy of Iloprost on vascular manifestation of SSc and also highlights its effect on the disease activity. Moreover this drug seems to influence, in a subgroup of patients, concentrations of CXCL4, an important chemokine involved in SSc pathogenesis that deserves further investigations.
References:
[1] Kowal-Bielecka O et al. Ann Rheum Dis. 2009 May;68(5):620–8.
[2] Clapp LH et al. Prostaglandins Other Lipid Mediat. 2015.
[3] Dorris SL et al. Mediators Inflamm. 2012;2012:926968.
[4] Zhu Y et al. Respir Res. 2010 Mar 20;11:34.
[5] Van Bon et al. N Engl J Med. 2014 Jan 30;370(5):433–43.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5731

SAT0348 ASSOCIATION OF VITAMIN D DEFICIENCY WITH REDUCED IL10-PRODUCING REGULATORY B CELLS IN SYSTEMIC SCLEROSIS

A. Mavropoulos, C. Liaskos, A. Gkoutzourelas, C.G. Katsiari, D.P. Bogdanos, L.I. Sakkas. *Rheumatology and Clinical Immunology, University of Thessaly, School of Health Sciences, LARISSA, Greece*

Background: IL-10-producing regulatory B cells (Bregs), also known as B10 cells, are decreased and functionally impaired in patients with systemic sclerosis (SSc), particularly in those with SSc-associated interstitial lung disease (1). As serum 25-OH-vitamin D (vitD) levels are associated with clinical aspects in patients with SSc (2), we investigated whether there is any link between vitD levels and Breg levels.
Objectives: To assess whether or not vitD deficiency in SSc is associated with the percentages of circulating IL-10-producing Breg cells.
Methods: PBMCs and serum samples were isolated from 55 patients with systemic sclerosis. Serum VitD levels were measured using a commercially available sandwich ELISA kit. Phenotypic analysis of CD19, CD24, CD27, CD38 and intracellular expression of cytoplasmic IL-10 following bacterial CpG (ODN2006) and PMA/ionomycin stimulation was examined by flow cytometry using specific fluorochrome-conjugated monoclonal antibodies (BD Biosciences).
Results: Systemic sclerosis patients were divided into two groups (vitD deficient or not) based on a serum concentration cut off value of 20 ng/ml. The mean vitD levels in the deficient group were 14.11±3.6 ng/ml (n=17) whereas the mean vitD levels in the non-deficient group were 37.5±12.9 ng/ml (n=38). IL-10-producing B cells (B10 cells) were significantly decreased in vitD deficient patients compared to those with medium/high levels (p=0.02). CD19+CD27+ (memory) B cells were also significantly reduced in patients with VitD deficiency (p=0.004). In addition the ratio of naïve/memory B cells was significantly higher in VitD deficient patients (p<0.05). Within the memory B cell fraction, the CD19+CD27+CD24hi cells also known as phenotypic memory Bregs, were mostly decreased (p=0.001). There was no significant association between CD19+CD38hiCD24hi (transitional) Bregs and VitD levels.
Conclusions: Our data suggest that vitamin D deficiency may account for reduced B10 cells in systemic sclerosis
References:
[1] Mavropoulos et al Arthritis Rheumatol. 2016;68:494–504.
[2] Arnson Y et al Autoimmun Rev. 2011;10:490–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5747

SAT0349 EVALUATION OF STANDARD SWALLOWING FUNCTION IN ASSESSING ASPIRATION RISK FOR PATIENTS WITH SYSTEMIC SCLEROSIS

L. Yan, P. Yunfeng, Y. Mengru. *Department of Rheumatology, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Swallowing dysfunction is a common symptom of systemic sclerosis, which usually induce aspiration pneumonia to aggravate lung progress. It is necessary to screen swallowing disorders effectively at an early stage.
Objectives: To investigate the value of standard swallowing function assessment (SSA) in aspiration screening for inpatients with Systemic sclerosis.
Methods: SSA and Video fluoroscopic swallowing study (VFSS) were performed in 120 inpatients with Systemic sclerosis from March 2014 to September 2016.The sensitivity, specificity, positive predictive value and negative predictive value of SSA in the diagnosis of aspiration in patients were calculated by taking VFSS examination as the gold standard. The incidence of pneumonia in SSA-positive and SSA-negative patients were compared.
Results: The diagnostic sensitivity of SSA was 81.2%, the specificity was 75%, the positive predictive value was 68.6% and the negative predictive value was 90.3%. The incidence of pneumonia in SSA positive patients was higher than that in SSA negative patients (54.1% vs 28.3%) (P<0.01).
Conclusions: SSA is a valuable screening tool for the evaluation of aspiration risk in patients with Systemic sclerosis.
References:
[1] Systemic Sclerosis with Multiple Pulmonary Manifestations. Kotnur MR, Suresh P, Reddy VS, Sharma T, Salim NA. J Clin Diagn Res. 2016 Jun;10(6):OD16–7. doi: 10.7860/JCDR/2016/18781.8032.
[2] Progression of esophageal dysmotility in systemic sclerosis. Vischio J, Saeed F, Karimeddini M, Mubashir A, Feinn R, Caldito G, Striegel K, Rothfield N. J Rheumatol. 2012 May;39(5):986–91. doi: 10.3899/jrheum.110923.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5441

SAT0350 DOES A SYSTEMIC SCLEROSIS PATIENT'S CLINICAL PHENOTYPE DEMONSTRATE HIS AUTOANTIBODY STATUS?

M. Boonstra[1], J.A. Bakker[2], M.K. Ninaber[3], N. Ajmone Marsan[4], T.W. Huizinga[1], J.K. de Vries-Bouwstra[1]. *[1]Rheumatology; [2]Clinical Chemistry and Laboratory Medicine; [3]Pulmonology; [4]Cardiology, LUMC, Leiden, Netherlands*

Background: Although antibody status has shown to improve clinical subsetting in Systemic sclerosis (SSc), it is far from perfect. For optimal clinical subsetting as well as for evaluating the possible pathogenic role of SSc specific antibodies, it is relevant to know to what extent clinical SSc phenotypes are determined by presence of these antibodies.
Objectives: To evaluate 1. if clinical relevant subsets of SSc patients are distinguishable using only clinical data, 2. how SSc specific autoantibodies are distributed among these subsets, and 3. whether adding antibody status to cluster analyses improves recognition of SSc subsets.
Methods: Using data from SSc patients of the Combined Care In Systemic Sclerosis (CCIS) cohort, Leiden University Medical Center, hierarchical clustering based on Ward Method was performed on the first obtained factor of principal component analysis of 7 organ systems (skin;lung;heart;kidney;muscle;vascular;gastro-

intestinal) and time since non-Raynaud phenomenon. Clinical characteristics and prevalence of auto-antibodies within clusters was evaluated. We assessed whether adding autoantibody status as additional factor improved clinical subsetting.

Results: Of 407 SSc patients included, 371 patients (91%) fulfilled ACR/EULAR 2013 criteria. Prevalence of anti-centromere (ACA) was 37%, anti-topoisomerase (ATA) 24%, anti-RNAPIII 5%, anti-fibrillarin 4%, anti-Pm/Scl 5%. Cluster analysis identified clinically recognisable clusters of SSc patients based on absence of skin involvement (cluster 1), peripheral vascular involvement (cluster 2), fibrotic complications (cluster 4), and severe vascular complications (pulmonary arterial hypertension [PH], renal crises; cluster 5). Except for cluster 4, where ATA was dominant, in all clusters ACA was the most prevalent auto-antibody. No cluster associated with any of the more rare SSc specific auto-antibodies. Adding of auto-antibodies resulted in increased clinical overlap, with a frequency of PH between 6 – 8% and a frequency of digital ulcers between 24 – 39% in clusters 2,4 and 5.

Table 1. Clustering of SSc patients based on clinics

	Cluster 1 (n=66)	Cluster 2 (n=50)	Cluster 3 (n=129)	Cluster 4 (n=81)	Cluster 5 (n=81)
Age in years, mean (SD)	53 (14)	54 (14)	54 (14)	53 (16)	62 (12.4)
Female, % (n)	90 (60)	86 (43)	85 (110)	72 (58)	74 (60)
Time since non-Raynaud, median (range)	3 (-3–14)	10 (-3–44)	2 (0–20)	3 (0–27)	13 (0–46)
dcSSc, % (n)	0 (0)	2 (1)	17 (22)	65 (53)	25 (20)
Mean mRSS (SD)	0 (0)	4 (3)	4 (3)	14 (11)	4 (6)
PAH, % (n)	3 (2)	4 (2)	0 (0)	5 (4)	20 (16)
DLCO, %predicted, mean (SD)	70 (18)	66 (16)	70 (15)	64 (16)	54 (18)
History of renal crisis, % (n)	0 (0)	0 (0)	0 (0)	3 (2)	17 (14)
Digital ulcers, % (n)	15 (10)	98 (49)	4 (5)	28 (23)	6 (5)
Anti-topisomerase, % (n)	5 (3)	15 (7)	22 (28)	48 (37)	24 (19)
Anti-centromere, % (n)	62 (39)	48 (23)	41 (53)	8 (6)	30 (24)

Conclusions: Based on clinical data alone, relevant subgroups in SSc can be distinguished. Adding antibody status to cluster analyses increases overlap of clinical features between subgroups. These findings show that solely presence of SSc specific antibodies is of limited clinical relevance. For optimal risk stratification more complex serological findings as antibody titers might be additive.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6004

SAT0351 DIFFERENCES AMONG PATIENTS WITH INTERSTITIAL LUNG DISEASE ACCORDING TO THEIR SYSTEMIC SCLEROSIS SUBCLASSIFICATION

M. Laffont[1], I. Catellvi[2], D. Castillo[3], M. Millan[2], C. Diaz-Torné[2], P. Moya[2], B.P. Magallares[2], A. Laiz[2], H.S. Park[2], J.M. De Llobet[2], J. Casademont[2].
[1]Reumatologia, Hospital Jose Maria Ramos Mejia, Ciudad Autónoma de Buenos Aires, Argentina; [2]Reumatologia; [3]Neumonologia, Hospital Universitario de la Santa Creu I Sant Pau, Barcelona, Spain

Background: Systemic Sclerosis (SSc) has been widely studied from a purely global standpoint, but only a few trials have analysed patients with interstitial lung disease (SSc-ILD) as well.

Objectives: 1. Describe the clinical features of a cohort of patients with SSc and SSc-ILD. 2. Determine whether there are disparities among different types of SSc-ILD and their progression in patients with either limited (lcSSc) or diffuse involvement (dcSSc). 3. Ascertain whether there are disparities among different types of SSc-ILD and their progression according to the SSc-specific autoantibody (AAb).

Methods: Retrospective study of a cohort of patients with ILD-SSc controlled during an SSc consultation. The following variables were collected: sex, age, SSc and ILD progress in years, type of SSc and ILD, smoking, digital ulcers (DU), pulmonary hypertension, digestive disorders, cancer, SSc treatment, corticosteroid doses and lastly, lung function tests upon diagnosis, at treatment onset, and 24 months later. Additionally, a record was kept on the types of AAb present in every SSc. Qualitative and quantitative variables were compared in relation to the clinical and immunological sub-classification. Chi-square and Student's T Tests were performed. A p-value$\leq$0.05 was considered significant.

Results: out of 266 patients with SSc, data from 47 patients with ILD-SSc were gathered; 89.4% were female, with an age range of 66.09±15.1 years old, and 9.85±10.2 and 4.38±9.24 years of progression of their SSc and ILD respectively. 33 out of 47 sustained lcSSc, and both Scl-70/ATA (29.8%) and ACA (26.1%) were the most frequently found AAb. Non-specific interstitial pneumonia (NSIP) was the most common ILD radiological pattern (76.6%). Most patients with SSc underwent treatment (51.1%), 24% with mycophenolate mofetil (MMF); 36.2% of the patients had been concomitantly administrated corticosteroids with a mean prednisone dose of 15.73±10.3 mg/d.

Upon comparing patients with lcSSc and dcSSc, prevalence of DU was higher in those with dcSSc (p<0.01), MMF was less frequently used (p<0.02), rituximab was more usually employed (p<0.03), and they presented worse values of FEV1/FVC ratio after 24 months of treatment (p<0.03). No differences were observed as to either type of ILD or progression. However, when variables were analysed regarding AAb in SSc, patients with ACA presented both fewer DU (p<0.02) and NSIP pattern (p<0.02), and more frequent compromise of the small airway (p<0.01), they were younger and thus, they had had shorter progression of the disease. ILD diagnosis was made significantly earlier in those patients with RNA polymerase, and later in those with anti-U1RNP. No AAb was observed associated with neoplasia. Considering the types of ILD, patients with NSIP pattern were younger (p0.054) and presented worse spirometric values.

	ILD-SSc n 47	lcSSc n 33	dcSSC n 14	P (lcSSc vs dcSSc)	P (ACA vs no ACA)	P (ATA vs no ATA)	P U1RNP vs noU1RNP	P RNApol vs noRNApol
Age ± SD (years)	66.09± 14.1	67.09± 14.04	63.71±15.67	Ns	<0.05	Ns	Ns	Ns
Progress in years SSc ± SD	9.85± 10.29	8.81±15. 04	12.31±9.59	Ns	<0.04	Ns	<0.02	Ns
Evolution in years ILD ± SD	4.38± 9.24	4.11±9.7 2	5.02± 8.29	Ns	Ns	Ns	<0.0001	<0.005
NSIP (%)	36(76.6)	24 (72.72)	12(85.71)	Ns	<0.02	Ns	Ns	Ns
IPF (%)	3 (6.4)	1 (3.03)	2(14.28)	Ns	Ns	Ns	Ns	Ns
LIP (%)	2 (4.3)	2 (6.06)	0	Ns	Ns	Ns	Ns	Ns
Small airway compromise(%)	4 (8.5)	4(12.12)	0	Ns	<0.005	Ns	Ns	Ns
PH (ultrasound)	3 (6.4)	3 (9.09)	0	Ns	Ns	Ns	Ns	Ns
Digital ulcers (%)	17 (36.2)	7 (21.21)	10(71.42)	<0.01	<0.02	<0.01	Ns	Ns
Neoplasia (%)	5 (10.6)	3 (9.09)	2(14.28)	Ns	Ns	Ns	Ns	Ns
Immunosuppressive treatment (%)	24 (51.1)	18 (54.54)	6(42.85)	Ns	Ns	Ns	Ns	Ns
Use of cyclophosphamide (%)	8 (17)	4 (12.12)	4(28.57)	Ns	Ns	Ns	Ns	Ns
Use of MMF (%)	16 (34)	15 (45.45)	1(7.14)	<0.02	Ns	Ns	Ns	Ns
Use of azathioprine (%)	1(24)	0	1 (7.14)	Ns	Ns	Ns	Ns	Ns
Use of rituximab (%)	3 (6.4)	0	3 (21.42)	<0.03	Ns	<0.03	Ns	Ns
Use of corticoids (%)	17 (36.2)	13 (39.39)	4 (28.57)	Ns	Ns	Ns	Ns	Ns
Doses of corticoids ± SD (mg/d)	15.73± 10.31	14.42± 9.79	20± 12.24	Ns	<0.02	Ns	Ns	Ns
%FVC ±SD upon diagnosis of SSc	82.29± 14.6	84.5± 13.41	77.89±16.67	Ns	Ns	Ns	Ns	<0.001
%FVC±SD upon diagnosis of ILD	77.8± 16.09	80.29± 18.13	71.92±13.96	Ns	Ns	Ns	Ns	Ns
%FVC±SD 24 months after diagnosis of ILD	77.65± 20.94	79.85± 22.6	73.45±17.58	Ns	Ns	Ns	Ns	Ns
%FEV1/FVC± SD upon diagnosis of SSc	83.78± 14.07	85.11± 15.71	81.11±10.21	Ns	Ns	Ns	Ns	Ns
%FEV1/FVC± SD upon diagnosis of ILD	87.79± 16.06	89.56± 16.85	83.69±13.79	Ns	Ns	Ns	Ns	Ns
%FEV1/FVC± SD 24 months after diagnosis of ILD	93.25±1 8.93	98.71±1 7.24	81.8± 17.83	<0.03	Ns	0.08	Ns	Ns
%DLCO±SD upon diagnosis of SSc	69.76± 17.8	70.93± 18.46	67.67±17.42	Ns	Ns	Ns	Ns	Ns
%DLCO±SD upon diagnosis of ILD	63.28± 18.31	65.69± 18.75	57.92±16.75	Ns	Ns	Ns	Ns	Ns
%DLCO 24 months after diagnosis of ILD	61.31± 17.47	63± 18.74	58.45±15.68	Ns	Ns	Ns	Ns	Ns

Conclusions: In terms of ILD-SSc patient stratification, sub-classification by AAb appears to be more specific than the clinical sub-classification. ACA is related to less frequency of NSIP pattern. Unlike what has been described for SSc from a global point of view, in patients with ILD-SSc no association between AAb and neoplasia could be established.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6138

SAT0352 MORTALITY IN IDIOPATHIC INFLAMMATORY MYOPATHY-RESULTS FROM A SWEDISH NATIONWIDE POPULATION-BASED COHORT STUDY

C. Dobloug[1], J. Svensson[2], I. Lundberg[2], M. Holmqvist[2]. *[1]Oslo University Hospital, Oslo, Norway; [2]Karolinska Institutet, Stockholm, Sweden*

Background: Little is known about mortality in idiopathic inflammatory myopathies (IIM) compared to the general population, especially the risk development since diagnosis. In a recently published study, the 5-, and 10-year mortality was lower for IIM than previously reported, suggesting improved outcomes in recent years.

Objectives: To assess the mortality following IIM diagnosis in a nationwide population-based cohort of IIM patients diagnosed 2002–2011 compared to the general population.

Methods: We used nationwide fully covering health care registers to identify all individuals who were treated by a rheumatologist, neurologist, or dermatologist for IIM and who had a listing of IIM at $\geq$two visits within 1–12 months between 2002 and 2011, general population comparators, and death during follow up. We calculated mortality rates with 95% confidence intervals (CI) and compared the mortality in IIM to that in the general population using Cox proportional hazards models adjusted for age, sex, year of diagnosis, and residential area.

Results: During a median follow up of 4 years, 228 (31%) of the 733 IIM patients and during a median follow up of 6 years, 888 (12%) of the 7,340 general population comparators died. This corresponded to a crude mortality of 61/1,000 person-years in IIM, and 20/1,000 person-years in the comparators. The cumulative mortality at 1 year after diagnosis was 10% in IIM and 1% in the general population, at 5 years it was 24% in IIM and 7% in general population, and at 10 years the proportion was 31% and 12%. The overall hazard ratio (HR) (95% CI) of death comparing the NPR cohort and its comparator, was 3.5 (3.0–4.0). When restricting the outcome to cardiovascular disease-, cancer-, infection-, or pulmonary disease- specific death we noted increased mortality from all outcomes in IIM compared to the risk in the general population. When we stratified on time since diagnosis we noted an increased absolute and relative risk of death in the first year of diagnosis in particular for pulmonary disease and cancer, whereas cardiovascular mortality was a major cause of death also after 10 years after IIM diagnosis (table).

Conclusions: IIM patients are still at increased risk of death. The highest mortality

Abstract SAT0352 – Table 1. Hazard ratio (HR) and 95% confidence intervals (CI) comparing the mortality in idiopathic inflammatory myopathy (IIM) patients identified in the National Patient register between 2002 and 2011 and in an individually matched general population comparator. Overall mortality and stratified by underlying cause of death and time since IIM diagnosis

	IIM duration categories HR (95% CI) Deaths per 1,000 person years IIM patients/comparators			
	<1 year	1–<5 years	5–10 years	>10 years
Overall	10.3 (7.5–14.2) 110.8/ 11.6	3.2 (2.5–4.0) 51.2/19.6	2.6 (1.8–3.6) 48.2/24.7	2.4 (0.6–9.2) 42.1/27.7
Cardiovascular disease	5.3 (2.8–9.9) 21.9/4.4	2.3 (1.6–3.5) 14.9/8.0	2.4 (1.4–4.2) 16.7/10.0	6.49 (1.1–40.0) 28.1/13.4
Cancer	12.4 (7.4–20.8) 46.7/4.2	3.2 (2.1–4.8) 15.4/5.5	3.1 (1.6–6.0) 12.8/5.6	1.5 (0.1–14.9) 14.0/6.7
Pulmonary disease	22.49 (4.2–119.7) 7.3/0.1	5.2 (2.5–10.8) 6.1/0.3	2.4 (0.7–8.5) 3.0/1.0	- -

was noted within a year of diagnosis due to pulmonary disease, cancer and cardiovascular disease which calls for extra vigilance with respect to comorbidities during the first year of IIM diagnosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2581

SAT0353 SMALL AIRWAYS INVOLVEMENT IN SCLERODERMA PATIENTS: RESULTS OF A CASE-CONTROL STUDY

M. Bonifazi[1], M. Mattioli[2], P. Fraticelli[3], C. Fischetti[2], L. Paolini[1], S. Gasparini[1], A. Gabrielli[2]. *[1]Pulmonary Diseases Unit, Department of Internal Medicine, Azienda Ospedaliero-Universitaria "Ospedali Riuniti"; [2]Department of Biomedical Sciences and Public Health, Università Politecnica delle Marche, Ancona; [3]Clinica Medica, Department of Internal Medicine, Azienda Ospedaliero-Universitaria "Ospedali Riuniti", Ancona, Italy*

Background: Interstitial lung disease (ILD) and pulmonary hypertension are the leading cause of morbidity and mortality in systemic sclerosis (SSc). Although a ventilatory obstructive pattern, due to large airways impairment, has been rarely observed in SSc, a potential involvement of smaller airways (SA) has been suggested in previous reports. Recently, impulse oscillometry (IOS), a non-invasive forced oscillation technique, has been advocated as a valuable diagnostic tool for a sensitive assessment of SA.

Objectives: The main objectives of the present study was to investigate the prevalence of SA dysfunction by IOS in SSc patients compared to healthy controls, and to evaluate the correlation between SA dysfunction and selected radiological and clinical disease-related features.

Methods: Consecutive SSc patients were included in the present study according to eligibility criteria; controls were health volunteers. Both cases and controls underwent IOS measurements; cases also underwent pulmonary function tests and St. George's respiratory questionnaire. Radiological features were assessed on the latest chest high resolution computed tomography (HRTC) scan available in the twelve months before study enrolment, evaluating for both SA signs of disease and ILD. A SA involvement at IOS was defined as R5-R20 $\geq$0.07 kPa/L/sec. Odds ratios and 95% confidence intervals for the IOS value was computed using multiple logistic regression models. Correlation between SA dysfunction and selected parameters were assessed using Pearson's correlation coefficient.

Results: 92 cases (M/F 14/78, mean age 57.06) and 84 controls (M/F 15/69, mean age 54.28) were included in the present study. The R5-R20$\geq$0.07 kpa/L/sec was found in 20.65% of cases and in 3.57% of controls. The OR was 7.027 (95% CI 1.99–24.72, p<0.01). This value did not significantly change after the adjustment for confounding variables (OR a* 7.091). Correlations between R5–20 $\geq$0,07 kPa/L/s and selected parameters showed a significant inverse association with vital capacity (FVC) and forced expiratory volume in first second (FEV1) and a direct correlation with pulmonary artery systolic pressure estimated. With reference to cutaneous subtype a SA dysfunction was more prevalent in the limited form compared to the diffuse, respectively in 23% and 12%. Radiologic HRCT assessment of SA pathological features and ILD extent were provided for 77 patients: 19 (24.7%) presented at least one sign of SA disease. An underlying ILD was detected in 40 patients, characterized by NSIP pattern in 37.

Conclusions: A significant involvement of SA was found in a substantial proportion of SSc patients, compared to healthy controls. Moreover, this seemed to be associated with a more severe functional obstructive and restrictive impairment, and with higher PAPs values. Therefore, our findings suggests that SA may be a potential, less known, target of disease, and further studies are needed to assess prognostic and therapeutic implications of this pathologic feature.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5385

SAT0354 NAILFOLD VIDEOCAPILLAROSCOPY AND RAYNAUD'S PHENOMENON IN A COHORT OF MESTIZO LATIN AMERICAN PATIENTS: A PRELIMINARY OBSERVATIONAL STUDY

C.J. Velásquez-Franco[1], A. Facio-Lince García[2], A.L. Zapata-Castellanos[1], L.M. Rodríguez-Padilla[2], M.A. Mesa-Navas[1] on behalf of Clinical Immunology and Rheumatology Group. Universidad Pontificia Bolivariana. *[1]Rheumatology, Clinica Universitaria Bolivariana. Universidad Pontificia Bolivariana; [2]School of Health Sciences. Universidad Pontificia Bolivariana, Medellin, Colombia*

Background: The prevalence of Raynaud's phenomenon (RP) has been reported between 3–22%. When associated with systemic autoimmune diseases (SAD), especially systemic sclerosis (SSc), it is the sentinel event of irreversible organic damage. Nailfold videocapillaroscopy (NVC) is a non-invasive and safe procedure that allows *in vivo* observation of the microcirculation. Between 15–20% of patients who have RP with videocapillaroscopic alterations and certain autoantibodies will develop a SAD over two years. In addition, 90% of individuals with SSc and 85% with mixed connective tissue disease (MCTD) had RP as the first symptom.

Objectives: To evaluate the role of NVC in the differential diagnosis of RP, as well as in the early detection of SAD, in a cohort of Colombian patients.

Methods: A prospective, longitudinal, analytical study was conducted in subjects with RP, over 18-year-old, not active smokers, without previous connective tissue disease, secondary causes or aggravating factors. Optilia NVC with OptiPix software was used (Optilia Instruments; Sollentuna, Sweden). Qualitative variables are described by means, as well as absolute and relative frequencies; quantitative variables, according to the distribution of data, were reported by means or median, with standard deviation (SD) and interquartile range (IQR), respectively. We are reporting the baseline characteristics of these individuals.

Results: Fifty-eight individuals were included; 91.4% were female. The mean age was 40.9 years (SD: 14.1). RP was biphasic in 63.6% of the patients, with a median of 30 episodes per month (IQR: 8–30). In 41 subjects (available data), antinuclear antibodies were positive; the most common patterns were: speckled (41.5%) and centromere (26.8%). The median of erythrosedimentation rate (ESR) was 9 (IQR 4–13). Ten individuals (19.2%) were diagnosed with SAD in the first NVC: Seven patients with limited SSc, two with MCTD, and one with diffuse SSc. The patterns observed in the individuals with SSc were: early (n=3), active (n=3), late (n=2), and minor and unspecific abnormalities in subjects with MCTD (one each). The most frequent NCV alterations in subjects with SAD were: megacapillaries (n=10), microhemorrhages (n=10), avascular zones (n=8), neovascularization (n=6), and capilar disorganization (n=6). In these subjects, the mean capillary diameter was 76.7±33.9 mm; the median of capillary number per mm was 7 (IQR: 6–8).

Conclusions: The frequency of systemic autoimmune disease was similar to the published reports in the literature. We highlight the following aspects: 1) The normal erythrosedimentation rate in subjects with a rheumatologic diagnosis, a particular finding when compared to previous data; 2) The important percentage of subjects with a specific diagnosis in the first nailfold capillaroscopy; one possible explanation could be a underdiagnosed disorder; this fact could be possibly demonstrated by the large capillary diameter found.

References:

[1] Ingegnoli F et al. Arthritis Rheum. 2008; 58 (7): 2174–82.
[2] Ingegnoli F et al. Rheumatology 2010; 49 (4): 797–805.

Acknowledgements: Clinica Universitaria Bolivariana. Universidad Pontificia Bolivariana.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4075

SAT0355 NEUROPATHIC PAIN: IS IT AN UNDERESTIMATED SYMPTOM IN SYSTEMIC SCLEROSIS?

N. Cuzdan Coskun[1], I. Turk[2], T. Sarpel[1], E. Erken[2], Z.N. Alparslan[3]. *[1]Department of Physical Therapy and Rehabilitation, Division of Rheumatology; [2]Department of Internal Medicine, Division of Rheumatology; [3]Department of Biostatistics, Cukurova University Faculty of Medicine, Adana, Turkey*

Background: Pain is one of the most common symptoms in SSc patients, yet not considered in the assessment of disease severity. Former studies have shown that pain has a neuropathic component; however there is still lack of evidence about its distribution in the body regions and the direct effect of neuropathic pain on the quality of life (QoL).

Objectives: We aimed to investigate the frequency of neuropathic pain syndrome (NPS) and to evaluate its interference with the quality of life in SSc patients.

Methods: Diffuse and Limited SSc patients diagnosed by *American College of Rheumatology* 2013 criteria were included in the study. Pain was evaluated with *Visual Analogue Scale* (VAS); painful body regions and pain intensity with *Brief Pain Inventory* (BPI); presence of neuropathic pain with *The Leeds Assessment of Neuropathic Symptoms and Signs* (LANNS) questionnaire; disease activity with *Medsger Disease Severity Scale* and QoL with *Short-form 36* (SF36). Multiple regression analysis was used to assess the associations of NPS with sociodemographic and clinical factors.

Results: One hundred twenty patients were included in the study (mean age 53.64±11.44 years, female/male 83.3%>16.7%). Total pain frequency was found 69.2% and NPS was 35.9% in the whole patient group. Mean VAS in the

group of patients with and without NPS were 5.44±2.03, 3.45±1.82; respectively ($P<0.001$). Pain was most frequently seen in wrist-hand (50.6%) and ankle-foot (43.4%) regions; albeit, NPS rates were highest in face (94.4%), lower leg (87.5%) and gluteal (78.6%) regions. SF 36 scores were lower in patients with NPS than the patients without NPS but the difference has not reached to a statistically significant level ($P>0.05$). The most associated factors with NPS were Medsger Disease Severity Score for muscle and drug consumption of the patient.
Conclusions: According to our results, high frequency of NPS is seen in SSc patients, and NPS is associated with low QoL. The highest rates of NPS presence were seen in face, gluteal and lower leg regions of the body. Differential diagnosis of NPS is important to consider right treatment options and accurate management of pain in all rheumatologic diseases including SSc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6213

SAT0356 VIDEOFLUOROSCOPY SWALLOW STUDY IN PATIENTS WITH SYSTEMIC SCLEROSIS. CORRELATION WITH CLINICAL PATTERNS

P. Fraticelli[1], C. Fischetti[2], A.M. Pisani[3], S. Barchiesi[2], G. Romanelli[2], A. Gabrielli[1,2]. *[1]Clinica medica, Department of internal medicine, Ospedali Riuniti; [2]Department of Clinical and Molecular Sciences, Università Politecnica delle Marche; [3]Department of Radiology, Ospedali Riuniti, Ancona, Italy*

Background: Systemic Sclerosis (SSc) is a chronic autoimmune disease characterized by proliferative vascular lesions and progressive fibrosis of skin and internal organs, including the gastrointestinal tract. Gastrointestinal involvement is a very frequent complication, reported in up to 90% of SSc patients in both limited (lSSc) and diffuse (dSSc) cutaneous forms, and it is one of the earliest events.
Objectives: To evaluate the correlation between radiological items analyzed by videofluoroscopy swallow study and clinical patterns of patients SSc.
Methods: 55 patients (M/F: 6/49; median age 56y; median disease 6y, lSSc /dSSc:36/19; anti-Scl70+:21/55, ACA+:18/55, only ANA+:16/55), with a diagnosis of SSc and a history of dysphagia underwent a dynamic and morphological study of the oral, pharyngeal and esophageal phases of swallowing with videofluoroscopy. The oral and pharyngeal esophageal phases were performed in the upright position, while the esophageal phase was performed in the prone-oblique position, after administration of contrast material either in bolus form or diluted. Data were analyzed by radiologist with experience in videofluoroscopy for the evaluation of 17 videofluoroscopy items, of which, 4 concerning the oral, 4 the pharyngeal and 9 the esophageal phase, respectively. Results were expressed in a binary system. Then the main relevant videofluoroscopy findings were correlated with the principal scleroderma pattern of disease: lSSc vs dSSc; disease duration (more than 2 years) and subset of autoantibodies.
Results: Radiological study of swallowing disorders showed for oral phase: inadequate velar elevation in 4%, leakage in 15%, drooling in none (0%) and stasis of bolus in mouth in 4% of the patients. As for pharyngeal phase: stasis of bolus on pharyngeal in 49%, penetration in the laryngeal aditus in 53%, post-swallowing aspiration in 22%, abnormal upper esophageal sphincter behavior in 13% of the cases. Concerning esophageal phase: inadequate primary peristalsis in 53%, abnormal secondary peristalsis in 29%, non-peristaltic contractions in 40%, defects of clearance in 69%, abnormal lower esophageal sphincter behavior in 76%, hiatal hernia in 80%, esophageal reflux in 56%, esophagitis in 82% of the patients, nobody presented esophageal luminal stenosis. When we analyzed the swallowing disorders in different conditions we found that these are prevalent in patients with more than 2 year of disease, although may be found also early. Conversely, we have not found a significant prevalence between the lSSc or the dSSc, or a particular correlation with different patterns of autoantibodies.

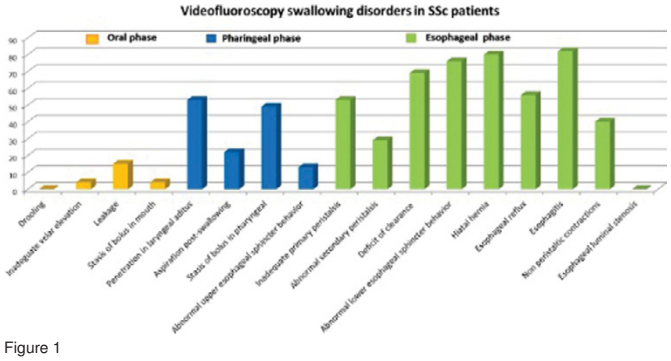


Figure 1

Conclusions: Our study demonstrated relevant abnormalities in swallowing functions in high number of patients with SSc. Pharyngeal and esophageal phases are the most affected, also early. Swallowing disorders increase with disease progression and involve similarly the limited or the diffuse SSc. An early and detailed diagnosis, supported by a semi-quantitative analysis with the use of videofluoroscopy scores, may be useful to guide the appropriate therapeutic approach, either rehabilitative or pharmacological, and finally, to improve the patient's quality of life. Extensive studies are necessary to confirm and transfer our data into clinical practice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5456

SAT0357 FEATURES ASSOCIATED WITH MODERATE TO HIGH RISK OF MALNUTRITION IN A COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS

P.M. Marcaida[1], D. Vanesa[1], V. Martire[1], F. Melo[1], A. Secco[1], M. Mamani[1], S. Scarafia[1], M. Lazaro[2], A. Cusa[2], F. Cusa[3], V. Caputo[4], J. Sarano[5], M. Molina[6], A. Nitsche[7], M. Gaona[8], C. Pena[9], M. Garcia[9], S. Gordon[10], N. Muñoz Cantos[8], S. Montoya[8]. *[1]Rheumatology, Rivadavia Hospital; [2]Rheumatology; [3]Nutrition, IARI; [4]Rheumatology, Military Hospital; [5]Rheumatology, Lanari Institute; [6]Rheumatology, Central Hospital of San Isidro; [7]Rheumatology, Diagnostic system-CM; [8]Rheumatology, Ramos Mejia Hospital, Buenos Aires; [9]Rheumatology, HIGA, la plata; [10]Rheumatology, HIGA, Mar del plata, Argentina*

Background: It is estimated that about 28% of Systemic Sclerosis (SS) patients have moderate to high risk of malnutrition.
Objectives: to evaluate differences between SS patients with moderate to high risk of malnutrition and those with low risk.
Methods: cross-sectional, observational, multicentric study. We included patients with SS according to ACR-EULAR 2013 classification criteria. Patients were classified in groups depending on whether they were in low or moderate-high risk of malnutrition, according to the screening method for detection of adult malnutrition (MUST). Were evaluated: disease duration, disease subtype (limited or diffuse), presence of microstomia, xerostomia, active or past digital ulcers, amputations, arthritis, Rodnan Score, gastroesophageal and bowel involvement, anxiety and depression, and hands functionality by Duruöz Index. Continuous variables were described as median (IQR) or mean (SD) and percentages for categorical variables. Mann Whitney or t-test was used for continuous variables, and Fisher exact test or chi squared for categorical variables. A $p<0.05$ was considered significant. A multivariate analysis was made taking MUST as a dependent variable.
Results: 116 patients were included. Thirty percent were at moderate to high risk of malnutrition. These patients experienced significantly higher frequency of diffuse SS (49% vs 21%, p=0,003), bowel involvement (49% vs 27%. p=0,02), gastroesophageal involvement (74% vs 48%, p=0,009), higher cutaneous involvement (*median* 12 vs 6, p=<0,01), microstomia (40% vs 15%, p=0,003), worst hand functionality (*median:* 11 vs 3, p=0,02), and moderate-severe depression (37% vs 16%, p=0,012). Also, men experienced a higher moderate-high risk of malnutrition (20% vs 6%, p=0,02). In the multivariate analysis, the male sex (OR 4.55, 95% CI 1.11–20, p=0.03), the Rodnan score >9 (OR 3.13, 95% CI, 95% CI, p=0,01), and gastroesophageal involvement (OR 2.87, 95% CI 1.07–7.73, p=0.03), were independently and statistically significant.
Conclusions: These results highlight the importance of assessing the nutritional status of our SS patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6535

SAT0358 DECREASED BODY FAT, LEAN BODY MASS AND BONE MINERAL DENSITY IN PATIENTS WITH SYSTEMIC SCLEROSIS ARE ASSOCIATED WITH DISEASE ACTIVITY AND PHYSICAL ACTIVITY

S. Oreska[1], M. Spiritovic[1,2], P. Cesak[2], M. Cesak[2], H. Storkanova[1], K. Kubinova[1], M. Klein[1], L. Vernerova[1], O. Ruzickova[1], H. Mann[1], K. Pavelka[1], L. Senolt[1], J. Vencovsky[1], R. Becvar[1], M. Tomcik[1]. *[1]Department of Rheumatology, 1st Medical Faculty, Charles University, Institute of Rheumatology; [2]Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic*

Background: Systemic sclerosis (SSc) is characterized by fibrosis of the skin and visceral organs, especially digestive tract, and musculoskeletal involvement, which limit mobility/self-sufficiency of patients, and can have a negative impact on body composition.
Objectives: To assess body composition and physical activity of SSc patients and healthy controls (HC).
Methods: 59 patients with SSc (50 females, 9 males; mean age 52.1; disease duration 6.7 years; limited cutaneous (lcSSc,36)/diffuse cutaneous (dcSSc,23)) and 36 age-/sex-matched HC (30 females, 6 males, mean age 51.4) without rheumatic/tumor diseases or manifest cardiovascular event were included. SSc patients fulfilled EULAR/ACR 2013 criteria. Anthropometric parameters and body composition were assessed (by densitometry-iDXA Lunar, and by bioelectric impedance-BIA-2000-M), and physical activity was evaluated using Human Activity Profile (HAP) questionnaire. Routine biochemistry analysis was performed after 8 hours of fasting. Disease activity was evaluated by EUSTAR SSc activity score. Data are presented as mean±SD.
Results: Compared to HC, patients with SSc had significantly lower body-mass index (BMI: 26.4±3.3 vs. 22.4±4.3 kg/m^2, p<0.0001) and body fat % assessed by both iDXA (BF%: 37.2±6.6 vs. 32.6±8.2%, p=0.0014) and BIA (BF%: 31.1±6.4 vs.

24.6±7.8%, p<0.0001), and a trend to decreased visceral fat weight (0.9±0.9 vs. 0.5±0.5kg, p=0.0670). Compared to HC, SSc patients demonstrated significantly decreased lean body mass assessed by both iDXA (LBM: 46.6±7.5 vs. 40.9±6.8kg, p=0.0003) and BIA (LBM: 53.2±8.7 vs. 47.7±7.0kg, p=0.0017), and increased ECM/BCM ratio (extracellular mass/body cell mass: 1.03±0.1 vs. 1.29±0.4, p<0.0001), which reflects worse muscle predispositions for physical exercise, aerobic fitness/performance, and usually increases with deteriorating nutritional status. Compared to HC, SSc patients had significantly lower bone mineral density (BMD: 1.16±0.10 vs. 1.05±0.11g/cm^2, p<0.0001), and were currently able to perform less energetically demanding physical activities according to HAP score (84.7±6.6 vs. 64.1±17.2, p<0.0001). Disease activity negatively correlated with BF% (r=-0.324, p=0.014), and physical activity (HAP) positively correlated with BMD (r=0.276, p=0.034) and negatively with ECM/BCM (r=-0.625, p<0.0001).

Conclusions: Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our SSc patients, which are associated with their disease activity and physical activity, and could reflect their nutritional status, and gastrointestinal and musculoskeletal involvement.

Acknowledgements: Supported by AZV-16–33574A, GAUK-214615.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4873

SAT0359 THE COURSE OF MOUTH OPENING AND ITS RELATIONSHIP WITH DISEASE CHARACTERISTICS, GLOBAL FUNCTIONING, HEALTH-RELATED QUALITY OF LIFE AND MOUTH HANDICAP IN PATIENTS WITH SYSTEMIC SCLEROSIS

S.J.H. Khidir[1], M. Boonstra[1], G.W.M. Boerrigter[2], E.M. Voogt-van der Harst[2], S.A. Bergstra[1], M.K. Ninaber[3], N. Ajmone Marsan[4], T.W.J. Huizinga[1], J.K. de Vries-Bouwstra[1]. *[1]Rheumatology; [2]Physiotherapy; [3]Pulmonology; [4]Cardiology, Leiden University Medical Center, Leiden, Netherlands*

Background: Systemic sclerosis (SSc) is a fibrotic disease which can lead to reduced maximal mouth opening (MMO). Previous cross-sectional research showed that reduced MMO in SSc correlated with higher disease severity and lower oral quality of life. Interpretation of interventions that possibly influence MMO is difficult, as the natural history of MMO in SSc is not well described.

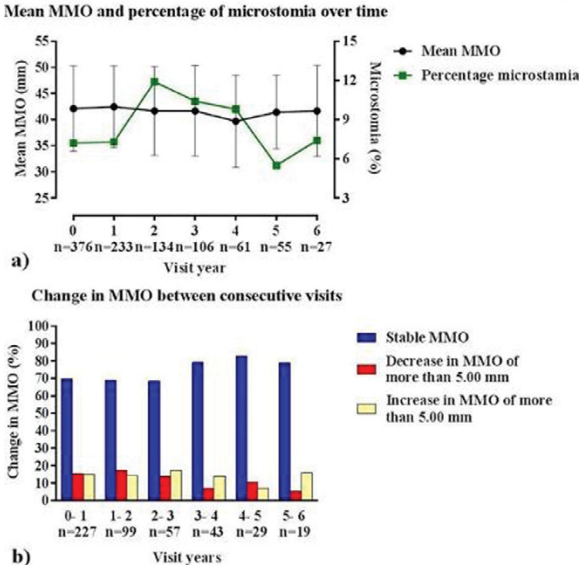
Objectives: To evaluate in SSc 1) the course of MMO 2) disease characteristics predictive for decreasing MMO and 3) the relationship between the course of MMO and global functioning, health-related quality of life (HRQoL) and mouth handicap.

Methods: SSc patients from the Leiden Combined Care In Systemic Sclerosis (CCIS) cohort, Leiden University Medical Center were included if at least one MMO measurement was available. Annual clinical assessment includes MMO measurement, global functioning (HAQ), HRQoL (Short Form-36; SF-36), mouth handicap (Mouth Handicap in Systemic Sclerosis scale; MHISS). We assessed mean MMO, prevalence of microstomia (MMO<30.00 mm) and decreasing MMO (decline >5.00 mm/year) over time. Predictors for decreasing MMO were assessed by a linear mixed model (LMM), including baseline clinical parameters reflecting 7 domains (peripheral vasculopathy, skin, heart, gastrointestinal, lung, renal, musculoskeletal). Additionally, MMO over time was correlated with baseline HAQ, SF-36 and MHISS in separate LMMs adjusted for gender, Body Mass Index, age and disease characteristics correlated significantly (p<0.05) with the course of MMO.

Table 1. Multivariate mixed model to determine the association between Maximal Mouth Opening (MMO) and baseline disease characteristics in SSc patients

	β	*p*-value	95% Confidence Interval	
			Lower limit	Upper limit
Non cutaneous SSc (3)			ref	
Limited SSc (2)	-2.2	**0.036**	-4.2	-0.2
Diffuse SSc (1)	-4.1	**0.004**	-6.9	-1.4
Gastrointestinal involvement	-2.6	**0.001**	-4.1	-1.1
Pulmonary involvement	-1.8	**0.032**	-3.4	-0.2
Peripheral vasculopathy	-2.3	**0.003**	-3.8	-0.8

Figure 1 Mean Maximal Mouth Opening (MMO), percentage of microstomia and change in MMO over time in SSc patients



Results: 382 patients were included with mean age 54±14 years, 83% female and 25% diffuse cutaneous SSc. Mean MMO during 6 years of follow-up ranged from 39.4 to 42.5 mm. The annual mean percentage of patients with microstomia was 9%, range 6 to 12% (Figure 1a). A decrease in MMO between two consecutive annual measurements was observed in 5 to 17% of patients, mean 12% (Figure 1b). More extended cutaneous involvement, peripheral vasculopathy, pulmonary and gastrointestinal involvement at baseline were predictive for decreasing MMO over time (Table 1). Baseline HAQ (β=-1.6, 95% CI=-2.7 to -0.6), SF-36 physical component (β=0.1, 95% CI=0.0 to 0.1) and MHISS (β=-0.2, 95% CI=-0.2 to -0.1) correlated with longitudinal MMO.

Conclusions: Over time, MMO is relatively stable in the majority of SSc patients. Microstomia is seen in 9% and important decrease of MMO in 12% and is associated with more severe organ involvement. Even though this concerns only a small subgroup of SSc patients, a significant association with global functioning and HRQoL was demonstrated, underlining the need for treatment strategies improving MMO.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6245

SAT0360 MYOSITIS-SPECIFIC AND MYOSITIS-ASSOCIATED AUTOANTIBODIES IN PATIENT WITH DERMATOMYOSITIS / POLYMYOSITIS; COMPARISON BETWEEN LINE BLOT AND ENZYME-IMMUNOASSAY ASSAYS

S. Nakashima, T. Kameda, M. Izumikawa, H. Shimada, H. Ozaki, R. Wakiya, A. Kondou, N. Kadowaki, H. Dobashi. *Department of Internal medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Kagawa University, Kagawa, Japan*

Background: MESACUP^{TM} test (enzyme-immunoassay assays; TIF1γ, MDA5, Jo-1, EJ, PL-7, PL-12, and KS; MBL) (MESA) is used for a diagnosis of idiopathic inflammatory myopathies (IIMs) in Japan. On the other hand, EUROLINE myositis Profile 3 (line blot; EUROIMMUN) (EURO) can analyze plural Myositis-specific autoantibodies (MSA: Mi-2, Jo-1, SRP, PL-7, PL-12, EJ, OJ) and Myositis-associated autoantibodies (MAA; Ku, PM-Scl) at the same time, which is used commercially in Western countries. However, the difference between utility of MESA and that of EURO haven't be disclosed.

Objectives: To clarify difference between utility of EURO and MESA, and extract the problem of respective examination.

Methods: We enrolled 58 patients diagnosed DM/PM in our facility. Polymyositis (PM) and dermatomyositis (DM) were diagnosed according to Bohan and Peter's criteria.[1)] The MAA and MSA were analyzed using MESA and EURO. In case of MESA (+), MSA (anti-Jo1, anti-PL7, anti-PL12, anti-KS) were identified by specific ELISA. When those results were different, we analyzed by immunoprecipitation. And we analyzed the association between each autoantibody and clinical features.

Results: MSA and MAA were detected in 43/58 (74%) (anti-PL7: 12, anti-Jo1: 7, anti-EJ: 3, anti-PL12: 1, anti-OJ: 0, anti-Ro52: 27, anti-PM-Scl75: 7, anti-Ku: 6, anti-PM-Scl100: 1) by EURO. On the other hand, MSA and MAA were detected in 30/58 (52%) (anti-PL7: 9, anti-Jo1: 7, anti-EJ: 4, TIF1γ: 4, MDA5: 3, U1RNP: 3) by MESA. Five patients were MESA (-) and EURO (-). In the case of ARS positive patient, Two of EURO (-) patients was positive in MESA, respectively Jo1 and EJ. Three of MESA (-) patients was positive in EURO. Although MESA(-) and EURO(+) patients had plural MSA and MAA (PL7+Jo1, PL7+PL12, PL7+Ku), MSA and MAA weren't detected by immunoprecipitation in MESA(-) and EURO(+) patients. Two of patients that detected plural MSA or MAA had rapid progressive ILD.

(Association between clinical manifestations and MSA, MAA)

All patients with anti-ARS (anti-Jo-1, anti-PL-7, anti-PL-12 and anti-EJ) had ILD. In addition, anti-ARS were associated with arthritis and mechanic's hands. Anti-Mi-2 positive patients didn't have ILD. Patients detected anti-PM-Scl75, anti-PM-Scl100, anti-Ku were almost overlap syndrome. All of Anti-SRP positive patients was PM.

Conclusions: EURO is a convenient and reliable method useful for detection of MSA and MAA. It was suggested the patients whom plural antibodies were detected by EURO have unique clinical course in others.

References:

[1] Bohan, A., Peter, J.B., 1975. Polymyositis and dermatomyositis (second of two parts). N. Engl. J. Med. 292, 403–407.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4762

SAT0361 CHEST COMPUTED TOMOGRAPHY AS AN ALTERNATIVE TO HIGH RESOLUTION MANOMETRY FOR THE DIAGNOSIS OF SCLERODERMA ESOPHAGUS

S. Panopoulos, V.K. Bournia, G. Karamanolis, K. Denaxas, A. Zorbala, P.P. Sfikakis. *First Department of Propedeutic Internal Medicine and Joint Academic Rheumatology Program, National and Kapodistrian University, Medical School, Athens, Greece*

Background: Severe esophageal disease in patients with systemic sclerosis (SSc), referred as scleroderma esophagus, is characterized by ineffective or absent peristalsis along with hypotensive esophagogastric junction (hEGJ). The associations between scleroderma esophagus and different clinical and laboratory manifestations of SSc are still controversial.
Objectives: To assess associations between scleroderma esophagus, diagnosed by high resolution manometry (HRM), and other manifestations of disease.
Methods: Fifty-four consecutive SSc patients (49 women, mean age 50.6±11.6 years) with esophageal symptoms underwent clinical interview, medical records review and HRM. HRMs were analyzed according to the Chicago Classification in order to provide esophageal motility diagnosis; EGJ <9 mmHg was considered hypotensive. Demographic characteristics, patient-reported symptoms, SSc subtypes, pulmonary fibrosis, cutaneous ulcers, and anti-Scl-70 positivity were compared between SSc patients with or without scleroderma esophagus. Comparison was also performed in chest computed tomography (CT) findings of esophageal lumen in 26 patients with available data. Esophageal dilatation was deemed present when the diameter was >9 mm.
Results: Absent contractility was present in 37 (68.5%) patients; among these patients hEGJP was found in 32, thus 32/54 (59.2%) patients had classic scleroderma esophagus. There were no associations with gender, age, esophageal symptoms, skin involvement extent, anti-Scl-70, pulmonary fibrosis and cutaneous ulcers. Notably, esophageal dilation on chest CT was more frequent in patients with scleroderma esophagus compared to those without (77% *vs.* 8%, p=0.04, respectively).

Table 1. Associations between scleroderma esophagus and various SSc manifestations

	Scleroderma esophagus (n=32)	No scleroderma esophagus (n=22)	p
Age (yrs)	52. 5±11.9	52. 5±11.9	
Sex (F, %)	28 (87.5)	21 (98.4)	0.362
Diffuse SSc (n, %)	12 (55.5)	14 (43.8)	0.646
Pulmonary fibrosis (n,%)	25 (78.1)	15 (68.1)	0.750
Cutaneous ulcers (n, %)	19 (59.4)	12 (54.5)	0.854
Anti-Scl-70 (n, %)	23 (71.9)	12 (54.5)	0.540
CT coronal diameters >9 cm (n, %)*	10 (76.9)	1 (7.7%)	0.045
Presence of symptoms (%)			
– dysphagia	18 (56.3)	13 (39.1)	0.914
– heartburn	25 (78.1)	21 (95.4)	0.620
– regurgitation	28 (87.5)	19 (86.4)	0.126
– chest pain	13 (56.3)	7 (31.8)	0.653

*Data available in 26 SSc patients (13 with and 13 without scleroderma esophagus).

Conclusions: Scleroderma esophagus diagnosed by HRM was present in less than 2/3 of symptomatic patients with SSc and associated only with esophageal dilation (>9mm) in CT. Although further studies are needed, esophageal dilation on chest CT may be a non-invasive alternative for evaluation of SSc patients with esophageal symptoms.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3182

SAT0362 RISK FACTORS AND OUTCOME OF THAI PATIENTS WITH SCLERODERMA RENAL CRISIS (SRC): A DISEASE DURATION-MATCHED CASE CONTROL STUDY

S. Wangkaew[1], S. Lertthanaphok[1], S. Puntana[1], K. Noppakun[2]. [1]*Rheumatology;* [2]*Nephrology, Chiang Mai University, Chiang Mai, Thailand*

Background: Data regarding the prevalence, risk factors and outcome of scleroderma renal crisis (SRC) in Asian patients with systemic sclerosis (SSc) are limited.
Objectives: To determine the prevalence, risk factors and outcome of SRC in Thai SSc patients.
Methods: Medical records of all SSc patients, fulfilling the 1980 American College of Rheumatology classification criteria for SSc, seen at the Division of Rheumatology, Maharaj Nakorn Chiang Mai Hospital, Thailand, from January 1990 and December 2015 were retrospectively reviewed. Patients younger than 18 years old or overlapping with rheumatoid arthritis, systemic lupus erythematosus or mixed connective tissue disease were excluded. Cases of SRC were identified based on the international Scleroderma Renal Crisis Study criteria[1]. Controls were selected from consecutive SSc patients without SRC from our database that was ranked closest to the cases based on hospital number, and matched for disease duration from the first non-Raynaud's phenomenon, by±1 year. The ratio for SRC patients to control patients was 1:4.
Results: Of 608 SSc patients seen during the study period, 19 SRC were identified resulting of the SRC prevalence of 3.13% and there were 76 matched controls. Of the 19 cases, mean±SD age and median (IQR1, 3) disease duration was 56.2±13.8 years and 9 (5.0, 16.0) months, respectively. Seventeen patients (89.5%) had dcSSc. There were 12 (63.2%) patients with hypertensive renal crisis (HRC) and 7 (16.8%) patients with normotensive renal crisis (NRC). Univariate conditional logistic regression analyses showed that current myositis (Odd ratio [OR]21.75, 95% CI 2.65– 178.71,p=0.004), cardiac involvement (OR5.68, 95% CI2.03 – 15.84,p=0.001), age >60 years (OR2.82,95% CI 1.01 – 7.94,p=0.049), WBC>10,000 cell/mm^3 (OR2.69,95% CI 0.99 – 7.26,p=0.050), serum albumin<3.0 mg/dl (OR11.08,95% CI 3.02 – 40.66,p<0.001), and current prednisolone used≥15 mg/day (OR19.36,95% CI 2.29 – 163.66,p=0.007) were associated with SRC. Digital gangrene tended to show an association with SRC in the univariate analysis (OR8.00,95% CI0.72 – 88.22,p=0.090). Variables with p<0.15 in univariate conditional logistic regression analysis were included in the multivariate conditional logistic regression analysis. When multivariate conditional logistic regression analysis was performed, digital gangrene (adjusted odd ratio [AOR]31.41,95% CI 1.16 – 852.23,p=0.041), current prednisolone use≥15 mg/day (AOR31.22, 95% CI 1.59 – 613.85,p=0.024), serum albumin <3 mg/dl (AOR7.97, 95% CI 1.49 – 42.56,p=0.015) and cardiac involvement (AOR 6.62,95% CI1.08 – 40.63,p=0.041) were confirmed to be independent risk factors for SRC. During a median (IQR 1, 3) follow-up of 1 (0, 2) months, 15 (78.9%) patients required hemodialysis, including 9 of 12 (75.0%) patients with HRC and 6 of 7 (85.7%) with NRC. Twelve (63.2%) patients received ACEI, including 9 of 12 (75.0%) patients with HRC and 3 of 7 (42.9%) patients with NRC. Ten (52.6%) patients died, including 5 of 12 patients (41.7%) with HRC and 5 of 7 (71.4%) patients with NRC.
Conclusions: SRC was an uncommon complication in Thai patients with SSc, but associated with high mortality. Digital gangrene, current prednisolone used≥15 mg/day, serum albumin<3 mg/dl and cardiac involvement were independent risk factors of SRC.
References:
[1] Hudson M, et al.Semin Arthritis Rheum 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1903

SAT0363 INTERSTITIAL LUNG DISEASE IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A REPORT FROM THE REMICAM REGISTRY

T. Cobo-Ibáñez[1], F.J. López-Longo[2], B. Joven[3], V. Maldonado[4], I. Llorente[5], C. Barbadillo[6], A. Gómez Gómez[7], L. Barrio Nogal[8], R. Almodóvar[9], L. Lojo[10], L. Ruiz[11], M.J. García de Yébenes[12], L. Nuño[13] on behalf of REMICAM. [1]*H. Infanta Sofía, Universidad Europea;* [2]*H. Gregorio Marañón;* [3]*H. Doce de Octubre;* [4]*H. Ramón y Cajal;* [5]*H. la Princesa;* [6]*H. Puerta de Hierro;* [7]*H. HM Sanchinarro;* [8]*H. Príncipe de Asturias;* [9]*H. Fundación Alcorcón;* [10]*H. Infanta Leonor;* [11]*H. Niño Jesús;* [12]*Instituto de Salud Musculoesquelética;* [13]*H. la Paz, Madrid, Spain*

Background: Interstitial lung disease (ILD) in idiopathic inflammatory myopathies (IIM) may appear at any time in evolution and is associated with a worse prognosis.
Objectives: To investigate sociodemographics data and clinical characteristics of patients with IIM and ILD from the REMICAM registry.
Methods: A multicenter retrospective study (1980–2014) was performed. Patients were classified as polymiosytis (PM), dermatomyositis (DM), IIM with anti-synthetase antibodies (AB) and overlap syndrome. In addition, ILD was classified according to HRCT pattern: usual interstitial pneumonia (IP), non specific IP, organizing pneumonia, and acute IP. We compared sociodemographic data, clinical characteristics, AB and treatments of patients with and without ILD, patients with ILD according to subgroup of myositis or ILD.
Results: 478 patients were included, of whom 129 (27%) had ILD. Patients with ILD had a higher age at diagnosis, ESR and CRP and worse initial respiratory function. They were characterized by increased frequency of arthritis, systemic and cardiac manifestations, Raynaud, cardiovascular disease, pulmonary hypertension, ischemic ulcers, sclerodactyly and anti-synthetase AB (p<0.001). The differences among patients with ILD were: less arthritis in PM, greater frequency of Raynaud and sclerodactyly in overlap and antisynthetase syndrome, more anti-RNP AB in the overlap syndrome, more anti-synthetase and anti-Ro AB in the antisynthetase syndrome, and a higher prevalence of cutaneous signs and mechanical hands in DM (p<0.001). There were no differences according to the type of ILD or treatments.
Conclusions: We found some clinical manifestations and AB that may help for detection of patients with IIM associated to ILD, as well as clinical manifestations to better differentiate myositis subtypes in patients with ILD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3268

SAT0364 HISTORY OF DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS IS ASSOCIATED WITH PERIPHERAL VASCULOPATHY AS ASSESSED BY VIDEOCAPILLAROSCOPY AND 22-MHZ POWER DOPPLER ULTRASONOGRAPHY

T. Schioppo[1,2], A. Orenti[1,3], P. Boracchi[1,3], O. De Lucia[2], A. Murgo[2], P.L. Meroni[1,2], F. Ingegnoli[1,2] on behalf of OPERA study group. [1]*Università degli Studi di Milano;* [2]*ASST Pini-CTO;* [3]*Lab of Medical Statistics, Epidemiology and Biometry GA Maccacaro, Milan, Italy*

Background: Vasculopathy is considered a primary pathogenic event in systemic

sclerosis (SSc) and it substantially contributes to prominent features of the disease such as digital ulcers (DUs). History of DUs (HDUs) has been shown to correlate with disease severity, new cardiovascular events, new DUs and overall poor prognosis [1]. Microvascular abnormalities as assessed by nailfold videocapillaroscopy (NVC) and power Doppler ultrasound (PDUS) have been demonstrated to be predictive of new DUs occurrence [2,3].

Objectives: To study the severity of microvascular involvement at the 3rd and 4th finger of the dominant hand in patients with SSc with or without HDUs as assessed by NVC and 22-MHz PDUS.

Methods: 100 SSc consecutive patients fulfilling the 2013 EULAR classification criteria were enrolled. PDUS was performed at the 3rd and 4th finger of the dominant hand after exclusion of ulnar artery occlusion (UAO). In case of UAO non-dominant hand was examined. Ultrasound investigation was performed with Esaote MyLab 70 XVG by means of linear array transducer (10–22 MHz). Power Doppler settings were standardized (Doppler frequency 14.3 MHz, Gain 55%, PRF 750 Hz). PDUS measurements included sagittal scan of nailbed and fingertip qualitatively graded from 1 (no signal) to 4 (marked hyperemia) [4], and resistivity index (RI) of ulnar and radial proper digital arteries. Capillary density (number/mm) was calculated by NVC with magnification 200X performed on two images of the same digits examined by PDUS.

Results: 100 SSc patients, 87 (87%) women, 86 (86%) limited cutaneous SSc, median age 62.2 years old, median disease duration 8 years were evaluated. 7 (7%) patients had UAO. 33 (33%) had HDUs among them 23 had experienced more than one DUs and 2 had active DUs at the moment of evaluation. Semiquantitative perfusion score of sagittal scan of nailbed and fingertip were not significantly associated with the presence of HDU. RI and capillary density were significantly different in the two groups as shown in the table below:

	Presence of HDUs	Absence of HDUs	Mean difference (95% CI)
Capillary density	3.023	3.884	-0.862 (-1.390, -0.333)
RI	0.740	0.792	-0.052 (-0.090, -0.014)

Conclusions: A significant lower RI of ulnar and radial proper digital arteries reported in patient with HDUs is novel. By contrast PDUS grading of nailfold and fingertip were not significantly different in patients with or without HDUs. The finding of a significant lower capillary number assed by NVC in patients with HDUs is consistent with previous results [2]. Adequately longitudinal studies exploring the predictive value of PDUS parameters are required to fully ascertain its role in SSc.

References:

[1] Mihai C et al. Ann Rheum Dis. 2016;75(4):681–6.
[2] Cutolo M et al. Arthritis Rheumatol. 2016;68(10):2527–39.
[3] Lescoat A et al. Arthritis Care Res. 2016;Epub ahead of print.
[4] Newman JS et al. Radiology. 1996,198:582–584.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3844

SAT0365 MUSCULOSKELETAL US AND MRI FINDINGS IN JUVENILE SCLERODERMA

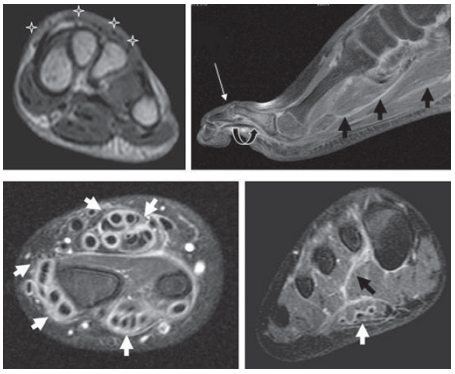
M. Tsinti, V. Dermentzoglou, E. Tsitsami. *Pediatric Rheumatology Unit, 1st Department of Pediatrics, University of Athens, Children's Hospital "Aghia Sofia", Athens, Greece*

Background: Musculoskeletal (MS) involvement and clinically evident arthritis occurs in up to 65% of patients with Juvenile Systemic or localized Scleroderma (JSc). It may be the first manifestation preceding even the onset of Raynaud or skin manifestations; patients presenting with arthritis, tenosynovitis or enthesistis may suffer from Sc. On the other hand clinical examination often underestimates MS involvement in Sc. US and MRI can help distinguish arthritis with effusion from dry tenosynovitis of Sc, define whether loss of range of motion (LOM) derives only from skin thickening or from bone and joint involvement and monitor disease progression.

Objectives: To describe the spectrum of MRI and US features in juvenile scleroderma with musculoskeletal involvement.

Methods: We describe MRI and color Doppler MSUS findings of clinically affected (with arthritis and/or LOM and/or overlying skin with edema or sclerosis) lower or upper extremities from 4 males and 2 females;2 with systemic sc (ssc), 2 with linear scleroderma, 1 with generalized morphea, 1 with mixed morphea (median age 8,5 years, range 7–10,5; median time from symptom onset to MRI 11 months, range 2–24). MRI sequences;T1, fluid-sensitive, and T1-FS contrast-enhanced. Comparisons were made to uninvolved areas of the extremity, and the contralateral extremity. Findings guiding diagnosis and evaluation of disease extent are depicted in the Figure.

Results: Thickening of the dermis and infiltration of the subcutaneous fat with increase in signal intensity on fluid sensitive sequences and contrast-enhanced T1w images and hypointense signal lesions on unenhanced T1w images (asterisks) was apparent in 4 patients. In 2 male patients with generalized scleroderma, clinical LOM of fingers and wrists preceded skin sclerosis by 2 months. Joint and tendon sheath synovitis, indicated by initial MSUS, was detected in fluid sensitive and T1w enhanced images (white arrows). The combination of tendon-sheath synovitis and muscular fascia thickening and enhancement (black arrows), and contractures (thin white arrow) very characteristic of scleroderma, helped identify sclerodermatous musculoskeletal involvement in the absence of skin induration. Focal bone marrow edema depicted as high signal intensity in fluid sensitive sequences (curved arrow) was found in 2 cases; 1 with generalized morphea without apparent overlying skin sclerodermatous lesion, 1 with linear scleroderma with atrophic lesions in all overlying structures



Conclusions: Musculoskeletal imaging features of juvenile scleroderma involving the skin, fascia, musculature and bones reflect pathomorphologic changes of this rare disorder and enable a complete assessment of the disease extent, including depth of infiltration and disease activity.In the described cases implementation of MSUS and MRI in Juvenile scleroderma led to earlier definition of the diagnosis and assisted the evaluation of disease extension.

References:

[1] Zulian F et al. Arthritis and Rheumatism 2007 Mar 15;57(2):203–12.
[2] Eusler E et al. Pediatr Radiol 2017 Jan 14.
[3] Schannz S et al. RSNA 2011.
[4] Torok K Pediatr Clin North Am. 2012 April;59(2):381–405.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5393

SAT0366 SMOKING BEHAVIOUR AND THE PROGRESSION OF ORGAN MANIFESTATIONS IN SYSTEMIC SCLEROSIS: A LONGITUDINAL EUROPEAN SCLERODERMA TRIALS AND RESEARCH GROUP STUDY

V.K. Jaeger[1], G. Valentini[2], E. Hachulla[3], L. Czirják[4], E. Siegert[5], O. Distler[6], L.M. Bambara[7], E. Rosato[8], Y. Allanore[9], M. Matucci-Cerinic[10], P. Airó[11], U. Walker[1] on behalf of EUSTAR co-authors. *[1]University Hospital Basel, Basel, Switzerland; [2]Second University of Naples, Naples, Italy; [3]Université de Lille, Lille, France; [4]University of Pécs, Pécs, Hungary; [5]University Hospital Charité, Berlin, Germany; [6]University Hospital Zurich, Zurich, Switzerland; [7]University of Verona, Verona; [8]Sapienza University of Rome, Rome, Italy; [9]Paris Descartes University, Paris, France; [10]University of Florence, Florence; [11]Spedali Civili, Brescia, Italy*

Background: Systemic sclerosis (SSc) is a rare, multisystem autoimmune disorder. It is characterised by generalized microangiopathy, in which hypoxia and oxidative stress have been implicated in its pathogenesis. Tobacco inhalation increases free radicals and strongly promotes vascular damage. So far, data available with regards to a role of tobacco exposure with SSc severity and progression are scarce.

Objectives: We aimed to assess the effects of smoking on the speed of worsening of organ manifestations, namely lung involvement (forced vital capacity, FVC; forced expiratory volume, FEV1/FVC ratio; diffusing capacity for carbon monoxide corrected for alveolar volume, DLCO/VA), skin involvement (modified Rodnan skin score; mRSS), and digital ulcers (DU) in the European scleroderma trials and research (EUSTAR) database.

Methods: Adult SSc patients from the EUSTAR cohort with a follow-up visit 12±4 months after their baseline visit and available data on their smoking habits were included.

The associations of smoking behaviour (never smokers *vs* ex-smokers *vs* current smokers) with the disease manifestations at follow up were assessed after adjusting for potentially confounding covariates using multivariable linear or logistic regression analyses.

Missing data were imputed using multiple imputations.

Results: Of the 3,023 patients included (mean age 57 years, SD 13; 85% female), 66% stated that they never smoked, 23% were ex-smokers and 11% were current smokers. On average, ex-smokers had smoked for 19.5 years (SD 12) while current smokers smoked for 29.1 years (SD 13). Ex-smokers had smoked on average 17.3 pack-years (SD 20) and current smokers 29.3 pack-years (SD 36). The mean time since smoking cessation in ex-smokers was 15.8 years (SD13).

The FEV1/FVC ratio changed from 96.3 (SD 14) at baseline to 96.2 (SD 13) at follow up. Taking into account the effect of age, sex, autoantibody status, disease duration and SSc subset as well as the baseline values of the outcome, the FEV1/FVC ratio decreased faster in currently smoking SSc patients than in never smokers (β=-2.8, p=0.001). Similarly, the DLCO/VA diminished faster in current

smokers (β=-3.7, p=0.006) while on average the DLCO/VA decreased from 78.1 (SD 18) to 76.5 (SD 17). Changes in FVC were however not associated with smoking behaviour (p=0.13).
The mRSS changed between baseline and follow-up from an average of 7.6 (SD 7) to 7.3 (SD 7); on average, in smokers the mRSS improved faster than in never smokers (β=-0.65, p=0.015). The presence of DUs at follow-up was not associated with current smoking (p=0.9).
Having previously smoked was not significantly associated with the progression of any of the assessed outcomes.
Conclusions: Although the adverse effects of smoking on bronchial airways that is known in the general population could be replicated in the SSc population, the lack of a measurable adverse effect of smoking on SSc organ manifestations argues against a major role of tobacco associated free radicals and vasoconstriction in the pathogenesis of SSc vasculopathy and fibrosis.
Disclosure of Interest: V. Jaeger: None declared, G. Valentini: None declared, E. Hachulla: None declared, L. Czirják: None declared, E. Siegert: None declared, O. Distler Grant/research support from: 4 D Science, AbbVie, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, iQone Healthcare, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm and Sinoxa, Consultant for: 4 D Science, AbbVie, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, iQone Healthcare, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm and Sinoxa, L. M. Bambara: None declared, E. Rosato: None declared, Y. Allanore: None declared, M. Matucci-Cerinic: None declared, P. Airó: None declared, U. Walker: None declared
DOI: 10.1136/annrheumdis-2017-eular.2729

SAT0367 CAPILLAROSCOPY PATTERNS AMONG SYSTEMIC SCLEROSIS PATIENTS WITH GASTROINTESTINAL INVOLVEMENT AND MALNUTRITION EVALUATED BY SELF-REPORTED QUESTIONNAIRES

Y. Yalçınkaya, Z. Ertürk, A.U. ÜNal, S. Kaymaz, P. Atagündüz, H. Direskeneli, N. Inanç. *Department of Internal Medicine, Division of Rheumatology, Marmara University, School of Medicine, Istanbul, Turkey*

Background: Gastrointestinal system (GI) is commonly involved in systemic sclerosis (SSc) beginning after early stages of disease.
Objectives: We aimed to investigate capillaroscopic findings among the SSc patients with GI involvement and malnutrition.
Methods: GI involvement was evaluated by UCLA SCTC GIT 2.0 questionnaire (Khanna D.) (7 multi-item; reflux, distension, soilage, diarrhea, social functioning, emotional wellbeing and constipation) in SSc patients ACR/EULAR classification criteria (2013). To report the nutrition status of the patients “malnutrition universal screening tool (MUST)” (sum of the scores of body mass index, weight loss in last 3–6 months and acute disease effect) scores were calculated. Simultaneously, nail fold video-capillaroscopy (NVC) was performed in all paatients to deterimine ealy, active late scleroderma patterns (Cutalo et al.).
Results: In 58 SSc patients (51 female); the mean age, duration of Raynaud’s, non-Raynaud symptom (year) and follow-up (month) were 46±13, 54±50, 10±9 and 7±7, respectively. Limited cutaneous form, positive ANA and anti-Scl70, telangiectases, dysphagia, digital ulcers, lung disease were found in 40 (71%), 48 (83%) and 21 (36%), 45 (78%), 39 (67%), 33 (57%), 23 (40%) in patients, respectively. Of the NVC patterns, early was found in 16 (28%), active was in 11 (19%), late was in 28 (48%) and normal in 3 (5%). The scores of disease activity, severity and GI were shown to be higher in patients with late NVC pattern (table-1). Of the patients with MUST score of >0 (n=10), 9 had late and 1 had early NVC pattern.

Table 1. The scores of disease activity and severity and UCLA SCTC GIT 2.0 in SSc patients

	NVC (early)	NVC (active)	NVC (late)	p
Modified Rodnan skin score	4,3±5,1	8,3±6,9	*12,3±7,5*	P=0,001*
Telangiectasia score (Shah)	2,3±2,4	4,6±1,9	*6±3,5*	P<0,001*
Disease activty score (Valentini)	0,9±0,9	1,1±1,2	*1,9±1,2*	P=0,014*
Disease severity score (Medsger)	3,4±2	4,6±3	*6,5±2,6*	P=0,001*
UCLA SCTC GIT 2.0	0,063±0,111	0,259±0,288	*0,353±0,327*	P=0,002*
Reflux	0,263±0,415	0,500±0,509	*0,874±0,667*	P=0,002*
Distension	0,118±0,357	0,296±0,498	0,564±0,881	NS
Soilage	0±0	0±0	0,107±0,315	NS
Diarrhea	0±0	0,500±0,741	0,268±0,552	NS
Social functioning	0±0	0,105±0,237	0,184±0,406	NS
Emotional wellbeing	0,011±0,050	0,211±0,372	0,118±0,308	NS
Constipation	0,184±0,380	0,159±0,322	0,259±0,469	NS

*Bonferroni, NS = not significant.

Conclusions: This SSc cohort predominantly had limited cutanous disease and vascular manifestations. In patients with late scleroderma pattern, severity of GI was higher similar to disease activity and severity. Undernutrition was frequently seen in patients with late pattern. NVC might be useful to predict the severity of GI and malnutrition and allow to direct the patients to required procedures earlier.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5394

SAT0368 THE PREVALENCE OF OSTEOMYELITIS IN INFECTED DIGITAL ULCERS IN SYSTEMIC SCLEROSIS PATIENTS

Y. Braun-Moscovici [1], Z. Keidar [2], M. Braun [3], D. Markovits [1], K. Toledano [1], Y. Tavor [1], F. Sabbah [1], A. Rozin [1], K. Dolnikov [1], A. Balbir-Gurman [1]. *[1] Rheumatology Department, Rambam Health Care Campus, Rappaport Faculty of Medicine, Technion; [2] Department of Nuclear Medicine, Rambam Health Care Campus Rappaport Faculty of Medicine Technion, Haifa; [3] Liver Institute, Beilinson Hospital Petach-Tikva, Sackler School of Medicine, Tel Aviv University, Petach-Tikva, Israel*

Background: Skin ulcers, particularly digital ulcers occur in at least 50% of systemic sclerosis (SSc) patients (pts) and cause significant morbidity. They are often complicated by local infection which can lead to contiguous osteomyelitis.
Objectives: Our aims were to evaluate the accuracy of clinical diagnosis of osteomyelitis and to assess whether there are clinical parameters that may improve the precision of the clinical diagnosis.
Methods: We retrospectively analyzed the clinical data of consecutive SSc patients hospitalized for skin ulcers in a tertiary referral center for SSc. Our cohort is part of the EUSTAR cohort. The patients were evaluated by rheumathologists skilled in managing SSc skin lesions. All the patients with infected ulcers and suspected for contiguous involvement of underlying bone had bone scans. All the positive scans were followed with 99m-Technetium-Tc-labeled white blood cells (WBC) scintigraphy, in order to differentiate true osteomyelitis from acro-osteolysis or soft tissue infection. We collected demographic data, disease type, extent and severity, routine lab data (CBC, C-reactive protein -CRP, erythrocyte sedimentation rate (ESR), alkaline phosphatase (ALKP), albumin) and wound culture. Each hospitalization was considered a separate event. Statistical analysis: descriptive, student’s T test, Mann-Whitney test.
Results: During the years 2003–2016, 220 SSc pts with skin/digital ulcers were hospitalized in our department for ilomedin treatment (993 hospitalizations). Most of the pts were hospitalized several times due to recurrent ulcers. Tc bone scan was performed in 39 pts (59 admissions) with infected ulcers (32 females, mean (SD) age 48 (15), disease duration 9 (6.6) years, 25 with diffuse SSc, skin score (MRSS) 9.9 (8)). Osteomyelitis was confirmed in 18 pts on 23 occasions. Osteomyelitis occurred twice in 5 pts in different locations. No statistically significant differences were found between the group with positive scans and the group with negative scans regarding demographic, clinical and lab data. 9 pts had 25 admissions for infected ulcers, osteomyelitis was confirmed in 14 of the admissions. No statistically significant differences were found for CBC ESR CRP ALKP between the osteomyelitis events and superficial infected ulcer admissions in these pts. The causative infectious agents were similar between the 2 groups. Positive bone and WBC scans confirmed osteomyelitis in 39% of clinical suspected cases. WBC scans confirmed osteomyelitis in 75% or the patients with positive Tc bone scans.
Conclusions: The prevalence of osteomyelitis among our SSc pts admitted for digital ulcers was 10%. The prevalence of confirmed osteomyelitis by scintigraphy in clinically highly suspected cases was 39%. Even when contiguous osteomyelitis was suspected by highly skilled rheumathologists, bone scan ruled out the diagnosis in 61% of the cases, thus avoiding unnecessary prolonged antibiotic therapy. No clinical predictors to rule osteomyelitis in or out could be identified.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6474

SAT0369 HETEROGENEITY IN THE UNDERLINING PATHOGENESIS IN PATIENTS WITH CONNECTIVE TISSUE DISEASE-ASSOCIATED BORDERLINE MEAN PULMONARY ARTERIAL PRESSURE AND ITS DISTINCTIVE HEMODYNAMIC CHARACTERISTICS FROM THOSE WITH NORMAL PULMONARY ARTERIAL PRESSURE

Y. Yamasaki [1], Y. Asari [1], K. Tsuchida [1], K. Suzuki [2], Y.J. Akashi [2], T. Okazaki [2], S. Ozaki [1], H. Yamada [3]. *[1] Rheumatology and Allergology; [2] Cardiology, St. Marianna University School of Medicine, Kawasaki; [3] Medical Center for Rheumatic diseases, Seirei Yokohama Hospital, Yokohama, Japan*

Background: Borderline mean pulmonary artery pressure (PAP) (21–24 mmHg) may comprise a transition phase from normal pulmonary hemodynamic condition to pulmonary arterial hypertension (PAH), which is one of the fatal complications in connective tissue diseases (CTD) [1]. The accumulated evidence is not enough to conclude that treatment for PAH in this stage may be associated with improving clinical outcomes. On the other hand, CTD-associated PH is caused by various cardiopulmonary comorbidities. It is possible that borderline mean PAP, like overt PH, is caused not only by pulmonary vasculopathy but also by cardiac and pulmonary complications [2].
Objectives: To clarify whether patients with borderline mean PAP associated with CTD have distinctive hemodynamic characteristics from those with normal mean PAP and its underlining pathogenesis is heterogeneous as those with manifest PH.
Methods: We retrospectively investigated 76 CTD patients who underwent right heart catheterization from 2008 through 2016. Of the 76 patients, 25 (33%) and 16 (21%) had manifest PH and borderline mean PAP, respectively. The rest of the 35 patients had normal mean PAP. Systemic sclerosis was the most common

CTD among the enrolled patients (61%), followed by MCTD (16%). Hemodynamic characteristics and findings after exercise echocardiography in patients having normal mean PAP, borderline mean PAP, and PH were compared. We also determined the validity of therapeutic intervention.

Results: The values of tricuspid regurgitation pressure gradient (TRPG) were comparable between patients with borderline (31.1±7.8 mmHg) and normal mean PAP (28.3±6.9 mmHg) (P=0.1572) but its value became significantly higher in patients with borderline mean PAP (39.1±8.0 mmHg) than in those with normal mean PAP (32.8±7.4 mmHg) after exercise echocardiography (P=0.0391). Pulmonary arterial wedge pressure was significantly elevated in patients with borderline mean PAP (12±3 mmHg) compared with that in normal mean PAP (7±3 mmHg) ($P<0.0001$) and its value was comparable to those with overt PH, suggesting the heterogeneity on the cause of borderline mean PAP among CTD patients. The clinical course of 10 patients with borderline mean PAP was studied. Five were treated for precapillary disease, 3 for postcapillary disease, and 2 for interstitial lung disease (ILD). Normalization of mean PAP was seen in 3/4 and 3/3 of the patients treated for precapillary and postcapillary disease, respectively. Deterioration of TRPG was seen in one patient after receiving pulmonary vasodilators. One with severe ILD developed PH.

Conclusions: The pathogenesis of borderline mean PAP, clearly distinctive from normal mean PAP, was heterogeneous as that of manifest PH in CTD patients. Though the clinical course may be altered with appropriate therapeutic intervention, repeated assessment is needed.

References:

[1] Kovacs G, Olschewski H. Borderline pulmonary pressures in scleraderma - "a pre-pulmonary arterial hypertension" condition? Arthritis Res Ther 2015; 17: 123, 015–0649–7.

[2] Kovacs G, Avian A, Tscherner M, et al. Characterization of patients with borderine pulmonary arterial pressure. Chest 2014; 146: 1486–93.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3592

SAT0370 EVALUATIONS OF EXERTION DYSPNEA IN PATIENTS WITH CONNECTIVE TISSUE DISEASE (CTD) BY CPET (CARDIOPULMONARY EXERCISE TESTING) FOR EARLY DETECTING ASSOCIATED PULMONARY HYPERTENSION (APAH)

Y. Nobuhara, Y. Kamei, Y. Fujikawa, T. Nakazawa. *Rheumatology, Osaka saiseikai nakatsu hospital, Osaka, Japan*

Background: Patients with CTD often complain of exertion dyspnea, due to lung diseases, heart diseases, musculoskeletal disorders and/or APAH. Although imaging and physiological tests could reveal pathophysiology, some of them remain unknown. Especially APAH is rarely diagnosed in WHO functional class I or II, because pulmonary vasculopathy (PV) cannot be detected until two-thirds of pulmonary blood vessels deteriorated, [1] with cardiac ultrasonography (UCG) or right heart catheterization (RHC) at rest. Pathophysiological considerations suggest that the haemodynamic/metabolic impairment in APAH may be observed during exercise before the disease becomes evident at rest.[2–3] We evaluated exertion dyspnea of unknown to find out early APAH with CPET.

Objectives: We performed CPET in patients who complained of exertion dyspnea and tried to detect early PV.

Methods: From June 13th in 2015 to October 28th in 2016, we performed CPET and evaluate their clinical state in 28 patients, 17–80 years 2 males/26 females, 5 mixed connective tissue disease (MCTD), 15 SSc, 3 SLE, 2 Sjögren's syndrome, 3 dermatomyositis. They underwent UCG, pulmonary function testing (PFT), 6-minutes walk test, and nailfold capillaroscopy by Cutolo's method.[4]

Results: Twenty cases presented decreased peak VO2. VE/VCO_2 ratio, which represent increased ventilation-perfusion mismatch, elevated in 12 cases. 8 cases, with decreased peak VO2 but normal VE/VCO_2, were regarded that muscle weakness mainly induced exertion dyspnea, and advised exercise. Twelve cases with decreased peak VO2 and elevated VE/VCO_2 were estimated to have APAH or/and interstitial lung disease (ILD). Seven of them underwent RHC and 1 case diagnosed as definite APAH, and another 1 case as post capillary PH.

A 34 years MCTD woman without ILD showed an active capillaroscopic pattern, her peak VO2 decreased (13.9ml/kg/min.) and nadir VE/VCO_2 elevated (39). Although her mean PAP was normal, we suspected she had early PV and administered PDE5 inhibitor to her and her dyspnea had gone soon and CPET parameters improved.

CPET was also useful for early detections of therapeutic gains in APAH. A SSc woman, diagnosed as APAH by RHC, was performed CPET only 9 days after administration of PDE5 inhibitor. Her peak VO2 elavated (13.3 to 15.4 ml/kg/min.) and nadir VE/VCO_2 decreased (43.4 to 38.9) promptly.

Thirteen patients showed an early capillaroscopic pattern, 7 an active pattern and 3 a late pattern. Median values of minimum VE/VCO_2 ratio significantly differed ($p<0.05$) in the three capillaroscopic groups, being progressively worse from early to late capillaroscopic pattern.

Conclusions: We performed CPET in every patient safely. Although more research is required, CPET may provide valuable information notably in APAH patients.

References:

[1] Hachulla E, et al. French PAH-SSc Network. PAH with SSc in patients with functional class? dyspnea; mild symptoms but severe outcome. Rheumatology 2010;49:940–4.

[2] Grunig E, et al. Non-invasive diagnosis of pulmonary hypertension: ESC/ERS Guidelines with Updated Commentary of the Cologne Consensus Conference 2011. Int J Cardiol 2011;154:53.

[3] Domitrescu C, et al. Developing PV in SSc, detected with non-invasive CPET. PLoS ONE 2010;5e14293.

[4] Cutolo M, et al. Nailfold videocapillaroscopy assessment of microvascular damage in SSc. J Rheumatol. 2000 Jan;27(1):155–60.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4184

SAT0371 BONE FRACTURE RISK ASSESSMENT IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: RESEMBLANCES TO RHEUMATOID ARTHRITIS

Z. Griger, A. Vincze, K. Szabó, J. Gaál, K. Dankó. *Division of Clinical Immunology, Department of Internal Medicine, University of Debrecen, Debrecen, Hungary*

Background: Idiopathic inflammatory myopathies are chronic, heterogeneous systemic autoimmune diseases with symmetrical proximal muscle weakness. During the disease course, osteoporosis and bone fractures are more common compared to the healthy population, which can be explained by the chronic inflammation, immobilization, spontaneous falls and steroid treatment, and affect crucially the patients' quality of life. Recently, a WHO fracture risk calculation tool, FRAX score is available, to measure the 10-year probability of osteoporotic fractures. It takes into account relevant clinical risk factors, such as rheumatoid arthritis, however myositis does not exist among the risk factors.

Objectives: Estimation the effect of myositis and myositis related bone mineral densities on bone fracture risk calculated by FRAX tool.

Methods: FRAX score was determined in 71 patients with idiopathic inflammatory myopathies and results were compared with the data from 50 age, sex and BMI matched patients with rheumatoid arthritis. Moreover, osteoporosis related biomarkers, disease related fractures and bone mineral densities were determined using DXA examinations. Statistical analysis was performed with IBM SPSS 20.0 software.

Results: There were no significant differences between the demographical data, biomarkers (Ca, Vitamin D, parathormone level) of the two groups. Disease duration and cumulative steroid dose were higher in the myositis group. Results of the FRAX score without BMD were significantly lower in the patients with myositis, in both fracture risk: major osteoporotic (8,61±6,36%, vs. 15,59±12,66%; p: 0,002) and femur neck (2,66±3,24%, vs. 6,34±9,018; p: 0.003). T score results of the DXA examination were not significantly different between the two populations (Lumbar1–4: -0,9±1,43 vs.-0,829±1,38; p:0,829; Femoral neck: -1,4±1,08 vs. -1,02±1,08; p: 0,93), but the presence of osteopenia (60% vs. 39,5%) and osteoporosis (13,5% vs. 7%) were more frequent in the myositis group (p: 0,045). Disease related fracture was associated with disease duration in the myositis group and with antibody (RF, ACPA) presence in the RA group. FRAX score with BMD results showed no significant differences between the two populations (Major osteoporotic: 9,44±6,72 vs. 13,25±9,43; p: 0,053; Hip: 2,77±3,01 vs. 3,57±5,08; p: 0,811).

Conclusions: As far as we know, this is the first study which examine the fracture risk using FRAX score in patients with idiopathic inflammatory myopathies. According to our data, we can conclude that existence of myositis might indicate similar, independent risk factor in fracture probability, like rheumatoid arthritis. Evaluation of fracture risk should be done with DXA result in patients with IIM, otherwise risk could be underestimated. An exact value of the "myositis related risk" could be determined by a 10-year prospective study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3784

SAT0372 CLINICAL AND SEROLOGICAL ASSOCIATIONS OF AUTOANTIBODIES TO BICD2 AS A NOVEL MARKER FOR SYSTEMIC SCLEROSIS

M. Mahler[1], C. Bentow[1], J. Milo[1], M. Hudson[2], H.-D. Zucht[3], P. Budde[3], D. Wirtz[3], J. Schulte-Pelkum[3], M. Choi[4], M. Fritzler[4]. *[1]Research and Development, Inova Diagnostics, San Diego, CA., United States; [2]Department of Medicine, McGill University, Quebec, Canada; [3]Protagen, Dortmund, Germany; [4]Cumming School of Medicine, University of Calgary, Calgary, Canada*

Background: Anti-nuclear antibodies (ANA), which are present in approximately 90% of systemic sclerosis (SSc) patient's sera, play an important role in establishing the diagnosis and predicting prognosis of SSc. Recently, a novel autoantibody has been described in SSc patients targeting Cytoskeleton-Like Bicaudal D Protein Homolog 2 (BICD2).

Objectives: The aim of this study was to assess the prevalence and titers of anti-BICD2 antibodies in SSc and controls and to study the clinical associations of this new antibody.

Methods: A total of 502 samples from SSc patients enrolled in the Canadian Scleroderma Research Group (CSRG) cohort were included in this study. Clinical associations were assessed either as anti-BICD2 antibody positivity

with and without other autoantibodies present using 451 SSc patients with complete dataset. Autoantibodies to several scleroderma-related autoantibodies were detected using commercial or research use only kits (Inova Diagnostics, San Diego, USA). P-values below 0.05 were considered significant.

Results: The sensitivity and specificity of anti-BICD2 antibodies were determined as 22.1% and 99.0%, respectively. Receiver operating characteristic (ROC) analysis showed an area under the curve of 0.79 (95% CI 0.75–0.84). The likelihood (LR) and odds ratios (OR) were 17.7 (LR+), 0.8 (LR-) and 20.4 (OR). The prevalence of these autoantibodies was equally distributed between limited and diffuse form of SSc (22.8% and 24.0%). When SSc patients without the classification criteria markers anti-Scl-70, anti-Centromere and anti-RNA Pol III (n=184) were compared with controls, similar performance was obtained as seen in the entire cohort. Results are summarized in table 1 below.

Table 1

Performance Characteristic	Entire SSc cohort (n=502)	Anti-Scl-70, anti-Centromere and anti-RNA Pol III negative (n=184)
Sensitivity	22.1%	13.6%
Specificity	99.0%	99.0%
AUC	0.79 (95% CI 0.75–0.84)	0.78 (95% CI 0.72–0.84)
LR+	28.1	15.6
LR-	0.21	0.13
OR	133.1	123.7

Several statistically relevant clinical associations were found for anti-BICD2 as summarized in table 2 below.

Conclusions: Our data confirm the presence of anti-BICD2 antibodies in SSc patients that may help to differentiate SSc from other systemic autoimmune rheumatic diseases and to stratify SSc patients into more defined subforms of the disease.

Disclosure of Interest: M. Mahler Employee of: Inova Diagnostics, C. Bentow Employee of: Inova Diagnostics, J. Milo Employee of: Inova Diagnostics, M. Hudson: None declared, H.-D. Zucht Employee of: Protagen, P. Budde Employee of: Protagen, D. Wirtz Employee of: Protagen, J. Schulte-Pelkum Employee of: Protagen, M. Choi: None declared, M. Fritzler: None declared

DOI: 10.1136/annrheumdis-2017-eular.2751

SAT0373 EVALUATION OF AMERICAN COLLEGE OF RHEUMATOLOGY PROVISIONAL COMPOSITE RESPONSE (CRISS) INDEX IN THE FASSCINATE TRIAL

D. Khanna[1], V. Berrocal[1], C. Denton[2], A. Jaheris[3], H. Spotwood[4], C. Lin[3], J. Siegel[3], D. Furst[5]. *[1]Univ Michigan, Ann Arbor, United States; [2]UCL, London, United Kingdom; [3]Genentech, San Francisco, United States; [4]Roche, Welwyn Garden, United Kingdom; [5]UCLA, Los Angeles, United States*

Background: Treatment with tocilizumab (TCZ) in early systemic sclerosis (SSc; FaSScinate trial) resulted in consistent, but not statistically significant, improvements in skin sclerosis (mRSS) at wks 24 and 48[1]. The CRISS index has been proposed as a composite index for trials in SSc[2]. CRISS is a 2-step process that assigns a probability of improvement for each subject ranging from 0.0 [no improvement] to 1.0 [marked improvement]. Step 1 assesses clinically meaningful decline in cardio-pulmonary-renal involvement and assigns a probability of 0.0. For remaining subjects, 5 variables are used to calculate probability of improvement. These are: FVC%, mRSS, patient (PT GA) and physician globals (MD GA), and HAQ-DI.

Objectives: To assess the performance of CRISS index in the FaSScinate trial.

Methods: In FaSScinate, pts ≥18 y with active SSc were randomized 1:1 to TCZ or placebo (PLA) for 48 wks. Step 1 CRISS was captured using review of serious adverse event data. Non-parametric Wilcoxon test was used to assess significant differences between the CRISS scores in both arms. Analyses were carried out for subject who had complete data at baseline and 24 weeks and at baseline and 48 weeks.

Results: 87 pts (43 TCZ, 44 PBO) were enrolled. Baseline characteristics were similar between arms. 4 subjects in the PBO group and none in TCZ met the pre-defined definition of worsening in Step 1 and were given a score of 0.0. For remaining subjects, we calculated probability score for each subject. Using CRISS as a continuous measure, the median score was statistically significant and favored TCZ compared to PBO at wks 24 and 48 (p=0.04 and 0.01; Table). Table also presents the individual components of Step 2 where only FVC% was statistically significant favoring TCZ at wk 48.

Table 1. Comparison of TCZ and PBO using CRISS index and individual variables at 24 and 48 weeks

	TCZ	PBO**	P value
CRISS, median [IQR] at 24 week	0.23 [0.003; 0.95], N=33	0.008 [0.00; 0.10], N=36	0.04*
CRISS, median [IQR] at 48 week	0.31 [0.008; 0.99], N=27	0.001 [0.00; 0.18], N=35	0.01*
MRSS, mean change at 24 week	-4.2, N=33	-2.1, N=34	0.24
MRSS, mean change at 48 week	-5.9, N=27	-3.2, N=31	0.35
FVC% predicted, mean change at 24 week	-0.78, N=33	-4.4, N=34	0.08
FVC% predicted, mean change at 48 week	-1.6, N=27	-5.1, N=31	0.02
PT GA, mean change at 24 week	-0.41, N=33	-0.10, N=34	0.64
PT GA, mean change at 48 week	-0.69, N=27	-0.45, N=31	0.72
MD GA, mean change at 24 week	-0.94, N=33	-0.80, N=34	0.76
MDGA, mean change at 48 week	-1.81, N=27	-0.73, N=31	0.07
HAQ-DI, mean change at 24 week	0.09, N=33	0.06, N=34	0.76
HAQ-DI, mean change at 48 week	0.00, N=27	0.16, N=31	0.10

*Using Wilcoxon test as CRISS data is not normally distributed. **There are 4 subjects in the PBO who met step 1 and were given a score of 0.0.

Conclusions: In this post-hoc analysis, CRISS index was able to discriminate TCZ from PBO, supporting its validity in an independent cohort.

References:

[1] Khanna D. Lancet. 2016.
[2] Khanna D. Arthritis Rheum. 2016.

Disclosure of Interest: D. Khanna Grant/research support from: NIH/NIAMS and NIH/NIAID, BMS, Pfizer, Consultant for: Actelion, Bayer, BMS, Boehringer Ingelheim, Genentech/Roche, Sanofi-aventis, GSK, Corbus, Cytori, EMD Serono, V. Berrocal: None declared, C. Denton Consultant for: Actelion, Bayer, GSK, CSL Behring, Merck-Serono, Genentech-Roche, Inventiva, Sanofi-Aventis, Boehringer Ingelheim, A. Jaheris Shareholder of: Roche stock and options, Employee of: Genentech, H. Spotwood Employee of: Roche, C. Lin Employee of: Genentech, J. Siegel Employee of: Genentech, D. Furst Grant/research support from: Amgen, BMS, NIH, Novartis, Pfizer, Roche/Genentech, Consultant for: AbbVie, Amgen, BMS, Cytori, Novartis, Pfizer, Roche/Genentech, UCB

DOI: 10.1136/annrheumdis-2017-eular.3754

SAT0374 THE EUROMYOSITIS REGISTRY: AN INTERNATIONAL DESCRIPTION OF MYOSITIS

J.B. Lilleker[1], J. Vencovsky[2], G. Wang[3], L.R. Wedderburn[4], L.P. Diederichsen[5], J. Schmidt[6], P. Jordan[7], O. Benveniste[8], M.G. Danieli[9], K. Dankó[10], N.T.P. Thuy[11], M. Vazquez-Del Mercado[12], Ø. Molberg[13], B. De Paepe[14], J. De Bleecker[15], B. Maurer[16], N. Pipitone[17], N. McHugh[18,19], Z. Betteridge[18,19], P. New[20], R.G. Cooper[20], W.E. Ollier[1], J.A. Lamb[1], N.S. Krogh[21], I.E. Lundberg[22], H. Chinoy[23] on behalf of UKMYONET and all contributors to the EuroMyositis Registry. *[1]Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, United Kingdom; [2]Institute of Rheumatology, Charles University, Prague, Czech Republic; [3]Rheumatology, China-Japan Friendship Hospital, Beijing, China; [4]UCL GOS Institute of Child Health, London, United Kingdom; [5]Rheumatology, Odense University Hospital, Odense, Denmark; [6]Neurology, University Medical Center, Göttingen, Germany; [7]Myositis UK, Southampton, United Kingdom; [8]Médecine Interne et Immunologie Clinique, Hôpital Pitié-Salpêtrière, Paris, France; [9]Scienze Cliniche e Molecolari, Università Politecnica delle Marche & Ospedali Riuniti, Ancona, Italy; [10]Immunology, University of Debrecen, Debrecen, Hungary; [11]Rheumatology, Bach Mai Hospital, Hanoi, Viet Nam; [12]Medicina Interna, Hospital Civil Dr. Juan I. Menchaca, Guadalajara, Mexico; [13]Rheumatology, Oslo University Hospital, Oslo, Norway; [14]Neurology; [15]Ghent University Hospital, Ghent, Belgium; [16]Rheumatology, University Hospital Zurich, Zurich, Switzerland; [17]Rheumatology, Arcispedale S. Maria Nuova, Reggio Emilia, Italy; [18]Royal National Hospital for Rheumatic Diseases; [19]Pharmacy and Pharmacology, University of Bath, Bath; [20]Rheumatology, Salford Royal NHS Foundation Trust, Salford, United Kingdom; [21]ZiteLab ApS, Frederiksberg, Denmark; [22]Karolinska University Hospital, Karolinska Institutet, Stockholm, Sweden; [23]NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom*

Background: The idiopathic inflammatory myopathies (IIM) represent a rare and heterogeneous group of multisystem autoimmune diseases. The rarity of IIM has

Abstract SAT0372 – Table 2

Clinical Association	Whole group (N=451)		BICD2 alone (N=29)	Overlapping BICD2 (N=107)	Negative BICD2 (N=315)	BICD2 alone vs Negative	Overlapping vs Negative
	Mean (sd) or N (%)	NA	Mean (sd) or N (%)	Mean (sd) or N (%)	Mean (sd) or N (%)	P Values	P Values
Disease duration since the onset of RP, years	15.4 (12.9%)	18	15.6 (13.7%)	17.5 (12.6%)	14.6 (12.9%)	0.728	0.013
Diffuse cutaneous disease	138.0 (30.7%)	1	9.0 (31.0%)	23.0 (21.5%)	106.0 (33.8%)	0.766	0.018
Calcinosis	104.0 (23.2%)	2	8.0 (27.6%)	33.0 (31.1%)	63.0 (20.1%)	0.339	0.019
Inflammatory myositis	43.0 (9.6%)	4	7.0 (24.1%)	4.0 (3.8%)	32.0 (10.3%)	0.003	0.040
GERD/reflux	285.0 (69.7%)	42	16.0 (59.3%)	79.0 (81.4%)	190.0 (66.7%)	0.437	0.006
Antibiotics for bacterial growth	47.0 (10.5%)	5	0.0 (0.0%)	8.0 (7.6%)	39.0 (12.5%)	0.043	0.160
Interstitial lung disease	123.0 (27.8%)	9	13.0 (46.4%)	17.0 (16.5%)	93.0 (29.9%)	0.071	0.008
FVC% predicted	93.5 (19.5%)	61	96.0 (20.8%)	98.3 (19.7%)	91.7 (19.1%)	0.304	0.004

hampered research efforts, resulting in remarkably limited therapeutic evidence. The EuroMyositis Registry was created to pool resources and expertise across the international IIM research community.

Objectives: To describe the phenotypic characteristics of different IIM subtypes. Associations with malignancy, interstitial lung disease (ILD), cardiac involvement and dysphagia were assessed.

Methods: Pooled data from the EuroMyositis Registry (from Belgium, China, Czech Republic, Hungary, Italy, Mexico, Norway, Sweden, Switzerland, UK, Vietnam) were obtained. Associations were assessed using logistic regression and multinomial logistic regression with polymyositis (PM) as the reference group.

Results: Data regarding 3,196 patients were analysed. The UK was the largest contributor (n=1,307). The most common diagnoses were dermatomyositis (34%), PM (32%) and connective tissue disease (CTD)-overlap myositis (15%). In those with anti-synthetase syndrome (7%), 85% had muscle weakness, 86% ILD and 58% arthritis. Overall, 43% had a myositis specific antibody, most commonly anti-Jo1 autoantibodies (20%). Glucocorticoid usage was noted in 98%. Most commonly used disease modifying agents were methotrexate (71%) and azathioprine (50%).

Malignancy occurred in 9% and was associated with a diagnosis of dermatomyositis (Relative Risk Ratio [RRR] 1.68, 95% CI 1.09–2.56, p=0.018). Cardiac involvement occurred in 9%, most commonly in those with CTD-overlap myositis (13%), and was associated with a higher Health Assessment Questionnaire disability index (1 versus 0.75, OR 1.40, 95% CI 1.03–1.91, p=0.031). Dysphagia occurred in 39% and was associated with a diagnosis of CTD-overlap myositis (RRR 2.25, 95% CI 1.61–3.15, p<0.001).

Conclusions: This large international cohort demonstrates the heterogeneity of IIM and the burden of associated malignancy, ILD, cardiac and gastrointestinal involvement. The EuroMyositis Registry facilitates international collaborative research outputs, underlining the benefits of harmonised data collection methodology between centres.

Acknowledgements: This work was supported by researchers at the National Institute for Health Research (NIHR) Biomedical Research Unit. The views expressed are those of the authors and not necessarily those of the UK National Health Service, the NIHR or the UK Department of Health

Disclosure of Interest: J. Lilleker: None declared, J. Vencovsky: None declared, G. Wang: None declared, L. Wedderburn Grant/research support from: The UK JDM Cohort and Biomarker study is supported by grants from the NIHR and Myositis UK, L. Diederichsen: None declared, J. Schmidt: None declared, P. Jordan: None declared, O. Benveniste: None declared, M. G. Danieli: None declared, K. Dankó: None declared, N. T. P. Thuy: None declared, M. Vazquez-Del Mercado: None declared, Ø. Molberg: None declared, B. De Paepe: None declared, J. De Bleecker: None declared, B. Maurer Grant/research support from: AbbVie, Protagen, EMDO, Novartis, Roche, Actelion, N. Pipitone Speakers bureau: GRAPPA Workshop, Alfa-Wassermann, N. McHugh: None declared, Z. Betteridge: None declared, P. New: None declared, R. Cooper: None declared, W. Ollier: None declared, J. Lamb Grant/research support from: MedImmune, N. S. Krogh: None declared, I. Lundberg Grant/research support from: Astra-Zeneca, Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Idera, H. Chinoy Grant/research support from: MedImmune, Novartis

DOI: 10.1136/annrheumdis-2017-eular.2742

SAT0375 METABOLOMICS OF SERA REVEALS POTENTIAL BIOMARKERS OF SKIN FIBROSIS IN SYSTEMIC SCLEROSIS THAT CORRELATE WITH PRO-FIBROTIC GENE EXPRESSION IN SKIN BIOPSIES

S. Ahmed[1], M.K. Rai[1], D. Dubey[2], A. Rawat[2], D.P. Misra[1], D. Kumar[2], V. Agarwal[1]. *[1]Clinical Immunology, Sanjay Gandhi Post Graduate Institute of Medical Sciences; [2]Centre for BioMedical Research, Lucknow, India*

Background: There is an unmet need for biomarkers in Systemic Sclerosis (SSc). Despite its shortcomings, the modified Rodnan skin score (mRSS) has remained the standard disease assessment tool for SSc. Expression of certain genes, cartilage oligomeric matrix protein (*COMP*), thrombospondin-1 (*THS1*), interferon-induced 44 (*IFI44*) and sialoadhesin (*SIG1*), and, more recently, Tenascin-C (*TNSC*), have been shown to correlate with skin fibrosis. However, assessment of the expression of these genes requires a skin biopsy. Hence, we used an open-ended approach to identify a serum-based biomarker of SSc.

Objectives: To identify small molecules in serum that correlate with mRSS and profibrotic genes that are upregulated in skin of SSc patients

Methods: We obtained serum and skin biopsies from 25 consenting adult patients with SSc and serum from 25 age- and sex-similar controls. mRNA levels of five genes: *COMP*, *THS1*, *IFI44*, *SIG1*, and *TNSC* were estimated as fold-change relative to Glyceraldehyde 3-phosphate dehydrogenase (*GAPDH*), a housekeeping gene. H^1NMR (Nuclear Magnetic Resonance) based metabolomics studies were performed on the sera using standard protocols. Principal component analysis (PCoA) and Partial Least Squares Discriminant Analysis (PLSDA) were used to delineate metabolites that were different between patients and healthy controls. Then spearman correlations (ρ) of these metabolites with mRSS and the fold-expression of the five pro-fibrotic genes were estimated.

Results: H^1NMR based metabolomics identified 126 peaks that were different between patients and controls. Out of these, the levels of glycine had the best correlation with pro-fibrotic gene expression (ρ=0.5, p<0.05 for *IFI44*; ρ=0.44, p<0.05 for *TNSC*). Choline inversely correlated with *SIG1* (ρ=-0.41; p=0.05) while Glycerophosphocholine correlated with mRSS (ρ=0.50, p<0.05).

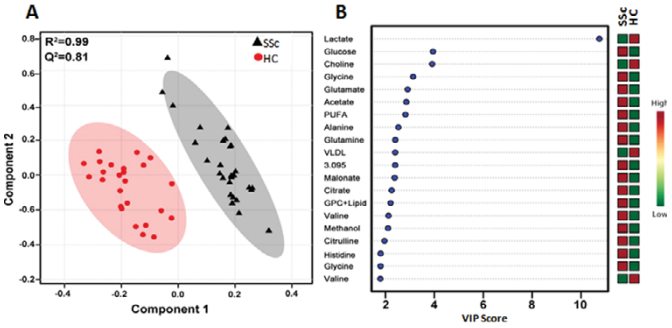


Figure 1: H^1-NMR Metabolomics data (A) PCoA plot showing metabolomics can clearly distinguish between patients of systemic sclerosis and healthy controls (B) Plot showing 20 representative metabolites that were significantly different between patients and controls; SSc: Systemic Sclerosis, HC: Healthy Controls, PUFA: Poly Unsaturated Fatty Acids; VLDL: Very Low Density Lipoproteins, GPC: Glycerophosphocholine, VIP: Variable Importance in Projection Score

Conclusions: H^1NMR based metabolomics identified glycine, choline and their metabolites as potential biomarkers for skin fibrosis in SSc. These findings require validation in a larger cohort.

References:

[1] Farina G, Lafyatis D, Lemaire R, Lafyatis R. A four-gene biomarker predicts skin disease in patients with diffuse cutaneous systemic sclerosis. Arthritis Rheum. 2010 Feb;62(2):580–8.

[2] Bhattacharyya S, Wang W, Morales-Nebreda L, Feng G, Wu M, Zhou X, Lafyatis R, Lee J, Hinchcliff M, Feghali-Bostwick C, Lakota K, Budinger GR, Raparia K, Tamaki Z, Varga J.Tenascin-C drives persistence of organ fibrosis. Nat Commun. 2016 Jun 3;7:11703.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3715

SAT0376 ANTI-NT5C1A AUTOANTIBODIES ARE FREQUENT IN JUVENILE MYOSITIS AND ASSOCIATED WITH INCREASED ILLNESS SEVERITY

R. Yeker[1], I. Pinal-Fernandez[1], T. Kishi[2], I.N. Targoff[3], F.W. Miller[2], L.G. Rider[2], A. Mammen[1]. *[1]Muscle Disease Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)/National Institutes of Health (NIH); [2]Environmental Autoimmunity Group, National Institute of Environmental Health Sciences (NIEHS)/National Institutes of Health (NIH), Bethesda; [3]University of Oklahoma Health Sciences Center, Oklahoma City, United States*

Background: Autoantibodies (Abs) against 5'-Nucleotidase, Cytosolic 1A (NT5C1A) have been portrayed as a potential diagnostic aide in distinguishing inclusion body myositis (IBM) and polymyositis (PM) in adults. However, 4–21% of dermatomyositis (DM) patients also have Abs to NT5C1A.

Objectives: The prevalence and clinical features of anti-NT5C1A Abs in juvenile-onset myositis (IIM) patients is unknown, so we sought to examine this in a large cohort.

Methods: We screened 384 juvenile IIM patients meeting probable or definite Bohan and Peter criteria for anti-NT5C1A Abs by immunoblotting for the full length NT5C1A protein in transfected and non-transfected lysates. Clinical characteristics and HLA typing were compared between juvenile IIM patients who were anti-NT5C1A positive (Ab+) and those who were anti-NT5C1A negative (Ab-).

Results: In this cohort, 29% (103) of juvenile DM, 15% (3) of juvenile PM, and 37% (15) of juvenile overlap myositis patients tested positive for anti-NT5C1A Abs. Compared with anti-NT5C1A Ab- patients, anti-NT5C1A Ab+ juvenile IIM patients showed a similar distribution of race, gender, and association with myositis-specific Abs. However, NT5C1A Ab was associated with anti-p155/140 Abs (p=0.05). The only observed clinical difference was an increased frequency of V- or shawl-sign rashes ever present (44% vs. 26%, p=0.002). Disease severity was increased in anti-NT5C1A Ab+ patients, based on more frequent hospitalizations (p=0.02), more medications used (p<0.001), and more treatment trials per year (p<0.001). Additionally, pulse steroids (p<0.001) and intravenous immunoglobulin therapy (p=0.008) were prescribed more frequently in anti-NT5C1A Ab+ than Ab- patients. The HLA alleles DRB1*07 (20% vs. 9%, p<0.05) and DQA1*0201 (21% vs. 7%, p<0.01) were present more frequently in anti-NT5C1A Ab- compared to Ab+ patients.

Conclusions: Anti-NT5C1A Abs are commonly present in juvenile DM and juvenile overlap myositis patients, and are present more frequently in patients with anti-p155/140 Abs, but are also seen in association with other myositis specific Abs. Consistent with data in adult IIM patients, anti-NT5C1A Abs have few distinguishing clinical features in juvenile myositis, but are associated with increased illness severity marked by increased hospitalizations and receipt of additional therapy.

Disclosure of Interest: R. Yeker: None declared, I. Pinal-Fernandez Grant/research support from: The Myositis Association, T. Kishi Grant/research support

from: The Myositis Association, I. Targoff Consultant for: Oklahoma Medical Research Foundation Clinical Immunology Laboratory regarding myositis autoantibody testing, F. Miller: None declared, L. Rider: None declared, A. Mammen: None declared
DOI: 10.1136/annrheumdis-2017-eular.6246

SAT0377 RELIABILITY OF A NEW AUTOMATED SYSTEM FOR ABSOLUTE CAPILLARY NUMBER COUNTING (AUTOCAPI) ON SYSTEMIC SCLEROSIS NAILFOLD VIDEOCAPILLAROSCOPIC IMAGES

M. Cutolo[1], K. Melsens[2], A.C. Trombetta[1], C. Pizzorni[1], E. Deschepper[3], A. Sulli[1], V. Smith[4]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa, Italy; [2]Department of Internal Medicine, Faculty of Medicine and Health Sciences; [3]Department of Public Health, Biostatistics Unit; [4]Department of Internal Medicine, Faculty of Medicine and Health Sciences; Department of Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium*

Background: Nailfold capillary density is a useful measure in systemic sclerosis (SSc) classification and evaluation. Its manual detection may be time-consuming, hampering its use in largescale investigations. We evaluated a new automated system to assess the absolute nailfold capillary number.
Objectives: To attest the instrumental reliability of automatic counting in SSc patients using nailfold video capillaroscopy (NVC) images.
Methods: 75 NVC random images, from SSc patients, were blindly analyzed by four raters (2 less and 2 more experienced; raters: 1,2,3,4) from two European centers. Each rater was asked to define the region of interest (ROI) on the NVC images and to manually count the number of capillaries, according to the following instructions: upper bound placed on top of the longest capillary head and lower bound placed on half of the length of that longest capillary (figure 1); if the common branch of an abnormal shape (neoangiogenesis) is in ROI it is counted as being one; if the common branch is out of ROI it is counted as separate capillaries; if the capillary is on the edge of the vertical line of ROI, it is only counted when the head of the capillary is half in ROI; if the capillary head is on the edge of lower bound, it is counted as soon as the "head" part is in the ROI; all "heads" in the ROI are counted (not only distal row). The dedicated automated system (AUTOCAPI-ds medica, IT) also counted the number of capillaries in the same ROI (figure 1). Reliability between the manual and automatic counting was investigated per rater through intraclass correlation coefficient (ICC) and reported with 95% confidence interval (CI). External validation was obtained by multi-rating of the same set of images. Average difference between automated and manual counting per rater was calculated.
Results: The ICC (95% CI) of manual versus automatic counting in ROI was 0.77 (0.61–0.86) for rater 1 ($p<0.0001$), 0.81 (0.71–0.88) for rater 2 ($p<0.0001$), 0.65 (0.50–0.76) for rater 3 ($p<0.0001$) and 0.81 (0.71–0.87) for rater 4 ($p<0.0001$). The average difference was -0.69 for rater 1, 0.04 for rater 2, -0.03 for rater 3 and 0.16 for rater 4.

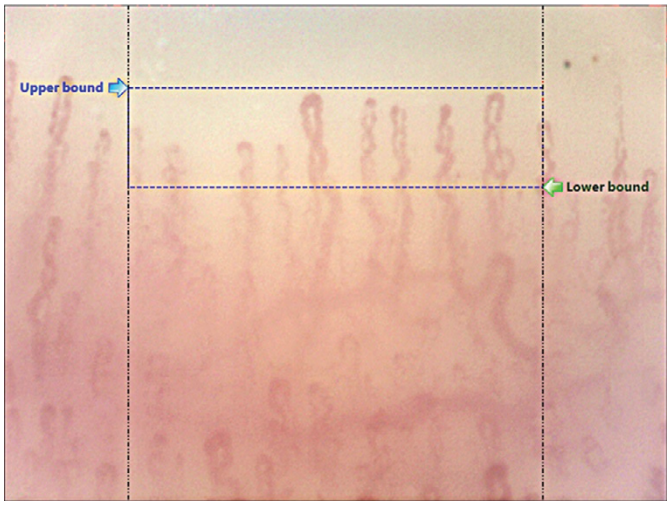


Figure 1. In the picture captured by the operator (normal subject), two vertical bars, with a distance of 1 mm appears automatically in the middle of the picture, together with two horizontal bars (upper bound and lower bound) to be placed manually (see text) in order to define the ROI.

Conclusions: This is a first study to attest the reliability of a new automated system to calculate the absolute number of capillaries in a ROI arising from SSc NVC images. High performance of the new automated counting system was confirmed in pathological conditions (SSc).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3191

SAT0378 BONE MARROW OEDEMA AND SYNOVITIS ON MRI OF THE HAND ARE ASSOCIATE WITH DIGITAL ULCERS, ACTIVE DISEASE AND IMPAIRED FUNCTIONAL CAPACITY IN SYSTEMIC SCLEROSIS

B. Stamenkovic[1,2], S. Stojanovic[1,2], J. Nedovic[2], V. Zivkovic[1,2], S. Milenkovic[2], J. Jovanovic[2], N. Damjanov[3], A. Stankovic[1,2]. *[1]Medical School; [2]Rheumatology, Institute Niska Banja, Nis; [3]Rheumatology, Institute for Rheumatology, Belgrade, Serbia*

Background: Hand inflammatory involvement is a major feature in patients with systemic sclerosis (SSc), responsible for major disability. Magnetic resonance imaging (MRI) can identify and characterize subclinical inflammation and joint damage on hand with much greater precision than clinical, radiographic and ultrasonography assessment in SSc.
Objectives: To determine the association of MR bone marrow oedema, synovitis and probability for the occurrence of listed inflammatory changes with clinical features and laboratory tests in SSc patients
Methods: 112 SSc patients were tested (mean age 54y). Contrast enhanced low field MRI of the wrist and MCP2–5 joints was performed to all the pts. MRI bone marrow oedema and synovitis were assessed and scored by OMERACT RAMRIS scoring system. Age, sex, SSc type, disease duration (date of first non Raynaud symptom), Raynaud phenomenon, articular or periarticular pain, joint swelling and contractures, digital ulceration, HAQ, acroosteolysis (by standard PA radiographs of hand and wrist) pulmonary arterial hypertension (PAP>40mmHg at rest on Doppler echocardiography), pulmonary fibrosis (by CT and pulmonary function tests) and laboratory tests (antibody profile, RF, CRP, Creatine phosphokinase) and disease activity (by Valentini index) were done.
Results: By multiple logistic regression analysis taking into account all clinical and laboratory variable, we found that MRI bone marrow oedema of the hand was associated and probability for the occurance of MRI bone marrow oedema was higher for the SSc pts with digital ulcers (OR=6.081;95%IP:1.295–28.550; $p<0.05$), HAQ>1.5 (OR=6.448; 95%IP: 1.714–24.257; $p<0.01$) and active disease (OR=3.377; 95%IP; 1.175–9.706; $p<0.05$).
MRI synovitis of the hand was associated and probability for the occurance of MRI synovitis was higher, also, for the SSc pts with digital ulcers (OR=5.128; 95%IP: 1.085–24.243; $p<0.05$), HAQ>1.5 (OR=9.067; 95%IP: 1.925–42.708; $p<0.01$) and active disease (OR=3.565; 95%IP: 1.181–10.764; $p<0.05$).
Conclusions: MRI bone marrow oedema and synovitis on the hand in SSc are associate with digital ulcers, impaired functional capacity and active disease. Monitoring and treatment of clinical features and organ involvement are essential in all the pts with SSc, especially those with proven bone marrow oedema and synovitis on MRI of the hand.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4522

SAT0379 NAILFOLD CAPILLAROSCOPY FINDINGS IN PATIENTS WITH INFLAMMATORY MYOPATHY AND/OR SPECIFIC OR ASSOCIATED ANTIBODIES

A.M. Millan Arciniegas[1], M.A. Martinez[2], A. Baucells[2], C. Juarez[2], L. Martinez[2], H.S. Park[1], B. Magallares[1], A. Laiz[1], P. Moya[1], J.M. Llobet[1], C. Diaz Torne[1], I. Castellvi[1]. *[1]Rheumatology; [2]Immunology, Hospital de Sant Pau, Barcelona, Spain*

Background: Nailfold videocapillaroscopy (NVC) is an easy, fast and non-aggressive tool, useful in the study of autoimmune diseases. The use of NVC in Inflammatory Myopathy (IM) is not clearly established.
Objectives: 1. To evaluate capillaroscopic findings in patients with IM and/or with presence of specific or associated antibodies with this pathology. 2. To analyze possible relationships with clinical characteristics of the patients.
Methods: Retrospective review of a cohort of patients with IM and/or with presence of specific or associated antibodies, followed in Rheumatology Unit of a University Hospital.
Patients underwent a NVC at 200x, being evaluated for the presence of: loss of capillary density, enlarged and giant capillaries, ramified capillaries, haemorrhages, thrombosis, tortuous capillaries, avascular areas, disorganization of capillary architecture and subpapilar venous plexus. The following variables were also collected: sex, age, active smoking, muscle weakness, CK elevation at diagnosis, compatible muscle EMG and biopsy, skin findings, cardiac disease, dysphagia, lung disease, Raynaud's phenomenon, cancer history and overlap syndromes.
For the comparison of qualitative and/or quantitative variables Fisher's exact Test or T-test was performed when necessary.
Results: Twenty patients with at least one NVC (45% with 2), 65% female, with a mean age of 58 years ± 11.6 were evaluated. The characteristics of the patients are detailed in table 1.
65% of patients had some capillaroscopic alteration. The findings in NVC-1 and NVC-2 were: loss of capillary density 30% and 33%, tortuous capillaries 90% and 89%, enlarged capillaries 65% and 66.7% (giants 30% and 33%), ramifications 40% and 55.6%, disorganization 10% and 33%, haemorrhages 25% and 44%, thrombosis 20% and 0%, avascular areas 25% and 22%, visible venous plexus 40% and 55%.
The presence of dysphagia was associated with the presence of loss of capillary

density ($p<0.02$) and haemorrhages ($p<0.01$) in the initial NVC, as well as the presence of ramifications in the control NVC ($p<0, 05$).
It was observed that patients with normal capillary organization presented better value of FVC ($p<0.01$), TLC ($p<0.01$), and lower FEV1/FVC ratio ($p<0.02$), the latter finding also found in control NVC ($p<0.03$). As additional data, we found that patients with anti-Ku+ presented better values of FVC ($p<0.04$) and TLC ($p<0.05$), but although they all had normal capillary organization, the association of this antibody with NVC was not statistically significant. We also did not find a statistically significant relationship between the alterations in NVC and the presence of Raynaud's phenomenon, the other clinical variables, cancer history and the presence of overlap syndromes.

Table 1	PATIENTS
N	20
Age at diagnosis (years)	55 ± 11,7
Time of evolution (years)	2,9 ± 1,8
Active smoking	5 (25%)
Muscle weakness	7 (35%)
CK elevation at diagnosis	8 (40%)
EMG compatible with IM	5/8 (62.5%)
Muscle biopsy compatible with IM	7/8 (87,5%)
Skin findings	6 (30%)
Cardiac disease	1 (5%)
Disphagia	5 (25%)
Lung disease	7 (35%)
Concomitant cancer	1 (5%)
Raynaud's phenomenon present	11 (55%)
Overlap:	5 (25%)
-With Systemic Sclerosis	4/5 (80%)
-With Sjögren Syndrome	1/5 (20%)
Anti-Mi2	4 (20%)
Anti-Ku	5 (25%)
Anti-Jo1	2 (10%)
Anti-PL7	2 (10%)
Anti-Ro52	5 (25%)
Other Ab (SRP, PL12, PM/SCL, OJ, MDA5, TIF1G)	6 (30%)

Conclusions: Patients with capillary disorganization in NVC showed worse values of FVC, TLC and FEV1/FVC. We found a statistically significant association between esophageal disease and haemorrhages, loss of capillary density and ramifications. Prospective studies with larger sample sizes are required to define the usefulness of NVC in the diagnosis, prognosis and follow-up of these patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6730

SAT0380 CLASSIFICATION, CATEGORISATION AND ESSENTIAL ITEMS FOR DIGITAL ULCER (DU) EVALUATION IN SYSTEMIC SCLEROSIS (SSC): A DESSCIPHER/EUSTAR SURVEY

J. Blagojevic[1,2,3], L. Cometi[1], G. Abignano[3,4], S. Guiducci[1], S. Bellando-Randone[1], D. Huscher[5], J. Avouac[6], L. Czirják[7], C. Denton[8], O. Distler[9], M. Frerix[10], V.K. Jaeger[11], V. Lóránd[7], B. Maurer[9], S. Nihtyanova[8], G. Riemekasten[12], E. Siegert[13], G. Valentini[14], S. Vettori[14], U. Walker[15], U. Müller-Ladner[10], Y. Allanore[16], F. Del Galdo[3,4], M. Matucci-Cerinic[1] on behalf of DeSScipher Consortium and contributing EUSTAR centres. *[1]Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy; [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [3]NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust; [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom; [5]Department of Rheumatology and Immunology, Charité University Hospital and German Rheumatism Research Centre, Berlin, Germany; [6]Department of Rheumatology, University of Paris Descartes, Paris, France; [7]Department of Rheumatology and Immunology, University of Pécs, Pécs, Hungary; [8]Department of Rheumatology, University College London, Royal Free Hospital, London, United Kingdom; [9]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [10]Department of Rheumatology and Clinical Immunology, Justus–Liebig University Giessen, Kerckhoff Clinic Bad Nauheim, Giessen/Bad Nauheim, Germany; [11]Department of Rheumatology, University of Basel, Basel, Switzerland; [12]University Schleswig-Holstein Lübeck, Lübeck; [13]Department of Rheumatology and Immunology, Charité University Hospital, Berlin, Germany; [14]Department of Rheumatology, Second University of Naples, Naples, Italy; [15]Department of Rheumatology, University of Basel, Basel, Switzerland; [16]Department of Rheumatology, University of Paris Descartes, Paris, France*

Background: A consensus on DU definition in SSc has been recently reached (1),while for their evaluation,classification and categorisation it is still missing.
Objectives: To identify in SSc a set of essential items for DU evaluation, to assess if the existing DU classification (2) was useful and feasible in clinical practice, and to investigate if the DU categorisation (3) was preferred to the simple division of DU in recurrent and not recurrent.
Methods: The DU Desscipher items that reached >60% of completion rate were administered to EUSTAR centres via online survey.These items were: DU distal to the proximal interphalangeal joints, recurrent DU, DU history, infection, gangrene, amputation, total number of DU, number of new DU, number of healed DU, number of DU defined as loss of tissue, number of DU due to calcinosis and number of DU due to digital pitting scars (DPS).Questions about feasibility and usefulness of the existing DU classification (DU due to DPS, to loss of tissue, derived from calcinosis and gangrene) (2) and newly proposed DU categorisation (episodic, recurrent and chronic) (3) were also administered.
Results: All Desscipher and 82/194 EUSTAR centres (42.3%) completed the questionnaire.Out of 27 items selected for the Desscipher study, those scored by>70% of participants as essential and feasible for DU evaluation in clinical practice were only the following: number of DU defined as a loss of tissue (level of agreement 91.1%), recurrent DU (84%) and number of new DU (74.4%).For 64.6% of the centres,the classification of DU was considered useful and feasible in clinical practice.Moreover, 80.3% of the centres preferred the categorization of DU in episodic,recurrent and chronic.
Conclusions: For clinical practice, EUSTAR centres identified only three essential items for DU evaluation and considered useful and feasible the proposed classification and categorisation of DU.The set of items needs to be further validated by Delphi voting in order to implement its use in clinical practice while further implementation of DU classification and categorisation is warranted.
References:
[1] Suliman Y et al.Preliminary musculoskeletal ultrasound (MSUS) ulcer definition does not correlate with visual observation in systemic sclerosis (SSc) patients. J. Scleroderma Relat. Disord.2017(in press).
[2] Amanzi L et al.Digital ulcers in scleroderma: staging, characteristics and subsetting through observation of 1614 digital lesions. Rheumatology (Oxford) 2010;49:1374–82.
[3] Matucci-Cerinic M et al.Elucidating the burden of recurrent and chronic digital ulcers in systemic sclerosis: long-term results from the DUO Registry. Ann Rheum Dis. 2016;75:1770–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6815

SAT0381 CORRELATION BETWEEN THREE DIFFERENT METHODS TO ASSESS DERMAL THICKNESS IN SYSTEMIC SCLEROSIS PATIENTS WITH DIFFERENT PATTERNS OF NAILFOLD MICROANGIOPATHY

B. Ruaro, A. Sulli, E. Alessandri, S. Paolino, M. Ghio, A.C. Trombetta, C. Pizzorni, V. Tomatis, M. Cutolo. *Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, IRCCS AOU San Martino, Genoa, Italy*

Background: Systemic sclerosis (SSc) is characterized by the increase of dermal thickness (DT) (1). The modified Rodnan skin score (mRss) is the validated method to evaluate the severity of skin impairment (2,3). Several studies have reported the capability of high frequency skin ultrasound (US) to reflect the overall severity of the skin damage in SSc patients (4–5). The plicometer skin test (PST) is another method to evaluated cutaneous involvement in SSc patients (6).
Objectives: The aim of this study was to identify possible correlations between US, mRss and PST to evaluate DT in SSc patients with different patterns of nailfold microangiopathy.
Methods: Sixty-three SSc patients (mean age 64±11SD years, mean disease duration 7±6 years, 43 lcSSc and 20 dcSSc) and 63 sex and age matched healthy subjects were enrolled after written informed consent. All subjects were assessed by mRss, US and PST to evaluate the DT in the seventeen skin areas of the body usually evaluated by mRss (zygoma, fingers, hands, dorsum of hands, forearms, arms, chest, abdomen, thighs, legs, feet) (1–6). Nailfold videocapillaroscopy (NVC) was used to assess the proper pattern of microangiopathy and to calculate the microangiopathy evolution score (MES) (7–8). Statistical evaluation was performed by non-parametric tests.
Results: As expected, the group of SSc patients had a statistically significant higher DT, as evaluated by the three methods, at level of all areas when compared to the control group ($p=0.0001$). All methods demonstrated a progressively higher DT in patients with "Early", vs. "Active" and vs "Late" pattern of nailfold microangiopathy ($p<0.005$), and a positive correlation was observed with MES ($r=0.71$ $p<0.001$). A positive correlation was observed in SSc patients between the three method to evaluate DT (PST vs mRss $r=0.98$, $p<0.0001$; PST vs US $r=0.53$, $p<0.0001$; US vs mRss $r=0.53$, $p<0.0001$).
Conclusions: This study demonstrates a relationship between different methods to assess DT (US, mRss and PST) in SSc patients and a relationship between skin damage and microangiopathy impairment.
References:
[1] Moore TL, et al. Rheumatology 2003;42:1559–63.
[2] Sulli A, et al. Ann Rheum Dis. 2014;69:1140–3.
[3] Kaldas M, et al. Rheumatology 2009;48:1143–6.
[4] Hesselstrand R, et al. Rheumatology 2008;47:84–7.
[5] Kaloudi O, et al. Ann Rheum Dis. 2010;69:1140–3.
[6] Parodi MN, et al. Br JRheumatol. 1997;36:244–50.
[7] Sulli A, et al. Ann Rheum Dis 2008;67:885–7.
[8] Cutolo et al. J Rheumatol 2000; 27;155.60.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2731

SATURDAY, 17 JUNE 2017

Spondyloarthritis - clinical aspects (other than treatment)

SAT0382 CHANGES IN VOLUMETRIC BONE MINERAL DENSITY AND BONE MICROARCHITECTURE IN PATIENTS WITH ANKYLOSING SPONDYLITIS. A FIVE-YEAR PROSPECTIVE STUDY USING HRPQCT

A. Deminger[1], E. Klingberg[1], M. Lorentzon[2], H. Carlsten[1], L.T. Jacobsson[1], H. Forsblad-d'Elia[1,3]. [1]*Department of Rheumatology and Inflammation Research, Sahlgrenska Academy at University of Gothenburg;* [2]*Geriatric Medicine, Institute of Medicine, Sahlgrenska Academy at University of Gothenburg and Sahlgrenska University Hospital, Göteborg;* [3]*Department of Public Health and Clinical Medicine, Rheumatology, Umeå University, Umeå, Sweden*

Background: Studies have demonstrated increased prevalence of osteoporosis in patients with ankylosing spondylitis (AS) in the hip and lumbar spine assessed by conventional DXA but the peripheral skeleton is less studied. The peripheral skeleton can be studied in detail by high-resolution peripheral quantitative computed tomography (HRpQCT) demonstrating data of the volumetric bone mineral density (vBMD) and bone microarchitecture. We have previously shown that patients with AS from Western Sweden had lower vBMD measured by HRpQCT in radius and tibia compared with healthy controls [1]. No prospective study in this matter has been published in AS.
Objectives: To investigate changes over 5 years in the peripheral vBMD and microarchitecture in patients with AS.
Methods: HRpQCT of ultra-distal radius and tibia was performed in male AS-patients (NY criteria) at baseline and at the five-year follow-up. The patients were also assessed with blood samples and questionnaires.
Results: Of the 69 patients included at baseline 57 (83%) patients were re-examined at the five-year follow-up. Baseline characteristics of the 57 patients [median (IQR)]: age 48 (35 to 61) years, symptom duration 21 (11 to 34) years, ESR 10 (5 to 17) mm/h, CRP 3 (1 to 7), $ASDAS_{CRP}$ 1.8 (1.3 to 2.8) and BASDAI 2.3 (1.2 to 4.2). 23% used TNF-inhibitors, 75% used NSAIDs and 2% bisphosphonates. All measurements at tibia had good quality and matched images had common regions $\geq$80%. The images of radius of 12 patients had to be excluded due to insufficient quality. At tibia, the total, cortical and trabecular vBMD decreased significantly. In the microarchitecture an increase in the trabecular separation was seen (Table). Changes in vBMD were negatively and significantly correlated; Spearman's correlation coefficient between -0.3 and -0.4, to Δ-values (difference between follow-up and baseline) for ESR, CRP (cortical vBMD), $ASDAS_{CRP}$ (total vBMD and cortical vBMD) and BASDAI (total vBMD). At radius, no significant change in vBMD was observed; however, less power for analyses of radius. An increase was seen in the cortical thickness and the trabecular number while the trabecular thickness decreased (Table). Changes in cortical vBMD was negatively and significantly correlated, r $\approx$ -0.3, to Δ-CRP and Δ-$ASDAS_{CRP}$.

Table.

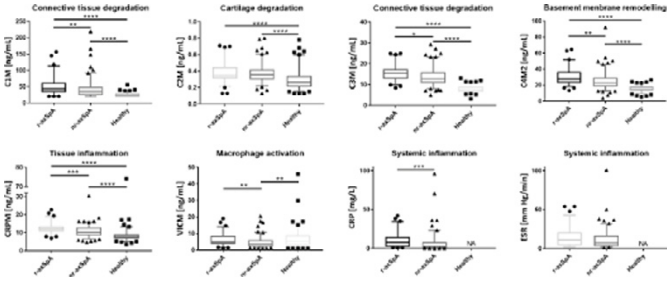
Site		Baseline mean ± SD	Five-year follow-up mean ± SD	Difference mean% ± SD	p-value
Tibia	**Total vBMD, mg/cm³**	297.9 ± 55.5	292.8 ± 55.8	**-1.7 ± 3.9**	**0.002**
	Cortical vBMD, mg/cm³	842.7 ± 54.8	834.1 ± 62.5	**-1.1 ± 1.9**	**0.001**
	Trabecular vBMD, mg/cm³	184.8 ± 34.6	179.5 ±31.9	**-2.6 ± 4.8**	**0.001**
	Cortical thickness, mm	1.22 ± 0.32	1.21 ± 0.32	-1.0 ± 5.2	0.35
	Trabecular thickness, mm	0.08 ± 0.01	0.07 ± 0.01	-1.5 ± 7.3	0.26
	Trabecular number in 1/mm	2.06 ± 0.30	2.04 ± 0.32	-0.7 ± 6.7	0.19
	Trabecular separation, mm	0.42 ± 0.08	0.43 ± 0.08	**1.8 ± 6.9**	**0.027**
Radius	Total vBMD, mg/cm³	319.6 ± 64.9	320.7 ± 69.9	0.1 ±4.7	0.47
	Cortical vBMD, mg/cm³	854.4 ± 54.9	854.1 ± 59.5	-0.1 ±1.9	0.98
	Trabecular vBMD, mg/cm³	177.5 ± 40.5	173.6 ± 41.9	-2.3 ± 6.2	0.082
	Cortical thickness, mm	0.83 ± 0.21	0.85 ± 0.21	**2.5 ± 5.4**	**0.004**
	Trabecular thickness, mm	0.08 ± 0.02	0.07 ± 0.01	**-5.4 ± 10.5**	**0.001**
	Trabecular number in 1/mm	1.96 ± 0.24	2.01 ± 0.24	**4.2 ± 10.8**	**0.041**
	Trabecular separation, mm	0.44 ± 0.07	0.43 ± 0.06	-2.7 ± 10.1	0.080

Conclusions: Over five years, this group of male patients with AS decreased in the vBMD of tibia, both trabecular and cortical. Even though there were alterations in the microarchitecture, no significant change in vBMD of radius was seen. Increases in inflammatory markers and disease activity had a negative impact on the cortical vBMD. The differences in the development of vBMD and microarchitecture in loaded and unloaded skeleton as well as factors associated with the changes needs to be further investigated.
References:
[1] Klingberg, E., et al., Bone microarchitecture in ankylosing spondylitis and the association with bone mineral density, fractures, and syndesmophytes. Arthritis Res Ther, 2013. 15: p. R179.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4950

SAT0383 BIOMARKERS OF ECM DEGRADATION REFLECT DISEASE ACTIVITY IN RADIOGRAPHIC AND NON-RADIOGRAPHIC SPONDYLARTHRITIS

A.S. Siebuhr[1], A.-C.S. Bay-Jensen[1], K. Pavelka[2], S. Forejtova[2], K. Zegzulkova[2], M. Tomcik[2], M.A. Karsdal[1], M. Urbanova[2], K. Grobelna[2], J. Horinkova[2], J. Gatterova[2], M. Husakova[2]. [1]*Biomarkers and Research, Nordic Bioscience, Herlev, Denmark;* [2]*Institute of Rheumatology and Department of Rheumatology, Charles University, Praugh, Czech Republic*

Background: Axial spondyloarthritis (axSpA) comprises two groups - radiographic (r-axSpA) and non-radiographic (nr-axSpA) with varying disease activity, spine involvement and response to biological therapy. An objective biomarker of disease activity may be able to select patients, which will benefit from a given biological treatment.
Objectives: We investigated the association of extracellular matrix (ECM) degradation biomarkers in axSpA patients (r-axSpA and nr-axSpA) with disease activity.
Methods: AxSpA patients (n=193; 72 r-axSpA and 121 nr-axSpA) and 100 healthy controls were included in the study. Biomarkers of type I, II, III and IV degradation (C1M, C2M, C3M, C4M2), MMP-degraded CRP (CRPM) and MMP-degraded and citrullinated vimentin (VICM) were detected by ELISA in serum. Mann-Whitney t-test tested the difference in the biomarker levels between groups and multiple regression analysis investigated the association between biomarkers and clinical manifestations with adjustment for age, gender, BMI, disease duration and CRP. ROC AUC tested the biomarkers capacity to differentiate the patient groups.
Results: Patients with r-axSpA compared to nr-axSpA patients had higher radiographic status and longer disease duration ($p<0.001$), whereas nr-axSpA had more swollen joints (p=0.0093). They were alike in age, BMI and disease activity (ASDAS-CRP, BASDAI and HAQ). All tested biomarkers except VICM were elevated in the axSpA patients compared to healthy subjects (all $p<0.001$). VICM was lower in the axSpA group, particularly in nr-axSpA compared to healthy (p=0.036 and p=0.002 respectively). R-axSpA compared to nr-axSpA patients had higher level of C1M, C3M, C4M2, CRPM and VICM ($p<0.001$, =0.001, <0.001, <0.001 and =0.003), but not C2M (p=0.92). C1M correlated to ASDAS-CRP in both r-axSpA and nr-axSpA (r-partiel: 0.46 and 0.44) with adjustment for age, gender, BMI and disease duration, but the correlation was lost by adjustment for CRP. Also C3M and C4M2 correlated to ASDAS-CRP in both axSpA groups. C2M was in r-axSpA patients moderately correlated to ASDAS-CRP, but minimal after adjustment of CRP (r-partiel: 0.32 unadjusted and 0.18 adjusted). CRPM correlated to ASDAS-CRP with adjustment to CRP in r-axSpA (r-partiel: 0.27 unadjusted, 0.26 adjusted), but not in nr-axSpA (r-partiel: 0.19 unadjusted, 0.03 adjusted).
Especially, C3M and C4M2 could differentiate between healthy and the axSpA patients (AUC 0.95 and 0.89), but also C1M, C2M, CRPM had AUC of $\geq$0.72. VICM was the only biomarker to differ between r-axSpA (AUC 0.92 and nr-axSpA (AUC 0.51).



Conclusions: Biomarkers of ECM turnover, C3M and C4M2 in particular, were associated with r-axSpA and nr-axSpA and could define disease. The biomarkers of ECM degradation, especially C1M, may reflect the pathogenetic background of axSpA.
Acknowledgements: Supported by Project for Conceptual development of MH CR – Inst. of Rheumatology (no.023728).
Disclosure of Interest: A. S. Siebuhr Employee of: Nordic Bioscience, A.-C. Bay-Jensen Employee of: Nordic Bioscience, K. Pavelka: None declared, S. Forejtova: None declared, K. Zegzulkova: None declared, M. Tomcik: None declared, M. Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, M. Urbanova: None declared, K. Grobelna: None declared, J. Horinkova: None declared, J. Gatterova: None declared, M. Husakova: None declared
DOI: 10.1136/annrheumdis-2017-eular.2432

SAT0384 RISK OF MYOCARDIAL INFARCTION AND CEREBROVASCULAR ACCIDENT IN ANKYLOSING SPONDYLITIS: A GENERAL POPULATION-BASED STUDY

A.C.L. So[1], J. Chan[1], E.C. Sayre[2], J.A. Avina-Zubieta[1]. [1]*UBC Division of Rheumatology;* [2]*Arthritis Research Canada, Vancouver, Canada*

Background: There is conflicting data on the risk of myocardial infarction (MI) and cerebrovascular accidents (CVA) in patients with Ankylosing Spondylitis (AS).

Objectives: 1) To assess the future risk of newly recorded MI and CVA events among incident cases of AS compared to non-AS controls from the general population by utilizing physician billing, medication, and hospitalization data that covers the entire province of British Columbia (BC), Canada.
Methods: Our data includes all outpatient visits and hospitalizations (1990–2012) and all dispensed medications (1996–2012) for all BC residents. We conducted a retrospective matched cohort study of all patients >18 years of age satisfying the following criteria: 1) two ICD-9 or 10 codes (720.0 or M45) for AS at least two months apart and within a 2-year period by any physician or hospitalization; 2) all AS cases had at least a 7-year run-in period before the 1st ICD code for AS in order to consider the case as incident. Each AS patient was matched with up to 10 controls by birth year, sex, and entry cohort time. The outcomes were a newly recorded MI (ICD-9-CM: 410 or ICD-10-CM: I21) or CVA (ICD-9 codes: 433–434, ICD-10 codes: I63-I66) event from hospital or death certificates. We estimated relative risks (RRs), adjusting for age, sex, and entry cohort time as well as multivariable models adjusting for confounders including glucocorticoids and non-steroidal anti-inflammatory drugs using a Cox proportional hazard model.
Results: 7,190 individuals with newly diagnosed AS were identified (48.7% female, mean age of 45.8 yrs). 7,148 and 7,107 were free of previous CVA/MI, respectively. 80 developed CVA (incidence rate=1.8 per 1000 patient years) and 115 had MI (incidence rate=2.6 per 1,000 patient years) (Table 1). The age-, sex-, and entry-time-matched RR for CVA was 1.60 (95% CI, 1.25–2.03) and MI was 1.52 (95% CI, 1.24–1.85). When adjusted for cardiovascular risk factors (obesity, angina, COPD, hospitalizations in year before index date, Charlson's comorbidity index, oral glucocorticoids, cardiovascular drugs, anti-diabetic medication, HRT, contraceptives, fibrates, statins, NSAIDs, and Cox-2 inhibitors), the estimated RR was 1.34 (1.04–1.73) for CVA and 1.21 (0.98–1.49) for MI.

Table 1. Relative risk of incident CVA and MI according to AS status

	AS (N=7,148)	Non-AS (N=71,489)
CVA events, n	80	492
Incidence Rate of CVA/1000 Person-Years	1.81	1.13
Incidence Rate Ratio of CVA (95% CI)	1.60 (1.25–2.03)	1.0
Multivariable RR of CVA (95% CI)	**1.34 (1.04–1.73)**	1.0
	AS (N=7,107)	Non-AS (N=71,033)
MI events, n	115	748
Incidence Rate of MI/1000 Person-Years	2.62	1.73
Incidence Rate Ratio of MI (95% CI)	1.52 (1.24–1.85)	1.0
Multivariable RR of MI (95% CI)	**1.21 (0.98–1.49)**	1.0

Conclusions: This large population-based study demonstrates an increased risk of CVA, but not for MI. These findings support that increased monitoring for this potentially fatal outcome and its modifiable risk factors is warranted for AS patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6544

SAT0385 SIMILARITIES AND DIFFERENCES BETWEEN PATIENTS FULFILLING NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND UNDIFFERENTIATED SPONDYLOARTHRITIS CRITERIA: RESULTS FROM THE ESPERANZA COHORT

A. Juan Mas[1], X. Juanola Roura[2], E. de Miguel Mendieta[3], E. Collantes Estévez[4], J.C. Quevedo Abeledo[5], E. Alonso Blanco-Morales[6], V. Navarro-Compán[3] on behalf of ESPeranza working group. *[1]Rheumatology, Hospital Son Llàtzer, Palma de Mallorca; [2]Hospital Bellvitge, Barcelona; [3]Hospital la Paz, IdiPaz, Madrid; [4]Hospital Reina Sofía, Córdoba; [5]Hospital Gran Canaria Dr. Negrín, Gran Canaria; [6]Hospital Juan Canalejo, A Coruña, Spain*

Background: Patients with spondyloarthritis (SpA) were classified in five subgroups: ankylosing spondylitis (AS), psoriatic arthritis, arthritis associated with inflammatory bowel disease, reactive arthritis and undifferentiated SpA (uSpA). ASAS criteria classify patients in peripheral SpA and axial SpA (axSpA), being the latest classified in two groups: classical AS and non-radiographic axSpA (nr-axSpa). Whether or not patients with nr-axSpA represent the same group of patients that used to be classified as uSpA remains unclear.
Objectives: To evaluate the similarities and differences between patients with predominant axial disease classified currently as nr-axSpA versus those traditionally classified as uSpA.
Methods: Baseline data from the ESPeranza program (a multicenter national initiative to early diagnose SpA between 2008 and 2011) was used. Inclusion criteria for this program were: age <45 years and inflammatory back pain plus ≥1 SpA features with symptoms duration between 3 and 24 months. Demographic, clinic, laboratory and image results were compared between two groups: 182 patients with nr-axSpA and 166 patients classified as uSpA. In order to get a deeper knowledge of the differences between nr-axSpA and uSpA, we also compared: i) 88 patients only classified as nr-axSpA, ii) 72 patients only classified as uSpA; iii) 94 patients fulfilling both criteria. Student-t test for continuous variables and Pearson Chi-square test for categorical variables were used.
Results: Compared to patients classified as uSpA patients with nr-axSpA were younger, had HLA-B27 positive more frequently and higher values of CRP. On the other hand, they had history of SpA less frequently and lower values for BASDAI, BASFI and ASQoL (table). No differences were observed for gender, work incapacity, dactilitis, enthesitis, Pt's and Phy's VAS, BASMI and BASRI.

Table 1. Results are presented in mean ± standard deviation for continuous variables and n (%) for categorical variables

	Both, nr-axSpA & undifferentiated SpA N (%) = 94	Only nr-axSpA N (%) = 88	Only undifferentiated SpA N (%) = 72	p value*
Age (years)	30.9±7.3	32.2±6.9	35.2±6.9	**<0.01**
Male	61 (64.9)	50 (56.8)	34 (47.2)	0.2
Family history	48 (51.1)	21 (23.9)	30 (41.7)	**<0.05**
HLA-B27	81 (86.2)	65 (73.9)	6 (8.3)	**<0.001**
Enthesitis	29 (30.9)	18 (20.5)	22 (30.6)	0.1
BASDAI	3.7±2.3	3.8±2.1	4.7±2.3	**<0.01**
BASFI	2.2±2.2	2.1±2.1	2.9±2.5	**<0.05**
ASQoL	5.9±4.7	5.2±4.5	7.4±5.2	**0.01**
CRP (mg/L)	10.7±14.3	9.8±16.5	5.1±9.1	**<0.05**

*p value for differences between nr-axSpA and undifferentiated SpA (Student-t test for continuous variables and Pearson Chi-square test for categorical variables).

Conclusions: Compared with patients traditionally classified as uSpA, patients who are currently classified as nr-axSpA are diagnosed earlier, are more frequently HLA-B27 carriers and have higher disease activity according to objective parameters. On the other hand, they report lower values for patient reported outcomes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5675

SAT0386 EXTREME PATIENT REPORTED OUTCOME (PRO) IN EARLY SPONDYLOARTHRITIS: A SURROGATE FOR FIBROMYALGIA? ITS IMPACT ON TNF-ALPHA BLOCKERS TREATMENT EFFECT?

B. Meghnathi[1], A. Etcheto[1], P. Claudepierre[2], M. Dougados[1], A. Moltó[1]. *[1]Paris Descartes University, Medicine Faculty; APHP, Rheumatology B Department, Cochin Hospital; [2]Paris XII University; Rheumatology Department, Hôpital Henri-Mondor, Paris, France*

Background: In case of a concomitant fibromyalgia (FM) with axial spondyloarthritis (axSpA), there is a risk of misclassifying a patient as active (e.g. BASDAI >4), and to falsely consider him as refractory to NSAIDs/ biologics, since FM patients often report higher level of pain and fatigue[1]. We hypothesized that not only are extreme patient reported outcome (PRO) potentially surrogate marker of FM in axSpA, but also that this extreme PRO may have an impact on the TNF-α blockers (TNFb) treatment effect
Objectives: A) To describe the prevalence of extreme PRO in an early axSpA cohort. B) To compare the phenotype of axSpA patients with and without extreme PRO. C) To assess the impact of extreme PRO on the TNFb efficacy.
Methods: This analysis was performed on the DESIR cohort which included 708 adult patients (>18 and <50 years) with inflammatory back pain suggestive of axSpA (according to the rheumatologist's conviction of ≥5/10) for >3 months but <3 years duration. All patients were biologic naïve at inclusion and were followed up every 6 months for the first 2 years. At baseline, data pertaining to demographics, BASDAI, history of depression, type of medications (antidepressants or muscle relaxants) used and concomitant diseases were collected. It is worth noting that no systematic assessment of the fulfilment of the ACR criteria for FM was performed in this study; thus, we created a "FM gold standard" according to the available data (i.e., presence of either Muscle relaxants/ Depression/ Anti-depressant drug treatment/ Fibromyalgia comorbidity reported in the CRF). BASDAI was the selected PRO for this study due to its widespread use in clinical practice. BASDAI was tested against this "FM gold standard": we plotted ROC curves to define the best cut-off to define an "extreme PRO" for BASDAI. Phenotype of patient's with/without extreme PRO scores was compared. Impact of extreme PRO score on TNFb efficacy was assessed by comparing the retention rate of the first TNFb by Cox analysis.
Results: ROC curves to define an "extreme PRO" determined a different cut-off for each BASDAI question (i.e. >6, >5, >1, >4, >5 and >3 for question 1 to 6, respectively), and the need of at least 4 out of these 6 cut-offs to fulfil the "extreme PRO" condition; giving us a prevalence of 42.9% (304 patients) of extreme PRO in DESIR. Phenotypically, this group with extreme PRO, consisted of older patients (34.6 (8.3) vs 33.1 (8.8)), had more females (184 (60.5%) vs 195 (48.8%)), reported less sacroiliitis [radiographic and MRI, (36 (12%) vs 76 (19.4%)) and (82 (27.6%) vs 148 (37.8%)), respectively], showed less HLA B27 positivity (160 (52.6%) vs 248 (62.2%)), had higher CRP values (102 (34.3%) vs 102 (26.5%)), and more arthritis/ enthesitis history (212 (69.7%) vs 190 (47.5%)/ 182 (59.9%) vs 166 (41.5%)). A lower retention rate was observed in the group of patients with "extreme PRO" (Figure 1)
Conclusions: Coexistence of extreme PRO might be considered as a surrogate marker for FM in axSpA patients. Moreover, it appears to have a negative impact on TNF-α blockers retention rate.
References:
[1] Wendling D, Prati C. Spondyloarthritis and fibromyalgia: interfering association or differential diagnosis? Clin Rheumatol 2016;35:2141–43.

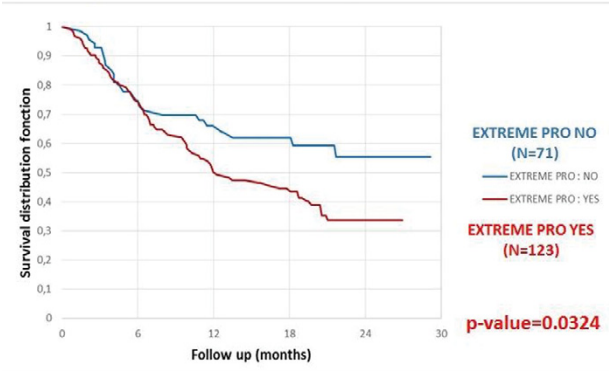


Figure 1. Impact of extreme PRO on first TNF-α blocker retention rate (first 2years) [Kaplan Meier curves and Log Rank test]

Acknowledgements: The DESIR cohort is financially supported by unrestricted grants from the French Society of Rheumatology and Pfizer France.
Disclosure of Interest: B. Meghnathi Grant/research support from: ASAS Society (ASAS FELLOW), A. Etcheto: None declared, P. Claudepierre: None declared, M. Dougados: None declared, A. Moltó: None declared
DOI: 10.1136/annrheumdis-2017-eular.3827

SAT0387 "DO NOT DO" RECOMMENDATIONS IN THE MANAGEMENT OF COMORBIDITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. GECOAX PROJECT

J.C. Torre-Alonso[1], C. González[2], S. Castañeda[3], R. Curbelo[4], E. Collantes[5], M.V. Hernández[6], A. Urruticoechea-Arana[7], J.C. Nieto[2], J. García[8], M.Á. Abad[9], J. Ramírez[6], C. Suárez[10], R. Dalmau[11], M.D. Martín-Arranz[12], L. León[13], J.C. Hermosa[14], J.C. Obaya[15], T. Otón[4], L. Carmona[4].
[1]Rheumatology, HU Monte Naranco, Oviedo; [2]Rheumatology, HU Gregorio Marañón; [3]Rheumatology, HU la Princesa, IIS-IP; [4]InMusc, Madrid; [5]Rheumatology, HU Reina Sofía, Córdoba; [6]Rheumatology, HU Clinic i Provincial, Barcelona; [7]Rheumatology, H Can Misses, Ibiza; [8]Rheumatology, HU 12 de Octubre, Madrid; [9]Rheumatology, H de Plasencia, Plasencia; [10]Internal Medicine, HU la Princesa, IIS-IP; [11]Cardiology; [12]Gastroenterology, HU la Paz; [13]Psychology, UCJC, Madrid; [14]Centro de Salud Ciudades, Getafe; [15]Centro de Salud Alcobendas, Alcobendas, Spain

Background: During the development of recommendations and implementation aids of the GECOAx project, the importance of avoiding certain situations was highlighted.
Objectives: To recognize what prescriptions, risk assessments, or preventive strategies are wrong practices and should thus be avoided in clinical practice. To establish not to do recommendations in the management of the comorbidity of AxSpA.
Methods: A multidisciplinary group was selected [10 rheumatologists, 1 internist, 1 cardiologist, 1 gastroenterologist, 1 psychologist and 2 family physicians]. With the support of 3 methodologists, and after interactions aimed to edit a document for the management of comorbidity launched by the same panel, a list of Not to do recommendations was issued. In a discussion meeting, evidence was provided to support the recommendations, items without sufficient basis were removed, and the final list was produced.
Results: A summary list of Not to do recommendations (Table 1) was issued.

Table 1

– DO NOT prescribe NSAIDs to patients with high cardiovascular (CV) risk and particularly with hypertension.
– DO NOT prescribe NSAIDs to patients with CKD, heart failure or liver cirrhosis and, if necessary, exert caution.
– DO NOT use CV risk scores in patients who already suffered a CV event or those with multiple risk factors (smoking, obesity, sedentary lifestyle, DM, hypertension, dyslipidemia) or a family history of premature CV disease; All should be considered high CV risk.
– DO NOT base renal disease screening on a single glomerular filtration test and/or albuminuria (ALWAYS should be confirmed); serum creatinine should not be used as the only test to evaluate renal function.
– DO NOT administer biological therapy in case of active, serious and uncontrolled infection, sepsis or risk of sepsis or tuberculosis or without a previous screening of chronic HBV, HCV, HIV and TB.
– DO NOT repeat HBV vaccination unless HBV antibody levels are not achieved.
– DO NOT vaccinate a patient in therapy with biological agents or in immunosuppressive treatment with live viruses

Conclusions: These recommendations aim to avoid making common mistakes in clinical practice and to help better management of frequent comorbidity in patients with AxSpA.
Acknowledgements: This project was funded by Merck Sharp & Dohme Spain. Merck Sharp & Dohme had no influence on either the development of the project or the final content of the manuscript.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5029

SAT0388 ANALYSIS OF THE MUSCULOSKELETAL MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASE PATIENTS AND ITS RELATIONSHIP WITH BIOLOGICAL TREATMENT

S. Mainero Mendoza[1,2], C.M. Feced Olmos[1], L. Gonzalez Puig[1], J. Ivorra Cortes[1], I. Martínez Cordellat[1], C. Nájera Herranz[1], R. Negueroles Albuixech[1], J.E. Oller Rodriguez[1], F.M. Ortiz-Sanjuan[1], E. Vicens Bernabeu[1], E. Grau Garcia[1], E. Labrador Sánchez[1], K. Arévalo Ruales[1], J.J. Fragio Gil[1], R. González Mazarío[1], C. Alcañiz Escandell[1], I. Cánovas Olmos[1], I. Chalmeta Verdejo[1], V. Fornés Ferrer[3], J.A. Román Ivorra[1,2]. *[1]Rheumatology Department, HUP la Fe; [2]Medical School, UCV; [3]Biostatistics Unit, IIS la Fe, Valencia, Spain*

Background: Crohn's disease (CD) and ulcerative colitis (UC) are the main entities of inflammatory bowel disease (IBD). Both present extraintestinal manifestations that do not always depend on the IBD activity. The most common manifestations involve the musculoskeletal system and they are included in the seronegative spondiloarthritis group. If there is active or known IBD, treatment of this is priority because it usually improves joint disease. However, joint disease can also have an independent course of the intestinal manifestations as in patients with IBD and ankylosing spondylitis (AS).
Objectives: To analyze the prevalence of extraintestinal manifestations in IBD patients and treatment provided.
Methods: Retrospective observational analysis of IBD patients that have been remitted to the rheumatology department of HUP La Fe with musculoskeletal manifestations. Demographic, clinical and treatment data of patient were collected. Biostatistical analysis with R (3.3.2.) was performed.
Results: We recruited 183 patients diagnosed with IBD (57.4% women), 117 with CD and 66 with UC, with a mean age at diagnosis of 37.03±14.02 years old. 29 of them have axial affection and 51 peripheral affection, and simultaneously in 22 cases. We observed no statistical differences in axial or peripheral affection according to the IBD diagnosis. 79 cases were on biological therapy, and these treatments were conducted by Rheumatology in the 44% of cases and by Digestive Department in the 66% of cases. We observed that patients with axial affection present higher probability that the treatment has been conducted by Rheumatology (P=0.007), and broken down axial affections AS diagnosis had the most probability to be conducted by Rheumatology (n=36 P=0.0102). Related to peripheral manifestations, uveitis diagnosis had the most probability to be conducted by Rheumatology (n=14 P=0.0337).
Conclusions: In our patient series with IBD and musculoskeletal manifestations, the most common were peripheral affection. Among patients with IBD and axial and/or peripheral manifestation, 44% were conducted by Rheumatology, and are cases with axial predominance, where IBD treatment does not improve musculoskeletal disease and a primary spondyloarthritis treatment is needed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5687

SAT0389 COMPARISON OF ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN A MULTI-ETHNIC ASIAN POPULATION OF SINGAPORE

C. Hong[1], Y.H. Kwan[2], W. Fong[1]. *[1]Department of Rheumatology and Immunology, Singapore General Hospital; [2]Programme in Health Services and Systems Research, Duke-NUS Medical School, Singapore, Singapore*

Background: The relationship between non-radiographic axial spondyloarthritis (nr-axSpA) and ankylosing spondylitis (AS) is currently debated. Till date, there is no study exploring the differences between AS and nr-axSpA in Asia.
Objectives: The primary objective of this study was to compare clinical characteristics, disease activity, patient-reported outcomes and associated co-morbidities between patients with AS and nr-axSpA in a multiethnic Asian population of Singapore.
Methods: All patients fulfilled 2009 ASAS classification criteria for axial SpA. Of these, all AS patients fulfilled the modified New York criteria. AS and nr-axSpA patients were retrieved from the PREcision medicine in SPONdyloarthritis for Better Outcomes and Disease Remission (PRESPOND) registry in Singapore General Hospital. Patients were followed up over 2 years. Baseline characteristics, medications, disease activity, patient-reported outcomes and inflammatory markers prior and 6 months post treatment were recorded using standardized questionnaires.
Results: 262 AxSpA patients (82% Chinese, 79% males) were included. Current mean age (S.D.) was 41.7 (13.7) years, mean age of diagnosis was 31.7 (12.5) years, mean length of disease was 10.1 (8.3) years and body mass index was 24.7 (6.3) kg/m^2, which was similar between AS and nr-axSpA patients. AS patients were older [mean age 42.7 (13.5) vs 37.4 (13.8) years, p=0.02], had longer disease duration [mean disease duration 10.9 (8.7) vs 6.4 (4.8) years, p<0.01], more frequently HLA-B27 positive (82% vs 68%, p=0.03), associated with uveitis (33% vs 17%, p=0.03), and hypertensive (17% vs 0%, p<0.01) compared to nr-AxSpA respectively. nr-axSpA patients had higher BASDAI [mean BASDAI 4.2 (1.6) vs 3.5 (1.9), p=0.02], BAS-G [mean BAS-G 4.7 (1.7) vs 3.9 (2.1), p<0.01] and ASQOL [mean ASQOL 4.9 (4.8) vs 3.5 (4.1), p=0.04] scores

compared to AS patients respectively at baseline. Peripheral arthritis, enthesitis, dactylitis, psoriasis, inflammatory bowel disease, hyperlipidemia, cardiac disease, diabetes mellitus, patient global assessment, BASFI, HAQ and SF-36 physical component summary and mental component summary were similar in both groups at baseline. Mean BASDAI, BAS-G, patient global assessment, HAQ and SF-36 physical component summary and mental component summary scores were similar at 12 months between both groups, except for BASFI, which was higher in AS patients ($p<0.001$). Medications used were similar between AS and nr-AxSpA patients (81% of axial SpA patients were on NSAIDs, 31% on concomitant DMARDs and 14% on biologics). Mean erythrocyte sedimentation rate and C-reactive protein were similar between both groups at baseline and 12 months post treatment.

Conclusions: In our multi-ethnic Asian cohort, patients with AS are more likely to be HLA-B27 positive, have uveitis, hypertension, and poorer physical function despite therapy; whilst nr-axSpA patients have higher baseline disease activity scores and tend to experience poorer well-being and quality of life. Although both groups represent different aspects of the same disease, they respond similarly to treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3366

SAT0390 DIFFUSION WEIGHTED IMAGING (DWI) IS MORE USEFUL THAN SHORT TAU INVERSION RECOVERY (STIR) SEQUENCE IN DIAGNOSIS OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS (SPA) AND BOTH SEQUENCES ARE PARTICULARLY USEFUL IN EARLY DISEASE STAGE

C.W.S. Chan, H.Y. Chung. *Medicine, Queen Mary Hospital, Hong Kong, Hong Kong*

Background: Diffusion weighted imaging (DWI) is a new Magnetic Resonance Imaging (MRI) sequence proposed for spondyloarthritis (SpA) diagnosis. Whether it is more useful than the traditional short tau inversion recovery (STIR) sequence in disease diagnosis had not been evaluated.

Objectives: By comparing with traditional STIR sequence in a group of back pain patients newly referred to rheumatology clinics, we evaluated the usefulness of DWI in SpA diagnosis at different stages.

Methods: All new patients referred to the rheumatology clinics with persistant back pain were recruited. DWI and STIR MRI were performed. Conventional radiographs of the pelvis were assessed according to the modified New York criteria for ankylosing spondylitis. Bone marrow edema (BME) and active sacroiliitis according to the ASAS definition were evaluated in STIR and DWI by two independent observers.

Results: One hundred and thirty-three patients were recruited. Ninety patients (67.7%) had a clinical diagnosis of SpA. Average back pain duration was 8.5±8.9 years. The presence of Human Leukocyte Antigen (HLA) B27 was found in 42.9% of the study population. Inter-observer correlations were excellent (STIR 95.4%, $p<0.001$; DWI 69.5%, $p<0001$). DWI was found to be comparable to STIR in disease diagnosis (sensitivity DWI 34.1% vs STIR 34.3%; specificity DWI 85% vs STIR 93.8%) and when applied to the Assessment of SpondyloArthritis international Society (ASAS) criteria for axial SpA (sensitivity DWI 78.9% vs 79.5%; specificity DWI 75.0% vs 78.8%). DWI is better than STIR in non-radiographic axial SpA group (sensitivity DWI 37.8% vs STIR 33.8%; specificity DWI 85.3% vs STIR 95.6%). In the group with disease duration less than 3 years, the two images showed improved sensitivity (sensitivity DWI 34.5% vs STIR 41.4%; specificity DWI 84.6% vs STIR 88.5%).

Conclusions: DWI is useful in SpA diagnosis especially in non-radiographic axial SpA group. Both DWI and STIR are especially useful for early disease diagnosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2173

SAT0391 LUMBAR FLEXION/RELAXATION PHENOMENON IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

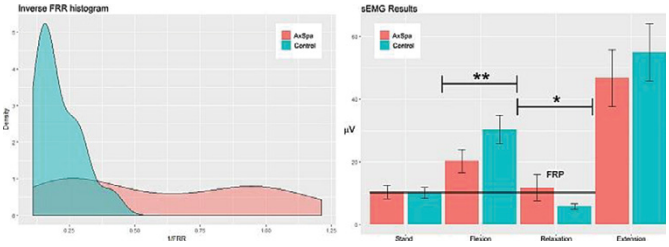
C. Aranda-Valera[1], J.L. Garrido-Castro[2], A.M. Galisteo[1], J. Peña-Amaro[1], C. González-Navas[2], P. Font-Ugalde[2], E. Collantes-Estevez[2]. *[1]University of Cordoba; [2]Maimonides Institute for Biomedical Research of Cordoba, Cordoba, Spain*

Background: Surface electromyography (sEMG) has been used in several studies to assess muscle activity in patients with low back pain (LBP). It has also been analyzed the lumbar flexion-relaxation phenomenon (FRP) defined by reduced lumbar erector spinae (ES) muscle myoelectric activity during full trunk flexion in healthy individuals, through the flexion relaxation ratio (FRR). In LBP patients, this relaxation, compared to the peak reached at the flexion phase, is smaller and even non-existent. There are very few studies that analyze this effect in patients with Axial Spondyloarthritis (axSpA).

Objectives: To evaluate muscular activity at the erector spinae using sEMG in patients with axSpA to analyze FRP.

Methods: 39 subjects were included: 25 patients with axSpA (49.3±5.6 years, 75% men) and 14 healthy subjects (46.7±8.7 years, 71% men) as control group. Demographic data, conventional metrology, advanced metrology using motion capture (UCOTrack) and PRO questionnaires were collected. Electrodes were placed on left and right side, at L4-L5 level and separated 2cm from the spinous process, on the ES. Muscle activity values were obtained in 4 phases (standing, flexion, relaxation and extension). With the values of flexion and relaxation, the FRR index and its inverse 1/FRR were calculated. Student t tests were used for differences between groups.

Results: There were no significant differences between the right and left sides of the measurements at ES, so mean values were considered for the analysis. There were also no significant differences in age and gender between the control group and patients. Results obtained in each of the phases are shown in the graph. The FRP appeared in healthy individuals, but not in patients, as show the FRP line in the graph: in axSpA, sEMG values at the Flexion phase are above values at the stand phase, and in control group is the opposite, so there is a truelly relaxation. There were significant differences between patients and control group in flexion, relaxation, and in the FRR and 1/FRR ratios. 1/FRR presented better correlations with several parameters (age, lateral flexion, Schöber, BASMI, BASFI, UCOASMI, BASG, all with $p<0.01$), but not with activity indexes (BASDAI, ASDAS). Distribution of 1/FRR values and results of sEMG between group (** $p<0.01$, * $p<0.05$) are shown at the chart. The area under a ROC curve to discriminate healthy patients using 1/FRR was 0.85 (95% CI 0.72–0.96 $p<0.001$).



Conclusions: In our study, there were differences between healthy and patients with axSpA in the FRP, as in other studies with LBP patients. The 1/FRR index shown the best results in correlation with other parameters and it was where major differences between groups appeared. There was good correlation with the patient global score (BASG) and with the functional BASFI index, so assessment with sEMG could be an objective and quantitative test to evaluate the patient's functional status. It would be very interesting to analyze, in future studies, the sensitivity to change to treatments which would give us a good indicator to assess their effectiveness.

Acknowledgements: This study was supported by the XXI Research Promotion Program of the University of Córdoba (Spain).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2575

SAT0392 THE DIAGNOSTIC ACCURACY OF EXISTING GRADING CRITERIA OF SACROILIAC JOINT CT IN ANKYLOSING SPONDYLITIS

D. Gao, K. Li, Y. Wang, J. Zhu, J. Zhang, F. Huang. *Rheumatology, Chinese PLA General Hospital, Beijing, China*

Background: Imaging modalities are essential for the diagnosis of ankylosing spondylitis (AS) due to the absence of specific clinical manifestations. Sacroiliac Joint (SIJ) CT has been used to identify sacroiliitis for decades with a higher diagnostic accuracy than radiography in detecting structural changes, and not reducing the specificity like MRI. However, no well-accepted grading system for SIJ CT existed.

Objectives: We evaluated the diagnostic accuracy of existing grading criteria of sacroiliitis, aiming to provide references for future better reading of SIJ CT in AS.

Methods: A total of 2714 patients who had received CT scanning for any reasons with complete SIJ structures displaying between June 2012 and December 2015 were included. The CT scans were read by 2 rheumatologists together who had received professional training in radiology. Patients with sacroiliitis were selected and bilateral SIJs of each patient were evaluated separately by the 1984 modified New York (mNY) criteria, the criteria proposed by Lee (Lee criteria)[1] and the criteria from Innsbruck workshop report (Innsbruck criteria)[2], respectively. The grading differences among these criteria were analyzed.

Results: Amount to 509 patients were detected having sacroiliitis with an average age of 34 years and 64% of male. Among 1018 SIJs of these patients, 45 SIJs graded 1∼3 by mNY criteria were graded 0 by Lee criteria, indicating the better specificity of Lee criteria. Lee criteria was much more convenient and reliable than mNY criteria for its more explicit definitions. The SIJs with definite sacroiliitis estimated by mNY and Lee criteria were 79.37% and 82.91%, respectively, and simply divided into grade 3 or grade 4. Conversely, 85.27% SIJs were identified as definite sacroiliitis and classified into 5 grades, from grade IIB to grade IVB, by Innsbruck criteria, and the percentages of each grade were 8.94%, 26.82%, 20.92%, 10.12% and 18.47%, respectively, which means a higher discrimination capability than the other two criteria. Other than graded by the extent of lesions in mNY criteria or Lee criteria, the grading assessment by Innsbruck criteria was based on the lesion types, which was more consistent with the natural progression of sacroiliitis.

Abstract SAT0392 – Table 1. The existing grading criteria of SIJ CT

mNY criteria	Lee criteria	Innsbruck criteria
0 = Normal	0 = Normal	IA = SIJ>4 mm
1 = Suspicious for erosions or sclerosis	1 = Focal erosions seen on only one of either semi-coronal or axial images	IB = SIJ<2 mm
2 = Mildly abnormal with definite erosions or sclerosis, but without alteration in the joint width	2 = ≤25% erosions*, but without alteration in the joint width	IIA = Contour irregularities
3 = Moderately abnormal with erosions or sclerosis, joint space narrowing or widening and/or partial ankylosis	3 = ≥25% erosions*, joint space alteration and/or partial ankylosis	IIB = Erosion
4 = Complete ankylosis	4 = Complete ankylosis	IIIA = Subchondral sclerosis
		IIIB = Spur formation
		IVA = Transarticular bony bridges
		IVB = Ankylosis

*Extent of erosions; (%) = number of slices with erosions/total number of slices × 100.

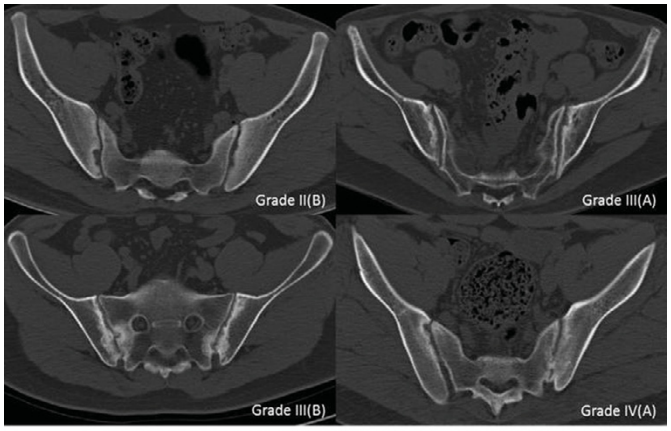


Figure 1 SIJ CT images graded 3 by mNY criteria or Lee criteria, while graded from II(B) to IV(A), respectively, by Innsbruck criteria.

Conclusions: Lee criteria has a better diagnostic specificity with a lower difficulty in the evaluation process, while Innsbruck criteria is a more detailed grading system, which has a higher consistency with the progression of sacroiliitis in AS.

References:

[1] Lee YH, et al. Rheumatol Int, 2013, 33(4): 1005–1011.
[2] Klauser A, et al. J Rheumatol 2004, 31(10): 2041–2047.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4224

SAT0393 PROTEIN FINGERPRINTING SCREENING SPECIFIC PROTEINS IN SERUM OF PATIENTS WITH ANKYLOSING SPONDYLITIS

D. Ma, L. Zhang. *Rheumatology Department, Shanxi DaYi Hospital, Shanxi Academy of Medical Sciences, Taiyuan, China*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic diseases which mainly affects the spine and sacroiliac joint. So far, the pathogenesis of AS remains elusive, making it difficult to improve early diagnosis and treatment. Proteomics is a new enabling technology to screen disease associated proteins which can be used in diagnostics or therapeutics.

Objectives:
The surface-enhanced laser desorption ionization/time of flight mass spectrometry (SELDI-TOF-MS) and protein chip screening specific biomarkers in serum of patients with ankylosing spondylitis (AS) are used to diagnose and assess the disease as well as to anticipate the program of disease.

Methods:
The serum samples of 69 AS patients, 10 rheumatoid arthritis (RA) and 12 healthy individuals were detected by SELDI-TOF-MS and weak cation exchange (WCX-2) chip. Then 69 AS patients were divided into several types such as the active and inactive stage of illness, axial arthritis involved and peripheral and axial arthritis involved, the positive and negative group of HLA-B27 to study differentially expressed proteins in the pathogenesis of AS by using Biomarker Wizard and Biomarker Pattern software of SELDI to screen the specific proteins and set up the diagnostic prediction models of disease.

Results: 1.The contents of 27 proteins between AS patients and healthy groups were significantly different. Of these proteins, 14 were up-regulated and 13 were down-regulated in patients with AS.The diagnostic model made up of 8085, 2640 and 2932 could be used to diagnose AS, which the sensitivity and specificity were 94.23% and 100% respectively.

2.The contents of 30 proteins were significantly different. Of these proteins, 14 were up-regulated and 16 were down-regulated in the active stage of AS. The diagnostic model made up of 3677, 3880, 2539, 3159 and 3242 could be used to determine the disease activity of AS, which the sensitivity and specificity were 98.11% and 100% respectively.

3.The contents of 3 proteins were significantly different. The protein of M/Z 8687 was up-regulated in the axial arthritis involved of AS, while the proteins of M/Z 4700, 18538 were down-regulated. The diagnostic model made up of the three proteins could be used to predict AS whether peripheral arthritis was involved or not, which the sensitivity and specificity were 80.00% and 82.35% respectively.

4.There were no different expressed proteins in serum between the positive and negative group of HLA-B27.

5.The contents of 23 proteins were significantly different. Of these proteins, 14 were up-regulated and 9 were down-regulated in the AS patient. The diagnostic model made up of 10259, 7972, 2048, 2154 and 2954 could be used to distinguish AS and RA, which the sensitivity and specificity were 100% and 100% respectively.

Conclusions:
The serum protein fingerprinting set up by SELDI-TOF-MS could screen new biomarkers in AS, which is expected to become a screening platform in diagnose and assessment of disease.

References:

[1] Kabeerdoss J, Kurien BT, Ganapati A, et al. Proteomics in rheumatology[J]. Int J Rheum Dis, 2015, 18(8): 815–817.
[2] Li Y, Sun X, Zhang X, et al. Establishment of a decision tree model for diagnosis of early rheumatoid arthritis by proteomic finger printing[J]. Int J Rheum Dis, 2015, 18(8): 835–841.
[3] Liu J, Zhu P, Peng J, et al. Identification of disease-associated proteins by proteomic approach in ankylosing spondylitis[J]. Biochem Biophys Res Commun, 2007, 357(2): 531–536.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3342

SAT0394 THE IMPAIRMENT OF HIP JOINTS IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS (CORSAR COHORT) BASED ON THE RESULTS OF THE TWO-YEAR OBSERVATION

D. Rumiantceva[1], T. Dubinina[1], O. Rumyantseva[1], A. Demina[1], E. Agafonova[1], S. Erdes[1], S. Krasnenko[1], A. Smirnov[2]. *[1]Laboratory of spondyloarthritis; [2]Laboratory of radiology, Nasonova Research Institute of Rheumatology, Moscow, Russia, Moscow, Russian Federation*

Background: Previous studies showed that the impairment of hip joints (HJ) - coxitis leads to a hip replacement and it is a frequent cause of early disability in patients (pts) with spondyloarthritis (SpA). Early detection of coxitis have a great clinical importance.

Objectives: To study the incidence and character of the impairment of HJ involvement in patients with early axial SpA (axSpA).

Methods: The study include 65 patients with axSpA (ASAS 2009) with disease duration <5 years and age at onset <45 years, mean age 28,5 (5,8) y., 32 (49,2%) males, 60 (92,2%) pts were HLAB27-positive, average disease duration was 24,1 (15,4) mo. The following evaluations were made: HJ pain (numerical rating scale – NRS - from 0 to 10), inter-malleolar distance (IMD), radiological HJ changes (BASRI-hip), ultrasound examination (US) and pts who had US evidence or/and clinical coxitis - MRI of hip joints. For 2 years pts taking NSAIDs at therapeutic doses. The dosages of NSAIDs accounted by the ASAS NSAID index.

Results: After 2 years follow-up reduce HJ functional limitations and pain in the

Table 1. Clinical characteristics of imparment HJ at baseline and after 2 years

	Baseline	After 2 years	P
Bilateral HJ pain, % pts	22 (33,8%)	17 (26,1%)	0,2
Pain in the right HJ, % pts	6 (9,2%)	5 (7,6%)	0,5
Pain in the left HJ, % pts	32 (49,2%)	8 (12,3%)	0,000003
HJ funcional limitations, % pts	13 (20,0%)	3 (4,6%)	0,007
Bilateral HJ funcional limitations, % pts	8 (12,3%)	3 (4,6%)	0,1
IMD, mean (s.d.)	110,8 (11,0)	110,8 (11,0)	1,0

Table 2. MRI symptoms of the impairment HJ and US symptoms of coxitis at baseline and after 2 years

	Baseline	After 2 years	P
MRI symptoms of the defeat HJ, % pts	22 (68,7%)	14 (43,7%)	0,08
Bilateral synovitis, % pts	17 (77,2%)	10 (71,4%)	0,5
One-side synovitis, % pts	4 (18,1%)	2 (14,2%)	0,5
Bilateral swelling of bone marrow in femoral head, % pts	1 (4,5%)	0	0,5
One-side swelling of bone marrow in femoral head, % pts	2 (9,0%)	0	0,2
Bilateral swelling of acetabular roof, % pts	2 (9,0%)	3 (21,4%)	0,3
One-side swelling of acetabular roof, % pts	0	1 (7,1%)	0,5
US symptoms* of coxitis, % pts	14 (21,5%)	11 (16,9%)	0,3
Bilateral US symptoms of coxitis, % pts	2 (14,2%)	4 (28,5%)	0,3
One-side US symptoms of coxitis, % pts	12 (85,7%)	7 (50,0%)	0,9

*The distance between the anterior joint capsule and the femoral neck, capsular-neck distance CND >7 mm.

left HJ (Table 1). There were no statistical differences between MRI symptoms of the impairment HJ and US symptoms of coxitis at baseline and after 2 years (Table 2).
Radiographic progression (BASRI-hip≥1 stage) after 2 years follow-up founded in 7 (31,8%) pts with MRI symptoms of the impairment HJ. There are radiographic progression from normal HJ to bilateral stage 1 in 5 (71,4%) pts, from bilateral stage 1 to bilateral stage 2 in 2 (28,6%) pts. Mean NSAID index in pts with radiographic progression (31,8%) amount 62,2%, while in pts without radiographic progression – 72,5% (p=0,2).
Conclusions: 1. In patients with early axial spondyloarthritis in two years of observation radiographic progression observed in 31,7% patients despite on regular intake of NSAIDs. 2. Further studies of the impairment HJ are required in patients with axial SpA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3985

SAT0395 SIMILARITIES AND DIFFERENCES BETWEEN NON-RADIOGRAPHIC AND RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN PROOF COHORT

D. Poddubnyy[1], R.D. Inman[2], J. Sieper[1], S. Akar[3], S. Muñoz-Fernández[4], M. Hojnik[5]. *[1]Charité Universitätsmedizin Berlin, Berlin, Germany; [2]Toronto Western Hospital, Toronto, Canada; [3]Izmir Katip Celebi University School of Medicine, Izmir, Turkey; [4]Hospital Universitario Infanta Sofía, Universidad Europea, Madrid, Spain; [5]AbbVie, Ljubljana, Slovenia*

Background: Previously, some differences between non-radiographic and radiographic axial spondyloarthritis (axSpA) – such as a higher prevalence of females and lower level of acute phase reactants in non-radiographic axSpA (nr-axSpA) – have been reported in national observational studies, mostly from Europe.
Objectives: To compare demographic and clinical characteristics of patients (pts) with nr-axSpA and radiographic axSpA (ankylosing spondylitis, AS) in a large multinational cohort of pts with recently diagnosed axSpA.
Methods: PROOF is a prospective observational study evaluating clinical and radiographic outcomes in axSpA pts in rheumatology clinical practice in 29 countries. Pts with axSpA fulfilling ASAS classification criteria were eligible if diagnosed ≤1 year prior to study enrolment. Investigator's confidence with the diagnosis of axSpA was ascertained on a numeric rating scale (NRS 0–10) at enrolment and end of follow-up. At baseline, demographic and clinical data related to the diagnosis, disease activity, quality of life and work productivity, as well as conventional radiographs of the sacroiliac joints were collected. Classification as nr-axSpA or AS was based on the results of the assessment of sacroiliac radiographs. Available radiographs were assessed first by a local reader and then by a central reader according to the grading system of the modified New York criteria. In the case of a disagreement in the classification (nr- axSpA or AS), the radiograph was evaluated by the 2nd central reader, who was blinded to the previous assessments and the final classification was made based on the decision of 2 out of 3 readers.
Results: Of the 2126 pts enrolled in PROOF, 1281 (60.3%) pts were classified as AS and 845 (39.7%) as nr-axSpA according to investigators. The confidence with the diagnosis of axSpA was 8.7±1.8. The final classification according to the central assessment of sacroiliac radiographs was confirmed in1583 pts included in this analysis. A total of 987 pts (62.3%) were classified as AS and 596 (37.7%) as nr-axSpA. AS pts expectedly had longer symptom duration, more frequently had elevated and higher CRP and were more often male and treated with TNF inhibitors (Table). In addition, HLA-B27 positivity was more frequent among AS pts, while pts with nr-axSpA had a significantly higher prevalence of enthesitis, psoriasis, and inflammatory bowel disease (IBD). The prevalence of other SpA features was comparable between the two subgroups of axSpA. Mostly, pt-reported outcomes reflecting burden of disease were comparable between the two subgroups, but BASDAI was significantly higher in the nr-axSpA subgroup (Table).
Conclusions: There were a few differences between nr-axSpA and AS pts in the PROOF cohort. The clinical constellation of female sex, low CRP, enthesitis, psoriasis, and IBD in nr-axSpA pts appears to reflect a phenotype less prone to structural damage in the sacroiliac joints. However, the clinical burden of disease was comparable between the two subgroups of axSpA.
Acknowledgements: AbbVie funded the PROOF study, contributed to its design and participated in data collection, analysis and interpretation of the data, and in writing, review, and approval of the publication. Medical writing support was provided by Deepa Venkitaramani, PhD, of AbbVie.
Disclosure of Interest: D. Poddubnyy Grant/research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, BMS, Boehringer, MSD, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, BMS, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, R. Inman Grant/research support from: AbbVie, Amgen, and Janssen, Consultant for: AbbVie, Amgen, Janssen, Lilly, Novartis, and Pfizer, J. Sieper Grant/research support from: AbbVie, Merck, and Pfizer, Consultant for: AbbVie, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Janssen, Merck, Novartis, Pfizer, Roche, and UCB, S. Akar Grant/research support from: AbbVie, BMS, MSD, Novartis, Pfizer, Roche, and UCB, Consultant for: AbbVie, BMS, MSD, Novartis, Pfizer, Roche, and UCB, Speakers bureau: AbbVie, BMS, MSD, Novartis, Pfizer, Roche, and UCB, S. Muñoz-Fernández Grant/research support from: Abbvie, BMS, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Consultant for: Abbvie, BMS, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Speakers bureau: Abbvie, BMS, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, M. Hojnik Shareholder of: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.2001

Table. Baseline demographic and clinical characteristics of patients from PROOF cohort.

Characteristic		nr-axSpA (N = 544)	AS (N = 1039)	P-value[a]
Age, years, mean ± SD		35.5 ± 9.8	34.5 ± 11.1	.070
Duration since back pain onset, months, mean ± SD		48.7 ± 69.2	62.4 ± 90.9	**.001**
Duration since diagnosis, months, mean ± SD		2.8 ± 5.6	4.0 ± 20.2	.119
Male sex, n (%)		264 (48.5)	737 (71.0)	**<.001**
SpA parameters	HLA-B27 (+), n (%)	254 (55.3)[b]	591 (69.0)[c]	**<.001**
	Inflammatory back pain, n (%)	512 (94.1)	991 (95.4)	.279
	Peripheral arthritis, n (%)	171 (31.4)	343 (33.0)	.535
	Enthesitis (heel), n (%)	214 (39.3)	348 (33.5)	**.023**
	Dactylitis, n (%)	32 (5.9)	57 (5.5)	.732
	Uveitis, n (%)	49 (9.0)	106 (10.2)	.477
	Psoriasis, n (%)	54 (9.9)	59 (5.7)	**.003**
	IBD, n (%)	23 (4.2)	18 (1.7)	**.004**
	Good response to NSAIDs, n (%)	324 (59.6)	636 (61.2)	.551
	Family history of SpA, n (%)	101 (18.6)	196 (18.9)	.946
	Elevated CRP, n (%)	178 (32.7)	555 (53.4)	**<.001**
Number of positive SpA parameters, mean ± SD		3.5 ± 1.4	3.8 ± 1.4	**.001**
CRP, mg/l, mean ± SD		11.5 ± 19.5	17.6 ± 24.3	**<.001**
ASDAS-CRP, mean ± SD		2.8 ± 1.1	3.0 ± 1.1	**.004**
BASDAI, points NRS (0-10), mean ± SD		4.8 ± 2.4	4.3 ± 2.3	**<.001**
Patient global, points NRS (0-10), mean ± SD		5.0 ± 4.8	4.8 ± 4.6	.183
BASFI, points NRS (0-10), mean ± SD		3.4 ± 2.5	3.3 ± 2.5	.815
SF-12v2, physical component score, mean ± SD		40.9 ± 8.9	41.0 ± 8.8	.698
SF-12v2, mental component score, mean ± SD		42.9 ± 10.9	43.7 ± 10.4	.166
WPAI-SHP – total activity impairment, mean ± SD		44.9 ± 28.1	43.1 ± 27.4	.208
Current Treatment	NSAIDs, n (%)	428 (78.7)	800 (77.0)	.485
	Methotrexate, n (%)	40 (7.4)	63 (6.1)	.335
	Sulfasalazine, n, (%)	117 (21.5)	253 (24.4)	.212
	Steroids, n (%)	40 (7.4)	85 (8.2)	.624
	Analgesics, n (%)	98 (18.0)	144 (13.9)	**.033**
	TNF α inhibitors, n (%)	48 (8.8)	165 (15.9)	**<.001**

[a]P-values from two-sided t-test for scale variables and Fisher's exact test for categorical variables.
[b]N = 459; [c]N = 856.
nr-axSpA = non-radiographic axial spondyloarthritis; AS = Ankylosing spondylitis; SD= standard deviation; SpA = spondyloarthritis; HLA-B27 = human leukocyte antigen B27; IBD = inflammatory bowel disease; NSAIDs = non-steroidal anti-inflammatory drugs; CRP=C-reactive protein; ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score containing CRP; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; NRS = numeric rating scale; BASFI = Bath Ankylosing Spondylitis Functional Index; SF-12v2=Short form 12-item health survey; WPAI-SHP = Work productivity impairment Questionnaire–specific health problem; TNF = tumor necrosis factor.

SAT0396 INVESTIGATION OF IRON DEFICIENCY ANEMIA IN ANKYLOSING SPONDYLITIS PATIENTS

Y. Bulut[1,2,3], D. Arslan Tas[4], O. Goruroglu Ozturk[2], U. Karaogullarindan[3]. *[1]Cukurova University, Faculty of Medicine, ADANA, Turkey; [2]Biochemistry; [3]Internal Medicine; [4]Rheumatology-Immunology Department, Cukurova University, Faculty of Medicine, ADANA, Turkey*

Background: It is reported that subclinic intestinal inflammation may occur in Ankylosing spondylitis (AS) patients, besides, using NSAIDs cause peptic and duedenal ulcers. %50–60 of AS patients have asymptomatic ileal and colonic mucosal inflammation. It is reported that inflammatory bowel disease (IBD) is found in 5–10% of AS patients and 4–10% of IBD patients have concomittant findings with AS. These conditions may cause iron deficiency anemia (IDA).
Objectives: It is well known that chronic disease anemia is a frequent finding in AS patients. But there is no study in the literature about relationship between AS patients and IDA. In this particular study we aimed to asses frequency of IDA in AS patients and to investigate the etiologies of IDA.
Methods: Ninety four consecutive AS patients who meet 2012 ASAS/EULAR criteria, who were followed Çukurova University Romatology Clinic, were icluded. We investigated the etiologies of IDA in anemic patients. Twenty six AS patients were diagnosed as IDA. Twenty six patients without anemia were assigned as a control group. Hepcidin, soluble transferrin receptor1 (sTfR1) and anemia parameters were tested in both groups. Findings were anayzed with SPSS version 23.
Results: Twenty six of 94 AS patients were diagnosed as IDA (%27). Frequency of IDA in our AS patients was higher when compared to the IDA prevalence in the society (%1–2). Endoscopy and colonoscopy were performed for searching etiology of IDA. Mucosal inflammation was found in 62% of patients by endoscopy and 11% of patients by colonoscopy. One patient was diagnosed as Crohn's disease and one patient was diagnosed as Coeliac disease histopathologically. Hepcidin was found to be significantly lower in IDA patients ($p<0.01$). We found sTfR1 levels significantly higher in IDA patients ($p<0,01$). BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and sedimentation values were found to be higher in IDA patients statistically ($p<0.01$and $p=0.01$ respectively). Although we found C- reactive protein (CRP) values were higher when compared to the non- anemic patients; however it was not statistically significant ($p>0.05$).
Conclusions: We found higher frequency of IDA when compared to the normal

population. We found that AS was more active in patients who were diagnosed as IDA. We suggest that AS activitiy may cause mucosal inflammation and subsequently may result as IDA. Also we found that mucosal inflammation in AS patients is not related to NSAIDs because there was no difference about mucosal lesions between NSAID taking and non-NSAID taking group. No study was met in the literature concerning AS and IDA. Our findings should be supported by further studies.

References:

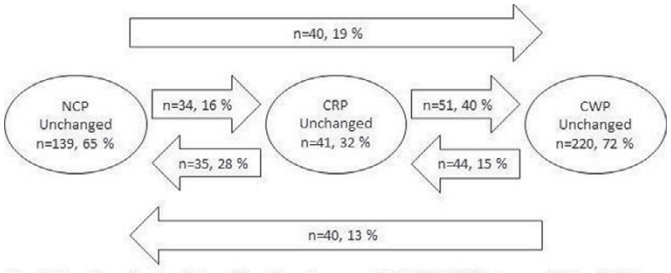
[1] Rudwaleit M, Baeten D. Ankylosing spondylitis and bowel disease. Best Pract Res Clin Rheumatol 2006; 20(3):451–71.
[2] Lanas A, Boers M, Nuevo J. Gastrointestinal events in at-risk patients starting non-steroidal anti-inflammatory drugs (NSAIDs) for rheumatic diseases: the EVIDENCE study of European routine practice. Ann Rheum Dis. 2015;74(4):675–81.
[3] Niccoli L, Nannini C, Cassarà E, Kaloudi O, Cantini F. Frequency of anemia of inflammation in patients with ankylosing spondylitis requiring anti-TNFα drugs and therapy-induced changes. Int J Rheum Dis. 2012;15(1):56–61.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5913

SAT0397 RISK FACTORS FOR DEVELOPMENT AND PERSISTENCE OF CHRONIC WIDESPREAD PAIN, IN ANKYLOSING SPONDYLITIS AND UNDIFFERENTIATED SPONDYLOARTHRITIS

E. Mogard[1], E. Lindqvist[1], A. Bremander[2,3], S. Bergman[2,4]. *[1]Department of Clinical Sciences, Section of Rheumatology and Skåne University Hospital; [2]Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund; [3]School of Business, Engineering and Science, Halmstad University, Halmstad; [4]Primary Health Care Unit, Department of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*

Background: Chronic back pain is a prominent symptom in Spondyloarthritis (SpA), and an important contributor to diminished quality of life (1,2). Chronic pain can develop in intensity, become more spread, and progress to chronic widespread pain (2). Mechanisms for this are yet inconsistent (3), and in SpA, knowledge of progression to chronic widespread pain (CWP) is lacking.
Objectives: To study the development of CWP in patients with SpA, and to identify risk factors for development and persistence of CWP.
Methods: A cohort study with baseline and 2.5-year follow-up postal surveys. 644 patients (47% women) with ankylosing spondylitis (AS) and undifferentiated spondyloarthritis (SpA) answered both surveys, and were categorized as no chronic pain (NCP), chronic regional pain (CRP), and CWP. Logistic regression analyses, with CWP as the main outcome were performed. Due to multicollinearity, each risk factor candidate (disease duration, BMI, smoking, and different patient-reported outcome measures; PROMs) were analysed in separate logistic regression models together with a base model (age, sex, and SpA-subgroup).
Results: At follow-up, prevalence estimates for NCP, CRP and CWP were similar to those at baseline, but 38% of the patients had transitioned between the groups. A large group, 72% of the patients with initial CWP, also reported persistent CWP at follow-up (Figure). Risk factors (OR and 95% CI) for development of CWP from initial NCP/CRP were more pain regions (1.36; 1.20–1.53), pain intensity (1.35; 1.20–1.52), fatigue (1.25; 1.13–1.38), global health (1.35; 1.19–1.54), EQ-5D (0.05; 0.01 – 0.19), BASDAI (1.25; 1.07 – 1.45), BASFI (1.32; 1.16 – 1.50), ASES pain (0.97; 0.96 – 0.99), ASES symtom (0.98; 0.97 – 0.99), and HADb (1.10; 1.02 – 1.19). The risk factors for persistent CWP, compared to patients transitioning to NCP or CRP, were similar to those predicting development of CWP, but in addition, also higher age (1.02; 1.00–1.04), and female sex (1.82; 1.06–3.10), predicted the outcome.



Figur 1. Transition of patients to and from the pain groups (NCP, CRP, CWP) between 2009 and 2011. Pearson Chi-Square test p≤0.001.

Conclusions: The total prevalence of CWP did not change over the study-period, although a substantial transition between the pain-groups were found. More pain regions, higher pain intensity, fatigue and worse self-reported health predicted the development into CWP, and persistent CWP. Also, higher age and female sex were risk factors for persistent CWP in SpA. Special attention in patients who report increased pain and related symtoms is essential, to early identify the development of CWP in patients with SpA.

References:

[1] Dougados M et al. The European Spondyloarthropathy Study Group preliminary criteria for the classification of spondyloarthropathy. Arthritis Rheum 1991;34:1218–27.
[2] Kiltz U et al. Do patients with non-radiographic axial spondyloarthrits differ from patients with ankylosing spondylitis? Arthritis Care Res (Hoboken) 2012;64:1415–22.
[3] Bergman S et al. Chronic widespread pain: a three year followup of pain distribution and risk factors J Rheumatol 2002;29:818–825.
[4] Larsson B et al. A systematic review of risk factors associated with transitioning from regional musculoskeletal pain to chronic widespread pain. Eur J Pain 2012;16:1084–1093.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3445

SAT0398 PREGNANCY OUTCOMES IN KOREAN WOMEN WITH ANKYLOSING SPONDYLITIS

E.H. Park[1], J.K. Jun[2], S.M. Lee[2], Y.W. Song[1], E.B. Lee[1]. *[1]Division of Rheumatology, Department of Internal Medicine; [2]Department of Obstetrics and Gynecology, Seoul National University College of Medicine, Seoul, Korea, Republic Of*

Background: Ankylosing spondylitis (AS) is a chronic, systemic, inflammatory disease that primarily affects the sacroiliac joints and spine. Despite overwhelming prevalence of AS in men, it can also occur in women. Since AS mainly affects the sacroiliac joints, a special attention should be paid to the normal labors and pregnancy outcomes in these female patients. However, very little is known about the impact of AS on pregnancy outcomes due to rare occurrence of the disease in women.
Objectives: To investigate the pregnancy outcomes in Korean female patients with AS.
Methods: All of the 27 deliveries from 20 AS female patients who had been cared at Seoul National University Hospital between February 1994 and June 2016 were retrospectively evaluated through medical record review. After matching each pregnancy of the AS women with the pregnancies of the control group on a 1 to 4 ratio based on maternal and gestational age, pregnancy outcomes of AS patients were compared with those of the control group. Pregnancy outcomes included cesarean section (CS) rate, preterm birth, low birth weight infant, fetal growth restriction (FGR), fetal malformations and preeclampsia. Each pregnancy was considered as a separate observation, and outcomes between the groups were compared by regression models estimated using Generalized Estimating Equations (GEEs) to account for the matched nature of the data. For zero events in either group in which GEE models do not converge, Fisher's exact test or Chi-square test were used.
Results: Caesarean section (CS) was performed in 44.4% of deliveries among women with AS compared with 20.4% in controls (p=0.002) (Table 1). The indications of CS included previous uterine surgery, breech position, placenta previa, placental abruption, fetal distress, and cephalopelvic disproportion (CPD), which were comparable between two groups. When excluding the cases of elective CS, 16 pregnant women with AS were tried for the vaginal delivery. Among them, 15 cases (93.8%) achieved successful vaginal deliveries, which was comparable to the successful vaginal delivery rate in controls (86/90 (95.6%), p=0.566). CS due to CPD was done in 1 case (8.3%) of AS women, while there was no case in the controls (p=0.353). Interestingly, the severity of sacroiliitis in AS patients did not show any association with CS (p=0.342). Women with AS had a higher frequency of LBW compared to the controls (22.2% vs 8.3%, p=0.024). However, there was no statistically significant difference in other adverse pregnancy outcomes, including preterm birth, FGR, fetal malformations, and pre-eclampsia.

Table 1. Overall pregnancy outcomes

Characteristics	Pregnancies with AS (n=27)	Pregnancies without AS (n=108)	*p*-value[1)]
Caesarian section delivery, n (%)	12(44.4)	22(20.4)	0.002
Fetal loss, n (%)	0(0.0)	0(0.0)	-
Maternal death, n (%)	0(0.0)	0(0.0)	-
Preeclampsia, n (%)	0(0.0)	4(3.7)	0.583*
Twin pregnancy, n (%)	5(18.5)	8(7.4)	0.016
Fetal malformation, n (%)	1(3.7)	1(0.9)	0.329
Transfusion, n (%)	1(3.7)	2(1.9)	0.577
Hospital stay, days, mean (SD)	4.1(2.9)	5.1(7.9)	0.283
Sex of child, female, n (%)**	17(53.1)	63(54.8)	0.883
Neonatal weight, g, mean (SD)**	2960.3(523.8)	3065.3(509.4)	0.370
1 min Apgar Score <4, n (%) **	1(3.1)	7(6.1)	> 0.999
5 min Apgar Score <7, n (%) **	1(3.1)	4(3.5)	> 0.999

1) P-value: calculated from regression models estimated using GEEs to account for the matched nature of the data
* P-value: calculated from Fisher's exact test because of zero events in either group in which GEE models do not converge
** Analyzed by neonates and information of twins reflected, pregnancies with AS, n=32; pregnancies without AS, n=115

Conclusions: Although pregnant women with AS are concerned about CPD during their labors due to the involvement of the sacroiliac joints, vaginal deliveries

can be tried in patients with AS. The obstetric and perinatal outcomes in women with AS were also comparable to normal pregnant women.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2511

SAT0399 HEADACHE AS A CLINICAL COMPLAINT AT INITIAL PRESENTATION AND DURING THE DISEASE COURSE IN PATIENTS WITH SPONDYLOARTHRITIS INDICATES CONCOMITANT / SECONDARY FIBROMYALGIA

E. Roussou, M. Karela, A. Georgiou. *Rheumatology, Barking, Havering and Redbridge University Hospitals NHS Trust, London, United Kingdom*

Objectives: To evaluate the symptom of headache as being able to clinically distinguish associated secondary fibromyalgia in patients with spondyloarthropathies (SpA). To compare the incidence of MSK complaints (related to SpA) in patients with headache to those that did not. To assess headache during the SpA disease course.
Methods: Registry data from 776 patients seen in clinic with SpA were analysed with reference to headache as symptom at presentation. The data of those patients presented with headache were compared with data of those patients who did not report headache with regards to demographics and disease characteristics. In addition, other MSK complaints, fatigue and pain during disease course were also analysed.
Results: From a total of 776 patients (m: f=265:508) age 48.3 (SD +14.1), 13 were excluded as no answer was recorded. 117/ 763 patients (15.08%) representing 28 males and 89 females (23.9% vs 76.1% ratio 1:3.1) reported headache at disease onset.
During the disease course, 13 patients out of the initial 117 did not record an answer to the question and were excluded. From remaining 104 patients, 95 patients (91.3%) continued to describe headache as a symptom.
From those not reporting headache as initial symptom, (n=659) 148 did not record an answer and were excluded. From the remaining 511 patients, 194 (37.9%) reported headache during the disease course.
On the data obtained from these 2 sub-groups, comparison took place using paired sample t-test.
Table shows demographics and disease characteristics as well as differences between the 2 SpA sub-groups. Those presenting with headache describe worse disease, more fatigue and a greater percentage describe pain at pressure points and MSK system.

	Headache at presentation (n=117)	No headache at presentation (n=656)	Statistical significance (p)	CI
Age (mean ± SD)	47.7 (13.16)	48.3 (14.3)	0.1	-5.757 to 0.912
Gender (M:F) ratio	28:89 (1:3.1)	219:419 (1:1.9)	0.3	-0.025 to 0.077
Disease duration (y) (mean ± SD)	11.4 (12.1)	10.9 (10.8)	0.4	-1.905 to 4.470
Delay in diagnosis (y) (mean ± SD)	6.43 (8.9)	6.3 (8.1)	0.7	-3.151 to 2.151
ESR (mean ± SD) mmHg	15.5 (14.8)	18.2 (18)	0.07	-11.064 to 0.582
CRP (mean ± SD) mg/dL	10.4 (36)	8.2 (9.8)	0.4	-6.106 to 12.536
BASDAI score (mean ± SD)	7.31 (3.7)	6.06 (2.08)	<0.005	0.783 to 2.624
BASFI score (mean ± SD)	5.6 (2.7)	5.04 (2.7)	0.09	-0.143 to 1.626
Buttock pain (%)	31.6	12.8	0.001	0.083 to 0.293
Back pain (%)	82.9	58.8	<0.005	0.125 to 0.337
Neck pain (%)	72.6	24.4	<0.005	0.340 to 0.583
Knee pain (%)	63.2	30.6	<0.005	0.284 to 0.520
Shoulder (%)	70.9	23	<0.005	0.312 to 0.559
Foot (%)	57.2	22	<0.005	0.279 to 0.524
Hip (%)	55.5	19.9	<0.005	0.217 to 0.467
Eye (%)	23	4.3	<0.005	0.102 to 0.274
Fatigue	77/116 (66.4%)	340/608 (55.9%)	0.018	0.029 to 0.299
Pain with pressure	71/117 (61.2%)	257/807 (42.4%)	0.000	0.122 to 0.378
Headache as co-morbidity	95 (109) 87.2%	195/509 (38.3%)	0.000	0.808 to 0.935

Conclusions: Headache can clinically represent secondary FM among SpA patients. A proportion of patients (representing 15%) report headache at presentation. The majority of those patients (>90%) continue to describe headache during the disease course. From those patients who did not have headache at presentation, 38% report headache during the disease course. Patients describing headache at presentation have more MSK complaints at presentation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5354

SAT0400 IS WHIPLASH INJURY A TRIGGERING OR EXACERBATING FACTOR FOR AXIAL SPONDYLOARTHRITIS?

F. Urano, S. Ono, R. Hara, M. Yasumura, T. Muramatsu, S. Suzuki. *Arthritis and Lupus Center, J a Nagano Koseiren Shinonoi General Hospital, Nagano City, Japan*

Background: Axial spondyloarthritis (AxSpA) can be triggered by infection and environmental factors, and some cases involve trauma. Whiplash injury in a traffic accident may lead to exacerbation of symptoms of AxSpA.
Objectives: The aims of this study are to survey the prevalence of trauma before or after onset of AxSpA and to examine the prevalences of neck trauma and other trauma in patients with a history of AxSpA.
Methods: The patients completed a questionnaire, and clinical presentation, inflammatory markers (ESR, CRP), radiographs, MRI of sacroiliac joints, Bath ankylosing spondylitis disease activity index (BASDAI), Bath ankylosing spondylitis functional index (BASFI), and Bath ankylosing spondylitis metrology index (BASMI) were assessed. Onset of symptoms was evaluated using European criteria for spondyloarthritis and patients were asked about mechanical stress (spinal trauma, extremity trauma, and internal organ injury). Patients with rheumatoid arthritis (RA) were included as controls and underwent the same evaluation. Patients with neck trauma were divided into four groups based on a short (<3 years) (group A) or long (≥3 years) (group B) period between disappearance of trauma symptoms and onset of inflammatory back pain (IBP); continuous IBP after trauma (group C); and a gradual change from minor symptoms to severe IBP after trauma (group D).
Results: The subjects were 124 patients with AxSpA and 102 with RA. Trauma occurred at a significantly higher rate in patients with AxSpA than in those with RA (66 (53.2%) vs. 12 (11.8%), p<0.0001). Neck trauma was also significantly more frequent in patients with AxSpA (63 (53.2%) vs. 9 (8.8%), P<0.0001) (Table 1). There were no significant differences in clinical background between patients with AxSpA with and without trauma (Table 2). Regarding the period from neck trauma to onset of IBP in patients with AxSpA, there were 4 (6.3%), 22 (34.9%), 14 (22.2%), and 23 (36.5%) cases in groups A, B, C and D, respectively.

Table 1. Prevalence of items related to mechanical stress in patients with axial spondyloarthritis (AxSpA) and rheumatoid arthritis (RA)

Item	AxSpA n (%) (95%CI)	RA n (%) (95%CI)	P value
Cases (male/female)	124 (46/78)	102 (15/87)	
Mean age (yrs)	51.8±12.9* (49.5-54.1)	66.0±11.7* (63.7-68.2)	<0.0001
Mean duration of illness (yrs)	25.8±14.4*(23.3-28.3)	23.4±10.5* (21.3-25.6)	0.1294
Trauma to date	66 (53.2%) (44.4-62.0)	12 (11.8%) (5.5-18.0)	<0.0001
Neck trauma to date	63 (50.8%) (41.2-58.8)	9 (8.8%) (3.3-14.3)	<0.0001
Neck trauma before onset	25 ** (20.2%) (13.1-27.2)	9 (8.8%) (3.3-14.3)	0.1046
Lumbar trauma	2 (1.6%) (-0.6-3.8)	1(1%) (-0.1-3.0)	0.9244
Operation before onset	33 (26.6%) (18.8-34.4)	16 (15.7%) (8.6-22.7)	0.1048
Fracture before onset	9 (7.3%) (2.7-11.8)	7(6.9%) (2.0-11.8)	0.9001

n: Number of patients, CI: confidence interval, * standard deviation, ** groups A and B

Table 2. Clinical features in patients with AxSpA and without trauma

	AxSpA with trauma average ± SD (95% CI)	AxSpA without trauma average ± SD (95% CI)	Statistical significance
ESR (mmHg/h)	10.48±9.39 (8.21-12.75)	12.84±15.32 (8.90-12.78)	ns
CRP (mg/dl)	0.23±0.42 (0.13-0.33)	0.35±0.78 (0.15-0.55)	ns
BASDAI	2.66±1.24 (2.36-2.96)	2.40±1.23 (2.08-2.72)	ns
BASFI	2.95±2.46 (2.36-3.54)	2.36±2.70 (1.67-3.05)	ns
BASMI	2.62±1.58 (2.24-3.00)	2.48±1.69 (2.05-2.91)	ns

SD: standard deviation, CI: confidence interval, ns: not significant (P>0.05)

Conclusions: The remarkable finding in this study is that half of patients with AxSpA had a history of whiplash injury. These results suggest that trauma may influence the course of AxSpA through the immunological system or hypothalamic-pituitary-adrenal axis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3953

SAT0401 PREVALENCE OF ULTRASONOGRAPHIC LOWER AND UPPER ENTHESITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

G. Cuomo [1], M. Zappia [2], M. Verde [1], D. Sgambato [2], M. Romano [2]. *[1] Dipartimento Assistenziale Integrato di Medicina Interna, UOC Medicina Interna - Università degli Studi della Campania - Luigi Vanvitelli; [2] Dipartimento di internistica Clinica e Sperimentale, Università degli studi della Campania - Luigi vanvitelli, Napoli, Italy*

Background: Spondyloarthritis (SpA) occurs in up to 20% of patients with inflammatory bowel disease (IBD) [1]. Symptomatic enthesitis is a characteristic feature of SpA and represents an early sign of SpA [2]. The prevalence of enthesitis in patients with IBD is not known.
Objectives: This study was designed to evaluate whether patients with IBD showed an increased prevalence of entheseal involvement, even in the absence of clinical symptoms.
Methods: Thirty-five IBD patients (25 M and 10 F, median age 41 yrs), 25 with Crohn's disease (CD) and 10 with ulcerative colitis (UC), all with moderate intestinal activity, and 22 (13 M and 12 F, median age 44 yrs) control subjects with irritable bowel syndrome underwent a thorough clinical evaluation followed by entheses ultrasonography of upper limb (brachial triceps) and lower limb (quadriceps, proximal and distal rotuleus, Achilles tendon and plantar fascia). The Madrid sonographic entheses index (MASEI) was used to score entheses abnormalities [thickness, enthesophytosis, bursitis, erosions with and without power doppler (PD)]. Correlation between IBD features (type, duration and

activity), age, sex and MASEI score was assessed with nonlinear Spearman's rho. Significance of differences was assessed by chi-square test. The level of statistical significance of differences was set at p

Results: All of 35 patients with IBD presented at least one entheses alteration with a mean MASEI of 5.43 (thickness 57.1%, enthesophytosis 42.8%, bursitis 0%, erosions 0%, PD abnormalities 14.2%) vs 3 patients of control group (enthesophytosis 14%) (p

Conclusions: 1) IBD patients showed a significantly higher prevalence of early entheses involvement, even in the absence of clinical symptoms; 2) the entity of entheses alteration as assessed by MASEI did not correlate with type, duration and activity of IBD; 3) age was the only variable which significantly correlated with ultrasonographic entheses involvement.; 4) we speculate that IBD patients should undergo ultrasonography evaluation of entheses and, if any alteration, be followed up for early detection of SpA.

References:

[1] Harbord M et al. J Crohns Colitis. 2016.
[2] Sakellariou G et Clin Exp Rheumatol. 2014.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4869

SAT0402 FREQUENCY AND HLA PHENOTYPE OF REACTIVE ARTHRITIS, UVEITIS, AND CONJUNCTIVITIS IN JAPANESE PATIENTS WITH BLADDER CANCER FOLLOWING INTRAVESICAL BCG THERAPY: A 20-YEAR, TWO-CENTER RETROSPECTIVE STUDY

H. Nishikawa[1], Y. Taniguchi[1], K. Inoue[1], Y. Yoshinaga[2], Y. Terada[1]. *[1]Kochi Medical school, Nankoku; [2]Kurashiki Medical center, Kurashiki, Japan*

Background: Intravesical instillation of Bacillus Calmette-Guerin (iBCG) is used as an effective immunotherapy of bladder cancer. However it may have, as adverse event, a reactive arthritis (ReA) and the frequencies are known as about 0.5 to 1% in Western countries.

Objectives: To evaluate the frequencies and HLA phenotype of reactive arthritis (ReA), uveitis, conjunctivitis and other adverse events in Japanese patients with bladder cancer following iBCG therapy.

Methods: The clinical findings of Japanese patients who received iBCG (n=555 [250 and 305 in Kochi Medical School Hospital {KMSH} and Kurashiki Medical Center {KMC}, respectively]) for bladder cancer from March 1997 to February 2016 were retrospectively assessed, with specific attention to patients with ReA and conjunctivitis/uveitis. We also looked at human leukocyte antigen (HLA) phenotypes of patients with ReA.

Results: Patient age was 73±10 and 70±11 years and male/female ratio was 198/52 and 240/65 in KMSH and KMC, respectively. 91/555 (16.4%), 121/555 (21.8%), and 196/555 (35.3%) of all enrolled patients presented with fever, haematuria, and dysuria, respectively. Of the 555 cases, ReA, uveitis and conjunctivitis were revealed in 11/555 (2.0%), 4/555 (0.7%) and 33/555 (5.9%), respectively. The frequency and the protocol of iBCG therapy were stable over the 20 years. Notably, HLA-B27, -B35, -B39 and -B51 positivity was more frequent in ReA patients (9.1%, 36.3%, 36.3% and 63.6%, respectively) ($p<0.05$) than in healthy subjects without ReA (0.3%, 8.3%, 4.0% and 9.1%, respectively).

Conclusions: The 2.0% ReA frequency in iBCG-treated Japanese patients exceeds that in Western countries. HLA phenotype, especially HLA-B51 and -B39 alleles in addition to -B27, may be a risk factor in iBCG-induced ReA in Japanese patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1768

SAT0403 ARTERIAL HYPERTENSION IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS – RESULTS OF 10-YEARS FOLLOW-UP

I.Z. Gaydukova, A. Aparkina, E. Kchondkaryan, A. Rebrov. *Hospital Therapy, Saratov State Medical University, Saratov, Russian Federation*

Background: Spondyloarthritis (SpA) (ankylosing spondylitis (AS) and psoriatic arthritis (PsA)) are associated with increased cardiovascular risk [1]. Destabilization of arterial pressure in chronic inflammation and anti-inflammatory treatment could be one of the reasons of early cardiovascular events onset.

Objectives: The purpose of this work is evaluate the occurrence and risk of arterial hypertension (AH) onset in patients with AS and PsA.

Methods: 663 patients were involved in the study: AS patients fulfilled mNew-York criteria (1984), PsA patients fulfilled CASPAR criteria (2006). Study included cross-sectional analyze, where 159 AS and 85 PsA patients participated, and 10-year prospective follow-up part, included 278 AS patients, 109 PsA patients. 276 patients were excluded due to lose the follow-up. In follow-up part of the study were involved SpA patients without AH at baseline. 182 healthy volunteers participated in the study like controls, 32 of them lost the follow-up. New cases of AH were registered after 4 and 10 years.

Statistics was performed in SPSS17 and GraphPadPrizm. All the results were adjusted to cardiovascular risk factors.

Results: Characteristics of the patients and controls with 10-years follow-up are presented in table 1.

Table 1. Baseline characteristics of the patients, involved in the study

	AS, n=278	PsA, n=109	Controls, n=150
Age, years (M ± SD)	40.0±11.4	40.55±10.6	39.0±11.2
Gender, male, n (%)	212 (76.25)#@	41 (48.2)	84 (56)
Disease duration, years (M ± SD)	13.7±10.03	14.8±14.4	–
Obesity, n (%)	32 (11.5)	24 (28.2)	22 (14.7)
Smoking, n (%)	151 (54,31)#@	30 (35,2)	40 (26,7%)

AS, ankylosing spondylitis; PsA, psoriatic arthritis; "–", absence of data. #$p<0.001$ for the difference with controls. @$p<0.001$ for the difference with PsA.

100% of patients recieved NSAIDs, 10% - glucocorticoids (5–10 mg prednisolone), 68.8% of PsA patients recieved methotrexate (10–25 mg/week), 14.3 of AS patients - sulfasalazine (2.0–3.0 g/day).

Due to cross-sectional analyses was shown that AH occurred in 48.7 of AS and in 67.5% of PsA patients, respectively, p=0.03.

Numbers of new AH cases during follow-up are presented in table 2.

Table 2. New cases of arterial hypertension in ankylosing spondylitis, psoriatic arthritis and healthy controls after 4 and 10-years of follow-up

	AS, n=278		PsA, n=85		Controls, n=150	
	4 years	10 years	4 years	10 years	4 years	10 years
AH cases, n (%)	95.0 (34.1)	139.0 (50)*	59.0 (69.4)	61.0 (71.7)*	31.0 (36.5)	31.0 (36.5)

*$p<0.0001$ for the difference with controls.

The relative risk (RR) of AH onset in patients with AS compared to healthy individuals is 2.22 (95% confidential interval (CI) 1.59 - 3.1); RR in PsA patients is 3.08 (95% CI 2.19 - 4.03), difference between risk of AH development in PsA and AS is significant, $p<0.0001$. Median to new AH cases in AS and PsA is 10±2.57 years from the first SpA symptoms appearance.

Conclusions: AH is frequently presented in PsA patients than in AS. Risk of new AH onset in patients with AS and PsA is superior compared with the healthy individuals. The number of new cases of hypertension increases with time, and in 10 years from diagnosis half of PsA/AS patients without cardiovascular disease will be in the risk of hypertension.

References:

[1] Agca R et al. Ann Rheum Dis. 2017 Jan;76(1):17–28.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6325

SAT0404 RELATIONSHIP OF SCLEROSTIN AND DICKKOPF-1 SERUM LEVELS WITH DISEASE ACTIVITY AND INFLAMMATORY MRI LESIONS IN PATIENTS WITH SPONDYLOARTHRITIS

I. Shynkaruk[1], O. Iaremenko[1], D. Fedkov[1], K. Iaremenko[2]. *[1]Bogomolets National Medical University; [2]Olexandrivska Kyiv City Hospital, Kyiv, Ukraine*

Background: Dickkopf-1 (Dkk-1) and sclerostin (Scl) are likely to play important roles in the process of ankylosis in Spondyloarthritis (SpA) [1]. Their serum levels are associated with the formation of new syndesmophytes [2]. But the relationship between these biomarkers and disease activity including active inflammatory lesions in sacroiliac joints (SIJ) on magnetic resonance imaging (MRI) still not clear.

Objectives: To estimate the relationship between the Scl and Dkk-1serum levels and active inflammatory MRI lesionsin SIJ, disease activity and functional status in SpA patients (pts).

Methods: Serum levels of Scl and Dkk-1 (pmol/l; ELISA) were measured at baseline in 79 pts with SpA. Mean age of pts (63.3% male) was 37.5±11.3, mean disease duration – 10.7±9.44 yrs. Radiological sacroiliitis defined according to Kellgren grade was: 0 – 1.6%, I – 22%, II – 49.2%, III – 13.6% and IV – 13.6%. Active inflammatory lesions in SIJ were evaluated with Spondyloarthritis Research Consortium of Canada (SPARCC) MRI SIJ score (0–72, n=46). Disease activity was measured by Ankylosing Spondylitis Disease Activity Score (ASDAS) using C-reactive protein (CRP), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI, mm), CRP (mg/l) and erythrocyte sedimentation rate (ESR, mm/hr). Functional status estimated using Bath Ankylosing Spondylitis Functional Index (BASFI, mm). For correlation the Spearman correlation coefficient was calculated.

Results: Mean value (M±σ) of biomarkers in all SpA pts were: Scl – 19.2±11.63, Dkk-1 – 30.7±19.5. The mean value of indices and laboratory parameters in all SpA pts were: ASDAS-CRP – 3.01±1.09, BASDAI – 4.36±1.88, CRP – 20.3±33.0, ESR – 25.8±20.7, BASFI – 3.01±2.33. SPARCC score was 24.6±10.9.

Scl level was significantly higher in pts with lower activity by SPARCC score (23.1±12.7) vs higher activity (16.6±7.63), p=0.043, in pts with moderate disease activity by ASDAS-CRP (22.3±15.6) vs very high disease activity (14.6±9.89), p=0.031, and in women (23.1±12.6) vs men (16.9±10.5), p=0.014. Its level didn't depend on CRP, ESR, BASDAI, BASFI and HLA B27 positivity.

Scl showed significantly negative correlation with BASDAI (r=-0.381, p=0.041) only in women.

There was no difference in Dkk-1 serum level depending on the gender, disease activity (by ASDAS-CRP), functional status, the presence of HLA B27 and inflammatory changes in SIJ (with quartile distribution). But the correlation analysis showed significant relationship of Dkk-1 with CRP (r=0.243, p=0.031) and SPARCC MRI SIJ score (r=0.351, p=0.017). The strength of the correlation between Dkk-1 and CRP was slightly higher in HLA B27 positive pts (90%; r=0.334, p=0.018).

In SpA pts with lower activity by SPARCC score significant correlation between Dkk-1 and inflammatory lesions in SIJ (r=0.400, p=0.043) and a negative correlation between Dkk-1 and BASDAI (r=-0.513, p=0.017) were found.
There was no correlation between Scl and Dkk-1 levels among all pts and different subgroups.
Conclusions: Scl level is significantly higher in pts with lower disease activity by SPARCC MRI SIJ score and ASDAS-CRP. Dkk-1 significantly positively correlates with disease activity due to CRP level and SPARCC score, but not to BASDAI.
References:
[1] Xie W. Ann N Y Acad Sci. 2016 Jan; 1364: 25–31.
[2] Song I-H. Ann Rheum Dis. 2011 Jul 1; 70(7): 1257–1263.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2430

SAT0405 CLINICAL, BIOLOGICAL AND GENETIC FACTORS, PREDICTORS OF TREATMENT NONRESPONSE TO TNF INHIBITORS (TNFI), IN ANKYLOSING SPONDYLITIS (AS) AND PSORIATIC ARTHRITIS (PSA)

J. Polo y La Borda, J. Campos, J. Sanz, J. Mulero, A. Sánchez. *Reumatología, Instituto de Investigación Biomédica, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain*

Background: TNF inhibitors (TNFi), are effective in controlling the activity of spondyloarthritis. But, there is a proportion of patients, who have to stop treatment due to its ineffectiveness or to the appearance of adverse events. In addition, these therapies imply high economic costs. To identify predictors of response, would help us to make decisions and to improve the risk/benefit ratio, in patients candidates who are candidates to initiate TNFi
Objectives: To determine clinical, biological and genetic predictors of nonresponse to treatment with TNFi in patients with AS and PsA.
Methods: We analyzed 118 patients [49 AS and 69 PsA (24 axial and peripheral involvement and 45 only peripheral)], under treatment or who were to start treatment with TNFi. Data were collected, prior to the start of the TNFi and at the last scheduled visit to the Rheumatology Service of the Hospital Puerta de Hierro, during the period 2013–2014. A clinical response was defined as the reduction ≥50% of the initial BASDAI, in patient with axial involvement, and if the final DAS 28 PCR was <2.6, in those patients with only peripheral involvement. A total of 73 men and 45 woman, mean age 53±11.2 years, and a median duration of illness of 15 years (IQR 10–23) were included. The baseline ESR and CRP were (10mm/hr IQR 5.0–27.0 and 2mg/l IQR 0.0–9.0) respectively. The mean and SD of BASDAI, DAS28 CPR and BASFI were (6.0±1.9, 3.0±0.6 and 5.4±2.5) respectively. A univariate analysis was performed using a Cox proportional hazard regression model which included: Smoker status, axial pain, peripheral arthritis, sacroiliitis, IBD, uveitis, psoriasis, HLA B27, VSG, PCR, BASDAI, BASFI, VGP, the number of TNFi and 45 single nucleotide polymorphism (SNPs) previously reported to be associated with response to TNFi. SNP genotyping was performed using de Sequenom MassARRAY plataform.Variables with a *P*-value <0.1 were included in a multivariate analysis. The discrimination capacity of the model was assessed using the Harrell C index. *P*-values <0.05 were considered statistically significant. Statistical analysis was performed with the SPSS v.17 software.
Results: The median duration of treatment was 62.9 months (IQR 40.7–96.5), the response to TNFi was 79.7% of patients, with mean and SD of BASDAI, BASFI and DAS 28 PCR (2.7±2.2, 4.2±2.8, 1.5±0.6) respectively. The factors that increased the non-response rate, were: the group of peripheral PsA versus AS (HR 2.94, *P*=0.023), VGP (HR 1.47, *P*<0.001), BASDAI (HR 1.80, *P*=0.001), BASFI (HR 1.52, *P*=0.001) and the number of TNFi used (*P*<0.001). There was a trend of significance (*P* <0.10) for females, with a 2.13-fold lower response rate than males *(P*=0.065). The SNPs associated were: rs4240847 of the *MAPKAPK2* gene (allele A, HR 1.63, *P*=0.019), rs11096957 of the *TLR-10* gene (T allele, HR 1.49, *P*=0.011), rs11541076 of the *IRAK-3* (allele T, HR 1.47, *P*=0.050), rs916344 of the *MAPK14* gene, in a recessive form,since CC alleles against CG or GG increased 10.12 times the non-response rate (HR 10,12; *P*=0.027) and rs11591741 of the *CHUK* gene (GG+GC/CC; HR 8.3, *P*=0.035).The mutivariable analysis is shown in the following table:

Table. Multivariate analysis and factors independently associated with the nonresponse rate

Variable	*P*-value	Hazard ratio	95% IC HR	
			Lower	Upper
Sex (Female/Male)	0,007	4,46	1,49	13,35
BASFI at the start of treatment	0.000	1,75	1,31	2,35
rs11591741 (GG/GC o CC)	0,022	3,83	1,21	12,12

Discriminatory capacity of the model, Harrell Index C 0.92

Conclusions: Female gender, basal BASFI elevated and SNP rs11591741 (GG) of *CHUCK* gene were identified as predictors of nonresponse to TNFi treatment in these patients.
Acknowledgements: This work has been supported by FIS (PI11/00400)
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3142

SAT0406 PREVALENCE OF VERTEBRAL FRACTURES IN AXIAL SPONDYLOARTHRITIS. A SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES

J.C. Nieto-González [1], R. Cubero [2], S. Castañeda [3], J. Ramírez [4], L. Carmona [2]. *[1] Rheumatology, Hospital G.U. Gregorio Marañón; [2] Statistics, Instituto de Salud Musculoesquelética; [3] Rheumatology, Hospital la Princesa, Madrid; [4] Rheumatology, Hospital Clinic, Barcelona, Spain*

Background: Some studies have described a higher rate of osteoporosis in axial spondyloarthritis (AxSpA). However, there are still some doubts about whether vertebral fractures (VF) should be a concern in AxSpA patients
Objectives: To evaluate the prevalence and incidence of VF in AxSpA
Methods: A systematic review was performed in Medline, Embase and Cochrane Library databases limited to studies published from Jan/2006 to Dec/2015) in Spanish, Italian and English. Search strategy combined synomyms of AxSpA, fractures, plus a filter study type. We selected cross-sectional or longitudinal studies estimating the prevalence and/or incidence of VF in adult AxSpA patients
Results: The search retrieved 3944 references which after screening by title and abstract ended in 90 studies to study in depth. Finally, 12 estudies were included. The majority of the studies evaluated the VF prevalence, and only 2 studies evaluated the incidence of VF. Prevalence estimates depended on VF definitions, varying between 4.1% (clinically diagnosed VF) and 32.4% (morphometric fracture by Genant definition). Table 1 shows all studies included and their data
Conclusions: The published studies that focus on VF in AxSpA are very heterogeneous, but in general showed a slight increase in the VF prevalence. More studies are need focused on VF incidence in AxSpA
Acknowledgements: Funding: This Project was funded by Merck Sharp & Dohme Spain. Merck Sharp & Dohme did not influenced neither the development of the review nor the confection of the abstract.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3574

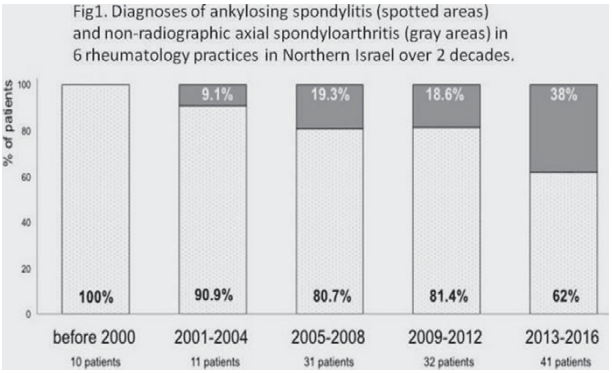
Abstract SAT0406 – Table 1

Author, year	Country/ies	Design	N	Population	Primary objective	Vertebral fracture	Incidence or Prevalence
Kang 2014	South Korea	Prospective	298	AS	VF incidence	Clinically diagnosed VF	4.1% at 2 years 13.6% at 4 years
Robinson 2013	Sweden	Cross-sectional (survey)	17764	AS	VF prevalence	Clinically diagnosed VF	4.1%
Feldtkeller, 2006	Germany Holand Belgium	Retrospective survey	1080	AS	VF prevalence and incidence	Clinically diagnosed VF	5.7% (4.3% after trauma)
Jun 2006	South Korea	Cross-sectional	68	AS	VF prevalence	Genant	16.2%
Klingberg 2013	Sweden	Cross-sectional	69	AS	VF prevalence	Genant	12%
Montala 2011	Spain	Cross-sectional	176	AS	VF prevalence	Genant	32.4% (25.5–39.3%)
Rossini 2015	Italy	Cross-sectional	71 AS 71 healthy	AS	VF and relation with bone remodeling	Genant	29%
Van der Weijden 2012	Holand	Cross-sectional	113 AxSpa 80 AS	EspAx	VF prevalence	Genant	15%
Mitra 2000	England	Cross-sectional	66 AS 39 healthy	AS (Males)	VF prevalence and relation with BMD	Mc Closkey	16.7%
Mehmet 2007	Turkey	Cross-sectional	59 AS 40 healthy	AS	VF prevalence	Tourissot	31%
Ulu 2013	Turkey	Cross-sectional	86 AS 50 Healthy	AS	VF prevalence	Tourissot	28%
Ulu 2014	Turkey	Cross-sectional Case y controls	59	AS	VF prevalence	Tourissot	32.5%

SAT0407 RISE IN THE DIAGNOSIS OF NON-RADIOGRAPHIC FORM OF AXIAL SPONDYLOARTHRITIS IN NORTHERN ISRAEL OVER TIME

K. Zilber, S. Ginsberg, D. Rimar, M. Rozenbaum, N. Boulman, L. Kaly, A. Awisat, N. Jaries, I. Rosner, G. Slobodin. *Rheumatology, Bnai Zion Medical Center, Haifa, Israel*

Background: Approach to the diagnosis of axial spondyloarthrithis (axSpA) has changed in the last decade, with the aim of diagnosing the disease in its early form.
Objectives: The objective of this study was to explore change in the diagnostic pattern of axSpA in Northern Israel over the last 15 years.
Methods: Patients with the clinical diagnosis of axSpA from six rheumatology practices affiliated with the Rheumatology Unit of the Bnai Zion Medical Center in Haifa, Israel were recruited to the study. Ankylosing Spondylitis (AS) was diagnosed in the presence of sacroiliitis grade 2 or more on X-ray films; all other patients were considered as having non-radiographic axSpA. All patients were subdivided by time periods to 5 groups, and percentages of patients diagnosed in the non-radiographic stage of the disease, as well as patient demographic data were compared using exact Fisher test.
Results: One hundred twenty five patients were subdivided to 5 groups by periods of diagnoses (before 2000, 2001–2004, 2005–2008, 2009–2012, 2013–2016). Gradual increase in a proportion of patients diagnosed with non-radiographic axSpA was observed over years, with statistical significance achieved in 2013–2016 ($p<0.05$) (Fig.1). Patients' gender and age distribution did not differ significantly among the groups.



Conclusions: Progressive increase in the proportion of patients diagnosed with non-radiographic form of axSpA over years was observed in this study. This finding, made on the basis of real life data, reflects change in the diagnostic approach to spondyloarthritis during the last decades.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5666

SAT0408 POSITIVE CORRELATION BETWEEN INFLAMMATION ON SACROILIAC JOINT MRI AND SERUM C-TERMINAL TELOPEPTIDE OF TYPE-I COLLAGEN IN ANKYLOSING SPONDYLITIS BUT NOT IN NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

K.Y. Kang [1], Y.S. Hong [2], J.H. Ju [3], S.-H. Park [3]. *[1]Division of Rheumatology, Internal Medicine, Catholic University of Korea, seoul; [2]Catholic University of Korea, Incheon; [3]Catholic University of Korea, seoul, Korea, Republic Of*

Background: The MRI-determined inflammatory score was suggested as a more objective measure of disease activity than clinical activity scores in axial spondyloarthritis. It would be useful to identify the disease activity scores and/or laboratory biomarkers that objectively reflect inflammation on MRI.
Objectives: To identify the clinical disease activity scores and laboratory markers that best reflect magnetic resonance imaging (MRI)-determined sacroiliac joint (SIJ) inflammation in ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA).
Methods: This cross-sectional study included all consecutive patients who presented with axial spondyloarthritis in 2013–2015. All underwent SIJ MRI. The bone marrow edema in the inflammatory lesions on MRI was scored using the SPondyloArthritis Research Consortium of Canada (SPARCC) method. Bone-specific alkaline phosphatase (BALP), serum C-terminal telopeptide of type-I collagen (sCTX-I), and inflammatory markers were measured. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS) were assessed. The correlations between the MRI-determined SIJ inflammation scores and disease activity scores and laboratory variables were evaluated.
Results: Of the 81 patients with axSpA, 45 had AS and 36 had nr-axSpA. The AS and nr-axSpA groups did not differ in terms of disease activity scores, physical functional index, or MRI-determined SIJ inflammation. Erythrocyte sedimentation rate, C-reactive protein, and ASDAS correlated with MRI inflammatory scores in nr-axSpA but not in AS. sCTX-I correlated with MRI-determined SIJ inflammatory scores in AS only. BASDAI and BALP levels did not associate with MRI inflammatory scores in either group. Multivariate analysis showed that sCTX-I associated independently with MRI inflammatory score in AS (β=17.047, p=0.038).
Conclusions: Inflammatory markers and ASDAS correlated with active sacroiliitis on MRI in nr-axSpA only. In AS, only sCTX-I correlated with active inflammation on SIJ MRI. sCTX-I may be useful as a marker of objective inflammation in AS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1253

SAT0409 IMPORTANCE OF ULTRASONOGRAPHY FOR THE DETECTION OF PERIPHERAL ENTHESITIS IN SPONDYLOARTHRITIS

L. Mani, K. Baccouche, S. Hmila, M. Bouhoula, B. Safaa, Z. Alaya, N. El Amri, H. Zeglaoui, E. Bouajina. *Rheumatology, Farhat Hached Hospital, Sousse, Tunisia*

Background: Peripheral enthesitis has been repeatedly described like the primary lesion in all forms of spondyloarthritis (SpA), and it may occur at any enthesis in SpA, though it is most common in the entheses of the lower limbs. Ultrasonography (US) has proved to be a highly sensitive and noninvasive tool, to assess the presence of enthesitis
Objectives: To estimate the prevalence and the US abnormalities of enthesitis in patients with SpA, compared to a control group.
Methods: We have consecutively included 40 patients with established SpA, including 30 patients with ankylosing spondylitis (AS), 8 patients with psoriatic arthritis (RP) and two patients with arthritis-associated with Crohn's disease. Control populations consisted of 20 patients with mechanical low back pain (MBP). Ultrasound (US) in B mode and power Doppler (PD) was performed at Achille tendon (AT) and plantar fascia (PF).
Results: The study sample included 40 control patients (4 male- 16 female) with a mean (SD) age of 51.05 (11.45) years (range 32–73) and mean duration of disease 8.40 (range 5–81) years.
SpA subtypes were: ankylosing spondylitis 30; psoriatic arthritis 8; arthritis-associated inflammatory bowel disease (AIBD) 2. 47.5% of entheses were tender at clinical examination. Axial form was found in 36 cases (90%) and peripheral form in 4 cases (10%).
In SpA patients, a total of 109/160 (68.12%) of the entheseal sites were abnormal compared with 27/80 (33.75%) in controls, which was statistically significantly fewer than in the SpA group for AT (p=0.000) and PF (p=0.023). Abnormal vascularization in the cortical bone insertion was found in 47 cases (29.375%) versus 4 cases in control group with a significant correlation. We also found a significant correlation for decreased echogenicity and bone erosions. No major variation in the proportion of abnormal entheses identified by US examination was observed between different forms of SpA.
US abnormalities were not correlated to the duration of the disease in patients with SpA, and there was no significant difference between US findings and either ESR, CRP, BASDAI score or BASFI score. We also, found no significant correlation between entheseal US abnormalities and the anti-TNF medications used among the SpA patients.
Conclusions: Ultrasonography can be useful for detecting subclinical enthesitis in SpA patient and the enthesis US score can be useful for improving the diagnostic of SpA.
References:
[1] Balint PV, Kane D, Wilson H. Ultrasonography of entheseal insertions in the lower limb in spondyloarthropathy. Ann Rheum Dis 2002;61:905–10.
[2] D'Agostino MA, Said-Nahal R, Hacquard-Bouder C. Assessment of peripheral enthesitis in the spondyloarthropathies by ultrasonography combined with power Doppler: a cross-sectional study. Arthritis Rheum 2003;48:523–33.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5230

SAT0410 HLA-B27 ROLE IN ANKYLOSING SPONDYLITIS PHENOTYPE: RESULTS FROM THE REGISPONSER DATABASE

M. Arevalo [1], P. Font [2], M. Moreno [1], D. Ruiz [2], M. Castro [2], P. Carreto [3], M. Larrosa [1], E. Collantes [2], J. Gratacós [1] on behalf of REGISPONSER group. *[1]Rheumatology, Parc Taulí Hospital Universitari. Institut d'Investigació i Innovació Parc Taulí I3PT. Universitat Autònoma de Barcelona. Sabadell, Spain, Sabadell; [2]Rheumatology, Hospital Universitario Reina Sofía/IMIBIC/Universidad de Córdoba., Córdoba; [3]Gerency MFyC de Valladolid East Area, Valladolid, Spain*

Objectives: To assess if there are different phenotypical patterns of Ankylosing Spondylitis (AS) patients depending on the positivity or negativity of HLAB27.
Methods: This is a multicentric, observational, transversal and descriptive study of AS patients from the spanish database REGISPONSER. We compared HLAB27 positive and HLAB27 negative patients regarding clinical and demographical data, disease activity and structural damage. In order to assess disease activity we used the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and acute phase reactants (VSG and PCR). Functional disability was measured by Bath Ankylosing Spondylitis Functional Index (BASFI), and structural damage by Bath Ankylosing Spondylitis Radiology Score (BASRI). For qualitative variables we used the Chi square test and for quantitative ones the t test. An univariate

and multivariate comparative analyisis was performed, in order to define which variables were related to the negativity or positivity of HLAB27.
Results: Data of 1235 AS pacients were analysed. Of them 1029 (83.3%) were HLAB27 positive and 206 (17.7%) HLAB27 negative. 924 (74.8%) were men. AS patients with HLAB27+ presented significantly more familiar history of spondyloarhritis (p=0.002), were younger (p=0.012) and had earlier disease onset and disease diagnosis (p<0.001), with a longer disease duration (p=0.037) and a trend to a higher percentage of uveitis compared to those with HLAB27-. On the other hand, AS patients with HLAB27- also presented significantly more peripheral arthritis (p=0.0022), dactylitis (p=0.001) and extraarticular manifestations (psoriasis, palmoplantar pustulosis, inflammatory bowel disease (IBD) and balanitis (p<0.001)) compared with those of HLAB27+. AS patients with HLAB27- also presented higher scores of BASDAI and BASFI (p=0.047 and p=0.005 respectively). The study didn't show differences between both groups of patients regarding sex distribution, axial manifestations, enthesitis nor radiological damage (assessed by BASRI). In the multivariate analysis, the family history of spondyloarthritis (OR 2.10, IC95% 1.27–3.49, p=0.004), the age at diagnosis (OR 0.97, IC95% 0.96–0.98, p<0.001), the presence of dactylitis (OR 0.16, IC95% 0.05–0.56, p=0.004), extraarticular manifestation specially IBD (OR 0.22, IC95% 0.12–0.40, p<0.001) and peripheral arthritis (OR 0.53, IC95% 0.32–0.89, p=0.016) were the variables independently associated with the presence of HLAB27.
Conclusions: The presence of HLAB27 in AS patients is associated to an earlier disease onset, a higher frequency of familiar history of spondyloarthritis, and a lower frequency of dactylitis, extraarticular manifestations and peripheral arthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1928

SAT0411 CORRELATION BETWEEN DISEASE ACTIVITY SCORES AND QUALITY OF LIFE IN SPONDYLOARTHRITIS

M. Linda, K. Baccouche, S. Lataoui, S. Belghali, Z. Alaya, N. El Amri, H. Zeglaoui, E. Bouajina. *Rheumatology, Farhat Hached Hospital, Sousse, Tunisia*

Background: Spondyloarthritis (SpA) is a group of chronic inflammatory rheumatism and it is known to be one of the leading causes of disability.
Objectives: This study aimed to investigate the quality of life and the psychological disorders (depression, anxiety and insomnia) in patients with SpA.
Methods: A total of 60 patients were included with the diagnosis of SpA meeting the Amor and New York modified criteria, in a prospective study. In a questionnaire, the characteristics of the disease and sociodemographic patient were collected. Also psychiatric assessment was done using the insomnia severity index score (ISI) and the Hospital Anxiety and Depression scale (HAD). In addition, patients answered to the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire and the SF-12.
Results: The sex-ratio (men/women) was 3.28 (46/14), the average age was 37.95 years (18–70). The average duration of disease progression was 11.5 years (1–30). The mean value of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was 5.11 and the Bath Ankylosing Spondylitis Functional Index (BASFI) was 5.22. Uveitis was reported in 11.7% of patients, osteoporosis in 35%, enthesitis in 36.7% and coxitis in 36.7%. 78.3% of patients received NSIAD and 30% were treated with biotheraby. On the psychological level, 25% of patients had an anxiety, 20% had depression. According to the ISI, 35% of patients had sub threshold insomnia, 20% had moderate insomnia and 10% had severe insomnia. The mean value of the ASQoL was 9 (0–16). The mean value of the physical health was 37.13 (19.34–60.41) and for the mental health was 41.65 (14.9–60.35). A significant positive correlation was found between the disease activity and the ASQoL (p=0.000), the physical health (p=0.000) and the mental health (p=0.002). Also, we found a significant positive correlation between the BASDAI and depression (p=0.01) and insomnia (p=0.001).
Conclusions: SpA is a chronic inflammatory disease that contributes to significant physical disability and decreased quality of life in a significant number of patients. The treatment of those patients must consider the improvement of quality of life, as part of a global approach.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6394

SAT0412 ASSOCIATION BETWEEN SMOKING WITH SPINAL LEVEL OF STIFFNESS AND FUNCTIONAL LIMITATION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE SPANISH ATLAS

M. Garrido-Cumbrera[1], J. Chacón-García[1], J. Gratacos-Masmitja[2], D. Galvez-Ruiz[1], V. Navarro-Compan[3], C. Blanch-Mur[4], E. Collantes-Estevez[5], P. Zarco-Montejo[6], O. Brace[1]. *[1]Universidad de Sevilla, Seville; [2]H. Parc Taulí, Sabadell; [3]H. la Paz, Madrid; [4]Novartis, Barcelona; [5]Universidad de Córdoba, Cordova; [6]H. Fundación Alarcón, Madrid, Spain*

Background: Smoking has been associated with greater disease activity and radiographic progression in patients with Axial Spondyloarthritis (ax-SpA). In addition, radiographic damage has been linked to greater functional limitation. However, clarification is still being sought as to whether or not this association exists.
Objectives: To investigate the association between smoking and both the area of spinal stiffness and functional limitation in patients with ax-SpA.
Methods: A sample of 680 patients diagnosed with ax-SpA was interviewed during 2016 as part of the Spanish Atlas, which aims to promote early referral and improve healthcare and the use of effective treatments in patients with ax-SpA. Tobacco consumption was recorded as: Smoker (62.4%), Occasional Smoker (8.9%) and Non-Smoker (28.7%). Spinal stiffness was assessed in the three different vertebral areas: cervical, dorsal and lumbar.
To determine de degree of functional limitation we used a composed index which includes the sum of the degree of limitation in the 18 daily activities well established (dressing, grooming, bathing, tying shoelaces, moving around the home, stairs, getting to/out of bed, toilet, shopping, preparing meals, eating, cleaning, walking, using public transportation, going to the doctor, driving, physical exercise, sexual relations) using an ordinal variable (0=none, 1=little, 2=some and 3=moderate). A descriptive analysis was used to compare the level of stiffness (chi-squared test) and the mean degree of limitation (Kruskal-Wallis test) in the different groups of smokers consumptions. Regression analysis was also used to assess the relation between smoking and degree of limitation (0–54).
Results: 53% were females, mean age 46 years and 77.1% were HLA-B27+. The percentage of patients with stiffness in the lumbar region was significantly higher in habitual/occasional smokers than in non-smokers (89.0%, 93.8%, 83.5% respectively; p<0.01) (Table). The mean degree of functional limitation increased with tobacco consumption, although this difference was not statistically significant (47.9±12.1 vs. 45.1±11.5 vs. 44.8±13.7 respectively; p=0.2). However, regression analysis showed a statistically significant correlation between smoking and functional limitation (r=0.096; p=0.02).

Relationship between tobacco consumption and spinal stiffness levels in patients with ax-SpA

	Smoker	Occasional smoker	Non smoker	*P*	χ^2
Cervical stiffness	84.2%	77.1%	73.1%	0.171	9.044
Dorsal stiffness	76.0%	76.6%	72.4%	0.408	6.141
Lumbar stiffness	89.0%	93.8%	83.5%	0.002	20.518

Source: Spanish Atlas.

Conclusions: Smoking in patients with ax SpA is associated to greater stiffness in the lumbar region, but is not related to stiffness in the cervical or dorsal regions. Additionally, smoking is associated to the degree of functional limitation in these patients.
Acknowledgements: This project has been supported by Novartis
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6519

SAT0413 INFECTIOUS PROFILE IN A TUBERCULOSIS-ENDEMIC POPULATION WITH SPONDYLOARTHROPATHIES

M.A. Alzate[1,1], F. Ramirez[2], F. Vargas[2], D. Hernandez-Parra[1], J.C. Salazar-Uribe[3], P. Ortiz-Salazar[1], R. Pineda[1] on behalf of Artmedica IPS, Medellin, Colombia. *[1]Clinical information group; [2]Rheumatology division, Artmedica IPS; [3]School of Statistics, Faculty of Sciences, National University of Colombia, Medellin, Colombia*

Background: Screening latent tuberculosis (TB) and other opportunistic infections in patients with spondyloarthropathies (SpA) with biologic or immunosuppression therapy is important in highly endemic population (1).
Objectives: To assess the prevalence of latent and active TB, hepatitis B, hepatitis C, HIV and Syphilis in a colombian cohort with SpA, as well as evaluate differences between treatments.
Methods: A cross-sectional study was conducted in 621 patients with SpAs, in whom TB, hepatitis B, hepatitis C, HIV and syphilis screening was analyzed based on type of diagnosis. Differences among immunomodulatory therapies were assessed. Statistical association was examined by means of Chi-square tests, Mann-Whitney test, and logistic regression analyses.
Results: The prevalence of latent and active TB in this cohort were 63,1%, and 2,9%, respectively. Significant differences were found in proportions of latent and active TB among types of SpAs, indicating a positive association with AS. A high

Table 1. Infectious profile in colombian patients with SpAs

	All N=621		AS N=340		PsA N=222		Und SpA N=59		p-value
	N	%	N	%	N	%	N	%	
Latent TB	251/398	63,1	156/244	63,9	76/126	60,3	19/28	67,9	0,009
Positive TST before immunotherapy	175/398	44	98/244	40,2	64/126	50,8	13/28	46,4	0,64
TST conversion during immunotherapy	76/398	19,1	59/244	24,2	13/126	10,3	4/28	14,3	<.0001
Active TB	18	2,9	12	3,5	4	1,8	2	3,4	0,03
Latent TB conversion to active TB	7	1,1	6	1,8	1	0,4	0	–	0,04
Active TB during immunotherapy	11	1,8	10	2,9	1	0,4	0	–	0,008
Hepatitis B	11/400	2,8	4/241	1,7	6/128	4,7	1/31	3,2	0,32
Hepatitis C	2/400	0,5	2/241	0,8	0/128	–	0/31	–	0,61
VDRL test	2/285	0,7	1/167	0,6	1/94	1,1	0/24	–	0,38
HIV	3/330	0,9	2/197	1	0/111	–	1/22	4,5	0,14

Ankylosing spondylitis (AS), psoriatic arthritis (PsA), undifferentiated spondyloarthritis (Und SpA), tuberculin skin test (TST).

proportion of TST conversion during immunotherapy was found. According to the immunomodulatory therapy, no differences were found among latent TB patients, active TB disease and no infection with the use of conventional DMARD therapy, but a positive association between latent TB and the use of biologic therapy was recognized. Low prevalences of opportunistic infections (i.e., Hepatitis B and C, syphilis and HIV) were found in this cohort, dispite the frequent use of biologic therapy.

Conclusions: In a TB-endemic population, higher prevalences of latent and active TB were found in patients with SpAs, when compared to the general population. Complete infectious screening is mandatory in patients under consideration of biologic agents, and close follow-up must be done to recognize TST conversion.

References:

[1] Pérez-Díaz CE, Uribe-Pardo E, Calixto OJ, Faccini-Martínez ÁA, Rodriguez-Morales AJ. Infections with biological therapy: strategies for risk minimization in tropical and developing countries. J Infect Dev Ctries. 2016;10(12).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3752

SAT0414 DIFFERENCES IN CLINICAL PRESENTATION BY GENDER IN COLOMBIAN PATIENTS WITH SPONDYLOARTHROPATHIES

M.A. Alzate[1], F. Vargas[2], F. Ramirez[2], D. Hernandez-Parra[1], J.C. Salazar-Uribe[3], P. Ortiz-Salazar[1], R. Pineda[1] on behalf of Artmedica IPS, Medellin, Colombia. *[1]Clinical information group; [2]Rheumatology division, Artmedica IPS; [3]School of Statistics, Faculty of Sciences, National University of Colombia, Medellin, Colombia*

Background: Spondyloarthropathies (SpAs) are a group of auto-inflammatory diseases, with overlapping symptoms, that include ankylosing spondylitis (AS), psoriatic arthritis (PsA), undifferentiated spondyloarthritis (Und SpA), enteropathic arthritis, and reactive arthritis (1). Historically, SpAs have been viewed as diseases that predominantly affected men (2).

Objectives: To analyze the influence of gender on disease patterns and therapeutic approach in a large cohort of Colombian patients with SpAs.

Methods: A cross-sectional study was conducted in 621 patients with SpAs, in whom clinical and therapeutic characteristics were analyzed based on gender. Statistical association was examined by means of Chi-square tests, Mann-Whitney test, and logistic regression analyses.

Results: The male-to-female ratio was 1,1:1 in this cohort. Younger age at diagnosis was found in males. AS was the most frequent disease (54,7%), followed by PsA (35,7%), and undifferentiated SpA (9,5%). The male gender was positively associated to the presence of AS (OR 2,29 95%IC 1,31–4,04), radiographic sacroilitis (OR 3,46 95%IC 1,82–6,56), HLAB27 positivity (OR 1,95 95%IC 1,31–2,91), low back pain (OR 1,85 95%IC 1,34–2,54) and axial involvement (OR 1,98 95%IC 1,42–2,77). According to the therapeutic profile, female gender was positively associated to the use of conventional DMARD therapy (i.e., methotrexate (p=0,03), leflunomide (p=0,0057), chloroquine (p=0,013)), while male patients were more associated to the use of biologic therapy.

Table 1. General characteristics of patients with SpAs by gender

	All (N=621)		Male (N=328)		Female (N=293)		p-value
Age (mean)	49,4		48,6		50,2		0,15
Age at diagnosis (mean)	38,9		37,2		40,6		**0,0042**
Years of evolution (mean)	9,8		10,6		9,1		**0,02**
	N	%	N	%	N	%	
Age at onset <45 years	469	75,5	257	78,3	212	72,3	0,008
Diagnosis							
AS	340	54,7	208	63,4	132	45,1	
PsA	222	35,7	96	29,2	126	43	**<0.0001**
Und SpA	59	9,5	24	7,3	35	11,9	
Low back pain	342	55,1	204	62,2	138	47,1	**0,0002**
Arthritis	411	66,2	215	65,5	196	66,9	0,72
Enthesitis	217	34,9	125	38,1	92	31,4	0,08
Dactylitis	116	18,6	54	16,4	62	21,2	0,13
Uveitis	92	14,8	52	15,8	40	13,6	0,44
Psoriasis	225	36,2	98	29,8	127	43,3	**0,0005**
Sacroilitis (Rx)	70/171	40,9	46/82	56,1	24/89	26,9	**0,0001**
Sacroilitis (MRI)	203/279	72,7	102/136	75	101/143	70,6	0,41
HLA-B27	284/438	64,8	176/246	71,5	108/192	56,2	**0,0009**
Axial	397	63,9	234	71,3	163	55,6	**<0.0001**
Peripheral	488	78,6	254	77,4	234	79,8	0,46
Both	264	42,5	160	48,8	104	35,5	**0,0008**

Conclusions: In this Colombian large sample with SpA, male patients have a younger onset of disease, higher proportion of axial involvement, HLAB27 positivity, evidence of radiographic sacroilitis and higher use of anti-TNF therapy.

References:

[1] Roussou E, Sultana S. Spondyloarthritis in women: differences in disease onset, clinical presentation, and Bath Ankylosing Spondylitis Disease Activity and Functional indices (BASDAI and BASFI) between men and women with spondyloarthritides. Clin Rheumatol. 2011;30(1):121–7.

[2] Ibn Yacoub Y, Amine B, Laatiris A, Hajjaj-Hassouni N. Gender and disease features in Moroccan patients with ankylosing spondylitis. Clin Rheumatol. 2012;31(2):293–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3560

SAT0415 HIGH PREVALANCE OF HIP ARTHRITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TNF INHIBITORS

M. Konsta[1,2], M.T. Nurmohamed[2], A. Iliopoulos[1], J.C. van Denderen[2], I. Visman[2], P.P. Sfikakis[1], I.E. van der Horst-Bruinsma[2]. *[1]First Department of Propaedeutic Internal Medicine, Rheumatology Department, Joined Rheumatology Program, National and Kapodistrian University of Athens, Medical School, Athens, Greece; [2]Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands*

Background: Hip involvement is the most frequent extraspinal arthritic manifestation of Ankylosing Spondylitis (AS) and a common cause of disability. It is present in 24% to 36% of AS patients, leading to total hip replacement (THR) in 5%.

Objectives: To examine the prevalence of hip arthritis in patients with AS under TNF-inhibitor (TNFi) treatment, to identify predictors of its development and possible gender differences.

Methods: Consecutive TNFi-naïve AS patients (fulfilling the modified New York criteria) who were eligible for TNFi treatment were included. At baseline (before the start of TNFi), disease activity and function were recorded by BASDAI, ASDAS-CRP/ESR, BASFI and BASMI. Anteroposterior x-rays of the pelvis and lateral x-rays of cervical and lumbar spine were obtained at baseline and scored according to the BASRI-hip scoring system and mSASSS. Hip involvement was assessed both clinically (as pain, reduced range of motion and intermalleolar distance) and radiographically (BASRI-h score $\geq$2 was defined as definitive hip involvement). Mann-Whitney, two-sample t-test and logistic regression analysis were applied. The groups' averages were expressed as mean±SD, or median (IQR) according to the normality of data.

Results: 298 consecutive AS patients (214 men, age: 49±12years (mean±SD), disease duration: 23.8±11.8 years) were included. Definite hip involvement was detected in 113/298 (38%) patients. Bilateral THR and unilateral THR underwent 10/298 (3.4%) and 9/298 (3%) patients respectively. No gender difference in the prevalence of hip arthritis was observed (females: 26/84 (31%) vs. males 87/214 (40.8%). The patients with hip arthritis compared to those without had significantly higher disease activity scores (BASDAI (6.1±1.7 vs. 5.5±1.9, p=0.008), ASDAS-CRP (3.9±0.8 vs. 3.4±0.9, p=0.0001), CRP [16 (7.7–32) median (IQR) vs. 7 (2.9–22), p=0.0001], ESR [26 (10–42) vs. 15.5 (7–33), p=0.004], higher BASFI-scores (6.3±2.1vs. 4.8±2.3, p<0.0001), BASMI-scores (5.1±2.3vs. 3.4±2, p<0.0001) and reduced intermalleolar distance (89±23 vs. 104.8±19 cm, p<0.0001). AS patients with hip arthritis also had significantly higher mSASSS-scores [15 (3- 39) vs. 4 (0–16), p<0.0001] more often syndesmophytes [75/107 (70.1%) vs.75/181 (41.4%), p<0.0001] and peripheral arthritis [54/111 (48.7%) vs. 68/184 (37%), p=0.048). According to multivariate logistic regression analysis, independent risk factors for hip arthritis were: raised CRP (OR: 1.01 CI: 1.001–1.02), presence of syndesmophytes (OR: 2.6, CI: 1.45–4.8) and a high BASFI (OR: 1.33, CI: 1.1–1.5).

Conclusions: The prevalence of hip arthritis in AS is very high (1/3) and significantly related to high disease activity and a high mSASSscore. No gender difference in prevalence of hip arthritis was found. Considering the large impact on function, this manifestation might need more attention.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6844

SAT0416 ANKYLOSING SPONDYLITIS DISEASE ACTIVITY SCORE (ASDAS) IS ASSOCIATED WITH NSAID USE OVER TIME

M.J. Carbo[1], S. Arends[1,2], F. Maas[1], E. Bouwer[1], R. Bos[2], H. Bootsma[1], E. van der Veer[3], F. Wink[2], A. Spoorenberg[1,2]. *[1]Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen; [2]Rheumatology, Medical Center Leeuwarden, Leeuwarden; [3]Laboratory Medicine, University Medical Center Groningen, Groningen, Netherlands*

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are the cornerstone of conventional treatment in ankylosing spondylitis (AS). In case of insufficient response, tumor necrosis factor-alpha (TNF-α) inhibitors are available. Still little is known about concomitant NSAID use.

Objectives: To investigate the longitudinal association between disease activity and NSAID use in established AS patients.

Methods: The present analysis is part of the GLAS cohort, an ongoing longitudinal observational axial spondyloarthritis (SpA) cohort study in daily clinical practice. During 52 weeks of follow-up, NSAID use was recorded prospectively. The ASAS-NSAID index was calculated using the dosage and frequency assessed retrospectively from clinical records. Disease activity was assessed using ASDAS, BASDAI, and serum CRP levels.

Generalized estimating equations (GEE) was used to evaluate NSAID use in relation to assessments of disease activity over time. NSAID use was analyzed using 4 parameters: NSAID use (yes/no), ASAS-NSAID index, low on demand use (index $\geq$10 versus <10), and high use (index $\geq$90 versus <90). Analyses were stratified for treatment regimen: patients starting TNF-α inhibitors and patients on conventional treatment.

Results: Of the 393 included AS patients, 67% were male, mean age was 44±13 years, median symptom duration 15 years (IQR 8–24), and 79% were

HLA-B27 positive. In total, 254 (66%) patients started TNF-α inhibitors and 139 (34%) patients received conventional treatment. Patient characteristics were comparable between both groups, except higher disease activity, more often peripheral arthritis, and worse physical functioning in patients starting TNF-α inhibitors. NSAID use and disease activity reduced significantly after starting TNF-α inhibitors and remained low and stable during follow-up. In the conventional treatment group, disease activity was low and NSAID remained stable at all visits. GEE analysis over time showed that NSAID use was significantly associated with disease activity (Table 1). In the TNF-α inhibitor group, a significant association of all NSAID parameters with ASDAS was found: NSAID use yes vs. no, ASAS-NSAID index, index ≥10 vs. <10, and index ≥90 vs. <90. Comparable results were found for BASDAI and CRP. The association between NSAID use and ASDAS remained significant in the 217 patients who used TNF-α inhibitors more than 80% of the follow-up time and when analyzing only 12 to 52 weeks of follow-up to exclude the initial effect of TNF-α inhibitors, although the regression coefficients were lower in these last analyses. In the conventional treatment group, a significant but less prominent association of NSAID parameters with ASDAS was found: NSAID use yes vs. no, index ≥10 vs. <10, and index ≥90 vs. <90. BASDAI was only significantly associated with on demand NSAID use. For CRP, no significant associations with NSAID use were found.

Table 1. Association between ASDAS and NSAID use over time in AS patients.

		B (95% CI)	P-value	Interval	n
TNF-α Inhibitors					
NSAID use Yes	Complete group	0.825 (0.664-0.985)	**<0.001**	1074	251
ASAS-NSAID index	Complete group	0.009 (0.007-0.012)	**<0.001**	1073	251
	TNF-α≥80%*	0.011 (0.009-0.013)	**<0.001**	953	214
	12-52 weeks**	0.005 (0.003-0.007)	**<0.001**	633	246
ASAS-NSAID index≥10	Complete group	0.831 (0.672-0.990)	**<0.001**	1073	251
ASAS-NSAID index≥90	Complete group	0.855 (0.682-1.028)	**<0.001**	1073	251
Conventional treatment					
NSAID use Yes	Complete group	0.250 (0.006-0.493)	**0.045**	315	131
ASAS-NSAID index	Complete group	0.002 (0.000-0.005)	0.059	314	131
ASAS-NSAID index≥10	Complete group	0.223 (0.022-0.425)	**0.030**	314	131
ASAS-NSAID index≥90	Complete group	0.269 (0.038-0.501)	**0.023**	314	131

*Subgroup analysis of patients who used TNF-α inhibitors ≥80% of the follow up time. ** Analysis for 12 to 52 weeks of follow-up (excluding baseline and 6 weeks).

Conclusions: In this observational cohort of established AS patients, NSAID use over time was significantly associated with ASDAS, which was most pronounced for patients treated with TNF-α inhibitors.

Acknowledgements: The GLAS cohort was supported by an unrestricted grant from Pfizer. Pfizer had no role in the design, conduct, interpretation, or publication of this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1971

SAT0417 GRADUAL PROGRESSIVE CHANGE TO EQUAL PREVALENCE OF ANKYLOSING SPONDYLITIS AMONG MALES AND FEMALES IN SWITZERLAND: DATA FROM THE SWISS ANKYLOSING SPONDYLITIS SOCIETY (SVMB)

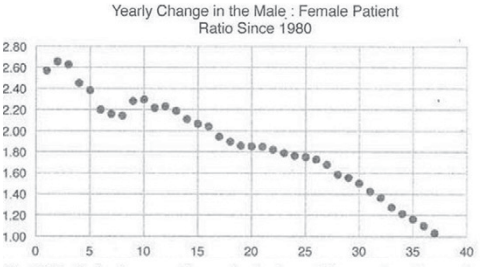
H. Baumberger[1], M.A. Khan[2]. *[1]PhD. First president of, Schweizerische Vereinigung Morbus Bechterew, Zurich, Switzerland; [2]Professor Emeritus of Medicine, Case Western Reserve University, Cleveland OH, United States*

Background: Classic ankylosing spondylitis (AS) with radiographic sacroiliitis has long been considered to be more common in men than women. But this difference has gradually decreased with increasing recognition of this condition in women so that the more recent data suggest a range of 2:1 to 1.2:1 ratio in favor of men [1].

Objectives: To document greater disease recognition in women during the last 30 years in Switzerland as reflected by AS patient membership in the Swiss Ankylosing Spondylitis Society (SVMB) since its foundation in 1978 [2].

Methods: We reviewed the Society's quarterly newsletters that have kept record since 1980 not only of the number of members, but also the percentage of males and females AS patients. We calculated yearly AS patient membership and also change in the male/female patient ratio (M:F).

Results: There has been a progressive decline in the M:F ratios since 1980 as shown in the Figure. There were 44 female forming 28% of the patient population, with a M:F ratio of 2.57 in 1980. At the end of 2016, there are 1731 females forming 49% of the total number of patients, and the M:F ratio is now 1.03.



The M:F ratio is shown on the vertical axis, and the number of years is shown on the horizontal axis.

Conclusions: AS is now being recognized as often in females as in males, as reflected in the membership of SVMB over the last 36 years. There can be various reasons for this observation, one of them being the availability of better imaging tools to recognize AS/axial spondyloarthritis (axSpA), especially among women whose disease is clinically and radiologically less pronounced and is therefore often overlooked [2]. For example, the use of MRI (for early detection of spinal inflammation) and the ASAS criteria have resulted in >50% females in a German cohort of patients with nonradiographic axSpA [3]. SVMB has played a major role in achieving greater disease recognition in Switzerland by increasing disease awareness and educating patients and their families, the general public, the governing bodies and the allied health professionals about AS, and by interacting closely with rheumatologists. Other possible factors influencing our data include: women outliving men, forming a little greater percentage of the general population, and possibly more likely to join patient self-help groups and societies, We did not investigate any gender difference in disease severity and clinical presentation. In conclusion, AS/axSpA almost equally afflicts men and women in Switzerland.

References:

[1] Khan MA. Accomplishments of Heinz Baumberger PhD: a remarkable patients with ankylosing spondylitis for 72 years. Clin Rheumatol. 2016;35(6):1637–41.
[2] Khan M.A. Ankylosing Spondylitis - Axial Spondylitis. Professional Communications Inc. 2016. pp. 1–333.
[3] Rudwaleit M, et al. The early disease stage in axial spondylarthritis: results from the German Spondyloarthritis Inception Cohort. Arthritis Rheum. 2009;60:717–27.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3961

SAT0418 ANXIETY AND DEPRESSION ON DISEASE ACTIVITY AND QUALITY OF LIFE OF SPONDYLOARTHRITIS PATIENTS UNDER BIOLOGIC THERAPIES

N. Madeira[1], J. Borges[1], A. Cardoso[2], L. Miranda[1], F. Barcelos[1], C. Miguel[1], C. Silva[1], S. Fernandes[1], R. Trinca[3], D. Medeiros[1], R. Campanilho-Marques[1], H. Santos[1], R. Leitão[1], A. Faustino[1]. *[1]Rheumatology; [2]Nutrition; [3]Nursing, Instituto Português de Reumatologia, Lisbon, Portugal*

Background: Several studies describe an association between anxiety, depression and disease activity in Spondyloarthritis (SpA).

Abstract SAT0418 – Table 1. Comparison of anxious vs non-anxious and depressive vs non-depressive patients

	HADS-A<8	HADS-A ≥8	*p*-value	HADS-D<8	HADS-D≥8	*p*-value
Current age, mean±SD (years)	48.9±11.9	52.6±10.8	0.045	49.2±11.4	53.2±11.5	0.072
Age at diagnosis, mean±SD (years)	34.3±11.9	40.2±11.5	0.004	34.9±11.5	40.9±12.5	0.015
Age at 1st bDMARD, mean±SD (years)	44.0±11.9	48.7±10.64	0.013	44.7±11.5	48.7±11.6	0.059
HADS-A, mean±SD	3.2±2.1	10.2±2.1	–	4.5±3.4	9.7±3.1	<0.001
HADS-D, mean±SD	2.9±3.3	8.3±2.7	<0.001	2.98±2.5	10.3±2.3	–
ASQoL, mean±SD	3.12±3.8	10.6±4.5	<0.001	4.6±4.7	9.63±5.8	<0.001
BASMI, mean±SD	3.1±1.8	3.9±1.6	0.003	3.2±1.7	3.9±1.6	0.016
BASFI, mean±SD	1.7±1.6	4.1±2.3	<0.001	2.0±1.7	4.3±2.6	<0.001
BASDAI, mean±SD	1.98±1.6	4.5±2.1	<0.001	2.4±1.9	4.5±2.3	<0.001
ASDAS, mean±SD	2.3±1.3	2.6±1.1	0.002	2.3±1.2	2.7±1.2	0.006
Patient's pain assessment (VAS), mean±SD	23.96±21.8	41.2±22.1	0.020	29.1±23.3	38.2±23.0	0.226
Patient's global assessment (VAS), mean±SD	19.1±19.9	42.8±23.1	<0.001	22.9±21.6	42.6±24.5	<0.001
physician's global assessment (VAS), mean±SD	10.6±12.9	20.1±16.8	<0.001	10.8±12.4	23.95±17.8	<0.001
TJC, mean±SD	1.4±4.2	4.3±9.99	0.002	1.79±5.3	4.45±10.3	0.002
FACIT-F, mean±SD	42.4±7.8	29.5±8.2	<0.001	40.4±8.6	29.3±9.5	<0.001
EQ5D, mean±SD	0.51±0.11	0.29±0.19	<0.001	0.48±0.13	0.28±0.23	<0.001

Objectives: To assess disease activity and quality of life in anxious and depressed SpA patients.
Methods: Observational, retrospective, cross-sectional study of SpA patients on bDMARDs, registered at Reuma.pt, Portuguese Rheumatology registry, with ≥1 clinical evaluation from November 2015 to July 2016. Demographic and clinical outcomes including: BASDAI, BASMI, BASFI, ASDAS, DAS 28–3V ESR in peripheral psoriatic arthritis, tender and swollen 44 joints count (TJC, SJC), patients' pain and global assessments, physician's global assessment, CRP, ESR, ASQoL, EQ-5D, FACIT-F for fatigue and HADS scale with 2 domains, HADS-A for anxiety and HADS-D for depression (a cutoff of 8 defining these symptoms), were collected. Statistics: Mann-Whitney test, $p<0.05$. SPSS® v.17.
Results: 160 patients were included, 41.9% were male, with mean: current age 50.7±11.9, age at diagnosis 36.9±11.96, at 1st bDMARD 46.2±11.8, time from diagnosis 18.5±10.3, years. The mean DAS 28–3V ESR was 3.2±1.4, BASDAI 2.98±2.2, ASDAS 2.4±1.2, BASFI 2.68±2.26, BASMI 3.36±1.7, patient's global assessment 28.8±24.1, physician's global assessment 14.5±15.2, ESR 18.8±18.1 mm/h, CRP 6.7±16.01 mg/L, ASQoL 6.2±5.6, FACIT-F 37.2±10.1 and EQ-5D 0.417±0.19. The mean HADS-A was 5.96±4.01 and HADS-D was 5.05±4.1 (HADS-A≥8 in 39.5% and HADS-D≥8 in 28.3% patients). Comparison of anxious vs non-anxious and depressive vs non-depressive groups appears on table 1.
Conclusions: These results suggest that anxious and depressed patients may have higher disease activity, more functional limitations and worse quality of life. These symptoms should not be underestimated, but instead, they should be controlled to achieve clinical improvement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5053

SAT0419 SIMILARITIES AND DIFFERENCES BETWEEN HLA B27 POSITIVE AND HLA B27 NEGATIVE SPONDYLOARTHRITIS: RESULTS FROM THE ESPERANZA COHORT

P. Serrano[1,2], V. Navarro-Compán[2], S. Rodríguez[3], M. Fernández[4], P. Zarco[5], E. de Miguel[2]. *[1]Universidad Autónoma; [2]Hospital la Paz, IdiPaz, Madrid; [3]Hospital Nuestra Señora de Valme, Sevilla; [4]Hospital Guadalajara, Guadalajara; [5]Hospital Fundación Alcorcón, Madrid, Spain*

Background: The diagnostic relevance of HLA B27 for spondyloarthritis (SpA) is well established and highlighted by its inclusion in the classification criteria. However, the clinical relevance of this gen on the disease manifestations is unclear.
Objectives: To investigate the influence of HLA B27 status on disease manifestations in patients with recent-onset SpA.

Table 1

Characteristic	Axial SpA			Peripheral SpA		
	HLA-B27+ N (%)=219 (75)	HLA-B27- N (%)=72 (25)	p value	HLA-B27+ N (%)=28 (33)	HLA-B27- N (%)=58 (67)	p value
Age (years)	31.4±7.1	33.8±6.5	**0.01**	30.6±8.6	33.9±7.2	0.07
Male	151 (68.9)	40 (55.6)	**<0.05**	16 (57.1)	34 (58.6)	0.9
Symptoms duration (months)	12.9±6.7	13.3±6.7	0.7	8.9±5.2	9.5±6.6	0.7
Peripheral arthritis	44 (20.1)	9 (12.5)	0.1	28 (100)	55 (94.8)	0.2
Enthesitis	48 (21.9)	9 (12.5)	0.08	18 (64.3)	25 (43.1)	0.07
Dactylitis	13 (5.9)	3 (4.2)	0.6	9 (32.1)	19 (32.8)	0.9
EAMs:						
– Uveitis	20 (9.1)	3 (4.2)	0.2	1 (3.6)	0 (0)	NA
– Psoriasis	18 (8.2)	15 (20.8)	**<0.01**	2 (7.1)	26 (44.8)	**<0.001**
– IBD	4 (1.8)	5 (6.9)	**<0.05**	2 (7.1)	8 (13.8)	0.4
Diarrhea, cervicitis, urethrtis	9 (4.1)	2 (2.8)	0.6	3 (10.7)	2 (3.4)	0.2
Inflammatory back pain	83 (37.9)	29 (40.3)	0.7			
Family history	84 (38.4)	17 (23.6)	**<0.05**	10 (35.7)	21 (36.2)	0.9
APRs:						
– ESR (mmHg)	13.6±13.2	13.5±14.3	0.9	13.8±14.6	14.2±12.9	0.9
– CRP (mg/L)	11.3±15.3	9.4±14.9	0.4	19.5±48.0	11.0±18.8	0.2
SJC	0.3±1.5	0.2±0.8	0.8	1.6±3.0	1.3±2.0	0.6
VAS (0–10) physician	2.8±2.2	3.2±2.1	0.2	2.2±2.2	2.5±2.2	0.5
VAS (0–10) patient	4.0±2.7	4.6±2.6	0.2	2.9±2.6	3.3±2.4	0.6
BASDAI	3.7±2.3	4.2±2.2	0.2	2.6±1.7	3.9±2.4	0.02
BASFI	2.2±2.3	2.8±2.2	0.1	1.2±1.4	1.9±2.1	0.09
Temporary disability	19 (8.7)	7 (9.7)	0.7	5 (17.9)	13 (22.4)	0.7
ASQoL	5.5±4.7	7.0±4.8	**<0.05**	3.3±4.0	5.0±5.3	0.2

Methods: Baseline database from ESPeranza cohort (<45 years, symptoms duration 3–24 months and with inflammatory back pain or asymmetrical arthritis or spinal/joint pain plus ≥1 SpA features) was used. Inclusion period in the program was 2008–2011. For this study, 377 fulfilling the ASAS classification criteria for SpA were included. A descriptive analysis was used to compare demographic and clinical characteristics between HLA B27+ and HLA B27- patients for both subgroups, axial SpA and peripheral SpA. Chi- square test for qualitative variables and Student-t test for quantitative variables were employed to compare variables among groups.
Results: A total of 291 patients (75% B27+ and 25% B27-) were classified as axial SpA and 86 (33% B27+ and 67% B27-) as peripheral SpA. Results (mean –standard deviation- and relative frequencies) are presented in the table. In axial SpA, B27+ patients were younger, more frequently males and with a family history of SpA while B27- patients had more frequently psoriasis, IBD and poorer quality of life. In peripheral SpA, B27- had more frequently psoriasis and reported higher BASDAI.
Conclusions: In patients with SpA, HLA B27 status influences on the presentation of the disease. In axial SpA, the presence of B27 is associated with an earlier onset, male predominance and more frequency of family history of SpA. In peripheral SpA, the presence of B27 is linked with lower subjective parameters of disease activity. In both, axial and peripheral SpA, the absence of B27 is associated with psoriasis, IBD and poor quality of life.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6011

SAT0420 RELATIONSHIP BETWEEN HEALTH-RELATED QUALITY OF LIFE WITH DISEASE ACTIVITY AND FUNCTIONAL STATUS, IN PATIENTS WITH ANKYLOSING SPONDYLITIS

P. Chiowchanwisawakit, V. Srinonprasert, W. Katchamart. *Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: Ankylosing spondylitis (AS) is a chronic disease resulting in diminished quality of life (QoL). There was no study regarding QoL in Thai patients with AS.
Objectives: To identify factors associated with quality of life, measured by EuroQol 5-dimension, 5-level questionnaire (EQ-5D-5L), in patients with AS.
Methods: This was a cross-sectional study. Demographic data and outcomes related to health utility or HU [Thai version EQ-5D-5L], disease activity [BASDAI (0–10), ASDAS-ESR or CRP, number of tender (TJC) and swollen joint (SJC), and enthesitis], and functional status [BASFI (0–10) and HAQ (0–3)] were collected. The HU was calculated on the basis of responses to 5-domains using the Thai value set. Regression analysis was used to explore factors associated with each EQ-5D domain and HU. Multiple models using different outcome measures for disease activity and functional status were performed to identify the best predictive model.
Results: Among 119 AS patients, most (73%) were male with mean (SD) age of 40.4 (11.6) years. Most (52.9%) were married and 92 (77.3%) were employed. The median (IQR) disease duration, BASDAI, BASFI, and HAQ were 7.5 (11.8) years, 3.2 (3.7), 2.3 (4.2), and 0.4 (0.9), respectively. The mean (SD, range) EQ-5D and VAS were 0.75 (0.20, -0.24–1.00) and 68.8 (18.8, 10–100), respectively. In univariate analysis, higher disease activity, higher functional index score, and more severe peripheral joint involvement were significantly associated with lower HU and moderate to very severe problem in each EQ-5D domain compared with no to mild problem with $p<0.05$, except SJC which was not associated with mobility problem. Conversely, age, gender, marital status, and disease duration were not associated with any EQ-5D domains or HU. In multivariate regression analysis, disease activity and functional status were significantly associated with HU (Table 1), when adjusted for age. The best predictive model using BASDAI, CRP, and HAQ with adjusted for age correctly predicted 77.4% of the variance in HU, while using BASFI instead of HAQ in the same model yielded slightly lower predictive value of 70.7%.
Conclusions: Disease activity and functional status were significantly factors related to QoL and HU in patients with AS. To improve QoL, the aim of treatment should be achieve remission or at least low disease activity and improve or at least maintain function.
Disclosure of Interest: P. Chiowchanwisawakit Grant/research support from: Siriraj Research fund, V. Srinonprasert: None declared, W. Katchamart: None declared
DOI: 10.1136/annrheumdis-2017-eular.3155

Abstract SAT0420 – Table 1. Multivariate linear regression analysis of factors associated with the health utility

Model	Adjusted R^2	Age (yr), Beta (95% CI)	Disease activity, Beta (95% CI)	Functional index, Beta (95% CI)
1	0.707	0.002 (-0.001, 0.005)‡	BASDAI: -0.030 (-0.054, -0.006)* CRP: -0.003 (-0.005, -0.002)*	BASFI: -0.036 (-0.062, -0.011)*
2	0.622	0.004 (0.001, 0.007)*	ASDAS-CRP: -0.049 (-0.091, -0.008)*	BASFI: -0.055 (-0.081, -0.029)*
3	0.592	0.003 (0.000, 0.005)*	ASDAS-ESR: -0.084 (-0.114, -0.054)*	BASFI: -0.032 (-0.049, -0.016)*
4	0.774	0.002 (-0.001, 0.005)‡	BASDAI: -0.034 (-0.050, -0.017)* CRP: -0.002 (-0.003, -0.001)*	HAQ: -0.197 (-0.270, -0.124)*
5	0.722	0.003 (0.000, 0.006)‡	ASDAS-CRP: -0.055 (-0.083, -0.026)*	HAQ: -0.248 (-0.319, -0.177)*
6	0.695	0.003 (0.001, 0.005)*	ASDAS-ESR: -0.069 (-0.093, -0.046)*	HAQ: -0.199 (-0.250, -0.147)*

*$p<0.05$; ‡$p\geq0.05$.

SAT0421 FAT MASS NEGATIVELY AFFECTS THE RESPONSE TO TNF ALPHA BLOCKERS IN ANKYLOSING SPONDYLITIS PATIENTS

S.E. Ibáñez Vodnizza[1,2], M.T. Nurmohamed[3,4], I.M. Visman[3], J.C. van Denderen[3], W.F. Lems[3,4], I.E. van der Horst-Bruinsma[4]. *[1]Rheumatology department, Clínica Alemana de Santiago; [2]Rheumatology department, Hospital Padre Hurtado, Santiago, Chile; [3]Amsterdam Rheumatology and immunology Center, Reade; [4]Amsterdam Rheumatology and immunology Center, VU University Medical Center, Amsterdam, Netherlands*

Background: Women with Ankylosing Spondylitis (AS) seem to be less responsive to TNF-α blockers and have a shorter drug survival. This might be explained by differences in body composition (BC), as women have higher total body fat (BF).
Objectives: Assess the relationship between gender, BC and response to TNF-α blocker treatment in a cohort of TNF-α blocker naïve AS patients.
Methods: AS patients (Modified New York criteria), ≥18 years old, who had a Dual-Energy X-ray Absorptiometry BC analysis before the start of TNF-α treatment and at least 6 months thereafter were included. Demographic information and the disease activity measures ASDAS CRP and BASDAI were reported. Fat Mass (FM) was reported as BF% (FM/Total body mass), and Fat Mass Index (FMI= FM kg/height m^2). Fat Free Mass (lean mass + bone mineral content) was reported as its index (FFMI kg/m^2). BF%, FMI, and FFMI percentiles, according to the reference population tables, stratified by age and gender, were also reported.
Results: Forty-one patients were included, 61% were men. Demographic characteristics were similar in men and women. The FFMI percentile was remarkably low in men, probably reflecting muscle wasting (figure 1). The percentiles increased in men and decreased in women after treatment. The clinically important improvement (CII) of ASDAS CRP was achieved by 52% of men and only 37.5% of women. The minimum CII for BASDAI was achieved by 64.7% of men, and only 35.7% of women that had a BASDAI ≥4 at baseline. After multivariate analysis we found a significant relationship between higher BF%, FMI or FMI percentile at baseline and a lower chance of achieving at least a CII of ASDAS CRP; the same relationship was found between FMI percentile at baseline and the minimum CII for BASDAI (table 1).

Table 1. Multivariate logistic regression analysis results[a]

Outcome	Variable	OR (95% CI)
Clinically important or major improvement of ASDAS CRP	Body Fat % at baseline	0.8 (0.7–0.98)
	Fat Mass Index at baseline	0.7 (0.4–0.99)
	FMI percentile[b] at baseline	0.9 (0.9–0.99)
BASDAI MCII[c]	FMI percentile[b] at baseline	0.95 (0.91–0.99)

[a]Controlled for gender, age, years with symptoms, days of follow up, use of DMARDs and NSAIDs and baseline outcome value. [b]Percentiles according to the reference population tables, stratified by age and gender. [c]Only for patients with a BASDAI ≥4 at baseline. CRP = C-reactive protein, ASDAS = Ankylosing Spondylitis Disease Activity Score, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, MCII = minimum clinically important improvement, FMI = Fat Mass Index.

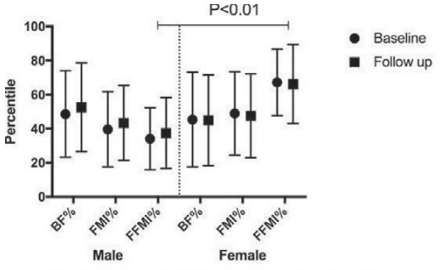


Figure 1. Body Fat % (BF%), Fat Mass Index (FMI) and Fat Free Mass Index (FFMI) percentiles according to reference population tables, stratified by gender. At baseline and follow-up the FFMI was significantly higher in female patients (*P* <0.001).

Conclusions: Higher body fat content at baseline is independently associated with a worse response to treatment with TNF-α blockers, measured by ASDAS-CRP and BASDAI change, and might contribute to the lower response to treatment rates in female patients. Also, there is a trend toward muscle mass recovery in male patients after treatment with TNF-α blockers.
Acknowledgements: This study was endorsed by an ASAS (Assessment of SpondyloArthritis international Society) Fellowship.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1189

SAT0422 EFFECTS OF VITAMIN D REPLACEMENT ON THE DISEASE ACTIVITY AND INFLAMMATORY PARAMETERS SUCH AS IL-1, IL-6, TNF-α, ASYMMETRIC DIMETHYLARGININE (ADMA) AND ARGININE/ADMA RATIO IN ANKYLOSING SPONDYLITIS

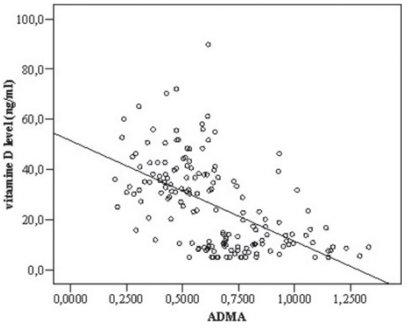
S. Ergulu Esmen[1], S. Yılmaz[2], L. Kebapcılar[3], A. Ünlü[4], S.H. İpekci[3], S. Abusoglu[4]. *[1]Rheumatology, Internal Medicine, Konya Education and Research Hospital; [2]Rheumatology, Internal Medicine; [3]Endocrinology and Metabolic Diseases, Internal Medicine; [4]Biochemistry, Selcuk University, Konya, Turkey*

Background: Asymmetric dimethylarginine (ADMA) levels in AS patients were found to be higher than controls (1).The relationship between vitamin D level and disease activity was shown in AS (2). But the effects of vitamin D replacement on the disease acitivity, inflammatory parameters and ADMA pathway were not investigated in AS.
Objectives: To determine the effects of vitamin D replacement on the disease activity, inflammatory parameters and ADMA pathway in AS.
Methods: All AS patients with vitamin D level of <20 ng/ml who consecutively attended the outpatient rheumatology clinic were enrolled.C-reactive protein, erythrocyte sedimentation rate, Bath AS disease activity index (BASDAI), Bath AS Functional Index (BASFI) TNF-α, IL-1, IL-6, ADMA, symmetric dimethylarginine (SDMA), NG-monomethyl-L-arginine (LNMMA), arginine, arginine/ADMA ratio and citrulline levels were analyzed when vitamin D level was <20 ng/ml and ≥20 ng/ml, after replacement.
Results: The study population was represented by 82 patients, 48 women (58.5%), mean age 39 years old and mean disease duration 5.5 years. When vitamin D levels were increased to normal levels, levels of IL-1 (4.8±9.7 and 3.1±4.0 p<0.001), IL-6 (7.1±14.1 and 4.7±2.1 p=0.009), ADMA (0.8±0.2 and 0.4±0.1 p<0.001), SDMA (0.9±0.2 and 0.4±0.2 p<0.001), LNMM (0.08±0.02 and 0.06±0.02 p<0.001), arginine (385.8±106.4 and 269.2±79.0 p<0.001) and citrulline (91,1±34,3 and 75,3±23,5 p<0,001) were reduced. Levels of arginine/ADMA ratio was increased (498.7±136.5 and 576.7±170.7 p<0.001) (Table 1). Also BASDAI, BASFI and erythrocyte sedimentation rate were decreased but it was statistically meaningless. In pearson correlation analysis, ADMA, SDMA, LNMMA, arginine and citrulline were negatively correlated with vitamin D levels.Multiple regression analysis showed that SDMA, arginine and citrulline were significantly related with vitamin D levels. Negative correlation between ADMA and vitamin D levels was shown in Figure 1

Table 1

	Vit D <20 (ng/ml)	Vit D ≥20 (ng/ml)	P
TNF-α (pg/mL)*	19.04±14.39	19.36±8.18	0.041
IL-6 (pg/mL)*	7.17±14.19	4.75±2.15	0.009
IL-1 (pg/mL)*	4.86±9.70	3.17±4.05	<0.001
ADMA (μmol/L) **	0.80±0.21	0.49±0.16	<0.001
SDMA (μmol/L) **	0.93±0.26	0.49±0.20	<0.001
LNMMA (μmol/L) **	0.08±0.02	0.06±0.02	<0.001
Arginine (μmol/L)**	385.83±106.43	269.22±79.08	<0.001
Arginine/ADMA	498.72±136.51	576.74±170.76	<0.001
Citrulline (μmol/L)**	91.14±34.34	75.30±23.52	<0.001

*Wilcoxon sign test **paired samples t test.



Conclusions: Vitamin D replacement in AS with low vitamin D levels improves antioxidant status via ADMA pathway and shows anti-inflammatory effects on IL-1 and IL-6. In literature, there is no other study investigating the effects of increased vitamin D levels on disease activity, inflammatory parameters and ADMA pathway in AS.
References:
[1] Sari I, Kebapcilar L, et al: Increased levels of asymmetric dimethylarginine (ADMA) in patients with ankylosing spondylitis. Intern Med 2009, 48(16):1363–1368.
[2] Lange U, Teichmann J, et al: Association of 1.25 vitamin D3 deficiency, disease activity and low bone mass in ankylosing spondylitis. Osteoporos Int 2005, 16(12):1999–2004.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3290

SAT0423 INCREASED PREVALENCE OF EXTRA-ARTICULAR MANIFESTATIONS AMONG INDIVIDUALS WITH ANKYLOSING SPONDYLITIS IN CANADA: RESULTS FROM THE RHUMADATA® MULTICENTRE REGISTRY

S. Szabo[1], S. Chehab[2], L. Coupal[3], D. Choquette[3]. *[1]Broadstreet HEOR, Vancouver; [2]Novartis Pharmaceuticals Canada; [3]Institut de Recherche en Rhumatologie de Montréal, Montreal, Canada*

Background: Among populations with ankylosing spondylitis (AS), the frequency and severity of extra-articular manifestations (EAMs) vary widely; due to underlying geographic and genetic differences, individual characteristics, and the impact of treatment with anti-tumour necrosis factor [TNF] agents. The frequency of EAMs

among Canadians with AS has not previously been examined, using data from a large clinical registry.
Objectives: To estimate the prevalence of EAMs, including uveitis, inflammatory bowel disease (IBD), dactylitis, and enthesitis, in a population of Canadians undergoing active management for AS.
Methods: This retrospective study used RHUMADATA®, a multicentre registry developed by rheumatologists of the IRRM and *Centre d'ostéoporose et de rhumatologie de Québec* to evaluate the effectiveness and safety of rheumatologic therapies. Up to 15 years of real-world observational data on the broad set of patients treated in clinical practice are available. The proportion with EAMs was estimated according to type. The frequency of EAMs was compared according to age at cohort entry (≤40 vs >40 years), sex, AS severity (by BASDAI score), and status of treatment with anti-TNFs (anti-TNF-naive, anti-TNF treated [without switching], and anti-TNF treated [with switching]).
Results: The mean (SD) age at cohort entry was 36.0 (12.6) years, and 60.0% were male. Of the 944 patients, 268 (28.4%) were ever diagnosed with an EAM over a median of 9.66 (10.58) years of follow-up. Prevalence was 14.7% for uveitis, 5.8% for IBD, 4.3% for dactylitis, and 9.0% for enthesitis (Table). The proportion with EAMs was: slightly higher among females versus males (31.0% vs. 26.7%), among older versus younger patients (29.5% vs. 25.9%), among those with more severe disease (from 29.2% [mild AS] vs. 34.1% [severe AS]), and among anti-TNF treated patients (18.8% [anti-TNF-naïve] to 47.0% [treated with anti-TNFs, with switching]).

Table 1. EAMs among Canadian patients with AS from the Rhumadata dataset; overall, and according to levels of treatment status, key clinical, and demographic characteristics

	N	Uveitis		IBD		Dactylitis		Enthesitis		Any EAM	
		n	%	n	%	n	%	n	%	n	%
Overall											
N			14.7		5.8		4.3		9.0		28.4
Males	566	81	14.3	29	5.1	23	4.1	47	8.3	151	26.7
Females	378	58	15.3	26	6.9	18	4.8	38	10.1	117	31.0
≤40 years at cohort entry	651	111	17.1	37	5.7	29	4.5	58	8.9	192	29.5
>40 years at cohort entry	293	28	9.6	18	6.1	12	4.1	27	9.2	76	25.9
Missing AS severity	166	12	7.2	7	4.2	2	1.2	3	1.8	21	12.7
Mild AS (BASDAI <3.5)	271	47	17.3	16	5.9	12	4.4	21	7.7	79	29.2
Moderate AS (3.5 ≤ BASDAI <6.0)	252	44	17.5	12	4.8	13	5.2	26	10.3	81	32.1
Severe AS (BASDAI ≥6.0)	255	36	14.1	20	7.8	14	5.5	35	13.7	87	34.1
Anti-TNF naïve	490	47	9.6	18	3.7	11	2.2	25	5.1	92	18.8
Anti-TNF treated [no switching]	286	51	17.8	21	7.3	15	5.2	28	9.8	97	33.9
Anti-TNF treated [with switching]	168	41	24.4	16	9.5	15	8.9	32	19.0	79	47.0

Conclusions: EAMs are common among Canadians with AS, occurring in up to 28% over almost 10 years of follow-up, with uveitis occurring the most frequently (in almost 15% of the cohort). EAMs were most frequent among those with more severe disease (in 34%) and among those treated with anti-TNFs (in 20–50% of such patients). These estimates are useful for comparing to other geographic areas, where the risk factor distribution for AS and its sequelae would differ; and for use in economic models to evaluate the benefits and costs of new therapies.
Disclosure of Interest: S. Szabo: None declared, S. Chehab Employee of: Novartis Canada, L. Coupal Consultant for: Novartis, Speakers bureau: Novartis, D. Choquette: None declared
DOI: 10.1136/annrheumdis-2017-eular.5021

SAT0424 AXIAL DISEASE IN PSORIATIC ARTHRITIS: BURDEN OF UNDERDIAGNOSED DISEASE AND RISK FACTORS IN REAL LIFE

S.Z. Aydin[1], U. Kalyoncu[2] on behalf of the PsART study group. *[1]University of Ottawa, Ottawa, Canada; [2]Hacettepe University, Ankara, Turkey*

Background: The frequency of axial disease in Psoriatic Arthritis (PsA) is around 24–78% with additional patients with subclinical disease who have spondylitic changes or sacroiliitis in the absence of clinical findings. Despite that most of the physicians do not perform routine imaging with the argument that subclinical disease has no effects on management decisions.
Objectives: We aimed to explore barriers for diagnosing axial disease in PsA and its implications in real life.
Methods: PsART (Psoriatic Arthritis Registry of Turkey) is a prospective, multicentre registry where PsA patients are consecutively recruited. Radiographs of the spine and sacroiliac joints were scored by one central reader, whenever available. Patients with axial disease according to the physician were compared with patients with imaging findings only and risk factors for being underdiagnosed were investigated.
Results: Among 1195 patients, 35% had axial disease according to the physician who were more frequently men (41.2% vs 32.2%; p=0.04), younger (44.4 (12.2) vs 47.9 (13); p<0.001), more frequently smokers (44.6% vs 34.1%; p<0.001), more on anti TNFs (37.1% vs 29.4%; p=0.01) and had more nail involvement (49.9% vs 43.2%; p=0.03). Within the IBP criteria, the ASAS criteria had the lowest sensitivity (59.7%) which was even lower in women (53.1%). Forty-nine (15.7%) patients were classified as having axial disease according to the rheumatologist despite not fulfilling any of the IBP criteria which was more frequent for women (21.1%) than men (8.2%, p=0.002). Among 71 patients that had syndesmophytes, 20 patients (28.2%) were not classified as having axial disease according to the physician. This was higher for women (15/42, 35.7%) then men (5/29, 17.2%).
There were 126 patients who had sacroiliitis fulfilling the ASAS criteria, despite not being categorized as having axial disease by the clinician. The risk of being underdiagnosed was higher for women (30.8% vs 18.4%; p=0.003). These patients had higher Leeds enthesitis scores, tender and swollen joint counts (table) and were less using anti-TNF medications (14.6% vs 38.7%; p<0.001). The PROs and the physician global assessment were similar, suggesting a similar disease activity state according to the patients and physicians in diagnosed and underdiagnosed groups.

Table 1. Comparison of outcomes in patients with axial disease according to the clinician and axial disease by imaging only

	Axial disease according to the Clinician (n=415)	Axial disease by imaging only (n=126)	p
Patient global assessment	47 (24.8)	49.2 (20.8)	0.4
Pain	46.4 (28.7)	50.1 (23.3)	0.3
Fatigue	47.1 (27.7)	51.9 (23.6)	0.1
BASDAI	4.5 (2.5)	3.9 (2.3)	0.08
BASFI	3.3 (2.5)	3.2 (2.4)	0.8
Physician's global assessment	38.7 (23.3)	41 (18.9)	0.2
Tender joint count	3.4 (4.7)	5.3 (6)	<0.001
Swollen joint count	1.3 (2.5)	2 (3)	<0.001
Leeds enthesitis index	0.3 (0.8)	0.4 (1)	0.05

Conclusions: Underdiagnosed axial disease is frequent in PsA, women having higher risk and IBP criteria being less sensitive in women. More complex patients (eg with higher enthesitis and peripheral arthritis) have a higher risk of being underdiagnosed. These patients are less frequently treated with biologic treatments, which could be the right treatment choice if were diagnosed. Axial disease needs to be ruled out using imaging modalities, even if back pain does not clinically suggest an inflammatory pattern.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3022

SAT0425 SYMPTOMOLOGY, DISEASE STATUS, AND REMISSION RATES OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND ANKYLOSING SPONDYLITIS PATIENTS IN EUROPE

T.M. Hunter[1], D. Sandoval[1], S. Lobosco[2], R. Moon[2], J. Birt[1], G. Miligan[2]. *[1]Eli Lilly and Company, Indianapolis, United States; [2]Adelphi Real World, Bollington, United Kingdom*

Background: Axial Spondyloarthritis (axSpA) is a chronic inflammatory disease predominantly affecting the sacroiliac joints and spine. Ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA) have been considered to represent the same axial spondyloarthritis disorder, but are differentiated by the presence or absence of structural changes in the sacroiliac joints as determined by common imaging modalities.
Objectives: To better understand the symptoms and clinical characteristics of nr-axSpA patients and how they compare to ankylosing spondylitis patients in Europe.
Methods: Data drom the 2015 SpA Disease Specific Programme, a cross-sectional, multi-national survey of patients and rheumatologists conducted in France, Germany, Italy, Spain, and the UNited Kingdom were analyzed. Rheumatologists (n=299) completed forms containing patient demographics, clinical results and symptomology. Symptoms, disease activity, and disease status (defined as improving, stable, unstable, deteriorating) of AS and nr-axSpA patients were compared.
Results: A total of 3,033 patients (AS: 1,520; nr-axSpA: 1,513) were included in the analysis. A higher proportion of AS patients were male (72% vs. 53%), older (mean age=44.8 vs. 41.0), had a higher BMI and were employed when compared to nr-axSpA patients. Nr-axSpA patients' current disease status was less likely to be stable (p<0.0001) in comparison to AS patients. Nr-axSpA patients were also less likely to be in remission (p<0.0001). Nr-axSpA patients were reported as having higher pain level (p=0.0333) than AS patients. AS patients had more axSpA symptoms, such as spinal fusion and loss of movement, however nr-axSpA patients were more likely to have inflammatory back pain, enthesitis, persistent lower back pain, and nocturnal wakening.
Conclusions: Both nr-axSpA and AS appear to have many similar clinical characteristics with few distinct features between them. However, in spite of these similarities, nr-axSpA patients show less stability and a lower likelihood of remission when compared to AS patients. These findings may suggest that nr-axSpA is as burdensome as AS, and that both conditions may warrant similar treatment approaches from an early stage.
Disclosure of Interest: T. Hunter Employee of: Eli Lilly and Company, D. Sandoval Employee of: Eli Lilly and Company, S. Lobosco Employee of: Adelphi Real World, R. Moon Employee of: Adelphi Real World, J. Birt Employee of: Eli Lilly and Company, G. Miligan Employee of: Adelphi Real World
DOI: 10.1136/annrheumdis-2017-eular.2956

SAT0426 HIGH LEVELS OF EMPLOYMENT BUT PERSISTING WORK PLACE IMPAIRMENT IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS ON BIOLOGIC THERAPY

T.G. Nadin[1], D. Wallis[1], C. Holroyd[1], P. Clayton[1], R. Armstrong[1], C. Cooper[2], B. Davidson[1], N. Harvey[2], E. Dennison[2], R. Seth[1], K.E. Walker-Bone[2], S. Bennett[1], C.J. Edwards[1,3]. *[1]Rheumatology; [2]MRC Lifecourse Epidemiology Unit; [3]NIHR Wellcome Trust Clinical Research Facility, University Hospital Southampton, NHS Foundation Trust., Southampton, United Kingdom*

Background: Axial spondyloarthritis (axSpA) is associated with reduced work productivity. Biologic therapies have demonstrated a positive impact on work-related outcomes in clinical trials but real world data are limited.
Objectives: To investigate the prevalence and predictors of work impairment and disability in patients with axSpA attending a biologic therapy clinic.
Methods: Data were collected from a single-centre, prospective cohort of patients with axSpA treated with biologic therapy. Standardised outcome measures, including the Work Productivity and Activity Impairment (WPAI) Questionnaire for axSpA, are collected every 6 months. Data from the most recent clinic visit were analysed using IBM SPSS Statistics 24. Disease activity was compared between employed patients and those unemployed due to disability from axSpA. The effect of smoking status and gender on work related outcomes was analysed. The relationship between work-related outcomes and disease severity was investigated using Pearson's correlation. Significance was defined as $p<0.05$ with Bonferroni correction.
Results: Data were available for 165 patients (mean age 47.6 years, 75% male, 21% current smokers). Mean time since diagnosis was 15.4 years and mean duration of biologic therapy 4.7 years, with 19/165 (12%) on a reduced dose regimen. Mean BASDAI was 4.0, ASQoL 6.6, BAS-G 3.9 and spinal pain VAS 4.0. Employment data were provided by 144 patients of whom 99/144 (69%) were employed; 17/144 (12%) not working due to disability caused by SpA; 19/144 (13%) retired; 5/144 (4%) unemployed; 2/144 (1%) full-time education; and 2/144 (1%) full-time parents. Of the 144 patients in employment, 8 (6%) had missed hours of work in the week prior to the last clinic visit due to axial SpA (mean hours missed =13). There was no difference between males and females in (i) the proportion of patients employed or (ii) the proportion not working due to disability from SpA.
Mean impairment while working due to axial SpA was 23% and impairment of regular daily activities 35%. There was no significant difference in percentage work impairment between males and females. BASDAI was higher in patients unemployed due to SpA (7.1±1.6) compared to those who were employed (3.5±2.2, $p<0.001$). Higher levels of work impairment were observed in current smokers compared to previous smokers and never smokers ($p=0.003$). Positive correlations were found between individual WPAI domains and each of BASDAI, BAS-G, ASQoL and spinal pain VAS ($p<0.001$).
Conclusions: In this cohort of axial SpA patients on biologic therapy, the majority were employed and few reported missing time at work. As expected, disease activity was higher in patients unemployed due to disability compared to those who were currently in paid work. Gender did not appear to affect employment rates, disability rates or work impairment. Smoking was associated with increased work impairment. The impact of disease on employment should be considered in the clinic and strategies for enhancing work participation directed towards those patients most at risk.
Disclosure of Interest: T. Nadin: None declared, D. Wallis Grant/research support from: Janssen, MSD and Pfizer, C. Holroyd Paid instructor for: BMS, Abbvie, Chugai and Janssen., P. Clayton: None declared, R. Armstrong: None declared, C. Cooper: None declared, B. Davidson: None declared, N. Harvey: None declared, E. Dennison: None declared, R. Seth: None declared, K. Walker-Bone: None declared, S. Bennett: None declared, C. Edwards Consultant for: Abbvie, Pfizer, Lilly, Celltrion, Mundipharma, Samsung, Anthera, UCB, Celgene, Roche, BMS, Jansen, Novartis and UCB., Speakers bureau: Abbvie, Pfizer, Lilly, Celltrion, Mundipharma, Samsung, Anthera, UCB, Celgene, Roche, BMS, Jansen, Novartis and UCB.
DOI: 10.1136/annrheumdis-2017-eular.2075

SAT0427 ASAS HEALTH INDEX: VALIDITY AND RELIABILITY IN ARGENTINEAN PATIENTS WITH SPONDYLOARTHRITIS

V.M. Duarte[1], U. Kiltz[2], V. Navarro-Compán[3], N. Lloves[1], G. Crespo Amaya[1], L. Ferreyra[4], C. Orozco[5], E.E. Schneeberger[5], H. Maldonado Ficco[6], D. Baenas[7], F. Colombres[8], M. Mamani[1], J.A. Maldonado Cocco[9], E. Soriano[4]. *[1]Hospital B. Rivadavia, Buenos Aires, Argentina; [2]Rheumazentrum Ruhrgebiet, Herne, Germany; [3]Hospital la Paz, IdiPaz, Madrid, Spain; [4]Hospital Italiano de Buenos Aires; [5]Instituto de Rehabilitación Psicofísica (IREP), Buenos Aires; [6]Hospital San Antonio de Padúa, Río Cuarto; [7]Hospital Privado de Córdoba, Córdoba; [8]Hospital de Clínicas Dr. Avellaneda, Tucumán; [9]Consulting Profesor of Rheumatology, University of Buenos Aires, Buenos Aires, Argentina*

Objectives: The aim of the study was to translate and validate the ASAS Health Index (ASAS-HI) for Argentinean patients with spondyloarthritis.
Methods: Translation was done using a forward-backward procedure and qualitative interview were done with the translation. Patients fulfilling ASAS classification criteria for either axial (axSpA) or peripheral SpA (pSpA) were included to test psychometric properties. Test-retest reliability was assessed by intraclass correlation coefficient (ICC) in patients without treatment changes (stable disease state). In patients who required therapeutic modifications due to changes of disease activity, responsiveness was evaluated using a standardized response mean (SRM). Construct validity against other health outcomes was evaluated by Spearman correlation. Internal consistency (Cronbach-alfa) and discriminative ability between ASAS-HI and ASDAS were assessed.
Results: Translation into Argentinean Spanish was accepted with minor changes. Fifty two patients were recruited [65% male, mean (SD) age 39. 5 (12.5) years and median (IQR) disease duration 72 (45–138) months]. Most of the patients had axSpA diagnosis (AS: 26, nr-axSpA: 18) while the rest had pSpA (8). The total score of the ASAS-HI was 7.4 (SD: 4.4), BASDAI: 4.4 (SD: 2.7), BASFI: 4.0 (SD: 3.1), ASDAS-CRP: 2.4 (SD: 0.9). Test-retest reliability (n: 20) was good ICC: 0.88 (95%IC 0.76 to 0.98). Sensitivity to change was tested in 13 patients and SMR was -0.61 for those patients receiving TNF inhibitors (n: 11). Convergent validity ranged as hypothesized with Spearman correlations from low (age: 0.27) to good (pain: 0.65), (table 1). The ASAS-HI discriminated well between patients with different stages of disease activity and function irrespective of the measure applied (ASDAS, BASDAI and BASFI) (table 2). The internal consistency according to Cronbach's alfa was 0.81.

Table 1. Spearmen correlation coefficient

Characteristics	Spearmen correlation coefficient	
	ASAS-HI (0–17)	p value
Age	0.27	<0.05
Pain (0–10)	0.65	<0.001
Night spinal pain (0–10)	0.54	<0.001
ASDAS	0.51	<0.001
BASDAI (0–10)	0.60	<0.001
BASFI (0–10)	0.54	<0.001
SF-36 Total	0.46	<0.001

Table 2. ASDAS Status Groups

	ASDAS Status Groups			
	Inactive (n: 9)	Moderate (n: 9)	High (n: 29)	very high (n: 5)
ASAS-HI (0–17)	3.44 (± 3.9)	5.77 (± 4.79)	9. 06 (± 3.49)	10.05 (± 4.5)
BASFI (0–10)	0,53 (± 0,35)	1.41 (± 1.40)	5.5 (± 2.46)	6.46 (± 3.12)
BASDAI (0–10)	1.21 (± 0.49)	2.37 (± 1.7)	5.73 (± 1.91)	6.46 (± 3.38)

Conclusions: The Argentinean version of the ASAS-HI was comprehensive and reliable by patients with SpA. The ASAS-HI is a valid tool for assessing overall functioning and health in spondyloarthritis.
References:
[1] The ASAS Health Index (ASAS HI)a new tool to assess the health status of patients with spondyloarthritis, Clin Exp Rheumatol 2014;32:S105-S108.
Disclosure of Interest: V. Duarte Employee of: Novartis Argentina, U. Kiltz: None declared, V. Navarro-Compán: None declared, N. Lloves: None declared, G. Crespo Amaya: None declared, L. Ferreyra: None declared, C. Orozco: None declared, E. Schneeberger: None declared, H. Maldonado Ficco: None declared, D. Baenas: None declared, F. Colombres: None declared, M. Mamani: None declared, J. Maldonado Cocco: None declared, E. Soriano: None declared
DOI: 10.1136/annrheumdis-2017-eular.4386

SAT0428 WHICH CRITERIA FOR INFLAMMATORY BACK PAIN IN SPONDYLOARTHRITIS ARE OPTIMAL? DATA FROM THE SCREENING FOR AXIAL SPONDYLOARTHRITIS IN PSORIASIS, IRITIS, AND COLITIS STUDY (SASPIC)

R. Carmona[1], J. Yeung[2], A. Masetto[3], L. Martin[4], S. Keeling[5], J. Chan[2], D. Mosher[6], O. Ziouzina[4], J. Paschke[7], A. Carapellucci[7], R.G. Lambert[8], W.P. Maksymowych[5,7]. *[1]St. Joseph's Healthcare Hamilton, Hamilton; [2]Medicine, University of British Columbia, Vancouver; [3]Medicine, Université de Sherbrooke, Sherbrooke; [4]Medicine, University of Calgary, Calgary; [5]Medicine, University of Alberta, Edmonton; [6]University of Calgary, Calgary; [7]CaRE Arthritis; [8]Radiology, University of Alberta, Edmonton, Canada*

Background: Criteria for inflammatory back pain (IBP) in spondyloarthritis (SpA) include the Calin, Berlin, and Assessments in SpA International Society (ASAS) criteria, although no studies have undertaken comparative validation to determine which are optimal versus the rheumatologist expert opinion gold standard assessment.
Objectives: We aimed to compare IBP criteria in unselected patients presenting with undiagnosed back pain to rheumatology practice.
Methods: The Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at the development and validation of a triage strategy for detection of axial SpA in patients presenting with undiagnosed back pain. Consecutive patients $\leq$45 years of age with $\geq$3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis, or colitis diagnosed by the relevant specialist undergo routine clinical evaluation by a rheumatologist for axial SpA. The rheumatologist determines the presence or absence of IBP (defined as <5 or >5 on 0–10 scale, respectively) and axial SpA (yes/no) after the clinical evaluation and review of labs (B27, CRP) and imaging (x-ray, MRI). Clinical and laboratory data, radiographs and MRI scans are also assessed centrally for diagnosis of axial SpA (yes/no). We assessed sensitivity and specificity of each

of the IBP criteria for diagnosis of IBP according to the local rheumatologist, diagnosis of axial SpA by local rheumatologist, diagnosis of axial SpA by central assessment, and concordant diagnosis of axial SpA by both local and central assessment.

Results: We recruited 185 patients (48.6% male, mean age 27.6 years, mean back pain duration 7.0 years) with iritis (30.3%), psoriasis (17.3%), Crohn's (38.4%) and ulcerative colitis (18.9%). IBP and/or axial SpA were considered present in 65.2% and 47.3%, respectively, of all patients by the local rheumatologist. By central assessment axial SpA was considered present in 32.7% while amongst patients with a concordant diagnosis by both local and central assessment 37.2% were considered to have axial SpA. Sensitivity was comparatively high for all IBP criteria but specificity was poor. The Berlin criteria consistently performed best while the Calin criteria consistently performed worst (Table).

Gold standard	IBP criteria	Sensitivity (%)	Specificity (%)	LR+	LR–
IBP by local rheumatologist	ASAS	83.8	58.8	2.03	0.28
	Berlin	88.9	76.5	3.78	0.15
	Calin	94.0	37.3	1.50	0.16
Axial SpA by local rheumatologist	ASAS	82.9	44.9	1.50	0.38
	Berlin	84.3	51.3	1.73	0.31
	Calin	90.0	19.2	1.11	0.52
Axial SpA by central assessment	ASAS	80.0	37.5	1.28	0.53
	Berlin	80.0	38.9	1.31	0.51
	Calin	94.3	20.8	1.19	0.27
Axial SpA by central and local assessment	ASAS	86.2	44.9	1.56	0.31
	Berlin	86.2	51.0	1.76	0.27
	Calin	93.1	22.4	1.20	0.31

Conclusions: IBP criteria lack specificity for rheumatologist diagnosed IBP or axial SpA but the Berlin criteria have consistently better performance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5151

SAT0429 THE PERFORMANCE OF MAGNETIC RESONANCE IMAGING USING THE VIBE TECHNIQUE TO DETECT STRUCTURAL CHANGES IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS IN COMPARISON TO CONVENTIONAL RADIOGRAPHY AND COMPUTED TOMOGRAPHY

X. Baraliakos[1], F. Hoffmann[1], X. Deng[2], Y. Wang[2], F. Huang[2], J. Braun[1]. *[1]Rheumazentrum Ruhrgebiet, Herne, Germany; [2]Department of Rheumatology, Chinese PLA General Hospital, Beijing, China*

Background: Magnetic resonance imaging (MRI) is the gold standard for detection of inflammation in the sacroiliac joints (SIJ) of patients (pts) with axial spondyloarthritis (axSpA), while for chronic, structural changes (erosions, sclerosis and ankylosis) conventional radiographs (CR) and computed tomography (CT) are often preferred. The 3D volumetric interpolated breath-hold sequence (VIBE) is an MRI technique, easy to acquire in daily practice, that can visualize cartilage especially well because of its good contrast to synovial tissue.

Objectives: To compare the ability of the VIBE technique to detect structural changes in comparison to CR and CT in SIJs of axSpA patients in relation to symptom duration and age.

Methods: Complete sets of MRI (T1 and VIBE techniques), CT and CR of SIJs of 109 AS patients were available. Two readers evaluated all images independently, blinded to demographic data and in separate sessions for each technique. The assessment of lesions was performed based on SIJ-quadrants (SQ) to score erosions, sclerosis and ankylosis (SIJ-halves). Lesions were counted as positive if both readers were in agreement. Comparisons between MRI techniques were performed by Wilcoxon-test. Linear regression analysis was used to evaluate the influence of age and disease duration on the occurrence of different structural lesions by modeling the differences in the number of lesions in different imaging techniques as dependent variable.

Results: The mean age ± standard deviation was 45.3±13.9 years (y), 55 pts (50.5%) were aged ≤45y, 67.9% male, 82.3% HLA-B27+, 58 pts (53.2%) had a disease duration ≤3y. Agreement for positive and negative findings between MRI and CT was generally high (>80% of SQs in all subgroups) and agreement between readers for all techniques and lesion types was excellent (ICC=0.979–0.997).

Overall, MRI detected significantly more SQ with erosions in pts ≤45y (n=134) and in pts with disease duration ≤3y (n=125) as compared to CT (n=91, p=0.002 and n=90, p=0.003, respectively) and in pts with age ≤45y (n=61, p<0.001) as compared to CR, while there were no differences between MRI and CT in pts. >45y or disease duration >3y. Linear regression analysis showed that MRI was superior in the detection of erosions in younger ages as compared to CT (B=0.032, p=0.001).

However, CT detected significantly more SIJ halves with ankylosis in all subgroups and more SQ with sclerosis in pts with disease duration ≤3y (n=64 vs. n=37, respectively, p=0.006), and it also detected more SQ with sclerosis in pts >45y (n=67 vs. n=38, p=0.001) and disease duration >3y (n=64 vs. n=40, p=0.003) as compared to MRI, while no differences were found in the assessment of ankylosis.

Conclusions: MRI in the T1 and VIBE technique is more sensitive in the detection of erosions as compared to CT and CR in axSpA pts with short disease duration and younger age. This is due to its ability to identify structural damage in the SIJ cartilage that has not yet extended to the underlying bone. These differences are not found in pts with longer disease duration or older age. This data suggests a more prominent role for MRI also for the early detection of structural changes in the SIJ of axSpA pts.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6501

SAT0430 THE RELATIONSHIP BETWEEN EXOSOMAL MIRNA21-5P AND ANKYLOSING SPONDYLITIS

Y. Huang, T. Li, Z. Huang, W. Deng, S. Zheng, Z. Huang. *Guangdong No. 2 Provincial People's Hospital, Guangzhou, China*

Background: Ankylosing Spondylitis (AS) affects human health seriously, which is difficult to diagnose in the early stages. It is reported that MicroRNAs (miRNAs) may serve as novel biomarkers for AS. Exosome can function as vehicles to deliver miRNAs in body fluids including saliva and plasma. Our previous study shows that exosomal miRNA21–5P is higher expressed in AS patients, compared with healthy subjects. However, the relationship between exosomal miRNA21–5P and AS has yet to be determined.

Objectives: The aim of the present study is to explore the relationship between exosomal miRNA21–5P and AS.

Methods: AS patients who fulfilled the modified New York criteria were enrolled for this study. Healthy subjects were also enrolled as control group. BASDAI, BASFI, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were evaluated. Quantitative reverse-transcription PCR (qRT-PCR) was used to confirm the expression of exosomal miRNA21-5P, and receiver-operator characteristic (ROC) curve was used to evaluate the diagnostic value of exosomal miRNA21-5P for AS. According to the cut off value, AS patients were divided into exosomal miRNA21–5P low value group (<cut off value) and exosomal miRNA21-5P high value group (≥cut off value), and the difference of AS patient's clinical characteristics between the two group were explored.

Results: Twenty healthy subjects and 38 AS patients were enrolled in the study. The qRT-PCR results indicated that the expression level of exsomal miRNA21-5P in AS patients was (2.041±0.975) times higher than that of healthy subjects. ROC curve analysis showed that exsomal miRNA21-5P had significant diagnostic value for AS with the AUC of 0.809 (CI95%: 0.691–0.921). In addition, the cut off value was 1.310, with the specifity of 80.0% and sensitivity of 76.32%. According to the cut off value of exsomal miRNA21–5P, AS patients were divided into the low exsomal miRNA21-5P group (<1.310) and the high exsomal miRNA21-5P group (≥1.310). Among the 38 AS patients, 12 cases were in the low exsomal miRNA21–5P group and 26 cases were in the high exsomal miRNA21-5P group. Comparations of the clinical characteristics of the two groups showed that BASDAI, BASFI, CRP and ESR were significantly increased in exsomal miRNA21-5P high value group.

Conclusions: Exsomal miRNA21-5P was significantly increased in AS patients, which may be used as a biomarker for AS.

References:

[1] Atayde VD, Aslan H, Townsend S, Hassani K, Kamhawi S, Olivier M. Exosome.
[2] Secretion by the Parasitic Protozoan Leishmania within the Sand Fly Midgut. Cell Reports, 2015, 13 (5): 957–67.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6836

SAT0431 THE RELATIONSHIP OF SEASONAL VARIATION, THE ONSET AND THE SYMPTOMS OF ANKYLOSING SPONDYLITIS MEASURED BY SELF-ADMINISTRATED QUESTIONNAIRES IN CHINESE PATIENTS

Y. Jiang, M. Yang, Z. Lin, Q. Wei, S. Cao, J. Gu. *Rheumatology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease which mainly involves sacroiliac joints, resulting in pain, functionally limitation and even less life expectancy. Seasonal variation was found in rheumatoid arthritis and gout [1,2]. No reports had been focused on seasonal variation of AS onset or symptoms in AS patients.

Objectives: Our study was to investigate the relationship of seasonal variation and the onset and symptoms of AS in Chinese patients.

Methods: Adult AS patients diagnosed with the modified New York criteria for AS whose disease duration was over 2 years were enrolled from several provinces all over China. Participants were required to complete a set of questionnaires and examinations, including demographic and clinical information. Questions included "in which season(s) did you have the initial symptoms of AS", and "in which season(s) were the symptoms aggravated/improved". The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis.

Results: Of all the 859 AS patients, 75.1% were male patients. 47.8% were married. Mean age was 30.60±9.50 years. Mean disease duration was 7.43±6.92 years. 27.7% of the patients had an onset of the disease in summer, while the lowest incidence happened in autumn (12.5%, p<0.05). 29.6% of the patients could not recall the exact season. 29.5% of the patients' symptoms got worse in winter,

while only 2.6% of the patients felt worse in autumn, in comparison of 10.3% in spring and 6.0% in summer. 24.4% of the patients felt relieved in summer, while surprising, only 2.7% felt better in spring, with a lowest rate in the four season. However, 48.1% of the patients believed there were no seasonal differences.

Conclusions: More patients had an onset of AS in summer, compared to other seasons. More patients felt worse in winter and better in summer. Nearly half of AS patients considered that there were no seasonal differences in the deterioration or improvement of the symptoms.

References:

[1] Karmacharya P, Pathak R, Aryal MR, Giri S, Donato AA (2016) Seasonal variation in acute gouty arthritis: data from Nationwide Inpatient Sample. Clin Rheumatol 35: 523–525.

[2] Feldthusen C, Grimby-Ekman A, Forsblad-d'Elia H, Jacobsson L, Mannerkorpi K (2016) Seasonal variations in fatigue in persons with rheumatoid arthritis: a longitudinal study. BMC Musculoskelet Disord 17: 59.

Disclosure of Interest: Y. Jiang: None declared, M. Yang: None declared, Z. Lin: None declared, Q. Wei: None declared, S. Cao: None declared, J. Gu Grant/research support from: Guangzhou Science and Technology Plan Projects [grant number 2006Z2-E0221] and 5010 Subject of Sun Yat-sen University (2009–2010)

DOI: 10.1136/annrheumdis-2017-eular.4167

SAT0432 CORRELATION BETWEEN THE SPINAL MRI FINDINGS AND NEW BONE FORMATION FACTOR (DKK-1)I N PATIENTS WITH SPONDYLOARTHRITIS

Z. Zhao, G. Wang, Y.Y. Wang, J.S. Yang, J. Zhu, F. Huang. *Rheumatology, Chinese PLA General Hospital, Beijing, China*

Background: Recent prospective data suggest that spinal inflammatory damage in patients with ankylosing spondylitis will eventually convert into fat. In these complex inflammatory lesions, bone formation and inflammation are not synchronized. The molecular basis responsible for new bone formation in SpA patients is still unclear. Serum level of dickkopf-1 (Dkk-1), the natural inhibitor of WNT protein, is a main factor in limiting new bone formation.

Objectives: In this study, we aimed to assess the correlation between the secreted protein Dkk-1 and abnormal findings on spinal MRI through a prospective study of SpA.

Methods: Thirty patients with active axial SpA (axSpA) who fulfilled the ASAS axSpA criteria were enrolled. All patients received an injection of recombinant human TNF receptor-antibody fusion protein (YISAIPU) at a dosage of 50 mg/week for 6 months. Patient report outcome measure questionnaires and physical examination, blood tests were completed according to the study protocol. All patients were scored for bone marrow edema and fat infiltration on spinal MRI imaging. The spinal MRI imaging of the patients before and after the treatment were blindly reviewed and scored using the SPARCC scoring system by two individuals who were familiar with the system.

Results: There are 28 male and two female patients (mean age: 31±5.5 yrs, range: 22–41; mean duration: 93.5±75.8; HLA-B27(+): 96.7% (29/30)). In patients who finished the 6 month anti-TNF treatment, the ESR, CRP, BASDAI, BASFI, BASMI and ASDAS-CRP were significantly decreased ($P<0.01$). Serum Dkk-1 concentration was also significantly decreased ($P<0.05$), as were the edema measurements of spinal bone marrow ($P<0.05$), but not with the before and after treatment differences in fat infiltration scores ($p>0.05$). (Table1). Correlation analysis found that serum Dkk-1 concentration before treatment was significantly correlated with spinal bone marrow edema scores ($P<0.01$). The differences in serum Dkk-1 levels significantly correlate with differences in spinal MRI bone marrow edema scores after treatment ($P<0.05$).(Figure 1 and 2).

Table 1. Clinical indexes, serum DKK-1 and spine imaging scores before and after treatment

	Before treatment	After treatment
ESR (mm/h)	23.78±22.27	5.03±4.63**
CRP (mg/dl)	2.59±2.90	0.40±0.52**
BASDIA	6.23±1.29	2.52±1.84**
BASFI	5.78±1.44	2.69±1.72**
BASMI	2.46±1.91	0.69±1.21**
ASDAS-CRP	3.77±0.83	1.58±0.74**
DKK-1 (ng/ml)	98.23±113.41	51.88±41.90*
Spine-BME	20.27±23.53	6.08±8.09**
Spine- FAT	10.08±10.38	13.81±15.34

*p<0.05; ** p<0.01.

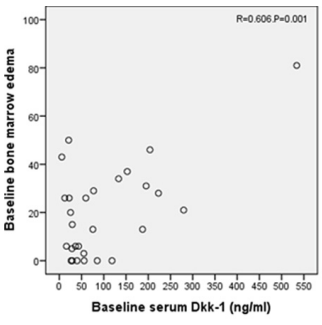


Figure 1. Serum Dkk-1 level is correlated with bone marrow edema at baseline

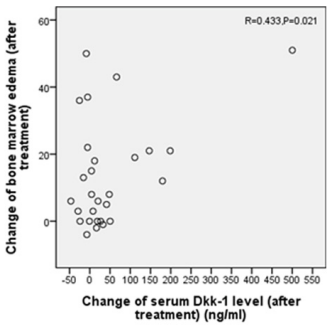


Figure 2. After treatment，the change of serum Dkk-1 level is correlated with change of bone marrow edema

Conclusions: Spinal marrow edema may have a role in predicting new bone formation in the spine, since the change of serum Dkk-1 level is correlated with change of spinal marrow edema. And Dkk-1 may participate in the molecular basis of the TNF inhibitor's blockade of new bone formation. Further research is needed on patients who have received long-term TNF antagonist treatment to find the time points when serum Dkk-1 level reaches a stabilized plateau. Increased knowledge in this area will be helpful when assessing a predictive marker for the timing of treatment withdrawal.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3160

SATURDAY, 17 JUNE 2017

Psoriatic arthritis

SAT0433 ANTI-TNF TREATMENT IN RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS PATIENTS IS ASSOCIATED WITH A STRONG INCREASE OF PALMOPLANTAR PUSTULOSIS BUT NOT OF PSORIASIS VULGARIS

J. Ruwaard[1], E. van der Vlugt[1], M. Nurmohamed[1], T. Rispens[2], G.J. Wolbink[1,2]. *[1]Amsterdam Rheumatology and immunology Center | Reade; [2]Department of Immunopathology, Sanquin Research and Landsteiner Laboratory Academic Medical Centre, Amsterdam, Netherlands*

Background: The prevalence of paradoxical psoriasis developed with biological use is already studied. However, none of these studies discriminate between psoriasis vulgaris (PV) and palmoplantar pustulosis (PPP), while these might be different entities (1). The prevalence in general population is 2–4% for PV and 0.01–0.05% for PPP (1–3). Moreover, most reports in the literature imply only a role for anti-Tumor necrosis factors (anti-TNF), although, a few cases described paradoxical psoriasis in patients treated with biologicals other than anti-TNF.

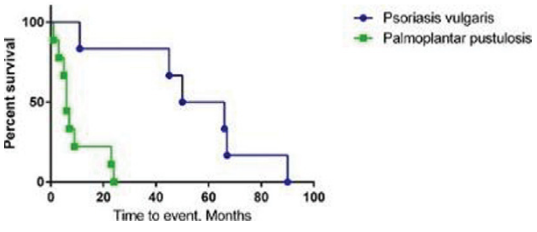
Objectives: To study the prevalence and incidence density of paradoxical psoriasis and palmoplantar pustulosis in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS) treated with biological therapy. Second to investigate differences between paradoxical psoriasis and palmoplantar pustulosis.

Methods: Data were collected from the observational cohorts of AS and RA patients. 1499 consecutive patients were included for calculating prevalence and incidence density. Incidence density is calculated per 1000 person years. For calculating differences, only biological naïve patients (n=830) were included. Kaplan Meier curve was used to show the difference in time in onset.

Results: In all, 13 cases of PPP and 16 cases of PV were observed in both the RA as AS cohorts. In AS patients 1.73% developed PPP and 1.38% PV. In RA patients respectively 0.66% and 0.99%.

The incidence density of PPP in RA was 2.1 (95% CI 0.7–3.6), for PV 3.2 (95% CI 1.4–5.0). In AS, 4.7 (95% CI 0.6–8.8) for PPP and 3.7 (95% CI 2.3–12.7) for PV. Although not statistically significant, PPP was more prevalent in adalimumab (0.94%) compared to etanercept (0.34%). In contrast, PV occurs in 0.53% in adalimumab and 0.92% in etanercept treated patients. PPP was only observed in anti-TNF, PV was also observed in 1 patient treated with tocilizumab and 1 with abatacept. A difference was observed in the time to event, with a median of 6 months (IQR 4–16 months) for PPP and 50 months (IQR 11–67 months) for PV; p=0.003 (figure 1). Discontinuation of biological treatment was indicated in 80% of the PPP patients and 18.2% PV patients.

Figure 1. Difference between patients who developed psoriasis vulgaris versus palmoplantar pustulosis on biological therapy.



Conclusions: Our findings show that biological therapy in patients with RA or AS is associated with a 13 to 35 fold increase in prevalence of PPP. While the prevalence of biological-associated PV is lower than the prevalence of PV in the general population. In this study PV and PPP are different from each other regarding prevalence, time to onset and consequences for biological treatment, and therefore should be considered as separate entities.

References:

[1] J Dermatolog Treat 2011 Apr;22(2):102–5.

[2] Lancet 2015 Sep 5;386(9997):983–94.

[3] Acta Derm Venereol 1971;51(4):284–8.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3758

SAT0434 NETWORK META-ANALYSIS ON THE EFFICACY OF NOVEL THERAPEUTIC AGENTS IN PATIENTS WITH PSORIATIC ARTHRITIS

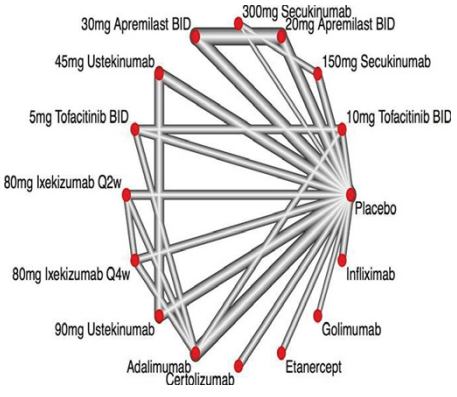
T.T. Cheung, M.F. Tsoi, Y. Fei, C.S. Lau, B.M.Y. Cheung. *Medicine, The University of Hong Kong, Hong Kong, Hong Kong*

Background: Novel therapeutic agents are more effective than DMARDs in the management of psoriatic arthritis. However, direct comparisons of efficacy between these novel therapeutic agents are lacking.
Objectives: This network meta-analysis aims to compare the relative efficacies between different novel therapeutic agents.
Methods: Literature searching was conducted in MEDLINE, EMBASE, Scopus, ISI Web of Science, Cochrane Library, Clinicaltrials.gov and recent rheumatology conference abstracts up to Nov 2016. 2 independent researchers analysed the articles. For inclusion, randomised, placebo-controlled trials must report the proportion of patients achieving ACR20, ACR50, ACR70 and PASI75 responses. The outcomes of this network meta-analysis were the proportion of patients achieving ACR20, ACR50, ACR70 and PASI75 responses with reference to placebo and etanercept.
Results were analysed using random effect model by R statistics (version 3.3.1) with statistical package netmeta (version 0.9–2). The heterogeneity of the study results was determined by the I^2 statistics.
Results: 18 trials were included into this study. In general, all novel therapeutic agents demonstrated superior efficacies than placebo. With reference to etanercept, apremilast and ustekinumab were associated with less proportions of patients achieving ACR20 response (odds ratio [95% confidence interval]: 20mg apremilast: 0.18 [0.07–0.48]; 30mg apremilast: 0.24 [0.09–0.62]; 45mg ustekinumab: 0.26 [0.09–0.73]; 90mg ustekinumab: 0.32 [0.11–0.90]).
Etanercept was not different from apremilast, ustekinumab, golimumab, adalimumab, ixekizumab, certolizumab, ixekizumab and secukinumab in terms of ACR20 and ACR50 responses.
Golimumab and infliximab were associated with greater proportions of patients achieving PASI75 response, though the difference did not reach statistical significance. (odds ratio [95% confidence interval]: golimumab: 3.51 [0.44–28.2]; infliximab: 5.97 [0.89–40.2]).

Table 1. Network meta-analysis on proportion of patients achieved ACR20 and PASI75 response with reference to etanercept

	ACR20 response	PASI75 response
10mg Tofacitinib BID	0.38 [0.12; 1.22]	0.68 [0.13; 3.54]
150mg Secukinumab	0.64 [0.22; 1.90]	0.49 [0.07; 3.19]
20mg Apremilast BID	0.18 [0.07; 0.49]	0.39 [0.08; 1.83]
300mg Secukinumab	0.77 [0.21; 2.80]	0.67 [0.10; 4.56]
30mg Apremilast BID	0.24 [0.09; 0.63]	0.48 [0.10; 2.22]
45mg Ustekinumab	0.26 [0.09; 0.75]	1.18 [0.15; 9.09]
5mg Tofacitinib BID	0.25 [0.08; 0.81]	0.64 [0.12; 3.29]
80mg Ixekizumab Q2w	0.40 [0.12; 1.27]	2.74 [0.49; 15.37]
80mg Ixekizumab Q4w	0.35 [0.11; 1.11]	1.73 [0.32; 9.31]
90mg Ustekinumab	0.32 [0.11; 0.92]	1.40 [0.18; 10.74]
Adalimumab	0.33 [0.13; 0.86]	0.77 [0.17; 3.50]
Certolizumab	0.42 [0.12; 1.39]	NA
Etanercept (reference)	1.00	1.00
Golimumab	0.93 [0.25; 3.40]	3.51 [0.44; 28.22]
Infliximab	0.74 [0.26; 2.12]	5.97 [0.89; 40.22]
Placebo	0.10 [0.04; 0.22]	0.09 [0.03; 0.35]

NA: not applicable.



Conclusions: Apremilast and ustekinumab were less efficacious than etanercept in terms of ACR20 response. All the novel therapeutic agents demonstrated comparable efficacies in terms of ACR50, ACR70 and PASI75 responses.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5096

SAT0435 IL17 CORRELATES POSITIVELY WITH TGF-BETA 1 AND DKK1 AND INVERSELY WITH BMP2 AND 4 IN SYNOVIAL MEMBRANE OF PATIENTS WITH PSORIATIC ARTHRITIS

J. Pinto-Tasende, M. Fernandez-Moreno, M.E. Vazquez-Mosquera, J.C. Fernandez-Lopez, N. Oreiro-Villar, M. Bejerano-Herrería, B. Acasuso-Pardo de Vera, F.J. Blanco-García. *INIBIC-Rheumatology, Complejo Hospitalario Universitario A Coruña, A Coruña, Spain*

Background: Immune and non-immune cells contribute to the pathology of chronic arthritis and they can contribute to tissue remodeling and repair as well as disease pathogenesis. An important role for their products such as TGF-beta 1, IL17 or BMPs has been suggested in homeostatic and remodeling mechanisms in arthritis. BMP signaling could have an anti-inflammatory role in the control and maintenance of low levels of pro-inflammatory factors in healthy joints or the early stage of RA.
Objectives: to analyze and compare serum levels, gene expression and immunohistochemistry (IHC) in synovial membrane of inflammation and bone destruction/regeneration biomarkers in patients with psoriatic arthritis (PsA), undetermined seronegative arthritis (USA), Osteoarthritis of the knee (kOA) and ankylosing spondylitis (AS).
Methods: We recruited 45 consecutive patients with chronic knee arthritis referred for undergoing arthroscopies (17 PsA, 12 USA, 12 kOA, 4 AS). Synovial membrane was processed for IHC analysis and quantification of mRNA expression ratio by qRT-PCR. Serum levels of TGF-beta 1, IL6, IL17 and IL22, DKK1, Sclerostin, BMP2, BMP4, Wnt1 and Wnt5a were measured (ELISA). We analyzed and compared these data with the demographic, clinical, analytical and radiological characteristics of the patients. Data were analyzed using the SPSS version 17.0 software and statistical significance was defined as $P<0.05$.
Results: We obtained valid synovial membrane samples from 41 patients for IHC, RNA extraction and purification from 29 patients for analyze mRNA expression and serum from 38 patients for protein levels measurement. IL17 gene expression was higher in PsA patients (p=0.027) and correlated positively with DKK1 (r=0.424, p=0.022) and negatively with BMP2 (r=-0.396, p=0.033) and BMP4 (r=-0.472, p=0.010). IHC reactivity for TGF-beta 1 in synovial tissue was higher in patients with psoriatic arthritis (p 0.010) and correlated positively with IL17 (r=0.389, p=0.012) and DKK1 (r=0.388, p=0.012). Moreover, serum levels of TGF-beta 1 were significantly increased in PsA with erosions (p=0.044).
Conclusions: IL17 gene expression in synovial membrane from patients with psoriatic arthritis was higher than in seronegative undetermined arthritis, osteoarthritis and ankylosing spondylitis patients, correlating positively with DKK1 and negatively with bone morphogenetic proteins 2 and 4. In addition, TGF-beta in synovial tissue, necessary for the activation of Th17 cells, was higher in patients with psoriatic arthritis, in relation to IL17 and DKK1 increased. Serum TGF beta 1 levels were also higher in patients with erosive disease.
References:
[1] Varas A, Valencia J, Lavocat F, Martínez VG, Thiam NN, Hidalgo L, et al. Blockade of bone morphogenetic protein signaling potentiates the pro-inflammatory phenotype induced by interleukin-17 and tumor necrosis factor-α combination in rheumatoid synoviocytes. Arthritis Res Ther. 2015;17:192. doi: 10.1186/s13075–015–0710–6.
Acknowledgements: This work has been supported by grant PI11/00390 from Plan Nacional de Investigación Científica, Desarrollo e Innovación Tecnológica 2008–2011 y cofinanciado por el ISCIII-Subdirección General de Evaluación y Fomento de la Investigación - Fondo Europeo de Desarrollo Regional (FEDER).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4427

SAT0436 DURABILITY OF APREMILAST RESPONSE IN PATIENTS WITH PSORIATIC ARTHRITIS: LONG-TERM (208-WEEK) RESULTS FROM THE PALACE 1 TRIAL

A. Kavanaugh[1], D.D. Gladman[2], J.J. Gomez-Reino[3], S. Hall[4], E. Lespessailles[5], P.J. Mease[6], G. Schett[7], M. McIlraith[8], N. Delev[8], M. Paris[8], L. Teng[8], J. Wollenhaupt[9]. *[1]UCSD School of Medicine, la Jolla, United States; [2]Toronto Western Research Institute, Toronto, Canada; [3]Hospital Clínico Universitario, Santiago, Spain; [4]Monash University, CabriniHealth, Melbourne, Australia; [5]University of Orléans, Orléans, France; [6]Swedish Medical Center and University of Washington School of Medicine, Seattle, United States; [7]University of Erlangen-Nuremberg, Erlangen, Germany; [8]Celgene Corporation, Summit, United States; [9]Schön Klinik Hamburg Eilbek, Hamburg, Germany*

Background: Optimizing treatment choice in psoriatic arthritis (PsA) necessitates an understanding of the long-term effects of therapies across varied manifestations of this complex disease. Data from 4 years of apremilast (APR) treatment in PALACE 1 were used to examine disease control across markers of active inflammation, such as SJC, as well as improvements in patient (pt) functionality, as assessed using the HAQ-DI.
Objectives: Evaluate long-term outcomes with APR treatment after ≥1 DMARD or biologic in pts with active PsA.
Methods: Pts were randomized (1:1:1) to placebo (PBO), APR 30 mg BID (APR30), or APR 20 mg BID (APR20). The PBO-controlled phase continued to Wk 24, at which time all remaining PBO pts were re-randomized to APR30 or

APR20. Double-blind APR treatment continued to Wk 52; pts could continue APR for up to 4 additional years in an open-label extension.

Results: 504 pts were randomized and received ≥1 dose of study medication (PBO: n=168; APR30: n=168; APR20: n=168); 86.9% (225/259) of pts entering the third year completed 208 wks of APR treatment; overall, this is 44.6% (225/504) of pts randomized at baseline (BL). At Wk 52, 53.2% of APR30 pts achieved a modified ACR20 response (Table), regardless of when APR was started (BL, Wk 16, or Wk 24). At Wk 208, a sustained response rate was observed in APR30 pts, as shown by an ACR20 response rate of 67.5%. Marked improvements in SJC were seen throughout the study, with a mean percent decrease of −84.2% at Wk 208; TJC reductions were consistent (Table). Functionality is of paramount importance to pts; large improvements were seen in HAQ-DI score, with a mean change of −0.47. Pts also note fatigue as a disease- or treatment-related impairment; a mean improvement of 5.7 was seen in FACIT-F score at Wk 208 (Table), and the pt population reached a mean score of 35.7. In addition, long-term treatment led to the maintenance of the proportions meeting the minimal clinically important difference in HAQ-DI score change, achieving ACR50/ACR70 responses and reaching PASI-75 and PASI-50 responses (Table). No new safety concerns were identified with APR treatment up to 208 wks. During Wks >156 to ≤208, the only adverse event (AE) occurring in ≥5% of APR30-exposed pts was URTI (5.2%); most AEs were mild/moderate in severity. Among APR30-exposed pts, serious AEs occurred in 6.7% of pts in Wks >156 to ≤208, consistent with earlier data. Importantly, few discontinuations due to AEs occurred throughout the long-term treatment period.

Outcomes at Wk 52 and Wk 208		
	Wk 52	Wk 208
	APR30 n=193*	APR30 n=123*
ACR20, n/m§ (%)	101/190 (53.2)	83/123 (67.5)
ACR50, n/m§ (%)	49/191 (25.7)	56/122 (45.9)
ACR70, n/m§ (%)	27/191 (14.1)	35/123 (28.5)
Swollen joint count, mean % change	−50.5	−84.2
Tender joint count, mean % change	−45.1	−78.1
HAQ-DI (0-3), mean change	−0.31	−0.47
HAQ-DI MCID ≥0.30, n/m (%)	85/193 (44.0)	72/123 (58.5)
HAQ-DI MCID ≥0.35, n/m (%)	85/193 (44.0)	72/123 (58.5)
DAS-28 (CRP) <2.6, n/m (%)	41/189 (21.7)	57/122 (46.7)
DAS-28 (CRP), mean change	−1.26	−2.08
FACIT-F, mean change	3.8	5.7
PASI-75‡, n/m (%)	31/95 (32.6)	21/60 (35.0)
PASI-50‡, n/m (%)	52/95 (54.7)	37/60 (61.7)

Data as observed. *The n reflects the number of pts treated with APR30, regardless of when treatment started (BL, Wk 16, or Wk 24), and who had data available at the specific time point; actual number of pts available for each end point may vary. §Denominators vary slightly due to availability of sufficient data for each level of ACR response assessment. ‡Examined among pts with psoriasis involvement of the body surface area ≥3% at BL and data at the specific time point. APR30=apremilast 30 mg BID; ACR20/50/70=20%/50%/70% improvement in modified American College of Rheumatology response criteria; n/m=number of responders/number of pts with sufficient data for evaluation; HAQ-DI=Health Assessment Questionnaire-Disability Index; MCID=minimal clinically important difference; DAS-28=28-joint count Disease Activity Score; CRP=C-reactive protein; FACIT-F=Functional Assessment of Chronic Illness Therapy-Fatigue; PASI-75/50=≥75%/≥50% reduction from BL Psoriasis Area and Severity Index score; pts=patients; BL=baseline.

Conclusions: APR30 demonstrated sustained, clinically meaningful improvements in signs and symptoms of PsA, physical function, and associated psoriasis over 208 wks. APR30 continued to demonstrate a favorable safety profile and was generally well tolerated.

Disclosure of Interest: A. Kavanaugh Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, D. Gladman Grant/research support from: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB, J. Gomez-Reino Grant/research support from: Roche and Schering-Plough, Consultant for: BMS, Pfizer, Roche, Schering-Plough, UCB, S. Hall Consultant for: Boehringer Ingelheim, MSD, Roche, Schering-Plough, Servier, Wyeth, Paid instructor for: Amgen, AstraZeneca, Boehringer Ingelheim, Centocor, GSK, MSD, Pfizer, Sanofi Aventis, Sanofi Pasteur, Schering-Plough, Serono, Wyeth, Speakers bureau: Boehringer Ingelheim, GSK, MSD, Pfizer, Roche, Sanofi Aventis, Schering-Plough, Wyeth, E. Lespessailles Grant/research support from: Amgen, Eli Lilly, Novartis, Servier, Speakers bureau: Amgen, Eli Lilly, Novartis, Servier, P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Consultant for: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Genentech, Janssen, Eli Lilly, Pfizer, UCB, G. Schett Grant/research support from: Abbott, Celgene Corporation, Roche, UCB, Consultant for: Abbott, Celgene Corporation, Roche, UCB, M. McIlraith Employee of: Celgene Corporation, N. Delev Employee of: Celgene Corporation, M. Paris Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, J. Wollenhaupt Grant/research support from: Abbott, BMS, MSD, Pfizer, UCB, Consultant for: Abbott, BMS, MSD, Pfizer, UCB

DOI: 10.1136/annrheumdis-2017-eular.3001

SAT0437 IXEKIZUMAB IMPROVES NAIL AND SKIN LESIONS IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND PRIOR TNF INADEQUATE RESPONSE

L.E. Kristensen[1], J.F. Merola[2,3], J. Dutz[4], D.H. Adams[5], L. Kerr[5], P. Rich[6].
[1]Copenhagen University Hospital, Bispebjerg and Frederiksberg, Denmark; [2]Brigham and Women's Hospital; [3]Harvard Medical School, Boston, United States; [4]The University of British Columbia, Vancouver, Canada; [5]Eli Lilly and Company, Indianapolis; [6]Oregon Health Science University, Portland, United States

Background: Ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A, significantly improved fingernail psoriasis by Week (Wk) 12 vs placebo (PBO) in patients (pts) with moderate-to-severe plaque psoriasis[1]. Moreover, IXE had significantly reduced signs and symptoms of psoriatic arthritis (PsA) at Wk 24 in biologic disease-modifying antirheumatic drug (bDMARD)-naïve pts with active PsA[2].

Objectives: To evaluate the impact of IXE on nail and skin lesions in active PsA pts who have previously received bDMARD therapy.

Methods: In this phase 3, multicentre, double-blind, PBO-controlled, outpatient study, pts (aged ≥18 years) with active PsA and bDMARD-experience randomly (1:1:1) received PBO for 24 Wks, 80 mg IXE as one injection every 2 (IXE Q2W) or 4 Wks (IXE Q4W) after starting dose of 160 mg. At Wk 16, inadequate responders received rescue medication and PBO pts were re-randomised (1:1) to receive either IXE Q2W or IXE Q4W. The efficacy of IXE was assessed by Nail Psoriasis Severity Index (NAPSI) in pts with nail psoriasis at baseline (PBO, n=73; IXE Q4W, n=89; IXE Q2W, n=74), Psoriasis Area and Severity Index (PASI) 75/90/100 response rate at Wk24 in pts with baseline body surface area (BSA) ≥3 (PBO, n=67; IXE Q4W, n=68; IXE Q2W, n=68) and percentage of pts achieving static Physician Global Assessment (sPGA) of psoriasis score of 0 (cleared) or 1 (minimal) in pts with baseline sPGA≥3 (PBO, n=55; IXEQ4W, n=60; IXEQ2W, n=62). Missing data and inadequate responder data were imputed using the nonresponder imputation for categorical variables. For continuous variables, least squares mean (LSM) changes were calculated using mixed effects models for repeated measures, observed data from Wks 16 to 24 was excluded for inadequate responders.

Results: Overall the demographics and baseline characteristics were comparable between the treatment groups. The mean (SD) NAPSI total score at baseline was 19 (19), 20 (20), and 21 (22) in PBO, IXE Q4W and IXE Q2W, respectively. At Wk 24, the change in NAPSI total score from baseline was significantly greater with IXE Q4W (LSM±SE -10.2±2.04) and IXE Q2W (-10.8±2.12) vs PBO (0.5±2.13, p<.001 each). Similarly, the mean percentage improvement in NAPSI total score was significantly greater with IXE Q4W (LSM±SE 35.4±22.14, p<.001) and IXE Q2W (30.9±22.95, p=.001) vs PBO (-45.2±23.04). At Wk 24, significantly greater percentage of pts achieved a NAPSI score of 0 with IXEQ4W or IXEQ2W treatment vs PBO (Table). At Wk 24, the percentage of pts achieving PASI 75/90/100 response was significantly greater with IXE Q4W and IXE Q2W vs PBO (Table). Overall, the safety profile of IXE was aligned with the general study population.

Table: Percentage of patients with improvement in skin and nail lesions

Efficacy endpoints (%)	Placebo	IXE Q4W	IXE Q2W
PASI 75[a]	14.9	55.9*	60.3*
PASI 90[a]	11.9	44.1*	50.0*
PASI 100[a]	4.5	35.3*	27.9*
sPGA (0, 1)[b]	9.1	66.7*	75.8*
NAPSI (0)[c]	6.8	20.2**	29.7*

*p<.001; **p=.022; [a]Patients with baseline ≥3% BSA; [b]in patients with baseline sPGA ≥3; [c]Patients with baseline fingernail psoriasis

Conclusions: In the present study, ixekizumab led to significantly greater reduction and clearance of the nail and skin lesions in active PsA pts who had previously received bDMARD therapy compared to placebo.

References:

[1] Dennehy EB et al. J Drugs Dermatol. 201615(8):958–61.
[2] Mease PJ, et al. Ann Rheum Dis. 2016 doi: 10.1136/annrheumdis-2016–209709.

Disclosure of Interest: L. Kristensen Grant/research support from: UCB, Janssen-Cilag and Biogen, Consultant for: Pfizer, AbbVie, Amgen, UCB, Celegene, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, Speakers bureau: Pfizer, AbbVie, Amgen, Biogen, UCB, Celegene, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, J. Merola Grant/research support from: Biogen IDEC, Consultant for: Biogen IDEC, Amgen, AbbVie, and Eli Lilly, Novartis, Pfizer, Janssen, UCB, Kiniksa, Momenta and Mallinckrodt, J. Dutz Grant/research support from: Abbvie, Novartis, Amgen, Consultant for: Cipher, Speakers bureau: Janssen, Abbvie, Novartis, Amgen, Leo, Celgene, D. Adams Employee of: Eli Lilly and Company, L. Kerr Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Rich Grant/research support from: UCB, Janssen-Cilag and Biogen, Consultant for: Pfizer, AbbVie, Amgen, UCB, Celegene, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals, Speakers bureau: Pfizer, AbbVie, Amgen, Biogen, UCB, Celegene, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals.

DOI: 10.1136/annrheumdis-2017-eular.3105

SAT0438 PSORIATIC ARTHRITIS AND NODAL OSTEOARTHRITIS CAN BE DIFFERENTIATED USING HAND RADIOGRAPHS: A NOVEL METHOD

S. Bahadur[1], A. Zavareh[2], C. Hughes[3], R. Mandegaran[3], S. Subesinghe[3], B. Kirkham[3]. *[1]Rheumatology; [2]Radiology; [3]Guys and St Thomas Trust, London, United Kingdom*

Background: One of the difficulties of rheumatology practice is the differentiation of Psoriatic Arthritis (PsA) and Nodal Osteoarthritis (NOA) in some patients with distal interphalangeal joint involvement. MRI and ultrasound imaging, have recently been demonstrated as inconclusive in some cases (1,2). This differentiation is critical, as treatment for these debilitating conditions is completely different.
Objectives: To establish a scoring system of radiographic joint and soft tissue features to differentiate PsA from NOA.
Methods: We devised a scoring system for hand radiographs of interphalangeal joints, soft tissue and bone features, allocated major and minor weighting. The scoring system was then tested in a single blind analysis of hand radiographs from 48 patients with PsA, 50 with NOA and 1 with RA (incorrectly classified as PsA at study entry) seen between 2008 and 2016. Anonymised patient images were assessed by a Musculoskeletal (MSK) Radiologist, blind to clinical information. Radiological diagnosis was then compared with clinical diagnosis. We taught the method to 2 rheumatology and 1 radiology trainees over 1 hour, who then independently assessed the same radiographs.
Results: The MSK radiologist reported normal hand radiographs in 5 patient sets. Of the remaining 94 patient sets, the scoring system correctly allocated 100% of images into PsA, NOA or RA. Notably, 2 patients with NOA who subsequently developed PsA several years later, and 1 patient with seropositive RA, initially misclassified as PsA, were correctly identified by the MSK radiologist.
Trainees using the system also achieved good agreement, after removing radiographs assessed as normal; Rheumatology trainees: 88% and 67% correct; Radiology trainee: 70% correct.
Conclusions: This initial single-centre study shows our novel radiological scoring system is effective at differentiating patients with PsA from NOA. Radiographs provide an accurate, time-efficient (for both clinician and patient) and inexpensive test. We also show that trainees can learn this scoring system with moderate accuracy after a short educational programme. We are currently carrying out a detailed analysis of the scoring system to optimise accuracy and ease of use by non-radiologists.
References:
[1] McGonagle D, Hermann KG, Tan AL. Differentiation between osteoarthritis and psoriatic arthritis: implications for pathogenesis and treatment in the biologic therapy era. Rheumatology. 2015;54:29–38.
[2] Yumusakhuylu Y, Kasapoglu-Gunal E, Murat S et al. A preliminary study showing that ultrasonography cannot differentiate between psoriatic arthritis and nodal osteoarthritis based on enthesopathy scores. Rheumatology. 2016; 55:1703–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6350

SAT0439 INTEGRATED SAFETY SUMMARY OF TOFACITINIB IN PSORIATIC ARTHRITIS CLINICAL STUDIES

G. Burmester[1], O. FitzGerald[2], K. Winthrop[3], G. Williams[4], V.F. Azevedo[5], W.F.C. Rigby[6], K. Kanik[7], C. Wang[7], P. Biswas[8], T. Jones[9], S. Menon[7], N. Palmetto[8], R. Rojo[7]. *[1]Charité - University Medicine Berlin, Berlin, Germany; [2]Department of Rheumatology, St. Vincent's University Hospital, Dublin, Ireland; [3]Oregon Health and Science University, Portland, OR; [4]Williams Cancer Drug Consulting LLC, Wayne, NJ, United States; [5]Universidade Federal do Paraná, Curitiba, Brazil; [6]Geisel School of Medicine at Dartmouth, Lebanon, NH; [7]Pfizer Inc, Groton, CT; [8]Pfizer Inc, New York, NY; [9]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for psoriatic arthritis (PsA).
Objectives: To describe the safety profile of tofacitinib from integrated Phase (P)3 and long-term extension (LTE) studies.
Methods: Data were analysed for patients (pts) who received ≥1 dose of tofacitinib 5 or 10 mg BID or placebo (PBO), integrated across 2 P3 studies (OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]) and 1 LTE study (OPAL Balance [ongoing, database not locked; NCT01976364]). Common adverse events (AEs; occurring in ≥2% of tofacitinib pts in any group) were analysed in the PBO-controlled portion (Months 0–3) of the P3 studies (Cohort 1 [C1]). Serious AEs (SAEs) and discontinuations due to AEs were analysed over 12 months in pts randomised to tofacitinib 5 or 10 mg BID in P3 studies (Cohort 2a [C2a]); pts randomised to PBO were excluded from this analysis. Deaths and AEs of special interest (serious infections [SI], herpes zoster [HZ], opportunistic infections [OI] including HZ, major adverse cardiac events [MACE], malignancies, non-melanoma skin cancer [NMSC]) were evaluated in all tofacitinib-treated pts in the P3 and LTE studies (Cohort 3 [C3]). Incidence rates (IR; pts with events/100 pt-years [PY] and 95% confidence intervals) are reported. Laboratory results will be reported in future publications.
Results: C1 included 474 tofacitinib- and 236 PBO-treated pts; C2a included 474 tofacitinib-treated pts; and C3 included 783 tofacitinib-treated pts (exposure: 776 PY). Nasopharyngitis (5.9%) and headache (8.5%) were the most commonly reported AEs at Month 3 in pts receiving tofacitinib 5 and 10 mg BID, respectively (Table). In pts randomised to tofacitinib 5 or 10 mg BID, over 12 months (C2a), the IRs for SAEs were 7.92 (4.09, 13.84) and 8.11 (4.19, 14.17), respectively. Discontinuation due to AEs occurred in 11 (4.6%) and 11 (4.7%) pts randomised to tofacitinib 5 and 10 mg BID, respectively, with IRs of 7.16 (3.58, 12.82) and 7.31 (3.65, 13.08), respectively, over 12 months (C2a). Across all tofacitinib-treated pts in the P3 and LTE studies (C3), SIs occurred in 11 pts (1.4%; IR 1.40 [0.70, 2.50]). HZ was reported in 16 pts (2.0%; IR 2.05 [1.17, 3.33]) receiving tofacitinib. All 3 cases of multidermatomal HZ were adjudicated as OIs; these were the only OIs (0.4%; IR 0.38 [0.08, 1.11]). In C3, 2 deaths occurred (0.3%; IR 0.25 [0.03, 0.91]); all were considered unrelated to the study drug. MACE were reported in 3 pts (0.4%; IR 0.38 [0.08, 1.11]), malignancies (excluding NMSC) in 5 pts (0.6%; IR 0.63 [0.21, 1.48]) and NMSC in 4 pts (0.5%; IR 0.51 [0.14, 1.30]).

Table: Common adverse events (≥2% occurrence in any group, all causalities) at Month 3 in patients receiving tofacitinib 5 or 10 mg BID or placebo

Common Adverse Events, n (%)	Tofacitinib 5 mg BID (N=238)	Tofacitinib 10 mg BID (N=236)	Placebo (N=236)
Diarrhoea	8 (3.4)	9 (3.8)	1 (0.4)
Dyspepsia	5 (2.1)	2 (0.8)	2 (0.8)
Nausea	6 (2.5)	5 (2.1)	7 (3.0)
Fatigue	0	7 (3.0)	1 (0.4)
Bronchitis	6 (2.5)	4 (1.7)	0
Nasopharyngitis	14 (5.9)	13 (5.5)	6 (2.5)
Pharyngitis	1 (0.4)	7 (3.0)	3 (1.3)
Upper respiratory tract infection	12 (5.0)	11 (4.7)	11 (4.7)
Urinary tract infection	3 (1.3)	6 (2.5)	5 (2.1)
Headache	9 (3.8)	20 (8.5)	11 (4.7)
Dizziness	6 (2.5)	1 (0.4)	3 (1.3)
Acne	3 (1.3)	5 (2.1)	0
Hypertension	4 (1.7)	5 (2.1)	3 (1.3)

BID, twice daily; N, number of patients evaluable

Conclusions: Tofacitinib was well tolerated in pts with PsA, with a safety profile consistent to that seen in RA; no new risks were identified. Longer-term follow-up and larger pt populations will provide further information on the safety profile of tofacitinib in pts with PsA.
Acknowledgements: These studies were sponsored by Pfizer Inc. Editorial support was provided by C Viegelmann of CMC and was funded by Pfizer Inc.
Disclosure of Interest: G. Burmester Grant/research support from: UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Hexal, Janssen, MSD, MedImmune, Novartis, Pfizer Inc, Sanofi, Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Hexal, MSD, Novartis, Pfizer Inc, Roche, O. FitzGerald Grant/research support from: AbbVie, Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer Inc, Speakers bureau: Celgene, Janssen, Novartis, K. Winthrop Grant/research support from: Bristol-Myers Squibb, Pfizer Inc, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Eli Lilly, Galapagos, Pfizer Inc, UCB, G. Williams Consultant for: Pfizer Inc, V. Azevedo Grant/research support from: Bristol-Myers Squibb, GSK, Pfizer Inc, UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Novartis, Pfizer Inc, Serono, W. F. Rigby Grant/research support from: Amgen, Pfizer Inc, Roche, Consultant for: Bristol-Myers Squibb, Eli Lilly, Pfizer Inc, Roche, K. Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, P. Biswas Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Jones Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, S. Menon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, N. Palmetto Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. Rojo Shareholder of: Pfizer Inc, Employee of: Pfizer Inc
DOI: 10.1136/annrheumdis-2017-eular.1573

SAT0440 DO DEPRESSION AND ANXIETY INFLUENCE THE CHANCE OF REMISSION IN PATIENTS WITH PSORIATIC ARTHRITIS? REAL LIFE DATA FROM THE NOR-DMARD STUDY

B. Michelsen[1,2], E.K. Kristianslund[1], K.M. Fageli[1], E. Lie[1], H.B. Hammer[1], G. Haugeberg[2,3], T.K. Kvien[1]. *[1]Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo; [2]Dept. of Rheumatology, Hospital of Southern Norway Trust, Kristiansand; [3]Dept. of Rheumatology, Martina Hansens Hospital, Oslo, Norway*

Background: Depression and anxiety are frequent comorbidities in psoriatic arthritis (PsA). Still, the potential influence of depression/anxiety on achievement of remission remains unexplored.
Objectives: To investigate the predictive value of baseline depression/anxiety on the likelihood of achieving remission in PsA, as well as the associations between

Abstract SAT0440 – Table 1

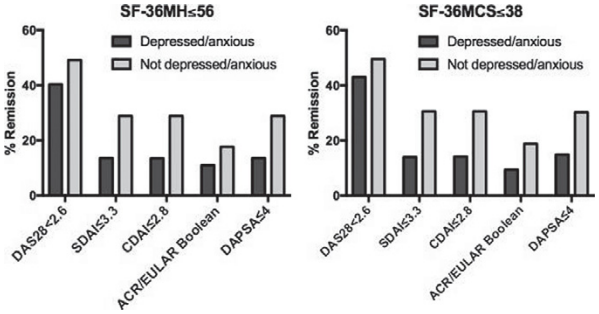
Months	Odds ratio (95% CI) for remission in patients with vs. without baseline depression/anxiety according to SF-36MH≤56				
	DAS28<2.6	SDAI≤3.3	CDAI≤2.8	ACR/EULAR Boolean	DAPSA≤4
3	0.61 (0.35–1.06), p=0.08	0.36 (0.17–0.76), p=0.007	0.48 (0.25–0.93), p=0.03	0.62 (0.29–1.30), p=0.20	0.37 (0.18–0.79), p=0.01
6	0.81 (0.44–1.51), p=0.51	0.38 (0.18–0.82), p=0.01	0.39 (0.19–0.81), p=0.01	0.61 (0.28–1.33), p=0.21	0.40 (0.19–0.84), p=0.02
Months	Odds ratio (95% CI) for remission in patients with vs. without baseline depression/anxiety according to SF-36MCS≤38				
	DAS28<2.6	SDAI≤3.3	CDAI≤2.8	ACR/EULAR Boolean	DAPSA≤4
3	0.68 (0.42–1.01), p=0.11	0.37 (0.20–0.69), p=0.002	0.45 (0.26–0.78), p=0.004	0.45 (0.23–0.88), p=0.02	0.42 (0.23–0.76), p=0.004
6	0.91 (0.54–1.56), p=0.74	0.42 (0.22–0.79), p=0.008	0.43 (0.24–0.78), p=0.005	0.51 (0.26–1.00), p=0.05	0.46 (0.25–0.86), p=0.02

baseline depression/anxiety and the components of the remission criteria at follow-up.

Methods: From the prospective multi-center observational NOR-DMARD study we included PsA patients starting first-time methotrexate/tumor necrosis factor inhibitors between year 2006 and 2012. The following criteria for depression/anxiety were assessed: 1) the Medical Outcomes Survey Short Form-36 (SF-36) Mental Health subscale (MH)≤56 and 2) SF-36 Mental Component Summary score (MCS)≤38.[1] The predictive value of baseline depression/anxiety on remission at 3 and 6 months was explored in prespecified logistic regression models adjusted for age, sex, disease duration and smoking, and the associations between baseline depression/anxiety and the components of the remission criteria at follow-up in prespecified multiple linear regression models adjusted for age, sex, disease duration and smoking.

Results: 805 PsA patients were included (mean (SD) age 48.0 (12.4) years, median (25th-75th percentile) disease duration 1.0 (0.07–6.8) years, 50.8% females, 28.6% current smokers). According to the SF-36MH≤56/SF-36MCS≤38 criteria 15.6/25.2% of the patients had depression/anxiety at baseline, respectively. Lower percentages of patients with vs. without baseline depression/anxiety achieved remission at 6 months (unadjusted analyses;figure). Patients with baseline depression/anxiety had consistently lower point estimates for achievement of remission at follow-up, but did not reach significance for all the analyses (adjusted analyses, table).

Baseline depression/anxiety was associated with increased patient's global assessment and joint pain at follow-up, but not with swollen joint count or levels of acute phase reactants.



Conclusions: Depression and anxiety may reduce likelihood of remission based on composite scores in PsA. These observations support a focus on depression and anxiety as comorbidities in a treat-to-target strategy and may also reflect that patient reported outcome measures are part of all these composite measures used to define remission.

References:

[1] Matcham et al. BMC Musculoskelet Disord. 2016;17:224.

Disclosure of Interest: B. Michelsen: None declared, E. Kristianslund: None declared, K. Fageli: None declared, E. Lie Consultant for: Hospira, Pfizer, UCB, Speakers bureau: AbbVie, Celgene, H. Hammer Consultant for: AbbVie, Pfizer, UCB, Roche, MSD, BMS and Novartis., Speakers bureau: AbbVie, Pfizer, UCB, Roche, MSD, BMS and Novartis., G. Haugeberg: None declared, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB

DOI: 10.1136/annrheumdis-2017-eular.3181

SAT0441 COMPARISON OF DIFFERENT REMISSION TARGETS IN PATIENTS WITH PSORIATIC ARTHRITIS AND EVALUATION OF THEIR PROGNOSTIC VALUE

L.C. Coates[1], L. Aikman[2], A. Szumski[3], A. Chhabra[4]. *[1]University of Leeds, Leeds; [2]Pfizer, Walton Oaks, United Kingdom; [3]inVentiv Health, Princeton; [4]Pfizer, New York, United States*

Background: Psoriatic arthritis (PsA) is a complex form of arthritis that develops in people with psoriasis. There is no agreement on the optimal criteria to identify remission in patients with PsA and some of them may miss skin lesions.

Objectives: To investigate the merits of different potential remission definitions using data from the PRESTA study.[1]

Methods: Remission was investigated for disease activity index for PsA for 3 definitions: very low disease activity (VLDA), Disease Activity in PsA (DAPSA), and clinical (c)DAPSA. VLDA index was defined as 7/7 met criteria of the minimal disease activity (MDA) cut-off points: tender joint count (TJC) ≤1, swollen joint count (SJC) ≤1, psoriasis activity and severity index (PASI) ≤1, patient global visual analog scale (Pt VAS) ≤20mm, Pt pain VAS ≤15mm, health assessment questionnaire (HAQ) ≤0.5, tender entheseal points ≤1. DAPSA remission was defined as DAPSA ≤4 (TJC, SJC, physician global VAS [cm], Pt VAS [cm], C-reactive protein [CRP]) and cDAPSA remission was defined as cDAPSA ≤4 (DAPSA without CRP).

Results: At Week 24, the proportion of patients achieving remission was 9.6%, 31.0%, and 34.7% for VLDA, DAPSA, and cDAPSA remission, respectively. Discordance between VLDA and DAPSA or cDAPSA remission was 21.7% or 25.1%, respectively. Only 0.2% of the patients that achieved VLDA did not achieve DAPSA remission and 21.5% vice versa (Kappa coefficient 0.38) and 0.0% in the case of cDAPSA remission and 25.1% vice versa (Kappa coefficient 0.33). At the end of the study, residual levels of dactylitis and enthesitis appeared to be similar among all definitions (all ≤3.0%); however, patients achieving DAPSA and cDAPSA remission had higher proportions of patients with PASI >1 than patients achieving VLDA remission (PASI 2–9: VLDA 0.0% vs DAPSA 46.4% vs cDAPSA 47.2%; PASI ≥10: VLDA 0.0% vs DAPSA 5.8% vs cDAPSA 6.4%). Raised CRP values (upper limit of normal >8.99) were 7.8%, 4.8%, and 7.3% for VLDA, DAPSA, and cDAPSA, respectively.

Conclusions: VLDA remission is a more stringent target than DAPSA and cDAPSA remission, with the advantage of including a measurement for psoriasis. Therefore, VLDA is more useful than DAPSA or cDAPSA in assessing a remission state in patients with PsA and extended skin lesions. Measurement of CRP levels does not appear to provide further information on current disease activity level in these patients and exclusion of this laboratory marker should facilitate remission assessment in clinical practice.

References:

[1] Sterry W, et al. BMJ 2010;340:c147.

Disclosure of Interest: L. Coates Grant/research support from: Abbvie, Janssen, Consultant for: Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Pfizer, L. Aikman Shareholder of: Pfizer, Employee of: Pfizer, A. Szumski Employee of: InVentiv Health, A. Chhabra Shareholder of: Pfizer, Employee of: Pfizer

DOI: 10.1136/annrheumdis-2017-eular.1188

SAT0442 FUNCTIONAL DISEASE STATUS AND HEALTHCARE COSTS IN PSORIATIC ARTHRITIS: A SIMILAR RELATIONSHIP TO THAT SEEN IN RHEUMATOID ARTHRITIS

A. Maguire[1], I. Handel[2], W. Tillett[3], F. Mughal[4], J. Morris[5], N. Hawkins[6], C. Cavill[3], E. Korendowych[3], N. McHugh[3]. *[1]Department of Psychology, University of Cambridge, Cambridge; [2]Royal (Dick) School of Veterinary Studies, University of Edinburgh, Edinburgh; [3]Royal National Hospital for Rheumatic Diseases NHS Foundation Trust, Bath; [4]Celgene Ltd, Uxbridge; [5]Cogentia Healthcare Consulting Ltd, Cambridge; [6]Health Economics and Health Technology Assessment, University of Glasgow, Glasgow, United Kingdom*

Background: The Health Assessment Questionnaire-Disability Index (HAQ-DI), an important, validated measure of functional status in patients with psoriatic arthritis (PsA), has been used as an intermediate variable in modelling of costs and quality-adjusted life-years. The relationship between HAQ-DI and costs has been well documented for rheumatoid arthritis (RA),[1,2] but less so for PsA. The HAQ-DI study data in PsA patients from the British Society for Rheumatology Biologics Registers was mapped to resource use data in the Health Improvement Network dataset.[3] A drawback of this approach relates to the HAQ-DI and resource use data being derived from separate patient cohorts.

Objectives: Estimate the HAQ-DI and cost relationship in PsA within a single cohort of patients.

Methods: Functional disease status, patient demographic, disease history and healthcare resource use data were extracted from a cohort of patients at the Royal National Hospital for Rheumatic Diseases. Resource data were available for primary and secondary care consultations, prescriptions, accident and emergency attendance, hospital admissions and tests, and collected for 6 months before and after HAQ-DI measurement. Medication costs were excluded from the modelling as it was not possible to specify which were PsA-related. Linear regression models were used to predict costs as a function of HAQ-DI and age at HAQ-DI

measurement. As cost data were not normally distributed, standard errors (SEs), 95% confidence intervals (CIs) and *P* values were estimated by bootstrap resampling (10,000 samples).

Results: Data were available for 95 PsA patients (female: n=43). Mean HAQ-DI score was 0.81 (SE 0.08); mean age at HAQ-DI measurement was 58.6 (SE 1.04). Mean total annual healthcare costs, excluding medication costs, were £ 1,588 (SE 172.3). Regression modelling indicated that a 1-point increase in HAQ-DI score was associated with an increase in total costs, excluding medications, of £ 547.49 (SE 222.7; 95% CI 191.7–1,103.8; *P*=0.004) (Table). Subgroup analyses suggested trends for higher cost increases within the lower HAQ-DI cutoff subgroup (HAQ-DI 0–1) and for those with greatest disease duration (>10 years). Costs associated with secondary care consultations seemed to be the primary factor in the association between HAQ-DI and total costs.

Estimated HAQ-DI Coefficient (£/Unit) From Regression of Costs on the HAQ-DI (Bootstrapped SE, 95% CI, and *P* Value)

Outcome	Estimate (SE)	95% CI	*P* Value
Tests	21.45 (14.18)	-7.93 – 47.5	0.130
Accident and emergency	15.67 (5.46)	6.46 – 28.89	0.002
Primary care consultation	69.98 (24.32)	20.97 – 115.90	0.004
Secondary care consultation	293.67 (48.26)	205.81 – 398.67	<0.001
Admitted care	162.25 (201.13)	-132.82 – 707.29	0.434
Total cost	547.49 (222.74)	191.69 – 1,103.82	0.004

Conclusions: Models incorporating total healthcare costs were highly significant; this association appears to be driven mainly by secondary care consultation costs. Costs in this study were similar to previous studies in RA populations. A study limitation was that only direct medical costs were considered, which may underestimate the true burden of PsA on healthcare systems and the wider society.

References:

[1] Lajas C, et al. Arthritis Rheum. 2003;49:64–70.
[2] Kobelt G, et al. Joint Bone Spine. 2008;75:408–15.
[3] Poole CD, et al. Rheumatology (Oxford). 2010;49:1949–56.

Disclosure of Interest: A. Maguire Grant/research support from: Cogentia Healthcare Consulting Ltd, UK, I. Handel Consultant for: Visible Analytics Limited, W. Tillett: None declared, F. Mughal Employee of: Celgene Ltd, J. Morris Grant/research support from: Celgene Ltd, N. Hawkins Grant/research support from: Celgene Ltd, C. Cavill Grant/research support from: Celgene Ltd, E. Korendowych Grant/research support from: Abbvie, Celgene and Pfizer, Consultant for: Janssen, Abbvie, Novartis, Pfizer and Celgene, Speakers bureau: Janssen, Abbvie, Novartis, Pfizer and Celgene, N. McHugh Grant/research support from: Celgene Ltd

DOI: 10.1136/annrheumdis-2017-eular.5332

SAT0443 IDENTIFICATION OF PREDICTORS OF MINIMAL DISEASE ACTIVITY IN EARLY PSORIATIC ARTHRITIS

A. Zabotti[1], L. Idolazzi[2], L. Quartuccio[1], M. Sartori[1], A. Fassio[2], F. Zuliani[1], D. Gatti[2], M. Rossini[2], S. De Vita[1]. *[1]Department of Medical and Biological Sciences, Rheumatology Clinic, "Santa Maria della Misericordia" University Hospital, Udine, Italy, Udine; [2]Rheumatology Clinic, Aoui Verona Reumatologia, Verona, Italy*

Background: Psoriatic arthritis (PsA) is a systemic inflammatory disease with articular and extra-articular features, the disease activity ranges from mild mono-oligoarthritis to destructive polyarthritis. Hence, establishing the prognosis of a patient with PsA is important to better define the treatment strategy. Furthermore, minimal disease activity (MDA) is a validated composite outcome measure since it correlates well with long-term outcomes (e.g. development of joint damage)[1].

Objectives: The aim of this study was to identify the baseline clinical variables associated with MDA at 12th month of follow up in two cohorts of early PsA.

Methods: Consecutive PsA patients, attending the outpatient Early Arthritis Clinic in Udine or Verona in the last two years, were assessed. All the included patients had: I) CASPAR score ≥ 2[2] II) new diagnosis of PsA III) a complete clinical data and follow-up of at least 12 months. The GRAPPA recommendations on the management of PsA were followed. Statistical analysis included T- test, ANOVA and Pearson's test in order to find possible predictors of MDA.

Results: Eighty-one early PsA patients were included in the study. 47/81 (58.2%) reached MDA at 12th month of follow-up; 68/81 (83.9%) were in c-DMARDs while 11/81 (13.6%) were in b-DMARDs. Two variables at baseline were selected comparing the groups based on achievement of MDA. These were: 1) LEI, which was significantly lower at baseline in patients reaching MDA (0.43 *Vs* 0.86, p=0.001); and 2) a lower baseline CRP (1.2 mg/dl *vs* 2.8 mg/dl, p=0.008). Of note, neither the baseline disease activity evaluated with DAPSA nor the time to referral were selected by statistical analysis.

Conclusions: Baseline lower LEI score and lower CRP were identified as clinical predictors of MDA after 12 months of treatment in PsA. Therefore, patients with a more active enthesitis or higher inflammation may have a less responsive disease. This may be relevant to select proper treatments at baseline, and indirectly confirms that enthesitis is a key therapeutic target in PsA.

References:

[1] Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis 2010; 69: 48–53.
[2] Coates LC, Conaghan PG, Emery P et al. Sensitivity and specificity of the classification of psoriatic arthritis criteria in early psoriatic arthritis. Arthritis Rheum 2012; 64: 3150–3155.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4987

SAT0444 DETECTION OF PSORIATIC ARTHRITIS AT EARLY ONSET: A MULTI-PROTEOMIC APPROACH TO DEVELOPING A NEW BLOOD TEST

A.F. Mc Ardle[1], A. Szentpetery[2], S. De Rook[3], B. Hernandez[1], O. FitzGerald[4], S.R. Pennington[1]. *[1]School of Medicine and Medical Sciences, University College Dublin; [2]Rheumatology, St. Vincents University Hospital, Dublin 4, Ireland; [3]Wilhelmina Kinderziekenhuis, Hospital, Utrecht, Netherlands; [4]Rheumatology, St. Vincents University Hospitla, Dublin 4, Ireland*

Background: Psoriatic Arthritis (PsA) is an inflammatory arthritis (IA) frequently associated with psoriasis. Clinically, it is a complex heterogeneous disease and there are no diagnostic tests or criteria [1]. At first presentation, PsA may resemble other disease types - especially rheumatoid arthritis (RA). Making an accurate and early diagnosis is particularly important to ensure that individual patients receive effective and safe medication and so optimise long-term patient outcomes. Thus, it is widely acknowledged by physicians and patients alike that a new diagnostic test is needed to facilitate the early and specific diagnosis of PsA [2].

Objectives: To (i) identify and verify candidate biomarkers with the potential to segregate patients with PsA from those with RA; and (ii) explore the value of combining different proteomic discovery platforms.

Methods: Serum samples were obtained from a cohort of 64 patients (32 PsA and 32 RA) defined as early onset (<12 months) and DMARD naïve. Individual baseline samples were analysed with label free LC-MS/MS (n=64), the Luminex xMAP (n=62) and an aptamer based platform called SOMAscan (n=36). The random forest test was applied to each individual data set as well as to a combined-matched data set (n=36). To verify MS data, a multiple reaction monitoring (MRM) assay was developed for 54 of the most discriminatory proteins to be applied to both pooled (PsA n=9, RA n=9) and individual patient samples (n=64).

Results: In this study, it was possible to quantify 387, 48 and 1129 proteins from LC-MS/MS, Luminex and SOMAscan analysis, respectively. Proteins with the ability to segregate PsA patients from those with RA were identified by random forest analysis; LC-MS/MS (AUC 0.94), Luminex (AUC 0.69) and SOMAscan (AUC 0.73). The application of the random forest model to the (i) combined data and (ii) MRM data set is part of ongoing work.

Conclusions: To date, statistical analysis revealed LC-MS/MS identified proteins were the most discriminatory. An MRM assay has been developed to the top 54 LC-MS/MS proteins and this assay has been applied to the discovery cohort (data analysis ongoing). The assay will next be applied to additional evaluation cohorts that include patients with spondyloarthritis and psoriasis. Discriminatory proteins verified here represent candidates for inclusion in a blood based multi-analyte test that could ultimately be used in the diagnosis of PsA.

References:

[1] Butt AQ, Mc Ardle A, Gibson DS, FitzGerald OF, Pennington SR. Psoriatic arthritis under a proteomic spotlight: application of novel technologies to advance diagnosis and management. Curr Rheumatology Reports 2015;17(5):35. doi: 1007/ss11926-015-0509–0.
[2] Mc Ardle, A. Butt AQ, Szentpetery, A. De Jager, Wilco. De Roock, Sytze. FitzGerald, O. Pennington, SR. Developing Clinically Relevant Biomarkers in Inflammatory Arthritis: A Multiplatform Approach for Serum Candidate Protein Discovery. Proteomics Clinical Applications, 2015. doi: 10.1002/prca.201500046.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5832

SAT0445 SHORT-TERM EFFECTS OF SECUKINUMAB ON BONE TURNOVER MARKERS AND WNT SIGNALING ANTAGONISTS IN PATIENTS WITH PSORIATIC ARTHRITIS

A. Fassio, L. Idolazzi, O. Viapiana, C. Benini, E. Vantaggiato, M. Rossini, D. Gatti. *Rheumatology, Aoui Verona Reumatologia, Verona, Italy*

Background: psoriatic arthritis (PsA) is a chronic inflammatory disease characterized also by increased levels of cells producing IL-17 [1], and these levels have been shown to correlate with measures of disease activity and structural damage and bone loss [2]. Secukinumab is a new monoclonal antibody licensed woth the treatment of PsA which selectively binds to and neutralizes interleukin-17 (IL-17). Currently, data about the effects on the activity of either bone-reabsorbing cells and bone-forming cells secondary to the inhibition of the IL-17 pathway are completely absent.

Objectives: the aim of our study was to explore the short-term effects of secukinumab on bone turnover markers (BTM) and Dkk-1 and sclerostin.

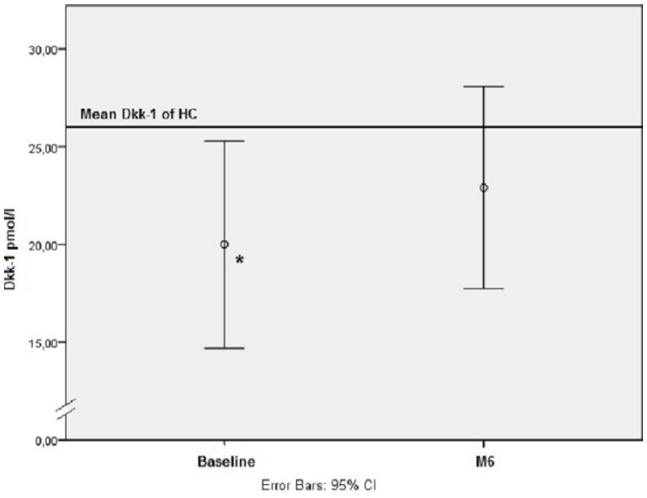
Methods: we enrolled 28 patients with PsA, classified with the CASPAR criteria and 43 healthy controls (HC). For the PsA group DAS28 was recorded and serum samples were stored at baseline and then at the first, the third and the sixth month of therapy. Intact N-propeptide of type I collagen (PINP) and C-terminal

telopeptide of type I collagen (CTX-I). Dickkopf-related-protein 1 (Dkk-1) and sclerostin were dosed too. For the HC group, a single blood sample was taken.
Results: Neither P1NP nor CTX showed any statistically significant variation. Baseline Dkk-1 for the PsA group was lower than HC. Both Dkk-1 and sclerostin demonstrated a significant increase at the sixth month. When the PsA groups was compared to HC, the difference between the levels of Dkk-1 lost significance at month six.

Table 1

	Healthy controls (N=43)			
Dkk-1 pmol/l	25,92±11,26†			
Sclerostin pmol/l	33,11±16,85			
	PsA patients (N=28)			
	Baseline values (Mean ± SD)	month 1	month 3	month 6
DAS28	3,97±1,30	3,78±1,21	3,57±1,58	3,41±1,55
P1NP ng/ml	43,5±14,5	-0,31±12,91	-0,81±11,97	0,96±14,87
CTX ng/ml	0,25±0,16	0,02±0,14	0,04±0,20	0,08±0,27
Dkk-1 pmol/l	20,0±13,64	-1,45±7,89	-1,38±9,49	2,90±7,45*
Sclerostin pmol/l	30,9±12,02	-0,76±8,39	3,09±7,54*	3,03±7,77*

*p<0,05 vs baseline, †p<0,05 vs Dkk-1 of the PsA group at baseline, month 1 and month 3.



Conclusions: our study demonstrated that the treatment with secukinumab has little influence on the levels of BTM within the first six months of treatment but a definite influence on some fine regulators of the bone cells activity such as the WNT inhibitors and it is able, in some way, to normalize the Dkk-1 levels in PsA patients. The clinical implications of this trend are currently unclear thought it might suggest an drug-induced inhibition of the over-proliferation of bone typical of the joint lesions of PsA. Further studies with greater numbers of patients are warranted to determine whether these preliminary results have clinical relevance.
References:
[1] Jandus C, Bioley G, Rivals J-P, et al. Increased numbers of circulating polyfunctional Th17 memory cells in patients with seronegative spondylarthritides. Arthritis Rheum 2008;58:2307–17. doi:10.1002/art.23655.
[2] Uluçkan Ö, Jimenez M, Karbach S, et al. Chronic skin inflammation leads to bone loss by IL-17-mediated inhibition of Wnt signaling in osteoblasts. Sci Transl Med 2016;8:330ra37. doi:10.1126/scitranslmed.aad8996.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2734

SAT0446 IXEKIZUMAB IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND PREVIOUS INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR-INHIBITORS

A. Kavanaugh[1], R. Vender[2], J. Birt[3], D.H. Adams[3], O. Benichou[3], C.-Y. Lin[3], P. Nash[4]. *[1]Univ of CA San Diego Health System, la Jolla, United States; [2]Dermatrials Research Inc., Hamilton, Canada; [3]Eli Lilly and Company, Indianapolis, United States; [4]University of Queensland, Brisbane, Australia*

Background: Ixekizumab (IXE), a monoclonal high affinity antibody that selectively targets interleukin-17A, was superior to placebo (PBO) in achieving clinical responses and improving health related quality of life (HRQoL) for psoriatic arthritis (PsA) patients who were biologic-naïve.[1] Herein, results are presented from a phase 3 trial (SPIRIT-P2; NCT02349295) with IXE in patients with active PsA and previous inadequate response to tumor necrosis factor-inhibitors (TNF-i).
Objectives: To explore the impact of IXE on patient reported HRQoL outcomes up to 24 weeks (wks) in patients with active PsA.
Methods: In this phase 3, multicentre, double-blind study, 363 adult patients with active PsA were randomly assigned in the ratio of 1:1:1 to subcutaneous administration of either 80-mg IXE every 4 wks (Q4W; N=122) or every 2 wks (Q2W; N=123) following a 160-mg starting dose at Wk 0 or PBO (N=118). All patients entering the study had an inadequate response to one or two TNF-i or were intolerant to TNF-i. At baseline and Wk 24, HRQoL was measured by the Short Form-36 Health Survey (SF-36) Physical Component Summary (PCS) and Mental Component Summary (MCS), European Quality of Life 5 Dimensions Visual Analog Scale (EQ-5D VAS), Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP; absenteeism; presenteeism, work productivity, and activity impairment), the itch Numeric Rating Scale (NRS), and the Dermatology Life Quality Index (DLQI). Itch NRS, DLQI, and Psoriasis Area Severity Index (PASI) responses were assessed in patients with baseline psoriatic lesion involving ≥3% body surface area (BSA; N=203). Treatment comparisons were made by a mixed model for repeated measures for continuous data and by a logistic regression model for categorical data with missing values imputed by nonresponder imputation.
Results: Mean baseline (Wk 0) scores for HRQoL measures indicated impaired physical and mental function, quality of life, and work productivity (Table). At Wk 24, clinical efficacy was shown by 50.6% and 58.1% of IXE-treated patients achieving ACR20 and PASI75 responses, respectively. Patients receiving IXE (Q4W or Q2W) reported significantly greater improvements in SF-36 PCS and MCS, EQ-5D VAS, and WPAI-SHP (presenteeism, work productivity, and activity impairment) than patients treated with PBO (Table; p<.05). For PsA patients with co-morbid psoriasis (≥3% BSA), IXE treatment (Q4W or Q2W) resulted in significantly greater improvements in itch NRS and DLQI than PBO treatment (Table; p<.001). Finally, 51.5% of IXEQ4W patients and 50.0% of IXEQ2W patients reached a DLQI total score of 0 or 1 at Wk 24, which is significantly greater than patients treated with PBO (9.0%, p<.001).

Table: Summary of Patient-Reported Outcomes at Baseline and Week 24

		PBO N=118	IXEQ4W N=122	IXEQ2W N=123
SF-36 PCS[a]	Baseline	33.9 (9.0)	34.8 (8.8)	34.3 (9.1)
	Change from Baseline	3.3 (1.4)	8.9 (1.3)***	8.2 (1.2)***
SF-36 MCS[a]	Baseline	48.0 (13.1)	49.6 (11.3)	49.1 (11.5)
	Change from Baseline	0.9 (1.3)	3.6 (1.2)*	4.0 (1.2)**
EQ-5D VAS[a]	Baseline	53.6 (20.0)	53.9 (22.4)	53.9 (19.7)
	Change from Baseline	1.8 (3.4)	15.3 (3.2)***	12.8 (3.0)***
WPAI-SHP: Absenteeism[b]	Baseline	11.9 (28.1)	11.6 (26.6)	8.8 (23.2)
	Change from Baseline	4.5 (5.0)	3.7 (4.6)	9.4 (4.4)
WPAI-SHP: Presenteeism[b]	Baseline	40.4 (28.8)	45.0 (25.7)	36.9 (25.0)
	Change from Baseline	-7.2 (4.9)	-26.6 (4.3)***	-24.0 (4.1)***
WPAI-SHP: Work Productivity[b]	Baseline	41.5 (29.6)	46.9 (26.7)	38.8 (26.6)
	Change from Baseline	-4.5 (5.4)	-23.2 (4.7)***	-17.6 (4.6)*
WPAI-SHP: Activity Impairment[b]	Baseline	54.0 (25.8)	53.9 (24.9)	49.3 (26.5)
	Change from Baseline	-14.8 (4.1)	-30.2 (3.9)***	-26.2 (3.7)**
		N=67	N=68	N=68
Itch NRS[b,c]	Baseline	5.7 (2.8)	5.5 (2.5)	5.6 (3.0)
	Change from Baseline	-1.2 (0.5)	-3.4 (0.4)***	-3.5 (0.4)***
DLQI[b,c]	Baseline	9.6 (8.1)	9.1 (7.4)	9.2 (7.8)
	Change from Baseline	-3.1 (0.9)	-7.7 (0.8)***	-7.3 (0.8)***

Baseline values are mean (SD); Change from baseline values are least squares mean (SE).
[a]Increase in score represents improvement.
[b]Decrease in score represents improvement.
[c]Patients were from the intent-to-treat population with ≥3% BSA at baseline.
*p<.05;**p<.01;***p<.001; with respect to placebo control; p-values are from a repeated measures mixed model.

Conclusions: In patients with active PsA and previous inadequate response to TNF-i, IXE provided significant improvement through 24 wks in all joint and skin associated HRQoL outcomes, including physical and mental function, quality of life, work productivity, DLQI, and itch.
References:
[1] Mease P et al. 2017 ARD 76(1):79.
Disclosure of Interest: A. Kavanaugh Consultant for: Eli Lilly and Company, R. Vender Grant/research support from: Abbvie, Amgen, Centocor, Dermira, Galderma, GSK, Leo, Eli Lilly and Company, Takeda, Novartis, Merck, Pfizer, Regeneron, Consultant for: Abbvie, Amgen, Janssen, Galderma, GSK, Leo, Eli Lilly and Company, Novartis, Pfizer, Valeant, Actelion, Celgene, Cipher, Palladin, Speakers bureau: Abbvie, Amgen, Janssen, Galderma, GSK, Leo, Eli Lilly and Company, Novartis, Pfizer, Valeant, Actelion, Celgene, Cipher, Palladin, J. Birt Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, D. Adams Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, O. Benichou Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, C.-Y. Lin Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Nash Grant/research support from: AbbVie, Amgen, BMS, Celgene, Eli Lilly and Company, Hospira, MSD, Pfizer, Janssen, UCB, Novartis, Roche, Sanofi, Consultant for: AbbVie, Amgen, BMS, Celgene, Eli Lilly and Company, Hospira, MSD, Pfizer, Janssen, UCB, Novartis, Roche; Sanofi, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Eli Lilly and Company, Hospira, MSD, Pfizer, Janssen, UCB, Novartis, Roche, Sanofi
DOI: 10.1136/annrheumdis-2017-eular.1580

SAT0447 **PREVALENCE OF RADIOGRAPHIC SACROILIITIS IN PATIENTS WITH PSORIATIC ARTHRITIS AND THE CLINICAL, ANALYTICAL AND DEMOGRAPHIC FACTORS ASSOCIATED TO ITS APPEARANCE**

C. López-Medina[1,2], S. León-Idougourram[2], M.D. López-Montilla[1,2], L. Bautista-Aguilar[1,2], L. Ladehesa-Pineda[1,2], E. Collantes-Estévez[1,2]. *[1]Hospital Universitario Reina Sofía de Córdoba/ Imibic; [2]Universidad de Córdoba, Córdoba, Spain*

Background: To date, published studies suggest that a significant proportion of patients with Psoriatic Arthritis (PsA) present asymptomatic sacroiliitis; that is to say, an inflammatory back pain (IBP) absence. This fact could result in the underdiagnosis of axial involvement in these patients (1).
Objectives: To evaluate the prevalence of radiographic sacroiliitis in patients with PsA and to determine its association with clinical, analytical and demographic factors.
Methods: A cross-sectional, observational, and unicentre study in which clinical, analytical and demographic data from 359 patients belonging to a PsA monographic consultation were analyzed. All patients met the CASPAR criteria. The presence of sacroiliitis in the sacroiliac x-ray image was used as a dependent variable, formerly evaluated by a trained Rheumatologist. Likewise, independent variables related to arthropathy, cutaneous involvement and sociodemographic characteristics of the patients were used as well. A descriptive analysis and two logistic regressions (univariate and multivariate), were performed to associate radiographic sacroiliitis to different covariates.
Results: Out of the 359 patients, 214 (59.6%) were men with a mean time of PsA evolution of 10.05±11.6 years. The x-ray image performed showed sacroiliitis in 127 patients (35.4%). Univariate analysis showed that radiographic sacroiliitis is related ($p<0.05$) to gender (men), psoriasic paternal family history, IBP, positive HLA-B27 antigen and psoriatic cutaneous involvement greater than 25%. The multivariate analysis showed that radiographic sacroiliitis in these patients is predominantly associated to the presence of IBP, the positive HLA-B27 antigen and gender (men). However, sacroiliitis is not not associated to the onset age of PsA ($p>0.05$).

Univariate logistic regression

	Sacroiliitis n=127 (n%)	No Sacroiliitis n=232 (n%)	OR (CI 95%)	p-value
Sex (men)	94 (74.0)	120 (51.7)	2.6 (1.6–4.2)	<0.001
Psoriasis duration, mean (SD)	12.6 (9.2)	10.8 (0.2)	1.0 (0.9–1.0)	0.082
PsA duration, mean (SD)	5.5 (5.9)	4.5 (6.3)	1.0 (1.0–1.0)	0.041
Onset age of PsA ≤45 years	76 (59.8)	131 (56.6)	1.1 (0.7–1.7)	0.536
Family history of Psoriasis – None	70 (56.5)	150 (65.8)	Reference	
– Paternal	29 (23.4)	35 (15.4)	1.7 (1.0–3.1)	0.048
– Maternal	25 (20.2)	43 (18.9)	1.2 (0.7–2.2)	par 0.449
IBP	93 (73.2)	22 (9.5)	26.1 (14.9–47.0)	<0.001
HLA-B27 +	22 (17.5)	11 (4.8)	4.1 (1.9–9.0)	<0.001
Psoriasis extension – <10%	177 (76.6)	78 (61.9)	Reference	
– 10–25%	21 (16.7)	21 (16.7)	1.5 (0.8–2.8)	0.170
– >25%	23 (10.0)	27 (21.4)	2.6 (1.4–4.9)	0.002

Conclusions: The prevalence of radiographic sacroiliitis in our population is 35.4%, higher than in other series due to the fact that the sacroiliac x-ray images were performed on all patients, regardless of the clinic. The radiographic sacroiliitis in patients with PsA is related to the presence of IBP, HLA-B27 antigen and gender. However, the time of evolution of arthropathy and the onset age of PsA are not related to sacroiliac radiographic involvement.
References:
[1] Jadon DR, Sengupta R, Nightingale A, et al. Axial Disease in Psoriatic Arthritis study: defining the clinical and radiographic phenotype of psoriatic spondyloarthritis. Ann Rheum Dis 2016;0:1–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3572

SAT0448 **APREMILAST TREATMENT AND LONG-TERM (UP TO 156 WEEKS) IMPROVEMENTS IN DACTYLITIS AND ENTHESITIS IN PATIENTS WITH PSORIATIC ARTHRITIS: ANALYSIS OF A LARGE DATABASE OF THE PHASE III CLINICAL DEVELOPMENT PROGRAM**

D.D. Gladman[1], A. Kavanaugh[2], J.J. Gomez-Reino[3], J. Wollenhaupt[4], M. Cutolo[5], G. Schett[6], E. Lespessailles[7], M. McIlraith[8], C. Hu[8], C.J. Edwards[9], C.A. Birbara[10], P.J. Mease[11]. *[1]Toronto Western Hospital, Toronto, Canada; [2]University of California, San Diego, School of Medicine, la Jolla, United States; [3]Hospital Clínico Universitario, Santiago, Spain; [4]Schön Klinik Hamburg Eilbek, Hamburg, Germany; [5]University of Genova, Genova, Italy; [6]University of Erlangen-Nuremberg, Erlangen, Germany; [7]University of Orléans, Orléans, France; [8]Celgene Corporation, Summit, United States; [9]University Hospital Southampton, Southampton, United Kingdom; [10]University of Massachusetts Medical School, Worcester; [11]Swedish Medical Center and University of Washington School of Medicine, Seattle, United States*

Background: Dactylitis and enthesitis, hallmark features of psoriatic arthritis (PsA), may be difficult to manage. PALACE 1, 2, and 3 compared the efficacy and safety of apremilast (APR) with placebo (PBO) in patients (pts) with active PsA despite prior conventional DMARDs and/or biologics.
Objectives: Report the impact of long-term APR 30 mg BID (APR30) treatment on dactylitis and enthesitis in pts with active PsA.
Methods: Pts were randomized (1:1:1) to PBO, APR30, or APR 20 mg BID (APR20) stratified by baseline (BL) DMARD use (yes/no). After the 24-wk PBO-controlled phase, all pts received APR30 or APR20 and could enroll in long-term follow-up. Data for pts entering the study with pre-existing dactylitis or enthesitis were pooled across PALACE 1–3, as prespecified, to allow for robust analysis. Dactylitis count (number of digits [hands/feet] with dactylitis present [0=absence, 1=presence]; range: 0–20) was used to assess dactylitis improvement. Enthesitis was evaluated based on MASES (range: 0–13), indicating the number of painful entheses out of 13 enthesis sites. Wk 24 analyses used LOCF for missing values and data for early escape pts; Wks 52 and 156 used data as observed.
Results: Among pts with dactylitis (n=610) or enthesitis (n=915) at BL and ≥1 post-BL value, BL mean dactylitis counts ranged from 3.2 to 3.4 and MASES ranged from 4.4 to 4.8. At Wk 24, mean change in dactylitis count was −1.8 (APR30) vs −1.3 (PBO) (P=0.0097); more APR30 pts achieved a dactylitis count of 0 vs PBO pts (Table). Mean change in MASES was −1.3 (APR30) vs −0.9 (PBO) (P=0.0194); more APR30 pts achieved a MASES of 0 vs PBO pts. Significant effect on enthesitis was confirmed in the PSA-006 (ACTIVE) study of APR in pts with a maximum of 1 previous DMARD treatment, in which the Gladman Enthesitis Index was used, focusing on more peripheral sites of activity: significant effect for APR vs PBO was seen as early as Wk 2, and at Wk 24, mean changes were −1.5 vs −0.5 (P=0.0032, MMRM). Sustained improvements in dactylitis and enthesitis severity were seen in APR pts at Wk 156 in PALACE 1–3 (Table): for dactylitis, 79.6% achieved a count of 0 and the mean percent change was −83.6%; for MASES, 55.0% of APR pts achieved a score of 0 and the mean percent change was −65.2%.

	Wk 24		Wk 52	Wk 156
Dactylitis Count*	**PBO n=205**	**APR30 n=221**	**APR30 n=249**	**APR30 n=181**
BL, mean	3.3	3.2	3.4	3.4
Mean change from BL	−1.3	−1.8‖	−2.5	−3.0
Mean % change from BL	−38.2	−48.6	−67.9	−83.6
Median % change from BL	−66.7	−79.3	−100.0	−100.0
Pts achieving score of 0, %	39.0	46.2	67.5	79.6
MASES§	**PBO n=311**	**APR30 n=327**	**APR30 n=377**	**APR30 n=278**
BL, mean	4.8	4.4	4.4	4.2
Mean change from BL	−0.9	−1.3‡	−2.0	−2.7
Mean % change from BL	−7.0	−23.6‡	−43.5	−65.2
Median % change from BL	−21.1	−50.0‡	−66.7	−100.0
Pts achieving score of 0, %	22.5	27.5	37.7	55.0

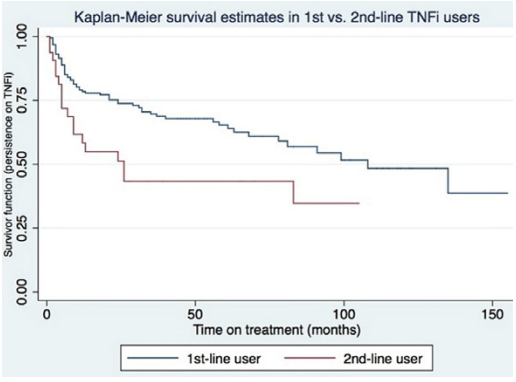
The n at Wk 24 represents pts with a BL value >0. The n at Wk 52 and Wk 156 represents the number of pts taking APR, regardless of when treatment started (BL, Wk 16, or Wk 24), with a BL value >0 and a value at Wk 52 or Wk 156.
*Dactylitis count is the sum of all scores (0=absence of dactylitis; 1=presence of dactylitis) from each of the 20 digits. §MASES ranges from 0 to 13, with 0 indicating no pain at any assessed enthesis and 13 indicating pain at all assessed entheses. ‡P<0.05 vs PBO. ‖P<0.01 vs PBO.
PBO=placebo; APR30=apremilast 30 mg BID; BL=baseline; pts=patients; MASES=Maastricht Ankylosing Spondylitis Enthesitis Score.

Conclusions: The majority of pts (63%) in PALACE 1–3 had active enthesitis and 42% had dactylitis at BL. APR30 demonstrated early and long-term benefit (up to 156 wks) in treating dactylitis and enthesitis, including resolution of BL disease in many pts.
Disclosure of Interest: D. Gladman Grant/research support from: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB, A. Kavanaugh Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, J. Gomez-Reino Grant/research support from: Roche and Schering-Plough, Consultant for: BMS, Pfizer, Roche, Schering-Plough, UCB, J. Wollenhaupt Grant/research support from: Abbott, BMS, MSD, Pfizer, UCB, Consultant for: Abbott, BMS, MSD, Pfizer, UCB, M. Cutolo Grant/research support from: Actelion, BMS, Sanofi-Aventis, Consultant for: Actelion, BMS, Sanofi-Aventis, G. Schett Grant/research support from: Abbott, Celgene Corporation, Roche, UCB, Consultant for: Abbott, Celgene Corporation, Roche, UCB, E. Lespessailles Grant/research support from: Amgen, Eli Lilly, Novartis, Servier, Speakers bureau: Amgen, Eli Lilly, Novartis, Servier, M. McIlraith Employee of: Celgene Corporation, C. Hu Employee of: Celgene Corporation, C. Edwards Grant/research support from: Celgene Corporation, Pfizer, Roche, Samsung, Consultant for: Celgene Corporation, Pfizer, Roche, Samsung, Speakers bureau: Abbott, GSK, Pfizer, Roche, C. Birbara Grant/research support from: Amgen, BMS, Incyte, Eli Lilly, Merck, Pfizer, P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Consultant for: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Genentech, Janssen, Eli Lilly, Pfizer, UCB
DOI: 10.1136/annrheumdis-2017-eular.3821

SAT0449 SEX, METABOLIC CO-MORBIDITIES AND LINE OF THERAPY PREDICT TNF-INHIBITOR THERAPY PERSISTENCE IN PSORIATIC ARTHRITIS: A RETROSPECTIVE COHORT STUDY

W. Ye[1], T. Guruparan[1], C. Stober[2], E.E.P. Htut[2], D.R. Jadon[2]. [1]*School of Clinical Medicine, University of Cambridge;* [2]*Department of Rheumatology, Cambridge University Hospitals, Cambridge, United Kingdom*

Background: Although tumour necrosis factor-alpha inhibitor (TNFi) therapy has proven efficacy in the management of psoriatic arthritis (PsA), relatively little is known about predictors of TNFi persistence. Such knowledge would assist the application of stratified medicine.
Objectives: To determine baseline clinical characteristics associated with TNFi persistence in patients receiving their first-line agent, and to compare TNFi persistence in first versus second-line users.
Methods: A retrospective cohort study was performed of all patients with PsA attending a single-centre between 2003–2016. Demographic, clinical and laboratory characteristics were compared with TNFi persistence, using Kaplan-Meier survival analysis and multivariable Cox proportional hazards models.
Results: A total of 188 PsA cases had used TNFi therapy as first-line over a period spanning 7,620 person months: 46% male; mean age at TNFi initiation 47.27 (SD 11.36) years; median disease duration at initiation 11 (IQR 7,16) years. Etanercept was used by 102 and adalimumab by 86. Concomitant DMARDs were used by 121/186 (65%) and 87/188 (46%) had metabolic co-morbidities (hypertension, dyslipidaemia, type-2 diabetes, obesity). TNFi therapy was terminated in 65/188 (35%) of cases (35% due to primary inefficacy, 22% secondary inefficacy, 43% adverse events), with a median duration of TNFi persistence of 26.5 (IQR 10.5, 62.0) months. Multivariable Cox proportional hazards modelling found the following parameters at TNFi initiation to be associated with shorter (poorer) TNFi persistence in first line users: female sex (hazard ratio, HR 2.57; 95% CI 1.26, 5.24; p=0.01); presence of metabolic co-morbidity (HR 2.65; 95% CI 1.24, 5.69; p=0.01); with a non-significant statistical trend towards younger age at TNFi initiation (HR 0.94; 95% CI 0.88, 1.00; p=0.06) and older age at PsA onset (HR 1.05; 95% CI 0.99, 1.12; p=0.08). Parameters not statistically associated with TNFi persistence included: choice of TNFi agent (adalimumab *vs.* etanercept), concomitant DMARD/methotrexate use, tender/swollen joint counts, patient global assessment (PGA) of disease activity, CRP, ESR and disease duration. Of 32 cases proceeding to a second TNFi (19 adalimumab, 13 etanercept), persistence was 14/32 (44%) over 954 person months. TNFi failure was two-fold more likely in second versus first-line users (HR 2.02; 95% CI 1.20, 3.42; p=0.009) [Figure 1], with no significant contribution from other co-variables.



Conclusions: Patients with PsA who are female and have metabolic co-morbidities appear to be more likely to fail first-line TNFi therapy. Contrary to observations in rheumatoid arthritis, and somewhat challenging the few studies in PsA, choice of TNFi agent (humanised monoclonal *vs.* chimeric), concomitant methotrexate use, acute-phase response and joint counts prior to TNFi initiation did not influence TNFi persistence. Although TNFi failure was more likely in second-line users, a significant proportion of PsA cases responded to second-line TNFi therapy, advocating this strategy in refractory cases.
Acknowledgements: TG and WY contributed equally to this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5178

SAT0450 SILENT AXIAL DISEASE IN THE RUSSIAN COHORT OF EARLY PERIFERAL PSORIATIC ARTHRITIS PATIENTS

E.E. Gubar, E.Y. Loginova, A.V. Smirnov, S.I. Glukhova, T.V. Korotaeva. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Axial involvement in early psoriatic arthritis (ePsA) patients (pts) is often asymptomatic, poorly diagnosed and has not been studied properly. Magnetic resonance imaging (MRI) of sacroiliac joints (SIJs) helps to better define spinal involvement in ePsA.
Objectives: to study the prevalence of axial involvement in peripheral ePsA pts.
Methods: 89 pts (M/F–42 /47) with peripheral ePsA according to CASPAR criteria were included; mean age 36.5±10.9 yrs, disease duration 12.1±10.1 mo., disease activity index (DAS) 5.2±2.8, C-RP 16.1 [6.6; 31.0] mg/l, ESR 22.5±19.2 mm/h. All patients were evaluated for the presence of inflammatory back pain (IBP) by ASAS criteria. In pts having IBP disease activity was also measured according to BASDAI. The examination included X-ray of sacroiliac joints (SIJs) (pelvic radiograph), HLA B27 antigen, MRI of SIJs was performed in 79 pts, both with and without IBP, on Signa Ovation 0,35T. Bone marrow edema on MRI (STIR), considered as active MRI sacroiliiitis (MRI-SI), was evaluated by an independent reader. Radiographic sacroiliitis (R-SI) was defined when 2 grade changes in at least one SIJ appear, and included definite radiographic SI (dR-SI) and "non-definite" radiographic SI (ndR-SI). dR-SI was determined according to New York criteria (unilateral grade≥3 or bilateral grade≥2). 2 grade changes in only one SIJ were qualified as ndR-SI.
Results: IBP was found in 58 out of 89 (65.1%) pts, 35 (60.3%) of them had short-term (episodic) IBP, and 23 (39.7%) pts had long-term IBP. MRI-SI was observed in 28 out of 79 (35.4%) pts. R-SI was determined in 42 out of 89 (47.2%) pts, while dR-SI was found in 27 out of 89 (30.3%) pts, the remaining 15 (16.9%) pts had ndR-SI. 34 (38. 2%) pts were HLA B27 positive. In pts having IBP disease activity according to BASDAI was 4.5±1.6. Correlation has been detected between MRI-SI and IBP: among the group of pts having MRI-SI IBP was observed in 92.9% cases while out of the group of patients without MRI-SI in 54.9% cases (p=0.0002). An association was found between MRI-SI and long-term IBP (p=0.003) as well as between MRI-SI and short-term IBP (p=0.006). Moderate correlation has been detected between the presence of dR-SI and IBP (p=0.038). It's worth noting that among the 26 pts having dR-SI, 5 (19.2%) pts never had IBP before. And among the 15 pts having ndR-SI, 6 (40.0%) pts never had IBP before. No association was found between the presence of MRI-SI/R-SI/dR-SI and HLA B27 status.
Conclusions: in the Russian cohort of early peripheral psoriatic arthritis pts, careful examination quite often revealed high prevalence of axial involvement: 65% of pts had IBP (moreover, more than half of them (60%) had short-term IBP), 35% of pts had MRI-SI, half of the pts had R-SI, one third of the pts had definite R-SI. A significant number of patients (40%) developed 2 grade changes in one SIJ without previous IBP. An association was found between IBP and SI revealed by any of the visualization methods used. No association has been detected between the presence of MRI-SI or R-SI and HLA B27 status. These data indicate that in peripheral ePsA pts axial involvement is often asymptomatic and is poorly diagnosed. Careful identification of IBP together with MRI of SIJs will help to better define spinal involvement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3044

SAT0451 THE ONE-YEAR RADIOGRAPHIC PROGRESSION AND MINIMAL DISEASE ACTIVITY IN EARLY PSORIATIC ARTHRITIS PATIENTS TREATED ACCORDING TO TREAT-TO-TARGET STRATEGY (RESULTS OF AN ONGOING OPEN-LABEL REMARCA STUDY)

E. Loginova, T. Korotaeva, A. Smirnov, A. Koltakova, D. Karateev. *V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Treat-to-target (T2T) strategy has benefit in early psoriatic arthritis (EPsA) treatment. Its influence on radiographic progression has limited data.
Objectives: to investigate radiographic outcomes and minimal disease activity (MDA) after 1-year of T2T strategy in patients with EPsA.
Methods: 40 (M-18/F-22) DMARD-naïve pts with active EPsA, according to the CASPAR criteria, mean age 38.4±11.1 yrs., PsA duration 11.9±10.6 months, psoriasis duration 73.8±84.6 months, median DAS 3.8 [3.2; 4.7] from the open-label REMARCA study were included. At baseline all pts were treated by Methotrexate (MTX) subcutaneous (s/c) 20–25 mg/week. Pts that still had medium or high activity after 3–6 months were treated by combination therapy MTX+ biologic therapy (BT) - anti-TNF or Ustekinumab (n=21). By the end of the study, 19 pts were treated by MTX-monotherapy. At baseline and after 1-yr. of treatment PsA activity index and digital radiographs of hands and feet were performed. All images were scored according to Sharp/van der Heijde (Sh.-v.d. H) method by a blinded musculoskeletal radiologist. Median total score (TS Sh.-v.d. H) = total erosion score (TES) + total narrowing score (TNS), the proportion of pts who reached MDA, M±SD, Me [Q75; Q50], W-test, U-test, (%) were calculated. All $p<0.05$ were considered to indicate statistical significance.
Results: At baseline, 23 out of 40 pts (57%) had erosion. By 1 yr., the number of pts with erosion increased up to 26 pts (65%). The median TS Sh.-v.d. H significantly increased from 91.5 [72–108.5] to 91.5 [73.5–111.5] (W-test, $p<0.01$), TES from 2 [0–4.5] to 2.5 [0–5] (W-test, $p<0.05$) and TNS from 85 [69–105] to 87 [71.5–107] (W-test, $p<0.01$). At 1 yr. of therapy there was no significant difference between the treatment groups in the value of TS Sh.-v.d. H (W-test $p>0.05$).
25 of pts (62.5%) had reached MDA by 1 yr. In pts who did not reach MDA (n=15) by 1 yr. TES was significantly higher at baseline compare to those who reached MDA: 3 [2–9] and 0 [0–3] accordingly (U-test, $p<0.05$). In the group of pts who did not reach MDA 1 yr. progression was significantly higher (table).
In 29 out of 40 pts (72.5%) there was no X-ray progression considering both erosion and joint space narrowing. 13 of them (45%) were treated by MTX and 16 pts (55%) by MTX+BT. Negative X-ray progression was found in 11 out of 40 pts (27.5%): 6 of them (54.5%) were treated by MTX and 5 pts (45.5%) by MTX+BT.

Table 1

Sh.-v. d.H score	MDA (n=25)		No MDA (n=15)	
	Baseline	After 1 yr.	Baseline	After 1 yr.
TES	0 [0–3]	1* [0–3]	3# [2–9]	5# [2–11]
TNS	88 [70–108]	88 [71–108]	84 [68–98]	84 [74–103]
TS Sh.-v.d. H.	89 [72–109]	89* [72–110]	93 [81–106]	93* [83–115]

#significant differences between groups (U-test, p<0.05). *- significant differences into group (W-test, p<0.05).

Conclusions: In the Russian cohort of active EPsA pts erosion was found in more than half of cases. Active EPsA pts treated according to T2T strategy during 1 year in 72.5% did not show any radiographic progression, only a quarter of pts (27.5%) had negative X-ray progression by the end of the study, regardless of the type of therapy. The pts who achieved MDA had less erosive progression.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3057

SAT0452 INFLUENCE OF ANTIRHEUMATIC THERAPY ADMINISTERED IN ACCORDANCE WITH "TREAT TO TARGET" PRINCIPLES ON HEART RATE VARIABILITY AND CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH ACTIVE EARLY PSORIATIC ARTHRITIS

E. Markelova, D. Novikova, T. Korotaeva, E. Loginova, I. Kirillova, L. Denisov, D. Karateev. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Psoriatic arthritis (PsA) is an inflammatory arthropathy, which is associated with range of co-morbid diseases and risk factors, such as dyslipidemia, obesity, metabolic syndrome, cardiovascular disease (CVD). Lower heart rate variability (HRV) is a well-established risk factor for CVD and all-cause mortality in the general population.
Objectives: to study dynamic of traditional risk factors (TRF) of CVD and parameters of HRV during antirheumatic therapy, administered inaccordance with "Treat to target" principles in PsA pts.
Methods: 44 (F.-21) DMARD-naive PsA pts, according to the CASPAR criteria, age 36 [27; 46] years (yrs.), PsA duration – 6 [4; 8] yrs, DAS 4.06 [3.51; 4.74]. TRFs of CVD were assessed according to ESC (2016): arterial hypertension (AH) – 11 (22.9%) pts, obesity (body mass index >30kg/m^2) – 11 (22.9%), abdominal obesity – 14 (29.2%), dyslipidemia – 31 (64.5%), family history of early CVD – 6 (12.5%), menopausal status – 5 (10.4%), smoking - 16 (33.3%). All pts were assessed for ECG, 24-h ECG monitoring, carotid ultrasound imaging. Antihypertensive therapy received all pts with AH. Methotrexate (MT) therapy was started in all pts with an escalation of the dose up to 25 mg/week subcutaneously. In case of no remission 3 months later, MT was added with biologic therapy: Adalimumab, Certolizumabpegol, Ustekinumab. 23 subjects were assessed after 18 months of therapy.
Results: After 18 months of therapy DAS and CRP level decreased significantly, p=0.001. DAS remission was achieved in 82.6% of pts. The incidence rate of AH (39% vs 39%), obesity (30% vs 21%), smokers (39% vs 39%), menopausal status (17% vs 17%), atherosclerotic plaques (39% vs 39%), did not change significantly. High-density lipoproteins increased significantly from 1.2 [1.1; 1.6] to 1.5 [1.2; 2.1]mmol/l, p=0.03. We didn't find significant differences between baseline and after treatment levels of total cholesterol/low-density lipoproteins level: from 5.2 [4.6; 6.0] to 5.2 [4.5; 5.9] (p=0.47) mmol/l and from 3.4 [2.8; 3.8] to 3.3 [2.6; 3.6] (p=0.60) mmol/l. HRVs parameters didn't change significant (table 1).

Table 1. HRV parameters in PsA pts baseline and after treatment

Parameters	Baseline	18 months
MeanNN (ms)	783 [734; 883]	803 [773; 852]
SDNN (ms)	132 [124;159]	147 [129; 163]
SDNNi (ms)	59 [45; 69]	61 [42; 80]
SDANN (ms)	121 [101; 146]	127 [109; 160]
RMSSD (ms)	39 [20; 50]	33 [18; 53]
pNN50 (%)	13 [2.6; 21]	10.7 [1.9; 22.7]

Data are present in median values and interquartile range, *p<0,05 before and after 18 months treatment (nonparametric paired Wilcoxon test).

Conclusions: antirheumatic therapy of early PsA pts in accordance with "T2T" principles improves lipid profile but not HRVs parameters. Lower HRV is a risk factor for cardiovascular disease and mortality that demands the further studying its influence on the cardiovascular prognosis in PsA pts.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5269

SAT0453 EFFICACY OF USTEKINUMAB IN PSORIATIC ARTHRITIS PATIENTS BY PRIOR TREATMENT EXPOSURE AND DISEASE DURATION: DATA FROM PSUMMIT 1 AND PSUMMIT 2

I. McInnes[1], S.D. Chakravarty[2,3], G.J. Morgan[3], I. Apaolaza[4], S. Kafka[3], E.C. Hsia[5,6], M. Song[5], Y. You[5], A. Kavanaugh[7]. *[1]University of Glasgow, Glasgow, United Kingdom; [2]Drexel University College of Medicine, Philadelphia; [3]Janssen Scientific Affairs, LLC, Horsham, United States; [4]Janssen Biologics BV, Leiden, Netherlands; [5]Janssen Research & Development, LLC, Spring House; [6]University of Pennsylvania, Philadelphia; [7]University of California, San Diego, la Jolla, United States*

Background: PSUMMIT 1 and PSUMMIT 2 were Phase 3 trials of ustekinumab (UST) in adults with PsA.
Objectives: Evaluate the efficacy of UST by prior treatment exposure and disease duration in PsA patients (pts) in PSUMMIT 1 and 2.
Methods: Pts had active PsA (≥5 swollen, ≥5 tender joints, CRP ≥3.0mg/dL,) for ≥6 mos despite treatment with DMARDs and/or NSAIDs (PSUMMIT 1) or DMARDs, NSAIDs, and/or anti-tumor necrosis factor (TNF) agents (PSUMMIT 2). In both studies, pts were randomized to SC injections of placebo (PBO) or UST 45mg or 90mg at wks 0, 4 and every 12 wks. PBO pts crossed over to UST 45mg at wk 24. At wk 16, early escape (PBO –> UST45mg; UST45mg –> UST90mg; UST90mg –> UST90mg) was possible. Stable doses of MTX were allowed. Pooled data from both PSUMMIT 1 and 2 were analyzed. Efficacy assessments included ACR response, DAS28-CRP response, DAS28-CRP remission (score <2.6), changes in enthesitis (modified MASES index) and dactylitis scores, and total van der Heijde-Sharp (vdH-S) score for radiographic progression. Pts who were anti-TNF-naïve, MTX- and anti-TNF-naïve, all DMARD- and anti-TNF-naïve were evaluated. ACR response at wks 4 and 16 to assess for early efficacy was also evaluated for anti-TNF-naïve pts with PsA duration <1 year, ≥1 to <3 years, and ≥3 years.
Results: In the pooled data, 747 pts were anti-TNF-naïve (53.8% were male; mean age=47 years); 179 pts were MTX- and anti-TNF-naïve (63.7% were male; mean age =47 years); 146 pts were all DMARD- and anti-TNF-naïve (61.0% male; mean age=46 years). In all three prior treatment populations significantly greater proportions of pts in the combined UST group vs PBO achieved an ACR20, ACR50, or ACR70 at wk 24. (Table). Similarly, greater proportions of pts in the combined UST group had DAS28-CRP response or remission vs PBO across all three prior treatment populations. In anti-TNF-naïve pts, improvements in enthesitis and dactylitis were significantly greater in the combined UST group vs PBO, and mean change in total vdH-S score was significantly greater for pts in the PBO group than the combined UST group; comparable trends were observed for the MTX- and anti-TNF-naïve pts and all DMARD- and anti-TNF-naïve pts, but did not reach statistical significance due to the smaller sample sizes in both subgroups. Among anti-TNF-naïve pts treated with UST, ACR20/50/70 response rates were similar across different PsA disease duration groups at early time-points (either wk4 or wk16).

Table. Efficacy at week 24 in PSUMMIT 1 and PSUMMIT 2 combined.

	Anti-TNF-naive		MTX- and anti-TNF-naive		All DMARD- and anti-TNF-naive	
	Placebo	Combined UST (45mg/90mg)	Placebo	Combined UST (45mg/90mg)	Placebo	Combined UST (45mg/90mg)
Randomized pts, n	248	499	56	123	45	101
ACR20	59 (23.8%)	237 (47.5%) p<0.001	10 (17.9%)	66 (53.7%) p<0.001	9 (20.0%)	57 (56.4%) p<0.001
ACR50	21 (8.5%)	132 (26.5%) p<0.001	7 (12.5%)	43 (35.0%) p=0.002	7 (15.6%)	38 (37.6%) p=0.007
ACR70	7 (2.8%)	64 (12.8%) p<0.001	2 (3.6%)	24 (19.5%) p=0.006	2 (4.4%)	20 (19.8%) p=0.017
DAS28-CRP response	90 (36.3%)	327 (65.5%) p <0.001	17 (30.4%)	87 (70.7%) p<0.001	16 (35.6%)	71 (70.3%) p<0.001
DAS28-CRP remission	19 (7.7%)	99 (19.8%) p <0.001	6 (10.7%)	34 (27.6%) p=0.012	6 (13.3%)	29 (28.7%) p=0.043
Enthesitis (modified MASES index)						
Pts with enthesitis at baseline, n	176	351	39	89	29	75
Pts with enthesitis at week 24	133/166 (80.1%)	217/340 (63.8%) p<0.001	30/37 (81.1%)	58/83 (65.2%) p=0.077	22/28 (78.5%)	46/75 (61.3%) p=0.096
Percent change in score	-18.0 ± 80.0	-44.6 ± 57.2) p<0.001	-16.7± 62.7	-36.0 ± 74.6 p=0.046	-20.2 ± 65.2	-36.2 ± 79.9 p=0.129
Dactylitis (0-3)						
Pts with dactylitis at baseline, n	113	233	23	56	16	46
Pts with dactylitis at week 24	79/106 (74.5%)	129/226 (57.1%) p<0.001	17/22 (77.3%)	32/55 (57.1%) p=0.073	12/15 (80.0%)	24/46 (52.2%) p=0.118
Percent change in score	-25.2 ± 63.1	-44.8 ± 94.4 p <0.001	-23.3 ± 51.0	-44.5 ± 70.3 p=0.104	-20.0 ± 52.8	-43.4 ± 75.5 p=0.206
Change from baseline in tota vdH-S score	1.1 ± 4.2	0.3 ± 1.7 p<0.001	0.8 ± 2.6	0.2 ± 1.4 p=0.197	1.0 ± 2.8	0.2 ± 1.4 p=0.105

Data presented as n (%) or mean ± SD unless otherwise noted. MASES, Maastricht Ankylosing Spondylitis Enthesitis Score

Conclusions: UST-treated patients had greater improvements in signs and symptoms of PsA regardless of prior treatment exposure and disease duration.
Disclosure of Interest: I. McInnes Consultant for: Janssen Research & Development, LLC, S. Chakravarty Employee of: Janssen Scientific Affairs, LLC, G. Morgan Employee of: Janssen Scientific Affairs, LLC, I. Apaolaza Employee of: Janssen Biologics, BV, S. Kafka Employee of: Janssen Scientific Affairs, LLC, E. Hsia Employee of: Janssen Research & Development, LLC, M. Song Employee of: Janssen Research & Development, LLC, Y. You Employee of: Janssen Research & Development, LLC, A. Kavanaugh Consultant for: Janssen Research & Development, LLC
DOI: 10.1136/annrheumdis-2017-eular.4538

SAT0454 FINGER FLEXOR TENDON PULLEY COMPLEX INVOLVEMENT IN PSA: AN HIGH RESOLUTION ULTRASONOGRAPHIC STUDY

I. Tinazzi[1], A. Marchetta[2], D. Chessa[3], D. Mc Gonagle[4], P. Macchioni[5]. [1]*UOS Reumatologia, Ospedale Sacro Cuore-Don Calabria, Negar (Verona);* [2]*Ospedale Sacro Cuore Negrar (Verona), Negrar Verona;* [3]*Ospedale Paolo Dettori, Tempio Pausania (OT), Italy;* [4]*Leeds Institute of Rheumatic and Muscoloskeletal Medicine, Leeds, United Kingdom;* [5]*Ospedale S.Maria Nuova UOC Reumatologia, Reggio Emilia, Italy*

Background: Psoriatic Arthritis (PsA) is often associated with hand involvement including synovitis and tenosynovitis and dactylitis. At the micro anatomical level PsA is strongly linked to disease localisation to entheses and other sites of high mechanical stressing. Recently high resolution MRI has shown prominent abnormalities at the mini-entheses of the flexor tendon pulleys, a site of high physical stressing during finger flexion

Objectives: This study tested the hypothesis that sonographic abnormalities were common at the hand flexor tendon mini-entheses in PsA including the A1, A2 and A4 in patients without active hand arthritis or dactylitis at the moment of ultrasound (US) scanning

Methods: Consecutive patients affected by psoriasis (PsO) (23 cases), PsA (17) and healthy controls (HC) (19) were collected. The demographic charateristics are shown in Table 1. The cases were matched for sex, age and BMI. We excluded PsA patients with active arthritis or dactylitis at the moment of US study, the majority being under therapy with conventional DMARDs. The 2nd to 4th flexor tendons of the dominant hand were scanned with a high resolution linear probe (10–22 MHz) using an Esaote MyLab Twice machine. The sonograrapher was expert in muscolo skeletal ultrasound (MSKUS) and was blinded to the clinical details.The following changes were scored: tenosynovitis, A1, A2 and A4 pulley tendon thickness and pseudotensynovitis (peritendinous oedema). Pulleys were explored with transverse e longitudinal scan

Results: The A1, A2 and A4 pulleys were significantly thicker in PsA compared to PsO and healthy controls measuring both longitudinal and transverse scan (table 2 shows mean±SD value of transverse measures).In PsA patients A1, A2 and A4 pulleys thickness were above than the 95th percentile of HCs values respectively in 84%,80% and 100% of cases.Considering HCs and PsA we found that having a A1 thickness over the 95th percentile of HCs shows a sensibility of 82% and specificity of 100% for PsA. Using ROC curve analysis we found that the presence of one A1 thickness over the 95th percentile of HCs have a sensibility of 82% and specificity of 100% for PsA. Peritendinous oedema evaluated scanning the palmar side of proximal and intermediate phalanx was common in PsA patients (6/17) and absent in PsO and HCs

Table 1 Demographic data

	Healthy (n 19)	PsO (n 23)	PsA (n 17)
M/F	7/11 (39%61%)	9/14 (40%60%)	12/5 70%30%
Age (y) med ± SD	57±12	56±9	56±6
BMI med ± SD	25.5±4.0	25.9±3.2	28±3
Nail involvment	0	1 (4%)	8 (47%)
Previous dactylitis	0	1 (4%)	8 (47%)
MS >30'	0	0	9 (53%)
Previous trigger finger	0	7 (32%)	8 (47%)

Table 2 Transverse measures of pulleys thickness (mm)

	PsA	PsO	HCs
A1	0.61±0.15	0.40±0.10	0.33±0.08
A2	0.56±0.11	0.40±0.10	0.34±0.07
A4	0.50±0.13	0.33±0.05	0.30±0.02

Conclusions: This study suggests that PsA cases have a much higher burden of abnormalities in the mini-entheses of the flexor tendons on the hand. With the improving resolution and capabilities of MKUS these findings may be relevant to understand the involvment of flexor tendon in PsA expecially in sites with high mechanical stressing. Measuring A1, A2 and A4 thickness could be useful in detecting PsA cases without clinical signs of sinovitis or dactylitis

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6777

SAT0455 IMPACT OF PSORIATIC ARTHRITIS IN THE WORKPLACE: RESULTS OF THE FRENCH SURVEY PSOPRO

P. Claudepierre[1], I. Bonnet[1], Y. Roquelaure[2], P. Levy[3], R. Aubert[4], H. Bachelez[5]. [1]*Rheumatology, CHU Henri Mondor Créteil, CreteIL;* [2]*Medicine and Occupational Health, CHU Angers, Angers;* [3]*Economics, Université Paris-Dauphine, PSL Research University, LEDa [LEGOS];* [4]*Patient advocacy groups France Psoriasis;* [5]*Dermatology, AP-HP Hôpital Saint-Louis, Sorbonne Paris Cité Université Paris Diderot, Paris, France*

Objectives: The PsoPRO (Psoriasis & PROfessional life) survey, run under the aegis of the patient advocacy groups France Psoriasis, was aimed at measuring, in comparison to the general population, the impacts of psoriasis occurring alone (PsO) or concurring with psoriatic arthritis (PsO+PsA) on patients' working life.

Methods: From 13/07/16 to 08/08/16, 714 PsO patients, 81 of whom were under systemic treatment (PsO-ST), and 84 patients PsO+PsA were surveyed using a questionnaire drawn up by a multi-disciplinary scientific committee and conducted via the Internet. In addition to medical and professional characteristics, patients provided their recent absenteeism and presenteeism data, using a WPAI-PSO standardized self-questionnaire, as well as information about the interactions between psoriasis and their working life. Using the Student, Chi-deux and Fischer tests, patients were compared with a sample of 604 working respondents representative of the French population and questioned about the impact of possible health problems on their working life.

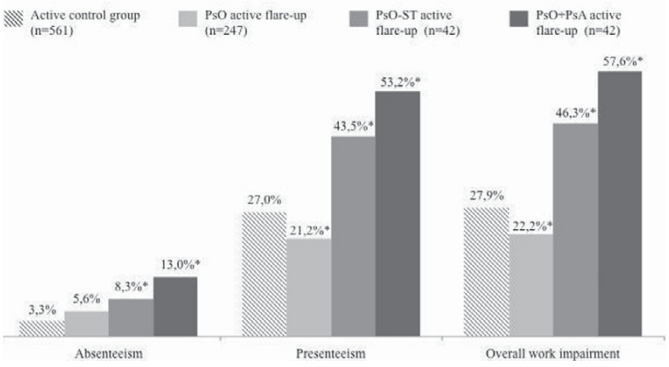
Results: The socio-demographic characteristics of the control group were similar to those of the total patient population with psoriasis, although men were slightly over-represented in the latter group. The duration of disease and cutaneous and rheumatismal locations were in line with those usually found in the literature. The unemployment rate over the previous 5 years and number of days of medical leave over the previous 12 months was higher in the PsO+PsA group as compared to the control group (Table 1). In the sub-group reporting a flare-up at the time of the survey, the impact of the disease on absenteeism, presenteeism and productivity was significantly higher in PsO-ST and PsO+PsA patients (Figure 1). Despite this, PsO-ST and PsO+PsA patients reported greater attachment to their work than did those in the control group (Table 1).

Table 1. Impact of psoriasis and psoriatic arthritis on functioning in the workplace and attachment to work

	Control group	PsO	PsO-ST	PsO+PsA
Unemployment over the past 5 years, % (n)	31 (187)	34 (243)	41 (33)	57* (42)
Number of days of medical leave over past 12 months, n	11	6	6	17*
Work considered more important than other aspects of life, % (n)	8 (45)	10 (62)	28* (20)	25* (17)
Work considered less important than other aspects of life % (n)	42 (236)	49* (301)	21* (15)	27* (18)

*p<0.05 versus control group respondents. PsO: psoriasis; PsO-ST: psoriasis under systemic treatment; PsO+PsA: psoriasis and psoriatic arthritis.

Figure 1: Impact of psoriasis and psoriatic arthritis on absenteeism, presenteeism and productivity over the past 7 day based on WPAI-PSO scores.
* p< 0.05 versus control group respondents PsO: psoriasis; PSO-ST: psoriasis under systemic treatment; PsO + PsA: psoriasis and psoriatic arthritis



Conclusions: In patients with PsO, placement under systemic treatment or the co-existence of PsA appears to be associated with greater impact on patients' working life, though they also reported higher attachment to their work. Close supervision and appropriate care in PSO patients developing PsA should limit these impacts.

Acknowledgements: This survey was made possible by funding from Celgene France and participation of the patient advocacy groups France Psoriasis.

Disclosure of Interest: P. CLAUDEPIERRE Grant/research support from: AbbVie, MSD, Roche, Pfizer, Consultant for: AbbVie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche, UCB, I. BONNET: None declared, Y. ROQUELAURE Consultant for: Abbott, Celgene, P. LEVY Consultant for: AbbVie, Actelion, Amgen, Anergis, Astellas, Bayer, Becton Dickinson, Biogen, BMS, Conceptus, Daïchi-Sankyo, Eli Lilly, EOS, Gilead, GSK, Hospira, Impeto Médical, Janssen, MSD, Mundipharma, Novartis, Novo Nordisk, Roche, Sanofi Pasteur MSD, Stallergènes. H., R. AUBERT: None declared, H. BACHELEZ Grant/research support from: Pfizer, Consultant for: Abbvie, Actelion, Amgen, Boehringer, Celgene, Eli- Lilly, Janssen, Leo Pharma, Novartis, Pfizer, Takeda, Abbott, Merck Serono, Roche, Schering-Plough, Wyeth

DOI: 10.1136/annrheumdis-2017-eular.4433

SAT0456 THERAPY MODIFICATIONS AMONG PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH A BIOLOGIC IN THE UNITED STATES – DESCRIPTIVE ANALYSES FROM AN ADMINISTRATIVE CLAIMS DATABASE

J.A. Walsh[1], O. Adejoro[2], B. Chastek[2], G. Chun[3], J.B. Palmer[3]. [1]*University of Utah School of Medicine, Salt Lake City, UT;* [2]*Optum, Eden Prairie, MN;* [3]*Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States*

Background: Biologic therapy used for the treatment of active psoriatic arthritis (PsA) can sometimes be augmented by adding non-biologic medications and/or

escalating the dose of the biologic therapy. Limited data exist on how theses therapy modifications are used in patients with PsA receiving biologic treatment in real-world settings.

Objectives: To describe therapy modifications (adding non-biologic medications or dose escalation of the current biologic therapy) in patients with PsA receiving biologic therapy in the United States.

Methods: This study used US administrative claims data from the Optum Research Database. Adults with PsA who newly initiated (no evidence of use in the 12 months prior) a biologic between January 1, 2013 and January 31, 2015, and were continuously enrolled in a commercial or Medicare Advantage health plan 12 months before (baseline period) and 15 months following the index date, defined as the date of first pharmacy fill or medical infusion, were included. To reduce confounding by patients with an early switch/discontinuation, therapy modifications were identified only in those patients who persisted with their index biologic for >90 days. Therapy modifications identified included initiation of add-on medications (disease-modifying antirheumatic drugs [DMARDs], nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, corticosteroids, antidepressants, anxiolytics, sleeping aids and topical analgesics) after the first 90 days of persistence, and dose escalation of the index biologic. Dose escalation was defined as a patient receiving a dose >10% above the reference dose from the product label for ≥90 days.

Results: Of the 1,010 patients included who persisted on their index biologic for >90 days, 80.5% initiated a subcutaneous tumor necrosis factor inhibitor (TNFi-SC; adalimumab, certolizumab pegol, etanercept or golimumab) as their index biologic, 12.0% initiated an intravenous TNFi (TNFi-IV; infliximab) and 7.5% initiated ustekinumab. During the 12-month baseline period, patients had a mean (standard deviation) number of claims of 2.9 (4.3) for conventional synthetic DMARDs (csDMARDs), 2.6 (5.0) for opioids, 2.2 (3.1) for NSAIDs and 2.0 (2.9) for corticosteroids. Overall, 45.5% of patients received ≥1 additional medication during the period from 90 days after the index date to the end of persistence with the index biologic or immediate 12-month post-index period. The most commonly added medications were corticosteroids (22.0%), opioids (17.1%), NSAIDs (12.9%) and csDMARDs (5.3%) (Table 1). Overall, 9.6% of patients had a dose escalation of the index biologic (33.9% for TNFi-IV, 6.4% for TNFi-SC and 5.3% for ustekinumab) in the immediate 12-month post-index period.

Table 1. Add-on medications initiated from 90 days after the index date to the end of persistence or 12 months among patients with PsA

Add-on Medication, n (%)	Total (N = 1010)	TNFi-SC* (n = 813)	Infliximab (n = 121)	Ustekinumab (n = 76)
Any medication	460 (45.4)	353 (43.4)	62 (51.2)	45 (59.2)
Corticosteroid	222 (22.0)	168 (20.7)	37 (30.6)	17 (22.4)
Opioid	173 (17.1)	126 (15.5)	20 (16.5)	27 (35.5)
NSAID	130 (12.9)	105 (12.9)	14 (11.6)	11 (14.5)
csDMARD	54 (5.3)	43 (5.3)	8 (6.6)	3 (3.9)
Antidepressant	49 (4.9)	34 (4.2)	8 (6.6)	7 (9.2)
Anxiolytic	48 (4.8)	34 (4.2)	10 (8.3)	4 (5.3)
Topical analgesic	31 (3.1)	24 (3.0)	4 (3.3)	3 (4.0)
Sleeping aid	22 (2.2)	17 (2.1)	4 (3.3)	1 (1.3)
tsDMARD	11 (1.1)	9 (1.1)	0 (0.0)	2 (2.6)

csDMARD, conventional synthetic disease-modifying antirheumatic drug; NSAID, nonsteroidal anti-inflammatory drug; PsA, psoriatic arthritis; SC, subcutaneous; TNFi, tumor necrosis factor inhibitor; tsDMARD, targeted synthetic DMARD.
* TNFi-SC includes adalimumab, certolizumab pegol, etanercept and golimumab.

Conclusions: In this descriptive, administrative claims-based study, nearly one-half (≈ 45%) of patients with PsA receiving biologic therapy initiated an add-on medication, most of which were pain medications. Further research is needed to better understand the reasons for therapy modifications during biologic treatment and the impact of insufficient control of pain in patients with PsA in the United States.

Acknowledgements: This study was sponsored by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

Disclosure of Interest: J. Walsh Consultant for: Novartis, O. Adejoro Employee of: Optum, B. Chastek Employee of: Optum, G. Chun Employee of: Novartis, J. Palmer Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.3014

SAT0457 MIXED ANXIETY-DEPRESSIVE DISORDER (MADD) IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH BIOLOGICAL THERAPY

C. García-Porrúa[1], J.A. Mosquera-Martínez[2], F.J. Maceiras-Pan[3], L. Fernandez-Dominguez[4], L. Guerra-Vazquez[5], J. Pinto-Tasende[6].
[1]Rheumatology, Hospital Universitario de Lugo, Lugo; [2]Rheumatology, Complejo Hospitalario Universitario de Pontevedra, Pontevedra; [3]Rheumatology, Complejo Hospitalario Universitario de Vigo, Vigo; [4]Rheumatology, Complejo Hospitalario Universitario de Ourense, Ourense; [5]Rheumatology, Complejo Hospitalario Universitario de Ferrol, Ferrol; [6]INIBIC-Rheumatology, Complejo Hospitalario Universitario A Coruña, A Coruña, Spain

Background: Psoriasis makes stress in patients and stress could play a role on the onset and exacerbation of psoriasis. Psoriasis and psoriatic arthritis (PsA) are associated with a variety of psychological problems, mainly anxiety and depression, although most of patients suffer from both anxiety and depressive symptoms of limited and equal intensity accompanied by at least some autonomic features and excluding severe anxiety and depressive symptoms (mixed anxiety-depressive disorder or MADD).

Objectives: The aim of this study was to describe the prevalence of MADD in clinical practice among PsA patients from our registry on treatment with biological therapy (bDMARDs) and to analyze their possible relation with characteristics of the disease or treatments in these patients.

Methods: We included all PsA patients (met CASPAR criteria) following treatment with bDMARDs and included in our regional registry (reference population 2.055.000). Was recorded the history of attending a mental health consultation since PsA diagnoses and before starting biologics therapy and if they were diagnosed as a mixed of anxiety and depression disorder (F41.2, ICD-10) and treated by non severe anxiety and depressive symptoms. We used for this analysis sex, age, disease duration, current bDMARDs with or without current co-medication with csDMARDs (methotrexate or leflunomide or sulfasalazine) and HLA-B27 status. Continuous variables were reported as mean ± standard deviation. Categorical variables were reported as percentages and frequencies. All analyses were performed using SPSS software. Differences were considered statistically significant if $p<0.05$ (two-tailed).

Results: We have registered 604 PsA patients who have been treated with bDMARDs. Three-hundred and twenty nine (54.5%) patients were men, mean age was 53.3±12.6 years and disease duration of PsA was 12.4±8.7 years. MADD was diagnosed in 99 patients (16.4%), and was more frequent in women than in men (21.1% vs 12.5%, p=0.004), with no differences in age of diagnosis and disease duration of PsA, nail disease, dactylitis, uveitis or HLA-B27. MADD was more prevalent in patients with enthesitis (31.9% vs 12.0%, $p<0.0001$) and PsA with axial involvement was associated with MADD (p=0.003). Etanercept (42%) and adalimumab (36%) were bDMARDs more used -56.2% with associated csDMARDs - and 67.9% of patients remained in the first biologic with a mean follow-up of 4.9 years. Infliximab was most used bDMARDs in patients with previous MADD (p=0.001).

Conclusions: Mixed anxiety-depressive disorder was more prevalent in women with PsA in our registry. It was associated more frequently with the axial disease, enthesitis and most use of infliximab like bDMARDs established in these patients.

References:

[1] McDonough E, Ayearst R, Eder L, Chandran V, Rosen CF, Thavaneswaran A, Gladman DD. Depression and anxiety in psoriatic disease: prevalence and associated factors. J Rheumatol. 2014;41(5):887–96.

Acknowledgements: The authors are grateful for the support of the members of the Galician Society of Rheumatology (SOGARE).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4015

SAT0458 IDENTIFICATION OF GENETIC VARIATION SPECIFICALLY ASSOCIATED WITH PSORIATIC ARTHRITIS USING GENOME-WIDE ASSOCIATION STUDIES

J.D. Cañete[1], A. Aterido[2], J.A. Pinto[3], J. Gratacós[4], R. Queiró[5], C. Montilla[6], J.C. Torre-Alonso[7], J.J. Pérez-Venegas[8], A. Fernández-Nebro[9], S. Muñoz-Fernández[10], C. González[11], D. Roig[12], P. Zarco[13], A. Erra[14], J. Rodríguez[15], S. Castañeda[16], E. Rubio[17], G. Salvador[18], C. Díaz-Torné[19], R. Blanco[20], A. Willisch-Domínguez[21], J.A. Mosquera[22], P. Vela[23], J. Tornero[24], S. Sánchez-Fernández[25], H. Corominas[12], J. Ramírez[1], A. Pluma[2], M. López-Corbeto[2], M. López-Lasanta[2], R. Tortosa[2], N. Palau[2], S. Marsal[2], A. Julià[2]. *[1]H. Clínic Barcelona and IDIBAPS; [2]Vall Hebron Research Institute; [3]CH. Juan Canalejo, Barcelona; [4]H. Parc Taulí, Sabadell; [5]H. Univ. Central Astúrias, Oviedo; [6]H. Virgen de la Vega, Salamanca; [7]H. Monte Naranco, Oviedo; [8]H. SAS Jerez Frontera, Cádiz; [9]H. Reg. Univ. Málaga, Málaga; [10]H. Univ. Infanta Sofía; [11]H. Univ. Gregorio Marañón, Madrid; [12]H. Moisès Broggi, Barcelona; [13]H. Univ. Fundación Alcorcón, Madrid; [14]H. Sant Rafael; [15]H. Univ. Bellvitge, Barcelona; [16]H. Univ. la Princesa, IIS-Princesa, Madrid; [17]Centro Salud Virgen Reyes, Sevilla; [18]H. Mútua Terrassa, Terrassa; [19]H. Santa Creu i Sant Pau, Barcelona; [20]H. Univ. Marqués Valdecilla, Santander; [21]CH. Ourense, Ourense; [22]CH. Pontevedra, Pontevedra; [23]H. Univ. Alicante, Alicante; [24]H. Univ. Guadalajara, Guadalajara; [25]H. General la Mancha Centro, Ciudad Real, Spain*

Background: PsA has a higher heritability than PsV, indicating the existence of additional PsA-specific genetic factors. To date, however, the specific genetic basis underlying PsA is poorly understood.

Objectives: The objective the present study was to identify new genetic variation specifically associated with PsA risk.

Methods: In order to characterize the genetic basis of PsA, we performed a GWAS meta-analysis at the single-marker level as well as at the pathway level (GWPA). A cohort of 835 PsA patients and 1,558 controls from the Spanish population was genotyped for >550,000 SNPs. GWAS data from a second cohort of 1,430 PsA patients and 1,417 controls from the North American population

was also used. In order to confirm the specificity of the new genetic variation associated with PsA risk, we analyzed the association with purely cutaneous psoriasis (PsC, n=614) and rheumatoid arthritis (RA, n=1,191). We performed a pharmacogenetic analysis to investigate the new PsA-specific pathways as a source for drug discovery in PsA.
Results: GWAS meta-analysis identified a new association between *B3GNT2* gene and PsA ($P<5e-08$). In the GWAS pathway analysis, we identified and validated a total of 14 genetic pathways associated with PsA risk. From these, the glycosaminoglycan (GAG) metabolism pathway was also found to be significantly associated with PsA risk when directly contrasted to the PsC cohort as well as the RA cohort. At the functional level, we detected a significant differential expression of GAG metabolism pathway genes in blood samples from PsA patients compared to PsC patients. The pharmacogenetic analysis identified several FDA-approved drugs likely to modify the GAG pathway.
Conclusions: The present study represents an important step towards the characterization of the genetic factors specific to PsA risk.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3685

SAT0459 LOW DOSE IL-2 RESTORES IMBALANCE BETWEEN TH17 AND REGULATORY T CELLS IN PATIENTS WITH PSORIATIC ARTHRITIS

K. Qin[1], Q. Chen[1], J. Fan[1], D. Xu[1], X. Li[1], C. Wang[1], C. Gao[2]. *[1]Rheumatology, the Second Hospital of Shanxi Medical University, Taiyuan, China; [2]Pathology, Joint Program in Transfusion Medicine, Brigham and Women's Hospital/Children's Hospital Boston, Harvard Medical School, Boston, United States*

Background: Psoriasis arthritis is one of chronic, relapsing, inflammatory autoimmune disorders with skin lesions and joint damage. A therapeutic revolution of psoriatic arthritis (PsA) is still a considerable unmet need in the past decades. It has been well known that the imbalance of Th17 cells and regulatory T cells (Tregs) may be a pivotal cause of PsA. Correction of this dysfunction can be a potential therapy of PsA.
Objectives: In this study, we measured and compared both absolute numbers and proportions of CD4+CD17+ Th17 cells and CD4+CD25+Foxp3+ Treg cells in peripheral blood of PsA patients and healthy controls to explore the immunopathogenesis of PsA; on the other hand, the effects of low-dose recombinant human IL-2 (rhIL-2) on Th17 and Treg cells were investigated in patients with PsA.
Methods: Both absolute numbers and proportions of Treg and Th17 cells in peripheral blood, defined as the CD4+CD25+Foxp3+T or CD4+IL-17+ T cell populations, were examined by flow cytometry in 40 healthy controls and 77 patients with PsA, including 39 patients who had never received disease-modifying antirheumatic drugs (DMARDs) and 38 patients who were receiving or had received DMARDs. Among these patients, 20 patients consented at enrollment to receive rhIL-2 treatment. Before and after treatment (50WIU/d for 5 days, IH), Th17 and Treg cells in peripheral blood were analyzed by flow cytometry.
Results: The absolute count of Th17 cells in patients with PsA was very significantly higher than that of healthy controls ($P<0.01$), but the proportions of Th17 cell were not seen difference between PsA and healthy controls ($P>0.05$). In contrast with treated-PsA patients, the absolute count of Th17 cells was significant higher in untreated-PsA patients ($P<0.05$). After the course of rhIL-2 treatment, there was a significant increase in the absolute count of Treg cells ($P<0.05$), but no diference in the absolute count of Th17 cells, Th17/Treg was significantly lower and went back to nomal.
Conclusions: The results suggest that, not the proportion, but the decrease in the absolute count of Th17 cells, defined as the CD4+CD17+ populations, contributes to the pathogenesis of PsA. After the treatment of rhIL-2, there was a more significant increase in the absolute count of Treg cells than that of Th17, and consequently the balance of Th17/Treg was restored to normal, leading to the development of new therapies.
References:
[1] Karczewski J, Dobrowolska A, Rychlewskahańczewska A, et al. New insights into the role of T cells in pathogenesis of psoriasis and psoriatic arthritis[J]. Autoimmunity, 2016:1.DOI:10.3109/08916934.2016.1166214.
[2] Yoo I S, Lee J H, Song S T, et al. T-helper 17 cells: the driving force of psoriasis and psoriatic arthritis.[J]. International Journal of Rheumatic Diseases, 2012, 15(6):531–537. DOI:10.1111/j.1756–185X.2012.01813.x.
[3] Szodoray P, Nakken B, Barath S, et al. Altered Th17 cells and Th17/regulatory T-cell ratios indicate the subsequent conversion from undifferentiated connective tissue disease to definitive systemic autoimmune disorders[J]. Human Immunology, 2013, 74(12):1510–8. DOI:10.1016/j.humimm.2013.08.003.
[4] Raychaudhuri S P. Role of IL-17 in psoriasis and psoriatic arthritis.[J]. Clinical Reviews in Allergy & Immunology, 2013, 44(2):183–193. DOI: 10.1007/s12016–012–8307–1.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6027

SAT0460 ASSOCIATION BETWEEN INFLAMMASOME-RELATED POLYMORPHISMS AND PSORIATIC ARTHRITIS

K. Juneblad[1], A. Kastbom[2], S. Rantapää-Dahlqvist[1], P. Söderkvist[3], G.-M. Alenius[1]. *[1]Dept of Public Health and Clinical Medicine/Rheumatology, University Hospital, Umeå, Umeå; [2]Department of Clinical and Experimental Medicine, Rheumatology; [3]Division of Cell Biology, Dept of Clinical and Experimental medicine, Linköping University, Linköping, Sweden*

Background: In recent years, research on the interleukin 1β(IL1 β)–regulating protein complex, called the inflammasome, has shown interesting associations with various inflammatory diseases. E.g. for Rheumatoid Arthritis (RA) (1) and psoriasis (Pso) (2, 3) associations with genetic polymorphisms in genes related to the inflammasome has been discovered. So far, no studies investigating genetic polymorphisms in inflammasome genes in Psoriatic Arthritis (PsA) patients have been published.
Objectives: To examine whether polymorphisms in genes related to inflammasomes confer increased risk for psoriatic arthritis.
Methods: DNA from 771 PsA patients and 793 healthy controls from Sweden were analyzed for different single nucleotide polymorphisms (SNPs) in *NLRP3* (rs35829419, rs10733113, rs4353135), *CARD8* (rs 2043211) and *NLRP1* (rs8079034, rs878329).
Results: Significant associations with PsA were found between carriage of allele, C, of rs878329 in *NLRP1* (Chi-2=6.5, OR (95% CI); 0.75 (0.60–0.94), P=0.011) and allele G in rs4353135 in *NLRP3* (Chi-2=4.8, OR (95% CI); 1.25 (1.02–1.53), p=0.028). Genotype distribution were also significantly different between patients and controls and for rs878329 in *NLRP1* there was a significant difference in allele frequency (G/C) between patients and controls (Chi-2=5.8, OR (95% CI); 1.20 (1.03–1.38), p=0.016). No significant associations with PsA were found for the other SNPs analyzed.
In genotype analysis, a significant higher frequency of genotype GG in rs878329 in PsA was detected (32.9% vs 26.9%, Chi-2=6.49, OR (95% CI); 1.34 (1.07–1.67), p=0.011), whilst no significant differences were detected for genotypes GC or CC. For rs4353135, a significantly higher frequency of genotype TG (43% vs 37.6%, Chi-2=4.66, OR (95% CI); 1.25 (1.02–1.53), P=0.033) and a significantly lower frequency of genotype TT (50.5% vs 56.1%, Chi-2=4.85, OR (95% CI); 0.80 (0.65–0.98), P=0.028) was seen in PsA, no significan difference was detected for genotype GG.
Conclusions: Carriage of rs878329C in *NLRP1* was less frequent in patients with PsA compared with controls indicating a protecting effect, but when different genotypes were analysed the difference likely results from an increased risk of PsA with genotype GG. The results are in contrast with the study of Ekman *et al*, where an increased transmission of rs878329C to family members with psoriasis was seen (3), indicating an increased risk of developing skin psoriasis for carriers of C, but in agreement with the study of Sui *et al* on patients with RA, where an association was detected for carriage of C (OR 0.82, p=0.02), with the risk genotype for RA being GG (4). Thus, the genotype GG possibly confers risk of arthritic disease whilst the C-allele seems associated with skin disease. Carriage of rs4353135G in *NLRP3* was more frequent in PsA patients compared with controls indicating an increased risk of disease, but only genotype GT was significantly increased in PsA. The study is, to our knowledge, the first to study possible associations between genes related to the inflammasome and PsA. In the study associations were found between one SNP in *NLRP3* and one SNP in *NLRP1*, indicating a possible involvement in pathogenesis of PsA disease.
References:
[1] Rheumatol 2008;47:415–7.
[2] Exp Dermatol 2012;21:932–7.
[3] Br J Rheumatol 2014;171:1517–20.
[4] Arthritis Rheum 2012;64:647–54.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3477

SAT0461 CHARACTERISATION OF DIFFERENT LOW DISEASE ACTIVITY MEASUREMENTS IN PATIENTS WITH PSORIATIC ARTHRITIS

L.C. Coates[1], A.B. Gottlieb[2], J.F. Merola[3], L. Aikman[4], A. Szumski[5], A. Chhabra[6]. *[1]University of Leeds, Leeds, United Kingdom; [2]New York Medical College, New York; [3]Harvard Medical School, Boston, United States; [4]Pfizer, Walton Oaks, United Kingdom; [5]InVentiv Health, Princeton; [6]Pfizer, New York, United States*

Background: Selection of the correct target to guide treatment is crucial for effective disease management in patients with psoriatic arthritis (PsA).
Objectives: To evaluate the prognostic value of several low disease activity (LDA) measurements in patients with PsA and psoriasis to assist physicians choose a valid target that facilitates assessment in clinical practice.
Methods: This was a post-hoc analysis from the PRESTA[1] clinical study. LDA targets analyzed were: Disease Activity in PsA (DAPSA) LDA ≤14 (tender joint count [TJC], swollen joint count [SJC], patient global visual analog scale [Pt VAS], pain VAS, C-reactive protein [CRP]; clinical (c)DAPSA LDA ≤13 (DAPSA without CRP); and minimal disease activity (MDA) measurement defined as 5/7 cut-offs (TJC ≤1, SJC ≤1, psoriasis activity and severity index [PASI] ≤1, Pt pain ≤15mm, Pt VAS ≤20mm, health assessment questionnaire ≤0.5, tender entheseal points ≤1). Additional MDA measurements were investigated where 5/7

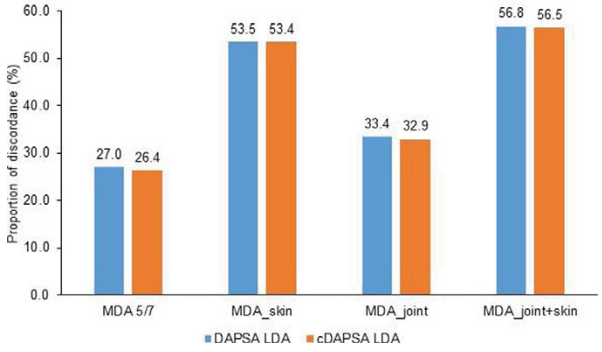
Abstract SAT0461 – Table 1. Proportion of patients with residual disease at Week 24

	MDA 5/7, n/N (%)	MDA_skin, n/N (%)	MDA_joint, n/N (%)	MDA_joint + skin, n/N (%)	DAPSA LDA, n/N (%)	cDAPSA LDA, n/N (%)
Dactylitis (1–12)	10/322 (3)	6/131 (5)	5/255 (2)	3/97 (3)	18/475 (4)	17/478 (4)
Enthesitis (1–5)	2/324 (1)	2/132 (2)	1/256 (0)	1/97 (1)	16/477 (3)	16/480 (3)
PASI (2–9)	142/324 (44)	0/132 (0)	119/256 (47)	0/97 (0)	237/477 (50)	237/480 (49)
PASI (≥10)	17/324 (5)	0/132 (0)	14/256 (6)	0/97 (0)	r 38/477 (8)	39/480 (8)
TJC (>1)	46/324 (14)	28/132 (21)	0/256 (0)	0/97 (0)	140/477 (29)	139/480 (29)
SJC (>1)	25/324 (8)	15/132 (11)	0/256 (0)	0/97 (0)	65/477 (14)	65/480 (14)

cut-offs were met but some were mandated: MDA_joint with both TJC and SJC cut-offs mandated, MDA_skin where PASI cut-off was mandated, MDA_joint+skin where the TJC, SJC, and skin cut-offs were mandated.

Results: At Week 24, the proportion of patients achieving LDA were 47%, 20%, 38%, 14% in MDA 5/7, MDA_skin, MDA_joint, MDA_joint+skin, respectively, vs ~71% in DAPSA and cDAPSA LDA. The highest proportion of discordance was observed between MDA_skin or MDA_joint+skin with DAPSA LDA or cDAPSA LDA (Figure). The majority of patients had no residual arthritis although levels were highest in the DAPSA measurements (Table). However, notable residual levels of psoriasis were observed in measurements that did not require skin disease control (Table 1). MDA_joint+skin had the lowest levels of residual disease across all cut-offs (Table 1). At Week 12, a significant difference ($P<0.05$) between the 50mg etanercept (ETN) once a week and 50mg ETN twice a week cohorts was observed in the measurements that required a skin cut-off (MDA_skin and MDA_joint+skin) and MDA 5/7 but not in DAPSA LDA, cDAPSA LDA, or MDA_joint.

Figure. Proportion with discordance for DAPSA LDA or cDAPSA LDA across different low disease activity definitions at Week 24



Conclusions: DAPSA and cDAPSA LDA provided the least stringent cut-offs with the highest percentages of patients with residual disease. Whilst choosing the optimal target for treatment requires more debate, it is clear from these data that levels of residual psoriasis are high in those measurements that do not require skin control. If this is not included in a treatment target for PsA, notable levels of psoriasis can be missed.

References:

[1] Sterry W, et al. BMJ 2010;340:c1471.

Disclosure of Interest: L. Coates Grant/research support from: Abbvie, Janssen, Consultant for: Abbvie, BMS, Janssen, Lilly, MSD, Novartis, Pfizer, A. Gottlieb Grant/research support from: Centocor (Janssen), Amgen, Abbvie, Novartis, Celgene, Pfizer, Lilly, Levia, Merck, Xenoport, Dermira, Baxalta, Consultant for: Amgen, Astellas, Akros, Centocor (Janssen), Celgene, Bristol Myers Squibb, Beiersdorf, Abbvie, TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dermipsor, Incyte, Pfizer, Canfite, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, Glaxo Smith Kline, Xenoport, Catabasis, Meiji Seika Pharma, Takeda, Mitsubishi,Tanabe Pharma Development America, Genentech, Baxalta, Kineta One, KPI Therapeutics, Crescendo Bioscience, Aclaris, Amicus, Reddy Labs, Speakers bureau: Abbvie, J. Merola Consultant for: Biogen IDEC, AbbVie, Amgen, Eli Lilly, Novartis, Pfizer, Janssen, UCB, Kiniksa, Momenta and Mallinckrodt, L. Aikman Shareholder of: Pfizer, Employee of: Pfizer, A. Szumski Employee of: InVentiv Health, A. Chhabra Shareholder of: Pfizer, Employee of: Pfizer

DOI: 10.1136/annrheumdis-2017-eular.1874

SAT0462 SECUKINUMAB PROVIDES SUSTAINED PASDAS RELATED LOW DISEASE ACTIVITY IN PSORIATIC ARTHRITIS: 2 YEAR RESULTS FROM THE FUTURE 2 STUDY

L.C. Coates[1,2], D.D. Gladman[3], P. Nash[4], O. Fitzgerald[5], A. Kavanaugh[6], L. Rasouliyan[7], L. Pricorp[8], K. Ding[8], C. Gaillez[9] on behalf of the FUTURE 2 study group. [1]*Leeds Teaching Hospitals NHS Trust;* [2]*University of Leeds, Leeds, United Kingdom;* [3]*Toronto western hospital, Toronto, Canada;* [4]*University of Queensland, Brisbane, Australia;* [5]*University College Dublin, Dublin, Ireland;* [6]*UC San Diego School of Medicine, la Jolla, United States;* [7]*RTI Health Solutions, Barcelona, Spain;* [8]*Novartis Pharmaceuticals Corporation, East Hanover, United States;* [9]*Novartis Pharma AG, Basel, Switzerland*

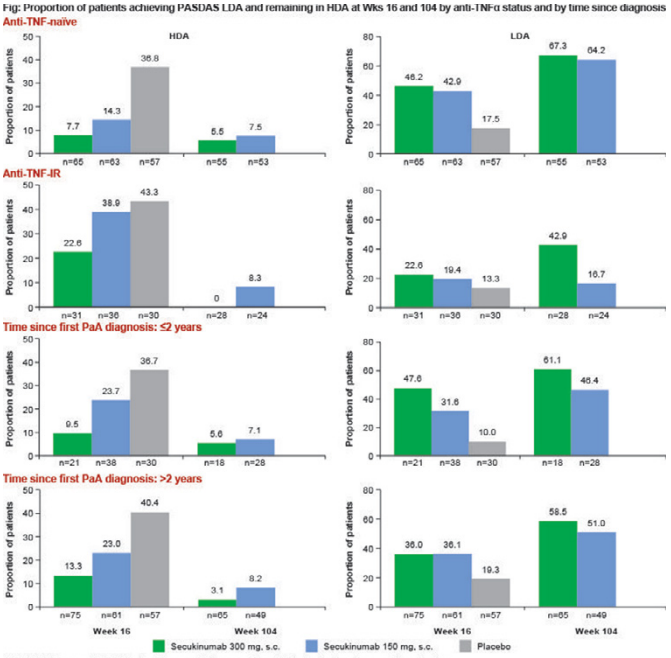
Background: Psoriatic arthritis (PsA) disease activity score (PASDAS) assessing multiple facets of PsA was demonstrated to distinguish treatment effect, perform better in statistical terms than traditional joint-only indices[1] and could be used as a treatment target in clinical trials in PsA.

Objectives: Secukinumab provided sustained improvement in the signs and symptoms of PsA over 104 weeks (wks) in the FUTURE 2 study.[2] Here, we report the ability of secukinumab to reach and sustain PASDAS based low disease activity (LDA) up to 104 wks in the FUTURE 2 study using a *post-hoc* exploratory analysis.

Methods: 397 patients (pts) with active PsA were randomised to subcutaneous (s.c.) secukinumab (300mg, 150mg, or 75mg) or placebo (PBO) at baseline (BL), Wks 1, 2, and 3, and every 4 wks (q4w) from Wk 4. PBO nonresponder and responder pts were re-randomised to secukinumab 300 or 150mg s.c. q4w from Wk 16 and 24, respectively. PASDAS is derived from physician's global VAS, patient's global VAS, SF-36 PCS, tender and swollen joints (TJC 68 and SJC 66), Leeds enthesitis count, dactylitis count and CRP level and has cut-points for high disease activity (HDA≥5.4), low disease activity (LDA<3.2) and remission (REM≤1.9).[3] PASDAS was assessed in the overall population and in pts stratified by prior anti-TNF use (naïve/inadequate response [IR]) and disease duration (≤2 years vs. >2 years since diagnosis) and reported using non-mutually exclusive categories at group level and as observed analysis. Secukinumab 75mg data are not reported as this was not considered an effective dose.[2]

Results: PASDAS score (mean [SD]) at baseline was 5.9 (0.9), 6.0 (1.0) and 5.8 (1.0) in the secukinumab 300mg, 150mg and PBO groups. In the overall population at Wk 16, PASDAS LDA was achieved in 37/96 (38.5%) and 34/99 (34.3%) of pts, treated with secukinumab 300mg and 150mg, respectively; vs. 14/87 (16.1%) with PBO. A high proportion of pts treated with secukinumab 300 and 150mg achieved LDA (49/83 [59.0%] and 38/77 [49.4%], respectively) at Wk 104. The proportion of pts achieving PASDAS LDA and remaining in HDA at Wks 16 and 104 by anti-TNFα status and by disease duration (≤2 years vs. >2 years) for secukinumab 300 and 150mg is reported in the figure.

Fig: Proportion of patients achieving PASDAS LDA and remaining in HDA at Wks 16 and 104 by anti-TNFα status and by time since diagnosis



HDA, high disease activity; LDA, low disease activity; n, number of pts in the treatment group with evaluation

Conclusions: A higher proportion of secukinumab-treated pts at Wk 16 achieved PASDAS LDA than PBO, with LDA sustained at group level at Wk 104. Discriminatory effect of PASDAS was consistent with that previously reported in the GRACE project.[4] A higher proportion of anti–TNFα-naïve pts treated with secukinumab achieved and sustained PASDAS LDA than anti–TNFα-IR pts whereas similar proportion of pts treated with secukinumab achieved PASDAS LDA irrespective of time since diagnosis (≤2 years vs. >2 years).

References:

[1] Helliwell PS and Kavanaugh A. Arth Care and Res. 2014;66:749–56.
[2] McInnes IB et al, Arthritis Rheumatol. 2016;68 (suppl 10).
[3] Coates LC and Helliwell PS, J Rheumatol. 2016;43:371–5.

[4] Helliwell PS et al, Ann Rheum Dis. 2013;72:986–91.
Disclosure of Interest: L. Coates Grant/research support from: Abbvie, Janssen, Consultant for: Abbvie, BMS, Celgene, Pfizer, UCB, MSD, Novartis, Lilly, Janssen, Sun Pharma, D. Gladman Grant/research support from: Amgen, AbbVie, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB, P. Nash Grant/research support from: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, Consultant for: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, Speakers bureau: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, O. Fitzgerald Grant/research support from: Bristol-Myers Squibb, Roche, Abbott, Consultant for: Bristol-Myers Squibb, Roche, Abbott, A. Kavanaugh Consultant for: Novartis, L. Rasouliyan Consultant for: Novartis through employment at RTI Health Solutions, Employee of: RTI Health Solutions, L. Pricorp Shareholder of: Novartis, Employee of: Novartis, K. Ding Shareholder of: Novartis, Employee of: Novartis, C. Gaillez Shareholder of: Novartis, BMS, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1458

SAT0463 SECUKINUMAB PROVIDES SUSTAINED REDUCTION IN FATIGUE IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS THROUGH 3 YEARS: LONG-TERM DATA FROM THE FUTURE 1 AND FUTURE 2 STUDIES

L. Gossec[1], T.K. Kvien[2], P.G. Conaghan[3], M. Østergaard[4], D. Gladman[5], P. Mease[6], L. Rasouliyan[7], L. Pricop[8], C. Gaillez[9], S. Jugl[9]. *[1]UPMC University Paris 06, Paris, France; [2]Diakonhjemmet Hospital, Oslo, Norway; [3]University of Leeds, Leeds, United Kingdom; [4]Copenhagen Center for Arthritis Research (COPECARE), Glostrup, Denmark; [5]University of Toronto, Toronto, Canada; [6]Swedish Medical Center, Seattle, WA, United States; [7]RTI Health Solutions, Barcelona, Spain; [8]Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States; [9]Novartis Pharma AG, Basel, Switzerland*

Background: Fatigue, a common symptom in patients (pts) with PsA, can negatively impact HRQoL and social functioning. Secukinumab (SEC), a fully human anti–IL-17A mAb, rapidly improved signs and symptoms, physical functioning, HRQoL, and fatigue in pts with PsA.[1,2]
Objectives: To assess the long-term effects of SEC on fatigue in TNF inhibitor (TNF)-naïve PsA pts and those with an inadequate response or intolerance to TNF inhibitor therapy (TNF-IR).
Methods: 606 and 397 pts were randomized to SEC or placebo (PBO) in FUTURE 1 (10 mg/kg IV followed by 150 or 75 mg SC) and FUTURE 2 (300, 150, or 75 mg SC), respectively. At Wk 16, PBO pts with ≤20% reduction in tender/swollen joint count (non-responders) were re-randomized to SEC 150 or 75 mg SC (FUTURE 1) and SEC 300 or 150 mg SC (FUTURE 2); responders were re-randomized at Wk 24. Pts in FUTURE 1 could enter a LTE study at Wk 104 (NCT01892436). Across both studies, approximately 68% of pts were TNF-naïve and 32% were TNF-IR. Fatigue was assessed at baseline (BL) and Wks 4, 8, 12, 16, 24, 52, 104, and 156 (FUTURE 1 only) using FACIT-F (higher scores = less fatigue). Fatigue response was defined by an increase in FACIT-F score of ≥4 from BL (corresponding to the MCID). Correlations between BL characteristics and improvements in fatigue were investigated using a logistical regression model. Only data with approved doses of SEC (300/150 mg) are shown.
Results: FACIT-F was 27.8–28.9 and 26.6–29.2 at BL across groups in FUTURE 1 and 2, respectively. Improvements in fatigue seen with all doses of SEC vs. PBO from Wks 4–24 were sustained through 156 wks in FUTURE 1 and 104 wks in FUTURE 2 in both the overall population and subgroups stratified by prior exposure to TNF (Table). The numerically higher responses with SEC 150 vs. 300 mg in this observed analysis were as a result of a higher rate of discontinuation due to lack of efficacy with the lower dose, which inflated the response rate. In the overall population, the LS mean change (±SEM) from BL in FACIT-F was significantly greater with SEC vs. PBO at Wk 16 in both FUTURE 1 (7.25±0.72 vs. 4.07±0.76; P=0.002) and FUTURE 2 (300 mg: 5.89±0.92 vs. 1.86±0.93, P=0.002; 150 mg: 7.40±0.90 vs. 1.86±0.93, P<0.0001); improvements were sustained throughout the entire follow up in both studies (FUTURE 1 Wk 156: 6.14±0.77; FUTURE 2 Wk 104: 300 mg 7.29±1.04, 150 mg 7.02±1.06). Improvements were generally somewhat larger in TNF-naïve pts than in TNF-IR pts. Correlation analyses did not identify any BL factors that consistently predicted change in fatigue score across Wks 16, 52, and 104.

Table. FACIT-Fatigue responders in FUTURE 1/FUTURE 2 until Week 156/104[a]

Proportion of Patients with FACIT-Fatigue Response[b], % (n/m)	FUTURE 1[c]	FUTURE 2	
	SEC IV–150 mg	SEC 300 mg	SEC 150 mg
Overall Population	**N=161**	**N=100**	**N=100**
Week 16	60.4 (96/159)	50.5 (48/95)	70.0 (70/100)
Week 52	66.9 (107/160)	60.2 (56/93)	68.5 (61/89)
Week 104	63.4 (90/142)	62.4 (53/85)	70.1 (54/77)
Week 156	57.4 (89/155)	–	–
TNF-naïve	**N=120**	**N=67**	**N=63**
Week 16	61.3 (73/119)	52.4 (33/63)	71.4 (45/63)
Week 52	69.2 (83/120)	60.7 (37/61)	72.9 (43/59)
Week 104	63.9 (69/108)	60.7 (34/56)	71.7 (38/53)
Week 156	58.3 (67/115)	–	–
TNF-IR	**N=41**	**N=33**	**N=37**
Week 16	57.5 (23/40)	46.9 (15/32)	67.6 (25/37)
Week 52	60.0 (24/40)	59.4 (19/32)	60.0 (18/30)
Week 104	61.8 (21/34)	65.5 (19/29)	66.7 (16/24)
Week 156	55.0 (22/40)	–	–

[a]Observed data are shown; [b]Defined as improvement ≥4.0 points; [c]Data shown are from patients who entered the FUTURE 1 long-term extension study at Week 104
m, number of patients with sufficient data for evaluation; N, number of patients randomized to SEC 150 mg or SEC 300 mg (FUTURE 2 only); n, number of responders.

Conclusions: SEC-treated PsA pts achieved rapid, sustained, and clinically meaningful improvements in fatigue for up to 156 wks, with higher responses in TNF-naïve pts.
References:
[1] McInnes et al. Lancet 2015;386:1137–46.
[2] Mease et al. N Engl J Med 2015;373:1329–39.
Disclosure of Interest: L. Gossec Grant/research support from: BMS, Lippy, Pfizer; Consultant for: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, P. Conaghan Consultant for: Abbvie, BMS, Lilly, Novartis, Pfizer, Roche, Speakers bureau: Abbvie, BMS, Lilly, Novartis, Pfizer, Roche, M. Østergaard Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Janssen, Merck, Novartis, Orion, Pfizer, Regeneron, Roche, UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Janssen, Merck, Novartis, Orion, Pfizer, Regeneron, Roche, UCB, D. Gladman Grant/research support from: Abbvie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Consultant for: Abbvie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, UCB, P. Mease Grant/research support from: Abbvie, Amgen, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Janssen, Merch, Novartis, Pfizer, SUN, UCB, Consultant for: Abbvie, Amgen, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Janssen, Merch, Novartis, Pfizer, SUN, UCB, Speakers bureau: Abbvie, Amgen, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Janssen, Merch, Novartis, Pfizer, SUN, UCB, L. Rasouliyan Consultant for: Novartis, L. Pricop Shareholder of: Novartis, Employee of: Novartis, C. Gaillez Shareholder of: Novartis and BMS, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1719

SAT0464 THE IDEAL TARGET FOR PSORIATIC ARTHRITIS? COMPARISON OF REMISSION AND INACTIVE DISEASE STATES IN A REAL LIFE COHORT

L.J.J. Van Mens[1], A.W.R. van Kuijk[2], D.L. Baeten[1,3], L.C. Coates[4]. *[1]AMC; [2]Reade, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands; [3]UCB, Brussels, Belgium; [4]LIRMM, University of Leeds, Leeds, United Kingdom*

Background: Recommendations on psoriatic arthritis (PsA) state that the target of treatment should be remission or inactive disease. Multiple potential targets have been developed and proposed, each with a different composition of clinical measurements.
Objectives: Our aim is to use an existing real life dataset of a large group of patients in a low disease activity state, to compare different targets and provide further evidence to choose a target.
Methods: This analysis uses data from a cross-sectional real life cohort of 250 PsA patients (EULAR16–2124). All patients were considered in an acceptable disease state according to the treating rheumatologist, defined by the fact that the rheumatologist did not consider to modify the current treatment. Remission/inactive disease targets were the DAPSA [TJC; SJC; patient global visual analogue scale (Pt VAS); pain VAS; CRP] and clinical (c)DAPSA [DAPSA minus CRP] remission (≤4), very low disease activity (VLDA) [7/7 of TJC ≤1; SJC ≤1; PASI ≤1; Pt pain ≤15mm; Pt VAS ≤20mm; HAQ ≤0.5; tender entheseal points ≤1], and PASDAS ≤1.9 or near remission (NR).
Results: 113 pts were in cDAPSA remission, 107 in DAPSA remission, 56 met VLDA and 37 in PASDAS NR. There was a very high percentage exact agreement between DAPSA and cDAPSA (96%) reflecting the similarity of the two definitions. DAPSA/cDAPSA and VLDA show a high correlation (pearson of 0,611 and 0,590 resp) but VLDA is more stringent in comparison with both DAPSA scores. The correlation between NR and DAPSA/cDAPSA/VLDA was lower, (pearson 0,400, 0,403 and 0,412 resp). Again PASDAS NR was generally more stringent than DAPSA/cDAPSA remission but greater dissimilarities are seen between PASDAS NR and VLDA where 14 patients are in VLDA but not PASDAS NR and 29 are in PASDAS NR but not VLDA.
Although presence of active joint disease was similar across the different measures, VLDA presents as a more stringent cutoff with less residual disease in PASI, TJC and less impact on DLQI and HAQ. All targets had similar % of patients

with a raised CRP. The DAPSA measures which do not include an enthesitis measure show more patients with an active enthesitis.
There was a limited consequence on QoL measures when residual disease activity was allowed in certain domains in these remission states. In those patients with active enthesitis or skin disease, no differences were found on PROs on quality of life and functionality. The presence of active skin disease with a PASI>2 (present in 20/110 pts achieving DAPSA) was reflected by an impact on DLQI (2,85 (SD2,9)v.s. 1 (2,3)p=0.003). This effect was not seen when the cutoff of for PASI>1 was used.

		cDAPSA (n=113)	DAPSA (n=107)	VLDA (n=56)	PASDASNR (n=37)
PASDAS mean (SD)		2,16 (0,52)	2,13 (0,49)	1,97 (0,42)	1,6 (0,20)
SJC	0	101 (89%)	96 (90%)	53 (95%)	33 (89%)
	1	10	10	3	1
	2	2	1	0	3
TJC	0	93 (82%)	89 (83%)	51 (91%)	28 (75%)
	1	11	11	5	2
	2	7	5	0	4
	3+	2	2	0	3
LEI	0	108 (96%)	102 (96%)	56 (100%)	37 (100%)
	1	1	1	0	0
	2+	4	4	0	0
PASI score	0–1	79 (70%)	74 (69%)	56 (100%)	32 (86%)
	>1	34	33	0	5
CRP >5mg/dl		11 (10%)	8 (7,5%)	5 (9%)	1 (3%)

Conclusions: This comparison of the different remission targets shows that VLDA presented as the most stringent target. Inclusion of laboratory markers seems not to be a necessity although the exclusion of a skin domain might result in a negligence of skin disease in some patients despite an impact on their QoL.
Disclosure of Interest: L. Van Mens: None declared, A. van Kuijk Grant/research support from: UCB, Pfizer, MSD, Janssen, Consultant for: Novartis, Celgene, D. Baeten Grant/research support from: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim. This cohort was funded by an unrestricted grant from Pfizer to DB, Consultant for: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim, Eli Lilly, Roche, BMS, Glenmark, Employee of: UCB, L. Coates: None declared
DOI: 10.1136/annrheumdis-2017-eular.2926

SAT0465 AN INTEGRATED SAFETY DATA ANALYSIS ACROSS ALL PHASE II AND PHASE III CLINICAL PROGRAMS FOR USTEKINUMAB IN PSORIATIC ARTHRITIS, CROHN'S DISEASE, AND PSORIASIS

L.S. Gensler[1], E. Hsia[2], C. Gasink[2], B. Randazzo[3], D. Parenti[4], S. Fakharzadeh[4], L.-L. Gao[3], S.D. Chakravarty[5]. *[1]University of California, San Francisco, San Francisco; [2]Janssen Research & Development, LLC/University of Pennsylvania, Spring House/Philadelphia; [3]Janssen Research & Development, LLC, Spring House; [4]Janssen Scientific Affairs, LLC, Horsham; [5]Janssen Scientific Affairs, LLC/Drexel University College of Medicine, Horsham/Philadelphia, United States*

Objectives: Therapeutic decisions are based on efficacy, but clinicians need to consider medication safety in this process. Here, we report ustekinumab (UST) integrated safety data in patients (pts) with psoriatic arthritis (PsA), Crohn's disease (CD), and psoriasis (PsO). We also compare a subset of PsA pts with & without baseline methotrexate (MTX).
Methods: Integrated safety data from 3 PsA, 5 CD, & 4 PsO trials were analyzed. PsA studies included the Ph2 trial [CNTO743T10] & the 2 Ph3 trials (PSUMMIT 1 & 2) with 222, 615 & 312 pts exposed to UST, respectively. The percentage of pts in the Ph2 study that received MTX was 20.5%. No concomitant DMARDs with the exception of MTX (approximately 50% of pts in each study) were permitted in the 2 Ph3 studies. In the 5 CD trials (Ph2/3Ph3) 1749 pts were exposed to UST. In the 3 Ph3 CD trials, pts received one dose of UST 130mg or ~6mg/kg IV at induction (UNITI-1 & UNITI-2), then 8 weeks later, entered the maintenance phase (IM UNITI) and received UST 90mg SC q8w or q12w for 44 weeks. The percentage of pts on background MTX in UNITI-1 was 9.2% & in UNITI-2, 4.8%. In the PsO studies (1Ph2/3Ph3), a total of 3117 pts received UST 45mg or 90mg SC; *no concomitant DMARD therapy (including MTX) was permitted*. The PsO studies were completed through 5-years of follow-up. All pts who received at least 1 dose of UST are included in this analysis. Safety events are reported in events per 100-pt years. 95% CI for events per 100 PY were estimated.
Results: Through 1 year of follow-up, a total of 1018 PsA pts were treated with UST, of which 465 were co-treated with MTX. Of the 1749 CD pts treated with UST, 139 received MTX. Discontinuation rates of UST due to adverse events (AEs) were comparable across disease states irrespective of MTX use (Table). AE rates (95% CIs for events/100 PY) were noted to be comparable in the UST vs PBO groups for all diseases pooled irrespective of MTX use-UST (420.39, 432.45) vs PBO (534.80, 570.44). Serious adverse event rates (SAEs) were also comparable in the UST vs PBO groups for all diseases pooled-UST (14.25, 16.56) vs PBO (24.05, 32.18). Infections and Serious infections (SIs) had numerically lower event rates in UST vs. PBO groups for all diseases pooled-UST (122.16, 128.72) vs PBO (120.94, 138.27) and UST (2.10, 3.05) vs PBO (2.76, 6.00), respectively (Table). Major adverse cardiovascular events (MACE) did not appear

	Psoriatic Arthritis				Crohn's disease				Psoriasis**		All Diseases Pooled	
	PBO		UST		PBO		UST		PBO^	UST^^	PBO	UST
	+MTX	-MTX	+MTX	-MTX	+MTX	-MTX	+MTX	-MTX	N/A	N/A	N/A	N/A
Pts treated	160	219	465	553	76	867	139	1610	733	3117	2055	5884
Pt years of follow-up	64	81	396	454	25	322	89	1017	182	2566	17.05	39.96
PTs D/C due to AE (%)	5.0	6.4	3.4	2.7	3.9	4.8	6.5	6.1	2.3	2.8	4.1	3.8
Event rate per 100-pt years												
AEs	381.53	313.34	255.55	253.10	849.48	701.45	646.96	641.16	414.81	390.60	552.41	426.39
SAEs	20.33	8.64	6.82	11.46	79.76	41.04	40.16	34.91	8.78	8.77	27.89	15.37
Infections	104.76	101.16	82.32	74.30	139.59	145.51	137.91	133.64	120.71	127.40	129.38	125.41
Serious infections	1.56	0.00	0.00	1.76	15.95	6.22	13.45	5.80	1.65	1.40	4.15	2.54
MACE*	0.00	1.23	0.25	1.10	0.00	0.00	0.00	0.10	0.55	0.55	0.3	0.46
Malignancies (excluding NMSC)	0.00	0.00	0.00	0.22	0.00	0.00	0.00	0.39	0.55	0.43	0.15	0.35
Deaths	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.19	0	0.11

*MACE adjudicated events includes CV death, non-fatal MI, or non-fatal stroke; **In the psoriasis studies, no concomitant DMARD therapy (including MTX) was permitted. ^includes data from the time of crossover, ^^includes data from the first UST dose onward for patients who crossed over from PBO

to significantly differ in both PBO & UST pts in PsA, PsO and CD. Event rates of malignancy (excluding non-melanoma skin cancer) were comparable across all disease states. No deaths in PsA or CD were reported.
Conclusions: UST demonstrates a favorable safety profile in an integrated safety data analysis across the PsA, CD, & PsO phase 2 & 3 clinical trials. The use of UST in PsA appears to be safe & well-tolerated, with fewer event rates of SAEs & SIs noted vs PBO. Despite higher overall rates of SAEs & SIs observed in CD pts, the data do not suggest an influence of UST on either.
Disclosure of Interest: L. Gensler Grant/research support from: Janssen Scientific Affairs, LLC, E. Hsia Employee of: Janssen Research & Development, LLC, C. Gasink Employee of: Janssen Research & Development, LLC, B. Randazzo Employee of: Janssen Research & Development, LLC, D. Parenti Employee of: Janssen Scientific Affairs, LLC, S. Fakharzadeh Employee of: Janssen Scientific Affairs, LLC, L.-L. Gao Employee of: Janssen Research & Development, LLC, S. Chakravarty Employee of: Janssen Scientific Affairs, LLC
DOI: 10.1136/annrheumdis-2017-eular.1116

SAT0466 PREGNANCY IN WOMEN WITH PSORIATIC ARTHRITIS: PREGNANCY OUTCOMES AND CHANGES IN DISEASE ACTIVITY

M.E.B. Clowse, G. McDaniel, A.M. Eudy. *Rheumatology, Duke University Medical Center, Durham, United States*

Background: Very little has been published about psoriatic arthritis (PsA) in pregnancy, and it remains unknown whether pregnancy outcomes are impacted by this disease or whether disease activity is changed by pregnancy or delivery.
Objectives: To discover the rate of pregnancy complications for women with psoriatic arthritis, and to determine whether psoriasis and the associated arthritis change during and following pregnancy.
Methods: A retrospective survey was completed by 40 women aged 20–50 years with psoriatic arthritis managed at a university center. Each survey collected information about infertility, pregnancy outcomes and complications, as well as patient-reported assessments of changes in both skin and joint disease activity at the onset of pregnancy, over the course of the pregnancy, and in the months following pregnancy. Simple statistics were used to compare outcomes before and after the diagnosis of PsA.
Results: The survey was completed by 40 women with PsA. The majority (93%) were white, non-Hispanic with a high level of education (40% completed college and another 30% either started or finished a graduate degree); 62.5% were married. The average age at the time of the study was 37.4 (SD 7.9) years and age at PsA diagnosis was 30.9 (8.4) years.
Twenty-five women reported they had ever tried to become pregnant, and of those, 9 had been unable to become pregnant after 12 months of trying or had been diagnosed with infertility by a physician (36%). The reasons for infertility or inability to become pregnant included polycystic ovarian syndrome (44%), problem with ovulation (11%), problem with uterus (11%), elevated prolactin (11%), infection in pelvic area (11%), and/or cervical problems (30%). Infertility was unexplained in 33%.
There were 70 pregnancies to 26 patients, with 37 pregnancies occurring after the diagnosis of PsA (see table). Pregnancy outcomes following PsA diagnosis were worse than those prior to PsA diagnosis, particularly the rate of pregnancy loss (32% compared to 12%; p=0.05) and preterm birth (48% compared to 21%; p=0.02). Only 24% of patients took psoriasis or arthritis medications during pregnancy. The most commonly used medications during pregnancy were TNF inhibitors (16%), corticosteroids (8%), and DMARDs (5%).
The large majority of patients had minimal arthritis and psoriasis during pregnancy.

Table. Pregnancy outcomes before and after psoriatic arthritis diagnosis.

	Overall	Prior to PsA Diagnosis	After PsA Diagnosis
Number of Pregnancies	70	33	37
Live Births	47 (67%)	24 (73%)	23 (62%)
Spontaneous Abortion	15 (21%)	4 (12%)	11 (30%)
Stillbirth	1 (1%)	0 (0%)	1 (3%)
Ectopic Pregnancies	1 (1%)	1 (3%)	0 (0%)
Elective Termination	6 (9%)	4 (12%)	2 (5%)
Preterm Birth	16/47 (34%)	5/24 (21%)	11/23 (49%)
Preeclampsia	11/46 (24%)	5/23 (22%)	8/23 (35%)
Abnormal Infant	1/47 (2%)	2/24 (8%)	2/25* (8%)
Adverse Pregnancy Outcome	33 (47%)	10 (30%)	23 (62%)

*two twin pregnancies

Only 12% had moderate and 6% had severe arthritis. Similarly, only 10% had moderate and 7% had severe psoriasis. During and following pregnancy, about half of all patients reported no change in either joint or skin activity during and follow pregnancy, with fairly equal numbers reporting improved and worsened arthritis. On the other hand, 42% had improved psoriasis during pregnancy compared to 6% with worsened. There did not appear to be a significant postpartum flare.

Conclusions: Our analysis found that among women with PsA who have tried to become pregnant, 36% experienced infertility, primarily due to PCOS. Compared to pregnancies occurring before the diagnosis of PsA, pregnancies after PsA diagnosis had a lower frequency of live births and a higher frequency of preterm births. Overall, in this cohort of women with mostly mild disease during pregnancy, arthritis pain and psoriasis activity did not appear to substantially worsen during pregnancy.

Acknowledgements: This study was funded by Janssen.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6392

SAT0467 ALL 10-YEAR CARDIOVASCULAR RISK SCORES ARE SIMILAR IN PATIENTS WITH PSORIATIC ARTHRITIS AND PSORIASIS

N. Ikumi[1], F. Farkas[1], A. Szentpetery[1], B. Kirby[2], O. FitzGerald[1].
[1]Rheumatology; [2]Dermatology, St. Vincent's University Hospital, Dublin, Ireland

Background: Psoriatic arthritis (PsA) and Psoriasis (PsO) are associated with higher cardiovascular (CV) risk with higher risk in patients with a severe disease phenotype[1,2]. Long-term CV risk is evaluated using several methods for the general population.

Objectives: The aim of the study was to compare CV risk factors and 10-year CV risk scores between patients with PsA and those with PsO only.

Methods: PsA patients fulfilling the CASPAR criteria and PsO with disease duration <10 years were enrolled consecutively from Rheumatology and Dermatology clinics. Fasting bloods were obtained for glucose, insulin and lipids. Patients underwent thorough physical examination, joint and skin assessments and completed questionnaires on health and quality of life. Four different CV risk scores were calculated: (1) Framingham Coronary risk score (FCS); (2) American College of Cardiology and American Heart Association (ACC/AHA) 10-year atherosclerotic cardiovascular disease (ASCVD) algorithm; (3) Systematic Coronary Risk Evaluation (SCORE) algorithm; and (4) QRISK2 (2016).

Results: 232 patients (100 PsA and 132 PsO) were recruited with mean age 52.4 (±10.5) for PsA and 39.7 (±14.4) for PsO. Mean disease duration for PsA was 17.9 (±10) years. There were significantly more patients with hypertension (HTN) and metabolic syndrome in PsA group, and the patients taking DMARDs and/or biologics treatment were also higher compared to PsO. Fasting glucose, insulin, lipids, BMI and waist/hip ratio did not show significant differences. The mean FCS, ASCVD, SCORE and QRISK2 were significantly higher in PsA as compared to PsO (7.6±7.0% vs. 4.7±6.1%, P=0.0002; 8.4±8.2% vs. 4.5±5.8%, P<0.0001; 2.1±2.6% vs. 1.1±1.8%, P=0.0002; 11.2±9.9% vs. 5.2±6.4%, P<0.0001, respectively). However, after adjusting for age and sex, all CV risk scores were similar (P=0.21). Multiple regression analysis revealed that waist/hip ratio significantly correlated with all CV risk scores in both PsA and PsO.

Conclusions: We found similar 10-year risk of CVD in PsA and PsO patients using FCS, ASCVD, SCORE and QRISK2. Waist/hip ratio had significant effect on all CV risk scores suggesting that central obesity should be managed appropriately to reduce long-term CVD in psoriatic disease.

References:

[1] Eder L. Ther Adv Musculoskel Dis 2015.
[2] Ogdie A. ARD 2015.

Disclosure of Interest: N. Ikumi: None declared, F. Farkas: None declared, A. Szentpetery: None declared, B. Kirby Grant/research support from: abbie, O. FitzGerald Grant/research support from: abbie, Pfizer, BMS, Consultant for: abbie, Pfizer, BMS, Celgene, Janssen, Novartis, UCB, Eli Lilly

DOI: 10.1136/annrheumdis-2017-eular.4404

SAT0468 PRESENCE OF POOR PROGNOSTIC FACTORS MAY PREDICT RESPONSE TO ABATACEPT IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A POST HOC ANALYSIS FROM A PHASE III STUDY

P. Mease[1], I. McInnes[2], V. Strand[3], O. FitzGerald[4], H. Ahmad[5], A. Johnsen[5], J. Ye[5], S. Banerjee[5]. *[1]Swedish Medical Center and University of Washington, Seattle, United States; [2]University of Glasgow, Glasgow, United Kingdom; [3]Stanford University, Palo Alto, United States; [4]St Vincent's University Hospital and University College Dublin, Dublin, Ireland; [5]Bristol-Myers Squibb, Princeton, United States*

Background: Abatacept, a selective T-cell co-stimulation modulator, significantly increased ACR20 response and had an overall beneficial effect on musculoskeletal symptoms in patients (pts) with active psoriatic arthritis (PsA) in the Phase III Active pSoriaTic athritis RAndomizEd triAl (ASTRAEA, NCT01860976).[1] Factors that may predict responses to abatacept were explored in this *post hoc* analysis.

Objectives: To evaluate the relationship between baseline characteristics and abatacept response in a *post hoc* analysis of ASTRAEA.

Methods: Pts were randomized (1:1) to SC abatacept 125 mg weekly or placebo for 24 weeks in this trial. Pts without >20% improvement in joint counts at Week 16 were switched to open-label abatacept (early escape). ACR20 response rate in pts stratified by baseline variables was investigated in a multivariate analysis and odds ratios (ORs) generated to identify differences in response. Using a cut-off of OR 1.2, indicating pt subgroups in whom abatacept appeared to have a meaningful treatment benefit, baseline variables were further investigated in a univariate analysis and estimated differences calculated.

Results: Of 424 pts enrolled, 213 received abatacept and 211 placebo. In abatacept-treated pts, the multivariate model showed a difference in ACR20 response (OR >1.2) for baseline CRP (>upper limit of normal [ULN] vs ≤ULN; OR 1.346 [95% CI 0.668, 2.712]), DAS28 (CRP) (>5.1 vs ≤5.1; 1.489 [0.782, 2.836]), dactylitis (>0 vs 0; 1.372 [0.708, 2.659]), and median baseline erosions (≥3 vs <3; 1.924 [1.032, 3.587]). In placebo-treated pts, the OR was >1.2 for dactylitis only (1.406 [0.619, 3.193]). These factors, which have been identified previously as indicating poor prognosis in PsA, were balanced between treatment arms at baseline. In the univariate model by poor prognostic factors, the differences in ACR20 response rates with abatacept treatment vs placebo in distinct subgroups were numerically greater in pts who were positive for these prognostic factors at baseline than in those who were not (Figure).

Figure. Univariate Analysis of ACR20 Response Rate by Poor Prognostic Factors at Week 24

	Responders, n/N (%)		
	Abatacept	Placebo	Estimated difference (95% CI)
All patients	84/213 (39.4)	47/211 (22.3)	17.2 (8.7, 25.6)
CRP ≤ULN	19/66 (28.8)	16/78 (20.5)	8.3 (–5.9, 22.4)
CRP >ULN	64/146 (43.8)	31/131 (23.7)	20.2 (9.3, 31.0)
CRP ≤ULN and baseline erosion score <3	9/43 (20.9)	10/44 (22.7)	–2.4 (–19.1, 14.3)
CRP ≤ULN and baseline erosion score ≥3	9/22 (40.9)	4/30 (13.3)	25.0 (2.5, 47.5)
CRP >ULN and baseline erosion score <3	28/72 (38.9)	16/69 (23.2)	12.9 (–2.1, 27.9)
CRP >ULN and baseline erosion score ≥3	32/68 (47.1)	14/57 (24.6)	24.5 (8.8, 40.1)
DAS28 (CRP) ≤5.1	38/111 (34.2)	26/121 (21.5)	12.5 (1.2, 23.8)
DAS28 (CRP) >5.1	42/99 (42.4)	21/87 (24.1)	19.0 (6.0, 31.9)
No baseline dactylitis digits	46/137 (33.6)	29/144 (20.1)	13.2 (3.0, 23.3)
With baseline dactylitis digits	32/66 (48.5)	14/55 (25.5)	21.5 (5.0, 37.9)
Baseline erosion score <3	37/115 (32.2)	26/114 (22.8)	8.2 (–2.9, 19.3)
Baseline erosion score ≥3	42/91 (46.2)	18/88 (20.5)	26.3 (13.2, 39.3)



ULN=upper limit of normal

Conclusions: These findings identified subgroups of pts with PsA with certain baseline characteristics in whom abatacept is most likely to be effective. The predictive factors identified are aligned with poor prognostic factors in the EULAR and Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) guidelines,[2,3] and may indicate pts with the highest unmet medical need.

References:

[1] Mease P, et al. Arthritis Rheumatol 2016;68(Suppl 10):[Abstract 1041].
[2] Gossec L, et al. Ann Rheum Dis 2016;75:499–510.
[3] Coates L, et al. Arthritis Rheumatol 2016;68:1060–71.

Disclosure of Interest: P. Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo Biosciences, Corrona, Demira, Janssen, Lilly, Novartis, Pfizer, Sun, UCB, Zynerba, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo Biosciences, Genentech, Janssen, Novartis, Pfizer, UCB, I. McInnes Grant/research support from: Bristol-Myers Squibb, Celgene, Janssen, UCB, Consultant for: Bristol-Myers Squibb, Celgene, Janssen, Novartis, Pfizer, AbbVie, UCB, V. Strand Consultant for: AbbVie, Amgen Corporation, AstraZeneca, Biogen Idec, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Celltrion, Corrona, Crescendo Biosciences/Myriad Genetics, EMD Serono, Genentech/Roche, GlaxoSmithKline, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, UCB, O. FitzGerald Grant/research support from: AbbVie, Pfizer, Bristol-Myers Squibb, Consultant for: AbbVie, Pfizer, Bristol-Myers Squibb, Celgene, Janssen, Novartis, UCB, Lilly, H. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, A. Johnsen Employee of: Bristol-Myers Squibb, Celgene, Janssen, Novartis, Pfizer, AbbVie, UCB, J. Ye Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Banerjee Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.1641

SAT0469 INTEGRATED EFFICACY ANALYSIS OF TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

P. Nash[1], L.C. Coates[2], R. Fleischmann[3], K.A. Papp[4], J.J. Gomez-Reino[5], K.S. Kanik[6], C. Wang[6], J. Wu[6], T. Hendrikx[7], W.C. Ports[6]. *[1]Department of Medicine, University of Queensland, St Lucia, Brisbane, Australia; [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom; [3]Metroplex Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX, United States; [4]Probity Medical Research and K Papp Clinical Research Inc, Waterloo, ON, Canada; [5]Fundacion Ramon Dominguez, Hospital Clinico Universitario, Santiago de Compostela, Spain; [6]Pfizer Inc, Groton, CT; [7]Pfizer Inc, Collegeville, PA, United States*

Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for treatment of psoriatic arthritis (PsA).

Objectives: To determine efficacy based on pooled data from 2 pivotal Phase 3 studies of tofacitinib in patients (pts) with active PsA.

Methods: Data were pooled from 2 placebo (PBO)-controlled, double-blind, multicentre, global Phase 3 studies (OPAL Broaden [N=422; 12 months; NCT01877668]; OPAL Beyond [N=394; 6 months; NCT01882439]). Pts had active PsA and either inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD) and were tumour necrosis factor inhibitor (TNFi)-naïve (OPAL Broaden), or had IR to ≥1 TNFi (OPAL Beyond). Pts were randomised to tofacitinib 5 mg twice daily (BID), 10 mg BID, adalimumab 40 mg subcutaneous injection once every 2 weeks (OPAL Broaden only) or PBO, in addition to a single, stable background csDMARD. PBO pts advanced to tofacitinib 5 mg or 10 mg BID at Month (M)3. Endpoints included ACR20/50/70 response rates (≥20%, ≥50% and ≥70% improvement), change from baseline (Δ) in HAQ-DI (Health Assessment Questionnaire-Disability Index), HAQ-DI response (decrease from baseline [BL] of ≥0.35), PASI75 (≥75% improvement from BL in Psoriasis Area and Severity Index), ΔLEI (Leeds Enthesitis Index) and enthesitis absence, ΔDSS (Dactylitis Severity Score) and dactylitis absence and ΔDLQI (Dermatology Life Quality Index). Pooled data only included tofacitinib 5 mg and 10 mg BID (to M6) and PBO (to M3). Significance was declared for $p \leq 0.05$ without correction for multiplicity.

Results: For pooled data, pts were predominantly white (94.2%) and female (55.4%) with ≥5 peripheral swollen or tender joints (98.0%), enthesitis (LEI>0; 67.5%), dactylitis (DSS>0; 52.5%), psoriatic body surface area ≥3% (67.7%) and CRP levels above the upper limit of normal (>2.87 mg/L; 62.5%) at BL. Mean age was 49.1 years and PsA duration was 8.0 years. Significant improvements vs PBO at M3 were observed for peripheral arthritis and physical function endpoints for tofacitinib 5 mg and 10 mg BID: ACR20, ACR50, ACR70, ΔHAQ-DI (least squares mean [LSM]), and HAQ-DI response (Table 1). Significant improvements in psoriasis, enthesitis and dactylitis endpoints vs PBO were also observed for tofacitinib 5 mg and 10 mg BID at M3: PASI75, ΔLEI, enthesitis absence based on LEI, ΔDSS (LSM), dactylitis absence based on DSS and ΔDLQI (Table 1). Efficacy was maintained or further improved at M6.

Table 1. Efficacy endpoints at Month 3 and Month 6; pooled data from OPAL Broaden and OPAL Beyond (Full Analysis Set[a])

	Month 3			Month 6[b]	
	Placebo (N=236)	Tofacitinib 5 mg BID (N=238)	Tofacitinib 10 mg BID (N=236)	Tofacitinib 5 mg BID (N=238)	Tofacitinib 10 mg BID (N=236)
ACR20,[c] n (%)	66 (28.0)	119 (50.0)***	125 (53.0)***	141 (59.2)	135 (57.2)
ACR50, n (%)	29 (12.3)	69 (29.0)***	79 (33.5)***	91 (38.2)	87 (36.9)
ACR70, n (%)	18 (7.6)	40 (16.8)*	34 (14.4)*	47 (19.8)	52 (22.0)
ΔHAQ-DI,[c] LSM (SE) [N1/N2]	-0.16 (0.03) [219/235]	-0.38 (0.03)*** [227/236]	-0.38 (0.03)*** [223/236]	-0.45 (0.03) [222/236]	-0.41 (0.04) [212/236]
HAQ-DI response,[d] n/N3 (%)	61/210 (29.1)	109/212*** (51.4)	101/215*** (47.0)	-	-
PASI75,[e] n/N3 (%)	24/168 (14.3)	52/162 (32.1)***	66/151 (43.7)***	65/162 (40.1)	79/151 (52.3)
ΔLEI,[f] LSM (SE) [N1/N2]	-0.5 (0.2) [145/156]	-1.2 (0.1)* [149/156]	-1.4 (0.2)*** [149/160]	-1.5 (0.2) [149/156]	-1.6 (0.2) [145/160]
Enthesitis absence rate (LEI),[f] n/N3 (%)	34/158 (21.5)	58/158* (36.7)	58/163* (35.6)	75/158 (47.5)	71/163 (43.6)
ΔDSS,[f] LSM (SE) [N1/N2]	-2.5 (0.7) [110/119]	-4.6 (0.6)* [122/125]	-5.8 (0.6)** [118/124]	-6.0 (0.7) [119/125]	-6.4 (0.7) [114/124]
Dactylitis absence rate (DSS),[f] n/N3 (%)	37/121 (30.6)	55/127* (43.3)	69/125*** (55.2)	71/127 (55.9)	76/125 (60.8)
ΔDLQI, LSM (SE) [N1/N2]	-2.1 (0.3) [219/233]	-4.1 (0.3)*** [226/234]	-5.5 (0.3)*** [222/234]	-4.4 (0.3) [222/234]	-5.7 (0.4) [211/234]

Nominal *p≤0.05; **p<0.001; ***p<0.0001 vs placebo at M3

[a]All randomised patients who received ≥1 dose of study medication; [b]p values not calculated at M6 as the placebo-controlled period ended at M3; [c]primary endpoint in each individual study at M3; [d]among patients with baseline HAQ-DI ≥0.35 (analysis at M6 not performed); [e]among patients with baseline BSA ≥3% and baseline PASI >0; [f]among patients with baseline score >0

Large sample approximation to the difference in binomial proportions was used to analyse ACR20/50/70, HAQ-DI response, enthesitis absence, dactylitis absence and PASI75; missing response considered as non-response. ΔHAQ-DI, ΔLEI, ΔDSS, and ΔDLQI were analysed with a mixed model for repeated measures without imputation for missing values

Δ, change from baseline; ACR20/50/70, American College of Rheumatology ≥20/50/70% improvement; BID twice daily; BSA, body surface area; DLQI, Dermatology Life Quality Index; DSS, Dactylitis Severity Score; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; LSM, least squares mean; M, Month; N, number of patients in the Full Analysis Set; n, number of patients with response; N1, number of patients evaluable at a visit; N2, number of patients included in the model; N3, number of patients evaluable at a visit (denominator); PASI, Psoriasis Area and Severity Index; PASI75, ≥75% improvement from baseline PASI; SE, standard error

Conclusions: In a pooled analysis of csDMARD-IR/TNFi-naïve and TNFi-IR pts, tofacitinib 5 mg and 10 mg BID were superior to PBO at M3 across four PsA disease domains: peripheral arthritis, psoriasis, enthesitis and dactylitis.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Haines of CMC and was funded by Pfizer Inc.

Disclosure of Interest: P. Nash Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer Inc, Roche, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Merck, Novartis, Pfizer Inc, Sanofi, Roche, UCB, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Novartis, Pfizer Inc, Roche, UCB, L. Coates Speakers bureau: Pfizer Inc, R. Fleischmann Grant/research support from: Abbott, Amgen, Astellas, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Genentech, Eli Lilly, Janssen, Novartis, Pfizer Inc, Regeneron, Sanofi Aventis, Roche, UCB, Consultant for: Abbott, Akros, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Eli Lilly, Janssen, Novartis, Pfizer Inc, Sanofi Aventis, UCB, K. Papp Grant/research support from: Abbott, Amgen, Anacor, Astellas, Celgene, Celtic, Dow Pharma, Eli Lilly, Galderma, Janssen, Janssen Biotech (Centocor), Merck, Novartis, Pfizer Inc, Consultant for: 3M, Abbott, Akros, Alza, Amgen, Astellas, Baxter, Boehringer Ingelheim, Celgene, Cipher, Eli Lilly, Forward Pharma, Funxional Therapeutics, Galderma, Genentech, Isotechnika, Janssen, Janssen Biotech (Centocor), J&J, Kirin, Kyowa, Meiji Seika Pharma, Merck, Mitsubishi Pharma, Mylan, Novartis, Pfizer Inc, Regeneron, Sanofi Aventis, Serono, Stiefel, Takeda, UCB, Speakers bureau: 3M, Abbott, Amgen, Astellas, Boehringer Ingelheim, Celgene, Eli Lilly, Galderma, Janssen, Merck, Novartis, Pfizer Inc, J. Gomez-Reino Grant/research support from: AbbVie, Novartis, Pfizer Inc, Roche, UCB, Consultant for: Pfizer Inc, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, MSD, Pfizer Inc, Roche, UCB, K. Kanik Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, C. Wang: None declared, J. Wu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Hendrikx Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, W. Ports Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.2444

SAT0470 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE PSORIATIC ARTHRITIS: 3-YEAR EFFICACY AND SAFETY RESULTS FROM PHASE 3 FUTURE 1 TRIAL

P.J. Mease[1], A. Kavanaugh[2], A. Reimold[3], H. Tahir[4], J. Rech[5], S. Hall[6], P. Geusens[7,8], P. Pascale[9], E.M. Delicha[9], L. Pricop[10], S. Mpofu[9] on behalf of the FUTURE 1 study group. *[1]Swedish Medical Centre and University of Washington, Seattle; [2]UC San Diego School of Medicine, la Jolla; [3]University of Texas Southwestern Medical Center, Dallas, United States; [4]Barts Health NHS Trust, London, United Kingdom; [5]University of Erlangen-Nuremberg, Erlangen, Germany; [6]Monash University, Melbourne, Australia; [7]University of Hasselt, Hasselt, Belgium; [8]Maastricht University Hospital, Maastricht, Netherlands; [9]Novartis Pharma AG, Basel, Switzerland; [10]Novartis Pharmaceuticals Corporation, East Hannover, United States*

Background: Secukinumab significantly improved the signs and symptoms of psoriatic arthritis (PsA) over 2 years (yrs) in the FUTURE 1 study.[1]

Objectives: To report efficacy and safety of secukinumab through 3 yrs in an extension of the FUTURE 1 study (NCT01892436).

Methods: After 2-yr core trial, patients (pts) receiving secukinumab 150/75mg s.c. entered the 3-yr extension phase. Efficacy results at Week (Wk) 156 are presented for those pts originally randomised to secukinumab (n=308) and included ACR20/50/70, PASI 75, DAS28-CRP, SF-36 PCS, HAQ-DI, dactylitis and enthesitis. Multiple imputation was used for analysis of binary variables while continuous variables are reported as observed. Analyses by anti-TNF status (naïve/inadequate response) were prespecified and reported as observed. Safety analysis included all pts (n=587) who received ≥1 dose of secukinumab.

Results: Overall, 457 of the original 606 pts entered the extension study of which 435 (95.2%) pts completed 156 wks (151 [93.8%] pts in IV→150 mg group; 142 [96.6%] in IV→75 mg group; 142 [95.3%] in PBO→ secukinumab groups). Sustained clinical improvements through Wk 156 were observed across all endpoints and were seen regardless of prior anti-TNF use (Table 1). Over

Abstract SAT0470 – Table 1. Summary of efficacy results at Week 156

Variables	Secukinumab IV→150 mg (n=161)	Secukinumab IV→75 mg (n=147)
ACR 20/50/70[a], % responders	77/55/33	65/39/26
PASI 75[a,b], % responders	76	59
DAS28-CRP[c], mean change (SD)	–1.9 (1.3)	–1.9 (1.5)
HAQ-DI[c], mean change (SD)	–0.43 (0.6)	–0.42 (0.6)
Resolution of dactylitis[a,d] (%)	88.1	86.8
Resolution of enthesitis[a,d] (%)	76.7	74.8

Analysis by anti-TNFα status[c]

	Anti-TNFα-naïve		Anti-TNFαIR	
	Secukinumab IV→150 mg (n=120)	Secukinumab IV→75 mg (n=110)	Secukinumab IV→150 mg (n=41)	Secukinumab IV→75 mg (n=37)
ACR20/50/70	81/63/39	67/43/28	62/36/18	56/28/19
PASI 75	76	60	75	56

[a]Multiple imputation (missing binary variables). [b]Analysis performed in pts with psoriasis ≥3% body surface area at time of randomisation (n=89 and n=82 in secukinumab IV→150 and IV→75 mg, respectively). [c]Observed data. [d]Data from the pts with these symptoms at BL (dactylitis, n=83 in secukinumab IV→150 mg and n=77 in secukinumab IV→75 mg and enthesitis, n=99 in secukinumab IV→150 mg and n=91 in secukinumab IV→75 mg). n, number of pts in the extension study.

the entire study period (mean [±SD] exposure to secukinumab of 1025.1±372.7 days), the exposure-adjusted incidence rate with secukinumab for serious infections/infestations, candida infections, Crohn's disease, and malignant/unspecified tumors was 1.7 (27), 1.2 (17), 0.1 (2), and 0.9 (14) per 100 pt-yrs, respectively.
Conclusions: Secukinumab provided sustained improvements in signs/symptoms and across multiple clinical domains of active PsA in pts who completed 3 yrs of therapy. Secukinumab was well tolerated with a favorable safety profile consistent with that previously reported.[1]
References:
[1] Kavanaugh A, et al. Arthritis Care Res. (Hoboken) 2016.
Disclosure of Interest: P. Mease Grant/research support from: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Consultant for: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, A. Kavanaugh Consultant for: Novartis, A. Reimold Grant/research support from: AbbVie, H. Tahir Speakers bureau: Novartis, Eli Lilly, and Abbvie, J. Rech Speakers bureau: Abbvie, BMS, Celgene, Fresenius, medicap, MSD, Novartis, Pfizer, and Roche, S. Hall: None declared, P. Geusens Grant/research support from: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Bio Minerals and Roche, Speakers bureau: Pfizer, Abbott, Lilly, Amgen, MSD, Will, Bio Minerals and Roche, P. Pascale Shareholder of: Novartis, Employee of: Novartis, E. M. Delicha Employee of: Novartis, L. Pricop Shareholder of: Novartis, Employee of: Novartis, S. Mpofu Shareholder of: Novartis, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1260

SAT0471 TRENDS IN CLINICAL CHARACTERISTICS ASSOCIATED WITH ACHIEVEMENT OF MINIMAL DISEASE ACTIVITY IN RESPONSE TO BIOLOGIC THERAPY IN PSORIATIC ARTHRITIS – ANALYSES FROM THE CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

P.J. Mease[1], C. Karki[2], M. Liu[2], A. Kavanaugh[3], C.T. Ritchlin[4], D.H. Hunyh[5], R. Pandurengan[2], J.B. Palmer[6], J.D. Greenberg[2,7]. *[1]Seattle Rheumatology Associates, Seattle, WA; [2]Corrona, LLC, Southborough, MA; [3]University of California San Diego, San Diego, CA; [4]University of Rochester, Rochester, NY; [5]Scripps Institute, la Jolla, CA; [6]Novartis, East Hanover, NJ; [7]New York University School of Medicine, New York, NY, United States*

Background: Achievement of minimal disease activity (MDA) may represent an objective target for treatment for patients with psoriatic arthritis (PsA).[1] A patient is considered to have achieved MDA when 5 of the following 7 criteria are met: tender joint count (TJC) ≤1, swollen joint count (SJC) ≤1, affected body surface area (BSA) ≤3%, patient pain VAS ≤15, patient global activity VAS ≤20, HAQ score ≤0.5 and tender entheseal points ≤1.[1]
Objectives: To retrospectively report the MDA and patient-reported outcomes (PROs) over time (baseline vs first follow-up [FU] visit vs second FU visit) that may contribute to achievement of MDA in responders versus non-responders to biologic treatment.
Methods: This analysis included all patients with PsA in the Corrona registry aged ≥18 years between March 2013 and March 2016 who received biologics (index biologics) at enrollment (baseline) and had ≥2 FU visits (at ≈ 6-month intervals, mean [SD] 2nd FU visit: 15.7 [3.7] months). Responders were defined as patients who achieved MDA at the second FU visit and remained on their index biologic. Demographics, clinical characteristics, PROs and treatment history were collected at enrollment and at both FU visits. Trend tests of MDA over time were performed using the Wilcoxon rank-sum nonparametric test for responders and non-responders separately.
Results: Of 148 patients who met the inclusion criteria (mean [SD] age, 54.7 [11.0] years; mean [SD] disease duration, 11.8 [10.1] years), 34 patients (23%) were classified as responders and 114 patients (77%) were non-responders at the second FU visit. The core components of MDA in these patients are shown in Table 1. Among responders, there were significant improvements in clinical characteristics and PROs such as mean TJC (3.4 vs 2.1 vs 0.6; P=0.004), SJC (2.5 vs 0.8 vs 0.5; P<0.0001), percentage of affected BSA (5.6% vs 2.4% vs 1.4%; P=0.03), patient pain (34.7 vs 26.1 vs 21.9; P=0.007) and HAQ scores (0.6 vs 0.4 vs 0.3; P=0.04); however, there were no significant changes over time for patient global assessment or enthesitis counts (P>0.05). Non-responders failed to have a significant improvement from baseline to the first and second FU visits in TJC, SJC, enthesitis, pain, patient global assessment and percentage of affected BSA (all P>0.05).
Conclusions: Only 23% of patients achieved MDA on their index biologic at the second FU visit and were considered responders. Over time, responders showed significant improvements in TJC and SJC, percentage of affected BSA, patient pain and HAQ scores; these most likely contributed to achievement of MDA response. A treat-to-target approach may be considered given the low number of patients in MDA.
References:
[1] Coates, LC et al. Ann Rheum Dis. 2010;69(1):48–53.
Acknowledgements: Corrona, LLC, has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly and Company, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.

Table 1. Clinical and patient-reported characteristics of patients with PsA in the Corrona registry stratified by response to index biologics over time

Characteristics*	At Enrollment		1st FU Visit		2nd FU Visit		*P* Value (R)	*P* Value (NR)
	R n = 34	NR n = 114	R n = 34	NR n = 114	R n = 34	NR n = 114		
MDA, n (%)†	0 (0)	0 (0)	17 (57)	13 (14)	34 (100)	10 (8.8)	< 0.0001	0.01
Tender joint count (0-68)	3.4 (5.3)	7.2 (11.0)	2.1 (5.1)	6.0 (8.2)	0.6 (1.4)	6.6 (11.7)	0.004	0.16
Swollen joint count (0-66)	2.5 (3.5)	2.8 (3.7)	0.8 (1.7)	2.5 (4.5)	0.5 (1.5)	2.3 (3.9)	< 0.0001	0.12
SPARCC enthesitis (0-16)	2.4 (0.5)	4.4 (3.3)	3.0 (2.8)	4.1 (3.3)	2.0 (1.4)	3.7 (1.9)	0.70	0.67
BSA, %	5.6 (8.1)	8.3 14.4)	2.4 (3.6)	5.1 (9.1)	1.4 (1.7)	4.8 (11.7)	0.03	0.006
Patient-reported pain (VAS 0-100)	35.7 (23.4)	51.2 (24.8)	26.1 (25.2)	54.6 (26.3)	21.9 (20.5)	54.6 (25.3)	0.007	0.28
Patient global assessment (VAS 0-100)	70 (17.8)	53.6 (24.0)	59.2 (30.2)	54.3 (24.5)	62 (31.4)	56.1 (22.5)	0.58	0.47
HAQ (0-3)	0.6 (0.5)	1.0 (0.6)	0.4 (0.5)	1.0 (0.6)	0.3 (0.4)	1.0 (0.6)	0.04	0.54

BSA, body surface area; FU, follow-up; HAQ, Health Assessment Questionnaire; MDA, minimal disease activity; NR, non-responders; R, responders; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale.
* All values are presented as "mean (SD)" unless otherwise stated.
† MDA was defined as "Yes" if a patient met ≥ 5 of the 7 following categories: tender joint count ≤ 1, swollen joint count ≤ 1, BSA ≤ 3%, patient pain VAS ≤ 15, patient global activity VAS ≤ 20, HAQ ≤ 0.5, tender entheseal points ≤ 1.

Disclosure of Interest: P. Mease Grant/research support from: Celgene, Novartis, AbbVie, Amgen, BMS, Lilly, Pfizer, UCB, Consultant for: Celgene, Corrona, Novartis, AbbVie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Merck, Pfizer, UCB, C. Karki Employee of: Corrona, LLC, M. Liu Employee of: Corrona, LLC, A. Kavanaugh Grant/research support from: Amgen, AbbVie, Janssen, Pfizer, Novartis, C. Ritchlin Grant/research support from: Amgen, Janssen, UCB, Consultant for: AbbVie, Amgen, Janssen, Regeneron, UCB, D. Hunyh Speakers bureau: AbbVie, BMS, R. Pandurengan Employee of: Corrona, LLC, J. Palmer Employee of: Novartis, J. Greenberg Shareholder of: Corrona, LLC, Consultant for: Lilly, Genentech, Janssen, Novartis, Pfizer, Employee of: Corrona, LLC
DOI: 10.1136/annrheumdis-2017-eular.1479

SAT0472 UTILIZATION OF THE PSORIASIS EPIDEMIOLOGY SCREENING TOOL TO IDENTIFY SIGNS AND SYMPTOMS OF EARLY PSORIATIC ARTHRITIS AMONG THOSE WITH PSORIASIS: ANALYSIS FROM THE CORRONA PSORIASIS REGISTRY

P.J. Mease[1], J.B. Palmer[2], M. Lebwohl[3], C. Karki[4], G.W. Reed[4,5], C.J. Etzel[4,6], J.D. Greenberg[4,7], P.S. Helliwell[8]. *[1]Swedish Medical Center and University of Washington, Seattle; [2]Novartis Pharmaceuticals Corporation, East Hanover; [3]Icahn School of Medicine at Mount Sinai, New York; [4]Corrona, LLC, Southborough; [5]University of Massachusetts Medical School, Worcester; [6]The University of Texas MD Anderson Cancer Center, Houston; [7]New York University School of Medicine, New York, United States; [8]University of Leeds, Leeds, United Kingdom*

Background: The Psoriasis Epidemiology Screening Tool (PEST) is a 5-item questionnaire developed to help identify psoriatic arthritis (PsA) at an early stage, with a score ≥3 indicative of PsA.[1] A recent Korean study found that a PEST score of 2 may be a more favorable cutoff for screening patients with psoriasis (PsO).[2]
Objectives: To assess the risk of undiagnosed PsA among patients with PsO and characterize patients based on PEST scores in a US cohort.
Methods: This study included all patients enrolled in the Corrona PsO Registry with data on all 5 PEST questions. Demographics, disease characteristics, patient-reported outcomes (PROs) and medication use were analyzed at the time of enrollment and stratified by PEST score (0, 1, 2 or ≥3). Pairwise comparisons were made between PEST score =0 (reference) and other PEST score groups using t-tests for continuous variables and χ^2 tests for categorical variables.
Results: As of June 2016, 99.1% (1516/1529) of patients in the Corrona PsO Registry had data on all 5 PEST questions; 612 patients (40.4%) had dermatologist-reported PsA at enrollment. Among the remaining 904 patients, 421 patients (46.6%) had a PEST score =0, 225 (24.9%) had a PEST score =1, 146 (16.2%) had a PEST score =2 and 112 (12.4%) had a PEST score ≥3. Of patients with a PEST score ≥3, patients most commonly answered "yes" to "have you ever had a swollen joint (or joints)?" (89%) and "has a doctor ever told you that you have arthritis?" (86%). Compared with patients with a PEST score =0, patients with a PEST score ≥1 all had a higher BMI, longer duration of PsO, increased family history of PsA, increased prevalence of nail PsO and worse EQ-VAS at enrollment (all P<0.05; Table 1). In addition, patients with PEST scores ≥2 were older, more likely to be female, less likely to be employed and had an increased family history of PsO, worse pain and fatigue, worse dermatology-related quality of life and higher percentage impairment of daily activities due to psoriasis at enrollment vs patients with a PEST score =0 (all P<0.05). There were no significant differences across PEST scores in affected body surface area or PASI scores.
Conclusions: In this cohort of PsO patients with no diagnosis of PsA, patients with PEST scores ≥2 were significantly different from those with PEST scores =0

Table 1. Baseline characteristics of patients with PsO and no diagnosis of PsA stratified by PEST score (0-5)

Characteristic*	PEST Score = 0 n = 421	PEST Score = 1 n = 225	PEST Score = 2 n = 146	PEST Score ≥ 3 n = 112
Age, years	48.0 (15.5)	48.5 (14.9)	53.7 (13.8)†	52.9 (14.4)†
Female, n (%)	164 (39.0)	103 (45.8)	72 (49.3)†	62 (55.4)†
Currently employed, n (%)	311 (74.0)	169 (75.1)	81 (55.9)†	60 (53.6)†
BMI, kg/m^2	28.8 (6.9)	29.7 (6.8)†	31.4 (7.0)†	32.2 (8.0)†
Categorical BMI (in kg/m^2), n (%)				
Normal/underweight (< 25.0)	133 (31.8)	63 (28.1)	22 (15.2)‡	22 (19.8)‡
Overweight (25.0 to < 30.0)	145 (34.7)	73 (32.6)	50 (34.5)‡	26 (23.4)‡
Obese (≥ 30.0)	140 (33.5)	88 (39.3)	73 (50.3)‡	63 (56.8)‡
Family history of PsO, n (%)	13 (3.1)	12 (5.4)	11 (7.5)†	14 (12.6)†
Family history of PsA, n (%)§	126 (30.1)	85 (38.1)†	67 (45.9)†	46 (41.4)†
Duration of PsO, years	12.8 (12.0)	15.3 (13.2)†	19.1 (15.6)†	17.3 (14.8)†
Nail PsO, n (%)	30 (7.1)	35 (15.6)†	21 (14.4)†	24 (21.4)†
BSA, % involvement	8.8 (12.2)	9.0 (12.0)	9.3 (13.9)	10.2 (13.3)
PASI (0-72)	5.5 (6.0)	6.1 (6.9)	6.2 (7.1)	6.3 (6.5)
Pain (VAS 0-100)	20.1 (28.3)	21.5 (29.1)	24.2 (29.2)†	28.3 (30.6)†
Fatigue (VAS 0-100)	24.2 (27.0)	23.0 (25.1)	30.4 (28.1)†	41.7 (27.8)†
EQ-VAS (VAS 0-100)	78.7 (19.6)	73.9 (22.9)†	73.8 (22.4)†	67.0 (22.9)†
DLQI (0-30)	5.8 (6.0)	6.6 (6.1)	6.9 (5.3)†	8.1 (6.5)†
WPAI-GH domain: % of daily activities impaired by PsO	14.2 (23.3)	14.8 (23.4)	17.6 (24.9)†	24.0 (28.6)†

BMI, body mass index; BSA, body surface area; DLQI, Dermatology Life Quality Index; EQ-VAS, EuroQol overall health status using the visual analog scale; PASI, Psoriasis Area and Severity Index; PEST, Psoriasis Epidemiology Screening Tool; PsA, psoriatic arthritis; PsO, psoriasis; VAS, visual analog scale; WPAI-GH, Work Productivity and Activity Impairment questionnaire: general health.
* All values are presented as "mean (SD)" unless otherwise indicated.
† $P < 0.05$ versus PEST score = 0.
‡ $P < 0.05$ for overall distribution of patients across BMI categories versus PEST score = 0.
§ Family history, but patient had no current diagnosis.

for many characteristics at enrollment, including BMI and PROs. These findings highlight the value of screening for PsA among patients with PsO in order to potentially improve patient outcomes.

References:

[1]) Ibrahim GH, et al. Clin Exp Rheumatol. 2009;27(3):469–74.
[2]) Ha YJ, et al. Arthritis Rheumatol. 2016;68(suppl 10):A2744.

Acknowledgements: The Corrona Psoriasis Registry is sponsored by Corrona, LLC and is funded by AbbVie, Boehringer Ingelheim, Eli Lilly and Company and Novartis Pharmaceuticals Corporation. Corrona, LLC has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, AstraZeneca, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.

Disclosure of Interest: P. Mease Grant/research support from: Celgene, Novartis, AbbVie, Amgen, BMS, Lilly, Pfizer and UCB, Consultant for: Celgene, Corrona, Novartis, AbbVie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Merck, Pfizer and UCB, Speakers bureau: AbbVie, Amgen, BMS, Crescendo, Celgene, Genentech, Janssen, Pfizer and UCB, J. Palmer Employee of: Novartis, M. Lebwohl Employee of: Mount Sinai, which received research funds from Amgen, Anacor, Boehringer Ingelheim, Celgene, Lilly, Janssen Biotech, Kadmon, LEO Pharmaceuticals, MedImmune, Novartis, Pfizer, Sun Pharmaceuticals and Valeant, C. Karki Employee of: Corrona, LLC, G. Reed Shareholder of: Corrona, LLC, Employee of: Corrona, LLC, C. Etzel Consultant for: Merck, Employee of: Corrona, LLC, J. Greenberg Shareholder of: Corrona, LLC, Consultant for: Eli Lilly, Genentech, Janssen, Novartis and Pfizer, Employee of: Corrona, LLC, P. Helliwell Consultant for: Amgen, BMS, Janssen, Lilly, Pfizer and UCB, Speakers bureau: Novartis, AbbVie, Janssen, Lilly, Pfizer and UCB

DOI: 10.1136/annrheumdis-2017-eular.1478

SAT0473 PREVALENCE OF ULTRASOUND ABNORMALITIES IN PATIENTS WITH PSORIATIC ARTHRITIS IN A CLINICAL PHASE OF MINIMAL DISEASE ACTIVITY UNDER ANTI-TNF TREATMENT

P. Macchioni[1], G. Ciancio[2], G. Sandri[3], A. Zabotti[4], G. Vukatana[5], L. Montaguti[6], M. Focherini[7], E. Verduci[1], D. Chessa[8], M. Govoni[2], A. Spinella[3], N. Malavolta[5], F. Zuliani[4], M. Bruschi[6], F. Mascella[7].
[1]Rheumatology, Arcispedale S Maria Nuova, Reggio Emilia; [2]Rheumatology, University of Ferrara and Azienda Ospedaliera-Universitaria Sant'Anna, Ferrara; [3]Rheumatology, University of Modena e Reggio Emilia, Modena; [4]Rheumatology Clinic, University of Udine, Udine; [5]Rheumatology, University of Bologna, Bologna; [6]Rheumatology, Ospedale Bufalini, Cesena; [7]Medicina Interna e Reumatologia, Ospedale degli Infermi, Rimini; [8]Internal Medicine, Ospedale Paolo Dettori, Tempio Pausania (OT), Italy

Background: Few studies have analized the persistence of ultrasound (US) abnormalities in patients (pts) with Psoriatic Artritis (PA) during the phase of minimal disease activity (MDA)

Objectives: To investigate the prevalence of US alterations at enthesis, joint and tendon levels in pts with psoriatic arthritis (PA) during a phase of MDA.

Methods: Pts treated with anti-tumor necrosis factor (TNF) for at least 12 months and with at least 6 months duration of MDA were consecutively recruited at 6 Italian centers. In every center, the local rheumatologists provided PA pts to be examined by US. Personal history, demographic and clinical data were recorded. Each patient underwent the following US examinations: metacarpophalangeal (MCP), knee and tibio-tarsal (TT) joint, flexor and extensor tendon of hand digit, flexor and extensor tendon at carpal area, flexor and extensor tendon of foot, and enthesis of common extensor tendon insertion on the lateral epicondyle of the humerus, quadriceps tendon, patellar tendon, Achilles tendon and plantar fascia insertions on the calcaneus. Each examination were performed by rheumatologists expert in US, to assess synovitis (joint effusion, synovial proliferation, and power Doppler (PD) signal), and bone erosions, flexor tendon tenosynovitis, hand finger extensor tendon tenonitis, and enthesel involvement using an Esaote MyLabClass with a 5–13 or 6–18 MHz linear probe. The following elementary lesions were assessed at each enthesis: morphologic abnormalities (hypoechogenicity and/or thickening), entheseal calcific deposits, cortical abnormalities (bone erosion and/or proliferation), adjacent bursitis and intraenthesis and perienthesis (tendon body and/or bursa) PD signal. All US findings were scored using a 4 degree semiquantitative scoring system. US acute enthesitis was defined by the presence of entheseal edema or PD signal. US chronic entheseal alterations by the presence of calcifications, erosions, or enthesophytes. US peripheral active synovitis if synovial hypertrophy was associated with the presence of PD signal. US examinator were blind of clinical data of the pts.

Results: Sixty-three pts were recruited (mean age 53±13y, mean PA duration 13±8y, mean MDA duration 21±11m). At US examination 66.7% of pts had at least one peripheral joint involved (17.5% had peripheral active synovitis), 47.6% had acute enthesitis and 95.2% chronic enthesopathy. US bursitis was present in 22.2% of pts, 3.7% had hand extensor finger tendon involvement.

Table 1 shows clinical and demographical data of the pts and table 2 the US results

	Nail involvement	Previous dactylitis	FamHyst	IBP
Patients with abnormality (%)	28.3	42.9	23.9	19.7

Table 2. US abnormalities in 63 pts in MDA

	Perypheral active sinovitis	Joint peripheral involvement	Chronic entheseal alterations	Acute entheseal alterations	Tenosynovitis
Patients with abnormality (%)	17.5	66.7	95.2	47.6	29.6

Conclusions: Joint, entheseal and tendon abnormalities have a high prevalence in PA patients treated with anti-TNF during MDA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5010

SAT0474 VERY LOW DISEASE ACTIVITY AND IMPACT OF DISEASE IN A SPANISH POPULATION WITH PSORIATIC ARTHRITIS

R. Queiro, J.D. Cañete, C. Montilla, M.A. Abad, S. Gómez, A. Cábez.
Rheumatology, Hospital Universitario Central de Asturias, Oviedo, Spain

Background: The target of treatment in psoriatic arthritis (PsA) should be remission or inactive disease. A potential definition that would fit with the Treat-to-Target Recommendations would be MDA meeting all 7 criteria[1], proposed as a definition of very low disease activity (VLDA) in PsA. Patient reported outcomes (PROs), such as those provided by the novel PsAID questionnaire [2], are also important to evaluate healthcare interventions and to reflect the impact of PsA on patients' lives.

Objectives: The aims of the present study were to evaluate the prevalence of VLDA in patients with PsA and how much residual active disease is still present, so as to determine whether PsAID could be an additional useful tool to assess PsA interventions in clinical practice.

Methods: This was a post-hoc analysis of data from a cross-sectional observational and multicenter study (MAAPS), aimed at evaluating the prevalence of MDA in a Spanish population with PsA, to describe their characteristics and to evaluate the association between MDA and the impact of the disease as assessed by the PsAID questionnaire in routine clinical practice The original study included adult patients of both genders diagnosed with PsA according to CASPAR criteria with at least one year of evolution time of disease and on treatment with biological and/or conventional synthetic disease modifying anti-rheumatic drugs (cDMARD). Patients were considered in VLDA when they met all the MDA criteria[1]: tender joint count $\leq$1, swollen joint count $\leq$1, Psoriasis Area Severity index (PASI) score $\leq$1 or body surface area $\leq$3%, patient pain visual analog scale (VAS) score $\leq$15, patient global disease activity VAS score $\leq$20, Health Assessment Questionnaire (HAQ) score $\leq$0.5, and tender entheseal points $\leq$1. Patient acceptable symptoms state (PASS) has been defined as a PsAID value $<$4.

Results: 227 patients were included, 133 (58.6%) in MDA state and 58 (25.6%) in VLDA state. VLDA patients suffered from a mild impact of the disease according to PsAID: the majority (82.5%) had a PsAID score $<$4 and a mean total score (SD) of 2.1 (2.6) IC95% [1.55–2.64], while, 66.7% of MDA patients had a PsAID score $<$4 and a mean total score (SD) of 3.3 (3.1) IC95% [2.82–3.87]. Disability, as measured by HAQ was greater in MDA patients (mean (SD) 0.3 (0.5) IC95% [0.21–0.43]) than in those who reached VLDA state (mean (SD) 0.2 (0.3) IC95% [0.11–0.25].

Conclusions: 26% of Spanish PsA patients achieve VLDA state in routine clinical practice. PsA patients who reached this state also had a very low impact of disease according to PsAID. VLDA state could represent a situation of clinical remission in PsA.

References:

[1] Coates LC, Fransen J, Helliwell PS. Ann Rheum Dis 2010;69(1):48–53.
[2] Gossec L, de WM, Kiltz U, Braun J, Kalyoncu U, Scrivo R et al. Ann Rheum Dis 2014;73(6):1012–1019.

Acknowledgements: MAAPS (Minimal Activity in Psoriatic Arthritis) study group:. J.C. Torre Alonso; J.A Román Ivorra; J. Sanz; J. Salvatierra; J. Calvo Alén;

A. Sellas; F.J. Rodriguez; A. Bermúdez; M.Romero; M. Riesco; J.C Cobeta; F.Medina; A. Aragón; ML. García; A. Urruticoechea; CM. González; E. Judez; B. González; P. Fernández; L. Pantoja; R. Morlá.
This study was funded by Pfizer.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3780

SAT0475 RECENT ONSET PSORIATIC ARTHRITIS: BASELINE DATA FROM THE REAPSER STUDY

R. Queiro, A. Laiz Alonso, H.S. Park, C. Montilla Morales, E. Galíndez Agirregoikoa, J.J. Bethencourt Baute, S. Bustabad Reyes, P. Tejón Menéndez, M.Á. Belmonte, J.A. Pinto Tasende, E.A. Blanco Morales, J. Ramír.
Rheumatology, Hospital Universitario Central de Asturias (Coordinating Center), Oviedo, Spain

Background: The natural history of psoriatic arthritis (PsA) is very little known and the information regarding prospective cohorts is very scarce worldwide, including our country. REAPSER (Spanish Rheumatology Society Registry of Psoriatic Arthritis) is the first registry of Spanish patients with recent onset PsA.
Objectives: To describe the baseline characteristics of patients included in the REAPSER cohort.
Methods: Observational, multicentric study (34 centers), with consecutive inclusion. We included adults of both sexes 18 years of age or older with PsA that met CASPAR criteria, and duration of less than two years since the appearance of symptoms attributed to PsA. Annual follow-up visits will be carried out for 5 years. Measurements: socio-demographic data; employment status and impact of the disease; family history of PsA and other inflammatory diseases; comorbidities and treatment; lifestyle; use of health services; clinical status at the time of diagnosis of PsA; anthropometric data; clinical evaluation of PsA manifestations; radiographic evaluation; analytical determinations; treatment of PsA. The study has been approved by the ethical committees of the participating centers.
Results: Two hundred and fifteen consecutive patients were included, mean age 49.8±13.9 years.

Baseline characteristics of the cohort

Parameter	N: 215
Men	67.4%
Women	32.6%
Active worker	59.5%
Unemployed	12.1%
Retired/pensioner	17.7%
Job change last year	4.7%
University studies	20%
Smoking	30.2%
BMI	27.7±5.2
Weekly alcohol consumption	0 SDU (0–4)
Family history of psoriasis	41.4%
Family history of PsA	9.3%
Family history of other arthritis	6.5%
Charlson's Comorbidity Index	0: 46.5%. 1–2: 35.3%. 3–4: 14.4%. >4: 3.8%
Psoriasis at baseline	88%
PASI	1.5 (0.6–4.3)
Joint pattern	Peripheral: 81.5%. Axial: 5.2%. Mixed: 13.3%
TJC68	4 (2–8)
SJC66	2 (1–4)
BASDAI	3.9 (3–4.4)
Dactylitis	41.9%
Enthesitis	25%
Uveitis	0.5%
Pain	5 (3–7)
Patient's global disease activity	5 (3–7)
PsAID	3.8 (1.8–6)
Steinbrocker Index (0–168)	0 (0–4)
Cardiovascular events	5.7%
HLA-B27	12.3%
ESR	13 (6–25)
NSAIDs	75%
GC	28.3%
Synthetic DMARDs	53.2%
Biological DMARDS	1.5%

Values are expressed as percentages, means with standard deviation and medians with their IQR (interquartile range). SDU: Standard Drink Units. PsAID: Psoriatic Arthritis Impact of Disease.
Conclusions: The baseline situation of Spanish patients with newly diagnosed PsA corresponds to that of a disease with slight cutaneous involvement and predominance of oligoarticular arthritis. Unsurprisingly, structural damage is scarce but not zero. The impact of the disease is still low in these early stages, however 18% of patients have a high Charlson's comorbidity index (>3) and almost 5% of patients have had to change their employment status in the last year due to its PsA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4268

SAT0476 DEMOGRAPHIC, CLINICAL, AND LABORATORY CHARACTERISTICS OF ELDERLY ONSET PSORIATIC ARTHRITIS

S. Kobak[1], M. Orman[2]. *[1]Rheumatology, Istinye University Faculty of Medicine, LIV Hospital, Istanbul; [2]Statistics, Ege University Faculty of Medicine, Izmir, Turkey*

Background: Psoriatic arthritis (PsA) is a chronic inflamatory disease characterized with axial and peripheral joints involvement. It is rarely affects patients older than 65 years old.
Objectives: The purpose of this study is to compare and evaluate the demographic, clinical and laboratory features of elderly-onset psoriatic arthritis (EOPsA) and young-onset (YOPsA) patients.
Methods: One hundred and eighty patients diagnosed with PsA according to CASPAR criteria and followed-up in single center were included in this study. The patients with initial symptoms started after age 65 were accepted as EOPsA. Demographic, clinical, and laboratory data and the medications which the patients recieved were recorded and retrospectively evaluated.
Results: Nineteen (10.5%)of 180 patients were diagnosed as EOPsA, and 161 (89.5%) patients were evaluated as YOPsA. Mean patient age was 42.1years for YOPsA group and 68.3years for elderly onset group. Mean duration of disease was 5.6 years for early onset group and 1.3 years for elderly onset group (p=0.001). Fourteen (73.3%) of 19 EOPsA patients were female and 5 of them were male. Higher rates of fatique, pain scores, comorbid diseases and acute phase reactants were detected in EOPsA patients comparing to YOPsA (p=0.000, p=0.000, p=0.001 and p=0.001 respectively). YOPsA patients have more dactilitis, nail involvement, elevated PASI scores, and smoking habitus when compared with EOPsA patients (p=0.019, p=0.03, p=0.005, p=0.004 respectively). In terms of the treatment options chosen, there was no significant difference in the use of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids (CS), methotrexate (MTX), and sulfasalazine (SSL), but there was a more frequent use of anti-tumor necrosis factor -alpha in YOPsA group.
Conclusions: Herein we showed that YOPsA and EOPsA patients may have different demographic, clinical, and laboratory features. EOPsA patients are characterized with higher rates of fatique, pain scores, comorbid diseases, and acute phase reactants and less dactilitis, nail involvement and anti-TNF-alpha usage.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1378

SAT0477 THE COMPARISON OF ULTRASOUND SYNOVITIS AND ENTHESITIS FINDINGS AND CLINICAL FINDINGS IN PATIENTS WITH PSORIATIC ARTHRITIS AND SKIN PSORIASIS

T. Okano[1], K. Inui[1], Y. Sugioka[2], K. Mamoto[1], H. Yoshimura[1], T. Koike[2,3], H. Nakamura[1]. *[1]Department of Orhopedic surgery; [2]Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, Osaka; [3]Search Institute for Bone and Arthritis Disease (SINBAD), Shirahama Foundation for Health and Welfare, Wakayama, Japan*

Background: Conventionally, the assessment of affected joint count in patients with psoriatic arthritis (PsA) was relied for the detection of swelling and tenderness in the joints and enthesis by clinical physical assessment. To date, the modern imaging tool such as ultrasound (US) can detect inflammation in the joint and enthesis more sensitively than clinical assessment.
Objectives: The aim of this study was to research the prevalence of US syovitis and enthesitis findings in patients with PsA and psoriasis (PsO) comparing with clinical assessment.
Methods: Total 100 patients, 54 patients with PsA and 46 patients with PsO, were consecutively included. HI VISION Ascendus (HitachiAloka Medical, Tokyo, Japan) was used with a 18-MHz linear array transducer. US examination was performed in MCP, PIP, DIP and wrist joints in both hand. Grayscale (GS) and power Doppler (PD) US were scored on a 0–3 semiquantitative scale for each joint. Moreover, the US assessment of enthesis was performed. Lateral epicondyle, triceps enthesis, the proximal and distal patella tendon enthesis, Achilles tendon and fascia plantaris tendon enthesis was scanned in both GS and PD assessment. Abnormal findings of enthesis was defined structure thickness, bursitis erosion, calcification and power Doppler signal.
Results: US synovitis was found in 81.5% (n=44) and 60.9% (n=28) by GS, 66.7% (n=36) and 45.7% (n=21) by PD assessment, respectively in patients with PsA and PsO. Active synovitis (GS grade ≧ 2 and/or PD grade ≧ 1) was found

	PsA (n=54)	PsO (n=46)	P value
Male (%)	26 (48.1%)	26 (56.5%)	0.429
Age (years)	55.4±15.0	57.5±15.3	0.508
Height (cm)	161.6±9.8	161.6±9.5	0.969
Weight (kg)	62.7±15.5	63.1±13.9	0.905
BMI	23.8±3.9	24.0±3.6	0.883
Duration of psoriasis (years)	15.6±13.6	17.5±19.7	0.584
PASI	11.7±13.4	8.9±7.5	0.432
PASE	45.8±14.6	29.8±11.9	<0.001
Active US synovitis (GS≥2, PD≥1)	37 (68.5%)	21 (45.7%)	0.026
US enthesitis (any pathological findings)	47 (87.0%)	26 (56.5%)	<0.001

68.5% (n=37) in PsA and 45.7% (n=21) in PsO. US synovitis was more frequently found than clinical assessment. The most common sites of inflammatory synovitis were the wrist. US enthesopathy was found in 87.0% (n=47) in patients with PsA 56.5% (n=26) in patients with PsO. US enthesitis was also more frequently found than clinical assessment. The most common sites of enthesopathy were the enthesis in lateral epicondyle, quadriceps and Achilles tendon.

Conclusions: Our results showed that US was able to detect a high prevalence of inflammatory synovitis in peripheral joints and enthesis in patients with PsA. Moreover, subclinical inflammatory findings were also found in patients with PsO by US. US examination is useful to detect the inflammatory condition in patients with PsA and PsO than clinical examination.

Acknowledgements: We wish to thank Setsuko Takeda, Ayumi Hashimoto and Emi Yamashita for their special efforts as a sonographer and collecting data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5028

SAT0478 RAPID3 QUESTIONNAIRE HAS HIGH DISCRIMINATING ABILITY IN MINIMAL DISEASE ACTIVITY ATTAINMENT IN PATIENTS WITH EARLY PSORIATIC ARTHRITIS TREATED ACCORDING TO TIGHT CONTROL STRATEGY IN DAILY CLINICAL PRACTICE (RESULTS OF ONE-YEAR OPEN-LABEL REMARCA STUDY)

T. Korotaeva, E. Loginova, A. Koltakova, L. Denisov, M. Chamurlieva, D. Karateev, E. Nasonov. *V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: RAPID3 is an instrument based on patient's report outcomes (PROs) for the assessment of remission and disease activity in rheumatoid arthritis. The advantages of this questionnaire in treat-to-target (T2T) strategy in early psoriatic arthritis (EPsA) have not been studied properly.

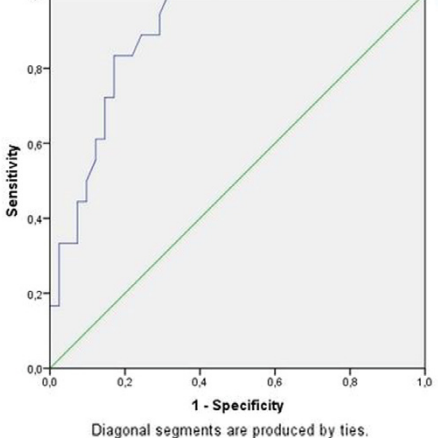
Objectives: to study discriminating ability of RAPID3 in minimal disease activity (MDA) attainment in patients with EPsA treated during one year according to tight control strategy.

Methods: 61 (M/F–29/32) patients (pts) with active EPsA, according to CASPAR criteria, mean age 37±10.6 years, PsA duration 11.3±10.2 months, psoriasis duration 75.4±80.9 months were included. All pts signed a consent form for participation in the open-label REMARCA study. At baseline and after 1year (yr.) of therapy all pts underwent evaluation of PsA activity by Tender Joint count (TJC78), Swollen Joint Count (SJC76), physician's global disease activity (PhGA) VAS, DAS, CRP (mg/l) and by PROs - patient pain global assessment VAS, Patient global disease activity (PGA) VAS, Health Assessment Questionnaire (HAQ) and RAPID3. The dose of Methotrexate (MTX) subcutaneous (s/c) was escalated by 5 mg every 2 weeks from 10 mg/wk up to 20–25 mg/wk. If pts did not achieve MDA after 3–6 months of MTX mono-therapy, combination therapy (CoT) of MTX+Adalimumab (ADA) was started in a standard regime; CoT was continued up to 1 yr. The proportion of pts who achieved MDA was calculated. M±SD, Me [Q25;Q75], %, Spearman rank correlation R, W-test, U-test, ROC-curve analysis were performed. All $p<0.05$ were considered to indicate statistical significance.

Results: By 1 yr. of therapy 36 out of 61 pts (59%) and 25 out of 61 pts (41%) were treated with MTX and with MTX+ADA accordingly. Significant improvements in PsA activity and PROs from baseline up to 1 yr. were observed: DAS 3.93 [3.20–4.58]/1.36 [0.82–2.25], SJC 7 [5–11]/1 [0–3], TJC 8 [6–1]/1 [0–3], PhGA 56 [48–69]/10 [5–20] and VAS pain 54 [48–68]/11 [1–20], PGA 55 [49–68]/14 [7–24], HAQ 0.75 [0.50–1]/0 [0–0.63] accordingly (for all W-test $p<0.001$). Significant positive correlations between RAPID3 and PsA activity, PROs and CRP are shown in table 1 (for all R $p<0.001$).

MDA was seen in 43 out of 61% pts (70.5%). At the same time RAPID3 and CRP significantly decreased from 12.7 [9.2–16.8] to 4.3 [2.0–7.8] and from 16.6 [8.6–34.6] to 2.1 [0.9–6.7] mg/l accordingly (for all W-test, $p<0.001$). Among those who have achieved MDA RAPID3 was in "near remission" status and significantly less compared to pts that did not achieve MDA-2.5 [1.3–5.3] and 8.1 [6.0–15.1] accordingly (U-test, $p<0.001$). According to the results of ROC-curve analysis RAPID3 score had a high discriminating ability for the presence of MDA - AUC 0.888 [0.808–0.969] (Fig. 1).

ROC-curve analysis: association of RAPID-3 values and presence of MDA



Diagonal segments are produced by ties.

Parameters	R
DAS	0.74
TJC78	0.68
SJC76	0.63
PGA VAS	0.82
Pain VAS	0.83
PtGA VAS	0.81
CRP	0.69

Conclusions: RAPID3 based on PROs is a simple instrument for evaluating PsA activity. RAPID3 has shown high discriminating ability in MDA attainment in EPsA pts treated according to tight-control strategy, and could be useful in daily clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3010

SAT0479 INCREASED CAROTID INTIMA-MEDIA THICKNESS CAN DISCRIMINATE SIGNIFICANT CORONARY ARTERY STENOSIS BY CORONARY CT ANGIOGRAM IN PATIENTS WITH PSORIATIC ARTHRITIS

T.H. Cheng[1], Q. Shang[1], E.K.M. Li[1], K.T. Wong[2], A.P.W. Lee[1], C.C. Szeto[1], L.S. Tam[1]. *[1]Department of Medicine and Therapeutics, the Chinese University of Hong Kong; [2]Department of Diagnostic and Interventional Radiology, The Prince of Wales Hospital, Hong Kong, Hong Kong*

Background: PsA patients have increased morbidity & mortality due to cardiovascular disease (CVD). However, their CV risk were underestimated by various CV risk score[1]. Subclinical carotid atherosclerosis may be considered as surrogate marker of coronary artery disease (CAD) in the general population[2]while it remained uncertain for PsA patients

Objectives: To assess the relationship between carotid artery disease by ultrasound (US) and CAD by coronary computed tomography angiography (CCTA) and identify US parameters predictive of significant CAD

Methods: 91subjects (56 males; age: 50±11 years; disease duration 9.4±9.2 years) without overt CVD who underwent CCTA & carotid US (interval between two exams:2 [1–7] months) were recruited. Carotid intima-media thickness (cIMT)& the presence of plaque were determined by high resolution US in the distal CCA, bulb & proximal ICA bilaterally. Significant coronary artery stenosis was defined as stenosis of the lumen >50%

Results: Carotid plaque was present in 33 (36%) patients & coronary plaque was present in 55 (60%) patients while 9 (10%) patients had significant coronary artery stenosis. 36 (40%) patients had non-zero calcium score (CAC+ group).The mean cIMT was significantly higher in CAC+ group compared to CAC=0 group [0.70±0.11mm vs0.64±0.11mm, p=0.031]. There was a trend suggesting the mean cIMT increases with increasing CAC score, while the prevalence of carotid plaque increased significantly with rising calcium score (Table1). The mean cIMT increased significantly with number of coronary vessels habouring plaque, while there was a trend suggesting the max cIMT and the prevalence of carotid plaque may increase in patients with rising number of coronary vessels harboring plaques The mean & max cIMT were significantly higher in SS+ group than SS- group [mean cIMT: 0.76±0.07mm vs0.65±0.12mm, p=0.011; max cIMT: 0.93±0.14mm vs 0.80±0.16mm, p=0.020] (Table1). The prevalence of carotid plaque was similar between SS+ & SS- group [29 (35.4%) vs 4 (44.4%), p=0.421]. Using multivariate logistic regression, mean & max cIMT were independent explanatory variable of significant coronary stenosis after adjusting age, gender, disease duration & damaged joint count. The OR of significant coronary stenosis of every 0.01mm increase in mean & max cIMT were 1.07 (95% CI: 1.00–1.15, p=0.042) and 1.06 (95% CI: 1.00–1.11,p=0.036). Mean cIMT of 0.66mm was the optimal cut off

	Coronary Artery Calcium (Agatston Score)						
	Normal (CAC=0) (n=55)		Minimal-mild (1-399) (n=25)		Severe (400+) (n=11)		p
Mean carotid IMT, mm	0.64 ± 0.11		0.70 ± 0.13		0.70 ± 0.07		0.099
Maximum carotid IMT, mm	0.79 ± 0.16		0.84 ± 0.16		0.86 ± 0.15		0.223
Carotid Plaque, n, %	16	29.1%	10	40.0%	7	63.6%	0.031
	Number of coronary artery with any plaques						
	0 (n=36)		1-2 (n=43)		3 (n=12)		p
Mean carotid IMT, mm	0.63 ± 0.12		0.68 ± 0.11		0.69 ± 0.08		0.029
Maximum carotid IMT, mm	0.77 ± 0.17		0.83 ± 0.17		0.83 ± 0.15		0.065
Carotid Plaque, n, %	10	27.8%	16	37.2%	6	58.3%	0.068
	Significant coronary artery stenosis						
	No (n=82)				Yes (n=9)		p
Mean carotid IMT, mm	0.65 ± 0.12				0.76 ± 0.07		0.011
Maximum carotid IMT, mm	0.80 ± 0.16				0.93 ± 0.14		0.020
Carotid Plaque, n, %	29	35.4%			4	44.4%	0.421

Table 1. Relationship between carotid artery disease by ultrasound and coronary artery disease by coronary computed tomography angiography.

for discriminating patients with significant coronary stenosis (sensitivity: 100%; specificity: 44%). ROC analyses demonstrated that mean cIMT (AUC=0.801, p=0.003)has higher power than Framingham CVD risk score (FRS) (AUC=0.756, p=0.012)

Conclusions: Increased cIMT is associated with the presence & severity of coronary calcification & obstructive coronary disease on CCTA in PsA patients. cIMT measurement can discriminate PsA patient with significant coronary stenosis better than FRS. PsA patients with moderate CVD risk should have carotid US for better CV risk stratification

References:

[1] LamHM, ShenJ., et al., Framingham Risk Score Discriminates Coronary Atherosclerosis in PsA Patient Better Than Other Cardiovascular Scores Do [abstract]. Arthritis Rheumatol. 2016;68.

[2] Cohen, G.I., et al., Relationship between carotid disease on ultrasound and coronary disease on CT angiography. JACC Cardiovasc Imaging, 2013.6(11).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1473

SAT0480 COMPARATIVE EFFECTIVENESS OF SECUKINUMAB AND INFLIXIMAB IN PSORIATIC ARTHRITIS ASSESSED BY MATCHING-ADJUSTED INDIRECT COMPARISON USING PIVOTAL PHASE 3 CLINICAL TRIAL DATA

V. Strand[1], I. McInnes[2], P. Mease[3], E. Choy[4], P. Nash[5], H. Thom[6], C. Kalyvas[7], K. Gandhi[8], L. Pricop[8], S. Jugl[9]. *[1]Stanford University, Palo Alto, United States; [2]University of Glasgow, Glasgow, United Kingdom; [3]Swedish Medical Center and University of Washington, Seattle, United States; [4]University of Cardiff, Cardiff, United Kingdom; [5]University of Queensland, Brisbane, Australia; [6]University of Bristol, Bristol, United Kingdom; [7]MAPI Group, Houten, Netherlands; [8]Novartis Pharmaceuticals Corporation, East Hanover, United States; [9]Novartis Pharma AG, Basel, Switzerland*

Background: Therapeutic options with discrete modes of action are now available for psoriatic arthritis (PsA). Clinicians require evidence to guide decision-making. No head-to-head RCTs have compared secukinumab 150 mg (SEC; anti-IL-17A) with infliximab 5 mg/kg (INF; TNFi) in patients with PsA. Matching-Adjusted Indirect Comparison (MAIC) can be used to estimate comparative effectiveness and enables treatment outcomes to be compared across effectively balanced trial populations. MAIC is an established method in health technology assessments, with NICE having recently published guidance.

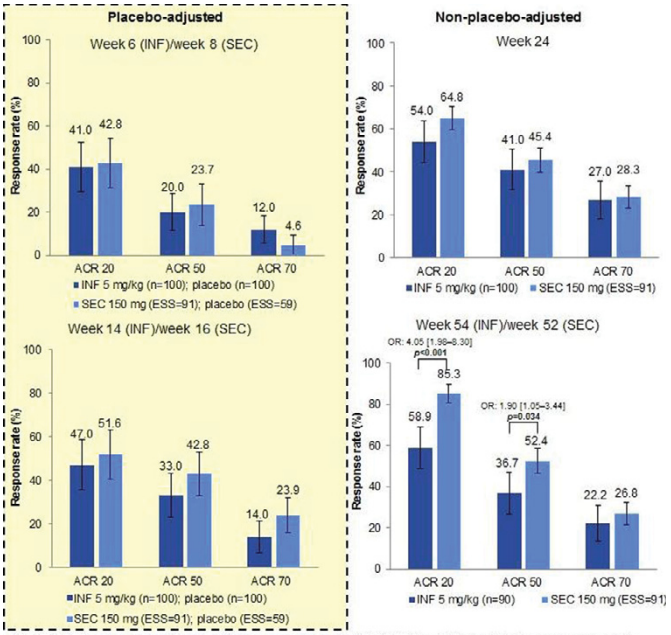
Objectives: To use MAIC to assess the comparative effectiveness of SEC and INF for up to 1 year using pooled FUTURE 1 (F1) and FUTURE 2 (F2) individual patient data (IPD) and published aggregate IMPACT 2 data, respectively.

Methods: Pooled F1 and F2 data were used to maximize the effective sample size (ESS) for SEC. IPD from the SEC arms of F1 and F2 (n=302) were weighted to match selected baseline characteristics of the INF arm of IMPACT 2 (n=100). Placebo arms were also matched; placebo-adjusted comparisons were possible only until week 16 because patients could receive active treatment from this time point onwards. Logistic regression was used to determine weights for age, sex, race, body weight, methotrexate use, presence of psoriasis (≥3% body surface area), mean PASI score, dactylitis, enthesitis, mean HAQ-DI score and previous TNFi therapy. Recalculated outcomes from F1 and F2 (SEC, ESS=91; placebo, ESS=59) were compared with data from IMPACT 2 (INF, n=100; placebo, n=100). Pairwise comparisons using odds ratios (ORs [95% CIs]) were performed for ACR 20, 50 and 70 responses at nearest-equivalent time points across trials: weeks 6/8, 14/16, 24 and 54/52. Mean changes from baseline in SF-36 Physical and Mental Component Summary (MCS) scores were also compared. Strict thresholds were avoided when interpreting p values, in line with American Statistical Association 2016 guidance.

Results: There was no evidence of differences in ACR 20, 50 and 70 responses between SEC and INF at weeks 6/8, 14/16 (both placebo-adjusted) and 24 (non-placebo-adjusted). At week 54/52, ACR 20 and 50 responses were higher with SEC than INF (OR [95% CI]: 4.05 [1.98–8.30], p<0.001 and 1.90 [1.05–3.44], p=0.034, respectively). Improvements in SF-36 MCS scores were greater with SEC than INF at weeks 14/16 (p=0.063), 24 (p=0.001) and 54/52 (p<0.001). A sensitivity analysis that added PsA duration, swollen joint count and CRP levels to the matching parameters yielded similar results.

Conclusions: In this MAIC, SEC showed evidence of superiority for symptomatic improvement (non-placebo-adjusted ACR 20 and 50) over INF for active PsA at 1 year. This was accompanied by greater improvements in SF-36 MCS scores. At earlier time points, there was no evidence of differences in ACR responses between SEC and INF.

Disclosure of Interest: V. Strand Consultant for: Abbvie, Amgen, AstraZeneca, Biogen Idec, Boehringer Ingelheim, Celltrion, Crescendo, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi and UCB, I. McInnes Consultant for: Abbvie, Celgene, Janssen, Novartis, Pfizer and UCB, P. Mease Grant/research support from: AbbVie, Amgen, BMS, Lilly, Novartis, Pfizer and UCB, Consultant for: AbbVie, Amgen, BMS, Corrona, Lilly, Merck, Novartis, Pfizer, Sun and UCB, Speakers bureau: AbbVie, Amgen, Celgene, Genentech, Novartis, Pfizer and UCB, E. Choy Grant/research support from: Pfizer, Roche and UCB, Consultant for: Chugai Pharma, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, Roche, R-Pharm and Sanofi, P. Nash Grant/research support from: Novartis, Consultant for: Novartis, Speakers bureau: Novartis, H. Thom Consultant for: Eli Lilly, F Hoffman-La Roche, Novartis Pharma AG and Pfizer, C. Kalyvas Employee of: Paid employee of the Mapi Group. The Mapi Group received funding from Novartis Pharma AG for this study, K. Gandhi Employee of: Novartis employee with stock, L. Pricop Employee of: Novartis employee with stock, S. Jugl Employee of: Novartis employee with stock



ACR 20/50/70 responses are the absolute mean response rate (IMPACT 2) and the predicted mean response rate (FUTURE 1 and FUTURE 2). Error bars show 95% CIs.
ACR, American College of Rheumatology; ACR 20/50/70, at least a 20%/50%/70% improvement according to the ACR response criteria; CI, confidence interval; ESS, effective sample size; INF, infliximab; OR, odds ratio, SEC, secukinumab.

DOI: 10.1136/annrheumdis-2017-eular.5802

SAT0481 THE RELATIONSHIP BETWEEN THE PATIENT ACCEPTABLE SYMPTOM STATE (PASS) AND DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS (PSA)

J.Z. Fei[1], A. Perruccio[2], Y. Ye[1], D.D. Gladman[1], V. Chandran[1]. *[1]Rheumatology; [2]Orthopaedics, Toronto Western Hospital, Universtiy of Toronto, Toronto, Canada*

Background: PASS is the highest level of symptoms beyond which patients consider themselves well. Psoriatic Arthritis Disease Activity Score (PASDAS) is a recently developed composite disease activity measure that summarizes a patient's disease in a single 0–10 score.

Objectives: In this study, we aimed to identify the PASDAS cut-off points for PASS, and to examine the agreement between PASS and the PASDAS thresholds for low (<3.2), moderate (3.2–5.4), and high disease activity (>5.4).

Methods: Patients were prospectively recruited from the University of Toronto PsA clinic. A standard protocol including physician assessment and patient-reported outcomes was used to record variables required to calculate PASDAS. In addition, each patient was asked to "think about all the ways your PsA has affected you during the last 48 hours. If you were to remain in the next few months as you were during the last 48 hours, would this be acceptable to you?" to assess PASS. For analysis, the PASDAS threshold for PASS was identified with the ROC analysis to maximize specificity and sensitivity. Furthermore, the agreement between PASS and low, moderate, and high PASDAS disease activity cut-offs were evaluated.

Results: 169 patients [61% male, mean age 56.1, mean disease duration 16.9 years, mean (SD) PASDAS 3.25 (1.1)] were recruited. The PASDAS threshold for the patient acceptable symptoms state (PASS+) was identified to be 3.84 (AUC – 0.88, sensitivity 0.82, specificity 0.94) using ROC curve analysis. 91% of patients with low disease activity (PASDAS <3.2) considered their symptoms state acceptable (PASS+), and 100% of the patients with high disease activity (PASDAS >5.4) considered their symptom state as unacceptable (PASS-). Furthermore, the mean (SD) PASDAS was 4.5 (1.0) in the PASS- group and 2.8 (1.1) in the PASS+ group.

Conclusions: The PASDAS threshold for patient acceptable symptoms state is 3.84, which is within the moderate disease activity range. Thus with a PASDAS of 3.84 or lower, PsA patients consider their symptom state acceptable for the next few months. This cut-off should be considered for shared decision making regarding treatments in PsA patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6186

SAT0482 SUBCLINICAL ENTHESOPATHY IN PSORIATIC PATIENTS AND ITS RELATION TO OTHER DISEASE PARAMETERS: AN ULTRASOUND STUDY

W. Gouda[1], M. Ismail[2], M. Doma[2]. [1]*Rheumatology, Aswan University, Aswan;* [2]*Rheumatology, Al-Azhar University, Assiut, Egypt*

Background: Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by reddish, thick patches covered with marked silvery scaling [1]. In about 70% of the patients, psoriasis is present many years before the onset of psoriatic arthritis [2]. The early recognition and therapeutic intervention especially with the new biologic treatments is critical to prevent the destructive and debilitating changes of psoriatic arthritis [3]. Enthesitis is inflammation at the attachment of tendons and ligaments to the bones, has been suggested as being the unifying feature of psoriatic arthritis, and the disease can be considered an enthesis associated disorder rather than primary synovitic arthropathy [4].
Objectives: We aimed to correlate the subclinical enthestitis in patients with psoriasis detected by means of power Doppler (PD) ultrasonography (US) with other disease parameters.
Methods: 50 persons with a definite diagnosis of psoriasis with no clinical evidence of arthritis or enthesitis were selected. All patients underwent complete clinical assessment included Psoriasis severity (PASI) score, body mass index (BMI), PDUS evaluation of Achilles, quadriceps, patellar entheses and plantar aponeurosis. US findings were scored according to the Glasgow Ultrasound Enthesitis Scoring System (GUESS).
Results: In 18 of 50 of patients (36%) PDUS found signs indicative of enthesopathy. The Achilles enthesis had the highest number of PDUS signs of enthesopathy (33.3%), followed by distal patellar enthesis (22.2%), proximal patellar enthesis (16.7%), quadriceps enthesis (16.7%), and plantar aponeurosis enthesis (11.1%) with variable enthesial morphostructural abnormalities. The GUESS score was directly correlated with age (p=0.012), disease duration (p=0.044), PASI (p=0.035), BMI (p=0.011), hyperuricemia (p=0.011).

Demographic findings of the study population

Characters	Patients
Age (range) mean (SD)	(19–70) 33.8±11.2
Gender	
Female N (%)	31 (62)
Male N (%)	19 (38)
Disease duration (range) mean (SD)	(2–12) 7.7±3.4
PASI score mean ±SD (range)	21.1±7.3 (2.7 - 33.2)
BMI mean ±SD (range)	29.9±6.4 (19.5–42)
Rheumatoid factor: N of patients (%)	
Positive (>1/8)	4 (8%)
Negative	46 (92%)
SUA: N of patients (%)	
Normal (<6 mg/dl)	38 (76%)
Elevated	12 (24%)
Radiographic sacroiliitis: N of patients (%)	6 (12%)
Ultrasonographic findings: (%)	
Normal	32 (64%)
Abnormal (enthesitis)	18 (36%)



Conclusions: In addition to the importance of PDUS as a complimentery tool in examination of entheses in psoriatic patients, the presence of high PASI score together with the increased BMI and hyperuricemia in addition to long disease duration could be considered as predictive parameters for the presence of psoriatic enthesitis.
References:
[1] Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis, section 1. Overview of psoriasis and guide lines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol. 2008; 58(5):826–50.
[2] Dimitrios TB, Ioannis OT. Psoriatic arthritis. In: Klippel JH, ed.Primer on the Rheumatic Diseases. Atlanta, GA: Arthritis Foundation, 1997: 175–179.
[3] Rozenblit M, Lebwohl M. New biologics for psoriasis and psoriatic arthritis. Dermatol Ther. 2009; 22(1):56–60.
[4] McGonagle D, Conaghan PG, Emery P. Psoriatic arthritis: a unified concept twenty years on. Arthritis Rheum. 1999; 42:1080–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1595

SATURDAY, 17 JUNE 2017

Osteoarthritis

SAT0483 OSTEOARTHRITIS (OA) AND SOCIO-ECONOMIC STATUS (SES) PREDICTS THE ONSET OF COMORBIDITIES LINKED TO FREQUENT HEALTHCARE CONSULTATION

R. Hayward[1], K. Kaur[2], R. Wilkie[1]. [1]*Research Institute for Primary Care & Health Sciences;* [2]*Medical Student, Keele University, Keele, United Kingdom*

Background: OA is the most common joint condition, the fourth leading cause of disability globally and the fastest increasing major health condition. In older adults, OA frequently coexists with other morbidities, but the temporal nature is unclear. There is abundant evidence that markers of low SES are associated with poor outcomes among people with musculoskeletal conditions, however the mechanism linking comorbidity may vary with SES.
Objectives: To examine if OA predicted the onset of comorbidities that are the reason for frequent consultation to primary care, and if this association was moderated by SES.
Methods: Cohort study combining questionnaire data at two time points (2005, 2008) in the North Staffordshire Osteoarthritis Project, and medical record data from 2000 to 2005 (n=3910). OA was defined by consultation to primary care for OA between 2000 and 2005, and the indication of moderate to extreme pain interference in the questionnaire (2005). Logistic regression examined the association between OA and the onset of seven comorbidities (anxiety, depression, widespread pain (WP), insomnia, cognitive impairment, neurosis, stress between 2005 and 2008) and restricted social participation, first unadjusted and then adjusting for putative confounders (comorbidity, socio-demographic and lifestyle factors). Moderation of the association between OA and new onset comorbidity by change in income, education and area-level deprivation was examined by including interaction terms in regression and stratified analyses. Results were reported as odds ratios with a 95% Confidence Interval (OR; 95% CI).
Results: Mean age was 63, 55% were female, and 942 (24%) had OA. In the unadjusted analysis, OA was significantly associated with new onset of seven comorbidities ($p<0.05$). After adjusting for confounders, OA was associated with the onset of WP (2.49; 1.96–3.17) and insomnia (1.58;1.14–2.19) There was a significant non-multiplicative interaction between OA and income and new onset cognitive impairment (P=0.047); new onset of cognitive impairment in those with OA whose income remains adequate 29.1% cf 38.1% in those with OA whose income remains inadequate), and between OA and education and new onset WP (P=0.012; new onset in those with OA and secondary education only was 37.4% cf 50% in those with OA and had more than a secondary education).
Conclusions: Consulters for OA were more likely to develop new physical and psychological comorbidities that lead to more frequent consultation to primary care than those without OA. Whilst confounders explained some of these associations, OA consulters may benefit from more proactive strategies to prevent further morbidity. Despite no significant multiplicative interactions, there were differences in the prevalence of new onset of morbidity in those with OA when stratified by SES. Onset of cognitive impairment was associated with inadequate income but WP was associated with those with higher education suggesting a "worried well" population seen both in other health surveys and in screening. OA and baseline morbidities were higher with lower SES and further exploration across the life-course will help to establish the role of SES on the natural history OA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2106

SAT0484 LOW MAGNESIUM INTAKE IS ASSOCIATED WITH INCREASED PAIN IN SUBJECTS WITH RADIOGRAPHIC KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

A. Shmagel[1], N. Onizuka[1], T. Vo[2], L. Langsetmo[2], K. Ensrud[3,4], R. Foley[5], P. Valen[1,6]. [1]*Medicine/Rheumatology;* [2]*School of Public Health;* [3]*Medicine, University of Minnesota;* [4]*Medicine, VA Medical Center;* [5]*Nephrology/Medicine, University of Minnesota;* [6]*Medicine/Rheumatology, VA Medical Center, Minneapolis, United States*

Background: Osteoarthritis pain appears to be caused, at least in part, by alterations in peripheral and/or central nociceptive pathways.[1] As magnesium is a known mediator of nociception, we hypothesized that low magnesium intake may be associated with increased pain in radiographic knee OA.
Objectives: To evaluate whether magnesium intake is associated with knee pain in radiographic knee osteoarthritis.
Methods: We investigated the associations between knee pain and magnesium intake from food and supplements in 2549 participants with prevalent radiographic knee OA (Kellgren-Lawrence score $\geq$2) in the Osteoarthritis Initiative cohort.[2] WOMAC pain scores in the affected knee were reported annually with total follow up period of 48 months. Magnesium intake was assessed at baseline by food frequency questionnaire and dietary supplement questionnaire, and expressed in gender-specific calorie-adjusted quintiles. Analyses used generalized linear mixed effects models with repeated measures.
Results: Among participants with baseline radiographic knee OA the mean total magnesium intake was 310 mg/day (SD 133) for men, and 288 mg/day (SD

118) for women, with 68% of men and 44% of women below the estimated average requirement (EAR). The mean WOMAC pain score at 0, 12, 24, 36, and 48 months of follow up was 3.5 (SD 3.8), median score 2 (IQR 0; 6). After adjustment for age, gender, BMI, caloric intake, physical activity, smoking status, alcohol use, renal insufficiency, and the use of analgesics, subjects in the lowest gender-specific quintile of magnesium intake (Q1) had, on average, 1 point higher WOMAC knee pain scores than subjects in the highest quintile (Q5): Q1 β (95% CI) 1.00 (0.61–1.39), Q2 0.69 (0.32–1.06), Q3 0.25 (-0.12–0.62), Q4 0.25 (-0.14–0.64); $p<0.0001$.

Conclusions: In a cohort of adults with prevalent radiographic knee osteoarthritis, magnesium intake overall was below recommended. Low magnesium intake at baseline was associated with increased pain in the affected knee over 48 months of follow up. These findings may be of growing importance as the average dietary magnesium intake for humans is declining.[3]

References:

[1] Thakur M, Dickenson AH, Baron R. Osteoarthritis pain: nociceptive or neuropathic? Nat Rev Rheumatol. 2014;10(6):374–380. doi: 10.1038/nrrheum.2014.47.
[2] Fawaz-Estrup F. The osteoarthritis initiative: an overview. Med Health R I. 2004;87(6):169–171.
[3] Rosanoff A, Weaver CM, Rude RK. Suboptimal magnesium status in the United States: are the health consequences underestimated? Nutr Rev. 2012;70(3):153–164. doi:10.1111/j.1753–4887.2011.00465.x.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3024

SAT0485 INCREASED EXPRESSION OF OSTEOPROTEGERIN IN CD271+ MULTIPOTENTIAL STROMAL CELLS FROM FEMORAL HEADS OF PATIENTS WITH HIP OSTEOARTHRITIS

D.C. Ilas[1], S.M. Churchman[1], J. Aderinto[2], P.V. Giannoudis[1], D. McGonnagle[1], E. Jones[1]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]Department of Orthopaedics, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom*

Background: Osteoarthritis is a disease of the whole joint, but subchodral bone marrow lesions (BMLs) closely correlate with disease progression [1]. We have previously shown that in OA femoral heads, subchondral bone multipotential stromal cells (MSCs) were 5-fold more abundant in MRI determined BML areas where they also showed reduced mineralisation capacity and altered RANKL expression compared to non-BML areas [2]. This offered novel insight into MSC involvement in the bone remodeling process in OA.

Objectives: The current study investigated a multi-lineage gene expression profile of native CD271+ MSCs from OA femoral heads focusing on osteogenesis and bone remodeling related genes compared to CD271+ MSCs from healthy trabecular bone.

Methods: Femoral heads were obtained from 17 OA patients undergoing total hip arthroplasty. Control samples included healthy iliac crest bone from 12 patients undergoing autograft harvesting for bone reconstruction and healthy femoral neck bone from 2 patients, extracted following core decompression surgery for avascular necrosis of the femoral head. CD271+ MSCs were extracted by enzymatic digestion and purified by FACS, as previously described [3, 4]. MSC cultures were generated by standard methods [4]. Quantitative real-time PCR was performed using TaqMan assays for 12 transcripts and gene expression was normalised to *HPRT1*.

Results: Sorted CD271+ cells from both groups displayed gene expression profiles indicative of their steady-state osteogenic, adipogenic, bone remodeling and stromal-support functions (Table 1). Three out of 11 transcripts showed significant increases in OA: alkaline phosphatase, melanoma cell adhesion molecule and osteoprotegerin (OPG) ($p<0.05$, Mann Whitney test). The proportion of CD271+ cells in relation to total live cells was more variable but on average 2-fold higher in OA (medians of 2.3 and 5.2%, respectively, not significant). Consistent with previous findings [4, 5], gene expression levels for the majority of transcripts were altered following MSC culture expansion (3 up-regulated and 8 down-regulated).

Table 1. Transcripts expression levels in CD271+ MSCs from OA and healthy bone

Transcript	Median (Range)		Fold increase in OA (*=p<0.05)
	OA	Healthy	
Osterix	0.5 (0.1-16.3)	0.2 (0.1-1.6)	2.4
Alkaline phosphatase	**17 (2.4-71.3)**	**7.1 (0.5-16.3)**	**2.4***
Collagen 1a1	3.1 (0.2-18.7)	1.1 (0.4-8.9)	2.9
Osteonectin	89.8 (6.1-163.1)	15.3 (11.3-81.6)	5.9
Osteopontin	49.2 (9.6-693)	46 (6.9-212.5)	1.1
Cadherin-11	15.6 (1.3-37.9)	5.0 (3.2-29.2)	3.1
Fatty acid-binding protein-4	1.9 (0.3-10.1)	0.8 (0.4-11)	2.5
Receptor activator of nuclear factor kappa-B ligand (RANKL)	0.3 (0.2-2.3)	0.2 (0.1-0.5)	1.1
Osteoprotegerin (OPG)	**0.5 (0.1-0.8)**	**0.1 (0.1-0.4)**	**3.8***
Stromal cell-derived factor 1	164.6 (22-1377)	128.3 (91.1-1956.8)	1.3
Melanoma cell adhesion molecule	**4.5 (1.0-16.3)**	**0.9 (0.9-3.1)**	**5.1***

Conclusions: This is the first study to show gene expression alterations in uncultured CD271+ MSCs from OA patients. A notable increase in OPG is suggestive of MSCs' bias towards inhibition of bone resorption in late hip OA and further incriminates the RANKL/OPG pathway, specifically in MSCs, in OA pathophysiology. Further studies are needed to define the role of native MSCs in lesion associated OA disease progression and to evaluate these as a possible target for treatment.

References:

[1] Goldring et al, Nat Rev Rheumatol. 2016;12:632.
[2] Campbell et al, Arthritis Rheumatol. 2016;68:1648-.
[3] Jones et al., Arthritis Rheum. 2010 Jul;62:1944.
[4] Churchman et al., Arthritis Rheum. 2012 Aug;64:2632.
[5] Churchman et al., Stem Cells Int, 2017 (in press).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5937

SAT0486 CATASTROPHIZING IN OSTEOARTHRITIS OF THE KNEE: DOES THE LEQUESNE SCORE TAKE IT IN COUNT? A PROSPECTIVE STUDY

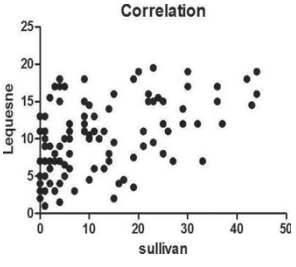
J. Lecorney, M. Chouk, X. Guillot, C. Prati, D. Wendling, F. Verhoeven. *Rhumatologie, CHRU de Besançon, Besançon, France*

Background: knee osteoarthritis is a frequent matter of consultation in both general practice and rheumatology. Pain is the main symptom leading to a consultation. This painful experience can be influenced by various factors such as the anxio-depressive state or catastrophizing. Catastrophizing is known to be associated with lower analgesia results in total knee arthroplasty (1).

Objectives: The aim of this study is to evaluate the correlation between the functional status (assessed by the Lequesne score) and the catastrophizing (assessed by the Sullivan score) in patient with osteoarthritis of the knee.

Methods: We included patients consulting for knee osteoarthritis, meeting the OARSI criteria (2), one of the three general practitioners participating in the study or a rheumatologist at University Hospital. We excluded those with surgical indication. For each patient we registered the epidemiological data, the radiographic stage as well as the scores of Lequesne and Sullivan questionnaires. The correlation between the different scores were assessed with a Spearman test.

Results: A total of 100 patients were included, 50 consulting a general practitioner and 50 consulting a rheumatologist, between November 2015 and April 2016. Among these 100 patients, there were mainly women (57%) with a mean age of 64.8±1.17 years old. The mean radiographic stage was 2.66±0.11 on the Kellgren and Lawrence scale. The Mean Sullivan score was 12.98±1.18 and the mean Lequesne score was 10.46±0.47. There was a close correlation ($r=0.3$, $p=0.006$) between the Lequesne score and the radiographic scale. There was no correlation between the Sullivan score and the radiographic scale. Howerver, the correlation between the Sullivan and the Lequesne scores was modest ($r=0.47$; $p<0.0001$) (Figure 1). Thus, the Lequesne score is correlated with the radiographic scale and the Sullivan score. When we compare the two populations, it appeared that the people consulting a rheumatologist are majority of women (72%) and younger (62.58±1.8 VS 67, 18±1.38 years, $p<0.05$) and with a shorter duration of symptoms (6.02±1.12 VS 12.96±1.5 Years, $p<0.001$). In terms of radiographic and functional impairment, the two populations were similar (Kellgren score of 2.59±0.15 VS 2.7±0.158 and Lequesne score of 11.13±0.67 VS 9.78±0,66. $p>0.05$) but there was a clear difference for the Sullivan score (16.96±1.67 VS 9±1.4; $p<0.001$).



Conclusions: Our study is the first to highlight a correlation between the Sullivan and the Lequesne scores in patient consulting for osteoarthritis of the knee. Moreover, unlike the Sullivan, score the Lequesne score is correlated with the radiographic scale. The strength of this study is the inclusion of both patients consulting the general practitioner and those consulting the rheumatologist to avoid a recruitment bias. Indeed, patients consulting the rheumatologist had a catastrophizing score more important for the same functional and radiological impairment than those consulting the general practitioner. Thus, our population is representative of the global population suffering from osteoarthritis of the knee in terms of age, sex-ratio, BMI.The Lequesne score is a global score correlated with structural damage and with psychological factors like catastrophizing.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2617

SAT0487 A RANDOMIZED, BLINDED, COMPARATOR-CONTROLLED TRIAL INVESTIGATING A 4-WEEK COURSE OF LYRICA IN SUBJECTS WITH KNEE OSTEOARTHRITIS WHO EXHIBIT NEUROPATHIC PAIN, COMPARED WITH A 4-WEEK COURSE OF PARACETAMOL

A. Wright[1], P. Moss[1], H.A. Benson[2], R. Will[3], P. Chowalloor[4]. *[1]School of Physiotherapy and Exercise Science; [2]School of Pharmacy, Curtin University; [3]School of Medicine and Pharmacology, University of Western Australia; [4]Department of Rheumatology, Royal Perth Hospital, Perth, Australia*

Background: Knee osteoarthritis (OA) has been considered the archetypal model of inflammatory or nociceptive pain [1] but it is apparent that people with knee OA may present with different pain phenotypes including some with features of neuropathic pain [2,3].
Objectives: The aim of the present study was to select people with knee OA who exhibited features of neuropathic pain based on elevated cold pain thresholds (≥15℃) and elevated PainDETECT scores (≥13) and to determine if pregabalin would be more effective in reducing pain and improving function in this cohort than paracetamol.
Methods: The study used a double-blind, randomized, comparator-controlled design in participants with knee OA to compare the effectiveness of a standard dose of paracetamol (1000mg qid) with a titrated dose of pregabalin (Lyrica) taken daily over 28 days. A cohort of 90 participants with moderate to severe painful knee OA (Pain rating ≥4/10) who demonstrated features of neuropathic pain were included in the study. Participants were selected from an initial cohort of 271 OA sufferers recruited from the Perth community based on screening of CPT and PainDETECT. Included participants were randomly assigned to receive either a four week course of pregabalin titrated to a maximum dose of 300mg or a four week course of paracetamol (4,000mg).
Participants were assessed at baseline, 14 and 28 Days. They completed the PainDETECT, WOMAC and PQAS questionnaires. Quantitative sensory testing was carried out at three sites (index knee, contralateral knee, ECRB) using standard methods. Cold and heat pain thresholds were tested using a Peltier thermode and pressure pain thresholds were assessed using a digital algometer. Physical function was assessed using three timed locomotor function tests (sit-to-stand, walk, stairs).
Results: Participants receiving pregabalin (300mg) exhibited greater reductions in WOMAC Pain scores (P=0.0001) and PainDETECT scores (P=0.0001) at Day 28 compared to the paracetamol group and a greater increase in pressure pain thresholds (reduced tenderness) (P=0.025) at the index knee. There was no significant difference between the groups in cold pain thresholds (P=0.33). Participants in the pregabalin group completed the physical tests more quickly than the paracetamol group (Sit-to-stand p=0.05, walk p=0.001, stairs p=0.05). The pregabalin group also had a significantly increased likelihood of reducing their PainDETECT score below the entry value of 13 compared to the paracetamol group (OR 9.20; P=0.001) but there was no significant difference in the likelihood of reducing their cold pain threshold below the 15℃ entry value (OR 2.26; P=0.14).
Conclusions: The group receiving pregabalin 300mg showed greater reductions in pain, reduced features of neuropathic pain and reduced tenderness at the affected knee. Further research is warranted to evaluate pregabalin in this specific patient cohort.
References:
[1] Harden, R.N., et al., J Pain, 2013. 14(3): p. 281–9.
[2] Hochman, J.R., et al., Osteoarthritis Cartilage, 2011. 19(6): p. 647–54.
[3] Ohtori, S., et al., Yonsei Med J, 2012. 53(4): p. 801–5.
Acknowledgements: The investigators thank Ms Lisa Webster for her contribution to the study.
Disclosure of Interest: A. Wright Grant/research support from: Pfizer Inc, P. Moss Grant/research support from: Pfizer Inc, H. Benson Grant/research support from: Pfizer Inc, R. Will Grant/research support from: Pfizer Inc, P. Chowalloor: None declared
DOI: 10.1136/annrheumdis-2017-eular.5656

SAT0488 COMPARATIVE EFFECTIVENESS OF AYURVEDA AND CONVENTIONAL CARE IN KNEE OSTEOARTHRITIS – A RANDOMIZED CONTROLLED TRIAL

C.S. Kessler[1], K. Dhiman[2], A. Kumar[3], T. Ostermann[4], S. Gupta[5], A. Morandi[6], M. Mittwede[7], E. Stapelfeldt[1], M. Spoo[1], K. Icke[8], A. Michalsen[1], C. Witt[8]. *[1]Complementary and Integrative Medicine, Immanuel Hospital Berlin, Berlin, Germany; [2]Central Council for Research in Ayurvedic Sciences; [3]All India Institute of Ayurveda, New Delhi, India; [4]Department of Psychology and Psychotherapy, University of Witten Herdecke, Witten, Germany; [5]Department of Kaya Cikitsa, J.S. Ayurveda College & P.D. Patel Ayurveda Hospital, Nadiad, India; [6]School of Ayurvedic Medicine, Ayurvedic Point, Milan, Italy; [7]European Academy of Ayurveda, Birstein; [8]Institute for Social Medicine, Epidemiology and Health Economics, Charité Medical University, Berlin, Germany*

Background: Traditional Indian Medicine Ayurveda is used to treat knee osteoarthritis (OA) despite limited evidence.
Objectives: We aimed to evaluate the effectiveness of complex Ayurvedic treatment compared to complex conventional care in knee OA patients.
Methods: According to ACR criteria patients with knee OA were included in a multicenter randomized, controlled trial and treated in 2 hospital outpatient clinics and 2 private outpatient clinics in Germany with 5 physicians and 20 therapists participating. Patients received either Ayurvedic treatment (n=77) or conventional care (n=74) with 15 treatments over 12 weeks. Primary outcome was the change on the Western Ontario and McMaster University Osteoarthritis (WOMAC) Index after 12 weeks (validated German version). Secondary outcomes included the WOMAC subscales; a pain disability index, numeric rating scales for pain and sleep quality, a pain experience scale, a quality-of-life index, a profile of mood index, rescue medication use, and safety issues.
Results: A total of 151 patients (Ayurveda n=77, conventional care n=74) were included. Changes of the WOMAC Index from baseline to 12 weeks were more pronounced in the Ayurveda group (mean difference 61.0 [95% CI 52.4;69.6]) than in the conventional group (32.0 [95% CI 21.4;42.6]) resulting in a significant difference between groups ($p<0.001$) and a clinically relevant effect size (Cohen's d 0.68 [95% CI 0.35;1.01]). Similar tendencies were observed for all secondary outcomes at week 12. Effects were sustainable at follow-ups after 6 and 12 months.
Conclusions: The results suggest that a complex Ayurvedic treatment might be clinically superior to a complex conventional intervention in the treatment of OA of the knee.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4692

SAT0489 ASSOCIATION OF CHILDHOOD OVERWEIGHT MEASURES WITH ADULTHOOD KNEE CARTILAGE DEFECTS AND BONE MARROW LESIONS: A 25-YEAR COHORT STUDY

T. Meng[1], S. Thayer[2], A. Venn[1], F. Cicuttini[3], L. March[4], T. Dwyer[5], A. Halliday[2], M. Cross[4], L. Laslett[1], G. Jones[1], C. Ding[1,3,6], B. Antony[1]. *[1]Menzies Institute for Medical Research; [2]Department of Radiology, Royal Hobart Hospital, Hobart; [3]Department of Epidemiology and Preventive Medicine, Monash University, Melbourne; [4]Institute of Bone and Joint Research, Sydney; [5]Murdoch Childrens Research Institute, Melbourne, Australia; [6]Translational Research Centre, Academy of Orthopaedics, Southern Medical University, Guangzhou, China*

Background: Obesity and overweight have been associated with increased risk of knee osteoarthritis (OA). Cartilage defects and bone marrow lesions (BMLs) are imaging biomarkers that predict the development and progression of knee OA. However, there are no studies describing the effect of childhood obesity or overweight on risk of adulthood knee structural abnormalities including cartilage defects and BMLs.
Objectives: To describe associations between body weight, body mass index (BMI), overweight status and fat mass in childhood and knee cartilage defects and BMLs measured using magnetic resonance imaging (MRI) in adulthood 25 years later.
Methods: Subjects broadly representative of the Australian population (n=327, aged 31–41 years) were selected from the Australian Schools Health and Fitness Survey of 1985 (n=8498, aged 7–15 years). Childhood measures, including weight, height and skinfolds were measured in 1985. BMI and fat mass were calculated. They underwent T1-weighted fat-suppressed and proton density-weighted fat-suppressed MRI scans 25 years later. Cartilage defects and BMLs were measured from MRI using a semi-quantitative scoring system. Log binomial regression analyses were used to determine the associations of childhood overweight measures with adulthood knee cartilage defects and BMLs.
Results: There were no associations between childhood overweight measures and adulthood tibio-femoral cartilage defects; however, body weight, BMI and overweight status were positively associated with patellar cartilage defects after adjustment for childhood age, duration of follow-up, sex, childhood height (if weight or fat mass was the predictor), childhood injury, adulthood injury and corresponding adulthood measures (RR 1.05, 95% CI 1.01 to 1.09 for weight; RR 1.10, 95% CI 1.01 to 1.19 for BMI; RR 2.06, 95% CI 1.19 to 3.58 for overweight). After further adjustment for patellar BMLs, these associations remained largely unchanged and the association of fat mass with patellar cartilage defects became significant (RR 1.10, 95% CI 1.01 to 1.21).
Childhood overweight measures were not associated with adulthood BMLs in either tibio-femoral or patellar compartments. However, sex-specific analyses showed BMI and overweight status were associated with higher risks of patellar BMLs after adjustment for covariates in men (RR 1.36, 95% CI 1.03 to 1.81 for BMI; RR 4.37, 95% CI 1.01 to 18.91 for overweight) but not in women.
Conclusions: Childhood overweight measures were significantly associated with increased risk of patellar cartilage defects and BMLs in young adults. In addition, overweight status was significantly associated with patellar BMLs in men which may explain why overweight was only associated with increased knee pain in men as we reported earlier. These results indicate the importance of addressing overweight in childhood to aid in preventing adulthood knee structural abnormalities which increase the risk of OA in later life.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5668

SAT0490 GENOME-WIDE DNA METHYLATION PROFILING OF OSTEOARTRHITIS PERIPHERAL BLOOD MONONUCLEAR CELLS REVEALS SLOWED EPIGENETIC AGING AMONG RAPID RADIOGRAPHIC PROGRESSORS: DATA FROM THE OSTEOARTHRITIS INITATIVE (OAI)

A. Rivas[1], M. Jeffries[1,2]. [1]*Rheumatology, Immunology, and Allergy, University of Oklahoma Health Sciences Center;* [2]*Arthritis & Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, United States*

Background: Extensive evidence has correlated epigenetic alterations in articular tissues with both the presence and progression of human osteoarthritis, but few analyses of blood cell epigenetic patterns have been done in OA.
Objectives: We examined the DNA methylation aging rate in peripheral blood mononuclear cells (PBMCs) at baseline from knee OA patients with rapid radiographic progression compared to well-matched nonprogressors enrolled in the Osteoarthritis Initiative (OAI).
Methods: PBMC DNA was obtained from baseline blood draws of 64 OA patients enrolled in the OAI longitudinal study. All patients had baseline symptomatic and radiographic OA. 32 rapidly-progressive OA patients, defined as $\geq$1.0mm radiographic joint space loss within 24 month follow-up were compared to 32 non-progressive patients. There were no differences in age, sex, race, BMI, baseline K/L grade, or calculated PBMC subset composition between rapid- and non-progressors. DNA methylation was quantified with Illumina HumanMethylation 450k arrays. Preprocessing was performed in GenomeStudio and normalized to internal controls. Epigenetic age was estimated with the algorithm described by Horvath et. al., using 353 age-associated CpG sites. This epigenetic age was compared to chronological age to calculate epigenetic-chronological age discordance (ΔAge) and group differences compared with a Student t-test. ΔAge was correlated with individual CpG methylation sites of rapid progressors, and Pearson values calculated. Correlation was considered significant if Pearson's r values were $\leq$-0.55 or $\geq$0.55 ($p \leq 0.001$). Pathway analysis of correlated genes was performed with the Ingenuity Pathway Analysis (IPA) system.
Results: The baseline DNA methylation aging rate in rapidly progressive (RP) knee OA patients was decelerated compared to nonprogressors (NP) and to chronological age (ΔAge-RP: -4.9±1.4 vs. ΔAge-NP: -0.071±1.3 mean±SEM years less than chronological age, p=0.015). 1165 CpG sites were correlated with ΔAge in rapid progressors, corresponding to 755 genes. Ontologic analysis of highly correlated genes showed association of the STAT3 pathway (p=6E-4), Notch signaling (p=1E-3), axonal guidance signaling (p=7E-3), CREB signaling (p=2E-2), NFAT signaling (p=2E-2), and autophagy (p=4E-2) among others. Associated upstream regulators included FGF2 (p=3E-5), SMAD4 (p=9E-4), SMAD5 (p=1E-3, TNF (p=4E-3), and TGFB1 (p=4E-3), among others
Conclusions: Our data reveal that a decelerated peripheral blood differential DNA methylation age epigenotype is present at baseline in rapidly progressive knee OA patients, but not in nonprogressive knee OA patients. The genes correlated with this methylation age deceleration cluster in pathways previously associated with OA in articular tissues, suggesting that these pathways may systemically epigenetically dysregulated. Our data reinforce the notion that OA is a heterogeneous disease composed of distinct subgroups, and suggests that future epigenetic investigation of immune cell subsets may be beneficial in unraveling OA pathogenesis.
Acknowledgements: We gratefully acknowledge the assistance of Dr. Michael Nevitt, PhD, MPH, and Dr. John Lynch, PhD, of the University of California San Francisco and the OAI for their assistance in sample selection.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6567

SAT0491 USE OF HISTAMINE H1-RECEPTOR ANTAGONISTS IS ASSOCIATED WITH DECREASED PREVALENCE OF RADIOGRAPHIC KNEE OSTEOARTHRITIS: A CROSS-SECTIONAL ANALYSIS OF OSTEOARTHRITIS INITIATIVE DATA

I. Shirinsky, V. Shirinsky. *Institute of Fundamental and Clinical Immunology, Novosibirsk, Russian Federation*

Background: Mast cells are prevalent in osteoarthritis (OA) synovial tissue and their presence is associated with structural damage [1]. H1-receptor antagonists block the action of histamine, which is the major mediator of mast cells, on specific receptors. Therefore, H1 receptor blockade may represent a way to prevent and treat OA. Currently, there is a lack of data investigating the effects of H1-receptor blockade on knee OA in humans.
Objectives: To evaluate cross-sectional association between the use of histamine H1-receptor antagonists and radiographic knee OA.
Methods: For the current analysis we used data from the publically available Osteoarthritis Initiative (OAI). We compared cross-sectionally the knees of OAI participants taking H1-receptor antagonists at baseline with knees of control participants. We used logistic regression models to assess the association between radiographic knee OA (defined as KL$\geq$2 and JSN) and the use of H1-receptor antagonists. Generalized estimating equations (GEE) were used to adjust for the correlation between knees. The models were adjusted for multiple covariates including age, race, and body mass index.
Results: A sample of 4377 OAI participants (8753 knees) was analyzed, 457 of them (914 knees) used histamine H1-receptors at baseline. The use of histamine H1-receptor antagonists was associated with lower prevalence of radiographic knee OA in both crude (OR 0.77, 95 CI 0.64–0.91, $p<0.01$) and adjusted (OR 0.79, 95 CI 0.66–0.95, p=0.01) analyses.
Conclusions: Histamine H1-receptor antagonists are associated with decreased prevalence of knee OA. Further studies are warranted to determine whether H1-receptor blockade may be of benefit in the prevention and treatment of knee OA.
References:
[1] de Lange-Brokaar BJ, Kloppenburg M, Andersen SN, Dorjee AL, Yusuf E, Herb-van Toorn L, et al. Characterization of synovial mast cells in knee osteoarthritis: association with clinical parameters. Osteoarthritis and Cartilage 2016; 24: 664–671.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2658

SAT0492 INTRAMUSCULAR CORTICOSTEROID INJECTION VERSUS PLACEBO INJECTION IN HIP OSTEOARTHRITIS: A 12- WEEK BLINDED RANDOMIZED CONTROLLED TRIAL

D. Dorleijn[1], P. Luijsterburg[1], M. Reijman[2], M. Kloppenburg[3], J. Verhaar[2], P. Bindels[1], K. Bos[2], S. Bierma-Zeinstra[1]. [1]*General Practice;* [2]*Orthopeadics, Erasmus MC, Rotterdam;* [3]*Rheumatology, LUMC, Leiden, Netherlands*

Background: Several international guidelines recommend intra-articular (IA) corticosteroid injections for patients with hip OA experiencing moderate to severe pain and no responding to oral analgesics. Previous research has shown a systemic effect of an intramuscular (IM) gluteal corticosteroid injection in patients with subacromial impingement shoulder pain. A clinically relevant effect of IM corticosteroid injections would offer a less complex, alternative treatment for patients' episodes of increased pain in hip OA.
Objectives: The trial aim was to assess the efficacy of an IM gluteal corticosteroid injection compared to a placebo injection on patients' reported hip pain severity in patients with hip OA, who were not responding on oral analgesics.
Methods: Patients in primary and secondary care were included if they met the clinical ACR and radiographic (KL score $\geq$2) criteria for hip OA and scored a severity of hip pain $\geq$3 on a scale of 0–10 (0=no hip pain). Patients were randomized to receive either 40mg of triamcinolone acetate or saline (placebo) with an IA injection into the ipsilateral gluteus muscle. Primary outcome was severity of hip pain at 2 weeks, measured with numerical rating scale (NRS) in rest and during walking (0–10;0=no pain) and with the WOMAC pain subscale (0–100;0=no pain). Secondary outcomes included hip pain severity (NRS, WOMAC pain, ICOAP), function (WOMAC function), stiffness (WOMAC stiffness), adverse events, and medical co-interventions at 2, 4, 6, and 12 weeks follow-up. Statistical analyses were performed based on the intention to treat principle. Linear mixed models with repeated measurements were used to analyze between group differences. The models were adjusted for variables that changed the effect estimate >10%.
Results: 107 of 422 screened patients were randomized. After informed consent, one randomized patient did not show up at the appointment for baseline measurement and subsequent injection and could, because of lack of data, not be included in the analyses. Finally, 52 patients in the corticosteroid injection group, and 54 in the placebo injection group were included in the analyses. 68% of the patients were female, and 25% were recruited by orthopedic surgeons. Mean age was 64 years (SD 11) and duration of OA was $\geq$1 year for 70%. At 2 weeks follow-up (table), the corticosteroid injection was statistically significant and clinically relevant associated with hip pain reduction at rest (coefficient -1.3, 95% CI -2.3 to -0.3) compared to placebo. The corticosteroid injection was also associated with significant hip pain reduction at 4, 6 and 12 weeks. Moreover, at almost all follow-up measurements the estimates showed significant differences in favor of the corticosteroid injection on WOMAC pain, function, stiffness and total score, and ICOAP. No significant differences between groups were found for adverse events and medical co-interventions.

Table. Results of the multivariable linear mixed model analyses with repeated measurements regarding primary outcomes between corticosteroid and placebo group.

				Adjusted mixed model	
		Corticosteroid (n=52)	Placebo (n=54)	Between group difference * (95% CI)	p- value
Outcome; Mean (SD)					
NRS pain (rest) (0-10)	baseline	4.3 (2.4)	4.2 (2.5)		
	2 w	2.6 (2.3)	3.9 (2.5)	-1.3 (-2.3 to -0.3)	0.01
	4 w	2.8 (2.1)	3.9 (2.5)	-1.2 (-2.1 to -0.2)	0.01
	6 w	2.6 (2.3)	4.0 (2.6)	-1.4 (-2.4 to -0.5)	<0.01
	12 w	3.2 (2.4)	4.2 (2.8)	-1.2 (-2.3 to -0.2)	0.02
NRS pain (walking) (0-10)	baseline	5.4 (2.1)	5.1 (2.3)		
	2 w	3.5 (2.4)	4.2 (2.5)	-0.9 (-1.9 to 0.1)	0.07
	4 w	3.5 (2.2)	4.5 (2.5)	-1.1 (-2.0 to -0.2)	0.01
	6 w	3.4 (2.2)	4.6 (2.5)	-1.4 (-2.3 to -0.4)	<0.01
	12 w	4.0 (2.5)	5.0 (2.7)	-1.3 (-2.2 to -0.3)	0.01
WOMAC pain (0-100)	baseline	43 (17)	43 (17)		
	2 w	35 (18)	39 (17)	-6.1 (-13.4 to 1.2)	0.10
	4 w	34 (19)	39 (18)	-7.0 (-14.4 to 0.4)	0.06
	6 w	32 (18)	40 (20)	-9.9 (-17.7 to -2.2)	0.01
	12 w	33 (18)	40 (23)	-9.6 (-18.0 to -1.2)	0.03

Models adjusted for baseline hip KL-score, ethnicity, hip stiffness, and patients expected effect; * placebo group is reference group; SD = standard deviation; 95%CI = 95% confidence interval; WOMAC = Western Ontario and McMaster Universities Index (0 = no pain); NRS = Numerical Rating Scale (0 = no pain); ICOAP = Intermittent and Constant OsteoArthritis Pain (0 = no pain); w = weeks

Conclusions: An IM gluteal corticosteroid injection was effective in hip pain reduction compared to placebo injection in patients with hip OA at 2 weeks

folow-up. Moreover, the effect of the corticosteriod injection prolonged the entire 12 week follow-up period.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4767

SAT0493 MAINTAINING SUFFICIENT SERUM VITAMIN D LEVELS OVER TWO YEARS IS ASSOCIATED WITH IMPROVED KNEE STRUCTURAL AND SYMPTOMATIC OUTCOMES IN PEOPLE WITH KNEE OSTEOARTHRITIS: A POST HOC ANALYSIS OF THE VIDEO TRIAL

S. Zheng[1], X. Jin[1], F. Cicuttini[2], X. Wang[1], Z. Zhu[1], A. Wluka[2], W. Han[1], T. Winzenberg[1], B.E. Antony[1], D. Aitken[1], L. Blizzard[1], G. Jones[1], C. Ding[1].
[1]Menzies Institute for Medical Research, University of Tasmania, Hobart; [2]Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia

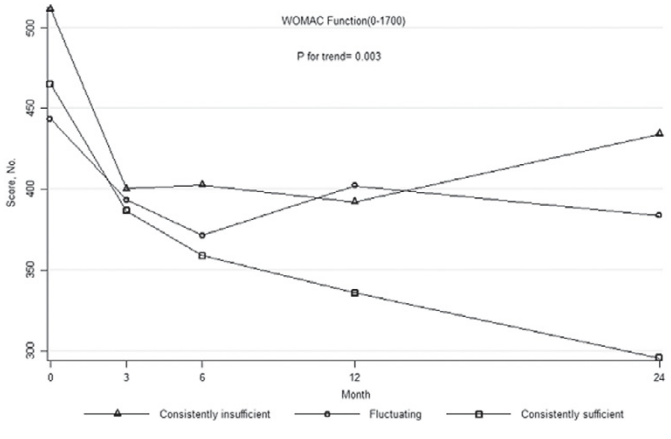
Objectives: To describe whether maintaining sufficient serum vitamin D levels in people with knee osteoarthritis (OA) and baseline vitamin D insufficiency has an association with change in knee structures and symptoms over two years.
Methods: Participants (n=413, age 63.2; 50% females) with symptomatic knee OA and vitamin D insufficiency were enrolled in a clinical trial. 340 participants (82.3%) completed the study with 25-hydroxyvitamin D [25(OH)D] measurements at month 0, 3 and 24. Participants were classified as consistently insufficient (serum 25(OH)D $\leq$50nmol/l at month 3 and 24, n=45), fluctuating (25(OH)D $>$50nmol/l at either point, n=68) and consistently sufficient (25(OH)D $>$50nmol/l at month 3 and 24, n=226) vitamin D groups. Knee cartilage volume, cartilage defects, bone marrow lesions (BMLs) and effusion-synovitis volume were assessed using MRI at baseline and month 24. Knee symptoms were assessed at baseline, month 3, 6 12 and 24 using Western Ontario and McMaster Universities Arthritis Index (WOMAC).
Results: The consistently sufficient group had significantly less loss of tibial cartilage volume (β: 2.1%, 95 CI%: 0.3%, 3.9%), less increase in effusion-synovitis volume (β: -2.5ml, 95 CI%: -4.7, -0.2) and less loss of WOMAC physical function (β: -94.2, 95% CI: -183.8, -4.5) compared to the consistently insufficient group in multivariable analyses. In contrast, there were no significant differences in these outcomes between the fluctuating and consistently insufficient groups. Changes in tibiofemoral cartilage defects, BMLs and knee pain were similar between groups.

Table 1. Associations between maintaining sufficient 25-(OH)D levels and changes in cartilage volume and effusion -volume over 24 months in patients with knee osteoarthritis

	Multivariable analysis	
	β (95% CI)	P Value
Total tibial Cartilage Volume Change (%/y)		
Consistently insufficient	*Reference*	
Fluctuating	1.5 (-0.5, 3.5)	0.15
Consistently sufficient	2.1 (0.3, 3.9)	**0.03**
P for trend		**0.02**
Effusion-Synovitis Absolute Volume Change (ml)		
Consistently insufficient	*Reference*	
Fluctuating	0.7 (-2.5, 3.9)	0.66
Consistently sufficient	-2.5 (-4.7, -0.2)	**0.03**
P for trend		**<0.01**

Adjusted age, sex and BMI and change in season of blood sampling.

Figure 1 Changes in WOMAC Function in knee OA patients with or without sufficient serum vitamin D levels over 24 months



Conclusions: This post hoc analysis suggests beneficial effects of maintaining vitamin D sufficiency on cartilage loss, effusion-synovitis and physical function in people with symptomatic knee OA.
References:
[1] Cao, Y., et al., Vitamin D supplementation in the management of knee osteoarthritis: study protocol for a randomized controlled trial. Trials 2012;13:131.
[2] Jin, X., et al., Effect of Vitamin D Supplementation on Tibial Cartilage Volume and Knee Pain Among Patients With Symptomatic Knee Osteoarthritis: A Randomized Clinical Trial. JAMA 2016; 315(10):1005–13.
Acknowledgements: We specially thank the participants who made this study possible, and we gratefully acknowledge the role of Vitamin D Effect on Osteoarthritis Study staff and volunteers in collecting the data. We thank the research assistants Jodi Barling, Kay Nguo, Judy Hankin and Alice Noone who were involved in the coordination of this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1056

SAT0494 EARLY TOLL-LIKE RECEPTOR 4 BLOCKADE IMPEDES THE BEHAVIOURAL AND HISTOLOGICAL CHARACTERISTICS OBSERVED IN A MIA-INDUCED ANIMAL MODEL OF OSTEOARTHRITIC PAIN

M.M. Garcia[1,2], D. Pascual[1,2], E. Quesada[2,3], J.A. Uranga[4], C. Goicoechea[2,5].
[1]Pharmacology, Universidad Rey Juan Carlos, Alcorcón; [2]Unidad Asociada URJC-IQM-CSIC, Madrid- Alcorcón; [3]Grupo Nucleósidos, Instituto química médica CSIC, Madrid; [4]Histología, Universidad Rey Juan Carlos, Alcorcón; [5]Pharmacology, Universidad Rey Juan Carlos, Madrid, Spain

Background: Contribution of Toll-Like Receptor 4 (TLR4) to pain sensitisation has been demonstrated to occur under chronic pain conditions. We previously described an antinociceptive effect of TLR4-A1, a TLR4 inhibitor, in two chronic pain conditions, peripheral neuropathic pain and osteoarthritis (OA).
Objectives: The aim of this study was to evaluate TLR4-A1 effect on allodynia and hyperalgesia in OA model, and to evaluate whether this effect is correlated with changes in spinal glial activation.
Methods: Wistar rats weighing 200–250g were used. OA was induced by a single intraarticular injection of 2mg of monosodium iodoacetate (MIA) into the right knee joint of anaesthetised rats. TLR4-A1, 10 $mgkg^{-1}$, was intraperitoneally administered during the first five days post-MIA injection. TLR4-A1 was synthesised by Dr Quesada. Vehicle-treatment (ethanol:saline, 1:9) was used as control. Each group was composed of 6 animals. After three weeks (day 22 post-MIA injection), animals were sacrificed for tissue collection. L3-L5 spinal segments were collected and embedded in paraffin wax. Eventually, samples were immune-stained with anti-GFAP or Iba-1 antibodies. Photomicrographs were recorded to make montages of the entire spinal cord at a final magnification of 20x (n=3 per lumbar section). Total number of GFAP or Iba-1 positive cells were counted separately in laminas I-II, III-IV and V-VI.
Results: Intraarticular injection of MIA increased microglial expression (Iba-1 labelling) in the ipsilateral spinal cord compared to the contralateral side, being the difference statistically significant for the superficial (I-II, +72.25%; $P<0.01$) and deeper (V-VI, +95.31%; $P<0.001$) laminae of L3 and for the superficial laminae of L4 (+87.5%; $P<0.01$). In animals treated with TLR4-A1, Iba-1 labelling in the ipsilateral dorsal horn showed a similar pattern to the contralateral dorsal horn. Pre-treatment with TLR4 blocker prevented microglia activation after MIA-injection in L3 and L4 segments.
Intraarticular injection of MIA also increased the number of GFAP-positive activated astrocytes in the ipsilateral spinal cord compared to the contralateral side; in this case, statistically significant differences were found for the superficial (I-II; +41.62%; $p<0.01$) and middle (III-IV; +64.35%, $p<0.001$) laminae of L3 sections. GFAP in TLR4-A1-treated rats showed a similar pattern for the ipsi- and the contra-lateral sides. That is, TLR4-A1 prevented L3 increased activated astroglia following MIA-injection.
Conclusions: Early toll-like receptor 4 blockade hampers spinal glial activation, which correlates with diminished allodynia and hyperalgesia observed in TLR4-A1-treated animals in a model of MIA-induced OA. Although further studies are needed, TLR4 blockade could be a good option in the treatment of osteoarthritis.
Acknowledgements: Franco R and Marquez A for technical support.
Granted: Ministerio de Economía y Competitividad. SAF2012–40075-C02–01.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6022

SAT0495 KNEE FUNCTION AND ENTHESITIS IN LONG STANDING OSTEOARTHRITIS, WHAT ULTRASOUND COULD TELL US?

A. Abogamal, H. Aly, S. Ghanem, H. Saad on behalf of AL-Azhar MSUS school.
Rheumatology, Alazhar Faculty of Medicine, Cairo, Egypt

Background: The enthesis around the knee including the quadriceps tendon and infrapatellar ligament insertions could be responsible for a significant cause of knee pain functional deterioration in long standing knee osteoarthritis.
Objectives: Ultrasound evaluation of the enthesis at the quadriceps tendon patellar insertion, infrapatellar ligament patellar and tibial insertions in patients with long standing knee osteoarthritis (KOA) and low knee function.
Methods: 410 Patients with KOA attending the outpatient rheumatology clinic of AL-Azhar university hospitals who had met the inclusion criteria:
- Primary Knee osteoarthritis.
- Kellegren – Lawrance scale grade III.
- At least 5 years disease duration.

Exclusion criteria:
- Patients with chronic diseases affects the patient function.

• Patients with previous knee surgery, recent trauma, or intraarticular intervention.
• Patients with knee effusion, active synovitis, or popliteal cysts.
All patients were subjected to ultrasound assessment in gray scale and Power Doppler was performed using a scanner with a multifrequency 12L linear array transducer (General electric Systems; LOGIQU-E). Ultrasound techniques were used for all patients included in the study. Knee was assessed for the following items in both sides while Patient lying supine with the knee flexed 40 degrees:
1) Superior pole of the patella – quadriceps tendon enthesis: • Quadriceps tendon thickness >6.1 mm • Suprapatellar bursitis • Superior pole of patella erosion • Superior pole of patella enthesophyte.
2) Inferior pole of the patella – proximal patellar ligament enthesis: • Patellar ligament thickness >4 mm • Inferior pole of patella erosion • Inferior pole of patella enthesophyte.
3) Tibial tuberosity – distal patellar ligament enthesis • Patellar ligament thickness >4 mm • Infrapatellar bursitis • Tibial tuberosity erosion • Tibial tuberosity enthesophyte.
Knee functional status was assessed using KOOS scale for Pain, other Symptoms, Activities of Daily Living (ADL), Sport and Recreation Function (Sport/Rec) and knee-related Quality of Life (QOL). Low knee function was considered if the patient had score 50 or more in any KOOS scale parameter.
Results: 172 (42%) patients were found with low knee function among them quadriceps enthesitis found in 114 (66.3%) patients, at the patellar attachment of infrapatellar ligament in 160 (93%) patients, and enthesitis at the tibial attachment of infrapatellar ligament in 44 (26%) patients. Good knee function were found in 238 (58%) patients among them quadriceps enthesitis found in 76 (31.9%) patients, at the patellar attachment of infrapatellar ligament in 87 (36.3%) patients, and no enthesitis at the tibial attachment of infrapatellar ligament were detected.
Conclusions: Enthesitis at the quadriceps and infrapatellar ligament represent a common ultrasonographic finding in patients with longstanding KOA, and significantly associated with low knee function.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4284

SAT0496 SAFETY OF DIACEREIN IN PATIENTS WITH OSTEOARTHRITIS – A REAL WORLD EXPERIENCE WITH UNEXPECTED RESULTS

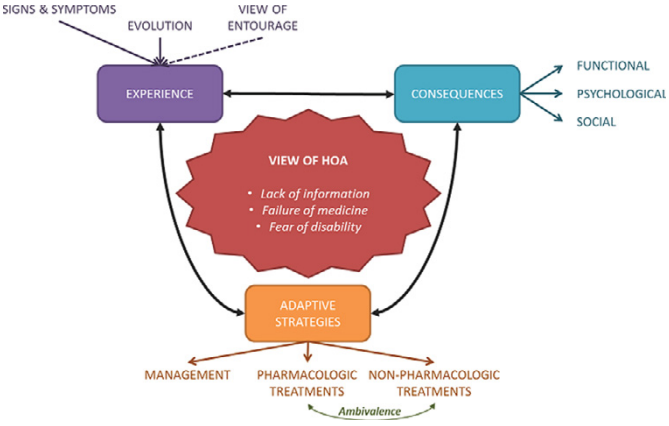
A. Malpica[1], K. Mendez[2], P. Santos-Moreno[3,3,3], L. Villarreal[4], D. Buitrago-Garcia[1]. *[1]Epidemiology; [2]Pharmaceutical chemist; [3]Rheumatology; [4]Psychology and processes, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: Osteoarthritis (OA) is a common joint disorder and may occur in any synovial joint in the body, the condition is common in hands, knees, hips and spine. Diacerein is a antraquinone derivate has shown the inhibition of cytokine interleukine 1-B (1). A Cochrane review published in in 2014 showed that diacerein could be effective for this condition, however the most frequent adverse event with this medication was diarrhea compared to placebo RR 3.52 (95% CI 2.42 to 5.11) or other symptomatic slow acting drugs for OA 3.20 (95% CI 1.58 to 6.49) (2).
Objectives: To describe the real-world safety of Diacerein in patients with OA in a specialized center in Bogotá, Colombia.
Methods: We performed a cross-sectional study; patients with confirmed criteria of osteoarthritis and treated on a regularly basis with Diacerein were included. Patients were followed during a 18 month period. Adverse events were classified according the Common Terminology Criteria for Adverse Events (CTCAE) of the World Health Organization. Descriptive epidemiology for continuous variables, measure of central tendency and dispersion for qualitative and categorical variables through percentages and averages were calculated, we analyzed bi-variated correlations with X2 test.
Results: 1278 patients meet inclusion criteria; mean age was 62 year ± 10 years. 88% were female and 12% male, due to our patient's condition 80% of them were polimedicated. 93% of our patients received diacerein in usual dose of 100 mg daily and remaining 7% in a 50 mg day dose. Regarding safety 7.5% (n=96) of our patients reported any event adverse, the most frequent event was diarrhea with 50%, followed by nausea and abdominal disturbances among others. According to the CTAE classification the events adverse were mild 98% and only 2% severe; that means only 0.075% of total of patients receiving Diacerein had severe AE. On the other hand, correlation between adverse events and polymedication were statistical significant (P=0.000). For this reason we consider that AE such as diarrhea can be attributed more to patients' polymedication than diacerein.
Conclusions: This evidence showed a low proportion of patients with adverse events taking Diacerein; also most of these patients were polymedicated giving as a result a higher risk of having an adverse event. When we compared our results to other studies diarrhea was the most frequent event, followed by nausea, but only a very low proportion of patients were forced to discontinue medication. It is important to continue following patients that take diacerein in order to report its true safety and effectiveness.
References:
[1] Bartels EM, Bliddal H, Schondorff PK, Altman RD, Zhang W, Christensen R. Symptomatic efficacy and safety of diacerein in the treatment of osteoarthritis: a meta-analysis of randomized placebo-controlled trials. Osteoarthritis and cartilage. 2010;18(3):289–96.
[2] Fidelix TS, Macedo CR, Maxwell LJ, Fernandes Moca Trevisani V. Diacerein for osteoarthritis. The Cochrane database of systematic reviews. 2014(2):Cd005117.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5272

SAT0497 WHAT ARE THE PATIENTS' EXPERIENCE, NEEDS AND EXPECTATIONS IN HAND OSTEOARTHRITIS? A QUALITATIVE EVALUATION

M.-A. Offroy, A. Frazier-Mironer. *Centre Viggo Petersen, Rheumatology Department, APHP Lariboisière Hospital, Paris, France*

Background: The objective of this study was to evaluate the patients' experience and needs with HOA, in order to establish a therapeutic education program for HOA patients.
Objectives: As the subject was about descriptive, not quantifiable elements, qualitative methodology was chosen. Patients were submitted to individual semi-directive interviews. Verbatim were analyzed following the grounded theory until saturation of data.
Methods: Twelve HOA patients accepted to participate to the study. There were 10 women and 2 men, aged 45 to 79 years. Body-mass indexes varied from 18.7 to 31.6 kg/m^2. Clinical and radiological severity of HOA varied among patients.
They provided data on the experience of HOA, which is influenced by clinical and functional signs and the evolution of the disease. Pain and deformity are the main clinical signs, and lead to severe functional impairment. The functional, psychological, social consequences of HOA also have an impact on the patient experience. Patients develop adaptive strategies, mainly recourse to medical management, and pharmacological and non-pharmacological therapies. The needs of HOA patients were also explored, and three main ideas emerged. First, they want to be better informed on HOA. Second, they have a feeling of failure of conventional medicine, and often use alternative medicines. Third, the fear of disability with the course of the disease is very strong. They have difficulty accepting pharmacological treatments, but often do not realize the therapeutic nature of non-pharmacological treatments.
Results: The main concerns of HOA patients are: information, non-pharmacological treatments and evolutionary risks. These themes should be included in the development of therapeutic education programs for HOA.



References:
[1] We thank Pr François Rannou, Pr Pascal Richette and Pr Eric Roulot for providing access to HOA consultation in their centers for recruitment. We thank Dr Laurence Baumann-Coblenz for her advice in qualitative methodology.
Acknowledgements: We thank Pr François Rannou, Pr Pascal Richette and Pr Eric Roulot for providing access to HOA consultation in their centers for recruitment. We thank Dr Laurence Baumann-Coblenz for her advice in qualitative methodology.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1203

SAT0498 THE PERFORMANCE OF URINARY COLLAGEN TYPE II C-TELOPEPTIDE (UCTX-II) IN KNEE OSTEOARTHRITIS: A META-ANALYSIS

B. Jeremiasse, F.P. Lafeber, W.E. Van Spil. *Department of Rheumatology and Clinical Immunology, UMC Utrecht, Utrecht, Netherlands*

Background: Among the currently available biochemical markers for osteoarthritis (OA), urinary collagen type II C-telopeptide (uCTX-II) is one of the most frequently investigated markers[1]. Much research has been performed into the performance of uCTX-II, but most of it in relatively small cohort studies[1]. Therefore, we performed a meta-analysis to summarize uCTX-II studies in a quantitative way.
Objectives: To perform a meta-analysis of the performance of uCTX-II as a biomarker for diagnosing knee osteoarthritis (KOA) and its association with radio-

graphic KOA severity. Furthermore, to look for patient and study characteristics that determine uCTX-II performance.

Methods: Medline and Embase databases were searched for studies into uCTX-II levels in adult subjects with radiographic KOA according to the Kellgren and Lawrence (K&L) classification system. uCTX-II levels were compared between subjects with KOA K&L ≥2 versus healthy control subjects and between subjects with KOA K&L 2 versus K&L 3–4 (i.e. moderate vs severe KOA). Controls were either selected based on lack of knee symptoms, based on K&L score, or were randomly selected from the general population. Differences between KOA subgroups were expressed as standardized mean differences (SMD). Subgroup analyses were performed to compare uCTX-performance between genders, ethnicities, and large and small studies. Differences between subgroups were considered relevant when SMDs differed >25% between groups.

Results: 2035 Studies were screened for eligibility, of which ten studies were included. A moderate pooled SMD of 0.52 (confidence interval (CI): 0.40–0.65, P<0.0001) was found for subjects with KOA K&L ≥2 versus controls, based on ten SMDs. For K&L3–4 versus K&L2 a moderate pooled SMD of 0.47 (CI: 0.32–0.63, P<0.0001) was found, based on five SMDs. No indications for publication bias were identified using funnel plots. Subgroup analyses of the K&L ≥2 versus control comparison showed that uCTX-II performs better in women as compared to men and in Caucasian subjects as compared to other ethnicities. Study size did not influence the pooled SMD. Subgroup analysis was considered infeasible for the K&L 2 versus K&L 3–4 comparison due to a limited number of studies.

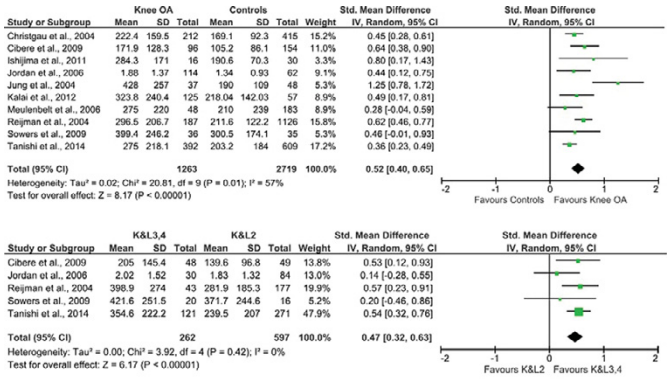


Figure 1: Forest plots for the comparisons of uCTX-II levels between subjects with radiographic KOA and controls and between subjects with KOA K&L3,4 and K&L2.

Conclusions: This is the first meta-analysis of uCTX-II performance in subjects with radiographic KOA. It appeared that uCTX-II levels can distinguish with moderate strength between radiographic KOA subjects and controls. Moreover, uCTX-II levels are consistently increased in severe versus moderate radiographic KOA. Female gender and Caucasian ethnicity were found to enhance uCTX-II performance in distinguishing radiographic KOA from controls. Yet, the number of studies was relatively small and criteria for KOA and control subjects differed between studies.

References:

[1] Van Spil WE, DeGroot J, Lems WF, Oostveen JCM, Lafeber FPJG. Serum and urinary biochemical markers for knee and hip-osteoarthritis: A systematic review applying the consensus BIPED criteria. Osteoarthr Cartil 2010;18(5):605–12. Doi: 10.1016/j.joca.2010.01.012.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2342

SAT0499 IDENTIFICATION OF BIOCHEMICAL PHENOTYPES IN KNEE OSTEOARTHRITIS: LONGITUDINAL DATA FROM THE FNIH OA BIOMARKER CONSORTIUM

B. Jeremiasse[1], P.M. Welsing[1], C. Fellows[2], F.P. Lafeber[1], W.E. Van Spil[1].
[1]Department of Rheumatology and Clinical Immunology, UMC Utrecht, Utrecht, Netherlands; [2]School of Veterinary Medicine, University of Surrey, Guildford, United Kingdom

Background: It is hypothesized that patients with knee osteoarthritis (OA) can be classified into different phenotypes. Knowledge of these phenotypes may contribute to developing effective targeted treatment strategies.

Objectives: To identify different longitudinal phenotypes of knee OA using biochemical markers and to compare these phenotypes with regard to radiographic joint space loss (JSL) and/or pain progression.

Methods: Baseline, 1-year, and 2-year biochemical marker data from the FNIH OA Biomarker Consortium were used. This consortium is a nested case-control study of 600 subjects with one symptomatic index knee showing radiographic OA changes of Kellgren and Lawrence grade 1 to 3[1]. Subjects were classified as either JSL progressors, pain progressors, JSL+pain progressors, or non-progressors according to predefined criteria (pain progression=persistent increase in WOMAC pain≥9 points (0–100 scale) from baseline to 2, 3 or 4 years, JSL progression=decrease in JSW≥0.7mm from baseline to 2, 3 or 4 years).
Biochemical markers included in the current analysis were sCTX-I, uαCTX-I, uβCTX-I, sNTX-I, uCTX-II, sCPII, sC2C, sC1,2C, sColl2–1 NO2, sCOMP, sHA, and sMMP (u=urinary, s=serum). First, using principal component analysis (PCA), the individual markers were reduced into a number of clusters of markers (components) that may represent common underlying domains. Second, a hierarchical cluster analysis (HCA) was performed to differentiate between longitudinal courses (phenotypes) of these marker clusters. The optimum number was determined from the additive value of each newly identified phenotype as compared to already identified phenotypes. Third, these longitudinal phenotypes were compared with regard to percentages of patients in each of the JSL and/or pain progression categories.

Results: PCA showed an optimal solution of three components. Looking at the markers that loaded maximally onto each of the components, they were interpreted as cluster of bone (sCTX-I, uαCTX-I, uβCTX-I, sNTX-I, uCTX-II), cartilage (sCPII, sC2C, sC1,2C, sColl2–1 NO2), and synovial (sCOMP, sHA, and sMMP) metabolism, respectively. HCA revealed an optimum of seven longitudinal phenotypes. Based on the relative predominance of the component(s) throughout follow-up, phenotypes were named “high bone”, “high cartilage”, “high synovium”, “low cartilage”, “low synovium”, “low bone, cartilage and synovium” and “low bone and high synovium” phenotype, respectively (Figure 1, dendrogram and heatmap). Phenotypes differed with regard to percentages of patients in JSL and/or pain progression categories (Figure 1, pie charts) as well as other demographic, clinical, and radiographic parameters (data not shown).

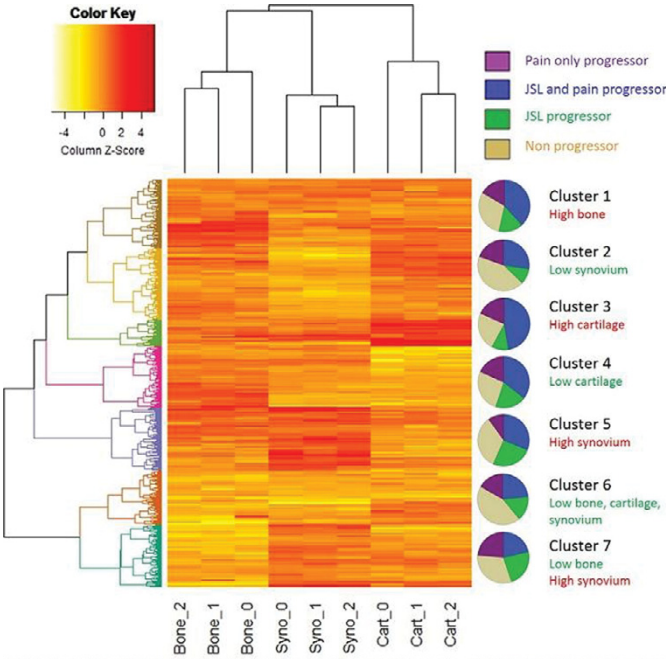


Figure 1: Heatmap depicting scores for the bone (bone), synovium (syno), and cartilage (cart) component for individual knee OA patients at baseline (_0), 1 year (_1), and 2 years (_2). Patients were classified into seven phenotypes using HCA, represented by the dendrogram at the left side. Percentages of subjects in the pain, JSL, pain+JSL, and no progression subgroups in each of the phenotypes are represented in the pie charts at the right side.

Conclusions: Seven longitudinal phenotypes of knee OA could be identified based on biochemical markers representing bone, cartilage and synovial metabolism. These phenotypes showed relevant differences in other characteristics, such as JSL and/or pain progression.

References:

[1] Kraus VB, Collins JE, Hargrove D, et al. Predictive validity of biochemical biomarkers in knee osteoarthritis: data from the FNIH OA Biomarkers Consortium. Ann Rheum Dis. 2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5825

SAT0500 SLEEP DISTURBANCE, KNEE INFLAMMATION, AND SYMPTOMS IN KNEE OSTEOARTHRITIS

C.K. Kwoh[1], E. Ashbeck[1], A. Guermazi[2], F.W. Roemer[2,3], S. Parthasarathy[4].
[1]Univ. of Arizona Arthritis Center, Univ. of Arizona (UA), Tucson; [2]Radiology, Boston Univ., Boston, United States; [3]Radiology, Univ. of Erlangen-Nuremberg, Erlangen, Germany; [4]UAHS Center for Sleep & Circadian Sciences, UA, Tucson, United States

Background: Sleep disturbance has been shown to contribute to systemic inflammation, as well as increased pain sensitization. The role of sleep disturbance in knee osteoarthritis (OA) has not been established. Sleep disturbance may be an aggravating contributor to and/or a consequence of knee OA symptoms, with inflammation serving as a potential mediator.

Objectives: To compare knee symptoms over nine years of follow-up by

frequency of sleep disturbance at baseline, among participants with or at risk for radiographic knee OA (ROA), and to estimate the association between the presence of inflammation on knee MRI and pain that disturbs sleep among knees that developed ROA.

Methods: Knees from the Osteoarthritis Initiative (OAI) with or at risk for ROA were included in this longitudinal analysis. Self-reported frequency of restless sleep in the past week was assessed using a CES-D question. Knee symptoms were assessed annually using the WOMAC. Knees that developed incident ROA (i.e., ≥2 Kellgren-Lawrence grade, KLG) through four years of follow-up were assessed for effusion-synovitis on non-contrast-enhanced 3T MRI using the MRI Osteoarthritis Knee Score (MOAKS) from annual clinic visits between four years prior to incident ROA and up to one year after ROA detection. Effusion-synovitis represents a combination of joint effusion and synovial thickening on fluid-sensitive sequences and scored as 0 (normal), 1 (mild), 2 (moderate), or 3 (severe). Annual mean WOMAC total score was estimated using a mixed model with participant and knee treated as random effects, in 5,028 knees at risk for ROA at baseline, and in 3,893 knees with ROA at baseline. Log-binomial regression with generalized estimating equations was used to estimate the association between effusion-synovitis and knee pain in bed that disturbs sleep, adjusted for age, sex, and BMI in a sample of 355 knees with an average of 3.8 MRI assessments.

Results: There was dose-dependent effect, with participants reporting restless sleep 1–2 days, 3–4 days, and 5–7 days in the past week having higher mean WOMAC total scores compared to those who reported <1 day of restless sleep (i.e., difference in means: 2.5 [95% CI: 1.3 to 3.8], 5.1 [95% CI: 3.2 to 7.1], and 10.1 [95% CI: 7.6 to 12.6], respectively) among knees with ROA (KLG≥2) at baseline. Differences in average WOMAC total score between groups were relatively persistent over nine years (Figure 1). A similar dose-dependent effect of restless sleep was observed among knees at risk of ROA (i.e., KLG 0 or 1). Among knees that developed incident ROA, those with mild effusion-synovitis had a 52% higher risk of knee pain in bed that disturbs sleep at the same visit (RR=1.52; 95% CI: 1.13 to 2.04), while knees that had moderate/severe effusion-synovitis had more than double the risk of knee pain that disturbs sleep (RR=2.55; 95% CI: 1.87 to 3.47), compared to knees with no MRI-detected effusion-synovitis.

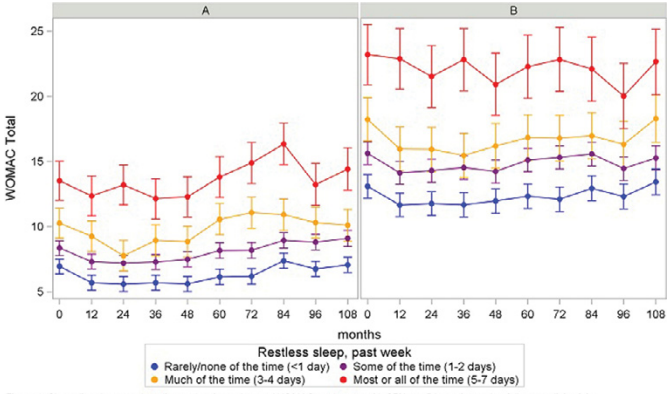


Figure 1. Sleep disturbance at baseline and estimated mean WOMAC total score with 95% confidence interval at follow-up clinic visits
A. Knees at risk for radiographic knee OA at baseline (KLG 0 or 1), B. Knees with radiographic knee OA at baseline (KLG 2+)

Conclusions: Restless sleep was associated with knee symptoms and disability in a dose-dependent manner, with average levels persistent over nine years of follow-up among knees with and at risk of ROA. Effusion-synovitis was associated with pain that disturbs sleep among knees that developed incident ROA. Sleep disturbance and knee inflammation may be important targets for interventions in knee osteoarthritis.

Disclosure of Interest: C. K. Kwoh Grant/research support from: Abbie, EMD Serono, E. Ashbeck: None declared, A. Guermazi Grant/research support from: Boston Imaging Core Laboratory, Consultant for: MerckSerono, TissueGene, Ortho Trophix, AstraZeneca, Genzyme, F. Roemer Grant/research support from: Boston Imaging Core Laboratory, S. Parthasarathy: None declared

DOI: 10.1136/annrheumdis-2017-eular.6273

SAT0501 PREVALENCE OF HAND OSTEOARTHRITIS IN A MODEL OF AUTO-IMMUNE DISEASE, SJÖGREN SYNDROME: RESULTS OF A PROSPECTIVE STUDY

C. Glanowski[1], J. Sellam[1], E. Bergé[2], R. Seror[2], A.-L. Tomi[3], X. Chevalier[3], F. Berenbaum[1], X. Mariette[2], R. Belkhir[2]. *[1]Rheumatology, Hôpital Saint Antoine, Paris; [2]Rheumatology, Hôpital de Bicêtre, le Kremlin-Bicêtre; [3]Rheumatology, Hôpital Henri Mondor, Créteil, France*

Background: Despite the role of chronic low-grade inflammation in osteoarthritis (OA), prevalence of OA during inflammatory or auto-immune diseases remains poorly assessed. A single study without a valid control group [1] and daily practice suggest an increased frequency of hand OA (HOA) in primary Sjögren Syndrome (pSS).

Objectives: We aimed investigate the prevalence of radiographic, symptomatic or erosive HOA in pSS and to compare these results with age and sex-matched control population suffering from dry eyes and mouth without auto-immune manifestation (sicca patients).

Methods: We included women with pSS fulfilling 2002 AECG European-American criteria and control women suffering from sicca symptoms without autoimunity who underwent a multidisciplinary day hospital. Standardized radiographs of hands were performed and were all read by an experimented reader. Radiographic HOA was defined as Kellgren-Lawrence score ≥2 on at least one joint. Erosive HOA was defined using the Verbruggen scoring system (phase E, subchondral erosion or R, remodelling of subchondral plate). Symptomatic HOA was defined as radiographic HOA associated with spontaneous hand joint pain and/or with a FIHOA ≥5 at the time of radiographs. We compared pSS versus sicca patients, pSS with radiographic HOA (pSS+, HOA+) versus pSS without radiographic HOA (pSS+, HOA-), and finally pSS with radiographic HOA (pSS+, HOA+) versus sicca patients with radiographic HOA (pSS-, HOA+).

Results: We included 34 patients with pSS (median age [range] 54.5 [28–84] years) and 54 patients with only sicca symptoms (57 [24–85] years). Among pSS patients, 41% had radiographic HOA, 12% had symptomatic HOA and 9% had erosive HOA. These prevalences did not differ from sicca patients (52% radiographic HOA p=0.45, 28% symptomatic HOA p=0.11, 9% erosive HOA p=1.0). The trend for a higher prevalence of symptomatic HOA in sicca patients compared to pSS is expected since these patients frequently suffer from dryness associated with fibromyalgia. In pSS patients, radiographic HOA was associated with a higher average age (pSS+HOA+:63,5 versus pSS+HOA-: 48,5 years old, p<0,01), with menopause (pSS+HOA+: 100% versus pSS+HOA-: 45%, p<0,01) and hypothyroidism (pSS+HOA+: 64% versus pSS+HOA-: 25%, p=0.04). There was no pSS feature such as autoantibodies profile or pSS disease activity, associated with radiographic or symptomatic HOA. Finally, HOA symptoms did not differ between patients with pSS and sicca symptoms. The prevalence of radiographic and erosive HOA in pSS and non-autoimmune sicca group seems in the same range as that observed in women from Framingham's cohort (44% and 10% respectively). And prevalence of symptomatic HOA seems similar in the pSS (12%) and in women from Framingham's cohort (16%).

Conclusions: The prevalence of HOA is not increased in pSS, a model of auto-immune diseases. Patients with pSS have the same HOA risk factors than in general population (age and menopause) and also hypothyroidism that may be involved in OA pathophysiology.

References:

[1] Aksoy and al, J Rheumatol 2016.
[2] Mariette and al, Rheumatology (Oxford) 2003.
[3] Haugen and al, Ann Rheum Dis 2011.

Acknowledgements: Osteoarthritis group of French Society of Rheumatology.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2476

SAT0502 A RANDOMIZED, PLACEBO-CONTROLLED, PROOF-OF-CONCEPT EFFICACY STUDY OF A MICROSOMAL PROSTAGLANDIN E SYNTHASE-1 (MPGES1) INHIBITOR AND A PROSTAGLANDIN E RECEPTOR (EP4) ANTAGONIST IN THE TREATMENT OF CANINE OSTEOARTHRITIS PAIN

C. Robertson-Plouch[1], J.R. Stille[2], P. Liu[1], S. Malcolm[2], D. Brown[3], M. Warner[1], M.J. Fisher[1]. *[1]Lilly Research Laboratories; [2]The Chorus Group, Eli Lilly and Company, Indianapolis; [3]School of Veterinary Medicine, University of Pennsylvania, Philadelphia, United States*

Background: Inflammation is a known contributor to osteoarthritis (OA) pain in animals and humans. While translation of human treatments to companion dogs is common, translation from companion dogs to humans is less frequent. We present results of a clinical study, in client-owned canines with moderate OA pain, which evaluated the efficacy of 2 molecules targeting the actions of prostaglandin E, either by modulating its production (mPGES1 inhibitor; LYA), or subsequent pharmacology through 1 of its 4 receptors (EP4 antagonist, LYB).

Objectives: To provide translational and comparative data to inform the potential utility of each of these mechanisms for treatment of chronic OA pain in humans and dogs.

Methods: A multicenter, randomized, double-blind, placebo (PBO)- and active-controlled trial in client-owned canine patients with moderate OA pain in ≥1 hindlimb/forelimb joint. Dogs ≥2 years of age with Liverpool Osteoarthritis in Dogs (LOAD) Mobility total score ≥13 to <46 were randomized (1:1:1:1) to 2 weeks of LYA (1.5 mg/kg/day), LYB (25 mg/kg/day), carprofen (4.4 mg/kg/day), or PBO. Efficacy versus PBO was assessed by mean change from baseline (CFB) to Week 2 in the Canine Brief Pain Inventory (CBPI) Pain Interference (PI) Score (primary endpoint), and for secondary endpoints: CBPI Pain Severity (PS) and Overall Impression (OI) subscores, and LOAD Mobility score. Data were analyzed by mixed-effect model for repeated measures with treatment, time, and interaction of treatment and time as fixed effects, and with baseline score, site, and weight as covariates. Posterior probability of treatments being superior to PBO was calculated with Bayesian methods.

Results: Of 163 dogs randomized, 158 (96.9%) completed the study. Treatment arms were well-balanced for baseline characteristics (mean [standard deviation] age: 9.3 [3.0] years, weight: 54.6% 15–32 kg, 45.4% >32–50 kg, CBPI PI: 5.1 [2.1]; CBPI PS: 4.2 [1.9]; LOAD Mobility: 24.1 [5.6]). Improvements (CFB) in CBPI PI were observed in all treatment groups after 2 weeks (Table). For LYA,

the probablility of superiority to PBO was 80% for CBPI PI and 89% to 96% for secondary endpoints. LYB showed inconsistent separation from PBO across the endpoints, with probablilty of superiority to PBO 54% to 89%. The separation of carprofen and PBO arms demonstrated assay sensitivity. The incidence of adverse events for LYA (35.9%) was comparable to that of carprofen (25.6%) and PBO (32.6%). For LYB, the incidence was significantly higher versus PBO (59.5%, P=.017).

Mean CFB to Week 2 in primary and secondary efficacy endpoints and probability of being superior to PBO

	LYA (n=39)	LYB (n=42)	Carprofen (n=39)	PBO (n=43)
CBPI PI (Primary)				
LS mean CFB (95% CI)	-1.85 (-2.44, -1.25)	-1.54 (-2.14, -0.95)	-2.12 (-2.73, -1.52)	-1.50 (-2.07, -0.92)
Prob. superior to PBO, %	80	54	93	
CBPI PS				
LS mean CFB (95% CI)	-1.66 (-2.14, -1.18)	-1.39 (-1.87, -0.91)	-1.56 (-2.05, -1.08)	-1.14 (-1.60,-0.68)
Prob. superior to PBO, %	94	78	90	
CBPI OI				
LS mean CFB (95% CI)	0.56 (0.30, 0.82)	0.37 (0.11, 0.63)	0.61 (0.35, 0.87)	0.35 (0.10, 0.59)
Prob. superior to PBO, %	89	56	93	
LOAD Mobility				
LS mean CFB (95% CI)	-6.18 (-8.38, -3.97)	-5.43 (-7.61, -3.24)	-7.52 (-9.75, -5.28)	-3.55 (-5.68, -1.42)
Prob. superior to PBO, %	96	89	99	

CI=confidence interval; LS=Least squares; Prob.=probability

Conclusions: The study results support an efficacy proof-of-concept signal for the mPGES1 inhibitor mechanism for treatment of chronic OA pain in canine patients.

Acknowledgements: We also thank Leijun Hu, Alain Frix, and Claire Smith of Eli Lilly and Company for their contributions to the study.

Disclosure of Interest: C. Robertson-Plouch Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, J. Stille Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, P. Liu Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Malcolm Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, D. Brown Grant/research support from: AlcheraBio, Centrexion Corporation, Enceladus, Integrated Chinese Medicine Holdings, and Regeneus, M. Warner Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, M. Fisher Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company

DOI: 10.1136/annrheumdis-2017-eular.3113

SAT0503 CAN BALNEOTHERAPY MODIFY MICRORNA EXPRESSION LEVELS IN OSTEOARTHRITIS? A COMPARATIVE STUDY IN PATIENTS WITH KNEE OSTEOARTHRITIS TREATED WITH MUD-BATH THERAPY

C. Giannitti, A. De Palma, S. Cheleschi, J. Facciolo, N.A. Pascarelli, M. Galeazzi, A. Fioravanti. *Department of Medicine, Surgery and Neurosciences., Rheumatology Unit, Policlinico le Scotte, Siena, Italy*

Background: MicroRNAs (miRNAs) are a class of 19–23 nucleotides long non-coding RNAs that post-transcriptionally regulate the activity of target mRNAs. MicroRNAs are involved in cartilage homeostasis and play an important role in the pathogenesis of osteoarthritis (OA). They have been detected in human plasma and in synovial fluid and are considered as potential diagnostic biomarkers and therapeutic targets of OA. Balneotherapy is a common non-pharmacological treatment for OA patients. In a previous published prospective single-blind randomized clinical trial in patients with knee OA, we showed that a cycle of mud-bath therapy (MBT) in addition to conventional treatments induced an improvement on pain, functional capacity and quality of life in comparison to standard treatment alone.

Objectives: as part of this study we evaluated the whole blood levels of miR-155, 223, 181a, 146a and miR-let-7e, which are involved in the pathogenesis of OA.

Methods: Thirty-two patients aged between 50 and 75 years with knee OA defined by the ACR criteria were included for the current analysis, based on the availability of blood sample at basal time and after 2 weeks. Twenty-one patients (MBT group) were daily treated with a combination of daily local mud-packs at 42°C and baths in mineral water, at 37°C for 15 min, for a total of 12 applications over a period of 2 weeks, in addition to standard therapy; the other eleven patients (control group) continued their conventional treatment alone.

Clinical parameters [global pain score by a 0–100 mm Visual Analog Scale (VAS); physical function, total pain score and total stiffness score (WOMAC)] and microRNAs expression were performed at basal time and after 2 weeks. Peripheral whole blood was collected into PAXgeneTM Blood RNA tubes and then stored a -80°C. Total RNA was extracted using the PAXgeneTM Blood miRNA kit and the relative expression of miR-146a, miR-155, miR-223, miR-181a and miR-let-7e were determined by qRT-PCR.

Results: At the end of MBT we observed a statistically significant improvement of clinical paramethers. Furthermore, we observed a significant decrease of miR-155, 181a and miR-146a ($p<0.001$) and of miR-223 ($p<0.01$) expression levels. On the contrary, no clinical and biochemical modifications were detected in the control group. Concerning miR-let-7e expression levels no significant variations were showed in both groups after 2 weeks.

Conclusions: Our data showed that MBT can modify the expression levels of miR-155, 181a, 146a and 223 expression levels, that are up-regulated in OA. This MBT effect could be explained considering the role of the heat stress and of the hydrostatic pressure, since some miRNAs were found to be temperature and mechano-responsive. Further studies are needed to better explain the mechanism of action of MBT and the role of miRNAs in OA.

References:

[1] Cheleschi S et al. Int J Mol Sci. 2017.
[2] De Palma A et al. Clin Exp Rheumatol. 2017.
[3] Fioravanti A et al. Int J Biometeorol. 2015.
[4] Potla R. et al. RNA. 2015.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6462

SAT0504 PREDICTIVE ABILITY OF BIOMARKERS LINKED WITH SYNOVITIS FOR FUTURE INCIDENCE OF PAINFUL KNEE OSTEOARTHRITIS IN A COMMUNITY BASED COHORT OF MIDDLE-AGE WOMEN

C.S. Thudium[1], S. Kluzek[2], J.L. Newton[2], T. Spector[3], D. Hart[3], M.A. Karsdal[1], A.C. Bay-Jensen[1], N. Arden[2]. *[1]Biomarkers & Research, Nordic Bioscience, Herlev, Denmark; [2]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford; [3]Department of Twin Research, King's College London, St. Thomas Hospital, London, United Kingdom*

Background: Radiographic knee osteoarthritis (RKOA) is associated with the knee pain. However, more than half of the middle-aged individuals with RKOA will report no concurrent knee pain. Specific matrix metalloproteinases (MMPs) generated protein fragments have been associated with knee synovitis and suggested as specific neo-epitope biomarkers of joint remodelling.

Objectives: The aim of the study was to evaluate the association between MMP-derived neo-epitope biomarkers measured in serum, and future incidence of either painful RKOA or RKOA without pain, in a cohort of middle-aged women with no RKOA at baseline.

Methods: 585 participants (mean age 53.2, mean BMI 25.1) from the Chingford 1000 Women Study Chingford Women Study had serum biomarker levels of MMP- degraded of CRP (CRPM), collagen type II (C2M) and collagen type III (C3M) measured at year 2 or 3 of the study. All participants had a Kellgren Lawrence (KL) score of 0 in both knees at baseline. Ten years following the recruitment, incidence of RKOA was determined as KL $\geq$2 and painful RKOA was defined as the presence of pain on any number of days in the preceding month in the knee with RKOA. Log-transformed normalised biomarker levels were utilised in separate logistic regression models adjusted for age. Outcomes were defined as either RKOA without pain or painful RKOA. Further analyses were performed adjusting for both age and BMI.

Results: 24.6% of women developed RKOA during 10 years after the recruitment, but only 8.9% of developed RKOA associated with concurrent knee pain. After adjusting for age, statistically significant positive associations were found between C3M and CRPM and the risk of developing painful RKOA with odds ratio (OR) =3.4 (95% confidence interval (CI): 1.4 to 8.2), and OR=2.5 (95% CI: 1.2, 5.2) respectively. After adjusting for age and BMI, only C3M was positively associated with risk of developing painful RKOA with OR=3.2 (95% CI: 1.3, 7.8).

Conclusions: In a population of middle-aged women without knee osteoarthritis, an MMP generated neo-epitope of collagen III previously linked with knee synovitis (C3M) can independently identify high-risk individuals for developing painful RKOA. These findings indicate that targeting MMP activity may be a promising therapeutic strategy in well-targeted populations.

Disclosure of Interest: C. Thudium Employee of: Nordic Bioscience, S. Kluzek: None declared, J. Newton: None declared, T. Spector: None declared, D. Hart: None declared, M. Karsdal: None declared, A. Bay-Jensen: None declared, N. Arden: None declared

DOI: 10.1136/annrheumdis-2017-eular.5761

SAT0505 SELF-REPORTED KNEE INSTABILITY ASSOCIATED WITH PAIN AND ACTIVITY LIMITATIONS PRIOR AND ONE YEAR AFTER TOTAL KNEE ARTHROPLASTY IN PATIENTS WITH KNEE OSTEOARTHRITIS

C. Leichtenberg[1], J.J. Meesters[1], J. Dekker[2,3], R.G. Nelissen[1], T.P. Vliet Vlieland[1], M. van der Esch[4]. *[1]Orthopedics, Leiden University Medical Center, Leiden; [2]Rehabilitation Medicine; [3]Psychiatry, VU University Medical Center; [4]Rehabilitation Research, Reade, Amsterdam, Netherlands*

Background: Sixty to 80% of the patients with knee osteoarthritis (OA) reported self-reported knee joint instability, which was associated with pain and activity limitations. One previous randomized control trial described the prevalence of retained self-reported knee joint instability after total knee arthroplasty (TKA) (32%). To better understand self-reported knee joint instability in usual care there is a need to replicate and extend the results.

Objectives: The aims of the study were to determine (i) the prevalence of self-reported knee instability prior and one year after TKA, (ii) the associations between self-reported knee instability, pain, activity limitations and quality of life prior and one year after TKA, (iii) the course of self-reported knee instability over time and (iv) the associations between retained knee instability, pain, activity limitations and quality of life.

Methods: Consecutive patients with knee OA undergoing primary TKA, extracted from the Longitudinal Leiden Orthopaedics and Outcomes of OsteoArthritis Study (LOAS Study), were included. Self-reported knee joint instability and the Knee injury and Osteoarthritis Outcome Score (KOOS) Pain, Activity Daily Living (ADL) and QoL subscales (0–100; worst-best) were assessed by questionnaires prior and one year after surgery. Multivariable regression analyses were performed to determine associations between knee joint instability, pain, activity limitations and quality of life, adjusted for potential confounders including age, sex, comorbidities, physical activity and preoperative frailty.
Results: 908 patients were included of which 649 patients (72%) reported preoperative knee joint instability (mean age 67 years (SD8.6), 453 females (70%)) and 187 patients (21%) postoperative knee joint instability. Preoperative knee joint instability was associated with preoperative KOOS Pain (B-7.2;95% CI-10.9–3.5) and ADL (B3.8;95% CI-7.5–0.09), but not QoL (B-0.4;95% CI-2.1–1.2). In addition, postoperative knee joint instability was associated with postoperative KOOS Pain (B-13.5;95% CI-17.0–10.0), ADL (B-15.1,95% CI-18.4–11.8) and QoL (B-11.0;95% CI-13.5–8.5). Among the patients with preoperative self-reported knee joint instability, 165 patients (25%) retained knee instability and among the patients with no preoperative self-reported knee joint instability, 22 (8%) developed knee instability one year after surgery. After adjusting for baseline scores and potential confounders, retained knee joint instability was associated with postoperative KOOS Pain (B-19.6;95% CI-30.9–8.3), ADL (B-16.5;95% CI-27.0–5.9) and QoL (B-13.0;95% CI-17.9–8.1).
Conclusions: In usual care, knee joint instability is prevalent one year after TKA (21%). Reported knee joint instability is associated with more pain, worse physical function (pre- and postoperatively) and worse QoL postoperatively. Besides, retained knee joint instability was associated with worse pain, physical function and QoL. This emphasizes the importance of further research into the genesis of pre- and postoperative knee joint instability.
Acknowledgements: The study was funded by the Dutch Arthritis Foundation (DAF).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5988

SAT0506 EARLY POSTOPERATIVE IDENTIFICATION OF PATIENTS AT RISK FOR UNFAVOURABLE LONG-TERM OUTCOMES

C. Leichtenberg[1], H.H. Kaptijn[2], S.H. Verdegaal[3], R. Onstenk[4], H.M. van der Linden-van der Zwaag[1], S.B. Vehmeijer[5], W.-J.C. Marijnissen[6], P.-J. Damen[7], R.G. Nelissen[1], T.P. Vliet Vlieland[1], M.G. Gademan[1] on behalf of LOAS Studygroup. *[1]Orthopedics, Leiden University Medical Center, Leiden; [2]Orthopedics, LangeLand Hospital, Zoetermeer; [3]Orthopedics, Alrijne Hospital, Leiden and Leiderdorp; [4]Orthopedics, Groene Hart Hospital, Gouda; [5]Orthopedics, Reinier de Graaf Hospital, Delft; [6]Orthopedics, Albert Schweitzer Hospital, Dordrecht; [7]Orthopedics, Waterlandziekenhuis, Purmerend, Netherlands*

Background: Identification of patients who benefit from Total Hip or Knee Arthroplasty (THA or TKA) is necessary to indicate the need for surgery. This seems difficult as 20% of all patients report unfavourable outcomes. To provide better treatment options for patients with unfavourable outcomes, they should be identified at an early stage after surgery.
Objectives: I To investigate the prevalence of four trajectories in THA and TKA patients for both pain and function separately: (1) Patients with favourable initial and long-term outcomes, (2) patients with favourable initial but unfavourable long-term outcomes, (3) patients with unfavourable initial and favourable long-term outcomes and (4) patients with unfavourable initial and long-term outcomes. II To determine if long-term outcomes in all patients and in patient groups stratified by initial outcome (favourable/unfavourable) can be predicted on the basis of pre- and early postoperative variables.
Methods: Prospective, multicentre, observational study including consecutive patients undergoing primary THA and TKA (Longitudinal Leiden Orthopaedics and Outcomes of OsteoArthritis Study (LOAS). Measurements were done preoperatively and at 6 and 12 months. Pain and function were assessed with the Hip Disability/ Knee injury and Osteoarthritis Outcome Scores (HOOS or KOOS) Pain and Activity Daily Living (ADL) subscales (score range 0–100). In addition, preoperative variables (sex, age, comorbidities) and early postoperative complications (reoperations or readmissions) were gathered by questionnaire. Scores of the Pain and ADL subscales above and below 70 were defined as favourable and unfavourable outcomes, whereas initial and long-term outcomes were defined as 6 months and 12 months after surgery, respectively. First the prevalence's of the trajectories were determined. Secondly, multivariable logistic regression analysis were done to examine if preoperative variables, postoperative complications and initial outcomes predicted long-term pain and function outcomes. Identical analyses were performed in the patients with favourable and unfavourable initial outcomes separately.
Results: 972 THA and 892 TKA patients were included. With respect to pain, the prevalence of trajectories 1, 2, 3 and 4 were 79% (n=740), 5% (n=47), 7% (n=63) and 9% (n=88) in THA and 75% (n=606), 4% (n=33), 9% (n=71) and 12% (n=93) for TKA. With respect to function, the prevalence's were 74% (n=696), 6 (n=53), 7% (n=63) and 14% (n=131) for THA and 72% (n=624), 5% (n=49), 9% (n=78) and 14% (n=119) for TKA, respectively. Moreover, one-third of the patients with initial unfavourable pain or function outcomes attained favourable long-term outcomes. Overall, only the initial postoperative HOOS/KOOS pain and function predicted long-term outcomes (Table 1).

Table 1. Multivariable associations of preoperative or early postoperative pain or function outcomes with long-term pain or function outcomes

	Early postoperative associations with long-term outcomes in all patients		Early postoperative associations with long-term outcomes in patients with unfavourable early outcomes		Early postoperative associations with long-term outcomes in patients with favourable early outcomes	
THA	Pain N=151, ADL N=194		Pain N=88, ADL N=131		Pain N=63, ADL N=63	
	OR	95% CI	OR	95% CI	OR	95% CI
HOOS Pain*	1.10	1.08-1.12	1.06	1.01-1.11	1.12	1.06-1.17
HOOS ADL*	1.13	1.10-1.16	1.07	1.02-1.12	1.13	1.06-1.20
TKA	Pain N=221, ADL N=197		Pain N=121, ADL N=119		Pain N=100, ADL N=78	
	OR	95% CI	OR	95% CI	OR	95% CI
KOOS Pain*	1.10	1.08-1.13	1.06	1.02-1.11	1.14	1.01-1.21
KOOS ADL*	1.11	1.08-1.13	1.06	1.02-1.10	1.12	1.06-1.18

*Included in the multivariable model were age, sex, comorbidities (musculoskeletal and non-musculoskeletal), postoperative complications and the HOOS/KOOS pain or ADL subscale.
THA or TKA = Total Hip or Knee Arthroplasty
ADL = Activity Daily Living
HOOS = Hip Disability and Outcomes of Osteoarthritis Score
KOOS = Knee Injury and Outcomes of Osteoarthritis Score
OR = Odds Ratio
CI = Confidence Interval

Conclusions: One-third of patients with unfavourable initial outcomes improved further after the first six months after surgery. More research into the recovery early after surgery may help to identify patients at risk for unfavourable outcomes and modify their course by appropriate interventions.
Acknowledgements: This study was funded by the Dutch Arthritis Foundation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2295

SAT0507 OXYTOCINE IN OSTEOARTHRITIS: FROM IN VITRO TO IN VIVO

C.H. Roux[1], E. Fontas[2], L. Euller-Ziegler[3], V. Breuil[3], E.Z. Amri[4]. *[1]Rheumatology, University of Nice Sofia Antipolis, IBV; [2]Biostatistical Department; [3]Rheumatology, CHU Nice, University Nice Sofia Antipolis; [4]Biological Department, University of Nice Sofia Antipolis, IBV, nice, France*

Background: The relationship between oxytocine (OT) and osteoarthritis (OA) is poorly studied and remains unknown. However the subchondral bone is considered as a major player in osteoarthritis, and a protective effect of OT on bone mineralization is described in recent studies.
Objectives: The aim of our work was to investigate a possible link between OT and OA
Methods: we used three different approaches: i) In vitro using MSC (adipose and bone marrow derived stem cells) that were maintained as mono-layer (2D) or as pellets in three dimension (3D) in the absence or the presence of OT. RT-PCR, histological and immunohistochemical analysis were performed. ii) in vivo using a rat animal model developing OA upon anterior cruciate ligament transection (ACLT). Twenty female Wistar rats were divided in 2 groups: one group was sham operated whereas the second was ACL transected. Half of each group received either OT (1 mg/kg/day) injections or saline buffer. Histological analysis was performed on day 28. The severity of OA lesions was assessed on a scale adapted from Mankin's score at medial part of the femur. iii) Clinical analysis using a *human cohort*. Samples issued from a hand OA cohort (ADEM). 63 OA women have been included; men were excluded because of their low number. At baseline, all subjects benefited of OT and leptin circulating levels measurements and hand X rays (Scoring systems including Kelgren and Lawrence and Verbruggen scores). The control group consists in subjects of the same age range without osteoporosis, OA or inflammatory disease.
Results: OT treatment of differentiating MSCs for 21 days induced a significant increase of agrecan, Col X and COMP mRNA levels without variation of Col 1a. Immunostaining experiments showed an improvement of Sox9 and Col II expression in the presence of OT. The histological analysis of rat knee showed no differences in the severity of lesions between the different ACLT groups. The characteristics of the women cohorts is as follow: 63 OA women age = 65 (+/-11), Body Mass Index (BMI) = 24 (+/-4), OT=1.4 (+/-2) and 19 control women age=63 (+/-10), BMI=26 (+/-5), OT=6.5 (+/-7).The multivariate analysis adjusted for age, BMI and leptin levels, showed a significant lower level of OT in hand OA women ($p=0.002$, $\beta=3.4$). In univariate analysis, there was no relationship between OT blood levels and the severity of OA (Verbruggen: p=0.7, KL: p=0.2), Joint Space Narrowing (p=0.2) and osteophytes (p=0.1).
Conclusions: Our study shows an anabolic effect of OT on chondrogenesis and that OT circulating levels was significantly lower in OA patients. OT might represents an interesting player in the pathophysiology of osteoarthritis and further studies will shed some light on its mechanism of action.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6821

SAT0508 LACK OF A CLEAR DISEASE MODIFYING ACTIVITY OF CELECOXIB IN TREATMENT OF END-STAGE KNEE OSTEOARTHRITIS: A RANDOMIZED OBSERVER BLINDED CLINICAL TRIAL

E.M. Van Helvoort[1], K. Coeleveld[1], T.N. de Boer[1], A.M. Huisman[2], A.A. Polak[3], J.W.J. Bijlsma[1], J.M. van Laar[1], F.J.P.G. Lafeber[1], S.C. Mastbergen[1].
[1]Rheumatology and Clinical Immunology, University Medical Centre Utrecht, Utrecht; [2]Rheumatology; [3]Orthopedics, Sint Franciscus Gasthuis, Rotterdam, Netherlands

Background: Several studies suggest that celecoxib has beneficial effects on degenerated cartilage (1, 2). Together with effects on synovial tissue and bone, celecoxib was postulated to have disease modifying osteoarthritic drug (DMOAD) activity.
Objectives: This study evaluated the DMOAD activity of celecoxib, a selective cyclooxygenase 2 (COX-2) inhibitor compared to no treatment and naproxen, treating end-stage knee osteoarthritis (OA), after in vivo exposure using detailed *ex vivo* tissue analyses.
Methods: 172 patients with end-stage knee OA were randomized to 4 groups and treated for 4 weeks prior to knee replacement surgery: celecoxib 2dd200g, naproxen 3dd250mg, celecoxib 2dd200mg stopped 3 days prior to surgery, or no treatment. To determine if treatment had reached the joint, intra-articular COX-2 expression was determined by Western Blot analysis in the celecoxib until surgery and no treatment group, considering these as most extremes. Proteoglycan release, as primary outcome and content were determined by staining and precipitation of glycosaminoglycans (GAGs) with Alcian Blue. Release of newly formed proteogylcans, as a measure of proteoglycan retention, was determined by loss of $^{35}SO_4^{2-}$-labeled GAGs in culture medium by precipitation of GAGs and subsequent liquid scintillation analysis. Synovial tissue inflammation markers interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) were determined by Enzyme Linked Immuno Sorbet Assay (ELISA) and nitric oxide (NO) production by standard Griess reaction. Western Ontario and McMaster University (WOMAC) questionnaire was used to evaluate clinical parameters.
Results: Intra-articular COX-2 expression was significantly decreased in both cartilage and synovial tissue (figure 1) indicating proper in vivo exposure of the treatment.
Despite this reduction, no significant effect on proteoglycan release, retention or content was found for none of the treatment groups (table 1). Synovial tissue showed only a small decrease in nitric oxide levels in celecoxib treated patients. No clear clinical effects could be observed as indicated by the WOMAC scores.

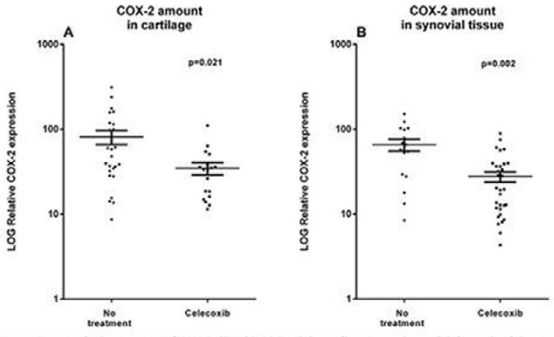


Figure 1. Intra-articular amount of COX-2. The COX-2 levels in cartilage (A) and synovial tissue (B) of the no treatment group and celecoxib until surgery group. Results are presented for each individual patient (dots) and mean ± SEM (dash with whiskers). P-values are given for celecoxib treated group compared to no treatment group. Due to limited amount of tissue available the analyses of COX-2 for cartilage was limited to 18 treated and 25 non-treated patients and for synovial tissue to 31 treated and 16 non-treated patients.

Table 1: Effects of 4 week treatment with celecoxib or naproxen on cartilage biochemistry, synovial tissue inflammation and WOMAC scores. Results are expressed as means (SD) and P-values represent comparison with no treatment

	No treatment	Celecoxib		Celecoxib -3		Naproxen	
	Mean (SD)	Mean (SD)	P-value	Mean (SD)	P-value	Mean (SD)	P-value
Cartilage biochemistry							
- % total PG release	12 (4.36)	11 (2.86)	0.630	11 (2.61)	0.826	12 (3.98)	0.720
- % newly formed PG release	15 (8.97)	14 (5.48)	0.795	13 (4.54)	0.531	15 (7.24)	0.755
- PG content	25 (6.63)	24 (4.81)	0.525	25 (4.61)	0.901	23 (6.02)	0.243
Synovial tissue inflammation							
- IL1β production (pg/ml/mg tissue)	17.88 (45.02)	15.71 (28.24)	0.901	14.04 (19.86)	0.481	11.44 (17.04)	0.880
- TNF-α production (pg/ml/mg tissue)	2.70 (2.56)	2.44 (2.42)	0.655	3.93 (5.21)	0.393	2.35 (1.77)	0.985
- NO production (uM/mg tissue)	0.08 (0.04)	0.06 (0.05)	***0.041***	0.07 (0.06)	0.270	0.09 (0.09)	0.745
WOMAC change after treatment							
- Pain	-3.93 (11.64)	2.13 (18.09)	0.127	4.91 (14.40)	***0.026***	0.46 (12.21)	0.258
- Stiffness	3.13 (21.74)	3.65 (20.01)	0.865	10.19 (19.62)	0.245	6.00 (14.03)	0.363
- Function	-1.82 (8.95)	2.98 (15.18)	0.115	2.07 (14.50)	0.191	1.73 (12.39)	0.193
- Total	-1.76 (8.03)	2.80 (15.12)	0.109	3.44 (13.84)	0.124	1.87 (10.77)	0.138

No treatment (n=38); Celecoxib until surgery (n=34); Celecoxib -3 represents celecoxib stopped 3 days before surgery (n=33); Naproxen stopped 3 days before surgery (n=32). P-values represent comparison to no-treatment group.

Conclusions: No effect of a 4-week in vivo celecoxib treatment on joint tissue in knee OA patients could be detected, although decreased expression of COX-2 confirmed its intra-articular availability. Effects on synovial inflammatory mediators and clinical outcome were very limited. No adverse effects were found either. As such the previous reported disease modifying effects of celecoxib in *in vitro* and pilot clinical studies could not unambiguously be confirmed in this randomized trial.
References:
[1] de Boer TN, Huisman AM, Polak AA, Niehoff AG, van Rinsum AC, Saris D, et al. The chondroprotective effect of selective COX-2 inhibition in osteoarthritis: ex vivo evaluation of human cartilage tissue after in vivo treatment. Osteoarthritis and cartilage/OARS, Osteoarthritis Research Society. 2009;17(4):482–8.
[2] Mastbergen SC, Jansen NW, Bijlsma JW, Lafeber FP. Differential direct effects of cyclo-oxygenase-1/2 inhibition on proteoglycan turnover of human osteoarthritic cartilage: an in vitro study. Arthritis research & therapy. 2006;8(1):R2.
Disclosure of Interest: E. Van Helvoort: None declared, K. Coeleveld: None declared, T. de Boer: None declared, A. Huisman: None declared, A. Polak: None declared, J. Bijlsma Grant/research support from: J.W.J. Bijlsma received a consultancy fee from Pfizer (<5.000 US$). J. van Laar: None declared, F. Lafeber: None declared, S. Mastbergen: None declared
DOI: 10.1136/annrheumdis-2017-eular.1454

SAT0509 DYNAMICS IN THE LEVELS OF ADIPOKINES AND CYTOKINES IN PARALLEL WITH WEIGHT LOSS AND THEIR RELATIONSHIP WITH CLINICAL MANIFESTATIONS OF KNEE OSTEOARTHRITIS

E. Strebkova[1], I. Solovyova[2], A. Mkrtumyan[2], L. Alekseeva[1]. *[1]Nasonova Research Institute of Rheumatology; [2]Moscow State Medical Stomatological Institute, Moscow, Russian Federation*

Background: Untoward effects of pro-inflammatory cytokines on a chondrocyte are implied in pathogenesis of osteoarthritis (OA), while adipokines would enhance these pathogenetic mechanisms and facilitate maintenance of inflammation and progression of OA when the latter is associated with obesity.
Objectives: To asses dynamic changes of adipokine (leptin) and pro-inflammatory cytokines (IL-6, TNF-α) levels and their relationship with clinical manifestations of knee OA in pts losing weight during orlistat therapy.
Methods: The study included 50 female pts aged 45–65 years with knee OA, Kellgren-Lawrence stage II-III, and obesity (BMI>30kg//m^2). Pts form Group 1 (n=25) were receiving orlistat 120 mg x 3 times a day for 6 month combined with low-caloric diet and therapeutic physical exercise. Pts from Group 2 (n=25) were administered only low-caloric diet and therapeutic physical exercise for 6 month. Anthropometry data (height, body weight, BMI), WOMAC and quality of life EQ-5D scores, as well as serum levels of leptin, IL-6 and TNF-α using ELISA were assessed at baseline and at 6 months in all pts.
Results: Following pharmacological and non-pharmacological therapy of obesity in pts with knee OA subjects from Group 1 reduced their body weight by 10,07% (p<0,05), and pts from Group 2 - by 0,84% (p>0,05). At baseline pts from both groups did not differ (p>0,05) by leptin, IL-6 and TNF-α levels. Decreased leptin levels were documented in pts from Group 1 after 6 months of orlistat therapy (p=0,05), which directly correlated with body weight loss (r=0,5, p=0,02), total WOMAC score reduction r=0,5, p=0,01), and score reduction in WOMAC subscales measuring pain r=0,5, p=0,01; stiffness r=0,4, p=0,04; and functional insufficiency r=0,4, p=0,03, thus reflecting improvement of OA symptoms; and inversely correlated with increased EQ-5D score (r=-0,4, p=0,03) reflecting improvement in quality of life. Besides, orlistat therapy was associated with decreased IL-6 levels (p<0,05). Both groups demonstrated high TNF-α levels, although some insignificant decrease was noticed in Group 1 (p=0,14) following weight loss with orlistat therapy. Persisting leptin, IL-6 and TNF-α levels were registered in pts from Group 2, who maintained their body weight following only life-modifying therapy of obesity. Clear correlations between IL-6 and TNF-α levels and changes in body weight and clinical manifestations of OA were not found in both groups.
Conclusions: Significant decrease in leptin and IL-6 levels were observed in knee OA pts following orlistat therapy and associated weight loss. There was a direct correlation between decreased leptin levels and body weight loss, as well as reduction in WOMAC scores reflecting improvement of knee OA clinical manifestations, and inverse correlation with EQ-5D score resulting in quality of life improvement. Therefore, body weight loss following pharmacotherapy of obesity is associated not only with improvement of OA clinical symptoms, but also with down-regulation in production of pro-inflammatory leptin and IL-6, most probably resulting in reduction of meta-inflammation in obese pts with OA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2822

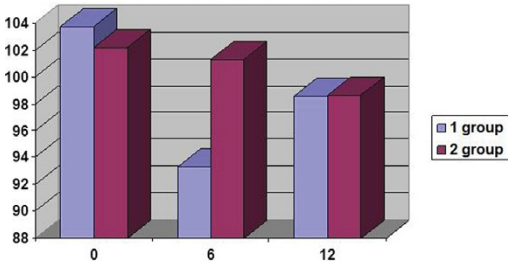
SAT0510 EFFECT OF PHARMACOLOGICAL AND NON-PHARMACOLOGICAL THERAPY OF OBESITY ON THE CLINICAL MANIFESTATIONS OF OSTEOARTHRITIS

E. Strebkova, L. Alekseeva. *Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Osteoarthritis (OA) and obesity are inter-related and most challenging conditions for the public health, leading to significant deterioration in quality of

life. Obesity is considered to be associated with the incidence and progression of OA, thus weight loss is of paramount importance in OA management.
Objectives: To evaluate the efficacy of pharmacological and non-pharmacological therapy of obesity in pts with knee OA.
Methods: The study included 50 female pts aged 45–65 years with knee OA, Kellgren-Lawrence stage II-III, and obesity (BMI>30kg//m^2). Pts form Group 1 (n=25) were administered orlistat at 120 mg x 3times a day for 6 month alongside with low-caloric diet and therapeutic physical exercise. Pts from Group 2 (n=25) adhered to life-modifying therapy only, i.e. low-caloric diet and therapeutic physical exercise for 6 month. Anthropometry data (height, body weight, BMI), as well as WOMAC and quality of life EQ-5D scores were assessed at baseline, at 6 and 12 months (i.e, 6 months after discontinuation of therapy) after initiation of treatment in all pts.
Results: After 6 months of pharmacological therapy pts from Group 1 achieved significant mean weight loss by 10,07% (p<0,05), while pts from Group 2 with non-pharmacological therapy demonstrated only <1% (0,84%) (p>0,05) weight loss. Pts receiving pharmacological therapy with orlistat demonstrated the following improvements by WOMAC subscales: pain reduction by 52,5% (p<0,05), stiffness reduction by 47,98% (p<0,05), and 51,55% function improvement, while total WOMAC score improved by 51,49% (p<0,05). Respective WOMAC subscale scores in pts from Group 2 were considerably less impressive vs Group 1. Pts from Group 1 demonstrated statistically significant improvement in the quality of life by 52,27% EQ-5D (p<0,05). EQ-5D score remained unchanged only in 2 pts from Group 1 who failed to lose weight. During the following 6 months after discontinuation of orlistat pts from Group 1 regained 5,6% of their body weight (p<0,05) (Fig.1), which was associated with OA worsening OA (deterioration of pain by 42,63% (p<0,05) WOMAC, and total WOMAC score decrease by 23,15%). After 12 months of follow up pts from Group 2 showed body weight loss by 3,5%, and continuing decrease of pain in knee joints by WOMAC pain subscale, reaching 22,3% (p<0,05) as compared to baseline.

Fig 1. Body weight dynamics during the study



Conclusions: The results of our study demonstrate significant >10% weight loss in OA pts induced by orlistat therapy. Such a noticeable weight loss was associated with reduced pain intensity, improved function and quality of life in OA pts. Partial regain of body weight during 6 months after discontinuation of orlistat was accompanied by worsening of OA clinical course. Thus, effective maintenance of optimal body weight in OA pts requires longer pharmacotherapy of obesity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2819

SAT0511 THUMB BASE OSTEOARTHRITIS: ASSOCIATIONS BETWEEN SYNOVITIS ON ULTRASOUND AND PAIN

S. Ermurat[1], F. Kroon[2], M. Kortekaas[2], M. Reijnierse[3], M. Kloppenburg[2,4].
[1]Rheumatology, Uludag University Medical Faculty, Bursa, Turkey; [2]Rheumatology; [3]Radiology; [4]Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands

Background: Hand osteoarthritis (OA) affects the interphalangeal (IP) joints but also the first carpometacarpal (CMC1) joint in the thumb base. Previous ultrasonography (US) studies of the IP joints have shown that inflammatory and structural features are frequently present and associated with clinical signs and symptoms. Until now, US studies specifically assessing the CMC1 joint have not been performed.
Objectives: To investigate associations between inflammatory features, structural damage and pain in CMC1 OA.
Methods: Cross-sectional data of 87 hand OA patients participating in the EChography in Hand OA (n=63) and the Etanercept in Hand OA (n=24) study at the Leiden University Medical Center were used in this analysis. Both CMC1 joints were assessed with US for synovial thickening, effusion and power Doppler signal (PDS) on a 0–3 scale by experienced ultrasonographers. Presence of pain upon palpation of the thumb base was assessed by trained research nurses on the same day as the US. Hand radiographs were scored blinded for clinical and US features, according to the Osteoarthritis Research Society International atlas for osteophytes (0–3), joint space narrowing (JSN, 0–3), sclerosis (0–1) and malalignment (0–1) in the CMC1 joint. Risk ratios (RRs) with 95% confidence intervals (CIs) were calculated using generalized estimating equations to investigate associations between US or radiographic features and thumb base pain on joint level.
Results: Of 87 patients (mean age 60.3 years, 82% women, mean BMI 27.2 kg/m^2) 174 CMC1 joints were assessed, of which 54 (31%) were painful. The US features synovial thickening, effusion and PDS were found in 26%, 33% and 25% of the joints, respectively. Radiographic features were present in 55% (osteophytes), 79% (JSN), 20% (sclerosis) and 12% (malalignment) of the joints. No associations were seen between inflammatory US features and pain upon palpation of the thumb base (Table). However, osteophytes and sclerosis were associated with more pain (RR 2.5 [95% CI 1.4 to 4.6] for osteophytes grade 3 versus no osteophytes, and RR 2.0 [95% CI 1.3 to 3.2] for presence of sclerosis). Other radiographic features (JSN, malalignment) showed a trend for increased risk of pain on palpation, and for osteophytes and JSN a dose-response relation was apparent.

Table. Associations of US and radiographic features with pain on palpation in thumb base OA (n=171 joints*)

	Tenderness yes/no, n	RR (95% CI)
US features		
Synovial thickening		
Absent	40/85	1
Grade 1	10/22	1.1 (0.6-1.8)
Grade 2/3	4/10	0.9 (0.4-2.4)
Effusion		
Absent	35/79	1
Grade 1	13/25	0.8 (0.4-1.5)
Grade 2/3	6/13	0.8 (0.3-2.0)
Power doppler signal		
Absent	41/86	1
Grade 1	8/24	0.9 (0.5-1.6)
Grade 2/3	5/7	1.2 (0.7-2.0)
Radiographic features		
Osteophytes		
Absent	18/58	1
Grade 1	16/40	1.2 (0.7-2.2)
Grade 2	11/13	1.5 (0.7-2.9)
Grade 3	9/6	2.5 (1.4-4.6)
Joint space narrowing		
Absent	8/27	1
Grade 1	36/77	1.6 (0.8-3.3)
Grade 2	7/9	2.1 (0.8-5.3)
Grade 3	3/4	2.5 (0.9-7.0)
Sclerosis		
Absent	38/104	1
Present	16/13	2.0 (1.3-3.2)
Malalignment		
Absent	44/107	1
Present	10/10	1.4 (0.7-2.7)

*3 joints no information on tenderness. CI, confidence interval; n, number; OA, osteoarthritis; RR, risk ratio; US, ultrasound.

Conclusions: Radiographic features, especially osteophytes and JSN, were prevalent and more frequently present than US inflammatory features in the CMC1 joints of hand OA patients. In contrast to what is known from studies in IP joints, the presence of inflammatory US features was not associated with pain in the thumb base, but structural damage was. These results suggest differences in etiology of pain in thumb base compared to IP OA, with a larger role for structural damage in thumb base OA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4921

SAT0512 MRI PROVIDING INSIGHTS IN ASSOCIATION OF SYNOVITIS AND BONE MARROW LESIONS (BMLS) WITH PAIN IN THUMB BASE OSTEOARTHRITIS (OA)

F. Kroon[1], S. van Beest[1], W. Damman[1], R. Liu[1], M. Reijnierse[2], M. Kloppenburg[1,3]. *[1]Rheumatology; [2]Radiology; [3]Clinical Epidemiology, Leiden University Medical Center, Leiden, Netherlands*

Background: Hand OA affects the interphalangeal (IP) and thumb base joints (first carpometacarpal [CMC1] and scaphotrapeziotrapezoid [STT]). Much is still unknown about the pathophysiology of thumb base OA. Magnetic resonance imaging (MRI) studies have led to new insights in IP OA, but in absence of a scoring system thumb base MRI studies are lacking.
Objectives: Investigate the prevalence of MRI synovitis and BMLs in the thumb base, and their association with pain, using the novel OMERACT thumb base OA MRI scoring system (TOMS)[1].
Methods: Cross-sectional data of the Hand OSTeoArthritis in Secondary care (HOSTAS) study, including consecutive patients diagnosed by their treating rheumatologist with primary hand OA, were used. Patients with an MRI of the right thumb base at baseline were included in the analysis. MRIs were scored by two readers using the TOMS for synovitis and bone marrow lesions (BMLs) in the CMC1 and STT joints (grade 0–3). BMLs were evaluated in the proximal and distal joint parts separately, resulting in a 0–6 and 0–9 sum score for CMC1 and STT, respectively. Pain on palpation of the thumb base was assessed by trained research nurses. Hand radiographs were assessed for presence of osteophytes in the CMC1 and STT joints. Associations between MRI lesions and thumb base tenderness were analysed using logistic regression, presented as odds ratios (ORs) with 95% confidence intervals (CIs), stratified for absence or presence of radiographic osteophytes. For the analyses synovitis and BML scores were

aggregated into a dichotomous total thumb base involvement score (0–1 in both joints vs ≥2 in at least one joint).
Results: 85 out of 202 patients (84% women, mean age 60.1 years) reported pain on palpation in the thumb base. Synovitis was seen in both thumb base joints (CMC1 42%, STT 37%), although prevalence of grade 2–3 synovitis was low in both the CMC1 (16%) and STT (14%). BMLs were present in CMC1 and STT in 54 and 53%, respectively, with 18 and 21% having a sum score of 2–3, and 16 and 7% a sum score ≥4. In absence of radiographic osteophytes, presence of synovitis or BMLs in either thumb base joint was not statistically significantly associated with thumb base tenderness (ORs 1.9 [95% CI 0.6–6.4] and 1.5 [0.5–4.3], respectively). However, in absence of synovitis or BMLs, radiographic osteophytes and pain were associated, with increasing ORs when MRI lesions were additionally present (Table). Similar results were found for self-reported thumb base pain (not shown).

Table. Number of tender joints (yes/no) and associations of MRI inflammation and radiographic osteophytes with pain on palpation in thumb base osteoarthritis (n=196*)

		Osteophyte CMC1 or STT	
		absent	*present*
Synovitis	*CMC1 and STT grade 0-1*	1 23/70	4.2 (2.0-8.6) 30/22
	CMC1 or STT grade ≥ 2	1.9 (0.6-6.4) 5/8	5.9 (2.6-13.3) 25/13
BML	*CMC1 and STT grade 0-1*	1 21/64	4.3 (1.7-11.0) 14/10
	CMC1 or STT grade ≥ 2	1.5 (0.5-4.3) 7/14	5.3 (2.6-10.8) 42/24

BML, bone marrow lesion; CI, confidence interval; CMC1, first carpometacarpal; MRI, magnetic resonance imaging; OR, odds ratio; STT, scaphotrapeziotrapezoid.
*n=196 patients with available radiographs and evaluable MRI for synovitis and BMLs.

Conclusions: Synovitis and BMLs are present in the thumb base, although severe MRI lesions were uncommon. Prevalence of synovitis was similar in the CMC1 and STT joints, although higher BML scores were more frequently seen in CMC1. Radiographic osteophytes seemed more important in predicting thumb base tenderness than MRI inflammation alone. Combined presence of radiographic osteophytes and MRI lesions had a small additive effect. These findings are in contrast to results from IP OA studies, supporting thumb base OA as a distinct hand OA subset. It might also explain why trials investigating intra-articular corticosteroids in thumb base OA have led to equivocal results.
References:
[1] Kroon F, Conaghan P, Foltz V, et al. J Rheumatol 2017 (in press).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2879

SAT0513 FUNCTIONAL IMPAIRMENT RATHER THAN BURDEN OF CO-MORBIDITIES IS ASSOCIATED WITH A 5-YEAR CHANGE IN HEALTH STATE UTILITY IN HIP AND KNEE OSTEOARTHRITIS: RESULTS FROM THE KHOALA COHORT STUDY

A.Y. Omorou[1,2], H. Achit[2], M. Wieczorek[1], B. Fautrel[3], A.-C. Rat[1], F. Guillemin[1,2]. [1]*Ea 4360 Apemac, University of Lorraine;* [2]*CIC-1433 Clinical Epidemiology, CHRU Nancy, Nancy;* [3]*UPMC Université Paris 6, Grc-Upmc 08 (Eemois), Sorbonne Universités, Paris, France*

Background: Functional impairment of hip and knee osteoarthritis (OA) and associated co-morbidities can independently impact patient's health state utility (HSU), a useful indicator for valuing health in medico-economic studies.
Objectives: This study aimed to examine the respective influence of the evolution of functional impairment and of burden of co-morbidities on a 5-year change in HSU for patients with OA.
Methods: 548 patients (Mean age of 61.1 years, 66.6% of women and 68.1% with knee OA) from the KHOALA study with 5 years follow-up were included. Functional impairment, co-morbidities and HSU were measured annually using the WOMAC (0–100) [1], FCI (1–18) [2] and SF-6D (0–1) [3], respectively. First, baseline clinical patterns were identified using hierarchical clustering methods [4]. Then, the role of these patterns as determinants of 5-year change in HSU was analysed using hierarchical mixed models.
Results: Two clusters were identified: cluster 1 *"Low functional impairment and few co-morbidities"* (65.3%) and cluster 2 "*Severe functional impairment and many co-morbidities*" (34.7%). Compared to the cluster 1, the functional impairment of cluster 2 significantly decreased (-14.5 [-18.1; -10.92]) at 5 year follow up, while the co-morbidity index significantly increased in the two clusters (+0.18 [-0.22; 0.57]). The mean baseline HSU score was 0.66 (0.70 for cluster 1 and 0.59 for cluster 2). Compared to cluster 1, patients in cluster 2 had a significantly higher increased in 5-year HSU (β=+0.0335 [0.0088; 0.0583]) (R^2=21%). The difference of 5-year change in HSU was no more significant when adjusted for change in functional impairment (β=+0.0335; p=0.008 vs. -0.0153; p=0.30) (R^2=42%) while it remained significant when adjusted for change in co-morbidity index (β=+0.0335; p=0.008 vs. +0.0386; p=0.002) (R^2=27%).
Conclusions: Cluster analysis showed that patients with severe functional impairment also had high rate of co-morbidities à baseline. The reduction of OA functional impairment is an important determinant of 5-year improvement of HSU while burden of co-morbidities was not associated with change in hip and knee OA HSU. This result highlights the importance of reducing functional impairment in clinical management of patients with hip and knee OA, and gives clues for interpretation of medico-economic analyses.
References:
[1] Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J. Rheumatol. 1988;15:1833–40.
[2] Groll DL, To T, Bombardier C, Wright JG. The development of a comorbidity index with physical function as the outcome. J. Clin. Epidemiol. 2005;58:595–602.
[3] Brazier J, Usherwood T, Harper R, Thomas K. Deriving a preference-based single index from the UK SF-36 Health Survey. J. Clin. Epidemiol. 1998;51:1115–28.
[4] Everitt BS. Unresolved Problems in Cluster Analysis. Biometrics. 1979;35:169.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3796

SAT0514 CAN IMMUNOPHENOTYPING OF SYNOVIAL FLUID CELLS HELP DISTINGUISH BETWEEN PATIENTS WITH OSTEOARTHRITIS?

G. Gabcova[1], G. Manukyan[2], Z. Mikulkova[1], E. Kriegová[1], J. Gallo[3]. [1]*Department of Immunology, Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic;* [2]*Group of Molecular and Cellular Immunology, Institute of Molecular Biology NAS RA, Yerevan, Armenia;* [3]*Department of Orthopaedics, Palacky University, Teaching Hospital Olomouc, Olomouc, Czech Republic*

Background: Osteoarthritis (OA) is a leading cause of chronic pain and functional disability in elder people. It is not a homogeneous but diverse group of synovial joint diseases. This could stay behind the therapeutic inconsistency observed in clinical practice caused probably by different diseases and/or different stages of a single disease. The comprehensive immunophenotyping of immune cells and their cell counts in synovial fluid (SF) might therefore advance our understanding of a particular type/stage of OA. This could have diagnostic value as well as provide novel insights into the pathophysiology of OA.
Objectives: To characterize immune cells present in SFs from OA patients in different stages of a disease.
Methods: We performed immunophenotyping of SFs from 63 patients with OA and 10 SFs from control patients (non-OA) without clinical/radiographic signs of OA using flow cytometry. We were able to characterize the following immune cells in the sampled SFs: T helper lymphocytes ($CD3^+/CD4^+$), T cytotoxic lymphocytes ($CD3^+/CD8^+$), NK cells ($CD3^-/CD16^+/CD56^+$), B lymphocytes ($CD19^+$), T regulatory (Treg) cells ($CD4^+/CD25^+/CD127^-$), mast cells ($CD203c^+/CD117^+$), M1- ($CD14^+/CD86^+/HLA\text{-}DR^{high}$) and M2-polarized macrophages ($CD14^+/CD163^+/CD206^+$), and neutrophils ($CD15^+/CD16^+$).
Results: A comparison between OA and control (non-OA) SFs revealed phenotypic alterations mainly in T cells, NK cells, macrophages, and neutrophils. T cells were the predominant population in the SFs, with $CD4^+$ T lymphocytes being more prevalent than $CD8^+$ T cells in OA (increased CD4/CD8 ratio). The second largest cell population was macrophages. Despite the dominant mixed-polarized (M1-M2) macrophage subpopulations in both the studied groups, SFs from the OA patients displayed a tendency towards greater M1 activity comparing to the controls. A markedly increased percentage of neutrophils found in the OA group was associated with their activated state compared to the controls (increased CD11b). No difference was found in percentages of B, Treg and mast cells. Despite the similar numbers of NK cells in both the groups, the activation-associated marker CD69 was up-regulated in NK cells from the OA patients. Representative dot-plots (FCS-SSC) of inter-individual variability of the main immune cell populations in synovial fluids from osteoarthritic patients is shown in Figure 1.

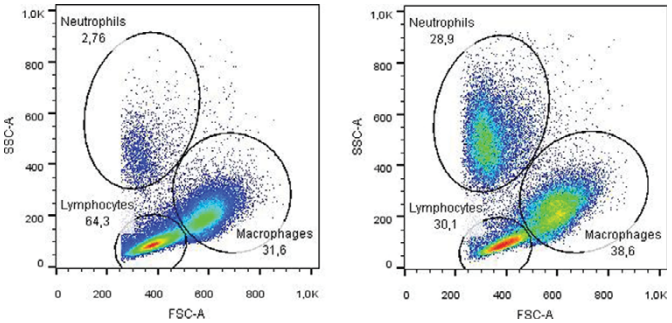


Figure 1. Representative dot-plots (FCS-SSC) of inter-individual variability of the main immune cell populations in synovial fluids from osteoarthritic patients.

Conclusions: We were able to distinguish between the OA cases and controls

in terms of their immune cells profiles (i.e. their numbers, activation status etc.). Additionally, we were able to follow specific immune cell patterns inside the OA group. Our study further emphasized the role of immune cells in the pathogenesis of OA. In particular, the results provide evidence suggesting ongoing activation of innate immunity as well as a shift towards T helper lymphocytes in fluids of the patients with OA. Our findings give a rational starting point to be addressed by the future research for clinically useful biomarkers associated with the OA development and progression.

Acknowledgements: Grant support: MZ CR VES16–31852A, MZ CR VES15–27726A.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4045

SAT0515 SONOGRAPHIC AND CLINICAL EXAMINATION OF TENDON INVOLVEMENT IN HAND OSTEOARTHRITIS

I. Gessl, A. Vinatzer, G. Supp, A. Kerschbaumer, P. Studenic, M. Zauner, D. Aletaha, J. Smolen, P. Mandl. *Dep. of Medicine 3, Div. of rheumatology, Medical University of Vienna, Vienna, Austria*

Background: Persistent tenosynovitis and degenerative tendinitis is associated with pain and can lead to dysfunction and tendon damage. While tenosynovitis is a common finding in rheumatoid arthritis, data on tendon involvement in hand osteoarthritis (HOA) is clearly limited. The clinical assessment of tendons is difficult and not fully standardized, but muculoskeletal ultrasound (MSUS) has been used successfully in inflammatory rheumatic disease as a sensitive method to detect tenosynovitis, tendon damage and osteophytes.

Objectives: To characterize tendon involvement in hand osteoarthritis and compare ultrasound with clinical assessment.

Methods: In this cross-sectional observational study 34 patients with HOA underwent MSUS and clinical examination on the same day. Each flexor and extensor tendon of the hand was scored independently for tenosynovitis and tendon damage (presence/absence) respectively by an expert in MSUS, blinded to the results of the clinical examination. Additionally, osteophytes in the proximal and distal interphalangeal joints of the fingers were assessed. Clinical assessment of tendons for tendon involvement included volar or dorsal pain, crepitus and swelling involving the hand, wrist or forearm during active movement of the tendon against resistance according to the Birmingham consensus criteria, by assessors who were blinded to the results of the MSUS. Conventional radiographs (CR) of the hands were also acquired and evaluated by the Interphalangeal Osteoarthritis Radiographic Simplified score.

Results: The majority of patients (30/34, 88.2%) were female, with a mean age of 69.5±8.5 years and a median of 10 (9–22.5) years disease duration. Clinical examination revealed tendon involvement in 21 (61.8%) patients with a median of 3 (range 1–14) affected tendons. In MSUS tenosynovitis was detected in 17/33 patients (51.5%) with a median of 1 (1–4) tendon involved. Tendon damage was found in 8/33 patients (24.2%) with a median of 2 (1–11) tendons involved. A total of 20/33 (60.6%) patients exhibited sonographic signs of tendon involvement (tenosynovitis/tendon damage) with a median of 2 (1–12) involved tendons. Tendon damage was found more often on the right hand ($p<0.05$) while tenosynovitis did not significantly differ. Similarly, no significant difference between male and female patients was found. The extensor digitorum and the extensor carpi ulnaris tendons were the most commonly affected tendons under US. Tenosynovitis was found to be more prevalent among extensor tendons ($p<0.001$), while tendon damage was demonstrated at a higher frequency in flexor tendons ($p<0.05$) (Fig. 1). The agreement between MSUS and clinical examination was moderate on the patient level and poor on the level of individual tendons. Osteophytes were found in 96.8% patients using MSUS and in 100% of patients assessed using CR. Osteophytes detected on MSUS or CR showed good agreement (p=0.01, Cronbach's Alpha=0.66).

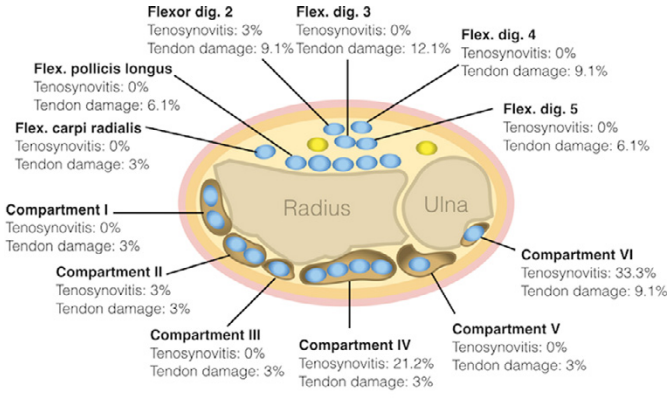


Fig.1 Distribution of tenosynovitis and tendon damage

Conclusions: The findings of our study reveal a high prevalence of tendon involvement in patients with hand OA. Sensitivity of MSUS in detecting tendon involvement coupled with the lack of agreement between clinical examination and MSUS on the level of individual tendons may suggest that while clinical examination is able to identify patients with overall tendon involvement, it does not allow the specific identification of involved tendons.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5853

SAT0516 INFLUENCE OF ETHNICITY ON CLINICAL PAIN IN PATIENTS WITH OSTEOARTHRITIS VERSUS RHEUMATOID ARTHRITIS: CONTRIBUTION OF LEVEL OF EDUCATION AND DEPRESSION

I. Castrejon[1], J. Chua[1], J.A. Block[1], L.A. Bradley[2], Y. Yazici[3], N. Shakoor[1]. *[1]Rheumatology, Rush University Medical Center, Chicago; [2]Clinical Immunology and Rheumatology, University of Alabama, Birmingham; [3]Rheumatology, NYU Hospital for Joint Diseases, New York, United States*

Background: The experience of pain is characterized by inter-individual and group variability, with ethnicity being one potential contributing factor. In a systematic review, it was shown how African Americans (AA) demonstrated lower pain tolerance in experimental studies[1]. Pain is the most common and troubling symptom in patients with osteoarthritis (OA) -maybe reflecting damage- and in patients with rheumatoid arthritis (RA) -maybe reflecting synovitis- but other pain mechanisms are important.

Objectives: To investigate the influence of ethnicity on clinical pain and other outcomes and to identify potential predictors of higher scores for pain in AA and Hispanic patients with OA or RA seen in routine care.

Methods: As part of their clinic visit, all patients complete a multidimensional health assessment questionnaire (MDHAQ) at 2 academic sites. MDHAQ includes 0–10 visual analogue scales (VAS) for pain, physical function, and a patient global evaluation (PATGL), and a depression score between others. The MDHAQ also include demographic data and patients "self-identify" their ethnicity. One random visit with complete questionnaire data for each OA (ICD-9=715.0) and RA (ICD-9=714.0) patient from each site was included in this analysis. Comparison according to patients' self-reported ethnicity -White, African-American (AA) or Hispanics- were performed using ANOVA and chi-squared. Multiple regression models were performed to identify independent explanatory variables for clinical pain in AA and Hispanics groups versus White.

Results: The study included 402 OA patients and RA 373. There were no differences in age and gender between ethnicity groups in both diagnostic groups. Years of education were highest in the White followed by AA and then Hispanics in both OA and RA. AA and Hispanics showed statistically significantly higher scores for pain (6.6 vs 5.3 in OA, $p<0.001$; 5.7 vs 4.4 in RA, $p<0.001$) and lower physical function (3.2 vs 1.9 in OA, $P<0.001$; 3.2 vs 1.9 in RA, $p<0.001$) in comparison with Whites in both diagnostic groups. A lower level of education and a higher level of depression predicted greater pain on a MDHAQ in OA in separate models for AA and Hispanic patients and in RA in Hispanic patients (Table).

Table 1. Multiple regression models predicting clinical pain on a MDHAQ stratified by ethnicity

DV: MDHAQ-Pain (0–10)	Osteoarthritis			Rheumatoid Arthritis		
	β	p	R squared	β	p	R squared
Model 1						
Age	-0.04	0.49	0.13*	0.08	0.25	0.10*
Sex	-0.07	0.21		0.03	0.65	
African-Americans	0.12	0.06		0.04	0.94	
Education	**-0.19**	**0.005**		-0.09	0.19	
Depression	**0.19**	**0.002**		**0.29**	**<0.001**	
Model 2						
Age	-0.05	0.39	0.15*	0.05	0.40	0.16*
Sex	-0.12	0.07		0.02	0.68	
Hispanic	0.09	0.19		0.03	0.63	
Education	**-0.19**	**0.01**		**-0.19**	**0.01**	
Depression	**0.21**	**0.002**		**0.30**	**<0.001**	

Conclusions: AA and Hispanic patients had higher level of pain than Whites, but these differences are mainly influenced by level of education and level of depression in OA and RA patients. These results support the biopsychosocio-cultural model of pain in which, ethnic group differences may be determined by multiple mechanisms including socio-cultural as education, and psychological as depression, in addition to biological pathways.

References:

[1] Rahim-Williams B, Riley JL, et al. Pain Med 2012, 13(4):522–540.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3843

SAT0517 FACTORS RELATED TO ANALGESIC USE IN PATIENTS WITH KNEE AND/OR HIP OSTEOARTHRITIS REFERRED TO AN OUTPATIENT CENTER: RESULTS FROM THE AMSTERDAM OSTEOARTHRITIS COHORT

J. Knoop[1], J. van Tunen[2], M. van der Esch[1], L.D. Roorda[1], J. Dekker[3], M. van der Leeden[1,3], W.F. Lems[4,5]. *[1]Amsterdam Rehabilitation Research Center, Reade, Center for Rehabilitation and Rheumatology, Amsterdam, Netherlands; [2]Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark; [3]Department of Rehabilitation Medicine, VU University Medical Center; [4]Jan van Breemen Research Institute, Reade, Center for Rehabilitation and Rheumatology; [5]Department of Rheumatology, VU University Medical Center, Amsterdam, Netherlands*

Background: Analgesics are recommended in current guidelines, but non-use and inadequate prescription have been reported in patients with knee and/or hip osteoarthritis (OA). Furthermore, predictors of analgesic use have not yet been clarified.
Objectives: To (i) describe the use of analgesics; and (ii) determine factors that are related to analgesic use in patients with knee and/or hip OA referred to an outpatient center.
Methods: Data from 656 patients with knee and/or hip OA referred to an outpatient center (Amsterdam Osteoarthritis (AMS-OA) cohort) were used. Self-reported use of analgesic (yes/no) was administered and subdivided into acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs, including coxibs) and opioids. Logistic regression analyses were performed to analyze the association between analgesic use and disease-related, predisposing, and enabling factors.
Results: Analgesic use was reported by 62% of the patients, with acetaminophen, NSAIDs and opioid use reported by 50%, 30% and 12%, respectively. Factors related to analgesic use were higher pain severity, longer duration of symptoms, higher radiographic hip OA severity, overweight/obesity, and psychological distress. These factors explained 21% of the variance of analgesic use.
Conclusions: Less than two-third of patients with knee and/or hip OA referred to an outpatient center reported analgesic use, which seems to be indicative for under-use. Although multiple, mostly disease-related factors were associated with analgesic use, it remained predominantly unexplained. Our findings may indicate that prescription of analgesics should be guided more dominantly by clinical symptoms and needs, and preceded by a thorough shared decision making process between patient and physician.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2286

SAT0518 ASSOCIATION BETWEEN GRIP STRENGTH AND HAND AND KNEE RADIOGRAPHIC OSTEOARTHRITIS IN OLDER ADULTS: DATA FROM THE DONG-GU STUDY

J.-E. Kim, J.-H. Kang, K.-E. Lee, D.-J. Park, S.-S. Lee on behalf of Chonnam. *Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic Of*

Objectives: Although some studies have shown a negative relationship between grip strength and hand osteoarthritis (OA), little is known about how grip strength is related to specific radiographic features of hand OA, such as osteophytes, joint space narrowing, and erosion. In addition, no reported study has examined whether grip strength, as a measure of muscle activity, is related to knee OA, which may also show a one-way effect of reduced muscle strength on OA. In this large, population-based cohort study, we took advantage of the availability of subjects without hand pain to evaluate the effect of grip strength on OA using a novel, semi-quantitative grading system. We also examined whether grip strength was related to detailed radiographic features of OA.
Methods: Data from 2,251 subjects enrolled in the Dong-gu study, who had no hand joint pain, were analyzed to investigate the relationship between grip strength and OA. Hand grip strength was measured using a hand-held dynamometer, and radiographs of the hand and knee were scored according to a semi-quantitative grading system. Multiple linear regressions were used to explore associations between grip strength and radiographic features of OA.
Results: Grip strength in men and women was negatively related to hand (both $p<0.001$) and knee (men, $p<0.001$; women, $p=0.010$) OA after adjusting for confounders. Hand (men, $p<0.001$; women, $p=0.001$) and knee (both $p<0.001$) joint space narrowing showed the strongest associations with low grip strength, regardless of sex. Moreover, the severity of hand osteophytes in women ($p=0.001$), knee osteophytes in men ($p=0.006$), hand malalignment (men, $p=0.008$; women, $p=0.041$), and subchondral cysts (men, $p<0.001$; women, $p=0.007$) was correlated with low grip strength in both sexes.
Conclusions: Among subjects without hand joint pain, low grip strength was associated significantly with hand and knee radiographic OA, regardless of sex. Among all types of OA radiographic damage, low grip strength showed the strongest association with joint space narrowing.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2355

SAT0519 THE VALUE OF HIGH-SENSITIVITY C-REACTIVE PROTEIN IN HAND AND KNEE RADIOGRAPHIC OSTEOARTHRITIS: DATA FROM THE DONG-GU STUDY

J.-E. Kim, J.-H. Kang, K.-E. Lee, D.-J. Park, S.-S. Lee[1,1]. *Chonnam National University Medical School and Hospital, Gwangju, Korea, Republic Of*

Objectives: Due to the inconsistent association between high-sensitivity C-reactive protein (hs-CRP) and osteoarthritis (OA), we evaluated the relationship between hs-CRP and various radiographic findings in older adults with OA.
Methods: This cross-sectional study recruited 2,400 participants from the population-based Dong-gu cohort. The scores of radiographic features in OA on X-rays of the knees and hands were computed using a semi-quantitative grading system. The hs-CRP levels were measured using a particle-enhanced immunonephelometry assay. Correlations showing the relationship between hs-CRP and OA were calculated using multiple linear correlation analysis.
Results: The hs-CRP levels were significantly higher in older subjects ($p<0.001$), those with a higher body mass index (BMI) ($p<0.001$), current smokers ($p<0.001$), current alcohol drinkers ($p=0.012$), those who were less physically active ($p=0.002$), and those with a lower level of education ($p=0.036$). After adjusting for BMI and other confounders, the total OA scores (knee, $p=0.048$; hand, $p=0.010$), erosion scores (knee, $p=0.035$; hand, $p=0.031$), and sclerosis (knee, $p=0.021$; hand, $p=0.029$) in the knees and hands were all significantly positively correlated with hs-CRP. A significant association was also observed between hs-CRP and the hand malalignment score ($p=0.012$).
Conclusions: In this large cross-sectional study, the hs-CRP level was a significant predictor of radiographic OA. Of the various types of OA radiographic damage, erosion, sclerosis, and malalignment showed significant associations with hs-CRP.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2358

SAT0520 MARKED REDUCTION OF OSTEOARTHRITIS PAIN WITH A HYDROGEN SULFIDE-RELEASING NAPROXEN DERIVATIVE

J.L. Wallace[1], D. Vaughan[2]. *[1]University of Calgary, Calgary; [2]Antibe Therapeutics Inc, Toronto, Canada*

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) remain a mainstay of therapy for osteoarthritis, but their use is limited by their propensity to cause significant gastrointestinal (GI) bleeding and ulceration. Hydrogen sulfide (H2S) is an endogenous signaling molecule that has been shown to exert protective and pro-healing effects in the GI tract. We developed a series of H2S-releasing NSAIDs, and have now tested the lead drug (ATB-346) in a phase 2a clinical trial in patients with osteoarthritis. ATB-346 is a derivative of naproxen, the most cardiovascular-safe of the NSAID family. Data from a phase 1 clinical trial suggested that ATB-346 was significantly more potent and long-lasting than naproxen in terms of suppressing cyclooxygenase (COX) activity.
Objectives: An open-label phase 2a trial was performed to determine if a low dose of ATB-346 (250 mg; equimolar to 160 mg naproxen), given once daily, would provide significant pain relief in patients with osteoarthritis. To be admitted to the trial, patients had to exhibit a $\geq$10 point increase in the WOMAC Visual Analog Score between their screening visit and the baseline study entry visit.
Methods: 12 patients with osteoarthritis of the knee who met the inclusion criteria were recruited for the trial (diagnosis of OA $\geq$2 years; age 40–75; BMI $\leq$40). The WOMAC subscale pain score (0–20) was the primary endpoint. The patients were off anti-inflammatory medication for 5 days prior to starting this study. After recording the initial WOMAC subscale pain score, they began once daily oral treatment with ATB-346 (250 mg). Pain scores were recorded on the day prior to starting ATB-346 treatment ("day -1"), and on days 4 and 10 of treatment. Blood samples were collected for measurement of COX activity on days -1, 1, 4 and 10.
Results: ATB-346 was safe and well tolerated. The mean WOMAC subscale pain score the day prior to initiation of treatment was 14.0 + 0.7. A significant decrease in the WOMAC subscale pain score was observed on day 4 (-4.3±1.0; $p<0.01$), with an even greater decrease on day 7 (-7.6±1.5; $p<0.001$). Whole blood COX activity was suppressed by more than 80% ($p<0.01$) on the first day of treatment, and continued to be suppressed throughout the study.
Conclusions: The results of this study demonstrate that a low dose of ATB-346, given only once daily, produces a clinically and statistically significant reduction of pain in patients with osteoarthritis, that may exceed what can be achieved with standard doses of napoxen or celecoxib (1,2). The observed suppression of COX activity was consistent with the pain reduction data, supporting the conclusion that ATB-346 is considerably more potent and long-acting than naproxen. Extensive pre-clinical studies have demonstrated that ATB-346 has greatly improved GI safety as compared to naproxen and other commonly used NSAIDs.
References:
[1] Wittenberg et al. Arth Res Therap 2006; 8: R35 (doi: 10.1186/ar1854.
[2] Boucher M. http://www.page-meeting.org/pdf_assets/8269-Bayesian%20Meta%20Analysis%20Final.pdf.
Disclosure of Interest: J. Wallace Shareholder of: Antibe Therapeutics Inc, Employee of: Antibe Therapeutics Inc, D. Vaughan: None declared
DOI: 10.1136/annrheumdis-2017-eular.1040

SAT0521 INCREASING PHYSICAL ACTIVITY IN OLDER PEOPLE WITH PAIN. PRELIMINARY RESULTS OF THE IPOPP PILOT TRIAL

J. McBeth[1,2], E. Nicholls[2,3], E. Healey[2], N.E. Foster[2,3], E.M. Hay[2], T. Pincus[4], S. Dent[2], C.A. Chew-Graham[2], L. Hartshorne[3], C. Jinks[2] on behalf of iPOPP team. *[1]Arthritis Research UK Centre for Epidemiology, The University of Manchester, Manchester; [2]Research Institute for Primary Care and Health Sciences; [3]Keele Clinical Trials Unit, Keele University, Keele; [4]Department of Psychology, University of London, London, United Kingdom*

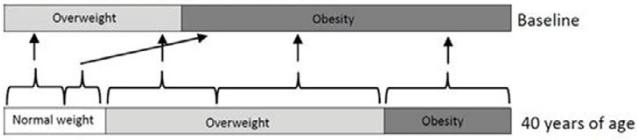
Background: Chronic (≥3 months) pain is associated with physical inactivity in older (≥65 years) people. Walking is an acceptable form of physical activity with health benefits. We have developed Increasing Physical Activity in Older People with Pain (iPOPP), a brief intervention to increase walking.
Objectives: To assess the acceptability and credibility of iPOPP, and to test the feasibility of trial processes, in a pilot randomised controlled trial.
Methods: Eligible responders to a screening questionnaire (≥65 years; consulted their general practitioner for chronic pain; Chronic Pain Grade score ≥2) collected 7-day accelerometer data before randomisation and at the end of follow-up. Participants were randomised to one of Usual primary care; Pedometer, walking diary, pain toolkit (written pain management information); or iPOPP comprising *week 1* face-to-face Health Care Assistant (HCA) consultation to develop a walking action plan, pedometer, walking diary, pain toolkit, discussion of walking behaviour and barriers, goal setting; *week 2* follow up face-to-face or telephone (participant preferred) HCA consultation to review progress and goals, relapse prevention strategies; *weeks 3–10* weekly motivational prompts (participant preferred postcard, email or text). A follow-up questionnaire was sent 12 weeks post-randomisation.
Success criteria were: 7% of those screened would be eligible, return an accelerometer and be randomised; follow-up rates ≥75% of those randomised; ≥50% of those in iPOPP would complete week 1 and 2 intervention sessions; and a median score of ≥5/10 across a four-item intervention acceptability and credibility questionnaire.
Results are number (%) or median (inter quartile range (IQR)).
Results: Of 2326 people mailed, 1256 (54%) responded and 695 (30%) were eligible. After mailing study information to 425 eligible participants, 161 (38%) agreed to participate, 159 (12% of those mailed) returned an accelerometer and were randomised, 7 withdrew, and 136 (86%) returned a follow-up questionnaire. Of those randomised to iPOPP 82% completed week 1 and 2 intervention sessions; 32% had a face-to-face week 2 follow-up; 48% preferred postcard motivational prompts, 10% email, 22% text, and 20% had no preference. Median (IQR) acceptability and credibility scores were: "how logical is treatment?" 8 (3, 9.8), "confidence in treatment success" 5.5 (3, 8), "would recommend treatment to friend" 7 (3.3, 9), and "treatment would be successful for another pain problem" 5 (3, 7.8). 152 participants were mailed a follow-up accelerometer and 144 (95%) were returned. 147 (91%) baseline and 117 (81%) follow-up accelerometers had useable data.
Conclusions: These data demonstrate the acceptability and credibility of the iPOPP intervention, and the feasibility of proposed trial processes. The effectiveness of iPOPP compared with usual care will be tested in a future main trial.
Acknowledgements: Funded by Arthritis Research UK (grant reference 20608). ELH, CJ, and CCG are part funded by the NIHR Collaborations for Leadership in Applied Health Research and Care West Midlands. The views expressed in this paper are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2699

SAT0522 SEARCHING FOR THE OPTIMAL TIMING FOR PREVENTIVE WEIGHT REDUCTION STRATEGIES FOR KNEE OSTEOARTHRITIS DEVELOPMENT

J. Runhaar[1], M. Landsmeer[1], M. van Middelkoop[1], S.M. Bierma-Zeinstra[2]. *[1]General Practice; [2]General Practice and Orthopaedics, Erasmus University Medical Center Rotterdam, Rotterdam, Netherlands*

Background: We previously showed that middle-aged women free of clinical knee osteoarthritis (OA), but at high-risk for future OA development due to a BMI ≥27 kg/m^2, had a high prevalence of OA features on MRI [1]. Subjects with a steadily decrease in body weight over 30 months (-9.0±7.2 kg), did not show a significantly different progression of these features, compared to those without loss in body weight [2].
Objectives: To explore the effects of differences in body weight in the years prior to inclusion on the prevalence of knee OA on MRI at baseline, to discuss the optimal timing for preventive weight loss strategies for OA development.
Methods: Data from the PROOF study (ISRCTN 42823086) were used [3]. At baseline, women aged 50–60, with a BMI ≥27 kg/m^2 were recruited. At inclusion, the women were free of clinical knee OA. At baseline, all participants filled-in a questionnaire for demographic data, including body weight at age 40, and body weight and height were measured. BMI at 40 years and at baseline was calculated and classified into normal weight (BMI <25 kg/m^2), overweight (BMI ≥25 and <30 kg/m^2) and obesity (BMI ≥30 kg/m^2). MRI scans of both knees was made on a 1.5 Tesla scanner. All MRIs were scored using the semi-quantitative MRI Osteoarthritis Knee Score (MOAKS) and MRI OA was defined in all knees was defined using published definitions [4]. Using logistic regression, the percentages of women with MRI OA, with unilateral MRI OA, bilateral MRI OA, and with ≥2 affected compartments were compared, using the normal/overweight group as reference.
Results: 374 women had all baseline measurements available and were selected. At baseline, 127 women were overweight and 248 were obese. Mean age was 55.7±3.2 years. Of the baseline obese women, 11% (26 women) reported normal weight, 52% (130 women) overweight and 37% (92 women) obesity at 40 years. Of the baseline overweight women, 39% (49 women) reported normal weight, 61% (77 women) overweight and 1 woman reported obesity at 40 years (see figure).
Baseline prevalence of MRI OA, of unilateral/bilateral MRI OA, and the percentage of women with ≥2 affected compartments, out of both TF and both PF compartments, are presented in the table.

Baseline and 40-years BMI groups and their course*.



*the one overweight woman at baseline that reported obesity at 40 years was omitted for clarity reasons

Prevalence of MRI OA for different subgroups by BMI course.

BMI group at 40 years	BMI group at baseline	N*	Prevalence of MRI OA overall (uni-/bilateral/2+ compartments)
Obesity	Obesity	92	44%# (25%# / 19%# / 23%#)
Overweight	Obesity	130	32%# (25%# / 7% / 9%)
Normal weight	Obesity	26	23% (15% / 8% / 12%)
Overweight	Overweight	77	27% (22% / 5% / 12%)
Normal weight	Overweight	49	16% (10% / 6% / 6%)

N = number of women. *the one overweight woman at baseline that reported obesity at 40 years was omitted for clarity reasons. #Significant difference compared to 'normal/overweight' group (p < 0.05).

Conclusions: Women with higher body weight at 40 years showed higher prevalence of knee OA on MRI at the age of 56. It is highly questionable whether OA related structural abnormalities seen on MRI are reversible. It is suggested that body weight reduction around the age of 40 might be much more effective for the prevention of future knee OA development than it would be at the age range of 50 to 60 years, where radiographic and clinical knee OA usually develops.
References:
[1] Landsmeer M, Runhaar J, et al. Reducing progression of knee OA features assessed by MRI in overweight and obese women: secondary outcomes of a preventive RCT. OA&C, 2016;24:982–90.
[2] Landsmeer M, de Vos B, et al. Effect of weight change on progression of knee OA features assessed by MRI in high-risk overweight and obese women. OA&C, 2016;24:S263–S264.
[3] Runhaar J, van Middelkoop M, et al. Prevention of knee osteoarthritis in overweight females: the first preventive randomized controlled trial in osteoarthritis. Am J Med. 2015;128(8):888–895.e4.
[4] Hunter D, Arden N, et al. Definition of osteoarthritis on MRI: results of a Delphi exercise. OA&C, 2011;19(8):963–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5795

SAT0523 NO TREATMENT EFFECTS OF ORAL GLUCOSAMINE FOR SUBGROUPS OF KNEE AND HIP OSTEOARTHRITIS PATIENTS; AN INDIVIDUAL PATIENT DATA META-ANALYSIS FROM THE OA TRIAL BANK

J. Runhaar[1], R. Rozendaal[1], M. van Middelkoop[1], J. Bijlsma[2], M. Doherty[2], K. Dziedzic[2], L. Lohmander[2], T. McAlindon[2], W. Zhang[2], S. Bierma-Zeinstra[2]. *[1]General Practice, Erasmus University Medical Center Rotterdam; [2]OA Trial Bank Steering Committee, Rotterdam, Netherlands*

Background: The effectiveness of oral glucosamine for symptoms of osteoarthritis (OA) is debated. Individual trials are not powered to show effects within subgroups of patients.
Objectives: To evaluate the effectiveness of oral glucosamine in clinical relevant subgroups of hip and knee OA patients based on pain severity, BMI, sex, structural abnormalities and inflammation, using individual patient data from published trials.
Methods: A systematic search for published randomized controlled trials on the effectiveness of any oral glucosamine substance in patients with clinically or radiologically defined knee or hip OA was performed. Additionally, trail registries were searched for ongoing studies. All authors and institutions of all eligible studies were approached and asked to share the trial data. All shared trials were assessed for their risk of bias, using the criteria recommended by the Cochrane. Missing data for covariates and outcome measures were imputed, using multiple imputation methods, within each original study. Subgroup factors were dichotomized, based on consensus of the OA Trial Bank Steering Committee. A multilevel regression analysis was performed to estimate the magnitude of the effect of glucosamine over the control intervention in the different subgroups with the individuals nested within each study. Pain at short-term (3 months)

and long-term (24 months) served as primary outcomes measure, function as secondary. Outcome measures measured on different scales were standardized to a 0–100 scale to pool the data. All analyses were performed with and without stratifying for affected joint and type of glucosamine substance.
Results: Out of 21 eligible studies, six studies (N=1663) shared their trial data with the OA Trial Bank. Only one of these studies (N=40) was industry driven. All six studies had a low risk of bias, of which five trials (all not industry driven) compared glucosamine to placebo. These five studies represented 50% of the total number of randomized subjects in all published trials for this comparison. No main effects of glucosamine were found on pain or function at short-term (mean difference 0.31 95% CI [-2.02 to 2.64] and 1.56 [-0.56 to 3.69], respectively) and at long-term follow-up (0.98 [-1.76 to 3.73] and 1.40 [-1.27 to 4.06], respectively). Also, no significant interactions with treatment were found for subgroups based on pain severity (WOMAC pain <70 vs. ≥70), BMI (<27 kg/m^2 vs. ≥27kg/m^2), sex (male vs. female) and structural abnormalities (KL-grade 0–2 vs. 3–4), see Table. Stratification for knee OA patients only and for type of glucosamine did not result in any differences in the outcomes. No data was available to adequately form subgroups based on degree of inflammation.

Estimated pooled differences between glucosamine and placebo on a 0-100 scale and p-values for treatment-subgroup interactions.

		All studies (N = 1394)	Knee OA only (N = 1172)	GH in knee OA (N = 671)	GS in knee and hip OA (N = 723)	GS in knee OA (N = 501)
Pain at short-term*	*Estimated pooled differences and 95% confidence interval*					
	Glucosamine vs placebo	0.31 (-2.02 – 2.64)	0.53 (-2.21 – 3.26)	1.97 (-1.14 – 5.09)	-2.62 (-6.03 – 0.79)	-5.99 (-11.50 – -0.48)
	p-values for treatment-subgroup interactions					
	Pain subgroup	0.80	0.92	0.94	0.59	0.81
	BMI subgroup	0.36	0.66	0.83	0.30	0.43
	Sex subgroup	0.80	0.70	0.80	0.67	0.62
	KL subgroup	-	-	-	-	-
Pain at long-term*	*Estimated pooled differences and 95% confidence interval*					
	Glucosamine vs placebo	0.98 (-1.76 - 3.73)	0.19 (-2.83 – 3.22)	0.78 (-4.33 – 5.89)	1.22 (-1.90 – 4.33)	-0.38 (-3.67 – 2.90)
	p-values for treatment-subgroup interactions					
	Pain subgroup	0.26	0.28	0.42	0.44	0.86
	BMI subgroup	0.55	0.10	0.51	0.72	0.10
	Sex subgroup	0.46	0.53	0.75	0.52	0.77
	KL subgroup	-	0.40	-	-	-
Function at short-term**	*Estimated pooled differences and 95% confidence interval*					
	Glucosamine vs placebo	1.56 (-0.56 – 3.69)	1.57 (-0.93 – 4.31)	2.13 (-0.82 – 5.09)	0.74 (-2.06 – 3.53)	-1.38 (-5.91 – 3.16)
	p-values for treatment-subgroup interactions					
	Pain subgroup	0.46	0.32	0.38	0.97	0.90
	BMI subgroup	0.92	0.87	1.00	0.83	0.45
	Sex subgroup	0.55	0.37	0.23	0.49	0.79
	KL subgroup	-	-	-	-	-
Function at long-term**	*Estimated pooled differences and 95% confidence interval*					
	Glucosamine vs placebo	1.40 (-1.27 – 4.06)	0.63 (-2.31 – 3.58)	0.85 (-4.43 – 6.13)	2.02 (-0.82 – 4.86)	0.62 (-2.29 – 3.52)
	p-values for treatment-subgroup interactions					
	Pain subgroup	0.49	0.38	0.55	0.94	0.91
	BMI subgroup	0.82	0.42	0.65	0.56	0.68
	Sex subgroup	0.72	0.61	0.80	1.00	0.94
	KL subgroup	-	0.77	-	-	-

*measured using WOMAC pain (0-100) and adjusted for age sex, BMI, WOMAC pain at baseline and study number. **measured using WOMAC function (0-100) and adjusted for age sex, BMI, WOMAC function at baseline and study number. Positive estimated pooled differences indicate a greater reduction in the outcome in the glucosamine group compared to the placebo group. GS = glucosamine sulphate; GH = glucosamine hydrochloride.

Conclusions: The majority of industry-led glucosamine studies for osteoarthritis did not wish to share data, challenging optimal use of available data. There is currently no evidence for the use of glucosamine for the treatment of hip or knee osteoarthritis and an absence of support for clinically relevant subgroups of OA patients according to baseline pain severity, BMI, sex, and structural abnormalities.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5986

SAT0524 UTILITY OF TOCILIZUMAB IN CLINICAL MANIFESTATIONS OF EROSIVE OSTEOARTHROSIS OF HANDS REGIONAL HOSPITAL ISSSTE PUEBLA, MÉXICO

J.M. Sánchez Huerta[1], J. Gálvez-Romero[2], W. López-Rodriguez[1], A. López[3]. *[1]Rheumatology; [2]ISSSTE, Puebla, Puebla; [3]UDLAP, Cholula, Puebla, Mexico*

Background: Erosive osteoarthritis (EOA) is a form of severe involvement of osteoarthrosis in the hands, characterized by inflammation of the synovium of the proximal interphalangeal (PIF) and distal joints (DIF); the last ones are the most affected in a symmetrical manner. Inhibition of interleukin 6 (IL-6) in joints with osteoarthrosis helps to improve the production of the cartilaginous matrix and microfractures of articular cartilage.
Objectives: To know if the application of TCZ is useful for the control of the clinical manifestations of EOA of the hands.
Methods: Twenty-four patients with EOA were studied, 18 females and 6 males with ages ranging from 42 to 72 years, with an evolution time of 4 to 30 years. The application of TCZ was intravenous (8 mg/kg of body weight per month).
Articular pain in the PIF and distal joints was evaluated by the visual analogue scale (VAS) (0 to 10) and joint pain (0 to 50), morning stiffness (0 to 10), and functional limitation (0–90) by the AUSCAN index.
Results: The VAS showed improvement of 30% (0% to 100%). The AUSCAN index showed improved pain (16.2), morning stiffness (0.6) and functional limitation (17.5). Decreased ESR, CRP, and IL-6 levels less than 1.56 to 59.1 pg/ml.
Conclusions: IV Tocilizumab is useful for the control of the clinical manifestations of OAE of the hands. More precise studies are needed to evaluate the improvement of the cartilaginous matrix in EOA by TCZ.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6483

SAT0525 THE EFFICACY OF PELOID THERAPY IN MANAGEMENT OF HAND OSTEOARTHRITIS

M. Aksoy Kasapoğlu[1], L. Altan[2], R. Eröksüz[3], B. ÖkmenMetin[1]. *[1]Physical Medicine and Rehabilitation, University of Health Sciences Bursa Yüksek Ihtisas Training and Research Hospital; [2]Physical Medicine and Rehabilitation, Uludağ University Medical Faculty; [3]Ecology and Hydroclimatology, University of Health Sciences Bursa Yüksek Ihtisas Training and Research Hospital, Bursa, Turkey*

Background: Hand osteoarthritis (OA) is associated with pain, reduced grip strength, loss of range of motion (ROM), and joint stiffness, leading to impaired hand function and difficulty in performance of daily living activities. Various randomized controlled clinical trials were conducted to assess the efficacy and tolerability of mud-pack therapy in patients with knee OA. Data from these clinical trials support the beneficial effect of mud-pack therapy on pain, function, and quality of life in knee OA. However, to the best of our knowledge, in spite of its significant impact of on the activities of daily life, there is a lack of adequate randomized controlled studies on peloid therapy in management of osteoarthritis of the hand
Objectives: To investigate the effects of peloid therapy in the patients with hand OA on pain, functional state, grip strength, and the quality of life
Methods: 63 patients aged between 35 and 75 years, who had been diagnosed with hand OA were included in the study. Patients were randomized into 2 groups with a random number table. Patients in Group 1 (n=33) underwent peloid therapy over 2 weeks, 5 sessions a week, for a total of 10 sessions and home exercise program. Patients in Group 2 (control, n=30) received only the same home exercise program as in Group 1. Patients were evaluated just before, and 2 and 6 weeks after the start of the study with Visual Analogue Scale (VAS), Australian/Canadian Osteoarthritis Hand Index (AUSCAN) Health Assessment Questionnaire (HAQ), Hand Grip Strength (HGS), Pinch strength (PS).
Results: Statistically significant improvements were observed in all parameters assessed at week 2 and week 6 in the Group 1 ($p<0.05$). Statistically significant differences were observed in HGS scores in the Group 2 at week 2, and in AUSCAN scores at week 6 ($p<0.05$). Intergroup comparisons of the scores revealed significant differences between the peloid therapy group and control group in VAS, HAQ, AUSCAN, HGS and PS scores at week 2 and week 6 ($p<0,05$).
Conclusions: This study demonstrates that peloid therapy is an effective and confident treatment modality in the management of symptomatic osteoarthritis of the hand and provides effective pain control and improvements in the hand functions, quality of life and grip strength
References:
[1] Zhang Y, Niu J, Kelly-Hayes M, Chaisson CE, Aliabadi P, Felson DT. Prevalence of symptomatic hand osteoarthritis and its impact on functional status among the elderly. Am J Epidemiol 2002;156:1021–7.
[2] Bellometti S, Cecchettin M, Galzigna L (1997) Mud-pack therapy in osteoarthrosis. Changes in serum levels of chondrocyte markers. Clin Chim Acta 268:101–106.
[3] Odabaşı E, Turan M, Erdem H, Pay S, Güleç M, Karagülle MZ. The Effect of Mud Pack Treatment in Knee Osteoarthritis. Turk J Rheumatol 2009; 24: 72–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2310

SAT0526 POSSIBILITY OF CARTILAGE REPAIR WITH PLATELET AUTOLOGOUS PLASMA (PAP)

L.V. Khimion[1], O.A. Burianov[2], L.O. Smolina[1], H. Havryliuk[1], T. Omelchenko[3]. *[1]Department of Family Medicine, Shupyk National Medical Academy of Postgraduate Education; [2]Traumatology and Orthopedic Department; [3]Traumatology and Orthopedic Department, Bogomolets National Medical University, Kiyv, Ukraine*

Background: The investigations of the platelet-derived biologic agents in osteoarthritis treatment had shown promising but often controversial results.
Objectives: To study the efficacy (in clinic & experiment) & safety (in clinic) of the platelet autologous plasma (PAP) in cartilage repair and treatment of early knee OA.
Methods: The study was conducted at the Department of Family Medicine and Traumatology and Orthopedic Department and consisted of 2 parts: experimental (20 rabbits with the traumatic damage of the knee cartilages) and clinical (included 146 patients with diagnosed knee OA (radiological stage I-II). Rabbits

were randomly divided in 4 groups: in 1st and 2nd grs. 10 animals received 3 intra-articular injections of PAP (on 5th,7th,14th day after knee trauma) as a control (gr.3 and 4) 10 rabbits received 3 intra-articular injections of 0,9% NaCl at the same days after trauma; histopathology was performed at 45th (1st and 3rd gr.) & at 90th day (2nd and 4th gr.) after trauma. 146 patients - 58 men (39.7%) & 88 women (60.3%), were divided into 2 grs. Gr.1 included 68 patients who consented to receive standard OA treatment and 3 weekly intra-articular injections of PAP (total 2 courses in 12 months) (plasma volume 12–15ml/course, total platelets number per injection 1260,24±22,1x10^9); Gr.2 consisted of 78 patients with the same diagnosis who received only standard OA treatment (non-steroidal anti-inflammatory drugs, physiotherapy, exercises). Both groups were of comparable age, gender and initial WOMAC data (Gr.1 40,9±0,7 Gr.2 39,7±0,9, $p>0,05$). WOMAC scale parameters were analyzed before treatment and after 3 weeks; 6 & 12 months after course of treatment in both groups.

Results: In animals histopathology has found better repair, ↓ inflammation, better structure of the knee cartilage after PAP injections comparing with the control groups animals; in addition in 3rd group of rabbits ↓ signs of early posttraumatic osteoarthritis were found (comparing to 4th gr.).

Clinical study demonstrated better changes in pain, stiffness and function in 3 weeks after treatment in patients of Gr.1 comparing to Gr.2 (WOMAC had decreased by 35.8% in Gr.2 and by 74.1% in Gr.1), $p<0,05$.

After 6 months of follow-up (before 2 course of PAP treatment), the mean number of OA exacerbations was (0,7±0,02) in Gr.1 & (1,6±0,04) in Gr.2 ($p<0,05$) and general WOMAC index in Gr.1 was significantly lower than in Gr.2 (accordingly (22,8±0,3) and (36,5±0,8); $p<0,05$).

In the next 6 months again patients in Gr.1 had less exacerbations (0,51±0,03) then patients in Gr.2 (1,4±0,03),$p<0,05$; & better WOMAC performance (Gr.1-(17,5±0,6 & Gr.2–37,1±0,5 accordingly,$p<0,05$).

Conclusions: 1. Histopathology of the knee cartilage has shown promising results concerning possibility of cartilage repair after trauma and prophylaxis of the early posttraumatic OA after PAP injections in animal model.

2. Repeating intra-artricular injections of PAP, added to the standard care in knee OA improves functional activity, reduces pain and number of OA exacerbations in 12 months of follow up.

3. The further studies (both experimental and clinical) are needed to obtain more accurate information and determine the most effective methods of PAP use in OA patients.

References:

[1] Autologous platelet-rich plasma (PRP) in osteoarthritis treatment [sat0462]. L. Smolina, L. Khimion, EULAR-2016. London, GB, (Suppl2): 838.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2720

SAT0527 ASSESSMENT OF SHORT-TERM EFFECTIVENESS OF FIVE LOCAL TREATMENT MODALITIES IN PATIENTS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS

M.L. Ladehesa Pineda, M.C. Castro Villegas, R. Ortega Castro, P. Font Ugalde, L. Bautista Aguilar, C. López Medina, R. Jiménez Gasco, L. Pérez Sánchez, M.Á. Caracuel Ruiz, A. Escudero Contreras, E. Collantes Estévez on behalf of Rheumatology, Hospital Universitario Reina Sofía de Córdoba/Instituto Maimónides de Investigación Biomédica (IMIBIC). *Rheumatology, Hospital Universitario Reina Sofía of Córdoba, Córdoba, Spain*

Background: Inside the therapeutic algorithm of knee osteoarthritis (OA) it is included the Non-Arthroscopic Joint Lavage (NAJL) since around 1934 Burman reported that arthroscopies improved the symptoms. Current medical treatment strategies are aimed at pain reduction and symptom control rather than disease modification (1). The large variety of potentially interventions available has raised the need to assess their effectiveness.

Objectives: To compare the short-term effectiveness among five treatment strategies in patients with symptomatic knee OA.

Methods: An open, controlled, randomized prospective study involving 150 patients of whom 76.7% were females. The average age was 65.37±8.35. Patients had knee OA according to American College of Rheumatology criteria, with Kellgren-Lawrence radiographic grades II-III. They were randomly assigned to five groups of treatment, 1)NAJL (n=30), 2)NAJL+hyaluronic acid (HA) (n=32), 3)NAJL+ corticosteroid (CS) (n=32), 4)HA (n=31), and 5)CS (n=25). Evaluations took place at baseline, one and three months. Western Ontario and McMaster University Osteoarthritis Index (WOMAC) and Lequesne scores were recorded. Statistical analysis included mixed analysis of variance, with post-hoc comparisons with Sidak's adjustment, and multiple linear regression (MLR) to identify those possible factors associated to WOMAC total at 3 months.

Results: Regarding WOMAC pain, significative differences were found in NAJL, at one month and at 3 months; and in NAJL+CS at one month. For WOMAC stiffness, there were significative differences in NAJL at one month and at 3 months; in NAJL+HA after one month and 3 months versus one month; and in NAJL+CS, at one month. For WOMAC function, significative differences were found in NAJL at one month and at three months; in NAJL+CS at one month; and in HA at 3 months. Regarding WOMAC total, significative differences were found in NAJL at one month ($p<0.001$) and at 3 months ($p<0.001$); and in NAJL+CS at one month ($p=0.018$). For Lequesne, significative differences were found in HA at one month ($p=0.003$) and at 3 months ($p=0.019$) versus baseline; and in CS, at one month ($p<0.001$). The WOMAC function at baseline, NAJL+HA, and infiltration with CS are the variables that show a significant association with WOMAC total at 3 months. The group that received NAJL+HA had poorer outcomes.

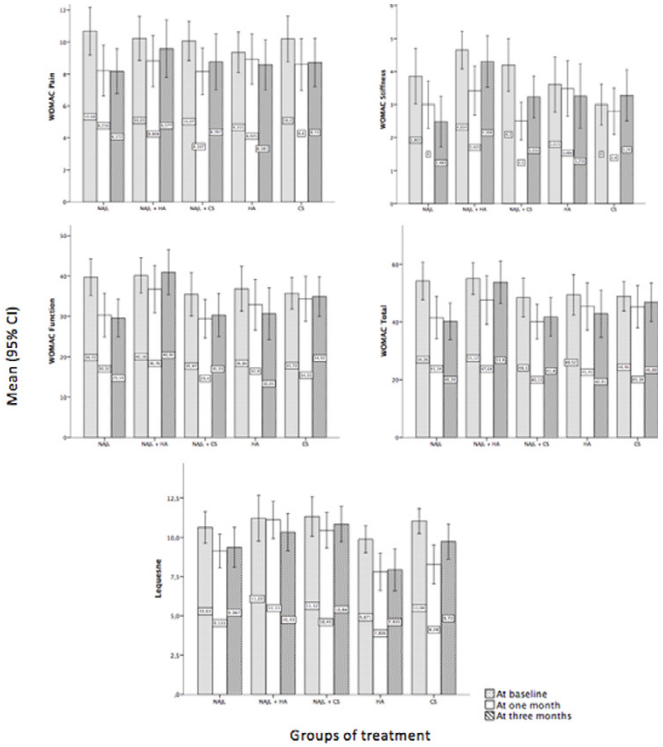


Figure 1. Clinical outcomes. WOMAC pain, stiffness, function and total, and Lequesne at baseline, at one month after treatment and three months after treatment.
Data are expressed as mean and confidence intervals are shown.
CI, confidence interval; NAJL, non arthroscopic joint lavage; HA, hyaluronic acid; CS, corticosteroid; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Conclusions: One month after treatment, best outcomes were obtained with HA due to the results found in Lequesne scale when comparing HA versus NAJL+HA, and NAJL+CS. Three months after the treatment, the most effective modality treatment was NAJL; since we did find significant differences regarding articular stiffness, physical function and Lequesne scale. The treatment with NAJL+HA appears to be less effective than the other modalities.

References:

[1] Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J et al. American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee. Arthritis Care & Research Vol. 64, No.4, April 2012,pp 465–474.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3555

SAT0528 MOLECULAR MODIFICATIONS INDUCED BY MUD-BATH THERAPY IN PATIENTS WITH OSTEOARTHRITIS

M.M. Angioni [1], A. Denotti [2], S. Pinna [1], C. Sanna [2], A. Floris [1], M. Piga [1], A. Loi [2], A. Cauli [1]. [1]*Scienze Mediche e Sanità Pubblica, Università degli Studi di Cagliari, Monserrato (CAGLIARI);* [2]*Antiche Terme di Sardara, Sardara (VS), Italy*

Background: Mud-bath therapy (MBT) is a non-pharmacological approach commonly used to treat osteoarthritis (OA). Several data indicate that MBT improve patient's symptoms (1), exerting a beneficial effect on pain and joint function, although the biological mechanisms involved in the therapeutic response are poorly defined.

Objectives: This study aimed to find molecular changes (proteins and mRNA variations) in patients with OA after MBT treatment.

Methods: The study included 39 patients whit primary diffuse osteoarthritis, assigned to receive a cycle of mud-bath therapy over a period of 2 weeks added to usual pharmacologic treatment. Whole blood and serum were collected before and after standard MBT treatment: for each time points two pools of patients sera were analyzed by the direct antigen-labeling technology (RayBio® Biotin Label-based Antibody Array, RayBiotech) obtaining a broad, panoramic view of protein expression. Using this semi-quantitative technique up to 1000 target proteins was simultaneously detected, making this approach ideally suited for proteomic studies. Again, pooled samples of mRNA were used to investigate genes expression and to perform the transcriptomic analysis using an high-resolution array design that contains >6.0 million distinct probes, covering coding and non-coding transcripts (GeneChip® HTA 2.0, Affymetrix).

Results: At the end of mud-bath therapy, using first a semi-quantitative approach, we observed in both biological replicates increased levels (>1.5 fold change) of: inhibin beta A subunit (INHBA), activin A receptor type 2B (ACVR2B), angiopoietin-1 (ANGPT1), beta-2-microglobulin (B2M), growth differentiation factor 10 (BMP-3b/GDF10), C-X-C motif chemokine ligand 5 (CXCL5), fibroblast growth factor 2 (FGF2), fibroblast growth factor 12 (FGF12), oxidized low density lipoprotein receptor 1 (OLR1), matrix metallopeptidase 13 (MMP13). We observed that some increased proteins belongs to the same family or pathway: INHBA, ACVR2B and BMP-3b are members of TGF-Beta superfamily; CXCL5 and MMP13 participate into IL-17 signaling pathway; FGF2 and FGF12 are proteins of FGF family. We are currently performing the transcriptome analysis, and the next step will be to correlate detected proteins with mRNA levels considering also post-transcriptional or epigenetic modifications. Finally we will validate these findings with other quantitative techniques (like ELISA and RT-PCR).
Conclusions: Our first proteomic and broad spectrum analysis suggest the implication of molecular pathways involved in a wide variety of cellular functions such as gene expression modulation, differentiation, angiogenesis, tissue repair, acute and chronic inflammatory response which may explain the beneficial effects of MBT observed in osteoarthritis. This "omic" approach (proteomic and transcriptomic), generated a huge amount of data that is currently under statistical and bioinformatic analysis.
References:
[1] Forestier R, Desfour H, Tessier JM, et al. Spa therapy in the treatment of knee osteoarthritis: a large randomised multicentre trial. Ann Rheum Dis. 2010;69:660–5.
Acknowledgements: Supported by Fondazione per la Ricerca Scientifica Termale (FORST) grant.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6874

SAT0529 PROLONGED TNF-INHIBITOR TREATMENT DURATION IS ASSOCIATED WITH LOWER RISK OF HAND OSTEOARTHRITIS PROGRESSION IN PATIENTS WITH RECENT-ONSET RHEUMATOID ARTHRITIS AFTER 10-YEAR FOLLOW-UP

M. Loef[1], F.P. Kroon[1], S.A. Bergstra[1], J.A. van der Pol[1], W.F. Lems[2], P.J. Kerstens[3], C.F. Allaart[1], M. Kloppenburg[1,4]. [1]*Rheumatology, Leiden University Medical Center, Leiden;* [2]*Rheumatology, VU University Medical Center, Amsterdam;* [3]*Rheumatology, Westfriesgasthuis, Hoorn;* [4]*Epidemiology, Leiden University Medical Center, Leiden, Netherlands*

Background: Increasing evidence indicates involvement of the pro-inflammatory cytokine TNF-α in hand osteoarthritis (OA) pathogenesis. Ten years clinical and radiologic follow-up of the BeSt study, a randomized trial primarily designed to investigate targeted treatment in rheumatoid arthritis (RA) patients, offered the unique opportunity to study the long-term effects of TNF inhibitors (TNFi) on the development and progression of hand OA. The distal interphalangeal joints (DIPs) are rarely affected in RA, which allowed to evaluate primary OA separately.
Objectives: To investigate the effect of TNFi on incidental and progressive radiographic hand OA after 10-year follow-up in recent-onset RA patients.
Methods: At baseline and 10-year follow-up 262 patients (mean age 52 years, 66% women) were available for radiologic assessment of hand OA. Eighteen interphalangeal joints (IPs) were scored for osteophytes (OP) using the Osteoarthritis Research Society International (OARSI) atlas (0–3; summated score 0–54), and according to the Kellgren-Lawrence (KL) scoring method (0–4; summated score 0–72). Incidental OA was defined as an increase ≥1 in summated OP score or ≥2 in summated KL score in absence of OA at baseline, and progressive OA as an increase ≥3 in summated OP or KL score in presence of OA at baseline, based on the smallest detectable change. TNFi treatment and disease activity score (DAS) were assessed on standardized visits at a three-monthly interval. Associations between duration of TNFi treatment in months and incidental and progressive OA were analyzed using generalized linear models with Poisson distribution and robust standard errors, while adjusting for age, gender, time averaged DAS, time averaged Sharp-van der Heijde score and hand OA severity at baseline.
Results: Based on the OP score, 126 patients (48%) were classified with OA at baseline in the DIPs and 82 patients (31%) in the proximal IPs (PIPs). Incidental OA developed in 33% of patients in DIPs and in 42% in PIPs. Progressive OA occurred in 30% of patients in DIPs and in 38% in PIPs. Of patients with and without OA at baseline, irrespective of joint location, 63% and 55% were treated with TNFi, with a median treatment duration of 47 and 36 months, respectively. No effect of TNFi treatment duration was seen on incidental hand OA. On progressive hand OA, every month of TNFi treatment resulted in a reduced relative risk (RR) of OA progression in DIPs with a RR (95% confidence interval) of 0.987 (0.978–0.996), but not in the PIPs. The results from the analyses with the KL scoring method were comparable to the OP score, as shown in table 1.

Table 1. Associations between TNFi treatment duration and progressive hand OA in 261* patients, defined by osteophyte score and Kellgren-Lawrence score.

Joint type	Number of patients treated/ median (IQR) duration of treatment	Adjusted RR (95% CI)^	P value
Patients with a ΔOP score ≥3 units in presence of OA at baseline			
DIPs	67/ 33 (12-72)	0.987 (0.978-0.996)	0.003
PIPs	43/ 30 (12-72)	0.995 (0.985-1.005)	0.321
Patients with a ΔKL score ≥3 units in presence of OA at baseline			
DIPs	51/ 39 (12-87)	0.991 (0.984-0.998)	0.007
PIPs	32/ 36 (12-72)	0.995 (0.986-1.004)	0.303

*1 patient missing due to poor quality of hand radiographs at 10 years. ^Adjusted for age, gender, time averaged DAS, time averaged SHS, severity of OA at baseline

Conclusions: Prolonged TNFi treatment is associated with a reduced relative risk on radiologic hand OA progression in DIPs, but not in PIPs, after 10 years. Although the effect sizes are small, these results provide evidence for influence of TNF-α in hand OA pathogenesis.
Disclosure of Interest: M. Loef: None declared, F. Kroon: None declared, S. A. Bergstra: None declared, J. van der Pol: None declared, W. Lems: None declared, P. Kerstens: None declared, C. Allaart Grant/research support from: The BeSt study was designed by the investigators and supported by a government grant from the Dutch Insurance Companies, with additional funding from Schering-Plough B.V. and Janssen B.V., M. Kloppenburg: None declared
DOI: 10.1136/annrheumdis-2017-eular.2337

SAT0530 CENTRAL SENSITISATION IN HAND OSTEOARTHRITIS: THE ANTERIOR CINGULATE CORTEX IS INVOLVED IN PAIN PROCESSING

M. Russell[1], F. Howe[2], T. Barrick[2], N. Sofat[1]. [1]*Institute of Infection & Immunity;* [2]*St George's, University of London, London, United Kingdom*

Background: We have previously shown that people suffering with chronic pain in hand OA have activation of central brain pain processing centres localised to the anterior cingulate cortex, insular cortex and thalamus by functional neuroimaging (1) and algometry (2).
Objectives: We hypothesised that hand OA subjects will have structural differences in 3 pain-processing regions of the brain - the anterior cingulate cortex (ACC), insular cortex and thalamus - based on activation of brain centres we have found previously (1). Our brain neuroimaging work was part of a randomised, placebo-controlled trial to assess the effect on clinical pain outcomes by intervention with centrally-acting analgesic agents: pregabalin or duloxetine.
Methods: The primary outcome measures for our clinical trial were hand pain Numerical Rating Scale (NRS) and AUSCAN pain after 12 weeks' treatment. In secondary outcome analyses, participants with hand OA (n=28) underwent T1-weighted MRI of the brain before and after 12 weeks of treatment with pregabalin, duloxetine or placebo therapy. Grey matter brain structure was compared using FreeSurfer regional volumetric analysis and voxel-based morphometry (VBM) to age-matched controls (n=11), and evaluated for volume changes in the ACC, insular cortex and thalamus.
Results: In our clinical trial, we observed clinically significant improvement in pregabalin, duloxetine and placebo treatment groups after 12 weeks (ANOVA p=0.0078). Most notably, pairwise comparisons for pregabalin vs placebo showed significant improvement for NRS pain and AUSCAN pain outcomes in the ITT analysis ($p<0.05$), but not for duloxetine vs placebo after 12 weeks' ($p>0.05$). Both voxel-wise and regional volumetric analyses demonstrated areas of reduced grey matter volume in the ACC of hand OA subjects, relative to control subjects, at baseline ($p<0.05$) (Figure 1). The structural differences in the ACC persisted following 12 weeks of treatment with pregabalin, duloxetine or placebo therapy ($p<0.05$). We did not observe structural differences in the insular cortex or thalamus in any of the three groups.

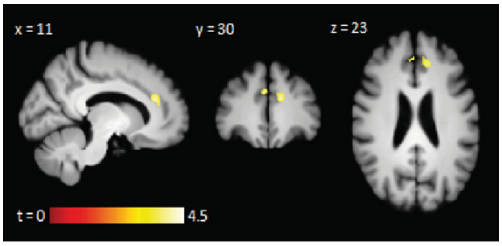


Figure 1. VBM analysis demonstrating clusters of reduced grey matter volume in the ACC in participants with hand OA, relative to control subjects, at baseline. The left side of the figure represents the left side of the brain.

Conclusions: We found that the ACC volume was reduced in participants with hand OA. The ACC is a key pain-processing region of the brain. Changes in ACC grey matter volume have previously been described in other painful conditions, but not hand OA. ACC grey matter volume reduction is thought to represent neural plasticity in chronic pain states. Our data supports the role of central sensitisation in hand OA and provides a rationale for the further investigation of centrally-acting analgesics in its management. Our trial demonstrated improvement in clinical endpoints for pain for pregabalin vs placebo and duloxetine vs placebo, respectively ($p<0.05$). However, structural differences in the ACC were still evident following 12 weeks of treatment with pregabalin or duloxetine. This may relate to the relatively short duration of treatment in our study. Alternatively, the baseline differences in the ACC may represent irreversible changes. Longitudinal studies with greater follow-up periods are necessary to further investigate this.

References:
[1] Sofat N, et al. Journal of Biomedical Graphics and Computing, 2013, 3(4). doi:. 10.5430/jbgc.v3n4p20.
[2] Wajed J, et al. International Journal of Rheumatology 2012; 2012:703138.
Acknowledgements: We acknowledge support from the Rosetree's Trust and the NIHR Clinical Research Network.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3537

SAT0531 MATRIX ASSISTED LASER DESORPTION IONIZATION IMAGING MASS SPECTROMETRY APPLIED TO HUMAN OSTEOARTHRITIS CARTILAGE REVEALS THE INTRA-TISSUE METABOLIC HETEROGENEITY

M. Eveque-Mourroux[1], P. Emans[2], T. Welting[2], A. Boonen[3], R. Heeren[1], B. Cillero-Pastor[1]. *[1]Division of Imaging Mass Spectrometry, Maastricht MultiModal Molecular Imaging (M4I) Institute; [2]Department of Orthopaedic Surgery; [3]Caphri Research institute, Maastricht University Medical Center, Maastricht, Netherlands*

Background: Osteoarthritis (OA) is one of the most common diseases, caused by a chronic degenerative disorder of the joint. OA can be related to the metabolic syndrome or metabolic abnormalities being recently defined as a subtype of the disease[1]. Matrix-assisted laser desorption/ionization (MALDI) imaging mass spectrometry (IMS) technology allows for the investigation of the bimolecular distribution of proteins, lipids or metabolites through the in situ analysis of tissue sections. In order to better understand the metabolic OA phenotype, the study of the endogenous metabolic profiles using MALDI-IMS should be considered.
Objectives: The main goal of this study is to apply MALDI-IMS methodology to study the metabolic spatial distribution of cartilage and to reveal intra-tissue and inter-patient heterogeneity.
Methods: Human OA cartilage was obtained from donors undergoing total knee joint replacement. Samples were heat stabilized by a stabilizer system, before being snap frozen. Cartilage punches were sectioned at 12 μm thickness in a cryostat and deposited on indium tin oxide (ITO) glass slides. 9-Aminoacridine (9AA) and N-(1-Naphthyl) Ethylenediamine DihydroChloride (NEDC) matrices were sprayed on the tissues. MALDI-MS profiling and imaging experiments were performed using different mass spectrometers. Data were analyzed by different software dedicated to mass spectrometry.
Results: Results showed that 9AA and NEDC matrices were both able to extract several and different compounds. MALDI-MS/MS was employed with 9AA matrix for molecular identification, confirming for the first time the presence of several metabolites in cartilage such as adenosine triphosphate, adenosine diphosphate, uridine triphosphate or N-Acetylglucosamine. Punches from lesioned and non-lesioned areas from the same OA patient were heat stabilized and sprayed with NEDC matrix. MALDI-IMS experiments at 40-μm of spatial resolution showed a different metabolic distribution between deep and superficial areas but also between lesioned and non-lesioned regions suggesting an evidence in the existence of intra-tissue heterogeneity (figure 1).

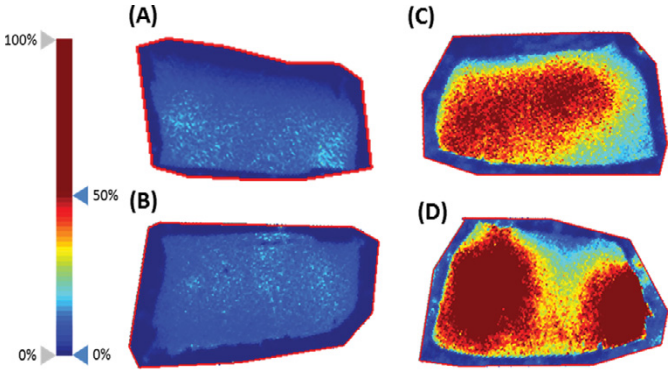


figure 1: Distribution of Hexose species (m/z 215. 03) in OA cartilage tissue sections from the same patient. (A, B) Duplicate of non-lesioned cartilage tissues sections. (C, D) Duplicate of lesioned cartilage tissues sections.

Conclusions: MALDI-IMS methodology is a useful technique for metabolite profiling of cartilage and could be employed to study OA patient heterogeneity. This fact will be especially relevant for OA patients suffering of metabolic syndrome.
References:
[1] Zhuo, Q., et al. (2012). Metabolic syndrome meets osteoarthritis. Nat Rev Rheumatol 8(12): 729–737.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6498

SAT0532 SLEEP QUALITY IN PATIENTS WITH KNEE OSTEOARTHRITIS

M. Sezgin[1], E. Yeşildal[1], S. Sevim[2], H. Ankaralı[3], G. Sahin[1]. *[1]Department of Physical Medicine and Rehabilitation; [2]Department of Neurology, Mersin University Medical Faculty, Mersin; [3]Department of Biostatistics and Medical Informatics, Duzce University Medical Faculty, Düzce, Turkey*

Objectives: The aim of this study was to investigate sleep quality in patients with knee osteoarthritis (OA).
Methods: One hundred patients with knee OA and age and gender-matched 75 healthy controls were enrolled into the study. Demographic characteristics of the participants were recorded. All patients was examined by a single physician, the findings were recorded. Knee radiographs of the patients were staged according to the Kellgren-Lawrence grading. In addition, to evaluate the clinical status and quality of life of patients was performed Western Ontario ve McMaster Universities Osteoarthritis Index (WOMAC) and Nottingham Health Profile (NHP). The sleep quality of two groups with MOS sleep scale and polysomnography (PSG) were subjectively and objectively evaluated.
Results: All scores of MOS sleep scale were significantly lower in patients with knee OA than controls ($p<0.001$). When PSG outcomes of the patients compared with the controls,waketime during sleep period (WTSP) (37.2±35.9, 13.1±19.4 p=0.012 respectively) and number of awakeness (NOAW) (9.2±18.2, 2.6±3.5, p=0.05 respectively) were significantly higher, sleep efficiency (SE) (84.2±21.1, 96.7±4.6 p=0.009 respectively) was significantly lower in patients with knee OA. There were significantly positive correlations between MOS sleep scale and PSG (sleep period, sleep onset, REM duration and REM latans) outcomes of the patients (r:0.44–0.59 p=0.04–0.006).
In addition, MOS sleep scale scores of patients were negatively related with both NHP (pain, emotional reaction, sleep and social isolation subgroup scores) and WOMAC (total and functional) scores (r:-0.20–0.47, p=0.04–0.0001).
Conclusions: The sleep quality of patients with knee OA was worse compared to healthy controls. The poor sleep and sleep quality in knee OA had adversely affected the clinical status and quality of life.
References:
[1] Hays RD, Martin SA, Sesti AM, Spritzer KL. Psychometric properties of the Medical Outcomes Study Sleep measure. Sleep Med 2005; 6:41–44.
[2] Wilcox S, Brenes GA, Levine D, et al. Factors related to sleep disturbance in older adults experiencing knee pain or knee pain with radiographic evidence of knee osteoarthritis. J Am Geriatr Soc 2000; 48:1241.
[3] Leigh TJ, Hindmarch I, Bird HA, Wright V. Comparison of sleep in osteoarthritic patients with age and sex matched healthy controls. Ann Rheum Dis 1988;47:40–2.
[4] Vivien CA, Priscilla SA, Christian G. Sleep and rheumatologic disorders. Sleep medicine reviews 2008;12: 211–228.97.
[5] Stewart AL, Sherbourn C, Hays RD, et al. Summary and discussion of MOS measures. Measuring functioning and well-being: The Medical Outcomes Study approach. Durham: Duke University Press, 1992:345–371.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2158

SAT0533 ASSOCIATION OF OSTEOARTHRITIS AND PERIODONTITIS BASED ON THE KOREA NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

M.K. Chung, N. Koo, B.W. Lee, J. Lee, S.-K. Kwok, S.-H. Park, J.H. Ju. *Division of Rheumatology, Department of Internal medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic Of*

Background: Osteoarthritis (OA) is a chronic joint disease with complex etiologies characterized by synovial inflammation, subchondral bone remodeling, and the formation of osteophytes, which leads to cartilage deterioration. Periodontitis (PD) is also a chronic inflammatory disease characterized by loss of periodontal ligament and alveolar bone. Recently, the association between OA and metabolic diseases has been proposed, and the association between several systemic diseases such as rheumatoid arthritis, metabolic syndrome and periodontitis has been also revealed.
Objectives: The aim of this study was to investigate the association between OA and PD in South Korea using data from the Korea National Health and Nutrition Examination Survey (KNHANES) during 2010–2014.
Methods: Cross-sectional data of 7,969 adults who completed the KHANES, and participated in both a periodontal examination and a knee imaging were analyzed. OA of knee was defined when a participant had knee arthralgia and showed radiographic change of Kellgren-Lawrence (KL) grade over 1. OA patients were grouped into mild (KL grade 1–2) and severe (KL grade 3–4) OA. The periodontal status was assessed by the Community Periodontal Index. Binary logistic regression analysis was performed according to the OA and PD status, severity of OA, and subgroups (age, gender) adjusting for the socio-demographics, oral health behaviors and status, smoking, and drinking.
Results: Of the 7,969 participants, 1408 (17.7%) had OA and 2987 (37.5%) had PD. OA and PD showed no significant association in overall analysis. However, in subgroup analysis, female patients with severe OA were more likely to have PD (adjusted odd ratio (OR) 1.377, P=0.0316); likewise, OR for severe OA in female patient with PD was 1.367. (P=0.0.54)
Conclusions: Severe OA and PD were associated with each other especially in

female in the Korean population. Further prospective and experimental studies are necessary to identify the impact and mechanisms of association between severe OA and PD in female.

References:
[1] Zhuo Q, Yang W, Chen J, Wang Y. Metabolic syndrome meets osteoarthritis. Nature reviews Rheumatology 2012; 8(12): 729–37.
[2] Kwon YE, Ha JE, Paik DI, Jin BH, Bae KH. The relationship between periodontitis and metabolic syndrome among a Korean nationally representative sample of adults. Journal of clinical periodontology 2011; 38(9): 781–6.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4849

SAT0534 EFFECT OF SUSTAINED- RELEASE SYMPTOMATIC DRUGS ON PROGRESSION OF KNEE JOINT OSTEOARTHROSIS IN PATIENTS WITH LESS THAN 5 YEARS DISEASE DURATION IN A 5-YEAR PROSPECTIVE STUDY

N. Kashevarova, E. Taskina, L. Alekseeva. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

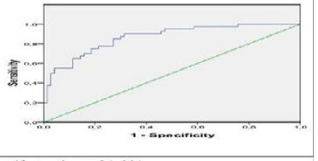
Objectives: To assess the effect of sustained release symptomatic drugs chondroitin sulfate (CS) + glucosamine hydrochloride (GH) on progression of knee OA in pts with <5 years disease duration during the 5year follow-up period (FUP).

Methods: This 5-year study included 52 female-patients with primary knee OA (ACR criteria), disease duration did not exceed 5 yrs (mean age–59,1±8,9). On each pts the individual file including 200 parameters was filled. Diagnostic modalities used in each patient included plain radiography of knee joints (gonarthrosis stage was classified using Kellgren J.- Lawrence J. scale), DEXA subchondral portions of the hip and tibia, ultrasound (US) and MRI examination of knee joints. First OA stage was documented in 22 (42,3%)pts, 2-nd - in 24 (46,2%), 3d- in 6 (11,5%). During 5 years of FUP 31 (60%) pts were administered the combined CS+GH regimen for more than 6 months a year. OA progression was documented based on radiographic criteria.

Results: During the 5 year FUP radiographic progression (upgrade in radiographic stage) of knee OA was documented in 14 pts (Group 1 - with OA progression), while in 38 pts radiographic stage remained unchanged (Group 2 - without progression). Patients from both groups were comparable in terms of age and disease duration (p>0,05). Although, pts from Group 1 with OA progression had more intense knee pain when walking: 60,4±18,3 vs 48,7±17,8mm, p=0,04; and higher BMI values: 34,5±4,6 vs 28,9±4,9 kg/m^2, p=0,001; US-findings based higher rate of synovitis:57,1% vs 18,4%, OR=5,9, 95% CI 1,6–22,5, p=0,009; bone marrow edema in medial tibia aspect 64,3% vs 13,2%, OR=11,9, 95% CI 2,8–50,3, p=0,0006 based on MRI findings. In pts with OA progression DEXA examination identified significantly higher absolute BMD values in the medial condyle of the tibia (0,9 (0,8–1,2) vs 0,8 (0,7–0,8) g/cm^2, p=0,001) as compared to pts from Group 2. Re-examination in 5yrs showed that statistically significant differences between the two groups still remained. Analysis of 5year therapy revealed, that the majority of pts without OA progression (68,4%) were taking combined CS+GH regimens for more than 6 months a year during 5-year FUP, while only 35,7% of pts who progressed (OR=4,3, 95% CI 1,1–16,3, p=0,03) managed to adhere to this regimen. Discriminant analysis showed that 5-year intake of combined CS+GH therapy for more than 6 months a year should be considered as a predictor of decreased risk of disease progression, while on the contrary, such symptoms as synovitis, bone marrow edema, and high BMD values in the medial condyle of the tibia should be viewed as predictors and risk factors for knee OA progression in pts with <5 years disease duration. Based on identified factors and their coefficients the authors designed a model (with area under the ROC curve equal to 0,93), allowing to predict the future course of the disease in an individual patient with high accuracy, i.e. 85,7% sensitivity and 84,2% specificity.

Factors	Discriminant function coefficients
US: synovitis	2,17
MRI: bone marrow edema	3,19
BMI in the medial condyle of the tibia	5,19
CS+GH	–1,03
Constant	11,83

ROC-curve (AUC=0,93)



The accuracy of prediction based on the variables (factors) was 84,6 %.

Conclusions: Use of combined CS+GH regimens for more than 6 months a year during 5 years is an important factor, decelerating the progression of knee OA in pts with <5 years disease duration by the factor of 4. While synovitis, bone marrow edema, and high BMD values in the medial condyle of the tibia are responsible for further OA progression on this group of pts.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2620

SAT0535 IMPACT OF THE METABOLIC SYNDROME ON THE PREVALENCE, SEVERITY INCIDENCE AND PROGRESSION OF KNEE OSTEOARTHRITIS

N. Oreiro-Villar[1,2], M. Fernandez-Moreno[1,2], E. Cortes-Pereira[1], M.E. Vazquez-Mosquera[1], S. Relaño[1], S. Pertega[3], C. Fernandez-Lopez[1], F.J. Blanco[1], I. Rego-Perez[1]. *[1]Servicio de Reumatología, Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). As Xubias, 15006, A Coruña; [2]Centro de Investigación Biomédica En Red, Ciber-Bbn, Madrid; [3]Unidad de Epidemiología Clínica y Bioestadística, Instituto de Investigación Biomédica de A Coruña (INIBIC). Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC). As Xubias, 15006, A Coruña, Spain*

Background: The contribution of metabolic factors on the development of OA has not been fully elucidated.

Objectives: The aim of this work is to analyze the influence of metabolic syndrome in the rate of radiographic incidence and progression of knee osteoarthritis, as well as its impact on the prevalence and severity of the disease.

Methods: For this work we used data from the Spanish cohort PROCOAC (PROgnostic Cohort of OsteoArthritis A Coruña). This cohort consists of subjects that visited the Rheumatology consultations at different time points and comprises 984 subjects at baseline including radiographic knee and hip KL grade, radiographic hand OA status, demographic and clinical data as well as the necessary information to assess the metabolic syndrome at baseline, that is, abdominal circumference (in cm) in addition to at least two of the following parameters: triglycerides above 200mg/dL, low HDL (<35 mg/dL), hypertension and increased glucose blood levels (>110 mg/dL). To assess the severity of the disease, the number of affected joints was coded as 0–1 and 2–3, according to the radiographic information of hands, knees and hips. Appropriate statistical analyses including Cox regression models with Kaplan-Meier survival curves and chi-square contingency tables were performed with SPSS v19.

Results: The mean age of subjects was 63,86 [32–88] years; 75,6,% were women. A total of 85% had radiographic hand OA and 11,8% suffered metabolic syndrome at baseline. In those OA patients that experienced radiographic knee OA progression over time (any KL increase from KL≥2 at baseline) the metabolic syndrome appeared as a significant risk factor (HR=3.696;95CI:1.085–14.520;p-value=0.037) (Figure 1). Similarly, in those subjects that developed incident radiographic knee OA over time (a new-onset KL grade 2), the metabolic syndrome at baseline also appeared as a significant risk factor with an increased magnitude (HR=12.931;95CI:3.037–55.051;p-value<0.001) (Figure 1). In addition, to have contralateral knee OA at baseline (HR=12.837;95CI:5.044 – 32.673;p-value <0.001) as well as radiographic hand OA (HR=5.671;95CI:0.854–37.649;p-value=0.07) associates with an increased rate of incident knee OA too. In terms of prevalence and severity of the disease, the metabolic syndrome associates with an increased risk of knee OA (OR=1.865;95% CI=1.080–3.220;p=0.024) as well as with increased number of affected joints, though in a non-significant manner (OR=1.582;95% CI=0.916–2.733;p=0.098)

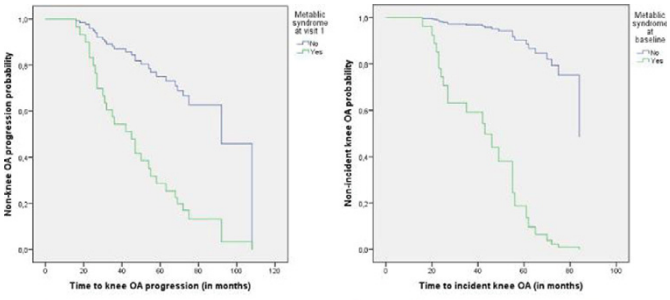


Figure 1. Kaplan-Meier survival curves showing the influence of the metabolic syndrome in the rate of radiographic knee OA progression and incidence over time

Conclusions: The alterations that underlie the metabolic syndrome condition the severity and prevalence of knee osteoarthritis, as well as the rate of incidence and progression of the disease

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3100

SAT0536 AXIAL ALIGNMENT OF THE KNEE – IMPORTANCE IN CARTILAGE REPAIR? HIGH TIBIAL OSTEOTOMY VS. DISTRACTION

N. Besselink[1], R. van Heerwaarden[2], J. van der Woude[3], K. Wiegant[4], S. Spruijt[5], F. Lafeber[1], W. van Spil[1], S. Mastbergen[1]. *[1]Rheumatology and Clinical Immunology, University Medical Centre Utrecht, Utrecht; [2]Orthophedics, ViaSana, Mill; [3]Orthophedics, Alrijne Hospital, Leiden; [4]Orthophedics, Sint Maartenskliniek, Nijmegen; [5]Orthophedics, Sint Maartenskliniek, Woerden, Netherlands*

Background: Opening-wedge high tibial osteotomy (HTO) is primarily indicated in treating varus gonarthrosis. The rationale behind HTO treatment of knee

osteoarthritis (OA) is to unload the affected compartment, this is accomplished by correcting the angular deformity towards the unaffected compartment, i.e. shifting the hip-knee-ankle angle (HKA; mechanical axis) towards varus for a medial lesion. Knee joint distraction (KJD) is an alternative joint-sparing treatment for knee OA and has been demonstrated to decrease pain, improve function, and increase joint space width (JSW)[1].

Objectives: To investigate the importance of axial alignment (and correction) in these two effective (joint-sparing) treatments of medial knee OA.

Methods: Patients with medial knee OA, a HKA less than 12° varus, normal knee stability, younger than 65 years, and a BMI less than 35 kg/m^2 were randomized to HTO (n=46) or KJD (n=23). WOMAC and VAS pain were collected at baseline and after twelve months. To assess structural outcome, JSW was measured on knee radiographs, before and after both treatments. HTO patients had full leg standing anteroposterior radiographs taken before and after surgery, KJD patients only had these taken before surgery. Therefore, the femur-tibia angle (FTA; anatomical axis), acquired using Knee Image Data Analysis (KIDA), was investigated as an alternative for assessing axial alignment. Agreement between axial alignment as defined by HKA and by FTA appeared to be fair (ICC=-0.414). WOMAC and VAS Pain were then related to (changes in) axial alignment, Kellgren & Lawrence (K&L) grade, BMI, gender, pre-operative range of motion (ROM), and age as independent variables in linear regression models.

Results: Patient baseline characteristics were not statistically significantly different between patients treated with KJD or HTO (see table 1). WOMAC increased statistically significantly one year after either treatment (KJD:Δ21.05±19.93; HTO:Δ27.80±15.32; both p<0.001). Likewise, VAS pain decreased (KJD:Δ-23.89±29.67,p=0.001; HTO:Δ-35.42±24.06,p<0.001). KJD led to a statistically significant increase in mean JSW (Δ0.50±0.88mm,p=0.014), and both treatments led to a statistically significant increase in medial (KJD:Δ0.81±1.16mm,p=0.004; HTO:Δ0.47±0.69mm,p<0.000) as well as minimal JSW (KJD:Δ0.85±0.96mm,p<0.000; HTO:Δ0.35±0.51mm,p<0.000) after one year. The FTA changed significantly in the HTO group after one year (Δ0.73°,p=0.005), while the KJD group showed a trend (Δ0.77°,p=0.105). In the KJD group, changes in clinical outcomes were not associated with pre-operative HKA, changes in FTA, K&L grade, BMI, gender, pre-operative ROM, or age. In contrast, in the HTO group a significant association was demonstrated for a change in WOMAC with a change in FTA (std.β=-0.341) and for a change in VAS Pain with baseline age (std.β=-0.323), as seen in table 2.

Table 1. Baseline characteristics

Characteristics	High tibial osteotomy	Knee joint distraction	
Mean (± SEM)	(n = 45)	(n = 22)	p-value
Male gender (n)	27/45 (60%)	16/22 (73%)	n.s.
Height (cm)	177 ± 2	178 ± 2	n.s.
Weight (kg)	85.2 ± 2.1	87.2 ± 2.8	n.s.
Body mass index (kg/m²)	27.2 ± 0.5	27.5 ± 0.7	n.s.
Affected knee (left)	20/45 (44%)	10/22 (45%)	n.s.
Age at surgery (yr)	49.4 ± 1.0	51.2 ± 1.1	n.s.
Kellgren & Lawrence			n.s.
Grade 0 (n)	1 (2%)	0 (0%)	
Grade 1 (n)	5 (11%)	6 (27%)	
Grade 2 (n)	12 (27%)	4 (18%)	
Grade 3 (n)	23 (51%)	11 (50%)	
Grade 4 (n)	4 (9%)	1 (5%)	
Tibiofemoral axis (°)	6.2 ± 0.3	5.8 ± 0.6	n.s.

Table 2: Linear regression with change in WOMAC and VAS Pain as dependent variables, and change in KIDA angle, pre-operative axial alignment, pre-operative range of motion (ROM), age, gender, BMI, baseline K&L grade, and either baseline WOMAC or VAS Pain as independent variables. [1]Standardized beta coefficients, *P<0.05

	High tibial osteotomy				Knee joint distraction			
	Δ WOMAC		Δ VAS Pain		Δ WOMAC		Δ VAS Pain	
	Std β[1]	Sig.*	Std β[1]	Sig.*	Std β[1]	Sig.*	Std β[1]	Sig.*
Δ Femur-tibia angle (FTA)	-0,341	0,029*	0,255	0,124	-0,049	0,840	-0,077	0,753
Pre-operative axial alignment (HKA)	0,128	0,368	-0,048	0,755	-0,076	0,768	-0,131	0,609
Pre-operative ROM	-0,172	0,234	0,083	0,595	0,124	0,684	0,033	0,902
Age	0,245	0,084	-0,323	0,045*	0,161	0,627	-0,077	0,786
Gender	-0,160	0,283	0,026	0,875	0,049	0,836	-0,159	0,481
BMI	-0,201	0,154	0,027	0,857	0,177	0,471	-0,150	0,537
Baseline K&L	-0,081	0,556	0,078	0,611	0,191	0,516	-0,037	0,885
Baseline WOMAC	-0,301	0,036*			-0,816	0,033*		
Baseline VAS Pain			-0,231	0,147			-0,682	0,016*

Conclusions: Both KJD and HTO lead to a statistically significant clinical and structural benefit after one year. Nevertheless, the change in FTA was associated with WOMAC change after one year in the HTO group, but not in the KJD group. This indicates that axial alignment correction may not per se be necessary for clinical benefit.

References:

[1] van der Woude et al. Five-Year Follow-up of Knee Joint Distraction. 2016 Cartilage.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3363

SAT0537 INFLUENCE OF MELOXICAM IN ORODISPERSIBLE FORM ON PLATELET AGGREGATION AND VON WILLEBRAND FACTOR IN PATIENTS WITH OSTEOARTHRITIS

O.S. Khmel, V.V. Rodionova. *Occupational Diseases and Clinical Immunology, State Establishment "Dnipropetrovsk Medical Academy, of Health Ministry of Ukraine", Dnepr, Ukraine*

Background: Meloxicam, which selectively inhibits COX-2, can cause inhibition of the biosynthesis of vascular endothelium vasodilator - prostacyclin, without impacting significantly on production of thromboxane, which promotes vasoconstriction [1]. Therefore, the effect of Meloxicam on the possibility of thrombotic complications need to be learn more accurately.

Objectives: To investigate the effect of orodispersible form of Meloxicam on platelet aggregation and von Willebrand factor in patients with knee osteoarthritis.

Methods: The study included 24 patients with knee osteoarthritis (OA) of the II stage according to the Kellgren-Lawrence. The control group consisted of 15 healthy individuals. Patients were prescribed the orodispersible form of Meloxicam in dose of 15 mg 1 time per day orally during 10 days. The survey was carried out before and after treatment. Patients had all-clinical studies, questionnaires (visual analogue scale (VAS), Western Ontario and McMaster Universities Arthritis Index (WOMAC), questionnaire Lequesne), optical aggregometry with adenosine diphosphate (ADP), collagen, thrombin and ristocetin for revealing the level of von Willebrand factor.

Results: As a result of treatment patients had a significant improvement of overall health and reduction of pain in knee joints according to the VAS (before treatment – 54.5 [50 – 71] mm, after treatment – 27 [18 – 41] mm; p≤0.05), WOMAC (before treatment – 143 [109 – 187] points, after treatment - 98 [13–168] points; p≤0.05), questionnaire Lequesne (before treatment – 16 [13 – 21] points, after treatment – 12 [3 – 22] points; p≤0.05). After treatment patients experienced a significant increase in the degree of platelet aggregation with ADP (before treatment – 52.6 [39.6 – 98.2]% after the treatment – 83.5 [41.3 – 127]%; p≤0.05), which may indicate a probable increase in the initiation of irreversible aggregation of circulating platelets. The degree of platelet aggregation with collagen also increased (before treatment – 46.5 [29.5 – 89]%, after treatment – 68.6 [37.9 – 115.4]%; p≤0.05), indicating the increased adhesion of platelets to collagen of the vascular endothelium. Before and after treatment, patients remained significantly elevated degree of aggregation with thrombin in comparison with the control group (before treatment – 65.6 [24.7 – 86.7], after treatment – 78 [62.3 – 92.7]%, control group – 37.8 [32.11 – 42.26]%; p≤0.05) which indicates the stimulation of the of the endothelin-1 synthesis with further infringements of procoagulants and anticoagulants. Von Willebrand factor, as an indirect indicator of endothelial damage, was significantly increased after treatment (before treatment – 151.4 [138.9 – 224]% after treatment – 206.8 [171.9 – 257.4]%), which may indicate increase of endothelial lesions because of meloxicam with further endothelial dysfunction (p≤0.05).

Conclusions: Intake of the orodyspersible form of Meloxicam in patients with osteoarthritis can cause an increase of platelet aggregation and level of von Willebrand factor that may contribute to the vascular endothelial dysfunction and increase in risk of thrombosis.

References:

[1] Wittenauer R., Smith L., Aden K. Update on 2004 Background Paper Written by Saloni Tanna, Pharm.D. MPH Background Paper 6.12 Osteoarthritis. Priority Medicines for Europe and the World "A Public Health Approach to Innovation"; 2013. P. 31.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5348

SAT0538 PROGRESSION OF PAIN, NUMBER OF CLINICALLY SWOLLEN JOINTS AND ULTRASOUND DETECTED SYNOVITIS AND OSTEOPHYTE FORMATION IN PATIENTS WITH HAND OSTEOARTHRITIS OVER TWO YEARS

O. Sleglova, O. Ruzickova, K. Pavelka, L. Senolt. *Institute of Rheumatology, Prague, Czech Republic*

Background: Hand osteoarthritis (HOA) is a common and frequent cause of pain. HOA is a heterogeneous group of disorders with two main subsets including non-erosive and erosive disease. Few studies demonstrated inflammatory ultrasound changes and more severe clinical symptoms in patients with erosive compared with non-erosive disease, however the results are inconsistent.

Objectives: he aim of this study was to evaluate progression of pain, stiffness, physical impairment and ultrasound features in patients with erosive and non-erosive HOA in a two years longitudinal study.

Methods: Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. Joint pain and swelling were assessed. Patients reported joint pain on 100 mm visual analogue scale (VAS). Pain, joint stiffness and disability were assessed by the Australian/Canadian OA hand index (AUSCAN). Radiographs of both hands were examined and erosive disease was defined by at least one erosive interphalangeal joint. Synovial hypertrophy and power Doppler signal (PDS) were scored with ultrasound. Synovitis was graded on a scale of 0–3 and osteophytes were defined as cortical protrusions seen in two planes. Patients were examined at baseline and at the two years follow-up.

Results: Altogether, 129 patients (12 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2017. Out of these patients, 72 had erosive disease. The disease duration ($p<0.01$) was significantly higher in patients with erosive compared with non-erosive disease.
Pain ($p<0.05$) and the number of clinically swollen joints ($p<0.05$) were significantly higher in patients with erosive compared with non-erosive disease at baseline. There were significant progression of pain ($p<0.05$) and the number of clinically swollen joints ($p<0.01$) at the two years follow up. The progression in clinically swollen joint count was about 21% higher in patients with erosive disease.
According to the AUSCAN, patients with erosive compared with non-erosive disease had more pain ($p<0.05$) and stiffness ($p<0.01$) at baseline. Pain and stiffness, but not function, got worse ($p<0.01$) in patients with erosive compared with non-erosive disease at the two years follow up.
US-detected pathologies such as gray-scale synovitis total score ($p<0.001$), intensity of PDS ($p<0.01$) and number of osteophytes ($p<0.01$) were significantly higher in patients with erosive compared with non-erosive disease at baseline. There were improvements in gray-scale synovitis total score and intensity of PDS in patients with non-erosive disease while patients with erosive disease worsened at the two years follow up. On the other hand, the progression of US-determined osteophyte formation was observed in both groups.
Conclusions: The findings of this study show that pain and number of clinically swollen joints associated with US-detected synovial hypertrophy inflammatory signs and osteophyte formation is more severe in patients with erosive HOA than in patients with non-erosive disease. In addition, osteophyte formation is more likely to progress independent of synovial inflammation.
Acknowledgements: This work was supported by the project (Ministry of Health, Czech Republic) for consensual development of research organization 023728.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2795

SAT0539 DIFFERENTIAL PROFILE OF ENDOGENOUS PEPTIDES DETECTED BY TARGETED PROTEOMICS IN HIP AND KNEE CARTILAGE SECRETOMES FROM OSTEOARTHRITIS PATIENTS

P. Fernandez-Puente, L. Gonzalez-Rodriguez, V. Calamia, L. Lourido, M. Camacho, C. Ruiz-Romero, F.J. Blanco. *Grupo de Proteomica-PBR2-ProteoRed/ISCIII-Servicio de Reumatología., Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC), A Coruña, Spain*

Background: Peptidomics can be defined as the comprehensive, qualitative and quantitative study of all native peptides in a sample in a defined space at a defined time under defined biological conditions. LC-MS/MS targeted proteomics have been used to identify and quantify candidate molecular biomarkers in diverse range of samples, including cells, tissues, serum/plasma, and other types of body fluids.
Objectives: In the present work, we have developed a targeted method to detect a panel of endogenous peptides that were identified as released from human healthy (N) and/or osteoarthritic (OA) hip and knee cartilage. Secretomes were obtained separately from the wounded (WZ) and unwounded (UZ) zones of OA cartilage. The enrichment of endogenous peptides was achieved by ultrafiltration and solid phase extraction (SPE). After peptide extraction, the different peptide profiles of these secretomes were relative quantified by target proteomics.
Methods: Proteins secreted from human articular cartilage (secretomes) were obtained by culture of tissue explants [1]. The enrichment of endogenous peptides was standardized using ultrafiltration procedures and solid phase extraction with reversed phase (C18) resins. A method for the targeted identification and relative quantitation of endogenous peptides by Multiple Reaction Monitoring (MRM)-mass spectrometry was developed employing cartilage secretome samples, and then applied on synovial fluid and serum. The peptides were separated by nano-LC coupled to a 5500 QTRAP mass spectrometer using stable isotope-labeled (SI) peptides as an internal control. Peptide identifications were searched using the ProteinPilot program. Data analysis was performed using the Skyline software.
Results: 23 endogenous peptides belonging to 9 proteins related with OA, as Cartilage Oligemeric Matrix Protein (COMP), Cartilage Intermediate Layer Protein (CILP), Prolargin (PRELP), Dermcidin (DCD), Fibronectin (FINC) and Glia Derived Nexin (GDN) among others, were differentially detected and relatively quantified in the cartilage secretomes. Some of the endogenous peptides belonging to COMP, FINC and GDN were found with a significant high release in the UZ of hip cartilage, however in knee cartilage the release is higher in the WZ. On the other hand, certain peptides belonging to proteins like CILP or PRELP were found to be mostly increased in the UZ of both hip and knee OA cartilages when compared to healthy tissue.
Conclusions: A panel of endogenous peptides has been identified in articular cartilage, which are differentially released between OA and healthy patients, as well as between knee and hip OA patients. These endogenous peptides may be potential biomarkers to differentiate osteoarthritis from hip and knee. Our targeted proteomics approach would be widely applicable to quantify low abundant peptides of interest in complex biological samples as synovial fluid and serum in order to unravel their putative biomarker value for osteoarthritis.

References:
[1] Lucía Lourido et al. "Quantitative Proteomic Profiling of Human Articular Cartilage Degradation in Osteoarthritis". J Proteome Res. 2014 Dec 5;13(12):6096–106.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6185

SAT0540 THE REDUCTION IN ADRENERGIC AND INFLAMMATORY SERUM MARKERS IN OSTEOARTHRITIS PATIENTS AFTER TREATMENT WITH CHONDROITIN SULFATE/GLUCOSAMINE HYDROCHLORIDE AND CELECOXIB IS DIFFERENT ACCORDING TO THE PRESENCE OF BACTERIAL DNA IN BLOOD

P. Zapater[1], M. Herrero[2], H. Martínez[2], R. Francés[3,4], J. Vergés[5], J.F. Horga[6]. *[1]Pharmacology Department, Miguel Hernández University, Alicante; [2]Clinical R&D, Bioiberica, Barcelona; [3]CIBERehd. Instituto de Salud Carlos III, Madrid; [4]Medicine Department, Miguel Hernández University, Alicante; [5]Osteoarthritis Foundation International (OAFI), Barcelona; [6]Pharmacology Department, Miguel Hernández University, Alicante, Spain*

Background: Inflammation in osteoarthritis (OA) has been characterized by infiltration of immune cells and secretion of cytokines into synovial tissues. Synovial macrophages production of IL-1beta and TNF-alfa is increased in response to lipopolysaccharide (LPS) suggesting a potential role of pathogen-associated molecular patterns (PAMPs) in OA development and/or evolution. Adrenergic activity have been associated with subchondral bone loss and increased osteoclast activity. Also, adrenergic activity is a main modulator of immune response to PAMPs in different settings. However,the relationship between activation of adrenergic and immune system with OA progression and treatment response remains still unknown.
Objectives: To assess the adrenergic and immune activation in OA patients according to the presence of bacterial DNA (bDNA) fragments in blood before and after Chondroitin Sulfate/Glucosamine Hydrochloride (CS/GH) or Celecoxib (CE) treatment.
Methods: Serum samples from patients participants in a 6-month controlled, double blind and randomized clinical trial comparing the analgesic efficacy of CS/GH and CE were analyzed to determine cytokines (IL-2, IL-4, IL-6, IL-10, IL-8, IL-1beta), catecholamines (noradrenaline, adrenaline and dopamine) and the presence of endotoxin or LPS and bDNA. Results are shown as mean±sd or median with ranges (Q25-Q75).
Results: Samples from 100 OA patients (age: 62±8yr.; BMI: 31±6kg/m^2 86 females; VAS: 73±15; WOMAC: 369±43) treated with CS/GH (50) or CE (50) were analyzed.There were no baseline significant differences between the two treatment groups regarding demographics,clinical and experimental variables. Thirty-four patients (17-CS/GH and 17-CE) showing bDNA in blood had significantly higher levels of noradrenaline compared with patients without bDNA (1993 [1354–3183] vs. 1324 [738–1899]; p=0.0002). After 6 months, both groups of treatment showed a similar reduction in VAS and WOMAC score (pain assessment) and serum adrenaline levels independent of presence or absence of bDNA (Table 1).Thirty-three patients showed bDNA presence at the end of the study (23 negative and 10 positive at baseline). Patients with bDNA at 6 months after treatment showed reduced serum noradrenaline levels compared with those observed in patients with bDNA at baseline (1993 [1354–3183] vs. 1561 [1174–2193]; p=0.0325). IL-8 was significantly reduced after 6 months of treatment only in patients without bDNA.There were no significant differences between baseline and 6 months samples in the other experimental variables.

Table 1

	Baseline				6 months			
	No bDNA		bDNA		No bDNA		bDNA	
	CS/GH	CE	CS/GH	CE	CS/GH	CE	CS/GH	CE
Adrenaline (pg/mL)	98 (88-127)	100 (77-118)	92 (78-114)	98 (75-115)	78* (65-92)	81* (62-92)	76* (58-97)	77* (66-105)
Noradrenaline (pg/mL)	1357 (790-1693)	1228 (738-1967)	1723# (1385-2381)	2765# (1232-3250)	1050 (811-1600)	1588 (882-2133)	1563 (1209-2180)	1528 (1174-2229)
IL-8 (pg/mL)	5.5 (1.3-9.4)	5.6 (1.7-14)	4.8 (3.9-5.7)	11 (1.9-15)	3.3* (0.0-11)	0.0* (0.0-5.9)	6.1 (3.7-14)	5.6 (1.5-16)
VAS score (0-100)	72 (66-82)	75 (65-81)	79 (67-90)	76 (70-80)	32* (22-45)	20* (10-60)	37* (27-50)	52* (24-60)
WOMAC score	364 (341-389)	354 (321-389)	382 (372-407)	360 (340-400)	150* (87-217)	135* (64-238)	180* (84-218)	282* (139-318)

* p < 0.05 vs baseline values (Mann-Whitney-Wilcoxon Test, # p<0.05 vs No bDNA values

Conclusions: OA patients show bDNA fragments in blood associated to higher serum noradrenaline levels. Six month treatment with CS/GH or CE reduces significantly and in a similar fashion the pain intensity and adrenaline levels. IL-8 levels were reduced with the treatment except in patients with presence of bDNA fragments in blood. Systemic adrenergic and inflammatory activity in OA patients is influenced by the presence of PAMPs as bDNA in blood and this may be a factor to take into consideration to evaluate the severity, evolution and response to treatments.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6147

SAT0541 INHIBITING αVβ3 INTEGRIN AND CD47 SIGNALING AMELIORATES THE PROGRESSION OF OSTEOARTHRITIS

Q. Wang[1], K. Onuma[2], R. Mao[1], H. Wong[1], W.H. Robinson[1]. [1]*Medicine;* [2]*Stanford University, Stanford, United States*

Background: Osteoarthritis is leading cause of disability, and its prevalence is rising due to the aging population and obesity epidemic[1]. Despite the substantial morbidity and health costs attributed to osteoarthritis, no treatment has been approved to prevent or slow disease progression, largely because the underlying pathogenic mechanism remains elusive. Both integrin αVβ3 and the integrin-associated receptor CD47 are considered important therapeutic targets for a number of diseases, but the potential involvement of these receptors in osteoarthritis remains unclear[2].
Objectives: Our study aimed at assessing the role of integrin αVβ3 and the integrin-associated receptor CD47 signaling pathways in the pathogenesis of osteoarthritis, and identifying potential targets for disease-modifying therapy.
Methods: We performed transcriptomic and proteomic analyses of human and murine osteoarthritic tissues to examine the involvement of integrin αVβ3 and CD47 with osteoarthritis. Further, we evaluated the effects of genetic deficiency in and pharmacological modulations of integrin αVβ3 subunits, CD47, and their downstream signaling molecules Fyn and FAK on the destabilization of the medial meniscus (DMM) mouse model. Additionally, we used microPET/CT imaging of the DMM mouse model to assess the ligand-binding capacities of integrin αVβ3 and CD47 in osteoarthritic joints. Finally, we carried out multiple *in vitro* assays to determine how integrin αVβ3 and CD47 signaling might become activated in osteoarthritis, and what the molecular consequences of such activation might be.
Results: Our transcriptomic and proteomic analyses revealed the involvement of dysregulated integrin αVβ3 and CD47 signaling in osteoarthritis. Data from investigations of genetically deficient mice and pharmacological modulations showed that αVβ3, CD47, Fyn, and FAK are crucial to the pathogenesis of arthritis. We detected elevated ligand-binding capacities of integrin αVβ3 and CD47 in osteoarthritic joints by microPET/CT imaging of mice subjected to DMM. Our *in vitro* studies demonstrated that chondrocyte breakdown products, derived from the articular cartilage of individuals with osteoarthritis, induced αVβ3/CD47-dependent expression of inflammatory and degradative mediators, and revealed that the signaling network involved the Ras-CRAF-MEK-ERK pathways.
Conclusions: Our findings identify a central role of deregulated αVβ3 and CD47 signaling in the pathogenesis of osteoarthritis, and provide a rationale for targeting these signaling pathways as a disease-modifying therapy.
References:
[1] Lawrence, R. C. et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum 58, 26–35, doi:10.1002/art.23176 (2008).
[2] Tian, J., Zhang, F. J. & Lei, G. H. Role of integrins and their ligands in osteoarthritic cartilage. Rheumatology international 35, 787–798, doi: 10.1007/s00296–014–3137–5 (2015).
Acknowledgements: We thank Tamsin M. Lindstrom for her scientific input. Our research is supported by VA I01BX002345, I01RX000934, and I01RX000588.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7024

SAT0542 SUBCLINICAL CRYSTAL ARTHROPATHY MIGHT INFLUENCE FUNCTIONAL DISABILITY IN PATIENTS WITH KNEE OSTEOARTHRITIS? AN EGYPTIAN CROSS SECTIONAL STUDY

R.H.A. Mohammed. *Department of Rheumatology and Rehabilitation, MD, FRCP, FACR, School OF MEDICINE, Cairo University Hospitals, Cairo, Egypt*

Background: Osteoarthritis is a complex slowly progressive degenerative disease that affects joint components.Concomittant articular crystal deposits are able to stimulate an inflammatory response in OA through stimulation of the innate immune system.
Objectives: Assess the contribution of sonographically detected crystal deposits to pain severity and functional disability in patients with knee OA (WOMAC score)
Methods: Single-center cross sectional study. Adult patients diagnosed with knee OA diagnosed in accordance with ACR criteria from the Department of Rheumatology and Rehabilitation, Kasr Alainy School of Medicine, Cairo University were recruited. Clinical assessment of pain and functional status in patients with knee osteoarthritis was measured using: Western Ontario and McMaster Universities Arthritis Index score. The Logic p5 ultrasound machine (GE) with linear array probe (8–13 MHz). Examination of the articular and periarticular structures was performed by a trained rheumatologist according to the standard EULAR guidelines for exam of the knee. Serum uric acid was investigated. Plain radiography was done for comparison.
Results: 53 patients (44 females 83% & 9 males 17%) were included, mean age 53.5 years ± 8.3 SD, disease duration 42.5 months ± 49.5 SD, body mass index mean 34.9±6.3 SD. Crystal deposits were sono-graphically diagnosed in 73 knees (68.9%), Monosodium urate deposits found in 33 knees (31.1%) and Calcium Pyrophosphate Dihydrate deposits were diagnosed in 67 knees (63.2%). Pain, stiffness and disability scores were significantly higher in OA knees with crystal deposition as compared to those without ($p<0.05$) that was in fact resistant to conventional analgesics, chondro-protectives and physiotherapy demanding the ongoing use of NSAIDs.

Table 1. WOMAC pain, stiffness and disability scores in the studied Patients with knee OA showing sonographic evidences of CDDs versus those without

WOMAC score	OA with CDDs (Mean ± SD)	OA without CDD (Mean ± SD)	Mann-Whitney U- test r	P-value (significance)
WOMAC pain score	15. 6±3.6 (8–20)	12.0 ±3.8 (5–20)	596	0.00*
WOMAC stiffness score	5. 5 ±2.0 (0–8)	3.8 ±1.8 (0–8)	643	0.00*
WOMAC disability score	53.4 ±11.6 (25–67)	41.5±12.8 (14–67)	606	0.00*

WOMAC = Western Ontario and McMaster Universities Arthritis Index score. *Significant difference ($p\leq0.05$).

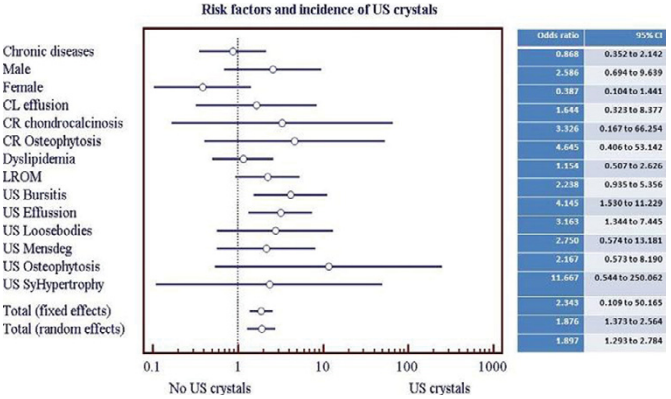


Conclusions: Crystal deposition was associated with significantly increased pain intensity, knee joint stiffness and functional disability as measured by WOMAC in patients with knee OA.
References:
[1] Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al., Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum. 1986; 29(8):1039–49.
[2] Naredo E, Cabero F, Palop MJ, Collado P, Cruz A, Crespo M. Ultrasonographic findings in knee osteoarthritis: A comparative study with clinical and radiographic assessment. Osteoarthr Cartil. 2005; 13(7):568–74.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1145

SAT0543 CLINICAL PREDICTORS AND RADIOGRAPHIC EVIDENCES OF OCCULT CRYSTAL DEPOSITION DISEASE WITH KNEE OSTEOARTHRITIS

R.H.A. Mohammed. *Department of Rheumatology, Rehabilitation and Clinical Immunology, MD, FRCP, FACR, School of Medicine, Cairo University Hospitals, Cairo, Egypt*

Background: Osteoarthritis is a slowly progressive degenerative disorder that affects joint components from cartilage to meniscus, subchondral bones and might even lead to synovial inflammation.
Objectives: To investigate the clinical and radiographic findings associated with asymptomatic crystal deposition disease in patients with knee osteoarthritis.
Methods: A single-center cross sectional study, sixty adult patients with knee OA diagnosed according to the ACR criteria were enrolled. Participants were all subjected to history taking, general as well as musculoskeletal clinical examination, serum uric acid, and plain radiography. Examination of the knee joints for intraarticular/periarticular crystal deposits was done using a Logic p5 ultrasound machine (GE) with linear array probe (8–13 MHz) according to the standard EULAR guidelines.
Results: A total of sixty adult patients were enrolled, fifty three patients satisfied the inclusion criteria, 44 females (83%) & 9 males (17%), mean values for; ages



Abstract SAT0543 – Table 1. Odds ratio and Forest plot analysis

Risk factors	Knees with sonographic crystals (Total: 73 knees) r	Knees without sonographic crystals (Total: 33 knees)	Odds ratio	95% CI	p value (significance)
Male Gender	15	3	2.6	0.7 to 9.6	0.16
Female Gender	58	30	0.4	0.1 to 1.4	0.16
Dyslipidemia	38	16	1.2	0.5 to 2.6	0.73
Chronic medical illness as Diabetes mellitus and hypertension	20	10	0.9	0.4 to 2.1	0.76
Clinically detected knee effusion	7	2	1.6	0.3 to 8.4	0.55
Limitation in ROM	36	10	2.2	0.9 to 5.4	0.07
Bursitis by sonography	35	6	4.1	1.5 to 11.2	**0.01***
Effusion by sonography	47	12	3.2	1.3 to 7.4	**0.01***
Total (fixed effects)	430/1022	156/462	1.9	1.4 to 2.6	0.23
Total (random effects)	430/1022	156/462	1.9	1.3 to 2.8	

53.5 years ± 8.3 SD, disease duration 42.5 months ± 49.5 SD. Crystal deposits were sono-graphically diagnosed in 73 knees with normal serum uric acid values (68.9%> MSU in 31.1%, CPPD in 63.2%, a picture of mixed deposits in 5.7%). Plain radiography revealed chondrocalcinosis in 3 patients only. Regression analysis models and Forest Plot test revealed a 4.1 fold incidence of crystal deposition in patients with sonographic bursitis than those without (OR=4.13, CI=1.5–11.2, p=0.01) and a 3.2 fold incidence of crystal deposition in patients with sonographic effusion than those without (OR=3.16, CI=1.34–7.44, p=0.01).

Conclusions: The study concluded a number of clinical as well as radiographic associates that might be considered as predictors of silent CDD in patients with knee OA as diagnosed by ultrasonography, the most commonly reported clinical associates were bursitis and effusion.

References:

[1] Naredo E, Cabero F, Palop MJ, Collado P, Cruz A, Crespo M. Ultrasonographic findings in knee osteoarthritis: A comparative study with clinical and radiographic assessment. Osteoarthr Cartil. 2005; 13(7):568–74.

[2] Doherty M, Jones A, Cawston T. Osteoarthritis. In: Oxford Textbook of Rheumatology. Isenberg D. Lanyon P.Muir K. Doherty S. eds. 3rd ed. Oxford University Press. 2004; 1091- 1118.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2376

SAT0544 SUBGROUPS IN RADIOGRAPHIC FEATURES IN PATIENTS WITH HIP OSTEOARTHRITIS: RESULTS OF THE AMS-OA COHORT

R.A.M. Pouw[1,2], M. van der Esch[1], M. van der Leeden[1,3], D. Reiding[4], L.D. Roorda[1], J. Dekker[5], W.F. Lems[6,7]. *[1]Amsterdam Rehabilitation Research Center, Reade, Center for Rehabilitation and Rheumatology; [2]Faculty of behavioural and movement sciences, VU University; [3]Department of Rehabilitation Medicine, VU University Medical Center; [4]Department of radiology, Reade, Center for Rehabilitation and Rheumatology; [5]Rehabilitation Medicine; [6]Department of Rheumatology, VU University Medical Center; [7]Jan van Breemen Research Institute, Reade, Center for Rehabilitation and Rheumatology, Amsterdam, Netherlands*

Background: Radiographic features are important in diagnosing hip osteoarthritis (OA)[1,2]. In daily practice, only the anterior-posterior view is visualized but not the false profile view. Since we assessed radiographic features in both types of radiographic hip images in the AMS-OA cohort, we were able to examine the differences in radiographic features in two regions of the hip (superior-lateral and central-axial region).

Objectives: (i) To describe the presence of radiographic features in patients with hip OA; and (ii) to determine whether radiographic features differ between the superior-lateral and central-axial region of the hip.

Methods: Data from 97 patients with bilateral hip pain and a Kellgren and Lawrence score of ≥1 of the Amsterdam Osteoarthritis (AMS-OA) cohort of patients with knee and/or hip OA were used. Standard radiographic images were examined of patients in an erect position, both with an anterior posterior view and with a false profile view, which is an oblique lateral view of the hip. Radiographic images were scored by an experienced radiologist (DR) and an independent researcher (ME). Consensus between two raters was achieved for each score. Four radiographic features were scored: presence of joint space narrowing, osteophytes, sclerosis and cysts. All joint features were scored separately for the superior-lateral and the central-axial region of the hip. A Fisher's exact test was performed for testing the significance of the differences between the two regions of the hip.

Results: Table 1 shows the frequencies of radiographic features (joint space narrowing, osteophytes, sclerosis and cysts) in the superior-lateral and the central-axial region of the left and right hip joint of patients with hip OA. Significant differences between the two regions were found for osteophytes, sclerosis and cysts with the highest frequency of these features in the superior-lateral region of the hip.

Conclusions: In our cohort we found as expected, that joint space narrowing of the hips was the most frequent feature (>80% in both the superior- lateral and central-axial region). Moreover, osteophytes, sclerosis and cysts were more frequently present in the superior-lateral region. Our findings indicate that hip OA may exist of two subgroups with differences in radiographic features (i.e., superior-lateral and central-axial). Future research should confirm these results and focus on possible associations with biomechanical and physical function variables.

Radiographic feature	Superior Lateral part				Central Axial part				Fisher's exact test	
	Left		Right		Left		Right		Left	Right
	N	%	N	%	N	%	N	%	P-value	P-value
JSN	77	79.4	78	80.4	81	84.4	83	85.6	NS	NS
Osteophytes	68	70.1	65	67.0	49	51.0	45	46.9	0.014*	0.003*
Sclerosis	43	44.8	44	45.8	15	15.6	11	11.5	0.023*	0.021*
Cysts	28	29.2	30	31.3	3	3.1	2	2.1	<0.001**	<0.001**

TABLE 1: presence of radiographic features in patients with bilateral hip pain. (*p<0.05) (**p<0.001)

References:

[1] Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. Osteoarthritis and Cartilage (2007); 15, A1-A56.

[2] Krishanu B, Gupta MD, Duryea J, Weissman BN. Radiographic evaluation of osteoarthritis. Radiol Clin N Am 42 (2004) 11–41.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2132

SAT0545 PREDICTIVE FACTORS FOR RESPONSE TO ULTRASOUND-GUIDED INTRA-ARTICULAR GLUCOCORTICOIDS IN KNEE OSTEOARTHRITIS

S. Slimani[1], A. Aissoug[2], S. Aouidane[1], H. Bounecer[1], M.M. Makhloufi[1], A. Ladjouze-Rezig[3]. *[1]Medicine, Univeristy of Batna 2; [2]Private practice, Batna; [3]Medicine, University of Algiers 1, Algiers, Algeria*

Objectives: To investigate predictive factors for good outcome of ultrasound intra-articular glucocorticoids in knee osteoarthritis (OA).

Methods: We conducted a prospective monocenter cohort study including 116 patients with knee OA, after failure to standard treatments, with pain >4 (numerical rating scale NRS 0–10). Patients received an ultrasound-guided injection of 40 mg triamcinolone acetonide in their most painful knee. We exhaustively collected demographic and clinical data at inclusion, as well as lab, radiographs and ultrasound parameters of the included knees. WOMAC score was calculated at inclusion and after 4 weeks. Responders were defined as patients with at least 40% improvement of their WOMAC score. Univariate analysis was performed in order to select possible predictive factors, and stepwise multiple logistic regression analyses were conducted to identify predictors of response.

Results: Among the 116 patients, 101 were females. Median age was 64 years (40–85) and mean duration of the disease was 14.1±14,8 years. Mean BMI was 29.9±3.8 Kg/m^2. Mean NRS of pain was 8.4±1.2 and mean WOMAC was 73.3±11,8 at inclusion. 70.0% of the knees were grade 3 or 4 of Kellgren-Lawrence. 98% of knees expressed ultrasound synovial effusion and/or hypertrophy at inclusion. After 4 weeks, 61.2% of patients were responders. Regression analysis showed that patients with a BMI <30 Kg/m^2 (OR=0.38, 95% CI 0.16–0.89) and an ESR <20 mm (OR=0.27, 95% CI 0.08–0.90) were more likely to respond to ultrasound-guided glucocorticoids injection. Having both predictive factors of good response increases the response rate to 73.5%, whereas having no predictive factor decreases the response rate to 25.0%.

Conclusions: Our study is the largest study evaluating predictive factors of response for intra-articular glucocorticoids injections in knee OA. Also, it is the first study of predictive factors for ultrasound-guided injections. Patients with high BMIs and high ESR seem less likely to respond to intra-articular injections.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1362

SAT0546 TOTAL OSTEOPHYTE SCORE IS A BIOMARKER OF CURRENT AND PERSISTENT PAIN IN KNEE OSTEOARTHRITIS SUBJECTS

S. Feng, M.C. Levesque. *AbbVie Inc., Worcester, MA, United States*

Background: X-ray and magnetic resonance imaging (MRI) demonstrated associations between osteophyte severity and current pain in knee osteoarthritis (OA) patients. Persistent pain over 5 years was also associated with x-ray osteophyte severity. A biomarker to identify knee OA subjects with persistent pain may reduce placebo response rates in clinical trials.
Objectives: To determine whether the total knee osteophyte score (TKOS), as measured by MRI Osteoarthritis Knee Score (MOAKS), is a biomarker of current and persistent pain severity in knee OA subjects.
Methods: Knee OA subjects from the Foundation for the National Institutes of Health Biomarker Consortium were longitudinally assessed over 4 years and categorized as pain and x-ray progressors (n=194), x-ray–only progressors (n=103), pain-only progressors (n=103), and non-progressors (n=200). Knee osteophyte severity was scored at baseline by MOAKS at 12 positions across the knee and summed to obtain the TKOS. TKOS was summarized as means and SDs in the 4 progression groups; each progression group TKOS was compared with the non-progression group using Wilcoxon rank sum tests (Table 1). The longitudinal Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores were plotted and tested with a linear mixed model, by high and low TKOS status, defined as above and below the TKOS median of 6 (Figure 1). Subjects with persistent pain were defined based on WOMAC pain scores at 4 out of 5 time points higher than the thresholds listed in Table 2; at each threshold, mean differences in TKOS were tested using analysis of variance among those with and without persistent pain.
Results: The distribution of baseline TKOS differed by progression group, with the highest TKOS among pain and x-ray progressors (Table 1). In all 4 progression groups, baseline WOMAC pain scores were higher in subjects with high (>6) versus low (≤ 6) baseline TKOS status (P=0.0001, 0.0383, 0.0035, and 0.0466, respectively). The difference in WOMAC pain scores between TKOS high and low subgroups was constant over time (Figure 1; solid curves above and parallel to dashed curves with TKOS main effect always significant [$P<0.01$] in all 4 progression groups), but the TKOS$\times$Time interaction term in the longitudinal mixed model was not statistically significant, indicating that the pain difference between the TKOS high and low subgroups did not change over time. TKOS was highly associated with persistent pain, with TKOS higher at all thresholds (Table 2).

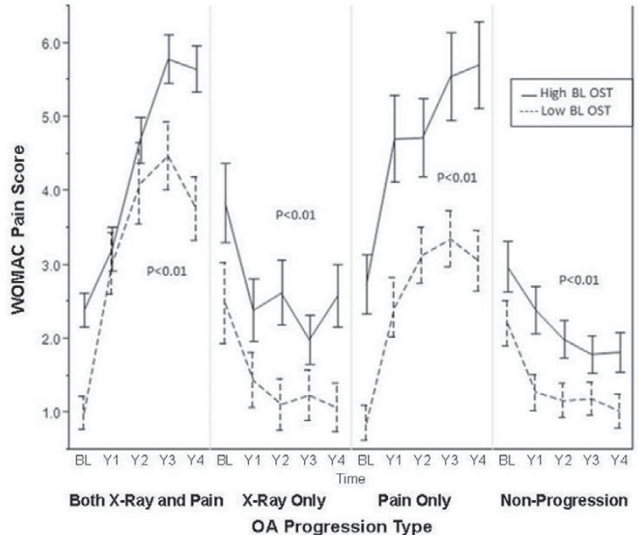
Table 1. Distribution Parameters of TKOS at Baseline by OA Progression Type

Progression Type	TKOS			*P* value)
	n	Mean	SD	
X-ray and pain	194	10.43	6.60	<0.0001
X-ray only	103	8.79	6.56	0.06
Pain only	103	8.03	5.91	0.22
None	200	7.32	6.07	–

Table 2. Group Sizes and TKOS Mean Differences for Different WOMAC Pain Thresholds for Persistent Pain

WOMAC Pain Threshold	Subjects With Persistent Pain, n	TKOS Difference for Subjects With Persistent Pain vs Those Without	*P* Value
2	211	2.5	<0.0001
3	150	2.4	<0.0001
4	112	2.4	0.0001
6	52	3.6	<0.0001
8	21	2.5	0.06

Figure 1. WOMAC pain score over 4 years stratified by baseline TKOS status and OA progression type.



Conclusions: TKOS is a candidate biomarker for current and persistent pain in knee OA patients and may be a predictive biomarker for reduced placebo response rates in clinical trials.
Acknowledgements: AbbVie funded the analysis; participated in analysis, design and interpretation and in abstract writing, review, and approval; and funded writing support by M. Theisen of CPS.
Disclosure of Interest: S. Feng Shareholder of: AbbVie, Employee of: AbbVie, M. Levesque Shareholder of: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.5095

SAT0547 THE INFLUENCE OF OSTEOARTHRITIS ON CLINICAL, LABORATORY AND ULTRASOUND PARAMETERS OF PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

T. Serban[1,2], I. Satulu[3], O. Vutcanu[2], M. Milicescu[1,2], C.M. Mihai[1,2], M. Bojinca[1,2]. *[1]Internal Medicine and Rheumatology, "Carol Davila" University of Medicine and Pharmacy; [2]Internal Medicine and Rheumatology, "Dr. I. Cantacuzino" Clinical Hospital, Bucharest, Romania; [3]Rheumatology, Kalmar County Hospital, Kalmar, Sweden*

Background: Osteoarthritis (OA) and rheumatoid arthritis (RA) are not infrequent in the general population. The two pathologic entities can overlap and the presence of OA can interfere with the evaluation of patients with RA.
Objectives: This study aims to evaluate the possible impact of OA on the clinical, laboratory and ultrasound parameters currently evaluated in patients with early RA (ERA).
Methods: We have evaluated the data obtained from patients with ERA referred to our Early Arthritis Research Center (EARC). Only data from patients who fulfilled EULAR/ACR 2010 criteria for RA (1) and had a symptom duration of less than 12 months were analyzed. 43 patients were diagnosed with ERA in the EARC between 2012 and 2016 and were enrolled in this study. Patients were evaluated at baseline and after 12 months. All patients underwent clinical examination, laboratory tests and ultrasound (US) examination. For the US examination we have calculated the score proposed by Naredo et al. considering that this simplified US score includes the evaluation of the hand and knee. (2)
Results: There was a clear predominance of women (62.8%). The mean age was 55.47±13.71 years. At baseline, 21 patients (48.8%) were diagnosed with OA. 15 patients (34.9%) presented hand OA and 9 patients (20.9%) presented knee OA. Hand OA didn't influence the values of DAS28, SDAI, patient's and physician's visual analogue scale (VAS) or ultrasound scores ($p>0.05$). For patients with knee OA, significantly higher values for DAS28 were observed at baseline (p=0.018) and were maintained significantly higher after 12 months of observation (p=0.031). All the other parameters were not influenced by the presence of knee OA ($p>0.05$). The median value and interquartile range for lab tests and for disease activity indices are shown in Table 1.

Table 1. Values for disease activity indices, laboratory tests and US scores for patients with ERA with/without OA

Lab test - Median (Interquartile range)	ERA patients with OA (n=21)	ERA patients without OA (n=22)	p
DAS28	5.07 (4.62–5.73)	4.94 (3.87–5.44)	0.280
SDAI	29.02 (24.95–36.59)	28.87 (16.18–33.97)	0.644
VAS patient (mm)	72.00 (55.00–81.00)	62.50 (50.50–72.25)	0.144
VAS physician (mm)	52.00 (40.00–66.50)	50.00 (33.75–57.00)	0.456
Naredo score - GS	8.00 (5.50–12.00)	9.00 (5.00–12.25)	0.932
Naredo score - PD	4.00 (0.00–6.50)	3.00 (0.00–4.00)	0.700

Conclusions: Significantly higher values of DAS28 were observed in patients with ERA who associated knee OA, while the values of SDAI were not influenced, suggesting that SDAI may be superior to DAS28 in evaluating patients with ERA and knee OA. Not the same tendency was observed in patients with ERA and hand OA. The values of patient's VAS were not influenced by the presence of hand or knee OA suggesting that these types of OA do not influence the patients' perception of the disease activity. Moreover, the values of ultrasound scores were not influenced by the presence of OA.
References:
[1] Aletaha D et al. Arhritis Rheum. 2010;62:2569–2581.
[2] Naredo E et al. Clin Exp Rheumatol. 2005;23:881–884.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4592

SAT0548 PLASMA CGRP CONCENTRATIONS WERE NOT ASSOCIATED WITH PATIENT OA SYMPTOMS OR RESPONSE TO GALCANEZUMAB, A MONOCLONAL ANTIBODY AGAINST CGRP

T.A. Mcnearney[1], C. Smith[2], R. Brown[3], A. Camporeale[4], M. Deeg[3], D. Montieth[5], E.C. Collins[3], T.J. Schnitzer[6], A.J. Kivitz[7], J. Talbot[3], Y. Jin[3]. *[1]Neuroscience/Pain, Eli Lilly and Company, Indianapolis, United States; [2]Eli Lilly and Company, Windlesham, United Kingdom; [3]Eli Lilly and Company, Indianapolis, United States; [4]Eli Lilly and Company, Sesto Fiorentino, Italy; [5]Xenon Pharmaceuticals Inc, Burnaby, Canada; [6]Northwestern University, Chicago, IL; [7]Altoona Center for Clinical Research, Duncansville, United States*

Background: The safety and efficacy of galcanezumab, a monoclonal antibody

directed against CGRP, were assessed in a phase 2 clinical trial NCT02192190 in patients with moderate to severe osteoarthritis (OA) knee pain. Patients were randomized to placebo, galcanezumab (5, 25, 120 and 300 mg subcutaneously every 4 weeks, at weeks 0 and 4) or celecoxib (200 mg once daily) for 16 weeks in a 2:1:1:1:1:1 ratio. The study was terminated after an interim analysis due to inadequate efficacy for OA pain.

Objectives: This study assessed the correlation of baseline plasma CGRP concentrations with signs, symptoms and radiographic severity of OA, and response to galcanezumab and celecoxib treatments.

Methods: Plasma samples were collected at baseline and weeks 4, 8, 12 and 16 after study drug treatment. CGRP concentrations were determined by a validated high sensitivity (HS) assay. Correlation of baseline CGRP levels to WOMAC scores, PGA and radiographic Kellgren-Lawrence (K-L) grades were assessed using Spearman's correlation and Wilcoxon test. Patients were stratified into high vs low groups by baseline CGRP concentrations and post-treatment changes from baseline WOMAC scores evaluated by mixed effect model repeated measures for each subset.

Results: At the interim analysis, baseline plasma CGRP samples were available for 262 patients with 54 patients providing samples at study termination through the week 8 visit. The median CGRP concentration at baseline was 1.07 pg/ml, range <0.78 to 33.91, and 31% of patients were below the level of quantitation (BLQ, <0.78 pg/ml). Median baseline CGRP levels were 1.0 pg/ml for K-L grade 2 (N=178), and 1.2 pg/ml for K-L grade 3 (N=84) (p=0.06). Correlations of WOMAC or PGA scores with baseline CGRP levels were all r <0.01 (showed no significant correlations). In OA patients receiving galcanezumab 300mg SC at week 0 and week 4, those with high baseline CGRP levels demonstrated a 14mm improvement in WOMAC Pain response at week 12, (95% CI 0, 29mm). The pain response to galcanezumab 300mg did not reach the magnitude of celecoxib response and no effects were seen at 5–120mg doses. Celecoxib treatment had larger pain reduction among patients with high baseline CGRP compared to low baseline CGRP levels. Treatment with celecoxib did not alter plasma CGRP concentrations.

Conclusions: At baseline, CGRP levels in OA patients were not associated with WOMAC or PGA scores. There was a modest association to radiographic K-L grade. Subgroup analyses of patients with high (>median) CGRP levels at baseline suggested a potential response to galcanezumab for the highest dose, 300mg, but not lower doses. Celecoxib response was greater in those with higher CGRP levels. However, interpretation was limited by small samples sizes at the latter time points. Further studies may determine if enriching the OA population for higher CGRP levels at baseline, or if increased or longer dosing of galcanezumab would improve pain responses or if CGRP blockade is relevant in relieving OA knee pain.

Disclosure of Interest: T. Mcnearney Shareholder of: Eli Lilly stock, Employee of: Eli Lilly and Company, C. Smith Shareholder of: Eli Lilly stock, Employee of: Eli Lilly and Company, R. Brown Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, A. Camporeale Shareholder of: Eli Lilly stock, Employee of: Eli Lilly and Company, M. Deeg Shareholder of: Eli Lilly stock, Employee of: Eli Lilly and Company, D. Montieth Shareholder of: Eli Lilly stock, E. Collins Employee of: Eli Lilly and Company, T. Schnitzer Consultant for: Eli Lilly and Company, A. Kivitz: None declared, J. Talbot Shareholder of: Eli Lilly stock, Employee of: Eli Lilly and Company, Y. Jin Shareholder of: Eli Lilly stock, Employee of: Eli Lilly and Company

DOI: 10.1136/annrheumdis-2017-eular.2155

SAT0549 ANTI-INFLAMMATORY PROPERTIES OF SM04690, A SMALL MOLECULE INHIBITOR OF THE WNT PATHWAY AS A POTENTIAL TREATMENT FOR KNEE OSTEOARTHRITIS

V. Deshmukh, C. Barroga, M. Ibanez, T. Seo, S. Kc, Y. Yazici. *Samumed, LLC, San Diego, CA, United States*

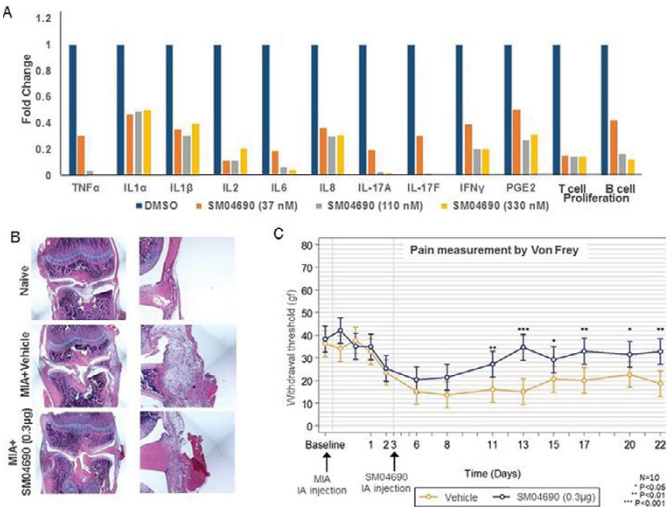
Background: Osteoarthritis (OA) is characterized by pain, deformity, and reduced function in the knee joint. Upregulated Wnt signaling affects the pathogenesis of OA through increased inflammation, increased subchondral bone and thinning cartilage. SM04690, a novel small molecule, was previously shown to inhibit the Wnt pathway and induce chondrogenesis *in vitro* and *in vivo*.[1]

Objectives: SM04690 was evaluated in preclinical studies to determine its capacity to reduce inflammation, and reduce pain in OA.

Methods: Anti-inflammatory activity was evaluated by measuring cytokine (IL-6 and TNF-α) secretion using ELISA with IL1-b stimulated synovial fibroblasts. A panel of pro-inflammatory cytokines (TNF-α, IL-1α, IL-1β, IL-2, IL-6, IL-8, IL-17A, IL-17F, IFN-γ and PGE2) was evaluated by ELISA; T and B cell proliferation by flow cytometry in peripheral blood mononuclear cells (PBMCs), and T and B cell co-cultures stimulated with super-antigen (SAg) or lipopolysaccharides (LPS), compared to vehicle or benchmark immunosuppressant or steroid (cyclosporin A and prednisolone). SM04690 effects on LPS-induced expression and phosphorylation of JNK, NFkB, Erk, cJun, Akt, Stat3 in THP-1 cells were measured by qPCR and Western Blot. *In vivo* SM04690 activity was evaluated in a rat monosodium iodoacetate (MIA) injection-induced OA model, immediately followed by a single intra-articular SM04690 or vehicle injection. Joint inflammation was evaluated by measuring synovial thickness and infiltrating cells histology; inflammatory cytokines (IL-1α, IL-1β, IL-2, IL-5, IL-6, IL-8, TNF-α and IFN-γ) by qPCR and ELISA and cartilage protection by qPCR for matrix metalloproteinases (MMPs). Pain was measured as paw withdrawal threshold using Von Frey apparatus.

Results: SM04690 inhibited IL-1b-induced TNF-α and IL-6 secretion in synovial fibroblasts (EC_{50} @30nM). SM04690 significantly inhibited ($p<0.01$) SAg and LPS stimulated pro-inflammatory cytokine production (TNF-α, IL1-α, IL1-β, IL-2, IL-6, IL-8, IL-17A, IL-17F, IFN-γ, PGE2), T and B cell proliferation in PBMCs and T and B cell co-cultures (Figure A), with activity comparable to or better than cyclosporin A and prednisolone. SM04690 treatment specifically decreased LPS-induced gene expression ($p<0.01$) and phosphorylation of NFkB in THP-1 cells with no effect on JNK, Erk, cJun, Akt and Stat3. Compared to vehicle in the rat MIA OA model, SM04690 injection reduced inflammatory cells, decreased synovial thickness ($p<0.05$,Figure B), inhibited production of pro-inflammatory cytokines and MMPs ($p<0.05$). SM04690 increased ($p<0.01$) paw withdrawal threshold in treated rats compared to vehicle at multiple time points (Figure C).

Figure. SM04690 inhibited inflammatory cytokine production *in vitro* and decreased inflammation and pain in the MIA model of OA



Conclusions: SM04690 demonstrated potent anti-inflammatory properties, comparable to or greater than cyclosporin A and prednisolone. In a rat knee OA model, SM04690 injection reduced inflammation, protease production and pain compared to vehicle. The anti-inflammatory properties of SM04690 may provide beneficial effects in the treatment of OA. Clinical studies are ongoing.

References:

[1] Hood et al. OAC 2016, s187.

Disclosure of Interest: V. Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, C. Barroga Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, M. Ibanez Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, T. Seo Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, S. KC Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Y. Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC

DOI: 10.1136/annrheumdis-2017-eular.6460

SAT0550 NEUROPATHIC PAIN AMONG PATIENTS WITH PRIMARY KNEE OSTEOARTHRITIS- RESULTS OF A CROSS SECTIONAL STUDY FROM A TERTIARY CARE CENTRE IN SOUTHERN INDIA

V. Narayan R[1], M.M. Thabah[2], M. Poduval[3]. [1]*MBBS Student;* [2]*Medicine;* [3]*Orthopedic Surgery, Jawaharlal Institute of PostgraduateMedical Education and Research, Puducherry, India*

Background: Pain in osteoarthritis (OA) is generally believed to be nociceptive because of local structural pathology and joint failure which so characterizes OA. However, there is often a discordance between the radiographic knee OA and pain, suggesting that the pain can be contributed by other mechanisms other than nociception.[1] Recently it is shown that pain in knee OA may have a neuropathic component.[2]

Objectives: The objective of the study was to assess the level of neuropathic pain in patients with knee OA, and identify the clinical and socio-demographical factors associated with neuropathic pain

Study design: Cross sectional study.

Setting: Medicine and Orthopaedic outpatient department (OPD) of a tertiary care centre located in southern India

Methods: One-hundred and sixty-one patients with knee OA satisfying the American College of Rheumatology 1986 clinical and radiographic classification criteria for knee OA were studied. Neuropathic pain was assessed by the Douleur Neuropathique in 4 questions (DN4) questionnaire;[3] score of 4/10 or more was classified as diagnostic for neuropathic pain. The Indian version of Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[4] was used to assess pain, stiffness and physical function of the patients. Factors associated with neuropathic pain were explored.

Results: Mean age was 55.7±8.8 years. The mean total Indian WOMAC was

75.07±13.8, WOMAC pain score was 16.1±3.6. Eighty-two patients of 161 (50.9%) had neuropathic pain. When diabetics were excluded (n=58), the proportion of patients with neuropathic pain reduced to 45.6%. The most frequently described pain characteristic was sensation of electric shock (58.4%). Mean total WOMAC and physical function subscale was significantly higher in neuropathic pain group when compared to no neuropathic pain group (DN4 score 3 or less), 77.5±11.5 versus 72.6±15.5, p=0.024; and 54.3±8.8 and 49.8±12.6 respectively, p=0.008

Conclusions: Neuropathic pain was seen in up to 50% patients with knee OA. Centrally acting drugs like tricyclic anti-depressants or duloxetine can be used to improve pain and physical function in patients of knee OA with neuropathic pain.

References:

[1] Hannan MT, Felson DT, Pincus T. Analysis of the discordance between radiographic changes and knee pain in osteoarthritis of the knee. J Rheumatol 2000;27(6):1513–1517.

[2] Havelin J, Imbert I, Cormier J, Allen J, Porreca F, King T. Central sensitization and neuropathic features of ongoing pain in a rat model of advanced osteoarthritis. J Pain 2016; 17: 374–82.

[3] Cruccu G, Truini A. Tools for Assessing Neuropathic Pain. PLoS Med 2009; 6(4): e1000045. [Internet] http://journals.plos.org/plosmedicine/article ?id=10.1371/journal.pmed.1000045.

[4] Chopra A, Lavin P, Patwardhan B, Chitre D. A 32 week randomized, placebo controlled evaluation of RA-11, an Ayurvedic drug, on osteoarthritis of the knees. Clin Rheumatol 2004; 10:236–245.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6192

SAT0551 INCREASED SERUM AND SYNOVIAL LEVELS OF MIDKINE ARE ASSOCIATED WITH RADIOLOGICAL PROGRESSION IN KNEE OSTEOARTHRITIS PATIENTS

W.A. Hassan[1], A.I. Mansour[2]. *[1]Rheumatology and Rehabilitation; [2]Clincal and Chemical Pathology, Benha university, Benha, Egypt*

Background: Midkine is a heparin-binding growth factor that plays an important role in mesoderm remodeling as in chondrogenesis and adipocyte formation. There is an increased expression of midkine in damaged tissues and it is believed to have functional antagonism, as it helps in tissue repair and survival while, on the other hand it can enhance inflammatory reactions resulting in more tissue injury [1].

Objectives: This study aimed to determine serum and synovial fluid (SF) levels of midkine in patients with primary knee osteoarthritis (KOA) and to examine the relationship between these levels with the clinical and functional parameters as well as radiological progression of KOA.

Methods: We measured midkne in the serum (n=52) and SF samples (n=23) from 52 KOA patients as well as in the serum from 20 healthy control (n=20). In the patients, numerical rating scale of pain (NRSP), body mass index (BMI) and The Western Ontario Mc Master scale (WOMAC) were recorded. Graded plain radiographs using Thomas score, and musculoskeletal ultrasound examination (MSUS) of both knees were performed at baseline and after 24 months to assess radiological progression [2,3]. Radiological progression was considered if there is an increase in the Thomas grading score or MSUS transition to a higher grade at the 24 months follow up period compared to baseline evaluation.

Results: Serum and SF midkine levels were significantly increased in KOA patients (mean ± SD 80.79±31.8 pg/mL and 216.31±94.93 pg/mL respectively) compared to serum level in the healthy controls (mean ± SD 65.6±14.76 pg/mL),$p<0.05$ and $p<0.001$ respectively. In KOA patients, the serum and SF concentrations of midkine significantly correlated with the baseline thickness of the cartilage on the medial condyle ($r= -0.41$ and -0.52 respectively, $p<0.05$) but not on the lateral condyle of the femur ($r=0.12$ and 0.15 respectively, $p>0.05$). Patients with elevated serum and SF midkine (defined as midkine level more than the mean plus 2 standard deviation of healthy controls's level) had a twofold increased risk of radiological progression with MSUS (age, sex and BMI adjusted RR 2.4 and 2.6, 95% CI respectively).With elevated serum and SF midkine levels, there was no increased risk of radiological progression detected with plain radiography in KOA Patients (age, sex and BMI adjusted RR 1.3 and 1.6, 95% CI respectively).

Conclusions: Osteoarthritis patients have significantly elevated serum and synovial levels of midkine that were obviously associated with radiological progression on MSUS suggesting that it could be a useful marker to reflect OA severity and implies a possible role in the pathogenesis of OA.

References:

[1] Muramatsu T. Midkine and pleiotrophin: two related proteins involved in development, survival, inflammation and tumorigenesis.J Biochem. 2002 Sep;132(3):359–71.

[2] Naredo E, Acebes C, Möller I, Canillas F, de Agustín JJ, de Miguel E, et al. Ultrasound validity in the measurement of knee cartilage thickness. Ann Rheum Dis 2009;68:1322–7.

[3] Saarakkala S, Waris P, Waris V, Tarkiainen I, Karvanen E, Aarnio J, et al. Diagnostic performance of knee ultrasonography for detecting degenerative changes of articular cartilage. Osteoarthritis Cartilage 2012;20:376–81.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5439

SAT0552 CLINICAL OUTCOMES FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 STUDY OF A NOVEL, INTRA-ARTICULAR, INJECTABLE, WNT PATHWAY INHIBITOR (SM04690) FOR THE TREATMENT OF KNEE OSTEOARTHRITIS: WEEK 26 INTERIM ANALYSIS

Y. Yazici[1], A. Gibofsky[2], N.E. Lane[3], N. Skrepnik[4], E. Armas[5], C.J. Swearingen[1], A. DiFrancesco[1], J.R. Tambiah[1], T.E. McAlindon[6]. *[1]Samumed, LLC, San Diego, CA; [2]Weill Cornell Medical College and Hospital for Special Surgery, New York, NY; [3]UC Davis Medical Center, Davis, CA; [4]Tucson Orthopedic Institute, Tucson, AZ; [5]Well Pharma, Miami, FL; [6]Tufts Medical Center, Boston, MA, United States*

Background: Knee osteoarthritis (OA) is characterized by pain, disability and joint deformity due to degradation of articular cartilage and bone remodeling. The Wnt signaling pathway has a role in these cellular processes, and it is also linked to inflammation. SM04690, a small molecule Wnt pathway inhibitor, is in development for the treatment of knee OA as a potential disease modifying drug. A phase 2, multicenter, 52-week, randomized controlled trial of a single intra-articular (IA) injection of SM04690 is ongoing in subjects with moderate to severe knee OA. Clinical results from an interim analysis are reported.

Objectives: To evaluate clinical outcomes from the treatment of moderate to severe knee OA by SM04690.

Methods: Subjects with ACR defined knee OA, Kellgren-Lawrence (KL) grades 2–3, received a 2 mL injection of 0.03 mg, 0.07 mg, 0.23 mg SM04690 or placebo in the target (most painful) knee. Clinical outcomes (Western Ontario and McMaster Universities Arthritis Index [WOMAC], patient global assessment [PTGA], physician global assessment [MDGA]), were assessed at 4, 13 and 26 weeks by analysis of covariance adjusted for subject baseline in the intention-to-treat (ITT) population and two subgroups: 1) with unilateral knee OA (pre-specified); 2) without chronic pain (Widespread Pain Index [WPI]≤4, post-hoc).

Results: 455 subjects (average age 60.3 [±8.7], female 58.9%, average BMI 29.9 [±4.6] kg/m^2, KL 3 [64.4%], and bilateral OA [64.0%]) were enrolled. SM04690 appeared well tolerated. In the ITT population clinically meaningful improvements in all clinical outcomes compared to baseline were seen for all groups and placebo at weeks 13 and 26 (Table). Moreover, clinically meaningful improvements in clinical outcomes were also seen in multiple groups over several outcomes at various time points compared to placebo. In the unilateral knee OA subgroup, PTGA (0.03 mg) and MDGA (0.07 mg) were significantly improved compared to placebo. In the WPI≤4 subgroup, WOMAC Pain (0.07 mg), PTGA (0.03 mg) and MDGA (0.07 mg) were significantly improved compared to placebo.

Table. Mean (SD) Baseline and Change in Clinical Outcomes over Time by Treatment Groups

All Subjects (ITT)	Timepoint	0.03 mg	0.07 mg	0.23 mg	Placebo
n*		106	114	103	105
WOMAC Pain [0-50]	*Baseline*	25.9 (8.3)	25.9 (8.2)	25.6 (7.7)	26.0 (7.6)
	Week 13	-11.9 (11.3)	-11.8 (11.2)	-10.8 (11.4)	-11.1 (11.1)
	Week 26	-12.4 (12.0)	-13.7 (10.8)	-12.0 (10.6)	-12.1 (10.8)
WOMAC Function [0-170]	*Baseline*	90.7 (28.7)	92.3 (25.7)	88.2 (28.9)	90.4 (25.4)
	Week 13	-41.6 (37.4)	-44.2 (36.4)	-38.7 (37.7)	-39.0 (37.7)
	Week 26	-43.3 (38.4)	-48.4 (37.0)	-41.3 (36.0)	-43.5 (36.3)
Physician Global [0-100]	*Baseline*	52.7 (20.0)	53.2 (18.4)	53.0 (20.5)	52.0 (18.2)
	Week 13	-23.2 (25.1)	-26.0 (23.5)	-23.3 (25.5)	-20.8 (25.8)
	Week 26	-25.3 (28.9)	-26.8 (23.6)	-25.6 (25.8)	-21.5 (24.8)
Patient Global [0-100]	*Baseline*	45.4 (22.0)	45.3 (20.5)	45.2 (20.9)	44.1 (21.1)
	Week 13	-18.5 (24.1)	-13.8 (24.8)	-15.0 (26.8)	-13.9 (24.1)
	Week 26	-21.7 (24.7)	-17.9 (25.2)	-17.8 (27.2)	-15.9 (27.4)
Unilateral Subjects (ITT)	**Timepoint**	**0.03 mg**	**0.07 mg**	**0.23 mg**	**Placebo**
n*		43	35	42	34
WOMAC Pain [0-50]	*Baseline*	25.5 (8.5)	24.3 (8.9)	24.5 (7.1)	27.0 (7.1)
	Week 13	-13.7 (11.1)	-11.7 (8.7)	-11.7 (12.0)	-12.6 (10.7)
	Week 26	-13.7 (11.9)	-13.7 (7.9)	-12.3 (10.6)	-11.7 (10.1)
WOMAC Function [0-170]	*Baseline*	92.7 (29.6)	85.3 (27.7)	84.2 (28.6)	91.2 (22.7)
	Week 13	-51.3 (34.9)	-44.8 (28.7)	-39.7 (40.7)	-39.7 (39.3)
	Week 26	-50.5 (39.5)	-47.6 (28.0)	-42.7 (38.0)	-40.8 (34.2)
Physician Global [0-100]	*Baseline*	54.5 (18.5)	50.6 (20.5)	52.8 (24.2)	50.5 (17.8)
	Week 13	-30.6 (24.6)†	-25.6 (19.7)	-24.5 (27.1)	-17.4 (26.5)
	Week 26	-29.2 (29.8)	-27.6 (25.7)†	-27.9 (24.6)	-17.4 (25.9)
Patient Global [0-100]	*Baseline*	44.2 (23.1)	44.3 (24.1)	48.8 (19.7)	45.7 (19.9)
	Week 13	-22.9 (24.0)†	-13.3 (24.3)	-20.0 (28.1)	-13.8 (24.4)
	Week 26	-26.8 (23.6)‡	-20.4 (29.1)	-20.2 (30.4)	-13.8 (31.0)
WPI ≤ 4 (ITT)	**Timepoint**	**0.03 mg**	**0.07 mg**	**0.23 mg**	**Placebo**
n*		64	66	63	64
WOMAC Pain [0-50]	*Baseline*	25.6 (7.4)	25.5 (8.7)	26.7 (5.8)	26.5 (7.0)
	Week 13	-13.4 (11.3)	-12.2 (11.5)	-11.6 (11.9)	-11.0 (11.6)
	Week 26	-12.4 (12.0)	-14.8 (11.1)†	-12.9 (10.5)	-11.5 (11.2)
WOMAC Function [0-170]	*Baseline*	90.6 (25.6)	88.7 (26.7)	93.6 (21.5)	91.1 (24.9)
	Week 13	-47.6 (39.2)	-44.0 (35.7)	-43.4 (36.2)	-35.9 (39.7)
	Week 26	-46.1 (41.2)	-49.8 (36.9)	-46.6 (34.2)	-39.5 (36.4)
Physician Global [0-100]	*Baseline*	53.2 (19.5)	53.4 (19.7)	56.9 (18.6)	51.6 (18.1)
	Week 13	-24.8 (25.7)	-26.1 (24.4)	-24.9 (27.5)	-18.7 (26.9)
	Week 26	-24.5 (29.6)	-28.4 (25.2)‡	-26.2 (27.3)	-18.0 (24.9)
Patient Global [0-100]	*Baseline*	44.3 (23.0)	43.9 (23.7)	47.8 (22.4)	42.8 (21.1)
	Week 13	-21.6 (24.9)‡	-15.1 (26.7)	-18.1 (28.6)	-12.1 (26.2)
	Week 26	-23.8 (25.7)†	-21.1 (27.6)	-21.1 (28.6)	-14.3 (29.1)

*Ns represent observations at Week 26.†P<0.05 compared to placebo. ‡ P<0.01 compared to placebo.

Conclusions: In this phase 2 interim analysis, the ITT population (SM04690 and placebo groups) demonstrated clinically relevant improvements in clinical outcomes at weeks 13 and 26 compared to baseline. In two subgroups, consistent

improvements over placebo were seen in 0.03 mg and 0.07 mg treatment arms, achieving statistical significance for PTGA and MDGA. Further studies to identify relevant sub-populations and evaluate the safety and efficacy of SM04690 are ongoing.

Disclosure of Interest: Y. Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, A. Gibofsky Shareholder of: AbbVie, Amgen, J&J, GSK, Regeneron, Consultant for: AbbVie, Pfizer, Horizon, Iroko, Celgene, Novartis/Sandoz, Samumed, Speakers bureau: AbbVie, Amgen, Celgene, Pfizer, N. Lane Consultant for: Samumed, LLC, N. Skrepnik Grant/research support from: Samumed, LLC, Consultant for: Orthofix and Sanofi, E. Armas Grant/research support from: Samumed, LLC, C. Swearingen Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, A. DiFrancesco Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, J. Tambiah Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, T. McAlindon Grant/research support from: Samumed, Consultant for: Astellas, Flexion, Pfizer, Regeneron, Samumed,and Seikugaku

DOI: 10.1136/annrheumdis-2017-eular.6382

SAT0553 DETECTION OF SERUM LEVEL CHANGES OF MATRIX METALLOPROTIENASE-13 AND INTER LEUKIN-1 BETA DURING REMISSION AND FLARE-UPS OF PRIMARY OSTEOARTHRITIS OF THE KNEES

Y. Hussein Gazar, H. Bassiouni. *Alazhar University Hospital, Cairo, Egypt*

Background: The diagnosis of osteoarthritis is currently based on radiographic criteria (eg, joint space width) and clinical symptoms (eg, pain and loss of function).

The evaluation of new disease-modifying osteoarthritis drugs (DMOADs) is performed on the same basis, since the regulatory bodies currently require evidence for an impact on radiographic joint space narrowing (JSN) and an impact on symptoms However, the limitations of radiography have led to research into alternative parameters for monitoring osteoarthritis that could serve as biomarkers in drug development.

Objectives: Detection the serum level of MMP-13 and IL-1 β In OA of the knee during remission and exacerbation and if these Biomarkers can be validated as gold biomarkers in assessing OA progression and drug development in OA treatment.

Methods: This study was performed on 60 patients with knee osteoarthritis, 18 males (30%) and 42 females (70%), all diagnosed as osteoarthritis of one or both knees. Their ages ranged from (40 -65) years. The duration of their disease ranged from one to 15years. The control groups were 8 males (32%) and 17 females (68%). their ages ranged from (40–65) years.

- The patients were allowed to continue on the medications that they have pro inflammatory cytokines (IL-1β) and degradative enzymes (MMP-13) are measured.
- Clinical assessing for pain using visual analogue scale (0–10)
- Assessing for pain, stiffness and physical functions by:
  (A) the WOMAC osteoarthritis index
  (B) Lequesne's algo functional index
- Asssesing the flare-ups using Knee Osteoarthritis Flare Ups Score (KOFUS).

Results: Patients who had 3 flare-ups (during one year follow up) showed the statistically significantly highest mean IL-1β & MMP13 level.

There was no statistically significant difference between patients with no flare-up, 1 flare-up and 2 flare-ups; all showed statistically significantly lower mean levels.

There was a statistically significant positive (direct) correlation between IL-1β, disease duration, KL, VAS, stiffness score, pain score, functional score, WOMAC and KOFUS. An increase in all these variables is associated with an increase in IL-1β & MMP13.

Conclusions:

- There is a potential role for IL1 beta and MMP 13 biomarkers in assessing the development in osteoarthritis.
- IL 1 β and MMP 13 were founded to be correlated positively in patients with knee OA this correlation sounded right as the expression of MMP 13 depends on the level of IL1 β.
- Although all medications groups failed to lower the level of IL 1 β and MMP 13,yet there was a numerical difference in favor of Diacerine and NSAID.
- patients on both Diacerine and NSAID had the lowerest rate of flare ups
- It is recommended that the early measurement of biomarkers may detect cases to progress and thus stronger treatment may be given for these groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1134

SAT0554 INVESTIGATION OF SELECTED BIOCHEMICAL MARKERS IN KNEE OSTEOARTHRITIS: THE FRAMINGHAM OSTEOARTHRITIS COHORT

Y. Luo[1], Y. He[1], A.S. Siebuhr[1], S. Hoielt[1], D. Felson[2], M. Karsdal[1], A.-C. Bay-Jensen[1]. *[1]Biomarkers & Research, Nordic Bioscience, Herlev, Denmark; [2]Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, United States*

Background: Osteoarthritis (OA) is a major cause of functional impairment and disability among the elderly. There is an unmet need for the development of biomarkers for identifying patients with high risk for OA and for monitoring drug efficacy. Specific and sensitive biochemical markers revealing the turnover of bone, cartilage, and synovial tissue may be useful for investigation and monitoring of OA.

Objectives: To investigate a targeted set of five biochemical markers, which reflect joint tissue turnover, for their ability to evaluate the prevalence of radiographic and symptomatic knee osteoarthritis (OA) in a substudy from the cross-sectional Framingham OA cohort (FOA).

Methods: The subjects from the community-based FOA cohort were divided up based on a terminology proposed by the FNIH-OAI consortium. Two main groups were defined: subjects with radiographic knee OA (RKOA, n=80) and a group with no radiographic OA (NRKOA, n=136). The presence of ROA as any Kellgren-Lawrence (KL) grade =2 or 3. The RKOA group were further divided into two groups; those with persistent symptoms of a joint (RKOA+S, n=30) and those without (RKOA-S, n=50). +S was defined as having pain, aching or stiffness in either knee on most days.

Serum levels of C1M, CRPM and huARGS (matrix metalloproteinases cleaved type I collagen and C-reactive protein neo-epitopes, aggrecanase cleaved ^{374}ARGS neoepitope of aggrecan, Nordic Bioscience) were determined by ELISA. Serum levels of cartilage synthesis and degradation biomarkers, hsPro-C2 and hsAGNx-1 (procollagen type IIB N-terminal propeptide, aggrecanase cleaved TEGE^{373} neoepitope of aggrecan, Nordic Bioscience) were measured by electrochemiluminescence immunoassay (ECLIA). Each measure was fisher transformed in order to be comparable across the biomarkers. The correlation between the biomarkers and covariates was assessed.

The subjects of substudy were segregated into two groups based on the cut-off values of each biomarker. The cut-off values of these markers were set as mean of their reference levels. We used logistic regression to compare these two groups, and to examine the association between each marker and the presence of OA and/or pain. All confounding factors were adjusted.

Results: The two main groups were well-matched by age, sex, and BMI. Two biomarkers correlated negatively with BMI: C1M and CRPM. Aggrecan degradation biomarker, hsAGNx-1 was negatively associated with age while the huARGS was not associated with it (Table 1).

CRPM was associated with a lower risk of RKOA+S. Interestingly, hsPro-C2 was associated with a higher risk of it (Table 2).

Table 1. Subject characteristics of substudy

Covariates	NRKOA (n=136)	RKOA-S (n=50)	RKOA+S (n=30)	Biomarker (Fisher transformed) associations with covariates
BMI, mean kg/m^2 (SD)	31.3 (3.79)	32.3 (6.05)	31.6 (5.12)	C1M, CRPM
WOMAC pain	0.182 (0.657)	0.820 (1.66)	4.83 (3.64)	
Age, mean years (SD)	62.6 (8.18)	63.7 (7.06)	62.4 (7.09)	hsAGNx-1
Sex, n (%) female	82 (60.3%)	33 (66.0%)	18 (60.0%)	C1M

Table 2. Odds ratio of OA in the substudy. Values in bold represent associations of p≤0.05. OR data are for each definition of OA, using logistic regression and adjusted for age, sex, and BMI (Upper: unadjusted, Lower: adjusted). ORs are for comparison with knees with NRKOA subjects.

Biomarker	OR of RKOA-S (95% CI)	OR of RKOA+S (95% CI)
C1M	1.07 (0.54 - 2.10)	0.47 (0.18 - 1.24)
CRPM	0.97 (0.51 - 1.88)	0.41 (0.16 - 1.02)
hsAGNx-1	1.20 (0.61 - 2.38)	0.68 (0.27 - 1.72)
hsPro-C2	1.27 (0.63 - 2.57)	**2.51 (1.10 - 5.73)**
huARGS	1.43 (0.71 - 2.88)	1.19 (0.50 - 2.84)
Biomarker	**OR of RKOA-S (95% CI)**	**OR of RKOA+S (95% CI)**
C1M	0.96 (0.47 - 1.95)	0.45 (0.17 - 1.20)
CRPM	0.87 (0.44 - 1.71)	**0.39 (0.16 – 1.00)**
hsAGNx-1	1.11 (0.55 - 2.23)	0.68 (0.27 - 1.72)
hsPro-C2	1.32 (0.64 - 2.72)	**2.55 (1.11 - 5.82)**
huARGS	1.49 (0.73 - 3.03)	1.21 (0.50 - 2.92)

Conclusions: This study provides two major findings: 1) aggrecan degradation is not just aggrecan degradation and different neo-epitopes have distinct clinical relevance; 2) CRPM is a candidate biomarker of disease activity and for patient profiling. These data suggest a reference for interpretation of OA subject biomarker data in future human studies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1744

SAT0555 MRI-DETECTED KNEE OSTEOPHYTE: NATURAL HISTORY AND STRUCTURAL RISK FACTORS AFFECTING CHANGE

Z. Zhu[1], W. Han[2], S. Zheng[2], T. Winzenberg[2], F. Cicuttini[3], C. Ding[2], G. Jones[2] on behalf of Musculoskeletal Unit, Menzies Institute for Medical Research. *[1]12779, Hobart, Australia; [2]Musculoskeletal Unit, 12779, Hobart; [3]Department of epidemiology and Preventive Medicine, Monash University, Melbourne, Australia*

Background: Although magnetic resonance imaging (MRI) has been proved to be far more sensitive than conventional radiographs to detect OP, the natural history of MRI-detected OP in older adults has not yet been described, and it is unclear whether knee structural abnormalities, including cartilage defects, cartilage volume, bone marrow lesions (BMLs), meniscal extrusion, infrapatellar fat pad (IPFP), and effusion-synovitis, can predict osteophyte change.

Objectives: To describe the natural history of knee MRI-detected OP, and to determine if knee structural risk factors are associated with change of MRI-detected OP in a longitudinal study of older adults.

Methods: 413 randomly selected older adults (mean age 63 years) had magnetic resonance imaging at baseline and approximately 2.6 years later to measure knee OP, cartilage defect, cartilage volume, BMLs, meniscal extrusion, IPFP quality score/maximum area and effusion-synovitis. Weight, height, body mass index (BMI) and leg muscle strength were measured by standard protocols.
Results: 85% participants had MRI-detected OP at baseline. Over 2.6 years, the average OP score increased significantly in all compartments. The OP score remained stable in 53% participants and worsened in 46% (≥1-point increase) OP, with 1% decreasing. Baseline factors associated with an increase in MRI-detected OPs over 2.6 years included BMI, cartilage defects, BMLs, meniscal extrusion, IPFP quality score and Effusion. In multivariable analyses, baseline cartilage defects, BMLs and meniscal extrusions and IPFP quality score were site-specifically and significantly associated with increased OP at medial tibiofemoral, lateral tibiofemoral and total compartments (p all <0.05). In contrast, total and suprapatellar pouch effusion-synovitis were significantly associated with increased OP at total and lateral compartments (p all <0.01). The significant associations between baseline cartilage volume and increased OPs at medial and total compartments became non-significant after further adjustment for other knee structural abnormalities. Age sex and smoking status were not associated with increased OPs over time.

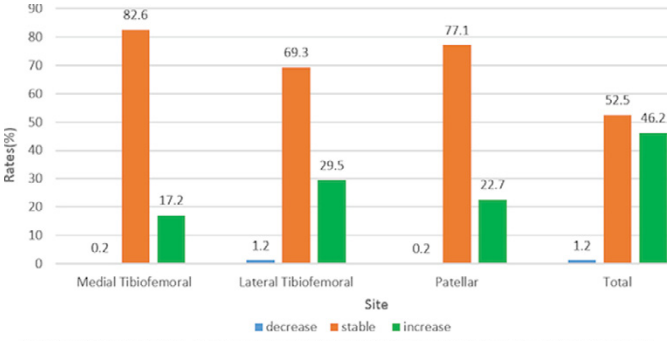


Figure 2. Change in MRI-detected osteophyte scores by site over 2.6 years. Total score was calculated by summing medial tibiofemoral, lateral tibiofemoral and patellar scores.

Conclusions: Knee MRI-detected OP in older adults is common and, in contrast to radiographs, is likely to progress over a relatively short period. Progression can be predicted by structural risk factors suggesting they are a consequence of these abnormalities.
References:
[1] McCauley TR, Kornaat PR, Jee WH. Central osteophytes in the knee: prevalence and association with cartilage defects on MR imaging. AJR Am J Roentgenol. 2001 Feb; 176(2):359–364.
Acknowledgements: The authors thank the participants who made this study possible, and acknowledge the role of the staff and volunteers in collecting the data, particularly research nurses Boon C and Boon P. Warren R assessed MRIs and Dr Srikanth V and Dr Cooley H assessed radiographs.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1161

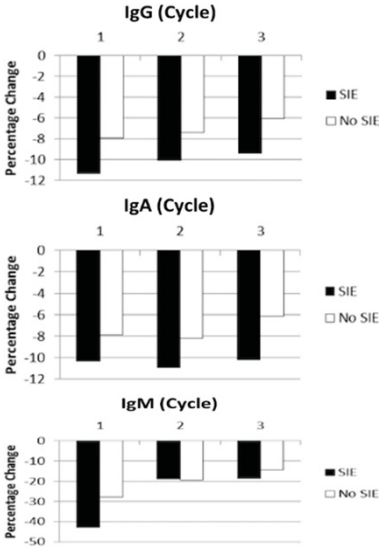
SATURDAY, 17 JUNE 2017

Infection-related rheumatic diseases

SAT0556 RISK FACTORS FOR SEVERE INFECTION AND RATIONALE FOR IMMUNOGLOBULIN MONITORING DURING RITUXIMAB TREATMENT IN AUTOIMMUNE RHEUMATIC DISEASES

M.Y. Md Yusof [1,2], E.M. Vital [1,2], D. McElvenny [3], E.M. Hensor [1,2], S. Das [1], M.H. Buch [1,2], P. Emery [1,2], S. Savic [1,2]. [1] *Rheumatology, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds;* [2] *NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds;* [3] *Institute of Population Health, University of Manchester, Manchester, United Kingdom*

Background: Rituximab (RTX) has been used in the treatment of various autoimmune rheumatic diseases (AIRDs) for over a decade. Repeat cycles are effective for maintenance but may lead to hypogammaglobulinaemia. Low IgG at baseline has been associated with post-treatment infection rate but may be confounded by other clinical variables and fully adjusted models with method for handling missing data have not been presented. Importance of post-treatment change in Igs has also not been proven.
Objectives: To evaluate risk factors for severe infection in multivariable analysis and assess outcome of hypogammaglobulinaemia.
Methods: The first 700 consecutive patients with AIRDs treated with RTX at a single centre were studied. Each cycle of RTX consisted of 2x1000mg infusions repeated on clinical relapse. IgM, IgA and IgG levels were measured at baseline and 4–6 months after each cycle. Multiple imputation was used for missing data. Baseline factors for predicting serious infection and low Ig were tested using univariable and multivariable (MVA) logistic regression analyses.
Results: 550 patients were female, median age (IQR) at RTX initiation 58 (46–68) years and median disease duration (IQR) 7.9 (3.4–15.0) years. 506 (72%) had RA, 94 (13%) SLE, 49 (7%) AAV, 14 (2%) DM, 5 (1%) APS, 6 (1%) SSc and 26 (4%) other CTD. 364 (52%) were biologic-naïve and 515 (74%) were on concomitant DMARDs. Total follow-up: 2940 patient-years (PY). 284 serious infections were recorded in 179 patients (9.7/100 PY); 88 cases within 12 months of cycle 1 (C1). In MVA, previous severe infection (OR 10.7, 95% CI 5.8–19.5), low IgG (OR 3.6, 95% CI 1.5–8.6), previous cancer (OR 2.9, 95% CI 1.2–6.6) and chronic lung disease (OR 1.7, 95% CI 0.9–3.1) increased the odds of a severe infection within 12 months of C1. A diagnosis of CTD was associated with lower risk (OR 0.5, 95% CI 0.2–0.9). Low IgG at RTX initiation was predicted by older age, previous cancer, RA diagnosis, previous severe infection and previous treatment with cyclophosphamide. In C1-C3, higher rate of change in IgA and IgG levels were associated with serious infections (Figure 1). Overall, only 7 (1%) of the patients required Ig replacement in this cohort.



Conclusions: Factors associated with serious infection at RTX initiation include previous serious infection, low IgG, previous cancer, a diagnosis of RA and chronic lung disease. This is the first study to show the rationale for monitoring the rate of change in Ig levels during repeat cycles of RTX, with reduction in all Ig subclasses being associated with increased risk of post-treatment infection. Further analysis including predictors of serious infections in repeat cycles is in progress and will be used to develop guidelines for safety monitoring of rituximab.
Acknowledgements: This research was funded/supported by the National Institute for Health Research (NIHR) and NIHR Leeds Musculoskeletal Biomedical Research Unit based at Leeds Teaching Hospitals NHS Trust; (DRF-2014–07–155). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6896

SAT0557 CHIKUNGUNYA OUTBREAK IN BRAZIL: DEMOGRAPHIC AND CLINICAL CHARACTERIZATION OF 732 PATIENTS – CHIKBRASIL COHORT

A.L. Duarte [1], C.D.L. Marques [1], P.R. Santos [1], A. Ranzolin [2], N.G. Cavalcanti [1], R.S. Gonçalves [3], A.T. Dantas [1], M.S. Luna [1], C.A. Andrade [1], L.F. Rocha Junior [3], M.R. Freitas [3], P.R. Melo [1], L.D. Valadares [4], C.A. da Fonte [4], M.L.D. Valadares [4], E. Freire [5], A.K.G. Melo [5], M.M. Medeiros [6], M.C. Bezerra [6], V.B. Marques [6], R.A. Océa [7]. [1] *Internal Medicine, Universidade Federal de Pernambuco;* [2] *Rheumatology;* [3] *Internal Medicine, Instituto de Medicina Integral Prof. Fernando Figueira;* [4] *Rheumatology, Hospital Getulio Vargas, Recife;* [5] *Rheumatology, Universidade Federal da Paraíba, João Pessoa;* [6] *Rheumatology, Universidade Federal do Ceará, Fortaleza;* [7] *Rheumatology, Universidade Federal de Sergipe, Aracaju, Brazil*

Background: Chikungunya Fever (CF) is a disease characterized by acute febrile arthritis and caused by a mosquito-transmitted alphavirus. Considering the wide distribution of the vector, the presence of imported cases from 2010 and Brazilian population's susceptibility, there was a dispersal and establishment of Chikungunya virus (CHIKV) throughout the country. Since 2014, the CF has achieved a large proportion of the Brazilian population and has been responsible for the development of chronic joint symptoms in thousands of people.
Objectives: To describe the demographic, clinical and serological characteristics of patients from specialized Rheumatology services from northeastern Brazil, in a large, multicenter cohort.
Methods: Data from 732 patients in a prospective, multicenter, observational cohort conducted in six research rheumatology centers were analyzed. Patients

18 years or older who fulfilled the clinical and epidemiological Health Ministry criteria for case definition of CF were included in the study, from April to December 2016.

Results: From 732 patients included, 83.1% were women. The mean age was 54.1 (± 13.4) years; 92.4% lived in urban area and 58.6% had only primary education. The most common comorbidities were hypertension (43.8%), hyperlipidemia (25.3%) and diabetes mellitus (13.7%). Prior rheumatologic disease was observed in 16.4% patients, being the most frequent rheumatoid arthritis (32.5%), osteoarthritis (32.5%) and spondyloarthritis (11.7%). Arthralgia was the most frequent symptom referred by all patients; fever and fatigue were also common manifestations, being referred by 95.3% and 87.1% of patients, respectively. Arthritis occurred in 84.3%. The most frequent joint pattern involvement was polyarticular (67.8%) and the additive (84.0%). At the first appointment with the rheumatologist, 75.9% had been or were under corticosteroid use, with the average dose of 15.4 mg (±8.7) of prednisone or equivalent; was observed an median of 8 painfull joints (IQR 4–21) and arthritis was found in 73.6% patients, with an median of 2 swollen joints (IQR 0–5). The median score of patient global assessment at the time of the initial evaluation was 6 (IQR 4–8) using a 10 points visual analogue scale. After resting stiffness was referred by 86.0%, with 58.4% of these longer than 30 minutes. The most commonly prescribed medications were corticosteroids (58.3%) and hydroxychloroquine (59.1%). The serological tests for CHIKV were positive for IgM in 97.1% and for IgG in 71.7% of patients.

Conclusions: This is the first descriptive study of a cohort Brazilian patients with CF, with an expressive number of patients when compared to those described in the literature. Most of the features of patients in our cohort were similar to the results described in studies/cohorts published.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4537

SAT0558 CONCORDANCE BETWEEN CLINICAL-EPIDEMIOLOGICAL CRITERIA AND CHIKUNGUNYA FEVER SEROLOGY

C.D.L. Marques[1,1,1], C.A. Andrade[1], M.S. Luna[1], P.R. Santos[1], A.T. Dantas[1], A. Ranzolin[2], N.G. Cavalcanti[1], R.S. Gonçalves[3], L.F. da Rocha Jr[4], P.R. Melo[1], R.M. Correia[3], L.D. Valadares[5], C.A. da Fonte[5], M.L.D. Valadares[5], E. Freire[6], A.K.G. Melo[6], M.M. Medeiros[7], M.C. Bezerra[7], V.B. Marques[7], R.A. Océa[8], A.L. Duarte[1]. *[1]Internal Medicine, Universidade Federal de Pernambuco; [2]Rheumatology; [3]Internal Medicine, Instituto de Medicina Integral Prof. Fernando Figueira; [4]Rheumatology, Instituto de medicina integral professor Fernandes Figueira; [5]Rheumatology, Hospital Getulio Vargas, Recife; [6]Rheumatology, Universidade Federal da Paraíba, João Pessoa; [7]Rheumatology, Universidade Federal do Ceará, Fortaleza; [8]Rheumatology, Universidade Federal de Sergipe, Aracaju, Brazil*

Background: The first autochthonous reports of Chikungunya fever (CF) in Brasil was confirmed in 2014, and by December 2016, there were 263.980 probable cases of CF, 55.03% confirmed. According to recommendations of the Ministry of Health (MH) of Brazil, in an established epidemic situation, the diagnosis of CF should be made by appliyng clinical and epidemiological criteria. There is no indication for the serology for Chikungunya virus (CHIKV) in the acute phase, except in atypical cases and complicated clinical situations, which may generate doubts in clinical practice about the correct diagnosis of these patients.

Objectives: The objective of this study was to evaluate the concordance of the clinical and epidemiological criteria with the serology results for CHIKV in a cohort of patients with CF.

Methods: The multicenter cohort CHIKBRASIL from the Northeast of Brazil has enrolled CF patients with joint manifestations since April 2016, using as inclusion criteria the presence of fever and arthralgia/arthritis in a patient residing or who had visited an endemic or epidemic area within 15 days prior to the onset of symptoms. For the present study, we selected patients in which IgM and/or IgG serology was performed, regardless of the results. For the analysis of agreement with the serology, the most characteristic symptoms of CF were used individually (fever, arthritis/arthralgia or exanthema) and three models of association of symptoms were created: (1) fever and arthralgia; (2) fever and arthritis; (3) fever, arthralgia/arthritis, and exanthema. The sensitivity (SENS), specificity (SPEC), positive predictive value (PPV) and negative predictive value (NPV) of the criteria were also assessed, with the serology result considered the gold standard.

Results: A total of 143 patients were evaluated, 119 (83.2%) of which were female, with a mean age of 53.89 years (± 13.5); 52.4% of the cases were in the subacute phase of the disease (15 days to 3 months) and 42.7% were in the chronic phase (over 3 months). The IgM positivity was observed in 95.1% of cases and IgG in 71.67%. The concordance rate between the IgM serology or combined positive serology (IgM or positive IgG) was over 80% for any of the symptoms/symptoms model analyzed, as well as the SENS and PPV of the symptoms/ symptoms model, which was over 95% in all situations evaluated. The concordance rate for IgG serology ranged from 51.9 to 72.1%. Model 1 presented the highest agreement with the result of positive combined serology.

Conclusions: During an epidemic situation, the use of clinical and epidemiological criteria shows high agreement with the serology result, regardless of the combination of symptoms presented, with high sensitivity and positive predictive value.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6431

SAT0559 SEPTIC ARTHRITIS IN COVENTRY IN THE UK: 5 YEAR DATA

A. Vivekanantham[1], A. Kahlon[1], M. Ali[1], A. Metcalfe[2], S. Dubey[1]. *[1]Rheumatology; [2]Orthopaedics, University Hospitals Coventry and Warwickshire, CV2 2DX, United Kingdom*

Background: Septic arthritis (SA) is a serious condition associated with significant morbidity and prolonged hospital stays, posing a large economic burden to healthcare systems. It affects 2–10 people per 100,000 and there has been a suggestion that the incidence is increasing due to iatrogenic causes [1]. Our local secondary centre, University Hospitals Coventry and Warwickshire NHS Trust (UHCW NHS Trust), provides care to Coventry and Rugby covering an estimated population of 550,000.

Objectives:

- To investigate the incidence of native joint SA in the adult population in a secondary care hospital in the UK.
- To investigate whether immunosuppression contributes significantly to the burden of SA.

Methods: Patients were retrospectively identified on the basis of the International Classification of Diseases (ICD)-10 coding generated following discharge from hospital for all patients between 2007–11. Exclusion criteria included paediatric patients, diabetic foot, prosthetic joint infections and those who on review were not thought to have SA. The data was analysed using Excel. Formal ethical approval was obtained via the research and development department within the UHCW NHS Trust.

Results: A total of 189 admissions were coded as SA. Of these, 103 were excluded (n=74 not thought to have SA on review of the notes, n=26 paediatric patients and n=3 prosthetic joints). Therefore, there were 86 adult admissions for 64 patients with SA.

The average age of these patients was 53.4 years, with the majority of them being males (n=43, 67.2%). The majority of patients had co-morbidities (n=44, 65.7%), with hypertension (n=10, 14.9%) and type 2 diabetes (n=10, 14.9%) being the most prevalent. Joint aspirates were performed on 63.2% (n=56) of admissions and blood cultures on 70.8% (n=63) of admissions. Staphylococcus aureus was the most commonly cultured microbe in both joint fluid (46.4%, n=13) and blood (42.9%, n=3). The knee was the commonest joint involved (n=31, 46.3%). Other commonly affected joints included the small joints of the hands (n=9, 13.4%) and shoulder/acromioclavicular/sternoclavicular joints (n=9, 13.4%).

Interestingly, 23 (35.9%) of the patients were immunocompromised. Of these, 4 patients had a diagnosis of rheumatoid arthritis (RA) and were on steroid treatment alone (n=2), or in combination with disease-modifying anti-rheumatic drugs (n=2). A total of 11 patients had a pre-existing rheumatological diagnosis of which RA was the most common condition (n=6). Two of these patients were not on immunosuppressants. The 5-year mortality was significant at 29.7% (n=19).

Conclusions: Our local data showed the incidence of SA to be approximately 3 per 100,000, which is in keeping with proposed figures. Our cohort highlighted that those with pre-existing co-morbidities or those who were immunocompromised were at greatest risk. An ageing population with multiple co-morbidities means the incidence of SA is set to rise. Greater emphasis therefore needs to be placed on improving awareness and optimising treatment.

References:

[1] Geirsson AJ, Statkevicius S, Vikingsson A. Septic arthritis in Iceland 1990–2002: increasing incidence due to iatrogenic infections. Ann Rheum Dis. 2008;67:638–43.

Acknowledgements: We would like to thank the PPMO team at UHCW NHS Trust.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4372

SAT0560 COEXISTENCE OF SEPTIC AND CRYSTAL-INDUCED ARTHRITIS: A DIAGNOSTIC CHALLENGE

Y. Garcia-Mira, A. Prior-Español, S. Minguez, J. Camins, M. Martínez-Morillo, S. Holgado, A. Olive, J. Cañellas, L. Gifre, L. Mateo. *H.UNIVERSITARI Germans Trias I Pujol, Badalona, Spain*

Background: Septic arthritis (SA) is a rheumatologic emergency as joint destruction occurs rapidly and can lead to significant morbidity and mortality. Accurate diagnosis can be particularly challenging in patients with underlying inflammatory joint disease. Crystal-induced arthritis (CA) is a risk factor for its appearance. When both conditions appear simultaneously, CA may mask diagnosis of infection and delay the antibiotic treatment.

Objectives: To describe the characteristics of patients with concurrent septic and CA.

Methods: Retrospective analysis of patients with coexistence of septic and CA attended between 1985 and 2015 in a university hospital with a reference area of 850,000 inhabitants. We collect demographic, clinical, laboratory and imaging data as well as patient medical treatment, complications and evolution records. All patients had positive bacterial culture (blood and/or joint fluid) and crystals in synovial fluid.

Results: A total of 123 patients with SA were identified. 20.3% (n=25) of them had concomitant CA, with mean age of 67 years (SD 14), 17 (68%) males and 8 (32%) females. Risk factors were: diabetes (24%), diuretic drugs (24%), chronic renal failure (16%) -2 of them undergoing hemodialysis and 4 kidney

transplant patients with immunosuppressive treatment. In only 2 cases there was a previous arthrocentesis. The mean diagnostic delay was 14 days (SD 13) (data available in 14 cases). The most commonly affected joint was the knee (48%), followed by the foot (20%) and the hip (12%). In 2 cases several joints were involved at the same time. In synovial fluid cytological studies, the most frequently identified crystals were: urate (60%), calcium pyrophosphate (20%) and hydroxyapatite (8%). In 32% of cases gram staining was positive, but 88% of patients had a positive joint fluid culture, with the most frequently isolated germs being methicillin-sensitive *S. aureus* (48%), methicillin-resistant *S. aureus* (MRSA) (12%) and *M. tuberculosis* (12%). 32% of patients presented positive blood cultures (12% with negative synovial fluid culture), although 48% of patients had fever at the time of diagnosis. It should be noted that 48% had radiological baseline damage. Surgical debridement was performed in 32% of patients. Evolution was successful in 56% of patients; although intercurrent complications were usual (40%). Mortality was 8% -one case due to acute pulmonary edema and the other because of septic shock.

Conclusions: Coexistence of infectious and CA represents a diagnostic challenge and requires a high suspicion index. It usually appears in elderly patients with comorbidities. Gout was the most prevalent CA. *S. aureus* was the most commonly causative pathogen, with a high rate of MRSA infection. If it's treated early the evolution is usually favorable, which makes synovial fluid microbiological study imperative.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4993

SAT0561 USEFULNESS OF POLYMERASE CHAIN REACTION FOR DIAGNOSING WHIPPLE'S DISEASE IN RHEUMATOLOGY

M. Herbette [1], J.B. Cren [2], L. Joffres [3], C. Lucas [4], E. Ricard [5], C. Salliot [6], J. Guinard [5], A. Perdriger [4], E. Solau-Gervais [3], B. Bouvard [2], A. Saraux [1] on behalf of Reseau Victor Hugo. *[1] Rheumatology, CHU Brest and Université Bretagne Occidentale, Brest; [2] Rheumatology, CHU, Angers; [3] Rheumatology, CHU, Poitiers; [4] Rheumatology, CHU, Rennes; [5] Rheumatology; [6] CHU, Orleans, France*

Background: No consensus exists about the combination of clinical, laboratory, and radiological findings that warrant tests for Whipple's disease.

Objectives: The primary aim of this multicentre retrospective study was to determine when patients evaluated for rheumatological symptoms should undergo *T. whipplei* PCR testing. Secondary aims were to describe the clinical patterns and treatments used, to determine the diagnostic yield of PCR testing, and to assess whether centres with higher numbers of tests also had a larger number of Whipple's disease diagnoses.

Methods: In a retrospective observational study done in five hospitals, we assessed the clinical and radiological signs that prompted *T. whipplei* PCR testing between 2010 and 2014, the proportion of patients diagnosed with Whipple's disease, the number of tests performed and the number of diagnoses according to the number of tests, the patterns of Whipple's disease, and the treatments used.

Results: At least one PCR test was performed in each of 267 patients. Rheumatic signs were peripheral arthralgia (n=239, 89%), peripheral arthritis (n=173, 65%), and inflammatory back pain (n=85, 32%). The main extra-articular signs were constitutional symptoms (n=111, 41.8%), diarrhoea (n=70, 26.5%), fever (n=53, 20%), lymphadenopathy (n=14, 5.3%), and neurological signs (n=11, 4.2%). Whipple's disease was diagnosed in 13 patients (4.9%). The main samples tested and the more frequently positive tests in the centres with diagnoses of Whipple's disease were saliva and stool. In the centres with no diagnoses of Whipple's disease, arthritis was less common, whereas constitutional symptoms, fever, and lymphadenopathy were more common. 11 patients with Whipple's disease had CRP elevation. The annual incidence ranged across centres from 0 to 3.6/100000 inhabitants. The patients group with Whipple's disease had a higher proportion of males, older age, and greater frequency of arthritis.

Conclusions: Males aged 40–75 years with unexplained intermittent seronegative peripheral polyarthritis, including those without constitutional symptoms, should have *T. whipplei* PCR tests on saliva, stool and, if possible, joint fluid.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5852

SAT0562 CHIKUNGUNYA FEVER IN PATIENTS WITH PRIOR RHEUMATIC DISEASES: IS IT MORE SEVERE?

A.T. Dantas [1], M.S. Luna [1], P.R. Santos [1], C.A. Andrade [1], C.D.L. Marques [1], A. Ranzolin [2], N.G. Cavalcanti [1], R.S. Gonçalves [3], L.F. Rocha Junior [2], H.D. Lima [2], P.R. Melo [3], L.D. Valadares [4], C.A. da Fonte [4], M.L.D. Valadares [4], E. Freire [5], A.K.G. Melo [5], M.M. Medeiros [6], M.C. Bezerra [6], V.B. Marques [6], R.A. Océa [7], A.L. Duarte [1]. *[1] Internal Medicine, Universidade Federal de Pernambuco; [2] Rheumatology; [3] Internal Medicine, Instituto de Medicina Integral Prof. Fernando Figueira; [4] Rheumatology, Hospital Getulio Vargas, Recife; [5] Rheumatology, Universidade Federal da Paraíba, João Pessoa; [6] Rheumatology, Universidade Federal do Ceará, Fortaleza; [7] Rheumatology, Universidade Federal de Sergipe, Aracaju, Brazil*

Background: Chikungunya fever (CF) is an infectious disease caused by a RNA virus and its transmission occurs by the inoculation of the virus by the female bite of *Aedes aegypti* mosquito. In Brazil, where the vetor is endemic, the virus rapidly disseminated and there was an epidemic, specially in the Northeast region of the country with 263.980 notified cases in 2016. It is known that CF may have a chronic course with articular symptons, however there is not consistent data in the medical literature on CF evolution in patients with prior rheumatic diseases.

Objectives: To assess whether there is any difference in the characteristics of articular manifestations of CF in patients with prior inflammatory rheumatic diseases (IRD), non-inflammatory rheumatic diseases (NIRD) and controls (patients with no diagnosed prior rheumatic diseases).

Methods: Cross-sectional study using a database from CHIKBRASIL cohort. Patients enrolled had clinical and epidemiological characteristics of CF and were classified in three groups: IRD (rheumatoid arthritis, axial spondyloarthritis and systemic lupus erythematosus), NIRD (fibromyalgia and osteoarthritis) and controls (no prior rheumatic diseases).

Results: A total of 150 patients were enrolled. There were 55 patients with IRD, 40 patients with NIRD and 55 controls, paired by age and sex. There were no differences in acute phase symptoms in the groups. There a was more frequent occurrence of arthritis in patients with IRD compared to NIRD (p=0.001) and to controls (p=0.002). In 89.1% of the patients with IRD there was an underlying disease exacerbation and 74% described an expressive worsening of symptoms compared to the period prior to infection. Patients with IRD had an increase in the current dose of corticosteroids (median 10mg, IQR 10–20) compared to previous dose used (median 6mg, IQR 5–10) after the onset of CF (p=0.0007). Importantly, there was more methotrexate prescription (23.5%) in IRD group, compared to NIRD group (0, p-0.001) and to controls (3.7%, p=0.003).

Conclusions: Patients with IRD and CF presented significantly more arthritis compared to NIRD or to controls. CF seems to induce underlying rheumatologic disease exacerbation in patients with inflammatory disease and a more aggressive therapeutic approach might be necessary in this group of patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6560

SAT0563 EVALUATION OF ROLE OF SLEEP DISTURBANCE, DEPRESSION, OBESITY, AND PHYSICAL INACTIVITY IN FATIGUE IN CHIKUNGUNYA ARTHRITIS

M. Bhama. *Orthopedics, Sardar Patel Medical College, Bikaner, India*

Background: Chikungunya virus (CHIKV) is a mosquito-borne alphavirus that circulates predominantly in tropical and subtropical regions, potentially affecting over 1 billion people.

Objectives: Fatigue is a major concern in individuals where CHIKV results severe chronic arthralgia and/or arthritis lasting months to years. However, in order to treat fatigue adequately, its sources need to be identified.

Methods: All participants had physician-diagnosed CHIKV arthralgia. Data regarding self-reported sleep quality, depression, physical activity, disease activity, muscle strength, functional limitations, and body composition were collected during a single home visit (number of participants=117). Information on demographics, medications, alcohol intake and smoking was collected. The Fatigue Severity Inventory (FSI; measuring average fatigue over the past 7 days) was used as the primary outcome. Analyses were conducted to evaluate bivariate relationships with fatigue and correlations among risk factors. Multivariate analyses identified independent predictors of fatigue.

Results: The mean age was 48±16 years, the mean disease duration was 7±6 years, and 71% (M:33, F:84) of subjects were female. The mean FSI rating was 4.1±2.0 (range 0–10). In multivariate analyses, self-reported disease activity, poor sleep, depression, and obesity were independently associated with fatigue. Physical inactivity was correlated with poor sleep, depression, and obesity. Mediation analyses indicated that physical inactivity had an indirect association with fatigue, mediated by poor sleep, depression, and obesity.

Conclusions: This cross-sectional study suggests that fatigue may not be solely a result of CHIKV arthralgia, but may result from a constellation of factors that includes CHIKV arthralgia disease activity or pain, but also includes inactivity, depression, obesity, and poor sleep. The results suggest need of various interventions to improve fatigue in individuals with CHIKV arthritis, including increasing physical activity or addressing depression or obesity.

References:

[1] Thiberville S.D., Moyen N., Dupuis-Maguiraga L., Nougairede A., Gould E.A., Roques P., de Lamballerie X. Chikungunya fever: epidemiology, clinical syndrome, pathogenesis and therapy. Antiviral Res. 2013;99(3):345–370.

[2] Vijayan V, Sukumaran S. Chikungunya Virus Disease: An Emerging Challenge for the Rheumatologist. J Clin Rheumatol. 2016 Jun;22(4):203–11.

[3] Stebbings S, Herbison P, Doyle T, Treharne GJ, Highton J. A comparison of fatigue correlates in rheumatoid arthritis and osteoarthritis: disparity in associations with disability, anxiety, and sleep disturbance. Rheumatology (Oxford)2010;49:361–7.

[4] Whitehead L. The measurement of fatigue in chronic illness: a systematic review of unidimensional and multidimensional fatigue measures. J Pain Symptom Manage2009;37:107–28.

Disclosure of Interest: M. Bhama Consultant for: Orthopedics Consultant

DOI: 10.1136/annrheumdis-2017-eular.6670

SAT0564 SUBLINGUAL VACCINE: NEW CHALLENGE IN THE PREVENTION OF RECURRENT INFECTIONS IN AUTOIMMUNE DISEASES

K. Llano Hernández[1], S. Sanchez Ramón[1], J. Ochoa Grullon[1], P. Macarron[2], C. Morado[2], C. Martínez-Prada[2], A. Rodríguez De La Peña[1], E. Rodríguez Frías[1], M. Nuñez Beltran[1], B. Fernández[2], J.Á. Jover[2], G. Candelas[2]. *[1]Inmunology; [2]Rheumatology, Madrid Clinic Hospital, Madrid, Spain*

Background: Disease-modifying antirheumatic drugs (DMARDs) and new biologicals have improved the prognosis of systemic autoimmune diseases (SAD), but reciprocally increase the risk of recurrent respiratory tract (RRTI) and urinary tract (RUTI) infections. Given the rising of antibiotic resistance, the search for new strategies for the prevention of recurrent infections is a priority.
Objectives: The purpose of this study was to evaluate the clinical benefit of the sublingual polybacterial vaccines on infections' rates in SAD patients.
Methods: A retrospective observational study on a cohort of SAD patients on active inmunosuppression with RRTI and RUTI was conducted. Patients were treated with multibacterial sublingual vaccine formulations either for RRTI (*Staphylococcus spp., S. pneumoniae, K. pneumoniae, M. catarrhalis, H. influenzae*)[3] or/and RUTI (*K. pneumoniae, E. coli, E. faecalis, P. vulgaris*)[4] (Bactek/Uromune®, Inmunotek SL Madrid, Spain) for 3-months period and clinical follow-up at 6- and 12-months. We monitored the frequency of infections, the intensity and severity of infections during follow-up. Immunological evaluation was performed, including: Serum immunoglobulin levels, IgG subclasses, specific antibodies' production: anti-pneumococcal, anti-Typhi polysaccharide and anti-tetanus toxoid antibodies, and B and T cell phenotype.
Results: A total of 50 patients were evaluated, and 34 were eligible at 12-months.The mean age of the patients was 58±13 years, 31 women (91.17%) and 3 men (8.82%), 44.11% (n=15) with rheumatoid arthritis (RA), 23.52% (n=8) with systemic lupus erythematosus (SLE), 8.82% (n=3) mixed connective tissue disease, 2.94% (n=1) ankylosing spondylitis, 2.94% (n=1) sacroileitis, 2,94% (n=1) psoriatic arthritis, 2,94% (n=1) SLE/RA, 2.94% (n=1) discoid LE/Sjögren, 2.94% (n=1) adult onset Still disease, 2,94% (n=1) sarcoidosis, 2.94% (n=1) SLE-like. All patients showed a significant decrease in RRTI (3.15±2.66 vs 0.46±1.07, $p<0.01$) and RUTI (1.85±2.49 vs 0.35±1.06, $p<0.01$) frequency and use of antibiotics at 6-months of vaccine, except one with sarcoidosis. 23 of 34 patients (67.64%) disclosed defects on specific antibody production to polysaccharide and protein immunization. Three patients with antibody production deficit and pneumonia required prophylactic intravenous Ig. No adverse effects or SAD relapses were noted during the 1-year observational period.
Conclusions: Mucosal vaccination in immunosuppressed patients due to SAD with recurrent infections resulted in lower rates of RRTIs and RUTIs with subsequent improvement in their quality of life. Our preliminary results need to be validated in controlled trials.
References:
[1] G. Avila, A. Alonso, A. Pluma, C. Diaz, R. Juvernau, M. Lüpez Lasanta, S. Marsal. FRI0252 Risk Analysis for Recurrent Infectionsduring Biological Therapy in Chronic Inflammatory Arthritis. Ann Rheum Dis 2014;73:474–475 doi:10.1136/annrheumdis-2014-eular.5736.
[2] Sánchez-Ramón S, de Diego RP, Dieli-Crimi R, Subiza JL. Extending the clinical horizons of mucosal bacterial vaccines: current evidence and future prospects. Curr Drug Targets. 2014;15(12):1132–43.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4802

SAT0565 THE FREQUENCY OF SEPTIC ARTHRITIS AFTER ARTHROCENTESIS AND INTRA ARTICULAR GLUCOCORTICOID INJECTION IS LOW

S.K. Petersen, R.A. Andreasen, I.M.J. Hansen. *Rheumatology, Odense University Hospital, Svendborg Hospital, Svendborg, Denmark*

Background: Intraarticular (IA) procedures have both diagnostic and therapeutic purposes in patients with arthritis. The therapeutic benefit of IA glucocorticoids (GC) injection in patients with rheumatologic diseases is well described. However, IA procedures are associated with increased risk of Septic arthritis (SA). Rapid diagnose and correct treatment is crucial to avoid joint damage, sepsis and potential fatal outcome. However, patients in risk of evolving SA secondarily to GC injection or arthrocentesis are not well defined.
Objectives: The aim of this study was to evaluate the risk of SA in patients who received an IA GC injection or an isolated joint puncture, and to describe possible characteristics for these patients.
Methods: All patients' undergoing IA procedures at the orthopaedic and rheumatological departments of Fuhnen from January 2006 to December 2013 were identified in the central database and included by register extraction. Patients who developed SA within 30 days after IA GC injection were registered as cases. SA was defined as clinically inflamed joint and positive synovial fluid culture.
Retrospectively, data on age, gender, affected joint location, bacterial agent, pre-existing inflammatory disorder and death within 30 days were extracted from the patient files.
According to local recommendations a non-touch sterile technic where used for IA procedures. Patients were informed about the risk for SA and motivated to seek medical attention if suspicion of infection or lack of improvement.
Results: 22370 IA procedures were registered; 14118 IA GC injections and 8252 arthrocentesis. Eleven patients with SA were registered.
Eleven patients developed SA subsequently to IA GC injection (0.08% of all GC injections). For patients' demography, joint distribution, bacterial agent and pre-excisting joint disease (Table 1). One patient died within 30 days after IA GC injection.

Sex	Age	Joint	Bacterial agent	Inflammatory Disease	Death, 30 days
M	83	Shoulder	Grp. A streptococcus	No	+
M	53	Elbow	S. Aureus	No	–
M	55	Ancle	S. Aureus	Gout	–
M	67	Knee	Grp. A streptococcus	No	–
F	83	Knee	E. Faecalis	No	–
M	58	Knee	S. Aureus	No	–
M	73	Knee	S. Aureus	Gout	–
F	50	Shoulder	Grp. A streptococcus	RA	–
F	66	Knee	S. Aureus	No	–
F	80	Knee	S. Aureus	RA	–
M	73	Elbow	E. coli	RA	–

Conclusions: This study demonstrates that IA procedures can be performed with little risk of SA. The risk factors identified i.e. elderly patients with inflammatory joint diseases are consistent with those described in the literature [1].
We consider joint puncture technique and patient information for being essential when doing IA procedures. However, if SA occurs it is potentially fatal and therefore GC injection should be preserved for doctors with experience in joint diseases.
References:
[1] RA Andreasen et al. Prognostic factors associated with mortality in patients with septic arthritis: a descriptive study. Scand J Rheumatoly 2016, 1–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1333

SAT0566 ELECTRONEUROGRAPHIC FINDINGS IN PATIENTS WITH SUBACUTE/CHRONIC ARTICULAR SYMPTOMS OF CHIKUNGUNYA FEVER AND NEUROPATHIC COMPLAINTS – PRELIMINARY RESULTS

L.F. da Rocha Jr[1,2], H.D. de Lima[1], R.M. Correia[1], M.R.D.A. Freitas[1], P.R.S. de Melo[1], A.G.L. de Mattos[1], A.F.R. de Oliveira[1], C.D.L. Marques[2], A.L.B.P. Duarte[2], O. Lins[1], A. Ranzolin[1,2]. *[1]Instituto de Medicina Integral Professor Fernando Figueira; [2]Hospital Das Clínicas of Pernambuco, Recife, Brazil*

Background: The mechanisms of nonarticular pain associated with Chikungunya virus (CHIKV) infection are still poorly understood. Many patients that progress to Subacute/Chronic phases have neuropathic pain (NP) besides the articular symptoms. The NP is associated with a less favorable outcome, with greater impact on quality of life and lower efficacy of treatment. The NP can reflect a dysfunction of the nervous system, rather than a neurological lesion induced by CHIKV, but the pathophysiology of the neural disfunction is not completely understood. There are no studies evaluating the electroneurographic findings in patients with CHIKV infection and neuropathic symptoms.
Objectives: To evaluate the results of electroneurography (ENoG) of patients with Chikungunya Fever (CF) and neuropathic symptoms.
Methods: Patients with diagnosis of CF (clinical and epidemiological) and symptoms of paresthesias underwent ENMG of upper and lower limbs. The electrodiagnostic evaluation consisted of nerve conduction study of median, ulnar, tibial, fibular, sural and plantar nerves. Clinical and epidemiological data were also recorded.
Results: The sample was composed by 18 patients (82.3% females) with mean age of 56 (±9.9) years. The mean duration of symptoms of CF at the time of the ENoG was 23.8 (±10.8) weeks and the average of tender and swollen joints (including ankle and foot) was 29.6 (±21.5) and 9 (±9.9), respectively. The mean score of visual analogic scale (VAS) for pain was 4.4 (±2.4) and for fatigue was 5.9 (±2.9), considering values between 0 and 10. No patient presented axial pain and the number of painful joints was higher in upper (19.4±13.9) compared to lower limbs (10.2±8.4). Only 3 patients reported unspecific paresthesias prior to the onset of arbovirosis and worsening after CF. However, these 3 patients had normal ENoG. Six patients had diabetes. Mononeuropathy was the most frequent result occurring in 12 subjects (67%). Bilateral mononeuropathy of median nerve (at carpal tunnel) was found in 11 patients and one subject had median neuropathy just on the left hand. Other mononeuropathies were also present: bilateral tibial nerve in 4, bilateral plantar nerve in 2 and bilateral fibular nerve in 1 patient. Distal axonal polyneuropathy was present in 8 cases (6 sensory and 2 sensorimotor); 5 of these were diabetic. The ENoG was normal in 4 cases. Ten patients were in use of prednisone (mean dose 11.4mg/d) and just 6 were using antineurophatic agents.
Conclusions: Our preliminary results indicate that the ENoG is altered in most patients with chronic articular manifestations of CF and associated paresthesias. Mononeuropathy is the most commom finding, even in the chronic phase of the disease when the nonarticular edema is not common. Further clinical studies with a larger number of patients and follow-up tests will be needed to confirm our data.
References:
[1] Andrade DC, Jean S, Clavelou P et al. Chronic pain associated with the

Chikungunya Fever: long lasting burden of an acute illness. BMC Infectious Diseases 2010 10:31.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5554

SAT0567 IMPACT OF CHIKUNGUNYA FEVER ON FUNCTIONAL STATUS AND QUALITY OF LIFE – A PROSPECTIVE COHORT STUDY OF BRAZILIAN PATIENTS

L.F. da Rocha Jr[1,2], M.R.D.A. Freitas[1], A.G.L. de Mattos[1], H.D. de Lima[1], R.M. Correia[1], F.G.T. Vieira[1], A.L.B.P. Duarte[2], C.D.L. Marques[2], W.L.M. de Oliveira[1], P.R.S. de Melo[1], A. Ranzolin[1,2]. *[1]Instituto de Medicina Integral Professor Fernando Figueira; [2]Hospital Das Clínicas of Pernambuco, Recife, Brazil*

Background: An epidemic of Chikungunya Fever (CF) spread throughout South America in 2014. The acute manifestation of CF typically consists of febrile arthritis. The burden of the chronic articular manifestations remains a public health issue affecting activities of daily life. There is a very important impact on quality of life in patients affected by CF, even at chronic phase. The long-term functional status may also be affected by CF.
Objectives: To evaluate longitudinally the disability, Health Related Quality of Life (HRQOL) and functional status of patients with CF and analyze the clinical and epidemiological factors associated with different outcomes.
Methods: Patients with clinical and demographic diagnosis of CF and persistent articular symptoms were evaluated in a cohort study between May 2016 and December 2016. HRQOL was rated by Short-Form 12 (SF-12) and the functional status was checked through Health Assessment Questionnaire (HAQ) and the Global Functional Status (GFS). Data were divided per weeks after disease onset and were analysed (Spearmans's correlation coefficient and Mann-Whitney test).
Results: Sixty-five patients (58 females), mean age of 51.3 (±13.3) were assessed. As expected, a significant correlation between pain related scores and Physical Health Composite Scale Score (PCS), HAQ and GFS was found ($p<0.05$)). Edema and morning stiffness correlated with PCS, HAQ and GFS status from 4 to 20 weeks after disease onset ($p<0.05$). There was improvement in scores of all instruments used from 4–8 weeks of disease to 12–16 weeks of disease (table 1). The worst indices of PCS, Mental Health Composite Scale Score (MCS) and GFS were scored in the first month, mean scores of 30.07±5.77, 38.13±8.54 and 3.15±1.07 respectively. Higher HAQ values were demonstrated between 4 and 8 weeks after disease onset (mean score 1.87±0.82).

HRQOL and Functional Status in patients with CF

	4–8 weeks of disease (mean score)	12–16 weeks of disease (mean score)	P value
PCS	30.12±8.21	35.86±11.11	0.0487
MCS	40.95±12.23	47.02±12.09	0.0326
HAQ	1.87±0.82	1.36±0.86	0.0228
Global Functional Status	3.03±0.98	2.53±0.95	0.0438

Conclusions: We demonstrated the impact of CF on HRQOL and Functional Status of patients. The SF-12 Health Survey, HAQ and GFS are influenced mostly by patients pain and worsening of this status are more prominent in the first 8 weeks of disease. Further clinical studies of the impact of CF on quality of life and functional studies are needed
References:
[1] Soumahoro MK, Gérardin P, Boëlle PY et al. Impact of Chikungunya virus infection on health status and quality of life: a retrospective cohort study. PLoS One. 2009 Nov 11;4(11):e7800.
[2] Rahim AA, Thekkekara RJ, Bina T et al. Disability with Persistent Pain Following an Epidemic of Chikungunya in Rural South India. J Rheumatol. 2016 Feb;43(2):440–4.
[3] Couturier E, Guillemin F, Mura M et al. Impaired quality of life after chikungunya virus infection: a 2-year follow-up study. Rheumatology (Oxford). 2012 Jul;51(7):1315–22.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5604

SAT0568 RHEUMATOLOGICAL MANIFESTATIONS IN A SERIES OF PATIENTS WITH CHIKUNGUNYA FEVER

A.M. Sapag Duran[1], A.M. Beron[2], S. Sapag Duran[2], C. Coral Cristado[1], G. Medina[2], G. Nasswetter[2], D. Dubinsky[2]. *[1]Rheumatology, Hospital Universitario Japones, Santa Cruz, Bolivia, Plurinational State Of; [2]Rheumatology, Clinical Hospital "Jose de San Martin", University of Buenos Aires., CABA, Argentina*

Background: Chikungunya fever is characterised by a high probability of persistent rheumatological manifestations, producing a negative impact in the work, social and economic fields.
Objectives: To determine the frequency and type of rheumatologic involvement in the subacute and chronic phase of Chikungunya fever.
Methods: Descriptive, cross-sectional study. We included patients>16 years old with Chikungunya infection (real time PCR, IgM or IgG for Chikungunya) who consulted consecutively for rheumatic symptoms/signs from March 2015 to March 2016. According to the time of evolution, the disease was divided in 2 Phases: acute ($\leq$10 days of duration) and subacute/chronic ($\geq$11 days). According to clinical presentation, patients were classified in two groups: 1) non-autoimmune rheumatologic compromise (NARC) and 2) autoimmune rheumatologic compromise (ARC). Current ACR/EULAR criteria for classification of autoimmune diseases were used.
Results: Two hundred and two patients were evaluated, 80 were excluded due to negative serology for Chikungunya. 122 were included: 107 (88%) female, mean age 52.52±13.19 years, and time of evolution of 116.66±91.61 days.
Acute phase. 122 patients: fever 85 (69.67%), rash and pruritus 54 (44.26%), tenosynovitis 23 (18.8%), polyarthralgias 100 (82%) and arthritis 56 (45.90%).
Chronic phase. 122 patients: 71 (58%) patients had a chronic persistent rheumatologic symptoms and 51 (42%) presented remission of symptoms but all of them presented subsequent recurrence in an 91±40 days. NARC in 33 patients (27%) and ARC in 89 (73%), with no significant differences in age and time of evolution was observed.
NARC: 14 (42.4%) exacerbation of previous osteoarthritis pain, 9 (27.3%) developed fibromyalgia and 10 (30.3%) had localized soft tissue pain.
ARC: 13 (14.6%) with a history of RA, SLE, psoriasis or DM reactivated the underlying disease and 76 (85.4%) developed ARC: Undifferentiated polyarthritis with negative antibodies 61 (80%), RA with positive antibodies 5 (6.5%), scleroderma 2 (2.6%), cutaneous vasculitis 2 (2.6%), polymyalgia rheumatica 1 (1.3%), Sjogren's Syndrome 2 (2.6%), Dermatomyositis 1, Erythema nodosum 1 (1.3%) and vitiligo 1 (1.3%).
Antibodies were requested according to clinical suspicion: FAN $\geq$320 in 5 patients, RF in 6, ACPA in 4 and anti RO in 1. Thyroid dysfunction was observed in 7 patients who had a previous normal thyroid profile.

	Acute Fase n 122 (%)	Chronic Fase n 122 (%)	p
Fever	85 (69,7)	0	0,01
Rash and pruritus	54 (44,2)	0	0,01
Tenosynovitis	23 (18,8)	41 (33,61)	NS
Polyarthralgias	100 (82)	83 (68,03)	NS
Arthritis	56 (45.9)	81 (66,39)	0,0005

Conclusions: The frequency of rheumatological manifestations post Chikungunya fever in our sample was high, and can trigger ARC. Patients presenting new immunological manifestations in an endemic area for Chikungunya fever should have a serologic test performed. This series of patients must be evaluated with long-term studies to define their evolution, under the possibility of developing definite autoimmune disease or remission.
References:
[1] *Chikungunya Pathology and Cytokines. Chow et al. JID 2011.*
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2755

SAT0569 OUTCOME OF PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES ADMITTED IN INTENSIVE CARE UNIT: A PROGNOSTIC STUDY OF 98 PATIENTS

A. Malézieux-Picard[1], H. Hivernat[2], N. Martis[1], J.-G. Fuzibet[1], G. Bernardin[2], V. Queyrel[1]. *[1]Internal medecine departement; [2]Intensive care unit, Centre Hospitalier Universitaire de Nice, Nice, France*

Background: Systemic rheumatic diseases (SRD) are a rare and heterogeneous group of diseases, associated with a high mortality rate due to the natural evolution of the disease and/or consequences of their specific treatments (infections, toxicity).
Objectives: To describe the clinical features, outcomes and prognostic factors for patients with SRD admitted to the intensive care unit (ICU).
Methods: Single-center retrospective observational cohort study of 98 patients with SRD over an 11-year period in an ICU of a French teaching hospital.
Results: Ninety-eight patients (57% women; median age, 57 years [19–81years]) accounted for 108 admissions. Connective tissue disease (primarily systemic lupus erythematosus) and systemic vasculitides (mainly ANCA-associated vasculitides) represented respectively 55% and 30% of SRD. For nineteen patients, diagnosis of SRD was made at admission. Reasons for admission were: SRD exacerbations (43%), isolated infections (34%), SRD exacerbations associated with infections (12%) or other (11%). Respiratory failure was the most common organ dysfunction. Mechanical ventilation was necessary for 43 patients (44%), vasoactive drugs for 47 (48%) and extra-renal replacement therapy for 38 (39%). The ICU mortality rate was 30% and 37% one year after admission. Infection was the main cause of death (69%). The factors significantly associated with mortality in the ICU were (multivariate analysis): diabetes, cardiovascular diseases and immunosuppressive treatments on admission. At 1 year of follow-up, additional risk factors were: number of organ dysfunction at ICU admission and mechanical ventilation. It is to be noted that at 1 year of follow-up, diabetes was not anymore a prognostic factor.
Conclusions: Patients with SRD admitted to the ICU have a severe prognosis. Causes of mortality are mainly infections. Our study points out the importance of vaccination and developing new therapeutic strategies. Diagnosis of SRD in the ICU is not rare and should be systematically considered on admission. Prognostic factors of mortality in the ICU were patient comorbidities and immunosuppressive

therapy at admission. In addition, mechanical ventilation and multiple organ failure were risk factors for mortality at 1 year.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3692

SAT0570 AN IGNORED DISEASE IN ADULTS: ACUTE RHEUMATIC FEVER

B. Bitik[1], O. Kucuksahin[2], N. Karahan Yesil[1], H. Yesil[2], S. Erten[2].
[1]Rheumatology, Ankara Research and Education Hospital; [2]Rheumatology, Yildirim Beyazit University, Ankara, Turkey

Background: Acute rheumatic fever (ARF) is a delayed, inflammatory sequela of pharyngitis secondary to Group A Streptococcus infection. ARF remains one of the most important causes of cardiovascular morbidity and mortality in developing countries. Although it is mainly known as a childhood disease, it is also encountered in adult clinics in developing countries.
Objectives: To investigate the clinical and laboratory characteristics of patients who were diagnosed with ARF in two rheumatology outpatient clinics from June 2015 to January 2017.
Methods: The data of 20 patients (12 female; median age 29.5 (21–40) years) were evaluated. The diagnosis of ARF was based on the 2015 Jones criteria. The data collected included patient age, gender, arthralgia, arthritis, erythema marginatum (EM), subcutaneous nodules (SN), ECG/ Doppler transthoracic echocardiography findings, and other rare findings. The erythrocyte sedimentation rate (ESR), antistreptolysin O (ASO) and CRP levels of the patients and the drugs initiated were also recorded. Anti-streptolysin O (ASO) test or throat culture were used for the evidence of preceding Streptococcus infection. Patients with post-streptococcal reactive arthritis were differentiated and excluded by clinically. Patients with positive rheumatoid factor or ACPA were also excluded. Joint fluid examination was done to exclude septic arthritis in patients with monoarthritis.
Results: All patients were referred to rheumatology for arthralgia or arthritis. Patients were taking some sort of nonsteroidal antiinflammatory (NSAI) drugs before the referral. The median follow-up time was 9 months (0–18). Sixteen out of 20 patients had mono-, oligo- or poliarthritis (25%, 25% and 30%, respectively). Knees and ankles were the most common involved joints. The median duration of arthritis was 1 week (1–50 weeks). Six out 20 patients had subclinical carditis (30%). Nine out of 20 patients had a history of ARF attack previously. Three patients had chronic rheumatic mitral valve thickening without any severe insufficiency. EM and SN were observed in 15% and 60% of patients, respectively. Chorea was diagnosed in one patient. NSAI drugs were given to all patients with maximum dosages. High dose salicylate therapy were not given to patients due to intolerance or side effects. Nine patients were given prednisolone therapy (5–20 mg/d). The median duration of prednisolone therapy was 2 weeks (0–6 weeks). Sulfasalazine was given to two patients for the prolonged arthritis. All patients received secondary prophylaxis with penicillin.
Conclusions: ARF should be considered in the differential diagnosis of arthritis in young adults in developing countries. Arthritis of ARF in adults seems to be resistant to classical NSAI drugs. Our data show that steroid therapy can be given safely instead of salicylates in carditis or arthritis.
References:
[1] GewitzMH,BaltimoreRS,TaniLY,etal. AmericanHeart Association Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease of the Council on Cardiovascu- lar Disease in the Young. Revision of the Jones criteria for the diagnosis of the rheumatic fever in the era of Doppler echocardiography: a scientific statement of the American Heart Association. Circulation 2015; 131: 1806–18.
[2] He VY, Condon JR, Ralph AP, et al. Long-Term Outcomes From Acute Rheumatic Fever and Rheumatic Heart Disease: A Data-Linkage and Survival Analysis Approach. Circulation. 2016 Jul 19;134(3):222–32.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4944

SAT0571 PERFORMING SEPTIC ARTHRITIS DIAGNOSIS IN SCENARIOS WHERE SYNOVIAL FLUID IS NOT AVAILABLE: MULTIVARIATE LOGISTIC REGRESSION ANALYSIS

C.A. Guillen-Astete[1], G.A. Gabilondo-Alvarez[2]. *[1]Rheumatology Department; [2]Microbiology, Ramon y Cajal University Hospital, Madrid, Spain*

Background: In order to establish the diagnosis of septic arthritis (SA) it is necessary to demonstrate the presence of bacteria into the synovial fluid. However, clinics should act according to its suspicious when the differential diagnosis included this possibility even when the microbiologic study of the synovial fluid in unavailable by any cause (small joints, lack of training or logistic deficiencies).
Objectives: The purpose of our study is to determine the relative weight of other clinical or analytical variables that should be useful in these scenarios.
Methods: A retrospective multivariate logistic regression analysis about the registries of monoarthritis assessed in our unit between 2013 and 2016. There were included only registries with cases of synovial joints with all parameters of interest available. The binary response variable was the microbiological demonstration of septic arthritis (culture/Gram stain of synovial fluid or tissue). Explanatory variables were age (stratified in <30, 30–39, 40–49, 50–59, 60–69 and >70 years old), gender, temperature above of 37.9ºC, recount of neutrophils in peripheral blood sample, measure of procalcitonine (PCT), and measure of C reactive protein (CRP). Synovial fluid study, although was available in almost all cases was deliberately omitted for purpose of this study. The logistic regression analysis used the forward model strategy.
Results: There were included 449 registries. One hundred an sisteen of them were SA. The fixed model showed a Chi-square=226.64 with 5 degrees of freedom and a P<0.0001. Explanatory variable gender was excluded from the forward model strategy due to its lack of impact on the binary response variable. The Odds Ratio for PCR, PCT >1.3 ng/dL, age, neutrofils recount and body temperature were 1.0175, 8.1588, 0.5135, 1.0001 and 3.4147, respectively. The model showed a sensibility of 68.1%, specificity of 94.8%, PPV of 82.2% and NPV of 89.5%. The following table shows the full results of the logistic regression analysis: Standard error, Wald index, p value and R coefficients.

Variable	Coefficient	E. E.	Chi2-Wald	G.F.	p-value
PCR	0.0174	0.0024	52.0092	1	<0.0001
PCT	2.0991	0.3407	37.9640	1	<0.0001
Age	-0.6665	0.1326	25.2763	1	<0.0001
Neutrophils recount	0.0001	0.0001	14.9630	1	0.0001
T>37.9	1.2281	0.3286	13.9674	1	0.0002
Constant	-3.7227	-	-	-	N.A.

Conclusions: Previous studies have demonstrated the usefulness of PCT measure for the diagnosis of SA however all of them have been based on joints which synovial fluid is quite easy to obtain for further analysis. Present study allows laying the ground for creation of future diagnostic models based on five clinical variables that could be useful on scenarios where the assessment by joint puncture is not available.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4240

SAT0572 LEVELS OF SERUM PROCALCITONINE AS DIAGNOSIS DISCERNING TOOL BETWEEN GOUT AND SEPTIC ARTHRITIS

C.A. Guillen-Astete, M. Terán-Tinedo. *Rheumatology Department, Ramon y Cajal University Hospital, Madrid, Spain*

Background: In a previous study we demonstrated the potential usefulness of the procalcitonine serum measure in order to diagnose septic arthritis. This utility is quite important on the differential diagnosis of knee arthritis in patients with known gout or other inflammatory joint disease which can express as a monoarthritis.
Objectives: Due to that, this study aims to determine sensibility, specificity, positive predictor value and negative predictor value of procalcinonine sereum measure (PCT) in patients with knee arthritis for the diagnosis of septic arthritis.
Methods: We reviewed the registries of patients who consulted due to knee acute monoarthritis between 2013 and 2015 in which a PCT was obtained. Registries were grouped according to the final diagnosis (gouty arthritis only (group I) and septic arthritis with or without gout (group II). Based on a previous study, PCT value of 1.47ng/mL was considered the cut point. Validation tests were applied fixed to demographic and clinical specific scenarios.
Results: Registries of 121 patients with gout and 47 patients with septic arthritis (SA) were included. From the 47 patients with SA, 9 were previously diagnosed by gout. All diagnosed were based on guidelines and clinical recomendations for SA and gout (Coakley et al. Rheumatology, 2006 and Zhang et al. Ann Rheum Dis, 2006).
Using the cut point of 1.47 ng/mL, test validation results were as follows: sensibility of 87.2%, specificity of 92.5%, PPV of 82.0% and NPV of 94.9%. Excluding patients with less than 48 hours of onset, there were 44 registries of patients with SA and 83 with gout. In this scenario the results of the validation tests were as follows: Sensibility of 93.1%, specificity of 96.3%, PPV of 93.1% and NPV of 96.38%. Excluding all patients with body temperature above 37.5ºC there remained 11 with SA and 81 with gout. In this scenario the results of the validation tests were as follows: Sensibility of 72.7%, specificity of 95.1%, PPV of 66.6% and NPV of 96.2%.
Conclusions: This is the first study aimed to validate previous observations about the usefulness of PCT determination in patients with acute knee monoarthritis. Altough the global results in the validation test are a bit inferior that our original observations in a shorter pilot study in terms of sensibility, the NPV remains over 95% in scenarios where the differential diagnosis could be harder to establish such as recent onset flares or cases without an associated febrile syndrome.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4289

SAT0573 SOCIODEMOGRAPHIC, CLINICAL CHARACTERISTICS AND JOINT INVOLVEMENT OF A CHIKUNGUNYA EPIDEMIC IN COLOMBIA

J.C. Rueda[1], J.-I. Angarita[1], A.M. Santos[1], E.-L. Saldarriaga[1], I. Pelaez-Ballestas[2], E. Couto-Luvie[1], J. Londono[3]. *[1]Reumatología, Universidad de la Sabana, Chia, Colombia; [2]Reumatología, Hospital General de México, México, Mexico; [3]Reumatología, Universidad de la Sabana-Hospital Militar Central, Bogotá, Colombia*

Background: During 2014 and 2015 a chikungunya epidemic took place in Colombia concurrently with a COPCORD study across the country.
Objectives: To describe the clinical characteristics of CHIKV infection in 6 different cities in Colombia and determine the most frequently associated clinical picture with CHIKV.
Methods: World Health Organization criteria was used to identify CHIKV patients. A complete characterization and confirmation was established with CHIKV immunoglobulin G and IgM serology. Four possible scenarios were stablished: patients who met or not the criteria for probable case, and patients who met or not the criteria for confirmed case. *P* values were calculated between patients who met or not met the criteria. Sensibility and specificity was calculated for the WHO criteria.
Results: A total of 604 patients with MSK symptoms were evaluated in 6 different cities. The sociodemographic, clinical characteristics and joint involvement of the studied population is depicted in tables 1 and 2. Sensibility and specificity of the WHO criteria were 56.2% and 91.1% respectively (PPV: 83.3%, NPV: 74.4%).

Table 1. Sociodemographic and Clinical Characteristics of Patients with Positive COPCORD

	WHO Probable Case Criteria		WHO Confirmed Case Criteria	
	Met Criteria (n: 180)	Did Not Met Criteria (n: 424)	Met Criteria (n: 150)	Did Not Met Criteria (n: 454)
Age (mean; SD) in years	46,1±16,2	49,5±17,8	44,9±16,3	49,7±17,6*
Gender Female (%)	133 (73,9)	285 (67,2)	113 (75,3)	305 (67,2)
CHIKV IgG in SU (mean; SD)	36,5±22,9*	16,2±18,3	42,9±19,4*	15,4±18,0
CHIKV IgM in SU (mean; SD)	9,0±6,9*	6,6±5,1	9,8±7,2*	6,5±4,9
Fever (%)	180 (100)*	0 (0,0)	150 (100)*	30 (6,6)
Rash (%)	126 (70,0)*	28 (6,6)	109 (72,7)*	45 (9,9)

*$p<0,005$.

Table 2. Clinical Characteristics of Joint Involvement

	WHO Probable Case Criteria		WHO Confirmed Case Criteria	
	Met Criteria (n: 180)	Did Not Met Criteria (n: 424)	Met Criteria (n: 150)	Did Not Met Criteria (n: 454)
Symmetry (%)				
Arthralgia	177 (98,3)*	215 (50,7)	147 (98,0)*	245 (54,0)
Arthritis	85 (47,2)*	14 (3,3)	80 (53,3)*	19 (4,2)
Arthralgia (%)				
Elbows	58 (32,2)*	60 (14,2)	48 (32,0)*	70 (15,4)
Wrists	78 (43,3)*	67 (15,8)	65 (43,3)*	80 (17,6)
Hands	120 (66,7)*	126 (29,7)	103 (68,7)*	143 (31,5)
Knees	128 (71,1)*	200 (47,2)	107 (71,3)*	221 (48,7)
Ankles	103 (57,2)*	95 (22,5)	92 (61,3)*	106 (23,4)
Feet	71 (39,4)*	94 (22,2)	65 (43,3)*	100 (22,0)
Arthritis (%)				
Wrists	17 (9,4)*	4 (0,9)	16 (10,7)*	5 (1,1)
Hands	44 (24,4)*	6 (1,4)	42 (28,0)*	8 (1,8)
Knees	21 (11,7)*	4 (0,9)	20 (13,3)*	5 (1,1)
Ankles	43 (23,9)*	8 (1,9)	42 (28,0)*	9 (2,0)
Feet	40 (22,2)*	7 (1,7)	39 (26,0)*	8 (1,8)
Myalgia (%)	130 (72,2)*	35 (8,3)	106 (70,7)*	59 (13,0)
Fatigue (%)	165 (91,7)*	41 (9,7)	137 (91,3)*	69 (15,2)

*$p<0,005$.

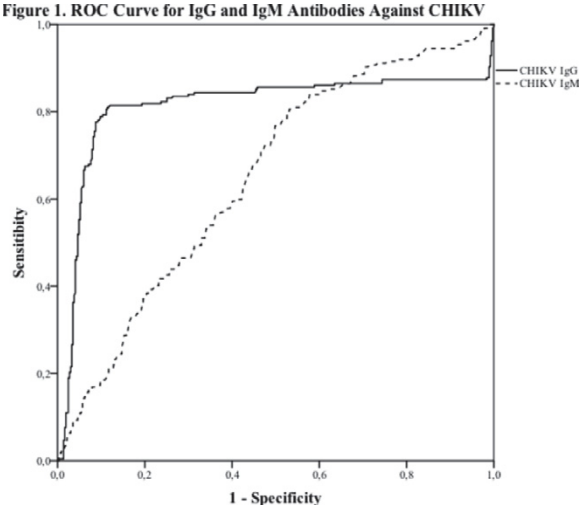
Conclusions: Our study shows a clear clinical picture of systemic symptoms, high titters of CHIKV immunoglobulins, and a defined joint involvement, which will help clinicians to identify and differentiate CHIKV infection from other viral infections and MSK diseases. Also, the sensibility of the WHO criteria applied to our cohort of patients demonstrates the need to improve clinical criteria without the use of laboratory tests.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1879

SAT0574 PERFORMANCE OF IMMUNOGLOBULIN M AND G (IGM AND IGG) ANTIBODIES AGAINST CHIKUNGUNYA VIRUS (CHIKV) BY ENZYME-LINKED IMMUNOSORBENT (ELISA) TECHNIQUE

J.C. Rueda[1], J.-I. Angarita[1], A.M. Santos[1], E.-L. Saldarriaga[1], I. Pelaez-Ballestas[2], P. López-Morales[1], J. Londono[3]. *[1]Reumatología, Universidad de la Sabana, Chia, Colombia; [2]Reumatología, Hospital General de México, México, Mexico; [3]Reumatología, Universidad de la Sabana-Hospital Militar Central, Bogotá, Colombia*

Background: CHIKV is suspected based on epidemiological and clinical criteria, however confirmation of the disease is only achieved by laboratory tests. Laboratory diagnosis is made by two approaches: the detection of viral RNA and identification of the specific immune response by serological methods. Serological tests are the most frequently used laboratory methods for the diagnosis of CHIKV. IgM is the first detected antibodies during 4 to 6 days after onset of symptoms followed by IgG. In Colombia, CHIKV's probable cases are not mandatory to be confirmed, so there is no standardization for laboratory confirmation tests
Objectives: To evaluate the performance of IgM and IgG antibodies against CHIKV in a cohort of patients with CHIKV
Methods: IgM and IgG antibodies against CHIKV were measured by ELISA (AbcamÒ ab177835 and ab177835 anti-chikungunya virus IgM and IgG human ELISA kit, Cambridge, UK) technique in 604 patients with CHIKV suspicion. A typical case of CHIKV with high sensitivity and specificity obtained from a previous study was used as gold standard for diagnosis of CHIKV. Since CHIKV epidemic of 2014–2015 was the first to be reported in our country (Colombia), no second measurements of IgG were needed to confirmed infection.
Results: Cut off point for IgG was 14,3 SU and for IgM was 11,2 SU. Mean values for IgG was 36,7 SU (±22,7) in patients with CHIKV and 8,6 SU (SD± 6,3) for IgM. Statistical significance was obtained for both IgG and IgM ($p<0,0001$) when comparing patients with and without CHIKV. Receiver operating characteristic (ROC) curves showed and area under the curve (AUC) of 0,81 for IgG and 0,65 for IgM (figure 1).

Figure 1. ROC Curve for IgG and IgM Antibodies Against CHIKV



Conclusions: Our study revealed a good performance of IgG and regular performance of IgM for the diagnosis of CHIKV in a cohort of CHIKV patients from Colombia's epidemic. Cut off points for both IgG and IgM were measured for future reference.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1886

SAT0575 ASSOCIATION OF HUMAN LEUKOCYTE A, B AND DR ANTIGENS IN PATIENTS WITH CHIKUNGUNYA VIRUS INFECTION

J.C. Rueda[1], J.-I. Angarita[1], A.M. Santos[1], E.-L. Saldarriaga[1], I. Pelaez-Ballestas[2], B. Zaldivar-Castaño[1], J. Londono[3]. *[1]Reumatología, Universidad de la Sabana, Chia, Colombia; [2]Reumatología, Hospital General de México, México, Mexico; [3]Reumatología, Universidad de la Sabana-Hospital Militar Central, Bogotá, Colombia*

Background: Host factors like innate and adaptive immune response play an important part in disease susceptibility. Also, the role of host genetics factors in the pathogenesis of viral diseases have been reported. Human leukocyte antigen (HLA) is responsible for initiating innate and adaptive immune responses. Studies have demonstrated HLA class II alleles association to susceptibility or resistance to chikungunya virus infection (CHIKV), however there is no evidence of association studies of HLA class I and II in the Latin-American CHIKV epidemic.
Objectives: To evaluate the association of human leukocyte A, B and DR antigens in a group of Colombian patients with CHIKV.
Methods: Characterization of HLA allele A, B, and DR of 62 patients with confirmed CHIKV was compared with 100 unrelated healthy subjects as a control group. The comparison between the different allele frequencies in the patient group and the control population was performed using chi^2, with Bonferroni correction. A p value <0.05 was considered to be significant. The magnitude of associations was assessed using odds ratio (OR) and confidence intervals (CI) of 95%. To establish the homogeneity of the studied groups, the Hardy-Weinberg disequilibrium was used.
Results: Of the 62 patients studied 46 were female (74,2%). The mean age was 45,0 (SD±16,8) years. Most of the patients were from Barranquilla (64,5%; n: 40). Mean CHIKV immunoglobulin G (IgG) was 38,6 SU (SD±21,7), while IgM was 13,3 SU (SD±7,6). Also C reactive protein levels were high (mean: 14,7

mg/L; SD±8,4). Association alleles of HLA-A, and DR are depicted in table 1. No association was found with HLA-B alleles.

Table 1. Associated Alleles with CHIKV

	Patients	Control	Odds Ratio	CI	*p*	C*p*
Resistance						
*A*28*	0	11	0,0	0,0-INF	0,002	0,040
*A*29*	6	24	0,2	0,0–0,6	0,002	0,048
Susceptibility						
*A*68*	14	2	9,9	2,1–45,1	0,000	0,008
*DRB1*01*	21	5	6,4	2,3–17,9	0,000	0,001
*DRB1*04*	26	11	3,6	1,6–8,0	0,000	0,010
*DRB1*13*	24	8	4,6	1,9–11,1	0,000	0,004

CHIKV: chikungunya virus infection; CI: confidence interval 95%; C*p*: Bonferroni corrected *p* value.

Conclusions: Our study demonstrated the alleles *A*28* and *A*29* to be associated with resistance to CHIKV, and alleles *A*68*, *DRB1*01*, *DRB1*04* and *DRB1*13* to be associated with susceptibility to CHIKV. No association was found in any HLA-B alleles.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1887

SAT0576 IMPROVED CLINICAL SCENARIO FOR CHIKUNGUNYA DIAGNOSIS

J.C. Rueda[1], J.-I. Angarita[1], A.M. Santos[1], E.-L. Saldarriaga[1], I. Pelaez-Ballestas[2], M.J. Soares-Santeugini[1], J. Londono[3]. *[1]Reumatología, Universidad de la Sabana, Chia, Colombia; [2]Reumatología, Hospital General de México, México, Mexico; [3]Reumatología, Universidad de la Sabana-Hospital Militar Central, Bogotá, Colombia*

Background: The World Health Organization (WHO) criteria for chikungunya virus infection (CHIKV) have a specificity of 91,1% with a low sensibility of 56,2%, which decreases the ability to detect patients with the infection. Because of this issue a group of rheumatology, epidemiology and bacteriology experts in diagnosing and treating CHIKV patients performed an agreement consensus on the clinical characteristics of CHIKV infection and proposed a set of clinical criteria. In order to test the performance of the new criteria and improve sensibility and specificity a clinical scenario was developed with the agreements from the expert panel and the clinical characteristics with higher odds ratios.

Objectives: To improve sensibility and specificity of a set of clinical criteria for the diagnosis CHIKV.

Methods: Odds ratios of the clinical features of patients with CHIKV infection were analysed. A clinical scenario was developed and sensitivity and specificity was calculated.

Results: 37 clinical characteristics were evaluated in a cohort of 604 patients with suspicion of CHIKV. From those, 29 exhibited statistical significance and only 10 had high odds ratios (table 1). A clinical scenario with the following joint involvement (symmetrical arthritis of shoulders or wrists or hands or knees or ankles or feet) or systemic symptoms (fever or rash or myalgia or fatigue) poised a sensitivity of 74,2% (PPV: 83,5%) and a specificity of 88,4% (NPV: 81,2%). The following clinical characteristics extracted from the agreements of the consensus group were added to the clinical picture: origin from an epidemic area and abrupt onset of symptoms.

Table 1. Clinical Characteristics with High Odds Ratios

	WHO Confirmed Case Criteria		Odds Ratio	CI (95%)	*p*
	Met Criteria (n: 150)	Did Not Met Criteria (n: 454)			
Symmetry (%)					
Arthritis	80 (53,3)	19 (4,2)	24,8	11,2–54,6	<0,0001
Arthritis (%)					
Wrists	16 (10,7)	5 (1,1)	22,2	3,6–204,1	<0,0001
Hands	42 (28,0)	8 (1,8)	36,7	8,8–152,6	<0,0001
Knees	20 (13,3)	5 (1,1)	10,0	2,8–33,8	<0,0001
Ankles	42 (28,0)	9 (2,0)	24,4	7,5–79,3	<0,0001
Feet	39 (26,0)	8 (1,8)	69,3	9,6–510,8	<0,0001
Myalgia (%)	106 (70,7)	59 (13,0)	13,0	8,1–20,7	<0,0001
Fatigue (%)	137 (91,3)	69 (15,2)	16,9	10,9–26,8	<0,0001
Fever (%)	150 (100)	30 (6,6)	13,1	8,4–20,5	<0,0001
Rash (%)	109 (72,7)	45 (9,9)	14,0	8,5–22,9	<0,0001

WHO: World Health Organization; CI: Confidence Interval.

Conclusions: Our study demonstrated that the proposed clinical scenario for suspicion of CHIKV improves diagnostic sensibility with a slight decrease in specificity, increasing the chance of diagnosis without the need for laboratory tests. We propose that a patient from an epidemic area (fulfilling epidemiological criteria according to the WHO) with an abrupt onset of a clinical picture of symmetrical arthritis of any of the following joints: hands, wrists, shoulders, knees or feet, or the presence of any of the following systemic symptoms: fever, rash, fatigue or myalgia, is more likely to have CHIKV infection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1883

SAT0577 MUSCULOSKELETAL MANIFESTATIONS OF TUBERCULOSIS: AN OBSERVATIONAL STUDY

N. Gupta[1], A. Bhatnagar[2]. *[1]Clinical Immunology & Rheumatology, CHRistian Medical College, VELLORE; [2]Pulmonology, Rajan Babu Tuberculosis Hospital, Delhi, India*

Background: Data of musculoskeletal manifestations of tuberculosis is limited to case reports, series or retrospective study. To our knowledge there is no prospective study which has addressed this issue. So, we conducted this study to create awareness among the doctors about musculoskeletal manifestations of tuberculosis.

Objectives: To study the musculoskeletal manifestations of tuberculosis.

Methods: It was a prospective observational study which was conducted at a referral Tuberculosis Hospital in North India in the month of September & October 2016. Patients from outpatient and inpatient department of pulmonology were recruited irrespective of the duration of anti tubercular therapy.

We included patients who had active tuberculosis as per World Health Organization (WHO) 2010 criteria. Patients with other chronic illnesses were excluded. A detailed history, examination and appropriate investigations (blood, urine, serological and radiological) of the 100 consecutive patients fulfilling the inclusion criteria was recorded

Results: Mean age of patients was 32.16±12.93 years. Male to female ratio was 43:57. Mean duration of disease was 6.85±8.83 months. Of the 100 patients, 60 (60%) had pulmonary tuberculosis. Pleural tuberculosis presenting as pleural effusion was seen in 17 (17%) patients. Abdominal tuberculosis was seen in 9 (9%), tuberculous lymphadenopathy in 8 (8%) and pott's spine in 4 (7%). Eye tuberculosis and tubercular breast lump was seen in 1 patient each.

83 (83%) patients had first episode of tuberculosis while the other 17 (17%) patients had second episode of tuberculosis. 74 (74%) patients were on category 1 anti tuberculosis treatment (ATT), while 23 (23%) were on category 2 ATT and 3 (3%) were on modified ATT. Mean duration of ATT was 1.79±1.34 months.

Fibromyalgia was classified in 21 (21%) patients, polyarthralgia's were seen in 9 (9%), pott's spine in 7 (7%), osteomyelitis in 4 (4%) and scleritis in 2 (2%) patients. Uveitis, tenosynovitis, erythema induratum, subcutaneous abscess and dactylitis was seen in 1 (1%) each. Rheumatological manifestations as septic arthritis, DILE, poncet's arthritis, tendinopathy, amyloidosis, gout, erythema nodosum and myositis were not seen in any patient.

In 21 patients who had fibromyalgia, 11 patients developed fibromyalgia with 2nd episode of tuberculosis amounting to 60.75% patients.

Conclusions: This is the first prospective study to look at the musculoskeletal manifestations of tuberculosis. Patients with active tuberculosis were found to have various rheumatological manifestations.

Acknowledgements: I acknowledge Dr Sushil Gupta, director of the Rajan Babu TB Hspital for allowing me to conduct this study

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1357

SAT0578 LEFLUNOMIDE INHIBITS THE APOPTOSIS OF HUMAN EMBRYONIC LUNG FIBROBLASTS INFECTED BY HUMAN CYTOMEGALOVIRUS

Q. Ren[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Background: The immunomodulatory drug leflunomide (LEF) is frequently used for treating human cytomegalovirus (HCMV), but its antiviral mechanism is still unclear.

Objectives: In this study,we therefore investigated the effects of the active LEF metabolite A771726 on the HCMV lifecycle in human embryonic lung fibroblasts. We clarified the mechanism of LEF antiviral infection, and provide a new way to treat immune dysfunction patients with HCMV infection.

Methods: The experiment was divided into four groups:the control group, the HCMV group, the ganciclovir + HCMV group as well as the LEF + HCMV group. MTT was usedfor assessmentof the cell inhibitory rate. Apoptosis was measured by staining with fluoresceinisothiocyanate Annexin V and propidium iodide. Statistical significance was determined by paired *t*-test using SPSS software.

Results: The results of the study showed that cell proliferation was significantly inhibited by HCMV at 24 hours and 48 hours. With increasing HCMV concentration, the value-added inhibition of the cells was significantly decreased compared with the control group, and was statistically significant ($P<0.01$). Ganciclovir can increase proliferation of cellsinfected with HCMV;compared with the control group it was statistically significant ($P<0.05$). Meanwhile,with LEF treatment cell proliferation was significantly improved at 24 hours and 48 hours, with statistical significance ($P<0.05$). The apoptosis rate of human embryonic lung fibroblasts infected with HCMV increased significantly at 24 hours, 48 hours and 72 hours,and as time goes on the apoptosis rate increases statistically significantly ($P<0.01$) compared with the control group The apoptosis rate of theHCMV infection group decreased by adding LEF,and was statistically significant ($P<0.05$).

Conclusions: In this studywe show that LEF is an exciting new drug for cytomegalovirus infection. LEF significantly inhibited HCMV infection-induced apoptosis and proliferation, playing an important role in the treatment of patients infected by HCMV. In this study we explored the potential usefulness of LEF for

cytomegalovirus infection and found it to be a cost-effective new treatment for cytomegalovirus infection that deserves further study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2128

SAT0579 LOW DOSE IL-2 RESTORES IMBALANCE BETWEEN TH17 AND REGULATORY T CELLS IN PATIENTS WITH CONNECTIVE DISEASE COMBINED EBV/CMV VIREMIA

Q. Wang, C. Wang. *Rheumatology, The second hospital of Shanxi medical university, TaiYuan, China*

Background: DMARDs are the most important medicine in treatment of autoimmune disease. However, excessive using DMARDs lead to decrease immune-function, which increasing opportunistic infection, such as EBV, CMV viremia. Recent study show the imbalance between T help cell 17 (Th17) and regulatory T cell (Treg cell) is a pivotal cause of autoimmune disease and correction of this imbalance to be a potential therapy. So whether low dose IL-2 restores the balance of Th17/Treg and improve immune function?
Objectives: To investigate the effect of low-dose IL-2 on Treg and effector lymphocyte subsets in patients with connective tissue disease (CTD) combined EBV or CMV viremia.
Methods: Clinical records of 70 CTD patients combined EBV or CMV viremia, hospitalized from May 2012 to January 2017 in the second Hospital of ShanXi medical university (Group infection), were analyzed. The group includes 21 patients who received rhIL-2 after infected CMV or EBV, and 12 continue receiving DMARDs. As control, we selected 70 health persons (Group health) whose age matched with group infection, 70 naïve CTD patients with no treatment (Group treatment-naïve), and 70 CTD without viremia patients having glucocorticoid and DMARDS medical history (Group Treatment-DMARDS). The two groups' underlying diseases are matched with the Group infection. The absolute numbers and proportions of peripheral lymphocytes (T cells, B cells, NK cells, the total number of the three cells, CD4+ T cells, CD8+ T cells), and CD4+ T cell subsets (Th1, Th2, Th17, Treg cells and Th1/Th2, Th17/Treg) were examined by flow cytometry.
Results: 1. The absolute count of Treg cells in the Group treatment-naïve was significantly low and Th17/Treg was notable increase compared with the Group health ($P<0.05$). The peripheral lymphocytes and Treg cells are notable low ($P<0.05$) and Th17/Treg was significantly increase ($P<0.05$) in the Group treatment-DMARDs compared with the Group treatment-naïve.
2. The peripheral lymphocytes, CD4+T cells subsets except Treg cells and Th1/Th2, Th17/Treg are significantly decrease in the Group infection compared with the Group treatment-DMARDs ($P<0.05$). While the absolute count of Treg cell was no different between the two groups.
3. After the course of rhIL-2 treatment, there were significantly increase of the peripheral lymphocytes and CD4+T cells subsets ($P<0.01$). Th17/Treg was significantly low after treatment. Compared with the patients who continue receiving DMARDs, all lymphocytes subsets had a rising trend in patients receiving rhIL-2 treatment.
Conclusions: The decrease of Treg cell number and imbalance of Th17/Treg may contribute to the pathogenesis of CTD. Excessive using glucocorticoid and DMARDs may augment this imbalance. On the other hand, these medicines decrease immune function, which leads to EBV and CMV viremia. Over the treatment of rhIL-2, immune function was improved and there was a more significant increase in the absolute count of Treg cells than Th17, and a consequently restore the balance of Th17/Treg.
References:
[1] Miyara M, Ito Y, Sakaguchi S. TREG-cell therapies for autoimmune rheumatic diseases. Nature reviews Rheumatology 2014;10:543–51.
[2] Klatzmann D, Abbas AK. The promise of low-dose interleukin-2 therapy for autoimmune and inflammatory diseases. Nature reviews Immunology 2015;15:283–94.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6247

SAT0580 OSTEOARTICULAR TUBERCULOSIS: A RETROSPECTIVE STUDY OF 119 CASES

R. Sonia, S. Boussaid, I. Abdelkafi, S. Hela, C. Ilhem, E. Mohamed. *Rheumatology, la Rabta, Tunis, Tunisia*

Background: Bone and joint involvement in tuberculosis is uncommon. Wile osteoarticular tuberculosis most commonly occurs in the vertebral column, less frequently affected sites are the hip, knee and sacroiliac joints. The multifocal form of skeletal tuberculosis is exceptional.
Objectives: To evaluate the clinical and diagnostic features of osteoarticular tuberculosis.
Methods: We reviewed the files of all patients admitted to our department from 2000 to 2015 with a diagnosis of osteoarticular tuberculosis.
Results: We identified 119 patients (52 men, 67 female), having osteoarticular tuberculosis lesions. Mean age was 43 years [21–82]. Diagnosis delay was 4 months. Pain, low-grade fever and loss of weight were the most common presenting symptoms. All the patients consulted because of pain. The spine was involved in 81 patients. Peripheral osteoarticular tuberculosis was diagnostic in 38 cases, mainly in the knee (21 cases). Five patients have a multifocal involvement of the osteoarticular tuberculosis. The tuberculin skin test was positive in 75% of the cases. The diagnosis of spondylodiscitis was provided by CT-scan and /or magnetic resonance imaging. Paraspinal and epidural abscesses has been reported in 11 cases. Bacteriological and /or pathological diagnosis was made in 72 cases (60.5%). The Quantiferon test was done in 7 cases and was positive. The antibiotic treatment led to recovery in all cases. Tree patients have presented neurological signs.
Conclusions: Our results were similar to those of the literature. Elderly population was especially at risk. The idiagnosis can be delayed espacially in negative investigations. Therefore it is recommendable to do a very large screening tests especially in endemic areas.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6911

SAT0581 NON-TUBERCULOUS MYCOBACTERIAL (NTM) INFECTION IN PATIENTS WITH RHEUMATIC DISEASES: POSSIBLE IMPORTANCE OF PULMONARY BARRIER FUNCTION RATHER THAN SYSTEMIC IMMUNE STATE IN THE DEVELOPMENT AND EXACERBATION OF NTM INFECTION

S. Takenaka[1], H. Kameda[1], T. Ogura[1], H. Oshima[2], K. Izumi[3], A. Hirata[1], H. Ito[1], Y. Fujisawa[1] on behalf of Department of Connective Tissue Diseases, National Tokyo Medical Center. *[1]Rheumatorogy, Toho University Ohashi Medical Center; [2]Rheumatorogy, Department of Connective Tissue Diseases, National Tokyo Medical Center; [3]Rheumatorogy, Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan*

Objectives: To identify the risk factors of the development and exacerbation of NTM infection in patients with rheumatic diseases.
Methods: Among 7013 patients with rheumatic diseases visiting Toho University Ohashi Medical Center and Tokyo Medical Center, 20 patients were enrolled in this study by fulfilling the diagnostic criteria of NTM infection by The Japanese Society for Tuberculosis and The Japanese Respiratory Society, and being followed-up for more than 1 year. The medical records of enrolled patients were retrospectively reviewed.
Results: Eleven patients with rheumatoid arthritis, 4 patients with vasculitis, 3 patients with Sjögren's syndrome and 1 patient with dermatomyositis and systemic lupus erythematosus for each were enrolled in this study. *Mycobacterium avium* complex (MAC) was detected in 13 patients, *M. chelonae* in 2 patients, *M. abscessus* and *M.kansasii* in 1 patient each, and undetermined mycobacterium in 3 patients. Notably, bronchiectasis was the predominant pulmonary complication observed in 13 patients, and interstitial lung disease was observed in 5 patients. Although 7 patients experienced the exacerbation of NTM during the observation period, immunological state on NTM diagnosis including peripheral blood leukocyte (median 5.8×10^3 versus $7.0\times10^3/\mu L$; p=0.72), lymphocyte (median 1.3×10^3 versus $1.1\times10^3/\mu L$; p=0.10) and the serum IgG level (median 1379 mg/dL versus 1207 mg/dL; p=0.20) were within normal ranges and comparable between ever and never exacerbated patients, respectively, as well as the treatments for rheumatic diseases such as glucocorticoids and biological agents.
Conclusions: NTM infection in patients with rheumatic diseases develops based on the dysfunction of pulmonary barrier rather than the systemic immunosuppression.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3357

SAT0582 CHAGAS' DISEASE IN PATIENTS WITH AUTOIMMUNE DISEASES RECEIVING IMMUNOSUPPRESSIVE THERAPY. ANALYSIS OF 48 CASES

S. Retamozo[1,2], M.J. Haye Salinas[2], A. Alvarellos[2], V. Saurit[2], F. Caeiro[2], J.P. Caeiro[3], V. Carballo[4], M. Medeot[4], O. Salomone[5], R. Albertini[6], F. Merschon[7], F. Bonisconti[8], A. Sanchez[8], T. Alvarellos[8]. *[1]INICSA, CONICET; [2]Rheumatology; [3]Infectious Diseases, Hospital Privado Universitario de Córdoba; [4]Infectious Diseases, Hospital Raúl A Ferreyra; [5]Cardiology, Hospital Privado Universitario de Córdoba; [6]Internal Medicine, Hospital Privado Universitario; [7]Cátedra de Física Biomédica, Secretaria de Ciencia y Tecnología (SECyT), Universidad Nacional de Córdoba; [8]Molecular Biology, Hospital Privado Universitario de Córdoba, Cordoba, Argentina*

Objectives: To analyze the main features at diagnosis and Chagas' Disease (CD) reactivation in patients with autoimmune diseases (AD) receiving immunosuppressive therapy (IT).
Methods: 13 patients with AD diagnosed with CD admitted to our Units between January to December 2016. In addition, we performed a systematic analysis of cases reported to date through a MEDLINE search. Inclusion criteria 1) adults with AD treat with iT (glucocorticoids [GC], disease-modifying anti rheumatic drugs [DMARDs] and biological drugs [BD]); 2) had confirmed or were positive for 2 serological test for CD. Reviews, experimental studies, duplicate publications, and abstracts were excluded.
Results: A total of 48 patients (13 from our Units and 35 from the literature search) fulfilled the inclusion criteria. There were 41 (85.4%) women, mean age of

43.8 years (range: 17–80). The main underlying disease was SLE in 22 (45.8%). Previous/current treatment at time CD diagnosis included GC >40mg/day in 27/48 (56.3%), DMARDs in 32/48 (66.7%) and 7 patients had previously received DB. CD was reactivated in 36 (75%) cases (mean 40.9 months [range: 0–252]) with the following patterns: high *T. cruzi* load by quantitative real-time polymerase chain reaction (qRTPCR) in 23 (63.8%) from which 20 (86.9%) had no clinical manifestation and 3 (13%) had panniculitis, the remaining 11 patients (30.5%) had positive XD with one of them had myositis, only one patient (2.7%) had fever. After a mean follow-up of 47 (range: 1–120) months, 4 patients with SLE died (8.3%), all had received GC>40mg/day, 3 had CD reactivation and all died due to SLE flare. No statistical differences were found with respect to CD diagnosis, use of GC, DMARDs, BD; in contrast, patients who had CD reactivation on therapy with GC >40mg/day showed higher cardiac involvement (83.3% vs 43.5%, p=0.03 OR 6.50 CI95% 1.15–36.57) where the time of immunosuppression in this group was lower in those who died median 0.53 (IQR 0.46–0.53) vs 3.00 (IQR 1.26–78.00) months, p=0.04. Patients with SLE and CD reactivation showed a higher risk of death (18.8% vs 0.0%, p=0.04, OR: 1.23, CI95% 0.97–1.57). Survival rate of the entire cohort was 91.5%. The poorest survival rates were observed in who had CD reactivation (log rank p=0.037).

Conclusions: Reactivation was presented mainly as high *T. cruzi* load by qRTPCR without clinical manifestation of CD. Use GC>40mg/day showed a higher risk of CD reactivation with cardiac involvement. Considering this data it's reasonable to screen serologic and molecular tests before to start treatment with immunosuppressive drugs.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4484

SATURDAY, 17 JUNE 2017

Back pain, mechanical musculoskeletal problems, local soft tissue disorders

SAT0583 LATERAL EPICONDYLITIS: WHAT IS NEW? DIAGNOSTIC, IMAGING AND TREATMENT. A SYSTEMATIC LITERATURE REVIEW

A. Pieren[1], M. Dougados[2], P. Le Goux[3], M. Lavielle[2], C. Roux[2], A. Moltó[2]. *[1]Rheumatology, Hospital Ia Paz, Madrid, Spain; [2]Rheumatology B., Hôpital Cochin; [3]Rheumatology, Hôpital Ambroise-Paré., Paris, France*

Background: Lateral epicondylitis or tennis elbow is an extremely frequent disease, secondary to intratendinous degeneration of the common carpi extensor tendon. However, diagnosis and therapeutic management are still a challenge for the rheumatologist.

Objectives: To determine the available evidence regarding the diagnostic, imaging and treatment of epicondylitis.

Methods: A systematic review literature was performed.using PUBMED. Only controlled trials, systematic literature reviews and meta-analysis were selected (Jan 1990 to May 2016). The MESH search words were " Tennis elbow "," Lateral elbow tendinopathy ", " Diagnostic imaging" and" Therapeutics ".

Results: 1314 potential articles were screened; 7 articles of clinical diagnosis, 21 of imaging and 18 of treatment were finally selected.

Diagnostic: No controlled trials were found about the diagnosis of the epicondylitis. The clinical tests employed in the retrieved clinical trials were based upon the experts' recommendation: lateral epicondyle palpation, resisted extension of the carpe and resisted extension of the 3rd and 4th fingers.

Imaging: Among the 21 articles identified, 1 article concerning plain Xray, 1 about scintigraphy, 10 of US and 10 of MRI were selected. One clinical trial, found plain Xrays were not helpful for the initial diagnosis. Ultrasound was found to be a sensitive (64–100%) and specific (36–100%) tool for the diagnosis, in one meta-analysis. Ten studies, within a systematic review, showed MRI was reported to be as sensitive (90–100%) as the ultrasound, with a greater specificity (83–100%). In addition, MRI showed better reliability (0.41–0.53 vs 0.73–1.00). Also, the two techniques showed a good correlation between the observed lesions and symptoms, severity and involvement of other structures. On the contrary, no data was found to support the use of imaging tests for follow-up.

Treatment: Among the 18 articles, 9 articles (within 4 systematic review and 5 randomized clinical trials) about pharmacological treatment, 10 about the non-pharmacologic approach and 1 about surgery were selected. Corticoids injections were found to be effective in one meta-analysis at short-term and preferably for acute epicondylitis (Pain reduction at 1–3 weeks =1.18 (95% CI 0.27–2.09), 4–8 =1.30 (95% CI 0.55–2.04), 12–24 =-0.38 (95% CI -0.85–0.08). Similar results were found for NSAIDs. Five prospective randomized clinical trials, showed braces and carpal extension splints were reported to improve pain at rest and during exercice, in short term. Physical therapy was reported to be efficacious in pain and function too, in a systematic review. Therapies like rich platelet plasma injections, autologous serum and botulinim toxin showed weak evidence.

Conclusions: No high quality trials for epicondylitis management were found in this systematic review. The diagnostic was based upon clinical presentation and physical exam. Ultrasounds and MRI seem to play a role on imaging diagnosis but not in follow-up. Corticoids injections and NSAIDs are effective in short term. Other studies are needed to evaluate other therapeutic modalities.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2301

SAT0584 THE ROLE OF MRI INTERPRETATION IN PATIENTS WITH ROTATOR CUFF DISEASE

S. Albina[1], A.-M. Ramazan[2], E.V. Ionescu[3], M.G. Iliescu[3]. *[1]Rehabilition Clinic, Clinical Hospital of Rehabilitation Eforie Nord; [2]Rheumatology, Emergency County Clinical Hospital "Sf Apostol Andrei"; [3]Faculty of Medicine, Ovidius University, Constanta, Romania*

Background: Shoulder pain is a common musculoskeletal complaint, roughly equal in incidence to neck pain (1). The shoulder pain syndrome has a prevalence to 47% in general population (2) and an incidence to 87–100.000 persons per year, an increasing indicator in the latest years (3). The identified etiology of painful shoulder were: rotator cuff tendinopathies (85%), impingement syndrome (74%), acromioclavicular joint involvement (24%), adhesive capsulitis (15%) si radiated pain (7%) (4). MRI imaging of rotator cuff disease, features of impingement are the techniques of choice at most institutions (5,6).

For all physicians, the shoulder is a complex joint, with difficulty in clinical and MRI examination. The type of therapy (medical, physical or surgical) can be estabilished according with MRI conclusion, but sometimes this was a debate between physicians.

Objectives: To assess the concordance between two radiologists in interpretation of the same shoulder MRI in patients with rotator cuff disease.

Methods: Our prospective observational study included 51 patients (median age 57±9.9 years, 70.6% female) with nontraumatic shoulder pain. The assessment had included a clinical examination of the shoulder for inclusion criterias, lab tests for exclusion an inflammatory diseases and shoulder MRI with purpose to pathological diagnose of cuff rotator disease. Two experienced radiologists independently, blindly and retrospectively interpreted the MRI images. One of the radiologist had more MRI trainnings and do daily musculoskeletal MRI images. We have analized the each MRI changes, as rotator cuff tendinopathies (tendinitis, tendinosis, tears), bicipital tendinopathy and other changes (subacromial bursitis, impingement syndrome, retractile capsulitis). Statistical analysis was performed using SPSS-18 and a p-value <0.05 was considered for statistical significance.

Results: There was identified a statistically significant difference between readers. There was a poor to moderate concordance (Cohen's Kappa$<$0,40, p$<$0.05) between MRI interpretations for supraspinos tendinopathy, subacromial bursitis, capsulitis, but a good agreement between for subscapular tendinosis (accuracy=98%, Kappa=0,79, p=0.000) and perfect compatibility (accuracy=100%, Kappa=1, p=0,000) for terres minor tendinitis. The poorest concordance between readers was in impingement syndrome (compatibility=55%, kappa=0,11, p$>$0,05).

Conclusions: The MRI examination is significant in rotator cuff disease only when the radiologist is overtrained for shoulder, otherwise the technique is unuseful and doubtful in clinical practice.

References:

[1] McCarthy DJ, Koopman WJ, Arthritis and Allied Conditions, 12th Edition.
[2] Ole M Ekeberg et al, Clinical, socio-demographic and radiological predictors of short-term outcome in rotator cuff disease. BMC Musculoskeletal Disorders 2010, 11:239.
[3] White JJ et al, An epidemiological study of rotator cuff pathology using The Health Improvement Network database. Bone Joint J. 2014 Mar; 96-B(3):350–3.
[4] Oster AJ et al, Diagnosis and relation to general health of shoulder disorders presenting to primary care, Rheumatology 2005; 44: 800–805.
[5] Berquist TH, Musculoskeletal Companion, Second Ed, Lippincot, 2007.
[6] Roy J-S et al, BrJSportsMed 2015; 49:1316–1328.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2609

SAT0585 IS IT SAFE TO PERFORM JOINT PUNCTURES IN PATIENTS TREATED WITH DABIGATRAN?

C.A. Guillen-Astete, J.R. Quiñones-Torres. *Rheumatology Department, Ramon y Cajal University Hospital, Madrid, Spain*

Background: The introduction of new oral anticoagulants provides us with a new therapeutic intervention and secondary prevention opportunity in stroke patients previously not well controlled with acenocumarol due to not compliance or other issues.

As with other anticoagulants or even antiplatelet agents, the attending doctor may hesitate to perform a joint puncture in patients receiving such treatments.

Objectives: The purpose of this study is to describe the four-year cumulative experience of joint and peri-articular punctures in patients receiving Dabigatran, a new oral anticoagulant recently introduced in our country.

Methods: We performed a systematic review of the records of patients who underwent a knee joint aspiration or periarticular shoulder joint puncture for diagnostic or therapeutic purposes and who were under treatment with dabigatran between the years 2012 and 2016.

For this purpose we conducted an search for electronic records within that period, using the search terms: "infiltration", "arthrocentesis" or "joint puncture" and "shoulder" or "knee" and "dabigatran" or it's brand names.

Follow up visits in either primary care (HORUS® Application) or emergency settings (CAJAL® Application) were analyzed, regardless of the main complain at admission, and the data was collected from this records.

Results: Between 2012 and 2016, 68 joint knee punctures and 49 periarticular shoulder punctures were performed in dabigatran patients. Of the 117 procedures, 78 (66.6%) were performed by attending physicians in Traumatology, Rheumatology or Physical Medicine and Rehabilitation, and the rest by internal medicine residents.

Of the 68 knee arthrocentesis, in 48 (70.5%) of the cases synovial fluid collection and infiltration were performed, while in the rest only infiltration was needed.

Of the 49 shoulder punctures, in 12 (24.4%) a bursocentesis was performed while in the rest only an infiltration was done.

16 knee and 17 shoulder punctures (23.5% and 34.6%) were ultrasound assisted procedures.

Among the patients with knee puncture, 11 (16.1%) came back before 15 days due to procedure related symptoms. Of these, 9 did so because of persistence of the main symptom or persistent pain and 2 because of increased pain. These two patients were studied sonographically and one of them had a hemarthrosis that was treated conservatively.

In the group of patients with shoulder puncture, 7 (14.2%) came back before the first 15 days and in all of them the cause was persistence of the main symptom. None of the patients required admission at the hospital. None of the patients with ecography-assisted procedures came back before the first 15 days.

No patient consulted due to bleeding after the first fifteen days. (There were no hemarthrosis cases after the fists 15 days). The outcome of the procedure was not influenced by the person performing it (attending vs resident), however, all the echocardiographic procedures were performed by an attending.

Conclusions: Although it is a small population, this is to the best of our knowledge, the biggest published serie of dabigatran anticoagulated patients who underwent a large joint or periarticular puncture. We can conclude that this type of punctures are safe in patients with this characteristics. On the other hand, there is evidence that ecography-assisted procedures are more effective in this group of patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6640

SAT0586 RELATIONSHIP BETWEEN CORE STABILIZATION AND LOW BACK PAIN IN YOUNG PEOPLE

E. Mete[1], V. Akduman[1], I. Demirbuken[1], G. Ogren[2]. *[1]Physiotherapy and Rehabilitation; [2]Nutrition and Dietetic, Marmara University, maltepe, Turkey*

Background: Low Back Pain (LBP) is a very common health problem that affects people of all ages. It has been observed that the increase in lumbar stabilization is effective in reducing back pain risk. A combination of local and global stability system is used to describe to core stability which is a key factor for enhancing lumbar stabilization. Exercise training focused on these groups of muscles could contribute to pain alleviation and spinal functional improvement.

Objectives: The aim of the study was to define relationship between core stabilization and low back pain in young people who were suffering from low back pain.

Methods: 290 individuals (144 male, 146 female), between 18 and 25 years of age were included in this study. Disability arising from low back pain was identified by using the Oswestry disability index, consisting of 10 questions with 6 choices (0–5 points for each question). The higher score is associated with more low back pain. The period of core stabilization was determined using Plank test in which the body is stand flat from shoulder to heels on foot and forearm and Side Plank test in which sitting on the forearm and standing on one side of the body with the legs parallel and the feet perpendicular and the body is held flat from the shoulder to the heels. The duration of ability to maintain Plank test was measured by a chronometer. Spearman correlation test used for statistical analyzing.

Results: In this study, the average of Plank test duration was 76.9±44.2 (sec), while the mean of the Side Plank test duration was 43.9±28.2 (sec) and Oswestry disability index total score was 6.3±5.5. A weak negative correlation was found between the Plank test and the Oswestry disability index (p=0,03; r =-0,111). And negatively correlated between the Side Plank and the Oswestry disability index (p>0.05). On the other hand, there was a positively modarate correlation between the Plank test and the Side Plank test (p=0,00; r =0,656). There was a weak negative correlation between age and Oswestry disability index (p=0,014; r =- 0,151).

Conclusions: Results of the study indicated that increasing the duration of stabilization reduces the low back pain. For this reason, core muscles deserve a great deal of interest in order to reduce the problem of low back pain which is common among young population.

References:

[1] Kibler, W. Ben, Joel Press, and Aaron Sciascia. The role of core stability in athletic function. Sports medicine 36.3 (2006): 189–198.

[2] Zazulak, Bohdanna T., et al. The effects of core proprioception on knee injury: a prospective biomechanical-epidemiological study. The American journal of sports medicine (2007).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5083

SAT0587 SCHOOL BAGS WEIGHT ARE NOT ASSOCIATED WITH LOW BACK PAIN IN SCHOOLCHILDREN IN CAMEROON

F. Kemta Lekpa, M.S. Doualla, H. Namme Luma. *Service de Médecine Interne, Douala General Hospital, Douala, Cameroon*

Background: Data are mixed on the role of school bags in the occurrence of low back pain in pupils.

Objectives: Thus, we carried out this study with the aim to determine if the school bags were a factor associated with low back pain in Cameroonian schoolchildren.

Methods: We performed a cross-sectional study between December 2015 and April 2016 in 10 primary schools of the city of Douala, Cameroon. A questionnaire was submitted to the students of these different schools. Informed and signed consent of their parents were obtained. Sociodemographic and clinical data were collected, as well as the weight of each school bags. A p<0.05 was significant.

Results: We included 1075 pupils (543 boys, 532 girls). The mean age was 11±1 years (8–16 years). BMI was normal in 928 children (86.5%). The prevalence of low back pain was 12.3% (132 children: 81 girls and 51 boys). Sixteen children had already met a physician for low back pain.

The mean weight of the school bag was 4.9±1.9 kg, with 369 children (57.7%) with a school bags weight ≥15% of their body weight in private schools compared with 56 (12.9%) in public schools. We had 99 children with low back pain with a school bag weight ≥10% of their body weight (Table 1). We didn't find any relationship between low back pain and the weight of the school bag, regardless of gender, BMI, age of pain, type of school, distance from home to school, way of transportation, and age (p>0.05). However, the exception was found in girls aged from 8 to 10 years with a school bag weight >15% of their body weight (p=0.05). Furthermore, in univariate analysis, factors associated with low back pain were (p<0.05): age, history of low back pain in at least one parent, competitive sport, a bad seated position on school benches. In multivariate analysis, factors associated with low back pain were female, competitive sport, and low back pain in at least one parent (Table 2).

Table 1. Relationship between weight of school bag and body weight of pupils with low back pain (n=132)

Weight of the school bag in relation to the weight of the child	Number of pupils, n (%)	*p*
<5%	3 (5,5)	–
5–10%	30 (11,7)	0,09
10–15%	46 (13,6)	0,10
>15%	53 (12,5)	0,19

Table 2. Factors associated with low back pain in children

Variable	OR	95% CI	*p*
Age	0.93	0.81–1,06	*0.25*
Sex	1.73	1.19–2,52	*0.004*
Competitive sport	1.61	1.03–2.53	*0.038*
Low back pain in parents	1.88	1.23–2.89	*0.004*

Conclusions: The weight of the school bags was not associated with low back pain in Cameroonian schoolchildren (except for girls aged from 8 to 10). However, female, competitive sport and low back pain in at least one parent were associated to low back pain.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6693

SAT0588 HEALTHCARE WORKERS ARE NOT MORE AT RISK TO LOW BACK PAIN THAN OTHER OCCUPATIONS

F. Kemta Lekpa, M.S. Doualla, H.B. Ngahane Mbatchou, A.S. Mkoh, H. Namme Luma. *Service de Médecine Interne, Douala General Hospital, Douala, Cameroon*

Background: Low back pain is common among healthcare workers but is it more frequent than in other occupations?

Objectives: In order to answer this question, we carried out this study with the aim of determining if healthcare workers was more at risk for low back pain in the same institution than non-healthcare workers, administrative and technical workers.

Methods: We performed a survey on all permanent workers (n=584) of the Douala General Hospital in Cameroon from January to May 2016. Socio-demographic characteristics of workers (distinction with different occupations – healthcare workers, administrative workers, technical workers) and the main features of low back pain were collected. A p<0.05 was significant.

Results: Of the 584 questionnaires distributed, 474 responses were obtained (81.1%). We excluded 27 for incomplete data. 447 were retained for the final analysis: 296 healthcare workers, 79 administrative workers, and 72 technical workers. The mean age was 40±10 years [22–66 years] and 258 (57.7%) were female. Mean BMI was 27±4.3 kg/m^2 with 103 (23%) obese.

At the end of the study, 252 (56.4%) workers described low back pain, including 170 (57.4%) healthcare workers, 44 (55.7) administrative workers and 38 (52.7) technical workers. There was no significant difference between the different groups (p>0.05). Same for sex (p=0.9). The overall independent risk factors associated with low back pain were: seniority in their current position (OR 4.97, 95% CI 1.80–13.68, p=0.002), office chair quality (OR 3.06, 95% CI 1.29–7.26,

Table 1. Risk factors for low back pain according to occupational class

Risk factors	Healthcare workers OR (95% CI)	Administrative workers OR (95% CI)	Technical workers OR (95% CI)
Age (years)	1.00 (0.98–1.03)	1.10 (1.04–1.16)***	1.04 (1.01–1.09)
Sex ratio	1.15 (0.71–1.84)	1.99 (0.55–7.24)	0.84 (0.28–2.54)
Seniority in the firm	1.42 (0.76–2.64)	0.95 (0.24–3.83)	5 (1.4–17.83)**
Seniority in their current position	3.5 (1.2–10.6)*	1.04 (0.35- 3.12)	11.3 (1.1–112.1)*
Number of hours worked per week	0.76 (0.26–2.21)	10.07 (1.02–99.69)*	–
Office chair quality	3.3 (1.1–10.4)*	5.97 (1.16–30.63)*	10 (0.6–164.9)
Heavy weight	1.10 (0.62–1.97)	2.27 (0.52–9.84)	4.2 (1.3–13.3)**
Vibrations	1.23 (0.67–2.27)	10.30 (0.81–130.73)	3.6 (1.2–10.6)**
Job satisfaction	0.35 (0.14–0.89)*	0.74 (0.10–5.58)	0.66 (0.17–2.53)

*p<0.05; **p<0.01; ***p<0.001.

p=0.01), and job satisfaction (OR 1.55, 95% CI 105–2.54, p=0.048). The specific risk factors for each occupation are presented in Table 1.

Conclusions: In an institution like Douala General Hospital, where the administrative, technical and healthcare workers are subjected to the same professional stress in terms of quality of care and performance, we did not find any difference on prevalence among these 3 occupations.

Preventive measures must be performed for all staff but need to be tailored to each occupation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6750

SAT0589 THERAPEUTIC EDUCATION IN THE MANAGEMENT OF FEARS AND BELIEFS IN PATIENTS WITH CHRONIC LOW BACK PAIN

R. Maaoui[1], A. Khezami[1], I. Ksibi[1], I. Lajnef[1], H. Rahali[1], R. Dhahri[2], I. Gharsallah[2], L. Metoui[2], F. Lajili[2], S. Othmani[2]. *[1]Physical and Rehabilitation Medicine; [2]Internal Medicine, military hospital Tunis, tunis, Tunisia*

Background: The notions of apprehension-avoidance and beliefs are among the psychosocial factors associated with the occurrence, maintenance and strengthening of the chronic painful process.

Therapeutic education is increasingly described in the literature as a means to manage these factors in order to limit the transition to a chronic stage.

Objectives: The aim of this study is to examine the effect of therapeutic education on fears and beliefs in chronic low back pain.

Methods: A prospective, comparative study was conducted with two groups of 50 patients each one having chronic low back pain. Both groups had benefited from the same physical rehabilitation program. The second group concurrently attended therapeutic education sessions.

Fears and beliefs of patients and their kinesiophobia were evaluated with the FABQ: Fear-Avoidance beliefs questionnaire and the TSK: Tampa scale of kinesiophobia for the evaluation of kinesiophobia index.

Results: The initial evaluation of apprehension-avoidance showed a high FABQ score in two groups. Management that was limited to physical rehabilitation demonstrated no effect on the apprehension-avoidance indices evaluated by the FABQ scale. However, there was a clear improvement in apprehension and avoidance in the G2 and with a statically significant difference (P=0.03).

An initial and high kinesiophobic score (≥48) was noted in two groups. G1 patients showed no significant improvement in their TSK scores after the end of the program. G2 patients who benefited from a therapeutic education workshop improved their TSK scores significantly after the program completion compared to G2.

Conclusions: The integration of the patient into the therapeutic education workshops improved the behavior of apprehension and kinesiophobia. This further supports the usefulness of applying cognitive therapy to our patients when restructuring of preconceived ideas about movement and physical activities.

References:

[1] Nguyen C, Poiraudeau S, Revel M. Lombalgie chronique: facteurs de passage à la chronicité. Rev rhum.2009;76:537–42.

[2] Butron AK, Waddel G, Tilloston KM, Sumerton N. Information and advice to patients with back pain can have positive effects. A randomized controlled trial of a novel educational book in primary care. Spine. 1999;24:2481–91.

[3] Fritz JM, George SZ, Delitto A.The role of fear-avoidance beliefs in acute low back pain: relationships with current and future disability and work status.Pain. 2000;94:7–15

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4373

SAT0590 FEARS AND BELIEFS IN PATIENTS WITH CHRONIC LOW BACK PAIN AND SICK LEAVE: WHAT RELATIONSHIP?

R. Maaoui[1,1], A. Khezami[1], I. Ksibi[1], I. Lajnef[1], H. Rahali[1], R. Dhahri[2], I. Gharsallah[2], L. Metoui[2], B. Louzir[2], F. Lajili[2], S. Othmani[2]. *[1]Physical and Rehabilitation Medicine; [2]Internal Medicine, military hospital Tunis, tunis, Tunisia*

Background: The occupational impact of low back pain is generally assessed in terms of absenteeism and duration of sick leave. A non-return to work greater than eight days has been considered a poor prognosis factor. Several psychosocial factors have been identified as the original cause.

Objectives: Studying the impact of erroneous beliefs, avoidance behaviors, apprehension and fear of movement on sick leave in patients with chronic low back pain.

Methods: A prospective study was conducted in patients with chronic low back pain patients. The notion of apprehension-avoidance was evaluated by the Fear Avoidance Beliefs questionnaire (FABQ), fear of movement by the Tampa scale of kinesiophobia (TSK) and functional disability by the Functional Disability Scale Of low back pain: EIFFEL (French version of Roland Disability Questionnaire).

A study of the correlations between these different parameters and the duration of sick leave was carried out subsequently.

Results: Our study included 100 patients. The findings revealed a 95% absenteeism rate including 67% with a sick leave of more than one month. The FABQ, TSK and EIFFEIL scores were high.

The statistical study concluded that there was a positive and significant correlation between sick leave time, fears and erroneous beliefs (r =0.147, P=0.033). We also found a positive and significant correlation between the duration of sick leave and kinesiophobia. There were no statistically significant correlations between sick leave and functional disability.

Conclusions: The high scores of FABQ and TSK confirm the important role of false beliefs and fear of movement in the genesis of chronicity in chronic low back pain as reported in the literature. The positive correlations found in our study reinforce the theory of the deconditioning of these patients following their beliefs. Management of these factors would be an important contribution to limit sick leave times in chronic low back pain.

References:

[1] Williams RA, Pruitt SD, Doctor JN, Epping-Jordan JE, Wahlgren DR, Grant I et al.The contribution of job satisfaction to the transition from acute to chronic low back pain. Arch Phys Med Rehab.1998;79:366–74.

[2] Ratinaud MC,Chamoux A,Glace B,Coudeyre E. Job satisfaction evaluation in low back pain: a literature review and tools appraisal. Ann Phys Rehabil Med. 2013;56(6):465–81.

[3] Fayad F, Lefevre-Colau MM, Poiraudeau S,Fermanian J, Rannou F, Wlodyka Demaille S et al. Chronicité, récidive et reprise du travail dans la lombalgie: facteurs communs de pronostic. Ann Readap Med Phy.2004; 47:179–88.

[4] Gronblad M, Jarvinen E, Airaksinen O, Ruuskanen M, Hamalainen H, Kouri JP. Relationship of subjective disability with pain intensity, pain duration, pain location and work –related factors in non operated patients with chronic low back pain. Clin J Pain. 1996;12:194–200.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4385

SAT0591 LOCAL STEROID INJECTION VERSUS WRIST SPLINTING FOR CARPAL TUNNEL SYNDROME: A RANDOMIZED CLINICAL TRIAL

H. So[1], V. Chung[2], J. Cheng[3], M.L. Yip[4]. *[1]Medicine and Geriatric, Kwong Wah Hospital, Kowloon; [2]Faculty of Medicine, The Chinese University of Hong Kong, New Territories; [3]Department of Occupational Therapy, Kwong Wah Hospital; [4]Integrated Diagnostic and Medical Centre, Tung Wah Groups of Hospitals, Kowloon, Hong Kong*

Background: Carpal tunnel syndrome (CTS) can lead to significant symptoms and loss of hand function. It also has a great socio-economic impact. However, there is no consensus regarding its best treatment up to this moment. Local steroid injection and wrist splinting are among the most popular nonsurgical treatment options. Previous studies have confirmed their respective effectiveness. However, there is no high quality head to head comparative study regarding the two treatments in the literature.

Objectives: To compare the efficacy of local steroid injection and nocturnal wrist spiniting for CTS.

Methods: We conducted a prospective randomised parallel clinical trial comparing the efficacy of local steroid injection and nocturnal wrist splinting in patients with CTS. The well validated and disease specific Boston Carpal Tunnel Questionnaire (BCTQ) was employed and its score at 4 weeks after treatment was used as the primary outcome measure. Important secondary outcomes included the patient satisfaction, the change of an objective finger dexterity test 9-hole-peg test, and the side effects.

Results: Twenty-five patients in the local steroid group and 25 patients in the wrist splinting group completed the study procedures. The baseline patient and clinical characteristics of the two treatment groups were similar. At 4 weeks after treatment, there was significant improvement of the BTCQ scores in both the steroid group and splinting group. There was improvement of the 9-hole-peg test only in the steroid group but not in the splinting group. However, there was no statistically significant difference in the changes of BTCQ scores between the two groups after treatment. Patient satisfaction score was higher in the steroid group. Patient in the steroid group took less painkillers after treatment. Four patients developed side effects after splinting and 3 after local steroid injection, which was not statistically significant.

Conclusions: Although local steroid injection and nocturnal wrist splinting were equally effective in the treatment of patients with CTS, only the former improved objective hand function. Local steroid injection also resulted in better patient satisfaction and less painkiller use without causing more side effects.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1122

SAT0592 EFFECT OF INTERFERENTIAL CURRENT THERAPY IN PATIENTS WITH SUBACROMIAL IMPINGEMENT SYNDROME: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

T. Nazligul, P. Akpinar, I. Aktas, F. Unlu Ozkan, H. Cagliyan. *Department of Physical Medicine and Rehabilitation, Fatih Sultan Mehmet Education and Research Hospital, Istanbul, Turkey*

Background: Shoulder pain is one of the most common types of musculoskeletal pain in the adult population. Subacromial impingement syndrome (SIS) has been reported to be the most frequent etiologic factor for shoulder pain (1). A conservative approach comprising non-steroid anti-inflammatory drugs (NSAID), subacromial injections, exercise, and several physical therapy agents is recommended as the first step treatment for SIS (2). Although interferential current (IFC) is a common electrotherapeutic modality used to treat musculoskeletal pain, there isn't any randomized controlled trial investigating its clinical efficacy on SIS (3).
Objectives: To investigate the effectiveness of IFC treatment in patients with SIS.
Methods: In this double blind, placebo controlled study, patients with shoulder pain, who had been diagnosed SIS according to clinical evaluation and subacromial injection test were randomly assigned to the IFC or placebo groups. Exercise, cryotherapy, and NSAID were applied to the all groups. Daily 20 min per session, 5 days per week, for 2 weeks 10 sessions IFC with alternative method were applied to the IFC group while sham IFC therapy were applied to the placebo group with the same protocol. Visual analog scale (VAS), Constant Murley Scale (CMS) and Shoulder Disability Questionnaire (SDQ) were used for evaluation at baseline, post-treatment and 1 month post-treatment.
Results: A total of 60 patients were completed the study; 26 (43.3%) were male and mean age was 50.02±9.10 years. There was not a significant difference in demographic and clinical data of the patients between the IFC (n=30) and placebo (n=30) groups ($p>0.05$). Significant improvement in all parameters was observed on post-treatment and 1 month post-treatment evaluations compared to baseline evaluations in both groups ($p<0.01$). Comparison of the VAS, CMS and SDQ scores between the two groups did not show significant difference either pre-treatment or post-treatment ($p>0.05$).
Conclusions: This study showed that IFC treatment does not provide additional benefit to NSAID, cryotherapy and exercise program in the treatment of SIS. Further studies are needed to investigate the long-term effects of IFC therapy.
References:
[1] Van der Windt DA, Koes BW, de Jong BA, Bouter LM. Shoulder disorders in general practice: Incidence, patient characteristics, and management. Ann Rheum Dis 1995;54(12):959–64.
[2] Merino LP, Brians'o MCC, Alarc'on GB, et al. Evaluation of the effectiveness of three physiotherapeutic treatments for subacromial impingement syndrome: a randomised clinical trial, Physiotherapy. 2016 Mar;102(1):57–63.
[3] Fuentes JP, Armijo Olivo S, Magee DJ, Gross DP. Effectiveness of Interferential Current Therapy in the Management of Musculoskeletal Pain: A Systematic Review and Meta-Analysis Phys Ther. 2010 Sep;90(9):1219–38.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2773

SAT0593 GENDER-SPECIFIC ASSOCIATIONS BETWEEN FAT MASS AND MUSCULOSKELETAL PAIN IN COMMUNITY RESIDENTS: A 3-YEAR LONGITUDINAL STUDY

K.M. Son[1], N.H. Cho[2], S.H. Lim[2], H.A. Kim[3]. *[1]Department of rheumatology., Hallym University Dongtan Sacred Heart Hospital; [2]Ajou University school of Medicine; [3]Hallym University Sacred Heart Hospital, Gyeonggi-Do, Korea, Republic Of*

Background: Increase in fat mass is correlated with musculoskeletal pain
Objectives: In this study, we sought to delineate the prospective relationship between fat mass parameters and the musculoskeletal pain in Korean community residents.
Methods: In the Korean Health and Genome Study, 1,325 participants (mean age 60.2 years, 56.2% women) who completed pain questionnaires and underwent dual x-ray absorptiometry to calculate body composition had 3 year follow-up data on pain. Pain was categorized according to number of pain regions. After 3 years of follow-up, subjects were classified into the followings: 1) no pain both at baseline and at 3 years (no pain), 2) any pain (one, two or more, or widespread regions) at baseline and no pain at 3 years (transient pain), 3) no pain at baseline and any pain at 3 years (new pain) 4) any pain both at baseline and at 3 years (persistent pain). 1) and 2) were grouped as no/transient pain group (no pain) and 3) and 4) as new/persistent pain group (pain)
Results: Female gender and obesity were 2 significant factors associated with the persistence or development of pain. Total fat mass and fat:muscle mass ratio were significantly correlated with pain, and the odds ratios for pain were significantly increased in subjects in the highest quartile of fat muscle ratio after adjustment among female subjects only. Among normal weight subjects, those without metabolic syndrome were less likely to belong to the pain group, especially among women.
Conclusions: The association of fat mass and pain was only significant among females
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2247

SAT0594 THE EFFECT OF RADİAL EXTRACORPOREAL SHOCK WAVE THERAPY (RESWT) İN THE TREATMENT OF TRİGGER FİNGER

M. Dogru[1], S. Narin[1], M. Erduran[2]. *[1]Department of Physiotherapy and Rehabilitation, Institute of Healty Science; [2]Department of Orthopedics and Traumatology, Faculty of Medicine, Izmir, Turkey*

Background: Trigger finger is a stenotic tendovaginitis characterized by hand pain and dysfunction, commonly encountered and easily recognizable (1). RESWT is frequently used in the treatment of soft tissue pathologies such as lateral epicondylitis, plantar fasciitis and calcific rotator cuff tendinitis (2–3). However, there is no study examining whether RESWT is effective on the trigger finger or not.
Objectives: The aim of this study was to investigate the effect of Radial Extracorporeal Shock Wave Therapy (RESWT) in the Treatment of Trigger Finger.
Methods: This study was carried out on 16 patients (18 patient hand) who had been diagnosed with trigger finger that grade 1,2,3 according to quinnel classification. Patients were carried out as a single group. 16 patients (18 patient hand) with trigger fingers were applied to ten-sessions,twice a week of RESWT (2000 impulses, 2 bar, 10 Hz). Pain scores (Numeric Pain Rating Scale - NRS), general funtional capasities (The Disabilities of the Arm, Shoulder and Hand Score (Quick-DASH)), range of motion, grip strength (GS) and pinch strenght (PS) were assessed at every week for five weeks during treatment and 3 months after treatment.
Results: 13 female and 3 male patients over 18 years of age were evaluated. In the evaluations performed every week during 10 sessions of RESWT treatment and 3 months after treatment, decrease in pain levels and increase in general functional capacity, range of motion, grip strength and pinch strength were observed in the patients treated ($p<0.001$) (tablo 1).

Tablo 1: Comparison of range of motion of the thump finger and 2-5. Finger , comparison of pain, grip streght, pinch streght and general functional capacity

	1.week (IQR)	2.week (IQR)	3.week (IQR)	4.week (IQR)	5.week (IQR)	3.month (IQR)	p value
MCF joint flexion thump finger	45.00 (40.00/50.00)	48.00 (40.00/50.00)	49.00 (40.00/52.00)	50.00 (40.00/58.00)	50.00 (40.00/60.00)	50.00 (50.00/65.00)	0.004
IF joint flexion Thump finger	15.00 (00.00/35.00)	20.00 (00.00/42.00)	28.00 (00.00/45.00)	39.50 (00.00/50.00)	45.00 (00.00/60.00)	55.00 (00.00/60.00)	<0.001
MCF joint flexion 2-5 finger	80.00 (50.00/90.00)	80.00 (50.00/90.00)	82.50 (52.00/90.00)	82.50 (54.00/90.00)	82.50 (55.00/90.00)	90.00 (60.00/90.00)	<0.001
PIF joint flexion 2-5 finger	100.00 (40.00/110.00)	100.00 (50.00/113.00)	100.00 (55.00/115.00)	100.00 (65.00/118.00)	100.00 (70.00/120.00)	110.00 (90.00/120.00)	<0.001
DIF joint flexion 2-5 finger	50.00 (20.00/75.00)	53.50 (20.00/75.00)	60.00 (30.00/77.00)	61.50 (40.00/77.00)	67.50 (50.00/80.00)	70.00 (60.00/85.00)	<0.001
NRS	7.00 (.00/10.00)	6.00 (.00/7.00)	4.00 (.00/7.00)	3.00 (.00/7.00)	2.00 (.00/7.00)	.00 (.00/7.00)	<0.001
GS	16.00 (4.00/30.00)	17.00 (12.00/40.00)	16.00 (10.00/36.00)	18.00 (8.00/36.00)	19.00 (8.00/28.00)	18.00 (12.00/36.00)	=0.001
PS	3.00 (1.00/10.00)	3.50 (2.00/11.00)	3.00 (1.00/9.00)	4.00 (2.00/12.00)	4.00 (2.00/12.00)	4.00 (2.00/12.00)	<0.001
Quick-DASH	42.04 (.00/70.45)	39.76 (.00/70.45)	28.40 (.00/68.18)	18.18 (.00/70.45)	4.54 (.00/68.18)	.00 (.00/25.00)	<0.001

Friedman test, $p<0.001$, MCF: Metacarpofalangeal, İF : İnterfalangeal, PİF: Proksimalinterfalangeal, DİF: Distalinterfalangeal, IQR: Interquartile Range

Conclusions: According to our results; RESWT might be an effective method to decrease pain severity, improve general functional capacity, range of motion, grip strength and pinch strength in patients with trigger finger.
References:
[1] Canale ST. Beaty JH. Canale & Beaty: Campbell's Operative Orthopaedics, (CD-ROM) 11th Edition. 2008. Philadelphia, Pennsylvania.
[2] Ogden JA, Toth-Kischkat A, Schultheiss R. Principles of shock wave therapy. Clin Orthop Relat Res 2001; 387: 8–17.
[3] Okay B, Mustafa E. Ortopedi ve travmatolojideekstrakorporeal şok dalga tedavisi uygulamaları. C. Ü. Tıp Fakültesi Dergisi. 2002; 24(3):161–164.
Acknowledgements: The authors declare that they have no conflict of interest.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4776

SAT0595 EFFECTIVENESS OF SHORT WAVE DIATHERMY TREATMENT IN PATIENTS WITH SUBACROMIAL IMPINGEMENT SYNDROME AND VALUE OF NIGHT PAIN ON PATIENT SELECTION: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL

M. Yilmaz Kaysin[1], P. Akpinar[1], I. Aktas[1], F. Unlu Ozkan[1], D. Karamanlioglu[2], H. Harteviogl u[1], N. Vural[1]. *[1]Department of Physical Medicine and Rehabilitation, Istanbul Fatih Sultan Mehmet Training and Research Hospital; [2]Department of Physical Medicine and Rehabilitation, Sultanbeyli State Hospital, Istanbul, Turkey*

Background: Shoulder impingement syndrome (SIS) is a common causes of shoulder pain and the night pain is a frequent symptom of this condition (1,2). Short wave diathermy (SWD) is a deep diathermic agents used in the treatment of

musculoskeletal system disorders. Local inflammation could be the major cause of night pain, and using a deep diathermic modality might be contradictory.
Objectives: Investigation of the effectiveness of short wave diathermy SWD treatment in patient with SIS and to emphasize the significance of night pain (NP) status on treatment response.
Methods: In this double-blind, randomized placebo controlled trial, 57 patients aged between 35 to 65 years, diagnosed as SIS were classified into two groups as night pain positive NP(+) (n=28) and night pain negative NP(-) (n=29). Both groups were randomly assigned to SWD treatment NP(+) n=14, NP(-) n=14 and sham NP(+) n=15, NP (-) n=14 subgroups. Exercise, cold pack application and a non-steroidal anti-inflammatory drug treatment were applied to all groups. 27.12 MHz continuous SWD (daily 20 min per session, 5 days per week, for 2 weeks, 10 sessions) was applied to the treatment groups while sham SWD was applied to the sham groups with the same protocol. Rest, activity and night visual analog scale (VAS), Constant (Murley) Score (CS) and Shoulder Disability Questionnaire (SDQ) were used for evaluation of patients at 2 weeks before the treatment, 1 month and 2 months after the treatment.
Results: There were no statistical differences between the SWD treatment and sham groups in all outcome parameters except for the Constant pain scores in NP (+) group. In NP(-) group, SWD treatment improved the parameters of pain, strength, total scores of CS, and SDQ compared to sham group at 1 month. SWD treatment was superior to sham for all parameters except for the Constant daily living activity scores at 2 months.
Conclusions: In conclusion, addition of 27.12 MHz continuous SWD treatment to conventional therapies provides long term benefits when compared to sham SWD in terms of rest and activity VAS scores, Constant-Murley scores, and SDQ scores in SIS patients without night pain. However, there was no convincing evidence that SWD treatment is of additional benefit in SIS patients with NP. Therefore; night pain as a symptom should be regarded in the selection of treatment modalities in order to use the deep heaters effectively in the management of SIS.
References:
[1] Van der Windt DA, Koes BW, de Jong BA, Bouter LM (1995) Shoulder disorders in general practice: incidence, patient characteristics, and management. Ann Rheum Dis 54(12), 959–964.
[2] Minns Lowe CJ, Moser J, Barker K (2014) Living with a symptomatic rotator cuff tear "bad days, bad nights": a qualitative study. BMC Musculoskelet Disord 15:228.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1297

SAT0596 EFFICACY OF EPIDURAL STEROID INJECTION IN LUMBAR SPINAL STENOSIS IS NOT RELATED TO THE DEGREE OF SEVERITY BY MRI

E.S. Elsayad[1], M.A. Mortada[1], T. Abd El Samad Elhawala[2], E.S.A. Abd El Hady[3], A. Hijab[4]. *[1]Rheumatology & Rehabilitation; [2]Orthopaedic Surgery, Zagazig University, Zagazig; [3]Rheumatology & Rehabilitation, El Mataria Hospital, Cairo; [4]Anesthesia, Zagazig University, Zagazig, Egypt*

Background: Lumbar spinal stenosis (LSS) is a common degenerative disease. Treatment modalities for LSS vary and include medication, exercise, interventional techniques, and surgery. Epidural steroid injection has been used for the treatment of LSS with variable results. The relationship between severity of lumbar spinal stenosis and efficacy of lumbar epidural steroid injection is still undetermined.
Objectives: The aim of our study was to determine the relationship between the severity of LSS using MRI grading system and the response to lumbar epidural steroid injection.
Methods: Thirty patients with degenerative LSS were enrolled in this prospective study. All subjects underwent lumbar spine MRI (T2-weighted axial images). LSS was graded using MRI grading system (grade 1 = mild stenosis with separation of all cauda equine; grade 2 = moderate stenosis with some cauda equine aggregated; grade 3 = severe stenosis with none of the cauda equine separated). All fluoroscopy guided transforaminal epidural steroid injections (FG- TFESI) were performed in the procedure room. Outcome measures were obtained using the visual analogue scale (VAS) for both back and leg pain, Oswestry disability index (ODI), Roland 5-point pain scale, walking tolerance and patient's satisfaction scale at 2 and 8 weeks post-treatment.
Results: Thirty LSS patients treated with FG- TFESI, who were completely followed up, were included in this study, the injection rate was one injection per patient. The patients were followed at 2 weeks and 8 weeks. Fifty-six percent of patients at 2 weeks and 70%% at 8 weeks had a successful outcome, reporting at least a >50% reduction between pre-injection and post-injection visual analogue pain scores.Roland 5 point pain scale showed pain reduction in 50% of patients by (26%) at 2 weeks and in 70% of patients by50%pain reduction at 8 weeks. Oswestry low back pain disability questionnaire (ODI) scores showed statistically significant improvement from initial scores to 2 weeks and from to 8 weeks in 70% of patients. Walking tolerance showed improvement at 2 weeks in 50% of patients and at 8 weeks in 70% of patients. The outcome was statistically significant even in severe stenotic patients when comparing initial scores of moderate and severe stenosis at 2 weeks and 8 weeks scores in walking tolerance (P=0.006), Back VAS (P=0.717), Leg VAS (P=0.139), ODI (0.139), and Roland (P=0.001).
Conclusions: FG-LESI may reduce pain and improve walking tolerance in the short term for the treatment of patients with LSS for a period of 8 weeks. The outcome does not seem to correlate with the degree of lumbar spinal stenosis. Patients with severe LSS may have the same chance to get benefits from FG-LESI as patients with moderate LSS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2233

SAT0597 RELATIONSHIP BETWEEN LUMBAR DISC HERNIATION AND BENIGN JOINT HYPERMOBILITY SYNDROME

M.R. Albeer[1], F.K. Abd alrazaq[2], M.H. Alosami[3]. *[1]Radiology, College of Medine of Baghdad; [2]Medicine, Baghdad Teaching Hospital; [3]Medicine, College of Medicine of Baghdad, BAGHDAD, Iraq*

Background: Benign joint hypermobility syndrome (BJHS) can present with a wide variety of musculoskeletal disorders.Benign joint hypermobility syndrome (BJHS) is a hereditary disorder characterized by the presence of musculoskeletal symptoms in persons with generalized joint laxity in the absence of systemic rheumatologic disease (1–3). Lumbar disc herniation (LDH) is a common cause of low back pain. On the other hand, low back pain may be a presenting symptom in patients with BJHS.
Objectives: to evaluate relationship between Lumbar disc herniation and BJHS.
Methods: The study included 100 patients diagnosed with LDH depending on history, clinical examination and MRI findings and another 100 healthy control participants. All, patients and healthy controls were assessed for BJHS using the revised (Brighton 1998) criteria.
Results: the mean age was (35.4±8.9) year and (33.72±8.3) for patients and controls respectively, there were 43 males and 57 females in each group. The mean BMI was (27.6±4.8) kg/m^2 in patients and (28.3±4.6) in controls. No significant differences found between the groups regarding the age, sex and BMI in all comparisons (P.value>0.05). The mean Beighton score was significantly higher among patients in comparison to controls; itwas (2.3±1.62) versus (1.2±1.35) in controls group; on the other hand major and minor criteria were significantly more prevalent among patients rather than controls, in all comparisons (P.value<0.05). BJHS was more prevalent among patients rather than controls, 55% of the patients had BJHS compared to 21% of controls, the odds ratio was (4.6) and (P.value <0.05). BJHS was more prevalent among females compared to males, from the total number of all participants, BJHS was present in 76 participants, and of them 47 were females versus 29 males, (P.value <0.05).
It had been significantly found that subjects with BJHS in both groups (patients and controls) were relatively shorter than those without BJHS, P.value <0.05. The correlation analysis of BJHS with the MRI findings of LDH in patients group showed no significant differences among patients with and without BJHS, in all comparisons P.value >0.05.
Conclusions: BJHS is more prevalent among patients with LDH. There is no significant relationship between presence of BJHS in LDH patients and MRI findings.
References:
[1] Hakim AJ, Grahame R. Joint hypermobility. Best Pract Res Clin Rheumatol 2003; 17:989–1004.
[2] Simmondsa JV, Keer RJ. Hypermobility and the hypermobility syndrome. Man Ther 2007; 12:298–309.
[3] Beighton P, Grahame R, Bird H. Hypermobility of Joints. New York, Verlag; 1983.p.125–49.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1030

SAT0598 EVALUATION OF THE QUALITY OF SEXUAL LIFE DURING CHRONIC LOW BACK PAIN

I. Haddada[1], M. Brahem[1], H. Hachfi[1], S. Ben Hammouda[1], M. Maraoui[1], M. Jguirim[2], M. Younes[1]. *[1]Rheumatology, Taher Sfar Hospital Mahdia, mahdia; [2]Rheumatology, Fattouma Bourguiba Hospital Monastir, Monastir, Tunisia*

Background: Sexual life has an important role in preserving the good quality of life of patients and their partners. Chronic low back pain (CLBP) as well as other musculoskeletal diseases, can affect all life activities including sexual function.
Objectives: The aim of this study is to assess the impact of chronic low back pain on sexual life and to identify the associated factors.
Methods: It's a study of 144 patients suffering from chronic low back pain, during a period of nine months (from February to October 2016).We have specifically studied the relationship between chronic low back pain and sexual quality of life, using the Sexual Quotient (QS) (a validated questionnaire), which consists in 10 questions, rated each one from 0 to 10, to have a final score rated from 0 to 100.
Results: The average age of our patients was 53.87years [23–79 years], with a female predominance in 64% of cases. The mean visual analogue scale for pain was 4.72 [1–9].
The average duration of low back pain was 6.5 years. The average score of Quebec was 45.3 [5–92], concerning the mean Dallas score,the segmental results were as follows: 53.1% of impact on daily activities, 47.6% of impact on work/leisure ratio, 45% of impact on anxiety/depression ratio and 33.4% of impact on sociability.
In our study, 57.2% of cases were under analgesic treatment, 85.5% were under

non-steroidal anti-inflammatory drugs, 20% had at least one local corticosteroid infiltration, 34% had functional rehabilitation and 4, 1% had surgical treatment.
Regarding sexual dysfunction, 34.5% of our patients didn't have any sexual activity, 2.1% had a catastrophic sexual life (score <20), 9% had a disappointing sexual life (score between 20 and 40), 20% had an average sexual life (score between 40 and 60), 17.9% had a satisfying sexual life (score between 60 and 80), while only 13.1% had a very fulfilling sexual life (score between 80 and 100. we showed that the alteration of the sexual quotient in our patients is more marked when the age of the patients is more advanced. But we didn't found a significant correlation with the duration of the disease, the mean visual analogue scale for pain and the functional scores of Quebec and Dallas.
Conclusions: Our study suggests that sexuality is profoundly disrupted in chronic low back pain. The advanced age is proved to be correlated with the deterioration of the sexual life. So, sexuality must be taken into account in the management of patients with chronic low back pain.
References:
[1] Kellie S.H. Kwan, Lindy J. Roberts, Delphin M. Swalm.
[1] Sexual dysfunction and chronic pain: the role of psychological variables and impact on quality of life.
[2] European Journal of Pain 9 (2005) 643–652.
[2] Ambler Nicholas, Williams Amanda, Hill Patrick, Gunary Rachel, Cratchley Gina.
[3] Difficultés sexuelles des patients douloureux chroniques.
[4] Clinical Journal of Pain 17 (2001) pp 138–145.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5339

SAT0599 LOW BACK PAIN IN MEDICAL STUDENTS LINKED TO POOR SLEEP QUALITY: RESULTS FROM THE PAX-I STUDY

N.R. Ziade[1,2], F. Fayad[1], B. Badra[3]. [1]*Rheumatology, Hotel Dieu de France;* [2]*Rheumatology;* [3]*Medicine, St-Joseph University, Beirut, Lebanon*

Background: Low Back Pain (LBP) is a major public health problem and is classified by the Global Burden of Disease Study among the ten diseases most responsible for Disability-Adjusted Life Years worldwide. All ages may be affected, mostly young adults, with a prevalence going up to 50%. Medical students may be particularly vulnerable due to sedentary lifestyle and high stress levels.
Objectives: The primary objective is to evaluate the prevalence of LBP in Lebanese medical students. The secondary objective is to identify predictive factors associated with LBP and to identify prevalence and components of inflammatory back pain (IBP).
Methods: PAX-I is a cross-sectional study, completed at the St-Joseph University of Beirut from April to June 2016. All students from the first to the sixth year of medicine were invited to fill a questionnaire about their demographic data, lifestyle habits, Patient Health Questionnaire for Depression and Anxiety (PHQ4) and LBP characteristics, including components of IBP as per ASAS criteria. Student test and ANOVA were used for quantitative variables, chi-square test was used for qualitative variables and logistic regression was used for predictive factors for low back pain. Analysis were performed on IBM SPSS Statistics 23.
Results: Response rate was 51.3% (258/502). Mean age was 20.86 years (SD 1.92). 54.3% were female, 76.7% drank caffeine, 66.3% had a regular sports activity and 9.7% were smokers. 38% had the habit of walking while studying. All habits were similar across years of studying except for sports activities which decreased over the years (p 0.018). 80% were satisfied with their studies. Only 46% were satisfied with their quality of sleep. Mean PHQ4 score was 7.17 and increased with the years of studies (p 0.045).
55.8% of students reported a LBP event during the past year, with a mean number of 3.6 episodes per year. 91% of these students had LBP while studying, with high reported intensity (5.18/10), 62.5% reported LBP after exercise. 80% had episodes of less than one month and 7% of more than three months duration. 12% had IBP according to the ASAS criteria (Details of IBP in Figure 1). Predictive factors for LBP in univariate analysis were: smoking (p 0.040), alcohol consumption (p 0.005), caffeine consumption (p 0.041), television watching (p 0.042) –positive association-, and number of hours of sleep (p 0.011) and satisfaction with sleep quality–negative association- (p 0.017). Satisfaction with sleep quality remained the only significant association in multivariate analysis (p 0.014).

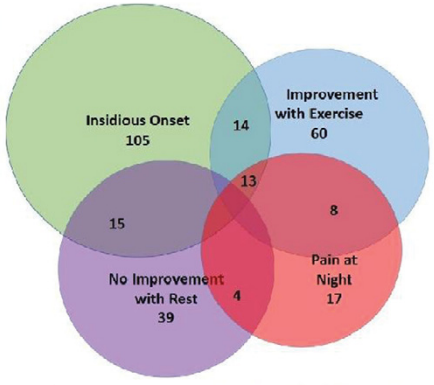


Figure 1. Components of Inflammatory Back Pain according to the ASAS criteria.

Conclusions: LBP is a frequent problem among medical students with high intensity, especially when studying, and a high recurrence rate. The main predictive factor was poor satisfaction with sleep quality. A significant percentage fulfills IBP criteria by auto-questionnaire and should benefit from further investigation.
References:
[1] Hoy D et al. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis 2014;968–74.
[2] Sieper J et al. New criteria for inflammatory back pain in patients with chronic back pain: a real patient exercise by experts from the Assessment of SpondyloArthritis International Society (ASAS). Ann Rheum Dis 2009;68:784–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3025

SAT0600 USEFULNESS OF VERTEBROPLASTY IN VERTEBRAL FRACTURES WITH PERSISTANT BACK PAIN. A REPORT OF 64 VERTEBRAL AUGMENTATION FROM A UNIVERSITY HOSPITAL

O. Fernandez-Berrizbeitia[1], M. González-de-Garay-Sanzo[2], A. López-Medina[2], M. García-Vivar[1], E. Ruíz-Lucea[1], I. Torre-Salaberri[1], A. Intxaurbe-Pellejero[1], J. Blanco-Madrigal[1], E. Guerrero-Basterretxea[1], I. Calvo-Zorrilla[1], O. Ibarguengoitia-Barrena[1], C. Pérez-Velásquez[1], L. Estopiñán-Fortea[1], C. Gómez-Arango[1], N. Rivera-García[1], M. Allande-López-Linares[1], A. Bilbao-González[3], E. Galíndez-Aguirregoikoa[1]. [1]*Rheumatology;* [2]*Radiodiagnostic;* [3]*Research, Basurto University Hospital, Bilbao, Spain*

Background: Management options for patients with persistent back pain after a vertebral fracture include vertebral augmentation, but its use is controversial.
Objectives: Our iam was to evaluate the fracture cause, efficacy and complications of consecutive vertebroplasties performed in our Hospital in a 12 years period.
Methods: Retrospective study of vertebroplasties performed at a University Hospital in the last 12 years (April 2004 to April 2016). The duration of follow-up was more than 12 months. Epidemiological variables, indications, time elapsed, efficacy and complications of the procedure were collected. The indication of vertebroplasties in fractures was pain refractory to usual symptomatic treatment in these pathologies: osteoporosis, trauma, leukemia/lymphoma, metastasis and hemangioma. Efficacy was assessed at 6 and 12 months with a simple verbal scale according to the pain response (improvement/non-improvement). Patients who died before 12 months period were excluded for the that parameter. A comparative study of the efficacy between a)cause of fracture, b)location, c)time elapsed, d)access route and e)complication was performed. For the descriptive analysis we used frequencies and percentages in the case of qualitative variables, and mean and standard deviation (SD) or median and interquartile range for quantitative variables. Chi-square test or Fisher's exact test was used in for qualitative variables, and Wilcoxon's non-parametric test for evolution time. Statistic analysis was performed with the SAS System for Windows V 9.2.
Results: 66 vertebroplasties were performed in 44 patients (75% female/25%

FRACTURE CAUSE, n(%)	
Osteoporosis	50 (78.13)
Trauma	6 (9.38)
Lymphoma/leukemia, n (%)	5 (7.81)
Metastasis	2 (3.13)
Hemangioma	1 (1.56)
FRACTURE LEVEL, n(%)	
Lumbar	25 (39.06)
Dorsal	37 (57.81)
Cervical	2 (3.13)
VERTEBROPLASTY ACCESS ROUT, n(%)	
Unipedicular	15 (23.44)
Bipedicular	44 (68.75)
Parapedicular	2 (3.13)
Spine-Jack	1 (1.56)
Anterior	2 (3.13)
CEMENT LEAKAGE, n(%)	
No	38 (59.38)
Mild	20 (31.25)
Moderate	5 (7.81)
Severe	1 (1.56)
REFRACTURE, n(%)	
No	56 (87.5)
Yes	8 (12.5)
EFFICACY AT 6 MONTHS/12 MONTHS, n(%)	
Improvement	38 (59.38)/43 (75.44)
Lack of improvement	26 (40.63)/14 (24.56)

male). Their mean age was 70.63±10.60 years (range, 46–96 years). The description of the causes of fracture, its level, the access route and the cement leaks are expressed in TABLE. The median time from fracture to vertebroplasty was 3 months [1–6]. 78% of the fractures were osteoporotic and had a better response to pain at 6 months than all other fractures ($p<0.05$), although at 12 months there were no differences ($p=0.42$). Only 12.5% had refracture. Pain control and vertebral refracture did not differ between neither the access rout nor the cement leakage and its magnitude. In the 12-month follow-up, 7 patients died (6 due to neoplasia, 1 due to sudden death) and no case was related to vertebroplasty.

Conclusions: In our experience vertebroplasty has been shown to be an effective technique for the control of refractory pain in vertebral fractures regardless of cause and time of evolution. Likewise, only 12.5% presented refracture in the following 12 months to the procedure. According to our study we can consider vertebroplasty as an effective and safe alternative in this type of patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3543

SAT0601 TREATMENT OF CARPAL TUNNEL SYNDROME (CTS) WITH ESWT: A SHAM CONTROLLED DOUBLE BLINDED RANDOMISED STUDY

Ö. Karataş[1], S. Catal[2], E.A. Gökmen[3], N. Samanci[4]. *[1]Physical Medicine and Rehabilitation, Korkuteli Public Hospital; [2]Physical Medicine and Rehabilitation, Akdeniz University School of Medicine; [3]Physical Medicine and Rehabilitation, Antalya Training and Research Hospita; [4]Physical Medicine and Rehabilitation, Akdeniz University School of Medicine, Antalya, Turkey*

Background: The carpal tunnel syndrome (CTS) is the most common neuropathy (1). The etiology isn't properly known, but CTS is produced by the chronic compression of median nerve while passing through carpal canal can be associated with this disease (2).

Objectives: The aim of this study was to investigate the efficiency of extracorporeal shockwave therapy (ESWT) in the treatment of CTS.

Methods: 49 hand with the diagnosis of CTS were included in the study. Patients were randomised in ESWT (n=29 hands) and sham (n=20 hands) groups. Patients were randomly allocated to receive 1 session per week for 3 weeks of either sham or active ESWT. All patients were prescribed with tendon and nerve gliding exercises and hand-wrist splint which used night. Patients were evaluated before the treatment, and at the end of the first week, first month and third month after the last ESWT treatment session with Boston Scale (symptom severity and functional capacity), Visual Analogue Scale (VAS) for pain and paresthesia assessment, for muscle strength hand gross grasp and electroneurophysiological parameters.

Results: A total of 38 patients completed the study with 29 wrists in active ESWT and 20 wrists in sham ESWT groups. Groups were similar in age, sex, duration of symptoms, hand gross grasp and electrodiagnostic parameters ($P>0.05$). In both groups, significant improvements were observed in VAS, Boston Scale and hand gross grasp after treatment. In both groups, there was no statistically significant improvement in electromyographic variables after treatment ($p>0.05$). However there was no significiant differrence between two groups in all of clinical and electrodiagnostic parameters.

Conclusions: Although ESWT was effective in symptoms in CTS but this efficacy isn't superior to placebo. Our results indicated that ESWT was effective in pain and clinical variables in CTS. Wider and high-quality studies are needed to further demonstrate the effectiveness of ESWT in treatment of CTS.

References:

[1] Ozturk K, Esenyel CZ, Sonmez M, et al: Comparison of carpal tunnel injection techniques: A cadaver study. Scand J Plast Reconstr Surg Hand Surg 2008;42:300–4.

[2] Gelberman RH, Hergenroeder PT, Hargens AR, Lunborg GN, Akeson WH. The carpal tunnel syndrome. A study of carpal canal pressures. J Bone Joint Surg Am 1981;63:380–3.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5363

SAT0602 MANAGEMENT OF EPICONDYLITIS WITH SINGLE LOCAL INJECTION OF SODIUM HYALURONATE

R. Petrella, A. Cogliano, A. Decruze. *Western University, London, Canada*

Background: Lateral elbow epicondylitis, also known as tennis elbow, is a common musculoskeletal condition causing pain and functional impairment in daily activities.[1] It affects between 40–50% of recreational tennis players at some time.[2] Sodium Hyaluronate (SH) is a natural biological substance which has proven to be effective to improve pain and function in osteoarthritic patients with low incidence of side effects.[3] Similarly, the administration of periarticular injections of SH can be an alternative approach to treat chronic epicondylitis.[4]

Objectives: To evaluate the efficacy and safety of a single periarticular injection with SH in the treatment of epicondylitis.

Methods: A single-site, and placebo-controlled trial was conducted in patients with chronic epicondylitis. Patients' condition was assessed at baseline and afterwards they were randomized 1:1 to receive a single 2.5ml injection of SH (manufactured by Tedec Meiji Farma SA) or placebo (saline) at the point of maximal pain at the lateral epicondyle. Additionally, standard of care (RICE: Rest, Ice, Compression and Elevation) was prescribed to both groups. Efficacy assessments were done at days 30 and 90 and included VAS (0–10cm) pain at rest and assessment of grip strength, patient global satisfaction, patient assessment of normal function and physician global assessment of elbow injury (all measured using 5-point categorical scale). Adverse events were recorded for safety purposes.

Results: A total of 60 patients were included and completed the study procedures. Both groups were homogeneous at baseline. A statistically significant reduction from baseline in VAS pain at rest and after grip testing was observed at 30 and 90 days in both treatment groups ($p<0.05$). Besides, inter-group comparison showed statistically significant differences in favour of SH group at 30 and 90 days ($p<0.05$). This was associated with significantly greater grip strength, patient global satisfaction and assessment of normal elbow function in SH group vs placebo ($p<0.05$). Improvement of elbow injury assessed by the physician was also statistically greater in patients treated with SH compared to placebo ($p<0.05$). No adverse events were recorded.

Conclusions: A single local injection of SH administered to patients with epicondylitis was significantly superior to placebo improving pain at rest and after grip testing, through all the study follow up period. The treatment was highly satisfactory for both physicians and patients and there were no safety concerns.

References:

[1] Chourasia AO, Buhr KA, Rabago DP, Kijowski R, Lee KS, Ryan MP, Grettie-Belling JM, Sesto ME. Relationships between biomechanics, tendon pathology, and function in individuals with lateral epicondylosis. J Orthop Sports Phys Ther. 2013 Jun;43(6):368–78. doi:. 10.2519/jospt.2013.4411.

[2] Taylor SA, Hannafin JA. Evaluation and management of elbow tendinopathy. Sports Health 2012; 4(5): 384–93.

[3] Bannuru RR, Schmid CH, Kent DM, Vaysbrot EE, Wong JB, McAlindon TE. Comparative Effectiveness of Pharmacologic Interventions for Knee Osteoarthritis: A Systematic Review and Network Meta-analysis. Ann Intern Med 2015; 162(1): 46–54.

[4] Petrella RJ, Cogliano A, Decaria J, Mohamed N, Lee R. Management of tennis elbow with sodium hyaluronate periarticular injections. Sports Med Arthrosc Rehabil Ther Technol 2010; 2:4.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2986

SAT0603 AN INNOVATIVE TREATMENT MODALITY FOR ACUTE ILIO-TIBIAL BAND SYNDROME IN RUNNERS: LOCAL HYALURONATE + BOTULINUM TOXIN IN A PROSPECTIVE COHORT OF 45 ATHLETES

R. Petrella, A. Decruze, J. Decaria. *Western University, London, Canada*

Background: Iliotibial band syndrome (ITBS) is the most common cause of lateral knee pain in runners[1]. It is an overuse injury that results from repetitive friction of the iliotibial band (ITB) over the lateral femoral epicondyle. Initial treatment includes activity modification, nonsteroidal anti-inflammatory medication, taping, stretching exercise and in severe cases, a corticosteroid injection[2]. Treatment of symptoms and return to activity are variable and can be intractable.

Objectives: To evaluate the efficacy and safety on pain and return to activity of a single, local injection of ITBS with combination hyaluronate and Botulinum toxin in 45 runners.

Methods: 45 runners with at least grade 2 ITBS underwent baseline investigations including pain following symptom-limited treadmill running test during which pain was recorded on a visual analogue scale (VAS 0–10) every minute. Runners then had injection in the area where the iliotibial band crosses the lateral femoral condyle with 2.5 ml combination hyaluronate (750–1300 kDa) with 40 U Botulinum toxin. Additionally, standard of care (RICE: Rest, Ice, Compression and Elevation) and stretching was prescribed but participants were instructed not to use NSAIDS or taping. The same pain VAS measures as well as peak exercise time, patient global satisfaction and patient assessment of normal running function (all measured using 5-point categorical scale) were repeated after 2, 7, 14 and 30 days. The primary outcome was peak pain during symptom-limited treadmill running.

Adverse events were recorded for safety purposes.

Results: 45 consecutive runners with acute (within 7 days) ITBS were included and completed the study procedures. A statistically significant reduction from baseline in VAS peak treadmill exercise was observed at all time points ($p<0.05$). This was associated with significantly longer exercise time at 7, 14 and 30 days. Patient global satisfaction was increased progressively after 7, 14 and 30 days and assessment of normal running function was described in >75% at 14 days. No serious adverse were reported. 3 subjects described transient (<24 hours) weakness in knee extension and 2 subjects described mild pain at the time and location of injection.

Conclusions: A single local injection of combination hyaluronate + Botulinum toxin for ITBS in runners improved pain and exercise time with treadmill running by 7 days post treatment and continued to 30 days. This treatment was satisfactory to runners and resulted in few, limited adverse events.

References:

[1] Louw M, Deary C. The biomechanical variables involved in the aetiology of iliotibial band syndrome in distance runners - A systematic review of the literature. Phys Ther Sport. 2014 Feb;15(1):64–75.

[2] Fredericson M, Wolf C. Iliotibial band syndrome in runners: innovations in treatment.Sports Med. 2005;35(5):451–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3552

SAT0604 AUTOLOGOUS BLOOD AND CORTICOSTEROID LOCAL INJECTION IN TREATMENT OF PLANTAR FASCIITIS (RANDOMIZED, CONTROLLED MULTICENTER CLINICAL TRIAL)

A. Karimzadeh, S.A. Raeissadat, S. Erfani fam, L. Sedighipour. *Physical Medicine & Rehabilitation Research Center, Tehran, Iran, Islamic Republic Of*

Background: Plantar fasciitis is the most common cause of heel pain. Local injection modalities are among treatment options in patients with resistant pain.
Objectives: The aim of the present study was to evaluate the effect of local autologous blood compared with corticosteroid local injection in treatment of plantar fasciitis.
Methods: In this randomized controlled multicenter study, 36 patients with chronic plantar fasciitis were recruited. Patients were allocated randomly into 3 treatment groups: local autologous blood, local corticosteroid injection and control groups receiving no injection. Patients were assessed with Visual Analogue Scale (VAS), Pressure Pain Threshold (PPT) and Plantar Fasciitis Pain/Disability Scale (PFPS) before treatment, 4 and 12 weeks post therapy.
Results: Variables of pain and function improved significantly in both corticosteroid and autologous blood groups compared to control group. At 4 weeks following treatment, patients in corticosteroid group had significantly lower levels of pain than patients in autologous blood and control groups (higher PPT level, lower PFPS and VAS). After 12 weeks of treatment both corticosteroid and autologous blood groups had lower average levels of pain than control group. The corticosteroid group showed an early sharp and then more gradual improvement in pain scores but autologous blood group had steady gradual drop in pain.
Conclusions: Autologous blood and corticosteroid local injection both can be considered as effective methods in the treatment of chronic plantar fasciitis. These treatments decrease pain and improve function significantly compared to control group.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1771

SAT0605 LOCAL PROGESTERONE INJECTION: NEW OPTION FOR MANAGEMENT OF CARPAL TUNNEL SYNDROME

S.A. Raeissadat[1], L. Sedighipour[1], S. Shahraeeni[2]. [1]*Physical Medicine & Rehabilitation Research Center;* [2]*Physical medicine and rehabilitation research center, Tehran, Iran, Islamic Republic Of*

Background: A number of studies, have demonstrated the neuroprotective effects of progesterone and its influence on the recovery after neural injury. Few studies investigated the efficacy of local progesterone in Carpal Tunnel Syndrome.
Objectives: The objective of this study was to compare the long term effects of progesterone versus corticosteroid local injections in patients with mild and moderate carpal tunnel syndrome.
Methods: In this randomized clinical trial, 78 hands with Carpal Tunnel Syndrome were assigned to two groups. Patients were treated with a single local injection of triamcinolone acetonide in one group and single local injection of hydroxy progesterone in the other group. Variables including pain (based on Visual Analogue Scale), symptom severity and functional status (based on Bostone/Levine symptom severity and functional status scale) and nerve conduction study were evaluated before and 6 months after the treatments.
Results: All outcome measures including pain, functional scales and electrophysiologic findings improved in both corticosteroid and progesterone groups and there were no meaningful differences between two groups regarding mentioned variables. However, functional outcome was significantly better in progesterone compared to corticosteroid group at 6 month follow up (P=0.04).
Conclusions: This study demonstrated the efficacy of progesterone local injection in mild and moderate CTS at long term follow up. Furthermore, local progesterone can be superior to corticosteroid injection for relieving symptoms and improving functional and electrophysiologic findings at long term follow up.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1774

SAT0606 IS THE LEVEL OF PHYSICAL ACTIVITY AN IMPORTANT FACTOR FOR LOW BACK PAIN AMONG STUDENTS OF UNIVERSITY?

V. Akduman[1], E. Mete[1], I. Demirbuken[1], G. Ogren[2]. [1]*Physiotherapy and Rehabilitation;* [2]*Nutrition and Dietetic, Marmara University, Istanbul, Turkey*

Background: Back pain is a major global health problem, causing greater disability worldwide than any other condition. Regular physical activity is widely believed to have important health benefits, such as improving quality of life and mobility, and reducing disabilities. Conversely, lack of physical activity is considered a risk factor for increasing chronic diseases, functional dependence and mortality. Patients with low back pain (LBP) often report disability to perform daily activities. Also, decreased physical activity level can lead to low back pain.
Objectives: The aim of the study was to determinewhether increasing the level of physical activity affects the low back pain or not in the population of univesity students.
Methods: The cross-sectional study included 350 students (181 females and 169 males) with a mean age of 19.8±1.9 years. LBP was determined using the validated Oswestry Disability Index (ODI). ODI consist of ten items and are completed in reference to the patient's functional status "today". Physical activity level was evaluated by the short form of the International Physical Activity Questionnaire (IPAQ). IPAQ is a scale to be recorded at different levels of physical activity time in the last week. IPAQ is a scale to be recorded at different levels of physical activity time in the last week. Individuals whose score is lower than 600 MET are described as inactive (IPAQ 1), between 600–1500 MET (IPAQ 3) are described as minimal active and higher than 3000 MET (IPAQ 5)are described as active. For the statistical analyzing we used spearman correlation test.
Results: According to the short form of IPAQ, %14.8 percent of students were found inactive, % 48.1 percent of students were found minimal inactive and %37.1 percent of students were found active. The total score of Oswestry disability index was found 6,2±5,0. There was a significant difference between the Oswestry disability index score of inactive, minimally active and active groups (p=0,02). In addition to this, between the Oswestry disability index and total score of IPAQ was found a weak correlation in the negative direction (p=0,01; r=-0,184). Between the IPAQwhich means vigorous intensity activity, and Oswestry disability index was found a weak correlation in the negative direction (p=0,00; r=-0,190). And also between IPAQ3, which means modarate intensity activity, and Oswestry disability index was found a significant but weak correlation in the negative direction (p=0,03; r=-0,157). Between Oswestry disability index and sedentary activity and walking was not found any significant correlation ($p>0.005$).
Conclusions: According to our study, increasing the level of physical activity may reduce low back pain. Especially vigorous and modarate intensity activity can be effective in prevention from low back pain. For reducing of low back pain, sedentary activity and walking did not have any significant effect in our study. Therefore, the level of physical activity should be increased at the young age to prevent of low back pain which is a major health problem.
References:
[1] Saglam, Melda, et al. International physical activity questionnaire: reliability and validity of the Turkish version. Perceptual and motor skills 111.1 (2010): 278–284.
[2] Fairbank, Jeremy CT, and Paul B. Pynsent. The Oswestry disability index. Spine 25.22 (2000): 2940–2953.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4953

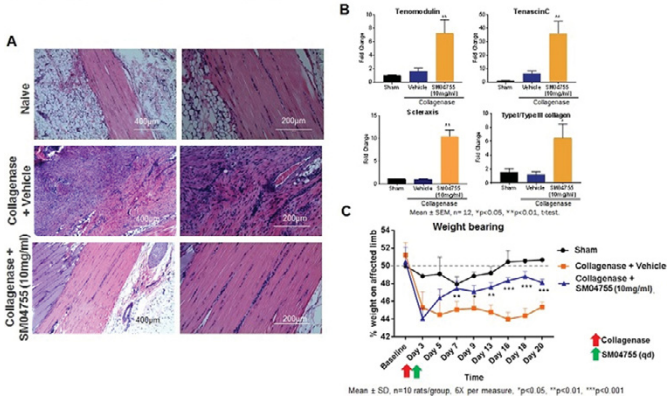
SAT0607 DISCOVERY OF A SMALL MOLECULE INHIBITOR OF THE WNT PATHWAY (SM04755) AS A POTENTIAL TOPICAL TREATMENT FOR TENDINOPATHY

V. Deshmukh, T. Seo, M. Ibanez, J. Stewart, B. Hofilena, Y. Yazici. *Samumed, LLC, San Diego, CA, United States*

Background: Tendinopathy is an inflammatory and degenerative disorder caused by injuries or overuse. It can progress to a chronic condition with failed healing, tendon fibrosis and micro-tears that lead to pain and sometimes rupture. Current therapeutic options focus mainly on pain relief rather than treatment of underlying disease. The Wnt pathway is upregulated in tendinopathy and has an important role in inflammation, fibrosis and tenocyte differentiation.
Objectives: SM04755, a novel, topical Wnt pathway inhibitor, was evaluated in preclinical studies to determine its potential to inhibit inflammation, reduce fibrosis and increase tenocyte differentiation, thereby promoting tendon healing.
Methods: Anti-inflammatory activity was measured by TNF-α and IL-6 secretion using ELISA in lipopolysaccharides (LPS) or anti-CD3/anti-CD28 stimulated peripheral blood mononuclear cells (PBMCs). Differentiation of human mesenchymal stem cells (hMSCs) and rat tendon derived stem cells (rTDSCs) into tenocytes was measured by high-content imaging for tenocyte markers scleraxis A (SCXA), tenomodulin and tenascin C. Pharmacokinetics were evaluated following topical application in rats. *In vivo* efficacy of SM04755 was evaluated in a single injection, collagenase-induced acute rodent tendinopathy model and a chronic, multiple injection, failed healing model, by scoring histological indicators of tendon health. Inflammation was measured by chemokine ligand 1 (CXCL1) levels in plasma by ELISA and pro-inflammatory markers (IL-6, TNF-α, IL-1β, IFN-γ, IL-8) in the tendon by qPCR. Tendon regeneration and healing were evaluated by qPCR based gene expression of tenocyte differentiation markers SCXA, tenomodulin and tenascin C, Type I/Type III collagen ratio and polarized light microscopy using Sirus Red staining. Pain in the rodent model was evaluated by measuring weight distribution with an incapacitance meter.
Results: SM04755 potently inhibited cytokine secretion in LPS and anti-CD3/anti-CD28 stimulated PBMCs (EC_{50}=500nM). SM04755 induced expression of tenocyte markers in differentiated hMSCs and rTDSCs (EC_{50}=200nM). A single topical application of SM04755 resulted in tendon concentrations $>EC_{50}$ for up to 24hrs, with minimal systemic exposure or toxicity. In both the acute and failed healing tendinopathy models, SM04755 (10mg/ml) treatment improved tendon morphology (Figure A), significantly increased mean tendon health

score ($p<0.01$), decreased plasma levels of CXCL1 ($p<0.05$) and reduced gene expression of pro-inflammatory markers (IL-6, TNF-a, IL-1b, INF-g, IL-8; $p<0.05$) compared to vehicle. SM04755 treatment promoted tendon regeneration measured as increased expression of tenocyte markers ($p<0.05$), increased Type I/Type III collagen ratio (Figure B; $p<0.01$) and Sirus Red stained collagen fibers in tendon compared to vehicle. SM04755 treatment increased % total weight bearing on the affected limb ($p<0.01$), at multiple time points (Figure C), indicating reduced pain in the rodent model.

Figure. SM04755 inhibited inflammation, promoted tendon healing and reduced pain in a rat collagenase-induced tendinopathy model



Conclusions: Topical SM04755, a Wnt pathway inhibitor, reduced inflammation, promoted tendon regeneration and healing, and reduced pain compared to vehicle in rodent tendinopathy models. SM04755 is a potential treatment for tendinopathy. Clinical studies are in progress.

Disclosure of Interest: V. Deshmukh Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, T. Seo Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, M. Ibanez Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, J. Stewart Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, B. Hofilena Shareholder of: Samumed, LLC, Employee of: Samumed, LLC, Y. Yazici Shareholder of: Samumed, LLC, Employee of: Samumed, LLC

DOI: 10.1136/annrheumdis-2017-eular.6427

SAT0608 RELATION BETWEEN SCAPULAR MUSCLE ENDURANCE, MUSCLE STRENGTH, PAIN AND FUNCTION IN PATIENTS WITH ROTATOR CUFF LESION

U. Sozlu, S. Basar, U. Kanatli, Z.B. Alkan. *Gazi University, Ankara, Turkey*

Background: Rotator cuff lesion (RCL) is an term that encompasses a spectrum of shoulder conditions including; subacromial impingement syndrome (SIS), partial and full thickness rotator cuff tears (RCT) and calcific tendinitis. Symptoms include pain, limited motion, muscle weakness and functional disability.

Objectives: To investigate the relationship between scapular muscle endurance (SME), muscle strength, pain and function in patients with shoulder RCL.

Methods: This study was conducted on 53 patients in shoulder RCL and 23 healthy controls. SIS was present in 25 patients (14 males, 11 females; mean age 41±9 years) and partial RCT in 28 patients (16 females, 12 males; mean age was 54±5 years) in the study group. In the control group, there were 12 females and 11 males and the mean age was 48±10 years. SME was measured as isometric based on the exercise developed by Sahrmann. Strength of the shoulder and scapular muscles were evaluated with digital manuel muscle dynamometer. Activity, night and rest pain levels were evaluated by visual analog scale. Functional activity status was assessed by the Functional Impairment Test-Head, and Neck/Shoulder/Arm (FIT-HaNSA).

Results: Statistically significant relationship was found positively in varying grades between SME and serratus anterior, middle trapezius, shoulder flexor, extensor, abductor, supraspinatus, pectoralis majör strength in partial RCT group and between lower trapezius muscle strength and SME in addition to these muscles in SIS group ($p<0.05$). Statistically significant relationship at varying degrees was found between SME and all muscles excluding shoulder internal, external rotators in control group ($p<0.05$). In SIS and partial RCT groups, negative, moderate and statistically significant relationship was found between SME and activity pain ($p<0.05$). In SIS and partial RCT groups significant correlation was not observed between SME and rest, night pain levels ($p>0.05$). In SIS and partial RCT groups, positive, excellent and statistically significant relationship was detected between SME and FIT-HaNSA ($p<0.05$). In control group, positive, moderate, again statistically significant relationship was detected ($p<0.05$).

Conclusions: Muscle strength may be reduced, upper extremity function may worsen and activity pain may increase in patients with reduced SME. It was concluded that shaping of exercise programs of muscle groups related to SME in rehabilitation studies and SME should be increased in patients with SIS and partial RCT in order to reduce shoulder pain and improve its functionality.

References:

[1] Cofield, R. H. (1985). Current concepts review rotator cuff disease of the shoulder. Journal of Bone and Joint Surgery. American volume, 67(5), 974–979.
[2] Neer, C. S. (1993). Impingement lesions. Clinical Orthopedia, 173, 71–7.
[3] Edmondston, S. J., Wallumrød, M. E., MacLéid, F., Kvamme, L. S., Joebges, S. and Brabham, G. C. (2008). Reliability of isometric muscle endurance tests in subjects with postural neck pain. Journal of Manipulative and Physiological Therapeutics, 31(5), 348–354.
[4] MacDermid, J. C., Ghobrial, M., Quirion, K. B., St-Amour, M., Tsui, T., Humphreys, D., McCluskie, J., Shewayhat, E. and Galea, V. (2007). Validation of a new test that assesses functional performance of the upper extremity and neck (FIT-HaNSA) in patients with shoulder pathology. BMC Musculoskeletal Disorders, 8(1), 42.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6310

SATURDAY, 17 JUNE 2017

Diagnostics and imaging procedures

SAT0609 GIANT CELL ARTERITIS: ATHEROSCLEROSIS AS PITFALL IN THE HALO SIGN

E. De Miguel[1], L.M. Beltran[2], F. Deodati[2], I. Monjo[1], W.A. Schmidt[3], J. García-Puig[2]. *[1]Rheumatology; [2]Internal Medicine, Hospital Universitario la Paz, Madrid, Spain; [3]Rheumatology, Immanuel Krankenhaus, Berlin, Germany*

Background: The halo sign (defined as an homogenous, hypoechoic wall thickening, well delineated towards the luminal side, visible in longitudinal and transverse planes). is the more accurate ultrasonographic (US) finding for the diagnosis of Giant Cell Arteritis (GCA). False-positive halos are seen in malignant and infectious diseases. The new US high frequencies probes make possible not only to see the halo sign but also measure the increase of the intima-media-thickness (IMT). Moreover, the US appearance of the IMT in atherosclerotic carotid artery may be hypoechoic as the halo sign.

Objectives: The aim of this study was to explore if the increase of the atherosclerotic IMT can mimic the halo sign in temporal arteries (TA) and to produce false positives in the diagnosis of GCA.

Methods: Consecutive non selected patients, ≥50 years-old with high vascular risk according to European Guidelines on Cardiovascular Disease Prevention, and without signs or symptoms of GCA, were included.

Ultrasonography of carotid artery: Carotid ultrasound examinations were performed on a Mylab Seven (Esaote Medical Systems, Italy) with a 4–13 MHz linear-array. The system employed dedicated software radiofrequency-tracking technology to obtain IMT (QIMT®).

Ultrasonography of temporal superficial artery: A color Doppler ultrasound (CDU) and grey scale measure of the IMT/halo sign in the branches of both TA was performed by a second experienced sonographer. A Mylab Twice equipment (Esaote, Geneve, Italy) was used, with a 22 MHz frequency for grey scale and a 12.5 MHz for CDU, with a color gain of 51 and a PRF of 2 kHz. The sonographer was blind to the clinical data and carotid ultrasound IMT measures. Examination videos were stored for reliability and an intra-reader was performed months after the examination.

Statistical analysis: Descriptive frequencies, Student's *t*-test, Cronbach's alpha and Spearman correlations was used.

Results: Forty patients were studied, 28 men (70%), with a mean age of 70,6±6,9 years. Three patients were active smoker and 27 ex-smokers. Arterial hypertension was present in 39 (97.5%), dyslipidemia in 34 (85%) and diabetes in 19 (47.5%). The mean erythrocyte sedimentation rate was 13.6±11.0. Eighty carotids were studied, 50 had plaques and 30 did not with a IMT ranged from 0.528 to 1.480 mm. The mean values of TA related with the carotid IMT are presented in the table: the increase in the carotid IMT is associated with an increase in the IMT of the TA with a weak Spearman correlation (parietal branches 0.282 p=0.012 and frontal branches 0.228 p=0.048).

Patients with a final GCA diagnosis (n=22)

Carotid IMT mm	Branches of Temporal arteries parietal and frontal			
	n	Mean Halo/IMT mm	SD	Min–Max
≤0.7	12	0.247	± 0.043	0.16–0.29
≤0.9	46	0.254	± 0.037	0.18–0.33
≤1	42	0.269	± 0.034	0.18–0.36
≤1.2	50	0.282	± 0.052	0.17–0.45
>1.2	10	0.284	± 0.067	0.19–0.40

From reliability a Cronbach's alpha of 0.900 and 0.876 were achieved for parietal and frontal branches respectively.

Some patients had a TA IMT that can be interpreted as halo sign: 18 (45%) patients and 33 (20.6%) TA branches if we choose a cutoff >0.30 mm of IMT/halo sign; 4 (10%) patients and 7 (4.4%) TA branches if the cutoff were >0.34 mm.

Conclusions: The atherosclerotic disease can produce false-positive GCA diagnosis. Carotid IMT >0.9 mm is associated with halo sign in TA. The IMT cutoff value for the diagnosis of GCA should be established.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1461

SAT0610 TEMPORAL ARTERY ULTRASOUND IN THE DIAGNOSIS OF GIANT CELL ARTERITIS IN A COHORT WITH ELEVATED CLINICAL IMPRESSION

P.V. Estrada[1], D. Reina[1], V. Navarro[1], D. Roig[1], D. Cerdà[2], V. Torrente[1], S. Heredia[1], H. Corominas[1]. *[1]Rheumatology; [2]Hospital Moisès Broggi-Hospital General de L'hospitalet. Consorci Sanitari Integral. Sant Joan Despí, Barcelona, Barcelona, Spain*

Background: Giant cell arteritis (GCA) is the most frequent vasculitis in adulthood. The delay in diagnosis sets back treatment and can lead to serious consequences. Diagnosis is complex, and is followed by the classification criteria according to the American College of Rheumatology (ACR). The is an increasing interest on the utility of temporal artery ultrasound (TAUS) as a tool to evaluate inflammation on the vessel wall.
Objectives: to evaluate the utility of TAUS in GCA.
Methods: During 2016, 120 TAUS were carried out in 60 patients with clinical suspicion for GCA. The TAUS was carried to completion by rheumatologist with experience. The symptoms that lead to a TAUS was either one or more of these clinical scenarios: 1) cranial symptoms (recent onset headache, mandibular claudication, visual disturbances) 2) polymyalgic syndrome 3) toxic o febril unspecific syndrome 4) vertebrobasilary (VB) stroke. Demographic and laboratory data were collected, and a follow-up was done to learn the final diagnosis. As for TAUS, the "halo" sign was considered positive if an anechoic image surrounded the vessel was present, and measured >0,30 mm in both, longitudinal and transverse cuts. Other more unspecific signs as stenosis or occlusion were also registered. A temporal artery biopsy was performed whenever the physicians considered necessary, based on clinical criteria, every case in no more than 30 days.
Results: Fifty-two percent were women, mean age 76±7.8 years old. Mean laboratory parameters: eritrosedimentation rate 85±41.9 mm/h, C-reactive protein 77±80 mg/L, Haemoglobin 11.4±2.2 g/L, white blood count 10,228±3,520, platelet count 310,603±123,918. The symptoms that motivated requesting the TAUS were: cranial symptoms (62.2%), toxic, unspecific, febrile syndrome (44%), polymyalgic syndrome (30%), VB stroke (5%). A temporal artery biopsy was carried out in 45% of patients (N=27); it was positive in 40.7%, negative in 40.7% and unspecific (given it reported an inflammatory histologic pattern, but without the characteristic giant cells) in 18.5%. From all 60 patients in whom a TAUS was performed, 36% were diagnosed with GCA, based on ACR criteria.

Patients with a final GCA diagnosis (n=22)

Ultrasound	Biopsy	%
Positive	Positive	40.7%
Positive	Unspecific	22.7%
Positive	Not done	9%
Negative	Not done	9%
Non-conclusive	Negative	9%
negative	Positive	9%

The sensibility and specificity for TAUS was 80% and 94% respectively, with a posivite predictive value of 88.9% and a negative predictive value of 89.2%
Conclusions: TAUS is a useful, non-invasive, fast, accessible tool for evaluating temporal arteries with a great diagnostic valu
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6810

SAT0611 INTIMA-MEDIA THICKNESS REFERENCE RANGES DEPICTING HALO SIGN FOR THE DIAGNOSING OF LARGE VESSEL GIANT CELL ARTERITIS BY ULTRASOUND

M. Milchert, M. Brzosko. *Department of Rheumatology Internal Medicine and Geriatrics, Pomeranian Medical University, Szczecin, Poland*

Background: Color duplex ultrasonography (CDU) is most promising tool for the assessment of large vessel giant cell arteritis (LV-GCA). There is a need to define ultrasound findings consistent with the diagnosis of GCA.
Objectives: We aimed to score intima-media thickness (IMT) reference ranges for LV-GCA in polish patients.
Methods: 214 patients suspected for GCA and evaluated with CDU were included in the study and followed up for min 9 months. Large vessel CDU, together with arteritis/non-arteritis categorization, were performed before or within 1 week after treatment initiation by a single physician. Vasculitis was defined as hypoechoic, homogenous, increase of IMT with distorted wall structure resulting in no clear intima-media structure, over long distance (not limited only to the place of arterial bifurcations). ROC curves were calculated.
Results: GCA was diagnosed in 81 patients, polymyalgia rheumatica (PMR) in 131 (characteristics – Table 1). Extracranial LV-GCA was diagnosed in 43 patients: axillary vasculitis in 23 patients, common carotid artery (CCA) – 24, subclavian – 18, superficial femoral – 11, brachial (all spreading per continuum from axillary arteritis) – 8. In 83 remaining patients other diagnosis was confirmed, and they served as non-GCA/PMR controls. Mean IMT in LV-GCA was significantly higher versus controls and isolated PMR (Fig. 1). IMT in GCA was not significantly influenced by gender, hypertension and smoking in contrast with IMT in controls. Proposed cut off values for IMT depicting vasculitis in GCA patients are presented in Table 2. 100% specificity for vasculitis (vs GCA without large vessel vasculitis) was reached with axillary IMT of 1.06 mm (62% sens.), subclavian – 1.35 mm (38% sens.), superficial femoral – 1.55 mm (60% sens.), CCA – 1.27 mm (22% sens.).

Table 1. Patient characteristics

	GCA (N=81)	Isolated PMR (N=50)	Non-GCA/PMR controls (N=83)	p
Female	53 (65%)	37 (74%)	54 (65%)	0.512
Age (mean ± SD; min-max)	73* ± 9; 55–95	69±9; 52–87	65±10; 44–89	0.001
Hypertension	53 (65%)	31 (62%)	44 (53%)	0.251
Smoking	36 (44%)	14 (28%)	29 (35%)	0.148
Diabetes	13 (16%)	6 (12%)	15 (18%)	0.649
Hypercholesterolemia**	25/66 (38%)	12/33 (36%)	19/38 (50%)	0.400
Arterial calcifications***	34 (42%)	11 (22%)*	33 (40%)	0.058
Upper limbs claudication	4 (4.9%)	0 (0.0%)	1 (1.2%)	0.131

*Significant findings ($p<0.05$); **Assessed in 137 patients; ***Of medium to high grade.

Table 2. Cut off values for IMT depicting vasculitis in GCA patients

Artery	IMT (mm)	AUC	Sens. (%)	Spec. (%)
Arteries classified as vasculitis vs GCA without large vessel vasculitis				
Axillary	0.82	0.959	85.7	92.7
Subclavian	0.84	0.954	87.5	96.8
Superficial femoral	0.97	0.945	90.0	96.3
Common carotid	0.96	0.877	72.2	93.7
Arteries classified as vasculitis vs controls				
Axillary	0.81	0.969	87.0	93.7
Subclavian	0.66	0.974	100	83.7
Superficial femoral	0.92	0.958	90.9	96.6
Common carotid	0.73	0.910	91.7	79.0

Maximal IMT value from bilateral CDU measurements was chosen. AUC = area under the curve.

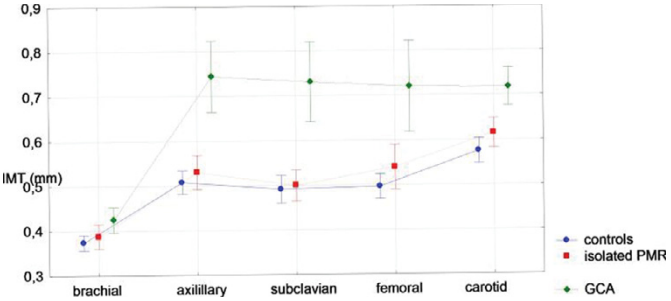


Figure 1. Mean IMT in different arteries in GCA, isolated PMR and controls.

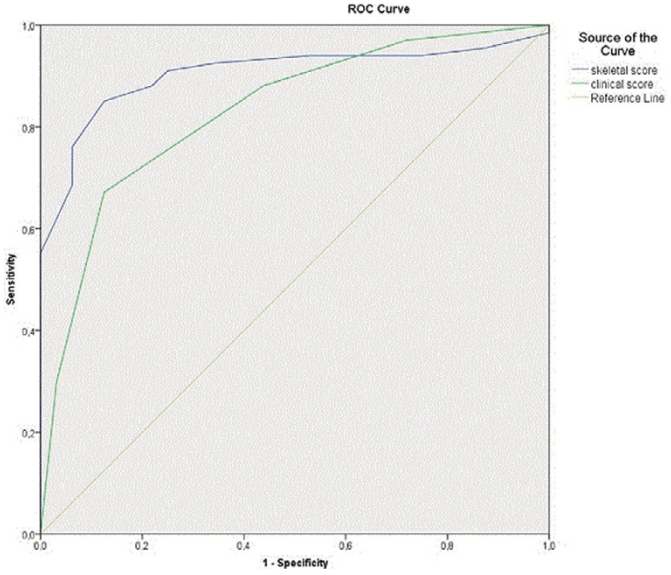
Conclusions: We demonstrated that cut off values may discriminate between GCA and its mimics as well as between presence and lack of vasculitis in different arteries in GCA.
References:
[1] Milchert M, Diamantopoulos A, Brzosko M. Atlas of ultrasound application in large vessel arteritis: giant cell arteritis and Takayasu arteritis. Wydawnictwo Pomorskiej Akademii Medycznej, Szczecin, 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4139

SAT0612 THE USE OF 18F-FDG-PET IN THE DIAGNOSIS OF POLYMYALGIA RHEUMATICA (PMR) – A PROSPECTIVE STUDY OF 99 PATIENTS SUSPECTED OF PMR

L. Henckaerts[1], O. Gheysens[2], S. Vanderschueren[1], K. Goffin[2], D. Blockmans[1]. *[1]General Internal Medicine; [2]Nuclear Medicine Department, University Hospital Gasthuisberg, Leuven, Belgium, Leuven, Belgium*

Background: Previous studies have shown that the majority of patients with polymyalgia rheumatica (PMR) have increased fluorodeoxyglucose (FDG)-uptake around the shoulders, hips and processes of the cervical and lumbar spine on positron emission tomography (PET) (1). The specificity of these findings for PMR is not known.
Objectives: To determine the specificity and sensitivity of FDG-PET findings for the diagnosis of PMR.
Methods: A prospective monocentric study in a tertiary care centre. All patients underwent FDG-PET scanning before treatment with glucocorticoids was started. The clinical suspicion of PMR was quantified by the treating physician on a scale from 1 to 5. FDG-uptake was scored visually in 12 articular regions (cervical spinous processes, lumbar spinous processes, left and right sternoclavicular joint, left and right ischial tuberosity, left and right greater trochanter, left and right hip and left and right shoulder) (score 0–2) and a total skeletal score was calculated reflecting the FDG-uptake in these 12 articular regions. ROC analysis was performed to determine the optimal clinical and total skeletal score for diagnosing PMR. The golden standard for a diagnosis of PMR was the judgment of an experienced clinician after at least six months of follow-up.
Results: 99 consecutive patients with a possible clicinal diagnosis of PMR were included in this study. Sixty-seven patients were finally diagnosed with PMR while 32 patients got another diagnosis. A clinical score of 4 or more had a sensitivity

of 67.2%, specificity of 87.5%, positive predictive value (PPV) of 91.8% and a negative predictive value (NPV) of 56.0% for the diagnosis of PMR. A total skeletal score of 16 or more had a sensitivity, specificity, PPV, NPV of respectively 85.1%, 87.5%, 93.4% and 73.7%.



Conclusions: FDG-PET before starting glucocorticoid therapy improves the diagnostic accuracy compared to a clinical scoring system in patients with clinical suspicion of PMR.

References:

[1] Blockmans D, De Ceuninck L, Vanderschueren S, Knockaert D, Mortelmans L, Bobbaers H. Repetitive 18-fluorodeoxyglucose positron emission tomography in isolated polymyalgia rheumatica: a prospective study in 35 patients. Rheumatology (Oxford) 2007; 46: 672–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3628

SAT0613 HIGH PREVALENCE OF SUBCLINICAL ATHEROSCLEROSIS IN GOUT AND ASYMPTOMATIC HYPERURICEMIA: A STUDY BASED ON CAROTID ULTRASOUND

C. Bertolazzi[1], M. Gutierrez[2], R. Espinosa[3], M. Martínez-Lavin[4], L.H. Silveira[4], C. Lozada[2], J. Moreno[3], E. Cruz[5], B. Olivares[5], C. Pineda[3], A.C. Lozada[2]. *[1]Division of Neuroscience; [2]Division of Musculoskeletal and Rheumatic Diseases; [3]Rheumatology Department, Instituto Nacional de Rehabilitación; [4]Rheumatology Department, Instituto Nacional de Cardiología Ignacio Chavez; [5]Epidemiology and Social Medicine Department, Instituto Nacional de Rehabilitación, Ciudad de Mexico, Mexico*

Background: Accelerated atherosclerosis is known in gout. Hyperuricemia is considered an independent risk factor for cardiovascular (CV) disease. Evidence supporting both proatherogenic and prothrombotic states in HU is also published Ultrasound (US) measurement of the carotid intima-media thickness (cIMT) is a recognized measure of premature subclinical atherosclerosis with a predictive value respect to vascular events.

Objectives: To determine the prevalence of increased cIMT, as sign of subclinical atherosclerosis, by an automated US method, and the associated risk factors in patients with gout and asymptomatic hyperuricemia (aHU)

Methods: 138 patients with gout, 105 with aHU and 99 age and sex matched healthy controls were enrrolled. For all patients were recorded: clinical history, disease duration, smoking, ischemic heart disease, comorbidities (diabetes mellitus, high blood pressure, dyslipidemia, renal insufficiency, obesity), and current therapy. ESR and serum CRP, total and HDL cholesterol, triglycerides, glucose, creatinine and uric acid were recorded. Patients with history of CV and cerebrovascular events or autoimmune diseases were excluded.

US examinations of both common carotids were performed by an experienced sonographer trained in cIMT examination, with a Esaote My Lab 70XVG, equipped with a linear probe (4–13 MHz) and an automatic IMT measure software. The definitions of Mannheim cIMT Consensus were adopted

Results: A total of 684 common carotids were assessed. The prevalence of increased cIMT was 47.1%, 47.6% and 1% in patients with gout, aHU, and control group, respectively. The final adjusted logistic regression for patients with gout showed that time of disease progression (OR =0.79, 95% CI 0.66–0.95) and previous smoking (OR =0.32, 95% CI, 0.10–0.97) were associated with cIMT increase ($p<0.05$) whereas the uric acid levels (OR =1.66, 95% CI 1.07–2.56) was associated with an increased cIMT in aHU. No significant correlation was found with the other variables. No differences in US findings were found between gout and aHU (p=0.936). There was a significant difference in cIMT in gout versus control (p=0.0001) and aHU versus control (p=0.0001).

Conclusions: Our results demonstrate that patients with gout and aHU without clinically evident cardiovascular disease have a high prevalence of subclinical atherosclerosis. Disease duration and levels of uric acid are independent factors related with increased cIMT in gout and aHU respectively. These results support the importance of screening for CV risk and to include carotid ultrasound in CV prevention strategies in these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6363

SAT0614 ULTRASOUND AND URATE CRYSTAL DEPOSITION: HOW MANY JOINTS TO SCREEN?

D. Bhadu[1], S.K. Das[2], A. Wakhlu[3], U. Dhakad[2]. *[1]Department of Rheumatology, All India Institute of Medical Sciences, New Delhi; [2]Department of Rheumatology; [3]Department of Radiodiagnosis, King george medical university, lucknow, India*

Background: Gout is one of the most common inflammatory joint disease in males. The new ACR/EULAR 2015 gout classification criteria has included imaging as a scoring item [1]. Naredo et al [2], found that in intercritical gout, assessment of one joint (ie, radiocarpal) and two tendons (ie, patellar and triceps) for HAGs, and three articular cartilages (ie, first metatarsal, talar and second metacarpal/femoral) for double contour sign (DCS) showed the best balance between sensitivity and specificity (84.6% and 83.3%, respectively). Ultrasound screening at these 6 sites is time consuming and not feasible in a busy outpatient service. So we aimed to compare the two sites (knee and 1st MTP joints) with these 6 sites for the ultrasound detected abnormalities namely DCS and HAGs in patients of gout particularly with the idea to find the best possible minimum joint combination without compromising the sensitivity and specificity.

Objectives: To compare the ultrasound-detected abnormalities namely double contour sign (DCS) and hyperechoic aggregates (HAGs) at knee and first metatarsophalangeal (1st MTP) joint (two sites) verses six sites (knee joint, 1st MTP joint, radiolcarpal joint, patellar tendon and triceps tendon) in patients of gout.

Methods: Forty seven gout and fifty controls (serum uric acid <7mg/dl) with age more than 18 years were included in this study. DCS was looked for at three articular cartilage sites (first metatarsal, tibiotalar and femoral condyle) whereas HAGs were looked for at one joint site (radiocarpal joint) and two tendon sites (patellar tendon and triceps tendon). Ultrasound findings of all three groups were compared.

Results: We found sensitivity, specificity, positive predictive value, negative predictive value and positive likelihood ratio of two joint areas (knee and 1st MTP) ultrasound findings for gout were 87.2%, 84%, 83.7%, 85.6% and 5.5 respectively. Similar sensitivity, specificity, positive predictive value, negative predictive value and positive likelihood ratio were observed with 6 sites ultrasound findings. Amongst controls 17.5% were found to have these abnormal ultrasound findings by both two joint area and 6 sites exams.

Applied Diagnostics	Sensitivity	Specificity	PPV	NPV	LR+	LR–
Knee joint DCS	53.2	94.0	89.3	68.1	8.9	0.49
1st MTP Joint DCS	51.1	84.0	75.0	64.6	3.2	0.58
1st MTP joint HAGs	44.7	100.0	100.0	65.8	–	0.55
1st MTP Joint DCS+HAGs	72.3	84.0	81.0	76.4	4.5	0.32
Talar joint DCS	40.5	100.0	100.0	69.4	–	0.59
Patellar tendon HAGs	23.4	100.0	100.0	58.1	–	0.76
Triceps tendon HAGs	14.9	100.0	100.0	55.6	–	0.85
Radiocarpal joint HAGs	4.3	100.0	100.0	52.6	–	0.95
Knee and MTP joint abnormalities	87.2	84.0	83.7	85.6	5.5	0.15
Ultrasound abnormalities at Six examined site	87.2	84.0	83.7	85.6	5.5	0.15

Conclusions: Screening of two joint areas (knee and 1st MTP) has similar sensitivity, specificity and positive likelihood ratio as compared to six sites in diagnosing gout. While utilizing lesser time in examination.

References:

[1] Neogi T, Tim L, Dalbeth N, Fransen J, Schumacher HR, Berendsen D, et al. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Annals of the Rheumatic Diseases. 2015;74:1789.

[2] Naredo E, Uson J, Jiménez-Palop M, Martínez A, Vicente E, Brito E, et al. Ultrasound-detected musculoskeletal urate crystal deposition: which joints and what findings should be assessed for diagnosing gout? Ann Rheum Dis 2014;73: 1522–1528.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1680

SAT0615 THE RS11803505 IL-23R POLYMORPHISM IS A RISK FACTOR FOR THE DEVELOPMENT OF MSUS-DETECTED EROSIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C. Perricone[1], F. Ceccarelli[1], V. Iorgoveanu[1], C. Ciccacci[2], S. Rufini[2], C. Alessandri[1], F.R. Spinelli[1], E. Cipriano[1], G. Novelli[2], G. Valesini[1], P. Borgiani[2], F. Conti[1]. *[1]Lupus Clinic, Rheumatology, Department of Internal Medicine, Sapienza University of Rome; [2]Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy*

Background: Articular involvement is a frequent and invalidating manifestation in patients with Systemic Lupus Erythematosus (SLE) ranging from arthralgia to erosive arthritis. Bone erosions are far less common in SLE but require a different management and may display a distinct pathogenesis. Musculoskeletal ultrasonography (MSUS) has proven useful in the assessment of inflammatory arthritis and it is now known that MSUS is more sensitive than radiography in detecting bone erosions.
Objectives: We aimed at analyzing, in a large monocentric cohort of SLE patients who suffered from arthritis, the relationship between 31 polymorphisms in 18 genes previously associated with SLE or other autoimmune/inflammatory arthritis [1] and the presence of bone erosions detected by MSUS.
Methods: Consecutive SLE patients who complained articular involvement (defined by 1997 ACR criteria, i.e. $\geq$2 joints with tenderness, swelling or effusion) were enrolled. Patients RF+ve and/or anti-CCP+ve were excluded. Thirty-one SNPs in 18 genes (STAT4, IL10, IL23R, IRAK1, PSORS1C1, HCP5, MIR146a, PTPN2, ERAP1, ATG16L1, IRGM, TRAF3IP2, VKORC1, CCR5, ATG5, TRAF6, TNFSF4, CD40) were genotyped by allelic discrimination assays. Bilateral high-resolution MSUS of the hands and feet was performed. Erosion number was recorded, the presence of erosive damage was assessed with a dichotomous score.
Results: Clinical and laboratory features of the 95 enrolled patients are described in table.

Clinical and laboratory features	N.	%
Sex	92	96.8
Age (mean ± SD)	43.38±11.49	
Age at diagnosis (mean ± SD)	31.14±11.83	
Anti-dsDNA	69	72.6
MSUS Erosive score (mean ± SD)	0.44±1.34	
MSUS Erosions (yes/no)	15/80	15.8

The presence of MSUS-detected erosions was demonstrated in 15/95 (15.8%) patients, with a mean±SD of 0.44±1.34. Bone erosions were more frequently observed at II metacarpophalangeal joint of the hands (29.4%), followed by the V metatarsophalangeal joint of the feet (16.1%). An association was found between anti-dsDNA and the presence of bone erosions (P=0.009, Fisher's exact test); indeed, all the 15 patients (100%) with bone erosions were anti-dsDNA positive vs 54/80 (67.5%) of those without erosions. After Bonferroni correction, IL-23R rs11803505 was found to be associated with the presence of MSUS-detected bone erosions both at genotypic (P_c=0.045) and at the allelic level [P_c=0.022, OR=8.27 (95% CI 1.02–66.90)]. The association of bone erosions with anti-dsDNA and IL-23R11803505 genotype was confirmed in a logistic regression analysis including also age, sex and disease duration (P=0.005 and P=0.02, respectively).
Conclusions: Our study is the first reporting a contribution of IL-23R gene to MSUS-detected erosive damage in SLE. IL-23R gene is a key player in several inflammatory conditions such as psoriatic arthritis, and variants of this gene have already been associated with peripheral erosive disease [2]. Moreover, we confirmed an association between anti-dsDNA and bone erosions in SLE [3], suggesting that the presence of these antibodies is linked with a more aggressive inflammatory pattern of disease.
References:
[1] Ciccacci C, Perricone C, et al. PLoS One. 2014.
[2] Jadon D, Tillett W, et al. Rheumatology (Oxford). 2013.
[3] Galvão V, Atta AM, et al. Joint Bone Spine. 2009.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5989

SAT0616 DIAGNOSTIC MODELING OF SYSTEMIC LUPUS ERYTHEMATOSUS BASED ON NEW AND TRADITIONAL AUTOANTIBODIES- DEMONSTRATION OF FEASIBILITY

P. Budde[1], H.-D. Zucht[1], J. Schulte-Pelkum[1], D.S. Wirtz[1], P. Rengers[1], T. Witte[2], P. Schulz-Knappe[1], M. Schneider[3]. *[1]Protagen Ag, Dortmund; [2]Department of Clinical Immunology, Medical School Hannover, Hannover; [3]Policlinic of Rheumatology, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany*

Background: Given the heterogeneity of clinical presentations, the diagnosis of Systemic Lupus Erythematosus (SLE) can be challenging, in particular in those patients presenting with early or incomplete disease, or with overlapping or atypical features. Autoantibodies (AABs) are important in aiding the clinical diagnosis of SLE, with some few AABs, anti-double-stranded DNA (dsDNA), anti-Smith (Sm), and anti-ribosomal P (riboP) being highly associated with SLE. As none of the traditional AABs has sufficient sensitivity to achieve diagnosis of SLE, current testing is based on measuring multiple AAB assays either in parallel or serial. We have recently identified novel AABs in SLE, which hold promise for improving diagnostic testing of SLE (1). We have developed quantitative ELISA-prototypes for five new AABs, which were tested in combination with traditional AABs.
Objectives: The objectives of this study were to evaluate the diagnostic value of novel AABs and to screen for an optimized combination of novel and traditional AABs using logistic regression to increase the diagnostic accuracy of SLE testing.
Methods: Serum samples were obtained from 156 SLE patients with European ancestry at the rheumatology department of the Heinrich-Heine University (Düsseldorf, Germany), and Hannover Medical School (Hannover, Germany). SLE samples were compared against 126 samples from autoimmune diseases (AID; myositis: n=20; Sjögren's syndrome (SjS): n=31; rheumatoid arthritis (RA) n=36; systemic sclerosis (SSc): n=39), and 77 healthy control samples. Prototype bead based ELISAs were developed for five novel antigens described in (1). Traditional diagnostic AABs were measured using IVD ELISAs and included: SSA/Ro60, SSA/Ro52, La/SSB, Sm, RNP, dsDNA, Scl70, CENPB, Jo-1, CCP, phospholipid and dsDNA. Optimized marker combinations of new and traditional markers were tested using logistic regression and receiver operating curve analysis (ROC).
Results: When comparing 156 SLE patients with 203 control samples, the area under the curve (AUC) of the five novel SLE ELISAs ranged from 0.63 to 0.75. A cut-off was set at a specificity of 95% and yielded a sensitivity ranging from 13.5% to 21.2% for the five novel assays. The sensitivity and specificity of new ELISAs was comparable to traditional ELISAs, which was in this cohort for anti-dsDNA 35% and 97%, anti-Sm 15% and 97%, and anti-RiboP 26% and 97%. A logistic regression model was used to combine the results of multiple tests. Compared to a logistic regression with traditional assays, a logistic regression with novel markers achieved higher sensitivity by pertaining high specificity. The logistic regression model based on a multimarker IVD assay with ten extracted nuclear antigens (ENA) yielded an AUC of 0.87 and a sensitivity of 58% at a specificity of 95%. By contrast, the optimal combination of traditional and novel ELISAs reached an AUC of 0.92 and a sensitivity of 75% at a specificity of 95%.
Conclusions: This study demonstrates the feasibility of combining test results of novel and traditional AABs using logistic regression to increase the diagnostic accuracy for SLE. Further studies are required to assess the impact of different ethnicities on marker selection and algorithm performance.
References:
[1] Budde P et al. (2016). Lupus. (8):812–22.
Disclosure of Interest: P. Budde Employee of: Protagen AG, H.-D. Zucht Employee of: Protagen AG, J. Schulte-Pelkum Employee of: Protagen AG, D. Wirtz Employee of: Protagen AG, P. Rengers Employee of: Protagen AG, T. Witte: None declared, P. Schulz-Knappe Employee of: Protagen AG, M. Schneider Consultant for: Protagen AG
DOI: 10.1136/annrheumdis-2017-eular.4995

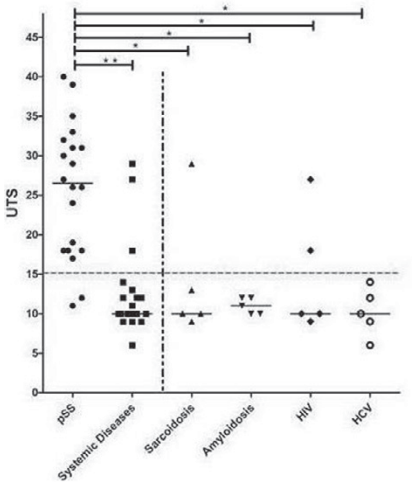
SAT0617 SALIVARY GLAND ULTRASOUND CAN DIFFERENTIATE PRIMARY SJÖGREN'S SYNDROME FROM SYSTEMIC DISEASES WITH SALIVARY GLAND INVOLVEMENT

K. Delli[1], J.F. Van Nimwegen[2], S. Arends[2], A.J. Stel[2], M. Van den Berge[3], W.F. Bierman[4], H. Bootsma[2], F.K.L. Spijkervet[1], A. Vissink[1] on behalf of EULAR US-pSS Study Group. *[1]Oral and Maxillofacial Surgery; [2]Rheumatology & Clinical Immunology; [3]Pulmonology; [4]Internal Medicine, Infectious Diseases Service, University of Groningen, University Medical Center Groningen, Groningen, Netherlands*

Background: Ultrasound of the major salivary glands (SGUS) has shown high diagnostic accuracy for primary Sjögren's syndrome (pSS) [1,2]. None of the existing studies, however, included a control group of patients with sarcoidosis, amyloidosis, human immunodeficiency virus (HIV) or hepatitis C (HCV) infection [2]. These diseases are known to frequently affect the major salivary glands, cause dry mouth or may have histopathology similar to pSS.
Objectives: To assess the diagnostic accuracy of SGUS to differentiate pSS from systemic diseases with salivary gland involvement.
Methods: Twenty consecutive patients fulfilling the AECG criteria for pSS and 20 consecutive patients with well-established systemic diseases, i.e., 5 patients with sarcoidosis, 5 patients with amyloidosis, 5 patients with HIV infection and 5 patients with HCV infection, were included. Echogenicity, parenchymal homogeneity, presence of hypoechogenic areas and clearness of posterior glandular border of both parotid and submandibular salivary glands were scored independently by two blinded observers and rated according to the Hocevar et al scoring system (ultrasound total score (UTS), range: 0–48) [3]. The optimal cut-off point was determined by using ROC curve. The agreement between SGUS positivity and classification as pSS was assessed.
Results: The median age of patients with pSS and systemic diseases was 50 and 53 years, respectively. Daily complaints of dry mouth longer than 3 months, need of liquid to swallow food and recurrent or persistent swelling of the major salivary glands were reported by 95%, 85% and 70% of patients with pSS compared to 45%, 30% and 20% of patients with systemic diseases. The accuracy of SGUS to discriminate pSS was excellent, with an area under ROC of 0.91 and optimal cut off point of 15. The agreement between SGUS and diagnosis for pSS was good (κ=0.75, percentage of absolute agreement 87.5) with a sensitivity of 90%,

specificity of 85%, positive predictive value of 86%, negative predictive value of 89% and diagnostic odds ratio of 51. UTS was positive in 2 patients with HIV infection and one patient with sarcoidosis. Patients with pSS had significantly higher UTS than patients with systemic diseases (median UTS 27 vs. 10, $p<0.001$) and patients of the various subgroups ($p<0.05$; Fig).

Figure: UTS in patient (sub)groups. ** p<0.001, * p<0.05. Black horizontal lines indicate median values. The intermittent horizontal line shows the cut-off point. The intermittent black vertical line separates the two major patient groups (pSS vs. systemic diseases) from the subgroups of patients with sarcoidosis, amyloidosis, HIV and HCV infection.



Conclusions: This pilot study indicates that SGUS has a high diagnostic accuracy to discriminate pSS from associated systemic diseases with salivary gland involvement. A minority of HIV and sarcoidosis patients, however, may show SGUS findings mimicking pSS.

References:

[1] Jousse-Joulin et al. Rheumatology (Oxford) 2016;55:789–800.
[2] Delli et al. Oral Dis 2015;21:792–800.
[3] Hocevar et al. Rheumatology (Oxford) 2005;44:768–72.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3117

SAT0618 DISTURBANCES OF THE ACRAL PERFUSION DETECTED BY FLUORESCENCE OPTICAL IMAGING ARE ASSOCIATED WITH THE DEVELOPMENT OF ISCHEMIC COMPLICATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS

S. Lüders[1], S. Friedrich[1], S. Ohrndorf[1], S. Werner[1], G.-R. Burmester[1], G. Riemekasten[2], M. Backhaus[3]. *[1]Division of Rheumatology and Clinical Immunology, Charité - Universitätsmedizin Berlin, Berlin; [2]Department of Rheumatology, Universität zu Lübeck, Lübeck; [3]Department of Rheumatology, Park-Klinik Weißensee, Berlin, Germany*

Background: Systemic sclerosis (SSc) is a condition causing an impaired microcirculation with the risk of ischemic complications such as digital ulcers and pitting scars (DU/PS). Fluorescence optical imaging (FOI) is an imaging method that detects enhanced microcirculation as a sign of joint inflammation in both hands of patients with rheumatoid arthritis and other arthritides [1, 2]. FOI's impact to record disturbed microcirculation in the hands of patients with systemic sclerosis has not yet been sufficiently investigated.

Objectives: To find associations of disturbed microcirculation initially detected by FOI and the development of new DU/PS throughout a follow-up of 12 months.

Methods: Sixty-three patients with SSc were included and received FOI examination following the Xiralite-System guidelines (ICG 0.1mg/kg BW i.v.; 6 minute duration) as well as capillaroscopy at baseline. After a mean follow-up time of 12 months (min-max: 8–20 months), all participants were followed regarding the development of new ulcers and pitting scars.

Results: A disruption of microcirculation in FOI was defined as a lack of a sufficient fluorescent signal in at least one fingertip over the entire course of the examination and was found in 11 of 63 SSc patients. All patients had a history of DU/PS and frequently presented with a *late pattern* capillaroscopy (9 out of 11) at baseline. Fingers with a disrupted microcirculation also showed a reduced capillary density to a greater extend (96.0%) than fingers with a sufficient signal in FOI (76.0%; p=0.0241).

30 of 60 patients developed digital ulcers or pitting scars during follow up (3 drop outs due to death (n=2) or withdrawal). 81.8% of patients with a disturbed microcirculation in FOI developed these complications during follow-up compared with 42.9% of patients without a disruption in FOI (p=0.0419; OR=6.0 [95% CI 1.2 - 30.7]). A disruption of microcirculation especially increased the risk of developing DU/PS in the same finger: 20.1% of fingers with normal, but 65.4% with a missing FOI signal in the fingertip presented with an ischemic complication during follow-up ($p<0.0001$; OR=7.5 [95% CI 3.3 - 17.3]).

Conclusions: Fluorescence optical imaging can reveal an impaired microcirculation in patients with systemic sclerosis, which is associated with microangiopathic changes as seen in capillaroscopy as well as the subsequent development of digital ulcers and pitting scars. Therefore, FOI might help to identify patients at risk for these complications.

References:

[1] Werner SG et al. Inflammation assessment in patients with arthritis using a novel in vivo fluorescence optical imaging technology. Ann Rheum Dis. 2012 Apr;71(4):504–10.
[2] Werner SG et al. Indocyanine green-enhanced fluorescence optical imaging in patients with early and very early arthritis: a comparative study with magnetic resonance imaging. Arthritis Rheum. 2013 Dec;65(12):3036–44.

Acknowledgements:.
We thank Gabriela Schmittat for technical and Dr. Bernd Schicke, PhD, for statistical assistance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4346

SAT0619 ANKLE EVALUATION IN ACTIVE RHEUMATOID ARTHRITIS BY ULTRASOUND: A CROSS SECTIONAL STUDY

A.M. Elsaman[1], E.S. Mostafa[2], A.R. Radwan[1]. *[1]Rheumatology, Sohag University Faculty of Medicine; [2]Rheumatology, Qena faculty of medicine, Sohag, Egypt*

Background: Ankle joint evaluation is underestimated in many clinical and sonographic scores used for evaluation and follow-up of rheumatoid arthritis (RA) patients. Moreover, sonographic scores which included the ankle joint had no agreement on examination parameters. More effort is needed to detect the value of the ankle joint examination in RA and also a description of the earliest and the most frequent ultrasonographic signs that should be considered in ankle assessment (1).

Objectives: detection of ankle affection by ultrasound (US) in active RA and correlate this finding with disease duration, DAS28-ESR 28 score and rheumatoid factor (RF).

Methods: 126 ankle joints and tendons of 63 active RA patients, aged above 18 years old were included in the study. US examination was done to the tibiotalar and talonavicular joints for synovitis and/or effusion on Greyscale (GS) mode and power doppler (PD). The anterior, lateral and posterior ankle tendons were examined for tenosynovitis and tendinosis.

Results: The mean age and ± standard deviation were 35.1±8.3 with the female-to-male ratio 2:1. The mean disease duration was 22.7±9.6 months. The mean DAS28-ESR 28 score was 3.05±0.66. The most frequent pathologies detected were tenosynovitis of the flexor, extensor or peroneal tendons (found in 30.2% of the affected ankles); followed by synovitis of the tibiotalar and talonavicular joints (18.3%); next was erosion (8.7%) and lastly tendinosis (4%). The earliest sonographic signs were tenosynovitis, followed by synovitis, erosion, and lastly tendinosis.

Conclusions: It can be stated that ankle evaluation should be considered more in RA assessment. The tibialis anterior and posterior tendons, the tibiotalar and talonavicular joints were the commonest and most frequent sites to be involved in the ankle. Tenosynovitis appears earlier than synovitis. DAS28-ESR score was correlated to synovitis and tenosynovitis but not to erosion. Bilaterality and erosion were correlated with disease duration. RF positivity has a positive correlation with positive US findings in the ankle region.

References:

[1] Alsuwaidi M, Ehrenstein BP, Fleck M, Hartung W: Ankle Joint Involvement In Rheumatoid Arthritis. An Ultrasound Study Using High Resolution-and Colour Doppler Ultrasound. In: *Arthritis and Rheumatism: 2013*: Wiley-Blackwell.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4957

SAT0620 POTENTIAL ROLE OF METACARPOPHALANGEAL JOINTS ULTRASOUND IN THE DIFFERENTIAL DIAGNOSIS BETWEEN EARLY RHEUMATOID ARTHRITIS AND EARLY SPONDYLOARTHRITIS

A. Batticciotto, G. Prato, M. Antivalle, M.C. Ditto, M.C. Gerardi, R. Talotta, F. Atzeni, P. Sarzi-Puttini. *Rheumatology Department, ASST-Fatebenefratelli–Sacco."L. Sacco" University Hospital, Milan, Italy*

Background: Several studies have demonstrated that musculoskeletal ultrasound (MSUS) is more sensitive in diagnosing arthritis when compared to clinical examination, although, as underlined in a recent review, still remains controversial whether it can improve substantial discriminatory value in an early arthritis (EA) setting.(1) In 2011 Gutierrez M. et al. published preliminary data on high frequency of peritenon extensor tendon inflammation in Psoriatic arthritis (PsA) patients, suggesting a relevant potential role for US in differential diagnosis between Rheumatoid Arthritis (RA) and PsA at metacarpophalangeal (MCP) joints level and recommending additional research in order to confirm these data.(2)

Objectives: To compare MSUS findings between early RA and early Spondyloarthritis (SpA) patients at MCP joints level.

Methods: From a consenting cohort of EA patients presenting to our Rheuma-

tology Department, we retrospectively selected 35 patients that within one year from the first visit had a defined diagnosis of RA (according with the 2010 ACR/EULAR criteria) or of axial/peripheral SpA (according with the 2009 ASAS criteria). Demographic, clinical parameters and MCPs' MSUS assessment at baseline were recorded during the patients' first EA clinic visit by an experienced Rheumatologist and by a blinded skilled sonographer. ESAOTE MyLAB 70 with 6–18 MHz linear array transducer was used for all patients scanning and US were scored according with OMERACT guidelines.

Results: MSUS data of twenty RA patients (17 F – 3 M; median age of 59 yrs with range 35–83 yrs, median time for defined diagnosis of 2,4 months with range 1–11 months) and 15 SpA patients (9F–6M; median age of 53 yrs with range 18–78 yrs, median time for defined diagnosis of 1,7 months with range 1–8 months) were retrospectively analyzed. At the first EA clinic visit, all patients showed at least one joint with synovial fluid and/or synovial hypertrophy in Grey scale (GS) with a score >1 and no statistically significant differences were found in the percentage of patients that presented at least one joint with power Doppler (PD) positivity (55% RA Vs 53% SpA,p=0,92) and that presented PD positivity tenosynovitis of the flexor tendons in at least one finger (10% RA Vs 33% SpA, p=0,08). A statistically significant difference was found in the percentage of patients with erosions in at least one MCP (25% RA Vs 0% SpA, p=0,036) and in the percentage of patients with PD positive paratenonitis of the extensor tendons in at least one finger (30% RA Vs 80% SpA pts, p=0,003).

Conclusions: Early RA patients showed a statistically higher percentage of erosions at MCPs' MSUS evaluation of the first visit of the EA clinic, when compared with early SpA group and early SpA patients presented at the level of the extensor tendons an higher percentage of PD positive paratenonitis when compared with the early RA group.

References:

[1] Lage-Hansen PR. et al. The role of ultrasound in diagnosing rheumatoid arthritis, what do we know? An updated review. Rheumatol Int.2017Feb;37(2):179–187.

[2] Gutierrez M. et al. Differential diagnosis between rheumatoid arthritis and psoriatic arthritis: the value of ultrasound findings at metacarpophalangeal joints level.Ann Rheum Dis.2011 Jun;70.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5658

SAT0621 AGREEMENT BETWEEN SEMIQUANTITATIVE AND QUANTITATIVE DOPPLER SCORING SYSTEMS FOR THE ASSESSMENT OF SYNOVIAL PATHOLOGICAL VASCULARIZATION IN RHEUMATOID ARTHRITIS

E. Naredo[1,2], I.M. Rutigliano[3], I. Janta[1], C. Scirocco[3], L. Valor[1], F. Figus[4], L. Carreño[1], J. Garrido[5], A. Iagnocco[6]. *[1]Department of Rheumatology, Hospital General Universitario Gregorio Marañón; [2]Department of Rheumatology, Hospital Universitario Fundación Jiménez Díaz. Autonoma University, Madrid, Spain; [3]Dipartimento Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Rome; [4]Dipartimento Reumatologia, Università degli Studi di Cagliari, Cagliari, Italy; [5]Department of Social Psychology and Methodology, Faculty of Psychology, Autonoma University of Madrid, Madrid, Spain; [6]Dipartimento Scienze Cliniche e Biologiche, Università degli Studi di Torino, Turin, Italy*

Objectives: To compare power Doppler (PD) vs colour Doppler (CD) semiquantitative and quantitative scoring of synovial vascularization (RA) and to evaluate the relationship between semiquantitative and quantitative scores in patients with rheumatoid arthritis (RA).

Methods: One hundred RA patients underwent B-mode, PD, and CD assessments of 12 joints at two European centres. Each joint with synovial hypertrophy detected on B-mode was semiquantitatively scored (0–3) for PD (SPD score) and CD (SCD score) synovial signal. PD and CD synovial signal were also quantitatively scored (0–100%) (QPD and QCD scores, respectively) using a software for counting the colour fraction.

Results: We found SH in 184 joints. SPD and SCD agreed in 92.3% (95% CI: 88.4; 96.2%) of paired scores, with Kendall rank correlation coefficient tau-b=0.95. Significant differences between marginal distributions of SPD and SCD were not found (p=0.565). QPD and QCD scores were highly correlated (Pearson's coefficient=0.70) but Blamd-Altman plot showed insufficient agreement, being the QCD scores systematically slightly higher than the QPD scores. The distribution of QPD and QCD values between SPD and SCD scores, respectively, showed significant differences between grade 0 and grade 1 ($p<0.001$), and grade 2 and grade 3 (p=0.042 and p=0.007, respectively) but not between grade 1 and 2 (p=0.154 and p=0.150, respectively).

Conclusions: SPD and SCD scores were concordant and QPD and QCD scores highly correlated although were not concordant. There was consistency between SPD and SCD moderate and severe scores and QPD and QCD scores. There was an overlapping between SPD and SCD mild and moderate scores regarding QPD and QCD scores.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3251

SAT0622 MULTICENTER 14-3-3ETA BIOMARKER REPRODUCIBILITY; THE JAPANESE EXPERIENCE

S. Hirata[1,2], M. Kaneda[3], T. Isayama[3], Y. Gui[4], A. Marotta[4], W.P. Maksymowych[5], Y. Tanaka[2]. *[1]Hiroshima University Hospital, Hiroshima; [2]University of Occupational and Environmental Health, Kitakyushu; [3]Medical & Biological Laboratories, Nagano-ken, Japan; [4]Augurex Life Sciences Corp, Vancouver; [5]University of Alberta, Edmonton, Canada*

Background: The soluble biomarker sub-committee of OMERACT has published validation criteria for biomarkers reflecting structural damage end-points. Within these, categories of Discrimination and Feasibility relate to assay reproducibility and performance. 14–3-3eta (η) is a joint-derived biomarker that drives joint damage processes and informs radiographic progression independently of acute phase reactants. As an ELISA assay, 14–3-3η is currently available for clinical use as a laboratory developed test (LDT) in the United States (US) and as an in-vitro diagnostic (IVD) in Canada. The ELISA is (CE) marked for Europe and is Therapeutics Good Administration (TGA) approved for Australia. Previous studies have described 14–3-3eta assay equivalence at independent laboratories in the US and Canada.

Objectives: The purpose of this study was to demonstrate the reproducibility of 14–3-3eta measurements at two independent laboratories in Japan and one in Canada.

Methods: A total of 212 samples from the University of Occupational and Environmental Health were provided for this study. Serum 14–3-3eta measurements were performed using the 14–3-3eta ELISA provided by Augurex. Testing in Canada occurred in August 2015; these 14–3-3eta values were set as the "standard". The 212 samples were shipped from Canada to Japan in January 2016 with testing being performed in February 2016. Testing at MBL was performed on a blinded-basis. Upon completion of testing, results were sent to the investigators at which point in time, MBL was unblinded. 14–3-3eta positivity was defined at $\geq$0.19ng/ml. Contigency and Spearman analyses were performed to assess the strength of the results between the two testing centres. Values above the linear range of the assay i.e. $\geq$20ng/ml were excluded for the Spearman analyses and determination of the median (IQR). A p-value of <0.05 established statistical significance.

Results: In Canada, of the 212 samples tested, 146 (68.8%) were 14–3-3eta positive and in Japan, 147 (69.3%) were positive. In Canada, 187 patients had reportable values in the linear range and in Japan 186 did. Median 14–3-3eta levels in Canada were 0.51 ng/ml (IQR: 0.11–2.09) and in Japan they were 0.58 ng/ml (IQR: 0.02–2.68), respectively. Spearman correlation analysis revealed a highly significant correlation between the two testing sites, r=0.92; $p<0.00001$. Contingency analysis revealed a strong concordance between the two sets of results delivering a likelihood ratio (LR) of 156, $p<0.0001$. Between the two sites, 58 of the samples were 14–3-3eta negative and 139 were positive; there was agreement in 197 (93%) of the 212 samples.

Conclusions: As defined by the soluble biomarker sub-committee of OMERACT, reliability and standardization of biomarker assessments in routine clinical practice across the globe and in clinical studies is of high importance. The results presented herein demonstrate that the 14–3-3eta assay is highly reliable, that testing/delivery of results can be standardized between two independent laboratories, and that it is very stable over time and when shipped between continents.

Disclosure of Interest: S. Hirata: None declared, M. Kaneda Employee of: Medical & Biological Laboratories, T. Isayama Employee of: Medical & Biological Laboratories, Y. Gui Employee of: Augurex Life Sciences Corp., A. Marotta Employee of: Augurex Life Sciences Corp., W. Maksymowych Consultant for: Augurex Life Sciences Corp, Y. Tanaka: None declared

DOI: 10.1136/annrheumdis-2017-eular.5543

SAT0623 CORRELATIONS BETWEEN CLINICAL, ULTRASOUND AND DISEASE ACTIVITY SCORES OF PERIPHERAL ENTHESITIS IN SPONDYLOARTHRITIS (SPA)

A. Haddouche, S. Haid, S. Bencheikh, S. Slimani, A. Abdessemed, N. Brahimi, A. Ladjouze. *Medicine, University of Algiers 2, Algiers, Algeria*

Objectives: To look for correlations between clinical, ultrasound (US) and disease activity scores of peripheral enthesitis in an SpA cohort.

Methods: A prospective study of all SpAs meeting SpA ASAS criteria followed at EHS Ben Aknoun, over a period from January 2015 to April 2016. Seventeen entheseal sites were assessed bilaterally: insertions of supra-spinatus, infra-spinatus, sub-scapular, medial and lateral epicondylars, triceps brachialis, gluteus midius and minimus, quadricipital, proximal and distal insertion (patellar ligament, medial and lateral collateral ligament), Achilles tendon and plantar aponeurosis. Peripheral entheses was assessed by the following clinical scores: Enthesitis Peripheral Score (PES= Sum of symptomatic peripheral entheses sites on clinical examination), Visual Analog Scale of peripheral enthesitis (VAS), Spondyloarthritis Research Consortium of Canada score (SPARCC) as well as the following US enthesitis scores: Acute Enthesitis score (Sum of acute enthesitis US scores for each site), Chronic Enthesitis score (Sum of US chronic enthesitis scores for each site), Global Enthesitis score (Sum of the acute and chronic US scores of enthesitis), Doppler signal Enthesitis score (Sum of Doppler signal scores less than 2mm from cortical bone for each site), Madrid Sonography Enthesitis Index (MASEI), Simplified Echographic Score (SES) wich assesses only the Achilles

tendon and the plantar aponeurosis. Correlations between clinical, activity and US scores were investigated by SPPSS software.

Results: A total of 208 patients were included. At examination 88.9% had an active disease and 64.4% of SpA were taking NSAIDs. 6240 entheses were assessed clinically and with US. A positive correlation was found between activity scores and two clinical scores (Peripheral Enthesitis Score, SPARCC). A good correlation was found between Activity scores and all US scores on one hand and with SPARCC scores and PES scores on the other hand. For US and clinical correlations, only Doppler scores was positively correlated with 2 clinical scores (SPARCC and PES scores), Acute Enthesitis scores was correlated with the PES scores. No correlation was found between clinical scores and MASEI or SES scores. No correlation was found with the mean enthesitis VAS scores.

Table 1. Correlations between clinical scores and activity scores with ultrasound scores

scores	PES	VASm Enthestis	SPARCC	ASDAS-vs	ASDAS-crp
Acute Enthesitis	r: 0,14	r: -0,03	r: 0,16	r: 0,43	r: 0,52
	p: 0,04	p: 0,72	p: 0,07	**p<0,001**	**p<0,001**
Chronic Enthesitis	r: 0,07	r: -0,15	r: 0,06	r: 0,19	r: 0,22
	p: 0,30	p: 0,03	p: 0,41	**p: 0,006**	**p: 0,002**
Global Enthesitis	r: 0,15	r: -0,08	r: 0,13	r: 0,43	r: 0,52
	p: 0,03	p: 0,24	p: 0,07	**p<0,001**	**p<0,001**
Doppler Enthesitis	r: 0,16	r: -0,001	r: 0,18	r: 0,34	r: 0,36
	p: 0,02	p: 0,99	**p: 0,01**	**p<0,001**	**p<0,001**
MASEI	r: 0,09	r: -0,08	r: 0,12	r: 0,44	r: 0,34
	p: 0,19	p: 0,23	p: 0,07	**p<0,001**	**p<0,001**
SES	r: 0,04	r: -0,04	r: 0,09	r: 0,31	r: 0,38
	p: 0,55	p: 0,59	p: 0,18	**p<0,001**	**p<0,001**

Table 2. Correlations between clinical scores and activity scores

	PES	VASm Enthestis	SPARCC
ASDAS-vs	r: 0,32	r: -0,04	r: 0,27
	p<0,001	p: 0,62	**p<0,001**
ASDAS-crp	r: 0,31	r: -0,03	r: 0,27
	p<0,001	p: 0,62	**p<0,001**

Conclusions: All US enthesitis scores were correlated with disease activity scores but those correlated with the clinical symptoms and not with its intensity were: Acute Enthesitis Scores, Global Enthesitis Scores and especially Doppler signal Enthesitis Scores.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1968

SAT0624 QUANTITATIVE 3D IMAGING OF TENOSYNOVITIS AND BONE MARROW EDEMA BY DCE-MRI IS A SENSITIVE MEASURE OF RESPONSE TO THERAPY IN RHEUMATOID ARTHRITIS

C. Roberts[1], G. Guillard[2], M.A. Bowes[2], J. Burlison[2], A. Khan[2], N. Maguire[1], S. Gotla[1], A. Morgan[1], G.J. Parker[1,3], R. Hodgson[3,4], J. Freeston[4], E.M. Vital[4], P. Bird[5], P. Emery[4], P.G. Conaghan[4]. *[1]Bioxydyn; [2]Imorphics; [3]Centre for Imaging Sciences, University of Manchester, Manchester; [4]University of Leeds, Leeds, United Kingdom; [5]Combined Rheumatology Practice, Sydney, Australia*

Background: Quantitative analysis of tissue microvascular function using dynamic contrast-enhanced MRI (DCE-MRI) shows promise for improved understanding of synovial pathophysiology in rheumatoid arthritis (RA). Assessing tenosynovitis and bone marrow edema (BME) using physiologically-interpretable measures such as *K*trans may offer additional insights; this will require increased precision in quantification.

Objectives: To apply a 3D DCE-MRI method to quantify capillary permeability (K^{trans}) in tendons, bone marrow edema, and to explore muscle involvement. To generate precise and consistent 3D regions of interest (ROI) of tenosynovitis and BME using active appearance models (AAMs)? and evaluate response to therapy within these regions.

Methods: MR images of the hand were acquired in 27 patients with established RA who had recently commenced the same biological therapy. Subjects were imaged at 0,3,6 months. The MRI protocol included pre- and post-contrast high-resolution 3D FLASH acquisitions. The DCE-MRI scan protocol included T1 mapping sequences followed by 15 sequential volumes acquired over 5 minutes, during which a bolus of gadolinium (0.1 mmol/kg) was administered at 2 ml/s at the beginning of the 5th volume measurement. The Extended Kety model was applied to each voxel concentration-time series within ROIs, allowing voxelwise estimates ofK^{trans}. Pre-contrast T1-weighted mages were searched using 3D active appearance models (AAMs) to reliably identify tendons and their sheath in the carpal tunnel region as well as bones and marrow area. Images from the dynamic series were registered to the high-resolution pre-contrast images, providing standardised 3D ROIs for each of the regions. Median K^{trans} was summarised in each patient for each ROI. T-test ($p<0.05$) determined significant differences from baseline.

Results: Differences in baseline *K*trans were observed in each tissue type and demonstrated that highest levels of inflammation within the synovium, followed by tenosynovitis, BME and detection of low grade inflammation in the muscle (Fig. 1). Significant post-therapy responses in *K*trans, indicating a reduction in perfusion and capillary permeability associated with reduced inflammation, were seen in each of these tissue types (Fig.1). RAMRIS scoring showed no significant change at either 3 or 6 months. 3D visualisation of *K*trans in tenosynovitis revealed additional spatial response to the biological treatment (Fig. 2) – most of the remaining tenosynovitis at 6 months had lower permeability with almost all of the higher permeability class of synovitis disappearing after therapy.

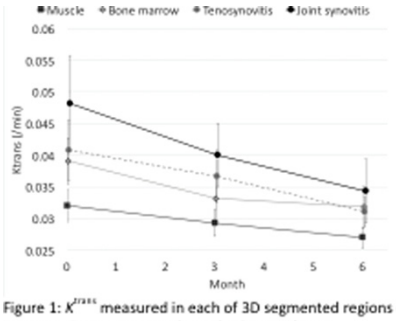


Figure 1: K^{trans} measured in each of 3D segmented regions of interest. Group mean and standard error shown.

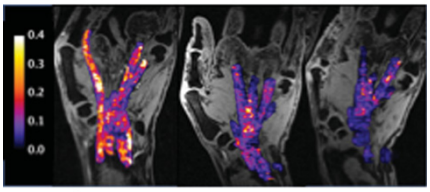


Figure 2: K^{trans} (/min) maps overlaid on post-contrast T_1-weighted images from an example patient imaged at baseline (left), 3 months post-therapy (centre) and 6 months (right).

Conclusions: 3D DCE-MRI measures of tenosynovitis and bone marrow edema are practical in RA MR imaging trials, and offer sensitivity to change and differential tissue response not visible with other methods. Therapy-induced response in muscle suggests that there may be an inflammatory process in RA affecting local muscle groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6584

SAT0625 ULTRASOUND ASSESSMENT OF JOINTS AND ENTHESIS IN A COHORT OF PATIENTS AFFECTED BY OCHRONOSIS: HOW COMMON IS INFLAMMATION?

C. Toscano[1], V. Di Sabatino[1], A. Adinolfi[1], M. Bardelli[1], V. Picerno[1], E. Selvi[1], A. Santucci[2], M. Galeazzi[1], B. Frediani[1], G. Filippou[1]. *[1]Department of Medicine, Surgery and Neuroscience; [2]Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Siena, Italy*

Background: Ochronosis, the musculoskeletal manifestation of alcaptonuria (AKU), is characterized by alterations of the spine and large joints of the limbs similar to those of osteoarthritis. However, some cases of spinal involvement that resembles spondiloarthritis (SpA) have been describe, suggesting a prevalent inflammatory involvement of the joints.

Objectives: To evaluate the prevalence of inflammatory abnormalities in peripheral joints and enthesis of a cohort of patients affected by AKU.

Methods: consecutive patients with definite diagnosis of AKU (with or without clinical manifestations) referred at our clinic from 2014 to 2016 were enrolled. All patients underwent a US examination of the following sites bilaterally: metacarpo-phalangeal joints (MCP), proximal interphalangeal joints (PIP), radiocarpal/mid carpal joints, elbow, gleno-humeral, hip, knee, ankle and metatarso-phalangeal (MTP) joints; flexor and extensor tendons of fingers and wrist and the ankle tendons. Further, the enthesis of the rotator cuff of the shoulder, triceps, quadriceps, patellar and Achilles tendon were assessed. Joints and tendons with a synovial sheath were assessed for effusion, synovial hypertrophy and power Doppler (PD) signal while enthesis were evaluated for the presence of PD signal, enthesophytes and calcifications. All the US lesions were scored using a dichotomous scale (presence/absence). All US exams were performed by an expert sonographer blind to clinical history, using an Esaote MyLab70 scanner equipped with high resolution linear probes.

Results: 11 patients (6 women) were enrolled in this study with a mean age of 57 yo (SD±11,50). the mean number of joints with effusion was 3,9 for each patient (median 3, range 2–8) while the mean number of joints with synovial hypertrophy was of 2,9 (median 2, range 2–7). =0,18 joints (median 0, range 0–2) presented also PD signal. I The mean number of exudative tenosynovitis was0,81 (median 2, range 0–3) while proliferative tenosynovitis (mean 0,54, median 0, range 0–2) and PD in tendons with sheaths (mean 0,27, median 0, range 0–2) were rare. Finally, the mean number of enthesis with PD was 1,27 (median 1, range 0–7), the mean number of enthesophytes was 0,63 (median 0, range 0–3) and for calcifications 4,27 (median 5, range 1–8).

Conclusions: Ochronotic arthropathy is believed to be characterized by a widespread articular damage, correlated mainly to degenerative processes due to the deposition of Homogentisinic Acid in the joints. The results of this US study

showed that joint inflammation is common in ochronotic patients, associated in some cases with peripheral enthesis involvement confirming previously published data (1). The prevalence and the characteristics of the inflammatory manifestations should be further studied in larger cohorts of patients as they could play an important role in the joint damage process in these patients and provide a rationale for the use of new drugs.

References:
[1] Filippou G, Frediani B, Selvi E et al, Tendon involvement in patients with ochronosis: an ultrasonographic study. Ann Rheum Dis 2008 Dec;67(12): 1785–6.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6678

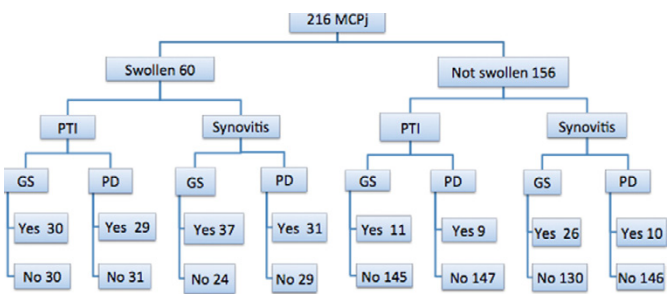
SAT0626 METACARPOPHALANGEAL JOINT SWELLING IN PSORIATIC ARTHRITIS: WHAT DOES IT MEAN?

C. Macía[1], S. Falcao[2], M. Gutierrez[3], J. Medina[4], H.B. Hammer[5], E. De Miguel[6]. *[1]Rheumatology, Hospital Universitario Severo Ochoa, Madrid, Spain; [2]Rheumatology, Chronic Diseases Study Center (CEDOC), NOVA Medical School, UNL, Lisboa, Portugal; [3]Rheumatology, Division of Musculoskeletal and Rheumatic Disorders. Instituto Nacional de Rehabilitación, Mexico City, Mexico; [4]Rheumatology, Hospital Clínico Universitario, Valladolid, Spain; [5]Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; [6]Rheumatology, Hospital Universitario la Paz, Madrid, Spain*

Background: Clinical metacarpophalangeal joint (MCPj) swelling is a frequent finding in psoriatic arthritis (PsA). It is assumed to be caused by intra-articular synovitis (IAS). However, ultrasound (US) have also demonstrated in PsA peritenon inflammation of the extensor digitorum tendon (PTI).To date the data about the significance of this two lesions (IAS and PTI) in MCPj swelling are sparse.
Objectives: Our objective was to explore PTI and IAS as the cause of clinical MCPj swelling in PsA patients.
Methods: 27 consecutive non selected PsA patients, fulfilling CASPAR criteria, with clinical involvement of at least one 2nd to 5th MCPj were included. A MyLab 70 XVG machine, Esaote, Genova, Italy, with a greyscale (GS) 13 MHz probe, and a 7.1 MHz power Doppler (PD) frequency (PRF 750 Hz, Gain 60) was used. Videos (3–5 sec) of each MCPj 2nd to 5th of both hands in transversal and longitudinal views were obtained for central reader analysis, scoring US as presence or absence in GS and PD of: 1) PTI (defined as an hypoechoic swelling of the soft tissue surrounding the extensor tendon at MCPj level with or without PD) and 2) IAS (OMERACT definition). US pathology for each joint and lesion was defined as at least three of five central readers having the same score. SPSS analysis was performed for frequencies, percentage of agreement and Cohen's Kappa test.
Results: 27 PsA patients with a mean (SD) age of 56 (11) years and disease duration 109 (101) months were included. Isolated peripheral involvement was present in 21 patients (78%) and 6 (22%) had both axial and peripheral affection. Mean (SD) CRP level was 8.3 (8.2) mg/l and ESR 21.9 (19.3) mm. The mean DAS28 ESR was 3.88 (1.23). Psoriasis involvement included skin and nails in 15 (55.5%) of the patients.
A total of 216 MCPj were examined, with 60 (27,7%) being clinically swollen. The figure illustrates the agreement between clinical and US assessments, and the table shows the kappa values for the agreements. PTI in at least one MCPj was found in 19/27 patients (70%) with a total of 41/216 locations (19%) in GS. For IAS, there was GS in at least one MCPj in 23/27 patients (85%) with a total of 63/216 locations (29%). 28 of 41 (68.3%) joints had both PTI and IAS.

Table 1. US findings versus Clinical joint swelling

	Agreement n (%)	Kappa
Any US lesion (vs. clinical swelling)	167/216 (77.3%)	0.471
Any grey scale lesion (vs. clinical swelling)	166/216 (76.8%)	0.426
Any power Doppler lesion (vs. clinical swelling)	169/216 (78.2%)	0.550
Grey scale IAS (vs. clinical swelling)	166/216 (76.8%)	0.426
Power Doppler IAS (vs. clinical swelling)	177/216 (81.9%)	0.499
Grey scale PTI (vs. clinical swelling)	175/216 (81.0%)	0.474
Power Doppler PTI (vs. clinical swelling)	176/216 (81.5%)	0.478



Conclusions: Our study identifies two different US lesions (IAS and PTI) causing clinical joint swelling. PTI is near as frequent as IAS as a cause of MCPj swelling, and future studies are necessary to explore the added value of assessing PTI for prognosis or treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1437

SAT0627 MUSCLE BIOPSY: MASTER ROLE IN DIFFERENTIAL DIAGNOSIS IN PATIENTS WITH SUSPECTED MYOPATHY

D. Santos-Faria, J. Sousa-Neves, M. Cerqueira, J.L. Silva, J.R. Rodrigues, D. Peixoto, J. Tavares-Costa, S. Alcino, C. Afonso, F. Teixeira. *Rheumatoloy, Unidade Local de Saúde do Alto Minho, Ponte de Lima, Portugal*

Background: The muscle biopsy may be a fundamental technique in the suspicion of myopathy, with high specificity to distinguish between normal or abnormal muscle tissue. In association with clinical and laboratory findings, the muscle biopsy has an important role to a more accurate diagnosis.
Objectives: To evaluate the usefulness and safety of muscle biopsies performed in a Rheumatology Unit in patients with suspected myopathy.
Methods: Retrospective analysis of the clinical charts of patients submitted to muscle biopsy between January 2010 and December 2016 at our Rheumatology Unit. Demographic, clinical, laboratory, electromyographic and histological data were collected. The histological study was performed in a Neuropathology Specialized Unit.
Results: A total of 46 patients, 19 men and 27 women, with a mean age of 53.3±17.1 years, were evaluated. Clinical manifestations included muscle weakness, myalgia and decreased muscle strength. Most patients also had increased muscle enzymes, particularly creatine kinase, but in a patient with generalized muscle atrophy, muscle enzymes were overall diminished. Of the 46 biopsies, 12 (26.1%) did not show alterations, 8 (17.4%) showed nonspecific alterations and only 1 biopsy was not conclusive because the sample was inadequate. In 4 patients, the histological features did not present specific characteristics of a myopathy, but revealed a preferential atrophy of type 2 fibbers, usually associated with prolonged corticosteroid therapy. Among the others, 9 (19.6%) were compatible with inflammatory myopathies, namely polymyositis (6), dermatomyositis (1), inclusion body myopathy (1), and localized nodular myositis (1). In the latter case, the patient had a different clinical presentation, with intermittent episodes of pain, oedema and flushing of different muscle groups. In addition, 5 metabolic myopathies (2 McArdle's diseases and 3 non-specific metabolic disorders), 2 muscular dystrophies (1 Becker's muscular dystrophy and 1 dystrophinopathy), 1 suspected case of myotonic dystrophy and 1 myopathy associated with statins use were diagnosed. In a patient with muscle weakness and prior diagnosis of systemic vasculitis, the histology showed a chronic inflammatory process with no specific alterations. In the patient with overall decrease in muscle enzymes, the biopsy revealed neurogenic atrophy, without inflammatory infiltrates. Overall, the results of electromyography (EMG) did not correlate with the histological findings, because EMG identified alterations both in cases with histologically compatible inflammatory myopathy and in cases without histological pathology. On the other hand, EMG did not reveal any changes in some of the metabolic myopathies. Muscle biopsies were performed mainly in the deltoid muscle. There were no relevant immediate or late complications with this technique.
Conclusions: Although muscle biopsy is an invasive technique, it is a safe technique and allows the differential diagnosis between the various myopathies, which is fundamental to an appropriate treatment.

References:
[1] Michelle EH, Mammen AL. Myositis Mimics. Curr Rheumatol Rep. 2015; 17(63):1–8.
[2] Barsotti S, Terenzi R et al. One year in review 2015: idiopathic inflammatory myopathies. Clin Exp Rheumatol. 2015;33(5):593–601.

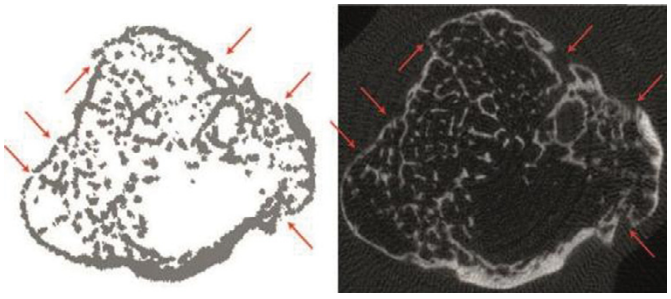
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5069

SAT0628 INCREASE OF CORTICAL MICRO-CHANNELS (COMICS) AS A NEW FEATURE OF STRUCTURAL DAMAGE IN PAIENTS WITH RHEUMATOID ARTHRITIS

D. Werner[1,2], D. Simon[1], M. Englbrecht[1], F. Stemmler[1], A. Berlin[1], J. Haschka[3], N. Renner[4], T. Buder[5], J. Rech[1], K. Engelke[6], A.J. Hueber[1], G. Schett[1], A. Kleyer[1]. *[1]Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Erlangen; [2]Rheumatologie & Nephrologie, Städtisches Klinikum Dresden, Dresden, Germany; [3]St.Vincent Hospital, Medical Department, Academic Teaching Hospital of Medical University of Vienna, Vienna, Austria; [4]Department of Trauma and Orthopedic Surgery, Friedrich-Alexander-Unviersity Erlangen-Nuremberg; [5]Institute of Anatomy, Friedrich-Alexander-University Erlangen-Nürnberg (FAU); [6]Institute of Medical Physics, Friedrich-Alexander-University Erlangen-Nuremberg Erlangen, Erlangen, Germany*

Background: Bone damage in rheumatoid arthritis (RA) typically emerges at certain anatomical hotspots corresponding to the so-called "bare area", an intra-articular region between the cartilage and the insertion site of the joint capsule (1,2). We hypothesized that this region exhibits certain micro-anatomical properties, which facilitates the emergence of bone erosions.

Objectives: To find the micro-structural correlate of the origin of bone erosions in the bare area of the human joint
Methods: Bare areas of human joints were analyzed for early microstructural changes by in-vivo high-resolution peripheral computed tomography (HR-pQCT). First, bare areas were exactly defined by scanning 6 cadaveric hands for localization of the bare area in the human metacarpal head. Bone lesions found in the cadaveric hand by HR-pQCT were additionally by super-resolution ex vivo micro-CT (μCT40). Then, number and distribution of the type of bare area bone lesion found in cadaveric study were analyzed in a cohort of 105 healthy individuals and 107 anti-citrullinated peptide (ACPA) positive RA patients with similar sex and age distribution.
Results: HR-pQCT combined with adaptive thresholding allowed the definition of a new type of bone lesions in the bare areas of the human joint termed "COMIC" standing for "cortical micro-channel". Their existence in the bare area was additionally validated by microCT (Figure 1). RA patients showed significantly ($p<0.001$) more CoMiCs (112.9±54.7/joint) than healthy individuals (75.2±41.9/joint) with 20–49 years old RA patients exhibiting similar CoMiC numbers as observed in over 65 year old healthy individuals. Importantly, CoMiCs were found in RA patients already very early in their disease course with enrichment in the erosion-prone radial side of the joint.

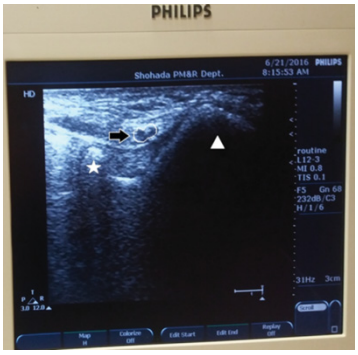


Conclusions: CoMiCs represent a new structural feature of the joint, which is characteristic for the bone of the bare area. COMICS at low level are also found in young healthy individuals but they significantly increase with age and particularly with RA. COMICs develop much earlier and much more pronounced in RA patients than in healthy individuals and therefore represent an interesting new early indicator for erosion development in ACPA positive RA patients.
References:
[1] Stach CM, Bauerle M, Englbrecht M, Kronke G, Engelke K, Manger B, et al. Periarticular bone structure in rheumatoid arthritis patients and healthy individuals assessed by high-resolution computed tomography. Arthritis & Rheumatism. 2010;62(2):330–9.
[2] Simon D, Kleyer A, Stemmler F, Simon C, Berlin A, Hueber AJ,Haschka J, Renner N, Figueiredo C, Neuhuber W, Buder T, Englbrecht M, Rech J, Engelke K, Schett G. Age- and Sex-Dependent Changes of Intra-articular Cortical and Trabecular Bone Structure and the Effects of Rheumatoid Arthritis. J Bone Miner Res. 2016 Oct 27. doi: 10.1002/jbmr.3025. [Epub ahead of print].
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3730

SAT0629 ELECTRODIAGNOSTIC VS ULTRASONOGRAPHY: WHICH ONE IS BETTER TO CONFIRM DIAGNOSIS OF ULNAR NEUROPATHY AT ELBOW?

S.M. Rayegani[1], E. Loni[2], S.A. Raeissadat[3], E. Kargozar[4], S. Rahimi Dehgolan[1]. *[1]Physical Medicine and Rehabilitation Research Center, Shahid Beheshti University of Medical Sciences; [2]Rofeideh rehabilitation Hospital, University of Social Welfare and Rehabilitation Sciences; [3]Physical Medicine and Rehabilitation Research Center, ShahidBeheshti University of Medical Sciences; [4]Physical Medicine and Rehabilitation, Baharloo Hospital, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran, Islamic Republic Of*

Background: Ulnar neuropathy at the elbow is the second most common compression neuropathy preceded by carpal tunnel syndrome. Although this diagnosis has been traditionally confirmed by electrodiagnosis (EDX), ultrasonography (US) is a re-emerging alternative method which can also evaluate the cubital zone anatomy. This study determines the maximum amount of US sensitivity and specificity by assessing different sonographic parameters and evaluates consistency and diagnostic value of the best US method in compare with EDX.
Methods: We included 66 participants (32 elbows of patient and 34 normal elbows) and performed physical exam, US and EDX for both groups. Patients were classified into four severity grades using EDX criteria. The parameters of US were cross sectional area (CSA) of ulnar nerve at three levels: medial epicondyle (CSA med), 2cm distal (CSA dist) and 2cm proximal (CSA prox) to medial epicondyle. Then we would be able to evaluate consistency between two tests using area under receiver operating curve (AU-ROC) method and also to determine the optimum CSA cut-off point to better diagnosis of ulnar neuropathy by US.
Results: Our findings showed that CSA med and CSA dist had significantly larger size in patients compared to normal participants (P-value =0.01 and 0.05, respectively). This increase in nerve size was more prominent among those who had axonal lesion rather than patients with demyelinated lesion (p-value <0.01). Moreover those who had longer duration of symptoms had significantly higher CSA med. and CSA dist. (p-value=0.015 and 0.001 respectively). The other promising findings were two important points; First a strong correlation between CSA med. and severity grade (p-value=0.034) and the second correlation was between CSA med and CSA dist. with a cross-elbow nerve conduction velocity (NCV) (p-value=0.01 and 0.02, respectively). Finally we assessed US diagnostic value as it showed AU-ROC =0.871, that means a very good coverage for an alternative diagnostic method. Also our results showed specificity of 80% and sensitivity of 84% for US in the CSA med cut-off point =9mm^2 for diagnosis of ulnar nerve entrapment at elbow.



Conclusions: Based on these results we can conclude that US is a highly sensitive and specific method to diagnose ulnar neuropathy at elbow and can be used as an alternative and complementary method in diagnosis of ulnar neuropathy at elbow in particular when EDX is not available. However it could not be still a definitive and substitute mutually exclusive method to EDX in diagnosis of ulnar neuropathy
Acknowledgements:
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1694

SAT0630 EXTRA-ARTICULAR MUSCULOSKELETAL INVOLVEMENT IN JUVENILE IDIOPATHIC ARTHRITIS: CLINICAL AND ULTRASONOGRAFIC FINDINGS

V. Ravagnani[1], F. Licciardi[2], D. Montin[2], F. Santarelli[3], S. Martino[4], C. Cirone[5]. *[1]Internal Medicine, ASST MANTOVA - C. Poma Hospital, Mantova; [2]ImmunoRheumatology Unit, Regina Margherita Children Hospital Città della Salute e della Scienza; [3]ImmunoRheumatology Unity, Regina Margherita Children Hospital, Città della Salute e della Scienza; [4]ImmunoRheumatology Unity, Regina Margherita Children Hospital Città della Salute e della Scienza; [5]ImmunoRheumatology Unit, Regina Margherita Children Hospital, Città della Salute e della Scienza, Torino, Italy*

Background: in Juvenile Idiopathic arthritis (JIA), musculoskeletal ultrasound (MSUS) has been proven to be more sensitive than clinical evaluation in detecting articular synovitis. Nevertheless, many studies report a variable percentage of clinically active joints, that are judged normal by ultrasound examination. In absence of a feasible and reliable gold standard for pediatric synovitis (histology or MRI), this point may weaken the confidence in ultrasound, that is nevertheless perceived as an interesting tool, in the management of JIA.
Objectives: This preliminary study investigates the possibility that sometimes the clinically detected synovitis could be missed by ultrasound, because of its extra-articular localization.
Methods: 43 consecutive children affected by JIA underwent separated clinical and ultrasound assessments, blindly, in the same day. Patients were followed up in a pediatric Rheumatology Unit. The following clinical data were collected: age, sex, disease duration, subset of JIA, ongoing therapy, previous therapy, disease activity. By MSUS, the synovitis was investigated bilaterally, both in gray scale and power Doppler, in the MCP and subtalar joints, wrists, knees, ankles, in the flexor and extensor tendons of the wrist and hand, in the anterior, medial and lateral tendons of the ankle, in the synovial bursae of knee and ankle. The possible involvement of the entheses was also investigated. The definition of ultrasonographic synovitis was based on the preliminary OMERACT definitions of synovitis in children. The inter and intra observer reproducibility of the MSUS examination was tested, independently, both between two operators and through a second assessment of the stored images.
Results: 43 children affected by JIA were recruited, in the outpatient clinic of the Regina Margherita Pediatric Hospital of Torino, Italy. They were 9 boys and 34 girls, median age 7,7 (IQR 5,5–10,1), 27 oligoarticular, 11 poliarticular, 4 psoriatic arthritis, 1 undifferentiated arthritis. The median disease duration was 44 months (IQR: 20,5–61,5), 20 patients in remission, 23 with active disease. 774 joints, 1548 synovial sheaths, 430 entheses and 258 synovial bursae were assessed. The physical examination detected inflammation in 54 joints, 33 tendons, 0 entheses,

0 bursae. Ultrasound abnormalities were found in 62 joints, 73 tendons, 8 bursae, 0 entheses. Overall physical examination and MSUS showed good concordance even if MSUS was more sensitive especially in detecting extra-articular locations.
Conclusions: If the extra-articular locations of synovitis are taken in consideration during the ultrasound examination, there is a good sensitivity of MSUS and a better concordance between clinical and MSUS assessment of JIA. MSUS seems more accurate than physical assessment in detecting the exact position of the inflamed synovial membrane in each anatomical location (joint, synovial sheath, synovial bursa). It could be helpful not only for better addressing the injective procedures, but also for a global quantification of the synovitis (both intra and extra-articular), even if the exact clinical meaning of these ultrasound findings is still unknown, in terms of response to treatments and prognosis.
References:
[1] Magni-Manzoni S. Arthritis and rheumatism. 2009 Nov 15; 61(11):1497–1504.
[2] Roth J. Arthritis Care Res (Hoboken). 2016 Oct 16.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6900

SAT0631 INTER-OBSERVER AND INTRA-OBSERVER RELIABILITY OF THE OMERACT ULTRASONOGRAPHIC (US) CRITERIA FOR THE DIAGNOSIS OF CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD) AT THE METACARPAL-PHALANGEAL (MCP), WRIST, ACROMION-CLAVICULAR (AC) AND HIP JOINTS

G. Filippou[1], C.A. Scirè[2], N. Damjanov[3], A. Adinolfi[1], G. Bruyn[4], G. Carrara[5], T. Cazenave[6], M.-A. D'Agostino[7], A. Delle Sedie[8], M.E. Diaz Cortes[9], E. Filippucci[10], F. Gandjbakhch[11], M. Gutierrez[12], D. MacCarter[13], M. Micu[14], I. Moller[15], G. Mouterde[16], M.A. Mortada[17], E. Naredo[18], V. Picerno[1], C. Pineda[12], F. Porta[19], A.M. Reginato[20], I. Satulu[21], W.A. Schmidt[22], T. Serban[23], L. Terslev[24], V. Vlad[25], F. Vreju[26], P. Zufferey[27], S. Bellavia[1], P. Bozios[28], V. Di Sabatino[1], C. Toscano[1], A. Iagnocco[29] on behalf of OMERACT US subtask force in CPPD. *[1]University of Siena, Siena; [2]University of Ferrara, Ferrara, Italy; [3]University of Belgrade, Belgrade, Serbia; [4]Department of Rheumatology, MC Groep, Lelystad, Netherlands; [5]SIR Epidemiology Unit, Milan, Italy; [6]Instituto de Rehabilitación Psicofísica, Buenos Aires, Argentina; [7]Université Versailles Saint-Quentin en Yvelines, Paris, France; [8]University of Pisa, Pisa, Italy; [9]Fundacion Santa Fe de Bogotà, Bogotà, Colombia; [10]Università Politecnica delle Marche, Jesi, Italy; [11]Hôpital la Pitié Salpêtrière, Paris, France; [12]Instituto Nacional de Rehabilitación, Mexico City, Mexico; [13]North Valley Hospital, MT, United States; [14]Rehabilitation Clinical Hospital, Cluj-Napoca, Romania; [15]InstitutoPoal, Barcellona, Spain; [16]Centre Hospitalier Universitaire de Montpellier, Montpellier, France; [17]Zagazig University, Zagazig, Egypt; [18]Hospital GU Gregorio Marañón, Madrid, Spain; [19]Hospital of Pistoia, Pistoia, Italy; [20]Brown University, RI, United States; [21]Kalmar County Hospital, Kalmar, Sweden; [22]Immanuel Krankenhaus Berlin, Berlin, Germany; [23]Cantacuzino Hospital, Bucharest, Romania; [24]Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark; [25]Sf. Maria Hospital, Bucharest; [26]University of Medicine and Pharmacy Craiova, Doja, Romania; [27]Lausanne University Hospital, Lausanne, Switzerland; [28]University of Ioannina, Ioannina, Greece; [29]University of Turin, Turin, Italy*

Background: The OMERACT US subtask force "US in CPPD" recently created the definitions for US identification of crystal deposits in joints and tested the reliability at the knee [1].
Objectives: To assess the inter/intra-observer reliability of US on detecting CPPD at triangular fibrocartilage complex (TFCC) of the wrists, fibrocartilage of the AC joint, hip labrum (HL), hyaline cartilage (HC) of the metacarpal (MC) and femoral head.
Methods: The OMERACT criteria for CPPD were used for the exercise [1] using a 2 steps approach. First, the panel of experts gave a dichotomous score (presence/absence of CPPD) of 120 images of the sites included, using a web platform. The images were evaluated twice to assess the inter/intra-observer reliability. Then, the experts met in Siena for a patient based exercise. Bilateral evaluation of TFCC, AC, HL /HC of the hip and HC of the II-III MCP of 8 patients was carried out twice in a day, using a dichotomous score for CPPD. 8 US machines (3 GE, 1 Samsung and 4 Esaote) equipped with high resolution linear probes were used.
Results: Reliability values of static exercise were high for all sites, demonstrating that definitions were clear. The results of the second step are presented in table 1. On live scanning, the TFCC resulted the most reliable site for CPPD assessment, followed by AC. Other sites demonstrated lower kappa values and thus are not reliable for CPPD assessment.
Conclusions: TFCC of the wrist is the most reliable site for CPPD. By adding these results to the previous [2], we confirm that the OMERACT definitions for CPPD can be applied reliably at the knee (meniscus and HC), TFCC and AC, usually the most involved sites in CPPD. The next step of the OMERACT subtask force will be to test these findings in a longitudinal observational study.
References:
[1] Filippou G, Scirè CA, Damjanov N et al. Definition and reliability assessment of elementary US findings in CPPD. Results of an international multi-observer study by the OMERACT sub-task force "US in CPPD". J Rheumatol, in press.
Disclosure of Interest: None declared

Section	Mean prevalence	Mean observed agreement	Mean kappa	Pabak*
Inter-Reader Agreement				
1) ALL	48,2	0,71	0,43	0,42
2) Fibrocartilage	72,7	0,75	0,39	0,51
3) Hyaline cartilage	23,7	0,67	0,09	0,34
4) Hand	22,6	0,69	0,12	0,38
5) Wrist Fibrocartilage	95,1	0,91	0,01	0,82
6) Acromion-Clavicular Joint	61,1	0,75	0,51	0,51
7) Hip	43,7	0,61	0,23	0,23
7a) Hip Labrum	61,8	0,6	0,16	0,19
7b) Hip Cartilage	25,7	0,63	0,04	0,26
Intra-Reader Agreement				
1) ALL	48,3	0,85	0,69	0,71
2) Fibrocartilage	73,1	0,85	0,57	0,71
3) Hyaline cartilage	23,4	0,86	0,53	0,73
4) Hand	23	0,84	0,48	0,69
5) Wrist Fibrocartilage	95,1	0,93	0,66	0,87
6) Acromion-Clavicular Joint	62,5	0,88	0,68	0,76
7) Hip	42,9	0,82	0,58	0,66
7a) Hip Labrum	61,7	0,73	0,32	0,47
7b) Hip Cartilage	23,9	0,91	0,67	0,83

Strength of agreement: < 0.20 Poor. 0.21 - 0.40 Fair. 0.41 - 0.60 Moderate. 0.61 - 0.80 Substantial. 0.81 - 1.00 Excellent
*Pabak: Prevalence-Adjusted Bias-Adjusted Kappa

DOI: 10.1136/annrheumdis-2017-eular.3515

SAT0632 IMPACT OF LUMBAR SPINE MORPHOLOGY (SCOLIOSIS) ON EARLY SPONDYLOARTHRITIS PATTERN (THE IMPALA-DESIR STUDY)

M. Voirin-Hertz[1], G. Carvajal Alegria[1], F. Garrigues[2], A. Simon[3], A. Feydi[4], F. de Bruin[5], M. Reijnierse[6], D. van der Heijde[7], D. Loeuille[8], P. Claudepierre[9], T. Marhadour[1], A. Saraux[1] on behalf of DESIR. *[1]Rheumatology; [2]Radiology; [3]Neurosurgery, CHU Brest and Université Bretagne Occidentale, Brest; [4]Radiology, CHU Cochin, Paris, France; [5]Radiology, 5Leiden University Medical Center; [6]Radiology; [7]Rheumatology, Leiden University Medical Center, Leiden, Netherlands; [8]Rheumatology, CHU, Nancy; [9]Rheumatology, CHU Creteil, Paris, France*

Objectives: To evaluate the impact of scoliosis on both clinical presentation and lumbar imaging of early inflammatory back pain suggestive of spondyloarthritis.
Methods: The DESIR cohort is a prospective longitudinal cohort study of adults aged 18–50 with inflammatory back pain (IBP) $\geq$3 months, $\leq$3 years. Baseline lumbar X-Rays of patients included in DESIR cohort were read by two central blinded fellow readers (and a rheumatologist spine specialist in case of discrepancy) for presence or not of scoliosis (defined as a Cobb angle$>$10° and a Nash Moe grade$\geq$1). Associations between scoliosis and baseline clinical variables, presence of X-Rays (New York) and MRI (ASAS and MORPHO proposal definition) sacroiliitis, presence of spinal signs of spondyloarthritis (mSASSS, BASRI-total, SPARCC scores), presence of spinal degenerative MRI signs on X-rays (yes or no) and MRI (presence of Modic abnormalities, Pfirrmann score, Canal stenosis, Extrusion, High intensity zone Facet osteoarthritis) according to central reading (two readers) and axSpA diagnostic confidence (according to local clinician's confidence on a 0–10 visual analogic scale) were assessed by univariate analysis using the chi-square test (or Fisher's exact test where appropriate) and the Mann-Whitney test. Adjustment for multiple testing was performed according to Bonferroni method.
Results: 675 patients (47.1% men, mean age of 33.6 years, 89.6% had lumbar pain, 65% fulfilling ASAS criteria) were studied. The mean Cobb angle was 3.2° (± 4.8) and 49/675 (7.3%) patients had lumbar scoliosis. The only significant difference was the lumbosacral sagittal balance. Indeed, scoliotic patients had greater lumbar lordosis (57.8° versus 50.9°; $p<0.001$) than non-scoliotic. About MRI findings, spinal degenerative manifestations were very scarce in both groups. The major part of degenerative changes was in the two last lumbar discs and vertebras, without significant difference between scoliotic and non-scoliotic patients.
Conclusions: Scoliotic patients with inflammatory back pain suggestive of spondyloarthritis do not have more lumbar degenerative lesions than non-scoliotic patients, nor difference of clinical presentation, but they have greater lumbar lordosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5168

SAT0633 NOT A REPLACEMENT BUT A POSSIBLE SUBSTITUTION: DETECTION OF SACROILIITIS ON MAGNETIC RESONANCE ENTEROGRAPHY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

I. Ergenç[1], R. Ergelen[2], A.U. Ünal[3], Z. Ertürk[3], Y. Yalçınkaya[3], N. İnanç[3], N. İmeryüz[4], H. Direskeneli[3], G. Ekinci[2], P. Atagündüz[3]. *[1]Internal Medicine; [2]Radiology; [3]Rheumatology; [4]Gastroenterology, Marmara University School of Medicine, Istanbil, Turkey*

Background: MR Enterography (MRE), a part of the diagnosis in patients with inflammatory bowel disease (IBD), is increasingly used to exclude Crohn's Disease (CD) in SpA patients with diarrhea. Two important retrospective studies[1,2], on IBD

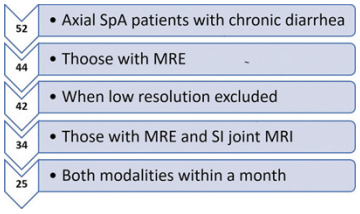
suggest that acute and structural findings of sacroiliitis can be evaluated on MRE. But, it needs to be verified whether it really correlates with sacroiliac MRI.

Objectives: We aimed to determine whether assessment of sacroiliitis on MRE correlates with magnetic resonance imaging (MRI) of sacroiliac (SI) joint.

Methods: MREs used for screening of IBD in Axial SpA patients with chronic diarrhea and routine semi-coronal SI joint MR images were screened for the presence of acute inflammatory lesions and structural changes of the SI joint by the same radiologist in a blinded fashion to time and diagnosis. Firstly, MRE images and then MR images were evaluated on two separate occasions. Only patients with two imaging modalities with a maximum time distance of a month were evaluated.

Results: Forty-four patients with MRE imaging were included. Two MRE studies were excluded because of low resolution. Of those 11 patients (26%) had active inflammatory lesions involving mostly both SI joints and 3 had accompanying chronic structural changes. Ten patients (%24) in the MRE group had chronic structural changes, only. In the remaining 20 (47%) MRE evaluated patients SI joint were not affected. Twenty-five axSpA patients had both MRE and SI joint MRIs performed within a month. In 19 cases, out of 25 with both modalities the finding "no sacroiliitis" overlapped. An additional four patients had acute inflammatory lesions on both investigations. In only two patients either MRE or SI joint MRI had acute inflammatory lesions. In general, chronic structural changes overlapped in both modalities as well; Fourteen out of 25 patients with no changes and eight with chronic changes overlapped in both examinations. Both modalities differ in only three patients; Chronic changes was present in two patients in SI joint MRI and one patient in MRE only.

		MRE (Sacroiliitis)	
		(+)	(–)
SI joint MRI (Sacroiliitis)	(+)	4	1
	(–)	1	19
		MRE (Structural Findings)	
		(+)	(–)
SI joint MRI (Structural Findings)	(+)	8	2
	(–)	1	14



Conclusions: In SpA patients with chronic diarrhea a present MRE may substitute a conventional semi-coronal MRI of the SI joints and may hence decrease diagnostic expenses. Evaluation of MRE for the acute inflammatory and chronic structural changes of the SI joints may also have a place in the diagnostic flow in IBD patients referred by the gastroenterology clinics, as well.

References:

[1] Leclerc-Jacob, S., et al. The prevalence of inflammatory sacroiliitis assessed on magnetic resonance imaging of inflammatory bowel disease: a retrospective study performed on 186 patients. Alimentary pharmacology & therapeutics, 2014, 39.9: 957–962.

[2] Gotler, Jakob, et al. Utilizing MR Enterography for detection of sacroiliitis in patients with inflammatory bowel disease. Journal of Magnetic Resonance Imaging, 2015, 42.1: 121–127.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6114

SAT0634 MUSCULOSKELETAL ULTRASOUND IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATISM POST-CHIKUNGUNYA

I. Monjo Henry[1], F. De la Calle[2], E. Trigo[2], E. Fernandez[1], D. Benavent[1], E. De Miguel[1], A. Balsa[1]. *[1]Rheumatology, Hospital la Paz; [2]Tropical Diseases and Travel Unit, Hospital la Paz-Carlos III, Madrid, Spain*

Background: Since 2013, Chikungunya fever (CHIK) has become a re-emerging disease, with an important number of cases imported in Europe, mainly from South America. At chronic stage (after third month) it can develop a chronic inflammatory rheumatism (CIR), in some cases indistinguishable from rheumatoid arthritis (RA) or spondyloarthritis (SpA).

Objectives: The aim of this study was to investigate the ultrasound (US) alteration in patients with persistent arthralgia at chronic stage of CHIK.

Methods: Observational study of patients with persistent arthralgias at the chronic stage of CHIK. We designed a protocol of derivation patients from the Tropical Diseases Unit to the Rheumatology Department which included patients had persistent arthritis after 6 weeks who did not respond to steroids, presence of bone erosion or any diagnosis doubt. In the basal rheumatological visit, we made the clinical history, physical examination, blood analysis, X-ray and US examination. A Mylab Twice equipment (Esaote, Geneve, Italy) was used, with a 5–13 MHz frequency for grey scale and 5–12.5 MHz for Power Doppler (PD). Wrist, metacarpophalangeal (MCP), interphalangeal (IP), knee, ankle and metatarsophalangeal joint were assesed and also enthesis if symptomatic. Three patterns of post-CHIK CIR were defined: 1) Post-CHIK RA (if meet RA ACR/EULAR 2010 criteria). 2) post-CHIK SpA (if meet ASAS criteria) and 3) post-CHIK undifferentiated arthritis (arthritis without meeting the previous criteria). Post-CHIK musculoskeletal disorders were defined as chronic polyarthralgia without objective physical signs of inflammation (without arthritis, tendinitis or enthesitis).

Results: 59 patients were included, 76.3% women, mean age of 46.08±13.65 years. 6 patients (10.2%) were derived to the Rheumatology Department, 5 women and 1 man. In one rheumatoid factor and anti-cyclic citrullinated peptide antibodies were detected. HLA B27 and antinuclear antibodies were negative in all patients. The physical and US data of these patients are shown in the table. 5 of these patients were diagnosed with post-CHIK CIR: 1 post-CHIK RA, 1 non-radiographic axial SpA with peripheral affectation (arthritis and enthesitis) and 3 patients with post-CHIK undifferentiated arthritis. The other patient was diagnosed with post-CHIK musculoskeletal disorder. All 59 patients received NSAIDs and steroids. In addition, post-CHIK CIR received methotrexate (2 patients) and sulfasalazine (1 patient), all with improvement. In the full cohort, only 5.9% of patients had arthralgias prior to CHIK infection, vs. 33.3% in the post-CHIK CIR (p=0.081). 3 patients (5.08%) had a family history of arthritis, all in the post-CHIK CIR.

Patient (n°)	Painful joints (n°)	Swollen joints (n°)	Tendinitis	Enthesitis	Sinovitis PD (n° joints)	Tenosynovitis PD (n°)	Enthesitis PD (n°)	Sacroiliitis magnetic resonance
1	33	3	1	0	1	2	0	
2	6	2	0	1	4	0	1	positive
3	5	0	0	0	0	0	0	
4	6	3	0	0	2	0	0	
5	11	1	1	1	2	2	0	
6	6	8	0	0	8	0	0	

Conclusions: Arthralgias are a frequent symptom even at chronic stage of CHIK. Sometimes it is true arthritis and in others cases edema. For this reason US is very useful in doubtful cases. In our cohort, patients that developed post-CHIK CIR were more frequently women, with a higher percentage of family history of arthritis. To the best of our knowledge, this is the first US study in patients with post-CHIK CIR.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6702

SAT0635 DESCRIPTIVE ANALYSIS OF THE QUANTICAP STUDY: A MULTICENTRIC PROSPECTIVE STUDY FOR THE VALIDATION OF QUANTITATIVE AND QUALITATIVE PARAMETERS OF NAILFOLD CAPILLAROSCOPY

I. Castellví[1], P. Reyner[2,3], S. Martinez[4], M. Moreno[5], M.S. Gelman[6], V. Ortiz-Santamaría[7], S. Ordoñez[8], P. Santo[9], S. Heredia[10], X. Juanola[11], H. Corominas[10]. *[1]Rheumatology, Hospital Universitari de la Santa Creu I Sant Pau, Barcelona; [2]Rheumatology, Hospital Universitari Dr. Josep Trueta, GIRONA; [3]Hospital de Santa Caterina, SALT; [4]Rheumatology, Hospital Universitari Mutua de Terrassa, Terrassa; [5]Rheumatology, Corporació Sanitaria Parc Taulí, Sabadell; [6]Rheumatology, Fundació Althaia, MANRESA; [7]Rheumatology, Hospital General de Granollers, Granollers; [8]Rheumatology, Hospital Universitari Arnau de Vilanova, LLEIDA; [9]Rheumatology, Hospital General Parc Sanitari Sant Joan de Deu, Sant Boi de Llobregat; [10]Rheumatology, Hospital Comarcal Sant Joan Despí-Moises Broggi, Sant Joan Despí; [11]Rheumatology, Hospital Universitari de Bellvitge, Hospitalet de Llobregat, Spain*

Background: Nailfold capillaroscopy (NC) is a useful tool to study Raynaud's phenomenon (RP) and other diseases. Different findings and patterns has been described however there is currently no work that validates the qualitative and quantitative NC findings.

Objectives: To describe the morphological and metrological findings of NC in patients with RP and autoimmune diseases.

2-Describe the morphological and metrological findings of CP in patients with RF and several systemic autoimmune diseases.To Describe the morphological and metrological findings of NC in patients with RP and other autoimmune diseases.

Methods: Observational study performed in 10 hospitals by rheumatologists with experience in NC. Patients with diffuse systemic sclerosis (dSSc), limited systemic sclerosis (lSSc), dermatomyositis (DM), polimyositis (PM), systemic lupus erythematosus (SLE) Primary Sjögren's syndrome (PSS), rheumatoid arthritis (RA), primary RP and a control group without RP or rheumatological condition were collected.A video NC 200x magnification were made in all patients. 8 Fingers in each hand were analyzed to find: megacapillary and dilated capillaries, giant capillaries, loss of density (<7/mm), tortuous capillaries, ramifications, haemorrhages, thrombosis and destructuration. Also we analyzed the diameter of the afferent and efferent loop, the capillary apex, the capillary diameter and density/mm. The following variables were also collected: sex, age, years of evolution of the disease and RP, history of digital ulcers or medication for

RP, smoking and presence of hypertension or diabetes. To compare qualitative variables, the test was used Chi-square or Fisher's test. To compare quantitative vs qualitative variables Student's T test was used. Significance was considered for those values with $p<0.05$.

Results: Between May 2014 to December 2016 images of 406 patients were collected: 24 dSSc, 41 lSSc, 19 DM, 14 PM, 40 SLE, 39 PSS, 37 RA, 44 PRP and 145 controls. C 84.5% were women, the age of the sample were 51.32±15.21 years. 28.9% had a history of smoking and 21.1% and 5.5% of hypertension or diabetes, respectively. Excluding the cases of dSSc, lSSc, PRP and the 145 controls, the presence of RP was observed in 18/152 (11.84%). The afferent, efferent, apical diameter And capillary was 26.01±19.01; 31.93±24.51um; 37.95±36.67um and 82.68±58.10um respectively. The most frequent qualitative finding were tortuosities. The control group showed no difference in the presence of hypertension or diabetes except in patients with PM. We also observed more women in SLE and PSS patients vs control group and greater presence of digital ulcers in lSSc, dSSc, SLE and DM. Only the lSSc presented differences in the presence of tortuosities with respect to the control group.

Conclusions: Except in the lSSc no differences were observed in the presence of tortuosities with the rest of groups and its presence may not be relevant in different diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4408

SAT0636 ULTRASONOGRAPHY DEFINITIONS FOR SYNOVITIS GRADING IN CHILDREN: THE OMERACT PEDIATRIC ULTRASOUND TASK FORCE

J. Vojinovic[1], S. Magni-Manzoni[2], P. Collado[3], D. Windschall[4], V. Ravagnani[5], C. Hernandez-Diaz[6], J.C. Nieto Gonzales[7], C. Malattia[8], N. Tzaribachev[9], G. Susic[10], N. Damjanov[11], S. Guillaume Czitrom[12], T. Herlin[13], S. Lanni[8], G. Bruyn[14], A. Iagnocco[15], L. Terslev[16], M.-A. D'Agostino[17], E. Naredo[7].
[1]Clinical Centre, Medical Faculty, University of Nis, Nis, Serbia; [2]Ospedale Pediatrico Bambino Gesu, Rome, Italy; [3]Hospital Universitario Severo Ochoa, Madrid, Spain; [4]Department of Pediatrics, Asklepios Hospital Weissenfels, Weissenfels, Germany; [5]Department of Medicine, University of Verona, Verona, Italy; [6]Instituto Nacional de Rehabilitación, Mexico City, Mexico; [7]Department of Rheumatology, Hospital General Universitario Gregorio Marañón and Complutense University, Madrid, Spain; [8]IRCCS Istituto Giannina Gaslini, Genova, Italy; [9]PRI - Pediatric Rheumatology Research Institute, Bad Bramstedt, Germany; [10]Institute for Rheumatology; [11]Institute for Rheumatology, University of Belgrade, Belgrade, Serbia; [12]Rhumatologie Pédiatrique, CHU Bicêtre, le Kremlin-Bicêtre, France; [13]Department of Pediatrics, Aarhus University Hospital Skejby, Aarhus N, Denmark; [14]Department of Rheumatology, MC Group, Lelystad, Netherlands; [15]Università degli Studi di Torino, Turin, Italy; [16]Department of Rheumatology, University of Copenhagen, Copenhagen, Denmark; [17]APHP, Hôpital Ambroise Paré, Rheumatology Department, UFR Simone Veil, Versailles-Saint-Quentin University, Saint-Quentin en Yvelines, France

Background: Ultrasound (US) was found to have face and content validity for detecting synovitis in juvenile idiopathic arthritis (JIA) with higher sensitivity than clinical examination. In order to test validity and improve the applicability of US in JIA, the OMERACT US pediatric subtask force recently published preliminary definitions for the sonographic features of synovitis in children.

	B-mode (GS)	color power/Doppler (PD)
0	No signs of synovial effusion or synovial hypertrophy (ie. no joint recess enlargement/capsular distension).	Absence of color/power Doppler signal within synovial hypertrophy with or without detection of normal physiological Doppler signals.
1	Synovial effusion and/or synovial hypertrophy that leads to a mild change of the joint recess appearance (ie. mild joint recess enlargement/capsular distension).	Detection of up to 3 single Doppler signals within the area of synovial hypertrophy with or without normal physiological Doppler signals.
2	Synovial effusion and/or synovial hypertrophy that leads to a moderate change of the joint recess appearance (ie. moderate joint recess enlargement/capsular distension).	Detection of more than 3 single Doppler signals but less than 30% of the area of synovial hypertrophy with or without normal physiological Doppler signals.
3	Synovial effusion and/or synovial hypertrophy that leads to a severe change of the joint recess appearance (ie. severe joint recess enlargement/capsular distension).	Detection of Doppler signals at more than 30% of the area of synovial hypertrophy with or without normal physiological Doppler signals

	Intra-observer				Inter-observer			
Grade	Percentage agreement		kappa Cohen		Percentage agreement		kappa PABAK	
	GS	PD	GS	PD	GS	PD	GS	PD
0	100	94	1.0	0.83	100	100	1.0	1.0
1	80	83	0.5	0.5	60	50	0.47	0.33
2	89	83	0.7	0.67	50	71	0.5	0.62
3	81	92	0.92	0.8	86	71	0.81	0.71

Figure 1. Synovitis grading definitions in children and inter- and intra-observer reliability in B-mode (GS) and color power/Doppler (PD).

Objectives: Aim of this study was to confirm and improve B-mode and color power/Doppler (PD) US definitions for synovial components and grading in children, by using an image and patient based exercise.

Methods: The definitions were confirmed and modified in a multi-step process. In the 1st step, definitions were developed in multi-round Delphi web based consensus process were ≥80% of participants would need to reach ≥80% of agreement on a Likert scale from 1–5 (1 strongly disagree, 2 disagree, 3 neutral, 4 agree, 5 strongly agree). In the 2nd step, in a face to face meeting, a subgroup of these experts revised the definitions for final wording and performed intra- and inter-observer reliability exercise study in JIA patients as the final 3rd phase of the process. The definitions were tested in four joints (wrist, 2nd MCP, knee and ankle) of JIA patients divided in four age groups following standardized image acquisition and machine setting protocol. Statistics program R (version 3.3.0) was used for the statistical analyses. For intra-rater agreement Cohen kappa and for inter-rater agreement prevalence and bias adjusted kappa (PABAK) were calculated if needed.

Results: Reliability exercise included 20 JIA patients (distributed in equal numbers by age groups), 14 observers, 4 joints/observer, 3 observers/joint, 360 intra- and 360 inter-observer tests. A 0–3 semi-quantitative B-mode and color power/Doppler US definitions for synovial components and grading, were agreed (presented in Figure 1).

Conclusions: The proposed synovitis grading for children showed to be reliable why the next step should be to test sensitivity to change in order to possibly be used as an outcome tool in JIA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6199

SAT0637 ULTRASOUND ASSESSMENT OF SKIN THICKNESS IN SYSTEMIC SCLEROSIS PATIENTS: CORRELATION WITH CLINICAL FEATURES

J. Sousa-Neves[1], M. Cerqueira[1], D. Santos-Faria[1], J. Leite Silva[1], A. Raposo[2], C. Afonso[1], F. Teixeira[1]. *[1]Rheumatology, Hospital Conde de Bertiandos, ULSAM, Ponte de Lima; [2]Rheumatology, Centro Hospitalar Trás-os-Montes e Alto Douro, Vila Real, Portugal*

Background: Although modified Rodnan skin score (mRSS) is the most widely used measure for assessment of skin involvement in Systemic Sclerosis (SSc), ultrasound (US) of skin thickness seems to be a promising complementary tool. (1)

Objectives: To compare skin thickness measured by US of a defined anatomical point between SSc patients and age and sex matched controls. To compare, among patients, US measurements of skin thickness with local and total mRSS and other specific clinical variables.

Methods: Forty-eight SSc patients and 45 age and sex matched controls were evaluated in a cross-sectional study at our Rheumatology Unit. SSc patients had a mean age of 56.98±12.73 years and mean disease duration of 9.77±6.12 years; 42 patients had limited cutaneous disease. Regarding US assessment, skin thickness was arbitrarily defined as thickness of epidermis, dermis and subcutaneous tissue, in millimetres, measured at the 2nd finger of both hands of each subject on the dorsal aspect of the proximal phalange. Examination was performed with a 15 MHz linear probe of a General Electric LOGIQ S8 US. For comparison between groups, mean skin thickness (mST) of combined right and left side was used. Patients' local and total mRSS were also assessed. Hand mobility in SSc (HAMIS) was calculated to evaluate functional disability and SSc Severity Scale (SScSS) to estimate activity and damage. Additional data was also collected from patients' clinical charts. Statistical analysis included Mann-Whitney U-test, Kruskal-Wallis and Spearman correlation coefficient test. Statistical significance was defined as P value <0.05.

Results: SSc patients showed higher mST (3.17 mm [2.56 to 3.58]) (median [interquartile range]) compared with controls (1.89 mm [1.55 to 2.08]) ($p<0.001$). Among SSc group, skin thickness measured by US of both 2nd fingers of each patient strongly correlated with local mRSS assessed by palpation (Spearman's rho=0.698, $p<0.001$ and rho=0.645, $p<0.001$ for right and left sides, respectively). US mST was also correlated with total mRSS (rho=0.568, $p<0.001$), HAMIS (rho=0.520, $p<0.001$) and SScSS (rho=0.524, $p<0.001$). A higher mST was found in patients clinically classified with oedematous phase ($p<0.001$) and in diffuse cutaneous subtype (p=0.039). A mild association was observed for patients with digital ulcers (p=0.05). Age, gender, disease duration and the presence of calcinosis were not associated with US mST ($p>0.05$).

Conclusions: US measurements of skin thickness of 2nd fingers were significantly higher in SSc patients compared with age and sex matched controls. US mST strongly correlated with local and total mRSS and was significantly higher in the presence of oedema, digital ulcers and in patients with diffuse subset. US mST also reflected functional disability and damage.

References:

[1] Hesselstrand R et al. High-frequency ultrasound of skin involvement in systemic sclerosis reflects oedema, extension and severity in early disease. Rheumatology (2008) 47 (1): 84–87.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4541

SAT0638 CLINICAL ACTIVITY, ULTRASOUND ASSESSMENT AND DRUG MONITORING IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING ANTI-TNF-α THERAPY WITH EXTENDED INTERVAL OF ADMINISTRATION

J.M. Senabre Gallego[1], J. Rosas Gómez de Salazar[1], M. Marco Mingot[2], A. Naranjo[3], F. Llinares-Tello[2], A. Pons[1], X. Barber-Vallés[4], G. Santos-Soler[1], E. Salas-Heredia[1], C. Cano[1], M. Lorente[1], J.A. García Gómez[4], J. Molina[2] on behalf of Asociación para la Investigación en Reumatología de la Marina Baixa (AIRE-MB). *[1]Rheumatology; [2]Laboratory, Hospital Marina Baixa, Villajoyosa (Alicante); [3]Rheumatology, Hospital Dr. Negrín, Las Palmas de Gran Canaria; [4]Centro de Investigación Operativa, Universidad Miguel Hernández, Elche, Spain*

Objectives: To assess clinical activity, ultrasound synovitis and drug levels in rheumatoid arthritis (RA) patients receiving anti-TNFα therapy with extended interval of administration (EIA).
Methods: Prospective observational study. Population: RA patients, in clinical remission, receiving adalimumab (ADL) or etanercept (ETN) with EIA. Clinical activity was assessed by DAS28-ESR, DAS28-CRP, CDAI and SDAI scores at each visit. Twelve-joint ultrasound assessment (elbows, wrists, 2nd and 3rd metacarpophalangeal joints, knees and ankles) was performed evaluating synovitis through B-mode (BM) and Color Doppler signal (CD). A BM and CD score was calculated summing the highest score from each joint to a maximum of 36 points. We consider positive score >1 point. Serum drug levels were measured using Promonitor® ELISA kits (Progenika Biopharma-Grifols, Spain).
Results: A total of 39 patients were included since February 2011 to December 2016. One patient was excluded due to blindness violation and 2 patients never reduced anti-TNFα due to low drug levels. 31 patients were women (82%) and the mean age was 61 (39–81) years. Most patients were RF positive (87%) and ACPA positive (74%). 22 patients were with ADL treatment and 16 with ETN. 32 patients (82%) were with DMARD concomitant treatment (18 MTX (46%), 11 LEF (18%), 2 HCQ (5%), 1 SSZ (2%)) and 7 patients were with low-dose CS (18%). Mean time from diagnosis was 14,95 years (range 2,15 – 52,31) and Mean time with current biologic drug was 4,21 years (range 1,39 – 11,07). Nine patients (24%) returned to standard interval due to worsening of clinical activity and one discontinued treatment due to septic arthritis. All of them returned to clinical remission and no anti-drug antibodies were detected. Clinical activity scores, ultrasound scores and drug levels are summarized in table 1.

Table 1. Clinical activity scores, ultrasound scores and drug levels

	Basal visit	6 months	12 months
N	32	31	20
DAS28-ESR	2,0 (0,91)	1,83 (0,83)	1,61 (0,70)
DAS28-CRP	1,71 (0,51)	1,78 (0,52)	1,62 (0,48)
SDAI	4,25 (2,55)	4,27 (3,04)	3,64 (3,13)
CDAI	3,82 (2,48)	3,61 (2,33)	2,76 (1,3)
BM score	3,57 (4,57)	3,29 (3,81)	4,7 (4,32)
CD score	0,78 (0,80)	1,19 (1,7)	1,15 (1,42)
BM score (%)	73,91	77,42	90,00
CD score (%)	56,52	45,16	50,00
ETN	4,61 (2,74	3,59 (2,9)	3,03 (0,84)
ADL	12,05 (6,88)	8,49 (5,01)	6,49 (2,78)*

*p<0,05. All results mean (SD) otherwise specified.

Conclusions: 1. Clinical remission was sustained in most patients receiving ADL or ETN in extended interval of administration (EIA). 2. Drug levels decrease over time. 3. Some patients (24%) returned to standard interval of administration due to clinical worsening. 4. Some patients show subclinical ultrasound synovitis in B-mode (90%) or Color Doppler (50%) 5. It would be advisable to perform periodic ultrasound and monitoring of anti-TNFα levels to maintain clinical remission in patients with EIA.
Acknowledgements: This study was supported by a research grant from Fundación Española de Reumatología and AIRE-MB.
Disclosure of Interest: J. Senabre Gallego Speakers bureau: MSD, Novartis, Abbvie, UCB, BMS, J. Rosas Gómez de Salazar: None declared, M. Marco Mingot: None declared, A. Naranjo: None declared, F. Llinares-Tello: None declared, A. Pons: None declared, X. Barber-Vallés: None declared, G. Santos-Soler: None declared, E. Salas-Heredia: None declared, C. Cano: None declared, M. Lorente: None declared, J. A. García Gómez: None declared, J. Molina: None declared
DOI: 10.1136/annrheumdis-2017-eular.3066

SAT0639 BIOLOGIC-ELIGIBLE RHEUMATOID ARTHRITIS PATIENTS DEMONSTRATE ABSENCE OF SYNOVITIS – UTILITY OF ULTRASOUND IN THE MANAGEMENT OF RA-BIOLOGIC POPULATION

K. Naraghi[1], T. Vojinovic[2], J. Nam[1], J. Freeston[1], P. Emery[1], R.J. Wakefield[1], M.H. Buch[1]. *[1]Leeds Institute of Rheumatic & Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom; [2]Faculty of Medicine and Surgery, University of Pavia, Pavia, Italy*

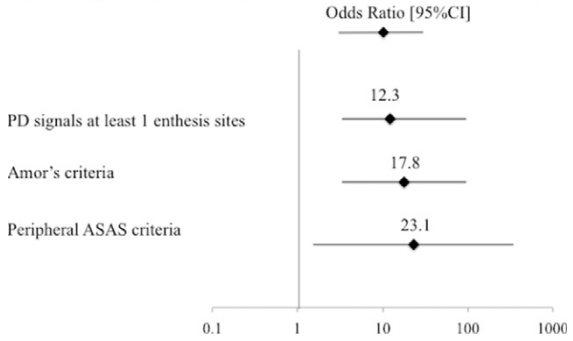
Background: Biologic drugs act by suppressing synovitis in patients with rheumatoid arthritis (RA). Clinical disease activity scores (DAS) are used to determine eligibility and assess biologic drug response. However, several drivers aside from synovitis may drive the DAS. Joint ultrasound (US) scan is more accurate than clinical examination in detecting inflammatory synovitis [1, 2], and is frequently used in clinical practice to assess need for biologic drug change [3].
Objectives: To phenotype DAS using US in patients eligible for a first/switch in biologic therapy and to evaluate whether and how this changed decision making.
Methods: A retrospective evaluation of RA patients who attended our tertiary centre biologic clinic between 2014 and 2016 and had an US to clarify basis for raised disease activity. Three-variable DAS28-CRP 28 joints (DAS28-CRP) was recorded and US reports were evaluated to determine which of the following characteristics were observed: presence of synovitis, tenosynovitis, osteoarthritis, tendinopathy and no abnormality. Clinic notes were reviewed to record change in the management of patients as a result of combined clinical and US scan findings.
Results: We identified 70 patients who had not received steroids within 4 weeks of the US, 84.3% female, median (range) age 58 (20–88) years. 66 (94.3%) patients were biologic experienced with 59 on ongoing treatment [3 (5.1%) abatacept, 22 (37.3%) anti-TNFα, 22 (37.3%) rituximab and 12 (20.3%) tocilizumab] of whom 47 (79.7%) were on combination with csDMARD therapy. 4 (5.7%) patients were biologic naive. 42 (63.6%) of bio-experienced patients, had a DAS28 ≥3.2 and were eligible for a change in their biologic however, only 17 of these patients had US-confirmed synovitis, 21 had evidence of osteoarthritis (OA), 1 tenosynovitis and 3 had no abnormalities. All biologic naïve patients had DAS28-CRP ≤5.1 before US however, 3 had US-confirmed synovitis and 1 had OA. Of bio-experienced, 13/66 (19.4%) patients, including 4 with DAS-28 <3.2 but US-confirmed synovitis, had a new biologic started. 3 rituximab patients (including one with subclinical synovitis) had re-treatment. Concomitant treatment was escalated in 13 (24.2%) patients. 35 (53.0%) patients, including 4 with US synovitis/tenosynovitis, had no change in their treatment. 2 (3.0%) patients self-discontinued treatment.
Conclusions: By identifying lack of inflammatory synovitis in biologic eligible patients US reduced the need for unnecessary and costly change of biologics. US also detected subclinical synovitis warranting modification of their treatment.
References:
[1] Colebatch AN, Edwards CJ, Ostergaard M, et al. EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis. Annals of the rheumatic diseases. 2013; 72:804–814.
[2] Saleem B, Brown AK, Keen H, et al. Should imaging be a component of rheumatoid arthritis remission criteria? A comparison between traditional and modified composite remission scores and imaging assessments. Annals of the rheumatic diseases. 2011; 70:792–798.
[3] Iagnocco A, Finucci A, Ceccarelli F, et al. Power Doppler ultrasound monitoring of response to anti-tumour necrosis factor alpha treatment in patients with rheumatoid arthritis. Rheumatology (Oxford). 2015; 54:1890–1896.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6633

SAT0640 DIAGNOSTIC UTILITY OF DETECTING ENTHESITIS BY ULTRASOUND IN PERIPHERAL SPONDYLOARTHRITIS

K. Fujikawa[1], Y. Endo[1], A. Mizokami[1], M. Mine[2], A. Kawakami[3]. *[1]Rheumatology, Japan Community Healthcare Organization, Isahaya General Hospital; [2]Rheumatology, Suga Orthopedic Hospital, Isahaya; [3]Department of Immunology and Rheumatology, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan*

Objectives: To evaluate the diagnostic utility of detecting enthesitis by ultrasound in patients with peripheral spondyloarthritis (SpA).
Methods: A single-center cohort study was performed in patients with symptoms suggestive of peripheral SpA (inflammatory back pain, arthritis of the lower limbs, tenderness of the entheses and dactylitis). Patients with only axial symptoms in the absence of peripheral symptoms were excluded. Fourteen sites of enthesis (both sides of lateral epicondyle, quadriceps tendon insertion into the patella, patellar ligament insertion into the patella and tibial tuberosity, medial and lateral femoral condyles, and Achilles tendon) were assessed at baseline by ultrasound. Ultrasound assessment was made by Japan College of Rheumatology (JCR)-registered sonographers. Furthermore, articular synovitis and tenosynovitis of both wrist and finger joints as well as symptomatic sites were examined. Clinical, laboratory (CRP, HLA typing), radiological (X-ray and MRI of sacroiliac joint) findings and SpA classification criteria (Amor's, ESSG and ASAS) were also evaluated. The gold standard was the diagnosis made by the JCR-certified rheumatologists during a six-month follow-up period.
Results: Between April 2014 and November 2016, one hundred-thirty six patients were consecutively enrolled. A definite diagnosis was obtained in 112 patients (72 SpA and 40 non-SpA). Diagnosis was not made in the remaining 24 patients. Seventy-two SpA patients (62 with undifferentiated SpA, 6 with psoriatic arthritis, 2 with AS, 1 with inflammatory bowel disease-associated arthritis and 1 with reactive arthritis) and 40 non-SpA patients were investigated in this study. In ultrasound findings, SpA patients showed power Doppler (PD) signals of the articular synovium (57%), tendon sheath synovium (71%) and enthesis (94%). A PD signal for at least one enthesis sites was the most useful finding for differentiation of SpA from non-SpA (sensitivity 94%; specificity 85%; accuracy 91%; positive likelihood ratio 6.3) regarding ultrasound findings. In logistic regression analysis, fulfillment of peripheral ASAS criteria, that of Amor's criteria, and presence of PD signals at least one enthesis sites were independent variables to the contribution of diagnosis of SpA (Figure 1).

Figure 1. Logistic regression analysis for the contribution of diagnosis of SpA



Conclusions: PD signals of entheses by ultrasound are useful for the diagnosis of SpA with peripheral joint symptoms. In addition to the consideration of axial SpA, the combination use of ultrasound with clinical classification criteria including ASAS and Amor's criteria is beneficial to diagnose peripheral SpA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3148

SAT0641 THE DIAGNOSTICS OF OSTEOPOROSIS IN MALE REUMATOID PATIENTS

K. Aminov. *Medical Radiology, Tashknet Institute for Postgraduate Medical Education, Tashkent, Uzbekistan*

Background: Rheumatoid arthritis (RA) - chronic immune inflammatory joint disease leading to early disability of patients at high risk for cardiovascular events and osteoporotic fractures. Of particular relevance, this problem becomes in men with RA, due to more frequent severe disease and increased mortality in the year after the fracture. Reduced bone mineral density (BMD) and muscle mass are significant predictors of fracture, which leads to the high importance of studying the state of the IPC and body composition.
Objectives: To improve the diagnosis of osteoporosis in patients with RA male subjects.
Methods: A total of 146 male patients with definite diagnosis of RA at the age of 59 years. Depending on the reception of glucocorticosteroids (GCS) is allocated two subgroups: I subgroup - 40 patients not receiving corticosteroids and II subgroup - 66 patients receiving corticosteroids. The control group consisted of 24 healthy men, matched by age and body mass index. IPC Study in the lumbar spine (L1-L4) and femoral carried out by dual-energy X-ray absorptiometry using osteodensitometry. Evaluation of body composition was carried out with the help of "Pod" program.
Results: In 63% of patients with RA revealed male BMD reduction corresponding to osteopenia/OP (OP was diagnosed in 36 (24.7%) patients with RA, and osteopenia - in 56 (38.4%)). The incidence of OP in the II subgroup was significantly higher ($p<0,05$), than in the I subgroup (48.5% and 5% respectively). The most significant decrease in BMD observed in femoral neck in the study group as a whole, and in individual subgroups. There was a negative correlation between the degree of RA activity and performance of the IPC as a lumbar spine ($r = -0,4$, $p<0.05$), and the proximal femur ($r = -0,38$, $p<0.05$). Evaluation of body composition showed that the treatment group had a significant decrease in total lean mass (TM) body, as well as the trunk and extremities TM compared with those of control group ($p<0,05$). Sarcopenia detected in 80 (55.8%) of RA patients, whereas in the control group it was absent. In 50 (67.6%) of patients with RA male sarcopenia observed to decrease the level of the IPC osteopenia (35.2%) and OD (32.4%). After receiving a negative correlation parameters TM and the absolute 10-year risk of osteoporotic fractures ($r = -0,302$, $p<0,05$) on the FRAX.
Conclusions: 63% of men suffering from RA, observed BMD decrease corresponding OP/osteopenia with a primary decrease in BMD at the femoral neck. Reduced BMD in patients with RA was significantly associated with a high degree of disease activity ($r = -0,4$, $p<0.05$). Receiving corticosteroids had no significant effect on BMD at the femoral neck. Analysis of body composition in 55% of RA patients revealed a decrease in TM limbs to the level of sarcopenia. Received correlation decrease BMD and TM limbs ($p<0,05$; $r =0,28$). Thus, in patients with RA males along with OP/osteopenia revealed a significant decrease in TM, that in view of the biomechanics of the movements may be an additional risk factor for falls and fractures.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3159

SAT0642 ULTRASONOGRAPHY AND INTRA-ARTICULAR INJECTION THERAPY IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE RANDOMISED ARCTIC TRIAL

L.B. Nordberg[1], S. Lillegraven[1], A.-B. Aga[1], I.C. Olsen[1], E. Lie[1], H.B. Hammer[1], T. Uhlig[1], D. van der Heijde[2], T.K. Kvien[1], E.A. Haavardsholm[1] on behalf of the ARCTIC study group. [1]*Diakonhjemmet Hospital, oslo, Norway;* [2]*Leiden University medical center, Leiden, Netherlands*

Background: Intra-articular (i.a.) corticosteroid injections are in many countries an integral part of rheumatoid arthritis (RA) treatment. Ultrasonography (US) is increasingly used in the management of RA as a tool to select joints for i.a. injections. How selection of joints based on US information affects distribution of injections has not been previously studied. US can detect joints with subclinical inflammation, however, it is unknown whether there is any added value of injecting these joints.
Objectives: We aimed to explore how US information influences the selection of joints for corticosteroid injection therapy. Additionally, we wanted to examine the efficacy of injecting joints with subclinical inflammation detected by US in terms of reduction of subclinical inflammation and prevention of clinical synovitis.
Methods: In the ARCTIC trial, DMARD-naive RA patients fulfilling the 2010 ACR/EULAR criteria were randomised 1:1 to follow-up with or without US.[1] In both arms the same DMARD treatment strategy was applied, and clinically swollen joints were treated with i.a. steroids when indicated. In the US arm, clinicians could also inject non-swollen joints with PD activity. Patients were assessed at 13 visits during 2 years of follow-up and injections could be performed at all visits. Distribution of injections in patients followed with and without US was assessed. The proportion of patients with any injection was compared between arms using logistic regression, adjusted for gender. In addition, we examined the effect of injections in clinically non-swollen joints with PD $\geq$2 (range 0–3) by comparing clinical joint swelling and estimated mean change in PD activity at the next visit in injected versus non-injected joints. We used logistic and linear mixed model with random intercept by patient in order to adjust for within-patient dependencies.
Results: 230 patients were included (US arm 118, conventional arm 112). Mean (SD) age was 50.6 (13.3)/ 52.3 (14.1) years, 71/51% were females and mean (SD) baseline DAS was 3.5 (1.2)/3.4 (1.2) in the US/conventional arms. [1] More injections occurred in the US arm than in the conventional arm (770 vs 548), especially in intercarpal (58 vs 5) and MTP joints (200 vs 104) (Table 1). In the US arm, 193 joints were clinically non-swollen, but had PD score $\geq$2. Of these, 77 joints were injected. 72/77 injected joints (93.5%) remained non-swollen at next visit compared to 88/116 non-injected joints (75.9%), with an odds ratio of 3.97 (CI: 1.25–12.57, p=0.019, NNT:6). Estimated mean (SE) reduction of PD activity was 2.3 (0.1) compared to 2.0 (0.1) in injected versus non-injected joints ($p<0.001$).

Joint	Number of injections, 0-24 months		Patients with any injection n (%)			
	Ultrasonography N=118	Conventional N=118	Ultrasonography N=118	Conventional N=112	OR (95% CI)	p-value*
DIP 2-5	2	5	2 (1.7)	3 (2.7)	0.62 (0.10-3.93)	0.61
PIP 1-5	74	122	37 (31.4)	36 (32.1)	1.15 (0.65-2.06)	0.63
MCP 1-5	163	113	55 (46.6)	44 (39.3)	1.45 (0.83-2.45)	0.19
Radioulnar	33	9	18 (15.3)	8 (7.1)	2.33 (0.95-5.69)	0.06
Radiocarpal	65	43	39 (33.1)	27 (24.1)	1.66 (0.92-3.03)	0.09
Intercarpal	58	5	33 (28.0)	4 (3.6)	13.38 (4.40-40.75)	**<0.001**
Elbow	15	13	10 (8.5)	9 (8.0)	1.22 (0.46-3.21)	0.90
Shoulder	26	26	14 (11.9)	16 (14.3)	0.78 (0.36-1.72)	0.54
Toes (IP)	7	22	6 (5.1)	13 (11.6)	0.43 (0.15-1.19)	0.10
MTP 1-5	200	104	63 (53.4)	36 (32.1)	2.61 (1.50-4.55)	**0.001**
Ankle	35	35	18 (15.3)	17 (15.2)	1.02 (0.49-2.13)	0.96
Knee	58	31	27 (22.9)	17 (15.2)	1.65 (0.83-3.28)	0.15
Other joints	34	20	14 (12.5)	22 (18.6)	1.59 (0.76-3.35)	0.20
Total	770	548	103 (87.3)	86 (76.8)	2.40 (1.17-4.93)	**0.017**

*Adjusted for gender

Conclusions: Our study shows that follow-up with US may lead to an increased number of joint injections with a different distribution of injected joints compared to follow-up without US. Joints with subclinical inflammation were more likely to remain non-swollen at next visit if injected. However, as the number of joints needed to treat to prevent one swollen joint was six, the clinical relevance of injecting joints with subclinical inflammation may be questionable.
References:
[1] Haavardsholm EA et al., BMJ 2016;354:i4205.
Disclosure of Interest: L. Nordberg: None declared, S. Lillegraven: None declared, A.-B. Aga: None declared, I. Olsen: None declared, E. Lie: None declared, H. Hammer Consultant for: Consultant for AbbVie, Pfizer, BMS, Roche, UCB, T. Uhlig: None declared, D. van der Heijde: None declared, T. Kvien: None declared, E. Haavardsholm Grant/research support from: Pfizer, MSD, UCB, AbbVie, Roche
DOI: 10.1136/annrheumdis-2017-eular.2505

SAT0643 VALUE OF POWER DOPPLER ULTRASONOGRAPHY FOR PREDICTION OF TREATMENT FOR RHEUMATOID ARTHRITIS (RA) IN EARLY ARTHRITIS DURING THE FIRST 12 MONTS OF FOLLOW-UP

L. Mayordomo [1,1], M.L. Velloso [1], C. Jurado [2], P. González-Moreno [3], C. Gomez-Cano [1], J.L. Marenco [1], C. Almeida [4]. *[1]Rheumatology Department; [2]Radiology Dp, Hospital Universitario Valme; [3]Rheumatology Department, HVM; [4]Research and Statistics Dp, Hospital Universitario Valme, SEVILLA, Spain*

Background: There is a short window of opportunity for early diagnosis and treatment of rheumatoid arthritis, that may be crucial for reaching remission and a low rate of radiographic progression. High resolution power doppler ultrasonography (PDUS) is helpful in early detection of synovitis and may help to select patients that will need early establishmet of treatment for RA.
Objectives: To study whether the presence of basal power doppler signal in patients with early arthritis in a clinical basis treatment decision could predict the risk of receive treatment for AR at 3 and 12 months of follow-up.
Methods: We studied the presence of ultrasonographic Power Doppler (PD) signal on 28 joints (shoulders, elbows, wrists, MCPs, knees) and 44 joints (28 joints and in addition hips, Tarsus, ankles and MTPs), with a mid-range equipment GE L5, in 70 patients with suspected early arthritis. The patients were included with at least one of the following inclusion criteria: a) Swelling in 2 or more joints b) pain in MCPs, MTPs and/or the wrists c) morning stiffness of more than 30 minutes with <12 months duration of the symptoms. Clinical treatment decision was not awared to basal power doppler results. Statistical study: Chi-square, Fisher exact test, p univariant and Odds Ratio calculation.
Results: The presence of basal power doppler signal in ≥1 joints of 44 (PD44) at baseline shows statistically significant association with treatment with oral steroids (p<0.001, OR 8,6 (2,4–30,5), DMARD p 0.028, OR 4,2 (1,3–13,3), metotrexato (MTX) p 0.002 OR 6,6 (1,9–22,1) but not sulfasalazine (SSZ) (p 0.145) at 3 months and with steroids (p<0.0005 OR 14,8 (3,9–44,4), DMARDs (p<0.0005, OR 10,3 (2,6–40,4), MTX (p<0.0005, OR 8,67 (82,6–29,2)), sulfasalazine (p=0.001, OR 8,7 (2,2–33,9), at 12 months The presence of at least one joint with power doppler signal of 28 joints (PD28) was significantly associated to esteroids (p=0.003, OR 5,4 (1,8–16,8) and metotrexate (p=0.016, OR 4,1 (1,4–12,7) treatments in the first 3 months but not to other DMARDs p=0.146 (including sulfasalazine p=0.416) and with esteroid (p=0.01 OR 7,3 (2.2–24,9), DMARD, (p=0.03, OR 5,8 (1,8–18,7), MTX (p=0.012, OR 4,3 (1,4–12,8),and sulfasalazine (p=0.008, OR 4,9 (1,5–15,6) during first 12 months of follow-up. Predictive value of other risk factors for RA (RF, basal erosions=EROS BAS) is shown in the table below.

BASAL N=70		ESTEROID 12M P univariate OR IC 95%	DMARD 12M P univariate OR IC 95%	MTX 12M P univariate OR IC 95%	SSZ 12M P univariate OR IC 95%
PD28	SI	44/50(88%)	33/50 (66%)	37/50(74%)	31/50(51,4%)
	NO	10/20(50%)	5/20 (7,1%)	8/20(40%)	5/20(25%)
		0,001	0,003	0,012	0,008
		OR 7,3 (2,2-24,9)	OR 5,8 (1,8-18,7)	OR 4,3 (1,4-12,8)	OR 4,9(1,5-15,6)
PD44	SI	47/52(90,4%)	35/52 (67,3%)	40/52(76,9%)	33/52(63,5%)
	NO	7/18(38,9%)	3/18 (16,7%)	5/18(27,8%)	3/18(16,7%)
		<0,0005	<0,0005	<0,0005	0,001
		OR 14,8(3,9-44,4)	OR 10,3(2,6-40,4)	OR 8,67 (2,6-29,2)	OR 8,7(2,2-33,9)
RCP	SI	40/45(88,9%)		37/45(82,2%)	
	NO	14/25(56%)	NS	8/25(32%)	NS
		0,003	1,000	P<0.0005	0,624
		OR 6,3 (1,9-21,3)		OR 9,8 (3,2-30,6)	
FR	SI	19/20(95%)		19/20(95%)	
	NO	35/50(70%)	NS	26/50(52%)	NS
		0,028	0,430	0,001	0,433
		OR 8,1(1-66,5)		OR 17,5 (2,1-141)	
ACPA	SI			12/13(92,3%)	
	NO	NS	NS	33/57(57,9%)	NS
		0,272	0,193	0,024	0,622
				OR 8,7(1,1-71,7)	
EROS BAS	SI			26/30(86,7%)	
	NO	NS	NS	17/35(48,6%)	NS
		0,139	0,161	0,002	0,622
n=65				OR 6,9(1,9-23,9)	

Conclusions: Power doppler ultrasonography in at least one joint of 44 (PD44) may predict the patients that will need esteroids, any DMARD, MTX and SSZ teraphy in early arthritis at 3 and 12 months of follow-up. PD28 may predict the patients that will need esteroids, any DMARD, MTX and SSZ teraphy in early arthritis at 12 months, but may only predict the need of esteroid and MTX at three months.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6910

SAT0644 IS ANKLE INVOLVEMENT IMPORTANT IN RHEUMATOID ARTHRITIS?

L. Enache, C. Mogosan, C. Popescu, G. Gutoiu, C. Codreanu. *Rheumatology, Clinical Center of Rheumatic Disease, Bucharest, Romania*

Background: The ankles may be affected by rheumatoid arthritis (RA). In daily evaluation of RA patients, the ankles are often neglected by clinical examinations, while composite activity scores do not include them
Objectives: The aim of the study is to assess the inflammatory lesions in RA ankles, regarding frequency and possible correlation with activity disease
Methods: The study included 76 RA patients fulfilling the 2010 ACR/EULAR classification criteria. In every patient we recorded clinical ankle involvement (ankle swelling and/or tenderness on physical examination); both ankles were evaluated by gray scale (GS) and Power Doppler (PD) ultrasound examination, graded from 0–3. In each joint we assessed: tibio-talar joint (TT); tibialis anterior (TA) tendon; extensor hallux (EH) and extensor digitorum (ED) tendons; talo-navicular joint (TN); tibialis posterior (TP) tendon; flexor digitorum (FD) and flexor hallux (FH) tendons; peroneus brevis (PB) and longus (PL) tendons; Achilles tendon (AT); subtalar joints (SJ; posterior, lateral, medial recesses); plantar fascia (PL). We recorded the following abnormalities: synovitis, tenosynovitis, bursitis, entesopathy and rupture. Activity scores (DAS28, DAS44, SDAI), inflammatory markers (ESR, CRP), serology (FR, ACPA) and HAQ were also assessed
Results: The mean age was 57.2±14.2 years; 88% were women; mean disease duration was 12.2±9.2 years; 56.6% had symptomatic ankles; 81.6% had ultrasound ankle abnormalities. The most frequent ultrasound pathology encountered was ST synovitis (56.6%), followed by TT synovitis (48.7%), TN synovitis (38.2%), TP tenosynovitis (30.3%), PL tenosynovitis (15.8%). Ultrasound abnormalities were recorded in 93% of the symptomatic ankle patients and in 66.7% of the asymptomatic ankle patients (p=0.008). Overall, 43% had positive PD signals, but the prevalence of positive PD signals was significantly higher in symptomatic ankle patients than in asymptomatic ankle patients (60.5% compared to 21.2%, p=0.011). Statistically significant correlations were found between ultrasound inflammatory pathology (synovitis and tenosynovitis), activity disease markers and quality of life (Table 1).

Table 1. Correlations of GS ultrasound measures with disease activity and HAQ

	ESR	CRP	$DAS28_{CRP}$	$DAS28_{ESR}$	DAS44	SDAI	HAQ
TT	0.104	0,360**	0,395***	0,283*	0,317**	0,352**	0.150
TN	0.159	0,426***	0,442***	0,330**	0,366**	0,391***	0.007
PL	0.272*	0.366**	0.368**	0.347**	0.362**	0.340**	0,292*
PB	0.074	0.139	0.200	0.215	0.231*	0.223	0,243*
TP	0.408***	0.466***	0.543***	0.548***	0.558***	0.542***	0,268*
FD	0.166	0.145	0.254*	0.260*	0.285*	0.259*	0,256*

Note: the reported values represent the *rho* coefficients of bivariate Spearman correlations: *p<0,05; **p<0,01; ***p<0,001.

Conclusions: Musculoskeletal ultrasound detected a high prevalence of inflammatory abnormalities in rheumatoid arthritis ankles, in both symptomatic and asymptomatic patients, while power Doppler signal was present mostly in symptomatic patients. The ultrasound pathology was highly correlated with activity disease markers and quality of life
References:
[1] M Backhaus, G-R Burmester, T Gerber et al., Guidelines for musculoskeletal ultrasound in rheumatology, Ann Rheum Dis 2001,; 60:641–649.
[2] M Alsuwaidi, B Ehrenstein, M Fleck et al., Ankle Joint in Rheumatoid Arthritis. An Ultrasound Study Using High Resolution- and Clour Doppler Ultrasound, 2013 ACR/ARHP Annual Meeting, Abstract No 1969.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6217

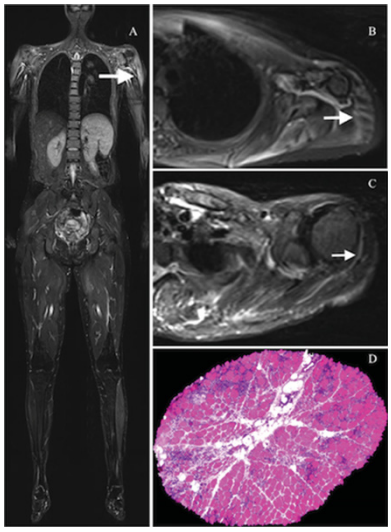
SAT0645 MAGNETIC RESONANCE IMAGING AND HISTOPATHOLOGICAL CORRELATION IN DERMATOMYOSITIS

M.V. Collado [1], J.C. Milisenda [2], X. Tomás [3], A.I. García [3], M. Faruch [4], J.M. Grau [2] on behalf of Muscle Research Unit, Internal Medicine Service, Hospital Clínic de Barcelona, Universidad de Barcelona and CIBERER. *[1]Reumatology, Instituto de Investigaciones Médicas Alfredo Lanari (UBA), Buenos Aires, Argentina; [2]Internal Medicine; [3]Radiology, Hospital Clínic de Barcelona, Barcelona, Spain; [4]Radiology, CHU Toulouse Purpan, Toulouse, France*

Background: Dermatomyositis represents one of the major forms among the inflammatory myopathies (IIM). Although the muscle biopsy remains the definitive test, MRI has been used to detect unique patterns of muscle involvement. To date, no studies have compared MRI with muscle pathology in naïve DM.
Objectives: To compare the pattern of muscle MRI with muscle pathology.
Methods: All the patients enrolled in the Hospital Clínic de Barcelona (HCB) from January 2009 to December 2016 with an available MRI, performed just before muscle biopsy were included. The HCB ethics committee approved this study, and written informed consent was obtained from each participant.
MRI data and the clinical and demographic features were prospectively collected. Patients were classified as having definite DM (ref 4). MRI was performed on a 1.5T with standardized protocol of whole body or scapular and pelvic girdle MRI, which include coronal and axial T1-weighted and STIR images. Image analysis was performed by two experienced musculoskeletal radiologists masked

to the disease activity. The presence of oedema, fatty replacement and fascial oedema was evaluated in the biopsied muscle. Muscle and fascial inflammation was scored using a 0–3 point scale. The extent of muscle involvement was also evaluated by the analysis of 12 to 14 axial images and a percentage of muscle volume was calculated. Fatty replacement was scored using a 0–3 point scale. Muscle biopsies were evaluated by two trained pathologists at the HCB. Muscle biopsies were routinely processed. Quantification of fiber necrosis, regeneration and inflammation infiltrate were recorded. All statistical analyses were performed using "SPSS v22.0 ®". In all statistical tests performed p value of 0.05 was considered significant.

Results: A total of 16 (13 female) patients were included. Except in one patient all of them had proximal muscle weakness, and all of them except one had typical DM skin lesions. In 12% of the patients a solid cancer was diagnosed. All patients had fascial edema at muscle MRI while no one had fatty replacement, and 65% had muscle oedema. Only one biopsy was normal. A significant correlation was found between muscle inflammation and MRI muscle edema (p=0,036) and the percentage of volume muscle involvement at MRI (p=0,027). Muscle necrosis was seen in those patients with moderate and severe fascial edema compared with those with mild fascial edema (p=0,032). More regenerating cells were seen in those patients with moderate and severe muscle edema compared with negative or mild muscle oedema (p=0,018).



Conclusions: A strong and significant correlation between histological and imaging findings was found. Fascial and muscle edema were the predominant findings in DM patients

References:

[1] Garcia J. MRI in inflammatory myopathies. Skeletal Radiol 2000;29:425–38.
[2] Connor A, Stebbings S, Hung N, et al. STIR MRI to Direct Muscle Biopsy in Suspected Idiopathic Inflammatory Myopathy. J Clin Rheumatol 2007;13: 341–45.
[3] Dalakas MC. Inflammatory muscle diseases. N Engl J Med 2015;373:393–4.
[4] Hoogendijk JE, Amato AA, Lecky BR, et al. 119th ENMC international workshop: trial design in adult idiopathic inflammatory myopathies, with the exception of inclusion body myositis, 10–12 October 2003, Naarden, the Netherlands. Neuromuscul Disord 2004;14:337–45.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5746

SAT0646 COMPARISON OF US, CT, X-RAY AND MRI EFFICACY FOR SEQUENTIAL ASSESSMENT OF CHRONIC GOUT MANIFESTATIONS

M. Eliseev, O. Zhelyabina, S. Vladimirov, M. Chikina, M. Severinova, A. Smirnov, D. Kudinsky, O. Mirovich. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Ultrasonography (US), magnetic resonance imaging (MRI), computed tomography (CT), and X-ray are the alternative diagnostic modalities used to identify affected joints and surrounding tissues (tophi, erosions and synovitis) in gout patients, but the potential of each method for sequential assessment of disease regression in pts receiving urate-lowering therapy is not sufficiently studied [1]

Objectives: Comparison of US, CT, X-ray and MRI efficacy for sequential assessment of affected joints in pts treated with urate-lowering agents.

Methods: The open prospective study was conducted in 2013–2015 yy at V.A. Nasonova Research Institute of Rheumatology. 22 pts with crystal-verified gout (4 (15%) f and 18 (85%) m), mean age – 54,5±12,7 years, were included. The dose of allopurinol administered in all pts was adjusted by titration starting from 100 mg/day. Instrumental diagnostic examination (US, MRI, CT and plain X-ray of knee joints) was performed at baseline and after one year of follow up. US of knee joints was performed using multi-frequency linear array transducer, at 7 to 17 MHz frequencies; for MRI examination "Esaote Artrosan 0.25TI" was used, GE "Light Speed" - for CT scans, and Stephanix – for plain X-ray examination. Applied descriptive statistics STATISTICA 10.0 (StatSoft/Inc., USA) package was used for statistical analysis.

Results: Mean serum level of uric acid decreased from 568±115 μmol/l to 302±135 μmol/l. The target level (<360 μmol/l) was achieved in 20 pts (91%), (<300 μmol/l) was achieved in 11 pts (50%). Median allopurinol dose was 400 [300; 600] mg/day, 9 (45%) pts had to take 600 mg/day and more. At baseline US examination detected periarticular tophi in 13 (59%) pts, MRI - in 6 (28%) pts, CT in 3 (14%), X-ray - 1 (5%) pts, after one year - by US in 9 (41%) pts and MRI - 3 (14%) pts, CT in 2 (9%), X-ray - 1 (5%) pts. At baseline intraosseous tophi were detected only by CT and X-ray in 18 (81%) and 2 (9%) pts respectively, after one year 17 (77%) pts and 3 (14%) pts respectively. At baseline erosions were detected in 19 (86%) pts by MRI, in 11 (50%) pts – by US, in 14 (65%) pts – by CT, and in 9 pts (41%) – by X-ray, after one year in 14 (64%) pts by MRI, 10 (45%) pts by US, 12 (54%) pts by CT, 8 (36%) pts by X-ray. At baseline synovitis was reliably diagnosed by MRI and US: in 15 (68%) pts and 17 (77%) pts, after one year in 2 (9%) pts and 3 (14%) pts respectively

Conclusions: MRI and US, as for synovitis, erosions and tophi dynamics, are comparable, at that for erosions MRI is more accurate. CT is the most informative approach to monitor intraosseous tohhi regression. X-ray is low- informative modality for sequential assessment of gout.

References:

[1] Grainger R, Dalbeth N, Keen H, et al. Imaging as an outcome measure in gout studies: report from the OMERACT gout working group. J Rheumatol 2015; 42(12):2460e4.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3722

SAT0647 LASER DOPPLER IMAGING: AN OBJECTIVE OUTCOME MEASURE FOR ASSESSMENT OF CUTANEOUS LUPUS ERYTHEMATOSUS

M.Y. Md Yusof[1,2], J. Britton[3], E.M. Hensor[1,4], M. Goodfield[2], M. Wittmann[2], P. Emery[1,2], E.M. Vital[1,2]. *[1]Rheumatology, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; [2]NIHR Leeds Musculoskeletal Biomedical Research Unit; [3]Medical Physics Department, Leeds Teaching Hospitals NHS Trust; [4]NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*

Background: Cutaneous lupus erythematosus (CLE) is the most common manifestation of SLE and may occur without systemic features. Skin disease is particularly heterogeneous, rendering assessment of activity difficult. Laser Doppler imaging (LDI) is a non-invasive imaging tool that monitors blood perfusion in dermal tissue. It has been shown to correlate with inflammation in psoriasis but no study has been undertaken in CLE.

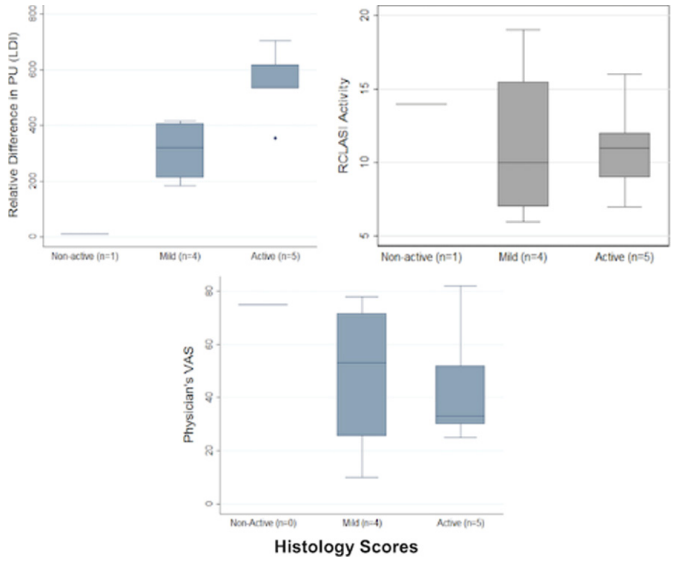
Objectives: To evaluate validity of LDI against the gold standard of histology from skin biopsy as well as other clinical tools including the Revised Cutaneous Lupus Erythematosus Disease Area and Severity Index (RCLASI) and Visual Analogue Scale (VAS) scoring of photographs.

Methods: A prospective observational study was conducted in consecutive patients with CLE flare at a single centre. Disease activity was assessed using RCLASI and measured using a high resolution LDI system (Moor Instruments) by JB and YY, both blinded to clinical assessment. Relative difference to the non-lesion area was calculated and expressed in perfusion unit (PU). Skin biopsy was obtained in those who consented and scored as 0=non-active, 1=mild activity and 2=active. Photographs were taken on the same day and were later assessed by a dermatologist and a rheumatologist who were blinded to LDI results using a 100mm VAS. The agreement of VAS between both clinicians was analysed using Bland-Altman limits of agreement (LOA) and the correlation between histology and LDI, RCLASI and VAS were analysed using Kendall's Tau-a.

Results: 20 patients were studied (19 female, median age 47.2 (range 21–62) years, 6 smokers, 2 CLE only, 14 (70%) ANA positive at the time of the scan). The distribution of CLE type were: acute CLE=7, subacute CLE=6 and chronic CLE=7. The agreement between the VAS scores of the two clinicians was fair; mean difference 7.8 (95% CI LOA -26 to 42) mm versus average. In 10 patients with skin biopsy, the correlation with histology was better for LDI (tau-a=0.56) than RCLASI [-0.09; difference (90% CI) 0.64 (0.10, 1.19)] or VAS [-0.16; 0.71 (0.13, 1.29)] (figure 1). One patient who was deemed to have a subacute CLE flare based on clinical assessment indeed had a negative histology and a low PU.

Conclusions: In this preliminary analysis, assessment of blood perfusion to dermal tissue using LDI provides a valid quantitative and objective measure of inflammation in cutaneous lupus. The findings from LDI also had a better correlation with histology from skin biopsy compared to currently used clinical tools. Further validation and longitudinal analysis including assessment of responsiveness to therapy will provide further evidence on the usefulness of LDI in clinical practice and trials.

Acknowledgements: The authors would like to acknowledge Lorraine Green for substantial contribution in the acquisition of data and NIHR for funding the Laser Doppler Imaging.



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6784

SAT0648 ULTRASOUND FINDINGS IN SYMPTOMATIC AND ASYMPTOMATIC JOINTS IN PATIENTS WITH GOUT

M.M. Basaric, G. Radunovic, N. Damjanov, M. Radak Perovic. *Institut of rheumatology, Belgrade, Serbia*

Objectives: To determine sensitivity and specificity of ultrasound (US) findings for gout: "double contours" (DC) and hyperechogenic aggregates (HAGs) of symptomatic and asymptomatic joints in patients with gout.
Methods: This prospective study included 69 persons (34 patients with primary gout and 35 healthy subjects). Including criteria for patients with gout were: age ≥18 years; diagnosis of primary gout; absence of acute gout attacks during the study tests; the absence of any other inflammatory and infectious joint disease, and secondary gout. The research included: demography and medical history. Physical and US examination covered following structures: 138 radiocarpal joint, 276 patellar and triceps tendon and 414 articular cartilages (first metatarsal, talar and femoral condyle).
Results: Both groups were compatible for age and gender. In the gout group 124 (30%) symptomatic and 284 (70%) asymptomatic joints were found and in healty group all joints was asymptomatic. The sensitivity of the DC for symptomatic joint was 56 to 84% and specificity also was very high 91 to 94% as well as positive and negative predictive value (69 - 86% and 38 - 71%). Sensitivity of DC finding for the asymptomatic joints was 42 to 73% and specificity was 91 to 94%, with also high positive and negative predictive value (69 - 89% and 44 - 62%). The specificity of the HAGs for both symptomatic and asymptomatic joints was very high 99% but sensitivity of HAGs symptomatic structures was moderate (41 do 56%), while its sensitivity for asymptomatic structures was low (18 to 34%), table 1.

Table 1

Structure		Sensitivity (%)	Specificity (%)	"Cut-off"	PPV (%)	NPV (%)
Symptomatic	DC	56–84	91–94	0.50	69–86	38–71
	HAGs	41–56	98–99	0.50	69–89	44–62
Asymptomatic	DC	42–73	91–94	0.50	58–86	38–71
	HAGs	18–34	98–99	0.50	49–75	31–60

DC - "double contours"; HAGs - hyperechogenic aggregates; PPV - positive predictive values; NPV - negative predictive values.

Conclusions: Ultrasound examination of symptomatic and asymptomatic joints in patients with gout equally observed structural changes characteristic of gout. The finding of "double contours" in the symptomatic and asymptomatic joints has a very high sensitivity and specificity. Consequently, future research should be focused on the ultrasound examination of asymptomatic joints in patients with gout.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4199

SAT0649 CHANGES IN CARTILAGE QUALITY (DGEMRIC) FOLLOWING KNEE JOINT DISTRACTION OR HIGH TIBIAL OSTEOTOMY: A TWO-YEAR FOLLOW-UP

N. Besselink[1], S. Mastbergen[1], K. Vincken[2], L. Bartels[2], A. Concepcion[1], A.K. Marijnissen[1], F. Lafeber[1]. *[1]Rheumatology and Clinical Immunology; [2]Image Sciences Institute, University Medical Centre Utrecht, Utrecht, Netherlands*

Background: Since abnormal loading can cause onset and progression of OA, unloading the affected compartment of an osteoarthritic knee, should slow down OA progression, or even enable joint repair. High tibial osteotomy (HTO) is a well-known unloading approach for treating unilateral compartment osteoarthritis (OA) with mechanical axis deviation. Transient unloading using knee joint distraction (KJD) has demonstrated a progressive decrease in pain, normalization of function, and an increase in cartilage thickness[1]. Although both treatments show indications of joint repair, there is limited information about the actual quality of the regenerated tissue.
Objectives: To evaluate the change in quality of the repaired cartilaginous tissue using dGEMRIC after KJD or HTO treatment.
Methods: 40 patients (20 with KJD, and 20 with HTO), treated for medial tibiofemoral OA, are included in this study. Radiographic changes, clinical changes, and changes in cartilage quality are evaluated after one and two years follow-up. Joint space width (JSW) is evaluated on weight-bearing radiographs. Clinical improvement is evaluated by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Visual Analogue Scale (VAS) pain score. In order to evaluate the quality of the (newly formed) cartilaginous tissue, quantitative MRI analysis, in the form of Delayed gadolinium enhance Magnetic Resonance Imaging of cartilage (dGEMRIC) is performed.
Results: A significantly increased medial (Δ1.15 mm,p<0.000), minimal (Δ0.93 mm,p<0.000) and mean (Δ0.79 mm,p=0.003) JSW one year after KJD, sustaining up until 2 years, was demonstrated (medial (Δ0.99 mm,p=0.002), minimal (Δ1.04 mm,p<0.000), mean JSW (Δ0.68 mm,p=0.027)). Similarly, medial (Δ0.49 mm,p=0.017) and minimal (Δ0.32 mm,p=0.023) JSW were significantly increased one year after HTO, sustaining up until 2 years (medial: Δ1.03 mm,p<0.000, minimal: Δ0.72 mm,p=0.015), after which mean JSW (Δ0.46 mm,p=0.030) is also significantly increased. Both interventions led to clinical improvement, observed as an increase in WOMAC after one year (KJD: Δ36.89,p<0.000, HTO: Δ33.74,p<0.000) and two years (KJD: Δ32.52,p<0.000, HTO: Δ24.19,p=0.002), and a decrease in VAS Pain, after one year (KJD: Δ-30.79,p=0.001, HTO: Δ-41.89,p<0.000) and two years (KJD: Δ-30.50,p=0.004, HTO: Δ-34.64,p<0.000). However, no statistically significant changes in cartilage quality were found after KJD or HTO, not in the medial and lateral compartments of the tibiofemoral joint, nor in the separate ROIs (see figure 1).

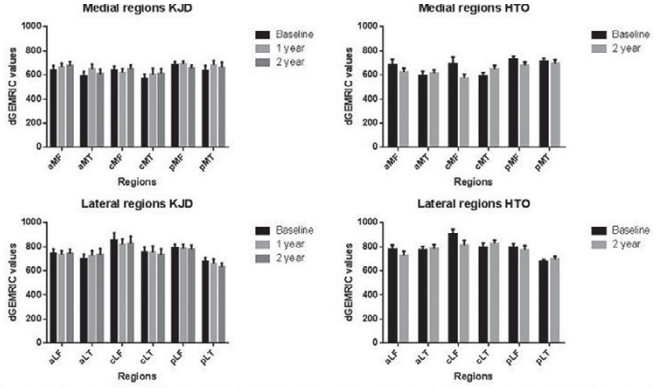


Figure 1: Average dGEMRIC indices (in ms) for the six ROIs of the medial and lateral compartment at baseline and after follow-up.

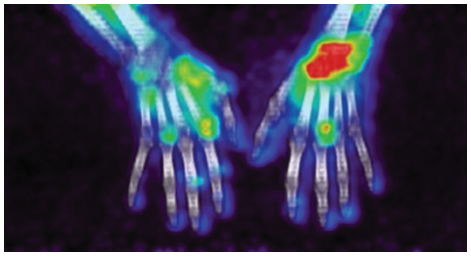
Conclusions: Treatment of medial compartmental OA by either HTO or KJD leads to alleviation of pain and recovery of function, achieved one year after either intervention, and maintained for another year. Within the first year after treatment, KJD shows a statistically significantly higher increase in WOMAC as compared to HTO. Both treatments led to a statistically significant increase in JSW after one and two years, postponing the natural osteoarthritis progression rate. No statistically significant change in the quality of newly formed cartilaginous tissue could be detected by dGEMRIC.
References:
[1] van der Woude et al. Knee joint distraction compared with high tibial osteotomy. 2016. Knee Surgery,Sports Traumatology,Arthroscopy,1–11.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3400

SAT0650 [18F]FLUORO-PEG-FOLATE PET: A NOVEL IMAGING TECHNIQUE TO VISUALIZE RHEUMATOID ARTHRITIS

N. Verweij[1], S. Bruijnen[1], Y. Gent[1], M. Huisman[2], G. Jansen[1], C. Molthoff[2], Q. Chen[3], P. Low[3], A. Windhorst[2], A. Lammertsma[2], O. Hoekstra[2], A. Voskuyl[1], C. van der Laken[1]. *[1]Dept. of Rheumatology, Amsterdam Rheumatology and Immunology Center - location VU University Medical Center; [2]Dept. of Radiology & Nuclear Medicine, VU University Medical Center, Amsterdam, Netherlands; [3]Dept. of Chemistry, Purdue University, West Lafayette, United States*

Background: Imaging arthritis activity in rheumatoid arthritis (RA) patients using PET macrophage tracers holds promise for both early diagnostics and monitoring response to therapy (1,2). Previously, (*R*)-[^{11}C]PK11195 has been used, but this macrophage tracer is limited due to high background uptake, especially in bone and bone marrow. Recently, a novel macrophage tracer, [^{18}F]fluoro-PEG-folate,

was developed, which showed excellent targeting of the folate receptor beta on activated macrophages in synovial tissue in a preclinical arthritic rat model (3).
Objectives: To assess the value of [^{18}F]fluoro-PEG-folate PET-CT for imaging inflamed joints in patients with clinically active RA.
Methods: Nine RA patients with at least two clinically inflamed hand joints were included. PET-CT scans of the hands were acquired after intravenous administration of either 185 MBq of [^{18}F]fluoro-PEG-folate (n=6) or 425 MBq of (*R*)-[^{11}C]PK11195 (n=3). Volumes of Interest (VOI) were drawn over joints with visually marked uptake and Standardized Uptake Values (SUVs) were calculated. Background VOIs were drawn on metacarpal bone in order to calculate Target-to-Background (T/B) ratios.
Results: No side effects were observed, establishing the safety of [^{18}F]fluoro-PEG-folate for use in humans. [^{18}F]fluoro-PEG-folate clearly showed uptake in arthritic joints, as shown in Figure 1. In patients scanned with [^{18}F]fluoro-PEG-folate, 25 positive joints were seen, with a minimum of two joints per patient. Clinical arthritis was confirmed in 10 of these 25 joints, and was absent in 15 positive joints, suggesting the presence of subclinical inflammation. Whilst both [^{18}F]fluoro-PEG-folate and (*R*)-[^{11}C]PK11195 accumulated in arthritic joints, [^{18}F]fluoro-PEG-folate showed a significantly lower background uptake than (*R*)-[^{11}C]PK11195 (SUV of 0.18 vs 0.75; $p<0.001$) respectively. T/B-ratios were significantly higher for [^{18}F]fluoro-PEG-folate (3.60vs 1.72, p=0.009).



Conclusions: This first in patient study clearly demonstrates the potential of [^{18}F]fluoro-PEG-folate PET-CT as macrophage tracer to image both clinically and sub-clinically affected joints in RA patients. [^{18}F]fluoro-PEG-folate showed better characteristics for arthritis imaging than the established tracer (*R*)-[^{11}C]PK11195 because of its lower background signal.
References:
[1] Gent YY, et al. J Rheumatology. 2014; 41: 2145–52.
[2] Gent YY, et al. Arthritis Rheum. 2012; 64: 62–6.
[3] Gent YY, et al. Arthritis Res Ther. 2013; 15: R37.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3249

SAT0651 QUANTIFICATION OF DYNAMIC MRI EXAMINATIONS IN JUVENILE IDIOPATHIC ARTHRITIS

N. Tzaribachev[1], R. Hagoug[2], P. Louka[2], J. Islam[2], M. Hinton[2], O. Kubassova[2], M. Boesen[3]. *[1]Pri - Pediatric Rheumatology Research Institute, Bad Bramstedt, Germany; [2]Image Analysis Group, London, United Kingdom; [3]Radiology, Copenhagen University Hospital Bispebjerg and Frederiksberg, Bispebjerg, Denmark*

Background: In chronic inflammatory conditions, the need for a more objective measurement of disease activity has been identified. Imaging biomarkers as outcome measurements based on the automated quantification of dynamic contrast enhanced magnetic resonance images (DCE-MRI) have been studied in adult patients with rheumatoid arthritis (RA)[1]. In children with juvenile idiopathic arthritis (JIA) similar knowledge is very limited.
Objectives: To compare treatment related changes of clinical scores in patients with JIA and automated DCE-MRI quantitative parameters analyzed with a dedicated software Dynamika^{tm} also compared to clinical outcomes of the patients.
Methods: In patients with polyarticular JIA with insufficient ($\geq$3 affected joints) response or intolerance to $\geq$3 months Methotrexate, Etanercept was started. Six Slice Axial DCE-MRI of the metacarpophaleangeal (MCP) 2–5 joints in the clinically most affected hand was performed at 3 time points: baseline (BL), month 3 and 6 of treatment using a 0.2 Tesla Esaote C-Scan. Clinical scores included active joint (AJ) counts. Clinical response was considered a state of $\leq$3 AJ. DCE-MRI was analyzed using regions of interest (ROI) covering synovium in slices where MCPs 2–5 were visible. Output parameters included dynamic MRI quantification scores (DEMRIQvol) corresponding to the volume of enhancing voxels within the synovial ROIs alone or multiplied with the mean of the maximum enhancement (ME) or the initial rate of enhancement (IRE). Differences in DEMRIQvol scores between visits were analyzed using t-test ($p<0.05$* = statistically significant, $p<0.25$** = clinically meaningful). Concordance between clinical and DEMRIQvol scores were described.
Results: 18 Caucasian patients (12 girls, median age 12,6 years, median disease duration 1,2 years) were included in the study. Two patients discontinued imaging after BL but continued treatment. In all but 3 of the remaining patients statistically significant and/or clinically meaningful changes were documented for DEMRIQvol ME between visits.
In 4 patients clinical and DEMRIQvol scores showed corresponded changes but these were non-concordant in all others patients.
Based on DEMRIQvol change (irrespective of the clinical scores) the outcome of the patient could be predicted:
- in 5 patients improvement of DEMRIQvol scores predicted response to treatment (within 2–6 months after last MRI examination)
- in 4 patients the increase or the persistence of a high DEMRIQvol predicted non-response to treatment
- in 7 patients increase in DEMRIQvol (after initial decrease) or persistence of a high DEMRIQ vol predicted flare (in 3 of the patients flare occurred after treatment discontinuation)

In all patients subclinical disease could be detected on MRI in clinically unaffected joints.
Conclusions: Dynamika based scores appear to be useful for depicting disease activity in JIA and seem to support clinical examination by detecting subclinical inflammation. More over, in the present study DEMRIQvol scores were predictive for the outcome of the patients and were able to "foresee" response to treatment, flare of disease, non-response to treatment in most patients possibly making DEMRIQvol scores supportive in research and clinical decision taking.
References:
[1] Kubassova O et al; Eur J Radiol. 2010 Jun;74(3):e67–72.
Acknowledgements: The study was supported by Pfizer.
Disclosure of Interest: N. Tzaribachev: None declared, R. Hagoug Employee of: Image Analysis Group, P. Louka Employee of: Image Analysis Group, J. Islam Employee of: Image Analysis Group, M. Hinton Employee of: Image Analysis Group, O. Kubassova Employee of: Image Analysis Group, M. Boesen Shareholder of: Image Analysis Group
DOI: 10.1136/annrheumdis-2017-eular.4341

SAT0652 CLINICAL AND IMMUNOLOGICAL SIGNIFICANCE OF RADIOGRAPHIC THYMIC ALTERATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

O. Murata[1], K. Suzuki[1], H. Sugiura[2], Y. Kondo[1], M. Takeshita[1], H. Yasuoka[1], K. Yamaoka[1], K. Koga[3], R. Morita[4], A. Yoshimura[4], T. Takeuchi[1]. *[1]Division of Rheumatology, Department of Internal Medicine, School of Medicine; [2]Division of Diagnostic Radiology, Department of Radiology, School of Medicine, Keio University, Tokyo; [3]Inflammation Drug Discovery Unit, Pharmaceutical Research Division, Takeda Pharmaceutical Company Limited, Kanagawa; [4]Department of Microbiology and Immunology, School of Medicine, Keio University, Tokyo, Japan*

Background: The thymus, a primary lymphoid organ, plays a crucial role in immune system homeostasis [1,2]. Although several small-scale studies of the association between radiographic thymus alterations and serological features have been reported in systemic autoimmune diseases, information in patients with rheumatoid arthritis (RA) is limited.
Objectives: We conducted a large-scale cross-sectional analysis of radiographic thymus alterations and their association with clinical and immunological features in patients with RA.
Methods: RA patients were randomly selected from all patients who visited our department and underwent chest CT scan between January 2013 and December 2015. Patients with thymoma or thymic cyst and those aged less than 30 years were excluded. Thymic enlargement and thymus attenuation score in axial images of CT scans were quantitatively interpreted. We defined thymic enlargement as a thickness of more than 13 mm and graded the score by a four-point scale (score 0–3) according to previous studies [3,4]. Associations with immunophenotyping data of peripheral blood by flow cytometry and clinical and serological information were statistically analyzed in some available patients.
Results: 387 RA patients were enrolled. 78% were women and mean age was 65.2±12.3 years. Thymic enlargement was found in 76 (19.6%) patients. Thymus attenuation (score $\geq$2) was found in 154 (39.8%) patients. These findings were more frequent than in undiagnosed controls (11.3% (P=0.078) and 22.5% (P=0.017)). Importantly, radiographic thymus alterations in these RA patients, especially thymus attenuation score, were significantly associated with serological features such as serum level of CRP, ESR, IgG, RF-positivity or ACPA-positivity (P=0.0003, 0.001, 0.0009, 0.005, and 0.0009 respectively). When we investigated the association with the proportion of 68 peripheral blood subpopulations in 83 RA patients, thymic enlargement was significantly associated with the proportions of CD45RA+CCR7+ naïve CD4+T cell or CD45RO+CCR7-effector memory CD4+T cell (P=0.04 and 0.009). Furthermore, thymus attenuation score was also significantly associated with the proportions of CD4+ naïve T cell, CD4+effector memory T cell, CXCR5-CXCR3+CXCR6+CD4+Th1/Th17 cell, CD45RO-CCR7+CD95+CD4+ stem cell memory T cell, and CD19+ B cell (P=0.03, 0.02, 0.04, 0.04, and 0.037 respectively).
Conclusions: Radiographic thymus alterations are frequent in RA patients and may reflect immunological features of autoantibody production or T cell differentiation and function.
References:
[1] Gorozny JJ, et al. Trends Immunol 2001;22:251–255.
[2] Seddon B, et al. Immunol Today 2000;21:94–99.
[3] Naidich P, et al. Lippincott-Raven 1999:57–73.
[4] Ackman JB, et al. Radiology 2013;268(1):245–253.
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3933

SAT0653 QUANTITATIVE ASSESSMENT OF INTERSTITIAL LUNG DISEASE IN SJÖGREN SYNDROME: A PILOT STUDY

P. Guisado Vasco[1], M. Silva[2], N. Sverzellati[2], I. Martín Garrido[1], D. Santilli[3], F. Mozzani[3], O. Martin Segarra[1], J.M. Luque Pinilla[1], A. Ariani[4]. *[1]Internal Medicine, Complejo Hospitalario Ruber Juan Bravo, Madrid, Spain; [2]Radiology, University of Parma; [3]Internal Medicine; [4]Internal Medicine and Rheumatology unit, UAzienda Ospedaliero-Universitaria di Parmaniversity of Parma, Parma, Italy*

Background: The interstitial lung disease (ILD) is the most frequent form of lung damage in Sjögren's syndrome (SjS). The diagnosis is still nowadays challenging: there are not specific test -autoantibodies, pulmonary function test- or symptoms. Chest CT is the gold standard. Semiquantitative (SQCT) assessment (such Taouli or Goh visual scores) could estimate ILD severity or burdened by relevant inter-rater variability. Quantitative chest CT (QCT) is a promising method to assess primary or secondary ILD, but there are not studies focused on SjS-ILD.
Objectives: Herein we designed a study to evaluate if QCT indexes might assess differences in SjS-ILD.
Methods: We conducted a multicenter, cross-sectional, and retrospective study, identifying subjects affected of SjS (per modified American-European consensus criteria) and with a thorax CT ordered by local physician by any reason. We enrolled 52 cases, splitted in two cohorts according to the presence/absence of ILD on chest CT. A centralized SQCT assessment was carried out to calculate both Goh and Taouli scores. A DICOM-viewer open-source software (Horos) was used to analyse, blindly and anonymously, all CT images and to calculate QCT indexes (pulmonary (p) and total (t) kurtosis, standard deviation, skewness and mean lung attenuation). QCT indexes and SQCT scores were compared using the Spearman rank and Mann-Whitney tests. ROC curves were calculated to assess the sensibility and specificity of the QCT indexes to detect ILD.
Results: Median age was 70.5 (95% CI 65.47–73.0); 96.2% were female. 9 cases have ILD, and 41 were not affected - two patients not assessable. The disease duration (till CT thorax) have a median of 21 (95% CI -6 – 42.41) months. 42.3% have secondary SjS and 57.7% a primary SjS. All QCT scores, except tSDev, were statistically different in ILD comparing those without ILD; the most relevant were: pKurt 2.05 (IQR 0.389 – 3.78) vs 4.34 (IQR 2.74- 6.0), p=0.008; pSdev (105.6 (IQR 101.4 - 122.95) vs 96.4 (IQR 92.38 to 104.94), p=0.006); pSkew (1.49 (IQR 0,49 -1,94) vs 2.01 (IQR 1.59 – 2.38), p=0.011); tKurt 7.62 (IQR 3.35 – 9.31) vs 10.00 (IQR 8.60 – 11.42),p=0,012 and tSkew 2.52 (1.63 – 2.85) vs 3.04 (2.81- 3.29), p=0.005). ROC analysis showed that tSkew could best discriminate ILD and those without: 0.8 (95% CI 0.66–0.9), cut off point $\leq$2.89; sensitivity 88.89% (95% CI 51.8–99.7), specificity 65.85% (95% CI 49.4–79.9), p$<$0.001. The correlation coefficients for QCT and Goh and Taouli's score ranges around ±0.4.
Conclusions: QCT indexes identified some differences between SjS-ILD and those not. These parameters could be useful both to improve imaging diagnosis and also the decision to treat those cases. This innovative tool migh open up a potential research area to be developed in SjS. Moreover, the operator independence of QCT makes it a time-saving method extremely suitable for multi-centre trials. Our pilot study have some handicaps: small sample, low number of events, different reasons for CT performing, no smoking identification, and biological differences between primary and secondary SjS. However, it could be point out that QTC could be a useful tool to identify and quantify ILD in SjS, and further data are need to ascertain this hypothesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6868

SAT0654 THE RECALL SURVEY: DIFFERENCIES OF ULTRASOUND EXAMINATION BETWEEN EARLY VS LONG LASTING RHEUMATOID ARTHRITIS PATIENTS IN CLINICAL REMISSION

P. Macchioni[1], A. Iagnocco[2], M. Canzoni[3], C. Bonali[4], O.M. Epis[5], E. Filippucci[6], A. Delle Sedie[7], S. Tropea[8]. *[1]Rheumatology, Arcispedale S Maria Nuova, Reggio Emilia; [2]2Academic Rheumatology Unit, Università degli Studi di Torino, Turin; [3]Rheumatology, Local Health Unit (ASL)Rome 1, Rome; [4]Rheumatology, Ospedale San Paolo, Bari; [5]Rheumatology, Ospedale Niguarda Milano, Milan; [6]Rheumatology, Università Politecnica delle Marche, Jesi (AN); [7]Rheumatology, Università di Pisa, Pisa; [8]Rheumatology, Busacca Hospital, Ragusa, Italy*

Background: Ultrasound (US) examination is able to show subclinical synovitis and structural changes of joints in patients (pts) with RA in clinical remission (CR).
Objectives: To investigate the differencies of US examination of small joints of hands, feet and wrists in pts with very early (VERA, $<$1y) vs early (ERA, $<$3y duration) vs long lasting RA (LRA, $>$7 y duration) in clinical remission (CR).
Methods: In 2015 an educational event (RECALL survey) focused on the added value of US in RA pts was held in 22 rheumatology centers in Italy. In every center, the local rheumatologists provided RA pts to be examined by US. Pts signed an informed consent and a brief history of them was collected by the local rheumatologists (previous and current therapy, DAS28, HAQ score). Bilateral US examinations of wrists, metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints were performed by rheumatologists expert in US, to assess synovitis (joint effusion, synovial proliferation, and power Doppler (PD) signal), and bone erosions, using a Logiq E R7, General Electrics, with a 4.2–13 MHz linear probe. All US findings were scored using a 4 degree semiquantitative scoring system.
Results: Eighty-eight pts were classified as VERA, 183 as ERA and 165 as LRA. Drug usage was not different among the three groups of pts. LRA patients were older (p$<$0.001), had longer disease remission before US examination (p$<$0.001) and had an higher prevalence of female sex (p$<$0.01). Table 1 reports the differences of US examination between VRA vs ERA vs LRA patients. LRA patients had more erosions at MTP and wrists with no differences at MCP joints. Synovial hypertrophy and PD signal had the same degree and distribution in the two groups of patients. LRA patients had more MTP joints with effusion with lower degree as compared to patients with ERA and VERA (see table 1).

Table 1

	VERA (A) 88 pts	VERA+ERA 183 pts	LRA (C) 165 pts	p
M/F	25/63	58/125	22/143	A vs C = 0.002 B vs C = $<$0.001
Number of pts aged $<$50y	30/88	58/183	21/165	A vs C = $<$0.001 B vs C = $<$0.001
% of pts with remission $<$12 months	85	80	48	A vs C = $<$0.001 B vs C = $<$0.001
% of pts with $>$1 eroded joint	39	54	62	A vs C = $<$0.001 B vs C = $<$0.001
% of pts with $>$1 joint with synovial hypertrophy	69	71	73	A vs C = ns B vs C = ns
% of pts with synovial hypertrophy $>$1	46	49	51	A vs C = ns B vs C = ns
% of pts with $>$1 joint positive for PD signal	48	50	45	A vs C = ns B vs C = ns
% of joints with PD signal $>$1	32	34	35	A vs C = ns B vs C = ns
% of pts with effusion at MTP joints	45	49	59	A vs C = 0.034 B vs C = 0.044
% of pts with MTP joints effusion $>$1	25	21	12	A vs C = 0.010 B vs C = 0.023

Conclusions: At US examination VERA, ERA and LRA pts in CR have the same degree of synovial hyperplasia and PD signal despite the differences of duration of CR. Higher degree of erosive disease (at wrist and MTP joints), lower degree of MTP effusion and higher prevalence of joint effusion at MTP joints were present among LRA vs ERA and VERA pts.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5047

SAT0655 EARLY ENDOTHELIAL DAMAGE IN PATIENTS WITH RAYNAUD'S PHENOMENON

R. Gualtierotti[1,2], F. Ingegnoli[2,3], T. Schioppo[2], S. Griffini[4,5], E. Grovetti[4,5], M.O. Borghi[6], M. Cugno[4,5], P.L. Meroni[1,2,3,6]. *[1]Lupus Clinic; [2]Division of Rheumatology, ASST G. Pini; [3]Department of Clinical Sciences and Community Health; [4]Dipartimento di Fisiopatologia Medico-Chirurgica e dei Trapianti, University of Milan; [5]Medicina Interna, Ospedale Maggiore Policlinico, Fondazione IRCCS Ca' Granda; [6]IRCCS Istituto Auxologico Italiano, Milan, Italy*

Background: Raynaud's phenomenon (RP) can be the first manifestation of systemic sclerosis (SSc) or other connective tissue diseases (CTDs), often preceding an overt disease by years. It is not known if markers of endothelial damage are detectable in those RP patients who subsequently develop a CTD.
Objectives: We studied RP patients at their first evaluation to correlate the levels of endothelial markers with the subsequent development of an overt disease 36 months later.
Methods: Eighty-two patients with RP at their first evaluation were recruited. We measured plasma levels of tissue-type plasminogen activator (t-PA) and von Willebrand factor (vWF), two markers of endothelial damage, and interleukin-6 (IL-6), a pro-inflammatory cytokine. Thirty healthy subjects served as healthy controls.
Results: At baseline, 67 patients showed capillaroscopic normal pattern and 15 patients, of which 11 were very early SSc, had scleroderma pattern. Plasma levels of t-PA, vWF and IL-6 were higher in patients with capillaroscopic normal pattern (p=0.0001) than in normal controls and even much higher in patients with scleroderma pattern (p=0.0001). In patients with capillaroscopic normal pattern and RP of recent onset ($<$18 months), vWF plasma levels were higher when autoantibodies were present (p=0.020). After 36 months, among 48 RP patients with capillaroscopic normal pattern who remained in follow-up, 24 were diagnosed as primary and 24 as secondary RP. In secondary RP, basal levels of t-PA, IL-6 and particularly vWF were higher than in primary RP (p=0.005, p=0.004, p=0.0001 respectively) and normal controls (p=0.0001 for all).
Conclusions: Our findings indicate that markers of endothelial damage are elevated in RP patients who subsequently develop SSc or other CTDs, even in the absence of capillaroscopic abnormalities.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5416

SAT0656 OPTICAL IMAGING OF PHAGOCYTE MIGRATION REPRESENTS A NOVEL METHOD TO DETERMINE DISEASE ACTIVITY IN CIA

S. Gran[1], L. Honold[2], O. Fehler[1], S. Zenker[1], S. Hermann[2], M. Schäfers[2], T. Vogl[1], J. Roth[1]. *[1]Institute of Immunology; [2]European Institute for Molecular Imaging, Münster, Germany*

Background: Recruitment and migration of phagocytes to the site of inflammation are key events in the onset of inflammation. Albeit crucial for pathogen elimination, tissue repair and restoration of tissue homeostasis, dysregulated phagocyte infiltration can also cause severe inflammatory disorders. Therefore, targeting and modulation of phagocyte infiltration represents a promising new approach to fight inflammatory disorders and diseases, such as rheumatoid arthritis. Additionally, non-invasive tracking of phagocyte migration to the site of inflammation could extend both scientific knowledge as well as the repertoire of diagnostic strategies in clinical use.
Objectives: The aim of this study was to establish a fluorescence reflectance imaging (FRI) based system to visualize and analyze migration properties of different cell populations in inflammatory disease models, like experimental arthritis, *in vivo*.
Methods: Immortalized murine myeloid progenitor ER-HoxB8 cells were differentiated to neutrophils or monocytes (1). Cells were labeled with the membrane-selective fluorescent dyes DIR (2) or DID, respectively. We analyzed viability and functionality of stained cells *in vitro* and investigated their ability to migrate to sites of inflammation *in vivo* in several mouse models - particularly in a collagen induced arthritis (CIA) mouse model - via fluorescence reflectance imaging (FRI). Using CRISPR-Cas9 technology we introduced targeted gene deletions for main adhesion molecules.
Results: Differentiated ER-HoxB8 cells could effectively be labeled with DIR or DID. Labeling of monocytes or neutrophils did not affect cellular viability or functionality *in vitro*. Subsequent *in vivo* imaging experiments allowed the visualization of migrated labeled phagocytes in different murine disease models, thereby cells could be detected at sites of inflammation with high sensitivity and specificity. In a CIA mouse model the amount of immigrated cells could even be associated closely to disease score and disease severity. Thus, the detection of immigration of labeled cells might also give hints about new inflammatory spots that are about to settle up before they can be detected macroscopically. Furthermore, differential cell labeling allowed direct quantitative comparison of differences in migration rates of wildtype and CD18 or CD49d knockout cells *in vivo*.
Conclusions: Specific and distinguishable labeling of diverse cell types allows *in vivo* tracking and subsequent quantification of migrated cells within the same animal. Targeted gene deletion allows analysis of molecular mechanisms relevant for leukocyte recruitment during different stages of arthritis. Correlation of the amount of immigrated cells to disease severity offers new opportunities to non-invasively detect and monitor inflammatory sites *in vivo*.
References:

[1] Wang GG, Calvo KR, Pasillas MP, Sykes DB, Häcker H, Kamps MP. Quantitative production of macrophages or neutrophils ex vivo using conditional Hoxb8. Nat Methods. 2006;3(4):287–93.
[2] Eisenblätter M, Ehrchen J, Varga G, Sunderkötter C, Heindel W, Roth J, et al. In vivo optical imaging of cellular inflammatory response in granuloma formation using fluorescence-labeled macrophages. J Nucl Med. 2009;50:1676–82.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6151

SAT0657 CAN VASCULAR INFLAMMATION IN RA BE DETECTED USING CONTRAST ENHANCED MRI? PRELIMINARY RESULTS

S. Skeoch[1,2], R. Little[3], Y. Watson[4], S. Cheung[3], J. O'Connor[3], Y. Alexander[5], I. Bruce[1,2], G. Parker[3], J. Waterton[3]. *[1]Manchester NIHR Musculoskeletal Biomedical Research Unit, Central Manchester University Hospitals NHS Foundation Trust; [2]Centre for Epidemiology; [3]Centre for Imaging Sciences; [4]University of Manchester; [5]Health Related Research, Manchester Metropolitan University, Manchester, United Kingdom*

Background: In rheumatoid arthritis (RA) vascular inflammation may contribute to excess cardiovascular (CV) risk. Contrast enhanced MRI has been used to detect vascular inflammation in Takayasu's arteritis. In RA, its utility has not been studied but it may provide a method of identifying and monitoring vascular inflammation and effects of therapy.
Objectives: We sought to compare carotid artery wall enhancement on contrast enhanced MRI in RA patients and controls and evaluate association with circulating markers of inflammation, endothelial activation and CV risk factors.
Methods: Patients and age/sex matched controls underwent clinical and serological assessment (details in Table 1) and a screening carotid ultrasound. Those with wall thickening>2mm had a carotid MRI. T_1-weighted images were acquired before and after gadopentate injection on a 3T scanner. Increase in mean signal intensity (SI) in the carotid vessel wall normalised to adjacent skeletal muscle provided a global enhancement metric (WE_G). Histograms of distribution of SIs on pre-and post- contrast images were generated and bimodal Gaussian distributions fitted to explore patterns of enhancement within the wall. MRI measurements were compared between groups and association with serological markers tested using non-parametric statistics.
Results: 27 patients and 10 controls underwent MR imaging. Key characteristics are seen in Table 1. There was no difference in WE_G between groups and no association with serological markers. However a bimodal distribution of SI in vessel wall was observed (Figure 1) and in exploratory analysis these two components were analysed separately. For the low-signal component enhancement (WE_{low}) correlated with ESR, I-CAM, e-selectin (r=0.39,p=0.03;r=0.44,p=0.01;r=0.37,p=0.04). There was a trend towards correlation with CRP (r=0.30,0.08) and towards higher values in patients (median 0.20 (0.15, 0.33) vs 0.14 (0.11, 0.22),p=0.051). Enhancement in the high-signal component (WE_{high}) was not associated with serological markers or RA status.

Table 1.Key characteristics (median (IQR) or frequency (%) where*)

	Cases	Controls	P value
Age (yrs)	61.0 (56.5, 64.6)	55.4 (54.0, 57.0)	0.07
Female*	22 (81)	5 (50)	0.06
LDL (mmol/L)	2.7 (2.25, 3.23)	3.80 (3.24, 4.53)	0.08
Glucose (mmol/L)	4.8 (4.6, 5.0)	5.8 (5.3, 6.0)	0.01
Hs-CRP (mg/l)	3.34 (2.04, 5.75)	0.81 (0.39, 4.58)	0.047
ESR (mm/hr)	18 (10, 35)	7 (5, 10)	0.01
ICAM (ng/ml)	161.5 (134.8, 213.4)	151.3 (106.9, 220.8)	0.51
V-CAM1 (ng/ml)	398 (352, 473)	376 (353, 390)	0.52
E-selectin (ng/ml)	7.55 (5.79, 21.1)	4.71 (3.01, 7.76)	0.11
WE_G	0.23 (0.23, 0.28)	0.25 (0.18, 0.27)	0.62
WE_{low}	0.20 (0.15, 0.33)	0.14 (0.11, 0.22)	0.05
WE_{high}	0.32 (0.22, 0.50)	0.33 (0.29, 0.38)	0.73

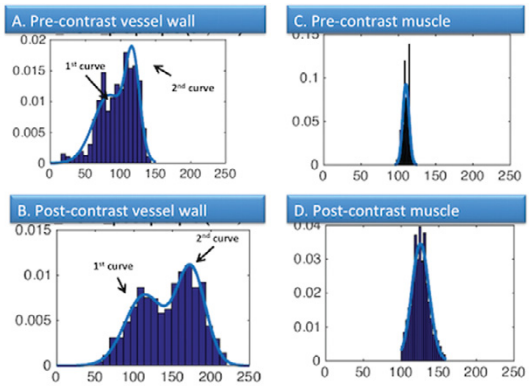


Figure 1. Distribution of signal intensity (SI) within the vessel wall and muscle referent before and after contrast injection (x axis signal intensity (a.u), y axis relative frequency). Gaussian curves were fitted and mean of fit values for each curve were calculated. A bimodal distribution with low and high signal intensity components can be seen in vessel wall (panel A & B) compared with a single curve in muscle (panel C& D). For each curve the difference between pre- and post- contrast mean SI was calculated (with normalisation to muscle signal). This provided a wall enhancement measurement for the 2 separate curves (WE_{low} and WE_{high})

Conclusions: Simple global SI measurement on MRI did not suggest vascular inflammation in RA. However, the bimodal SI distribution may represent different wall components e.g. intima and adventitia. The differential enhancement, and association of WE_{low} with inflammation, endothelial activation and RA status, warrants further investigation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6657

SAT0658 THE STIFFNESS OF MEDIAN NERVE MEASURED BY ELASTOSONOGRAPHY IN PATIENTS WITH RHEUMATOID ARTHRITIS

S. Anno[1], T. Okano[2], Y. Sugioka[3], K. Mamoto[2], T. Koike[3,4], K. Inui[2], H. Nakamura[2]. *[1]Yodogawa Christian Hospital; [2]Department of Orthopedic Surgery, Osaka City University Graduate School of Medicine; [3]Center for Senile Degenerative Disorders (CSDD), Osaka City University Medical School, Osaka; [4]Search Institute for Bone and Arthritis Disease (SINBAD), Wakayama, Japan*

Background: Carpal tunnel syndrome (CTS) is the most frequent neuropathy of all entrapment neuropathies in the general population. Rheumatoid arthritis (RA) is one of the disease generate secondary CTS. The pathophysiology of CTS of RA might be different from idiopathic CTS. RA is a disease that has the characteristics to generate inflammatory synovial proliferation of the joint and also tendon. Although inflammation of the wrist joint and synovial tissue of the flexor tendons can cause increased pressure in the carpal tunnel, there is a possibility that even RA patients without symptoms of CTS also have subclinical median nerve damage because of the synovial proliferation and inflammation.
Objectives: The aim of this study was to assess and compare the stiffness of the median nerve measured by quantitative elastosonography between patients with RA without symptom of CTS and controls.
Methods: Four hundred two hands in 201 patients with RA and 222 hands in controls were included. All participants were examined both wrists. Ultrasound (US) examination was performed by using a 5- to 18-MHz linear array transducer (HI VISION Ascendus; HitachiAloka Medical,Tokyo, Japan). As a reference medium, an acoustic coupler (EZUTECPL1; HitachiAloka Medical) with a standardized

elasticity was attached to the transducer during the elastosonography. The inlet of the carpal tunnel at the scaphoidpisiform level and the proximal portion of the carpal tunnel inlet were scanned in a transverse plane. The crosssectional area (CSA) and the elasticity of the median nerve, which was measured as the acoustic coupler/median nerve strain ratio, were evaluated. The measurements were repeated two times, and the average strain ratio was used for analysis.

Results: We analyzed 342 hands in 177 RA patients (139 female, mean age: 63.5±11.6 years) and 158 hands in 81 non-RA (68 female, mean age: 71.5±14 years) finally. There were no significant differences in the cross-sectional area of median nerve (left: 8.9 vs 8.7 mm^2, p=0.91, right: 8.2 vs 8.4 mm^2, p=0.62) or the circumference of median nerve (left: 13.1 vs 13.4 mm, p=0.41, right: 13.7 vs 13.7 mm, p=0.95) within carpal tunnel between RA group and non-RA group. Strain ratio within carpal tunnel in RA group was higher than that of non-RA group (left: 2.6 vs 2.1, p=0.002, right: 2.7 vs 2.2, p=0.003). There were no significant differences in the cross-sectional area of median nerve (left: 7.5 vs 8.1 mm^2, p=0.07, right: 8.8 vs 8.3 mm^2, p=0.6), the circumference of median nerve (left: 13.1 vs 13.5 mm, p=0.3, right: 13.7 vs 13.9 mm, p=0.71) and strain ratio (left: 2.1 vs 2.0, p=0.88, right: 2.3 vs 2.1, p=0.01) at the entrance of the carpal tunnel between RA group and non-RA group.

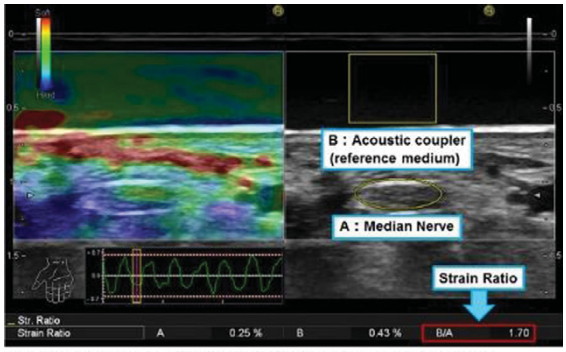


Figure: The images of acoustic coupler /median nerve strain ratio.

Conclusions: Real-time Elastosonography showed the stiffness of the median nerve with RA patients without any symptoms of CTS was higher than controls. It suggests that inflammation of flexor tenosynovitis and wrist joint may generate fibrotic change of median nerve in patients with RA.

References:

[1] Miyamoto H, Halpern EJ, Kastlunger M, et al. Carpal tunnel syndrome: diagnosis by means of median nerve elasticity–improved diagnostic accuracy of US with sonoelastography. Radiology. 2014;270:481–6.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1632

SAT0659 COMPARISON BETWEEN EIGHT DIFFERENT ULTRASONOGRAPHIC SCORES FOR HAND ASSESSMENT IN RHEUMATOID ARTHRITIS -A CROSS-SECTIONAL STUDY

S. Hussain[1,2], P. Sivakumaran[1,2], L. Attipoe[2], C. Ciurtin[2]. *[1]University College London Medical School; [2]Department of Rheumatology, University College London Hospitals NHS Foundation Trust, London, United Kingdom*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory condition associated with well-recognised inflammatory joint features, which are amenable to ultrasound (US) examination. The implementation of US scoring systems in addition to clinical examination could help standardise the way RA is monitored; however, due to variation in local availability of US and sonographer expertise, different scoring systems have been used in clinical practice (1). Despite significant research progress in supporting the role of US in RA, there is no consensus as to which scoring system is most useful.

Objectives: To assess whether simplified US protocols for hand examination correlate significantly with a 22 hand joint US score in patients with established rheumatoid arthritis, and correlate the US examination with the disease activity score (DAS-28 score).

Methods: This is a cross-sectional study of 224 RA patients stratified based on their DAS-28 scores and assessed using eight preselected US examination protocols including 22, 18, 16, 14, 10, 8 and two different combinations of 4 joints, respectively. Student T, Mann-Whitney U and Kuskal-Wallis tests were employed for analysis of clinical, laboratory and US parameters in the RA patient groups ($P<0.05$ was considered significant). Spearman's coefficients were used to correlate permutations of pairs of US scores, and US and DAS-28 scores.

Results: We found a significant difference between different US hand scores and their ability to detect the presence of active and chronic inflammation in RA patients. The DAS-28 scores correlated very well (R=0.89–1, $P<0.05$) with the total Power Doppler (PD) scores generated by all US protocols irrespective of patients' disease activity. Simplified US scores missed information on presence of erosions ($P<0.05$), but were equivalent to the extensive 22 joint score in appreciating the amount of chronic and active inflammation compared to the extensive 22 joint score (P=0.15, P=0.11, respectively).

Conclusions: This study showed that preselected simplified US scores could be used in clinical practice to appreciate reliably the disease activity in patients with established RA; however they are less reliable in appreciating the disease burden when compared with an extended protocol for US examination of 22 hand joints. All the simplified US scores correlated very well with DAS-28 scores.

References:

[1] Mandl, P., et al., A systematic literature review analysis of ultrasound joint count and scoring systems to assess synovitis in rheumatoid arthritis according to the OMERACT filter. J Rheumatol, 2011. 38(9): p. 2055–62.

Acknowledgements: S. Hussain and P. Sivakumaran contributed equally to the study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2722

SAT0660 SAFETY, FEASIBILITY AND TOLERABILITY OF PERFORMING CONSECUTIVE MINIMAL INVASIVE ULTRASOUND-GUIDED SYNOVIAL BIOPSY PROCEDURES ON THE SAME WRIST IN A PROSPECTIVE RHEUMATOID ARTHRITIS STUDY

S.A. Just[1], C. Nielsen[2], E.K. Hejbøl[3], H.D. Schrøder[3], I.M.J. Hansen[4], T. Barington[2], H.M. Lindegaard[1]. *[1]Rheumatology; [2]Clinical Immunology; [3]Clinical Pathology, Odense University Hospital, Odense; [4]Medicine, Svendborg Hospital, Odense University Hospital, Svendborg, Denmark*

Background: Studies on synovial tissue retrieved using the minimal invasive ultrasound-guided synovial biopsy (USG-SB) method have led to major advances in the understanding of Rheumatoid Arthritis (RA). The method is now used in multicenter RA studies and recommended in the phases of RA drug development. Only to biopsy disease active joints at start and end of a study, can lead to biopsies being retrieved from different joints. This can make interpretation of the changes in the synovial tissue and gene-expression profile difficult, as synovial histology patterns can vary between joints. We here present an approach where we biopsied the wrist with disease activity at presentation and the same wrist after six month of disease duration. We use the wrist, as it is the joint most commonly involved in the upper extremity in RA. The joint is easily accessible for USG-SB and therefore ideal to use to follow disease activity/treatment response/biomarker change in prospective RA studies.

Objectives: To assess the safety, tolerability and feasibility to perform repeated synovial biopsies from the same wrist, using a minimally invasive USG-SB technique in patients suffering from RA.

Methods: Patients with newly diagnosed untreated RA or longstanding (>5 years) RA and at least one clinically swollen wrist, underwent x-ray, magnetic resonance imaging (MRI) and ultrasound examination of the affected wrist and hand on the day of the biopsy. This was repeated 6 months later, where the second biopsy from the same wrist was taken. EULAR guidelines for RA treatment were followed in the 6 months between biopsies. Patient-reported outcomes (PRO) included a standard questionnaire given to all patients on the day of the biopsy as well as 2 weeks after the biopsy. Tolerability and the patient-reported willingness to repeat the procedure was assessed using the 5-point Likert scale.

Results: 38 RA patients (22 early, 16 longstanding) underwent USG-SB procedure at inclusion and after 6 months. One patient was excluded and did not have second biopsy due to diagnosis of CPPD. All patients have undergone first biopsy and at present time and 50% second biopsy. At the EULAR congress complete data will be presented. At present time, at both first and second biopsy no worsening in PRO of the biopsied joints was reported 2w after the biopsy, as compared before the biopsy. No infection, hemorrhage, nerve or tendon damage has currently been observed. One patient developed a tenosynovitis after biopsy (the CPPD patient), successfully treated with glucocorticoid injection. 10% of the patients were somewhat or very unlikely to have another biopsy procedure after the first procedure, and 6% after the second. All included RA patients accepted to have a second biopsy. Detailed data on differences in tolerability between early untreated RA patients versus patients with longstanding RA, will be presented at the conference.

Conclusions: To our knowledge, we are the first, to demonstrate that retrieving synovial tissue using the USG-SB method on the same wrist, at start and end of a prospective RA study, is safe and well tolerated.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2453

SAT0661 FINGER JOINT CARTILAGE THICKNESS EVALUATED BY ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

T. Ogura, A. Hirata, N. Hayashi, H. Ito, S. Takenaka, Y. Fujisawa, K. Mizushina, T. Katagiri, R. Kujime, M. Imamura, N. Yamashita, H. Kameda. *Toho University Ohashi Medical Center, Tokyo, Japan*

Background: Joint destruction in RA includes both bone and cartilage lesions. By X-ray examination, cartilage destruction is evaluated as a joint space narrowing (JSN). However, joint space narrowing is not a direct evaluation of cartilage.

Objectives: We aimed to examine the finger joint cartilage thickness (CT) by ultrasound (US) imaging and clarify its clinical significance in patients with RA.

Methods: We enrolled 121 RA patients in low disease activity or clinical remission

(DAS28-CRP <2.7) in this study. The CT of metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of 2nd to 5th fingers was bilaterally visualized and measured at the middle portion of MCP and PIP joints from a longitudinal dorsal view, with approximately 90 degrees flexion. In addition, JSN of finger were scored by van der Heijde- modified Sharp method for patients who had a hand X-ray within 2 months.

Results: CT in MCP joints ranged from 0.0 to 1.1 mm (median 0.5 mm), and CT in PIP ranged from 0.0 to 0.6mm (median 0.3mm), respectively. The sum of total CT from 8 fingers ranged from 4.0 to 9.4 mm (median 6.9 mm), and there was a significant difference in total CT, but not in JSN score, between male and female patients (7.4 versus 6.7, p=0.006; and 11 versus 10, p=0.899, respectively). CT was well correlated with JSN (ρ=-0.589, p<0.001; ρ=-0.595, p<0.001 for MCP joints andρ=-0.448, p<0.001 for PIP joints), and both CT and JSN were significantly correlated with disease duration (ρ=-0.282, p=0.002, andρ=0.286, p=0.005, respectively). Notably, CT of MCP, but not of PIP, was inversely correlated with disease duration (ρ=-0.328, p<0.001). Height was correlated with CT (ρ=0.244, p=0.008), but not with JSN (ρ=-0.057, p=0.589). CT and JSN were not correlated with age, functional disability, and seropositivity.

Conclusions: A direct visualization and quantification of finger joint CT, especially MCP joints, by US is valid and useful in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4703

SAT0662 EVALUATION OF ANTI-DOUBLE STRANDED DNA ANTIBODIES IN THE MONITORING OF SYSTEMIC LUPUS ERYTHEMATOSUS

T. Dervieux[1], T. O'Malley[1], J. Conklin[1], C. Ibarra[1], C. Bentow[2], M.A. Aure[2], M. Mahler[2]. *[1]Exagen Diagnostics, Vista, CA; [2]Research and Development, Inova Diagnostics, San Diego, CA, United States*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune rheumatic disease characterized by the production of pathogenic autoantibodies. Amongst these antibodies, those directed to dsDNA are routinely used to monitor disease activity and are components of the SELENA-SLEDAI index to score severity of SLE disease. Because the predictive value of anti-dsDNA is dependent on the sensitivity and robustness of the assays used, the choice of anti-dsDNA is crucial in the clinical laboratory and clinical research setting.

Objectives: The objective was to compare four anti-dsDNA assays for their performance characteristics of SLE disease activity.

Methods: A cohort of 36 subjects with active SLE presenting with classical complement activation were enrolled and followed monthly for 1 year. At each study visit blood was collected, serum isolated and frozen until analysis. A total of 371 specimens were collected. Disease activity was scored on the day of each study visit according to the SELENA-SLEDAI method excluding anti-dsDNA or complement components (non-serological [ns] SELENA-SLEDAI). All specimens were tested using four different anti-dsDNA kits; QUANTA Lite, QUANTA Flash, a high Avidity anti-dsDNA ELISA, and the *Crithidia luciliae* indirect immunofluorescence assay (CLIFT) (Inova Diagnostics, San Diego, CA). Study visits presenting with inactive disease (ns-SELENA- SLEDAI score=0) were compared to those presenting with active disease (ns-SELENA- SLEDAI>0). The longitudinal data were analyzed using linear mixed effect modeling with the ns-SELENA-SLEDAI as dependent variable and the anti-dsDNA titers as fixed effect predictors. Marginal R^2 was calculated for each assay.

Results: At enrollment the sensitivity of the QUANTA Lite and High Avidity anti-dsDNA both reached 64%; whereas anti-dsDNA positivity was 83% by QUANTA Flash and reached 96% by CLIFT. Study visits with active disease presented with several fold higher anti-dsDNA titers than those with inactive disease status (Table 1). Linear mixed effect modeling indicated that the decrease in ns-SELENA-SLEDAI scores were associated with significant reduction in titers of all three anti-dsDNA kits (Table 2). QUANTA Flash yielded highest marginal R^2 (0.112) (Table 2).

Table 1. Anti-dsDNA antibody and disease activity

Anti-dsDNA		Inactive Disease 0 (n=141)	Active disease 1+ (n=230)	*p* value
QUANTA Flash	Titers (units)	72 (30–134)	170 (56–813)	<0.001
	Percent positive (>35 Units)	72%	86%	<0.001
High Avidity	Titers (units)	36 (12–170)	129 (47–775)	<0.001
	Percent positive (>30 Units)	56%	77%	<0.001
QUANTA Lite	Titers (units)	343 (106–624)	545 (293–879)	<0.001
	Percent positive (>301 Units)	53%	74%	<0.001
CLIFT	Titers (units)	1:160 (1:80 – 1:320)	1:320 (1:160–1:320)	<0.001
	Percent positive (>1:10)	99%	97%	0.26

Titers are presented as median inter-quartile range.

Table 2. Linear Mixed model effects of anti-dsDNA with ns-SELENA-SLEDAI scores

Assay	Intercept + Estimate SE	*p* value	Marginal R^2
QUANTA Flash	3.3±0.5 + 0.0011±0.001	<0.001	0.112
High Avidity	2.8±0.8 + 0.0023±0.0011	0.001	0.082
QUANTA Lite	2.9±0.6 + 0.0037±0.001	0.022	0.037
CLIFT	3.3±0.8 + 0.0031±0.003	0.28	0.006

Conclusions: These preliminary data indicate that anti-dsDNA antibodies determined by QUANTA Flash have value in monitoring SLE disease activity.

Disclosure of Interest: T. Dervieux: None declared, T. O'Malley: None declared, J. Conklin: None declared, C. Ibarra: None declared, C. Bentow Employee of: Inova Diagnostics, M. A. Aure Employee of: Inova Diagnostics, M. Mahler Employee of: Inova Diagnostics

DOI: 10.1136/annrheumdis-2017-eular.5317

SAT0663 TWO-STEP ALGORITHM FOR EARLY DIAGNOSIS OF OSTEOARTHRITIS BASED ON PLASMA DAMAGED AMINO ACIDS PROVIDES SIMPLE AND LOW COST SCREENING TEST

N. Rabbani, U. Ahmed, P.J. Thornalley. *Warwick Medical School, University of Warwick, Coventry, United Kingdom*

Background: Currently, magnetic resonance imaging techniques have been developed for evaluation of cartilage damage in early-stage osteoarthritis (eOA). These imaging techniques have approximately 70% sensitivity and 90% specificity compared to reference diagnosis by arthroscopy. They require expensive instrumentation, time and facilities. In searching for biomarkers for clinical diagnosis we found that the proteolysis of damaged (oxidised, glycated and nitrated) proteins gives a unique pattern in the plasma of arthritic patients with the severity of the disease – trace level oxidised, glycated and nitrated amino acids. In this study we developed a two-step algorithm using these analytes as features.

Objectives: The objective was to distinguish between the following four groups: healthy control, eOA, early stage rheumatoid arthritis (eRA) and other inflammatory joint disease (non-RA).

Methods: Four algorithm types were tested for performance using random forests, multiclass logistic regression, multi-class sparse logistic regression and support vector machines. In all cases, the diagnostic algorithms were trained on the training data set, before being used to predict the disease class for each sample in the test data set. A two-stage approach was taken: (i) to distinguish between disease and healthy control; and (ii) to distinguish between eOA, eRA and non-RA. The area under the curve of the receiver operating characteristic plot (AUROC) statistic was used as measure of performance

Results: Random forest was the best-performing method. Application of two algorithms consecutively gave the best diagnostic outcome. The AUROC (sensitivity/specificity) values for disease/health were: eOA, 0.99 (0.92/0.91); eRA, 0.96 (0.89/0.90) and non-RA, 0.77 (0.73/0.72) for the training set and test set validations. A random outcome is 0.50. For typing arthritis, eOA, eRA and non-RA, AUROC values were in the range 0.68–0.98, 0.77–0.93 and 0.62–0.91 for training set and test set cross-validations and test set validation, respectively. A random outcome is 0.33.

Conclusions: A two-step algorithm approach based on trace level damaged amino acids gave better diagnostic performance that MRI for detecting and typing eOA. It is low cost and suitable for rollout as a clinical screening test.

References:

[1] Menashe, L., Hirko, K., Losina, E., Kloppenburg, M., Zhang, W., Li, L. and Hunter, D. J. (2012) The diagnostic performance of MRI in osteoarthritis: a systematic review and meta-analysis. Osteoarthritis and Cartilage. 20, 13–21.

[2] Ahmed, U., Anwar, A., Savage, R.S., Thornalley, P.J. and Rabbani, N. (2016) Application of protein glycation, oxidation and nitration for early-stage diagnosis and severity of osteoarthritis and other arthritic disease. Arthritis Research & Therapy 18:250.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6904

SAT0664 IS THERE AN EARLY ULTRASONOGRAPHIC PATTERN IN SALIVARY GLANDS IN BOTH PRIMARY AND SECONDARY SJOGREN SYNDROME?

V.C. Iorgoveanu[1], D. Mazilu[2], I. Saulescu[3], V. Vlad[4], V. Bojinca[3], L. Groseanu[3], D. Opris[3], A. Balanescu[3], C. Constantinescu[3], D. Predeteanu[3], R. Ionescu[3]. *[1]Rheumatology, Carol Davila University of Medicine and Pharmacy; [2]Saint Mary Clinical Hospital, UMF Carol Davila, Bucharest, Romania; [3]Rheumatology, Saint Mary Clinical Hospital, UMF Carol Davila; [4]Rheumatology, Saint Mary Clinical Hospital, Bucharest, Romania*

Background: Sjogren Syndrome (SS) affects mainly exocrine glands. Ultrasonography (US) demonstrates specificity and sensibility in major salivary glands (SG) evaluation. Recent data confirm US might be used as primary evaluation technique for its ability to show structural alterations of parenchyma [1].

Objectives: To assess the gray scale (GS) parenchymal inhomogeneity of major SG in patients with established primary and secondary SS and correlate with clinical and biological data.

Methods: Consecutive patients with SS were recruited and SG US was performed. Inhomogeneity of glandular parenchyma was quantified binary on each gland. ESSDAI and ESSPRI scores were calculated. Statistics was performed with SPSS.

Results: Twenty one (42.85% primary SS, 90.47% female) consecutive patients were included. Mean age was 53.66+/-12.99 years and disease duration 5.33+/-3.74 years. Antibody SSA/SSB presence was found in 85.7% (18/21). ESSDAI mean was 8.67+/-8.9 (0–29), ESSPRI 10.13+/-5.59 (0–20). There were no differences regarding ESSDAI and ESSPRI in the two groups (primary and secondary SS). Right parotid gland showed alterations in 71.4% patients (77%

with primary SS, 66% with secondary SS). Frequently inhomogeneity was found in all major SG (33%, 22% left and right submandibular, 77%, 44.4% left and right parotid glands) in primary SS. Both submandibular glands were symmetrically involved ($p<0.02$). Duration of disease was negatively correlated to inhomogeneity of right parotid gland ($p<0.02$).

Conclusions: Inhomogeneity in major SG in GS US was found in the majority of patients with primary and secondary SS. The symmetrical involvement of submandibular glands was significant. The inhomogeneity appears in the early period of diagnosis. No major differences were found between two groups.

References:

[1] Damjanov N, Milic V, Nieto-González JC, Janta I, Naredo E. Multiobserver Reliability of Ultrasound Assessment of Salivary Glands in Patients with Established Primary Sjögren Syndrome. J Rheumatol. 2016 Oct;43(10):1858–1863.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2104

SAT0665 DOES PATIENTS' OPINION OF REMISSION IN RHEUMATOID ARTHRITIS OVERLAP US "TRUE" REMISSION?

V. Vlad[1], F. Berghea[2], M. Popescu[1], V. Iorgoveanu[1], D. Predeteanu[1], R. Ionescu[2]. *[1]Rheumatology, Clinical Hospital Sf Maria Bucharest; [2]Rheumatology, UMF Carol Davila, Bucharest, Romania*

Background: Patients describe RA remission as the absence of any symptoms or return to normality. Ultrasound (US) in RA remission patients did not exactly overlap clinical evaluation of remission in previous studies (residual synovitis frequently described). US tenosynovitis evaluation and scoring seemed to better follow clinical remission scores than synovitis in RA [1].

Objectives: To verify with US/clinical evaluations if patients' reported remission is "true" remission, and if and which clinical and US scores are lowest possible in that cohort.

Methods: Forty-eight RA patients were enrolled in this pilot study between 2015–2017 according to their positive answer to the question "Are you feeling free of symptoms, like before RA started for you?"; the enrollment was regardless of the treatment they were on. Written informed consent was obtained. Clinical evaluation of tender and swollen joints was performed the same day with US evaluation of 24 joints and 26 tendon sites and with lab CRP evaluation, blinded from one another. DAS28 and SDAI were calculated after, counting VAS=1, for both physician and patients.

Results: Mean patients age was 58, 35/48 (72.9%) patients were also in remission per DAS28 criteria. Except for CRP value, no other variables (tender, swollen joints, RF, CCP, remission duration) were significantly different in the group with overlapping DAS28 remission. Considering 1.00 as the "ideal" situation (absolute overlapping of US remission and remission felt by patients), the closest was PD scoring in tenosynovitis of the ankle and feet (100%) and the furthest was GS scoring of synovitis in superior and inferior limbs (mean 17.1%)-table 1. Although residual synovitis and tenosynovitis in remission RA patients did not exhibit a statistically significant difference, PD tenosynovitis in both upper and lower limbs was found in less than 10% of patients. This confirms the results from our previous cohort [1], that tenosynovitis better overlaps RA remission than synovitis.

Table 1. Prevalence of US remission in patients with clinical remission – bootstraping for CI

MSUS Remission	DAS28 remission	SDAI Remission
PD Tenosynovitis	94.3 (5.7–100)	90.9 (77.3–100)
GS Tenosynovitis	57.1 (40.0–74.3)	54.5 (36.4–72.7)
PD Synovitis	62.9 (45.7–80.0)	59.1 (36.4–77.3)
GS Synovitis	17.1 (5.7–31.7)	13.6 (0–31.8)
PD Lower limb tenosynovitis	100 (100)	100 (100)
GS Lower limb tenosynovitis	91.4 (82.9–100)	86.4 (72.7–100)

Conclusions: The way patients perceive their disease activity is not related to either DAS28, SDAI scores or to objective US assessment of joints and tendons (GS or PD). However, PD signal especially in tendons sheaths seems to be absent in patients having a normal life, according to their own opinion. Consequently, patients in remission could benefit from US evaluation on any machine, regardless of its costs and Doppler settings. GSUS synovitis/tenosynovitis can be residual finding and does not imply any dissatisfaction in patients' health. An ongoing cohort of active RA patients is currently conducted to explore the validity of this conclusion in these cases, too.

References:

[1] Vlad V et al. Tenosynovitis US scoring systems follow synovitis and clinical scoring systems in RA and are responsive to change after biologic therapy. Med Ultrason 2015 Sep;17(3):352–60.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4244

SAT0666 SAMPLE SIZE FOR RA CLINICAL TRIALS USING ULTRASOUND OUTCOME MEASURES MAY BE REDUCED BY NOVEL JOINT SELECTION METHODS: A PILOT STUDY

J.C. Allen Jr[1], J. Thumboo[2,3,4], W.K. Lye[1], P.G. Conaghan[5,6], L.C. Chew[2,3,4], Y.K. Tan[2,3,4]. *[1]Office of Clinical Sciences, Centre for Quantitative Medicine, Duke-NUS Medical School; [2]Yong Loo Lin School of Medicine, National University of Singapore; [3]Duke-NUS Medical School; [4]Department of Rheumatology and Immunology, Singapore General Hospital, Singapore, Singapore; [5]NIHR Leeds Musculoskeletal Biomedical Research Unit; [6]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom*

Background: Novel outcome measures selecting a reduced joint count for ultrasonography can be highly responsive in demonstrating the improvement in joint inflammation seen in rheumatoid arthritis (RA) patients on treatment [1].

Objectives: To determine whether the use of the novel methods can translate into smaller sample sizes for subject recruitment into RA clinical trials. Results from the existing methods are used for comparison.

Methods: 24 RA patients with treatment starts or escalation had clinical and ultrasound joint assessment at baseline and 3 months. The novel methods select joints based on (A) ultrasound joint findings (i.e. Individualized Ultrasound (IUS) method) or (B) a composite of ultrasound and clinical joint findings (i.e. Individualized Composite Ultrasound (ICUS) method). In contrast, the existing methods utilize pre-determined joint sites for ultrasonography. Scores at the relevant joints per patient are summed up to obtain the total inflammatory score (TIS). The effect size (ES) was measured as the mean change of the TIS divided by the standard deviation of the change in the TIS. Sample sizes were calculated from confidence intervals (CIs) on ES that reflect uncertainty in estimating ES. For a given CI on ES, sample sizes are computed as the minimum number of patients required to provide $\geq$80% power at α =0.05 for rejecting the null hypothesis (defined as no difference in the 3-month mean change in TIS comparing novel versus existing methods).

Results: Based on the 95% CI analysis, sample sizes using existing joint assessment methods in conjunction with the 12-joint approach ranged from 10 to 234. The corresponding sample sizes using the ICUS method with the 12-joint approach ranged from 7 to 39, and using the IUS method with the 12-joint approach ranged from 6 to 37. The corresponding sample sizes using the ICUS method with the 7-joint approach ranged from 6 to 24, and using the IUS method with the 7-joint approach ranged from 6 to 35.

Table 1. Summary statistics for novel versus existing methods on 3-month change in scores

Method/Approach	Sample Estimates				95% CI	
	Mean 3-month change in TIS	SD of change in TIS	Effect Size	Post-hoc Sample Size	Effect Size	Sample Size
ICUS/7-joint	0.61	0.54	1.13	9	0.61, 1.64	6, 24
ICUS/12-joint	0.87	0.91	0.96	11	0.46, 1.43	7, 39
IUS/7-joint	0.66	0.67	0.99	11	0.49, 1.47	6, 35
IUS/12-joint	0.91	0.94	0.97	11	0.47, 1.45	6, 37
Existing/7-joint	0.10	0.29	0.34	70	-0.07, 0.75	16, –[1]
Existing/12-joint	0.22	0.35	0.63	68	0.18, 1.06	10, 234

CI: Confidence Interval; SD: Standard Deviation. [1]Interval contains zero which corresponds to the null hypothesis, so upper limit cannot be calculated.

Conclusions: Our findings strongly suggest that novel ultrasound joint selection methods result in smaller sample size requirements compared to existing methods, and provide justification for larger studies to confirm these observations.

References:

[1] Tan YK et al. Novel Ultrasound Joint Selection Methods Using a Reduced Joint Number Demonstrate Inflammatory Improvement when Compared to Existing Methods and Disease Activity Score at 28 Joints. J Rheumatol. 2016;43:34–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1430

SAT0667 PRESEPSIN AND PROCALCITONIN ARE OF DIAGNOSTIC VALUE FOR BACTERIAL INFECTION IN PATIENTS WITH CONNECTIVE TISSUE DISEASES

Y. Ichimura, Y. Kawaguchi, A. Tochimoto, T. Higuchi, M. Tochihara, Y. Katsumata, H. Yamanaka. *Institute of Rheumatology, Tokyo women's medical university, Tokyo, Japan*

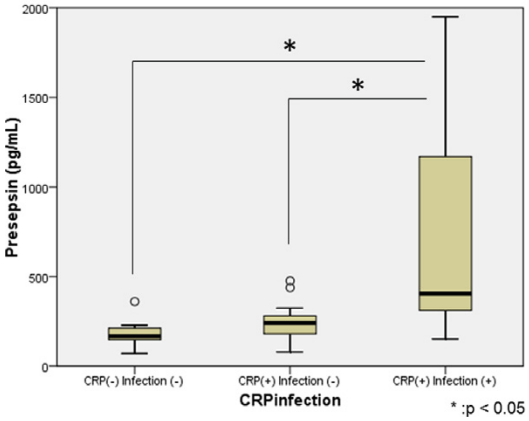
Background: Recently, presepsin (soluble CD14-subtype) and procalcitonin are reported as a good diagnostic markers of bacterial infection, especially sepsis. However, their utility in patients with connective tissue diseases (CTDs) has been unknown.

Objectives: To assess the diagnostic value of presepsin and procalcitonin in patients with CTDs.

Methods: We enrolled the consecutive patients with CTDs, who checked the level of procalcitonin and/or presepsin during January to September, 2016, retrospectively. We divided two groups; the infection group and non-infectious group. Infection was diagnosed by symptoms, micro-bacterial methods and the good response to antibiotics. The data analysis were assessed using IBM SPSS statistics 22.

Results: Eighty-four patients with CTDs were enrolled, including 42 patients with rheumatoid arthritis (RA). The level of procalcitonin was evaluated in all patients, and the level of presepsin was in 48 patients. Thirty-six patients were classified in infection group; 38 patients in the CRP-positive non-infection group; and 10 patients in CRP-negative non-infection group. The level of presepsin was significant higher in infection group than CRP-positive non-infection group (693 +/- 577 pg/mL vs. 250 +/- 101 pg/mL, $p<0.01$) (Fig. 1). Among the patients with RA, the level of presepsin was significant higher in infection group than non-infection group (809 +/- 637 pg/mL vs. 233 +/- 135 pg/mL, $p<0.01$). AUCs of procalcitonin (0.823) and presepsin (0.821) showed similar diagnostic value. The cut-off value of presepsin and procalcitonin were 265 pg/mL and 0.16 ng/mL, respectively (sensitivity: 78.3% and 82.6%, specificity: 76.0% and 76.0%).

【Fig. 1】The level of presepsin in each group



Conclusions: Procalcitonin and presepsin may be of diagnostic value for bacterial infection in patients with CTDs, especially may distinguish bactrial infection from active phase in patients with CTDs.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4763

SAT0668 ASSESSMENT OF INTRACRANIAL VESSELS AND VASCULAR LESIONS IN RHEUMATOID ARTHRITIS. A DETAILED TRANSCRANIAL DOPPLER, CAROTID ULTRASOUND AND BRAIN MRI STUDY

C. Oláh[1], Z. Kardos[2], M. Sepsi[3], A. Sas[4], L. Kostyál[3], H.P. Bhattoa[5], K. Hodosi[6], G. Kerekes[7], L. Tamási[2], A. Valikovics[4], D. Bereczki[8], Z. Szekanecz[6]. *[1]Department of Neurosurgery, Borsod County Teaching Horspital; [2]Department of Rheumatology, Semmelweis Teaching Hospital; [3]Department of Radiology; [4]Department of Neurology, Borsod County Teaching Horspital, Miskolc; [5]Department of Laboratory Medicine; [6]Department of Rheumatology; [7]Department of Angiology, University of Debrecen, Faculty of Medicine, Debrecen; [8]Department of Neurology, Semmelweis University, Budapest, Hungary*

Background: Stroke has been associated with rheumatoid arthritis (RA). Vascular physiology should be assessed in the preclinical vascular state.
Objectives: We assessed RA patients and healthy controls by transcranial Doppler (TCD), carotid ultrasonography and brain MRI. We wished to determine preclinical pathophysiological changes in the cerebral vasculature.
Methods: Altogether 63 female RA patients and 60 age-matched controls underwent TCD assessment of the medium cerebral (MCA), basilar and vertebral arteries. Pulsatility (PI), resistance (RI) indices and circulatory reserve capacity (CRC) were determined. The presence of carotid plaques and intima-media thickness (cIMT) were also determined. Intracerebral vascular lesions were investigated by brain MRI. RA subsets include MTX- and biologic-treated patients.
Results: MCA PI and RI values at rest and after apnea are significantly increased in the total RA population vs controls. MCA PI (r) and RI (r) is also lower in biologic-treated patients. MCA CRC was also impaired and basilar artery PI was higher in RA. More RA patients had carotid plaques and had increased cIMT. Correlation analysis suggested multiple associations between right and left TCD parameters. There may be an association of TCD and carotid features with cerebral atrophy and age. Disease duration, disease activity and anti-CCP may influence left MCA PI and RI, as well as CRC. Lp(a) may also influence the development of carotid plaques.
Conclusions: This may be the first study to show increased distal MCA and basilar artery occlusion in RA as determined by TCD. RA patients also exert CRC defect. We also confirmed increased carotid plaque formation, increased cIMT. Biologics may beneficially influence some parameters in the intracranial vessels.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2846

SATURDAY, 17 JUNE 2017

Epidemiology, risk factors for disease or disease progression

SAT0669 HOW DO WE USE BIOLOGICS IN PATIENTS WITH A HISTORY OF MALIGNANCY? AN ASSESSMENT OF TREATMENT PATTERNS USING SCANDINAVIAN REGISTERS

K. Chatzidionysiou[1], K. Aaltonen[2], D. Nordström[2], B. Gudbjornsson[3], G. Grondal[4], A.J. Geirsson[4], L. Steingrimsdottir[5], T. Frisell[1], J. Askling[1] on behalf of for the Nordic Rheumatology Register Collaboration. *[1]Clinical Epidemiology Unit, Dept of Medicine Solna, Karolinska Institutet, Stockholm, Sweden; [2]Department of Medicine, Helsinki University Central Hospital, Helsinki, Finland; [3]Centre for Rheumatology Research, University Hospital & Faculty of Medicine, University of Iceland; [4]Department of Rheumatology, University Hospital Reykjavik; [5]Icelandic Cancer Registry, Reykjavik, Iceland*

Background: Immune competence is of importance for the occurrence and outcome of malignancies. Robust data on risk of relapse of previous cancer following treatment with biological immune-modulators are scarce. Most treatment guidelines caution about their use in patients with a history of cancer, leaving rheumatologists with the decision whether a potential treatment benefit may offset any potential risk of cancer relapse.
Objectives: To assess the overall use of biologics and the relative use of different biological drugs in RA patients with a history of cancer.
Methods: As part of a Nordic collaboration, and using data from the ARTIS (Sweden), ROB-FIN (Finland), and ICEBIO (Iceland) biologics registers, we identified all patients with RA who initiated a first ever biological treatment 2010 through 2014. Through linkage to the national cancer registers, we identified those patients who had a history of any invasive malignancy (including squamous cell skin cancer) either within the five years preceding start of biological treatment ("recent history of malignancy") or more than five years before start of biological treatment ("non-recent history malignancy).
Results: The age- and gender distributions were similar across countries and drugs. Initiators of non-TNFi biologics were older than TNFI-initiators; the median age at start was the highest for rituximab. Out of a total of 8065 bio-initiations, 6% occurred in individuals with a history of cancer (2% with a cancer within 5 years, and 4% with a cancer more than 5 years before treatment start. Whereas there was little variation (around 5%) across TNFi initiators, the proportion of patients with a history of cancer at treatment start was higher among rituximab initiators, in part explained by age (Table). There were only small variations across country (not shown).
Conclusions: In Sweden, Finland and Iceland, one out of 20 biologics-initiators (and almost one out of five rituximab initiators) have a history of an invasive cancer, underscoring the need for more data on benefit/risks in this treatment context. The higher proportion in rituximab initiators is partly explained by differences in age at treatment start and reflects the preference for rituximab by clinicians for treatment of patients with history of cancer.
Disclosure of Interest: K. Chatzidionysiou Consultant for: Roche, Pfizer, Abbvie, Elli-Lilly, UCB, K. Aaltonen: None declared, D. Nordström Speakers bureau: AbbVie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, UCB, B. Gudbjornsson Speakers bureau: Actavis, Celgene, MSD, Pfizer, G. Grondal: None declared, A. Geirsson: None declared, L. Steingrimsdottir: None declared, T. Frisell: None declared, J. Askling Grant/research support from: AbbVie, Eli Lilly, Janssen, Merck, Pfizer, Roche, UCB, Samsung
DOI: 10.1136/annrheumdis-2017-eular.6665

Abstract SAT0669 – Table 1

	Etanercept	Infliximab	Adalimumab	Certolizumab	Golimumab	Rituximab	Abatacept	Tocilizumab	All
Total number of pts	2072	1538	1236	1036	795	883	281	224	8065
Age at treatment start (Swedish pts)	57	58	57	57	57	66	62	61	
Age at treatment start (Finnish pts)	55	50	54	55	54	67	58	54	
Age at treatment start (Icelandic pts)	52	53			53	66			
Total number of pts with cancer <5 yrs before start	41	20	9	18	15	76	6	12	197
Total number of pts with cancer ≥5 yrs before start	70	48	34	36	19	87	19	10	323
Total number of pts with a history of cancer	111	68	43	54	34	163	25	22	520
Proportion of pts with history of cancer <5 yrs before start	2%	1%	1%	2%	2%	9%	2%	5%	2%
Proportion of pts with history of cancer ≥5 yrs before start	3%	3%	3%	3%	2%	10%	7%	4%	4%
Proportion of pts with any history of cancer	5%	4%	3%	5%	4%	18%	9%	10%	6%

SAT0670 THE PREVALENCE OF NEUROPATHIC PAIN-LIKE SYMPTOMS AND ASSOCIATED RISK FACTORS IN THE NOTTINGHAM COMMUNITY: A CROSS-SECTIONAL STUDY

G.S. Fernandes[1,2,3], A. Sarmanova[1,3], S. Warner[1], H. Harvey[1], H. Richardson[1], N. Frowd[1,3], L. Marshall[1,3], J. Stocks[1,3], M. Hall[1,3], A. Valdes[1,2,3], D. Walsh[1,2,3], W. Zhang[1,2,3], M. Doherty[1,2,3]. *[1]Division of Rheumatology, Orthopaedics and Dermatology; [2]Arthritis Research UK Centre for Sports, Exercise and Osteoarthritis; [3]Arthritis Research UK Pain Centre, University of Nottingham, Nottingham, United Kingdom*

Background: Knee pain (KP) affects 1 in 4 adults over the age of 50. Aside from structural joint changes, person-specific factors influence the KP experience. Increased central sensitisation of neural pathways due to localised joint pain or ineffective descending inhibitory mechanisms can cause an enhanced pain response and neuropathic pain-like (NP) symptoms. Understanding these person-specific factors and how they modulate the pain experience might help profile different KP and NP phenotypes.
Objectives: a) To determine the prevalence of NP in a KP community population b) to identify significant risk factors associated with NP and those with both NP and non-NP KP.
Methods: 9,513 men and women, aged 40+ years, were recruited from the East Midlands region (United Kingdom) via postal questionnaire. The questionnaire included sections on KP severity (numerical rating scale) and type (NP versus nociceptive) using the modified PainDETECT Questionnaire (mPDQ); quality of KP using the intermittent and constant osteoarthritis pain (ICOAP) instrument) as well as other risk factors including age, body mass index (BMI), injury, pain catastrophizing scale (PCS) and mental wellness (Hospital Anxiety and Depression Scale). KP participants were those who reported *"knee pain for most days of the past one month"* while likely NP was mPDQ scores of $\geq$13 and definite NP, $\geq$19. Differences between groups were assessed using t-tests for continuous data and chi^2 for categorical data. We used multinomial regression analysis to determine the odds ratios (ORs) of risk factors with 95% confidence intervals (CI) and significance set $p<0.05$.
Results: The prevalence of definite NP in the Nottingham Community was 366 (13.62%). There were more women (p=0.04) and higher BMI (p<0.001) in KP vs. non-KP responders but no age difference (p>0.05). When comparing the neuropathic-like KP to non-neuropathic KP responders, significant risk factors after adjustment for age, BMI, gender and pain severity included: anxiety (OR 3.17 (95% CI 2.38;4.23)); depression (OR 2.99 (95% CI 2.14;4.19)); PCS in highest tertile (OR 5.39 (95% CI 2.94;9.88)); fibromyalgia (OR 4.06 (95% CI 2.48;6.66)) and previous knee injury (OR 1.5 (95% CI 1.12;2.00)). When comparing neuropathic-like KP to non-KP responders, anxiety (1.74 (95% CI 1.31; 2.30), depression (2.05 (95% CI 1.40; 3.01), PCS 3.78 (95% CI 2.57; 5.56)), fibromyalgia (OR 1.94 (95% CI 1.10; 3.40)) and previous injury (OR 1.35 (95% CI 1.05; 1.73)) were significant risk factors after adjustment.
Conclusions: This is the first population based cross-sectional study in the UK to determine prevalence of NP in people with KP. The results suggest that both psychological factors (depression, anxiety, high catastrophising) and peripheral risk factors (injury) associate with NP reporting. These factors can augment pain sensitivity and produce an amplified response via central and peripheral pathways. Phenotypes based on these risk factor profiles may warrant specific management in KP populations.
Acknowledgements: Arthritis Research UK Grant Refs: 20777, 20194
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4930

SAT0671 THE IMPACT OF OBESITY ON TREAT TO TARGET GOALS AND FUNCTIONAL ABILITY IN THE ERAS/ERAN UK PROSPECTIVE COHORTS

E. Nikiphorou[1], S. Norton[1], P. Kiely[2], A. Young[3] on behalf of ERAS/ERAN. *[1]KCL; [2]St George's Hospital, London; [3]St Albans Hospital, St Albans, United Kingdom*

Background: The links between adipose tissue and inflammation on the one hand and obesity and joint dysfunction on the other, are well established. However, how these translate into clinical disease activity and functional disability in rheumatoid arthritis (RA), remains to be clearly defined.
Objectives: To investigate the association between BMI and 1. The achievement of disease remission or low disease activity and 2. Functional ability, in RA.
Methods: Data from two consecutive UK multi-centre RA inception cohorts with similar design were used: the Early RA Study (ERAS) and Early RA Network (ERAN). Recruitment figures/median follow up for ERAS and ERAN were 1465/10 years (maximum 25 years), and 1236/6 years (maximum 10 years) respectively. Standard demographic and clinical variables were recorded at baseline and then annually until loss to follow-up or the end of study follow-up. Multilevel logistic regression analysis was used with either remission (R-DAS) or low disease activity status (L-DAS) and health assessment questionnaire (HAQ, <1 vs $\geq$1) as the dependent categorical variables of interest in models adjusting for patient, disease-related clinical variables and recruitment year. BMI was examined in separate models as both a continuous and categorical predictor variable according to WHO definitions: underweight (BMI less than 18.5), normal (BMI between 18.5 and 25), overweight (BMI between 25 and 30) and obese (BMI greater than 30). BMI was included in the models relating to the same time point as the outcome assessed.
Results: Baseline BMI data from 2420 patients (90%) indicated that 40.0% had BMI scores in the normal range, 1.8% were underweight, 37.2% were overweight and 21.3% were obese. Mean BMI increased slightly over time from 26.5 at baseline to 26.8 at 2 years and then 27.1 at 5 years. In multilevel logistic models adjusting for age, sex, smoking status, antibody status, haemoglobin, erosions and year of recruitment, higher BMI was associated with reduced odds of achieving R-DAS (OR 0.97;95% CI 0.95, 0.99) (table) and L-DAS, although the latter did not reach statistical significance (OR 0.98;95% CI0.96, 1.00). Obesity was related to a significantly lower chance of R-DAS by 29% (OR 0.71;95% CI 0.55, 0.93) and L-DAS by 31% (OR 0.69;95% CI 0.55,0.87). Higher BMI was predictive of higher disability (OR 1.04;95% CI 1.01,1.06). More specifically, obesity increased the odds of higher disability by 63% (OR 1.63;95% CI 1.20,2.23) and in the same models, higher DAS was also strongly predictive of higher disability (OR 3.67;95% CI 3.41,3.95).

Table. Impact of BMI category on disease activity and functional ability in models adjusting for patient demographic, clinical & disease variables.

Independent predictors	MODELS		
	Remission DAS OR (95% CI) (n=1690)	Low DAS OR (95% CI) (n=1690)	HAQ OR (95% CI) (n=1688)
Age at disease onset (years)	0.98(0.97,0.99)	0.98(0.97,0.99)	1.03(1.02,1.05)
Female gender	0.32(0.25,0.41)	0.31(0.24,0.39)	2.47(1.76,3.45)
Past smoking (vs no smoking)	0.58(0.43,0.78)	0.58(0.44,0.77)	1.77(1.20,2.62)
Current smoking (vs no smoking)	0.56(0.42,0.75)	0.66(0.51,0.86)	1.73(1.19,2.51)
Positive rheumatoid factor/anti-CCP	0.83(0.65,1.06)	0.82(0.66,1.02)	1.09(0.79,1.49)
Disease activity score (DAS)	-	-	3.67(3.41,3.95)
Presence of baseline erosions	0.80(0.61,1.04)	0.85(0.67,1.09)	0.63(0.45,0.89)
Haemoglobin (g/dL)	1.03(1.01,1.04)	1.01(1.00,1.03)	1.00(0.98,1.02)
Recruitment year	1.09(1.07,1.11)	1.07(1.06,1.09)	1.09(1.07,1.12)
BMI category* (kg/m^2)			
-Underweight	1.28(0.73,2.26)	1.23(0.75,1.99)	1.83(0.99,3.38)
-Overweight	0.97(0.80,1.18)	0.88(0.74,1.05)	0.97(0.77,1.22)
-Obese	0.71(0.55,0.93)	0.69(0.55,0.87)	1.63(1.20,2.23)

**Reference category = normal BMI*

Conclusions: The findings support a link between higher BMI and worse clinical outcomes, namely disease activity and functional ability. Obesity was associated with lower levels of both remission and low disease activity states, and of higher disability. The findings highlight the importance of monitoring the patients' weight, screening and targeting obesity as part of routine clinical practice, in order to improve disease outcomes. This work provides clinical insights into the role of BMI on disease outcomes in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5510

SAT0672 RISK OF FRAGILITY FRACTURE AMONG PATIENTS WITH PSORIASIS: A POPULATION BASED MATCHED COHORT STUDY FROM THE UNITED KINGDOM

Z. Paskins[1,2], R. Whittle[1], A. Abdul Sultan[1], S. Muller[1], M. Blagojevic-Bucknall[1], T. Helliwell[1], S. Hider[1,2], E. Roddy[1,2], C. Mallen[1]. *[1]Research Institute for Primary Care and Health Sciences, Keele University, Keele; [2]Haywood Rheumatology Centre, Haywood Hospital, Burslem, Stoke-on-Trent, United Kingdom*

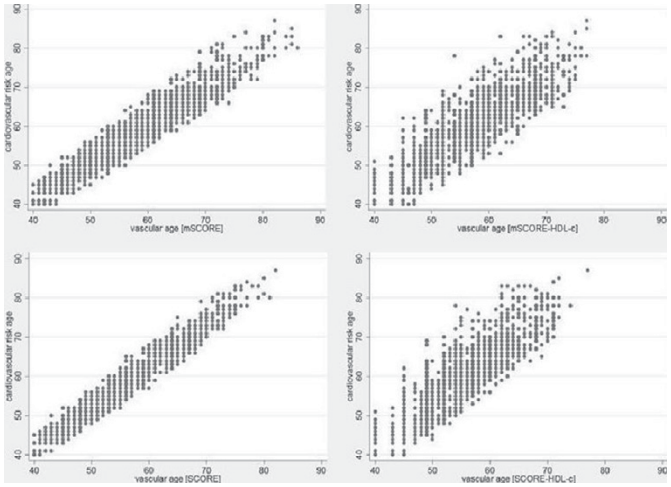
Background: Psoriasis is a common inflammatory skin disease affecting 2–4% of the population and of these a subset will develop an associated inflammatory arthritis (psoriatic arthritis - PsA). An increased risk of osteoporosis has previously been reported in psoriasis patients but the risk of fracture in patients with both psoriasis and PsA has not been established.
Objectives: To estimate the effect of psoriasis, and PsA, on the risk of fracture using a large electronic primary health care database.
Methods: A matched cohort study was conducted utilizing data from the Clinical Practice Research Datalink, a large UK database of primary care medical records. The exposed population was defined as psoriasis patients aged over 40 years with an incident diagnosis between 1990–2004, who were followed up until 2015. Four unexposed patients were matched to each exposed based on age, sex and general practice. The incidence rate of fracture were calculated as the number of incident diagnoses per 10,000 person-years, stratified by sex. Hazard ratios (HR) and 95% confidence intervals were estimated using a Cox proportional hazards model to compare the hazard rate between the exposed and unexposed, adjusting for BMI, alcohol consumption, smoking status, Charlson comorbidity index and steroid use. Fracture risk was estimated for patients with both psoriasis and PsA, identified as patients with an incident diagnosis of psoriasis and a diagnosis of PsA between 1990–2004.
Results: 24,219 patients with psoriasis and 94,820 controls were included in the study. The mean age was 59 years at study entry and just over half (51%) of the patients were male. The incidence rate of fracture was 58.4 (95% CI:55.6–61.3) and 53.1 (51.7–54.5) per 10,000 person-years for the exposed and unexposed, respectively. After adjusting for confounding factors, patients with psoriasis had 12% increased risk of fracture (HR: 1.12; 95% CI: 1.06–1.19) compared to the matched unexposed group. The risk was slightly higher in males (1.22 (1.09–

1.36)) than females (1.09 (1.03–1.17)). Among those with psoriasis, 4.1% were also diagnosed with PsA. An increased risk of 45% was found in those exposed to both psoriasis and PsA compared to the unexposed group (1.45 (1.09–1.94)).
Conclusions: This study reports for the first time, an increase in fracture risk in patients with psoriasis. A higher risk was found in males than females and the risk was further increased if the patient also had PsA. These findings suggest that fracture risk assessment needs to be considered for individuals with psoriasis and PsA.
Acknowledgements: This study was funded by the National Institute for Health Research School for Primary Care Research (NIHR SPCR). CDM is funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care West Midlands, the NIHR School for Primary Care Research and a NIHR Research Professorship in General Practice (NIHR-RP-2014–04–026). TH is funded by an NIHR Clinical Lectureship in General Practice. AAS is funded by an NIHR Postdoctoral Fellowship. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3379

SAT0673 RISK AGE AND RELATIVE RISK OF CVD IN INFLAMMATORY JOINT DISEASES

G. Wibetoe[1], E. Ikdahl[1], S. Rollefstad[1], I. Olsen[1], K. Bergsmark[1], T. Kvien[1], A. Salberg[2], D. Soldal[3], G. Bakland[4], Å. Lexberg[5], B.T. Fevang[6], H.C. Gulseth[7], G. Haugeberg[8], A.G. Semb[1]. *[1]Diakonhjemmet Hospital, Oslo; [2]Lillehammer Hospital for Rheumatic Diseases, Lillehammer; [3]Hospital of Southern Norway, Kristiansand; [4]University Hospital of Northern Norway, Tromsø; [5]Vestre Viken Hospital, Drammen; [6]Haukeland University Hospital, Bergen; [7]Betanien Hospital, Skien; [8]Martina Hansens Hospital, Bærum, Norway*

Background: Individuals with inflammatory joint diseases (IJD) [rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA)] have increased risk of cardiovascular disease (CVD). In the European guidelines for CVD prevention, calculation of relative risk and risk age is advised in patients with low absolute risk of fatal CVD events the next 10 years estimated by the systematic coronary risk evaluation [SCORE] algorithm; the rational being that low absolute risk may conceal high relative risk and risk ages far beyond chronological age. Thus, more patients needing intensive CVD prevention may be identified.
Relative risk is a ratio comparing absolute CVD risk in a specific patient to the risk given optimal CVD risk factor levels (CVDRFs). Risk age denotes the age with similar CVD risk and optimal CVDRFs. To this date, no studies have evaluated relative risk and risk age across IJD entities, neither has the agreement between different risk age models been investigated.
Objectives: 1) Estimate relative risk and risk age across IJD entities. 2) Investigate agreement between different risk age models.
Methods: RA/axSpA/PsA patients aged 40≤65 years with low/moderate 10-year risk of fatal CVD were included from a nationwide quality assurance project implementing CVD risk assessment. Relative risk and cardiovascular risk age was calculated in accordance with risk charts published by the European Society of Cardiology (2016) and Cooney et al (2012), respectively. Vascular age was calculated by matching SCORE to estimated risk ages in accordance with Cuende et al (2010). Four different vascular age estimations were calculated, depending on whether the EULAR 1.5 multiplication factor in RA was applied (mSCORE) and if SCORE version with HDL-c (SCORE-HDL-c) was used: SCORE, SCORE-HDL-c, mSCORE and mSCORE-HDL-c. Risk years beyond chronologic age, were calculated. Linear regression models were used to investigate agreement between risk age estimations.
Results: Relative risk was increased in 53% of all patients and 20% had three times the risk or higher compared to individuals with optimal CVDRF levels. In total, 42% and 20% had a risk age ≥5 years higher than their chronologic age, according to the cardiovascular risk age model and the vascular age model derived from SCORE, respectively. There were minor differences between RA, axSpA and PsA patients in terms of relative risk and risk age. Agreement between cardiovascular risk age and various vascular age models varied (Figure). Discrepancies ≥5 years in estimated risk age were observed in 14–43% of estimations. The largest observed difference in calculated risk age was 24 years. Similarly, linear regression models yielded a R^2 of 0.81–0.96. Across all models, median difference between risk age and age increased with advancing relative risk. Moreover, several patients had high relative risk despite a risk age close to their chronologic age.



Conclusions: Relative risk and risk age may identify several patients at high need of intensive CVD preventive efforts despite low estimated absolute risk. However, there are considerable discrepancies between risk age models.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2856

SAT0674 EARLY TREATMENT RESPONSE TO CONVENTIONAL DMARD THERAPY IN RHEUMATOID ARTHRITIS IS A BETTER PREDICTOR OF LOW DISEASE ACTIVITY OR TREATMENT ESCALATION AT 12 AND 24 MONTHS THAN AUTOANTIBODIES OR EROSIONS

A. Richter[1], A. Strangfeld[1], P. Herzer[2], J. Kaufmann[3], T. Klopsch[4], S. Zinke[5], J. Listing[1], A. Zink[1,6]. *[1]German Rheumatism Research Center, Berlin; [2]Scientific Advisory Board, Munich; [3]Rheumatologist, Ludwigsfelde; [4]Rheumatologist, Neubrandenburg; [5]Rheumatologist; [6]Charité University Medicine, Berlin, Germany*

Background: The EULAR guidelines recommend using the presence of seropositivity or erosions to support treatment decisions. The prognostic value of these factors regarding the primary treatment target in rheumatoid arthritis, remission or low disease activity (LDA), is unclear.
Objectives: To investigate biomarkers, csDMARD treatments and response to treatment regarding their usefulness to predict LDA or the need to escalate treatment within 24 month.
Methods: The control group in RABBIT (Rheumatoid Arthritis: Observation of biologic therapy) comprises N=2,228 patients who were enrolled at treatment start with conventional-synthetic (cs)DMARDs after failure of at least one csDMARD therapy, mostly methotrexate (MTX) monotherapy. We excluded patients with a DAS28-ESR<3.2 at enrollment and those with ≥2 csDMARD failures (n=618). 102 patients were excluded due to enrollment less than 12 month prior to closure of the data base (April 30th, 2016). The DAS28-ESR, physical function, age, seropositivity (RF+/ACPA+), comorbidities (≥3 vs. <3) and the presence of erosions at baseline were evaluated as prognostic factors. Concomitant treatment with glucocorticoids (mg/d) and csDMARDs, response to treatment (3–6 month after enrollment) were additionally examined. We applied a multinomial generalized-estimating-equation (GEE) model to investigate: (1) achievement of LDA at month 12/24 or (2) treatment escalation (biologic treatment) in year one and two after enrollment.
Results: More than one third of patients (34.2%) were treated with a combination of MTX and leflunomide (LEF), 23.6% with LEF mono, 20.8% with MTX + hydroxychloroquine (HCQ) or sulfasalazine (SSZ), 16.5% with MTX mono, and 4.9% with SSZ mono. We found no major differences across treatment regimens except for patients treated with MTX+HCQ who had a lower DAS28, better physical function and shorter disease duration at treatment start. Significant predictors for achieving LDA were low DAS28 at baseline, improvement in DAS28 within 3–6 month, better physical function and less than 3 comorbidities (table). Escalation to bDMARD therapy was significantly more frequent in younger patients, those with no improvement in DAS28 or concomitant glucocorticoid treatment, and in patients with less than 3 comorbidities. There were no differences between treatments regarding achievement of LDA. However, switching to bDMARDs was

Table: Results of the multinomial GEE-model in odds-ratios (OR) and 95% confidence interval (CI).

	Achievement of LDA at month 12 or 24	Escalation of Therapy within 12 or 24 month
	OR [95% CI]	OR [95% CI]
Age (per 10 years)	0.97 [0.87; 1.07]	**0.77 [0.70; 0.86]**
DAS28 improvement ≤6 month (per unit)	**1.68 [1.51; 1.87]**	**0.86 [0.76; 0.97]**
Erosions (Yes vs. No)	0.95 [0.75; 1.20]	1.16 [0.86; 1.55]
Seropositivity (Yes vs. No)	0.83 [0.67; 1.02]	0.89 [0.68; 1.17]
DAS at Baseline	**0.67 [0.59; 0.76]**	1.14 [1.00; 1.30]
Physical function	**1.13 [1.07; 1.19]**	1.04 [0.97; 1.11]
≥3 Comorbidities (vs. <3 comorbidities)	**0.73 [0.55; 0.97]**	**0.69 [0.49; 0.98]**
Glucocorticoids (per 5mg/d)	0.96 [0.79; 1.16]	**1.45 [1.23; 1.71]**
MTX monotherapy (Reference)		
LEF	0.81 [0.58; 1.13]	**1.55 [1.01; 2.39]**
MTX + HCQ | SSZ	1.20 [0.86; 1.66]	1.19 [0.74; 1.90]
MTX + LEF	0.81 [0.59; 1.11]	**1.85 [1.24; 2.77]**
SSZ	0.89 [0.50; 1.59]	1.47 [0.74; 2.89]
Year 2 vs. Year 1	1.20 [0.92; 1.56]	**1.47 [1.11; 1.96]**

most frequent in patients treated with LEF mono or with LEF+MTX. The presence of erosions or seropositivity were not associated with any of the outcomes (table).

Conclusions: The highest impact on achieving LDA was found in disease activity at baseline and response to treatment within 3–6 month. The relevance of erosions and/or seropositivity regarding the prediction of a poorer outcome is disputable.

Acknowledements: RABBIT is supported by a joint, unconditional grant from AbbVie, Bristol-Myers Squibb, Celltrion, MSD Sharp & Dohme, Pfizer, Roche, Samsung Bioepis and UCB.

Disclosure of Interest: A. Richter Consultant for: Pfizer, A. Strangfeld Speakers bureau: BMS, MSD, Pfizer, Roche, Sanofi-Aventis, P. Herzer Consultant for: AbbVie, Pfizer, J. Kaufmann: None declared, T. Klopsch: None declared, S. Zinke: None declared, J. Listing Consultant for: Sandoz, Pfizer, A. Zink Speakers bureau: AbbVie, BMS, MSD, Pfizer, Roche, UCB

DOI: 10.1136/annrheumdis-2017-eular.4979

SAT0675 THE ROLE OF EROSIONS TYPICAL OF RHEUMATOID ARTHRITIS IN THE 2010 ACR/EULAR RHEUMATOID CLASSIFICATION CRITERIA: RESULTS FROM A VERY EARLY ARTHRITIS COHORT

G.H. Brinkmann[1,2], E.S. Norli[2,3], P. Bøyesen[2], D. van der Heijde[4], L. Grøvle[1], A.J. Haugen[1], H. Nygaard[5], O. Bjørneboe[3], C. Thunem[2], T.K. Kvien[2], M.D. Mjaavatten[2], E. Lie[2]. *[1]Østfold Hospital Trust, Moss; [2]Diakonhjemmet Hospital, Oslo; [3]Martina Hansens Hospital, Sandvika, Norway; [4]Leiden University Medical Center, Leiden, Netherlands; [5]Lillehammer Hospital of Rheumatic diseases, Lillehammer, Norway*

Background: A EULAR task force has proposed that in addition to the 2010 ACR/EULAR rheumatoid arthritis (RA) classification criteria (2010 RA criteria), patients can still be classified as having RA with less than 6 criteria points on the presence of ≥3 joints with typical erosions on conventional radiographs of hands and feet (erosion criterion) (1).

Objectives: To determine how the EULAR definition of erosive disease contributes to the number of patients classified as RA according to the 2010 RA criteria in an early arthritis cohort.

Methods: Patients with arthritis of ≤16 weeks duration and a clinical diagnosis of RA or undifferentiated arthritis (UA) with available hand and feet radiographs were included from the Norwegian Very Early Arthritis Clinic (NOR-VEAC) study. Erosive disease was defined according to the EULAR definition accompanying the 2010 RA criteria, i.e. ≥3 erosive joints (1). We calculated the additional number of patients being classified as RA based on the erosion criteria at baseline and during follow-up. Other cut-offs and the distribution of erosive joints was also examined.

Results: The current study included 289 patients (mean (SD) age 48 (14.7) years, 54.3% females, median (25, 75 perc) duration of joint swelling 46 (19.5, 79.0) days). At baseline, 120 patients (41.5%) fulfilled the 2010 RA criteria. Of the remaining 169 not fulfilling the 2010 RA criteria, 55 patients had ≥1 erosive joint (40 with hand erosions, 28 with feet erosions and 13 with hand and feet erosions) and 15 (5.2%) patients fulfilled the erosion criterion (Figure 1). The distribution of erosive joints in the 169 patients not fulfilling the 2010 RA criteria at baseline is shown in the table.

	Erosive joints at baseline					
	PIP	MCP	Wrist	CMC + os trapezium	MTP	IP1 feet
≥1 erosive joint (n=55)	23	17	12	8	22	12
≥2 erosive joints (n=27)	11	13	10	8	12	8
≥3 erosive joints (n=15)	6	8	9	6	8	7

118 patients had radiographic follow-up at 2 years, of whom only 1 additional patient solely fulfilled the erosion criterion during follow-up (7 additional patients fulfilled both the 2010 criteria and the erosion criterion). Among patients with no erosions at baseline (N=74), 13 (17.6%) developed erosions during follow-up (PIP joints n=3, MCP n=4, wrist n=3, CMC joint n=1, MTP joints n=9 and IP1 joint in the foot n=3).

Conclusions: Among this cohort of patients with very early arthritis, 5.2% were classified as RA at baseline based solely on the erosion criterion. Of the 118 patients with 2-year follow-up data, only 1 additional patient was classified based on the erosion criterion alone during follow-up, thus, follow-up radiographs in patients with early UA do not seem to provide additional information in classifying patients with RA.

References:

[1] van der Heijde D, van der Helm-van Mil AH, Aletaha D, Bingham CO, Burmester GR, Dougados M, et al. EULAR definition of erosive disease in light of the 2010 ACR/EULAR rheumatoid arthritis classification criteria. Ann Rheum Dis2013 Apr;72(4):479–81.

Disclosure of Interest: G. Brinkmann: None declared, E. Norli: None declared, P. Bøyesen: None declared, D. van der Heijde: None declared, L. Grøvle: None declared, A. Haugen: None declared, H. Nygaard: None declared, O. Bjørneboe: None declared, C. Thunem: None declared, T. Kvien Consultant for: Has received fees for speaking and/ or consulting from AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, M. Mjaavatten: None declared, E. Lie: None declared

DOI: 10.1136/annrheumdis-2017-eular.1484

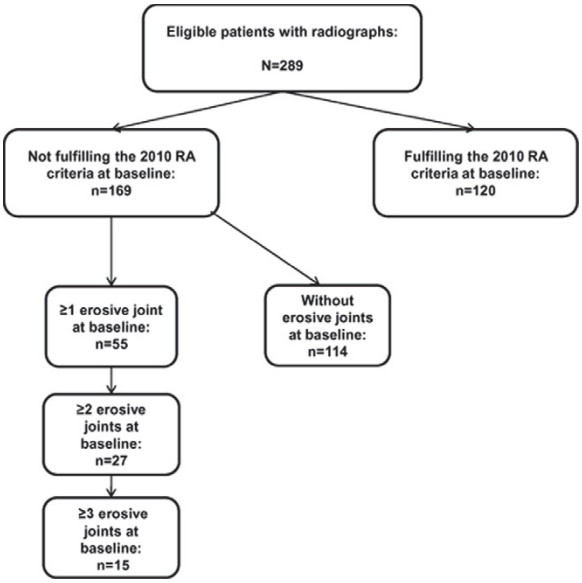


Figure 1

SAT0676 (SERONEGATIVE) MALES SHOW BETTER EULAR TREATMENT RESPONSE THAN FEMALES IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS (RA)

M. Yates[1], J. Galloway[1], A. Rivett[2], S. Norton[1], J.M. Ledingham[3], E.M. Dennison[4], A.J. Macgregor[5], K. Bechman[1], A. Rutherford[1], N. Snowden[6]. *[1]Academic Rheumatology, King's College London; [2]The British Society for Rheumatology, London; [3]Rheumatology Dept, Portsmouth Hospitals NHS Trust, Portsmouth; [4]MRC, Southampton University, Southampton; [5]Rheumatology Dept, Norfolk and Norwich University Hospital, Norwich; [6]Rheumatology Dept, Pennine MSK Partnership, Oldham, United Kingdom*

Background: Gender has been reported to play a role in attainment of RA remission (1), but the data are inconsistent. The impact of gender in early RA therefore warrants further investigation.

Objectives: To assess the impact of gender on early RA outcomes.

Methods: An audit, designed as a national prospective longitudinal observational study, was conducted to assess early RA care. All NHS providers in England and Wales were required to participate. Follow up data were captured over 3 months for subjects with a diagnosis of RA. Logistic regression was used to estimate associations between gender and DAS-28 response. Smoking status, baseline disease activity, age, antibody status, symptom duration, referral times, and treatment were considered in multivariate models.

Results: 136 of 146 eligible trusts submitted data. 11,752 subjects consented, 5,622 were diagnosed with RA. DAS-28 response was available for 2234/5622 (39.7%). Male patients had a similar 3 month improvement in their DAS-28 to females, despite having a lower mean baseline score. Male gender associated with a higher rate of good EULAR response (DAS improvement >1.2, follow up DAS <3.3), with an adjusted odds ratio of 1.42 (CI 1.17–1.72). There were no differences between the genders in their treatment use or in other aspects of care including speed of referral (Table 1).

Table 1

	Male N=786	Female N=1432	P value
Age mean (SD)	61.6 (13.2)	58.1 (15.1)	0*
Smoker %	28	21	0**
Social deprivation decile mean (SD)	5.4 (2.9)	5.5 (2.9)	0.6**
Seropositive %	66	70	0.05**
symptom duration days	230	226	0.8*
Baseline DAS-28 mean (SD)	5.1 (1.4)	5.3 (1.3)	0.03*
FU DAS-28 mean (SD)	3.3 (1.5)	3.6 (1.5)	0.0001*
Change in DAS-28 mean (SD)	1.8 (1.7)	1.7 (1.6)	0.08*
EULAR good response %	43.4	36.7	0.002**
Timely referral %	16	15	0.3**
Timely rheumatology assessment %	39	39	0.7**
Steroids commenced at baseline %	87	86	0.7**
Early DMARD treatment %	28	27	0.9**
Any DMARD prescribed within 6 weeks %	70	70	0.9**
DMARD choice; Methotrexate monotherapy %	69	68	0.6**
DMARD choice; combination therapy %	44	44	0.8**

*t-test **chi-squared. Social deprivation decile from deprivation rank calculated via super output area.

The male excess in good EULAR response was more pronounced in seronegative compared with seropositive RA (1.98 (CI 1.4–2.8) compared to 1.21 (0.96–1.53)).
Conclusions: The association of male gender with improved outcomes in early RA has not been shown before in a national cohort of this scope. Previous work suggests seronegative individuals achieve greater clinical response (2), here we present this effect amplified in men. To the authors' knowledge this is a new finding. This is likely multifactorial, with biological effect of gender, greater diagnostic uncertainty and higher reporting of global scores in women all potentially playing a role.
References:
[1] Svensson B, Andersson M, Forslind K, Ajeganova S, Hafstrom I. Persistently active disease is common in patients with rheumatoid arthritis, particularly in women: a long-term inception cohort study. Scan rheum. 2016;45(6):448–55.
[2] Barra L, Pope JE, Orav JE, et al. Prognosis of seronegative patients in a large prospective cohort of patients with early inflammatory arthritis. Rheum. 2014;41(12):2361–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1560

SAT0677 THE IMPACT OF DISEASE ACTIVITY DURING PREGNANCY IN WOMEN WITH SLE ON THE OCCURRENCE OF PREECLAMPSIA AND PREMATURE BIRTH

A.C.G. Skorpen[1,2], S. Lydersen[3], I.-M. Gilboe[4], K.Å. Salvesen[5], M. Wallenius[1,2]. *[1]National advisory unit on Pregnancy and Rheumatic Diseases, Trondheim University Hospital; [2]Department of Neuromedicine and Movement Science; [3]Regional Center for Child and Youth Mental health and Child Welfare, Norwegian University of Science and Technology, Trondheim; [4]Department of Rheumatology, Oslo University Hospital Rikshospitalet, Oslo; [5]Department of Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology, Trondheim, Norway*

Background: Pregnancy in women with systemic lupus erythematosus (SLE) is associated with an increased risk of complications such as preeclampsia and premature birth. Active disease is considered one of the risk factors.
Objectives: The aim of this study was to explore the impact of disease activity in pregnant women with SLE on preeclampsia and premature birth, and compare the occurrence with pregnancies from the general obstetric population.
Methods: We linked data from RevNatus with data from the Medical Birth Registry of Norway (MBRN). RevNatus is a Norwegian nationwide prospective observational register including women with an inflammatory rheumatic disease when planning pregnancy or after conception. The register was established in 2006 and is administered by the National advisory unit on pregnancy and rheumatic diseases. Women 18 years or older are recruited and followed-up in each trimester of pregnancy and at 6 weeks, 6 months and 12 months after birth. MBRN is a national birth registry. The population constituted all singleton live births recorded in MBRN in the period 2006 – 2014. The births in women diagnosed with SLE in MBRN and included in RevNatus formed the patient group (n=180). The references were all other births (n=498849). We performed logistic regression, and calculated OR for preeclampsia and premature birth in the patient population compared to the references from the general obstetric population. The target population was then split in two groups according to disease activity assessed in the 2nd trimester, and compared to references.
Results: Women with SLE had a significantly higher risk of preeclampsia and premature birth than references after adjustment for maternal age, parity and smoking (Table 1).
Concerning preeclampsia, there was no significant difference in women with no disease activity compared to references, whereas active disease resulted in a significantly higher odds. We observed a two-fold and eight-fold increase in risk of premature birth in women with quiescent and active disease, respectively (Table 2).

Table 1. Preeclampsia and premature birth in references and in women with SLE

Adverse event, n (%)	References n=498,849	SLE n=180	Adj OR* (95% CI)	p
Preeclampsia	15132 (3.0)	14 (7.8)	2.64 (1.53, 4.58)	0.001
Premature birth	27063 (5.5)	34 (18.9)	4.25 (2.92, 6.19)	<0.001

*Adjusted for maternal age, parity and smoking in pregnancy.

Table 2. Preeclampsia and premature birth in references and in women with SLE according to disease activity status

Adverse event, n (%)	References n=498,849	No disease activity† n=85	Adj OR* (95% CI)	p
Preeclampsia	15132 (3.0)	4 (4.7)	1.60 (0.58, 4.38)	0.36
Premature birth	27063 (5.4)	11 (12.9)	2.78 (1.47, 5.24)	0.002
Adverse event, n (%)	References n=498,849	Disease activity‡ n=63	Adj OR* (95% CI)	p
Preeclampsia	15132 (3.0)	9 (14.3)	5.05 (2.48, 10.30)	<0.001
Premature birth	27063 (5.4)	21 (33.3)	8.63 (5.10, 14.60)	<0.001

†LAI-P=0. ‡LAI-P>0. *Adjusted for maternal age, parity and smoking in pregnancy.

Conclusions: Women with SLE have a higher risk of preeclampsia and premature birth than references from the general obstetric population. Women with active disease in pregnancy are most prone to these complications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1509

SAT0678 SIGNIFICANTLY INCREASED SEROPOSITIVITY, RHEUMATOID FACTOR TITRES AND RHEUMATOID NODULES IN CORNISH KAOLIN WORKERS

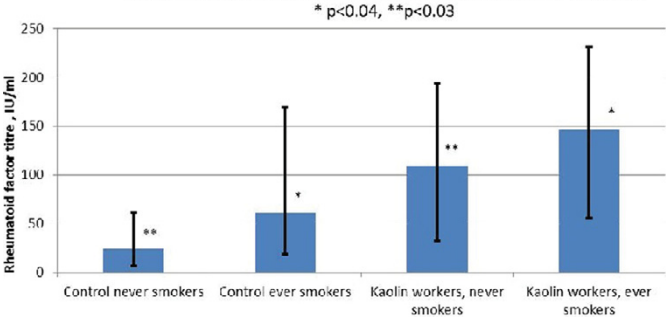
D. Murphy[1,2], E. Fleeming[2], K. Bellis[1], D. Hutchinson[1,2]. *[1]Rheumatology, Royal Cornwall Hospital; [2]University of Exeter Medical School, Cornwall Campus, Truro, United Kingdom*

Background: Kaolin has been mined in Cornwall, UK for over 250 years, with half of the world's production originating from the area at the turn of the 20th century. Mineral kaolinite does not react as free silica, and is used in heavy metal contamination containment due to its adsorption capabilities.[1]
Objectives: To investigate the prevalence of occupational kaolin dust exposure in male rheumatoid arthritis (RA) patients in Cornwall, UK.
Methods: All males diagnosed with RA under follow up at the Royal Cornwall Hospital, UK, during the study period April 2015-January 2017, were invited to complete an occupational questionnaire, detailing current occupation, last occupation (if retired) and other occupations for >1 year.
Results: 39/720 (5%) cases were excluded on non-return of initial questionnaires. 41/720 (6%) cases died during the study period (22 months). 54/640 (8%) remaining cases had occupational kaolin exposure, approximately 12 times higher than expected based on current census employment rates. 30/54 had long term kaolin dust exposure, living in the post code region PL22-PL26 (total male population 33693). These were matched for age ±2 years, sex and index of multiple deprivation (IMD) ±1 decile, to RA patients with no occupational dust or fume exposure. 40/110 potential controls were successfully matched.
Significantly more RA kaolin workers were seropositive for RF and ACPA than non-dust exposed RA controls (Table 1). Of RF seropositive patients, median RF titres were significantly higher in kaolin workers than unexposed controls (p<0.01). No significant differences were seen in ACPA titre. Smoking prevalence rates were not significantly different between kaolin workers and controls. Amongst ever smokers, median pack years smoked showed no difference between cases and controls.

	Kaolin workers (n=30)	Control (n=40)	Significance
RF+	28/30 (93%)	30/40 (75%)	p<0.05
ACPA+	27/30 (90%)	24/40 (60%)	p<0.01
Median seropositive RF titre (IQR)	142 (68–124)	61 (25–162)	p<0.01
Median seropositive ACPA titre (IQR)	375 (169–500)	283 (199–500)	Not sig.
Ever smokers (%)	23/30 (77%)	26/40 (65%)	Not sig.
Median pack years ever smokers (IQR)	18 (15.5–32)	17 (10.75–32.25)	Not sig.

Kaolin exposed never smokers demonstrated significantly higher RF titres than unexposed never smokers (kaolin median RF 109 (IQR 32–193.5), control median RF 24 (IQR 7–61), p<0.04), as did kaolin exposed smokers (kaolin median RF 146.7 (IQR 56–231.5), control median RF 61 (IQR 18.5–170), p<0.03, figure 1). Interestingly, 7/30 (23%) kaolin workers demonstrated nodular disease, compared to 3/40 (7.5%) matched controls, p=0.06, significantly higher than the background nodular rate 79/720 (11%) of male RA patients throughout Cornwall, p<0.04.

Figure 1. Rheumatoid factor titres, RA Kaolin workers vs RA controls.
*** p<0.04, **p<0.03**



Conclusions: Kaolin dust exposure in RA confers higher RF and ACPA seropositivity rates and higher RF titres. Smoking and kaolin dust exposure have an additive effect on RF titres. Higher rates of nodular disease are seen in RA patients exposed to kaolin dust, independent of smoking. We hypothesise that this interaction is due to adsorption of heavy metals from tobacco smoke or other environmental sources by kaolin particles, stimulating autoantibody production.
References:
[1] Matlok M, Petrus R, Warchol JK. Equilibrium study of heavy metals adsorption on Kaolin. Ind Eng Chem Res 2015; 54(27):6975–84.
Acknowledgements: Cornwall Arthritis Trust.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1890

SAT0679 ARE ADULT TRAJECTORIES OF WEIGHT OVER A LIFETIME LINKED TO FOOT PROBLEMS YEARS LATER?

A.B. Dufour[1], E. Losina[2], H.B. Menz[3], M.P. LaValley[4], M.T. Hannan[1]. *[1]Institute for Aging Research, Hebrew SeniorLife; [2]Brigham and Women's Hospital, Boston, United States; [3]School of Allied Health, la Trobe University, Bundoora, Australia; [4]Biostatistics, Boston University, School of Public Health, Boston, United States*

Background: Obesity and foot problems are common in older adults and associated with many negative health outcomes. Better understanding of the consequences of patterns of weight change may lead to better prediction and dealing with foot pain and foot disorders.
Objectives: This study identified longitudinal trajectories of weight in a population-based study and examined the association of these groups with current foot problems.
Methods: We used 28 measures of weight over 57 years to identify trajectories of weight in 2445 members of the Framingham Foot Study using k-means longitudinal cluster analysis. Foot examinations (2002–2008) recorded presence of foot pain, hallux valgus, claw toes, hammer toes and overlapping toes on each foot. Associations between weight group membership and foot problems at time of foot exam, adjusted for age and sex, were examined using logistic regression with generalized estimating equation correction for two feet per subject. The reference group used for analysis was the group with the lowest weight trajectory ("E").
Results: We found 5 trajectories of weight, representing relatively constant patterns over time, with weight increasing from groups E to A. Those in group "E" were more likely to be older, while the youngest were in group "A" group. "E" had the lowest prevalence of foot pain (14%) while group "A" had the highest (22%). Similarly, group "A" had the lowest prevalence of hallux valgus, while group "E" had the highest (36%) (Table 1).
Compared to group "E", other groups were more likely to have foot pain (ORs 1.57–3.50, Table 2) and less likely to have hallux valgus (ORs 0.73–0.99). For claw toes, all but one group were more likely to have claw toes compared to group "E". Groups "A" and "D" were more likely to have hammer toes (ORs 2.40 and 1.35, respectively) compared to group "E". We found no associations between overlapping toes and group membership.

Table 1. Participant characteristics by weight trajectory group

	A N=201/ 402 feet	B N=644/ 1288 feet	C N=617/ 1233 feet	D N=506/ 1011 feet	E N=477/ 954 feet
Age (years)	63±9.0	69±11.2	68±10.5	66±9.7	71±11.9
Body mass index (kg/m^2)	37±6.3	27±3.3	29±4.0	31±4.3	23±2.9
Female	76 (19%)	1036 (80%)	478 (39%)	230 (23%)	918 (96%)
Foot pain	88 (22%)	240 (19%)	222 (18%)	186 (18%)	135 (14%)
Hallux Valgus	57 (14%)	408 (32%)	267 (22%)	169 (17%)	341 (36%)
Claw Toes	9 (2%)	29 (2%)	29 (2%)	24 (2%)	18 (2%)
Hammer toes	89 (22%)	246 (19%)	197 (16%)	165 (16%)	174 (18%)
Overlapping toes	14 (3%)	99 (8%)	73 (6%)	48 (5%)	90 (9%)

Table 2. Association between weight trajectory group membership and foot problems, adjusted for age and sex

	A vs. E	B vs. E	C vs. E	D vs. E
Foot pain	3.5 (2.49, 4.9)*	1.57 (1.25, 1.98)*	2.16 (1.68, 2.77)*	2.63 (2.00, 3.47)*
Hallux Valgus	0.72 (0.51, 1.02)	0.99 (0.82, 1.18)	0.86 (0.7, 1.06)	0.77 (0.61, 0.99)*
Claw toes	3.97 (1.57, 10)*	1.52 (0.83, 2.79)	2.24 (1.17, 4.29)*	3.1 (1.51, 6.38)*
Hammer toes	2.4 (1.71, 3.38)*	1.2 (0.96, 1.5)	1.12 (0.87, 1.45)	1.35 (1.02, 1.79)*
Overlapping toes	0.78 (0.41, 1.48)	0.93 (0.68, 1.27)	0.87 (0.6, 1.25)	0.85 (0.55, 1.32)

*$p<0.05$.

Conclusions: Trajectories with higher weight over a lifetime had increased odds of foot pain and claw toes, and decreased odds of hallux valgus later in life. These results provide evidence that having lower weight over one's lifetime can reduce the likelihood of foot problems later in life.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3018

SAT0680 THE IMPACT OF DISEASE ACTIVITY DURING PREGNANCY IN WOMEN WITH SLE ON THE BIRTH WEIGHT OF THE CHILD

A.C.G. Skorpen[1,2], S. Lydersen[3], I.-M. Gilboe[4], K.Å. Salvesen[5], M. Wallenius[1,2]. *[1]National advisory unit on Pregnancy and Rheumatic Diseases, Trondheim University Hospital; [2]Department of Neuromedicine and Movement Science; [3]Regional Center for Child and Youth Mental health and Child Welfare, Norwegian University of Science and Technology, Trondheim; [4]Department of Rheumatology, Oslo University Hospital Rikshospitalet, Oslo; [5]Department of Laboratory Medicine, Children's and Women's Health, Norwegian University of Science and Technology, Trondheim, Norway*

Background: Mean birthweight is lower in children of SLE-mothers than in references. Active disease in pregnancy is considered one of the risk factors.
Objectives: The aim of this study was to explore the association of disease activity in women with SLE in pregnancy and the birth weight of the child expressed as mean birth weight and mean z-score for birth weight.
Methods: We linked data from RevNatus with data from the Medical Birth Registry of Norway (MBRN). RevNatus is a Norwegian nationwide prospective observational register including women with an inflammatory rheumatic disease when planning pregnancy or after conception. The register is administered by the National advisory unit on pregnancy and rheumatic diseases. Women 18 years or older are recruited and followed-up in each trimester of pregnancy and at 6 weeks, 6 months and 12 months after birth. MBRN is a national birth registry. The population constituted all singleton live births recorded in MBRN in the period 2006 – 2014. The births in women diagnosed with SLE in MBRN and included in RevNatus formed the patient group (n=180). The references were all other births (n=498849). Mean birth weight in the patient group was compared to mean birth weight in the general obstetric population. We calculated z-score for birth weight adjusted for gestational age and sex. The target population was then split in two groups according to disease activity assessed in the 2nd trimester, and compared to references. One-way ANOVA was performed to compare SLE-women without active disease, SLE-women with active disease and references from the general obstetric population.
Results: The mean birth weight and mean z-score were both significantly lower in women with SLE compared to references.

Table 1. Mean birth weight and z-score in references and in women with SLE

Mean (SD)	References n=497959	SLE n=180	Mean difference (95% CI)	p
Birth weight g	3518 (588)	3091 (691)	426 (325, 528)	<0.001
Z-score	-0.11 (0.98)	-0.59 (0.87)	0.47 (0.33, 0.62)	<0.001

When comparing three groups, a significantly lower mean birth weight and mean z-score remained between women without active disease and references and women with active disease and references. There were no significant differences between the two disease groups.

Table 2. Mean birth weight and z-score in references and in women with SLE according to disease activity status

Mean (SD)	References n=497,959	No disease activity† n=85	Mean difference (95% CI)	p
Birth weight g	3518 (482)	3133 (587)	385 (260, 510)	<0.001
Z-score	-0.11 (0.98)	-0.64 (0.81)	0.53 (0.32, 0.74)	<0.001
Mean (SD)	References n=497,959	Disease activity‡ n=63	Mean difference (95% CI)	p
Birth weight g	3518 (588)	2991 (802)	526 (62- 354)	<0.001
Z-score	-0.11 (0.98)	-0.54 (0.90)	0.43 (0.18, 0.67)	0.001
Mean (SD)	No disease activity n=85	Disease activity n=63	Mean difference (95% CI)	p
Birth weight g	3133 (587)	2991 (802)	141 (-50, 333)	0.15
Z-score	-0.64 (0.81)	-0.54 (0.90)	-0.10 (-0.40, 0.22)	0.53

†LAI-P=0. ‡LAI-P>0.

Conclusions: Mean birth weight and Z-score was significantly lower in women with SLE compared to the general obstetric population. There were no significant differences in diseased women with active as opposed to quiescent disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5820

SAT0681 RISK OF ACTIVE TUBERCULOSIS IN PATIENTS WITH INFLAMMATORY ARTHRITIS RECEIVING TNF-INHIBITORS

A.M. Gheorghiu[1,2], A. Garaiman[1,2], A. Radu[1,2], A. Soare[1,2], V. Aramă[2,3], D. Bumbăcea[2,4], R. Dobrotă[1,2], R. Oneata[1,2], S. Pintilie[1,2], M. Milicescu[1,2], I. Ancuta[1,2], A. Martin[1,2], M. Sasu[1], C. Ciofu[1,2], L. Macovei[1,2], V. Stoica[1,2], M. Bojinca[1,2], C. Mihai[1,2]. *[1]Internal Medicine and Rheumatology, Cantacuzino Hospital; [2]Carol Davila University of Medicine and Pharmacy; [3]Infectious Diseases 1, Matei Bals National Institute for Infectious Diseases; [4]Dept. of Pneumology, Elias Emergency University Hospital, Bucharest, Romania*

Background: Tuberculosis (TB) is a major concern in patients receiving TNF inhibitors (TNFi).
Objectives: To assess the incidence of active TB and the efficacy of TB prevention measures in a large, single-center cohort of patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) receiving TNFi.
Methods: Data of all patients in whom treatment with TNFi was initiated in our rheumatology clinic from January 1st 2002 until December 31st 2015 have been retrospectively analysed. The cohort was divided into 2 groups per the mandatory latent TB infection (LTBI) screening method at baseline: tuberculin skin test (group TST), and QuantiFERON®-TB Gold test (group QFT). The incidence of active TB was analysed for each group and compared to TB incidence data in general population.
Results: 653 patients were included (344 RA, 52 PsA, 257 AS); 324 patients belonged to the TST and 329 to the QFT group. The number of active TB cases/ time of exposure to TNFi (person-years, PY) was 17/2002.6 and 7/1041.2 respectively, accounting for an incidence of 848.9 and 672.3 cases per 10^5 PY, about 8 times higher (8.3 and 8.8 for TST, respectively QFT group) than the average TB during the period of exposure to TNFi. LTBI reactivations per total TB cases were only 4/17 and 2/7, respectively, too few to identify statistically significant differences between the 2 LTBI screening protocols. Only 10 patients

Table 1. LTBI screening results and TB occurrence in the 653 TNFi-treated patients (Pearson χ^2 test)

	TST (n=324)	QFT (n=329)	All (n=653)	p value
Positive immuno-diagnostic test at baseline	52 (16.0%)	63 (19.1%)	115 (17.6%)	<0.001*
Active TB	17 (5.2%)	7 (2.1%)	24 (3.7%)	0.185*
Reactivation TB	4 (1.2%)	2 (0.6%)	6 (0.9%)	**
New infection TB	13 (4.0%)	5 (1.5%)	18 (2.8%)	0.052*
Total TB incidence (per 10^5 PY)	848.9	672.3	788.5	–
Maximal period of TNFi exposure in group	2002–2016	2011–2016	2002–2016	–
Mean TB incidence in Romania in the respective time period (per 10^5 PY)	102.3	76.7	102.3	–
TB incidence patients/general population	8.3	8.8	7.7	0.88†

*Pearson χ^2 test comparing TST and QFT. **Reactivation TB cases were too few to perform statistical testing. †Pearson χ^2 test comparing total TB incidence in the TST and QFT groups to the average TB incidence in our region in the respective period of exposure.

had pulmonary TB, whereas the rest were disseminated TB (8 cases), TB pleurisy and/or pericarditis (4 cases), one mediastinal lymph node TB and one isolated hepatic TB. Using Pearson chi-square test, we found no significant differences between LTBI group and active TB (Table 1).

Conclusions: In our cohort, new infection TB exceeds reactivation TB, suggesting the necessity of periodical LTBI re-screening.

Disclosure of Interest: A. M. Gheorghiu: None declared, A. Garaiman: None declared, A. Radu: None declared, A. Soare: None declared, V. Aramă: None declared, D. Bumbăcea: None declared, R. Dobrotă: None declared, R. Oneata: None declared, S. Pintilie: None declared, M. Milicescu Speakers bureau: Has received sponsoring from Abbvie, MSD and Pfizer., I. Ancuta Grant/research support from: Abbvie, Pfizer, Roche, UCB, BMS, Consultant for: Abbvie, Pfizer, Roche, UCB, BMS, Speakers bureau: Abbvie, Pfizer, Roche, UCB, BMS, A. Martin Grant/research support from: Abbvie, MSD, Pfizer, Roche, UCB, BMS, M. Sasu Grant/research support from: Abbvie, MSD, Pfizer, Roche, UCB, BMS, C. Ciofu Grant/research support from: Abbvie, MSD, L. Macovei Grant/research support from: MSD, Pfizer, Roche, V. Stoica: None declared, M. Bojinca Grant/research support from: Abbvie, MSD, Pfizer, Roche, UCB, BMS, Consultant for: Abbvie, MSD, Pfizer, Roche, UCB, BMS, Paid instructor for: Abbvie, MSD, Pfizer, Roche, UCB, BMS, C. Mihai Grant/research support from: Abbvie, MSD, Pfizer, Roche, UCB, BMS, Consultant for: Abbvie, MSD, Speakers bureau: Abbvie, MSD, Pfizer, Roche, UCB, BMS

DOI: 10.1136/annrheumdis-2017-eular.5835

SAT0682 PREVALENCE OF SARCOPENIA IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES

A. Tournadre[1,2], P. Jaffeux[3], T. Frayssac[1], A. Fan[1], M. Couderc[1], J.J. Dubost[1], S. Malochet-Guinamand[1], S. Mathieu[1], Z. Tatar[1], J.C. Jourdy[3], M. Soubrier[1,2]. *[1]Rheumatology, CHU Clermont Ferrand; [2]UNH, University Clermont Auvergne INRA; [3]Medical Information, CHU Clermont Ferrand, Clermont Ferrand, France*

Background: Evaluation of sarcopenia is of major relevance because of these clinical repercussions on morbidity and mortality. Although the definition should include both low muscle mass and function, a combination of the 2 criteria was not reported in inflammatory rheumatic diseases (IRDs).

Objectives: To determine in a cohort of IRDs the prevalence of sarcopenia using established combined criteria (EWGSOP) (1).

Methods: Sarcopenia defined as both low muscle mass (skeletal muscle index (SMI) <7.26 kg/m^2 for men; <5.45 kg/m^2 for women) and impaired muscular function (handgrip strength or gait speed) (1) was assessed in active rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PsoA) patients before initiating first biologic. Body composition (DXA) and related factors were compared using univariate, multivariate and correlation analysis.

Results: 148 patients were included (Table). Sarcopenia with decrease in muscle mass and function was observed in 5 RA (7.8%), one SpA (1.7%) and one PsoA (9.1%). Sarcopenia in terms of reduced SMI only (1) was not more frequent occuring in 5 RA (7.8%), 3 SpA (5.1%) and one PsoA (9.1%). Grip strength was decreased in RA as well as muscle mass compared to SpA and PsoA but the difference was no longer significant when adjusted on age, sex, disease duration (Table). Only fat distribution differed with a trunk/peripheral fat ratio higher in PsoA. In RA, lean mass was negatively correlated with disease duration and sedentary time. In SpA and PsoA, fat mass was correlated with age, disease activity, HAQ. HAQ and CRP level negatively correlated with lean mass. No association between treatments and body composition was observed.

Table 1. Characteristics and body composition of patients with RA, SpA, PsoA [mean±SD; n (%)]

	RA (n=74)	SPA (n=63)	PsoA (n=11)	p/p*
Age, years	59.5±11.7	44.1±12.0	54.6±11.0	<0.0001
Women	54 (73)	27 (43)	6 (55)	0.001
Disease duration, years	9±15.9	6.4±9.4	5.5±6.8	0.4
Body Mass Index	25.8±6.3	26.6±5.8	28.7±5.1	0.3
DAS28	4.37±1.08	2.78±0.91	3.63±1.06	<0.0001
BASDAI		50.8±17.2	49.6±17.7	0.8
HAQ	0.9±0.6	0.7±0.5	1.0±0.7	0.09
CRP, mg/l	16.4±21.3	11.9±14.3	10.7±13.6	0.3
MTX	54 (73.0)	6 (9.5)	6 (54.6)	<0.0001
Steroids	41 (55.4)	1 (1.6)	1 (9.1)	<0.0001
NSAIDs	18 (24.3)	38 (60.3)	7 (63.6)	<0.0001
Total lean mass, kg	46.7±10.8	53.3±11.1	51.1±9.8	**0.004**/0.6
SMI, Kg/m^2	7.2±1.4	8.1±1.6	8.0±1.7	**0.009**/0.5
Total fat mass, kg	21.9±8.1	21.8±10.3	25.5±10.7	0.5/0.1
Fat mass index (FMI), kg/m^2	8.2±3.2	7.8±4.2	9.6±4.3	0.3/0.05
Overfat (Body fat percentage >27% for men and 38% for women)	18 (28)	18 (30.5)	4 (36)	0.8
Trunk/peripheral fat ratio	0.97±0.30	0.99±0.33	1.23±0.26	**0.04**/**0.02**

*Adjusted for age, sex, disease duration.

Conclusions: Sarcopenia with combined criteria (muscle mass and function) occurred in 7.8% of RA corresponding to the values of the general population aged over 70 years-old (2). Reduced muscle mass only was not highly prevalent and lower than that reported in elderly suggesting important cofactors such as functional limitations or muscle quality in sarcopenia associated with rheumatic diseases.

References:

[1] Cruz-Jentoft AJ et al. Age Ageing 2010;39:412–23.
[2] Spira D, et al. Z Gerontol Geriatr 2016;49:94–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5122

SAT0683 PREVALENCE OF OSTEOPOROSIS IN ALBANIAN POSTMENOPAUSE WOMEN AND THE ROLE OF RISK FACTORS IN OSTEOPOROSIS

A. Kollcaku, J. Kollcaku, V. Duraj. *Rheumatology, University Hospital Center "Nene Tereza", Tirana, Albania*

Background: Menopause is the time in woman's life when production of sex hormones ceases. Sex hormones deficiency leads to increasing bone fragility and, thus, fracture risk. Bone turnover and bone mass could be affected by too many other risk factors. Osteoporosis threatens the health and quality of life of women with postmenopausal osteoporosis.

Objectives: The aims of this study were to assess the prevalence of osteoporosis in Albanian postmenopause women and the role of risk factors in osteoporosis.

Methods: A cross-sectional study was conducted in Tirana city in a period 2009–2013, including a population-based sample of 4,789 women. All subjects enrolled in the study were asked for risk factors for osteoporosis by completing a specific questionnaire. Low bone mineral density (osteopenia defined as a bone mineral density T-score less than -1 and osteoporosis for T-score less than -2.5) was assessed with a bone ultrasound device which is simple and easy to use for screening of bone mineral density in population-based studies. Binary logistic regression was used to determine the relationship of osteoporosis and independent factors in this study population.

Results: The prevalence of osteoporosis in this study population was 6.2% (N=286) and prevalence of osteopenia was 16.6%; 77.1% of osteoporosis women were in postmenopause. In logistic regression models was seen that menopausal women had 69% more chances than no menopausal women to have osteoporosis (OR=1.69, 95% CI=1.45–1.77, P<0.001). Osteoporosis was positively associated with multiparity (P<0.001) and long treatment with glucocorticoids (OR: 1.52; CI95% 1.46–1.94; p=0.02). In multivariable analysis osteoporosis was positively associated with rheumatoid arthritis (OR=1.62, 95% CI=1.47–1.81, P<0.001). In Kendal's correlation coeficient, osteoporosis was negatively associated with level of education (r=-0.101, p<0.001) and body mass index (r=-0.0033, p<0.009) and positively associated with white color of skin (r=0.003, p<0.027) and treatment with diuretics (r=0.007, p<0.001).

Conclusions: This study offers useful evidence about the osteoporosis and osteopenia prevalence among postmenopausal albanian women. Caucasian females with early menopause, multiparous, lower body-weight, suffering from rheumatoid arthritis, long treated with glucocorticoids and diuretics and lower education should be followed-up more carefully for development of osteoporosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4495

SAT0684 DETERMINANTS OF 12-MONTHS PERSISTENCE IN RHEUMATOID ARTHRITIS PATIENTS INITIATING SUBCUTANEOUS TNF-ALPHA INHIBITORS

B. Fautrel[1], M. Belhassen[2], C. Hudry[3], M.-C. Woronoff[4], N. Gouyette[5], A. Clément[5], E. Van Ganse[6], F. Tubach[7]. *[1]Sorbonne Universités, UPMC Univ Paris 06; AP-HP, Rheumatology Department, Pitié Salpétrière University Hospital, Paris, France., Paris; [2]Hesper 7425, Health Services and Performance Research, University Claude Bernard Lyon 1; PELyon, Pharmacoepidemiologie Lyon, Lyon; [3]AP-HP Hôpital Cochin, Paris; [4]CHU Besançon, Université Franche-Comté, Comue UBFC, UMR INSERM 1098, Besançon; [5]Merck Sharp & Dohme, Paris; [6]Hesper 7425, Health Services and Performance Research, University Claude Bernard Lyon 1, PELyon, Pharmacoepidemiologie Lyon, Lyon; [7]APHP, Hôpital Pitié-Salpêtrière, Département de Biostatistiques, Santé publique et Information médicale, APHP, Centre de Pharmacoépidémiologie (Cephepi); INSERM, UMR 1123 ECEVE; Université Pierre et Marie Curie Paris 6, Sorbonne Universités, Paris, France*

Background: Biotherapies such as subcutaneous tumor necrosis factor-alpha

inhibitors (SC-TNFis) have transformed the management of inflammatory joint diseases such as rheumatoid arthritis (RA). The assessment of SC- TNFis persistence and its determinants is needed.

Objectives: The objective of this study was to describe treatment persistence in real-world settings, and identify the determinants of persistence among RA patients initiating treatment with an SC-TNFi.

Methods: The French national health insurance scheme database lists all outpatient and inpatient healthcare consumption for individuals covered by the general health insurance scheme. Using French claims data, RA was diagnosed using Long Term Disease status and hospital admission, based on ICD-10 codes. Patients were then identified through prescription filled for adalimumab (ADA), etanercept (ETA), certolizumab pegol (CZP) and golimumab (GLM) between 2012/07/01 and 2013/12/31. A patient was considered as non-persistent in the event of a prolonged interruption of the therapy lasting 91 days or more. Persistence was estimated with Kaplan Meier analysis. Determinants of persistence in the 12 months before initiation were identified using Cox models.

Results: A total of 7,204 patients with RA were identified. In the descriptive analyses of the 12 months persistence, differences were observed for RA patients, with raw/non-adjusted persistence rates of 51.8% for CZP, 57.4% for ETA, 53.7% for ADA and 56.6% for GLM. Results of the Cox model are presented below, including hazard ratio for biotherapy, adjusted on sex, age, socio-economic status, and criteria on disease severity. The variables biotherapy, sex and socio-economic status did not meet the proportionality hypothesis of risks, and were corrected by the addition of a variable integrating the interaction with time.

Table 1: Determinants of 12-month non-persistence (Cox model)

	Hazard Ratio	IC 95%		P-value
SC-TNFis				
GLM	1.000	–	–	–
CZP	1.642	1.343	2.006	<0.0001
ETA	1.512	1.297	1.763	<0.0001
ADA	1.418	1.258	1.599	<0.0001
Sex				
Male	1.000	–	–	–
Female	1.610	1.367	1.897	**<0.0001**
Age	1.000	0.998	1.003	0.6833
Deprived socio-economic status : Yes vs No	0.901	0.712	1.141	0.3882
Number of comorbid conditions (per additional condition)	1.122	1.086	1.160	**<0.0001**
Biotherapy line (per additional line)	1.364	1.296	1.435	**<0.0001**
DMARD dispensation: Yes vs No	0.952	0.884	1.025	0.1924
Sulfasalazine dispensation : Yes vs No	1.101	0.964	1.258	0.1545
Long term oral steroids : Yes vs No	1.026	0.958	1.099	0.4629
Hospital admission for IRMD	0.932	0.871	0.997	**0.0419**
Visits to rheumatologist				
0	1.000	–	–	–
1–4	0.681	0.578	0.803	**<0.0001**
>4	0.704	0.599	0.828	**<0.0001**
Interaction with time				
Interaction biotherapy * time	1.001	1.000	1.001	**0.0025**
Interaction sex * time	0.999	0.998	0.999	**0.0023**
Interaction socio-economic status * time	1.002	1.000	1.003	**0.0084**

Conclusions: Non-persistent patients were more likely female, with multiple comorbid conditions, and multiple line of biotherapy. Hospital admission for IRMD, visits to rheumatologist and treatment with GLM (compared to CZP, ETA and ADA) decreased the risk of non-persistence. Further analyses are needed to better understand behaviours of patients and to assess the impact of non-persistence on clinical and economics outcomes.

Disclosure of Interest: B. Fautrel Grant/research support from: AbbVie, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgène, Hospira, Janssen, Lilly, MSD, NORDIC Pharma, Pfizer, Roche, SOBI, UCB, M. Belhassen Employee of: PELyon, C. Hudry Consultant for: ABBVIE, MSD, BMS, PFIZER, ROCHE, CELGENE, NOVARTIS, BIOGEN, UCB, SANDOZ, AMGEN., Employee of: COCHIN Hospital, M.-C. Woronoff: None declared, N. Gouyette Employee of: MSD France, A. Clément Employee of: MSD France, E. Van Ganse Consultant for: PELyon; ALK ABELLO; AstraZeneca; Bayer; BMS; BIF; GSK; IMS; LASER; MSD, F. Tubach: None declared

DOI: 10.1136/annrheumdis-2017-eular.5023

SAT0685 DETERMINANTS OF 12-MONTHS PERSISTENCE IN PSORIATIC ARTHRITIS PATIENTS INITIATING SUBCUTANEOUS TNF-ALPHA INHIBITORS

B. Fautrel[1], M. Belhassen[2], C. Hudry[3], M.-C. Woronoff[4], N. Gouyette[5], A. Clément[5], E. Van Ganse[6], F. Tubach[7]. *[1]Sorbonne Universités, UPMC Univ Paris 06; AP-HP, Rheumatology Department, Pitié Salpétrière University Hospital, Paris, France., Paris; [2]Hesper 7425, Health Services and Performance Research, University Claude Bernard Lyon 1; PELyon, Pharmacoepidemiologie Lyon, Lyon; [3]AP-HP Hôpital Cochin, Paris; [4]CHU Besançon, Université Franche-Comté, Comue Ubfc, UMR INSERM 1098, Besançon; [5]Merck Sharp & Dohme, Paris; [6]Hesper 7425, Health Services and Performance Research, University Claude Bernard Lyon 1, PELyon, Pharmacoepidemiologie Lyon, Lyon; [7]APHP, Hôpital Pitié-Salpêtrière, Département de Biostatistiques, Santé publique et Information médicale, APHP, Centre de Pharmacoépidémiologie (Cephepi); INSERM, UMR 1123 ECEVE; Université Pierre et Marie Curie Paris 6, Sorbonne Universités, Paris, France*

Background: Biotherapies such as subcutaneous tumour necrosis factor-alpha inhibitors (SC-TNFis) have transformed the management of inflammatory joint diseases such as psoriatic arthritis (PsA). The assessment of SC- TNFis persistence and its determinants is needed.

Objectives: The objective of this study was to describe treatment persistence in real-world settings, and identify the determinants of persistence among PsA patients initiating treatment with an SC-TNFi.

Methods: The French national health insurance scheme database lists all outpatient and inpatient healthcare consumption for individuals covered by the general health insurance scheme. Using French claims data, PsA was diagnosed using Long Term Disease status and hospital admission, based on ICD-10 codes. Patients were then identified through prescription filled for adalimumab (ADA), etanercept (ETA), certolizumab pegol (CZP) and golimumab (GLM) between 2012/07/01 and 2013/12/31. A patient was considered as non-persistent in the event of a prolonged interruption of the therapy lasting 91 days or more. Persistence was estimated with Kaplan Meier analysis. Determinants of persistence in the 12 months before initiation were identified using Cox models.

Results: A total of 2,011 patients with PsA were identified. In the descriptive analyses of the 12 months persistence, differences were observed for PsA patients, with raw/non-adjusted persistence rates of 37.3% for CZP, 51.8% for ETA, 54.7% for ADA and 50.8% for GLM. Results of the Cox model are presented, including hazard ratio for biotherapy, adjusted on sex, age, socio-economic status, and criteria on disease severity. The variables biotherapy, biotherapy line, comorbid conditions and hospital admission for IRMD did not meet the proportionality hypothesis of risks, and were corrected by the addition of a variable integrating the interaction with time.

Table 1. Determinants of 12-month non-persistence (Cox model)

	Hazard Ratio	IC 95%		P-value
SC-TNFis				
GLM	1.000	–	–	–
CZP	2.315	1.438	3.726	**0.0005**
ETA	1.631	1.199	2.217	**0.0018**
ADA	1.167	0.944	1.443	0.1525
Sex				
Male	1.000	–	–	–
Female	1.480	1.301	1.684	**<0.0001**
Age	0.996	0.991	1.001	0.1544
Deprived socio-economic status : Yes vs No	1.486	1.197	1.843	**0.0003**
Number of comorbid conditions (per additional condition)	0.993	0.885	1.115	0.9114
Biotherapy line (per additional line)	1.422	1.188	1.702	**0.0001**
DMARD dispensation: Yes vs No	0.965	0.854	1.090	0.5649
Sulfasalazine dispensation : Yes vs No	1.127	0.907	1.401	0.2789
Long-term oral steroids : Yes vs No	1.101	0.918	1.320	0.2980
Hospital admission for IRMD	0.784	0.611	1.007	0.0565
Visits to rheumatologist				
0	1.000	–	–	–
1–4	0.808	0.598	1.093	0.1673
>4	0.779	0.577	1.052	0.1035
Interaction with time				
Interaction biotherapy * time	1.001	1.001	1.002	**0.0013**
Interaction comorbid conditions * time	1.001	1.000	1.001	**0.0138**
Interaction biotherapy line * time	0.998	0.997	0.999	**0.0006**
Interaction hospital admission for IRMD * time	1.002	1.000	1.003	**0.0303**

Conclusions: Non-persistent patients were more likely female, with deprived socio-economic status, and multiple line of biotherapy. Treatment with GLM (compared to CZP and ETA) decreased the risk of non-persistence. Further analyses are needed to assess the impact of non-persistence on clinical and economics outcomes.

Disclosure of Interest: B. Fautrel Grant/research support from: AbbVie, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgène, Hospira, Janssen, Lilly, MSD, NORDIC Pharma, Pfizer, Roche, SOBI, UCB, M. Belhassen: None declared, C. Hudry Consultant for: ABBVIE, MSD, BMS, PFIZER, ROCHE, CELGENE, NOVARTIS, BIOGEN, UCB, SANDOZ, AMGEN., Employee of: COCHIN Hospital, M.-C. Woronoff: None declared, N. Gouyette Employee of: MSD France, A. Clément Employee of: MSD France, E. Van Ganse Consultant for: PELyon; ALK ABELLO; AstraZeneca; Bayer; BMS; BIF; GSK; IMS; LASER; MSD, F. Tubach: None declared

DOI: 10.1136/annrheumdis-2017-eular.5081

SAT0686 MAJOR ADVERSE CARDIOVASCULAR EVENTS: RISK FACTORS IN PATIENTS WITH RA TREATED WITH TOFACITINIB

C. Charles-Schoeman[1], H. Valdez[2], K. Soma[3], L. Hwang[2], R. DeMasi[4], M. Boy[3], I.B. McInnes[5]. *[1]University of California, Los Angeles, CA; [2]Pfizer Inc, New York, NY; [3]Pfizer Inc, Groton, CT; [4]Pfizer Inc, Collegeville, PA, United States; [5]Glasgow Biomedical Research Centre, University of Glasgow, Glasgow, United Kingdom*

Background: Patients (pts) with RA have increased risk of myocardial infarction (MI) and stroke that cannot be completely explained by traditional cardiovascular

(CV) risk factors. Tofacitinib is an oral JAK inhibitor for the treatment of RA. Treatment with tofacitinib may increase total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-c) and high-density lipoprotein-cholesterol (HDL-c), without affecting TC/HDL-c ratio.

Objectives: To evaluate major adverse CV event (MACE) risk factors in tofacitinib-treated pts with RA in the clinical development programme.

Methods: Data were pooled from pts with moderately to severely active RA receiving ≥1 tofacitinib dose in 6 Phase 3 and 2 long-term extension (LTE) studies (1 LTE study ongoing, data cut-off: April 2015). MACE was any MI, stroke or CV death (coronary, cerebrovascular, cardiac). Cox regression models evaluated associations between baseline (BL) values and time (BL to first tofacitinib dose) to first MACE. Changes (BL to Week [wk] 24) in MACE predictors and time to future MACE (first occurrence after 24 wks) were evaluated after adjusting for age, BL values and time-varying tofacitinib dose. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated.

Results: 52 MACE cases occurred over 12,873 pt-years (py) of exposure in 4076 pts (incidence rate: 0.4 pts with events/100 py). At BL, compared with pts without MACE, pts with MACE were older (mean age 60.2 vs 52.7 years) with a higher mean BMI (29.2 vs 27.0 kg/m^2) and longer mean RA disease duration (10.1 vs 7.7 years), and were more likely to have a history of diabetes (15.4% vs 7.6%) and hypertension (57.7% vs 33.7%). Pts with MACE had higher mean TC (208.2 vs 198.3 mg/dL), LDL-c (123.3 vs 114.0 mg/dL), TC/HDL-c ratio (4.0 vs 3.5) and triglycerides (152.1 vs 125.3 mg/dL) at BL, and lower HDL-c (55.3 vs 59.4 mg/dL) vs pts without MACE. In univariate analyses, traditional CV risk factors and corticosteroid and statin use at BL were associated with MACE risk (Table). BL disease activity and inflammation measures were not associated with MACE risk (Table). In multivariate analysis, BL age, hypertension and the TC/HDL-c ratio were significantly associated with MACE risk. Increases in HDL-c ($p<0.001$) and decreases in TC/HDL-c ratio ($p<0.05$) after 24 wks of tofacitinib therapy were significantly associated with decreased risk of future MACE (Figure). Increases in erythrocyte sedimentation rate (ESR; p=0.09) may be associated with increased future MACE risk. Changes in TC, LDL-c or other disease activity measures were not associated with future MACE risk.

Conclusions: In pooled analyses of tofacitinib-treated pts (age and BL value adjusted), increases in LDL-c and TC after 24 wks of tofacitinib therapy were not associated with future MACE risk. Increases in HDL-c and decreases in the TC/HDL-c ratio after 24 wks of tofacitinib therapy were associated with reduced future MACE risk. Increases in ESR after 24 wks may be associated with increased future MACE risk. More data are needed to confirm these findings.

Acknowledgements: Previously presented at ACR 2016 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by C Viegelmann of CMC and was funded by Pfizer Inc.

Disclosure of Interest: C. Charles-Schoeman Grant/research support from: AbbVie, Bristol-Myers Squibb, Pfizer Inc, Consultant for: Amgen, Pfizer Inc, Regeneron-Sanofi, H. Valdez Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, K. Soma Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Hwang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, R. DeMasi Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Boy Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, I. McInnes Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Merck, Novartis, Pfizer Inc, Roche

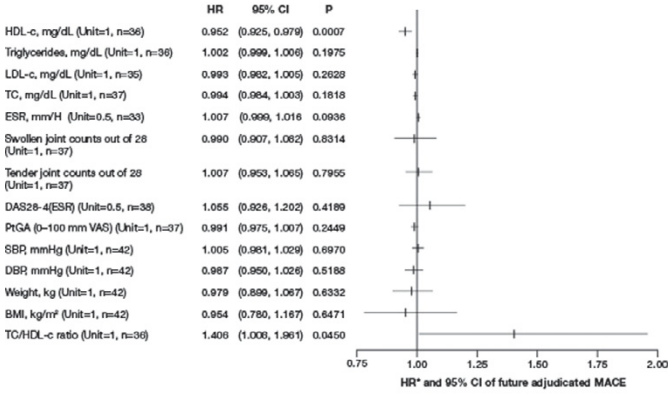
DOI: 10.1136/annrheumdis-2017-eular.2434

Table. Association of baseline risk factors and development of MACE based on univariate Cox analysis

Baseline variable	HR	(95% CI)
Age (years, n=52)	2.02***	(1.53, 2.67)
BMI (kg/m^2, n=52)	1.05**	(1.01, 1.09)
Baseline statin users (Y/N, n=52)	2.77**	(1.45, 5.28)
Baseline corticosteroid users (Y/N, n=52)	0.55*	(0.31, 0.98)
Duration of RA, (years, n=52)	1.03*	(1.00, 1.06)
Triglycerides (mg/dL, n=51)	1.00**	(1.00, 1.01)
TC/HDL-c ratio (n=51)	1.42***	(1.16, 1.74)
Apolipoprotein B (mg/dL, n=48)	1.02**	(1.01, 1.03)
Apolipoprotein B/Apolipoprotein A-1 ratio (n=48)	2.76**	(1.50, 5.09)
SBP (mmHg, n=51)	1.02*	(1.01, 1.04)
DBP (mmHg, n=51)	1.04*	(1.01, 1.07)
History of diabetes (Y/N, n=52)	2.56*	(1.20, 5.43)
History of hypertension (Y/N, n=52)	2.86***	(1.65, 4.96)

*p<0.05; **p<0.01; ***p<0.001
Other BL variables assessed as not being statistically significant were gender, weight, smoking status, DAS28-4(ESR), ESR, CRP, swollen joint count out of 28, tender joint count out of 28, baseline MTX users, baseline MTX dose, TC, HDL-c, LDL-c and history of cardiac disorders
n represents number of patients with MACE (uncensored) analysed for each variable
BL, baseline; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; DAS28-4, disease activity score in 28 joints; DBP, diastolic blood pressure; ESR, erythrocyte sedimentation rate; HDL-c, high-density lipoprotein-cholesterol; HR, hazard ratio; LDL-c, low-density lipoprotein-cholesterol; MACE, major adverse cardiovascular event; MTX, methotrexate; RA, rheumatoid arthritis; SBP, systolic blood pressure; TC, total cholesterol

Figure. Age-adjusted and baseline parameter-adjusted association of change from baseline to Week 24 in lipid levels, inflammation parameters and RA disease activity measures with future MACE



These data show results from a Cox regression model; age-adjusted and baseline parameter-adjusted association of changes from baseline to Week 24, for future MACE risk
*For each variable listed, a Cox regression model was fitted, with change in variable at Week 24, the variable at baseline, age at baseline and time varying dose as predictors
In this model, only patients with exposure after the tofacitinib-week 24 were considered (ie, patients who had MACE before tofacitinib-week 24 or who had withdrawn or completed the study by tofacitinib-week 24 were excluded). Additionally, patients with missing data for a tofacitinib-week 24 variable were excluded from the analysis of that variable (no imputation method). The HR corresponds to increased risk of MACE per 1-unit increase in the parameter
n is the number of patients with future MACE for each predictor
BMI, body mass index; CI, confidence interval; DAS28-4, disease activity score in 28 joints; DBP, diastolic blood pressure; ESR, erythrocyte sedimentation rate; HDL-c, high-density lipoprotein-cholesterol; HR, hazard ratio; LDL-c, low-density lipoprotein-cholesterol; MACE, major adverse cardiovascular event; PtGA, patient's global assessment; RA, rheumatoid arthritis; SBP, systolic blood pressure; TC, total cholesterol

SAT0687 ADHERENCE OF RHEUMATIC PATIENTS TO INH PROPHYLAXIS PRESCRIBED BEFORE BIOLOGICAL TREATMENT: HUR-BIO SINGLE CENTER REAL LIFE RESULTS

E. Şeyhoğlu[1], O.A. Uyaroğlu[1], A. Erden[2], L. Kılıç[2], B. Armağan[2], A. Sarı[2], M. Baykal[2], S. Ak[2], Ö. Karadağ[2], A. Akdoğan[2], S. Apraş Bilgen[2], S. Kiraz[2], I. Ertenli[2], U. Kalyoncu[2]. *[1]Department of Internal Medicine; [2]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey*

Background: Isoniazid (INH) prophylaxis is strongly recommended for the patients who have latent tuberculosis (TB) and who are going to be under anti-TNF treatment. INH is prescribed for 9 months and patient adherence to INH affects the risk of active TB development.

Objectives: In this study we aimed to assess the levels of patient adherence to INH prophylaxis.

Methods: Patients, who are under biological treatment and who have a quantiferon (QFT) test result, were evaluated with a questionnaire between August 2015-August 2016. Questionnaire included the demographic and clinical characteristics. Besides, patients were asked whether they had been prescribed INH. Patients, who were given INH prophylaxis, were asked to answer those questions: i) Did you take INH daily and regularly for 9 months? ii) If not what was the reason? The reasons are classified into three categories: 1) The patient discontinued INH of his/her own volition before 9 months. 2) Continued INH for 9 months but did not take regularly due to forgetfulness. 3) Treatment stopped by physicisan due to an adverse effect (elevation of liver enzymes, neuropathy, etc.)

Results: 1. 710 patients were recruited. INH was prescribed to 169 (23.8%) of 710. Demographic characteristics of INH-prescribed patients: 88 (52.1%) of 169 were female, mean age was 46.2 (SD:11.4), 82 (48.5%) of 169 at least graduated from a high school. Diagnosis were followed; RA 65 (38.4%), SpA 85 (50.3%), PsA 13 (7.7%), others 6 (3.6%). Totally 34 (20.1%) of 169 took INH irregularly. 19 (11.2%) of 169 patients discontinued INH of his/her own volition before 9 months. During follow-up 5 of 19 were prescribed INH again by the physician and they completed the 9-months duration. 9 (5.3%) of 169 patients did not take INH regularly due to forgetting. INH was stopped by a physician due to liver enzyme elevation in 6 (3.5%) of 169 patients. There was not a statistically difference in demographical and clinical characteristics between regular and irregular INH takers.

Conclusions: There is an inadherence to INH treatment approximately in one of five patients. Only 3.5% of INH-recommended patients had a medical reason of inadherence. Among other patients, causes of inadherence were discontinuance of own volition and forgetfulness or perfunctoriness. Physicians should be aware that reminding of INH is one of the question in every outpatient clinic visits. Other reminding methods such as regular calling should be considered in those of high risk population. Further studies were needed for reminding process.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4093

SAT0688 JOINT INVOLVEMENT IN PATIENTS WITH KNEE AND HIP OA SCHEDULED FOR SURGERY: MULTI-JOINT OA, THE RULE NOT THE EXCEPTION?

E.M. Badley[1], C. Yip[1], J.D. Power[2], R. Gandhi[2], N. Mahomed[2], J.R. Davey[2], K. Syed[2], Y.R. Rampersaud[2], C. Veillette[2], A.V. Perruccio[1,2]. *[1]Division of Health Care and Outcomes Research, Krembil Research Institute; [2]The Arthritis Program, Toronto Western Hospital, Toronto, Canada*

Background: Multijoint involvement in osteoarthritis (OA) has long been documented clinically and in the literature. Even so, the vast majority of OA research has focused on OA in individual joints, particularly the knees, hips or hands. In many "joint-specific" studies, the presence of multijoint symptoms are either ignored or peripherally considered in descriptive and analytical work. The implicit assumption is often that OA is OA, irrespective of whether a single joint or several joints are involved.

Objectives: To document the occurrence of multijoint symptoms in a clinical sample of individuals with knee and hip OA scheduled for orthopaedic surgery. To examine the joint sites involved and investigate whether the extent of joint involvement is related to demographic and health characteristics.

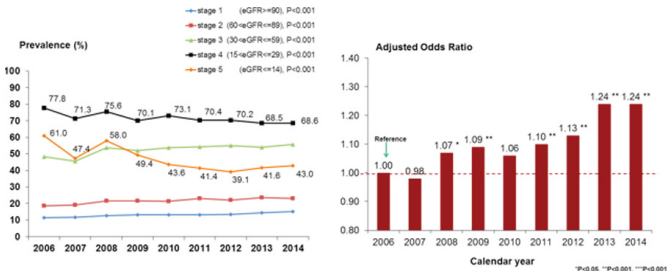
Methods: Patients scheduled for total knee or hip replacement for end-stage OA were consecutively recruited from an academic hospital in Toronto, Canada. A health questionnaire completed prior to surgery captured demographic

characteristics (age, sex), symptomatic joints other than the surgical joint (right and left shoulders, elbows, wrists, hands, hips, knees, feet, ankle, neck and back), body mass index (BMI), comorbidities (hypertension, depression, diabetes, migraine headaches, cancer, respiratory disease, heart disease, stomach/bowel disease, stroke) and WOMAC hip- and knee-specific pain and function.
Results: Study questionnaires were completed by 366 hip and 407 knee patients. The mean age of the sample was 65 years (SD=9.2; range 38–89 years), 57% were female. The most frequently reported symptomatic joints among knee patients were the contralateral knee (53.2%), one or both hands (32.1%), and the upper-, mid- or lower-back (31.0%), and among hip patients were one or both knees (49.4%), the back (36.6%), and the contralateral hip (21.3%). The overall mean number of symptomatic joints other than the surgical joint was 3.0 (SD=3.2; range 0–17). Only 19.0% reported the surgical joint as the only symptomatic joint; 23.0% reported 5 or more additional symptomatic joints. Mean hip/knee-specific pain and function scores were significantly worse with increasing symptomatic joint count ($p<0.01$). Additional symptomatic joints were significantly more frequent in women than men; mean count 3.6 vs. 2.3 ($p<0.01$). No significant difference in mean joint count (p=0.64) was observed by age. Similarly, no difference was found by BMI (i.e. overweight/obese vs. normal); p=0.24 for mean count. However, the number of co-occurring conditions increased with increasing joint count: 27.2% reported 2+ co-occurring conditions among those with 1–4 symptomatic joints, and 42.8% among those with 5+ symptomatic joints ($p<0.01$).
Conclusions: In this clinical OA sample, the "average" patient reported multiple symptomatic joints. Increasing age was not associated with increasing frequency of symptomatic joints. Irrespective of age and obesity, multiple symptomatic joints were the rule, not the exception. It was notable that the frequency of co-occurring conditions increased with increasing symptomatic joint count. This may suggest a need to re-examine how OA is characterized and perhaps its underlying etiology as it relates to single vs. multi-joint involvement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6432

SAT0689 PREVALENCE OF AND TEMPORAL TRENDS IN HYPERURICAEMIA AMONG ADULT PATIENTS WITH CHRONIC KIDNEY DISEASE IN IRELAND

F. Adeeb[1,2], A.A. Udayakumar[2,3], D. Ryan[2], X. Li[2], A.D. Fraser[1,2], A.G. Stack[2,3] on behalf of Health Research Institute, University of Limerick. *[1]Department of Rheumatology, University Hospital Limerick; [2]Graduate Entry Medical School, University of Limerick; [3]Department of Nephrology, University Hospital Limerick, Limerick, Ireland*

Background: An increasing body of evidence links hyperuricaemia with the development of several metabolic disorders and major cardiovascular outcomes. A better understanding of the burden and variation of hyperuricemia within the health system is important in order to identify high-risk groups and facilitate early intervention with effective management strategies.
Objectives: The aim of this study was to describe the prevalence of hyperuricaemia, and period trends within the Irish Health System among patients with chronic kidney disease (CKD).
Methods: 136,325 adult CKD patients aged 18 and above with valid measurements of serum uric acid and creatinine levels were identified between 2006 and 2014 from the laboratory systems within the Irish health system. Hyperuricaemia was defined as serum uric acid $\geq$420μmol/L in men and $\geq$360μmol/L in women. Estimated glomerular filtration rates were determined using the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation and patients were classified by CKD stage according to the Kidney Disease Improving Global Outcomes (KDIGO) staging system. Age- and sex-specific prevalence of hyperuricemia estimates with 95% confidence intervals were determined for each group and across calendar years. Comparisons among groups and across years were conducted using chi-square and multivariate logistic regression was used to explore associations using adjusted odds ratios (AOR) and 95% Confidence Intervals (CI).
Results: Patients with hyperuricaemia were noted to be older [58.2 (18.5) vs. 51.2 (17.4) years]. The prevalence of hyperuricaemia increased progressively between 2006 and 2014 from 20.3% (19.5, 21.0) to 26.5% (25.8, 27.2%) in men and from 17.9% (17.2, 18.6) to 20.4% (19.8, 21.0) in women, $p<0.001$. Age-specific prevalence increased significantly over time for all age groups (18–39, 40–59, 60–79, and $\geq$80 years) for men and women, $p<0.001$. Prevalence was significantly higher with more advanced CKD stage: 15.1% (14.5, 15.6) in Stage 1 CKD compared to 43.0% (34.8, 51.1) in Stage 5 CKD, $p<0.001$. However, rates fell significantly for those Stage 4 and 5 CKD respectively (Figure1). In multi-variable models, the adjusted likelihood of hyperuricaemia increased with each successive year (Figure 2).



Conclusions: The prevalence of hyperuricaemia is substantial in the Irish health system and has increased in frequency over the past decade. Although the burden was highest among patients with more advanced CKD, an encouraging decline in prevalence was observed in recent years. Greater management of gout and hyperuricaemia from increasing utilization of urate-lowering therapies may be responsible for this trend.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5556

SAT0690 RISK OF HOSPITALIZED INFECTION IN CANCER PATIENTS WITH AUTOIMMUNE DISEASES: A SINGLE-CENTER COHORT STUDY

H.-H. Chen[1], D.-Y. Chen[2]. *[1]Department of Medical Research; [2]Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, Province of China*

Background: Whether the risk of hospitalized infection is associated with autoimmune diseases in incident cancer patients is unknown.
Objectives: To examine the risk of hospitalized infection in incident cancer patients with autoimmune diseases compared with those without autoimmune diseases.
Methods: During 2000–2016, we identified 37,027 incident cancer patients from the Cancer Registry database of Taichung Veterans General Hospital. Autoimmune diseases included rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), ankylosing spondylitis (AS), psoriasis (PSO)/psoriatic arthritis (PSA), antiphospholipid syndrome, polymyositis, dermatomyositis, systemic sclerosis, Sjögren's syndrome, mixed connective tissue disease, multiple sclerosis, neuromyelitis optica, palindromic rheumatism, myasthenia gravis, Hashimoto's thyroiditis, immune thrombocytopenic purpura, autoimmune hemolytic anemia, juvenile idiopathic arthritis, adult onset Still's disease, Crohn's disease, ulcerative colitis, Wegner's granulomatosis, and uveitis. Of all subjects, 1,334 had autoimmune diseases. The association between autoimmune diaseases and hospitalized infection risk was shown by calculating hazard ratios (HRs) with 95% confidence intervals (CIs) using cox proportional regression analyses after adjusting for baseline age, sex, cancer stage, hemoglobulin (Hgb), creatinine (CR), log(ALT), log(WBC), and use of biologic agents or tofacitinib.
Results: Among all cancer subjects, the mean ± SD age was 60.2±14.7 years, and the proportion of male gender was 55.7%. Of the 1,334 patients with autoimmune diseases, 338 (25.3%) patients had RA, 221 (16.6%) patients had SLE, 61 (4.6%) patients had AS, 151 (11.4%) patients had PSO/PSA, and 563 (46.8%) had other autoimmune diseases. The incidence rates of hospitalized infection were 143.8 per 10^3 years in patients with autoimmune diseases and 118.9 per 10^3 years in patients without autoimmune diseases. The risk of hospitalized infection was higher in patients with RA and SLE, but not in patients with AS, PSO/PSA, or other autoimmune diseases. Prior use of biologic agents or tofaitinib did not increase hospitalized infection risk. Other risk factors for hospitalized infection included elder age (HR, 1.01; 95% CI, 1.01–1.1), higher cancer stage, CR (HR, 1.04; 95% CI, 1.02–1.06), log(WBC) (HR, 1.21; 95% CI, 1.14–1.28). Female gender (HR, 0.65; 95% CI, 0.62–0.68) and Hgb (HR, 0.89; 95% CI, 0.88–0.90) were associated lower hospitalized infection risk.

Table 1. Univariable and multivariable analyses for the association between autoimmune diseases and hospitalized infection among cancer patients

	Univariate analysis HR (95% CI)	Multivariable analysis* HR (95% CI)
No autoimmune diseases	Reference	Reference
Autoimmune diseases		
RA	1.32 (1.10–1.59)	1.37 (1.13–1.66)
SLE	1.21 (0.95–1.54)	1.41 (1.10–1.80)
AS	0.67 (0.37–1.21)	0.88 (0.46–1.70)
PSO/PSA	1.36 (1.05–1.78)	1.05 (0.80–1.38)
Others	1.17 (1.01–1.36)	1.15 (0.99–1.34)

*Adjusted for age, gender, cancer stage, prior use of biologic agents or tofacitinib, baseline hemoglobulin, creatinine, log (ALT) and log (WBC).

Conclusions: Hospitalized infection was associated with a comorbidity of RA or SLE in incident cancer patients.
Acknowledgements: With thanks to Cancer Registry database and Clinical Informatics Research & Development Center of Taichung Veterans General Hospital for the Support of Clinical data.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4676

SAT0691 INFLUENCE OF SMOKING IN THE EXPRESSION OF CHRONIC PERIODONTITIS AND ANTI-CITRULLINATED PROTEINS ANTIBODIES IN RHEUMATOID ARTHRITIS

J. González Febles[1], J.L. Garnier Rodríguez[2], F. Sánchez Alonso[3], S. Dadlani[2], Y. Barrios[4], S. Bustabad[5], F. Díaz González[5], M. Sanz Alonso[1], B. Rodríguez Lozano[5]. *[1]Periodontology, UCM, Madrid; [2]Odontology/Periodontology, Dental Clinic Dr Garnier, Santa Cruz de Tenerife; [3]Research Unit, Sociedad Española de Reumatologia, Madrid; [4]Immunology Section.Central Laboratory; [5]Rheumatology, Hospital Universitario de Canarias, Tenerife, Spain*

Background: Environmental, genetic and epigenetic factors can induce citrullination of structural peptides by the enzyme PAD,which induce anti-citrullinated protein antibodies (ACPA) preceding RA. Among the environmental factors are cigarette smoke, infections, such as *P. gingivalis* in periodontitis (PD) and *Prevotella copri* of intestinal microflora, and silica dust. Given the implication of these two exogenous factors, tobacco and PD,in citrullination, and tobacco enhancer factor in PD, we studied:
Objectives: 1. The risk of smoking for developing advanced PD in patients with RA. 2. Possible influence of smoking on the expression of severe PD and ACPA in RA patients.
Methods: Observational, descriptive, cross-sectional study in RA patients older tan 18y.o.(ACR/EULAR 2010), with ≥4 teeth, without tooth cleaning nor antibiotic intake 6 months previously. Socio-demographic and anthropometric variables included smoking status, social indicators such as Graffar scale, stress level, annual dental prophylaxis, and co-morbidities such as diabetes mellitus, dyslipidemia, ischemic cardiovascular disease. Serum ACPA detection: semiquantification Ab IgG against citrullinated peptides (ELISA) with Immunoscan CCPlus®test kit. Eurodiagnostica: positive >25; ACPA title stratification: Low (25–75), moderate (76–300) and high (>300). Periodontal parameters: plaque index (PI), Bleeding on probing (Bop), probing pocket depth, recession, clinical attachment level (CAL). CAL loss was categorized according to European Workshop 2005 (Tonetti)[1]: T level 0 (abscence), TL1 (mild), TL2 (severe). Statistical analysis: t-student, Kruskal Wallis, Chi-cuadrado by Stata program 13.1.
Results: We studied 187 patients, F/M 78.6%/21.4%, mean age 54.4 y.o. Follow-up time 8.8 y.o. RF+ 74.2%, ACPA positive in 114/168 patients (67.86%). Smoking habit:Current smoker (19.25%), former smoker (24.6%); low socioeconomical status (36.4%)/ relative poverty (33.7%).PD was observed in 97.3%: TL1 52.4%, TL2 44.9%. A "risk gradient" was observed for PD related to smoking habit: former smoker OR 1.62 (95% CI 0.81–3.27),p=0.174; smokers, OR 2.27 (95% CI 1.05–4.91), p=0.037. When analyzing the influence of smoking on PD development according to ACPA profile, a gradient effect of developing severe PD was observed from former smokers OR 2.37 (IC95% 0.52–7.64) to current smokers OR 6.99 (IC95% 1.53–32.07) (p=0.029) in ACPA(-) patients. This relationship was not observed in ACPA (+) patients (p=0.383).
Conclusions: 1.There is a "risk gradient" to develop PD in RA in relation to past or current exposure to tobacco, so that, although not significant, former smokers are at greater risk than non-smokers, and current smokers have a significant risk 2.3 times higher. 2. This risk gradient is shown in ACPA (-) patients, but not in ACPA (+) patients, which suggests an independent relationship between PD and ACPA (+) RA.
References:
[1] Tonetti MS, et al. J Clin Periodontol 2005.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5201

SAT0692 PREDICTORS AND PERSISTENCE OF UNACCEPTABLE PAIN DURING THE FIRST YEAR OF RHEUMATOID ARTHRITIS IN SWEDEN

H. Westerlind[1], M.E. Schelin[1], R. Altawil[2], L. Klareskog[3], L. Alfredsson[1], J. Lampa[3]. *[1]Institute of Environmental Medicine; [2]Rheumatology Unit, Department of Medicine, Center for Molecular Medicine (CMM); [3]Rheumatology Unit, Department of Medicine, Center for Molecular Medicine (CMM), Karolinska Institutet, Stockholm, Sweden*

Background: Pain is a dominant symptom in rheumatoid arthritis (RA).
Objectives: Investigate unacceptable pain (VAS-pain ≥40) during the first year of the disease and whether it can be predicted from baseline disease characteristics.
Methods: The cohort included all incident RA cases from the Swedish population-based case-control Epidemiological Investigation of Rheumatoid Arthritis study (EIRA), who also were in the Swedish Rheumatology Register. Unacceptable pain was defined as scoring 40 mm or above on the pain visual analog scale (VAS) (i.e. not reaching the patient acceptable symptom state (PASS) (1)), and the proportion of patients going in and out of PASS was traced over the first year. Association between baseline parameters, divided into quartiles, and unacceptable pain at one year was assessed using modified Poisson regression and expressed as risk ratios with 95% confidence intervals (95% CI), adjusted for sex and age at diagnosis.
Results: A total of 2808 patients were included in the study and 33.8% of the patients presented with PASS (i.e.VAS pain below 40) at inclusion. If a patient had PASS at any given visit, there was over 70% chance that the patient remained in PASS at the following visit. The most common PASS pattern (25.6%), was to present with unacceptable pain, reach PASS at the 3 month visit, and then remain in PASS. However, one year after diagnosis, only two thirds of the patients had PASS. Higher disability (measured as HAQ) at baseline was significantly and independently associated with an increased risk for unacceptable pain at one year (for the highest quartile of HAQ; RR=1.97 [95% CI:1.60–2.42]). Also high tender joint count at baseline was associated with an increased risk for unacceptable pain; RR=1.40 [95% CI: 1.18–1.65] for the highest quartile, whereas high swollen joint count at baseline was associated with a decreased risk; RR=0.79 [95% CI: 0.66–0.95] for the highest quartile.
Conclusions: The results highlight the need for efficient pain treatment strategies early in the disease.
References:
[1] Tubach F, Ravaud P, Martin-Mola E, Awada H, Bellamy N, Bombardier C, et al. Minimum clinically important improvement and patient acceptable symptom state in pain and function in rheumatoid arthritis, ankylosing spondylitis, chronic back pain, hand osteoarthritis, and hip and knee osteoarthritis: Results from a prospective multina. Arthritis Care Res (Hoboken) 2012;64:1699–1707.
Acknowledgements: We would like to acknowledge the EIRA study group and the EIRA data collectors.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6133

SAT0693 SERUM URIC ACID LEVELS AND HORMONE REPLACEMENT THERAPY TYPE: A RETROSPECTIVE CASE-CONTROL STUDY OF POSTMENOPAUSAL WOMEN

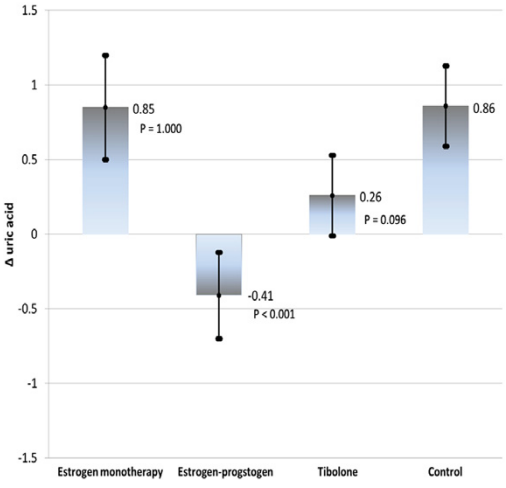
J.H. Jung, J.-H. Kim, Y.H. Lee, G.G. Song, S.J. Choi. *Internal Medicine, Korea University Medical Center, Seoul, Korea, Republic Of*

Background: Serum uric acid levels increase in postmenopausal women but decrease when hormone replacement therapy (HRT) is administered. However, no study has evaluated the effects of different types of HRT on serum uric acid levels.
Objectives: We examined whether estrogen monotherapy, estrogen-progestogen combination therapy, and tibolone use affected serum uric acid levels in this population.
Methods: We performed a retrospective case-control study of postmenopausal women. From 2005 to 2015, postmenopausal women measured serum uric acid levels more than twice were included. Patients were grouped according to HRT regimen: estrogen monotherapy, estrogen-progestogen combination therapy, or tibolone. The control group did not receive HRT. Differences in serum uric acid levels were examined in each group. Our analysis was adjusted to accommodate different follow-up intervals for individual patients. Multiple variables were adjusted using the Tukey-Kramer method. Age, body mass index, hypertension, diabetes mellitus, dyslipidemia, alcohol consumption, smoking status, and co-medications were also adjusted.
Results: In the control group, the serum uric acid level increased to 0.86±0.27 mg/dL (least squares mean ± standard error). In comparison, after adjusting for multiple variables, the serum uric levels in the estrogen-progestogen combination

Table 1. Degrees of changes in serum uric acid levels by hormone replacement therapy type

	Estrogen mono		Estrogen-progestogen		Tibolone		Control
	Δ uric acid	P	Δ uric acid	P	Δ uric acid	P	Δ uric acid
Crude	0.64±0.26	1.000	-0.50±0.17	<0.001	0.16±0.18	0.097	0.67±0.13
Model I	0.63±0.26	0.994	-0.51±0.17	<0.001	0.15±0.18	0.059	0.71±0.13
Model II	0.63±0.26	0.994	-0.51±0.17	<0.001	0.14±0.18	0.060	0.71±0.13
Model III	0.67±0.27	0.988	-0.42±0.19	<0.001	0.30±0.21	0.206	0.77±0.14
Model IV	0.64±0.34	0.986	-0.47±0.29	<0.001	0.23±0.26	0.195	0.74±0.26
Model V	0.85±0.35	1.000	-0.41±0.29	<0.001	0.26±0.27	0.096	0.86±0.27

All models that included crude values were adjusted for follow-up intervals. Model I: adjusted age. Model II: adjusted age and BMI. Model III: adjusted age, BMI, HTN, DM, and dyslipidemia. Model IV: adjusted age, BMI, HTN, DM, dyslipidemia, alcohol consumption, and smoking status. Model V: adjusted age, BMI, HTN, DM, dyslipidemia, alcohol consumption, smoking status and co-medications.



therapy group were found to be significantly lower (-0.41±0.29 mg/dL, P<0.001). However, the serum uric acid levels in the estrogen monotherapy and tibolone groups did not differ significantly from the control group level.

Conclusions: Serum uric acid levels decreased in response to estrogen-progestogen combination therapy in postmenopausal women. We attribute our findings to the effects of progesterone, rather than estrogen.

References:

[1] Roddy E, Doherty M. Epidemiology of gout. Arthritis Res Ther. 2010;12:223.
[2] Hak AE, Curhan GC, Grodstein F, Choi HK. Menopause, postmenopausal hormone use and risk of incident gout. Ann Rheum Dis. 2010;69:1305–9.
[3] Hak AE, Choi HK. Menopause, postmenopausal hormone use and serum uric acid levels in US women–the Third National Health and Nutrition Examination Survey. Arthritis Res Ther. 2008;10:R116.
[4] Bruderer SG, Bodmer M, Jick SS, Meier CR. Association of hormone therapy and incident gout: population-based case-control study. Menopause. 2015;22:1335–42.

Acknowledgements: No grants or other support were received for this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1950

SAT0694 SUBGROUPING OF EARLY RA-PATIENTS IDENTIFIED CLUSTER OF PATIENTS WITH HIGH LEVELS OF PAIN, FATIGUE AND PSYCHOSOCIAL DISTRESS 3 YEARS AFTER DIAGNOSIS

J. Lindqvist[1], H. Westerlind[2], L. Klareskog[1], L. Alfredsson[2], J. Lampa[1]. *[1]Unit of Rheumatology, Department of Medicine Solna; [2]Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden*

Background: The wide range of effective treatment alternatives for rheumatoid arthritis (RA) makes treating the disease to inflammatory remission a feasible goal for a majority of patients. However, earlier studies have reported that symptoms other than inflammatory disease activity causes a substantial burden of illness for RA-patients. These unmet needs include persistent pain, fatigue, impaired physical function and mental health status (1).

Objectives: To identify clusters of early RA-patients based on pain, fatigue, sleep, physical function, mental health status and perceptions of quality of life, 3 years after diagnosis. Withal investigate associations between clusters and clinical parameters at the time of diagnosis.

Methods: Data was compiled from the Swedish case-control cohort Epidemiological Investigation of Rheumatoid Arthritis (EIRA) and linked to the Swedish Rheumatology Quality Register (SRQ). All patients were diagnosed with RA according to the 1987 ACR criteria. Early RA-patients with clinical data from diagnosis and 3 year follow-up questionnaire data were included (N=618; 74% women, median age at diagnosis 58 years). Measurements of pain, fatigue, sleep problems, physical and mental functioning and quality of life was entered into a hierarchical agglomerative clustering procedure using Ward's method of squared Euclidian distances. Number of clusters was determined by largest changes in distances at which clusters were formed. Associations between clusters and clinical variables at diagnosis were calculated using contingency analysis. All statistical analysis was performed using jmp statistical software (SAS, US). p<0.05 was considered significant.

Results: The cluster analysis identified three distinct clusters. Cluster 1 consisted of 178 patients (29%) doing significantly worse for all included variables. Cluster 3 consisted of 209 patients (34%) doing very well and cluster 2, consisting of 231 patients (37%), constituted an intermediate group doing fairly well. Cluster 1 was associated with female sex (p=0.0007) and lower education level (p=0.0003) compared to cluster 3. Cluster 1 was also associated to higher HAQ (p<0,0001), higher patient global assessment of health (p<0.0001), higher pain ratings (p<0.0001) and lower swollen/tender joint count ratio (STR) (p=0.0065) at the time of diagnosis compared to cluster 3.

Conclusions: Through cluster analysis, we could identify a subgroup of almost a third of the RA-patients with high levels of pain, fatigue, sleep problems and poor physical and mental health related quality of life 3 years after RA-diagnosis. These symptoms are indicative of a central sensitization syndrome and these findings indicate that other factors than inflammatory disease activity causes a significant burden of illness also at an early stage of RA and that there is a need of additional intervention strategies for these patients.

References:

[1] Taylor PC, Moore A, Vasilescu R, Alvir J, Tarallo M. A structured literature review of the burden of illness and unmet needs in patients with rheumatoid arthritis: a current perspective. Rheumatol Int. 2016;36(5):685–95.

Acknowledgements: All patients and staff involved in EIRA ans SRQ.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3740

SAT0695 NO ASSOCIATION BETWEEN VITAMIN D LEVELS AND CARDIOVASCULAR DISEASES IN INFLAMMATORY JOINT DISEASES AND SYSTEMIC AUTOIMMUNE DISEASES – A SYSTEMATIC REVIEW

J.E.S. Ling[1], M. Ter Wee[2], W. Lems[3], M. Nurmohamed[3], H. Raterman[3]. *[1]Newcastle University Medicine Malaysia, Johor Bahru, Malaysia; [2]Epidemiology and Statistics; [3]Amsterdam Rheumatology and Immunology Centre, VU University Medical Centre, Amsterdam, Netherlands*

Background: In recent years, vitamin D deficiency has been linked to disease activity and pathogenesis of systemic autoimmune diseases (SAD) like systemic lupus erythematosus (SLE) and inflammatory joint diseases (IJD) such as rheumatoid arthritis (RA). In the general population, the association between vitamin D with risk for cardiovascular diseases (CVD) is still debatable. While people with IJD and SAD tend to be vitamin D deficient and suffer from an elevated CVD burden, the effect of vitamin D on their cardiometabolic risk factors is of much interest.

Objectives: To provide an overall conclusion on whether vitamin D deficiency contributes to an increased cardiovascular morbidity in these patients, a systematic literature review was done.

Methods: A systematic literature search was done in PubMed/MEDLINE and EMBASE to identify all articles that assessed the association of vitamin D with cardiovascular disease and its risk factors in patients with IJD (rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis) and SAD (systemic lupus erythematosus (SLE), Behcet's disease, vasculitis, Sjogren syndromes, systemic sclerosis). Eligible studies were assessed for quality and risk of bias according to the Cochrane Handbook Chapter 13.5.2.1. (Higgins JPT. GS. Cochrane Handbook for Systematic Review of Interventions The Cochrane Collaboration 2011.)

Results: In total 3273 abstracts were identified. After screening, selection and quality assessment, 16 studies were included (6 case-control and 10 cohort studies), which described only RA and SLE except for one study which focused on PsA. Therefore, this study focused on RA and SLE because they are the most frequent IJD and with highest CVD risk respectively. In RA patients (n=812) vitamin D deficiency was associated with presence of (components)of metabolic syndrome (OR =1.8 (95% CI: 1.3; 2.5), P=0.001) in RA, especially dyslipidemia (OR 1.7; 95% CI:1.1–2.5; P=0.013) and obesity. No studies with prospective design in RA have assessed CVD risk in relation to vitamin D. In SLE patients (n=1850) the only prospective study observed no association between vitamin D deficiency and CVD, although weak associations with dyslipidemia and obesity were observed in some studies.

Conclusions: No clear association between vitamin D deficiency and CVD was found in patients with RA and SLE, probably due to large heterogeneity in terms of sample sizes, designs, analyses and outcome measures. As conclusions were mainly drawn on cross-sectional data, there is an urgent need for adequate prospective studies to assess if vitamin D levels are associated with cardiovascular outcomes.

References:

[1] Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4302

SAT0696 ENDOTHELIAL NITRIC OXIDE SYNTHASE T-786C GENE PROMOTER POLYMORPHISM IS A POTENTIAL PREDICTOR OF LOW RESPONSE TO THE THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS, UKRAINE POPULATION

K. Zaichko, M. Stanislavhuk, I. Shapoval. *The Internal Medicine, National Pirogov Memorial Medical University, Vinnytsya, Ukraine*

Background: Recently endothelial nitric oxide synthase (eNOS) T-786C gene promoter polymorphism was considered to be a factor of a high severity of RA [1,2]. It is possible that the eNOS T-786C gene promoter polymorphism can modify the efficacy and safety of treatment in patients with RA, but there is no information on the subject.

Objectives: To evaluate efficacy of treatment of patients with RA in accordance to the eNOS T-786C gene promoter polymorphism.

Methods: Patients who were enrolled in the study satisfied follows criteria: MTX 10–15 mg/week during the past 12 weeks, stable oral NSAIDs and corticosteroids (CCS), ≤10 mg/day prednisone or equivalent during the past 2 weeks, DAS28 ≥3.2, >6 tender and swollen joints. We excluded patients with previous biologic agent treatment history. All patients received treatment that included MTX, folic acid, CCS, NSAIDs. We evaluated RA activity (DAS28), number of swollen and tender joints, ESR, CRP, and HAQ before enrollment in the study and at the 12 week. Efficacy of the treatment was assessed by the ACR 20; 50; 70 at the end of the study.

The 12-week study completed 148 patients with RA, 100% female, aged 45.7±8.54 years (mean ± SD), with moderate (DAS28 3.2–5.1; 34.5%) and high disease activity (DAS28 >5.1; 65.5%). Among the patients with RA, seropositive were 81.8% and 84.5% by the RF and the anti-CCP, respectively. Polymorphism of NOS3 T786C gene (rs2070744) was performed by Real-Time PCR. All studied polymorphism satisfied Hardy-Weinberg equilibrium. The study was conducted in accordance with the Declaration of Helsinki of the World Medical Association

"Ethical principles of medical research involving human subjects" (2000), the requirements of GCP, the applicable national legislation.

Results: Among patients with RA frequency of the genotypes was as follows: TT – 37.2%, TC – 42.6%, CC – 20.3%. Age, seropositivity and the duration of the disease were not differing in patients with RA, carriers of the different genotypes of eNOS. Though, CC genotype was associated with high disease activity according to DAS28-ESR >5.2 (OR=9.60; 95% CI 2.18–42.2), HAQ >2 (OR =2.38; 95% CI: 0.94–6.02) and extraarticular manifestations (OR =3.26; 95% CI 1.40–7.56).

After 12 weeks treatment we estimated, that among patients with TT genotype there were 58.3; 16.7; and 8.3% responders ACR20; ACR50; ACR70, and among patients with CC genotype - 20.0; 10.0; 0.0% ($p<0.05$). TC heterozygotes patients had lower (by 22–25%, $p<0.05$) clinical response to the treatment by DAS28 and HAQ than the homozygotes TT.

Conclusions: eNOS T-786C gene promoter polymorphism influence on the efficacy of the treatment, and CC genotype can be considered as a possible predictor of a low response to the treatment in patients with rheumatoid arthritis.

References:

[1] Breedveld F.C., Weisman M.H., Kavanaugh A.F. et al. (2006) The PREMIER study. Arthr. Reum., 54: 26–37.

[2] Gonzalez-Gay M.A., Llorca J., Palomino-Morales R. et al. (2009) Influence of nitric oxide synthase gene polymorphisms on the risk of cardiovascular events in rheumatoid arthritis. Clin. Exp. Rheumatol., 27 (1): 116–119.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3962

SAT0697 PREVALENCE OF HEPATITIS B AND C INFECTION AND REACTIVATION IN PATIENTS RECEIVING BIOLOGIC IV THERAPIES

K. Arévalo Ruales[1], B. Soler Bas[2], J. Ivorra Cortes[1], E. Grau Garcia[1], E. Vicens Bernabeu[1], E. Labrador Sánchez[1], J.J. Fragio Gil[1], R. González Mazarío[1], C. Alcañiz Escandell[1], I. Cánovas Olmos[1], I. Chalmeta Verdejo[1], C.M. Feced Olmos[1], L. Gonzalez Puig[1], I. Martínez Cordellat[1], C. Nájera Herranz[1], R. Negueroles Albuixech[1], J.E. Oller Rodriguez[1], F.M. Ortiz-Sanjuan[1], J.A. Román Ivorra[1,2]. *[1]Rheumatology Department, HUP la Fe; [2]Medical School, UCV, Valencia, Spain*

Background: With the use of biological therapy, cases of reactivation of hepatitis B (HBV) and C (HCV) have been described, consequently its use has to be carefully evaluated. In some cases these therapies have to be administered together with antiviral treatment. Despite the fact that before the beginning of the biological therapy the screening of HBV and HCV virus is done, during the course of treatment serologies are no longer used to detect serovonversions.

Objectives: To analyze the prevalence of HBV and HCV in patients with rheumatic disease at the beginning of biological therapies. To identify the cases of hepatitis reactivation.

Methods: Retrospective observational analysis of the biological treatments administered to patients with rheumatic Disease of the rheumatology department of La Fe hospital, during the period 2000–2015 who had HBV and/or HCV serology at the beginning of treatment. Demographic data and diagnosis of the patient, months of treatment and the results of the serologies performed at the beginning and in the follow-up of the treatment, and the cases of reactivation of hepatitis have been collected.

Results: A total of 388 patients were selected of which 62.4% were female; the mean age at diagnosis of was 38.96±14.36 years. 49.5% of the patients were diagnosed with rheumatoid arthritis (RA), 25.3% of ankylosing spondylitis (AE), 18.6% of psoriatic arthritis (APSO) and 6.7% with other diagnoses. The mean treatment time with patients' biological therapy is 200±118 months (3–464 months), and the mean time between the two serologies is 172±102 months (18–460 months). An incidence of 10% of cases with HBV infection (39 patients) is observed. The serological pattern was 8 cases with Ac-core (+) HBV/Ac-surface (-)/Ag-surface (-) HBV and 31 HBV/Ac- surface (-). The incidence of HCV at the start of treatment was 1.1% (4 patients). A case of reactivation (12.5%) was detected among the 8 patients with Ac-core (+)/Ac-surface (-)/Ag-surface (-) HBV. The patient had infliximab and methotrexate, and reactivation was observed after 12 years of treatment. No reactivation of HCV has been detected.

Conclusions: In our series of patients the incidence of HBV and HCV has been 10% and 1.1%, respectively. One of the 8 patients with Ac-core (+)/Ac-surface (-)/Ag-surface (-) HBV, had reactivation of the virus.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4827

SAT0698 DISEASE ACTIVITY DURING AND AFTER PREGNANCY IN WOMEN WITH AXIAL SPONDYLOARTHRITIS

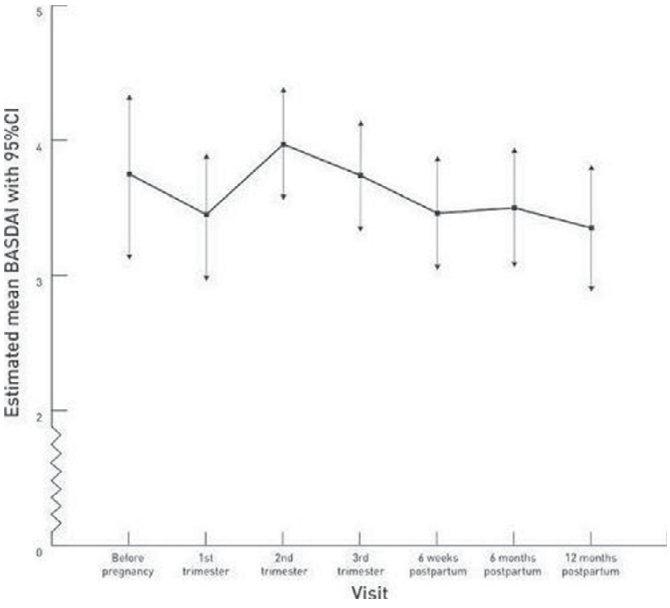
K. Ursin[1,2], S. Lydersen[3], J. Skomsvoll[1], M. Wallenius[1,2]. *[1]National Advisory Unit on Pregnancy and Rheumatic Diseases, St. Olavs Hospital - Trondheim University Hospital; [2]Department of Neuromedicine and Movement Science; [3]Regional Centre for Child and Youth Mental Health, NTNU, Norwegian University of Science and Technology, Trondheim, Norway*

Background: Studies on disease activity of ankylosing spondylitis in pregnancy have shown diverging results. A large retrospective study from 1998 without validated disease activity scores found no particular pattern of disease course during pregnancy (1). Later two small studies demonstrated a tendency towards lower disease activity in the beginning of pregnancy and deterioration in late pregnancy (2,3). None of these studies included women with non-radiographic axial spondyloarthritis. The only large study was conducted before the widespread use of biological DMARDs.

Objectives: The aim of this project was to prospectively study disease activity in women with axial spondyloarthritis before, during and after pregnancy with BASDAI as disease activity measure.

Methods: RevNatus is a Norwegian nationwide register designed for the follow-up of pregnant women with rheumatic diseases. RevNatus included 181 full term pregnancies in 168 women with axial spondyloarthritis between 2006 and 2016. The women had seven visits at a rheumatology unit; before pregnancy, in each trimester, and six weeks, six months and twelve months postpartum. BASDAI-values from each visit were analyzed in a linear mixed model.

Results: Even though we found a statistically significant relationship between disease activity and time point in the follow-up period, our study demonstrated that women with axial spondyloarthritis had stable, low disease activity during and after pregnancy. Disease activity in second trimester was significantly higher than six weeks after delivery, but the change in estimated mean BASDAI was small (BASDAI 3.97 vs. BASDAI 3.46, p=0.005). The figure below shows changes in disease activity throughout the study period.



Conclusions: Studying women with axial spondyloarthritis, we found that disease activity was highest in second trimester, but altogether stable in the period from planning pregnancy to one year after delivery.

References:

[1] Ostensen M, Ostensen H. Ankylosing spondylitis - The female aspect. J Rheumatol. 1998;25(1):120–4.

[2] Ostensen M, Fuhrer L, Mathieu R, Seitz M, Villiger PM. A prospective study of pregnant patients with rheumatoid arthritis and ankylosing spondylitis using validated clinical instruments. Ann Rheum Dis. 2004;63(10):1212–7.

[3] Lui NL, Haroon N, Carty A, Shen H, Cook RJ, Shanmugarajah S, et al. Effect of pregnancy on ankylosing spondylitis: A case-control study. J Rheumatol. 2011;38(11):2442–4.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1604

SAT0699 RAPID ASSESSMENT PREDICTS DISEASE ACTIVITY IMPROVEMENT IN NEWLY DIAGNOSED RHEUMATOID ARTHRITIS (RA)

M. Yates[1], J. Galloway[1], N. Snowden[2], S. Norton[1], J.M. Ledingham[3], E.M. Dennison[4], A. Rivett[5], A.J. Macgregor[6]. *[1]Academic Rheumatology, King's College London, London; [2]Rheumatology Dept, Pennine MSK Partnership, Oldham; [3]Rheumatology Dept, Portsmouth Hospitals NHS Trust, Portsmouth; [4]MRC, Southampton University, Southampton; [5]BSR, The British Society for Rheumatology, London; [6]Rheumatology Dept, Norfolk and Norwich University Hospital, Norwich, United Kingdom*

Background: Early intervention in RA is associated with improved outcomes in randomised trials. UK guidelines stipulate that those with suspected RA are assessed by a rheumatologist within 3 weeks of referral. However, there are limited real world data confirming the value of early assessment. Previous work suggests social deprivation predicts severe disease at presentation and a worse

clinical course (1). The impact of deprivation in early assessment has yet to be characterised on a national level.
Objectives: To investigate if rapid assessment in secondary care associates with achieving a good treatment response, and if this is modulated by social deprivation.
Methods: An audit, designed as a prospective longitudinal observational study, was conducted to assess early RA care. All NHS providers in England and Wales were required to participate. Follow up data were captured over 3 months for subjects with a diagnosis of RA. Rheumatologist assessment within 3 weeks of referral was the predictor variable. The primary outcome was good EULAR DAS response; the secondary outcome was meaningful improvement in RAID score. Logistic regression was used to estimate for associations. Confounders including age, gender, baseline DAS28 and RAID scores were considered in analyses. The index of multiple deprivation (IMD) rank was calculated for each individual based on super-output geographical areas. The IMD rank was then stratified into quintiles and included as a confounder.
Results: 136 of 146 eligible trusts submitted data. 11,752 subjects consented, 5,622 were diagnosed with RA. 94/5622 (1.7%) had incomplete assessment date data. DAS28 response was available for 2234/5622 (39.7%), and RAID response for 901/5622 (16%). The table shows baseline characteristics and response for subjects with complete data. Assessment within 3 weeks associated with a significantly greater improvement in DAS28 and RAID scores, with an adjusted odds ratio for a good EULAR response 1.38 (1.15–1.66) and meaningful RAID reduction 1.44 (1.03–2.02).

	Seen within 3 weeks	Not seen within 3 weeks	P Value
N	878	1356	
Age (SD)	58.6 (14.8)	59.9 (14.1)	0.046*
Female (%)	65.2	64.4	0.24**
White British (%)	86	88.9	0.015**
Current smoker (%)	21.1	25.4	0.009**
IMD quintile mean	3	3	
DAS28 EULAR good response (%)	43.7	35.8	0.001**
DAS28 EULAR moderate response (%)	31.2	35	
DAS28 EULAR no response (%)	25.1	29.1	
Achieved MCID† RAID (%)	48	40.7	0.026*

*t-test; **chi-squared. †Minimal clinically important difference (reduction by 50% or absolute reduction >3).

Conclusions: These real world data confirm rapid assessment significantly predicts treatment response, in terms of clinical disease activity and patient reported outcomes. Amongst those who were assessed within 3 weeks of referral, an additional 8% achieved a good EULAR response. The association with RAID response was strengthened when social deprivation was included as a confounder. The relationship between IMD and RAID response appears to be non-linear and requires further study.
References:
[1] ERAS Study Group. Socioeconomic deprivation and rheumatoid disease:What lessons for the health service? Ann rheum dis. 2000;59(10):794–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2462

SAT0700 COMPARATIVE RISK OF RESPIRATORY DEPRESSION IN PATIENTS TREATED WITH OPIOIDS FOR NON-MALIGNANT PAIN

M. Jani[1], K. Kopec-Harding[1], M. Lunt[1], W.G. Dixon[1,2,3]. [1]*Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester;* [2]*Rheumatology department, Salford Royal NHS Foundation Trust, Salford;* [3]*Health eResearch Centre, University of Manchester, Manchester, United Kingdom*

Background: Opioid use for non-cancer pain has increased considerably over the last 30 years. The U.S. Food and Drug Administration announced several boxed warnings in 2016 to highlight serious opioid-related risks (1) in an effort to reduce fatal overdoses, 80% of which are unintentional (2). The most serious opioid related adverse event is respiratory depression (RD), which can be potentially fatal. There are few data on the incidence of RD in opioids users for non-malignant pain and no comparative data between drugs.
Objectives: To assess the comparative risk of RD in new users of opioids for non-malignant pain using routinely collected electronic patient records (EPR).
Methods: Opioid users from Salford hospital EPR were identified between 2014–2016. Patients with prior malignancy were excluded on the basis of ICD-10 codes and health issues. Those with prior history of opioid use were excluded using keyword searches within the medicines reconciliation document. The primary analysis was on drug + 1 day lag window, unless patient switched to another opioid. Exposure was categorised as opioid monotherapy by drug or combination of opioids (so that RD events could be assigned to a single exposure category). Electronic National Early Warning Scores, used to regularly monitor physiological parameters during inpatient visits, were used to classify RD. An RD event was defined as any one of the following: respiratory rate (RR) ≤8/min, RR ≤10/min and oxygen saturations <94%, RR ≤10/min and altered consciousness, or dispensed naloxone use. Crude rates per 1000 person years of follow up were calculated and Cox proportional hazards models were used to examine the comparative risk of dispensed opioids and RD. Patients contributed follow up time for a particular drug from dispensed drug start date until day after discontinuation, first RD event, death or end of last hospital admission (by 31/05/16).
Results: 8007 opioid users were included in the study, 3,976 female (50%) and a mean age (SD) of 53 (21) years. There were 255 RD events observed on treatment, 87 with severe respiratory depression (RR <8/min), 114 requiring naloxone and 3 respiratory arrests. Patients on fentanyl, morphine, oxycodone and combination treatment had the highest crude rates of RD (table). In the age and gender adjusted Cox-model, using codeine as the referent, patients on fentanyl, morphine, oxycodone and combination opioids had the highest risk of RD [(table), adjusted HR (95% CI) for combination opioids: 2.22 (1.56, 3.16)]. Compared to morphine, combination opioids had an adjusted HR of 1.52 (1.09, 2.13).

Opioid (no. of patients)	Codeine (n=4,638)	Fentanyl (n=577)	Morphine (n=3,783)	Oxycodone (n=1,740)	Tramadol (n=189)	Alfentanil (n=372)	Buphrenorphine (n=93)	Combination (n=3,175)
Mean age (years, SD)	51 (20)	62(20)	48 (18)	68 (18)	48 (18)	52 (17)	75 (17)	49 (19)
Females (%)	50	49	49	55	49	35	66	50
Median follow up per patient (days)	7 (3-15)	12 (6-24)	8 (4-15)	14 (7-28)	15 (7-36)	37 (17-78)	36 (21-67)	9 (5-19)
Number of RD events	63	11	79	37	2	2	1	60
Crude rate per 1000 patient years (95% CI)	58 (46, 75)	120 (66, 217)	89 (72, 111)	102 (74, 141)	40 (10, 160)	70 (17, 283)	61 (9, 433)	152 (118, 195)
Hazard ratio (95% CI)	Ref	1.99 (1.05, 3.77)*	1.49 (1.06, 2.07)*	1.79 (1.19, 2.69)*	1.05 (0.26, 4.31)	0.48 (0.12, 1.98)	1.73(0.24, 12.51)	2.23 (1.56, 3.17)*
Age and gender adjusted hazard ratio (95% CI)	Ref	2.05 (1.08, 3.90)*	1.46 (1.05, 2.03)*	1.99(1.31, 3.03)*	1.03 (0.25, 4.20)	0.45 (0.11, 1.86)	1.83 (0.25, 13.24)	2.22 (1.56, 3.16)*
Hazard ratio (95% CI)	0.67 (0.48, 0.94)*	1.34 (0.71, 2.51)	Ref	1.21 (0.82, 1.78)	0.71 (0.17, 2.89)	0.33 (0.08, 1.32)	1.16 (0.16, 8.39)	1.50 (1.07, 2.10)*
Age and gender adjusted hazard ratio (95% CI)	0.69 (0.49, 0.95)*	1.40 (0.74, 2.65)	Ref	1.37 (0.91, 2.06)	0.70 (0.17, 2.87)	0.31 (0.08, 1.27)	1.25 (0.17, 9.06)	1.52 (1.09, 2.13)*

* p<0.05

Conclusions: Fentanyl, oxycodone, morphine monotherapy have a significantly higher risk of RD than codeine, but these are not significantly different from each other. Combination opioids confer the highest risk of RD, compared to both codeine and morphine. The strengths of this study include capture of real time physiological parameters to define RD and dispensed medication use (rather than prescribed) to define exposure.
References:
[1] FDA Drug Safety Communication: March 2016. http://www.fda.gov/Drugs/DrugSafety/ucm489676.htm. 2016.
[2] CDC. Wide-ranging OnLine Data for Epidemiologic Research (WONDER); 2014. http://wonder. cdc.gov/mortSQL.html.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1802

SAT0701 TOWARDS DIAGNOSIS-SPECIFIC LIFETIME RISKS FOR TOTAL HIP ARTHROPLASTY REVISION SURGERY

M. Gademan[1], L.N. van Steenbergen[2], S.C. Cannegieter[3], R.G. Nelissen[4], P.J. Marang-van de Mheen[5]. [1]*Orthopaedics/ Clinical Epidemiology, LUMC, Leiden;* [2]*Dutch Arthroplasty Register (LROI), 's Hertogenbosch;* [3]*Clinical Epidemiology;* [4]*Orthopaedics;* [5]*Medical Decision Making, LUMC, Leiden, Netherlands*

Background: An important aspect regarding optimal timing of primary hip arthroplasty (THA) is to weigh the benefit associated with the primary surgery at a certain point in time against the risk for revision surgery. Revision surgery should be avoided, as outcomes after revision surgery are less favourable than outcomes after primary surgery. Information on lifetime revision risks is needed to guide decision making for individual patients regarding timing of primary surgery.
Objectives: Our aim was to provide the 7 year cumulative percentages for revision surgery stratified for diagnosis, sex, type of fixation and age at which primary THA was performed.
Methods: Data on arthroplasties was available from the Dutch Arthroplasty Register (LROI), a nationwide population-based registry with information on all joint arthroplasties in the Netherlands from 2007 onwards. For the current study, all patients who received a primary THA in the period 2007 to 2015 were included except patients with a metal on metal prosthesis, patients with a hybrid or reversed hybrid fixation type or patients with revision surgery without primary surgery registered. Revision surgery was defined as any change of one or more components of the prosthesis. For the current study age at primary surgery, diagnosis, sex, type of fixation (uncemented, cemented) and survival (alive/dead) and revision of prosthesis (yes/no) were extracted from the LROI database.

Diagnosis was dichotomized into osteoarthritis (OA) and other diagnoses. Annual revision risks were calculated for each subsequent year after primary arthroplasty by dividing the number of revisions by the total number of patients at risk during that year. The risks were stratified according to the underlying diagnosis, sex, age at primary arthroplasty and fixation type. In addition cumulative annual revision percentages were calculated for the full follow-up period. Furthermore we estimated the percentage of avoided OA revisions by assuming that all OA patients received their primary THA 5 years later (in all age groups <85 yrs) and that the revision risks remained the same in all age categories.

Results: In total 134463 primary THA patients were included of whom 68% were female, 89% had OA as underlying indication and 66% of the THAs were uncemented. The 7th year cumulative risk percentage varied between 2.0 and 11.7% (Table 1). Overall cumulative revision percentages were higher in younger age categories (Table 1), with the exception of a 11.7% revision in the group aged 85–90 yrs (uncemented, male, other diagnosis), but this finding is likely due to chance as this group existed of 67 patients. We estimated that by delaying THA for 5 years, a total of 197 revision surgeries (4.4% of all revision surgeries) could be avoided, 48 (14.0%) in the OA male cemented group, 11 (0.9%) in the OA male uncemented group, 69 (3.3%) in the OA female cemented group and 69 (8.6%) in the female uncemented group. This could result in a yearly cost reduction of approximately 4 million euros.

Table 1. Cumulative revision percentages within 7 years after index surgery.

	Osteoarthritis				Other diagnosis			
	Male		Female		Male		Female	
Age-categories	Cemented	Uncemented	Cemented	Uncemented	Cemented	Uncemented	Cemented	Uncemented
50-54	4,10	4,46	3,14	5,27	8,31	6,56	4,44	7,19
55-59	4,55	5,46	6,70	4,63	8,94	5,38	8,02	5,95
60-64	4,72	4,34	3,55	4,24	5,03	5,54	7,23	3,82
65-69	4,23	4,06	2,36	3,63	5,92	7,30	6,86	4,99
70-74	3,71	4,53	2,92	4,50	5,24	7,34	2,46	4,28
75-79	3,00	4,67	2,47	3,78	4,15	7,25	3,87	2,94
80-84	2,69	3,84	2,20	3,59	5,94	3,76	3,48	3,79
85-90	2,02	4,93	2,11	3,73	2,04	11,65	2,47	2,51
Total	3,45	4,50	2,62	4,11	5,53	6,39	4,31	4,54

Conclusions: Cumulative 7th year risk percentages decreased by age in all different categories. By delaying the primary THA surgery, revisions might be avoided thereby resulting in cost reduction.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4274

SAT0702 LOCAL AND SYSTEMIC INFLAMMATION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS WITH CHLAMYDIA TRACHOMATIS INFECTION

M. Natalia, K. Svetlana. *Belorussian State Medical University, minsk, Belarus*

Objectives: We had to study local and systemic inflammation in rheumatoid arthritis patients with persistence Chlamydia trachomatis (Ch tr) in the joint

Methods: 31 patients with early RA; mean age 54,5 (10,6) years, disease duration 21,5 (14,4) weeks witch persistence Ch tr in the joint (mRNP Ch tr had been revealed in synovial fluid by NASBA PCR) were enrolled in this study. The comarison group was patients with RA (n=42) without mRNP in synovial fluid (Ch tr-). Mean age was 51,7 (15,4) years, disease duration 20,8 (13,3) weeks. All the patients had been received only symptomatic treatment (NSAID). Disease activity had been detected by DAS 28. Systemic inflammation was estimated by levels of erythrocyte sedimentation rate (ESR), hsp C-reactive protein (hspCRP), orozomucoid (OR) in the blood samples; local inflammation- by detection hsp CRP, OR in synovial fluid. Also we had been detected level of ACCP in the blood samples and synovial fluid.

Results: We didn't reveal statistically significant differences between levels of ESR, hsp CPR, OR, ACCP in blood samples patients with RA Chtr+ and RA Ch tr-. Level of hsp CPR and OR in synovial fluid of research group (Ch tr+) were significantly higher than comparison group (4,1±0,3 mg/l versus 2,4±0,2 mg/l, $p<0,05$ –hspCRP and 157,4±17,5mg/dl versus 78,5±18,9 mg/dl, $p<0,001$- OR). In the group of research (Ch tr+) level of ACCP in synovial fluid was statistically significant higher than comparison group (Ch.tr -) (195,6±37,3 versus 67,9±15,4; $p<0,001$)

Conclusions: Patients with early RA detected by NASBA PCR in synovial fluid Ch tr+, had been characterized by absence differences compared RA Ch tr- patients in the level of systemic inflammation and had differences in the level of local inflammation. We revealed high level of ACCP in RA patients with Ch tr in the joints, that may be important for understanding some aspects of RA pathogenesis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6876

SAT0703 INFLUENCE OF PHYSICAL ACTIVITY AND SLEEP ON FUNCTIONAL CAPACITY AND PAIN IN PATIENTS WITH KNEE OSTEOARTHRITIS

M. Nuñez[1], E. Nuñez[2], J.M. Segur[3], L. Lozano[3], J. Montañana[3], V. Segura[3], M. Marti[4], A. Garcia-Cardo[4], S. Sastre[3], X. Alemany[3]. *[1]Rheumatology and IDIBAPS Area 1, Hospital Clinic;[2]SAP Suport al Diagnòstic i al Tractament, Institut Català de la Salut;[3]Orthopedic Surgery and IDIBAPS;[4]Rheumatology, Hospital Clinic, Barcelona, Spain*

Background: Knee osteoarthritis (OA) is a degenerative disease in which pain and functional disability progression tend to increase with reducing the health-related quality of life (HRQOL). Factors related to healthy lifestyles, such as physical activity and sleep, are known to have restorative benefits on function and pain in these patients. A previous study found that patients with reparative sleep achieved better WOMAC and SF-36 HRQOL questionnaire dimension scores.

Objectives: To determine the influence of physical activity and sleep on functional capacity and pain in patients with long-term knee OA.

Methods: Cross-sectional study. Sociodemographic and clinical variables, physical activity (PA) (regular physical exercise ≥3 times a week ≥30 minutes per session (PE) and sitting ≤6 hours/day [S]) and sleep quality/reparative sleep (RS) were determined using the question: How do you usually sleep? (1=well [RS], 2=regular, 3=badly, 4 =with medication/treatment [NRS]). Functional capacity and pain were evaluated using the WOMAC (specific) and SF-36 (generic) HRQOL questionnaires. Associations were analysed using multiple regression models.

Results: 453 patients (84.3% female), mean age 69.73 (8.4), BMI 35.27 [SD 6.3], comorbidities 2.43 (SD 1.5), 78.6% with obesity (BMI 33.68 [SD 6.7]), depression/anxiety in 36.4%, PE 60.5%, S 72.2% and PA 48.6%, were included. 22.5% reported RS. Bivariate analysis showed patients with PA and those with RS had better functional capacity and less pain intensity (>10, $p>0.001$, in both WOMAC and SF-36). The four multiple regression showed that patients with PA and SR had better scores, both in functional capacity (dependent variables, WOMAC and SF-36) and pain (dependent variables, WOMAC and SF-36), $p<0.006$. Age, gender, number of comorbidities and obesity were included in the models as potential confounders. Obesity was associated with worse function and more pain in the four models ($p<0.05$). Being female and greater comorbidity were associated with poorer functional capacity and pain assessed by the SF-36.

Conclusions: Physical activity and sleep were associated with less pain and better functional capacity, suggesting these variables should be determined systematically in clinical practice due to their significant relationship with HRQOL. Obesity was negatively associated with function and pain. There was also a negative relationship between female gender and comorbidity according to the SF-36. Differences in generic and specific questionnaires mean they should be used together to provide more detailed information.

Acknowledgements: This work was funded by project PI/13/00948, integrated in the Plan Nacional I+D+I and cofounded by ISCIIISubdirección General de Evaluación and European Regional Development Fund (ERDF).

References:

[1] Uthman OA, van der Windt DA, Jordan JL, Dziedzic KS, Healey EL, Peat GM, et al. Exercise for lower limb osteoarthritis: systematic review incorporating trial sequential analysis and network meta-analysis. BMJ. 2013;347:f5555.

[2] Abad VC, Sarinas PS, Guilleminault C. Sleep and rheumatologic disorders. Sleep Med Rev 2008;12:211–28.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2180

SAT0704 THE IMPACT OF AUTOIMMUNE DISEASE IN THE MANAGEMENT AND PROGNOSIS OF ACUTE CORONARY SYNDROME

N. Lozano[1], F.J. Pastor Perez[2], L.F. LInares Ferrando[1], J. Martinez Ferrin[1], J. Ruiz Sara[1], A. Paños Iniesta[1], P. Castillo Dayer[1], A. Bermudez Torrente[1], F.A. Marinez Angosto[1], S. Manzano Fernandez[2]. *[1]Rheumatology;[2]Cardiology, University Hospital Virgen de la Arrixaca, Murcia, Spain*

Background: Patients with autoimmune diseases (AID) have a high burden of cardiovascular disease leading to premature morbidity and mortality. But it is unclear if it is due to a higher prevalence of cardiovascular disease, to a worse case fatality or to a different management after an index event.

Objectives: The primary aim of the study is to assess the prognostic implications of the presence of AID both during the hospitalization and after discharge after an acute coronary syndrome (ACS). The secondary objectives included the assessment of the prevalence of AID in patients with ACS, their clinical profile and the management of this index event

Methods: The study included consecutive patients admitted after ACS from January 2011 to December 2015 at the University Hospital Virgen de la Arrixaca, Murcia (Spain). For AID patients, in-hospital management and ACS presentation was compared to non-AID patients. We also compared in-hospital and major adverse events during follow-up (death, recurrent non-fatal myocardial infarction, stroke and major bleeding, between groups). A multivariate Cox regression model was performed to assess the independent role of the presence of AID in the occurrence of the events of interest.

Results: Of 2236 patients included with ACS, 78 had AID (3.3%): 24 rheumatoid arthritis, 10 inflammatory bowel disease, 7 ankylosing spondylitis, 6 psoriatic arthritis, 5 polymyalgia rheumatica, 2 systemic lupus erythematosus and 20 miscellanea. Mean age of AID patients was 67±13 years and median evolution of the disease was 10 [4–14] years. Seventy percent of AID patients were taking corticosteroids, 50% disease modifying antirheumatic drugs, 22% non-steroidal anti-inflammatory drugs and 8 biological theraphy. No significant differences were found in clinical and demographics characteristics between groups except for a

higher percentage of atrial fibrillation and chronic obstructive pulmonary disease in AID patients. Compared to non-AID patients, AID patients had similar clinical ACS presentation and no differences were found with respect to revascularization strategies or medical treatment at discharge. With respect to prognosis the two groups had comparable rates of adverse events during hospitalization (10% vs 10%, p=0.920) with no statistically significant differences in any single event studied. However after a follow-up of 397 [375–559] years, AID patients had higher rate of combined adverse events (44% vs 28% p<0,001). After multivariate adjustment the presence of AID was associated with increased total mortality (hazard ratio 2.1, 95% CI 1.2 to 3.7, p=0.008) and it was also a borderline risk factor for higher bleeding complications (hazard ratio 2.2, 95% CI 0.9 to 5.5). The presence of AID was not an independent risk factor for neither stroke or recurrent non-fatal myocardial infarction.

Conclusions: The presence of AID did not change ACS presentation and clinical management. Although AID is not associated with worse outcomes during hospitalization it is independently linked to higher total mortality and a trend to an increased risk of major bleeding during follow-up.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6758

SAT0705 DO DIET CHARACTERISTICS IMPACT EFFECT OF A 12-MONTH VITAMIN D SUPPLEMENTATION ON 25OH-VITAMIN D SERUM LEVEL AMONG OVERWEIGHT ELDERLY?

R.M. Baddoura[1], N.A. Yaghi[2], A. Arabi[3], G. Halaby[4], G. El-Hajj-Fuleihan[3].
[1]Rheumatology, Hotel-Dieu de France, St Joseph University; [2]Nutrition, School of Pharmacy, St Joseph University; [3]Calcium Metabolism, American University of Beirut Medical Center; [4]Endocrinology, Hotel-Dieu de France, St Joseph University, Beirut, Lebanon

Background: Achieving desirable 25OHvitamin D serum levels with vitamin D supplementation may be influenced by many confounders including lifestyle patterns and vitamin D receptor genetic polymorphisms.

Objectives: To test the effect of dietary intake confounding variables such total as calories, dietary intake of vitamin D, calcium, proteins, carbohydrates and fats, on the variance in serum 25-hydroxy vitamin D (25OHD) level after vitamin D supplementation.

Methods: Study population: All subjects from one out of three centers who participated in a randomized clinical trial comparing high (3750 IU/day) versus low (600 IU/day) dose of vitamin D supplementation in ambulatory overweight (BMI exceeding 25) elderly subjects (age ≥65 years), with serum 25OHD level between 10 and 30 ng/ml at screening.

Outcome measure: 25OH D serum levels at 12 months of follow-up.

Confounders included gender, body mass index, baseline 25OHD serum level, genetic polymorphism of vitamin D receptor (Fok, BsmI and Taq) and dietary intake of vitamin D, calcium, proteins, carbohydrates, fats and total calories assessed by food frequency and 24h recall questionnaires, administered a year after the termination of the trial.

Statistical analysis: ANOVA for repeated measures and regression using STATA version 13. Numbers expressed as mean (SD).

Results: We studied 117 Participants, 62 females and 55 males, age was 71 (5) years, of who 61 received 3,750 IU of vitamin D, and 55 received 600 IU/day. Vitamin D receptor genetic polymorphisms distribution was comparable in both arms. Daily vitamin D intake excluding provided supplements was 7.59 (1.21) mcg and 8.53 (1.36) mcg from the 24 h recall, and food frequency questionnaires, respectively (p was NS between the two arms). Calories, calcium, protein, carbohydrate and fat mean intake was also similar across both arms. The high-dose group achieved significantly higher 25OH-vitamin D serum levels at twelve months 34.9 (9.3) ng/ml compared to low-dose, 21.9 (6.1) ng/ml (p<0.0001). Difference between arms remained significant adjusting for gender, baseline BMI, Fok, BsmI and Taq genetic polymorphism, baseline serum vitamin D and dietary intake of vitamin D, calcium, calories, proteins, carbohydrates and fats. None of these dietary intake measures was found to have significant contribution to the model variance. Supplementation dose was the only significant predictor of 25OHvitamin D serum levels achieved at 12 months.

Conclusions: Diet composition was not a confounder for the effect of high versus low dose vitamin D 12-month supplementation, on achieved 25OHD vitamin D serum levels.

Acknowledgements: St Joseph University, Hotel-Dieu de France hospital
American University of Beirut Medical Centre
Lebanese National Council for Scientific Research
Lebanese Ministry of Social Affairs

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2206

SAT0706 END-STAGE ORGAN FAILURE IN SARCOIDOSIS: CHARACTERIZATION AND PREDICTIVE FACTORS IN 1082 PATIENTS

R. Pérez-Alvarez[1], B. Kostov[2], A. González García[3], R. Gómez De La Torre[4], M. Lopez Dupla[5], B. De Escalante[6], A. Alguacil[7], J. Chara[8], J. Velilla[9], J. Rascón[10], J.S. Garcia Morillo[11], C. Feijoo[12], E. Fonseca[13], M. Bonet[14], J.L. Callejas[15], G. de la Red[16], A.B. Madroñero Vuelta[17], C. Soler[18], E. Peral[19], J.F. Gómez Cerezo[20], G. Cruz[21], P. Perez[22], S. Rodríguez Fernández[23], B. Pinilla[24], A. Gato[25], M. Akasbi[26], A. Robles[27], I. Ojeda[28], M.J. Vives[29], C. Morcillo[30], M. Penadés[31], M. De Vicente[32], M. Ramos-Casals[33], L. Pallarés[10], P. Brito-Zerón[30,33] on behalf of the SARCOGEAS-SEMI Registry.
[1]Hosp Alvaro Cunqueiro, Vigo; [2]IDIBAPS, Barcelona; [3]Hosp Ramón y Cajal, Madrid; [4]HUCA, Oviedo; [5]Hosp Joan XXIII, Tarragona; [6]Hosp Clínico, Zaragoza; [7]Hosp Virgen de la Salud, Toledo; [8]Hosp Josep Trueta, Girona; [9]Hosp Miguel Servet, Zaragoza; [10]Hosp Son Espases, Palma de Mallorca; [11]Hosp Virgen del Rocio, Sevilla; [12]Hosp Parc Taulí, Sabadell; [13]Hosp de Cabueñes, Gijón; [14]Althaia, Manresa; [15]Hosp Clínico San Cecilio, Granada; [16]Hosp Esperit Sant, Santa Coloma; [17]Hosp San Jorge, Huesca; [18]Hosp de Sta Caterina, Girona; [19]Hosp Virgen Macarena, Sevilla; [20]Hosp Infanta Sofía, Madrid; [21]Hosp de Poniente, Almería; [22]Hosp Puerta del Mar, Cádiz; [23]Hosp da Barbanza, A Coruña; [24]Hosp Gregorio Marañón, Madrid; [25]CH, Albacete; [26]Hosp Infanta Leonor; [27]Hosp la Paz, Madrid; [28]Hosp Valle del Guadiato, Córdoba; [29]San Joan de Déu, San Boi; [30]Hosp CIMA-Sanitas, Barcelona; [31]Hosp de Manises, Valencia; [32]Hosp Nuestra Señora del Prado, Talavera; [33]Hosp Clínic, Barcelona, Spain

Objectives: To characterize the main features at presentation of sarcoidosis associated with the development of end-stage organ failure in a large multicenter cohort of patients from Southern Europe.

Methods: In January 2017, the Spanish National Registry of Sarcoidosis (SARCOGEAS-SEMI) included 1082 consecutive patients diagnosed with sarcoidosis according to the ATS/ERS/WASOG 1999 statement and extrathoracic involvement to the 2014 WASOG instrument. The development of end-stage organ failure was assessed at the last visit.

Results: The cohort consisted of 618 (57%) women and 464 (43%) men, with a mean age at diagnosis of 47yrs. After a mean follow-up of 82 months, 90 (8%) patients developed end-stage organ failure, including respiratory failure (n=56), chronic renal failure (n=13), cardiac failure/permanent cardiac device (n=8) and liver cirrhosis (n=3). The following baseline features were associated with end-stage organ failure in the univariate analysis: patients born in Spain (p=0.008), a higher mean age at diagnosis (p<0.001) and a radiological stage III/IV (p<0.001) With respect to extrathoracic involvement, spleen (p=0.015), renal (p=0.001), cardiac (p=0.028) and bone marrow (p=0.003) involvements, hypercalcemia (p=0.018) and use of corticosteroids (p<0.001) were associated with end-stage organ failure, while patients with cutaneous sarcoidosis had a lower risk (p=0.029). Multivariate analysis identified age at diagnosis (OR 1.05), radiological stages III/IV (OR 3.12) and use of corticosteroids (OR 4.55) as independent variables associated with the development of end-stage organ failure.

Conclusions: Nearly 10% of patients with sarcoidosis developed end-stage organ failure. Respiratory failure represented two thirds of cases of sarcoidosis-related organ failure, followed by renal (15% of cases) and cardiac (9%). Older patients, as well as those presenting with advanced radiological stages, had an enhanced risk of developing end-stage organ failure.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3376

SAT0707 EFFICACY AND SAFETY OF PROPHYLACTIC TREATMENT ON ACTIVIATION OF LATENT TUBERCULOSIS DURING GLUCOCORTICOID THERAPY IN PATIENTS WITH RHEUMATIC DISEASES

R. Wu. *Department of Rheumatology, the First Affiliated Hospital of Nanchang University, Nanchang, China*

Background: More than 80% of cases of tuberculosis are the result of reactivated latent infection, and nearly all these cases could be prevented by the administration of a course of antibiotic treatment. Therefore, it is suggested screening and treatment are most beneficial for those patients taking immunosuppressive medications. Although the prevalence of latent tuberculosis infection in China was much higher than the United States on the basis of tuberculin skin testing, In China, so far, no study has been done about prophylactic treatment on prevention of tuberculosis activation during glucocorticoid therapy in patients with rheumatic diseases. Should it been recommended that all patients with rheumatic diseases be screened for the presence of active tuberculosis or LTBI before the use of long term glucocorticoid or immunosuppressive medications in China? It is reported only about 5% of immunocompetent persons with a positive test will have progression from latent infection to disease in their lifetime. and decisions about whether to treat latent tuberculosis should take into account the individual patient's risk for the development of active tuberculosis and the risks of therapy.

Objectives: To evaluate the risk of reactivation of LTBI in patients with rheumatic diseases who were undergoing prednisone use and the efficacy and safety of prophylactic treatment on prevention of tuberculosis reactivation.

Methods: 1000 patients with rheumatic diseases who were treated with prednisone were enrolled since 2012. IGRA test (the T-SPOT.TB test) were performed for all subjects. 50 patients with a IGRA-positive were administrated with rifampin for 4 months. 2-years follow-up was conducted to evaluate the risk factors of reactivation of LTBI and the efficacy and safety of rifampin treatment on prevention of tuberculosis reactivation.

Results: the IGRA-positive rates were 20.6% (206/1000). Forty-eight patients with a IGRA-positive finished the treatment with rifampin for 4 months. 2-years follow-up shows no latent tuberculosis developed into active tuberculosis in the patients with prevention of rifampin, while 3 (0.38%) patients with negative IGRA and 22 (10.7%) patients with positive IGRA without rifampin treatment developed into active tuberculosis. 25 patients had active tuberculosis disease in two years, which 24 patients with SLE and one patient with systemic vasculitis while 20 cases had pulmonary tuberculosis, 3 cases had vertebral tuberculosis and tuberculous peritonitis, tuberculous meningitis was 1 case, respectively. Univariate analysis showed that age, entities of rheumatic disease, dosage of glucocorticoid, DMARDs using, comorbidity with interstitial lung disease and cancer were significantly associated with tuberculosis activation ($P<0.05$), with the ORs of 0.959, 0.592, 4.45, 0.226, A3.51 and 69.9, respectively. Entities of rheumatic diseases, Dosage of glucocorticoid, DMARDs using, comorbidity of cancer entered the final multivariate Logistic model. No severe adverse effects occurred in all subjects.
Conclusions: Medium or high dosage of glucocorticoid treatment appears to increase the risk of activation of latent tuberculosis infection. Latent tuberculosis activation could be safely prevented by 4-months rifampin treatment while starting glucocorticoid and DMARDs therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3937

SAT0708 SYMPTOMS INDICATIVE OF INFLAMMATORY ARTHRITIS ARE COMMON IN THE PRIMARY CARE POPULATION: FINDINGS FROM THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS SURVEY

S.L. Hider[1,2], S. Muller[1], J. Prior[1], T. Helliwell[1], D. van Schaardenburg[3], A. van der Helm-van Mil[4], K. Raza[5], C.D. Mallen[1]. *[1]Arthritis Research UK Primary Care Centre, Keele University, Keele; [2]Haywood Academic Rheumatology Centre, Haywood Hospital, Staffordshire, United Kingdom; [3]Reade, Amsterdam; [4]Department Rheumatology, Leiden University Medical Centre, Leiden, Netherlands; [5]Rheumatology Research Group, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom*

Background: Early, accurate diagnosis of RA is critical to improving outcomes. Patients with RA may develop a variety of symptoms including joint pain, swelling and stiffness. The Symptoms in Persons at Risk of Rheumatoid Arthritis (SPARRA) questionnaire was derived to assess the presence, severity and impact of common symptoms in patients at risk of RA (1). However, to date there is little data available on how common these symptoms are in primary care consulters.
Objectives: To describe the prevalence of self-reported inflammatory joint symptoms in primary care patients consulting for both musculoskeletal and non-musculoskeletal complaints.
Methods: Questionnaires were sent to 10161 individuals, of whom 5050 had consulted primary care for musculoskeletal problems. The remainder were matched to this sample by age, gender and general practice and had consulted for any non-musculoskeletal indication. Respondents provided data on presence of common symptoms such as joint pain, stiffness and swelling. The prevalence of these symptoms, their severity and impact was compared between musculoskeletal and non-musculoskeletal consulters.
Results: 4549 people responded to the survey (adjusted response 45.8%) of whom 52.3% were in the musculoskeletal consultation group. The mean (SD) age was 61.6 (14.8) years and 58.9% were female. Symptoms commonly associated with inflammatory arthritis were common in both groups. 89.1% of musculoskeletal consulters reported current joint pain, compared with 74.9% in the non-MSK consulter group, 48.7% of MSK consulters reported joint swelling compared to 37.3% of non-MSK consulters and 77.9% of MSK consulters reported joint stiffness (64.3% in non-MSK group). A similar proportion in each group reported fatigue (59.5% vs 55%). Joint symptoms remained common symptoms in both groups even when severity and impact of symptoms was considered.
Conclusions: Although symptoms such as joint pain, swelling, and stiffness are predictive of inflammatory arthritis, a large proportion of those consulting primary care for non-musculoskeletal reasons routinely report these symptoms when prompted. This compounds the challenges of diagnosing inflammatory arthritis in a non-specialist setting where new approaches are needed to ensure accurate, early diagnosis, facilitating a treat to target approach.
References:
[1] van Tuyl, et al. Musculoskeletal Care 2016;14:169–73.
Acknowledgements: This study represents independent research funded by the National Institute for Health Research (NIHR). TH is funded by a NIHR Clinical Lectureship in General Practice. CDM is funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care West Midlands, the NIHR School for Primary Care Research and a NIHR Research Professorship in General Practice (NIHR-RP-2014–04–026). The views expressed are those of the authors and not necessarily those of the NHS, NIHR or the Department of Health.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5503

SAT0709 MORTALITY PREDICTION IN MIXED CONNECTIVE TISSUE DISEASE

S. Reiseter[1], R. Gunnarsson[2], T.M. Aaløkken[3], M.B. Lund[4], J. Corander[5], Ø. Molberg[6]. *[1]Institute of Clinical Medicine, University of Oslo, Norway; [2]Dept. of Rheumatology; [3]Dept. of Radiology and Nuclear Medicine; [4]Dept. of Respiratory Medicine, Oslo University Hospital; [5]Institute of Basic Medical Sciences; [6]Institute of Clinical Medicine, University of Oslo, Oslo, Norway*

Background: Mixed Connective Tissue Disease (MCTD) is a chronic, immune-mediated disorder defined by the combined presence of serum anti-ribonucleoprotein (RNP) antibodies and selected clinical features of Systemic Sclerosis, Systemic Lupus Erythematosus, Rheumatoid Arthritis and Polymyositis. Several clinical manifestations and laboratory findings have been found to be associated to increased risk of mortality in univariable analyses (1).
Objectives: Here we present a mortality predicting model in a long-term observational unselected nationwide cohort aiming to enhance the knowledge of long-term prognosis in MCTD.
Methods: 135 patients were included from our nationwide MCTD cohort. Abnormal high resolution computed tomography (CT) findings of ground glass attenuation and reticular patterns were defined as Interstitial Lung Disease (ILD) and expressed as percentage of Total Lung Volume (TLV). Pulmonary function tests and laboratory tests were performed within 2 months of the HRCT examination. Pleuritis was defined as typical pleurisy for more than one day, pleural effusions or pleural rub present at or before baseline. Pericarditis was defined as typical pericardial pain for more than one day, pericardial effusion, pericardial rub or pericarditis by electrocardiography at or before baseline. Myositis was confirmed by muscle biopsy and/or electromyogram and CK elevation at or before baseline. Cox regression analyses were used to find the predictive factors of mortality. Variables at a significant level of $P<.25$ where considered a candidate in the prediction model by manual backward elimination procedure.
Results: 21 patients died after a mean (standard deviation) observation of 9 (2) years. The predictive model is shown in Table 1. According to the Harrell's C index, patient outcomes were accurately predicted by this model 85% of the time.

Table 1

	Univariable			Multivariable		
	HR	95% CI	P value	HR	95% CI	P value
Pericarditis ever	4.0	1.6–9.7	0.003	5.5	1.9–16.0	0.002
Male gender	2.5	1.1–5.9	0.038	5.8	1.9–17.9	0.002
% ILD of TLV	1.1	1.03–1.1	0.001	1.1	1.0–1.1	0.010
DLCO <60%	3.1	1.3–7.5	0.011	3.1	1.0–9.2	0.046
Agegroups* at diagnosis	1.8	1.4–2.4	<0.001	1.9	1.4–2.5	<0.0001
Baseline ESR >30 mm	3.3	1.4–7.7	0.007			
FVC <75%	3.6	1.4–8.8	0.006			
Arthritis present at or before baseline	2.1	0.85–5.2	0.109			
Pleuritis ever	2.2	0.81–6.1	0.121			
Baseline Hb <12 g/dL	2.7	1.0–7.0	0.041			
Myositis	0.22	0.03–1.7	0.144			

*Patients were divided in 6 age groups at diagnosis (<25 years, 26 to 35 years, 36 to 45 years, 46 to 55 years, 56–65 years and above 65 years). FVC = Forced Vital Capacity % of predicted, DLCO = diffusing capacity of the lung for carbon monoxide % of predicted, ESR = erythrocyte sedimentation rate, TLV = total lung volume, Hb = Haemoglobin.

Conclusions: The strongest predicting factors of mortality in MCTD is increasing % ILD of TLV, pericarditis, male gender, DLCO less than 60% of predicted and increasing age at diagnosis.
References:
[1] Hajas A, Szodoray P, Nakken B, Gaal J, Zold E, Laczik R, et al. Clinical course, prognosis, and causes of death in mixed connective tissue disease. The Journal of rheumatology. 2013;40(7):1134–42.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1855

SAT0710 RENAL FUNCTION CONTRIBUTE TO RISK OF CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS

S. Hannawi[1], I. Alsalmi[2]. *[1]Rheumatology, Ministry of Health and Prevention of UAE, Dubai, United Arab Emirates; [2]Renal, Royal Hospital, Muscat, Oman*

Background: The excess mortality associated with rheumatoid arthritis (RA) is due largely to cardiovascular disease. This highest risk is not related primarily to traditional cardiovasculr/atherosclerosis risk factors. The presence of RA indepedently, as well as high inflammation associated with RA has been reported as a cardiovascular risk factors. Also, subclinical decreased kidney function has been identified as an independent risk factor for CV events in patients with RA. The potential impact of impaired kidney function on atherosclerosis in RA requires more elucidation.
Objectives: To assess the role of renal parameters, alongside with inflammation and traditional cardiovascular risk factors in predicting cardiovascular disease; as manifested by carotid intima media thickness (cIMT), among RA population.
Methods: cIMT measurement was carried out in 68 RA patients, and correlated with renal function parameters with adjustment for traditional CV risk factors and RA associated inflammation. Glomerular filtration rate (GFR) was estimated with the abbreviated Modification of Diet in Renal Disease formula. Linear regression determined the association between renal parameters and the thickness of cIMT.

Results: Carotid intima media thickness was positively associated with 1-demographic characteristics of the participants such as age of the participants ($p<0.001$), and age at RA sumptoms onset (p=0.001). 2-traditional cardiovascular risk factors such as systolic blood pressure ($p<0.001$), diastolic blood pressure (p=0.016), triglycerid level (p=0.016), and low densilty lipoprotein (LDL) (p=0.001). 3-inflammatory markers such as erythrocytes sedimentation rate (ESR) (p=0.020) and c-reactive protein (CRP) (0.020), and 4-renal function parameters such as uric acid level (p=0.006), urine microalbumin level (p=0.030). cIMT negativlely associated with high density lipoprotein (HDL) (p=0.037), 24 hours urine creatinine level (p=0.020) and glomerular filtration rate (p=0.008).
Conclusions: Subclinical renal function in conjunction with tarditional and non-traditional cardiovascular risk factors work synergistically to accelerate atheroscrlerosis in RA population.
References:
[1] Maradit-Kremer H, Crowson, Nicola PJ, Ballman KV, Roger VL, Jacobsen, Gabriel SE. Increased unrecognized coronary heart disease and sudden deaths in rheumatoid arthritis: a population-based cohort study. Arthritis Rheum, 2005;52:402–411.
[2] Roman MJ, Moeller E, Davis A, Paget SA, Crow MK, Lockshin MD, Sammaritano L. Preclinical carotid atherosclerosis in patients with rheumatoid arthritis: prevalence and associated factors. Ann Intern Med, 2006; 144:249–256.
[3] van Sijl AM, van den Oever IA, Peters MJ, et al. Subclinical renal dysfunction is independently associated with cardiovascular events in rheumatoid arthritis: the CARRE Study. AnnRheum Dis. 2012;71(3):341–344.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1664

SAT0711 CHECKPOINT INHIBITOR THERAPY IN PATIENTS WITH ADVANCED MALIGNANCIES AND PREEXISTING RHEUMATOLOGIC DISEASE: THE MAYO CLINIC EXPERIENCE

U. Thanarajasingam[1], O. Pinkston[2], L. Kottschade[3], H. Finnes[3], S. Markovic[3].
[1]Rheumatology, Mayo Clinic, Rochester; [2]Rheumatology, Mayo Clinic, Jacksonville; [3]Oncology, Mayo Clinic, Rochester MN, Rochester, United States

Background: Immune checkpoint inhibitors (specifically the anti-CTLA-4 antibody ipilimumab, and the anti-PD-1 antibodies nivolumab and pembrolizumab, have revolutionized the treatment of advanced malignancies. However, by virtue of their mechanism of action – that is, loss of T-cell inhibition and impaired self-tolerance, patients with underlying autoimmune and rheumatologic diseases were typically excluded from the clinical trials leading to the approval of these agents. Limited data, typically of single checkpoint inhibitors, exist for their safety in patients with autoimmune diseases. However, the risk for rheumatologic disease flare in patients exposed to checkpoint inhibitors is unknown.
Objectives: To determine the risk of rheumatologic disease flare in patients receiving checkpoint inhibitor therapy.
Methods: We retrospectively studied all patients who had received a checkpoint inhibitor (i.e. ipilimumab, nivolumab, pembrolizumab, or any combination thereof) for any malignancy on the Mayo Clinic Rochester, Minnesota campus between January 1st, 2011 and May 16th, 2016 (approximately 5,200 patients.) Of these patients, we identified those with preexisting rheumatologic disease according to specific diagnostic codes.
Results: Of the 16 patients identified (13 [81%] female; median [range] age, 68.5 [34–86]y), 6 had inflammatory arthritis, 3 had polymyalgia rheumatica, 2 had lupus, 2 had Sjogren's syndrome, 1 had temporal arteritis, 1 had IBD-associated spondyloarthropathy and 1 had gout. Patients were treated for the following metastatic/advanced malignancies: melanoma (9 [56%]), lung (5 [31%]) and lymphoma (2 [12%]) with; ipilimumab (4 [25%]), nivolumab (7 [44%]), pembrolizumab (5 [31.2%]) and ipilimumab/nivolumab (1 [6%]). Notably, in all cases, checkpoint inhibitor therapy was offered after failure of numerous other chemotherapies. Ten (62.5%) patients were on immunosuppressive therapy (mainly low dose prednisone and methotrexate) at the time of cancer diagnosis, and the majority (10 [62.5%]) were well-controlled/in remission from the standpoint of their rheumatologic disease. Three (19%) patients had flares of their rheumatologic disease after treatment for the following cancers as noted: Patient 1 - temporal arteritis – nivolumab - non-small cell lung cancer, Patient 2 - Sjogren's (severe sicca)– pembrolizumab - melanoma, and Patient 3 - spondylitis-ipilimumab/pembrolizumab combination –melanoma. All flares responded to steroids or supportive therapy. Checkpoint inhibitor therapy was discontinued in all three patients for the following reasons: Patient 1 – flare of temporal arteritis, Patients 2 & 3 – cancer progression.
Conclusions: To our knowledge, we have identified the largest cohort (16) of patients from a single academic with preexisting rheumatologic disease who had been exposed to checkpoint inhibitor therapy for advanced malignancy. Of these patients, only a minority experienced a flare of their disease during cancer treatment, and responded to standard therapies. With close monitoring and in the appropriate clinical context, checkpoint inhibitor therapies should be considered and made available to patients with preexisting rheumatologic disease who develop advanced malignancies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5461

SAT0712 SELF-REPORTED SEDENTARY BEHAVIOUR IS ADVERSELY ASSOCIATED WITH MICROVASCULAR ENDOTHELIAL FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

S.A.M. Fenton[1,2], J.J. Veldhuijzen van Zanten[1,2], A. Sandoo[3], J.L. Duda[1], G.S. Metsios[2,4], G.D. Kitas[2]. *[1]School of Sport Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham; [2]Rheumatology, Russells Hall Hospital, Dudley; [3]School of Sport, Health and Exercise Sciences, Bangor University, Gwynedd, Wales; [4]Faculty of Education Health & Wellbeing, University of Wolverhampton, Wolverhampton, United Kingdom*

Background: Patients with Rheumatoid Arthritis (RA) are at increased risk for cardiovascular disease (CVD). Research suggests impaired vascular function contributes to this heightened risk. At present, little is known regarding factors associated with vascular function in RA. Epidemiological evidence demonstrates sedentary behaviour (i.e., waking behaviour $\leq$1.5 metabolic equivalents whilst sitting or lying), to be adversely linked to CVD risk in the general population. Whilst the biological processes underlying this relationship are not understood, vascular dysfunction may play a role (1, 2). However, research is yet to examine the association between sedentary behaviour and vascular function in healthy adults and/or clinical populations. Studies investigating this relationship in RA, will help to determine the extent to which sedentary behaviour may represent a modifiable risk factor for CVD in these patients.
Objectives: To investigate the cross-sectional associations between sedentary behaviour and microvascular and large vessel endothelial function among patients with RA.
Methods: Fifty-three patients with RA participated in the study (*M* age=52.9±12.8, 72% female). Laser Doppler imaging with iontophoresis was used to assess microvascular endothelium-dependent (acetylcholine, ACh) and endothelium-independent (sodium nitroprusside, SNP) function. Large vessel endothelium-dependent and endothelium-independent functions were measured via flow-mediated dilation (FMD) and glyceryl trinitrate dilation (GTN), respectively. Sedentary behaviour was self-reported via the International Physical Activity Questionnaire (hours/week sitting). Data were analysed using multiple linear regressions adjusted for traditional CVD risk factors; age, gender, total cholesterol, smoking status, family history of CVD, hypertension and body-mass-index.
Results: Sitting time (hours/week, M =39.2±17.9) was significantly negatively related to % increase in perfusion in response to ACh (β=–0.30, $p<0.05$) and SNP (β=–0.37, $p<0.01$) after adjustment for traditional CVD risk factors. Sitting time accounted for 8% and 12% of the variance in microvascular endothelium-dependent function (ACh) and endothelium-independent function (SNP), respectively (traditional CVD risk factors, R^2=0.3). No significant associations were observed between self-reported sitting time and large vessel endothelium-dependent vasodilation (FMD, β=0.16, p=0.29) or independent vasodilation (GTN, β=–0.08, p=0.55).
Conclusions: Sedentary behaviour appears to adversely affect microvascular endothelial function, but not large vessel function in patients with RA. It may therefore represent a modifiable risk factor for CVD in this population. Experimental studies employing objective measures of sedentary behaviour are necessary to confirm these findings, and to determine the utility of sedentary behaviour interventions for improving vascular function and reducing CVD risk in RA.
References:
[1] Thosar SS, Bielko SL, Mather KJ, et al. Effect of Prolonged Sitting and Breaks in Sitting Time on Endothelial Function. Med Sci Sports Exerc 2015:47(4);843–9.
[2] Fenton SAM & Kitas GD. Rheumatoid Arthritis: Sedentary behaviour in RA – a new research agenda. Nat Rev Rheumatol 2016:12(12):698–700.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4821

SAT0713 SURVEY ON PREVALENCE OF RHEUMATIC DISORDERS IN BANGLADESHI ADULTS

S. Ahmed[1], S.A. Haq[1], A.Z. Al-qadir[1], M.M. Rahman[2], S. Paul[3].
[1]Rheumatology, Bangabandhu Sheikh Mujib Medical University; [2]Medicine, Dhaka Medical College, Dhaka; [3]Medicine, Chittagong Medical College, Chittagong, Bangladesh

Background: From Community based COPCORD (community oriented program for control of rheumatic diseases) study in Bangladesh about a quarter of people is suffering from musculoskeletal disorders. But the study was conducted over a small number of samples and some specific localities of the country. So further study was required, covering the whole Bangladesh to justify this high prevalence.
Objectives: To determine the prevalence of musculoskeletal symptoms and specific rheumatic disorders in adult population of Bangladesh.
Methods: In this survey, a total of 2000 individuals aged 18 years or older were selected in twenty clusters (primary sample unit) from the seven divisions of the country. Modified COPCORD (Community Oriented Program for Control of Rheumatic Disorders) questionnaire was used to detect positive respondents. Standard criteria were used for diagnosing rheumatic disorders. Clinical judgment was used to solve diagnostic problems.
Results: In total 1843 individuals were interviewed with a response rate of 92.1%. The point prevalence of musculoskeletal pain was 33.7%. It was higher in women (38.7%) than men (28.4%) and higher in rural (34.5%) than that in urban (32.4%) areas. Higher prevalence rates were observed in homemakers (16.0%), laborers

(3.0%), business professionals (2.9%) and cultivators (2.8%). Low back (23.3%), knee (12.7%) and shoulder (6.1%) were the most frequent site of complaint. Non specific low back pain (12.7%) and knee osteoarthritis (7.3%) were the two top ranking disorders. The prevalence of rheumatoid arthritis was 1.6% and spondyloarthritis 1.2%. 5.5% of the respondents had disability from rheumatic problems.
Conclusions: About one third of the Bangladeshi adults suffer from musculoskeletal pain at a given point of time. There are residence and gender variation in the prevalence rates. Low back and knee pain were the principal sites of complaints.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2562

SAT0714 INCREASED RISK OF OPPORTUNISTIC INFECTION IN THE EARLY STAGE OF RHEUMATOID ARTHRITIS

H. Kim[1], S.-K. Cho[1,2], M.J. Kim[1], G.Y. Ahn[1], H.H. Kwon[1], D. Kim[1], J. Lee[2], S.-C. Bae[1,2], Y.-K. Sung[1]. *[1]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases; [2]Clinical Research Center for Rheumatoid Arthritis (CRCRA), Seoul, Korea, Republic Of*

Background: The increased risk of opportunistic infections (OIs) in rheumatoid arthritis (RA) patients who started biologic disease modifying anti-rheumatic drugs (DMARDs) has been well known. However, it has not been studied regarding the increased risk of OIs in the early stage of RA.
Objectives: To study the increased risk of incidence rate (IR) of OIs in early RA patients compared with established RA patients, and to evaluate the risk factors for developing the OIs in the early stage of RA.
Methods: Retrospective cohorts of early and established RA patients were conducted independently using the Korean National Healthcare claims database. Early RA patients (n=14,081) were identified in 2010 having disease free period for 1 year before index date, and receiving continuous treatment for over three years. Established RA patients (n=226,838) were recruited between 2010 and 2012 with using the ICD10 code of RA and any DMARD use. Follow-up started on the index date and ended on the data of the development of OIs, at 12 months, or at the time of death. The incidence rates of OIs were compared between two groups by calculating incidence rates ratio (IRR) and standardized incidence ratio (SIR) for overall or each OIs. The multivariable regression model was used to evaluate the risk factors for OIs in the early stage of RA.

Table 1

Type of opportunistic infection	Established RA N=226,838		Early RA N=14,081		SIR comparing early RA patients with established RA patients	
	IR/100PY	95% CI	IR/100PY	95% CI	SIR	95% CI
Total	3.67	3.59–3.74	3.81	3.52–4.11	1.14	1.05–1.23
Tuberculosis	0.71	0.67–0.75	0.70	0.54–0.87	1.06	0.82–1.33
Herpes zoster	2.79	2.72–2.85	2.89	2.64–3.13	1.12	1.03–1.22
Cytomegalovirus	0.02	0.02–0.03	0.03	0.00–0.06	0.98	0.20–2.86
Epstein–Barr virus	0.01	0.00–0.01	0.04	0.00–0.07	3.54	0.96–9.06
Pneumocystis jiroveci pneumonia (PJP)	0.01	0.01 - 0.02	0.02	-0.01–0.04	1.20	0.15–4.34
Candidiasis	0.10	0.08–0.11	0.11	0.07–0.16	2.40	1.55–3.54
Aspergillosis	0.02	0.02–0.03	0.02	0.00–0.05	0.84	0.17–2.47
Cryptococcosis	0.01	0.00–0.01	0.01	-0.01–0.02	1.15	0.03–6.39

RA = rheumatoid arthritis, SIR = standardized incidence ratio, PY = person year, N = number, IR = incidence rate, CI = confidence interval.

Results: The IRs of overall OI in early and established RA patients were 3.81 (95% CI 3.52–4.11)/100PY and 3.67 (95% CI, 3.59–3.74)/100PY, respectively. The SIR for overall OIs in early RA patients was 1.14 (95% CI, 1.05–1.23). The herpes zoster (SIR 1.12, 95% CI 1.03–1.22) and candidiasis (SIR 2.40; 95% CI 1.55–3.54) were commonly affected in the early stage of RA patients. Older age more than 50 years old [50<age≤60 (OR 1.74, 95% CI 1.30–2.33), 60<age≤70 (OR 1.85, 95% CI 1.36–2.52), 70<age (OR 1.89, 95% CI 1.34–2.68)], more comorbidities [one comorbidities (OR 1.53, 95% CI 1.24–1.89), ≥2 of comorbidities (OR 1.84, 95% CI 1.47–2.29)], and corticosteroid ≥5mg per day (OR 1.38, 95% CI 1.13–1.69) were associated with increased risk of OIs in the early stage of RA patients.
Conclusions: The incidence of OIs is increased in early stage of RA patients compared with established RA patients. Old age, comorbidities, high corticosteroid dose were related with the development of OI. Physicians should be aware of the possible occurrence of OIs in early stage of RA treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4882

SAT0715 CLINICAL SIGNIFICANCE OF FIBROMYALGIA SYNDROME IN DIFFERENT RHEUMATIC DISEASES: RELATION TO DISEASE ACTIVITY AND QUALITY OF LIFE

T.A. Gheita, S.M. El-Rabbat, N.K. Mahmoud. *Rheumatology and Clinical Immunology Department, Faculty of Medicine - Kasr Al-Ainy School of Medicine - Cairo University, Cairo, Egypt*

Background: In clinical practice, the co-expression of fibromyalgia syndrome (FMS) and a rheumatologic disease deserves special attention as FMS may go unrecognized especially when it develops after the disease or more commonly when it is misdiagnosed as an autoimmune disorder.
Objectives: The aim of the present work was to compare the frequency of FMS in rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and Behçets disease (BD) patients and to study the relation of FMS to the clinical manifestations, laboratory features, disease activity and/or damage as well as the quality of life (QoL).
Methods: One hundred and sixty patients (50 RA, 50 SLE, 30 SSc and 30 BD) consequently recruited from those attending the Rheumatology outpatient clinic and department, Faculty of Medicine, Cairo University Hospital. and 141 age and sex matched corresponding healthy controls were included. Disease activity was assessed using Disease Activity Score in 28 joints (DAS28) for RA, SLE Disease Activity index (SLEDAI), modified Rodnan skin score for SSc and BD Current Activity Form (BDCAF). The Systemic Lupus International Collaborating Clinics (SLICC)/ACR damage index was assessed in SLE patients. The quality of life (QoL) was also recorded. Severity in FMS cases was estimated using the revised Fibromyalgia Impact Questionnaire (FIQ) score.
Results: In the RA, SLE, SSc and BD patients, FMS was found in 14%, 18%, 6.67% and 3.33% respectively compared to 2.1%, 3%, 3.3% and 0% in their corresponding controls. In RA patients, DAS28 was significantly higher in those with FMS (5.5±0.9) compared to those without (4.3±1.3) (p=0.009); significantly correlated with both Widespread Pain Index (WPI) (p=0.011) and Symptom Severity (SS) scale (p=0.012) and the QoL scale in those with FMS was significantly worse (62.3±7.9) compared to those without (71.7±14.4) (p=0.023). In SLE patients, The WPI and SS both significantly correlated with the presence of thrombosis (r=0.28, p=0.049 and r=0.43, p=0.002 respectively). The SS scale tended to correlate with the SLEDAI (r=0.28, p=0.05). In BD patients, BDCAF and WPI significantly correlated (p=0.03). On comparing the WPI among the rheumatic diseases patients, the mean was significantly higher in the SLE patients (2.3±3.2) compared to that in the RA (1.96±2.6), SSc (1.9±2.2) and BD (0.7±1.1) patients (p=0.047).
Conclusions: Fibromyalgia syndrome is more frequent in rheumatic diseases. The significance of this study is boosted by the fact that it was among the first to investigate the prevalence of FMS in patients with SSc. Also, adds to the limited insights on the relation of FMS to BD. It is novel to present the relative prevalence of FMS in different Egyptian rheumatic diseases patients and to throw light on the association with disease activity in RA and BD as well as thrombosis in SLE. The impact of FMS on the QoL in RA patients requires special attention.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2207

SAT0716 A FIRST TIME HOSPITAL ADMISSION FOR COMORBID CONDITIONS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IS MORE FREQUENTLY DUE TO CARDIOVASCULAR AND RENAL COMPLICATIONS THAN IN CONTROLS AND SUBSEQUENTLY INCREASES THE RISK FOR DEATH

W.D. Raymond[1], D. Preen[2], C. Inderjeeth[1,3], H. Keen[4,5], J. Nossent[1,6]. *[1]School of Medicine & Pharmacology; [2]School of Population Health, University of Western Australia; [3]Rehabilitation and Aged Care, Sir Charles Gairdner Hospital; [4]Rheumatology, Fiona Stanley Hospital; [5]School of Medicine, Murdoch University; [6]Rheumatology, Sir Charles Gairdner Hospital, Perth, Australia*

Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that runs an unpredictable disease course.
Objectives: We aimed to understand the characteristics and outcomes of incident hospitalisation for conditions other than the underlying disease in SLE patients.
Methods: Using whole-population data linkage of hospital admissions and death records in Western Australia (WA) WA between 1980 and 2015, we performed a retrospective analysis for patients where SLE (ICD-9-CM 695.4, 710.0 and ICD-10-AM L93.0 & M32) was a *co-existing* discharge diagnosis. All SLE patients were age- and gender-matched with hospital controls free of rheumatic disease. We investigated the rate and characteristics of the index hospitalisation for comorbidity and the risk of subsequent death by Kaplan-Meier survival and Cox regression.

Table 1: Patient Characteristics (at index hospitalisation) and study outcomes.

	Lupus was secondary to the Admitting Diagnosis	Matched Controls	χ2 or t-test
	MoCT or n(%)	MoCT or n(%)	(p-value)
Age	54.31 ± 18.76	54.32 ± 22.13	0.120
Female	1911 (82.3%)	1755 (82.8%)	0.210
Indigenous Status	82 (3.5%)	26 (1.2%)	<0.001
Length of Stay (days)	5 (IQR 2, 11)	2 (IQR 1, 5)	<0.001
Privately Insured	438 (35.4%)	469 (48.8%)	<0.001
Diagnosed with an Ischaemic Heart Disorder	184 (7.9%)	73 (3.4%)	<0.001
Diagnosed with a Cerebral Ischaemic Disorder	33 (1.4%)	18 (0.8%)	0.074
Diagnosed with a Hypertension Disorder	348 (15.0%)	136 (6.4%)	<0.001
Diagnosed with an Atherosclerotic Disorder	158 (6.8%)	19 (0.9%)	<0.001
Diagnosed with a Kidney Disorder	295 (12.7%)	39 (1.8%)	<0.001
Diagnosed with a Thrombotic Disorder	54 (2.3%)	4 (0.2%)	<0.001
Patient died during the hospital admission	87 (3.7%)	40 (1.9%)	<0.001

MoCT: Measure of Central Tendency, i.e. mean ± standard deviation or median (interquartile range).

Results: Hospitalisation rates for comorbidity were 13.9/million/year in SLE patients. SLE patients were similar to controls for age and gender, but more likely to be Indigenous, have renal failure, cardiovascular and thrombotic conditions (Table 1). Independent predictors of mortality risk following hospitalisation for a comorbid condition included: SLE diagnosis (OR 1.6, CI: 1.3–1.9, $p<0.001$) (Fig. 1), cerebrovascular events (OR 2.0, CI: 1.2–3.7, $p<0.001$), renal disease (OR 1.75, CI: 1.4–2.3 $p<0.001$), thrombotic events (OR 1.8 CI: 1.1–2.8, $p=0.001$) and reliance on Medicare (OR 1.5, CI: 1.3–1.8, $p<0.001$) (Table 2).

Conclusions: SLE patients were more frequently hospitalised than controls for cardiovascular or renal conditions and this increased their mortality risk. These results strengthen the need for close monitoring and interventions to prevent such comorbidity in all SLE patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5902

Abstracts Accepted for Publication

Genomics, genetic basis of disease and HLA / T cell recognition

AB0001 FIRST DESCRIPTION AND FUNCTIONAL PROTEOMIC ANALYSIS OF A PROTECTIVE FOR RHEUMATOID ARTHRITIS GENE POLYMORPHISM

A. Sarantopoulos[1], I. Theodorou[2], A. Notopoulos[3], I. Koulas[1], P. Boura[1].
[1]Clinical Immunology Unit, 2nd Dpt of Internal Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Laboratoire d' Histocompatibilite et Immunogenetique, Departement d' Immunologie., Groupe Hospitalier Pitie Salpetriere Charles Foix, Paris, France; [3]Department of Nuclear Medicine, Hippokration General Hospital, Thessaloniki, Greece

Background: Rheumatoid Arthritis (RA) is the most common systemic autoimmune disease, with a respective expanded genetic research[1]. Immunogenetic studies have documented the positive correlation of various gene loci with incidence and/or disease profile. However, the description of gene loci negatively related to the incidence of RA is rarely documented. Apart from an early study involving HLA class II, there has been no reference to any genetic locus associated with a protective role against RA incidence.
Objectives: To identify the sequence of the functional areas of the TRAF1 (TNF receptor associated factor 1 - a protein involved in the intracellular signaling pathway of TNF) gene.
Methods: 172 patients and 95 controls were genetically assessed for the sequence of the seven exons of the gene TRAF1.
Results: On the position 9:120905076 of exon 7, the registered polymorphism G/A (rs143265058) was described in the controls group. The same polymorphism was not confirmed in any of the patients. Further functional proteomic study of the polymorphism with computing programs (software), revealed that the presence of this polymorphism leads to a differentiation of the quaternary structure of TRAF1 protein, possibly affecting the cohesion of intracellular TNF signaling pathway[2].
Conclusions: The present reference is one of the extremely rare genetic studies describing a protective gene locus against rheumatoid arthritis, and a pioneer of its kind in the use of Applied Informatics in the depiction of the quaternary structure of the encoded protein. At the same time, it is one of the few immunogenetic studies describing the functional proteomics of the encoded protein, plotting on a molecular level specific interaction modifications affecting the intracellular signaling pathway of TNF.
References:
[1] Kim K, Bang SY, Lee HS, Bae SC. Update on the genetic architecture of rheumatoid arthritis. Nat Rev Rheumatol. 2017 Jan; 13 (1): 13–24.
[2] A. Sarantopoulos. TRAF-1 immunogenic study in Rheumatoid Arthritis. PhD Thesis, Aristotle University of Thessaloniki, 2016. (Http://thesis.ekt.gr/thesisBookReader/id/38410#page/1/mode/2up).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6818

AB0002 GENETIC STUDY OF THREE-PRIME REPAIR EXONUCLEASE (TREX1) IN THE SUSCEPTIBILITY TO SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) AMONG EGYPTIAN PATIENTS

D. El Dessouki[1], M.S. Abdel-Hamid[2], L. Effat[6], M. Niazy[3], N. Kholoussi[4], G. Abdel Moneim[3], G.M. Abdel-Salam[5]. *[1]Rheumatology; [2]Medical Molecular Genetics, National Research Centre; [3]Rheumatology, Faculty of Medicinie, Cairo University; [4]Immunogenetics; [5]Clinial Genetics, National Research Centre, Cairo, Egypt; [6]Affiliation not provided*

Background: Interferon-alpha (IFNα) pathway has a crucial role in the pathogenesis of SLE. Many genes have been encoding with this pathway and their impaired expression have been reported in patients with SLE. *TREX1* is a DNA exonuclease involved in the metabolism and clearance of single stranded DNA from apoptotic cells, which is impaired in SLE[1]. *TREX1* mutations have been reported in SLE[2].
Objectives: Our study was aiming to assess the role of *TREX1* in the genetic susceptibility to systemic lupus erythematosus (SLE) among Egyptian patients.
Methods: Fifty SLE Egyptian patients and 50 age & sex matched healthy controls were included in this study. Based on the clinical history and immunological investigations, the 50 SLE patients were divided into two groups according to the presence of positive family history of autoimmune disease: Group I: 28 patients with positive family history & Group II: 22 patients with no family history. Further, the single exon of *TREX1* and its flanking sequences were amplified by PCR and sequenced in both directions.
Results: Our work showed a recurrent *TREX1* polymorphism rs11797 (c.531C>T) among Egyptian patients (56%) in comparison to control group (36%) (p value of 0.070) especially in cases with NPSLE, seizures and chilblains; with minor allele frequency of 0.28 in cases and 0.18 in controls (p value=0.342). *TREX1* polymorphism was present in 57.1% patients (16/28) of SLE patients in group I versus 54.5% patients (12/22) of SLE cases in, group II. The polymorphism was positively associated with neuropsychiatric manifestations (OR=7.000, 95% CI=0.791–61.975) and chilblains (OR=10.532, 95% CI=0.550–201.679). Furthermore, there was a statistically significant difference in cases with oral ulcers (p value=0.004), photosensitivity (p value=0.047) and seizures (p value=0.029).
Conclusions: We confirm that rs11797 (c.531C>T) could be associated with the susceptibility to neurological manifestations among the studied SLE patients.
References:
[1] Hur JW, Sung YK, Shin HD, Park BL, Cheong HS, and Bae SC (2008): TREX1 polymorphisms associated with autoantibodies in patients with systemic lupus erythematosus. Rheumatol Int; 28:783–789.
[2] Lee-Kirsch MA, Gong M, Chowdhury D, Senenko L, Engel K, Lee YA, et al. (2007): Mutations in the gene encoding the 3'-5' DNA exonuclease TREX1 are associated with systemic lupus erythematosus. Nat Genet; 39(9):1065–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2000

AB0003 A MIF PROMOTER POLYMORPHISM IS ASSOCIATED WITH THE SUSCEPTIBILITY TO PULMONARY ARTERIAL HYPERTENSION IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS PATIENTS

E. López-Isac[1], L. Bossini-Castillo[1], D. Campillo-Davó[1], F.D. Carmona[1], C.P. Simeón[2], P. Carreira[3], J.L. Callejas-Rubio[4], I. Castellví[5], A. Fernández-Nebro[6], L. Rodríguez-Rodríguez[7], M. Rubio Rivas[8], F.J. García Hernández[9], A.B. Madroñero[10], S. Scleroderma Group[1], L. Beretta[11], A. Santaniello[11], C. Lunardi[12], P. Airó[13], A.-M. Hoffmann-Vold[14], A. Kreuter[15], G. Riemekasten[16], T. Witte[17], N. Hunzelmann[18], M.C. Vonk[19], A.E. Voskuyl[20], J.D.V. Bouwstra[21], P. Shiels[22], A. Herrick[23], J. Worthington[23], T.R.D.J. Radstake[24], J. Martin[1]. *[1]Biología Celular e Inmunología, Instituto de Parasitología y Biomedicina López Neyra (CSIC)., Armilla (Granada); [2]Department of Internal Medicine, Hospital Valle de Hebrón, Barcelona; [3]Department of Rheumatology, Hospital Universitario 12 de Octubre, Madrid; [4]Unidad de Enfermedades Sistémicas Autoinmunes, Department of Internal Medicine, Hospital Clínico Universitario San Cecilio, Granada; [5]Department of Rheumatology, Hospital de la Santa CreuiSant Pau, Barcelona; [6]Department of Rheumatology, Hospital Carlos Haya, Málaga; [7]Department of Rheumatology, Hospital Clínico San Carlos, Madrid; [8]Department of Internal Medicine, Hospital Universitario de Bellvitge, Barcelona; [9]Department of Internal Medicine, Hospital Virgen del Rocio, Sevilla; [10]Department of Internal Medicine, Hospital General San Jorge, Huesca, Spain; [11]Referral Center for Systemic Autoimmune Diseases, Fondazione IRCCS Ca' GrandaOspedale Maggiore Policlinico and University of Milan, Milán; [12]Department of Medicine, UniversitadegliStudi di Verona, Verona; [13]Servizio di Reumatologia ed Immunologia, Clinica Spedali Civili, Brescia, Italy; [14]Department of Rheumatology, Rikshospitalet, Oslo University Hospital, Oslo, Norway; [15]Department of Dermatology, Josefs-Hospital, Ruhr University Bochum, Bochum; [16]Clinic of Rheumatology, University of Lübeck, Lübeck; [17]Klinik fürImmunologie und Rheumatologie, Hannover Medical School, Hannover; [18]Department of Dermatology, University of Cologne, Cologne, Germany; [19]Department of Rheumatology, Radboud University Nijmegen Medical Centre, Nijmegen; [20]VU University Medical Center, Amsterdam; [21]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; [22]Glasgow Biomedical Research Centre, University of Glasgow, Glasgow; [23]Arthritis Research UK Epidemiology Unit, The University of Manchester, Manchester Academic Health Science Centre, Manchester, United Kingdom; [24]Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands*

Background: Systemic sclerosis (SSc) is a fibrotic immune-mediated disease of unknown etiology. Among its clinical manifestations, pulmonary involvement is the leading cause of mortality in SSc patients. However, the genetic factors involved in lung complication are not well-defined.
Objectives: We aimed to revisit the association of the MIF gene, which encodes a cytokine implicated in idiopathic pulmonary hypertension among other diseases, with the susceptibility and clinical expression of SSc, besides testing the association of this polymorphism with SScrelated pulmonary involvement.
Methods: A total of 4,393SSc patients and 16,591 unaffected controls from six cohorts of European origin were genotyped for the MIF promoter variant rs755622. An inverse variance method was used to meta-analyze the data.
Results: A statistically significant increase of the MIF rs755622*C allele frequency compared to controls was observed in the subgroups of patients with diffuse cutaneous SSc (dcSSc) and with pulmonary arterial hypertension (PAH) indepen-

dently (dcSSc: P=3.20E-2, OR=1.13; PAH: P=2.19E-02, OR=1.32). However, our data revealed a stronger effect size with the subset of SSc patients showing both clinical manifestations (dcSSc with PAH: P=6.91E-3, OR=2.05).
Conclusions: We revisited the association of the MIF rs755622*C allele with SSc and described a phenotype-specific association of this variant with the susceptibility to develop PAH in dSSc patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1907

AB0004 PSORIATIC ARTHRITIS. GENES INVOLVED IN THE MESTIZO POPULATION

L.A. Gutierrez-Gonzalez[1], F. Herrera[2], M.T. Fernandez Mestre[2] on behalf of GRUVES (Grupo Venezolano para el Estudio de las Espondiloartritis). *[1]Centro Nacional de Enfermedades Reumaticas (Cner); [2]Laboratorio de Fisiopatología, Instituto Venezolano de Investigaciones Científicas (IVIC), Caracas, Venezuela, Bolivarian Republic Of*

Background: Psoriatic Arthritis (PsA) is not a regular systemic autoimmune disease, many expert define it with autoinflammatory disease, resulting in chronic inflammation of the synovium and consequent cartilage and bone erosion in approximately 10% of patients with skin psoriasis. It is important to identify novel genomic biomarkers associated with disease susceptibility but also able to detect early those patients with negative prognostic factors who may benefit from a more aggressive therapeutic approach. The over-expression of tumor necrosis factor (TNF)-a is a central element in the pathogenesis of psoriasis and psoriatic arthritis (2). The levels of TNF-alpha are under genetic control. An "A" at position *-308* in the *TNFA* promoter has been shown to be associated with increased level of TNF-alpha expression and "A" at position *-238* with a diminished level of TNF-α expression (3,4). Many authors consider that it is a disease only of Europeans descendants or Caucasians, however never be studied in mestizo population
Objectives: We investigate the potential association between the *TNFA*-238 G/A, *TNFA*-308 G/A, *IL10 -1082 G/A,-819C/T, -592C/A* polymorphisms and the Psoriatic Arthritis susceptibility.
Methods: The study included 52 PsA patients diagnosed by CASPAR criteria and 52 controls. The polymorphism of TNFA-308 G/A (rs1800629), TNFA-238 G/A (rs361525), IL10 -1082 G/A (rs1800896), -819C/T (rs1800871) and -592C/A (rs1800872) were genotyped by single specific primers -polymerase chain reaction (SSP-PCR). All subjects were from an unrelated Venezuelan-Mestizo population with a history of ancestors, at least back to the third generation
Results: When comparing allele and genotype frequencies between the groups studied, no significant differences were observed for the TNFA-308 G/A (rs1800629) and IL10 -1082 G/A (rs1800896), -819C/T (rs1800871) and -592C/A (rs1800872). However, our results showed a significant decrease in the frequency of the TNF-*238A* allele among PsA patients compared to healthy individuals (3.8% vs. 10.57%, respectively, OR: 0.31, 95% CI: 0.92 -1.05, p: 0.02), suggesting that *TNFA-238A* allele may have a protective effect (Table 1).

Table 1. Genotypic and allelic frequencies of the 308 G / AG (rs1800629) and -238 G / A (rs36152! variants of the TNFA gene in patients with psoriatic arthritis and healthy controls

TNFA-308 G/A (rs1800629)	PsA n=73	Controls n= 52	OR (IC95%)	*P*
Genotype				
GG	80,7%	84,6% (44)	0,76(0,27-2,12)	0,302
GA	19,3%	15,4% (8)	1,30(0,47-3,63)	0.302
AA	0%	0 % (0)		
Allele				
G	92,3%	90,4% (94)	1,27(0,48-3,37)	0,311
A	7,3 %	9,6% (10)	0,78(0,29-2,07)	0,311
TNFA-238 G/A (rs361525)	PsA n=73	Controls n= 52	OR (IC95%)	*P*
Genotype				
GG	92,3%	78,8% (41)	3,22(0,95-10,8)	*0,025
GA	7,7 %	21,2% (11)	0,31(0,09-1,05)	*0,025
AA	0	0		
Allele				
G	96,2%	89,4%(93)	2,95(0,91-9,61)	*0,0306
A	3,8%	10,6 %(11)	0,39(0,10-1,09)	*0,0306

NOTE: The values shown in parentheses represent the number of individuals carrying the genotype for the polymorphic site studied. The frequency is expressed as a percentage (p> 0.05: not significant, p <0.05: significant) psoriatic arthritis and healthy controls

Conclusions: This is the first genetic study carried out in Venezuelan mestizo patients with Psoriatic Arthritis to establish associations between genetic markers such as the polymorphisms of the promoter region of the TNFA and IL10 genes and the disease. In conclusion the *TNFA*-238 G/A polymorphism might play an important role in the development of Psoriatic Arthritis in Venezuelan mestizos and this association could not only clarify the different factors involved in a multifactorial disease, such as Psoriatic Arthritis, but also establish the relationship of these molecular markers with some clinical manifestations of the disease, which would allow in the future to determine the suitability or not to use some types of treatments, such as the use of anti-TNF therapy, for example.
References:
[1] Morales-Zambrano, et al. Int J Clin Exp Med. 2014; 7(9): 2605–2614.
[2] Bowes J, Barton A. Discov Med. 2010;10 (52):177–83.
[3] Liu Y, Helms C, et al. PLoS Genet, 2008;4(3): 1000041.
Acknowledgements: To bioanalyst Esther Guzmán, Marion DiMuro, Elena Flores and Mercedes Flores from the Clinica El Ávila and the University Hospital of Caracas (HUC/UCV), as well as Eva Salazar, Omar Balbas y Fernando Hernandez (IVIC).
Disclosure of Interest: L. A. Gutierrez-Gonzalez Grant/research support from: IIR/PFIZER, F. Herrera Grant/research support from: Grant Award (Pfizer), M. Fernandez Mestre: None declared
DOI: 10.1136/annrheumdis-2017-eular.1490

AB0005 CYTOKINE MRNA GENE EXPRESSION ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

L. Miteva[1], M. Ivanova Goycheva[2], I. Manolova[1], G. Vasilev[2], R. Stoilov[2], S. Stanilova[1]. *[1]Department of Molecular Biology, Immunology and Medical Genetics, Medical Faculty, Trakia University, Stara Zagora; [2]Clinic of Rheumatology, University Hospital "St. Iv. Rilski", Medical Faculty, Medical University, Sofia, Bulgaria*

Background: Systemic lupus erythematosus (SLE) is a complex polygenic autoimmune disease, characterized by autoantibody production, inflammatory manifestation and imbalanced cytokine production. In accordance with the pivotal role of Th17 cell in autoimmunity and the altered Th17/Tregs balance in response to changes in the cytokine milieu we analyzed mRNA expression of several cytokines in peripheral blood of SLE patients. Quantification of mRNA expression in peripheral blood could be useful to assess the disease activity of SLE patients.
Objectives: The aim of the present study was to investigate the gene expressions at mRNA level of proinflammatory (TNFA, IL18, IL12B); Th17-related (IL23A); immunosuppressive (TGFB1 and IL10) cytokines and Treg-specific transcription factor Foxp3 in peripheral blood of women with SLE.
Methods: Total RNA from peripheral blood was isolated from 28 female patients with SLE and 17 healthy women. Quantitative real-time polymerase chain reaction was performed for 7 genes of interests, using the TaqMan detection system. Relative quantitative evaluation of mRNAs was performed by the comparative ΔΔCt method and results are presented as n-fold mean difference (RQ-relative quantity) of target genes relative to calibrator (healthy controls) after normalization to the reference gene-GAPDH. Disease activity in SLE was determined by SLEDAI and divided into three categories: mild (0–5), moderate (6–10) and high (>10).
Results: The results reveal considerable overexpression of IL23A in SLE patients compared to healthy controls (RQ=5.347; $p<0.001$). According to the level of disease activity we found the highest elevation of IL23A in patients with SLEDAI>10 (RQ=8.54; $p<0.001$) compared to the controls. In inactive to mild (SLEDAI 0–5) and moderate SLE (SLEDAI 6–10), IL23A was also upregulated in approximately equal rate (RQ=4.976; $p<0.001$ and RQ=4.64; $p<0.001$). In addition, immunosuppressive cytokines IL10 and TGFB1 mRNA were elevated significantly in SLE patients than in controls (RQ=1.79; p=0.0077 and RQ=1.78; p=0.02, respectively). We also found that the expression of proinflammatory TNFA and IL12B were significantly downregulated approximately 2-fold. The mRNA level of Foxp3 was downregulated only for patients with SLEDAI>10. A significant good correlation between IL18 and the SLEDAI score was found (r=0.5548; p=0.002). Higher IL18 expression was observed among patients with worsened SLE compared to those with mild (RQ=1.656; p=0.008) and moderate (RQ=1.474; p=0.034) disease activity. We further demonstrated positively correlation between the expression levels of IL23A and TGFB1 (r=0.7276; $p<0.001$) among SLE patients.
Conclusions: These results suggest that upregulation of IL23 and TGFB1 in addition to downregulated Foxp3 expression may contribute to skewing towards Th17 profile in SLE pathogenesis and this was the most markedly manifested at the highest level of disease activity. Our results support indirectly the idea for restoring Th17/Treg balance as a therapeutic target in SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2299

AB0006 MICRORNA-499 IN BEHCET DISEASE AND POSSIBLE ASSOCIATION WITH DISEASE ACTIVITY

M. Eissa[1], M. Al Kaffas[2], S. Abdel Wahab[2], L. Rashed[2]. *[1]Department of rheumatology and rehabilitation; [2]Medical Biochemistry, Cairo University, Cairo, Egypt*

Background: Behçet Disease (BD) is a relapsing inflammatory autoimmune disease. Although the etiology of BD is not yet known, genetic predisposition and immune dysregulation are thought to be critical factors in the pathogenesis of the disease. MicroRNAs (miRNAs) are small RNA fragments that can regulate the gene expression. miRNAs play a critical role in the pathogenesis of autoimmune or auto inflammatory diseases. Sinngle nucleotide polymorphisms (SNPs) may change the property of miRNAs through altering miRNA expression and/or maturation.
Objectives: The aim of this work was to detect miRNA-499 (rs3746444) genotyping and relative expression in BD patients in order to find out the possible association between them and disease activity and severity.
Methods: Relative expression of miRNA-499 was measured by Real-Time PCR and miRNA-499 gene (rs 3746444) genotyping was performed by TaqMan SNP

Genotyping Assay in blood samples obtained from 47 patients BD diagnosed according to 1990 international criteria for behcet disease and 50 matched healthy controls. Disease activity was done using BD current activity form (BDCAF).
Results: Study of miRNA-499 polymorphism, showed that the genotype frequencies of TT, CT, and CC were 21.3%, 63.8%, and 14.9% in BD patients and 18.0%, 52.0%, and 30.0% in the control group respectively. A significant increase in the relative expression of miRNA-499 was found in BD patients compared to control ($P<0.05$). There was no significant relation between relative expression of miRNA-499 and activity of BD patients assessed by BDCAF ($P>0.05$). In addition there was association between genotypes of miRNA-499 and posterior uveitis ($P<0.05$). There was association of the relative expression of miRNA-499 with miRNA-499 (rs3746444) polymorphism and vascular manifestations ($P<0.05$).
Conclusions: Genotyping of miRNA-499 showed higher percentage of TT genotype in BD patients than control and also miRNA relative expession, they may be implicated in pathogenesis of the disease. Genotype TT for miRNA-499 is associated with posterior uveitis. miRNA relative expression is associated with vascular manifestations and aneurysm.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4476

AB0007 SHARED GENETIC PREDISPOSITION IN RHEUMATOID ARTHRITIS–INTERSTITIAL LUNG DISEASE AND FAMILIAL PULMONARY FIBROSIS

P.-A. Juge[1], R. Borie[2], C. Kannengiesser[3], S. Gazal[3], P. Revy[4], L. Wemeau-Stervinou[5], M.-P. Debray[6], S. Ottaviani[1], S. Marchand-Adam[7], N. Nathan[8], G. Thabut[9], C. Richez[10], H. Nunes[11], I. Callebaut[12], A. Justet[2], P. Richette[13], H. Lioté[14], Y. Allanore[15], O. Sand[16], C. Dromer[17], R.-M. Flipo[18], A. Clément[8], J. Sibilia[19], B. Coustet[1], V. Cottin[20], M.-C. Boissier[21], B. Wallaert[22], T. Schaeverbeke[10], D.L.M. Florence[8], A. Frazier[13], C. Ménard[23], M. Soubrier[24], N. Saidenberg[21], D. Valeyre[11], S. Amselem[8], C. Boileau[3], B. Crestani[2], P. Dieudé[1]. *[1]Rheumatology; [2]Pulmonology A; [3]Genetic, Hopital Bichat; [4]INSERM UMR_1163, Paris; [5]CHRU de Lille, Lille; [6]Radiologie, Hopital Bichat, Paris; [7]CHU de Tours, Tours; [8]Pneumologie pédiatrique, Hôpital Trousseau; [9]Pulmonology B, Hopital Bichat, Paris; [10]Rheumatology, CHU Bordeaux, Bordeaux; [11]Pulmonology, Hôpital Avicenne, Bobigny; [12]CNRS UMR_7590; [13]Rheumatology, Hôpital Lariboisière; [14]Pulmonology, Hôpital Tenon; [15]Rheumatology, Hôpital Cochin, Paris; [16]UMR_8199, Lille; [17]CHU Bordeaux, Bordeaux; [18]Rheumatology, CHRU de Lille, Lille; [19]Rheumatology, CHU de Strasbourg, Strasbourg; [20]UMR_754, Lyon; [21]Rheumatology, Hôpital Avicenne, Bobigny; [22]Pulmonology, CHRU de Lille; [23]UMR_s933, Paris; [24]CHU Clermont Ferrand, Clermont Ferrand, France*

Background: Despite its high prevalence and mortality, little is known about the pathogenesis of RA–associated interstitial lung disease (RA-ILD). Given that familial pulmonary fibrosis (FPF) and RA–ILD frequently share the usual interstitial pneumonia pattern and common environmental risk factors, we hypothesized that the two diseases may share additional risk factors including FPF-linked genes.
Objectives: Our aim was to identify coding mutations of FPF-risk genes associated with RA-ILD.
Methods: We used whole-exome sequencing (WES) followed by restricted analysis of a discrete number of FPF-linked genes and performed a Burden test to assess the excess number of mutations in RA–ILD patients compared to controls.
Results: Among the 101 RA–ILD patients included, 12 (11.9%) had 13 WES-identified heterozygous mutations in the *TERT*, *RTEL1*, *PARN* or *SFTPC* coding regions. The burden test, based on 81 RA–ILD patients and 1010 controls of European ancestry, revealed an excess of *TERT*, *RTEL1*, *PARN* or *SFTPC* mutations for RA–ILD patients ($p=9.45'10^{-4}$, odds ratio [OR] 3.17 95% CI 1.53–6.12). Telomeres were shorter for RA-ILD patients with a *TERT*, *RTEL1* or *PARN* mutation than controls ($p=2.87x10^{-2}$).
Conclusions: Our results support the contribution of FPF-linked genes to RA–ILD susceptibility.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5237

AB0008 THE ASSOCIATION OF THE PTPN22 RS2476601 GENE POLYMORPHISM WITH JUVENILE IDIOPATHIC ARTHRITIS IN CHILDREN FROM RUSSIA

L.S. Nazarova[1], K.V. Danilko[1], V.A. Malievsky[1], T.V. Viktorova[1,2]. *[1]Bashkir State Medical University; [2]Institute of Biochemistry and Genetics, Ufa, Russian Federation*

Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. The exact cause of the disease is still unknown, but seems to be related to both genetic and environmental factors [1]. The protein tyrosine phosphatase non-receptor type 22 (*PTPN22*) gene single-nucleotide polymorphism (SNP) rs2476601 was shown to be associated with JIA in different populations, but according to resent reports this association is restricted only to females [2,3].
Objectives: The aim of the study was to determine whether the *PTPN22* rs2476601 SNP is associated with the development of JIA and its subtypes in children from Russia.
Methods: The study included 330 patients with JIA and 346 healthy controls from Russia. Genotyping was performed using real-time PCR method and statistical analysis - using two-tailed Fisher's exact test (p), odds ratio (OR), 95% confidence interval (95% CI).
Results: The frequencies of the genotype AG and the allele A were significantly higher and the frequencies of the genotype GG and the allele G were significantly lower in patients with JIA than in controls (p=0.016, OR=1.65, 95% CI 1.10–2.48; p=0.028, OR=1.48, 95% CI 1.05–2.08; p=0.016, OR=0.62, 95% CI 0.43–0.91; p=0.028, OR=0.68, 95% CI 0.48–0.95, correspondingly). The same analysis was then performed separately for patients with two the most frequent ILAR subtypes: persistent oligoarthritis (n=106) and RF-negative polyarthritis (n=85). Significant associations similar to those in the whole JIA group were found only for persistent oligoarthritis (p=0.018 for the genotype AG; p=0.037 for the allele A; p=0.022 for the genotype GG; p=0.037 for the allele G). No significant differences were found for patients with RF-negative polyarthritis ($p>0.6$). Sex-stratified analysis showed that for the whole JIA group and for persistent oligoarthritis the association with the *PTPN22* rs2476601 SNP is restricted only for girls (for girls with the genotype AG: p=0.024 and p=0.0098; with the allele A: p=0.016 and p=0.0061; with the genotype GG: p=0.015 and p=0.0047; with the allele G: p=0.016 and p=0.0061, correspondingly; for boys: $p>0.2$ for all comparisons).
Conclusions: In this study we revealed the association of the *PTPN22* rs2476601 SNP with the development of JIA and its persistent oligoarticular subtype in girls from Russia.
References:
[1] Ravelli A, Martini A. Juvenile idiopathic arthritis. Lancet. 2007;369:767–778.
[2] Chiaroni-Clarke RC, Li YR, Munro JE, Chavez RA, Scurrah KJ, Pezic A, et al. The association of PTPN22 rs2476601 with juvenile idiopathic arthritis is specific to females. Genes Immun. 2015;16:495–498.
[3] Goulielmos GN, Chiaroni-Clarke RC, Dimopoulou DG, Zervou MI, Trachana M, Pratsidou-Gertsi P, Garyfallos A, Ellis JA. Association of juvenile idiopathic arthritis with PTPN22 rs2476601 is specific to females in a Greek population. Pediatr Rheumatol Online J. 2016 Apr 23;14(1):25.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4377

AB0009 GENOMIC SIGNATURES MAY BE ASSOCIATED WITH VASCULAR PATHOLOGY ASSOCIATED WITH RHEUMATOID ARTHRITIS

S. Poliska[1], E. Végh[2], A. Váncsa[2], S. Szamosi[2], M. Csumita[2], G. Zahuczky[3], G. Szücs[2], S. Szántó[2], L. Nagy[1], Z. Szekanecz[2]. *[1]Clinical Genomics Centre; [2]Department of Rheumatology, University of Debrecen, Faculty of Medicine; [3]UD-Genomed Ltd, Debrecen, Hungary*

Background: Accelerated atherosclerosis and cardiovascular (CV) disease have been associated with rheumatoid arthritis (RA). Many genes have been implicated in atherosclerosis, RA or both. However, most of these studies described SNPs in *CD40, SMAD3, HLADR, CTLA4* and other alleles. Very few studies on genetic signatures have been performed that would link RA and CV pathology. We have previously associated some genomic profiles with pathological carotid atherosclerosis (ccIMT), arterial stiffness (PWV) and brachial artery flow-mediated vasodilation (FMD). In other studies we have also found 165 genes that separated anti-TNF responder patients from non-responders.
Objectives: Here we looked for associations between clinical and "vascular" response to biologics and vascular pathology in RA patients.
Methods: In this study, 19 RA patients were treated with either etanercept (ETN) or certolizumab pegol (CZP) for one year. We separated responders (R) and non-responders (NR) according to EULAR response criteria. Microarray gene expression study was performed (Affymetrix) followed by analysis using the GeneSpring software, hierarchy clustering and principal component analysis (PCA). "Vascular response" (VR) to biologics was defined as an at least 20% improvement in FMD, ccIMT or PWV. Good Vascular Response (GVR) was defined as an at least 20% improvement in two or three of these variables.
Results: Among the 19 patients, 13 were R and 6 were NR. With respect to VR, FMD, ccIMT and PWV responded to anti-TNF treatment in 10, 9 and 8 patients, respectively. GVR was observed in 8 patients and 5 patients had VR in all 3 parameters. When comparing clinical response and VR, 7 out of 8 patients showing GVR also had good clinical response to biologics. Up-regulation of 99 and down-regulation of 67 genes separated clinical R and NR patients. Significant correlation was found between ccIMT improvement upon biological therapy and clinical response (R=0.418, p=0.04).
Conclusions: Genomic signature analysis may be able to separate clinical responders and non-responders to biologics, as well as patients that show or do not show imporvement of vascular pathology.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3208

Adaptive immunity (T cells and B cells) in rheumatic diseases

AB0010 LILRB3 EXPRESSION ON T CELLS CORRELATES WITH DISEASE ACTIVITY IN RA

A. Holz, T. Witte, R.E. Schmidt. *Department of Clinical Immunology and Rheumatology, Hannover Medical School, Hannover, Germany*

Background: Leukocyte immunoglobulin-like receptors (LILR) participate in the generation of immunological tolerance (1,2). LILRB3 can be expressed on T cells and is an inhibiting receptor (3).
Objectives: We wanted to study LILR expression on T cells in RA compared to SLE and controls.
Methods: Heparinised human blood from blood donors was obtained from the Institute of Transfusion Medicine, Medical School Hannover (Germany). Blood samples from RA (DAS28 <3.2 n=11; DAS28>3.2 n=8) and SLE patients (n=9) were obtained from Outpatients' Clinic of the Department of Rheumatology and Immunology after informed consent. PBMCs were stained with LILRA2 (Biolegend, APC), LILRB3 (Biolegend, PE), CD3 (Biolegend, APC-Cy 7), CD4 (BD, PerCP-Cy5.5), CD8 (Biolegend, V500), CD25 (Biolegend, PE/Cy5), CD28 (Biolegend, Pacific Blue). Results were compared to isotype controls.
Statistical analyses and figures were made with GraphPad Prism, ANOVA and the Mann-Whitney Test.
Results: The percentage of both CD4+ and CD8+ T cells expressing LILRB3 was significantly higher in both inactive as well as active RA compared to controls or SLE (See Fig. 1) (p=0.0397 ANOVA: RA all vs. SLE vs. controls). Within the group of RA patients, the percentage of LILRB3 expressing T cells was highest in active compared to inactive (DAS28<3.2) RA (p=0.0287). LILRA2 was not expressed on T cells.

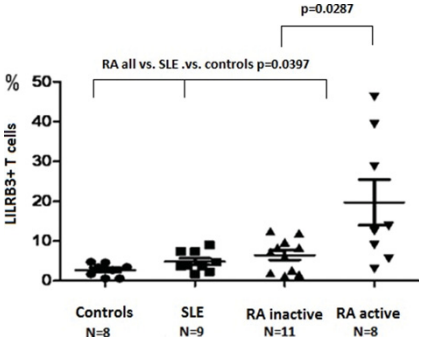


Figure 1

Conclusions: Expression of LILRB3 correlates with disease activity of RA and is decreased after successful treatment with DMARDS or biologicals. Since LILRB3 is an inhibiting receptor the increased expression in active RA may be a counterregulation to reduce disease activity.
References:
[1] Anderson KJ, Allen RL. Regulation of T-cell immunity by leucocyte immunoglobulin-like receptors: innate immune receptors for self on antigen-presenting cells. Immunology 2009 May;127(1):8–17.
[2] Thomas R, Matthias T, Witte T. Leukocyte immunoglobulin-like receptors as new players in autoimmunity. Clin Rev Allergy Immunol 2010 Apr;38(2–3):159–162.
[3] Brown D, Trowsdale J, Allen R. The LILR family: modulators of innate and adaptive immune pathways in health and disease. Tissue Antigens 2004 Sep;64(3):215–225.
Acknowledgements: We thank the StrucMed program for the support, and Katja Kniesch for technical assistance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1697

AB0011 KLRG1 AS A MARKER OF CD28 NEGATIVITY IN RHEUMATOID ARTHRITIS, COMPARISON WITH CD57 AND CD45RA

C. Rawlings, E. Choy, R. Davies, G. Jones, A. Williams. *Cardiff University, Cardiff, United Kingdom*

Background: Our research has shown that patients with RA have higher proportions of peripheral blood CD3+CD8+CD28- Treg cells compared to healthy individuals. CD3+CD8+CD28- Treg cells in patients with RA have lost their ability to suppress lymphocyte proliferation[1]. Thus CD28 negativity may mark senescent T cells. CD57[2] CD45RA[3,4] and killer-cell lectin like receptor G1 (KLRG1)[5] cell surface molecules have been associated with CD8+ T cell activation and senescence. Defining the phenotypic signature of CD8+CD28- Treg cells will help establish their significance in the immunoregulation of RA.
Objectives: To use immunofluorescence and flow cytometry to define the phenotype of CD3+CD8+CD28+/- cells in relation to early RA progression.
Methods: The effector characteristics of peripheral blood CD8 T cells were evaluated by flow cytometry. RA patients with established (n=21) and early disease (n=20) were recruited, and compared to twenty four healthy controls. The mean age of the subjects was 59 (SD=12.5), 25/38 (66%) were female, 27/38 (71%) were anti-CCP positive and 25/38 (66%) rheumatoid factor positive. The mean age for the controls was 43 (SD=11.6), 14/20 (70%) were female.
Results: Confirming our previous work, a significantly higher proportion of CD3+CD8+CD28- cells was observed in RA patients compared to healthy individuals (P=0.03) (Figure 1).
Flow cytometric evaluation of peripheral blood demonstrated a significantly higher expression of CD57, CD45Ra and KLRG1 in CD28- compared to CD28+ T cells.

Table 1. CD57, CD45Ra, KLRG1 and CD28 on CD3+CD8+ T cells

	CD28–	CD28+	P value
CD57+	40	9	<0.0001
CD45Ra+	38	23	0.0026
KLRG1+	36	20	0.0012

A further evaluation of these markers revealed that 69% of the CD8+CD28- cell pool was KLRG1+, in comparison to 66% being CD57+ and 55% KLRG1+CD57+ double positive. This suggests that KLRG1 is a robust and clinically relevant marker of CD28- T cells in RA. Our current research is investigating the significance of KLRG1 and CD8+CD28- cells as prognostic markers in RA.

CD3+CD8+CD28- cells in Controls (n=24) v.s RA patients (n=41) with median.

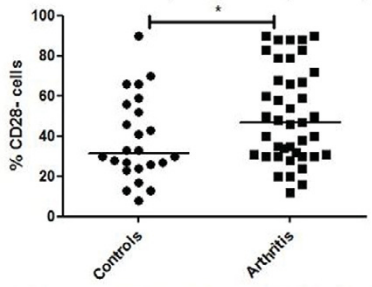


Figure 1: Graph showing the percentage of CD3+CD8+CD28- in RA patients and healthy controls.

Conclusions: CD3+CD8+CD28- cells are enriched in the peripheral blood of RA patients. KLRG1 expression is increased in line with CD57 and CD45Ra in CD8+CD28- cells, and will be used to evaluate the functional significance of these cells in relation to their activation status and potential senescence in the immunoregulation of RA pathogenesis.
References:
[1] Ceeraz S, Hall C, Choy EH, Spencer J, Corrigall VM. Defective CD8+CD28+ regulatory T cell suppressor function in rheumatoid arthritis is restored by tumour necrosis factor inhibitor therapy. Clin Exp Immunol. 2013 Oct;174(1):18–26.
[2] Progressive decrease of CD8high+ CD28+ CD57- cells with ageing.Merino J, Martínez-González MA, Rubio M, Inogés S, Sánchez-Ibarrola A, Subirá ML Clin Exp Immunol. 1998 Apr; 112(1):48–51.
[3] CD28(-)CD8(+) T cells do not contain unique clonotypes and are therefore dispensable. Weinberger B, Welzl K, Herndler-Brandstetter D, Parson W, Grubeck-Loebenstein BImmunol Lett. 2009 Dec 2; 127(1):27–32.
[4] KLRG1 signaling induces defective Akt (ser473) phosphorylation and proliferative dysfunction of highly differentiated CD8+ T cells. Henson SM, Franzese O, Macaulay R, Libri V, Azevedo RI, Kiani-Alikhan S, Plunkett FJ, Masters JE, Jackson S, Griffiths SJ, Pircher HP, Soares MV, Akbar AN. Blood. 2009 Jun 25; 113(26):6619–28.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1562

AB0012 IN THE ELDERLY ACPA-NEGATIVE RA IS MORE PREVALENT THAN ACPA-POSITIVE RA WHILE THE COMPOSITION OF THE ACPA-RESPONSE APPEARS IDENTICAL

D. Boeters[1], L. Mangnus[1], S. Ajeganova[1,2], E. Lindqvist[3], B. Svensson[4], R. Toes[1], L. Trouw[1], T. Huizinga[1], F. Berenbaum[5], J. Morel[6], S. Rantapää-Dahlqvist[7], A. van der Helm-van Mil[1]. *[1]Department of Rheumatology, Leiden University Medical Center, Leiden, Netherlands; [2]Department of Medicine Huddinge, Karolinska Institutet, Stockholm; [3]Department of Clinical Sciences, Section of Rheumatology, Lund University and Skåne University hospital; [4]Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund, Sweden; [5]Department of Rheumatology, Sorbonne University, INSERM UMR_s938, DHU i2B, Assistance Publique-Hôpitaux de Paris, Saint-Antoine Hospital, Paris; [6]Department of Rheumatology, Teaching hospital Lapeyronie and Montpellier University, Montpellier, France; [7]Department of Public Health and Clinical Medicine/Rheumatology, University Hospital, Umeå, Sweden*

Background: Rheumatoid arthritis (RA) consists of two syndromes, one autoantibody-positive and one autoantibody-negative. This multi-cohort study

assessed the age of onset in relation to the presence of autoantibodies. The association with characteristics of the anti-citrullinated protein antibodies (ACPA)-response was also explored.
Objectives: 1) determine the association between age of RA-onset and the presence of ACPA, rheumatoid factor (RF) and anti-carbamylated protein (anti-CarP) antibodies, 2) study if age of onset was associated with characteristics of the ACPA-response, 3) substantiate previously reported associations between age of onset and clinical characteristics.
Methods: 3,321 1987-positive RA-patients included in the Leiden-EAC, BARFOT, ESPOIR, Umeå and Lund cohorts were studied at presentation on age of onset and the presence of ACPA, RF and anti-CarP antibodies. Logistic regression analyses were performed; effect sizes were summarized in inverse-weighted meta-analyses. Within ACPA-positive RA, ACPA-level was studied in all cohorts; ACPA-isotypes, ACPA-fine-specificity and ACPA-avidity index and clinical characteristics were studied in the Leiden-EAC.
Results: From the age of fifty onwards, the proportion of ACPA-negative RA-patients increased in Dutch, Swedish and French cohorts. Similar observations were done for RF and anti-CarP. The composition of the ACPA-response did not change with increasing age of onset with respect to titer, isotype distribution, fine specificity and avidity index. With increasing age of onset RA-patients smoked less often, had higher acute phase reactants and more often a sub(acute) symptom onset.
Conclusions: Data of five cohorts revealed that with higher age of onset ACPA-negative RA is more frequent than ACPA-positive RA, while characteristics of ACPA-positive RA as judged by the composition of the ACPA-response appeared not age-dependent. Although more biologic studies are needed to characterize the pathogenesis of ACPA-negative polyarthritis at older age, the present data can promote personalized treatment decisions in ACPA-negative patients in daily practice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3781

AB0013 IS THERE IMMUNE DISREGULATION IN NON-SJÖGREN SICCA SYNDROME? A STUDY OF BLOOD LYMPHOCYTE SUBPOPULATIONS

F. Barcelos[1,2,3], C. Martins[3], G. Nunes[3], T. Lopes[3], J. Vaz Patto[1], J. Amaral[4], J.C. Branco[3], L.M. Borrego[3]. *[1]Instituto Português Reumatologia; [2]Hospital CUF Descobertas; [3]Nova Medical School; [4]Faculdade Med Dentária, UL, Lisboa, Portugal*

Background: A large number of patients with sicca syndrome not fulfilling Sjögren's syndrome (SS) classification criteria, present manifestations of autoimmunity, like arthritis, Raynaud's, rash or hematologic disturbances, and have anti-nuclear antibodies, lacking however more specific antibodies. The designation Undifferentiated Connective Tissue Disease was coined to refer to those patients, and some will eventually progress to a definite disease, of which SS would be a likely candidate. Immune cell disturbances could be progression markerr, since diseases like pSS have distinct lymphocyte profiles.
Objectives: We aim to study the circulating lymphocyte subsets in non-Sjögren sicca patients (n-SS), and compare them with pSS and healthy controls.
Methods: We included 65 n-SS patients, 53 pSS patients (2002 AECG criteria) and 22 healthy controls. Lymphocyte subsets were characterized by flow cytometry, including follicular and regulatory T cells and naïve, mature, memory, plasmablasts and regulatory B cells. Statistical analysis was performed with GraphPad, and significance was considered for $p<0.05$
Results: Comparing to controls, n-SS patients had lower counts of T cells (p=0.016), with lower CD4 (p=0.0028), however that difference was not as pronounced as between SS and controls. n-SS patients had higher percentages of CD4 (p=0.0005) and lower CD8 percentages (p=0.0009) than pSS. Additionally, there was a decrease in absolute counts of Tregs (p=0.0028) in n-SS patients compared to controls, which was less pronounced than the comparison between SS and controls (p=0.0008). Th17 cells were decreased in SS compared to controls (p=0.0005), but not in-SS patients. Compared with controls, both n-SS and SS patients presented decreased absolute count (p=0.0001 and p<0,0001, respectively) of $CXCR5^+$ Tfh cells, with no differences between n-SS and SS patients. However, higher levels of $IL21^+CD4$ T cells and Tfh1 cells were found comparing SS patients with both controls (p=0,0209 and p=0,0092 respectively) and n-SS patients (p=0,0051 and 0,0028 respectively).
Absolute counts of memory, unswitched and switched memory cells in n-SS patients present intermediate levels between controls with significantly higher levels, and SS patients with significantly lower levels. Accordingly, using the Bm1–5 classification, we have found decreased Bm1 (p=0.004), eBm5 (Abs, p=0.0273) and Bm5 cells (Abs, p=0.0444) in n-SS patients compared to controls. Though not significant, there was an increase in eBm5 (Abs, p=0.063) and Bm5 cells (Abs, p=0.05) in n-SS compared to SS patients. Again, $CD24^+CD27^+$ Bregs were also decreased in n-SS patients compared to controls (p=0.036), but increased in n-SS compared to SS patients (p=0,0007).
Conclusions: Our data showed that n-SS patients present immune disregulation, represented by alterations in the B cell compartment but also in Tfh subset, known to modulate the humoral immune response. Although less pronounced, these modifications resemble the ones found in SS patients. Wether n-SS is a stage in the evolution to SS remains to be clarified. The identification of a characteristic disregulation of the immune system in n-SS could be usefull for diagnostic and prognostic purposes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6367

AB0014 DIFFERENTIAL EFFECTS OF A SINGLE DOSE OF CYCLOPHOSPHAMIDE ON CIRCULATING CELL SUBPOPULATIONS IN PATIENTS WITH VASCULITIDES AND AUTOIMMUNE SYSTEMIC DISEASES

G. Gabcova[1], Z. Mikulkova[1], M. Skacelova[2], A. Petrackova[1], A. Smrzova[2], M. Schubertova[2], F. Mrazek[3], P. Horak[2], E. Kriegova[1]. *[1]Department of Immunology, Faculty of Medicine and Dentistry, Palacky University, Olomouc; [2]Department of Internal Medicine III - Nephrology, Rheumatology and Endocrinology, Faculty of Medicine and Dentistry, Palacky University Olomouc, University Hospital, Olomouc; [3]Department of Immunology, University Hospital Olomouc, Olomouc, Czech Republic*

Background: High-dose cyclophosphamide (CFA) is used for treatment of patients with severe manifestations of systemic autoimmune diseases. The knowledge about the effect of CFA on circulating cell populations in these diseases is still limited.
Objectives: To identify the effect of a single dose of CFA on circulating cell populations in patients with vasculitides and autoimmune systemic diseases.
Methods: We immunophenotyped T lymphocytes (CD3, CD4, CD8, CD25, CD127, HLA-DR), B lymphocytes (CD19, CD20, CD27), NK cells (CD3, CD16, CD56, CD69), neutrophils (CD15, CD11b, CD16, CD54, CD62L, CD64), and monocytes (CD11b, CD14, CD16, CD64, HLA-DR) using 6-color cytometer BD FACSCanto II (Becton Dickinson) in peripheral blood of patients with vasculitides (n=6) and systemic disorders of connective tissue (n=6). From each patient, we obtained paired samples before and one month after a single CFA dose. Statistical tests were performed using GraphPad Prism (GraphPad Software, Inc). *P*-value <0.05 was considered as significant.
Results: Single dose of CFA resulted in increase of percentage of CD8+ T lymphocytes (*P*=0.002), leading to marked decrease of CD4+/CD8+ ratio (*P*=0.009). Except three patients, overall percentage of neutrophils decreased after the treatment (*P*=0.01). Although CFA pulse did not influence the percentage of NK cells, the percentage of NK cells carrying stimulatory receptor CD69 increased after CFA (*P*=0.037). Similarly, CFA enhanced the percentage of co-stimulatory molecule CD27 on B lymphocytes (*P*=0.048). Among subsets of monocytes, CFA treatment increased percentage of CD14-CD16+ monocytes (*P*=0.006) and increased expression (MFI) of Fc fragment CD64 (*P*=0.02). Moreover, increase of HLA-DR was observed on CD14-CD16+ monocytes (*P*=0.037). The investigations whether the changes in immune cell subpopulations in treated patients have prognostic potential are ongoing.
Conclusions: Single dose of CFA resulted in increase of CD8+ T lymphocytes, activation of NK, B lymphocytes and monocytes as well as in some patients decrease in neutrophil counts. Further investigation of selected markers may lead to identification of new prognostic markers and predict the effectiveness of the treatment.
Acknowledgements: Grant support: MZ CR VES15–28659A, IGA_LF_2017_009
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4663

AB0015 CAPTURE OF IGA IMMUNE COMPLEXES AND ENRICHMENT IN IGA IG GENE EXPRESSION BOTH SUGGEST A ROLE FOR FCRL4+ B CELLS IN THE LINK BETWEEN MUCOSAL AND JOINT INFLAMMATION

J. Cameron[1], E. Clay[1], K. Amara[2], N. Sippl[2], A. Filer[1], K. Raza[1], V. Malmström[2], D. Scheel-Toellner[1]. *[1]Rheumatology Research Group, RACE AR UK Centre of Excellence in RA Pathogenesis, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom; [2]Rheumatology Unit, Department of Medicine, Karolinska Universitetssjukhuset, Stockholm, Sweden*

Background: Increasing evidence points to the autoimmune process of rheumatoid arthritis (RA) originating at mucosal surfaces. Previous work from our group described a subset of B cells in the synovium and synovial fluid (SF) of RA patients which can be distinguished by their expression of the Fc-like receptor 4 (FcRL4) and elevated expression of RANKL, indicating a unique pathogenic function[1,2]. B cells expressing FcRL4 were originally described as a distinct memory B cell subset in human tonsils where they accumulate in the epithelium[3]. We have recently shown that they are enriched in cells recognizing citrullinated autoantigens (Amara, K. et al. under revision). Recent *in vitro* work suggested that FcRL4 is a low affinity receptor for aggregated IgA[4].
Objectives: 1) To investigate the interaction of RA synovial fluid FCRL4+ B cells with IgA
2) To examine the distribution of Ig classes by flow cytometry and PCR
Methods: SF mononuclear cells were isolated, labelled for FcRL4, IgA and CD19 and analysed by flow cytometry. In experiments identifying IgA B cell receptors, SF mononuclear cells were briefly incubated in an acidic buffer to remove surface receptor bound antibodies before staining. Heat-aggregated purified human IgA

was added to assess IgA binding to FcRL4+ B cells. Single B cells were sorted from SF of RA patients and their constant region genes probed for identification of their Ig subclass by PCR.

Results: *Ex vivo*, FcRL4$^+$ B cells in SF of RA patients have a higher load of IgA bound to their surface compared to their FcRL4- counterparts. After in vitro removal of surface bound IgA, they can bind heat-aggregated IgA (p=0.0313). We also demonstrate that a significantly higher proportion of FcRL4+ B cells use IgA BCRs (p=0.0061) by flow cytometry and further more by probing constant region genes by PCR an enrichment for Ig genes for coding the IgA1 isotype (p=0.009) was found.

Conclusions: Both their ability to capture IgA immune complexes through binding to FcRL4 and their enrichment in IgA Ig gene expression suggest a potential role for synovial fluid FcRL4$^+$ B cells in the mucosal origin of joint inflammation.

References:

[1] Yeo, L. et al. Cytokine mRNA profiling identifies B cells as a major source of RANKL in rheumatoid arthritis. Ann Rheum Dis 70, 2022–2028, doi:10.1136/ard.2011.153312 (2011).
[2] Yeo, L. et al. Expression of FcRL4 defines a pro-inflammatory, RANKL-producing B cell subset in rheumatoid arthritis. Ann Rheum Dis 74, 928–935, doi:10.1136/annrheumdis-2013–204116 (2015).
[3] Falini, B. et al. Expression of the IRTA1 receptor identifies intraepithelial and subepithelial marginal zone B cells of the mucosa-associated lymphoid tissue (MALT). Blood 102, 3684–3692, doi:10.1182/blood-2003–03–0750 (2003).
[4] Wilson, T. J., Fuchs, A. & Colonna, M. Cutting edge: human FcRL4 and FcRL5 are receptors for IgA and IgG. J Immunol 188, 4741–4745, doi:10.4049/jimmunol.1102651 (2012).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6488

AB0016 B-CELL SUBSETS DIFFERENCES IN INFLAMMATORY RHEUMATIC DISEASES

J.L. Gomes[1,2], D. Ligeiro[3], A. Lima[3], A. Sepriano[2,4], C. Teixeira[3], C. Lopes[1], T. Costa[1], S. Ramiro[4], M. Mateus[1], M. Costa[1], J.C. Branco[1,2], F. Pimentel-Santos[1,2]. *[1]Rheumatology, Hospital Egas Moniz - CHLO; [2]CEDOC, NOVA Medical School-Universidade Nova de Lisboa; [3]Centro de Sangue e Transplantação de Lisboa, IPST-IP, Lisboa, Portugal; [4]Rheumatology, LUMC, Leiden, Netherlands*

Background: Targeting humoral immunity has been proved effective in several inflammatory rheumatic diseases (IRD). Though clinical trials have shown some efficacy of B-cell depletion in ankylosing spondylitis (AS), results are less convincing. Other studies have revealed an association between mutations and expression of immune regulatory genes suggesting B-cell dysfunction in the development and progression of AS. Yet, there is still lack of data describing B-cell subsets in AS, how these compare to other IRD and an evaluation of B cell compartment homeostasis in the pathophysiology of this disease.

Table 1. Patient and healthy controls demographics, clinical variables and absolute cell counts.

	AS (n=22)	RA (n=20)	SLE (n=18)	HC (n=12)
Patients				
Male, Female; n (%)	11 (50); 11 (50)	9 (45); 11 (55)	5 (27.8); 13 (72.2)	3 (30); 7 (70)
Age; median (IQR)	56 (45.8-65.5)	55 (51-65.5)	44 (37.5-52.5)*	60.5 (32-64.5)
ESR mm/hour	14 (10-29.3)	21 (10.3-37.8)	23 (6-34.5)	11 (8-22.5)
CRP mg/dL	1.1 (0.9-1.7)	0.98 (0.7-3.2)	0.6 (0.5-1.6)	-
HLA B27+: n (%)	11 (68.8)	-	-	-
With csDMARS, n (%)	6 (30)	18 (90)	15 (83.3)	0
Ig seric levels, mg/dl; median (IQR)				
IgG	1165 (881.3-1247.5)	1021 (830.3-1265)	1140 (1003-1325	1033.5 (823.3-123
IgA	230 (158.8-340)	250.5 (164.3-315.3)	261 (205-323)	236.5 (150.3-339.8
IgM	95.3 (65.6-119.5)	112 (67.7-164.8)	103 (60.6-131.5	122 (71.5-158.3)
Absolute cell counts/µl blood; median (IQR)				
Lymphocytes	1685 (1217-2007.5)	1555 (1097.5-2085)	1250 (625-1892.5)	2170 (1830-2377)*
Total B-cells (CD20$^+$)	186.3 (110.9-238.6)	96.2 (50.3-180.6)***	65.8 (20.9-116.1)***	182.1 (100.9-269.3
Immature Transitional B-cells (CD5$^+$CD27$^-$IgD$^+$), median (IQR)				
CD24^{++}CD38^{++}(T1)	2.8 (1.8-3.9)	0.6 (0.1-2.7)**	1.5 (0.2-2.8)**	4.3 (2.3-6.5)
CD24^{++}CD38^{++}(T2)	8.3 (5.1-14.9)	2.6 (0.2-8.0)**	3.0 (1.0-8.0)**	13.7 (5.7-18.8)
CD24$^+$CD38$^+$(T3)	9.0 (5.5-17.7)	2.2 (0.3-4.6)**	1.9 (0.2-3.7)**	7.7 (4.1-12.3)
Mature B-Cells, median (IQR)				
CD27$^-$IgD$^+$ (*naïve*)	73.2 (49.7-121.7)	40.1(19.2-76.9)**	27.2(11.9-57.1) †	78.6 (48.4-163.4)
CD27$^+$IgD$^+$(mem. *MZ-like*)	25.9 (13.6-39.9)	13.0 (3.5-27.2)**	2.6 (1.8-9.6) †	18.9 (11.2-27.1)
CD27$^+$IgD$^-$(*switch mem.*)	18.8 (12.2-37.9)	13.5 (3.9-37.6)	4.9 (2.2-17.2)***	29.3 (14.51-37.9)
CD27$^-$IgD$^-$(*double neg.*)	2.4 (1.8-5.2)	3.1 (2.0-6.4)	2.9 (1.0-5.0)	5.2 (2.6-8.1)

Mann-Whitney and the Fisher´s exact test were used for comparison between AS and other groups
* p<0.05; **p<0.02; ***p<0.01; †p<0.0001

Objectives: To assess and compare the immature, naive and antigen differentiated subsets of peripheral B-cell compartment in AS with those in healthy controls (HC) and other IRD

Methods: Patients (pts) with AS, RA and SLE according to respective classification criteria were included in this study. Pts under biologic DMARDS were not included. Sociodemographic and clinical variables were recorded. Blood samples were collected for quantification of inflammatory markers (ESR and CRP), immunoglobulin serum levels and assessment of B-cell immature transitional stages and mature subsets by flow cytometry (figure). Mann-Whitney and Fisher's exact test were used for comparison of AS with other groups

Results: Overall, 60 pts and 12 HC were included (Table). All patient groups presented similar and rather low levels of inflammation, as measured by CRP, ESR and immunoglobulins, in addition to a decreased lymphocyte count by comparison with HC. There were no differences in the B-cell counts between AS pts and HC, with both groups having higher B-cell counts than RA and SLE pts. Regarding B-cell subsets, the immature transitional compartment of AS pts was found in normal range, but not in the RA and SLE groups. In fact, the latter presented a significant decrease in all transitional cell maturity stages (T1-T3). The next step in B-cell differentiation is mature naïve cells, also found in normal levels in AS and decreased in RA and in particular in SLE. AS pts presented slightly higher counts of CD27+IgD+ MZ-like and class able to switch memory cells with reference to HC and these cell numbers were found to be low in RA and even lower in SLE pts. Switched memory CD27+IgD- B-cells were reduced in all patient groups, however, only SLE pts presented highly decreased cell levels.

Conclusions: We found that while a severe dysfunction is present in the homeostasis of the B-cell compartment in RA and in particular SLE pts, which are lymphopenic in both immature and mature B-cell compartments, it appears that AS pts are not affected in the same way. At this stage, functional studies appear to be necessary in order to identify differences in key mechanisms of B cell development and differentiation that may play a role in the aetiology and progression of these inflammatory rheumatic diseases. Our first results, however, establish that pathophysiological mechanisms involving B-cells clearly differentiate AS from RA and SLE

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5553

AB0017 THERAPEUTIC EFFECT OF UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS TRANSPLANTATION IN A MOUSE MODEL OF PRIMARY BILIARY CIRRHOSIS

J. Fan, Q. Wang, R. Feng, G. Yao, X. Tang, L. Sun. *Department of Rheumatology and Immunology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, nanjing, China*

Background: Primary biliary cirrhosis (PBC) is a cholestatic liver disease characterized by slowly progressive non-suppurative cholangitis with immune mediated destruction of intrahepatic bile ducts. Previous studies have shown beneficial effects of mesenchymal stem cells (MSCs) transplantation in many autoimmune diseases. However, few studies have focused on the effects of MSCs on PBC.

Objectives: In our study, we investigated the therapeutic effect of umbilical cord-derived mesenchymal stem cells (UC-MSCs) transplantation in a well-defined mouse model of PBC and explored the potential mechanism.

Methods: After 2OA-BSA-induced autoimmune cholangitis was created in C57BL/6 mice, cultured human UC-MSCs or a vehicle control was administered. Liver injury severity was assessed by clinical and histologic analysis. The immunity suppression effects and mechanism of UC-MSCs were tested.

Results: UC-MSCs administration alleviated bile duct damage and intrahepatic inflammatory cell infiltration in C57BL/6 mice that had undergone 2OA-BSA immunization. Serum levels of ALT and ALP were significantly decreased. Also, UC-MSCs reduced the production of anti-mitochondrial autoantibodies (AMA) in PBC mice. UC-MSCs downregulated inflammatory cytokine, such as IFN-γ, TNF-α, IL-12 and IL-17A production both in peripheral blood and local liver. Notably, Infusion of UC-MSCs resulted in an increase in regulatory T cells (Tregs) in peripheral blood but a decrease of this kind of cells in liver tissues. Furthermore, UC-MSCs significantly suppressed Th1- and Th17-cell responses and these alternations could be detected in spleen, peripheral blood and liver in PBC mice.

Conclusions: In summary, the current study shows that UC-MSCs based therapy has profound inhibitory effects on inflammatory responses and immunoregulatory effects both in local and systemic abnormalities in PBC. These findings also provide further evidence regarding the role of MSCs in the clinical trials of PBC.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3346

AB0018 B CELL DISTURBANCE IN RHEUMATOID ARTHRITIS PATIENTS: COMPARATIVE STUDY BETWEEN TREATED AND NON-TREATED PATIENTS

M.H. Nassr[1], E. Gomaa[2], M.M. Eid[3], A.A. Hamdy[2], A.A. Wegdan[2].
[1]Rheumatology department; [2]Microbiology and Immunology; [3]Clinical Pathology Department, Fayoum University, Fayoum, Egypt

Background: B cells have been shown to play a key role in the pathogenesis of rheumatoid arthritis (RA). Alterations of B cell homeostasis as well as B cell activation markers, such as B-cell activating factor (BAFF) and A Proliferation-Inducing Ligand (APRIL) have been described in RA patients. Up to our knowledge, no data is currently available on differences between treatment naïve patients and those receiving disease modifying anti-rheumatic drugs (DMARDs), regarding B-cell surface expression as well as levels of circulating BAFF/APRIL.
Objectives: The aim of this study is to investigate disturbance of B cell as well as B cell activation markers namely BAFF and APRIL in patients with rheumatoid arthritis comparing treatment naive patients with those receiving disease modifying anti-rheumatic drugs.
Methods: Sixty RA patients and 30 healthy controls were enrolled. Thirty patients receiving non biologic DMARDs and had not received prior biological treatment and 30 treatment naïve patients. Absolute number of blood CD19 B cells was determined by flow cytometry using the CD19-PE Kit (Immunotech, France). BAFF and APRIL blood concentration was measured using commercially available ELISA kits (Bosterbio, USA).
Results: There was statistically significant difference (p-value <0.05) between different study groups as regard B cell count with *low* mean among treated RA patients (137.2±60.5) and *high* mean among controls (243.7±22.5). The B cell count was diminished in the two groups of RA patients, however it is more pronounced in treated patients. Circulating BAFF levels were increased in RA compared to HC (p-value <0.05) with more increase in patients on treatment. Circulating APRIL levels were significantly lower (p-value <0.05) in treatment naïve rheumatoid arthritis patients (343.9±21.7) than the control group (371.5±24.3). However, there was no statistical significant difference (p-value >0.05) between each of treated rheumatoid arthritis group and controls or with non treated rheumatoid arthritis group.

Variables	B cell count		p-value
	Mean	SD	
G1: Treated RA patients	137.2	60.5	**<0.001**
G2: Non treated patients	179.3	59.1	
G3: Controls	243.7	22.5	
Variables	baff Concentration (pg/ml)		p-value
	Mean	SD	
G1: Treated RA patients	1419.4	417.3	**<0.001**
G2: Non treated patients	886.2	258.4	
G3: Controls	444.4	120.1	

Conclusions: More decrease in B cell count and more increase in BAFF level were observed in RA patients receiving non-biologic DMARDs. Conversely, APRIL levels were not affected by treatment.
The contribution of B lymphocyte to RA pathogenesis goes beyond autoantibody production. Disturbances in B cell homeostasis in RA are not only due to disease process itself but closely related to the use of anti-rheumatic drugs.
References:
[1] Kotzin BL (2005) The role of B cells in the pathogenesis of rheumatoid arthritis. J Rheumatol Suppl 73: 14–18.
[2] Edwards JC, Cambridge G.(2006) B-cell targeting in rheumatoid arthritis and other autoimmune diseases. Nat Rev Immunol. May;6(5):394–403.
[3] Ng LG, Mackay CR, Mackay F (2005) The BAFF/APRIL system: life beyond B lymphocytes. Mol Immunol 42: 763–772.
[4] Vincent F., Saulep-Easton D., Figgett W., Fairfax K., Mackay F. (2013) The BAFF/APRIL system: emerging functions beyond B cell biology and autoimmunity. Cytokine Growth Factor Rev 24: 203–215.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2014

AB0019 HDL PROMOTES A REGULATORY PHENOTYPE OF THE IMMUNE SYSTEM BY INDUCING THE PROLIFERATION OF HUMAN CD4+ T CELLS WHILE INCREASING THE EXPRESSION OF FOXP3 IN REGULATOR T CELLS

M. Fernandes Das Neves[1,2], J.R. Batuca[2], E.C. Jury[3], J. Delgado Alves[1,2].
[1]Medicine IV, Professor Doutor Fernando Fonseca Hospital, Amadora; [2]CEDOC - Chronic Disease Research Center, NOVA Medical School/Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon, Portugal; [3]Centre for Rheumatology Research, University College London, London, United Kingdom

Background: High-density lipoproteins (HDL) are the plasma lipoproteins responsible for reverse cholesterol transport. Its protective effect on cardiovascular disease is attributed to the cholesterol efflux capacity as well as to its anti-oxidant and anti-inflammatory properties. HDL low levels are associated with immune diseases, including systemic lupus erythematosus and rheumatoid arthritis, implying a potential link between HDL and immunity.
There is few evidence on the effects of HDL on human T cells. Animal studies suggested that HDL inhibits lymphocyte proliferation[1], but the only study in humans showed that HDL from young and healthy subjects increases the proliferation of lymphocytes[2]. Previous studies also showed that HDL levels are positively correlated with the prevalence of regulator T cells in peripheral blood[3]. Furthermore, it has been shown that one of the main actions of HDL in lymphocytes is the disaggregation of lipid rafts provoked by cholesterol efflux from the membrane, but the final consequences of this effect are not known.
Objectives: To determine the *in vitro* effects of HDL in human T cell proliferation and in the frequency of FoxP3+ regulator T cells.
Methods: Peripheral blood mononuclear cells from six healthy donors were cultured with and without HDL to measure membrane cholesterol and proliferative response to CD3/CD28 stimulation. Membrane cholesterol was measured by filipin binding, assessed by flow cytometry. T cell proliferation was studied by Ki-67 expression and cell trace staining for multiple generations. T cell phenotyping and FoxP3 fluorescence were analyzed by flow cytometry.
Results: HDL significantly reduced the amount of membrane cholesterol in CD4+ T cells, after 24 hours in culture. When added in the absence of stimulation, HDL did not induce any proliferation in CD4+ T cells. When added in conjunction with CD3/CD28 stimulation, HDL significantly increased the proliferation of CD4+ T cells. T cell phenotyping showed a significant increase in CD4+CD25+ FoxP3 fluorescence, after culture with HDL.
Conclusions: This study shows that HDL promotes cholesterol efflux from the membrane of CD4+ T cells *in vitro* and increases CD4+ T cell proliferation. However, the increase in T cell numbers seem to favor the expression of FoxP3 in regulator in T cells, which is associated with suppression of inflammation. With the development of therapies to increase HDL levels, the knowledge of the HDL effects on T cell subsets is very important for the future management of cardiovascular and rheumatic diseases.
References:
[1] Wilhem AJ, Zabalawi M, Owen JS, et al. Apolipoprotein A-I modulates regulatory T cells in autoimmune LDLr-/-, ApoA-I-/- mice. J Biol Chem. 2010; 285:36158–36169.
[2] Larbi A, Fortin C, Dupuis G, et al. Immunomodulatory role of high-density lipoproteins: impact on immunosenescence. Age. 2014; 36(5):9712.
[3] Ammirati E, Cianflone D, Banfi M, et al. Circulating CD4+CD25hiCD127lo regulatory T-cell levels do not reflect the extent or severity of carotid and coronary atherosclerosis. Arterioscler Thromb Vasc Biol. 2010; 30:1832–1841.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6681

AB0020 EXPRESSION LEVELS OF SIGNALING LYMPHOCYTE ACTIVATION MOLECULE FAMILY 6 (SLAMF6) ON CIRCULATING FOLLICULAR HELPER T CELLS ARE ASSOCIATED WITH DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

S.E. Kang[1], S.J. Lee[1,2], D.J. Go[1,2], H.M. Kwon[2], E.Y. Ahn[2], J.K. Park[1,2], E.Y. Lee[2], E.B. Lee[2], Y.W. Song[1,2]. *[1]Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul National University; [2]Division of Rheumatology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea, Republic Of*

Background: T follicular helper cells (Tfh) are necessary for B-cell maturation and differentiation in the germinal centers (GC). The signaling lymphocyte activation molecule family (SLAMF) receptors on the cell surface mediate T cell:B cell interaction for formation and maintenance of GC. But it remains to be elucidated whether SLAMF is expressed in circulating T follicular helper cells (cTfh).
Objectives: The aim of this study was to investigate the levels of SLAMF3 and SLAMF6 on cTfh and to analyze their association with disease activity in systemic lupus erythematosus (SLE) patients.
Methods: Blood samples were collected from 50 SLE patients, 24 Sjogren's syndrome (SS) patients and 25 age- and sex-matched healthy controls (HCs). In this study, CXCR5, programmed cell death protein 1 (PD-1), and CD4 were used as markers to define cTfh in peripheral blood mononuclear cells (PBMCs). The expression levels of SLMAF3 and SLMAF6 on cTfh were compared to that of circulating B cell subsets by flow cytometry. Clinical features including disease activity and laboratory tests were analyzed according to expression of SLAMF3 and SLAMF6.
Results: Surface expression of SLAMF6 on CD4 T cells was significantly increased in SLE patients compared to SS patients (mean fluorescence intensity [MFI], mean ± SD: 1291±319 vs 1098±147, p=0.015) and HCs (1291±319 vs 1094±243, p=0.011). But there was no difference in expression of SLAMF3 on CD4 T cells between SLE patients and SS patients or HCs. SLAMF6 expressions on cTfh cells, identified as $CD4^+CXCR5^+PD\text{-}1^+$, were significantly increased in SLE patients than in SS patients (1500±270 vs 1296±140, p=0.001) and HCs (1500±270 vs 1295±161, p=0.001). SLAMF6 expressions on cTfh cells had correlation with systemic lupus erythematosus disease activity index (SLEDAI) (Spearman's rho=0.477, p=0.001), proteinuria (rho=0.321, p=0.030) and double strand DNA (rho=0.340, p=0.026) in SLE patients. Moreover, expression levels of SLAMF6 on cTfh cells were correlated with those of several B cell subsets including total B cells ($CD19^+$), naïve B cells ($CD19^+CD27^-IgD^+$) and class-

switched memory B cells ($CD19^+CD27^+IgD^-$). But SLAMF6 expressions of B cell subsets were not correlated with disease activity.
Conclusions: Surface expression of SLAMF6 was increased in cTfh cells in patients of SLE and had correlation with disease activity.
References:
[4] T cells indicate Tfh cell activity and promote antibody responses upon antigen reexposure. Immunity. 2013;17;39(4):770–81.
[1] Choi JY, His-enHo J, Pasoto SG, et al. Circulating follicular helper-like T cells in systemic lupus erythematosus: association with disease activity. Arthritis Rheumatol. 2015;67(4):988–99.
[2] Zhang X, Lindwall E, Gauthier C, et al. Circulating CXCR5+CD4+helper T cells in systemic lupus erythematosus patients share phenotypic properties with germinal center follicular helper T cells and promote antibody production. Lupus. 2015;24(9):909–17.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6078

Innate immunity in rheumatic diseases

AB0021 HUMAN T CELL LEUKEMIA VIRUS TYPE 1 (HTLV-1) EXACERBATES RHEUMATOID ARTHRITIS; EXOSOMES AND IFN-GAMMA DERIVED FROM HTLV-1 INFECTED CELLS ENHANCE THE INFLAMMATORY RESPONSE OF RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS VIA PATTERN RECOGNITION RECEPTOR, RIG-I

K. Umekita, S. Miyauchi, K. Kubo, A. Kawano, K. Iwao, M. Komura, M. Matsuda, I. Takajo, H. Nomura, Y. Nagatomo, A. Okayama. *Division of Rheumatology, Infectious Diseases and Laboratory Medicine, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan*

Background: Human T cell leukemia type 1 (HTLV-1) positive rheumatoid arthritis (RA) patients show severe inflammatory state and resistance to anti-rheumatic therapy, including biologic agents (1). HTLV-1 infected T cells was increased in the synovial fluid and tissue from an HTLV-1 positive RA patients (2). However the mechanism of worsening RA by HTLV-1 infection remains unclear. We focused on the role of HTLV-1 infected T cells as a key player in the exacerbation of RA.
Objectives: To clarify the role of HTLV-1 infected T cells in the pathogenesis of RA. We investigate inflammatory mediators derived from HTLV-1 infected cells.
Methods: Peripheral blood mononuclear cells (PBMCs) were collected from asymptomatic HTLV-1 carriers (AC) (n=5) and healthy subjects (HS) (n=5). Rheumatoid arthritis synovial fibroblasts (RASFs) were co-cultured with PBMCs for 5 days. Cytokine profiles of supernatants were analyzed by multiplex. Exosomes were isolated and purified from cultured medium of HTLV-1 infected cell line (MT2). RASF was cultured with MT2 derived exosomes with and without IFN-gamma for 24hours. Total RNA was extracted using TRIZOL method. The expression of RIG-I, IL-6, CXCL10, and CCL5 mRNA in RASF was measured using real-time quantitative PCR. The expression of pattern recognition receptor, RIG-I was determined by immune blotting. Silencing of RIG-I in RASF was performed by transfection of siRNA against RIG-I.
Results: The levels of cytokine, including IFN-gamma, IL-2, IL-9, IL-13, IL-6, and CCL20, were higher in supernatants co-cultured with HTLV-1 positive PBMCs than in those of negative PBMC ($p<0.05$). The expression of CXCL10 and IL-6 mRNA was increased in RASF co-cultured with HTLV-1 positive PBMCs compared to those of negative PBMCs. IFN-gamma is well known to be an important cytokine in the pathogenesis of HTLV-1 associated inflammatory diseases. IFN-gamma induced the expression of IL-6, CCL5, and CXCL10 mRNA in RASF. HTLV-1 infected cell line, MT2, autonomously released a large amount of exosomes which contain nucleic acids such as RNA and DNA. MT2 derived exosomes significantly enhanced the expression of CXCL10 mRNA, but not IL-6 and CCL5, in RASF activated by IFN-gamma. Therefore, we hypothesized that exosomes play the role of ligand for pattern recognition receptors. IFN-gamma increased the expression of RIG-I protein in RASF in a dose-dependent manner. The expression of RIG-I protein also increased in RASF co-cultured with HTLV-1 positive PBMCs compared to those of negative PBMCs. Finally, the silencing of RIG-I suppressed the expression of CXCL10 in RASF induced by co-stimulation of both exosomes and IFN-gamma.
Conclusions: It is possible that HTLV-1 infected T cells exacerbate the inflammatory responses of RASFs. Exosomes derived from HTLV-1 infected cells enhance the expression of CXCL10 in RASF induced by IFN-gamma via pattern recognition receptor, RIG-I.
References:
[1] Umekita K, et al. Arthritis Care Res (Hoboken). 2014 May;66(5):788–92.
[2] Yakova M, et al. Retrovirology. 2005 Feb 1;2:4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2036

AB0022 CYTOTOXIC PROFILE CHARACTERIZATION OF NK AND NKT CELLS IN PATIENTS WITH BEHÇET DISEASE

M. Bonacini[1], A. Soriano[2], E. Calò[1], A. Zerbini[1], L. Cimino[3], L. Fontana[3], M. Parmeggiani[1], C. Salvarani[2], S. Croci[1]. *[1]Clinical Immunology, Allergy and Advanced Biotechnologies Unit; [2]Rheumatology Unit; [3]Ocular Immunology Unit, Arcispedale Santa Maria Nuova – IRCCS, Reggio Emilia, Italy, Reggio Emilia, Italy*

Background: Behçhet disease (BD) is a rare inflammatory small vessel vasculitis. It is a chronic systemic disorder with multiorgan damage and various clinical manifestations such as oral ulcers, genital ulcers and uveitis. Etiology is still unknown. Some gene polymorphisms have been associated with BD [1]. In addition, a high frequency of circulating Natural Killer T cells (NKT cells) has been found in BD patients respect to patients with other inflammatory uveitis such as Vogt-Koyanagi-Harada disease (VKH) [2].
Objectives: The objective of this study was to characterize the cytotoxic profile of circulating Nautral Killer (NK) and NKT cells in BD patients.
Methods: Peripheral Blood Mononuclear Cells (PBMCs) were collected from 23 BD patients (according to 1990 ISGB criteria), 7 VKH patients (according to 2001 Revised Diagnostic Criteria) and 9 healthy subjects [3,4]. BD activity was evaluated with BD Current Activity Form 2003. Anti-CD56 and anti-CD3 antibodies were used to identify NK ($CD56^+CD3^-$) and NKT ($CD56^+CD3^+$) cells by flow-cytometry. Expression of one inhibiting receptor (NKG2A) and five activating receptors (CD16, CD69, NKG2D, Nkp30 and Nkp46) was determined on the surface of NK and NKT cells. Cytotoxic potential of NK and NKT cells was assessed through incubation of PBMCs with K526 cells in presence or absence of IL-15 followed by flow-cytometry detection of the surface marker CD107a on NK and NKT cells [5].
Results: A higher frequency of NKT cells was detected in peripheral blood of BD patients than VKH patients. Compared to healthy subjects, an increased proportion of CD16 positive NKT cells was found in BD patients. Furthermore it was observed a higher percentage of NKG2D positive cells in both NK and NKT lymphocytes. No difference in the other markers was detected. In BD patients, the incubation of PBMCs with K562 cells in absence of IL-15 induced a higher percentage of NK cells expressing CD107a compared to VKH patients. Frequency of CD107a positive NKT cells was $<1\%$ and similar between groups. Finally, no differences were found between BD patients with active and inactive phase of the disease.
Conclusions: Our study confirms previous reports about an increased level of NKT cells in peripheral blood of BD patients, but we additionally identified a cytotoxic profile of NK and NKT cells characteristic of BD patients when compared to healthy subjects and patients with VKH. Our data revealed for the first time a potential involvement of NKG2D in the pathogenesis of BD. We can speculate that NK and NKT cells of BD patients are more prone to respond to stress/danger signals when exposed on target cells leading to cyclic auto-inflammation.
References:
[1] Ombrello MJ. Et al. Proc Natl Acad Sci U S A. 2014, 111:8867–72.
[2] Hamzaoui K. et al. J Neuroimmunol. 2006, 175:160–8.
[3] International Study Group for Behçet's Disease. Lancet 1990, 335:1078–80.
[4] Read RW. et al. Am J Ophtalmol. 2001, 131:647–52.
[5] Alter G. et al. J Immunol Methods. 2004, 294:15–22.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3493

AB0023 ASSOCIATION BETWEEN MEX-SLEDAI AND INFECTIONS WITH MBL STRUCTURAL AND PROMOTER GENOTYPES IN MEXICAN-MESTIZO PATIENTS

M.A. Villarreal-Alarcón[1], J.A. Esquivel-Valerio[2], D. Vega-Morales[2], R. Ortiz-Lopez[3], A. Rojas-Martínez[3], A.C. Arana-Guajardo[2], M.A. Garza-Elizondo[2]. *[1]Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Monterrey, -; [2]Rheumatology Service; [3]Rheumatology, Hospital Universitario Dr. José Eleuterio González, Monterrey, Mexico*

Background: The mannose-binding lectin protein (MBL) is a multimeric molecule with a structure that is the analogue to the C1q protein. Deficient and low MBL concentrations in serum are due to the presence of mutations in the structural or promoter region
Objectives: To investigate the role of alleles and haplotypes of MBL2 gene in the clinical expression of systemic lupus erythematosus (SLE) and its association with infections in Mexican-mestizo patients.
Methods: An observational, cross-sectional, retrospective study. We included 74 SLE patients and 75 matched controls. All $\geq$16 years-old who met at least four 1982 or revised 1997 ACR criteria for SLE were included. The association of MBL locus haplotypes with disease activity and past history of infection was studied in those patients. Allele and haplotype determinations in the promoter and structural regions of the MBL2 gene were performed from genomic DNA isolated peripheral blood. Probes were sent to Invitrogen (Carlsbad, California) for synthesis. The disease activity was determined by MEX-SLEDAI. Infections were categorized arbitrarily if patients had $\geq$4 events. The associations between the codons, clinical activity, and having $\geq$4 infection events were by odds ratio.
Results: There were 13/73 (17.8%) SLE patients with $\geq$4 infections. The presence of homozygous C/C codon 57 was observed to be greater risk for SLE activity and

present more than 4 infections. The significance of heterozygous HYLX promoter was observed only for the presence of infection. Table 1.

Table 1. Association between MEX-SLEDAI and Infections with MBL structural and promoter genotypes in SLE patients

	MEX-SLEDAI median (IQR)	p*	Patients with infections events ≥4, n (%)	Total patients with infections events ≥4, n (%)	p**	OR
Codon 52, n=71		0.68		12 (16.9)	0.44	
A/A	3 (6)		10 (17.5)			
A/D	3 (8)		0 (0)			
D/D	1 (7)		2 (25)			
Codon 57, n=73		0.02		13 (17.8)	0.03	8.7 (1.2–58)
A/A	2 (6)		10 (14.7)			
A/C	0 (0)		0 (0)			
C/C	9 (0)		3 (60)			
Promoter, n=74		0.35		13 (17.6)	0.01	
HYHY	3 (7)		2 (18.2)			
LYLY	2 (8)		5 (21.7)			
LXLX	1.5 (6)		1 (4.8)			
LXLY	2.5 (5)		2 (13.3)			
HYLY	5 (0)		1 (50)			
HYLX	0 (0)		2 (100)			

MEX-SLEDAI: Mexican Systemic Lupus Erythematosus Disease Activity Index, IQR: interquartile range, OR: Odds ratio. *Kruskal–Wallis H test, ** Chi-square test.

Conclusions: MBL2 gene polymorphisms of the homozygous C/C in codon 57 of the structural region and heterozygous HYLX of the promoter region are associated with increased risk of a higher number of infections. Also, we observed that homozygous C/C in codon 57 was asociated to a higher MEX-SLEDAI.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3304

AB0024 A NOVEL REAL-TIME IMAGING TECHNIQUE TO CHARACTERIZE MECHANISMS OF CELL DEATH IN NEUTROPHILS

S. Gupta[1], D.W. Chan[1], K.J. Zaal[2], E. Ralston[2], M.J. Kaplan[1]. *[1]Systemic Autoimmunity Branch; [2]Light Imaging Section, NIAMS/NIH, Bethesda, United States*

Background: Neutrophils play a key role in the pathogenesis of autoimmune diseases through various mechanisms including the formation of neutrophil extracellular traps (NETs). NETosis, a recently described distinct form of program neutrophil cell death, is characterized by reactive oxygen species generation, chromatin and nuclear decondensation, membrane rupture and extrusion of a meshwork of chromatin bound to granule peptides.
Objectives: Techniques to assess and quantitate NETosis in an unbiased, reproducible and efficient way are lacking. We developed a new method to automatically quantify the percentage of neutrophils undergoing NETosis using real-time quantitative live-cell analysis with IncuCyte ZOOM™ (Essen BioScience, Inc.) platform and a dual-dye system dependent on membrane integrity to stain DNA, to image neutrophils and characterize their mechanisms of cell death.
Methods: Neutrophils were isolated from healthy controls using density gradient methods and their DNA was stained with a membrane permeable NUCLEAR-ID Red DNA dye. Neutrophils were plated and incubated with various stimuli to induce NETosis (PMA, ionomycin and/or SLE sera), apoptosis (Staurosporin) or necroptosis (TNF with a pan-caspase inhibitor, Z-VAD) and with Sytox, a membrane-impermeable DNA dye. Three 20x magnification images from different areas per well were captured at 10-minute intervals. A processing definition was set and optimized to count all neutrophils (NUCLEAR-ID stained) at baseline and neutrophils undergoing cell death (Sytox stained) at three hours using fluorescence intensity and stained area size (Figure 1).

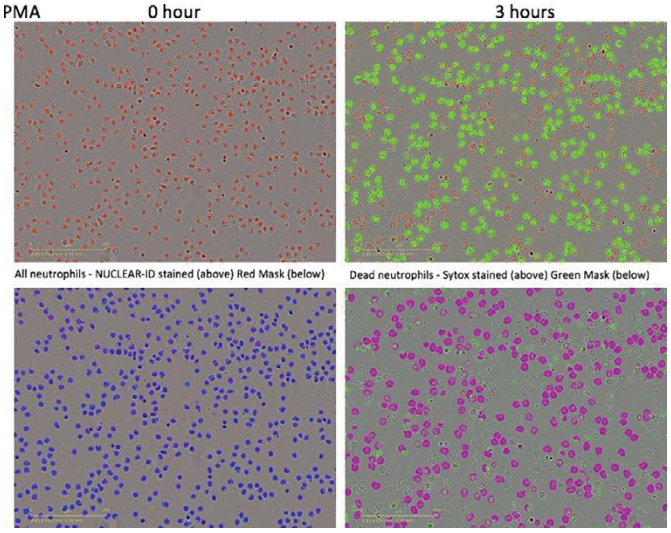


Figure 1

Results: Percentage of neutrophils undergoing cell death using various stimuli was highly reproducible. Characterization of changes in nuclear morphology, quantified by the processing definition, distinguished between NETosis, apoptosis and necroptosis. Findings were confirmed and counts correlated with previously established method using immunofluorescence microscopy.
Conclusions: This novel real time assay distinguishes types of neutrophil cell death and quantifies NETosis in a rapid, accurate and reproducible way. This technique may facilitate studies in neutrophil biology.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3593

AB0025 PREGNANCY RESULTS IN THE SELECTIVE MODULATION OF PLATELET TISSUE FACTOR EXPRESSION INDEPENDENTLY OF THE PRESENCE OF ANTIPHOSPHOLIPID ANTIBODIES OR OF OTHER AUTOIMMUNE FEATURES

V. Canti[1], M.T. Castiglioni[2], M. Angelo A[2], P. Rovere-Querini[2], N. Maugeri[2]. *[1]San Raffaele Scientific Institute, Milano, Italy; [2]via Olgettina 58, San Raffaele Scientific Institute, Milano, Italy*

Background: Neutrophils and platelets are key innate immune cells that productively interact upon activation, generating/releasing moieties that can damage the bystander tissue and prompt vasculogenesis. Successful pregnancy critically depends on a tight regulation of the latter events. Conversely pregnancy complications are associated with alteration/damage of the vasculature associated to the placenta. Blood-born tissue factor (TF) due to the expression of the moiety by platelets and leukocytes has been involved in the pro-thrombotic diathesis associated with sustained human autoimmunity, including that associated with anti-phospholipid syndrome (APS).
Objectives: To test the modulation of parameters related to blood-born TF during normal and pathological pregnancy
Methods: The expression of TF by platelets, monocytes and neutrophils has been studied in 40 women at the 12th week of gestation (wg) including twelve healthy women, 14 patients with insulin-dependent diabetes mellitus (IDDM) and 14 patients with a previous history of pregnancy complications, six of them with APS. 30 healthy age-matched non-pregnant women served as controls. When possible, patients were studied again at least one year after the pregnancy completion. Blood samples were collected and processed as described[1,2]. Other features reflecting cell activation were assessed in parallel[1,2].
Results: The expression of platelet TF was significantly higher in pregnant women compared with age-matched controls. Platelet P-selectin was as well significantly up-regulated. Neutrophils circulating in all pregnant women were mildly degranulated. The content of the neutrophil secondary granules was depleted in particular in subiects with previous pregnancy complications *sine causa*.
Conclusions: Our data support the contention that the activation of the innate immune system is a key feature of pregnancy, regardless of the presence of features of systemic or organ-specific autoimmunity. This implies an important modulation of the machinery involved in the reciprocal activation of platelets and neutrophils and in the pro-thrombotic phenotype of circulating cells. The analysis of the potential modulation of these parameters by ongoing treatment is currently being carried out.
References:
[1] Manfredi A & al. Ann Rheum Dis. 2016;75(8):1511–20. doi: 10.1136/annrheumdis-2015-208442.
[2] Maugeri N et al. Blood. 2011 Sep 22;118(12):3359–66. doi: 10.1182/blood-2011-02-337337.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6429

Cytokines and inflammatory mediators

AB0026 CHEMOKINE SIGNALS ARE CRITICAL FOR HOMING AND ENHANCED DIFFERENTIATION OF CIRCULATING OSTEOCLAST PROGENITOR CELLS

A. Sucur[1], Z. Jajic[2], M. Artukovic[3], M. Ikic Matijasevic[3], F. Grubisic[2], B. Anic[4], S. Ivcevic[1], D. Flegar[1], D. Grcevic[1]. *[1]Department of Physiology and Immunology, University of Zagreb School of Medicine; [2]Department of Rheumatology, Physical Medicine and Rehabilitation, Clinical Hospital Center "Sestre Milosrdnice", University of Zagreb School of Medicine; [3]Department of Clinical Immunology and Pulmology, Clinical Hospital "Sveti Duh"; [4]Department of Clinical Immunology and Rheumatology, Clinical Hospital Center "Zagreb", Zagreb, Croatia*

Background: Peripheral blood (PB) monocyte pool contains cells capable of differentiating into osteoclasts (OCs). These osteoclast progenitors (OCPs) contribute to osteoresorption in inflammatory arthritides under influence of the cytokine milieu and chemokine mediated trafficking.

Objectives: Our study aimed to define chemokine receptor profile of peripheral OCPs in rheumatoid arthritis (RA), with comparison to psoriatic arthritis (PSA), as well as their susceptibility to chemotactic signals.
Methods: 129 RA, 53 PSA and 110 control patients were enrolled after Ethical approval. PB samples and synovial fluid (SF) samples, with clinical data of disease activity, inflammation and autoantibody levels were collected. Patients starting anti-TNF therapy were followed up 6 months. TNF-α and CTX serum levels were measured by ELISA. Frequency of OCP-rich subpopulation (CD3-CD19-CD56-CD11b+CD14+), expression of OC differentiation (CD115, RANK) and chemokine (CCR1, CCR2, CCR4, CXCR4) receptors was assessed by flow cytometry. OCPs were sorted using FACS, cultured with M-CSF and RANKL, stained for TRAP enzyme and mature OCs counted. Levels of CCL2, CCL3, CCL4, CCL5, CXCL9 and CXCL10 were measured using cytometric bead array, and of CXCL12 by ELISA. Osteoclastogenic effects of CCL2, CCL5 and CXCL10 were analyzed in cell culture, and chemotactic effects on OCPs were studied by cell migration assay using Transwell, with count of number of migrated cells and subsequently differentiated mature osteoclasts.
Results: OCP population was moderately enlarged in PB, further expanded in SF and correlated with TNF-α and rheumatoid factor (RF) levels in patients with RA. However, sorted OCPs generated similar number of mature OCs as control. RANK+ subpopulation was enlarged in SF vs PB and correlated with number of tender joints. In PSA, the OCP population was not enlarged, but had a higher RANK expression. OCPs in RA and PSA had higher expression of CCR1, CCR2, CCR4, CXCR4, and all except CCR4 showed positive PB-to-SF gradient. RA had higher levels of CCL2, CCL3, CCL4, CCL5, CXCL9 and CXCL10, with a positive PB-to-SF gradient for all except CCL5 and CXCL9. OCP frequency correlated with levels of CCL2 and CCL5. Subset expressing CXCR4 was associated with TNF-α, CTX and RF levels and was lower in patients treated with DMARD, who at the same time had lower osteoresorption (CTX). Subset expressing CCR4 showed significant negative trend during anti-TNF treatment. CCL2, CCL5 and CXCL10 showed significant osteoclastogenic effect. CCL5 showed greatest chemotactic effect, attracting the highest number of cells in the migration assay. At the same time, attracted cells possessed greater osteoclastogenic potential.
Conclusions: Our study provides evidence of the specific importance of certain chemokine signals for stimulation of OCP mobilization, subsequent tissue homing, and maturation, explaining local as well as generalized bone loss seen in RA. Novel insights in regards to migratory behavior and functional properties of PB OCPs in response to chemotactic signals could open way to new therapeutic targets in RA.
Acknowledgements: This work was supported by a grant from the Croatian Science Foundation (project number 5699).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2317

AB0027 EXPRESSION DENSITY OF RECEPTORS TO TNF-ALPHA IS ASSOCIATED WITH DAS-28 SCORE IN RHEUMATOID ARTHRITIS

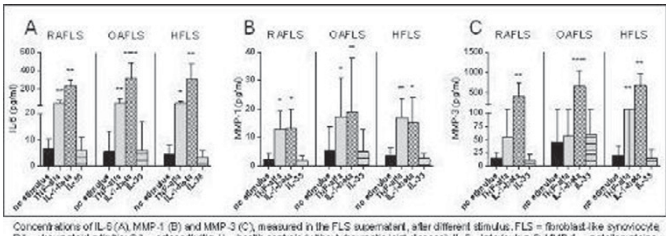
A.A. Alshevskaya[1], J. Lopatnikova[1], N. Shkaruba[1], O. Chumasova[1], A. Sizikov[1], V. Lukinov[2], A. Moskalev[2,3], S. Sennikov[1]. [1]*Federal State Budgetary Scientific Institution "Research Institute of Fundamental and Clinical Immunology"; [2]EOL Labs Ltd; [3]Biostatistics and Clinical Trials Center, Novosibirsk, Russian Federation*

Background: For a number of cytokines and growth factors density of receptors expression has been shown to be important in regulation of action intensity and variation. Although TNF-alpha is actively involved in the development and progression of chronic inflammation in rheumatoid arthritis (RA) role of membrane receptors and their regulatory function in RA remains unclear.
Objectives: To assess associations of membrane-bound receptors expression and soluble receptors and cytokine content with disease activity score in patients with rheumatoid arthritis.
Methods: To reveal linear relationships among integrated score DAS-28 and studied parameters of intact T-cells, B-cells and monocytes (evaluated by flow cytometry) and parameters of mediators soluble content (evaluated by ELISA) building of multiple linear regression model (MLRM) with a standard assessment of the regression coefficients by least squares method were used. To determine receptor number on the cells QuantibritePE Beads (BD) were used.
Results: For the group of patients with acute stage of RA MLRMs with best statistical quality characteristics revealed that for lymphocytes both TNFR1 and TNFR2 number had significant associations with DAS-28; for monocytes only number of TNFR2 was significant. Lower DAS-28 index is associated with higher number of TNFR2 per cell and lower number of TNFR1.
Comparison of models with different combinations of studied TNFR-parameters revealed that percentages of cells expressing receptors for TNFα validated not more than 20% of DAS-28 variation, while the number of receptors indicators on cells validated 40–50% of DAS-28 variation. Full MLRM with all 15 studied parameters validated about 70% of DAS-28 variation.
For the group of patients with acute stage of RA MLRMs with best statistical quality characteristics revealed that for lymphocytes both TNFR1 and TNFR2 number had significant associations with DAS-28; for monocytes only number of TNFR2 was significant. Lower DAS-28 index is associated with higher number of TNFR2 per cell and lower number of TNFR1. Comparison of models with different combinations of studied TNFR-parameters revealed that percentages of cells expressing receptors for TNFα validated not more than 20% of DAS-28 variation, while the number of receptors indicators on cells validated 40–50% of DAS-28 variation. Full MLRM with all 15 studied parameters validated about 70% of DAS-28 variation.
Conclusions: Number of receptors to TNF-alpha is more associated with RA activity score as compared with soluble receptors or cytokine. Number of receptors type 1 and type 2 to TNF-alpha per cell have opposite influence on disease activity score. Our findings indicate the involvement of receptors expression density changes in the pathological process in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2643

AB0028 FIBROBLAST-LIKE SYNOVIOCYTES MAY NOT BE THE TARGET OF IL-33 IN THE JOINT PHISIOPATHOLOGY

C.R.L. Machado[1], G.G. Resende[2], R.B.V. Macedo[2], V.C. Nascimento[2], T.P. Silva[2], A.M. Kakehasi[2], M.V.M. Andrade[2]. [1]*Universidade Federal Minas Gerais; [2]Universidade Federal de Minas Gerais, Belo Horizonte, Brazil*

Background: Rheumatoid arthritis (RA) and osteoarthritis (OA) are chronic joint diseases in which fibroblast-like synoviocytes (FLS) actively participate in the synovitis- damage cycle, trough production of cytokines such as IL-6 and metalloproteinases (MMPs)[(1)]. It has already been showed that serum IL-33 levels correlated with disease activity in RA[(2)]. IL-33 is capable to enhance TNF-α effects in FLS[(3)]. In the collagen-induced arthritis (CIA) model, the injection of IL-33 exacerbated the disease[(4)]. Since ST2 receptor is expressed in FLS, it is hypothesized that IL-33 could activate FLS and increase downstream production of inflammatory cytokines.
Objectives: To evaluate the production of IL-6, MMP-1, and MMP-3 by FLS stimulated with IL-33, TNF-α, and IL-1β.
Methods: FLS were cultured from samples of synovial fluid and tissue of OA patients (OAFLS n=8), RA patients (RAFLS n=3), and patients without rheumatic disease (health) (HFLS n=4). FLS were stimulate with TNF-α at concentrations of 1; 5; 10 and 50 ng/ml, IL-1β at concentrations of 0.1; 0.2; 0.3; 0.5 and 1 ng/ml and IL-33 at concentrations of 1; 3; 10; 30; 100 ng/ml, soon after, IL-6, MMP-1, and MMP-3 levels were evaluated by ELISA, in the cell supernatant.
Results: MMP-1, MMP-3 and IL-6 were constitutively expressed by FLS at baseline in all groups. Both TNF-α and IL-1β stimulated the production of IL-6 and MMP-1 with statistical significance in a dose-dependent manner in all three groups. Only IL-1β increased the production of MMP-3. TNF-α stimulated the production of MMP-3 only on HFLS. There was no difference between the concentration of MMP-1, MMP-3 and IL6 in the supernatant of OAFLS, ARFLS and HFLS when IL-33 stimulated and non-stimulated were compared.



Concentrations of IL-6 (A), MMP-1 (B) and MMP-3 (C), measured in the FLS supernatant, after different stimulus. FLS = fibroblast-like synoviocyte; RA = rheumatoid arthritis; OA = osteoarthritis; H = health controls (without rheumatic joint disease); IL-6 = Interleukin-6; MMP-1 = metalloproteinase-1; MMP-3 = metaloproteinase-3; TNF-alpha = Tumor Necrosis Factor-alpha; IL-1-beta = Interleukin-1-beta; IL-33 = Interleukin-33. * p < 0.05; ** p < 0.01; *** p < 0.001; **** p < 0.0001.

Conclusions: This study demonstrated that IL-33 failed to induce the production of IL-6, MMP-1 and MMP-3 by FLS of different diseases sources, suggesting that must be another cell type that plays the role of target to IL-33 in physiopathology of joint inflammation. The absence MMP-3 in response to TNF-α stimulus in RAFLS and OAFLS could be explain by saturation of this cytokine in synovial cells from these diseases.
References:
[1] Bartok B, Firestein GS. Fibroblast-like synoviocytes: key effector cells in rheumatoid arthritis. Immunological reviews. 2010;233(1):233–55.
[2] Matsuyama Y, Okazaki H, Tamemoto H, Kimura H, Kamata Y, Nagatani K, et al. Increased levels of interleukin 33 in sera and synovial fluid from patients with active rheumatoid arthritis. The Journal of rheumatology. 2010;37(1):18–25.
[3] Kunisch E, Chakilam S, Gandesiri M, Kinne RW. IL-33 regulates TNF-alpha dependent effects in synovial fibroblasts. International journal of molecular medicine. 2012;29(4):530–40.
[4] Xu D, Jiang HR, Kewin P, Li Y, Mu R, Fraser AR, et al. IL-33 exacerbates antigen-induced arthritis by activating mast cells. Proceedings of the National Academy of Sciences of the United States of America. 2008;105(31):10913–8.
Acknowledgements: Capes, Fapemig and Fundo de Apoio a Pesquisa e Ensino da Sociedade Brasileira de Reumatologia - FAPE-SBR.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6673

AB0029 ANTI INFLAMMATORY EFFECT OF PDE5 INHIBITION: SCOPE FOR A NEW POTENTIAL INDICATION IN SSC ASSOCIATED MYOSITIS

C. Corinaldesi[1,2], G. Abignano[1,3], C. Antinozzi[2], V. Riccieri[4], G. Valesini[4], M. Vasile[4], F. Marampon[2], A. Lenzi[4], K. Ballard[5], F. Del Galdo[1,3], C. Crescioli[2]. *[1]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom; [2]University of Rome Foro Italico, Rome, Italy; [3]NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; [4]Sapienza University of Rome, Rome, Italy; [5]Myriad RBM, Austin-TX, United States*

Background: Skeletal muscle damage can occur as clinical manifestation of Systemic Sclerosis (SSc) [1], and it is known to be associated to type I IFN pathway activation [2]. The type I IFN-induced chemokine CXCL10 is associated with a more severe SSc prognosis and skeletal muscle disease [3,4], and it has been reported to play a role in inflammatory myopathy (IM) and in diabetic cardiomyopathy (DCM) [5,6]. In DCM the phosphodiesterase type 5 inhibitor (PDE5i) sildenafil significantly decreased CXCL10 systemic and cellular release [7]. In SSc, sildenafil is used to treat pulmonary artery hypertension (PAH) and digital ulcers disease.
Objectives: To determine the serum levels of CXCL10 in SSc patients with or without muscle involvement and treated or not with sildenafil. To determine the role of sildenafil on IFNγ+TNFα-induced CXCL10 release in human skeletal muscle cells (Hfsmc).
Methods: Sera from 109 patients fulfilling ACR/EULAR 2013 classification criteria for SSc and 34 age and gender matched healthy controls (HC) were analysed by multiplexed, bead-based immunoassay. Hfsmc were cultured and analysed as previously described [5].
Results: CXCL10 serum level was significantly higher in SSc vs. HC (602.1±155.1 pg/ml vs 197.5±14.9 pg/ml, $P<0.001$) independently of diffuse or limited clinical subset ($p>0.05$); the presence of sildenafil in therapeutic regimen was associated with lower serum CXCL10 (455.2±211.8 pg/ml vs 633.1±183.02 pg/ml, $P<0.05$). CXCL10 was significantly higher in patients with increased Creatine Kinase (CK) (2703±2172 vs 454±82.51, $P<0.01$) and its concentration strongly correlated with the levels of CK ($r=0.986$, $P<0.001$) and with Medsger muscle Severity score ($r=0.445$, $P<0.001$). *In vitro*, sildenafil suppressed IFNγ+TNFα-induced CXCL10 release by Hfsmc in a dose dependent manner, down to 50% secretion at 1mM ($P<0.05$). The inhibition of CXCL10 secretion was associated with significant reduction in cytokine-induced STAT1, NFKB and JNK phosphorylation ($P<0.01$).
Conclusions: High CXCL10 level is associated with SSc independently from local or diffuse clinical subset and is lower in patients assuming sildenafil independently of other therapies. The strong correlation of CXCL10 and severity of muscle damage as assessed by serum CK and Medsger Muscle severity score, strongly indicate/confirm the involvement of IFN-I pathway activation during myositis in SSc. The direct inhibitory effect of PDE5 inhibitor Sildenafil on proinflammatory induced CXCL10 secretion warrant further research on the potential role of PDE5 inhibitors as disease modifying agents in SSc.
References:
[1] Varga J et al., J Clin Invest 2007, 117: 557–67.
[2] Higgs BW et al., Ann Rheum Dis 2011, 70:2029–36.
[3] Corrado A, Clin Ter 2014, 165:e436–41.
[4] Liu X et al., Arthritis Rheum 2013, 65:226–35.
[5] Crescioli C et al. Eur J Cell Biol. 2012,91:139–49.
[6] Di Luigi L et al., PLoS One. 2013 Oct 30;8(10):e77745.
[7] Di Luigi et al., Inflammation 2016,39(3):1238–52.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6233

AB0030 THE EFFECT OF SILDENAFIL AND ILOPROST ON CXCL10 LEVEL IN SYSTEMIC SCLEROSIS: IN VIVO AND IN VITRO COMPARISON

C. Antinozzi[1], C. Corinaldesi[2], F. Marampon[1], V. Riccieri[3], G. Valesini[3], M. Vasile[3], A. Lenzi[4], F. Del Galdo[5], C. Crescioli[1]. *[1]University of Rome, Foro Italico, Rome, Italy; [2]University of Leeds, Leeds, United Kingdom; [3]University of Rome, Sapienza; [4]University of Rome Sapienza, Rome, Italy; [5]Univerisity of Leeds, Leeds, United Kingdom*

Background: Th1 cell/cytokine repertoire contributes to systemic sclerosis (SSc) pathogenesis from early autoimmune/vascular stages while Th2 dominance prevails later, when (multi)organ fibrosis occurs [1]. The Th1-type chemokine IFNγ-induced 10 kDa protein (CXCL10), involved in several autoimmune diseases (thyroiditis, rheumatoid arthritis, systemic lupus erythematosus, inflammatory myopathy) exerts detrimental effects at systemic and tissue/cell level; it is reported in association with more severe SSc prognosis [2–4].
Objectives: To compare circulating CXCL10 level in SSc patients starting iloprost (I), prostacyclin analogue with or without sildenafil (S), phosphodiesterase type 5 inhibitor, both vasoactive drugs used in SSc for Raynaud's phenomenon digital ischemic ulcers and/or secondary pulmonary arterial hypertension; SSc subjects under immunosuppressants (DMARDs) or corticosteroids (CCs) - first choice treatments at disease onset - before and after I were also evaluated. Intracellular path activation underlying Th1 cytokine-induced CXCL10 release by human skeletal muscle cells (Hfsmc), endothelial cells (Hfaec), cardiomyocytes (Hfcm) and fibroblasts (hFbs) were compared after iloprost or sildenafil.
Methods: Sera of 27 SSc patients satisfying ACR/EULAR 2013 classification criteria for SSc were analyzed by ELISA before (T0, baseline) and 3 months after I intake (T3) vs. 15 age/gender-matched healthy subjects. Protein extracts from different human cell types were tested by Western blot for IFNγ+TNFα-induced NFkB, Stat1, JNK activation after S or I.
Results: CXCL10 serum level was higher in all SSc under each drug/drug combination (range ~300–500 pg/ml) vs. healthy subjects (~150 pg/ml, $P<0.05$). I intake did not modify baseline CXCL10 in SSc subjects taking only I, DMARDs or CCs, while it significantly decreased CXCL10 in subjects under S (~150 pg/ml, $P<0.05$). In Hfsmc S-induced inhibition of Stat-1/NFkB/JNK phosphorylation was higher vs. I (67/66/66% S vs. 28/30/38% I $P<0.01$). In Hfaec inhibition of Stat1/NFkB phosphorylation was higher and virtually prevented with I (99/92% I vs. 58/66% S $P<0.01$); conversely S-induced inhibition on JNK activation was significantly higher (66% S vs. 20% I $P<0.01$). In Hfcm I-induced inhibition was stronger on Stat1/JNK phosphorylation (67/83% I vs. 33/52% S $P<0.05$/$P<0.01$), while inhibition on NFkB was similar (70% I vs. 71% S). In hFbs, neither S nor I affected IFNγ+TNFα-induced activation of each analyzed path.
Conclusions: Our *in vivo* results show that S and I combination is the more effective in targeting circulating CXCL10 in SSc patients. Our *in vitro* findings show a different inhibitory drug-induced effect onto paths underlying CXCL10 production, depending on cellular/intracellular targets. Thus, we suggest I and S combination as potential pharmacological tool in SSc not limited to treat vascular dysfunction but likely helpful to control different cell/tissue involvement and damage.
References:
[1] Pattanaik D et al., Front Immunol 2015.
[2] Eloranta ML et al., Ann Rheum Dis 2010.
[3] Corrado A, Clin Ter 2014.
[4] Liu X et al., Arthritis Rheum 2013.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6638

AB0031 IL37 INHIBITS GAG RELEASE FROM HUMAN OA CARTILAGE EXPLANTS

E. Van Geffen, A. van Caam, H. van Beuningen, E. Vitters, C. Dinarello, E. Blaney Davidson, P. van der Kraan. *Radboud Univeristy Medical Center, Nijmegen, Netherlands*

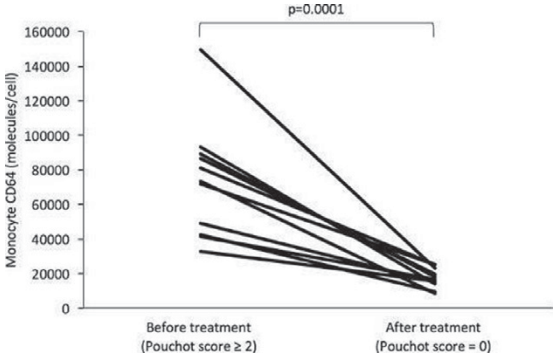
Background: In healthy cartilage, there is a balance between anabolic and catabolic activities of chondrocytes that maintains the functional integrity of the extracellular matrix. However, during osteoarthritis (OA), chondrocytes become more catabolically active and express increased levels of matrix degrading enzymes, such as MMPs and ADAMTSs. Increased MMP and ADAMTS activity results in a net loss of the extracellular matrix and therefore leads to cartilage damage. Previously, we found that the anti-inflammatory cytokine Interleukin 37 (IL37) is able to counter-regulate the catabolic status of chondrocytes by reducing the IL1β-driven expression of pro-inflammatory cytokines and catabolic enzymes.
Objectives: The goal of this study was to investigate, in human OA cartilage explants, the effect of IL37 on sulfated glycosaminoglycans (GAG) content and synthesis of extracellular matrix molecules and cartilage degrading enzymes to investigate its therapeutic potential in OA.
Methods: Human cartilage was obtained from eighteen OA patients undergoing total knee or hip arthroplasty. Biopsy punches of 4 mm in diameter were made to equalize explant size. After culturing overnight, explants were incubated for 48 h with three doses (1, 10 or 100 ng/ml) of recombinant-human IL37 (rhIL37). In the supernatant of the explant cultures, GAG release was measured with the DMB assay and levels of the ARGS neoepitope, which is one of the products of aggrecan degradation by ADAMTS5, were detected using Western Blot. Furthermore, gene and protein expression of extracellular matrix molecules and cartilage degrading enzymes were measured. Nitric oxide (NO), an important effector molecule that may suppress cartilage matrix synthesis, levels were measured in the supernatant of the explants culture using Griess reagens.
Results: Adding rhIL37 (100 ng/ml) to OA cartilage explants caused a highly significant reduction in GAG release to the supernatant of, on average, 32% in eighteen donors (Figure 1). Gene expression of the matrix molecules aggrecan and collagen type II was not affected, indicating that this effect of rhIL37 was not due to a loss of aggrecan synthesis. Another mechanism to prevent GAG release in cartilage is via inhibition of NO synthesis, but NO levels in the supernatant were comparable between rhIL37 treated groups and the control group. In contrast, after addition of rhIL37, ARGS neoeptiope levels, which reflect ADAMTS5 activity, were dose-dependently down regulated in the supernatant. Furthermore, protein analysis of the explants showed that rhIL37 reduced ADAMTS5 levels. These data indicate that IL37 interferes with the amount active matrix degrading enzymes in the cartilage matrix. However, gene expression of ADAMTS5 was not affected by rhIL37, indicating that the effect of IL37 on ADAMTS5 is post translational.
Conclusions: Our data show that rhIL37 reduces GAG release by OA cartilage explants. The mechanism behind this protective effect of IL37 probably runs via a reduction in ADAMTS5 abundance in the cartilage matrix, which is the main aggrecanase involved in OA This effect of IL37 on ADAMTS5 is probably post translational. Our data indicate that IL37 can maintain cartilage matrix integrity

under OA conditions and is able to reduce the severity of cartilage destruction during OA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3689

AB0032 UPREGULATION OF CD64 EXPRESSION ON MONOCYTES IN PATIENTS WITH ACTIVE ADULT-ONSET STILL'S DISEASE: A POSSIBLE BIOMARKER FOR ASSESSING DISEASE ACTIVITY

E. Oguro[1], T. Shimizu[1], A. Kikuchi-Taura[2], S. Tsuji[1], Y. Okita[1], M. Shigesaka[1], H. Matsuoka[1], T. Nii[1], S. Teshigawara[1], E. Kudo-Tanaka[1], Y. Harada[1], M. Matsushita[1], S. Ohshima[2], Y. Saeki[2]. *[1]Department of Rheumatology and Allergology; [2]Department of Clinical Research, NHO Osaka Minami Medical Center, Osaka, Japan*

Background: Adult-onset Still's disease (AOSD) is a systemic inflammatory disease of unknown etiology. Overproduction of multiple inflammatory cytokines and subsequent hyperactivation of monocytes/macrophages are prominent characteristics of AOSD. However, there are no convenient and precise methods for evaluating monocyte/macrophage activation in AOSD. We previously reported that monocyte CD64 (mCD64) expression could be quantitatively measured by flow cytometry and its expression was tightly correlated with the activity of systemic lupus erythematosus.
Objectives: We examined the association between mCD64 expression and AOSD disease activity.
Methods: This was a prospective, single-center, observational study conducted between January 2013 and December 2016. Eleven active AOSD patients who fulfilled the Yamaguchi's criteria for AOSD and had the modified Pouchot score of $\geq$2 were enrolled. The mCD64 expression levels were quantitatively measured by flow cytometry and individually assessed both before (Pouchot score $\geq$2) and after treatment (score 0). Other disease-related laboratory data, such as C-reactive protein, ferritin, and white blood cell count, were simultaneously measured. As a control, 16 active systemic lupus erythematosus (SLE) patients (SLE disease activity index $\geq$6), 22 active rheumatoid arthritis (RA) patients (disease activity score with 28-joint counts $>$3.2), and 20 healthy controls (HC) (female, 55%; mean age, 38.7±9.1 years) were enrolled. Statistical analysis was performed by the Mann-Whitney and Wilcoxon-paired tests.
Results: The median mCD64 expression levels were 73,339 [interquartile range (IQR), 45,861–88,181] and 16,443 (IQR, 45,891–88,181) molecules/cell before and after treatment, respectively. Thus, mCD64 expression levels were significantly decreased during the inactive phase compared with those in the active phase in AOSD (p=0.0001). The mCD64 expression levels were significantly higher in patients with active AOSD than in those with active SLE [34,648 (IQR, 44,204–24,657) molecules/cell, p=0.001], active RA [25,167 (IQR, 35,778–22,301) molecules/cell, p$<$0.0001], and in HC [14,174 (IQR, 13,413–17,774) molecules/cell, p$<$0.0001].



Conclusions: These results suggest that mCD64 expression levels are highly upregulated in AOSD and tightly correlated with disease activity. The mCD64 expression level may be a useful biomarker for assessing the disease activity of AOSD.
References:
[1] Rau M, et al. J Rheumatol. 2010 Nov;37(11):2369–76.
[2] Kikuchi-Taura A, et al. Lupus. 2015 Sep;24(10):1076–80.
[3] Pouchot J, et al. Medicine. 1991;70:118–36.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3337

AB0033 THE IDENTIFICATION OF IL-17A+, IL-17RA+ AND IL-17RC+ LYMPHOID AND MYELOID CELLS IN BLOOD OF TREATMENT NAÏVE EARLY AND IN SYNOVIAL FLUID OF ESTABLISHED PSORIATIC ARTHRITIS PATIENTS

X. Xu[1], N. Davelaar[1], A.-M. Otten-Mus[1], P.S. Asmawidjaja[1], H. den Braanker[1], H. Alves[1], J.P. van Hamburg[1], C. Gaillez[2], J.M. Hazes[3], R. Bisoendial[4], M. Vis[3], F. Kolbinger[5], E. Lubberts[1]. *[1]Rheumatology and Immunology, Erasmus Mc, University Medical Center, Rotterdam, Netherlands; [2]Novartis Pharma AG, Basel, Switzerland; [3]Rheumatology, Erasmus Mc, University Medical Center; [4]Rheumatology, Maasstad Hospital, Rotterdam, Netherlands; [5]Novartis, Basel, Switzerland*

Background: Interleukin (IL)-17A is a pro-inflammatory cytokine and is involved in the pathogenesis of psoriatic arthritis (PsA) (1,2). Various cells can produce IL-17A. However, it is not clear which cell types in PsA patients are responsible for the production of IL-17A. In addition, the expression of IL-17RA and IL-17RC on different cell types is not well defined.
Objectives: To identify IL-17A, IL-17RA and IL-17RC positive cells in blood of first diagnosed PsA patients with arthritis and in synovial fluid of established PsA patients with active disease.
Methods: Fresh blood was taken from first diagnosed DMARD and steroid naïve PsA patients (n=10), having arthritis in 1 or more joints (PsA blood). The diagnosis was made by a rheumatologist according to the CASPAR-criteria. In addition, fresh synovial fluid was obtained from established PsA patients (PsA SF) with active disease (n=10) and treated with either methotrexate (n=3) or adalumimab (n=3) or NSAIDs (n=4). Multicolor flow cytometric analysis was performed on PsA blood and PsA SF. For the detection of IL-17A, IL-17RA or IL-17RC the following antibodies were used: IL-17A-PE (eBioscience), IL-17RA or isotype control IgG1k (both Biolegend), IL-17RC or isotype control IgG2b (both R&D systems). The following markers were used to discriminate between different cell populations: T cell subsets (CD3, CD4, CD8, CD45RO, CCR6, TCR$\gamma\delta$), B cells (CD19), NK cells (CD15-CD16+), neutrophils (CD15+CD16+), monocytes (CD33+CD14+CD16+/-), mast cells (CD117+FcER1a+) and eosinophils (CD15+FcER1a+).
Results: Different lymphoid and myeloid cell types were IL-17A positive in PsA blood of first diagnosed PsA patients such as CD3+, TCR$\gamma\delta$+, CD4+, CD8+ lymphoid cells, CD14+ monocytes and eosinophils. In PsA SF of established PsA patients TCR$\gamma\delta$+ T cells, neutrophils, NK cells and eosinophils were IL-17A positive.
In both groups, no difference in expression of IL-17RA and IL-17RC was found on CD4+, CD8+, CD4+CD45RO+CCR6+/-, TCR$\gamma\delta$+ and CD19+ lymphoid cells compared to their isotype control. In contrast, the expression of IL-17RA and IL-17RC was increased compared to their isotype control on neutrophils and monocytes in PsA blood and on neutrophils, monocytes, mast cells and eosinophils in PsA SF.
Conclusions: These preliminary data show that not only lymphoid cells but also specific myeloid cell types may be sources of IL-17A in PsA. Furthermore, not lymphoid cells but IL-17RA/IL-17RC positive myeloid cells such as monocytes, neutrophils, mast cells and eosinophils may be potential target cells for IL-17A.
Together, these data suggest a more broad, but specific IL-17A-IL-17RA/RC signaling network between different cell types important in the IL-17A-driven pathogenesis of PsA.
References:
[1] Lubberts E. Nat Rev Rheumatol 2015, 11: 415–29.
[2] McInnes IB, et al. Lancet 2015, 386: 1137–46.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5916

AB0034 PARAMETERS OF TOTAL BLOOD COUNT; MIGHT THEY BE INDICATORS OF INFLAMMATION IN RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS?

O.G. Illeez, F. Unlu Ozkan, I. Aktas. *PMR, University of Saglık Bilimleri, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey*

Background: Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are launched as recent markers of inflammation in chronic inflammation principally in cancer and cardiovascular diseases (1–2).
Objectives: Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) are chronic inflammatory disorders marked by variable periods of remissions and relapses.Inflammation is most likely the underlying cause in disability, increased comorbidity therefore need to be closely monitored and kept under control (3).For this reason cost effective, accessible and reliable parameters are needed in daily practice. Our aim is to analyze the relation between inflammation and NLR and PLR which are easily calculated from whole blood count parameters.
Methods: Medical records of 425 subjects were analyzed retrospectively.Mean age of the subjects was 44,64±14,07 years (17–89 years),52.9% was female (n=225) and 47.1% was male (n=200).105 of them had RA, 216 of them had AS and 104 were healthy controls.2010 ACR/EULAR classification criteria and modified New York criteria were used for the diagnosis of RA and AS.Erythrocyte sedimentation rate (ESR), C reactive protein (CRP) and whole blood count were recorded with simultaneous DAS28 scores of patients with RA and BASDAI scores of patients with AS.
Results: Hemoglobin levels of RA patients were significantly (p$<$0.05) lower then the levels of control group (p=0.001).ESR, CRP, NLR and PLR were significantly higher then the control group respectively (p=0.001, p=0.001, p=0.001, p=0.040).In AS group hemoglobin, ESR, CRP and NLR values were significantly higher then the control group respectively (p=0.001, p=0.006, p=0.001, p=0.001). No difference was detected between AS and control groups in terms of PLR (p$>$0.05).When patients with high disease activity and patients in remission were compared for both RA and AS groups ESR (p=0.001, p=0.001)

and CRP scores (p=0.005, p=0.003) were significantly lower respectively. No statistical significance was found in terms of NLR and PLR (p>0.05).Significant positive correlation was found in RA patients with high disease activity between ESR, CRP, NLR and PLR. In AS patients with high disease activity significant positive correlation was found between ESR, NLR and PLR. No correlation was found between disease activity indices, NLR and PLR.

Conclusions: With the advantage of cost effectiveness and easy calculation NLR and PLR in RA patients, and NLR in AS patients might be used as indicators of inflammation together with ESR and CRP or instances when they are not applicable.Although NLR and PLR are useful in the discrimination of healthy and diseased subjects, they are not sufficient to determine disease activity because not only laboratory parameters but clinical findings and self assessment of the patient are also included in activity measurement.

References:

[1] Yang HB, Xing M, Ma LN, Feng LX, Yu Z.Prognostic significance of neutrophil-lymphocyte ratio/platelet-lymphocyte ratio in lung cancers:a meta-analysis. Oncotarget. 2016 Nov 22;7(47):76769–76778.

[2] Wiwanitkit V. Neutrophil-to-Lymphocyte Ratio,Platelet-to-Lymphocyte Ratio and Heart Failure.Arq Bras Cardiol. 2016 Mar;106(3):265.

[3] Mercan R, Bitik B, Tufan A, Bozbulut UB, Atas N, Ozturk MA, Haznedaroglu S, Goker B. The Association Between Neutrophil/Lymphocyte Ratio and Disease Activity in Rheumatoid Arthritis and Ankylosing Spondylitis. J Clin Lab Anal. 2016 Sep;30(5):597–601.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4800

AB0035 ANGIOPOIETINS: THE MISSING LINK IN POEMS SYNDROME?

F. Coutant[1], Z. Tatar[2], P. Rouzaire[1], B. Evrard[1], A. Dosgilbert[1], O. Tournilhac[3], G. Le Guenno[4], R. Lemal[3], M. Soubrier[2]. *[1]Laboratoire d'Immunologie; [2]Rhumatologie et Immunologie Clinique, CHU Gabriel Montpied; [3]Hématologie Clinique; [4]Médecine Interne, CHU Estaing, Clermont-Ferrand, France*

Background: POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy and Skin changes) is a rare multiorgan disease related to plasma cell dyscrasia. The pathogenesis of the POEMS syndrome is currently unknown, but microangiopathy involving neoangiogenesis and increased vascular permeability may explain some of the features of the disorder. Although vascular endothelial growth factor (VEGF) is constantly highly abundant in the serum of patients with POEMS syndrome, therapeutic approaches targeting the VEGF have led to conflicting results, suggesting that other mediators sharing functional similarities with the VEGF contribute to the pathogenesis. Angiopoietins are known to be involved in the development, remodeling and stability of blood vessels. It is thus tempting to speculate that altered expression of angiopoietins might contribute to the pathogenesis.

Objectives: The aim of this study was to evaluate the circulating levels of three major angiogenic cytokines in patients before and after treatment: VEGF, angiopoietin-1, which plays an essential role in the stabilization and the maturation of blood vessels, and angiopoietin-2 that facilitates angiogenesis in the presence of VEGF.

Methods: Circulating levels of VEGF, Angiopoietin-1 and angiopoietin-2 were determined by ELISA in the serum of 3 patients with POEMS syndrome, before and after therapy. All patients had polyneuropathy, organomegaly, a monoclonal gammopathy (2 IgAl, 1 IgGk) and osteosclerotic lesions. Two patients had typical skin lesions, oedema and one patient had a Castleman disease.

Results: As expected, the serum of patients before treatment exhibited high levels of VEGF (2901±920 pg/mL). Strikingly, angiopoietin-1 levels were highly abundant before treatment (67286±20395 pg/mL) and successful treatment led to a strong reduction in both VEGF and angiopoietin-1. Angiopoietin-1 levels strongly correlated with levels of VEGF (r=0.83). By contrast, angiopoietin-2 levels did not differ significantly before and after treatment.

Conclusions: Thus, angiopoietin-1 seems to be a crucial proangiogenic cytokine overproduced in patients with POEMS syndrome that might explain some of the features of the pathology. The overproduction of VEGF and angiopoietin-1 is likely to promote manifestations encountered in POEMS syndrome such as organomegaly, osteosclerotic lesions or glomeruloid hemangioma. Restoring the balance between angiopoitein-1, angiopoietin-2 and VEGF could constitute a very promising therapeutic strategy in this disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3697

AB0036 ASSOCIATION BETWEEN SYNOVITIS AND INFLAMMATORY CITOKINES SERUM LEVELS IN A COHORT OF PATIENTS AFFECTED BY PRIMARY KNEE OSTEOARTHRITIS

F. Ceccarelli[1], C. Perricone[1], V.A. Pacucci[2], C. Scirocco[1], C. Alessandri[1], G. Valesini[3], F. Conti[3]. *[1]Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma; [2]Reumatologia, Dipartimento Medicina Interna e Specialità Mediche; [3]Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza, Università di Roma, Roma, Italy*

Background: Osteoarthritis (OA) is characterized by progressive loss of cartilage, deterioration of subchondral bone and mild synovial inflammation. Classified for a long time as a non-inflammatory arthropathy, a growing number of evidences has suggested that OA course could be driven by systemic and localized inflammation. In particular, serum levels of Interleukin (IL)-6 have been associated with higher prevalence of osteophytes in older adults with knee OA. Furthermore, high levels of other inflammatory cytokines have been identified in serum and synovial fluid of OA patients.

Objectives: In the present cross-sectional study, we aimed at analyzing the correlation between articular inflammatory state, reflected by ultrasonographically-detected synovitis, and the serum levels of 27 cytokines, chemokines and growth factors in a cohort of primary knee OA.

Methods: We consecutively enrolled 47 patients (M/F 16/31, mean age ±SD 63.8±7.8 years, mean onset interval ±SD 70.0±78.6 months) affected by knees OA according to clinical and radiographic ACR criteria. Patients were excluded if they had received non-steroidal anti-inflammatory drugs or other analgesics within the 2 days before enrollment. Pain was assessed with a 100-mm visual analogue scale (VAS), and the Lequesne algo-functional index was used to measure the OA severity. BMI was registered. Each patient underwent ultrasonographic (US) assessment of both knees performed by a single operator. According with OMERACT definitions, we assessed the presence of synovial effusion, synovial hypertrophy and power Doppler. These elementary lesions were scored according to a semi-quantitative scale (0 = absent, 1 = mild, 2 = moderate and 3 = severe), the sum of them allows obtaining a total score of the patient's inflammatory state (0–18). Finally, blood samples for laboratory assays were obtained and commercially available multiplex bead based immunoassay kits (Human 27-plex, Bio-Rad laboratories, Hercules, CA) were used to measure concentrations of IL-1β, IL-1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-17, FGF-Basic, G-CSF, GM-CSF, interferon-γ, IP-10, MCP-1, MIP-1α, MIP-1β, PDGF, RANTES, TNF, VEGF.

Results: At the study enrollment, OA patients showed a mean±SD US synovitis score of 4.4±2.7, a mean±SD VAS pain rating of 53.3±16.6 mm (range 18–90 mm), a mean±SD Lequesne index of 10.2±4.2 (range 1.5–19), a mean±SD BMI of 26.8±4.2 (range 20–34.7). Positive correlations among US synovitis score and serum levels of IL-6 (r=0.3, p=0.01), IL-2 (r=0.3, p=0.01), IL-5 (r=0.3, p=0.01), IL-7 (r=0.3, p=0.03), MIP-1b (r=0.3, p=0.01), VEGF (r=0.3, p=0.02) were found. Moreover, US synovitis score positively correlated with Lequesne index (r=0.4, p=0.004) and BMI (r=0.4, p=0.04).

Conclusions: The results of the present study confirmed that OA may be associated with systemic inflammatory changes, as demonstrated by the positive correlation between US synovitis and several inflammatory cytokines serum levels.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5289

AB0037 SERUM CYTOKINE SIGNATURE IN MUCOCUTANEOUS AND OCULAR BEHÇET'S DISEASE

G. Lopalco[1], O.M. Lucherini[2], L. Cantarini[2], A. Lopalco[3], V. Venerito[1], M. Fornaro[1], D. Natuzzi[1], M. Galeazzi[2], G. Lapadula[1], F. Iannone[1]. *[1]Department of Emergency and Organ Transplantation, University of Bari, Bari; [2]Research Center of Systemic Autoinflammatory Diseases and Behcet's Disease Clinic, Department of Medical Sciences, Surgery and Neurosciences, University of Siena, Siena, Italy; [3]Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, United States*

Background: Behçet's disease (BD) is a multi-systemic inflammatory disorder consisting of recurrent oral aphthosis, genital ulcers, and chronic relapsing bilateral uveitis. However, many other organs including the vascular, gastrointestinal, neurological, and musculoskeletal systems can be affected. Pathogenetically, both innate and adaptive immunity have shown to play a pivotal role, and several proinflammatory cytokines derived from Th1 and Th17 lymphocytes seem to be involved in different pathogenic pathways leading to development of the clinical manifestations.

Objectives: The primary aim of our study was to compare a core set of proinflammatory cytokines between patients with BD and healthy control (HC). The secondary aim was to evaluate potential correlations between these putative circulating biomarkers, the status of disease activity, and the specific organ involvement at the time of sample collection.

Methods: Fifty-four serum samples were collected from 46 BD patients (17 males, 29 females, mean age 45,5±11,3 years), and 19 HC (10 males, 9 females, mean age 43±8.3 years). Twenty-five serum cytokines (APRIL/TNFS13, BAFF/TNFSF13B, sCD30/TNFRSF8, sCD163, Chitinase3-like1, gp130/sIL-6Rb, IFNb, sIL-6Ra, IL-10, IL-11, IL-19, IL-20, IL-26, IL-27 (p28), IL-28A/IFN-lambda2, IL-29/IFN-lambda1, IL-32, IL-34, IL-35, LIGHT/TNFSF-14, Pentraxin-3, sTNF-R1, sTNF-R2, TSLP and TWEAK/TNFSF-12) were simultaneously quantified using a Bio-Rad cytokine bead arrays.

Results: Serum levels of Chitinase3-like1, gp130/sIL-6Rb, IL-11, IL-26, sTNF-R1, sTNF-R2 were significantly higher in BD patients than in HC. Specifically, serum concentration of sTNF-R1 (p<0.01) and sTNF-R2 (p<0.01) resulted higher in both active- and inactive-BD than HC, whilst Chi-tinase3-like1 (p<0.05) and gp130/sIL-6Rb (p<0.01) serum levels were significantly higher in in-active-BD, and IL-26 (p<0.01) in active-BD than HC. No differences were observed between inactive- and active- BD group. In addition, comparing cytokines levels in patients affected by mucocutenous manifestations with (MO-BD) or without (M-BD) ocular

involvement we observed that gp130/sIL-6Rb, sIL-6Ra, IL-35, and TSLP serum levels were significant enhanced in MO-BD compared to M-BD subgroup.

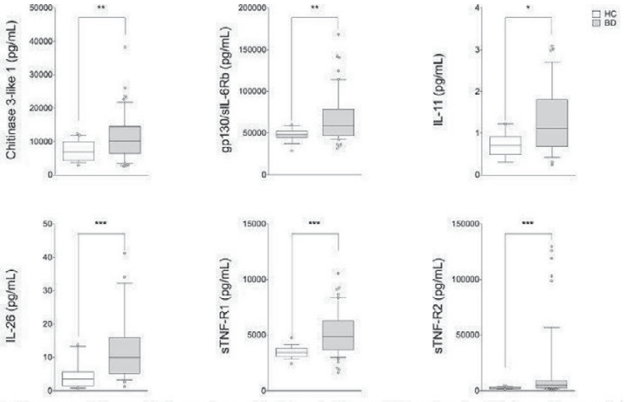


Fig.1. Serum cytokine profile in patients with Behçet's disease. BD patients (n=54) showed up-regulation of serum levels of Chitinase3-like1, gp130/sIL-6Rb, IL-11, IL-26, sTNF-R1 and sTNF-R2 compared with HC (n=19). Mann-Whitney U-test as well as Student's t-test were carried out to check for statistical significance between groups when required (***p<0.001, **p<0.01, *p<0.05). The central line represents the distribution median, boxes span 25th to 75th percentiles, and error bars extend from 10th to 90th percentiles. Dots (°) are outlier values, higher than the 90th percentile. Abbreviations: HC, healthy controls; BD, Behçet's disease.

Conclusions: Our findings showed a signature of IL-6, TNF-α as well as of Th17 response in BD patients due to increased levels of gp130/sIL-6Rb, sTNF-R1, sTNF-R2, IL-26 respectively. This evidence could contribute to improve the knowledge regarding the role of these citokines in the induction of specific BD clinical features

References:

[1] Lopalco G, Lucherini OM, Vitale A, Talarico R, Lopalco A, Galeazzi M, et al. Putative Role of Serum Amyloid-A and Proinflammatory Cytokines as Biomarkers for Behcet's Disease. Medicine (Baltimore) (2015) 94(42):e1858.
[2] Lucherini OM, Lopalco G, Cantarini L, Vitale A, Rotondo C, Lopalco A, et al. Correlation between serum amyloid-A and serum levels of proinflammatory cytokines in patients with Behçet's disease. Pediatric Rheumatology Online Journal (2015) 13(Suppl 1):P6.
[3] Turan B, Pfister K, Diener PA, Hell M, Möller B, Boyvat A, et al. Soluble tumour necrosis factor receptors sTNFR1 and sTNFR2 are produced at sites of inflammation and are markers of arthritis activity in Behçet's disease. Scand J Rheumatol (2008) 37(2):135–41.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1935

AB0038 INCREASED INTERFERON-ALPHA PRODUCTION BY PLASMACYTOID DENDRITIC CELLS STIMULATED WITH A TLR-7 AGONIST IN SYSTEMIC LUPUS ERYTHEMATOSUS

G. Murayama [1,2], N. Furusawa [2], A. Chiba [2], K. Yamaji [1], N. Tamura [1], S. Miyake [2].
[1] Department of Internal Medicine and Rheumatology; [2] Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan

Background: Type I interferon (IFN) appears to contribute to the development of systemic lupus erythematosus (SLE). IFN-α production is known to be increased in peripheral blood mononuclear cells (PBMCs) from SLE patients. Although plasmacytoid dendritic cells (pDCs) is a major source of IFN-α, previous reports showed that IFN-α production by pDCs stimulated with a TLR-9 agonist was decreased in SLE compared to healthy controls (HC).
Objectives: We set out to investigate an other endosomal TLR-signaling pathway in SLE by using TLR-7 agonist stimulation.
Methods: Blood samples were obtained from 55 HC and 73 SLE patients, diagnosed according to the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus (2012). PBMC from SLE patients and HC were stimulated with a TLR-9 agonist, CpG-A oligodeoxynucleotides (CpG-A ODN)-2216, and a TLR-7 agonist, imiquimod. The proportion of pDCs producing IFN-α was investigated by intracellular cytokine staining and flowcytometory. PBMC were pretreated with IFN-α for 24 hours, and then IFN-α production by pDCs was assessed after imiquimod stimulation.
Results: As previously reported, the level of IFN-α production by pDCs stimulated with CpG-A ODN was reduced in SLE compared with HC. However, the proportion of IFN-α producing pDCs stimulated with imiquimod was significantly increased in SLE patients. The percentage of IFN-α producing pDCs stimulated with imiquimod was positively correlated with SLE disease activity index (SLEDAI) score, and that of pDCs stimulated with CpG-A ODN was negatively correlated with SLEDAI. The expression of TLR-7 on pDCs, but not TLR-9, was upregulated in SLE patients compared with HC. Furthermore, pretreatment with IFN-α increased IFN-α production by pDCs upon imiquimod stimulation.
Conclusions: IFN-α production by pDCs form SLE patients was increased when stimulated with a TLR-7 agonist, and this was accompanied with upregulated TLR-7 expression in these cells. In murine lupus-models, TLR7-deletion has been shown to reduce autoimmune disease. The enhanced TLR-7 signaling pathway in pDC may play an important role in lupus pathology.

References:

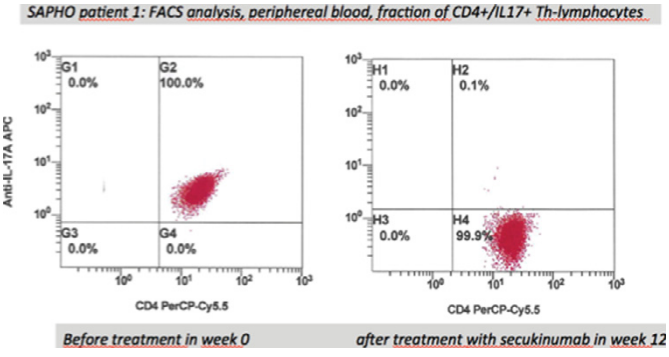
[1] Christensen SR, et al. Toll-like receptor 7 and TLR9 dictate autoantibody specificity and have opposing inflammatory and regulatory roles in a murine model of lupus. Immunity. 2006; 25: 417–28.
[2] Sacre K, et al. Hydroxychloroquine is associated with impaired interferon-alpha and tumor necrosis factor-alpha production by plasmacytoid dendritic cells in systemic lupus erythematosus. Arthritis Res Ther. 2012;R155.
[3] Fukui R, et al. Unc93B1 restricts systemic lethal inflammation by orchestrating Toll-like receptor 7 and 9 trafficking. Immunity 2011; 35: 69–81.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3074

AB0039 REDUCTION OF TH17+ LYMPHOCYTES IN PART OF SAPHO PATIENTS ON TREATMENT WITH SECUKINUMAB

G. Assmann [1], A. Tajali [2], S. Bamberger [1], M. Pfreundschuh [1], C. Schormann [1], F. Neumann [1]. *[1] Rheumatology and Oncology, University Medical School of Saarland, Homburg; [2] Rheumatology, Püttlingen Hospital, Püttlingen, Germany*

Background: The SAPHO syndrome has to be considered as a rare subtype of the disease entity of the seronegative spondylarthritis. The characteristic defining symptoms are synovitis, acne, palmoplantar pustulosis (PPP), and hyperostosis with osteitis. In general, most of SAPHO patients complete the diagnostic criteria for spondylarthritis and/or psoriatic arthritis. The etiology of SAPHO syndrome remains unclear so far, autoimmune dysregulations potentially triggered by bacterial infection with propionibacterium acnes has been discussed. Firinu D et. al (Ref.) has previously published data of higher Th17+ lymphocytes in the peripheral blood in SAPHO patients compared with psoriatic arthritis patients or healthy controls. Activation of the TH17 pathway leads to pro-inflammatory effects mediated by interleukin 17 with stimulation of osteoblast, macrophages, and fibroblasts with the consequences of secretion f pro-inflammatory cytokines such as interleukin 6 and 1, TNF alpha, and MMPs. The interleukin 17 blocking agent secukinumab has been introduced in the armentarium of antirheumatic drugs against seronegative spondylarthritis including psoriatic arthritis.
Objectives: To evaluate the count of Th17+ lymphocytes in patients with SAPHO syndrome and psoriatic arthritis before and under treatment with secukinumab.
Methods: Peripheral blood was derived from 4 patients with SAPHO syndrome and 4 patients with psoriatic arthritis, respectively before and under 12 week treatment with secukinumab 300mg (dosage: 4 times weekly, then monthly). All patients had received at least one conventional DMARDs and one TNF blocking agent in their medical history. All patients showed active disease with elevated scores of DAS28 and/or HAQ, for SAPHO patients the activity scores of osteitis (from 0 to 6) and PPP (0–6) were estimated by physician. The blood specimen were separated in EDTA containing tubes to separate lymphocytes, which were measured using FACS analysis to evaluate the fraction of Th 17+/CD4+ lymphocytes. The Ethics Committee of Saarland has proven the study, all patients gave their consent to take part in the study.
Results: The Th17+lymphocytes were not detectable in 4 patients with psoriatic arthritis and 2 of 4 SAPHO patients before and under 12 week treatment with secukinumab. In 2 of 4 SAPHO patients the fractions of Th17+ lymphocytes were prominent prior to secukinumab application; after treatment duration of 12 weeks one of both developed a depletion of Th17+ cells (figure), the other SAPHO patient a Th17+ cell reduction. Only the two SAPHO patients with diminishing Th17+ lymphocytes have developed treatment response evaluated by reduction of HAQ score (from 1.75 to 1.25), osteitis score (4.5 to 3.0), and PPP score (5.0 to 4.0). Three of 4 psoriatic arthritis patients showed reduced diseases activity under treatment with secukinumab (DAS28 score from 4.22 to 3.45, HAQ 2.25 to 1.5).



Conclusions: The measurement of Th17+lymphocytes in the peripheral blood of SAPHO patients could be suggested for further evaluation as possible predictor of treatment response by secukinumab.

References:

[1] Firinu D, Barca MP, Lorrai MM, Perra S, Cabras S, Muggianu E, Di Martino ML,

Manconi PE, Del Giacco SR. TH17 cells are increased in the peripheral blood of patients with SAPHO syndrome. Autoimmunity. 2014 Sep;47(6):389–94. doi: 10.3109/08916934.2014.906582. Epub 2014 Apr 10.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4360

AB0040 IMMUNE MODULATORY EFFECTS OF MESENCHYMAL STEM CELL TO MONONUCLEAR CELLS FROM PATIENTS WITH ACTIVE ADULT ONSET STILL'S DISEASE

I.W. Sohn[1], H.-J. Jeong[2], G.Y. Ahn[1], M.J. Kim[1], H. Kim[1], S. Kang[1], D.H. Yoo[1]. *[1]Rheumatology, Hanyang University Hospital for Rheumtic diseases, Seoul; [2]Rheumatology, Keimyung University Dongsan Medical Center, Daegu, Korea, Republic Of*

Background: Adult onset Still's disease (AOSD) is an inflammatory disorder of unknown etiology, which is accompanied by increased levels of serum pro-inflammatory cytokine. Mesenchymal stem cells (MSCs) have immunomodulatory capacities and might be a promising therapeutic option in the treatment of refractory autoimmune diseases. Both cell-to-cell contact and the release of soluble factors mediate immune modulatory functions of MSCs.
Objectives: We aimed to determine if MSCs could modulate serum cytokine level in patients with active untreated AOSD, either through paracrine secretion or via direct contacts with the MSCs.
Methods: Human peripheral blood mononuclear cells (hPBMCs) from 6 patients with active AOSD were co-cultured for 72 hours with human MSCs (hMSCs at a ratio of 10 to 1). We compared the cytokine levels before and after direct or indirect (transwell cultures) exposition to activated mononuclear cells (LPS, 10ng/ml) or T cell-inducing conditions (anti-CD3 [5 μg/ml], anti-CD28 [5 μg/ml], recombinant human IL-2 [5 ng/ml]). Cytokine levels were detected by multiplex cytokine detection kit by flow cytometry, or ELISA with culture supernatant. In vitro platform for studying the effects of MSCs on individual cytokines, the Wilcoxon signed-rank test was employed for comparison of serum cytokine levels.
Results: Treatment of mononuclear cells with hMSCs resulted in significant reduction of mean TNF-α level (mean 463.4 pg/ml vs 137.8 pg/ml, $p<0.05$) and IL-1 β (mean 1887.1 pg/ml vs 1127.9 pg/ml, $p<0.05$). When the hMSCs were present during the T-cell differentiation, there was a significant decrease in the mean secreted TNF-α (mean 10953.5 pg/ml vs 454.9 pg/ml, $p<0.05$), IFN-γ (mean 14301.0 pg/ml vs 5090.4 pg/ml, $p<0.05$) and sIL-2 receptor (mean 3550.8 pg/ml vs 2506.4 pg/ml, $p<0.05$). On the contrary, level of TGF-β was significantly increased (mean 4088.8 pg/ml vs 5104.8 pg/ml, $p<0.05$). But, there was a significant increase in the amount of IL-6 (mean 2215.5 pg/ml vs 25130.6 pg/ml, $p<0.05$) and IL-17 α (mean 1357.0 pg/ml vs 2453.6 pg/ml, $p<0.05$). Two chamber experiments also showed similar pattern of cytokine modulation.
Conclusions: This preliminary experiment demonstrated that MSCs can modulate cyokine profiles of AOSD mononuclear cells by decreasing pro-inflammatory cytokines, and increasing anti-inflammatory cytokine such as TGF-β. However, up-regulation of IL-6 and IL-17 might be a hurdle to overvome in the clinical application of MSCs in AOSD patients.
References:
[1] Serum cytokine profiles in patients with Adult onset Still's disease. J Rheumatol. 2003 Nov;30(11):2422–7.
[2] Human mesenchymal stem cells modulated allogeneic immune cell responses. Blood. 2005 Feb 15;105(4):1815–22. Epub 2004 Oct 19.
Acknowledgements: none.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5719

AB0041 LARGE VESSEL VASCULITIS INDUCED BY CANDIDA ALBICAN WATER-SOLUBLE-FRACTION (CAWS) IN THE C57BL/6J MOUSE MODEL IS ASSOCIATED WITH OVEREXPRESSION OF IL-6, TNF-α, AND IL-10 WITH MODEST CHANGE IN SOCS-1

J.M. Springer[1], M. Zhang[2], D. Smith[1], N. Miura[3], N. Ohno[3], O. Tawfik[4], M. Maz[1], K. Dileepan[1]. *[1]Allergy, Immunology and Rheumatology; [2]Department of Orthopedics, Kansas University Medical Center, Kansas City, United States; [3]Department of Pharmacy and Life Sciences, Tokyo University, Hachioji, Japan; [4]Department of Pathology and Laboratory Medicine, Kansas University Medical Center, Kansas City, United States*

Background: We have previously demonstrated that mast cell degranulation acutely downregulates lipopolysaccharide induced aortic expression and serum levels of IL-6 in vivo. This is accompanied by aortic upregulation of suppressor of cytokine signaling-1 (SOCS-1) gene expression[1]. This effect is not seen in histamine H1 receptor-knockout mice suggesting that mast cell-derived histamine is a key mediator involved in IL-6 homoeostasis[2]. Mice injected with *Candida albican* water-soluble-fraction (CAWS) have been shown to develop coronary and aortic vasculitis[3]. Our long-term objective is to determine the pathogenic mechanism of large vessel vasculitis (LVV).
Objectives: The aim of this pilot study was to replicate and develop a working mouse model to determine the regulatory role of mast cells in LVV.
Methods: Eight to ten weeks-old male C57Bl6/J mice were randomly distributed into two groups [CAWS, N=8; and Control, N=8] and were injected i.p. daily for 5 days with either CAWS in normal saline (2 mg/day/mouse) or normal saline alone (controls). All mice were sacrificed 30 days after the 5th injection. We examined serum levels of IL-6 and TNF-α, as well as aortic tissue expressions of IL-6, TNF-a, IL-10 and SOCS-1 mRNA. Heart and aortic sections were evaluated for inflammation and mast cells after staining with H & E and toluidine blue, respectively.
Results: Treatment of mice with CAWS for 5-consecutive days led to overexpression of IL-6, TNF-a and IL-10 genes in the aortic tissue with modest upregulation of SOCS-1. At the root of the aorta, all animals in the CAWS group had intense inflammatory infiltrates composed of mixed acute and chronic inflammatory cells. There is also evidence of vasculitis in the coronary arteries. In contrast, none of the control mice had any evidence of aortic inflammation or vasculitis. Serum IL-6 concentrations were below detectable levels in both controls and CAWS-treated mice whereas TNF-a levels were elevated in 3 out of 8 mice in the CAWS group. There were no signs or increased presence of intact or degranulating mast cells in the area of inflammation.
Conclusions: These results suggest that CAWS-induced LVV involves acute and chronic inflammatory response and vascular tissue expression of both pro- and anti-inflammatory cytokines and SOC-1. Detailed kinetic studies are warranted to determine the optimum windows of peak inflammatory response and the expression of these genes to understand the pathobiology of CAWS-induced LVV.
References:
[1] Springer J, Raveendan V, Smith D, et al. [abstract] Ann Rheum Dis 2014; 73:112–113.
[2] Raveendran V, Springer J, Smith D, et al. [abstract]. Arthritis Rheumatol 2015; 67(suppl 10).
[3] Miura N, Shingo Y, Adachi Y, et al. Immunopharmacol Immunotoxicol 2004; 26(4):527–43.
Acknowledgements: Supported by Basic Science Development Award from Department of Medicine at the University of Kansas.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4884

AB0042 HIGH EXPRESSION OF S100 CALGRANULINS GENES IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF PATIENTS WITH TAKAYASU ARTERITIS

J. Kabeerdoss, R. Goel, H. Mohan, D. Danda. *Department of Rheumatology, CHRistian Medical College, Vellore, India*

Background: Takayasu arteritis (TA) is inflammatory disorder that affects aorta and its branches. Toll-like receptors (TLR) 1 to 4 are highly expressed in aorta (1). Activation of TLR4 causes transmural arteritis in human temporal artery–SCID chimera model (2). Ligand responsible for TLR4 activation is not known in TA.
Objectives: Aim of the study is to examine the expression of TLR4 and its endogenous ligands in peripheral blood mononuclear cells (PBMCs) of patient with TA.
Methods: RNA from PBMCs of 24 TA patients and 19 sex and age matched healthy controls were extracted. The mRNA expression of various endogenous TLR4 ligands, TLR4, RAGE, interleukin-6 (IL-6) and IL-8 were quantified in real time PCR using specific primers and SYBR Green qPCR master mix. Serum S100A8/A9 and S100A12 levels were measured using commercial ELISA kits. S100A8/A9 and S100A12 were measured in cell culture supernatant of un-stimulated and lipopolysaccharides (LPS) stimulated PBMCs, cultured for 4 hours. t-test was used to compare between the groups. $P<0.05$ was considered as statistically significant.
Results: The mRNA of S100A8, S100A9, S100A12 and TLR4 were highly expressed in TA as compared to healthy controls, while RAGE, HSP70 and IL-6 had lower expression in TA. No difference in serum levels of S100A8/A9 and S100A12 was noted between TA and healthy controls. LPS induced high secretion of both S100A8/A9 and S100A12 levels in both TA and healthy controls (Figure-1). However, the stimulatory response in healthy controls [2.88 (1.7–3.53) fold] was significantly higher as compared to TA [1.345 (1–1.82) fold; $p<0.05$] as measured by delta S100A12 (LPS/unstimulated control). Numerically delta S100A8/A9 was also higher in healthy controls [2.04 (1.7–5.6) fold] as compared to TA [1.38 (1.09–3.6) fold; p=0.129].

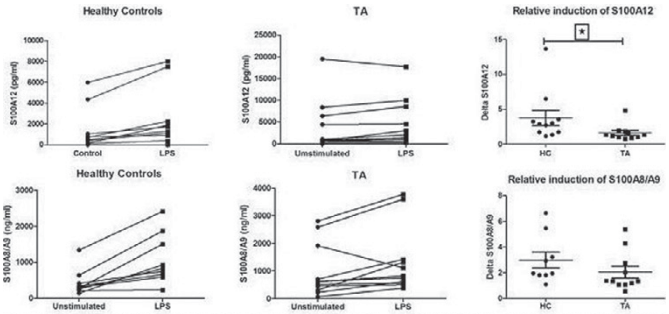


Figure -1. S100A8/A9 and S100A12 secretion by PBMCs cultured with and without LPS (100ng/ml) in RPMI medium for 4 hours for TA (n=10) and Healthy controls (n=10). Each circle represents each subjects and connecting line represents their corresponding S100A8/A9 and S10012 secretion levels in unstimulated control (without LPS) and LPS treatment on PBMCs. *=p<0.05.

Conclusions: mRNA expression of S100A8, S100A9, S100A12 and TLR4 in PBMCs of TA patients were higher as compared to healthy controls. Despite this, S100A12 secretion was lower in TA as compared to healthy controls upon LPS challenge.

References:
[1] Pryshchep O, Ma-Krupa W, Younge BR, et al (2008) Vessel-specific Toll-like receptor profiles in human medium and large arteries. Circulation 118:1276–1284.
[2] Deng J, Ma-Krupa W, Gewirtz AT, et al (2009) TLR4 and TLR5 induce distinct types of vasculitis. Circ Res 104:488–495.

Acknowledgements: This study was funded by grants-in-aid from Science and Engineering Research Board (SERB), Department of Science and Technology (DST), Government of India under young investigator scheme to JK (SB/YS/LS-14/2014).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5682

AB0043 TLR4 INHIBITION REDUCES MOVEMENT-INDUCED NOCICEPTION AND ATF-3 EXPRESSION IN EXPERIMENTAL OSTEOARTHRITIS

J. Ferreira-Gomes[1,2,3], M.M. Garcia[4], D. Nascimento[1,2,3], L. Almeida[1,2,3], E. Quesada[5], C. Goicoechea[4], J. Castro-Lopes[1,2,3], F. Neto[1,2,3]. *[1]Departamento de Biomedicina – Unidade de Biologia Experimental, Faculdade de Medicina da Universidade do Porto; [2]Instituto de Investigação e Inovação em Saúde, Universidade do Porto; [3]IBMC-Instituto de Biologia Molecular e Celular, Universidade do Porto, Porto, Portugal; [4]Area de Farmacologia, Facultad de Ciencias de la Salud, Universidad Rey Juan Carlos. Unidad Asociada URJC-IQM-CSIC, Alcorcon; [5]Instituto de Química Médica, Consejo Superior de Investigaciones Científicas. Unidad Asociada URJC- IQM-CSIC, Madrid, Spain*

Background: Toll-like receptor 4 (TLR4) is a pattern recognition receptor involved in the initiation of inflammatory responses to control pathogen infections, but is also a "danger-sensing" receptor that recognizes host-derived endogenous molecules called damage-associated molecular patterns (DAMPs). The role of TLR4 in rheumatic diseases is becoming evident, as well as its potential role as a therapeutic option.

Objectives: The aim of this study was to evaluate the effect, both on articular histopathology and pain behaviour, of a TLR4 antagonist (TLR4-A1) on an experimental model of OA. The effect of the TLR4-A1 on the activating transcription factor-3 (ATF-3) signalling pathway was also assessed.

Methods: OA was induced in adult Wistar rats through an intra-articular injection of 2mg of sodium mono-iodoacetate (MIA) into the left knee. Control animals received a similar injection with saline. TLR4-A1 (10 mg/kg), synthesized by Dr. Quesada from a compound previously described by the Peri Laboratory (Piazza et al., 2009), was intraperitoneally administered, daily, from days 14 to 28 after OA induction. Under the same procedure a control group of animals received the vehicle. Movement- and loading- induced nociception was evaluated in all animals, by the Knee-Bend and CatWalk tests, before and after TLR4-A1 or vehicle administration, at several time-points. Animals were sacrificed 28 days after OA induction. L3-L5 Dorsal Root Ganglia (DRG) were used for immunohistochemistry for TLR4 and ATF-3, spinal cords were immunoreacted for TLR4 and knee joints were processed for histopathological evaluation.

Results: Antagonism by TLR4-A1 significantly reduced the nociceptive behavior of OA animals both in the Knee-Bend and Catwalk tests. The effect was immediately observed 1 day after TLR4-A1 administration, but became more evident 4 days later, maintaining thereafter. No improvement in the cartilage histology was observed. The increased ATF-3 expression observed in DRG of OA animals was significantly reduced by TLR4-A1. On the contrary, TLR4 expression slightly increased after antagonist administration both at DRG and superficial dorsal horn levels.

Conclusions: Chronic treatment with TLR4-A1 showed an antinociceptive effect on OA animals, not related to articular histopathological improvement, possibly through an ATF-3 dependent mechanism.

References:
[1] Piazza M, Rossini C, Fiorentina SD, Pozzi C, Cornelli F, Bettoni I, Fusi P, Costa B and Peri F. Glycolipids and Benzylammonium Lipids as Novel Antisepsis Agents: Synthesis and Biological Characterization. J Med Chem 2009, 52, 1209–1213.

Acknowledgements: Granted by FEDER funds through COMPETE – Programa Operacional Factores de Competitividade (FCOMP-01–0124-FEDER-021359) and by National Funds through FCT – Fundação para a Ciência e a Tecnologia (PTDC/SAU-NSC/119986/2010); and by Ministerio de Economia y Competitividad (SAF2012–40075-C02–02).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2878

AB0044 THE INHIBITORY EFFECTS OF TACROLIMUS ON GLIOSTATIN PRODUCTION IN RA SYNOVIOCYTES

K. Ikuta[1], Y. Waguri-Nagaya[2], T. Yamagami[3], N. Tatematsu[3], Y. Kawaguchi[3], Y. Oguri[3], T. Terazawa[1], M. Kobayashi[3], K. Asai[4], T. Otsuka[3]. *[1]Orthopaedic Surgery, Daido Hospital; [2]Joint Surgery for Rheumatic Diseases; [3]Orthopaedic Surgery; [4]Molecular Neurobiology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan*

Background: Gliostatin (GLS) is known to have angiogenic and arthritogenic activities[1]. We also reported a decrease in serum GLS levels in RA patient responders treated with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs)[2]. Tacrolimus (TAC), an orally available calcineurin inhibitor, is a potent immunosuppressant. The efficacy of TAC monotherapy and the combination therapy with TAC and methotrexate in the treatment of RA has been previously described[3]. Although the principal TAC action is thought to be the inhibition of T cell activation, its beneficial effect on RA synoviocytes has not been yet elucidated.

Objectives: To determine the inhibitory effects of TAC on GLS production in RA, we investigated the modulation of serum GLS by TAC therapy and the effect of TAC on the production of GLS in cultured fibroblast-like synoviocytes (FLSs).

Methods: Serum samples were collected from eleven RA patients with active disease at baseline and after 12 weeks of TAC treatment. These RA patients had a history of unsatisfied response with at least one csDMARD or biological DMARD. Serum concentrations of GLS and matrix metalloproteinase (MMP)-3 were measured by enzyme immunoassay (EIA). Synovial specimens were obtained from RA patients at the time of total knee arthroplasty. FLSs were cultured and stimulated by TNF alfa with or without TAC. The expression levels of GLS were determined using RT-PCR and EIA. MMP-3 protein in conditioned media was measured by using EIA.

Results: Six patients fulfilled good and moderate responder and the other five patients fulfilled no responder with EULAR response criteria. DAS28, serum GLS, CRP and MMP-3 were significantly down-regulated in TAC responders. In RA FLSs, GLS mRNA and protein were significantly induced after treatment with TNF alfa alone (GLS mRNA 21.9-fold, protein 1.5-fold compared to control). These inductions were suppressed by TAC in a dose-dependent manner. MMP-3 protein was induced by TNF alfa and was similarly suppressed by TAC in a dose-dependent manner (MMP-3 protein 2.9-fold compared to control).

Conclusions: This study is the first to demonstrate that TAC down-regulates GLS mRNA and protein in FLSs treated by TNF alfa. Our data suggests that the beneficial effect of TAC in RA might be due to, at least in part, to anti-angiogenic and anti-arthritogenic activity following the down-regulation of GLS.

References:
[1] Asai K, et al. High concentration of immunoreactive gliostatin/ platelet-derived endothelial cell growth factor in synovial fluid and serum of rheumatoid arthritis. Clin Chim Acta 1993;218:1–4.
[2] Kusabe T, et al. The inhibitory effect of disease-modifying anti-rheumatic drugs and steroids on gliostatin/platelet-derived endothelial cell growth factor production in human fibroblast-like synoviocytes. Rheumatol Int 2005;25:625–630.
[3] Kremer JM, et al. Tacrolimus in rheumatoid arthritis patients receiving concomitant methotrexate: a six-month, open-label study. Arthritis Rheum 2003;48:2763–2768.

Acknowledgements: This research was supported by Grand-in-Aid for Scientific Research(C) (26462309) and 16K10913 from the Japan Society for the Promotion of Science.

Disclosure of Interest: K. Ikuta: None declared, Y. Waguri-Nagaya Grant/research support from: Biomet Japan, Inc, Chugai Pharmaceutical Co., Ltd., Astellas Pharma Inc., Merck Sharp & Dohme Co., AbbVie Japan Co., Ltd., Ono Pharmaceutical Co., Ltd., T. Yamagami: None declared, N. Tatematsu: None declared, Y. Kawaguchi: None declared, Y. Oguri: None declared, T. Terazawa: None declared, M. Kobayashi: None declared, K. Asai: None declared, T. Otsuka: None declared

DOI: 10.1136/annrheumdis-2017-eular.2527

AB0045 IL-17 INDUCED GLUCOCORTICOID INSENSITIVITY MIGHT BE DEPENDENT ON THE REDUCED 11BETA-HSD1 ENZYME ACTIVITY

M. Vitiello[1], V. Kunnathully[1], G. Orsolini[1], O. Viapiana[1], F. Poli[1], A. Mattè[2], L. De Franceschi[2], L. Idolazzi[1], D. Gatti[1], M. Rossini[1]. *[1]Rheumatology Unit; [2]Internal Medicine Section, University of Verona, Verona, Italy*

Background: It has been demonstrated that IL-17A is able to induce GC insensitivity. Although several studies have reported the role of IL-17 in GC insensitivity the mechanism underlying remains still largely unclear.

Objectives: To understand the effects of interleukin-17 (IL-17) on the enzyme 11β-hydroxysteroid dehydrogenases (11β-HSDs) in the two main classes of monocytes, CD14 and CD16.

Methods: Peripheral Blood Mononuclear Cells (PBMCs) were isolated from 5 healthy donors and were sorted into CD14 and CD16 subpopulations using cell sorting. Effect of IL-17 on 11β-HSD1 enzyme activity was measured in terms of conversion of cortisone to cortisol in sorted and unsorted monocytes using Homogeneous Time-Resolved Fluorescence (HTRF). The direct involvement of 11β-HSD1 in the conversion of cortisone to cortisol was confirmed using carbenoxolone, an inhibitor of 11β-HSD1.

Results: Monocytes showed a concentration-dependent decrease in the 11β-HSD1 enzyme activity when incubated with increasing concentrations of IL-17. CD14 and CD16 cells stimulated similarly with IL-17 showed a significant

difference in the enzyme activity between the untreated and stimulated cells in all treatment groups. However, a dose dependent decrease was observed only in case of CD14 cells. Both unsorted monocytes and monocyte sub-populations showed a significant decrease in the concentration of cortisol measured when co-incubated with carbenoxolone, indicative of the direct involvement of 11β-HSD1 enzyme in the conversion of cortisone to cortisol.

Conclusions: The results of this study showed that IL-17 induced GC insensitivity might be dependent on the reduced 11β-HSD1 enzyme activity in inflammatory conditions. We showed that the pro-inflammatory cytokine IL-17 causes a significant decrease in the 11β-HSD1 enzyme activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2681

AB0046 METABOLISM AND OSTEOARTHRITIS ARE LINKED BY ADIPOKINES

M.-L. Hülser[1], C. Schreiyäck[1], Y. Luo[2], A. Bozec[2], G. Schett[2], E. Neumann[1], U. Müller-Ladner[1]. *[1]Internal Medicine and Rheumatology, Justus-Liebig-University Giessen, Bad Nauheim; [2]Clinic of Medicine 3 - Immunology and Rheumatology, University of Erlangen-Nuremberg, Erlangen, Germany*

Background: Obesity and hyperinsulinemia are of increasing importance in the Western society. Both obesity and insulin resistance lead to changes in expression of adipokines such as adiponectin, visfatin or leptin, which appear to be immunomodulatory factors also in rheumatic diseases.

Objectives: Since osteoarthritis (OA) is often accompanied by hyperinsulinemia and obesity, we combined both mouse models (destabilization of the medial meniscus (DMM) and high-fat diet (HFD)). Here, we evaluated and correlated the systemic and local effects of both models at different states of OA development with special focus on the local/systemic expression of the adipokines adiponectin, visfatin and leptin over time.

Methods: HFD (mainly consisting of saturated fatty acids) to induce obesity and hyperinsulinemia, and ND (normal diet) as control were fed to C57Bl/6 mice for 3 months followed by surgical OA induction (time point 0). Tissues and sera were collected at different time points after DMM-mediated OA induction (4, 6, 8 weeks). Adipocytokine (leptin, visfatin, adiponectin and IL-6) serum levels were measured by ELISA. Histological stainings of the joints (H/E, safranin O, pappenheim and Masson-Goldner's trichrome) were evaluated and arthritis progress was scored. Immunohistochemical stainings of the joints were performed to evaluate the local distribution of adipokines, which were correlated to systemic adipocytokine levels and the respective arthritis score.

Results: Low systemic IL-6 levels confirmed that no acute inflammation due to surgery or infection was present in all animals. OA induction was visible at all time points, which was aggravated in HFD compared to ND mice (OA score: 4 weeks ND 0.87 vs. HFD 0.93, 6 weeks ND 1.44 vs. HFD 3.69, 8 weeks ND 1.78 vs. HFD 2.18). Systemic levels of leptin were significantly induced by HFD confirming the induction of insulin resistance, but DMM decreased leptin levels at all time points (significantly for 3 out of 6 groups, e.g. 4 weeks: HFD healthy vs. HFD DMM 18.4 ng/ml vs. 3.7 ng/ml). Interestingly, the systemic increase of adiponectin by DMM was time dependent (only 8 weeks after surgery: HFD healthy vs. HFD DMM 5176 ng/ml vs. 6149 ng/ml) but independent of diet. However, HFD in combination with DMM did not show significant effects on systemic levels of adiponectin, visfatin or IL-6.

Conclusions: HFD deteriorates OA in the DMM model. Systemic leptin levels were elevated by HFD/insulin resistance but reduced by DMM, which could not be observed for the mainly proinflammatory adipokine visfatin. Of note, systemic inflammation as shown by systemic IL-6 levels was low in all animals. The stage of OA development influences adiponectin levels, which were only increased systemically 8 weeks after surgery. In summary, systemic levels of adipokines are altered by DMM and HFD as well as the combination of both models and the analyzed adipokines show differing reactions to these factors.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4913

AB0047 TYPE I INTERFERON IS HIGHLY EXPRESSED IN RA SYNOVIAL FLUID AND JOINT CARTILAGE CORRELATED WITH SERUM RHEUMATOID FACTOR; A PRELIMINARY EXPERIMENTAL STUDY

M. Nakayama[1], H. Tobimatsu[1], H. Imamura[1], Y. Sakuma[1], K. Yano[1], Y. Niki[2], K. Ikari[1]. *[1]Department of Orthopedic Surgery, Institute of Rheumatology, Tokyo Women's Medical University; [2]Department of Orthopedic Surgery, Keio University, Tokyo, Japan*

Background: It was reported that type I interferon (IFN) is involved in the pathogenesis of rheumatoid arthritis (RA) [1–3], while the relevance of the IFN signature to RA disease activity and progression remains unclear. There were few reports about the expression of IFN in synovial fluid and joint cartilage.

Objectives: The aim of this study is to investigate the role of IFN in the pathogenesis of RA by means of the analysis of joint tissues of RA patients comparing with those of osteoarthritis (OA) patients.

Methods: Synovial fluid, synovia and cartilage were collected from RA and OA patients (n=10 for each) during total knee arthroplasty in our hospital and blood samples were collected just before surgery. As preoperative therapy for RA, Methotrexate (MTX) was administered to 9 patients (dose ranged (4–12mg), DMARDS without MTX to 2, biological DMARDS to 2, Prednisolone (PSL) to 6 (dose 1–5mg). Quantities of IFN alpha or beta of blood and joint fluid were measured with ELISA (PBL Assay Science, USA), and expression of IFN alpha, beta and TNF alpha of synovia and joint cartilage were measured with real time PCR. In RA patients. Serum biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Rheumatoid Factor (RF), hemoglobin and platelet were measured and investigated correlation with the quantities of IFN of blood or joint tissues. Medication for RA were investigated as well.

Results: In blood and synovial fluid of RA patients, IFN alpha and beta were highly detected, while they were not detected in those of OA patients. The expression of IFN alpha and beta of RA cartilage were much higher than those of OA whereas they were not expressed in synovium of both RA and OA. Expression of IFN was not correlated with that of TNF alpha in RA patients. Statistical analysis revealed that RF was related with blood and joint IFN and other markers were not. Medications for RA were not correlated with IFN expression.

Conclusions: IFN was highly expressed in RA synovial fluid, joint cartilage and blood, not in OA. IFN immunotherapy has been reported to induce RA [4–5], therefore abundant IFN might induce RA and inhibit cure of RA. Our results showed that RF was related with blood and joint IFN. It can be speculated that RF might be an index of IFN regulation in RA patient, however, more samples must be investigated to prove this speculation.

References:

[1] de Padiila CML and Niewold TB. The Type I Interferons: Basic Concepts and Clinical Relevance in Immune-mediated Inflammatory Diseases. Gene. 2016; 15, 576, 14–21.

[2] Carrio JR, de Paz B, et al. IFN alpha Serum Levels Are Associated with Endothelial Progenitor Cells Imbalance and Disease Features in Rheumatoid Arthritis Patients. Plos One, 2014;9, e86069.

[3] van Holten J, Smeets TJM, et al. Expression of interferon b in synovial tissue from patients with rheumatoid arthritis: comparison with patients with osteoarthritis and reactive arthritis. Ann Rheum Dis. 2005; 64: 1780–2.

[4] Passos SE, Evangelista SPT, et al. Rheumatoid arthritis induced by alpha-interferon therapy. Clin Rheumatol. 2001;20(4):297–9.

[5] Cacopardo B, Benanti F, et al. Rheumatoid arthritis following PEG-interferon-alfa-2a plus ribavirin treatment for chronic hepatitis C: a case report and review of the literature. BMC research notes. 2013; 6:437.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4978

AB0048 ANTIPHOSPHOLIPID ANTIBODIES, INTERLEUKIN-6 AND TUMOR NECROSIS FACTOR-α IN ATHEROSCLEROTIC PROCESS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

N.A. Bashlakova[1], T.D. Tyabut[2], A.E. Buglova[2]. *[1]Ultrasound Diagnostics Department; [2]Cardiology and Rheumatology Department, Belarusian Medical Academy of Postgraduate Education, Minsk, Belarus*

Background: Systemic inflammation has been postulated to be an independent cardiovascular risk factor, particularly in patients with autoimmune rheumatic disorders (ARD), such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), and is associated with accelerated atherosclerosis. There is some evidence to suggest that antiphospholipid antibodies (aPL) may also play a role in the development of atherosclerosis. However, it is few data about the relationship between these autoantibodies and inflammatory mediators in the development of atherosclerosis.

Objectives: To clarify the involvement of inflammatory mediators and aPL in the atherosclerotic process in patients with ARD.

Methods: The study included 87 female patients with ARD (RA (n=47), mean age 45,0 (33,0; 51,0) years old, disease duration 9,0 (3,0; 14,0) years, disease activity (DAS28=5,37 (4,69; 5,86) points); SLE (n=40), mean age 33,5 (27,5; 44,5) years old, disease duration 8,0 (5,0; 14,5) years, disease activity SLEDAI-2K 7,0 (4,0; 11,5) points). Sixty healthy women (mean age 40,5 (36,0; 47,0) years old) formed the control group.

The levels of high sensitive C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor - α (TNF-α), LA, IgG/IgM antibodies to cardiolipin (aCL), β2-glucoprotein-1(aβ2-GP1), annexin V (aAnV) and prothrombin (aPT)) were determined with ELISA. Intima-media thickness (IMT) of the carotid artery wall and the presence of atherosclerotic plaques were revealed ultrasonographically according to the described ESH/ESC Guidelines.

Results: The levels of hs-CRP, IL-6, TNF-α were significantly higher in ARD patients than in the control group, which indicates the disease activity. Furthermore, the patients with SLE had a significant correlation between IL-6 and SLEDAI-2K (r=0,471, p=0,002), TNF-α and SLEDAI-2K (r=0,499, p=0,001), whereas the patients with RA had only significant correlation between hs-CRP and DAS28 (r=0,355, p=0,031).

The concentration of IgG aCL, IgG and IgM aβ2-GP1, IgM aAnV, IgG aPT, LA were higher in patients with SLE than in the control group, and the levels of IgG and IgM aCL, IgM aβ2-GP1, IgG and IgM aAnV, LA were higher in patients with RA v.s. the control group.

We revealed a correlation between IgG aCL, IgG aβ2-GP1, IgG aAnV and TNF-α, IgG aCL and IL-6 in SLE patients, and only one between IgG aAnV and hs-CRP in RA patients. There wasn't any correlation between aPL and inflammatory mediators in the control group.
Univariate analysis has demonstrated an association of IgG aAnV with IMT (r=0,320, p=0,044) in SLE patients and positive association between TNF-α and IMT (r=0,362, p=0,028) in RA patients. Furthermore, we found an association between IL-6 and IgG aPT (r=0,426, p=0,038), TNF-α and IgG aCL (r=0,419, p=0,042) in SLE patients with carotid atherosclerosis. There wasn't any association between investigated parameters in the control group.
Conclusions: The association between inflammatory mediators and disease activity has been confirmed in ARD patients. Increased autoimmune activity has been verified both in patients with SLE and RA. It has been determined that IgG aAnV had more significance for IMT in patients with SLE, TNF-α - in RA patients. Our data can suggest that inflammatory mediators and antiphospholipid antibodies are involved in the atherosclerotic process in patients with ARD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5306

AB0049 NF-κB-INDUCING KINASE REGULATES LTβR-DRIVEN NF-κB SIGNALING AND INFLAMMATORY ACTIVATION OF ENDOTHELIUM

P. Kucharzewka[1], C.X. Maracle[2], J.P. van Hamburg[2], K.C. Jeucken[2], H. Olsson[1], S.W. Tas[2]. *[1]Imed Ria, AstraZeneca, Mölndal, Sweden; [2]Department of Clinical Immunology & Rheumatology and Laboratory for Experimental Immunology, AMC, University of Amsterdam, Amsterdam, Netherlands*

Background: Sites of chronic inflammation, such as rheumatoid arthritis synovial tissue, are characterized by neovascularization and often contain tertiary lymphoid structures with characteristic features of lymphoid organs such as endothelial venules (HEV), and sometimes even true germinal centers. Ligation of the lymphotoxin (LT)-β receptor (LTβR) results in activation of both canonical and NF-κB-Inducing Kinase (NIK)-dependent non-canonical NF-κB signaling in endothelial cells (ECs) and plays a crucial role in lymphoid neogenesis. Non-canonical NF-κB signaling in ECs promotes inflammation-induced angiogenesis and triggers the development of the cuboidal HEV appearance. However, the relative contribution of the individual pathways to the acquisition of leukocyte traffic-regulating properties by ECs is less well understood.
Objectives: To identify the molecular pathways by which LTβR drives inflammatory activation of ECs to promote interactions with leukocytes.
Methods: Primary human ECs were treated with LTβ or LIGHT to activate LTβR. Induction of downstream signaling pathways was assessed by western blot analysis and NF-κB transcription factor ELISA. The expression of adhesion molecules, inflammatory cytokines and chemokines, such as CXCL1, CXCL5, CXCL8 and GM-CSF in ECs was measured by RT-qPCR and cytokine antibody arrays. EC interactions with leukocytes were determined by an adhesion assay, and EC barrier integrity was assessed by a permeability assay. To repress canonical NF-κB signaling pathway, a small molecule inhibitor of IKKβ was used, and inactivation of non-canonical NF-κB signaling was achieved with siRNAs targeting NFκB2. The role of NIK in LTβR signaling was investigated using small molecule inhibitors of NIK, siRNAs targeting NIK and adenoviral vectors encoding wild type and kinase-deficient NIK.
Results: LTβR triggering in ECs resulted in activation of both canonical and non-canonical NF-κB signaling pathways and induced the expression of inflammatory cytokines and chemokines (CXCL1, CXCL5, CXCL8, MCP-1, GM-CSF, CCL5). Consistent with inflammatory activation of ECs, LTβR ligation also induced adhesion of immune cells to activated endothelium and increased permeability across EC monolayers. IKKβ inhibition completely repressed LTβR-induced inflammatory activation of ECs, indicating that this process was mediated through canonical NF-κB signaling. Interestingly, inactivation of NIK with small molecule inhibitors and siRNAs significantly decreased LTβR-induced expression of inflammatory cytokines and adhesion of immune cells to endothelium, whereas silencing of NFκB2 had no effect. This suggests that the non-canonical pathway is dispensable for NIK-dependent activation of endothelial cells through the canonical NF-kB pathway. Further analyses, including silencing of NIK and NIK overexpression, demonstrated a role for NIK in activation of the canonical NF-kB pathway by amplifying IKK complex activity.
Conclusions: These findings suggest that in addition to its pivotal role in the non-canonical pathway, NIK can serve as an amplifier of the canonical NF-κB pathway and associated inflammatory responses in ECs mediated by LTβR ligation, which may play a role in development and maintenance of chronic inflammation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5498

AB0050 IMPAIRED ADIPONECTIN AND LEPTIN LEVELS DURING OSTEOARTHRITIS ONSET AND DEVELOPMENT IN STR/ORT MICE

R. Giambelli, S.K. Bernini, M. Perrella, A. Grotti, R. Cavagnoli, G. Samuelli, P. Garofalo, T. Zanelli, G. Caselli, L.C. Rovati. *Rottapharm Biotech, Monza, Italy*

Background: Obesity is a risk factor for osteoarthritis (OA). In obese subjects OA develops not only in weight-bearing joints but also in non-weight-bearing joints, suggesting that dysregulated metabolism in obese patients may promote OA onset.
As obesity evolves many physiological parameters are dysregulated, including the levels of adipokine hormones such as leptin and adiponectin. For this reason, it has been suggested that adipokine levels in serum and synovial fluid are associated with a worsening of synovial inflammation and OA progression in these patients(1).
In vivo and in vitro studies show that high levels of leptin induce the synthesis of metalloproteases involved in cartilage degradation(2). Conversely, dietary-induced weight loss is associated with increased adiponectin serum levels and reduced loss of tibial and femoral cartilage volume, suggesting a protective role of adiponectin in OA.
STR/ort mice are an animal model of spontaneous OA characterized by early pathology development (at about 20 weeks) and dysregulated metabolism(3). Notably, these mice have adiponectin serum levels lower than those found in control mouse strains(4).
Objectives: To evaluate whether adiponectin and leptin serum levels are associated with OA development and/or progression in STR/ort mice.
Methods: First, we measured the time course of adipokine levels in STR/ort mice before the onset of OA (at 8, 14 and 20 weeks of age), and in age-matched CBA control mice. Then, we calculated the ratio leptin/adiponectin (L/A) in the serum of STR/ort mice during OA progression (at 20, 30 and 40 weeks). Blood samples were collected from caudal vein (time course) or from vena cava at sacrifice, when knee joints were collected, processed for histology and blindly scored according to OARSI and Mankin's methods.
Results: Adiponectin serum levels in STR/ort mice at 8, 14 and 20 weeks were significantly lower than in age-matched CBA mice. Instead, leptin serum levels in STR/ort mice were higher than in CBA strain at 14 and 20 weeks. Consequently, there was a relevant difference in the ratio L/A between the two strains, with greater L/A values in STR/ort mice at 14 and 20 weeks. (Table 1)
In STR/ort mice, the ratio L/A tended to further increase between 30 and 20 weeks (1.73±0.16 from 1.28±0.17, respectively), in parallel with the increase in OARSI scores of knee joints (11.1±1.5 vs 8.4±1.3). The histopathological score increased in STR/ort mice even between 30 and 40 weeks, but without a concomitant increase in the ratio L/A.

Adipokines levels (mean ± SEM)

Age (Weeks)	8	14	20
CBA (n=10)			
Adiponectin (µg/ml)	20.2 ± 0.7	16.0 ± 0.4	14.5 ± 0.3
Leptin (ng/ml)	1.5 ± 0.3	2.5 ± 0.3	3.1 ± 0.4
L/A	0.07 ± 0.02	0.16 ± 0.02	0.21 ± 0.03
STR/ort (n=14)			
Adiponectin (µg/ml)	9.2 ± 0.3**	7.3 ± 0.2**	6.0 ± 0.2**
Leptin (ng/ml)	3.3 ± 0.5	8.7 ± 1.3**	7.9 ± 1.1**
L/A	0.36 ± 0.05	1.15 ± 0.16**	1.28 ± 0.17**

**p<0.001 STR/ort vs CBA

Conclusions: We show for the first time that leptin serum levels and the ratio L/A in STR/ort mice are higher than in CBA mice, and that the ratio L/A in STR/ort mice increases as their histopathological scores worsen. We suggest that dysregulated levels of these adipokines may be associated or even precede OA development in this animal model.
References:
[1] King L.K. et al. Osteoarthritis and Cartilage, 2015.
[2] Bao J.P. et all. Mol Biol Rep. 2010.
[3] Uchida K. et al. Experimental Animals, 2009.
[4] Giambelli R. et al. Osteoarthtis and Cartilage Volume 24, Supplement 1, April 2016, Pages S85.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3083

AB0051 INTERLEUKIN-6 BLOCKADE WITH TOCILIZUMAB DECREASES METALLOPROTEINASE-9 ACTIVITY IN SYNOVIAL FIBROBLASTS STIMULATED WITH SYNOVIAL FLUIDS OF PATIENTS WITH RHEUMATOID ARTHRITIS OR SPONDYLOARTHRITIS

R. Blas[1], H. Tamashiro[2], A. Munarriz[3], R. Pardo-Hidalgo[4], M.S. Di Genaro[5,6]. *[1]Centro Médico MEDICI; [2]Clínica Bolivar; [3]Centro Médico CENYR, San Luis; [4]Centro de Rehabilitación Médica CER, San Juan; [5]National University of San Luis; [6]Laboratory of Immunopathology, Multidisciplinary Institute of Biological Investigations - San Luis (IMIBIO-SL), National Council of Scientific and Technical Investigations (CONICET), San Luis, Argentina*

Background: Fibroblast-like synoviocytes (FLS) exhibit a transformed aggressive phenotype characterized by increased secretion of pro-inflammatory cytokines and matrix metalloproteinases (MMPs). Early pathological mechanisms that explain the change to an altered phenotype in FLS of chronic inflammatory arthropathies remain largely unknown. The composition of synovial fluids (SF) is very complex and strongly influences the microenvironment of joints including FLS thus representing an inseparable element of the disease. The MMP-9 is a

gelatinase expressed in three major forms: dimer, monomer and a complex with neutrophil gelatin-associated lipocalin (NGAL). Interleukin-(IL)-6 is a pleiotropic cytokine expressed by a variety of immune and non-immune cells. However, the mechanisms by which IL-6 contributes to the pathogenesis of chronic arthropathies are not fully understood.
Objectives: The purpose of the present work was to perform a comparative study of the IL-6 production and MMP-9 activity in FLS stimulated with SF from patients with osteoarthritis (OA), rheumatoid arthritis (RA) or spondyloarthritis (SpA). In addition, the effect of IL-6 blockade on MMP-9 activity was evaluated.
Methods: Primary FLS were obtained from SF of the RA patients. Furthermore, the SW982 human synovial cell line was used. The SF of patients with OA (n=11), RA (n=11) or SpA (n=9) patients were pooled. The FLS were stimulated with OA, RA or SpA SF pools and supernatants (SN) were collected after 24, 48 and 72 h. The IL-6 levels were assessed in the SN by ELISA. The gelatinase activity of the SN was determined by zymography. The IL-6 function was blocked with the anti-IL-6 receptor antagonist tocilizumab (TCZ) (200μg/ml).
Results: Earlier induction of IL-6 in SW982 cell line was observed by RA and SpA SF stimulation since significant levels were detected at 24 h ($p<0.001$ and $p<0.01$ compared with non-stimulated cells, respectively), whilst OA SF induced significant IL-6 secretion at 72 h ($p<0.01$). Similar results were observed in primary FLS. In contrast to SF of OA patients, SF of patients with RA or SpA induced increased and sustained secretion of active MMP-9. Moreover, the molecular weight band corresponding with NGAL-MMP-9 complex, considered a protected form of MMP-9, was detected with higher intensity in the SN of FLS stimulated with RA or SpA SF compared with OA SF ($p<0.001$). In the presence of TCZ, significant inhibition in the gelatinase activity of all MMP-9 forms was observed at 48h of stimulation with RA or SpA SF ($p<0.001$ for MMP-9 dimer and NGAL-MMP-9 complex; $p<0.01$ for MMP-9 monomer, compared with FLS stimulated in absence of TCZ).
Conclusions: We conclude that SF of patients with inflammatory arthritis recreate a differential microenvironment for FLS that impacts on early phenotypic changes of these cells. The IL-6 provokes augmented and persistent MMP-9 activity in FLS stimulated with RA or SpA SF. This work identifies TCZ as an inhibitor of all forms of MMP-9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2940

AB0052 INCREASED PERIPHERAL CD8+ T CELL RESPONSES IN SLE BY LOW-DOSE IL-2 TREATMENT

R. Zhang, J. He, X. Sun, Y. Zou, Y. Gan, Z. Li. *Peking University People's Hospital, Beijing, China*

Background: CD8+ T cell responses to viral pathogens is crucial for the prompt resolution of acute infections. SLE patients are more likely to have infections due to suppression of immune system by long-term glucocorticoid and immunosuppressive agent intake. Our previous study showed that low-dose IL-2 is effective in SLE.
Objectives: The present study is to evaluate the potential anti-infection effect of low-dose IL-2 in refractory SLE patients.
Methods: Nine refractory SLE patients and 9 health controls (HCs) were recruited three cycles of 1 million IU recombinant human IL-2 (rhIL-2), administered subcutaneously every other day for 2 weeks, followed by a 2-week break. The disease activitise were evaluated by rheumatologist. The frequencies of T cell subsets were assayed by flow cytometry. Virus-specific CD8 T cells responses were determined based on TNF-a, IFN-g and Grazmy B producing CD8 T cells upon CMV-EBV-Flu (CEF) viral peptide pool stimulation and subsequent intracellular staining.
Results: Most patients showed good clinical responses after three cycles of low-dose IL-2 treatment. Clinical improvement was observed in SIR-4 response, improved complement 3 and 4 serum level and decreased anti-ds-DNA serum level. Functional profiling of CD8 T cells in low-dose IL-2 treated patients revealed an increased in the frequencies of CEF viral peptide specific TNF-a$^+$ and Grazmy-B$^+$ CD8 T cells. Moreover, low-dose IL-2 treated patients showed stronger antigen-specific response demonstrated by an increased stimulated/non-stimulate TNF-a-producing CD 8 T cells proliferation fold. Compared with HCs, SLE patients showed significantly lower frequencies of CEF specific Grazmy-B producing CD8 T cell, and treatment with low-dose IL-2 significantly increased the frequency of these Grazmy-B$^+$ CD8 T cells in SLE patients.
Conclusions: Low-dose IL-2 treatment was effective and safe in refractory SLE patients. Virus-specific antigen-specific CD8 T cell response could be enhanced upon this treatment which might be potentially valuable in anti-infection in SLE.
References:
[1] Bilate AM, Lafaille JJ. Induced CD4+Foxp3+ regulatory T cells in immune tolerance. Annu Rev Immunol. 2012;30:733–58.
[2] Blattman JN, Grayson JM, Wherry EJ, Kaech SM, Smith KA, Ahmed R. Therapeutic use of IL-2 to enhance antiviral T-cell responses in vivo. Nat Med. 2003;9(5):540–7.
[3] Palucka K, Banchereau J. Diversity and collaboration for effective immunotherapy. Nat Med. 2016;22(12):1390–1.
Acknowledgements: We thank Pro. Xin Lin for valuable suggestions to this manuscript. The research in the laboratory was funded by grants from the NSFC (21010000237, NSFC by Pro. Jing He and Zhanguo Li.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3196

AB0053 MANGIFERIN MODULATES TNF-ALPHA AND MMP-9 SIGNALING

S. Somani[1,2], K. Modi[3]. *[1]Pharmacology, RK University, Rajkot; [2]Pharmacology, Torrent Pharmaceuticals, Gandhinagar; [3]Pharmacology, B K Mody Government Pharmacy College, Rajkot, India*

Background: Rheumatic manifestation such as arthritis, spondylitis are the most common frequent extra-intestinal manifestations of inflammatory bowel disease (IBD), affecting 6 to 46% of patients. IBD is an umbrella term with two most prevalent entities namely Crohn's disease and Ulcerative colitis, defined as idiopathic chronic, relapsing and remitting inflammatory condition of intestinal tract. MMP-9, a matrixin is involved in the degradation of extracellular matrix promoting inflammation. Studies on MMP-9 knockout mice illustrated protection from collagen induced rheumatoid arthritis (RA) and Dextran sulphate sodium (DSS) induced colitis. Furthermore elevated MMP9 levels can be found in the synovial fluid of RA patients as well as IBD patients signifying that targeting MMP9 may have therapeutic importance. Mangiferin, an active component of Mango has demonstrated anti-inflammatory effects in the treatment of rheumatoid arthritis with low side-effects [1,2]; but its usefulness in chronic remission and relapse phases of human IBD i.e. chronic DSS model have not screened till date.
Objectives: We investigated the therapeutic potential of Mangiferin; in a clinical relevant chronic model of DSS induced colitis in mice.
Methods: Female BALB/c mice (8 to 12 wks) were randomized into four groups. Colitis was induced by cyclical administration of 5% DSS to mice i.e. 3 cycles of DSS with every cycle consisting of 7 days DSS followed by 7 days of autoclaved drinking water (7D DSS + 7D water). Group I (Normal control): free access to autoclaved drinking water. Group II (DSS control): free access to 5% DSS. Group III (DSS + Mangiferin_30mg/kg): free access to 5% DSS + oral Mangiferin at 30mg/kg. Group IV (DSS + Mangiferin_60mg/kg): free access to 5% DSS + oral Mangiferin at 60mg/kg. Mangiferin treatment was initiated following second cycle of DSS (i.e. Day 21); after assuring that colitis relapsed in mice. One fragment of the colon was fixed in 10% neutral buffered formalin for microscopic examination while the remaining tissue was divided into parts and stored at -70℃ for assessment of biochemical markers of oxidative stress and inflammatory cytokines such as TNF-α, IL-1β, MMP-9.
Results: Mangiferin treatment ameliorated the *clinical parameters* (body weight loss, stool consistency, occult blood), reduced *microscopic damage* (re-established mucosal architecture, abridged neutrophil infiltration), restored *epithelial barrier integrity* (diminished goblet cell loss), attenuated biochemical markers of *oxidative stress* (GSH, CAT, SOD, MDA, MPO), crucial *inflammatory cytokines* TNF-α, IL-1β and attenuates *MMP-9* levels implicated in the pathogenesis of arthritis and IBD.
Conclusions: Considering the beneficial effects of Mangiferin in arthritis and IBD, we suggest that it would be valuable to use Mangiferin in IBD patients with arthritis as its extra-intestinal manifestation.
References:
[1] Luczkiewicz, P., et al., Mangiferin: A promising therapeutic agent for rheumatoid arthritis treatment. Med Hypotheses, 2014. 83(5): p. 570–4.
[2] Tsubaki, M., et al., Mangiferin suppresses CIA by suppressing the expression of TNF-alpha, IL-6, IL-1beta, and RANKL through inhibiting the activation of NF-kappaB and ERK1/2. Am J Transl Res, 2015. 7(8): p. 1371–81.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4936

AB0054 CXCL4 POTENTIATES TLR-DRIVEN POLARIZATION OF HUMAN DENDRITIC CELLS TOWARDS CYTOKINE PRODUCTION, ANTIGEN CROSS-PRESENTATION AND INCREASES STIMULATION OF CD8+T-CELLS

S.C. Silva-Cardoso[1,2], A.J. Affandi[1,2], L. Spel[2,3], M. Cossu[1,2], M. Boes[2,3], T.R. Radstake[1,2]. *[1]Depart. of Rheumatology & Clinical Immunology; [2]Laboratory of Translational Immunology; [3]Department of Pediatrics, University Medical Center, Utrecht, Netherlands*

Background: CXCL4 is a chemokine produced by activated platelets and immune cells. Several studies have reported that CXCL4 plays a critical role on physiological processes since it affects the proliferation and maturation of megakaryocytic and hematopoietic progenitor cells, regulates coagulation and wound healing, displays anti-tumoral and angiostatic activity and induces immune cell modulation. Dysregulation of these processes causes the disturbance of the immune system and homeostasis, and might lead to pathological conditions. Indeed, a strong correlation was previously found between elevated CXCL4 levels in the circulation and the clinical features of patients with systemic sclerosis (SSc) (1). Dendritic cells are essential players in innate defence and bridging towards adaptive immune responses, thereby contributing to both immune activation and maintenance of homeostasis.
Objectives: Considering previous observations on the association of dendritic cells and T-cell dysfunction in SSc, we here investigated the effect of CXCL4 on monocyte-derived DC (moDC) differentiation, on Toll-like receptor (TLR)-mediated responses and on activation of polyclonal and antigen-specific CD8$^+$T-cells.

Methods: To this end, we compared the phenotype, TLR-mediated responses and CD8$^+$T-cell activation by moDCs and CXCL4 exposed moDCs.
Results: Already prior to TLR stimulation, CXCL4-moDCs displayed a more matured phenotype. We found that CXCL4 exposure can sensitize moDCs for TLR-ligand responsiveness, as illustrated by a dramatic upregulation of CD83, CD86 and MHC class I, and markedly increased secretion of IL-12 and TNF-α in response to TLR3 and TLR7/8-agonists. Next, we analyzed the effect of CXCL4 in modulating DC-mediated CD8$^+$ T-cell activation. CXCL4-moDCs strongly potentiated proliferation of polyclonal CD8$^+$ T-cells and production of interferon (IFN)-γ and IL-4, in an antigen-independent manner. While the internalization of antigen was comparable to moDCs, antigen processing by CXCL4-moDCs was impaired. Yet, these cells were more potent at stimulating antigen-specific CD8$^+$ T-cell responses.
Conclusions: Together our data supports that increased levels of circulating CXCL4 may contribute to immune dysregulation through the modulation of innate and adaptive responses by dendritic cells.
References:
[1] Van Bon, L & Affandi, A J; et al. 2014. Proteome-wide analysis and CXCL4 as a biomarker in systemic sclerosis. N. Engl. J. Med. 370: 433–43.
Acknowledgements: Supported by a PhD grant from the Portuguese Fundação para a Ciência e a Tecnologia (SFRH/BD/89643/2012) to S.C.S.C.; A.J.A. was supported by the grants from the Dutch Arthritis Association (Reumafonds grant NR-10–1-301) and the Netherlands Organization for Science Research (Mosaic grant 017.008.014); T.R.D.J.R. was funded by an ERC Starting grant, a grant from the Dutch Arthritis Foundation and Pre-Seed grant Dutch Association of Science (NWO).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4890

AB0055 IL-1 BETA AND CASPASE-1 P45 EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF PATIENTS WITH ADULT-ONSET STILL'S DISEASE

S. Bindoli, F. Fabris, L. Punzi, P. Galozzi, P. Sfriso. *Rheumatology Unit-Department of Medicine, University of Padova, Padova, Italy*

Background: Adult-onset Still's disease (AOSD) is a systemic inflammatory condition characterized by episodes of spiking fever, evanescent rash, arthralgia, leukocytosis and hyperferritinemia. The inflammatory status of AOSD could result from a deregulation of the NLRP3 inflammasome as Interleukin-1 (IL-1) is pivotal in the pathogenesis of AOSD.
Objectives: To evaluate IL-1 beta and caspase-1 p45 expression in AOSD patients.
Methods: 11 AOSD patients with systemic chronic disease (mean age: 44.5±15.6 years; mean disease duration: 3.0±1.7 years) and 5 healthy donors (mean age: 41.8±7.5) were enrolled. Anakinra (in 6 patients) and DMARDs (in 5 patients) adequately controlled the disease. PBMCs (peripheral blood mononuclear cells) obtained by Ficoll centrifugation were stimulated with lipopolysaccharide (LPS) [10 ng/ml] and ATP [1 mM] for 0.5, 1, 6 and 24 hours. IL-1β level was measured in the supernatant by ELISA and the expression of caspase-1 p45 at protein level was detected by Western Blotting.
Results: In unstimulated PBMCs minimal IL-1β production was found both in AOSD patients and controls. After 6 hours stimulation, IL-1β level was increased whereas we observed a reduced processing of caspase-1 p45 particularly in AOSD patients treated with Anakinra.

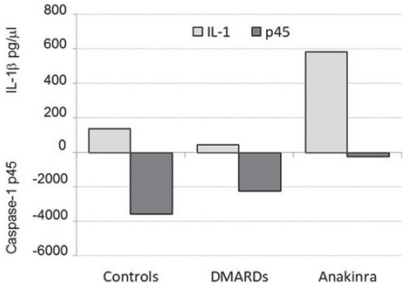


Figure 1. IL-1β secretion and caspase-1 p45 intracellular expression: differences between stimulated and unstimulated PMBCs in anakinra and DMARDs treated AOSD patients and in healthy controls.

Conclusions: Patients with refractory AOSD, who therefore need Anakinra, seem to have an increased production of IL-1β compared to healthy controls and to AOSD patients who respond to standard therapies. Altered processing of caspase-1 p45 in AOSD patients support the involvement of the NLRP3 inflammasome pathway in the pathogenesis of the disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6889

AB0056 EMERGING ROLE OF IL-33/ST2 AXIS IN ENDOTHELIAL CELL INJURY OF LUPUS NEPHRITIS

S. Yu, Y. Tao. *Rheumatology, The Second Affiliated Hospital of Guangzhou Medical, Guangzhou, China*

Background: "Alarmins" are prototypic endogenous pro-inflammatory factors as they are released from necotic cells and provoke local damage or systemic inflammation. Evidences are accumulating to support the inclusion of "Alarmins" as targets of autoreactivity as well as inducers in the pathogenesis of Systemic Lupus Erythematosus (SLE). Interleukin (IL)-33 is a novel member of the family of "Alarmins" because of its characteristics and functions in mediating host immune responses. On this background, we sought to determine the role of IL-33/ST2 axis in lupus pathogenesis. The role of IL-33/ST2 axis has not previously been described in lupus nephritis.
Objectives: This project will study the followings: (1) To determine whether IL-33 was present in renal glomerular endothelial cells; (2) To assess the functional and intracellular signal transuction mechanisms regulating the link between IL-33/ST2-mediated innate immunity and inflammation in CD4$^+$ T cells-endothelial cells co-culture system of lupus patients.
Results: Immunofluorescence (IF) for IL-33 in the kidney were performed in both MRL^{lpr} lupus mice and C57BL/6J mice. On double staining for IL-33 and lectin, IL-33 was clearly seen in glomeruli and also in peritubular areas. To determine whether the IL-33 staining in glomeruli and peritubular areas was in endothelium, double IF staining for IL-33 and von Willebrand factor (vWF) was performed. IL-33 co-localized with vWF in glomeruli and in peritubular areas. The increased levels of IL-33 mRNA transcripts were detected in kidney of MRL^{lpr} lupus mice compared with C57BL/6J mice. Expression of cell-surface ST2 was increased on the CD4$^+$ T cells of lupus patients when compared with healthy controls. Serum sST2 level was significantly higher in SLE patients with *flare* than those without *flare* ($p<0.05$).
Conclusions: As a result of external stimuli or infection, renal glomerular endothelial cells undergo cellular death and release the "Alarmin", IL-33, to alert the lupus immune system. Released IL-33 interact with their target cells, CD4$^+$ T cells via their specific receptor ST2 to subsequently induce innate and adaptive responses, activate inflammatory pathways in the pathogenesis of lupus nephritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1700

AB0057 THE ROLE OF GROWTH DIFFERENTIATION FACTOR (GDF)-15 AND TRANSFORMING GROWTH FACTOR (TGF)-β IN THE DEVELOPMENT OF PULMONARY FIBROSIS

V. Yazisiz, S. Oygen, M. Çavuşoğlu, M. Kahraman, E.G. Gök, S. Karahan, I. Uçar, M.E. Terzioğlu. *Rheumatology, Akdeniz University, Antalya, Turkey*

Background: The pathogenesis of pulmonary fibrosis is not fully understood and it is thought to develop secondary to inflammation. The main cause of pulmonary fibrosis is considered to be interstitial lung disease (ILD), which can be associted with connective tissue disorders (CTD).
Objectives: The aim of this study was to investigate serum GDF-15 and TGF-β levels in patients with diagnosis of CTD associated with ILD.
Methods: A total of 103 adult patients (19 rheumatoid arthritis, 18 Sjögren's syndrome, 32 systemic sclerosis, 3 systemic lupus erythematosus and 31 healthy controls) were included in the study. Pregnant, acute coronary syndrome, previous myocardial infarction and/or stroke history, heart failure and malignancy were excluded. Serum GDF-15 and TGF-β levels were studied by ELISA method in peripheral blood samples.
Results: There were 44 patients with CTD-ILD, 28 patients without ILD and 31 healthy controls. The age and gender distributions of participants in all three groups were not different. Serum TGF-β and GDF-15 levels in patients with CTD-ILD and CTD without ILD were significantly higher than healthy controls (respectively, 3.05±0.26, 3.05±0.22, 1.39±0.33 pg/ml, $p<0.001$ for TGF-β and 1.17±0.17, 1.12±0.05, 0.95±0.21 pg/ml, $p<0.001$ for GDF-15). There were no statistically different from patients with ILD and without ILD for both TGF-β (p:0.864) and GDF-15 levels (p:0.146) in CTD. Also, GDF-15 and TGF-β levels of patients with systemic sclerosis were not different from other CTD's.

Table 1. Comparison of analysis results of patient and control groups

	Connective tissue disorders		Healty Controls (n: 31)	p
	ILD (+) (n: 44)	ILD (–) (n: 28)		
Gender (Female) (n, %)	35 (79.5%)	22 (78.5%)	23 (74.2%)	0.831
Age (years) (Mean±SD)	53.95±11.9	53.61±9.2	51.68±12.8	0.641
TGF-β(pg/ml) (Mean±SD)	3.05±0.26	3.05±0.22†	1.39±0.33	<0.001
GDF-15 (pg/ml) (Mean±SD)	1.17±0.17	1.12±0.05‡	0.95±0.21	<0.001

†ILD vs non-ILD p=0.864. ‡ILD vs non-ILD p=0.146.

Conclusions: Our findings indicate that TGF-β and GDF-15 are increased in CTD patients but, they are not a specific markers for CTD-ILD
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1586

AB0058 LEVEL OF VASCULAR ENDOTHELIAL GROWTH FACTOR A AND INTIMA-MEDIA THICKNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

V.O. Omelchenko, E.A. Letyagina, M.A. Korolev. *FSBSI "Scientific Institute of clinical and experimental lymphology", Novosibirsk, Russian Federation*

Background: Early development of atherosclerosis (AS) with higher mortality risk is observed in patients with rheumatoid arthritis (RA). Actually, this problem hasn't been solved. That's why researches devoted to finding of relationships between RA and AS is still of current interest. In RA pannus formation accompanied by the development of new blood vessels forms main clinical manifestation. Vascular endothelial growth factor A (VEGF-A) is a heparin-binding glycoprotein, that induces the growth of blood vessels and plays a role in differentiation of endothelial cells. The expression of VEGF-A increases when plaque developes.
Objectives: To determine the particular qualities of VEGF-A production in patients with RA and various atherosclerotic damage of vessels.
Methods: 67 Caucasian patients with RA (age - 52 yr., [38;59], DAS28 5,25 [5,5;6,4]) were included in our study. Patients had American College of Rheumatology (ACR)-defined RA (1987 classification criteria). 45 Europeoid patients with OA (56 yr., [50;63]) were in control group. All patients gave written informed consent before enrollment. Level of VEGF-A was determined by ELISA for quantitative detection of human VEGF-A (Bender MedSystem GmbH, Austria). Range of atherosclerotic damage was assessed by ultrasonography with measurement of carotid intima-media thickness (IMT). IMT measured was compared with normal values according to the age and sex classes: younger 40 yr - 0,7 mm, 40–50 yr - 0,8 mm, elder 50 yr - 0,9 mm for men; younger 45 yr - 0,7 mm, 45–60 yr - 0,8 mm, elder 60 yr - 0,9 mm for women. Results is presented as median and 25th/75th percentiles (Me [25th percentile; 75th percentile]. Descriptive statistics, non-parametric Mann-Whitney U-test, Kruskal – Wallis test were used for analysis of the results.
Results: No significant differences of IMT were found between groups with RA and OA. Abnormal IMT were observed in about half of patients (Table 1).

Table 1. IMT in patients with RA and OA

	IMT	IMT>N	Plaque
RA, n (%)	35 (52.2)	20 (29.9)	12 (17.9)
OA, n (%)	18 (40)	12 (26.7)	15 (33.3)

The highest level of VEGF-A was in OA-group with stenosing plaque ($p<0,01$). No significant differences were found between other OA-subgroup. In patients with RA the highest level of VEGF-A was observed in subgroup with abnormal IMT ($p<0,05$), but not with pluques. Generally, VEGF-A production in patients with normal IMT was higher in RA-patients, but not sugnificially.

Table 2. Level of VEGF-A in groups with different values of IMT

	IMT	IMT>N	Plaque without stesosis	Stenosing plaque
VEGF-A in OA-patients, pg/ml	392,30 [225,60;641,33]	396,90 [213,08;519,95]	651,05 [318,58;1041,25]	1148,50 [1041,3;1164,25]
VEGF-A in RA-patients, pg/ml	753,6 [434,4;1301,15]	1013 [595,6;1319,1]	837,25 [677,28;1267,25]	712,75 [505,28;1036,85]

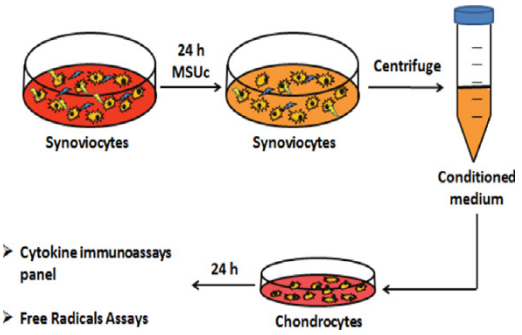
Conclusions: Regulation of VEGF-A production may play a role in earlier onset of atherosclerosis in patients with RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4556

Cartilage, synovium and osteoimmunology

AB0059 SYNOVIAL SECRETION OF PRO-INFLAMMATORY AND PRO-OXIDANT MOLECULES TRIGGERED BY MONOSODIUM URATE CRYSTALS INDUCES NGF AND H2O2 PAIN MEDIATORS IN THE CHONDROCYTE

A.G. Lopez-Reyes[1], D. Medina-Luna[2], M. Satamaria-Olmedo[2], K. Martinez-Flores[3], Y. Zamudio-Cuevas[3], J. Fernandez-Torres[3], G. Martinez-Nava[3], D. Clavijo-Cornejo[3], A. Olivos-Meza[4], M. Gutierrez[5], M. Fernandez-Moreno[6], F. Blanco[6], C. Pineda[5]. *[1]Laboratorio de Liquido Sinovial, Instituto Nacional de Rehabilitación "LGII"; [2]Laboratorio de Liquido Sinovial, Instituto Nacional de Rehabilitacion "LGII"; [3]Laboratorio de Liquido Sinovial, Instituto Nacional de Rehabilitacion "LGII"; [4]Arthroscopy Service, Instituto Nacional de Rehabilitación "LGII"; [5]Department of Rheumatic and Musculoskeletal Diseases, Instituto Nacional de Rehabilitacion "LGII", Mexico City, Mexico; [6]Rheumatology Service, INIBIC, CIBER-BBN, A Coruña, Spain*

Background: Gout is the most prevalent inflammatory arthropathy in young men, in which clinical manifestations are triggered by the deposits of monosodium urate (MSU) crystals in and around joints. From a clinical perspective, gouty attacks and tophaceous deposits have been associated to nodal osteoarthritis [1,2].
Objectives: To determine the molecular mechanisms associating MSU crystal deposits with chondrocyte activation and changes in articular cartilage.
Methods: Primary cultures of synoviocytes were activated with MSU crystals for 24 h, the resulting supernatant was used as a supplementary conditioning basal medium (CBM) for 24 h chondrocyte growth. The expression level profile of cytokines (IL-6, IL-8) and nerve growth factor (NGF) in the supernatant was measured. Production of reactive oxygen and nitrogen species, such as $O_2^{\bullet}$, H_2O_2, and $NO^{\bullet}$, was also measured intracellularly.
Results: Upon activation by MSU crystals, synoviocytes increased secretion of IL-6 and IL-8, as well as intracellular production of $O_2^{\bullet}$, H_2O_2, and $NO^{\bullet}$ in comparison to non-stimulated synoviocytes. Additionally, the chondrocytes incubated with CBM for 24 h increased significantly IL-6, IL-8, and NGF levels, as well as $O_2^{\bullet}$, H_2O_2, and $NO^{\bullet}$ levels when compared to non-stimulated chondrocytes. Secretion of these soluble mediators was even higher than the one observed in the synoviocytes and chondrocytes directly stimulated with MSU crystals.



Conclusions: Pro-inflammatory cytokine secretion induced by MSU crystals in synoviocytes triggers chondrocyte activation, intensifying the articular inflammatory state in gouty attacks. Furthermore, the increase in reactive species (particularly $NO^{\bullet}$, which inhibits proteoglycan synthesis) compromises the homeostasis of the extracellular matrix of the cartilage. Finally, overproduction of NGF and H_2O_2 by the chondrocyte functions a pain modulator during gout attacks.
References:
[1] Fam AG, et al. Gouty arthritis in nodal osteoarthritis. J Rheumatol 1996; 23:684–9.
[2] Roddy E, et al. Gout and nodal osteoarthritis: a case-control study. Rheumatology (Oxford) 2008; 47:732–3.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2401

AB0060 MODELLING DELAYED BONE HEALING IN A MOUSE-OSTEOTOMY MODEL TO EVALUATE THERAPEUTIC STRATEGIES FOR AFFECTED PATIENTS WITH RA

A. Lang[1,2,3], S. Fügener[1], P. Hoff[1], K. Schmidt-Bleek[4], T. Gaber[1,3], F. Buttgereit[1,3]. *[1]Department of Rheumatology and Clinical Immunology; [2]Berlin-Brandenburg School for Regenerative Medicine, Charité University Hospital; [3]German Arthritis Research Center; [4]Julius Wolff Institute and Center for Musculoskeletal Surgery, Charité University Hospital, Berlin, Germany*

Background: Anti-inflammatory treatment of rheumatoid arthritis (RA) using non-steroidal anti-inflammatory drugs (NSAID) or glucocorticoids (GC) as well as the disease itself, are supposed to negatively influence bone metabolism and healing. However, *in vivo* models allowing to evaluate therapeutic strategies for patients suffering from delayed bone healing are scarce and mainly created by critical size defects that are not representative for comorbity-induced disorders. In addition, there are no adequate rodent models allowing the analyses of the influence on the bone metabolism by the complete dysregulation of the immune system in RA as well as long-term medications with NSAID or GC. Previously, we have shown that immunologically restricted patients lack an adequate adaptation to hypoxia in the fracture hematoma thus facilitating healing disorders (1). The hypoxic microenvironment during the initial fracture-healing phase is known to be essential for activating the immunological reactions, which induce the regeneration. Furthermore, we performed a single-center retrospective study on fracture healing disorders showing a significant high prevalence for RA patients to be affected by delayed bone healing.
Objectives: In order to evaluate therapeutic strategies for affected patients with RA, we developed a model for delayed bone healing in a mouse-osteotomy model.
Methods: Female C57BL aged 12 weeks underwent osteotomy of the femur (fracture gap 0,7 mm) that was fixated with an external fixator (RIS-System). Lyostypt® (based on bovine Col I; mimicking extracellular bone matrix) was applied in the fracture gap and analysis was performed 2 and 3 weeks after surgery. The ratio of bone volume (BV) per total volume (TV) in the fracture gap was evaluated using *in vitro* μCT. In addition, Movat's pentachrome staining was performed to analyze the cellular and tissue composition within the fracture gap. To investigate the number of cells as well as the vessel formation, we used immunofluorescence to stain for Endomucin, PECAM-1 and DAPI. Quantitative analysis of histological staining was conducted by using ImageJ.
Results: We developed an *in vivo* mouse-osteotomy model showing delayed bone healing by applying Lyostypt® in the fracture gap. The BV, TV as well as the

ratio was significantly higher in the controls (empty gap = normal healing; n=8 per timepoint) as compared to the Lyostypt® group (n=8 per timepoint) 2 weeks after osteotomy and slightly higher after 3 weeks. Histological investigation showed the clear presence of the scaffold on both timepoints without briding cartilaginous tissue. The cell number as well as the vessel formation was significantly reduced within the fracture gap.

Conclusions: The results obtained so far support the hypothesis that we were able to develop a delayed healing or even non-union osteotomy model in mice by avoiding to create a critical size defect. Therefore, this approach represents a promising alternative animal model to evaluate therapeutic strategies to overcome bone healing complications in RA patients and perhaps other immunologically restricted patients.

References:
[1] Hoff et al. 2011 Immunol Res 51(1):116–22.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6578

AB0061 35SULPHATE INCORPORATION ASSAY AS A NEW TOOL FOR MEASURING EARLY CARTILAGE DEGRADATION FOLLOWING BLOOD EXPOSURE IN VITRO AND IN VIVO IN F8 KO RATS

A.E. Pulles[1,2], K.R. Christensen[3,4], K. Coeleveld[1], M. Kjelgaard-Hansen[4], R.E. Schutgens[2], F.P. Lafeber[1], K. Roepstorff[4], S.C. Mastbergen[1]. *[1]Department of Rheumatology & Clinical Immunology; [2]Van Creveldkliniek, University Medical Center Utrecht, Utrecht, Netherlands; [3]Veterinary Disease Biology, University of Copenhagen, Copenhagen; [4]Global research, Novo Nordisk A/S, Maaloev, Denmark*

Background: Joint damage upon bleeding causes significant morbidity in patients with hemophilia, and adds to joint degeneration after trauma or major joint surgery. To study the pathophysiology, rodent models with histology as primary outcome measure are often used. However, histological changes take time to develop and are subject to interpretation. Determining proteoglycan synthesis rate (PSR) in cartilage, by incorporation of radioactive ^{35}sulphate, is a sensitive method previously applied in human tissue and larger animal models to detect early cartilage changes. Isolating cartilage of small animals can be challenging, so a technique to shave off rat cartilage was developed.

Objectives: To study cartilage degradation following blood exposure, applying the ^{35}sulphate incorporation assay on rat tibial cartilage.

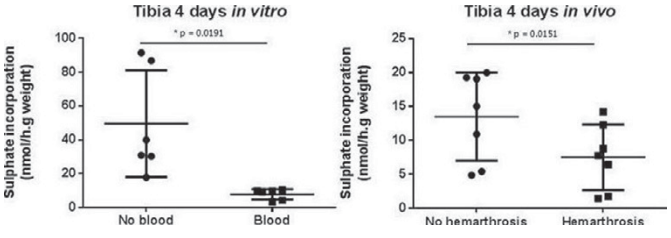
Methods: A total of 13 factor VIII knock out (F8KO) rats were bred and housed at Novo Nordisk A/S, Maaloev, Denmark. After euthanasia, the legs were removed and transported to UMC Utrecht, The Netherlands.

In vitro: within 24 hours after euthanasia the cartilage of 6 healthy F8KO rats was obtained by shaving off cartilage pieces of the tibia plateau by use of a scalpel. All cartilage explants were cultured for four days; in addition to culture medium, half of the cartilage samples were cultured with 50% v/v whole blood. After four days PSR was determined by adding 4uCi $Na_2{}^{35}SO_4$ to the cultures for four hours. $^{35}SO_4^{2-}$ is incorporated into newly synthesized proteoglycans. After digesting the cartilage pieces and precipitating the proteoglycans with cetylpyridinium chloride, the amount of radioactivity was measured by liquid scintillation analysis and normalized to the specific activity of the pulse medium, labeling time and wet cartilage weight.

In vivo: in 7 F8KO rats a unilateral joint bleed was induced by needle puncture and in the following four days until euthanasia, the animals received analgesia. At UMCU, the tibial cartilage was removed and PSR determined as described above.

All animal experiments were performed in accordance with and approved by the Danish Animal Experiments Council, Ministry of Food, Agriculture and Fisheries, Denmark.

Results: On average, a total of 1.6mg (0.8–3.1mg) cartilage per tibia could be obtained. The PSR of healthy cartilage determined after four days of culturing *in vitro* was on average 49.5 nmol/h.g. *In vitro* blood exposure resulted in a diminished synthesis: 7.7 nmol/h.g (p=0.0191), corresponding to an 84% decrease comparable to previously published experiments using human tissue [1]. *In vivo*, an induced joint bleed led to a 44% decrease in PSR (13.5 vs 7.5 nmol/h.g, p=0.0151).



Conclusions: This study demonstrates for the first time that PSR, by use of the ^{35}sulphate incorporation assay, can be determined in rat tibial cartilage and is affected by blood exposure *in vitro* and *in vivo*. As such, this assay can be a valuable tool to detect cartilage changes using joint degenerative rat models.

References:
[1] L. van Vulpen, R. Schutgens, K. Coeleveld, E. Alsema, G. Roosendaal, S. Mastbergen, F. Lafeber. IL-1beta: in contrast to TNFalpha, is pivotal in blood-induced cartilage damage and is a potential target for therapy. Blood, 2015;126(19):2015, pp.2239–2246.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1468

AB0062 EX VIVO BACK-TRANSLATION OF FOSTAMATINIB'S EFFECT ON JOINT ECM TURNOVER SHOWS SIGNIFICANT EFFECT ON BONE BUT NO EFFECT ON THE SYNOVIUM

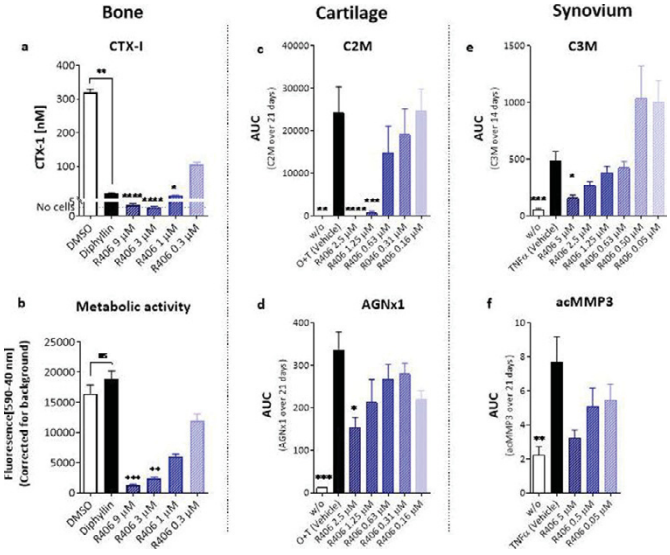
C.F. Kjelgaard-Petersen[1,2], T.G. Christensen[3], P. Hägglund[2], M.A. Karsdal[4], C.S. Thudium[4], A.-C. Bay-Jensen[4]. *[1]Biomarkers and Reseach, Rheumatology, Nordic Bioscience, Herlev; [2]Bioengineering, Technical University of Denmark, Lyngby; [3]Orthopaedic surgery Unit, Gentofte University Hospital, Gentofte; [4]Biomarkers and Research, Rheumatology, Nordic Bioscience, Herlev, Denmark*

Background: It is important to establish translational methods that aid in pre-clinical go/no-go decision points to increase the success rate of approved DMARDs. The Spleen tyrosine kinase (Syk) inhibitor Fostamatinib (Fosta) was terminated for development for RA, due to insufficient effect on joint structure in phase III.

Objectives: The objective was to use a translational system of *ex vivo* cultures to back-translate the insufficient effect on joint structure described in clinical studies.

Methods: Human mature osteoclasts (HOC) seeded on bone, bovine cartilage explants (BEX) and human synovial explants (SME) were treated with R406 (API of Fosta) at 5μM-0.05μM. Osteoclasts were co-stimulated with 25 ng/ml M-CSF and RANKL, while BEX and SME were co-stimulated with TNFα 2 ng/mL and OSM 10 ng/mL (O+T) or TNFα 10 ng/mL, respectively. CTX-1 and Ca^{2+} were measured in conditioned medium (CM) from HOC. Metabolic activity of HOC was assessed with Alamar Blue. C2M and AGNx1 were measured in CM from BEX, while acMMP3, C1M, and C3M were measured in CM from SME. The biomarkers in BEX and SME CM were measured at 4 time points and the total release were quantified by area under the curve (AUC). CTX-1, C2M, AGNx1, acMMP3, C1M, C2M and C3M were measured with ELISA. $Ca^{2+}$was measured with ADVIA Chemistry system. Statistical differences of metabolic activity was calculated with One-way ANOVA with Dunnett's multiple comparison test. Statistical differences between biomarkers levels or AUC were calculated with Kruskall Wallis test with Dunn's multiple comparision test.

Results: R406 decreased the release of CTX-1 (Fig 1A) and Ca^{2+} in a dose-dependent manner, with a significant decrease at 1μM ($P<0.01$). This might be due to a toxic effect of R406 on HOC (Fig 1B) ($P<0.05$). R406 decreased the total release of C2M and AGNx1 in a dose-dependent manner in BEX. C2M was inhibited a concentrations down to 1.25μM ($P=0.034$), and AGNx1 down to 5μM ($P=0.012$). In SME R406 only decreased the release of C1M and C3M (Fig 1e) significantly at 5 μM (C1M: $P=0.03$, C3M: $P=0.046$), and tended to decrease release of acMMP3 (Fig 1f) at 5μM. The later was however not significant.



Conclusions: Serum-based biomarkers of the joint ECM turnover were measured in CM from HOC, cartilage and synovial explant cultures. R406 decreased bone resorption and HOC metabolic activity in a dose-dependent manner, together with the MMP-mediated degradation of type II (C2M) collagen and aggrecanse degradation of aggrecan (AGNx1) in cartilage. However, R406 had limited effect on the inflammation driven MMP-mediated degradation of type I (C1M) and III (C3M) collagen and activation of MMP-3. CTX-1, C2M, and C3M have previously been measured in OSKIRA-1, with a profile identical to the *ex vivo* measurements here [1].

References:
[1] Platt A, Bay-Jensen AC, Braddock M, et al. The Effect of Fostamatinib with

Methotrexate on Circulating Biomarkers of Synovium, Cartilage and Bone Metabolism: Potential Utility for Clinical Development Decision Making in Rheumatoid Arthriti [abstract]. Arthritis Rheumatol. 2016; 68 (suppl 10).
Disclosure of Interest: C. Kjelgaard-Petersen: None declared, T. Christensen: None declared, P. Hägglund: None declared, M. Karsdal Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S, C. Thudium Employee of: Nordic Bioscience A/S, A.-C. Bay-Jensen Shareholder of: Nordic Bioscience A/S, Employee of: Nordic Bioscience A/S
DOI: 10.1136/annrheumdis-2017-eular.6788

AB0063 THE PROTECTIVE EFFECT OF PFTα ON ALCOHOL-INDUCED OSTEONECROSIS OF THE FEMORAL HEAD

C. Yixuan. *Orthopedics, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China*

Background: Epidemiologic studies have shown that alcohol plays a pivotal role in the development of osteonecrosis of the femoral head (ONFH). However, few studies have discussed the pathogenesis of or interventions for alcohol-induced ONFH.
Objectives: The aim of this study was to explore the underlying mechanism of alcohol-induced ONFH and the protective effect of pifithrin-α (PFTα).
Results: Through a series of *in vitro* assessments, we found that ethanol treatment significantly activated p53, suppressed Wnt/β-catenin signaling and inhibited osteogenic-related proteins, including runt-related transcription factor 2 (RUNX2), osteocalcin (OCN), osteopontin (OPN) and collagen I (COL1). Furthermore, by separating the cytoplasmic and nuclear proteins, we found that ethanol inhibited osteogenesisby impairing the accumulation of β-cateninin both the cytoplasm and nucleus in human bone mesenchymal stem cells (hBMSCs), which resulted from activating glycogen synthase kinase-3β (GSK-3β). In this *in vivo* study, we established alcohol-induced ONFH in rats and investigated the protective effect of PFTα. Micro-CT, hematoxylin & eosin (H&E) staining, immunohistochemical analyses, immunofluorescence staining, TUNEL staining, and fluorochrome labeling were performed to reveal the PFTα-induced therapeutic effects. H&E findings combined with TUNEL, caspase-3-cleaved immunohistochemical staining, and micro-CT images revealed obvious ONFH in the alcohol-administered rats, whereas significantly less osteonecrosis developed in the rats injected with PFTα. As the initiator of osteogenesis, RUNX2 and its downstream targets OCN, OPN, COL1 were immunostained in the femoral heads. These results indicated that those osteogenic-related proteins were significantly decreased in the alcohol-administered rats, whereas these results were reversed in the PFTα-injected rats. Fluorochrome labeling showed a similar result in that alcohol significantly reduced the osteogenic activity in the rat femoral head, which was blocked by the injection of PFTα.
Conclusions: Pifithrin-α, a p53 inhibitor, was able to block the ethanol-triggered activation of p53 in hBMSCs and alcohol-induced ONFH in a rat model. Its antagonistic effect against ethanol's effect on hBMSCs could be a clinical strategy to prevent the development of alcohol-induced ONFH.
Acknowledgements: The current study was supported by grants from the National Natural Science Foundation of China (no. 81272003 andno. 81301572) and the SMC-Chen Xing Plan for Splendid Young Investigators of Shanghai Jiao Tong University.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1981

AB0064 ADIPOSE STROMAL CELLS EXERT SPECIFIC EFFECTS ON OSTEOARTHRITIC SYNOVIAL MACROPHAGES

C. Manferdini[1], F. Paolella[1], E. Gabusi[1], L. Gambari[2], A. Piacentini[1], S. Fleury-Cappellesso[3], A. Barbero[4], M. Murphy[5], G. Lisignoli[1]. *[1]Laboratory of Immunorheumatology and tissue regeneration; [2]RAMSES Laboratory, Rizzoli Orthopaedic Institute, Bologna, Italy; [3]4EFS-Pyrénées-Méditerranée, Toulouse, France; [4]Department of Biomedicine, University Hospital Basel, Basel, Switzerland; [5]Regenerative Medicine Institute, Galway, Ireland*

Background: Osteoarthritis (OA) is the most common joint disease and the major cause of pain and disability in the aging population [1]. Adipose stromal cells (ASC) are promising candidate for cell therapy in OA, because they have immunomodulatory, trophic and differentiation capacities [2,3]. Synovial inflammation is accepted as important OA feature for the symptoms and disease progression [4]. Synovial tissue is mainly composed of synovial fibroblasts (SF), macrophages (SM) and a low percentage of other cell types [5].
Objectives: Aim of the study was to analyze the effects of adipose stromal cells in co-culture with SF and SM.
Methods: GMP clinical grade ASC were isolated from subcutaneous adipose tissue. Synoviocytes were isolated from synovial tissue of OA patients undergoing total joint replacement. Synovial cells at passage 1 and 5 were analyzed for: 1. different phenotypical markers by flow cytometric analysis, 2. inflammatory factors by multiplex immunoassay, 3.anabolic and degradative factors by qRT-PCR. Both p.1 (mix of SF and SM) and p.5 (only SF) synovial cells, as different cell models, were co-cultured with adipose stem cells (ASC) to define their effects. Furthermore macrophages type 1 (M1) were isolated and co-cultured with ASC.
Results: Synoviocytes at passage 1 were positive to typical markers of SM (CD14,CD16,CD68, CD80,CD163) and SF (CD55,CD73,CD90,CD105,CD106), whereas at passage 5 were positive only to SF markers and showed a higher percentage of CD55 and CD106. At p.1 synovial cells released a significantly higher amount of all inflammatory (IL6,CXCL8,CCL2,CCL3,CCL5) and anabolic (IL10) factors than those at p.5. Moreover, p.1 synovial cells expressed also higher amount of some degradative factors (MMP13, S100A8, S100A9) than p.5 synovial cells. Co-culture experiments showed that the amount of SM in p.1 synovial cells specifically orchestrate the up or down-modulation of some inflammatory (IL6,CXCL8,CCL2,CCL3,CCL5) and degradative factors (ADAMTS5,MMP13, S100A8,S100A9) analyzed. Interestingly, p.5 synovial cells induced all factors analyzed, except CCL5. Finally, we demonstrated that ASC effects were strictly dependent by M1, that decreased the release of typical macrophages cytokines (IL1β, IL6, TNFα and CCL3/MIP1α) and that ASC effects are responsible for the switching by M1 like inflammatory macrophages to M2 like phenotype mainly due to PGE2 involvement.
Conclusions: These data demonstrate that the GMP-ASC effects on OA synovial inflammation are strictly dependent by macrophages, that orchestrate the switching activated-M1 inflammatory macrophages to a M2-like phenotype, mainly through PGE2
References:
[1] Loeser RF (2012) Arthritis Rheum 64:1697–707.
[2] C. Manferdini (2013) Arthritis Rheum 65:1271–81.
[3] M. Maumus (2013) Stem Cell Research 11, 834–844.
[4] Y. Henrotin (2014) Semin Arthritis Rheum 43(5):579–87.
[5] MD. Smith (2011) The Open Rheumatology Journal 5:100–6.
Acknowledgements: This research was supported by Horizon 2020 Programme (project ADIPOA2, grant agreement no: 643809). The materials presented and views expressed here are the responsibility of the authors only. The EU Commission takes no responsibility for any use made of the information set out.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6081

AB0065 2-CARBA-CYCLIC PHOSPHATIDIC ACID SUPPRESSES EXPRESSION OF CARTILAGE DEGRADING ENZYMES SUCH AS MMP-13 IN INFLAMMATORY SYNOVIAL FIBROBLASTS AND ARTICULAR CHONDROCYTES INDUCED BY IL-1 BETA AND/OR TNF ALFA

I. Masuda[1,2], K. Okada[3], H. Yamanaka[1], S. Momohara[1,4]. *[1]Inst. of Rheumatology, Tokyo Women's Medical University, Tokyo; [2]Rheumatology, Inst. for Rheumatic diseases, Jyujyo-Takeda Rehabilitation Hospital, Kyoto; [3]SANSHO, CO., Ltd; [4]Keio University, Tokyo, Japan*

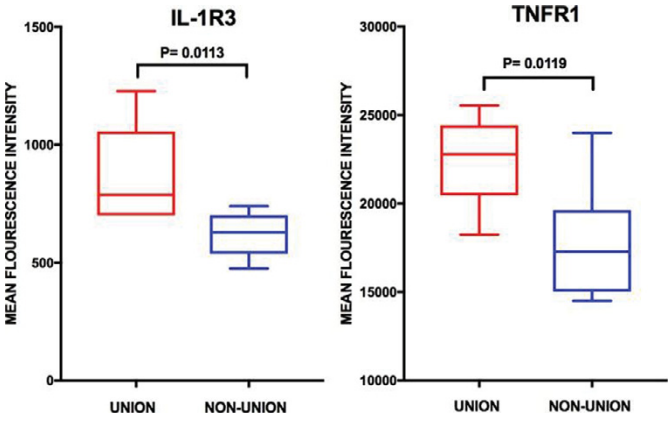
Background: Cyclic phosphatidic acid (cPA) is one of bioactive lipid, has been implicated as a mediator of various biological effects including inhibitory effects of proliferation, invasion and metastasis of cancer cells. cPA is naturally occurring mediator even exists in human serum. 2-carba-cPA (2ccPA) is structurally modified formula of cPA and has shown improved bioactivity. We have previously confirmed that 2ccPA stimulated HAS-2 production on human osteoarthritic chondrocytes and synovial fibroblasts (SFs) in vitro. Furthermore, intra-articular administration of 2ccPA has shown its suppressing effect of pain, swelling, and articular cartilage destruction in rabbit experimental osteoarthritis (OA). We have shown that 2ccPA might had direct inhibitory effect of cartilage degrading enzymes on rheumatoid synovial fibroblasts (SFs) in vitro. Inflammatory arthritis such as rheumatoid arthritis (RA) and early stage of OA involves synovial inflammation and subsequent production of cartilage degrading enzymes also from chondrocytes. 2ccPA may be possible another therapeutic option for degenerative arthritis.
Objectives: The aim of this study was to evaluate the direct effects of 2ccPA on cartilage matrix degrading enzymes using SFs and articular chondrocytes under influence of inflammatory cytokines.
Methods: In vitro studies were performed using SFs and chondrocytes obtained from arthritis patients (RA and OA) at joint replacement surgery. First, 2ccPA 0–25 μM was added to cell cultures and effects of 2ccPA on ADAMTS-4, -5, MMP-3, 9, -13 expression was assessed by real time PCR using specific primers to corresponding genes. Beta-actin was used as endogenous expression control for PCR. As we confirmed that 2ccPA had dose-dependent inhibitory effects on expression of above enzymes, the second experiment was performed. SFs or chondrocytes were pre-cultured with IL-1β (1 ng/ml) and/or TNF-α (10 ng/ml) for 24 hours, then added 10 μM 2ccPA to study attenuated effect of 2ccPA on synthesis of above cartilage matrix degrading enzymes. Newly synthesized MMP-3, -13 from SFs or chondrocytes in cultured media after 24 hours of 2ccPA addition were measured by sandwich ELISA.
Results: 2ccPA itself repressed cartilage degrading enzymes, ADAMTS-4, ADAMTS-5, MMP-3, MMP-9 and MMP-13 expression in both SFs and chondrocytes was all repressed by low dose of 2ccPA. Even after cells had been stimulated by cytokines, 10 μM 2ccPA repressed expression of cartilage degenerating enzymes in SFs or chondrocytes. Expression of MMP-13 were repressed more in chondrocytes by 2ccPA. ELISA results also confirmed the inhibitory effect of 2ccPA on MMP-13 production in RA SFs (n=5) by 52% or in RA chondrocytes (n=3) by 43%. In OA, MMP-13 production was reduced by 31% in OA SFs (n=6) and 34% in OA chondrocytes (n=4). However, not significant reduction of MMP-3 in both SFs or chondrocytes. MMP-9 expression by ELISA was under the detectable limit.

Conclusions: The in vitro results confirmed that 2ccPA had suppressing effect of cartilage degrading enzymes expression on SFs and chondrocytes, supports the hypothesis that 2ccPA might have played direct role to suppress inflammation and also protect articular cartilage in arthritic condition.
Disclosure of Interest: I. Masuda Grant/research support from: SANSHO, K. Okada: None declared, H. Yamanaka: None declared, S. Momohara: None declared
DOI: 10.1136/annrheumdis-2017-eular.5680

AB0066 HUMAN MULTIPOTENTIAL STROMAL CELLS EXPRESS LOW SURFACE LEVELS OF PRO-INFLAMMATORY CYTOKINE RECEPTORS IN BONE HEALING DEFECTS

J.J. El-Jawhari[1], G. Kleftouris[1], Y.M. El-sherbiny[1], R. West[2], E. Jones[1], P.V. Giannoudis[1]. [1]*Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM);* [2]*Leeds Institute of Health Sciences, University of Leeds, Leeds, United Kingdom*

Background: Osteoimmunology is an evolving field where the multipotential stromal cells (MSCs) can be considered as an important player linking immune response with bone generation. A group of pro-inflammatory cytokines including IFN-γ, TNF-α, IL-17 and IL-1, has been proven to have a licensing effect on MSCs promoting the immunomodulatory activities of MSCs (1). Importantly, these cytokines can regulate the osteogenic differentiation capability of MSCs and in particular, IL-1 and IL-17 can enhance the MSC osteogenesis as shown in previous in vitro studies (2,3). However, little is known about the role of these cytokine-MSC interactions in the bone-related diseases in humans.
Objectives: The main focus of this study was to assess if the immune-dependent licensing process of MSCs could be involved in defective bone regeneration.
Methods: We used samples of bone marrow aspirates (n=15) from two groups of traumatic bone fracture patients; normal union and non-union. Bone marrow MSCs were analyzed for the surface expression of the receptors of the pro-inflammatory licensing cytokines using flowcytometry-optimized panels. Additionally, a comparison of the cytokine effect on the proliferation of cultured MSCs was compared between normal union and non-union groups using the cell proliferation XTT test.
Results: Interestingly, there were significant lower expression levels of IL-1 receptors 1 and 3 (IL-1R1 and IL-1R3) on non-union MSCs compared to normal-union MSCs (p=0.0478 and p=0.0113 respectively). Furthermore, the surface levels of TNF-αR1 (CD120a) were significantly lesser on non-union MSCs (p=0.0119). There was a clear trend of reduced expression of IL-17 receptors (CD217) on the surface of non-union MSCs, but it was not statistically significant compared to normal-union (p=0.0726). The XTT data showed a significant less proliferation index for IL-1-treated non-union MSCs compared to normal-union MSCs (p=0.0446). Also, a consistent trend of lower proliferation index of non-union MSCs was detected when these cells were treated by IFN-γ, TNF-α or IL-17.



Conclusions: Together, the lower levels of the pro-inflammatory cytokine receptors indicated a possible mechanism for a defective response of non-union MSCs to the inflammatory signals (particularly IL-1). Further understating of the impact of immune-MSC interactions on human bone healing and regeneration will help to develop new therapies for musculoskeletal diseases involving osteolytic lesions.
References:
[1] Mesenchymal stromal cell 'licensing': a multistep process. Krampera M. Leukemia. 2011 Sep;25(9):1408–14.
[2] Interleukin-1β induces differentiation of human mesenchymal stem cells into osteoblasts via the Wnt-5a/receptor tyrosine kinase-like orphan receptor 2 pathways. Sonomoto K, Yamaoka K, Oshita K, Fukuyo S, Zhang X, Nakano K, Okada Y, Tanaka Y. Arthritis Rheum. 2012 Oct;64(10):3355–63.
[3] Proinflammatory T cells and IL-17 stimulate osteoblast differentiation. Croes M, Öner FC, van Neerven D, Sabir E, Kruyt MC, Blokhuis TJ, Dhert WJ, Alblas J. Bone. 2016 Mar; 84:262–70.
Acknowledgements: This project (no. S-16–132E) was supported by the AO Foundation.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6309

AB0067 INFLUENCE OF ADIPOKINES ON DIFFERENTIATION OF SPONGIOSA-DERIVED MESENCHYMAL STROMAL CELLS FROM OSTEOPOROTIC AND OSTEOARTHRITIS PATIENTS

L. Tsiklauri[1], E. Neumann[1], J. Werner[2], K. Frommer[1], R. Engel[1], S. Rehart[3], S. Wenisch[2], U. Müller-Ladner[1]. [1]*Department of Internal Medicine and Rheumatology, Justus-Liebig-University Giessen, Kerckhoff-Klinik, Bad Nauheim;* [2]*Institute of Veterinary-Anatomy, -Histology and –Embryology, Clinic of Small Animals, Justus-Liebig-University, Giessen;* [3]*Department of Orthopedics and Trauma Surgery, Agaplesion Markus Hospital, Frankfurt, Germany*

Background: Osteoporosis (OP) and osteoarthritis (OA) are two common age-related disorders leading to chronic pain and disability in elderly people. Age-related bone loss and articular cartilage damage are associated with increased bone marrow adiposity due to a possible shift of osteogenic differentiation towards adipogenic differentiation of bone marrow mesenchymal stem cells (MSC). The differentiation of MSC into adipocytes or osteoblasts is an important determinant of bone structural integrity. Adipose tissue is an metabolically active tissue. Therefore adipocyte-derived factors -adipokines- might influence differentiation of bone marrow-derived MSC.
Objectives: The role of fat-bone interactions in the pathogenesis of OP is poorly understood. Therefore, we analyzed the presence of distinct adipokines (visfatin, resistin and leptin) in the bone marrow cavity and their effects on MSC differentiation.
Methods: Spongiosa from femoral heads was collected (hip replacement surgery of OA patients or after osteoporotic femoral neck fracture). MSC were cultured in adipogenic and osteogenic media with/without adipokines. For the transfer and differentiation of MSC on cancellous bone, bone fragments were purified and sterilized. mRNA expression of adipokines, bone marker genes, TIMPs and MMPs of stimulated MSC and bone samples were evaluated by realtime PCR. Matrix mineralization was assayed using Alizarin red S staining. Proinflammatory factors were measured by ELISA.
Results: Visfatin and leptin levels were increased in OP bone vs. non-osteoporotic bone (n=14). In contrast to leptin and resistin, visfatin induced the secretion of proinflammatory factors (IL-6, IL-8, MCP-1) during both, osteogenic and adipogenic differentiation. Visfatin significantly increased the matrix mineralization and downregulated collagen type 1-expression (e.g. d21: -4.6-fold) in osteogenic differentiated cells. Visfatin also reduced the expression of MMP2, MMP13, RunX2, TIMP1 and TIMP2 (e.g. d21: -2.4-fold/-3.18-fold/-5.85-fold/-3.2-fold/-4.3 fold respectively) during osteogenic differentiation, but not leptin and resistin. In contrast to osteogenesis, visfatin significantly induced MMP13 expression (e.g. d21: 104-fold) during adipogenic differentiation under standard cell culture conditions. However, visfatin-induced MMP13-expression was markedly reduced during differentiation on purified autologous cancellous bone.
Conclusions: Visfatin and leptin levels were elevated in osteoporotic bone tissue. Therefore, the visfatin-mediated increase of matrix mineralization and reduction of collagen type 1 expression might lead to enhanced bone fragility and contribute to the pathogenesis of OP. Visfatin induced release of proinflammatory cytokines and dysregulated expression of MMPs and TIMPs during osteogenic and adipogenic MSC-differentiation might influence bone turnover specifically at the adipose tissue/bone interface.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2845

AB0068 HYPOXIA AND RHEUMATOID PHENOTYPE DECREASE THE CAPACITY OF SYNOVIAL FIBROBLASTS TO SUPPRESS T HELPER CELL PROLIFERATION THROUGH IDO1-MEDIATED TRYPTOPHAN CATABOLISM

L.-O. Tykocinski[1], N.-C. Kaul[1], I. Adam[2], S.R. Mohapatra[2], S. Krienke[1], C.A. Opitz[2], H.-M. Lorenz[1]. [1]*Department of Medicine V, Division of Rheumatology, University of Heidelberg;* [2]*Brain Cancer Metabolism, German Cancer Research Center (DKFZ), Heidelberg, Germany*

Background: The pathogenesis of rheumatoid arthritis (RA) is linked to functional changes in synovial fibroblasts (SF) and local infiltration of T lymphocytes. Increased synovial inflammation is also associated with a hypoxic joint microenvironment. Oxygen levels in the joints of RA patients are significantly decreased compared to those of osteoarthritis (OA) patients with values of about 22.5mmHg corresponding to ambient oxygen tensions of 3.2%. So far, little is known about the effects of hypoxia on the interaction between fibroblasts and T lymphocytes and its implications on the pathophysiology of RA.
Objectives: The aim of this study was to compare the influence of SF from RA versus OA patients on T helper (Th) cell responses both under normoxic and hypoxic conditions.
Methods: SF were isolated from synovectomy tissues of OA or RA patients, Th cells were isolated from peripheral blood of RA patients or healthy donors. Cell cultures were performed under normoxic or hypoxic (3% O_2) conditions. Th cell proliferation was determined by PKH26 labelling and flow cytometry. Cytokine secretion was quantified by ELISA. Indoleamine 2,3-dioxygenase 1

(IDO1) expression was analysed by Western Blot and expression of enzymes of the kynurenine pathway by real-time PCR. Tryptophan/ kynurenine levels in culture supernatants were quantified by HPLC.
Results: SF strongly inhibited the proliferation of co-cultured Th cells. Tryptophan was completely depleted within a few days in co-cultures of SF and Th cells, resulting in eukaryotic initiation factor (eIF)2α phosphorylation, TCRζ-chain down-regulation and proliferation arrest. Blocking of IDO1 completely restored Th cell proliferation, indicating that SF suppressed the proliferation of Th cells through IDO1-mediated tryptophan catabolism. Interestingly, RASF showed a significantly lower IDO1 expression, tryptophan metabolism and a weaker Th cell suppressive capacity compared to OASF. Under hypoxic conditions, the secretion of IFNg, the expression of IDO1, the tryptophan metabolism and the Th cell suppressive capacity of both OASF and RASF were significantly reduced.
Conclusions: SF suppressed Th cell growth through IDO1-mediated tryptophan catabolism. This mechanism may play an important role in preventing inappropriate Th cell responses under normal conditions. The reduced tryptophan metabolism under hypoxia together with the inferior efficiency of RASF to restrict T cell proliferation likely supports the development of synovitis in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5146

AB0069 STRONG AGE-DEPENDENT EFFECTS OF DOPAMINE ON JOINT INVASION IN ARTHRITIS

L. Van Nie[1], S. Rehart[2], E. Neumann[1], U. Müller-Ladner[1], S. Capellino[3].
[1]Department of Internal Medicine and Rheumatology, Justus-Liebig-University Gießen, Kerckhoff-Klinik, Bad Nauheim, Bad Nauheim; [2]Department of Orthopedics and Trauma Surgery, Apaglesion Markus Hospital, Frankfurt am Main, Frankfurt am Main; [3]Dept. of Immunology, Leibniz Research Centre for Working Environment and Human Factors, Dortmund, Germany

Background: Preventing synovial fibroblasts (SF) from migrating into the adjacent cartilage is a desirable therapeutic target in rheumatoid arthritis (RA) in order to avoid joint destruction and disability. In our previous studies we could show that RASF as well as SF from osteoarthritis (OA) patients express all dopamine receptor (DR) subtypes and dopamine stimulation alters pro-inflammatory cytokines (*Capellino S et al, A&R 2014*).
Objectives: Therefore, we aimed to elucidate a potential dopamine-mediated impact on joint invasion and destruction in arthritis.
Methods: SF from RA and OA patients were obtained from patients undergoing knee joint replacement surgery (mean age: 74.3±11.3yrs at OA and 73.7±10.3 yrs at RA patients) to investigate dopamine receptor (DR)-distribution within the RA synovium and in the invasion zone, immunohistochemistry was performed for all five DR-subtypes. Migration and motility assays were performed under D1-like (D1DR and D5DR) and D2-like (D2DR, D3DR and D4DR) receptor stimulation. Dopamine effects on MMP3 and proMMP1 were evaluated using ELISA.
Results: D1DR, D4DR and D5DR were found to be stronger expressed close to the invasion zone and more cells were expressing the respective DR. Migration of RASF and OASF was significantly correlated with patients' age at surgery: younger patients ($\leq$75years) showed an increase in migration up to 78% whereas older patients ($\geq$75years) showed a reduced migration of up to 50% (OA n=8; RA n=7). There was no difference between RA and OA patients and between D1-like and D2-like receptor stimulation. The same effect could be observed in the motility assay (OA n=5; RA n=6). MMP3 levels are altered under DR activation (OA n=6; RA n=6).
Conclusions: The high DR expression close to the invasion zone suggests a direct role of dopamine on RASF aggressiveness and may contribute to cartilage invasion. This was confirmed in the in vitro assays, and supports the idea of a therapeutic potential of the dopamine pathway in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5266

AB0070 CHONDROPROTECTIVE EFFECTS LINKED TO REDUCTION OF ADIPOGENESIS AND REGULATION OF GAP JUNCTION INTERCELLULAR COMMUNICATION: REGENERATIVE POTENTIAL THERAPEUTIC APPROACH FOR OSTEOARTHRITIS

M. Varela Eirin[1], A. Casado-Díaz[2], J. Loureiro[3], J.R. Caeiro[3], J.M. Quesada-Gómez[2], M.D. Mayán[1]. *[1]Translational Research in Cell Communication and Signaling (CellCOM Research Group), Instituto de Investigación Biomédica de A Coruña (INIBIC). CH-Universitario A Coruña (XXIAC). Servizo Galego de Saúde (SERGAS). University of A Coruña, A Coruña; [2]Clinical Management Unit of Endocrinology and Nutrition, Maimónides Biomedical Research Institute of Córdoba (IMIBIC). Hospital Universitario Reina Sofía – RETICEF. Universidad de Córdoba, Córdoba; [3]Department of Orthopaedic Surgery and Traumatology, Complexo Hospitalario Universitario de Santiago de Compostela (CHUS-XXIS). SERGAS, Santiago de Compostela, Spain*

Background: Human bone marrow mesenchymal stem cells (hMSCs) exhibit an age-dependent reduction in osteogenesis and an increased propensity toward adipocyte differentiation. This switch has been associated with different bone disorders characterized by reduced bone formation and increased bone marrow fat accumulation. Connexin43 (Cx43) is an integral membrane protein that forms gap junction channels (GJs) and it is implicated in multiple cellular functions including cellular differentiation and control of bone remodelling and cartilage structure and function.
Objectives: In this study we investigated the effect of oleuropein and other molecules isolated from the *Olea europaea* in cellular differentiation to test if these molecules act as adipogenic suppressors in order to promote bone ad cartilage regeneration through a Cx43-dependent mechanism.
Methods: hMSCs were obtained from bone marrow donors. Human chondrocytes were isolated from cartilage of healthy donors and patients with osteoarthritis (OA). Differentiation assays were carried out in the presence of different concentrations of oleuropein and olive extract (OE). Cellular differentiation was evaluated using histological stains. Scrape loading assays, western-blot, real-time qPCR and immunohistochemistry (IHC) assays were used to study the cellular communication through gap junction (GJs) and the levels and changes in subcellular localization of Cx43 and extracellular matrix (ECM) proteins such as Collagen type II (Col2).
Results: hMSCs treated with olive derived molecules showed a two-fold decrease in adipogenic differentiation, while osteogenesis and chondrogenesis were significantly increased. IHC, RT-qPCR and Western-Bot analysis of hMSCs supplemented with oleuropein/OE showed increased levels of Cx43. On the other hand, OA chondrocytes showed higher levels of Cx43 in comparison with normal chondrocytes; oleuropein and OE treatments significantly decreased Cx43 levels and dye transference through GJ channels. The treatment of OA chondrocytes micromasses with oleuropein and OE increased the levels of proteoglycans and Col2 in the extracellular matrix. These changes in the micromasses were accompanied by a decrease in Cx43 levels improving protein subcellular localization.
Conclusions: Together, our results suggest that the molecules used in this assays, via Cx43 and GJ intercellular communication increase the propensity towards osteogenesis and chondrogenesis, reducing adipocyte differentiation. Our assays indicate that these molecules may represent a potential therapeutic approach for cartilage and bone age-related disorders such as OA in order to promote cartilage regeneration.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4830

AB0071 ANALYSIS OF SYNOVIAL EXPRESSION OF PARVOVIRUS B19 ASSESSED IMMUNOHISTOCHEMICALLY AND CORRELATED TO SYNOVITIS SCORE

M. Tarasovs[1], A. Kadisa[2], A. Mihailova[3], S. Skuja[4], M. Murovska[5], V. Groma[4]. *[1]Riga Stradins University; [2]Department of Internal Diseases, Riga East Hospital Clinic "Gailezers"; [3]Orto Clinic; [4]Institute of Anatomy and Anthropology; [5]A. Kirchenstein Institute of Microbiology and Virology, Riga Stradins University, Riga, Latvia*

Background: Apart from systemic symptoms of viral infection parvovirus B19 (B19) could lead to acute and chronic arthropathy. It has been found in synovial tissue of rheumatoid arthritis (RA) patients, sometimes, being associated with some forms of undifferentiated arthritis. Possibly, it could promote inflammation in various forms of arthritis.
Objectives: To determine the expression of B19 antigens in different compartments of synovial membrane; correlate these findings to the estimated synovitis score.
Methods: 7 RA and 54 osteoarthritis (OA) patients were enrolled in this study. nPCR was used to detect the presence of B19 genomic sequence in 61 samples of synovial tissue. PCR B19 positive tissue samples were immunohistochemically treated with the anti-B19 antibodies detecting B19 capsid proteins' VP1/VP2 expression estimated thereafter semiquantitatively. The intimal and subintimal layers of synovium as well as vasculature were estimated. Synovial inflammation was evaluated using synovitis score.
Results: 3 RA and 3 OA patients were PCR B19 tissue positive. B19 antigens' expression was observed in synovial lining, immune infiltrates and vascular endothelium. Correlation between B19 expression observed in synovial cells and inflammatory infiltrates' lymphocytes and macrophages was r=0.555 ($p<0.0001$) and r=0.793 ($p<0.0001$), respectively. Likewise, correlation between vascular endothelial B19 expression and synovial lymphocytic infiltrates was demonstrated r=0.616 ($p<0.0001$). Determined synovitis score varied from low up to intermediate revealing median value 2. Simultaneously, there was no correlation found between the synovitis score and B19 antigens' expression.
Conclusions: B19 capsid proteins' VP1/VP2 expression is detectable in different structural constituents of synovial membrane. Under conditions studied, the tissue expression of B19 antigens does not correlate with the inflammatory indices scored.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6411

AB0072 RATIONAL DESIGNED GOLD NANOPARTICLE SUPPRESSES RANKL-INDUCED OSTEOCLASTOGENESIS IN RAW264.7 CELLS VIA NF-KAPPA B PATHWAY AND MAPK PATHWAYS

Q. Yuan[1,2], X. Gao[1,2]. [1]*Key Laboratory for Biological Effects of Nanomaterial and Nanosafety, Institute of High Energy Physics, CAS;* [2]*Department of Chemistry and Chemical Engineering, Beijing University of Technology, Beijing, China*

Background: Bone erosion in joint is the most deleterious effect induced by rheumatoid arthritis (RA) and is the major cause of disability. New therapies are urgently required to prevent RA-associated bone destruction. The excessive bone resorption in RA was proved to be mediated by osteoclasts which are derived from the monocyte/macrophage lineage and induced by RANKL. Therefore, RANKL could be a potential target for the preservation of bone mass in RA.
Objectives: Chrysotherapy showed potential effects in reducing of joint destruction but with serious side-effects in RA therapy. A rational designed gold nanoparticle named GN was prepared to provide a choice for suppressing bone loss in RA therapy with more safety.
Methods: Mice macrophage cell line RAW264.7 was activated by RANKL to evaluate the potential osteoclastogenesis suppressing effects of GN. The differentiation, fusion and function of osteoclast were assessed by tartrate-resistant acid (TRAP) staining, actin ring formation assay and osteologic discs detection respectively. Relative expressions of osteoclast-specific genes were evaluated by RT-PCR and the activity of NF-κB pathway as well as MAPK pathways were analyzed by immunoblotting.
Results: Osteoclast differentiation, fusion and bone resorption were activated by RANKL in RAW264.7 cell, while GN significantly attenuates this process in a dose-dependent manner. The expressions of osteoclast-specific genes including TRAP and OSCAR were increased by RANKL stimulation but were effectively suppressed by GN. The activation of NF-kappa B pathway and MAPK pathways induced by RANKL was also suppressed by GN treatment.
Conclusions: Our findings revealed that treatment with GN could prevent RANKL-induced osteoclastogenesis and reduce increased expression of osteoclast-specific genes which may through the suppression of NF-kB and MAPK activation in macrophage. GN may provide a basis for the design of chrysotherapy drugs that effect in progression of RA-associated articular erosions.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2087

AB0073 ACCUMULATION OF ADVANCED GLYCATION END PRODUCTS (AGES) IN OSTEOARTHRITIC CARTILAGE IS RELATED TO AN IMPAIRMENT OF THE ADAPTATIVE MECHANISM OF GLYOXALASE-1

S. Trellu[1], A. Courties[1], S. Jaisson[2], B. Friguet[3], X. Houard[4], F.-P. Ehkirch[5], C. Jacques[4], F. Berenbaum[1], J. Sellam[1]. [1]*UPMC Univ Paris 06, Inserm UMRS_938, Rheumatology department, AP- HP, Saint-Antoine Hospital, Paris;* [2]*University of Reims Champagne-Ardenne, UMR CNRS 7369, Laboratory of Biochemistry and Molecular Biology, Reims;* [3]*UPMC Univ Paris 06, UMR 8256, Biological Adaptation and Ageing-IBPS;* [4]*UPMC Univ Paris 06, Inserm UMRS_938, Saint-Antoine Hospital;* [5]*Groupe Maussins, Clinique des Maussins-Ramsay, Général de Santé, Paris, France*

Background: Advanced glycation end-products (AGEs) that result from a non-enzymatic reaction between a sugar and a protein, are generated during tissular ageing. Accumulation of AGEs could also be part of the osteoarthritis (OA) process by modifying the biomechanic properties of cartilage and by inducing chondrocyte activation. Glyoxalase-1 (Glo-1) is the main enzyme involved in the removal of AGEs precursors, especially the AGE carboxymethyllysine (CML).
Objectives: We aimed to quantify CML in human osteoarthritic cartilage, to investigate Glo-1 expression in chondrocytes and to study chondrocytic Glo-1 regulation in an inflammatory context.
Methods: 1) *Ex vivo:* Osteoarthritic cartilages from patients undergoing knee replacement were collected, dissected and incubated for 24h with or without IL-1β (5ng/ml). We quantified CML in these cartilage explants using liquid chromatography and mass spectrometry, Glo-1 protein expression (Western Blot and immunohistochemistry) and Glo-1 enzymatic activity by measuring the kinetic of formation of the Glo-1 product (S-D lactoylglutathione) using spectrophotometry at 240nm during 10 minutes. 2) *In vitro:* Primary cultured murine chondrocytes (C57B6) were stimulated 72 h with increasing IL-1β doses (0 to 10ng/mL). Glo-1 expression was assessed by quantitative RT-PCR, Western blot and enzymatic activity. To analyze whether oxidative stress is involved in Glo-1 regulation induced by IL-1β, cells were treated with inhibitors of mitochondrial oxidative stress (MitoTEMPO) or of nitric oxide (NO) synthase (L-NAME).
Results: 1) *Ex vivo*, CML was found in all human OA cartilage samples and its level increased according to age (correlation coefficient CML/age: $r=0.78$, $p<0.01$). In parallel to CML increase, Glo-1 protein was expressed in chondrocytes on all layers of cartilage. A positive correlation was found between Glo-1 enzymatic activity and the age of the patients ($r=0.45$, $p<0.05$) but was lost in case of incubation with IL-1β ($r=-0.09$, p non significant). 2) *In vitro*, in murine chondrocytes cultures, we observed a dose-dependent decrease of IL1β-induced Glo-1 mRNA (0.67 fold, $p<0.05$), protein quantity (0.56 fold, $p<0.05$) and enzymatic activity (0.7 fold, $p<0.05$) (n=5). The blockade of NO by L-NAME, and of mitochondrial oxidative stress by MitoTEMPO counteracted the downregulation of IL1β-induced Glo-1 expression and enzymatic activity (n=5).
Conclusions: We show here that the age-dependent accumulation of AGEs in OA cartilage could be due to an impairment of the adaptative mechanism of Glo-1, mediated by oxidative stress. Further studies aiming at targeting Glo-1 restauration as a therapeutical strategy for ageing-related OA are needed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1452

AB0074 INFLUENCE OF COBALT AND CHROMIUM IONS ON TGF-BETA EXPRESSION AND MINERALIZATION OF BONE FORMING CELLS IN-VITRO

S. Drynda[1,2], A. Drynda[1], J. Kekow[2], C.H. Lohmann[1]. [1]*Department of Orthopaedic Surgery, Magdeburg;* [2]*Clinic of Rheumatology, Vogelsang, Germany*

Background: Bone homeostasis is regulated at different levels. Transforming growth factor-beta (TGF-β) which exists in three isoforms in human and is stored in the latent form in the extracellular matrix is a major player in the regulation of osteoblast and osteoclast maturation, development, and function. The balance of bone formation and resorption is affected by numerous influences, such as hormone status, inflammation, and mechanical load.
In the aging population, supplied increasingly with artificial joint replacements, release of particles or ions from arthroplasty may exert local effects in the periprosthetic tissue. Cobalt and chromium ions are released through corrosion from metal-on-metal arthroplasty and modulate the gene expression level of several cytokines, chemokines and other mediators in bone cells.
Objectives: It was the aim of the study to analyse the effect of Co^{2+} and Cr^{3+} ions on the expression of TGF-β isoforms in bone forming cells and their impact on mineralization.
Methods: The study investigated the effect of Co^{2+} and Cr^{3+} ions on the expression of TGF-β1–3 in the human osteosarcoma cell lines (MG63 and SaOs2) and primary human osteoblasts.
Cells ($3x10^5$) were seeded in 2 ml DMEM (10%FCS) into 12 well plates and stimulated with $CoCl_2$ and $CrCl_3$ in concentrations between 50–250 μM for 24 hours. Total RNA was extracted and changes of expression levels of TGF-β1–3 were analysed by real-time PCR using sequence-specific primers and probes.
For mineralization cells were cultivated for up to 4 weeks in DMEM (10% FCS) supplemented with 0.2mM ascorbic acid, 10nm dexamethasone and 10mM glycerophosphate and Co^{2+} and Cr^{3+}. Calcium deposits were detected by 1% Alizarin Red S (pH 4.1) staining.
Results: The osteosarcoma cell lines as well as primary human osteoblasts isolated from bone explants expressed all three TGF-β isoforms, with TGF-β1 as most abundently expressed isoform. A dose dependent reduction of all TGF-β isoforms by Co^{2+} ions was observed, the strongest effect was found for TGF-β2. In MG63 cells and primary osteoblasts the mRNA levels of TGF-β2 decreased to 15±4% and 17±15% compared to the unstimulated control. The effect was lesser in SaOs2 cells with a reduction to 61±7% compared to control. In contrast to bivalent Co ions, the trivalent Cr ions had no significant effect on the expression of all TGF-β isoforms.
While Co^{2+} in a concentration range of 50–250 μM did not impair the mineralization, Cr^{3+} exerted a strong inhibitory effect on the mineralization in osteosarcoma cells and primary osteoblasts. In a dose dependent fashion mineralization was influenced already at concentrations of 50 μM CrCl3 and showed the strongest effect at 250 μM.
Conclusions: The results of our study show that bivalent cobalt ions and trivalent chromium ions have different effects on bone forming cells. While Cr^{2+} affects the expression of the different TGF-β isoforms in osteoblast-like cells and primary osteoblasts, no inhibitory effect on mineralization in the tested concentrations was seen. Cr^{3+} however, did not influence the expression of TGF-β but strongly inhibited the mineralization in vitro.
Our data implicate that the inhibitory effect of metal ions such as Co and Cr ions on the transcription of the bone regulating cytokines TGF-β1–3 and on bone forming activity may influence bone homeostasis.
Acknowledgements: Study supported by Stiftung Endoprothetik (S01/16).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6218

AB0075 TARGETING IMMUNE AND NON-IMMUNO SYNOVITIS BY 1,3,5-TRIAZINE-THIAZOLE VIA DUAL INHIBITION OF NF-KB AND EGFR-TKS FOR POSSIBLE BENEFIT IN RHEUMATOID ARTHRITIS

U.P. Singh[1], J.K. Shrivastava[1], A. Verma[1], H.R. Bhat[2]. [1]*Department of Pharmaceutical Sciences, Sam Higginbottom University of Agriculture, Technology & Sciences, Allahabad;* [2]*Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh, India*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease which is easily recognised by unrelenting inflammation, joint erosion, joint immobility and severe debilitation. The cause of the disease suggests that, T cells, B cells, macrophages, and dendritic cells gain access to the inflamed synovium causing progression of disease via generation of cytokines and autoantibodies.

The current available therapies to treat RA target the immune response which in turn adversely affects the immunity of the patients.
Objectives: The presents study deals with the discovery of 1,3,5-triazine-thiazoles targeting immune and non-immuno synovitis by via dual inhibition of NF-κB and EGFR-TKs for possible benefit in rheumatoid arthritis.
Methods: The 1,3,5-triazine-thiazole hybrid derivatives were synthesized via cascade of nucleophillic and cyclo-condensation reaction. These inhibitors was screened for NF-kB transcriptional activity in RAW264.7 macrophages, whereas, EGFR-TKs inhibitor activity was assessed via kinase inhibition assay kit. The docking study was carried out with 3D-crystal structure of NF-κB and EGFR-TK to explicate the inhibitory action.
Results: The designed hybrid analogues showed excellent inhibitory activity against both NF-κB and EGFR-TK. Particularly, against NF-κB, methyl (5c) containing molecule showed most significant activity (respectively with relative NF-κB activity: 1.82±1.87). Docking study suggests that, 5c was deeply buried in the DNA binding domain of NF-κB interacting with Tyr57, Val58, Cys59, His141, and Val142. In EGFR-TK inhibitory assay, the synthesized molecules showed IC_{50} ranging from 4.23–39.32μ M via interacting with Leu788, Met766, Lys745, Glu762 with 3D crystal structure of EGFR-TK.
Conclusions: These results demonstrate the feasibility of 1,3,5-triazine-thiazole as dual inhibitior of NF-κB and EGFR-TKs for the treatment of inflammatory disorders such as rheumatoid arthritis in more efficient way.
References:
[1] Collison J. Features of synovium in RA remission revealed. Nat. Rev. Rheumatol. 12, 316 (2016).
[2] Singh B, Bhat HR, Kumawat MK, Singh UP. Structure-guided discovery of 1,3,5-triazine-pyrazole conjugates as antibacterial and antibiofilm agent against pathogens causing human diseases with favorable metabolic fate. Bioorg Med Chem Lett. 24, 3321 (2014).
[3] Singh UP, Pathak M, Dubey V, Bhat HR, Gahtori P, Singh RK. Design, synthesis, antibacterial activity, and molecular docking studies of novel hybrid 1,3-thiazine-1,3,5-triazine derivatives as potential bacterial translation inhibitor. Chem Biol Drug Des. 80, 572 (2012).
Acknowledgements: Authors are thankfull to SHUATS for providing necessary infrastructural facilities.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5612

Rheumatoid arthritis - etiology, pathogenesis and animal models

AB0076 PERIODONTAL MICROBIOTA IN EGYPTIAN RA PATIENTS AND THEIR RELATION TO SERUM AND GINGIVAL ANTI-CITRULLINATED PROTEIN ANTIBODIES AND OTHER DISEASE PARAMETERS

A.A. Abdelati. *Internal Medicine, Rheumatology Unit, Faculty of Medicine, Alexandria University, Alexandria, Egypt*

Background: A possible infectious trigger for RA is suspected at the gingival site. Emerging data implicates the microbiome in RA pathogenesis. Mucosal sites exposed to a high load of bacterial antigens, such as the periodontium, may represent the initial site of autoimmune generation. If validated, these findings could lead to the discovery of potential biomarkers and therapeutic approaches in the pre-clinical and clinical phases of RA[(1)].
Objectives: To determine the organisms causing periodontitis in Egyptian RA patients and their relation to serum and gingival ACPA level and other disease parameters.
Methods: This study was carried out on 100 Egyptian RA patients fulfilling the 2010 ACR/EULAR classification criteria for RA and of less than 5 years disease duration, recruited from Rheumatology Unit, outpatient clinic and Dental clinic at Alexandria Main University Hospital. RA disease activity was assessed by applying DAS28 and functional state of the patients was assessed by applying HAQ score. Dental examination, serum RF, and ACPA in serum and GCF were done for all patients. X-ray of both hands to detect erosions and severity of the disease. Gingival Crevicular Fluid (GCF) culture was performed for all cases with periodontitis for the three micro-organisms most reported in the literature to produce periodontitis (Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia).
Results: Of the 100 patient, 66 patient had periodontitis, for them, GCF culture was performed and Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia were found in 60.6%, 15.2%, and 30.3% of RA patients with periodontitis respectively. Gingival ACPA was detected in the 3 studied organisms, being of significant higher level with P.gingivalis than P.intermedia positive cases (p=0.047). No statistical significant difference detected on comparing P.gingivalis with A.actinomycetemcomitans or A.actinomycetemcomitans with P.intermedia. A. actinomycetemcomitans positive cases were associated with significantly higher level of CRP than P. intermedia positive cases (p=0.029), while no statistical significant difference was detected between P.gingivalis and A. actinomycetemcomitans or P. intermedia positive cases. There was no statistical significant difference between the three studied organisms regarding serum ACPA level, DAS 28, HAQ score, or X-ray findings of hands.
Conclusions: P.gingivalis is the most prevalent periodontal microbiota in Egyptian RA patients with periodontitis, that associated with significant higher level of gingival ACPA. None of the detected organisms correlated with the degree of RA activity or other disease parameters, apart from significantly higher CRP level with A. actinomycetemcomitans.
References:
[1] Brusca SB, Abramson SB, Scher JU. Microbiome and mucosal inflammation as extra-articular triggers for rheumatoid arthritis and autoimmunity. Curr Opin Rheumatol 2014;26:101–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3557

AB0077 INVESTIGATION OF THE INFLUENCE OF TERIFLUNOMIDE PLASMA CONCENTRATIONS ON DISEASEACTIVITY IN LEFLUNOMIDE-TREATED PATIENTS WITHRHEUMATOIDARTHRITIS

R. Tekaya, A. Ben Tekaya, H. Sahli, O. Saidane, I. Mahmoud, L. Abdelmoula. *Rheumatology charles Nicolle, Tunis, Tunisia*

Background: Leflunomide has become of increasing value for the treatment of rheumatoidarthritis (RA), and leflunomideisused via its active metabolite teriflunomide. The European League Against Rheumatism (EULAR) suggestedthatboth LEF and methotrexatewerefundamentalmedicines for the treatment of RA.
Objectives: To investigate the relationshipbetweenteriflunomideplasma concentrations and diseaseactivity in patients with RA.
Methods: This was a cross-sectional multicenter study (four rheumatology departments) over a four years period.Patients withRA on a stable and dailyleflunomide dose for >2 monthswereincluded.
Socio-demographic data and clinical data were recorded. Respectively, disease status and functional disability were assessed by disease activity score (DAS28) and Health Assessment Questionnaire (HAQ). Treatment response was evaluated according to the EULAR criteria (variation of DAS28).
Quantitative determination of teriflunomide (active metabolite of leflunomide) plasma concentrationswas carried out by high-performance liquid chromatography with ultraviolet detection.
Results: A total of 24 patients were enrolled; sex ratio =1. The mean age of the sample was 51,71 (±15,3) years; the mean disease duration at study baseline was 135,2 (±80,26) months; 70% of patients were RF positive, and 58% ACPA positive.The mean score on VAS pain was 43 mm (±22,92). Respectively, the mean swollen and tender joint counts (SJC-28, TJC-28) were4,3 (±6,1) and 2,8 (±3,09). The mean HAQ was 2,01 (±0,78). At baseline, the mean DAS28 score was 4,17 (±1,12); 56% weregood and moderate EULAR responders.
The mean leflunomide treatment duration was 34,94 months (±32,47). The meanteriflunomide plasma concentrations was 38,34 ug/ml (±24,92).
Residualteriflunomide plasma concentrations was significantly associated SCJ-28 and DAS28 decrease (p=0,0027). However, all these parameters (VAS pain, TJC-28, HAQ, C reactive protein, prescription duration of leflunomide and EULAR response) were not correlated with residualteriflunomide plasma concentrations.
Conclusions: This studyconcludedthatresidualteriflunomide plasma concentration isassociatedwithlow active disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6892

AB0078 ROLE OF EXPERIMENTAL RESEARCH IN STUDY OF RHEUMATOID ARTHRITIS ETIOPATHOGENESIS

A.N. Goltsev, E.D. Lutsenko, M.V. Ostankov, N.A. Bondarovich. *Cryopathophysiology and Immunology Dept, Institute for Problems of Cryobiology and Cryomedicine of NAS of Ukraine, Kharkov, Ukraine*

Background: To study the pathogenesis, diagnosis and therapy of rheumatoid arthritis (RA) there are used numerous experimental *in vivo* and *in vitro* models. Topical issue of this problem is to study the causes of disorder and rehabilitation of immune tolerance mechanisms in RA. The concept about the role of different cells in central and peripheral tolerance formation in this pathology is often contradictory and not clear. A tolerogenic activity of products of fetoplacental complex has long been studied at the Cryopathophysiology and Immunology Department of the Institute for Problems of Cryobiology and Cryomedicine of NAS of Ukraine. The presence of a wide range of immunotropic substances in placenta is a premise to use placental cell suspension (PCS) for immunocompetent sphere recovery in autoimmune diseases.
Objectives: The research aim was to determine the possibilities and features of implementation of a tolerogenic activity by native and cryopreserved placental cells in experimental models of RA development: adjuvant arthritis (AA).
Methods: Research was carried out in CBA/H mice. The PCS was obtained via homogenizing the murine placenta to days 18–19 of gestation. The AA was induced by subplantar administration of the complete Freund's adjuvant. The AA development was expressed as the arthritis index. Either native (nPCS) or cryopreserved PCS were administered intravenously to day 7 after pathology induction. The PCS was cryopreserved under protection of either 10% dimethyl sulfoxide solution (suspension CD) or Propandiosakharol (suspension CP). A number of $CD4^+CD25^+$ T reg cells was determined by direct immunofluorescence

using monoclonal antibodies (BD Pharmingen TM) with flow cytometry (FACS Calibur, BD) in AA animal spleen. The *foxp3* gene expression in murine spleen cells was assessed by multiplex reverse transcription polymerase chain reaction (RT-PCR). In PCR we used the primer pairs to *foxp3* gene and that of housekeeping: β-actin. A number of gene transcripts was compared basing on the relative semi-quantitative estimation of amplification products using Agilent Bioanalyzer 2100 (USA).

Results: A disordered $CD4^+CD25^+$ cell accumulation in spleen of experimental animals with AA was established and possible use of PCS for its correction was demonstrated. The *foxp3* expression level in AA animal spleen cells reduced on day 28, suggesting a contribution of this factor into AA pathogenesis within a long-term period of pathology development. During this period a decrease in joint swelling correlated with an increased content of T-reg cells and *foxp3* expression level in spleen of animals after either nPCS or CD administration.

Conclusions: Therapeutic effect of either native or cryopreserved PCS in AA animals is manifested on molecular level, as evidenced by an increased *foxp3* expression in spleen cells after suspension administration. The effect of introduced cryopreserved placental cells as for this gene activation and, consequently, T-reg, was herewith determined by cryopreservation regimen.

References:

[1] Goltsev A.N., Lutsenko E.D. Ostankov M.V. Effect of different cryopreservation regimens on manifestation of immune modulating activity of placenta at development of adjuvant arthritis. Problems of Cryobiology 2008; 18(4): 456–459.

[2] Haque R., Lei F. Foxp3 and Bcl-xL cooperatively promote regulatory T cell persistence and prevention of arthritis development. Arthritis Research and Therapy 2010; 12: R.66.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6113

AB0079 TRANSDERMAL DELIVERY OF METHOTREXATE IN RHEUMATOID ARTHRITIS: ARE WE DEEP ENOUGH?

B. Sadarani[1], A. Majumdar[1], P. Kamble[1], S. Paradkar[2], A. Mathur[2], S. Sachdev[2], P. Chaudhari[3], B. Mohanty[3]. *[1]Pharmacology, Bombay College of Pharmacy, Mumbai; [2]Radiopharmaceuticals Program, Board of Radiation and Isotope Technology (BRIT); [3]Small Animal Imaging Facility, Advanced Center for Treatment, Research and Education in Cancer (ACTREC), Navi Mumbai, India*

Background: Methotrexate (MTX), at low doses, is the first choice in the management of rheumatoid arthritis (RA). Despite its effectiveness, the probability of its discontinuation remains high due to adverse effects such as gastrointestinal intolerance, bone marrow toxicity as well as hepatotoxicity with conventional oral and parenteral therapy.[1] Transdermal delivery epitomizes an attractive alternative for drugs with systemic toxicities. The physicochemical characteristics of MTX such as high polarity and ionisation at physiologic pH make the development of its topical route of delivery challenging.[2] A new class of liposomes termed deformable or flexible liposomes have been reported to possess the virtue of stress-dependent adaptability that enables them to squeeze through interstices of stratum corneum and increase the depth of skin penetration.[3]

Objectives: This study is intended to explore the transdermal route for the delivery of MTX in ameliorating its systemic toxicity without compromising the therapeutic effect in RA.

Methods: MTX entrapped in deformable liposomes were prepared and characterised for particle size (PS) and entrapment efficiency (EE). They were incorporated into a hydroxyethyl cellulose gel base and evaluated for *ex vivo* skin permeation. Optimized liposomal gel was applied on the back of rats (3x4 cm area) and evaluated for its acute dermal toxicity and pharmacokinetics. Biodistribution was studied by topical application of ^{125}I labelled MTX incorporated liposomal gel in rats. Furthermore the efficacy of optimized gel was determined in collagen induced arthritis (CIA) in rats.

Results: The optimized deformable liposomes exhibited a small PS of 110±20 nm and EE 35–50% while the liposomal gel showed a transdermal flux of 17.37±1.5 $\mu g/cm^2/hr$ in *ex vivo* skin permeation study. Topical application of liposomal gel depicted no clinical abnormalities or pathological changes at the site of application in rats. Pharmacokinetic data indicated sustained systemic delivery of MTX from its liposomal gel up to 48 hours. The gel resulted in lower accumulation of MTX in liver, kidneys and gut in contrast to intravenous administration of plain ^{125}I labelled MTX solution. In the CIA model, topical MTX gel administration demonstrated significant reduction in hind paw swelling and arthritic score, also validated by histological and radiographic examination of ankle joints and lowering of serum levels of cytokines like TNF-α and IL-6 in comparison to disease control group.

Conclusions: The liposomal gel displayed dermal safety, sustained systemic delivery of MTX and its lower distribution to the organs of toxicity which may enable alleviating systemic side effects. Moreover, liposomal gel of MTX showed appreciable therapeutic efficacy in the CIA model.

References:

[1] Braun J, Rau R. An update on methotrexate. Curr Opin Rheumatol. 2009;21(3):216–23.

[2] Prausnitz MR, Langer R. Transdermal drug delivery. Nat. Biotechnol. 2008;26(11):1261–68.

[3] Benson HA. Transfersomes for Transdermal Drug Delivery. Expert. Opin. Drug Deliv. 2006;3(6):727–37.

Acknowledgements: DAE-BRNS Research Grant (sanction no. 2012/35/17/BRNS).
Lipoids, Germany for gift sample of Phospholipon 90G, Gattefosse for gift sample of Labrasol and Signet for gift sample of Hydroxyethyl cellulose.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3703

AB0080 MODUALTION OF IMMUNOGLOBULIN G2B BINDING IN COMBINATION OF METHOTREXATE AND ACONITE IN A COLLAGEN-INDUCED ARTHRITIS SETTING

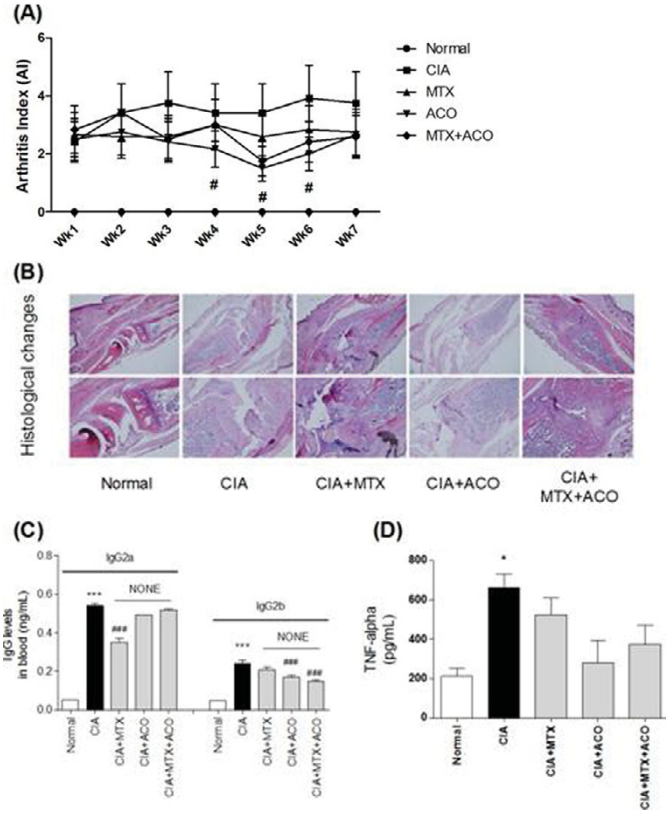
D.-S. Oh, G. Park, S.H. Lee. *The K-herb Research Centre, Korea Institute of Oriental Medicine, Daejeon, Korea, Republic Of*

Background: Our previous study showed synergistic responses in TNF-alpha (TNF-α) and interleukin-6 with the combination of methotrexate (MTX) and aconite. Modulation of those cytokines has not been applied to rheumatoid arthritis (RA)-mimicked in vivo models.

Objectives: To translate in vitro effects of MTX, aconite, and MTX/aconite combination towards anti-arthritic responses in vivo, we investigated arthritis index (AI), histopathologic changes, and levels of TNF-α, immunoglobulin G (IgG) 2a and 2b in a collagen-induced arthritis (CIA) setting.

Methods: CIA was induced in five male DBA/OlaHsd mouse per group by intradermal injection of bovine collagen type II and Complete Freund's Adjuvant. In Day21, a bovine collagen type II and Incomplete Freund's Adjuvant were given for booster infection. The mice of arthritis onset were treated daily throughout Day49 with per oral administration of pre-investigated ratios of three to one; MTX (3 mg/kg), aconite (Aconibal®, 1 mg/kg), and MTX/aconite (3 and 1 mg/kg) combination. The AIs were evaluated every week. Histological changes, levels of TNF-α as well as IgG2a and IgG2b in blood using ELISA kit were evaluated at finals. Repeat measure and one-way ANOVA were analysed using SPSS (ver. 18.0 KO for Windows; SPSS Inc., Chicago, IL, USA) to evaluate inter-period and inter-group differences with Tukey's post-hoc tests.

Results: The CIA phenotypes adequately presented through three groups' AI reductions (CIA vs. MTX, aconite, or MTX/aconite; $p<0.001$, for three). There were differences of AI scores in aconite group from MTX one in week 4, 5, and 6 (MTX vs. aconite; $p=0.038$, $p=0.001$, $p=0.042$, respectively). Synergistic responses of AI were not shown any of three groups. The recoveries of synovial tissues were observed in MTX and MTX/aconite groups. The levels of TNF-α were not changed (aconite vs. MTX/aconite; $p=0.200$ and MTX vs. MTX/aconite; $p=0.700$). MTX group showed IgG2a reduction (CIA vs. MTX; $p<0.001$). Interestingly, MTX/aconite combination and aconite group slightly downregulated IgG2b levels as 80.8±5.6% and 90.5±7.4%, respectively (CIA vs. MTX/aconite; $p=0.001$ and CIA vs. aconite; $p=0.010$).



Conclusions: Synergistic in vitro effects of MTX and aconite combination brought

the partial in vivo phenotypic responses: Aconite showed more AI changes than MTX did in 4, 5, and 6 weeks. However, we found the presence of partial FcγRIIB affinity of binding modulation that MTX/aconite could enhance preventing monocyte/macrophage activation via immune complex in RA pathogenesis, as was other benefits of the combination except direct synergies.

References:

[1] Oh DS, Park G, Choi S. Characterising multiple molecule-modulating response of TNF-alpha and interleukin-6 by combination of methotrexate and aconite in interferon gamma-induced toxicity setting. Ann Rheum Dis 2016;75:Suppl2 909–910.

[2] Wijngaarden S, van Roon JA, van de Winkel JG, Bijlsma JW, Lafeber FP. Down-regulation of activating Fcgamma receptors on monocytes of patients with rheumatoid arthritis upon methotrexate treatment. Rheumatology (Oxford) 2005;44:729–734.

[3] Stewart R, Hammond SA, Oberst M, Wilkinson RW. Down-regulation of activating Fcgamma receptors on monocytes of patients with rheumatoid arthritis upon methotrexate treatment. J Immunother Cancer 2014;2:29.

Acknowledgements: This study was supported by KIOM (Grant # K17252). The commercial product was donated by the virtue of HanPoong Pharmaceutical Company.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2802

AB0081 REACTIVE OXYGEN SPECIES INHIBIT CATALYTIC ACTIVITY OF PEPTIDYLARGININE DEIMINASE

D. Damgaard[1,2], M.E. Bjørn[1], C.H. Nielsen[1,2]. [1]*Center for Rheumatology and Spine Diseases, Copenhagen University Hospital, Rigshospitalet, Institute for Inflammation Research;* [2]*Department of Odontology, Faculty of Health and Medical Sciences, University of Copenhagen, Section for Periodontology, Microbiology and Community Dentistry, Department of Odontology, Faculty of Health and Medical Sciences, University, Copenhagen, Denmark*

Background: Protein citrullination is catalysed by pepdidylarginine deiminase (PAD) and plays an important pathogenic role in anti-citrullinated protein antibody (ACPA)-positive rheumatoid arthritis (RA), and possibly in other inflammatory diseases. PAD activity is dependent on calcium and reducing conditions.

Objectives: To determine the ability of H_2O_2 and reactive oxygen species (ROS) induced by the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase to regulate PAD activity.

Methods: Activity of recombinant human (rh) PAD2, rhPAD4 and PADs released from phorbol 12-myristate 13-acetate (PMA)-stimulated leucocytes was measured using an in-house PAD activity assay detecting citrullination of fibrinogen. PAD2 released from cells was measured using a luminex-based assay. The NADPH oxidase inhibitor diphenyleneiodonium (DPI) was used to inhibit ROS production in cells.

Results: At concentrations above 40 μM, H_2O_2 inhibited the catalytic activity of reduced rhPAD2 and rhPAD4. The inhibitory effect increased with increasing H_2O_2 concentration, reaching complete abrogation at 600 μM. PMA-stimulated leucocytes showed markedly higher PAD activity following inhibition of ROS formation with DPI. At a concentration of 10,000 μM, exogenously added H_2O_2 inhibited the catalytic activity of PAD released from PMA-stimulated leukocytes.

Conclusions: The ROS H_2O_2 directly inhibits enzymatic activity of PAD, and generation of ROS by NADPH oxidase down-regulates the activity of PAD released from stimulated leucocytes. This mechanism may play an important role in preventing hypercitrullination of proteins and thereby generation of self-antigens in RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3162

AB0082 ALKALINE PHOSPHATASE ELICITS PROPHYLACTIC AND THERAPEUTIC EFFECTS IN ARTHRITIC RATS

D.M.S.H. Chandrupatla[1], C.F.M. Molthoff[2], E. Elshof[2], W. Ritsema[2], M. Verlaan[2], R. Vos[2], A. Hammond[3], A.A. Lammertsma[2], C.J. van der Laken[1], R. Brands[4], G. Jansen[1]. [1]*Amsterdam Rheumatology and immunology Centre – location VUmc;* [2]*Radiology and Nuclear Medicine, VU University Medical Center, Amsterdam, Netherlands;* [3]*KIMS Hospital, Kent, United Kingdom;* [4]*AMRIF BV, Wageningen, Netherlands*

Background: Alkaline phosphatase (AP) functions as a gate-keeper of the innate immune system [1] by detoxifying inflammation triggering moieties (ITMs). As an ectophosphatase, AP thus acts extracellularly by dephosphorylating ITMs that originate and are released from endogenous sources, e.g. by converting ADP and ATP nucleotides into adenosine to establish a key signalling anti-inflammatory effect. Consequently, AP activity prevents the production of pro-inflammatory cytokines by activated leucocytes and their downstream effects. Due to its broad mechanism of action, AP may potentially serve as an attractive therapeutic moiety in chronic inflammatory disorders, including rheumatoid arthritis (RA).

Objectives: To examine the anti-arthritic effects of prophylactic and therapeutic AP interventions in arthritic rats.

Methods: Wistar rats were immunized twice with methylated bovine serum albumin (mBSA), followed by local arthritis induction (intra-articular (i.a.) mBSA injection with 3 repeated injections) in the right knee (arthritic knee) with the contralateral left knee serving as internal control [2]. Interventions were performed using 200 μg human recombinant placental AP, administered subcutaneously, either before i.a. mBSA injections (2x, every 3 days, 2 rats/group; *prophylactic* setting) or after arthritis induction (4x, every 3 days, 4 rats/group; *therapeutic* setting). After *ex vivo* tissue distribution, knees were excised, fixed, decalcified and paraffin-embedded. Knee sections were examined for synovial macrophage infiltration by immunohistochemistry with ED1 (∼CD68) and ED2 (∼CD163) macrophage specific antibodies. Results were compared with untreated arthritic rats and arthritic rats receiving MTX therapy (1 mg/kg, intraperitoneally, 4x, every 3 days, 4 rats/group).

Results: Prophylactic and therapeutic schedules of AP treatment were well tolerated and reduced knee swelling comparable with MTX treatment. Following AP prophylactic intervention, synovial macrophage infiltration in the arthritic knees was reduced 4-fold (ED1) and 6-fold (ED2) when compared with affected knees of untreated arthritic rats, approaching macrophage counts in contralateral (non-arthritic) knees of AP treated rats. Therapeutic AP interventions resulted in 3.5-fold lower synovial infiltration of both ED1 and ED2 macrophages in arthritic knees, comparable with effects of MTX treatment.

Conclusions: AP, both as prophylactic and as therapeutic intervention, demonstrated favourable anti-arthritic efficacy in a rat model of arthritis. These studies warrant further preclinical and clinical evaluation as a putative novel therapeutic entity for arthritis.

References:

[1] Pike AF et al, Biochim Biophys Acta (2013);1832:2044–2056.

[2] Chandrupatla DM et al, Biomed Res Int. (2015), 509295.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4630

AB0083 SINGLE NUCLEOTIDE POLYMORPHISMS IN LEP – 2548 G>A AND LEPR + 668 A>G IN RHEUMATOID ARTHRITIS MEXICAN MESTIZOS ARE ASSOCIATED WITH AGE AT DIAGNOSIS, DISEASE ACTIVITY AND ANTI-CCP ANTIBODIES

E. Gomez-Bañuelos[1], E. Chavarria-Avila[1], K. Arrona-Rios[2], L. González-Rosas[3], J. Aguilar-Arreola[3], S. Duran-Barragan[1], H. Avila-Armengol[3], F. Corona-Meraz[1], A. Saldaña-Millan[1], R.-E. Navarro-Hernandez[1], M. Vázquez-Del Mercado[1,3]. [1]*Instituto de Investigación en Reumatología y del Sistema Musculoesquelético, Universidad de Guadalajara;* [2]*Servicio de Reumatologia, Division de medicina interna, Posgrado PNPC 004086, CONACYT;* [3]*Servicio de Reumatologia, Division de medicina interna, Posgrado PNPC 004086, CONACYT, Hospital Civil de Guadalajara, "Juan I. Menchaca", Guadalajara, Mexico*

Background: The role of adipose tissue in RA pathogenesis has been acknowledged since the high frequency of dyslipidemia and insulin resistance in these patients. Leptin, a pleiotropic adipokine, has been associated with inflammation markers and articular damage in RA and the anti-citrullinated protein antibodies. Notwithstanding, these findings have not been constant across different populations. These points towards that single nucleotide polymorphism (SNP) in leptin and its receptor might influence the participation of this adipokine in RA pathogenesis.

Objectives: To determine the association of the SNPs *LEP* -2548 G>A and *LEPR* 668 A>G with adiposity, metabolic and inflammation markers in RA patients.

Methods: We enrolled 116 patients with RA (ACR 1987) matched with 133 control subjects by age, gender, and body mass index (BMI). Subjects were evaluated for fat mass and skinfold thickness. Also, serum glucose, insulin, lipid profile, serum leptin (sLep), soluble leptin receptor, TNFa. In patients with RA we evaluated disease activity and anti-CCP. Genotypes of *LEP* -2548 G>A and *LEPR* 668 A>G were determined by PCR-RFPL using *HhaI* and *MspI* restriction enzymes.

Results: There was no difference in genotypes distribution of LEP -2548 G>A and *LEPR* 668 A>G between RA and control. *LEPR* 668 G allele was associated with higher anti-CCP titers and disease activity score compared to *LEPR* 668A/A homozygotes, 4.2±1.7 vs. 3.46±1.2 *P*=0.012. *LEP* -2548A allele was associated with younger age of RA diagnosis vs. G/G homozygotes, 35.9±11.5 vs. 41.8±13.9 years old (*P* =0.045). OR for diagnosis before 40 years old was 2.7 (CI95% 1.04 – 7.45).

Conclusions: *LEP* -2548 G>A is related with a younger age at diagnosis of RA and *LEPR* 668 G/G was associated with increased anti-CCP titers and disease activity. This suggests that there is an additive effect between chronic inflammation of RA and obesity were leptin may favor humoral immune response against citrullinated proteins and influence the severity of RA.

In preobese and obese patients with RA anti-CCP (+) there is an increased sLep production. *LEP* -2548 G>A is related with a younger age at diagnosis of RA and *LEPR* 668 G/G was associated with increased anti-CCP titers and disease activity. These suggests that there is an additive effect between chronic inflammation of RA and obesity were leptin may favors humoral immune response against citrullinated proteins and influence the severity of RA.

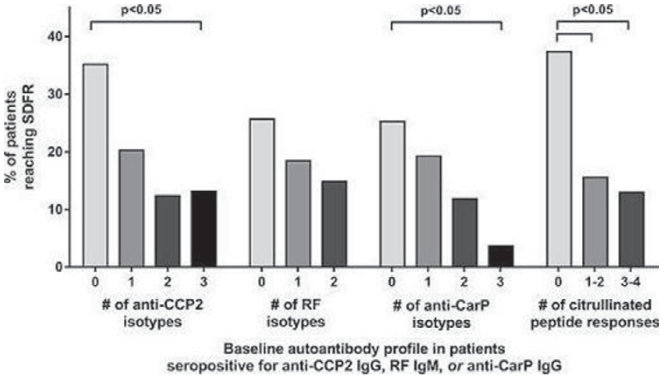
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6729

AB0084 BREADTH OF BASELINE AUTOANTIBODY PROFILE AND TREATMENT RESPONSE IN RHEUMATOID ARTHRITIS PATIENTS

V.F.A.M. Derksen[1], E.C. de Moel[1], L.A. Trouw[1], R.J. Goekoop[2], I. Speyer[3], T.W.J. Huizinga[1], C.F. Allaart[1], R.E.M. Toes[1], D. van der Woude[1].
[1]Rheumatology, Leiden University Medical Center, Leiden; [2]Rheumatology, Haga Hospital; [3]Rheumatology, Haaglanden Medical Center, The Hague, Netherlands

Background: Seropositive and seronegative rheumatoid arthritis (RA) are distinct disease entities with regard to pathophysiological mechanisms and disease outcomes. However, over the past years it has become clear that the autoantibody profile of seropositive RA is very diverse, involving multiple post-translational modifications and isotypes, and it seems unlikely that a single autoantibody will be informative for identifying groups at risk of poor treatment response. Instead of individual autoantibodies, we hypothesized that the breadth of seropositive patients' profile may be the best reflection of the underlying immunopathology, and would be able to identify homogenous treatment response and inform treatment decisions.
Objectives: To investigate whether baseline autoantibody profile is associated with treatment response and the ability to taper off medication in RA patients.
Methods: All RA patients fulfilling the 2010 ACR/EULAR Criteria included in the IMPROVED study[1] that were seropositive for routine clinical testing for anti-cyclic citrullinated peptide-2 (anti-CCP2 IgG), rheumatoid factor (RF IgM), or our in-house assay for anti-carbamylated protein antibodies (anti-CarP IgG) were selected (n=381). In baseline sera of these patients, we measured IgG, IgM, and IgA isotypes for each family (except IgG for RF) and reactivity against 4 citrullinated peptides (cit-vimentin 59–74, cit-fibrinogen β 36–52 and α 27–43, and cit-enolase 5–20). We investigated associations between autoantibody profile and 1) change in disease activity score (DAS)-44 over time and 2) sustained drug-free remission, defined as the ability to taper off medication and remain in remission for ≥1 year after achieving DAS44<1.6.
Results: The initial treatment response (mean ΔDAS 0–4 months) in seropositive patients with a broad autoantibody profile (7–8 isotypes present) was better than in those with fewer isotypes present (ΔDAS 0–4 months of 7–8 isotypes vs 1–2, 3–4, and 5–6 isotypes, respectively: -2.2 vs -1.5 [p<0.001], -1.7 [p=0.04], and -1.8 [p=0.04]). In contrast, the presence of multiple autoantibodies was unfavorable regarding the long-term outcome of sustained drug-free remission. Within seropositive disease, patients with more isotypes and more reactivities to citrullinated peptides significantly less often achieved sustained drug-free remission (SDFR) (Figure).



Conclusions: Seropositive patients with a broader autoantibody profile at baseline initially react better to treatment, but are not able to taper off medication and remain in remission. This may be relevant in individualized decision-making for tapering medication, as these results suggest that disease with a broad autoantibody response, as proxy for an active humoral autoimmunity, is more difficult to control in the long-term without sustained therapy.
References:
[1] Heimans, AR&T 2016, 18:23.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3193

AB0085 INTERACTION OF HLA-SHARED EPITOPE (SE) AND SMOKING ON THE DEVELOPMENT OF ANTI-CCP POSITIVE RHEUMATOID ARTHRITIS IN GREEK POPULATION

E.N. Mole[1], K. Tarassi[2], V. Kitsiou[2], T. Athanassiades[2], D. Kouniaki[2], K. Soufleros[2], C. Korkou[1], A. Tsirogianni[2], C. Sfontouris[1]. *[1]Department of Rheumatology; [2]Department of Immunology-Histocompatibility, Evangelismos General Hospital, Athens, Greece*

Background: Rheumatoid Arthritis (RA) is a complex, multifactorial autoimmune disease, whose etiopathogenesis involves genetic and environmental factors.
Objectives: The aim of the study was the assessment of the association of HLA-DRB1*-SE in the presence/absence of anti-CCP autoimmunity in Greek patients with RA (smokers and non-smokers).
Methods: Eighty-three (83) RA patients (41 smokers, 42 have never smoked) were typed for HLA-DRB1* alleles by molecular techniques (PCR-SSOP and -SSP). In 62 out of 83 (74.7%) anti-CCP abs were detected by ELISA.
Results: In RA pts and in comparison to the controls, increased frequency of HLA-DRB1*01:01 (28.9% *vs* 6.8%, OR=4.4), *10:01 (16.9% *vs* 2.4%, OR=8.4), *04:01 (3.6% *vs* 2%, OR=1.8), *04:04 (7.2% *vs* 1%, OR=7.6) and *04:05 (15.7% *vs* 3.7%, OR=4.8), as well as decreased frequency of *04:02 (1.2% *vs* 2%, OR=0.6) and *04:03 (4.8% *vs* 6.8%, OR=0.7) were found. Among the RA patients, 77.1% possess 1SE *vs* 18.9% of controls (OR=14.4), whereas 10.8% possess 2SE *vs* 1% of controls (OR=11.8). In CCP (+) RA patients and in comparison to CCP (-) an increased frequency of HLA-DRB1*01:01 (27.4% *vs* 14.3%, OR=2.3) and *10:01 (21% *vs* 4.8%, OR=5.3) was observed. Furthermore, 88.7% of CCP (+) carry 1SE *vs* 42.9% of CCP (-) patients (OR=10.5). CCP (+) smokers patients in comparison to CCP (+) non-smokers are presented with an increased frequency of DRB1*01:01 (41.9% *vs* 12.9%, OR=4.9). Among the CCP (+) smokers, 96.8% possess 1SE *vs* 80.6% of CCP (+) non-smokers (OR=7.2), whereas 12.9% possess 2SE *vs* 12.9% of CCP (+) non-smokers (OR=1).
Conclusions: a) An increased frequency of HLA-DRB1*01:01, *10:01, *04:05 alleles, as well as the protective role of *04:02, *04:03 alleles in Greek patients with RA were confirmed b) The presence of any SE, particularly *10:01 allele, strongly influences the production of anti-CCP abs and c) Interaction between smoking and any SE, particularly *01:01 allele, is associated with anti-CCP positive RA in Greek patients.
References:
[1] Klareskog L, Stolt P, Lundberg K, Kallberg H, Bengtsson C, Grunewald J, et al. A new model for an etiology of rheumatoid arthritis: smoking may trigger HLA-DR (shared epitope)-restricted immune reactions to autoantigens modified by citrullination. Arthritis and rheumatism. 2006;54(1):38–46.
[2] Ioannidis JP, Tarassi K, Papadopoulos IA, Voulgari PV, Boki KA, Papasteriades CA, et al. Shared epitopes and rheumatoid arthritis: disease associations in Greece and meta-analysis of Mediterranean European populations. Seminars in arthritis and rheumatism. 2002;31(6):361–70.
[3] Lee YH, Bae SC, Song GG. Gene-environmental interaction between smoking and shared epitope on the development of anti-cyclic citrullinated peptide antibodies in rheumatoid arthritis: a meta-analysis. International journal of rheumatic diseases. 2014;17(5):528–35.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5213

AB0086 PREVENTIVE EFFECTS OF ANGIOTENSIN 1-7 ON NEOANGIOGENESIS AND LEUKOCYTE TRAFFICKING INCREASE IN THE EARLY PHASES OF AN EXPERIMENTAL MODEL OF ANTIGEN INDUCED ARTHRITIS

F. Fischetti, P. Durigutto, D. De Nardo, R. Carretta. *University of Trieste Italy, Trieste, Italy*

Background: Renin Angiotensin System (RAS) might be supposed to be involved in the early and late phases of development of synovitis, since data exist showing that Angiotensin (AT)-II contributes to the development of vascular damage under early inflammatory conditions (1, 2). Little is known about AT 1–7 functions, which is supposed to play counteracting actions vs AT II, under these conditions (2, 3)
Objectives: to evaluate if, in the early phases of an experimental model of arthritis, namely the antigen-induced arthritis (AIA), treatment with AT 1–7 could interfere with the synovial development of capillary vascular growth, and prevent leukocyte trafficking activation, in vivo, either at synovial and at mesentery post-capillary venules.
Methods: in compliance with European (86/609/EEC) and the Italian (D.L.116/92) ethics committees, 2 groups each of 8 male (240–270 gr) Wistar rats were randomly chosen and treated respectively with sterile saline, or with AT 1–7 (576 μg/kg/day), during the time of immunization with methylated serum bovine albumin (mBSA). Arthritis was induced by intraarticular administration of mBSA (0.1mg in 100ml sterile saline) into the right knee of each animal, after previous immunization to mBSA emulsified in complete Freund's adjuvant. The left knee, injected with only saline, served as a control. Two and 5 days after arthritis induction, the count of capillary branches, and the number of fluorescently-labelled leukocytes, showing transient or stable adhesion to the endothelial microvascular layer (EL), were assessed by using an in vivo videomicroscopy technique.
Results: synovial branching vessels with diameter >20μm were not modified after AIA induction, while microvessels having diameter less than 20 μm were significantly increased. After 2 and 5 days, AT 1–7 reduced the number of neo expressed <20μm diameter vessels (Day2: 3.7±3.4 vs 7.7±5.05, p=ns; Day5: 12.7±6.9 vs 21.0±7.3, p<0.05; both significantly greater than control joints). Transient and stable adhesion to EL showed to be partially reduced 2 days after AIA induction and significantly reduced after 5 days (Day5, transient=12.5±6.2 vs 26.0±9.0, p<0.05; stable=27.0±8.3 vs 41.7±10.6, p<0.05; both significantly greater than control joints). Comparable results were found when analysing the number of leukocytes adhering to mesentery EL.
Conclusions: we suggest that AT 1–7 could play an immune modulating role in the early phase of synovitis with possible prevention of further inflammatory and secondary structural tissue alterations. These data further support the hypothesis that mechanisms leading to synovial AT-II activation have a detrimental role in the development of arthritis.

References:
[1] Candido R, et al. Circulation 2004;109:1536–1542.
[2] Zhang F et al, Sci Rep. 2016; 6: 34621.
[3] Villalobos LA et al, Front Pharmacol. 2016; 7: 482.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5493

AB0087 SONIC HEDGEHOG PROMOTES FIBROBLAST-LIKE SYNOVIOCYTES PROLIFERATION VIA MODULATING THE MAPK/ERK SIGNALING PATHWAY IN RHEUMATOID ARTHRITIS

F. Liu[1], S.-L. Zhu[2], Y.-F. Pan[1], J.-L. Huang[2]. *[1]Rheumatology, the Third Affiliated Hospital of Sun Yat-Sen University; [2]Rheumatology, the Sixth Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China*

Background: The Sonic hedgehog (Shh) signaling has been reported to be activated in synovium of RA patients and RA-FLS in vitro [1]. Further, Shh signaling plays an important role in RA-FLS proliferation [2]. As for the extracellular signal-regulated kinase (ERK),is a member of mitogen-activated protein kinase (MAPK) [3], which has been reported to be involved in proliferation of RA-FLS [4]. However, the role of MAPK/ERK signaling pathway in the proliferation of RA-FLS modulating by Shh is unclear.
Objectives: To study the effect of MAPK/ERK signaling pathway on cell proliferation modulated by Sonic hedgehog (Shh) signaling in fibroblast-like synoviocytes isolated from patients with active rheumatoid arthritis (RA-FLS).
Methods: The RA-FLS were primarily cultured by the explant culture, and then were treated with Shh agonist Purmorphamine,inhibitor Cyclopamine or MAPK/ERK signaling pathway inhibitor U0126, respectively. Western blots was used to examine the phosphorylation level of ERK 1/2 (p-ERK1/2), which was the critical protein of MAPK/ERK signaling. The cell proliferation activity was detected using cell proliferation and cytotoxicity kit-8 (CCK8),and the cell proliferation rate was detected using a flow cytometry.
Results: Compared with the control group, Purmorphamine transiently increased p-ERK1/2 protein at the concentration of 1 μM, and the peak activations of p-ERK1/2 took place at 15min ($P<0.01$). Cyclopamine and U0126 decreased the expression of p-ERK1/2 protein ($P<0.01$). After the RA-FLS treated with Purmorphmine (1μM) for 48 hours, the cell proliferation activity was 114±4% and the percentage of S phase cells was 8.39±0.60%, significantly higher than those of the control group 100±0% ($P<0.01$) and 3.29±0.69% ($P<0.01$). After treated with Cyclopamine (10μM) for 48 hours, the cell proliferation activity of RA-FLS was 89±1% ($P<0.05$) and the percentage of S phase cells was 1.53±0.22% ($P<0.05$). When co-treated with purmorphamine (1μM) and U0126 (10μM), the cells proliferative activity was 892% ($P<0.05$) and the percentage of S phase cells was 1.07±0.25% ($P<0.05$).
Conclusions: Shh might promote proliferaton of RA-FLS via modulating MAPK/ERK signaling, subsequently contributing to hyperlasia of synovium and ultimately leading to RA disease.
References:
[1] Wang M, et al. Sonic hedgehog signaling drives proliferation of synoviocytes in rheumatoid arthritis: a possible novel therapeutic target[J]. J Immunol Res, 2014, 2014: 401903.
[2] Zhu SL, et al. Inhibition of smoothened decreases proliferation of synoviocytes in rheumatoid arthritis[J]. Cell Mol Immunol, 2015. DOI: 10.1038/cmi.2015.67.
[3] Elia D, et al. Sonic hedgehog promotes proliferation and differentiation of adult muscle cells: Involvement of MAPK/ERK and PI3K/Akt pathways[J]. Biochim Biophys Acta, 2007. 1773(9): 1438–46.
[4] Morel J, Audo R, Hahne M, Cet al. umor necrosis factor related apoptosis inducing ligand (TRAIL) induces rheumatoid arthritis synovial fibroblast proliferation through mitogen activated protein kinases and phosphatidylinositol3-kinase/Akt[J]. J Biol Chem 2005. 280(16):15709–15718.
Acknowledgements: This study was supported by the National Natural Science Foundation of China (No.81571584). I thank Jianlin Huang for protocols.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4027

AB0088 THE ROLE OF HIGH MOBILITY GROUP BOX-1 (HMGB1) IN INFLAMMATORY VASCULOPATHY IN COLLAGEN ANTIBODY-INDUCED ARTHRITIS (CAIA)

F. Biscetti[1], A. Flex[2], F. Angelini[2], E. Gremese[1], B. Tolusso[1], G. Ferraccioli[1]. *[1]Rheumatology; [2]Internal Medicine, Catholic University School of Medicine, Rome, Italy*

Background: Rheumatoid arthritis (RA) is associated with vascular disease (1). Recent findings demonstrated that the risk of peripheral arterial occlusive disease is increased in patients with RA compared to the general population (2). However, the pathogenesis is not fully understood. High-mobility group box-1 (HMGB1) is a nuclear protein involved in inflammatory responses (3) and RA-like synovitis (4).
Objectives: Aim of the present study was to analyze the relationship between HMGB1 and peripheral arterial disease in collagen antibody-induced arthritis (CAIA).
Methods: BALB/c mice were injected with monoclonal anti-collagen antibody cocktail followed by lipopolysaccharide to induce arthritis. After the induction of arthritis, we studied ischemia-induced neovascularization in the ischemic hind limb of arthritic and control mice.
Results: We found that the perfusion recovery was significantly attenuated arthritic mice, compared to control mice. The immunohistochemical analysis for the CD31 demonstrated a reduced number of vessel in mice with experimental arthritis. The selective blockade of HMGB1 in arthritic mice resulted in restored blood flow recovery and capillary density in the ischemic muscle. Cytokine enzyme-linked immunosorbent assay (ELISA) analyses performed on peripheral blood demonstrated a significant reduction of interleukin (IL)-1β, IL-6 and tumor necrosis factor (TNF)-α in mice where HMGB1 was blocked. Interestingly, the selective blockade of HMGB1 resulted in an increase of the peripheral IL-17A concentration.
Conclusions: HMGB1 pathway is involved in an experimental vasculopathy induced in a RA-like model. The proangiogenic cytokine IL-17A is increased when HMGB1 is inhibited. Although further data are needed, these findings provide new evidence regarding the pathogenesis of vascular complications observed in patients with RA.
References:
[1] Roman MJ, Salmon JE. Cardiovascular manifestations of rheumatologic diseases. Circulation. 2007 Nov 13;116(20):2346–55.
[2] Chuang YW, Yu MC, Lin CL, Yu TM, Shu KH, Huang ST, Kao CH. Risk of peripheral arterial occlusive disease in patients with rheumatoid arthritis. A nationwide population-based cohort study. Thromb Haemost. 2016 Jan;115(2):439–45.
[3] Biscetti F, Ghirlanda G, Flex A. Therapeutic potential of high mobility group box-1 in ischemic injury and tissue regeneration. Curr Vasc Pharmacol. 2011 Nov;9(6):677–81.
[4] Biscetti F, Flex A, Pecorini G, Angelini F, Arena V, Stigliano E, Gremese E, Tolusso B, Ferraccioli G. The role of high-mobility group box protein 1 in collagen antibody-induced arthritis is dependent on vascular endothelial growth factor. Clin Exp Immunol. 2016 Apr;184(1):62–72.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4111

AB0089 ELECTROKINETIC CHARACTERISTICS OF SYNOVIOCYTES (SC) AND THE LEVEL OF ANTIOXIDANT PROTECTION IN RHEUMATOID ARTHRITIS (RA)

G. Kudriavtseva, V.I. Shishkin, V.V. Shishkin, Y.A. Malenkov. *Saint Petersburg State University, Saint Petersburg, Russian Federation*

Background: Known role of SC in the pathogenesis of RA. It is impossible, however, at this level of knowledge to ascertain all the mechanisms for their involvement in the pathological process. Reduced tissue antioxidant protection can affect cellular metabolism, and as might be expected, through the mechanism of autophagy inducing mitochondrial and lysosomal degradation, facilitating cell membrane depolarization.
Objectives: The aim of this work was to study the electrophoretic mobility (EM) of SC of RA patients and its relationship with the activity of antioxidant enzymes: Cu-Zn superoxidismutase (Cu-Zn SOD), Se-glutathione peroxidase (Se-GPO) and catalase (the CAT) in synovial fluid (SF).
Methods: SF has been obtained from the knee of 7 patients with RA and 5 donors. SC isolated by standard methods. EM of SC determined by the automatic microscope. Se level in SF recorded by atomic absorption spectrometry. The activity of the antioxidant enzymes was determined by classical methods of enzymology.
Results: A significant depolarization of the RA SC, resulting in a reduction of their EM as compared to the normal level of the average in 4 times. Activity of antioxidant enzymes is dramatically reduced by a significant decrease of Se concentrations in SF (150 μg/l normally up to 80 μ g/l in RA), which is particularly reflected in the activity of Se GPO (note that SF can be up to 100 Se-containing proteins).

Table 1

	EM of SC (m/v sec)	Cu-Zn SOD (Units/mg of protein)	Se-GPO (Units/mg of protein)	CAT (μmol/min/mg of protein)
Normal SF	$1{,}62\times10^{-8}$	23,4±0,8	1,3±0,3	10,3±0,1
RA SF	$0{,}37\times10^{-8}$	11,7±0,4	0,4±0,1	0,47±0,04

Conclusions: We can assume that aggravated by RA catabolic processes that caused the dysfunction of the lysosomal and mitochondrial structures (autophagy), consistently shoot antioxidant protection of SC and cause depolarization and the decrease in electrophoretic mobility of these cells.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5364

AB0090 N-ACETYL-L-CYSTEINE (NAC) CONTROLS OSTEOCLASTOGENESIS THROUGH REGULATING TH17 DIFFERENTIATION AND RANKL PRODUCTION IN RHEUMATOID ARTHRITIS

H.-R. Kim, K.-A. Lee, S.-H. Lee. *Rheumatology, Konkuk University School of Medicine, Seoul, Korea, Republic Of*

Background: NAC is a thiolic antioxidant produced by the body and serves as a precursor of glutathione synthesis. In rheumatoid arthritis (RA), oxidative stress is an important mechanism causing destructive proliferative synovitis.
Objectives: This study aimed to determine the regulatory role of N-Acetyl-L-cysteine (NAC), an antioxidant, in IL-17-induced osteoclast differentiation in RA.
Methods: After RA synovial fibroblasts were stimulated by IL-17, the expression and production of RANKL was determined by real-time PCR and ELISA. Human peripheral blood monocytes were cultured with M-CSF, IL-17, RANKL, and/or various concentrations of NAC, followed by counting of the cells for tartrate-resistant acid phosphatase activity to determine osteoclast formation. Osteoclastogenesis was also determined after cocultures of IL-17-stimulated RA synovial fibroblasts, Th17 cells and various concentrations of NAC with monocytes. After human peripheral $CD4^+$ T cells were cultured with NAC under Th17 condition, IL-17, IFN-g, IL-4, Foxp3, RANKL and IL-2 expression and production was determined by flow cytometry or ELISA.
Results: When RA synovial fibroblasts were stimulated by IL-17, IL-17 stimulated the production of RANKL, and NAC reduced the IL-17-induced RANKL production in a dose-dependent manner. NAC decreased IL-17-activated phosphorylation of mTOR, JNK and IkB. When human peripheral blood $CD14^+$ monocytes were cultured with M-CSF and IL-17 or RANKL, osteoclasts were differentiated, and NAC reduced the osteoclastogenesis. After human peripheral $CD4^+$ T cells were co-cultured with IL-17-pretreated RA synovial fibroblasts or Th17 cells, NAC reduced their osteoclastogenesis. Under Th17 polarizing condition, NAC decreased Th17 cell differentiation and IL-17 and RANKL production.
Conclusions: NAC inhibits the IL-17-induced RANKL production in RA synovial fibroblasts and IL-17-induced osteoclast differentiation. NAC also reduced Th17 polarization. NAC could be a supplementary therapeutic option for inflammatory and bony destructive processes in RA.
Acknowledgements: This research was supported by a grant of the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology, Republic of Korea (NRF-2014R1A2A2A01007223) and the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (HI13C1704).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1506

AB0091 SURFACE PHENOTYPE OF CIRCULATING PLATELETS IS ALTERED IN PATIENTS WITH RHEUMATOID ARTHRITIS

H. Yasuoka, K. Yoshimoto, K. Yamaoka, T. Takeuchi. *Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan*

Background: Rheumatoid arthritis (RA) is a connective tissue disease and characterized with multiple synovitis. However, pathogenesis of RA and systemic characteristic of RA is still under the investigation (1). Platelets distribute systemically through blood circulation and classically contribute to hemostasis physiologically (2). On the other hand, platelets can contribute to disease process by producing humoral factors such as cytokines or growth factors (3). Also, platelets have surface molecules not only associated with hemostasis but with other functional properties. Thus, these molecules can trigger the activation of other cells by cell-to-cell contact (4).
Objectives: To examine the association between characteristics of phenotype of circulating platelets based on the expression of surface molecules and clinical characteristics of RA and to seek the possibility as novel biomarkers.
Methods: Eight patients with RA were involved and 9 with scleroderma and 13 healthy controls were used as controls in this study. Surface expression of CD62P (P-selectin), membrane-bound TGF (transforming growth factor)-beta, CD147 (emmprin), CD142 (tissue factor), CD31 (platelet endothelial cell adhesion molecule (PECAM)-1) on CD41+CD45-CD14- platelets was examined using flow cytometry. Comparison between two groups was by non-parametric Mann-Whitney U-test. Clinical parameters at blood drawing were retrospectively obtained from clinical records, and correlation between proportion of platelet subsets and clinical parameters were examined.
Results: Proportion of CD62P+ activated platelets were higher in both RA and SSc compared to HC ($P<0.0005$, $P<0.0002$, respectively). Interestingly, CD147+ platelets were significantly higher in RA ($P<0.0004$), whereas not only proportion of CD147+ platelets but that of TGF-beta+ platelets were higher in SSc compared to healthy controls ($P<0.0001$, respectively). In patients with RA, proportion of CD62P+ activated platelets was correlated with inflammatory markers such as CRP and ESR and markers for disease activity such as SDAI ($P<0.05$, respectively) and these proportion were decreased after treatment ($P<0.03$).
Conclusions: In patients with RA, proportion of CD62P+ and CD147+ platelets were increased compared to healthy controls. Furthermore, phenotype of platelets of RA was altered compared to SSc. Interestingly, proportion of CD62P+ platelet is associated with the inflammatory markers and disease activity of RA. These results suggest that platelets reflect disease process of RA and could be utilized as novel biomarkers.
References:
[1] Smolen JS et al. Rheumatoid arthritis. Lancet 388: 2023–2038, 2016.
[2] Bizzozero G et al. Sur un nouvel element morphologue du sang chez les mammiferes et son importance dans la thombose et dans la coagulation. Arch Ital Biol 1:1–5, 1882.
[3] Morrell CN et al. Emerging roles for platelets as immune and inflammatory cells. Blood 123:2759–2767, 2014.
[4] Van Velzen JF et al. Multicolor flow cytometry for evaluation of platelet surface antigens and activation markers. Thromb Res 130:92–8, 2012.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4596

AB0092 EFFECT OF METHOTREXATE, LEFLUNOMIDE AND HYDROXYCHLOROQUINE ON THE INSULIN RESISTANCE AND OBESITY ASSOCIATED WITH RHEUMATOID ARTHRITIS: OBESE MOUSE MODELS OF RHEUMATOID ARTHRITIS

I. Arias de la Rosa[1], S. Rodriguez-Cuenca[2], Y. Jimenez-Gomez[1], P. Ruiz-Limon[1], C. Perez-Sanchez[1], M.C. Abalos[1], E. Collantes[1], A. Vidal-Puig[2], A. Escudero-Contreras[1], C. Lopez-Pedrera[1], N. Barbarroja[1]. *[1]Rheumatology Service, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain; [2]Metabolic Research Laboratories, Wellcome Trust-MRC Institute of Metabolic Science, Addenbroke's Hospital, Universidad de Cambridge, Cambridge, United Kingdom*

Background: Numerous studies have demonstrated the closely association between rheumatoid arthritis (RA) and metabolic complications such as obesity and insulin resistance. Thus, there is an urgent need for the use of therapies targeting both the activity of the disease and such metabolic disorders. Nowadays, the conventional treatment of RA consists of disease-modifying antirheumatic drugs (DMARDs) in monotherapy or combined. Yet, its beneficial/negative effect on the metabolic complications associated with cardiovascular disease prominent in RA patients is still unravelled.
Objectives: To analyze and compare the effects of methotrexate, leflunomide and hydroxychloroquine on the obesity and insulin resistance in an obese collagen-induced arthritis (CIA) mouse model.
Methods: CIA was developed in obese and lean mice. 55 C57Bl/6 mice (4–5 weeks) were used. Forty-one mice were fed with high fat diet (60%) until reaching 30g (obese) (OB). Groups of study: 5 non-diseased lean mice, 9 CIA lean mice, 5 non-diseased OB mice, 9 OB-CIA mice, 9 OB-CIA mice treated with leflunomide (10 mg/kg daily), 9 OB-CIA mice treated with methotrexate (3mg/kg three times/week) and 9 OB-CIA mice treated with hydroxychloroquine (60 mg/kg daily) for 15 days. Mice were weighted and the number of total inflamed digits was recorded daily. After treatment, before 72 hours of termination, glucose tolerance test (GTT) was performed. Buffy coat, plasma and metabolic tissues (gonadal and inguinal adipose tissue, skeletal muscle and liver) were collected.
Results: CIA obese mice developed the arthritis earlier and more severe (increased number of inflamed digits) compared with CIA lean mice. Regarding the progression of the disease, the three drugs significantly reduced the number of affected joints from the second day of treatment. However, after 15 days of treatment, the therapies more effective inhibiting the generation of inflamed digits were hydroxychloroquine and methotrexate. The development of RA in both obese and lean mice did not have effect on the body weight. Among the therapies used, only the hydroxychloroquine significantly reduced the body weight after 11 days of treatment. Glucose tolerance test revealed that the area under the curve was markedly smaller in OB-CIA mice after treatment with hydroxychloroquine compared to other treatments and OB-CIA mice untreated, suggesting an improvement of insulin sensitivity. Analysis on the metabolic tissues of these mice is currently ongoing in order to completely elucidate the effect of these therapies in the metabolic state.
Conclusions: 1) Obesity accelerates the development and aggravates the outcome of the arthritis in CIA mice. 2) Among the three DMARDs administered, hydroxychloroquine promoted a beneficial effect on the metabolism of CIA obese mice, reducing body weight and improving the insulin sensitivity. These results suggest that hydroxychloroquine could be used as a valuable therapeutic strategy in RA patients to reduce the disease activity and ameliorate the metabolic complications associated.
Acknowledgements: Funded by PI2013–0191, ISCIII-FIS (CP15/00158), RD16/0012/0015 and Roche Pharma S.A
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4684

AB0093 BLYS AND APRIL OVEREXPRESSION IN EARLY RHEUMATOID ARTHRITIS: ASSOCIATION WITH B CELLS AND MYELOID SUBSETS

J. Rodríguez-Carrio[1], M. Alperi-López[2], P. López[1], F.J. Ballina-García[2], A. Suárez[1]. [1]*Area of Immunology, University of Oviedo;* [2]*Department of Rheumatology, Hospital Universitario Central de Asturias, Oviedo, Spain*

Background: studies on B cell-mediated autoimmune diseases highlight the relevance of the B Lymphocyte Stimulator (BLyS) and A Proliferation-Inducing Ligand (APRIL), but emerging evidence points to an interaction with cell lineages other than B subsets. Although disturbances in the B cell compartment underlie the early stages of rheumatoid arthritis (RA), this phenomenon is poorly understood.
Objectives: to investigate the cellular populations responsible of BLyS expression and their association with the soluble forms of BLyS, APRIL and its receptor TACI (Transmembrane Activator and CALM Interactor) in early RA and to evaluate the changes in these parameters upon TNFα-blockade.
Methods: membrane BLyS (mBLyS) expression was assessed on B cells, monocytes (MØ), myeloid (mDC) and plasmacytoid (pDC) dendritic cells and neutrophils (NØ) by flow cytometry in fresh blood samples from 37 RA patients [DAS28 score (mean±SD): 4.84±1.44, disease duration (mean (range)): 1.26 (0–11) years, 23 (62.1%) RF+, 19 (51.3%) ACPA+, 19 untreated] and 31 healthy controls (HC). A subgroup of 13 biologic-naïve RA patients was prospectively followed for three months upon TNFα-blockade. Serum levels of soluble BLyS (sBLyS), APRIL (sAPRIL) and TACI (sTACI) were quantified by immunoassays.
Results: mBLyS expression was increased on B cells ($p=0.002$), MØ ($p<0.001$), mDC ($p<0.001$) and NØ ($p=0.014$) in RA patients. Higher sBLyS ($p=0.018$) and sAPRIL ($p<0.001$) serum levels were found in RA, whereas those of sTACI were not different compared to HC ($p=0.460$). Serum sAPRIL levels paralleled those of sTACI ($r=0.325$, $p=0.040$), and mBLyS expression on B cells ($r=0.463$, $p=0.009$), MØ ($r=0.521$, $p=0.003$), mDC ($r=0.438$, $p=0.014$) and NØ ($r=0.509$, $p=0.009$) in HC but not in RA patients. Serum levels of sTACI were negatively associated with DAS28 score ($r=-0.272$, $p=0.006$) in RA. However, sAPRIL was associated with mBLyS expression on mDC in patients with longer disease duration (>3 months) ($r=0.779$, $p<0.001$), but not in those recruited at onset ($r=0.245$, $p=0.361$). In the whole RA group, TNFα serum levels were found to be correlated with sAPRIL ($r=0.499$, $p<0.001$) and sBLyS ($r=0.362$, $p=0.013$). Similarly, IFNα and sAPRIL were positively associated ($r=0.423$, $p<0.001$). TNFα-blockade was associated with decreasing mBLyS expression on B cells, MØ, mDC and NØ (all $p<0.050$) and a slight increase in sTACI ($p=0.064$). Higher levels of mBLyS on MØ and mDC at baseline were associated with a poor clinical response upon TNFα-blockade ($n=8$; $p=0.006$ and $p=0.010$ compared to HC, respectively).
Conclusions: a role for B cell-activating factors in the pathogenesis of early RA is supported. B cells and myeloid populations (MØ, mDC and NØ) can account for the BLyS overexpression in RA, although important differences arise in their involvement. TNFα and IFNα are related to sBLyS and sAPRIL levels. An increased production of the soluble forms of BLyS and APRIL in addition to a less efficient feedback from their decoy receptors may delineate its detrimental effect.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2687

AB0094 MIGRATION, COLONIZATION AND DISTRIBUTION OF BONE MARROW MESENCHYMAL STEM CELLS TRANSPLANTED IN CIA RATS WERE TRACED BY GREEN FLUORESCENT PROTEIN

J. Hou, K. Xu, L. Zhang, G. Zhang, J. Gao, D. Ma, J. Fan. *Shanxi Academy of Medical Sciences, Shan xi Da Yi Hospita, Taiyuan, China*

Background: The mechanism of mesenchymal stem cells involved in injury and repair in vivo is not fully understood, so it is difficult to evaluate the effect of stem cells on rheumatoid arthritis.
Objectives: To investigate the migration, colonization and distribution of bone marrow mesenchymal stem cells (BM-MSCs) traced by green fluorescent protein (GFP) in the immune organs and joints of CIA rats, and study the mechanism of MSCs in repairing damage.
Methods: 1.MSCs labeled with GFP was cultured, amplified and identified in vitro.
2.Injected with mixture of II type collagen and complete Freund's adjuvant into Wistar rats space at 14 days: It was randomly divided into five groups, including early intervention group (n=20), late intervention group (n=20), CIA early control group (n=12), late control group (n=12) and normal control group (n=12).(2) MSCs were injected from tail veins according to the number of 1×10^7/kg,and the control groups were given equal volume of normal saline. (3) Observe the changes of arthritis index, arthritis swelling degree,and appearance of imageology and pathology.
3.The spleen, thymus, lymph nodes and joint tissues of the rats were made into pathological sections when transplanted at 3, 11, 30 and 42 days.The migration and distribution of the transplanted cells in the immune organs and the inflammatory joints were detected by immunohistochemistry.
Results: 1.(1)The arthritis index and degree of joint swelling in early and later intervention groups were decreased significantly than that of CIA control groups ($P<0.05$). (2)The early intervention group had lower arthritis index and the degree of joint swelling than the later intervention group ($P<0.05$).
2.The positive results of GFP was successfully detected by immunohistochemical method in the immune organs and joints of CIA rats, and sustainable for at least 42 days.
Conclusions: 1.MSCs transplanted through tail vein can migrate to the spleen, lymph nodes and thymus and joints,and can be long-term (42 days) colonization in these organizations.
2.The intervention of MSCs for CIA rats was effective, and early intervention effect was better than advanced intervention.
References:
[1] Gordon I. A. MacDonald, Andrea Augello, Cosimo De Bar. Role of mesenchymal stem cells in reestablishing immunologic tolerance in autoimmune rheumatic diseases. Arthritis &Rheumatism. 2011 Spe, 63(9): 2547–557.
[2] David Guéit, Marie Maumus, Florence Apparailly, Christian Jorgensen & Daniè Noë.Therapeutic mesenchymal stem or stromal cells in rheumatic diseases: rationale, clinicaldata and perspectivesClinical. Investigation. 2011 Sep, 1(9): 1269–1277.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4018

AB0095 BY INTRAVENOUS INFUSION MARKED BY GREEN FLUORESCENT PROTEIN TO REVEAL BONE MARROW MESENCHYMAL STEM CELLS' DISTRIBUTION AND DIFFERENTIATION OF COLLAGEN INDUCED ARTHRITIS RATS

J. Gao, L. Zhang. *Rheumatology Department, Shanxi Dayi Hospital, Taiyuan, China*

Background: Rheumatoid arthritis (RA) is a autoimmune disease,which is characterized by the osteoclasia or the high deformity rate of cartilage and bone. According to some materials, Mesenchymal stem cells (MSCs) were definited as the cell full of proliferation, differentiation capacity, and potential immune regulation. MSCs transplantation could be a appropriate-designed pattern to the joint damaging from rheumatoid arthritis (RA).However, the repairing mechanism against osteoclasia of cartilage and bone is still unclear.
Objectives: This study used collagen induced arthritis (CIA) rats as animal model to explore MSCs' tissue repairing mechanism.
Methods: We observed the ability of BMSCs differentiating into cartilage cells by toluidine blue staining in vitro;Then,BMSCs were labeled by the green fluorescent protein (GFP), infused into CIA through rats' tail vein infusion. In different point time, the rat's joints were made paraffin section,we observed the differentation of GFP positive cells and the distribution of GFP-positive cells differentiated chondrocytes by immunohistochemicale method.
Results: First,we found BMSCs in vitro can differentiate into cartilage cells under a certain-culture condition. Then, BMSCs were labeled by the green fluorescent protein (GFP), infused into CIA through rats' tail vein infusion. In different point time, the rat's joints were made paraffin section,which the GFP positive cells were observed in synovium and bone marrow tissues after transplantation on the 3th day, and in cartilage tissues on the 11th day, then increased in cartilage tissues on the 30th day,42th day, by laser scanning confocal microscope. Anti-type II collagen, GFP double positive cells were found in articular cartilages (especially damaged part)by Anti-II collagen immunofluorescence technology.

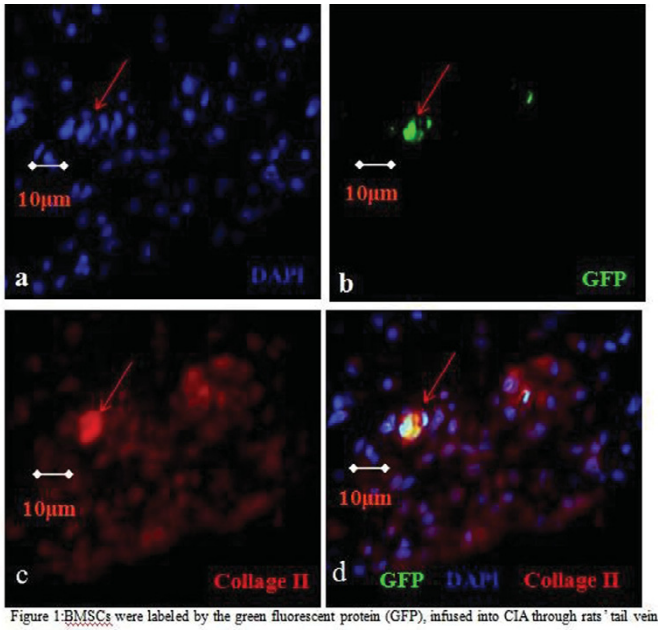


Figure 1:BMSCs were labeled by the green fluorescent protein (GFP), infused into CIA through rats' tail vein infusion. Fluorescence microscopic observation of joint paraffin section. Chondrocyte were stained with an antibody specific to type II collagen and observed by fluorescence microscopy (red fluorescence). Nucles were stained with DAPI (blue fluorescence).GFP-MSCs were observed by fluorescence microscopy (green fluorescence).Anti-type II collagen and GFP double positive cells were found in articular cartilages.

Conclusions: BMSCs were restricted to the joint injury or inflammatory site,differentiated into chondrocytes, and then participated in the cartilage repairing.

References:

[1] Zhao, C., L. Zhang, W. Kong, J. Liang, X. Xu, H. Wu, X. Feng, B. Hua, H. Wang, and L. Sun, Umbilical Cord-Derived Mesenchymal Stem Cells Inhibit Cadherin-11 Expression by Fibroblast-Like Synoviocytes in Rheumatoid Arthritis. J Immunol Res, 2015. 2015: p. 137695.
[2] Arend, W.P., G. Mehta, A.H. Antonioli, M. Takahashi, K. Takahashi, G.L. Stahl, V.M. Holers, and N.K. Banda, Roles of adipocytes and fibroblasts in activation of the alternative pathway of complement in inflammatory arthritis in mice. J Immunol, 2013. 190(12): p. 6423–33.
[3] Takano, T., Y.J. Li, A. Kukita, T. Yamaza, Y. Ayukawa, K. Moriyama, N. Uehara, H. Nomiyama, K. Koyano, and T. Kukita, Mesenchymal stemcells markedly suppress inflammatory bone destruction in rats with adjuvant-induced arthritis. Lab Invest, 2014. 94(3): p. 286–96.
[4] Gupta, A., C.D. Kaur, M. Jangdey, and S. Saraf, Matrix metalloproteinase enzymes and their naturally derived inhibitors: novel targets in photocarcinoma therapy. Ageing Res Rev, 2014. 13: p. 65–74.
[5] Oshita, K., K. Yamaoka and Y. Tanaka, [Regulation of osteoclastogenesis by human mesenchymal stem cells leading to application of a novel treatment for rheumatoid arthritis]. J UOEH, 2013. 35(1): p. 33–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3090

AB0096 EFFICACY AND SAFETY OF ORAL ADMINISTRATION OF PURE CELASTROL IN AIA RATS

R. Cascão [1], T. Carvalho [1], J. Goncalves [2], L.F. Moita [3], J.E. Fonseca [4]. *[1] Instituto de Medicina Molecular; [2] iMed – Research Institute of Medicines, Faculdade de Farmácia, Universidade de Lisboa, Lisbon; [3] Instituto Gulbenkian de Ciência, Oeiras; [4] Instituto de Medicina Molecular and Rheumatology Department, Centro Hospitalar de Lisboa Norte, EPE, Hospital de Santa Maria, Lisbon Academic Medical Centre, Lisbon, Portugal*

Background: Celastrol, a pentacyclic-triterpene isolated from *Tripterigium wilfordii* roots, has shown great therapeutic potential for the treatment of several inflammatory diseases, including rheumatoid arthritis (RA). We have previously demonstrated that celastrol has significant anti-inflammatory and bone protective effects in the adjuvant-induced rat model of arthritis (AIA), when administered via intraperitoneal route. For further preclinical evaluation of celastrol as a candidate compound for RA treatment, an effective and safe oral administration is crucial.

Objectives: In this work we aimed to study the dose range for both therapeutic and toxic effects for oral administration of pure celastrol using the AIA rat model.

Methods: Celastrol (1, 2.5, 5, 7.5, 12.5 and 25μg/g/day, N=5/group) was administrated orally in female AIA rats after 8 days of disease induction (therapeutic model) for a period of 14-days. A group of healthy (N=8) and untreated arthritic (vehicle, N=15) gender and age-matched Wistar rats were used as control. During the period of treatment, the inflammatory score, ankle perimeter and body weight were measured. At the end of the treatment, animals were sacrificed, blood was collected for clinical pathology, and necropsy was performed, with collection of internal organs for histopathological analysis and of paw samples for disease scoring.

Results: Oral administration of pure celastrol at 2.5, 5 and 7.5μ g/g/day reduced the inflammatory score and ankle swelling, preserved articular joint structure with a reduction in synovial inflammatory infiltrates and proliferation, halted articular bone destruction, and diminished the number of synovial CD68+ macrophages (a biomarker of response to anti-arthritic treatment). This compound also reduced the number of osteoclasts and osteoblasts present in joints. Bone resorption and turnover was also reduced at both 5 and 7.5μg/g/day, with a significant decrease in serum levels of TRACP-5b, P1NP and CTX-I. Of note, no significant variation in body weight, evidence of nephro-, hepato- or cardiotoxic effects, nor alterations in blood cell counts were observed at these concentrations. However, the dose of 7.5μ g/g/day was already associated with thymic and hepatotoxic changes, and higher doses showed toxicity signs. The lethal dose (LD) and LD_{50} were defined as 25μg/g/day and 12.5μg/g/day, respectively. Of note, oral celastrol at 1μg/g/day had no effect in arthritis progression.

Conclusions: Our results clearly show that 2.5μg/g/day is the lowest and 5μg/g/day is the highest effective and safe oral doses of celastrol in the setting of AIA rat model. These findings suggest that while celastrol is potentially very effective to treat RA, it has a narrow therapeutic window.

Acknowledgements: The authors would like to acknowledge Bruno Vidal and Inês Lopes for technical assistance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2868

AB0097 METHOTREXATE AND LOW DOSE PREDNISOLONE DOWNREGULATE OSTEOCLAST FUNCTION IN MONOCYTES FROM EARLY RHEUMATOID ARTHRITIS PATIENTS

I.P. Perpétuo [1], J. Caetano-Lopes [1], A.M. Rodrigues [1], R. Campanilho-Marques [1,2], C. Ponte [1,2], H. Canhão [3], M. Ainola [4], J.E. Fonseca [1,2]. *[1] Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa; [2] Rheumatology Department, Centro Hospitalar de Lisboa Norte, EPE, Hospital de Santa Maria; [3] EpiDoC Unit, CEDOC, NOVA Medical School, Universidade Nova de Lisboa, Lisbon, Portugal; [4] University of Helsinki, Institute of Clinical Medicine, Helsinki, Finland*

Background: Rheumatoid arthritis (RA) is a systemic, immune mediated inflammatory disease that is associated with bone erosions and joint destruction. Methotrexate (MTX) slows bone damage but the mechanism by which it acts is still unknown.

Objectives: In this study we aimed to assess the effect of MTX and low dose prednisolone (MTX+PDN) on circulating osteoclast (OC) precursors and OC differentiation in RA patients.

Methods: RA patients before and at least 6 months after MTX therapy were analyzed and compared with healthy donors. A blood sample was collected in order to assess receptor activator of NF-κB (RANK) ligand (RANKL) surface expression on circulating leukocytes and frequency and phenotype of monocyte subpopulations. Serum quantification of bone turnover markers and cytokines and *in vitro* OC differentiation assays were performed.

Results: The number or $RANKL^+$ neutrophils increased in RA patients when compared to healthy donors (p=0.006) and after treatment with MTX+PDN their count was reduced to healthy control numbers (p=0.0155). Classical activation markers of monocytes such as HLA-DR, CD86, CCR2 and CD11b, and also RANK were increased in RA patients at baseline, comparing to control healthy donors. After MTX+PDN exposure, expression decreased to healthy control levels. Serum RANKL levels were increased at baseline comparing to healthy donors (p=0.0164) and normalized after therapy.

Although the number of OC was not different between groups, resorbed area and resorbed area/pit were elevated when compared to controls (p=0.0436 and 0.0249, respectively) and reduced after treatment ($p<0.0001$).

Conclusions: Our results suggest that MTX+PDN play an important role in downregulating OC function, which we believe occurs through a decrease in RANK surface expression in monocytes.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6935

AB0098 EFFECTS OF TOFACITINIB IN EARLY ARTHRITIS BONE LOSS

B. Vidal [1], R. Cascão [1], M. Finnilä [2,3], I. Lopes [1], S. Saarakkala [2,4,5], P. Zioupos [6], H. Canhão [7], J. Fonseca [1,8]. *[1] Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal; [2] Research Unit of Medical Imaging, Physics and Technology, Faculty of Medicine, University of Oulu, Oulo; [3] Department of Applied Physics, University of Eastern Finland, Kuopio; [4] Medical Research Center, University of Oulu; [5] Department of Diagnostic Radiology, Oulu University Hospital, Oulo, Finland; [6] Biomechanics Labs, Cranfield Forensic Institute, Cranfield University, Swindon, United Kingdom; [7] EpiDoC Unit, CEDOC, NOVA Medical School, NOVA University; [8] Rheumatology Department, Centro Hospitalar de Lisboa Norte, EPE, Hospital de Santa Maria, Lisbon Academic Medical Centre, Lisboa, Portugal*

Background: Rheumatoid arthritis (RA) causes immune mediated local and systemic bone damage.

Objectives: The main goal of this work was to analyze, how treatment intervention with tofacitinib prevents the early disturbances on bone structure and mechanics in adjuvant induced arthritis rat model. This is the first study to access the impact of tofacitinib on the systemic bone effects of inflammation.

Methods: Fifty Wistar adjuvant-induced arthritis (AIA) rats were randomly housed in experimental groups, as follows: non-arthritic healthy group (N=20), arthritic non-treated (N=20) and 10 animals under tofacitinib treatment. Rats were monitored during 22 days after disease induction for the inflammatory score, ankle perimeter and body weight. Healthy non-arthritic rats were used as controls for comparison. After 22 days of disease progression rats were sacrificed and bone samples were collected for histology, micro-CT, 3-point bending and nanoindentation analysis. Blood samples were also collected for bone turnover markers and systemic cytokine quantification.

Results: At tissue level, measured by nanoindentation, tofacitinib increased bone cortical and trabecular hardness. However, micro-CT and 3-point bending tests revealed that tofacitinib did not revert the effects of arthritis on cortical and trabecular bone structure and on mechanical properties.

Conclusions: Possible reasons for these observations might be related with the mechanism of action of tofacitinib, which leads to direct interactions with bone metabolism, and/or with kinetics of its bone effects that might need longer exposure.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3491

AB0099 TAXOL ALLEVIATES COLLAGEN-INDUCED ARTHRITIS IN MICE BY INHIBITING THE FORMATION OF MICROVESSELS

J. Xu[1], Z. Feng[2], J. Zhu[3], S. Chen[1], X. Chen[4], J. Li[3]. *[1]Department of Internal Medicine of Traditional Chinese Medicine, College of Traditional Chinese Medicine, Southern Medical University, Guangzhou; [2]Department of Traditional Chinese Medicine, Medical College of China Three Gorges University, Yichang; [3]Department of Rheumatology, Nanfang Hospital, Southern Medical University; [4]Department of Pathogen Biology, School of Public Health, Southern Medical University, Guangzhou, China*

Background: Angiogenesis is one of the critical features in rheumatoid arthritis (RA). Uncontrolled neovascularization could help the infiltration of inflammatory cells and lead to synovial hyperplasia and bone destruction further. Precious studies have demonstrated that the medicine taxol (PTX) has anti-angiogenesis effects.
Objectives: To evaluate the inhibitory effects of PTX on angiogenesis in a collagen-induced arthritis (CIA) mouse model.
Methods: A total of 50 mice were used to induce a CIA mouse model with collagen II (CII) and complete Freund's adjuvant (CFA). Twenty-four with obvious arthritis syndrome were randomly divided into four groups: CIA model group, PTX 1.5 mg/kg group, PTX 1.0 mg/kg group, PTX 0.5 mg/kg group. In addition, 6 normal mice was regarded as the control group. PTX was administered by intraperitoneal injection in the PTX treatment groups 8 times every other day. Arthritis index scores, tissue pathology scores after HE staining and synovium microvessel density (MVD) analysis after immunohistochemical (IHC) staining were performed. Immunohistochemistry and ELISA were used to detect the expression of vascular endothelial growth factor (VEGF) and hypoxia-inducible factor-α (HIF-1α). Additionally, the correlation between MVD and pathological scores, level of VEGF and HIF-1α in the synovium were also evaluated.
Results: After PTX treatment, the three intervention group arthritis index scores (1.33±0.52, 2.00±0.63, 3.33±1.03) declined when compared with the CIA group (5.67±1.03, $p<0.001$, $p<0.001$, $p=0.016$). The total histological scores in the three PTX treatment groups (2.50±0.66, 3.89±0.86, 3.89±0.86) were lower than those in the CIA group (7.67±0.79, $p<0.001$, $p<0.001$, $p=0.007$). Similarly, PTX significantly alleviated the scores for synovitis, pannus formation and bone destruction. Compared with the CIA group (110.32±5.06/mm^2), the MVD of the three intervention groups decreased in dose-dependent manner (17.05±1.97/mm^2, 34.73±2.36/mm^2, 57.55±2.72/mm^2; $p<0.001$, respectively). In addition, the expression of VEGF and HIF-1α in synovial tissues and serum also decreased significantly after PTX treatment. Further analysis showed that MVD and pathological scores and levels of VEGF and HIF-1α in the synovium were positively correlated ($r=0.921$, $r=0.944$, $r=0.889$, $r=0.969$, $r=0.933$; $p<0.001$, respectively).
Conclusions: PTX may alleviate CIA by suppressing angiogenesis, providing new insights into the treatment of RA. VEGF and HIF-1α may be the target for PTX suppression of microvessel formation.
References:
[1] Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. The Lancet 2016.
[2] Park KS, Park MJ, Cho ML, et al. Type II collagen oral tolerance; mechanism and role in collagen-induced arthritis and rheumatoid arthritis. Mod Rheumatol 2009;19:581–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2515

AB0100 MTX COMBINED WITH CTX INHIBITED IL-6 INDUCED JAK2-STAT3 ACTIVATION AND THE INDUCTION OF P-GP IN PERIPHERAL BLOOD LYMPHOCYTES OF RHEUMATOID ARTHRITIS PATIENTS

K. Chen[1], Y. Mu[1], K. Qin[1], X. Zhao[1], J. Dong[1], X. Li[1], C. Gao[2], C. Wang[1]. *[1]Rheumatology, the Second Hospital of Shanxi Medical University, Taiyuan, China; [2]Pathology, Joint Program in Transfusion Medicine, Brigham and Women's Hospital/Children's Hospital Boston, Harvard Medical School, Boston, United States*

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by irreversible joint destruction and disability. At present, the biggest challenge in the field of RA treatment is the emergence of multidrug resistance (MDR) in the application of disease-modifying anti-rheumatic drugs (DMARDs).The Multidrug resistance Related Protein and Multi Drug Resistance protein 1, also called P-glycoprotein can decreases the intracellular concentration of different drugs. Moreover, cytokines play an increasingly important role in the expression regulation mechanisms of P-gp, especially inflammatory cytokines IL-6. Previously, We have indicated that Interleukin-6 up-regulates P-gp in peripheral blood lymphocytes via the JAK2-STAT3 pathway in RA patients. Through more than ten-years' clinical research, we observed that the therapeutic cycle alliance of methotrexate (MTX) and cyclophosphamide (CTX) has had better curative effect and lower rate of adverse reaction in treating RA. And we didn't found the emergence of MDR. How can the therapeutic alliance of MTX and CTX overcome MDR in RA patients? This study will give the answer.
Objectives: To Clarify whether the therapeutic alliance of MTX and 4-hydroperoxycyclophosphamide (4-HC) suppress expression and mRNA of P-gp in peripheral blood lymphocytes of RA through JAK2-STAT3 pathway.
Methods: RA patients without any DMARDs and biologic therapy (n=15) were enrolled. P-gp expression level was detected by Flow Cytometry. P-gp mRNA of peripheral blood lymphocytes and the intracellular signaling pathway mediating the effects of MTX and 4-HC on IL-6-stimulated JAK2-STAT3 activation was assessed by RT-PCR.
Results: Compared with blank control group, IL-6 induced P-gp, JAK2 and STAT3 expression levels increased significantly ($P<0.05$). Compared with IL-6 group, P-gp, JAK2 and STAT3 expression levels of 4-HC group and low MTX+4-HC group both decreased ($P<0.05$). the expression levels of P-gp, JAK2 and STAT3 in low MTX group, middle MTX group and high MTX group were lower than IL-6 group, but there were no statistically significant differences ($P>0.05$).
Conclusions: Our data indicated that MTX combined with CTX significantly inhibited IL-6 induced JAK2-STAT3 activation, as well as the induction of P-gp. Inhibition of IL-6-mediated multidrug resistance signaling pathways by the alliance of MTX and CTX may represents a new reversing drug-resistance therapeutic strategy for RA.
References:
[1] Li HX, Zhao W, Shi Y, et al. Retinoic acid amide inhibits JAK/STAT pathway in lung cancer which leads to apoptosis. Tumour Biol. 2015; 36(11): 8671–8678.
[2] Oh HM, Lee SW, Yun BR, et al. Vigna angularis inhibits IL-6-induced cellular signalling and ameliorates collagen-induced arthritis. Rheumatology (Oxford). 2014; 53(1): 56–64.
[3] Li R, Cai L, Ren DY, Xie XF, Hu CM, Li J. Therapeutic effect of 7, 3'-dimethoxy hesperetin on adjuvant arthritis in rats through inhibiting JAK2-STAT3 signal pathway. Int Immunopharmacol. 2012; 14(2): 157–163.
[4] Yun M, Lee D, Park MN, et al. Cinnamaldehyde derivative (CB-PIC) sensitizes chemo-resistant cancer cells to drug-induced apoptosis via suppression of MDR1 and its upstream STAT3 and AKT signalling. Cell Physiol Biochem. 2015; 35(5): 1821–1830.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5019

AB0101 NEW MUTATED PEPTIDYLARGININE DEIMINASE FROM PORPHYROMONAS GINGIVALIS A TARGET IN EARLY RA CITRULLINATES MAJOR RA-AUTOANTIGENS

M. Jenning[1], B. Marklein[1], J. Yetterberg[2], G. Burmester[1], K. Skriner[1]. *[1]Department of Rheumatology and Clinical Immunology, Charité University Medicine, Berlin; [2]Department of Rheumatology and Clinical Immunology, Karolinska Institutet, Stockholm, Germany*

Objectives: Previous reports showed that peptidylarginine deiminase (PPAD) form *Porphyromonas gingivalis (P.g.)* is not able to citrullinate proteins internaly. New mutated PPAD (mPPAD) from *P.g.* involved in periodontal disease (PD) cloned out of *P.g.* strain was characterized and analyzed for its reactivity in sera from patients with systemic autoimmune diseases
Methods: We cloned a new enzymatically active recombinant mutated PPAD from *P.g. mPPAD* mutations and citrullination sites were analyzed by DNA sequencing and/or protein mass spectrometry. Autocitrullination activity it's enzymatic-activity and human autoantigen protein citrullination was investigated by 2D-Elektrophoresis, MS, immunoblot analysis and ELISA. Furthermore we tested anti-mPPAD/cit-mPPAD with human sera (n=93) from early RA before and after onset of RA (n=30), established RA (n=32), SLE (n=16) and healthy blood donors (n=15) in ELISA assays. To study a potential impact on the RA mouse model (CAIA), mPPAD-containing vesicles from *P.g.* were injected by intraperitoneal injection (IP).
Results: Recombinant mPPAD lacks 43 amino acids at the N-terminus and exhibits so far two new amino acid mutations (amino acid position 73 (F>L) and 447 (E>V). We were able to demonstrate, mPPAD is enzymatically active over a huge pH-range (3–10) and autocitrullinates at amino acid position 63 the arginine to citrulline. Moreover mPPAd citrullinates major autoantigens in RA (Fibrinogen, Vimentin and hnRNP-A2/B1) which are detectable by RA patient sera and specific anti-citrulline monoclonal antibodies. mPPAD citrullinates HeLa-protein extracts and these specific citrullinated proteins are recognized by RA patient sera. Anti-citrullinated mPPAD antibodies were detected in 41% (n=32) of patients with RA but not in SLE (n=16) and control sera (n=15). In a RA follow-up study (n=30), we detected nearly similar antibody-sensitivities for citrullinated mPPAD before and after onset of RA (13/20%). Only a minority (7%) of RA patients show higher mPPAD antibody levels after RA diagnosis. In the Collagen antibody-induced arthritis (CAIA) RA mouse model mPPAD containing *P.g.* vesicles when injected IP showed a TLR2-dependent protective anti- inflammatory effect like *P.g.* LPS and Lipomannan.
Conclusions: Pg. infection and RA disease diagnosis occurs on different time-points and Pg. infection induces a TLR2-dependent protective anti-inflammatory effect.We show the first time that mPPAD can citrullinate major human autoantigens internally and their immunologically and diagnostic relevance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3651

AB0102 IMPAIRMENT OF GRANZYME B-PRODUCING REGULATORY B CELLS EXACERBATED RHEUMATOID ARTHRITIS

L. Xu, F. Hu, X. Liu, L. Zhu, L. Ren, H. Liu, H. Zhu, Y. Su. *Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China*

Background: Rheumatoid arthritis (RA) is a common and complex autoimmune disease characterized by chronic inflammation and cartilage/bone damage involving numerous cells, such as T cells, B cells, chondrocytes, fibroblasts [1]. B cells had long been well-demonstrated to participant in the development of RA [2]. Except producing specific antibody and inducing T cell activation, impaired immunosuppressive function of B cells further emphasized their roles in RA recently [3].
Objectives: To investigate whether B cells could produce granzyme B and the potential role in the pathogenesis of Rheumatoid arthritis (RA).
Methods: To reveal the expression of granzyme B in B cells, flow cytometry, PCR and Elispot were performed. The role of IL-21 and anti-BCR stimulation on granzyme B expression was assessed by in vitro stimulation assay. $CD4^+$ T cell-B cell co-culture in the presence of granzyme B neutralizing antibody was performed to demonstrate the function of these cells. Then the levels of granzyme B in B cells between RA patients, OA patients as well as HCs were compared. Next,the correlation analysis between granzyme B-producing B cells and clinical features in RA patients was performed. Finally, the frequencies of granzyme B-producing B cells in RA patients before and after therapy were also evaluated using flow cytometry.
Results: B cells could spontaneously produce granzyme B, which could be perpetuated by IL-21 and anti-BCR stimulation. The frequencies of Th1 and Th17 cells were significantly elevated under the condition of granzyme B blockade when granzyme B was neutralized in $CD4^+$ T cell-B cell co-culture. In RA patients, but not OA patients and HCs, the frequencies of granzyme-B producing Bregs decreased significantly, which was functionally impaired and negatively correlated with disease activity score 28. Moreover, after effective clinical therapy, the frequencies could recover to nomal levels.
Conclusions: B cells could exert the regulatory functions via granzyme B production. Under RA circumstance, these granzyme B-producing Bregs were impaired and contributed to the disease progression.
References:
[1] Smolen JS, Aletaha D, McInnes IB, Rheumatoid arthritis, Lancet. 2016 Oct 22;388(10055):2023–2038. doi: 10.1016/S0140–6736(16)30173–8.
[2] Nakken B, Munthe LA, Konttinen YT, et al,B-cells and their targeting in rheumatoid arthritis–current concepts and future perspectives. Autoimmun Rev. 2011 Nov;11(1):28–34. doi: 10.1016/j.autrev.2011.06.010.
[3] Daien CI, Gailhac S, Mura T, Regulatory B10 cells are decreased in patients with rheumatoid arthritis and are inversely correlated with disease activity. Arthritis Rheumatol. 2014 Aug;66(8):2037–46. doi: 10.1002/art.38666.
Acknowledgements: This study was supported by grants from the Natural Science Foundation of China (81671609, 81671604,31470039).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2269

AB0103 ANTI-INFLAMMATORY AND IMMUNOMODULATORY EFFECTS BY HUMAN UMBILICAL CORD MESENCHYMAL STEM CELL DERIVED MICROVESICLES IN RATS WITH COLLAGEN INDUCED

M. Tian, K. Xu, L. Zhang, J. Gao. *Rheumatology, Shanxi DaYi Hospital, Shanxi Academy of Medical Sciences, Taiyuan, China*

Background: Immunologic deranging and persistent inflammation is closely associated with the arising and developing of rheumatoid arthritis (RA). Increasing investigators demonstrated microvesicles (MVs) derived from mesenchymal stem cell (MSC-MVs) might simulate immune regulation and tissue repair of the parental cells. However,the immunotherapeutic potential of MVs in RA remains unknown.
Objectives: We investigated the therapeutic effects of MSC-MVs in RA model collagen induced arthritis (CIA) rats.
Methods: We tested the therapeutic effects of MSC-MVs on CIA rats,levels of T helper 17(Th17), regulatory T cell,and cytokines related,as well as specific transcriptional regulation factor Foxp3 and ROR-γT analysis was performed.
Results: Here, we show that MSC-MVs administration effectively improve arthritic symptoms, inhibit synovial hyperplasia,thus delaying the progression to inflammatory bone destruction, as effective as their original cells, exerting arthralprotective effects. MSC-MVs treating inhibited the proliferation of T cell,accelerated the apoptosis. MSC-MVs treating reduce proinflammatory cell Th17,cytokines IL-17, while a incline in the level of an-inflammatory cell Treg,ncytokines TGF-β. In the spllen and ankle joint of CIA rats, MSC-MVs treating increased the expression level of Foxp3 and coinciding with the ROR-γT suppressed, which, the enhanced therapeutic effects correlated with the increase of dosage in a certain range.
Conclusions: MSC-MVs showing anti-inflammatory and immunomodulatory activities on CIA rats, suggesting a new and feasible strategy for protection against RA.
References:
[1] E.M. Gravallese, S.R. Goldring, Cellular mechanisms and the role of cytokines in bone erosions in rheumatoid arthritis, Arthritis Rheum. 43 (10) (2000) 2143–2151.
[2] S. Culshaw, I.B. McInnes, F.Y. Liew, What can the periodontal community learn from the pathophysiology of rheumatoid arthritis? J. Clin. Periodontol. 38(Suppl. 11) (2011) 106–113.
[3] Schett, G., D. Elewaut, I.B. McInnes, J.M. Dayer, and M.F. Neurath, How cytokine networks fuel inflammation: Toward a cytokine-based disease taxonomy. Nat Med, 2013. 19(7): p. 822–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3462

AB0104 ALTERATIONS OF SPLICEOSOME COMPONENTS IN LEUKOCYTES FROM PATIENTS WITH RHEUMATOID ARTHRITIS INFLUENCE THEIR AUTOIMMUNE AND INFLAMMATORY PROFILE, AND THE DEVELOPMENT OF CARDIOVASCULAR DISEASE

P. Ruiz-Limon[1], C. Perez-Sanchez[1], R. Ortega-Castro[1], S. Pedraza-Arevalo[2], M. del Rio-Moreno[2], Y. Jimenez-Gomez[1], I. Arias de la Rosa[1], M. Ábalos-Aguilera[1], M. Aguirre[1], P. Segui[1], E. Collantes[1], A. Escudero[1], J. Castaño[2], R.M. Luque[2], N. Barbarroja[1], C. Lopez-Pedrera[1]. *[1]Rheumatology Service; [2]Department of Cell Biology, Physiology, and Immunology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain*

Background: A significant percentage of genetic and inflammatory diseases derive from splicing alterations. Therefore, the understanding of what modifications in spliceosome determine an alternative splicing and its association with the development of such pathologies is of critical importance.
Objectives: To identify the alterations present in the spliceosome machinery of patients with rheumatoid arthritis (RA),its influence on the development and activity of the disease and their atherothrombotic profile.
Methods: An array of selected components of the major- (n=12) and minor-spliceosome (n=4) and associated splicing factors (n=28) was developed, and their expression levels were evaluated using a Fluidigm methodology, in purified leukocytes from 14 RA patients and 14 healthy donors (HD). In parallel, an extensive clinical/serological evaluation was performed. Carotid intimate media thickness (CIMT) was used as atherosclerosis marker. Endothelial activity was monitored by laser-doppler flowmetry, and pro-inflammatory and oxidative stress markers were quantified. Association of these splicing components with clinical and analytical features were investigated.
Results: A significant alteration in various components of spliceosome and splicing factors was found in all the leukocytes subtypes from RA patients vs HD. Interestingly, we found a specific altered profile of splicing factors and spliceosome components when compared monocytes (CA150, PRP8, SRM160, U2AF1, RNU4atac, PTBB1, RAVER1, RBM17, SRSF4, SRSF10), lymphocytes (RNU12, RNU4, RNU6, PRP8, MAGOH, NOVA1, SRSF3) and neutrophils (RNU11, RNU6, SC35, RBM3).
Altered levels of various spliceosome elements in monocytes were associated with the presence of *atheromatous* plaques, while in neutrophils were found related to radiological involvement. In lymphocytes, the alteration of these components were linked to the positivity for Rheumatoid Factor and anti-CCPs antibodies, indicating that modifications in the spliceosome machinery could contribute to the increase in the production and assembly of autoantigens, inducing autoantibody production.
Correlation studies showed a significant relationship between altered levels of various spliceosome components in different leukocyte subtypes and high disease activity (DAS, HAQ), increased expression of proinflammatory mediators (CRF, TF, TNF, IL-8, TLR4) and oxidative stress markers (peroxides, GPX, SOD)as well as with parameters associated with insulin resistance.
Conclusions: These results reveal that there is a significant alteration of spliceosome components in RA patients that could be associated with the development and activity of this autoimmune condition, and influence mechanisms that drive the development of cardiovascular disease. Studies in progress will help to clarify the physiological implications of these findings, which could constitute new diagnostic biomarkers, as well as new therapeutic tools for the treatment of RA.
Acknowledgements: Funded by CTS7940, and ISCIII (PI15/01333, CP15/00158, and RIER RD16/0012/0015).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4907

AB0105 DOXYCYCLINE AND DEXAMETHASONE-INDUCED REPROGRAMMING OF PERIPHERAL BLOOD MONONUCLEAR CELLS IN A MODEL OF ARTHRITIS WITH THE SYSTEMIC MANIFESTATIONS IN WISTAR RATS

P. Litvitskiy[1], V. Sakharov[1], E. Alexeeva[2], N. Mayansky[2], R. Zakirov[2]. *[1]Pathophysiology, Sechenov First Moscow State Medical University; [2]Scientific Center of Children's Health, Moscow, Russian Federation*

Background: The systemic juvenile idiopathic arthritis (sJIA) is a problem with high social significance all over the world. Targeted cell reprogramming becomes one of the most important lines for modern medicine and can be regarded as

an origin for new highly improved treatment strategy of sJIA. As rat monocytes exhibited CD163 expression in a similar level with that shown for peritoneal macrophages [1], we decided to use CD163 as a key factor indicating cell reprogramming in the study.

Objectives: To investigate the dynamical changes in subpopulations of peripheral blood mononuclear cells (PBMC) and to assess doxycycline and dexamethasone effects in a model of arthritis with the systemic manifestations.

Methods: Animal model [2] was adapted in 24 Wistar rats (males, 6 month old). On the day of the last stimulation all the rats were divided into 3 equal groups and additional subcutaneous (s.c.) injections were performed as follows: DOXY-group – doxycycline (50 mg/kg, Saratov, Russia), DEXA-group – dexamethasone (4 mg/kg, KRKA, Slovenia), control group – 0,9% sodium chloride solution (Belarus). The s.c. injections were repeated on Day 54. Time points were 0, 21, 41, and 55 Days. PBMC were assessed by flow cytometry (BD FACSCanto II, USA) according to manufacturer's instructions. Staining was performed with FITC Anti-Rat CD11b (BD Pharmingen), anti-rat CD68 RPE (Serotec, UK), anti-rat CD163 ALEXA FLUOR 647 (Serotec, UK). CD11b+CD68+ and CD11b-CD68+ cells were regarded as monocytes and circulating dendritic cells consequently. At the termination animal organ masses were measured.

Results: Up to Day 55 proportions of CD163+ in CD11b+CD68+ population changed synchronically in all groups. On Day 55 the proportions (in comparison with the data of Day 41) were significantly higher in DEXA-group ($p<0,05$) but didn't change in DOXY- and control groups ($p>0,05$). Cell reprogramming was also observed in population of CD11b-CD68+. So, on Day 41 the proportions of CD163+ cells in CD11b-CD68+ population were significantly increased (in comparison with the data of Days 0 and 21) in DOXY- and DEXA-groups ($p<0,05$) but not in control group ($p>0,05$). Mentioned changes were subsequent with other parameters of inflammation. We observed significantly lower heart masses in DOXY- and DEXA-groups (median=0,63 and 0,635g consequently) in comparison with control group (median=0,74g) ($p<0,05$), but no difference between DOXY- and DEXA- groups ($p>0,05$).

Conclusions: In a model of arthritis with the systemic manifestations in Wistar rats we demonstrated that subpopulations of PBMC (CD11b-CD68+ and CD11b+CD68+) underwent reprogramming. Doxycycline and dexamethasone modyfied the dynamics of the reprogramming. In DOXY- and DEXA-groups there were lower heart masses than in the control group, the last fact is subsequent with the data by De P. et al. [3]. We can speculate that monocytes and dendritic cells undergo reprogramming (CD163neg and CD163+) in a similar way with M1 and M2 macrophages.

References:

[1] Moghaddami M, Cleland LG, Mayrhofer G. Int Immunol. 2005; 17(8):1103–15.
[2] Litvitskiy P, Sakharov V, Alexeeva E, et al. Annals of the Rheumatic Diseases. 2016;75:264.
[3] De P, Roy SG, Kar D et al. J Endocrinol. 2011;209(1):105–14.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3996

AB0106 EFFECT OF SERUM CYTOKINES ON COLLAGEN INDUCED ARTHRITIS RATS AFTER INTRA-ARTICULAR INIECTION OF OZONE

R. Guo, G. Zhang, L. Zhang, N. Liu. *Department of Rheumatology, Shanxi Dayi Hospital, Taiyuan, taiyuan, China*

Background: Ozone is a new treatment method, study confirmed that the ozone intra-articular injection can reduce the level of TNFR II CIA in rat synovial TNF-a, synovial tissue, the regulation of rat apoptosis inhibiting gene Bcl-2 decreased expression of proapoptotic gene Bax expression increased, thereby promoting apoptosis of synovial cells. However, there are few reports on the effects of ozone on the inflammatory cytokines such as serum TNF-a in the pathogenesis of RA.

Objectives: To observe the effects of intra-articular ozone iniection on the contents of tumor necrosis factor-α(TNF-α),Interleukin-6 (IL-6), IL-17A,and vascular endothelial growth factor (VEGF)in the serum of rats with collagen-induced arthritis (CIA) and explore the therapeutic mechanism of ozone in RA treatment.

Methods: Thrity-two Wistar rats were randomized into 4 groups,including ozone groups receiving intra-articularinjection of 40 μg/ml ozone (O_3 group), Ca blank control group (normal group), a methotrexate group (MTX group) and a collagen-induced arthritismodel (CIA group). All the rats, except for those in the blank control group, were subjected to hypodermic iniection of bovine collagen II and complete Freund'S adiuvant to induce CIA. DOzone treatment was administered once weekly for 3 weeks starting at 14 days after the modeling.MTX group of 0.9 mg/kg, once a week, a total of three weeks.The swelling degree of the foot were observed,the serum contents of TNF-α,IL-6,IL-17A and VEGF were detected. One-way analysis of variance or Kruskal-Wallis test was used to evaluate the experimental data.

Results: At the end of treatment,the foot swelling degree was reduced significantly in rats with O_3 group compared with that in the CIA group [4.21±0.14 ml and 9.12±0.17 ml, t=8.43, P=0.023]. The serum contents of TNF-a, IL-6 and VEGF showed significant difference between the CIA group and O_3 group [93.86±12.49 pg/ml and 14.33±1.85 pg/ml, c^2=6.216, P=0.002; 189.12±164.62 pg/ml and 5.84 (5.47,15.93) pg/ml, c^2=13.136, P=0.00451.56 (46.09,74.10) pg/ml and 37.77±7.88 pg/ml, c^2=3.732, CP=0.002, there was no statistically significant difference between the O_3 group and MTX group [14.33±1.85 pg/ml and 12.45 (11.8,15.6)) pg/ml, c^2=0.243, P>0.05; 5.84 (5.47,15.93 pg/ml, vs 9.59±5.13 pg/ml, c^2=0.058, P>0.05; 37.77±7.88 pg/ml and 41.99±8.78 pg/ml, c^2=0.516, P>0.05]. The serum contents of IL-17A showed no significant difference between the normal group,CIA group,MTX group and the O_3 group (F=1.827, P=0.165).

Comparison of serum levels of inflammatory cytokines in each group rats

	TNF-α (MFI)	IL-6(pg/ml)	IL-17A(pg/ml)	VEGF(pg/ml)
control group	11.21±1.44	10.23±3.18	0.49±0.34	27.65±9.84
CIA group	93.86±12.49[a]	189.12±164.62[a]	0.77±0.18	51.56(46.09,74.10)[a]
MTX group	12.45(11.8,15.6)[b]	9.59±5.13[b]	0.49±0.32	41.99±8.78[a]
O_3 group	14.33±1.85[b]	5.84(5.47,15.93)[b]	0.64±0.27	37.77±7.88[b]
χ^2/F	23.148	17.116	1.827	12.574
P	0.000	0.001	0.165	0.006

Note: [a] indicated that P<0.05 was compared with the control group; [b]indicated that P<0.05 was compared with CIA group;

Conclusions: Intra-articular iniecfion of 40 ug/ml ozone Can attenuate svnovitis in rats with CIA, the mechanism of which may involve the inhibition of TNF-a, IL-6 and VEGF in the serum.

References:

[1] Huiqiang Chen,Bin Yu.Efficacy and Mechanism of Using Different Concentrations Ozone to Treat Rheumatoid Arthritis Rats[D]. Southern Medical University, 2011.
[2] Vaillant JD, Fraga A, Díaz MT, et al.Ozone oxidative postconditioning ameliorates joint damage and decreases pro-inflammatory cytokinelevels and oxidative stress in PG/PS-induced arthritis in rats[J]. EurJ Pharmacol 2013;14(1–3):318–324. doi:10.1016/j.ejphar.2013.07.034.
[3] Bocci V, Borrelli E, Travag li V, et al. The ozone paradox: ozone is a strong oxidant as well as a medical drug[J]. Med Res Rev, 2009;29(4):646–682. doi:10.1002/med.20150.

Acknowledgements: Thanks to my tutor, my parterner, and the group medical staff.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3447

AB0107 THE MODULATION OF MACROPHAGE POLARIZATION BY SIRT1 MAYBE NEW TARGET THERAPY IN RHEUMATOID ARTHRITIS

S.Y. Lee[1], S.W. Lee[1], W.T. Chung[1], S.Y. Park[2], J.H. Bae[3]. *[1]Rheumatology of Internal Medicine, Dong-A University Hospital; [2]Rheumatology of Internal Medicine; [3]Biochemistry, Pusan national university, Pusan, Korea, Republic Of*

Background: The polarization of macrophages was the expressed to M1/M2 phenotype by various stimuli or environment signals. The M1 macrophage was pro-inflammatory phenotype and was key effector cells in the immune response of rheumatoid arthritis (RA). So, M1 macrophage influenced the inflammation of RA synovial membrane and joint destruction in RA, whereas M2 macrophage was anti-inflammatory phenotype and could down-regulate the production of proinflammatory cytokines in RA. The SIRT1 attenuated the RA inflammation via down-regulation of NF-κB signaling. However, the effect of SIRT1 on macrophages polarization remained uncler.

Objectives: We aimed to check out that activated SIRT1 modulated macrophages polarization into M1 phenotype and controlled the inflammation of RA.

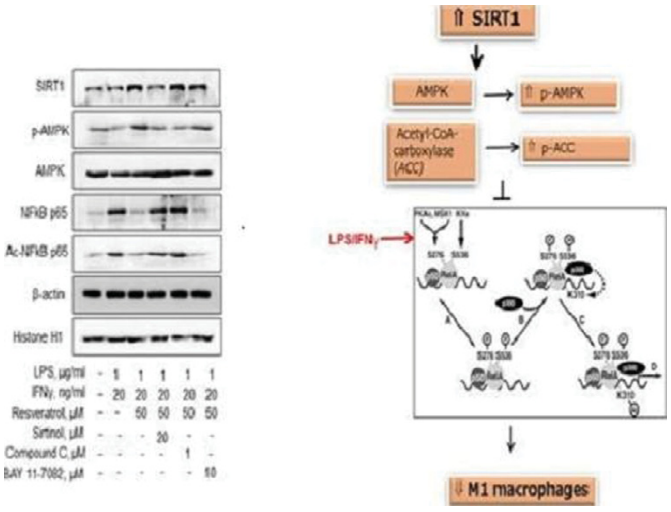
Methods: Monocytes from synovial fluid of RA patients, bone marrow–derived monocytes (BMDCs) from mice were studied. monocytes were cultured with M-CSF for 7days to differentiate into M0 macrophages (monocyte-derived mature macrophages M0 phenotype). M0 macrophages were incubated with LPS and IFN-gamma in order to obtain M1 macrophages. M1 macrophage markers were detected by real-time PCR.

Results: Activation of SIRT1 was achieved by Resveratrol, activated SIRT1 attenuated M1 macrophage phenotypes and pro-inflammatory cytokine expression. macrophages obtained from SIRT1-tg mice, which were overexpression of SIRT1, exhibited decreased M1 markers in association with enhanced activation of AMPK/ACC compared with macrophage from control C57BL/6 mice. In addition to SIRT1 activation, M1 polarizing signal, acetylation of NF-κB p65, was suppressed. In SIRT1-deficient macrophages, resveratrol fail to increase AMPK activity and to decrease the expression M1 markers owing to enhanced acetylation of NF-κB p65.

Conclusions: SIRT1 maybe an important modulator of M1 macrophages polarization and increased AMPK activity, which suppressed acetylation of NF-κB p65 during inflammation of RA. so, modulation of SIRT1 maybe a new target in RA treatment.

References:

[1] SIRT1 inhibits differentiation of monocytes to macrophages: amelioration of synovial inflammation in rheumatoid arthritis. J Mol Med (Berl). 2016 Aug;94(8):921–31.



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2646

AB0108 DECREASED EXPRESSION OF PTPN22 GENE IN PATIENTS WITH RHEUMATOID ARTHRITIS CARRYING THE RISK ALLELE OF PTPN22 RS2488457 POLYMORPHISM

S. Remuzgo-Martínez[1], S. Castañeda[2], A. Corrales[1], F. Genre[1], R. López-Mejías[1], P. Moreno-Fresneda[2], B. Ubilla[1], V. Mijares[1], V. Portilla[1], J. González-Vela[1], T. Pina[1], G. Ocejo-Vinyals[3], J. Irure-Ventura[3], R. Blanco[1], J. Martín[4], J. Llorca[5], M.A. González-Gay[1,6]. *[1]Epidemiology, Genetics and Atherosclerosis Research Group on Systemic Inflammatory Diseases, Rheumatology Department, IDIVAL, Santander; [2]Rheumatology Department, Hospital Universitario la Princesa, IIS-IP, Madrid; [3]Immunology Department, Hospital Universitario Marqués de Valdecilla, Santander; [4]Instituto de Parasitología y Biomedicina "López-Neyra", CSIC, PTS Granada, Granada; [5]Department of Epidemiology and Computational Biology, School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), IDIVAL; [6]School of Medicine, University of Cantabria, Santander, Spain*

Background: Mutations in the protein tyrosine phosphatase non-receptor 22 (*PTPN22*) gene are associated with numerous connective tissue and autoimmune diseases [1]. In particular, *PTPN22* has been recognized as the main non-HLA genetic risk factor involved in rheumatoid arthritis (RA) susceptibility [2]. Moreover, it has been suggested that *PTPN22* modulation may influence on inflammatory processes associated with RA [3,4].
Objectives: To determine if *PTPN22* (rs2476601, rs33996649 and rs2488457) polymorphisms, associated with RA, may influence on *PTPN22* expression in RA patients compared to healthy controls. Moreover, the association between *PTPN22* expression in patients with RA and their clinical characteristics was studied.
Methods: *PTPN22* messenger RNA (mRNA) expression was quantified by quantitative real-time PCR in peripheral blood samples from 42 RA patients and 24 healthy controls. *PTPN22* rs2476601 (G>A), *PTPN22* rs3399649 (C>T), and *PTPN22* rs2488457 (C>G) single-nucleotide polymorphisms (SNP) were genotyped by TaqMan SNP genotyping assays. Differences in *PTPN22* expression between patients and controls were analyzed by Student's t test, according to their genotype. Correlation coefficients were also assessed between *PTPN22* expression in RA patients and their clinical characteristics.
Results: A significant down-regulation of *PTPN22* expression in patients with RA carrying *PTPN22* rs2488457 risk allele (G) compared to controls was observed (relative mean values of *PTPN22* mRNA levels ± standard deviation: 2.93±0.76 vs 4.33±0.63, p=0.0004). Furthermore, an inverse relationship between *PTPN22* expression and disease duration (r=-0.38, p=0.03) was found. These results were adjusted by sex, age at time of study and cardiovascular risk factors.
Conclusions: Our study shows for the first time that the risk allele of *PTPN22* rs2488457 polymorphism influences on the down-regulation of *PTPN22* in patients with RA. This result suggests a transcriptional suppression of *PTPN22* gene in RA, which in turn may play an important role in disease diagnosis and progression.
References:
[1] Stanford and Bottini. Nat Rev Rheumatol 2014, 10(10):602–11.
[2] Messemaker et al. J Autoimmun 2015, 64:74–81.
[3] Ronninger et al. Genome Med 2012;4(1):2.
[4] Díaz-Gallo and Martín. Genome Med 2012;4(2):13.
Acknowledgements: This study was supported by European Union FEDER funds and "Fondo de Investigación Sanitaria" (PI12/00060 and PI15/00525) from "Instituto de Salud Carlos III" (ISCIII, Health Ministry, Spain). It was also partially supported by RETICS Programs RD12/0009 and RD16/0012 (RIER) from ISCIII. SR-M is supported by fund from the RETICS Program (RIER) (RD16/0012/0009). FG is a recipient of a Sara Borrell postdoctoral fellowship from ISCII (CD15/00095). RL-M is supported by a "Miguel Servet tipo-I" contract from ISCIII (CP16/00033). BU is supported by funds from the RETICS Program (RIER) (RD12/0009/0013) from ISCIII (Health Ministry, Spain).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5839

AB0109 AUTOPHAGY INHIBITOR REGULATES APOPTOSIS AND PROLIFERATION OF SYNOVIAL FIBROBLASTS THROUGH THE INHIBITION OF PI3K/AKT PATHWAY IN COLLAGEN-INDUCED ARTHRITIS RAT MODEL

S. Li, F. Li, W.J. Chen, C. Deng. *Department of Rheumatology and Immunology, the Second Xiang Ya Hospital, Central South University, Changsha, Hunan, China, Changsha, China*

Background: Mounting studies have illustrated an important role of autophagy in various diseases, but few studies have reported its contribution to rheumatoid arthritis (RA) and the underlying mechanism is largely unknown.
Objectives: This study aimed to investigate whether autophagy inhibitors could regulate apoptosis and proliferation through PI3K/AKT pathway in RA.
Methods: RA animal model was established by collagen induction. General observations and degree of joint swelling were observed. Inflammatory response, cell survival related factors and apoptosis were also detected in synovial fibroblasts. In addition, cultured rheumatoid arthritis fibroblast-like synoviocytes (RA-FLS) were subjected to TNF-α treatment *in vitro*, and TNF-α induced cell autophagy, synovial cell proliferation and apoptosis were detected. Moreover, cell cycle and cytokine secretion protein, along with the above parameters, were analyzed.
Results: Results from the animal model showed that autophagy inhibitors could attenuate inflammatory reaction and synovial hyperplasia, while promoted synovial fibroblasts apoptosis. Meanwhile, inhibition of autophagy promoted cell apoptosis and reversed cell proliferation *in vitro*, also blocked cell in the G2/M arrest and reduced the S phase cells. Furthermore, inhibition of PI3K/AKT pathway reversed TNF-α mediated autophagy and cytokine secretion.
Conclusions: autophagy inhibitors could mitigate inflammation response, inhibiting RA-FLS cell proliferation while promoting cell apoptosis by PI3K/AKT pathway.
References:
[1] Neumann, E., et al., Rheumatoid arthritis progression mediated by activated synovial fibroblasts. Trends in Molecular Medicine, 2010. 16(10): p. 458–68.
[2] Feng, Y., et al., The Role of Autophagy in Rheumatic Disease. Current Drug Targets, 2016.
[3] Kenific, et al., Cellular and metabolic functions for autophagy in cancer cells. Trends in Cell Biology, 2015. 25(1): p. 37–45.
[4] Yan, H., et al., Suppression of experimental arthritis through AMP-activated protein kinase activation and autophagy modulation. Journal of Rheumatic Diseases & Treatment, 2011. 1(1).
[5] Qu, Y., et al., MicroRNA-126 affects rheumatoid arthritis synovial fibroblast proliferation and apoptosis by targeting PIK3R2 and regulating PI3K-AKT signal pathway. 2016.
[6] García, S., et al., Akt activity protects rheumatoid synovial fibroblasts from Fas-induced apoptosis by inhibition of Bid cleavage. Arthritis Research & Therapy, 2010. 12(1): p.: R33.
Acknowledgements: This work was supported by grants from the National Natural Science Foundation of China Youth Foud (81302567) and Basic scientific research service fee of Central South University (2012QNZT138) to Dr. Shu Li.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2044

AB0110 EVALUATION OF THE EFFECT OF CHUANTENGTONGBI DECOCTION ON DBA / 1 MICE CIA MODEL

X.-Q. Wang, X.-D. Shen, X.-Y. Zhang, X. Du. *Department of Traditional Chinese Medicine, School of Basic Medical Sciences, Beijing University of Chinese Medicine, Beijing, China*

Background: DBA/1 mouse ($H2^q$ type) CIA model as a mature model of rheumatoid arthritis is widely used in pharmacology and pharmacodynamics research[1]. Chinese medicine treatment of rheumatoid arthritis has accumulated rich experience. The study of Tripterygium glycosides is quite representative, and it has been widely used in the past 30 years. Some Clinical studies showed that tripterygium glycosides treatment of rheumatoid arthritis had good effect[2]. ChuanTengTongBi decoction is also the effective prescription commonly used for the treatment of rheumatoid arthritis.
Objectives: To investigate the pathological damage degree of DBA/1 mouse CIA model and the effects of different doses of ChuanTengTongBi decoction on the CIA model mice.
Methods: The mice were divided into normal group, model group, leflunomide group (3.11mg/kg/d), low-dose of ChuanTengTongBi group (0.44g/ml/d), medium-dose group (0.88g/ml/d) and high-dose group (1.76g/ml/d).
Results: The arthritis index (AI) was evaluated every week to determine whether the model was successful. We defined AI score ≥4 as successful model (AI score

standard:0, No swelling;1, Slight redness and swelling;2, Moderate redness and swelling of ankle; 3, Severe redness and swelling of the entire paw;4, Maximally inflamed limb with involvement of multiple joints [3]). Day 28–42, hind foot redness and swelling of the mouse continued to develop and extended to the forefoot. Compared with the normal group, incidence of CIA model group reached 100%. Day 49, compared with the model group by joint scores, medium-dose group, high-dose group and leflunomide group have Significant differences on CIA model ($p<0.01$). Compared with the Leflunomide group, low-dose group, medium-dose group and high-dose group have no obvious difference ($p>0.05$). Compared with the low-dose group, medium-dose group and high-dose group have no difference ($p>0.05$).

Table 1. Joint scores (mean ± SD)

groups	28d	35d	42d	49d
a	o	o	o	o
b	8.05±1.62	12.40±2.10	14.68±1.77	12.33±1.68
c	8.66±0.14	11.99±0.23	12.10±0.23**	11.30±0.22**
d	7.90±0.34	11.40±0.18	12.80±0.20**	12.00±0.13
e	7.40±0.23	10.90±0.13*	10.40±0.44**	10.60±0.36**
f	8.80±0.24	10.60±0.30*	11.30±0.22**	8.80±0.55**

a. Blank group. b. Model group. c. Leflunomide group. d. Low-dose group. e. Medium-dose group. f. High-dose group. Compared with the model group, *$p<0.05$, **$p<0.01$.

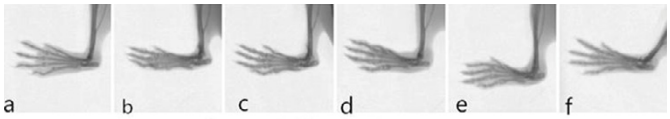


figure 1. Ankle Joint X-ray

a.blank group b.model group c.leflunomide group d.low-dose group e.medium-dose group f.high-dose group

Conclusions: CIA model has a high morbidity, long duration, macroscopic pathological manifestation and irreversible ankle joint deformation, which is consistent with the progress of human RA disease and pathological damage. Medium-dose of ChuanTengTongBi decoction, high-dose and leflunomide group had inhibitory effect on the progress of arthritis, and the effect of high-dose was better than that of leflunomide group.

References:

[1] Brand, D.D. Rodent models of rheumatoid arthritis. Comp. Med. 55, 114–122(2005).

[2] Shen S, Yang Z, Yiyang H U, et al. The Effect of Tripterygium Wilfordii glycoside on the Expression of CD_4+CD_(25)~(high) Regulatory T cells,Th1 and Th2 with IgA Nephropathy[J]. Chinese Journal of Integrated Traditional & Western Nephrology, 2013.

[3] David D Brand, Kary A Latham, & Edward F Rosloniec. Collagen-induced arthritis. Nature Protocol.5.1270–1274(2007).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3396

AB0111 CADMIUM NANOPARTICLES CITRULLINATE INTRACELLULAR CYTOKERATINS: CADMIUM POTENTIALLY LINKS RHEUMATOID ARTHRITIS TO SMOKING AND NUMEROUS WORKING CLASS OCCUPATIONS

D. Hutchinson[1], J. Müller[2], J.E. McCarthy[3], Y. Gun'ko[3], N. Verma[4], X. Bi[5], L. Di Cristo[3], L. Kickham[3], D. Movia[3], A. Prina-Mello[3], Y. Volkov[3]. *[1]Royal Cornwall Hospital Trust, University of Exeter Medical School, Truro, United Kingdom; [2]University of Basel, Switzerland, Basel., Switzerland; [3]Trinity College, Dublin, Ireland; [4]Nanyang Technological University; [5]Bioprocessing Technology Institute, Singapore, Singapore*

Background: Smoking has emerged as a consistent risk factor for ACPA positive RA, although the specific constituents of cigarette smoke that induce citrullination are unknown. It has been hypothesised that cadmium triggers RA as its inhalation links various well established risk factors for RA such as smoking (the most important environmental source of cadmium) and numerous working class occupations [1].

Objectives: To determine whether the cadmium-derived materials induce intracellular citrullination.

Methods: Human A549 lung epithelial cells were exposed to cadmium in ionic and particulate form represented by cadmium chloride and cadmium oxide, respectively, and their combinations with ultrafine carbon black (ufCB) nanoparticles produced following high temperature combustion, imitating cigarette burning. Protein citrullination in cell lysates was analysed by SDS-PAGE electrophoresis with western blotting and verified by immunofluorescence staining and confocal microscopy. Target citrullinated proteins were identified by proteomic analysis.

Results: Cytotoxicity studies demonstrated that cadmium compounds were toxic to the cells. Based on the results of cytotoxicity measurements, all the materials utilised in the experiments were subsequently applied to the cells in sub-toxic concentrations. Cadmium oxide, ufCB and its combination with cadmium chloride and cadmium oxide after high temperature combustion induced citrullination of multiple proteins in cultured human lung epithelial cells of A549 cell line, as demonstrated by SDS-SDS-PAGE electrophoresis and western blotting. This phenomenon develops via a peptidylargininedeiminase-dependent mechanism, as demonstrated in our previous studies [2]. The majority of citrullinated proteins were represented by the bands corresponding to the molecular weights between 55 and 72 kDa, and several less abundant bands at the level of ~25kDa and over 130 kDa. Acidic cytokeratins of type I (9, 10) and basic/neutral cytokeratins type II (1, 2, 5, 6A, 6B and 77) were identified as major intracellular citrullination targets. Immunofluorescent staining demonstrated that the citrullinated proteins were localised both in the cytoplasm and nuclei of cells exposed to cadmium particles, similar to the distribution patterns observed in cells exposed to ufCB.

Conclusions: Cadmium nanoparticle exposure facilitates post-translational citrullination of proteins.

References:

[1] Hutchinson D. Cadmium, one of the villains behind the curtain:has exposure to cadmium helped to pull the strings of seropositive rheumatoid arthritis pathogenesis all along? International journal of rheumatic diseases 2015;18:570–3.

[2] Mohamed BM, Verma NK, Davies AM, McGowan A, Crosbie-staunton K, Prina-Mello A, et al. Citrullination of proteins:a common post-translational modification pathway induced by different nanoparticles in vitro and in vivo. Nanomedicine 2012;7:1181–95.

Acknowledgements: This work has been supported by the Higher Education Authority of Ireland, Science Foundation of Ireland through the Advanced Materials and BioEngineering Research (AMBER) project (Grant #SFI/12/RC/2278) and the Cornwall Arthritis Trust.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3620

Spondyloarthritis - etiology, pathogenesis and animal models

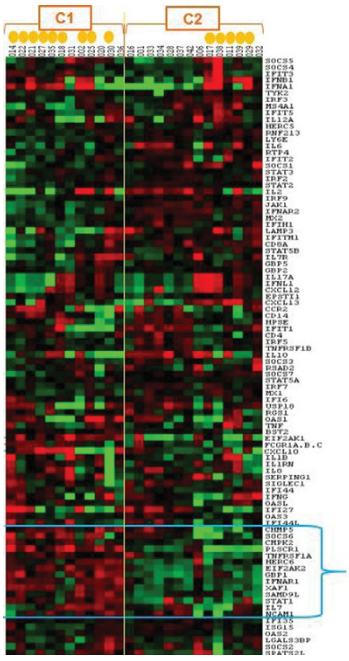
AB0112 INTERFERON-REGULATED GENES (IRG) SIGNATURES DIFFERENTIATE GROUPS OF AS PATIENTS AND ARE ASSOCIATED WITH ANTI-TNF RESPONSE: PILOT DATA

S.R. Harrison, A.N. Burska, P. Emery, H. Marzo-Ortega, F. Ponchel. *Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom*

Background: Ankylosing Spondylitis (AS) is a chronic inflammatory arthritis characterised by sacroiliac/ lumbar spinal inflammation and extra-articular manifestations. Currently, TNF inhibitors (TNFi) are licensed for treatment-refractory AS; however, many patients do not respond to treatment and there is no way to predict Response/Non-Response (R/NR). The expression of several Interferon (IFN) signalling related genes (IRG) are associated with inflammatory diseases, including AS. Furthermore, an IRG expression signature has been used to predict treatment response in phase-Ia trials in systemic lupus erythematosus (1), demonstrating the feasibility of the use of IRG signatures as biomarkers in routine clinical practice.

Objectives: To explore whether IRG signatures differentiate groups of AS patients, and can be associated with response to TNFi in AS.

Methods: Twenty-six week-0 peripheral blood mononuclear cell (PBMC) samples



Unsupervised Hierarchical Clustering of IRG in AS patients

Red represents higher levels of gene expression and green represents lower levels of gene expression of the corresponding gene following normalisation to the housekeeping gene, GAPDH. Clustering defined two groups (C1 and C2), driven by expression of the 14 IRG (blue box). Patient study numbers are listed at the top of the cluster. An orange dot adjacent to a particular patient indicates that they were an ASDAS NR.

from AS patients participating in a previously reported in-house clinical trial [infliximab (IFX), n=15 vs. placebo (P), n=11] (2) were selected from our tissue bank. R/NR was defined as a ≥1.1 point reduction in AS Disease Activity Score (ASDAS) at week-30, or a reduction in the number of sacroiliac/vertebral MRI lesions. Expression of 96 IRG was quantified from PBMCs using custom TaqMan assays and analysed using unsupervised hierarchical clustering, Chi-Squared, and Mann-Whitney U tests.

Results: A total of 11 patients were clinical responders [IFX=7/15; P=4/11]. At week-0, patients clustered into 2 groups (C1/C2) based on expression of 14 IRG. Clinical/demographic characteristics were not significantly different between C1/C2 and groups were not biased for treatment (C1, IFX=8, P=4; C2, IFX=7, P=7, p=0.735). Improvement in ASDAS was weakly associated with C2 (C2, R=8/14, C1, R=7/12, p=0.098). Looking at IFX treated patients only (n=15), 2 cluster groups were observed (T1/T2) driven by 12 IRG. T2 was associated with a reduction in MRI lesions (T2 R=6/7, T1 R=3/8, p=0.057). Finally, paired week-0 and week-22 samples from 10 IFX-treated patients were analysed and clustered in 2 groups (H1/H2). Changes in IRG signature following treatment were observed towards segregating pre- and post- IFX treatment samples (H1, 6/8 week-0; H2, 8/12 week-22 p=?).

Conclusions: This pilot study suggests a possible association between IRG and response to IFX treatment in AS. These results now require assessment in a larger cohort in order to determine statistical and possible clinical significance, and to refine the signature further to construct potential predictive algorithms.

References:

[1] Yao Y, et al. Arthritis Rheum 2009.
[2] Marzo-Ortega H, et al. Ann Rheum Dis 2005.

Acknowledgements: The authors would like to thank the George Drecler Foundation and BTCure EU/IMI for funding this project.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4471

AB0113 THE RELATIONSHIP OF POLYMORPHISMS OF ANTXR2 GENE WITH ANKYLOSING SPONDYLITIS IN CHINESE HAN

Q. Lv, X. Wu, J. Gu. *Third Affiliated Hospital of Sun Yat-Sen Universit, Guangzhou, China*

Background: ANTXR2 as the protein binding to collagen IV and laminin, may be involved in extracellular matrix adhesion. GWAS study in European had found its SNPs has relationship with ankylosing spondylitis, but these variations were not related to Chinese people.

Objectives: In this study, we would find susceptibility locus in ANTXR2 associated with ankylosing spondylitis.

Methods: After the haplotype analysis from the 1000 Genomes Project data, we chose tags SNPs validated on 254 cases and 170 matched controls through Mass Spectrometry method. The patients were diagnosed accoding to the Modified New York Criteria for Ankylosing Spondylitis (1984).

Results: In 197 Chinese people from the 1000genome database, there are 16 Haplotype blocks of ANTXR2 gene. 5 SNPs were verified (rs78740643, rs11098964, rs28688624, rs4389526 and rs7689197) by mass spectrometry. Case/control association analysis showed rs11098964 having relationship with AS (P=0.01721, OR (95% CI) = 0.4793 (0.2554–0.8621)). Dominant model of rs11098964 were significant difference from controls (P=0.0109).

Conclusions: our study found the rs11098964 also has relationship with AS. rs11098964 was protective against AS. ANTXR2 is related to susceptibility to AS

References:

[1] Ng SC, Liao Z, Yu DT, Chan ES, Zhao L, Gu J. Epidemiology of spondyloarthritis in the People's Republic of China: review of the literature and commentary. Semin Arthritis Rheum 2007;37:39–47.
[2] Reveille JD, Sims AM, Danoy P, Evans DM, Leo P, Pointon JJ, et al. Genome-wide association study of ankylosing spondylitis identifies non-MHC susceptibility loci. Nat Genet 2010;42:123–7.
[3] Momenzadeh P, Mahmoudi M, Beigy M, Garshasbi M, Vodjdanian M, Farazmand A, et al. Determination of IL1 R2, ANTXR2, CARD9, and SNAPC4 single nucleotide polymorphisms in Iranian patients with ankylosing spondylitis. Rheumatol Int 2016;36:429–35.
[4] Guo C, Xia Y, Yang Q, Qiu R, Zhao H, Liu Q. Association of the ANTXR2 gene polymorphism and ankylosing spondylitis in Chinese Han. Scand J Rheumatol 2012;41:29–32.
[5] van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361–8.
[6] Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MA, Bender D, et al. PLINK: a tool set for whole-genome association and population-based linkage analyses. Am J Hum Genet 2007;81:559–75.
[7] Wu Z, Mou Y, Lin Z, Huang J, Wei Q, Gu J. HLA-B27 polymorphism in Han Chinese patients with ankylosing spondylitis: a distinctive disease association for B*2715 in a multiplex family. J Rheumatol 2009;36:2849–50.
[8] Goedecke V, Crane AM, Jaakkola E, Kaluza W, Laiho K, Weeks DE, et al. Interleukin 10 polymorphisms in ankylosing spondylitis. Genes Immun 2003;4:74–6.
[9] van der Paardt M, Crusius JB, Garcia-Gonzalez MA, Baudoin P, Kostense PJ, Alizadeh BZ, et al. Interleukin-1beta and interleukin-1 receptor antagonist gene polymorphisms in ankylosing spondylitis. Rheumatology (Oxford) 2002;41:1419–23.
[10] Burton PR, Clayton DG, Cardon LR, Craddock N, Deloukas P, Duncanson A, et al. Association scan of 14,500 nonsynonymous SNPs in four diseases identifies autoimmunity variants. Nat Genet 2007;39:1329–37.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4673

AB0114 EFFECTS OF ANTI-IL17A BLOCKADE WITH SECUKINUMAB ON SYSTEMIC AND LOCAL IMMUNE RESPONSES: A MECHANISM-OF-ACTION STUDY IN PERIPHERAL SPONDYLOARTHRITIS

L.J.J. Van Mens[1], M.G. van de Sande[1], S. Menegatti[2], I.C.J. Blijdorp[1], H.M. de Jong[1], I.A. Fluri[1], T.E. Latuhihin[1], A.W.R. van Kuijk[3], N.G. Yeremenko[1], D.L. Baeten[1,4]. *[1]AMC, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands; [2]Immunology, Institut Pasteur, Paris, France; [3]Reade, Amsterdam Immunology and Rheumatology Center, Amsterdam, Netherlands; [4]UCB, Brussels, Belgium*

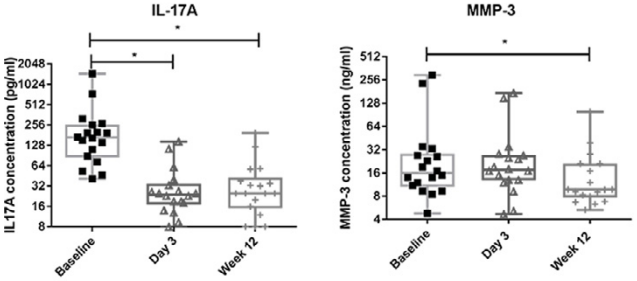
Background: IL-17A blockade is an effective therapy for ankylosing spondylitis (AS) and psoriatic arthritis (PsA), the two prototypical forms of spondyloarthritis (SpA). How IL-17A blockade affects the systemic and local immune responses in SpA remains incompletely understood.

Objectives: To assess the effect of anti-IL17A treatment with secukinumab on the systemic cytokine responses and the synovial immunopathology in SpA patients with peripheral disease (pSpA).

Methods: 20 active SpA patients were included in a 12wk open-label trial followed by 2yrs non-investigational extension. All patients received secukinumab 300mg/wk from baseline to wk4 and then every 4wks. Clinical response was measured 4wkly. TruCulture tubes with SEB and zymosan were drawn at baseline, day3, and wk12. Synovial biopsies were obtained by needle arthroscopy at baseline and wk12, analyzed by immunohistochemistry (IHC) and qPCR.

Results: The 20 pSpA patients consisted of 13 PsA, 3 undifferentiated SpA, 2 AS with peripheral arthritis, 1 reactive arthritis and 1 IBD associated pSpA. There were no SAEs in the 12wk core study. However, two SAEs occurred in the extension of the study: tonsillitis (suspected to be related to study drug) and myocardial infarction (non related), both fully recovered. Secukinumab induced a rapid and highly significant improvement in SJC (Baseline: 2,5 [IQR1–4] vs wk12: 0,5 [IQR0–1]p=0.001), TJC (6 [2–8] vs 0,5 [0–3]p<0.001); VASptglobal (46 [28–65] vs 13 [6–24]p<0.001). 18/20patients reached EULAR DAS response at wk 12 (10 good and 8 moderate responders). This was paralleled by significant improvements in other activity outcomes such as BASDAI (53 [25–63] vs 20 [9–40]p=0.001) and PASI (5,7 [4,5–7,1] vs 0,6 [0,1–1,8]p=0.001). Systemic inflammatory response revealed a decrease in CRP (3,85 [1,35–16,6] vs 2 [1,15–6,3]p=0,001) and ESR (16 [6–35] vs 6 [2,8–16,3]p=0,001), which was associated with decreased production of MMP-3, a validated biomarker of inflammation in pSpA,[1] by peripheral blood cells in the TruCulture system (see figure). With exception of a decrease in IL-17A, the TruCulture system did not reveal any impact of secukinumab on the capacity of peripheral blood cells to produce a broad panel of cytokines and chemokines upon stimulation. In contrast with this preserved systemic immune response, IHC confirmed the positive impact of 12wks of secukinumab on peripheral joint immunopathology as reflected by a significant decrease of infiltration of the synovial sublining with macrophages (2 [1–3] vs 1,5 [1–2]p=0.028) and neutrophils (1 [0,5–3,5] vs 0 [0–1]p=0.004), sensitive synovial biomarkers of treatment response in pSpA.[2] mRNA analysis of synovial biopsies before and after 12wks of secukimumab shows a decrease in IL-17A but not TNF expression.

Figure 1 - Reduction in secretion of IL-17 and MMP-3 in response to SEB in the whole blood TruCulture system after treatment with anti-IL17A.



Significance of the comparisons is determined by a paired T-Test. Concentrations shown are pg/ml (IL-17) and ng/ml MMP-3. P value <0.05 was considered significant and indicated with an (*).

Conclusions: This mechanism-of-action study indicates that IL-17A blockade with secukinumab has a profound beneficial clinical and biological impact on pSpA without compromising systemic immune responses. Further gene expression analysis will delineate which inflammatory pathways are blocked by secukinumab in the diseased target tissue.

References:

[1] van Dooren, Arthritis & Rheumatism, 2004.
[2] Kruithof, Arthritis & Rheumatism, 2005.

Disclosure of Interest: L. Van Mens: None declared, M. van de Sande Speakers

bureau: Benecke, Takeda, Tillots, MSD, Cellgene, S. Menegatti: None declared, I. Blijdorp: None declared, H. de Jong: None declared, I. Fluri: None declared, T. Latuhihin: None declared, A. van Kuijk Grant/research support from: UCB, Pfizer, MSD, Janssen, Consultant for: Novartis, Celgene, N. Yeremenko: None declared, D. Baeten Grant/research support from: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim, Consultant for: Pfizer, MSD, AbbVie, UCB, Novartis, Janssen, Boehringer Ingelheim, Eli Lilly, Roche, BMS, Glenmark, This study was funded by an unrestricted grant from Novartis, Employee of: UCB
DOI: 10.1136/annrheumdis-2017-eular.1915

AB0115 COMPARISON OF THE BACTERIAL STOOL MICROBIOTA IN ESTABLISHED PSORIATIC ARTHRITIS (PSA) AND PSORIASIS (PSC) - EXPLORATORY ANALYSIS OF PILOT DATA

M. Castelino[1,2], M. Tutino[2], J. Moat[3], U.Z. Ijaz[4], R. Parslew[5], A. Al-Sharqi[5], R.B. Warren[6], C. Quince[7], P. Ho[1], M. Upton[8], S. Eyre[2], A. Barton[1,2]. *[1]NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester Foundation Trust, Manchester Academic Health Sciences Centre; [2]Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research; [3]Microbiology and Virology Unit, Institute of Inflammation and Repair, University of Manchester, Manchester; [4]School of Engineering, University of Glasgow, Glasgow; [5]Department of Dermatology, Royal Liverpool and Broadgreen Univesrity Hospitals Trust, Liverpool, UK, Liverpool; [6]The Dermatology Centre, Salford Royal NHS Foundation Trust, University of Manchester, Manchester; [7]Warwick Medical School, University of Warwick, Warwick; [8]Faculty of Medicine and Dentistry, University of Plymouth, Plymouth, United Kingdom*

Background: Psoriatic arthritis (PsA) is a complex inflammatory condition with both genetic and environmental risk factors contributing to disease. A potential environmental risk factor, known to modify the immune system, is the intestinal microbiota. In PsA there is evidence of intestinal inflammation [1,2] and recently dysbiosis of the gut microbiota has been reported in treatment naïve PsA patients [3]. However, there is no information on the temporal stability of the microbiota over time in established PsA on treatment compared to matched PsC controls.
Objectives: To explore the temporal stability of gut microbiota composition and reveal associations with PsA compared to PsC while on stable on treatment with methotrexate.
Methods: Patients with PsA and PsC were recruited to the study if they had been on a stable dose of methotrexate for 6 months. Bacterial DNA was extracted and the V3-V4 hypervariable region of the 16S rRNA was amplified and sequenced on MiSeq. The resultant data was analysed using a bespoke bioinformatics pipeline and taxa were assigned using the Ribosomal Database Project classifier according to the SILVA119 database. The Wilcoxon rank sum test was used to assess alpha diversity indices, while permanova testing using Bray Curtis distance and DESeq2 values corrected for false-discovery rate (FDR) were used to compare beta diversity indices after removing low abundance (<0.5%) Operational Taxonomic Units (OTU). The ALDEx2 analysis package was used to assess effect size.
Results: Stool samples were available 9 PsA (n=13) and 6 PsC (n=12) individuals. Second stool samples were also obtained from the PsA (n=5) and PsC (n=4) groups.
No significant difference in the alpha diversity indices was observed between PsA and PsC. The beta diversity index showed no significant difference between the two conditions using permanova test. However, using the DESeq2-FDR analysis,

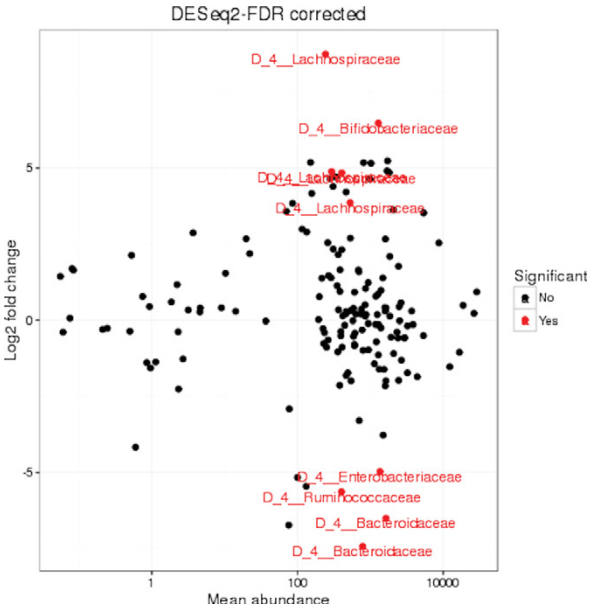


Table 1. Baseline Demographics

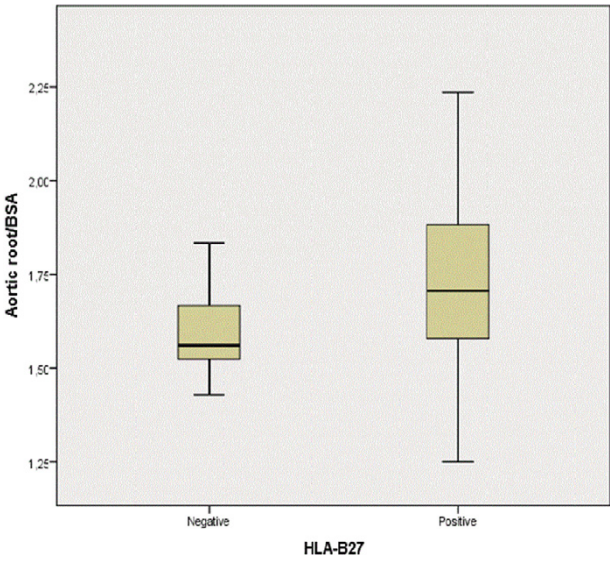
Demographic variables	PsA (n=9)	PsC (n=6)
Age mean (range) yrs	56.8 (40–72)	58.5 (27–79)
Gender Female (%)	2 (22)	4 (67)
Duration of Psoriasis mean (median) yrs	23.7 (26)	26.7 (30)
Type 1 Psorasis (Age at onset <40yrs) (%)	7 (77.8)	3 (50)

8 OTUs were identified which had significantly ($p<0.01$) different abundances in PsA compared to PsC. The taxa (Lachnospiraceae & Ruminococcaceae) predominantly belonged to the Firmicutes phylum, family Lachnospiraceae and Actinobacteria phylum, family Bifidobacteriaceae (Bifidobacteriaceae). The significant OTUs with DESEq2 had an effect size >1 using ALDEx2 but the BH p-value was not significant ($p<0.01$), which may be due to the small sample size. There were no significant differences in the diversity measures over time.
Conclusions: These results suggest that a gut enterotype with predominant Firmicutes/Actinobacteria composition is associated with stable/well controlled disease and is stable over time. This requires replication in a larger cohort.
References:
[1] Lindqvist, 2006.
[2] Scarpa, 2000.
[3] Scher, 2015.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3404

AB0116 IDENTIFYING THE AS PATIENT AT RISK: IS AORTIC ROOT DILATATION ASSOCIATED WITH HLA-B27?

M. Baniaamam[1], S. Heslinga[2], T. Konings[3], O. Kamp[3], I. van der Horst-Bruinsma[1], M. Nurmohamed[1]. *[1]Rheumatology; [2]Reade/VU medical centre; [3]Cardiology, VU Medical Centre, Amsterdam, Netherlands*

Background: Cardiac involvement is more common in *Ankylosing Spondylitis* (AS) patients with HLA-B27 genotype, especially aortic valvular regurgitation (AVR). AVR in AS is caused by aortic root dilatation and fibrotic thickening of the aortic cusps, both linked to inflammation. Inflammation of the aortic root might lead to a weakening in aortic wall strength and dilatation with AVR. Severe AVR can result in heart failure and is an indication for valve replacement or repair. The prevalence of AVR in AS is estimated at 14–18%, which is significantly higher compared to the general population. Therefore, some advocate regular echocardiographic screening of AS patients [1]. However, the cost-benefit of echocardiographic screening in AS is currently unknown and the precise effect of AS specific cardiac pathology on clinically overt cardiovascular morbidity and mortality remains to be elucidated. Hence, we should aim to identify a specific "at risk" AS population that might benefit from routine echocardiographic monitoring.
Objectives: Primary: To assess the association between the aortic root diameter in HLA-B27 positive versus HLA-B27 negative patients.
Secondary: To assess the association between the aortic root diameter with disease duration and inflammation biomarkers.
Methods: We performed a cross-sectional study in AS patients between 50–75 years who were recruited from a large rheumatology outpatient clinic. Patients underwent echocardiography, with 2D, spectral and colour flow Doppler. The aortic root was measured at sinuses of Valsalva during diastole. The aortic root diameter was corrected for body surface area (BSA). Correlation between aortic root diameter/BSA and disease duration and inflammation biomarkers were assessed.
Results: 132 Consecutive AS patients were included with a mean age of 60.5 years, of whom 110 (83%) were HLA-B27 positive. The median aortic



root diameter/BSA ratio was significantly higher in HLA-B27 positive patients compared to HLA-B27 negative patients: 1.75±0.22 mm vs. 1.61±0.14 mm (p=0.001). Eight AS patients (6%) had aortic root dilatation (>2.1mm corrected for BSA), who were all HLA-B27 positive. Patients with and without aortic root dilatation did not significantly differ in age or disease duration. The median aortic root diameter/BSA ratio was correlated with disease duration (r=0.229, p=0.012), but not with inflammatory biomarkers.

Conclusions: HLA-B27 positive AS patients with a long disease duration have an increased aortic root diameter and a higher risk for aortic root dilatation compared to HLA-B27 negative AS patients. The risk of developing aortic root dilatation in AS patients is comparable to patients with essential hypertension (6%)[2].

Future prospective studies should assess which AS patients phenotype are at the highest risk of this AS specific cardiac disease, thus candidates for regular echocardiographic screening.

References:

[1] Klingberg et al. Aortic Regurgitation Is Common in AS: Time for Routine Echocardiography Evaluation? Am J Med 2015Nov;128(11)1244–1250.

[2] Cuspidi C et al. Prevalence and correlates of aortic root dilatation in patients with essential hypertension. J Hypertens 2006 Mar;24(3)573–80.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4616

AB0117 CADHERIN-11 MRNA EXPRESSION IS INCREASED IN THE PERIPHERAL BLOOD OF PATIENTS WITH ACTIVE SPONDYLARTHROPATHY: A PILOT STUDY

N.I. Vlachogiannis, P.F. Christopoulos, G. Bamias, K. Fragiadaki, M. Tektonidou, P.P. Sfikakis. *Joint Academic Rheumatology Program, National and Kapodistrian University of Athens Medical School, Athens, Greece*

Background: Cadherin-11 is a key regulator of synovial architecture and has a central role in the formation of the rheumatoid pannus. Immunohistochemical studies have shown upregulation of cadherin-11 in the synovium of patients with seronegative spondylarthropathies (SpA), comparable to that in rheumatoid arthritis (RA), as well as in the intestinal tissue of patients with inflammatory bowel disease (IBD). Moreover, cadherin-11 mRNA transcripts have been identified in the peripheral blood of patients with RA and independently associated, among various disease characteristics, with the presence of active inflammation in multiple joints [1].

Objectives: To test the hypothesis that cadherin-11 mRNA transcripts are increased in the peripheral blood of patients with active SpA and search for possible associations with clinical features.

Methods: Fifteen patients with active SpA (BASDAI>4), aged between 21 and 71 years, 11 men, and 30 age- and gender-matched healthy controls were examined. Peripheral whole blood samples (3 ml) were subjected to cDNA synthesis and cadherin-11 mRNA expression was quantified by real-time PCR. Available cDNA from 33 IBD patients without axial or peripheral active arthritis served as disease control and were studied in parallel.

Results: Cadherin-11 mRNA was detected in the peripheral blood of 9/15 (60%) patients with SpA versus 5/30 (17%) healthy controls and 10/33 (30%) patients with IBD (SpA vs healthy controls p: 0.006, SpA vs IBD p: 0.06). Notably, cadherin-11 was not associated with BASDAI or skin/nail psoriasis present in 10 patients, but was detected with increased frequency among SpA patients with clinically active peripheral arthritis at the time of sampling (7 out of 10, 70%) than the remaining patients (2 out of 5, 40%). Moreover, cadherin-11 positivity associated significantly with increased erythrocyte sedimentation rate in SpA but not in IBD.

Conclusions: Cadherin-11 mRNA is upregulated in the peripheral blood of patients with SpA and may correlate with "spreading" of inflammation in peripheral joints. Since an anti-cadherin-11 mAb is in early clinical development for RA, further studies in patients with inflammatory arthritis are warranted.

References:

[1] Sfikakis PP, Christopoulos PF, Vaiopoulos AG, et al. Cadherin-11 mRNA transcripts are frequently found in rheumatoid arthritis peripheral blood and correlate with established polyarthritis. Clin Immunol 2014;155:33–41. doi:10.1016/j.clim.2014.08.008.

Disclosure of Interest: N. Vlachogiannis: None declared, P. Christopoulos: None declared, G. Bamias: None declared, K. Fragiadaki: None declared, M. Tektonidou: None declared, P. Sfikakis Grant/research support from: Educational grant from Janssen

DOI: 10.1136/annrheumdis-2017-eular.3650

AB0118 THE LYMPHATIC SYSTEM: A GATEKEEPER FOR MIGRATION OF PATHOGENIC T-CELLS TOWARDS SYNOVIAL JOINTS AND ENTHESES IN PSORIASIS

R. Bisoendial[1], E. Prens[2], A. Mus[3], P. Asmawidjaja[3], N. Davelaar[3], A. Hofman[4], J.-B. Jaquet[4], J. Hazes[3], M. Kok[5], E. Lubberts[3]. *[1]Department of Rheumatology, Maasstad hospital and Erasmus Medical Center; [2]Department of Dermatology; [3]Department of Rheumatology, Erasmus University Medical Center; [4]Department of Plastic surgery; [5]Department of Rheumatology, Maasstad hospital, Rotterdam, Netherlands*

Background: The factors underlying the transition of psoriasis (PsO) to psoriatic arthritis (PsA) are poorly understood. The lymphatic system may control the homing of disease-associated T-cells to skin and extra-cutaneous sites like synovial joints and entheses.

Objectives: To study the capacity of lymphatic endothelial cells (LEC) to regulate T-cell homing capabilities in PsA.

Methods: Human dermal LEC ($0.5x10^4$), and fibroblast-like synoviocytes of a patient with PsA (PsA-FLS; $1.0x10^4$) were pre-incubated for 3 days with PsA synovial fluid (PsA-SF; 0/10/20% v/v) and co-cultured with $2.5x10^4$ allogeneic CD4+CD45RO+CD25- T-cells that were sorted from peripheral blood mononuclear cells of 3 donors (with or without stimulation with αCD3/αCD28). After 72 h, T-cells were analyzed by flow cytometry. The CCR6+ T-helper (Th) subsets Th17.1 (CCR4-/CXCR3+), Th17/Th22 (CCR4+/CXCR3-), Th17 (CCR4+/CXCR3-/CCR10-) and Th22 (CCR4+/CXCR3-/CCR10+), and CCR6- subsets Th1 (CCR4-/CXCR3+), and Th2 (CCR4+/CXCR3-) were identified. We also looked at cutaneous lymphocyte- associated antigen (CLA). IL-17A, IL-22, and TNF protein levels were determined by ELISA. Statistical analysis included unpaired t-test (two-sided) for two-group comparison or one-way ANOVA with the Tukey-Kramer post hoc test for multi-group comparisons.

Results: Stimulation of CD4+CD45RO+ T-cells in co-culture with PsA-FLS skewed towards the CCR6+ subset Th17/Th22, which were predominantly Th17 cells. Th17 differentiation upon stimulation was suppressed in co-culture with LEC, even when LEC were pre-incubated with PsA-SF. T-cell stimulation in co-culture with LEC, as compared to PsA-FLS, promoted the generation of the Th22 subset. Upon co-culture with untreated LEC, stimulated T-cells showed higher expression of the skin homing receptor CLA than those that were co-cultured with PsA-FLS. The proportional reduction in CLA expression on T-cells in the co-cultures with LEC pre-incubated with PsA-SF 20% was comparable to PsA-FLS, however LEC conserved CLA expression on CD4+CD45RO T-cells at a higher level than PsA-FLS; this phenomenon particularly affected the CCR6+ T-cells. In line, a trend towards lower IL-17A and higher IL-22 levels were observed in the co-cultures with LEC that were pretreated with PsA-SF 20%, as compared to the co-culture with PsA-FLS. No differences were seen for TNF protein levels.

Conclusions: LECs are directly involved in T-cell differentiation and homing capabilities, as shown by suppression of Th17 differentiation upon stimulation, as compared to PsA-FLS. Also, LEC promoted Th22 generation, and conserved CLA expression in CCR6+ T-cells, even when LEC were preincubated with PsA-SF. Studies are underway to confirm that LECs from relevant biological tissues (e.g. synovium and lymph nodes) are critical for tissue-restricted T-cell migration to skin and synovial membranes in PsA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5360

AB0119 ANTI-FIBROTICS TO PREVENT NEW BONE FORMATION IN SPONDYLOARTHRITIS: PROOF OF CONCEPT USING PIRFENIDONE IN CELL CULTURE MODELS

J. Laustsen[1,2], S. Lomholt[3], P. Andersen[3], J. Kelsen[4], T.W. Kragstrup[1]. *[1]Department of Rheumatology, Aarhus University Hospital; [2]Department of Biomedicine; [3]Aarhus University; [4]Aarhus University Hospital, Aarhus C, Denmark*

Background: The pathogenesis of spondyloarthritis (SpA) involves both inflammation and new bone formation in the spine. In line with this, the disease has been characterized as both inflammatory and fibrotic. Current treatment including inhibitors of tumour necrosis factor alpha (TNFα) seem to dampen inflammation while new bone formation can progress. Therefore, there is an unmet therapeutic need for the treatment of new bone formation in SpA. Fibrosis is mediated by myofibroblasts and new bone formation is the result of increased osteoblast mineralization and decreased osteoclast bone degradation. Here, we evaluate the potential effect of the newly approved anti-fibrotic agent pirfenidone (Esbriet, Pirespa) on fibrosis and new bone formation in cell culture models of SpA.

Objectives: We hypothesized that pirfenidone inhibits SpA myofibroblast formation and activity and osteoblast mineralization.

Methods: Synovial fluid mononuclear cells from patients with SpA (n=6) were included for culturing fibroblast-like synovial cells (FLSs) while osteoblasts were purchased. The cells were cultured with pirfenidone in increasing concentrations (0.25, 0.5, and 1.0 mg/ml) with or without stimulation with tumor necrosis factor alpha (TNFα), transforming growth factor beta (TGFβ), or interferon gamma (INFγ). The proliferation of FLSs was analyzed with light microscopy and flow cytometry using the marker Ki67. The differentiation and activation of FLSs was assessed with flow cytometry, a proteome profiler assay and enzyme-linked immunosorbant assays. The mineralization capacity of the osteoblasts was measured as deposition of hydroxyapatite.

Results: Pirfenidone reduced the Ki67 expression 7.1-fold in untreated FLSs (p=0.001) and 11.0-fold in FLSs stimulated with TGFβ, TNFα, and INFγ (p=0.022). PFD further inhibited TGFβ induced upregulation of αSMA (Figure 2A) and INFγ induced upregulation of HLA-DR (Figure 2C) in all cultures. There was no difference between the percentage of ICAM-1 positive FLSs in cultures treated with or without pirfenidone. In supernatants from FLSs stimulated with TGFβ, TNFα, and INFγ a total of 12 cytokines or chemokines had values above the detection limit in the membrane-based antibody array. Pirfenidone decreased the secretion of 3 of these 12 cytokines or chemokines more than 2-fold. The changes in secretion of monocyte chemoattractant protein 1 (MCP-1) and chitinase-3-like

protein 1 (CHI3L1, also known as YKL-40) were validated with ELISA. Further, pirfenidone decreased the secretion of both DKK1 (p=0.006) and OPG (p=0.02) by SpA FLSs stimulated with TGFβ, TNFα, and INFγ, while the concentration of RANKL was below the detection limit of the ELISA assay in all cultures. Finally, pirfenidone inhibited the deposition of hydroxyapatite by osteoblasts in a dose-dependent manner (p=0.0001). This inhibition was partly reversible when removing pirfenidone after the first week of the mineralization assay.
Conclusions: Taken together, pirfenidone inhibited SpA myofibroblast formation and activity and osteoblast mineralization. This encourages further research in anti-fibrotics as treatment of new bone formation in SpA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1503

AB0120 ACCELERATED OSTEOGENIC DIFFERENTIATION OF HUMAN BONE-DERIVED CELLS IN ANKYLOSING SPONDYLITIS

Y.-S. Park[1], S. Jo[2], I.-H. Sung[3], T.-H. Kim[2]. *[1]Orthopaedic Surgery, Hanyang University Hospital, Guri; [2]Rheumatology, Hanyang University Hospital for Rheumatic Disease; [3]Orthopaedic Surgery, Hanyang University Hospital, Seoul, Korea, Republic Of*

Background: Ankylosing spondylitis (AS) is characterized by excessive bone formation with syndesmophytes, leading to bony ankylosis. The contribution of osteoblasts to the pathogenesis of ankylosis is poorly understood.
Objectives: The aim of this study was to determine molecular differences between disease controls (Ct) and AS bone-derived cells (BdCs) during osteogenic differentiation.
Methods: We confirmed osteoblastic differentiation of Ct and AS BdCs under osteogenic medium by observing morphological changes and measuring osteoblastic differentiation markers. Osteoblast differentiation was detected by alkaline phosphatase (ALP) staining and activity, and alizarin red S and hydroxyapatite staining. Osteoblast-specific markers were analyzed by qRT-PCR, immunoblotting, and immunostaining. To examine the effects of inflammation, we added AS and healthy control serum to Ct and AS BdCs, and then analyzed osteoblast-specific markers.
Results: AS BdCs showed elevated basal intercellular and extracellular ALP activity compared to Ct. When osteoblast differentiation was induced, AS BdCs exhibited higher expression of osteoblast-specific marker genes and faster mineralization than Ct BdCs, indicating that these cells differentiated more rapidly into osteoblasts. ALP activity and mineralization accelerated when serum from AS patients was added to Ct and AS BdCs.
Conclusions: Our results revealed that AS BdCs showed significantly increased osteoblastic activity and differentiation capacity by regulating osteoblast-specific transcription factors and proteins compared to Ct BdCs. Active inflammation caused by adding AS serum accelerated bony ankylosis. Our study could provide useful basic data for understanding the molecular mechanism of ankyloses in AS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4885

SLE, Sjögren's and APS - etiology, pathogenesis and animal models

AB0121 DYSREGULATED CIRCULATING MIRNA LEVELS ARE CHARACTERISTIC OF BOTH NON SJÖGREN'S SICCA AND PRIMARY SJÖGREN'S SYNDROME PATIENTS

A.P. Lopes[1,2], M.R. Hillen[1,2], E. Chouri[1,2], S.L. Blokland[1,2], A.A. Kruize[1], M. Rossato[1,2], T.R. Radstake[1,2], J.A. van Roon[1,2]. *[1]Department of Rheumatology & Clinical Immunology; [2]Laboratory of Translational Immunology, University Medical Centre Utrecht, Utrecht, Netherlands*

Background: MicroRNAs are small non-coding RNAs that play important regulatory roles in a variety of biological processes. They can regulate the post–transcriptional expression of target genes and play an important role in gene regulation. Specific microRNAs are stably present in serum and changes in their abundance are potentially disease-specific. Considering their important role in regulation of the immune system, we investigated circulating levels of miRNAs in patients with primary Sjögren's syndrome (pSS) and those with non-Sjögren's sicca (nSS) in relation to disease activity.
Objectives: To assess the expression of a large number of miRNAs in the serum of pSS and nSS patients as compared to healthy controls and to investigate their correlation with disease activity.
Methods: Two independent cohorts (discovery and validation) were established, consisting of a total of 37 pSS patients classified according to the 2002 criteria, 20 nSS patients that were not clinically considered to be pSS and did not meet the classification criteria, and 18 healthy controls (HC). Serum miRNAs were isolated and miRNA profiling of 758 miRNA was performed using the OpenArray platform in the discovery cohort. A selection of 10 miRNAs found to be differentially expressed between the groups was measured in the independent validation cohort using single TaqMan microRNA Assays.
Results: miRNA profiling revealed 10 miRNAs to be differentially expressed between the groups; 2 in pSS vs HC, 7 in nSS vs HC and 1 in both pSS and nSS vs HC. One miRNA was excluded from further analysis after technical validation by single TaqMan microRNA Assay. The other 9 miRNAs were measured in the validation cohort. Surprisingly, 2 miRNAs were validated to be increased in the nSS group as compared to HC (snRNA-U6 and miR-661). Using the data from both cohorts combined, the levels of snRNA-U6 and miR-661 was associated with serum Ig and C4 in the nSS group, but also in the pSS group. This prompted us to investigate miRNA expression in subgroups of pSS patients. snRNA-U6 and miR-661 levels are significantly increased compared to HC in pSS patients negative for autoantibodies. In autoantibody positive pSS patients, levels of snRNA-U6 and miR-661 are comparable to those found in HC and both miRNAs are significantly increased in autoantibody negative patients as compared to autoantibody positive pSS patients. In addition, their expression is strongly associated with leukocyte numbers in the autoantibody positive patients, but not in the negative patients.
Conclusions: Increased circulating levels of snRNA-U6 and miR-661 in patients with nSS and autoantibody negative pSS patients are associated with normal B cell activity and normal numbers of circulating leukocytes. Reduced miRNA levels in autoantibody positive pSS patients are associated with B cell hyperactivity and decreased leukocyte counts, which is possibly the result of immune cells migration to the inflammatory sites. Considering the important role of miRNAs in the control of immune cell activation, this work points to a significant role of miRNAs in pSS and nSS patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4961

AB0122 DETECTION OF AN INTRIGUING VIRUS-LIKE SEQUENCE IN THE SALIVARY GLAND EPITHELIAL CELLS OF SJÖGREN'S SYNDROME PATIENTS

A.G. Vakrakou[1,2], E. Karamichali[3], O. Georgopoulou[3], M.N. Manoussakis[1,2]. *[1]Pathophysiology, University of Athens; [2]Laboratory of molecular immunology; [3]Molecular Virology Laboratory, Hellenic Pasteur Institute, Athens, Greece*

Background: Several previous studies from our laboratory had indicated that the salivary gland epithelial cells (SGEC) of primary Sjögren's syndrome (SS) patients manifest cell autonomous (intrinsic) activation, which is demonstrated in non-neoplastic cell lines derived from patients (SS-SGEC). As for other autoimmune diseases, it is widely proposed that infectious factors may incite SS. In fact, several viral agents have been proposed to be involved in the development of SS, including EBV, retroviruses (such as HTLV-1 and endogenous retrotransposons) and the Coxsackie virus. Recently, the sequence and antigen of HDV were detected in the salivary gland tissues of approximately half of SS patients studied [Weller et al., 2016], however, in the absence of detectable hepatitis B virus (HBV) surface antigen and antibodies to HBV or HDV. Therefore, we hypothesized that HDV may be causally related with the cell-autonomous aberrations observed in the SS-SGEC lines and may trigger the inflammatory and autoimmune reactions that characterize SS.
Objectives: Herein, using non-neoplastic SGEC lines derived from SS patients, we sought to address directly whether the SGEC of these patients manifest evidence for infection by the HDV virus, despite the fact that patients studied did not display any evidence of infection by HBV or HDV viruses.
Methods: For that purpose, we purified total RNA from SGEC lines from non-SS controls (n=7) and SS patients (n=7). Reverse transcription of RNA isolated from salivary gland epithelial cells (SGEC) was performed using random hexamer primers as per the manufacturer's specifications. We performed PCR for the identification of HDV RNA sequences with three sets of primers from different regions of the viral sequence. RNA extracted from HDV-positive sera was used as positive control in HDV-specific PCR.
Results: All SGEC lines from SS patients and non-SS controls tested were found positive for HDV RNA, as tested by the first two sets of primers (two sets of primers for first and nested PCR with expected PCR products 329bp and 234bp, respectively). Nevertheless, when we selected primers for another region of the HDV genome (set of primers with expected PCR products 375bp) all RNA samples from SGEC lines tested were found negative for HDV RNA, whereas the HDV RNA control specimen was positive.
Conclusions: We conclude that SS-SGEC are not actually infected by the HDV virus, but are probably carriers of an HDV-like sequence. In fact, the putative HDV virus-like sequence has been previously shown be highly homologous to the RNA binding-protein cytoplasmic polyadenylation element-binding protein-3 (CPEB3), which belongs to a family of genes regulating messenger RNA polyadenylation and is structurally and biochemically related to the human HDV ribozymes (Salehi-Ashtiani et al, 2006). We are currently in the process of further analyzing the nature of this HDV-like sequence, through cloning and Sanger sequencing of the RT-PCR products, as well as performing of HDV-specific immunostaining studies in both SGEC lines and salivary gland tissues.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6308

AB0123 T-CELL SURFACE GLYCOSYLATION PATTERN ALTERATIONS IN SLE – A PUTATIVE LINK TO GALECTIN-1-MEDIATED IMMUNOREGULATORY DEFICIENCY

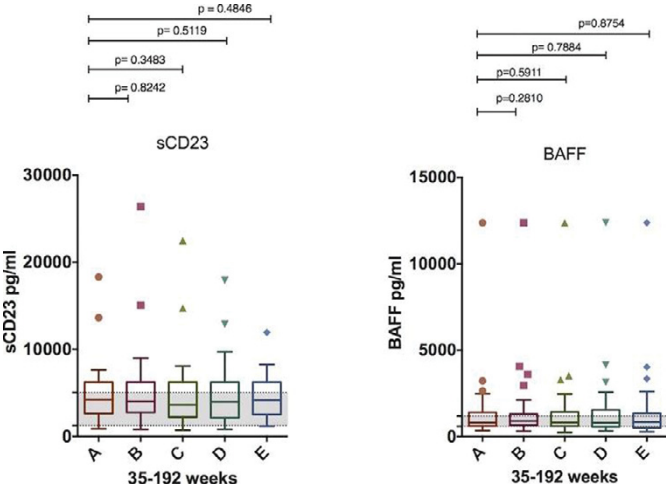
Á. Hornung[1], E. Szabó[2], Á. Czibula[2], É. Monostori[2], L. Kovács[1]. *[1]Department of Rheumatology and Immunology, University of Szeged; [2]Department of Genetics, Hungarian Academy of Sciences, Biological Research Centre, Szeged, Hungary*

Background: We have previously found that activated T-cells from systemic lupus erythematosus (SLE) patients express lower amount of intracellular galectin-1 (icGal-1) than those of healthy controls and are resistant to the apoptotic effect of extracellular galectin-1 (ecGal-1), an endogenous immunoregulatory lectin. We also demonstrated that the *de novo* synthesized icGal-1 level affects apoptosis of T-cells induced by ecGal-1, since low icGal-1 expression resulted in reduced sentsitivity to ecGal-1 (Deák M *et al*). We have therefore proposed the defective icGal-1 production to be an explanation to the insufficient regulatory effects of ecGal-1 in SLE. However, altered binding of ecGal-1 to T-cells due to changes in surface glycosylation may also regulate the apoptotic activity of ecGal-1.
Objectives: We have herein hypothesized that the cell-surface glycosylation pattern, and consequently, lectin-binding ability in SLE T-cells is altered, and that an abnormal expression of glycosylation enzymes may account for these changes.
Methods: In order to analyse the glycosylation pattern of cell surface glycoproteins, lectin-binding assays were performed using 5 different plant lectins and human recombinant Gal-1 on resting and activated T-cells from patients with active SLE (n=8) with multi-colour flow-cytometry, and were compared with 15 healthy controls. mRNA levels of 13 glycosylation enzymes involved in the development of N-glycan structures on T-cells were measured with qPCR, and were correlated with the specific lectin binding data.
Results: As compared with the resting state, the increase in Gal-1 binding during activation was significantly lower in SLE T-cells than in controls, and the level of Gal-1 binding maximum was significantly reduced in SLE activated T-cells than in controls. Binding maximum of plant lectins that recognise high complexity N-glycans also increased less in SLE T-cells than in controls during activation. mRNA level of sialyltransferase ST3GAL6 was increased and neuraminidase Neu1 was decreased in active SLE patients as compared to controls. The ST6GAL1/NEU1 ratio in SLE patients positively correlated with the SLEDAI disease activity index.
Conclusions: SLE T-cells show decreased complexity of N-glycan structures. Increased ST3GAL6 and decreased Neu1 expression result in an increased density of terminal sialic acids, and this may explain the impaired Gal-1 binding. In addition to the previously described deficiency in icGal-1 expression upon activation, our present findings of an attenuated glycan complexity and a shift toward terminal sialylation provide a further mechanism of pathological T-cell activation and regulation of T-cell viability in SLE.
References:
[1] Deák M, Hornung Á, Novák J, Demydenko D, Szabó E, Czibula Á, Fajka-Boja R, Kriston-Pál É, Monostori É, Kovács L. Novel role for galectin-1 in T-cells under physiological and pathological conditions. Immunobiology. 2015 Apr;220(4):483–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5657

AB0124 SEROLOGICAL MEASURES OF B CELL FUNCTION IN PATIENTS WITH SLE; HOW ROBUST ARE THEY OVER TIME?

A. Hennessey[1,2], R. Marques[3], M. Leandro[1,2], D. Isenberg[1,2], G. Cambridge[2]. *[1]Division of Rheumatology, Department of Medicine, University College London Hospitals; [2]Centre for Rheumatology and Bloomsbury Rheumatology Unit, University College London, London, United Kingdom; [3]Serviço de Medicina Interna B, Centro Hospitalar Universitário de Coimbra, Coimbra, Portugal*

Background: In SLE the precise mechanisms whereby parent autoreactive B cells are generated and permitted to escape tolerance checkpoints, proliferate, persist and switch to pathogenic autoantibody production remains poorly understood. Hypotheses include defective negative central selection, defective peripheral selection with enhanced germinal center activity as well as positive selection of B cells via autoantigen presentation or T-independent mechanisms. Biomarkers to identify possible breaches in tolerance checkpoints would allow more effective intervention. We have therefore measured relative levels of soluble (s)CD23 (released during B cell differentiation from naive to memory B cell status) and the B cell activation factor, BAFF (survival factor and class-switch/differentiation promoter) in SLE sera to determine if relative levels of sCD23 and BAFF were of use as biomarkers to group patients based on B cell kinetics rather than clinical features. BAFF is often raised in SLE patients and can stimulate the aberrant differentiation of transitional B cells and of plasmablasts in vitro. Combining the 2 biomarkers could therefore indicate whether there was increased expansion of naïve B cells, and whether BAFF was a possible driver/consequence of autoimmunity in different patients.
Objectives: To determine whether relative levels of sCD23 and BAFF reflect disease activity or remain stable over time.
Methods: Stored SLE serum from patients who were Rituximab-naive, had >5 samples available in the biobank over at least 6 months (n=38). Samples were analysed for levels of sCD23 and BAFF via ELISA. Wilcoxon matched-pairs signed rank test were used to compare serial values. Clinical details including BILAG scores were also collected for the available time points. If positive dsDNA at any time during the time period this was deemed positive. The latest BILAG was utilised and reviewed, a patient was deemed not to have system involvement if they had an "E" for that system.
Results: Sera from 38 SLE patients (32 female, 6 male) with mean age of first sample 42 (range: 25–72). Minimum interval between 1st and last sample was 101 weeks (range: 35–192 weeks). Patients were then sorted into clinical groups according to levels of these serum markers. Normal ranges defined as: sCD23 (1235–5023pg/ml), BAFF (584–1186pg/ml). Group I (n=9): – High (H) sCD23, Normal (N) BAFF; Group II (n=11) – H sCD23, H BAFF; Group III (n=17) – N sCD23, N BAFF; Group IV (n=2) – N sCD23, H BAFF. Figure 1 shows the p values generated from the Wilcoxon matched-pairs signed rank test for each time period demonstrating nil significant change over time. Analysis of clinical data showed no differences in terms of organ involvement or anti-dsDNA -Ab status.



Conclusions: Within a cohort of SLE patients, soluble CD23 and BAFF is stable over time despite variation in disease activity. Grouping patients based on sCD23 and BAFF profile may be useful in identifying distinct B cell maturation pathways reflecting underlying autoimmune pathways which vary between patients.
Disclosure of Interest: A. Hennessey: None declared, R. Marques: None declared, M. Leandro Consultant for: Roche UK, Roche Basel and Genentech, D. Isenberg: None declared, G. Cambridge: None declared
DOI: 10.1136/annrheumdis-2017-eular.6780

AB0125 BRAIN IMMUNOPATHOLOGY OF LUPUS-PRONE FCΓRIIB-/-YAA MICE - IMPLICATION TO THE INNATE IMMUNE RELATED MECHANISM OF NEUROPSYCHIATRIC SLE

A. Nomura[1], G. Murayama[1,2], A. Chiba[1], S. Miyake[1]. *[1]Immunology; [2]Rheumatology, Juntendo University, Tokyo, Japan*

Background: Neuropsychiatric SLE (NPSLE) is a common manifestation of SLE and problems such as cognitive impairment or depression are elusive. The importance of innate immune related inflammation in the pathomechanism of neurodegenerative or psychiatric diseases has been recognized recently, and the importance of innate immunity in the pathogenesis of NPSLE has also been suggested[1)]. Therefore, we investigated innate immune mechanism of NPSLE by using lupus prone mice.
Objectives: This study is conducted to understand the brain immune pathology of lupus-prone FcγRIIB$^{-/-}$ *Yaa* mice in which innate immune stimulation is potentiated by the duplication of Toll-like receptor 7[2)].
Methods: Immune cell subsets and histopathology of brains were analyzed by flow cytometry and immunohistochemistry in FcγRIIB$^{-/-}$ *Yaa* mice compared with congenic mice at around 16 week-old when glomerulonephritis had developed. For flow cytometric analysis, microglia, myeloid lineage cells and lymphocytes were defined by staining with CD11b and CD45. Subsets of those cells and their activation status were analyzed. For histopathological analysis, microglia, brain macrophages, astrocytes and lymphocytes were immunostained and expression of MHC class I and class II were also analyzed.
Results: Flow cytometric analysis revealed increase in the number of microglial cells (CD11b^{+} CD45^{int}) and myeloid lineage cells (CD11b^{+} CD45^{high}) in the brains of FcγRIIB$^{-/-}$ *Yaa* mice compared with congenic FcγRIIB$^{+/+}$ mice. Mean fluorescence intensity of MHC class I was increased in microglia and myeloid lineage cells in FcγRIIB$^{-/-}$ *Yaa* mice. An increased percentage of CD3 positive cells compared to CD19 positive cells were observed and their expression of CD69, an activation marker, were increased in FcγRIIB$^{-/-}$ *Yaa* mice. In histopathology, number of macrophages and microglia identified by Iba1 (Ionized calcium binding adapter molecule 1) positive cells were increased in FcγRIIB$^{-/-}$ *Yaa* mice. In areas where MHC class I and class II were highly expressed on macrophages,

reaction of astrocytes and patchy increase of lymphocytes were also observed. Furthermore, MHC class I and class II were also highly expressed in the vascular endothelium in FcγRIIB$^{-/-}$ *Yaa* mice.

Conclusions: Activation of myeloid lineage cells and reactive changes of glial cells and endothelial cells were observed in the central nervous system of lupus-prone FcγRIIB$^{-/-}$ *Yaa* mice. These results imply the role of innate immune mechanisms in the pathology of NPSLE.

References:

[1] Stock AD, Wen J, Doerner J, et al. Neuropsychiatric systemic lupus erythematosus persists despite attenuation of systemic disease in MRL/lpr mice. J Neuroinflammation.2015;12:205.

[2] Kawano S, Lin Q, Amano H, et al. Phenotype conversion from rheumatoid arthritis to systemic lupus erythematosus by introduction of Yaa mutation into FcγRIIB-deficient C57BL/6 mice. Eur J Immunol.2013;43:770–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2849

AB0126 AUTOPHAGY AND SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL SIGNIFICANCE OF ATG14+, FOXP3+, AND CD25+ EXPRESSION ON T REGULATORY CELLS AND NK CELLS

A. Rodríguez[1], E.J. Zurita[1], A.R. Durán[2], R. Bustamante[3], A. Sánchez[3], M.Á. Saavedra[3], C. Arroyo[4], G. Medina[5], L.J. Jara[3]. *[1]Immunology Department, Escuela Nacional de Ciencias Biologicas; [2]Immunology Department, Escuela Nacional de Ciencias Biológicas; [3]Rheumatology Department; [4]Banco de Sangre, Hospital de Especialidades "Dr. Antonio Fraga Mouret", Centro Médico la Raza, IMSS; [5]Rheumatology Department, Hospital de Especialidades "Dr. Antonio Fraga Mouret", CENTRO, Mexico City, Mexico*

Background: Autophagy is a highly conserved protein degradation pathway, essential for removing protein aggregates and misfolded proteins in healthy cells. Autophagy and autophagy-molecules expression have been implicated in autoimmune diseases. Systemic Lupus Erythematosus (SLE) is a prototype of autoimmune disease whose main characteristic is the loss of immune tolerance. Recent evidences suggest that autophagy, and autophagy-related proteins participate in SLE immune regulation. However, little is known about the SLE clinical significance of autophagy-related proteins, T regulatory, and NK cells.

Objectives: To evaluate the expression of ATG14$^+$ (autophagy-related key regulator protein), FOXP3$^+$, CD25$^+$T regulators, CD56$^+$NK cells in active and inactive SLE patients.

Methods: The expression of ATG14$^+$, FOXP3$^+$, CD25$^+$, and CD56$^+$ were measured by flow cytometry, and expressed in percentages in T and NK cells of SLE patients (1997, ACR criteria), and healthy controls. Active SLE was considered by SLEDAI ($\geq$4). The organs affected and treatments were evaluated.

Results: A total of 40 SLE patients and 20 healthy controls were included. The mean expression of autophagy in 20 active SLE patients was 11.19% in comparison with inactive SLE patients, 7.13%, (p=0.04), and in healthy donors, 7.445% (p=0.0281). The FOXP3$^+$ expression in NK cells in active SLE was lower in comparison with inactive patients (0.98% vs 3.82% respectively). In healthy donors was 2.89%.

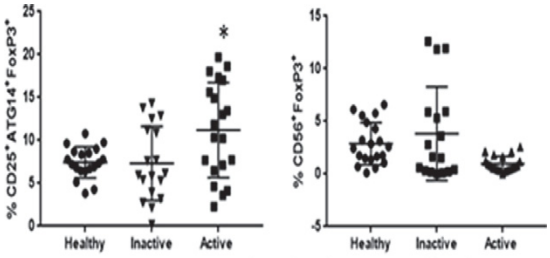


Figure 1: Expression in percentage of CD25$^+$ATG14$^+$FoxP3$^+$ (T reg) and CD56$^+$FoxP3$^+$ (NK cells) in SLE active and inactive patients and healthy controls. *p=0.04 Mann Whitney U test.

Conclusions: We found that in active patients autophagy is higher than in inactive patients. In inactive patients FOXP3 expression in NK cells is normal. These results can be due to the effect of the different treatments given according to clinical manifestations. Autophagy-related key regulator protein may be a new target of SLE treatment

References:

[1] Lech M, Anders HJ. The pathogenesis of lupus nephritis. J Am Soc Nephrol. 2013, 24, 1357–1366.

[2] Chikte S, et. al. use of LysoTracker dyes: A flow cytometric study of autophagy. Cytometry. 2014, 85(2), 169–78.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6883

AB0127 ANTI-DS-DNA ANTIBODIES REGULATE ATHEROTHROMBOSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS THROUGH THE INDUCTION OF NETOSIS, INFLAMMATION AND ENDOTHELIAL ACTIVATION

C. Perez-Sanchez[1], M.A. Aguirre[1], P. Ruiz-Limon[1], M.C. Abalos-Aguilera[1], I. Arias-de la Rosa[1], N. Barbarroja[1], Y. Jimenez-Gomez[1], P. Segui[1], E. Collantes-Estevez[1], J.A. Gonzalez-Reyes[2], J.M. Villalba[2], M.J. Cuadrado[3], C. Lopez-Pedrera[1]. *[1]IMIBIC/Reina Sofia Hospital/University of Cordoba; [2]Department of Cell Biology, Physiology and Immunology, ceiA3, University of Cordoba, Cordoba, Spain; [3]Lupus Research Unit and St. Thomas Hospital, London, United Kingdom*

Background: The role of anti-dsDNA in the pathogenesis of the systemic lupus erythematosus (SLE) has been clearly established. However, the influence of these autoantibodies in the atherothrombotic status of SLE patients has not yet been evaluated

Objectives: 1. To analyse in vivo the involvement of anti-dsDNA antibodies in the development of CVD in SLE patients. 2. To evaluate in vitro the mechanisms underlying the effects of anti-dsDNA antibodies in these processes

Methods: The study was conducted in 50 SLE patients and 38 healthy donors. Endothelial function was assessed by measuring the post-occlusive hyperaemia using Laser-Doppler. Various markers of oxidative stress, inflammatory cytokines, prothrombotic mediators and NETosis, were quantified in purified leukocytes and plasma from SLE patients and controls. Activation of intracellular pathways was analyzed in monocytes using pathscan intracellular signaling array. In vitro, purified neutrophils, monocytes and lymphocytes from healthy donors and endothelial cells (ECs) were treated separately and in a trans-well co-culture system with anti-dsDNA antibodies isolated from the serum of SLE patients. Then, markers of inflammation, thrombosis, oxidative stress and NETosis were evaluated by flow cytometry (protein), RT-PCR (mRNA) and electron microscopy

Results: SLE patients showed impaired micro-vascular endothelial function (reduction of hyperaemia post occlusion area) and altered expression levels of pro-inflammatory proteins (IL6, IL8, MCP-1 and PCR), prothrombotic molecules (TF), oxidative stress markers (peroxides and mitochondrial membrane potential) and netosis-related molecules (NE, MPO and cell free-DNA). Monocytes from anti-dsDNA-positive SLE patients showed activation of various pathways related to inflammation, thrombosis and apoptosis (ErK, STAT-3, p38, JNK, GSK, Bad and Caspase-3). Association studies demonstrated that molecules related to inflammation and thrombosis, endothelial dysfunction, oxidative status and netosis were linked to the occurrence of thrombotic events, as well as to the presence of anti-dsDNA antibodies. In vitro treatment of purified leukocytes with anti-dsDNA antibodies promoted an increase in the production of NETosis, levels of peroxides and percentage of cells with altered mitochondrial membrane potential, as well as enlarged expression of a number of proinflammatory and prothrombotic molecules. In vitro treatment of HUVEC with anti-dsDNA antibodies promoted an increase in endothelial activation molecules (ICAM-1, VCAM-1 and E-selectin).

Conclusions: 1. Positivity for anti-dsDNA antibodies is linked to an increased pro-atherothrombotic status in SLE patients. 2. Anti-dsDNA antibodies, in vitro, promote NETosis on neutrophils, apoptosis on monocytes, modulate the expression of molecules related to inflammation and thrombosis, and induce endothelial activation. Together, that data suggest the involvement of such autoantibodies on atherothrombosis development in SLE

Acknowledgements: CTS-794 and ISCIII (FIS15/1333;RIER RD16/0012/0015)

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4735

AB0128 ALTERATIONS OF THE SPLICING MACHINERY COMPONENTS IN LEUKOCYTES FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS INFLUENCES ITS DEVELOPMENT AND ATHEROTHROMBOTIC PROFILE AND DRIVES THE THERAPEUTIC RESPONSE

C. Perez-Sanchez[1], M.A. Aguirre[1], S. Pedraza-Arévalo[1], M. del Río-Moreno[1], P. Ruiz-Limón[1], N. Barbarroja[1], Y. Jimenez-Gomez[1], I. Arias-de la Rosa[1], M.C. Abalos-Aguilera[1], P. Segui[1], E. Collantes[1], J. Castaño[1], R.M. Luque[1], M.J. Cuadrado[2], C. Lopez-Pedrera[1]. *[1]IMIBIC/Reina Sofia University Hospital/University of Cordoba, Cordoba, Spain; [2]Lupus Research Unit, St Thomas Hospital, London, United Kingdom*

Background: Recent studies emphasize the relevance of alternative splicing in the development of genetic and autoimmune diseases and suggest therapeutic possibilities based on the modulation of this process.

Objectives: To identify alterations in the leukocyte splicing machinery of patients with systemic lupus erythematosus (SLE) and to evaluate its influence on the development and activity of the disease, its atherothrombotic profile, and the response to specific therapies.

Methods: An array of selected components of the major-(n=12) and minor-spliceosome (n=4) and associated splicing factors (n=28) was developed, and their expression levels were evaluated using a Fluidigm methodology, in purified leukocytes from 36 SLE patients and 29 healthy donors (HD). In parallel, an extensive clinical/serological evaluation was performed. Carotid intimate media thickness (CIMT) was used as atherosclerosis marker. Endothelial activity was

monitored by laser-doppler, and pro-inflammatory and oxidative stress markers were quantified by flow cytometry and RT-PCR. In a parallel cohort of SLE patients (n=12), the effects of in vivo treatment with ubiquinol on spliceosome components was evaluated.

Results: As a general feature, a significant reduction in splicing factors and spliceosome components was found in all the leukocytes of SLE patients. Interestingly, we found a specific altered profile of splicing factors and spliceosome components when compared monocytes (U2AF1, FBP11, SRSF9), lymphocytes (RBM22, PRP8, SRSF5) and neutrophils (RNU4, CA150). The reduced levels of some components of spliceosome in both monocytes and neutrophils were linked to the occurrence of thrombotic events, foetal loss and arterial hypertension. In lymphocytes, those reduced levels were strongly related to the positivity for anti-dsDNA antibodies in SLE patients, thus suggesting that reduced spliceosome machinery would contribute to increase in altered autoantigen assembly, inducing increased autoantibody production. Correlation studies demonstrated an inverse relationship among reduced levels of spliceosome components/splicing factors and high activity of the disease (measured as SLEDAI), endothelial dysfunction, and increased expression levels of peroxides and peroxynitrites, as well as of altered mitochondrial membrane potential in monocytes and neutrophils. In vitro treatment of leukocytes from HDs with anti-dsDNA promoted a reduction in spliceosome components associated with the expression of proinflammatory and oxidative mediators. Finally, in vivo treatment with ubiquinol reversed reduced expression in SLE of spliceosome components related to their proaterothrombotic profile.

Conclusions: These results reveal the existence of SLE- associated spliceosome alterations -promoted by anti-dsDNA antibodies-which could be related to the development and activity of this autoimmune condition and have influence on the induction of mechanisms that drive atherothrombosis as well as the therapeutic response.

Acknowledgements: Funded by CTS7940 and ISCIII (PI15/01333 and RIER RD16/0012/0015).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5036

AB0129 HMGB1+ MICROPARTICLES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH LUPUS NEPHRITIS

C. Burbano [1], J.A. Gómez-Puerta [1], M. Rojas [1], G. Vasquez [1], J. Orejuela [1], C.H. Muñoz [2], A. Vanegas-García [2], D. Castaño [1]. *[1]Universidad de Antioquia; [2]Hospital Universitario de San Vicente Fundación, Medellín, Colombia*

Background: High mobility group box protein 1 (HMGB1) is a nuclear DNA-binding protein that can function as an alarmin when is released from activated and dying cells. In association with nucleosomes, HMGB1 may contribute to the pathogenesis of systemic lupus erythematosus (SLE). Some previous reports have associated HMGB1 with the pathogenesis of cutaneous lupus and lupus nephritis (LN). HMGB1 may also be contained in microparticles (MPs). These vesicles have a wide spectrum of biological activities in intercellular communication, and they compete with apoptotic cells to bind mononuclear phagocytes.

Objectives: To evaluate the association of MP-HMGB1+ circulating with LN and to correlate them with LN activity.

Methods: Blood samples from 60 SLE patients were used to isolated MPs from platelet-poor plasma by centrifugation and their count, cell source and phenotype were characterized by flow cytometry. Renal pathology was reported using the standardized International Society of Nephrology/Renal Pathological Society classification. Inactive lupus nephritis (LN) was defined by the presence of one or more of the following criteria: 24 hrs proteinuria 500 mg/dl or inactive urine sediments (<5 red cells/HPF) and no red cell casts and no leucocyturia (<5 white cells/HPF) and stable serum creatinine.

Results: Mean age of SLE patients was 31.9±10.8 years, and mean disease duration was 7.8±6.2 years. 73% patients had LN and 89% were female. Patients with LN had significantly higher frequency of MP-HMGB1+, no significant differences were found among patients with active versus inactive LN or among patients with proliferative vs non-proliferative LN; MP-HMGB1+ had a moderate positive correlation with disease activity (SLEDAI, r=0.367, p=0.020), anti-C1q antibodies titers (r=0.42, p=001) and 24 hours proteinuria (r=0,33, p=,032), but no correlation was found with activity or chronicity indexes on renal biopsies. A ROC curve for MP-HMGB1+ and renal involvement showed a good discriminative ability (AUC 0.706). A cutoff of 15.7% of MP-HMGB1+ showed the best discrimination threshold with a sensitivity of 63.3% and specificity of 83.3%.

Conclusions: In our cohort of patients with SLE, MP-HMGB1+ was significantly higher in patients with LN and in patients with active disease. Given the multiple implication of HMGB1 in SLE, including the active kidney recruitment of mononuclear phagocytes, we consider that MP-HMGB1+ could be considered as a potential biomarker for LN in SLE patients.

References:

[1] Harris, H. E. et al. HMGB1: A multifunctional alarmin driving autoimmune and inflammatory disease. Nat Rev Rheumatol. 8, 195–202 (2012).

[2] Zickert, A. et al. Renal expression and serum levels of high mobility group box 1 protein in lupus nephritis. Arthritis Res Ther. 20;14(1):R36 (2012).

Acknowledgements: C. Burbano is recipient of a doctoral scholarship from COLCIENCIAS (call 617–2013). The authors are grateful to the grants "Sostenibilidad and Sistema Universitario de Investigaciones, CODI (2013–05–42869836) from Universidad de Antioquia, and to COLCIENCIAS (111565740575)".

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4397

AB0130 MESENCHYMAL STEM CELLS ALLEVIATE SLE THROUGH PROMOTING TREG CELLS BY HLA-G

C. Chen, J. Liang, G. Yao, Z. Zhang, S. Huang, L. Sun. *The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China*

Background: Soluble human leukocyte antigen-G (sHLA-G) is a non-classical HLA class I molecule, exhibiting strong immunosuppressive properties by inducing the differentiation of T regulatory cells (Treg). Mesenchymal stem cells (MSCs) transplantation alleviates disease progression in systemic lupus erythematosus (SLE) patients. However, the underlying mechanisms are largely unknown.

Objectives: The aim of the present study is to explore whether sHLA-G is involved in upregulating Treg cells by MSCs, which contributes to therapeutic effects of MSCs transplantation in SLE.

Methods: The serum sHLA-G levels of SLE patients and healthy controls were detected by ELISA. The percentages of peripheral blood CD4 + ILT2 +, CD8 + ILT2 +, CD19 + ILT2 + cells and Treg cells were determined by flow cytometry. Ten patients with active SLE, refractory to conventional therapies, were infused with MSCs and serum sHLA-G was measured 24 h after infusion. Peripheral blood mononuclear cells (PBMCs) were isolated from SLE patients and co-cultured with UC-MSCs for 3 days at different ratios (50:1, 10:1, and 2:1) with or without anti-HLA-G antibodies, and the frequencies of CD4 + CD25 + Foxp3 + T cells were then determined by flow cytometry.

Results: The concentrations of serum sHLA-G were comparable between SLE patients and healthy controls. However, there was a negative correlation between sHLA-G levels and SLE disease activity index (SLEDAI) scores in active SLE patients (SLEDAI >4). We found that serum sHLA-G levels were negatively correlated with blood urea nitrogen, serum creatinine and 24-hour urine protein in SLE patients. The sHLA-G levels were significantly lower in SLE patients with renal involvement than those without renal involvement. The expression of ILT2 on CD4 + T cells from SLE patients decreased significantly compared to that of healthy controls. A positive correlation between the frequencies of Treg and CD4 + ILT2 + T cells was found in SLE patients. The levels of sHLA-G increased 24 h after UC-MSC transplantation. The frequencies of Treg cells and the expressions of ILT2 on CD4 + Tcells were significantly increased 24 h after transplantations. *In vitro* studies showed that MSCs increased the frequency of Treg cells in SLE patients in a dose-dependent manner, which was partly abrogated by the anti-HLA-G antibody.

Conclusions: Our results suggested that MSCs might alleviate SLE through upregulating Treg cells, which was partly dependent on sHLA-G.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3600

AB0131 PLATELET MICROPARTICLES (PMPS) ARE HIGHER IN PATIENTS WITH SLE COMPARED TO HEALTHY CONTROLS

C.-L.M. Murphy, V. Ripoll-Nunez, C. Periculeous, T. McDonnell, S. Croca, I. Giles, A. Rahman. *Rheumatology, University College London Hospital, London, United Kingdom*

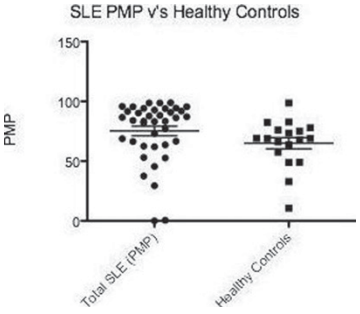
Background: Patients with SLE have an increased risk of cardiovascular disease (CVD) and reasons for this are unknown. Microparticles (MPs) are membrane-bound particles released by many cells, 70–90% are derived from platelets. MPs are a rich source of autoantigens, including DNA and have many functions including thrombosis and inflammation. PMPs can induce foam cell formation and promote adherence of platelets to endothelial lesions. MPs are potentially important in the pathogenesis of autoimmune rheumatic disease and in cardiovascular disease.

Objectives: To determine if EMPs and PMPs are increased in patients with SLE. Our secondary aim was to determine if there was a difference between those with/without subclinical cardiovascular disease and healthy controls.

Methods: Atherosclerotic plaque was previously determined in patients with SLE who had no known history of CVD by carotid and femoral ultrasound scans. Plaque and thickened intima media thickness (IMT) >0.1cm were defined according to the Mannheim Carotid Consensus. Data regarding plaque area, IMT and echolucency were collected. Plasma was stored at -80° at the time of scan. Plasma from n=57; plaque (n=16), no plaque (n=23) and healthy controls (HC) (n=18) were analysed for presence of endothelial and platelet microparticles (EMPs and PMPs), as per protocol. Samples were stained with Annexin V and platelet and endothelial antibodies, CD42a, CD31, CD105 and CD144. MPs were measured using flow cytometry. Statistical analysis was carried out using PRISM.

Results: A total of 57 plasma samples were tested. The average age of those with SLE was 45±12 years. 96% were female. 56% were Caucasian, 18% Asian, 21% Afrocaribbean, 5% other ethnicity. 18% of the SLE patients were smokers. Of the 18 HC, the average age was 37±7 years, 83% were female. 88% were Caucasian and 12% other ethnicity. 11% of the HCs were smokers. PMPs were significantly higher in patients with SLE compared to healthy controls (p=0.025). Patients with SLE without plaque had more PMPs compared to healthy controls

(p=0.037). There was no correlation between age and PMPs. There was no statistical significance between those with SLE with plaque and healthy controls or in EMP levels between the three groups. There was no correlation between EMPs or PMPs with disease activity as measured by BILAG.



Conclusions: PMPs were raised in patients with SLE compared to the healthy controls regardless of whether there was atherosclerotic plaque evident on imaging. Therefore, raised PMPs were associated with SLE itself and did not stratify a subset of patients with subclinical CVD. Further research is required to define whether PMP are important in the pathogenesis of SLE and to clarify the relationship of subclinical CVD in larger cohorts.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5525

AB0132 ANTIPHOSPHOLIPID SYNDROME PATIENTS SHOW AN ALTERED PROFILE OF ENDOTHELIAL PROGENITOR CELLS AND ENDOTHELIAL MICROPARTICLES

C. Barbati, F.R. Spinelli, F. Miranda, F. Ceccarelli, M. Vomero, L. Massaro, T. Colasanti, G. Valesini, C. Alessandri, F. Conti. *Department of Internal Medicine and Medical Specialties, Lupus Clinic, Sapienza University of Rome, Rome, Italy*

Background: Antiphospholipid Syndrome (APS) is an autoimmune disease characterized by recurrent thromboembolic events and pregnancy morbidity associated to the presence of specific serum antibodies directed against membrane phospholipids and proteic co-factors (1). Endothelial dysfunction represents the earlier and reversible stage of subclinical atherosclerosis that characterizes these patients. An altered profile of endothelial progenitor cells (EPCs) and endothelial microparticles (EMPs) could promote endothelial damage (2). Few studies suggested that EMP release is stimulated by circulating anti-phospholipids (aPL). A previous study on EPC reservoir in 7 APS patients showed no difference compared to healthy subjects.

Objectives: Our aim was to evaluate circulating EPCs and EMPs in primary APS patients (PAPS).

Methods: We studied primary APS patients with previous thromboembolic events and sex and age-matched healthy controls (HC). Circulating EPCs was identified by flow cytometry analysis as CD34+/KDR+ positive cells isolated from peripheral blood mononuclear cells (PBMCs); EMPs was obtained by centrifugation of whole blood and quantified by flow cytometry (CD31+/CD41a-). Data were expressed a s mean±standard deviation or median (interquartile range) when appropriate; correlations between EPC and EMP levels with aPL were investigated by Spearman test. P values <0.05 were considered statistically significant.

Results: We enrolled 12 PAPS patients (mean age 44±12 years) and 12 HC. Compared to HC, PAPS patients showed a lower EPC percentage (0.01±0.006% *vs* 0.04±0.003%, p=0.0008) and a higher EMP number (104±80 MPs/microliter *vs* 20±8, $p<0.0001$). EMPs number positively correlated with *anticardiolipin* and *antibeta2 glicoprotein* I, both IgM and IgG ($p<0.05$ and $r>0.7$ for all correlations).

Conclusions: The results of this study suggest that endothelial cells, activated by circulating aPL, release EMPs that can perpetuate the endothelial damage. Moreover, our cohort of APS patients has a reduced number of circulating EPC that could contribute to the impairment of endothelial repair. Both the chronic endothelial damage and the lack of an efficient repair could contribute to the progression of atherosclerosis in PAPS patients.

References:

[1] Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, Derksen RH, DE Groot PG, Koike T, Meroni PL, Reber G, Shoenfeld Y, Tincani A,Vlachoyiannopoulos PG, Krilis SA. International consensus statement on an update of the classification criteria for definiteantiphospholipid syndrome (APS). J. Thromb. Haemost. 2006 Feb;4:295–306.

[2] Bartoloni E, Alunno A, Bistoni O, Caterbi S, Luccioli F, Santoboni G, Mirabelli G, Cannarile F, Gerli R. Characterization of circulating endothelial microparticles and endothelial progenitor cells in primary Sjögren's syndrome: new markers of chronic endothelial damage? Rheumatology (Oxford). 2015 Mar;54:536–44.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3712

AB0133 BLOOD CONCENTRATION OF IMMUNOGLOBULIN BINDING PROTEIN 1 AS A BIOMARKER TO PREDICT LUPUS NEPHRITIS

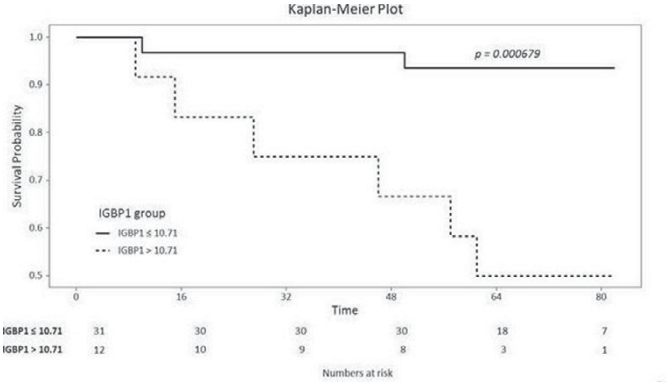
D.-H. Lim[1], E.-J. Lee[2], W.-J. Seo[3], O.C. Kwon[2], S. Hong[2], C.-K. Lee[2], B. Yoo[2], Y.-G. Kim[2]. *[1]Division of Allergy and Rheumatology, Ulsan University Hospital, Ulsan; [2]Division of Rheumatology, University of Ulsan College of Medicine, Asan Medical Center; [3]Division of Rheumatology, Seoul Veterans Hospital, Seoul, Korea, Republic Of*

Background: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease of unknown etiology, and renal involvement is an important factor associated with a high morbidity and mortality. Immunoglobulin binding protein 1 (IGBP1) is a phosphoprotein associated with Ig-α of the B cell receptor complex. Intracellular IGBP1 interacts with the catalytic subunit of protein phosphatase (PP2A) and regulates differentiation, proliferation, and apoptosis of B cells. Functional studies reported that high PP2A levels alter the phenotype and function of T cells in SLE patients. Recently, we reported that urinary IGBP1 levels were associated with the pathologic activity in lupus nephritis (LN). However, the role of plasma IGBP1 (pIGBP1) in the clinical features including the development of nephritis has not been identified in SLE.

Objectives: To determine the role of pIGBP1 as a biomarker related with LN.

Methods: Blood samples of SLE patients were collected between Jan 2009 and Dec 2010 in a tertiary hospital. The levels of pIGBP1 were measured in SLE patients with (n=44) or without (n=39) nephritis, and healthy subjects (n=14). Clinical parameters including baseline characteristics, laboratory data, medications and SLE Disease Activity Index (SLEDAI) were collected from electronic medical record. Activity and chronicity index in renal pathology of LN were scored blindly by a renal pathologist. To identify factors related to the development of LN, Cox proportional hazard regression model and Kaplan-Meier curves were used.

Results: The concentrations of pIGBP1 in SLE patient were higher than those in healthy individual (9.6±8.4 ng/mL vs 4.5±2.4 ng/ml) and positively correlated with SLEDAI score. However, the concentrations were not different between LN and non-nephritis SLE and were not associated with activity index score in renal pathology. During follow-up more than 5 years, nephritis was developed in 8 patients (20.5%) among 39 SLE patients who did not have renal involvement at baseline. Interestingly, levels of pIGBP1 (p=0.002), CRP (p=0.009), or anti-dsDNA antibody (p=0.03) were significantly elevated in 8 patients who developed LN compared to who did not. Kaplan-Meier survival curve showed that initial pIGBP1 (>10.71 ng/mL) as well as anti-dsDNA (>30.7 IU/mL) were associated with high probability of LN development in the future.



Conclusions: Based on our results, high concentration of pIGBP1 could be a valuable marker to represent high SLE activity and a predictor for developing nephritis in SLE patients.

References:

[1] Lee EJ, Hong S, Lim DH, et al. Increased levels of immunoglobulin binding protein 1 are associated with disease activity including renal damage in patients with systemic lupus erythematosus. Presented in 2015 ACR/ARHP Annual meeting.

[2] Sunahori K, Nagpal K, Hedrich CM, et al. The catalytic subunit of protein phosphatase 2A (PP2Ac) promotes DNA hypomethylation by suppressing the phosphorylated mitogen-activated protein kinase/extracellular signal-regulated kinase (ERK) kinase (MEK)/phosphorylated ERK/DNMT1 protein pathway in T-cells from controls and systemic lupus erythematosus patients. J Biol Chem. 2013, 288(30):21936–44.

Acknowledgements: This work was supported by the National Research Foundation of Korea (NRF-2016R1A6A3A11930269).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4292

AB0134 BLOOD LYMPHOCYTE SUBSETS ACCORDING TO THE CLINICAL PROFILE IN SJÖGREN'S SYNDROME

F. Barcelos[1,2,3], C. Martins[3], G. Nunes[3], T. Lopes[3], J. Vaz Patto[1], J. Amaral[4], J.C. Branco[3], L.M. Borrego[3]. *[1]Instituto Português Reumatologia; [2]Hospital CUF Descobertas; [3]Nova Medical School; [4]Faculdade Med Dentária, UL, Lisboa, Portugal*

Background: It has been recently described the occurrence of disturbances in lymphocyte subsets in Sjögren's syndrome (SS) which may reflect B cell hyper activation and a T cell adjuvant role.
Objectives: We aim to characterize circulating lymphocyte subsets in SS patients, according to disease activity and antibody profile.
Methods: We have included in this study 53 SS patients (2002 AECG criteria) of which 22 with >10 years since diagnosis and 31 with <2 years since diagnosis, and 22 healthy controls. Lymphocyte subsets, including follicular (Tfh) and regulatory T (Treg) cells, maturation subsets, plasmablasts (PB) and regulatory B (Breg) cells, were characterized by flow cytometry. Statistical analysis was performed with GraphPad. Significance was considered for $p<0.05$.
Results: Compared to controls, SS patients had lower absolute counts of B (p=0.0337) and T cells (p=0.0012), lower CD4 (p=0.0002) and higher CD8 percentages (p=0.0006), resulting in an increased CD4/CD8 ratio (p=0.0006). Additionally, there was decrease in absolute counts of Tregs (p=0.0008) and Th17 cells (p=0.0005) in SS patients. Moreover, there was a decreased absolute counts ($p<0.0001$) of Tfh cells, identified by CXCR5 expression, though higher levels of IL21$^+$CD4 T cells (p=0.0209) and Tfh1 cells (p=0.0092). SS patients also presented higher % of naïve B cells (p=0.0412), lower % and absolute counts of memory (%, p=0.0161; abs p=0.0002) and unswitched memory (%, p=0.0106; abs p=0.0005) B cells and lower absolute counts (p=0.0001) of switched memory B cells, with higher naive/memory B cell ratios, compared to healthy subjects (p=0.0219). Accordingly, using the Bm1–5 classification, we have found decreased Bm1 (%, p=0.0087; Abs, p=0.0007), eBm5 (Abs, p=0.0005) and Bm5 cells (Abs, p=0.0015) in SS patients. Similar Bm2+Bm2'/eBm5+Bm5 ratios were observed in patients and controls. CD24$^+$CD27$^+$ Bregs were also decreased ($p\leq0.0012$) in SS patients.
SS patients had also an increase in IL21$^+$CD4 T cells, particularly in patients with extra-glandular manifestations (EGM) (n=12), who also presented less Tfh17 cells (p=0.0409) comparing to patients without EGM. PB were decreased in patients with EGM only when compared to controls (p=0.0434).
SSA$^+$ patients (n=36) had more frequently EGM than SSA$^-$, higher ESSDAI score, γ-globulin levels and lower salivary flow. Compared to SSA$^-$ and controls, increased IL21$^+$CD4 T cells were detected in SSA$^+$patients ($p\leq0.0284$), who also had higher Tfh1 cells than controls ($p\leq0.0065$). Lower Bm1 cells ($p\leq0.0305$) were observed in SSA$^+$patients compared to SSA$^-$ and controls, with an increase % of Bm3+Bm4 cells (p=0.011) compared to SSA$^-$.
Conclusions: The immune profile of SS patients has distinctive features, with decreased memory B cell subsets, including CD24$^+$CD27$^+$ Bregs. Moreover, an increased capacity of IL21 secretion by T cells, together with a more prominent Tfh1 signature seem to be the hallmark of SS, particularly in patients with EGM and autoantibody production, suggesting an immune environment prone to proinflammatory processes, in severe patients. Comprehending the immune dynamics in SS may be valuable for diagnosis, follow-up and future therapeutic decisions.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3030

AB0135 PLASMATIC AND URINARY ENDOTHELIAL MICROPARTICLES ARE INCREASED IN PATIENTS WITH LUPUS NEPHRITIS

F. Miranda, C. Barbati, S. Truglia, F.R. Spinelli, F. Ceccarelli, C. Alessandri, G. Valesini, F. Conti. *Dipartimento di Medicina Interna e Specialità Mediche, Reumatologia, Sapienza Università di Roma, Rome, Italy*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease presenting with a wide array of clinical manifestations and incompletely understood pathogenesis. SLE is characterized by alterations in both the innate and adaptive immune system ultimately leading to the loss of immunologic tolerance and occurrence of autoantibodies against nuclear material. Lupus nephritis is one of the most severe features of SLE determining an increase in morbidity e mortality rates. Renal biopsy still represent a fundamental diagnostic and prognostic tool for LN. Therefore, non-invasive surrogate biomarkers of active LN are urgently needed. Circulating, heterogeneous subcellular microparticles (MPs) are released from cells and platelets constitutively and upon cellular activation or apoptosis. Such MPs may reflect the state of their parental cells and tissues, and could serve as markers of pathology. Particularly in SLE, MPs are potential biomarkers and triggers of autoimmunity. Recent studies have demonstrated increased levels of plasmatic EMPs in patients with SLE active disease and their reduction after treatment.
Objectives: The aim of this study was to investigate plasmatic and urinary levels of endothelial microparticles in a cohort of SLE patients with and without renal involvement compared to healthy controls.
Methods: Consecutive SLE patients and sex- and age-matched HC were included in the study. MPs were isolated from plasma and urine and characterized by flow cytometry using AnxV (a probe that binds to the exposed phosphatidilserine - PS) and antibodies against surface markers endothelial cells (CD31+CD41-). Mann-Whitney and Spearman correlation tests were used. A p value <0.05 was considered statistically significant.
Results: Sixty SLE patients (55F:5M, age 41,7±9.6 Y disease duration 149±112 months) and 29 healthy controls were studied. Twenty-eight patients had renal involvement.The total number of plasmatic MPs was lower in SLE patients than HC (p=0.001). In contrast there was no significant difference in levels of EMPs between the two groups. When the patients were divided according to renal involvement, the patients with active lupus nephritis (A-LN) showed lower plasmatic level of EMPs in comparison to inactive LN (I-LN) (p=0.01), while the patients with I-LN had higher levels of EMPs than HC (p=0.002). There was no significant difference of total urinary level of MPs between SLE patients and HC. Urinary levels of EMPs were higher in SLE and in lupus nephritis patients than HC.
Conclusions: The results of the present study show increased urinary and plasmatic levels of EMPs in patients with lupus nephritis in remission. Circulating EMPs have been considered as a potential biomarker of endothelial activation and damage in several autoimmune disorders, and higher EMP levels have been detected in patients with vasculitis and associated with disease activation. According to our results, plasmatic EMPs levels are higher in inactive LN patients than in healthy donors. These results may suggest a potential role of EMP as a biomarker of lupus nephritis
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5003

AB0136 MICROPARTICLES FROM SLE PATIENTS ARE A SOURCE OF INTERFERON-ALPHA

F. Miranda, C. Barbati, F.R. Spinelli, F. Ceccarelli, S. Truglia, C. Alessandri, G. Valesini, F. Conti. *Dipartimento di Medicina Interna e Specialità Mediche, Reumatologia, Sapienza Università di Roma, Rome, Italy*

Background: Systemic lupus erythematosus (SLE) is the prototype of systemic autoimmune disorders. In the late 1970s, increased serum levels of interferon (IFN) were shown for the first time to be significantly associated with SLE and to correlate with disease activity. IFNα is a pleiotropic cytokine that can affect multiple cell types involved in lupus.Plasmacytoid dendritic cells have a special role in the production of IFN and are the main sources of serum interferon. IFN has the potential to dramatically influence the development, progression, and pathogenesis of SLE as it can influence the function and activation state of most major immune cell subsets and function as a bridge between innate and adaptive immunity.Lupus-prone mouse models, indicates that the type I interferon system may play a pivotal role in the pathogenesis of several lupus and associated clinical features, such as nephritis, neuropsychiatric and cutaneous lupus.Circulating microparticles (MPs) are ubiquitous in the blood of healthy individuals, These MPs play an active role in coagulation and intercellular communication and assist in activation or suppression of the immune system, depending on their parental cell origin. Changes in the concentration and/or composition of circulating microparticles have been described in various autoimmune diseases, including rheumatoid arthritis (RA) systemic sclerosis (SSc) and systemic lupus erythematosus (SLE). For SLE, the reported microparticle-related changes remain somewhat inconclusive.
Objectives: To better understand the role of MPs in SLE patients, we analyzed the presence of interferon alpha on MPs surface.
Methods: MPs were isolated from citrate-treated plasma; blood cells were removed by two steps of centrifugation process (2500g for 15min at 20 C two time). The resulting platelet-poor-plasma (PPP), was analyzed by flow cytometry with specific antibody against IFN alpha
Results: 20 consecutive SLE patients (10 with active lupus nephritis) and 10 sex- and age-matched healthy control subjects were included in the study. We found that MPs from SLE patients carry on their surface IFN alpha.Moreover, the percentage IFNalpha + MPs was higher in SLE patients and in lupus nephritis patients than in HC, but there was not significant difference between patients with and without renal involvement.
Conclusions: The results of the present study show for the first time the presence of IFN alpha on MPs surface.We may assume that INF+ MPs derive from dendritic cells. In lupus nephritis patients the increased recruitment of dendritic cells was at tubular interstitial level, with subsequent IFN alpha production. Interestingly, MPs (containing RNA and DNA) could stimulate type I IFN production in plasmacytoid dendritic cells and MPs releasing.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5171

AB0137 ALTERATIONS IN MICRORNA EXPRESSION PROFILES IN PRIMARY SJÖGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS

G. Papp[1], J.-Q. Chen[1], S. Póliska[2], K. Szabó[1], T. Tarr[1], B.L. Bálint[2], P. Szodoray[3], M. Zeher[1]. *[1]Division of Clinical Immunology; [2]Department of Biochemistry and Molecular Biology, University of Debrecen; [3]Centre for Immune Regulation, University of Oslo, Debrecen, Hungary*

Background: MicroRNAs (miRNAs) are single-stranded, endogenous non-

coding small RNAs, ranging from 18 to 25 nucleotides in length. MiRNAs are essential in regulating gene expression, cell development, differentiation and function. Dysregulation in miRNAs expression may contribute to the development of autoimmunity. However, a given miRNA may have hundreds of different mRNA targets and a target might be regulated by multiple miRNAs, thus the characterisation of dysregulated miRNA expression profiles could give a better insight into the development of immunological disturbances in autoimmune diseases.

Objectives: The aim of our study was to examine the changes in miRNA expression profiles in patients with primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE).

Methods: Eight pSS patients, 8 SLE patients and 7 healthy control subjects were enrolled in the investigation. MiRNAs were isolated from peripheral blood mononuclear cells, and expression patterns were determined with Illumina next-generation sequencing technology. Since the immunopathogenesis of pSS and SLE encompasses pronounced B cell hyperactivity along with specific autoantibody production, we paid a special attention on the association between miRNA expression levels and altered peripheral B cell distribution.

Results: In SLE patients 135, while in pSS patients 26 miRNAs showed altered expression. Interestingly, the 25 miRNAs including miR-146a, miR-16 and miR-21, which were over-expressed in pSS patients, were found to be elevated in SLE group, as well. On the contrary, we observed the down-regulation of miR-150–5p, which is a novel and unique finding in pSS. Levels of several miRNAs over-expressed in SLE, were not changed in pSS, such as miR-148a-3p, miR-152, miR-155, miR-223, miR-224, miR-326 and miR-342. Expression levels of miR-223–5p, miR-150–5p, miR-155–5p and miR-342–3p, which miRNAs are potentially linked to B cell functions, showed associations with the B cell proportions within peripheral blood mononuclear cells.

Conclusions: The observed differences in miRNA expression profiles and the better understanding of immune regulatory mechanisms of miRNAs may help to elucidate the pathogenesis of pSS and SLE.

Acknowledgements: This work was supported by the ÚNKP-16–4-III New National Excellence Program of the Ministry of Human Capacities.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3205

AB0138 INTERFERON-GAMMA CHALLENGE OF PBMC FROM PATIENTS WITH LUPUS NEPHRITIS IN REMISSION DECREASES SUPPRESSOR OF CYTOKINE SIGNALING 1 (SOCS1) AND REGULATORY T CELLS (TREGS) AND PROMOTES IMMUNE ACTIVATION

G. Gibor[1], U. Arad[1], J. Wallman[1], J. Ablin[1], V. Aloush[1], I. Kaufman[1], S. Jacky[2], D. Caspi[1], O. Elkayam[1], D. Paran[1], A. Sharabi[3]. *[1]Rheumatology; [2]Tel Aviv Medical Center, Tel Aviv, Israel; [3]Harvard BIDMC, Boston MA, United States*

Background: Interferon-gamma (IFN-γ) plays an important role in the development of lupus nephritis (LN). Regulation of IFN-γ signaling that occurs in disease remission and in active LN is herein addressed.

Objectives: To study the impact of IFN-γ on PBMC obtained from patients with LN in remission as compared to active LN.

Methods: Sixteen patients fulfilling the ACR classification criteria for systemic lupus erythematosus were recruited. All patients had a history of LN of whom 10 were in remission (as defined by EULAR criteria) and 6 had active LN (as defined by SLEDAI-2K or BILAG). Healthy subjects (n=10) were included as a control group. Sera and PBMC were obtained from each individual. Flow cytometry, western blots and real time RT-PCR were used in processing and detection of cell subtypes, protein and mRNA levels. Recombinant human IFN-γ (rhIFN-γ) and anti-IFN-γ neutralizing antibody were used in vitro. Mann-Whitney and student t-tests were used for statistical analysis.

Results: In active LN there was a significant 2-fold increase in $CD4^+CD69^+$ activated T cells as compared to healthy subjects and patients in remission. Reactivity to interferon-gamma receptor was determined by the phosphorylation of its predominant transcription factor, signal transducer and activator of transcription 1 (STAT1) in the cells that were incubated with rhIFN-γ or with media alone. In active LN, 3- and 6-fold increase in pSTAT1 occurred with rhIFN-γ incubation during 24h and 48h, respectively, and healthy subjects responded likewise. In patients in remission, pSTAT1 increase was even higher (by 8- and 10-fold at 24h and 48h, respectively). After 24h incubation with rhIFN-g all groups had elevated (mRNA) expression of SOCS1, but at 48h, it significantly decreased in healthy subjects and in patients in remission by 34% and 50%, respectively. Further, at 24h the frequency of $CD4^+CD127^{low}FoxP3^+$ regulatory T cells (e.g. Tregs) increased by 27–30% in active LN and in healthy subjects, and in remission it was minimally changed. At 48h, the frequency of Tregs significantly decreased in healthy subjects (to baseline levels before rhIFN-γ challenge) and in patients in remission (by 24%, p=0.003). A challenge of PBMC from LN patients in remission with sera (at 1% concentration) derived from patients with active LN resulted in 7.5-fold increase in pSTAT1 expression and 20–30% decrease in Tregs, however, combination of sera and anti-IFN-g neutralizing antibody resulted in 5-fold decrease in pSTAT1 expression and significantly diminished the decrease in Tregs.

Conclusions: In LN in remission a challenge with IFN-γ could lead to immune activation and a risk of flare-up, as it results in a decrease in both SOCS1 and Tregs and a robust STAT1 phosphorylation. In active LN, STAT1 phosphorylation is less diminishing, as both SOCS1 and Tregs are saturated, which could affect their suppressive effectiveness.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4281

AB0139 ROLE OF MUCOSAL-ASSOCIATED INVARIANT T (MAIT) CELLS IN A LUPUS MODEL

G. Murayama[1,2], A. Chiba[2], A. Nomura[2], H. Amano[1], K. Yamaji[1], N. Tamura[1], S. Miyake[2]. *[1]Department of Internal Medicine and Rheumatology; [2]Department of Immunology, Juntendo University School of Medicine, Tokyo, Japan*

Background: Mucosal-associated invariant T (MAIT) cells are innate T cells that are restricted by MHC-related molecule-1 (MR1) and express a semi-invariant TCRα chain: Vα7.2-Jα33 in humans and Vα19-Jα33 in mice. Previously, we have demonstrated that MAIT cells played a protective role against experimental autoimmune encephalomyelitis, an animal model of human multiple sclerosis. We found that MAIT cells are activated in patients with systemic lupus erythematosus (SLE) and that the activation state of MAIT cells correlated with SLE disease activity index (SLEDAI) score, suggesting their association in lupus pathology.

Objectives: We set out to clarify functions of MAIT cells in a lupus model by using $Fc\gamma RIIB^{-/-}$ Yaa mice.

Methods: $Fc\gamma RIIB^{-/-}$ Yaa mice were crossed to MR1 deficient mice lacking MAIT cells, and disease progression was compared between $MR1^{-/-}$ $Fc\gamma RIIB^{-/-}$ Yaa and $MR1^{+/+}Fc\gamma RIIB^{-/-}$ Yaa mice at 1–4 months of age. Serum anti-dsDNA antibody levels were measured and urinary microalbumin were evaluated. At the time of sacrifice, at 4 months of age, the severity of nephritis and dermatitis were assessed by histologically and IgG deposition in skin and glomeruli was measured.

Results: Survival rate was significantly reduced in $MR1^{-/-}$ $Fc\gamma RIIb^{-/-}$ Yaa mice compared with $MR1^{+/+}$ $Fc\gamma RIIb^{-/-}$ Yaa mice. Anti-dsDNA antibody levels were remarkably higher in $MR1^{+/+}$ than $MR1^{-/-}$ $Fc\gamma RIIb^{-/-}$ Yaa mice at 4 months of age. Even though Glomeruli were significantly enlarged both in $MR1^{+/+}$ and $MR1^{-/-}$ $Fc\gamma RIIb^{-/-}$ Yaa mice due to a marked cellular proliferation in glomeruli, the glomerulonephritis score tended to be lower in $MR1^{-/-}$ $Fc\gamma RIIb^{-/-}$ Yaa mice compared with $MR1^{+/+}$ $Fc\gamma RIIb^{-/-}$ Yaa mice. A larger amount of IgG deposition was observed in mesangial area and along glomerular capillary walls in $MR1^{-/-}$ than $MR1^{+/+}$ $Fc\gamma RIIb^{-/-}$ Yaa mice. However, $MR1^{-/-}$ $Fc\gamma RIIB^{-/-}$ Yaa mice showed exacerbated inflammation in the skin lesions. There was a high degree of inflammatory cells infiltration into the skin and a significant worsening of dermatitis score in $MR1^{-/-}$ $Fc\gamma RIIb^{-/-}$ Yaa mice compared to $MR1^{+/+}Fc\gamma RIIb^{-/-}$ Yaa mice.

Conclusions: These data suggests that MAIT cells exhibit dual roles in lupus pathogenesis. MAIT cells enhance autoantibody production and the disease severity of nephritis, but have a suppressive effect on dermatitis. Further studies are under going to uncover the mechanisms by which MAIT cells are involved in each target tissues.

References:

[1] Croxford JL, et al. Invariant V(alpha)19i T cells regulate autoimmune inflammation. Nat Immunol. 2006; 7(9): 987–94.

[2] Chiba A, et al. Mucosal-associated invariant T cells promote inflammation and exacerbate disease in murine models of arthritis. Arthritis Rheum. 2012; 64(1): 153–61.

[3] Kawano S, et al. Phenotype conversion from rheumatoid arthritis to systemic lupus erythematosus by introduction of Yaa mutation into FcγRIIB-deficient C57BL/6 mice. Eur J Immunol. 2013; 43(3): 770–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3086

AB0140 LUPUS-PRONE SLAM HAPLOTYPE EXERTS MONOCYTOSIS AND DEVELOPS SPECIFIC PHENOTYPE OF AUTOIMMUNE DISEASE INTRODUCED BY YAA MUTATION

H. Amano[1], K. Nishikawa[2], Q. Lin[3], S. Kawano[1], K. Yamaji[1], S. Hirose[3], N. Tamura[1]. *[1]Department of Internal Medicine and Rheumatology; [2]Department of Pathology, Juntendo University School of Medicine, Tokyo; [3]Department of Biomedical Engineering, Toin Human Science and Technology Center, Toin University of Yokohama, Yokohama, Japan*

Background: We previously obtained a 129-derive FcγRIIB-deficient C57BL/6 (B6) congenic strain of mice, which spontaneously developed severe rheumatoid arthritis (RA)[1]. The introduction of the *Yaa* (Y-linked autoimmune acceleration) mutation, which is a consequence of a translocation from the telomeric end of the X chromosome containing the *Tlr7* gene onto the Y chromosome, to the FcγRIIB-deficient B6 mice (B6.FcγRIIB-/-. *Yaa*) developed lupus like nephritis but not RA[2].

Objectives: By extensively backcrossing 129-based FcγRIIB-deficient mice to B6 mice, we established wildtype FcγRIIB and 129-derive autoimmune-prone SLAM haplotype ($Slam^{129}$). We examined the phenotype of $Slam^{129}$ mice, and also $Slam^{129}$.*Yaa* mice by introducing *Yaa* mutation to these mice.

Methods: We analyzed peripheral blood monocyte subset and also serum autoantibodies as well as immunohistopathological findings of kidneys and lungs.

Results: $Slam^{129}$ mice showed age-associated monocytosis with marked expan-

sion of Gr-1 negative monocytes, also perivascular inflammatory cell infiltration in lungs. But they did not show any pathogenic autoantibodies. When introducing *Yaa* mutation, *Slam*^{129}.*Yaa* mice showed significant increase the serum levels of anti-RNP antibodies and anti-Sm antibodies. Although they showed significant increase of serum levels of IgM class anti-dsDNA antibodies, they did not show the elevation of IgG class anti-dsDNA antibodies. Also they developed nephritis but the pathological score was significantly lower than B6.FcγRIIB-/-.*Yaa* mice.
Conclusions: Autoimmune-prone SLAM haplotype plays a role for Gr-1 negative monocytosis and *Slam*^{129}.*Yaa* mice developed specific lupus phenotype with elevation of anti-RNP and anti-Sm autoantibodies.
References:
[1] Sato-Hayashizaki A, Ohtsuji M, Lin Q, Hou R, Ohtsuji N, Nishikawa K, Tsurui H, Sudo K, Ono M, Izui S, Shirai T, Takai T, Nishimura H, Hirose S. Presumptive role of 129 strain-derived Sle16 locus in rheumatoid arthritis in a new mouse model with Fcγ receptor type IIb-deficient C57BL/6 genetic background. Arthritis Rheum. 63(10):2930–8, 2011.
[2] Kawano S, Lin Q, Amano H, Kaneko T, Nishikawa K, Tsurui H, Tada N, Nishimura H, Takai T, Shirai T, Takasaki Y, Hirose S. Phenotype conversion from rheumatoid arthritis to systemic lupus erythematosus by introduction of Yaa mutation into FcγRIIB-de ficient C57BL/6 mice. Eur J Immunol. 43:1–9, 2013.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4175

AB0141 LOW DOSE IL-2 CIRCUMVENTED MTOR SIGNALING IN T CELLS IN THE TREATMENT OF SLE

J. He[1], X. Sun[1], J. Li[1], R. Zhang[1], D. Yu[2], Z. Li[1]. *[1]Peking University People's Hospital, Beijing, China; [2]School of Biomedical Sciences, Monash University, Melbourne, Australia*

Background: mTOR signaling is proved to be one of the most important pathway in the pathogenesis in SLE. However, in patients with SLE, whether mTOR pathway can be activated by low-dose IL-2 remained unclear.
Objectives: To clarify the effects of low-dose IL-2 therapy on mTOR signaling in the treatment of SLE.
Methods: Eight patients with active SLE were treated with 1 million IU IL-2. Phophrylation of S6 ribosomal protein (S6RP), AKT and pSTAT5 were measured before and after the first 2 week of low-dose rhIL-2 administration. C57BL/6 mice (male, 8–12 weeks old) were intraperitoneally immunized with SRB and followed by administration of different doses (low:10,000 IU and hight:300,000 IU) of rhIL-2 or PBS from day 3 to day 9. The ratio of Th1, Th2, Tfh, Th17, Tfh and Treg as well as the level of S6RP, AKT and pSTAT5 were assayed by flow cytometry
Results: Low-dose IL-2 was efficient and well tolerated in active SLE, and was associated with expansion of Treg cells ($p<0.001$) and reductions of Tfh and Th17 cells ($p\leq0.001$). No significant change of pS6RP and pAKT was observed. On the other hand, there was a signficiant induction of the activation of STAT5. In mouse studies, low-dose IL-2 inhibited the differentiation of Th17 cells and Tfh cells. Comparing with high dose IL-2 group, there was no significantly increased mTOR activity after low-dose IL-2 administration.
Conclusions: Low-dose IL-2 might circumvent mTOR pathway and play a regulatory role in the T cells in lupus
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3482

AB0142 IGM ANTIBODIES AGAINST PHOSPHORYLCHOLINE PROMOTE POLARIZATION OF T REGULATORY CELLS FROM PATIENTS WITH ATHEROSCLEROTIC PLAQUES, SYSTEMIC LUPUS ERYTHEMATOSUS AND HEALTHY DONORS: A NOVEL IMMUNOLOGICAL CONCEPT

J. Sun, S. Lundström, B. Zhang, R. Zubarev, J. Steuer, P. Gillgren, M. Rahman, S. Ajeganova, A. Liu, J. Frostegård. *Karolinska Institutet, Stockholm, Sweden*

Background: IgM antibodies against Phosphorylcholine (anti-PC) are negatively associated with atherosclerosis, cardiovascular disease (CVD) and systemic lupus erythematosus (SLE) where the risk of CVD and atherosclerosis is very high. We here study effects of IgM anti-PC on Th17 and T regulatory cells (Tregs).
Objectives: Immunomodulation in atherosclerosis and SLE could have a huge impact on disease prevention and treatment.
Methods: Mononuclear leukocytes were isolated from peripheral blood (PBMC) obtained from healthy blood donors, from six SLE patients with age- and sex-matched controls and from symptom-giving human atherosclerotic plaques. The proportion of Th17 ($CD4^+CCR6^+$) and Treg ($CD4^+CD25^+CD127^{dim/-}$) cells were determined by flow cytometry in $CD4^+$T cells after 6 days culture with Th17 or Treg-polarizing cytokines, with PMA and Ionomycin stimulation. IgM anti-PC were extracted from total IgM, with flow-through IgM as controls. Dendritic cells (DC) were differentiated from PBMC. Antibody peptide/protein characterization was done by a proteomics de novo sequencing approach.
Results: IgM anti-PC increased significantly the proportion of Tregs from healthy donors, SLE patients and from atherosclerotic plaque cells while control antibodies did not. T cells from SLE patients had a significantly lower proportion of Tregs and higher proportion of Th17 cells as compared to matched controls. IgM anti-PC but not control antibodies significantly reduced production of IL-17 and TNF-alpha in cell culture from SLE patients and from atherosclerotic plaque cells. IgM anti-PC interacted with CD40 and kept DCs in an immature stage potentially being tolerogenic. We identify differences on the IgM peptide expression level in anti-PC compared to control antibodies.
Conclusions: IgM anti-PC increase Tregs and having low levels could contribute to both SLE and atherosclerosis (and CVD) and could thus represent a novel underlying mechanism in these conditions. This finding could also have therapeutic implications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5076

AB0143 IMMUNOMODULATION FOLLOWED BY QUANTITATIVE TRANSCRIPTIONAL PROFILING TO CHARACTERIZE THE FUNCTIONAL ROLE OF THE SJÖGREN'S-ASSOCIATED NCRNA AC092580.4

J.A. Ice, I. Adrianto, A. Rasmussen, M. Joachims, A. Johnston, C. Montgomery, K. Sivils, C.J. Lessard. *Arthritis & Clinical Immunology, Oklahoma Medical Research Foundation, Oklahoma City, United States*

Background: Despite concerted efforts to characterize dysregulated transcriptional responses observed in Sjögren's syndrome and related autoimmune disorders (both in whole blood and target tissues), the functional roles of non-coding RNAs (ncRNAs), many of which have been identified as critical players in transcriptional regulation of disease, remain poorly defined.
Objectives: In the present study, we describe ongoing efforts to functionally characterize the upregulated ncRNA identified by RNA-seq and *in silico* approaches, *AC092580.4* (FC=2.54), which we hypothesize plays a role in T and NK cell responses.
Methods: To study the immunomodulation of the ncRNA *AC092580.4*, we carried out a time-course experiment (0–36 hrs) using either PMA/I (500x dil) or universal Type I Interferon. Relative gene expression changes were determined using the Livak method by qPCR using optimized primers for *GZMA* and *AC092580.4* normalized to *GAPD*. Healthy PBMCs were subjected to stimulation by PHA (1mg/mL; 3 days), PMA/I (500x dil; 3 days), or anti-CD3/CD28 ($50uL/1x10^6$cells; 1 day). An average 150-bp RNA-seq reads were generated for each sample; alignment was carried out using STAR (hg38) and comparisions of stimulated vs unstimulated cells were done using DEseq. Pearson's correlation (r) was calculated for all 3,748 differentially expressed (DE) transcripts to identify transcripts co-expressed with *AC092580.4*.
Results: Of the transcripts showing DE in our SS RNA-seq study, we identified 8 as having significantly correlated expression with *AC092580.4* in the SS^{Ro-} expression matrix ($r>0.70$ or <-0.65). To understand the possible effects of immunomodulation on relevant cells, we stimulated HSB-2 cells with PMA/I at various time points and assessed *AC092580.4* expression by. We observed downregulation of *AC092580.4* and the co-expressed transcript *GZMA* by PMA/I (trough: 12–16hrs; FC=0.09) followed by slow recovery at 36hrs (FC=0.59). To characterize these transcriptional changes further, we performed RNA-seq using healthy PBMCs exposed to various T cell stimulants. We observed marked upregulation of both *AC092580.4* and *GZMA* at 24/36hrs by all stimulants (FC=4.89–5.98). Other transcripts showed variable responses. *CAV2* is upregulated by PMA/I, but downregulated by CD3/CD28 and PHA. Stimulation by PHA leads to upregulation of *CD3D* (FC=1.56) and *SNRPD1* (FC=3.28) with little change in *RPL36A* (FC=1.09). Stimulation by CD3/CD28 similarly leads to upregulation of *CD3D* (FC=2.85) and *SNRPD1* (FC=10.04), but clear downregulation of *RPL36A (*FC=0.64*)*. We assessed *AC092580.4* expression in HSB-2 cells exposed to I IFN and observed initial upregulation (6hrs, FC=1.46) followed by gradual downregulation (36hrs, FC=0.18).
Conclusions: In the present study, we have initiated stimulation studies with to understand the immune relevance of *AC092580.4* and co-expressed targets. *AC092580.4* shows transcriptional induction by potent inducers of T cell responses (PMA/I, PHA, CD3/CD28) but is downregulated by type I IFN. Transcripts showing co-expressed with *AC092580.4* by whole-blood RNA-seq show divergent expression patterns according to the specific stimulus, suggesting a complex regulatory network governing dysregulated T and NK responses.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6872

AB0144 PREGNANCY OUTCOMES IN IMMUNE-MEDIATED RHEUMATIC DISEASES: A RETROSPECTIVE LONGITUDINAL STUDY IN A TERTIARY HOSPITAL

J. Bernardo[1], I. Brito[1], H. Guimarães[2], M. Guimarães[3], R. Fonseca[1]. *[1]Rheumatology; [2]Pediatrics; [3]Gynecology and Obstetrics, Faculty of Medicine of the University of Porto, Porto, Portugal*

Background: Autoimmune rheumatic diseases such as systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome (APS) and Sjögren's syndrome (SS) are part of a clinical spectrum eligible to affect women in child-bearing ages, increasing pregnancy morbidity and affecting neonatal outcomes. Pregnancy complications include the teratogenic risk from immunosuppressive drugs, pregnancy-related disease flares, recurrent pregnancy loss, premature

delivery, intrauterine growth restriction (IUGR) and preeclampsia. Conceiving in periods of low disease activity helps to reduce these complications.
Objectives: This project aims to describe the occurrence of pregnancy complications among women with immune-mediated rheumatic diseases and to study the associated clinical factors.
Methods: A retrospective longitudinal study was performed including consecutive pregnant women with immune-mediated rheumatic diseases seen in a multidisciplinary group for autoimmune diseases during pregnancy, in a tertiary hospital, between January 2010 and December 2015. Clinical and demographic data, as well as and pregnancy outcomes, were collected through consultation of clinical files. The factors associated with pregnancy manifestations (premature delivery, flares during pregnancy, recurrent pregnancy loss and foetal growth restriction) were studied using Mann-Whitney, qui-square and fisher tests (SPSS 24.0). Significance level was set as <0.05.
Results: We included 151 gestations from a total of 140 women with a mean age of 32,5±4,4 years; 4 gestations were twin pregnancies. Within these 151 gestations, 54 (35,8%) women had SLE, 17 (11,3%) had Sjögren's syndrome, 17 (11,3%) had rheumatoid arthritis, 41 had APS (27,2%), 11 (7,3%) had Behçet's disease, 4 (2,6%) had systemic sclerosis, 8 (5,3%) had mixed connective tissue disease and 16 (10,6%) had other immune-mediated diseases. 35 (23,2%) had anti-SSA/La antibodies, 18 (11,9%) had anti-SSB antibodies, 6 (4,0%) had anti-URNP antibodies and 43 (28,5%) had anti-nuclear antibodies. Seven (4,6%) of the women developed gestational diabetes and 4 (2,6%) developed gestational hypertension. Furthermore, 54 (35,8%) women had had previous miscarriages. Prematurity occurred more frequently among neonates with IUGR (53.8% vs 46.1%; p=0.04), and was associated with gestational diabetes (21.4% vs 2.9%; p=0.018). It also occurred more frequently in multiple pregnancies (75% vs 16.4%; p=0.001), mothers taking glucocorticoids (28.6% vs 9.2%; p=0.003) and active rheumatic disease at conception (23% vs 6.8% p=0.03). No statistically significant differences were observed in the occurrence of different pregnancy complications among different diseases or in presence of different antibodies.
Conclusions: Our study proved a link between immune-mediated rheumatic diseases and specific pregnancy outcomes such as prematurity and IUGR. Outcomes were worse when taking glucocorticoids, when gestational diabetes were developed and when conception occurred in a period of active disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6095

AB0145 TLR4 SIGNALING PATHWAY MEDIATES THE SENESCENCE OF BONE MARROW- MESENCHYMAL STEM CELLS FROM SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

J. Ji, Y. Wu, X. Kong, Z. Zhang, Z. Gu. *Department of Rheumatology, Affiliated Hospital of Nantong University, Nantong, China*

Background: Previous studies of our research group revealed the senescence of bone marrow-mesenchymal stem cells from systemic lupus erythematosus patients,which participated in the development of SLE. "Inflammatory microenvironment" played a very important role in cellular senescence. In the preliminary experiments, we discovered the level of HMGB1 in serum and Peripheral blood mononuclear cells from SLE patients was higher than those of The healthy control group.
Objectives: The aim of this study was to investigate whether HMGB-1 can lead to senescence BM-MSCs from SLE patients and its possible mechanism.
Methods: Tewelve female SLE patients and healthy subjects were enrolled in the study. All patients were females, and their age distribution was similar to that of the cases. All BM-MSCs were Isolated by density gradient centrifugation. Western Blotting and immunofluorescence were used to distinguish the difference of expression and localization of TLR4 signaling pathway between normal group and SLE group. Different concentrations (0.01,0.1,1,10ug/ml) of HMGB-1 (the endogenous ligand of TLR4) stimulated normal BM-MSCs, then detecting expression of TLR4 signal by WB, observing the activity of β-gal of cells, the changes of cytoskeletal structure by F-actin staining and the distribution of cell cycle by flow cytometry. We used small interfering RNA (siRNA) to interfere the expression of TLR4.
Results: BM-MSCs from SLE patients showed prominent features of senescence, characterized by impaired capacities of proliferation, increased SA-β-gal activity, and disordered cytoskeleton distribution, and abnormal activation of TLR4 signaling transduction, high level of phosphorylated p65. IκBα. After stimulation of HMGB1 in normal MSCs,TLR4 signaling was activated. And, the cell volume and the number of SA-β-gal positive in SLE BM-MSCs was increased. The organization of cytoskeleton was neatly disordered. The rate of cell proliferation was decreased. The inhibitors of HMGB-1 and small interfering RNA (siRNA) of TLR4 can significantly reverse the senescence.
Conclusions: HMGB-1 binded to TLR4, and by activating MyD88/IRAK/TRAF pathway, promoted NF-κB signal transduction, thereby affected the expression of cell cycle-related proteins, and then resulted in senescence of MSCs from SLE patients.
Acknowledgements: This research was supported by grants from the National Natural Science Foundation of China (81471603).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5375

AB0146 INVOLVEMENT OF PERIPHERAL CD8 T CELL SUBSETS IN SYSTEMIC LUPUS ERYTHEMATOSUS

J. Kikuchi[1], M. Ushikubo[1,2], S. Saito[1], K. Yamaoka[1], K. Sugahara[3], K. Chiba[3], T. Takeuchi[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine; [2]Department of Connective Tissue Diseases, National Tokyo Medical Center, Tokyo; [3]Sohyaku. Innovative Research Division, Mitsubishi Tanabe Pharma Corporation, Kanagawa, Japan*

Background: Although the mainstream of pathogenesis of systemic lupus erythematosus (SLE) is thought to be interactions between antigen-presenting cells like dendritic cells, helper T cells, B cells and cytokines, previous reports suggested CD8 T cells also involve in the pathogenesis of SLE[1,2]. However the associations between subsets of CD8 T cells and clinical manifestations remains unclear.
Objectives: We conducted standard immunophenotyping analysis with peripheral blood from SLE patients and focused on CD8 T cell subsets to elucidate the association with clinical phenotype and serological markers.
Methods: Peripheral blood was obtained from inactive SLE patients and healthy subjects as controls and also from active SLE before and 3 months after treatment. CD8 T cell subsets were measured by flow cytometry with fresh whole blood samples.
Results: Thirty-four active SLE patients and 38 inactive patients and 22 healthy controls (HCs) whose age and sex were matched with those in SLE patients were enrolled. Mean SLE disease activity index (SLEDAI) was 14.2 and 1.8 in active and inactive patients, respectively. Among CD8 T cell subsets, the proportion of HLA-DR+ cells was significantly higher in SLE patients than HCs and positively correlated with SLEDAI (p=0.016, rho =0.283), and was also higher in patients with nephritis than patients without nephritis (p=0.074), though it did not reach statistical significance. The proportion of naive CD8 T cells positively correlated with the titer of anti-dsDNA antibody (p=0.011, rho =0.30) and C1q immune complex levels (p=0.043, rho =0.25), and negatively correlated with serum complement levels (p=0.019, rho = -0.34). The proportion of central memory CD8 T cells (Tcm) negatively correlated with SLEDAI ($p<0.001$, rho = -0.43), the titer of dsDNA antibody ($p<0.001$, rho = -0.51) and C1q immune complex levels ($p<0.001$, rho = -0.44), and positively correlated with serum complement levels ($p<0.001$, rho =0.49), and was lower in the patients with nephritis (p=0.041), skin rash ($p<0.001$), and fever (p=0.002) than the patients without them. The proportion of effector memory CD8 T cells (Tem) was lower in SLE and negatively correlated with the titer of anti-dsDNA antibody (p=0.028, rho = -0.26). Sixteen active patients were treated with prednisolone (PSL) 50mg (mean) with concomitant immunosuppressant; eight were treated with cyclophosphamide. Mean SLEDAI decreased from 15.9 to 3.9 at 3 months after the treatments. The proportion of naïve CD8 T cells significantly decreased (p=0.003), and the proportions of HLA-DR+ cells and Tem increased at 3 months (p=0.011 and p=0.007, respectively). The proportion of Tem increased and negatively correlated with SLEDAI only with those who were treated with cyclophosphamide.
Conclusions: Pathological state of SLE positively correlated with the proportion of naïve CD8 T cells and negatively correlated with the proportion of Tem and these subsets were affected by treatment with PSL and immunosuppressant particularly cyclophosphamide. These results indicate that CD8 T cells are involved in pathophysiology and could potentially become a biomarker or a treatment target in SLE patients.
References:
[1] Blanco P, et al. Arthritis Rheum 2005; 52: 201–11.
[2] Kim JS, et al. Rheumatology (Oxford) 2012; 51: 1587–94.
Disclosure of Interest: J. Kikuchi: None declared, M. Ushikubo: None declared, S. Saito: None declared, K. Yamaoka: None declared, K. Sugahara Employee of: Mitsubishi Tanabe Pharma Corporation, K. Chiba Employee of: Mitsubishi Tanabe Pharma Corporation, T. Takeuchi: None declared
DOI: 10.1136/annrheumdis-2017-eular.4948

AB0147 THE EFFECT OF TREATMENT WITH HYDROXYCHLOROQUINE ON SOLUBLE TISSUE FACTOR LEVELS IN PATIENTS WITH ANTIPHOSPHOLIPID ANTIBODIES AND ANTIPHOSPHOLIPID SYNDROME WITH AND WITHOUT UNDERLYING SYSTEMIC LUPUS ERYTHEMATOSUS

K. Schreiber[1,2], K. Breen[1], K. Parmar[1], B.J. Hunt[1]. *[1]Centre for Thrombosis and Haemostasis, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; [2]Department of Rheumatology, Copenhagen University Hospital, Copenhagen, Denmark*

Background: Antiphospholipid syndrome (APS) is characterized by venous, microvascular and/or arterial and/or obstetric morbidity (obstetric APS) in patients who are persistently positive for antiphospholipid antibodies (aPL)[1]. The mainstay of treatment is based on anticoagulation therapy; however, increasing interest is currently received by the antimalarial hydroxychloroquine (HCQ). The use of HCQ has been associated with a reduced risk of thrombosis but HCQ's antithrombotic mechanism of action is unclear particularly in patients with aPL and APS.
Objectives: The aim of our study was to assess soluble tissue factor (TF) levels in HCQ naïve-patients with persistent aPL or APS at baseline and 12 weeks after commencing HCQ. We hypothesise that HCQ lowers levels of soluble TF.

Methods: Twenty- two individuals with APS with or without other associated autoimmune disease (20 females, two males, median age 55 (range 18–70) years) had blood samples taken before and 12 weeks after starting HCQ 200mg. Plasma was stored at -80°C and thawed to measure TF using Imubind TF kit (Invitech Ltd, Cambridgeshire, UK). The assay was performed according to the manufacturer's instructions. Patient characteristics are outlined in table 1. Statistical analysis was performed using SPSS Version 22. For continuous normally distributed data a two-tailed student's paired t-test was performed. A value of p=0.05 was considered as significant. There are no previous data in this area, so we were unable to do a power calculation to work out study size. Our study is therefore a pilot study.
Results: Soluble TF levels were above our normal range (40–300 pg/ml) prior to the commencement of HCQ and were significantly reduced (pre level mean (SD) 401.8 (152.8) pg/ml versus post 300.9 (108) pg/ml (p=0.010).

Table 1: Demographic data

Variables	APS (N=22)
Age: median (range)	47 (18-69)
Sex (female:male)	20:02
Ethnicity (white:asian:black)	(20:1:1)
aPL subtype	
LA* positive	19
IgG or IgM aCL positive (>99th centile)	5
IgG or IgM anti-Beta2GPI antibody positive (>99th centile)	0
aCL and anti-Beta2GPI antibody positive (>99th centile)	0
aCL antibody and LA* positive (>99th centile)	3
Anti-Beta2GPI antibody and LA* positive (>99th centile)	0
aPL complication	
Thrombosic APS	
Previous arterial thrombosis	10
Previous venous thrombosis	7
Previous arterial and venous thromboses	4
Obstetric APS	
Previous recurrent 1st trimester pregnancy loss	2
Previous pre-eclampsia	1
Previous intrauterine growth restriction	1
Previous stillbirth	3
Treatment	
Warfarin	14
Heparin	0
Aspirin	3
Autoimmune profile	
Antinuclear antibodies (ANA)	10
Extractable nuclear antibodies (ENA)	2
Double stranded DNA antibodies (dsDNA)	1

Key: aCL - anticardiolipin; anti-Beta2GPI - anti-Beta2glycoproteinI; LA - lupus anticoagulant. *LA detected by either DRVVT, dilute aPTT or TSVT

Conclusions: There was a significant reduction in soluble TF levels in this patient cohort of patients with apL and APS after commencing HCQ. Our previous work has shown that HCQ has not affected complement turnover, VEGF levels, thromboelastometry findings or CRP levels. Our findings of a reduction of soluble TF levels in aPL positive patients after the commencement of HCQ maybe a key mechanism by which HCQ reduces thrombotic risk. Further studies of a larger patient cohort are required to confirm our observation.
References:
[1] Miyakis, S., et al., International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost, 2006. 4(2): p. 295–306.
Disclosure of Interest: K. Schreiber Shareholder of: Novo Nordisk, Grant/research support from: educational support from Daiichi Sankyo, K. Breen: None declared, K. Parmar: None declared, B. Hunt: None declared
DOI: 10.1136/annrheumdis-2017-eular.4746

AB0148 INDUCTION OF HO-1 EXPRESSION IN MONOCYTES MIGHT PREVENT KIDNEY DAMAGE IN LUPUS NEPHRITIS (LN)

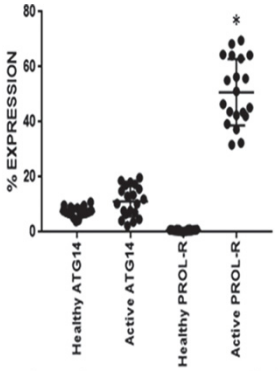
L. Cuitino[1], J. Obreque[1], P. Gajardo-Meneses[1], N. Crisostomo[1], A. Torres[1], A.M. Kalergis[2], C. Llanos[1]. [1]*Departamento de Inmunologia Clinica y Reumatologia;* [2]*Millennium Institute on Immunology and Immunotherapy, Departamento de Endocrinologia, Pontificia Universidad Catolica de Chile, Santiago, Chile*

Background: Systemic lupus erythematous (SLE), is an autoimmune disease characterized by autoantibody synthesis and inflammation. During disease course, up to 70% of SLE patients will develop LN. Emerging evidence has demonstrated that infiltrating monocytes and macrophages are associated with LN pathogenesis. We have previously demonstrated that HO-1, a haem-degrading enzyme with anti-inflammatory properties is decreased in peripheral monocytes of SLE patients. Therefore, we decided to explore the contribution of HO-1 expression to LN pathogenesis.
Objectives: To explore the role of HO-1 in modulating innate immunity through a cytoprotective effect in monocytes of LN nephritis patients. Accordingly, we examined the expression of HO-1 in circulating monocytes, and the effect of HO-1 induction in reactive oxygen species (ROS) production and the phagocytic activity of monocytes from peripheral blood of LN patients and healthy controls (HC).
Methods: SLE patients with proliferative LN confirmed by renal biopsy (Class III, IV or V ISN/RPS) were recruited at Hospital Clinico of PUC. All individuals signed an informed consent form. Monocytes were purified from peripheral blood mononuclear cells (PBMCs) of LN patients and HC using pan-monocytes MACS kit. Subpopulations of monocytes and HO-1 expression were measured by FACS. ROS was determined using CellRox Kit. The phagocytic ability of monocytes was assessed by FACS and the total phagocytosis was calculated as the percentage of cells with engulfed beads.
Results: We found that monocytes from LN patients show significant differences when compared to HC in all the parameters analyzed. The percentage of CD16+ inflammatory monocytes was higher in LN patients (6.72±0.98%) compared to HC (4.07±0.48%) ($p<0.05$). HO-1 protein expression is decreased in circulating LN monocytes (4789±911 vs 1572±481, p=0.005). Baseline levels of ROS are elevated in LN monocytes with similar values that the ones found in monocytes from HC treated with a ROS inducer (HC: 3509±584; HC+TBHP: 8436±1909; LN: 8355±1714). Furthermore, phagocytic activity is increased in LN monocytes (77.97±3.31%) compared to HC (39.63±2.75%). Moreover, our preliminary data indicate that HO-1 induction, using cobalt protoporphyrin (CoPP), leads to downregulation of ROS production in LN (~60%) and HC (~40%) leaving both in similar levels of ROS production. In addition, phagocytic activity is also decreased in LN and HC monocytes in the presence of CoPP (~30%).
Conclusions: Decreased HO-1 expression in circulating monocytes of LN patients leads to higher ROS production and phagocitic activity. ROS level and phagocytosis are reduced when we induce HO-1 expression with CoPP. We propose that HO-1 induction might exert a cytoprotective role in LN by regulating innate immunity. FONDECYT N° 1150173.
Acknowledgements: We would like to extend our appreciation to all the volunteers that participated in this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6428

AB0149 PROLACTIN AND AUTOPHAGY IN SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL SIGNIFICANCE OF CORRELATION BETWEEN PRL-R+ (RECEPTOR), CD19+, ATG14+, AND CD25+ EXPRESSION ON B AND T REGULATORY CELLS

L. Jara[1], E. Zurita[2], A. Durán[3], G. Medina[1], C. Arroyo[4], M.A. Saavedra[5], A. Sanchez[5], R. Bustamante[5], A. Rodriguez[3]. [1]*Direction of Education and Research, Instituto Mexicano del Seguro Social, Hospital de Especialidades Centro Medico la Raza;* [2]*Escuela Nacional de Ciencias Biologicas, Institutu}o Politecnico Nacional;* [3]*Escuela Nacional de Ciencias Biologicas, Instituto Politecnico Nacional;* [4]*Banco de Sangre Hospital de Especialidades Centro Medico la Raza;* [5]*Rheumatology Department, Instituto Mexicano del Seguro Social, Hospital de Especialidades Centro Medico la Raza, Mexico City, Mexico*

Background: Systemic Lupus Erythematosus (SLE) is a prototype of autoinmune diseases with excessive anti-nuclear autoantibodies production. B cells activation with immune complex formation is the main characteristic of SLE with abnormalities in immune cells, dysregulation of apoptosis, and defects in the clearance of apoptotic materials. Autophagy, a highly conserved protein degradation pathway, is essential for removing protein aggregates and misfolded proteins in cells and its defects contributes to SLE pathogenesis. On the other hand, multiple evidences in humans and experimental models suggest that prolactin (PRL) is associated with active SLE and participates in the immune dysregulation, and one of the mechanisms of PRL action is the inhibition of apoptosis.
Objectives: Analyze the relationship between PRL receptors (PRL-R) on B cells and markers of autophagy on T regulatory cells and the association, if any, with clinical characteristics of SLE.



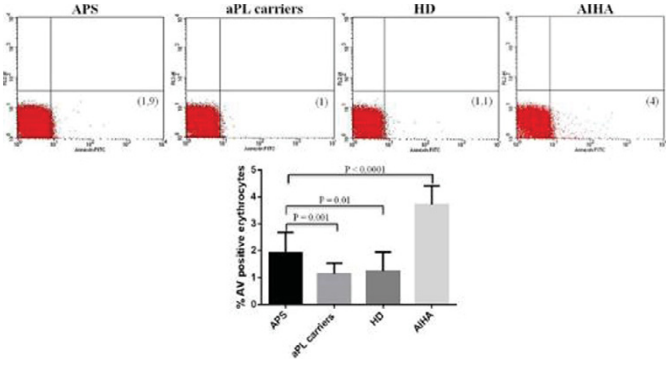
Expresssion of PRL-R and ATG14 in active SLE patients and healthy controls. *p=0.026 Dunn´s multiple comparisons test.

Methods: The expression of PRL-R on B cells CD19$^+$, and autophagy-related key regulator protein ATG14$^+$, on T regulatory cells CD25$^+$, were measured by flow cytometry, and expressed in percentages of SLE patients (1997, ACR criteria), and healthy controls. Active SLE was considered by SLEDAI ($\geq$4). The organs affected and treatments were evaluated.
Results: A total of 40 SLE patients and 20 healthy controls were included. Mean age of patients and controls was 30.67±4.16. Mean duration of disease was 6±4.6 years. Twenty patients were active (SLEDAI 8.45±1.9) and of these, lupus glomerulonephritis was observed in 13 patients (65%). The expression of PRL-R on B cells of active SLE was higher than in inactive SLE (50.5% vs 26.5%). In active SLE especially in patients with glomerulonephritis, the mean amount of PRL-R on B cells/ml was 6,645/ml (range 3167–6957). In contrast, patients with inactive SLE, had a low amount of PRL-R, 522.5/ml (range 15–895). In the relation of autophagy, the mean expression of ATG14$^+$ in 20 active SLE patients was 11.19% in comparison with inactive SLE patients, 7.13%, (p=0.04), and in healthy donors, 7.445% (p=0.0281).
Conclusions: Our study suggest: In active SLE patients the expression of PRL-R and autophagy-related key regulator protein ATG14+ are very high in B cells and T regulators respectively, in comparison with inactive SLE and healthy donors.
These novel findings suggest the interaction between PRL-R and autophagy in order to promote clinical/immune activation with overproduction of autoantibodies. PRL-R and ATG14$^+$ may be a new target of SLE treatment.
References:
[1] Lech M, Anders HJ, The pathogenesis of lupus nephritis. J Am Soc Nephrol, 2013, 24, 1357–1366.
[2] Jara LJ, Medina G, Saavedra MA, et al. Prolactic has a patogenyc role in systemic lupus erythematosus, Inmmunol Res, 2017, Jan 28.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6887

AB0150 INCREASED ERYPTOSIS LEVELS IN PRIMARY ANTIPHOSPHOLIPID SYNDROME PATIENTS

M. Vomero[1], F. Ceccarelli[1], A. Finucci[1], C. Pensa[1], C. Barbati[1], T. Colasanti[1], F.R. Spinelli[1], L. Massaro[1], S. Truglia[1], C. Perricone[1], F. Miranda[1], F.R. Mauro[2], R. Foà[2], F. Conti[1], G. Valesini[1], C. Alessandri[1]. *[1]Department of Internal Medicine and Medical Specialties, Lupus Clinic, Sapienza University of Rome; [2]Department of Cellular Biotechnologies and Hematology, Hematology, Sapienza University of Rome, Rome, Italy*

Background: Erythrocytes (RBCs) hold a crucial role in hemostasis and their integrity is influenced by different stimuli including circulating inflammatory mediators. Even though RBCs do not have nuclei and mitochondria, they have developed a process allowing them to undergo a rapid self-destruction named eryptosis. The exact mechanism of erythrocytes cell death is not fully clarified yet but it seems to involve Ca^{2+} and ceramide formation, leading to cell shrinkage and externalization of phosphatidylserine (PS) (1). Interaction between platelets and erythrocytes could participate in an increasing risk of thrombotic episodes typical of several diseases including antiphospholipid syndrome (APS). In fact, not only signals triggering eryptosis are involved in thrombosis activation, but also recent studies have demonstrated how PS-exposing erythrocytes are able to adhere to the vascular wall causing an impairment of circulation (2,3).
Objectives: Enhanced eryptosis is known to contribute to several pathological conditions (1) but the involvement of this process in APS has not been investigated yet. For this reason the aim of the study was to evaluate eryptosis levels in APS, healthy subjects positive for antiphospolipid antibodies without clinical manifestations (aPL carriers), autoimmune haemolytic anaemia (AIHA) and healthy donors (HD).
Methods: 27 patients with primary APS (M/F 5/22, mean age 51.1±7.6 years), 14 aPL carriers (M/F 3/11, mean age 48.9±8.4 years) were recruited after written informed consent. Moreover 10 AIHA patients and 12 HD were also enrolled as positive and negative control group respectively. RBCs were isolated from whole blood after centrifugation and eryptosis levels were analysed by flow cytometry, evaluating the percentage of annexin V-positive cells (PS-exposing cells). Flow cytometry was also use to estimated cellular volume from forward scatter (FSC).
Results: APS patients showed higher levels of eryptosis compared to HD (p=0.01). Interestingly, the percentage of annexin V-positive RBCs was lower in aPL carriers respect to APS patients (p=0.001). Moreover, an inverse correlation between RBCs volume and eryptosis was found in APS patients (r=-0.4, p=0.03). No clinical correlation between eryptosis and clinical manifestations were noticed. As expected, eryptosis was upregulated in AIHA patients compared to all populations studied ($p<0.0001$).
Conclusions: Our study provides for the first time evidence of eryptosis enhancement in APS patients suggesting a possible contribution of RBCs apoptosis in the pathogenesis of the disease.
References:
[1] Lang E, Lang F. Triggers, inhibitors, mechanisms, and significance of eryptosis: the suicidal erythrocyte death. Biomed Res Int. 2015;2015:513518.
[2] Borst O, Abed M, Alesutan I, Towhid ST, Qadri SM, Foller M, Gawaz M, Lang F. Dynamic adhesion of eryptotic erythrocytes to endothelial cells via CXCL16/SR-PSOX. Am J Physiol Cell Physiol. 2012;302:C644-C651.
[3] Pretorius E, du Plooy JN, Bester J. A Comprehensive Review on Eryptosis. Cell Physiol Biochem. 2016;39:1977–2000.

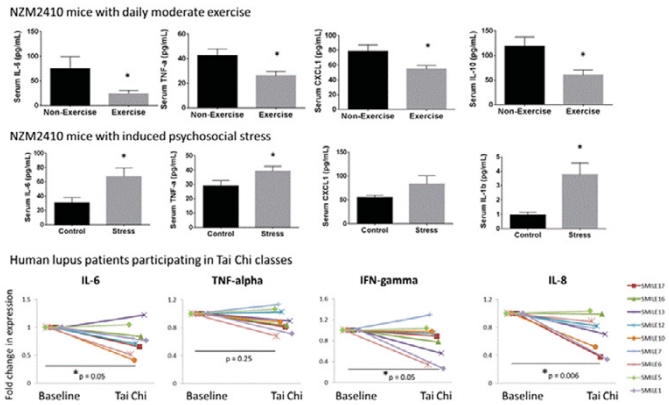


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4734

AB0151 STRESS MODERATION IMPACTING LUPUS WITH EXERCISE (S.M.I.L.E.): INFLUENCE OF DAILY MODERATE EXERCISE AND STRESS MODIFICATION ON AUTOIMMUNE-MEDIATED INFLAMMATION IN MICE AND HUMANS WITH LUPUS

N.A. Young[1], E. Thomas[1], B. Snoad[1], J. Sharma[1], M. Mobeen[1], J. Yedimenko[1], H. Steigelman[1], A. Meara[1], G. Valiente[2], S. Ardoin[1], N. Powell[3], J. Sheridan[3], W. Jarjour[1]. *[1]Rheumatology and Immunology; [2]Medical Oncology; [3]Institute for Behavioral Medicine Research, The Ohio State University Wexner Medical Center, Columbus, United States*

Background: Despite numerous studies indicating the positive effects of exercise and psychological stress reduction in patients with autoimmune disease, these therapeutic modalities are currently underemphasized due to the absence of comprehensive immunological characterization and regimen standardization.
Objectives: In order to examine the influence on the immune system at the cellular and tissue level, disease pathology was analyzed in the NZM2410 mouse model of lupus nephritis. To translate these results and begin to characterize a consensus treatment regimen, a pilot cohort of systemic lupus erythematosus (SLE) patients with active disease was enrolled into a daily Tai Chi program, which emphasized moderate exercise levels with meditative breathing to provide daily physical activity and stress reduction.
Methods: Mice were exercised daily by treadmill walking at moderate intensity. Social disruption stress was induced in mice by disturbing the social order within an established hierarchy. All mice were removed from the study when experimental removal criteria was reached [blood urea nitrogen (BUN)>50 mg/dL; weight loss>20%]. Kidney tissue and serum were collected from mice at experimental endpoint. SLE patients completed daily Tai Chi exercises and data was collected at baseline and throughout the study via questionnaires to access physical activity and stress levels, activity trackers (Fitbit), and serum sample analysis.
Results: Histopathological analysis of NZM2410 mice demonstrated that psychosocial stress induction significantly exacerbated and daily moderate exercise significantly reduced lupus nephritis disease pathology, as measured by BUN levels, complement component 3 and IgG complex deposition in glomeruli, pathological grading of H&E-stained kidney sections, and renal macrophage infiltration. Furthermore, stressors induced levels of IL-6, TNF-α, and IL-1β, while exercise suppressed IL-6, TNF-α, IL-10, and CXCL1 in mice. Compared to baseline data, questionnaires confirmed a significant reduction in perceived social stress and an increase in combined metabolic equivalent of task (MET) and overall physical activity in SLE patients. Moreover, fitness activity tracker data showed a significant increase in steps, distance, and activity calories with no changes in body mass index or vigorous activity levels. Interestingly, this correlated with an increased average time in bed each night. Analysis of pro-inflammatory serum cytokine



expression revealed suppression in the relative fold change of IL-6 by 23%, IL-8 by 30%, TNF-α by 11%, and IFN-γ by 21% with Tai Chi.
Conclusions: These data suggest that moderate exercise and stress management can have potent immunoregulatory effects on the chronic, systemic inflammation associated with SLE and identify daily Tai Chi exercise as a viable adjunct therapy to compliment current pharmacological interventions.
References:
[1] Wang C, et al. A randomized trial of tai chi for fibromyalgia. The New England journal of medicine 2010, 363(8): 743–754.
Acknowledgements: Funding: Center for Integrative Health and Wellness and Wexner Medical Center.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5455

AB0152 DISEASE ACTIVITY AND DAMAGE SCORES CORRELATED DIFFERENTLY WITH THE PATIENT REPORTED OUTCOMES IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME COMPARED TO LUPUS ASSOCIATED WITH SECONDARY SJÖGREN'S SYNDROME

N. Thompson, V. Gupta, A. Gandhi, R. Radmore, S. Cho, D.A. Isenberg, E.C. Jury, C. Ciurtin. *Rheumatology, University College London, London, United Kingdom*

Background: Previous studies showed a poor correlation between EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) and EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) in patients with Sjögren's syndrome (SS) (1). There are no previous studies correlating these scores with the SS Disease Damage Index (SSDDI) or assessing comparatively patients with primary (pSS) and secondary SS associated with lupus (SLE/SS).
Objectives: We aimed to assess how well scores assessing disease activity, damage and patient reported outcomes correlate with each other in patients with pSS compared to SLE/SS.
Methods: We conducted a cross-sectional study of 55 patients with pSS and 15 SLE/SS. Detailed clinical and laboratory data, along with patient reported outcomes (ESSPRI) and disease activity and damage scores (ESSDAI, BILAG and SSDDI) were collected. We compared the clinical and laboratory parameters of the two patient groups (pSS and SLE/SS) and assessed the correlations between maximum ESSDAI score since diagnosis and ESSDAI, ESSPRI, SSDDI and BILAG scores at the time of assessment.
Results: The table below shows comparatively the differences between the pSS and SLE/SS patient groups.

Table 1

Demographic	pSS (n=55)	SLE/SS (n=15)	Significance
Sex n (female/male %)	55 (100/0)	15 (100/0)	
Ethnicity n (C/A/MN/O)	43/6/3/3	9/1/5/0	P=0.4571
Age mean (range)	58 (28–84)	56 (25–78)	P=0.5923
Disease duration mean (range)	12 (2–34)	23 (3–40)	P=**0.005
Anti-Ro+ % (n)	76 (42)	73 (11)	P=0.7273
Anti-La+ % (n)	49 (27)	27 (4)	P=0.0565
ESSPRI median [IQR]	5 [3–7]	4 [2– 6]	P=0.3382
ESSDAI median [IQR]	2 [0– 4]	2 [1–4]	P=0.8884
Maximum ESSDAI [IQR]	4 [2–6]	3 [2–6]	P=0.9519
SSDDI median [IQR]	1 [1–2]	1 [0–2]	P=0.1992
Global BILAG median [IQR]		0 [0–2]	
Treatment			
Hydroxychloroquine (%)	65	40	P=0.0775
Methotrexate (%)	5	33	P=**0.0092

Unpaired T test performed; **p<0.01, n = total number, % percentage, IQR = interquartile range, ethnicity: C = Caucasian, A = Asian, MN = African Caribbean, O = Chinese, anti-Ro = anti-Sjögren's-syndrome-related antigen A, anti-La = anti-Sjögren's-syndrome-related antigen B.

We found significant correlations of SSDDI score with disease duration and maximum ESSDAI score in patients with pSS (r=0.27, p=0.05 and r=0.67, p=0.0001, respectively). In SLE/SS patients, ESSPRI scores correlated with both BILAG and maximum ESSDAI score (r=0.55, p=0.03 and r=0.7, p=0.02, respectively). The SSDDI score correlated with the disease duration only in pSS patients (r=0.27, p=0.05).
Conclusions: Our study showed that there was no similar correlation between various disease scores in patients with pSS compared to SLE/SS patients. If the patient reported outcomes correlated with the disease activity (ESSDAI and BILAG) in SLE/SS patients, this correlation was not seen in pSS patients, in which the significant correlations were found only between damage scores, highest disease activity score and disease duration.
References:
[1] Responsiveness of disease activity indices ESSPRI and ESSDAI in patients with primary Sjögren's syndrome treated with rituximab, Ann Rheum Dis 2012;71:.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2470

AB0153 DELETION OF RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS (RAGE) DOES NEITHER AFFECT AUTO-ANTIBODY PRODUCTION NOR DEVELOPMENT OF RENAL DISEASE IN PRISTANE-INDUCED LUPUS

N. Chevalier, R. Rzepka, R. Voll. *University Freiburg Medical Center, Freiburg, Germany*

Background: Systemic lupus erythematosus (SLE) is characterized by autoantibodies to diverse autoantigens, especially to nuclear components such as double-stranded DNA (dsDNA) or nucleosomes. Still, it remains unclear why poorly immunogenic molecules such as dsDNA and nucleosomes become targets of humoral autoimmunity in SLE. Increased signaling via pattern-recognition receptors (PRRs) through pathogen-associated molecular patterns (PAMPs) or endogenous damage-associated molecular patterns (DAMPs) released from damaged or stressed host cells and tissues, may be critically involved in the break of tolerance against such nuclear antigens. One important PRR in this context may be RAGE. Among many others, RAGE recognizes High mobility group box 1 (HMGB1). HMGB1 is a DNA-binding nuclear protein that has been found at elevated levels in patients with SLE and other autoimmune diseases; likewise perpetuation of RAGE signaling sustains inflammation and leads to the establishment of chronic inflammatory disorders.
Objectives: We therefore examined, using the Pristane-induced SLE model, if increased RAGE signaling may be involved in the break of tolerance against nuclear antigens and contributes to chronic inflammation.
Methods: To that end, WT and RAGE-/- animals were injected intra-peritoneally with a single dose of pristane. Disease manifestations were determined after 7 months and included the determination of proteinuria and renal pathology by evaluating the glomerular cellularity and matrix on H&E stained paraffin-embedded kidney sections and glomerular depositions of IgG and C3c. In addition to that we checked for auto-antibody production at several time points during disease development and immune cell distribution, differentiation and phenotype in inflamed kidneys and spleen.
Results: Apart from a slight decrease in $GL7^{hi}Fas^{hi}$ germinal center B cells and $B220^{+}CD21^{low}CD23^{hi}$ follicular B cells in RAGE-/- animals, we did not detect differences in auto-antibody secretion or disease manifestations between RAGE-/- and WT mice.
Conclusions: Our data contrast with recently published data showing that a deletion of RAGE exacerbated lupus nephritis and lymphoproliferation in a different SLE model (B6-MRL Fas lpr/j). Therefore, we are currently looking into the effects of RAGE deletion in additional models of auto-antibody-mediated immune disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6419

AB0154 CIRCULATING CPG DNA PROMOTER FRAGMENTS IN SLE ACTIVATE INTRARENAL TLR9 SIGNALING AND ACCELERATE RENAL INFLAMMATION AND FIBROGENESIS

P. Korsten, B. Tampe. *Department of Nephrology and Rheumatology, Universitätsmedizin Göttingen, Göttingen, Germany*

Background: In systemic lupus erythematosus (SLE), lupus nephritis (LN) is associated with chronic inflammation and perpetuated fibroblast activation, both determined by epigenetic mechanisms involving aberrant CpG DNA promoter methylation. During SLE progression, global methylation patterns are commonly lost. These CpG DNA promoter methylation patterns are not limited to the kidney, circulating CpG-rich DNA is also detectable in the blood allowing for biomonitoring ("liquid biopsy"). However, little is known about its specific contribution to determining disease progression. In the kidney, CpG-rich DNA activates TLR9 signaling mechanisms involved in inflammation and fibrogenesis. Based on these observations, we hypothesized that CpG-rich DNA promoter fragments potentially accelerate renal inflammation and fibrogenesis in SLE-associated LN.
Objectives: To analyze the role of circulating CpG-rich DNA on endothelial TLR9 signalling and the effect of experimental modification of oligodinucleotides on kidney inflammation in the Pristane-induced murine model of SLE.
Methods: We isolated circulating CpG-rich DNA from blood samples in a cohort of SLE patients. Then, we tested how these DNA promoter fragments influenced the LN phenotype in a TMPD ("pristane")-induced mouse model. Further, we investigated how this renal response could be influenced by the administration of either human or synthetic methylated/unmethylated CpG-rich DNA oligodinucleotides. Additionally, the effects of the administration of cicruclating CpG-rich DNA fragments on TLR9-signalling was analyzed in endothelial cell cultures.
Results: We show that circulating CpG-rich DNA promoter fragments are detectable in SLE patients' blood. Furthermore, SLE-associated LN is associated with accumulation of unmethylated CpG-rich DNA promoter fragments, implicating a mechanistic connection. These observations were further corroborated in a rodent model of TMPD-induced SLE where administration of CpG-rich DNA (isolated from LN patients or synthetic unmethylated CpG-rich DNA oligonucleotides) worsened the renal phenotype in terms of inflammation and fibrogenesis.
Causal contribution of TLR9 was further confirmed in *Tlr9*$^{+/-}$-knockout mice with protection from renal inflammation and kidney fibrosis after administration of unmethylated CpG-rich DNA promoter oligonucleotides. TLR9-mediated intrarenal

inflammation can be therapeutically targeted by administration of synthetic methylated CpG-rich DNA oligonucleotides, ultimately associated with suppression of TLR9-mediated signaling responses and renal injury in experimental SLE/LN.
Conclusions: Collectively, our results implicate accumulation of unmethylated CpG-rich promoter DNA fragments in SLE-associated LN. Furthermore. these unmethylated CpG-rich promoter DNA fragments causally contribute to TLR9-mediated inflammation and renal fibrogenesis. Administration of methylated CpG-rich oligonucleotides antagonized intrarenal TLR9-mediated inflammatory signaling responses and fibrogenesis. Therefore, biomonitoring of CpG-rich promoter DNA fragments and modulation of intrarenal TLR9 signaling is a promising therapeutical target in SLE-associated LN.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4493

AB0155 LEARNING SLE PATHOLOGICAL MECHANISMS FROM MULTI 'OMICS PROFILES

S.S. Pfister[1], N. Kelley[2], T. Schlitt[3], A. Fernandez[3], M. Sultan[3], M. Hasan[1], A. Mir[1], J.S. Rush[1]. *[1]Autoimmunity, Transplantation and Inflammation; [2]Analytical Sciences and Imaging; [3]BioMarker Development, Novartis Institutes for BioMedical Research, Basel, Switzerland*

Background: Precision medicine aims at providing intervention based on clinical and molecular stratification of patients, and is an important approach for targeting heterogeneous diseases. A diverse autoimmune disease is systemic lupus erythematosus (SLE), where dysregulation of several immune processes affects multiple organs. Fundamental for targeted treatment of such a heterogeneous disease is the identification of biomarkers predictive for the biological basis of clinical phenotypes.
Objectives: Despite recent progress, few markers for SLE are currently used in the clinic. In order to learn SLE pathological mechanisms and associated biomarkers, we obtained a diverse dataset from a cohort of active SLE patients (SLEDAI >6), including blood transcriptomics, serum proteomics, cytokines, and auto-antibody profiles. Integration of multi-omics data provides a rich dataset to explore associations between molecular and clinical readouts.
Methods: From a machine-learning perspective, biomarker discovery is defined as the process of selecting an optimal subset of variables for the prediction of parameters of interest. However, variable selection approaches are often underpowered for datasets that contain fewer samples than the number of variables. To overcome this problem we present a method based on L1 regularized regression and recursive variable elimination to generate networks of predictive markers across multiple data types.
Results: The proposed method allows us to graphically visualize the relationships among SLE phenotypes, and their molecular fingerprints. Identified networks of markers are validated by mapping to known biological pathways, and when available by comparison to independent patient cohorts. Despite the small number of patients (n=20), we identify known pathological mechanisms, including a type I IFN gene signature, several cell type specific signatures, and potential novel markers of clinically defined SLE subtypes.
Conclusions: Systemic lupus erythematosus is a complex autoimmune disease characterized by a variety of clinical manifestations. While multi-omics profiles from SLE patients pose challenges because of their intrinsic high dimensionality, they also provide a unique insight into the molecular processes of disease. Our integrated analysis gives a novel perspective on the pathological mechanisms of clinical SLE phenotypes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5009

AB0156 THYMIC STROMAL LYMPHOPOIETIN (TSLP) IN PRIMARY SJÖGREN'S SYNDROME AND RELATED LYMPHOMA: THE POSSIBLE CONTRIBUTION OF A NOVEL GROWTH FACTOR

S. Gandolfo[1,2], C. Fabro[1,2], M. Bulfoni[2,3], S. Russi[4], P. Masolini[1], L. Quartuccio[1,2], D. Cesselli[2,3], S. De Vita[1,2]. *[1]Rheumatology Clinic, Udine University Hospital S. Maria della Misericordia; [2]Department of Medical and Biologic Sciences, University of Udine; [3]Institute of Anatomic Pathology, Udine University Hospital S. Maria della Misericordia, Udine; [4]Department of Biomedical Sciences and Human Oncology, University of Bari, Bari, Italy*

Background: Primary Sjögren's syndrome (pSS) is an autoimmune lymphoproliferative systemic disease with a higher risk of non-Hodgkin B cell lymphoma (NHL) evolution. In SS, salivary gland (SG) epithelium plays a crucial role in initiating and perpetuating the autoimmune response. Thymic stromal lymphopoietin (TSLP) is both an epithelial and lymphopoietic cytokine involved in the maintenance of immune tolerance at interfaces between body and environment and in the regulation of lymphocytes homeostasis.
Objectives: To study TSLP in serum and SG biopsies of pSS patients stratified by the lymphoproliferative histopathologic status, from fully benign lesions (fbSS) to myoepithelial sialoadenitis (MESA) and to NHL, in order to evaluate a possible role of TSLP in SS pathogenesis and in lymphoma evolution.
Methods: Serum TSLP levels were determined by ELISA in pSS patients (n=30: 12 fbSS, 10 MESA, 8 NHL) and in controls (healthy blood donors - HD n=20; non-autoimmune sicca without SS - nSS n=10). TSLP was also studied by immunohistochemistry in SG biopsies of the same patients and nSS controls. Correlations with clinical and histopathologic parameters were performed. Of note, sequential samples were also included from three patients evolving from fbSS to NHL.
Results: TSLP serum levels were significantly higher in pSS compared to nSS (p=0.03) and HD (p=0.0002), with a progressive significant increase from fbSS to MESA (p=0.004) and finally to NHL (NHL vs fbSS p<0.0001; NHL vs MESA p=0.003), where the increase was dramatic. This was observed also in metachronous samples from the three pSS patients evolving to NHL. A positive significant correlation between TSLP serum levels and disease activity assessed by ESSDAI was found (p<0.0001).
Of note, in the affected tissue, TSLP showed an opposite pattern of expression than in the serum. Concerning the salivary epithelium, a declining expression of TSLP was shown from fbSS (expression was similar to nSS) to MESA and finally to NHL. Strikingly, however, the three pSS patients evolving to lymphoma were the only ones showing a low TSLP epithelial expression also at baseline. Concerning the glandular lymphoid infiltrate, the TSLP expression again decreased with progression to NHL. Again, the three pSS patients evolving to lymphoma were the only ones showing a low TSLP inflammatory expression also at baseline.
Conclusions: Serum TSLP increases in pSS and correlates with lymphoma progression. Discrepancies are however observed between serum levels and tissue TSLP expression: while the baseline TSLP tissue expression is evident and similar to controls, tissue TSLP decreases with lymphoma progression. TSLP likely represents an additional growth factor and biomarker for pSS pathogenesis and lymphoproliferation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6450

AB0157 TREX 1 MUTATION IN THE MEMBERS OF A FAMILY WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

S. Ugurlu[1], I. Karacan[2], H. Ozdogan[1], A. Tolun[3], E. Tahir Turanli[4]. *[1]Division of Rheumatology, Department of Internal Medicine, Cerrahpasa Medical Faculty, University of Istanbul; [2]Graduate School of Science, Engineering and Technology, Molecular Biology, Biotechnology and Genetics Program, Dr. Orhan Ocalgiray Molecular Biology-Biotechnology and Genetics Research Centre, Istanbul Technical University; [3]Department of Molecular Biology and Genetics, Boğaziçi University; [4]Dr. Orhan Ocalgiray Molecular Biology Biotechnology and Genetics (MOBGAM) Research Centre, Istanbul Technical University, Istanbul, Turkey*

Background: There are reports showing Three Prime Repair Exonuclease 1 (*TREX1*) mutations in atypical Systemic Lupus Erythematosus (SLE) patients.
Objectives: Here we report a family with SLE and Antiphospholipid Syndrome (aPL) who are positive for *TREX1* mutation and complicated with AA amyloidosis
Methods: DNA samples were extracted from peripheral blood samples of two affected (mother and daughter) and two unaffected individuals of the same family. Exome sequencing was performed for the daughter and data was processed according to GATK Best Practices recommendations. Exome variants were used to search for a rare candidate variant causing the disease. Identified variant was screened in four family members using Sanger sequencing.
Results: The index case (mother) was a 63 year-old woman who had developed polyarthritis and recurrent cerebrovascular accident (CVA) at the age of 44. She was positive for ANA, anti-ds-DNA and IgG anti-cardiolipin antibodies. On anticoagulant therapy she still experiences frequent CVAs. The daughter who is 43 years old had experienced depression, non-erosive arthritis and alopecia at the age of 13. She was positive for ANA, dsDNA and ACA and was treated with hydroxychloroquine, prednisolone, and rituximab. She had attacks of deep vein thrombosis despite anticoagulant therapy. A renal biopsy was performed because of an increase in her creatinine level, with no proteinuria and normal urinary sediment, which revealed AA amyloidosis. She was heterozygous for p.R202Q variant in *MEFV* gene. Further genetic testing was performed for the mother and the daughter as well as two other non-affected members of the family.
Candidate variant search in exome data resulted a novel c.2T>A (p.M1?) variant in *TREX1* gene. The variant was in heterozygous state for both affected members. Since the variant disrupts translation initiation codon (ATG/AAG), it is predicted to cause loss of complete protein production.
Conclusions: There is evidence that *TREX1* is involved in the pathogenesis of SLE, especially with neuropsychiatric disease. Here we report a familial SLE and aPL syndrome complicated with AA amyloidosis, with a novel *TREX1* variant. Such cases will increase our ability to understand the genetic spectrum of SLE and may allow the development of more effective therapies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6231

AB0158 TAUROURSODEOXYCHOLIC ACID DECREASES THE EXPRESSION OF ERAD COMPONENTS AND THE ACCUMULATION OF SALIVARY MUCINS INDUCED BY PRO-INFLAMMATORY CYTOKINES

N. Albornoz[1], S. Aguilera[2], M.-J. Barrera[1], I. Castro[1], P. Carvajal[1], S. González[3], C. Molina[3], U. Urzúa[1], D. Jara[1], C. Leyton[1], M.-J. González[1]. *[1]ICBM, Faculty of Medicine, University of Chile; [2]Reumatología, Clínica Indisa; [3]Patología Oral, Universidad Mayor, Santiago, Chile*

Background: The salivary glands of Sjögren's syndrome patients show endoplasmic reticulum (ER) stress characterized by intracellular accumulation of secretory products such as MUC1[1], dilated ER cisternae[2] and high levels of pro-inflammatory cytokines. Previous results from our laboratory revealed an increase of the ATF6α pathway of the UPR[3] and activation of ER-associated protein degradation (ERAD)[3]. Increased expression of proteins involved in ERAD (SEL1L and EDEM1) has been reproduced *in vitro* in human submandibular gland (HSG) cells treated with TNF-α or IFN-γ[2]. Tauroursodeoxycholic acid (TUDCA) is a chemical chaperone utilized for alleviate ER stress by enhancing the folding of proteins[3].
Objectives: The aim of this study was to evaluate if TUDCA decreases EDEM1, SEL1L, and MUC1 expression induced by pro-inflammatory cytokines in salivary gland epithelial cells.
Methods: HSG-cells were incubated with 10 ng/mL of IFN-γ or TNF-α for 24h. Alternatively, cells were incubated with cytokines for 6h and then co-incubated with TUDCA (150 and 250 μM) up to 24h. EDEM1, SEL1L and MUC1 protein and mRNA levels were determined by Western-blot and RT-qPCR, respectively. EDEM1 and SEL1L localization was determined by immunofluorescence.
Results: HSG cells stimulated with IFN-γ or TNF-α showed a significant increase of EDEM1 and SEL1L protein and mRNA levels. Importantly, TUDCA co-incubation caused a significant decreased expression of both molecules. Treatment with both cytokines induced a cytoplasmic increase of staining intensity of EDEM1 and SEL1L, which was suppressed by TUDCA. HSG cells stimulated with cytokines showed a significant increase of MUC1 protein and mRNA levels, which was also suppressed by TUDCA.
Conclusions: Decreased expression of MUC1, SEL1L and EDEM1 in the presence of TUDCA suggests that this chemical chaperone promotes folding of proteins in the ER, by decreasing ERAD activity and ER stress induced by pro-inflammatory cytokines in HSG cells. These results enable us to propose that TUDCA might alleviate the ER stress of salivary glands from Sjögren's syndrome patients.
References:
[1] Oral Dis. 2015;21(6):730–8.
[2] Arthritis Rheum. 2003 Sep;48(9):2573–84.
[3] J Autoimmun. 2016;75:68–81.
[4] Prion. 2014;8(2). pii: 28938.
Acknowledgements: Supported by Fondecyt-Chile [#1160015] (MJG, SA, CM, SG, IC).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2003

AB0159 AUTOIMMUNE REACTIVITY TO MALONDIALDEHYDE ADDUCTS IN SYSTEMIC LUPUS ERYTHEMATOSUS

U. Hardt[1], A. Larsson[2], I. Gunnarsson[1], G.J. Silverman[3], E. Svenungsson[1], C. Grönwall[1]. *[1]Dept. of Medicine, Rheumatology Unit, Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden; [2]Dept. of Medical Sciences, Clinical Chemistry, Uppsala University, Uppsala, Sweden; [3]Dept. of Medicine, NYU School of Medicine, New York, NY, United States*

Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by recurrent disease activity flares, multiple organ involvement, and often with a presentation of nephritis. Malondialdehyde (MDA) post-translational modification of proteins occurs upon inflammation and oxidative stress. Natural IgM anti-MDA autoreactivity is present from birth and may be beneficial. However, both IgM and IgG anti-MDA can also be increased in autoimmune disease. Yet, the role for potentially pro-inflammatory autoreactive IgG anti-MDA in SLE remains elusive.
Objectives: Here, we study the association between serum IgG anti-MDA and clinical features of SLE.
Methods: This cross-sectional study included 398 SLE patients at the Karolinska University Hospital fulfilling at least four of the 1982 ACR criteria. Data was compared to the previously reported combined US east coast cohorts (1, 2). Disease activity was assessed by SLEDAI-2K. Total IgG and ANA IgGs were assessed in the clinical laboratory and sTNFR by ELISA. IgG anti-MDA was measured by a quantitative ELISA using modified BSA. As a comparison, we measured IgG anti-phosphorylcholine (PC), another oxidation-associated natural IgG. Cutoff for positivity was based on highest control quartile. Specific IgGs were normalized for total IgG levels in the analysis. Means were compared with Mann-Whitney test, correlations with Spearman's analysis, and meta-analysis used Mantel-Haenszel fixed effect model.
Results: Serum IgG anti-MDA significantly correlated with SLE-associated auto-IgG (e.g. anti-dsDNA, n=398 R=0.42 $p<0.0001$). IgG anti-MDA correlated with higher disease activity by SLEDAI in two independent cohorts (Sweden KS, n=397 R=0.33 $p<0.0001$; US east coast, n=219 R=0.34 $p<0.0001$) and was confirmed in meta-analysis of dichotomized data showing an Odds Ratio of 3.9 (CI 2.6–5.8 $p<0.0001$) for IgG anti-MDA positivity in patients with active disease (SLEDAI≥6). Association of anti-MDA with disease activity was supported by an inverse correlation of IgG anti-MDA normalized for total IgG with complement (C2, n=304 R=-0.24 $p<0.0001$, C3 and C4, n=385 R=-0.24 $p<0.0001$). Furthermore, we observed elevated IgG anti-MDA/total IgG reactivity in SLE patients with current or history of nephritis compared to no history of nephritis (n=389 4.5+/-4.0 vs 3.4+/-3.3 $p<0.0001$) and inverse weak correlation of IgG anti-MDA/total IgG with markers of kidney function (serum cystatin C, n=283 R=0.20 p=0.0008, urine albumin, n=373 R=0.23 $p<0.0001$). Anti-MDA IgG/total IgG also directly correlated with serum soluble TNF receptors (sTNFR1, n=286 R=0.21 p=0.0003, sTNFR2, n=287 R=0.35, $p<0.0001$). IgG anti-PC either did not correlate or inversely correlated with disease measurements, consistent with its previously reported more protective properties.
Conclusions: IgG to MDA-modifications correlates with other autoreactivities, disease activity and nephritis in SLE, and should be further evaluated for its potential prognostic utility. Yet, it remains unclear, if IgG anti-MDA directly contributes to pathogenesis in SLE.
References:
[1] Clin Immunol. 2012 Mar;142(3):390–8.
[2] Clin Immunol. 2014 Jul;153(1):1–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5822

AB0160 INTERFERON-Γ-INDUCIBLE KYNURENINES INFLAMMATION PATHWAY: THE MISSING LINK BETWEEN DISEASE ACTIVITY AND SYMPTOMS IN SJÖGREN'S SYNDROME

V. Valim[1], W.M. Sardemberg[1], J.G. Brun[2], E. Zandonade[3], G.M. Balarini[1], L.V. Tanure[4], G.V. Ferreira[4], É.V. Serrano[1], J.F.V. Tonini[1], K.A. Brokstad[5], P.M. Ueland[6], R. Jonsson[5], P.M. Mydel[5]. *[1]Medicine, Federal University of Espírito Santo, Vitória, Brazil; [2]Clinical Science Department, University of Bergen, Bergen, Norway; [3]Statistic Department, Federal University of Espírito Santo; [4]Locomotor System Department, Federal University of Minas Gerais, Vitória, Brazil; [5]Broegelmann Research Laboratory, University of Bergen, Bergen, Norway; [6]Bevital Laboratory A/S, University of Bergen, Vitória, Brazil*

Background: Tryptophan (TRYP) can be converted to kynurenine (KYN) by indoleamine 2,3-dioxygenase (IDO) drived by interferon-γ. Recent studies have suggested that the KYN pathway reflects an important interface between the immune and nervous system modulation.
Objectives: The aim was to study KYN pathway and their correlation to clinical and immunological parameters in primary Sjögren's syndrome (pSS).
Methods: We included 97 pSS (AECG) and 63 healthy controls matched to age, sex, ethnicity, and body mass index (BMI). KYN metabolites and TRYP were analysed by liquid chromatography mass spectrometry.
Results: Patients aged 50±11 years showed anti-SSA-Ro of 63%, anti-SSB-La 31%, anti-nuclear antibody 81%, rheumatoid factor 24%, and systemic manifestations 67%. Most (68%) showed low disease activity measured by Eular Sjögren's Syndrome Disease Activity Index (ESSDAI), 22% moderate and 10% high ESSDAI. The kynurenine:tryptophan ratio (KTR) was (0.031±0.014 vs. 0.024±0.007, p=0.001), KYN (1.890±0.580 vs. 1.652±0.426, p=0.005), quinolinic acid (QA) (477.82±251.55 vs. 382.05±128.06, p=0.018), hydroxikynurenine (3HK) (53.45±52.05 vs. 39.15±9.67, p=0.056), anthranilic acid (AA) (19.86±6.26 vs. 16.78±4.71, p=0.001) were higher while xanthurenic acid (XA) (11.52±7.88 vs.13.00±5.68, p=0.019), and TRYP (64.90±13.43 vs. 71.02±8.88, p=0.012) were lower in pSS compared to controls. Higher KTR was associated with disease duration (r=0.211,p=0.042), CRP (r=0.254,p=0.029), lower hemoglobin (r=-0.219, p=0.34), creatinine (r=0.588, p=0.000), hypergammaglobulinemia (r=0.254, p=0.014), hyper IgG (r=0.354, p=0.004), lower C3 (r=0.262, p=0.011) and C4 (r=-0.294, p=0.004). Higher KTR was observed in those with Biological ESSDAI domain involvement (0.033±0.016 vs. 0.029±0.013, p=0.003), glandular manifestation (0.037±0.014 vs.0.029±0.013, p=0.007), in the other hand lower KTR in those with presence of musculoskeletal pain (0.029±0.011 vs. 0.032±0.015, p=0.003). ESSDAI showed a tendency to correlate with KTR (r=0.177, p=0.091) and ESSPRI inversely correlated with AA (r=-0.233, p=0.071). Either patient with pain showed lower AA (20.66±6.66 vs. 17.22±5.07, p=0.021).
Conclusions: TRYP is decreased and KYN metabolites pathway is increased in pSS. IDO activity expressed like KTR was positively correlated with disease activity and glandular manifestations but negatively with pain. A better understanding of the KYN pathway can clear the dissociation of symptoms and disease activity in pSS.
References:
[1] Maria NI, van Helden-Meeuwsen CG, Brkic Z, et al. Association of Increased Treg Cell LevelsWith Elevated Indoleamine 2,3-Dioxygenase Activity and an Imbalanced KynureninePathway in Interferon-Positive Primary Sjögren's Syndrome. Arthritis Rheumatol.2016 Jul;68(7):1688–99.
[2] Midttun Ø, Hustad S, Ueland PM. Quantitative profiling of biomarkers relatedto B-vitamin status, tryptophan metabolism and inflammation in human plasma byliquid chromatography/tandem mass spectrometry. Rapid Commun Mass Spectrom. 2009 May;23(9):1371–9.
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6015

AB0161 ANTIPHOSPHOLIPID ANTIBODIES DIFFERENTIALLY REGULATE THE EXPRESSION & ACTIVITY OF THE LYSOSOMAL PROTEASES WITH EFFECTS UPON MONOCYTE AUTOPHAGY

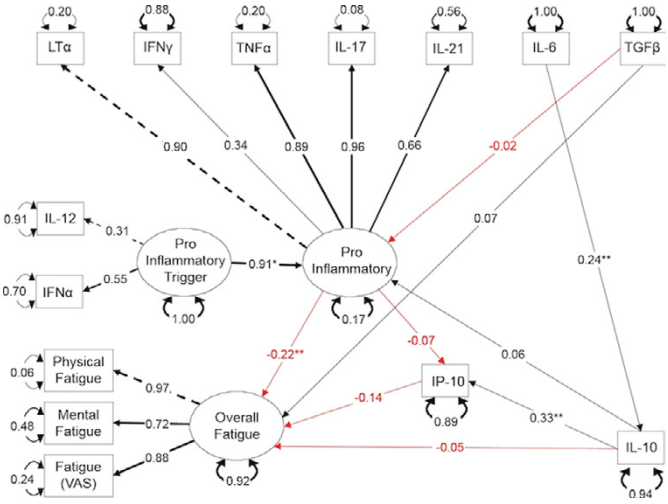
V.M. Ripoll-Nunez, A. Khawaja, I.P. Giles, A. Rahman. *Division of Medicine, University College London, London, United Kingdom*

Background: Antiphosholipid antibodies (aPLs) are known to activate monocytes in the pathogenesis of antiphospholipid syndrome (APS), although the precise mechanisms by which this activation occurs are not fully understood. We have recently identified several novel protein targets using a comprehensive proteomic analysis of human monocytes treated with IgG from patients with APS. Amongst these novel targets lysosomal proteases, including cathepsin B and cathepsin D were identified. These proteases are important in protein degradation, clearance of autolysosomes, apoptosis and autophagy. Dysregulation of these homeostatic cellular functions may be important in the exposure of autoantigens and pathogenesis of the APS. Therefore, we have now studied the effects of APS IgG upon the expression/activity of different cathepsins and their effects upon autophagy.
Objectives: Determine the effect of pathogenic aPL antibodies on monocyte autophagy and its association with the regulation of lysosomal activity.
Methods: Healthy monocytes were treated with 200 μg/ml of IgG purified from (n=9) patients with APS or (n=9) healthy control (HC) IgG for 6 h. The expression of cathepsin B and cathepsin D were measured by western blotting. Activity assays for lysosomal proteases cathepsin D, cathepsin B and cathepsin L were performed using fluorescence based assays (RayBio®). Intracellular proteolytic activity of monocytes was determined using DQ-BSA (Molecular probes) and flow cytometry analysis. Autophagy was induced by treating monocytes with 50 μg/ml GM-CSF for 14 h.
Results: Consistent with our previous label free quantification mass spectrometry proteomic analysis, western blot analysis confirmed that levels of cathepsin B and cathepsin D were decreased in monocytes treated with APS IgG compared to HC IgG. Similarly, enzymatic assays revealed that cathepsin B and cathepsin D activities were significantly reduced in monocytes treated with IgG from patients with APS compared to HC (p=0.0188, 0.0323). In contrast, levels of enzymatic activity of cathepsin L were increased in monocytes treated with APS IgG compared to HC IgG (p=0.0106). To determine the effect of APS IgG on autophagy, we exposed healthy monocytes to IgG and induced autophagy by treating them with GM-CSF for 14 h. Subsequently we tested the intracellular proteolytic activity with DQ-BSA. Stimulation of monocytes with APS IgG reduced the lysosomal activity of GM-CSF-treated monocytes whereas HC IgG had no effect, indicating that APS IgG disrupts lysosomal degradation during monocyte autophagy.
Conclusions: We found that IgG from patients with APS regulate the expression and activity of lysosomal proteases cathepsins B/D and cathepsin L in opposite directions. Activity of cathepsin B and D was down-regulated by exposure to IgG from patients with APS whereas cathepsin L was up-regulated. Furthermore, we found APS IgG disrupts lysosomal degradation during monocyte autophagy. Additional experiments are now underway to increase our understanding of how modulation of cathepsin activity and autophagy may be important in the pathogenesis of APS and provide new therapeutic targets.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3417

AB0162 SERUM LEVEL OF PROINFLAMMATORY CYTOKINES IS NEGATIVELY ASSOCIATED WITH FATIGUE IN PRIMARY SJÖGREN'S SYNDROME

D. Gardiner[1], W.D. Reid[2], J.R. Tarn[1], D. Lendrem[1], N. Howard-Tripp[1], S. Bowman[3], B. Griffiths[4], S. Rushton[2], W.-F. Ng[1] on behalf of UKPSSR.
[1]Institute of Cellular Medicine & NIHR Newcastle Biomedical Research Centre; [2]School of Biology, Newcastle University, Newcastle upon Tyne; [3]Rheumatology, University Hospital Birmingham, Birmingham; [4]Rheumatology, Freeman Hospital, Newcastle upon Tyne, United Kingdom

Background: We have previously described a model of fatigue in patients with primary Sjogren's syndrome (PSS) based on the levels of serum cytokines, pain and depression scores. Importantly, removal of cytokines from this model substantially reduced the accuracy suggesting that cytokines may have a key role in the biological basis of fatigue [1]. However, interpreting the model is complicated by the complexity of the immune system and the likely multiple interactions between numerous cytokines and other variables [2]. Structural equation modelling (SEM) is a statistical technique that allows for analysis of one or multiple independent variables with one or multiple dependent variables. SEM consists of two components – the structural model, which represents the relationships between the theoretical variables, and the measurement model, which are the relationships between the latent variables and their measures [3].
Objectives: To use SEM to test our hypothesis that the balance between pro-inflammatory and anti-inflammatory cytokines play an important role in determining severity of fatigue in patients with PSS.
Methods: We used Canonical Correpondence Analysis (CCA) to investigate the variation in cytokine expression across our spectrum of fatigue patietns to explore interactions and dependencies between cytokines. We then built a conceptual model based on the literature representing the likely relationships between fatigue and various proinflammatory and anti-inflammatory cytokines and other soluble molecules in the serum. This conceptual model was then challenged using serum data and fatigue scores of 161 PSS patients from the UK primary Sjogren's syndrome registry. Model fit was assessed using the Confirmatory Factor Index, the Root Mean Square Error of Association and the Standardised Root Mean Square Residual. We also analysed changes in fatigue scores over a period between 1–4 years.
Results: CCA revealed the first axis of ordination (CCA1) broadly correlates with fatigue, consists of many pro-inflammatory cytokines including TNFα, LTα and IFNγ, IL17, which were negatively correlated with fatigue while IL-6 and MCP1, which were positively associated with increased fatigue severity. The second axis (CCA2) reflects a trend in cytokines which appear to relate to patients' age. Fatigue scores were largely stable over time and therefore data were not included in the SEM analysis. The main pro-inflammatory SEM model showed fatigue was negatively associated with pro-inflammatory cytokine activity (p=0.019); IL-10 drove IP-10 (p=0.000); and IL-10 was driven by IL-6 (p=0.006) (Fig. 1)



Conclusions: Chronic fatigue in PSS is negatively associated with many pro-inflammatory cytokines. We hypothesize that it reflects adaptive biological processes, which occurs after chronic exposure to inflammation in conditions such as PSS.
References:
[1] Howard-Tripp N, et al. *RMD Open.* 2016;2:e000282.
[2] Genser B, et al. *BMC immunology*. 2007;8:1.
[3] Beran TN & Violato C. *BMC Research Notes*. 2010;3:267.
Acknowledgements: All UKPSSR participants.
Disclosure of Interest: D. Gardiner: None declared, W. Reid: None declared, J. Tarn: None declared, D. Lendrem: None declared, N. Howard-Tripp: None declared, S. Bowman Consultant for: Cellgene, Glenmark, GSK, Eli Lilly, Novartis, Roche, Takeda, UCB, B. Griffiths: None declared, S. Rushton: None declared, W.-F. Ng Consultant for: Pfizer, UCB, MedImmune, Takeda and Sanofi
DOI: 10.1136/annrheumdis-2017-eular.5811

AB0163 MESENCHYMAL STEM CELLS INDUCE CD1C+ TOLEROGENIC DENDRITIC CELLS IN HUMAN SYSTEMIC LUPUS ERYTHEMATOSUS VIA UP-REGULATING FLT-3 LIGAND

X. Yuan, D. Wang, Z. Zhang, Q. Wang, W. Li, X. Tang, W. Chen, G. Yao, L. Sun. *Department of Rheumatology and Immunology, The Affiliated Drum Tower hospital of Nanjing University Medical School, Nanjing, China*

Background: $CD1c^+$ tolerogenic dendritic cells (DCs) play important roles in the induction of peripheral tolerance and control of adaptive immune response. Umbilical cord (UC)-derived mesenchymal stem cells (MSCs) exhibit immunoregulation effects in systemic lupus erythematosus (SLE). However, the underlying immunosuppression mechanism of MSCs via tolerogenic DCs in SLE remains largely unknown.
Objectives: The aim of this study was to examine tolerogenic DCs levels in SLE patients, and to further investigate the mechanism of MSCs in the regulation of tolerogenic DCs.
Methods: Tolerogenic DCs were isolated as Lin $(CD3/19/56/14)^-$ HLA $DR^+CD11c^+CD1c^+$ from peripheral blood mononuclear cells (PBMCs). Levels of tolerogenic DCs were determined by flow cytometry, and serum concentration of Flt-3 ligand (FLT3L) were determined by ELISA from 17 healthy controls and 25 SLE patients. Eight SLE patients were given UC MSCs infusions. We compared the levels of tolerogenic DCs and serum FLT3L before and 24 hours after UC

MSCs transplantation. PBMCs from 8 patients were collected and co-cultured with UC MSCs at ratios of 1:1, 10:1 and 50:1, for 24 hours, 48 hours and 72 hours, respectively, to detect the levels of tolerogenic DCs. The FLT3L in the supernatant solution were determined. FLT3L siRNA was added to the co-culture system, and the level of tolerogenic DCs were detected.
Results: The levels of peripheral $CD1c^+$ DCs and serum FLT3L were significantly decreased in SLE patients compared to healthy controls. After UC MSCs transplantation, the levels of $CD1c^+$ DCs increased, along with an increase in serum FLT3L. In vitro studies showed that UC MSCs time-dependently up-regulated peripheral $CD1c^+$ DCs, but not dose-dependently. The supernatant FLT3L level significantly increased after co-cultured with MSCs. However, the addition of FLT3L siRNA significantly abrogated the up-regulation of $CD1c^+$ DCs by MSCs.
Conclusions: UC MSCs induce $CD1c^+$ tolerogenic DCs through up-regulating FLT3L in lupus patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3334

Scleroderma, myositis and related syndromes - etiology, pathogenesis and animal models

AB0164 AMYLOIDOSIS IN PROGRESSIVE SYSTEMIC SCLEROSIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 12 PATIENTS

Á. Apáthy[1], M. Bély[2]. *[1]Department of Rheumatology, St. Margaret Clinic Budapest; [2]Department of Pathology, Hospital of the Order of the Brothers of Saint John of God, Budapest, Hungary*

Background: Systemic sclerosis (SSc), like all chronic autoimmune disorders, may be complicated by AA amyloidosis (AAa). An associated B-cell lymphoma my cause amyloid λ or κ light-chain deposition and AL amyloidosis (ALa) in SSc as well.
Objectives: The aim of this study was to determine the prevalence and type of amyloidosis in SSc patients, appraise the extent of amyloid deposits in various organs.
Methods: 12 patients (females 11, age: 54.82 years, range 66–32, onset of SSc: 48.86, disease duration: 6.43 years; one male, age: 65.0 years at death, onset of SSc and disease duration not known) were studied. All patients were autopsied. SSc was diagnosed clinically according to the criteria of the ACR [1].
Amyloid deposits on different tissue structures [arteriole, small artery, medium size artery, venule, small vein, medium size vein, interstitial collagen fiber, reticulin fiber (collagen IV), basal lamina, nerve, renal glomerulus] of 6 organs [heart, lungs, kidney, gastrointestinal tract, skin and brain] were determined histologically. The extent of amyloid A deposits was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale, based on the number of involved tissue structures per light microscopic field [2] ("0": no amyloid deposits, "1": Sporadic, minimal amyloid deposits on different tissue structures, "2": less than five, "3": five or more involved tissue structures per microscopic field at objective magnification of x20)
The prevalence and extent of amyloid deposits in various organs were compared by Student (Welch) t-probe.
Results: Systemic AL-l light-chain amyloidosis was diagnosed in 1 (8.0%) 67 year old female patient (onset of SSc: 66 years, disease duration 1 year), and systemic AAa in 1 (8.0%) 53 year old female patient (onset of SSc: 41 years, disease duration 12 years).
The prevalence (in %) and the average extent of AL-l light-chain and amyloid A deposits (absolute value) in various organs of SSc patients are summarized in Table 1.

Tab;e 1

Organs	SSc-λ Prevalence in %	SSc-AAa Prevalence in %	p<	SSc-λ Average extent	SSc-AAa Average extent	p<
Skin	80.00	0.00	**0.0001**	1.45	0.00	**0.0002**
Heart	72.73	63.64	0.3329	1.45	0.91	0.117
Kidney	63.64	63.64	0.1228	1.09	0.73	0.185
G-I Tract	41.67	66.67	0.1185	1.08	1.00	0.433
Lung	40.00	40.00	0.5000	1.00	0.50	0.077
Brain	0.00	0.00		0.00	0.00	–
Average/Organ	50.79	41.27	**0.052**	1.040	0.556	**0.0036**
Average/Patient	45.56	35.96	0.144	0.965	0.494	**0.0006**

Conclusions: AL-λ deposits were present earlier and were more prominent in the skin, heart and kidney, than in the, G-I tract and the lung. Amyloid A deposits were present earlier and were more prominent in the G-I tract, heart and kidney, than in the, lung and the skin. In the brain AL-λ and amyloid A deposits were absent in both diseases.
Higher prevalence (80.0% versus 0.0%; $p<0.0001$) and massive AL-λ deposition in the skin (1.45 versus 0.0; $p<0.0002$) may be explained by qualitative differences of AL-λ and amyloid A and by a diverse affinity of circulating amyloid precursors to the qualitative changed interstitial collagen and reticulin fibers. In systemic sclerosis patients qualitative change of collagens has been demonstrated [3–5].

References:
[1] van den Hoogen F et al: Ann Rheum Dis 2013; 72:1747–1755.
[2] Bély M, Apáthy Á: Clinical Pathology of rheumatoid arthritis. Akadémiai Kiadó, Budapest 2012 http://www.akkrt.hu.
[3] Istok R, et al. Annals Rheum Dis 1999; 58(Suppl1): 192.
[4] Istok R, et al: Reumatologia 2000; 2: 91.
[5] Istok R, et al: Exp Dermatol 2001; 26:545–547.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1226

AB0165 CXCL4 MAY PLAY A KEY ROLE IN SYSTEMIC SCLEROSIS BY DRIVING CD4 T CELLS TO PRODUCE IL-17

A.J. Affandi[1,2], S.C. Silva Cardoso[1,2], S. Garcia-Perez[1,2], W. Marut[1,2], J.A.G. van Roon[1,2], T.R.D.J. Radstake[1,2]. *[1]Laboratory of Translational Immunology; [2]Dept. of Rheumatology & Clinical Immunology, UMC Utrecht, Utrecht, Netherlands*

Background: CXCL4 regulates multiple facets of immune response and its level is highly increased in various Th17-associated rheumatic diseases, including systemic sclerosis (SSc)[1–4]. Recently, CXCL4 was shown to induce type I interferon production as well as endothelial activation in SSc patients[1]. Th17 skewing has been demonstrated in SSc[5–6], however, whether CXCL4 plays a role in the induction of IL-17 production by human CD4 T cells is currently unclear.
Objectives: To investigate the effect of CXCL4 on human CD4 T cell phenotype in particular IL-17 production in the absence or presence of antigen presenting cells.
Methods: Blood was obtained from healthy donors and CD4 T cells, monocytes, dendritic cells, were isolated using magnetic-based sorting (n=20). In addition, CD4 T cells from SSc patients were isolated (n=10). CD4 T cells were activated using anti-CD3/CD28, or in co-cultures with antigen presenting cells, stimulated using superantigen Staphylococcal enterotoxin B. Exogenous recombinant human CXCL4 was added during (co-)culture in different concentrations. Cytokine production and proliferation were analyzed using Luminex immunoassays, intracellular cytokine staining, and flow cytometry.
Results: CXCL4 directly induced CD4 T cells secreting both IL-17 and IFN-γ, as well as IL-22, when costimulated with anti-CD3/CD28 ($p<0.05$). In many SSc patients, similar IL-17 increase upon CXCL4 treatment was observed, although this did not reach statistical significance. This might be due to the fact that CD4 T cells from SSc patients had already significant higher levels of IL-17 as compared to healthy donors (2182±722.2 vs 1053±263.6 pg/ml, mean±SEM, $p<0.05$). Furthermore, in co-culture system of CD4 T cells with monocytes or myeloid dendritic cells, CXCL4 treatment induced IL-17 production upon triggering by superantigen ($p<0.05$). Moreover, when monocyte-derived dendritic cells were differentiated in the presence of CXCL4, they orchestrated significantly increased levels of IL-17, IFN-γ, and proliferation by CD4 T cells (all $p<0.05$).
Conclusions: Altogether, we demonstrate that CXCL4 boosts pro-inflammatory cytokine production especially IL-17 by human CD4 T cells, either by acting directly or indirectly via antigen presenting cells. This indicates that targeting CXCL4 may potentially alleviate immune responses in Th17-mediated rheumatic diseases such as systemic sclerosis.
References:
[1] van Bon L, Affandi AJ, Broen J, et al. N Engl J Med 2014.
[2] Tamagawa-Mineoka R, et al. Allergol Int 2008.
[3] Vettori S, et al. Clin Rheumatol 2016.
[4] Yeo L, et al. Ann Rheum Dis 2015.
[5] Radstake TRDJ, van Bon L, et al. PLoS One 2009.
[6] Yang X, et al. Arthritis Res Ther 2014.
Acknowledgements: This study was supported by the Dutch Arthritis Association (Reumafonds) to A.J.A. and T.R.D.J.R., the Netherlands Organization for Scientific Research (NWO) to A.J.A. (Mosaic grant 017.008.014) and T.R.D.J.R. (Pre-Seed grant), the Portuguese Fundação para a Ciência e a Tecnologia to S.C.S.C. (SFRH/BD/89643/2012) and the European Research Council to T.R.D.J.R. (ERC Starting grant).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6100

AB0166 INTERLEUKIN-6-POLARISED MACROPHAGES PROMOTE DERMAL MYOFIBROBLAST DIFFERENTIATION

A. Tam, X. Shi Wen, B. Ahmed-Abdi, C. Denton, D. Abraham, V. Ong. *University College London, London, United Kingdom*

Background: Macrophages and fibroblasts are key effector cell types present in scleroderma tissue[1]. While the effect of scleroderma fibroblast conditioned medium on macrophages has been previously studied[2], less is known about the effect of scleroderma macrophages on fibroblasts. Interleukin-6 (IL-6) is an important mediator of fibrosis and is overexpressed in scleroderma sera and cells such as skin fibroblasts, monocytes and endothelial cells[3]. Given the increase in IL-6 levels in scleroderma and presence of the IL-6 receptor on the cell surface of macrophages, we are now investigating the phenotype of macrophages exposed to IL-6. Here we present our work into the paracrine function of IL-6-treated macrophages in stimulating fibroblasts using a media transfer approach.

Objectives: To investigate the effect of macrophage conditioned media on fibroblast activation.
Methods: PBMC-derived macrophages from healthy control (n=3 females, mean age 50.8±21.9 years) and diffuse scleroderma (n=4 females, mean age 54.8±15.7 years, mean disease duration 73.2±90.3 months, 2 with antiScl70 and 2 with antiRNA polymerase antibodies) individuals were cultured in RPMI/10% FBS/M-CSF (4ng/ml)/P/S, quiesced in media with 1% BSA replacing the FBS, and left untreated (M0) or treated with IL-6 (50ng/ml, M (IL-6)) for 24 hours. The cultures were replaced with fresh media and collected after 24 hours. Conditioned media were applied to healthy control skin fibroblasts (24 hours) and fibroblast expression of fibrotic proteins was assessed by Western Blot, using β-tublin and TBP as loading controls. As control, fibroblasts from healthy volunteers were left untreated by culturing in non-conditioned media (fresh RPMI/ 1% BSA/M-CSF (4ng/ml)/P/S).
Results: Fibroblast expression of collagen type I and connective tissue growth factor (CTGF) were not significantly different between untreated and macrophage conditioned medium treatment groups. Baseline levels of collagen type I were high in the fibroblasts cultured in non-conditioned media, and there was a trend towards increased CTGF expression in all conditioned media-treated groups compared to untreated fibroblasts in non-conditioned media. A 2.6-fold increase in α-smooth muscle actin (α-SMA) was observed in the healthy control M (IL-6)-conditioned medium-treated group compared to the group of fibroblasts cultured in non-conditioned media (one-way ANOVA with Sidak multiple comparison, p=0.048).
Conclusions: After 24 hours treatment, control dermal fibroblasts treated with media of IL-6-polarised healthy control macrophages expressed higher levels of α-SMA compared to fibroblasts cultured in non-conditioned medium. A trend towards increased CTGF was also observed. These results suggest that paracrine factors in the IL-6-activated macrophage secretome may promote differentiation of fibroblasts into myofibroblasts, which is a key component of wound healing and scleroderma fibrosis.
References:
[1] Fuschiotti P. Current perspectives on the immunopathogenesis of systemic sclerosis. Immunotargets Ther. 2016;5:21–35.
[2] Denton CP, Shi-Wen X, Sutton A, et al. Scleroderma fibroblasts promote migration of mononuclear leucocytes across endothelial cell monolayers. Clin Exp Immunol. 1998;114:293–300.
[3] Khan K, Xu S, Nihtyanova S, et al. Clinical and pathological significance of interleukin 6 overexpression in systemic sclerosis. Ann Rheum Dis. 2012;71:1235–42.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4868

AB0167 CALCIUM INFLUX KINETICS AND THE CHARACTERISTICS OF POTASSIUM CHANNELS IN PERIPHERAL T LYMPHOCYTES IN SYSTEMIC SCLEROSIS

N. Legány[1], G. Toldi[2], I. Ocsovszki[3], L. Kovács[1], A. Balog[1]. *[1]Department of Rheumatology and Immunology, Faculty of Medicine, Albert Szent-Györgyi Health Center, University of Szeged, Szeged; [2]First Department of Obstetrics and Gynecology, Semmelweis University, Budapest; [3]Department of Biochemistry, Faculty of Medicine, Albert Szent-Györgyi Health Center, University of Szeged, Szeged, Hungary*

Background: Systemic sclerosis (SSc) is a chronic connective tissue disorder characterized by microvascular injury, fibrosis and autoimmunity that affects the skin and internal organs. The short-term activation of peripheral blood T lymphocytes plays a crucial role in initiating and maintaining the chronic inflammation. The transient increase of the cytoplasmic free calcium level plays a key role in the process of lymphocyte activation. Kv1.3 and IKCa1 potassium channels are important regulators of the maintenance of calcium influx during lymphocyte activation. The influx of calcium is maintained by the function of potassium channels that conserve the electrochemical potential gradient via the efflux of potassium from the cytoplasm. Recent reports raised the notion that the inhibition of lymphocyte potassium channels, especially that of the Kv1.3 channel would be an straightforward solution for specific immunosuppression in autoimmune disorders. Furthermore, our previous studies described an alteration of the short-term activation of peripheral lymphocytes in rheumatoid arthritis and primary Sjögren's syndrome (pSS), and the overexpression of Kv1.3 channels in pSS.
Objectives: Therefore, in this study we aimed to characterize the effects of lymphocyte potassium channel inhibition on short-term peripheral blood T lymphocyte activation in major lymphocyte subsets in SSc.
Methods: We enrolled 12 healthy individuals and 16 SSc patients. We evaluated calcium influx kinetics following activation in CD4, Th1, Th2 and CD8 cells applying a novel kinetic flow cytometry approach. We assessed the sensitivity of the above subsets to specific inhibition of the Kv1.3 and IKCa1 potassium channels. We also assessed the Kv1.3 expression on lymphocytes.
Results: We observed increased parameters of calcium influx in CD8+ lymphocytes' as compared with Th1 cells in SSc. However, the activation of CD8+ cells was lower in SSc compared to healthy controls. Moreover, activation of Th1 lymphocytes was slower in SSc than in healthy controls. The inhibition of IKCa1 potassium channel decreased the activation of CD8+ lymphocytes in healthy controls and the activation of Th1 cells in SSc. The inhibition of Kv1.3 channel modified the dynamics of activation of Th1 and Th2 lymphocytes in SSc.
Conclusions: The altered function of CD8+ cells and the specific inhibition of potassium channels seem to be a consequence of altered calcium influx kinetics in SSc, distinguishing it both from healthy controls and other autoimmune diseases.
Acknowledgements: Attila Balog and Gergely Toldi were supported by the János Bolyai Scholarship. Gergely Toldi is an International Society for the Advanecement of Cytometry (ISAC) Scholar.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5310

AB0168 PROTECTIVE EFFECTS OF EPIGALLOCATECHIN 3 GALLATE ON FIBROSIS IN SCLERODERMA MODEL

A. Kocak[1], D. Harmancı[1], M. Birlik[2], S. Sarioglu[3], G. Guner Akdogan[4]. *[1]Department of Molecular Medicine, Institute of Health Sciences, Dokuz Eylul University; [2]Department of Internal Medicine, Division of Rheumatology & Immunology; [3]Department of Medical Pathology, School of Medicine, Dokuz Eylul University; [4]Department of Biochemistry, School of Medicine, Izmir University of Economics, Izmir, Turkey*

Background: Scleroderma (SSc) is a disease that shows involvement in internal organs or on the skin characterized by fibrosis (1). Dermis thickening and uncontrolled extracellular matrix (ECM) increase are seen in this disease whose pathogenesis is not fully understood. TGF-β/Smad 2&3 pathway is pivotal role in SSc pathogenesis via induction of profibrotic molecules including collagen and by decrease of matrix metalloproteinases (MMPs) synthesis (2,3). The occurrence of the myofibroblast phenotype at fibrosis is thought to be responsible for the contracted regions of the affected tissues (4).
Objectives: The aim of this study with bleomycin (BLM) formed in an experimental model of scleroderma is to investigate the potential effects of epigallocatechin-3-gallate (EGCG) against fibrosis.
Methods: 32 *Balb/c* female mice were randomly selected into four groups.For 21 days: (1) Control group (n: 8) was given 100 μ L *subcutan (sc)* saline (SF) once a day, 100 μL *intraperitoneal (ip)* SF twice a week, (2) BLM group (n: 8) was given 100 μL (100 ug) *sc* BLM once a day, 100 μL *ip* SF twice a week, (3) BLM + EGCG group (n:8) was given 100 μL (100 ug) *sc* BLM once a day, 100 μL (100 μg) *ip* EGCG twice a week, (4) EGCG group (n: 8) was given 100 μL *sc* SF once a day, 100 mL (100 μg) *ip* ECCG twice a week. Hematoxylin&eosin and Masson trichrome staining of dermal areas were performed. Myofibroblast activity was measured using alpha smooth muscle actin antibody (αSMA) by immunohistochemistry.Expression levels of MMP-1, MMP-8, MMP-13 and p-SMAD protein were examined by western blot. Expression levels of TGF-β mRNA were examined by qPCR. All of the statistical analyses were performed using SPSS software and the quantitative data were expressed as the means±SEM.The quantitative variables were compared using the a ANOVA-Sidak. Statistical significance was defined as $p<0.05$

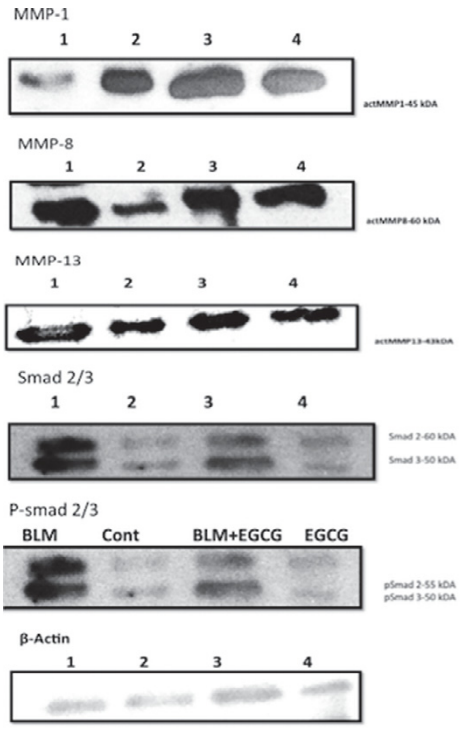


Figure 5. MMP-1, MMP-8, MMP-13, SMAD 2/3 and p-SMAD2/3 expression. β- Actin used for internal control.

Results: When compared to sham,control and experimental groups was observed to have reduced connective tissue fibrosis in dermis area, according to Masson Trichrome results. EGCG group showed a significant reduction in fibrosis at the dermal surface area with respect to hematoxylin measurements. MMP-1, MMP-8, p-SMAD 2/3 protein levels and TGF- β mRNA expression were slightly decreased in EGCG Group compared with the other tested groups ($p<0.05$). Otherwise, MMP-13 wasn't change between groups.
Conclusions: This study contributes to the potential use of EGCG as a treatment for fibrosis in SSc patients. Also, MMP-1&MMP-8 may play an important role in the etiology of SSc.
References:
[1] Varga, J. 2012. 15. Scleroderma-from pathogenesis to comprehensive management.Varga, J., Denton, C., Wigley, F.M./Denton C. New York: Springer.
[2] Ihn H. 2008. Autocrine TGF-beta signaling in the pathogenesis of systemic sclerosis. J Dermatol Sci 49: 103–113.
[3] Derk CT. 2007. Transforming growth factor-beta (TGF-beta) and its role in the pathogenesis of systemic sclerosis: a novel target for therapy? Recent Pat Inflamm Allergy Drug Discov 1: 142–145.
[4] Desmouliere A, Chaponnier C, Gabbiani G. 2005. Tissue repair, contraction, and the myofibroblast. Wound Repair Regen. 13(1):7–12.
Acknowledgements: This research was supported by a grant supplied from "Dokuz Eylul University Research Fund" and carried out at Dokuz Eylul University Medicine Faculty of Research Laboratory (R-LAB).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2076

AB0169 EVALUATION OF FREQUENCY AND TYPE OF PHYSICAL THERAPY IN MORE THAN 3400 PATIENTS WITH SYSTEMIC SCLEROSIS

D. Belz[1], P. Moinzadeh[1], N. Blank[2], E. Siegert[3], J. Henes[4], M. Worm[5], C. Sunderkoetter[6], M. Schmalzing[7], A. Kreuter[8], C. Gunther[9], L. Susok[10], G. Zeidler[11], I. Koetter[12], U. Mueller-Ladner[13], T. Krieg[1], A. Juche[14], T. Schmeiser[15], G. Riemekasten[16], E. Aberer[17], N. Gaebelein-Wissing[18], J.H.W. Distler[19], M. Sárdy[20], C. Pfeiffer[21], K. Kuhr[22], N. Hunzelmann[1].
[1]Dermatology, University Hospital Cologne, Cologne; [2]Rheumatology, University Hospital Heidelberg, Heidelberg; [3]Rheumatology, Charité Universitätsmedizin Berlin, Berlin; [4]Rheumatology, University Hospital Tuebingen, Tuebingen; [5]Dermatology, Charité Universitätsmedizin Berlin, Berlin; [6]Dermatology, University Hospital Muenster, Muenster; [7]Rheumatology, University Hospital Wuerzburg, Wuerzburg; [8]Dermatology, HELIOS St. Elisabeth Klinik Oberhausen, Oberhausen; [9]Dermatology, University Hospital Carl Gustav Carus, Dresden; [10]Dermatology, St. Josef Hospital Bochum, Bochum; [11]Rheumatology, Johanniter-Krankenhaus im Fläming Treuenbrietzen, Treuenbrietzen; [12]Rheumatology, Asklepios Klinik Altona, Hamburg; [13]Rheumatology, Justus Liebig University Giessen, Kerckhoff Clinic, Bad Nauheim; [14]Immanuel Krankenhaus Berlin-Buch, Berlin; [15]Rheumatology, Krankenhaus St. Josef, Wuppertal; [16]Rheumatology, University Medical Center-UKSH, Luebeck, Germany; [17]Dermatology, Medical University of Graz, Graz, Austria; [18]Dermatology, HELIOS University Hospital Wuppertal, Wuppertal; [19]Rheumatology, University Hospital Erlangen, Erlangen; [20]Dermatology, Ludwig Maximilians University Hospital, Munich; [21]Dermatology, University Medical Center Ulm, Ulm; [22]IMSIE, University of Cologne, Cologne, Germany

Background: Systemic sclerosis (SSc) is a chronic fibrosing autoimmune disease which leads to severe musculoskeletal dysfunction, disability and contractures. Little is known on the type and extent of physical therapy (PT) prescribed to SSc patients in daily practice.
Objectives: To determine the type and frequency of PT received by SSc patients.
Methods: The data of 3430 clinically well defined SSc patients registered in the database of the German Network for Systemic Sclerosis were analyzed using SPSS.
Results: 48,5% (1662/3430) of the patients were treated with PT. The most frequently used form of PT was lymphatic drainage (23,6%/876), followed by physical exercise therapy (22%/817) and paraffin wax bath (10,5%/389). About half of the patients (46,9%) received two or three different forms of PT simultaneously. The prescription of PT did not correlate with the SSc subtype, as 49,5% (503/1016) of dcSSc patients, 50,3% (850/1689) of lcSSc patients and 45,7% (143/313) of SSc-Overlap patients received PT. PT was significantly more often prescribed to patients with pulmonary fibrosis in 51,1% (617/1208), synovitis in 61,6% (299/485) and CK elevation in 61,1% (174/285) (p=0,001–0,029). PT did not correlate with the extent of skin fibrosis as measured by mRSS. Interestingly, patients with joint contractures (45,5%) (388/853) or tendon friction rubs (40,6%) (114/281) received significantly less often PT (p=0,006/ 0,045). Comparing the prescription of PT during the initial period 2003–2008 (49,1%; 1937/3942) with the follow up period 2009–2013 (45,3%; 2217/4899), a significant decrease of PT prescription was observed ($p<0,001$). Patterns of PT prescription differed significantly between medical subspecialties ($p<0,005$) i.e. rheumatologists, dermatologists.
Conclusions: Although SSc is characterized by considerable disability and restriction of motion, less than 50% of patients received PT. The significant decrease in PT prescription during recent years may reflect lack of knowledge how to prescribe PT and more restrictive insurance regulations.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3361

AB0170 DIMINISHED PERIPHERAL T-CELL ACTIVATION ALONG WITH MARKED TH17 CIRCULATING PROFILE IN SSC

E. Krasimirova[1], D. Kalinova[2], T. Velikova[1], E. Ivanova-Todorova[1], K. Tumangelova-Yuzeir[1], R. Rashkov[2], D. Kyurkchiev[1]. *[1]Laboratory of Clinical immunology; [2]Clinic of Rheumatology, University Hospital St. Ivan Rilski, Medical University of Sofia, Sofia, Bulgaria*

Background: Systemic sclerosis (SSc) is a rare, debilitating connective tissue disease characterized by immunological alterations, vasculopathy and progressive skin and multiorgan fibrosis. The autoimmune dysregulation in SSc comprises lymphocyte activation that leads to autoantibody production, abnormal production of cytokines and chemokines, and impairment of the innate immunity. Recent research has shown that the T cell activation and especially T helper cells play an important role in the pathogenesis of SSc. Amongst them are the proinflammatory Th17 cells.
Objectives: To investigate T-cell activation, the percentage of Th17 cells and the circulating cytokine profile in SSc.
Methods: We enrolled a total of 24 SSc patients and 16 healthy controls in the study and divided the patients as having diffuse cutaneous SSc (dcSSc, n=13) or limited cutaneous SSc (lcSSc, n=11). Peripheral venous blood samples were collected from all subjects. We examined the percentage of activated T cells (unstimulated and upon stimulation with PHA-M) and of Th17 cells by flow cytometry in both patients and controls. We used ELISA to quantitate the serum levels of human IL-6, TGF-β1, and IL-17A.
Results: We identified a decreased percentage of activated T cells (CD3+CD69+) in PHA-stimulated samples from SSc patients in comparison with healthy controls, $p<0.001$. However, we did not establish a correlation between the down-regulated CD3+CD69+ cells and the SSc phenotype.
With regard to Th17 cells, our patients demonstrated increased percentage as opposed to controls, p=0.031. We detected up-regulated Th17 cells within the lcSSc subset against controls, p=0.025. However, no difference was found between dcSSc and lcSSc patients. Regarding the peripheral cytokine profile, we detected raised levels of IL-6, $p<0.001$, TGF-β1, p=0.02, and IL-17A, $p<0.001$ in patients when compared to controls. Furthermore, we found increased circulating TGF-β, IL-6 and IL-17A in the lcSSc subset versus healthy individuals, as it follows TGF-β1, p=0.031, IL-6, $p<0.001$, and IL-17A, $p<0.001$. Furthermore, circulating IL-17A was higher in lcSSc as opposed to dcSSc subset, p=0.008. Within the dcSSc phenotype, we detected raised levels of IL-17A and IL-6 versus controls: IL-17A, $p<0.001$, IL-6, $p<0.001$.
Conclusions: Our results demonstrate down-regulated T-cell activation upon PHA-stimulation along with pronounced peripheral Th17 profile, and related cytokines in SSc patients, suggesting their implication in the pathogenesis of SSc.
References:
[1] Brembilla NC, Chizzolini C. T cell abnormalities in systemic sclerosis with a focus on Th17 cells. Eur Cytokine Netw 2012; 23 (4): 128–139.
[2] Raja J, Denton CP. Cytokines in immunopathology of systemic sclerosis. Semin Immunopathol 2015; 37 (5): 543–557.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5767

AB0171 ANTI-CARBAMYLATED PROTEIN ANTIBODIES IN PATIENTS WITH SYSTEMIC SCLEROSIS: AN INTRIGUING ASSOCIATION WITH SKIN INVOLVEMENT

E. Favoino[1], M. Prete[1], S. Vettori[2], A. Corrado[3], F.P. Cantatore[3], G. Valentini[2], F. Perosa[1]. *[1]Department of Biomedical Sciences and Human Oncology, Systemic Rheumatic and Autoimmune Disease Unit, University of Bari Medical School, Bari; [2]Department of Clinical and Experimental Internal Medicine, Rheumatology Section, Second University of Naples, Naples; [3]Department of Medical and Surgery Sciences, Rheumatology Unit, University of Foggia, Foggia, Italy*

Background: Systemic sclerosis (SSc), one of the most complex connective tissue disease, is characterized by three pathogenic events namely, vascular damage, autoimmunity and fibroblast activation, leading to a widespread fibrosis of skin and internal organs (1,2). Previous studies showed that 1) carbamylation mainly affects structural proteins undergoing to a low turn-over rate, namely dermal skin and tendons-associated proteins; and that 2) carbamylated proteins accumulate in skin in an age-dependent manner, contributing to tissue alteration (3).
Objectives: As dermis is a disease target and anti-carbamylated protein antibodies (anti-CarP Ab) have been reported in patients with SSc (4), we sought to evaluate any relationship between anti-CarP Ab and clinical parameters reflecting skin involvement in SSc.
Methods: Serum samples and clinical data from 123 patients with SSc were collected. Anti-CarP Ab were detected by indirect ELISA, using carbamylated bovine serum albumin as the antigen. Serum Anti-CarP Ab levels were also measured in 41 healthy aged-matched individuals. Clinical data were retrieved as previously reported (5).
Results: The mean serum levels of anti-CarP Ab did not statistically differ

between healthy and SSc group. In SSc, Spearman analysis showed that anti-CarP inversely correlated with the modified Rodnan skin score (RSS) (R= -0.325, $p<0.001$), independently of patients' age. Receiver operating characteristics (ROC) analysis identified the anti-CarP cutoff that best discriminated dichotomized clinical variables related to skin involvement. This cutoff that was employed to subdivide SSc patients into anti-CarP positive and anti-CarP negative patients. Three SSc skin-related clinical parameters were significantly different between groups: RSS (p=0.001), SI skin (p=0.002), and scleredema ($p<0.001$). A worse skin involvement was associated with low anti-CarP levels.

Conclusions: The study shows that anti-CarP Ab serum level inversely associates to the severity of skin involvement in SSc patients. One possible mechanism to explain the inverse association is that the disease-dependent accumulation of carbamylated proteins in the skin may neutralize circulating anti-CarP Ab, thus contributing to their serum levels decrease. However, further investigation is needed to clarify this issue and to assess whether the levels anti-CarP Ab can be useful in the clinical setting of SSc.

References:

[1] Varga J, Abraham D. J Clin Invest 117:557–67, 2007.
[2] Guy S, Kong J, Cheema GS, Keen CL, Wick G, Gershwin ME. Semin Arthritis Rheum 38:132–60, 2008.
[3] Gorisse L, Pietrement C, Vuiblet V, Schmelzer CEH, Köhler M, *DucaL*, *DebelleL*, *FornèsP*, *SJaisson*,and Gillery P. Proc Natl Acad Sci U S A 113(5): 1191–1196, 2016.
[4] Pecani A, Alessandri C, Spinelli FR, Priori R, Riccieri V, Di Franco M, Ceccarelli F, Colasanti T, Pendolino M, Mancini R, Truglia S, Barbati C, Vomero M, Sabatinelli D, Morello F, Valesini G, Conti F. Arthritis Res Ther 18(1):276, 2016.
[5] Perosa F, Favoino E, Favia IE, Vettori S, Prete M, Corrado A, Cantatore FP, Valentini G. Medicine (Baltimore) 95(25), 2016.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6377

AB0172 PSGL-1 AND ADAM8 ON DENDRITIC CELLS ARE ASSOCIATED WITH SYSTEMIC SCLEROSIS AND COULD ACT AS BIOMARKERS FOR INTERSTITIAL LUNG DISEASE

J. Silván[1], R. González-Tajuelo[1], E. Vicente-Rabaneda[2], A. Pérez-Frías[1], M. Espartero-Santos[1], E. García-Lorenzo[2], I. González-Alvaro[2], S. Castañeda[2], A. Urzainqui[1]. *[1]Immunology; [2]Rheumatology, Hospital Universitario de la Princesa, Madrid, Spain*

Background: Systemic sclerosis (SSc) is a chronic autoimmune disorder with cutaneous, vascular and immune cells abnormalities that lead to extensive cutaneous and visceral fibrosis with high morbidity and mortality. P-Selectin glycoprotein ligand-1 (PSGL-1) is the major ligand for P-selectin. PSGL-1 mediates the initial contacts with endothelial cells during extravasation to inflamed tissues or homing to several tissues in homeostatic conditions. In addition, PSGL-1/P-Selectin interaction contributes to the homeostasis of the immune system by generating regulatory T cells[1]. Importantly, the metalloprotease ADAM8 interacts with PSGL-1 and proteolytically processes it, what could be a regulatory mechanism to control the expression of PSGL-1[2]. Interestingly, mice lacking PSGL-1 develop a progressive SSc-like syndrome[3].

Objectives: To investigate whether PSGL-1 and ADAM8 expression on leukocytes could be implicated in the pathogenesis of SSc.

Methods: PBLs from 47 SSc patients and 35 healthy donors were analyzed by flow cytometry. The percentage of cells expressing PSGL-1, HLA-DR and ADAM8, as well as the membrane (without cell permeabilization) and total (after cell permeabilization) expression were assessed for each leukocyte subset. For cell permeabilization, cells were incubated for 15 min at room temperature with a fixation/permeabilization solution. Positivity was stablished using isotype control antibodies. Comparisons between groups were analyzed with Student t tests or Mann-Whitney U test. For pairwise multiple comparisons one-way ANOVA with Tukey's post hoc test was applied ($p<0.05$, 95% CI). To analyze the possible contribution of PSGL-1, ADAM8 and HLA-DR to SSc pathogenesis, and to explore whether they could be used as biomarkers for SSc, we studied the influence of these molecules using a multivariate logistic regression model.

Results: SSc patients showed increased expression of HLA-DR in antigen presenting cells (B cells, monocytes and dendritic cells), indicating a higher activation of these cells. PSGL-1 expression in B cells was decreased in SSc patients but increased in monocytes, dendritic cells (DC) and T cells. ADAM8 was increased in B and T lymphocytes, monocytes and DC from SSc patients. Overall, we have identified three variables that are associated with SSc: high percentage of ADAM8-expressing pDC, high PSGL-1 expression in cDC and high HLA-DR expression in CD16+ monocytes. Remarkably, highest PSGL-1 expression on conventional DC (cDC) and high levels of ADAM8 on plasmacytoid DC (pDC) associate with interstitial lung disease (ILD), one of the most severe SSc clinical manifestations, suggesting that PSGL-1 and ADAM8 could be prognostic markers of ILD.

Conclusions: This study highlights that PSGL-1 and ADAM8 expression on DC, monocytes and lymphocytes could be implicated in SSc pathogenesis and particularly on DC might act as biomarkers for ILD.

References:

[1] Urzainqui et al., J. Immunol 2007; Domínguez-Luis et al., Eur J Immunol 2011.
[2] Pérez-Frías et al., Arthritis Rheumatol 2014.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5038

AB0173 MYCOBACTERIAL INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS: CLINICAL SIGNIFICANCE AND ASSOCIATED FACTORS. DATA FROM THE REGISTRY OF PATIENTS WITH SLE OF THE SPANISH SOCIETY OF RHEUMATOLOGY (RELESSER)

J. Pego-Reigosa[1], V. Campo[2], A. Lois-Iglesias[3], C. Mouriño[2], F. López-Longo[4], M. Galindo[5], J. Calvo[6], J. Ibañez[7], A. Olivé[8], R. Melero[9], A. FdezNebro[10], J. Bernal[11], C. Erausquin[12], E. Tomero[13], L. Horcada[14], E. Uriarte[15], M. Freire[3], I. Rua-Figueroa[12] on behalf of EASSER-RELESSER. *[1]Hospital e IISGS; [2]H, Vigo; [3]H, Coruña; [4]H Gregorio Marañon; [5]H 12Octubre, Madrid; [6]H, Araba; [7]Povisa, Vigo; [8]H, Germans Trias; [9]H, Ourense; [10]H, Carlos Haya; [11]H, Alicante; [12]H, GCanaria; [13]H, la Princesa; [14]H, Navarra; [15]H, Donostia, Spain*

Objectives: To study the prevalence of mycobacterial infection (MI), the associated factors and their clinical significance in patients included in a large SLE cohort.

Methods: Retrospective descriptive study of RELESSER patients with a history of MI and analysis of the factors associated with this infection.

Results: In RELESSER 3,658 patients with ≥4 ACR SLE criteria were included. 90% are women with a mean age of 32.9 years. 93% are Caucasians. The mean follow-up time (± SD) was 120.2 (± 87.6) months. 705 (19.3%) patients had ≥1 severe infection (defined as requiring admission); 1,227 severe infections occurred. MI were diagnosed in 42 patients (1.2% of all RELESSER patients, 3.4% of all severe infections), 85.7% women. The incidence rate of MI was 1 per 1,000 patients/year (95% CI:0.7–1.4).

MI presentation was pulmonary in 18 (42.9%) patients and extrapulmonary in 24 (57.1%) patients [joints in 8 (19.0%) patients, soft tissue in 6 (14.3%) and other sites in 10 (23.8%)]. The extrapulmonary form was associated with immunosuppressants use: 84.6% of the 13 patients treated with immunosuppressive drugs versus 44.4% of the 27 patients without (p=0.01). We did not observe this association with the use of corticosteroids.

To study the factors associated with MI, we performed a bivariate analysis including the variables associated with severe infection in RELESSER (age, sex, ethnicity, corticosteroids, immunosuppressants, antimalarials, previous admission by SLE activity, rituximab and anti-TNF use, Katz severity index, SDI index, SLEDAI index and Charlson comorbidity index). There is a statistically significant association with previous admission by SLE activity (RR:2.9, 95–95%:1.3–6.2, p=0.007), renal impairment (RR:2.0, CI 95%:1,1–3,7, p=0,04), the Katz score (RR:2.1, 95% CI:1.1- 4.0, p=0.04) and the Charlson index (RR: 2.5; 95% CI: 1.3–4.8, p=0.009). Damage (SDI>0) was closely associated with significance:RR: 2.0; 95% CI: 1.0–4.0, p=0.07. Iimmunosuppressants use was associated with an important increase in the risk of MI: RR:4.3; 95% CI:2.2–8.3, p=0.31.

Two patients (4.8%) died (1 respiratory and 1 extrapulmonary). Mean survival after MI diagnosis in these cases was 21 days.

Conclusions: MI in RELESSER affects 1.15% of patients. Its incidence rate is 1 per 1,000 patients/year (95% CI:0.7–1.4). Extrapulmonary localization affects more than half of the patients and is associated with immunosuppressants use. Previous admission by SLE activity, renal involvement, SLE severity and increased number of comorbidities are factors associated with MI.

Acknowledgements: Work supported by Spanish Society of Rheumatology, FIS/ISCIII/FEDER (PI11/02857), BIOCAPS from the European Union 7th Framework Programme/REGPOT-2012–2013.1(316265), GSK, Roche, Novartis, UCB.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2974

AB0174 LYMPHOCYTE SUBSETS T, B AND NK CELS IN SYSTEMIC SCLEROSIS

L. Schneider[1], V. Hax[1], N. Marcondes[2], R.M. Xavier[1], R. Chakr[1]. *[1]Rheumatology; [2]HCPA, Porto Alegre, Brazil*

Background: Systemic sclerosis (SSc) is a rare multisystem disease with underlying immune mechanisms, whose pathogenesis remains unclear. Few previous reports have evaluated lymphocyte subpopulations in SSc and your results are conflicting.

Objectives: The present study aimed to analyze the lymphocyte subsets in SSc patients in comparison to healthy individuals.

Methods: Peripheral blood (PB) samples to analyze lymphocyte subsets were obtained from a non-random convenience sample of 20 SSc patients. Twenty healthy individuals recruited from the blood bank were used as sex and age-matched controls. Blood samples were analyzed by flow cytometry for total T cells, CD4+ and CD8+ T cells subsets, CD19+ B cells and total NK cells. Statistical analyses were performed using the IBM Statistical Package for Social Sciences (SPSS 18.0). Data are expressed as mean ± SD and median and range. Non-parametric Mann–Whitney U test was used for analyses of the flow cytometry. A probability $p<0.05$ was considered statistically significant.

Results: The mean (SD) age of SSc patients was 57.9 (14.2) years, 95% were female and 31.6% presented diffuse cutaneous SSc (dcSSc). Patients presented a lower mean total lymphocyte count compared to healthy controls (23.7% vs.

29.6%, p=0.026) (Table 1.). No statistically significant differences were found in the percentages or the absolute numbers of T, B or NK cells.
Conclusions: Our data support previous reports indicating that depletion of lymphocyte in the PB of SSc patients. However, we found no significant difference in relation to lymphocyte subtypes, which differs from the literature data.
References:
[1] T and NK Cell Phenotypic Abnormalities in Systemic Sclerosis: a Cohort Study and a Comprehensive Literature Review. Almeida et al, 2015.
[2] Liu M, Wu W, Sun X, Yang J, Xu J, Fu W, Li M. New insights into CD4+ T cell abnormalities in systemic sclerosis. Cytokine & Growth Factor Reviews, 2016; 28:31–36.
[3] Gambichler T, Tigges C, Burkert B, Höxtermann S, Altmeyer P, Kreuter A. Absolute count of T and B lymphocyte subsets is decreased in systemic sclerosis. Eur J Med Res 2010; 15:44–46.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7028

AB0175 INHIBITORY EFFECT OF ENDOTHELIN-1 TYPE A RECEPTOR ANTAGONISTS ON MIGRATION OF NEUTROPHILS AND TUMOUR CELLS

L.M. Kappes[1], S. Sommerlatte[1], C. Plattfaut[2], S. Pitann[1], G. Marschner[1], H. Heidecke[3], P. Lamprecht[1], A. Müller[1], F. Gieseler[2], O. Cabral-Marques[1], G. Riemekasten[1]. *[1]Department of Rheumatology; [2]Department of Oncology, University of Lübeck, Lübeck; [3]Celltrend GmbH, Luckenwalde, Germany*

Background: Endothelin-1 type A receptor (ETAR) antagonists (e.g. ambrisentan) are currently approved by the U.S Food and Drug administration, representing a well-tolerated treatment of pulmonary arterial hypertension (PAH)[1] for patients with connective tissue diseases such as systemic sclerosis (SSc). Noteworthy, increased numbers of infiltrating neutrophils have been associated with worse clinical outcome in PAH patients. In another context, several studies have reported that endothelin-1 and its receptor ETAR also play a central role in the development of tumour cell invasion and metastasis. However, the effects of ETAR antagonists on migration of neutrophils and tumour cells remain to be determined.
Objectives: The objective was to analyse the effects of two ETAR antagonists on migration of neutrophils and tumour cell lines.
Methods: The migratory ability of peripheral neutrophils from healthy donors (HD) and different tumour cell lines (myeloid leukaemia HL60 cells and human pancreatic adenocarcinoma COLO357 cells) was analysed in response to N-Formylmethionyl-leucyl-phenylalanine (FMLP) or Protease-activated receptor 2 (Par-2) agonist. Because it has been shown before [2], IgGs from HD and SSc patients were used as additional stimulus for migration. Neutrophils and HL60 cells were preincubated (1h) with sitaxentan or ambrisentan, respectively, before being tested for migration (1h) using the Transwell assay. COLO357 cells were incubated (48h) in the presence of sitaxentan and migration was tested in the Oris Pro Cell assay. Migration was analysed by automatic cell counting or digital photo analysis and a migration index was calculated.
Results: Sitaxentan and/or ambrisentan significantly blocked the migration of neutrophils and tumour cell lines. In more detail, neutrophil migration in response to FMLP, being set to 100%, was completely inhibited by sitaxentan (0,46%). Further, neutrophil migration in response to IgGs from HD and SSc patients was induced equally, again being set to 100%. In the presence of sitaxentan migration was reduced to 60%, respectively. In DMSO-differentiated HL60 cells the migratory capacity in response to FMLP (100%) was reduced to 66% by ambrisentan and to 14% by sitaxentan. Moreover, in the presence of sitaxentan and a Par-2 agonist the migratory ability of COLO357 cells was significantly decreased to 89% compared to Par-2 agonist only, being set to 100%.
Conclusions: Our results suggest a pivotal and non-redundant role of ETAR in cell migration, which needs further clarification in order to repurpose the use of ETAR inhibitors. Therapeutic switching of ETAR antagonists from PAH to cancer therapies is a promising adjuvant therapy.
References:
[1] Waxman AB. A review of sitaxsentan sodium in patients with pulmonary arterial hypertension. Vasc Health Risk Manag 2007;3:151–7.
[2] Kill A, Tabelin C, Undeutsch R, et al. Autoantibodies to angiotensin and endothelin receptors in systemic sclerosis induce cellular and systemic events associated with disease pathogenesis. Arthritis R&T, 2014, 16:R29.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6173

AB0176 MITOCHONDRIAL DYSFUNCTION IN IDIOPATHIC INFLAMMATORY MYOPATHY DERIVED MYOBLASTS

C. Basualto-Alarcón[1], M.F. Bozán[2], J. Bevilacqua[1,2], F. Urra[1], D. González[1], H. Gatica[2], A. Göecke[2], P. Wurmann[2], M.F. Sabugo[2], S. Saavedra[2], C. Cárdenas[1,3,4]. *[1]Cellular Metabolism and Bioenergetics Laboratory; Anatomy and Developmental Biology Program; ICBM; Faculty of Medicine., Universidad de Chile; [2]Hospital Clínico Universidad de Chile; [3]Geroscience Center for Brain Health and Metabolism, Universidad de Chile, Santiago, Chile; [4]Buck Institute for Research on Aging, Novato, United States*

Background: Idiopathic inflammatory myopathies (IIM) are acquired skeletal muscle diseases, characterized by proximal muscle weakness. This syndrome includes five different (1) diseases, nevertheless, in this work, we included dermatomyositis (DM) and polymyositis (PM) patients. Has been reported that despite treating inflammation, muscle atrophy and weakness persist in some patients, suggesting an inherent muscle cause (2,3). In addition, histological studies show some mitochondrial abnormalities. Our aim was to evaluate a possible role for mitochondrial dysfunction in the pathophysiology of this diseases.
Objectives: To compare the mitochondrial status of myoblast obtained from myositis patients -and healthy control- biopsies.
Methods: Primary cultured myoblasts extracted from the deltoid of IIM patients were used and compared with myoblasts obtained from normal patients subjected to shoulder surgery. Also, a human skeletal muscle cell line (RCMH) was used as control. The bioenergetic profile was analyzed with an Extracellular flux analyzer^{e}96 (Seahorse Biosciences). Also, biopsy tissue was used for Western blot (WB) and immunofluorescence experiments.
Results: Basal oxygen consumption rate, ATP-linked oxygen consumption, maximal oxygen consumption and spare respiratory capacity were lower in IIM myoblasts when compared to RCMH myoblasts, however, when compare to control primary cultured myoblasts we only find differences in ATP-linked oxygen consumption. Expression levels of mitochondrial complexes (I, III, IV and V) were analyzed by WB in tissue samples. No differences were observed between control and IIM patients. Mitochondrial area was estimated by immunofluorescence of the voltage dependent anion channel (VDAC), which show no differences between control and patients.
Conclusions: IIM derived myoblasts present a compromised mitochondrial function, compared to control myoblasts. Specially, oxygen consumption associated with ATP synthesis show decreased levels in patients. Although, expression levels of the mitochondrial complexes as well as mitochondrial area were not different between control and patients. Future experiments should address if IIM mitochondria are consuming less oxygen because of a lower ATP demand or because a primary mitochondrial damage.
References:
[1] Dalakas M. Inflammatory Muscle Diseases. N Engl J Med. 372:1734–1747, 2015.
[2] Park, J. H. et al. Magnetic resonance imaging and P-31 magnetic resonance spectroscopy provideunique quantitative data useful in the longitudinal management of patients with dermatomyositis. Arthritis Rheum.37, 736–46, 1994.
[3] Lee, H.-K. et al. Foxo/Atrogin induction in human and experimental myositis. Neurobiol. Dis.46, 463–475, 2012.
Acknowledgements: FONDECYT 3150623 & 1151383; FONDAP 15150012.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3889

AB0177 INCREASED LEVELS OF THE INFLAMMATORY PROTEINS CXCL10, CXCL11, TNFR2 AND YLK-40 TYPIFY THE EARLIEST PHASE OF SYSTEMIC SCLEROSIS (SSC)

M. Cossu[1,2], L. van Bon[1], M. Rossato[1,2], L. Beretta[3], T.R.D.J. Radstake[1,2]. *[1]Rheumatology & Clinical Immunology; [2]Laboratory of Translational Immunology (LTI), UMC Utrecht, Utrecht, Netherlands; [3]Referral Center for Systemic Autoimmune Diseases, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy*

Background: Definite systemic sclerosis (defSSc) patients yet lacking the prototypical signs of fibrosis stratify in an intermediate severity stage between pre-clinical and fibrotic, limited cutaneous (lcSSc) and diffuse cutaneous (dcSSc) phenotypical subsets[1].
Objectives: We aimed to molecularly position defSSc patients in respect to healthy controls (HC) and early SSc (EaSSc) patients with a broad panel of serum mediators of inflammation and tissue damage in an attempt to increase the knowledge in pathophysiologic mechanisms and biomarkers availability, thereby offering new ground for disease interception before fibrosis develops.
Methods: To this end, an 88-plex immunoassay was performed in sera from an identification cohort composed of 21 EaSSc according to LeRoy and Medsger criteria[2] without other signs and symptoms of evolutive disease, 15 defSSc patients according to the 2013 ACR/EULAR criteria[3] without skin or lung fibrosis and 11 HC. A larger cohort comprising 47 EaSSc, 48 defSSc and 43 HC was used for replication purposes. Fifty-one lcSSc and 35 dcSSc as comparison with established, fibrotic disease were recruited in parallel.
Results: Sixteen mediators differentially expressed in EaSSc and defSSc were selected for replication (one-way ANOVA and/or ANOVA polynomial test for trend with exploratory threshold $p<0.1$). Amongst these, after correction for multiple comparisons, CXCL10/IP-10, CXCL11/I-TAC, TNFR2 and CHI3L1/YKL-40 showed a significant upregulation in defSSc and EaSSc with a linear increase from HC to EaSSc to defSSc. The level of upregulation observed in defSSc individuals was similar (CXCL10/IP-10, CXCL11/I-TAC) or further increased (TNFR2, CHI3L1/YKL-40) in lcSSc and dcSSc patients. A set of 7 ranked markers (Angiopoietin-2, TNFR2, CXCL11/I-TAC, CXCL10/IP-10, sICAM-1, CHI3L1/YKL-40, CXCL9/MIG) provided a good visualization of the gradually increasing pattern from HC to EaSSc to defSSc to lcSSc and dcSSc.
Conclusions: This is the first attempt to validate circulating biomarkers defining the earliest phases of SSc. Despite the need for confirmation in a prospective

setting, our results confirm that defSSc might represent an intermediate entity between pre-clinical stages and the most severe subsets of disease, thereby opening new perspectives on SSc pathophysiology and disease interception.

References:
[1] Cossu M, et al. Rheumatology 2016.
[2] LeRoy EC, et al. J Rheumatol 2001.
[3] van den Hoogen F, et al. Arthritis Rheum 2013.

Acknowledgements: Supported by a grant from Gruppo Italiano per la Lotta alla Sclerodermia (GILS). MC and TR are partly supported by the VIDI laureate and Dutch Arthritis Foundation (NWO, Netherlands Institute for Science) and ERC starting grant (EU) obtained by TR. The LTI MultiPlex Core Facility is acknowledged for technical performance of the multiplex immune assays.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5295

AB0178 PHENOTYPING OF NATURAL KILLER (NK) RECEPTORS ON NK AND NKT-LIKE CELLS DISCLOSES DEFECTIVE IMMUNE-REGULATORY CAPABILITY IN PATIENTS WITH SYSTEMIC SCLEROSIS

M. Cossu[1,2], L. Beretta[3], E. Trombetta[4], S.T.A. van Bijnen[5,6], M. Rossato[1,2], L. van Bon[1], M. van der Kroef[1,2], E.C. Chouri[1,2], C.G.K. Wichers[1,2], N. Vazirpanah[1,2], M.C. Vonk[7], L. Porretti[4], F. Preijers[6], H. Dolstra[6], T.R.D.J. Radstake[1,2]. *[1]Rheumatology & Clinical Immunology; [2]Laboratory of Translational Immunology (LTI), UMC Utrecht, Utrecht, Netherlands; [3]Referral Center for Systemic Autoimmune Diseases; [4]Flow Cytometry Service, Clinical Chemistry and Microbiology Laboratory, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy; [5]Hematology; [6]Laboratory Medicine, Laboratory of Hematology; [7]Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands*

Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by dysregulation of the immune system, vasculopathy and fibrosis of the skin and internal organs. Natural Killer ($CD56^+CD3^-$, NK) and NKT-like ($CD56^+CD3^+$) cells display receptors (NKR) whose expression pattern determines their cytotoxic and immune-regulatory activity. The role of NK and NKT-like cells in the dysregulation of the immune system in SSc has not been fully elucidated yet.
Objectives: To improve our knowledge on the contribution of NK, NKT-like and a subset of NKT cells expressing invariant TCR (iNKT) in SSc development, we performed a broad phenotyping of NKR in the circulation of SSc patients, including subjects with pre-clinical SSc.
Methods: NKR were assessed by flow cytometry using two 13-color panels on whole blood of 84 SSc patients and 20 healthy controls (HC). In particular, 15 patients with early SSc (EaSSc) without signs or symptoms of evolutive disease (2001 LeRoy and Medsger criteria[1]), 24 patients with definite SSc without skin or lung fibrosis (defSSc), 26 patients with limited (lcSSc) and 19 patients with diffuse cutaneous SSc (dcSSc) (2013 ACR/EULAR classification criteria for SSc[2]) were included. NK degranulation in response to K562 target cells was assessed in lcSSc and dcSSc patients versus HC.
Results: The number of circulating lymphocytes, NKT-like and iNKT cells - but neither $CD3^+$ T nor NK cells - was reduced in dcSSc versus HC. $NKp46^+$ NK cells co-expressing NKG2D and CD16 were decreased in dcSSc versus HC and EaSSc. Consistently with these observations, dcSSc exhibited lower degranulation capability. $(CD57^+)KIR^+$ and activating NKR-expressing NKT-like cells were diminished in both dcSSc and lcSSc versus HC.
Conclusions: dcSSc patients showed a defective NK cytotoxicity potential, possibly due to the decreased $NKp46^+$ fraction. The regulatory, cytolytic KIR^+ NKT-like fraction was also reduced with a parallel decrease of activating receptors expression in both lcSSc and dcSSc. Overall these results point towards an impairment of NK and NKT-like cells as immune check-points in fibrotic SSc.

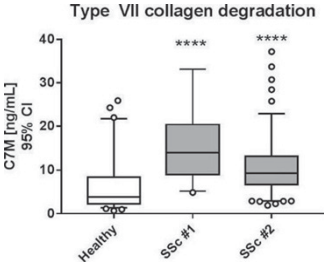
References:
[1] LeRoy EC, et al. J Rheumatol 2001.
[2] van den Hoogen F, et al. Arthritis Rheum 2013.

Acknowledgements: Supported by a grant from Gruppo Italiano per la Lotta alla Sclerodermia (GILS). MC and TR are partly supported by the VIDI laureate and Dutch Arthritis Foundation (NWO, Netherlands Institute for Science) and ERC starting grant (EU) obtained by TR. The authors would like to thank Koos Gaiser (U-DAIR, LTI, UMC Utrecht) for the technical assistance in developing the 13-color flow cytometry panels; Dr F. Montero, L. Nieto-Gligorovski and E. Gautherot (Beckman Coulter Inc, Marseille) for providing the NKG2A-PB antibody; the NIH Tetramer Facility for providing the CD1d tetramers.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5059

AB0179 DEGRADATION OF TYPE VII COLLAGEN (C7M) IS ASSOCIATED WITH SYSTEMIC SCLEROSIS – DEVELOPMENT OF A NOVEL NEO-EPITOPE SPECIFIC ASSAY

J. Sand[1], P. Juhl[1], L. Iversen[2], T. Karlsmark[2], M. Karsdal[1], A.-C. Bay-Jensen[1], M. Mogensen[2], A.S. Siebuhr[1], D. Leeming[1]. *[1]Nordic Bioscience, Herlev; [2]Department of dermatology, Bispebjerg Hospital, Copenhagen, Denmark*

Background: Type VII collagen (col7) is the main component of the anchoring fibrils that connects the basement membrane to the underlying interstitial matrix and has mainly been investigated for its role in blistering skin diseases. It has been investigated for its role in dystrophic epidermolysis bullosa, a severe skin disease. Furthermore, increased levels of type VII collagen in skin has been reported for patients with systemic sclerosis (SSc).
Objectives: The objective was to develop and characterize a blood-based marker assessing col7 degradation in patients with SSc.
Methods: We identified a specific fragment of col7 in serum from COPD patients, which was not found in controls, using mass spectrometry. A monoclonal antibody was raised against the first ten amino acids of the neo-epitope (KLH-CGG-GPPGPPGRLV) and employed in a competitive ELISA (C7M). The C7M assay was validated technically and was subsequently evaluated in 2 cohorts including SSc patients. The first cohort (SSc#1; n=35) consisted of early (<2 years of SSc symptoms; n=16) and late (>10 years of disease with stable skin for at least 6 months, n=19) diffuse SSc patients, while the second cohort (SSc#2; n=119) consisted of limited (n=78) and diffuse (n=41) SSc patients. Serum C7M levels were likewise measured in healthy subjects and compared to the levels of SSc patients using the Kruskal-Wallis test with Dunn's multiple comparisons test comparing healthy individuals with the two SSc cohorts.
Results: A technically robust competitive ELISA (C7M), which was highly specific for a col7 fragment was developed. The assay showed acceptable inter- (13%) and intra-assay (9%) variation, linearity (102% dilution recovery), analyte stability (102% recovery after 4 freeze/thaw cycles), and interference.
The C7M marker was evaluated by comparing serum levels in healthy donors with patients with SSc (Figure). Serum C7M levels were not associated with age, gender, BMI, or disease duration. The geometric mean serum C7M level in healthy donors was 4.6 ng/mL (95% CI 3.7–5.6 ng/mL). The geometric mean serum C7M levels were significantly elevated in both cohorts of patients with SSc (SSc#1, 13.6 ng/mL [95% CI 11.1–16.5], $p<0.0001$; SSc#2, 9.2 ng/mL [95% CI 8.3–10.2], $p<0.0001$). Furthermore, a significant difference were observed between the two cohorts (P=0.05).



Conclusions: The C7M ELISA enabled quantification of type VII collagen degradation in serum. Elevated serum C7M levels indicated that the remodeling of type VII collagen was significantly increased in patients with SSc, suggesting a pathological role.

Acknowledgements: We thank Biogen Idec's SSc department for their contribution.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5689

AB0180 BIOMARKERS OF EXTRACELLULAR MATRIX REMODELING ARE ASSOCIATED WITH ACUTE EXACERBATIONS OF IDIOPATHIC INTERSTITIAL PNEUMONIA

J. Sand[1], P. Juhl[1], Y. Tanino[2], T. Nikaido[2], K. Misa[2], Y. Sato[2], R. Togawa[2], X. Wang[2], M. Karsdal[1], A.-C. Bay-Jensen[1], D. Leeming[1], A.S. Siebuhr[1], M. Munakata[2]. *[1]Nordic Bioscience, Herlev, Denmark; [2]Department of Pulmonary Medicine, Fukushima Medical University School of Medicine, Fukushima, Japan*

Background: Idiopathic interstitial pneumonia (IIP) is characterized by an increased rate of extracellular matrix (ECM) turnover resulting in fibrosis. The pathogenic remodeling includes increased levels of protein synthesis and degradation mediated by proteases such as matrix metalloproteinases (MMPs). Acute exacerbations of IIP (AE-IIP) represent periods of increased disease activity. Pulmonary involvement, especially pulmonary fibrosis, is common in patients suffering from systemic sclerosis (SSc) and ankylosing spondylitis (AS)
Objectives: The objective was to investigate if ECM remodeling was altered during AE-IIP by serological neo-epitope biomarkers.
Methods: Serum samples were collected from patients with IIP at clinically stable disease (S-IIP, n=29) and at AE-IIP (n=68). Of these, 11 and 28 patients, respectively, had idiopathic pulmonary fibrosis (IPF). 28 IIP patients had paired samples. Biomarkers released from MMP-mediated degradation of collagen type I (C1M), III (C3M), IV (C4M), and VI (C6M), elastin (ELM7), versican (VCANM), biglycan (BGM), and C-reactive protein (CRPM) were assessed in serum by competitive ELISAs utilizing neo-epitope specific monoclonal antibodies. Data were analysed using Mann-Whitney test, Wilcoxon test, Spearman's rank correlation, and Kaplan-Meier curves as appropriate.
Results: Mean age of patients was 71 (range 54–86) at AE-IIP and 69 (range 55–83) at S-IIP. Mean forced vital capacity in percentage of predicted value (%FVC) was 55.6% (SD 19.5) at AE-IIP and 79.0% (SD 26.5) at S-IIP. Serum

levels of C4M, C6M, and CRPM at AE-IIP were positively correlated with %FVC (r=0.37, p=0.008; r=0.36, p=0.011; r=0.33, p=0.020; respectively). Serum levels of C4M (p=0.002) and C6M (p=0.024) were increased while ELM7 (p=0.024) and VCANM (p<0.0001) were decreased at AE-IIP as compared with S-IIP when analyzing all patients. IPF patients had lower levels of VCANM at AE-IPF (p=0.0001). Patients with paired samples showed significantly elevated serum levels of C4M (p=0.004) and decreased levels of ELM7 and VCANM (p=0.036 and p=0.0001, respectively) at AE-IIP. C1M and C6M levels at AE-IIP were borderline related to mortality outcome for IPF patients (both p=0.059) with levels above median associated with a higher risk of mortality. Analyses of all or paired patients showed no associations with mortality.

Conclusions: Serological levels of neo-epitope biomarkers of ECM degradation were associated with AE-IIP and weakly with mortality outcome. These results indicate that the rate of ECM remodeling in the lungs of patients with IIP is significantly altered during periods of high disease activity such as an acute exacerbation. The difference in degradation profile for the proteins studied is intriguing and indicate activation of different processes contributing to AE-IIP.

Neo-epitope biomarkers of the ECM might be useful in identifying patients diagnosed with rheumatic disease as SSc and AS with pulmonary involvement.

Acknowledgements: The Danish Research Foundation

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5699

AB0181 DIFFUSING CAPACITY AND CLINICAL CHARACTERISTICS OF PATIENTS WITH SYSTEMIC SCLEROSIS – DATA FROM THE GERMAN NETWORK FOR SYSTEMIC SCLEROSIS

P. Moinzadeh[1], N. Blank[2], E. Siegert[3], J. Henes[4], M. Worm[5], C. Sunderkoetter[6], M. Schmalzing[7], A. Kreuter[8], C. Gunther[9], L. Susok[10], G. Zeidler[11], I. Koetter[12], U. Mueller-Ladner[13], T. Krieg[1], A. Juche[14], T. Schmeiser[15], G. Riemekasten[16], E. Aberer[17], N. Gaebelein-Wissing[18], J.H.W. Distler[19], M. Sárdy[20], C. Pfeiffer[21], K. Kuhr[22], N. Hunzelmann[1], F. Bonella[23], M. Kreuter[24]. *[1]Dermatology, University Hospital Cologne, Cologne; [2]Rheumatology, University Hospital Heidelberg, Heidelberg; [3]Rheumatology, Charité Universitätsmedizin Berlin, Berlin; [4]Rheumatology, University Hospital Tuebingen, Tuebingen; [5]Dermatology, Charité Universitätsmedizin Berlin, Berlin; [6]Dermatology, University Hospital Muenster, Muenster; [7]Rheumatology, University Hospital Wuerzburg, Wuerzburg; [8]Dermatology, HELIOS St. Elisabeth Klinik Oberhausen, Oberhausen; [9]Dermatology, University Hospital Carl Gustav Carus, Dresden; [10]Dermatology, St. Josef Hospital Bochum, Bochum; [11]Rheumatology, Johanniter-Krankenhaus im Fläming Treuenbrietzen, Treuenbrietzen; [12]Rheumatology, Asklepios Klinik Altona, Hamburg; [13]Rheumatology, Justus Liebig University Giessen, Kerckhoff Clinic, Bad Nauheim; [14]Immanuel Krankenhaus Berlin-Buch, Berlin; [15]Rheumatology, Krankenhaus St. Josef, Wuppertal; [16]Rheumatology, University Medical Center-UKSH, Luebeck, Germany; [17]Dermatology, Medical University of Graz, Graz, Austria; [18]Dermatology, HELIOS University Hospital Wuppertal, Wuppertal; [19]Rheumatology, University Hospital Erlangen, Erlangen; [20]Dermatology, Ludwig Maximilians University Hospital, Munich; [21]Dermatology, University Medical Center Ulm, Ulm; [22]IMSIE, University of Cologne, Cologne; [23]Unit for interstitial lung diseases, Ruhrlandklinik University Hospital Essen, Essen; [24]Center for interstitial and rare lung diseases, Thoraxklinik, University Hospital Heidelberg, Heidelberg, Germany*

Background: Lung involvement, i.e. interstitial lung disease (ILD) and pulmonary hypertension (PH), is common in patients with systemic sclerosis (SSc), significantly limiting quality of life and survival. Data on clinical correlations between lung function and clinical subsets of SSc are sparse.

Objectives: To investigate the relationship of DLCO and clinical characteristics in patients SSc patients within the registry of the German Network for Systemic Scleroderma.

Methods: Clinical data of the patient registry, currently including DLCO data of 1917 patients were evaluated. In total, these patients were clinically evaluated 5997 times (i.e., at the first visit and during follow-up visits). At the initial visit and during follow-up DLCO levels were correlated with clinical characteristics.

Results: At initial presentation, 64% of the patients had DLCO levels <75% predicted. Impaired DLCO levels were observed in 74% of dcSSc patients, in 64% of SSc-Overlap patients and 57% of lcSSc patients (p<0.0001). Furthermore, male patients (62%), patients with PH (80%), ILD (80%), dyspnea (78%), and those with presence of anti-topoisomerase I antibodies (71%) exhibited significantly more often DLCO levels <75% (p<0.01). Patients suffering from dcSSc had the lowest DLCO levels (mean value, 62%), followed by patients with SSc-Overlap syndromes (mean value, 67%) and lcSSc patients (mean value, 70%) revealing significant differences between subsets. Long-term follow-up evaluation (mean follow up, 6.0 years) revealed that in comparison to lcSSc patients dcSSc patients (OR 2.1; p<0.0001; 95%>CI 1.7–2.5) and SSc-Overlap patients (OR, 1.55; p<0.0001; 95% CI, 1.2–2.0) had a significantly increased risk to a decrease in DLCO levels <75%.

Conclusions: Impairment of pulmonary function as determined by diffusing capacity DLCO is more common and more pronounced in patients with dcSSc and SSc-Overlap Syndrome compared to lcSSc. DLCO may be useful for diagnosing and monitoring pulmonary involvement in SSc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3474

AB0182 IN VITRO CHARACTERIZATION OF DERMAL FIBROBLASTS FROM SYSTEMIC SCLEROSIS PATIENTS

R. Brizzolara[1], P. Montagna[1], S. Soldano[1], A.C. Trombetta[1], B. Ruaro[1], A. Sulli[1], S. Scabini[2], E. Stratta[2], V. Smith[3], M. Cutolo[4]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, IRCCS San Martino; [2]Oncologic Surgery, Department of Surgery, IRCCS San Martino IST, Genoa, Italy; [3]Department of Rheumatology, Ghent University Hospital, Ghent, Belgium; [4]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa, Italy*

Background: Systemic sclerosis (SSc) is characterized by progressive fibrosis of the skin and/or internal organs. Skin fibrosis is mainly due to the excessive production of extracellular matrix (ECM) proteins from dermal activated fibroblasts. The high amounts of transforming growth factor-beta (TGFbeta) production induce fibroblast proliferation and their transition into profibrotic myofibroblasts. Consequently, the increased presence of alpha-smooth muscle actin (alpha-SMA)-positive myofibroblasts in affected tissues is associated with fibrotic tissue remodelling, that characterize SSc [1–4].

Objectives: To characterize dermal fibroblasts from SSc patients by evaluating the gene expression of specific phenotypic and profibrotic markers: fibrillar collagen type I (COL I), fibronectin (FN), fibroblast-specific protein 1 (S100A4), TGFbeta and alpha-SMA (marker of myofibroblasts).

Methods: Human dermal fibroblasts were obtained by skin biopsy from affected areas of 6 active lcSSc patients after written informed consent and approval of medical ethics committee. SSc patients fulfilled the new EULAR/ACR criteria for SSc and they were treated only with various vasodilators (no severe clinical SSc complications were present at the time of skin sampling). Human SSc dermal fibroblasts were cultured up to 80% of confluence and at the third to fifth subpassages were used for experiments. Total RNA was extracted and quantitative real-time PCR (qRT-PCR) was performed to evaluate the gene expression of relevant fibroblast markers: COL I, FN, S100A4, TGFbeta and alpha-SMA.

Results: In human SSc fibroblasts the gene expression of the relevant markers COL I, FN and S100A4 resulted of 10^7 RNA copies for each gene. Interestingly, in the same tested fibroblasts, the profibrotic alpha-SMA gene expression (marker of myofibroblasts) was similarly found highly expressed, with a result of 10^7 gene copies. On the contrary, TGFbeta showed a much lower gene expression (10^3 copies) compared to the other investigated genes.

Conclusions: In human SSc cultured dermal fibroblasts, the gene expression of ECM proteins (COL I and FN), was found associated with a relevant gene expression of S100A4 and alpha-SMA, confirming their myofibroblast phenotype, as highly differentiated. Interestingly, TGFbeta gene appears to be less expressed. It could be concluded that myofibroblasts from the SSc skin mainly undergo the effects of the tissutal TGFbeta, since it seems that they do not contribute to its further production once differentiated.

References:

[1] Cutolo M. et al. J Rheumatol 2015;42:3.
[2] Brunasso A.M. et al. F1000Research 2016;5:723.
[3] Hinz B et al. Am J Pathol 2012;180:1340–55.
[4] Dumoitier N. et al. Arthritis Rheumatol 2016 [Epub ahead of print].

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3687

AB0183 ISOLATION AND CHARACTERIZATION OF CIRCULATING FIBROCYTES FROM SYSTEMIC SCLEROSIS PATIENTS: AN VITRO INVESTIGATION

R. Brizzolara[1], P. Montagna[1], S. Soldano[1], A.C. Trombetta[1], P. Contini[2], V. Smith[3], B. Ruaro[1], A. Sulli[1], M. Cutolo[1]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, IRCCS San Martino; [2]Division of Clinical Immunology, Department of Internal Medicine, University of Genoa, Genoa, Italy; [3]Department of Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium*

Background: In physiological and pathological conditions, such as in tissue repair and in fibrosing diseases (i.e. systemic sclerosis, SSc), the importance of circulating fibrocytes relies on the capacity of such cells to migrate into scleroderma-affected tissues (through CXCR4/CXCL12 interaction) and to differentiate into fibroblasts/myofibroblasts, inducing fibrosis (through matrix protein deposition) (or both) [1–3]. In addition, fibrocytes seem to exert immunomodulatory effects, expressing class II major histocompatability complex molecules (HLA-DP, -DQ, and -DR) [4].

Objectives: To isolate fibrocytes from Circulating Progenitor Cells (CPCs - peripheral blood mononuclear cells PBMCs) of SSc patients and healthy subjects and to identify them by fluorescence-activated cell sorter analysis (FACS), using their specific markers: the leukocyte common antigen CD45, collagen I (COL I), the chemokine receptor CXCR4 and HLA-DR [2].

Methods: Samples were collected, at basal time (t0), from 11 SSc patients, affected by SSc (treated only with different vasodilator drugs) and 5 healthy

subjects (CNTs). PBMCs, isolated from 9 among the SSc patients, were cultured on fibronectin-coated plates [5]. The non-adherent cells were removed and after 8 days (t8) of culture (standardized time), the adherent spindle shaped cells were lifted through incubation in 0.05% EDTA (ice-cold). Fibrocyte identification (at both t0, t8), was performed by FACS, using anti-CD45, anti-COL I, anti-CXCR4 and anti-HLA-DR monoclonal antibodies.

Results: FACS analysis revealed that, at basal time (t0), among the CD45+ cells, the percentage of fibrocytes, identified as triple positive (CD45+, COL I+, CXCR4+) was 1.0±1.2% in SSc patients and 0.4±0.3% in healthy subjects (CNTs). In addition, the HLA-DR expression on fibrocytes in both SSc patients and CNTs showed low values (22.1±21.1% and 7.1±6.1%, respectively).

After 8 days (t8) of culture, fibrocytes presented adherent and spindle shaped morphology. Interestingly, the FACS analysis at t8 of culture, demonstrated that the percentage of SSc fibrocytes CD45+, COL I+, CXCR4+ increased up to 52.8±27.1%, compared to basal time (t0), as well as strongly increasing the HLA-DR+ expression (90.1±22.7%).

Conclusions: Fibrocytes isolated from CPCs of SSc patients were confirmed to express CD45, COL I and CXCR4 molecules, but in very low percentage at the beginning. Already after 8 days of culture in proper conditions, the percentage of differentiated fibrocytes (CD45+, COL I+ and CXCR4+) from SSc patients, increased up to 50 times and the HLA-DR expression increased up to 68%. Additional markers of progressive fibrocyte differentiation are now under test to further characterize the fibrocytes phenotype(s) of SSc patients vs healthy controls.

References:

[1] Chesney J et al. Proc. Natl. Acad. Sci. 1997; 94:6307–6312.
[2] Bucala R. Mol Med 2015;21:S3–S5.
[3] Brunasso A.M. et al. F1000Research 2016;5:723.
[4] Blakaj and Bucala. Fibrogenesis & Tissue Repair 2012;5:S6.
[5] Pilling D et al. J Immunol Methods 2009; 351:62–70.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4963

AB0184 CHROMOSOMAL ABERRATIONS ARE ASSOCIATED WITH DISEASE SEVERITY IN A MOUSE MODEL OF BLEOMYCIN-INDUCED SCLERODERMA

R. Luisetto[1], M. Beggio[2], A. Scanu[2], F. Leite de Oliveira[3], E. Pigatto[2], A. Peruffo[4], E. Zanatta[2], F. Oliviero[2], P. Sfriso[2], L. Punzi[2], F. Cozzi[2]. *[1]Dept of Surgery, Oncology and Gastroenterology; [2]Dept of Medicine- Rheumatology Unit, University of Padova, Padova, Italy; [3]Institute of Biomedical Sciences, Federal University Rio de Janeiro, Rio de Janeiro, Brazil; [4]Dept. of Comparative Biomedicine and Food Science, University of Padova, Padova, Italy*

Background: Scleroderma (SSc) is a connective tissue disease characterized by immunomediated inflammation and fibrosis. The presence of autoantibodies against chromosome associate proteins,such as anti-centromere proteins and anti-topoisomerase I, was observed in SSc patients, however genotoxic events have never been evaluated (2).

Objectives: To assess the presence of aneuploidia, micronuclei (MN) and other chromosomal aberrations in peripheral lymphocytes in a bleomycin (BLM)-induced scleroderma mouse model.

Methods: BALB/c mice (n=20 per condition) were injected subcutaneously daily with BLM 2mg/kg or PBS (control) for 14 days. Urine was collected weekly and proteinuria was measured. At day 15 mice were sacrificed and organs harvested for histological analysis. The MN assay was performed on cultured peripheral lymphocytes isolated from mice spleens. Cells were treated with cytochalasin B (10 μg/ml) for 24 h and a minimum of 1000 binucleated cells/mouse were scored following the criteria of Fenech (1). The antikinetochore (CREST) staining was used to determine the origin of MN observed.

Results: In BLM treated mice was observed huge perivascular lung fibrosis and significant skin involvement. 17 out of 20 mice developed acute renal involvement with mean proteinuria levels of 730±48 mg/dl. In comparison with the control mice, a significant increase in MN number was observed in BLM treated mice (57,8±4,4 vs 6,3±0,6, $p<0.05$). CREST staining was higher in MN derived from BLM treated mice (16,4±1,1 vs 3,7±0,7, $p<0,025$), indicating that in this group lymphocyte MN arised mainly from lagging chromosomes. In addition, an increased frequency of ring chromosome was observed in mice with greater skin fibrosis and renal involvement.A correlation between the presence of CREST stained MN and disease severity parameters as renal failure, lung and skin fibrosis was observed (respectively R=0,4095; R=0,7507 and R=0,9471).

Conclusions: This study provides experimental evidence that significant chromosomal aberrations seem to be related to the severity of disease in a mouse model of SSc. Further investigations on lymphocytes obtained from SSc patients could be matched with results observed in mouse model to confirm the relationship between severity of the disease and chromosomal abnormalities.

References:

[1] Fenech M. Cytokinesis-block micronucleus cytome assay. Nature Protocols 2006, 2(5): 1084–1199.
[2] Korman BD and Criswell LA. Recent advances in the genetics of systemic sclerosis: toward biological and clinical significance. Curr Rheumatol Rep 2015, 17(3): 21–34.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5043

AB0185 ENDOTHELIN-1 STIMULATES THE PROFIBROTIC ALTERNATIVE ACTIVATED PHENOTYPE IN CULTURED HUMAN MACROPHAGES ISOLATED FROM SYSTEMIC SCLEROSIS PATIENTS

S. Soldano[1], P. Montagna[1], R. Brizzolara[1], A.C. Trombetta[1], C. Corallo[2], C. Pizzorni[1], S. Paolino[1], A. Sulli[1], M. Ghio[1], V. Smith[3], N. Giordano[2], M. Cutolo[1]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa; [2]Medicine, Surgery and Neurosciences, University of Siena, Siena, Italy; [3]Department of Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium*

Background: In the damaged tissue of systemic sclerosis (SSc) patients, the presence of immune inflammatory infiltrate, characterized by T-cells and macrophages, represents an important early pathological event in the fibrotic process (1).

In the macrophage population, the alternatively activated (M2) macrophages were observed in both peripheral blood and damage tissues of SSc patients and they participate in the fibrotic process exerting profibrotic effects, primarily by the production and release of transforming growth factor β1 (TGFβ1) (1,2). These cells are characterized by the expression of specific phenotype markers, such as mannose receptor (CD206) and scavenger receptors (CD204 and CD163), and the production of specific chemokines (i.e. macrophage derived chemokine, CCL-22) (3).

Endothelin-1 (ET1) plays an important role in the fibrotic process of SSc by inducing the profibrotic phenotype in endothelial cells and fibroblasts (4).

Objectives: To evaluate the ability of ET1 to upregulate the profibrotic gene expression profile characterizing the M2 macrophages in cultured monocytes/macrophages isolated from SSc patients.

Methods: Human monocytes were isolated from peripheral blood mononuclear cells of 4 SSc patients (mean age 59±11years, 2 females and 2 males, treated with vasodilator drugs) using a monocyte isolation kit. Cultured cells were maintained in RPMI growth medium for 24hrs and then treated with ET1 (100nM) for 6 days or treated for 1hr with ET receptor antagonist ($ET_{A/B}$RA, bosentan 10μM) before stimulation with ET1. Cultured cells maintained in RPMI growth medium were used as untreated cells.

Gene and protein expression of M2 phenotype markers and TGFβ1 were evaluated by quantitative real-time polymerase chain reaction (qRT-PCR) and Western blotting (WB). Statistical analysis was carried out using a Mann-Whitney non-parametric test.

Results: In cultured SSc macrophages, ET1 induced the upregulation of the gene expression of CD206, CD204, CD163, and CCL22 compared to untreated cells. Moreover, ET1 increased the TGFβ1 gene expression compared to untreated cells. $ET_{A/B}$RA partially contrasted the gene expression of CD204 and CD206. However, $ET_{A/B}$RA antagonized the ET1-mediated increase in the gene expression of CD163, CCL22 and TGFβ1. WB confirmed the results obtained by qRT-PCR.

Conclusions: Preliminary results showed the ability of ET1 to stimulate a profibrotic M2 phenotype in cultured human SSc macrophages characterized by the overexpression of TGFβ1, and this process is partially contrasted by the action of $ET_{A/B}$RA.

References:

[1] Higashi-Kuwata N et al. Arthrit Res Ther. 2010;12:R128.
[2] Stifano G et al. Curr Rheumatol Rep. 2016;18:2.
[3] Wynn TA et al. Nat Rev. 2013;496:445–55.
[4] Cipriani P et al. J Rheumatol. 2015;42:1808–16.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5857

AB0186 ASCA (ANTI-SACCHAROMYCES CEREVISAE ANTIBODY) IN SCLERODERMA

A. Fedrigo, T.A.F.G. dos Santos, A. Bortoluzzi, T. Skare, R. Nisihara.
Rheumatology Unit, Hospital Universitário Evangelico de Curitiba, Curitiba, Brazil

Background: The majority of Scleroderma (SSc) patients have gastrointestinal involvement. Motility is usually compromised but few studies address permeability changes in the intestinal wall. ASCA is an antibody direct against mannan in the cell wall of Saccharomyces cerevisiae, the baker's yeast that is found mainly when the small bowel is involved in Chron's disease. Nowadays ASCA is regarded more as a marker of increased gastrointestinal permeability than as a serological autoimmune marker of intestinal inflammatory disease. ASCA levels (anti-Sacharomyces Cerevisae antibodies) are associated with increased intestinal permeability.

Objectives: At present we study the presence of ASCA in the serum of SSc patients aiming to know if there is increased intestinal permeability in this disease and if this is related to any clinical, demographic and treatment data.

Methods: Seventy four SSc patients and 57 healthy controls were studied for ASCA (IgG and IgA) positivity by ELISA. ASCA positivity was associated with demographic, clinical, severity index (Medsger score) and serological data in SSc patients.

Results: ASCA IgG levels were high in 26/74 (43.7%) patients from SSc group and 1/57 (5.2%) of controls ($p<0.001$); IgA ASCA was high in 12/74 (16.2%) from SSc group and 3/57 (1.7%) of controls ($p=0.006$). In univariated analysis IgG ASCA high levels associated positively with African background ($p<0.0001$) and

TABLE 1 - COMPARISON OF EPIDEMIOLOGICAL, CLINICAL, SEROLOGICAL DATA IN SCLERODERMA PATIENTS WITH AND WITHOUT HIGH ASCA LEVELS.

	ASCA IgG			ASCA IgA		
	Positive N=21	Negative N=53	p	Positive N=12	Negative N=62	p
Mean age (years)	51.4±12.7	52.0±12.1	0.84	52.08±13.8	51.6±12.1	0.92
Gender (male /female)	4/32 (12.5%)	13/39 (33.3%)	1.00	0/12	8/62 (12.9%)	0.33
Median Disease duration (IQR)	6.5 (4.2-14.0)	9.0 (3.5-12.0)	0.83	9.0 (6.5-17.5)	7.0 (3.0-11.5)	0.15
Tobacco exposure	5/32 (14.2%)	4/31 (12.9%)	0.72	1/12 (8.3%)	8/62 (12.9%)	1.00
Afrodescent/caucasians	18/30 (60%)	4/42 (9.5%)	< 0.0001	6/11 (54.5%)	25/58 (43.1%)	0.48
Median BMI (Kg/m^2) (IQR)	24.01 (22.04-28.4)	26.02 (23.1-30.9)	0.09	24.9 (22.1-29.3)	25.4 (22.3-28.6)	0.84
Median Medsger index (IQR)	4 (3.0-8.0)	4.0 (2.5-6.0)	0.98	4.0 (1.0-4.0)	5.0 (3.0-8.0)	0.05
Median Rodnan m (IQR)	4 (2.0-10.5)	6 (2.5-14.0)	0.44	3 (0-10)	6.0 (3.0-13.0)	0.13
Raynaud	32/32 (100%)	40/42 (95.2%)	0.50	12/12 (100%)	60/62 (96.7%)	1.00
Telangiectasias	6/32 (18.7%)	16/42 (38.09%)	0.07	3/12 (25%)	19/62 (30.6%)	1.00
Digital scars	14/32 (43.7%)	19/42 (45.2%)	0.89	3/12 (25%)	30/62 (48.3%)	0.20
Pneumonitis	13/32 (40.6%)	25/42 (59.5%)	0.10	4/12 (33.3%)	34/62 (54.8%)	0.21
Calcinosis	3/32 (9.3%)	2/41 (4.8%)	0.72	1/12 (8.3%)	4/61 (6.5%)	1.00
Arthritis	11/32 (34.3%)	8/42 (19.04%)	0.13	3/12 (25%)	16/62 (25.8%)	1.00
Myositis	3/32 (9.3%)	4/42 (9.5%)	1.00	1/12 (8.3%)	6/62 (9.2%)	1.00
Esophageal dismotility	19/30 (63.3%)	23/40 (57.5%)	0.62	6/12 (50%)	36/58 (62.0%)	0.43
Pulmonary hypertension	4/26 (15.3%)	8/32 (25%)	0.51	1/10 (10%)	10/46 (21.7%)	0.67
Anti centromere	8/30 (36.4%)	22/39	**0.01**	4/10 (40%)	26/59 (42.3%)	1.00
Anti Scl-70	2/31 (6.4%)	9/41 (21.9%)	0.10	0/11	11/61 (18.03%)	0.19
Anti Ro	7/31 (22.5%)	4/40 (10%)	0.19	4/12 (33.3%)	7/59 (11.8%)	0.08
Anti La	4/31 (12.9%)	3/40 (7.5%)	0.69	2/12 (16.6%)	5/59 (8.4%)	0.33
Median ESR (mm) (IQR)	32.5 (13.2-48.5)	25.0 (14.0-41.0)	0.30	32.0 (14.2-55.2)	27 (14.0-41)	0.49
Median C reactive protein (mg/dL) (IQR)	8 (2.4-14.2)	9.5 (4.0-17.5)	0.64	9.0 (5.7-14.7)	8.8 (1.07-16.7)	0.60
Median hemoglobin (g/dL) (IQR)	13 (12-13.5)	13.0 (12.0-14.1)	0.68	13.2 (12.8-13.4)	13.0 (12.0-13.7)	0.34
Scleroderma subset:			0.36			0.13
Limited	19/32(59.3%)	18/42(42.8%)		7/12 (58.3%)	31/62 (50%)	
Generalized	11/32(34.3%)	21/42 (50%)		3/12 (25%)	28/62 (42.1%)	
Others	02/32 (6.2%)	03/42 (7.1%)		2/12 (16.6%)	3/62 (4.9%)	

IQR= interquartile rate; ESR= erythrosedimentation rate;BMI= Body mass index.

negatively with anticentromere antibodies (p=0.013); ASCA IgA had a negative association with Medsger score (p=0.05). In multivariated analysis IgG ASCA associated independently only with African ethnic background.

Conclusions: Positivity for IgG and IgA ASCA are higher among scleroderma patients than controls. African descendants have more positivity for IgG ASCA and ASCA IgA were less commonly seen in patients with more severe disease.

References:

[1] Sallam H, McNearney TA, Chen JD. Systematic review: pathophysiology and management of gastrointestinal dysmotility in systemic sclerosis (scleroderma). Aliment Pharmacol Ther. 2006; 23: 691–712.

[2] Cobden I, Rothwell J, Axon ATR, Dixon MF, Lintott DJ, Rowell NR. Small intestinal structure and passive permeability in systemic sclerosis. Gut. 1980; 21:293–8.

[3] Ghoshal UC, Ghoshal U, Singh H, Tiwari S.Anti-Saccharomyces cerevisiae antibody is not useful to differentiate between Crohn's disease and intestinal tuberculosis in India. J Postgrad Med. 2007; 53:166–70.

[4] Assessment of intestinal permeability and orocecal transit time in patients with systemic sclerosis: analysis of relationships with epidemiologic and clinical parameters. Rheumatol Int. 2003; 23:226–30.

[5] Catanoso M, Lo Gullo R, Giofré MR, Pallio S, Tortora A, Lo Presti M, et al. Gastro-intestinal permeability is increased in patients with limited systemic sclerosis. Scand J Rheumatol. 2001; 30: 77–81.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4305

Basic science in paediatric rheumatology

AB0187 LONG-TERM ADMINISTRATION OF FENSPIRIDE HAS NO NEGATIVE IMPACT ON BONE MINERAL DENSITY AND BONE TURNOVER IN YOUNG GROWING RATS

A. Matuszewska[1], B. Nowak[1], D. Jędrzejuk[2], M. Landwójtowicz[2], M. Bolanowski[2], W. Dziewiszek[1], E. Szelag[3], K. Zduniak[4], J. Kwiatkowska[1], A. Szeląg[1]. *[1]Department of Pharmacology; [2]Department of Endocrinology, Diabetology and Isotopes Therapy; [3]Department of Maxillofacial Orthopaedics and Orthodontics; [4]Department of Pathomorphology, Wroclaw Medical University, Wroclaw, Poland*

Background: In young organisms intensive bone turnover is observed and it allows the skeleton to achieve proper side, shape and weight of bones. It is extremely important to assess the influence on various drugs on growing bones. Fenspiride is registered for therapy of acute and chronic respiratory tract infections in children and adolescence. It decreases the synthesis of proinflammatory cytokines, blocks H1 receptors and has bronchodilatotory properties.

Objectives: The aim of the study was to assess the influence of long-term administration of fenspiride on bone mineral density and selected markers on bone turnover in young growing rats.

Methods: The experiment was carried out on18 young (8-week-old) male Wistar rats receiving standard diet containing 1.2% of calcium ans 0.7% of phosphate. Rats were randomly assigned to one of two groups (9 animals in each group): group F – rats receiving fespiride (15 mg /kg) in saline solution (4ml/kg), and group C (control group) - rats receiving saline solution (4ml/kg). Saline solution and fenspiride were given intragastrically once daily for 90 days (from day 3 to day 92). On day 1 and 93 blood samples for serum isolation were collected. Markers of bone turnover were assessed with commercial ELISA kits according to producers' instruction. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry (DXA) with Hologic DXA equipment (Hologic Dicovery W 81507) using a small animal software. The experiment was performed with the approval of the First Local Ethics Committee for Experiments on Animals in Wroclaw.

Results: On Day 1 there was no difference in age and body weight between groups. On Day 1 no difference in total body bone mineral density (BMD) (0.160±0.0065 g/cm^2 vs. 0.1608±0.0056 g/cm^2), lower limbs BMD (0.232±0.0267 g/cm^2 vs. 0.2274±0.0314 g/cm^2), serum levels of bone turnover markers (osteocalcin: 1000.921±109.0705 pg/ml vs. 952.5777±178.5306 pg/ml; bCTX: 280.089±54.4298 pg/ml vs. 292.8979±116.0042 pg/ml; osteoprotegerin: 3.5±0.6338 pg/ml vs. 3.7963±0.6894 pg/ml; RANKL: 0.167±0.4099 pg/ml vs. 1.0218±1.2717 pg/ml) was detected.

On Day 93 there was no difference in body weight, total body BMD and lower limbs (0.212±0.0104 g/cm^2 vs. 0.2035±0.0242 g/cm^2; 0.264±0.0159 g/cm^2 vs. 0.2520±0.0271 g/cm^2, respectivelly) between groups. On Day 93 no difference between groups in serum bone turnover markes was detected (OC: 422.758±92.3316 pg/ml vs. 429.2071±83.0520 pg/ml; bCTX: 307.748±77.6733 pg/ml vs. 285.3486±79.16334; OPG: 5.466±0.7815 pg/ml vs. 5.3520±1.6458 pg/ml; RANKL:0.647±0.8457 pg/ml vs. 0.5630±0.8608 pg/ml).

Conclusions: Long-term administration of fenspiride has no negative impact on bone mineral density and bone turnover in young growing rats

Acknowledgements: Research was supported with Wroclaw Medical University Grant for Young Researchers Pbmn 138.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2855

AB0188 EFFECT OF MIR-19A AND MIR-21 ON THE JAK/STAT SIGNALING PATHWAY IN THE PERIPHERAL BLOOD MONONUCLEAR CELLS OF PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

H. Li[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]epartment of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Background: Overexpression of the components of the Janus kinase/signal transducer and activator of transcription (JAK/STAT) signaling pathway are key factors of the pathogenic mechanisms underlying systematic juvenile idiopathic arthritis (SJIA).

Objectives: The present study aimed to investigate the association between microRNA (miR)-19a, miR-21 and the JAK/STAT signaling pathway.

Methods: A total of 20 patients with SJIA were included in the study, and peripheral blood mononuclear cells (PBMCs) from 20 normal controls were also collected.RNAiso was used to extract total RNA, and the RNA was then reverse transcribed into cDNA. Primers were designedto detect the mRNA of miR-19a and miR-21, and U6 was set as the internal parameter. In addition, the mRNA of STAT3, suppressor of cytokine signaling 3 (SOCS3), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) was detected, and β-actin was set as the internal parameter. Reverse transcription-quantitative polymerase chain reaction was performed to detect the expression levels of these proteins in patients with SJIA and control subjects, and non-parametric tests were used to analyze the statistical differences in 2-$\Delta\Delta$Cq between the two groups.

Results: The expression levels of miR-19a and miR-21 were significantly lower in the SJIA group compared with the control group ($P<0.05$). SOCS3, TNF-α and STAT3 were shown to be the target genes of miR-19a and miR-21, as determined by Targetscan. The expression levels of STAT3, SOCS3,TNF-α and IL-6 mRNA were significantly higher compared with those of the control group ($P<0.05$).

Conclusions: In the PBMCs of the patients with SJIA, miR-19a and miR-21 expression levels were lower compared with those of the control group, and the JAK/STAT signaling pathway was activated, which indicated that miR-19a and miR-21 may participate in the activation ofthe JAK/STAT signaling pathway.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2060

Rheumatoid arthritis - prognosis, predictors and outcome

AB0189 RAID COMPOSITE INDEX IN THE EVALUATION OF RA PATIENTS RECEIVING BIOLOGICAL TREATMENT: HUR-BIO REAL-LIFE RESULTS

A. Erden, L. Kilic, B. Armagan, A. Sari, A. Akdogan, S.A. Bilgen, O. Karadag, I. Ertenli, S. Kiraz, U. Kalyoncu. *Department of Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey*

Background: Rheumatoid Arthritis Impact of Disease (RAID) is a composite index. There are seven domains of this index (pain, function, fatigue, sleep disturbance, physical wellbeing, psychological/emotional well-being and coping). Daily activity in last week is evaluated. This score, is reccommended to be used in clinical trials to measure the effect of RA.
Objectives: The aim of this study is to examine the relationship between RAID composite index and other indexes.
Methods: This study was carried out from the HUR-BIO reserved database since August, 2016. In addition to the demographic characteristics of the patients, DAS-28, HAQ-DI, pain, fatigue, Patient global Assesment (PGA), Tender joint counts (TJC), swollen joint counts (SJC), CRP and ESR are recorded. Since 2015, a RAID form is filled for our patients. While this composite scale was being created, Gazi University Turkey carried out Turkish validation, in the original study. RAID composite index includes 7 questions, each scored from 0 to 10, 0 being the best score while 10 points is worst. The relationship between RAID composite index and other indexes were studied with Spearman correlation test.
Results: HUR-BIO database containts 1235 RA patients as of August 2016. A RAID form was filled for 149 of these patients before initiating biological agent. 124 patients (83.2%) were female. Mean age was 49±13 years and mean disease duration was 7.8±7.2 years. Positive ACPA and RF ratios were detected as 48/104 (45.7%) and 78/137 (56.9%) respectively. 77.9% of our patients had education of high school or less. RAID average score was detected as 6.72 (1.98). In female patients RAID disease activity was significantly higher than in men [RAID 6.8 (2.0) vs. 5.9 (1.6), p=0.038]. There was no significant difference among RF, CCP positive patients and auto antibody-negative patients in terms of RAID disease activity. [RAID for RF + vs -; 6.75 (2.05) vs 6.68 (1.86), p=0.82, RAID for CCP + vs -; 6.74 (1.96) vs 6.98 (1.82), p=0.52]. RAID disease activity measurements were correlated moderately acute phase reactants, it was very weak. In table, it is grouped by level of education and re-evaluated. In those with an education higher than college, rising parameters were seen in good level of correlation. [RAID vs Pain, r =0.65, p<0.005; RAID vs PGA, r =0.68, p<0.005].

Table 1. Correlation of RAID composite index according to education level

	RAID Query			
	RAID Total Score n: 149	Lower than High School n: 92	High School and Beyond n: 57	College and Beyond n: 33
DAS-28	0.28*	0.25*	0.42*	0.44*
HAQ-DI	0.49*	0.47*	0.50*	0.54*
Pain	0.51*	0.56*	0.58*	0.65*
Fatigue	0.45*	0.35*	0.52*	0.49*
PGA	0.50*	0.52*	0.59*	0.68*
TJC	0.27*	0.20*	0.30*	0.32
SJC	0.16*	0.06	0.29*	0.25
CRP	0.05	0.09	0.04	0.17
ESR	0.01	-0.01	0.12	0.20

DAS-28: Disease Activity Score, HAQ-DI: The Health assessment questionnaire disability index, PGA: Patient global Assesment, TJC: Tender joint counts, SJC: Swollen joint counts, CRP: C-Reactive Protein, ESR: Sedimentation. *p<0.005.

Conclusions: RAID has low correlation with other composite index such as DAS-28 score. RAID also has moderate correlation with pain, fatigue ad PGA VAS. On the other hand, patient with high education level had better perception for those patient reported composite index. RAID can be used confidently in these selected cases.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4202

AB0190 ASSESSMENT OF PLASMA MICRO-RNA 155 IN RHEUMATOID ARTHRITIS

A.A. Negm[1], S. Al Araby[1], E. Abdulazim[1], H. Raslan[2], K. Mohamed[3], M. Abdelhady[2], M. Hamed[4], S. Ismail[2]. *[1]Rheumatology, Al-Azhar University, Cairo; [2]Internal Medicine; [3]Molecular Biology; [4]Clinical Pathology, National Research Center, Giza, Egypt*

Background: Several observations have indicated that Epigenetics now play a role in the pathogenesis of many diseases including Rheumatological and Immunological disorders such as Rheumatoid Arthritis.(RA). Unlike the genetic code, the epigenome is altered by endogenous (e.g. hormonal) and environmental (e.g. diet, exercise) factors and changes with age. There are three main and interrelated mechanisms: DNA methylation, post-translational modification of histone proteins and non-coding RNA which includes Micro RNA (miR).
Objectives: 1. To determine the level of miR- 155 in plasma of RA patients.
2. To determine the potential value of miR-155 as molecular biomarker for diagnosis, prognosis of disease outcome, and prediction of therapeutic response in RA patients, and to test the relation miR-155 and serum levels of Matrix Metalloproteinase 3.(MMP)
Methods: The study group consisted of 50 female RA patients in active disease and 25 controls of matched age and sex. Disease duration of 1 to 10 years and age range from 20 to 45 years old. They underwent detailed history taking including questionnaire for disability and health assessment scoring, clinical examination, radiological assessment by modified Sharp score. Routine laboratory investigations in addition to assessment of Plasma miR -155 expression levels and serum MMP-3 levels were done for all patients. Ten of the cases were resampled for miR-155 and MMP-3 after receiving treatment and entering disease remission (By DAS 28 score).
Results: Plasma miR–155 expression levels and serum MMP-3 titers were significantly higher in RA patients than in controls (mean 4.071 and 1, $p<0.001$, mean 323.7 and 84.5, $p<0.001$) respectively. MMP-3 titers in serum were significantly higher in erosive than in non-erosive arthritis (mean 366.9 and 163.4, $p<0.001$). There was a significant positive difference between serum MMP-3 levels in disease activity and remission (mean 630 and 380, $p<0.001$). Mean values of the clinical parameters of our study group: STLW score (37.44±15.90), HAQ score (56.86±16.69), ACR disability class (2.224±0.872), DAS 28 score (4.856±1.222), ESR (58.16±29.44), Sharp score (32.36±23.9), There was a significant positive correlation between serum MMP-3 and DAS 28 score and ESR (r=0.022, p_0.022 and r=0.013, p=0.013 respectively). There was a significant positive moderate correlation between Plasma miR-155 and serum MMP-3 ($r=0.596$, $p<0.001$). Correlation between Plasma miR-155 expression levels and HAQ (p=0.612, r=0.0744), with ESR (p=0.13, r=0.219) with DAS 28 score (p=0.187, r=0.192), with Sharp score (p=0.675, r=0.0797).
Conclusions: miR-155 is indeed related to the presence of Rheumatoid arthritis, though not directly related to disease activity like MMP-3. miR-155 significantly but moderately correlates with MMP-3 in blood, but whether it plays a role in the pathogenesis of the disease with or without directly influencing MMP-3 in the joint will require more work on both markers inside the synovial fluid, synovial tissue and the synovial fibroblasts. MMP-3 was re-established in our study as a marker of disease activity and predictor of erosive arthritis.
References:
[1] Annabelle Grolleau-Julius, Donna Ray, and Raymond L. Yung,The Role of Epigenetics in Aging and Autoimmunity, Clin Rev Allergy Immunol. 2010 Aug; 39(1): 42–50.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4469

AB0191 CLINICAL SIGNIFICANCE OF MULTIPLE AUTOANTIBODY SPECIFICITIES IN RHEUMATOID ARTHRITIS: THE ROLE OF ANTI-CITRULLINATED ALPHA ENOLASE AND ANTI-INTERFERON INDUCIBLE PROTEIN 16

A. Alunno[1], O. Bistoni[1], F. Pratesi[2], V. Caneparo[3], G.M.C. La Paglia[1], I. Puxeddu[2], M. De Andrea[4], E. Bartoloni[1], S. Landolfo[4], P. Migliorini[2], R. Gerli[1]. *[1]Department of Medicine, Rheumatology Unit, University of Perugia, Perugia; [2]Department of Clinical and Experimental Medicine, University of Pisa, Pisa; [3]Department of Traslational Medicine, University of Piemonte Orientale Amedeo Avogadro, Novara; [4]Department of Public Health and Pediatric Sciences, University of Turin, Turin, Italy*

Background: Anti-cyclic citrullinated peptide (anti-CCP) auto-antibodies (auto-Abs) represent the current gold standard for the diagnosis of rheumatoid arthritis (RA). However, growing evidence suggests that a variety of other citrullinated or not citrullinated self-proteins may act as autoantigens and lead to the production of auto-Abs. The identification of the diagnostic and/or prognostic value of such novel auto-Abs is under intense investigation. We recently demonstrated that RA patients display a higher prevalence of auto-Abs against the interferon-inducible protein 16 (anti-IFI16) but these auto-Abs do not have a good diagnostic value (1). Recent data showed that auto-Abs against citrullinated alpha-enolase (anti-CEP1) are associated with erosive RA (2).
Objectives: The purpose of this study was to investigate the possible prognostic value of anti-CEP-1 and anti-IFI16 as well as the clinical implication of their association with anti-CCP in a cohort or RA patients.
Methods: Two hundred and fifty two RA patients were enrolled and serum samples were obtained. Auto-Abs were assessed as follows: anti-CCP EDIA 2nd generation ELISA kit (Eurodiagnostica); anti-CEP-1 IgG ELISA kit (Euroimmun). In a subgroup of 113 patients also anti-IFI16 auto-Abs were assessed with an in-house ELISA kit (1). Clinical and serological records of patients were collected and statistical analysis was performed with SPSS 21.0 software.
Results: One hundred and twenty patients (44%) displayed anti-CEP-1 auto-Abs and of these 97 patients (87%) also displayed anti-CCP. Logistic regression analysis revealed an association between both auto-Abs and RA-associated pulmonary disease (odds ratio-OR=2.9; 95% CI=1.06–7.9; p=0.04). We also confirmed that anti-CEP-1 are associated with erosive RA but of interest to a greater extent compared to anti-CCP (anti-CEP-1: OR=4.12; p=0.04; anti-CCP: OR=2.1; p=0.03). The analysis that included anti-IFI16 auto-Abs revealed that a small proportion of patients display all the three auto-Abs (9%) but

the triple positivity was significantly associated with male gender (OR=3.5; p=0.02), the presence of rheumatoid nodules (OR=5,3; p=0.015) and pulmonary involvement (OR=2.6; p=0.007). Anti-IFI16 auto-Abs were associated to male gender independently of the presence of the other two auto-Abs.

Conclusions: Our study demonstrated that anti-CEP-1 auto-Abs may participate to the development of RA-associated pulmonary manifestation together with anti-CCP and that the assessment of multiple auto-Abs in daily practice may help clinician to stratify RA patients at identify those at higher risk to develop extra-articular manifestations.

References:

[1] Alunno A et al. Arthritis Care Res (Hoboken) 2016;68(4):440–5.
[2] Montes A et al. Arthritis Rheum 2012;64(10):3102–3110.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3564

AB0192 SERUM MEASURES OF TYPE I COLLAGEN DEGRADATION ARE SURROGATE MARKERS OF JOINT DESTRUCTION AND PROGRESSION; FIRST STEPS TOWARDS A PROGNOSTIC SCORE

A.C. Bay-Jensen[1], C. Bager[2], A.S. Siebuhr[1], H. Bay Nielsen[2], M.A. Karsdal[1]. *[1]Rheumatology, Nordic Bioscience Biomarkers and Research; [2]Proscion, Herlev, Denmark*

Background: Monitoring of patients with rheumatoid arthritis (RA) requires assessment of biomarkers reflecting disease activity and its progression. There is a need for non-invasive markers for frequent monitoring of disease severity and progression as well as response to therapy.

Objectives: Serological markers together with clinical parameters was tested in a multi-marker model to assess its ability to objectively predict progression of RA.

Methods: Current post-hoc analysis included RA patients from the biomarker substudy of the phase III clinical study LITHE investigating the safety and efficacy of tocilizumab[1–4]. Patients had moderate/severe, active RA. In addition, only patients of the placebo arm and with total sharp score (SHP) recorded at baseline (BL), week 24 (W24) and W52 were included. Progressors were defined as the delta from BL to W24 and W24 to W52. Biochemical markers reflecting tissue turnover (table) were assessed at BL and W16. Associations with structural progression (deltaSHP) were investigated by spearman's r, least squared multivariate and logistic regression. Covariates were CRP, sex, BMI, age, disease duration, DAS-ESR, no. prior DMARDs/aTNF use and SHP/BL. The data were divided into a training and confirmation set; 1) association between markers/W16 and deltaSHP/W52 (n=31 prog./42 non-prog.), 2) association between markers/BL and deltaSHP/W24 (n=33/48).

Results: *The training set.* Eight markers were correlated (R>0.2) with deltaSHP/W52. Of these C1M, PINP, ICTP and MMP3 were predictive for of progression (deltaSHP/W52>0) with ORs of 3.2 [1.3–8.0], 4.0 [1.4–12], 8.5 [2.4–31], and 2.5 [1.3–5.1]; all p<0.01, respectively. A logistic model for prediction of disease progression incorporating C1M, ICTP, disease duration and BMI demonstrated an AUC of 0.77 [0.66–0.86], p<0.01. The model correctly identified 72% of the progressors. textitThe confirmation set: The results were confirmed in the second dataset with an AUC of 0.75 [0.64–0.81], p<0.01. The model correctly identified 65% of the progressors.

Biochemical marker	Description	Biomarker of	Spearman correlation between DeltaSHP/W52 and baseline biochemical marker R>0.2
C1M	MMP-mediated type I collagen degradation	Connective tissue destruction	**0.377**
C2M	MMP-mediated type II collagen degradation	Cartilage degradation	0.088
C3M	MMP-mediated type III collagen degradation	Connective tissue destruction	**0.277**
C4M	MMP-mediated type IV collagen degradation	Basement membrane destruction	0.157
C6M	MMP-mediated type VI collagen degradation	Connective tissue destruction	0.175
CRP	C-reactive protein	Acute reactant	**0.354**
CRPM	C-reactive degradation	Tissue inflammation	**0.290**
CTX-I/OC	Ratio between cathepsin K-mediated type I collagen degradation and osteocalcin	Bone turnover balance (Bone resporption/formation)	0.063
Gender	-	-	0.090
HAQ	Health assessment questionnaire		-0.032
ICTP	MMP-mediated type I collagen degradation	Connective tissue destruction /bone degradation	**0.334**
MMP3	Matrix metalloproteinase 3	Joint inflammation	**0.226**
Pain (VAS)	-	-	0.073
Patient global score (VAS)	-	-	0.110
Physician global score (VAS)	-	-	0.051
PIIANP	Propeptide of type II collagen	Cartilage formation	-0.077
PINP	Propeptide of type I collagen	Connective tissue and bone formation	**0.217**
VCAM	MMP-mediated Versican degradation	Epithelial turnover	-0.054
VICM	MMP-mediated degradation of citrullinated vimentin	Macrophage activity	**0.232**

Conclusions: We demonstrated that a multi-marker model was able to pint-point, which patients were more likely to be structural progressors. Such first steps to build a progression model, rather than a score reflecting disease activity only, may enrich clinical studies with structurally active diseaese. Importantly, the markers with strongest influence were those associated with MMP-driven bone (ICTP) and connective tissue (C1M) remodelling.

References:

[1] Smolen JS.Tocilizumab inhibits progression of joint damage in rheumatoid arthritis irrespective of its anti-inflammatory effects: disassociation of the link between inflammation and destruction. Ann Rheum Dis 2012.
[2] Kremer JM.Tocilizumab inhibits structural joint damage in rheumatoid arthritis patients with inadequate responses to methotrexate: results from the double-blind treatment phase of a randomized placebo-controlled trial of tocilizumab safety and prevention of structu. Arthritis Rheum 2011.
[3] Bay-Jensen AC. Effect of tocilizumab combined with methotrexate on circulating biomarkers of synovium, cartilage, and bone in the LITHE study. Semin Arthritis Rheum 2014.
[4] Bay-Jensen AC. Early changes in blood-based joint tissue destruction biomarkers are predictive of response to tocilizumab in the LITHE study.Arthritis Res Ther 2016.

Disclosure of Interest: A. Bay-Jensen Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience, C. Bager Employee of: Proscion, A. S. Siebuhr Employee of: Nordic Bioscience, H. Bay Nielsen Employee of: Proscion, M. Karsdal Shareholder of: Nordic Bioscience, Employee of: Nordic Bioscience

DOI: 10.1136/annrheumdis-2017-eular.6676

AB0193 MEDICAL ADHERENCE IN PATIENTS WITH TIGHTLY CONTROLLED RHEUMATOID ARTHRITIS

A. Caliskan Uckun, F.G. Yurdakul, H. Bodur. *Physical Medicine and Rehabilitation, Ankara Numune Research and Education Hospital, Ankara, Turkey*

Background: Medication adherence is very important in the treatment of rheumatoid arthritis (RA). However, medication adherence of the patients with RA was not optimal in many of the studies (1–2).

Objectives: The purpose of this study was to investigate the medication adherence in tightly controlled RA patients and reasons of non-adherence.

Methods: A total of 82 RA patients (65 women and 17 men) who followed regularly in our outpatient clinic were included. Socio-demographic features and medical history were collected. The eight-item Morisky scale (MMAS-8) was used to evaluate adherence to medication. Disease activity score (DAS28), health assessment questionnaire (HAQ), mini mental state examination (MMSE) test and Beck depression inventory (BDI) were evaluated.

Results: According to Morisky scale, 34.1%, 15.9% and 50% of our patients were categorized as low, moderate and high adherence, respectively. The most prevalent noticed barriers for adherence were forgetting medication, inadequate information about using instructions, side effects of medications (Table 1). Socio demographic features, duration of disease, type and number of drugs used per day, the route of drug administration, co-morbid diseases, body mass index, smoking and alcohol consumption were not found to be associated with medication adherence, whereas low MMSE and high BDI score were associated with low medication adherence (p=0.009 and p=0.011, respectively). We found that the disease activity was significantly higher in non-adherent cases (p=0.00) (Table 2).

Table 1. Barriers to medication adherence

Barriers	%
Forgetfulness	41.4%
Inadequate information	22%
Side effects of medications	17%
Fears about drug benefit	12.2%
Anxiety about side effects	4.8%
Cost of medications	2.6%

Table 2. Medication adherence and disease activity

DAS 28	Low adherence (Morisky <6)	Moderate adherence (Morisky 6–7)	High adherence (Morisky = 8)	Total
Remission (<2.6)	2 (5.6%)	5 (13.9%)	29 (80.6%)	36
Low disease activity (2.6–<3.2)	7 (36.8%)	3 (15.8%)	9 (47.4%)	19
Moderate disease activity (3.2–<5.1)	17 (68.0%)	5 (20%)	3 (12%)	25
High disease activity (≥5.1)	2 (100%)	0 (0%)	0 (0%)	2
Total	28	13	41	82

DAS: Disease activity score.

Conclusions: Our RA patients who were closely followed had 50% high medication adherence. This rate is quite high compared to other studies using MMAS-8. It should be kept in mind that tight control and adequate communication increase medication adherence but different parameters may also be effective. Assessing cognitive disorders and emotional problems of the patient will be beneficial for improving adherence and controlling disease activity.

References:

[1] Gadallah MA, Boulos DN, Gebrel A, Dewedar S, Morisky DE. Assessment of rheumatoid arthritis patients' adherence to treatment. Am J Med Sci. 2015;349:151–6.
[2] Ferguson A, Ibrahim FA, Thomas V, Weinman J, Simpson C, Cope AP, Scott

DL, Lempp H. Improving medication adherence in rheumatoid arthritis (RA): a pilot study. Psychol Health Med. 2015;20(7):781–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2837

AB0194 JOURNEY OF A PATIENT WITH RHEUMATOID ARTHRITIS: DELAY IN DIAGNOSIS AND TREATMENT

A. Luissi, J.E. Rosa, F. Vergara, F.S. Pierini, M. Scolnik, M.V. Garcia, E.R. Soriano. *Rheumatology section, Medical Services, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina*

Background: It has been shown that there is a window of opportunity for treatment in Rheumatoid Arthritis (RA). Several Argentinean studies showed an average of 8 months to arrive to a rheumatology visit and 12 months to receive DMARDs. There aren't recent studies.
Objectives: To establish delay time from onset of rheumatoid arthritis (RA) symptoms to the first rheumatology visit, to diagnosis of the disease and to the beginning of treatment with DMARDs; and to assess impact of such delay on structural damage, in a cohort of RA patients.
Methods: A retrospective study was performed including all patients with RA (fulfilling ACR/EULAR 2010 criteria) seen at a Prepaid Medical Health Plan between 2002–2015. Diagnosis delay and its impact on functional capacity measured by HAQ-A and structural damage by Sharp van der Hejde score (SvdH) was estimated. Demographic and clinical data, and dates ofdiagnosis, onset of symptoms and HAQ-A were extracted from electronic medical records. Svdh score was performed by an experienced rheumatologist.
Results: 246 patients (mean age at diagnosis 67.25±14 years, 199 (81%) female) were included. Clinical presentation was poliarticularin 49% of the cases, oligoarticularin 47% and monoarticular in 3%. 79% had high titers of anti-cyclic citrullinated peptide antibodies, 12% low titers, and 9% were negative. Rheumatoid factor was positive in 82.5%. Mean time of follow up was 7 years (SD: 3.8). At the end of the follow-up,median HAQ-A (n=145) was 0.125 (IRQ: 0–0.87). Hands and feet lastxray available were analized in 171 patients. Median Svdh score was 15 (IQR: 6–33). 242 patients (98.4%) received DMARDs as initial treatment: methotrexate monotherapy (76%) was the most frequent one. 41 patients (17%) received biological agents at some point of their disease. Table 1 shows different delay times in accessing rheumatology consultation, diagnosis and beginning of treatment.
At the end of follow up, 21 patients (12.28%) had noradiological damage (Svdh score =0). In the ROC curve (AUC 0.57,95% CI: 0.45 - 0.69), 5.6 months of diagnosis delay was the best cut off valueto discriminate the presence of erosions (SvdH erosions score>0), with a sensitivity and specificity of 54.17% and 61.90%, respectively. Delay in diagnosis greater than 12 months (n=70) was associated with significantly radiological damage: Svdh mean 30.91 (IC 95% 21.99–39.79) vs 21.32 (IC 95% 16.93–25.72); p=0.0325.

Table 1. different delay times

Variable	Mean (SD)	Median (IQR)
Time from first symptoms to first rheumatology visit (months)	9.21 (20.50)	3 (1–7)
Time from first symptoms to diagnosis (months)	14.2 (24)	4.8 (2.4–13)
Time fromfirst symptoms to DMARDs indication (months)	16.9 (25.4)	7 (3–17)
Time from first symptoms to biological indication (years)	6.2 (4.8)	5.7 (2.4–7.2)

Conclusions: In a Prepaid Medical Health Planwith ease of referral, there is still a significant delay in diagnosis and treatment of RA patients.Delay in diagnosis greater than 12 months was associated with more radiological damage.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2967

AB0195 IS THERE AN ASSOCIATION BETWEEN PERIODONTITIS AND LEVELS OF ANTI-CITRULLINATED PEPTIDES ANTIBODIES IN RHEUMATOID ARTHRITIS?

B. Rodríguez-Lozano[1], J. González Febles[2], F. Sánchez Alonso[3], J.L. Garnier Rodríguez[4], S. Dadlani[4], Y. Barrios[5], M. Sanz Alonso[6], F. Díaz González[1]. *[1]Rheumatology, Hospital Universitario de Canarias, Tenerife; [2]Periodontology, UCM, Madrid; [3]Research Unit, Sociedad Española de Reumatología, Madrid; [4]Odontology/Periodontology, Dental Clinic Dr Garnier, S/C Tenerife; [5]Immunology Unit. Central Laboratory, Hospital Universitario de Canarias, Tenerife; [6]Periodontology, UCM, Madrid, Spain*

Background: Positivity of anti-citrullinated peptides antibodies (ACPA) indicates severity in Rheumatoid Arthritis (RA). There is evidence for chronic periodontitis (PD) in RA autoimmune response by periodontopathogenic bacteria such as *P.gingivalis*, through citrullination of L-arginine.
Objectives: 1.To determine whether there is an association between PD and its severity with ACPA(+).2.To assess relationship between PD and ACPA titres.3.To identify association between certain periodontal parameters and ACPA titres and their possible cutoff points.
Methods: Observational, cross-sectional study RA patients ≥18 with ≥4 teeth, no tooth cleaning, antibiotic intake 6 months before.Socio-demographic and anthropometric variables, annual dental prophylaxis and comorbidities.Serum ACPA detection:Ab IgG against CCP2 (ELISA)Eurodiagnostica:positive≥25; ACPA titres stratification:Low (25–75), moderate (76–300) and high (>300). Periodontal parameters: plaque index (PI), bleeding on probing (Bop), probing pocket depth,clinical attachment level (CAL). CAL loss was categorized according to European Workshop 2005 (Tonetti):T level0 (absence), TL1 (mild), TL2 (severe). Statistical analysis:t-student, Kruskal Wallis, Chi- squared tests by Stata program 13.1.
Results: 187 RA patients included (table 1),ACPA determined in 168 patients: 67.86% (+) with similar titres distribution: low 18%, moderate 26%, high 23%. PD:182 patients (97.3%):TL1 52.4%,TL2 44.9%. Although prevalence of severe PD/ACPA(+) was higher compared to PD/ACPA(-) (69.2% vs 30.7%), there was no association between PD and ACPA positivity/titres. Regarding the association with periodontal parameters, there was tendency of association between ACPA(+) and number of periodontal pockets ≥5mm (NPP),OR 1.02 (95% CI 0.9–1.04) adjusted. There was a gradient effect, where NPP increased as ACPA titles increased, which was significant for high ACPA titres (p≤0.05,OR 1.03 95% CI 1.0–1.05). When ACPA(+) was related to %PI and BoP, a strong association was observed for PI, OR 10.32 (p<0,026), and only a tendency for BoP (p<0.062). With cutoff points of 8% PI and 65% BoP, a risk for ACPA(+) was detected with an OR 2.19 and OR 2.45, respectively.

Table 1

	RA (N)	RA (%)
Female sex	147	78.6
Mean age (SD)	54.4 (10.8)	
Follow up time, median (SD), years	8.88 (7.32)	
Early RA	35	18.7
Rheumatoid factor, seropositive	138	74.2
Disease Activity Ranges		
Remission	39	20.9
Low	45	24.1
Moderate	85	45.4
High	18	9.6
Medication RA		
Without Treatment	10	5.3
DMARDs	99	52.9
≥2 DMARDs	22	11.8
Biologic Drugs	56	29.9

Conclusions: 1.Despite higher prevalence of severe PD in ACPA(+) patients, we found no association between the presence of PD and ACPA positivity nor with serum titres. 2. On analysis of ACPA titres in relation to the severity of the periodontal parameters, there was a "gradient" risk, where NPP increased as ACPA titres increased, which was significant for high ACPA titres.3. Risk cutoff points for ACPA(+) were 8% for PI and 65% for BoP.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4420

AB0196 VASCULAR ENDOTHELIAL GROWTH FACTOR IN PATIENTS WITH RHEUMATOID ARTHRITIS

B. Rebrov[1], E. Komarova[1], A. Blagodarenko[1], G. Belkina[2], I. Pokryshka[3]. *[1]Internal Medcine; [2]Medical Chemistry, SI "Lugansk State Medical University"; [3]Rheumatology, Lugansk Clinical Regional Hospital, Lugansk, Ukraine*

Background: The level of vascular endothelial growth factor (VEGF) may reflect the intensity of angiogenesis, which is an important step in the initiation and development of chronic rheumatoid arthritis (RA).
Objectives: to study features of VEGF level changes in the blood of RA patients, depending on the duration of the disease, the degree of activity, the level of antibodies to cyclic citrullinated peptide (anti-CCP)
Methods: 194 patients were examined with a diagnosis of RA (verified according to criteria ACR/EULAR 2010), without concomitant pathology. Among the examined patients with RA women predominated 168 (86.6%), and there were 26 men (13.4%). The age of patients was 22 to 65 years (mean age 47,7±10,22 years), mean duration of the disease was 3,82±3,43 years. Assessment of RA activity was done by DAS 28 index, using blood CRP in the formula. 152 patients were positive for the presence of anti-CCP (≥20 U/ml) (78%) and 42 (22%) - negative. Serum CRP concentrations (Vector-Best, Russia), anti-CCP (Orgentec, Germany), VEGF (BCM Diagnostic, Canada) were determined by ELISA. Statistical processing of the data was performed using non-parametric methods, univariate (ANOVA) variance analysis on a personal computer using a licensed software packages ("Microsoft-Excel" and "Statistica-Stat-Soft", USA)
Results: Analysis of VEGF level changes in the blood depending on the duration of RA revealed that the measure was high in patients with small diseases duration 0–23 months (472.96 (341.1; 582.1) pg/ml) compared with the group 5 years (324.1 (199.2; 556.2) pg/ml) (p<0,04). Analysis of VEGF level in blood depending on the degree of RA activity showed that the VEGF concentration in blood increased with increasing degree of RA activity and it was the greatest - 564.4 (340.1; 758.4) pg/ml in the group with a high degree (DAS28 >5.2) compared to the minimum (DAS28 ≤3,2) - 230,5 (178,1; 385,3) pg/ml, and moderate (DAS28 3,3–5,2) - 356,4 (278 9; 553.1) pg/ml, (p<0,001; p=0,005, respectively). Using ANOVA variance analysis, it was found that the degree of RA activity influenced the VEGF levels in the blood (KW =17,37; p<0,001).
Analysis of the VEGF levels in the blood depending on the level of anti-CCP

showed a significant increase in VEGF level (343.35 (190.62; 561.28) pg/ml) in the group of high positive ACCP (>60 U/ml) compared with the group of low positive ACCP (≤60 U/ml) - 470.23 (324.3, 676.85) pg/ml (p=0,005). Using ANOVA variance analysis, it was found that the level of anti-CCP in the blood of studied RA patients influences the VEGF level in blood (KW =7,88; p=0,005)
Conclusions: In patients with RA duration <2 years VEGF levels in the blood was 30% higher than in patients with a prolonged course of RA. Concentration of VEGF in the blood increased 2-fold with a high degree of RA activity. Levels of VEGF in the blood were 1.5 times higher in the patients with anti-CCP levels>60 U/ml compared to low positive anti-CCP patients. The high level of VEGF may be a marker of severe clinical course of RA, the high rate of disease progression and the development of early joint destruction
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2373

AB0197 SUBCLINICAL INTERSTICIAL LUNG DISEASE IN EARLY RHEUMATOID ARTHRITIS

C. Fernández-Díaz [1], M. Calderón-Goerckel [1], J. Martin-Varillas [1], B. Atienza-Mateo [1], A. Corrales-Martinez [1], V. Portilla-Gonzalez [1], V. Calvo-Rio [1], J. Rueda-Gotor [1], N. Palmou-Fontana [1], M. Agudo-Bilbao [1], N. Vegas-revenga [1], L. Domingues-Casas [1], J. Cifrian-Martinez [2], M.A. Gonzalez-Gay [1], R. Blanco [1]. *[1]Rheumatology, Hospital Universitario Marques de Valdecilla, IDIVAL; [2]Pneumology, Hospital Universitario Marques de Valdecilla., Santander, Spain*

Background: Interstitial lung disease (ILD) is a severe extra-articular complication of Rheumatoid Arthritis (RA). The decrease in DLCO diffusion is the most sensitive value for the detection of ILD, DLCO is also a prognostic factor.
Objectives: To study the prevalence of subclinical lung involvement in early RA.
Methods: Cross-sectional study of lung involvement in early RA. The following criteria were used: A) RA according to the EULAR-2010 criteria. B) Early RA if evolution from the onset of symptoms to the diagnosis of RA was less than one year. C) Lung affectation if DLCO diffusion was lower than 80%. In each patient we evaluate: a) presence of dyspnea according to MMRC (Modified British Medical Research Council) scale; B) Respiratory function tests (FVC, FEV1, FEV1/FVC; C) DLCO; classifying the degree in: i) normal>80% (mild decrease 80–60%); ii) Moderate decrease (60–40%) and iii) Severe reduction (<40%); D) Chest x-ray: assessed by radiologist. E) Joint activity of RA (DAS28), F) CRP and ESR. G) RF, CCPA, H) Presence of atheroma plaque on carotid ultrasound. Quantitative variables were expressed as mean±SD or median [IQR] and were compared with the Student t or Mann Whitney U test, respectively. Dichotomous variables were expressed as percentages and compared using the chi-square test. Statistical analysis was performed with the SPSS 15.0 program.
Results: 20 patients (15 women/5 men) with early RA were studied; mean age of 54.1±13.4 years. Some patients were using disease-modifying antirheumatic drugs (DMARDs) prior to performing respiratory function tests (PFR): methotrexate (7) 3 of them with less than 14 days of treatment, hydroxychloroquine (4), sulfasalazine (1). The table shows the main characteristics of patients according to pressence of lung disease. We observed a decrease in DLCO in 15/20 patients (75%) who were mild (DLCO <80%) in 4 (27%); Moderate (DLCO <60%) in 9 (60%) and severe (DLCO <40%) in 2 (13%). Chest x-ray showed these alterations in 3 patients: signs of air trapping, laminar atelectasis and scarring tracts. There were no alterations in FVC in any patient.

Table 1

	With lung involvement (n=15)	Without lung involvement (n=5)	P
Age. mean	56.3±13.11	55.6±15.69	0.55
Sex (W/M)	13/2	3/2	**0.03**
Smokers or ex smokers, n (%)	10 (66.7)	1 (20)	0.06
CCP Antibody, positive n (%)	8 (53.3)	2 (40)	0.60
Titer, median [IQR]	430.5 [165.8–1874.2]	47 [35–59]	0.23
RF Positive, n (%)	8 (53.3)	2 (66)	0.6
RF titer. median [IQR]	213 [67.5–334.75]	135 [74–196]	0.6
ESR mean/ CRP mean	32.1±21.4/ 4.7±7.8	24.6±21.8/ 0.80±0.83	0.84/0.21
DAS28, mean	5.04±1.03	4.48±0.85	0.49
Bone erosions X ray, n (%)	1 (6.7)	1 (20)	0.60
Carotid plaque, n (%)	8 (53.3)	2 (40)	0.60
Extra articular manifestation, n (%)	3 (20)	0	0.16
– Sjögren Syndrome	2		
Abnormalities in thorax Rx. n (%)	3 (20)	0	0.16
Dyspnea, n (%)	1 (6.7)	0	0.60
DMARDs, n (%)	8	4	0.60
Methotrexate,n (%)	5 (55)	2 (50)	
Hydroxichloroquine, n (%)	2 (33)	2 (50)	
Sulfasalazine, n (%)	1 (12)	0	

Conclusions: We find a high frequent of lung involvement in early RA, in most of cases subclinical. Performing Respiratory function tests may help in early detection of lung involvement. These results should be ratified in larger series.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3267

AB0198 DIFFERENTIAL CHARACTERISTICS OF PATIENTS DISCONTINUATING SEVERAL BIOLOGICAL THERAPIES IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS

C. Tornero [1], C. Plasencia [1], D. Pascual-Salcedo [2], B. Hernández [1], M. González [1], M.G. Bonilla [1], L. Nuño [1], A. Villalba [1], D. Peiteado [1], P. Bogas [1], E. Moral [1], A. Balsa [1]. *[1]Rheumatology; [2]Immunology, la Paz University Hospital, Madrid, Spain*

Background: The treatment of Rheumatoid Arthritis (RA) has been transformed in the last decade with the introduction of biologic therapy. Nevertheless, a substantial proportion of patients (pts) are found to be primary or secondary nonresponders and will receive several biologics during the course of the disease. Evidence is lacking on the characterization of patients failing several agents and those who have adequate clinical response to their first biological treatment.
Objectives: To compare demographic, clinical and analytical characteristics in a cohort of RA pts who have failed treatment with at least two biological agents ("switchers") and another cohort of RA patients showing a sustained clinical good response to their first therapy ("maintainers"). As a secondary objective, reasons for therapy discontinuation were also evaluated.
Methods: A total of 186 patients under biological therapy of the RA-PAZ cohort were included in this observational study. In this cohort, 63 pts were switchers and 123, maintainers. Baseline demographic data and clinical disease activity (DAS 28 -ESR), clinical improvement (delta-DAS 28) and serological data (CRP and ESR) were evaluated at baseline and sixth months after starting the first biological treatment.Serum anti-drug antibodies (ADA) were measured by bridging ELISA at the last visit available during the follow-up period under the first treatment. Reasons for discontinuation of the first therapy and the number of biologic treatments received during the course of the disease were also evaluated.
Results: Demographic and clinical characteristics of both groups are shown in Table 1.Mean Age (49,96±10,82 vs 53,77±12,91,p=0,046) and disease duration (6,79±6,19 vs 9,97±8,56,p=0,001) prior to biologic therapy initiation were lower in the switchers.Furthermore, a higher proportion of switchers had extraarticular manifestations in comparison to the maintainers (18/63 (28,6%) vs 16/121 (13,2%),p=0,016). Clinical activity at baseline (DAS28: 5,74±1,26 vs 5,01±1,14,p=0,01) and after 6 months of starting the first biological therapy (DAS28: 4,45±1,6 vs 3,22±1,1,p=0,001) were statistically significant higher in the switchers. At the last visit under the first biologic, there were also more ADA-positive pts in the switchers (6/25 (24%) vs 1/73 (1,4%), p=0,01).Moreover, duration under biologic treatment was higher in this group. In terms of the reason for discontinuation of the first biologic, 22,2% of pts showed primary lack of efficacy;38,1%, secondary loss of efficacy; 33,3%, adverse effects;4,8%interrupted because of other reasons and 1,6% because of

Pts characteristics	Switchers n= 63	Maintainers n= 123	P value
Baseline characteristics at the initiation of the 1st biological therapy (1BT)			
Female, n/N (%)	49 / 63 (77,8%)	102 / 122 (83,6%)	NS
BMI (kg/m2.) ± DS	27,31 ± 5,37	26,23 ± 4,96	NS
Smoking habit - Non-smoker - Smoker - Ex smoker	38/ 61 (62,3%) 11/61 /18%) 12/61 (19,7%)	69 / 115 (60%) 19 / 115 (16,5%) 27/ 115 (23,5%)	NS
Age at the starting of the 1BT ± DS	49,96 ± 10,82	53,77 ± 12,91	P= 0,046
Time from diagnosis to 1BT ± DS (y)	6,79 ± 6,19	9,97 ± 8,56	P= 0,001
Co-therapy (DMARDs) ± DS	27,31 ± 5,37	26,22 ± 4,96	NS
Auto-antibodies (UI/ml) - FR +, n/N (%) - ACPA +, n/N(%)	50 / 63 (79,4%) 97/118 (82,2%)	93/121 (76,9%) 53/62 (85,5%)	NS NS
Erosions, n/N(%)	36 / 52 (69,2%)	67/101 (66,3%)	NS
Extraarticular manifestations, n/N(%)	18/63 (28,6%)	16/121 (13,2%)	P= 0,011
Monotherapy, n/N (%)	3/ 63 (4,8%)	6 /122 (4,9%)	NS
Baseline activity ± DS - DAS – 28 ± DS - PCR ± DS - VSG ± DS	5,74 ± 1,26 13,82 ± 20,8 33,63 ± 22,03	5,01 ±1,14 10,26 ± 13,6 29.4 ±18,36	P=0,001 NS NS
6 months after the initiation of the 1st biological therapy			
Six months activity ± DS - DAS-28 ± DS - Delta-DAS 28 ± DS	4,44 ± 1,61 1,40 ± 1,6	3,22 ± 1,10 1,77 ±1,2	P= 0,001 NS
Last visit available after the initiation of the 1BT			
ADA+, n/N (%)	6 /25 (24%)	1/ 73 (1,4%)	P= 0,01
At the last visit available after the initiation of the 1st biological therapy			
Age, mean ± DS	61,23 ± 11,8	61,05 ± 12,8	NS
Time of follow-up until the last visit available ± DS, (years)	16,48 ± 7,5	16,71 ± 9,9	NS
Mean time under biologic ± DS, (y)	9,48 ± 4,3	6,72 ± 4,6	P=0,001

remission. There was no association between reasons for discontinuation of the first therapy because of primary or secondary failure and adverse effects (3,4±0,9 vs 3,75±1,11vs 3,86±1,3, p=0,6) with the number of treatments received.
Conclusions: In our biologic therapy RA-PAZ cohort, we found a subgroup of younger pts, with a more systemic phenotype of the disease and a higher disease activity,who required a prompter biological therapy initiation. This subgroup of pts is more susceptible to biological treatment failures. The development of ADA after the first biological agent was also associated with the need to use more biologics.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5494

AB0199 METHOTREXATE RESPONSE IN EARLY RHEUMATOID ARTHRITIS ASSESSED USING A SOMAMER PROTEOMIC ASSAY

C. Hitchon, V. Spicer, X. Meng, A. Gao, H.S. El-Gabalawy, J. Wilkins. *University of Manitoba, Winnipeg, Canada*

Background: Optimizing treatment in early rheumatoid arthritis (ERA) improves clinical outcomes. Developing approaches that would allow for accurate outcome predictions would be useful. We examined the possibility of employing SOMAscan to identify biomarkers that predict treatment response.
Objectives: To define methotrexate (MTX) 6 month treatment associated response protein changes using SOMAscan.
Methods: Sera from 14 Disease Modifying Antirheumatic Drug (DMARD) naive ERA patients at baseline (PRE) and after six months of MTX (POST) were analyzed using SOMAscan, an aptamer based assay that offers simultaneous relative quantitation of 1310 proteins. RA activity was measured by DAS28ESR3var abbrev DAS3; RF and ACPA were measured at baseline. SOMAmer intensity data was log2 transformed and differences (D=POST-PRE) clustered using undirected hierarchical self-organization. Kolmogorov-Smirnov differential analysis determined SOMAmers contributing to these populations at $p<0.05$. Potential processes associated with these SOMAmer regulation groups were identified using an in-house biological enrichment tool.
The potential for SOMAmers to predict treatment response was also explored; for this we defined a fractional clinical response metric dDAS3= (DAS3_POST-DAS3_PRE)/DAS3_PRE. We then selected a population of proteins (n=3 to avoid over-fitting) with PRE expression levels best correlating to dDAS3. These three PRE expression values formed a weighted average, with weighting coefficients optimized by a simple Monte-Carlo method. We included this weighted average with clinical variables in logistic regression models, where 6 month DAS3 was the dependent variable.
Results: Clustering gave two populations of 6 and 8 patients (POP0, POP1) with mean delta DAS3 values of -1.71 and -0.46 respectively. In POP0 compared to POP1, 113 proteins were upregulated and 121 proteins were downregulated. The upregulated proteins were involved in VEGF signalling and platelet activation. The downregulated proteins were involved in regulation of immune response, cellular response to TNF and cytokine –cytokine receptor interactions. The fractional change dDAS3 correlated well with the treatment response panel (R^2=0.8645; p=6.8e-5), with the caution that expression values of the 3 best-correlating proteins exhibited low coefficients of variation (<0.1). However, these proteins did reflect RA responses or inflammation. This weighted sum was also independently associated with treatment response in regression models including baseline DAS3 (or components) and RF/ACPA.
Conclusions: This pilot study suggests that high content proteomic approaches such as SOMAscan may be useful for developing prediction tools of patient responses to treatment. Extension of this work into a larger patient population is ongoing.
References:
[1] Journal of Statistical Software, 8(18) 1–4, 2004.
[2] Nature Protocols, 4(1) 44–57, 2009.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1747

AB0200 MUSCULOSKELETAL ULTRASOUND ADDED TO ROUTINE EVALUATIONS OF RHEUMATOID ARTHRITIS PATIENTS HAS A DIFFERENT IMPACT ON THE TREATMENT PROPOSAL DEPENDING ON PHYSICIAN EXPERIENCE

C. Sifuentes[1], I. Contreras-Yáñez[1], M. Gutíerrez[2], V. Pascual[1]. [1]*Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran;* [2]*Instituto Nacional de Rehabilitación y Ortopedia, México, D.F, Mexico*

Background: Disease activity (DA) is the most important factor in the treatment decision/monitoring during rheumatoid arthritis (RA) patient's follow-up. In routine clinical practice, it is recommended to regularly evaluate DA level from patients with RA. Musculoskeletal ultrasound has been suggested to add value to establish the level of DA; evaluations that assess a reduced number of joints, as the German ultrasound score of 7 joints (GUS-7) are easy to incorporate in clinical practice (1).
Objectives: To explore the real impact of GUS-7 in the treatment recommendation to RA outpatients, currently attending an Early Arthritis Clinic (EAC). The primary objective was to determine the proportion of patients in whom treatment recommendation differed after GUS-7 examination. We additionally tested the variations of GUS-7 impact according to the physician's experience (senior rheumatologist [SR] vs. trainee in rheumatology [TR]).
Methods: A sample size of 84 evaluations was calculated to achieve the primary objective. Eighty-seven consecutive and randomly selected RA outpatients were invited to participate; 2 patients denied because of administrative reasons and the 85 patients left underwent 170 assessments (85 each by the SR and the TR). At first, both physicians (blinded to each other evaluations) performed a clinical evaluation that included DAS28 scoring and recommended a RA-treatment. Then, patients underwent GUS-7 by a blinded (to clinical evaluations) rheumatologist that additionally determined the sonographic disease activity. In the final step, the TR and the SR integrated the US findings to their previous evaluation and reviewed their prescription; GUS-7 findings, pre- and post-GUS-7 treatments were recorded on standardized formats. Patients received final recommendation only from the SR. All the patients signed informed consent and were instructed about the process. Descriptive statistics was used.
Results: Patients were primarily middle-aged [(mean±SD) 45.13±12.4 years] female (91.4%), with (mean±SD) disease duration of 7.5±3.9 years. Most of the patients (69.2% according to TR and 71.8% to SR) were in DAS28-ESR-remission, although the four levels of DA were represented. Agreement between both physicians was good (Kappa: 0.82, $p\leq0.001$). Most frequent GUS-7 findings were grey scale synovitis in at least one joint in 98.8% of the patients, among whom 22.6% had Power Doppler activity (PD); one third of the patients had tenosynovitis although few (12%) had PD; erosions were detected in 38.8% of the patients.
In 34 of 170 clinical scenarios (20%), GUS-7 findings modified treatment; treatment changes (after GUS-7 findings were incorporated to clinical findings) consisted of an increase in 24 (70.6%) scenarios, a decrease in 8 (23.5%) and joint injection with corticosteroids in 2 (5.9%). Interestingly, 24 of the 34 clinical scenarios with GUS-7 treatment impact were performed by the TR vs. 10 performed by the SR: 70.5% vs. 29.5%, p=0.01. Treatment changes (increase, decrease and joint injection) were similar among both specialists.
Conclusions: In routine clinical practice of RA patients, GUS-7 assessments impacted treatment decision in 20% of the patients; the impact was stronger among TR than among SR.
References:
[1] Backhaus et al. Arthritis Rheum 2009; 61: 1194–201.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1435

AB0201 INFLUENCE OF SIGA ON CLINICAL ACTIVITY MARKERS IN SPA PATIENTS WITH NON-RADIOGRAPHIC AND PERIPHERAL COMPROMISE

C. Romero-Sanchez[1], F. Salas-Cuesta[2], I. Arias[3], J.M. Bello-Gualtero[4], W. Bautista-Molano[1], D. Herrera[3], D. Castillo[5], R. Valle-Oñate[1]. [1]*Department of Rheumatology and Inmunology, Hospital Militar Central;* [2]*School of Medicine, Universidad Militar Nueva Granada;* [3]*Universidad Javeriana;* [4]*Department of Rheumatology and Inmunology, Hospital Militar Central, Bogotá, Colombia;* [5]*UIBO Institute, Universidad El Bosque, Bogotá D.C., Colombia*

Background: There are previous evidence about inflammatory signs related with the intestinal mucosa in spondyloarthritis patients with seronegative arthritis and them relation with articular inflammatory activity. It is uncertain the role of these serological markers on the inflammatory/clinical activity in patients with SpA
Objectives: To establish the relationship among activity variables and indices, and soluble markers associated to mucosal associated lymphoid tissue in a group of SpA patients.
Methods: Patients were selected by rheumatologists with the ESSG criteria. Levels of SIgA, IgA, IgA *Chlamydia trachomatis*, *Shigella spp*, *Yersinia ssp*, *Campilobacter ssp* and *Salmonella ssp*, CRP,ESR,HLA-B27,BASDAI,ASDAS-CRP and ASDAS-ESR were determined. A principal components analysis (PCA), Poisson Regression and multiple correspondence analysis were performed to find relationships between clinical and laboratory variables and SIgA. This study was approved for Ethics Committee.
Results: 46 patients were included (78.2% males with a mean age 34.8±12.3 years). It was reported at least one gastrointestinal sing in 69.2% of patients:abdominal bloating (45%), abdominal pain (43%); all patients showed at least one musculoskeletal symptom, 69.5% enthesitis, 63% inflammatory back pain and 58.6% arthritis, as well as 43.4% previous infection and 47.8% presented HLA-B27.The PCA showed three principal factors which cover a contribution of 82.2% to explain the SIgA variation.The ASDAS-CRP, ASDAS-ESR, BASDAI variables which provide the 47.12%;the regression model shows an inverse association among SIgA and BASDAI (prevalence ratio (PR):0.43, 95% CI:0.26–0.70 p=0.001), ASDAS-CRP (PR:0.72, 95% CI:0.24–0.95 p=0.021) and ASDAS-ESR (PR:0.69, 95% CI:0.39–0.95 p=0.007); however, a risk was demonstrated among BASDAI and Yersinia IgA (PR:1.68 95% CI:1.03–2.74 p=0.036) and between ASDAS-CRP with HLA-B27 (PR:1.62 95% CI:1.18–2.19 p=0.0002). There was a relationship between the absence of clinical activity (ASDAS-CRP, ASDAS-ESR and BASDAI), previous infection, Yersinia IgA with SIgA Q1 (27.8–43.0 ug/mL); the presence of arthritis, Salmonella IgA, and high levels of CRP and ESR were related with SIgA Q2; SIgA levels among (Q3)12.2–18.0 ug/mL were associated with inflammatory back pain, obesity and Salmonella IgA <1/1600. High scores

of BASDAI and ASDAS-CRP, absence of previous infection had a strong relation with low levels of SIgA.
Conclusions: SIgA serum level were the only one serologic maker, which had an inverse correlation with all clinical activity variables of disease, previous infection and some specific antibodies associated with intestinal mucosal infection, suggesting a protective role of this molecular shape of IgA that is characteristic of mucosal immune responses
References:
[1] Mantis NJ. Mucosal Immunol (2011) 4:603–11.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6159

AB0202 LOW DOSE ACETYLSALICYLIC ACID AS PRIMARY PROPHYLAXIS OF CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS. A LONGITUDINAL, RETROSPECTIVE STUDY

D. Iacono, S. Fasano, V. D'Abrosca, I. Pantano, R. Chieffo, G. Valentini.
Rheumatology Unit, University of Campania "Luigi Vanvitelli", Naples, Italy

Background: Cardiovascular events (CV) i.e. acute myocardial infarction and stroke are recognized as a leading cause of mortality in patients with Rheumatoid Arthritis (RA) [1,2]. Acetylsalicylic acid (ASA) is known to be associated with a significant decrease in the incidence of CV events in patients at high risk for atherosclerosis like patients with diabetes [3] and has been recently reported to play a primary prophylactic role of CV events in Systemic Lupus Erythematosus by our team [4].
Objectives: To investigate the so far unexplored role of ASA in reducing CV morbidity in RA.
Methods: We analysed patients admitted to our Outpatient clinic from January to December 2015. Out of 199, 155 patients, who had been followed from January 2000 and had not experienced any CV event at the first visit, were enrolled. The incidence of CV morbidity was recorded at December 2016.
Results: The 155 patients had been followed-up for a median of 8 years (range 1–15 years). Out of them, 111 patients had been treated with ASA, that we currently administer to patients undergoing steroid treatment. During the 15-years of follow up, 5 CV events (2 cerebrovascular, 3 acute myocardial infarction) had occurred (Incidence rate 3.93/1000 person/year). Interestingly, only 1 CV event had occurred in ASA treated patients (Incidence rate 1.12/1000 person/year) with respect to 4 in the non-ASA group (44 patients) (Incidence rate 10.48/1000 person/year) (p=0.0146).
Conclusions: Our study has several limitations including the low number of patients and CV events. Nevertheless, it might suggest a primary prophylactic role of ASA in RA, that awaits to be investigated in large controlled prospective studies.
References:
[1] Arthritis Rheum. 2001 Dec;44(12):2737–45. High incidence of cardiovascular events in a rheumatoid arthritis cohort not explained by traditionalcardiac risk factors. del Rincón ID, Williams K, Stern MP, Freeman GL, Escalante A.
[2] BMC Musculoskelet Disord. 2014 Apr 29;15:142. Cardiovascular case fatality in rheumatoid arthritis is decreasing; first prospective analysis of a current low disease activity rheumatoid arthritis cohort and review of the literature. Meek IL, Vonkeman HE, van de Laar MA.
[3] Diabetes Res Clin Pract. 2016 Oct;120:31–9. Aspirin for primary prevention of cardiovascular disease in patients with diabetes: A meta-analysis. Kokoska LA, Wilhelm SM, Garwood CL, Berlie HD.
[4] Rheumatology (Oxford). 2016 Sep;55(9):1623–30. Low-dose aspirin as primary prophylaxis for cardiovascular events in systemic lupus erythematosus: a long-term retrospective cohort study. Iudici M, Fasano S, Gabriele Falcone L, Pantano I, La Montagna G, Migliaresi S, Valentini G.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2858

AB0203 EXPRESSION LEVELS OF SELECTED GENES CAN PREDICT THE INDIVIDUAL RHEUMATOID ARTHRITIS PATIENT RESPONSE TO TUMOR NECROSIS FACTOR ALPHA BLOCKER TREATMENT

D. Paran[1], Y. Smith[2], S. Pundak[3], U. Arad[1], D. Levartovsky[1], I. Kaufman[1], J. Wollman[1], V. Furer[1], A. Broyde[1], O. Elalouf[1], D. Caspi[1], S. Pel[4], O. Elkayam[1]. *[1]Rheumatology, Tel Aviv Medical Center and the Sackler school of Medicine, Tel Aviv University, Tel Aviv; [2]Genomic Data analysis, Hadassah Medical School Hebrew University, Jerusalem Israel; [3]Genefron Ltd, Jerusalem; [4]Rheumatology, Tel Aviv Medical Center, Tel Aviv, Israel*

Background: Rheumatoid arthritis (RA) patients have many therapeutic options. However, there are limited tools to predict the individual patient's response to therapy. The Genefron personal diagnostic kit (IFR 300) has been developed based on analysis of large databases to select interferon stimulated gene (ISG) expressions which could predict response to a biologic agent
Objectives: This study aims to evaluate the ability of the Genefron diagnostic kit to predict the individual RA patient response to TNFα blockers.
Methods: Two separate analyses were performed, one retrospective and one prospective analysis. The response of 61 RA patients reported in 2 published data sets was analyzed retrospectively utilizing the Genefron kit. In addition, 18 patients with RA were assessed prospectively, before and 3 months after starting treatment with a TNFα blocker. Clinical assessment included swollen and tender joint counts, patient and physician assessments of disease activity. Patients' blood samples were obtained before administration of the TNFα blocker and were analyzed utilizing the Genefron diagnostic kit which measures expression levels of selected genes by quantitative real time PCR.
Results: Genefron kit analysis of retrospective data correctly predicted the response to a TNFα blocker in 53 of 61 RA patients (accuracy - 86.8%). In the prospective analysis 6 patients achieved a moderate EULAR response, 6 achieved a good EULAR response and 6 did not respond. According to the EULAR moderate response, the Genefron diagnostic kit predicted the response correctly in 16 of 18 patients (accuracy-89%, sensitivity -100%, specificity - 67%). According to the EULAR good response, the kit predicted the response correctly in 15 of 18 patients (accuracy - 83.3%, sensitivity - 100%, specificity - 75%).
Conclusions: The Genefron diagnostic kit predicted the response to TNFα blockers in a high percentage of RA patients assessed either retrospectively or prospectively in a real life setting. This personal diagnostic kit has the ability to guide selection of a suitable biological drug for the individual RA patient
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2653

AB0204 DISEASE FACTORS ASSOCIATED TO ABNORMAL INTIMA-MEDIA THICKNESS IN MEXICAN MESTIZO RHEUMATOID ARTHRITIS PATIENTS

D.A. Galarza-Delgado[1], J.R. Azpiri-Lopez[2], I.J. Colunga-Pedraza[1], R.E. Ramos-Cazares[1], F.J. Torres-Quintanilla[2], A. Valdovinos-Bañuelos[1], R.I. Arvizu-Rivera[3], A. Martinez-Moreno[3], J.A. Cardenas-de la Garza[3], R. Vera-Pineda[3], G. Elizondo-Riojas[4], J.I. Garcia-Colunga[4]. *[1]Rheumatology; [2]Cardiology; [3]Internal Medicine; [4]Radiology and Imaging, Hospital Universitario Dr. José Eleuterio Gonzalez, Monterrey, Mexico*

Background: Atherosclerotic cardiovascular disease (ASCVD) is the main mortality cause in patients with rheumatoid arthritis (RA) (1). It has been proven that the carotid intima-media thickness (CIMT) measured with carotid duplex ultrasonography (US) is an important ASCVD predictor with a measurement ≥0.9 mm (2–4).
Objectives: To characterize the disease factors related with abnormal carotid duplex US findings in Mexican mestizo patients with RA.
Methods: In a cross-sectional setting, we enrolled consecutive RA patients. Patients with overlap syndromes, personal history of ASCVD, dyslipidemia and previous use of any statin were excluded. A board-certified radiologist performed a bilateral carotid duplex US to all patients. Abnormal CIMT was defined as ≥0.9 mm (hypertrophy ≥0.9 – 1.2 mm and carotid plaque ≥1.2 mm). A clinical history and blood tests were performed at the time of the patient's visit. Disease activity was measured with Disease Activity Score using 28 joints–C-reactive protein (DAS28-CRP).
Results: We enrolled 57 patients. Demographic characteristics are shown in table 1. A total of 30 (52.2%) patients had an abnormal CIMT. US findings are shown in table 2. A significant correlation between abnormal CIMT and RA disease duration (p=0.04), as well as between the former and anti-cyclic citrullinated peptide antibodies (ACPA) positivity (p=0.033) was found.

Table 1. Demographic and disease characteristics

Variable	Results
Female gender, n (%)	54 (94.7)
Age (years), mean ± SD	56±9.9
Disease duration (years), mean ± SD	12.4±8.3
BMI (kg/m^2), mean ± SD	28.22±4.9
Smoking status, n (%)	5 (8.77)
DAS 28- CRP, mean ± SD	3.33±1.19
Disease Activity, n (%)	
Remission	17 (29.8)
Low	11 (19.3)
Moderate	25 (43.8)
Severe	4 (7.1)
Positive Anti-CCP, n (%)	44 (77.19)
Positive RF, n (%)	51 (89.47)

BMI: Body Mass Index.

Table 2.- *Carotid Doppler ultrasound findings.*

Ultrasound findings, n (%)		Disease duration	Disease Activity	Positive Anti-CCP	Positive RF
				P	
Abnormal CIMT	32 (56.14)	***0.022***	0.57	***0.034***	0.14
Plaque	11 (19.29)	0.33	0.75	0.65	0.67
Hypertrophy	21 (36.84)	0.52	0.59	0.54	0.38

Conclusions: There is a strong relationship between CIMT and the chronic inflammatory process of RA, as well as ACPA positivity. These results might be influenced by the high mean disease duration of our patients. Prospective studies that evaluate CIMT among disease duration intervals are necessary to support these findings.

References:
[1] Avina-Zubieta JA, Thomas J, Sadatsafavi M, Lehman AJ, Lacaille D. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis. 2012;71(9):1524–9.
[2] Galarza-Delgado DA, Esquivel-Valerio JA, Garza-Elizondo MA, Gongora-Rivera F, Munoz-De Hoyos JL, Serna-Pena G. Carotid atherosclerosis in patients with rheumatoid arthritis and rheumatoid nodules. Reumatol Clin. 2013;9(3):136–41.
[3] Mateo I, Morillas P, Quiles J, Castillo J, Andrade H, Roldan J, et al. What measure of carotid wall thickening is the best atherosclerotic loading score in the hypertensive patient: maximum or mean value? Rev Esp Cardiol. 2011;64(5):417–20.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5660

AB0205 CAROTID INTIMA-MEDIA THICKNESS LINKED TO THE PRESENCE OF CARDIOVASCULAR RISK FACTORS IN MEXICAN MESTIZO PATIENTS WITH RHEUMATOID ARTHRITIS

D.A. Galarza-Delgado[1], J.R. Azpiri-Lopez[2], I.J. Colunga-Pedraza[1], R.E. Ramos-Cazares[1], F.J. Torres-Quintanilla[2], A. Valdovinos-Bañuelos[1], R.I. Arvizu-Rivera[3], A. Martinez-Moreno[3], J.A. Cardenas-de la Garza[3], J.I. Garcia-Colunga[4], G. Elizondo-Riojas[4]. *[1]Rheumatology; [2]Cardiology; [3]Internal Medicine; [4]Radiology and Imaging, Hospital Universitario Dr. José Eleuterio Gonzalez, Monterrey, Mexico*

Background: Rheumatoid Arthritis (RA) is associated to subclinical atherosclerosis. Traditional risk factors for cardiovascular outcomes do not explain completely the higher risk, which could be caused by chronic systemic inflammation.
Objectives: The aim of this study is to relate abnormal carotid intima-media thickness (CIMT) to the presence of cardiovascular risk factors.
Methods: Observational cross-section design. We included patients who fulfilled the 1987 ACR and/or 2010 ACR/EULAR classification criteria for RA, 40 to 75 years old, with no personal history of atherosclerotic CV disease. A board-certified radiologist performed carotid duplex ultrasounds. Patients were distributed in two groups according to the absence (Group 1) or presence (Group 2) of traditional risk factors for cardiovascular disease (smoking status, dyslipidemia, high blood pressure and diabetes).
Results: A total of 82 patients were included. Demographic characteristics for each group are shown in Table 1. Ultrasound findings are shown in Table 2. CIMT alterations were more common in Group 2 (66.7%) than in Group 1 (38.7%), with statistical significance (*p=0.013*). Presence of carotid plaque was more common in Group 2 (27.5%) than in Group 1 (16.1%), shown clinical relevance, although did not shown statistical significance (*p=0.18*).

Table 1. Demographic characteristics

Variable	Total	Group 1 (n=31) (CVRF–)	Group 2 (n=51) (CVRF+)	*p*
Patients, n (%)	82 (100)	31 (37.80)	51 (62.20)	–
Female gender, n (%)	77 (93.9)	29 (93.5)	48 (94.1)	0.0917
Age (years), mean ± SD	57±9.96	51.90±8.43	59.82±9.69	**0.001**
Disease duration (years), mean ± SD	12.45±8.39	11.74±8.76	12.89±8.32	0.554
BMI (kg/m^2), mean ± SD	28.22±4.9	29.05±5.09	27.72±4.92	0.248
Smoking status, n (%)	8 (9.75)	–	8 (15.68)	–
Diabetes, n (%)	13 (15.85)	–	13 (25.49)	–
HBP, n (%)	28 (34.14)	–	28 (54.90)	–
Dyslipidemia, n (%)	8 (9.75)	–	8 (15.68)	–

CVRF: Cardiovascular Risk Factors, HBP: High Blood Pressure.

Table 2.- *Carotid ultrasound findings*

	Total n=46	Group 1 (CVRF -) n=12	Group 2 (CVRF +) n=34	*p*
Abnormal CIMT, n (%)	46 (56.1)	12 (38.7)	34 (66.7)	***0.013***
Plaque, n (%)	19 (23.2)	5 (16.1)	14 (27.5)	0.18
Bilateral, n (%)	12 (14.6)	1 (3.2)	11 (21.6)	***0.02***
Hypertrophy, n (%)	28 (34.1)	7 (22.6)	21 (41.2)	0.068
Bilateral, n (%)	12 (14.6)	2 (6.5)	10 (19.6)	0.091

CVRF: Cardiovascular Risk Factors

Conclusions: In this cohort of Mexican patients with RA, we demonstrate relation between the presence of alterations in CIMT (carotid hypertrophy and carotid plaque) and risk factors for cardiovascular disease, which can be enhanced by intrinsic risk of RA. These findings reaffirm the importance of global health assessment in patients with RA to reduce morbidity.
References:
[1] Avina-Zubieta JA. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis. 2012;71(9):1524–9.
[2] Galarza-Delgado DA, Serna-Pena G. Carotid atherosclerosis in patients with rheumatoid arthritis and rheumatoid nodules. Reumatol Clin. 2013;9(3):136–41.
[3] Mateo I, What measure of carotid wall thickening is the best atherosclerotic loading score in the hypertensive patient: maximum or mean value?]. Rev Esp Cardiol. 2011;64(5):417–20.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5616

AB0206 INTERLEUKIN-17 AND CC-CHEMOKINE LIGAND 20 ARE NOT USEFUL MARKERS OF RHEUMATOID ARTHRITIS ACTIVITY IN PATIENTS UNDERGOING BIOLOGIC TREATMENT

D. Sikorska[1], R. Rutkowski[2], J. Łuczak[2], W. Samborski[1], J. Witowski[2]. *[1]Department of Rheumatology and Rehabilitation; [2]Department of Pathophysiology, Poznan University of Medical Sciences, Poznan, Poland*

Background: Interleukin-17 (IL-17) and IL-17-induced CC-chemokine ligand 20 (CCL20) are increasingly implicated in the pathogenesis of rheumatoid arthritis (RA). A correlation has been reported to exist between serum levels of IL-17 and CCL20 and the disease activity following biologic treatment [1]. However, such an effect has not been universally demonstrated [2].
Objectives: The aim of the present study was to investigate if serum IL-17 and CCL20 reflect activity of the disease and whether they could be of prognostic value for predicting therapeutic response to biologic therapy in RA.
Methods: Thirty RA patients qualified to receive biologic treatment were prospectively assessed before and 12 weeks of therapy with either TNFα inhibitors or anti-IL-6 receptor antibodies. Serum concentrations of IL-17 and CCL20 were measured with high sensitivity ELISA with estimated detection levels 0.01 pg/ml and 0.47 pg/ml, respectively. Successful response to therapy was defined by the EULAR criteria.
Results: The patient baseline characteristics were summarized in Table 1.

Table 1. Patient characteristics: data presented as the mean ± SD or %

Age (years)	54.3±11.5
Sex (% of male)	4 (13%)
Disease duration (years)	9.6±6.0
Prednisone (<5 mg/24h) (%)	17 (57%)
NSAIDS (%)	22 (73%)
Methotrexate (%)	12 (40%)
Biologic treatment (%)	– TNFα inhibitors (adalimumab, certolizumab, golimumab, infliximab): 22 (73%) – IL-6R blocker (tocilizumab): 8 (27%)

Twelve weeks of biologic treatment resulted in a significant improvement in the majority of the patients with only 2 patients (7%) identified as non-responders. The favorable response to therapy was reflected both by clinical and standard biochemical criteria (Table 2). However, the mean serum concentrations of IL-17 and CCL20 did not change significantly over the course of therapy and they did not correlate with the disease activity, response to therapy, the type of biologic intervention and other medication used.

Table 2. Selected parameters before and after treatment: data presented as the median (interquartile range)

	Before treatment (n=30)	After 12-weeks of treatment (n=30)	P-value (Wilcoxon test)
DAS28 (ESR)	5.53 (5.26–6.08)	3.23 (2.19–3.75)	<0.001
ESR (mm/h)	24.0 (16.0–32.0)	10.0 (4.0–20.0)	<0.001
CRP (mg/l)	7.37 (2.3–15.8)	0.8 (0.1–5.5)	<0.001
WBC (10^3/l)	9.0 (7.6–9.9)	7.8 (6.6–9.6)	0.014
IL-17 (pg/ml)	0.65 (0.00–5.81)	0.53 (0.00–4.45)	0.355
CCL20 (pg/ml)	22.0 (18.0–28.0)	22.5 (20.0–31.0)	0.322

Serum IL-17 and CCL20 levels showed no correlation with DAS28, and standard inflammatory markers.
Conclusions: Serum levels of IL-17 and CCL20 did not parallel changes in the clinical status and standard biochemical parameters in patients undergoing biologic treatment for RA. Thus, the measurement of IL-17 and CCL20 in serum does not seem to provide additional information that would help to monitor the response to biologic treatment in RA more effectively.
References:
[1] Rosu A, Margaritescu C, Stepan A, et al.: IL-17 patterns in synovium, serum and synovial fluid from treatment-naive, early rheumatoid arthritis patients. Rom J Morphol Embryol 2012; 53(1):73–80.
[2] Silosi I, Boldeanu MV, Cojocaru M, et al.: The Relationship of Cytokines IL-13 and IL-17 with Autoantibodies Profile in Early Rheumatoid Arthritis. J Immunol Res. 2016;2016:3109135.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2178

AB0207 CHANGE IN ANTI-CITRULLINATED PROTEIN AUTOANTIBODY LEVELS IN CLINICAL PRACTICE ARE ASSOCIATED WITH RESOURCE USE AND DISEASE ACTIVITY MEASURES

E. Alemao[1], Z. Guo[1], C. Iannaccone[2], M. Frits[2], N. Shadick[2], M. Weinblatt[2]. *[1]Bristol-Myers Squibb, Princeton; [2]Brigham and Women's Hospital, Boston, United States*

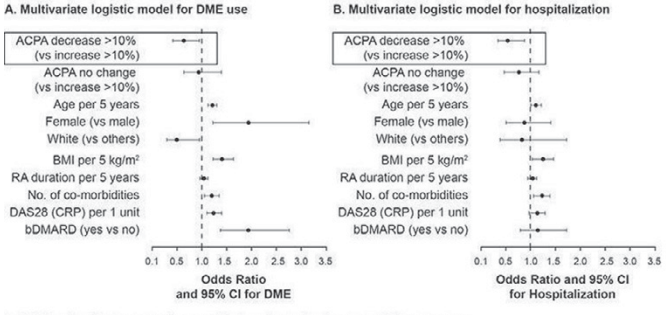
Background: High anti-citrullinated protein antibody (ACPA) concentration, beyond ACPA positivity, is indicative of more aggressive radiographic progression in patients (pts) with RA.[1] However, there is limited information on changes in ACPA levels in clinical practice settings, and the association of changes in ACPA with measures of resource use and/or disease activity.

Objectives: To evaluate the association between change in ACPA levels with hospitalizations/durable medical equipment (DME) use and change in disease activity.

Methods: Pts enrolled in a tertiary care centre RA registry, established in 2003, were analysed. The registry mostly comprises pts with established RA who were evaluated semi-annually for multiple clinical patient-reported outcomes as well as resource utilization parameters, and annually for disease activity measures such as DAS28 (CRP), SDAI and CDAI. The current analysis is based on pts enrolled in the registry with ACPA values at the time of baseline (BL) and follow-up visits. BL and follow-up ACPA levels were based on well-documented and validated ELISAs from Euro-Diagnostica (distributed by IBL-America, Minneapolis, MN, USA). Annual mean ACPA change from BL over the first year of enrolment in the registry was calculated. Changes ([follow-up – BL]/BL x 100) in ACPA levels were categorized as decrease (<–10%), no change (–10% to +10%) or increase (>+10%). Use of DME (canes, wheelchairs, walkers and commodes) as well as hospitalizations during 12-month follow-up and annual change in disease activity (DAS28 [CRP], SDAI, CDAI, swollen painful joint counts and pain) were assessed. Multivariate logistic regression analyses for binary outcome variables (DME and hospitalizations) and linear regression for change in disease activity measures were conducted, controlling for BL covariates.

Results: A total of 840 (65%) pts in the registry had BL and follow-up ACPA values and were included in the analysis. Overall, 34.6% (n=291) of pts had a decrease, 31.7% (n=266) had no change and 33.7% (n=283) had an increase in ACPA levels. There were no significant differences in BL characteristics between the three groups except for disease duration. Pts with RA with an increase in ACPA levels had significantly longer disease duration at BL. In univariate analyses, DME use was 23.4%, 30.1% and 28.6%, and hospitalization rate was 13.4%, 16.5% and 20.1% in pts with a decrease, no change or an increase in ACPA levels, respectively. Unadjusted mean (SD) change from BL in DAS28 (CRP), SDAI and CDAI in pts with reductions in ACPA levels was –0.7 (1.4), –6.1 (15.7) and –5.9 (15.1), and –0.5 (1.4), –5.0 (15.7) and –4.7 (14.6) in pts with an increase in ACPA levels. After controlling for BL covariates, the odds ratio (OR) for DME in patients who had a decrease in ACPA levels (vs increase) was 0.62 (95% CI 0.40, 0.94; p=0.026), and the OR for hospitalization was 0.54 (0.33, 0.86; p=0.010). Similarly, reductions in ACPA levels were associated with greater reductions in disease activity measures (Fig).

Figure. Association of Reductions in ACPA Levels With Resource Use (Panel A and B) and Disease Activity (Panel C) in Clinical Practice



C. Multivariate linear regression models for change in disease activity measures

Independent variable of interest*	Outcome modelled	Regression coefficient (p value)
ACPA decrease (vs no change and increase)	Change in DAS28 (CRP)	**–1.97 (0.024)**
	Change in CDAI	–1.68 (0.087)
	Change in SDAI	–1.68 (0.099)
	Change in joint counts	**–2.00 (0.010)**
	Change in pain VAS	**–0.39 (0.026)**

*Other variables in the models included age, sex, race, BMI, RA duration, co-morbidities, biologic use and baseline disease activity. ACPA=anti-citrullinated protein antibody; bDMARD=biologic DMARD; DME=hospitalizations/durable medical equipment; VAS=visual analogue scale

Conclusions: Reductions in ACPA levels were associated with reductions in DME use and hospitalizations as well as reductions in disease activity measures.

References:

[1] Ronnelid J, et al. Ann Rheum Dis 2005;64:1744–9.

Disclosure of Interest: E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Z. Guo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, C. Iannaccone: None declared, M. Frits: None declared, N. Shadick Grant/research support from: Bristol-Myers Squibb, UCB, Mallinckrodt, Amgen, Crescendo Biosciences, Consultant for: Bristol-Myers Squibb, M. Weinblatt Grant/research support from: Amgen, Bristol-Myers Squibb, Crescendo, UCB, Dxterity, Consultant for: Amgen, Bristol-Myers Squibb, Crescendo Biosciences, UCB, AbbVie, Lilly, Pfizer, Roche

DOI: 10.1136/annrheumdis-2017-eular.1569

AB0208 HOSPITALIZATION RATES IN PATIENTS WITH RA BY POOR PROGNOSTIC FACTORS: IMPACT OF ABATACEPT AND OTHER DISEASE-MODIFYING ANTIRHEUMATIC THERAPIES

E. Alemao, L. Burns, Z. Guo. *Bristol-Myers Squibb, Princeton, United States*

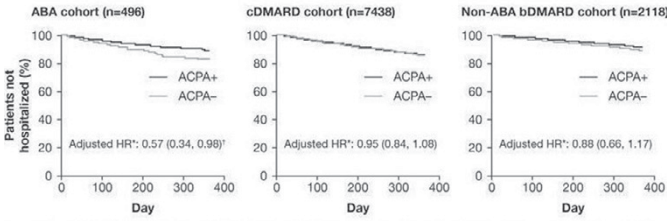
Background: Studies have reported that poor prognostic factors (PPF) in RA, such as high anti-citrullinated protein antibodies (ACPA), are associated with erosions, rapid radiographic progression and/or extra-articular manifestations.[1,2] Evidence from clinical trials and clinical practice indicate differences in treatment effects of biologic (b)DMARDs by ACPA status and/or level.[3,4] PPF also play an important role in clinical management of patients (pts) with RA, including inpatient admissions.

Objectives: To compare hospitalization rates of ACPA-positive (+) with ACPA-negative (–) pts managed with abatacept (ABA), non-ABA bDMARDs or conventional (c)DMARDs.

Methods: This is a retrospective cohort analysis of Clinformatics Data Mart, a database of administrative health claims including results for outpatient laboratory tests, processed by national laboratory vendors under contract with the managed care organization, for a total of ~53 million unique lives over 13 years. This analysis was restricted to adult pts (aged ≥18 years) who had at least two ICD-9-CM diagnosis codes for RA between Jan 2007 and Dec 2014 (identification period) and 12 months (M) of membership/drug benefit. Pts with ankylosing spondylitis, Crohn's disease, lupus, psoriasis or ulcerative colitis at or before the index date were excluded. ACPA+ was based on >19 or >5 U/mL, depending on the test utlilized. Follow-up for pts initiating ABA was from first day of treatment to first hospitalization, end of enrolment or end of 12M follow-up. The primary outcome was all-cause hospitalization at 12M. Descriptive statistics such as Wilcoxon rank-sum test for continuous variables or Pearson's chi-square test for categorical variables were used. Cox proportional hazard model was used to examine all-cause hospitalization adjusted for age, sex, region and past hospitalization. Additional covariates included co-morbidities that were different between ACPA+/– pts. Similar analyses were performed for pts treated with cDMARDs and non-ABA bDMARDs.

Results: A total of 496 ABA, 7438 cDMARD and 2118 non-ABA bDMARD pts were included, with an overall past hospitalization rate of 35.5, 25.4 and 23.2%, respectively. Overall, 59.5, 41.5 and 51.7% of pts were ACPA+ in the ABA, cDMARD and non-ABA bDMARD cohorts, respectively. ACPA+ pts were older and less likely to have obstructive sleep apnoea, depression and myalgia/myositis across all cohorts. Unadjusted 12M hospitalization rate in ACPA+ vs ACPA– pts was 10.8 vs 16.4%, 13.7 vs 14.3% and 8.5 vs 10.8% in the ABA, cDMARD and non-ABA bDMARD cohorts, respectively. After controlling for baseline covariates, the hazard ratio for hospitalization in the ACPA+ (vs ACPA–) group was 0.57 (95% CI: 0.34, 0.98; p=0.04), 0.95 (95% CI: 0.84, 1.08; p=0.47) and 0.88 (95% CI; 0.66, 1.17; p=0.38) in the ABA, cDMARD and non-ABA bDMARD cohorts, respectively (Figure).

Figure. Kaplan–Meier Plot for 1-Year Hospitalization According to ACPA Status



*HR of hospitalization for ACPA+ vs ACPA– from a Cox model adjusted for age, sex, region, past hospitalization and co-morbidities. †p<0.05. ABA=abatacept; bDMARD=biologic DMARD; cDMARD=conventional DMARD; HR=hazard ratio

Conclusions: ACPA+ pts with RA treated with abatacept have a lower rate of hospitalization than ACPA– pts. This pattern was not observed with cDMARDs or non-abatacept bDMARDs. Further efforts including matching and subgroup analysis should be explored for direct comparisons between the cohorts.

References:

[1] Visser K, et al. Ann Rheum Dis 2010;69:1333–7.
[2] Combe B, et al Ann Rheum Dis 2016; doi: 10.1136/annrheumdis-2016–210602. [Epub ahead of print].
[3] Gottenberg JE, et al. Ann Rheum Dis 2012;71:1815–9.
[4] Sokolove J, et al. Ann Rheum Dis 2016;75:709–14.

Disclosure of Interest: E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, L. Burns Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Z. Guo Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.1565

AB0209 THE CHANGES OF SIGNAL PEPTIDE- CUB-EGF DOMAIN-CONTAINING PROTEIN (SCUBE) AND OTHER ANGIOGENESIS PROTEINS DURING DISEASE ACTIVITY AND RELATIONSHIP WITH THE JOINT ULTRASOUND FINDINGS IN RHEUMATOID ARTHRITIS PATIENTS

E. Capkin, N. Cılesızoglu, S. Ozer Yaman, M. Garıpoglu, D. Altay. *Karadeniz Technical University, Trabzon, Turkey*

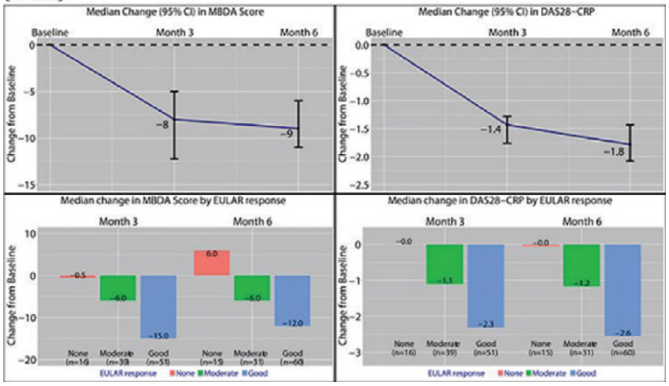
Background: Rheumatoid arthritis (RA)is a multifactorial, systemic, progressive, inflammatory disease which is characterized with bone and cartilage destruction. Synovial angiogenesis is important at the etiopathology. SCUBE (Signal peptide-CUB-EGF domain-containing protein) is rather a new surface cell protein. Its secretion increases with inflammation and hypoxic conditions. Its relations with inflammation and angiogenesis are shown in preclinical studies.
Objectives: The purpose is to study levels of newly identified plasmaSCUBE 1 and 3 and other angiogenesis markers and analysis of changes after treatment in RA patients. Moreover, to determine whether a correlation with this change in SCUBE proteins after treatment, clinical parameters and with joint ultrasound findings.
Methods: This study covers patients diagnosed with RA associated with 2010 American Collage of Rheumatology (ACR) diagnosis criteria matched with healthy controllers who are equivalent of RA patients in terms of age and gender. Detailed background information and examination of the patients were recorded and disease activity scores (DAS28) were figured out and US7 scores were calculated. The levels of SCUBE 1–3, Vascular Endotedial Groving Factor (VEGF), Matrix metaloproteinaz-9 (MM-9), Interlökin-6 (IL-6), CD40L were evaluated with the method of Enzyme-Linked ImmunoSorbent Assay (ELISA). Clinical and laboratory measurements were re-evaluated at the third month after treatment.
Results: This study covers 56 individuals; 28 of whom were diagnosed with RA and 28 of them were healthy controllers. Significant differences were observed between RA patients and healthy controller groups in terms of MMP-9 levels ($p<0,05$). Levels of SCUBE-1, SCUBE-3, VEGF, İL-6 ve CD-40 were similar ($p>0,05$).After treatment VEGF levels were significantly lower compared to pre-treatment ($p<0,05$), the changes in SCUBE-1, SCUBE-3, İL-6, CD-40 ve MMP-9 levels were not statistically significant ($p>0.05$). After treatment ultrasound scores were significantly lower than before treatment ($p<0.05$).
Conclusions: In our study, significant improvements were observed in clinical, laboratory and ultrasound findings after treatment. MMP-9 and VEGF were associated with disease activity. SCUBE proteins which have been newly identified markers of angiogenesis were shown no relationship with disease activity.
References:
[1] Szekanecz Z, Besenyei T, Paragh G, Koch AE Angiogenesis in rheumatoid arthritis.Autoimmunity. 2009;7:563–731.
[2] Yanga M, Mingyang G, Yonghe H Jiang y. Scube regulates synovial angiogenesis-related signaling. Medical Hypotheses 2013;27: 948–953.
[3] Lainer-Carr D, Brahn E. Angiogenesis inhibition as a therapeutic approach for inflammatory synovitis. Nat Clin Pract Rheumatol. 2007;3:434–42.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5949

AB0210 THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE FOR ASSESSING RESPONSE TO TREATMENT WITH ADALIMUMAB

D. Pappas[1,2], E.H. Sasso[3], R.J. Bolce[3], X. Liu[3], C.J. Etzel[1,4]. *[1]CORRONA, LLC, Southborough; [2]Columbia University Medical Center, New York; [3]Crescendo Bioscience Inc., South San Francisco; [4]University of Texas MD Anderson Cancer Center, Houston, United States*

Background: The multi-biomarker disease activity (MBDA) score measures 12 serum biomarkers to assess disease activity in patients with rheumatoid arthritis (RA) on a scale of 1–100. The MBDA score was validated in several different cohorts but has not been evaluated in a cohort consisting only of patients initiating TNF inhibitor therapy in clinical practice. We utilized patients enrolled in the Corrona-CERTAIN study to evaluate MBDA scores for patients initiating adalimumab (ADA) in several clinical practices in the US.
Objectives: Evaluate the ability of the MBDA score to assess response to treatment with ADA.
Methods: We studied 106 biologic-naïve RA patients who had been treated with ADA for at least 12 months, had initiated ADA in CERTAIN while in moderate or high disease activity by CDAI, and for whom sera were available at baseline (BL) and Months 3 and 6. Changes (Δ) in MBDA score and DAS28-CRP were evaluated from BL to Months 3 and 6 by the one-sample paired t-test. ΔMBDA scores were evaluated for patients grouped by EULAR response categories, using the Cochran-Armitage test for trend. Receiver Operating Characteristic (ROC) analysis with bootstrap sampling (20,000 iterations) was used to evaluate MBDA score ability to discriminate ΔDAS28-CRP improvement >1.2 units at Month 3, and to determine the optimal MBDA threshold by maximizing the sum of sensitivity and specificity (Youden's index criterion).
Results: At BL, median values were age 54.5 years, disease duration 2 years, BMI 28.2, DAS28-CRP 4.7, CDAI 24, SDAI 25.4; 74.5%/65.4% were RF+/ACPA+. Median MBDA score was 49 with 17 (16%) patients in low (<30), 23 (22%) patients in moderate (30–44), and 66 (62%) patients in high (>44) MBDA categories. The relative magnitude and the direction of median change from BL to Months 3 and 6 were similar for MBDA score (–8, –9) and DAS28-CRP (–1.4, –1.8), with statistically significant changes from BL for each (line graphs in Figure). Similar results were observed for SDAI and CDAI. Pearson's correlations with ΔMBDA score at Months 3 and 6 were 0.58, 0.59, respectively, for ΔDAS28-CRP; 0.48, 0.47 for ΔSDAI; and 0.42, 0.42 for ΔCDAI (all $p<0.0001$). Median reductions in MBDA score were significantly greater for patients with concurrent DAS28-CRP improvement >1.2 units (n=67) vs. ≤ 1.2 units (n=39) at Month 3 (15 vs. 2) and Month 6 (13 vs. 1.5) (both $p<0.0001$); and for patients with EULAR Good vs. Moderate vs. Non-responses (p=0.0002 at Month 3, $p<0.0001$ at Month 6) (bar graphs in Figure). Area under the ROC curve (AUROC) for the ability of ΔMBDA score from BL to Month 3 to discriminate DAS28-CRP improvement >1.2 units at Month 3 was 0.82 (95% CI, 0.74–0.90). The optimal threshold for this discrimination was a reduction in MBDA score >9 units, with sensitivity/specificity=0.63/0.82 and PPV/NPV =0.86/0.56.

Figure. Median changes from baseline in MBDA score and DAS28-CRP at 3 and 6 months: in line graphs with 95% CI (above) and by EULAR response category (below).



Conclusions: This study expands the previous validation of the MBDA score by demonstrating its ability to assess response to treatment with adalimumab in a US clinical practice cohort. The AUROC value of 0.82 for discriminating improvements in DAS28-CRP >1.2 units indicates a significant association between change in MBDA score and clinical improvement.
Disclosure of Interest: D. Pappas Grant/research support from: AbbVie, Consultant for: AbbVie, Employee of: CORRONA, LLC, E. Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., R. Bolce Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., X. Liu Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience Inc., C. Etzel Consultant for: Merck, Employee of: CORRONA, LLC
DOI: 10.1136/annrheumdis-2017-eular.5602

AB0211 THE EFFECT OF SMOKING, ALCOHOL AND CAFFEINE ON EARLY RHEUMATOID ARTHRITIS OUTCOMES

E. Chamizo-Carmona[1], C. Carrasco Cubero[2], J.J. Aznar Sanchez[1], R. Veroz Gonzalez[1], P.J. Cossío Jimenez[1], S.M. Rojas Herrera[1]. *[1]Rheumatology, H. Merida, Merida; [2]Rheumatology, CHU Badajoz, Badajoz, Spain*

Background: The aim of early RA treatment is remission. Intensive treatment with MTX achieve remission in 30–50% patients (pts). Modifiable risk factors, as smoking, alcohol, coffee and tea, may affect response to MTX.
Objectives: To study the influence of tobacco, alcohol, caffeine on the MTX response in early RA pats.
Methods: A case-control study (2010–2015): cases were pts who achieved DAS28<2.6 (remission) and controls were pts who did not. We collected information from pts$>$18years with early RA, treated with MTX, evaluated quarterly in a specialized unit early RA. All the pts underwent a structured interview about their smoking history and others habits. A descriptive and comparative study, was performed (SPSS21).
Results: 182 pts (age 50,96±13,11y, 67,6% female, 81,3% FR+ and 65,7% ACPA+) was treated with MTX and followed 105,03±7,15 months since 1995. More than 95% pts received MTX (in rapid escalation) in the first 24 months of the onset of symptoms. DAS28<2.6 was achieved for 67 (36,8%) pts, who required an lower average dose of MTX (15,07mg/w) than those who did not (18,04mg/w) (p=0,000). Age, DAS28 and physical function at baseline, treatment delay, smoking and adverse events by MTX were related to remission.The univariate and multivariate analysis of the baseline pts characteristics and the relationship of their smoking history with age, RF, ACPA and outcome of MTX monotherapy are shown in table 1and 2, respectively. The median survival of MTX monotherapy was 87,39 months (100.27 non-smokers and 47.70 months for current smokers (Log Rank 10.32, p 0.001) (see graphic).
Conclusions: The treatment of early RA with MTX alone achieved high rates of remission, especially in non-smokers. Smoking cessation could significantly improve the response to MTX and therefore should be an integral part of the treatment of early RA patients.

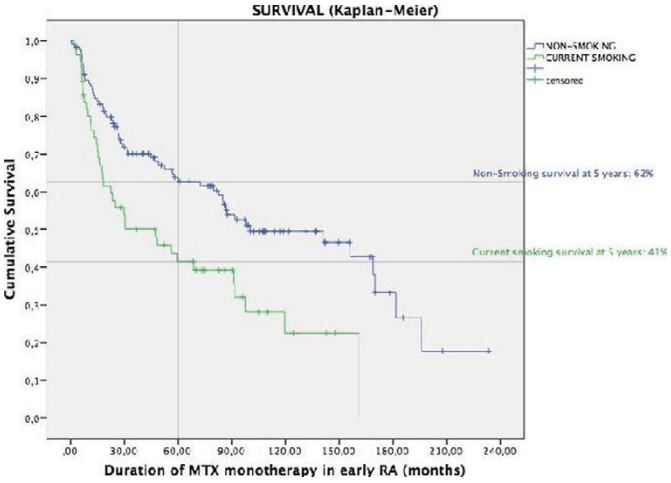
Abstract AB0211 – Table 1

Baseline Characteristic	Univariate analysis			Multivariate analysis
	DAS28<2.6	No remission	OR (95%IC)	OR (95% CI)
Age, mean (SD), years	55.46 (13.21)	48.34 (12.38)	7.11 (3.26, 10.96)**	0.124
Female, n (%)	41 (33.3)	82 (66.7)	ns	0.173
Current smoking, n (%)	12 (21.4%)	54478.6)	2,84 (1.37–5.89)**	0.37 (0.16, 0.86)*
Caffeine, n (%)	33 (29,2%)	80 (70,8)	2.35 (1.26 -4.39)**	0.092
Functional status > In (%)	38 (29.0%)	93 (71.0)	3,23 (1.65–6.31)**	2.39 (1.06, 5.40)*
Extra-articular involv, n (%)	7 (20,6%)	27 (79.4)	2,63 (1.08–6.43)*	0.107
MTX adverse events, n (%)	20 (24,1%)	63 (75,9)	2.85 (1.50–5.40)**	0.44 (0.20, 0.95)*
Baseline DAS28PCR, mean (SD)	3.88 (0.56)	4,75 (0,76)	-0,87 (-1.06, -0.67)**	5.79 (2.99, 11.20)**
MTX delay, mean (SD), m	1.66 (3.91)	5,39 (18.57)	-3.73 (-7.28, -0.18)*	0.089

Abstract AB0211 – Table 2

Smoking history	Edad	ACPA	MTX dose	Remission (n=67)	Low activity (n=98)	Need for biological (n=60)
Never Smoking (n=67), % (SD),	53,85 (15.23)*	126.03 (146.91)*	16,86 (3.92)	28 (41.8)	39 (58.2)	19 (28.4) ns
diff (95% CI)	4.58 (0.32 to 8.82)	-3.97 (-103.03 to -4.90)	ns	ns	ns	ns
Former Smoker (n=59), % (SD),	65.97 (58.68)	188.81 (159.17)	15.97 (3.34)*	27 (45.8)	39 (66.1)*	14 (23.3)
diff (95% CI)	ns	ns	-1.44 (-0.29 to -2.59)	ns	1.67 (1.06 to 2.63)	ns
Current smoker (n=56), % (SD),	45.34 (9.94)**	171.03 (166.99)	18.08 (3.63)**	12 (21.4)**	20 (35.7)**	27 (48.2)**
diff (95% CI)	-8.11 (-2.02 to -4.12)	ns	1.63 (2.79 to 0.47)	0.46 (.26 to 0.82)	0.47 (0.3 to 0.75)	2.62 (1.36 to 5.06)

*p<0.05, **p<0.01.



References:
[1] Söderlin, et al. Scandinavian Journal of Rheumatology. 2011;40(4):249–55.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6739

AB0212 CLINICAL AND SOCIODEMOGRAPHIC CHARACTERISTICS ASSOCIATED WITH RESPONSE TO METHOTREXATE (MTX) IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) NAÏVE TO DMARD

E. Chamizo-Carmona[1], C. Carrasco Cubero[2], P.J. Cossio Jimenez[1], S.M. Rojas Herrera[1], T.L. Rodriguez Araya[1], R. Veroz Gonzalez[1], J.J. Aznar Sanchez[1]. *[1]Rheumatology, Hospital de Merida, Merida; [2]Rheumatology, CHU Badajoz, Badajoz, Spain*

Background: RA treatment involves starting early with a DMARD. MTX achieves good sustained response in 30–40% of patients (pts). When MTX response is insufficient add other DMARD by achieve RA remission. Different factors may affect the response to MTX
Objectives: To analyze the clinical and demographic characteristics related to response to MTX in RA pts DMARD-naïve
Methods: We enrolled between 2011 and 2015, pts>18years RA diagnosed (ACR 1987 criteria), treated firs with MTX monotherapy (MTXm). A case-control study (MTXm persistence with CRP-DAS28<3.2 and suspension of MTXm by ineffectiveness or toxicity, respectively) was performed. We collected information that can influence the response to MTXm by medical records review and patient survey. A descriptive and analitical study with SPSS statistics 21 was performed
Results: We included 222 pts (70 men and 152 women). The characteristics of cases (123) and controls (99) are shown in the table. The causes of MTXm suspension were remission (7), intolerance/toxicity (19) and inefficiency (79). MTX was discontinued in 40 (18.2%) pts, 28 (12.7%) of them by intolerance/toxicity. Of 123 (55.4%) responders, 71 (32.0%) were CRP-DAS28<2.6. MTXm response was associated with age at onset ≥60 years (χ2 18.47, p<0.01, OR 3.67), rheumatoid factor (RF) <100 IU (χ2 10.92, p<0.01, OR 3.16) and current smoking (χ2 12.71, p<0.01, OR 2.95). Tobacco was associated with RF+ (χ2 8.9 p<0.01 OR 2.59 (1.37; 4.89) and ACPA+ (χ2 4.49 p<0.05 OR 1.88 (1.04, 3.38). We found no association with gender, education, job, coffee, tea or alcoho drinks, comorbidities, cardiovascular risk, possitivity ACPA or FR, RA presentation, treatment delay, or corticosteroid use. We found no correlation between age of RA-onset and RF or ACPA levels and MTXm duration. MTXm persistence at 5 years was 59% pts and their median survival was 93 months (77.14 to 108.8). We only found significant differences in favor of non-smokers and RF<100

Table 1. Clinical and sociodemographics characterisitics of RA patients

Characteristics	Responders n=125	Nonresponders n=99	Statistic Significancy
Age at onset (y) (mean, SD)	53.48 (13.0)	46.65 (11.5)	t=4.08 p=00006
Female n (%)	80 (65.0)	72 (72.7)	ns
Current Smokers n (%)	23 (18.7)	40 (40.4)	χ^2 12.7 (p<0,01) OR 2.95 (1.6, 5.4)
Alcohol consumers n (%)	35 (28.5)	28 (28.3)	ns
Comorbidity n (%)	92 (74.8)	61 (61.6)	χ^2 4.45 (p<0.05) OR 1.21 (1.0, 1.5)
CV risk factors n (%)	92 (74.8)	81 (81.8)	ns
Polyarticular onset of AR n (%)	61 (49.6)	61 (61.6)	ns
Extraarticular involvement n (%)	17 (13.8)	21 (21.2)	ns
Possitive RF n (%)	89 (72.4)	79 (79.8)	ns
Possitive ACPA n (%)	70 (60.3)	64 (68.1)	ns
Duration of RA (m) (mean (SD)	96.1 (63.1)	96,0 (73.9)	ns
MTX toxicity n (%)	47 (38.2)	59 (59.6)	χ^2 10.0 (p<0.01) OR 2.38 (1.4, 4.1))
MTX dose (mg) (mean, SD)	15.6 (0.32)	17.8 (0.37)	t=-4.52 p=00001

Conclusions: The initial treatment of RA with MTX is an effective and safe option, with a high drug survival. MTX response was not associated with antibody positivity (RF or ACPA), but it was significantly better in non-smokers patients and RF <100. Smoking cessation could significantly improve the response to MTX of RA patients

References:
[1] Saevarsdottir S, et al. Arthritis Rheum 2011;63:26–36.
[2] V. K. Ranganath et al. Rheumatology 2013;52:1809–1817.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1109

AB0213 HIGH POWER DOPPLER SIGNALS SEEMS MORE IMPORTANT THAN SYNOVITIS SCORES IN ESTABLISHED RHEUMATOID ARTHRITIS

E.D. Keskin[1], F.G. Yurdakul[2], H. Bodur[2], A. Akıncı Tan[3], L. Özçakar[3]. *[1]Physical Medicine and Rehabilitation, Kırıkkale University Faculty of Medicine, Kırıkkale; [2]Physical Medicine and Rehabilitation, Ankara Numune Training and Research Hospital; [3]Physical Medicine and Rehabilitation, Hacettepe University Faculty of Medicine, Ankara, Turkey*

Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease characterized by synovial inflammation, potential cartilage and bone damages. Evaluation with ultrasound (US) has come into prominence due to conventional radiography is relatively insensitive on soft tissue inflammatory changes and early bone erosions (1,2).
Objectives: The value of US has been shown in early arthritis, but is not well known for established RA. The aim of this study is to determine the relation between US signal, disease activity, articular damage and disability in established RA patients.
Methods: Forty-four RA patients (21 women, 23 men) were enrolled to the study. Age and gender, duration of disease, morning stiffness, disease activity score 28 (DAS28), The Rheumatoid Arthritis Articular Damage (RAAD) score, Hand disability Index (HDI), DASH (Disabilities of the Arm, Shoulder and Hand) scale, and grip strength values were recorded. Wrist, I-II- III. metacarpophalangeal and proximal interphalangeal joints of dominant hand were examined by both B mode US (BMOD) and Power Doppler US (PDUS).
Results: All of the 44 patients were established RA. The median of disease

duration was 156 (48–420) months. DAS 28 score was 2.86 (0.68–5.70) and 54.5% of the patients were in remission. BMOD synovitis, erosion and PDUS synovitis total scores were 20 (6–36); 6 (0–17); 1 (0–14) respectively. Although US findings were not correlated with DAS 28 and grip strength; there was poor correlation between US findings and DASH, RAAD and disease duration (Table 1). Signs of synovitis indicated with PDUS in 63.3% of the joints assessed. High-grade PDUS signal (grade 3) was found in 10 (22.7%) of the patients. Duration of morning stiffness, HDI and DASH scores were worse in the patients with high-grade PDUS signals (p=0.01, 0.04, 0.01 respectively)

Table 1. Correlation coefficients between clinical, ultrasound and functional variables

	BMOD synovitis Total		BMOD erosions Total		PDUS synovitis Total	
	r	p	r	p	r	P
DASH	0.37	0.02*	0.19	0.20	0.13	0.38
HDI	0.21	0.17	0.17	0.28	0.21	0.17
RAAD	0.33	0.02*	0.41	0.00*	0.22	0.15
DAS 28	-0.04	0.78	0.01	0.95	-0.05	0.75
MS	0.24	0.12	-0.10	0.51	0.20	0.19
Disease duration	0.13	0.38	0.46	0.00*	-0.31	0.03*
Lateral GS	0.07	0.64	-0.06	0.69	-0.06	0.70
Tip GS	0.11	0.49	-0.27	0.08	0.09	0.56
Three fingered GS	0.21	0.89	-0.17	0.27	0.05	0.76
Mass grasp	-0.08	0.59	-0.078	0.61	-0.12	0.43

BMOD: B mode ultrasound, PDUS: Power Doppler ultrasound, DASH: Disabilities of the Arm, Shoulder and Hand, HDI: Hand disability index, RAAD: Rheumatoid Arthritis Articular Damage, DAS 28: Disease activity score, MS: Morning stiffness, GS: Grip strength. *P<0.05.

Conclusions: US scores in established RA patients are usually high because of synovial hypertrophy. It is considered that the high grade PDUS signals are more appropriate for evaluation of long-standing RA patients. Furthermore in this study, grade 3 PDUS signals were found to be a good indicator of synovial inflammation, morning stiffness, and disability.

References:

[1] Concordance between Clinical and ultrasound findings in rheumatoid arthritis. Garrigues F, Jousse-Joulin S, Bouttier R et al. Joint Bone Spine 80 (2013) 597–603.

[2] Severity and Diurnal Improvement of Morning Stiffness Independently Associate with Tenosynovitis in Patients with Rheumatoid Arthritis. Kobayashi Y, Ikeda K, Nakamura T et al. Plos One (11) Doi: 10.1371/journal.pone.0166616.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2898

AB0214 METHOTREXATE IN EARLY RHEUMATOID ARTHRITIS: A SINGLE-CENTER EVALUATION OF CLINICAL OUTCOME COMPARING TWO STARTING TREATMENT STRATEGIES

F. Benaglio, S. Bugatti, G. Sakellariou, G. Crepaldi, G. Zanframundo, C. Montecucco, R. Caporali. *Early Arthritis Clinic, Division of Rheumatology, University of Pavia, IRCCS Policlinico San Matteo Foundation, Pavia, Italy*

Background: methotrexate (MTX) is considered the 'anchor drug' in the treatment of rheumatoid arthritis (RA) and it should be part of the first treatment strategy: there are many indications about the correct way to optimize the dosage, depending on clinical response and tolerability, but currently there is no shared evidence about the optimal starting dosage.

Objectives: to compare two different starting treatment strategies with MTX in patients with early RA evaluated at our Early Arthritis Clinic (EAC) in order to assess the rate of patients who reaches the target (remission/low disease activity) at 6 months, according with EULAR guidelines.

Methods: patients with RA (disease duration <12 months) evaluated at our EAC between 2005 and 2016 and treated with MTX parenterally and glucocorticoids (GC) were included. Patients followed a treat-to-target strategy to reach low disease activity with bimonthly tight control. Patients evaluated between 2005 and 2009 were initially treated with MTX 10 mg/week + GC (group A) with increase of MTX to 15 and then 20 mg/week in case of failure to reach the target; patients evaluated between 2010 and 2016 were initially treated with MTX 15 mg/week + GC (group B) with possible increase to 20 and 25 mg/week. The DAS28 response was assessed after 6 months.

Results: 260 patients were analyzed: 123 in group A vs 137 in group B. At baseline patients showed differences in DAS28 (5.2±1.15 vs 4.6±1.16, p<0.0001) and HAQ (1,125 vs 1 IQR IQR 0.75–1.875 0.375–1.5, p=0.006); there were no differences in terms of autoimmunity. After 6 months of therapy there were no differences in clinical response: 32% of patients in the group A reached the DAS28 remission vs 40% of the group B (p= ns), 27% in the group A reached the DAS28 low disease activity vs 24% of the group B (p= ns), 41% of the group A was in moderate disease activity vs 36% in the group B (p= ns). The need to increase the dosage of MTX during the first 6 months was similar: 27.6% of the group A vs 29.9% of the group B (p= ns), conversely, the need to reduce the dosage of MTX due to intolerance and/or adverse event was significantly higher in the group B (group A: 1.6% vs group B: 9.5%, p=0.014).

Conclusions: the use of higher dose of MTX is associated with a higher rate of side effects but does not provide, at short term, a significant improvement in term of clinical outcome. Conversely, the initial use of MTX 10 mg/week, with a quick dose titration in case of persistent disease activity, seems to be an appropriate option for many patients with early RA, as also recently suggested by the Utrecht Arthritis Cohort Study Group; in spite of this, there is an amount of patients who do not achieve the clinical target at short term regardless of the initial dose of MTX. Our experience suggests that in the early phase of RA treatment, in a context based on early diagnosis, tight control and treat to target, the clinical outcome seems to be linked more to the treatment strategy than to the drug dosage used.

References:

[1] Combe B, et al. 2016 update of the EULAR recommendations for the management of early arthritis. Ann Rheum Dis-2016–210602.

[2] Nair SC, et al. Determining the lowest optimally effective methotrexate dose for Individual RA patients using their dose response relation in a tight control treatment approach. PLoS ONE 11:e0148791.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6437

AB0215 A LONGER MEAN SURVIVAL OF BIOLOGIC TREATMENTS IS ASSOCIATED WITH DAS28 REMISSION IN RHEUMATOID ARTHRITIS PATIENTS

F. Ometto, C. Botsios, B. Raffeiner, D. Astorri, L. Friso, L. Bernardi, L. Punzi, A. Doria. *Rheumatology Unit, Department of Medicine - Dimed, University of Padova, PADOVA, Italy*

Objectives: To determine factors associated with remission (DAS28<2.6). We specifically considered the association of biologic treatment duration, number of biologic switches and survival of biologic treatment with remission.

Methods: We conducted a retrospective analysis on a monocentric cohort of rheumatoid arthritis patients. We included patients who were on biologic drugs at the time of the analysis (31st December 2016). We considered patients starting the first biologic treatment since January 2000 and with a follow-up ≥12 months. We considered the following variables: demographics, positive rheumatoid factor (RF)/ anti-citrullinated peptides (ACPA), disease duration at the start of the first biologic treatment, number of biologic switches, clinical assessment at the last follow-up, concomitant DMARDs, prednisone dose, current biologic treatment. We also considered the mean survival of biologic treatments, defined as the duration of the biologic treatment of each patient divided by the number of biologics undergone by the patient.

Mann-Whitney test and chi-square test were used to assess the association of continuous and categorical variables with the outcome. Continuous measures are reported as medians and interquartile range. Multivariate regression analysis included all variables reaching a p value <0.2 in univariate analysis

Results: We collected data of 330 patients. All patients had complete data. One hundred thirty-five patients (40.9%) were in DAS28 remission. Characteristics of the patients are reported in Table I. We considered 609 biologic treatments (abatacept n=61; anti-TNF alpha n=445; anakinra n=43; tocilizumab n=56; rituximab n=5). Total biologic treatment duration in all patients was 9.62 years (5.68–12.53), in patients in remission 8.95 (4.70–12.53) and in patients not in remission 10.12 (6.28–12.62) (p=0.248). Median number of previous biologic switches was 1.00 (0–1.00) in patients in remission and not in remission (p=0.436). Survival of biologic treatments was 5.33 years (2.89–7.72) in all patients, 4.57 (2.54–7.28) in patients in remission and 5.81 (3.49–7.93) in patients not in remission (p=0.013).

All clinical assessments at the last follow-up were significantly associated with DAS28 remission. Mean prednisone dose was significantly lower in patients in DAS28 remission but was considered as a consequence of remission rather than a predictor (Table I). The type of current biologic treatment was not significantly associated with DAS28 remission.

Variables included in the multivariate regression analysis were: BMI, age, disease duration, positive RF/ACPA mean survival of each biologic treatment. All variables included in the model were independently associated with DAS28 remission. A higher BMI, older age, longer disease duration and positive RF/ACPA were negatively associated with remission. A longer mean survival of biologic

Table I. Characteristics of the patients according to the achievement of DAS28 remission at the last follow-up: results of univariate and multivariate analysis.

		Univariate analysis			Multivariate regression analysis		
	All Patients	Patients not in DAS28 Remission	Patients in DAS28 Remission	p value*		OR (95% C.I.)	p value
Number	330	195	135				
Females, n (%)	58 (17.6)	34 (17.4)	24 (17.8)	0.936			
Age, median (IQR), years	62.14 (51.11-70.04)	63.62 (54.14-71.64)	60.69 (47.61-68.03)	0.009	per 10-year increase	0.83 (0.69-0.99)	0.037
BMI, median (IQR)	23.52 (21.29-27.22)	24.54 (22.09-27.68)	22.95 (20.45-26.17)	0.001		0.91 (0.86-0.96)	0.001
Disease duration, median (IQR), years	8.63 (3.83-14.43)	9.33 (4.92-15.17)	7.33 (2.92-12.08)	0.017	per 5-year increase	0.86 (0.75-0.99)	0.038
Positive rheumatoid factor or anti-citrullinated peptides, n(%)	189 (57.4)	123 (63.1)	66 (49.3)	0.013		0.58 (0.36-0.92)	0.022
Combined DMARD, n (%)	117 (35.5)	75 (38.5)	42 (31.1)	0.262			
Daily prednisone dose, median (IQR), grams	2.50 (0.00-5.00)	0.00 (0.00-5.00)	0.00 (0.00-5.00)	<0.001†			
Current anti-TNF use, n(%)	95 (28.8)	60 (30.8)	35 (25.9)	0.339			
Subcutaneous administration, n(%)	292 (88.5)	175 (89.7)	117 (86.7)	0.369			
Biologic treatment duration, median (IQR) (years)	9.62 (5.68-12.53)	8.95 (4.70-12.53)	10.12 (6.28-12.62)	0.248			
Mean survival of biologic treatments, median (IQR), years	5.33 (2.89-7.72)	4.57 (2.54-7.28)	5.81 (3.49-7.93)	0.013	per year increase	1.11 (1.03-1.18)	0.003
Biologic switches, median (IQR)	1.00 (0.00-1.00)	1.00 (0.00-1.00)	1.00 (0.00-1.00)	0.436			
Tender joints, median (IQR)	0.00 (0.00-2.00)	2.00 (0.00-2.00)	0.00 (0.00-0.00)	<0.001¶			
Swollen joints, median (IQR)	2.00 (0.00-3.00)	3.00 (2.00-5.00)	0.00 (0.00-1.00)	<0.001¶			
Patient VAS, median (IQR)	30.00 (20.00-40.00)	35.00 (30.00-50.00)	20.00 (10.00-25.00)	<0.001¶			
C-reactive protein, median (IQR)	4.00 (1.74-8.00)	5.00 (3.49-8.90)	2.00 (0.40-3.90)	<0.001¶			
DAS28, median (IQR)	2.82 (2.59-3.44)	3.28 (2.96-3.91)	1.80 (1.52-2.23)	<0.001			

*Continuous variables are presented as medians and the respective interquartile range IQR, and were tested with the Mann-Whitney test. Categorical variables are presented as frequencies and were tested with the chi-square test. † Not included in multivariate analysis. ¶ Not included in multivariate analysis as they are components of the DAS28.

treatments was positively associated with DAS28 remission (OR 1.11 per year increase, 95% C.I. 1.03–1.18, p=0.003).
Conclusions: The duration of biologic treatment and the number of previous biologic switches were not associated with of DAS28 remission. Indeed, a longer survival of biologic treatments was associated with remission. The mean survival of biologic treatments reflects both a smaller number of biologic failures and a prolonged response to each biologic treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4482

AB0216 EFFECTS OF ANTI-CITRULLINATED PROTEIN ANTIBODIES ON SYSTEMIC BONE MASS IN RHEUMATOID ARTHRITIS PATIENTS

G. Orsolini, C. Caimmi, O. Viapiana, L. Idolazzi, E. Fracassi, D. Gatti, G. Adami, M. Rossini. *Rheumatology Unit, University of Verona, Verona, Italy*

Background: Bone loss in rheumatoid arthritis (RA) is a key feature both local and systemic. Anti-citrullinated protein antibodies (ACPA) have recently been found to directly induce differentiation and activation of osteoclasts and therefore contribute to periarticular bone loss.
Objectives: The aim of this study was to analyze the effect of ACPA on systemic bone mineral density (BMD) in patients with established RA.
Methods: This is a cross-sectional study with a single-center RA population. BMD was measured with Dual X-ray absorptiometry at lumbar and femoral sites. ACPA were measured by EIA. Multivariate analysis was performed adjusting for the main confounding variables.
Results: One hundred twenty-seven RA patients were enrolled. In univariate analysis ACPA-positive patients showed lower BMD Z-score (SD below the age- and gendermatched mean reference value) at femoral sites ($p<0.01$). A negative correlation between ACPA titer and BMD Z-score at all sites was observed ($p<0.01$). The multivariate analysis adjusted for the main confounding variables confirmed the negative effect of ACPA at femoral sites ($p<0.05$), but not at lumbar spine BMD. No significant effect of rheumatoid factor has been observed.
Conclusions: ACPA have a negative titer-dependent effect on BMD at femoral sites, mainly constituted by cortical bone. ACPA-positive patients, especially if at high titer, should undergo bone investigations and be treated with bone protecting agents. Disease-modifying anti-rheumatic drugs lowering ACPA titer might have positive effects on systemic bone mass.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2672

AB0217 THE PROGNOSTIC VALUE OF IGA AUTOANTIBODIES (RHEUMATOID FACTOR AND ACPA) FOR PREDICTION OF THERAPEUTIC RESPONSES TO ANTI-TNF THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS

G. Steiner[1], D. Sieghart[1], F. Alasti[1], P. Studenic[1], T. Perkmann[2], T. Horn[3], D. Aletaha[1], J.S. Smolen[1]. *[1]Internal Medicine III-Rheumatology; [2]Laboratory Medicine, Medical University Vienna; [3]Phadia Austria GmbH, Thermo Fisher Scientific, Vienna, Austria*

Background: Anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) are important diagnostic markers in rheumatoid arthritis (RA). These antibodies are predominantly of the IgM (RF) or IgG (ACPA) isotype. The added diagnostic and prognostic value of IgA autoantibodies is being debated.
Objectives: To determine the prevalence of IgA-RF and IgA-ACPA in patients with RA and to investigate their potential predictive value regarding response to treatment with methotrexate (MTX) and TNF inhibitors.
Methods: A total of 255 patients were tested for the presence of IgA-RF, IgA-ACPA and IgG-ACPA by EliA® (Thermo Fisher Scientific); IgM-RF was measured by nephelometry. Therapeutic responses to MTX and TNF blocking biologicals were calculated in an inception cohort (n=104) who had started their DMARD therapy at our clinic. To define therapeutic responses simplified disease activity index (SDAI) 50 and American College of Rheumatology (ACR) 20 responses were calculated.
Results: Among the 255 patients tested 125 (49%) had at least one type of IgA autoantibody: 114 (44.7%) were found to be IgA-RF positive and of these 10.5% were negative for IgM-RF and 5.2% were double negative for both IgM-RF and IgG-ACPA; thus, in these patients IgA-RF was the only detectable antibody. IgA-ACPA were detected in 79 (31%) patients and apart from one exception all of them had also IgG-ACPA. Remarkably, the percentage of patients showing a SDAI50 response to TNF inhibitors was significantly lower in patients positive for IgA-RF and/or IgA-ACPA ($p<0.0001$) compared to IgA negative patients. Thus, 58% of IgA negative (but IgM-RF and/or IgG ACPA positive) patients showed a SDAI50 response whereas only 25% of the IgA-RF and/or IgA-ACPA positive ones were responders. Interestingly, while the presence of both IgA specificities did not further change the percentage of responders, patients positive for IgA-ACPA but negative for IgA-RF showed the lowest response rate to anti-TNF treatment. Completely seronegative patients also showed a significantly lower SDAI50 response ($p<0.0001$) to TNF inhibitors compared with the IgA negative (but IgM-RF and/or IgG-ACPA positive) patients. Similar results were obtained when ACR20 was used as response criteria. No differences between the various serological groups were seen with respect to treatment with MTX.
Conclusions: While the added diagnostic value of IgA antibody measurement was moderate, IgA-RF and particularly IgA-ACPA appear to be associated with poorer therapeutic responses to TNF inhibitory biological drugs and therefore may help in further stratification of RA patients and therapeutic decision making.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5210

AB0218 CORRELATION OF GRAY SCALE AND POWER DOPPLER ULTRASONOGRAPHY WITH CLINICAL EVALUATION IN RHEUMATOID ARTHRITIS

I.E. Okatan, M. Torgutalp, M.E. Yayla, A.B. Keleşoğlu Dinçer, E. Uslu Yurteri, A. Ateş, T.M. Turgay, G. Kınıklı. *Department of Internal Medicine, Division of Rheumatology, Ankara University Faculty of Medicine, Ankara, Turkey*

Objectives: Ultrasonography (US) is a useful method for assessing synovial vascularization and proliferation in rheumatoid arthritis (RA). The aim of the study is to compare the tender joint and swollen joint in patients with rheumatoid arthritis (RA) with gray scale (GS) and power doppler (PD) ultrasonography (US).
Methods: Thirty RA patients were included. Median disease duration was 53.7 months. Demographic and clinical data, C reactive protein (CRP) level and erythrocyte sedimentation rate (ESR) were recorded for each patient. Disease activity was evaluated using the Disease Activity Score in 28-joints (DAS28) with a median score 3.8.The joint tenderness and swelling were assessed for 10 joints (wrists, second and third proximal interphalangeal and metacarpophalangeal) in each patient.These joints were evaluated by GS and PD by ultrasonography. US joint effusion, synovitis and PD signals were graded from 1 to 3 for each joints. The 10-joint GS and 10-joint PD scores were then calculated. Correlations were tested using the Spearman coefficient.
Results: GS effusion, synovitis scores ($r=0.565$, $p<0.001$) and PD signals ($r=0.883$, $p<0.001$) correlated highly with the corresponding swollen joints. There was a significant correlation between DAS28 and number of tender joints ($r=0.745$, $p<0.001$) but no correlation was found between the tender joints and ultrasonographycal effusion, synovitis grade ($r=0.073$, $p>0.001$) and the PD signal ($r=0.069$, $p>0.001$). There was moderate correlation between 10 joints GS, 10 joints PD and DAS28, but it was not statistically significant.

Table 1. Demographic and clinical characteristics of the patients (n=30)

Age (years) – mean (SD)	53.7±11.9
Female, n (%)	28 (93.3)
RA duration (months)	42 (67)
Rheumatoid factor positive, n (%)	15 (50)
CCP positive, n (%)	20 (66.7)
Smoking, n (%)	5 (16)
Prednisone, n (%)	11 (36.7)
DAS28 (ESR), (IQR)	3.8 (2.9)
TJC (0–10), (IQR)	2 (5)
SJC (0–10), (IQR)	0 (0)
10 Joint GS score, (IQR)	0 (1)
10 Joint PD score, (IQR)	0 (0)
ESH mm/h (IQR)	23.5 (21)
CRP mg/L (IQR)	4.6 (6.5)

SD: standard deviation, RA: rheumatoid arthritis, CCP: cyclic citrullinated peptide, DAS28: disease activity score in 28 joints, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, GS: gray scale, PD: power doppler, TJC: tender joint count, SJC: swollen joint count.

Conclusions: Evaluating the swollen joints with clinical examination and combining it with US is a sensitive method. As joint tenderness is a more subjective finding than the joint swelling, this may explain the lack of correlation between tender joints and ultrasonography findings. We suggest to use Gray scale US and PD as a complementary method in addition to clinical assessment of joint tenderness in patients with RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4859

AB0219 INTENSIVE COMBINATION THERAPY WITH MEDICATION AND ORTHOPEDIC SURGICAL INTERVENTION FOR TREATING RHEUMATOID ARTHRITIS PATIENTS WITH DETERIORATED JOINTS

H. Ishikawa[1], A. Abe[1], Y. Nomura[1], S. Ito[1], T. Kojima[2], M. Kojima[3], N. Ishiguro[2], A. Murasawa[1]. *[1]Rheumatology, Niigata Rheumatic Center, Shibata; [2]Orthopedic Surgery, Nagoya University Hospital; [3]Medical Education, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan*

Background: The treatment aim of rheumatoid arthritis (RA) is achieving and maintaining remission (REM) or low disease activity (LDA) via tight medical control. However, despite remarkable advances in medication, progressive deterioration and/or deformity of the joint sometimes occurs, if adequate medication is not administered in the early stage. Surgical reconstruction is still required in the joints with functional loss caused by structural damage. Recently, patients have expressed a desire to achieve functional REM with a higher quality of life (QOL) and improved mental wellness.
Objectives: The objective of this study was to clarify the effectiveness of intensive combination therapy with medication and orthopedic surgical intervention in patients who have already achieved REM or LDA.

Methods: A prospective cohort study was performed on 294 sites in 276 patients with functional loss due to RA scheduled to undergo primary elective surgery between October 2012 and September 2014. There were 99 sites in 96 patients (males: 10, females: 86) whose disease activity was REM or LDA just before surgery. In the REM/LDA group, the average age was 63 (29–82) years, and the average disease duration was 17 (2–60) years. The surgical site was the shoulder in 1 patient, elbow in 7, wrist in 21, hand in 24, hip in 5, knee in 10, ankle in 4, and forefoot in 27. The procedures performed included 38 alloarthroplasties, 41 arthroplasties without prosthesis, 19 arthrodesis, and 9 synovectomies. The patient-reported outcome (PRO) was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI), EuroQol-5 Dimensions (EQ-5D), Beck Depression Inventory-II (BDI-II), Patient's General Health using visual analogue scale of 100 mm (Pt-GH), and the Disabilities of the Arm, Shoulder and Hand (DASH) for the upper extremity surgery. The Time Up &Go test (TUG) was administered for patients receiving lower extremity surgery. The disease activity was assessed based on the 28-joint Disease Activity Score using C reactive protein (DAS28-CRP). All of these items were investigated just before surgery (baseline) and again at 6 and 12 months after surgery.

Results: On the whole, the physical function (HAQ-DI, DASH, TUG), QOL (HAQ-DI, EQ-5D, Pt-GH), mental wellness (BDI-II, Pt-GH), and disease activity (DAS28-CRP)[1)] were significantly improved at 6 and 12 months after surgery compared to baseline ($p<0.01$). In the REM/LDA group, a significant improvement was noted in the physical function (DASH, TUG) and QOL (EQ-5D) at 6 and 12 months after surgery; however, we did not observe any significant changes in any other items (Table 1).

Table 1: Outcome of combination therapy with medication and orthopedic surgical intervention

		HAQ-DI	EQ-5D	BDI-II	Pt-GH mm	DASH (UE)	TUG (LE) sec	DAS28-CRP
Total n=276 (UE: n=151, LE: n=125)	baseline	1.08 (0.74)	0.69 (0.11)	13.0 (8.7)	39 (25)	43.8 (22.2)	13.0 (9.5)	3.1 (1.0)
	PO# 6mos.	1.00** (0.78)	0.74** (0.14)	11.7** (8.2)	26** (21)	37.3** (29.1)	10.5** (5.4)	2.4** (1.5)
	PO# 12mos	0.98** (0.78)	0.75** (0.14)	11.6** (8.5)	27** (21)	36.2** (23.0)	10.7** (7.0)	2.4** (0.8)
REM+LDA n=96 (UE: n=50, LE: n=46)	baseline	0.84 (0.63)	0.73 (0.13)	11.0 (8.1)	18 (18)	35.2 (20.9)	9.8 (3.2)	2.1 (0.4)
	PO# 6mos.	0.81 (0.67)	0.79** (0.15)	9.9 (7.7)	18 (16)	30.2** (18.9)	9.0** (2.6)	1.9** (0.6)
	PO# 12mos	0.83 (0.70)	0.79** (0.16)	10.1 (8.1)	18 (18)	29.9** (20.3)	9.0** (3.0)	1.9 (0.6)

Mean(SD), **: p<0.01 compared to baseline

Conclusions: Achieving REM or LDA is not the ultimate goal of treatment for patients with functional loss caused by structural damage. Further "wellness" can be achieved by surgical intervention. Intensive combination therapy with medication and orthopedic surgical intervention is effective in improving the QOL and mental health as well as the physical function. Such intervention can also ameliorate the disease activity.

References:

[1] Oh K, Ishikawa H, Abe A, et al. Effects of surgical intervention on disease activity of rheumatoid arthritis: cases of surgery for rheumatoid arthritis of the lower limbs treated with biologics. Mod Rheumatol. 2014;24(4):606–11.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2415

AB0220 THE PROMISE OF ULTRASOUND GUIDED MINIMALLY INVASIVE SYNOVIAL BIOPSIES IN THE UNITED STATES

A.M. Mandelin[1], P. Homan[2], C.M. Cuda[1], S.T. Dominguez[1], S.L. Bridges[3], J.M. Bathon[4], J. Atkinson[5], D. Fox[6], E.L. Matteson[7], C.D. Buckley[8], C. Pitzalis[9], D. Parks[5], L.B. Hughes[3], L. Geraldino-Pardilla[4], R. Ike[10], K. Wright[7], A. Filer[8], S. Kelly[9], E. Bacalao[1], E.M. Ruderman[1], R. Pope[1], H. Perlman[1], D.R. Winter[1]. *[1]Northwestern University, Chicago, United States; [2]Medicine/Rheumatology, Northwestern University, Chicago; [3]UAB, Birmingham; [4]Columbia University, New York; [5]Washington University, St. Louis; [6]Medicine/Rheumatology, University of Michigan, Ann Arbour; [7]Mayo Clinic, Rochester, United States; [8]University of Birmingham Research Laboratories, Birmingham; [9]Queen Mary University of London, London, United Kingdom; [10]University of Michigan, Ann Arbour, United States*

Background: Currently we are in the golden age of therapy for patients with rheumatoid arthritis (RA). However, currently there exists no available assay to predict the response to a particular therapy for an individual patient. Today, rheumatologists do not have information at han for therapeutic decisions. It is clear that the target organ in RA patients, i.e. the synovium, has the potential to unlock the secret for determining therapeutic response. Ideally, a sufficient synovial sample would be obtained from each patient to perform histology, sorting of individual cell populations and transcriptional analyses.

Objectives: Our goal is to establish a minimally invasive ultrasound guided synovial biopsy program in the United States to obtain synovial tissue for determining therapeutic response.

Methods: Rheumatologists from six Universities in the United States were trained in ultrasound guided minimally invasive synovial tissue biopsy procedures. Only patients with a grey scale synovitis score of 2 or greater were selected. A disposable semi-automatic-guillotine type biopsy needle (Quick-Core) was utilized for all patients and 25/26 patients had the biopsy performed on the wrist. Histology was performed on whole tissue. RNA was extracted from whole tissue and from FACS sorted macrophages in order for RNA sequencing (RNA-seq) analysis to be performed.

Results: Our group has already performed over 26 minimally invasive ultrasound guided synovial tissue biopsies on RA patients with active disease. We had minimal adverse effects and patients tolerated the procedure very well. At least 6–12 needle biopsies of synovial tissue were obtained via biopsy per patient. A minimum of 4 needle biopsies were placed in formalin and synovial lining was confirmed via histologic analyses. The remaining pieces were used to prepare libraries for RNA-seq. We observed comparable RNA integrity numbers, a measure of RNA quality, between the whole synovial tissue from RA (biopsy obtained) and OA (surgically-obtained) patients. OA patients segregated together transcriptionally, while RA patients are more heterogeneous as demonstrated via RNAseq analysis. We also optimized a protocol for digestion of synovial tissue biopsies for isolation of macrophages. We identified genes differentially associated with macrophage activity in RA versus OA synovial macrophages that were not evident in the whole tissue transcriptional profile.

Conclusions: Ultrasound guided synovial tissue biopsies are feasible in the United States. Based on our recent success using minimally invasive ultrasound guided synovial biopsies, we believe that this procedure coupled with cutting-edge technologies will provide the critical information to rheumatologists to establish precision based medicine as a reality for RA patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5488

AB0221 IMPACT OF SMALL TO MEDIUM DOSE OF PREDNISOLONE ON BONE MINERAL DENSITY AMONG EARLY RHEUMATOID ARTHRITIS PATIENTS

H.M. Lam[1], M.C. Wan[2], L.S. Tam[1] on behalf of CRYSTAL study group, The Hong Kong Society of Rheumatology. *[1]Dept. of Medicine and Therapeutics, The Chinese University of Hong Kong, Shatin; [2]Dept. of Medicine, Ruttonjee Hospital, Wanchai, Hong Kong*

Background: Recent randomized trials in rheumatoid arthritis (RA) using low to medium dose of corticosteroid showed that bone mineral density (BMD) loss over 2 years was not significantly different from that with placebo. Another study in early RA and undifferentiated arthritis even showed a positive correlation between cumulative glucocorticoid (GC) dose with an increase in BMD at the ultradistal forearm. Whether the use of prednisolone (pred) can prevent bone loss in early RA patients remained controversial.

Objectives: The aim of this study was to investigate the impact of small dose pred (≤10mg/day) on BMD in early RA patients.

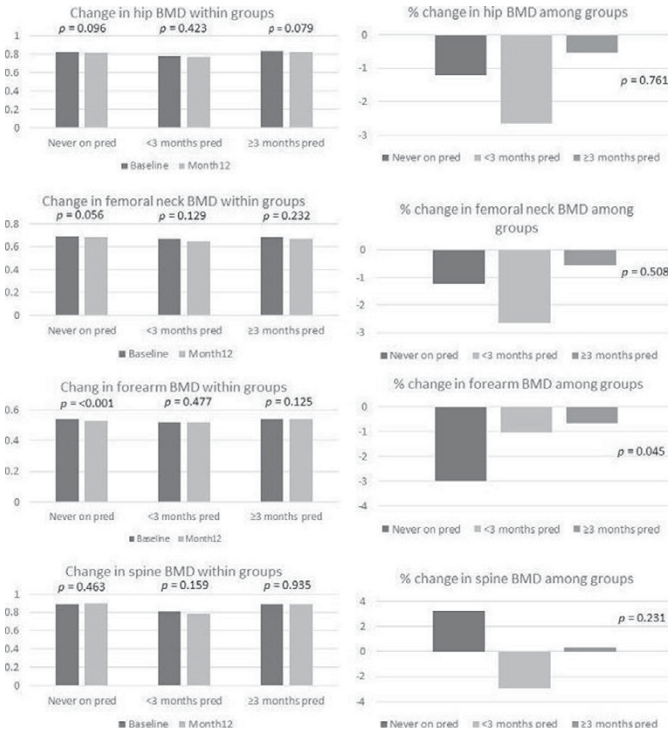
Methods: Data from 107 patients ((age: 53.3±11.92 years; females: 79 [73.8%], median disease duration at entry: 7-month (IQR, 4–12)) from the Hong Kong early arthritis registry (Clinical Rheumatology Systematic Treat to Target in Asia Leadership [CRYSTAL] project)were analyzed. In this register, clinical and treatment information were recorded systematically, including cumulative GC dose. Hip, spine and forearm BMDs were measured by duel-energy X-ray absorptiometry (DXA) at baseline and month 12. Patients were categorized into three groups according to pred use (never/<3/≥3 months) during the first year of follow-up. Patients who ever took>10mg/day of pred were excluded. The change in BMD was compared between groups and between the two time points.

Results: The baseline characteristics of patients were shown in Table 1. Patients

Table 1. Baseline characteristics

	Duration of pred use			
	Never (n=58)	<3 months (n=8)	≥3 months (n=41)	*p*
Female	46 (79.3%)	5 (62.5%)	28 (68.3%)	0.249
Age (years)	50.66±11.86	48.25±16.4	57.61±10.24	0.004
BMI (kg/m^2)	22.80±3.56	22.27±2.19	23.55±3.84	0.496
RF+ve	46 (79.3%)	6 (75.0%)	32 (80.0%)	0.950
AntiCCP+ve	41 (83.7%)	4 (80.0%)	31 (83.8%)	0.976
Osteoporosis	14 (24.1%)	2 (25.0%)	14 (34.1%)	0.540
Disease duration	10.80±11.41	7.49±3.99	6.73±6.11	0.032
Tender joints	6.77±5.19	6.25±4.17	9.85±7.92	0.218
Swollen joints	4.05±3.70	4.13±2.85	5.98±5.17	0.146
ESR (mm/1st hr)	56.93±35.62	40.75±18.97	62.20±35.72	0.387
CRP (mg/L)	15.18±21.68	14.8619.56	27.31±34.77	0.265
DAS-CRP	4.28±1.20	4.40±1.03	4.95±1.41	0.042
DAS remission	3 (5.3%)	0 (0.0%)	2 (4.9%)	0.436
Pred	0 (0.0%)	5 (62.5%)	25 (61.0%)	<0.001
Osteoporotic drug	0 (0.0%)	0 (0.0%)	2 (5.6%)	0.172
DMARDS	30 (54.5%)	4 (57.1%)	13 (36.1%)	0.332
Biologics	0 (0.00%)	0 (0.00%)	0 (0.00%)	–
NSAID	40 (72.7%)	5 (71.4%)	28 (77.8%)	0.766

who required ≥3 months of pred treatment are older, with a shorter disease duration and a higher disease activity. Significant differences in the percentage change of BMD in forearm was found among the groups (Pred never/Pred<3 months/Pred≥3 months: -2.99±4.21/-1.05±3.10/-0.65±3.45, p=0.045). Post-hoc analysis revealed that the percentage reduction of forearm BMD was significantly less in the Pred ≥3 months group compared to the Pred never group (p=0.043). After adjusting for age, gender, disease duration and baseline DAS-CRP, the changes in forearm BMD was still significantly different among the three groups (p=0.015). No significant differences in the changes of hip and spine BMD were observed. Significant changes in forearm BMD were observed between baseline and month 12 only in the Pred never group (0.54±0.08/0.53±0.0 p<0.001,graph1).



Conclusions: Small to medium dose of prednisolone might protect bone loss in forearm among early RA patients. These results need to be further validated.

References:

[1] Safety of low- to medium-dose glucocorticoid treatment in rheumatoid arthritis: myths and reality over the years. Ann N Y Acad Sci 2014.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2842

AB0222 THE SERUM ANTI-CITRULLINATED PROTEIN/PEPTIDE ANTIBODIES IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

H. Zeng. *Department of Pediatric Allergy, Immunology and Rheumatolog, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: To investigate the diagnostic value and prognostic usefulness of anti-citrullinated protein/peptide antibodies (ACPA) in children with juvenile idiopathic arthritis (JIA).

Methods: The presence of ACPAs in the serum samples from 81 JIA patients were determined using Anti-CCP IgG, CCCP3.1 IgG and IgA ELISA. Citrullinated Protein Antibodies, Anti-MCV, and Aeskulisa RA/CP-Detect which coated various citrullinated antigen substrates: synthetic cyclic peptide, recombinant rat filaggrin, mutated human vimentin, and IgG-derived peptides. 55 children with other joint diseases and 49 healthy donors were control groups. The diagnostic performance of ACPAs was analyzed and correlations between ACPAs and radiological damage were evaluated.

Results: CPAs in 8.8–28.4% of JIA group were detected with specificity of 84.6–98.1%. ACPAs could be seen in all subtypes of JIA, and high levels of ACPAs were particularly found in the RF positive JIA patients No healthy control had increased ACPA tested for CCP, CCP3.1, and CPA, whilst 3and 2 of healthy controls were found positive to MCV and RA/CP, respectively. The presence of ACPAs correlated more frequently with the presence of RF (P<0.05). The ACPA positivities in 18 JIA patients with radiological damage were 27.8–55.6%, which higher than that in patients without damage, and of the ACPA (CCP, CCP3.1, CPA, or MCV) positive JIA patients, 62.5%, 62.5%, 52.9%, 43.5% respectively had radiological damage, which significantly higher than that in JIA patients without ACPA (P<0.05).

Conclusions: This study confirms the main presence of ACPAs in children with polyarticular JIA, especially those with RF positive using ELISA based methods, and ACPAs relate significantly with joint erosions in JIA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2058

AB0223 PROGNOSTIC FACTORS FOR RADIOGRAPHIC DAMAGE IN PATIENTS WITH SERONEGATIVE RHEUMATOID ARTHRITIS

H.Y. Lee[1], E.-J. Park[2], W.S. Jeong[2], J. Kim[2]. *[1]Department of Medicine; [2]Dvision of Rheumatology, Department of Medicine, Jeju National University Hospital, Jeju-si, Jeju-do, Korea, Republic Of*

Background: Long since it have been suggested that seronegative rheumatoid arthritis (RA) represents a clinical entity quite distinct from that of seropositive RA. However, analytical studies dedicated to clinical outcomes regarding radiographic progression and risk factors for that are scarce[1,2].

Objectives: The aim of this study is to evaluate radiographic outcome and prognostic factors for radiographic damage in patients with seronegative RA.

Methods: RA pateints reportedly seronegative for both rheumatoid factor and anti-cyclic citrullinated peptide antibody who were seen at Jeju National University Hospital in South Korea between August 2003 and December 2016, and followed-up at least 2 years were included. Medical records, laboratory and radiographic data was retrospectively analyzed and multivariate analysis was performed to evaluate prognostic factors for radiographic damage in patients with seronegative RA.

Results: One hundred six patients with seronegative RA were observed and 16 (15.1%) patients demonstrated newly-developed joint damage during follow-up period. Age at diagnosis was 38.9 years and 64 (60.4%) patients were female. Symptom duration at diagnosis was 1.1 years and follow-up duration was 4.4 years. Baseline characteristics including sex, symptom duration, smoking status, number of active joints, acute phase reactant, joint erosion at diagnosis were not significantly different in patients with joint damage compared to those without joint damage. Joint erosion at diagnosis and smoking status were associated with radiographic damage in seronegative RA adjusting age, symptom duration, ESR, CRP values at diagnosis, and follow-up duration, whereas it was not statistically significant (adjusted odds ratio 1.45;p=0.061 and 1.58;p=0.072 respectively).

Conclusions: Our study demonstrated a rate of joint damage in patients with seronegative RA comparable to recent studies. Joint erosion at diagnosis and smoking status showed tendency to correlate with progression of radiographic damage in patients with seronegative RA. A large comparative study dedicated to this issue in seronegative RA is required.

References:

[1] Ajeganova, S. & Huizinga, T. W. J. Nat. Rev. Rheumatol. 11, 8–9 (2015).
[2] A.G. Pratt, J.D. 652 Isaacs/Best Practice & Research Clinical Rheumatology 28 (2014) 651e659.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6898

AB0224 SIMULATION FOR CHOICE OF BDMARDS AND TSDMARDS IN ORDER TO SUCCESS FOR THREE-YEAR SURVIVAL IN RHEUMATOID ARTHRITIS TREATMENT

I. Yoshii. *Rheumatology, Yoshii Hospital, Shimanto City, Japan*

Background: In rheumatoid arthritis (RA) treatment, bDMARDs and tsDMARDs (BIO) perform tremendous disease activity control, however, its effectiveness is uncertain and unstable, because their survival ratio is not good enough to tolerate. If more right choice is done in guided by some simulation.

Objectives: This study aims more than 80% of three-year survival ratio (SR@3Y) in simulating risk of BIO by using statistical clinical data and post marketing surveillance (PMS) data with Bayes estimation.

Methods: Infection risk and survival risk were harvested from Japanese PMS data, and our clinical data. All our cases were calculated with last observation carried forward method (LOCF). If BIO was continued for more than three years or discontinued by attaining clinical remission, it was evaluated as success, while other cases were evaluated as failure. Patient's clinical data and general status were calculated for each case, and SR@3Y for success was statistically evaluated with Binary Logistic Analysis for success. Evaluation methods for parameters were divided according to general risk and drug specific possibility. If calculated general risk went above 0.2, selection of BIO was discarded. In other case which had gone below, choice of BIO is done in according to point that had been cumulated by drug specific possibility in choosing what took maximum calculated expectation value.

If chosen drug have matched used BIO, it was evaluated as true, if not, it was evaluated as false, while if true case was in success, it was evaluated as true success, and if in failure, it was evaluated as true failure, while false case was in success, it was evaluated as false success, and if in failure, it was evaluated as true failure. Sensitivity in success cases and specificity in failure cases was evaluated in patients in whom BIO was administered. Statistical evaluation was done with chi-square test.

Results: 188 cases have had enough data for simulating. In these, 108 were success and 80 were failure. In success cases, simulated TNF inhibitor (TNF-i) counted 73, Tocilizumab (TCZ) counted 11, Abatacept (ABT) counted 12, and

Tofacitinib (TOF) counted 2 while real chosen cases were TNF-i counted 65, TCZ counted 11, ABT counted 21, and TOF counted 11. Overall success ratio was 57.4%. In these cases, true choice had been done in 97 cases of 108. In failure cases, simulated TNF-i counted 44, TCZ counted 16, ABT counted 2, and TOF counted 1, while real chosen cases were TNF-i counted 49, TCZ counted 17, ABT counted 10, and TOF counted 4. True success counted 97, and false success counted 11, while false success counted 37 and true failure counted 54. Then, sensitivity was 89.8% and specificity was 67.5% (<0.01).

Conclusions: Drug choice of BIO supported with simulation was superior to real choice. If risk management was adequately performed, SR@3Y is expected more than 85%.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6499

AB0225 CHARACTERISTICS OF MHAQ FOR UPPER AND LOWER EXTREMITY FUNCTION, AND RELATIONSHIP WITH AGE AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENT

I. Yoshii [1], T. Chijiwa [2]. [1] *Rheumatology, Yoshii Hospital, Shimanto City;* [2] *Rheumatology, Kochi Memorial Hospital, Kochi, Japan*

Background: Activity in daily living (ADL) is one of main target to maintain patient's quality of life in rheumatoid arthritis (RA) treatment. Modified Health Assessment Questionnaire (mHAQ) is a most popular index for ADL in routine practice. mHAQ is separated according to function of extremity; namely the first four categories are reflections of upper extremities (mHAQ-UE), while the latter are of lower extremities (mHAQ-LE). If function of each extremity is separately disabled, it should be reflected on each part of mHAQ.

Objectives: mHAQ was separately investigated in order to evaluate characteristics of each part of mHAQ.

Methods: 964 RA patients since January 2010 had been treated. In these, patients who have been treated consecutively for more than five years at December 2016 were recruited in this study. Patient who had been operated musculoskeletal surgery was eliminated. mHAQ, mHAQ-UE and mHAQ-LE, and 28-joint disease activity index with C-reactive protein (DAS28-CRP) were measured every time since first consult. Average value of these parameters including Sharp/van der Heijde Score (SvdHS) were calculated annually. Relationship between each of mHAQ and parameters for each year were evaluated used with multiple linear regression analysis.

Predominant extremity in mHAQ was evaluated as in what upper extremity predominant (G-UE), lower extremity predominant (G-LE), same weight (G-EV), and both of them were zero (G-Z). Changes of the evaluation from first to the last period were evaluated year by year.

Results: One hundred and two male and three hundred and thirty-three female, totally four hundred and thirty five patients were picked up. Their average value of age, SvdHS, DAS28-CRP, mHAQ, mHAQ-UE, and mHAQ-LE were 64.65, 52.1, 2.96, 0.439, 0.386 and 0.491 at first consult, and 71.05, 52.1, 1.72, 0.425, 0.344, and 0.505 at last time follow up, respectively. Both of mHAQ-UE and mHAQ-LE have demonstrated significant regression with both age and SvdHS throughout treatment, while not significant with DAS28-CRP, however, mHAQ-UE correlated with tenderness joint except of knee, and mHAQ-LE have correlated with swelling of the knee joint significantly.

G-UE had counted for 85 patients, G-LE for 136, G-EV for 49, and G-Z for 165 at first consult. Once evaluation had changed, then have continued to the last in all patients. G-UE resulted in G-UE for 83, while G-LE for 2 at last. G-LE resulted in G-LE for 133, G-Z for 2, and G-EV for 1. G-EV resulted in G-LE for24, G-UE for 7, and G-EV for 18. G-Z resulted in G-Z for 137, G-LE for 19, G-UE for 4, and G-EV for 5. G-EV to G-EV demonstrated significant higher DAS28-CRP improvement from first to the last than to G-LE, and to G-UE, and G-EV to G-LE demonstrated significant higher DAS28-CRP improvement than to G-UE, although no significant difference demonstrated for mHAQ improvement among groups. G-UE to G-LE demonstrated significant higher DAS28-CRP improvement than to G-UE, as well as G-UE to G-LE demonstrated significant higher mHAQ improvement than to G-UE.

Conclusions: From these results, it is suggested that mHAQ-UE and mHAQ-LE move under common influence. However, mHAQ-UE change may be reflected by upper exrtremities joint tenderness, while mHAQ-LE can move more sensitively with knee swelling. Tight disease activity control may reduce mHAQ both of them, however, reduces more predominantly with mHAQ-UE than mHAQ-LE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2012

AB0226 FUNCTIONAL DISABILITY IN RA PATIENTS TREATED WITH BIOLOGICS: HUR-BIO REAL LIFE RESULTS

A. Sari, B. Armagan, A. Erden, L. Kilic, O. Karadag, A. Akdogan, S. Apras Bilgen, S. Kiraz, U. Kalyoncu, I. Ertenli. *Rheumatology, Hacettepe University School of Medicine, Ankara, Turkey*

Background: Rheumatoid arthritis (RA) is a chronic, erozive disorder which may lead to permanent joints damage. Health assessment questionnaire (HAQ) is frequently used for evaluating functional disability in RA patients.

Objectives: The aim of this study is to determine the effect of biologic treatment on functional disability in RA patients.

Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a prospective, monocentric database of biological treatments including 1229 RA patients by August 2016. 523 patients in whom HAQ assessment before biologics was avaliable, were recruited in this retrospective analysis. HAQ score $\geq$1.0 was defined as severe functional disability.[1] HAQ assesment at last follow-up visit were evaluated. Demographic,clinical and serologic data of patients were also collected. Improvement of HAQ score 0,22 points or more was considered as clinically significant response to treatment.[1]

Results: Among 523 patients (80.5% female), mean age was 52.6±12.5 and mean disease duration was 9.4±7.3 years. Seropositivity for RF and/or CCP was present in 67.2% of patients. At baseline visit, HAQ score was $\geq$1.0 in 268 patients (51.2%). Baseline and last follow-up HAQ scores were 1.07±0.62 and 0.64±0.57. Minimal clinically significant improvement of HAQ score was observed in 238/377 patients (63.1%). Clinically significant response was more frequent in patients with baseline HAQ score of $\geq$1 (153/195 (78.4%) vs 85/182 (46.7%), $p<0.001$). Table 1 represents features of patients according to baseline HAQ score. Mean follow-up time was 16.4±16.4 months. Data of at least one visit was available for 377 (72.0%) patients.

Table 1. Comparison of demographic an clinical data of patients according to baseline HAQ score

	HAQ $\geq$1 (n=268)	HAQ<1 (n=255)	p
Age, mean ± SD	55.1±12.3	50.0±12.3	<0.001
Disease duration (years), mean ± SD	10.2±8.0	8.6±6.3	0.01
BMI, mean ± SD	31.3±6.4	28.9±5.9	<0.001
High school or collage graduate n (%)	68 (25.3)	110 (43.1)	<0.001
Smoking (current or previous),n (%)	95 (35.4)	123 (4.,4)	<0.001
Hypertension, n (%)	101 (37.7)	59 (23.1)	<0.001
Patient global assesment VAS, mean±SD	6.8±1.4	5.7±1.8	<0.001
Fatigue VAS, mean ± SD	6.7±2.0	5.0±2.8	<0.001
Pain VAS, mean ± SD	7.1±1.6	6.1±2.1	<0.001
Biologic switch, n (%)	63 (23.5)	41 (16.1)	0.033

Conclusions: Functional disabilty was observed approximately half of patients. Clinically significant improvement was more frequent among patients with higher baseline HAQ scores particularly. Biologic treatment seems to be provide significant functional improvement. However significant functional disability persists in one fourth of patients.

References:

[1] Lillegraven S., Kvien T.K. Measuring disability and quality of life in established rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2007;21:827–840.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4098

AB0227 IMPACT OF EARLY ARTHRITIS CLINIC ON THE RATE OF TREATMENT WITH BIOLOGICS IN RHEUMATOID ARTHRITIS: INTERRUPTED TIME SERIES ANALYSIS

I. Farina, E. Galuppi, G. Ciancio, C. De Giorgio, C.A. Scire', M. Govoni. *Department of Medical Sciences, UOL Rheumatology, Section of Haematology and Rheumatology, University of Ferrara and Azienda Ospedaliero-Universitaria Sant'Anna, Ferrara, Italy*

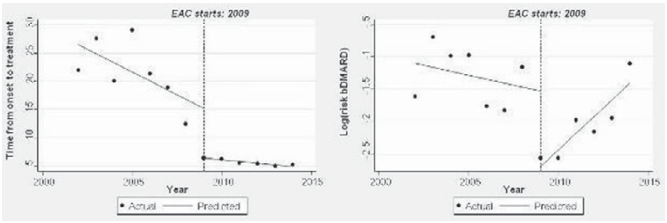
Background: Early diagnosis is one of the mainstay of rheumatoid arthritis (RA) management. Early diagnosis reflects on early treatment, better response with reduction of long-term detrimental disease outcomes. Early arthritis clinics (EAC) are the healthcare services devoted to facilitate early diagnosis and optimize treatment of early onset inflammatory arthritis. Despite the a priori beneficial potential of EAC, no strong experimental data support EAC efficacy. Interrupted time series analysis is one of the "next best" approaches for dealing with interventions when randomisation is not possible or clinical trial data are not available.

Objectives: To evaluate the impact of the implementation of an EAC in terms of probability of starting second-line biologic DMARDs, using a quasi-experimental approach.

Methods: RA patients fulfilling 1987 ACR criteria who attended the outpatient rheumatology clinic (RC) between 2002 and 2008 and the Early Arthritis Clinic between 2009 and 2014 were retrospectively analyzed. The EAC was developed as a healthcare service integrating primary care with tertiary rheumatology care to provide early referral of suspected inflammatory arthritis and tight monitoring and standardized therapeutic approach according to "treat to target" (T2T) strategy and EULAR guidelines to early RA. The two sub-cohorts were compared in terms of: 1) lag time from symptoms onset to RA treatment with DMARDs; and 2) risk of treatment with bDMARDs at 24 months. Interrupted time analysis was performed to compare lag time from onset to treatment and log-transformed 24-month risk of biologics periods before the implementation of the EAC with subsequent periods.

Results: A total of 353 RA patients were included: 208 (mean±SD age 58.7±12.6 years, 164 F, baseline DAS28 4.76±1–23) followed in RC and 145 (mean±SD age 58.8±14.9 years, 106 F, DAS28 5.09±1.31) in EAC. Lag time from symptoms onset to treatment resulted significantly lower (median [IQR] months 4 [2–7] vs 12 [5–24]; $p<0.0001$) in patients managed in EAC compared with RC. Within 24 months a biologic therapy was started in 62/208 (29.8%) of patients followed in RC, and 21/145 (14.5%) in EAC group (p=0.001), along with an increased remission rate at 24 months (43% vs 62%, $p<0.001$). Analyzing the time series "interrupted" by the implementation of the EAC, comparing before and after

intervention periods, a significant change in slope was observed for both lag time (coefficient -8.85 [95% CI -17.25, -0.44], p=0.04) and risk of treatment with biologics (coefficient -1.17 [95% CI -2.09, -0.24], p=0.01). As expected in more recent years - according to a T2T approach - a monotonous positive trend in percentage of patients treated with biologics is also observed in EAC (coefficient 0.31 [95% CI 0.05, 0.58]).



Conclusions: The implementation of an EAC that integrates care and applies tight control and standard of care, leads to early diagnosis and treatment and may lower the need – overtime - of second-line biologic drugs, with a significant impact both on individuals and health care systems.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6481

AB0228 IMMUNOLOGICAL APPROACH TO THE DIAGNOSIS OF LESIONS OF THE NERVOUS SYSTEM IN PATIENTS WITH RHEUMATOID ARTHRITIS

I.P. Gontar[1], E.V. Baranov[1], L.A. Maslakova[1], A.S. Trofimenko[1], O.V. Paramonova[2]. *[1]Clinical Immunology Lab, FSBSU Research Institute for Clinical and Experimental Rheumatology; [2] Department of Hospital Therapy, Volgograd State Medical University, Volgograd, Russian Federation*

Background: Although S100 proteins represent 40% of the neutrophil cytoplasmic proteins, their physiological and pathological functions are still unclear. S100 protein concentrations are dramatically enhanced in synovial fluid and synovium of patients suffering from rheumatoid arthritis (RA). Their expression seems to correlate with disease activity and joint damage [1].
Objectives: Improvement of immunological detection of neurological involvement in RA by means of polyacrylamide magnetic beads with immobilized S- 100 protein.
Methods: The research was carried out in agreement with the principles of the World Medical Association Declaration of Helsinki. The informed consent had been signed by all involved persons, another obligate requirement was age 18 years or more. The patients were from the rheumatologic wards in Volgograd Municipal Hospital No. 25 and Volzhsky Municipal Hospital No. 1. Diagnosis of RA was established by ACR-EULAR criteria (2010), RA activity was evaluated using DAS28. Serum anti-S-100 protein antibodies were measured by ELISA, with S-100 protein immobilized on polyacrylamide magnetic beads as an antigen. The antibody concentrations were expressed as optical density units (ODU) and were considered positive if the cutoff value ($M+2\sigma$ of the reference group, 0.050 ODU) was exceeded. The results were expressed as mean$\pm\sigma$, differences were considered significant when $p<0.05$. Pearson correlation coefficient (r) was also used.
Results: 40 healthy persons (29 mans and 11 women), and 95 female patients with RA and the neurological signs, appeared during active phase of the disease, were recruited for this study. Mean age of the healthy controls was 36±7 years, and for the RA group it was equal to 55±11 years. Mean RA duration was 4.2±2.9 years. 13 patients had low, 52 – moderate, and 8 – high disease activity. The most common types of neurological involvement were mononeuropathy (n=29), polyneuropathy (n=65), radiculopathy (n=80); cervicocranialgias (n=51), and trigeminal neuralgias (n=14). The symptoms of central nervous system damage (TIA, seizures, cerebellar ataxia, dysarthria) were found in 21 patients. In RA group, anti-S-100 protein antibodies were detected in 11 (32.4%) cases, with mean concentration 0.078±0.028 ODU. The patients with different neurological signs had mean anti-S-100 protein antibody concentration 0.138±0.046 ODU, the subgroup without any neurological signs had 0.060±0.024 ODU (p=0.022). In all cases analyzed index correlated with the degree of activity of the pathological process. High levels of antibodies to S-100 protein in RA associated with central nervous system (CNS) and peripheral nervous system (PNS).
Conclusions: We found an association between neurological involvement in RA and elevation of anti-S-100 protein antibody concentrations. These findings give us an opportunity to improve the diagnosis of minor neurological damage in RA and thus to make more precise adjustment of the treatment.
References:
[1] Baillet A. S100A8, S100A9 and S100A12 proteins in rheumatoid arthritis. Rev Med Interne. 2010 Jun;31(6):458–61.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3123

AB0229 DOES EXPRESSION LEVEL OF VIP AND ITS RECEPTORS CORRELATED WITH DISEASE SEVERITY IN EARLY ARTHRITIS?

I.V. Seoane[1], A. Lamana[2], M. Carrión[1], Y. Juarranz[1], R. García-Vicuña[2], I. González-Álvaro[2], C. Martínez[3], R.P. Gomariz[1]. *[1]Dpto. Biología Celular, Facultad de Biología, Universidad Complutense de Madrid; [2]Rheumatology Service, Hospital Universitario de la Princesa, Instituto de Investigación Sanitaria Princesa; [3]Dpto. Biología Celular, Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain*

Background: Rheumatoid Arthritis (RA) is a heterogeneous disease, not only in the course but also in the response to treatment (1). So, a major challenge is the classification of patients according to the disease severity/mildness to apply customized therapeutic strategies. Low vasoactive intestinal peptide (VIP) serum levels are associated to a worse clinical course in Early Arthritis (EA) (2) and the expression of its receptor VPAC1 is associated with disease activity (3).
Objectives: To identify in an Early Arthritis cohort associations between clinical parameters of severity and serum VIP levels or expression of their receptors VPAC1 and VPAC2.
Methods: We studied 212 patients from the PEARL (Princesa Early Arthritis Registry Longitudinal) study. Follow-up includes five visits (0, 6, 12, 24 and 60 months) in which we collect demographic, clinical, laboratory, therapeutic and radiological data, as well as biological samples. Since there is not a global disease severity variable for RA, we stratified severity as follows: A) remission after two years of follow-up defined as SDAI <3.3 (4). B) Global Disease Assessment by Physician >75th percentile of the population (severe disease) or >25th percentile (mild disease). C) Median value in our population of the Δ erosion score (SvdH method assessed in hands) after two years of follow-up. VIP levels were determined by enzyme immunoassay and mRNA expression levels of VIP receptors in PBMCs by real-time PCR. To analyze the association between severity/mildness and the expression of VIP/VPAC we use several parametric and non-parametric hypothesis testing (t-test, ANOVA and Kruskal-Wallis) using Stata 12 for Windows (StataCorp PL, College Station, TX, USA).
Results: We observed a trend towards higher baseline VIP serum levels in patients who reached remission in terms of SDAI (p=0.1169). Patients no achieving remission showed lower VPAC1 expression (p=0.0494). Severe patients defined by GDAPh displayed a clear trend to lower VIP levels (p=0.081). Those patients also exhibited significant lower VPAC1 expression levels (p=0.0276). Concerning bone erosion score, we did not observe a significant association with VIP levels; interestingly we found that those patients classified as “severe” by erosion score displayed lower VPAC1 expression levels (p=0.0722) and higher levels of VPAC2 (p=0.0253).
Conclusions: VIP serum levels and VPAC1 and 2 receptors expression are associated with a more severe phenotype in EA patients stratified by SDAI, GDAPh and bone erosion.
References:
[1] Firestein GS. Nature. 2003;423(6937):356–61.
[2] Martínez C, Ortiz AM, Juarranz Y, et al. PloS one. 2014;9(1):e85248.
[3] Seoane IV, Ortiz AM, Piris L, et al. PloS one. 2016;11(2):e0149141.
[4] Aletaha D, Smolen J. Clin Exp Rheumatol. 2005;23(5 Suppl 39):S100–8.
Acknowledgements: This work has been supported by Instituto de Salud Carlos III, Spain, cofinanced by FEDER, European Union: RETICS program, Red de Investigación en Inflamación y Enfermedades Reumáticas (RD16/0012/0008 (RPG) and RD16/0012/0011 (IGA) and the projects PI12/00758 (RPG), PI14/00477 (CMM) and PI14/00442 (IGA).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4817

AB0230 POLYMORPHISM OF CYTOTOXIC T-LYMPHOCYTE 4 +49A/G IS ASSOCIATED WITH EARLY PRESCRIBING THE BIOLOGICAL THERAPY IN ACTIVE EARLY RHEUMATOID ARTHRITIS PATIENTS (ERA PTS) REFRACTORY TO THE PREVIOUS SUBCUTANEOUS METHOTREXATE (SC MTX) MONOTHERAPY

I. Guseva[1], A.S. Avdeeva[1], E.L. Luchikhina[1], D.D. Abramov[2], N.V. Demidova[1], E.N. Alexandrova[1], A.A. Novikov[1], M.Y. Krylov[1], E.Y. Samarkina[1], D.Y. Trofimov[2], D.E. Karateev[1], E.L. Nasonov[1]. *[1]V.A.Nasonova Research Institute of Rheumatology; [2]NRC Institute of Immunology of FMBA of Russia, Moscow, Russian Federation, Moscow, Russian Federation*

Background: Monotherapy with MTX is the first step of RA therapy as recommended by EULAR. According to “Treat to Target” (T2T) strategy principles insufficient response to MTX requires prompt switch to a combination therapy with biological agents.
Objectives: To find out whether polymorphisms of immune response genes are associated with early prescribing the biological treatment in eRA pts, refractory to the SC MTX monotherapy.
Methods: By January 2014, 210 pts with RA were included in the REMARCA study (Russian InvEstigation of MethotrexAte and biologics in eaRly aCtive inflammatory Arthritis), and 88 pts have passed the 12 months control point. All pts started SC MTX monotherapy with rapid up-titration of the dose from 10 to 25–30 mg/week. Therapy was revised every 3 months using DAS28, SDAI and CDAI indices. Combination with biologics (in most cases TNF inhibitors)

was used in 57 (65%) of pts at (median) 3 [3;6] month [1]. Retrospectively, 45 out of 88 active eRA pts (35 woman, mean age 53,5; 46–59,5 years, mean disease duration 7,0; 4,0–11,5 months, mean DAS28 5,8; 4,9–6,4, mean hs-CRP 27,0; 9,7–61,0 mg/l) were selected to evaluate the changes in cytokine profile in MTX-naive pts during SC MTX and SC MTX + adalimumab (SC MTX+ADA) therapy [2]. These 45 pts were genotyped for the following gene polymorphisms (SNPs): PTPN22 (+1858 C/T, rs2476601), CTLA4 (+49A/G, rs231775), TNFAIP3 (rs675520, rs6920220, rs10499194), IL6 (-174G/C, rs1800795), IL6R (+358A/C, rs8192284), TNFA (-308A/G, rs1800629), MCP1/ CCL2 (+2581A/G, rs1024611), IL10 (-592A/C, rs1800872, -1082 A/G, rs1800896), IL1A (-889C/T, rs1800587), IL1B (+3953C/T, rs1143634).

Results: By the end of 3 months of SC MTX therapy, 23 out of 45 eRA pts (51,1%) adequately responded to SC MTX (EULAR criteria) and continued on SC MTX monotherapy. In 22 pts (48,9%) SC MTX monotherapy failed, thus they were switched to SC MTX + ADA combination therapy. CTLA-4 gene polymorphism (+49A/G) was the only predictor for the administration of biological therapy in eRA pts, that was confirmed by a logistic regression analysis [OR=7,7 95% CI 1,4–40,9, p=0,017]. The carriers of at least one G allele (AG/GG genotypes) received the biological therapy more often than subjects with AA genotype (20/22, 90,9% and 13/23, 56,5% respectively). Moreover, the CTLA-4 (+49A/G) genotypes (AG/GG vs AA respectively) were associated with DAS28 (3,6±1,1 and 4,6±1,6, p=0,04), the number of tender joints (3,1±3,1 and 7,1±5,1, p=0,016), the number of swollen joints (2,7±2,5 and 5,3±4,9 p=0,024), SDAI (11,1±7,2 and 20,2±12,1, p=0,018), CDAI (10,6±7,1 and 18,6±10,6, p=0,025) and CRP (6,3±12,1 and 21,8±37,1 p=0,018) values after 3 months of SC MTX monotherapy.

Conclusions: Our data suggest that CTLA-4 (+49A/G) genetic polymorphism is associated with more severe rheumatoid arthritis and may predict the need for early administration of biological therapy.

References:

[1] Karateev D., E. Luchikhina E., N. Demidova N. et al. Ann Rheum Dis 2014;73(Suppl2): 235–236.

[2] Avdeeva A.S. Novikov A. A, Aleksandrova E. N. et al. Ann Rheum Dis 2014;73(Suppl2): 215–216.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3023

AB0231 PHYSICIAN VISUAL ANALOG SCALE ESTIMATES FOR DAMAGE ARE HIGHER THAN FOR INFLAMMATION IN PATIENTS WITH OSTEOARTHRITIS AND ALSO IN PATIENTS WITH RHEUMATOID ARTHRITIS AT ALL LEVELS OF CLINICAL SEVERITY ACCORDING TO RAPID3

I. Castrejon, J. Chua, J.A. Block, T. Pincus. *Rheumatology, Rush University Medical Center, Chicago, United States*

Background: A visual analog scale (VAS) to estimate the patient's global status (DOCGL) often is the most efficient of all 7 RA core data set measures to distinguish active from control treatments in clinical trials[1]. DOCGL is designed to assess inflammatory activity, but it may be influenced variably in different doctors by irreversible joint damage and/or distress. Therefore, 3 additional 0–10 VAS have been developed to estimate levels of inflammation, damage, and distress that may impact DOCGL.

Objectives: To analyze 4 estimates for overall global, inflammation, damage and distress according to 4 RAPID3 (routine assessment of patient index data) severity categories in patients with RA or OA.

Methods: Patients seen at one academic clinical setting are assigned 4 0–10 VAS estimates: overall DOCGL, inflammation (reversible), damage (irreversible), and distress (symptoms explained by neither inflammation nor damage, eg, fibromyalgia). All patients complete a self-reported MDHAQ questionnaire as part of routine care. The MDHAQ includes 0–10 scores for physical function (FN), pain (PN), patient global estimate (PATGL), compiled into a 0–30 RAPID3. Patients with a primary diagnosis of RA or OA according to their rheumatologists were included. The percentage of RA and OA patients in each RAPID3 severity category was compared according to mean DOCGL and the 3 subscale estimates using chi-square and ANOVA.

Results: The study included 232 patients with RA and 274 with OA. Patients with OA were older than RA patients (66.5 versus 57.3, $p<0.001$) and had higher scores for RAPID3 (14.4 vs 11.7, $p<0.001$). A higher percentage of patients with OA had high RAPID3 severity compared with RA patients (66% vs 48%, $p<0.001$) (Table). DOCGL and each subscale estimate were higher according to each of 4 RAPID3 categories from remission to high severity in RA and OA (Table). The level of inflammation was higher in RA than in OA, but estimates for damage higher in OA than RA. However, estimates for damage were higher than for inflammation in RA in each RAPID3 category.

Conclusions: Physician VAS for inflammation, damage, and distress may supplement the overall physician global estimate as quantitative physician estimates of reversible findings, irreversible findings, and distress to support clinical management decisions. Estimates of joint damage are higher in OA than in RA, although higher than estimates of inflammation in both RA and OA, in patients in all 4 RAPID3 severity categories.

Table 1. Mean and SD for the four physician estimates according to RAPID3 categories in RA and OA patients

	RAPID3 Severity Categories				P
	Remission (<3)	Low (3–6)	Moderate (6–12)	High (>12)	
Rheumatoid Arthritis	N=45 (19%)	N=19 (8%)	N=57 (25%)	N=111 (48%)	
Overall DOCGL (0–10 scale)	1.7 (1.4)	2.7 (1.5)	3.3 (1.4)	5.1 (1.9)	<0.001
Inflammation (0–10)	1.3 (1.9)	1.4 (1.8)	1.6 (1.3)	3.3 (2.5)	<0.001
Damage (0–10)	1.7 (1.5)	2.9 (2.0)	2.9 (2.0)	3.7 (2.2)	<0.001
Distress (0–10)	0.2 (0.7)	0.3 (0.8)	0.4 (0.9)	1.6 (2.4)	<0.001
Osteoarthritis	N=14 (5%)	N=18 (7%)	N=60 (22%)	N=182 (66%)	
Overall DOCGL (0–10 scale)	1.3 (1.2)	2.5 (0.8)	3.2 (1.4)	4.7 (1.6)	<0.001
Inflammation (0–10)	0.4 (0.6)	0.7 (1.1)	0.8 (1.4)	1.0 (1.4)	0.25
Damage (0–10)	2.5 (1.5)	3.0 (0.9)	3.5 (1.5)	4.5 (1.8)	<0.001
Distress (0–10)	0.0 (0.0)	0.3 (0.6)	1.1 (2.1)	2.0 (2.8)	<0.001

References:

[1] Pincus T, et al. Clin Exp Rheumatol 2014; 32 (Suppl. 85): S47-S54.

Disclosure of Interest: I. Castrejon: None declared, J. Chua: None declared, J. Block: None declared, T. Pincus Shareholder of: Health Report Services, Inc

DOI: 10.1136/annrheumdis-2017-eular.3556

AB0232 MINIMAL CLINICALLY IMPORTANT IMPROVEMENT (MCII) OF RAPID3 (ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3), AN INDEX OF ONLY PATIENT SELF-REPORT SCORES, PERFORMS SIMILARLY TO TRADITIONAL RHEUMATOID ARTHRITIS (RA) INDICES, DAS28 AND CDAI

I. Castrejon[1], M.M. Ward[2], M.J. Bergman[3], L.C. Guthrie[2], M.I. Alba[2], T. Pincus[1]. *[1]Rheumatology, Rush University Medical Center, Chicago; [2]Intramural Research Program, NIAMS/NIH, Bethesda; [3]Rheumatology, Taylor Hospital, Ridley Park, United States*

Background: No single "gold standard" measure is available to assess patients with rheumatoid arthritis (RA) in clinical trials and routine care, as in hypertension, diabetes, and other diseases. Therefore, an index of several measures, such as a DAS28 (Disease Activity Score-28) and CDAI (Clinical Disease Activity Index), based on 7 RA core data set measures; is needed. However, the only quantitative data in many (most) patients in routine rheumatology care are laboratory test results. RAPID3 (routine assessment of patient index data), which includes only patient self-report scores, is considerably more feasible than DAS28 or CDAI for routine care, distinguishes active from control treatments in RA clinical trials similarly and is correlated significantly with these indices. A minimal clinically important improvement (MCII) to interpret changes in clinical trials and clinical care has not been established for RAPID3

Objectives: To estimate MCII of RAPID3, and compare results to MCIIs of DAS28 and CDAI.

Methods: Post hoc analyses were performed of a reported longitudinal study of 250 patients with active RA (1). All 7 RA core data set measures were collected at baseline and after treatment escalation with prednisone 1 month later or with disease modifying medications or biologic agents 4 months later (1). Patient judgment of improvement in arthritis status was obtained as "improved", "the same" or "worsened", and analyzed in relation to changes in RAPID3, DAS28 and CDAI. RAPID3 is the sum of 3 0–10 measures: physical function on a HAQ recalculated from 0–3 to 0–10, pain and patient global estimate on 0–10 VAS (visual analog scales), total=0–30. DAS28-ESR (erythrocyte sedimentation rate) and CDAI were computed as described in the literature. Changes in all indices, standardized response means (SRM), MCIIs as changes that had a specificity of 0.80 for improvement based on receiver-operating characteristic curves, and MCII as a proportion of the maximum score were computed.

Results: Among 250 patients, 167 (66.8%) reported improvement. RA activity and SRMs improved similarly per the 3 indices (Table). ROC curve areas were ≥0.77 (Table). MCIIs with specificity for improvement of 0.80 were -3.5 for RAPID3, -1.17 for DAS28-ESR, and -12.5 for CDAI. MCIIs were in a similar range of 11.6% to 16.8% of maximum score (Table).

Conclusions: MCIIs for RAPID3, DAS28, and CDAI were in a similar range. Knowledge concerning MCII thresholds can improve interpretation of data from clinical trials and routine clinical care.

References:

[1] Ward, M et al, Ann Rheum Dis 2015, 74:1691–1696.

Disclosure of Interest: I. Castrejon: None declared, M. Ward: None declared, M.

Abstract AB0232 – Table 1. Changes in rheumatoid arthritis activity measures during the study

Measure (range)	Baseline	Follow-up	Mean (%) change	SRM (95% CI)	ROC Curve Area (95% CI)	MCII (95% CI)	% of Total
RAPID3 (0 – 30)	16.3±6.3	11.1±6.7	-5.2±6.5 (32%)	-0.79 (-0.71, -0.88)	0.80 (0.74, 0.86)	-3.5 (-2.9, -4.3)	11.6%
DAS28-ESR (0–9.4)	6.16±1.2	4.8±1.38	-1.31±1.34 (21%)	-0.98 (-0.90, -1.07)	0.77 (0.71, 0.82)	-1.17 (-1.36, -0.87)	12.4%
CDAI (0–76)	36.8±13.5	23.0±13.6	-13.7±14.1 (37%)	0.98 (-0.90, -1.08)	0.78 (0.73, 0.84)	-12.5 (-14.7, -10.5)	16.4%

*SRM = standardized response mean; CI = confidence interval.

Bergman: None declared, L. Guthrie: None declared, M. Alba: None declared, T. Pincus Shareholder of: Health Report Services, Inc
DOI: 10.1136/annrheumdis-2017-eular.3500

AB0233 REMISSION ACCORDING TO RAPID3 (ROUTINE ASSESSMENT OF PATIENT INDEX DATA 3) IN PATIENTS WITH RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY FROM ROUTINE CARE AT 3 USA SITES

I. Castrejon[1], M.J. Bergman[2], K.A. Gibson[3,4,5], Y. Yazici[6], J.A. Block[1], T. Pincus[1]. *[1]Rheumatology, Rush University Medical Center, Chicago; [2]Rheumatology, Taylor Hospital, Ridley Park, United States; [3]Rheumatology, Liverpool Hospital; [4]Ingham Research Institute, Liverpool; [5]University of NSW, Sydney, Australia; [6]Rheumatology, NYU Hospital for Joint Diseases, New York, United States*

Background: RAPID3 remission criteria provide similar results to DAS28 criteria, although less stringent compared to ACR/EULAR Boolean criteria. RAPID3 remission criteria are more feasible in routine care[1] and have been reported at 25% in patients from France[1] and 21% from Norway[2].
Objectives: We examined the proportion of patients in remission and 3 other severity categories according to RAPID3 at 3 sites at which MDHAQ is completed by all patients in routine care.
Methods: All patients seen at each rheumatology site complete an MDHAQ/RAPID3 at all visits in the waiting area as part of their routine care. The MDHAQ includes 0–10 scores for physical function, pain and patient global estimate, compiled into a 0–30 RAPID3, as well as scores for fatigue, RADAI self-report of painful joints, and demographic data. Physicians complete a global assessment (DOCGL) on a 0–10 visual analog scale (VAS). A random visit with complete questionnaire data for each RA patient from each site was included in the analyses. The proportion of patients in 4 RAPID3 categories, high severity (>12/30), moderate severity (6.1–12), low severity (3.1–6), and remission (≤3), was computed. MDHAQ demographic and clinical measures and DOCGL were compared in the 4 RAPID3 severity groups using chi-square and ANOVA tests.
Results: 420 RA patients from the 3 sites were analyzed. Remission rates according to RAPID3 severity ranged from 23% to 26%, similar to reported rates from France and Norway. Low severity ranged from 7–24%, moderate severity from 23–29% and high severity from 21–46%. Age and sex were similar in the disease severity categories at the 3 sites (Table). Patients in the moderate and high severity groups at each site had higher scores for fatigue, RADAI self-reported joint pain, and DOCGL.

Table 1. Mean (SD) for demographic and clinical characteristic of patients in remission versus other disease severity categories according to RAPID3 in each site. *p<0.001

	Remission (≤3)	Low (3.1–6)	Moderate (6.1–12)	High (>12)
Site 1 (N=137)	32 (23.4%)	11 (8%)	31 (22.6%)	63 (46%)
Female, n (%)	27 (84.4%)	9 (81.8%)	26 (83.9%)	59 (93.6%)
Age, yrs	58.5 (16.9)	57.9 (18.8)	56.8 (17.5)	55.6 (14.5)
Fatigue (0–10)	1.1 (1.5)	2.3 (2.0)	3.1 (2.1)	6.6 (2.3)*
Self-report RADAI (0–48)	1.9 (2.9)	5.0 (3.9)	7.5 (5.60	17.0 (9.2)*
DOCGL (0–10)	1.6 (1.2)	3.7 (1.7)	3.2 (1.4)	5.3 (1.9)*
Site 2 (N=144)	37 (25.7%)	35 (24.3%)	42 (29.2%)	30 (20.8%)
Female, n (%)	28 (75.7%)	22 (62.9%)	34 (80.9%)	24 (80%)
Age, yrs	56.6 (16.9)	62.0 (14.6)	62.3 (14.7)	62.5 (15.9)
Fatigue (0–10)	0.9 (1.0)	2.7 (1.9)	4.1 (2.4)	5.6 (3.0)*
Self-report RADAI (0–48)	NA	NA	NA	NA
DOCGL (0–10)	0.9 (1.3)	1.0 (1.0)	1.7 (1.5)	3.4 (2.7)*
Site 3 (N=139)	32 (23%)	10 (7%)	33 (23.7%)	64 (46%)
Female, n (%)	23 (72%)	9 (90%)	20 (62%)	50 (79%)
Age, yrs	44.4 (13.8)	43.8 (17.0)	50.3 (17.8)	50.9 (15.0)
Fatigue (0–10)	0.4 (0.8)	2.6 (2.7)	4.1 (2.7)	6.9 (2.9)*
Self-report RADAI (0–48)	1.3 (1.9)	4.7 (4.2)	5.7 (5.1)	18.3 (12.2)*
DOCGL (0–10)	1.1 (1.1)	3.2 (1.9)	2.5 (1.2)	3.2 (1.5)*

Conclusions: Similar RAPID3 remission rates were seen at 3 USA sites (about 24%), comparable to results from France and Norway.
References:
[1] Castrejon I, Dougados M, et al. J Rheumatol 2013, 40(4):386–393.
[2] Uhlig T, Lie E, et al. J Rheumatol 2016, 43(4):716–723.
Disclosure of Interest: I. Castrejon: None declared, M. Bergman: None declared, K. Gibson: None declared, Y. Yazici: None declared, J. Block: None declared, T. Pincus Shareholder of: Health Report Services, Inc
DOI: 10.1136/annrheumdis-2017-eular.2749

AB0234 ORAL CONTRACEPTIVES, MENOPAUSE AND RHEUMATOID ARTHRITIS IN KOREAN WOMEN: A NATIONWIDE STUDY

J.H. Jung, H.S. Jeong, J.-H. Kim, G.G. Song, S.J. Choi, Y.H. Seo. *Internal Medicine, Korea University Medical Center, Seoul, Korea, Republic Of*

Background: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease with a multifactorial etiology. Hormonal factors, ethnicity and their interaction may result in the development of RA.
Objectives: We investigated the effects of oral contraceptives (OCs) and menopause on RA in South Korea women using nationwide data.
Methods: Data were collected from the 2008–2012 Korea National Health and Nutrition Examination Surveys. A total of 17,890 eligible participants were included. As there were significant differences in baseline characteristics between the patients on OCs and those not taking OCs, we used propensity score-matching to adjust for such differences. We calculated the odds ratios (ORs) and 95% confidence intervals (95% CIs) of OCs leading to RA development.
Results: The peak incidence of RA was between 50–59 years old. The overall rate of OC usage was 16.5% and mean duration of OC using was 18.41±28.78 (ranged from 0 to 360) months. Before propensity score-matching, using multivariable logistic regression adjusted for traditional risk factors, taking OC was a significantly associated with RA development (OR 1.18, 95% CI 1.18–1.19, p <0.001). After propensity score-matching, taking OCs was not associated with RA (OR 1.05, 95% CI 0.83–1.34, p <0.001). Menopausal status showed strongly significant increase in the risk of RA.
Conclusions: There was an association between menopausal status and RA development in South Korean women. However, usage of OCs did not show significant effects on the development of RA.
References:
[1] Pikwer M, Bergstrom U, Nilsson JA, Jacobsson L, Berglund G, Turesson C. Breast feeding, but not use of oral contraceptives, is associated with a reduced risk of rheumatoid arthritis. Ann Rheum Dis 2009;68:526–30.
[2] Hazes JM, van Zeben D. Oral contraception and its possible protection against rheumatoid arthritis. Ann Rheum Dis 1991;50:72–4.
[3] Pullerits R, d'Elia HF, Tarkowski A, Carlsten H. The decrease of soluble RAGE levels in rheumatoid arthritis patients following hormone replacement therapy is associated with increased bone mineral density and diminished bone/cartilage turnover: a randomized controlled trial. Rheumatology (Oxford) 2009;48:785–90.
[4] Doran MF, Crowson CS, O'Fallon WM, Gabriel SE. The effect of oral contraceptives and estrogen replacement therapy on the risk of rheumatoid arthritis: a population based study. J Rheumatol 2004;31:207–13.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4769

AB0235 EFFECT OF BASELINE DISEASE ACTIVITY ON ACHIEVING SUSTAINED LOW DISEASE ACTIVITY IN BARICITINIB PHASE 3 STUDIES

J.R. Curtis[1], A. Kavanaugh[2], D. van der Heijde[3], D. Muram[4], J. Alam[4], J.S. Smolen[5]. *[1]Univ of Alabama at Birmingham, Birmingham; [2]UC San Diego School of Medicine, la Jolla, United States; [3]Leiden University Medical Centre, Leiden, Netherlands; [4]Eli Lilly and Company, Indianapolis, United States; [5]Medical University of Vienna, Vienna, Austria*

Background: In the Phase 3 studies RA-BUILD[1] and RA-BEAM[2], baricitinib (bari) has demonstrated clinical efficacy including reduced disease activity in RA patients (pts) with an inadequate response (IR) to conventional synthetic DMARDs (csDMARDs).
Objectives: To determine whether disease activity at baseline (BL) affects the achievement of sustained low disease activity (LDA) with bari treatment.
Methods: In this post hoc analysis, pts from the placebo (PBO) and bari 4 mg treatment arms of the RA-BUILD and RA-BEAM studies were categorised based on their level of disease activity at BL; either CDAI ≤median or CDAI >median, where median was 34.8 for RA-BUILD and 36.2 for RA-BEAM. Pts who achieved CDAI ≤10 at ≥2 consecutive visits (sustained LDA) within 12 and 24 weeks (wks) were considered as responders. The length of time required by pts to achieve sustained LDA was determined for each group using the incidence rate (percent pts responding per month). In addition, the association between response and dose of bari was explored in csDMARD-IR pts randomised to bari (2 mg or 4 mg) once daily from the RA-BUILD study.
Results: Within the bari 4 mg arm, a greater proportion of pts with CDAI ≤median at BL achieved sustained LDA and within a shorter treatment duration as indicated by higher incidence rates, compared to pts with CDAI >median at BL. In pts with CDAI ≤34.8 at BL, the 2 mg and 4 mg doses showed similar efficacy, but a larger proportion of pts with CDAI >34.8 reached sustained LDA at 24 wks with bari 4 mg than 2 mg (41.4% and 32.4%, respectively).

Table 1. Proportions and Rates of Sustained LDA Achievement with Baricitinib Treatment

Pts achieving CDAI ≤10		BL CDAI ≤ median			BL CDAI > median		
		PBO	Bari 4 mg	Bari 2 mg	PBO	Bari 4 mg	Bari 2 mg
RA-BUILD	N	116	108	114	108	116	111
Wk12	%	19.8	42.6	40.4	7.4	21.6	18.0
	i-rate	4.36	11.78	10.50	1.55	4.69	3.90
Wk24	%	44.8	63.9	63.2	17.6	41.4	32.4
	i-rate	10.63	19.20	17.59	3.80	9.59	7.27
RA-BEAM	N	249	236		235	246	
Wk12	%	23.7	39.8		4.3	18.7	
	i-rate	2.71	5.40		0.42	1.98	
Wk24	%	34.5	69.1		14.0	41.9	
	i-rate	4.35	12.97		1.49	5.47	

Pts were defined as responders if they met the response criterion within the stated time frame, prior to any rescue or discontinuation. % = percent of pts meeting response criteria; CDAI median = 34.8 (RA-BUILD) or 36.2 (RA-BEAM); i-rate = exposure-adjusted incidence rate (% pts/month); N = number of randomised and treated pts.

Conclusions: Pts with CDAI ≤35–36 at BL achieved sustained LDA more frequently and more rapidly than pts in the higher disease category at BL. In pts with higher disease activity at BL a more robust response was observed with bari 4 mg treatment.

References:
[1] Dougados M et al. Ann Rheum Dis 2017; 76(1):88–95.
[2] Taylor P et al. Arthritis Rheumatol 2015; 67(Suppl 10):1–4046.

Disclosure of Interest: J. Curtis Grant/research support from: AbbVie, Amgen, BMS, Corrona, Eli Lilly and Company, Janssen, Myriad, Pfizer, Roche/Genentech, UCB, Consultant for: AbbVie, Amgen, BMS, Corrona, Eli Lilly and Company, Janssen, Myriad, Pfizer, Roche/Genentech, UCB, A. Kavanaugh Consultant for: Eli Lilly and Company, D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, Astra-Zeneca, BMS, Boeringer Ingelheim, Celgene, Daiichi Sankyo, Eli Lilly and Company, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, UCB, Employee of: Director of Imaging Rheumatology bv, D. Muram Employee of: Eli Lilly and Company, J. Alam Employee of: Eli Lilly and Company, J. Smolen Grant/research support from: Abbvie, Janssen, Eli Lilly and Company, MSD, Pfizer, Roche, Consultant for: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB, Speakers bureau: Abbvie, Amgen, Astra-Zeneca, Astro, BMS, Celgene, Celltrion, Chugai, Gilead, Glaxo, ILTOO, Janssen, Eli Lilly and Company, Medimmune, MSD, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi-Aventis, UCB

DOI: 10.1136/annrheumdis-2017-eular.1340

AB0236 ASSOCIATION OF LYVE-1 PROTEIN IN EXOSOME WITH DISEASE ACTIVITY AS A NEW CANDIDATE BIOMARKER FOR RHEUMATOID ARTHRITIS

J. Yoo[1], S.K. Lee[2], M. Lim[1], D. Sheen[1], E.-H. Choi[2], S.A. Kim[1]. *[1]School of Medicine; [2]Eulji Medi-Bio Research Institute, Eulji University, Daejeon, Korea, Republic Of*

Background: Exosomes, membrane-bound vesicles of 40–100 nm in diameter, have protein and lipid composition that depends on the cell origin, the state of activation, infection and/or transformation of the parent cells. Those proteins and lipid have a role in mediating inflammatory and autoimmune disease as well. Discovery of inflammatory marker to evaluate appropriate response of treatment could give effective timing to adjust treatment for rheumatoid arthritis patients.

Objectives: The aim of the study was to identify protein candidates in exosome being related with other inflammatory parameters.

Methods: The study population consisted of 60 RA patients, in which there were 30 patients of clinical remission (CR) group with DAS28-ESR≦2.6 and 30 patients of non-clinical remission (non-CR) group with DAS28-ESR>2.6. By exosome preparation with ExoQuick™ kit and protein identification with tandem mass tags labeling/mass spectrometry between the groups, potent protein markers were selected. Level of the proteins was measured by ELISA.

Results: We identified 6 proteins by proteomics approach. Amyloid A (AA) and lymphatic vessel endothelial hyaluronic acid receptor-1 (LYVE-1) was identified with different levels in exosome between CR group and non-CR group. AA levels of both serum and exosome were higher in non-CR group than CR group (p value=0.001). Significant positive correlations were found between exosome AA level and CRP as well as between serum AA level and CRP (ρ=0.614, p value=0.001 and ρ=0.624, p value=0.001). Though LYVE-1 level of serum was not different between non-CR group and CR group, LYVE-1 level of exosome was lower in non-CR group than CR group (p value=0.01). We found positive correlations between serum/exosome of LYVE-1 and CRP in only non-CR group (serum ρ=0.376, p value=0.04; exosome ρ=0.545, p value=0.002).

Conclusions: We suggest that LYVE-1 in exosome can be used as an additional marker of disease activity in RA patients and this study provides the evidence about the role of exosome for RA as the carrier of useful marker.

References:
[1] Mathivanan S, Ji H, Simpson RJ. Exosomes: extracellular organelles important in intercellular communication. J Proteomics. 2010 Sep;73(10):1907–20.
[2] Shen C, Sun X-G, Liu N, et al. Increased serum amyloid A and its association with autoantibodies, acute phase reactants and disease activity in patients with rheumatoid arthritis. Mol Med Rep. 2015;11(2):1528–34.
[3] Nunomiya K, Shibata Y, Abe S, et al. Relationship between serum level of lymphatic vessel endothelial hyaluronan receptor-1 and prognosis in patients with lung cancer. J Cancer. 2014;5(3):242–7.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1194

AB0237 PREVALENCE AND CLINICAL CHARACTERISTICS OF MALIGNANCY IN SEROPOSITIVE RHEUMATOID ARTHRITIS PATIENTS

J. Park, C. Lee. *Nhis Ilsan Hospital, Goyang, Korea, Republic Of*

Background: Patients with rheumatoid arthritis (RA) are at an increased risk of malignancies compared with the general population.

Objectives: The aim of this study was to evaluate the prevalence and risk factors of malignancy in National Health Insurance Service Ilsan hospital patients with seropositive RA.

Methods: We found patients with seropositive RA who fulfilled the American College of Rheumatology criteria and American College of Rheumatology criteria/European League Against Rheumatism criteria, from May 2008 to September 2015. Occurrence of malignancy was originally collected by electronic medical record reports and diagnostic code. We consecutively enrolled patients with newly diagnosed malignancy. Control group was selected as five times the number of patients randomized.

Results: Total 12 malignancies in 647 patients were newly identified during the retrospective observation period of 2051 person-years. Malignancy types were 3 lung cancers, 2 colon cancers, gastric cancer, breast cancer, thyroid cancer, cervix cancer, cholangiocarcinoma, lymphoma and parotid gland cancer. In multivariate logistic regression, the variables with independent predictive value were older age (age: odds ratio =1.11, 95% CI =1.01–1.22, p-value =0.02), rheumatoid factor (RF) negativity (RF positivity: odds ratio =0.06. 95% CI =0.01–1.27, p-value 0.07) In cox regression, the variables with independent predictive value were older age (age: hazard ratio =1.12, 95% CI =1.01–1.24, p-value =0.02), negative RF (RF positivity: hazard ratio =0.12. 95% CI =0.02–0.78, p-value 0.02), lower anti-cyclic citrullinated peptide (CCP) antibody titer (anti-CCP antibody titer: hazard ratio =0.98. 95% CI =0.96–0.99, p-value 0.03) and positive antinuclear-antibody (ANA) (ANA positivity: hazard ratio =14.97, 95% CI =0.87–255.05, p-value 0.06).

Table 1. Associations between variables and malignancy event in subjects: longitudinal data

Variables	Univariable			Multivariable		
	Hazard ratio	95% CI	p-value	Hazard ratio	95% CI	p-value
Etiology						
Age	1.14	1.05–1.24	<0.01	1.12	1.01–1.24	0.02
Gender	3.71	0.47–29.08	0.21			
Laboratory results						
RF positivity	0.33	0.09–1.13	0.07	0.12	0.02–0.78	0.02
Anti-CCP Ab titer	0.99	0.98–1.00	0.10	0.98	0.96–0.99	0.03
ANA positivity	5.56	0.69–44.64	0.10	14.97	0.87–255.05	0.06

Conclusions: Age, RF positivity, anti-CCP antibody titer, ANA positivity may be associated with malignancy risk in seropositive rheumatoid arthritis. So, continued vigilance and regular cancer screening are recommended for case of older age, RF negativity, lower anti-CCP antibody titer and ANA positivity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1587

AB0238 THE INFLUENCE OF FATIGUE IN THE DEFINITION OF REMISSION IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB

J. Caetano[1], S. Oliveira[1], J. Delgado Alves[1,2]. *[1]Systemic Autoimmune Diseases Unit, Department of Medicine IV, Fernando Fonseca Hospital, Amadora; [2]CEDOC, NOVA Medical School, Lisbon, Portugal*

Background: Achieving disease remission or low disease activity is the therapeutic goal in rheumatoid arthritis' (RA) treatment. Disease activity is defined through established criteria most of them requiring the evaluation of patient global assessment (PGA). PGA is considered a limiting factor for achieving remission definition, as it can be influenced by many factors not RA-related, namely fatigue which is commonly reported in RA and has been correlated with increased levels of interleukin-6 (IL-6).

Objectives: To evaluate the relation between PGA and fatigue, and whether fatigue influences disease remission definition in RA patients treated with tocilizumab (TCZ), an anti-IL-6 receptor monoclonal antibody.

Methods: We prospectively recruited 18 consecutive patients with RA (ACR/EULAR 2010 criteria), on TCZ treatment (≥3 months), from a single referral centre. Disease activity was evaluated by disease activity score for 28-joints (DAS28), and the ACR/EULAR Boolean-based criteria for remission were calculated. Visual Analog Scale for Fatigue (VASF) and Multidimensional Assessment of Fatigue scale (MAF) were used to measure fatigue.

Results: 89% of the patients were female and mean age was 55.5±13.8 years (yrs). Mean disease duration was 8.8±6.8yrs and mean duration of TCZ treatment was 2.3±1.3yrs (50% 1st line). Mean PGA score was 3.3±2.0 (0-best health) and mean DAS28 C-reactive protein (CRP) was 2.27. According to DAS28-CRP 44% of the patients were in remission, 22% had low disease activity and 33% had moderate activity. 3 patients (17%) fullfield the ACR/EULAR Boolean criteria for remission. Considering all the composits of the Boolean criteria, PGA was the only reason for not achieving remission in 10 patients (56%). The mean fatigue scores were: VASF 6.6±2.3 (0-best health), Global Fatigue Index (GFI), calculated through MAF scale, 24.3±14.9 (1-best health). Amongst the 18 patients, PGA correlated with higher fatigue scores on VASF (r=0.50, p=0.00951) and on GFI (r=0.49, p=0.037). In the group of patients not fulfilling Boolean remission, a similar correlation between PGA and higher fatigues scores was found (VASF: r=0.54, p=0.036; GFI: r=0.79, p=0.00041). In the sub-group of patients in which PGA was the only factor for not achieving Boolean remission, there was a significant correlation between PGA and fatigue scores (GFI: r=0.79, p=0.009), that was not present in the other patients (GFI: r=0.24; p=0.49).

Conclusions: We found a positive correlation between higher PGA and fatigue

scores in RA patients treated with TCZ. PGA was the major limiting factor for not achieving ACR/EULAR Boolean remission criteria, and in this sub-group of patients the same positive correlation between higher PGA and fatigue scores was found, not present in the rest of the cohort. These results enhance the influence of fatigue in patients' perspectives of disease and reinforce the limitations of using PGA to define RA activity and remission. Furthermore, considering the influence of TCZ in fatigue mechanisms, by blocking IL-6 receptor, we still found high fatigue scores in this cohort, which can enhance the complex physiopathology of fatigue in chronic inflammatory diseases, and the role of several other cytokines (IL-1, TNF-α). This effect and comparison with RA patients treated with anti-TNF-α can be explored further in larger prospective studies.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2502

AB0239 DKK1 IS NOT ASSOCIATED WITH INFLAMMATORY ACTIVITY INDEXES IN RHEUMATOID ARTHRITIS, BUT WITH FUNCTIONAL DISABILITY RELATED TO THE LONG EVOLUTION OF THE DISEASE

R. Giraldo-Bustos[1], E.L. Saldarriaga[1], A.M. Santos[1], J.I. Angarita[1], J.G. Ballesteros[1], J.C. Rueda-Sanchez[1], A. Vasquez[1], L. Valero[1], S. Arias[2], J. Londono[1] on behalf of Grupo de Espondiloartropatías Universidad de La Sabana – Hospital Militar Central. *[1]Department of Rheumatology; [2]Universidad de la Sabana – Hospital Militar Central., Bogotá, Colombia*

Background: Rheumatoid arthritis (RA) is a systemic chronic inflammatory disease characterized by joint destruction, deformity, lower functional status and decrease in life expectancy. Wnt signaling pathway recently it has been implicated in bone homeostasis. Studies suggest that overexpression of inhibitors of the way, like the Dickkopf 1 protein (DKK1) has been implicated in bone destruction

Objectives: To compare circulating levels of DKK1 in patients with RA to their disease activity and functional status

Methods: 379 consecutive patients with early and established RA were evaluated at the Hospital Militar Central in Bogota-Colombia, between March 2015 and November 2016. A complete medical history related to RA was obtained. Disease activity was evaluated by DAS28-CRP, CDAI, SDAI and RAPID3. functional status was measurement using MDHAQ and the Steinbrocker functional classification. DKK1 levels measured by ELISA using an Abcam® kit

Results: The mean age was 60,7±13,1 years, disease duration 13,1±10,9 years, 80,4% were female. Higher levels of DKK1 were not associated with higher disease activity by CDAI (p=0,70), SDAI (p=0,84), DAS28 with CRP (p=0,80) or RAPID3 (p=0,70). Interestingly Higher levels of DKK1 were significantly associated to greater disability and lower functional status according to the Steinbrocker functional grading (p=0.013) and with severe disability by MDHAQ (p=0.004), Table 1.

Other variables associated with joint destruction were osteoporosis, elevated rheumatoid factor, smoking, and hospitalization

Steinbrocker functional grading	n (%)	DKK1 (pg/mL) M±ds	P
Class I-II	286 (75,2)	4930,9±8061,5	0,013
Class III-IV	93 (24,5)	7930,6±10811,3	
MDHAQ			
Without or low disability	334 (88,0)	3192,0±2729,4	0,004
Moderate or severe disability	45 (12,0)	4445,67±2821,0	

Conclusions: Higher levels of DKK1 were found in patients with lower functional status. This association was not found in patients with greater disease activity according to CDAI, SDAI, DAS28 and RAPID3. This could be explaining by greater structural damage though more studies would be needed to explore this possibility

References:

[1] Huizinga TW, Pincus T. In the Clinic. Rheumatoid arthritis. Ann Intern Med. 2010 Jul 6;153(1):ITC1–1-ITC-15.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1518

AB0240 ASSOCIATION BETWEEN LEPTIN CONCENTRATIONS AND CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS

J.A.D.J. Batún Garrido[1], I.E. Juárez Rojop[2], M. Salas Magaña[2], É. Hernández Núñez[1], F. Olán[1]. *[1]Hospital Regional de Alta Especialidad Dr. Gustavo A. Rovirosa Pérez; [2]Universidad Juárez Autónoma de Tabasco, Villahermosa, Mexico*

Background: It has been observed that leptin plays a role in the development of cardiovascular risk, independently associated with the development of atherosclerosis, as well as with traditional risk factors such as obesity and arterial hypertension, on the other hand, its participation in carbohydrate and lipid metabolism and in coagulation, makes leptin a promoter of the complications of obesity and therefore increase cardiovascular risk.

Objectives: Identify whether there is a relationship between serum leptin concentrations and cardiovascular risk assessed using the Framingham scale.

Methods: We studied patients with the diagnosis of rheumatoid arthritis (RA) according to the ACR/EULAR 2010 criteria; the leptin determination was through an enzyme immunoassay (ELISA) with the TECO® Test Kit. Cardiovascular risk was calculated using the modified Framingham score, as reported by EULAR, the result obtained was multiplied by 1.5. Were considered as risk values of <1% as low; 1–5% moderate and >5% high. Statistical analysis was performed using the SPSS 22.0 package. A p≤0.05 was considered a significant result. Categorical variables were compared with Chi square test. Continuous variables were compared with either the Student's T test or the Mann-Whitney non-parametric test, according the case.

Results: We studied 77 patients. The traditional CVR factors that presented the highest prevalence were age, hypoalphalipoproteinemia and obesity; With regard to the prevalence of non-traditional factors, hyperleptinemia, glucocorticoid use and positive RF were predominant. More than ¾ parts of the study population consumed methotrexate and hydroxychloroquine, which have been considered as CVR protective factors. Serum leptin concentrations and CVR factors were compared and found that there was a significant difference between higher leptin values and disease activity (p=0.047), obesity (p=0.038), positive rheumatoid factor (p=0.009), Tobacco (0.009) and metabolic syndrome (p=0.001). Likewise, a significant relationship was found between lower leptin concentrations and hydroxychloroquine consumption (p=0.023). Framingahm CVR was calculated and the result obtained was multiplied by 1.5. The 35.2% of the population studied had a low Framingahm RCV, 38.9% moderate and 25.9% presented a high risk. We compared the level of CVR and serum leptin concentrations, finding that the highest CVR were the leptin values.

Conclusions: There is a positive association between CVR and serum leptin concentrations. It is also significantly associated with traditional and non-traditional risk factors

References:

[1] Raggi P. Epicardial Adipose Tissue as a Marker of Coronary Artery Disease Risk. J Am Coll Cardiol. 2013; 61(13): 1396–139.
[2] Correia M, Haynes W. Leptin, obesity and cardiovascular disease. Curr Opin Nephrol Hypertens. 2004; 13 (2): 215–23.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6968

AB0241 RELATIONSHIP BETWEEN LEPTIN AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

J.A.D.J. Batún Garrido[1], I.E. Juárez Rojop[2], M. Salas Magaña[2], É. Hernández Núñez[3], F. Olán[3]. *[1]Medicina Interna, Hospital Regional de Alta Especialidad Dr. Gustavo A. Rovirosa Pérez; [2]Universidad Juárez Autónoma de Tabasco; [3]Hospital Regional de Alta Especialidad Dr. Gustavo A. Rovirosa Pérez, Villahermosa, Mexico*

Background: Increased concentrations of leptin have been observed during infectious processes and inflammation, in such a way that it plays a role in the inflammatory and the immune response

Objectives: Determine the association between serum leptin and disease activity measured through DAS-28 PCR.

Methods: Patients with the diagnosis of rheumatoid arthritis (RA) according to the ACR/EULAR 2010 criteria were studied. Leptin was determined by enzyme immunoassay (ELISA) with the TECO® Test Kit, the values higher than 17ng/mL were considered as hyperleptinemia. Disease activity was assessed by the DAS-28 PCR, classifying as remission <2.3, low activity ≥2.3 to <3.8, moderate activity as ≥3.8 to <4.9 and high activity ≥4.9. Statistical analysis was performed using the SPSS 22.0 package. A p≤0.05 was considered a significant result. A multivariate logistic regression model was used to determine the association between significant variables and leptin concentrations.

Results: 77 patients were studied, 93,5% were female. The activity of the disease was determined, finding that 40,3% of patients were in remission, 41,6% had low activity, 11,7% had moderate activity and 6,5% had high activity. The 46,8% had obesity, 32,5% were overweight, 18,2% had normal weight and 2,5% were underweight. The 37,7% of the patients studied had metabolic syndrome, being the main factor the presence of an altered abdominal perimeter. The 63,6% had positive rheumatoid factor. The 71,4% had leptin levels ≥17 ng/ml. A multivariate logistic regression was performed with leptin as dependent variable. The results show an independent association between higher concentrations of leptin and disease activity (OR 1,9; 95% CI 1,3–3,8; p=0,045), obesity (OR 3,63; 95% CI 1,1–11,9; p=0,033), the presence of metabolic syndrome (OR 2,74; 95% CI 1,7–10,4; p=0,038), and positive rheumatoid factor (OR 3,5; 95% IC 1,2–11,3; p=0,033). It was also found that at higher disease activity, there were higher concentrations of serum leptin. Patients with severe activity had higher leptin media than patients in remission

Conclusions: There is a positive relationship between the activity of the disease and the serum leptin concentration, likewise this hormone is related to other inflammatory processes such as metabolic syndrome and rheumatoid factor.

References:

[1] Tilg H, Moschen A. Adipocytokines: Mediators linking adipose tissue, inflammation and immunity. Nat Rev Immunol. 2006; 6: 772–83.
[2] Otero M, Lago R, Lago F, Casanueva F, Dieguez C, Gómez J. Leptin, from

fat to inflammation: Old questions and new insights. Febs Lett. 2005; 579: 295–301.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6722

AB0242 EVALUATION OF VARIANTS IN MIR-146A, MIR-196A-2 AND MIR-499 AND THEIR ASSOCIATION WITH SUSCEPTIBILITY FOR RHEUMATOID ARTHRITIS AND ITS EXTRA-ARTICULAR MANIFESTATIONS

J.C. De La Cruz-Castillejos, R.E. Barbosa-Cobos, L.T. Becerril-Mendoza, G.E. Lugo-Zamudio, J. Ramírez-Bello, M. Matias-Carmona, I. Alemán-Ávila. *Hospital Juárez de México, Ciudad de México, Mexico*

Background: The miRNAs, small non-coding RNA, regulate the genetic expression to posttranscriptional level, inhibiting the translation. The role of miRNAs in the evolution of RA is not clear.
Objectives: To evaluate the variants rs 2910164G/C in *miR-146a*, rs11614913C/T in *miR-196a-2* and rs3746444A/G in *miR-499* and their association with susceptibility and severiry to Rheumatoid arthritis (RA) and its extra-articular manifestations (EAM)
Methods: 133 cases with RA were included (ACR/EULAR criteria 2010) and 430 healthy controls. There were evaluated EAM (rheumatoid nodules [RN], Raynaud phenomenon [RP], cutaneous vasculitis (CV), episcleritis, scleritis, peripheral ulcerative keratitis [PUK], multiple mononeuritis [MM] and multiple polyneuritis [MP]) and levels of ESR, CRP, RF and CCP. It was performed genotyping of singe nucleotide polymorphisms (SNPs) rs2910164G/C in *miR-146a*, rs11614913C/T of *miR-196a-2* and rs3746444A/G of *miR-499*. The descriptive and inferential statistical analysis was performed with the software SPSS and Finetti.
Results: Patients with RA, women 126 (94.7%); age Me 48.9 (IQR 40–58); patients with EAM 23 (17.2%; women 22 [95.6%]; RN 14 [60.8%], RP 4 [17.3%], CV 1 [4.3%], episcleritis 1 [4.3%], PUK 1 [4.3%], MM 1 [4.3%], MP 1 [4.3%]); ESR Me 37 (IQR 22–45), CRP Me 0.11 (IQR 0.03–0.27); positive RF 125 patients (93.9%, high positive 106 [79.7%], low positive 19 [14.3%]; EAM with high positive RF, 100%), positive CCP 70 (52.6%, high positive 48.9%, low positive 3.8%; EAM high positive 94.1%, negative 5.9%). The alleles and genotypic frequencies did not show statistically significant difference between cases and the healthy controls ($p>0.05$). It was identified statistical difference between the patients with and without EAM in CPR (p=0.032). The genotypic and allelic frequencies and association analysis of *miRNAs* in patients with and without EAM are shown in table 1

Table 1. Analysis of the genotypic and alleles frequencies of the SNPs rs2010164G-C from *miR-146a*, rs11614913C/T from *miR-196a-2* and rs3746444A/G from *miR-499* in patients with RA with and without EAM

Genotype	Patients without EAM		Patients with EAM		OR	CI 95%	p
rs2010164G/C Genotype	n	%	n	%			
GG	54	(49.1)	9	(39.1)	–	–	–
GC	47	(42.7)	11	(47.8)	1.40	0.54-3.68	0.49
CC	9	(8.2)	3	(13.0)	2.00	0.45-8.83	0.35
Allele							
G	155	(70.4)	29	(63.0)	–	–	–
C	65	(29.6)	17	(37.0)	1.34	0.72-2.71	0.32
rs11614913C/T Genotype							
CC	42	(38.2)	2	(8.7)	–	–	–
CT	55	(50.0)	14	(60.9)	5.34	1.15-24.81	0.02
TT	13	(11.8)	7	(30.4)	11.31	2.09-61.29	0.001
Allele							
C	139	(63.2)	18	(39.1)	–	–	–
T	81	(36.8)	28	(60.9)	2.67	1.39-5.12	0.002
rs3746444A/G Genotype							
AA	100	(90.9)	21	(91.3)	–	–	–
AG	9	(8.2)	2	(8.7)	1.06	0.21-5.26	0.94
GG	1	(0.9)	0	(0.0)	1.56	0.06-39.6	0.65
Allele							
A	209	(95.0)	44	(95.6)	–	–	–
G	11	(5.0)	2	(4.4)	0.86	0.18-4.03	1.03

O: Odds Ratio, CI: confidence interval, EAM: extra articular manifestations

Conclusions: None of the evaluated variants in *miRNAs* are associated with susceptibility for RA, however, the SNP re11614913C/T licated in *miR-196a-2* is associated with EAM.
References:
[1] Churov AV, Oleinik EK, Knip M. MicroRNAs in rheumatoid arthritis: altered expression and diagnostic potential. Autoimmun Rev 2015;14:1029–37.
[2] Singh RP, Massachi I, Manickavel S, Singh S, Rao NP, Hasan S et al. The role of miRNA in inflammation and autoimmunity. Autoimmun Rev 2013;12:1160–5.
[3] Nakasa T, Nagata Y, Yamasaki K, Ochi M. A mini-review: microRNA in arthritis. Physiol Genomics 2011;1:566–70.
[4] Chung IM, Ketharmathan S, Thiruvengadam M, Rajajumar G. Rheumatoid Arthritis: The Stride from Research to Clinical Practice. Int J Mol Sci 2016;17. piiE900.
[5] LI K, Tie H, Hu N, Chen H, Yin X, Peng C et al. Association of two polymorphisms rs2910164 in miRNA-146a and rs3746444 in miRNA-499 with rheumatoid arthritis: a meta-analysis. Hum Immunol 2014;75:602–8.
[6] Hashemi M, Eskandari-Nasab E, Zakeri Z, Atabaki M, Bahari G, Jahantigh. Association of pre-miRNA-146a rs2910164 and pre-miRNA-499 rs3746444 polymorphisms and susceptibility to rheumatoid arthritis. Mol Med Rep 2013;7:287–9.
[7] Lu L, Tu Y, Liu L, Qi J, He L. MicroRNA-499 rs3746444 polymorphism and autoimmune diseases risk: a meta-analysis. Mol Diagn Ther 2014;18:237–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6500

AB0243 SERUM LEVELS OF ANGIOGENIC AND PROINFLAMMATORY CYTOKINES TO DISCRIMINATE BETWEEN 6 SETS OF REMISSION CRITERIA IN RA

J. Ramírez García, A. Cuervo, R. Celis, V. Ruiz-Esquide, M.V. Hernández, R. Sanmartí, J.D. Cañete. *Rheumatology, Hospital Clínic, Barcelona, Spain*

Background: The ideal definition of remission in RA remains to be agreed. Angiogenic factors and proinflammatory cytokines are key in RA pathogenesis.
Objectives: The aim of this study was to analyse serum levels differences of angiogenic and inflammatory biomarkers between SDAI, CDAI, ACR, DAS28 and sonographic remission in patients with (RA).
Methods: We selected patients with RA in clinical remission (DAS28-ESR<2.6 for >6 months). PDUS of knees and hands was performed. Serum levels of biomarkers of inflammation/angiogenesis were determined by Quantibody® Human Array. Patients were classified according to 6 sets of remission criteria: SDAI (<3.3), CDAI (<2.8), ACR, DAS28-ESR (<2.6), Doppler (score Doppler=0) and UdAS (ultrasound defined active synovitis:no joints with SH$\geq$2+PD)
Results: 60 patients with RA were collected. 76% female, aged (mean) 53 years; disease duration 110 months. 47 (76%) csDMARDs, and 27 (45%) biological therapies. At baseline, 67% of patients had PD signal and 48% fulfilled criteria for previously defined UdAS. Although patients in sonographic remission had lower levels of inflammatory biomarkers such as IL-6, IL-17 or IL-23, no significant differences were found between the 6 sets of remission criteria. Angiogenic biomarkers such as CXCL6 (0.039), ENA78 (0.007), SDF1 (0.047) and VEGF-R1 (0.025) were significantly lower in patients fulfilling CDAI remission. Patients with no PD signal (0.009) and no UdAS (0.006) had significantly lower levels of bFGF.
Conclusions: RA patients in CDAI remission had significantly-lower levels of angiogenic cytokines. However, no differences in serum levels of proinflammatory cytokines were found between the 6 sets of remission criteria.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3504

AB0244 MICROWAVE RADIOMETRY-DERIVED THERMAL CHANGES OF SMALL JOINTS AS POTENTIAL ADDITIONAL BIOMARKER IN RHEUMATOID ARTHRITIS: A PROSPECTIVE STUDY

K. Laskari[1], G. Pentazos[1], K. Prekas[2], I. Raftakis[3], E. Siores[4], P.P. Sfikakis[1]. *[1]Rheumatology Unit, 1st Dept. of Propaedeutic Internal Medicine and Joint Rheumatology Program, National & Kapodistrian University of Athens Medical School; [2]Technological Education Institute; [3]Department of Rheumatology, Asklepion General Hospital, Athens, Greece; [4]Institute of Materials Research and Innovation, University of Bolton, Bolton, United Kingdom*

Background: Microwave Radiometry (MR) is a rapid, non-invasive method that detects in-depth tissue temperatures. Using joint ultrasound as reference method, in a proof-of-concept study, we have found that an increased temperature at the knee joint detected by MR in the absence of relevant clinical signs reflects the presence of subclinical synovial inflammation in rheumatoid arthritis (RA) (1).
Objectives: To test the hypothesis that temperature of small joints assessed by MR correlates to global disease activity levels in RA, a disease in which small joints are primarily affected.
Methods: Ten patients with active, untreated RA underwent clinical and laboratory assessments, joint ultrasound and MR of hand and foot small joints (RTM 01 RES microwave computer based system, Bolton, UK) at baseline, as well as 15, 30 and 90 days after treatment onset. Twenty aged-matched healthy individuals served as controls.
Results: Using 1248 separate MR-derived recordings from RA patients we created several thermo-scores involving different small joint combinations and compared them with clinical and ultrasound data. The best performing thermo-score involved the sum of temperatures of 16 small joints (2nd-5th metacarpal and proximal inter-phalangeal joints, bilaterally). This thermo-score correlated positively to DAS28 disease activity score (p=0.001), tender joint count (p=0.002), swollen joint count (p=0.001), patient's visual analogue scale ($p<0.001$), CRP

(p=0.040), but not ESR levels, as well as to the standard Ultrasound Score of 7 joints (p≤0.025) (2). The MR-derived thermo-score could also discriminate patients in high [mean (SD) 9.2 (5.6)], moderate [mean (SD) 7.1 (3.5)] and low disease activity/remission [mean (SD) 4.2 (1.8)] (p=0.015), or aged-matched healthy subjects [mean (SD) 5.0 (1.7)] (p=0.002). Moreover, individual changes from baseline to follow-up end mirrored the corresponding DAS28 changes in 7/10 patients.

Conclusions: Increased in-depth temperatures of small joints detected by MR, which are indicative of local inflammation, may serve as an additional biomarker in RA. Optimization of MR equipment and technique may result in an objective measurement of RA disease activity in clinical practice.

References:

[1] E. Zampeli, et al. Detection of subclinical synovial inflammation by microwave radiometry. PLoS ONE. 2013;(8)5:e64606.

[2] Backhaus M, et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. Arthritis Rheum. 2009;61(9):1194–201.

Acknowledgements: None.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3279

AB0245 DISTRICT DIFFERENCES BETWEEN THE SEXES OF PREDICTIVE VALUE OF MATRIX METALLOPROTEINASE-3 AT BASELINE REGARDING CHANGES IN MODIFIED TOTAL SHARP SCORE AT 1 YEAR IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Inui[1], T. Okano[1], K. Orita[2], Y. Sugioka[3], K. Mamoto[1], T. Koike[3,4], M. Tada[5], H. Nakamura[1]. *[1]Department of Orthopaedic Surgery, Osaka City University Graduate School of Medicine, Osaka; [2]Department of Orthopaedic Surgery, Shirahama Hamayu Hospital, Shirahama; [3]Center for Senile Degenerative Disorders, Osaka City University Graduate School of Medicine, Osaka; [4]Search Institute for Bone and Arthritis Disease, Shirahama Foundation for Health and Welfare, Shirahama; [5]Department of Orthopaedic Surgery, Department of Orthopaedic Surgery, Osaka City General Hospital, Osaka, Japan*

Background: Matrix metalloproteinase (MMP)-3, also known as stromelysis-1, is expressed in inflamed synovium of patients with rheumatoid arthritis (RA). It degrades components of articular cartilage, such as proteoglycans. In Japan MMP-3 has been used as a clinical biomarker of joint destruction and its predictive value for radiographic progression has been reported.

Objectives: W aimed to confirm a relation between baseline MMP-3 and radiographic progression at 1 year and to examine the association of the MMP-3 level with ultrasonography (US) findings.

Methods: A total of 259 (213 women) consecutive patients with RA were enrolled. We collected baseline data, that included the patient's age, sex, disease duration, use of glucocorticoid or disease modifying antirheumatic drugs, Disease Activity Score-28, and modified total Sharp score (mTSS); MMP-3 and, C reactive protein levels;, rheumatoid factor or anti-citrullinated peptide antibody status,; and the power doppler score (PD) of US assessment of digits and wrists. Baseline MMP-3 level was analyzed in association with the baseline PD value and changes (Δ) in mTSS, erosion score (ΔERN), joint space narrowing (ΔJSN) at 1 year from baseline by Pearson's correlation method. Correlations between ΔMMP-3 and ΔmTSS, or ΔPD were also analyzed. Multiple regression analysis was performed, with ΔmTSS as the outcome for baseline variables. Statistical analysis was performed separately by sex because the upper normal limits of MMP-3 differ between the sexes (men ≤121ng/ml, women ≤59.7 ng/ml).

Results: There was a weak correlation between the baseline MMP-3 level and baseline PD score in men. There was also moderate correlations between baseline MMP-3 level and structural damage at 1 year only in men. There was no predictive value for baseline MMP-3 level in women in terms of structural damage at 1 year. Multiple regression analysis revealed that the baseline MMP-3 level correlated independently with the ΔmTSS only in men (p=0.0031), whereas in the women the baseline PD score was correlated independently with the ΔmTSS (p=0.0003).

Table 1

	Variables	Correlation coefficient	Confidence interval	p
Male patients				
Baseline MMP-3	ΔmTSS	0.501[a]	[0.246, 0.691]	<0.001
	ΔERN	0.336[b]	[0.051, 0.571]	0.022
	ΔJSN	0.542[a]	[0.299, 0.719]	<0.0001
	Baseline-PD	0.228[b]	[-0.074, 0.492]	0.136
ΔMMP-3	ΔmTSS	-0.435[a]	[-0.644, -0.165]	0.003
	ΔERN	-0.325[b]	[-0.562, -0.038]	0.028
	ΔJSN	-0.436[a]	[-0.645, -0.167]	0.002
	ΔPD	0.134	[-0.170, 0.414]	0.387
Female patients				
Baseline MMP-3	ΔmTSS	0.0011	[-0.130, 0.132]	0.987
	ΔERN	0.0188	[-0.113, 0.150]	0.780
	ΔJSN	-0.0148	[-0.146, 0.117]	0.826
	Baseline -PD	0.0985	[-0.040, 0.233]	0.163
ΔMMP-3	ΔmTSS	-0.0344	[-0.165, 0.098]	0.610
	ΔERN	-0.0485	[-0.179, 0.083]	0.472
	ΔJSN	-0.0127	[-0.144, 0.119]	0.851
	ΔPD	0.134	[-0.0058, 0.270]	0.060

[a]Moderate correlation, [b]Weak correlation. Statistical analysis was performed using Pearson's correlation.

Conclusions: The baseline MMP-3 level was a good predictor of deterioration of the mTSS at 1 year in male patients with RA, but not in female patients. On the other hand, the baseline PD score was a useful predictor of joint destruction in female patients with RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2431

AB0246 IMPACT OF TREAT TO TARGET STRATEGY WITH COMPLEMENTARY ULTRASOUND ON REAL WORLD RADIOGRAPHIC OUTCOMES IN EARLY RHEUMATOID ARTHRITIS OVER THE PAST DECADE

K. Kobayashi[1], K. Minegishi[1], S. Ohno[1], H. Nakajima[2]. *[1]Center for Rheumatic Diseases, Yokohama City University Medical Center; [2]Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, Japan*

Background: Treatment for rheumatoid arthritis (RA) has changed over the past decade. Early diagnosis and prompt agressive treatment based on treat to target strategy, as well as complementary ultrasound have been adopted and proven to improve patient clinical and radiological outcomes in clinical trials.

Objectives: The aim of this study was to compare radiographic progression of early RA patients starting their first DMARD 10 years ago vs more recently in daily clinical practice.

Methods: We reviewed the medical records of consecutive patients with symptom of 3 years duration who fulfilled the 1987 ACR classification criteria or the 2010 ACR/EULAR classification criteria in a single center retrospectively. In the first cohort (2000s), 70 patients (55.3±13.3y.o, Female 77%) who were diagnosed with RA during 2003–2005 were included. in the second cohort (2010s), 71 patients (54.5±17.3y.o,Female90%) who were diagnosed with RA during 2013–2015 were included. Radiographs of hands were assessed at baseline and one year after according to the van der Heijde modified Sharp score (range 0–280) without clinical information and chronological orders of radiographs in the individual patients.

Results: Mean changes in radiographic joint damage for joint space narrowing score, erosion score, total radiographic score were higher in 2000s than 2010s (0.92±2.70 vs 0.28±1.86; p=0.010, 0.54±1.35 vs 0.35±0.99; p=0.390, 1.45±3.54 vs 0.68±2.55; p=0.015, respectively). Radiographic progression defined as total radiographic score >0 and >5 were 31.4% vs 22.5% and 8.6% vs 8.5% between 2000s and 2010s (p=0.230 and p=0.970, respectively). Methotrexate (MTX) was frequently used for initial treatment in 2010s than 2000s (86% vs55%, p≤0.001), and initial dose and maximum dose of MTX were higher in 2010s than 2000s (9.13±2.09 mg/week vs 4.67±1.54 mg/week; p≤0.001 and 12.04±3.73 mg/week vs 8.13±1.88 mg/week; p≤0.001, respectively). The mean duration from symptom onset to diagnosis was earlier in 2010s than 2000s (5.75±5.04 months vs 7.85.±6.85 months, p=0.001). CRP at baseline and 1 year after were lower in 2010s than in 2000s (2.74±1.90 mg/dL vs 3.35±3.94 mg/dl; p=0.001 and 0.60±1.19 mg/dL vs 1.20±1.99 mg/dl; p=0.03 respectively). There were no significant differences in sex, age, positive rate of RF and ACPA, the Sharp score at baseline, steroid use, and biological agents use between two cohorts.

Conclusions: In recent 10 years, early diagnosis with complementary ultrasound and appropriate MTX use based on treat to target strategy led to prevent joint destruction of RA patients in daily clinical practice.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5649

AB0247 EVALUATION OF RHEUMATOID ARTHRITIS CASES WITH HIGH ANTI-CCP ANTIBODY LEVEL

K. Suzuki, M. Minami, Y. Nishio, N. Hara, S. Nakamura. *Hokkaido Orthopedic Memorial Hospital, Sapporo, Japan*

Background: Anti-cyclic citrullinated peptide antibodies (Anti-CCP Ab) are well-established serological markers that show high sensitivity and specificity in diagnosing early rheumatoid arthritis (RA). Furthermore, Anti-CCP Ab is reported to be associated with bone erosions of RA. Therefore, Anti-CCP Ab positive RA patient can be a candidate for intensive treatment.

Objectives: Upper measurement limit of Anti-CCP Ab increased recently up to 1200 units. High level of Anti-CCP Ab may be a predictor of the profound therapy for RA. To understand the importance of Anti-CCP Ab level, we evaluated RA patients with high titer Anti-CCP Ab in relationship to the other activity markers of RA and the intensity of the treatment for RA.

Methods: Total of 186 RA patients with Anti-CCP Ab higher than 30 units was included in this study. Baseline markers such as CRP, MMP-3, RF and anti-CCP Ab were measured at the entry of the study. Relationship among these markers ware evaluated and examined using statistical significance for the single-factor ANOVA and the multiple comparisons. Among those cases 131 cases were treated conservatively with biologics and/or DMARDs and were followed up more than one year. We graded them from I to IV by the intensity of the treatment. Grade I: Biological agent. Grade II: Methotrexate (MTX) more than 12mg or combination with more than 3 DMARDS Grade III: MTX 6–11mg or combination

with two recommended DMARDS Grade IV: single use of DMARDS including MTX less than 5mg.

Results: There was no relationship between titers of Anti-CCP Ab and titers of RF. We found significant statistical correlation between anti-CCP antibody titers and inflammatory markers such as CRP and MMP-3. There was significant statistical correlation between CRP and MMP-3.

In terms of treatment intensity, strong intensity group showed high titer of anti-CCP Ab and CRP. Titer of RF and MMP-3 level did not have any relationship with the treatment intensity. In cases treated with biologics, anti-CCP Ab and CRP were significantly higher compared to non-biologic case group. In 80% of cases treated with biologics titer of anti-CCP was more than 200 units. However, non-biologic treatment was continued in more than 50% of cases with anti-CCP Ab higher than 200 units.

Conclusions: Even though we treated cases based on the severity of the symptoms of the patient and response in laboratory data, high anti-CCP Ab titers and CRP at the base line were most associated with the treatment intensity after 1 year. The results of our study suggest that the titer of anti-CCP Ab can be better a predictor of the treatment intensity than MMP-3 and RF.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4989

AB0248 THE IMPACT OF THERAPY ON ANTI-CARBAMYLATED PROTEIN ANTIBODY ISOTYPES AND SEROSTATUS IN PATIENTS WITH EARLY RA TREATED WITH ABATACEPT AND METHOTREXATE

L. Trouw[1], S. Connolly[2], A. Johnsen[2], J. Ye[2], M. Maldonado[2], R. Toes[1], T. Huizinga[1]. *[1]Leiden University Medical Center, Leiden, Netherlands; [2]Bristol-Myers Squibb, Princeton, United States*

Background: Maturation of autoantibody responses has been suggested to be a proxy for disease maturation. Autoantibody responses against post-translationally modified antigens are present in autoimmune diseases and antibodies directed against carbamylated proteins (anti-CarP antibodies) are a marker of RA. Anti-CarP antibody analysis in patients with early RA offers the opportunity to estimate whether specific intervention during such early stages of autoantibody development may have an impact on the maturation of the anti-CarP antibody response.

Objectives: We assessed the relationship between changes in anti-CarP isotypes and rates of seroconverson to negative in patients with early RA.

Methods: In the Assessing Very Early Rheumatoid arthritis Treatment study (AVERT; NCT01142726), patients with early RA were treated with abatacept (ABA)+MTX, ABA monotherapy or MTX alone.[1] Patients in AVERT were anti-cyclic citrullinated peptide-2 positive at baseline for study entry.[1] In this *post hoc* analysis, concentrations of anti-CarP isotypes were measured using custom ELISAs. Anti-CarP ELISAs for immunoglobulin (Ig)G, IgM or IgA isotypes were performed in patient serum at baseline, and at Days 85 and 365 on treatment. Baseline levels of each anti-CarP antibody isotype and % seropositivity were comparable across the three treatment arms. Adjusted mean change from baseline was calculated using a longitudinal repeated measures model.

Results: At baseline, 51.3, 42.5 and 29.3% of all patients with serum available in AVERT were positive for IgG, IgM (indicative of an ongoing immunoresponse) and IgA anti-CarP isotypes, respectively. Overall, approximatly 65% of patients were positive for at least one anti-CarP antibody isotype. Median % change from baseline (25%, 75%) for anti-CarP isotypes levels from baseline to Days 85 and 365 are shown (Table). Analysing patients who were positive at baseline for each of the isotypes, we observed that 19/48 (40%), 16/43 (37%) and 11/48 (23%) of the patients positive for the IgG isotype became negative on ABA+MTX, ABA and MTX, respectively, at 1 year. For the IgM isotype, 26/48 (54%), 14/36 (39%) and 15/38 (39%) became negative on ABA+MTX, ABA and MTX, respectively. For the IgA isotype, 12/26 (46%), 10/23 (43%) and 13/31 (42%) became negative on ABA+MTX, ABA and MTX, respectively.

Conclusions: Concentrations of all anti-CarP isotypes (IgM, IgA, IgG) were numerically reduced by abatacept+MTX therapy compared with MTX or abatacept alone. Abatacept+MTX trended towards higher rates of seroconversion to negative for all isotypes over 1 year of treatment. These results indicate that the extent of the anti-CarP antibody response can be modulated by intervention with abatacept on background MTX in anti-citrullinated protein antibody-positive patients with early RA.

References:

[1] Emery P, et al. Ann Rheum Dis 2015;74:19–26.

Disclosure of Interest: L. Trouw: None declared, S. Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, A. Johnsen Employee of: Bristol-Myers Squibb, J. Ye Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Maldonado Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, R. Toes: None declared, T. Huizinga Grant/research support from: EU & Dutch Arthritis Foundation, Consultant for: Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Crescendo Bioscience, Inc, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, UCB, Inc., Eli Lilly, Speakers bureau: Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough

DOI: 10.1136/annrheumdis-2017-eular.2935

AB0249 IDENTIFICATION OF INFLAMMATORY- AND IMMUNE DISORDER- RELATED PROTEINS AS PUTATIVE BIOMARKER CANDIDATES FOR IMPROVING RHEUMATOID ARTHRITIS MONITORING

L. González-Rodríguez[1], V. Calamia[1], L. Lourido[1], P. Fernández-Puente[1], M. Camacho-Encina[1], C. Ruiz-Romero[1], A. Julià[2], A. Fernández-Nebro[3], J. Tornero[4], S. Marsal[2], F.J. Blanco[1]. *[1]Proteomics Group, Rheumatology Division, ProteoRed, PRB2-ISCIII, INIBIC-Hospital Universitario A Coruña, A Coruña; [2]Rheumatology Research Group, Vall d'Hebron Hospital Research Institute, Barcelona; [3]UGC Reumatología, Instituto de Investigación Biomédica (IBIMA), Hospital Regional Universitario de Málaga, Málaga; [4]Hospital Universitario Guadalajara, Guadalajara, Spain*

Background: Rheumatoid arthritis (RA) is a long-lasting inflammatory autoimmune disorder that ultimately leads to the destruction of joint architecture.

Objectives: Using the DAS28 activity index, 80 RA serum samples (40 with low activity and 40 with high activity) were selected in order to be analyzed by mass spectrometry. The aim of this study was to find possible protein biomarkers that could discriminate patients with different RA activity in the daily clinical routine.

Methods: In order to facilitate the complex measurement of these serum samples, a simple, fast and reproducible albumin-specific depletion method using ethanol was optimized and applied to this study. Four independent pools of the 40 high RA activity samples (10 samples per pool) and 4 pools of the 40 low RA activity samples were firstly albumin-depleted, and then the remnant serum proteins were digested and differentially labelled with iTRAQ 8-plex reagents. Subsequently, the 8 labelled pools were combined and cleaned using StageTips-C18. Finally, the pool mixture was fractionated by HPLC (Zorbax-C18) and the resulting fractions were analyzed by nanoLC-MS/MS using two different equipments for validation (MALDI-TOF/TOF and TripleTOF).

Results: The mass spectrometry analysis led to the identification of 186 proteins. Among these, Haptoglobin, Kininogen-1, Alpha-2-HS-glycoprotein, Serum Amyloid A, Afamin and Histidine-rich-glycoprotein, exhibited a differential relative abundance depending on the RA activity of the patients ($p<0.03$) in both analysis. These proteins were also validated by other orthogonal techniques (western blot, ELISA and protein arrays).

Conclusions: In this proteomic study, 9 proteins were found to be modulated between patients with high and low RA activity. Most of these proteins are related with the RA process and the effects caused by this type of disease (inflammation and immune disorder in joints). Therefore, these proteins are possible biomarker candidates for improving RA monitoring. Future validation experiments and prospective studies are needed to facilitate their implementation in the clinical routine.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4912

AB0250 THE ADIPOSE TISSUE AS PREDICTIVE FACTOR OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS: EVALUATION OF BODY FAT COMPOSITION BY BIOELECTRICAL IMPEDANCE ANALYSIS AND ULTRASONOGRAPHY

M.G. Anelli[1], C. Rotondo[2], R. Fanizzi[2], O. Magazzino[2], M. Giannotta[2], M. Giannini[2], O. Lorusso[3], E. Praino[2], M.T. Viggiani[3], F. Cacciapaglia[2], M. Barone[3], G. Lapadula[2], F. Iannone[2]. *[1]DIM; [2]DETO, Unit of Rheumatology; [3]DETO, Gastroenterology Unit, Bari, Italy*

Background: Adipose tissue (AT) is an endocrine organ able to secrete the "adipokine" molecules that contribute to the low-grade inflammatory state in obese subjects and to the local inflammation that affects joints and bone (1,2). High-grade inflammation, in course of RA, leads to an altered body composition (3,4), characterized by the increasing of fat mass and the decreasing of lean mass, mostly not associated to body mass index (BMI) variations (3,5). The BMI is not able to differentiate visceral (VTH) and subcutaneous (STH) fat tissue and to distinguish between muscle mass and fat mass body composition (BC) (6,7). Alternative methods proposed for assessment of visceral fat deposition, are bioelectrical impedance analysis (BIA) and ultrasonography (US).

Objectives: The aim of the study is to investigate if BC, assessed by BIA and US,

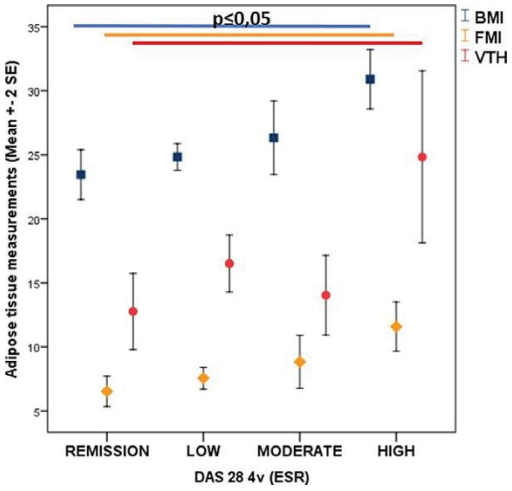
Abstract AB0248 – Table 1. Median % change from baseline (25%, 75%) for anti-CarP isotypes

	Day 85			Day 365		
	IgG	IgM	IgA	IgG	IgM	IgA
ABA	–17.3 (–55.7, 0.0)	–26.3 (–57.9, 0.0)	–6.8 (–35.1, 0.0)	–31.2 (–67.4, 0.0)	26.0 (-81.2, 0.0)	–26.7 (–72.9, 13.0)
MTX	–19.3 (–53.6, 0.0)	–35.7 (–54.4, –6.9)	–27.2 (–42.4, –3.9)	–17.7 (–65.1, 0.0)	–38.3 (–63.7, 0.0)	–21.9 (–50.3, 0.0)
ABA+ MTX	–38.8 (–62.3, 0.0)	–44.2 (–59.5, –13.8)	–41.3 (–54.9, –28.3)	–55.7 (–76.7, 0.0)	–45.7 (–72.5, –0.2)	–46.4 (–66.7, 0.0)

correlates with disease activity (assessed by the Disease Activity Score using 28 joint counts – DAS28) and affects the response to the therapy (DAS 28 variation from first evaluation).

Methods: 87 consecutive RA patients (pts) (72 women and 15 men; aged 52.4±13.2 years; disease duration of 10.7±8.6 years), treated with DMARDs and/or biologics (bDMARDs), were recruited during their regular visit. The inclusion criteria were the 1987 American College of Rheumatology (ACR) or ACR/EULAR 2010 classification criteria. The pts underwent to anthropometric measures (BMI); abdominal US to assess STH and VTH and derived computing of peritoneal circumference (PC); and BIA to the indices of body composition (fat-free mass index (FFMI) and fat mass index (FMI).

Results: We observed increasing values of BMI, FMI, VTH (fig. 1) and CP with the worsening of disease activity phases, evaluated by DAS 28. In particular, pts with DAS28≥5.1 had highest BMI (30,9±2; p=0,036), FMI (11,5±1,6; p=0,05), CP (92,7±12,5 cm; p=0,035) and VTH (24,8±5,8 mm; p=0,046) than pts in less severe disease activity. By linear regression analysis the predictor of higher DAS28 is the BMI (p=0,028). As regard the drug response, the predictors of DAS 28 improvement are higher FFMI (p=0,044) and lower BMI (p=0,015), independently by bDMARDs or DMARDs treatment. A trend to higher FMI and US AT measures was observed in female with high disease activity, in particular in menopause pts.



Conclusions: An altered fat distribution is observed in active RA phases; in particular, the FMI increasing is attributable just to visceral AT (VTH and CP). An inflammatory hyperactivity of visceral adiposity could be supposed in RA. The body composition, in addition to BMI, seems to predict the disease activity and drug response in RA patients. The evaluation of VTH by US could be useful to not overestimate the disease activity; instead the BIA could be a useful tool to support the clinicians in a more aggressive treatment management.

References:

[1] Nat Clin Pract Rheumatol 2007; 3(12):716–24.
[2] J Mol Endocrinol 2009; 43(1):11–8.
[3] Mediators Inflamm 2013; 2013:710928.
[4] Arthritis Care Res (Hoboken) 2012; 64(10):1471–9.
[5] Nat Rev Rheumatol 2010; 6(8):445–51.
[6] Curr Opin Clin Nutr Metab Care 2003; 6(4):387–93.
[7] Ann Rheum Dis 2007; 66(10):1316–21.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4260

AB0251 IN RHEUMATOID ARTHRITIS EROSIONS ARE MORE FREQUENT IN THE FEET THAN IN THE HANDS

M.L. Andersson, B. Svensson, K. Forslind. *Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund and Helsingborg, Sweden*

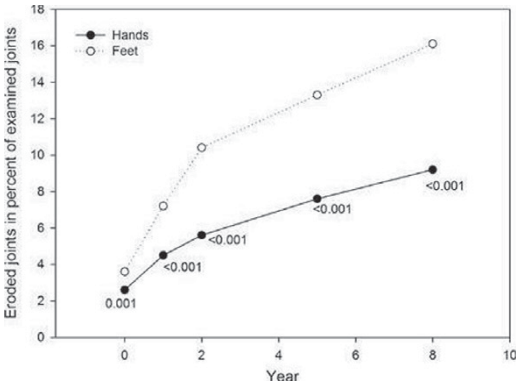
Background: Joint destruction in patients with rheumatoid arthritis (RA) is mostly evaluated by scoring radiographs of both hands and feet using the Sharp van der Heijde or Larsen scoring methods. In contrast, DAS28, the most commonly used composite measure of inflammation measure, does not include the feet.

Objectives: To study the distribution of erosions in hand and wrist (hands) and feet in early RA and elucidate if the feet should be included also in composite measures of inflammation

Methods: This study comprises 1 052 patients from the BARFOT study of patients with early RA, recruited 1992–2006. Radiographs of hands and feet were performed at baseline, 1, 2, 5 and 8 years and evaluated by the Sharp van der Heijde scoring (SHS) method (32 joints in the hands and 12 in the feet). Disease activity at baseline was measured by the DAS28.

Results: In the feet there were significantly more eroded joints in percent of examined joints at all time points (p<0.001), and higher erosion scores in percent of maximum erosion score at 5 and 8 years (0.037 and 0.021 respectively), compared with the hands.

There were no differences in mean joint space narrowing (JSN) between hands and feet at any time point. Patients with erosions only in the feet had significantly lower DAS28, mean 4.59, compared with the patients in the other groups, mean 5.03 in the no erosions group p=0.031, mean 5.17 in the group with erosions only in the hands, p=0.013, and mean 5.15 in the group with erosions in both hands and feet, p=0.031.



Conclusions: Joint destruction over time was more pronounced in the feet than in the hands. Baseline erosions limited to the feet were associated with low disease activity, suggesting that inflammation localized to the feet may not be reflected by DAS28. These observations may have relevance to the evaluating of disease activity and progression in the individual patient. Possibly inclusion of the feet to DAS28 might improve the validity of this disease activity measure.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3634

AB0252 THE IMPACT OF THE RHEUMATOID FOOT ON FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS EVALUATED BY FFI AND LFIS

M. Erraoui, B. Amine, L. Tahiri, I. El Binoune, J. Bahha, S. Fellous, Y. Boujenane, F. Allali, R. Bahiri. *Rheumatology, Mohammed V University, Faculty of Medicine and Pharmacy of Rabat, El Ayachi Hospital, SALE, Morocco*

Background: The impairment of function in patients with rheumatoid arthritis (RA) is determined by several factors related to the disease including joint damage. The foot, a location frequently affected during course of the disease, has a major impact on the lower limb and could cause functional disability.

Objectives: The purpose of this study is to evaluate the impact of the rheumatoid foot on function of patients with RA.

Methods: Cross-sectional study was conducted in 33 patients with RA. Patients with static lower limb disorder or foot injury from other origin were excluded. Demographic and clinical characteristics were collected: age, sex, BMI, disease duration, tender joint count, swollen joint count, foot pain evaluated on an VAS, foot squeeze test and various podiatric abnormalities observed clinically (forefoot, midfoot and rearfoot). Biological characteristics also collected: sedimentation rate in the first hour, C reactive protein, rheumatoid factor and anti-CCP. Disease activity was evaluated by DAS28, CDAI, SDAI and DAS44. Functional repercussions were estimated by the French Functional Index (FFI), comprising 23 items, divided into 3 sections: pain, function and limitation of activity. Functional disability was studied by the Leeds Foot Impact Scale (LFIS), which includes 51 items (21 items specific to foot function alteration (LFIS-I) and 30 related to foot disability (LFIS-D)). Statistical analysis was performed using SPSS21 software.

Results: Thirty-three patients followed for RA were included. The mean age of our patients was 49.39±10.52 with a female predominance (87.9%). Mean disease duration was 9.96±7.49 years. In all patients; 21 (95.5%) were seropositive. The mean DAS28 was 5.53±1.38 and the mean HAQ was 1.37±0.83. 93.9% of our patients had bilateral foot pain; 69.7% in the forefoot, 18.2% in the midfoot and 42.4% in the hindfoot. The medial retromalleolar tumefaction was found in 21.2% of the patients and the lateral retromalleolar tumefaction in 45.5% of them. The squeeze test was positive in 23 (69.7%) patients. Prevalences of Podiatric abnormalities were noted in the following ordre: hallux valgus (48.5%), quintus varus (12.1%), hallux rigidus (6.1%), claw toe (15.2%), triangular forefoot (9.1%), rearfoot valgus (27.3%) and rearfoot varus (27.3%).

Mean FFI was 52.35±25.63 (FFI-pain: 58.69±24.41, FFI-function: 53.66±30.48 and FFI- limitation of activity: 39.33±30.58). Mean LFIS-I was 11.48±5.36 and mean LFIS-D was 19.96.

A high FFI was associated with foot pain (p=0.034); in midfoot (p=0.029) and rearfoot (p=0.005) and with high disease activity: DAS28 (P=0.005), CDAI, SDAI and DAS44 (p=0.0001).

LFIS-I and LFIS-D were statistically related to pain in foot (p=0.019) (midfoot (0.042), hindfoot (0.003)), and to a positive squeeze test. The disease activity was positively correlated with high LFIS-I and LFIS-D (p=0.0001). The presence of medial retro-malleolar swelling, posterior gutter filling and calcaneal varus is responsible for a high FFI, LFIS-I and LFIS-D with respectively: p=0.0001, p=0.003, p=0.003.

Conclusions: The rheumatoid foot alters function. It causes disability which is related to foot pain, rearfoot podiatric abnormalities and disease activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5508

AB0253 TIPS ON SELECTION OF BIOLOGICS FOR PATIENTS WITH RHEUMATOID ARTHRITIS BASED ON TREATMENT PATTERNS

M. Kamiya[1], S. Soen[1], H. Kikuchi[2], N. Okada[3]. *[1]Department of Orthopaedic Surgery and Rheumatology, Kindai University Nara Hospital, Ikoma-City; [2]Department of Orthopaedic Surgery and Rheumatology, Kindai University Sakai Hospital, Sakai-City; [3]Department of Orthopaedic Surgery, Sumoto Itsuki Hospital, Sumoto-City, Japan*

Background: The emergence of biologics has led to innovation in the treatment of rheumatoid arthritis (RA). In the clinical setting, biologics are administered with careful consideration of complications and medical history in accordance with the treat-to-target recommendations. However, the progression of joint damage, the costs incurred before finding an effective biologic are serious concerns. It is therefore desirable to use biologics with long-term efficacy and less financial burden from the early stage.
Objectives: Participants were RA patients treated with one of three biologics having different mechanisms of action who achieved therapy targets with long-term treatment efficacy and consequently achieved either reduction or withdrawal of therapy. Patients' background characteristics and long-term treatment patterns were evaluated.
Methods: Between November 2004 and October 2016, 196, 57, and 85 RA patients were treated with etanercept (ETN), tocilizumab (TCZ), and abatacept (ABT), respectively, in first- or second-line therapy. These patients were divided into the continuation group, who underwent therapy with the same agent for $\geq$3 years without disease flare (DAS28-ESR $>$3.2) persisting 3 months, and the discontinuation group, who experienced primary failure resulting in discontinuation of the therapy within 3 months. Student's t test or Mann-Whitney's U test were used to compare patients' background characteristics between the two groups for each biologic. Further, log-rank test and Steel-Dwass test, respectively, were used to compare therapy continuation rates and reasons for discontinuation among the three biologics. Finally, relative dose intensity (RDI) was calculated to evaluate the treatment patterns of the individual biologics.
Results: The Kaplan-Meier method showed that the 3-year continuation rates of therapy with ETN, TCZ, and ABT were 54.2%, 23.8%, and 35.8%, respectively: the continuation rate of ETN was significantly higher than that of the other two agents. The numbers of patients treated with ETN, TCZ, and ABT were respectively 46, 9, and 14 in the continuation group and 16, 12, and 11 in the discontinuation group. The proportion of patients treated with ETN plus concomitant MTX was significantly higher in the continuation group than in the discontinuation group (P=0.0057). No significant differences were found in patients' background characteristics (disease duration, rheumatoid or anti-cyclic citrullinated peptide positivity, number of biologics previously used, and DAS28-ESR). Mean RDI values (median value, 95% confidence interval) over a 3-year period were as follows: 0.95 (0.92, 0.83–1.06) for 25 mg/week ETN therapy; 0.78 (0.90, 0.66–0.89) for 50 mg/week ETN therapy; 0.84 (0.84, 0.76–0.89) for TCZ therapy; and 0.87 (0.94, 0.79–0.95) for ABT therapy. The cumulative costs for 3 years of the respective treatments were 19,700, 32,200, 27,300, and 39,000 euros (1 euro =115 Japanese yen). After targets were reached, the dose of ETN was maintained at 25 mg/week or reduced from 50 mg/week, while the TCZ and ABT therapies were continued over the long term with a longer dosing interval.
Conclusions: Treatment with ETN plus concomitant MTX showed high continuation rates, and long-term achievement of therapy targets was maintained at a lower dosage (and thus, lower costs). It is beneficial to choose this method over non-TNF inhibitors.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1146

AB0254 COMPARISON OF DYNAMIC PEDOBAROGRAPHIC FINDINGS BETWEEN RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY INDIVIDUALS

S. Ghadimy, M. Aarabi, N. Abdolahi, N. Nematollahi, M. Aghaei. *Rheumatology Reasearch Center, Gorgan, Iran, Islamic Republic Of*

Background: Foot involvement happens early in RA patients and situation becomes ugly and painful rather very fast. There is a blank gap between starting of foot involvement and the time where patient needs surgical intervention for correcting the damages done by RA. No guideline exists for determining when and what we can do in these patients to detect and prevent the changes or at least reduce their damages.(1)
Objectives: 1. Evaluating foot pressure changes by pedobaroghy:
- comparing maximum force/peak pressure distributed in different regions of foot between RA patients and healthy individuals.
- comparing maximum force/peak pressure distributed in different regions of foot between men and women.
- determining effects of aging on maximum force/peak pressureby comparing them between two age groups.
- determining effects of duration of RA on force/peak pressure in RA patients.

2. Evaluating radiologic findings in symptomatic RA patients and comparing them with pedobarographic findings.
3. Evaluating and comparing quality of life in RA patients and healthy individuals with SF36 questionnaire.
Methods: 90 RA patients and 45 healthy individuals were chosen and entered this research. Patients divided into two groups: 45 patients without any previous foot symptoms, 45 with foot symptoms. All these groups underwent dynamic pedobarography with Novel emed pedobargraphy.
We took foot and ankle X-rays for symptomatic group.
Based on Larsen score, symptomatic patients were divided into individuals with and without radiologic changes.
Results: There was a significant difference in total maximum force between patients and healthy individuals; healthy individuals had lesser amount of maximum force in different parts of their feet compared to RA patients.
Fore foot region endured the most amount of maximum force and pressure in all three groups with no significant difference between groups.
RA patients both symptomatic and asymptomatic had more force and pressure upon their midfoot regions compared to the healthy group p-value:.000.
Since we excluded patients with severe deformities and those who couldn't walk alone from the study, and our cases were relatively in early stages of disease, we didn't find any significant difference in pressure or force between symptomatic patients with and without radiographic findings. This can be explained by the fact that foot pressure alteration detectable in pedobarography is already begun in all patients with foot symptoms but radiologically evident pathologies had not happened yet.
Conclusions: RA has considerable effect on patients' feet along with other physical and mental issues. While conventional radiologic methods has a limited eficacy in predicting and diagnosing the pathologic changes in foot region, pedobarography can easily shows these changes in foot pressure values and can be used to detect RA patients that need simple interventions like using proper insoles to prevent surgical interventions
References:
[1] Schmiegel A, Rosenbaum D, Schorat A, Hilker A, Gaubitz M. Assessment of foot impairment in rheumatoid arthritis patients by dynamic pedobarography. Gait & posture. 2008;27(1):110–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4445

AB0255 EVALUATION OF KINESIOPHOBIA IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

M. Aykut[1], B. Cakit[2], E. Mert[2], S. Aslan[2], E. Sahingoz[2], H. Genc[2], F.F. Ayhan[2], A. Karagoz[2]. *[1]Physical Medicine and Rehabilitation, Ankara Training and Research Hospital; [2]Physical Medicine and Rehabilitation, Ankara Training and Research Hospital, Ankara, Turkey*

Background: Fear avoidance behavior which is caused by painful injury resulting precision and extreme fear is defined as kinesiophobia. Rheumatoid arthritis (RA) is a chronic, inflammatory and systemic disease with symmetrical arthritis and visceral involvement. Ankylosing spondylitis (AS) is a chronic, inflammatory disease with involvement of the spine or peripheral joints.
Objectives: In our study, we aimed to evaluate the relationships between kinesophobia and disease activity, quality of life (QoL), level of physical activity and emotional status in RA and AS patients.
Methods: We included 42 patients with RA (8 males-M, 34 females-F) (group 1), 49 patients with AS (34 M, 15 F) (group 2) and 29 healthy controls (9 M, 20 F) (group 3) in our study. The QoL was assessed using the health assessment questionnaire (HAQ), kinesiophobia was assesed with Tampa scale of kinesiophobia (TSK), pain was assesed with visual analog scale (VAS), fatigue was assesed with VAS and emotional status was assesed with Beck depression inventory (BDI). Disease activity was assesed with Bath ankylosing spondylitis disease acitivity index (BASDAI) and functional status was assesed with Bath ankylosing spondylitis functional index (BASFI) in patients with AS. Disease activity was assesed with DAS28 in patients with RA.
Results: The mean age was 46.2 in group 1, 43.2 in group 2 and 40.17 in group 3. There was no difference among groups with respect to mean age ($p>0.05$). Kinesiophobia was present in 37 patients in group 1, 22 patients in group 2 and 7 patients in group 3. Statistically significant differences were found among groups

Table 1. Baseline features of the patients of AS and RA and healthy controls

	Group 1	Group 2	Group 3
Age	46,2±11,47	43,2±10,73	40,17±7,77
Gender (F/ M)	34/8	15/34	20/9
VAS*	47,02±24,42	32,44±26,75	1,72±4,68
TKS**	44,73±7,26	36±12,03	29,58±9,37
Fatigue (VAS)†	55,47±24,31	36,93±27,70	37,93±20,59
HAQ‡	0,73±0,83	0,43±0,41	0,06±0,19
BDI§	14,17±9,49	12,23±9,63	5,25±6,13

*p=0.008 between group 1 and 2; p<0.001 between group 2 and 3; p<0.001 between group 1 and 3. **p<0.001between group 1 and 2; p=0.023 between group 2 and 3; p<0.001 between group 1 and 3. †p<0,05 between group 1 and 2; 2 and 3; 1 and 3. ‡p=0.039 between group 1 and 2; p=0.021 betwen group 2 and 3; p<0.001 between group 1 and 3. §p>0.05 between group 1 and 2; p=0.004 betwen group 2 and 3; p<0.001 between group 1 and 3.

with respect to the number of patients with kinesiophobia and to mean scores of pain intensity, fatigue, HAQ and BDI (p<0,05-<0,001). Patients with RA had higher rates of kinesiophobia than patients with AS and healthy controls (p=0.001, p=0,001). Patients with RA had worser scores than patients with AS and healthy controls. Patients with AS had worser scores than healthy controls. In patients with RA and AS, kinesiophobia is associated with pain severity, fatigue, emotional status and QoL.

Conclusions: In our study, patients with RA and AS had higher rates of kinesiophobia. We found that kinesiophobia was related with pain severity, fatigue, depression, disease activity and QoL of the patients. The QoL can be improved through controlling kinesiophobia by reducing pain, depression and fatigue.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6163

AB0256 SERUM AND SYNOVIAL KYNURENIC ACID CONCENTRATION AND ITS CORRELATION WITH DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: CLINICAL AND ULTRASONOGRAPHIC STUDY

F. Elshabacy[1], T. Fathy Mohammed[1], M.A. Mortada[2], H.A. EL-Saadany[3], S.M. Farouk[4], E.R. Amer[4]. *[1]Rheumatology, Benha Teaching Hospital, Benha; [2]Rheumatology & Rehabilitation, Zagazig University, Zagazig; [3]internal medicine and Rheumatology, Military Medical Academy, Cairo; [4]Clinical Pathology, Benha Teaching Hospital, Benha, Egypt*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease. kynurenic acid has anti-inflammatory effects, because it is the most important agonist of the orphan G-protein-coupled receptor (GPR35) which expressed on various types of cells associated with the immune system. Stimulation of these receptors by kynurenic acid lead to reduction in the synthesis of proinflammatory cytokines, nitric oxide, and reactive oxygen species (1).

Objectives: Detection and quantification of kynurenic acid in serum and synovial fluid obtained from the affected joints in patients with rheumatoid arthritis and its relation to different clinical aspects of disease activity and signs of synovitis and synovial hyperplasia detected by musculoskeletal diagnostic ultrasound.

Methods: Thirty RA patients diagnosed according to ACR and EULAR revised criteria and thirty patients of idiopathic knee osteoarthritis as a control group were enrolled in the study. These patients were collected from outpatient clinic of rheumatology department Benha Teaching Hospital. Kynurenic acid was assessed in Serum samples from all patients and controls coupled synovial fluid samples aspirated from knee joint of all RA patients and fourteen OA patients after musculoskeletal ultrasonographic examination of these joints.

Results: Serum and synovial level of kynurenic acid was assessed in the studied groups. Comparison between RA and OA patients as regard serum kynurenic acid showed no differences where it's level was *29.80±13.86 pg/ml in RA versus 30.98±11.03 pg/ml in OA patients)*, while synovial kynurenic acid was significantly lower in RA 16.38±6.45 pg/ml than in OA patients 26.22±2.99 pg/ml ($p<0.001$). kynurenic acid was significantly lower in synovial fluid (16.38±6.45 pg/ml) than in serum (29.80±13.86 pg/ml) in RA group of patients ($p<0.001$). Comparison among different grades of synovitis detected by grey scale U/S and by Doppler signals in RA patients as regard synovial kynurenic acid showed that it was significantly lower in higher grades of synovitis ($P<0.001$). Synovial kynurenic acid level was negatively correlated with grades of synovitis and Doppler signals ($p<0.001$).

Conclusions: The negative correlation between Kynurenic acid concentration in the synovial fluid and both the synovial thickness detected by ultrasonography and the hyperaemia of synovial tissues as represented by the Doppler activity, may support its use as a local marker of the two faces of rheumatoid arthritis (chronicity and activity) at the joint level.

To the best of our knowledge, this is the first study that gives correlation between the serum and synovial levels of kynurenic acid concentrations and the grade of synovitis detected by grey scale and Doppler ultrasonography.

References:

[1] Tistzlavicz Z, Nemeth B, Fulop F et al (2011). Naunyn Schmiedebregs Arch Phrmacol; 383(5):447–55.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2198

AB0257 SCREENING OF DIFFERENTIALLY EXPRESSED SERUM PROTEINS FOR RHEUMATOID ARTHRITIS BY SURFACE-ENHANCED LASER DESORPTION/INIONATION-TIME OF FLIGHT-MASS SPECTRA

N. Liang, L. Zhang, K. Xu. *Shanxi academy of medical sciences Shanxi dayi hospital, TaiYuan, China*

Background: RA is a chronic inflammatory rheumatic disease, and early diagnosis and treatment can improve prognosis[1].Surface-enhanced laser parsing ionization/time of flight mass spectrometry (SELDI-TOF-MS) combining a protein chip and mass spectrometry technology own the advantages of low dosage of samples, direct point sample detection and high sensitivity.

Objectives: SELDI used to profile and compare the proteomes in serum samples of RA patients including complicated with Sjogren's syndrome (SS), interstitial lung disease (ILD). Using Biomarker Wizard software and Biomarker Pattern Software established diagnostic model, and calculate sensitivity and specificity,which can simplify clinical procedures, save medical costs and explore the pathogenesis.

Methods: Using the Biomarker Wizard and Biomarker Pattern software to establish the diagnosis prediction model to predict RA disease progression between the following groups, including simple RA patients (n=44) and RA-SS patients (n=18), RA patients (n=44) and RA-ILD (n=22), RA patients (n=44) and RA-ONFH (n=6). Also 96 RA patients and 77 healthy control, which were randomly allocated to the training set (83 RA patients and 56 healthy controls) and test set (14 RA patients and 20 healthy controls)to develop and verify a pattern by means of decision treealgorithm.

Using the Biomarker Wizard and Biomarker Pattern software to establish the diagnosis prediction model to predict RA disease progression between the following groups, including simple RA patients (n=44) and RA-SS patients (n=18), RA patients (n=44) and RA-ILD (n=22). Also 96 RA patients and 77 healthy control, which were randomly allocated to the training set (83 RA patients and 56 healthy controls) and test set (14 RA patients and 20 healthy controls)to develop and verify a pattern by means of decision treealgorithm.

Results: 1. Comparison of RA patients and healthy controls: there are 22 up-regulated expression in RA, 36 down-regulated. The diagnostic model of M/Z3448.857,4716.712,8214.285 and 10645. The sensitivity and specificity is 91.566% and 92.857%, the area under the ROC curve was 0.937, to verify the diagnosis model, we get a sensitivity of 100% and a specificity of 95%. 2. Comparison of the simple RA and RA -ILD. The diagnostic model of M/Z10645.1, M/Z12595.86. The sensitivity and specificity is 86.4% and 84.1% and the area under the ROC curve was 0.856.3. Comparison of the simple RA and RA -SS: The diagnostic model of M/Z6635.623, M/Z33897.72. The sensitivity and specificity is 77.8% and 79.5% and the area under the ROC curve was 0.794.

Conclusions: The serum protein fingerprinting by SELDI-TOF-MS could identify new biomarkers in RA. The biomarkers may play an important role in pathogenesis of RA. We could diagnose RA in early stage, predict disease progression and determine disease activity by these biomarkers.

References:

[1] Vincent Goëb1, Marlène Thomas-L'Otellier2,et al. Candidate autoantigens identified by mass spectrometry in early rheumatoid arthritis are chaperones and citrullinated glycolytic enzymes. Arthritis Research & Therapy, 2009, 11:R38.

[2] Jr GW, Cazares LH, Leung SM, Nasim S, Adam BL, Yip TT. Protein chip surface enhanced laser desorption/ionization (SELDI) mass spectrometry: a novel protein biochip technology for detection of prostate cancer biomarkers in complex protein mixtures. Prostate Cancer Prostate Dis.1992;2:264–76.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3698

AB0258 AGE AND QUALITY OF LIFE AMONG RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BIOLOGIC AGENTS

N. Oguro, N. Yajima, Y. Miwa. *Rheumatology, Showa University School of Medicine, Nishinakanobu, Shinagawa Ward, Tokyo, Japan*

Background: Rheumatoid arthritis (RA) is a common autoimmune disease of unknown etiology which is characterized by symmetric, chronic inflammatory, peripheral polyarthritis. If it is untreated or unresponsive to therapy, inflammation and joint destruction lead to loss of physical function, inability to carry out daily tasks of living.

In addition to problems related to pain and inflammation, patients with RA are also affected by psychological problems such as anxiety and depression.

It has been a while since, the biologic agents have let RA patients to early remmision, and improved their Quality of life (QOL).

A few studies show relevance between age and QOL among RA patients. Lambert et al. found that age was positively correlated with pain, indicating that increasing age made the situation worse.

Objectives: This study aimed to assess the relationship between age and QOL of RA patients who has been treated with biologic agents.

Methods: 149 RA patients who treated with biologic agents at Showa University Hospital, Showa University Northern Yokohama Hospital and Showa University Koto Toyosu Hospital were recruited from 2005 to 2016. This study design was retrospective cohort study. Loss to follow-up was eliminated. The patients were divided into two groups, whose age was 65 years old and over (elderly) and under 65 (adults). The primary outcome was the change of QOL in 6months'. QOL was measure using SF-36, and we use physical component scale (PCS) and mental component scale (MCS). Logistic regression analysis was performed.

Results: Among 149 RA patients, the mean age was 57 years old and 85.9% was female. 92 out of 149 patients (61.7%) were adult group and 57 (38.3%) were elderly group. Adjusted with sex, disease duration, DAS28-ESR, HAQ, and with or without complications which are interstitial lung disease, diabetes mellitus, and chronic kidney disease, there was no significant difference in change of MCS in 6 months'. But those of PCS was significantly higher in adult's group (regression coefficients -7.25; 95% Confidence Interval (CI) -11.7 to -2.77; $p=0.0018$).

Conclusions: There is a possibility that, younger patient who suffers with RA could achieve better quality of life than those of elderly patients after treatment with biologic agents.

Table1.

		Total (n=149)	Adults (n=92)	Elderly (n=57)
Age	mean(SD)	57(15.4)	47(12.2)	71(5.63)
Female	n(%)	128 (85.9)	77 (83.7)	51 (89.4)
Disease duration (year)	mean(SD)	8.4(10.0)	7.1(7.55)	10(12.9)
DAS28 ESR	mean (SD)	4.74(1.37)	4.54(1.38)	5.08(1.30)
HAQ	mean (SD)	0.61(0.66)	0.49(0.56)	0.78(0.76)

Table2.

	regression coefficient	95%CI	*p* value
Adults	reference	–	–
Elderly	-7.24	-11.7 to -2.7	0.0018

Multiple liner regression analysis
Adjuseted with sex, disease duration, DAS28-ESR, HAQ, and complications (interstitial lung disease, diabetes mellitus, and chronic kidney disease).

References:
[1] Izabela Roma (2014) Quality of life and elderly patients with rheumatoid arthritis, Rev Bras Reumatol 2014;54(4):279–286.
[2] ULF Jakobsson (2002) Pain and quality of life among a older people with rheumatoid arthritis and/or osteoarthritis, Journal of clinical Nursing 2002;11;430–443.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4708

AB0259 PREDICTORS OF HIGH DISEASE ACTIVITY IN A COHORT OF GREEK PATIENTS WITH ACPA POSITIVE EARLY RHEUMATOID ARTHRITIS

N. Papadopoulos[1], A. Gkagkalis[2], E. Konstantinidou[3], L. Mentesidou[1], G. Tzatzagou[4], V. Galanopoulou[1]. *[1]Rheumatology Unit; [2]Gastroenterology Unit, Papageorgiou General Hospital; [3]Molecular Biologist, PRIVATE; [4]1st INTERNAL MEDICINE CLINIC, Papageorgiou General Hospital, Thessaloniki, Greece*

Background: In Early Rheumatoid Arthritis, the presence of ACPA positivity is associated with increased disease activity.
Objectives: To investigate possible predictors, for high disease activity (DAS-28 >5.1), in a cohort of Greek patients with ACPA positive early RA.
Methods: From 2000 until December 2016, 156 patients with ACPA positive early RA, were diagnosed and subsequently followed up as outpatients at the Rheumatology Unit of our hospital. Demographic, clinical, laboratory and therapeutic parameters were evaluated during every follow-up. At the end of the study (last visit during 2016), all the above parameters were re-evaluated, considering the high disase activity (DAS-28 >5.1). The used methods were χ^2, ANOVA, Binary Logistic Regression (BLR) and ROC Curve.
Results: From 156 patients, 25% were males, 37.8% were current smokers, 76.9% were RF positive, 34.6% presenting with extra-articular manifestations and 16% with anemia of chronic disease (ACD). At the time of diagnosis, Univariate analysis revealed that smokers, RF positivity, high levels of CRP, patients with extra-articular manifestations and those with ACD, corellate statstically significant with high disease activity (p=0.011, p=0.006, p=0.03, p=0.001 and p=0.001 respectively). Using the BRL we found that the odds ratio for DAS-28 >5.1, were for smokers 2.95, for RF positivity 3.397 and for CRP 1.066 respectively. Based on the previous results the severity of disease can be predicted with sensitivity 80% (area unedr the curve: p<0.001, CI=0.723–0.878) using the ROC curve.
Conclusions: |High Diseasae Activity in ACPA positive early RA, at diagnosis, is best predicted by smoking, RF positivity and high levels of CRP.
References:
[1] Aletaha D et al, Rheum Dis North Am 2006;32:9–44.
[2] ScottDL et al, Lancet 2020;376:1094–1108.
[3] Papadopoulos N et al, Clin Rev Allerg Immunol 2008;34:11–15.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6763

AB0260 THE PREDICTORS OF FRAGILITY FRACTURES IN PATIENTS ON AROMATASE INHIBITORS: AN OBSERVATIONAL STUDY

N. Meah[1], R. Sinha[2], M. Bukhari[2]. *[1]Lancaster Medical School; [2]Rheumatology, Royal Lancaster Infirmary, Lancaster, United Kingdom*

Background: The use of aromatase inhibitors (AIs), given after breast cancer, has been associated with a low bone mineral density (BMD) and as a risk factor for fragility fractures. We have reported on the risk factor for low BMD in a previous abstract and it showed that the use of AIs significantly reduced lumbar spine BMD and femoral neck BMD (1). The FRAX ™ tool uses the femoral neck BMD to predict fractures on a population basis but ignores the lumbar spine. Some patients who have undergone bilateral hip replacements would not be able to estimate their FRAX ™ risk accurately.
Objectives: To determine the predictors of fragility fractures in an observational cohort of female patients on aromatase inhibitors.
Methods: Female patients referred for BMD estimation in a scanner in the North West of England between 2004 and 2014 on aromatase inhibitors were identified from a dual X-ray absorptiometry database. Demographics and other risk factors, as well as fragility fractures, were recorded. Initially, those who had sustained a fracture were compared to those who had not sustained a fracture using chi-squared tests for categorical variables and T-tests for continuous variables. Following that, univariate and multivariate logistic regression models were fitted looking at the predictors of fracture. Variables included age at scan, height, weight, alcohol, smoking, family history, rheumatoid arthritis, secondary osteoporosis as defined by FRAX™, body mass index and steroid exposure, in addition to BMD in the lumbar spine and femoral neck.
Results: 2029 female patients were scanned in the referral period. The mean age at scan was 66 (SD 10.46). 356/2029 (17.55%) had sustained a fracture. Results of the univariate analysis are shown in table 1, significant predictors are indicated with an asterisk (*).

Predictor	All Pts	Pts with Fracture	Pts without Fracture	p-value	Odds ratio (95% CI)
Age at scan (years)	65.85	69.41	65.09	0.00	1.04 (1.03,1.05)*
Height (cm)	160.40	159.60	160.57	0.02	0.98 (0.96,1.00)*
Weight (kg)	72.38	71.35	72.60	0.15	1.00 (0.99,1.00)*
Alcohol	123 (6.06%)	22 (6.18%)	101 (6.04%)	0.92	1.03 (0.64,1.65)
Smoking	698 (34.40%)	132 (37.08%)	566 (33.83%)	0.24	1.15 (0.91, 1.46)
Family Hx	247 (12.17%)	48 (13.48%)	199 (11.89%)	0.41	1.15 (0.82,1.62)
RA	32 (1.58%)	10 (2.81%)	22 (1.32%)	0.04	2.17 (1.02,4.62)*
Secondary op	183 (9.02%)	46 (12.92%)	137 (8.19%)	0.01	1.66 (1.17,2.37)*
Femoral Neck BMD (g/cm^2)	0.87	0.82	0.88	0.00	0.02 (0.01,0.05)*
Lumbar Spine BMD (g/cm^2)	1.10	1.05	1.12	0.00	0.12 (0.06,0.24)*
BMI (kg/m^2)	28.13	28.00	28.16	0.61	0.99 (0.97,1.02)
Steroid	466 (22.97%)	77 (21.63%)	389 (23.25%)	0.51	0.91 (0.69,1.20)

In the multivariate model, the variables that predicted fractures in this cohort were age at scan (OR 1.03 95% CI 1.02,1.05), femoral neck BMD (OR 0.74 95% CI 0.02,0.29) and lumbar spine BMD (OR 0.34 95% CI 0.14,0.80). Using the femoral neck multivariate model resulted in an area under the curve of 0.6720 and using the lumbar spine was 0.6653.
Conclusions: In the univariate analysis, many risk factors are associated with fractures within this cohort of female patients on aromatase inhibitors but both univariate analysis and multivariate analysis showed that lumbar spine BMD is a good predictor of fractures. This is not included in the FRAX ™ tool and would enable fracture risk to be calculated in patients who have undergone hip replacements.
References:
[1] Ann Rheum Dis 2014;73 Suppl3 SAT0472.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1406

AB0261 CLINICAL AND STRUCTURAL RESPONSES OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS (RA) USING STEP-UP DOSAGES OF TOFACITINIB IN A TREAT TO TARGET APPROACH

N.B. Gaylis[1], J. Sagliani[1], S. Needell[2]. *[1]Arthritis and Rheumatic Disease Specialties, Aventura; [2]Boca Radiology, Boca Raton, United States*

Background: Tofacitinib has been shown to reduce the clinical signs and symptoms of some RA patients at an approved dose of 5 mg bid. Studies report that 10 mg bid is an effective dose. This is the first community practice trial to measure the clinical and structural benefits of stepping up the initial dose of 5 mg bid in non-responders to 10 mg bid in order to achieve a clinical response using a treat to target approach.
Objectives: This study evaluates the optimal dose of tofacitinib (5 mg bid VS 10 mg bid) needed to reach treatment target in a cohort of patients with active RA while comparing the corresponding structural findings measured by low field MRI.
Methods: 20 RA patients who were unresponsive to either methotrexate (10–25 mg weekly) or MTX plus up to 2 prior biologics with synovitis, osteitis or erosions on Baseline MRI (Esaote 0.3T) were treated with 5 mg bid tofacitinib with a treat to target goal of Low Disease Activity (LDA) or remission depending on the Clinical Activity Index (CDAI) score at Baseline. If the target was not met and sustained for 3 months, the dose of tofacitinib was increased to 10 mg bid in an attempt to reach target. MRIs of the hand/wrist were blindly read by a musculoskeletal radiologist using a rheumatoid arthritis MRI scoring system (RAMRIS). A CDAI score of >10 was needed at study entry.
Results: Of the 20 enrolled patients, 6 remained at 5 mg bid and 14 were dose escalated to 10 mg bid most at the 12 week period. Of the 5 mg bid group, 3 completed the trial at target and 3 early termed (ET) for lack of efficacy, relocation and AE. Structurally, there was no change in erosions in all 3 patients; 2 showed regression of synovitis and 1 showed no change; 2 showed regression in osteitis and 1 no change. Of the 14 patients escalated to 10 mg bid, 11 completed the trial with 7 remissions, 2 at LDA, and 1 at MDA. 3 patients ET due to lack of efficacy. In the 10 mg bid group, 9 patients showed no change in erosions, 1 regression and 1 progression. 5 patients showed no change in synovitis and 6 showed regression, and 7 showed no change in osteitis, 3 showed regression and 1 showed progression. The CRP values correlated with the improvement of

the clinical and structural results, in particular, the levels improved after the dose was increased to 10 mg bid.

Patient	CDAI BSL	CDAI 3 Mnth All taking 5 mg bid	CDAI 12 Mnth Remain on 5 mg bid	CDAI 12 Mnth Dose Increased 10 mg bid
001	24.9	0.6	6	
002	56.1	20.9		2.7
003	45.9	27.4		2.3
004	65.2	33.8		0
005	56.1	15.5		3.1
006	34.7	38.9		19.4
007	27.9	56		1.5
008	34.3	18.4		1.8
009	43.6	3.3	2.3	
010	33.5	12.6		ET
011	32.7	5.1	ET	
012	25.3	13		0
013	21.2	2.4	ET	
014	21.6	9.9		2.9
015	21.6	5.2		ET
016	27.7	0.4	ET	
018	31.8	16.9		2.1
019	27.3	0.9		5.2
020	14.5	5.2		ET
021	30.5	2.1	1.9	

Conclusions: Our results suggest that a significant number of patients treated with the standard dose of 5 mg bid may potentially have improved outcomes including LDA or remission when treated at a higher dose (10 mg bid). As is evidenced by the results in this study, 11 of the 14 patients had significant improved response after treatment with the step up dose. It would appear that this improved result occurs by 3 months of therapy. Furthermore, the structural findings correlate in large part to the clinical findings showing stabilization or improvement in the majority of patients. A larger study is needed to validate these clinical and structural responses as well as to evaluate the safety outcomes using 10 mg bid for intervals of more than 12 months.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1806

AB0262 EVALUATION OF PATIENT REPORTED OUTCOME USING RAPID3 AND HAQ-DI COMPARED TO DAS28: EXPERIENCE FROM ROUTINE CLINICAL PRACTICE IN MALAYSIA

N. Mohd Jamid[1], B. D'Souza[1], H.C. Hong[1], N. Mohd Noor[1], C.K. Cheah[1], Y.L. Lee[2], S.C. Gun[1]. *[1]Hospital Tuanku Jaafar, Seremban; [2]PFIZER, Kuala Lumpur, Malaysia*

Background: Patient reported outcome (PRO) is an important measure to physician in management of patient with rheumatic diseases. Health assessment questionnaire disability index (HAQ-DI) is the most widely used PRO tool in rheumatoid arthritis (RA) clinical trials. Previous studies have shown that HAQ-DI correlates well with disease activity score of 28-joints (DAS28). However, routine assessment of patient index data 3 (RAPID3) is much simpler and faster questionnaire to score.

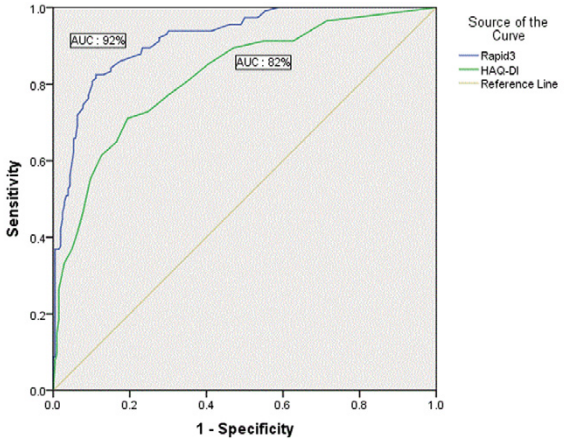
Objectives: This study aims to evaluate the correlation between RAPID3 and DAS28 compared to HAQ-DI and DAS28 in our population.

Methods: RA patients who received routine treatment in Hospital Tuanku Ja'afar from March to November 2016 were included in this study. Validated RAPID3 and HAQ-DI questionnaire were made available in other languages; Malay, Chinese and Tamil, for patients who were not English literate. Descriptive analysis were conducted. Pearson correlation was used to measure the correlation between these PRO tools while area under the curve of the receiver operating characteristic (ROC) curves evaluate the sensitivity to detect disease activity. DAS28-ESR and DAS28-CRP were used as the reference variable in ROC analysis to stratified the disease activity into two groups; low (remission and low) and high (moderate and high) disease activity.

Results: A total of 400 patients completed PRO assessments were available for analysis. The median age of our cohort was 57 years old (range 22 to 88) and 87.5% were female. Ethnic distribution in this cohort were as follows; 38.5% Indian, 31.8% Malay and 27.8% Chinese. Both RAPID3 ($r=0.74, p<0.001$) and HAQ-DI ($r=0.57, p<0.001$) were correlated with DAS28-ESR. The area under the curve was significantly higher in RAPID3 (83%) compared to HAQ-DI (75%) which implied greater performance in discriminating low and high disease activity using DAS28-ESR as reference. We observed similar performance trend between RAPID3 (92%) and HAQ-DI (82%) compared to DAS28-CRP.

Conclusions: In conclusion, RAPID3 is an effective quantitative measure of disease activity compared to HAQ-DI in our population. Furthermore, RAPID3 yield similar disease activity categories as DAS28 without the need of joint counts

ROC Curve to discriminate low and high disease activity using DAS28CRP as reference.



and laboratory tests. Hence is an informative assessment of disease activity in busy clinic settings.

References:

[1] Patient Reported Outcome in Rheumatoid Arthritis Clinical Trials. Ana-Maria Orbai, Clifton O. Bingham III. Current Rheumatology Reports. 2015 Apr;174(4):501.

[2] RAPID3 (Routine Assessment of Patient Index Data) on an MDHAQ (Multidimensional Health Assessment Questionnaire): Agreement with DAS28 (Disease Activity Index) and CDAI (Clinical Disease Activity Index) Activities Categories, Scored in Five Versus More Than Ninety Seconds. T. Pincus, C.J. Sweringen, M.J. Bergman, C.L. Colglazier, A.T. Kaell, A.M. Kunath, E.L. Siegel, Y, Yazici. Arthritis Care Res 2010;62:181.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2166

AB0263 PREDICTIVE VALUE OF A SINGLE MEASUREMENT OF THE MULTI-BIOMARKER DISEASE ACTIVITY (MBDA) SCORE FOR DISEASE FLARES WITHIN 6 AND 12 MONTHS IN RHEUMATOID ARTHRITIS PATIENTS USING TUMOR NECROSIS FACTOR INHIBITORS AND CONVENTIONAL SYNTHETIC DMARDS

P.M.T. Klooster[1], M. Ghiti-Moghadam[1], F. Lamers-Karnebeek[2], H. Vonkeman[3], E. Sasso[4], P.V. Riel[2], M.V.D. Laar[3], T.L. Jansen[5]. *[1]Rheumatology, University of Twente, Enschede; [2]Rheumatology, Bernhoven hospital, Uden; [3]Rheumatology, Medical Spectrum Twente, Enschede, Netherlands; [4]Medical&Scientific Affairs, Crescendo Bioscience, SanFrancisco, United States; [5]Rheumatology, VieCuri MC, Venlo, Netherlands*

Background: Rheumatoid Arthritis (RA) patients in the maintenance phase should be treated by escalating antirheumatics up to stable low disease activity and then often are treated with tumor necrosis factor inhibitors (TNFi) and conventional synthetic disease modifyers (csDMARD). Once this phase has been reached the risk of flare is an issue once drugs are to be tapered or discontinued.

Objectives: To examine the ability of the multi-biomarker disease activity (MBDA) score as predictor for disease flare in rheumatoid arthritis (RA) patients with stable low disease activity using tumor necrosis factor inhibitors (TNFi) and conventional synthetic disease modifyers (csDMARD).

Methods: Data were used from the continuation control group of the Dutch multicenter, open-label, POET trial, in which patients with stable low disease activity (disease activity score [DAS28] <3.2 for at least 6 months] were randomized to either stop or continue TNFi treatment. Three indicators of disease relapse were assessed: 1) flare based on DAS28 (DAS28 ≥ 3.2 with ΔDAS28 >0.6), 2) flare based on escalation of any DMARD therapy, and 3) flare based on physician-reported disease activity. Associations between baseline MBDA score and meeting the different criteria for disease flare within 6 or 12 months of follow-up were examined using univariate analysis and multivariate logistic regression adjusting for baseline DAS28 score.

Results: For this post-hoc analysis, baseline serum samples to measure MBDA scores were available for 225/286 (78.7%) of the patients randomized to the TNFi continuation group (88.9% also used methotrexate, another 8.0% used another csDMARD and 3.1% used no csDMARD): 86.2% with a first TNFi, 11.6% with second TNFi and 2.2% with a third TNFi. Within 12 months, 19.1% of patients had experienced a DAS28 flare, 12.0% had medication escalation and 8.0% had ≥ 1 physician-reported flare. Median time to DAS28-based flare was 26 weeks (IQR:13–28). Univariately, patients with high baseline MBDA (>44) scores (n=31) were at increased risk of experiencing a DAS28 flare within 6 (OR =4.39, P=0.001) or 12 (OR =2.78, P=0.015) months. MBDA scores were not associated with increased risk of medication escalation or physician-reported flare. After adjustment for baseline DAS28 scores, high MBDA score remained predictive for risk of flare within 6 months (OR =3.15, P=0.017), but not for flare within 12 months (OR =2.05, P=0.107).

Conclusions: MBDA score may be of additional value in predicting DAS28 flares but not in predicting medication escalations or physician-reported flares in RA patients on TNFi in stable low disease activity.
Acknowledgements: We wish to acknowledge all POET investigators and all who gave their contributions to the POET project.
Disclosure of Interest: P. M. Klooster: None declared, M. Ghiti-Moghadam: None declared, F. Lamers-Karnebeek: None declared, H. Vonkeman: None declared, E. Sasso Shareholder of: Myriad Genetics, Employee of: Crescendo Bioscience, P. Riel: None declared, M. Laar: None declared, T. L. Jansen: None declared
DOI: 10.1136/annrheumdis-2017-eular.4998

AB0264 THE PERFORIN A91V GENE AND CLINICAL FEATURES ANALYSIS IN CHINESE SO-JIA CASES WITH MACROPHAGE ACTIVATION SYNDROME

P. Wei[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: Macrophage activation syndrome (MAS) is a severe, potentially fatal complication of rheumatoid disease, especially in the systemic onset juvenile idiopathic arthritis (SoJIA). we aimed to investigate the clinical characteristics of 31 SOJIA cases with MAS and the perforin A91V gene were detected in part cases
Methods: gene-specific polymerase chain reaction (PCR) primers were used to analyze the perforin A91Vgene polymorphism.
Results: 31 soJIA cases were associated with MAS.25 out of 31 cases (83%) had infections prior to MAS. Serum ferritin was significantly increased in 27 cases (87.10%). High concentrations of triglycerides (23cases, 74.19%) and lactic dehydrogenase (27cases, 87.10%) are observed. What is more, Creatine Kinase (CK) increased in all cases that had been checked. Well-differentiated macrophages phagocytosing hematopoietic elements were found in all cases (100%).6 cases (19.35%) merged with multiple organ dysfunctions (MODS). The perforin A91V (NCBI: SNP rs35947132) variant gene was detected in twenty cases, but no mutation was found. Corticosteroids, immunosuppressant, cell cycle inhibitors, immunoglobulin, Tumor necrosis factor (TNF) antagonist and plasmapheresis were effective. After treatment, 28cases (90.32%) children were in remission, while 3 out of 31 cases died with mortality of 9.68%.
Conclusions: MAS is a life-threatening complication of systemic onset juvenile idiopathic arthritis. Most cases were preceded by infection. Unremitted fever, progressive hepatosplenomegaly, lymphadenopathy, cytopenias, elevated serum liver enzymes significantly increased serum ferritin are the main feature. Early diagnosis and treatment is the key to improve prognosis. The perforin gene mutations in our patients have not found yet.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2061

AB0265 THE SIGNIFICANCE OF EARLY DIAGNOSIS AND PROGNOSTIC EVALUATION OF FOUR KINDS OF ANTI-CCP ANTIBODIES IN VARIOUS TYPES OF JUVENILE IDIOPATHIC ARTHRITIS

P. Zeng[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: To investigate the relationship between immunological parameters AKA, anti - CCP, the RF- IGG, RF-IGM and the early diagnosis and prognosis in sub- JIA patients.
Methods: Collection of 76 JIA patients in our hospital with system treatment and adhere to the follow-up treatment for at least six months, detect the immunological parameters of AKA, anti- CCP, RF-IGG, RF-IGM in the early diagnosis, compare the Positive rate in different subtypes and prognosis, and make the statistical analysis of sensitivity, specificity and relevant risk, compare to the normal control group of blood of 49 healthy children.
Results: There is a significant difference between polyarticular group and normal control group in positive rate of AKA, anti-CCP, RF-IGG, RF-IGM, there is no significant difference between the type of systemic, oligoarticular, enthesitis and the normal control group in autoantibody-positive detection rate. Polyarticular group's sensitivity AKA > anti-CCP, RF-IGG > RF-IGM and four kinds of joint detection, specificity RF-IGM, four kinds of joint detection > AKA > RFIGG > anti-CCP. There is a significantly different between refractory JIA and general JIA patients in AKA positive rate, relative risk OR is 3.514%.
Conclusions: The effect of AKA, anti-CCP, RF- IGG, RF-IGM in the different subtypes of JIA about early diagnosis are different, it is found that AKA, anti-CCP has good sensitivity and specificity in polyarticular JIA, AKA appears relate with refractory JIA, it is a large sample of the study to be confirmed that whether it can be a serological marker in the early diagnosis and prognosis of Polyarticular JIA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2054

AB0266 EFFECTS OF PERIODONTAL BASIC TREATMENT ON PERIODONTAL CONDITION,CLINICAL RESPONSE AND SERUM INFLAMMATORY PARAMETERS IN RHEUMATOID ARTHRITIS (RA) PATIENTS WITH MODERATE TO SEVERE PERIODONTITIS

F. Xiao, P. Zhang, X. Li, Y. Mou, H. Chen, Y. Cai. *The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China*

Background: Periodontal disease (PD) shares several clinical and pathogenic characteristics with Rheumatoid Arthritis (RA). Some intervention studies have suggested that periodontal treatment can reduce serum inflammatory biomarkers such as C-reactive protein, or erythrocyte sedimentation rate. Periodontal diseases are not only a threat to dentition, but may also be an aggravating factor in patients with RA, its treatment may improve the RA outcomes.In this study we assessed the effect of periodontal basic therapy in relieving the PD symptoms and the clinical signs of RA in order to evaluate the importance of periodontal treatment in the control of inflammation.
Objectives: To evaluate the effects of periodontal basic treatment on periodontal condition, clinical response and serum inflammatory parameters in RA patients with moderate to severe periodontitis.
Methods: A total of 46 subjects with confirmed diagnosis of RA and moderate to severe periodontitis were included in the study. 18 subjects completing the study received periodontal basic treatment consisting of scaling/root planing and oral hygiene instruction at baseline and at 6 weeks; 28 subjects completing the study received no treatment as control group. Participants continued their usual disease-modifying medications for RA without any changes in DMARD therapy during the study period. Periodontal indices and RA measurements, such as probing depth (Pd), clinical attachment level (CAL), bleeding on probing (BOP), high-sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), disease activity score in 28 joints (DAS28) and subjective symptom were recorded at baseline, 6 and 12 weeks for each participant.
Results: After periodontal basic treatment,significantly lower Pd, CAL and BOP were observed in the treatment group ($P<0.01$),hsCRP,ESR,DAS28 and patients' subjective symptom improved significantly ($p<0.05$).Besides,the Pd and BOP were statistically significant between treatment subjects after therapy and controls ($P<0.001$).Although hsCRP was significantly lower in the treatment group after therapy than controls ($P<0.01$),there was no significant difference in the DAS 28 level between the two groups after periodontal basic therapy ($P>0.05$). Visual analog scale (VAS)was used to evalue patients' subjective symptom,the results show that the improvement was much better in patients received periodontal therapy than controls ($P<0.001$).
Conclusions: Periodontal basic treatment can effectively improve periodontal status, patients' subjective symptom and circulating inflammatory status.
References:
[1] Al-Katma MK, Bissada NF, Bordeaux JM, Sue J, Askari AD.Control of periodontal infection reduces the severity of active rheumatoid arthritis.J Clin Rheumatol. 2007 Jun;13(3):134–7.
[2] Ortiz P, Bissada NF, Palomo L, Han YW, Al-Zahrani MS, Panneerselvam A, Askari A.Periodontal therapy reduces the severity of active rheumatoid arthritis in patients treated with or withouttumor necrosis factor inhibitors.J Periodontol. 2009 Apr;80(4):535–40.
[3] Calderaro DC, Corrêa JD, Ferreira GA, Barbosa IG, Martins CC, Silva TA, Teixeira AL.Influence of periodontal treatment on rheumatoid arthritis: a systematic review and meta-analysis.Rev Bras Reumatol. 2016 Nov 26. pii: S0482–5004(16)30144–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6098

AB0267 TREATMENT PARADIGMS IN REAL-WORLD PRACTICE: BIOLOGIC AGENT USE PRIOR TO AND AFTER DISCONTINUATION OF ABATACEPT IN THE ACTION STUDY

R. Alten[1], H.-M. Lorenz[2], X. Mariette[3], H. Nüßlein[4], M. Galeazzi[5], F. Navarro[6], M. Chartier[7], Y. Elbez[8], C. Rauch[9], M. Le Bars[7]. *[1]Schlosspark-Klinik University Medicine, Berlin; [2]University Hospital, Heidelberg, Germany; [3]Université Paris-Sud, Paris, France; [4]University of Erlangen-Nuremberg, Nuremberg, Germany; [5]University of Siena, Siena, Italy; [6]Hospital Universitario Virgen Macarena, Seville, Spain; [7]Bristol-Myers Squibb, Rueil-Malmaison; [8]Excelya, Boulogne-Billancourt, France; [9]Bristol-Myers Squibb, Munich, Germany*

Background: ACTION is a 2-year, observational study of patients (pts) with moderate-to-severe RA who initiated IV abatacept (ABA) in Canada and Europe (NCT02109666).
Objectives: To determine pt biologic (b)DMARD use prior to initiation and after discontinuation of ABA overall and by treatment line in ACTION.
Methods: Pts with RA initiated IV ABA as first- or second-/further-line therapy. Biologic-naïve and biologic-failure pts were enrolled during three periods between May 2008 and December 2013. Pts could switch administration routes (IV to SC) during treatment. Crude retention rates (Kaplan–Meier) were compared by log-rank test.
Results: Of the 2364 pts enrolled, 2350 were evaluable for analysis: 673 (28.6%) were biologic naïve and 1677 (71.4%) biologic failures. Baseline characteristics differed: biologic-failure pts had longer RA duration, higher CRP levels and prevalence of radiographic erosions, and lower rates of chronic obstructive

pulmonary disease and neoplasms vs biologic-naïve pts. Most biologic-failure pts (96.7%) had previously received ≥1 TNF inhibitor (TNFi): 48.7% had received 1 and 48.0% ≥2 TNFi; 56.6% had received ≥2 bDMARDs. The overall 2-year retention rate was 47.9% and was higher for biologic-naïve vs biologic-failure pts (54.5 vs 45.2%; p<0.001); the most common reasons for ABA discontinuation were inefficacy (61.4 vs 67.7%) and safety (21.3 vs 21.2%). In pts who discontinued ABA, 83.0% started a bDMARD ≤6 months after discontinuation (Table), most commonly ABA IV. Mean (SD) days from stopping ABA to starting a bDMARD was similar for biologic-naïve (93.4 [51.3]) and biologic-failure pts (93.6 [48.0]). Among pts who restarted ABA, 62 (80.5%) biologic-naïve and 158 (85.0%) biologic-failure pts were considered to have discontinued as the time from last dose was >84 (IV) or >28 (SC) days, and thus were no longer temporary discontinuations, as predefined in the protocol. Three pts discontinued for bad compliance, 3 for lack of efficacy, 3 for remission/major improvement, 12 for safety and 15 for surgery. A good/moderate EULAR response was achieved by 76.7% of pts at the last follow-up before ABA discontinuation and 58.3% at ABA restart; mean (SD) DAS28 (CRP) was 3.2 (1.1) and 3.8 (1.4), respectively.

	bDMARD ≤6 months after ABA discontinuation		bDMARD prior to initial ABA treatment in pts who restarted ABA
	Biologic naïve n=186	Biologic failure n=526	Biologic failure n=186
None	35 (18.8)	86 (16.3)	
Abatacept	77 (41.4)	186 (35.4)	–
IV	71 (38.2)	170 (32.3)	
SC	6 (3.2)	16 (3.0)	
TNFi	41 (22.0)	74 (14.1)	181 (97.3)
Adalimumab	10 (5.4)	12 (2.3)	108 (58.1)
Etanercept	13 (7.0)	21 (4.0)	125 (67.2)
Infliximab	7 (3.8)	13 (2.5)	55 (29.6)
Certolizumab	7 (3.8)	17 (3.2)	5 (2.7)
Golimumab	4 (2.2)	11 (2.1)	2 (1.1)
Other bDMARD	33 (17.7)	180 (34.2)	51 (27.4)
Anakinra	1 (0.5)	4 (0.8)	5 (2.7)
Rituximab	6 (3.2)	58 (11.0)	30 (16.1)
Tocilizumab	26 (14.0)	118 (22.4)	21 (11.3)
		Data are n (%)	

Conclusions: Prior to abatacept treatment, over half of biologic-failure pts had received ≥2 bDMARDs and most had received a TNFi. After initial discontinuation (protocol defined), over one-third of pts restarted abatacept.

Disclosure of Interest: R. Alten Grant/research support from: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, H.-M. Lorenz Consultant for: AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, Speakers bureau: AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, AstraZeneca, Pfizer, Actelion, X. Mariette Grant/research support from: Biogen, Pfizer, UCB, Consultant for: Bristol-Myers Squibb, LFB, Pfizer, GSK, UCB, H. Nüßlein Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, M. Galeazzi: None declared, F. Navarro Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, Jansen, Lilly, Speakers bureau: Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, M. Chartier Employee of: Bristol-Myers Squibb, Y. Elbez: None declared, C. Rauch Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Le Bars Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.1392

AB0268 ACPA SEROPOSITIVITY AND PERIPHERAL NATURAL KILLER CELLS AS PREDICTIVE MARKERS OF CLINICAL RESPONSE TO RITUXIMAB IN RHEUMATOID ARTHRITIS PATIENTS

R.M. Ferreira, R. Fonseca, D.R. Gonçalves, F. Aguiar, T.M. Rocha, A. Bernardo, S. Pimenta, M. Bernardes, L. Costa. *São João Hospital Centre, Porto, Portugal*

Background: The efficacy of B cell-depletion therapy confirms the importance of B lymphocytes in rheumatoid arthritis's (RA) pathogenesis. Rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) are prognostic factors for a more severe disease. Others immune elements, namely natural killer (NK) cells, seems to influence RA clinical response to rituximab (RTX), but data are lacking.

Objectives: To analyze the influence of baseline status/levels of RF, ACPA and serum immunoglobulin G (IgG) level in RTX treatment. To study the effect of RTX on NK and CD19+ cells in RA patients and their association with clinical response at 6, 12 and 18 months (M).

Methods: An observational retrospective study was conducted, including all the consecutive patients with diagnosis of RA under rituximab, followed at our Rheumatology department. Demographic and clinical data were obtained by consulting the national database (Reuma.pt) and the analysis was limited until december 2016. RF, ACPA and IgG titres were evaluated at baseline. NK (CD56+CD16+) and B lymphocytes (CD19+) absolute counts were assessed by flow cytometry prior to the first RTX cycle and 6 M after. Clinical responses were assessed by DAS28 and EULAR criteria at 6, 12 and 18 M. Correlations were studied using Spearman coefficient analysis (SPSS 20.0). Significance level was set as 0.05.

Results: We included 63 RA patients (81% of women), with a mean (SD) age of 61 (10) years and a mean disease duration of 19 (10) years, 86% RF-positive and 87% ACPA-positive. Bone erosions were present in 86% of the patients. At baseline, the mean DAS28 was 5.79 (1.55). Combination therapy with methotrexate or with others cDMARDs was used in 48% and 30% of the patients, respectively; RTX monotherapy in 22% of our sample. Thirty three patients were previously exposed to other biologics. The magnitude of response was greater in ACPA-positive vs ACPA-negative patients in terms of DAS28 variation at 6, 12 and 18M (medians of 1.09 vs -0.08; 2.03 vs 0.35 and 2.10 vs 0.19; p=0.029, p=0.039 and p=0.004, respectively), without significant differences between groups in terms of initial DAS28 (5.91 (1.60) vs 5.00 (0.90), p=0.051). The presence of ACPA was also significantly associated with EULAR response at 6, 12 and 18 M (64%, 75% and 85% in ACPA-positive patients vs 25%, 16% and 25% in ACPA-negative patients; p=0.034, p=0.010 and p=0.001, respectively). Outcomes did not differ according FR status. There were no associations between the values of FR, ACPA and IgG at baseline with the clinical response (DAS28 variation). CD19+ cells depletion occurred in all patients (mean of 146.4/mm^3 at baseline vs 10.6/mm^3 at 6M). An increase of peripheral NK cells was seen at 6M (mean 231mm/3 at baseline vs 289/mm^3 at 6 M). We only have found a positive correlation between NK cells number at baseline and DAS28 variation at 6 M (r=0.35, p=0.023). There were no associations between, neither NK cells, nor CD19 cells variations at 6M with clinical response to RTX.

Conclusions: Our data suggest that ACPA seropositivity is associated with a better clinical response to RTX in RA patients. NK cells at baseline may be useful to identify early responders to RTX.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4505

AB0269 RAPID RADIOGRAPHIC PROGRESSION PROGNOSTIC FACTORS IN A LATIN AMERICAN COHORT OF RHEUMATOID ARTHRITIS

R. Gamboa-Cárdenas[1], M. Ugarte-Gil[2], F. Zevallos-Miranda[2], M. Medina-Chinchòn[2], C. Elera-Fitzcarrald[2], V. Pimentel-Quiroz[2], J. Cucho-Venegas[2], O. Sarmiento-Velasquez[2], C. Reàtegui-Solokova[1], J. Alfaro-Lozano[2], Z. Rodriguez Bellido[2], C. Pastor-Asurza[2], R. Perich-Campos[2]. *[1]Rheumatology; [2]HNGAI, Lima, Peru*

Background: Rapid Radiographic Progression (RRP) in Rheumatoid Arthritis (RA) patients predicts long-term disability (1), high related economic costs (2) and loss of working time (3). Detection of RRP predictors as a necessary tool for aggressive therapeutic interventions has been proved, but in Latin-American cohorts, no available data had been reported.

Objectives: To determine independent risk factors associated with RRP in a cohort of RA patients

Methods: A prospective analysis of RA Almenara cohort (January 2015-April 2016), 500 patients followed up with annual evaluations (background clinical/epidemiology, clinimetric, laboratory, health questionnaires and X-rays) who meet ACR 87/ACR-EULAR 2010 criteria's, older than 16 years at diagnosis,sign informed consent. Patients with overlap (except Sjögren), with active infections and/or pregnancy are excluded. Patients with at least two radiographs (baseline/final) were included. The X-rays were taken in a standardized protocol (each hand and foot). Joint damage was measured by Sharp-VDH (erosions, decreased joint space, and total scores). Radiographic Progression (RP) as a annual difference in Sharp-VDH score and RRP (>5 units in RP) were determined. A blinded rheumatologist for the RA condition read all films. Associated factors were analyzed (gender, socioeconomic level, smoking, age at diagnosis, time disease, use of biological and non-biological DMARDs, DAS 28, current steroids, HAQ/functional capacity, RF and basal SharpVDH score). Diagnosis delay and CRP were included to analyze risk factors in the RRP group. Statistical analyzesTweedie regression models with logarithm link. SPSS v. 21.0 was used

Results: 153 patients, 90.8% women, middle low (37.9%) and middle (35.3%) the most prevalent socioeconomic status. Age at diagnosis was 46.06 (12.73) years, time disease 14.25 (10.26) years. DAS28 average: 4.51 (1.33). Basal Sharp VDH:104.53 (90.09), CRP: 9.77 (10.35) UI/L, RF: 352.49 (538.08) UI/L, ACPA: 563.64 (782.2)UI/dL. PR annual rate was 7.64 (2.4 years of follow up),94.8% increased damage and 74 patients (48.36%) had PRR. Most subjects (94.1%) were using DMARDs but only 15 (9.8%) biologicals. The mean dose of prednisone was 4.88 (3.33) mg/d. In the univariate analysis, only DMARDs was associated with RP (B=50.8; CI=40.13–51.48, p<0.001), remaining this association in the multivariate analysis (B=50.56;CI=49.80–51.33,p<0.001). In the multivariate analysis of RRP group, no variables was associated with risk and subjects with steroids use had less radiographic impairment (B=0.859; CI 0.759–0, 893,p=0.017).

Conclusions: In this prospective study of an established RA cohort, a large proportion of patients had RRP and there was few percentage of biologic use. In the RRP subset only steroids use was a protective factor.

References:

[1] van den Broek M, Ann Rheum Dis. 2012;71(9):1530–3.
[2] Furneri. Clin Exp Rheumatol. 2012;30(4 Suppl 73): S72–84.
[3] Kavanaugh A. J Rheumatol. 2004;31(5):849–55.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3145

AB0270 HOW DOES THE ACTIVITY OF RHEUMATOID ARTHRITIS EVOLVE WITHIN A COHORT OF RECENT ONSET PATIENTS WITH A 5-YEAR FOLLOW-UP?

R. Jiménez Gasco, R. Ortega Castro, J. Calvo Gutierrez, P. Font Ugalde, A. Escudero Contreras, E. Collantes Estevez. *Reumatología, Hospital Universitario Reina Sofia de Córdoba, Cordoba, Spain*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory joint disease affecting 0.5% of Spanish population. This disease results in a significant radiological and functional deterioration, decreasing the quality of life and increasing its mortality if an specific treatment is not applied. Although the radiological and functional deterioration progress slowly during the whole course of the disease, it has been proven that early and aggressive approach to the disease is important in order for its control because the final outcome can be improved with a close, intense and early follow-up.
Objectives: To describe the clinical characteristics and evolution during 5 years of disease activity in RA patients derived from a recent arthritis clinic.
Methods: A prospective longitudinal study was carried out of 154 patients diagnosed from 2003 to 2012. They included patients over 18 years old diagnosed with RA (ACR criteria 1987) and with 5 years of follow-up. Socio-demographic and clinical variables such as Rheumatoid factor (FR) and anti-citrullinated peptide antibodies (ACPA) or disease activity (DAS28-VSG) as well as treatment were assessed in those patients. Mean and standard deviation of quantitative variables and frequencies and percentages of qualitative variables were calculated. Proportions were compared using the Cochran Q test statistic in order to compare differences between remission (determined by DAS-28 <2.6) measured at 1 year, 2 years and 5 years from diagnosis. Data were analyzed using SPSS v17 program.
Results: Of the 154 patients, 66.2% were females with a mean age at diagnosis of 52.88±14.64 years. Only 18.8% (29) patients were smokers; 67.5% (104) of patients were RF positive and 57% (88) of them were ACPA positive. Clinical remission measured by means of DAS 28-VSG (<2.6) was achieved in 84 patients (54.5%), 92 patients (59.7%) and 95 patients (61.7%) after 1, 2 and 5 years, respectively. Mean values of DAS 28 were 2.58 (2.02) at first year, 2.56 (1.99) at two years and 2.59 (2.02) at 5 years. Of the 154 patients, 108 (78.8%) started treatment with monotherapy (mostly methotrexate) and after 5 years only 18 (25.7%) patients were on biological treatment. No differences were found when remission was compared at first, second and 5 years of follow-up.
Subsequent comparison of two-to-two ratios among the three groups using χ^2 contrast also indicated that there were no statistically significant differences between groups. However a tendency in data was observed, so that once patients had reached the remission at first year there was no increase in the number of them showing remission in the successive years of follow-up.
Conclusions: These results suggest that achieving an early control of the disease is of importance, since control of the disease becomes more difficult as the delay of the diagnosis increases.
References:
[1] Villaverde Garcia V, Balsa A, Carmona L, Sanmartí R, Maese J, Pascual D, Ivorra J. What are patients with early rheumatoid arthritis like in Spain? Description of the PROAR cohort. Reumatología clínica.2009;5:115–120.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6878

AB0271 T2T ADHERENCE MEASUREMENT TOOL PERFORMANCE IN RHEUMATOID ARTHRITIS

R. Garcia Salinas, M.P. Girard Bosch, M.V. Martire, P. Arturi, S. Magri. *Hospital Italiano de la Plata, la Plata, Buenos Aires, Argentina*

Background: The purpose of the T2T approach in RA is to achieve remission or LDA according to results from objective activity measurements. This strategy has proven clinical benefits, however objective adherence T2T measurement tools are lacked in daily practice.
Objectives: To evaluate the setting, usage of a T2T adherence measure: T2T70 and T2T100, and its association with sustained low disease activity (LDAS) as a measure of outcome.
Methods: Prospective study, consecutive patients with RA diagnosis (ACR/EULAR 2010) and follow-up between 1 and 24 months were included. Data from electronic medical record (EHR) were collected. Demographic variables, characteristics of the disease and treatment were recorded. The following T2T characteristics were defined and collected from each patient: number of visits, visits where treatment was adjusted, CDAI measurements, use of ultrasound to measure disease activity and achievement of LDA. Sustained LDA (LDAS) was defined when the patient had 2 or more records of that consecutive state of activity. Measures of adherence to T2T were defined as follows: T2T-70, when therapeutic decisions were accompanied by the measurement of activity by 70% and the interval between visits did not exceed 6 months; And T2T-100, when 100% of the decisions were accompanied with the activity measurement and the interval between each visit did not exceed 6 months. Statistical analysis: a descriptive analysis of the variables was performed and Chi2 test (categorical) and Student or MannWhitney test (continuous) were applied. For multivariate logistic regression analysis we considered as dependent variable LDAs.
Results: 96 patients were included, with a mean follow-up of 15 months (DS 7.8), equivalent to 120.6 patients/year. Eighty percent of the patients were women, mean age 53.7 years (SD 13), disease duration 36 months (RIC, 12–52), 64% had early diagnosis, 85% and 75% positive For FR and ACPA, respectively. According to T2T characteristics, 526 visits were recorded, 270 were treatment adjustment and 208 (78%) of them were performed according to the CDAI value. The frequency of LDAS was 20% (IC95: 12–30). The frequency of T2T-70 compliance was 62.5% (IC95: 52–72) and T2T-100 was 42% (IC95: 32–52). Compliance with T2T-70 and T2T-100 presented a statistically significant association to the achievement of LDAS in the uni and multivariate analysis (p: 0.000). Compliance with T2T-70 and T2T-100 was associated with a shorter time course of disease; And T2T-70 also showed association with early diagnosis.
Conclusions: T2T-70 and T2T-100 adherence were 62% and 42%, respectively, patients who met these criteria reached more LDAS. The early diagnosis and shorter time to disease evolution at baseline were variables that were variables that were associated with more compliance of these tools.
Acknowledgements: Dra Josefina Marcos.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3051

AB0272 THE PERFORMANCE OF A SINGLE CENTRE INTERVENTIONAL CLINIC IN EARLY RHEUMATOID ARTHRITIS

R. Jese, A. Ambrožič, N. Gašperšič, A. Hočevar, K. Perdan Pirkmajer, B. Lestan, M. Pavič Nikolič, M. Plešivčnik Novljan, S. Praprotnik, Ž. Rotar, A. Šipek Dolničar, D. Šuput Skvarča, M. Tomšič. *Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia*

Background: In early rheumatoid arthritis (RA), first assessment by a rheumatologist and/or initiation of disease-modifying anti-rheumatic drugs (DMARD) within 12 weeks of symptom onset are associated with a significant benefit in long-term disease outcome.
Objectives: Our objective was to determine the proportion of patients with newly diagnosed RA in whom first rheumatology assessment and/or initiation of DMARD therapy was within the desired time frame.
Methods: A retrospective chart review of adult patients diagnosed with RA during years 2014 and 2015 was performed at the rheumatology department of an integrated secondary/tertiary teaching hospital that provides rheumatology services for a population of more than 500.000 residents. Potential cases were identified by searching the electronic medical records for ICD-10 codes M05.* and M06.* Electronic and paper records of patients were then thoroughly reviewed. In addition to demographic and clinical data, dates were recorded for onset of inflammatory joint symptoms, referral to rheumatologist, initial assessment by a rheumatologist and initiation of DMARD therapy. The percentage of patients assessed by a rheumatologist and/or treated with a DMARD within 12 weeks of symptom onset and the median times for delay were then calculated.
Results: Between January 1st 2014 and December 31st 2015, 243 new cases of RA were identified at our Department of Rheumatology. Of those, 197 (81.1%) were referred to our early interventional clinic. Within 12 weeks of symptom onset, 111 (45.7%) new RA patients were examined by a rheumatologist and 87 (35.8%) were started on DMARD therapy; the median time from symptom onset to consultation was 13.0 (IQR 4.6–27.8) weeks, median time from referral to consultation was 1 (IQR 1–3) days and median DMARD treatment delay was 15.7 (IQR 8.7–31.9) weeks.

Table 1. Demographic data, clinical history, and delays

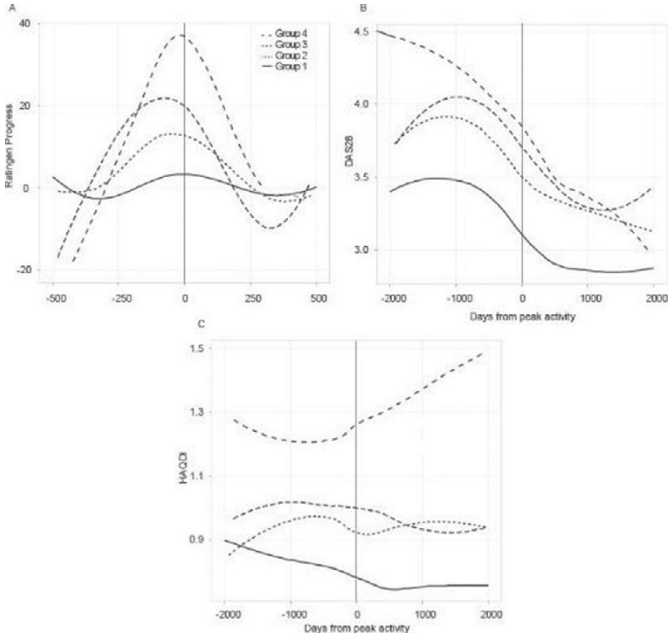
Gender (female/male) (%)	183/60 (75/25)
Age, years (median)	64.2 (IQR, 52.1–75.9)
Patients fulfilling 2010 ACR/EULAR classification criteria for RA, N (%)	228 (93.8)
DAS28 3v (mean ± SD)	5.3±1.3
Erosive disease (plain radiographs) at first rheumatologist assessment, N (%)	67 (31.5)
Time from symptom onset to first rheumatologist assessment, weeks (median)	13.0 (IQR, 4.6–27.8)
Time from referral to first rheumatologist assessment, weeks (median)	0.14 (IQR, 0.14–0.43)
Time from symptom onset to glucocorticoid initiation, weeks (median)	13.1 (IQR, 5.6–26.9)
Time from symptom onset to DMARD initiation, weeks (median)	15.7 (IQR, 8.7–31.9)

Conclusions: 46% of new RA patients were assessed by a rheumatologist and 36% were treated with a DMARD within the recommended time frame of 12 weeks. Most of the treatment delay was due to the time elapsed between symptom onset and referral to a rheumatologist. These results substantiate the efficacy of our early interventional clinic in diagnosing and treating patients with early RA: despite the heavily protracted nationwide waiting times for first rheumatologist assessment and significantly (40%) lower number of rheumatologists per capita compared to European Union average, the percentage of timely treated patients was comparable to recent reports.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5276

AB0273 VERY HIGH, BUT NOT LOWER, RADIOGRAPHIC PROGRESSION LEADS TO AN INCREASE IN HAQ-DI. RESULTS FROM THE SWISS SCQM RA COHORT

R. Mueller[1], R. Thalmann[1], N. Graf[2], H. Schulze-Koops[3], J. von Kempis[1].
[1]Division of Rheumatology, Kantonsspital St. Gallen, St. Gallen; [2]Graf Biostatistics, Winterthurthur, Switzerland; [3]Rheumaeinheit, Klinikum der Universität München, Campus Innenstadt, Munich, Germany

Background: Numerous predictors of radiographic progression in RA patients have been identified over the last years. In general, analyses of radiographic progression in RA rather focus on radiographic non-progression or repair. High radiographic progression in spite of therapy has, to our knowledge not been analysed in detail in the last years, neither in RCTs nor in cohort studies.
Objectives: To analyse radiographic, demographical and clinical data in RA patients with high radiographic progression before and after the individual peak radiographic progression.
Methods: We included all RA patients from the Swiss registry SCQM with at least two subsequently scored radiographs. Radiographic destruction was scored using the Ratingen erosion score. To analyse high radiographic progression we selected for the highest (peak) radiographic progression in every individual patient for the analysis. The individual peak radiographic progression was analysed in groups as change of Ratingen scores/year: 0-≤10, 10-≤20, 20-≤30, >30 (groups 1–4, follow up 1998 – 2015). The baseline disease characteristics were compared using standard descriptive statistics (Kruskal-Wallis or Chi-square tests). The change of DAS 28 and HAQ-DI scores before and after peak progression was analysed with the Wilcoxon signed rank tests.
Results: 3 patients were included into the analysis. 3'049 patients had a peak radiographic progression between 0 and ≤10/year, 773 between 10 and ≤20, 150 between 20 and ≤30, and 61 of >30. All patient groups were within the same age range (mean: 56.5 – 60.5 years). Rheumatoid factor and ACPA were more frequent in patient groups with higher peak radiographic progression (RF: 73.6, 80.0, 88.9, 90.0; ACPA: 66.8, 73.4, 74.3, 82.1, groups 1–4, respectively). When the rate of radiographic progression before and after peak progression was analysed, 69.7%, 74.7%, 76.9%, and 93.3% of the patients had a radiographic progression of 25% or lower as compared to peak progression before and 76.1%, 81.8%, 91.1%, and 93.8% after this peak progression, respectively for patients in groups 1 to 4 (Figure A).
The disease activity, as assessed by DAS 28, was significantly higher in all patient groups before peak progression and lower thereafter (Figure B, p<0.001). Average HAQ-DI scores increased after peak radiographic progression in group 4 (Figure C, p=0.005) whereas it is stable or even decreases among the patients of the other patient groups.



Conclusions: These data show that higher disease activity precedes radiographic peak progression, which is, if high, overall rare. Radiographic progression before and after the individual peak radiographic progression was far lower as compared to the time of radiographic peak progression. Only the highest individual peak (change of Ratingen score >30/year) radiographic progression was followed by an increase of HAQ-DI scores.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4253

AB0274 THE ASSOCIATION BETWEEN REPEATEDLY INFECTION AND DISEASE OUTCOME IN PATIENTS WITH RHEUMATOID ARTHRITIS

R. Zhang[1], J. He[2], C. Li[2], J. Li[2], J. Chen[2], Y. Jin[2], Y. Gan[2], Z. Li[2].
[1]Department of Rheumatology and Immunology; [2]Peking University People's Hospital, Beijing, China

Background: Some publications shows some therapies in rheumatoid arthritis (RA) could cause infections and it also can react the disease prognosis. But there was no report about the relationship between the repeated infections during the disease duration and its outcome.
Objectives: Our study was to evaluate the association between the history of repeated infectious agents that occurred more than three times during the duration of RA and the current disease status of RA, such as disease activity and physical disability.
Methods: 688 pure RA patients were selected from December 2015 to June 2016 in Peking People's hospital and divided into two groups according to their current disease status. Clinical data were collected including DAS28, HAQ, disease duration and therapies. Infectious agents occurred repeatedly during the duration were identified as history repeated infectious agents. T test, ANOVA, chi-squared test and multivariate analysis of covariance were used for analyzing the association between the infections and disease outcome.
Results: 688 RA patients were divided into two groups based on whether their DAS28 reached 3.2 (active or inactive). The HAQ score and the incidence of airway infection has a significant difference among these two groups (P=0.000; P=0.002). Logistic regression analysis shows that smoking, airway infection and age were the risk factor for RA activite (OR=4.844, 95% CI (0.193,1.001); OR=1.326, 95% CI (0.655,2.687); OR=1.013, 95% CI (0.989,1.037)), and the disease duration and the therapy were also effect the disease outcome (OR=0.650;OR=1.560). Than we divided these patients into four groups based on their infectious site such as airway, urinary, intestinal and no-infection. After adjusting for the disease duration, only airway infection incidence has statistically significantly different (P=0.000). DAS 28 has statistical different only among the groups whether they have airway infectious agents after adjusting the smoking and therapy (P=0.002; P=0.002). Compared with infection free group, patients with airway infection has a higher DAS28 because they have more swollen or painful joints, while patients with urinary infection perform a higher scores because they have a high level of ESR.

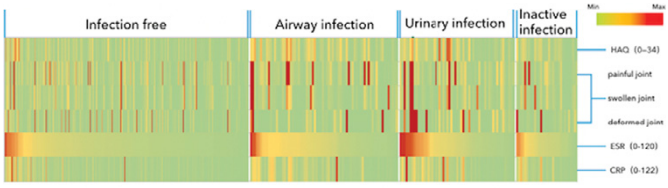


Figure 1. Levels of clinical data include HAQ, abnormal joints number,ESR and CRP were compared among subgroups of infection free(n=469), airway(n=121), urinary(n=75) and inactive infection(n=81).This figure shows which factor contribute to the difference of disease activity between subgroups.

Conclusions: The repeated infectious agents during the disease duration might lead to poor outcome. We should pay more attention to those patients who have repeatedly infectious agents during their disease duration in order to improve their prognosis.
References:
[1] Sokolove J, Wagner CA, Lahey LJ, et al. Increased inflammation and disease activity among current cigarette smokers with rheumatoid arthritis: a cross-sectional analysis of US veterans. Rheumatology (Oxford). 2016;55(11):1969–77.
[1] Sokolove J, Wagner CA, Lahey LJ, et al. Increased inflammation and disease activity among current cigarette smokers with rheumatoid arthritis: a cross-sectional analysis of US veterans. Rheumatology (Oxford). 2016;55(11):1969–77.
[2] Iguchi-Hashimoto M, Hashimoto M, Fujii T, et al. The association between serious infection and disease outcome in patients with rheumatoid arthritis. Clin Rheumatol. 2016;35(1):213–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3976

AB0275 THE CORRELATION OF CARTILAGE OLIGOMERIC MATRIX PROTEIN WITH SONOGRAPHIC KNEE CARTILAGE THICKNESS AND DISEASE CHARACTERISTICS IN RHEUMATOID ARTHRITIS

S. Rajalingham[1], S. Rajalingam[2], H. Hussein[2], R. Sridharan[3], A.A. Wahab[4].
[1]Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur; [2]Medicine, Putrajaya Hospital, Putrajaya; [3]Radiology; [4]Microbiology, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

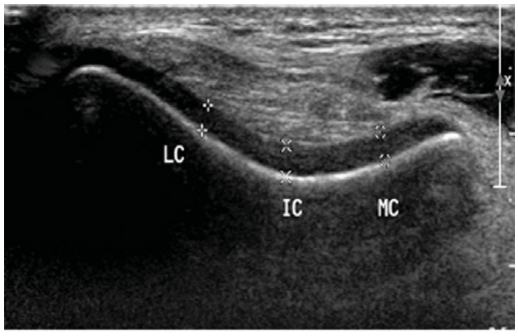
Background: Cartilage Oligomeric Matrix Protein (COMP) is an extracellular protein which is primarily found in the cartilage and to a lesser extent in ligaments, meniscus, tendons and synovium. Experimental models of rheumatoid arthritis (RA) and osteoarthritis have pointed out that serum COMP levels are reflective of the cartilage turnover rate.

Objectives: To investigate the correlation of serum COMP levels with the articular cartilage damage based on sonographic knee cartilage thickness (KCT) and disease characteristics in RA.
Methods: A total of 61 RA patients and 27 healthy controls were recruited in this study. Serum samples were obtained from all subjects to determine the COMP levels. All subjects had bilateral ultrasound scan of their knees performed by a single radiologist; who was blinded to the details of the subjects. The KCT was based on the mean of measurements at 3 sites; the medial condyle, lateral condyle and intercondylar notch (Figure 1). Besides, the RA patients were assessed for their disease activity based on DAS 28.
Results: Serum COMP concentrations were significantly elevated in the RA patients compared to the controls (p=0.001). The serum COMP levels had an inverse relationship with bilateral KCT in RA subjects and the healthy controls. However, the association was statistically insignificant for bilateral knees in the control arm. COMP correlated significantly with disease activity based on DAS 28 (r =0.299, p=0.010), disease duration (r =0.439,p = <0.05) and mean left KCT (r = -0.285,p=0.014) in RA (Table 1). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) which are the traditional markers of inflammation; demonstrated a significant positive correlation with the DAS 28 scores (r =0.372, p=0.003 for ESR; r =0.305, p=0.017 for CRP) comparable to the serum COMP. However, neither ESR nor CRP had a significant association with the KCT, as opposed to the serum COMP.

Table 1. Correlation of Serum COMP levels with Clinical Parameters in RA

Parameter	r	p value
Age	0.214	0.094
BMI	0.122	0.259
DAS 28	0.299	0.010
ESR	0.065	0.311
CRP	0.027	0.418
Disease duration	0.439	<0.05
Mean Right KCT	-0.177	0.088
Mean Left KCT	-0.285	0.014

KCT: knee cartilage thickness.



LC: Lateral Condyle, MC : Medial Condyle, IC :Intercondylar notch

Figure 1 : Sites of sonographic knee cartilage thickness measurement

Conclusions: The serum COMP is a promising biomarker in RA which reflects disease activity and damage to the articular cartilage. Serum COMP appeared superior to the traditional markers in RA i.e ESR and CRP in predicting sonographic KCT.
References:
[1] Andersson ML, Svensson B, Petersson IF, et al. Early increase in serum-COMP is associated with joint damage progression over the first five years in patients with rheumatoid arthritis. BMC Musculoskelet Disord. 2013;14:229.
[2] Happonen KE, Saxne T, Aspberg A, et al. Regulation of complement by cartilage oligomeric matrix protein allows for a novel molecular diagnostic principle in rheumatoid arthritis. Arthritis Rheum. 2010;62:3574–83.
[3] Happonen KE, Saxne T, Geborek P, et al. Serum COMP-C3b complexes in rheumatic diseases and relation to anti-TNF-alpha treatment. Arthritis Res Ther. 2012;14:R15.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1213

AB0276 EVALUATION OF ADHERENCE TO DRUG TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

A.E.-A.M. Alhefny[1], S.A. Mobasher[2], M.A. Abd El-Rahman[1], N.H. Shedid[1], H.M. Sakr[3], R.M. Hassan[1]. *[1]Ain Shams University Hospitals, Cairo, Egypt; [2]Internal Medicine and Rheumatology; [3]Radiology, Ain Shams University Hospitals, Cairo, Egypt*

Background: the medication adherence is very vital issue nowadays, especially in RA patients.
Objectives: to measure the frequency of the adherence in RA patients, and evaluate the common factors influencing RA patients adherence to drug treatment aiming at improving disease outcome.
Methods: a Prospective cohort study of 100 patients with RA under treatment, fulfilled the American College of Rheumatology/European League Against Rheumatism (ACR/ EULAR) (1) criteria. All patients subjected to Full history taking and clinical examination, (DAS 28 ESR), Health Assesment Questionnaire (HAQ) score, Visual Analouge Scalez (VAS) scale, CBC, ESR, CRP titer, RF titer, ACPA titer and Power Doppler U/S for both hands, patients also respond to specific questionnair containing questions about sociodemographic data, medication, health care system and Compliance Questionnaire of Rheumaology (CQR).
Results: The baseline adherence rate (CQR≥80) was 37%. The nonadherent RA patients to drug treatment were older, living outside Cairo, with low educational level and smokers, they also had higher DAS28ESR score, HAQscore, ESR, CRP titer and more frequent active synovitis in Doppler ultrasound. The cost of medication (61%), non-availability of medication in pharmacy (58%), forgetting the medication (36%), patients' lack of belief in the benefit of treatment (38%), inadequate follow up or discharge planning (23%) and polypharmacy (medication load) (20%) were the most common factors in nonadherent patients table (3). After 9 months of the follow up and trying to correct the causes of nonadherence, the adherence rate increased to (68.75%).Also there was improvement in disease activity, improvement in functional state and improvement in the quality of life.
Conclusions: Low adherence rate was associated with higher disease activity, functional disability. Patient education, financial support, good physician patient relationship, simplification of the prescription, facilitation their communication, using MSUS were found to improve the patient adherence and improve the disease outcome.
References:
[1] Aletaha D, Neogi T, Silman A et al, Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League against Rheumatism collaborative initiative. Arthritis Rheum 2010:62:2569–2581.
[2] Dowman B, Campbell R, Zgaga L et al, Estimating the burden of rheumatoid arthritis in Africa: A systematic analysis. J Global Health 2012;2(2):1–9.
[3] Wasserman A, Diagnosis and Management of Rheumatoid Arthritis.American Family Physician J 2011:84(11):1245–1252.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5785

AB0277 PATIENT REPORTED OUTCOMES EXPLAIN THE LACK OF AGREEMENT BETWEEN PHYSICIAN AND PATIENT PERCEIVED REMISSION IN EARLY RHEUMATOID ARTHRITIS

S.A. Turk[1], L. Rasch[2], W.F. Lems[1,2], L. van Tuyl[2], D. van Schaardenburg[1,3], M.M. ter Wee[2]. *[1]Amsterdam Rheumatology and Immunology Center| Reade; [2]Amsterdam Rheumatology and Immunology Center| VU University Medical Center; [3]Amsterdam Rheumatology and Immunology Center| Academical Medical Center, Amsterdam, Netherlands*

Background: Rheumatoid arthritis (RA) patients increasingly reach a state of absence of disease activity, or remission. However, the proportion of patients classified as in remission varies substantially between definitions and are often determined by disease activity score (DAS). But, the importance of patients' perspective is increasingly recognized, which often result in discordance between patients and physician assessment.
Objectives: To determine how often patients and physicians agree on a state of remission according to different definitions, as well as the difference in patient reported and clinical outcomes between patients in and not in self-perceived remission.
Methods: In 84 consecutive early RA patients, Boolean remission, EULAR

Table 1

Physician	Remission according to physician		
	PhR	NPhR	T
PatR	41 (61)	4 (23)	45 (54)
NPatR	26 (39)	13 (77)	39 (46)
T	67 (80)	17 (20)	84

Boolean	Remission			No remission		
	PhR	NPhR	T	PhR	NPhR	T
PatR	20 (87)	0 (0)	20 (87)	21 (48)	4 (24)	25 (41)
NPatR	3 (13)	0 (0)	3 (13)	23 (52)	13 (77)	36 (59)
T	23 (100)	0 (0)	23	44 (72)	17 (28)	61

EULAR response	Good			Moderate			None		
	PhR	NPhR	T	PhR	NPhR	T	PhR	NPhR	T
PatR	39 (65)	3 (60)	42 (65)	1 (20)	1 (14)	2 (17)	1 (50)	0 (0)	1 (14)
NPatR	21 (35)	2 (40)	23 (35)	4 (80)	6 (86)	10 (83)	1 (50)	5 (100)	6 (86)
T	60 (92)	5 (8)	65	5 (42)	7 (58)	12	2 (29)	5 (71)	7

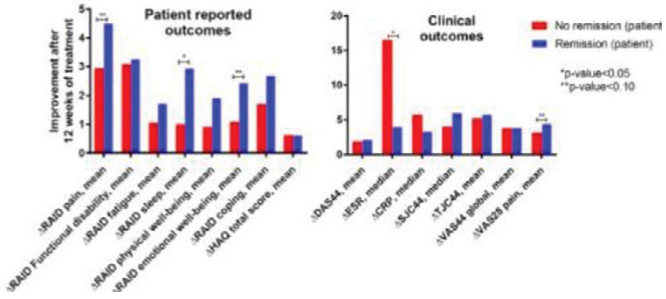
ACR	ACR 70			ACR 50 (not 70)			non (not 50)		
	PhR	NPhR	T	PhR	NPhR	T	PhR	NPhR	T
PatR	20 (87)	2 (100)	22 (88)	5 (56)	1 (100)	6 (60)	16 (46)	1 (7)	17 (35)
NPatR	3 (13)	0 (0)	3 (12)	4 (44)	0 (0)	4 (40)	19 (54)	13 (93)	32 (65)
T	23 (92)	2 (8)	25	9 (90)	1 (10)	10	35 (71)	14 (29)	49

Values are expressed as number (%). PhR = physician perceived remission, NPhR = no physician perceived remission, PatR = patient perceived remission, NPatR = no patient perceived remission, T = total.

response and ACR 70 criteria were determined after 12 weeks of treatment with a fixed schedule methotrexate and prednisone. Physician perceived remission (PhR) was defined as a global assessment of ≤20 on a visual analogue scale, phrased: "*How active do you think the RA of your patient is today?*". Patient perceived remission (PatR) was phrased as: "*Would you say that, at this moment, your disease activity is as good as gone? Yes/no*". In patients in PhR, the change in components of the DAS44 and questions of the Rheumatoid Arthritis Impact of Disease (RAID) and Health Assessment Questionnaire (HAQ) were compared between patients in and not in self-perceived remission.

Results: The agreement on remission between patients and physicians was 64% and was dependent of the definition of remission. In Boolean remission, EULAR good response and ACR70 remission agreement was: 86%, 63% and 80% respectively (table). Patients in PhR, the patients in PatR had more improvement on all RAID subdomains. There were no significant differences in clinical outcomes (ESR was significantly different at baseline, but not after 12 weeks; see figure).

Figure. Comparison in improvement in patient reported and clinical outcomes after 12 weeks of treatment, in patients in physician remission, who are and are not in self-perceived remission.



Conclusions: Two-third of the patients agreed with the physician on being in remission. In all different definitions for remission, this discordance between physician and patient on perceived remission remained similar. Patients in self-perceived remission had more improvement in components of the RAID, but not in clinical outcomes. Further research is needed to identify domains of patients perceived remission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3406

AB0278 ULTRASOUND EXAMINATION IN DIAGNOSIS OF EARLY RHEUMATOID ARTHRITIS

W. Hamdi [1], S. Miladi [1], K. Matallah [1], M. Bouaziz [2], D. Kaffel [1], I. Zouch [1], M.M. Kchir [1]. [1]*Rheumatology department;* [2]*Radiology department, Institute Kassab of Orthopedics, Manouba. Tunisia, Tunis, Tunisia*

Background: Fortunately, management of RA at the early stage has become possible thanks to both the emergence of new biotherapies and the strategy treat to target. Musculoskeletal ultrasound (US) is a potent tool for the detection of synovitis, effusion and bone erosion in RA.

Objectives: The aim of this study was to assess the contribution of US in diagnosing RA at the early stage of the disease.

Methods: A cross-sectional study was performed during 2 years. Patients with a history of inflammatory joint pain for ≥6 weeks and ≤2 years with synovitis of at least one joint were enrolled in this study. All patients underwent clinical assessement, laboratory tests and plain radiography of hands and feet.US was assessed within one week of clinical examination. Synovitis and erosion were defined according to the OMERACT.

Results: One hundred patients were included in this study with an average age of 51,8±14,6 years-old. Female outnumbered male with a sex ratio of 3,8. The mean duration of the disease was 10,9±7,4 months. When admitted to our department and after clinical examination it was found that 31% of patients presented polyarthritis, 4% had oligoarthritis and 7% suffered from monoarthritis. *US findings:* US was found to be more sensitive than clinical examination to detect synovitis. Among the 2200 joints assessed by US, a synovitis was detected in 81% patients, an intra-articular effusion in 36% patients and PD signals in 51% patients. Also, flexor tenosynovitis were present in 55% patients and extensor tenosynovitis in 59% patients. Erosions were more detected in plain radiography (70%) than in US (41%). Clinical parameters (VAS, duration of morning stiffness, number of night awakens, TJC) were not correlated with most US findings. Nevertheless, correlation was detected for US effusion (r=0,250, p=0,028) and for US Doppler (r=0,289, p=0,011) with SJC. PDUS examination correlated with CRP results (r=0,302, p=0,023) but not with ESR results. A significant, positive correlation was observed between erosions in X-rays or US assessment (r=0,342, p=0,002). The US detected synovitis in 25% of patients who had no swollen joint at the clinical examination when admitted to our department and had detected erosions in 9% of patients having negative plain X rays.

Conclusions: Ultrasound appears as a sensitive tool to detect subclinical synovitis (25%) and infra- radiological erosions (9%). It helps us to make an early diagnosis and start appropriate treatment before the onset of irreversible joint destruction.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6230

AB0279 HIGH RATE OF DISABILITY PENSION IN CHILEAN RHEUMATOID ARTHRITIS PATIENTS WITHOUT ACCESS TO BIOLOGICS. HOSPITAL PADRE HURTADO EXPERIENCE

S.E. Ibáñez Vodnizza, O. Valenzuela, F. Silva, M.J. Villar. *Rheumatology department, Clínica Alemana de Santiago/Hospital Padre Hurtado, Santiago, Chile*

Background: Until the year 2016, most of the Chilean rheumatoid arthritis patients in the public health system did not have acces to biologic treatment. Now the access is limited to those with high disease activity (DAS 28 >5.1).

Objectives: Our main objective was to evaluate the rate of patients benefited by disability pension within the group of rheumatoid arthritis patients seen in our center, before the introduction of biologic treatment for those with high disease activity. Our secondary objective was to estimate the association between having a disability pension and the characteristics of the patients.

Methods: Consecutive rheumatoid arthritis patients (according to the ACR 2010 criteria), 18 years old or older, that attended to our rheumatology consult between September and December of 2015, were included. Patients with other types of pensions (retirement) were excluded. Information about work status, gender, age, years since diagnosis, medications used, DAS 28 ESR and its variables was collected.

Results: 104 patients were included. 38.5% had a disability pension. We found significant differences between the patients with and without disability pensions for age, years since diagnosis, tramadol use, the number of tender joints, the number of swollen joints and DAS 28 ESR (Table 1). After multivariate logistic regression, age (OR 1, 95% CI 1.02–1.15), tramadol use (OR 0.3, 95% CI 0.08–0.92) and the number of swollen joints (OR 1.4, 95% CI 1–1.96) continued to be significantly associated.

Table 1. Disease characteristics

	All	Without Disability Pension	With Disability Pension	P
Number of patients (%)	104 (100)	64 (61.5)	40 (38.5)	NA
Female (%)	86 (82.7)	53 (82.8)	33 (82.5)	NS
Age (median, IQR)	55.5 (15)	52.5 (18)	58 (15)	0.002
Years since diagnosis (median, IQR)	8.8 (12.2)	5.8 (8.2)	12.3 (19.1)	<0.001
Number of DMARDs used (median, IQR)	2 (2)	1 (2)	2 (2)	NS
Prednisone users (%)	89 (85.6)	52 (81.3)	37 (92.5)	NS
NSAIDs users (%)	75 (72.1)	46 (71.9)	29 (72.9)	NS
Acetaminophen users (%)	68 (65.4)	39 (60.9)	29 (72.5)	NS
Tramadol users (%)	35 (33.7)	13 (20.3)	22 (55)	0.001
Number of tender joints (median, IQR)	4 (6)	3 (5)	6 (11)	0.018
Number of swollen joints (median, IQR)	2 (4)	1 (4)	3 (8)	0.012
ESR (median, IQR)	20.5 (21)	16.5 (18)	25 (31)	NS
VAS pain (median, IQR)	60 (40)	60 (40)	80 (40)	NS
DAS 28 ESR (mean, SD)	4.5 (1.6)	4.1 (1.4)	5 (1.8)	0.026

IQR = interquartile range, DMARDs = Disease-Modifying Antirheumatic Drugs, NSAIDs = Non-steroidal anti-inflammatory drugs, ESR = Erythrocyte Sedimentation Rate, VAS = Visual Analog Scale, DAS = Disease Activity Score, NS = Not significant.

Conclusions: Near forty percent of our rheumatoid arthritis patients, that did not have access to biologic treatment, were being paid a disability pension, and this condition was significatly associated with more years of age, tramadol use, and the number of swollen joints. The mean DAS 28 ESR in the patients with disability pension was 5. The limit of a DAS 28 >5.1 to authorize the use of biologic treatment possibly will not help to reduce the rate of patients with disability pension in our group.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2557

AB0280 INFLUENCE OF HLA CLASS II ANTIGEN (DRB1 AND DQB1) ON THE PRODUCTION OF ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODIES IN A TUNISIAN POPULATION

S. Boussaid [1], S. Kochbati [2]. [1]*Departement of Rheumatologie, la Rabta Hospital;* [2]*Departement of Rheumatologie, Habib Thameur Hspital, tunis, Tunisia*

Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatism. It's a complex autoimmune disorder. The aim of this study is to focus on the relationship between HLA-DRB1 genes and RA specific antibodies against cyclic citrullinated peptides (anti-CCP antibodies).

Methods: This prospective study was performed on a total of 81 Tunisian patients with rheumatoid arthritis. All patients fulfilled the American College of Rheumatology (ACR 1987) criteria for RA. For each patient we assessed DNA and serum samples. The DNA was extracted from lymphocytes using a commercial kit (Quiagen). The HLA class II (DQB1 and DRB1) was performed by Polymerase Chain Reaction technique Specifying-sequence primers (PCR-SSP). The specific products of PCR were analyzed by 2.5% agarose gel electrophoresis. All tests include positive and negative controls appropriate for each blood sample. The phenotypes of patients were obtained through the Software One Lambda DNA/SOFTWARE (SSP2L-generic DRB/DQB).

Results: The mean age of our population was 49.17±11.21 years (age 24–78). The disease average duration was 7.44±2.12 years (4 months - 29 years), 82.71% of RA were women and 17.29% were men. Seropositive RA were 80.24%, and 71% of RA have anti CCP positive antibody. Univariate analysis of the presence of anti-CCP antibodies in conjunction with HLA DRB1 and DQB1 was performed. Carriership of HLA DR*0301, 0401 and 1501 were significantly associated with the presence of anti-CCP antibodies ($p<0.0001$). Four DRB1 0401 carriers were homozygotes with three out of them having anti-CCP antibodies.
Carriership of HLA DQB1*0201, 0301, 0302,0501 and 0601 was associated with the presence of anti-CCP antibodies and so was HLA-DQB1*0401, but with a less significant association.
Conclusions: Although no formal conclusions on causality can be drawn from this association study, these findings suggest that anti-CCP antibodies are associated with different phenotypes; which suggest that various pathogenetic mechanisms underlie the positivity for anti-CCP in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2924

AB0281 CHARACTERIZATION OF CHANGES IN LYMPHOCYTE SUBSETS IN BARICITINIB-TREATED PATIENTS WITH EARLY, DMARD NAÏVE, RHEUMATOID ARTHRITIS IN A PHASE 3 STUDY

T. Takeuchi[1], R. Fleischmann[2], M. Schiff[3], M. Issa[4], W. Macias[4], T. Rooney[4], S. Zuckerman[4], D. Schlichting[4], I. McInnes[5]. *[1]Keio Univ., Tokyo, Japan; [2]Univ. Texas SW Med Center, Dallas; [3]Univ. Colorado, Denver; [4]Eli Lilly and Company, Indianapolis, United States; [5]Univ. Glasgow, Glasgow, United Kingdom*

Background: In RA-BEGIN (NCT01711359), baricitinib (bari), an oral Janus Kinase (JAK)1/JAK2 inhibitor, improved signs and symptoms of moderately to severely active RA in patients (pts) who had received no or limited prior csDMARD and no prior bDMARD therapy.[1]
Objectives: To analyse changes in absolute lymphocyte count (ALC) and cell subsets (LCS) in RA-BEGIN.
Methods: Pts (N=588) were randomised 4:3:4 (MTX up to 20mg QW, bari 4mg QD, bari 4mg+MTX) for 52 Wks. T and B cells plus subsets and natural killer (NK) cells were quantified by flow cytometry at baseline (BL) and Wks 4, 12, and 32.
Results: At BL, low cell counts were observed in 4.3%, 8.2%, 5.3%, 18.3%, and 19.7% of pts for ALC, CD3+, CD8+, B (CD19+), and NK cells. In the MTX group, slight declines in mean counts were observed for all cell types at post-BL visits (Table). For bari and bari+MTX, cell counts increased for all cell types at Wks 4 and 12, with, except for B cells, a return towards BL, or slightly below, at Wk 32. Changes in other T and B cell subsets generally reflected these patterns (data not shown). Treatment emergent (TE) low NK cell counts occurred in 11.6%, 13.4%, and 20.5% of pts for MTX, bari, and bari+MTX; TE low CD8+ cell counts occurred in 5.2%, 3.2%, and 8.3% of pts. Overall serious infection (SI) rates were 3.8%, 3.8%, and 2.3% for all pts in MTX, bari, and bari+MTX; rates were 6.8% (4 of 59 pts), 4.8% (2 of 42), and 2.8% (2 of 72) for pts with ≥1 low post-BL NK cell count and 15.8% (3 of 19), 25.0% (2 of 8), and 5.3% (1 of 19) for pts with ≥1 low post-BL CD8+ cell count. Herpes zoster (HZ) rates were 1.0% 2.5%, and 2.3% for all pts in MTX, bari, and bari+MTX; rates were 3.4% (2 of 59 pts), 4.8% (2 of 42), and 4.2% (3 of 72) for pts with ≥1 low post-BL NK cell count and 10.5% (2 of 19), 12.5% (1 of 8), and 5.3% (1 of 19) for pts with ≥1 low post-BL CD8+ cell count.

	MTX (N=210)				Bari 4 mg (N=159)				Bari 4 mg + MTX (N=215)			
Week: 0	4	12	32	0	4	12	32	0	4	12	32	
ALC: 1890	-110*	-110*	-80	1920	310***	380***	-20	1940	410***	220***	-100*	
CD3+: 1384	-108***	-98.5**	-102.5***	1369	148***	207***	-78*	1403.5	210***	90**	-150***	
CD8+: 435	-36**	-45***	-48***	422	52***	69***	-34**	435	80.5***	27*	-63***	
CD19+: 261	-17.5	-10	-13	258	103***	113***	51***	269	119***	101***	46***	
NK: 218	-11	-25**	-23**	247	74***	49***	-24**	234	64***	14	-44***	

Data are mean (Wk 0) and LSM Δ from BL (Wks 4, 12, 32), last observation carried forward. *p<0.05, **p≤0.01, ***p≤0.001 within grp comparison, LSM Δ from BL. Reference ranges (cells/μL): ALC=800–4280; CD3+=603–2990; CD8+=125–1312; CD19+=107–698; NK=95–64.

Conclusions: Low B and NK cell counts were common at BL, and post-BL changes within normality occurred in all treatment groups. Compared to MTX, bari was not associated with an increase in the % of pts with low NK or CD8+ cell counts while bari+MTX did show an increase in the % of pts with a low NK cell count. Changes appear distinct for LCS suggesting different mechanisms may underscore the effect of JAK inhibition. Whether low NK or CD8+ cell counts predispose to increased risk for SI or HZ was difficult to assess due to few pts with low counts experiencing these events.
References:
[1] Fleischmann R, et al. A & R. 2016.
Disclosure of Interest: T. Takeuchi Consultant for: Pfizer Japan, Astra Zeneca KK, Eli Lilly Japan KK, Novartis Pharma KK, Daiichi Sankyo Ltd, Nipponkayaku Ltd, Janssen Pharma KK, Merck Serono Ltd, Takeda Pharma Ltd, Mitsubishi Tanabe Pharma, Astellas Pharma, Abbvie GK, Bristol-Myers KK, Asahi Kasei Medical KK, Speakers bureau: Celtrion, Nipponkayaku Ltd, Pfizer Japan, UCB Japan, Daiichi Sankyo Ltd, Takeda Pharma Ltd, Chugai Pharma Ltd, Abbvie GK, Bristol-Myers KK, Eisai Co Ltd, Mitsubishi Tanabe Pharma, Janssen Pharmac KK, Astellas Pharma, R. Fleischmann Grant/research support from: Abbvie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Genetech, GSK, Janssen, Pfizer, Merck, Regeneron, Roche, Sanofi-Aventis, UCB, Consultant for: Abbvie, Akros, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly and Company, Genentech, GSK, Janssen, Pfizer, Sanofi-Aventis, UCB, M. Schiff Consultant for: Abbvie, BMS, Eli Lilly and Company, Johnson & Johnson, Speakers bureau: Abbvie, M. Issa Employee of: Eli Lilly and Company, W. Macias Employee of: Eli Lilly and Company, T. Rooney Employee of: Eli Lilly and Company, S. Zuckerman Employee of: Eli Lilly and Company, D. Schlichting Employee of: Eli Lilly and Company, I. McInnes Grant/research support from: Eli Lilly and Company, Abbvie, Pfizer, Novartis, Roche, Janssen, Consultant for: Eli Lilly and Company, Abbvie, Pfizer, Novartis, Roche, Janssen
DOI: 10.1136/annrheumdis-2017-eular.1336

AB0282 RHEUMATOID ARTHRITIS PATIENTS ACHIEVED BETTER QUALITY OF LIFE THAN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AT SUSTAINED REMISSION: THE IMPACT OF DISEASE DIAGNOSIS ON HEALTH-RELATED QUALITY OF LIFE OUTCOMES

V. Pascual Ramos, I. Contreras-Yáñez, L. Llorente, K.R. Valencia-Quiñones, J. Romero-Díaz. *Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico*

Background: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) impact the health related quality of life (HRQoL) of the patients. The 36 item Medical Outcome Study Short-Form survey (SF-36) assesses HRQoL and allows comparison of outcomes among different conditions. Whether remission represents similar status in terms of QoL in RA and SLE patients is unknown. In 2004 and 1999, respectively, recent-onset RA and SLE cohorts were initiated in a referral center for rheumatic diseases in México City; the SF-36 was applied beginning from enrollment.
Objectives: To compare the SF-36v2 scores between patients from both cohorts who achieved for the first time sustained remission (SR) and to define the role of disease diagnosis as associated to SF-36v2 normative data in SR patients.
Methods: First SR was considered when RA and SLE patients achieved at least 12 months of continuous follow-up with either SLE disease activity index 2000 update =0 or Disease Activity Score (28 joints) ≤2.4, respectively. Up to December 2015, updated data from 172 RA patients and 211 SLE patients with at least one year of follow-up were reviewed. In the SLE cohort, SF-36 was incorporated to routine assessments from 2005 onwards, meanwhile in the RA cohort it was applied since the beginning of enrollment. The SF-36v2 licensee re-scored the SF-36 used in the SLE cohort. In all the cases, Spanish versions were used and scoring was adjusted by gender and age. SF-36v2 scores were available for the totality of SR assessments. Logistic regression models were used to investigate factors associated with normative SF-36v2. Written informed consent was obtained from all patients.
Results: Cohorts were integrated primarily by middle-aged females (89%), with recent-onset disease (5.3±3.2 months); at inclusion, RA patients were older and lesser educated; follow-up was longer in SLE patients (10.6±2.9 vs. 7.5±3.2 years, p≤0.001) and a higher number of them died (15% vs. 2%, p≤0.001).
A higher proportion of patients achieved SR sooner in the recent-onset RA cohort than in the SLE cohort: 58% vs. 30.6% of the patients, after 30.8±23.9 vs. 59.4±37.5 months, respectively, p≤0.001. At SR, RA patients achieved better scores in 6 out of 8 SF-36v2 domains and in the physical health component summary (PHCS) compared with SLE patients; also, a greater proportion of RA patients achieved norms in five domains and in the PHCS; SLE patients achieved more frequent roles (physical and emotional) norms and scored higher mental health component summary than their counterpart. Finally, at SR RA patients had greater improvement in the majority of SF-36v2 domains and both summary components, despite having worse SF-36v2 scores at baseline evaluation.
In SR patients from both cohorts, age (β: 1.06, 95% CI: 1.02–1.1, p=0.03) and SLE diagnosis (β: 9.64, 95% CI: 3.61–25.75, p≤0.001) were predictors of not achieving normative PHCS.
Conclusions: RA patients who achieved SR had better HRQoL than their SLE counterparts. Age and SLE diagnosis were associated with not achieving HRQoL norms in SR patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1187

AB0283 ONE-YEAR FOLLOW-UP OF QUALITY OF LIFE IN RHEUMATOID ARTHRITIS PATIENTS FROM BULGARIAN POPULATION TREATED WITH CSDMARDS AND BDMARDS

V.V. Boyadzhieva, N.R. Stoilov, M. Ivanova, R. Stoilov. *Rheumatology, University Hospital "St. Iv. Rilski", Medical faculty, Medical University, Sofia, Bulgaria*

Background: Rheumatoid arthritis is a chronic systemic disabling condition associated with pathology mainly of the peripheral joints. Quality of Life (QoL) encompasses the impact of the disease and its treatment on the ability of the patient to fulfill/satisfy his or her needs. Assessing QoL in RA is an attempt to ensure the concern of patients that this important aspect of their daily lives will be measured.
Objectives: To evaluate the change of QoL of Bulgarian patients with RA after 6 months to 1-year of treatment with csDMARDs and bDMARDs by using two

generic questionnaires (HAQ-DI and SF-36) and a disease-specific measurement RAQoL.
Methods: A total of 220 patients with a mean age 55.05±10.63SD meeting the 1987 ACR classification criteria for RA were included in the study. The mean disease duration was 9.97±5.78SD. Patients were stratified according to treatment regimens into 2 age-matched treatment groups: 96 on csDMARDs and 124 on bDMARD therapy. Subjects with significant comorbidity, infectious disease, congestive heart failure (NYHA class III or IV), malignant hypertension, psychiatric illness, a history of lymphoproliferative disease or neoplasia were excluded from the study. All participants completed the HAQ-DI, SF-36v2TM and RAQoL at baseline, at months 6 and 12 thereafter. The scores of the three instruments were calculated via licensed calculator. Comparison was performed by analysis variance ANOVA.
Results: At baseline the mean scores of HAQ-DI and RAQoL did not differ greatly among patients on csDMARDs and bDMARDs (1.29±0.78SD *vs* 1.13±0.54SD, p=0.063; 16.31±8.26SD *vs* 15.03±7.13SD, p=0.219, respectively). However, the mean physical component summary score of SF-36 was significantly higher in bDMARDs compared with csDMARDs (32.98±5.97 *vs* 31.05±7.82, p=0.039), while in the mental component of this scoring system not such a difference was found (p=0.983). After 6 months subjects treated with bDMARD showed a significant decreasing of the means of the HAQ-DI and RAQoL, as opposed to the other treatment group (0.86±0.5SD *vs* 1.17±0.76SD, $p<0.001$; 10.98±6.53SD *vs* 14.55±7.96SD, $p<0.001$ respectively). Similar results were obtained for both physical and mental component summary scores of SF-36 (39.49±6.43SD *vs* 33.48±8.04SD, $p<0.001$; 43.69±7,99SD *vs* 39.66±10.19SD, p=0.001 respectively). At month 12 a significant improvement of QoL, measured by the three assessment tools was registered in patient receiving bDMARDs compared with the csDMARD treatment group ($p<0.001$).
Conclusions: Patient treated with bDMARDs showed better results for QoL than those on therapy with csDMARDs within a period of 12 months of treatment. Current management strategies should focus on improving the symptoms of activity and maintaining physical function in order to increase QoL in patients with RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3538

AB0284 ASSESSMENT OF DISEASE ACTIVITY BY DAS28-CRP, CDAI, SDAI AND RESPONSE TO TREATMENT WITH CSDMARDS AND BDMARDS AFTER ONE-YEAR FOLLOW-UP IN RHEUMATOID ARTHRITIS PATIENTS FROM BULGARIAN POPULATION

V.V. Boyadzhieva, N. Stoilov, M. Ivanova, R. Stoilov, R. Rashkov. *Rheumatology, University Hospital "St. Iv. Rilski" Medical Faculty - Medical University, Sofia, Bulgaria*

Background: The assessment of disease activity is an essential component in the selection of therapeutic approach for the prevention of disability of patients with RA.
Objectives: The current study was conducted to evaluate the disease activity in patients on csDMARDs and bDMARDs after 6 months to 1-year of treatment and to determine whether the benefits of different therapies were sustained over time.
Methods: For the purpose of the study were selected 220 patients with a mean age 55.05±10.63SD years, meeting the 1987 ACR classification criteria for RA. Patients were stratified according to treatment regimens into 2 age-matched treatment groups: 96 on csDMARDs and 124 on bDMARD therapy. Patient's assessment of disease related pain, global health and physician assessment of global health was made by visual analogue scale (VAS) – 100mm. Disease activity was the primary outcome domain. Independent joint assessor evaluate 28 joints on baseline, 6th and 12th month of the follow-up period. C-reactive protein (CRP) was used to measure the inflammation process. DAS28-CRP, CDAI and SDAI were calculated according to the standard formulas. Comparison was performed by analysis variance ANOVA.
Results: On baseline, patients on bDMARDs had a significantly higher mean time-averaged 28-joint disease activity score (5.03±0.84SD vs. 4.35±1.20SD, $p<0,001$), CDAI (25.06±7.32SD vs. 20.83±10.53SD, $p<0.001$) and SDAI (28.27±8.74 SD vs. 23.19±11.89 SD, $p<0.001$) compared to those on csDMARDs. On the 6th month in both groups (bDMARDS and csDMARDs) we found significant decrease in mean DAS28 ($p<0.001$, $p<0.001$), although no significant difference in disease activity between the groups was measured by this indicator (3.75±2.49 SD vs 3.90±1.10 SD, p=0.566). Patients on bDMARDs had significantly lower disease activity compared to those on csDMARDs after 6th and 12th month of treatment assessed by CDAI (13.43±4.98 SD vs 16.81±9.94 SD, p=0.001; 8.65±4.53 SD vs 15.86±10.02 SD, $p<0.001$), and SDAI (14.63±5.42 SD vs 18.38±10.49 SD, $p<0.001$; 9.39±4.92 SD vs 16.79±10.5 SD, $p<0.001$). Unlike results reported by DAS28-CRP which showed no change between the 6th and 12th month in patients receiving csDMARDs (3.90±1.10 SD, 3.82±1.12 SD, p=0.156) we observed a statistically significant difference in all three time intervals (0,6th,12th month) of the follow up period regarding to CDAI and SDAI.
Conclusions: After a year prospective follow-up, therapy with biologic DMARDs results in sustained suppression – minimal disease activity assessed by DAS28-CRP, CDAI and SDAI, compared to patients receiving DMARDs who had moderate disease activity according to these tools. The therapy with bDMARDs was superior to csDMARDs therapy for suppressing disease activity (assessed by DAS28-CRP, CDAI and SDAI) of rheumatoid arthritis (RA) on 6th and 12th month of the follow-up period.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6650

AB0285 CLINICAL SIGNIFICANCE OF GLUCOCORTICOID-INDUCED TUMOR NECROSIS FACTOR RECEPTOR RELATED PROTEIN LIGAND (GITRL) IN RHEUMATOID ARTHRITIS: RELATION TO DISEASE ACTIVITY AND TREATMENT OUTCOME

W.A. Hassan[1], A.I. Mansour[2]. [1]*Rheumatology and Rehabilitation;* [2]*Clinical and chemical pathology, Benha university, Benha, Egypt*

Background: Glucocorticoid-induced tumor necrosis factor receptor related protein (GITR) is a member of the tumor necrosis factor receptor superfamily that is activated by its specific ligand (GITRL). GITR is mainly expressed in immature and mature T cells especially regulatory (Treg) cells (CD4+ CD25+) and effector T cells (CD25–) [1]. GITRL is mainly expressed in endothelial cells, dendritic cells, macrophages and B cells but not in T cells. GITR-GITRL system is known to have important regulatory role on inflammatory response and immune reactivity.
Objectives: This study aimed to measure serum and synovial fluid (SF) levels of GITRL in patients with recent onset rheumatoid arthritis (RA) before and after initiation of therapy and to evaluate the relationship between GITRL and RA clinical and laboratory characteristics, disease activity and response to therapy.
Methods: We measured GITRL in the serum (n=48) and SF samples (n=21) from 48 recent onset RA patients and in the serum from 20 healthy control (n=20) at baseline and 6 months after initiation therapy with non-biological disease modifying anti-rheumatic drugs (DMARDS). In the patients Disease activity was calculated by the 28 joint counts (DAS28) and musculoskeletal ultrasound examination (MSUS) was performed at baseline and after 6 months using a 12-joint score (bilateral elbow, wrist, 2nd metacarpophalangeal (MCP), 3rd MCP, knee, ankle) [2]; immunoglobulin-M rheumatoid factor (IgM-RF) titre, anti-cyclic citrullinated peptide (anti-CCP) antibodies titre and C-reactive protein (CRP) levels were measured and the health assessment questionnaire (HAQ) score were recorded.
Results: Serum and SF GITRL levels were highly significantly increased in RA (39.38±16.78 ng/mL and 30.6±16.79 ng/mL respectively) compared to serum level in the healthy controls (10.3±5.46 ng/mL) ($p<0.001$). In RA patients, baseline serum and SF levels of GITRL significantly correlated with DAS28 (r=0.52 and 0.56 respectively, $p<0.05$), anti-CCP titres (r=0.46 and 0.51 respectively, $p<0.05$), grey scale (GS) (r=0.5 and 0.52 respectively, $p<0.05$) and power Doppler (PD) (r=0.65 and 0.68 respectively, $p<0.001$) synovitis scores. Also, serum and SF levels of GITRL at 6 months follow up significantly correlated with the DAS28 (r=0.42 and 0.48 respectively, $p<0.05$), GS score (r=0.46 and 0.51 respectively, $p<0.05$), PD signal (r=0.43 and 0.45 respectively, $p<0.05$). Logistic regression analysis showed that baseline serum levels of GITRL were predictive of follow up DAS 28 and PD synovitis score (p=0.009 and 0.03 respectively).
Conclusions: Rheumatoid arthritis patients have significantly increased serum and synovial levels of GITRL that remarkably correlated with the DAS28 and MSUS parameters of inflammations suggesting that it could be a useful marker to reflect RA disease activity. GITRL could be a useful biomarker to predict treatment outcome in RA patients.
References:
[1] Kim SH, Youn J. Rheumatoid Fibroblast-like Synoviocytes Downregulate Foxp3 Expression by Regulatory T Cells Via GITRL/GITR Interaction. Immune Netw. 2012;12(5):217–21.
[2] Naredo E, Rodríguez M, Campos C, Rodríguez-Heredia JM, Medina JA, Giner E, et al. Validity, reproducibility, and responsiveness of a twelve-joint simplified power Doppler ultrasonographic assessment of joint inflammation in rheumatoid arthritis. Arthritis Rheum 2008;59(4):515–22.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5476

AB0286 14 CASES STUDY OF MACROPHAGE ACTIVATION SYNDROME (MAS) IN SYSTEMIC ONSET JUVENILE IDIOPATHIC ARTHRITIS

X. Chen[1], H. Zeng[2]. [1]*Department of Pediatric Allergy, Immunology and Rheumatolog;* [2]*Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Background: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening syndrome.
Objectives: we aim to review the precipitating events,clinical features, treatment, and outcome of macrophage activation syndrome (MAS).Part patients were analysed the Polymorphisms of Perforin A91V (NCBI:SNP rs35947132) using special primers by polymerase chain reaction (PCR).
Methods: Retrospective review of cases of MAS from a prospectively collected database of children with autoimmune diseases from 2003 to 2008.
Results: Fourteen patients (nine boys) were considered to have evidence of MAS.The primary diagnosis was systemic onset juvenile idiopathic arthristis, with age ranged from 5 months to 12 years. No medication was identified as trigger. Eleven had infections prior to MAS,specific infectious agents were identified in four. High grade fever, new onset hepatosplenomegaly, lymphadenopathy, dysfunction

of liver,abnormal fat metabolism and hemophagocytosis were common clinical features.Two cases were with ARDS and MOF in three and three died. The perforin A91V (NCBI:SNP rs35947132) gene was detected in seven systemic onset juvenile idiopathic arthritis compolicated with MAS cases, but no mutation were found. Glucocorticoid, intravenous immunoglobulin, immunoimpressive therapy were effective and HP (Plasmapheresis) used in one serious case was also effective.
Conclusions: MAS is a rare and potentially fatal complication of childhood rheumatoid diseases,especially systemic onset juvenile idiopathic arthritis. Most of our patients were male, and most cases were preceded by infection. Bone marrow studies support the diagnosis. MOF may be a poor prognostic sign.Aggressive early therapy is essential.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1791

AB0287 MUTUAL ASSENT TOWARDS COMPREHENSIVE DISEASE CONTROL: THE RELATIONSHIP BETWEEN US MEASURES AND PATIENT REPORTED OUTCOMES IN EARLY RHEUMATOID ARTHRITIS

Y. El Miedany[1], M. El Gaafary[2], N. El Arousi[3], S.S. Youssef[3], A. Nasr[4].
[1]Rheumatology, Darent Valley Hospital, Dartford, United Kingdom; [2]Community and Public health; [3]Rheumatology and Rehabilitation; [4]Radiology, Ain Shams University, Cairo, Egypt

Objectives: Assessment of the relationship between US measures of joint inflammation/damage and patient reported outcomes (PROs): HAQ, pain and patient global assessment in early rheumatoid arthritis (early RA) patients over 5-years follow up period.
Methods: This longitudinal cohort of 261 patients with early RA was derived from the US monitoring study [1]. Adopting OMERACT definitions; correlations between total US scores (synovial hypertrophy, synovial fluid, Power Doppler, bone erosion and tenosynovitis) and PROs [2] namely functional disability (HAQ), pain and patient global scores were determined at 0, 1, and 5years. Radiological damage was assessed using modified Total Sharp score (mTSS). Univariate correlations as well as correlations between interval changes were assessed. Multivariable regression models were used to evaluate the associations over all time-points and their relationship to clinical disease activity measures.
Results: There were significant correlations ($p<0.01$) between total US score and HAQ (r=0.71), pain (r=0.69) and patient global scores (r=0.66) at all timepoints. The association tends to be stronger with increase disease duration (Spearman correlation 0.12 at baseline, 0.22 at 1-year and 0.41 at 5-years). Change in mTSS score at 5-years was not associated with changes in PROs. Improvements in US scores were also associated with improvements in PROs. Multivariate models revealed that synovial hypertrophy and Power Doppler scores were associated ($p<0.01$) with functional disability, pain and patient global assessment, controlling for clinical disease activity measures. Studying the pattern of joint involvement, it was associated significantly ($p<0.01$) with the US score of the affected joints. US total score at 1-year predicted subsequent 5-year HAQ score (R2=0.17). At 0, 1- and 5-years, total US scores were higher in patients whose HAQ score was >1 (9.26) compared to those below 1 (4.16, $p<0.01$).
Conclusions: the link between joint inflammation/structural damage and PROs is of critical importance to the care of patients with inflammatory arthritis. US measures of inflammation and structural damage correlated independently with physical function, pain and patient global assessments. A clear relationship between radiographic structure damage and the patient's perceived remission/flare provide the basis for comprehensive disease assessment and management.
References:
[1] El Miedany et al. Current Rheumatology Reviews 2015; 11, 18–27.
[2] El Miedany et al. Clin Exp Rheumatol 2010; 28(5):734–44.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4485

AB0288 LABORATORY MARKERS OF INFLAMMATION AND SERUM NICOTINAMIDE PHOSPHORIBOSYLTRANSFERASE LEVEL IN RHEUMATOID ARTHRITIS PATIENTS

Y. Akhverdyan[1], B. Zavodovsky[1], J. Polyakova[1], L. Seewordova[1], I. Zborovskaya[1], T. Rogatkina[2]. *[1]Federal State Budgetary Institution "Research Institute of Clinical and Experimental Rheumatology" Under the Russion Academy of Medical Sciences; [2]Volgograd State Medical University, Volgograd, Russian Federation*

Objectives: To study relationship between serum levels of nicotinamide phosphoribosyltransferase and laboratory markers of inflammation in patients with rheumatoid arthritis (RA).
Methods: We determined nicotinamide phosphoribosyltransferase level in sera of 140 patients with RA (96 women and 44 men) by indirect enzyme-linked immunosorbent assay (RaiBiotech, cat No. EIA-VIS-1). The control group consisted of 20 women and 10 men aged 22 to 55 years without complaints of pain in the joints throughout life. The mean duration of disease was 5.94±0.37 years.
Results: We divided all RA patients into 2 groups: one group (118 patients) with elevated levels of nicotinamide phosphoribosyltransferase serum (more than 3.9 ng/ml) and second group (22 patients) - with normal range.
In each of the two groups, the levels of CRP and ESR were determined.
Patients with elevated levels of Nampt had the following laboratory parameters (M±m): ESR – 37.83±1,57, CRP – 56.09±3,73 (rate - less than 5.0 mg/l). The second group had following data: ESR 22.46±0,56, CRP 21,65±1.38. Thus, patients with elevated levels of nicotinamide phosphoribosyltransferase had significantly higher concentrations of ESR and CRP ($p<0,001$).
Conclusions: There is the relationship between the level of nicotinamide phosphoribosyltransferase serum and laboratory markers of inflammation in RA (CRP and ESR). The data indirectly confirm the hypothesis that increased levels of nicotinamide phosphoribosyltransferase in RA patients is associated with disease activity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1958

AB0289 PREDICTOR OF THE SIMPLIFIED DISEASE ACTIVITY INDEX 50 (SDAI 50) AT MONTH 6 DURING BDMARDS TREATMENT IN PATIENTS WITH LONG-ESTABLISHED RHEUMATOID ARTHRITIS: A SINGLE-CENTER, RETROSPECTIVE STUDY

Y. Miwa, A. Nishimi, S. Nishimi, T. Tokunaga, S. Ishii, T. Kasama on behalf of ASHURA Registry Group. *Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan*

Background: The simplified disease activity index (SDAI) 50 has good agreement with the EULAR response measures for early rheumatoid arthritis (RA). Although there are reports on early RA, there have been no reports on long-established RA.
Objectives: In this study, we analyzed the relationships between various baseline factors and SDAI 50 after six months of biological disease-modifying antirheumatic drugs (bDMARDs) treatment to determine the prognostic factors for long-established RA.
Methods: The subjects were 332 RA patients who had been treated with bDMARDs for 6 months. The following characteristics were investigated: age, gender, disease duration, smoking history, body mass index, steroid and methotrexate dosage, previous bDMARDs use, combined csDMARDs use, ESR, CRP, serum matrix metalloproteinase-3 levels, SDAI score, health assessment questionnaire disability index score (for daily living activities) and short form-36 score (for quality of life). As a primary outcome index, SDAI response was defined as a 50% reduction in SDAI score between baseline and 6 months (SDAI 50).
Results: The group of RA patients who achieved SDAI 50 (Group A: 204 patients) had a higher tender joint count (p=0.041), swollen joint count (p=0.001), evaluator's global assessment (p=0.027) and SDAI (p=0.006) than did those who did not achieve SDAI 50 (Group B: 152 patients). Before the start of the treatment, steroid dosage (p=0.0187, odds ratio: 1.119, 95% CI: 1.029–1.229) and SDAI (p=0.0003, odds ratio: 0.953, 95% CI: 0.928–0.978) were determined based on logistic regression analysis. Comparisons were performed between Groups A and B and between before treatment and after 6 months of SDAI. Group A showed a significant improvement compared to Group B by repeated measure analysis of variance (ANOVA) (Interaction: p=0.000, Group A vs. Group B: p=0.000, before vs. after treatment: p=0.000).
Conclusions: Our study demonstrated that RA patients with a lower steroid dosage and higher SDAI baseline are more likely to achieve SDAI 50 with bDMARD treatment.
Acknowledgements: ASHURA Resistry Groups
Disclosure of Interest: Y. Miwa Grant/research support from: Astellas Pharma Inc., Mitsubishi Tanabe Pharma Corporation, AbbVie CK, Pfizer Japan Inc., Chugai Pharmaceutical Co., Ltd., Eizai Co., Ltd, Asahi Kasei Pharm Co., Ltd, YL biologics Ltd., Japan Blood Products Organization,. Ono Pharmaceutical Co., Ltd., Nippon Kayaku Co., Ltd., and Teijin Pharma Ltd., A. Nishimi: None declared, S. Nishimi: None declared, T. Tokunaga: None declared, S. Ishii: None declared, T. Kasama Grant/research support from: Mitsubishi Tanabe Pharma Corporation and AbbVie CK.
DOI: 10.1136/annrheumdis-2017-eular.1818

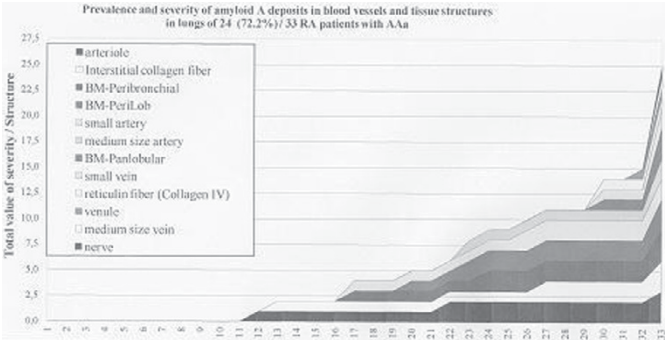
Rheumatoid arthritis - comorbidity and clinical aspects

AB0290 PULMONARY AMYLOIDOSIS IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS

Á. Apáthy[1], M. Bély[2]. *[1]Department of Rheumatology, St. Margaret Clinic Budapest; [2]Department of Pathology, Hospital of the Order of the Brothers of Saint John of God, Budapest, Hungary*

Background: AA amyloidosis (AAa) is one of the most insidious systemic complications of rheumatoid arthritis (RA), which furtively may lead to death [1].
Objectives: The aim of this study was to determine the prevalence and location of amyloid A deposition in the lungs of RA patients at the time of death.
Methods: A randomized autopsy population of 161 in-patients with RA was studied. AAa complicated RA in 34 (21.1%) cases [1].

At least four tissue samples of lungs (from apical and basal regions of both lungs) were available for histologic evaluation in 33 of these 34 patients.
RA was confirmed clinically according to the criteria of the ACR.
The presence of amyloid A deposits in various structures of the lungs was determined histologically by amyloid specific Congo red staining, according to Romhányi [2].
The extent of amyloid A deposition was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale, based on the number of involved tissue structures per light microscopic field [1]. ("0": no amyloid deposits, "1": Sporadic, minimal amyloid deposits on different tissue structures, "2": less than five, "3": five or more involved tissue structures per microscopic field at objective magnification of x20)
Results: Amyloid A deposition in the lungs was detected in 24 of 33 (72.2%) patients.
Amyloid deposition in various structures does not begin at the same time.
In the early stage of systemic amyloidosis there were histologically detectable amyloid deposits only in a few structures (arterioles, interstitial collagen fibers, peribronchial and perilobular basement membranes). In other structures (small and medium size arteries, panlobular basement membranes, small veins, collagen IV reticulin fibres, venules, medium size veins and nerves) deposits were seen only in late stages of amyloidosis (with massive involvement of the mentioned structures).

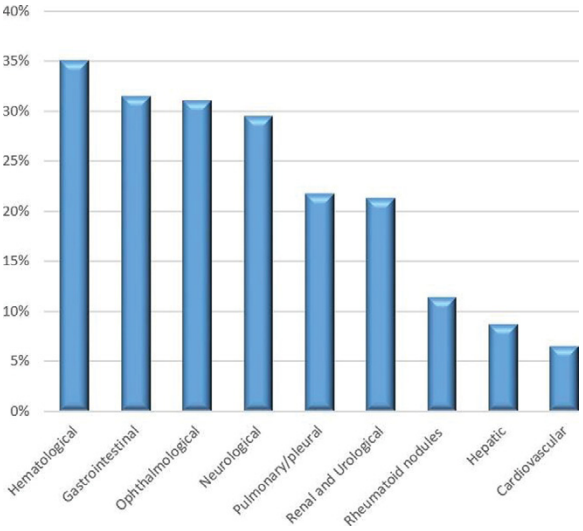


Conclusions: Amyloidosis is a progressive, cumulative process, involving in its early stage only a few structures in some organs, and increasingly more in the later stages of the disease [1]. Amyloid A deposition starts in the most frequently involved structures of the most frequently involved organ [1].
In the lungs amyloid A deposition starts in the wall of arterioles and in interstitial collagen fibers. As time progresses, basement membranes of peribronchial and peripheral regions of lobules, small and medium sizes arteries become involved. Still later panlobular deposition of basement membranes, small veins, reticulin fibers (collagen IV) of subpleural fat tissue, venules and medium size veins become involved. The involvement of nerves indicates advanced stages of amyloid deposition in the lung.
This chronology of amyloid A deposition allows an indirect assessment of the stage of amyloidosis. Based on the involvement of structures in lung biopsy specimens the pathologist may be able to estimate involvement of the other structures, even if not present in the sections. Involvement of arterioles alone (without involvement of small arteries) indicates an early stage of amyloidosis, whereas amyloid A deposits in veins or peripheral nerves suggests an advanced stage with massive involvement of other pulmonary structures.
References:
[1] Bély M, Apáthy Á: Clinical pathology of rheumatoid arthritis: Cause of death, lethal complications and associated diseases. 1–440 pp. Akadémiai Kiadó, Budapest 2012 http://www.akkrt.hu.
[2] Romhányi G (1971) Virchows Arch 354, 209–222.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1225

AB0291 EPIDEMIOLOGY AND COMORBIDITY OF RHEUMATOID ARTHRITIS IN UPPER EGYPT, A HOSPITAL BASED STUDY

A.M. Elsaman, A.R. Radwan, M.H. Abou Dahab, A.M. Sherif, E.M. Abu Al-Fadl.
Rheumatology, Sohag University Faculty of Medicine, Egypt, Egypt

Background: Rheumatoid arthritis (RA) is one of the commonest autoimmune diseases. It affects about 1% of the population worldwide (1). The prevalence of RA varies widely between different countries (2). Not only the prevalence of the disease which differs among different continents, races, ages and socioeconomic levels but also the disease pattern. Studies explaining the epidemiology of RA in Egypt in general and in upper-Egypt, in particular, are very limited (3).
Objectives: To estimate the comorbidity of rheumatoid arthritis and its relation to disease activity, duration, disease pattern and demographic features of RA patients in upper Egypt.
Methods: This study was carried out on 923 patients who fulfilled ACR/EULAR criteria 2010. All of them live in Sohag governorate and aged 18 years or older DAS28-ESR score, first involved joint, joint distribution, disease pattern, extra-articular comorbidities including gastrointestinal, urinary, cardiac, haematological and neurological were estimated. The activity of daily living was valued by Erlangen score (E-ADL).
Results: The mean age of the participants was 45±10.9 years, with a range (19–70). The median of the disease duration was 5 years, with a range (0.5–40 years). Most of the participants were female (691, 74.9%). Disease onset was gradual or insidious in 94.3% of cases and acute in 5.7% of them. First joint group affected were the small joints of the hands (MCPs and PIPs), recorded in 48.9% of cases, Followed by wrist joints (29.3% of cases), then knees (9%), ankles and small joints of the foot (6%) and lastly other joints collectively recorded in only 6.8%. The commonest extra-articular comorbidities were haematological, seen in 323 cases; 35%, followed by gastrointestinal in 290 cases (31.4%), then ophthalmological in 31%, entrapment syndromes in 29.4%, pulmonary in 21.7%, urological in 12.4%, rheumatoid nodules in 11.4%, liver cirrhosis in 8.7%, renal impairment in 8.5% and Cardiovascular diseases in 6.5%. The activity of daily living (E-ADL) showed that most of the cases fell in score 4 (58.2%). Regarding DMARDs treatment of the study population, Methotrexate (MTX) was used regularly by 78.3% of cases, hydroxychloroquine (HCQ) by 78.1%, followed by Leflunomide (LEF) by 26.4% and sulfasalazine (SSZ) by 13.1%. The majority of cases used combination therapy of either MTX+HCQ, MTX+SSZ, MTX+HCQ+SSZ or MTX+LEF. Regarding other drugs, 99% of cases used NSAIDs (regularly in 30.2% and on demand in 68.8%). Steroids were regularly used by 28.8% of cases.



Conclusions: The commonest comorbidities were haematological, gastrointestinal, ophthalmological and neurological ones; respectively. Erosion, deformity and Das28-ESR score have a great impact on E-ADL score.
References:
[1] Gibofsky A. Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. Am J Manag Care. 2012;18(13 Suppl):S295–302.
[2] Ferucci ED, Templin DW, Lanier AP, editors. Rheumatoid arthritis in American Indians and Alaska Natives: a review of the literature. Seminars in arthritis and rheumatism; 2005: Elsevier.
[3] El-Labban AS, Omar HAA, El-Shereif RR, Ali F, El-Mansoury TM. Pattern of young and old onset rheumatoid arthritis (YORA and EORA) among a group of Egyptian patients with rheumatoid arthritis. Clinical medicine insights Arthritis and musculoskeletal disorders. 2010;3:25.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1440

AB0292 CLINICAL FEATURES OF RHEUMATOID ARTHRITIS AT 75 YEARS OF AGE AND OLDER IN JAPAN – COMPARISON WITH POLYMYALGIA RHEUMATICA IN THE SAME AGE GROUP

A. Aoki[1], H. Oka[1], I. Aoki[2]. *[1]Dept. of Rheumatology, Tokyo Medical University Hachioji Medical Center, Tokyo; [2]Dept. of Pathology, Kanagawa Prefectural Ashigarakami Hospital, Kanagawa, Japan*

Background: As Japan is a super-aged society, we have many chances to care for elderly patients in our hospital. Elderly-onset rheumatoid arthritis (RA) (onset age >60 years) may present similar symptoms to those of polymyalgia rheumatica (PMR). We consider that differential diagnosis of RA and PMR is more difficult in patients over 75 than those under 74 in clinical practice.
Anti-cyclic citrullinated peptide antibody (ACPA) was reported to be a helpful tool in the differential diagnosis of EORA from PMR. However, when elderly patients with negative ACPA complained of bilateral shoulder and/or girdle pain, it was difficult to differentiate PMR from RA.
Objectives: The study aimed to explore clinical features of RA and PMR at onset age 75 years. For the present investigation, we used a novel diagnostic

tool to distinguish ACPA-negative elderly RA patients from PMR patients at initial presentation.

Methods: From April 2011 to December 2016, 21 RA patients and 24 PMR patients in our hospital, whose onset age was over 75 years, were recruited for this study. PMR patients did not have any evidence of giant cell arteritis. The diagnosis of RA was made based on 2010 ACR/EULAR RA classification criteria. The diagnosis of PMR was made based on 2012 EULAR/ACR classification criteria or Bird's criteria. Data were obtained from medical records under informed consent. Statistical analysis was performed using the Mann-Whitney U-test to compare median values and Fisher's exact test to compare frequencies (IBM SPSS version 24). $P<0.05$ indicated statistical significance.

Results: RA patients (6 men and 15 women) consisted of fifteen ACPA+ (11 RF+, 4 RF–), six ACPA– (1 RF+, 5 RF–). PMR patients consisted of 12 men and 12 women. All of them were ACPA–/RF– and did not meet 2010 RA criteria. Twenty patients met 2012 PMR classification criteria, and 4 patients without bilateral shoulder pain met Bird's criteria. Clinical features and statistical results are shown in the Table. Sixty-seven percent of RA patients and 13% of PMR patients had left-right differences in joint pain.

Scoring was performed based on clinical findings. Tenderness and/or swelling joint counts among wrists, fingers, ankles, and knees = each 1 point, left-right difference =1 point, no bilateral shoulder pain =1 point, no girdle pain =1 point, no fever =1 point; the maximum score was 8. The mean score in RA patients was 4.8 (SD =1.44), whereas that in PMR patients was significantly lower at 1.5 (0.98) ($P<0.001$). Receiver operating characteristic (ROC) curve analysis was used to determine the most suitable cut-off level to find RA. A score over 3 was 100% sensitivity and 87.5% specificity. All 6 ACPA-negative RA patients showed a score over 4.

Table Clinical features in patients with rheumatoid arthritis (RA) and polymyalgia rheumatica (PMR)

			RA≧75 (n=21)	PMR≧75 (n=24)	*P*-value
Age at onset (years)		mean (SD)	81.5 (4.18)	80.5 (3.95)	0.4
Male		n (%)	6 (33)	12 (50)	0.1
Time from onset to start of treatment (months)		median (IQR)	2.0 (1.5)	1.5 (1.4)	0.09
Joint/muscle pain at onset	Bilateral shoulder	n (%)	10 (48)	20 (83)	0.03
	Girdle	n (%)	0 (0)	12 (50)	<0.001
	Wrist	n (%)	19 (91)	7 (30)	<0.001
	Finger	n (%)	4 (19)	0 (0)	0.04
	Foot	n (%)	6 (29)	0 (0)	0.007
	Knee	n (%)	13 (62)	2 (8)	<0.001
Systemic symptoms	Fever	n (%)	3 (14)	14 (58)	0.002
	Body weight loss	n (%)	6 (29)	14 (58)	0.07
Rheumatoid factor positive		n (%)	12 (57)	0	<0.001
Anti-CCP antibody positive		n (%)	15 (71)	0	<0.001
C-reactive protein (mg/dL) at onset		mean (SD)	6.1 (5.66)	8.4 (4.61)	0.1
Matrix metalloproteinase 3 (ng/mL) at onset		mean (SD)	431 (373.6)	421 (342.0)	0.9

SD, standard deviation; IQR, interquantile range; CCP, cyclic citrullinated peptide

Conclusions: Pease et al studied RA at onset 60 years and over and PMR, and reported that arthritis of wrists and fingers was suggestive of RA[1]. However, in our study, small joint swelling was rare in RA patients 75 years and older. The scoring system we made might be useful for the differential diagnosis of ACPA-negative RA and PMR in elderly patients 75 years and older.

References:

[1] Pease CT, et al. Diagnosing late onset rheumatoid arthritis, polymyalgia rheumatica, and temporal arteritis in patients presenting with polymyalgic symptoms. A prospective longterm evaluation. J Rheumatol 32: 1043–1046, 2005.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2016

AB0293 METABOLIC SYNDROME AND INSULIN RESISTANCE IN ADULT EGYPTIAN FEMALES WITH RHEUMATOID ARTHRITIS

A.A.-R. Youssef[1,1], N.O. Neseem[1], M.A.-B. Omar[2], O.M. El-Siri[1].
[1]Rheumatology & Rehabilitation; [2]Clinical Pathology, Mansoura University, Mansoura, Egypt

Background: Patients with Rheumatoid Arthritis (RA) have an increased risk for cardiovascular disease (CVD) due to higher prevalence of traditional risk factors (1), Insulin resistance (IR) is implicated in inflammatory diseases such as RA (2). The prevalence of Met.Syn and IR in Egyptian female RA patients has not been studied before.

Objectives: To find out the prevalence of Met.Syn and IR in a cohort of Egyptian females with RA and in controls and to study the associated risk factors

Methods: 60 female RA patients and 30 healthy females matched for age were included according to the ACR/EULAR 2010 classification criteria. Disease activity was assessed using DAS- 28. IR using HOMA- index (HOMA- IR) (3) Met.Syn was defined according to the updated third report of the National Cholesterol Education Program's Adult Treatment Panel (NCEP-ATP III) criteria (4).

Results: Prevalence of Met.Syn in female RA patients is significantly (sig.) higher (56.7%) than that of controls (33.3%, P=0.04). IR is prevalent in RA patients (63.4%), Patients with Met.Syn exhibited sig. higher serum levels of TG ($P<0.001$,) FBG (P=0.02), CRP (P=0.02), Fasting insulin (P=0.01) and IR (P=0.03) than those without. Median CRP (24) and mean DAS- 28 (5.6±1.5) in RA patients with increased IR are sig. higher than those of RA Patients with normal IR (6.5, $P<0.01$) & (4.7±1.5 $P<0.04$) respectively. Significant positive correlation was found between DAS-28 and IR (Rs =0.3, P=0.03). Using logistic regression, high systolic blood presser (OR =1.2, 95% CI: 1.02 – 1.39, P=0.03) and elevated CRP (OR =1.07, 95% CI: 1.01 – 1.14, P=0.04) have shown to be the significant independent predictors for the development of Met.Syn

Conclusions: Met.Syn. and IR are prevalent in female Egyptian RA patients adding to the CV risk of the disease and both are related to increased disease activity. Rheumatologists should pay an attention to control RA disease activity in addition to screen patients for components of the Met.Syn and introduce appropriate treatment strategies. Further studies are warranted to get more conclusive results.

References:

[1] Gremese, E., & Ferraccioli, G. (2011). The metabolic syndrome: the crossroads between rheumatoid arthritis and cardiovascular risk. Autoimmunity Reviews, 10(10), 582–589.

[2] Goodwin, P. J., Ennis, M., Bahl, M., Fantus, I. G., Pritchard, K. I., Trudeau, M. E., ... & Hood, N. (2009). High insulin levels in newly diagnosed breast cancer patients reflect underlying insulin resistance and are associated with components of the insulin resistance syndrome. Breast Cancer Research and Treatment, 114(3), 517–525.

[3] Reilly, M. P., Wolfe, M. L., Rhodes, T., Girman, C., Mehta, N., & Rader, D. J. (2004). Measures of insulin resistance add incremental value to the clinical diagnosis of metabolic syndrome in association with coronary atherosclerosis. Circulation, 110(7), 803–809.

[4] Grundy, S. M., Cleeman, J. I., Daniels, S. R., Donato, K. A., Eckel, R. H., Franklin, B. A., ... & Spertus, J. A. (2005). Diagnosis and management of the metabolic syndrome an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation, 112(17), 2735–2752.

Acknowledgements: We acknowledge the efforts received by all staff members of departments of Rheumatology and clinical pathology at Mansoura University Hospital, Egypt.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1320

AB0294 PREGNANCY IN RHEUMATOID ARTHRITIS – A ROMANIAN COHORT

A. Bobirca[1], F. Bobirca[2], I. Ancuta[1], C. Mihai[1], C. Tataru[1], C. Comsa[1], M. Bojinca[1], M. Micu[3], A. Musetescu[4], C. Ancuta[5], V. Stoica[1]. *[1]Internal Medicine and Rheumatology; [2]General Surgery, Cantacuzino Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest; [3]Division of Rheumatology, Department of Rehabilitation II, Clinical Rehabilitation Hospital, Cluj-Napoca; [4]Rheumatology Department, University of Medicine and Pharmacy, Craiova; [5]Clinical Hospital of Rehabilitation, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania*

Background: Planning a pregnancy in rheumatoid arthritis (RA) meets several issues, mostly concerning potential drug toxicity and disease flares

Objectives: The purpose of this study is to evaluate pregnancy planning, RA activity during pregnancy and postpartum, pregnancy and fetal outcomes in a Romanian cohort of female patients diagnosed with RA.

Methods: This is an observational, ambispective study, including 58 RA Caucasian females with obstetric history after the onset of RA (20 females - prospective, 38 - retrospective). The cases were obtained from several Clinics of Rheumatology from Romania

Results: The mean age at inclusion was 37.1 years, age at RA diagnosis 3.9 years and mean age at conception 32.2 years. We recorded a total number of 96 pregnancies: 48 deliveries at term, 4 premature births, 15 elective abortions, 24 spontaneous abortions, and 5 ongoing. 34/96 (35.4%) had at least one unplanned pregnancy, while being on treatment.

Concerning the exposure to synthetic DMARDs during the pregnancy: 6 patients received Leflunomide and 4 received Methotrexate during the first trimester, the pregnancy outcomes being: 3 spontaneous and 3 elective abortions, 3 normal birth (1- Cholestiramine wash-out), 1 premature twin pregnancy.

Regarding biologic DMARDs: 5 were exposed to Etanercept - 3 less than 3 weeks, (2 normal births and one elective abortion- due to Methotrexate use), 2 treated in second trimester: 1 only in the 15th and 16th weeks due to relapse - normal birth, and the other one until week 20, pregnancy still ongoing.

One patient was treated with Certolizumab until week 12, the pregnancy is ongoing, and one with Adalimumab until week 4, the fetus had intrauterine growth restriction, premature birth.

6 patients treated with Rituximab were included, last infusions were: 4 weeks before conception (1- spontaneous abortion and 1 normal birth), 48 weeks (2 normal births and 1 premature), and one at 4 weeks after conception - normal birth.

In 4 cases the patients stopped the biological DMARD before conception: Etanercept 6 months and 2 years, Adalimu-mab,6 months with normal outcome, and for Tocilizumab 9 months (growth restriction)

81.25% of our patients were in Remission or Low Disease Activity (by DAS28CRP) at conception and generally this status was maintained, excepting several situations.

The average pregnancy length was 36.36 weeks and the mean birthweight was 2878.90 grams.2 growth restriction was identified and several atopic dermatitis, no teratogenic effect.
13 patients never had a new flare postpartum and in the others the mean time of postpartum flare was 12.1 weeks
Conclusions: Patients with RA can have successful pregnancies. More than 60% of pregnancies have been planned. Pregnancy decreases disease activity, but many deliveries are followed by RA flares. No fetal abnormalities were diagnosed.
References:
[1] Østensen M, et all. State of the art: Reproduction and pregnancy in rheumatic diseases: Autoimmun Rev. 2015 May;14(5):376–86. doi: 10.1016/j.autrev.2014.12.011. Epub 2014 Dec 30.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6605

AB0295 THE RECALL SURVEY: DATA FROM A MULTICENTER EDUCATIONAL EVENT ON PATIENTS WITH RA

A. Delle Sedie[1], E. Filippucci[2], O. Epis[3], P. Macchioni[4], S. Tropea[5], C. Bonali[6], M. Canzoni[7], A. Iagnocco[8]. *[1]Rheumatology Unit, University of Pisa, PISA; [2]Rheumatology Department, Università Politecnica delle Marche, Jesi; [3]Rheumatology Unit, Ospedale Niguarda Milano, Milano; [4]Rheumatology Unit, Reggio Emilia Hospital, Reggio Emilia; [5]5ASP7 Busacca Hospital, Ragusa; [6]Rheumatology Unit, Ospedale San Paolo, Bari; [7]Local Health Unit (ASL) Rome 1, Rome; [8]Academic Rheumatology Unit, Università degli Studi di Torino, Torino, Italy*

Background: Ultrasound (US) is able to show subclinical synovitis in patients (pts) with rheumatoid arthritis (RA) who are in clinical remission (CR); this has been proposed as a predictive factor for both clinical flares and progression of the structural damage in CR pts.
Objectives: To investigate the US characteristics of RA pts presenting either CR or low disease activity (LDA).
Methods: In 2015 an educational event focused on the added value of US in RA pts was held in 22 rheumatology centers in Italy. After a brief presentation on the evidence of US added value for the clinician given by expert sonographers (rheumatologists with a special interest in US that were performing US as their usual activity for many years), in every center, the local rheumatologists provided RA pts to be examined by US. All the US machines were identical both for type (Logiq E R7, General Electrics, with a 4.2–13 MHz linear probe) and settings (both for grey-scale and power Doppler (PD)). Pts signed an informed consent and a brief history of them was collected by the local rheumatologists (previous and current therapy, DAS28, HAQ score). The US examination was performed bilaterally on wrists, MCP and MTP joints, looking for synovitis (effusion, synovial proliferation and PD signal) and bone erosions. The positive findings were scored according to a 0–3 score for synovitis components and presence/absence for erosions; the number and size of the largest erosion was also registered.
Results: Demographic and descriptive data of the 433 pts examined are reported in Table I. Pts were divided on the basis of the DAS28 result. Statistically significant differences in age and disease duration were registered between the group in CR and the group with DAS28≥3.2 (p=0,019 and p=0,012, respectively), while no differences were found for HAQ or MTX use. Higher positivity of findings, regardless which was the score, was present in LDA group for effusion, synovial proliferation and PD signal. Significant differences were seen between CR and LDA group for effusion (general, MCP and MTP joints; p=0,011, p=0,026, p=0,017 and p=0,013, respectively), PD positivity (general, wrist, MCP and MTP joints; p=0,006, p=0,023 and p=0,05, respectively) and erosions (p=0,002), with higher positivity for pts in LDA.

Table 1. demographic data

	DAS28 <2.6	DAS28 2.6–3.2	DAS28≥3.2
N (M:F)	155 (34:121)	170 (39:131)	108 (20:88)
Age (mean±SD; yy)	56.1±14.3	59.2±12.2	60.5±11.4
Disease duration (mean±SD; dd)	2368.49±2565.39	3274.16±2948.36	1966.53±1884.58

Conclusions: The US assessment in this large cohort of RA pts showed frequent positive findings both in the CR and in the LDA group, confirming the results from previous studies. US is a useful imaging tool for the detection of subclinical joint abnormalities in RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4475

AB0296 HMG-COA REDUCTASE INHIBITOR DRUGS (STATINS) BENEFIT IN CARDIOVASCULAR RISK PREVENTION AND AMELIORATE DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

A. Hon, M. Sultanova. *Cardiorheumatology, Tashkent Medical Academy, Tashkent, Uzbekistan*

Background: Patients with active rheumatoid arthritis (RA) are frequently diagnosed with an atherogenic lipid profile and supra-aortic vessel ultrasound signs of atheromatous plaques, which have been linked to the inflammatory activity of RA. Recent experimental and clinical evidences suggest that the beneficial effects of statins are pleiotropic and have been proposed to have anti-inflammatory and immunomodulatory effects, inhibiting proinflammatory cytokines (IL-1β, 6, 8, TNF-α), adhesion molecules (sICAM 1, E-, P-selectin), osteoprotegerin, which are implicated in RA pathogenesis. However, the beneficial role of statin therapy in clinical improvement and their benefit-risk profile are still debatable.
Objectives: To evaluate the effect of medium-term rosuvastatin therapy on lipid profile, endothelial dysfunction and RA activity in patients with rheumatoid arthritis (RA) in comparison with conventional disease modifying antirheumatic drugs (DMARD) therapy.
Methods: The study included 82 patients in the Specialized Course Outpatient Therapy Department of the 1st Clinic of Tashkent Medical Academy of age group between 44 and 65 years (mean 52±8.4), predominantly female gender (n=57, 69.5%), with early RA (mean disease duration 9.2±2.4 months), and divided into 2 groups. Group 1 (n=40) received methotrexate (MTX; 7.5 mg/week; plus prednisolone (10 mg/day). Group 2 (n=42) received MTX and prednisolone with the same previous doses plus rosuvastatin (40 mg/day). Lipid profile assessment comprised triglycerides, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C). Disease activity was assessed by the disease activity score of 28 joints (DAS28), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and visual analog scale (VAS). Disease activity, lipid profile and intima-media thickness (IMT) of common carotid arteries were measured before and after 85 days (6 months) of treatment.
Results: 4 patients receiving rosuvastatin were excluded due to abnormal liver function test parameters (De Ritis ratio <0.9), further assessment was thus performed on 78 (Group 2, n=38) early RA patients. Overall ESR (Group 1: 24.4±7.26; Group 2: 37.4±12.3) and CRP (Group 1: 5.56±0.58; Group 2: 3.71±1.23) declined significantly during the treatment. The mean DAS28, unconditionally considered as the most important index of clinical disease activity in RA, was found to be lower ($p<0.05$) in the adjunct statin-treated group (Group 2: 3.68±0.77) than that of the conventional DMARD treated group (Group 1: 4.45±1.08). Statin significantly reduced LDL-C (3.9±1.2 mmol/l to 3.3±0.8 mmol/l; p=0.08) and increased HDL-C (1.3±0.6 mmol/l to 2.0±0.4 mmol/l; p=0.06) after 6 months of treatment. However, rosuvastatin therapy showed no significant improvement in VAS score (6.7±1.5 to 6.9±0.6; p=0.41) and IMT (1.04±0.09 to 1.08±0.07; p=0.05).
Conclusions: Statins ameliorate RA activity, reduce potential cardiovascular risk in the context of atherosclerosis and mediate clinically apparent anti-inflammatory effects, but long-term effects and benefit-risk profile should be addressed in the management of elevated risk of cardiovascular events in RA patients.
References:
[1] Husain K., Hernandez W., Ansari R. A., Ferder L. Inflammation, oxidative stress and renin angiotensin system in atherosclerosis. World Journal of Biological Chemistry. 2015;6(3):209–217.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6577

AB0297 TREATMENT WITH LOW-DOSE PREDNISONE DOES NOT INFLUENCE BODY COMPOSITION DURING THE FIRST YEAR OF RHEUMATOID ARTHRITIS- A PILOT STUDY

A. Raczkiewicz, O. Bujakowska, A. Juszkiewicz, B. Kisiel, J. Kur-Zalewska, M. Tłustochowicz, W. Tłustochowicz. *Internal Medicine and Rheumatology, Military Institute of Medicine, Warsaw, Warsaw, Poland*

Background: Early change in body composition is one of the risk factors of CVD in rheumatoid arthritis (RA). These changes have been atributed to inflammation and decreased physical activity. Glucocorticosteroids (GCS) reduces inflammation but may influence body composition. There is limited information about the effects of low-dose GCS on body composition in early RA.
Objectives: The aim of the study was to assess the presence of altered body composition in patients with early rheumatoid arthritis (eRA) and to determine whether low-dose prednisone affects body composition.
Methods: 65 consecutive eRA patients (49 women) aged 61±14 years were assessed at the time of diagnosis and after 12 months of treatment. All the patients had been treated with methotrexate (target dose 25–30mg/week) and tapered doses of prednisone (mean dose 4.8±3.4 mg/day). Disease activity score (DAS28), Health Assesment Questionnaire (HAQ), body mass index (BMI), waist/hip ratio, comorbidities, physical activity and smoking were recorded. Total and regional lean mass and fat mass were measured with dual energy X-ray absorptiometry (DXA). DXA measures were repeated after 12 months in 34 patients (24 women) and compared with baseline data.
Results: At baseline fat free mass index (FFMI; kg/m^2) was below the 10th percentile of a reference population in 32% of the women and 25% of the men. Reduced FFMI correlated with baseline ESR. Fat mass index (FMI) was above 90th percentile in 28% of the women and 42% of the men. Fat mass index (FMI;kg/m^2) correlated with HAQ, age and femoral BMD in women. After 12 months FFMI and FMI did not change significantly. There was no correlation between prednisone doses and the duration of prednisone treatment and changes in regional lean mass and fat mass. The decrase of FFMI (in 16 patients) was associated with higher mean ESR and lower vitamin D3 serum concentration.
Conclusions: Low FFMI was common in patients with eRA. The treatment with

low-dose glucocorticosteroids did not influence altered body composition during the first year of eRA therapy.

References:
[1] Book C, Karlsson MK, Nilsson JA et al. Changes in body composition after 2 years with rheumatoid arthritis. Scandinavian Journal of Rheumatology 2011(40:2); 95–100.
[2] Schtz Y, Kyle UUG, Pichard C. Fat-free mass index and fat mass index percentiles in Caucasians aged 18–98 y. International Journal of Obesity 2002(26);953–960.
[3] Engvall IL, Brisman K, Hafström I et al. Treatment with low-dose prednisolone is associated with altered body composition but no difference in bone mineral density in rheumatoid atrhritis patients: a controlled cross-sectional study. Scandinavian Journal of Rheumatology 2010(40:3)161–168.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3124

AB0298 ANTIBODIES TO CYCLIC CITRULLINATED PEPTIDE AND MODIFIED CITRULLINATED VIMENTIN: A ROLE IN RHEUMATOID ARTHRITIS ASSOCIATED WITH AUTOIMMUNE THYROIDITIS

A. Dvorovkin[1], V. Odin[1], O. Inamova[2], V. Tyrenko[1], M. Toporkov[1]. *[1]Faculty therapy, Military Medical Academy Named After S.M. Kirov; [2]Clinical Rheumatic Hospital No. 25, St. Petersburg, Russian Federation*

Background: Specific antibodies, including antibodies to cyclic citrullinated peptide (ACCP) and modified citrullinated vimentin (AMCV) are markers of severe course of rheumatoid arthritis (RA). At the same time, rheumatoid arthritis often associated with autoimmune thyroiditis (Hashimoto's thyroiditis (HT)).
Objectives: Evaluate the role of antibodies to ACCP and AMCV on the clinical and laboratory features of rheumatoid arthritis in association with autoimmune thyroiditis.
Methods: The study included two groups of patients. The first group of patients included 16 patients (14 men and 2 women, mean age - 62.37±2.12 years) with RA in combination with HT and detection in the blood only ACCP (group 1). The second group also included 16 patients (14 women and 2 men, mean age – 52.31±4.94 years) with RA in combination with HT and detection of ACCP and AMCV in the blood (group 2). In the first group of patients 10 patients had euthyreose, from 5 - hypothyroidism, compensated intake of L - thyroxine, 1 patient - thyrotoxicosis underway medikal euthyreose. In the second group of patients was observed in 14 patients euthyreose, from 2 - hypothyroidism, compensated reception L-thyroxine.
Results: Both groups of patients differed on the following parameters studied: erosion detected in 68% in group 1 and 50% in group 2 ($p<0,05$), in the first group of patients predominated (62%) the high degree of activity of RA by DAS-28, in while in group 2 - the average (56%, $p<0,05$).
By using correlation analysis Spearman correlation relationships among the studied attracted attention significant ($R=0,62$, $p<0,05$) relationship between erosions and detection in the blood of antibodies to ACCP in the second group of patients (a combination of RA and HT and identifying in blood ACCP and AMCV), which was repeatedly weakened and unreliable in group 1 (combination of RA and HT and only detect of ACCP) in the blood.
Conclusions: Second group patients (a combination of RA with HT and detection in blood ACCP and AMCV) are closer correlations with indicators of joint destruction than group 1 patients, that in the future may use as a prognostic marker of a more severe course of RA in combination with HT.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4172

AB0299 ATLANTOAXIAL SUBLUXATION AS A PROBLEM IN PATIENTS WITH RHEUMATOID ARTHRITIS

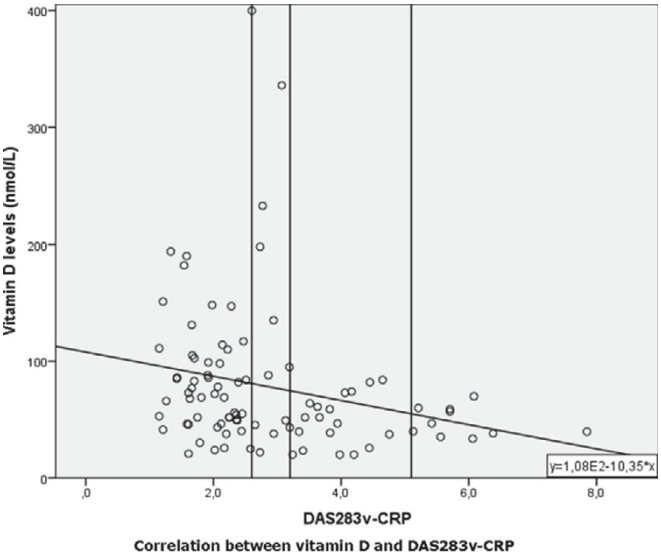
S. Misevska Percinkova[1], A.A. Kuchi[2]. *[1]Dept. for Inflamatory Rheumatic Disease, University Rheumatology Clinic; [2]Dept. for Internal Medicine, PHO City Health Centre Skopje 1, Skopje, Macedonia, The Former Yugoslav Republic Of*

Background: Atlantoaxial subluxation (AAS) is important and potentially life threatening complication of Rheumatoid arthritis (RA). It is defined when the space between odontoid process from C2 and arch of the atlas exceeds more than 3 mm. Instability in atlantoaxial joint may result with numerous neurological symptoms, compression of spinal cord and ultimately quadriparesis or quadriplegia.
Objectives: Aim of the study was to determine the frequency and the characteristics of atlantoaxial instability among our patients with RA and its dependence on the nature of the disease.
Methods: 92 outpatients from University Rheumatology Clinic in Skopje, with classical RA (ACR criteria 1988) were examined for the AAS. In all cases were analysed the duration of the disease, haematological and serological tests, disease activity (DAS 28), visual analogue scale (VAS) for the degree of articular pain and verbal rating scale (VRS).for cervical-occipital pain. All patients underwent native and functional x-ray, CT scan and MRI of cervical spine. A complete neurological examination was obtained, with SEP of the n. medianus et n. tibialis.
Results: Atlantoaxial instability, with expressed cervical-occipital symptomatology, occurred in 54 from 92 (58,69%) patients with RA. AAS appeared significantly more often in patients with longer duration of the disease ($p<0,0001$), in cases with significant cervical-occipital pain (VRS $p<0,0001$), with stronger joint pains (VAS), with higher values of SR ($p=0,002$), CRP ($p=0,023$), RF ($p=0,000005$), anti CCP ($p=0,00003$), and DAS 28 ($p<0,0001$). Anaemia and thrombocytosis ($p=0,0008$) appeared significantly more in cases with AAS. Anterior AAS, (mostly combined with other types) was the most frequent type, presented in 41 participants (75,92%). In one case posterior AAS was detected, what is very rare finding. Positive SEP was significantly higher in the group with AAS
Conclusions: AAS is serious extra-articular manifestation of RA. Cervical subluxation may be a general anesthetic risk and risk for a neck injury. Routine cervical radiographs with the head in flexed position should be recommended in need of general anaesthesia and in situations with risk for a neck injury.
Acknowledgements: Rheumatoid arthritis, atlantoaxial subluxation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5033

AB0300 ASSOCIATION OF VITAMIN D STATUS WITH RHEUMATOID ARTHRITIS DISEASE ACTIVITY AND UV INDEX

C. Lopes[1], J.L. Gomes[1,2], T. Costa[1], M. Mateus[1], F. Pimentel-Santos[1,2], J.C. Branco[1,2]. *[1]Rheumatology Department, Hospital de Egas Moniz | CHLO; [2]CEDOC, NOVA Medical School | Faculdade de Ciências Médicas - NOVA University of Lisbon, Lisbon, Portugal*

Background: Lower serum vitamin D levels have been shown to be associated with various autoimmune disorders, including Rheumatoid Arthritis (RA). Vitamin D deficiency is common in RA patients, despite profiting from a sunny country.
Objectives: The aim of the study is to evaluate (1) – the association between vitamin D serum levels and disease activity in patients with RA; (2) – seasonal distribution of vitamin D levels.
Methods: Patients fulfilling the 2010 EULAR/ACR Rheumatoid Arthritis Classification Criteria, which had serum vitamin D [25(OH)D3] levels measured between January 2013 and December of 2016 were included. Demographic data, disease activity scores, including DAS283v-CRP and DAS283v-ESR, vitamin D supplementation with cholecalciferol and other therapeutic approaches were recorded. Vitamin D insufficiency was considered between 25–75 nmol/L and deficiency if <25 nmol/L. According to the national agency for the study of sea and atmosphere, UV Index levels were grouped into low UV Index 3–6 (October to April) and high UV Index 9–10 (May to September). Correlation between variables was analyzed using Spearman's rho.
Results: A sample composed by 95 patients, 79 females (83.16%), with an average age (SD) of 68.57 (11.92) years within 40–88 years range were included. Average disease duration was 13.46 (11.41) years. The average age at diagnosis was 57.10 (14.25) years. The average vitamin D levels were 78.13 (60.98) nmol/L in a range between 20–400 nmol/L. Vitamin D levels were not significantly different in male *vs.* females patients. The prevalence of vitamin D insufficiency and deficiency was 53.68% and 8.42% respectively, despite 57.89% of the patients taking supplementation (average 6141 (4800) UI/week). The univariable analysis showed that albeit vitamin D levels presented a negative poor correlation with DAS283v-CRP (rho=-0.348, p-value<0.001) and DAS283v-ESR (rho=-0.271, p-value<0.01), there was a direct reduction in dispersion of the vitamin D values for increasing values of DAS283v-CRP and ESR. It was observed that vitamin D levels increase with patient age and decrease with disease duration. Sazonality and supplementation didn't affect vitamin D levels in our population.



Correlation between vitamin D and DAS283v-CRP

Conclusions: Vitamin D insufficiency/deficiency was frequent among RA patients (62.1%), independently of seasonality or supplementation. An interesting pattern

behavior was observed in this study, which indicates that the likelihood of encountering a very narrowband of vitamin D values for patients with high disease activity is very high, and thus, the forecast capability of vitamin D values for patients with increasingly active disease is quite good. Future research will aim at strengthening the statistical parameters of relevance, identifying and characterizing the more specific behaviours of this global pattern.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4062

AB0301 CARDIOVASCULAR RISK AND END ORGAN DAMAGE IN AN ITALIAN GROUP OF PATIENTS WITH RHEUMATOID ARTHRITIS

C.A. Valena[1], S. Barbarossa[1], G. Erba[1], R. Facchetti[2], A. Maloberti[1], P. Villa[1], I. Boggioni[1], M. Riva[1], G. Grassi[1], M.R. Pozzi[1]. *[1]Clinica Medica Università Milano Bicocca; [2]Dipartimento di Medicina Clinica e Prevenzione, Università Milano Bicocca, Monza, Italy*

Background: The elevated cardiovascular burden of rheumatoid arthritis is well known and the recent update of EULAR recommendations for cardiovascular disease management (1) establish as overarching principle that the rheumatologist is responsible for CVD risk management in patients with RA. They highlight the need of optimal disease activity control, regular CVD risk assessment, lifestyle counseling, appropriate prescription of NSAIDS,corticosteroids,antihypertensives and statins. Screening for asymptomatic atherosclerotic plaques by use of carotid ultrasound is also suggested: the presence of carotid plaques is associated with poor CVD-free survival and is strongly linked to future acute coronary syndrome in RA patients.
Objectives: We performed an overall cardiovascular assessment to evaluate the presence of end-organ damage in a group of RA patients.
Methods: We carried out non-invasive 24 hours ambulatory blood pressure monitoring, echocardiography, carotid doppler ultrasound and pulse wave velocity (PWV) in a group of RA patients to optimize non-DMARDs therapy and to evaluate end organ damage.
Results: 55 RA patients, 76.4% female, mean age 62.8±9 yrs were examined. The median disease duration was 12 yrs. 84% were RF +, 80% ACPA + and 51% had erosions. Mean DAS 28 CRP was 2.82±1.23 and HAQ 0.54±0.6. All pts were treated with cDMARDs and/or bDMARDs (54%) and Pd mean dosage was $\leq$5 mg/day. Only 3 patients had previous CV event. 49% were hypertensive, 25% had high cholesterol, 13% diabetes and 16% were smokers: median BMI was 25. MAP monitoring revealed that 43/55 (78%) pts were hypertensive: 13 of them had unknown or not/under treated hypertension: 63% had dipper profile and only 12% were reverse dipper. We did not find increased left ventricular mass and wall thickness, but left ventricular diastolic dysfunction grade I-II was found in 26/55 pts, not related to hypertension nor to RA activity. The IMT median value was 655 mm; only in 3 pts was $>$900 mm: no relation with disease activity was found. In 11 pts carotid plaques were present and related with age, BMI and ambulatory mean pressure values, but not with RA activity or duration. In one patient the plaque required carotid endarterectomy. The PWV median value was $>$10m/s in 16 pts, all hypertensive.
Conclusions: The accurate evaluation of cardiovascular involvement of this small group of RA patients shows that hypertension is frequent and often not appropriately treated and seems to be the main cause of the increased PWV. Low grade LV diastolic dysfunction was found in half of patients, with no relation with hypertension or RA features, except for CCP presence, but the small numbers do not allow any speculation. Carotid artery involvement was present in 20% of pts, but only in 1 was clinically significant. Once again no relation with RA features was found: the small number of patients, the low disease activity and the tight and overall clinical control could be partial explanations. The clinical tight control of patients with RA is an unique opportunity to fulfill EULAR reccomendations.
References:
[1] Agca R, et al. Ann Rheum Dis 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4127

AB0302 WORKABILITY IN PATIENTS WITH SEROPOSITIVE RHEUMATOID ARTHRITIS

C. Berner[1], T. Lamprecht[2], K.H. Fenzl[2], L. Erlacher[1], T.E. Dorner[3]. *[1]2nd Medical Division, Rheumatology, Kaiser Franz Josef Hospital, SMZ-Süd; [2]Karl Landsteiner Society, Institute for Autoimmune Illnesses and Rheumatology; [3]Institute of Social Medicine, Centre for Public Health, Medical University of Vienna, Vienna, Austria*

Background: Rheumatoid arthritis (RA) and other rheumatic conditions can lead to work disability, and temporary or permanent exit from the labour market. The indirect costs related to work disability, are higher than direct treatment costs, and pose an economic burden on patients and society. Workability in RA is influenced by many factors, including symptoms, such as pain, swelling and stiffness, muscle strength, or physical or mental exhaustion, which are components of the frailty syndrome.
Objectives: This study aimed to determine the association of workability with disease activity, pain, functional disability and frailty in patients with seropositive rheumatoid arthritis.
Methods: We conducted a monocentric cross-sectional study at a rheumatologic outpatient clinic and day hospital including 100 seropositive RA patients (according to 2010 EULAR classification) in the working age ($<$65 years). Workability was assessed with the self-administered Work Ability Index questionnaire. For disease activity, we used the Clinical Disease Activity Index (CDAI), a Visual analogue scale for pain assessment, for functional disability the self-administered Health Assessment Questionnaire Disability Index (HAQ-DI) and for the degree of frailty the SHARE Frailty Instrument (SHARE-FI). After testing for normal distribution, bivariate correlations between workability and associated variables were calculated using Spearman's correlation coefficients.
Results: Of 100 patients for 58 the workability index could be assessed. The remaining 42 were either unemployed, on disability pension, or employed but currently not working. These 58 patients, 37 women and 21 men, had an average age of 64.8 years (min-max=22–59, SD=9.3) and an average disease duration of 93.9 months (min-max=3–360, SD=86.7). 8 patients reported excellent workability, 27 good workability, 16 moderate workability and 7 poor workability. The workability was weakly correlated with age (r_s= -0.37, p$<$0.004), and moderately correlated with pain intensity (r_s=0.42, p$<$0.001), disease activity (r_s=0.40, p$<$0.002), functional disability (r_s=0.64, p$<$0.000) and frailty (r_s=0.623, p$<$0.000).
Conclusions: A considerable portion of employed RA patients reported poor or moderate workability, which is significantly associated with disease activity but also with the other parameters assessed. An adequate therapy may therefore not only improve well-being and state of health in RA patients but also provide socioeconomically advantage by maintaining patients' workability.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3567

AB0303 DOES COMORBIDITY ADVERSELY IMPACT ON TREATMENT RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

C.D. Hughes, N. Gullick. *Rheumatology, King's College Hospital, London, United Kingdom*

Background: The burden of comorbid illness in Rheumatoid Arthritis is high. Whilst there can be coincidental existence of comorbidity, it can be attributed to the disease process itself or therapeutic agents. Recent EULAR guidelines recommend reporting, screening and prevention of six common co-morbidities (cardiovascular, malignancy, infections, gastrointestinal, osteoporosis, depression). Limited research is available evaluating the impact of comorbidity on disease response following biologic treatment.
Objectives: To analyse retrospective data from the King's College Hospital (KCH) Virtual Biologic Clinic (VBC) to assess the impact of comorbidity on disease response following treatment with biologics.
Methods: Retrospective patient note review data was collected for patients referred to the VBC from May 2013 to July 2016. The following data was recorded: age, sex, disease duration, smoking status, BMI, presence or absence of Anti CCP antibody +/-Rheumatoid factor and the six specified comorbidities. Disease Activity Score in 28 joints (DAS28) at time of referral for biologic and within 6 months of commencing treatment was also recorded in order to calculate treatment response.
The impact of comorbidity and disease variables on 6 month EULAR response were analysed using logistic regression (SPSS version 23).
Results: The database contained 150 patients. 18 patients were excluded due to no follow-up DAS28, leaving 132 for analysis. Mean age and disease duration were 58 years and 10.45 years respectively. Comorbidity was present in 70% of patients. 70% of patients achieved a EULAR moderate response (improvement of $>$1.2 of DAS28) and 36% of this group achieved EULAR good response (DAS28$<$3.2). The most prevalent comorbidities were infection, cardiovascular disease and depression.
Logistic regression analysis was run analysing EULAR moderate response against presence of comorbidity and dataset variables (age, gender, serostatus, baseline DAS, HAQ and polypharmacy). The resulting model was not statistically significant (p=0.975).
Logistic regression analysis looking at EULAR good response against presence of comorbidity was also not statistically signifiicant (p=0.149). Analysis looking at EULAR good response against three variables (HAQ, baseline DAS and serostatus) was found to be statistically significant (p$<$0.001)

Characteristics	All N=132	No EULAR moderate response N=40	EULAR moderate response N=92	EULAR good response N=34
Age years (SD)	58 (13)	56 (10)	59 (14)	57 (11)
Gender (%F)	79%	72.5%	81.5%	76%
Positive serostatus	77%	65%	82%	74%
RA Disease duration (years) (SD)	10.45 (10.81)	10.70 (11.47)	10.34 (10.52)	10.54 (10.74)
Prior biologic use	55%	60%	52.2%	32%
Comorbidity	70%	80%	82%	62%
Baseline DAS28 (SD)	6.27 (0.93)	6.27 (0.93)	6.28 (0.93)	6.26 (0.93)
Mean DAS improvement (SD)	1.97 (1.57)	1.97 (1.57)	1.99 (1.58)	1.95 (1.58)

Conclusions: Comorbidities were present in the majority of patients assessed

(70%). Results show no significant relationship between EULAR moderate response or EULAR good response and the presence of comorbidity. Lower HAQ, lower baseline DAS28 and seronegativity contribute towards good treatment response.The limitations of this study include gaps in clinical records, absence of patient reported questionnaires, and small size of database.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2025

AB0304 SERUM LEVELS OF SCLEROSTIN AND DICKKOPF-1, AND THEIR CORRELATION WITH BONE MINERAL DENSITY AND BONE MARKERS IN RHEUMATOID ARTHRITIS

C.A. Nava-Valdivia[1], E. Corona-Sanchez[2], J. Ponce-Guarneros[3], A. Saldaña-Cruz[2], J. Murillo-Vazquez[2], E. Perez-Guerrero[2], P. Hernandez-Cuervo[2], M. Salazar-Paramo[3], D. Cardona-Müller[2], E. Cardona-Muñoz[2], L. Gonzalez-Lopez[3], J. Gamez-Nava[1]. *[1]Unidad Biomédica 02, IMSS; [2]Universidad de Guadalajara; [3]IMSS, Guadalajara, Mexico*

Background: Sclerostin (SOST) and dickkopf-1 (DKK1) are involved in the development of primary osteoporosis. Although to date, it is controverted does exist about if serum levels of these molecules may reflex adequately a subgroup of patients with decrement of Bone Mineral Density (BMD) being useful as clinical biomarkers. Some non-conclusive observations made in postmenopausal osteoporosis have shown abnormalities in serum levels. To date, there is a lack of information about if these serum molecules are associated with a decrease of BMD in RA. This information is relevant for to know if the measurement of these serum molecules could be useful in the clinical care to identify a subgroup of patients with low BMD.
Objectives: To evaluate if serum levels of SOST and DKK1 correlate with bone mineral density and other bone markers in RA.
Methods: In this Cross-sectional study, we included 115 women with RA >40 years old. All patients were assessed for clinical characteristics disease activity (DAS28) and functioning (HAQ-Di). BMD was measured in lumbar spine, hip and forearm using DXA. According to their results, osteoporosis was identified if the BMD in a patient had a T-score with a decrement of ≤-2.5 standard deviation (SD). According to their results we classified these patients in two groups: a) low BMD (T-score≤-1SD on lumbar spine or total hip) and b)normal BMD (T-score>-1SD). Serum SOST, DKK1, including serum Receptor Activator of NF-κB Ligand (sRANKL) and osteoprotegerin (OPG) were quantified by ELISA. We compared serum levels between the groups using Student t-tests. For comparisons between proportions we performed Chi-square test (or Fisher exact test if required). Correlations between serum levels of SOST, DKK1, with BMD, clinical variables, sRANKL and OPG we performed Pearson correlation tests.
Results: From the 115 women with RA, 58 patients had low BMD (50.4%), from them 44 patients (38.3%) had osteoporosis. Patients in the group with low BMD had higher age (63±8 vs 53±9,p<0.0001), DAS28 (4.1±1.5 vs 3.3±1.4, p=0.011), and HAQ-Di score (0.69±0.53 vs 0.36±0.47, p=0.001) compared with normal BMD; whereas lower serum levels of sclerostin was observed in the low BMD group (128.5±75.0 vs 178.2±103.3, p=0.004). SOST levels were correlated with BMD in lumbar spine (r=0.393, p<0.0001), hip (r=0.388,p<0.0001) and forearm (r=0.319, p=0.001). sRANKL serum levels had a negative correlation with BMD in hip (r=-0.17, p=0.03). No correlations were observed between serum DKK1 and OPG with BMD in hip or lumbar spine.
Conclusions: These results indicate that SOST, and RANKL are biomarkers may associated with abnormal BMD in RA. Further long-term follow-up studies should evaluate if high levels of these serum biomarkers could be useful as tests to predict the future development of osteoporotic fractures.
References:
[1] Xu et al. Chin Med J. 2013;126:2480–84.
[2] Xu et al. Rheumatol Int. 2012;32:3397–403.
Acknowledgements: This project was supported by grant from the Fondo de Investigación en Salud del Instituto Mexicano del Seguro Social: FIS/IMSS/PROT/GIS/1455.
Disclosure of Interest: C. Nava-Valdivia: None declared, E. Corona-Sanchez: None declared, J. Ponce-Guarneros: None declared, A. Saldaña-Cruz: None declared, J. Murillo-Vazquez: None declared, E. Perez-Guerrero: None declared, P. Hernandez-Cuervo: None declared, M. Salazar-Paramo: None declared, D. Cardona-Müller: None declared, E. Cardona-Muñoz: None declared, L. Gonzalez-Lopez Grant/research support from: Is a recipient of a Fundación IMSS Scholarship, México., J. Gamez-Nava: None declared
DOI: 10.1136/annrheumdis-2017-eular.5652

AB0305 FACTORS CONSIDERED BY RHEUMATOLOGISTS TO DECIDE TREATMENT DURING RHEUMATOID ARTHRITIS PATIENT'S FOLLOW-UP

C. Sifuentes-Cantu[1], I. Contreras-Yañez[1], M. Gutierrez[2], V. Pascual-Ramos[1]. *[1]Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran; [2]Division of musculoskeletal and rheumatic diseases, Instituto Nacional de Rehabilitación, México, D.F, Mexico*

Background: Disease activity (DA) is the most important factor in the treatment decision during rheumatoid arthritis (RA) patient's follow-up. In routine clinical practice, it is recommended to regularly evaluate DA and musculoskeletal ultrasound has been suggested to add value to establish the level of DA. Nevertheless, the final treatment proposal also requires considering additional factors. In a previous clinical study performed in the setting of an early arthritis clinic, we found that in 20% of the clinical scenarios evaluated, the German ultrasound score of 7 joints (GUS-7) (1) findings impacted the rheumatologist 's treatment proposal; the impact was more frequent among the trainee in rheumatology (TR) than among the senior rheumatologist (SR).
Objectives: To determine and rate, which among the following factors were determinant to recommend a treatment in the same population of RA patients above described: the clinical assessment, the GUS-7, comorbidities, treatment-related adverse events, DMARDs costs/availability, patient's preference and DMARD maximum dose. We also compared if factors differed between both physicians.
Methods: Eighty-seven consecutive and randomly selected RA outpatients were invited to participate; 2 patients denied and 85 patients underwent 170 assessments (85 each by the SR and the TR); at first, both physicians (blinded to each other) performed a clinical evaluation that included DAS28 scoring and recommended a RA-treatment. Then, patients underwent GUS-7 by a blinded (to clinical evaluations) rheumatologist. In the final step, the TR and the SR integrated the US findings to their previous evaluation and reviewed their prescription; also, both physicians recorded and rated on a standardized format which of the factors above described were determinant in the final treatment proposal. Patients signed informed consent and were instructed about the process. Only the SR met each patient for the final recommendation. Descriptive statistics was used.
Results: Patients were primarily middle-aged female (91.4%) and had (mean±SD) follow-up of 7.5±3.9 years. The majority of them were in DAS28-remission (72%). Clinical assessment (DAS28) was rated as determinant in the totality of the clinical scenarios (100%), followed by GUS-7 in 84.7%, DMARD maximum dose in 41.2%, comorbidities in 23.5%, DMARD cost/availability in 21.2%, treatment-related adverse events in 20% and patient's preference in 14.1% of them. The SR and the TR differed in their selection: GUS-7 and treatment-related adverse events were more frequently considered determinant for the TR (45.9% vs. 38.8%, p=0.01 and 12.9% vs. 7.1%, p=0.08), meanwhile the opposite figure was true for DMARD cost/availability (4.7% vs. 16.5%, p≤0.001) and DMARDs maximum doses (17.1% vs. 24.1%, p=0.08).
Conclusions: in a real clinical setting, DA assessed by DAS28 and by musculoskeletal ultrasound were the most important factors to determine the treatment of RA outpatients; additional factors were considered and differently rated by TR and SR.
References:
[1] Backhaus et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. Arthritis Rheum. 2009;61: 1194–201.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1103

AB0306 CAPLAN'S SYNDROME, CADMIUM AND CHINA CLAY: COULD OCCUPATIONAL KAOLIN INHALATION ENHANCE CADMIUM EXPOSURE TO EXPLAIN THE SIXTY YEAR CONUNDRUM OF CAPLAN'S SYNDROME FIRST REPORTED IN COAL MINERS?

D. Murphy[1,2], K. Bellis[1], D. Hutchinson[1,2]. *[1]Rheumatology, Royal Cornwall Hospital; [2]University of Exeter Medical School, Cornwall Campus, Truro, United Kingdom*

Background: Caplan's syndrome was first described in the coal miners of South Wales (UK). The specific cause for rheumatoid pulmonary nodules associated with coal dust exposure remains unknown. Coal dust exposure alone does not appear to explain Caplan's syndrome as almost all of these men were also smokers. Cigarette smoke is the most important environmental cause of cadmium exposure. We describe Caplan's syndrome in an ex-smoking kaolin worker associated with a significantly raised urinary cadmium level.
Objectives: A 65 year old Cornish kaolin worker and ex-smoker of 20 pack years with life limiting nodular erosive rheumatoid arthritis (RA), developed extra-articular manifestations including pulmonary nodules suggestive of Caplan's syndrome. We review the literature on kaolin, with respect to inhalation and mechanism of action for heavy metal adsorption and nodular disease development.
Methods: Pubmed searches were undertaken using the keywords "kaolinosis", "kaolin", "cadmium" "nodules", "adsorption", "coal". First pass mid-stream urine was analysed for cadmium using inductively coupled plasma–mass spectrometry (ICP-MS).[1]
Results: Urinary cadmium was significantly raised at 0.66 μmol/mol creatinine (non-occupationally exposed UK male median 0.17μmol/mol creatinine[1]), 20 years post-industrial exposure and 35 years post-smoking cessation. Contemporary serology levels demonstrated a rheumatoid factor of 481.7 iu/ml (0–10 normal range) and an anti-cyclic citrullinated peptide of >500 u/ml (0–17 normal range). CT scan of the chest demonstrated multiple pulmonary nodules consistent with Caplan's syndrome.
The prevalence of Caplan's syndrome in kaolin workers is the highest of any occupation ever reported.[2] Elevated cadmium levels of 11.2–15.9 mg/kg have been observed in kaolin,[3] fifty- fold higher than those reported in coal.[4] Coal contains variable amounts of clays and minerals such as kaolinite. Cadmium content in coal is strongly associated with levels of kaolinite contamination.[4] Cadmium

nanoparticles have been observed to cause lung parenchyma inflammation and granuloma formation in an animal model.[5]
Conclusions: Kaolinite mineral capacity for adsorption of heavy metals, in particular cadmium, could explain the scale and pattern of Caplan's syndrome incidence seen in Welsh coal miners and Cornish kaolin workers, and further explains the interactive risk seen in sequential dust and cigarette smoke exposure.
References:
[1] Morton J, Tan E, Leese E, Cocker J. Determination of 61 elements in urine samples collected from a non-occupationally exposed UK adult population. Toxicol Lett. 2014;231(2):179–93.
[2] Wells IP, Bhatt RC, Flanagan M. Kaolinosis: a radiological review. Clin Radiol. 1985;36(6):579–82.
[3] Bonglaisin JN, Mbofung CMF, Lantum DN. Intake of Lead, Cadmium and Mercury in Kaolin-eating: A Quality Assessment. J Med Sci 2011;11(7):267–273.
[4] Song D, Wang M, Zhang J, Zheng C. Contents and occurrence of cadmium in the coals from Guizhou province, China. Ann N Y Acad Sci. 2008;1140:274–81.
[5] Coccini T, Barni S, Vaccarone R, et al. Pulmonary toxicity of instilled cadmium-doped silica nanoparticles during acute and subacute stages in rats. Histol Histopathol. 2013 1;28(2):195–209.
Acknowledgements: Cornwall Arthritis Trust.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3727

AB0307 DIFFERENTIAL ASSOCIATION OF AGE AND DISEASE ACTIVITY WITH CAROTID INTIMA-MEDIA THICKNESS IN MEN AND WOMEN WITH RHEUMATOID ARTHRITIS

D. Taverner[1], S. Paredes[1], R. Ferre[2], L. Masana[2], A. Castro[2], J.C. Vallve[3].
[1]Rheumatology; [2]Internal Medicine; [3]Biologyst, Hospital Sant Joan de Reus, Reus, Spain

Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory condition and is characterized by an increase risk in cardiovascular (CV) disease. Carotid intima-media thickness (cIMT) is a surrogate marker of CV disease and many studies have evaluated the relationship between cIMT and RA disease activity with contradictory results.
Objectives: To evaluate in RA patients the association between both cIMT and carotid plaque presence and clinical RA features and analytical measurements.
Methods: We selected 214 RA patients according to the American College of Rheumatology criteria. Conventional clinical evaluation and analytical measurements were performed, including a standard lipid profile. We used My Lab 50 X-Vision sonograph to measure cIMT and atherosclerotic plaque presence
Results: No differences between men and women regarding age, body mass index, glycaemia, LDL-C and TG were observed. However, men had a significantly higher waist circumference, systolic and diastolic BP and lower levels of HDLc. On the other hand, women had significantly higher values of DAS28 (3.7 vs 2.99), HAQ, and VSG with no differences in other inflammatory variables (rheumatoid factor, ACPA, CRP or fibrinogen). Moreover, 74% of patients had pathological cIMT without gender differences and 43% had plaque presence in the carotid artery with a significant higher percentage in men (57%) than women (36%). Overall, men had significantly higher cIMT (0.678 vs 0.627 mm) but when disease activity (DAS28) was considered, we observed that such difference was due to patients that were in remission or in low activity. Men and women with moderate and high disease activity had no statistical differences in cIMT. Furthermore, across women cIMT was significantly higher in those with high disease activity compared with remission. This effect was not observed in men. Multivariate linear regression with cIMT showed a significant interaction between age and gender, so that the effect of age on cIMT was significantly more pronounced in men than in women.
Conclusions: We have described that in our RA cohort, disease activity measured with DAS28 and age are differentially associated with cIMT in men and women. Our results could explain the contradictory results published in the literature and it can be justified by a higher incidence of RA in women and by the hormonal-genetic status.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2704

AB0308 DISEASE ACTIVITY, GRIP STRENGTHS AND HAND DEXTERITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

D. Palamar[1], G. Er[1], R. Terlemez[1], U. Isil[2], G. Can[3], M. Saridogan[1].
[1]Department of Physical Medicine and Rehabilitation, Istanbul University Cerrahpasa Medical Faculty; [2]Physical Medicine and Rehabilitation Clinic, Bagcilar Training Hospital; [3]Department of Public Health, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting hand joints, and leading impairment in hand functions. To date many scientific studies assessed the disease activity of patients with RA, but little attention has been carried out to assess hand functions, and dexterity (1–2).
Objectives: The purpose of this study was to determine the clinical relevance of the Quick Disabilities of Arm, Shoulder and Hand (QuickDASH), hand dexterity with the Purdue Pegboard Test (PPT), and grip and pinch strengths of RA patients.
Methods: Eighty-two women with a diagnosis of RA according to the 2010 American College of Rheumatology/the European League Against Rheumatism (ACR/EULAR) criterion were recruited to the study. The disease activity scores were determined by using Disease activity score-28 (DAS-28). Grip strengths was measured with a Jamar dynamometer, and pinch strengths were measured by pinchmeter. Hand functions were evaluated with the PPT, and functional outcomes were assessed with the QuickDASH questionnaire.
Results: The mean age of the study group was 49.27±10.69 years. Average values of DAS-28, the QuickDASH values were found to be 4.22±1.28, 38.33±19.78, consecutively. High correlation was observed between DAS-28 and the QuickDASH values ($p<0.001$). The mean grip strengths were significantly correlated with the QuickDASH and DAS-28 values ($p<0.01$) (Table 1). The mean lateral pinch strengths were correlated significantly with DAS-28 and the QuickDASH scores ($p<0.001$). DAS-28 was correlated with PPT performance just on the dominant hand ($p<0.05$). The QuickDASH values were not correlated with all PPT performances ($p>0.05$). Grip strengths were positively correlated with the PPT performances ($p<0.05$).

Table 1. Showing the correlation coefficients of DAS 28 and QuickDASH scores between other parameters

	Correlation coefficients (r)	
	DAS 28	QuickDASH
QuickDASH	0.616***	
Grip strength (dominant hand)	-0.412***	-0.409***
Grip strength (nondominant hand)	-0.329**	-0.404***
Lateral pinch strength (dominant hand)	-0.320***	-0.327***
Lateral pinch strength (nondominant hand)	-0.276*	-0.310**
Palmar pinch strength (dominant hand)	-0.215	-0.157
Palmar pinch strength (nondominant hand)	-0.190	-0.165
Tip pinch strength (dominant hand)	-0.248*	-0.237*
Tip pinch strength (nondominant hand)	-0.227*	-0.201
Dexterity (dominant hand)	-0.277*	-0.033
Dexterity (nondominant hand)	-0.128	-0.098
Dexterity (both hands)	0.004	0.059
Dexterity (assembly)	-0.084	0.047

Spearman correlation analysis used for all parameters. *$p<0.05$, **$p<0.01$, ***$p<0.001$.

Conclusions: In conclusion, we determined that grip strengths were significantly related to disability and disease activity in RA patients in our study. The clinical significance of QuickDASH is high, and the questionnaire can be used effectively.
References:
[1] Aktekin LA, Eser F, Baskan BM, et al. Disability of Arm Shoulder and Hand Questionnaire in rheumatoid arthritis patients: relationship with disease activity, HAQ, SF-36. Rheumatol Int.2011;31:823–6.
[2] Singh H, Kumar S, Talapatra P, et al. Assessment of hand functions in rheumatoid arthritis using SF-SACRAH (short form score for the assessment and quantification of chronic rheumatoid affections of the hands) and its correlation to disease activity. Rheumatol Int. 2012;32:3413–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3541

AB0309 LIPID-LOWERING INTERVENTION OF A PREVENTIVE CARDIO-RHEUMA CLINIC IN MEXICAN MESTIZO PATIENTS WITH RHEUMATOID ARTHRITIS

D.Á. Galarza-Delgado[1], J.R. Azpiri-López[2], I.J. Colunga-Pedraza[1], R.E. Ramos-Cázares[1], F.J. Torres-Quintanilla[2], A. Valdovinos-Bañuelos[1], R.I. Arvizu-Rivera[3], A. Martínez-Moreno[3], J.A. Cárdenas-de la Garza[3], R. Vera-Pineda[3], J. García-Colunga[4], M.A. Garza-Elizondo[1], G. Elizondo-Riojas[4]. *[1]Rheumatology; [2]Cardiology; [3]Internal Medicine; [4]Radiology, Universidad Autónoma de Nuevo León, Monterrey, Mexico*

Background: Patients with rheumatoid arthritis (RA) have a significantly increased risk for cardiovascular (CV) morbidity and mortality when compared to general population (1). Preventive cardio-rheuma clinics have been created in recent years and proven to be effective to manage CV risk in patients with inflammatory joint diseases around the world (2).
Objectives: To evaluate the need for lipid-lowering intervention in Mexican mestizo patients with RA.
Methods: We initiated a preventive cardio-rheuma clinic for appropriate CV disease prevention in patients with RA in our population. A complete evaluation and CV risk stratification was performed to our patients, including blood tests and ultrasound examination of both carotid arteries. Each patient was classified to lifestyle changes only, a lifestyle intervention plus lipid-lowering treatment, or to have a low risk with no need for intervention, in accordance to the 2012 European Guidelines on cardiovascular disease prevention in clinical practice and the 2016 ESC/EAS Guidelines for the Management of Dyslipidemias.
Results: A total of 100 patients were evaluated, patient characteristics and intervention group distribution are shown in Table 1. Among these patients, 49 were found not to need any lipid-lowering intervention. The remaining 51 were classified into lifestyle change (n=18, 35.3%) or lipid-lowering drug regimens (n=33, 64.7%). A significant difference between intervention groups was only found regarding age ($p<0.001$). A multiple regression analysis was performed to predict the kind of intervention needed from age, disease duration, disease

Table 1 Patient characteristics and group distribution

	General n = 100	Group 1 (No intervention) n = 49	Group 2 (Lifestyle changes) n = 18	Group 3 (LLD) n = 33	p
Female gender, n (%)	96 (96)	47 (95.9)	18 (100)	31 (93.9)	0.58
Age (years), mean ± SD	56.7 ± 9.7	52.2 ± 8.8	62.4 ± 9.9	60.2 ± 7.6	< 0.001
Disease duration (years), median (IQR)	10.3 (4.2 – 17.9)	10.1 (3.8 – 16.2)	13.8 (9.3 – 21.5)	9 (3 – 19.7)	0.181
Disease activity (DAS28-CRP), median (IQR)	3.2 (1.9 – 4.1)	2.9 (1.9 – 4.1)	3.7 (2.2 – 4.2)	3.4 (1.8 – 4.2)	0.639
RF IgG (IU/ml), median (IQR)	8.8 (4.1 – 22.9)	8.4 (4.1 – 24.7)	7.25 (4 – 15)	11.5 (4.8 – 31.7)	0.381
RF IgM (IU/ml), median (IQR)	145.9 (52 – 200)	160.1 (35.4 – 200)	160.7 (57.8 – 200)	100 (48.9 – 200)	0.933
RF IgA (IU/ml), median (IQR)	44.3 (14.3 – 148.6)	41 (13.1 – 144.9)	38.3 (15.3 – 187.2)	67.1 (16.4 – 116.7)	0.935
ACPA (IU/ml), median (IQR)	99.2 (4.5 – 198.4)	100 (4.1 – 196.6)	18.4 (5.2 – 199.1)	114.4 (5 – 198.6)	0.970

SD: Standard deviation, IQR: Interquatrile range, DAS28-CRP: Disease activity scale using 28 joints – C-reactive protein, RF: Rheumatoid factor, ACPA: Anti-cyclic citrullinated peptide antibodies. LLD: Lipid-lowering drug.

activity and autoantibody levels, only age added statistically significantly to the prediction ($p<0.001$).

Conclusions: There was indication for preventive intervention in more than half of our patients. Age is a determinant factor that increases CV risk in RA patients independently from disease-specific factors. Treatment to lipid targets is essential to reduce their risk of CV morbidity and mortality (3). A prospective study evaluating treatment success rate is needed to further evaluate the intervention of the clinic.

References:

[1] Galarza-Delgado DA, Azpiri-Lopez JR, Colunga-Pedraza IJ, et al. Comparison of statin eligibility according to the Adult Treatment Panel III, ACC/AHA blood cholesterol guideline, and presence of carotid plaque by ultrasound in Mexican mestizo patients with rheumatoid arthritis. Clin Rheumatol. 2016;35(11):2823–7.

[2] Rollefstad S, Kvien TK, Holme I, et al. Treatment to lipid targets in patients with inflammatory joint diseases in a preventive cardio-rheuma clinic. Ann Rheum Dis. 2013;72(12):1968–74.

[3] Rollefstad S, Ikdahl E, Hisdal J, Olsen IC, et al. Rosuvastatin-Induced Carotid Plaque Regression in Patients With Inflammatory Joint Diseases: The Rosuvastatin in Rheumatoid Arthritis, Ankylosing Spondylitis and Other Inflammatory Joint Diseases Study. Arthritis Rheumatol. 2015;67(7):1718–28.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5574

AB0310 PREVALENCE OF COMORBIDITIES OF RHEUMATOID ARTHRITIS IN A MEXICAN MESTIZO POPULATION

D.Á. Galarza-Delgado[1], J.R. Azpiri-López[2], I.J. Colunga-Pedraza[1], R.E. Ramos-Cázares[1], F.J. Torres-Quintanilla[2], A. Valdovinos-Bañuelos[1], R.I. Arvizu-Rivera[3], A. Martínez-Moreno[3], J.A. Cárdenas-de la Garza[3], R. Vera-Pineda[3]. *[1]Rheumatology; [2]Cardiology; [3]Internal Medicine, Universidad Autónoma de Nuevo León, Monterrey, Mexico*

Background: Patients with rheumatoid arthritis (RA) have an increased risk of developing comorbid conditions which are associated to increased mortality, hospital admissions, higher costs of care and inability to work (1, 2).

Objectives: To evaluate the prevalence of comorbidities in a Mexican mestizo population of RA patients.

Methods: We performed a cross-sectional study in which RA patients who were admitted to our outpatient clinic between August 2014 and December 2016 were consecutively enrolled. We collected data regarding demographics, disease characteristics (activity, severity, treatment), comorbidities (cardiovascular, infections, cancer, and osteoporosis), and performed blood tests at the time of the patient's visit to the clinic.

Results: We analyzed 225 patients. Their characteristics are shown in Table 1. Age, 55.7±8.3 years (mean ± SD); disease duration, 9.5 (4 – 15.5) (median (IQR)); female gender, 93.7%; Disease Activity Score using 28 joints–C-reactive protein (DAS28-CRP), 3 (2 – 4) (median (IQR)); past or current methotrexate use, 84.9%; past or current use of any other conventional disease modifying anti-rheumatic drug (cDMARD), 52.4%; past or current use of biological agents, 8%. The most frequently associated diseases were: hypertension, 29.8%; dyslipidemia, 27.1%; osteoporosis, 19.1%; diabetes, 12.4%; hypothyroidism, 6.2%; solid malignancies (excluding basal cell carcinoma), 4.4%. Risk factors were also evaluated, the most prevalent was overweight (BMI $\geq$25 <30) present in 101 (44.9%) of our patients. A total of 71 (31.6%) had obesity (BMI $\geq$30). The systematic evaluation of our patients allowed us to detect abnormalities in vital signs, such as elevated blood pressure in 12.4%, and to identify conditions that manifest as laboratory test abnormalities, such as hyperglycemia in 27.1% and hyperlipidemia in 49.8%.

Conclusions: This study confirms the high prevalence of comorbidities in RA patients. Among our cohort, 63.5% had at least one comorbidity, being those associated with cardiovascular disease the most common. With a systematic assessment (3) including a thorough physical examination, vital signs and laboratory tests, it is possible to detect comorbid conditions that would otherwise remain unrecognized.

Table 1 Demographic characteristics

Variable	Result
Women, n (%)	211 (93.8)
Age (Years), mean ± SD	55.71 ± 8.38
Disease duration (years), median (IQR)	9.57 (4 – 15.58)
BMI (kg/m2), median (IQR)	27.41 (25.16 – 31.62)
Normal, n (%)	53 (23.6)
Overweight, n (%)	101 (44.9)
Obese, n (%)	71 (31.6)
Smoking, n (%)	20 (8.9)
DAS28-CRP, median (IQR)	3.01 (2.04 – 4.08)
Joint surgery due to RA, n (%)	25 (11.1)
Medication, n (%)	
Prednisone	135 (60)
Methotrexate	191 (84.9)
Other non-biologic DMARDs	118 (52.4)
Biologic DMARDs	18 (8)

References:

[1] Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis. 2014;73(1):62–8.

[2] Gabriel SE, Michaud K. Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis Res Ther. 2009;11(3):229.

[3] Baillet A, Gossec L, Carmona L, Wit M, van Eijk-Hustings Y, Bertheussen H, et al. Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. Ann Rheum Dis. 2016;75(6):965–73.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1523

AB0311 RESULTS OF SCREENING FOR TUBERCULOSIS INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS BEFORE AND ON TREATMENT WITH BIOLOGICAL DMARDS

D. Karateev[1], S. Borisov[2], T. Fomina[2], G. Loukina[3], E. Luchikhina[4], L. Guntupova[2], A. Satybaldyev[4]. *[1]Nasonova Research Institute of Rheumatology; [2]Moscow Centre against tuberculosis; [3]Moscow clinical scientific center; [4]Early arthritis department, Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: The prevalence of tuberculosis infection in Russia is much higher than in Western Europe. Therefore, screening for TB infection in patients with RA before therapy with biological agents is of particular importance. At the same time, reliable information on the results of screening are very few.

Objectives: Explore the results of the application of different methods of diagnosis of tuberculosis infection in RA patients before and during treatment with biological agents.

Methods: We used the data from the Russian register "Observational REgister of arthritis in cLinical practice" (OREL). 1471 RA patients were screened for TB infection before prescribing biologics, of whom 829 patients were exposed to TB infection monitoring on therapy by biologics. The group included 21.1% men, 78.9% women; at the time of initial screening age was 50,0±0,4 years, the duration of the disease 8,5±3,8 yrs, 68,3% RF +, 85.1% anti-CCP +, DAS28-ESR 5,7±1,1, 95,7% used synthetic DMARDs, 60,1% used systemic steroids. We used PPD (Mantoux) test, Diaskin test (intradermal test with tuberculosis recombinant allergens CFP10-ESAT6) and QuantiFERON-TB Gold (QFT) test (in some patients), chest X-ray, chest CT scan (if needed), all the patients were consulted by phthisiatrician. PPD and Diaskin test results were considered positive if the papule was $\geq$5 mm. Duration of treatment with biologics (anti-TNFs and others) varied widely (2–154 months), making a total of 2552,4 patient-years.

Results: At screening, we got 40,3% positive results of PPD test (significantly more in younger patients and patients who did not receive steroids), 16,5% positive results of Diaskin test (with no significant correlations with age and steroids). Positive results matched in 19.9% of cases, negative - in 51.9%. Discordant results in 217 patients were in 92,2% cases related to negative results of Diaskin in PPD-positive persons. Active TB was found after additional examination in 3 (0,2%) patients, inactive TB-related changes were revealed in 124 (8,8%) patients. Positive PPD and Diaskin results, but not QFT, correlated with signs of inactive TB lesions. Positive results of PPD and QFT tests matched in 36.5% of cases, negative - in 18.7%, Diaskin and QFT – in 33,6% and 41,1% of cases resp. As a result of screening, 224 pts were treated by isoniazid or combination of anti-TB drugs before initiation of biologics. On treatment with biologics, 114 (13,7%) pts became PPD-positive and 56 (6,8%) Diaskin positive, active TB was diagnosed in 8 (0,97%) pts.

Conclusions: In carrying out TB screening before prescribing biologics in high-

risk population of TB infection it is reasonable to use both PPD and Diaskin tests, and repeat them every 6 months on treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6988

AB0312 US7 SCORING SYSTEMS FOLLOW-UP 48 WEEKS TNF-A ANTAGONISTS PLUS MTX TREATMENT FOR HIGH DISEASE ACTIVITY REFRACTORY RHEUMATOID ARTHRITIS

D.F. Lin[1], X. Gu[1], J. Cao[1], Y. Pan[2], J. Gu[1]. [1]*Rheumatology department;* [2]*Ultrasound department, the 3rd Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China*

Background: US7 score is the ultrasound scoring system for rheumatic arthritis (RA) with the most clinical evidence so far. Several reports accessed its inter-, intra-observer agreement, its specificity, sensitivity and practical possibility compared to more complex scoring systems such as 72-joints scoring systems, which showed it is an convenient tool for clinical use.
Objectives: Our goal is to employ US7 to investigate the ultrasonic changes during biological agents plus MTX Treatment in high disease activity refractory RA patients in Yellow people.
Methods: All cases were diagnosed as RA fulfilling 2009 ACR/EULAR classification criteria and evaluated as high disease activity for DAS28>5.1 with MTX+HCQ+SASP or MTX+LEF invalid therapy for more than 3 months before baseline. Biological agents including TNF-a antagonist or IL-6 antagonist plus with MTX 10mg qw were then given and ultrasound was performed by 2 observers blinded to physicial examinations and blood tests at 0, 4, 12, 24, 48w. US examination referred to US7 scores by Backhaus et al. DAS28 were employed to assess disease activity.
Results: 1) 26 subjects were enrolled in the program up to now. 22 were given TNF-a antagonists and 4 were given IL-6 antagonists. 17 finished 24 weeks follow-up. 1 withdrew for TB infection at 12 week and 1 withdrew for fungi pneumonia at 8 weeks. Mean age of 17 was 44.3±11.8 years old, female-male ratio was 15:2, and disease duration was 71 months. All were RF and ACPA postIve.
2) DAS28-CRP, DAS28-ESR had prominent decrease from 0 to 24 week (DAS28-CRP: 0w: 4w: 12w: 24w = 6.76, 5.98, 5.09, 4.48, DAS28-ESR: 0w: 4w: 12w: 24w = 6.36, 4.94, 3.99, 3.35, paired Wilcoxon test, all sig<0.05)
3) The same prominent improvement also well reflected by the ultrasonic scores: average sum scores (0w:4w:12w:24w = 22.9:15.6:13:9.3, all sig <0.05 except 4w: 12w, sig=0.126), synovitis grey scale scores (0w:4w:12w:24w = 11.6:9.3:8.1:6.0, all sig <0.05, except 0w:4w, sig=0.068), synovitis Power Doppler scores (0w:4w:12w:24w = 8.5:4.9:3.8:2.7, all sig <0.05, except 4w:12w,4w:24w, 12w:24w, sig = 0.361,0.227, 0.235), tenosynovitis grey scale scores (0w:4w:12w:24w = 0.63:0.25:0.25:0.07, all sig <0.05, except 4w:12w,4w:24w, 12w:24w, sig = 1.0 , 0.26, 0.26), tenosynovitis Power Doppler scores (0w:4w:12w:24w = 1.00:0.19:0:0 all sig <0.05, except 4w:12w,4w:24w, 12w:24w, sig = 0.18, 0.18, 1.0), bone erosion scores (0w:4w:12w:24w = 1.2:1.0:0.94:0.53, all sig <0.05 except 0w:4w, 4w: 12w, 4w:24w, 12w:24w, sig = 0.083, 0.317, 0.102, 0.102). The above data showed the sum scores found biological agents improved thorough the whole course as Das28 did. Synovitis seemed to be eliminiated faster than tenosynovitis and the repair of bone erosion was the latest event compared to decreased synovitis and tenosynovitis.
Conclusions: It is recommended US7 used in clinic for US7 scoring system could reflect more exquisitely than DAS28 in more refined aspects including the changes of tendon, joint, bone at different phrases during biological agent treatment for RA. However, more samples should be included in our study to illuminate above conclusion with sufficient evidence.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2640

AB0313 CARDIOVASCULAR RISK, BIOLOGICS AND ANTI-CYCLIC CITRULLINATED PEPTIDE POSITIVITY IN RHEUMATOID ARTHRITIS

E.A. Jauregui, C.A. Agudelo, C. Aldana, Y.A. Muñoz. *Rheumatology, Riesgo de fractura S.A-CAYRE, Bogotá, Colombia*

Background: Co-factors and traditional cardiovascular disease (CVD) risk factors contribute to atherosclerosis in rheumatoid arthritis (RA). Several records since 1953 have reported an increase of up to 4 times the CVD risk and mortality in RA patients. Physicians who evaluate these patients forget to perform or record this assessments in medical records. Since 1948, the Framingham Heart Study became an ambitious project in health research, to identify the general causes of heart disease and stroke, they proposed a new risk estimator of general cardiovascular risk defined as CVD.This estimator was calibrated for Colombia and should be multiplied by a factor of 0.7
Objectives: To describe whether the request and registration of CV risk factors is performed. Also to estimate 10-year risk of CVD in RA patients and to compare the CVD risk among patients receiving or not biological therapy and those with positive and negative anti-cyclic citrullinated peptide (anti-CCP)
Methods: We conducted an observational descriptive study of patients who attended a specialized rheumatology clinic in Bogotá, Colombia from 2010 to 2015. Patients with RA were enrolled who had completed at least 5 year of follow-up. The information required to estimate CVD risk was obtained from medical records. Other variables included were biological therapy and test result of anti-CCP. For the calculation of CVD risk, the Framingham estimator was used and adjusted for the Colombian population. Additionally, patients who had 2 or more of these criteria: More than 10 years of evolution of RA, positive rheumatoid factor and/or extra-articular compromise, the risk was adjusted by multiplying by 1.5. Nonparametric statistics (Mann-Whitney U test) was used.
Results: We identified 273 eligible patients with RA with mean age 61, 66% women. Only 117 (42.8%) had recorded in their charts all variables to calculate CVD risk. We found that 32% had high blood pressure, 7% type II DM, 11% Obesity and 13% smoking. For the population evaluated, 10-year CVD risk median was 12.42% and for Colombia was 8.69%, adjusting this risk according to the disease in Colombia, increased to 13.03%. When we compare the 10-year CVD risk in anti-CCP positive patients (median: 11.15) and anti-CCP negative (median: 8.22) we did not find difference (p: 0.614). However, we found differences in the 10-year CVD risk median 9.04 vs. 23.25, 10-year CVD risk adjusted to Colombia median 6.32 vs. 16.31 and 10-year CVD risk adjusted to Colombia and RA median 6.81 vs. 13.39 between patients using biological therapy versus patients without receiving respectively (p: <0.001)
Conclusions: Only 42.8% of the sample had all CV risk factors requested and registered in the clinical record, so should promote improvement in the health team to increase this. The average 10-year CVD risk in all people with RA was 12.42%, and in patients who met the criteria to be multiplied by the factor 1.5 increased to 13.03%, which means that these patients should be reported this and applied risk prevention guidelines regarding obesity and cholesterol levels. Despite population receiving biologics are younger, they had lower CV risk. We need more research to confirm this results
References:
[1] Goff DC Jr, et al. 2013 ACC/AHA Cardiovascular Risk Guideline.
[2] M J L Peters, D P M Symmons, D McCarey et al. Ann Rheum Dis 2010;69:325–331.
[3] Arnett D, Goodman R, Halperin J, et al. Circulation. 2014; 130: 1662–1667.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6465

AB0314 HIGH INFLAMMATORY ACTIVITY AS A PREDICTOR OF INCREASED ARTERIAL STIFFNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Troitskaya, S. Velmakin, S. Villevalde, Z. Kobalava. *Propaedeutics of internal disease, RUDN University, Moscow, Russian Federation*

Background: Patients with rheumatoid arthritis (RA) have a high risk of cardiovascular (CV) morbidity and mortality. Arterial stiffness (AS) is a known predictor of CVD. Relationships between inflammation and arterial stiffness in patients with RA are not well understood.
Objectives: The aim of the study was to evaluate parameters of (AS) and their associations with inflammatory activity in patients with RA.
Methods: 62 patients with RA (EULAR 2010) without known CVD were examined (73% females,age 58,5±15,4 (M±SD) years, 13% smokers, 61% with AH, 34% with dyslipidemia). Median duration of RA was 8 years (IQR 3–17). Seropositive RA was diagnosed in 69% of patients. Median hsCRP was 12,1 mg/dl (IQR 2,2;23,4 mg/dl), median rheumatoid factor (RF) was 32,5 IU/ml (IQR 8,3;173 IU/ml). Mean DAS-28 (ESR) was 4,7±1,2. All patients received disease-modifying antirheumatic drugs, 22 (38%) - biological treatment. Parameters of AS were assessed by applanation tonometry (SphygmoCor, AtCor). Cardio-ankle vascular index (CAVI), ankle-brachial index (ABI) and vascular age were measured by VaSera 1500. Carotid intima-media thickness (CIMT) was evaluated by ultrasound. Pulse wave velocity>10,0 m/s and CAVI>9,0 were considered as AS increase. ABI<0,9 and CIMT>0,9 were considered as markers of subclinical atherosclerosis. p<0.05 was significant.
Results: Mean PWV was 9,3±3,2 m/s. PWV>10m/s was observed in 32,3% patients, CAVI>9,0 - in 25,8%, ABI<0,9 – in 6,5% and CIMT>0,9 – in 21%. Patients with PWV>10m/s were older (69,8±8,5 vs 53,2±15,1 years), had higher BMI (29,3±6,5 vs 24,7±4,8 kg/m^2), longer duration of AH (median 11,5 [IQR 5,5;17] vs 0 [IQR 0;5] years), higher BP levels (144±20/85±9 vs 123±14/77±10 mmHg), lower level of GFR (64±17 vs 89±19 ml/min/1,73m^2), higher levels of LDL-C (3,7±0,9 vs 3,2±1,0 mmol/l), plasma glucose (5,6±0,9 vs 4,8±0,7 mmol/l), hs-CRP (median 22 [IQR 13,3;60] vs 6,7 [IQR 1,6;17,2] mg/dl), higher CAVI (9,5±1,1 vs 7,6±1,4), vascular age (71±8,4 vs 53,4±17,5 years) and CIMT (1,01±0,3 vs 0,7±0,2 mm), p<0,05 for trend. Spearmen analysis revealed significant positive correlations between PWV and age (r=0,7), BMI (r=0,4), duration of AH (r=0,6), SBP (r=0,6), DBP (r=0,4), plasma glucose (r=0,3), hs-CRP (r=0,3), vascular age (r=0,6), CIMT (r=0,7), CAVI (r=0,6) and negative correlations with eGFR (r=-0,6). hsCRP correlated with PWV, aortic pulse pressure (r=0,3), CAVI (r=0,5), vascular age (r=0,5) and ABI (r=-0,5). Multiple regression analysis confirmed that AH duration (β=0,2, p=0.03), SBP (β=0,6, p<0.0001), GFR (β=-0,3, p=0,005) and hs-CRP-level (β=0,3, p=0.000009) were independent predictors of AS increase.
Conclusions: High prevalence of AS increase is observed in patients with RA without known CVD. Elevation of hsCRP as well as other traditional risk factors is an independent predictor of PWV increase in patients with RA.
References:
[1] Ambrosino P. et al. Subclinical atherosclerosis in patients with rheumatoid

arthritis. a meta-analysis of literature studies. Thromb Haemost 2015;113:916–930.
[2] Crilly M. et al. Arterial stiffness and cumulative inflammatory burden in rheumatoid arthritis:a dose–response relationship independent of established cardiovascular risk factors Rheumatology 2009;48:1606–1612.
[3] Silem H., Nasr G. Change of the aortic elasticity in rheumatoid arthritis: Relationship to associated cardiovascular risk factors J Cardiovasc Dis Res. 2010;1:110–115.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6495

AB0315 THE POTENTIAL ASSOCIATION BETWEEN RHEUMATOID ARTHRITIS AND TRADITIONAL CARDIOVASCULAR RISK FACTORS: A META-ANALYSIS OF CONTROLLED STUDIES

E. Filhol[1], C. Gaujoux-Viala[2], B. Combe[1], J. Morel[1], C. Hua[1], A. Nutz[2], C. Lukas[1], F. Flaisler[2]. *[1]Lapeyronie Hospital, Montpellier; [2]Nimes Hospital, Nimes, France*

Background: Systemic inflammation is the cornerstone of both rheumatoid arthritis (RA) and atherosclerosis. RA is currently considered as a cardiovascular risk factor.
Objectives: The aim of this systematic review was to assess the association between RA and the traditional cardiovascular risk factors (hypertension, dyslipidemia, diabete mellitus, and atherosclerosis) in RA patients in comparison to the general population.
Methods: We systematically searched literature (via Pubmed, Cochrane and abstracts from recent ACR and EULAR congresses) up to March 2016 for observational studies providing data concerning the presence of a traditional cardiovascular risk factor (among hypertension, dyslipidemia, diabetes mellitus, atherosclerosis) in patients with RA and in a control group. A meta-analysis of the relative risk (RR) concerning patients with RA in relation to the control group was performed for each cardiovascular risk factor.
Results: Out of 5714 screened references, 13 studies were included. Due to lack of data, atherosclerosis studies could not be included in this meta-analysis. For hypertension and diabetes, an increased risk was observed: RR =1.15 [95% CI 1.07–1.24], p=0.0003 and RR=1.11 [1.04–1.19], p=0.001, respectively. On the contrary, not any association was found with the dyslipidemia (RR=0.93 [0.77–1.12], p=0.43).
Conclusions: This meta-analysis highlights a moderate excess risk of hypertension and diabetes among patients with RA relative to the general population. A comprehensive identification of cardiovascular risk profile of RA is an opportunity to improve health management of these patients. Future research is crucial in order to establish to what extent the control of modifiable risk factors can improve cardiovascular outcome of these patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5432

AB0316 HOSPITAL ADMISSIONS OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH DMARD

E.C. Cervantes Pérez, J.R. Maneiro, A. Souto Vilas, J.A. Mera Varela, J.J. Gómez-Reino. *Ramón Domínguez Foundation, University Hospital Complex of Santiago de Compostela, Santiago de Compostela, Spain*

Objectives: To describe hospital admissions and contributing factors in patients with rheumatoid arthritis (RA) treated biological DMARD (b-DMAR) and conventional synthetic DMARD (cs-DMAR).
Methods: Retrospective observational study of RA patients admitted to the hospital for any cause from 2010 to 2015. Demographic, clinical and therapeutic characteristics were collected from the medical charts. Multivariate and univariate models were used to identify variables associated with admissions for any cause, major adverse cardiovascular events (MACE), and infection. The statistical program Stata 14.0 was used for the analysis.
Results: In the period 2010–2015, 26% of all RA patients were treated with b-DMARD. There were a total of 1251 hospital admissions for any cause in 600 patients; 1055 admissions in 477 patients treated with cs-DMAR and 196 admissions in 123 patients treated with b-DMAR. Of the 1251 admissions, 251 were due to infections and 60 to MACE. Demographic characteristics, comorbidities and treatment are disclosed in table. In the multivariate analysis, diabetes mellitus (p<0.001), and hypertension (p=0.029) were associated with admission for infections, and hypertension (p 0.011), and dyslipidemia (p=0.02) with admissions for MACE.
Conclusions: infections and MACE are a significant cause of hospital admission in patients with rheumatoid arthritis. Comorbidities as diabetes, hypertension and dyslipidemia but not b-DMARD are significantly associated with admission for infection or MACE.

Table. Demographic characteristics, comorbidities and treatment in 600 patients admitted to an university hospital.

	AR patients admitted (600)	Patients b-DMAR treated (123)	Patients cs-DMAR treated (477)	p*
Age > 65 years	428	59 (47.97%)	369 (77.36%)	0.03
Female	412	88 (71.54%)	324 (67.93%)	0.269
COPD[1]	59	8 (6.96%)	51 (10.81%)	0.062
Diabetes mellitus	109	10 (8.70%)	99 (20.97%)	0.364
Dyslipemia	161	23 (20.00%)	138 (29.30%)	0.025
Arterial hypertension	295	41(35.65%)	254 (53.93%)	<0.001
Corticoids	490	87(76.32%)	403 (85.74%)	0.162

[1]Chronic obstructive pulmonary disease.
*Univariate analysis comparing cs-DMARD treated patients with b-DMARD treated patients

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6769

AB0317 RHEUMATIC DISEASES AND PREGNANCY: PRACTICE PATTERNS AMONG RHEUMATOLOGISTS AND OBSTETRICIANS IN LEBANON

F. Fayad[1,2], N. Ziade[1,2], G. Abi Karam[1,2], W. Ghaname[3,4]. *[1]Saint Joseph University; [2]Hotel Dieu de France University Hospital, Beirut; [3]Holy Spirit University, Kaslik; [4]Notre Dame de Secours University Hospital, Jbeil, Lebanon*

Background: For years, women with potentially serious systemic diseases, such as rheumatic diseases (RD), have been advised against getting pregnant. However, with careful clinical management, most of these women can have successful pregnancies. The use of RD drugs before or during pregnancy is problematic due to the lack of knowledge about their compatibility with pregnancy. Recently, the British Society of Rheumatology (BSR) and the European League Against Rheumatism (EULAR) published guidelines on prescribing drugs in pregnancy and breastfeeding.
Objectives: To evaluate the perceptions and clinical practices of rheumatologists and obstetricians in Lebanon regarding the use of medications prior and during pregnancy and breastfeeding. The secondary objective was to assess the variables that are significantly associated with the physicians' adherence to guidelines.
Methods: A national, observational, cross-sectional physician survey was conducted among a representative sample of rheumatologists and obstetricians throughout Lebanon. Collected data included physicians' information (age, gen-

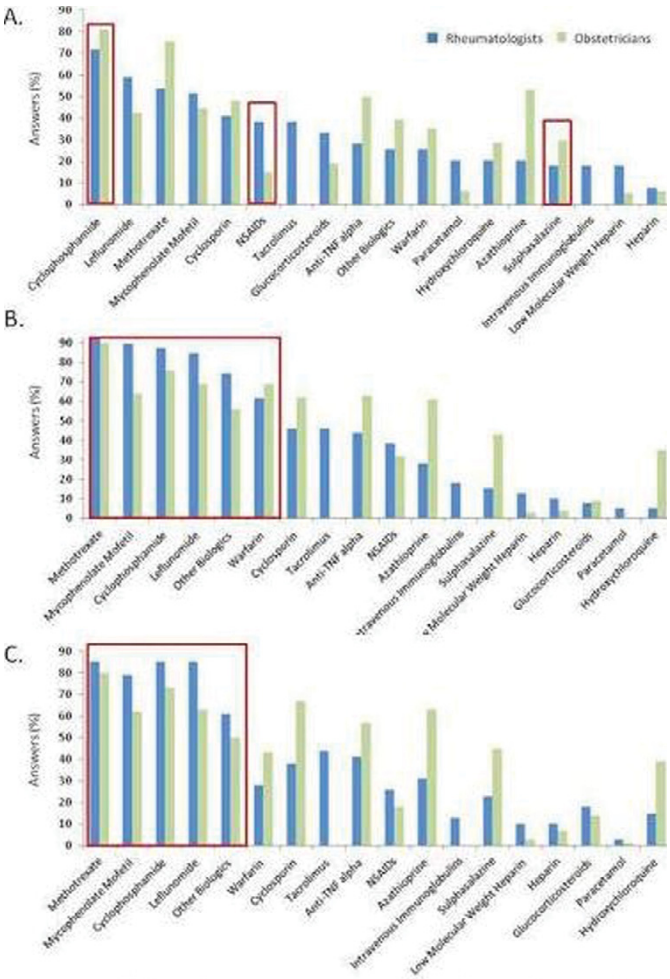


Figure 1. Percentage of rheumatologists and obstetricians who consider RD medications detrimental to fertility (A), pregnancy (B) and breastfeeding (C). Red squares indicate answers in accordance with EULAR/BSR guidelines.

der, years of experience, practice setting and number of pregnant patients with RD seen per month), their opinion on pregnancy in RD patients (pre-conception status of RD and counseling, remission length before allowing pregnancy) and compatible RD drugs with pregnancy and lactation. Qualitative variables were analyzed using Chi-square or Fisher's exact tests, while quantitative variables were analyzed using Wilcoxon or Student t tests. A total score of answers per physician in accordance with EULAR/BSR guidelines was calculated. Univariate and multivariate analysis assessed the variables significantly associated with this score. P value <0.05 indicated statistical significance.

Results: Thirty-nine (90.7%) rheumatologists participated in this survey. They had 22.2±11.6 years of practice. Ninety-four (41.4%) obstetricians participated in this survey. They had 26.0±12.8 years of practice. Figure 1 displays the percentage of physicians who consider the selected RD medications detrimental to/not compatible with fertility, pregnancy and breastfeeding.

Average score of answers in accordance with EULAR/BSR guidelines was 0.654±0.154 and results were significantly different between specialties ($p<0.001$): rheumatologists scored between 0.41 and 1, with an average of 0.777±0.152 and obstetricians scored between 0.36 and 1 with an average of 0.603±0.124. Multivariable analysis showed that the scores reflecting adherence to recommendations were significantly associated with type of specialty (rheumatology v/s obstetrics) and number of pregnant patients with RD seen per month.

Conclusions: Advices given to RD patients who plan on becoming pregnant in Lebanon vary largely, especially among the physicians' specialty and experience in RD, which highlights the urgency of disseminating the EULAR/BSR guidelines among rheumatologists and obstetricians alike.

References:

[1] Flint J et al, Rheumatology 2016.
[2] Gõtestam Skorpen C et al, Ann Rheum Dis 2016.
[3] Panchal S et al, Rheum Int 2013.
[4] Ruiz-Irastorza G and Khamashta MA, ACR 2014.

Acknowledgements: Sponsor: Newbridge Pharmaceuticals. MW support: KBP-Biomak.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3430

AB0318 CLINICAL AND SEROLOGIC CHARACTERISTICS OF A COHORT OF ECUADORIAN MEN WITH RHEUMATOID ARTHRITIS

G. Maldonado[1], C. Ferro[2], R. Guerrero[3], C. Paredes[3], C. Rios[4]. *[1]Universidad Espiritu Santo, Universidad Espíritu Santo; [2]Universidad Católica Santiago de Guayaquil; [3]Universidad Espíritu Santo; [4]Centro de Reumatología y Rehabilitación, Guayaquil, Ecuador*

Background: Rheumatoid arthritis (RA) is an inflammatory and disabling disease whose expression and clinical course is influenced by gender. In developed countries the prevalence of RA is 0.5–1%, with a ratio 3:1 female:male. Comparative gender studies have shown that women have greater functional disability, disease activity and pain than men1.

Objectives: The purpose of this study is to describe and compare the clinical and serological characteristics of a cohort of men with RA.

Methods: A cross-sectional study was conducted in patients with established diagnosis of RA (American College of Rheumatology criteria 1988) from the Luis Vernaza Hospital and a private rheumatology center (CERER). The data included clinical manifestations, demographic data, comorbidities, habits, treatment, activity index DAS28-CRP, HAQ-DI disability index and the PHQ-9 questionnaire. The statistical program SPSS V. 22 was used to analyze the data and calculate frequencies, percentages, means, ranges, Spearman correlation and ANOVA coefficient. Statistical significance used was 0.05, with a 95% reliability.

Results: A cohort of 50 men was compared with a control group of 50 women. Most men worked while women stayed at home (72% and 66%, respectively, p=0.000). Tobacco and alcohol were more common in men (34% vs 8% p=0.001 and 38% vs. 0% p=0.000 respectively). The delay in the first visit to the specialist was shorter in men than in women (24 vs 32 months) and they had a longer follow-up (55 vs 41 months). In clinical manifestations, women had greater fatigue (60% vs 30% p=0.003), weight loss (44% vs 20% p=0.010), loss of appetite (54% vs 12% p=0.000) and depression (60% vs 22% p=0.000). There was no significant difference in comorbidities and treatment between the groups. Men had lower disease activity: VSG (23 vs 47 p=0.046), DAS 28 (2.5 vs 3.4 p=0.011), HAQ DI (0.37 vs 1.12 p=0.000), functional disability (12% vs 36% p=0.005), severe disability (2% vs 22% p=0.002), painful joints (2 vs 8 p=0.000), swollen joints (2 vs 6 p=0.000) and VAS of doctor (2 vs 3 p=0.047).

Conclusions: This is the first cohort study of men with RA in Ecuador. As shown in other international studies2–3, our results confirm that men have a less aggressive disease.

References:

[1] Lesuis N, Befrits R, Nyberg F, van Vollenhoven RF. Gender and the treatment of immune-mediated chronic inflammatory diseases: rheumatoid arthritis, inflammatory bowel disease and psoriasis: an observational study. BMC Med. BioMed Central Ltd;2012;10(1):82.
[2] Sokka T, Toloza S, Cutolo M, Kautuainen H, Makinen H. Women, men, and rheumatoid arthritis: analyses of disease activity, disease characteristics, and treatments in the QUEST-RA Study. Arthritis Res Ther. 2009;11(1):1–12.
[3] Hallert E, Thyberg I, Hass U, Skargren E, Skogh T. Comparison between women and men with recent onset rheumatoid arthritis of disease activity and functional ability over two years (the TIRA project). Ann Rheum Dis. 2003;62(7):667–70.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1409

AB0319 COMORBIDITIES IN ECUADORIAN PATIENTS WITH RHEUMATOID ARTHRITIS

G. Maldonado[1], C. Rios[2], C. Ferro[3], R. Guerrero[4], C. Paredes[4], M. Moreno[5], C. Vallejo[6]. *[1]Universidad Espiritu Santo, Universidad Espíritu Santo; [2]Centro de Reumatología y Rehabilitación; [3]Universidad Católica Santiago de Guayaquil; [4]Universidad Espíritu Santo; [5]Hospital Luis Vernaza; [6]Sociedad Ecuatoriana de Reumatología, Guayaquil, Ecuador*

Background: Rheumatoid arthritis (RA) is associated with several comorbidities that reduce life expectancy. These comorbidities may be due to the rheumatic process itself, treatment or be independent, and include: anemia, osteoporosis, fractures, infections, gastric ulcers, myocardial infarction, depression, lymphoma and other malignancies.

Objectives: The aim of this study is to determine the comorbidities in patients with an establish diagnosis of rheumatoid arthritis.

Methods: A cross-sectional descriptive study was conducted in patients with an established diagnosis of RA according to the ACR 1987 criteria, from public and private rheumatology clinics in Guayaquil, Ecuador. The database included; demographics, comorbidities, habits, treatments, laboratory exams, number of swollen and tender joints, Visual Analog Scale (VAS), activity and disability index (DAS28 and HAQ-DI) and PHQ-9 for depression. The statistical program SPSS V. 22 was used to analyze the data and calculate frequencies, percentages, means, ranges, Spearman correlation and ANOVA coefficient. Statistical significance used was 0.05, with a 95% reliability.

Results: 402 patients with a mean age of 50 years were included, 87.8% (353) women and 12.2% (49) men. 93.8% (377) were mestizos, 3.5% (14) White, 1.5% (6) Indigenous and 1.2% (5) Afro-Ecuadorians. As for the marital status 55.5% (223) were married, 15.4% (62) cohabiting, 12.4% (50) divorced, 8.5% (34) singles and 8.2% (33) widowers. 9.7% (39) of the patients smoked, 7.5% (30) ingested alcohol and 0.5% (2) drugs. The average age of onset of the disease was 41 years, with a median time from onset of symptoms and the first rheumatology visit of 28.7 months, median follow-up time of 51.8 months and average disease duration of 11 years. For comorbidities, 54.8% (147/268) had dyslipidemia, 28.4% (114) gastric disease, 23.6% (95) hypertension, 20.1% (81) obesity, 19.6% (79) depression, 15.2% (61) thyroid disease, 12.4% (50) of the sexual involvement, 10.7% (43) allergies, 10.4% (32/307) hypertransaminasemia, 9.3% (21/225) anemia, and 6.7% (27) diabetes mellitus. 32.3% (114) of women have had at least one abortion. The PHQ-9 medium was 5.3; according to this 11.2% (45) corresponded to mild depression, 4.5% (18) moderate depression, 3.2% (13) moderately severe depression and 0.7% (3) severe depression. As for the other indicators of disease activity, the average for the number of painful joints was 5 (0–28), swollen joints 4 (0–26), patient VAS 3.9 (0–10) and doctor VAS 3.4 (0–10). In laboratory data, 67.4% (215/319) had positive ESR, 64.8% (149/230) PCR, 90.5% (182/201) anti CCP positive, and 94.4% (286/303) RF.

Conclusions: This is the first study of comorbidities in patients with RA in Ecuador. Patients with RA have a high prevalence of comorbidities and risk factors, which is why physicians should be prepared to prevent them and offer an early treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1408

AB0320 RHEUMATOID ARTHRITIS IN BRAZIL – THE "REAL" STUDY: A NATIONWIDE PROSPECTIVE STUDY

G. Castelar-Pinheiro[1], A.B. Vargas-Santos[1], C. Albuquerque[2], R. Amorim[1], R. Giorgi[3], S. Radominski[4], I. Pereira[5], M.F. Guimarães[6], M. Bértolo[7], P. Louzada Jr.[8], M.F. Cunha[9], K. Bonfiglioli[10], C. Brenol[11], L.M.H. Mota[2]. *[1]Internal Medicine, Rheumatology Unit, Universidade do Estado do Rio de Janeiro, Rio de Janeiro; [2]Universidade de Brasília, Brasília; [3]Instituto de Assistência Médica ao Servidor Público Estadual, São Paulo; [4]Universidade Federal do Paraná, Curitiba; [5]Universidade Federal de Santa Catarina, Florianópolis; [6]Universidade Federal de Minas Gerais, Belo Horizonte; [7]Universidade Estadual de Campinas, Campinas; [8]Universidade de São Paulo - Ribeirão Preto, Ribeirão Preto; [9]Universidade Federal do Pará, Belém; [10]Universidade de São Paulo, São Paulo; [11]Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil*

Background: Early diagnosis and immediate treatment are critical in achieving optimal outcomes in rheumatoid arthritis (RA). However, anecdotal evidence suggests that in Brazil there is still a significant delay in patient referral, RA diagnosis and DMARD initiation. The lack of national data hinders effective advocacy for proper public health policies, which led the RA commission of the Brazilian Society of Rheumatology to create a nationally-representative multicenter RA cohort to provide the necessary data.

Objectives: To describe the development process and baseline characteristics of a large, nationally-representative multicenter cohort of RA patients in Brazil.

Methods: Eleven public rheumatology centers from all of the 5 regions of Brazil enrolled ~100 consecutive RA patients each (1987 ARA or 2010 ACR-EULAR). This cohort is being followed prospectively for 1 year, with systematic data collection at time 0, 6±1 months and 12±1 months, and registration of all other visits during this 1-year period. Data collection began in 08–2015, using a single online electronic medical record, and included demographic, socioeconomic, clinical, lab, radiographic and therapeutic characteristics, along with functional status, quality of life and adherence to treatment information.
Results: 1125 patients were enrolled (Table), ~90% were female, with a mean age of 56 years and median disease duration of 13 years. Median BMI was 27 kg/m^2, with 64% of the patients classified as overweight or obese. The interval between symptoms and diagnosis varied from 1 to 457 months (median 12 months). Almost half of the patients were on glucocorticoids, 96% on DMARDs, with 36% on biologics. Only 7% were seronegative for both rheumatoid factor and ACPA. Median HAQ-DI was 0.875 and median DAS28-ESR was 3.5, with 58.6% of patients presenting moderate or high disease activity.

Table 1. Patients baseline characteristics

	N	
Age, years*	1125	56.7 (22.1–88.8)
Female	1125	89.5%
Current or former smoker	1125	39.6%
BMI, kg/m^2*	1055	26.6 (15.8–56.2)
Disease duration, years*	1124	12.7 (0.7–56.7)
Rheumatoid factor+	1105	78.7%
ACPA+	479	76.8%
Erosive disease	1105	55.2%
Extra-articular manifestation ≥1	1118	23.3%
Drugs in use:		%
– Glucocorticoids	1125	47.0
– NSAIDs	1125	9.0
– Synthetic DMARDs	1125	90.8
– Methotrexate	1125	66.5
– Biologic DMARDs	1125	36.1
Erythrocyte sedimentation rate (ESR), mm/1st hour*	933	21 (1–140)
C-reactive protein, mg/dL*	954	0.7 (0–76.1)
DAS28-ESR*	932	3.5 (0.3–8.2)
HAQ-DI*	1121	0.875 (0–3)

*Results in median (range).

Conclusions: The delay in diagnosis may explain the high percentage of patients with moderate or high disease activity and erosive disease. The low level of physical dysfunction observed in this established, predominantly seropositive RA population may be explained by the large proportion of patients on glucocorticoid and biologic therapy. Our findings suggest that, despite current treatment concepts being well known and accepted by Brazilian rheumatologists, there is still a gap in early diagnosis and management of RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1740

AB0321 RELATIONSHIP OF CAROTID FEMORAL PULSE WAVE VELOCITY WITH AGE AND TIME OF EVOLUTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

C. Ramos[1], G. Alanis[1], D. Cardona[2], S. Totsuka[1], E. Cardona[1], F. Pérez[1], A. Coldivar[1], J. Gómez[1], M. Vázquez del Mercado[1]. *[1]Physiology, University of Guadalajara; [2]Physiology, University of Gudalajara, Guadalajara, Mexico*

Background: Early vascular aging occurring in Rheumatoid Arthritis (RA) may be a consequence of chronic inflammation. The measurement of Carotid-femoral pulse wave velocity (cfPWV) is the gold standard to evaluate arterial stiffness. Vascular aging is a result of a change in the biomechanical properties of the vascular wall. This process can be accelerated by the accumulated damage of high mechanical stress (high blood pressure), chronic inflammation and comorbidities such as smoking, Diabetes Mellitus and dyslipidemia[1]
Objectives: The aim of this study was to evaluate variations in the Carotid-Femoral Pulse Wave Velocity (cfPWV) and it's association to age and time of disease evolution in patients with rheumatoid arthritis.
Methods: RA patients were matched for age and sex with healthy controls. Subjects with a history of smoking, cardiovascular disease, hypertension, diabetes mellitus, cancer, liver disease, thyroid disease and kidney disease were excluded. The cfPWV was calculated using the Pulse Pen ® (Diatechne, Italy) device.
Results: We included 76 women with RA and 28 healthy women, mean age (44.3±10.92 vs. 43.0±16.26, P=0.654). cfPWV demonstrated good correlation with age (r=0.459, P<0.01), disease evolution time (r=0.311, P=0.008), triglycerides (r=0.289, P=0.03), total cholesterol (r=0.421, P<0.01) and atherogenic index (r=0.320, P=0.02). No association with disease activity was found. cfPWV was higher in those patients with RA >10 years evolution compared to patients with <10 years of disease evolution and to controls (P<0.05).
Conclusions: A significant association between cfPWV was seen in patients with RA, and was also correlated to age and to a disease evolution >10 years long without finding a significant association with increased disease activity.
References:
[1] -Kozakova M, Morizzo C, Guarino D, et al. The impact of age and risk factors on carotid and carotid-femoral pulse wave velocity. Journal of hypertension 2015;33(7):1446–51 doi: 10.1097/HJH.0000000000000582 [published Online First: Epub Date]|.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6405

AB0322 THE ROLE OF HOMA-IR AND HOMA-ISLET INDICES IN DIFFERENT CARBOHYDRATE METABOLISM DISORDERS DURING GLUCOCORTICOID THERAPY

G. Nurullina. *Kazan Medical State University, KAZAN, Russian Federation*

Background: Diabetogenic effect limits the use of glucocorticoids (GC), especially in patients with diabetes risk factors. At present HOMA index is widely used for the evaluation of insulin resistance (IR) and β-cell function. HOMA-IR index increase is an indirect measure of IR progression and cardiovascular risk elevation.
Objectives: To evaluate the role of modified HOMA-IR and HOMA-islet indices in different carbohydrate metabolism disorders (CMD) during oral (OGCT) and PULSE (GCPT) glucocorticoid therapy (GCT).
Methods: A prospective study including 118 patients with systemic lupus erythematosus (SLE) (n=63) and systemic vasculitis (SV) (n=55) was performed. Seventy one patients received GCPT (i.v. infusion of 10–15 mg/kg of prednisolone with 250 ml of normal saline per day, for 3 consecutive days (1 course of 3 sessions); course dose was 1800–3000 mg; 47 patients received oral GC 15–30 mg/day. HOMA-IR index and β-cell function (HOMA-islet index) were calculated as follows: Homa-IR =1.5 + fasting blood glucose (mmol/l) x fasting C-peptide level (pmol/l) /2800. HOMA-islet =0.27 x fasting C-peptide level (pmol/l)/(fasting blood glucose (mmol/l) – 3,5).
Results: GCPT was associated with less CMD compared to OGCT. Impaired fasting glucose (IFG) was observed in 7 (9.9%) and 9 (19.1%), impaired glucose tolerance (IGT) – in 9 (12.7%) and 14 (29.8%) and diabetes mellitus (DM) – in 9 (12.7%) and 13 (27.7%) patients in GCPT and OGCT groups, respectively. There was a significant decrease of HOMA-islet during glycemic peak in DM patients from 13.96 to 6.17 after GCPT (p<0.05), compared to insignificant changes in other groups. Decrease of HOMA-islet index reflects a disturbance of overall functional activity of β-cells in DM patients. After a course of GCPT HOMA-islet index was significantly lower in DM patients compared to patients with no CMD (11.8 vs. 15.4), as GCPT is associated with a decrease of β-cell function which does not return to baseline as a consequence of β-cell reserve depletion. No rapid decrease of β–cell function was observed in OGCT group, instead there was a compensatory increase, which was insufficient to maintain normoglycia because of high insulin resistance. C-peptide, HOMA-IR and HOMA-islet levels in OGCT patients demonstrated the same trend as in GCPT patients. Significant differences were observed in patients with IGT and DM before and after oral glucose tolerance test (OGTT) on C-peptide (1042 pmol/l vs. 1978 pmol/l in IGT; 1306 pmol/l vs. 2286 pmol/l in DM) and HOMA-IR (4.53 vs. 9.81 in IGT; 5.6 vs. 11.27 in DM patients), whereas in patients without CMD and in patients with IFG, C-peptide before OGTT was 489 pmol/l vs. 743 pmol/l, after - 1295 pmol/l vs. 1488 pmol/l, HOMA-IR – 2.59 vs. 2.88 before OGTT and 2.88 vs. 5.85 after the test in the absence of CMD and in IFG patients, respectively. A significant decrease of β–cell function was observed in DM patients, reflected by a decrease of HOMA-islet index after OGTT compared to baseline (147 vs. 78.4).
Conclusions: Evaluation of blood glucose level, which was normal in all included patients, and isolated C-peptide evaluation are insufficient for the evaluation of carbohydrate metabolism before GCPT and long-term OGCT. The evaluation of modified HOMAA-IR and HOMA-islet indices before the start of intensive GC treatment and during OGCT may improve early detection of risk groups for serious CMDs – IGT and DM.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5721

AB0323 CARBOHYDRATE METABOLISM AND GLUCOCORTICOID THERAPY IN PATIENTS WITH SYSTEMIC INFLAMMATORY DISEASES

G. Nurullina. *Kazan Medical State University, Kazan, Russian Federation*

Background: Glucocorticoid therapy (GCT) is one of the risk factors of carbohydrate metabolism disorders (CMD) in patents with systemic inflammatory diseases. CMD development is a concern not only with long-term therapy, but also during intensive short-term GC administration, which can lead to different CMDs, including impaired glucose tolerance (IGT) and diabetes mellitus (DM).
Objectives: to evaluate the prevalence of CMD after long-term and intensive GC treatment (GCT) in patients with systemic lupus erythematosus (SLE), systemic vasculitis (SV) and chronic glomerulonephritis (CGN).
Methods: Ninety eight patients with systemic inflammatory diseases were included (SLE - 53, SV – 35), among them 68 received GC pulse-therapy (GCPT) (1 series of 3 sessions), and 30 – oral GCT (OGCT). All patients underwent standard clinical and laboratory evaluation, oral glucose tolerance test (OGTT), evaluation of C-peptide, HOMA-IR and HOMA-islet indices.
Results: CMDs developed less often in patients receiving GCPT compared to long-term OGCT (p=0.035). In patients receiving OGCT the most prevalent CMDs were IGT and DM – in 9 (30.0%) and 8 (26.7%) patients respectively, which

was significantly higher compared to patients in GCPT group – 7 (10.3%) and 6 (8.8%) respectively (p=0.038 and p=0.049). Baseline C-peptide was elevated in patients who developed IGT after a course of GCPT (850 pmol/l before GCPT, 4099 pmol/l 4–6 hours after GCPT and 1904 pmol/l after a 3-days course of GCPT) or DM (1050 pmol/l, 3170 pmol/l and 1796 pmol/l before GCPT, at peak blood glucose level and after a 3-days course of GCPT, respectively) ($p<0.05$). C-peptide remained normal in the absence of CMD and in IGT patients.
Baseline HOMA-IR index was elevated in patients with IGT (4.52, 17.47, 9.67 before GCPT, at peak blood glucose level and after a 3-days course of GCPT, respectively) and DM (5.04, 15.2, 10.4 respectively) ($p<0.05$), and normal in patients without CMD (2.2, 5.84 and 4.01 respectively) and patients with impaired fasting glucose (IFG) (2.46, 7.08 and 5.46).
HOMA-islet index analysis revealed that in the absence of CMD and at earlier stages of CMDs (IFG, IGT) insulin resistance is compensated via an increase of β-cell secretory activity. In DM patients there is a trend towards decreased β-cell secretory activity, which is associated with a significant decrease of HOMA-islet index to 64,6 at peak blood glucose levels after GCPT compared to baseline level (170) ($p<0.05$). C-peptide, HOMA-IR and HOMA-islet index levels in OGCT patients demonstrated same trend as in GCPT patients. Significant differences were observed in patients with IGT and DM before and after oral glucose tolerance test (OGTT) on C-peptide (1042 pmol/l vs. 1978 pmol/l in IGT; 1306 pmol/l vs. 2286 pmol/l in DM) and HOMA-IR (4.53 vs. 9.81 in IGT; 5.6 vs. 11.27 in DM patients), whereas in patients without CMD and in patients with IFG, C-peptide before OGTT was 489 pmol/l vs. 743 pmol/l, after - 1295 pmol/l vs. 1488 pmol/l, HOMA-IR – 2.59 vs. 2.88 before OGTT and 2.88 vs. 5.85 after the test in the absence of CMD and in IFG patients, respectively. A significant decrease of β–cell function was observed in DM patients, reflected by a decrease of HOMA-islet after OGTT compared to baseline (147 vs. 78.4).
Conclusions: GCT leads to IGT and DM in patients with increased IR both during GCPT and long-term OGCT. Long-term OGCT is associated with more CMDs compared to GCPT.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5748

AB0324 IS LOW SERUM VITAMIN D LEVEL ASSOCIATED WITH INCREASED NEUROPATHIC PAIN IN RHEUMATOID ARTHRITIS PATIENTS? A CROSS-SECTIONAL STUDY

H. Yesil[1], U. Sungur[2], S. Akdeniz[3], G. Gurer[3], B. Yalcın[4], U. Dundar[1]. *[1]Physical Medicine and Rehabilitation, Afyon Kocatepe University, Afyonkarahisar; [2]Physical Medicine and Rehabilitation, Ege University, Faculty of Medicine, Izmir; [3]Physical Medicine and Rehabilitation, Adnan Menderes University, Faculty of Medicine, Aydın; [4]Afyon Kocatepe University, Afyonkarahisar, Turkey*

Background: Rheumatoid arthritis (RA) is a systemic, autoimmune, progressive condition characterised by progressive synovitis with resultant joint destruction, functional disability and significant pain. Recent experimental data indicates that there may be a neuropathic component of pain perception in RA.
Objectives: The aim of this study was to examine the development of neuropathic pain (NP) in patients with RA and its relationship with vitamin D.
Methods: We used the Leeds assessment of neuropathic symptoms and signs (LANSS) questionnaire to evaluate NP in 93 patients with RA. Clinical parameters included general demographics, and disease activity scores were evaluated. The patients also completed Short form-36 survey, and Health Assessment Questionnaire.
Results: Of all the patients who were eligible for the study, 75 were female (80.6%). Mean serum vitamin D level of the participants was calculated to be 22.8±11.9 ng/mL. According to the LANSS questionnaire 31 patients (33.3%) were classified as having NP. There was a negative correlation between vitamin D levels and LANSS value (p=0.001). We have determined that patients with vitamin D serum levels below 20 ng/mL have significantly higher NP positivity rate (p=0.012), besides they have 5.8 times more risk of developing NP when compared to patients with vitamin D serum levels ≥30 ng/mL.
Conclusions: We conclude that Vitamin D deficiency is prevalent in RA patients with NP. Once it is the right diagnosis, Vitamin D deficiency treatment is relatively easy, safe, inexpensive and with satisfactory outcomes; therefore, an underlying vitamin D deficiency should be explored in the etiology of NP in patients with RA.
References:
[1] Bellucci E, Terenzi R, La Paglia GM, Gentileschi S, Tripoli A, Tani C, Alunno A. One year in review 2016: pathogenesis of rheumatoid arthritis. Clin Exp Rheumatol. 2016; 34(5):793–801.
[2] Koop SM, Klooster PM, Vonkeman HE, Steunebrink LM, van de Laar MA. Neuropathic-like pain features and cross-sectional associations in rheumatoid arthritis. Arthritis Research & Therapy.2015; 17:237.
[3] Shehab D, Jarallah KA, Abdella N, Mojiminiyi OA, Mohamedy HA. Prospective Evaluation of the Effect of Short-Term Oral Vitamin D Supplementation on Peripheral Neuropathy in Type 2 Diabetes Mellitus. Med Princ Pract. 2015; 24:250–256.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4395

AB0325 TREAT TO TARGET AND THE REAL LIFE EXPERIENCE – DATA FROM A COHORT OF RHEUMATOID ARTHRTIS PATIENTS IN SOUTH EAST ROMANIA (CONSTANTA COUNTY)

V.C. Suta[1,2], I.-T. Andronache[1], M. Suta[2]. *[1]Rheumatology Department, IInd Internal Medicine Clinic, "Sf. Apostol Andrei" Emergency Clinical County Hospital Constanta; [2]Faculty of Medicine, "OVIDIUS" University Constanta, Constanta, Romania*

Background: Treatment target in rheumatoid arthritis (RA) is remission or low disease activity. Considering that there is no quantitative "gold standard " for measuring the disease activity, monitoring and evaluation of RA patients is made through composite scores, which have an important subjective component. Moreover, the laboratory investigations used (ESR and CRP) are commonly discordant with the clinical findings
Objectives: To evaluate disease activity and establish relations between disease activity scores and their components in RA patients
Methods: We performed a transversal study which included 447 RA patients (aged 18 to 86-years-old) admitted to our Rheumatology Department between January 2014 and December 2015. Patients' evaluation was performed by the rheumatologist. All the data obtained from the medical history, clinical examination, laboratory tests and imaging studies was recorded at the same date. All patients signed a dated informed consent at the time of admission.
Results: The study included 447 patients, mean age 62.13±11.44, 85% women, accounting for a female:male ratio (F:M) of almost 6:1 (5.7:1) with an average disease duration of 10,75±8,85 years. 48% of our patients presented with normal CRP values (≤0.5mg/dl) and values of ≤1mg/dl for CRP, compatible with Boolean remission, were present in 66.6% of the patients. A significant percentage of our sample population (194 patients: 43.4%) registered normal ESR values (≤28 mm/h)
Remission and LDA were registered in 18.1% up to 29.8%.of the patients, depanding on the score used. The lowest rate of remission and low activity is registered through the DAS28 ESR evaluation (18.1%). The other three scores outline similar percentages for T2T group of patients: 27.1% (SDAI), 28.7% (CDAI), and 29.7% (DAS28 CRP). The LDA group is characterized in our study by a small number of swollen joints (<1), medium-normal ESR values (<30mm/h) and CRP values <1mg/dl (with the exception of SDAI). Consequently, patients with low activity based on the afore mentioned scores meet remission according to Boolean definition.
Conclusions: The disease activity and implicitly the remission rate are appreciated differently depending on the scale used. The limit between remission and low disease activity is fragile, influenced mainly by the purely subjective components of the assessment instruments. The important differences between the subjective and objective components of the evaluation scales recommend the supplementation of methods used in order to emphasize the real degree of joint inflammation.
References:
[1] Jonathan Kay, Olga Morgacheva, Daniel E Furst et al. Clinical disease activity and acute phase reactant levels are discordant among patients with active rheumatoid arthritis: acute phase reactant levels contribute separately to predicting outcome at one year. Arthritis Research & Therapy 2014, 16:R40.
[2] Tuulikki Sokka et al. Remission and Rheumatoid Arthritis. Data on Patients Receiving Usual Care in Twenty-Four Countries. ARTHRITIS & RHEUMATISM Vol. 58, No. 9, September 2008, pp 2642–2651.
[3] Glenn Haugeberg et al. Ten years of change in clinical disease status and treatment in rheumatoid arthritis: results based on standardized monitoring of patients in an ordinary outpatient clinic in southern Norway. Arthritis Research & Therapy (2015) 17:219.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6920

AB0326 INFLUENCE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS ON ARTERIAL STIFFNESS IN PATIENTS WITH RHEUMATIC DISEASES

J.N. Kim, J.-Y. Choe, S.-K. Kim, S.-H. Park, H. Lee, C.U. Lee, J.-W. Kim. *Division of Rheumatology, Department of Internal Medicine, Catholic University of Daegu School of Medicine, Daegu, Korea, Republic Of*

Background: The association with adverse cardiovascular (CV) events and NSAIDs has been the topic of much debate.
Objectives: The aim of the present study was to investigate the effects of continuing NSAIDs therapy on predictable parameters for CV events.
Methods: We enrolled 155 patients with variable rheumatic diseases (95 rheumatoid arthritis, 49 systemic lupus erythematosus, 3 behçet's disease, 3 gout, 5others.) who were free from established CV diseases and had taken cardiovascular function tests from June 2015 to June 2016. They were divided into two groups depending on whether or not to have taken NSAIDs therapy for at least 5 years: NSAIDs taking group (91 patients) vs. non NSAIDs taking group (64 patients). For evaluating heart function, transthoracic echocardiography was used. Arterial stiffness was assessed using brachial-ankle pulse wave analysis.
Results: There were no significant differences in blood pressure, serum creatinine, serum hemoglobin, total cholesterol, erythrocyte sediment rate, C-reactive protein, disease duration, age, and smoking history between the groups. The NSAIDs

taking group had a higher median (95% CI) baPWV (brachial-ankle pulse wave velocity) and median (95% CI) mean pulmonary artery pressure (mPAP) than non-NSAIDs taking group: baPWV 13.72 (12.77–15.62) vs. 15.29 (13.93–17.63) m/s, p=0.005; mPAP 26.5 (22.8–30.5) vs. 30.5 (27.3–32.3) mmHg, p=0.011. But baPWV and mPAP were not significantly different between selective cyclooxygenase-2 inhibitor (22 patients) and nonselective NSAIDs (69patients): baPWV 15.33 (13.98–17.63) vs. 14.83 (13.82–17.39) m/s, p=0.191; mPAP 29.0 (24.5–34.5) vs. 30.0 (26.0–33.0) mmHg, p=0.960.

Conclusions: Our study suggests that continuing NSAIDs therapy is associated with increased arterial stiffness in patients with rheumatic diseases, independently noted to increase the incidence of cardiovascular disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2403

AB0327 FEAR OF FALLING AND FOOT PAIN, IMPAIRMENT AND DISABILITY IN RHEUMATOID ARTHRITIS

J. Bahha, B. Amine, M. Erraoui, Y. Boujenane, S. Fellous, I. El Binoune, R. Bahiri. *Rheumatology, Mohammed V University, Faculty of Medicine and Pharmacy of Rabat, El Ayachi Hospital, sale, Morocco*

Background: Fear of falling, foot pain and functional disability are commonly reported in rheumatoid arthritis. Moreover, the relationship between the fear of falling and foot pain, impairment and disability has rarely been studied.

Objectives: To evaluate the relationship between fear of falling and foot pain, impairment and disability in patients with established RA.

Methods: A cross-sectional study that included patients with rheumatoid arthritis. We collected the following data: age, sex, duration of disease, foot pain assessed by the Visual Analogue Scale (VAS), Disease activity assessed by DAS 28, HAQ disability index (HAQ-DI). Fear of falling was assessed by Falls Efficacy Scale-International (FES-I) which consists of 16 different activities, scored using a four point scale (1=not at all concerned, 2=somewhat concerned, 3=fairly concerned and 4=very concerned). The summed scores for the 16 activities for each participant were calculated. Scores of ≥23 indicated a significant fear of falling. Foot disability and impairment were measured using the Leeds Foot Impact Scale (LFIS), Foot disability was represented by the total score (LFIST; range 0 to 51) of the LFIS and foot impairment by the first subscale (LFISIF; range 0 to 21). Correlations were used to assess the relationship between fear of falling and foot pain, impairment and disability.

Results: Thirty-three patients were included. The mean age was 49.3±10.5 years with female predominance (n=29 (87.9%)). The mean disease duration was 9.9±7.5 years. The mean HAQ-DI was 1.3±0.8. The mean DAS28 score was 5.5±1.3 and the mean EVA foot pain was 5.5±2.4. The mean FES-I score was 37.4±15.1 and 69.7% (n=23) of patients had a significant fear of falling. Positive correlations were found between fear of falling and foot impairment (r=0.66; p<0.0001) and disability (r=0.80; p<0.0001). No correlation was found between fear of falling and foot pain (r =0.29, p=0.07).

Conclusions: The results of this study have demonstrated the importance of the relationship between fear of falling and foot impairment and disability.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5912

AB0328 RHEUMATOID ARTHRITIS AND FEAR OF FALLING: THE INFLUENCE OF DISEASE ACTIVITY

J. Bahha, B. Amine, M. Erraoui, Y. Boujenane, S. Fellous, I. El Binoune, R. Bahiri. *Rheumatology, Mohammed V University, Faculty of Medicine and Pharmacy of Rabat, El Ayachi Hospital, sale, Morocco*

Objectives: The objective of this study was to evaluate fear of falling in patients with established RA and its relation to disease activity.

Methods: A cross-sectional study that included patients with rheumatoid arthritis. We collected the following data: age, sex, duration of disease, body mass index (BMI). Fear of falling was evaluated by the Falls Efficacy Scale-International score (FES-I) which consists of 16 different activities, scored using a four point scale (1=not at all concerned, 2=somewhat concerned, 3=fairly concerned and 4=very concerned). The summed scores for the 16 activities for each participant were calculated. Scores of ≥23 indicated a significant fear of falling. Disease activity was measured with swollen and tender joint count (SJC28, TJC28), pain on a visual analogue scale (VAS pain), patient and evaluator global assessment of disease activity (PGA, EGA), HAQ disability index (HAQ-DI), 28-joint DAS (DAS-28) and the clinical and simple disease activity indexes (CDAI, SDAI). Correlations were used to assess the relationship between fear of falling and disease activity.

Results: Thirty-three patients were included. The mean age was 49.3±10.5 years with female predominance (n=29 (87.9%)). The mean disease duration was 9.9±7.5 years.

The mean FES-I score was 37.4±15.1 and 69.7% (n=23) of patients had significant fear of falling. The mean VAS pain was 5.3±2.5, the PGA was 6.2±2.1 and the EGA was 5.7±1.7. The mean HAQ-DI was 1.3±0.8. The mean DAS28 score was 5.5±1.3. The mean CDAI was 29.9±13.6 and the SDAI was 31.6±13.7.

FES-I was significantly correlated with TJC28 (r =0.52, p=0.02), PGA (r=0,56, p=0,01), EGA (r=0,39, p=0,025), HAQ-DI (r =0.70, p=0001), DAS28 (r =0, 38, p=0.029), CDAI (r =0.48, p=0.005) and SDAI (r =0.52, p=0.002).

Conclusions: This study suggests that fear of falling is frequent in patients with rheumatoid arthritis and demonstrated that fear of falling is significantly correlated with disease activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6029

AB0329 DO ANXIOUS OR DEPRESSIVE RHEUMATOID ARTHRITIS PATIENTS ON BIOTECHNOLOGIC THERAPY HAVE WORSE DISEASE ACTIVITY, FUNCTION AND QUALITY OF LIFE?

J. Borges[1], N. Madeira[1], A. Cardoso[2], L. Cunha-Miranda[1], F. Barcelos[1], C. Miguel[1], C. Silva[1], S. Fernandes[1], R. Trinca[3], D. Medeiros[1], R. Campanilho-Marques[1], H. Santos[1], R. Leitão[1], A. Faustino[1]. *[1]Rheumatology; [2]Nutrition; [3]Nursing, Instituto Portugues de Reumatologia, Lisboa, Portugal*

Background: Depression, anxiety and fatigue are common symptoms in rheumatoid arthritis (RA) patients, and seem to influence disease activity, pain, quality of life (QoL) and treatment response.

Objectives: To assess disease activity, function and QoL in RA patients with symptoms of anxiety/depression.

Methods: Observational, cross-sectional study including RA patients on bDMARD followed at our centre, registered at Reuma.pt with ≥1 evaluation from 2015/11 to 2016/07. Clinical data including DAS28, CDAI, SDAI, TJC, SJC, patients' and physicians' pain/global assessments (VAS), ESR, CRP, HAQ, EQ5D, HADS score (anxiety and depression domains, cutoff ≥8) and FACIT-F were collected. Data were analyzed using Mann-Whitney, Qui-Squared and Spearman correlation, p<0.05.

Results: 182 patients enrolled, 84.6% female, mean: age at 1st bDMARD 53.8±11.1; time since diagnosis 16.2±9.3 years; DAS28 3.54±1.3; CDAI 10.2±9.6; SDAI 11.2±10.4; HAQ 0.97±0.6; HADS-Anxiety 7.13±4.5; HADS-Depression 6.62±4.54, FACIT-F 35.1±9.2, EQ-5D 0.36±0.2. 77 (44.5%) patients scored ≥8 in the HADS-Anxiety domain and 71 (41.0%) scored ≥8 in the HADS-Depression domain. Comparison of depressive *vs* non-depressive and anxious *vs* non-anxious groups appears on table 1. There was a correlation of *HADS-Anxiety* with DAS28 (r=0.391, p<0.001), CDAI (r=0.441, p<0.001), SDAI (r=0.426, p<0.001), HAQ (r=0.509, p<0.001), FACIT-F (r=-0.669, p<0.001) and EQ5D (r=-0.592, p<0.001). There was a correlation of *HADS-Depression* with DAS28 (r=0.389, p<0.001), CDAI (r=0.455, p<0.001), SDAI (r=0.439, p<0.001), HAQ (0.596, p<0.001), FACIT-F (r=-0.679, p<0.001) and EQ5D (r=-0.659, p<0.001).

Abstract AB0329 – Table 1. Comparison of anxious vs non-anxious and depressive vs non-depressive patients

	HADS-A <8	HADS-A ≥8	p	HADS-D<8	HADS-D ≥8	p
N	96	77		102	71	
Gender (M%)	18.8%	9.1%	0.073	18.6%	8.5%	0.061
Age at diagnosis, mean ± SD (years)	44.5±13.2	45.4±12.7	0.606	42.3±12.7	48.5±12.5	0.009
Age at 1st bMARD, mean ± SD (years)	53.6±11.1	54.9±10.0	0.422	52.4±10.3	56.8±10.6	0.008
HADS-A, mean ± SD				4.99±3.5	10.2±4.04	<0.001
HADS-D, mean ± SD	4.1±3.6	9.6±3.7	<0.001			
HAQ, mean ± SD	0.75±0.6	1.26±0.6	<0.001	0.7±0.5	1.3±0.6	<0.001
DAS28 ESR, mean ± SD	3.1±1.1	4.0±1.4	<0.001	3.1±1.0	4.1±1.5	<0.001
28 TJC, mean ± SD	1.83±3.3	4.95±5.8	<0.001	1.92±3.1	5.08±6.1	<0.001
28 SJC, mean ± SD	1.02±1.7	1.86±2.7	0.042	0.97±1.5	2.00±2.9	0.020
PGA (VAS), mean ± SD	28.46±23.2	46.3±24.1	<0.001	28.9±23.03	47.3±24.2	<0.001
Patients' pain assessment (VAS), mean ± SD	28.4±22.5	46.4±26.2	<0.001	28.8±22.4	47.3±26.5	<0.001
PhGA (VAS), mean ± SD	15.9±13.9	23.8±20.6	0.022	14.4±12.7	26.5±20.8	<0.001
ESR (mm/H), mean ± SD	26.42±19.6	28.43±21.2	0.513	25.3±18.4	30.2±22.6	0.190
CRP (mg/L), mean ± SD	6.9±10.9	9.3±23.5	0.771	6.1±8.9	10.6±25.3	0.808
CDAI, mean ± SD	7.3±7.1	13.8±11.2	<0.001	7.2±6.4	14.5±11.7	<0.001
SDAI, mean ± SD	8.2±7.4	14.96±12.4	<0.001	7.97±6.7	15.8±12.97	<0.001
FACIT-F, mean ± SD	39.8±7.5	29.3±7.7	<0.001	39.1±7.8	29.4±8.2	<0.001
EQ5D, mean ± SD	0.43±0.17	0.28±0.20	<0.001	0.44±0.17	0.26±0.19	<0.001

Conclusions: Anxious or depressive patients showed higher disease activity, especially in measures with some subjectivity (such as TJC and PGA) but not regarding ESR or CRP and worse function and QoL. This fact must be taken into account when evaluating therapeutic efficacy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6345

AB0330 RHEUMATOID FACTOR AND RO52KDA ANTIBODIES ARE INDEPENDENT PREDICTORS OF INSULIN RESISTANCE IN RHEUMATOID ARTHRITIS

J. Aguilar-Arreola[1], F.D.J. Perez-Vazquez[2], E. Gomez-Bañuelos[2], G.-I. Diaz-Rubio[2], S. Duran-Barragan[2], F.-I. Corona-Meraz[2], A. Saldaña-Millan[2], R.-E. Navarro-Hernández[2], M. Vázquez-Del Mercado[2]. *[1]Servicio de Reumatología, División de Medicina Interna, Pnpc 004086, CONACyT, Hospital Civil, "Juan I. Menchaca"; [2]Instituto de Invesgitación en Reumatología y del Sistema Musculoesquelético, Universidad de Guadalajara, Guadalajara, Mexico*

Background: The rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) autoantibodies in rheumatoid arthritis (RA), have been used as diagnostic and prognostic tools [1]. However, this traditional perspective has changed toward a major role in RA pathogenesis. Several studies have demonstrated that FR and ACPA autoantibodies positivity beyond its level, might influence disease activity, bone erosions and development of comorbidities. Anti-Ro52kDa antibodies have also been associated with disease severity in RA and might influence the development of comorbidities such as insulin resistance (IR) in RA.
Objectives: To evaluate the association between RF, ACPA and anti-Ro52 kDa and IR in RA patients.
Methods: We included 83 RA patients classified according to ACR 1987 and ACR/EULAR 2010 criteria and 90 controls matched for age, gender and body mass index (BMI). Homeostasis Model Assessment-Insulin Resistance (HOMA-IR), anthropometric parameters and antibody positivity (RF, ACPA, Ro52 kDa) were evaluated. Multivariate regressión analysis was used to assess the contribution of autoantibodies, adiposity and disease activity to insulin resistance in RA.
Results: Patients positive for RF or anti-Ro52 kDa showed higher levels of basal insulin (P=0.009, P=0.006) and HOMA-IR. DAS-28 ESR was correlated with basal insulin (r=0.31, P=0.01) and HOMA-IR (r=0.29, P=0.02). We also observed positive correlations between serum triglycerides (r=0.47, P=0.01) and HDL-c (r=-0.38, P=0.02) and basal insulin. Multivariate analysis showed that Triglycerides, HDL-c, DAS-28, RF and anti-Ro52 kDa were independent predictors of basal insulin and HOMA-IR in patients with RA.
Conclusions: In RA, RF or anti-Ro52 kDa are independent predictors of IR. This phenomenon might be linked to the network of inflammation, adipokine secretion, since disease activity was also precitive of higher basal insulin. Both RF and anti Ro52 kDa, along with disease activity are independent predictors of IR in RA patients without comorbidities.
References:
[1] Watad A, Amital H: ACPAs Are Much More Than Diagnostic Autoantibodies. Rambam Maimonides Medical Journal 2016, 7(4).
[2] England BR, Thiele GM, Mikuls TR: Anticitrullinated protein antibodies: origin and role in the pathogenesis of rheumatoid arthritis. Current Opinion in Rheumatology 2016.
[3] Schuntermann MF: [References for evaluation scales in quality assurance in rehabilitation–1. I. Scales for determining adverse sequelae of illnesses–an introduction]. Die Rehabilitation 1995, 34(1):I-III.
[4] Matsudaira R, Tamura N, Sekiya F, Ogasawara M, Yamanaka K, Takasaki Y: Anti-Ro/SSA antibodies are an independent factor associated with an insufficient response to tumor necrosis factor inhibitors in patients with rheumatoid arthritis. Journal of Rheumatology 2011, 38(11):2346–2354.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7003

AB0331 BEHAVIOR OF THE VALUE OF RED CELL DISTRIBUTION WIDTH IN PATIENTS WITH RHEUMATOID ARTHRITIS IN TREATMENT WITH DAILY DOSE OF METOTREXATE

J.E. Espinoza Martinez, M.U. Martinez MArtinez, C. Abud-Mendoza. *Unidad de Reumatología y Osteoporosis, Hospital Central Dr. Ignacio Morones Prieto, San Luis Potosí, Mexico*

Background: Recently the relationship between inflammatory biomarkers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) has been found, with the increase in the percentage of red cell distribution width (RDW), events related to increase in cardiovascular risk in patients with rheumatoid arthritis (RA). RDW is a parameter that represents the heterogeneity of erythrocyte size and is calculated by an automatic blood analyzer, translates anisocytosis and in turn is related to atherosclerosis, is a predictor of mortality in patients with cardiovascular diseases such as acute myocardial infarction (AMI) and Congestive Heart Failure (CHF) plus it has the advantage of being very cheap. In patients with RA who receive treatment with methotrexate (MTX), particularly those with good therapeutic response with decreased disease activity, the values of ESR and CRP decrease.
Objectives: The aim of this study is to verify if there is a decrease, increase or neither change in the value of RDW in the patients receiving or not MTX comparing the value prior to the start of treatment and the last value measured during their therapy.
Methods: In this descriptive, non-experimental cross-sectional study, men and women older than 18 years of age with a diagnosis of rheumatoid arthritis according to ACR criteria (Aletaha et al., 2010) who were or not treated with methotrexate and other DMARDs. We excluded patients with less than two visits in this unit and the elimination criteria were patients who did not have baseline or last RDW test. The records of all patients included name, age, sex, date of diagnosis of RA, comorbidities, baseline and final laboratory exams during follow-up that included tests with RDW and medications.
Results: A total of 403 all with a diagnosis of RA and an average of 4.62 years of evolution, of which 51 they do not take methotrexate in daily dose and 352 receive treatment and only 4.2% suffered from a cardiovascular event. The comparison was made grouping the patients in whom they received and not treatment with methotrexate and correlated with the value of baseline and final RDW as shown in Table 1.

Table 1

	Methotrexate			
	Receive		Do not Receive	
	Baseline RDW	Final RDW	Baseline RDW	Final RDW
Minimum	10.70	10.40	11.10	12.20
Median	15.70	15.70	15.85	15.35
Mean	15.97	16.01	15.97	15.93
Maximum	32.60	26.60	27.30	21.80

The results shown in Table 1, do not appear to reveal a significant change in RDW values between the different subgroups; in the figures we compared the median of RDW for each group of patients who take methotrexate from all patients included in this study.

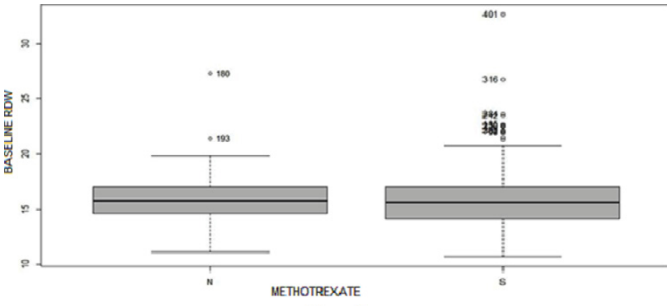
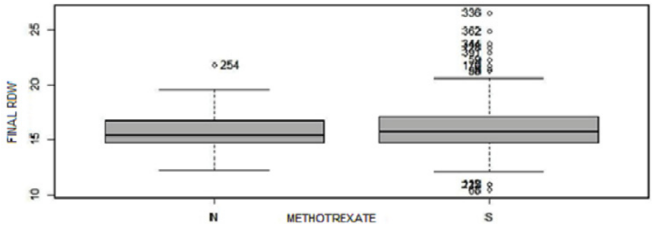


Figure. 2.



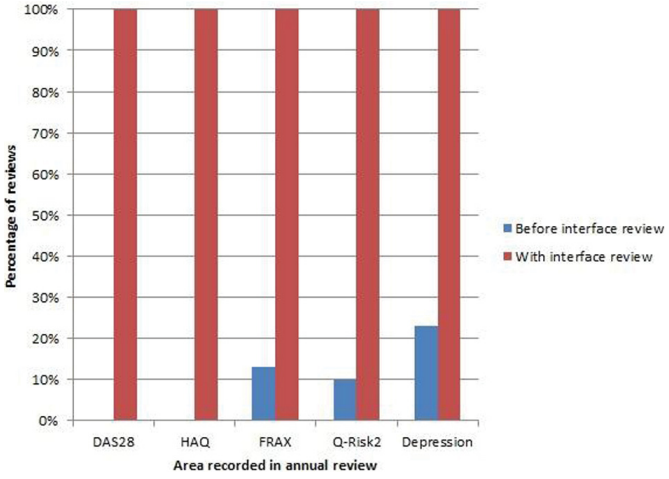
Conclusions: The value of RDW does not appear to significantly change its value when taking methotrexate at a daily dose in RA patients. The value of RDW may have weight in the assessment of the risk of suffering a cardiovascular event in patients with rheumatoid arthritis.
References:
[1] Hassan, S. et al. (2015). Red Cell Distribution Width: a measure of cardiovascular risk in rheumathoid arthtritis patiens? Clin Rheumatol.
[2] Woong Soo, L. et al. (2010). Relation between red cell distribution width and inflammatory biomarkers in rheumatoid arthritis. Seoul, Republic of Korea.
[3] Aletaha, et al. (2010). 2010 Rheumatoid arthritis classification criteria, Arthritis & Rheumatism.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3896

AB0332 DOES A COMMUNITY INTERFACE RHEUMATOID ARTHRITIS ANNUAL REVIEW IMPROVE PATIENT CARE?

J. Mcdonald, R. Haigh, D. Murphy. *Rheumatology, Royal Devon and Exeter Hospital, Exeter, United Kingdom*

Background: Patients with rheumatoid arthritis are known to have a long term disability and increased risk of extra-articular comorbidities. EULAR guidelines suggest annual review of cardiovascular risk in patients with rheumatoid arthritis [1] whilst UK national (NICE) guidelines suggest a more holistic annual review to look at the impact of the disease on quality of life as well as co-morbidities [2].

Objectives: Our aim was to look at the annual reviews currently taking place in primary care to see how frequently patient co-morbidities were assessed and documented. We then implemented a formal community rheumatology interface review to assess whether this improved patient care.
Methods: A large primary care practice (16,000 patients) was offered a community rheumatology interface review by a secondary care clinician. A search was undertaken for patients with rheumatoid arthritis who had attended for an annual primary care review between December 2015–2016. Of these 30 reviews were selected and we assessed how frequently the following were recorded; DAS28, HAQ score, FRAX score, Q-Risk2 (CV risk assessment tool) and screening for depression. Once we had analysed these results we implemented a community rheumatology interface review and assessed compliance with the above outcomes had improved compared to standard primary care management.
Results: In patients assessed prior to implementation of interface review, we found that a DAS28 score was recorded in 0%, HAQ score in 0%, FRAX in 13%, Q-Risk2 in 10% and depression screening in 23%.
In comparison, patients assessed by a community rheumatology interface clinician recorded DAS28 in 100%, HAQ score in 100%, FRAX in 100%, Q-Risk2 in 100% and depression screening was recorded in 100%. Based on improved interface review 7 patients (23%) were sent for DEXA scanning or started on a bisphosphonate, we discussed cardiovascular risk and starting a statin in 8 patients (26%) and 7 patients (23%) required follow-up for mental health. Of the 30 patients in this cohort all patients reported full adherence to their anti-rheumatic regime.



Conclusions: 1. An annual review with a rheumatology interface practitioner is of benefit in holistic patient care and improved compliance with all domains of the annual review.
2. Management of metabolic bone, cardiovascular and mental health issues was improved, according to current national guidelines.
References:
[1] Peters M et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis 2010 69:325–331.
[2] National Institute for Health and Clinical Excellence (NICE) (2009). Rheumatoid Arthritis in Adults: Management. Clinical Guideline 79. London: NICE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4804

AB0333 USE OF BIOLOGICAL DMARDS, BUT NOT OF CONVENTIONAL SYNTHETIC DMARDS OR STEROIDS, MAY BE RELEVANT TO INCREASED ENERGY INTAKE IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Masuko[1,2], Y. Mizukami[3], S. Tohma[4], T. Matsui[5]. *[1]Clinical Research Center for Medicine, International University of Health and Welfare; [2]Health Evaluation and Promotion Center, Sanno Medical Center, Tokyo; [3]Graduate School of Nutritional Science, Sagami Women's University; [4]Clinical Research Center for Allergy and Rheumatology, National Hospital Organization Sagamihara National Hospital, Kanagawa; [5]Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan*

Background: Dietary and nutritional factors may modulate the onset and/or outcome and comorbidities including cardiovascular diseases in rheumatoid arthritis (RA)[1]. For instance, a potential contribution of sodium intake and the occurrence of autoimmunity has been suggested, however the role of sodium in disease activity of RA is unclear.
Objectives: To investigate the potential relationship between dietary intake and current medications and the disease activity of RA.
Methods: Patients with RA in outpatient clinic of National Hospital Organization, Sagamihara National Hospital (n=89, M/F=18/71, age 65.0±12.8 yo, mean disease duration 16.8±13.2 y) were enrolled to the study. A questionnaire regarding dietary habit and the brief-type self-administered diet history questionnaire (BDHQ) were used to assess the relationship between clinical activity, status of medication and intake of each foodstuff and nutritional factors. The results were analyzed using IBM SPSS software using Pearson's correlation test and Levene test.
Results: The number of current medication was found to weakly correlate with DAS-28 (r=0.386), and negatively with intake of ethanol (r=-0.277). When users of biological disease modulating anti-rheumatic drugs (bDMARDs) were compared with non-users, the biologics-taking patients tended to have higher intake of total energy and carbohydrates than non-users. Use of oral corticosteroids, nor other anti-rheumatic DMARDs, did not significantly impact the total energy or carbo intake in RA patients. Sodium intake did not correlate with the disease status or the number of medications.
Conclusions: Although salt intake has been suggested to evoke autoimmunity, the amount of dairy intake of salt does not significantly modulate the current disease activity of RA. Use of biologics, but not of corticosteroids, may lead to increased energy and carbohydrate intake in RA patients.
References:
[1] Mizukami Y, et al. Distinct Patterns of Dietary Intake in Different Functional Classes of Patients with Rheumatoid Arthritis. Topics in Clinical Nutrition (in press).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4603

AB0334 KNEE FUNCTION AFTER TOTAL KNEE ARTHROPLASTY IS INFLUENCED BY DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Harigane[1,2], K. Kumagai[2], Y. Mochida[1], K. Ishii[1], Y. Miyamae[1], H. Choe[2], A. Nagaoka[2], Y. Inaba[2], N. Mitsugi[3], T. Saito[2]. *[1]Center for Rheumatic Diseases, Yokohama City University Medical Center; [2]Department of Orthopaedic Surgery, Yokohama City University; [3]Department of Orthopaedic Surgery, Yokohama City University Medical Center, Yokohama, Japan*

Background: Several studies reported that development of phaemacological treatment for rheumatoid arthritis (RA) contributed to decreased number of orthopaedic surgery. [1–3] Surgical treatment is, however, still required in many cases, and the impact of orthopaedic surgery on disease activity remain unclear.
Objectives: The aims of current study was to evaluate the effect of total knee arthroplasty (TKA) with capsulosynovectomy on changes of disease activity and knee function after TKA in patients with RA.
Methods: Seventy-seven serial patients with RA (61 female and 16 male) who underwent primary TKA with more than one year of follow-up were retrospectively reviewed to assess postoperative disease activity and knee function. The mean age at the time of surgery was 68.3 years old. The disease activity of RA was measured using Disease Activity Score in 28 Joints (DAS28). Clinical outcome was measured by treatment score for RA knee of the Japanese Orthopaedic Association (JOA) score. To evaluate the effects of disease activity on knee function, outcomes at before and one year after surgery were separately investigated following two groups; patients who had remission or low disease activity in DAS28-CRP (good controlled group), and patients who had moderate or high disease activity (poor controlled group) one year after surgery.
Results: The disease activity of RA was significantly decreased in DAS28-CRP one year after surgery. (3.9 vs. 2.7, $p<0.01$) Postoperative knee function was significantly improved in JOA scores one year after surgery. (48.9 vs. 86.0, $p<0.01$) As for differences of knee function between good and poor controlled group, the mean JOA score in good controlled group was significantly better than in poor controlled group. (90.4 vs. 82.1, $p<0.01$) Postoperative knee function was negatively correlated with RA disease activity. ($R^2=0.21$, $p<0.01$)
Conclusions: TKA with capsulosynovectomy improves both knee function and disease activity in patients with RA. Based on the results, knee function after TKA is influenced with disease activity.
References:
[1] Dusad A et al. Impact of Total Knee Arthroplasty as Assessed Using Patient-Reported Pain and Health-Related Quality of Life Indices: Rheumatoid Arthritis Versus Osteoarthritis. Arthritis Rheumatol. 2015; 67: 2503–11.
[2] Yano K et al. Effect of total knee arthroplasty on disease activity in patients with established rheumatoid arthritis: 3-year follow-up results of combined medical therapy and surgical intervention. Mod Rheumatol. 2010; 20: 452–7.
[3] Oh K et al. Effects of surgical intervention on disease activity of rheumatoid arthritis: cases of surgery for rheumatoid arthritis of the lower limbs treated with biologics. Mod Rheumatol. 2014; 24: 606–11.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3029

AB0335 EFFECT OF TOTAL KNEE ARTHROPLASTY ON MEDICATION IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Harigane[1,2], Y. Mochida[1], K. Kumagai[2], K. Ishii[1], Y. Miyamae[1], N. Mitsugi[3], H. Choe[2], A. Nagaoka[2], Y. Inaba[2], T. Saito[2]. *[1]Center for Rheumatic Diseases, Yokohama City University Medical Center; [2]Orthopaedic Surgery, Yokohama City University; [3]Orthopaedic Surgery, Yokohama City University Medical Center, Yokohama, Japan*

Background: Several studies reported that development of phaemacological treatment for rheumatoid arthritis (RA) contributed to decreased number of orthopaedic surgery. [1–3] Surgical treatment is, however, still required in many cases, and the impact of orthopaedic surgery on disease activity remain unclear.
Objectives: This study evaluated the effect of total knee arthroplasty (TKA) with capsulosynovectomy on chenges of disease activity and medication in patients with RA.
Methods: Seventy-seven serial patients with RA (61 female and 16 male) who underwent primary TKA with more than one year of follow-up were retrospectively reviewed to assess postoperative disease activity and drug administration. The mean age at the time of surgery was 68.3 years old. The disease activity of RA was measured using Disease Activity Score in 28 Joints (DAS28). To evaluate the effects of medication on preoperative and postoperative disease activity, outcomes at before surgery and one year after surgery were separately investigated following two groups; patients who were treated with the same or reduced medication (same group) and patients who were administered with additional or altered medication (change group).
Results: Seventy-two patients (97.3%) were administered with at least one DMRDs before or after surgery. The mean dose of methotrexate (MTX) was 7.7mg/week before surgery and 8.0mg/week after surgery respectively. The number of patients who were treated with biological DMARDs was increased after surgery (17 patients vs.21 patients), however there was not significant differences. RA disease activity was significantly decreased in DAS28-CRP one year after surgery. (3.9 vs. 2.7, $p<0.01$) As for difference of the disease activity in same and change groups, DAS28-CRP was significantly decreased after surgery. (same group; 3.7 vs. 2.5, $p<0.01$, change group; 4.5 vs. 3.2, $p<0.01$) DAS28-CRP in change group was significantly higher both before and after surgery compared with those in same group. ($p<0.01$)
Conclusions: TKA with capsulosynovectomy improves disease activity after surgery in patients with RA. Based on the results, patients with higher disease activity before surgery required further medication after surgery.
References:
[1] Dusad A et al. Impact of Total Knee Arthroplasty as Assessed Using Patient-Reported Pain and Health-Related Quality of Life Indices: Rheumatoid Arthritis Versus Osteoarthritis. Arthritis Rheumatol. 2015; 67: 2503–11.
[2] Yano K et al. Effect of total knee arthroplasty on disease activity in patients with established rheumatoid arthritis: 3-year follow-up results of combined medical therapy and surgical intervention. Mod Rheumatol. 2010; 20: 452–7.
[3] Oh K et al. Effects of surgical intervention on disease activity of rheumatoid arthritis: cases of surgery for rheumatoid arthritis of the lower limbs treated with biologics. Mod Rheumatol. 2014; 24: 606–11.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2416

AB0336 MAGNETIC RESONANCE IMAGING-ASSESSED SYNOVIAL AND BONE CHANGES IN HAND AND WRIST JOINTS OF RHEUMATOID ARTHRITIS PATIENTS

K.A. Lee, S.-H. Min, T.-H. Kim, S.-H. Lee, H.-R. Kim. *Internal Medicine, Konkuk University Medical Center, Seoul, Korea, Republic Of*

Background: Magnetic resonance imaging (MRI) is a sensitive and useful method for the detection of synovitis and joint destruction in rheumatoid arthritis (RA) patients. However, the patterns of MRI-detected bone erosion, bone marrow edema (BME), synovitis, and tenosynovitis have received insufficient attention.
Objectives: Therefore, this study evaluated the patterns of bone erosion, BME, synovitis, and tenosynovitis, and calculated the RA-MRI score (RAMRIS) of patients with RA at the carpal and metacarpophalangeal (MCP) joints using MRI.
Methods: MRI datasets from 43 RA patients were analyzed. All patients had undergone MRI of one wrist. In addition, 36 patients had MCP joint images taken, and 3 had also received MRI of the contralateral wrist and MCP joints. The MR images were evaluated for bone erosion, BME, and synovitis in consensus by 2 blinded readers according to the OMERACT RA-MRI score (RAMRIS). The MRI-detected tenosynovitis was evaluated based on Haavardsholm's tenosynovitis score.
Results: The capitate, lunate, triquetrum, and hamate bones were the most common sites of erosion and BME and showed the highest RAMRIS erosion and BME scores. Moreover, MRI-detected tenosynovitis was present in 78.3% of all patients with RA, and the extensor compartment 4 and flexor digitorum profundus and superficialis were frequently affected.
Conclusions: This study identified the distribution and prevalence of MRI-detected bone erosion, BME, synovitis, and tenosynovitis of the wrist and MCP joints in RA patients. The patterns of the MRI-detected abnormalities may help to select sites for the application of MRI protocols in clinical trials and practice.

References:
[1] Ejbjerg B, McQueen F, Lassere M, Haavardsholm E, Conaghan P, O'Connor P, et al. The EULAR-OMERACT rheumatoid arthritis MRI reference image atlas: the wrist joint. Annals of the rheumatic diseases. 2005;64 Suppl 1:i23–47.
[2] Ostergaard M, Edmonds J, McQueen F, Peterfy C, Lassere M, Ejbjerg B, et al. An introduction to the EULAR-OMERACT rheumatoid arthritis MRI reference image atlas. Annals of the rheumatic diseases. 2005;64 Suppl 1:i3–7.
[3] Conaghan P, Bird P, Ejbjerg B, O'Connor P, Peterfy C, McQueen F, et al. The EULAR-OMERACT rheumatoid arthritis MRI reference image atlas: the metacarpophalangeal joints. Annals of the rheumatic diseases. 2005;64 Suppl 1:i11–21.
[4] Haavardsholm EA, Ostergaard M, Ejbjerg BJ, Kvan NP, Kvien TK. Introduction of a novel magnetic resonance imaging tenosynovitis score for rheumatoid arthritis: reliability in a multireader longitudinal study. Annals of the rheumatic diseases. 2007;66(9):1216–20.
Acknowledgements: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1507

AB0337 BIOLOGIC THERAPY IN SEVERE PERIPHERAL ULCERATIVE KERATITIS (PUK). MULTICENTER STUDY OF 27 PATIENTS

L. Domínguez-Casas[1], V. Calvo-Río[1], O. Maíz[2], A. Blanco[2], E. Beltrán[3], L. Martínez-Costa[4], M. Alvarez del Buergo[5], E. Rubio-Romero[6], D. Díaz-Valle[7], R. López-González[8], A. García Aparicio[9], A. Juan Mas[10], N. Palmou[1], M. González-Gay[1], R. Blanco[1]. *[1]HUMV, Santander; [2]H, Donostia; [3]H; [4]H Peset, Valencia; [5]H; [6]H Río Carrión, Palencia; [7]H San Carlos, Madrid; [8]C Hospitalario, Zamora; [9]H, Toledo; [10]H S Llàtzer, P Mallorca, Spain*

Background: Peripheric Ulcerative Keratitis (PUK) is a severe inflammation that may lead to ocular perforation. PUK may be primary or associated with systemic conditions. Treatment is based on corticosteroids and conventional systemic immunosuppressive drugs.
Objectives: To evaluate biologic therapy in cases with severe and refractory PUK.
Methods: Multicenter study from 9 hospitals. Patients presented inadequate response or intolerance to conventional therapy with corticosteroids and at least 1 systemic traditional immunosuppressive drug.
The main outcome measures were visual acuity, signs of inflammation, progression to corneal thinning, central keratolysis and ocular perforation. Comparisons were made between baseline and 1st week, 1st month, 6th month and 1st year. Statistical analysis was performed using the software STATISTICA (StatSoft). Results were expressed as mean±SD for variables with a normal distribution, or as median [IQR] when they were not normally distributed. The comparison of continuous variables was performed using the Wilcoxon test and categorical variables with chi-square test.
Results: We studied 27 patients/35 affected eyes (7 men/20 women), mean age, 57.2±16.3 years (range 28–89). PUK was primary in 1 case whereas in the 26 remaining cases, the underlying diseases were Rheumatoid Arthritis (RA) (n=19), Psoriasic Arthritis (n=2), RA+Felty syndrome+common variable immunodeficiency (n=1), Behçet Disease (n=1), Type I diabetes mellitus (n=1), granulomatous polyangiitis (n=1) and microscopic polyangiitis (n=1). They received the following topical therapy: corticosteroids (n=18), antibiotics (n=17), lubricants (n=18), autologous serum (n=11), topical cyclosporin 2% (n=11) and topical tacrolimus 0.03% (n=1). Besides oral corticosteroids and before the onset of the biologic therapy they had received iv pulses of methylprednisolone (n=8), methotrexate (16), oral doxycycline (9), azathioprine (3) and ascorbic acid (2). Moreover, 10 patients required surgery: amniotic membrane (n=7), penetrating keratoplasty (n=4), conjunctival resection (n=3), tissue adhesives (n=2), conjunctival flap (n=1) and lamellar keratoplasty (n=1).
Anti-TNFα drugs were the most common biologic agents used in these cases (n=19): Adalimumab (ADA) (n=10; 37%), Infliximab (IFX) (n=8; 29.6%) and etanercept (n=1; 3.7%). In the remaining 8 cases the biologic agents were rituximab (n=7; 25.9%) and tocilizumab (n=1; 3.7%). The main outcome measures are summarized in the Table.
After a mean follow-up of 23.7±20 months, all objective outcomes had improved with a reduction of the median prednisone dose from 33.7 [17.5–52.5] mg at baseline to 0 [0–2.5] mg (p=0.028). The main observed adverse effects were supraventricular tachycardia (n=1) and pulmonary Tuberculosis (n=1).

	Basal	1 week	1 month	6 months	1 year
Visual acuity, mean±SD	0.54±0.37	0.55±0.35	0.58±0.33	0.67±0.3*	0.69±0.27*
Peripheral thinning #	85.7	80*	57.1*	40*	34.3*
Central keratolysis #*	17.1	8.6*	0*	8.6*	5.7*
Ocular perforation #	11.4	14.3*	0*	0*	2.8*
Scleritis #	34.3	22.8*	8.6*	0*	0*
Episcleritis #	22.8	11.4*	5.7*	2.8*	2.8*
Uveitis #	14.3	14.3	8.6*	2.8*	2.8*

Data expressed as % of the active eyes
*$p < 0.05$ compared with basal data

Conclusions: In our series, biological therapy, especially IFX and ADA, is effective and relatively safe in patients with PUK refractory to standard systemic treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3576

AB0338 HEADS-UP! SARCOIDOSIS AND RHEUMATOID ARTHRITIS CO-EXIST

L. Zickuhr, R. Hajj-Ali. *Rheumatology, Cleveland Clinic Foundation, Cleveland, United States*

Background: Sarcoidosis and rheumatoid arthritis (RA) uncommonly co-occur. How dual diagnosis affects these patients' clinical phenotype is unknown.
Objectives: To characterize the clinical and laboratory phenotype and to increase awareness of the coexistence of sarcoidosis and RA.
Methods: We searched PubMed from 1980–2016 for relevant articles using key words "sarcoidosis" and "rheumatoid arthritis," excluding cases with tumor necrosis factor inhibitors. We found 12 cases, omitted 5 lacking clinical detail, and added 2 from our experience at the Cleveland Clinic. Clinical features, laboratory and imaging findings were reviewed and summarized.
Results: Females comprised 7/9 cases (77%). Our cases are the first to describe men with dual diagnosis. Of the 8 cases reporting ethnicity, 4 (50%) were white. The mean age at time of diagnosis was 35.3 years for RA and 51.0 years for sarcoidosis. In 5/9 cases (55%), RA preceded sarcoidosis. RA affected the hands in 8/9 patients (88.9%). Of the 8 cases reporting symptoms of sarcoidosis, 5 (62.5%) had dyspnea. All cases (100%) had elevated rheumatoid factor (RF) and, when checked, anti-citrullinated peptide (anti-CCP) antibodies. Angiotensin converting enzyme (ACE) was elevated in 6/9 patients (66.6%). Of the 5 patients with joint imaging, 4 (80%) had inflammatory changes. All sarcoidosis (100%) was biopsy-proven. One case (11.1%) demonstrated concomitant pulmonary RA and sarcoidosis.
Conclusions: Sarcoidosis and RA coexist in seropositive patients, most commonly in women in their fourth through sixth decades of life. RA preceded sarcoidosis about half the time. Hand arthritis and dyspnea were the most common symptoms for RA and sarcoidosis, respectively. Awareness of this dual diagnosis may help identify RA and sarcoidosis earlier and prevent treatment delay.
References:
[1] Enzenauer RJ and West SG. Sarcoidosis in autoimmune disease. Arth & Rheum, 1992; 22(1):1–17.
[2] Menard O, et al. Association of histologically proven rheumatoid arthritis with pulmonary sarcoidosis. Eur Respir J, 1995; 8;472–3.
[3] Kobak S, et al. Co-occurrence of rheumatoid arthritis and sarcoidosis. BMJ Case Rep, 2015;1–3.
[4] Kucera, MRF. A possible association of rheumatoid arthritis and sarcoidosis. Chest, 1989; 95:604–06.
[5] Leo G, et al. Simultaneous pulmonary involvement, histologically proven, of sarcoidosis and rheumatoid arthritis. Clin Exp Rheumatol, 2009;27(1):164.
[6] Takashita M, et al. Mutilating rheumatoid arthritis associated with sarcoidosis: A case report. Clin rheum, 1995;14(5):576–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5401

AB0339 COMORBIDITIES AND RISK FACTORS OF CARDIOVASCULAR DISEASES IN RHEUMATOID ARTHRITIS PATIENTS

L.V. Khimion[1], I.V. Klymas[1], I.M. Naishtetik[2]. *[1]Department of Family Medicine, Shupyk National Medical Academy of Postgraduate Education; [2]Kyiv Regional Clinical Hospital, Kyiv, Ukraine*

Background: It is well known, that atherosclerosis associated cardiovascular diseases in many cases determine the life expectancy in RA patients. At the same time, risk factors which promote the development of premature atherosclerosis, including comorbidities, remain uncertain.
Objectives: to analyze comorbid conditions in RA patients under age of 50 years and assess their impact on the vascular wall (evaluated by ultrasound investigation of the carotid arteries).
Methods: The study was conducted at the Department of Family Medicine, Shupyk NMAPE at the Kyiv Regional Clinical Hospital. The study included 126 RA patients, aged from 18 to 49 years (women - 102 (81%), men - 24 (19%), average age 43.82±8.8 years, who provided written consent to participate in research. As a control group 30 persons without any autoimmune diseases (women - 25 (83.3%) men - 5 (16.7%), average age 42.4±8.6 years) were examined.
All RA patients and control group underwent comprehensive clinical, laboratory and instrumental examination to identify comorbid conditions including evaluation of atherogenesis by use of ultrasound examination of the carotid arteries with intima-media thickness (IMT) measurement and atherosclerosis plagues (AP) assessment.
Results: The frequency of identified comorbid conditions and diseases in RA patients and control group are presented in Table 1.
The average number of comorbid diseases/conditions per RA patient significantly exceeded its number in controls (4.13 and 1.67 respectively, $p<0.05$); most frequently among RA patients was determined: dyslipidemia (60.32%), nonalcoholic fatty liver disease (61.11%), chronic cholecystitis (36.51%), cholesterosis of the gallbladder (30.16%), hypertension (37.30%), autoimmune thyroiditis (27.77%), spinal osteoarthritis (33.33%).

Table 1. The frequency of comorbidities in RA patients and control group

Diseases and conditions	RA (n=126)		Control (n=30)	
	n	%	n	%
Coronary heart disease	12	9.52*	0	0
Arterial hypertension	47	37.30*	0	0
Neurocirculatory asthenia	2	1.58*	1	3.3
Dyslipidemia	76	60.32*	2	6.67
Peptic ulcer	6	4.76*	1	3.30
Chronic gastritis	29	23.00	3	10.0
Chronic pancreatitis	19	15.08	5	16.67
Nonalcohol fatty liver disease	77	61.11*	2	6.67
Cholesterosis of the gallbladder	38	30.16*	1	3.33
Chronic cholecystitis	46	36.51*	3	10.00
Gall stones	8	8.25*	0	0
Diabetes mellitus type 2	3	2.38*	0	0
Diffuse goiter	5	3.97*	0	0
Autoimmune thyroiditis	35	27.77*	1	3.33
Chronic obstructive pulmonary disease	5	3.97	4	13.33
Osteoarthritis of the spine	42	33.33	9	30.00
Chronic kidney disease	5	3.97	1	3.33
Abdominal obesity	21	16.67	4	13.33

*The difference between groups is significant, $p<0.05$.

Results of the carotid ultrasonography and assessment of atherosclerosis surrogate markers (IMT, AP) showed higher severity of atherosclerotic process in patients with RA compared to controls; the most important risk factors for increasing IMT and atherosclerotic plaques in carotid arteries were dyslipidemia, autoimmune thyroiditis with hypothyroidism and nonalcoholic fatty liver disease.
Conclusions: Patients with RA have a higher frequency of comorbid conditions and diseases than controls without RA; some of comorbidities have significant influence on atherogenesis; RA patients require a multidisciplinary and holistic approach for effective management of their health related problems.
References:
[1] Characteristics of comorbid stennov u hvorih on rheumatoid arthritis. Characteristics of comorbid conditions in patients with rheumatoid arthritis. Family Medicine 2015;3(59):219-222.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3027

AB0340 CLINICAL EFFICACY OF STATINS IN PATIENTS WITH RHEUMATOID ARTHRITIS

L. Mikulets, T. Ilashchuk. *Department of Propedeutics of Internal Diseases, Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsi, Ukraine*

Background: Cardiovascular disease (CVD) is a major cause of mortality in patients with rheumatoid arthritis (RA). In the literature there are conflicting data on the use of statins in patients with RA, indicating a lack of attention to the issue of prevention of CVD in this category of patients.
Objectives: The aim of the study was to improve the efficiency of the treatment of rheumatoid arthritis by including to the basic treatment rosuvastatin.
Methods: The study included 43 patients with RA. A survey conducted by the protocol patients (DAS28 index, visual analog scale (VAS), morning stiffness). The study of lipid metabolism included: determining the level of total cholesterol (total cholesterol), HDL cholesterol (HDL) and low density (LDL), atherogenic index (AI), triglycerides (TG). Total cardiovascular risk assessment was performed using a table SCORE. Surveyed patients divided into groups: primary (n=20) (basic therapy and rosuvastatin, 10 mg 1 time per day) and comparison (n=23) (basic therapy that included methotrexate, non-steroidal anti-inflammatory drugs, glucocorticoids in medium therapeutic doses).
Results: As a result of the treatment found that patients with a primary and group comparison, there was a positive dynamics of clinical indicators of inflammatory activity (DAS28, VAS, morning stiffness). In the study group experienced a significant decrease ($p<0.05$) at the same time as in the comparison group had a tendency to decrease. Noted a reduction parameters: CRP ($\Delta_1$37% main group and the comparison group $\Delta_2$21%), ESR ($\Delta_1$39% and $\Delta_2$26% respectively). Also noted the changes in the lipid profile. Significantly decreased in the study group performance total cholesterol ($\Delta_1$31% versus $\Delta_2$15%), LDL cholesterol ($\Delta_1$19% against $\Delta_2$8%) and AI ($\Delta_1$29% and $\Delta_2$16% respectively).
Conclusions: Inclusion in the complex therapy of patients with RA statins contributes to a significant reduction in total cholesterol, LDL cholesterol, and positively affects the activity of the process, reducing the levels of acute phase proteins. Additional indications for the purpose of statins have high activity process and late onset. The use of statins in RA, given their lipid-lowering and anti-inflammatory effects, may be an effective means for the successful prevention of cardiovascular complications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5983

AB0341 HOW COMMON IS DISCORDANCE IN DAS COMPONENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS

M. Shaikh. *Rheumatology, Addenbrooke's Hospital, Cambridge, United Kingdom*

Background: Chronic pain remains a significant problem for patients with rheumatoid arthritis (RA) despite advances in the management of joint inflammation (1–3). Pain that persists in the absence of significant inflammatory disease activity is thought to arise from sensitisation of the central nervous system. Composite scores such as DAS28, combine both objective and subjective aspects of disease. This may overestimate inflammatory disease in patients in whom pain occurs independently and has implications for treatment. However, the proportions of patients with such discordance is not clear.
Objectives: 1. To assess the degree of discordance between objective and subjective components of the DAS28 score in patients attending rheumatology clinics in a teaching hospital in Cambridge.
2. To assess the association between such discordance and the DAS28-P measure
Methods: A retrospective review of clinic notes was conducted of patients attending the rheumatology department at Addenbrooke's Hospital, Cambridge. Patients attending the early arthritis clinic, nurse practitioner follow up clinic and biologics clinic were included. Demographic information was collected including age, gender, current use of synthetic and biologic DMARDs. DAS28 scores and the individual components were retrieved and analysed. DAS28P was calculated as well as the difference between tender and swollen joint count (TJC-SJC) which has also been noted to be a measure of discordance between subjective and objective symptoms.
Results: 120 patients with RA were studied. The mean age was 59.4 years (range 27–86). 74% (89) were female. 88% (106) were on synthetic DMARDs: MTX 48% (58), HCQ 37% (45), SSZ 12% (15), LEF 3% (4), Gold 0.8% (1). 30% (36) were on biologic DMARDs: RTX 30% (11), ETA 30% (11), TOCI 17% (6), ADA 14% (5), ABA 6% (2).
Mean DAS28 was 3.42, SD 1.39. Mean TJC 4, mean SJC 2. Mean PGA 43, SD 24. DAS28-P was calculated as per previous studies (3). Mean TJC-SJC was 2, median 1. PGA and TJC-SJC (r=0.33) and TJC-SJC and DAS28P were correlated (r=0.44).
Conclusions: Discordance between subjective and objective components of DAS scores is relatively frequent in patients with RA. This can lead to confounding of DAS scores. There is currently no formal system of assessing the degree of such discordance which can have implications for treatment of inflammatory disease as compared to pain management strategies.
References:
[1] Taylor, P. et al., 2010. J. Int. Med. Res. 38, 1213–1224.
[2] Strand, V. et al., 2015. J. Rheumatol. 42, 2046–2054.
[3] McWilliams, D.F. et al., 2012. Arthritis Care Res. 64, 1505–1513.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6938

AB0342 POOR SLEEP QUALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS RELATED TO SUBCLINICAL CERVICAL SPINE AFFECTION MEASURED BY MRI

M. Hassanien[1], A. Al-johi[2], A. Al-awamy[3], N. Abas[4], R. Abdel-Razek[2]. *[1]Rheumatology Department; [2]Rheumatology Department; [3]Anathesia pain subdivision; [4]Radiology, Assuit University, assuit, Egypt*

Background: Rheumatoid arthritis is a chronic systemic inflammatory disease that often affects the cervical spine. Cervical disorders in rheumatoid arthritis (RA) patients have been an important problem for a long time
Objectives: investigate association between poor sleep complaints in rheumatoid arthritis patients and subclinical cervical spine involvement measured by MRI and its relation to disease activity in a population-based cross-sectional study.
Methods: 200 Egyptian RA patients fullfilling the American college of Rheumatology Criteria 2010 who were under follow up in the rheumatology and pain clinic, Assuit university hospital, Egypt. All patients underwent a complete history and physical examination with a focus on the cervical spine to assess disease duration, age of disease onset, swollen and tender joint counts. ESR, Hb, CRP, RF levels and disease activity was measured using the disease activity score 28 (DAS28). Oswestry-Neck-Pain-Questionnaire were completed. All patients filled out the Pittsburgh sleep quality index to evaluate their sleep quality, anxiety and depression scale. Symptomatic patients and previously diagnosed cervical subluxation were excluded. Radiographs of the cervical spine included lateral views taken in flexion, extension, neutral position of neck and antero-posteriorly and odontoid projection view.Patients suspicious for atlantoaxial affection underwent Magnetic Resonance Imaging to evaluate the cervicomedullary angle, dens erosion, amount of hypervascular –active pannus, atlantoaxial impaction, vertebral plate erosion, subaxial subluxation, apophyseal joints and disc material
Results: Asymptomatic cervical spine subluxation was found in 46 of the 200 RA patients (23%). The prevalence among involved patients of, anterior atlanto-axial subluxation, atlantoaxial impaction and subaxial subluxation was 25 (54.3%), 8 (17.4%) and 13 (28.2%), respectively. Posterior subluxation was not detected. There is significant relationship with cervical spine subluxation and sleep disturbance (interruption pattern) (P=0.006). The main baseline risk factor for difficulty falling asleep was anterior atlanto-axial subluxation, whereas for cervical spine subluxation it was higher patient age. Logistic regression confirmed early final awakening and short sleep respectively (HR 1.109, 95% CI 1.120–1.260, p=0.05) and (HR 1.095, 95% CI 0.991–0.998, p=0.005) as independent predictors of anterior atlanto-axial subluxation. The main risk factors for incident hypervascular atlantoaxial joint active pannus was disease activity score and older age. The frequency of early final awakening and short sleep were higher in relation to cervical spine involvement. Male sex, CRP positivity, and older age were risk factors for incident anterior atlantoaxial subluxation.
Conclusions: Cervical spine involvement is common and may be asymptomatic indicating routine cervical spine imaging is needed in patients with RA specially patients with sleep disturbances and high disease activity
References:
[1] Delamarter RB, Bohlman HH. Postmortem osseous and neuropathologic analysis of the rheumatoid cervical spine.Spine (Phila Pa 1976) 1994; 19: 2267–2274.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1434

AB0343 THE RHEUMATOID FOREFOOT: WHICH FREQUENT INJURY? WHAT IMPACT ON WALK?

M. Erraoui, B. Amine, L. Tahiri, I. El Binoune, J. Bahha, S. Fellous, Y. Boujenane, F. Allali, R. Bahiri. *Rheumatology, Mohammed V University, Faculty of Medicine and Pharmacy of Rabat, El Ayachi Hospital, SALE, Morocco*

Background: Foot involvement is the most common cause of disability in patients with rheumatoid arthritis (RA). The forefoot remains the most affected location.
Objectives: Investigate the forefoot injuries in patients with RA and evaluate its impact on walking.
Methods: Cross-sectional study of 33 patients with rheumatoid arthritis. Patients with static lower limb disorder or foot injury from other origin were excluded.Demographic and clinico-biological characteristics were collected: age, sex, BMI, disease duration, tender joint count, swollen joint count, foot pain evaluated on an VAS, squeeze test in foot, various podiatric abnormalities, sedimentation rate in the first hour, C reactive protein, rheumatoid factor and anti-CCP. Disease activity was evaluated by DAS28, CDAI, SDAI and DAS44. The effect on walking was studied by the HAQ (specific item of walking) and the French version of FFI (Foot Functional Index) which consists on 23 items, divided into 3 sections: pain, function and limitation of activity. Statistical analysis was performed using SPSS21 software.
Results: 33 patients followed for RA were included. The mean age of our patients was 49.39±10.52 with a female predominance (87.9%). Mean duration of the disease was 9.96±7.49 years. 21 (95.5%) of patients were seropositive. Mean DAS28 was 5.53 (4.58–6.50) and mean HAQ was 1.37 (0.70–2.10). 54.5% of our patients reported right forfoot pain and 57.6% of them reported left forefoot pain; with predominant metatarsalgia (right 54.5% and left 57.6%). 33.3% had forfoot pain in the day of the examination and 69.7% (23) had a positive squeeze test. 18 (54.5%) patients had a foot podiatric abnormalities. They are represented by: right hallux valgus (39.4%), left hallux valgus (39.4%), right quintus varus (12.1%), left quintus varus (9.1%), right claw toe (9.1%), left claw toe (12.1%), right triangular foot (6.1%) and left triangular foot (6.1%).
Mean FFI was 52.35 (34.73–71.43), and mean FFI-function was 53.66 (34.44–74.99). 27.3% (9) of patients had walking difficulty according to item 4 of HAQ. A statistically significant association was found between a high FFI-function and metatarso-phalangeal pain (p=0.029), anterior plantar pain (p=0.018) and a positive squeeze test (p=0.01). Impairment of walking assessed by FFI-function was positively correlated with pain (r=0.58,p=0.0001) and discomfort in forfoot (r=0.452,p=0.008), VAS pain (r=0.48,p=0.005) and global gene VAS (r=0.70,p=0.001) associated with disease. Disease activity was positively correlated with FFI-function (DAS28 (r=0.48,p=0.005), CDAI (r=0.6-p=0.0001), SDAI (r=0.60,P=0.0001) and DAS44 (r=0.55, p=0.001)). The difficulty of walking assessed by item 4 of HAQ was associated with metatarso-phalangeal pain (p=0.01), and was not influenced by adaptation of the footwear (p=0.015). Also, item 4 was statistically associated with disease activity (DAS28 (p=0.028) and SDAI (p=0.049)) and impaired function evaluated by FFI (p=0.001) and particularly FFI-Function (p=0.0001). Podological abnormalities were not statistically associated with either functional FFI or the item 4 of HAQ.
Conclusions: Forefoot involvement is frequent during RA, particularly podiatric abnormalities. It generates a functional repercussion on walking which would be rather related to pain and disease activity than to podiatric abnormalities.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5536

AB0344 SUBCLINICAL VASCULAR DAMAGE AND ITS ASSOCIATION WITH ACPA AND RF IN PATIENTS WITH RHEUMATOID ARTHRITIS

M. Aguilar-Zamora, M. Robustillo-Villarino, C. Vergara-Dangond, L. Montolio-Chiva, E. Valls-Pascual, A. Martínez-Ferrer, D. Ybañez-Garcia, V. Nuñez-Monje, J.J. Alegre-Sancho. *Rheumatology, Hospital Universitario Dr. Peset, Valencia, Spain*

Background: Accelerated atherosclerosis (AE) and increased arterial stiffness

are comorbidities of rheumatoid arthritis (RA) and are related to the inflammatory burden of the disease, as well as to certain clinical and genetic characteristics of the disease. There is controversy about the role of ACPA in the development of AE in these patients.
Objectives: To explore the relation between ACPA and RF titres and subclinical vascular damage in RA patients.
Methods: Descriptive cross-sectional study with analytical components. A total of 244 RA patients were recruited consecutively over a period of 18 months (2013–2014) in a rheumatology department of a tertiary hospital. Patients with high vascular risk (vascular ischemic events, renal failure and diabetes mellitus) were excluded. Demographics, clinical data (ACPA and RF titres, duration of disease, hypertension and dyslipidemia) and vascular damage (atheroma plaque, carotid intima thickness [IMTc] and pulse wave velocity [PWV]) were collected. The atheroma plaque and IMTc measurement was performed by ultrasonography of the carotid arterial tree using an Esaote® MyLab70XVG with a 7–12 MHz linear transducer and an automated program measuring intima-media thickness (IMT) through radiofrequency (Quality intima media Thickness in real time, QIMT). PWV was obtained by analysis of brachial pulse waves with an automated and validated system (Mobil O Graph®). Statistical analysis was performed with the SPSS 17.0 program.
Results: We included 181 patients, 141 (77.9%) women and 40 (22.1%) men, with a mean age of 60.4 years (SD 13.2) and a mean duration of the disease of 13.1 years (SD 10.5); 107 patients (59.1%) were smokers or ex-smokers, 56 (30.9%) hypertensive and 77 (42.5%) dyslipemic. 118 patients (65.2%) had positive ACPA, with a mean value of 330 (SD 621.5), and 107 (59.1%) had a positive value of RF with a mean of 114 (SD 164.5).
No association was found between the positivity of ACPA and RF and the presence of atheroma plaques or with the values of IMTc and/or PWV. In patients with positive ACPA, a positive correlation was observed between ACPA titers and PWV values ($p<0.05$). In particular, ACPA titers over 1600 were the ones that discriminated the highest values of PWV in our population ($p<0.009$). The ACPA and RF values, on the other hand, were not related to the presence of plaques or to IMTc.
Conclusions: No relation was found between the positivity of RF and ACPA titers and the presence of pathological carotid ultrasound in our RA patient population. However, higher arterial stiffness was observed in patients with high ACPA titers.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3245

AB0345 PSYCHIATRIC DISORDERS RELATED TO HYPERLEPTINEMIA AND RHEUMATOID ARTHRITIS CLINICAL ACTIVITY MEASURED BY DAS28

M. Vázquez-Del Mercado[1,2], A.-M. Rodrígez-Ramírez[2], E. Chavarria-Avila[2], F. Sandoval-García[2], B.-T. Martin-Marquez[2], R.-E. Navarro-Hernandez[2], F. Corona-Meraz[2], E. Gomez-Bañuelos[2]. *[1]Servicio de Reumatología, División de Medicina Interna, Pnpc 004086, CONACYT, Hospital Civil Juan I. Menchaca; [2]Instituto de Invesgitación en Reumatología y del Sistema Musculoesquelético, Universidad de Guadalajara, Guadalajara, Mexico*

Background: Leptin is an adipose-derived hormone with a role in depression related to chronic stress, anxiety and pain disorders, disturbs with a high prevalence in RA patients. In previous studies, it has been demonstrated the role of leptin in the pathogenesis of RA, in particular, its association with anti-CCP. The purpose of this study was to evaluate the psychiatric disorders risk related to serum soluble leptin (sLep) levels with clinical activity in RA patients.
Objectives: To evaluate the association between psychiatric disorders and serum leptin (sLep) levels and RA disease activity
Methods: 76 outpatients diagnosed with RA (ACR1987/ ACR/ EULAR2010) were evaluated with clinical, laboratory and image assessment. Disease activity was measured using DAS28 CRP, the Mini International Neuropsychiatric Interview Plus (M. I. N. I. Plus) was used for the psychiatric evaluation. sLep levels were measured by ELISA method.
Results: sLep levels were significantly higher in RA patients M.I.N.I. plus (+) ($P<0.001$). DAS28 CRP score was significantly higher in patients with a present psychiatric disorder ($P=0.006$) with an odds ratio of 1.6 ([1.04–2.46] $P=0.03$) for present psychiatric comorbidity. After adjustment with age and years of RA diagnosis, the odds ratio increased to 1.72 ([1.08–2.73] $P=0.02$). Also, DAS28 CRP had a moderate correlation with the number of psychiatric diagnosis present, past and for lifetime ($r=0.485$, $P<0.001$, IC95% [0.99–0.636]).
Conclusions: sLep levels and DAS28-CRP were associated with symptoms of depression, such as anxiety and pain disorder in RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6808

AB0346 MOOD DISORDERS (ANXIETY AND DEPRESSION) IN RHEUMATOID ARTHRITIS

M. Brahem[1], M. Maraoui[1], H. Hachfi[1], S. Ben Hammouda[1], I. Haddada[1], M. Jguirim[2], M. Younes[1]. *[1]Rheumatology, Taher Sfar Hospital Mahdia, mahdia; [2]Rheumatology, Fattouma Bourguiba Hospital Monastir, Monastir, Tunisia*

Background: In addition to recurrent pain, fatigue, and increased rates of physical disability, individuals with rheumatoid arthritis (RA) have an increased prevalence of some mental health disorders, particularly those involving affective or mood disturbances.Many researchers have shown that mood disturbance and disability may serve as important pathways through which disease burden contributes to poor health functioning in RA.
Objectives: Our aim is to estimate the mood disorders (anxiety and depression) in patients with RA and to evaluate the associated factors.
Methods: This is a cross-sectional and descriptive study during a period of the year 2016, including 37 patients followed in the department of Rheumatology in Mahdia Tunisia. All patients were diagnosed with RA based in ACR 1987/EULAR2010.We evaluated for each patient the parameters of activity of the disease, the quality of life by the HAQ questionnaire and the mood disorders using the Hospital Anxiety and Depression Scale (HAD).
Results: The age of the RA patients (32 females/5 males) ranged from 21 to 76 years. The mean age was 53.1±12 years. The mean duration of the disease was 11±10 years [1–34]. The mean number of tender joints was 13.2±9.6 and swollen joint was 5.9±7. The mean DAS28 was 5.5±1.5 [2.9–8.2] and HAQ was 1.6±0.9 [0–2.8]. 51.3% of patients had specific joint deformations, 83.8% had radiologic involvement and 29.7% had osteoporosis.
The biologic analysis showed that the mean ESR was 45±27.1 and the CRP was 13.7±25.3. Rheumatoid factors were positive in 37.8% of cases, the ACPA were positive in 32.4% of cases. 81.1% of RA patients were treated by methotrexate and 13.5% were treated by biologic treatments.
The average score of depression was 9±2.6 [1–14]. Basing on this score, 12 patients (32.4% of cases) didn't have depression (score <8), 14 patients (37.8% of cases) suffered probably from depression (score between 8 and 10) and 11 patients (29.7%) had a certain depression (score$\geq$10). Our study didn't found any correlation between the score of depression and the age, the score and clinical parameters of RA (duration of disease, DAS28, number of tender and swollen joints and deformations), the score and biologic parameters (ESR, CRP, Rheumatoid factor, ACPA).
The average score of anxiety was 9.2±4.2 [0–20]. 12 patients (32.4%) didn't have signs of anxiety (score <8), 12 patients (32.4%) had probably an anxiety (score between 8 and 10) and 13 patients (35.2%) presented a certain anxiety (score$\geq$10). We found a significant correlation between the score of anxiety and the number of tender joints, the anxiety score and the HAQ (Health Assessment Quality).
Conclusions: Our study showed that the majority of our RA patients suffered from mood disorders; 67.5% had signs of depression and 65.6% had signs of anxiety.So, it's important to evaluate the mood disturbances in RA patients to ameliorate their quality of life.
References:
[1] John A. Sturgeon et al, Affective disturbance in rheumatoid arthritis: psychological and disease-related pathways; reviews Rheumatology 2016.
[2] SARAH R. ORMSETH et al, Multidimensional Model of Disability and Role Functioning in Rheumatoid Arthritis; Arthritis Care & Research, Vol. 67, No. 12, December 2015, pp 1686–1692.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5279

AB0347 EVALUATION OF THE IMPACT OF RHEUMATOID ARTHRITIS ON SEXUAL FUNCTION

M. Brahem[1], H. Hachfi[1], S. Ben Hammouda[1], I. Haddada[1], M. Maraoui[1], M. Jguirim[2], M. Younes[1]. *[1]Rheumatology, Taher Sfar Hospital Mahdia, mahdia; [2]Rheumatology, Fattouma Bourguiba Hospital Monastir, Monastir, Tunisia*

Background: Rheumatoid arthritis (RA) may affect all aspects of life including sexual functioning.The percentage of arthritic patients who experience sexual problems ranged in various studies from 31% to 76%.The reasons for disturbing sexual functioning are multi-factorial and comprise disease-related factors as well as therapy.It can occur before, during and after sexual activities, and can affect sexual health in different perspectives.
Objectives: The aim of our study is to evaluate the impact of the RA in sexual function and its associated factors.
Methods: This is a cross-sectional and descriptive study during a period of the year 2016, including 37 patients followed in the department of Rheumatology in Mahdia Tunisia. All patients were diagnosed with RA based in ACR 1987/EULAR 2010. We evaluated for each patient the sexual quotient (QS). It is a validated scale which estimates the degree of satisfaction of the sex life.
Results: The age of the RA patients (32 females/5 males) ranged from 21 to 76 years. The mean age was 53.1±12 years. The mean duration of the disease was 11±10 years [1–34]. The mean number of tender joints was 13.2±9.6 and swollen joint was 5.9±7. The mean DAS28 was 5.5±1.5 [2.9–8.2] and HAQ was 1.6±0.9 [0–2.8]. 51.3% of patients had specific joint deformations, 83.8% had radiologic involvement and 29.7% had osteoporosis.
The biologic analysis showed that the mean ESR was 45±27.1 and the CRP was 13.7±25.3. Rheumatoid factors were positive in 37.8% of cases, the ACPA were positive in 32.4% of cases. 81.1% of RA patients were treated by methotrexate and 13.5% were treated by biologic treatments.
The mean sexual quotient was 50.25±20.8 [6–87.5]; only 8.1% of patients had a great sexual life (QS between 80 and 100), 16.2% expressed some sexual satisfaction (QS between 60 and 80), 21.6% had a mild sexual life (QS between

40 and 60), 18.9% presented a disappointing sexual life (QS between 20 and 40) and 35.4% didn't have any partner.
Our study showed a significant correlation between the duration of the disease and the alteration of the sexual quotient, but no correlation with the clinical and biological parameters of RA.
Conclusions: We conclude that only 24.3% of our RA patients had satisfaction in their sexual life. This alteration of the sexual quotient was found to be correlated with the duration of the disease.
This fact may be explicated by the disability, fatigue and pain caused by this chronic inflammatory disease. This relation should be confirmed by future studies.
References:
[1] Antonio G Tristano, Impact of rheumatoid arthritis on sexual function, World J Orthop 2014 April 18; 5(2): 107–111.
[2] Abdo J. Sex Med. 2007;4:382–389.
[3] Kraaimaat FW, et al, Intrusiveness of rheumatoid arthritis on sexuality in male and female patients living with a spouse. Arthritis Care Res 1996; 9:120–125.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5298

AB0348 SLEEP DISORDERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

M. Brahem[1], S. Ben Hammouda[1], H. Hachfi[1], M. Maraoui[1], I. Haddada[1], M. Jguirim[2], M. Younes[1]. *[1]Rheumatology, Taher Sfar Hospital Mahdia, mahdia; [2]Rheumatology, Fattouma Bourguiba Hospital, Monastir, Tunisia*

Background: Rheumatoid arthritis (RA)as one of the most common autoimmune diseases is known to be one of the leading causes of disability.Sleep disorders have direct influence on patient's life. But the exact nature of relationship between sleep disorders and Rheumatoid arthritis is not completely understood.
Objectives: The aim of our study is to evaluate the impact of RA in sleep quality and to establish associated factors.
Methods: This is a cross-sectional and descriptive study during a period of the year 2016, including 37 patients followed in the department of Rheumatology in Mahdia Tunisia. All patients were diagnosed with RA based on ACR 1987/EULAR2010. We evaluated for each patient the parameters of activity of the disease, the quality of life by the HAQ questionnaire and the quality of sleep using two scales: Epworth (ESS) and Pittsburg scale (PSQI) which is composed from 7 components rated each one from 0 to 3.
Results: The age of the RA patients (32 females/5 males) ranged from 21 to 76 years. The mean age was 53.1±12 years. The mean duration of the disease was 11±10 years [1–34]. The mean number of tender joints was 13.2±9.6 and swollen joint was 5.9±7. The mean DAS28 was 5.5±1.5 [2.9–8.2] and HAQ was 1.6±0.9 [0–2.8]. 51.3% of patients had specific joint deformations, 83.8% had radiologic involvement and 29.7% had osteoporosis.
The biologic analysis showed that the mean ESR was 45±27.1 and the CRP was 13.7±25.3. Rheumatoid factors were positive in 37.8% of cases, the ACPA were positive in 32.4% of cases. 81.1% of RA patients were treated by methotrexate and 13.5% were treated by biologic treatments.
The mean Epworth score was 9±5.7 (0–23). 56.8% of patients had no sleep debt, 32.4% had a sleep deficit and only 10.8% had signs of somnolence. Our study confirmed a significant correlation between the Epwoeth score and the number of tender joints, the ESR, the Health assessment quality (HAQ) score.
Regarding the overall score of Pitsburg, the average was 8.4±4.1 (1–16). The average of the "subjective sleep quality" was 1.35, "latency to sleep" was 1.81, "sleep duration" was 1.24, "habitual sleep efficiency" was 1.08, "sleep disorders" was 1.62, "the use of a sleep medicine" was 0.27 and finally the average of the 7th component about "poor form during the day" was 1.11 out of 3. So the latency to sleep and sleep disorders were the most affected components. We had a significant correlation between PSQI and the number of swollen joints, the HAQ score. The value of the ACPA was found to be associated with high score of PSQI.
Conclusions: Our study showed that the sleep disruption wasn't rare in patients with RA. This can be related to the disability and pain caused by this disease. Further studies with large sample size, as well as more careful tools of sleep disorders, would help to generalize results and suggestions. By providing adequate health care, and recognition of the patients' pain conditions we would ameliorate sleep quality and increase the QOL of RA patients.
References:
[1] Majid Purabdollah, et al, Relationship between Sleep Disorders, Pain and Quality of Life in Patients with Rheumatoid Arthritis; Journal of Caring Sciences, 2015, 4(3), 233–241.
[2] Seda PEHLİVAN et al, Sleep quality and factors affecting sleep in elderly patients with rheumatoid arthritis in Turkey; Turk J Med Sci (2016) 46: 1114–1121.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5251

AB0349 THE SERUM LEVEL OF IRISIN IS DECREASED IN THE PATIENTS WITH RHEUMATOID ARTHRITIS

A.T. Kalkan[1], M. Ozmen[2], B. Birlik[3], D. Kozaci[4], I. Turkmen[5], D. Solmaz[2], O. Gercik[2], S. Gucenmez[2], S. Akar[2]. *[1]Department of Internal Medicine; [2]Department of Internal Medicine, Division of Rheumatology; [3]Department of Radyology, Izmir Katip Celebi University, School of Medicine; [4]Department of Medical Biochemistry; [5]Department of Musculoskeletal System and Regenerative Medicine, Ankara Yıldırım Beyazıt University, School of Medicine, Izmir, Turkey*

Background: *Adipomyokines* are proteins that are synthesized by and secreted from both skeletal muscle and adipose tissue, and show their effects through autocrine, paracrine or endocrine pathways (1). *Irisin*, a novel adipomyokine, is secreted in association with exercise from the skeletal muscle, and from the white fat tissue to help the brown fat tissue gain the energy expenditure phenotype (2). There is evidence that the irisin is associated with metabolic syndrome (MetS) and cardiovascular risk (3,4).
Objectives: Rheumatoid arthritis (RA) is associated with an increased risk of cardiovascular disease (CVD) and MetS compared with the general population (5,6). The aims of this study were to assess the serum level of irisin, and the possible relationships of irisin with disease activity in patients with RA.
Methods: Eighty four consecutive RA patients fulfilling the 2010 ACR/EULAR RA Classification Criteria were included in the study. Fifty age- and sex-matched healthy volunteers were enrolled as the control group. Disease duration, medications, history of traditional risk factors of CVD and demographic data of patients were noted. Body Mass Index (BMI) was calculated as "weight (kg)/height (m)^2". HbA1c, lipid profile, insulin were measured. Insulin resistance was assessed with the Homeostasis Model Assessment (HOMA) Index. RA disease activity was assessed by disease activity score based on evaluation of 28 joints (DAS28). Serum irisin level was assessed by ELISA. Measurement of carotid intima media thickness by carotid doppler ultrasonography was performed by a radiologist for cardiovascular risk assessment.
Results: There was no significant difference between the groups in terms of BMI (p=0,20), HbA1c (p=0,15), lipid profiles ($p<0.05$), insulin resistance (p=0.72) and carotid intima-media thickness (p=0.216).
Serum irisin levels were found to be significantly lower in RA patients (20,65 (minimum:16,94- maximum:99,35) ng/mL) than healthy controls (37,56 (18,37–84,70) ng/mL) ($p<0.001$). There was no relationship between RA disease activity and irisin levels.
Conclusions: This study showed that irisin was significantly lower than controls. Irisin may be responsible for increased cardiovascular risk in RA patients. But before a definite judgment; prospective studies with a larger sample size assessing the exercise behaviour of patients and the presence of CVD are necessary.
References:
[1] Raschke S, Eckel J. Adipo-myokines: two sides of the same coin - mediators of inflammation and mediators of exercise. Mediators Inflamm. 2013;320724:1–16.
[2] Roca-Rivada A, et al. FNDC5/irisin is not only a myokine but also an adipokine. PLoS One. 2013; 8(4):e60563.
[3] Yan B, et al. Association of serum irisin with metabolic syndrome in obese Chinese adults. PLoS One. 2014 Apr 7;9(4):e94235.
[4] Deng W. Association of Serum Irisin Concentrations with Presence and Severity of Coronary Artery Disease. Med Sci Monit. 2016 Nov 5;22:4193–4197.
[5] Wolfe F,et al. Increase in cardiovascular and cerebrovascular disease prevalence in rheumatoid arthritis. J Rheumatol 2003;30: 36–40.
[6] Ozmen M, et al. Prevalence of the metabolic syndrome in rheumatoid arthritis. Eur J Rheum 2014; 1: 1–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2040

AB0350 FUNCTIONAL DISABILITY MEASURED BY HEALTH ASSESSMENT QUESTIONNAIRE (HAQ) CORRELATES WITH DISEASE ACTIVITY IN ELDERLY RHEUMATOID ARTHRITIS PATIENTS

N. Alpay-Kanıtez[1], Ö. Pehlivan[2], A. Omma[3], S. Can-Sandıkçı[3], S. Yılmaz-Öner[1], C. Bes[1], S. Çelik[1]. *[1]Bakırköy Dr. Sadi Konuk Research and Training Hospital; [2]Umraniye Research and Training Hospital, Istanbil; [3]Ankara Numune Research and Training Hospital, Ankara, Turkey*

Background: Rheumatoid arthritis (RA)'s prevalence increases with age and the recognition of functional disability related to RA could be challenging in elderly patients (1).
Objectives: In this study, we aimed to look at the correlation between disease activity and the functional disability by using HAQ score in elderly RA patients.
Methods: Elderly RA patients, $\geq$65 years old at their routine visits were included to the study. The composite "disease activity score" in 28 joints (DAS-28) and "Physician Global Assessment" (PhGA) were used to determine disease activity. Health assessment questionnaire (HAQ) scores were calculated to describe the functional disability and compared across the disease activity groups according to DAS-28.
Results: Two hundred and fifty eight RA patients with the mean age of 71±5

(65–90) were included. Seropositivity rate was 71% and 47% of the patients had erosive disease. Joint deformity was seen in 72 (28%) of patients and 28 (11%) patients had undergone total arthroplasty. Lung involvement (8.5%) and Sjogren's syndrome (7.4%) were found as the most frequent extra-articular manifestations. Hypertension (66%) and osteoporosis (36%) were the common co-morbidities. The proportion of patients with high and moderate disease activity was found as 70%. HAQ and PhGA scores were significantly correlated with the disease activity (Figure).

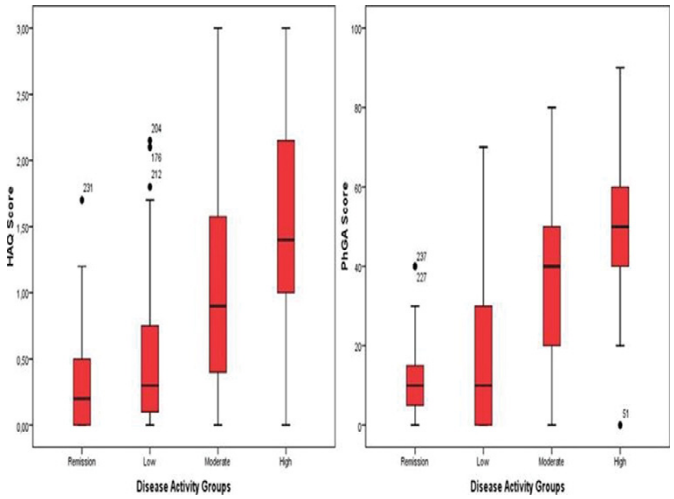


Figure 1. HAQ and PhGA distribution in disease activity subgroups. Both of them were found correlated with disease activity (p: 0.000).

Conclusions: We provided a novel data concerning the usefulness of HAQ for prediction of disease activity in RA patients who are elderly as well. In the future, our report will be supported by the studies which suggest that HAQ score improve with effective treatment in elderly RA patients.

References:

[1] Uhlig T, Loge JH, Kristiansen IS, Kvien TK. Quantification of reduced health-related quality of life in patients with rheumatoid arthritis compared to the general population. J Rheumatol 2007;34: 1241–1247.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6662

AB0351 CORRELATION BETWEEN SERUM ANTI-CITRULLINATED PROTEIN ANTIBODIES AND SUBCLINICAL CARDIC AFFECTION IN RHEUMATOID ARTHRITIS PATIENTS

A. Helal[1], G. Younis[1], N. Hussein[1], E. Elsharkawy[2], N. Abdelhady Abdelsadek[1]. *[1]Physical Medicine, Rheumatology and Rehabilitation, Alexandria University Hospital; [2]Cardiology and Angiology, Faculty of Medicine, Alexandria, Egypt*

Background: Cardiovascular disease (CVD) is a major cause of morbidity and mortality in rheumatoid arthritis (RA) patients. It has been postulated that chronic inflammatory activity is important for the development of CVD in RA even after adjustment for traditional cardiovascular risk factors.(1) One of the changes occurring in the context of inflammation is citrullination. Development of anti-citrullinated protein antibodies (ACPA) is implicated in higher frequency of extra-articular manifestations including cardiovascular complications.(2)

Objectives: To assess the relation of ACPA to subclinical cardiac affection in RA patients.

Methods: Thirty RA patients fulfilling the 2010 ACR-EULAR classification criteria for RA with no clinically evident CVD were subjected to full history taking and clinical examination. Disease activity was assessed by 28-joint disease activity score based on C-reactive protein (DAS28-CRP) (4 variables). The levels of ACPA, CRP, total cholesterol, triglycerides, high density lipoprotein cholesterol and low density lipoprotein cholesterol were measured. The patients were subjected to M-mode and colour Doppler echocardiographic examination.

Patients were subdivided into two subgroups according to ACPA positivity (ACPA positive patients represented "group A" and ACPA negative patients represented "group B").

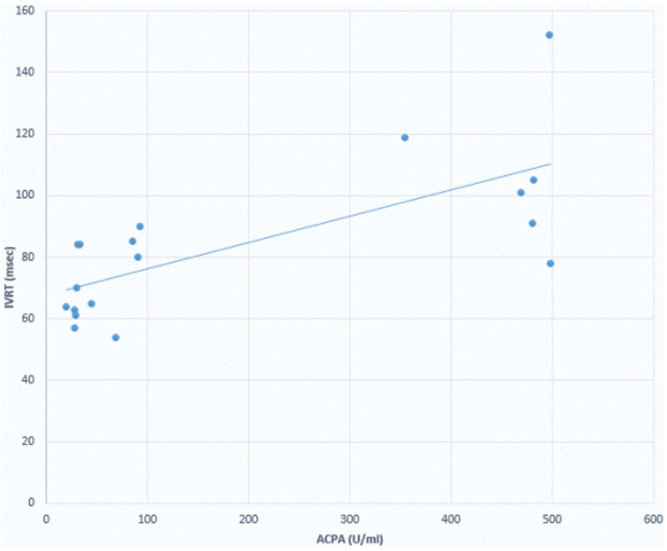
Results: The frequency of subclinical cardiac affection by echocardiographic examination was significantly higher among group A patients (4 patients had valvular lesion and 9 patients had diastolic dysfunction) than in group B patients (3 patients had diastolic dysfunction), (p=0.011). ACPA level showed significant positive correlation with isovolumic relaxation time (IVRT) in group A patients (prolongation of IVRT is a sign of diastolic dysfunction), (p=<0.001).

Conclusions: The presence of ACPA is related to development of subclinical cardiac involvement in RA patients and all RA patients with high level of ACPA should be routinely evaluated with echocardiography to assess their cardiovascular status.

Comparison between the two studied groups according to subclinical cardiac affection

	Group A (n=18)		Group B (n=12)		Test of sig.	p
	No.	%	No.	%		
Subclinical cardiac affection						
Present	13	72.2	3	25.0	$^{FE}\chi^2$=6.451	0.011*
Absent	5	27.8	9	75.0		

FE: Fisher Exact for Chi square test, χ^2: Chi square test. *Statistically significant at p≤0.05.



References:

[1] Arnab B, Biswadip G, Arindam P, Shyamash M, Anirban G, Rajan P. Anti-CCP antibody in patients with established rheumatoid arthritis: Does it predict adverse cardiovascular profile? J Cardiovasc Dis 2013; 4(2):102–6.
[2] Crowson C, Liao K, Davis J, Solomon D, Matteson E, Knutson K, et al. Rheumatoid arthritis and cardiovascular disease. Am Heart J 2013; 166(4):622–28.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2801

AB0352 RISK FACTORS AND SUBCLINICAL ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS FEMALES COMORBID WITH HYPERTENSION

O. Kuryta, T. Lusynets, O. Sirenko. *State Establishment "Dnipropetrovsk medical academy of Health Ministry of Ukraine", Dnipropetrovsk, Ukraine*

Background: Rheumatoid arthritis (RA) associates with accelerated atherosclerosis and high cardiovascular mortality. Cardiovascular risk management in RA comorbid with HT pts is do not fully reflected by traditional risk scales, thus additional factors searching is required.

Objectives: We aimed to estimate the subclinical manifestations of atherosclerosis in RA females comorbid with HT and its relationship with traditional, additional risk factors.

Methods: The study included 112 *RA* females with comorbid *HT* (mean age of 54 [50,3; 61,5] years) and 105 *RA* females without *HT* (control group). All pts received stable therapy of RA more than 6 months. Pts with coronary artery disease were excluded. The risk of fatal cardiovascular disease was calculated using m SCORE (EULAR 2010). RA disese activity was measured using DAS28 scale. Carotid ultrasound with stiffness indexes detection and endothelial-dependent flow mediated vasodilatation (EDVD) by Celermajer method were performed. The levels of adiponectin, insulin were measured using ELISA kit test, insulin resistance was estimated using HOMA2 index.

Results: Subclinical manifestations of atherosclerosis were established in 88 (78.6%) RA females with HT and 55 (52,4%) control group pts. The majority of main group pts have atherosclerotic plaques - 62 (55.4%), unstable plaques had 26 (23.2%) pts. While only 33 (29,5%) patients were high and very high cardiovascular risk assessed by mSCORE. In compare, 35 (33,3%) control group pts have atherosclerotic plaques, unstable plaques had only 14 (13.3%) control pts (p<0.05). The presence of atherosclerotic plaques in RA females with HT was associated with age, RA disease activity, endothelial dysfunction, carotid stiffness, LDL cholesterol level, insulin resistance, adiponectin level, duration of steroid therapy. AUROC index for adiponectin and HOMA2 were 0.83 (95% CI 0.74–0.95; p<0.05 and 0.75 (95% CI 0.68–0.91; p<0.05 respectively, that indicate a good quality of diagnostic models.

Conclusions: RA females with comorbid HT are characterized by higher frequency of subclinical atherosclerosis with unstable atherosclerotic plaques in compare with controls. Endothelial function, insulin resistance, adiponectin level,

carotid stiffness determining may be useful additional tools for cardiovascular risk evaluating in this pts.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5343

AB0353 ASSOCIATED FACTORS FOR FALLS AND FEAR OF FALLING IN AMBULATORY PATIENTS WITH RHEUMATOID ARTHRITIS: A COMPARATIVE STUDY WITH HEALTHY SUBJECTS

A. Yesim[1], Y. Ulus[1], T. Berna[1], L. Tomak[2], Y. Zahiroglu[1], A. Bilgici[1], O. Kuru[1]. *[1]Department of Physical Therapy and Rehabilitation, Faculty of Medicine; [2]Department of Biostatistics, Faculty of Medicine, Ondokuzmayıs University, Samsun, Turkey*

Background: Rheumatoid arthritis (RA) is a chronic disease that affects the bone and joints. Patients with RA migth be considered to be at increased risk of falls and FOF for a variety of reasons, including the presence of muscle weakness and stiff or painful joints of the lower extremities resulting in impaired physical activity, mobility, balance, and postural stability (1,2).
Objectives: The aim of the present study was to compare fall history and fear of falling (FOF) in patients with RA with healthy controls, and to investigate their relationships between the demographic features, severity of pain, disability, disease activity, walking velocity, balance and emotional status in patients with RA.
Methods: One hundred-twenty patients with RA and 60 healthy volunteers were included in the study. Their fall history (yes, no) and the number of falls within the last year were questioned. FOF by presence of FOF (yes/no) and by Falls Efficacy Scale-International-I (FES-I), walking time by 10 Meter Walk Test (10MWT), balance by One-Leg Stand Test (OLST) and Berg Balance Scale (BBS), emotional status by Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) were performed in both groups. Pain severity and patient global assessment (PGA) by Visual Analogue Scale (VAS), disability by the Health Assessment Questionnaire (HAQ), disease activity by Disease Activity Score-28 (DAS-28) were evaluated in patients with RA.
Results: There was no statistically difference between the RA patients and controls in terms of presence of fall history while presence of FOF and FES-I scores were significantly high in patients. PGA, 10MWT, pain VAS, HAQ, FES-I, BAI and BDI scores were significantly high, BBS score and OLST were significantly low fallers when compared to the non-fallers in the patients ($p<0.05$). In the patient group, FES-I score was significantly correlated with pain VAS, PGA, DAS-28, HAQ, BAI, BDI, 10MWT positively, and BBS, OLST negatively ($p<0.05$). In regression analysis; the number of falls, HAQ, BBS and BDI scores were detected to be the apparent independent risk factors affecting variations in FES-I scores ($p<0.001$).
Conclusions: According to the results of our study, ambulatory patients with RA have increased FOF, disturbed balance, increased walking time and impaired emotional status compared with controls. On the other hand; walking time, pain severity, disability, scores of emotional status and PGA were higher, while the balance scores were lower in the RA patients with fallers. There were relationships between FOF and increased pain, high disease activity and anxiety level, impaired PGA, increased walking time but the most important factors associated with FOF were impaired balance, increased disability and depression, and number of falls in RA patients. Strategies for preventing falls, maintaining balance, improving emotional status and againts FOF are of the utmost importance in patients with RA.
References:
[1] Armstrong C, Swarbrick CM, Pye SR, O'Neill TW. Occurrence and risk factors for falls in rheumatoid arthritis. Ann Rheum Dis.2005;64:1602–4.
[2] Jamison M, Neuberger GB, Miller PA. Correlates of falls and fear of falling among adults with rheumatoid arthritis. Arthritis Rheum. 2003;49:673–80.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2888

AB0354 PREVALENCE OF SIGNS OF CONNECTIVE TISSUE DYSPLASIA IN PATIENTS WITH RHEUMATOID ARTHRITIS AND CHARACTERISTICS OF THE COURSE OF COMBINED PATHOLOGY

R. Demidov, S. Lapshina, L. Myasoutova. *Kazan State Medical University, Kazan, Russian Federation*

Background: Connective tissue dysplasia (CTD) has a common pathogenesis with rheumatoid arthritis (RA). Question of peculiarities in such combination remains little known.
Objectives: To analyze the peculiarities of RA in patients with signs of CTD.
Methods: Among the 107 patients with RA, seen in the rheumatology departments in Kazan city, 18 (16.8%) patients (15 women and 3 men, mean age 47,9±12,89 years) with reliable signs of CTD were selected, identified clinically and the analysis of their documentation was performed. By DAS28 low RA activity was detected in 1 (5.6%) patients, average - 13 (72.2%), high - 4 (22.2%). The clinical-laboratory and instrumental methods of diagnosis, standardized and independently developed questionnaire for the presence of CTD in selected group of patientswere used
Results: The most frequently following signs of CTD syndrome - vegetative-vascular dystonia - 14 (77.7%), myopia - in 9 (50%), mitral valve prolapse- in 6 (33.3%), small heart abnormalities - in 8 (44.4%), flat feet - 6 (33.3%), scoliosis - in 5 (27.7%), hyperkyphosis - in 2 (11.1%), hypermobility of joints - in 2 (11 1%), anomaly of kidney structure- in 2 (11.1%), rhythm and conduction disturbances- in 7 (38.8%). Osteoporosis was observed in 11 (61.1%) patients.
We select two group of patients: the first (n=9) from 1 to 5 CTD signes and the second (n=9) – from 6 to 9 dysplasia symptoms. In the second group RA activity by DAS28 was significantly ($p\leq0.05$) higher (4.52±1,20) than in the first (DAS28 =3.95±0.81). Obtained differences in RA activity, depending on the availability of myopia (DAS28 =4,68±0,87) or its absence (DAS28 =3,78±1,06); flatfoot (DAS28 =4,53±1,05) or its absence (DAS28 =4,04±1,02) were evaluated. A significant ($p\leq0.05$) difference was found in patients with osteoporosis, the availability for activity (DAS28 =4.68±0.97), pain intensity VAS (1,44sm ± 6.90), compared with normal bone density tissue (DAS28 =3,36±0,36, pain VAS =5,83±2,22 cm).
Conclusions: Among patients with RA CTD signes occur more frequently than in the population (16.8% versus 10%). The most frequently detected are myopia, vegetative-vascular dystonia, cardiac diseases, osteoporosis. Patients with signs of dysplasia had a trend towards a higher activity of RA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3968

AB0355 MUSCLE POWER AND FALL RISK IN RHEUMATOID ARTHRITIS

R. Dietzel, D. Felsenberg, G. Armbrecht. *Centre of Muscle and Bone Research, Charite, Berlin, Germany*

Background: One of the serious consequences of aging is the gradual loss of muscle function, a phenomenon called sarcopenia. Skeletal muscle power refers to the ability to generate high-velocity movements and current evidence suggests that it declines earlier with advancing age [1] and is more strongly related to functional status than muscle force [2]. A decreased capacity for high-velocity movements in the legs has been linked to delayed responses in maintaining postural stability and thus with age-associated fall risk [3]. People with rheumatoid arthritis (RA) may be at high risk of falling due to disease-related impairments such as pain, joint deformity, muscle weakness, altered gait and decline in postural stability.
Objectives: As role of muscle power in fall-risk assessment of RA patients has not been investigated, so far, the aim of the present study was to determine the association between muscle power, muscle force, functional performance and falls in the last 12 months in RA patients.
Methods: 98 subjects with RA older than 60 years from a cross-sectional study on the prevalence of corticoid-induced osteoporosis in Germany (PSIO-D Berlin) and 98 age-matched controls without inflammatory disease, randomly chosen from a cross-sectional study collecting reference values for body composition, were analyzed in this case-control study. Muscle function was determined by muscle power per body mass in vertical countermovement jumps ($2LJP_{rel}$) on a force plate, the chair rise test (CRT), gait speed, grip strength and the Short Physical Performance Battery. Differences in muscle function measures between the RA group and the healthy reference were derived separately by sex with Student-T-test or Mann-Whitney-U-test. Using logistic regression adjusted for age and sex the association between muscle function and falls was determined.
Results: In bivariate analysis RA patients showed significantly weaker performance in all muscle function tests compared to controls in both sexes. Applying logistic regression, age (OR 1.10, 95%>CI 1.00–1.24) and female sex (OR 5.99, 95%>CI 1.25–28.57) were significantly associated with retrospective falls in RA subjects but not in controls. Gait speed (OR 0.09, 95%>CI 0.01–0.88) remained a significant correlate for falls independent of age and sex in RA patients. In controls only the CRT (OR 1.13, 95%>CI 1.02–1.26) could differentiate individuals who had past fall events in the age and sex adjusted model. No association was found for the $2LJP_{rel}$ and retrospective falls.
Conclusions: The results of the present study could not confirm an association between fall risk and muscle power in RA patients, but they highlight the importance of monitoring neuromuscular function such as gait speed, in order to prevent falls and consequently to prevent fractures, contributing to a better prognosis of rheumatic disease.
References:
[1] Lauretani, F., et al., Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol, 2003. 95(5): p. 1851–60.
[2] Bean, J.F., et al., A comparison of leg power and leg strength within the InCHIANTI study: which influences mobility more? J Gerontol A Biol Sci Med Sci, 2003. 58(8): p. 728–33.
[3] Pereira, A., et al., Effects of high-speed power training on functional capacity and muscle performance in older women. Exp Gerontol, 2012. 47(3): p. 250–5.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1957

AB0356 ASSOCIATION BETWEEN CARDIOVASCULAR RISK FACTORS AND CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS

R. González Mazarío[1], J.J. Fragio Gil[1], J. Ivorra Cortes[1], C.M. Feced Olmos[1], F.M. Ortiz-Sanjuan[1], E. Grau Garcia[1], E. Labrador Sánchez[1], S. Huerta Barberá[2], K. Arévalo Ruales[1], R. Negueroles Albuixech[1], I. Martínez Cordellat[1], I. Chalmeta Verdejo[1], L. Gonzalez Puig[1], C. Alcañiz Escandell[1], C. Nájera Herranz[1], I. Cánovas Olmos[1], E. Vicens Bernabeu[1], J.E. Oller Rodriguez[1], V. Fornés Ferrer[3], J.A. Román Ivorra[1,2]. *[1]Rheumatology Department, HUP la Fe; [2]Medical School, UCV; [3]Biostatistic Unit, IIS la Fe, Valencia, Spain*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease which affects 0.5% of adults, especially women. This disorder is associated with increased morbidity and mortality due to atherosclerotic cardiovascular diseases. In addition to classical cardiovascular risk factors, inflammation plays a key role in this fact. Intima-media thickness (IMT) measured by carotid ultrasound is currently used to detect the presence of atherosclerotic disease and its value could be a predictor of subclinical cardiovascular disease.
Objectives: To study cardiovascular risk factors, disease activity and carotid IMT in a RA patients series.
Methods: Cross-sectional observational study of patients diagnosed with RA according to ACR/EULAR 2010 criteria. Patients with age under 75 years old and up of 5 years of disease evolution were included. Cardiovascular established disease patients were excluded. During a unique visit, patients underwent anamnesis, physical examination, laboratory test, electrocardiogram, chest X-ray and carotid ultrasound with *Esaote-MyLabClassC* equipment. Statistical analyses were performed using software R (version 3.3.2).
Results: A total of 31 patients (57.1±9.7 years, 83.6% female, with 19.2±11.2 years of average disease course) were included. In relation to the classic cardiovascular risk factors, 19.4% were active smokers, 41.9% hypertensives and 45.2% had hypolipidemic treatment (85.7% with a statin), three of the patients were diabetic (9.7%). All patients were treated with monotherapy or combination therapy and 41.9% were also given glucocorticoid at low doses during the last 6 months. The median DAS28-VSG was 2.49 (1ºQ=1.6; 3ºQ=3.9), with an average HAQ of 0.88±0.68. As for extra-articular manifestations, 45.2% had xerophthalmia, 29% xerostomia, and 19.4% had rheumatoid nodules. The median total cholesterol was 195 mg/dL (174–221), and LDL of 116 mg/dL (96.5–138). The mean of the right carotid IMT was 576.13±118.78 mm and the carotid left IMT was 616.32±134.31 mm, resulting in 12 determinations higher values than expected to their age and sex provided by the ultrasound developer (38.7%). Using the SCORE table (modified by EULAR), only 5 patients (16.1%) had moderate-to -high cardiovascular risk. Statistical analysis showed a significative association between an increased IMT with tobacco consumption (classic cardiovascular risk factor) (p=0.028) and the modified SCORE (p=0.04). Neither years of evolution of disease nor the analytical biomarkers showed a significant association.
Conclusions: Our study shows that in patients with good disease control data, classic cardiovascular risk factors are related to increased carotid intima-media thickness. However, these factors may underestimate overall cardiovascular risk over other measures of subclinical cardiovascular disease, such as carotid IMT.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5868

AB0357 SEXUALITY IN WOMEN WITH RHEUMATOID ARTHRITIS - RESULTS OF A SURVEY

R. Puchner[1], J. Sautner[2], J. Gruber[3], A. Trenkler[4], E. Bragagna[5], G. Eberl[6], A. Alkin[7], H. Pieringer[8]. *[1]Rheumatologist in private practice Wels, Wels; [2]Lower Austrian State Hospital, Stockerau, Stockerau; [3]Medical University of Innsbruck, Innsbruck; [4]Elisabethinen Hospital Linz, Linz; [5]Specialist in Sexual Medicine in private practice Vienna, Vienna; [6]Klinikum Malcherhof Baden, Baden bei Wien; [7]Centre of Excellence in Medicine Linz; [8]2nd Department of Medicine, General Hospital Linz and Faculty of Medicine, Johannes Kepler University Linz, Linz, Austria*

Background: Diseases such as rheumatoid arthritis (RA) are distinguished by their chronic and progressive characteristics; they may lead to premature loss of joint function and constitute major social, economic and health burdens. Rheumatic diseases may affect all aspects of life including patients' sexuality.
Objectives: The objective of the study was to evaluate the impact of RA on women's sexuality regarding sexual motivation, activity, and satisfaction and to assess the correlation of disease related physical impairment within sexual functioning.
Methods: A group of rheumatologists, a sociologist and a specialist in sexual medicine initiated a substantial survey, including standardised questionnaires. The items asked were assessments of disease activity with the Clinical Disease Activity Index (CDAI) and measurements of illness and medically induced changes in sexual functioning with the Changes in Sexual Functioning Questionnaire-short form (CSFQ-14). Levels of depression were evaluated with the Beck Depression Inventory FastScreen (BDI FastScreen) and to establish disability the Health assessment questionnaire (HAQ) was used. Further questions were concerning demographic and health related data such as comorbidities, medication, alcohol and smoking habits.
Results: 319 questionnaires were distributed to RA-patients and 319 to healthy controls (HCOs). 235 questionnaires from patients (73, 7%) and 180 HCO-questionnaires (58, 8%) were sent back.
Women with RA had a significantly lower CSRQ Score than HCOs. 48% of the patients had a total CSFQ score of $\leq$41, which is defined as an indicator of sexual dysfunction. However, only 14% of the healthy respondents scored similarly.
29.3% of the surveyed patients were in remission, 45.1% in low disease activity, 18.9% in a moderate disease activity and 6.8% in high disease activity. There was no relationship between CDAI and CSFQ.
Age and level of education were the most important demographic parameters connected with sexual dysfunction. There was also a moderate and significant relationship between depression and sexual dysfunction.
A significant correlation between the HAQ index and the level of sexual dysfunction was to be observed.
Conclusions: Due to the lack of substantive surveys in this field, we tried to undertake a comprehensive study covering sexual dysfunction in women with RA. The study shows that RA has a significant effect on the sexuality of women, compared to healthy individuals.
Disclosure of Interest: R. Puchner Grant/research support from: unrestricted industrial grant Pfizer Austria WI205954, J. Sautner: None declared, J. Gruber: None declared, A. Trenkler: None declared, E. Bragagna: None declared, G. Eberl: None declared, A. Alkin: None declared, H. Pieringer: None declared
DOI: 10.1136/annrheumdis-2017-eular.3437

AB0358 PATIENTS WITH EARLY RHEUMATOID ARTHRITIS HAVE INCREASED CARDIOVASCULAR RISK AT THE TIME OF DIAGNOSIS

R. Davies[1], C.R. Thompson[1], H.S. Jin[1], E.A. Ellins[2], J.P. Halcox[2], A.S. Williams[1], E.H.S. Choy[1]. *[1]CREATE centre, Institute of Infection and Immunity, Cardiff University, Cardiff; [2]Institute of Life Sciences, Swansea University Medical School, Swansea, United Kingdom*

Background: Cardiovascular (CV) mortality in patients with rheumatoid arthritis (RA) is up to 50% higher than the general population. Whilst traditional CV risk factors such as smoking, diabetes and hypertension contribute to this increased mortality in RA, they do not fully explain the increase in risk. The British Society for Rheumatology, National Institute for Health and Clinical Excellence and European League Against Rheumatism (EULAR) recommend annual assessment of CV risk in RA patients. Furthermore, EULAR recommends multiplying such traditional CV risk scores by 1.5 for RA patients who meet two of three criteria consisting of (1) disease duration >10 years, (2) positive rheumatoid factor or anti-cyclic citrullinated peptide (anti-CCP) serology, (3) presence of severe extra-articular manifestation, to account for the unexplained increased CV risk in RA.
Objectives: This study assessed CV risk by QRISK2 score and used carotid ultrasound to determine cardiovascular risk and prevalence of subclinical atherosclerosis at the time of diagnosis of RA.
Methods: Patients $\geq$18 years-old with early RA, defined by ACR/EULAR 2010 criteria and diagnosis of RA <6 months were recruited from The University Hospital of Wales, Cardiff. Exclusion criteria included definite other autoimmune or inflammatory rheumatic disease, ACR Classification of Functional Status stage IV, previous history of CV disease and diabetes mellitus. Demographic details were collected, blood pressure, body mass index, ESR, CRP and lipid profile were measured and QRISK2 was calculated. Carotid ultrasound was performed and mean carotid intima media thickness (CIMT) and presence of plaque were measured. The study was approved by Research Ethics Committee for Wales (11/WA/0326).
Results: 40 patients, 10 males and 30 females with early RA were recruited. Mean age was 55.7±14.8 years. Rheumatoid factor and anti-CCP antibodies were positive in 62% and 80% of patients respectively. Mean BMI was 27.2±5.9. Twenty-nine percent were current smokers. Mean DAS28 was 3.8±1.3. According to the QRISK2, 54% of patients had >10% risk of CV disease over 10 years. Carotid ultrasound was conducted in 35 patients. Mean CIMT was 0.71±0.19 mm. 10 patients (29%) had carotid plaques. Fourteen patients (40%) had either plaque or CIMT >0.9mm, both considered markers of high CV risk. These patients were termed "ultrasound positive" patients. The sensitivity and specificity of the QRISK2 to predict US positive patients was 82% and 56% respectively. The positive predictive value of the QRISK2 was 63% and the negative predictive value of the QRISK2 was 88%. No patients met >1 criteria for EULAR adjustment of risk as all patients had early RA and none had severe extra-articular manifestations.
Conclusions: Many patients with early RA have significant CV disease at the time of diagnosis. This suggests subclinical CV disease may be developing before patients become symptomatic. More than half of the patients with early RA fulfil current NICE guidelines for starting lipid-lowering therapy, although of these, over one-third had no subclinical disease on carotid ultrasound. There is scope to improve the sensitivity and specificity of the QRISK2 calculation in RA patients, perhaps with a biomarker.
Acknowledgements: This work was funded by Arthritis Research UK, grant number 20760
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3240

AB0359 ASSESSING DEPRESSION IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS-HOW DO DIFFERENT APPROACHES COMPARE?

S.L. Hider[1,2], S. Ryan[1], N. Dale[1], N. Stanyer[1], A. Machin[2], C.A. Chew-Graham[2,3]. *[1]Haywood Academic Rheumatology Group, Haywood Hospital, Staffordshire; [2]Research Institute Primary Care and Health Sciences, Keele University, Keele; [3]Collaboration for Leadership in Applied Health Research and Care (CLARHC), West Midlands, United Kingdom*

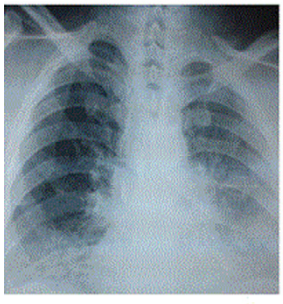
Background: Depression is common in patients with rheumatoid arthritis and negatively impacts on their quality of life and disease outcomes, including disease activity and treatment response. Several case-finding tools for depression are available, including the PHQ2, which is both valid (1) and easy to use.
Objectives: The aim of this study was to compare the prevalence of depression using case finding tools and self-report measures in patients with established RA.
Methods: Patients with established RA, attending a nurse-led annual review clinic, which aimed to offer patients a holistic review, were asked to complete a short questionnaire including demographics and self-reported comorbidity. The presence of depression was assessed in 3 ways a) PHQ2 score $\geq$3 b) Self recorded "ever" depression using the self-administered report comorbidity questionnaire (2) and c) Self report health status using the EQ5D - which includes a statement regarding current anxiety/depression (dichotomised into no anxiety/depression vs. slight/moderate/severe/extremely anxious or depressed. Ethical approval was obtained (15-WS-0063).
Results: 179 RA patients provided data. Of these 119 (66%) were female and the mean (sd) age was 67.1 (11.7) years. 59 patients (33%) reported they had ever had depression using the self-report comorbidity questionnaire and 25 (14%) indicated they were currently receiving treatment. 68 (38%) indicated they were currently slightly (or more) anxious or depressed when assessed with the EQ5D. 37 (21%) scored positively on the PHQ2. There was good concordance between the PHQ2 and EQ5D at higher levels of depression, in that all those with severe or extreme anxiety or depression on EQ5D also scored positively on the PHQ2. However, of those with moderate anxiety/depression on EQ5D, 4/14 patients scored less than 3 using the PHQ2 score.
Conclusions: Depression is common in patients with established RA. Use of the PHQ2 case-finding questions in patients with established RA, may help clinicians identify patients who may benefit from more detailed assessment of mood and interventions to improve their outcomes. Reliance should not be placed on a single tool, and exploration of mood should be part of routine assessment of a patient with RA.
References:
[1] Meader N,et al. BJGP 2011:61: 733–734.
[2] Sangha O, et al.Arthritis Rheum 2003;49:156–63.
Acknowledgements: ND was funded by the Haywood Foundation. CCG is funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care West Midlands. The views expressed are those of the authors and not necessarily those of the NHS, NIHR or the Department of Health.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5996

AB0360 CLINICAL AND HIGH RESOLUTION CT STUDY OF THE LUNGS IN 96 EGYPTIAN PATIENTS WITH RHEUMATOID ARTHRITIS

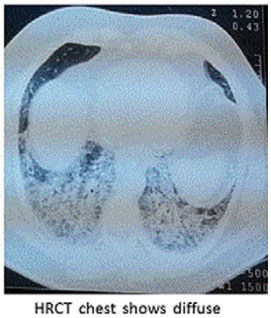
S. Tharwat, D. Shahin, A. Abdesalam, A.F. Barakat. *Internal Medicine (Rheumatology &Immunology), Mansoura University Hospital, Mansoura, Egypt*

Background: Lung involvement is a common extra-articular manifestation of rheumatoid arthritis (RA) that confers significant morbidity and mortality. However, this issue has not been sufficiently studied in Egyptian patients.
Objectives: To assess the prevalence of pulmonary abnormalities by high resolution computed tomography (HRCT) chest in RA patients and their association with clinical variables.
Methods: Ninty-six patients with RA were assessed regarding their age, gender, duration of RA disease, sicca symptoms, presence of subcutaneous rheumatoid nodules, rheumatoid factor, respiratory symptoms, use of medications, disease activity of RA using Disease Activity Score 28 (DAS28), basic laboratory investigations and pulmonary abnormalities in plain x-ray and HRCT.
Results: HRCT abnormalities were identified in 25% of the patients; 58.3% had respiratory symptoms while 41.7% were subclinical. Dyspnea and cough were the most frequent symptoms. HRCT abnormalities were interstitial lung disease (ILD) in 11 patients (11.5%), pleural involvement in 8 patients (8.3%), consolidation in 4 patients (4.2%), diffuse alveolar hemorrhage in 3 patients (3.1%), bronchiectasis in 2 patients (2.1%), and apical fibrosis with cavitation in only 1 patient (1%). Patients with dyspnea, cough, chest rales, cutaneous rheumatoid nodules, and who received disease modifying antirheumatic drugs (DMARDs) combination were more likely to have HRCT abnormalities.
Conclusions: Pulmonary involvement is not uncommon in RA patients, and HRCT is a sensitive tool in pulmonary evaluation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5037

44 year old male RA patient diagnosed as RA 5 years ago



Chest x-ray shows reduced lung volumes with bilateral reticular opacities



HRCT chest shows diffuse reticulo-nodular shadows suggestive of interstitial lung disease

AB0361 BODY COMPOSITION AND PHYSICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS (AR)

S. Manrique-Arija, N. Mena-Vazquez, M. Rojas-Giménez, C. Fuego, S. Abad-Sanchez, I. Ureña-Garnica, C. Domic, F.G. Jiménez-Núñez, M.C. Ordoñez-Cañizares, R. Caparros-Ruiz, L. Cano-Garcia, A. Belmonte, B. Panero-Lamothe, A. Fernandez-Nebro. *Department of Rheumatology at the University Regional Hospital of Malaga (HRUM). Institute for Biomedical Research in Malaga (IBIMA). Malaga University., Malaga, Spain*

Objectives: To describe the body composition and physical activity of patients with RA
Methods: *Design:* Observational case-control study. *Population:* 31 consecutive RA-patients (ACR/EULAR 2010 criteria) selected from a prospective inception cohort (diagnosis of RA between 2005 and 2012),and 31 sex and age-matched voluntary controls.*Protocol:* We included 62 subjects who were assessed using dual-body X-ray absorptiometry (DEXA) for the assessment of body composition at study entry. Data on clinical activity were also collected from the onset of the disease.The level of physical activity was assessed according to the abbreviated protocol of the International Physical Activity Questionnaire (IPAQ). *Main outcome:* Fat mass index (FMI) and fat free mass index (FFMI).FMI was defined as fat mass (kg)/ height (m^2) and FFMI as lean mass (kg)/height (m^2).*Secondary outcome:* description of the anthropometric parameters:BMI (body mass index),waist-hip index. *Variables:* Demographic, treatment, clinical-analytical variables: Disease Activity Score of 28 joints (DAS28-ESR), Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI);Anti–cyclic citrullinated peptide (ACPA), Rheumatoid factor (RF),Health Assessment Questionnaire (HAQ)and erosions.BMI was categorized according to the OMS classification. Waist- hip index (central obesity>1 for men and>0.8 for women). *Statistical analysis:* Descriptive and paired T-test or ranks test and Wilcoxon signed rank,as required
Results: We included 62 subjects,31 RA (50%) and 31 controls (50%).The mean duration of the disease of RA patients was 84.4 months. With a DAS28 mean of 3.04 (0.8), mean HAQ of 0.77 (0.6). The majority presented erosions (64.5%) RF (83.9%) and ACPA (77.4%) positive. Differences in clinical and densitometric anthropometric parameters between cases and controls are shown in Table 1. Significant differences were observed in the proportion of overweight subjects between cases and controls (p=0.03). A higher percentage of controls had moderate to high physical activity compared with the patients (65.5% vs 34.8%). The majority of patients with RApatients had low physical activity (74.2%).These had a mean (SD) of HAQ higher than patients with moderate-high physical activity [1.2 (0.9) vs 0.66 (0.6); p=0.09].Finally, patients performing moderate-high physical activity had less inflammatory activity than those performing low physical activity,with a DAS28 mean of 2.69 (0.7) vs 3.08 (0.9) ;p=0.308, respectively

Variable	Cases (n=31)	Controls (n=31)	P
Age (years), mean (SD)	53.6 (12.1)	53.6 (12.3)	0.999
Sex (Female), n (%)	27 (87)	27 (87)	1
Body mass index (BMI), mean (SD)>25 n (%)	25 (80.6)	17 (54.8)	0.03
Waist perimeter (cm), mean (SD)	88.7 (13.2)	89.1 (14.4)	0.891
Hip perimeter (cm), mean (SD)	103.9 (9.5)	106.8 (15.8)	0.395
Waist-hip index, mean (SD)	0.85 (0.1)	0.84 (0.1)	0.653
– Total fat (kg), mean (SD)	28.2 (9.3)	29.1 (10.9)	0.737
– Total lean (kg), mean (SD)	39.5 (7.6)	38.2 (9.6)	0.555
– Total mass (kg), mean (SD)	70.08 (13.8)	69.2 (15.5)	0.817
FMI (%) median (p25-p75)	10.44 (8.3–12.4)	9.51 (8.2–13.8)	0.882
FFMI (%) median (p25-p75)	14.27 (13.1–15.8)	13.83 (13.1- 15.7)	0.522

Conclusions: Patients with RA compared to controls show more overweight and less physical activity
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6056

AB0362 ANALYSIS OF INSULIN RESISTANCE IN A RHEUMATOID ARTHRITIS INCEPTION COHORT: CASE-CONTROL STUDY

S. Manrique-Arija[1], N. Mena-Vázquez[1], I. Ureña[1], S. Abad[2], M. Rojas-Gimenez[1], L. Ginel[2], L. Cano-Garcia[1], C. Fuego[1], C. Domic[1], M.C. Ordoñez-Cañizares[1], F.G. Jimenez-Nuñez[1], G. Diaz-Cordoves[1], A. Belmonte[1], V. Coret[1], M.V. Irigoyen[1], A. Fernandez-Nebro[1]. *[1]Department of Reumatology at the University Regional Hospital of Malaga (HRUM). Institute for Biomedical Research in Málaga (IBIMA). Malaga University; [2]Ciudad Jardín (Guadalmedina) Health center. Hospital Regional de Málaga., Málaga, Spain*

Objectives: To describe insulin resistance (IR) in patients with rheumatoid arthritis (RA) and compare it with healthy controls and to analyze the association between the accumulated inflammatory burden in patients with RA and IR.
Methods: *Design:* Observational case-control study. *Population:* consecutive RA-patients (ACR/EULAR 2010 criteria), >16 years, selected from a prospective inception cohort (diagnosis of RA between 2007 and 2011). Patients with Diabetes Mellitus (according to ADA 2010 criteria) were excluded. *Controls:* sex- age and BMI -matched controls were collected from a health center in our hospital area. *Protocol:* Cases and controls were evaluated by a rheumatologist. Clinical data of disease activity (RA patients), analytical values and oral glucose tolerance test (OGTT) were determined. All participants signed informed consent. *Main outcome:* IR measured by the homeostasis model for insulin resistance (HOMA-IR) (IR>2.29 μU * mmol/ml). *Secondary outcome:* IR measured by quantitative insulin sensitivity check index (QUICKI) (<0.337μU * mmol/ml) and by the homeostatic model assessment of β-cell function (HOMAβ). *Variables:* Demographic, clinical-analytical variables, Disease Activity Score of 28 joints (DAS28-ESR), Health Assessment Questionnaire (HAQ), BMI (according to OMS classification) and glucose and insulin before and after OGTT values. *Statistical analysis:* Descriptive and paired T-test or Chi-square test followed by binary logistic regression in RA patients (Dependent variable: Insulin Resistance).
Results: Sixty-two subjects were studied, 8 of them were excluded after OGTT (4 diabetic patients and their respective controls). Finally, 54 subjects were included; 27 RA and 27 healthy controls. The mean age of patients with RA was 52.2 (12.1) years. Most of them were women (88.9%), with seropositive (FR 81.5% and ACPA 74.1%) and erosive (63%) RA. The mean duration of the disease was 85.6 months (27.1) and mean DAS 28 index since the onset of the disease of 2.98 (0.9).
Differences between clinical characteristics and in relation to IR between cases and controls are shown in Table 1. No significant differences in the proportion of subjects with IR in cases and controls were observed. 33.3% of patients with RA had IR. In multivariate analysis, the only independent variable associated with IR in RA patients was disease activity score (DAS28) (OR [95% CI] = 3.6 [1.0–12.9], p=0.045).

Table 1

VARIABLE	CASES n=27	CONTROLS n=27	P - VALUE
Age, years; mean(±SD)	52.2(12.0)	52.3(12.3)	0.979
Sex, women; n(%)	24(88.9)	24(88.9)	1
Comorbidities			
BMI > 30 (obesity) n(%)	5(18.5)	4(14.8)	0.715
BMI, mean(±SD)	26.7(4.6)	26.3(5.4)	0.776
Waist perimeter(cm), mean(±SD)	88.7(13.2)	89.1(14.4)	0.891
Hip perimeter (cm), mean(±SD)	103.9(9.5)	106.8(15.8)	0.395
Dyslipemia, n(%)	5(18.5)	7(25.9)	0.513
Hypertension, n(%)	3(11.1)	6(22.2)	0.273
Insulin Resistance Indexes			
HOMA-IR>2,25, n(%)	9(33.3)	7(25.9)	0.551
HOMA-IR, mean(±SD)	1.9(10)	1.7(1.1)	0.514
HOMA-β, mean(±SD)	41.03(22.3)	37.7(25.26)	0.630
QUICKI, mean(±SD)	0.35(0.0)	0.36(0.0)	0.255

Conclusions: The only predictor of IR in RA patients was the inflammatory activity measured by DAS28. We did not find a higher IR in RA patients than in healthy controls, it could be because the patients were well treated and the inflammatory activity was controlled in the most of them.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6469

AB0363 RESULTS OF SCREENING FOR VIRAL HEPATITIS IN RA PATIENTS TREATED WITH BIOLOGICS: HUR-BIO REAL LIFE RESULTS

A. Sari, B. Armagan, A. Erden, L. Kilic, A. Akdogan, S. Apras Bilgen, I. Ertenli, U. Kalyoncu, S. Kiraz. *Rheumatology, Hacettepe University School of Medicine, Ankara, Turkey*

Background: Turkish Society of Rheumatology (TSR) proposed a guideline of recommendations for viral hepatitis screening before biological therapy in 2015.[1]
Objectives: The aim of this study was to assess results of viral hepatitis serological tests performed before biologics in RA patients.
Methods: HUR-BIO (Hacettepe University Rheumatology Biologic Registry) is a prospective,single center database of biological treatments including 1229 RA patients by August 2016. Results of serological tests for HBV of 468 RA patients were evaluated. The guideline includes 5 groups according to hepatitis B virus (HBV) serology; group 1 –HBV seronegative [HbsAg (-),anti HbS (-), anti-Hbc total (-)], group 2-vaccinated [HBsAg (-), anti-HBs (+), anti-HBc total (-)], group 3-previous HBV infection [HBsAg (-), anti-HBs (-), anti-HBc total (+)], group 4-Chronic HBV infection [HBsAg (+), anti-HBs (-), anti-HBc total (+)], group 5-secondary immunity [HBsAg (-), anti-HBs (+), anti-HBc total (+)]. Patients were also classified according to risk for HBV reactivation as very high risk (Group 4 patients receiving rituximab), high risk (group 3 patients receiving rituximab) and medium risk (Group3 or Group 4 patients receiving TNFi or T-cell blockers,IL12/23 pathway inhibitor). Screening results for hepatitis C virus (HCV) were also evaluated.
Results: Among 1229 patients (79.7% female), mean age was 54.9±11.7 and mean disease duration was 12.3±8.2 years. In total, 104 (22.2%) of patients had received rituximab. Serology for HbsAg, anti-Hbs and anti-HbC were avaliable in 468 patients. There were 273 (58.3%) patients in group 1, 81 (17.3%) in group 2, 19 (4.1%) in group 3, 9 (1.9%) in group 4 and 86 (18.3%) in group 5. Table 1 represents distribution of patients according to HBV reactivation risk. Anti-HCV was positive in 21 (2.5%) of patients.

Table 1. Distribution of patients according to HBV reactivation risk

HBV reactivation risk (%)	N (%)
Very high risk (>%20)	2 (%0.4)
High risk (%11–20)	22 (%4.7)
Medium risk (%1–10)	81 (%17.3)
No risk	363 (%77.6)

Conclusions: Among patients registered in HUR-BIO, 1.9% had chronic HBV infection and 2.5% anti-HCV positivity. 5.0% of them were under high and/or very high risk for HBV reactivation. Medium risk group which includes 17.0% of patients, seems to deserve most of the attention. Screening for viral hepatitis must be performed before biologics and TSR guideline may be useful in this matter.
References:
[1] Karadag O, Kasifoglu T et al. Guideline of the viral hepatitis screening before biologic agents use in patients with rheumatic diseases. RAED Journal;7:28–32.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4030

AB0364 CHARACTERISTICS OF BLOOD PRESSURE PHEHOTYPES IN PATIENTS WITH RHEUMATOID ARTHRITIS - EULAR

S. Velmakin, E. Troitskaya, S. Villevalde, Z. Kobalava. *Propaedeutics of Internal Diseases, Rudn University, Moscow, Russian Federation*

Background: Patients with rheumatoid arthritis (RA) have increased cardio-vascular risk. Arterial hypertension (AH) is highly prevalent, and seems to be under-diagnosed and under-treated among patients with RA. Data on ABPM profile in patients with rheumatoid arthritis are lacking.
Objectives: The aim of the study was to evaluate ABPM parameters and characterize phenotypes of blood pressure (BP) in patients with RA.
Methods: 62 patients with RA (EULAR 2010) without known cardio-vascular disease were examined (73% females, age 58,5±15,4 (M±SD) years, 13% smokers, 61% with AH, 34% with dyslipidemia). Median duration of RA was 8 years (IQR 3–17). Seropositive RA was diagnosed in 69% of patients. Median CRP was 12,1 mg/dl (IQR 2,2–23,4 mg/dl), median rheumatoid factor (RF) was 32,5 IU/ml (IQR 8,3–173 IU/ml). All patients received disease-modifying antirheumatic drugs (DMARDs), 22 (38%) - biological treatment. Median duration of AH was 6,1 years (IQR 0–10 years). All patients with AH received antihypertensive treatment. 24-h peripheral and central BP monitoring was performed (BPLab Vasotens, “Petr Telegin”). P<0.05 was considered significant.
Results: Mean office BP was 130±15/80±10 mmHg (peripheral) and 123±21/80±10 mmHg (central). 10 (17%) patients had elevated office BP (>140/90 mmHg). Mean BP values for peripheral and central BP were as follows: 125±15/73±9 and 116±14/75±9 mmHg for 24-h BP; 127±15/74±9 and 117±14/77±9 mmHg for daytime BP; 119±15/69±10 and 112±15/70±10 mmHg for nighttime BP. AH according to daytime BP was found in 15 (24,2%) pts, nighttime BP – in 29 (46,8%) pts, 24-h BP - in 19 (30,6%) pts. Phenotypes of BP were as follows: sustained normotension – in 38 (61,2%), masked hypertension in 12 (19,4%), sustained AH – in 10 (16,1%), white-coat hypertension in 2 (3,2%) patients. Isolated nocturnal AH was observed in 12 (19,4%) pts. 10 (16,1%) patients had isolated elevated central BP. 20 (32,3%) pts had elevated central SBP according to individual reference values; all patients with high office BP had elevated central BP.
Conclusions: Patients with RA free of CVD are characterized by high prevalence of with the satisfactory control of office BP in the majority of patients. Relatively high prevalence of masked and isolated nocturnal hypertension despite antihy-pertensive treatment is observed in this population. These findings may help to optimize hypertension treatment in patients with RA.

References:
[1] Ambrosino P. et al. Subclinical Atherosclerosis in Patients With Rheumatoid Arthritis. A Meta-Analysis of Literature StudiesThromb Haemost 2015; 113: 916–930.
[2] Avina-Zubieta JA et al. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. Arthritis Rheum 2008; 59:1690–7.
[3] Protogerou A.D., Panagiotakos D.B., Zampeli E. Arterial hypertension assessed "out-of-office" in a contemporary cohort of rheumatoid arthritis patients free of cardiovascular disease is characterized by high prevalence, low awareness, poor control and increased vascular damage-associated "white coat" phenomenon. Arthritis Res Ther. 2013;15(5):R142.
[4] Panoulas V.F., Metsios G.S., Pace A.V. Hypertension in rheumatoid arthritis. Rheumatology (Oxford). 2008;47(9):1286–98.
[5] Hamamoto K., Yamada S., Yasumoto M. Et al. Association of nocturnal hypertension with disease activity in rheumatoid arthritis. Am J Hypertens 2016;29(3):340–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5382

AB0365 HENOCH-SCHÖNLEIN PURPURA IN TUNISIAN ADULTS: MONOCENTRIC STUDY

S. Hammami, M. Nasr, N. Sassi, R. Klii, M. Kechida, I. Kochtali. *Internal medicine, University Hospital F Bourguiba Monastir, Monastir, Tunisia*

Background: Henoch-Schonlein purpura (HSP) is a non thrombopenic leucocytoclasic acute systemic vasculitis of the small vessels with IgA-immun complex deposits, most commonly affecting the skin, joints, gastro-intestinal tract and the kidneys. It commonly affects the children aged between 4 to 10 years. The occurrence of HSP in adults is significantly less frequent with atypical profile, and more serious complications.
Objectives: Analysis of the clinical presentations, biological characteristics, treatment and evolutions of HSP in this population, compared with other tunisian and international studies.
Methods: This is a monocentric retrospective study using an operating record data from 30 adult patients aged 16 to 82 years hospitalized for HSP in Internal Medicine Department in Monastir university hospital between May 2005 to July 2015. Inclusion criteria's where those defined in 2006 by the European League Against Rheumatism (ELAR) and the Pediatric Rheumatology European Society (PRES) for the diagnosis of HSP.
Results: Thirty patients with Henoch-Schönlein purpura (18 women and 12 men) were included in the study. The mean age at onset of the disease was 48.80±18.77 years (16 -82 years). The vascular purpura was the most frequent inaugural clinical manifestation (90%). It was diffuse and necrotic in 3.3% of cases. Cutaneous biopsy practiced in 26 cases (86.6%), found leukocytoclastic vasculitis in 21 cases (80.7%). Joint involvement was present in 80%: Inflammatory arthralgia in 56.6% and arthritis in 23,3%. Sixteen patients (53.3%) had gastro-intestinal involvement: Gastric and duodenal ulcers, occlusive syndrome, gastrointestinal bleeding and pancreatitis in 26,6%, 16,6%, 10% and 3,3% respectively. Eighteen patients (60%) had renal involvement. Nephritic syndrome was observed in thirteen patients (43,33%). Hematuria was objectified in 11 patients. Four patients had renal failure (13,33%). The renal biopsy practiced in 4 cases, objectified IgA nephropathy in 3 patients and glomerulonephritis extra-capillary in 1 case. Interstitial lung disease with bilateral pleurisy was observed in a patient. A woman had a cerebral vasculitis. Corticosteroids were prescribed in 8 patients for gastrointestinal and renal impairment. Two patients received cyclophosphamide cures for cerebral vasculitis and severe digestive impairment. Anti-inflammatory drugs were prescribed in 9 cases. A favorable spontaneous development was observed in 9 patients. A recurrence was reported in 2 cases. One patient dead by severe sepsis.
Conclusions: HSP manifests in adult patients as a more severe and atypical disease with more relapses and more frequent and severe gastro-intestinal and renal disease. HSP in adults requires a sustainable monitoring and more aggressive treatment
References:
[1] José M et al Henoch-SchöNlein Purpura in Adults; Clinics. 2008 Apr; 63(2): 273–276.
[2] Danhua Shu et al. Risk factors of progressive IgA nephropathy which progress to end stage renal disease within ten years: a case–control study, BMC Nephrol. 2017; 18: 11.
Acknowledgements: Department of Immunology, university Hospital, F Bourguiba Monastir Tunisia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4479

AB0366 "I JUST WANT MY LIFE BACK": PHYSICAL FUNCTION AND FATIGUE ARE CRITICAL TARGETS FOR IMPROVING PARTICIPATION AND HRQL IN RHEUMATOID ARTHRITIS

S.J. Bartlett[1,1], A. Sirois[2], N. Chiarlitti[2], M. Inceer[2], M. Jones[3], C.O. Bingham[3]. *[1]Medicine; [2]Mcgill University, Montreal, Canada; [3]Johns Hopkins, Baltimore, USA*

Background: The primary goal of treatment for rheumatoid arthritis (RA) is to maximize health-related quality of life (HRQL) through symptom and damage control, and normalize function and participation in social and life activities. Although fatigue is recognized as one of the most debilitating symptoms of RA, little is known about how fatigue impacts participation.
Objectives: We hypothesized that fatigue, along with pain, mood, disease activity, and disability would be associated with reduced participation.
Methods: RA patients enrolled in an observational study at an academic center completed PROMIS measures assessing fatigue, physical function, mood (depression and anxiety), pain interference, sleep disturbance, and participation. RA clinical indicators were also collected at the visit. Variance inflation factors were examined to evaluate collinearity among variables. Covariates/confounders independently associated with participation included pain, mood (depression, anxiety), sleep, disease activity (CDAI), and physical function. Multiple regression models that did and did not include pain were compared using likelihood ratio tests with SPSS and R.
Results: Participants were mostly female (82%) and white (83%) with mean (SD) age of 56 (13) years; 24% had $\leq$ high school, 29% had RA $\leq$5 years with 13% $\leq$2 years, and 22% were disabled. Mean CDAI was 7.9 (7.8). Most were in CDAI remission (n=56; 32%) or LDA (n=67; 38%); 39 (22%) were in MDA and 14 (8%) in HDA. Mean PROMIS fatigue was 53.9 (10.0); fatigue increased across CDAI levels from 46.2 (8.6) in remission to 64.0 (9.6). Only those with HDA had mean sleep, depression or anxiety scores $>$55 (i.e., above population norms).
In the full model, fatigue, depression, CDAI, and physical function were significant independent predictors of reduced participation in social roles and activities ($F(2, 162) = 29.75$, $p < .001$, adjusted $r^2 = .55$). Contrary to our hypothesis, pain was not associated with participation in univariate or multivariate models.
Conclusions: Our results suggest that in RA patients, high levels or fatigue are common; conversely, depression, anxiety, and sleep disturbance were elevated only in people with HDA. Disability and fatigue appear to have the greatest impact on participation in social roles and activities. RA treatments and interventions that attenuate fatigue and improve mood in people with active RA may improve their ability to participate in social and life situations restoring a sense of normalcy and improving HRQL.
Acknowledgements: Funding: PCORI IP2-PI0000737 and SC14–1402–10818, CIHR 312205.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5597

AB0367 THE PROPHYLACTIC EFFECT OF SULFASALAZINE AGAINST PNEUMOCYSTIS PNEUMONIA: AN ANALYSIS OF INCIDENCE FOR PNEUMOCYSTIS PNEUMONIA IN PATIENTS WITH RHEUMATOID ARTHRITIS IN JAPAN

T. Nunokawa, N. Yokogawa, K. Shimada, S. Sugii. *Department of Rheumatic Diseases, Tokyo Metropolitan Tama Medical Center, Fuchu-shi, Japan*

Background: Cases with *Pneumocystis* pneumonia (PCP) have been reported in patients with rheumatoid arthritis, mainly treated with biologics. An experimental study in the mouse revealed that sulfasalazine enhances the clearance of the *Pneumocystis* organism from the lung (1). Furthermore, a case-control study with small sample size indicated possible preventive effect of sulfasalazine against PCP (2).
Objectives: The aim of this study is to clarify the prophylactic effect of sulfasalazine against PCP in patients with rheumatoid arthritis with a large sample size.
Methods: This retrospective study focused on all patients with rheumatoid arthritis seen between April, 2011 and October, 2016. at department of rheumatology, Tokyo Metropolitan Tama Medical Center. We investigated their demographics and medication, including corticosteroids, disease-modifying antirheumatic drugs and prophylactic drugs against PCP. The person-time at risk was calculated from prescription records. We compared the incidence during the period of follow-up in which the patients received sulfasalazine with that in which they did not received sulfasalazine. The incidents were assumed to follow a Poisson distribution and statistical analysis was performed using z-test.
Results: In the study period, 2,394 patients with rheumatoid arthritis were treated at our hospital. Among them, 24 patients received the treatment for PCP because the infection was diagnosed or was strongly suspected. All the cases developed the condition while they were not taking sulfasalazine. The incidence rate of PCP was significantly lower in the treatment period with sulfasalazine than that without sulfasalazine ($p < 0.001$).
Conclusions: Our study confirmed that sulfasalazine has a preventive effect against PCP in patients with rheumatoid arthritis.
References:
[1] Wang J, Gigliotti F, Bhagwat SP, George TC, Wright TW. Immune modulation with sulfasalazine attenuates immunopathogenesis but enhances macrophage- mediated fungal clearance during pneumocystis pneumonia. PLoS Pathog. 2010;6(8):59–60.
[2] Mizushina K, Hirata A, Hayashi N, et al. Possible preventive effect of salazosulfapyridine against development of Pneumocystis pneumonia in methotrexate-receiving patients with rheumatoid arthritis. Mod Rheumatol. 2015;7595(November):1–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6083

AB0368 PREDICTORS OF NEUROPATHIC PAIN IN RHEUMATOID ARTHRITIS

T. Martins Rocha[1], S. Pimenta[1], M. Bernardes[1], A. Bernardo[1], M. Barbosa[2], R. Lucas[3], L. Costa[1]. *[1]Rheumatology; [2]Pain Unit, Centro Hospitalar de São João; [3]Clinical Epidemiology, Faculty of Medicine University of Porto (FMUP), Porto, Portugal*

Background: Significant pain persists in a substantial proportion of Rheumatoid Arthritis (RA) patients in spite of disease remission. Recent evidence indicates that features suggestive of neuropathic pain (NP) are present in RA patients with a prevalence range of 33–38% using the painDETECT questionnaire (PDQ).
Objectives: To estimate the clinical predictors of NP in a cohort of RA patients.
Methods: Observational, cross-sectional study was performed with RA patients followed at our Rheumatology department with unchanged DMARD treatment during the last 3 months. Patients with diagnosed neuropathy or non-RA risk factors for NP were excluded. Selected patients were evaluated in a medical visit. Demographic, clinical and laboratorial data were collected and disease activity and functional measures were evaluated. Two questionnaires were applied to assess NP: the Leeds Assessment of Neuropathic Symptoms (LANSS) and the PDQ. Univariate and multivariate logistic regression were performed to identify the predictors of NP. Significance level was set as <0.05.
Results: 112 RA patients were included. 86 (77%) were females, with a mean (SD) age of 55.1 (10.8) years and median disease duration of 13 years (range: 2–41). 84% patients were seropositive for Rheumatoid Factor and/or ACPA. 102 (91%) were treated with DMARDs and 42% with a biologic DMARD, whom 8% in monotherapy. The mean (SD) DAS28 4V was 3.61 (1.01) and 12% were in remission. 45 (40%) patients had NP by the LANSS ($\geq$12), 28% had a possible/likely NP in the PDQ ($>$12) and 21% were positive in the both tests. Female sex was predictive of LANSS and PDQ NP (OR: 3.44, p=0.02 and OR: 3.70; p=0.05, respectively) and disease duration was a predictor of LANSS (OR: 0.92 per year, p=0.004). After adjusting for these variables, pain VAS, patient global activity and the tender joint count were positive predictors of NP by both tests. Swollen joint count, ESR or CRP levels were not significantly associated with NP. DAS28 CRP and HAQ scores were both significant positive predictors of PDQ NP (OR: 1.77 and OR: 3.61, $p<0.01$, respectively). DAS28 CRP, dichotomized as remission/non-remission, and the HAQ score were also significantly positive predictors of LANSS NP (OR: 5.55, p=0.01 (DAS28 CRP$\geq$2.6); OR: 2.15, p=0.03). Positivity for ACPA was a negative predictor of LANSS NP (OR: 0.23, p=0.009), remaining significant after adjusting for DAS28 CRP, HAQ and current methotrexate (MTX). Number of analgesics and current NSAIDs treatment were associated with PDQ NP (OR: 2.72 and OR: 3.40, respectively, $p<0.05$). Current MTX and previous/current Hydroxychloroquine (HCQ) treatment were both negative predictors for PDQ NP (OR: 0.41 and OR: 0.20, respectively, $p<0.05$). No other significant associations were found. In a subgroup with dosed TSH levels (n=18), there was a positive though non-significant association with LANSS and PDQ (OR: 3.12, OR: 14.98, p=0.09).
Conclusions: NP was present in sizable proportion of RA patients. Consistently with previous data, our study supports the association between NP and disease activity/functional scores but not with objective inflammatory measures. This study newly points to a possible protective role of ACPA positivity, MTX and HCQ treatment in NP risk.
References:
[1] Koop SM, et al. Arthritis Res Ther. 2015; 17:237.
[2] AW Christensen et al. Scand J Rheumatol 2016;1–9.
Disclosure of Interest: T. Martins Rocha Grant/research support from: Portuguese Society of Rheumatology/Alfa Wassermann on May 2015, S. Pimenta: None declared, M. Bernardes: None declared, A. Bernardo: None declared, M. Barbosa: None declared, R. Lucas: None declared, L. Costa: None declared
DOI: 10.1136/annrheumdis-2017-eular.2634

AB0369 VITAMIN D STATUS AND DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

V. Povoroznyuk[1], O. Synenky[2], N. Balatska[1]. *[1]D.F. Chebotarev Institute of Gerontology Nams Ukraine, Kyiv; [2]Lviv Regional Clinical Hospital, Lviv, Ukraine*

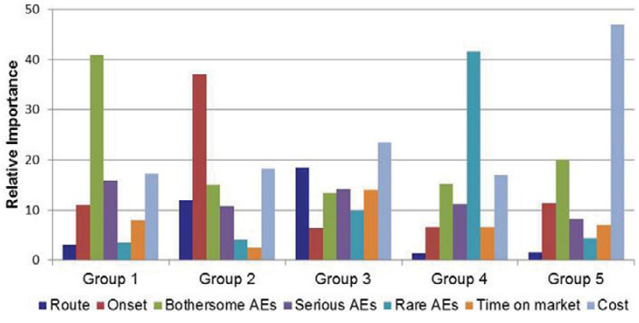
Background: The purpose of the study was to define the associations between serum level of 25-hydroxyvitamin D (25(OH)D) and disease activity in patients with rheumatoid arthritis (RA).
Objectives: The study group comprised 93 patients aged 27–80 years suffering from RA (74.2% women) and 93 controls.
Methods: The levels of rheumatoid factor (RF) and C-reactive protein (CRP) were measured by immunoturbidimetric assay. Erythrocyte sedimentation rate (ESR) was measured by Westergren method. Serum $25(OH)D_{total}$ level was determined by electrochemiluminescence (ECL) method. The optimal vitamin D status was defined when serum 25(OH)D level was 30–50 ng/ml.
Results: In general, 54.8% of RA patients revealed vitamin D deficiency, and 37.6% - vitamin D insufficiency. No significant difference was found when mean serum 25(OH)D levels in RA patients and healthy controls where compared. 25(OH)D levels appeared markedly lower in patients with the highest activity of RA compared to values noted in patients with the minimal RA activity (16.55±9.26 vs 22.59±9.74 ng/ml, $p<0.05$). In RA patients 25(OH)D levels were significantly and negatively associated with markers of disease activity (DAS28-ESR (β = -0.33; 95% CI =0.05, -0.01), CRP (β = -0.23; 95% CI = -0.72; 0.00), and ESR (β = -0.26; 95% CI = -0.78; -0.10). All these associations remained statistically significant after adjustment for gender, age and BMI.
Conclusions: Vitamin D deficiency should be considered as an important predictor of the high RA activity (AUROC =0.67; 95% CI =0.513–0.83, P=0.05).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4600

AB0370 DEVELOPMENT OF PATIENT PREFERENCE PHENOTYPES FOR RHEUMATOID ARTHRITIS

W.B. Nowell[1], C. Wiedmeyer[1], G. Herath[2], G. Michel[3], L. Fraenkel[2]. *[1]Global Healthy Living Foundation, Upper Nyack; [2]Yale University School of Medicine; [3]Yale University, New Haven, CT, United States*

Background: Many important treatment decisions for patients with rheumatoid arthritis (RA) are conditional on patient preferences and, according to the U.S. National Academy of Medicine, mandate a shared decision making approach (SDM). Furthermore, SDM is being increasingly recognized as an important quality measure. One of the most common preference sensitive decisions in RA is how to escalate care when response to methotrexate monotherapy is inadequate. However, the number of RA medications currently approved makes it challenging for patients to weigh the pros and cons related to each of the treatment options in order to develop a preference.
Objectives: The objective of this study was to develop representative patient preference phenotypes to enable patient-physician dyads to effectively incorporate patient preferences at the point-of-care.
Methods: People living with RA were invited to complete a Choice-Based Conjoint analysis survey including seven attributes (route of administration, time to onset of action, bothersome adverse events (AEs), serious AEs, extremely rare AEs, duration of time on the market and affordability) developed iteratively based on patient feedback. Each attribute was described across three or four levels using plain language. Preference phenotypes were identified by applying latent class analysis to the conjoint data. Class solutions were replicated five times from random starting seeds. A five-group solution was chosen based on Akaike's information criterion. We calculated the percentage of importance assigned to each attribute and performed simulations to estimate preferences for triple therapy, SC and IV biologics, or tofacitinib.
Results: 1100 U.S. subjects recruited via the CreakyJoints online patient community completed the survey. Of these, 49 were eliminated because they completed the survey in less than 10 minutes and an additional 45 people were excluded because they did not respond correctly to a dominant choice task. The mean age was 51.7 (11.2). The majority were female; (92%) and Caucasian (93%). Preferences (assuming low cost across options), and the reasons underlying each respondent's preference, clustered into five groups (Figure 1). There were no differences in the distribution of demographic or clinical characteristics across the five groups. Phenotypes were created based on the stated preference data.

Figure 1. Relative Importances



Conclusions: RA patients' preferences vary and can be classified into distinct phenotypes. Ongoing research is evaluating whether enabling patients to identify with a preference phenotype facilitates SDM at the point-of-care.
Acknowledgements: This research was supported by a grant from the Rheumatology Research Foundation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5024

AB0371 THE QUALITY OF LIFE CAN BE IMPROVED BY FOREFOOT RECONSTRUCTION EVEN IN PATIENTS WITH WELL-CONTROLLED RHEUMATOID ARTHRITIS

Y. Nomura[1], H. Ishikawa[1], A. Abe[1], S. Ito[1], T. Kojima[2], M. Kojima[3], N. Ishiguro[2], A. Murasawa[1]. *[1]Rheumatology, Niigata Rheumtic Center, Shibata; [2]Orthopedic Surgery, Nagoya University Hospital; [3]Medical Education, Nagoya City University Hospital Graduate School of Medicine, Nagoya, Japan*

Background: The treatment aim of rheumatoid arthritis (RA) is achieving and

maintaining remission (REM) or low disease activity (LDA) via tight medical control[1)]. However, despite remarkable advances in medication, progressive deterioration and deformity of the forefoot sometimes occur if adequate medication is not administered in the early stage. Surgical reconstruction is still required in patients with painful callosity and footwear problems caused by typical forefoot deformity. Recently, patients have expressed a desire to achieve functional REM with a higher quality of life (QOL) and improved mental wellness.

Objectives: The objective of this study was to clarify the systemic effects of forefoot reconstruction on the impaired foot, even in patients who have achieved REM or LDA.

Methods: A prospective cohort study was performed for 63 feet of 50 patients (males: 6, females: 44) with RA who underwent primary elective surgery between October 2012 and September 2014. Both feet underwent surgery on the same day in 13 patients. The average (range) age was 64 (42–89) years, and the average (range) disease duration was 20 (2–36) years. The procedures performed included shortening oblique osteotomy at the metatarsal neck of the lessor toes in 47 feet, first metatarsophalangeal joint arthroplasty (Swanson) in 44 feet, correction shortening osteotomy (modified Mitchell) at the first metatarsal in 4 feet, and fusion at the first interphalangeal joint in 7 feet, among others. A total of 30 feet in 27 patients (males: 5, females: 22) had a disease activity of REM or LDA just before surgery. The patient-reported outcomes (PROs) were assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI), EuroQol-5 Dimensions (EQ-5D), Beck Depression Inventory-II (BDI-II), and Patient's General Health using a visual analogue scale of 100 mm (Pt-GH). The 28-joint Disease Activity Score using C reactive protein (DAS28-CRP), the Japanese Society of Surgery of the Foot (JSSF) standard rating system (JSSF) for the RA foot and ankle scale[2)], and the Time Up&Go test (TUG) were also evaluated. All of these items were investigated just before surgery (baseline) and again at 6 and 12 months after surgery.

Results: Overall, the physical function (JSSF, TUG), QOL (EQ-5D), and mental wellness (depression) (BDI-II) were significantly improved at 6 and 12 months after surgery compared to the baseline values ($p<0.05$). In the REM/LDA group, significant improvement was noted in the physical function (JSSF), QOL (EQ-5D) both at 6 and 12 months after surgery; however, we did not observe any significant changes in the Pt-GH or DAS28-CRP (Table 1).

Table 1: Outcome of surgical intervention in the deformed forefoot for the patients with rheumatoid arthritis

		HAQ-DI	EQ-5D	BDI-II	Pt-GH (mm)	DAS28-CRP	JSSF	TUG (sec)
Total n=50	baseline	0.98 (0.77)	0.71 (0.11)	11.7 (8.2)	30.4 (22.9)	2.63 (1.1)	61.9 (16.4)	10.0 (4.0)
	PO# 6mos.	1.01 (0.8)	0.75* (0.13)	9.9* (7.0)	25 (20.9)	2.43 (0.92)	78.7** (14.7)	9.2* (3.0)
	PO# 12mos	1.04 (0.71)	0.76* (0.15)	9.7* (6.9)	25.4 (19.7)	2.40 (0.89)	78.2** (14.3)	9.3* (3.0)
REM+LDA n=27	baseline	0.78 (0.66)	0.73 (0.13)	10.3 (7.8)	18.9 (18.6)	1.85 (0.49)	68.0** (15.4)	8.6 (2.4)
	PO# 6mos.	0.81 (0.65)	0.80* (0.13)	8.1* (6.3)	19.5 (16.7)	2.0 (0.60)	82.8** (11.5)	8.4* (2.0)
	PO# 12mos	0.89 (0.66)	0.80* (0.16)	8.7 (7.6)	19.4 (16.1)	2.0 (0.57)	81.4** (11.8)	8.4 (2.5)

Mean(SD) *: p<0.05 compared to baseline, **: p<0.01 compared to baseline

Conclusions: Achieving REM or LDA is not the ultimate goal of treatment for patients with painful callosity and footwear problem functional loss. A higher QOL and improved function can be achieved by surgical intervention in the deformed forefoot.

References:

[1] Smolen JS, Breedveld FC, Burmester GR, et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. Ann Rheum Dis. 2016;75(1):3–15.

[2] Niki H, Aoki H, Inokuchi S, et al. Development and reliability of a standard rating system for outcome measurement of foot and ankle disorders I: development of standard rating system. J Orthop Sci. 2005:10:457–465.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3393

AB0372 ASSOCIATED FACTORS OF CERVICAL AND LUMBAR SPINAL INSTABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

Y. Sugimura[1], N. Miyakoshi[2], T. Kashiwagura[3], M. Kobayashi[4], T. Aizawa[5], H. Aonuma[6], Y. Shimada[2]. *[1]Orthopedic Surgery, Nakadori General Hospital; [2]Orthopedic Surgery, Akita University Graduate School of Medicine; [3]Orthopedic Surgery, Akita City Hospital, Akita; [4]Orthopedic Surgery, Hiraka General Hospital, Yokote; [5]Orthopedic Surgery, Kita Akita Municipal Hospital, Kitaakita; [6]Orthopedic Surgery, Kakunodate Municipal Hospital, Senboku, Japan*

Background: Few studies have compared rheumatoid arthritis (RA)-related disorders of the cervical and lumbar spine.

Objectives: The objectives of this study were to examine the prevalence of and risk factors for cervical and lumbar spinal instability in patients with RA.

Methods: From a total of 1,843 patients registered in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA), 135 patients [118 women, 17 men; mean age, 66 (41–84) years; mean disease duration, 14 (1–63) years] who underwent a radiographic examination were enrolled in this study. In the cervical spine, we defined instability as one of the following characteristics: (1) atlantodental interval (ADI) >3 mm, (2) Ranawat value <13 mm on a neutral plain radiograph, or (3) anteroposterior translation >3 mm at the subaxial cervical spine on an anteroposterior bending plain radiograph. In the lumbar spine, instability was defined as anteroposterior translation >3 mm on a neutral plain radiograph.

At the time of radiographs evaluation, demographic characteristics, clinical variables, medical history and current medications were investigated.

The patients were classified into two groups: with both cervical and lumbar spinal instabilities and without. The independent risk factors for both cervical and lumbar spinal instabilities were then determined using multivariate logistic regression analysis.

Results: Forty-six (34.1%) patients exhibited cervical spinal instability, and 50 (37.0%) patients exhibited lumbar spinal instability. Twenty-four patients (17.8%) exhibited both cervical and lumbar spinal instability. The presence of both cervical and lumbar spinal instability was significantly and independently associated with disease duration (OR: 1.06; 95% CI: 1.01–1.12).

Conclusions: The prevalence of both cervical and lumbar spinal instability in patients with RA was 17.8%. Disease duration was independent risk factor for presence of both cervical and lumbar spinal instability in this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6649

AB0373 ANALYSIS OF RISK FACTOR FOR LOCOMOTIVE SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM CHIKARA STUDY

Y. Yamada, M. Tada, K. Mandai, N. Hidaka. *Department of orthopedics surgery, Osaka City General Hospital, Osaka City, Japan*

Background: Patients with rheumatoid arthritis (RA) are at a higher risk for sarcopenia due to joint destruction and chronic inflammation*1, which can lead to locomotive syndrome (LS), i.e., being restricted in the ability to walk or lead a normal life owing to a dysfunction in one or more of the parts of the musculoskeletal system*2. The prospective observational CHIKARA study (Correlation research of sarcopenia, skeletal muscle and disease activity in rheumatoid arthritis; registration number UMIN000023744) was begun in 2016 to investigate the correlation between RA disease activity and sarcopenia and LS.

Objectives: We investigated the relationship between LS and disease activity at baseline in patients with RA.

Methods: One hundred patients (78% women; average age, 66y) enrolled in the CHIKARA study were examined for body weight, muscle mass, fat mass, predicted bone mass, basal metabolic rate (BMR), leg muscle score, etc., using a body composition analyzer. Laboratory data, disease activity, Health Assessment Questionnaire (HAQ) and treatment were also investigated. LS was diagnosed using a questionnaire called Locomo-5. We investigated the correlation between LS and each status using univariate and multivariate analyses.

Results: Fifty-two percent of the patients with RA that we examined had LS. Mean disease duration was 5.5 years and mean DAS28-ESR was 3.55. Table 1 shows the risk factors for LS. Univariate analysis showed that age, percent body fat, body weight, visceral fat rating, leg muscles score, rheumatoid factor status and HAQ had significant associations to LS. Leg muscle score and HAQ were detected as significant factors by multivariate analysis. Patients whose leg muscle score was less than 90 had a significantly higher prevalence of LS by ROC curve analysis (Odds ratio 3.77, p=0.001). Disease activity and use of glucocorticoids or biological agents showed no significant relationship.

Table 1. Risk factors for locomotive syndrome in patients with rheumatoid arthritis

	Univariate		Multivariate		
	R	p value	Odds ratio	95% Confidence Interval	P value
Age, y	0.255	0.01	–	–	–
% body fat	0.244	0.014	–	–	–
% body water	-0.215	0.032	–	–	–
Visceral fat rating	0.205	0.041	–	–	–
Leg muscle score	-0.359	<0.001	0.91	0.84–0.97	0.005
Rheumatoid factor	0.221	0.027	–	–	–
Health Assessment Questionnaire	0.460	<0.001	8.78	2.66–29.0	0.001

Conclusions: Lower leg muscle score and higher HAQ score are independent risk factors for LS among patients with RA.

References:

[1] Inui K., Koike T., Tada M., et al. Sarcopenia is apparent in patients with rheumatoid arthritis, especially those with biologics -TOMORROW study-. EULAR 2015 abstract (AB0359).

[2] Nakamura K., Ogata T. Locomotive Syndrome: Definition and Management. Clin Rev Bone Miner Metab. 2016; 14(2): 56–67.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3637

Rheumatoid arthritis - anti-TNF therapy

AB0374 FLARE INCIDENCE AND PREDICTIVE FACTORS IN A POPULATION OF PATIENTS WITH RHEUMATOID ARTHRITIS UNDER OPTIMISED TREATMENT WITH ADALIMUMAB AND INFLIXIMAB

A. Pieren[1], C. Plasencia[1], D. Pascual-Salcedo[2], M.B. Paredes[1], A. Balsa[1].
[1]Rheumatology; [2]Immunology, Hospital la Paz, Madrid, Spain

Background: Anti-TNF are nowadays widely used for the treatment of Rheumatoid Arthritis (RA),which has drastically changed the prognostic of the disease,carrying an important healthcare expense.This is why,optimisation seems a successful strategy that should not be linked to a worse become of our patients' clinical evolution.
Objectives: Describe a population of patients with RA under optimised treatment with Adalimumab (Ada) and Infliximab (Ifx).Study the incidence of flares and establish predictive factors of flares at baseline and pre-optimization.
Methods: Observational study of the prospective cohort RA-Paz. All the patients diagnosed of RA under treatment with Ifx and Ada between Jan.2000 and Dec.2016 of the day-care unit of La Paz Hospital,were included.Demographic data,clinical activity and blood sample results were collected at baseline, pre-optimization (pre-op)and at 3,6,9,12,18 and 24 months.Drug serum trough levels were measured under ELISA in each visit.Optimal range for Ifx was described as drug concentration between 1000- 4000 ng/ml and 1500- 5000 ng/ml for Ada.Optimisation was defined as drug use below standard dose.Flares were collected from the pre-op visit.Flare was described as clinical worsening which led to a therapeutic change or a DAS28>3.2 and DeltaDAS28>0,6.Predictive factors of flare at baseline and pre-op were evaluated with a uni and multivariate analysis. Statistical study was performed with the statistical program SPSS.
Results: Of the 271 patients diagnosed of RA, 74 patients were optimised (44 under Ada and 30 under Ifx). Baseline demographic caracteristics are shown in the table below.During the 24 months after the pre-op visit, 55,4% (41)of the patients presented at least one flare,with an average of 1,38 flares [1–5]. Most of the patients (53.7%,22/41),were controlled with the adjustment of non biological treatment.Only 39,0% (16) of the patients,had to go back to the previous optimised dose and 7,3% (3)to the standard dose.88% (39/41)were controlled after the dose modification.104 flares were collected,33% (34) happened at the 3rd month and 20% (21) at 24th. In the population who presented flares, we observed a persistent higher DAS Vs the patients who never presented flares (DAS pre-op 3,20±1,16 Vs 2,26±0,59;DAS 24month 3,61±1,13Vs2,10±0,65;p=0,007). A least proportion of patients with flares were in supra-optimal range (13,3% with flares vs 26% without, p=0,007). At baseline, no clinical factors were predictive of flare. Nor were blood sample results. In contrast, a higher disease activity, measured by DAS pre-op (p=0,004),a worst EULAR answer (p=0,027) and not being in supra-optimal range (p=0,032),were statistically correlated with flares development at the univariate analysis. Time to the optimisation tended to the significance (OR=1,152; p=0.08). In the multivariate analysis, only a higher DAS pre-op (OR:2,00,[1,08–3,73])and being in optimal (OR:5,90, [1,38–25,2])and sub-optimal range (OR=6,05 [1,28–28,7]), were independently correlated.

	N Total= 74
Sex	Women 83,8 % (62) Men 16,2 % (12)
Age	64,1 (+/-12,6)
Age at diagnosis	41,6 (+/-14,0)
bDMARD	Ada 59,5% (44) IFX 40,5% (30)
Time to the beginning of bDMARD (years)	10,7 (+/- 7,50)
Time to optimisation (years)	4,70 (+/-3,12)
Treatment duration (years)	8,80 (+/-4,00)
RF +	75,7% (56)
ACPA +	73,0% (54)
Smoking	No smokers 68.9% (51) Smokers 17,6% (13) Ex smokers 12,2% (9)
BMI	25,6 (+/-4,61)
Methotrexate (MTX)	74,3% (55)
Average dose MTX (mg/sem)	12,3 (+/-8,60)
Other sDMARD	54,1% (40)
sDMARD	Leflunomide 62,5% (25) Salazopyrine 15% (6) Hydroxychloquine 10% (4) Leflunomide+SZP 5% (2) Leflunomida+HCQ 5% (2) SZP+HCQ 2,5% (1)
Prednisone	37,8% (28)
Prednisone dose (mg/día)	1,89 (+/-2,62)
DAS baseline	5,03 (+/-1,35)
VSG baseline	34,7 (+/-18,9)
PCR baseline	10,2 (+/-12,5)

Conclusions: In our cohort of optimised patients, we noted a high proportion of flares. However, flares were controlled with dosage readjustment without needing a treatment change. Independently correlated predictive factors for flares were a higher disease activity measured by DAS and not being in therapeutic range in the pre-optimisation visit.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6859

AB0375 THE EFFECT OF CONCOMITANT USE OF METHOTREXATE ON THE CLINICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDER ANTI-TNFTHERAPY

A. Martinez-Feito[1], C. Plasencia[2], B. Hernandez-Breijo[1], A. Jochems[1], C. Diego[3], A. Villalba[2], D. Peiteado[2], L. Nuño[2], P. Nozal[3], A. Balsa[2], D. Pascual-Salcedo[1]. *[1]Immuno-Rheumatology research group; [2]Rheumatology; [3]Immunology, University Hospital la Paz, madrid, Spain*

Background: Several publications in rheumatoid arthritis (RA) have demonstrated a beneficial effect of concomitant methotrexate (MTX) use with TNF inhibitors (TNFi), mainly because of the MTX effect in reducing immunogenicity. In a previous work in the RA-La Paz cohort, we found that the concomitant use of MTX had a positive effect on the pharmacokinetics of serum TNFi levels, decreasing the immunogenicity of these drugs. Furthermore, the MTX effect was dose-dependent, being greater at high MTX dose. Currently, we investigate the effect of concomitant MTX use on the clinical response.
Objectives: To investigate the MTX influence on the clinical response in the RA-La Paz cohort treated with Infliximab (Ifx), Adalimumab (Ada) or Etanercept (Etn) at one year of treatment.
Methods: This is an observational study from a prospective cohort from the Biological Unit of the University Hospital La Paz, Madrid, Spain that analysed a total of 293 RA patients treated with Ifx (112 patients), Ada (71 patients) and Etn (110 patients). Patients were grouped according to the MTX dose: no MTX, low dose (LD: ≤12.5 mg/week), intermediate dose (ID: 15–17.5 mg/week) and high dose (HD: ≥20 mg/week). For this study, the clinical response was evaluated by DAS28-ESR and the clinical improvement by∆DAS28. Data were collected at baseline, 0.5 and 1 year of TNFi treatment. Statistical analysis was performed using GraphPad Prism 6.0 software.
Results: Out of 293 RA patients (pts) under TNFi treatment, 184 (71 with Ifx, 40 with Ada and 73 with Etn) were included. In this cohort, 128 (70%) pts used concomitantly MTX (91% oral administration) and 56 (30%) pts were in monotherapy. No differences in DAS28 were found at baseline between patients with or without MTX (p=0.8).
After one year of treatment, pts with TNFi +MTX have a significantly lower DAS28 than patients without MTX (3.3±1.3 vs 3.9±1.1; p=0.004). When analyzing the DAS28 values in relationship to the MTX dose, statistical differences are observed with use of HD (≥20 mg/week) (3.1±1.3 with HD vs 3.9±1.1 without MTX; p=0.001) but not with intermediate (3.4±1.2 with ID vs3.9±1.1 without MTX; p=0.06) or low MTX dose (3.8±1.6 with LD vs 3.9±1.1 without MTX; p=0.4) at 1 year of therapy.
Clinical improvement by∆DAS28 was higher in patients with TNFi +MTX than in patients without MTX (1.7±1.4 vs 1±1.3p=0.007). This effect was observed with all MTX doses (1.7±1.5 with HD vs 1±1.3 without MTX, p=0.01; 1.6±1.3 vs with ID 1±1.3without MTX, p=0.03; 1.8±1.3 with LD vs 1±1.3 without MTX, p=0.01).
Conclusions: In the RA-La Paz cohort under TNFi treatment, the concomitant use of MTX has a positive effect on the clinical activity, mainly when high dose of MTX is used. Moreover, we demonstrate a positive effect of any MTX dose on the clinical improvement at one year of treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2884

AB0376 CARTILAGE OLIGOMERIC MATRIX PROTEIN, A BIOMARKER OF ARTHRITIS, COULD BE USEFUL FOR PREDICTING THE RESPONSE TO BIOLOGIC THERAPY IN RHEUMATOID ARTHRITIS?

B.I. Gavrila[1], C. Ciofu[1], C. Mihai[1], G. Udrea[1], M. Bojinca[1], V. Stoica[1], E. Panaitescu[2]. *[1]Department of Internal Medicine and Rheumatology Cantacuzino Hospital; [2]Medical Informatics and Biostatistics, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

Background: introduction of biologic therapy has revolutionized the treatment of Rheumatoid Arthritis (RA). Despite these advances, 20–40% of the patients are declared nonresponders to at least one of the therapies (1).High costs and patient exposure to severe adverse reactions (ex. infections) determined the need to identify biomarkers that can distinguish pretreatment responders versus nonresponder patients.
Objectives: evaluating the predictive role for the response to anti tumor necrosis factor therapy (anti-TNF) of cartilage oligomeric matrix protein (COMP), a specific serological marker, which evaluates the articular cartilage degradation and its turnover.(2)
Methods: prospective and observational study including 64 patients followed 12 months with active RA, uncontrolled by conventional synthetic DMARDs.Clinical assessment was performed at 0, 6 and 12 months according to ACR criteria approved by OMERACT and evaluation of treatment response according to EULAR criteria (good /moderate /nonresponder).

Results: of the 64 patients included in the study, 59 (92.2%) were women and 5 (7.8%) men, mean age 57.55±9.42 years. After 6 months, 7 patients were declared nonresponders, 38 achieved a moderate response and 19 good response.
Following baseline COMP titres and the EULAR response at 6 months, general tests identified significant differences between groups. Lower baseline titres had predictive value for achieving a good response (746.04±130.095 ng/ml) comparing with moderate responders (1032.8±188.671ng/ml) and nonresponders (1042.2±181.717 ng/ml, p=0.0000).
After 12 months 11 patients achieved moderate response, 44 a good response and just 1 patient was declared nonresponder. At this visit, even if we didn't find significant differences between baseline COMP titres and the EULAR response (p=0.1430), we observed lower baseline titres for good responders (917.8±219.943 ng/ml) versus moderate responders (1042.7±193.117 ng/ml).
Grouping patients in 2 categories (responders/nonresponders) there were no differences between groups at 6 months (937.27±218.106 ng/ml versus 1042.2±181.717 ng/ml, p=0.227) or 12 months (942.82±219.025 ng/ml versus 896.5±0.000 ng/ml, p=0.9753).
Following the status pretreatment of COMP and EULAR response at 6 months, we identified differences between groups (p=0,0001), all 7 patients declared nonresponders were COMP positive and only 13/19 (68.4%) of good responders were tested positive. At 12 months there were no differences between pretreatment status of COMP and response to treatment (p=0.2805).
Regarding the evolution of serum levels, we noticed a decrease statistically significant from baseline (948.75±215.683 ng/ml) to 12 months (740.88±227.04 ng/ml, p=0.0000).
Conclusions: COMP could be one of the biomarkers for identifying pretreatment the patients who will respond to biologic therapy in Rheumatoid Arthritis.
References:
[1] Chaves Chaparro LM, Salvatierra Ossorio J, Raya Álvarez E Reumatol Clin. 2011 Mar-Apr; 7(2):141–4.
[2] Morozzi G, Fabbroni M, Bellisai F, Cucini S, Simpatico A, Galeazzi MClin Rheumatol. 2007 Aug; 26(8):1335–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1241

AB0377 SWITCHING FROM BIO-ORIGINAL ETANERCEPT TO BIOSIMILAR ETANERCEPT SB4: PATIENT ACCEPTABILITY AND OUTCOMES IN THE REAL WORLD

C. Holroyd[1], D. Wallis[1], S. Bennett[1], P. Clayton[1], C.J. Edwards[2].
[1]Rheumatology; [2]NIHR Wellcome Trust Clinical Research Facility, University Hospital Southampton, Southampton, United Kingdom

Background: A number of studies have demonstrated the efficacy of biosimilar therapies including SB4 (a biosimilar-etanercept). However, real world data of the process of switching, acceptability to patients, efficacy and safety is lacking.
Objectives: To obtain real world data of the acceptability and outcomes of patients with severe (eligible for TNFi therapy as defined by UK NICE) rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) who switch from bio-original etanercept (boDMARD-ETN) to the bsDMARD etanercept SB4 (bsDMARD-ETN).
Methods: Adult patients, with RA, PsA & AS, currently enrolled in the SMaRT study and switching from boDMARD-ETN to bsDMARD-ETN were followed for 6 months. Primary outcome was change in DAS28, PsARC response or BASDAI following switching. Additional outcomes included; % change of remission rate, HAQ-DI, CRP or ESR levels, patient satisfaction, PDUS and SAEs leading to discontinuation. All patients had severe disease and were receiving boDMARD-ETN as per local guidelines of UK NICE. Analysis was performed in a similar way to a cross-over RCT trial design where patients act as their own control with the experience in the 6 and 12 months prior to switching used as the control for experience after switching.
Patient education and support during the switch included: rheumatologist face to face discussion, letter giving details of the switch and bsDMARD-ETN information sheet, patients invited to discuss switch in clinic, helpline number with patients advised to call for further information or to report adverse events (AEs), routine review in clinic 3 months after switching, and then 6 monthly thereafter or more often if clinically necessary.
Results: Following the education and support programme 99% of patients agreed to switch to bsDMARD-ETN (one declined due to concerns about allergic reactions to previous therapies). To date 92 patients have switched from boDMARD-ETN to bsDMARD-ETN and been followed up for more than 6 months (58 RA, 15, AS, 16 PSA and 4 enteropathic arthritis; mean age 55.9 (14.9) yrs, (56 female, 36 male), mean disease duration 16.8 (10.9) yrs, duration on boDMARD-ETN before switch mean 4.85 (3.92) yrs and duration since switch 204.1 (51.4) days. After 6 months following the switch 91% of patients using bsDMARD-ETN have continued with mean last DAS28 – 2.67 (1.32) for RA patients and mean last BASDAI – 4.58 (2.47). Following the switch 8 patients stopped bsDMARD-ETN after mean of 93.6 (56.4) days, the reasons for this were 7/8 clinician/patient determined inefficacy (6 returned to boDMARD-ETN, 1 switched to certolizumab), 1/8 switched after reporting palpitations and poor concentration. In the control period 6 months before switching 17/110 patients stopped boDMARD-ETN (85% continued) including 7 due to primary failure, 7 due to secondary failure, 1 adverse event (AE), 1 patient choice, 1 death (Lung cancer in male ex-smoker with longstanding RA who had received boDMARD-ETN for 10 yrs).
Conclusions: An education programme prior to switching to a biosimilar TNFi leads to a high uptake by patients. In follow-up of 6 months after switching from boDMARD-ETN to a bsDMARD-ETN there appears to be a low rate of discontinuation due to inefficacy or AEs.
Acknowledgements: Biogen supported this work through an unrestricted grant.
Disclosure of Interest: C. Holroyd Speakers bureau: Abbvie, UCB, Roche, Pfizer, D. Wallis: None declared, S. Bennett: None declared, P. Clayton: None declared, C. Edwards Grant/research support from: Abbvie, Roche, Pfizer, Biogen, Speakers bureau: Merk, Abbvie, UCB, Roche, Pfizer, Celgene, Janssen, Celltrion, Lilly
DOI: 10.1136/annrheumdis-2017-eular.3672

AB0378 IMPROVED CLINICAL OUTCOMES AND PHYSICAL ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ADALIMUMAB IN CENTRAL AND EASTERN EUROPE

D. Karateev[1], C. Codreanu[2], B. Rojkovich[3], M. Hojnik[4], E. Smirnova[5].
[1]Nasonova Research Institute of rheumatology, Moscow, Russian Federation; [2]"Dr. Stoia" Center for Rheumatic Diseases, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania; [3]Hospital of Hospitaller Brothers of St. John of God, Budapest, Hungary; [4]AbbVie, Ljubljana, Slovenia; [5]AbbVie, Moscow, Russian Federation

Background: Although physical activity has known positive impacts upon pain, disease activity and functional status in patients with rheumatoid arthritis (RA), very little is known about physical activity in patients with RA on biologic therapy.
Objectives: To evaluate the effect of adalimumab treatment on physical activity and relationship with improvements in disease activity and physical function in patients with RA in routine clinical practice.
Methods: This was a 52-week multi-center, post-marketing observational study conducted in 7 countries in Central and Eastern Europe (CEE). Eligible RA patients were prescribed originator adalimumab according to the local practice; visits were performed approximately 3 months apart. Physical activity was assessed by validated Short QUestionnaire to ASsess Health-enhancing physical activity (SQUASH)[1,2], which measures habitual physical activity across four domains: commuting, leisure time and sport, household, work and school. RA disease activity was assessed by DAS28 and physical function by HAQ-DI; clinical remission (REM) and low disease activity (LDA) were defined as DAS28<2.6 and <3.2, respectively. Descriptive statistical analyses were performed, observed data are presented.
Results: 462 patients were enrolled and 255 patients completed the study. Mean age was 53.9 (±12.1) yrs; 82.2% of enrolled patients were female; average disease duration was 7.8 (±7.5) yrs. DAS28 decreased from 6.1 (±1.1) at baseline to 2.9 (±1.0) at study end, whereas the mean HAQ-DI from 1.6 (±0.6) to 0.7 (±0.5). The proportion of patients in LDA and REM at study end was 56.0% and 31.1%, respectively. Total SQUASH score increased from 4772 (±4132) to 6104 (±4921), representing 28% improvement in overall physical activity. The largest score improvements were seen in the SQUASH domains of leisure time and sport (by 43%), followed by household activities and activities at work and school (each by 19%). The correlations between the total SQUASH score and its subscores with DAS28 were weak both at baseline and study end. A significant correlation between the total SQUASH and HAQ-DI scores was seen at baseline (r -0.30), but not at the study end (r -0.22). Correlations between SQUASH subscores and HAQ-DI were not significant. The percentage of work disabled subjects decreased from 22% to 17%. According to linear regression analysis, sociodemographic factors did not substantially influence habitual physical activity.
Conclusions: Treatment with adalimumab in clinical practice in CEE resulted in clinically meaningful improvements in disease activity and physical function as well as improvements in physical activity. The correlation between the scores for disease activity, physical function and physical activity were however poor and there was no clear influence of the standard sociodemographic factors on physical activity.
References:
[1] Wendel-Vos WGC. et al. J Clin Epidemiol 2003; 56: 1163–9.
[2] Campbell N. et al. J Phys Act Health. 2016;13(2):154–8.
Acknowledgements: Funding: The design, study conduct, and financial support for the clinical trial were provided by AbbVie. AbbVie participated in the interpretation of data, drafting, review, and approval of the abstract.
Disclosure of Interest: D. Karateev Grant/research support from: Pfizer, Consultant for: Pfizer, Tirupharm, Biocad, Egis, R-Pharm, Novartis, Speakers bureau: Abbvie, Bristol Myers Squibb, Pfizer, Roche, Tirupharm, Biocad, R-Pharm, Novartis, Egis, MSD, UCB, C. Codreanu Grant/research support from: AbbVie, Amgen, BMS, Egis, MSD, Pfizer, Roche, Sanofi, UCB, Consultant for: AbbVie, Amgen, Angellini, Astra Zeneca, BMS, Egis, MSD, Pfizer, Richter, Roche, Sanofi, Servier, Teva, UCB, Zentiva, Speakers bureau: AbbVie, Amgen, Angellini, Astra Zeneca, BMS, Egis, MSD, Pfizer, Richter, Roche, Sanofi, Servier, Teva, UCB, Zentiva, B. Rojkovich Grant/research support from: AbbVie, Amgen, Novartis, Sanofi, UCB, Consultant for: Abbvie, Pfizer, Roche, Speakers bureau: Abbvie, Pfizer, Roche, M. Hojnik Employee of: AbbVie, E. Smirnova Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.4034

AB0379 EFFICACY OUTCOMES FOR ORIGINATOR TNF INHIBITORS AND BIOSIMILARS IN RHEUMATOID ARTHRITIS AND PSORIASIS TRIALS: A SYSTEMATIC LITERATURE REVIEW

R. Moots[1], C. Curiale[2], D. Petersel[2], C. Rolland[3], H. Jones[2], E. Singh[2], E. Mysler[4]. *[1]University of Liverpool, Liverpool, United Kingdom; [2]Pfizer, Collegeville, United States; [3]Envision Pharma Group, London, United Kingdom; [4]Organización Médica de Investigación, Buenos Aires, Argentina*

Background: Regulatory approval of biosimilar versions of innovator biotherapeutics requires that new biological products be highly similar to innovator products, with no clinically meaningful differences in safety, purity, and potency.[1,2] Pre-specified margins for equivalence in efficacy have been met in comparative trials of biosimilars of tumour necrosis factor inhibitors (TNFis) in rheumatoid arthritis (RA)[3] and plaque psoriasis (PsO),[4] supporting biosimilarity, but differences in treatment responses between originator pivotal trials and biosimilar trials have posed some interesting questions.
Objectives: To compare American College of Rheumatology 20% response (ACR20) and Psoriasis Area Severity Index 75% (PASI75) responses to originator TNFis in pivotal trials with those to originator TNFis and TNFi biosimilars in biosimilar trials in RA and PsO.
Methods: Historical data from originator pivotal trials (averaged across trials) were obtained from published systematic literature reviews. Searches were conducted to identify comparative randomized clinical trials of approved or proposed biosimilars of adalimumab (ADA), etanercept (ETN), and infliximab (INF) using Embase®, MEDLINE®, the Cochrane Central Trials Register and Database of Systematic Reviews, and other Cochrane Library databases, and 2015/16 congress abstracts. To reduce variability, only studies conducted in disease-modifying antirheumatic drug-experienced patients treated with the same biologic dosages and assessed at the same time points were selected for analysis.
Results: Of 83 publications initially identified, 16 publications were included for analysis (RA: originators, n=4; biosimilars, n=6; PsO: originators, n=3; biosimilars, n=3). Higher proportions of ACR20 responders were found among RA patients receiving the originator biologics and biosimilars in biosimilar trials, than among patients receiving the originator biologics in pivotal trials (Table). Insufficient data were available from ADA and INF biosimilar studies in PsO; in ETN studies in PsO, a difference was also observed in the proportions of PASI75 responders between biosimilar and pivotal trials.

Table: ACR20 and PASI75 responders in pivotal vs biosimilar trials and differences in response rates

Product	RA trial type	Time point (wk)	ACR20 responders, %	Difference, pivotal vs biosim, %
ADA	Pivotal[5,6]	24	65	—
ADA	Biosim[7]	24	72	10
	Biosim[8]	24	72	9
ABP 501	Biosim[7]	24	75	13
SB5	Biosim[8]	24	73	10
ETN	Pivotal[9]	24	71	—
ETN	Biosim[3]	24	80	12
	Biosim[10]	24	91	22
SB4	Biosim[3]	24	78	9
CHS-0214	Biosim[10]	24	91	22
INF	Pivotal[11]	30	50	—
INF	Biosim[12]	30	59	15
	Biosim[13]	30	59	15
CT-P13	Biosim[12]	30	61	18
SB2	Biosim[13]	30	56	10
Product	**PsO trial type**	**Time point (wk)**	**PASI75 responders, %**	**Difference, pivotal vs biosim, %**
ETN	Pivotal[14,15]	12	43	—
ETN	Biosim[4]	12	72	40
GP2015	Biosim[4]	12	70	39

5. Keystone EC, et al. *Arthritis Rheum* 2004;50:1400-11; **6.** Weinblatt ME, et al. *Arthritis Rheum* 2003;48:35-45; **7.** Cohen SB, et al. *Arthritis Rheumatol* 2015;67(suppl 10); **8.** Weinblatt ME, et al *Arthritis Rheumatol* 2015;67(suppl 10); **9.** Weinblatt ME, et al. *N Engl J Med 1999;340:253-9*; **10.** O'Dell J, et al. *Ann Rheum Dis* 2016;75(suppl 2):143; **11.** Maini R, et al. *Lancet* 1999;354:1932-9; **12.** Yoo DH, et al. *Ann Rheum Dis* 2013;72:1613-20; **13.** Choe JY, et al. *Ann Rheum Dis* 2017;76:58-64; **14.** Papp KA, et al. *Br J Dermatol* 2005;152:1304-12; **15.** van de Kerkhof PC, et al. *Br J Dermatol* 2008;159:1177-85.

Conclusions: Differences were observed in treatment response rates between originator pivotal trials and more recent trials of originator biologics and their respective biosimilars. Such differences in outcomes may be attributable to fundamental differences in study design and/or baseline patient characteristics, which require further analysis. Additional research is also needed to explore the clinical relevance of these differences.
References:
[1] US Food and Drug Administration. http://www.fda.gov/downloads/Drugs/ GuidanceComplianceRegulatoryInformation/ Guidances/UCM291128.pdf.
[2] European Medicines Agency. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/01/WC500180219.pdf.
[3] Emery P, et al. Ann Rheum Dis. 2017;76:51–7.
[4] Griffiths CE. Br J Dermatol. 2016. Oct 27 [e-pub].
Disclosure of Interest: R. Moots Grant/research support from: Novartis, Pfizer, Consultant for: Abbvie, BMS, Cellgene, Chugai, C. Curiale Shareholder of: Pfizer, Employee of: Pfizer, D. Petersel Shareholder of: Pfizer, Employee of: Pfizer, C. Rolland Employee of: Envision Pharma Group, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, E. Singh Shareholder of: Pfizer, Employee of: Pfizer, E. Mysler Consultant for: Abbvie, BMS, Pfizer, Roche, Pharma, GEMMA, Mabxience
DOI: 10.1136/annrheumdis-2017-eular.1851

AB0380 RESULTS FROM A RANDOMIZED, SINGLE-BLIND, SINGLE-DOSE, PARALLEL-GROUP STUDY IN HEALTHY SUBJECTS DEMONSTRATING PHARMACOKINETIC SIMILARITY BETWEEN ABP 710 AND INFLIXIMAB

E. Krishnan, V. Chow, N. Zhang, A. Kaliyaperumal, P. Kaur. *Amgen, Thousand Oaks, United States*

Background: ABP 710 is being developed as a biosimilar with the same amino acid sequence as infliximab, an anti-tumor necrosis factor therapy. Analytical and functional comparisons between ABP 710 and infliximab have been conducted and completed.
Objectives: This report describes the results of analyses comparing the pharmacokinetics (PK), safety, and immunogenicity of ABP 710 and infliximab sourced from the European Union (EU).
Methods: This was a single-blind, single-dose, parallel-group study among healthy adults, 18 to 45 years of age and with a body mass index of 18 to 30 kg/m^2. Subjects were randomized to receive a 5 mg/kg intravenous infusion of either ABP 710 or infliximab. The primary objective of this analysis was demonstration of PK similarity of ABP 710 to infliximab based on area under the serum concentration-time curve from time 0 extrapolated to infinity (AUC_{inf}; primary endpoint). PK equivalence was deemed achieved if the geometric mean (GM) ratio and its 90% confidence interval (CI) for AUC_{inf} was within the range of 0.80 and 1.25. Secondary endpoints included maximum observed serum concentration (C_{max}), area under the serum concentration-time curve from time 0 to last quantifiable concentration (AUC_{last}), safety, and immunogenicity.
Results: *Pharmacokinetics:* A total of 49 subjects received ABP 710 and 49 subjects received infliximab. Following a single dose, the adjusted least square (LS) GM of AUC_{inf}, AUC_{last}, and C_{max} for ABP 710 was 33559 μg·h/mL, 31789 μg·h/mL, and 123 μg/mL, respectively. The adjusted LS GM of AUC_{inf}, AUC_{last}, and C_{max} for infliximab was 33706 μg·h/mL, 31847 μg·h/mL, and121 μg/mL, respectively. Ratios of adjusted LS GMs (90% CIs) between ABP 710 and infliximab for AUC_{inf}, AUC_{last}, and C_{max} were 0.996 (0.904, 1.096), 0.998 (0.918, 1.086), and 1.021 (0.962, 1.083), respectively.
Safety: There was one subject in the infliximab group who developed polyarthritis that resolved with treatment and the subject completed the study. There were no deaths, other serious adverse events, or treatment-emergent adverse events (TEAEs) leading to discontinuation from the study. The incidence of TEAEs was similar in the two treatment groups (ABP 710: 83.7%; infliximab: 83.7%); the majority of TEAEs were mild or moderate. The most frequently reported TEAEs were somnolence, headache, nasopharyngitis, upper respiratory tract infection, nausea, and lethargy.
Immunogenicity: All subjects tested negative for antidrug antibodies (ADAs) prior to dosing. At the end of study (Day 57), 40% of subjects in the ABP 710 group and 27% in the infliximab group were positive for binding ADAs, and 13% of subjects in the ABP 710 group and 19% in the infliximab group were positive for neutralizing ADAs.
Conclusions: Results of this phase 1 study demonstrate PK similarity between ABP 710 and infliximab sourced from the EU among healthy subjects. The safety and immunogenicity profile were comparable between the treatment groups.
Disclosure of Interest: E. Krishnan Shareholder of: Amgen Inc., Employee of: Amgen Inc., V. Chow Shareholder of: Amgen Inc., Employee of: Amgen Inc., N. Zhang Shareholder of: Amgen Inc., Employee of: Amgen Inc., A. Kaliyaperumal Shareholder of: Amgen Inc., Employee of: Amgen Inc., P. Kaur Shareholder of: Amgen Inc., Employee of: Amgen Inc.
DOI: 10.1136/annrheumdis-2017-eular.3281

AB0381 CHANGE IS GOOD, BUT WHAT IS BETTER? RETROSPECTIVE STUDY IN CLINICAL PRACTICE FIRST SWITCH WITH DIFFERENT BIOLOGICAL THERAPIES IN RHEUMATOID ARTHRITIS

F.A. Ojeda, C. Pérez-García, E. Beltran, A. Pros, T. Salman-Monte, F. Castro, L. Polino, P. Corzo, I. Carrión, S. Castell, P. Benito. *Rheumatology, Hospital del Mar, Barcelona, Spain*

Background: The effectiveness of the switch when the first anti-TNF failure in patients with rheumatoid arthritis has been demonstrated in multiple studies. But what is more effective, if you make the switch to another anti-TNF or another molecule, is not clearly defined.
Objectives: A retrospective study was performed in clinical practice to determine if there is a response to DAS 28 at 6 months of change and whether there is a difference in response if the switch is performed on another anti-TNF or another biological.
Methods: From a total of 254 that met ACR 2010 criteria for RA, which have been biologically treated at Rheumatology of the Parc Salut Mar from 2000 to 2016, 61 (24%) were the first switch and the DAS 28 response at 3 and 6 months of follow-up. The following variables were analyzed: age, sex, years of evolution RA, erosions, FR, ACPA, type of biological treatment, DAS 28 at the start of the switch, 3 months and 6 months,% of patients presenting DAS 28 <2, 6 at 6 months.The statistical study was performed with SPSS 20 for paired and independent quantitative variables with Student's T and chi2 for qualitative variables
Results: Of the total of 61 first treatment changes, 27 (44.3%) were to another anti-TNF alpha, 23 (37.7) to tocilizumab (TCZ), 7 to abatacept (11.5%) and 4

to RTX (6,6). The demographic and response data DAS 28 are shown in Table 1. There are no differences in the years of evolution,% of women, FR or ACPA positive, erosions and disease activity, as measured by DAS 28, before the switch, between The two groups (anti-TNF vs non-anti-TNF). Patients in the anti-TNF group were slightly younger than non-anti-TNF.When the DAS 28 response is evaluated at 3 and 6 months, modifying the treatment is effective (DAS 28 beginning 4,40 vs DAS 28 6 months 2.8 $p<0.001$). When assessing the response to change, there is no difference in the DAS 28 response at 3 months or 6 months, if you switched to anti-TNF or non-anti-TNF (3.18 vs 2.52 p=0.122).
When comparing the patients with anti TNF alpha vs TCZ, 62.5% of the patients with TCZ are in remission compared to 38, 5% (p=0.047).

Table 1

	Total n=61	Swich anti-TNF alpha n=26	Swich No anti-TNF alpha n=35	p
Age (years)	60.08±11,5	56.19±8,4	62.97±12,8	0.023
Sex (% M)	80.3	84.6	77.1	0.532
Years evolution (years)	17.44±9,4	18.92±11,6	16.34±7,4	0.298
Erosion (%)	90.2	92.3	88.6	1.000
FR+ (%)	77.0	76.9	77.1	1.000
ACPA+ (%)	91.8	88.5	94.3	0.642

Table 2

	Total n=61	Swich anti-TNF alpha n=26	Swich No anti-TNF alpha n=35	p
DAS 28 Swich	4.40±1,38	4.61±1,5	4.21±1,3	0.216
DAS 28 3 months	3.18±1,52	3.52±1,09	2.96±1,7	0.167
DAS 28 6 months	2.8±1,54	3.18±1,74	2.52±1,3	0.122
DAS 28 <2.6 6 m (%)	52.5	38.5	62.5	0.047

Conclusions: In this retrospective study in daily clinical practice, it is evident that the change in treatment after failure of the first biological one, without differences if the change is to an anti TNF or another treatment. The percentage of patients who are remission at 6 months is higher if the change is at TCZ. Given the small number of patients, larger studies would be needed to confirm the results.
References:
[1] Johnston SS et col. Comparison of Biologic Disease-Modifying Antirheumatic Drug Therapy Persistence Between Biologics Among Rheumatoid Arthritis Patients Switching from Another Biologic. Rheumatol Ther.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3375

AB0382 OUTCOMES OF ETANERCEPT THERAPY IN ELDERLY RHEUMATOID ARTHRITIS PATIENTS: AN INVESTIGATION OF THE AKITA ORTHOPEDIC GROUP ON RHEUMATOID ARTHRITIS REGISTRY

H. Aonuma[1], T. Kashiwagura[2], M. Urayama[3], M. Kobayashi[4], T. Aizawa[5], Y. Sugimura[6], N. Miyakoshi[7], Y. Shimada[7]. *[1]Orthopedic Surgery, Kakunodate Municipal Hospital, Senboku; [2]Orthopedic Surgery, Akita City Hospital, Akita; [3]Orthopedic Surgery, Ogachi Central Hospital, Yuzawa; [4]Orthopedic Surgery, Hiraka General Hospital, Yokote; [5]Orthopedic Surgery, Kita Akita Municipal Hospital, Kita Akita; [6]Orthopedic Surgery, Nakadori General Hospital; [7]Orthopedic Surgery, Akita University Graduate School of Medicine, Akita, Japan*

Background: The Akita Orthopedic Group on Rheumatoid Arthritis (AORA) encompasses 32 physicians and 28 clinics providing medical care to rheumatoid arthritis (RA) patients in Akita Prefecture, Japan. The patient registry for this group (the AORA registry) reflects actual clinical data on RA therapy in Akita, where the proportion of elderly (age ≥65 years) residents in the population is the highest in Japan. Etanercept (ETN) is a tumor necrosis factor inhibitor reportedly associated with fewer adverse event-related treatment discontinuations than other drugs of this class. However, few evaluations of the efficacy and safety of ETN have been reported for elderly populations.
Objectives: Based on data from the AORA registry, we aimed to investigate the continuation rate for ETN therapy, reasons for discontinuation, and therapeutic effects among elderly RA patients living in Akita.
Methods: Among 204 AORA-registered patients starting ETN therapy between January 2009 and August 2014, data for the 73 patients (35.8%) who were ≥65 years old at the initiation of therapy were evaluated. Mean age was 72.4±4.7 years (range 65–83 years), and 79.5% were women. Mean disease duration was 15.1±12.6 years (range 9 months-55 years), 13.7% of patients were switching from another biologic agent, 49.3% could perform activities of daily living (ADL) independently, and 65.8% had at least one of the following comorbidities: hypertension, diabetes, respiratory disorder, cardiovascular disease, and cerebrovascular disease. We evaluated the 1-year cumulative continuation rate for ETN therapy using the Kaplan–Meier method, and investigated the characteristics of patients who discontinued treatment because of adverse events (AE cohort) or lack of efficacy (LOE cohort). We evaluated efficacy in 55 patients for whom Disease Activity Score – C-reactive protein assessments were possible, based on European League Against Rheumatism (EULAR) criteria.
Results: The 1-year cumulative continuation rate for ETN therapy was 87.2%, and 24 patients discontinued treatment. The AE and LOE cohorts contained 12 and 7 patients, respectively. The AE cohort had a mean age of 75.5 years at the start of treatment, with a mean disease duration of 20.7 years, 8.3% of patients switching from another biologic agent, 16.7% performing ADL independently, and a comorbidity rate of 100%. Corresponding values for the LOE cohort were: mean age, 71.4 years; disease duration, 12.7 years; switching from another biologic agent, 42.9%; performing ADL independently, 57.1%; and comorbidity rate, 28.6%. Efficacy was noted for 81.8% of all patients with 52 weeks of ETN therapy, achieving good efficacy in 21 cases and moderate efficacy in 24 cases.
Conclusions: Retention rate and efficacy were considered satisfactory in elderly RA patients receiving ETN therapy. The risk of adverse events was suggested to increase with increasing age, declining ADL, and presence of comorbidities. These factors require attention when prescribing ETN therapy.
References:
[1] Cho SK, Sung YK, Kim D, et al. Drug retention and safety of TNF inhibitors in elderly patients with rheumatoid arthritis. BMC Musculoskelet Disord. 2016; 17: 333.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6102

AB0383 SUBCLINICAL BRAIN DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS RELATIONSHIP TO TNF BLOCKER THERAPY

S. Sağ, I. Tekeoğlu, M.S. Sağ, A. Kamanlı, K. Nas. *Department of Physical Medicine and Rehabilitation, Rheumatology, Faculty of Medicine, Sakarya University, Sakarya, Turkey, sakarya, Turkey*

Background: RA is a chronic disease with a yet unclarified etiology, which causes the activation of pro-inflammatory pathways that bring about joint and systemic inflammations (1).In recent years, the pathophysiology of brain damage that can occur in RA has drawn attention. Emphasis is being put on the possibility that brain damage occurs due to blood-brain barrier (BBB) damage that is linked to chronic inflammation
Objectives: In this study, we aimed to investigate the peripheral blood levels of brain-specific proteins such as S100 beta and GFAP (glial fibrillary acidic protein), the differences in these proteins in patients who did and did not undergo TNF blocker therapy and their relationship with cranial MR lesions, disease activity and cognitive functions with the purpose of determining CNS (central nervous system) damage in patients with rheumatoid arthritis (RA).
Methods: 58 RA patients (47 (81.0%) females, 11 (19.0%) males) and 34 healthy controls (24 (70.6%) females, 10 (29.4%) males) were included in the study. All RA patients were on synthetic DMARD therapy at the beginning. While 30 patients continued sDMARD therapy, 28 patients with high disease activity were started on TNF blocker therapy. All demographic characteristics of the patients were recorded. Disease activity was evaluated using DAS28. The Mini-Mental State Examination (MMSE) was used to evaluate cognitive functions, and the Fazekas Scale was used to assess the cranial MRI lesions. The peripheral blood S100 beta, GFAP, claudin, IL-17, IL-1 beta levels of the patients were measured at the beginning and on the 6th month.
Results: Demographic characteristics were similar between the two groups and no statistical difference was detected between the patient group and the control group in terms of sex, age, and BMI. ($p>0.05$) S100 beta and GFAP levels were higher to a significant degree compared to the control group. ($p<0.05$) In the group that was started on TNF blocker therapy, S100 beta and GFAP levels were detected to have decreased significantly 6 months after treatment compared to the start of treatment. ($p<0.05$) No difference was found between the RA and control groups in terms of hyperintense lesions seen in the cranial MRI. ($p>0.05$) As the lesions in the deep white matter seen in the cranial MRI of RA patients increased, their S100 beta levels were also seen to increase. ($p<0.05$)
Conclusions: In conclusion, next to decreasing disease activity and joint erosions by suppressing inflammation, anti-TNF therapy in RA can also suppress potential brain damage linked to subclinical BBB (blood-brain-barrier) dysfunction. Further studies with broader participation and longer patient follow-up are needed to reinforce this hypothesis.
References:
[1] McInnes, I.B. and Schett, G. (2011). Thepathogenesis of rheumatoidarthritis. N Engl J Med 365, 2205 2219.doi:10.1056/ NEJMra1004965.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2315

AB0384 CLINICAL AND RADIOLOGICAL EVOLUTION IN RHEUMATOID ARTHRITIS (RA) PATIENTS AFTER DEINTESIFICATE BIOLOGICS

J. Uceda, R. Hernandez, J.L. Marenco. *Rheumatology, Valme University Hospital, Seville, Spain*

Background: RA is the most common chronic inflammatory arthritis. About 30% of patients are treated with biological therapy (BT). Deintensification of BT for patients in clinical remission, is a strategy used in clinical practice to reduce side effects and burden.
Objectives: The primary endpoint was evaluate clinical and radiological behavior of the RA in patients receiving BT at reduced doses.

The secondary endpoint was to analyze the characteristics of patients who remain for a longer period of time in an optimized dose regimen.
Methods: In our Rheumatology Unit we are treating 271 RA patients with BT, the dose was deintensificated for 62 (23%) patients in remission or low disease activity for at least 6 months. We have selected 32 patients with BT reduced for at least 6 years in an observational, descriptive, longitudinal and retrospective study. Disease activity was measured by the DAS 28 index. Structural damage was evaluated by SENS method.
Results: We analyze 32, 20 female, 12 male, mean age at diagnosis 42.6 years old; BT was started after RA evolution of 98.63 months. Drug reduction was performed after full BT for 62 months, mean DAS 28 was 2,47.
Patients were 75% FR positive and 56.7% ACPA positive. Etanercept was the BT more commonly reduced 59.4%, followed by adalimumab 21.9%, infliximab 12.5% and certolizumab 6.3%.
BT dose returned to normal for 11 patients because of disease activity worsening after an average time of 15.90 months.
For 21 patients remaining on reduced doses, the mean DAS28 at time for analysis was 2.67.
BT reduction as different drugs: none infliximab reduced dose patients required return to normal dose. All certolizumab reduced (2 patients) patients needed to back to normal dose. Etanercept in 36,8% and adalimumab 28,6%.
The mean of SENS score before the optimization was 8.78 and at time for analysis 10.67 for both kind of patients, who continued reduced and those who needed to increase BT dose.
For the secondary endpoint 10 out of 12 male continue with deintensificated BT (83%) in the other hand only 11 out of 20 female (55%) maintained reduced dose.More negative for FR (69,2%) and ACPA (75%) patients keep on reduced dose regimen.
Conclusions: We have deintensificated 62 out of 271 RA patients on BT (23%). All patients were in clinical remission at the beginning of BT dose reduction for more than 6 months.
Most patients (65%) analyzed remain long time with reduced BT in clinical remission.
We have not observed significant X-ray progression for reduced patients, even if they increase disease activity and need to back to the original BT dose.
The increase in disease activity was the main reason to interrupt the optimization regime.
Infliximab was the drug that remained more time optimized.
According to the results of our study, male patients negative for ACPA and FR remain longer with reduced doses
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5273

AB0385 STRATEGIES FOR THE OPTIMIZATION OF BIOLOGICAL THERAPY IN PATIENTS WITH JOINT INFLAMMATORY DISEASE: ANALYSIS OF CLINICAL RESULTS AT 4 YEARS

M.J. Rodriguez Valls, M.D. Toledo Coello, Y. Cabello Fernandez, M.V. Perez Romera, J.J. Perez Venegas. *Reumatologia, Hospital de Jerez, Jerez de la Frontera, Spain*

Background: Biological therapies optimization in joint inflammatory diseases is indicated in patients who have more than six months in clinical remission. The main objective is to limit the occurrence of adverse effects, which are dosage-dependent. In addition, the cost savings suppose a better access of new patients to these treatments. Given the increasing importance of this topic in recent years, we present the optimization experience in our center at the last 4 years
Objectives: 1.To analyze the clinical evolution evaluated by DAS28 in patients with rheumatoid arthritis (RA) and polyarticular psoriatic arthritis (PPSA) in biological therapy (BT) followed in a university hospital in the south of Spain which are performed in optimization of BT. 2.To analyze the optimization strategies used with the different BT
Methods: Observational, longitudinal, retrospective and descriptive study by the review of clinical records, between January 2013 and January 2017, of patients with RA and PPSA who underwent BT optimization for more than 6 months at follow-up (DAS28 $<$2.6) or minimal activity (DAS28 2.6–3.2). We analyze demographic data, time of evolution of illness before the use of BT, time of TB until optimization, clinical evaluation by DAS28 and therapeutic strategies. Statistical analysis was performed with the IBM SPSS Statistics program
Results: From 294 patients in BT (174 RA and 120 PPsA), 95 (32.3%) were submitted to optimization treatment: 58 in RA group and 37 in PPSA group. 57 were women and 38 men, with 56±12 years mean age. The mean treatment time at optimized doses was 32±17 months. At the optimization time, 85 (89.5%) patients presented DAS28 remission and 10 (10.5%) had low activity; at the study cut time, 67 (70.5%) of them continue at clinical remission,14 (14.7%) low activity, 11 (11.6%) moderate and 3 (3.2%)high activity according to DAS28. A 69.5% (66) of the patients continued with optimized doses at the end of the study. From the 58 patients included in the RA group, 14 (5 with adalimumab 40 mg/21 days, 8 with etanercept 25 mg/7–10 days or 50 mg/10 days and 1 with certolizumab 200 mg/month) need the standard dose of the drug for disease control; a patient receiving etanercept discontinued the treatment after the diagnosis of breast cancer, as well as three other patients treated with adalimumab who were diagnosed of pancreatic cancer, septic arthritis and cognitive impairment respectively. On the other hand, 9 patients from of the PPSA group needed to restart the treatment at standard doses, either for articular (4) or cutaneous (5) worsening, 3 of them being treated with adalimumab and 6 with etanercept. In addition, a patient had to be discontinued due to the diagnosis of decompensated liver cirrhosis; another patient suspended it voluntarily
Conclusions: After 4 years, we can conclude that in our cohort of patients with inflammatory joint disease in BT that have been submitted to dose optimization because they were in remission or low disease activity, a high percentage (69.5%) remain in the same clinical situation for an average of 32 months. The response rate obtained for optimization in the RA group and in the PPSA group are comparable. The most frequent optimization strategies employed were adalimumab 40mg/21 days, etanercept 25mg/7 days and etanercept 50mg/10 days.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4326

AB0386 A STUDY OF RETENTION AND SWITCHING RATES OF 1ST LINE BIOLOGICS FOR RHEUMATOID ARTHRITIS

M. Sato, T. Tani, T. Ohashi. *Rheumatology, Ohashi and Tani Orthopedics, Gifu, Japan*

Background: Since the introduction of biologics for rheumatoid arthritis (RA) treatment, significant improvements in joint inflammation control, prevention of bone/joint destruction, activities of daily living (ADL), and quality of life (QOL) have been observed. Tumor necrosis factor (TNF) inhibitors, such as anti-TNF drugs and TNF receptor drugs, accounted for the majority of biologics. However, the use of non-TNF inhibitors, including interleukin (IL)-6 receptor antibodies and selective modulators of T-cell co-stimulation, has been approved, and their efficacy has been demonstrated.
Objectives: This study aimed to analyze the effective usage retention rate of TNF inhibitors and non-TNF inhibitors in RA patients.
Methods: Among 475 RA patients who were administered biologics up to the end of 2015, 329 patients who had been treated for more than 5 years (treatment initiated before the end of December 2010) since the first introduction of biologics (1st line) were included in this study. These patients were divided into TNF inhibitor (infliximab: IFX, etanercept: ETN, and adalimumab: ADA) and non-TNF inhibitor groups (tocilizumab: TCZ, and abatacept: ABT) to investigate the number of patients who progressed to 2nd or 3rd line therapy by 5 years after introduction, and which biologic was administered as the 2nd or 3rd line therapy in each group.
Results: Of 329 patients, 67 were men and 262 were women. Patient age ranged between 22 and 83 years with a mean of 58.7±13.5 years. RA disease duration ranged between 1 and 50 years with a mean of 9.6±8.1 years. TNF inhibitors and non-TNF inhibitors were used as 1st line therapy in 278 and 51 patients respectively. In the TNF inhibitor group, IFX, ETN, and ADA were administered to 145, 87, and 46 patients respectively. In the non-TNF inhibitor group, TCZ and ABT were administered to 48 and 3 patients respectively. In the TNF inhibitor group, 94 of 278 patients (33.8%) progressed to 2nd line therapy owing to efficacy attenuation and adverse events. Thirty-four of these patients were switched to TNF inhibitors and 60 to non-TNF inhibitors. Conversely, 6 of 51 patients in the non-TNF inhibitor group (11.8%) advanced to 2nd line therapy, with 2 switching to TNF inhibitors and 4 to non-TNF inhibitors. Additionally, 25 and 3 patients advanced to 3rd line therapy in the TNF inhibitor and non-TNF inhibitor groups respectively. Throughout the 5 years, 154 (55.4%) patients in the TNF inhibitor group did not change their treatment agent while 69 (24.8%), 24 (8.6%), and 1 (0.4%) switched once, twice, or 3 times or more, respectively. Thirty (10.8%) patients discontinued biologic usage. In the non-TNF inhibitor group, 3 (5.9%), 2 (3.9%), and 1 (2.0%) patients switched once, twice, or 3 times, respectively. Six (11.8%) patients discontinued biologic usage, and no change in treatment occurred in 39 (76.5%) patients. The mean number of biologic agent switches per patient in each group over 5 years was 0.43 times in the TNF inhibitor group and 0.20 times in the non-TNF inhibitor group, indicating that the number was significantly lower in the non-TNF inhibitor group (p=0.0032).
Conclusions: While the sample size was small and patient characteristics varied, it appears that non-TNF inhibitors are not inferior to TNF inhibitors as 1st line therapy biologics in terms of retention rate and number of switches to TNF inhibitors.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3356

AB0387 COMPARISON OF ETANERCEPT IN MONOTHERAPY AND COMBINATION WITH SYNTHETIC DMARDS: DATA FROM ATTRA REGISTRY

P. Horák[1], M. Skácelová[1], L. Szczuková[2], A. Smržová[1], J. Vencovský[3], J. Závada[3], K. Pavelka[3] on behalf of ATTRA registry Czech Republic. *[1]III Department of internal Medicine, Faculty of Medicine and Dentistry, University Olomouc, Olomouc; [2]Institute of Biostatistics And analysis, Masaryk University Brno, Brno; [3]Institute of Rheumatolgy, Charles University of Prague, Prague, Czech Republic*

Background: Etanercept (ETN) is an established bDMARDs for therapy of rheumatoid arthritis and some other inflammatory diseases. In rheumatoid arthritis patients ETN could be given in combination therapy with sDMARDs as well as in monotherapy.

Objectives: To investigate and compare etanercept monotherapy versus combination with sDMARDs in RA patients regarding survival on drug, efficacy, quality of life and reason for discontinuation.
Methods: Observational, open, long-term study of patients from the ATTRA registry starting the ETN therapy since 2010 either on monotherapy or in combination with sDMARDs (n=605). 461 patients (80.7%) were females, rheumatoid factor was positive in 429 (76.6%), anti CCP antibodies in 412 (74.5%) patients. The following groups of patients were assessed: Etanercept monotherapy (ETN-mono, n=83), combination with methotrexate (Combo-MTX, n=378), combination with other sDMARDs (Combo-other sDMARDs, n=110).
Mean ± SD and absolute/relative frequencies were used to describe continuous and categorical variables, respectively. P-value of Pearson Chi-square test and Kruskal-Wallis test is given when assessing differences between groups in categorical and continuous variables. Results are presented as hazard ratio (HR) with corresponding p-value. Statistical evaluation was processed by IBM SPSS Statistics ver. 24.
Results: In the first measurement of activity after 3 months, there were significantly lower disease activity in both Combo groups compared to ETN mono (3.2±0.1 resp. 2.9±0.1 versus 3.7±0.2, $p<0.001$). However since the month 6 the differences lost their significance and the disease activity were comparable in all groups up to the month 24.
The HAQ value was significantly higher already at the time of ETN onset at month 0 in the ETN-mono group (1.7 versus 1.4 resp. 1.5, $p<0.001$) and stayed significantly higher at the month 3 and 12.
The hazard ratio (HR) for ETN discontinuation was higher in ETN mono group compared to Combo-MTX (HR=1.330) and also compared to Combo-other sDMARDs (HR=1.098), even if the differences did not reach statistical significance (p=0.131, resp. 0.671). Similar trend was evident, if the etanercept was given in the first and any subsequent line of biological therapy. The HR for ETN discontinuation was also numerically higher in Combo-other sDMARDs than in Combo MTX group (HR=1.211, p=0.244).
The patients on ETN mono have higher risk of discontinuation due to inefficacy compared to Combo-MTX (HR=1.415) and also to Combo-other sDMARDs (HR=1.670). The patients of combo-other sDMARDs group had lower risk of discontinuation due to inefficacy also in comparison with combo-MTX (HR=0.847). None of the differences reach statistical significance.
The patients on ETN mono have higher risk of discontinuation due to adverse event compared to Combo-MTX and also to Combo-other sDMARDs. This trend is higher, if ETN is given in the subsequent line of biological therapy, but not in first line. Nevertheless like in other situations, the differences showed some trend, but were not statistically significant.
Conclusions: Results support the evidence of advantages of ETN combination with methotrexate – quicker onset of efficacy and give some evidence of better survival on etanercept therapy in combination with methotrexate.
Acknowledgements: Supported by AZV 15–28659A
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2583

AB0388 RESULTS AT 3 YEARS OF AN OPTIMIZATION GUIDELINE OF BIOLOGICAL THERAPIES IN RHEUMATOID ARTHRITIS. CREATE RECORD RESULTS

P. Font[1], M.C. Castro[2], M. Romero[2], R. Ortega[2], J. Calvo[2], D. Ruiz[2], M. Cardenas[2], R. Alejandre[2], P. Carreto[3], E. Collantes[2]. *[1]Hospital Reina Sofia - Imibic-Universidad de Córdoba; [2]Hospital Reina Sofia - Imibic-Universidad de Córdoba, Cordoba; [3]MFyC de Valladolid, Area Este, Valladolid, Spain*

Background: Dose optimization, such as dose reduction or dose spacing, is nowadays presented as a therapeutic strategy to be followed in patients with rheumatoid arthritis (RA) who have managed to reach and maintain clinical remission for a while. This strategy reduces the frequency of adverse effects and promotes cost savings
Methods: Patients with RA (Criteria ACR 1987) of the CREATE registry (patients who was treated in real life conditions) who had clinical remission (DAS28 <2.6) of at least 6 months of duration on November 1, 2013, constituted the cohort of patients who were optimized for the dose received. According to the consensus of the Spanish Societies of Rheumatology and Hospital Pharmacy, the optimization of doses meant the reduction of between 20 and 50% of the same.
A multidisciplinary team of rheumatologists and clinical pharmacists in a third-level hospital was involved in decision-making on treatment and dose reduction, which involved the application of protocols and the follow-up of patients at least every two months.
Results: A prospective follow-up of 70 patients with RA who had received optimized doses of biological therapy for 3 years, with a mean age of 56.9 (13.7) years, of which 78.6% were women, 68.8% were positive rheumatoid factor and 66.7% ACPA +.
The relapse occurred in 41.8% (at first year), 56.7% (at second year) and 62.7% (at third year). There were no statistical differences between these last 2 percentages. The median survival time of the optimization regimen was 15.24 (4.65) months (95% CI: 4.66–25.83). No statistically significant differences were found when comparing patients according to the optimized drug (antiTNF versus non-anti-TNF) (test log.rank: 0.239, p: 0.625).
When relapse occurs, the patient returns to normal doses prior to optimization of the drug. Our data show that 62.7% of the patients in whom the relapse occurs at 3 years, maintains DAS28 <2,6 ($P<0.05$) when dose was returned to the manufacturer recommended dose.
The 37.3% (95% CI: 26.72%, 49.28%) patients maintained the optimization pattern throughout the follow-up without relapse, with an average DAS28 of 1.99 (1.07) at 3 years. Comparing these patients with those who relapse, they achieved significantly lower DAS28 values at both (p: 0.028) and at three years (p: 0.025)
Conclusions:
- The strategy of dose reduction of biological therapies in patients with established RA that achieve sustained remission is possible in 37.3% of cases in real clinical practice (CREATE Registry) and it was maintained for 3 years.
- The probability of occurrence of relapse decreases after 2 years of treatment with an optimized regimen in those patients who have not relapsed before.
- This strategy is possible in patients with persistently controlled disease and in view of our results, it is independent of the drug administered (antiTNF versus non-antiTNF).
- After 3 years of follow-up, all patients maintained clinical remission (DAS 28 <2.6) despite relapses, and after resumption of the usual dose, all of them reached the therapeutic goal again.
- Patients who maintain clinical remission for 3 years achieve DAS28 values statistically lower than those who did not after 2 years.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2156

AB0389 THE IMMUNOGENICITY OF BRANDED AND BIOSIMILAR INFLIXIMAB IN RHEUMATOID ARTHRITIS ACCORDING TO TH9-RELATED RESPONSES

R. Talotta[1], A. Berzi[2], A. Doria[3], A. Batticciotto[1], M.C. Ditto[1], D. Trabattoni[1], P. Sarzi Puttini[1]. *[1]Rheumatology Unit; [2]Department of Biomedical and Clinical Sciences, University Hospital "Luigi Sacco", Milan; [3]Rheumatology Unit, University Hospital, Padua, Italy*

Background: There are many evidences that Th9 lymphocytes take part to the pathogenesis of rheumatoid arthritis (RA), however it is unclear whether these cells are implicated in the immunogenicity of biologic agents.
Objectives: We aimed to evaluate the immunogenicity of branded and biosimilar infliximab by detecting changes in Th9 percentages following an *"in vitro"* stimulation test.
Methods: PBMCs from 55 consecutive RA outpatients (15 drug-free, 20 successfully treated with branded infliximab and 20 failing branded infliximab) and from 10 healthy controls were collected. PBMCs were cultured with/without 50 μg/mL infliximab originator (Remicade®) or 50 μg/mL infliximab biosimilar (Remsima®), 50 μg/mL Human IgG1kappa and 50 μg/mL recombinant Human IgG Fc for 18 hours. Th9 lymphocytes were identified by means of flow cytometry as PU.1+, IRF4+, IL9+ CD4+ cells. Furthermore, the markers CCR7 and CD45RA were used to distinguish naive from memory IL-9-producer cells.
Results: In unstimulated condition, RA patients showed the highest percentages of Th9 lymphocytes. Following stimulation with branded infliximab, the percentage of PU.1+, IRF4+ Th9 cells, CCR7+, CD45RA- central memory and CCR7-, CD45RA- effector memory IL-9 producer cells significantly increased in the group of infliximab non responder RA patients. On the contrary, no significant variation was observed after biosimilar exposure. Figures 1,2,3,4 resume the results.

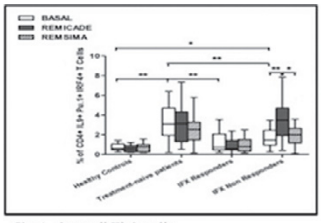


Fig.1 Overall Th9 cells

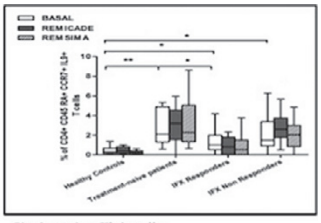


Fig.2 Naive Th9 cells

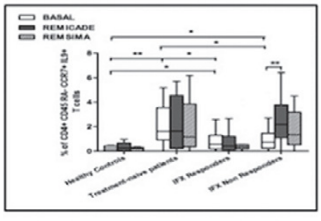


Fig.3 Central memory Th9 cells

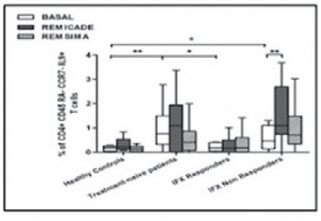


Fig.4 Effector memory Th9 cells

Conclusions: According to our results, Th9 cells seem to be involved in the immune response against the epitopes of branded but not biosimilar infliximab and this condition could rely on the recall and the stimulation of both central and effector memory cells. Further studies are indeed needed to confirm these data.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4401

AB0390 EFFICACY AND SAFETY OF YISAIPU, A RECOMBINANT HUMAN TUMOR NECROSIS FACTOR-α RECEPTOR II IGG FC FUSION PROTEIN IN CHINESE PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

R. Wu. *Department of rheumatology, the First Affiliated Hospital of Nanchang University, Nanchang, China*

Background: Rheumatoid arthritis (RA) is characterized by chronic autoimmune diseases of progressive synovitis and joint destruction, which can eventually lead to joint deformation and disability. A number of clinical studies showed the effectiveness of tumor necrosis factor antagonist combined with methotrexate in the treatment of RA. Yisaipu used in this study is produced by CPGC Company (Shanghai, China), which was approved to treat RA by Chinese Food and Drug Administration, in 2005, which is biosimilar of etanercept (a soluble recombinant human receptor antibody fusion protein, an immunoglobulin molecule which connects two TNF receptors (p75) to the human IgG1 FC division). Etanercept had been confirmed the effectiveness in rheumatoid arthritis already in many clinical trial.[5–8] However, there is rare randomized control study published regarding Yisaipu in international journals. We conducted an open-label, randomized controlled study for 24 weeks to evaluate the efficacy and safety of Yisaipu in combination with DMARDs in comparison with low or medium dose of glucocorticoid in patients with moderate to severe RA.

Objectives: to evaluate the efficacy and safety of Yisaipu in combination with DMARDs in comparison with low or medium dose of glucocorticoid in patients with moderate to severe RA.

Methods: Eighty four patients with moderate to severe rheumatoid arthritis were randomly assigned into 4 groups: group 1: methotrexate plus Yisaipu; group 2: methotrexate plus medium-dose prednisone (30mg/d, reduced to 15 mg/d after 2 weeks); group 3: methotrexate plus low-dose prednisone (prednisone 7.5mg/d); group 4: methotrexate alone. Each group was treated with MTX (12.5mg once weekly, the next day with folic acid 10mg) and hydroxychloroquine sulfate (200 mg twice a day) concomitantly. The primary endpoint was ACR20 response rate at week 24. Secondary efficacy endpoints were ACR20, ACR50, ACR70, DAS-28, Health Assessment Questionnaire (HAQ) and EULAR remission rate at week 4, 12 and 24.

Results: At week 24, a higher proportion of patients in the group 1and group 2 than the other two groups met the ACR20 response criteria (85.7% in group 1 and 71.4% in group 2 vs. group 3 and group 4, $P<0.05$). The reductions of HAQ at week 24 showed significant improvement in group 1 and group 2 compared to group 3 and 4 (-2.96 and -2.69 respectively, $P<0.05$). Reduction of DAS-28 in group 1 and group 2 were significantly higher than the other two groups ($P<0.05$). The percentage of EULAR remission rate of group 1 and group 2 is significantly higher than group 3 and group 4 at week 24 (47.6% in group 1, 33.3% in group 2, 23.8% in group 3 and 14.3% in group 4, $P<0.05$). There were no significant differences of adverse event among four groups.

Conclusions: Yisaipu plus MTX or GCs plus MTX in Chinese patients with moderate to severe RA is safe and effective in our study. More studies are needed to compare the long-term safety and cost-effectiveness between Yisaipu and GCs in treatment with RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1867

AB0391 SIMILAR PHARMACOKINETICS, SAFETY AND TOLERABILITY OF THE ADALIMUMAB BIOSIMILAR CANDIDATE BI 695501 ADMINISTERED SUBCUTANEOUSLY VIA PREFILLED SYRINGE (PFS) OR AUTOINJECTOR (AI) (VOLTAIRE®-AI)

S. Ramael[1], V. Moschetti[2], N. Peter[2], I. Sonderegger[2], S. Wiebe[2], B. Liedert[2]. *[1]SGS Life Science Services, CPU, Antwerp, Belgium; [2]Boehringer Ingelheim, Ingelheim a.R., Germany*

Background: PK bioequivalence of BI 695501, an adalimumab biosimilar candidate, and the adalimumab originator was demonstrated previously (VOLTAIRE®-PK: Wynne et al., Expert Opin Investig Drugs 2016;25:1361–70). Administration in chronic inflammatory diseases benefits from patient-friendly PFSs or AIs, the development of which requires assessment of PK, safety, immunogenicity, and local tolerability.

Objectives: To compare PK, safety, immunogenicity, and tolerability of BI 695501 after subcutaneous (SC) injection using either a PFS or an AI.

Methods: In this 16-week randomised, single-dose, open-label, parallel-group study (NCT02606903), 40mg BI 695501 was administered either via PFS or AI in healthy, Caucasian, male, non-athletic volunteers aged 18–65 years with body mass index (BMI) of ≥18 to ≤30 kg/m^2. The study end points included AUC_{0-1032}, C_{max}, and $AUC_{0-\infty}$, analysed using an ANOVA model with fixed effects for treatment and BMI group. Safety assessment included the proportion of subjects with drug-related adverse events (AEs). Immunogenicity parameters were: proportion of subjects with binding/neutralising anti-drug antibodies (ADAs), and ADA titers.

Results: Seventy-one volunteers were randomised: PFS, n=36; AI, n=35. Key demographic and baseline characteristics were well balanced between the treatment groups. PK end point results are shown in Table 1. Estimates for AI/PFS geometric mean (gMean) ratios were within the standard bioequivalence acceptance range (80–125%). Mean plasma concentration-time profiles and total exposure for BI 695501 administered via PFS or AI were similar over the observation period; treatment-emergent AEs (TEAEs) and administration site conditions (ASC) are shown in Table 2.

Table 1. PK Parameters over All Subjects for BI 695501 via PFS or AI

Parameter	PFS		AI		Adjusted gMean ratio (AI/PFS)*	2-sided 90% CI*
	n	Adjusted gMean*	n	Adjusted gMean*		
$AUC_{0-\infty}$† [μg·h/mL]	35‡	2270	35	2280	100.22	82.13, 122.29
AUC_{0-1032} [μg·h/mL]	35‡	1960	35	1960	100.14	85.15, 117.76
C_{max} [μg/mL]	36	3.76	35	4.14	110.19	96.80, 125.44

*Adjusted for treatment and BMI group as fixed effects; †Based on observed last concentration values; ‡AUC values could not be calculated for one subject (Subject 1001-0110), due to the lack of appropriate terminal phase (only one non-BLQ [below the limit of quantification] value in the elimination phase).

Table 2. TEAEs and ASC

n (%)	PFS (n=36)	AI (n=35)
≥1 TEAE	29 (80.6)	29 (82.9)
≥1 TEAE related to trial drug	16 (44.4)	20 (57.1)
≥1 non-serious TEAE	29 (80.6)	29 (82.9)
≥1 serious TEAE	0	0
ASC*	14 (38.9)	20 (57.1)
Injection site erythema	13 (36.1)	18 (51.4)
Injection site swelling	3 (8.3)	7 (20.0)
Injection site induration	1 (2.8)	4 (11.4)

*Injection-site reactions are those events recorded within the electronic case report form "Administration site reactions" (narrow) list.

Similar frequencies of patients tested positive for ADAs (57.6% in the PFS group and 51.5% in the AI group), and for neutralising antibodies (33.3%% in the PFS group and 30.3% in the AI group) at the end of the study.

Conclusions: PK, safety, tolerability, and immunogenicity of BI 695501 after SC injection with a PFS or an AI were comparable.

Disclosure of Interest: S. Ramael: None declared, V. Moschetti Employee of: Boehringer Ingelheim, N. Peter Employee of: Boehringer Ingelheim, I. Sonderegger Employee of: Boehringer Ingelheim, S. Wiebe Employee of: Boehringer Ingelheim, B. Liedert Employee of: Boehringer Ingelheim

DOI: 10.1136/annrheumdis-2017-eular.3507

AB0392 SAFETY AND EFFECTIVENESS OF CT-P13 IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM 24 MONTHS NATIONWIDE REGISTRY IN KOREA

S.H. Park[1], S.S. Nah[2], S.H. Chang[2], K.J. Kim[3], K.S. Park[3], S.S. Lee[4], S.R. Kwon[5], S.I. Lee[6], C.H. Suh[7], S.H. Kim[8], C.N. Son[8], J.K. Min[9], H.R. Kim[10], H.J. Beak[11], H.S. Kim[12], J.Y. Choe[13], H.I. Yang[14], M.K. Lim[15], S.J. Hong[16], Y.S. Kim[17], J.H. Lee[18], J. Suh[19], S. Lee[19]. *[1]The Catholic University of Korea Seoul St.Mary's Hospital, Seoul; [2]Soonchunhyang University Cheonan Hospital, Cheonan; [3]The Catholic University of Korea St. Vincent's Hospital, Suwon; [4]Chonnam National University Hospital, Gwangju; [5]Inha University Hospital, Incheon; [6]Gyeongsang National University School of Medicine, Jinju; [7]Ajou University School of Medicine, Suwon; [8]Keimyung University Dongsan Medial Center, Daegu; [9]Bucheon St.Mary's Hospital, Bucheon; [10]Konkuk University School of Medicine, Seoul; [11]Gachon University Gil Medical Center, Incheon; [12]The Soonchunhyang University Seoul Hospital, Seoul; [13]Daegu Catholic University Medical Center, Daegu; [14]Kyung Hee University Hospital at Gang Dong, Seoul; [15]Eulji University School of Medicine, Daejeon; [16]Kyung Hee University Medical Center, Seoul; [17]Chosun University Hospital, Gwangju; [18]Inje University Ilsan Paik Hospital, Goyang; [19]Celltrion, Inc, Incheon, Korea, Republic Of*

Background: CT-P13 is approved in both European Union and United States, and licensed for use in 79 countries around the world as a biosimilar to innovator infliximab (INX). The independent registries of CT-P13 have been conducted in a number of European countries and Korea [1].

Objectives: To evaluate safety and effectiveness of CT-P13 when administered in a real-life setting in active RA patients.

Methods: This study collected data of patients who were treated with CT-P13 from 2013 December to 2016 June. Efficacy was assessed at baseline and every 6 months thereafter using DAS28 (ESR) and/or DAS28 (CRP) and collection of adverse events (AEs) was performed. Immunogenicity was assessed at baseline, Week 30 and every year during CT-P13 treatment period.

Results: Total 125 patients were enrolled; 104 patients started treatment with CT-P13 (Naïve group) and 21 patients (8 from INX, 13 from other anti-TNFs) switched treatment to CT-P13 (Switching group). The mean (SD) duration since RA diagnosis was 6.5 (±6.85) years for all patients.

Of all patients treated with CT-P13, only 4.8% (6/125) of patients changed to other anti-TNFs. Two of six patients changed treatment within 8 month after starting CT-P13.

The proportion of patients achieving clinical remission by DAS28 (ESR/CRP) increased gradually (Figure 1). DAS28 (ESR/CRP) value decreased from baseline at 6 months and it maintained thereafter (Table 1). Switching group also showed similar results that remission rate by DAS28 (CRP) was 42.9% (3/7) and mean actual value was 2.85 at 12 months.

For Naïve group, 50% (52/104) of patients had at least one positive anti-drug antibody result and it is consistent to other published study [2].
Overall safety summarized as the percentage of patients with at least one treatment emergent AE (TEAE) was similar or lower after switching to CT-P13 (Table 2). No cases of active tuberculosis were reported.

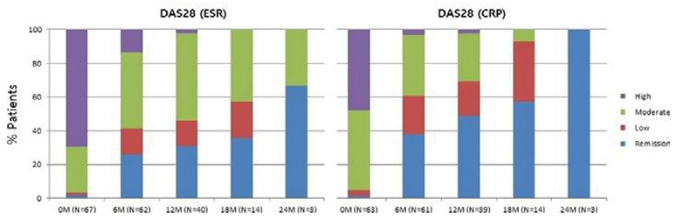
Table 1. DAS28 in CT-P13 Naïve group over 24 months

		Baseline	6 months	12 months	18 months	24 months
DAS28 (ESR)	n	67	62	40	14	3
	Mean	5.78	3.61	3.30	3.01	2.42
	SD	1.14	1.40	1.22	1.03	0.74
DAS28 (CRP)	n	63	61	39	14	3
	Mean	5.06	2.97	2.59	2.35	1.81
	SD	1.19	1.21	1.06	0.69	0.63

Table 2. Safety results in CT-P13 Naïve and Switching group

	Naïve group	Switching group
TEAEs	80.8% (84/104)	66.7% (14/21)
Related TEAEs	31.7% (33/104)	28.6% (6/21)
Infection and Infestation	42.3% (44/104)	33.3% (7/21)

Figure 1. Disease Activity by DAS28 in CT-P13 Naïve group



Conclusions: The overall safety profile revealed that CT-P13 is well-tolerated in patients with RA and remission rate for 24 months also showed that CT-P13 is efficacious under real world practice.
References:
[1] Glintborg et al. ACR 2016.
[2] Krintel et al. Rheumatology 2013.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2413

AB0393 ADVERSE SKIN REACTIONS IN RHEUMATOID ARTHRITIS PATIENTS RECIEVING TUMOR NECROSIS FACTOR ALPHA INHIBITOR – AN ANALYSIS OF DATA FROM THE SLOVENIAN BIOLOGICAL REGISTRY

S. Drljača[1], A. Podovšovnik[1], Ž. Rotar[2], A. Hočevar[2], S. Praprotnik[2], M. Tomšič[2] on behalf of rheumatologist participating in BioRx.si registry.
[1]Department of Internal medicine, Izola General Hospital, Izola; [2]Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia

Background: Paradoxical skin reactions (PSR) are defined as a new onset or worsening of skin conditions during treatment with tumour necrosis factor alpha (TNF-α) inhibitors that generally improve or respond to this therapy. The list of PSR is growing. The most commonly reported are psoriasiform skin eruptions.
Objectives: To evaluate the frequency of PSR in the group of rheumatoid arthritis (RA) patients treated with TNF-α inhibitor at the time of development of skin eruption.
Methods: We conducted the analysis of the data from the mandatory Slovenian national registry of patients treated with bDMARDs (BioRx.si) which includes spontaneous adverse reaction reports between 01.01.2008–31.05.2016. The analyses were limited to patients with RA.
Results: During the observation period, 1,046 RA (82% female; median (IQR) age at initiation of TNF-α inhibitors 56 (49–63) years) patients treated with TNF-α inhibitors for 3,140 person years. We identified 14 cases with PSR (71% female, median age (IQR) 45 (53–62)). There were 6 PSR cases on adalimumab, 4 on etanercept, 3 on certolizumab – pegol, and 1 on infliximab. 10 patients developed psoriatic/psoriasiform eruptions, 2 patient leucocytoclastic vasculitis, one had lichen planus, and one undifferentiated skin changes. The incidence rate of new onset of psoriasis in RA patients treated with TNF-α inhibitors was estimated at 3.2 cases/1000 patient-years (95% CI 2.58 to 3.82). The incidence rate of leucocytolastic vasculitis was 0.64/1000 person-years (95% CI 0.36 to 0.92), and of lichen planus 0.32/1000 person-years (95% CI 0.12 to 0.52).
Conclusions: The most commonly reported PSR in RA patients treated with TNF-α inhibitor was psoriasiorm PSR, which is in line with published data.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5287

AB0394 TAPERING TNF INHIBITORS IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE STUDY

A. Hacioglu, G. Hatemi, S.N. Esatoglu, Y. Ozguler, S. Ugurlu, E. Seyahi, M. Melikoglu, I. Fresko, H. Ozdogan, S. Yurdakul, V. Hamuryudan. *Division Rheumatology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey*

Background: Increasing evidence suggests the feasibility of biologic DMARD tapering in RA patients after achieving and maintaining good control of disease activity. Current guidelines on RA treatment also recommend tapering of biologic and non-biologic DMARDs for patients in remission. Data on biologic DMARD tapering reflecting real life settings are limited.
Objectives: To collect information on biologic DMARD tapering and its outcome in RA patients who are followed-up in a rheumatology outpatient clinic.
Methods: In this retrospective study we used the hospital administrative database to identify patients with a diagnosis of RA and a first time prescription of a biologic DMARD that was specifically limited to one of the 3 TNF inhibitors (etanercept, adalimumab, infliximab) between January 2012 and the end of December 2013. Demographics and information regarding treatment and outcome were taken from the medical charts.
Results: Of the 125 patients identified at the database search, 104 were belonging to our clinic and had available follow-up data until June 2016. Seventy-nine of them were women and 25 were men. Their mean age was 47.7±13 SD years and their mean disease duration was 7.4±6.9 SD years. 60% were prescribed etanercept, 23% adalimumab and 17% infliximab. After a mean duration of 14.0±7.6 SD months a dose reduction of TNF inhibitors was made in 44 patients (42%). This was in the form of spacing in 39 patients (Etanercept =16, Infliximab =14, Adalimumab =9) and dose tapering in 5 (all Etanercept). All of these were due to good clinical response except for 1 patient's own request for fear from adverse effects. Following dose reduction increased disease activity was seen in 16 patients (36%) mandating restoration to original dose within a mean of 8.8±9.7 SD months with good response. Twenty-eight patients (64%) preserved their good clinical response during a mean follow-up of 46.1±6.3 SD months which enabled further dose reductions in 20 patients. There was also reductions in the mean number of synthetic DMARD's (1.4±0.8 SD at the initiation of TNF inhibitors and 0.7±0.8 SD at the end of follow-up) and in the percentage of patients using steroids (78% to 33%). At the end of the follow-up, among the whole group of 104 patients, only 73 (70%) were using biologics (TNF inhibitors =49, non-TNF biologics =24). The reasons for stopping biologics in the remaining 31 patients were ongoing remission (16 patients), pregnancy (1 patient), non-compliance (4 patients), injection site reactions (3 patients), fear from adverse events (1 patient), deciding to try complementary medicine (1 patient) and other issues such as losing insurance and family issues (5 patients).
Conclusions: Tapering of TNF inhibitors was possible in 40% of RA patients during their routine follow-up. Half of the patients maintained good clinical response after tapering allowing further dose reductions in one third.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1934

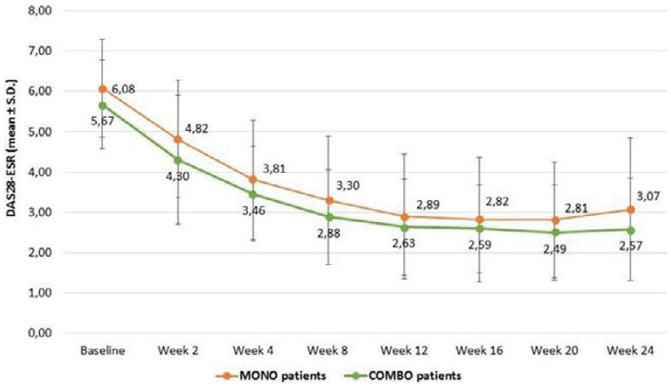
Rheumatoid arthritis - other biologic treatment

AB0395 SUBCUTANEOUS TOCILIZUMAB AS MONOTHERAPY OR IN COMBINATION WITH A CSDMARD IN PATIENTS WITH RHEUMATOID ARTHRITIS: 24 WEEKS RESULTS OF THE FRENCH PHASE IIIB STUDY, "TOSCA"

B. Fautrel[1], E. Senbel[2], O. Vittecoq[3], S. Rist[4], B. Combe[5], T. Schaeverbeke[6], F. Lioté[7], R.-M. Flipo[8], C. Baffie[9], D. Pau[10], E. Condé Da Silva Fraga[10], A. Pinta[11], P. Gaudin[12]. *[1]Rheumatology, Hôpital Pitié-Salpêtrière, Paris; [2]Rheumatology, Cabinet médical, Marseille; [3]Rheumatology, CIC/CRB 1404 CHU de Rouen, Rouen; [4]Rheumatology, CHG Orléans, Orleans; [5]Rheumatology, CHU Montpellier, Montpellier; [6]Rheumatology, CHU Bordeaux, Bordeaux; [7]Rheumatology, CHU Lariboisière, Paris; [8]Rheumatology, CHRU Lille, Lille; [9]Opérations cliniques, Altizem on behalf of Roche; [10]Clinical operations; [11]Medical department, Roche, Boulogne-Billancourt; [12]Rheumatology, CHU Grenoble, Grenoble, France*

Background: After the two global pivotal studies, which evaluated the safety and efficacy of subcutaneous tocilizumab (TCZ-SC) in combination (combo) with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), it was important to understand the efficacy and safety profile of TCZ-SC both as monotherapy (mono) and in combo with csDMARDs in patients (pts) managed in conditions less strict than those of pivotal clinical trials.
Objectives: To evaluate the efficacy and safety of TCZ-SC 162 mg once weekly (qw) as mono and in combo with csDMARDs over 24 weeks in adult pts with moderate to severe RA. The primary efficacy criterion was the change in DAS28-ESR from baseline to week 24 (W24).
Methods: TOSCA is a national, multicenter, open-label phase IIIb study, part of the international umbrella study (TOZURA). It aimed to enroll TCZ-naïve pts who were csdMARDs inadequate responders (IR) and/or biological DMARD-IR. Pts received TCZ-SC 162 mg qw for 24 weeks, administered at the investigator's discretion as mono or in combo with a csDMARD. Stable oral corticosteroids (CCS), ≤10 mg/day prednisone or equivalent (eq.pred), were allowed.

Results: The baseline characteristics of the 139 included patients were: mean age 57.3 years (±13.8), 74.1% female, mean RA disease duration 10.8 years (±9.2), immunopositivity 85.5%, structural joint damage 65.6%, mean DAS28 5.8 (±1.1). 52.5% of patients were bDMARD-IR. TCZ-SC was initiated in mono TCZ in 30.9% of pts and in combo in 69.1% (79.1% MTX). Oral CCS were used by 56.8% of pts (mean 7.4 mg/d/eq.pred.±2.7). In comparison with combo pts, the mono pts were older (58.7 vs 56.7 years), with a higher mean DAS28 (6.1 vs 5.7), a longer disease duration (11.5 vs 10.6 years), and a higher CCS mean dose (8.3 vs 6.9 mg/d/eq.pred.). At W24, the mean DAS28 score variation vs baseline was -3.1 overall ($p<0.0001$); -3.0 in mono TCZ vs -3.1 in combo TCZ ($p=0.76$) (Fig.). The proportion of pts who achieved DAS28 remission was 51.1% (41.9% in mono vs 55.2% in combo ($p=0.14$)). CDAI remission, which does not include acute phase reactants, was achieved in 17% pts, 16% in mono vs 17% in combo ($p=0.95$). At W24, 27.9% of pts receiving >5 mg CCS at baseline decreased the daily dose ≤5 mg/d/eq.pred. (30.1% in mono TCZ and 26.7% in combo). Out of the 23 pts (16.5%) who withdrew, 13.0% did so for lack of efficacy and 52.1% for safety reasons; one death occurred following a septic shock after surgery for gastric volvulus, not related to TCZ. At W24 95.7% of patients had experienced at least one adverse event (AE) and 10.1% at least one serious AE with similar rates between groups.



Conclusions: TCZ-SC demonstrated at 6 months comparable efficacy, safety and steroid sparing results in mono- and combo therapy consistent with the known profile of TCZ-IV.

Disclosure of Interest: B. Fautrel: None declared, E. Senbel: None declared, O. Vittecoq: None declared, S. Rist: None declared, B. Combe: None declared, T. Schaeverbeke: None declared, F. Lioté: None declared, R.-M. Flipo: None declared, C. Baffie Employee of: Altizem on behalf of Roche, D. Pau Employee of: Roche, E. Condé Da Silva Fraga Employee of: Roche, A. Pinta Employee of: Roche, P. Gaudin: None declared

DOI: 10.1136/annrheumdis-2017-eular.4440

AB0396 TOCILIZUMAB I.V. EFFECTIVENESS IN RA PATIENTS IS INDEPENDENT OF SMOKING STATUS

C. Specker[1], H. Kellner[2], P. Kästner[3], C. Volberg[4], V. Braunewell[5], I. Schwarze[6], M. Aringer[7], M. Sieburg[8], M.W. Hofmann[9], J.P. Flacke[10], H.-P. Tony[11], G. Fliedner[12]. *[1]Kliniken Essen Süd, Essen; [2]Schwerpunktpraxis für Rheumatologie und Gastroenterologie, München; [3]MVZ Ambulantes Rheumazentrum Erfurt, Erfurt; [4]Rheumazentrum Neuss, Neuss; [5]Schwerpunktpraxis Rheumatologie, Mönchengladbach; [6]Praxis für Internistische Rheumatologie, Leipzig; [7]Medizinische Klinik III, Rheumatologie, Technischen Universität Dresden, Dresden; [8]Rheumatologische Gemeinschaftspraxis, Magdeburg; [9]Rheumatologie, Chugai Pharma Europe Ltd., Frankfurt; [10]Rheumatologie, Roche Pharma AG, Grenzach-Wyhlen; [11]Rheumatologie/Immunologie der Medizinischen Klinik und Poliklinik II, Universitätsklinikum Wuerzburg, Wuerzburg; [12]Rheumapraxis, Osnabrueck, Germany*

Background: Cigarette smoking is considered an established risk factor for the development of rheumatoid arthritis (RA) and for poor response in RA patients to treatment with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and with anti-tumor necrosis factor (anti-TNF) agents [1,2].

Objectives: This interim analysis of the German non-interventional study ICHIBAN (NCT01194401) assessed the effectiveness and safety of intravenously administered Tocilizumab (TCZ i.v.) with respect to patients' smoking status (smoker, ex-smoker, non-smoker).

Methods: Since 2010 the ICHIBAN study collects clinical data of the routine use of TCZ i.v. in RA patients. The observation period for each patient is up to two years. At the due date of the current interim analysis (Dec 10, 2015) 2999 patients were enrolled. 902 patients have completed the maximal 104 weeks observation period (Group W104). Patients were subgrouped according to their smoking status at baseline (BL).

Results: At BL the subgroups showed the following distribution: smokers 19.0%, non-smokers 52.5%, and ex-smokers 17.0%. The mean TCZ i.v. treatment duration was 1.7, 1.8, and 1.6 years, respectively, for the three groups.

In comparison to non-smokers and ex-smokers, smokers comprised a higher percentage of male patients, were younger, and showed shorter disease duration. Smokers showed slightly lower overall comorbidity rates, while COPD was observed almost three times more among smokers (3.5%) and ex-smokers (3.9%) than in non-smokers (1.3%). Concomitant use of csDMARDs and glucocorticoids (GC) was more frequent among smokers.

DAS28-ESR disease activity at BL was similar between the 3 subgroups. After 2 years TCZ i.v. therapy, disease activity was comparably decreased in all 3 groups. The mean reduction from BL in DAS28-ESR was 2.6 (smokers), 2.8 (non-smokers), and 2.5 (ex-smokers). At last visit, DAS28-ESR remission (<2.6) was reached by 48.0%, 52.3%, and 51.6% of patients, respectively The similar effectiveness of TCZ i.v. was also shown by patient reported outcomes via visual analogue scales (VAS).

Regarding safety, smokers showed higher event rates of adverse events (AE), serious adverse events (SAE), infections, and serious infections [Tab. 1]

Table 1 Effectiveness and safety of TCZ i.v. in RA patients

		W104 (Total)	Smokers	Non-smokers	Ex-smokers
Baseline characteristics, % (n)		100.0 (902)	19.0 (171)*	52.5 (474)*	17.0 (153)*
Sex (male), % (n)		23.8 (215)	40.9 (70)	15.8 (75)	33.3 (51)
Age [years], mean ± SD		55.7 ± 12.4	51.8 ± 10.1	56.8 ± 13.6	56.6 ± 11.4
Duration of RA [years], median		8.0	6.0	8.0	8.0
Comedication, % (n)					
• DMARDs		42.6 (384)	49.7 (85)	41.4 (196)	37.9 (58)
• GC		61.5 (555)	68.4 (117)	59.7 (283)	56.2 (86)
Comorbidities, % (n)		72.5 (654)	68.4 (117)	72.4 (343)	78.4 (120)
Effectiveness					
DAS28-ESR					
• Week 0 (Baseline), mean ± SD		5.5 ± 1.1	5.5 ± 1.1	5.5 ± 1.1	5.3 ± 1.0
• Last visit under TCZ, mean ± SD		2.7 ± 1.5	2.9 ± 1.7	2.7 ± 1.5	2.8 ± 1.5
• Change from BL, mean ± SD		-2.7 ± 1.6	-2.6 ± 1.7	-2.8 ± 1.7	-2.5 ± 1.5
• Remission (< 2.6), % (n)		51.9 (468)	48.0 (82)	52.3 (248)	51.6 (79)
VAS [mm], median (Q1, Q3)					
• Exhaustion/Tiredness	(Baseline)	60.0 (36, 79)	62.0 (31, 80)	59.0 (40, 78)	55.0 (34, 75)
•	(Last visit)	37.0 (14, 60)	39.0 (13, 62)	35.0 (15, 60)	40.5 (12, 57)
• Intensity of pain	(Baseline)	65.0 (45, 79)	67.0 (42, 80)	63.0 (45, 77)	62.0 (46, 78)
•	(Last visit)	30.0 (13, 56)	32.0 (16, 58)	30.0 (11, 53)	38.5 (15, 60)
• Sleep disturbances	(Baseline)	50.0 (21, 74)	48.0 (15, 80)	45.0 (21, 72)	50.0 (25, 72)
•	(Last visit)	30.0 (10, 60)	27.0 (5, 57)	28.0 (10, 59)	35.0 (12, 62)
Safety (event rate per 100 patient years)					
Adverse events (AEs)		80.1	99.0	74.6	97.9
Serious adverse events (SAEs)		19.4	30.4	15.7	22.2
Infections (AEs) **		21.8	29.4	20.5	26.3
Infections (SAEs) **		2.9	5.2	2.0	2.4
Discontinuations due to AEs		2.9	3.5	2.2	5.7

SD: Standard deviation; VAS: Visual Analogue Scale; Q1, Q3 = 1st / 3rd quartile

* Please note, that for 104 patients (11.5%) the smoking status is unknown

** Infections: All AEs/SAEs with a MedDRA Preferred Term indicating an infection

Conclusions: TCZ i.v. treatment over two years resulted in improvements of all disease activity parameters. Contrary to csDMARDs and TNF-blockers, the results show that smokers benefit from TCZ i.v. to the same extent as non-smokers and ex-smokers. The similar effectiveness of TCZ i.v. was confirmed by distinctly improved patient reported outcomes (PROs) in all subgroups. On the other hand, smoking seems to coincide with a higher rate of adverse events and an increased risk of infections. However, due to differences in baseline characteristics between the subgroups, this has to be interpreted with caution.

References:

[1] Chang K, et al. Int J Mol Sci. 2014 Dec 3;15(12):22279–95.

[2] Theander E, et al. EULAR 2015: FRI0163.

Acknowledgements: This study was funded by Roche/Chugai, Germany.

Writing assistance was provided by Ecron Acunova GmbH, Germany with support from Roche/Chugai.

Disclosure of Interest: C. Specker Grant/research support from: Chugai, DRFZ, Consultant for: Abbvie, Janssen, Chugai, MSD, Novartis, UCB, Lilly, Boehringer, Speakers bureau: Abbvie, Celgene, Chugai, Euroimmun, MSD, Pfizer, UCB, H. Kellner: None declared, P. Kästner: None declared, C. Volberg: None declared, V. Braunewell: None declared, I. Schwarze: None declared, M. Aringer: None declared, M. Sieburg: None declared, M. Hofmann Employee of: Chugai Pharma Europe Ltd., Zweigniederlassung Deutschland, J. Flacke Employee of: Roche Pharma AG, Germany, H.-P. Tony Consultant for: Roche Pharma, Abbvie, BMS, Chugai, Janssen, Novartis, Pfizer, Sanofi, Lilly, MSD, Astra-Zeneca., G. Fliedner: None declared

DOI: 10.1136/annrheumdis-2017-eular.5923

AB0397 ABATACEPT SHOWS BETTER SUSTAINABILITY THAN TNF INHIBITORS WHEN USED FOLLOWING INITIAL BIOLOGIC DMARD FAILURE IN THE TREATMENT OF RHEUMATOID ARTHRITIS: 8 YEARS OF REAL-WORLD OBSERVATIONS FROM THE RHUMADATA® CLINICAL DATABASE AND REGISTRY

D. Choquette[1], L. Bessette[2], E. Alemao[3], B. Haraoui[1], F. Massicotte[1], M. Mtibaa[4], E. Muratti[4], J.-P. Pelletier[1], R. Postema[5], J.-P. Raynauld[1], M.-A. Rémillard[1], D. Sauvageau[1], A. Turcotte[2], É. Villeneuve[1], L. Coupal[1]. *[1]Rheumatology, Institut de recherche en rhumatologie de Montréal (IRRM), Montréal; [2]Rheumatology, Centre d'ostéoporose et de rhumatologie de Québec (CORQ), Québec, Canada; [3]Bristol-Myers Squibb, Princeton, United States; [4]Bristol-Myers Squibb, Montréal, Canada; [5]Bristol-Myers Squibb, Uxbridge, United Kingdom*

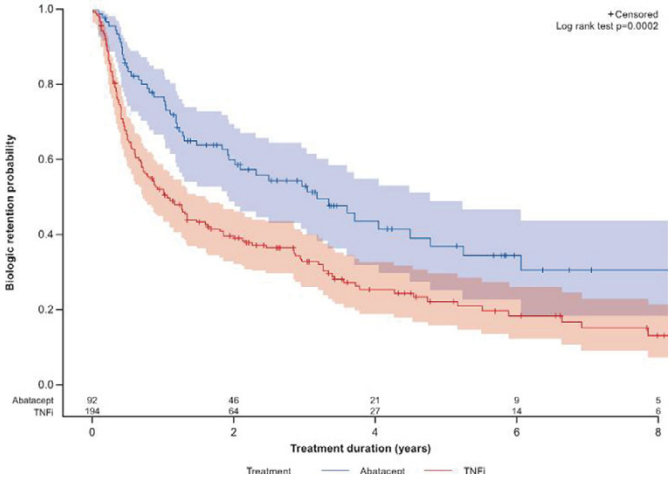
Background: In the absence of biomarkers predicting response to a specific therapy, the choice of second biologic is based mostly on habit and availability of an alternative agent. Traditionally, a second anti-TNF was the preferred option, but recent registry data point to better responses and retention if a drug with a different mode of action is prescribed.
Objectives: Assess the long-term retention of abatacept (ABA) and TNFi following first biologic (b)DMARD inadequate response in RHUMADATA® registry patients (pts) with RA.
Methods: Data from RHUMADATA® pts with RA prescribed either ABA or TNFi as the second bDMARD after 1 January 2006 were analysed. Pts were followed until treatment discontinuation or 9 January 2017 cut-off. Pt characteristics were compared using descriptive statistics, bDMARD discontinuation rates using Kaplan-Meier methods, and proportional hazard models were used to identify predictors of treatment discontinuation.
Results: Data for 92 and 194 pts prescribed ABA or a TNFi, respectively, as second-line treatment were extracted. No clinically significant differences in baseline characteristics were noted between treatment groups. Most pts were women (76.2%), average age (SD) was 45.1 (13.3) years at diagnosis and disease duration 10.8 (9.0) years. Most pts were stopping an anti-TNF agent: 97% of those who were switched to ABA and 83% of those who were prescribed a second anti-TNF. Overall, 77.6% of pts stopped their first bDMARD after >6 months of treatment (secondary failure). Significant differences in retention between ABA and TNFi groups (log-rank p=0.0002) were observed (Table, Figure). Results remained unchanged for pts treated with TNFi only in first line, and primary/secondary failure of the first bDMARD did not affect sustainability of the second agent. Lack of efficacy (57.7%) and AEs (16.5%) were the most commonly cited reasons for treatment discontinuation.
Conclusions: Abatacept has better sustainability over a second line TNFi in RA patients having failed one prior bDMARD.
Disclosure of Interest: D. Choquette Consultant for: BMS, Speakers bureau: BMS, L. Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant for: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Celgene, Lilly, Novartis, E. Alemao Shareholder of: BMS, Employee of: BMS, B. Haraoui Grant/research support from: BMS, Janssen, Roche, Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Merck, Pfizer, Roche, Sandoz, UCB, Speakers bureau: Pfizer, UCB, F. Massicotte: None declared, M. Mtibaa Shareholder of: BMS, Employee of: BMS, E. Muratti Employee of: BMS, J.-P. Pelletier: None declared, R. Postema Shareholder of: BMS, Employee of: BMS, J.-P. Raynauld Speakers bureau: AbbVie, Amgen, BMS, Janssen, Pfizer, Roche, Sanofi, Novartis, UCB, M.-A. Rémillard: None declared, D. Sauvageau: None declared, A. Turcotte Consultant for: Amgen, Abbvie, BMS, Celegene, Janssen, Roche, Pfizer, Lilly, Novartis, Merck, Sanofi, UCB, Speakers bureau: Amgen, Abbvie, BMS, Celegene, Janssen, Roche, Pfizer, Lilly, Novartis, Merck, É. Villeneuve Speakers bureau: Abbvie, Roche, BMS Consultant - Celgene, Cimzia, Pfizer, L. Coupal: None declared
DOI: 10.1136/annrheumdis-2017-eular.2379

Table 1. First bDMARD failure and retention characteristics of the second bDMARD

First bDMARD Failed	Second bDMARD					
	TNFi			Abatacept		
	Failure type		All	Failure type		All
	Primary	Secondary		Primary	Secondary	
TNF inhibitor, n, %	41, 25.5%	120, 74.5%	161, 100%	17, 19.1%	72, 80.9%	89, 100%
Other mode of action	6, 18.2%	27, 81.8%	33, 100%	0, 0%	3, 100%	3, 100%
Total	47, 24.2%	147, 75.8%	194, 100%	17, 18.5%	75, 81.5%	92, 100%
Second bDMARD Retention Probability at[1]:						
6 Months	64.68% (3.45%)			83.51% (3.89%)		
12 Months	50.54% (3.61%)			76.73% (4.45%)		
24 Months	39.77% (3.59%)			59.97% (5.29%)		
60 Months	22.26% (3.53%)			36.95% (6.17%)		
96 Months	13.22% (3.62%)			30.66% (6.61%)		
Biologic Retention Time (years)						
Mean, mean (SE)	2.71 (0.25)			3.33 (0.26)		
Lower Quartile (95% CI)	0.36 (0.28–0.44)			1.02 (0.49–1.29)		
Median (95% CI)	1.08 (0.71–1.60)			3.17 (1.92–4.78)		
Upper Quartile (95% CI)	4.26 (3.25–6.64)			++ (5.24-++)		

[1]% survival (standard error of % survival).

Figure. Retention Rates of Abatacept and TNFi Groups



AB0398 IMPACT OF BODY COMPOSITION ON RESPONSE TO BIOTHERAPY IN RHEUMATOID ARTHRITIS

S. Bouden, D. Kaffel, W. Hamdi[1,1], M.M. Kchir. *Rheumatology, Institut kassab, tunis, Tunisia*

Background: Biological therapies had greatly improved the treatment of rheumatoid arthritis (RA). The response to biologics may be influenced by many factors. Little is known about the impact of body composition inRA biologics.
Objectives: We aimed to investigate the impact of obesity (BMI≥30) andbody composition (lean mass/ fat mass)on response to biotherapy in RA.
Methods: A retrospective study was performed over a period of 11 years (2006–2016). Patients diagnosed RA (according to the ACR 1987 criteria) and treated by biologics were enrolled. Body composition (lean mass/ fat mass) was measured by X-ray biphotonic absorption (DXA). The threshold of signification was set for a value of $p<0.05$.
Results: Fifty patients were enrolled, including 5 men and 45 women (sex ratio=0.11). The mean age was 66 years [38–79]. The mean duration of RA was 5 years [1–30]. The mean duration of treatment with biologics was 38 months [6–120]. Thirty nine patients were treated by TNF alpha inhibitors (25 etanercept, 7 adalimumab, 6 infliximab and 1 certolizumabpegol), 6 rituximab and 5 tocilizumab. Nine patients had a normal weight (18%), 17 had overweight (34%) and 24 had obesity (49%). The average percentage of fat mass was 44.8 [23–54], with a median of 46. While comparing obese patients with others, we did not notice a significant difference in the mean variation of the DAS28 at 6 months for TNF alpha inhibitors nor for all biotherapies combined (respectively p=0.6 and p=0.9). The same result was observed while comparing the DAS28 according to the body composition (relative to the median of the percentage of the fat mass: for TNF alpha inhibitors (p=0,6) and for all biotherapies combined (p=0,09)).
Conclusions: In our study, there was no change in response to biologics in patients with RA. Further prospective studies with a larger size will be required to confirm or reverse these results.
References:
[1] Iannone F, Lopalco G and al. Impact of obesity on the clinical outcome of rheumatologic patients in biotherapy. Autoimmun Rev. 2016 May;15(5):447–50. doi: 10.1016.
[2] Gardette A, Ottaviani S. Body mass index and response to tocilizumab in rheumatoid arthritis: a real life study. Clin Rheumatol. 2016 Apr;35(4):857–61. doi: 10.1007.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6107

AB0399 RITUXIMAB TREATMENT AND IMMUNOGLOBULIN LEVELS MONITORING

G. Kasavkar, S. Kamath. *Rheumatology, Haywood hospital, Stoke on Trent, United Kingdom*

Background: Rheumatoid arthritis is a well-known inflammatory condition with a prevalence around 1% in females and 0.5% in males in UK (as per NOAR study). In the past decade use of biologic therapy has helped clinicians to treat rheumatoid arthritis more effectively. Rituximab is one of the biologics which is used commonly for treating rheumatoid arthritis. Rituximab is chimeric monoclonal antibody targeting CD20 molecule of B cells. First trial of rituximab in treating rheumatoid arthritis was published in 2004 and since then it has shown promising results in trials. In order to guide clinicians British society of rheumatology proposed recommendations in March 2010. An audit is required to ensure adherence to clinical guidelines at Haywood hospital.
Objectives: To assess whether patients receiving Rituximab are appropriately monitored with pretherapy evaluation of immunoglobulin levels

To assess the effects of rituximab on immunoglobulin levels and incidence of infection among patients on rituximab
Methods: Data was collected of all (N=105) patients who received Rituximab between May 2014 until April 2015 at the Haywood Hospital where patients attend for Rituximab injections.
Data was collected retrospectively from the Diamond System, Medisec system and Clinical Information System and entered onto an excel spread sheet which included following details
- Start date of Rituximab
- IgG levels prior to Rituximab and current IgG levels
- Total doses of rituximab and frequency of IgG monitoring
- Intermittent infections and type of infections.

Results: We observed that 82 out of 105 patients were started on rituximab after February 2011 when the BSR guidance was published and 53 out of 105 patients had their immunoglobulin levels checked prior to commencing rituximab
35/76 (46%) patients had 1 or more episodes of infections whilst on Rituximab which required treatment. Of these, 16 (46%) had recurrent infections.
39 patients had dropped their IgG levels after starting rituximab 18 (46%) of these suffered from infections.
17 patients had a drop in IgG ≥20% and 6 of these (36%) had recurrent infections and 1 patient had 1 episode of infection.
None of the patients had dropped their IgG levels below 5
Conclusions: A significant number of patients (35/76 =46%) had 1 or more episodes of infections despite IgG levels being above lower normal limit
Among patients who dropped their IgG levels had increased number infections. Also they had more than 1 episodes of infection
Patients who dropped IgG levels ≥20% suffered with recurrent infections
References:
[1] BSR and BHPR guidelines on the use of rituximab in rheumatoid arthritis doi:10.1093/rheumatology/ker106b.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1160

AB0400 EFFICACY AND SAFETY OF INTRAVENOUS AND SUBCUTANEOUS TOCILIZUMAB IN A COHORT OF PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS IN REAL-LIFE

G. Pomponio, C. Tontini, A. Angeletti, D. Olivari, D. Benfaremo, L. Manfredi, M.G. Danieli, P. Fraticelli, M.M. Luchetti, G. Moroncini, A. Gabrielli. *Department of Internal Medicine, Azienda Ospedaliero-universitaria 'Ospedali Riuniti', Ancona, Italy*

Background: Tocilizumab (TCZ) is a humanized monoclonal anti-interleukin-6 receptor antibody, used for the treatment of moderate to severe rheumatoid arthritis (RA). Although TCZ has been proved to be highly effective and safe in RA patients in large clinical trials, few data are available from real-life practice [1].
Objectives: To evaluate efficacy, safety and retention rate of intravenous (IV) and subcutaneous (SC) TCZ in a real-world setting.
Methods: We evaluated patients affected by moderate-to-severe RA and treated with TCZ from April 2010 to January 2017. Data of patients treated with IV-TCZ until January 2017 were collected retrospectively, while patients treated with either IV or SC-TCZ from January 2015 were included in a prospective cohort and assessed for disease activity, treatment discontinuation and/or onset of adverse events (AEs). DAS28-CRP, CDAI and SDAI scores were used for disease activity assessment and paired t test was used for statistical analysis. Treatment retention rate was estimated by Kaplan-Meier method.
Results: We evaluated 100 patients, 58 treated with IV-TCZ (8 mg/kg every 4w), 16 with SC-TCZ (162 mg every week), 26 switched from IV to SC during followup and 6 of these returned to IV-TCZ for cutaneous intolerance (80 females, median age 63 y, median duration of disease 11 y, median follow-up 16 months). Seventy-eight patients (78%) were treated with monotherapy and twenty-two (22%) in combination with methotrexate. At baseline, disease activity was severe in 87% of patients, moderate in 6% and mild or inactive in 7%; at the latest follow-up 60% of patients are in clinical remission. The mean DAS28-CRP in IV-TCZ and SW-TCZ groups considered as a whole was 4.34 at baseline and 2.71 at the latest follow-up available ($p<0.0001$). In the SC-TCZ group, mean basal DAS28-CRP was 3.70 vs 1.89 measured at the latest follow-up ($p<0.0001$). Fifty-three patients (53%) discontinued TCZ because of inefficacy (19), AEs (13) or other reasons (21, mostly lost to follow-up). Infections were the most frequent AE (45.1/100 person-years), 3 cases of severe pneumonia, one required treatment discontinuation. Infusion reactions were reported in 6/58 IV-TCZ patients, while injection site reactions in 14/42 SC-TCZ patients. Six of these intolerant patients were subsequently treated with i.v. tocilizumab without reactions. We observed an overall high retention rate of IV-TCZ and SW-TCZ (91.1%, 81.2%, 70.6%, 61.3%, 57.1% and 50% at 1, 2, 3, 4, 5, and 6 years respectively). The retention rate of SC-TCZ patients at 3 years was about 77%. The difference between IV/SW-TCZ and SC-TCZ groups was not significant (Fig. 2).
Conclusions: TCZ is effective, well tolerated and safe in a population of RA patients followed in a real-life setting.
No unexpected AE was observed in this large population followed for a long period. Interestingly retention rate was not affected by the administration route and in real life many patients can safely shift across different administration modalities.
References:
[1] Gabay C, Riek M, Hetland ML, Hauge EM, Pavelka K, Tomšič M, et al. Effectiveness of tocilizumab with and without synthetic disease-modifying antirheumatic drugs in rheumatoid arthritis: results from a European collaborative study. Ann Rheum Dis. 2015 Sep 15.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6724

AB0401 THE EFFICENT REGULATION OF TOCILIZUMAB FOR THE EXPRESSION OF CD4+/CD8+ T/CD19 + B CELLS AND THE IMMUNOGLOBULIN IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

H. Li[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: To study the influence of tocilizumab on lymphocyte subsets, immunoglobulin and biochemical indicators of Systemic juvenile idiopathic arthritis.
Methods: DMARDs poor efficacy in children with severe SJIA 18 patients were divided into two groups, of which eight patients tocilizumab + DMARDs group (in cluding a case of refractory MAS), 10 patients in the placebo + DMARDs control group, according to the weight>30kg, 8mg/kg, <30kg, 12mg/kg, injected once every two weeks in hospital.Symptoms and CD3 +, CD4 +, CD8 + T, CD19 + B, CD16 + 56-NK cell ratio in two groups were observed by the flow cytometry before or after 12 weeks treatment. Comparing immunoglobulin IgG, IgM, IgA, IgE with baseline after the therepy in two group, and continuous observe inflammatory markers (CRP, ESR, FER, WBC) and ALT/AST changes, adverse reactions and reduce stopping hormone case inductive analysis in following 12 weeks.
Results: After 12 weeks, tocilizumab + DMARDs group, CRP, ESR, FER were significantly decreased, the most frequently occurring adverse reaction was infection, mostly upper respiratory tract infection, followed by elevated transaminase, cholesterol, low-density lipoprotein High-density lipoprotein and triglyceride levels increased; two groups no serious adverse events (three-line reduction, severe infections, etc.). the proportion of CD4 + T, CD19 + B cells in Tocilizumab group were lower than baseline ($P<0.05$), CD8, CD3 + T cells were increased in comparing with baseline, however,no significant change with CD16 + 56-NK cells ($P>0.05$), and immunoglobulins IgG, IgM, IgA lower than baseline ($P<0.05$). The control group had no significant difference ($P>0.05$).
Conclusions: Tocilizumab can significantly reduce inflammatory markers (CRP, ESR, FER), but affect lipid metabolism and ALT/AST.Blocking IL-6 can be adjusted hyperthyroidism humoral and regulate CD4 + T, CD19 + B cells, reduce joint destruction. Tocilizumab can effectively control the development of DMARDs poor efficacy SJIA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2114

AB0402 RITUXIMAB MAY DELAY THE MOVEMENT OF RHEUMATOID ARTHRITIS PATIENTS ON CARDIORENAL CONTINUUM: RESULTS FROM A PROSPECTIVE OBSERVATIONAL SINGLE-CENTRE COHORT STUDY

I.R. Gaisin[1], L.V. Ivanova[2], A.A. Trukchina[2], A.A. Tukmacheva[2], Y.A. Volkova[1], A.A. Tebenkova[1], N.I. Maximov[1]. *[1]Izhevsk State Medical Academy; [2]Clinical Diagnostic Centre of the Udmurt Republic, Izhevsk, Russian Federation*

Background: Similarities in risk factors, initial stages, progression and final stage of both atherosclerotic cardiovascular disease (CVD) and chronic kidney disease (CKD) allowed formulating a concept of cardiorenal continuum.[1] CVD and CKD remain the main causes of mortality in rheumatoid arthritis (RA) patients.[2,3]
Objectives: We aimed to evaluate the effects of rituximab biologic therapy on cardiorenal continuum of RA patients.
Methods: Biologics-naïve RA patients (n=50; age 55.1±10.3) were followed up for 72 months after commencing and continuing rituximab therapy (1–10 standard courses) compared with 30 control RA patients (age 53.2±9.8).
Results: At year 6, rituximab patients have fewer incidences of hypertension, anxiety/depression, atherosclerosis and diastolic dysfunction than control patients (Table).
There were no significant differences in frequencies of other risk factors, signs of asymptomatic multiorgan damage and cases of established heart, cerebrovascular and renal diseases/complications.
Conclusions: Rituximab may be effective in delay of the movement of RA patients on cardiorenal continuum. The clinical implications of rituximab for cardiorenal correlations in RA patients need to be confirmed in large-scale clinical outcome trials.
References:
[1] Sarnak MJ, Levey AS. Cardiovascular disease and chronic renal disease: a new paradigm. Am J Kidney Dis 2000;35(4, Suppl. 1):117–31.
[2] Avina-Zubieta JA, Choi HK, Sadatsafarvi M, et al. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. Arthritis Rheum 2008;59:1690–7.
[3] Gullick NJ, Scott DL. Co-morbidities in established rheumatoid arthritis. Best Pract Res Clin Rheumatol 2011;25:469–83.

Abstract AB0402 – Table 1. Cardiorenal continuum features of rheumatoid arthritis patients (%)

	Features	Rituximab group			Control group			P_{R-C}
		1 year, n=50	3 years, n=47	6 years, n=31	1 year, n=30	3 years, n=26	6 years, n=16	
Risk factors	Hypertension	50.0	38.3	25.8 p_{6-1}=0.028	40.0	38.5	50.0	p_6=0.032
	Dyslipidaemia	44.0	36.2	38.7	40.0	46.2	50.0	>0.05
	Pre-diabetes	52.0	36.2	41.9	33.3	34.6	56.3	>0.05
	Metabolic syndrome	12.0	6.4	3.2	10.0	7.7	12.5	>0.05
	Diabetes mellitus	4.0	0	0	0	0	0	>0.05
	Anxiety/depression	83.2	41.5 p_{3-1}=0.006	35.3 p_{6-1}<0.001	80.0	73.1	68.8	p_3=0.009 p_6=0.008
Initial stages	Atherosclerosis	32.0	21.3	12.9 p_{6-1}=0.048	40.0	34.6	37.5	p_6=0.02
	Left ventricular hypertrophy	8.0	4.3	0	6.7	7.7	0	>0.05
	Diastolic dysfunction	48.0	38.3	22.6 p_{6-1}=0.022	46.7	50.0	56.3	p_6=0.04
	Albuminuria	8.0	0	0	0	0	6.3	>0.05
	Kidney impairment	6.0	2.1	0	13.3	0	0	>0.05
Progression	Angina	6.0	0	0	3.3	0	0	>0.05
	Chronic kidney disease	16.0	8.5	9.7	13.4	0	0	>0.05
End stage	Myocardial infarction/stroke	0	0	0	0	0	0	>0.05
	Heart failure	2.0	0	0	0	0	0	>0.05
	Acute/chronic renal failure	0	0	0	0	0	0	>0.05
	Death	0	0	12.9	0	0	0	>0.05

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5704

AB0403 ADHERENCE AND ACCESS TO BIOLOGICAL THERAPY AND TOFACITINIB IN A COHORT OF COLOMBIAN PATIENTS WITH RHEUMATOLOGICAL DISEASES

J.E. Machado-Alba, M.E. Machado-Duque, S. Granada on behalf of Grupo de Investigación en Farmacoepidemiología y Farmacovigilancia, Universidad Tecnológica de Pereira-Audifarma S.A, Pereira, Colombia. *Grupo de Investigación en Farmacoepidemiología y Farmacovigilancia, Universidad Tecnológica de Pereira-Audifarma S.A, Pereira, Colombia*

Background: Biological disease-modifying antirheumatic drug (bDMARD) and tofacitinib are highly effective, but with different pharmaceutical forms, adverse reactions and cost that could affect adherence therapy and drug access.
Objectives: To determine patient adherence and administrative access to the treatment with bDMARDs and tofacitnib in patients with rheumatological diseases in Colombia.
Methods: A retrospective cohort study, which included all patients in management with bDMARD and tofactinib initiated between July 1, 2015 and June 30, 2016. A monthly follow-up of the administrative adherence were evaluated by holding or applying the medication, as well as the application of Morisky-Green test in self-administered oral and subcutaneous therapies (non-adherent patient was considered when at least one doses is lost), other variables such as sociodemographic, comorbidities, and co-prescriptions were evaluated. A descriptive analysis, χ^2 for comparison and multivariate logistic regression were performed.
Results: A total of 1102 patients were evaluated, with a mean age of 52.8±15.4 years and a female predominance (72.8%). The most frequent comorbidities were hypertension (22.6%) and dyslipidemia (15.9%). The most prescribed drugs studied were adalimumab (31.9%), etanercept (22.2%) and tofacitinib (12.5%). 52.8% use conventional DMARDs and 42.2% use glucocorticoids. Global adherence was 66.3% as measured by Morisky-Green test. Adherence was better with self-administered subcutaneous drugs every week or longer, compared to daily dosing of oral drug; these data are detailed in table 1. In 42.4% of the patients, at least one delay per year in the application or dispensation occurred, leading to 36.1% of patients experiencing dose losses due to difficulties in access. The main reason (23%) for delays and dose losses is the failures by health-insurance companies to allow timely access to the therapy. In the multivariate analysis treatment with adalimumab or tofacitinib was associated with a greater probability of presenting delays in access after adjustment of variables.

Drug	(n)	(%)	Drug administration route and interval	Morisky-Green test adherence (%)	At least one dose application delay in the year of follow up (%)	Missed dose (%)
Adalimumab	351	31.9	SC – Every two weeks	74.8	62.7	51.3
Etanercept	245	22.2	SC – weekly	72	27.3	22.4
Tofacitinib	138	12.5	OA – every 12 hours	48.8	52.2	52.2
Golimumab	82	7.4	SC - monthly	64.7	32.9	28
Rituximab	66	6.0	IV - biannual and annual	Not apply	3.0	1.5
Certolizumab	58	5.3	SC - monthly	83.3	32.8	32.8
Infliximab	40	3.6	IV - monthly and every two months	Not apply	35.0	27.5
Abatacept	62	5.6	IV y SC - monthly and weekly	42.9 - (SC route)	38.7	27.4
Tocilizumab	60	5.4	IV y SC - monthly	50.0 - (SC route)	36.7	33.3

Conclusions: Subcutaneous self-applications of bDMARD have better adherence rates compared to oral drug. However, the limitations in access to treatment decrease the adherence. On the other hand the impact of the adherence could be major in the case of self-administered DMARD when weekly or longer intervals doses are lost, compared with the loss of one daily dose of tofacitinib.

References:
[1] Scott DL, et al. Rheumatoid arthritis. Lancet. 2010;376(9746):1094–108.
[2] Machado-Alba JE, et al. Effectiveness of treatment with biologic- and DMARD in rheumatoid arthritis patients in Colombia. Int J Clin Pract. 2016;70(6):506–11.
[3] Jorgensen TS, et al. Effectiveness and drug adherence of biologic monotherapy in routine care of patients with rheumatoid arthritis: a cohort study of patients registered in the Danish biologics registry. Rheumatology. 2015;54(12):2156–65.

Acknowledgements: To Universidad Tecnológica de Pereira and Audifarma S.A.
Disclosure of Interest: J. Machado-Alba Grant/research support from: The authors declare that Pfizer Colombia financed the data collection process in medical records. There was no intervention in the stages of processing, analysis or publication of that data. No non-financial conflicts of interest exist for any of the authors., M. Machado-Duque: None declared, S. Granada: None declared
DOI: 10.1136/annrheumdis-2017-eular.5263

AB0404 SIMILAR REMISSION RATES AMONG RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ANTI TNF AND NON-ANTI TNF THERAPIES: REAL-LIFE DATA

J.A. Gómez-Puerta [1,2], N. Duque [1], M. Saldarriaga [1], L.A. González [1,2], C. Cerón [1], L. Uribe Botero [1], O.J. Felipe-Díaz [1]. *[1]Medicarte IPS; [2]Grupo de Reumatología, Universidad de Antioquia, Medellín, Colombia*

Background: Several biological DMARD (bDMARD) therapies have been approved for use in rheumatoid arthritis (RA) and are classified according to their respective therapeutic target: Anti TNF therapies and non-Anti TNF therapies. They are very effective in most of patients but their comparative efficacy in daily clinical is less well known.
Objectives: Our aim was to compare the efficacy of anti-TNF therapies vs non-Anti TNF therapies in a cohort of Colombian RA patients followed in different arthritis clinics under daily clinical practice conditions.
Methods: We conducted a cross-sectional study including with RA patients treated at Medicarte IPS from March 2009 to December 2016. Medicarte is a referral center for the integral medical care and pharmaco-surveillance of patients under biologic therapies in 13 cities in Colombia for inflammatory arthropathies, mainly RA, psoriatic arthritis and spondyloartropathies. Clinical information was obtained from electronic clinical records and medical claims. Only those patients with disease activity scores (DAS-28) at baseline and at the last visit were included. Remission was defined as DAS-28 <2.6 on the last visit. Patients treated only with conventional DMARD and/or tofacitinib were excluded.
Results: A total of 1,020 patients with RA were identified. 844 patients (88% female) were included in the final analysis, 416 patients with anti TNF and 428 with non-anti TNF therapies (Rituximab 199, Tocilizumab 125 and Abatacept in 104 patients). The mean age was 55.2±11.8 years, with a mean disease duration

Table 1. General Characteristics of patients with RA under bDMARD therapy

	Total N=844	Anti TNF N=416	Non-Anti TNF N=428	p value
Gender (female) %	88.0	88.7	87.6	NS
Age (years, SD)	55.2±11.8	55.0±11.8	55.4±11.8	NS
Disease duration (years, SD)	15.2±9.5	15.0±9.9	15.5±9.0	NS
bDMARD therapy duration (years)	3.2±2.5	3.2±2.5	3.2±2.4	NS
First line bDMARD therapy,%	64.0	75.2	53.2	p<0.001
Combined therapy, %	83.0	90.9	75.0	p<0.001
Seropositive (either CCP and/or RF) %	80.1	82.0	78.3	NS
DAS-28 at baseline (± SD)	4.3±1.1	4.20±1.14	4.4±1.21	NS
HAQ at baseline (± SD)	1.13±0.77	1.09±0.78	1.16±0.77	NS

of 15.2±9.5 years. bDMARD therapy was used for a mean time period of 3.2±2.5 years. Eighty three percent of patients were treated in combination therapy and 80% of patients were seropositive (CCP and/or RF). Both groups did not differ significantly on baseline clinical characteristics (see Table), with 2 exceptions: patients who received Anti-TNF therapies were treated more frequently as first line therapy (75.2% vs 53.2%, $p<0.001$) and received in a higher proportion combined therapy (90.9% vs 75.0%, $p<0.001$). A total of 59% of patient achieved remission at the last visit. Three year remission rates were slightly higher but not significant in patients treated with non-anti TNF therapies vs anti-TNF therapies (59.6% vs 53.3%, p=NS). We did not find significant differences in remission rates according serological status.

Conclusions: In real-life setting, a meaningful proportion of RA patients achieved remission on the last visit. Patients treated with anti-TNF and non-anti TNF therapies had similar baseline characteristics and after a mean time period of treatment of 3 years, achieved similar remission rates.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5293

AB0405 SAFETY OF RITUXIMAB THERAPY IN AUTOIMMUNE DISEASES:SYSTEMATIC REVIEW AND META-ANALYSIS

K. Kobayashi[1], K.M. Minegishi[1], N. Horita[2], S. Ohno[1], H.N. Nakajima[3]. *[1]Center for Rheumatic Diseases, Yokohama City University Medical Center; [2]Department of Pulmonology; [3]Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, Japan*

Background: Treatment with rituximab (RTX), a chimeric CD20 monoclonal antibody, has demonstrated efficacy for patients with several autoimmune diseases. There is a growing concern, however, safety evidence of RTX is still lacking.

Objectives: We conducted to evaluate the safety of rituximab (RTX) for autoimmune diseases.

Methods: A literature review was performed based on the randomized clinical trials (RCTs) that assessed adverse events by comparing RTX and placebo or no treatment for autoimmune diseases. The same add-on treatment for both arms were allowed. Study selection and data extraction were independently conducted in duplicate. Meta-analyses were performed for each outcome separately using fixed model and generic inverse variance method.

Results: In the primary analysis, 16 eligible RCTs, with a total of 4147 patients for five autoimmune diseases (n=8: rheumatoid arthritis, n=3: Sjogren syndrome, n=1: systemic lupus erythematosus, multiple sclerosis, ulcerative colitis, Graves orbitopathy, immune thrombocytopenia) were analyzed. The incidence of infusion related reactions and the human antichimeric antibody (HACA) were higher in RTX group than placebo/no treatment group (OR 1.49, 95% CI 1.25–1.77 and OR 2.25, 95% CI 1.35–3.76, respectively). However, there were no significant differences the odds of total adverse events, serious adverse events, withdrawal for adverse events, infections, serious infections, malignancy, and all-cause death between two groups.

Conclusions: Our meta-analysis revealed that RTX was not associated with an increased risk of adverse events except for infusion related reactions and the incidence of HACA compared with placebo.

Acknowledgements:

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5643

AB0406 STABLE EFFICACY AND SAFETY AFTER SWITCHING FROM TOCILIZUMAB INTRAVENOUS TO SUBCUTANEOUS IN RHEUMATOID ARTHRITIS: RESULTS OF A COHORT OF 200 PATIENTS

L. Joffres[1], E. Ricard[2], C. Pereira Gillion[3], M. Herbette[4], C. Lucas[5], J.B. Cren[6], E. Bergeal[7], Y. Maugars[8], C. Saillot[2], P. Goupille[3], A. Saraux[4], A. Perdriger[5], B. Bouvard[6], E. Solau Gervais[1,9]. *[1]Rheumatology, University Hospital, Poitiers; [2]Rheumatology, General Hospital, Orleans; [3]Rheumatology, University Hospital, Tours; [4]Rheumatology, University Hospital, Brest; [5]Rheumatology, University Hospital, Rennes; [6]Rheumatology, University Hospital, Angers; [7]Medical information, General Hospital, la Rochelle; [8]Rheumatology, University Hospital, Nantes; [9]LITEC, Immunology Laboratory, Poitiers, France*

Background: Intravenous tocilizumab has been used since 2009 in Europe for the treatment of active rheumatoid arthritis. Since 2015, a subcutaneous formulation is available. The switch from a monthly, intravenous, with dose adjusted for bodyweight treatment to a weekly, subcutaneous, fixed dose, leads to various questions about efficacy and toxicity.

Objectives: The objectives were to evaluate the efficacy maintenance (maintenance rate and DAS28 variation), the safety, the dose variation after the switch and the characteristics of patients switching to the subcutaneous form respect to those following with the intravenous tocilizumab.

Methods: Multicenter and retrospective study was performed from a cohort of 203 patients undergoing intravenous tocilizumab from the rheumatology unit of 7 university hospitals between September 2015 and May 2016. Assessment has been done on the records, effectiveness was assessed using the DAS28, adverse events and reasons for staying on IV form were reported.

Results: On the 203 records analyzed, 3 were secondarily excluded. Of the 200 patients, 77 have switched for the subcutaneous form. Mean age of the 200 patients was 58 years (+/- 13.3) with 155 women (78%) and the mean duration of rheumatoid arthritis was 14 years (+/- 10.4). 72% of patients received a standard intravenous dose (8mg/kg/month) at baseline.

At the first visit after the prescription of the subcutaneous treatment, 58 patients on 65 (89%) maintained the treatment. The mean DAS28 was 1.53 (+/-1.00) at baseline and 1.19 (+/-0.78) at T1 (45 patients). Three patients received a reduced subcutaneous dose of 162mg/2 weeks following a reduced IV dose (<8 mg/kg/month) and maintained the subcutaneous treatment.

About safety, there was no new case of neutropenia $<1000/mm^3$. One severe adverse effect occurred (gastro intestinal perforation).

Regard to the dose variation, for the 77 patients switching, the mean difference between intravenous and subcutaneous dose was + 29mg/week (+/-35mg) with the subcutaneous tocilizumab.

Reasons for staying on IV form were essentially: the subcutaneous tocilizumab was not proposed in 55% of the cases and 17% of patients refused the subcutaneous form.

Conclusions: 89% of patients maintained the subcutaneous treatment after 4 months; efficacy was maintained in patients who received a reduced subcutaneous dose. Despite the higher dose after the switch (+29mg/week), there was no new case of neutropenia.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6008

AB0407 COMPARATIVE EFFECTIVENESS OF TOCILIZUMAB (TCZ) MONOTHERAPY WITH TUMOR NECROSIS FACTOR INHIBITORS (TNFI) IN COMBINATION WITH VARYING DOSES OF METHOTREXATE (MTX) IN PATIENTS WITH RHEUMATOID ARTHRITIS

L.R. Harrold[1,2], G.W. Reed[1,2], J. Best[3], S. Zlotnick[3], G. Persuitte[2], J.M. Kremer[2,4]. *[1]University of Massachusetts Medical School, Worcester; [2]Corrona, LLC, Southborough; [3]Genentech, Inc, South San Francisco; [4]Albany Medical College and The Center for Rheumatology, Albany, United States*

Background: Clinical studies have shown that the efficacy of TCZ monotherapy (TCZ mono) is superior to that of TNFi monotherapy and comparable to that of TCZ in combination with MTX.

Objectives: To compare the effectiveness of TCZ mono vs TNFi plus varying doses of MTX in patients with rheumatoid arthritis (RA) and prior exposure to TNFi in routine clinical practice.

Methods: Eligible participants were TCZ-naïve patients from the Corrona RA registry who had prior exposure to ≥1 TNFi, initiated TCZ mono or a TNFi + MTX between 2010 and 2016 and had a 6-month follow-up visit. The primary outcome was mean change from baseline in Clinical Disease Activity Index (CDAI) at 6 months. Secondary outcomes included achievement of low disease activity (LDA; CDAI ≤10) at 6 months. Patients initiating a TNFi + MTX were grouped by MTX dose (≤10 mg; >10 to ≤15 mg; >15 to ≤20 mg; >20 mg); outcomes in each group were compared with those initiating TCZ mono using trimmed populations, excluding patients outside the propensity score (PS) distribution overlap (not on common support). The PS included age, sex, race, body mass index, smoking status, work status, disease duration, concomitant prednisone use/dose, prior biologic use, American College of Rheumatology functional class and baseline modified Health Assessment Questionnaire, CDAI and patient pain scores. As a sensitivity analysis, stratified-matched populations were created (stratified by 1 vs ≥2 prior biologics, then matched on PS). Linear and logistic regression models were estimated in the trimmed populations, adjusting for the same covariates as in the PS.

Results: Baseline demographics were generally comparable between the TNFi + MTX groups and their matched TCZ mono groups. Overall, the mean age was 54 to 59 years, and the mean disease duration was 10.5 to 15 years. A higher proportion of patients initiating TCZ mono had received ≥3 prior biologics compared with those initiating TNFi + MTX. Patients initiating TCZ mono had significantly longer mean disease duration than those initiating TNFi + MTX >15 to ≤20 mg (13.0 vs 10.5 years) or TNFi + MTX >20 mg (12.3 vs 9.3 years) and a higher mean baseline CDAI than those initiating TNFi + MTX ≤10 mg (28.1 vs 25.4). Patients in all groups had improvement in CDAI scores at 6 months. In adjusted models, improvement in CDAI and the likelihood of achieving LDA were similar between the TCZ mono group and all TNFi + MTX groups (Table). Similar results were observed in the PS-matched cohorts.

Conclusions: TCZ mono was as effective as TNFi + MTX, regardless of MTX dose, for improving disease activity in patients with prior TNFi exposure. These data suggest that TCZ mono is an effective treatment option for patients with RA who cannot tolerate or prefer not to use MTX.

Acknowledgements: This study is sponsored by Corrona, LLC. Corrona, LLC, has been supported through contracted subscriptions in the past 2 years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.

Disclosure of Interest: L. Harrold Shareholder of: Corrona, LLC, Grant/research support from: Pfizer, Consultant for: Roche, Employee of: University of Massachusetts Medical School; Corrona, LLC, G. Reed Shareholder of: Corrona, LLC, Employee of: Corrona, LLC, J. Best Employee of: Genentech, Inc, S. Zlotnick

Table 1. Disease activity outcomes at 6 months in patients who initiated TCZ mono compared with those who initiated TNFi + MTX.

	Change in CDAI		Achievement of LDA	
	Unadjusted Mean (SD)	Adjusted β (95% CI)*	Unadjusted Response Rate, n (%)	Adjusted OR (95% CI)*
TCZ mono (n = 283)	−9.7 (14.6)	—	82 (29)	—
TNFi + MTX ≤ 10 mg (n = 108)	−7.8 (13.6)	−0.15 (−2.92 to 2.62)	33 (31)	1.22 (0.71 to 2.10)
TCZ mono (n = 300)	−9.6 (14.5)	—	88 (29)	—
TNFi + MTX > 10 to ≤ 15 mg (n = 186)	−9.0 (14.2)	−0.3 (−2.83 to 2.22)	70 (38)	0.94 (0.60 to 1.48)
TCZ mono (n = 292)	−9.6 (14.7)	—	85 (29)	—
TNFi + MTX > 15 to ≤ 20 mg (n = 273)	−6.9 (12.8)	−1.65 (−3.84 to 0.54)	73 (27)	1.4 (0.89 to 2.18)
TCZ mono (n = 285)	−9.7 (14.7)	—	85 (30)	—
TNFi + MTX > 20 mg (n = 107)	−8.4 (15.0)	−1.43 (−5.12 to 2.25)	32 (30)	1.26 (0.70 to 2.25)

CDAI, Clinical Disease Activity Index; LDA, low disease activity; MTX, methotrexate; OR, odds ratio; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor.
*TCZ compared with TNFi + MTX. Adjusted for sex, age, race (white vs nonwhite), disabled, retired, baseline CDAI, baseline modified Health Assessment Questionnaire, baseline patient pain scores, baseline prednisone use/dose, baseline body mass index, prior biologic use, prior TNFi use and American College of Rheumatology functional class.

Employee of: Genentech, Inc, G. Persuitte Employee of: Corrona, LLC, J. Kremer Shareholder of: Corrona, LLC, Consultant for: AbbVie; Amgen; Bristol-Meyers Squibb; Genentec, Inc; GlaxoSmithKline; Lilly; Pfizer; Regeron; Sanofi, Employee of: Corrona, LLC

DOI: 10.1136/annrheumdis-2017-eular.3295

AB0408 COMPARATIVE EFFECTIVENESS OF ABATACEPT VERSUS TNFI IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE CCP+ IN THE UNITED STATES CORRONA REGISTRY

L. Harrold[1], H. Litman[2], S. Connolly[3], E. Alemao[3], K. Price[3], S. Kelly[3], S. Rebello[2], W. Hua[2], J. Kremer[4]. *[1]University of Massachusetts, Worcester; [2]Corrona, LLC, Southborough; [3]Bristol-Myers Squibb, Princeton; [4]Albany Medical College and The Center for Rheumatology, Albany, United States*

Background: Anti-cyclic citrullinated peptide positivity (CCP+) is associated with a better response to abatacept (ABA) than anti-CCP negativity in patients (pts) with RA[1,2]; however, there are no head-to-head or comparative effectiveness research studies available evaluating responses to biologics in CCP+ pts in a real-world setting.
Objectives: To compare the effectiveness of ABA vs a TNF inhibitor (TNFi) in pts with RA who are CCP+.
Methods: We identified adult pts with RA from a large observational US cohort (1 Dec 2005–31 Aug 2016) who initiated ABA or a TNFi and who were CCP+ (≥20 U/mL) at or prior to initiation. Both groups had to have no prior exposure to other non-TNFi biologics or targeted synthetic DMARDs. TNFi initiators were excluded if they had prior use of ABA. Using propensity score matching (1:1) stratified by prior TNFi use (0, 1 and 2+), effectiveness at 6 months after initiation was evaluated. Mean change in CDAI over 6 months following initiation was the primary outcome, and secondary outcomes were: achievement of remission (CDAI ≤2.8), modified (m)ACR20, 50 and 70 responses and achievement of LDA/remission (CDAI ≤10) in those with moderate/high disease activity at initiation. A subset analysis was performed to consider separately pts who were biologic naïve and those who were biologic experienced at initiation.
Results: The 330 pairs of propensity score-matched ABA and TNFi initiators had no substantial differences in baseline characteristics. Both treatment groups had similar mean change in CDAI at 6 months as well as achievement of LDA, remission and mACR20/50/70 responses (Table). Among the 97 matched biologic-naïve pairs, there was no significant difference in change in CDAI for ABA initiators vs TNFi initiators (p=0.19). However, in the 233 matched biologic-experienced pairs, those initiating ABA had a greater improvement in mean change in CDAI (p=0.033) and were more likely to achieve an mACR50 response (p=0.014).
Conclusions: Pts with RA who were CCP+ and received either ABA or TNFi had a substantial improvement in clinical disease activity. In the overall propensity score-matched sample, similar outcomes were observed for both treatment groups. However, analysis of the biologic-experienced cohort found that ABA initiators had a greater improvement in disease activity than TNFi initiators.
References:
[1] Sokolove J, et al. Ann Rheum Dis 2016;75:709–14.
[2] Harrold LR, et al. Ann Rheum Dis 2016;75(Suppl 2):505–6.
Disclosure of Interest: L. Harrold Shareholder of: Corrona, LLC, Grant/research support from: Pfizer, Consultant for: Roche, Employee of: Corrona, LLC, H. Litman Employee of: Corrona, LLC, S. Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, K. Price Employee of: Bristol-Myers Squibb, S. Kelly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Rebello Employee of: Corrona, LLC, W. Hua Employee of: Corrona, LLC, J. Kremer Shareholder of: Corrona, LLC, Grant/research support from: AbbVie, Genentech, Lilly, Novartis, Pfizer, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Genentech, GSK, Lilly, MedImmune, Pfizer, Sanofi, Employee of: Corrona, LLC

DOI: 10.1136/annrheumdis-2017-eular.1643

AB0409 CORTICOSTEROID-SPARING IN PATIENTS WITH RHEUMATOID ARTHRITIS ON TOCILIZUMAB: FIRST EXPERIENCE OF BAB -EL- OUED HOSPITAL

M.A. Ifticene, H. Hafirassou, R. Benaziez, F. Mechid, F. Hanni, C. Dahou Makhloufi. *Hospital, algiers, Algeria*

Background: Tocilizumab (TCZ) is a monoclonal antibody directed against the IL-6 receptors. This treatment (TRT) allows for the cortisone weaning in preventing of its complications.
Objectives: The goal of this study is to evaluate the corticosteroid sparing in patients with RA treated with TCZ.
Methods: Prospective, descriptive study of patients hospitalized between 2012 and 2016, the diagnosis was made according to the ACR 1987 ACR/EULAR 2010 criteria. Included, are the patients treated with TCZ for at least 3 months associated with corticosteroids.
We have studied the following: the epidemiology, the associated DMARDs, the average DAS28VS, the average dosage of prednisone-equivalent and the percentage of patients with decreased or interrupted corticosteroids at M0, M3, M6 and M12.
Results: 26 patients (sex ratio: 0.7) treated with TCZ and corticosteroids, average age is 43.4 years (range 30–62). Average duration of the development of RA: 9.1±6.4 years. DMARDs was associated in 15 patient.
At baseline, 46.2% of patients were on 10 mg/day of cortisone, the average dose of prednisone-equivalent was at 7.7±3.6mg at M0, 5.3±3.2 mg at M3, 4.6±2.3 mg at M6, 2.6±2.6 mg at M12 with a statistically significant difference (p=0.000003). The average DASVS28 activity index was 5.6±0.9 at M0, 3.5±1.3 at M3, 3.04±1.2 at M6 and 2.6 ± M6 at M12 with a statistically significant difference (p<0.000001). Corticosteroid treatment was stopped in 12 patients after 1 year of treatment.
Conclusions: Through this study we note that the TRT using TCZ has enabled a significant reduction in the dose of corticosteroids. Stopping prednisone was possible in 50% of patients after 1 year of biotherapy.
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3965

Abstract AB0408 – Table 1

	Total population			Biologic naive			Biologic experienced		
	CCP+ abatacept initiators n=330 n=330	CCP+ TNFi initiators n=330		CCP+ abatacept initiators n=97	CCP+ TNFi initiators n=97		CCP+ abatacept initiators n=233	CCP+ TNFi initiators n=233	
Primary outcome:	Mean (±SE)	Mean (±SE)	p value*	Mean (±SE)	Mean (±SE)	p value*	Mean (±SE)	Mean (±SE)	p value*
Change in CDAI	–9.9 (±0.8)	–8.5 (±0.8)	0.24	–9.8 (±1.4)	–12.3 (±1.4)	0.19	–9.9 (±1.0)	–7.0 (±1.0)	0.033
Secondary outcomes:	Response rate (%)	Response rate (%)	p value†	Response rate (%)	Response rate (%)	p value†	Response rate (%)	Response rate (%)	p value†
LDA	41.3	39.7	0.69	50.0	57.0	0.36	37.6	32.1	0.26
Remission	15.5	14.8	0.83	19.6	21.6	0.72	13.7	12.0	0.58
mACR20	36.4	36.4	>0.99	40.2	45.4	0.47	34.8	32.6	0.62
mACR50	24.8	21.5	0.31	26.8 7 37.1	0.12	24.0	15.0	0.014	
mACR70	13.6	10.6	0.23	17.5	19.6	0.71	12.0	6.9	0.057

*t-test, †chi-square test.

AB0410 THE INTERPLAY BETWEEN C3 AND C4 AND DISEASE ACTIVITY IN PATIENTS AFFECTED BY RHEUMATOID ARTHRITIS DURING TREATMENT WITH ANTI-IL6 RECEPTOR

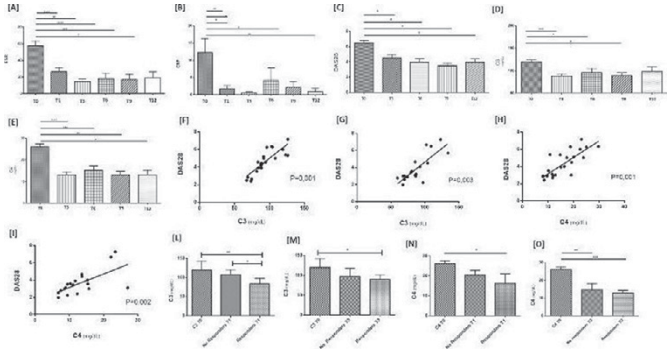
P. Conigliaro[1], P. Triggianese[1], M.S. Chimenti[1], I. Duca[2], B. Kroegler[1], R. Perricone[1]. *[1]Rheumatology, Allergology and Clinical Immunology, University of Rome Tor Vergata; [2]Dipartimento di Medicina Interna e Specialità Mediche, Reumatologia, Sapienza Università di Roma, Rome, Italy*

Background: The complement system (CS) is involved in the pathogenesis of rheumatoid arthritis (RA). Evidence reported that high C3 levels C3 in RA patients might reflect a pro-inflammatory status and represent a negative prognostic factor for TNF-inhibitors therapy.
Objectives: We evaluated CS in a cohort of RA patients treated with tocilizumab (TCZ) to explore whether there was any correlation between CS and both disease activity and response to therapy.
Methods: Consecutive outpatients affected by RA who started TCZ treatment i.v. at the Rheumatology Unit of "Policlinico Tor Vergata" in Rome (Italy) were enrolled (n=25) (Table I). We included 25 healthy subjects as controls. Disease activity was assessed by using DAS28 ESR-based while clinical response to therapy by EULAR response criteria. Peripheral blood samples were obtained from all patients at the time of each infusion. Laboratory assessment included ESR, CRP, RF, ACPA, C3, C4, CH50 assay. Clinical and laboratory data were registered at baseline (T0), after 1 (T1), 3 (T3), 6 (T6), 9 (T9), and 12 (T12) months from the beginning of the TCZ treatment.
Results: At baseline, both C3 and C4 were significantly higher in RA than in controls (Table 1).

Table 1

	RA (N=25)	Controls (N=25)	P value
Female (N/%)	23/92	23/92	N.S.
Age (years)	65.4±11.5	60.1±9.3	N.S.
Disease duration (years)	13±8.2	N.A.	N.A.
DAS28	6.5±1.3	N.A.	N.A.
HAQ	1.9±0.8	N.A.	N.A.
Positivity of RF (N/%)	17/68	N.A.	N.A.
Positivity of ACPA (N/%)	20/80	N.A.	N.A.
ESR (mm/h)	58±28	N.A.	N.A.
CRP (mg/l)	8.5±7.6	N.A.	N.A.
C3 (mg/dl)	119.4±22.4	104±18	0.04
C4 (mg/dl)	26±6.7	22±4	0.013
CH50 (%)	108±24	100±18	N.S.
Therapy:		N.A.	
PDN ≤7.5 mg/die (N/%)	9/36		
At least one DMARD (N/%)	13/52		
– MTX (N/%)	9/69.2		
– HCQ (N/%)	4/30.7		
– SSZ (N/%)	2/15.4		
– LEF (N/%)	2/15.4		
I line TCZ (N/%)	3/12		
II line TCZ (N/%)	3/12		
III line TCZ (N/%)	9/36		
IV line TCZ (N/%)	7/28		
V line TCZ (N/%)	3/12		

No difference in C3 and C4 resulted between ACPA positive and ACPA negative patients during the follow up. ESR, CRP and DAS28 levels were significanlty reduced at T1, T3, T6, T9, and T12 with the respect to T0 (Figure 1A-C). C3 levels were significantly reduced at T3, T6, and T9 with the respect to T0 while C4 levels were significantly reduced at T3, T6, T9, and T12 with the respect to T0 (Figure 1D-E). Positive correlations resulted between DAS28 and both C3 and C4 at T1 and T3 (Figure 1F-I). C3 and C4 were directly related with ESR at T1 (C3: P 0.002; C4: P 0.005), T3 (C3: P 0.04; C4: P 0.03), and T6 (C3: P<0.0001; C4: P 0.002) and with CRP at T1 (C3: P 0.03; C4: P 0.01) and T6 (C3: P<0.0001; C4: P 0.03). When stratifying patients in accordance with the EULAR response to therapy, C3 decreased significantly in responders than in no-responders at T1; moreover, responders showed lower levels of both C3 and C4 at T1 and T3 with the respect to T0 (Figure 1L-O).



Conclusions: In RA patients, treatment with TCZ is able to reduce C3 and C4 levels in an early and substained way. The disease activity is directly related with the reduction of C3 and C4 serum levels. RA patients with a good/moderate clinical response show significantly lower C3 and C4 levels than no-responder patients. Our preliminary data suggest that C3 and C4 can be a reliable marker of both the disease activity and the response to therapy in RA patients treated with TCZ.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4643

AB0411 COMPARISON OF TUBERCULIN SKIN TEST AND INTERFERON-GAMMA RELEASE ASSAY SCREENING IN PATIENTS WITH RHEUMATOID ARTHRITIS STARTING ANTI-TUMOR NECROSIS FACTOR THERAPY

D.T. Archimandriti[1], C. Iliou[1], A.T. Tzallas[2], E. Pelechas[1], A.A. Drosos[1], P.V. Voulgari[1]. *[1]Rheumatology Clinic, Department of Internal Medicine, Medical School, University of Ioannina; [2]Department of Computer Engineering, Technological Educational Institute of Epirus, Greece, School of Applied Technology, Ioannina, Greece*

Background: Biologic agents provide clinical benefits in patients with Rheumatoid Arthritis (RA) but they are associated with an increased risk of tuberculosis (TB) infection.
Objectives: We investigated the accordance between the tuberculin skin test (TST) and the interferon-gamma (IFN-γ) release assay (IGRA) for the diagnosis of latent tuberculosis infection (LTBI) in patients with RA. The objective of our study was a direct comparison between the IGRA and the TST regarding LTBI diagnosis in RA patients before starting anti-TNF agents and at least one year after the initiation of treatment.
Methods: RA consecutive patients have been included in the study both before and after 1 year of the initiation of TNF-α antagonist therapy. A standard questionnaire was completed for each patient, including basic demographic data and concurrent immunosuppressive therapy (corticosteroids, disease-modifying anti-rheumatic drugs [DMARDs], synthetic and biologics). The patients were screened for LTBI using IGRA and TST methods.
All analyses were performed with IBM-SPSS Statistics for Windows (version 21). The kappa coefficient (κ) was calculated to determine the concordance between the two tests: TST and IGRA. The strength of the agreement was considered "poor" for $\kappa \leq 0.20$, "low-moderate" for $0.20 < \kappa \leq 0.40$, moderate for $0.40 < \kappa \leq 0.60$, "substantial" for $0.60 < \kappa \leq 0.80$, and "optimal" for $0.80 < \kappa \leq 1$.
Results: 78 patients (67 female, 11 male) have been screened with TST and IGRA. The accordance between TST and IGRA was 89.7% (κ 0.514, $\kappa<0.001$). A κ value of 0.514 represents a moderate accordance between the two tests. 6 female patients converted TST (4 became positive, and 2 became negative). No patient developed active tuberculosis.
Conclusions: A moderate accordance between the two methods (TST and IGRA) was obtained. In the absence of a diagnostic gold standard for LTBI, different issues should be taken into consideration regarding the two methods (cost, laboratory expertise and equipment etc). More studies are needed in the field in order to elucidate the cost-effectiveness but also the appropriateness of both methods.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6400

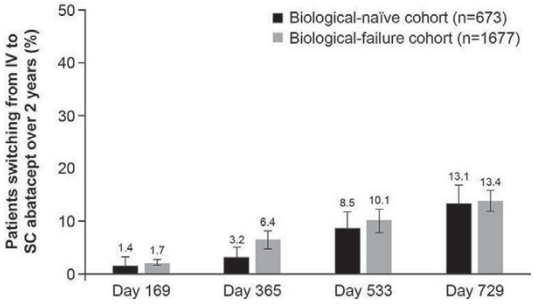
AB0412 LESS THAN 5% OF REAL-LIFE PATIENTS WHO SWITCH FROM IV TO SC ABATACEPT IN REAL-WORLD CLINICAL PRACTICE SUBSEQUENTLY SWITCH BACK TO THE IV FORMULATION

R. Alten[1], H.-M. Lorenz[2], X. Mariette[3], H. Nüßlein[4], M. Galeazzi[5], F. Navarro[6], M. Chartier[7], J. Heitzmann[8], C. Rauch[9], M. Le Bars[7]. *[1]Schlosspark-Klinik University Medicine, Berlin; [2]University Hospital, Heidelberg, Germany; [3]Université Paris-Sud, Paris, France; [4]University of Erlangen-Nuremberg, Nuremberg, Germany; [5]University of Siena, Siena, Italy; [6]Hospital Univesitario Virgen Macarena, Seville, Spain; [7]Bristol-Myers Squibb, Rueil-Malmaison; [8]Excelya, Boulogne-Billancourt, France; [9]Bristol-Myers Squibb, Munich, Germany*

Background: Patients (pts) with RA may be able to switch from IV to SC abatacept with no loss of efficacy or safety concerns, but data are inconclusive.[1–4] In the ACTION (AbataCepTIn rOutiNe clinical practice; NCT02109666) study, a 1-year interim analysis showed that switching had no adverse clinical effect.[5]
Objectives: To examine treatment patterns and explore abatacept formulation switching over 2 years in ACTION.
Methods: ACTION is a 2-year, prospective, observational study of pts with moderate-to-severe RA who initiated IV abatacept in Europe and Canada between May 2008 and December 2013. Assessments in biologic-naïve and biologic-failure pts were: baseline characteristics, rates of and reasons for switching (IV to SC), and re-switching to IV over 2 years. Descriptive data were generated: mean (SD) for continuous variables and n (%) for categorical variables. Rates of switching were estimated by Kaplan–Meier analysis. Cohorts were pooled to analyse further pts who switched owing to low numbers.
Results: In the ACTION cohort, 2350/2364 pts (99.4%) were evaluable for this analysis (673 [28.6%] biologic naïve, 1677 [71.4%] biologic failure). A total of 729

(43.4%) biologic-failure pts had received 1, and 948 (56.6%) had received ≥2 previous biologics. Baseline characteristics in biologic-naïve and biologic-failure pts, respectively, were: mean (SD) age 59.9 (12.7) and 56.9 (12.5) years; RA duration 7.2 (8.22) and 12.1 (9.13) years; 496 (73.7%) and 1379 (82.2%) were women; 621 (92.3%) and 1552 (92.5%) had received prior MTX; and 533 (79.2%) and 1386 (82.6%) had received corticosteroids. Over 2 years, 195 pts switched from IV to SC abatacept (57 biologic naïve, 138 biologic failure; Fig.). Reasons for switching were available for 172 pts (51 biologic naïve, 121 biologic failure; some had >1 reason); biologic naïve/biologic failure: pt wish 54.9%/62.0%, physician choice 31.4%/19.8%, safety 5.9%/9.9%, remission/major improvement 3.9%/5.0%, poor compliance 0%/4.1%, lack of efficacy 2.0%/3.3%, surgery 2.0%/0.8%, weight adjustment 2.0%/0%, other 49.0%/36.4%. Only eight pts (2.6%) re-switched to IV abatacept (2 biologic naïve, 6 biologic failure). Reasons for re-switching were: pt wish (n=4), lack of efficacy (n=4), safety issue (n=1) and other (n=2).

Figure. Patients Who Switched From IV to SC Abatacept Over 2 Years (Kaplan–Meier Analysis)



Conclusions: Less than 5% of pts who switched formulation from IV to SC abatacept in real-world clinical practice re-switched to the IV formulation, suggesting that switching has no adverse clinical impact. A change in formulation was mainly due to pt wish, reflecting their involvement in decision-making.

References:

[1] Keystone EC, et al. Ann Rheum Dis 2012;71:857–61.
[2] Mueller R, et al. Arthritis Rheumatol 2015;67(Suppl. 10):651–52.
[3] Reggia R, et al. J Rheumatol 2015;42:193–5.
[4] Monti S, et al. J Rheumatol 2015;42:1993–4.
[5] Alten R, et al. Ann Rheum Dis 2016;75(Suppl. 2):202.

Disclosure of Interest: R. Alten Grant/research support from: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, H.-M. Lorenz Consultant for: AbbVie, Bristol-Myers Squibb, Roche-Chugai, UCB, MSD, GSK, SOBI, Medac, Novartis, Janssen-Cilag, Astra-Zeneca, Pfizer, Actelion, X. Mariette Grant/research support from: Biogen, Pfizer, UCB, Consultant for: Bristol-Myers Squibb, LFB, Pfizer, GSK, UCB, H. Nüßlein Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, M. Galeazzi: None declared, F. Navarro Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, Jansen, Lilly, Speakers bureau: Pfizer, MSD, Roche, UCB, AbbVie, Bristol-Myers Squibb, M. Chartier Employee of: Bristol-Myers Squibb, J. Heitzmann: None declared, C. Rauch Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, M. Le Bars Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.1379

AB0413 INDUCTION AND PROGRESSION OF SUBCUTANEOUS NODULOSIS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOCILIZUMAB

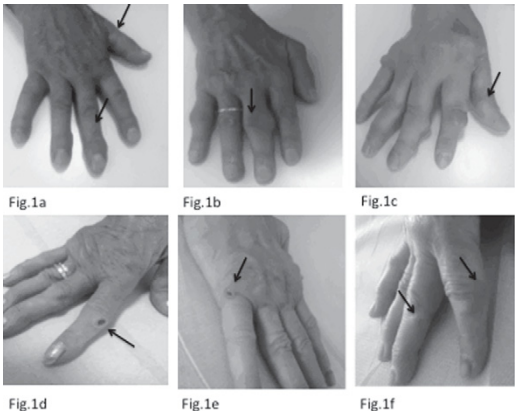
R. Talotta, A. Batticciotto, M.C. Ditto, M.C. Gerardi, D. Ventura, P. Sarzi Puttini.
Rheumatology Unit, University Hospital "Luigi Sacco", Milan, Italy

Background: Tocilizumab (TCZ) is a monoclonal antibody (moAb) directed against the IL-6 receptor approved for moderate-to severe rheumatoid arthritis (RA) treatment. Some authors have reported a beneficial effect of TCZ in preventing lung and subcutaneous nodulosis in RA patients. On the contrary, to our knowledge no data concerning the acceleration of subcutaneous nodulosis under TCZ therapy are currently available.

Objectives: We report a small case series of 5 RA patients experimenting an evident worsening of subcutaneous nodulosis during the treatment with intravenous tocilizumab.

Methods: Our cohort included 5 patients (1 male and 4 females, mean age ± Standard Deviation (SD) 64±10.6 years, mean disease duration ± SD 21.8±10.9 years). Four patients were rheumatoid factor and anti-citrullinated peptide antibodies positive. Each patient had been previously treated with several conventional and biologic drugs. At the time of observation, three subjects were practicing methotrexate (MTX), two patients were taking hydroxychloroquine (HCQ) and one patient was taking prednisone. Intravenous tocilizumab 8 mg/kg every 4 weeks was administered for a mean ± SD of 43.4±32.4 months, with a good disease control in 3 cases. All the patients had a previous history of subcutaneous nodulosis that considerably worsened during the treatment with tocilizumab. Patients experimented the development of new subcutaneous nodules localized at the fingers, elbows or the inframammary fold, tending to ulceration. The management of this medical event included the tapering of MTX, the administration of steroids, the addition of HCQ, the use of antibiotics and surgery. However, neither pharmacological nor surgical treatment was completely effective, as nodules tended to recur and to increase in number and dimensions.

Results: To our knowledge this is the first report describing an accelerated subcutaneous nodulosis in a small cohort of RA patients treated with tocilizumab.



Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4419

AB0414 THE USE OF RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS: IN WHICH INFUSION INTERVALS WERE GIVEN AND HOW DID THEY RESPOND? HUR-BIO REAL LIFE RESULTS

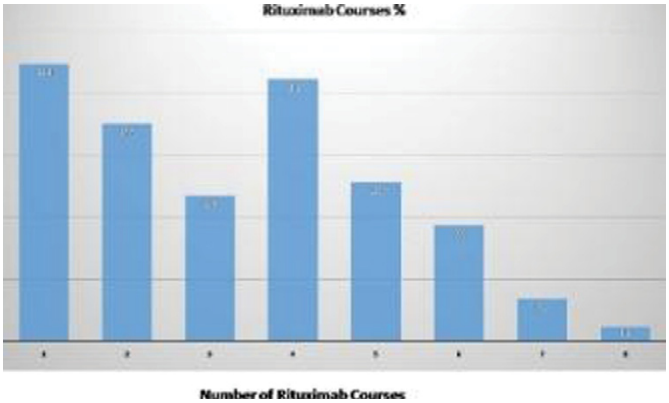
B. Armagan, A. Sari, A. Erden, L. Kilic, O. Karadag, A. Akdogan, S. Apras Bilgen, U. Kalyoncu, I. Ertenli, S. Kiraz. *Hacettepe University, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey*

Background: Rituximab is one of the treatment options in rheumatoid arthritis (RA) patients and officially recommended as a maintanance treatment given every 6 months after the initial loading of first course.

Objectives: In this real life study, it was aimed to investigate the infusion frequency of rituximab maintanance treatment and possible effects on disease activity.

Methods: The HUR-BIO is a single-center biologic registry of Hacettepe University which is established in Ankara and in which patients have been prospectively recorded since 2012. This database has 1235 RA patient records as of August 2016. Rituximab was prescribed at least once in 273 (22.1%) patients. The residence address of 85 those patients was within the boundaries of center city (Ankara) and they were included in to the study. In our clinic, the dates and the DAS-28 scores at the time of rituximab courses were recorded. Rituximab infusion compliance was classified as; "regular " if there is less than one month delay, "slightly irregular" if less than 3 months delay and "irregular" if more than 3 months delay.

Results: The mean age of the 85 patients (80% female) was 59.1 (10.1), the mean disease duration was 12.9 (8.6) years and 74.1% of patients were seropositive. 39/85 (46%) patients previously used at least one biological agent (46 (54%) patients were biologic naive before Rituximab therapy). Median rituximab course number was 3 (1–8). A total of 211 rituximab courses were given to 85 patients. Rituximab course number and percentage is shown in figure. The mean interval time between rituximab courses was 7.9 (2.8) months. Total of 102 (52.6%)



courses were admistred at normal times regularly, 60 (30.9%) were slightly irregular and 32 (16.5%) were irregular. There was no significant difference between the mean DAS-28 responses in the time of the courses and the rituximab infusion compliances [in regular group mean DAS-28 was 3.31 (1,19), in slightly irregular group mean DAS-28 was 3.26 (1.35) and irregular group mean DAS-28 was 3,57 (1.34), $p>0.05$]. Before rituximab courses, 33.7% of patients had remission, 19.1% had low disease activity, 36.3% had moderate disease activity and 10.9% had high disease activity.

Conclusions: Rituximab administration was approximately 2 months delayed in RA patients who were living in center-city boundaries. The pre-treatment mean disease activity scores were similar, even if there was a delay in rituximab administration. In our center, about 85% of patients were taking RTX courses regular and/or slightly irregular and about half of the patients before treatment were in remission and/or low disease activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4430

AB0415 TENDENCY TO CHOOSE FIRST BIOLOGIC AGENT THERAPY OF RHEUMATOID ARTHRITIS IN THE ELDERLY: RESULTS FROM JAPANESE MULTICENTER REGISTRY

T. Watanabe, T. Kojima, N. Takahashi, S. Asai, N. Asai, T. Matsumoto, Y. Sobue, N. Ishiguro. *Orthopaedic Surgery and Rheumatology, Nagoya University Graduate School of Medicine Department of Orthopaedic Surgery, Nagoya, Japan*

Background: Of the treatment of rheumatoid arthritis (RA), biologic agent therapies are chosen, if disease activity remains moderate or high despite csDMARDs therapy. In the elderly, with comorbidity and their less spare ability, safety is often concerned in the choice of biologic agent.

Objectives: We investigated the tendency to choose biologic agent and drug continuation rates in elderly in last decade.

Methods: Records of relevant patients with RA were collected from the Tsurumai Biologic Communication Registry, wherein the department of Nagoya University and 20 affiliated hospitals in Japan are enrolled. A total of 873 biologics-naïve and age 65 and older patients were recruited from January 2004 to December 2014. We studied the choice of the biologic agent year by, and baseline disease activity and concomitant methotrexate (MTX) among TNF inhibiters, tocilizumab (TCZ), and abatacept (ABT) groups. Drug continuation rates were compared among TNF inhibiters, TCZ, and ABT groups.

Results: From 2005 to 2010, etanercept (ETN) was used the most (2007; 73.5%, 2009; 65.9%). After the advent of ABT, ABT was used the most (2011; 44.3%, 2014; 38.8%).

Baseline disease activity slightly decreased as a whole (DAS28-CRP; 4.88 to 4.44). Despite baseline disease activity of TNF inhibitors group decreased (DAS28-CRP; 4.88 to 4.37), that of TCZ group increased (DAS28-CRP; 4.94 to 6.24).

In 2011–2014, baseline disease activity of TCZ group (5.85) was higher than that of TNF inhibiters group (5.11) ($p<0.05$). Concomitant MTX rate and dose were lower in ABT group (40.2%, 7.6mg) than that of TNF inhibiters group (79.0%, 8.9mg). 2 years drug continuation rate due to all unfavorable causes; ABT group was 92.4%, better than that of TNF inhibitors 87.1% and TCZ 69.2% ($p<0.05$). 2 years drug continuation rate due to adverse events; TCZ group was 80. 8%, lower than that of TNF inhibitors 94.6% and ABT 96.2% ($p<0.05$).

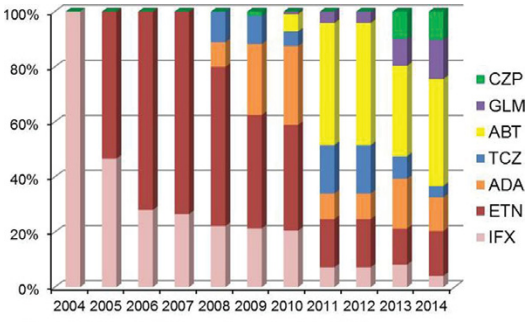


Figure 1. Changes of biologic agent from 2004 to 2014 (IFX:infliximab, ETN: etanercept ,ADA: adalimumab, TCZ:tocilizumab, ABT:abatacept,GLM: golimumab, CZP:certolizumab pegol)

Conclusions: ETN was used most before the advent of ABT. After the advent of ABT, ABT was used most and ETN decreased. This selection was made for speculation that ABT is lower risk than other biological agents. Baseline disease activity slightly decreased showing that tight control management became also popular among elderly. In 2011–2014, concomitant MTX rate and dose were lower in ABT group, but 2 years drug continuation rate was the highest.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1679

AB0416 WHICH FACTORS PREDICT THE RESPONSIVENESS TO TOCILIZUMAB IN RHEUMATOID ARTHRITIS? THE DIFFERENCE BETWEEN THE USAGE AS THE FIRST BIOLOGIC AND AS THE SECOND BIOLOGIC

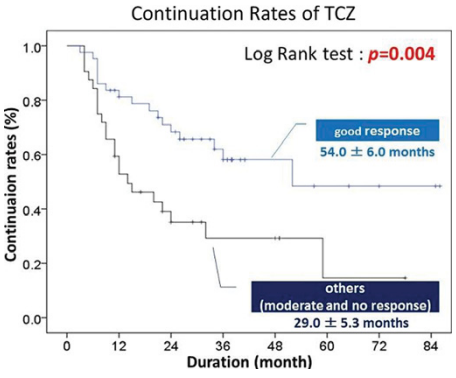
Y. Kunishita, R. Yoshimi, H. Nagai, N. Hamada, Y. Soejima, Y. Sugiyama, N. Tsuchida, H. Nakano, D. Kishimoto, R. Kamiyama, Y. Asami, Y. Kirino, H. Nakajima. *Department of Stem Cell and Immune Regulation, Yokohama City University Graduate School of Medicine, Yokohama, Japan*

Background: Although recent development of a variety of biologics has dramatically improved treatment for rheumatoid arthritis (RA), it is still unclear which biologics is better for use in each patient. Some previous studies have shown the predictive factors for good response (GR) to tocilizumab (TCZ), including low HAQ, high DAS28[1], low levels of serum soluble IL-6 receptor[2], and low numbers of previous use of other biologics[3]. However, the consensus is not immediately available.

Objectives: To compare continuation rates (CR) of TCZ by the responsiveness to the therapy and to identify predictive factors for GR to TCZ in RA.

Methods: Patient with RA who newly started receiving TCZ after April 2008 in our hospital, were included in the study. We collected patient records, medication histories, laboratory data, and clinical parameters longitudinally after starting TCZ. Statistical analyses were performed using the chi-square test, binomial *logistic regression* analysis, Kaplan-Meier method, and the log-rank test.

Results: Ninety-two patients were included in the study. The mean age and disease duration at baseline were 60.0±13.5 years and 8.7±8.0 years, respectively. The seroprevalence of the anti-cyclic citrullinated peptide antibody and the rheumatoid factor were 95.4% and 95.7%, respectively. The rate of methotrexate and prednisolone at baseline were 45.7% and 64.1%, respectively. TCZ was administered as the first biologic in 42 patients, and as the second biologic in 33. DAS28(ESR) and CDAI revealed high disease activity at baseline (5.2±1.5 and 25.4±14.1, respectively). The mean CR of all patients was 42.1±4.0 months. The CR was significantly higher in patients who achieved GR in EULAR response criteria at 6 months after starting TCZ than those who did not achieve GR (54.0±6.0 months vs 29.0±5.3 months, p=0.004). Multivariate statistical analysis revealed two predictive factors for achieving GR at 6 months after starting TCZ, the low number of previous use of other biologics and the low CDAI at baseline (p=0.018, odds ratio (OR) =0.386, and p=0.011, OR=0.944, respectively). We divided the patients into two groups, patients using TCZ as the first biologic and patients using it as the second biologic. Univariate statistical analyses revealed low usage rate and dose of prednisolone (PSL) and low serum creatinine level at baseline as the predictive factors for achieving GR in patients using TCZ as the first biologic, and low DAS28(ESR), CDAI and HAQ-DI in the patients using TCZ as the second biologic. By multivariate statistical analysis, we identified the low CDAI as a predictive factor in the patients using TCZ as the second biologic.



Conclusions: RA patients who achieved GR at 6 months after starting TCZ showed higher CR than the others. This study also suggests that low number of biologics usage and low CDAI at baseline are the predictive factors for GR. The history of biologics usage may be important to identify the predictive factors for GR to TCZ.

References:

[1] Ann Rheum Dis 2011;70:1216–22.
[2] Ann Rheum Dis 2014;73:945–7.
[3] Pharmacological Research 2016;111:264–71.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4059

Rheumatoid arthritis - non biologic treatment

AB0417 EFFICACY AND SAFETY OF METHOTREXATE AND LEFLUNOMIDE AS A COMBINATION THERAPY IN RHEUMATOID ARTHRITIS PATIENTS WITH HIGH DISEASE ACTIVITY PRESENTING AT A TERTIARY CARE SETTING IN PAKISTAN

B. Salim, S. Samreen, A. Nasim, H. Gul, A. Masood. *Rheumatology, Rawalpindi, Pakistan*

Background: In the management of rheumatoid arthritis (RA), the goal is remission. However it is not easy to attain this goal in all patients. Its not only the high disease activity, but rather other factors like availability and cost of biologics in developing countries. Therefore various combination therapies of conventional DMARDs are in vogue in such scenarios. Methotrexate (MTX) and Leflunomide (LEF) in combination is an effective option which can be fairly utilized in resource constraint settings to induce remission.
Objectives: To study the efficacy and safety profile of MTX+LEF combination in patients with active RA at 24 weeks.
Methods: This is a quasi-experimental study conducted at Rheumatology department, Fauji Foundation Hospital, Rawalpindi. 95 patients with active RA despite optimal dose (20–25 mg/week) of MTX. Leflunomide 20mg/day was added. Patients underwent clinical and laboratory review at 0, 4, 12 and 24 weeks to note down primary efficacy end points and adverse effects.
Results: Ninety five patients were enrolled with a mean age (years) ± SD of 51.7±8.9 and a mean duration of disease (years) of 8.6±7.1.Patients had active disease at baseline with a mean disease activity score (DAS28) of 5.99±0.6. At 24 weeks the mean change in tender joint count (TJ), swollen joint count (SJ), patients pain score on visual analogue scale (VAS) and DAS 28 were all statistically significant (p-value 0.000).The mean change in m HAQ was also statistically significant (p-value 0.000).
At 6 months the most frequent side effects (though mostly mild); were abdominal pain and nausea. 78 patients (79.1%) continued with the combination therapy. Only 3 patients stopped the treatment temporarily (due to raised ALT and vomiting).14 patients discontinued treatment mainly due to diarrhea, severe oral ulcers and markedly raised ALT.

Table 1. Baseline clinical and demographic feature of patients enrolled for MTX+LEF combination therapy

Total patients	95 (100%)
Age mean ± SD (years)	51.7±8.9
Gender m/f	2/93
Duration of diseasemean± SD (years)	8.6±7.1
RA factor (positive)	72 (75.8%)
Anti CCP (positive)	61 (64.2%)
Premorbids	
Diabetic (DM)	10 (10.5%)
Hypertensive (HTN)	16 (16.2%)
DM+HTN	3 (3.2%)

Table 2. Outcome/efficacy measure of MTX+LEF (n=95)

	Baseline (0 week)	24 weeks	p-value
Mean Tj	14.92±6.44	3.38±2.38	0.000
Mean Sj	4.29±2.30	0.90±1.28	0.000
Mean pain VAS (Patient)	7.19±1.86	2.91±1.85	0.000
Mean ESR	33.3±9.10	16.78±5.99	0.000
Mean DAS 28	5.99±0.64	3.52±0.86	0.000
Mhaq	1.75±0.64	0.59±0.42	0.000

Conclusions: MTX+LEF combination is an effective and safe option in RA patients failing MTX monotherapy provided regular clinical and laboratory monitoring is done.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1399

AB0418 COMPARISON OF ANTI-INFLAMMATORY DRUGS WITH GLUCOCORTICOIDS IN TREATMENT OF RHEUMATOID ARTHRITIS

B.N. Coskun[1], F. Ulutaş[2], S. Ermurat[1], E. Dalkılıc[1]. *[1]Rheumatology; [2]Internal Medicine, Uludag University, Bursa, Turkey*

Background: Rheumatoid arthritis (RA) is a chronical autoimmune disease that commonly presented with symmetrical polyarthritis of hands and feet. Pharmacological treatment options are non-steroid anti-inflammatory drugs (NSAIDs), glucocorticoids (GK) and disease modifying anti rheumatoid drugs (DMARDs) ([csDMARDs] or [tsDMARDs or [bDMARD].
Objectives: In this study we aimed to review the use of NSAID and GK in our patients.
Methods: The patients who diagnosed as RA at our office were included in the study. Patients were classified with EULAR 2010 RA criteria. The demographics and medications of the patients were recorded. All patients we examined pain with visual analog scale (VAS), global assessment of patient and doctor, number of tender and swollen joints (28 joints), health assessment questionnaire (HAQ), C – reactive protein (CRP), eritrocyte sedimentation rate (ESR), rheumatoid factor (RF) and anti – CCP. We assessed activity of disease by using disease activity score DAS28.
Results: A total of 686 patients were enrolled in the study (580 female [84.5%], 106 male [15.5%]). Mean age was 53.23±12.21 and mean length of diagnosis was 10.74±7.59 months. The rate of extra-articular disease was 17.9% and the deformity rate was 31.3%. In all patients, activity of disease was mild in 55%, moderate in 37.8% and severe in 7.3% with regard to DAS28 score. The disease activity was mild in 54.6%, moderate in 43.11% and severe in 2.3% in patients who were using only NSAIDS. These rates of diseases activity was 57.2%, 40.7% and 2.1% in mild, moderate and severe disease respectively for the patients using only GK. In patients using both NSAIDs and GK, the disease activity was mild in 55%, moderate in 44% and severe in 1%. Comparison of the disease activity with medications revealed statistically significant difference in patients that using only NSAID and using both, but not in that using only steroid (respectively p: 0.022, p: 0.025, p: 0.46).

DAS 28	Mild <3,2	Moderate ≥3,2-<5,1	Severe ≥5,1
All patients %	55	37,8	7,3
Only NSAIDS %	54,6	43,11	2,3
Only GK %	57,2	40,7	2,1
Both NSAIDs and GK %	55	44	1,0
p	**0,022**	**0,025**	0,46

Conclusions: In our study we found that patients has mild activity of disease use highly rates of NSAID and GC. It is important for providing remission using NSAIDs and GC along with DMARD. Our results demonstrate use of both GK and NSAIDS results in better outcomes.
References:
[1] Singh JA, Saag KG, Bridges SL Jr et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2016 Jan;68(1):1–26.
[2] Gaujoux-Viala C, Gossec L. When and for how long should glucocorticoids be used in rheumatoid arthritis? International guidelines and recommendations. Ann N Y Acad Sci. 2014 May; 1318:32–40.
Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5926

AB0419 REAL WORLD USE OF TOFACITINIB IN RHEUMATOID ARTHRITIS: DATA FROM LATIN AMERICA

E.E. Schneeberger[1], A. Salas[2], L.F. Medina[3], J.B. Zacariaz[4], R.D. Mantilla[5], J.C. Sarmiento-Monroy[5], L.J. Elizondo[6], B. Garro[7], H. Madariaga[8], L. Górriz[9], R.D.N. Giorgi[10], M. Pinheiro[11], D. Ponce de Leon[12]. *[1]Servicio de Reumatología, Instituto de Rehabilitación Psicofísica; [2]Servicio de Reumatología, HIGA San Martin de la Plata, Buenos Aires, Argentina; [3]Servicio de Reumatología, Hospital Universitario del Valle, Cali, Colombia; [4]Servicio de Reumatología, Hospital Italiano, Buenos Aires, Argentina; [5]Epidemiólogo, Centro de Dermatología y Reumatología FUNINDERMA, Bogotá, Colombia; [6]Reumatólogo, Centro de Investigación Clínica de Ciudad Obregón, Sonora, Mexico; [7]Reumatólogo, Centro de Excelencia en Reumatología, Lima; [8]Reumatólogo, Clínica del Sur, Arequipa, Peru; [9]Servicio de Reumatología, Hospital Santo Tomas, Panamá, Panama; [10]Servicio de Reumatología, Hospital do Servidor Público Estadual; [11]Pfizer Inc, São Paulo, Brazil; [12]Pfizer Inc, Lima, Peru*

Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. Tofacitinib can be given as monotherapy or with csDMARDs. Published data on real world (RW) tofacitinib use in Latin America (LA) are limited. We characterise the patient (pt) population starting tofacitinib and gain insights into the safety profile in the RW LA setting.
Methods: Initial tofacitinib therapies in adult RA pts from 10 private/public centres in 6 countries (Argentina, Brazil, Colombia, México, Panamá, Perú) were considered. Data were retrospectively obtained via a standardised format, focusing on demographics, drug history, adverse events (AEs), safety events of special interest, latent tuberculosis (TB) screening, selected confirmed laboratory abnormalities and discontinuation rates. Tofacitinib use as monotherapy or with csDMARDs was at the rheumatologist's discretion.
Results: 288 pts with severe active RA were included; most were female (n=263; 91%), mean (SD) age was 51.3 (6.36) years (yrs) and mean (SD) disease duration was 10.4 (4.0) yrs. 89% of pts were RF+ or ACPA+. The max (range) follow-up period was 22 (10–34) months. Tofacitinib was given as 2nd-line therapy (post-csDMARD) in 44% of pts, after one biologic DMARD (bDMARD) in 18% of pts and after ≥2 bDMARDs in 38% of pts. Tofacitinib was given as monotherapy in 117/283 (41%) pts and with csDMARDs in 171/283 (59%) pts. Tofacitinib usage corresponds to 13% of advanced therapies (JAK inhibitors, bDMARDs and biosimilars). Thirty-eight AEs were observed; upper respiratory infections (n=11), skin infection (n=5), herpes zoster (HZ; n=4) and urinary infections (n=4) were most common. Gastrointestinal intolerance was seen in 2 pts. Three (1%) pts had serious infection events (SIEs); no opportunistic infections (OIs), including TB, occurred. All HZ cases (n=4; 1.4%) were monomeric, non-serious and resolved without complication after antiviral therapy. Before starting tofacitinib, 5 pts (1.7%) were vaccinated against HZ and 5.6% were diagnosed with latent TB. No active

TB cases occurred with tofacitinib treatment. One malignancy (thyroid cancer) was reported. Severe (>3 ULN) elevation of liver enzymes or increases of CPK above normal were infrequent (<1%); no severe cytopenias were reported. Lipid increases occurred in 10% of pts. Tofacitinib was withdrawn in 40 pts (13.9%) due to lack of efficacy (n=20; 7%), AEs (n=11; 3.8%) or other reasons (n=9; 3.1%), such as loss of follow-up, pregnancy, access issues or travel. Limitations include limited pt numbers and follow-up of exposure.

Conclusions: In the RW LA setting, tofacitinib was used mostly as 2nd-line therapy; no new safety signals emerged vs clinical trials. SIEs and HZ were uncommon; no cases of TB/other OIs occurred, but were seen in the clinical program.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Irving of CMC and funded by Pfizer Inc.

Disclosure of Interest: E. Schneeberger: None declared, A. Salas Speakers bureau: AbbVie, Pfizer Inc, L. F. Medina: None declared, J. B. Zacariaz: None declared, R. D. Mantilla Grant/research support from: Abbott, AbbVie, Biopas, Bristol-Myers Squibb, Novartis, Pfizer Inc, Roche, Consultant for: Abbott, AbbVie, Biopas, Bristol-Myers Squibb, Novartis, Pfizer Inc, Roche, Speakers bureau: Abbott, AbbVie, Biopas, Bristol-Myers Squibb, Novartis, Pfizer Inc, Roche, J. C. Sarmiento-Monroy: None declared, L. J. Elizondo Grant/research support from: Amgen, Roche, Consultant for: Instituto Mexicano del Seguro Social, B. Garro: None declared, H. Madariaga: None declared, L. Górriz: None declared, R. D. N. Giorgi: None declared, M. Pinheiro Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, D. Ponce de Leon Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.1607

AB0420 THE SAME TREATMENT RESPONSE OF MONO- AND COMBINED-MTX TREATMENT IN DMARDS-NAÏVE TURKISH PATIENTS WITH SEROPOSITIVE RHEUMATOID ARTHRITIS AND THE IMPORTANCE OF PULMONARY TOXICITY

F.F. Ayhan[1,2], A. Gümüştepe[1], B. Nacır[1], A. Karagöz[1]. *[1]Physical medicine & rehabilitation, Ankara Training and Research Hospital, Ankara; [2]Physical therapy & rehabilitation, Uşak University, School of Health Sciences, Uşak, Turkey*

Background: Methotrexate (MTX) is the anchor drug for the treatment of rheumatoid arthritis (RA). There are important guidelines suggesting mono-MTX treatment at first for pharmacologic treatment of RA (1,2). We thought that these recommendations should be evaluated in different geographic regions and ethnic groups because of genetic factors.

Objectives: Therefore, we aimed to compare the efficacy and adverse effect profile of mono-MTX and combined-MTX treatments in patients with DMARDs-naïve Turkish patients with seropositive RA.

Methods: Hundred patients with seropositive RA (mean age: 47.4±12.0 years, 63 females and 37 males) were included. Patients were excluded the past history of using for synthetic or biologic DMARDs or moderate-high dose steroid (>10mg/day), viral hepatitis, transaminase elevations, and other contra-indications for MTX. Then they were divided as mono-MTX (n=57) and combined-MTX (n=43) groups.

Results: There was no difference between groups in age (p=0.34), sex (p=0.104), age of onset (p=0.10), MTX-weekly dose (p=0.228), the score of DAS28 (p=0.783), RF level (p=0.473), and CCP level (p=0.592) at the beginning. Patients of combined-DMARDs group used higher dose of prednisolone than patients of mono-MTX group (p=0.011). The change of DAS28 scores was not different between groups. CRP levels of combined-MTX group were higher than mono-MTX group both beginning and at 6th month. The frequencies of adverse events were not different between groups. GI adverse events are the first line in both groups (28% vs.16.3%). The frequencies of dose decrease (7% vs. 14%) or stop (7% vs. 4.7%) for MTX were also not different between groups (p=0.288, p=0.257). The frequencies of other adverse effects were less than 5%. MTX dose decrease or stop have been moderately correlated with pulmonary involvement (r=0.4, p=0.02).

Conclusions: Both mono-MTX and combined-MTX treatment had similar efficacy and safety profile in Turkish patients with seropositive RA as reported in studies of other countries suggesting no any advantage of combined MTX compared to mono-MTX (3). The frequency of MTX-stopping in our study was similar to this systematic review (9%). As a conclusion, MTX should also be the first choice of the treatment of RA in our country. Pulmonary adverse events should not be ignored.

References:

[1] Singh JA, Saag KG, Bridges SL J, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Rheumatol. 2016;68(1):1–26.

[2] Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis. 2014;73(3):492–509.

[3] Katchamart W, Trudeau J, Phumethum V, et al. Methotrexate monotherapy versus methotrexate combination therapy with non-biologic disease modifying anti-theumatic drugs for RA. Cochrane Database od Systematic Reviews 2010;Issue 4.Art.No.:CD008495.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2147

AB0421 RAPAMYCIN REDUCES DISEASE ACTIVITY THROUGH RESTORING REGULATORY T CELL NUMBERS IN PATIENTS WITH ACTIVE REFRACTORY RHEUMATOID ARTHRITIS

H. Niu[1], Z. Li[1], J. He[1], R. Jia[1], J. Luo[1], C. Gao[2], C. Wang[1], X. Li[1]. *[1]Department of Rheumatology, the Second Hospital of Shanxi Medical University, Taiyuan, China; [2]Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, United States*

Background: $CD4^+CD25^+Foxp3^+$ T regulatory (Treg) cells play a key role in peripheral tolerance. Rapamycin was approved by the FDA to preserve renal allografts and to be efficacious in patients with several autoimmune diseases [1].

Objectives: To investigate the status of Treg cells in active refractory rheumatoid arthritis (RA) and the effects of rapamycin on patients with RA.

Methods: Forty-five active refractory RA patients were enrolled. Rapamycin was used at a dose of 0.5 mg every 2 days [the preliminary, open-label clinical trial of rapamycin (Clinical Trials.gov number: ChiCTR-IPR-17010307)]. Clinical improvement and immunological assessments were performed before 1st rapamycin dose and 12 weeks post treatment. Blood samples were obtained from RA patients and 75 healthy volunteers for estimation of $CD4^+$ T cell subsets.

Results: Two patients dropped out due to non-compliance. As compared to healthy controls (median of Treg cells: 33.32 cell/ul), the absolute counts of circulating Treg cells were significantly decreased in patients with active refractory RA (median: 27.17 cell/ul; P=0.046). While the median ratios of Th17/Treg cells in patients with active refractory RA (median: 0.26) were significantly higher than those of healthy volunteers (median: 0.19; P=0.029). No difference in the absolute counts of circulating Th17 cells and Th1 cells was observed between patients with active refractory RA and healthy subjects. Rapamycin treatment led to clinical improvement with the median post-treatment DAS28-ESR decreasing when compared to baseline (from 4.19 to 3.78) in active refractory RA patients. Sixteen patients (16/43 patients, 37.21%) achieved an EULAR moderate response and 6 patients (6/43 patients, 13.95%) reached good response at week 12. Rapamycin administration resulted in an increase in the absolute counts of Treg cells in active refractory RA patients, from a median of 27.17 cell/ul (at week 0) to 37.57 cell/ul (at week 12) (P=0.041). The ratios of Th17/Treg cells shows a reduction from a median of 0.26 at baseline to 0.20 at week 12, but the difference is not significant (P =0.376). No significant difference was observed in the absolute counts of circulating Th17 and Th1 cells after rapamycin treatment. Interestingly, we observed that Treg cells increased before the complete remission of the disease (DAS28 score <2.6) in patients with active refractory RA. At week 12, the mean dose of prednisone which refractory RA patients were receiving decreased from 11.98 mg/d to 8.31 mg/d, with a dose reduced by ≥30% than that at baseline. The categories of DMARDs use were also reduced (P<0.05). No serious adverse events was observed during the 12-week period of rapamycin treatment.

Conclusions: Reduced absolute number of Treg cells was found in the patients with active refractory RA, indicating an imbalance between Th17 and Treg cells. Rapamycin elicits rapid improvement of disease activity via restoring circulating Treg cells numbers in patients with active refractory RA.

References:

[1] Perl A. Activation of mTOR (mechanistic target of rapamycin) in rheumatic diseases. Nat Rev Rheumatol. 2016. 12(3): 169–82.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2701

AB0422 1,25-DIHYDROXYVITAMIN D3 MODULATES T CELLS DIFFERENTIATION AND IMPACTS ON THE PRODUCTION OF ASSOCIATED-CYTOKINES FROM CHINESE HAN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

H. Wen[1], X. Li[2]. *[1]Rheumatology; [2]the Second Hospital of Shanxi Medical University, Taiyuan, China*

Background: Recent studies have suggested that vitamin D may play a role in select inflammatory diseases including rheumatoid arthritis (RA). Epidemiological studies suggest that there is an association between vitamin D deficiency and susceptibility to RA.

The present study sought to investigate effects of 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) on T cells differentiation and associated cytokines in Chinese Han patients with early rheumatoid arthritis (RA). The results reported that 1,25(OH)2D3 inhibits the synthesis of Th1 cytokines IFN-γ, Th17 cytokines IL-17, IL-22, IL-6, TNF-α, and up-regulates Th2 cytokine IL-4, which indicated that the possible immunoregulatory role and bone-sparing effects of 1,25(OH)2D3 in RA through modulation of the Th1/Th17 and Th2 cytokine balance.

Objectives: To study effects of 1,25-dihydroxyvitamin D3 ($1,25(OH)_2D_3$) on T cells differentiation and associated cytokines in patients with early rheumatoid arthritis (RA).

Methods: The level of Th1, Th2, Th17 and Treg cell were detected with BDFACS Calibur flow cytometer. IFN-γ, TNF-α, IL-2, IL-4, IL-6, IL-10, IL-17 and IL-22 were examined in 54 patients with incipient RA using a cytometric bead array (CBA).

Results: After 72 hours of incubation of peripheral blood mononuclear cells (PBMCs) with $1,25(OH)_2D_3$ in RA patients, the levels of IFN-γ, TNF-α, IL-2, IL-6 and IL-17 significantly decreased compared to those of the control. $1,25(OH)_2D_3$ had no significantly impact on the levels of IL-4, IL-10 and IL-22. The levels of Th17 and the ratio of Th17/Treg significantly decreased in $1,25(OH)_2D_3$ treated

groups compared to those of the control. 1,25$(OH)_2D_3$ had no significantly impact on the level of Th1, Th2, Treg and the ratio of Th1/Th2.
Conclusions: The present study demonstrated that 1,25$(OH)_2D_3$ inhibits the synthesis of Th1 cytokines IFN-γ, Th17 cytokines IL-17, IL-22, IL-6, TNF-α, and up-regulates Th2 cytokine IL-4, which indicated that the possible immunoregulatory role and bone-sparing effects of 1,25$(OH)_2D_3$ in RA through modulation of the Th1/Th17 and Th2 cytokine balance.
References:
[1] Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet 2016 May 3. pii: S0140-6736(16)30173-8. doi: 10.1016/S0140-6736(16)30173-8. [Epub ahead of print].
[2] Wen H, Baker JF. Vitamin D, immunoregulation, and rheumatoid arthritis. J Clin Rheumatol 2011;17(2):102–7.
[3] H. Takayanagi. Osteoimmunology and the efects of the immune system on bone. Nature Reviews Rheumatology 2009;5:667–76.
[4] N. J. Horwood, V. Kartsogiannis, J. M. W. Quinn, et al. Activated T lymphocytes support osteoclast formation in vitro. Biochemical and Biophysical Research Communications 1999;265(1):144–50.
[5] Y. Choi, K. M. Woo, S. H. Ko et al. Osteoclastogenesis is enhanced by activated B cells but suppressed by activated CD8+ T cells. European Journal of Immunology 2001;.31(7):2179–88.
Acknowledgements: This work was supported by a Research Grant from the National Natural Science Foundation of China (no.81301532) and the Shanxi Science and Technology research projects of China (no.201603D321074).
The authors thank Dr Alexis Ogdie for reviewing the manuscript.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3177

AB0423 MINIMALLY INVASIVE SURGICAL TREATMENT OF TEMPOROMANDIBULAR JOINT IN PATIENTS WITH VARIOUS RHEUMATIC DISORDERS

I. Zaslavskiy[1], A. Drobyshev[1], T. Dubinina[2], S. Erdes[2], A. Kuznetsov[1]. *[1]A.I. Yevdokimov Moscow State University of Medicine and Dentistry; [2]"Va Nasonova Research Institute of Rheumatology, RUSSIA, MOSCOW, Moscow, Russian Federation*

Background: Currently, maxillofacial surgery to actively develop and improve minimally invasive surgical methods for the treatment of patients with diseases of temporomandibular joint (TMJ). These types of surgical treatments like arthroscopy and artrolavazh TMJ are less traumatic and therefore can be effective in patients with rheumatic pathology.
Objectives: To evaluate the efficacy of minimally invasive surgical treatment of TMJ in patients with rheumatic diseases (RD).
Methods: In the study were included 64 pts aged from 18 to 65 years with various rheumatic disorders and lesions of the TMJ. Of these, rheumatoid arthritis (RA) - 43 (67.2%), psoriatic arthritis (PsA) 11 (17.2%), systemic lupus erythematosus - 8 (12.5%) and ankylosing spondylitis (AS) - 2 (3.1%). Before and after 14 days, a month and 6 months after surgery were assessed the following parameters: the level of pain in the TMJ (VAS), the aperture of mouth opening. All the patients at baseline and at 6 months after treatment was performed MRI of the TMJ. Interpretation of the TMJ MRI studies performed by the presence of signs of pathological changes in the joint, which were scored according to the number of pathological signs (from 0 to 8 points). As a preparatory stage before surgery all patients – splint therapy during 1 month was performed. Surgery included arthrolavage and arthroscopy TMJ followed by the introduction of hyaluronic acid.
Results: Before treatment all patients had severe involvement of the TMJ by Wilkes international classification: III of St is 62.5%, IV – by 21.9%, V – 15,6%. 6 months after surgical treatment the level of pain in the TMJ decreased 9.8 times (from 4.9 to 0.5, $p<0,0001$). Mouth opening increased 2.3 times (from 17.5 mm to 40.9 mm, $p<0,0001$), was reached from 96.7% of patients normal value. In the control MRI study of the TMJ at 6 months after surgery, the quantity of signs of pathological changes in the joints were reduced by 2.7 times in comparison with the initial level. The best results were achieved in patients with RA and PsA. The lowest result was achieved in the group of patients with AS.
Conclusions: Minimally invasive methods of surgical treatment of TMJ (arthrolavage and arthroscopy), the most effective and appropriate for the treatment of patients with RD lesion of the temporomandibular joint.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4562

AB0424 THE EFFECT OF HIGH LEVEL OF ANTI-CITRULLINATED PROTEIN ANTIBODIES AND RHEUMATOID FACTOR ON BONE EROSIONS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS– A CROSS-SECTIONAL AND LONGITUDINAL ANALYSIS

J. Yue[1], J. Griffith[2], J. Xu[3], L. Shi[1], D. Wang[4], P. Wong[1], E.K. Li[1], M. Li[1], T.K. Li[1], T.Y. Zhu[5], L. Qin[5], L.-S. Tam[1]. *[1]Department of Medicine & Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong; [2]Department of Imaging and Interventional Radiology, The Prince of Wales Hospital, The Chinese University of Hong Kong;[3]Department of Orthopedics & Traumatology; [4]Department of Imaging and Interventional Radiology; [5]Bone Quality and Health Center of the Department of Orthopedics & Traumatology, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hongkong, Hong Kong*

Background: Bone erosions are a key feature of rheumatoid arthritis (RA) reflecting both disease severity and disease progression. Recent studies using HR-pQCT demonstrated impairment in the bone microstructure of the metacarpophalangeal (MCP) joints of ACPAs-positive healthy individuals despite no signs of arthritis. In patients with established RA, ACPAs and rheumatoid factor (RF) showed an additive effect on erosion number and erosion size. Furthermore, RF influences erosion size only in ACPAs-positive but not in ACPAs-negative patients.
Objectives: To determine the effect of high titre of anticitrullinated protein antibodies (ACPAs) and rheumatoid factor (RF) on the number and size of bone erosions in patients with early rheumatoid arthritis (ERA) by high-resolution peripheral quantitative computed tomography (HR-pQCT) at baseline and whether these antibodies are associated with the progression of erosion after one year of follow-up.
Methods: In the cross-sectional study, HR-pQCT of the second metacarpophalangeal joint (MCP2) was performed in 124 patients with ERA at baseline, images were analysable in 117 patients. Erosions were visualized in 72 patients and parameters of bone erosions were assessed. In the prospective study, 63 ERA patients who had completed one year of follow-up with repeat HR-pQCT scan were also analysed. The number and volume of the erosions as well as bone mineral density (BMD) surrounding erosion were quantified. Data on demographic and disease-specific parameters including ESR, CRP, DAS 28, ACPAs and RF levels and treatment were recorded.
Results: At baseline, 90/117 patients were both ACPAs and RF positive (ACPAs+/RF+ group), 7/117 were only RF (RF+), 13/117 were only ACPAs (ACPAs+) and 7/117 were antibody negative (non-ACPAs+/RF+ group, n=27). Erosion depth and volume were increased in the ACPAs+/RF+ group compared with the non-ACPAs+/RF+ group (both $P<0.05$) (Table 1). Independent explanatory variables associated with a larger erosion volume included RF>16U (P=0.012), older age (P=0.003) and a higher damage joint count (P=0.028). Images from 63 patients who completed 12 months follow-up were analysed. Erosion volume were significantly lower in patients who achieved simplified disease activity score (SDAI) remission at 12 months compared to those who did not (P=0.045). Linear regression analysis indicated that independent predictors for an increase in erosion volume included RF>16U (P=0.032) and a higher damage joint count (P=0.009) at baseline and failure to achieve SDAI remission at 1 year (P=0. 043).

parameters	Total sample	RF+/ACPAs+	Not RF+/ACPA+	P value
N (total)	117	90	27	
Females N (%)	87 (74.36%)	66 (73.33%)	21 (77.78%)	0.500
Age (years)	53.024±13.0155	52.993±13.0250	53.129±13.2313	0.962
Disease duration (months)	7.1207±5.15862	7.4157±5.31466	6.1481±4.56326	0.265
ESR(mm/1st hr)	58.955±32.6734	59.942±34.5028	55.704±26.0455	0.497
CRP(mg/dl)	18.738±10.950	18.712±26.4026	18.822±19.0308	0.984
DAS28-CPR(4)	4.8615±0.92659	4.8068±0.92384	5.0418±0.92999	0.250
DAS28-ESR(4)	6.8612±1.05333	6.8406±1.05429	6.9291±1.06729	0.704
SDAI score	28.0363±11.14522	27.7124±10.94763	29.1041±11.92582	0.572
HAQ	1.02283±0.742946	0.96449±0.664134	1.21296±0.946155	0.129
Tender joint count (0-68)	8.00 (5-12.75)	8.00 (5-12)	8.00 (4-15)	0.345
Swollen joint count (0-66)	5.00 (2-7)	4.00 (2.5-7)	5.00 (2-6)	0.780
Damage joint count (0-68)	2.00 (1-3)	2.00 (1-3)	2.00 (1-4)	0.485
Treatment				
no	82	62	20	0.50
ever	16	12	4	0.52
current	19	14	5	0.49
Erosions(MCP2,N)	135	109	26	
Erosions/patients(N)	1.1538	1.2111	0.96296	0.307
Width(mm)	2.7218±1.87087	2.7729±2.02280	2.5558±1.34248	0.531
Depth(mm)	1.0686±0.88600	1.1392±0.98107	0.8615±0.44234	0.048
Volume(mm3)	4.4756±6.38831	5.3472±5.98738	1.8312±1.38206	0.017
BMD(mg/cm3)	423.8868±103.8231	420.1646±109.6622	431.2889±83.10927	0.585

Conclusions: ACPAs and RF show an additive effect on erosion volume in ERA patients. Higher RF titre was associated with larger erosion volume at baseline and predicted progression of erosion volume after adjusting for baseline parameters and treatment response.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2962

AB0425 TREATMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS IN POLAND - ESTIMATE THE FREQUENCY OF USE OF METHOTREXATE DURING A RANDOM APPOINTMENT WITH A RHEUMATOLOGIST

K. Sikorska-Siudek[1], M. Przygodzka[1], R. Radomski[2], S. Bojanowski[2]. *[1]Mazovian Centre of Rheumatology and Osteoporosis; [2]iEHR.eu, Warsaw, Poland*

Background: In accordance with the EULAR/ACR reomendations disease-modifying antirheumatic drugs (DMARDs), particulary metotrexate (Mtx) should be applied after diagnosis of rheumatoid arthritis (RA). The goal of the treatment is to get remission/low disease activity
Objectives: The aim of this study was evaluation of the RA treatment, the frequency of use of Mtx and its dose application during control visits to rheumatologist in Poland. The disease activity was evaluated by using disease activity 28 joint score (DAS-28).
Results: There were analysed 301 case records of patients diagnosed with RA on the basis of the ACR 1997 and/or ACR/EULAR 2010 criteria. Patients recently diagnosed were excluded from analysis. In the examined group were 226 women and 75 men, median age 58.0, disease duration 5.0 Patients were divided in groups depending on the type of applied therapy 215 (71%) patients were treated with Mtx monotherapy or combined with other DMARDs. 161 patients (53%) took glucocorticosteroids simultaneously. Average DAS28 – 5.09, disease duration 6.2 At 18 patients (6%) contraindications against the Mtx were stated. 127 patients (59%) took high dosage of Mtx (20–30 mg/week), 84 (39%) low dosage (7.5–15 mg /week) 31 patients (10%) were treated other than Mtx DMARDs in monotherapy or in combined therapy 14 (45%) took glucocorticosteroids simultaneously, average DAS 28 – 4.82, disease duration 5.0 55 (18%) patients didn't undergo treatment of DMARDs in the moment of analysis, 11 (20%) patients underwent treatment with glucocorticosteroids. Duration of disease 2.1 average DAS 28 5,43.
Conclusions: In patients treated with DMARDs in it also with Mtx a remission and/or a low activity of illness weren't being observed what is indicating for the ineffective treatment with RA.
Mtx wasn't applied in recommended doses in spite of the moderate or high activity of illness
There were patients who never had been treated with DMARDs. Causes of this occurrence require further research
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6773

AB0426 THE EFFICACY OF THE TRIPLE COMBINATION THERAPY WITH METHOTREXATE, LEFLUNOMIDE AND METHYLPREDNISOLONE IN RHEUMATOID ARTHRITIS

L. Groppa[1], E. Russu[1], L. Chislari[1], O. Bujor[2]. *[1]Rheumatology and Nephrology, State University of Medicine and Pharmacy "Nicolae Testemitanu"; [2]Arthrology, Republican Clinical Hospital, Chisinau, Moldova, Republic of*

Background: The RA modern treatment approaches are based on "aggressive therapy", which aims at suppressing autoimmune inflammation and prevent joint destructionsat the early stages of the disease.
Objectives: To evaluate the effectiveness and tolerability of the triple combination therapy with methotrexate, leflunomide and methylprednisolone in patients with rheumatoid arthritis.
Methods: The study included 150 patients with rheumatoid arthritis. As a result of randomization, 50 patients received triple combination therapy (methotrexate +methylprednisolone+leflunomide), 50 patients with monotherapy with methotrexate, leflunomide 50 others. As a result all patient groups were comparable after all clinical and demographic indices.
Results: Our results showed that triple therapy is very effective in treating patients with RA. A significant improvement on the criteria of the AAR (ACR>50) at the end of the study was observed in most patients receiving methotrexate, leflunomide and methylprednisolone. This is confirmed statistically and clinically positive dynamics significantly in almost all indicators used of efficacy (pain, stiffness, number of tender and swollen joints, the activity of AR, the value VSH index functional HAQ) In addition, the use of triple therapy decreased average dose simultaneous use of glucocorticosteroids daily (from 5.0 to 2.5 mg) and 76% of patients canceled anti-inflammatory non-steroid drugs.
Conclusions: After randomized trial data lasting 24 months based triple therapy (methotrexate, leflunomide and methylprednisolone) was highly effective in patients with high RA activity. A significant improvement according to the criteria of ACR (ACR>50) was obtained in 31 of 39 patients (79.48%), including the nine patients (23.07%) had developed clinical remission.
Administration of the basic triple therapy was characterized by a significant clinical effect ACR stability of>50. It was maintained during not less than 15 months of research in 28 (90.32%) of patients who received this treatment and only 3 of 11 (27.27%) patients who received methotrexate alone group and 8 in 10 (80%) who administered LF (p=0.039). Evidence recovery (ACR>50), as well as clinical remission was kept stable in all 28 patients that triple therapy was extended after the ending of basic research.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6317

AB0427 EFFICACY OF HYPNOTIC ANALGESIA FOR THE REDUCTION OF PAIN AND NEGATIVE EMOTIONAL STATES IN PATIENTS WITH RHEUMATOID ARTHRITIS OF THE "HOSPITAL CIVIL DE GUADALAJARA "FRAY ANTONIO ALCALDE"

F. Bolaños-Chamorro[1], L.A. Hernandez-Palma[2], G. Vazquez-Murillo[1], S. Cerpa-Cruz[3], J.F. Muñoz-Valle[2], R.M. Meda-Lara[1]. *[1]Basic Psychology; [2]Research Institute in Biomedical Sciences, University of Guadalajara; [3]Division of Rheumatology, Guadalajara Civil Hospital Fray Antonio Alcalde, Guadalajara, Mexico*

Background: Rheumatoid arthritis is a autoimmune and multisystemic disease. However, the negative emotions of anxiety and depression are the ones that have been most addressed, and there is a close relationship between pain associated with pain. Hypnosis is one of the best documented behavioral interventions in the management of acute and chronic pain in adults.
Objectives: To evaluate the efficacy of hypnotic analgesia for pain reduction and negative emotional states in patients with Rheumatoid Arthritis of the Guadalajara Civil Hospital Fray Antonio Alcalde
Methods: The method was developed through a quasi-experimental study, in which had two groups: a control group (CG) of 11 patients and an experimental group (EG) of 17, the women's age group were developed between 18 and 65 years old diagnosed with arthritis. The medition of Pain was realized through an instrument called EVA, and for the case of the Anxiety and depression were through HAD, achieving the baseline of each one of the variables. The EG group attended three psychological sessions of Hypnosis, with intervals of one month each. In these sessions, the perception of pain with an EVA was measured at the beginning and at the end. After a month, the subsequent evaluation was performed, measuring the same initial variables, in order to make the comparison of the pre and pos.
Results: The U of MANN Whitney was applied and it was identified that in the pre-test measurement, there were no statistically significant differences in the variables. However, in the pos measurement, differences were found in the patient's pain perception ($z=-2.84$, $p<0.05$), anxiety ($z=-2.36$, $p<0.05$) and The depression ($z=-2.68$, $p<0.05$). In addition, a Wilcoxon test was developed to determine differences between the pre-test score and the pos-test score in the EVA of each session. Statistically significant differences were found in the first session ($Z=-3.65$, $p=0.001$), second session ($Z=-3.67$, $p=0.001$) and third session ($Z=-3.56$, $p=0.001$).
Conclusions: Hypnosis, as a behavioral technique, has shown efficacy in patients with chronic pain. In this research, a significant decrease in patients' perception of pain has been demonstrated.
References:
[1] Chopra, A. (2013). The COPCORD world of musculoskeletal pain and arthritis. Rheumatology (United Kingdom), 52(11), 1925–1928.
[2] Matcham, F., Rayner, L., Steer, S., & Hotopf, M. (2013). The prevalence of depression in rheumatoid arthritis: A systematic review and meta-analysis. Rheumatology (United Kingdom), 52(12), 2136–2148.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6983

AB0428 A SYSTEMATIC REVIEW ON EFFICACY AND SAFETY OF SELECTIVE GLUCOCORTICOID RECEPTOR MODULATORS IN COMPARISON TO GLUCOCORTICOIDS IN ARTHRITIS

M. Safy[1], M.J. De Hair[1], J.W. Jacobs[1], F. Buttgereit[2], M.C. Kraan[3], J.M. van Laar[1]. *[1]Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Netherlands; [2]Rheumatology and Clinical Immunology, Charité - Universitätsmedizin, Berlin, Germany; [3]Department of Rheumatology and Inflammation Research, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden*

Background: Glucocorticoids (GCs) can cause unwanted effects. Both rheumatologists and patients classify osteoporosis, hyperglycemia/diabetes mellitus, cardiovascular diseases, and infections as the most worrisome adverse effects of GCs. Alternatives with less adverse effects but with good efficacy are needed, thus with a better efficacy/safety ratio. Selective GC receptor modulators (SGMRs) are designed to engage the receptor with dissociative characteristics: less transactivation of genes, mainly responsible for unwanted effects, while trans-repression of genes, inducing anti-inflammation, is maintained. Hereby, SGRMs are expected to have a better efficacy/safety ratio. A systematic review providing an overview of the efficacy and safety data of SGRMs is lacking.
Objectives: To systematically review the current literature on efficacy and safety of SGRMs in arthritis, compared to those of GCs.
Methods: A search was performed in Medline, Embase and the Cochrane Library, from inception dates of databases to October 5th, 2016. Experimental studies involving animal arthritis models or human material of arthritis patients, as well as clinical studies in patients of arthritis were included, if they reported original data. All types of arthritis were included. Data was extracted on the SGRM studied and on the GC as reference standard, design or setting of the study and whether or not safety and efficacy parameters had been reported.
Results: A total of 437 articles was retrieved of which 15 articles were eligible for our analysis. The following SGRMs were investigated: Compound A[1–6], PF-04171327[7], LGD-5552[8–9], Compounds 4[10], 5[10], and 14[11], (R)-16[12], (R)-18[13],

(R)-21[13], (R)-35[14], (R)-37[12], Ginsenoside Rg1[15] and Org 214007–0[16]. Results are shown in Table 1. (R)-16 showed better efficacy and safety compared to prednisone. Compound A, Ginsenoside Rg 1, Compounds 14, (R)-18, and (R)-21 had better safety profiles than a GC, but with similar efficacy. (R)-35 and (R)-37 showed better efficacy than a GC, but safety data was lacking. Org 214007–0, LGD-5552, Compounds 4 and 5 and PF-04171327 showed similar efficacy as a GC, but no safety data was provided.

Author, year	SGRM tested	Reference compound	Clinical trial	Pre-clinical human	Pre-clinical animal	Efficacy	Safety	Conclusion on efficacy and safety in comparison to reference compound
Dewint et al., 2008	Compound A	Dex		X	X	X	X	Similar efficacy. Better safety of Compound A.
Gossye et al., 2009	Compound A	Dex		x				Similar efficacy. No safety data
Gossye et al., 2010	Compound A	Dex		X	X			Less efficacy of Compound A. No safety data.
Rauch et al., 2011	Compound A	Dex		X		X	X	Similar efficacy. Better safety of Compound A.
Rauner et al., 2013	Compound A	Dex			X	X	X	Less efficacy of Compound A. Better safety of Compound A.
Malaise et al., 2015	Compound A	Pred		X		X	X	Similar efficacy. Better safety of Compound A.
Yang et al., 2015	Compound 4 and 5	Pred			X	X		Similar efficacy of compound 4, better efficacy of compound 5. No safety data.
Razavi et al., 2014	Compound 14	Pred			X	X	X	Similar efficacy. Better safety of Compound 14.
Riether et al., 2010	Compound (R)-16 and (R)-37	Pred			X	X	X	Better efficacy of (R)-16. Better safety of (R)-16 and (R)-37.
Harcken et al., 2014	Compound (R)-18 and (R)-21	Pred			X	X	X	Similar efficacy. Better safety of R)-18 and (R)-21.
Weinstein et al., 2011	Compound 35 and 37	Pred, dex			X	X		Better efficacy of compounds 35 and 37. No safety data.
Miner et al., 2007	LGD-5552	Pred			X	X		Similar efficacy. No safety data.
Lopez et al., 2008	LGD-5552	Pred			X	X		Similar efficacy. No safety data.
Du et al., 2011	Ginsenoside Rg1	Dex			X	X		Similar efficacy. Better safety of Ginsenoside Rg1.
Van Lierop et al., 2012	Org 214007-0	Pred			X	X	X	Similar efficacy of Org-214007-0.No safety data.
Conrado et al., 2015	PF-04171327	Pred	X			X		Similar efficacy. No safety data.

Table 1. Efficacy and safety results of selective glucocorticoid receptor modulators (SGRMs).

Conclusions: Studies both assessing efficacy and safety parameters of SGRMs are scarce. Currently, there is insufficient evidence for the presumed superior efficacy/toxicity balance of SGRMs compared to that of GCs.

References:

[1] Dewint P et al. J Immunol. 2008;180:2608–15.
[2] Rauch A et al. FASEB J. 2011;25:1323–32.
[3] Rauner M et al. Endocrinology. 2013;154:3719–28.
[4] Malaise O et al. Rheumatology. 2015;54:1087–92.
[5] Gossye V et al. Arthritis Rheum. 2009;60:3241–50.
[6] Gossye V et al. Ann Rheum Dis. 2010;69:291–6.
[7] Conrado DJ et al. J Pharmacokinet Pharmacodyn. 2016;43:325–41.
[8] Miner JN et al. Proc Natl Acad Sci U S A. 2007;104:19244–9.
[9] López et al. Endocrinology. 2008;149:2080–9.
[10] Yang MG et al. J Med Chem. 2015;58:4278–90.
[11] Razavi H et al. Bioorg Med Chem Lett. 2014;24:1934–40.
[12] Riether D et al. J Med Chem. 2010;53:6681–98.
[13] Harcken C et al. J ed Chem. 2014;57:1583–98.
[14] Weinstein DS et al. J Med Chem. 2011;54:7318–33.
[15] Du J et al. J Immunol. 2011;187:942–50.
[16] Van Lierop MJ et al. PLoS One.2012;7:e48385.

Disclosure of Interest: M. Safy Grant/research support from: MS was supported by a research grant from Astra Zeneca. Astra Zeneca was not involved in this study., M. De Hair: None declared, J. Jacobs: None declared, F. Buttgereit: None declared, M. Kraan: None declared, J. van Laar: None declared
DOI: 10.1136/annrheumdis-2017-eular.3254

AB0429 SHORT-TERM EFFECTS OF LOW DOSE GLUCOCORTICOIDS ON BONE METABOLISM IN EARLY RHEUMATOID ARTHRITIS

M. Vitiello[1], O. Viapiana[1], N. Malavolta[2], G. Saviola[3], R. Bortolotti[4], L. Idolazzi[1], F. Bertoldo[1], G. Orsolini[1], M. Risoli[1], D. Gatti[1], M. Rossini[1].
[1]Rheumatology Unit, University of Verona, Verona; [2]Rheumatology Unit, AOU of Bologna, Bologna; [3]Rheumatology and Rehabilitation Unit, Salvatore Maugeri Foundation IRCCS, Castel Goffredo, Mantua; [4]Rheumatology Unit, Santa Chiara Hospital, Trento, Italy

Background: Glucocorticoids (GCs) are frequently used in the treatment of Rheumatoid Arthritis (RA). Studies in humans about the effects on bone turnover markers and modulators are poor, and results are discordant and controverse, probably because conducted with different doses and underlying diseases.
Objectives: To evaluate changes in serum bone turnover markers and Wnt inhibitors at 7- and 30-days after initiation of low dose GCs treatment of early RA.
Methods: 27 adult patients suffering from early RA were prospectively enrolled. Blood tests including C-Reactive Protein (CRP), amino-terminal propeptide of type 1 procollagen (P1NP, marker of bone formation), carboxy-terminal telopeptide of type 1 collagen (CTX, marker of bone resorption), Sclerostin, and Dickkopf-related protein 1 (DKK1) were detected at baseline and 7 and 30 days after starting low dose of GC (methylprednisolone 4 mg/day).
Results: At baseline we observed a significant positive correlation between CRP and DKK1 serum levels ($r=0,63$; $p<0,05$) and between DKK1 and CTX serum levels ($r=0,38$; $p<0,05$). A significant decrease in serum levels of CRP, P1NP, and Sclerostin was observed after 7 and 30 days of GC treatment ($p<0,05$). About DKK1, it has been detected a not significant tendency to decrease after starting GC. CTX serum levels showed no significant changes.
Conclusions: This study has shown that a low dose GC treatment might have complex and conflicting short-term effects on bone metabolism in early RA (a reduction of bone formation, without increase of bone resorption), different from those observed with higher dose, in other diseases or in healthy subjects. The observed decrease in P1NP and Sclerostin serum levels might mean that also low dose of GC could acutely suppress bone formation and induce loss of function and/or number of osteocytes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4667

AB0430 LEFLUNOMIDE AS A SECOND LINE DMARD AFTER METHOTREXATE HAS LIMITED IMPACT ON RHEUMATOID ARTHRITIS IN REAL LIFE

G. Weigt, A. Erler, M. Aringer. *Medicine III, University Medical Center TU Dresden, Dresden, Germany*

Background: If rheumatoid arthritis (RA) is not in remission or at least low disease under methotrexate (MTX), leflunomide is an approved conventional synthetic DMARD, which is commonly used in some countries.
Objectives: To investigate in a real life situation whether patients with RA benefit from instituting leflunomide after methotrexate.
Methods: The clinical data of all RA patients who had at least once received leflunomide, and who agreed to the pseudonymized analysis of their data (approved by the local ethics committee), were analyzed from the time of leflunomide initiation on to the time of stopping leflunomide or the last visit in 2015, which ever came first.
Results: In total, 145 RA patients treated with leflunomide were identified. Of these, 87 received leflunomide after MTX had failed as a first line DMARD, and 8 received leflunomide as a first line DMARD. 50 patients had another first line therapy. Of the first line leflunomide patients 3 (38%) were still on leflunomide at the last visit, as compared to 7 of the 44 patients (16%) who were switched from MTX to leflunomide, and 0 of the 27 patients in whom leflunomide was added to MTX ($p<0.01$ vs 1st line leflunomide). For leflunomide monotherapy, 29% and 19% were still on the drug after 24 and 48 months, respectively, as compared to 14 and 0% under the combination with MTX. Of all patients who started leflunomide, remission (at least low disease activity) as per CDAI ($\leq$2.8 ($\leq$10)) was reached by 23% (57%) 3 months, 20% (40%) 6 months, and 16% (34%) one year after initiating leflunomide monotherapy, with corresponding percentages of patients of 39% switched to other approaches at six months and of 60% switched at one year. Under the combination of leflunomide and MTX, remission (at least low disease activity) was seen in 18% (53%) at 3 months, 20% (37%) at 6 months, and 8% (20%) at one year, and 55% and 71% had switched to other modes of action at six months and one year, respectively. Gastrointestinal and mucocutaneous adverse events and hypertension were common, and 4 our patients experienced serious bacterial infections.
Conclusions: Leflunomide constitutes a longer term option for a subgroup of RA patients with contraindications to MTX or after MTX failure. After one year, leflunomide had led to sustained acceptable disease control in approximately one third of the patients, but only in one in five under leflunomide combined with MTX. These results are supportive of the EULAR recommendations that patients should be switched to a second conventional DMARD in the absence of predictors of bad outcome only. If leflunomide is initiated, the patients need to be followed closely for potential secondary loss of efficacy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3531

AB0431 POST-MARKETING SURVEILLANCE OF TOFACITINIB IN JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS: AN INTERIM REPORT OF SAFETY DATA

T. Mimori[1], M. Harigai[2], T. Atsumi[3], M. Kuwana[4], S. Takei[5], N. Tamura[6], T. Fujii[7], H. Matsuno[8], S. Momohara[9], K. Yamamoto[10], T. Kokubo[11], Y. Endo[11], N. Sugiyama[11], T. Hirose[11], Y. Morishima[11], N. Yoshii[11]. *[1]Kyoto University, Kyoto; [2]Tokyo Women's Medical University, Tokyo; [3]Hokkaido University, Sapporo; [4]Nippon Medical School, Tokyo; [5]Kagoshima University, Kagoshima; [6]Juntendo University, Tokyo; [7]Wakayama Medical University, Wakayama; [8]Matsuno Clinic for Rheumatic Diseases, Toyama; [9]Hakkeikai Inc Medical Institution, Shizuoka; [10]The University of Tokyo; [11]Pfizer Japan Inc, Tokyo, Japan*

Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Efficacy and safety of tofacitinib have been shown in RA patients in global Phase 2, Phase 3 (one study included Japanese patients) and long-term extension (LTE) studies and in two Phase 2 and one LTE study in Japanese patients.

Objectives: We evaluated the safety of tofacitinib following drug approval in Japanese patients with RA using all-case post-marketing surveillance (PMS) data.
Methods: A 6-month interim analysis of safety data from an ongoing 3-year PMS study was conducted (5 Nov 2016 data-cut). All Japanese patients with RA who were treated with tofacitinib were consecutively and prospectively registered in the PMS study and were monitored for all adverse events (AEs) for 3 years. Baseline and follow-up data were collected from booklet-type survey forms. Follow-up surveillance after discontinuation of tofacitinib treatment was implemented: 12 months for serious infections and 3 years for malignancy or AEs leading to death from the date of treatment initiation with tofacitinib. AEs were coded using MedDRA/J.
Results: Overall, 2387 tofacitinib-treated patients were enrolled (1020.0 patient-years [pt-yrs] of exposure); of these, 594 patients (24.9%) discontinued treatment, mainly due to AEs (n=236; 9.9%) or lack of effectiveness (n=225; 9.4%). In total, 1793 (75.1%) patients continued treatment for 6 months. At least one AE was observed in 815 patients (34.1%), the most frequent of which was herpes zoster (n=78; 3.3%), including 12 serious cases. Serious AEs occurred in 190 patients (8.0%); the most frequent were pneumonia (n=20; 0.8%), interstitial lung disease (n=14; 0.6%) and condition aggravated (n=13; 0.5%). Infections (n=304; 12.7%) were serious in 88 patients (3.7%). Thirteen patients (0.5%) reported malignancy, including ovarian cancer (n=2; 0.1%), diffuse large B-cell lymphoma (n=2; 0.1%) and lymphoproliferative disorder (n=1, 0.04%). Sixteen (0.7%) deaths were reported.
Conclusions: Interim analyses of AEs during the initial 6-month treatment period from PMS reports of tofacitinib in Japanese patients did not reveal any new or unexpected safety signals vs the tofacitinib RA clinical programme. The target sample size for the final PMS analysis is 6000 patients (4000 tofactinib-treated, 2000 control patients).
Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by K Nicholson of CMC and was funded by Pfizer Inc.
Disclosure of Interest: T. Mimori Grant/research support from: Astellas, Ayumi, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Nippon Shinyaku, Takeda, Speakers bureau: Astellas, Bristol-Myers Squibb, Chugai, Eisai, Mitsubishi-Tanabe, M. Harigai Grant/research support from: Bristol-Myers Squibb, Eisai, Eli Lilly, Ono, Takeda, T. Atsumi Grant/research support from: Alexion, Astellas, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Sanofi. Scholarship donations from: Bayer, Daiichi-Sankyo, Takeda, Speakers bureau: AbbVie, Astellas, Chugai, Eisai, Mitsubishi-Tanabe, Pfizer Inc, Takeda, UCB Japan, M. Kuwana Grant/research support from: Chugai, Eisai, Mitsubishi-Tanabe, Ono, Pfizer Inc, Santen, Speakers bureau: Astellas, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Ono, Pfizer Inc, UCB, S. Takei Grant/research support from: Chugai, Eisai, Mitsubishi-Tanabe, Takeda, Speakers bureau: Asahi Kasei, Ayumi, Chugai, Mitsubishi-Tanabe, Ono, N. Tamura Grant/research support from: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Takeda, Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Eisai, Janssen, Mitsubishi-Tanabe, T. Fujii Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Eisai, Janssen, Kissei, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, Taisho Toyama, Takeda, UCB Japan, Speakers bureau: AbbVie, Actelion, Astellas, Ayumi, Chugai, Daiichi-Sankyo, Kissei, Mitsubishi-Tanabe, Nippon Kayaku, Ono, Pfizer Japan Inc, Taisho Toyama, Takeda, H. Matsuno Consultant for: Ayumi, Meiji Seika, Mochida, Nichi-Iko, S. Momohara Speakers bureau: AbbVie, Bristol-Myers Squibb, Eisai, Janssen, Mitsubishi-Tanabe, Ono, Pfizer Japan Inc, Takeda, K. Yamamoto Grant/research support from: AbbVie, Astellas, Ayumi, Chugai, Eisai, Mitsubishi-Tanabe, Nippon Kayaku, Pfizer Japan Inc, Taisho Toyama, Takeda, Teijin, UCB, Speakers bureau: Asahi Kasei, AstraZeneca, Ayumi, Boehringer Ingelheim, Bristol-Myers Squibb, Chugai, Eisai, Janssen, Mitsubishi-Tanabe, Pfizer Inc, Sanofi, Sumitomo Dainippon, Taisho Toyama, Takeda, Teijin, Toyama Chemical, UCB, T. Kokubo Employee of: Pfizer Japan Inc, Y. Endo Shareholder of: Pfizer Inc, Employee of: Pfizer Japan Inc, N. Sugiyama Shareholder of: Pfizer Inc, Employee of: Pfizer Japan Inc, T. Hirose Shareholder of: Pfizer Inc, Employee of: Pfizer Japan Inc, Y. Morishima Shareholder of: Pfizer Inc, Employee of: Pfizer Japan Inc, N. Yoshii Shareholder of: Pfizer Inc, Employee of: Pfizer Japan Inc
DOI: 10.1136/annrheumdis-2017-eular.1420

AB0432 ABT-494 HAS NO EFFECT ON THE QT INTERVAL AT THE DOSES BEING EVALUATED IN RHEUMATOID ARTHRITIS PHASE 3 TRIALS

M.-E.F. Mohamed, J. Zeng, P. Jiang, B. Hosmane, A.A. Othman. *Clinical Pharmacology and Pharmacometrics, AbbVie, North Chicago, United States*

Background: ABT-494 is a selective Janus Kinase 1 inhibitor currently being evaluated in Phase 3 trials for treatment of rheumatoid arthritis (RA) at doses of 15 mg and 30 mg once daily using the extended-release tablet formulation. Exposure-response analysis of ECG data collected at early stage clinical trials has been recently adopted in regulatory guidelines as a tool to assess the proarrhythmic risk of investigational new drugs.
Objectives: The objective of this work was to evaluate ABT-494 QT prolongation potential using exposure-response analysis of data collected in early Phase 1 studies.
Methods: Doses of ABT-494 or placebo were administered to healthy subjects in two Phase 1 studies. Evaluated ABT-494 immediate-release regimens ranged from 1 mg to 48 mg single doses under fasting conditions and 3 mg to 24 mg twice daily under non-fasting conditions. Serial triplicate electrocardiograms and pharmacokinetic assessments were conducted. The relationship between change from baseline in Fridericia-corrected QT interval (QTcF) and ABT-494 plasma concentrations was characterized using linear mixed-effects modeling. To evaluate the ECG assay sensitivity, the change in QTcF from baseline to 2 hours post-dose was compared for subjects who received placebo under fasting and non-fasting conditions.
Results: There was no statistically significant relationship between the change from baseline in the QTcF interval and ABT-494 plasma concentrations. The point estimate of the effect on QTcF for the highest concentration observed in the evaluated studies, which is approximately 4-fold higher than the mean C_{max} of the highest RA Phase 3 dose, is –1.77 msec (with upper bound of the 95% one-sided confidence interval of 3.33 msec; lower than the regulatory threshold of concern of 10 msec). Food shortened the QTcF interval by 5.9 msec (2-sided 90% confidence interval of -9.6 to -2.1 msec), indicating that the ECG assay used in the studies had adequate sensitivity to detect the small change in QTcF caused by food.
Conclusions: ABT-494 showed no potential for QT prolongation at the expected therapeutic and supra-therapeutic plasma exposures for the doses being used in Phase 3 RA trials.
Disclosure of Interest: M.-E. Mohamed Shareholder of: AbbVie, Employee of: AbbVie, J. Zeng Shareholder of: AbbVie, Employee of: AbbVie, P. Jiang Shareholder of: AbbVie, Employee of: AbbVie, B. Hosmane Shareholder of: AbbVie, Employee of: AbbVie, A. Othman Shareholder of: AbbVie, Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.3230

AB0433 CORRECTION OF LIPID AND ENDOTHELIAL DYSFUNCTION BY USING NO DONATORS (4,2% SOLUTION OF ARGININE HYDROCHLORIDE AND L-ARGININE ASPARTATE) IN PATIENT WITH RHEUMATOID ARTHRITIS IN COMBINATION WITH THE RAYNAUD'S SYNDROME

O. Shtefiuk, R. Yatsyshyn. *Internal Medicine #1, Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine*

Background: Lesion of the cardiovascular system is associated with uncontrolled inflammation and immune defects in patients with Rheumatoid Arthritis (RA). There is an evidence of the close pathogenetic connection between rheumatoid inflammation and accelerated development of atherosclerosis. The first sing of atherosclerosis is endothelial dysfunction (ED).
Objectives: Evaluate the effectiveness of NO donators (4,2% solution of arginine hydrochloride and L-arginine aspartate) in the correction of lipid and ED in patients with RA and secondary Raynaud's syndrome (RS).
Methods: 68 patients with RA were examined. All patients were divided into 2 groups: (37 people with RA in combination with secondary RS) received basic therapy of RA (methotrexate 10–15 mg/wk.), antiplatelet and vasodilatory drugs; II group (31 people – RA in combination with secondary RS) got similar therapy plus NO donators (4,2% solution of arginine hydrochloride and L-arginine aspartate). The examination was carried out at the patient's admission to the hospital and the hospital and 3 months after the beginning of treatment. Endothelial function was assessed by determining the flow-mediated vasodilation of brachial artery (FMD), levels of endothelin-1, rheumatoid factor (RF), C-reactive protein (CRP), lipid profile (total cholesterol – TC, low density lipoprotein – LDL, high-densitylipoprotein – HDL and triglycerides – TG), index of intima/media (IM) and atherogenic index (AI).
Results: Levels of TC, LDL, AI and MI indexes were significantly higher than the norm in 2 compared groups before the treatment and 3 months after its start ($p<0,05$). There were significant decreases in levels of lipid profile, IA and MI index in II group 3 months after treatment in comparison to benchmarks (TC by 13,3%, LDL by 16,1%, TG by 14,7%, AI index by 13,8% MI index by 12,7%,$p<0,05$) and they were significantly unchanged in I group ($p<0,05$). It was elucidated a direct reliable strong correlation in patients of II group between the level of FMD and endothelin-1 before treatment ($r=0,73$, $p<0,05$) and after treatment ($r=0,69$, $p<0,05$). Symptoms of ED, levels of endothelin-1, RF, CRP were decreased in patients of both groups after the conducted therapy. It was established a proportionately reliable correction between CRP and LDL levels after treatment in II group of patient ($r=0,63$, $p<0,05$).
Conclusions: 1.There is a lack of flow-mediated vasodilation of brachial artery in patients with RA and secondary RS, which can indicate a dysregulation of endothelial function.
2. The level of CRP is increased in patients with RA and secondary RS and is associated with the risk of hyperlipemia and atherosclerosis. 3. The usage of NO donators (4,2% solution of arginine hydrochloride and L-arginine aspartate) in the treatment of RA with secondary RS significantly reduces the levels of IA and IM index, the level of atherogenic lipoprotein fractions (TC, LDL and TG) and decreases the severity of ED, which leads to minimizing the risk of atherogenesis and its complications.
References:
[1] Kuryliszyn-Moskal A, Klimiuk PA, Sierakowski S, Ciolkiewicz M. /A study on vascular endothelial growth factor and endothelin-1 in patients withextra-articular involvement of rheumatoid arthritis // ClinRheumatol. 2006 May; 25 (3): 314–9.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1132

AB0434 TOFACITINIB IN RHEUMATOID ARTHRITIS: REAL LIFE EXPERIENCE

P. Sansinanea[1], A.C. Costi[1], A. Vulcano[2], A.P. Salas[2], J. Marcos[3], M.A. Belini[4], M.A. García[2]. *[1]Rheumatology Unit, Sanatorio Ipensa, HIGA San Martín la Plata; [2]Rheumatology Unit, HIGA San Martín la Plata; [3]Rheumatology Unit, Sanatorio IPENSA, Pfizer Inc., la Plata; [4]Medical Affairs, Pfizer Inc, CABA, Argentina*

Background: Tofacitinib is a new small molecule, Janus kinase 1 and 3 inhibitor, interfering with the JAK-STAT signaling pathway. The JAK-STAT transmits the extracellular information in the cell nucleus, influencing DNA transcription. Its efficacy and safety in Rheumatoid Arthritis (RA) has been demonstrated in different phase II, III and long-term clinical studies. It has been approved in Argentina for the treatment of patients with moderate to severe rheumatoid arthritis RA with failure to conventional DMARDs.
Objectives: To communicate real world safety data from patients with RA under treatment with Tofacitinib.
Methods: A retrospective, descriptive study from patients with RA (ACR/EULAR2010) under treatment with Tofacitinib from September 2014 to December 2016 was conducted. Medical records from patients being treated with Tofacitinib were reviewed and demographic data were recorded. Comorbidities, concomitant treatments, and reported adverse effects were documented.
Results: 62 patients were treated with Tofacitinib. 53 were female and 9 were male, with a mean age of 57.91±14.72 years and average disease duration of 140.09±130.83 months. 18 patients (29%) had at least one comorbidity, the most frequent being hypertension (77%).
Of the 62 patients studied, 54 (87%) had established RA (duration of illness greater than 24 months) and 8 patients (13%) with early RA (less than 24 months). In 54 patients Tofacitinib was indicated in combination with another DMARD (87%), and only 6 patients received treatment as monotherapy.
The most commonly used DMARD in combination therapy was methotrexate (MTX) in 92.5%
Treatments were indicated by failure to MTX or other conventional DMARDs, 12/62 treatments were indicated by failure to treatment with 1 biological DMARD and 13/62 treatments were indicated by failure to two or more biological DMARDs. The maximum exposure time was 21 months.
During the time of exposure to Tofacitinib the following adverse events were observed: Herpes Zoster infection 2 cases (monometameric, no visceral involvement in unvaccinated patients), upper airway infection 1 case, transient increase in liver enzymes 1 case, peripheral facial paralysis 1 case, tachycardia 1 case. There were no cases of serious infections, opportunistic infections, cytopenias, dyslipidemia, or increased CPK.
Three patients discontinued Tofacitinib: one due to tachycardia, another case peripheral facial paralysis and another case due inefficacy.
Conclusions: Most patients received combined treatment with DMARDs being the most commonly used Methotrexate. There were no cases of serious infections, opportunistic infections, cytopenias or dyslipidemia. The use of Tofacitinib in RA patients in our cohort showed a comparable safety profile with long-term extension studies in the treatment of patients with RA diagnosed with failure of conventional or biological DMARDs.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3861

AB0435 COMBINATION THERAPY IN EARLY STAGE OF RHEUMATOID ARTHRITIS

S.X. Matchanov. *Internal disease, Tashkent Medical Academy, Tashkent, Uzbekistan*

Background: It is known that the early period of rheumatoid arthritis (RA) has a critical role in the development and progression of immune inflammation. Allocation of early RA is due to the need for timely appointment of basic anti-inflammatory drugs to prevent the development of destructive changes in the joints and improve its current forecast. We have proposed a combination of two basic drugs for the treatment of RA, methotrexate (MTX) and leflunomide (LF). While this combination, we proceeded from the basic principles of combination therapy: each of the drugs has an independent clinical effect in early RA, the drugs have different mechanisms of action and different spectrum of side effects.
Objectives: Investigating of clinical efficacy of combination therapy with MT and LF in patients with RA in its early stages
Methods: We observed 80 patients with early RA, 50 patients of them were women and 30 patients were male. The age of patients ranged from 24 up to 42 years old (31,7±7,6), the duration of illness was 6 months. Activity of RA was corresponded to the II degree (DAS 28 <4.7) in 48 patients, III degree (DAS28>5,1) was in 32 patients. 1st group consisted of 40 patients and the 2nd group involved 40 patients. Patients in 1st group received combination therapy with LF in doses 20 mg/day and MT in doses 7.5 mg/week. 2nd group received just MT as a single basic anti-inflammatory drug in doses 7.5 mg/week. In order to improve portability of MT was administered to all patients folic acid in doses 1.2 mg/day, 5 days in a week. The efficiency of the intervention was evaluated after 6 months by reducing of the final value of the indicator of inflammatory activity.
Results: The results of observation of patients for 6 months were showed that, combination therapy with MT and LF provides a quick and pronounced clinical effect in patients in the early stages of RA. Patients of 1st group according to criteria ACR 50- 70% improvement was achieved in 50% of patients, while figure of all indicators of patients in 2nd group was 33.4%. During the treatment was indicated improvement of laboratory parameters of disease activity of RA in both groups, features of activity of 1st group were decreased up to (DAS28 =2,9), signs of 2nd group were (DAS28 =3,6). However, there were 26% of cases of clinical remission of the disease in patients of 1st group than patients of 2nd group. Known side effects of combination therapy with MT and LF in most cases have not been severe, reversible and demanded the abolition of drugs in rare (11.2%) cases.
Conclusions: Combined basic therapy of patients in the early stages of RA with LF and MT has more efficiency than mono therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4770

AB0436 COMPARISON OF TOFACITINIB EFFICACY IN PATIENTS WITH MODERATE VS SEVERE RHEUMATOID ARTHRITIS: POOLED ANALYSIS OF PHASE 3 STUDIES

S. Schwartzman[1], P. Sunkureddi[2], L. Takiya[3], M. Snyder[3], H. Fan[4], T. Lukic[5], J. Roberts[6], W.F.C. Rigby[7]. *[1]Hospital for Special Surgery, New York, NY; [2]Clear Lake Rheumatology, Nassau Bay, TX; [3]Pfizer Inc, Collegeville, PA; [4]Pfizer Inc, Groton, CT; [5]Pfizer Inc, New York, NY, United States; [6]Pfizer Inc, Tadworth, United Kingdom; [7]Geisel School of Medicine at Dartmouth, Lebanon, NH, United States*

Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA.
Objectives: To evaluate tofacitinib 5 and 10 mg twice daily (BID) efficacy in patients (pts) with moderate vs severe RA.
Methods: Tofacitinib 5 and 10 mg BID efficacy data were obtained from 6 randomised double-blind Phase 3 studies of 6–24 months' duration. Tofacitinib was administered as monotherapy (NCT00814307 ORAL Solo; NCT01039688 ORAL Start) or with csDMARDs, mainly MTX (NCT00960440 ORAL Step; NCT00847613 ORAL Scan; NCT00856544 ORAL Sync; NCT00853385 ORAL Standard). Pts receiving MTX monotherapy (ORAL Start), or placebo (±csDMARDs) were combined as a single "placebo" group. Baseline (BL) disease severity was classified as moderate or severe using Disease Activity Score in 28 joints with erythrocyte sedimentation rate (DAS28: moderate 3.2 to ≤5.1; severe >5.1) and Clinical Disease Activity Index (CDAI: moderate 10 to ≤22; severe >22). Month 3 (M3) efficacy outcomes included: pts (%) achieving low disease activity (LDA; DAS28 ≤3.2, CDAI ≤10), remission (DAS28 <2.6, CDAI ≤2.8), HAQ-DI <0.5 (normal physical functioning), HAQ-DI improvement >0.22 and mean change from BL (Δ) in DAS28, CDAI and HAQ-DI. This post hoc analysis had no multiplicity adjustments.
Results: Overall, more pts had severe BL disease by DAS28 (91.0%) and CDAI (89.5%). The table shows BL disease characteristics and M3 efficacy outcomes for pts classified by BL DAS28 disease severity; CDAI classification demonstrated similar trends.

Table. Baseline disease characteristics (A) and Month 3 efficacy outcomes (B) by baseline disease severity assessment using DAS28
A) Mean (SD) baseline demographics and characteristics

Baseline disease severity	Moderate (3.2 to ≤5.1)			Severe (>5.1)		
Treatment group	Tofacitinib 5 mg BID N=120	Tofacitinib 10 mg BID N=127	Placebo N=76	Tofacitinib 5 mg BID N=1427	Tofacitinib 10 mg BID N=1438	Placebo N=766
Disease duration, years	7.1 (7.6)	7.7 (9.2)	8.7 (8.1)	7.4 (7.9)	7.7 (8.0)	7.7 (8.3)
CDAI	20.7 (6.2)	19.5 (5.4)	20.3 (6.9)	39.4 (11.7)	39.1 (11.8)	39.3 (12.1)
DAS28	4.6 (0.5)	4.7 (0.4)	4.7 (0.4)	6.7 (0.8)	6.6 (0.8)	6.6 (0.9)
HAQ-DI	1.0 (0.7)	0.8 (0.7)	0.9 (0.7)	1.5 (0.6)	1.5 (0.6)	1.5 (0.6)
B) Month 3 efficacy outcomes						
Remission (DAS28<2.6), % (CI)	20.0** (14.9, 31.5)	22.8** (18.3, 35.3)	5.3 (1.7, 14.6)	6.2*** (5.6, 8.5)	9.0*** (8.5, 11.9)	2.0 (1.2, 3.5)
LDA (DAS28≤3.2), % (CI)	36.7*** (31.7, 51.1)	32.3*** (28.0, 46.6)	9.2 (4.3, 20.4)	13.8*** (13.6, 17.6)	19.1*** (19.1, 23.6)	4.6 (3.5, 6.9)
HAQ-DI <0.5, % (CI)	45.0 (35.9, 54.4)	60.6*** (51.6, 69.2)	32.9 (22.5, 44.6)	24.5*** (22.6, 27.2)	30.0*** (28.0, 32.8)	12.8 (10.6, 15.5)
HAQ-DI improvement >0.22, % (CI)	50.8* (41.6, 60.1)	55.9** (46.8, 64.7)	31.6 (21.7, 43.8)	66.2*** (64.8, 69.8)	72.4*** (71.0, 75.7)	50.7 (47.6, 54.8)
ΔDAS28, LS mean (CI)	-1.1*** (-1.4, -0.9)	-1.3*** (-1.6, -1.1)	-0.1 (-0.3, 0.2)	-2.0*** (-2.1, -2.0)	-2.3*** (-2.3, -2.2)	-1.1 (-1.2, -1.0)
ΔHAQ-DI LS mean (CI)	-0.3*** (-0.4, -0.3)	-0.4*** (-0.5, -0.3)	-0.1 (-0.1, 0.1)	-0.5*** (-0.6, -0.5)	-0.6*** (-0.7, -0.6)	-0.3 (-0.3, -0.2)

*p<0.05, **p<0.001, ***p<0.0001 vs placebo
BID, twice daily; CDAI, clinical disease activity index; CI, 95% confidence interval; DAS28, Disease Activity Score in 28 joints with erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDA, low disease activity; LS, least squares; SD, standard deviation

BL characteristics were balanced between treatment groups in each disease severity category. M3 efficacy was significantly greater with tofacitinib 5 and 10 mg BID vs placebo, regardless of BL disease severity. As expected, larger proportions of tofacitinib-treated pts with moderate vs severe BL RA achieved LDA by either DAS28 (32.3–36.7% vs 13.8–19.1%) or CDAI (49.2–55.0% vs 26.0–31.7%). Similarly, a higher proportion of pts achieved remission in the moderate vs severe BL groups by DAS28 (20.0–22.8% vs 6.2–9.0%) or CDAI (11.5–12.1% vs 5.1–6.7%). A greater proportion of pts achieved HAQ-DI <0.5 with moderate vs severe RA classified by BL DAS28 (45.0–60.6% vs 24.5–30.0%) or BL CDAI (40.8–52.4% vs 24.7–30.4%). Greater improvements from BL in disease activity and HAQ-DI were seen for pts with severe vs moderate RA classified by BL DAS28 (Table), and by BL CDAI (Tofacitinib 5/10 mg BID ΔCDAI: -21.1/-23.0 vs -8.1/-9.4; ΔHAQ DI: -0.5/-0.6 vs -0.3/-0.4).

Conclusions: Tofacitinib 5 and 10 mg BID demonstrated efficacy in treating pts with moderate and severe RA with >7 years' mean disease duration. By M3, pts with severe vs moderate BL disease activity had greater improvements in disease activity and physical functioning; higher proportions of pts with moderate vs severe BL disease activity achieved remission, LDA or normal physical functioning. Interpretation of this post hoc analysis may be limited by the smaller sample size of the moderate disease group and the combining of mono- and combination-therapy results.

Acknowledgements: This study was sponsored by Pfizer Inc. Editorial support was provided by A Pedder of CMC and funded by Pfizer Inc.

Disclosure of Interest: S. Schwartzman Consultant for: Pfizer Inc, P. Sunkureddi Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, L. Takiya Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, M. Snyder Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, H. Fan Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, T. Lukic Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Roberts Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, W. F. Rigby Grant/research support from: Amgen, Pfizer Inc, Roche, Consultant for: Bristol-Myers Squibb, Eli Lilly, Pfizer Inc, Roche

DOI: 10.1136/annrheumdis-2017-eular.1846

AB0437 EFFICACY AND SAFETY OF LONG-TERM ANALGESIC THERAPY WITH ETORICOXIB FOR PATIENTS WITH RHEUMATIC DISEASES

S. Lapshina, L. Myasoutova. *Kazan State Medical University, Kazan, Russian Federation*

Background: There are some data in literature on decompensation of arterial hypertension and other chronic diseases during the treatment with coxibs which in practice unfortunately limits their administration for patients with comorbidities.

Objectives: To evaluate the efficacy of analgesic effect of etoricoxib and frequency of comorbidities exacerbation on such treatment.

Methods: 58 patients with rheumatoid arthritis (34,4%), osteoarthritis (29,2%), ankylosing spondylitis (19%), gout (14%), psoriatic arthritis (3,4%) at the age of 25 to 75 years (the average age, 52,9±13,03 years) were included. 79,3% patients had comorbidities (diseases of digestive system – 37,9%, arterial hypertension – 53,4% (including 3,2% with decompensated hypertension), bronchial asthma – 1,7%). All the patients before the appointment had taken NSAIDs (diclofenac, nimesulid, ketoprofen, meloxicam, aceclofenac, ibuprofen) with lack of effect (84,4%) or minimal effect (15,6%). Etoricoxib was administered in 100% cases. Pain severity according to visual analogue scale (VAS), comorbidities exacerbation and blood pressure were assessed at the beginning and during the first month of treatment.

Results: The average time period between 2 appointments was 20,72±9,3 days. By the second appointment 98,2% patients were taking etoricoxib regularly, and good tolerability of the medication was noted (63,8% excellent, 36,2% good). The average VAS score at the first appointment was 7,27±1,04, at the second appointment – 2,75±1,12, in the meantime VAS score improvement was noted mostly in the group of patients with long disease duration (more than 3 years). At the time of second examination total relief of back pain was revealed in 16,7%, in knee joint – 35,5%, in hip joint – 68,1%, in the neck – 61,9%, in small joints – 30,8%, of shoulder blade pain – 82,4%. No comorbidities exacerbation was noted. There were also no cases of sudden blood pressure increase on the administered therapy, including patients with arterial hypertension.

Conclusions: Etoricoxib administration leads to significant decrease of pain syndrome and its relief without increasing blood pressure and exacerbations of chronic comorbidities.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3972

AB0438 RHEUMATOID ARTHRITIS DRUG THERAPY IN THE PERIOPERATIVE PERIOD OF LARGE JOINTS ARTHROPLASTY, ITS IMPACT ON THE LONG-TERM RESULTS OF SURGERY

S. Lapshina[1], I. Akhtyamov[1,2], I. Gilmutdinov[2], L. Myasoutova[1]. *[1]Kazan State Medical University; [2]Republic Clinical Hospital, Kazan, Russian Federation*

Objectives: To analyze the results of large joints arthroplasty depending on the received rheumatoid arthritis (RA) drug therapy

Methods: Knee and hip joints arthroplasty was performed for 54 RA patients (48 women, 6 men), mean age 51,4±12,8 years. At the time of the operation disease duration was 11,8±3,8 years, high activity (DAS28) - in 26%, moderate - in 55.5%, the low - at 18.5% patients. At the time of surgery 39 (72.2%) pts continued to take basic anti-rheumatic drugs (DMARDs) (methotrexate at a dose of 10–20 mg per week - 32, leflunomide (20 mg daily) -5). Corticosteroids (prednisone at a dose of 5–15 mg, an average of 7.1 mg per day) - 25 (46.2%) patients, of which in combination with DMARDs - 10 (18.6%). Before the operation, and after the 6 months joint pain (VAS), disease activity - DAS28, functional ability HAQ index were evaluated. In 32 patients, these same indexes were estimated after 12 months.

Results: The reduction of pain intensity VAS was observed in the first month after a joint arthroplasty, after 6 months VAS fell almost to 31.8 mm ($p<0.05$). Activity of the disease decreased (high - 11.2%, moderate - 44.4%, low - 44.4%), HAQ - from 1,61±0,41 to 1,09±0,26 ($p<0$, 05). After 12 months HAQ - 1,01±0,28.

The analysis showed that in patients not receiving corticosteroids (n=29) arthroplasty was conducted in 13,6±3,2 years after RA onset, and receiving long-term steroids (n=25) significantly earlier ($p<0,05$) - through 9,9±3,5 years. The functional capacity of patients in the group receiving DMARDs without corticosteroids (n=29) (the HAQ 6 months - 0,9±0,24, 12 months - 0 81±0,16) was significantly ($p<0.05$) higher compared with patients receiving corticosteroids (n=25) without the basic treatment (HAQ 6 months -1.13±0.21, over 12 months-1,24±0,19)

Conclusions: Large joints arthroplasty is an effective method to improve the functional capacity of patients with RA. For patients receiving corticosteroids need of arthroplasty arises a few years earlier. The function of the joints after surgery and in the remote period is better when patients continuously receive DMARDs compared to steroid therapy, the dose should be reduced to a reasonable minimum for the time of surgical treatment.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3955

AB0439 EFFICACY AT THREE YEARS OF DAILY CLINICAL USE OF IGURATIMOD IN PATIENTS WITH RHEUMATOID ARTHRITIS

T. Suto[1], Y. Yonemoto[1], K. Okamura[1], M. Tachibana[1], C. Okura[1], M. Matsushita[2], K. Takeuchi[2], K. Otsuka[2], K. Ayabe[3], T. Kaneko[4], Y. Tamura[4], M. Inoue[5], H. Inoue[4], H. Chikuda[1]. *[1]Department of Orthopaedic Surgery, Gunma University Graduate School of Medicine, Maebashishi; [2]Department of Orthopaedic Surgery, Isesaki Fukushima Hospital, Isesakishi; [3]Department of Orthopaedic Surgery, Keiyu Hospital, Tatebayashishi; [4]Department of Orthopaedic Surgery, Inoue Hospital; [5]Department of Medicine, Inoue Hospital, Takasaki, Gunma, Japan*

Background: Iguratimod (IGU) is a small-molecule antirheumatic drug that was developed in Japan and is currently only approved for treatment of rheumatoid arthritis (RA) in Japan and China. IGU suppresses tumor necrosis factor-alpha-induced production of interleukin (IL)-6, IL-8 and monocyte chemoattractant protein 1 via the inhibition of nuclear factor-kappa B activation in cultured human synovial cells and human acute monocytic leukemia cells. There are some reports about the efficacy and safety of IGU in patients with RA. However, the assessment about efficacy of the clinical use of IGU has mainly been restricted to short-term (within one year) outcome.

Objectives: The purpose of this study was to assess the efficacy of IGU in 3 years

Methods: Sixty-nine RA patients (14 males and 55 females, mean age of 63.9 years, mean disease duration of 14.9 years) were enrolled in this study. The clinical course of RA was evaluated during 3 years. The patients who discontinued the IGU therapy were analyzed by the last observation carried forward method.

Results: The survival rate at 3 years was 49.3%, and 8 patients discontinued the IGU therapies due to insufficient response, 12 patients due to adverse events such as exanthema, pneumonitis or hepatic disorder, and other patients based on their requests. The DAS28-CRP, DAS28-ESR, SDAI and CDAI significantly decreased at 6 months, 1, 2, 3 years compared with baseline. The low DAS28-CRP at 3 months and younger age were associated to the continuation of IGU. Furthermore, 27 patients (39.1%) were in remission at 3 years. In the remission achievement group, the DAS28-CRP and the usage rate of prednisolone at baseline were significantly lower and patients' age was younger. A logistic regression analysis revealed the low DAS28-CRP and low usage rate of prednisolone at baseline were significant factors contributing to the achievement of a clinical remission at 3 years.

Conclusions: We assessed middle-term outcome of the clinical use of iguratimod therapy in RA patients. The low DAS28-CRP and low usage rate of prednisolone at the initiation of IGU were significant factors of clinical remission achievement at 3 years.

References:

[1] Duan XW, Zhang XL, Mao SY, Shang JJ, Shi XD. Efficacy and safety evaluation of a combination of iguratimod and methotrexate therapy for active rheumatoid arthritis patients: a randomized controlled trial. Clin Rheumatol. 2015 Sep;34(9):1513–9.

[2] Mimori T, Harigai M, Atsumi T, Fujii T, Kuwana M, Matsuno H, Momohara S, Takei S, Tamura N, Takasaki Y, Ikeuchi S, Kushimoto S, Koike T. Safety and effectiveness of 24-week treatment with iguratimod, a new oral disease-modifying antirheumatic drug, for patients with rheumatoid arthritis: interim

analysis of a post-marketing surveillance study of 2679 patients in Japan. Mod Rheumatol. 2016 Dec 21:1–11.
[3] Okamura K, Yonemoto Y, Suto T, Okura C, Takagishi K. Efficacy at 52 weeks of daily clinical use of iguratimod in patients with rheumatoid arthritis. Mod Rheumatol. 2015 Jul;25(4):534–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6040

AB0440 IMPACT OF VITAMIN D DEFICIENCY UPON DISEASE ACTIVITY AND IMMUNE DISORDER IN RHEUMATOID ARTHRITIS PATIENTS

Y. Liu, H.Y. Wen. *Rheumatology, the Second Hospital of Shanxi Medical University, Taiyuan, China*

Background: Emerging evidence suggests that vitamin D plays an important role in immune regulation.
Objectives: The objective of this work was to determine if patients with rheumatoid arthritis (RA) are at risk for vitamin D deficiency and whether vitamin D levels correlate with disease activity or immune disorders.
Methods: This study was a retrospective research. RA patients who had vitamin D levels and immune function indexes of each other were included. Patients receiving or have received vitamin D, corticosteroids, disease-modifying anti-rheumatic drugs or a tumor necrosis factor antagonist and those who had hepatic or renal insufficiency were excluded. Multivariate analysis was performed to examine correlations and control for confounding factors.
Results: As suggested threshold (≤25 ng/ml), the overall prevalence of vitamin D insufficiency was 265 of 280 (94.8%). Mean serum vitamin D insufficiency levels of 11.15±4.74 ng/ml for RA patients were significantly lower compared to controls (31.62±6.46) (p=0.001). Among all the subjects, 208 (72.7%) were females. Vitamin D levels in high disease activity group were lower compared to vitamin D level in patients with low and moderate disease activity (DAS-28 score >5.1, 3.2–5.1, <3.2, respectively, p<0.001) and vitamin D levels had an inverse correlation with DAS28 score (β-coefficient-0.164, p=0.018, per 1 ng/ml). In patients with RA, the levels of vitamin D were moderately and inversely associated with Th 17 (β-coefficient-0.158, p=0.019, per 1 ng/ml). However, no significant relationship was found between vitamin D and these variables (T cell, B cell, NK cell, Treg, Th1, Th2, Th17/Treg) in patients.
Conclusions: Lower levels of vitamin D are associated with worse DAS28 and higher levels of Th17 with RA, especially in female patients. The levels of 1,25-dihydroxycholecalciferol (1,25$(OH)_2D_3$) could be a marker to monitor the disease activity in RA patients and vitamin D may be an alternative supplementary treatment for RA.
Acknowledgements: This work was supported by research grants from the National Natural Science Foundation of China (no. 81301532/H0603) and the Shanxi Science and Technology research projects of China (no. 201603D321074).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3202

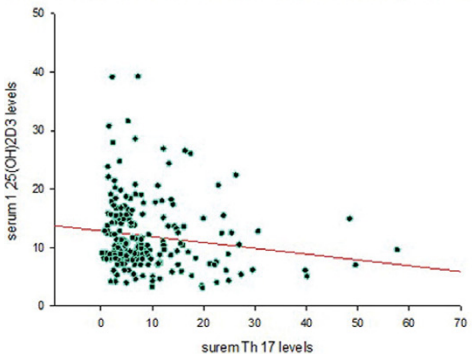
Table 1. Disease activity, immune function indexes with RA as mean ± standard deviation or number (%) for total group and based on vitamin D status

Variables	All patients N=280	Patients with Vitamin D insufficiency N=265	Patients without Vitamin D insufficiency N=15	P (Insufficiency vs no insufficiency)
Women	208 (72.7)	201 (74.2)	7 (33.3)	0.012
Age (yr)	56.421±12.325	56.109±12.225	61.933±13.215	0.075
Disease duration (yr)	9.004±9.336	9.017±9.374	8.782±8.938	0.925
ESR	59.064±36.483	59.325±36.731	54.467±32.544	0.617
DAS 28	4.754±1.429	4.768±1.426	4.508±1.526	0.494
T cell	1242.473±585.533	1249.317±586.751	1122.933±569.670	0.417
B cell	204.397±182.279	208.206±185.967	137.867±72.572	0.146
NK cell	237.419±187.449	233.782±188.784	300.933±153.989	0.178
Th1	88.290±116.113	87.583±116.660	103.377±108.907	0.691
Th2	12.729±10.819	12.852±10.992	10.121±5.788	0.461
Th17	9.271±9.023	9.330±9.145	8.010±6.059	0.669
Treg	33.710±28.519	34.060±29.025	26.257±12.426	0.424
Th17/Treg	0.421±0.639	0.421±0.647	0.411±0.445	0.964

Table 2. Multivariate associations of serum 1,25$(OH)_2$ D_3 concentrations with RA (n=280)

Variables	β-coefficient	95% CI	p
Gender	-0.241	-5.337 to -1.562	0.001
Age	0.182	0.024 to 0.168	0.009
DAS 28	-0.164	-1.243 to -1.116	0.018
Th 17	-0.158	-0.199 to -0.018	0.019

Figure 3: The correlations between of serum 1,25$(OH)_2D_3$ levels and Th 17 levels.



AB0441 USING OF SUBCUTANEOUS METHOTREXATE IN AGED PATIENTS WITH SEROPOSITIVE RA

Y. Muraviev, G. Gridneva, E. Luchikhina, N. Demidova, V. Lebedeva, D. Karateev. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russia, Moscow, Russian Federation*

Background: Increasing life expectancy is a global process involving multiple nations, thus deeper insights into methotrexate (MTX) therapeutic potential in aged people is of paramount importance, as MTX still remains an anchor DMARD in RA management.
Objectives: To assess the results of 12-months therapy with subcutaneous MTX (SC MTX) injections in RA patients aged more than 60 years.
Methods: The 12 months open study included pts with active RA (DAS28 >3,2), meeting ACR/EULAR (or ACR 1987) criteria, with RA lasting up to 3 years, and naïve to SC MTX. All pts were RF and/or ACPA-positive, 68% had increased BMI, 31% - obesity, 8% were smokers, 25% were taking oral GCS (≤10 mg/day equivalent to *prednisolone*).All pts were administered SC MTX monotherapy once a week as a DMARD, starting at 10–15 mg/week, with subsequent 5 mg up-titration each 1–2 weeks (to max 30 mg/week) up to achieving the target (remission or minimum disease activity) or up to emergence of an adverse drug reaction (ADR). Folic acid (min 5 mg/week) was administered at any day(s) except for the day of SC MTX injection for ADR prophylaxis. Disease activity was scored using DAS28. GEBA were administered in pts with insufficient SC MTX clinical effect. Pts were monitored within universal institutional REMARKA program, envisaging physical examination, blood analysis and biochemistry panel (including liver enzymes and creatinine). STATISTICA 10 software was used for data processing.
Results: 32 RA pts (28 females, 4 males) were included (mean disease duration 12±10 months, mean age - 65,7±4,7 years, mean DAS28 score -5,6±0,9. Cumulative SCMT dose by the end of the study reached 264±180 mg). The therapeutic target (remission or minimum disease activity based on DAS28 score) was achieved in 20 pts receiving SCMT monotherpay, 12 pts required administration of GEBAs. Adverse drug reactions (ADRs) were documented in 10 pts, including cases of more than one ADR at a time: breast abscess (1), alopecia (2), diarrhea (2), skin rash (1), a metallic aftertaste (1), local post-injection reactions (1), nausea (2), elevation of liver enzymes (3), leucopenia (1), pneumonia (1). There were 5 cases of SC MTX monotherpay discontinuation (2 - temporary, and 3 - permanent). The majority of pts (88%) could manage self-injection without additional training or assistance from medical staff.
Conclusions: 62,5% of aged RA pts participating in the study managed to achieve the therapeutic target after 12 months of SC MT monotherapy, although 31% ADRs rate required temporary (2)/permanent (3) SCMT discontinuation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2418

SLE, Sjögren's and APS - treatment

AB0442 REAL-LIFE EXPERIENCE WITH BELIMUMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): CONTROL OF DISEASE ACTIVITY AND FLARES IN A MULTICENTER COHORT

A. Fanouriakis[1], C. Adamichou[2], S. Koutsoviti[3], A. Klagou[4], C. Tsalapaki[5], S. Konsta[6], D. Dimopoulou[7], S. Ntali[8], D. Vassilopoulos[5], P. Konstantopoulou[9], A. Elezoglou[3], P. Sidiropoulos[2], A. Erden[10], G. Bertsias[2], D. Boumpas[1]. *[1]Rheumatology and Clinical Immunology, "Attikon" University Hospital, Athens; [2]Rheumatology, Clinical Immunology and Allergy, University Hospital of Heraklion, Heraklion; [3]Dept of Rheumatology, "Asklipieion" General Hospital; [4]Dept of Rheumatology, "G. Gennimatas" General Hospital; [5]2nd Dept of Internal Medicine, "Ippokrateion" General Hospital; [6]Dept of Rheumatology, "Evangelismos" General Hospital, Athens; [7]Dept of Rheumatology, "Ippokrateion" General Hospital; [8]Private rheumatologist, Thessaloniki; [9]Dept. of Rheumatology, "G. Gennimatas" General Hospital, Athens, Greece; [10]Dept. of Rheumatology, Hacettepe University, Faculty of Medicine, Ankara, Turkey*

Background: Data on the efficacy of belimumab in SLE mainly originate from large randomized clinical trials, whereas reports from real-life clinical practice are lacking.
Objectives: To describe the clinical experience from the use of belimumab in Greece since the approval of the drug.
Methods: Multicentre observational study of patients receiving belimumab, with documentation of disease activity (SLEDAI-2K index), achievement of low disease

activity states [remission (SLEDAI-2K=0) and lupus low disease activity state (LLDAS)], accrual of irreversible damage (SLICC damage index, SDI), number and severity of flares, and side-effects. Analyses were performed at quarterly intervals and only patients with at least 3 months of follow-up were included in the study.

Results: A total of 56 patients were included [53 women (94.6%), mean (SD) age 46.3 (12.7) years]. Evidence of serologic activity (low C3/C4 and/or high anti-ds DNA) was evident in 30 patients (53.5%). Most frequent manifestations were arthritis (82.1%), inflammatory rash (73.2%), active hair loss (57.1%), mucosal ulcers (26.8%) and leukopenia (10.7%).

Median (range) duration of follow-up was 9.1 (2.9 - 34.6) months. We observed a significant decrease in the SLEDAI-2K, physician global assessment (PGA) and daily prednisone dose over time, starting as early as 3 months after belimumab initiation (Table 1). This effect was significantly more pronounced in patients who were serologically active (SA) at baseline, even after exclusion of the serologic component of the SLEDAI [median (range) *clinical* SLEDAI-2K for SA patients: 7 (1–24) at baseline vs. 2 (0–16) at 6 months and 2 (0–16) at 12 months, $p<0.0001$ and p=0.013, respectively; for serologically inactive patients: 6 (2–23) at baseline vs. 6 (0–14) at 6 months and 5 (0–18) at 12 months, p=0.017 and p=0.024, respectively]. For patients with $\geq$12 months of follow-up (n=20), belimumab treatment resulted in a significant decrease in flare rate [median (range) total number of flares for the 12 months before and after belimumab treatment, 3 (0–7) and 0 (0–2), respectively, $p<0.0001$). 10 patients (17.8%) discontinued belimumab due to inefficacy after a median (range) 7.1 (5.5 - 20.4) months of therapy and 5 patients discontinued due to planned pregnancy. There were no drug discontinuations due to side-effects.

Table 1. Changes in disease activity and daily prednisone dose during treatment with belimumab

	Baseline (reference) n=56	3 months n=56	6 months n=47	9 months n=26	12 months n=22	18 months n=10	p value
SLEDAI, median (range)	8 (2-28)	6 (0-24)*	4 (0-20)*	4 (0-18)*	4 (0-18)*	3 (0-14)**	*p<0.001 **p=0.01
	Baseline (reference)	3 months	6 months	9 months	12 months	18 months	p value
PGA, median (range)	1.9 (1-3)	1.5 (0.3-3)*	1.5 (0.5-3)*	1.5 (0-2.2)*	1.15 (0-3)*	1 (0-2)***	*p<0.001 **p=0.18 ***p=0.01
	Baseline (reference)	3 months	6 months	9 months	12 months	18 months	p value
Pr dose, median (range)	7.5 (0-40)	7.5 (0-30)*	5 (0-25)*	5 (0-10)*	5 (0-30)**	4.3 (0-7.5)***	*p<0.001 **p=0.001 ***p=0.021
Low disease activity states, n(%)	Baseline	3 months	6 months	9 months	12 months	18 months	
LLDAS	0 (0)	10 (17.9)	15 (31.9)	10 (34.5)	5 (21.7)	4 (40)	
Remission	0 (0)	3 (5.4)	4 (7.1)	3 (5.4)	4 (7.1)	2 (3.6)	

Conclusions: In real-life clinical settings, belimumab is efficacious in controlling disease activity of SLE and permitting tapering of glucocorticoid dose. Similar to data from RCTs, this effect seems to be more pronounced in serologically active patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4825

AB0443 INFUSION REACTIONS TO RITUXIMAB IN SYSTEMIC LUPUS ERYTHEMATOSUS: A RETROSPECTIVE ANALYSIS

A. Hennessey[1,2], J. Lukawska[3], G. Cambridge[1], D. Isenberg[1,2], M. Leandro[1,2]. *[1]Centre for Rheumatology and Bloomsbury Rheumatology Unit, University College London; [2]Division of Rheumatology, Department of Medicine; [3]Allergy Medicine, University College London Hospitals, London, United Kingdom*

Background: B-cell depletion with Rituximab (RTX) has been used since since 2000 in the treatment of Systemic Lupus Erythematosus (SLE). An issue with the use of RTX is the attrition rate due reactions during of following infusions. This can prevent re-treatment with RTX in patients with a good initial response to RTX and in whom other treatments had failed, this is especially important in SLE patients with limited biologic options.

Objectives: To identify the rates and patient characteristics of infusion reactions to RTX in patients with SLE.

Methods: A retrospective analysis of the SLE patient cohort receiving RTX at University College London Hospitals via examination of patient records was used to determine if there was a clinically significant reaction (from clinic letters or discharge summary) for each RTX infusion. One cycle of RTX refers to 2 infusions given 2 weeks apart. A descriptive analysis of the reaction was recorded as was the decision making surrounding the infusions.

Results: Records from 151 RTX-treated patients were reviewed with 13 excluded due to missing data. 138 remaining patients (130 females and 8 males, mean age (1st infusion) =33 years; range: 16–73) received a total of 478 individual RTX infusions (between 1–9 cycles). Prior to 2007, standard of care was to receive Cyclophosphamide (CYC) with each cycle. The total rate of infusion reactions was 5.85% (23 patients had 28 reactions). Of these 4 (50%) were males, 19 females (14.6%; *p*=0.009, Chi square). Average number of cycles in those without, compared to with a reaction was 1.61 vs 1.64. With 1st dose, 7 patients (25%) had reactions, 19 with 2nd (67.9%). 3 patients were retreated (1 twice); 2/3 had further reactions and the 3rd two further cycles without issues. Most were not retreated. Reactions ranged from mild to severe (Table 1). A total of 24 RTX reactions were categorized into: Immediate- unlikely immune mediated 4; likely cytokine release 7; IgE mediated 5; and bone pain reactions 2. Delayed-early (24–48hours) 1; and late (>48hours) 5; by a Clinical Allergist. 4 reactions were excluded from this analysis; 1 death as likely CYC induced (but occurred within 24 hours of RTX) and 3 due to lack of data.

Table 1. Severity of Infusion Reactions

Severity of reaction	Number of patients	% of total infusion reactions	Retreated?
Death	1	3.6%	N
Severe	3	10.7%	Y – 1 (had further reaction)
Moderate	7	25.0%	Y – 1 (2 further cycles)
Mild	8	28.6%	Y – 1 (2 further cycles)
Delayed	5	17.9%	Y – 1 (1 further cycle)
Unclassified	4	14.3%	N

Mild (infusion resumed/completed), Moderate (had to cease infusion reaction), Severe (hospital admission), Delayed/serum sickness.

Conclusions: The number of previous cycles was similar in patients who reacted versus those who did not. Patients were most likely to experience a clinically significant reaction with the second infusion. Males had higher incidence of reactions. Most (19%) were immediate and the majority (79%) of immediate and delayed reactions occurred during 1st (10) and 2nd (9) cycles. The total rate of infusion reactions in this cohort was lower than previously reported however this is likely contributed to by the limitations of a retrospective review. However 64% of reactions (11/17) in this cohort were significant, necessitating cessation of infusion or hospital admission.

Disclosure of Interest: A. Hennessey: None declared, J. Lukawska: None declared, G. Cambridge: None declared, D. Isenberg: None declared, M. Leandro Consultant for: Roche UK and Roche Basel and Genentech

DOI: 10.1136/annrheumdis-2017-eular.5875

AB0444 EFFECT OF RITUXIMAB ON A SALIVARY GLAND ULTRASOUND SCORE IN PRIMARY SJÖGREN'S SYNDROME: RESULTS OF THE TRACTISS MULTICENTRE RANDOMISED TRIAL SUB-STUDY

B.A. Fisher[1], C.C. Everett[2], J. Rout[3], J.L. O'Dywer[4], P. Emery[5], C. Pitzalis[6], W.-F. Ng[7], A. Carr[8], C.T. Pease[5], E.J. Price[9], N. Sutcliffe[10], J. Makdissi[10], N.S. Gendi[11], F.C. Hall[12], S.P. Ruddock[2], C. Fernandez[2], C.T. Hulme[4], K.A. Davies[13], C.J. Edwards[14], P.C. Lanyon[15], R.J. Moots[16], E. Roussou[17], L.D. Sharples[18], M. Bombardieri[6], S.J. Bowman[1]. *[1]Rheumatology, University of Birmingham, Birmingham; [2]Leeds Institute for Clinical Trials Research, Leeds; [3]Dental Hospital, Birmingham; [4]Health Economics; [5]LMBRU, University of Leeds, Leeds; [6]Barts and the London School of Medicine, London; [7]Musculoskeletal Research Group, University of Newcastle; [8]Newcastle University, Newcastle; [9]Great Western Hospital, Swindon; [10]Royal London Hospital, London; [11]Basildon and Thurrock University Hospital, Basildon; [12]University of Cambridge, Cambridge; [13]Brighton and Sussex Medical School, Brighton; [14]University Hospital Southampton, Southampton; [15]University of Nottingham, Nottingham; [16]University of Liverpool, Liverpool; [17]BHRUT, Goodmayes; [18]London School of Hygiene and Tropical Medicine, London, United Kingdom*

Background: B lymphocytes are important in the pathogenesis of primary Sjögren's syndrome (PSS), but two phase III trials (TEARS and TRACTISS) of the B cell depleting agent rituximab (RTX) failed to show an effect on their primary endpoints in PSS. Whilst RTX may lack efficacy in a non-stratified PSS population, other possible explanations for these negative results include the choice and timing of primary outcome. In a small single-site salivary gland ultrasound (SGUS) substudy in TEARS, more subjects in the RTX arm demonstrated improvement in parotid gland echostructure. Importantly, SGUS is an operator-dependent technique.

Objectives: To compare the effects of RTX versus placebo on SGUS in PSS, in a multicentre, multiobserver substudy of TRACTISS.

Methods: Subjects consenting to SGUS were randomised to 1000mg RTX or placebo given at weeks 0, 2, 24 and 26, and scanned at baseline and weeks 16 and 48. Sonographers completed a 0–11 total ultrasound score (TUS) comprising domains of echogenicity, homogeneity, glandular definition, glands involved, and size of hypoechoic foci. Baseline-adjusted values of TUS were analysed over time, modelling change from baseline at each time point. For each TUS domain we fitted a repeated measures logistic regression model to model the odds of a response in the RTX arm (defined as a 1 point improvement) as a function of the baseline score, age category, disease duration and time point.

Results: 66 patients (49.6% of the total study population) consented to SGUS, and 52 (39.1%; n=26 RTX and n=26 placebo) completed the baseline and at least one follow-up visit. Estimated baseline-adjusted TUS at week 16 was 6.2 (95% CI 5.4–7.0) for placebo and 5.0 (95% CI 4.4–5.6) for RTX, and at week 48, 6.1 (95% CI 5.5–6.6) and 4.8 (95% CI 4.2–5.4) respectively. Estimated between group differences (RTX-placebo) in baseline adjusted TUS were -1.2 (95% CI -2.1 to -0.3; p=0.0099) and -1.2 (95% CI -2.0 to –0.5; p=0.0023) at weeks 16 and 48. Glandular definition was the only domain to show statistically significant improvement with an OR of 6.8 (95% CI 1.1–43.0; p=0.043) at week 16 and 10.3 (95% CI 1.0–105.9; p=0.050) at week 48. Improvement of $\geq$1 point in TUS was associated with improvement in oral dryness VAS at week 16 (diff=15.9; CI 1.5 to 30.3; p=0.030) but not week 48 in the RTX arm.

Conclusions: TUS differed between study arms, favouring RTX. This encourages further research into SGUS as an imaging biomarker in PSS clinical trials.
Acknowledgements: Funded by Arthritis Research UK. Roche provided RTX.
Disclosure of Interest: B. Fisher Paid instructor for: Novartis, Roche, Virtualscopics, C. Everett: None declared, J. Rout: None declared, J. O'Dywer: None declared, P. Emery: None declared, C. Pitzalis: None declared, W.-F. Ng Consultant for: Pfizer, UCB, MedImmune, Takeda and Sanofi, A. Carr: None declared, C. Pease: None declared, E. Price: None declared, N. Sutcliffe: None declared, J. Makdissi: None declared, N. Gendi: None declared, F. Hall: None declared, S. Ruddock: None declared, C. Fernandez: None declared, C. Hulme: None declared, K. Davies: None declared, C. Edwards: None declared, P. Lanyon: None declared, R. Moots: None declared, E. Roussou: None declared, L. Sharples: None declared, M. Bombardieri Consultant for: GSK, Amgen/MedImmune and UCB, S. Bowman Consultant for: Cellgene, Glenmark, GSK, Eli Lilly, Novartis, Roche, Takeda, UCB
DOI: 10.1136/annrheumdis-2017-eular.3138

AB0445 HYDROXYCHLOROQUINE'S IMPACT IN RENAL BIOPSY AND OUTCOMES OF LUPUS NEPHRITIS

D. Navarro, A.C. Ferreira, H. Viana, F. Carvalho, F. Nolasco. *Nephrology Department, Hospital Curry Cabral, Lisboa, Portugal*

Background: Given its immunomodulatory effects, hydroxychloroquine use is recommended in systemic lupus erythematosus (SLE). It is associated with a lower rate of appearance and of relapse of lupus nephritis (LN). LN is classically classified using ISN/RPS classification, but others indexes, such as the ones described by Austin and Hill, allow for the quantification of SLE activity in the kidney tissue.
Objectives: To analyze the association between the use of hydroxychloroquine and the activity of LN in the kidney biopsy.
Methods: Retrospective single center study of consecutive SLE and biopsy proven LN patients, diagnosed from 2010 to 2016. We evaluated the following outcomes: clinical remission, renal function and proteinuria at end of follow-up (g/24h). Complete remission was defined as a reduction of proteinuria to <0,5g/24h, inactive urinary sediment and serum creatinine <115% of baseline; partial remission same parameters, except proteinuria <1g/24h if initial value <3h/24h, or reduction to <3g/24h if initial value >3g/24h. Kidney biopsies were evaluated by the INS/RPS LN classification and the morphological indexes described by Austin and Hill, obtained after histomorphological review of renal biopsies. The studied predictor was the use of hydroxychloroquine. Statistical analysis was performed with STATA software, using one-way ANOVA, Qui2 and Pearson/Sperman test were appropriate.
Results: During 6 years, there were 46 biopsy-proven LN cases, 84,8% (n=39) woman, median 35 years old (27–42,5) and 57,6% (n=19) caucasian. 39 patients were already known to have SLE, 7,44 (1,13–12,3) years previously. Of those 39 patients, 46% were under hydroxychloroquine and 77% under other immunosuppression.
The median follow-up was 31,9 (13,2–45,6) months. Based on biopsy findings, 35 patients were started on immunosuppression – induction in 50% of cases with MMF and in 50% with cyclophosphamide; maintenance in 81% with MMF, the rest with azathioprine. Complete remission was achieved in 58% of patients, 27% achieving partial remission. We observed 4 LN relapses. At the end of FUP, we saw a 96% (n=44) patient survival, with a median serum creatinine of 0,8 mg/dl (0,7–0,99), eGFR 99,8 ml/min (71,2–116,8) and proteinuria of 0,6 g/24h (0,2–1,6). From those 46 patients, 30 were under immunosuppressive therapy at time of LN presentation, and 60% (n=18) were also under hydroxychloroquine. Table 1 summarizes the clinical findings:
With the use of hydroxychloroquine, we observed a lower histomorphological activity, as represented by a lower Hill biopsy index, and tendency towards lower Activity index. We also saw a tendency towards lower proteinuria.
Conclusions: Our data reinforces the recommendations of using hydroxychloroquine for its adjuvant role in SLE patients, as we saw a lower histomorphological activity in kidney biopsy, and a trend towards lower proteinuria.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5546

AB0446 ADDITIVE INHIBITION OF INTERFERONS, B AND T CELL ACTIVATION AND TFH-RELATED CYTOKINE CXCL13 BY LEFLUNOMIDE AND HYDROXYCHLOROQUINE SUPPORTS RATIONALE FOR COMBINATION THERAPY IN PSS PATIENTS

E.H. van der Heijden[1,2], S.A. Hartgring[1,2], A.A. Kruize[2], T.R. Radstake[1,2], J.A. van Roon[1,2]. *[1]Laboratory of Translational Immunology; [2]Dept. of Rheumatology & Clinical Immunology, UMC Utrecht, Utrecht, Netherlands*

Background: T and B cell-driven immunity is critically involved in immunopathology of pSS. Recently we demonstrated synergistic T and B-cell activation upon T cell triggering and TLR7/9-driven B cell activation in pSS patients, accompanied by synergistic induction of immunoglobulins and IFN-γ- and IL-17-producing T cells[1]. In addition, TLR7/9-expressing activated pDCs associated with increased type I IFNs and IFN-inducible genes are increased pSS patients. Several studies have shown that the DMARDs leflunomide and hydroxycholoroquine inhibit immune activation in pSS but only show moderate efficacy. However, LEF and HCQ target different pathways with overlapping, but also potentially additive mechanisms, where LEF primarily targets T and B cells and HCQ TLR7/9-driven B cell and pDC activation.
Objectives: To assess the additive effects of LEF and HCQ on CD4 T- and B-cell activation and production of interferons IFN-α and IFN-γ, Tfh-related cytokine CXCL13, as well as IgG and IgM *in vitro* employing SEB/TLR9-triggered PBMC.
Methods: PBMCs of healthy individuals (n=9) and of pSS patients (n=8) were cultured with antigen (SEB), TLR9 and their combination, in presence or absence of LEF, HCQ and their combination in clinical relevant concentrations. Proliferation of T and B cells and release of IFN-α, IFN-γ, CXCL13, IgG and IgM were measured.
Results: In line with robust T and B cell activation, IFN-γ, IFNα, CXCL13, IgG and IgM production was achieved by a combination of SEB and TLR9 (all at least $p<0.001$). LEF dose dependently inhibited B and T cell proliferation, Interferon, CXCL13 and immunoglobulin production. HCQ dose dependently inhibited B cell proliferation, IFN-α, CXCL13, and immunoglobulin production. T cell proliferation and IFN-γ production were inhibited by HCQ only at higher concentrations. At several suboptimal concentrations LEF and HCQ additively inhibited T cell proliferation both in healthy individuals and in pSS patients. (Figure 1). Significant additive effects were seen for all outcome measures except IFN-α. Since IFNa was already robustly inhibited by HCQ alone (eg.for pSS 90% at 3.3 μM, $p<0.001$), only trends towards additive effects were observed.

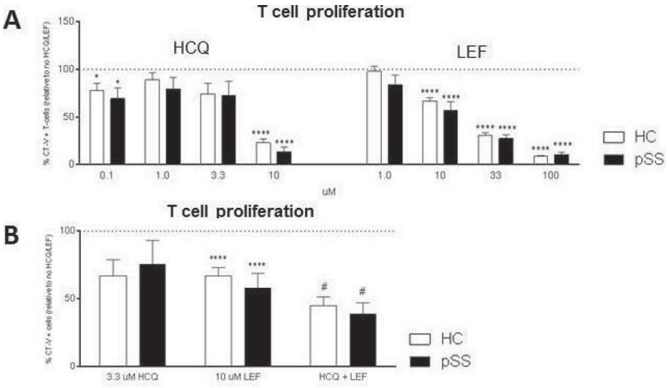


Figure 1. HCQ and LEF additively inhibit T cell activation. T cell proliferation is dose dependently inhibited by LEF and by HCQ at 0.1 and 10 μM **(A).** Significant additive inhibition of T cell proliferation is achieved by combination of suboptimal concentrations of LEF and HCQ both in HC and pSS patients **(B).** *and **** indicates statistical significance of p<0.05 and p<0.0001 resp. vs control, # indicates statistical significance of p<0.05 of the combination vs each of the single drugs.

Conclusions: LEF and HCQ robustly inhibited proliferation of T and B cells, cytokine production and immunoglobulin production with clear additive efficacy in both healthy individuals as in pSS patients. These data support the potential surplus value of combination therapy with LEF and HCQ for patients with pSS.
References:
[1] Bikker et al. Interleukin-7 and Toll-Like Receptor 7 induce synergistic B cell and T cell activation. PLoS ONE 9(4): e94756.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5022

AB0447 ANTIMALARIALS IMPROVE SURVIVAL OF SYSTEMIC LUPUS ERYTHEMATOSUS ON CHOLESTEROL: RESULTS OF A FIFTEEN-YEAR CHINESE MULTICENTER RETROSPECTIVE STUDY IN JIANGSU PROVINCE

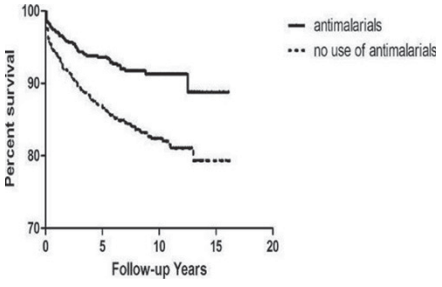
F. Wang[1], W. Zhang[1], S. Wang[1], W. Pan[2], L. Liu[3], M. Wu[4], X. Ding[5], H. Wei[6], Y. Zou[7], X. Feng[1], L. Sun[1]. *[1]Department of Rheumatology and Immunology, the Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing; [2]2Department of Rheumatology, Huaian First People's Hospital, Huaian; [3]Department of Rheumatology, Xuzhou Central Hospital, Xuzhou;*

Abstract AB0445 – Table 1

Hydroxychloroquine use	Class II	Class III	Class IV	Class V	Hill Biopsy Index	Activity Index	Chronicity Index	End of FUP eGFR (ml/min)	End of FUP serum creatinine (mg/dl)	End of FUP proteinuria (g/24h)
Yes (n=18)	39%	28%	28%	22%	0,86 (0,2 – 1,8)	1 (0 – 4,25)	0,75 (0 – 3,25)	99,8 (81,9 – 112,1)	0,74 (0,7 – 0,8)	0,3 (0,1 – 0,6)
No (n=12)	8%	17%	58%	33%	1,52 (0,98 – 2,01)	7,25 (1,38 – 9)	2,25 (0,13 – 5,25)	98,6 (56,4 – 120,3)	0,78 (0,7 – 1,3)	0,75 (0,15 – 2,6)
p-value	0,09	NS	NS	NS	0,03	0,07	NS	NS	NS	0,09

[4]Department of Rheumatology, Third Affiliated Hospital of Soochow University, Changzhou; [5]Department of Rheumatology, Liangyungang First People's Hospital, Liangyungang; [6 8]Department of Rheumatology, Subei People's Hospital of Jiangsu province, Yangzhou; [7]Department of Rheumatology, Wuxi People's Hospital, Wuxi, China

Background: Nowadays the importance of antimalarials, especially hydroxychloroquine (HCQ) and chloroquine (CQ), in treatment of systemic lupus erythematosus (SLE) has been demonstrated. However, few have examined the efficacy of HCQ and CQ on eastern Chinese SLE patients.
Methods: The analysis is based on 1372 patients who were enrolled in a retrospective study of 26 centers from January 1st, 1999 through December 31st, 2009, during which time is their first hospitalization. Baseline and follow-up clinical, laboratory and therapeutic data and survival status before April 30th, 2015 were recorded. Statistical analysis consist of Chi-square test, *t*-test, Kaplan-Meier curves and logrank test.
Results: Compared with 562 patients without HCQ or CQ treatment, the hazard ratio (HR) of deaths in 810 patients taking those was reduced (HR 0.52, 95% CI 0.38–0.70, $p<0.001$). 376 of these 1372 patients experienced their second hospitalization, during which treating group (165 of 376) showed lower blood level of total cholesterol (TG), compared to control group (4.47 (0.13) vs 5.03 (0.21), p=0.027), while no statistical difference of TG exists between the two groups' first hospitalization ($p>0.05$). Other metabolic data, such as systolic and diastolic blood pressure, fasting blood sugar, Triglyceride and uric acid were similar between the two groups in two times of hospitalization. On second inpatient visit, disease activity (SLEDAI, blood sedimentation rate, complement) and organ involvements (SLICC) of those who took antimalarials and no users have no significant differences.



Conclusions: Use of HCQ or CQ lower the risk of mortality and TG levels of eastern Chinese SLE patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4208

AB0448 USE OF DENOSUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A REAL LIFE MULTI-CENTRIC EXPERIENCE

F. Crisafulli[1], M. Fredi[2], A. Bortoluzzi[3], I. Cavazzana[2], F. Furini[3], M. Govoni[3], A. Tincani[1], F. Franceschini[2]. *[1]Rheumatology Unit and University of Brescia; [2]Rheumatology Unit, Brescia; [3]Department of Medical Sciences, Rheumatology Unit and University of Ferrara, Ferrara, Italy*

Background: The occurrence of osteoporosis (OP) and fragility fractures (FF) is a frequent comorbidity in patients with systemic lupus erythematosus (SLE), mainly due to the concomitant presence of many risks factors for secondary osteoporosis (drugs, gender, concomitant diseases). The use of corticosteroids (CS) increases the risk of osteoporosis induced by corticosteroid (GIOP) and FF [1]. Denosumab is monoclonal antibody that binds to RANKL, inhibiting osteoclast formation and activation, used for both male and women OP to prevent FFx [2,3]. Previous RCT [2] reported a numerically higher serious adverse events of infections in the denosumab users. In particular severe skin infections were significantly more frequent [4]. The possible increase in infection risk might be a concern in subjects treated with CS. The use of denosumab in SLE with GIOP patients is recently reported in 17 cases within a RCT [5]. Anyway, no data regarding the tolerability and disease activity during therapy were reported
Objectives: Our aim was to analyze the prevalence, the tolerability, and relevant changes in disease activity or damage in a cohort of SLE patients treated with denosumab
Methods: among all SLE patients currently followed in two referral Center we selected the ones that received at least one dose of denosumab. Clinical, serological manifestations, concomitant diseases and therapies were collected from clinical charts. Damage index (SDI), activity index (SLEDAI-2K) were calculated when denosumab was introduced (first cycle) and at the last evaluation (last cycle). For statistical analysis Chi-squared test or Fisher exact test was used
Results: Among 793 patients in our cohorts, 21 (2.6%) were treated with denosumab. Demographic data reported a female prevalence (19 cases,90%), mean age at onset of 38±12years, mean duration of disease of 28±10years and mean follow-up of 21±7.8years; most frequent manifestations were arthritis (90%), cutaneous (67%) and neurological (67%). All patients were still treated with CS (mean duration of 25±6.8 years) with a daily dose of 8.5±3.5mg/day. Other risk factors for OP were present in the majority of them: drugs (anticoagulants in 6pts, cyclosporin in 3 and antiepileptic in 2), chronic kidney disease (CKD) (4pts), hypovitaminosis D (15pts), anorexia, celiac disease and hemochromatosis (1pt, each). Indication for denosumab was OP with FFx in 17 cases: denosumab was used for a new FF during biphosphonates or after teriparatide. In the other 4 the indication was primary prevention with contraindications at the use of biphosphonates for concomitant severe CKD. Mean duration therapy was 4 cycles (range 1–8): data regarding disease activity, damage and adverse events are reported in table 1. No new FFx developed in any of the included patients at the last evaluation available.

Efficacy/adverse events	First cycle (N=21 pts)	Last cycle (N=21 pts)	P value
New fracture	Not applicable	0 (0%)	na
Mean dose of GC, mg/day (mean±DS)	6.9±3.4	5.8±3.1	ns
T score hip*	-2.6±1.4	-2±1	ns
T score lumbar spine *	-2.61±1.1	-2.3±0.8	ns
Hypovitaminosis D **	15 (71%)	13 (62%)	ns
SLEDAI-2k (mean±DS)	3.5±3.3	2.36±2.65	ns
SDI (mean±DS)	4 ±1.18	4.1±1.21	ns
Any adverse event	1	1	ns
Infective episodes	1 (not requiring antibiotic	1 (not requiring antibiotic)	
Skin infection	0	0	ns
Flare SLE	0	1 (arthritis)	ns
Therapy withdrawal	na	0	ns

*available for 18 patients at first cycle and 13 at last evaluation; **=all patients received vitamin D supplementation; na=not applicable; ns=not significant

Conclusions: In our cohorts denosumab is still used in few selected patients. However it could be considered as a valid option in GIOP patients because it was globally well tolerated and in our cohort it's efficacy in the prevention of new fragility fractures was confirmed
References:
[1] Gudbjornsson, et al. Ann Rheum Dis 2002;61,32–36.
[2] Cummings SR et al. N Eng J Med 2009; 61:756–65.
[3] Austin M et al. J Bone Miner Res 2012;27:687–93.
[4] Watts NB, Osteoporos Int 2012;23:327–37.
[5] Mok CC, et al. Bone 2015;75:222–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2740

AB0449 OFF LABEL OF BIOLOLOGICS IN CONNECTIVE TISSUE DISEASES. A SINGLE CENTER EXPERIENCE

G. Orsolini[1], C. Crowson[2], O. Viapiana[1], M. Rossini[1], K.G. Moder[2]. *[1]Rheumatology, University of Verona, Verona, Italy; [2]Rheumatology, Mayo Clinic, Rochester, United States*

Background: Connective tissue diseases (CTDs) are a broad spectrum of autoimmune conditions including different entities such as systemic sclerosis (SSc), Sjogren syndrome (SSj), systemic lupus erythematosus (SLE) and autoimmune myositis. There are many patients that do not meet the classification or diagnostic criteria and they fall under the diagnosis of Undifferentiated connective tissue disease (UCTD). Treatment of refractory forms of these could be challenging and clinicians sometimes are forced to try off label drugs such as biologics on the basis of scarce literature support and the experience on different rheumatic disease.
Objectives: To evaluate duration of biologic drug administered off label for the treatment of CTD and investigate variables possibly associated to drug suspension.
Methods: We used ACE program to search among Mayo Clinic clinical records all the patients that had in their records the words "undifferentiated connective tissue disease" or "lupus" or "myositis" or "Sjogren" or "systemic sclerosis" or "scleroderma"(and acronyms) AND "infliximab" or "etanercept" or "golimumab" or "certolizumab" or "tocilizumab" or "abatacept" or "adalimumab" (and their brand names).
All records were checked for definite diagnosis and patients with uncertain ones where excluded. Also medications were checked, patients without any information about treatments where excluded. All the records of the selected patients were used to collect information about the off label biologic treatment but also clinical, serological and demographic variables.
Results: We collected data on 122 patients with connective tissue diseases, some of them had other concomitant autoimmune diseases with indication for biologic treatment (e.g. rheumatoid arthritis, etc). We analyze the group with some CTD alone (n=72) considering SLE (n=18 – 25%), inflammatory myositis (n=22 – 31%) and UCTD (n=32 – 44%). In this group the first biologic was etanercept in 55%, adalimumab in 18%, infliximab in 17%, golimumab in 1% and abatacept in 8%. The 22% tried also a second biologic and 4% a third. We consider for analysis the first treatment.
Mean treatment duration was 0.8 (±1.1)years. In our population 12,5% experienced a flare of CTD, 12,5% had infections, 18% had allergic reactions (of any type). The 44% experienced primary failure, 11% loss of efficacy, 31% had minor adverse events, 14% major ones (possible more than one reason for interruption).
Analysis showed no definite factors correlated with treatment duration or failure or adverse events, No difference due to type of CTD.
Conclusions: The study is retrospective and this limits the conclusions to be taken from it, however is one of largest population of off label treatments in CTDs

so far. Due to retrospective data we choose as outcome only treatment duration and adverse events, direct outcomes of efficacy were impossible to evaluate. Our results indicates a poor treatment duration of biologics given off label in CTDs with a relevant prevalence of adverse events and failures. It has to be underlined that our population was mainly on TNF blockers.
These data discourage the use of biologics, mainly of TNF blockers in CTDs, even if they still can be considered with caution in very selected cases after failure of the other on label medications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2952

AB0450 THE DARK SIDE OF GLUCOCORTICOID THERAPY IN SYSTEMIC LUPUS ERYTHEMATOSUS: CAN WE DO SOMETHING ABOUT THAT?

I. Saulescu, T. Gudu, A. Neagu, D. Opris, A. Borangiu, S. Daia-Iliescu, L. Groseanu, A. Balanescu, V. Bojinca, R. Ionescu. *Internal Medicine and Rheumatology, Umf Carol Davila, Sf. Maria Hospital, Bucharest, Bucharest, Romania*

Background: Corticosteroids are still one of the main treatment in Systemic Lupus Erythematosus (SLE). Beside the effect on controlling disease activity, they are also implicated in damage accrual. Both patients and physicians are some time afraid to adopt a steroid free regimen when possible.
Objectives: To evaluate the knowledge and perception of patients with SLE upon glucocorticoids.
Methods: 84 patients with SLE were evaluated and data about demographic, clinical, serological characteristics or treatment were collected. Presence of steroids related side effects like hypertension, osteoporosis, cataracts or diabetes mellitus were also assessed. All patients completed a questionnaire in order to evaluate patient's knowledge about steroids. They were asked if they had a discussion with the doctors about corticotherapy and side effects related to them, if they consider that this treatment could be stopped with specialist approval. Statistics was performed with SPSS program.
Results: All patients had treatment with corticosteroids during disease evolution. 57.14% of them experienced at least one steroids related side effect. This patients were significant older: mean age at evaluation 49.50 versus 36.47 ($p<0.0001$), had a longer disease duration: mean SLE duration 9.27 versus 4.69 (p0.016), a higher mean Prednisone equivalent dose: 8.86 versus 4.71 (p 0.031), a higher mean SLICC Damage Index: 1.53 versus 0.44 (p 0.001) than patients without steroids related side effects. This complications were significantly more rare in patients that were on a steroid free regimen at the moment of evaluation versus those on a continuum steroid regimen (7.14% versus 50%, $p<0.0001$).
When patients were asked if they will stop steroids according to medical advice, almost 1/3 of patients - 28.57% - responded "no- to afraid to do that". Patients willingness to adhere to a steroid free regimen in the future according to a physician recommendation was significant more frequent in younger patients (p 0.031, r -0.235), in those with steroids initiated in less than 1 year (p 0.016, r -0.297) and in those with less damage accrual (p 0.017, r-0.267). Flare at the moment of evaluation significantly reduced this possibility, at least from the patient perspective (p0.041, r 0.224). The likelihood of a future steroid free regimen was increased by a previous discussion patient-doctor about steroids (p0.002).
Conclusions: This study clearly shows that an open discussion with our SLE patients about corticosteroids is mandatory from the beginning. Patients should be informed about possibility of a steroid free regimen when disease status permits. This will increase patient willingness to get free of steroids when possible, helping physician to limit the continuum damage accrual of SLE patients.
References:
[1] Duru N, van der Goes MC, Jacobs JWG et al, " EULAR evidence-based and consensus-based recommendations on the management of medium to high-dose glucocorticoid therapy in rheumatic diseases", Ann Rheum Dis 2013; 72: 1905–1913.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3978

AB0451 RIVAROXABAN VERSUS WARFARIN AS SECONDARY THROMBOPROPHYLAXIS IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME PROTOCOL: A RANDOMIZED, MULTICENTRE, OPEN-LABEL, CLINICAL TRIAL

J. Cortés-Hernández[1], L. Saez-Comet[2], M. Perez-Conesa[2], A. Riera Mestre[3], A. Castro-Salomo[4], S. Parra[4], J. Cuquet-Pedragosa[5], V. Ortiz-Santamaria[6], M. Mauri-Plana[7], P. Suñe[8], J. Ordi-Ros[9]. *[1]Vall Hebron Institute Research (Vhir), Barcelona; [2]Autoimmune Unit. Internal Medicine Department, Miguel Servet Hospital, Zaragoza; [3]VTE Unit. Internal Medicine Department, Bellvitge University Hospital, Barcelona; [4]Internal Medicine Department, Sant Joan de Reus University Hospital, Reus; [5]Internal Medicine Department; [6]Rheumatology Unit, Granollers University Hospital, Granollers; [7]Internal Medicine Department., Mataró Hospital, Mataró; [8]Pharmacy Department, Vall d'Hebron Hospital; [9]Autoimmune Unit. Internal Medicine Department, Vall Hebron Institute Research (Vhir), Barcelona, Spain*

Background: Long-term anticoagulation is widely used for secondary thromboprophylaxis in the antiphospholipid syndrome (APS) due to the high risk of recurrent events. Currently anticoagulation with vitamin K antagonists (VKAs) is the standard of care but have unpredictable pharmacodynamic properties that requiere monitoring for dose adjustment. Rivaroxaban, an orally active direct factor Xa inhibitor, has been shown to be effective and safe compared with warfarin for the treatment of venous thromboembolism and non valvular atrial fibrillation in major RCTs. No studies had been published in APS.
Objectives: To investigate the efficacy and safety of rivaroxaban in preventing recurrent thrombosis in patients with APS compared with warfarin.
Methods: This is a phase 3 randomized, multicenter, non-inferiority open-label RCT. 190 eligible APS patients with arterial or venous thrombotic history receiving warfarin will be stratified according the presence of SLE and venous/arterial thrombotic history and randomized (1:1) either to continue warfarin (standard of care, normalized ratio (INR) 2–3 or 2.5 to 3.5 in those with recurrent thrombotic episodes) or to switch to rivaroxaban (20 mg/day). The primary efficacy outcome is the development of any thrombotic event during the study period. Secondary efficacy outcomes include time to thrombosis, type of thrombosis (arterial or venous), overall causes of death, evaluation of a prognostic biomarker panel of recurrent thrombosis. The primary safety outcome will be major bleeding. Secondary safety outcomes include any adverse event and minor bleeding. The study has 3 years follow-up. First patient was included in March 2013 (EUDRA-CT:2010–019764–36).
Conclusions: If the study demonstrates a non-inferior anticoagulant effect compared with warfarin, this would provide sufficient supporting evidence to make rivaroxaban a standard of care for the treatment of patients with APS with previous thrombotic history.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6286

AB0452 CASE REPORT OF ALLOGENEIC UNRELATED-DONOR MESENCHYMAL STEM CELLS (MSC) INFUSION IN SJOGREN SYNDROME (SS) WITH REFRACTORY THROMBOCYTOPENIA

J. Qi, M. Qiu, J. Gu. *Department of Rheumatology, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Intravenous MSC infusion has been reported occasionally in SS treatmen and Immune Thrombocytopenia ttreament. To our knowledge,there is rare report of allogeneic unrelated-donor intravenous MSC infusion in SS with thrombocytopenia without immunosuppresive induction of MSC transplantation.
Objectives: To report the case of a Sjogren syndrome with refractory thrombocytopenia treated with MSC infusion. To review the current literature on intravenous MSC infusion for SS.
Methods: Literature review and multidisciplinary discussion were thoroughly performed before treatment protocol was approved by institutional ethics committee and patient and family signed informed consent form.
Results: A 48 year-old female with a 2-year history of SS, manifested by severe thrombocytopenia (PLT 14–30*10E9/L, after each injection of recombinant human interleukin 11, platelets can be transiently recovered.) refractory to Methylprednisolone, methotrexate, azathioprine and cyclophosphamide received Four infusions (Once a month) of allogeneic unrelated-donor $2x10^6$/Kg MSC. After two infusiong of MSC, the PLT increased gradually to greater than 100*10E9/L. After 1 year of follow-up, Platelet counts remained normal.
Conclusions: These results suggest that mesenchymal stem cells may be a therapeutic strategy for Sjogren syndrome with Refractory thrombocytopenia patients. Larger studies are needed to validate clinical efficacy and safety and to standardize treatment protocol of MSC infusion in SS.
References:
[1] Zhang D, Li H, Ma L, et al. The defective bone marrow-derived mesenchymal stem cells in patients with chronic immune thrombocytopenia. Autoimmunity 2014, 47 (8), 519–29.
[2] Xu J, Wang D, Liu D, et al. Allogeneic mesenchymal stem cell treatment alleviates experimental and clinical Sjogren syndrome. Blood 2012, 120 (15), 3142–51.
[3] Wu M, Ge H, Li S, et al. Mesenchymal Stem Cells Immunosuppressed IL-22 in Patients with Immune Thrombocytopenia via Soluble Cellular Factors. Journal of immunology research 2015, 2015, 316351.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6643

AB0453 OFF-LABEL USE OF MYCOPHENOLATE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN A RHEUMATOLOGY CENTER IN COLOMBIA

K. Mendez[1], D. Buitrago-Garcia[2], P. Santos-Moreno[3], J. Urrego[4]. *[1]Pharmaceutical chemist; [2]Epidemiology; [3]Rheumatology, Biomab, Center for Rheumatoid Arthritis, Bogota; [4]Pharmaceutical chemist, UDCA University, Bogota, Colombia*

Background: Immunosuppressants such as mycophenolate are widely used in people with systemic lupus erythematosus (SLE), but not all are specifically licensed by FDA, EMA (1) and in the case of Colombia the Regulatory Agency for Food and Drugs (INVIMA) has not approved it for this indication, only for the

prevention of the rejection of some transplants. Mycophenolate mofetil was found to be associated with a lower risk of toxic adverse events such as ovarian failure, alopecia and leucopenia, compared with cyclophosphamide (1).
Objectives: To describe the population of patients with SLE receiving mycophenolate during a five year period.
Methods: We conducted a retrospective observational study, extracting information from a database in our rheumatic diseases center; we reviewed the clinical record of each patient with diagnosis of SLE and receiving mycophenolate. Descriptive epidemiology was performed for each variable presented.
Results: 1989 patients were diagnosed with Systemic Lupus Erythematosus (SLE) during 2011 and 2016 and 287 were receiving mycophenolate. Regarding demographic characteristics 94% were woman and 6% men, mean age was 49 years ± 15. 41% of patients were employed, 40% were housekeepers, 11% students and 8% retired. The indication for mycophenolate was mainly for lupus nephritis 62%, SLE in overlapping with systemic sclerosis 30% and only for SLE in 8% of cases. 36% of patients received a daily dose of 2000 mg, 30% 1500 mg, 20% 1000 mg, 8% 3000 mg, 3.5% 4000 mg and 1.5% 6000 mg and 1% 500mg. The mean value for 24 hour urine protein was 792 mg/dl ± 140 and for creatinine was 0.84 mg/dl ± 0.36. In our population patients were taking mycophenolate during a median of 24 months with a minimum of 6 and a maximum of 132. In combination with mycophenolate 28% of the patients were taking corticoids, 21% hydroxichloroquine, 20% chloroquine, 17% antihypertensive drugs, 7% other medications and only 4% were taking the mycophenolate alone.
Conclusions: Despite of the absence of a license for mycophenolate for the management of Systemic Lupus Erythematosus, the use off-label of this drug continues to be frequently as an alternative and effective treatment in patients with lupus nephritis and other conditions associated to SLE.
References:
[1] National Institute for Health Care Excellence. NICE. Systemic lupus erythematosus: oral mycophenolate. England: NICE 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5559

AB0454 CLINICAL AND IMMUNOLOGICAL ACTIVITY IN POLISH COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS TREATED WITH GLUCOCORTICOIDS

K. Pawlak-Bus, P. Leszczynski. *Department of Rheumatology and Rehabilitation, University of Medical Sciences, Poznan, Poland*

Background: Nowadays the lupus treatment strategy is based on background therapy, immunosuppressive drugs and glucocorticoids (GC). Using minimal effective dose of GC only in flares is a recomandation for preventing complications which increase mortality.
Objectives: To evaluate SLE clinical and immunological activity in lupus patients during the standard clinical care and analyze GC treatment
Methods: We observed Polish cohort of patients with SLE 127 patients (118 female and 9 male) with average age 43±6 years, average disease duration 7,8±5,6 years. All of them were treated with oral and pulse GC and standard immunosuppressive therapies (CTX, MMF, AZT,MTX, CsA). As a background therapy 77% of these patients were on chloroquine or hydroksychloroquine. All patients were assessed according to Systemic Lupus Erythematosus Disease Activity Index assessed by SLEDAI (version 2000) and divided into 5 groups: no GC, low dose, medium dose, high dose and puls GC therapy group. Immunological activity was assessed by anti-dsDNA and C3 and C4 complements levels.
Results: In analyzed group 28 of patients wihout GC the average SLEDAI score was 7 and 50% of this pts not revealed any immunological activity. Low dose of GC was used in 50 pts with average SLEDAI score 13 and in 24 pts of this group anti-dsDNA and C3 or C4 levels upper limit were not observed. Medium dose of GC was used in 20 pts with average SLEDAI score 19 and it was contained with high immunological activity in 55% (n=11) of pts. In 27 of pts, high doses of GC including puls therapy were needed, the average SLEDAI score was very high 30 and most of pts from this group 70% were immunologicaly active.
Conclusions: In this Polish cohort lupus patients GC doses depended on lupus activity. Minimazing glucocorticoid exposure is an important part of appropriate management of lupus patients. Proper assessment of clinical and immunolgical lupus activity is critically for treatment decisions, especially for long-term GC use.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5400

AB0455 SURVIVAL OF PREDNISONE-FREE REMISSION IN SLE PATIENTS WITH SEROLOGICALLY ACTIVE CLINICAL QUIESCENT DISEASE

L. Nalotto, F. Ometto, M. Zen, L. Iaccarino, M. Gatto, M. Larosa, A. Doria. *Department of Medicine, Rheumatology Unit, University of Padova (Italy), Padova, Italy*

Objectives: To evaluate survival of prednisone (PDN) – free remission in systemic lupus erythematosus (SLE) patients and to investigate the potential predictors of disease flares.
Methods: Inclusion criteria were: (1) Diagnosis of SLE according to American College of Rheumatology (ACR) Classification Criteria of SLE; (2) Caucasian ethnicity; (3) Clinical remission (clinical SLEDAI-2K=0) at the time of PDN-withdrawal; (4) Stop of PDN treatment between 2010 and 2016; (5) At least two visits per year between January 2010 and April 2016.
Disease activity was assessed according to SLE Disease Activity Index-2000 (SLEDAI-2K). Damage was measured by the SLICC/American College of Rheumatology Damage Index (SDI). Flares were defined according to Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI criteria.
We evaluated whether gender, age, age at PDN-stop, disease duration, duration of corticosteroid therapy, duration of remission before PDN withdrawal, time to flare, SLICC/American College of Rheumatology Damage Index (SDI) – score >3, positive anti-dsDNA antibodies (abs) and-or low C3/C4, type of SLE-involvement and concomitant immunosuppressive treatment could be predictors of flare. Multivariate logistic regression analysis was run to investigate the predictors of flare. Covariates included in the analysis were all variables reaching $p<0.20$ in the univariate analyses.
Results: Among 400 patients evaluated, 104 (26%) fulfilled inclusion criteria. Baseline characteristics are reported in table 1. Twenty-two (21.2%) patients flared. Mean time to flare was 19.91±13.14 months. Types of flare were 7 renal, 7 articular, 4 cutaneous, 2 haematological, 1 serositic and 1 neurological. Variables included in the multivariate logistic regression analysis were: positive anti-dsDNA abs and-or low C3/C4, skin, articular and haematological involvement. Skin involvement resulted predictive of flare (OR 3.07, 95% CI 1.11–8.53, P 0.031) as reported in table 2.

Demographic and clinical variables in all patients and according to survival of prednisone-free remission

	All patients	Patients maintaining PDN-free remission	Patients who flared	p Value
Patients, N	104	82	22	-
Female, N (%)	91 (87.5%)	69 (84.1%)	22(100.0%)	0.046
Age in 2016, years, mean±SD	41.25±10.95	41.46±11.13	40.45±10.46	0.723
Age at PDN-stop, years, mean±SD	39.08±11.2	39.32±11.27	38.18±10.68	0.644
Disease duration, months, mean±SD	188.54±101.57	187.61±97.96	192.0±116.52	0.817
Duration of corticosteroid therapy, months, mean±SD	131.77±89.74	128.34±88.3	140.73±96.16	0.607
Duration of remission before PDN-withdrawal, months, mean±SD	36.80±33.01	38.24±34.95	31.91±23.51	0.765
Time to flare, months, mean±SD	-	-	19.91±13.14	-
SDI >3, N (%)	10 (9.6%)	8 (9.8%)	2 (9.1%)	0.925
Positive anti-ds-DNA abs and-or low C3/C4, N (%)	89 (85.6%)	68 (82.9%)	21 (95.5%)	0.138
Skin rashes, N (%)	35 (37.7%)	22 (26.8%)	13 (59.1)	0.004
Arthritis, N (%)	69 (66.3%)	51 (62.2%)	18 (81.8%)	0.084
Serositis, N (%)	16 (15.4%)	13 (15.9%)	3 (13.6%)	0.798
Glomerulonephritis, N (%)	65 (62.5%)	53 (64.6%)	12 (54.5%)	0.385
Neuropsychiatric manifestations, N (%)	10 (9.6%)	8 (9.8%)	2 (9.1%)	0.925
Vasculitis, N (%)	6 (5.8%)	4 (4.9%)	2 (9.1%)	0.452
Haematological involvement, N (%)	25 (24.0%)	17 (20.7%)	8 (36.4%)	0.128
Concomitant immunosuppressive treatment, N (%)	41 (39.4%)	32 (39.0%)	9 (40.9%)	0.872

PDN: prednisone; SD: standard deviation; SDI: SLICC/American College of Rheumatology Damage Index

Risk of flare in prednisone-free remission. Logistic regression analysis

	OR (95% C.I.)	p Value
Skin involvement	3.07 (1.11;8.53)	0.031
Articular involvement	2.75 (0.80;9.44)	0.106
Haematological involvement	1.89 (0.62;5.73)	0.261
Positive anti-ds-DNA abs and-or low C3/C4	3.17 (0.37;27.05)	0.292

OR: Odds Ratio; C.I.: Confidence Interval

Conclusions: In SLE patients who stopped corticosteroid therapy, previous skin involvement resulted to be a predictor of disease flare.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5925

AB0456 SAFETY AND RETENTION RATE OF BELIMUMAB: DATA FROM A MULTICENTRIC ITALIAN STUDY

L. Iaccarino[1], M. Larosa[1], L. Andreoli[2], E. Bartoloni-Bocci[3], A. Bortoluzzi[4], F. Ceccarelli[5], F. Conti[5], R. De Angelis[6], G. De Marchi[7], S. De Vita[7], A. Di Matteo[6], G. Emmi[8], L. Emmi[8], R. Gerli[3], M. Gerosa[9], M. Govoni[4], M. Mosca[10], P.L. Meroni[9], G. Pazzola[11], R. Reggia[2], C. Salvarani[11], C. Tani[10], M. Zen[1], A. Tincani[2], A. Doria[1]. *[1]University of Padova, PADOVA; [2]University of Brescia, BRESCIA; [3]University of Perugia, PERUGIA; [4]University of Ferrara, FERRARA; [5]University la Sapienza, ROMA; [6]University of Ancona, ANCONA; [7]University of Udine, UDINE; [8]University of Firenze, Firenze; [9]University of Milano, MILANO; [10]University of Pisa, PISA; [11]University of Reggio Emilia, Reggio Emilia, Italy*

Background: Belimumab is used in the treatment of systemic lupus erithematosus (SLE), but few data on its safety in daily clinical practice are available to date.
Objectives: To investigate safety, retention rate (RR), reasons and predictors of belimumab discontinuation in a prospective multicentric Italian study.
Methods: A total of 188 active SLE patients refractory to standard therapy were treated with belimumab as add-on-therapy in 11 Italian centers. Adverse events (AEs) were defined as “any untoward medical occurrence in a patient

treated with a pharmaceutical product which does not necessarily have a causal relationship with this treatment". AEs were subdivided in non-infectious, infectious, infusion and hypersensitivity reactions. Infusion and hypersensitivity reactions were defined as transient AEs related to belimumab occurring within 6 hours and 6–48 hours after drug administration, respectively. AEs was defined as severe (SAE) in case of hospitalization and/or death and/or life-threatening manifestations. Infections were considered severe in case of hospitalization and/or intravenous antibiotic use and/or death. Infusion and hypersensitivity reactions were considered severe when intensive care unit support was required. As baseline predictors of discontinuation the following variables were analyzed: gender, age, age at SLE onset, disease duration, disease activity pattern (relapsing remitting or chronic active), SLEDAI-2K $\geq$10, prednisone $>$7.5 mg/day, concomitant immunosuppressant, antimalarial drug use, number and type of comorbidities, number of previous organ involvement, type of major involvement and number of flares in the 12 months before belimumab initiation. Data were analyzed using the SPSS (version 23.0, Chicago, IL) software.

Results: A total of 453 EAs were recorded in 132 patients after a mean follow-up period of 17.5±10.6 months (range 3–36): 443 (97.8%) were non severe and 10 (2.2%) SAEs (Table 1). No deaths and severe infusion/hypersensitivity reactions occurred. Belimumab discontinuation was observed in 58 patients (30.8%) after 10.4±7.5 months of follow-up (Table 2). RR was 91.5% at 6 months, 81.4% at 12 months, 72.9% at 18 months, 72.4% at 24 months, 69.7% at 30 months and 69.2% at 36 months. No associations were found between baseline variables and drug discontinuation.

Table 1. AEs observed in 188 patients with refractory SLE treated with belimumab

	Pts with AEs (N)	Pts with AEs (%)	AEs (N)	AEs (%
Non severe AEs	*129*	*68.6*	*443*	*97.8*
Infectious AEs	101	53.7	273	60.3
Non infectious AEs	57	30.3	84	18.5
Hypersensitivity reactions	26	13.8	81	17.9
Infusion reactions	4	2.1	5	1.1
SAEs	*9*	*4.8*	*10*	*2.2*
Infectious SAEs	1	0.5	1	0.2
Non infectious SEAs	8	4.3	9	2.0
Total	**132**	**70.2**	**453**	**100.0**

Pts: patients; AEs: adverse events; SAEs: severe adverse events.

Table 2. Reasons of discontinuation of belimumab

	Pts (N)	Pts (%)
AEs	22	37.9
Non-responder (articular/renal/cutaneous/haematological)	16	27.6
Pregnancy	8	13.8
Flare (renal/articular)	6	10.3
Lost of follow-up	4	6.9
Remission	2	3.4
Total	**58**	**100.0**

Pts: patients.

Conclusions: Belimumab demonstrated a good safety profile with a low rate of SAEs. Discontinuation occurred in less than 1/3 of subjects with a low rate of discontinuation due to AEs.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6088

AB0457 LONG-TERM EFFECTIVENESS OF TREATMENTS FOR NEUROPSYCHIATRIC MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS

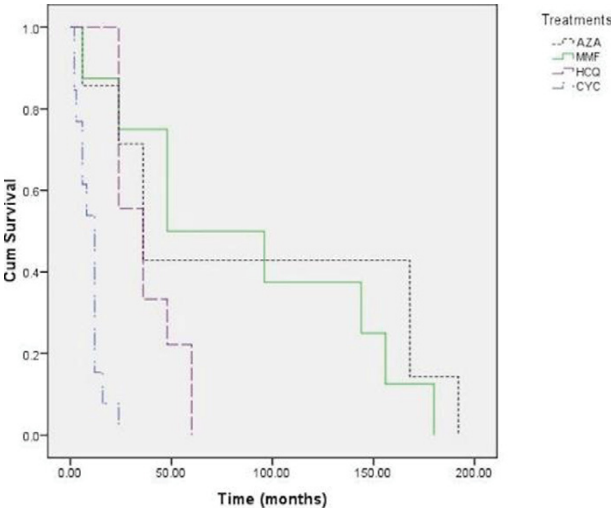
L.D. Fajardo Hermosillo. *Rheumatology, IMSS, Guadalajara, Mexico*

Background: Neuropsychiatric involvement of systemic lupus erythematosus (NPSLE) is one of the most deleterious complications of the disease, leading to great decrease of quality of life and poor prognosis [1]. Factors such as activity of disease have been associated NPSLE [1,2]. The current treatment of NPSLE remains mostly empiric, requiring high-dose corticosteroids and extensive immunosuppressive therapy [3,4]. Short-term efficacy of treatments in NPSLE have been evaluated by several studies, however few studies have been performed to evaluate long-term efficacy of these drugs [4].

Objectives: To compare the long-term effectiveness among drugs and associated factors in the treatment of NPSLE.

Methods: 209 patients ($\geq$14 years) from a Mexican cohort from 2011 to 2017 were examined. SLE and NPSLE cases fulfilled 1997 ACR and 1999 ACR criteria respectively. Demographic factors, comorbidities and pharmacologic treatments were reviewed for patients with NPSLE. Variables were studied by bivariate, multivariate and survival analyses.

Results: Of 209 SLE patients, 37 (17.7%) had NPSLE; of them 32 were women. The mean age [standard deviation (SD)] was 38.8 (14.6) years. The mean of time at onset of SLE (SD) was 6.2 (5.4) years. SLEDAI and SLICC mean (SD) were 22.1 (10.2) and 1.83 (1.2) separately. Diffuse and focal manifestations of NPSLE were presented in 20 and 17 cases. Central and peripheral nervous system events of NPSLE were described in 34 and 3 of patients. The NPSLE manifestations more prevalent were cerebrovascular disease (n=15), psychosis (n=8) and seizure disorders (n=5). A total of 112 cycles of treatment were analyzed [prednisone (PDN) n=30, intravenous (iv) methylprednisolone (MTP) n=23, iv cyclophosphamide (CYC) n=13, azathioprine (AZA) n=12, mycophenolate mofetil (MMF) n=11, rituximab (RTX) n=10, hydroxichloroquine (HCQ) n=9, plasmapheresis (PPH) n=2 and iv immunoglobulin (IVIg) n=2]. Cognitive dysfunction was more associated to higher SLE activity, damage and mortality. Also, psychosis was more associated to receive higher doses of oral PDN or iv MTP, to employ iv CYC and to be linked with renal SLE disease activity. On the other hand, cerebral vascular disease was more associated to receive HCQ and to have antiphospholipid antibodies. The main cause to therapy discontinuation was inefficacy and was more common in patients treated with iv CYC. Corticosteroids survival in months was higher in-group PDN $<$15 mg/d (97.89±16.4; IC95% 65.8–130). AZA survival in months (90±30.8; IC95% 29.6–150) was higher than others treatments for NPSLE and was more associated to use IVIg (OR 10.8, 95% CI 1.04–111, p=0.04). When the first therapy was failed, the drug as second therapy used with higher survival in months was MMF (100±60.5; IC95% 1.6–218).



Conclusions: This study suggests that patients with diffuse manifestations and central nervous system involvement in NPSLE presented more activity, damage and mortality and therefore used more PDN, MTP and CYC. Among the treatments as first therapy for NPSLE with the better long-term efficacy was AZA and when it failed, MMF remained as better second therapy.

References:

[1] Arthritis Rheum 1999;42:599–608.
[2] Semin Arhtritis Rheum 2011;41;1–11.
[3] Ann Rheum Dis 2010;69(3):529–535.
[4] CNS DRugs 2011;25(9):721–736.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2815

AB0458 B CELLS DEPLETION FOR THE TREATMENT OF SYSTEMIC AUTOIMMUNE DISEASES

M.L. Velloso Feijoo, S. Rodriguez Montero, N. Plaza Aulestia, J.L. Marenco de la Fuente. *Rheumatology Unit, Valme University Hospital, Seville, Spain*

Background: Systemic autoimmune diseases (SAD) have traditionally been treated with steroids and immunosuppressants, but not all patients respond to these measures.

Rituximab (RTX) has been used in several SAD with favorable results, but there are only a few reports of isolated clinical experiences, with a very small number of patients.

Data about use of this drug under conditions of daily clinical practice may be relevant.

Objectives: To describe the characteristics of patients with SAD who are candidates for treatment with RTX.

To evaluate the response to this drug in the different SAD.

Methods: Demographic data and disease, treatment and response variables were included.

We use the EULAR definitions of partial response (improvement of at least 50% of the main manifestations of the disease) and complete response (disappearance of the manifestations of the disease), because of the heterogeneity of the SAD and their multiple manifestations.

Results: We included 53 patients, 90.6% were women. The mean age at diagnosis was 31.42±14.33 years; and the median duration of disease at the onset of RTX 1.99 (0–7.5) years. Patients received a median of 2 cycles (1–3 min

-1, max 12); and the median interval between cycles was 14.81 months (6–15.75, min 6, max 120).
The EAS included SLE with 23 (43.4%) cases, systemic sclerosis with 7 (13.2%) cases, Sjögren's syndrome with 6 (11.3%) cases, vasculitis with 5 (9.4%) cases, Still disease with 3 (5.7%) cases, autoinmune cytopenias with 3 (5.7%) cases, dermatomyositis with 2 (3.8%) cases, Behçet's disease with 2 (3.8%) cases, IgG4 disease with 1 (1.9%) case and sarcoidosis with 1 case (1.9%).
A partial response was observed in 27 patients (50.9%) and complete in 20 patients (37.7%). There was no response in 6 of the 53 patients (11.3%). The response by disease groups is detailed in Table 1.

SAD	Partial response	Complete response	No response
SLE (n=23)	9 (39,1%)	12 (52,2%)	2 (8,7%)
Systemic Sclerosis (n=7)	5 (71,4%)	2 (28,6%)	0
Vasculitis (n=5)	5 (100%)	0	0
Sjögren (n=6)	3 (50%)	3 (50%)	0
AI cytopenias (n=3)	1 (33,3%)	1 (33,3%)	1 (33,3%)
Dermatomyositis (n=2)	1 (50%)	1 (50%)	0
Behçet's disease (n=2)	0	0	2 (100%)
IgG4 related disease (n=1)	0	1 (100%)	0
Sarcoidosis (n=1)	1 (100%)	0	0

Conclusions: In our study, patients treated with RTX achieved response in 88.7%; similar than some experiences of RTX off-label use.
Remision of the disease occurs in 50% of the patients.
The best results are observed in SLE, especially in lupus nephritis, and Sjögren disease.
The results in SS are promising due to the limited therapeutic resources for this disease.
References:
[1] Ramos-Casals M, García-Hernández FJ, de Ramón E, Callejas JL, Martínez-Berriotxoa A, Pallarés L, et al. Off-label use of rituximab in 196 patients with severe, refractory systemic autoimmune diseases. Clinical and experimental rheumatology 2010; 28 (4): 468–76.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6402

AB0459 TREATMENT OF SYSTEMIC AUTOIMMUNE DISEASES WITH RITUXIMAB: SAFETY DATA

M.L. Velloso Feijoo, N. Plaza Aulestia, S. Rodriguez Montero, J.L. Marenco de la Fuente. *Rheumatology Unit, Valme University Hospital, Seville, Spain*

Background: Systemic autoimmune diseases (SAD) have traditionally been treated with steroids and immunosuppressants, but not all patients respond to this strategy. Rituximab (RTX) has been used in several SAD with favorable efficacy and safety results; there are only reports of isolated clinical experiences of small series of patients. The description of this drug safety data in daily clinical practice may be relevant.
Objectives: To describe the adverse events and the hospital admissions during the treatment of a series of patients with SAD with RTX.
Methods: Demographic data, related to disease and treatment, response and safety variables were included. We use the EULAR definitions of partial response (improvement of at least 50% of the main manifestations) and complete response (disappearance of the manifestations), because of the heterogeneity of the SAD.
Results: We included 53 patients, 90.6% were women; the mean age at diagnosis was 31.42±14.33 years; and the median duration of disease at the onset of RTX 1.99 (0–7.5) years. Patients received a median of 2 cycles (1–3; min -1, max 12); and the median interval between cycles was 14.81 months (6–15.75;min 6, max 120).
The SAD were SLE with 23 cases (43.4%), systemic sclerosis with 7 cases (13.2%), Sjögren's syndrome with 6 cases (11.3%), vasculitis with 5 cases (9.4%), Still disease with 3 cases (5.7%), autoinmune cytopenias with 3 cases (5.7%), dermatomyositis with 2 cases (3.8%), Behçet's disease with 2 cases (3.8%), IgG4 disease with 1 case (1.9%) and sarcoidosis with 1 case (1.9%).
A partial response was observed in 27 patients (50.9%) and complete in 20 patients (37.7%). There was no response in 6 of the 53 patients (11.3%).
Adverse events were detected in 15 of the 53 patients (28.3%) and 20 were hospitalized (37.7%) during the treatment with RTX (Table 1).

Infecctions (9)	Disease activity (8)	Others (3)
Respiratory: 7	LES: 8	Acute coronary syndrome: 1
Pyelonephritis: 1		Vertebral fracture: 1
Stomach flu: 1		Metrorrhagia: 1

Three patients developed hypogammaglobulinemia, only one of them was associated with recurrent respiratory infections and even hospitalized in one occasion. Febrile neutropenia was detected in 2 patients, and one of them required admission. Three patients were diagnosed with pneumonia and admitted for supportive and antibiotic treatment. Three other patients suffered gastroenteritis requiring admission in one of them. In two cases, low respiratory infections were repeated requiring admission on 7 occasions. There was also recurrent otitis and a severe hypersensitivity reaction.
Conclusions: The most frequent adverse event were the infectious, mainly respiratory tract infections followed by an infusion reaction. No patient developed opportunistic diseases. This findings are similar than observed in other studies on patients with SAD treated with RTX. Infusion reactions are becoming less frequent, due in part to premedication.
We are dealing with a large number of patients with refractory EAS treated with RTX, so the data obtained from this study show an acceptable safety profile.
References:
[1] Ramos-Casals M, García-Hernández FJ, de Ramón E, Callejas JL, Martínez-Berriotxoa A, Pallarés L, et al. Off-label use of rituximab in 196 patients with severe, refractory systemic autoimmune diseases. Clinical and experimental rheumatology 2010;28(4):468–76.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3890

AB0460 USE OF INTRAVENOUS IMMUNOGLOBULIN (IVIG) IN AUTOIMMUNE RHEUMATIC DISEASES: EXPERIENCE IN A THIRD LEVEL MEDICAL CENTER

M. Pérez Cristóbal[1,2], R. Ricaño Rocha[2], G. Horta Baas[2], L. Barile Fabris[2], M. Portela Hernández[2]. *[1]Rheumatology; [2]Imss, Mexico City, Mexico*

Background: IGIV therapy in rheumatology has been used as an alternative treatment for patients with refractory, severe disease, or with contraindication to the use of conventional immunosuppressive therapy as serious infections; it has recently been increased its use to treat multiple autoimmune diseases, however with a limited number of precise indications as there are not enough studies to increase the level of evidence for the administration of IVIG
Objectives: To describe the experience gained with the use of IVIG in autoimmune rheumatic diseases in a third level medical center
Methods: This is an observational, descriptive and retrospective study. We report the use of IVIG in our clinical practice, efficacy and adverse effects. We included consecutive patients with autoimmune rheumatic diseases that received IVIG between 2012 and 2015. The information was extracted from clinical records
Results: We included 35 patients: 19 women, 16 men, 18 with systemic lupus erythematosus (SLE), 15 with autoimmune inflammatory myopathy, 1 with primary Sjögren's syndrome (SSp) and 1 with polyarteritis nodosa (PAN).
The most common indication was active disease associated with severe infection that contraindicated the use of immunosuppressants in 24 patients and in 11 patients refractory activity disease to conventional therapy. The most frequent indications in patients with SLE were: 6 thrombocytopenias, 5 lupus nephritis, 4 pulmonary hemorrhage and 3 neurolupus; of the group of inflammatory myopathy the indications were: 6 dysphagia, 5 respiratory insufficiency and 4 refractory myopathy. In patients with SSp and PAN the indication was peripheral neuropathy.
The mean number of IVIG applications was 3.3 (range 1–15). Activity scales were decreased in all patients with IVIG: mean SLEDAI at baseline 15.6 and in the follow up 4.5; in inflammatory myopathies remission was reached in 86% of the cases.
The steroid dose was significantly reduced in most patients in the follow up.
Four patients had adverse effects associated with IGIV: 2 with tachycardia and hypertension, one with acute pulmonary edema and one with hemolytic anemia.
Conclusions: In our experience, IGIV administration was effective in controlling the activity of the autoimmune rheumatic disease, mainly in patients with concomitant infection, and with a good safety profile.
Discussion: IGIV was an effective alternative treatment in patients with contraindication of conventional treatment or in refractory disease, however it is a high cost treatment and should be used in well selected cases
References:
[1] Erwin W. Gelfand, M.D. Intravenous Immune Globulin in Autoimmune and Inflammatory Diseases. N Engl J Med 2012;367:2015–25.
[2] Bem Mulhearn I, and Ian N. Bruce. Indications for IVIG in rheumatic disease. Rheumatology 2015; 54: 383–391.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6694

AB0461 BENEFITS OF VITAMIN D IN SLE DEPEND ON THE ORGAN SYSTEM

M. Petri[1], L.S. Magder[2]. *[1]Johns Hopkins University School of Medicine; [2]Biostatistics, University of Maryland, Baltimore, United States*

Background: Low 25-OH Vitamin D is associated with SLE. Both a randomized clinical trial and a longitudinal cohort study proved that supplementation reduced SLE disease activity.
Objectives: We examined whether Vitamin D benefits in SLE are dependent on the organ system.
Methods: Vitamin D and SLEDAI components were measured at each cohort visit starting in 2010 and 16,519 visits of 1,345 different patients were included. The patients were 92% female, 50% Caucasian, 41% African American.
Organ-specific disease activity was defined as a set of binary variables based on SLEDAI. If the patient received any score for any component, then the patient was defined as having that type of activity.
Interestingly, after adjustment for repeated measures and covariates, the relationship between vitamin D and immunologic disease activity totally disappeared.

Table 1. Estimated association between vitamin D levels and odds of organ-specific lupus disease activity, adjusting for age, race, sex, calendar year, prednisone use and plaquenil use

Vitamin D Level (ng/mL)	Immunologic Disease Activity		Skin Disease Activity		Renal Disease Activity	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
<10 (n=163)	1.0 (0.7, 1.5)	0.88	1.4 (1.0, 2.1)	0.049	3.1 (2.0, 4.9)	<0.0001
10–20 (n=1039)	1.0 (0.9, 1.1)	0.93	0.9 (0.8, 1.1)	0.41	2.2 (1.5, 3.1)	<0.0001
20–30 (n=2760)	1.0 (0.9, 1.1)	0.97	1.0 (0.9, 1.2)	0.53	1.6 (1.2, 2.0)	0.0008
30–40 (n=3959)	1.0 (0.9, 1.1)	0.78	1.1 (1.0, 1.2)	0.13	1.2 (0.9, 1.5)	0.23
40–50 (n=3578)	1.0 (Ref Grp)		1.0 (Ref Grp)		1.0 (Ref Grp)	
50–60 (n=2308)	1.0 (0.9, 1.1)	0.78	1.1 (0.9, 1.3)	0.19	1.0 (0.7, 1.3)	0.91
60–70 (n=929)	1.0 (0.9, 1.2)	0.98	1.0 (0.8, 1.3)	0.74	0.8 (0.5, 1.3)	0.33
70–80 (n=504)	1.1 (0.8, 1.2)	0.92	1.3 (1.0, 1.7)	0.072	0.8 (0.4, 1.4)	0.41
80+ (n=356)	(1.1 (0.9, 1.4)	0.42	1.4 (1.0, 1.9)	0.072	0.6 (0.3, 1.6)	0.32

However, for skin activity, there was a significantly elevated risk among those in the very extreme levels of vitamin D. For Renal Disease Activity, there was a significantly higher rate of renal disease activity among those with low levels of vitamin D. In addition, there was a clear trend such that the higher the vitamin D, the lower the risk of renal disease activity.

We then conducted a "within person" analysis. In this analysis, each person serves as his own control, and the question is: "When a person has a vitamin D level lower than his/her average, are they more likely to have renal disease activity". Note, this analysis implicitly adjusts for race, sex, and all variables (measured and unmeasured) that are invariant within a person. The results are shown in Table 2.

Table 2. Within-person analysis of the relationship between vitamin D levels and renal activity adjusting for prednisone use, plaquenil use, and implicitly for all time-invariant characteristics

Vitamin D Level	Odds Ratio	P-value
10 ng/mL or more lower than personal average	1.5 (1.3, 1.8)	<0.0001
Within 10 ng/mL of the personal average	1.0 (Ref Grp)	
10 ng/mL or more higher than personal average	0.8 (0.7, 1.0)	0.080

For Renal, it appears (based on the within-person analysis), that increasing vitamin D results in a reduction in renal activity. Based on other analyses, it is clear this drop was mostly among those in the vitamin D deficiency range.

Conclusions: Low vitamin D is associated with cutaneous and renal SLE activity, but not with immunologic (low C3 or high anti-DNA) activity, in adjusted analyses.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4526

AB0462 VITAMIN D SUPPLEMENTATION SIGNIFICANTLY REDUCES CHOLESTEROL IN SLE

M. Petri[1], L.S. Magder[2]. [1]*Johns Hopkins University School of Medicine;* [2]*University of Maryland, Baltimore, United States*

Background: The benefit of vitamin D on SLE global and renal activity have now been proven by both cohort studies and a clinical trial. The benefits on cardiovascular risk factors, however, are less well understood.

Objectives: We present the first longitudinal study on hyperlipidemia.

Methods: A within-person aanalysis addressed the question of whether a person tends to have higher cholesterol when her vitamin D is lower than her average vitamin D. To assess this, for each visit, we calculated the difference between the vitamin D level at that visit and the person's average of vitamin D. Differences in the range of vitamin D <50 ng/mL were distinguished from differences in the range above 50 ng/mL. Then we modelled the relationship between these differences in vitamin D and the difference between the person's cholesterol at each visit and the person's average cholesterol.

Results:

Table 1. Difference in Cholesterol at each visit per 10 ng/mL difference in between the patient's vitamin D at that visit and the patient's average vitamin D

Range of Vitamin D	Estimated difference in cholesterol (relative to a patient's average cholesterol) as a function of differences in a patient's Vitamin D levels (relative to her average Vitamin D levels)			
	Unadjusted	P-value	Adjusted[1]	P-value
0–50 ng/mL	-3.4 (-3.9, -2.9)	<0.0001	-3.1 (-3.6, -2.6)	<0.0001
50+ ng/mL	-1.1 (-1.7, -0.5)	0.0003	-1.0 (-1.7, -0.4)	0.0016

[1]Adjusted for age, age-squared, sex, race, proportion of time on Plaquenil, mean prednisone dose, mean BM and systolic blood pressure.

Table 2. Difference in Cholesterol per 10 ng/mL Difference in Vitamin D

Range of mean Vitamin D	Estimated difference in cholesterol per 10 ng/mL difference in Vitamin D (95% CI)			
	Unadjusted	P-value	Adjusted[1]	P-value
0–50 ng/mL	-3.7 (-4.2, -3.2)	<0.0001	-3.0 (-3.5, -2.4)	<0.0001
50+ ng/mL	-0.9 (-1.5, -0.2)	0.014	-1.1 (-1.8, -0.3)	0.0037

[1]Adjusted for age, age-squared, sex, race, proportion of time on Plaquenil, mean prednisone dose, mean BMI and SBP.

This means that at a particular clinic visit, if a person's vitamin D is higher than the person's mean vitamin D by 10 ng/mL and the person has vitamin D below 40 ng/mL, then the expected cholesterol will decrease by 3.4 mg/dL. There is no significant effect of higher vitamin D among those whose mean vitamin D exceeds 50.

Conclusions: Vitamin D supplementation (in those whose level is below 40 ng/mL) has a significant benefit on total cholesterol that is independent of age, sex, ethnicity, Plaquenil, prednisone and body mass index. Vitamin D supplementation - as it also helps systolic blood pressure - is both important for SLE activity and for reduction of cardiovascular disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1647

AB0463 THERAPEUTIC PLASMA EXCHANGE (TPE) FOR REFRACTORY SLE: A COMPARISON OF OUTCOMES BETWEEN DIFFERENT SUB-PHENOTYPES?

A. Soyuoz[1], O. Karadag[2], L. Kilic[2], T. Karaagac Akyol[3], S. Apras Bilgen[2], O.I. Ozcebe[4]. [1]*Department of Internal Medicine;* [2]*Department of Internal Medicine, Division of Rheumatology, Hacettepe University Faculty of Medicine;* [3]*Blood and Apheresis Unit, Hacettepe University Hospitals;* [4]*Department of Internal Medicine, Division of Haematology, Hacettepe University Faculty of Medicine, Ankara, Turkey*

Background: Therapeutic plasma exchange (TPE) offers an alternative therapeutic modality for patients with systemic lupus erythematosus (SLE) and primary antiphospholipid syndrome (APS). However, there is conflicting evidence regarding its efficacy in different sub-phenotypes.

Objectives: This study aims to investigate the main clinical characteristics and outcomes of patients with different phenotypes of SLE and APS treated with TPE at a tertiary care centre.

Methods: Database of Blood and Apheresis Unit between 2001–2013 was screened for patients with SLE and primary APS. SLE disease activity index (SELENA-SLEDAI), the indications for treatment, complications and outcomes were obtained from review of medical records and phone calls. A total of 24 patients (SLE: 20, APS: 4) were recruited for the study.

Results: Mean ages of SLE (M/F: 1/19) and primary APS (PAPS) patients (M/F: 2/2) were 32.4±12.89 and 52.0±10.7, respectively. The main indications for TPE were haematologic, neurologic, pulmonary involvement and APS-related. TPE was preferred in 8 patients because of leukopenia, and co-infection. SLEDAI was significantly decreased after TPE (16.7±8.3 vs. 8.8±3.1, p=0.001). Both primary APS and SLE related CAPS patients had completely responded to TPE. Success rate of TPE in patients with thrombocytopenia were lower than patients with haemolytic anaemia. Median (IQR 25%>75%) TPE sessions were 6.5 (5–10.5).

Table 1. Clinical, disease activity, treatment findings and TPE outcomes of SLE patients

Patient number	Major TPE Indication	Age/ Sex	H/o Nephr itis	Pre-TPE Drugs	preTPE SLEDAI	Concomitant problem, synchronous treatment/ procedures	PostTPE SLEDAI	Outcome	Follow-up
1	TTP	29	no	MP, CYC	13		13	CR	144 months
2	Thrombocytopenia, bleeding	59	no	MP	5		4	PR	5 months
3	Thrombocytopenia, cerebral hematoma	24	yes	MP, CYC, MG	37	L, MP, HD	NA	Exitus	
4	Thrombocytopenia, bleeding	22	yes	MP, CYC	31	MP, RTX, HD	14	PR, HD	58 months
5	Thrombocytopenia, bleeding	15	no	MG	9	L	9	TF	12 months
6	Renal Failure, Cytopenia	54	yes	MP, CYC, MMF	27	L, MP, CYC, HD	5	CR	31 months
7	Renal Failure	22	yes	MP, CYC, MMF, RTX, IVIG	16	PR, HD	8	CR	3 months
8	Alveolar hemorrhage	30	yes	MP, CYC, MG	16	MP, CYC, HD, MV	NA	Exitus	
9	Alveolar hemorrhage	18	yes	MP, CYC	38	MP, CYC, RTX, HD, MV	NA	Exitus	
10	Pulmonary Fibrosis, Dyspnea, Skin	33	no	MP, CYC, MG	13	MP, CYC	7	PR, pulm HT	21 months
11	Psychosis, Active Disease	26	no	MP, CYC	23	L, MP, CYC	11	CR	48 months
12	Neuromyelitis optica, vision loss, paraplegia	32	no	MP, CYC, MG	20	MP, CYC	10	CR	96 months,
13	Myasthenia Gravis, generalized weakness	32	no	AZA	12	L	12	CR	132 months
14	Myasthenia Gravis, generalized weakness	30	no	MG	11		NA	Exitus	
15	Longitudinal myelitis, quadriplegia	23	yes		29	PR, MP, CYC, RTX	10	PR, paraplegia	16 months
16	CAPS	25	no		24	MP, CYC	10	CR	84 months
17	APS-widespread thrombosis	60	no	MP, CYC, MG	11		8	CR	4 months
18	Evans syndrome	33	no		9		8	CR	36 months
19	Hemolytic anemia	47-M	yes	MP, CYC, MG	28	MP, CYC	NA	Give up TPE	12 months
20	Hemolytic anemia	34	no	MP, CYC	8		3	CR	73 months

Abbreviations: L, leukopenia, PN: Pneumonia, MP: Pulse methyl prednisolone, CYC: Cyclophosphamide, AZA: Azathioprine, RTX:Rituximab, HD: Hemodialysis, MV: Mechanical Ventilation, CR: complete Response, PR: partial response, TF: Treatment Failure

Conclusions: This study suggests catastrophic antiphospholipid syndrome (CAPS) and other APS related problems respond well to the TPE treatment. TPE should be kept in mind for the treatment of patients with other features of SLE, especially those resistant to other agents and in the presence of leukopenia and psychosis

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4426

AB0464 AZATHIOPRIONE METABOLITES IN CONNECTIVE TISSUE DISEASE

P. Pentony, T.Y.-E. Tsai. *Rheumatology, the Canberra Hospital, Canberra, Australia*

Background: Azathioprine (AZA) is a common treatment for connective tissue diseases (CTD). AZA is a pro-drug which is metabolised to active moieties of

6-thioguanine (6-TGN) and 6-methylmercaptopurine (6-MMP). These metabolites, rather than the absolute dose of AZA, are associated with clinical efficacy and toxicity. An idiosyncratic skewed metabolism towards 6-MMP in some patients ("shunters") increases the risk of hepatotoxicity and treatment failure. Allopurinol can correct such shunts[1]. Therapeutic protocols using metabolite concentrations have been shown to be cost effective, improve efficacy, and decrease treatment morbidity in IBD[1]. Only one small study estimated a therapeutic 6-TGN level for SLE patients[2]. There are scant data on AZA shunters in connective tissue disease[3].

Objectives: Explore the proportion of AZA therapeutic failure, toxicity, and shunters in CTD patients.

Methods: Retrospective, multicentre audit of AZA metabolite levels in CTD patients from 2012–2016. Patient demographics, treatments, disease activity and drug toxicity were also extracted.

Results: 61 testing episodes occurred in 34 patients whose mean age was 55 (32–79) years; predominantly female (N=26, 77%), with SLE (N=19, 56%). Active disease was present in 15/61 (25%) episodes. 20/34 (60%) patients were on HCQ + AZA. 25/34 (76%) of patients were either on no or <10mg/day of prednisone. 22/61 (36%) episodes had bone marrow suppression, and 8/61 (13%) had moderate liver function derangement. 12/35 (34%) patients were AZA shunters.

Based on AZA metabolite levels, patients were classified into four categories:

Classification[3]	6-TGN	6-MMP	Prevalence in Study (N)
Underdosed/ noncompliant	Low	≤ Normal	9
Appropriately dosed	Therapeutic	≥ Normal	23
Overdosed	High	≥ Normal	16
6-MMP Shunter	Low	> Normal	13

SLE patients were over-represented in the underdosed/non-compliant category (7/9). Patients in underdosed and 6-MMP shunter categories had more active disease (44% & 31%), compared with appropriate and overdosed (17% and 19% p=0.24). Surprisingly, patients who were overdosed by 6TGN levels had the lowest mean AZA dose. 6-MMP shunters had significantly lower median 6TGN levels (147pmol/8x10^8 RBC), yet toxic MMP levels (9630pmol/8x10^8 RBC) that was associated with worst LFT derangement prevalence (4/13, 31% vs <13%, p=0.16).

Conclusions: AZA dose is poorly predictive of 6-TGN and 6-MMP levels. Overall, one third of CTD patients were shunters, with lower 6-TGN levels and more hepatotoxicity. Only 40% of test episodes were appropriately dosed. Patients with low disease activity are more likely to have adequate 6TGN levels, however, 40% of patients with CTD won't have adequate disease control despite therapeutic 6-TGN levels. AZA metabolites can identify the multiple causes for therapeutic failure (under dosing, shunter, or true non-response), and enable early detection of shunters to avoid liver toxicity.

References:

[1] Croyle, L., & Morand, E. F. (2015). Optimizing the use of existing therapies in lupus. Int J Rheum Dis 18(2), 129–37.
[2] Askanase, AD et al (2009). Use of pharmacogenetics, enzymatic phenotyping, and metabolite monitoring to guide treatment with azathioprine in patients with systemic lupus erythematosus. J Rheum, 36(1), 89–95.
[3] Haines, ML et al (2011). Clinical usefulness of therapeutic drug monitoring of thiopurines in patients with inadequately controlled inflammatory bowel disease. Inflam Bowel Dis, 17(6), 1301–7.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2405

AB0465 ASSOCIATION BETWEEN SAFETY, EFFICACY AND HYDROXYCHLOROQUINE DOSAGE IN THE TREATMENT OF CUTANEOUS LUPUS ERYTHEMATOSUS AND SYSTEMIC LUPUS ERYTHEMATOSUS

R. Wakiya, T. Kameda, M. Izumikawa, S. Nakashima, H. Shimada, H. Ozaki, A. Kondo, N. Kadowaki, H. Dobashi. *Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Kagawa University, Kagawa, Japan*

Background: Hydroxychloroquine (HCQ) are considered to be effective against cutaneous lupus erythematosus (CLE) and symptoms associated with systemic lupus erythematosus (SLE) such as rashes, joint pain, and fatigue. In a randomized controlled trial in stable active patients with SLE on HCQ treatment, those who achieved blood HCQ levels greater than or equal to 1000ng/ml had a tendency for reduced SLE flares during a 7 month period [1]. To prevent ocular toxicity, HCQ should be maintained at a dose of 6.5mg/kg or less for ideal body weight [2], however, optimal HCQ dosage is unclear.

Objectives: To extract the problem of the dosage based on ideal body weight and identify safer and more effective HCQ dosage.

Methods: We enrolled patients who took HCQ for SLE or CLE more than 3 months in our institute and 2 related facilities from September 2015. We used Cutaneous Lupus Erythematous Disease Area and Severity Index (CLASI) to evaluate cutaneous symptoms and evaluated effect at start of administration and 3 months of that. The attending doctors assessed the adverse events (AEs). We investigated the change of serum biomarker, such as the value of serum complement and anti-ds-DNA body, the number of white blood cells, lymphocytes and platelets.

Results: We enrolled the 30 patients with administration of HCQ more than 3 months and in CLE were 2 cases, in SLE were 28 cases. In 21 cases HCQ dosage were based on ideal weight. The AEs were in 13/30 cases (43.3%). The AEs were the new cutaneous symptoms in 5 cases, eye manifestation in 3 cases (abnormal visual field in 2 cases, color anomaly in 1 case), diarrhea in 2 cases, fever in 2 cases, feeling of fatigue in 2 cases, renal dysfunction in 1 case, muscular pain in 1 case, and pericarditis in 1 case. The eye manifestation in the 3 cases disappeared for a few days by stopping or reducing HCQ dosage. Although we needed glucocorticoid treatment for pericarditis, the other AEs improved by reducing HCQ dosage or stopping. The AEs of taking HCQ 200mg/day were in 6 cases, 200mg and 400mg alternatively on every other day in 6 cases, and 400mg/day in 1 case. The AEs of taking HCQ dosage based on ideal body weight were in 10/21 cases (47.6%) and by minimal dosage in 3/9 cases (33.3%). 22/28 cases (78.6%) significant improved cutaneous symptoms (amount of mean change of CLASI -4.57, p=0.024). There is no difference in the efficacy of cutaneous symptoms between group received HCQ based on ideal body weight (80.0%) and the others (92.3%). 5/21 cases of HCQ based on ideal body weight were made to reduce HCQ dosage due to AEs, but all 5 cases improved cutaneous symptoms. 53.3% (16/30) cases increased complement, but other biomarkers didn't change.

Conclusions: HCQ was effective for the treatment of CLE even when HCQ dosage was reduced due to AEs. These findings suggest that low-dose HCQ is also effective and safe, and HCQ initial dosage wasn't the need to adjust for ideal body weight.

References:

[1] Costedoat-Chalumeau N, et al. Hydroxychloroquine in systemic lupus erythematosus: results of a French multicentre controlled trial (PLUS Study). Ann Rheum Dis. 2013;72(11):1786–92.
[2] Ronald B. Melles, Michael F.Marmor. The risk of toxic retinopathy in patients on long-term hydroxychloroquine therapy. JAMA Ophthalmol. 2014;132(12): 1453–60.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3928

AB0466 THE EFFECT OF OMEGA-3 FATTY ACIDS ON DISEASE ACTIVITY, ENDOTHELIAL FUNCTION, INFLAMMATORY MARKERS, AND LIPID PROFILE IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED, CONTROLLED TRIALS

R. Castillo[1], P.P. Uy[1], D.M. Francisco[1], S. Lakshminarayanan[2]. *[1]Internal Medicine; [2]Rheumatology, University of Connecticut, Farmington, United States*

Background: Omega-3 fatty acids have been shown to have potentially beneficial immunomodulatory activity in autoimmune conditions such as rheumatoid arthritis and Sjogren's syndrome. Whether this extends to systemic lupus erythematosus (SLE) remains unclear.

Objectives: We undertook this study to summarize the body of evidence available from published clinical trials on the effectiveness of omega-3 fatty acids on clinical and laboratory outcomes in SLE.

Methods: Two independent reviewers systematically searched PubMed, MEDLINE, Scopus, and the reference lists of related articles for studies published from inception to November 2016 using relevant keywords. Randomized, controlled trials (RCTs) on SLE patients comparing omega-3 fatty acids with placebo were included in the analysis. The quality of the included RCTs was assessed in accordance with the Cochrane Handbook. A random effects model was used to pool extracted data. Heterogeneity was evaluated with Chi^2 test and I^2, with *p*-values <0.05 considered significant. Data presented in median and interquartile range were converted to mean and standard deviation using the method described by Wan et al.

Results: A total of seven clinical trials consisting of 303 subjects with a duration of treatment ranging from 12 to 52 weeks were included. In studies using SLAM-R as the measurement of disease activity (n=82), there was a statistically significant mean score reduction in the omega-3 fatty acid group vs. the placebo group at 24 weeks. However, in studies that used mean change in SELENA-SLEDAI (n=117, WMD: -0.87, 95% CI: -3.9, 2.17, I^2=0%, p=0.58) and PGA (n=117, WMD -0.46, 95% CI: -1.16, 0.24, I^2=85%, p=0.20) scores, there was no significant effect (Figure 1). Mean brachial artery diameter after 12 weeks likewise did not reveal

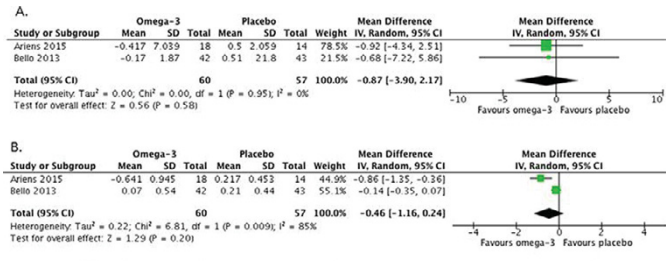


Figure 1. Effect of omega-3 fatty acids on SLE disease activity as measured by mean change in SELENA-SLEDAI (A) and PGA (B) scores.

any difference between the two groups (n=141, WMD: -0.01, 95% CI: -0.03, 0.01, I^2=0%, p=0.26). The data on percent increase in flow-mediated dilation was conflicting. In terms of inflammatory markers, there were likewise no clear associations, with some studies reporting significant changes in ESR, CRP, IL-12, and IL-13 levels which were not observed in others. With regards to lipid profile, treatment with omega-3 fatty acids was associated with a non-significant trend toward increase in all lipid profile parameters at 12 weeks including HDL (WMD 6.83, 95% CI: -4.37, 18.02, I^2=12, p=0.23), LDL (WMD 5.41, 95% CI: -1.27, 12.10, I^2=0%, p=0.11), and total cholesterol (WMD 8.48, 95% CI: -0.38, 17.33, I^2=0, p=0.06).

Conclusions: The limited data on the use of omega-3 fatty acids has not shown clear benefit in improving disease activity, endothelial function, inflammatory markers, or lipid profile in patients with SLE. Larger studies for longer durations using standardized scales for measuring outcomes are needed.

References:

[1] Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014;14:135–148.

Acknowledgements: Dr. Chia-Ling Kuo.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2666

AB0467 EFFICACY AND SAFETY OF ASSISTED REPRODUCTIVE TECHNOLOGIES (ART) IN RHEUMATIC PATIENTS: A MULTICENTER STUDY

R. Reggia[1], H. Sebbar[1], L. Andreoli[1], A. Hoxha[2], M. Larosa[3], F. Ceccarelli[4], V. Canti[5], V. Ramoni[6], A. Inversetti[7], A. Ruffatti[2], A. Doria[3], F. Conti[4], G. Valesini[4], P. Rovere Querini[5], C. Montecucco[6], A. Lojacono[8], L. Fallo[8], A. Tincani[1]. *[1]Rheumatology and Clinical Immunology, ASST Spedali Civili di Brescia, BRESCIA; [2]Rheumatology Unit, Department of Medicine - DIMED; [3]Rheumatology Unit, Hospital and University of Padua, Padua; [4]Internal Medicine and Medical Specialties Department, Policlinico Umberto I, "La Sapienza" University of Rome, Rome; [5]Allergology and Clinical Immunology, U.O. Internal medicine, Ospedale San Raffaele, Milan; [6]Rheumatology Unit, IRCCS Policlinico San Matteo and University of Pavia, Pavia; [7]Department of Obstetrics and Gynaecology, Ospedale San Raffaele, Milan; [8]Maternal-Fetal Medicine, ASST Spedali Civili di Brescia, BRESCIA, Italy*

Background: Always more frequently rheumatic patients (pts) ask for Assisted Reproductive Technologies (ART) for infertility problems. The main concern is determined by the ovarian stimulation, associated with an increased risk of disease flare and thrombosis.

Objectives: To describe a case series of ART cycles in pts affected by rheumatic diseases, analyzing pregnacy rate and outcome, fetal-maternal complications and disease flares.

Methods: We included all the consecutive pts evaluated in the Pregnancy Clinic of 5 Italian Rheumatology Units after having performed ≥1 ART cycle from 1997 to 2016.

Results: We included 60 pts: infertility was primary (no previous spontaneous conception) in 68% of cases, idiopathic in 76.5%, of male origin in 8.3%, of female origin in 15%, mixed in 0.2%. One hundred and eleven ART cycles were performed: 13IUI, 44FIVET (3eterologous), 53ICSI (14eterologous), 1embryodonation. Antiphospholipid antibodies were positive in 23 (38.3%) pts and in 45 (40.5%) cycles. Procedures were unstimulated in 14 (12.6%) stimulated in 97 (59.5%) cases: with GnRH-Antagonist in 26 (26.8%), GnRH-agonist in 60 (61.8%), gonadotropins only in 7 (7.3%) and with clomiphene in 4 (4.1%) cases. We registered 3 (3%) cases of Ovarian Hyperstimulation Syndrome, all after Agonist protocol. Overall we observed 46 pregnancies, with a *pregnancy rate* of 38.7% for omologous procedures and of 55.5% for eterologous. No miscarriages were reported. Pregnancies ended with 35 single and 5 twin birth, 6 are still ongoing: we recorded 4 (8.9%) perinatal deaths: 1 baby died at birth for multiple malformations and 3 died in the first days of life for extreme prematurity. One or more fetal complications were reported in 11 (27.5%) pregnancies: 3PROM, 3IUGR, 3oligohydramnios, 4fetal malformation (2 severe, 1multiple and fatal). The mean age of the women suffering from fetal complications was significantly lower (p:0.03). One or more maternal complications were reported in 13 (32.5%) pregnancies: 4gestational diabetis, 2thrombocytopenia, 2pre-eclampsia, 2placenta previa, 1hypothyroidism, 1gestational hypertension, 1cholestasis of pregnancy. Disease Flares were reported in 5 (12.5%) pregnancies: 4 articular (2 in RA patients, 2 in SLE patients), 1haematological (in SLE patient, after spontaneous therapy discontinuation). No cases of thrombosis were reported.During puerperium: 1 (2.5%) post-partum hemorrage (no LMWH ongoing), 1 articular flare (2.5%). Additional informations are available in Table 1.

Mean age at procedure; [median]; range	36.4; [37]; 19-45	
Diagnosis	22 SLE (2+APS), 12 UCTD, 5 PAPS, 8 RA, 5 AS, 2 SjS, 1 DM, 1PA, 1 Takayasu Arteritis, 1 Churg-Strauss Vasculitis, 1 Behcet Disease, 1SSc.	
Mean disease duration at procedure; [median]; range	6.9 years; [6]; 1-22	
Prophylactic therapy during ovarian stimulation (data available in 109 cycles) Mean n' of embryos transferred in utero; [median]; range	yes in 71 (65.1%)	LDA only n:23 (32.4%)
		LMWH only n:25 (35.2%) Prophylactic dose in 25(100%)
		LDA+LMWH n:23 (32.4%)
	no in 38 (34.9%)	
	1.6; [2];1-4	
Single embyo-transfer vs Multiple embryo-transfer	n:32 (31.2%), *pregnancy rate*: 50% n:48 (68.8%), *pregnancy rate: 39.6%* (p:0.37)	
Prophylactic therapy during pregnancy (administered in 35 pregnancies)	-LDA only n:9 (25.7%); -LMWH prophyilactic only n:4 (11.4%); -LDA+LMWH prophyilactic n:20 (57.1%); -LDA+LMWH therapeutic n:1 (2.9%); -UH therapeutic n:1 (2.9%).	
Deliveries	vaginal n:17 (42.5%), cesarean section n:23 (57.3%); at term n:33 (82.5%), pre-term n:7 (17.5%).	
Mean age at delivery; [median]; range	37 weeks; [38]; 24-41.	
Mean weight and lenght at delivery; [median], range	2780.8g; [3005g]; 420-3900g. 47.6cm; [49]; 28-53.	

Tab.1 Main features of patients, procedures and newborns

SLE: Systemic Lupus Erythematosus; PAPS: Primary Antiphospholipid Syndrome; UCTD: Undifferentiated Connective Tissue Disease; SjS: Sjögren Syndrome; SSc: Systemic Sclerosis; PA: Psoriasic Arthritis; AS: Ankylosing Spondylitis.

Conclusions: We didn't found any good reasons to discourage ART performance in rheumatic pts: the safety seems to be high and the *complications rate* is in line with that reported in general population. An adequate prophylaxis during stimulation, pregnancy and puerperium seems to provide a good protection from thrombotic complications.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2351

AB0468 POSSIBLE EFFECTS OF BELIMUMAB THERAPY ON T- AND B-CELL PHENOTYPE IN A COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

S. Piantoni[1], F. Regola[1], M. Scarsi[2], F. Dall'Ara[1], L. Andreoli[1], A. Tincani[1], P. Airò[1]. *[1]Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Brescia; [2]Internal Medicine Unit, Esine-Vallecamonica Hospital, Esine, Italy*

Background: B- and T-cell activation are one of the pathogenic mechanisms of systemic lupus erythematosus (SLE). After repeated antigenic stimulation, T-cells undergo different modifications, leading to the differentiation into effector memory T-cells (CCR7-CD45RA-) and highly experienced memory T-cells (CCR7-CD45RA+). Similarly, down-modulation of CD28 may lead to the expansion of the CD28neg T-cells, a subpopulation with peculiar effector activities (1).

Recent studies showed that memory CD4+ T-cells are increased in the peripheral blood of SLE patients, whereas contradictory data are reported on CD28 neg T-cells (2).

Peripheral transitional B-cells (38high24high) are immature B-cells transiting to secondary lymphoid organs, where their maturation into follicular or marginal zone B-cells is driven by a stimulating factor called BLyS. This population is expanded in patients with SLE (3). The anti-BLyS therapy agent belimumab is approved for treatment of SLE.

Objectives: The aims of this study were to characterize B- and T-cell phenotype in a cohort of patients with SLE, according with disease activity, and to analyse their modifications therapy with belimumab.

Methods: Phenotypic analysis of peripheral blood B and T lymphocytes was made by flow-cytometry. First, a cross-sectional study on 51 consecutive SLE patients (F/M: 48/51; median age: 35 years; anti-dsDNA: 16 UI/ml; C3: 79 mg/dl; C4: 10 mg/dl) was performed.

Second, 18 patients treated with belimumab were longitudinally followed.

Disease activity was evaluated by SLEDAI-2K score.

Results: SLE patients were divided in two groups according disease activity: patients with SLEDAI-2K ≥6 (n:13) had a higher percentage of circulating CD4+T-cells with CD28neg phenotype: median value (25th-75th percentile)=13 (5–19) vs 3 (1–5) % of CD4+ T-cells, p<0.01), as well as of those with an effector memory (37 (29–40) vs 18 (12–27) % of CD4+ T-cells, p<0.01), highly experienced memory phenotype (9 (7–12) vs 1 (1–3) % of CD4+ T-cells, p<0.01), and of B-cells with a transitional phenotype (3 (0.5–5) vs 0.2 (0–0.4) % of CD19+ cells, p=0.02), in comparison with patients with low disease activity (n:38).

After 6 months of treatment with belimumab, no significant variation in the T-cell subset was observed, but there was a reduction in the number of circulating naïve B-cells (from 49 (30–71) to 21 (11–36) % of CD19+ cells; p<0.01). Among these patients, the proportion of transitional B-cells, was raised (as compared with normal controls) at baseline in 3/11 patients with SLEDAI-2K ≥6, and 0/7 with low disease activity. After 6 month of therapy, their number normalized in 2 of these 3 patients.

Conclusions: CD4+ T-cells subpopulations displaying phenotype characteristics of effector lymphocytes, and transitional B-cells are expanded in peripheral blood of patients with active SLE. Therapy with belimumab may inhibit the production of transitional and naïve B-cells.

References:

[1] Strioga M, et al. Immunology 2011.
[2] Ugarte-Gil M, et al. Lupus 2016.
[3] Jacobi AM, et al. Arthritis Rheum 2008.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5976

AB0469 **EVALUATION OF PILOCARPINE TREATMENT IN XEROSTOMIA BY PULSED DOPPLER COLOR ULTRASONOGRAPHY: ECHOPILO STUDY**

T. Depinoy[1], A. Saraux[1], S. Boisrame[2], D. Cornec[1], J.O. Pers[3], T. Marhadour[1], D. Guellec[1], V. Devauchelle-Pensec[1], S. Jousse-Joulin[1]. *[1]Rheumatology, Cavale Blanche Hospital; [2]Odontology Department; [3]Immunology Department, Morvan Hospital, Brest, France*

Background: The ultrasonography of salivary glands (USSG) has proved its utility in diagnosing and following primary Sjögren patient's (pSS) (1,2). The evaluation of disease activity is still of interest and can be studied by assessing the inflammatory status of SG using US Doppler.
Objectives: To evaluate the vascularization of salivary glands, and particularly the parotid gland (PG) using Pulsed Doppler color ultrasonography (USSGPD) in patients complaining of xerostomia before and after treatment by pilocarpine.
Methods: We prospectively included patients with objective dry mouth syndrome (using salivary flow rate) at Brest University Hospital (DiapSS cohort). The vascularization was assessed by the resistive index (RI) at the left parotid. Only patients with pathological RI (<0.8) were included in order to observe evolution after pilocarpine. USSGPD was carried out by the same operator. A dental consultation with measure of salivary flows before and after stimulation was performed. These examinations were performed at baseline and after 3 months of treatment with pilocarpine at 4 mg 3 times daily.
Results: Among the 19 patients included, 11 received pilocarpine treatment for the whole 3 months period, 6 of the 8 remaining patients stopped the pilocarpine due to side effects. Among the 11 patients with a follow-up evaluation at 3 months, 5 had pSS according to AECG criteria. The differences of RI before and after lemon stimulation were on average of -0.04 at baseline and -0.04 at M3. The sum of ultrasound's grades average of the four glands was 3.47 at M0 and 4.18 at M3. The non-simulated salivary flow was on average of 1.96 mL/mn at M0 and 5.23 mL/mn at M3, whereas the average of stimulated salivary flow was 2.84 mL/mn at M0 and 8.51 mL/mn at M3. None of these observed differences were statistically significant before and after 3 months of treatment by Pilocarpine: RI before and after lemon stimulation (p=0.953), the sum of the four glands' grades (p=0.858), the non-stimulated (p=0.26) and stimulated salivary flow (p=0.139). Concerning the 3 patients with Sjögren's syndrome, there was no differences using RI before and after treatment but the RI was lower in this subgroup compared to the xerostomia patients.The study was marked by a large number of pilocarpine's discontinuation (31%) due to adverse effects.
Conclusions: Preliminary results showed no significant differences between the 4 gland's grade, ultrasound's RI and salivary non and stimulated flow before and after three months of pilocarpine's treatment. The vascularisation of salivary glands could be an opportunity to follow our treated patients with Sjögren's syndrome or with xerostomia but more studies are needed to prove the interest of this procedure.
References:
[1] Cornec D, et al. Contribution of salivary gland ultrasonography to the diagnosis of Sjögren's syndrome: toward new diagnostic criteria? Arthritis Rheum. 2013 Jan;65(1):216–25.
[2] Jousse-Joulin S et al. Brief Report: Ultrasonographic Assessment of Salivary Gland Response to Rituximab in Primary Sjögren's Syndrome. Arthritis Rheumatol. 2015 Jun;67(6):1623–8.
Acknowledgements: We thank the Professor luc Bressollette and Muriel Korpet for their contribution in the study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2937

AB0470 **RESPONSIVENESS OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AFTER RITUXIMAB TREATMENT: A SINGLE CENTER EXPERIENCE**

Y.P. Tsao, C.Y. Tsai. *Medicine, Taipei Veterans General Hospital, Division of Allergy, Immunology, Rheumatology (Air), Taipei, Taiwan, Province of China*

Background: Systemic lupus erythematosus (SLE) is a complex disease with multi-organ presentations. Lupus nephritis, which results from autoantibody deposition at glomerulus, induces inflammation and damage. Lupus nephritis is also the leading cause of comorbidity in SLE patient and associated with poor prognosis.
Objectives: To evaluate the treatment responsiveness of rituximab in patients with SLE.
Methods: Patients should fulfill the criteria of 1997 American College of Rheumatology classification criteria for SLE. Patients underwent chemotherapy, with severe infection, under hemodialysis or after kidney transplantation were excluded. Total 37 patients were evaluated receiving rituximab infusion from 2009 to 2013. Clinical parameters were measured before and after rituximab usage.
Results: Among the 37 patients, the female patient was 89.2%. Mean age was 39.53 years old. The mean creatinine level remained similar during the 36 months of follow-up. In the beginning of the treatment, the mean creatinine level was 1.40mg/dl (SD 0.84). After 12, 24, 36 months of follow-up, the mean creatinine levels were 1.73mg/dl, 2.16mg/dl, and 2.40mg/dl, respectively (p=0.431, 0.148, 0.328). The mean proteinuria level was 3.51g/day initially (SD 2.52), but it rapidly decreased to 1.60g/dl after 6 months of follow-up (p<0.001), and further decreased to 1.40g/day, 1.12g/day, and 0.90g/day after 12, 24, 36 months of follow-up (p=0.001, 0.002, 0.012). The mean ds-DNA level was 216IU/ml in the starting of the treatment, and it decreased to 97.04IU/ml, 88.28IU/ml, 94.6IU/ml after 12, 24, 36 months of follow-up (p=0.002, 0.003, 0.05). The C3 level revealed elevation after 36 months of follow-up. The mean C3 level was 70.63mg/dl initially, and increased to 88.60mg/dl, 90.65mg/dl, and 96.20mg/dl after 12, 24, 36 months of follow-up (p<0.001, 0.002, 0.011). The platelet level remained similar from the beginning of the study to 36 months of follow-up (269.97K/cumm to 253.5K/cumm, p=0.929). The improvement of proteinuria was significant and could be detected in 6 months, which had significant correlations with the reduction level in 24 months (p<0.001). This suggested that early improvement of proteinuria may predict the further responsiveness.
Conclusions: Although the role of rituximab still remained controversial in the treatment of systemic lupus erythematosus, it showed positive effects in our single center's experience. Early response to rituximab was an important predictor of further sustained responsiveness and reduction of proteinuria and other clinical parameters.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6648

SLE, Sjögren's and APS - clinical aspects (other than treatment)

AB0471 **WIDE HETEROGENEITY IN TREATMENT PROTOCOLS AND INAPPROPIATE USE OF PREDNISOLONE FOR ANTI-RO/LA ASSOCIATED-CONGENITAL HEART BLOCK: A SYSTEMATIC REVIEW OF 492 CASES**

A. Erden[1], L. Kilic[1], E. Bilgin[2], A. Fanouriakis[3], S. Ceylan[2], B. Hymabaccus[2], Y.Z. Sener[2], F. Gurler[2], A. Sari[1], B. Armagan[1], O. Karadag[1], S. Kiraz[1], D. Boumpas[3], U. Kalyoncu[1]. *[1]Department of Rheumatology; [2]Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey; [3]Rheumatology and Clinical Immunology, 4th Department of Internal Medicine, "Attikon" University Hospital, Athens, Greece*

Background: Congenital heart block (CHB) risk is 1–2% in case of maternal anti SSA/Ro and/or anti SSB/La antibody positivity. CHB have significant mortality (20–30%) and available therapeutic options' efficacy is contradictory.

Table. Treatments after diagnosis of CHB

General treatment, n(%)			
Only glucocorticoids	92 (39.3)		
Glucocorticoids and IVIG	10 (4.2)		
Only IVIG	2 (0.8)		
Glucocorticoids and hydroxychloroquine (HCQ)	2 (0.8)		
Glucocorticoids, HCQ and IVIG	2 (0.8)		
Only HCQ	1 (0.4)		
No treatment	134 (57.2)		
Glucocorticoid type, n(%)			
Dexamethasone	54 (50.9)		
Prednisolone	27 (25.4)		
Betamethazone	11 (10.3)		
Not known	14 (13.2)		
Dosing regimen of glucocorticoids, n(%)			
Dexamethasone 4 mg/day, until birth	25 (30.4)		
Prednisolone 40-60 mg/day, until birth	11 (13.4)		
Dexamethasone but not know dosage or time period	9 (10.9)		
Dexamethasone or Betamethasone cumulative dose over 100 mg's'	7 (8.5)		
Dexamethasone 8 mg/day until birth	5 (6.0)		
Dexamethasone or Betamethasone cumulative dose over 100 mg's'	3 (3.6)		
Dexamethasone 2 mg/day, until birth	3 (3.6)		
Prednisolone until birth, dosage not specified	3 (3.6)		
Prednisolone 10 mg/day, until birth	2 (2.4)		
Dexamethasone 12 mg/week, until birth	2 (2.4)		
Dexamethasone or Betamethasone 12 mg/day, until birth	2 (2.4)		
Dexamethasone or Betamethasone 25 mg/ twice a week, until birth	1 (1.2)		
Dexamethasone 10 mg/day, until birth	1 (1.2)		
Dexamethasone 6 mg/day, until birth	1 (1.2)		
Prednisolone 2 mg/kg/day, no time period	1 (1.2)		
Use of betamimetics, n(%)			
Yes	17 (12.4)		
No	120 (87.6)		
Dosing regimen of IVIG, n(%)			
0.4gr/kg/day for 5 days, then one per month or 1 g/kg 2 consequent day in a month	4 (28.6)		
1gr/kg per week	3 (21.4)		
0.4 gr/ kg per 3 weeks	3 (21.4)		
1 gr/kg per 3 weeks	2 (14.3)		
1 gr/kg per 15 days until birth	1 (7.1)		
1gr/day for 2 times totally	1 (7.1)		
CHB type, n(%)	**Taking glucocorticoids?**		**p**
	Yes	**No**	
First degree block	6 (32)	13 (68)	0.6
Second degree block	5 (18)	22 (82)	
Third degree block	46 (20)	185 (80)	
Sinus bradycardia	5 (26)	14 (74)	
Total	62 (21)	234 (79)	
Plasma exchange schedule n(%)			
Two consequtive days, then weekly	13 (61.9)		
Totally 3 plasma exchanges in 48 hours, 1 cycle	2 (9.5)		
Totally 3 plasma exchanges in 48 hours, 2 cycles	1 (4.7)		
Totally 3 plasma exchanges in 48 hours, one per 4 weeks	2 (9.5)		
Totally 3 plasma exchanges in 48 hours, one per 3 weeks	1 (4.7)		
Unknown time period	2 (9.5)		

Objectives: To review the literature regarding different treatment modalities for CHB.
Methods: We performed a systematic review (August 2015) on Pubmed, using the following MeSH terms: "neonatal lupus", "congenital heart block"; results were restricted to human studies and English language. 1125 articles were assessed in abstract form and, after employing exclusion criteria, 267 original articles/case reports were evaluated in full text. Finally, 199 studies were included, reporting on a total of 492 CHB patients. All administered treatments were assessed on a patient-by-patient basis.
Results: A total of 243 cases reported data for CHB treatment: glucocorticoids (GCs) in 106 (43.6%) cases, intravenous immunoglobulin (IVIG) in 14 (5.7%) cases, and hydroxychloroquine in 5 (2.0%) cases. 21 patients received plasmapheresis treatment. 134 (55.1%) cases received no treatment. Both GCs and IVIG were mostly used in cases with complete atrioventricular (AV) block (74.1% and 61.5% of cases, respectively). Different types of GCs were used: Dexamethasone in 54 (58.6%) patients, prednisolone in 27 (29.3%) and betamethasone in 11 (11.9%) patients (total 92 patients with available data). Dosing schemes and regimens were also widely heterogeneous, with fifteen different regimens used by different centres (Table). Regarding IVIG treatment, six different algorithms were used. Similarly, five different plasmapheresis protocols were used.
Conclusions: There is no consensus in the treatment of CHB. Drug selection and dosing regimens have wide heterogeneity. More than half cases received no treatment. Of note, prednisolone has often been used, despite its inability to cross the placenta.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5909

AB0472 IMPACT OF DISEASE ON FAMILY AND SOCIAL LIFE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

H. Babaoglu[1], Ö. Varan[1], S.C. Guven[2], D. Tecer[2], H. Küçük[1], A. Tufan[1], S. Haznedaroglu[1], M.A. Öztürk[1], B. Goker[1]. *[1]Department of Internal Medicine, Division of Rheumatology; [2]Department of Physical and Rehabilitation Medicine, Division of Rheumatology, Gazi University Faculty of Medicine, Ankara, Turkey*

Background: Systemic lupus erythematosus (SLE) is a chronic connective tissue disease with involvement of various organ systems and characteristically has a higher incidence in women than men[1]. The disease, as well as its treatment, could have significant effects on the quality of life of lupus patients.
Objectives: Here, we aimed to investigate the impact of SLE on quality of the social and family life of women.
Methods: One hundred and twenty women diagnosed with SLE were included in the study. A questionnaire including questions about family and social relations were applied and demographic information, educational status, marital status, organ involvement and treatment data were obtained. The results of this study are preliminary and the study is still ongoing.
Results: One hundred and twenty patients were studied. The average age was 37 (± 10). 77 patients were married, 29 patients were single, 12 patients were divorced and 2 patients were widows. 29% of the patients were employed. 10,8% of the patients declared having difficulty in accepting their illnesses. 94,8% of the married patients had nuclear families. Relationship with partners and family members detoriated in 15,5% of the married patients after the diagnosis of SLE. 10,7% of single patients ended their serious relationships and 28,6% developed negative thoughts about marriage after the diagnosis of SLE.
17,6% of the married patients were exposed to verbal or physical violence by their partners. 33% of the patients declared having worse social life compared to prior to diagnosis and 20,7% declared having poor relations with their friends due to their disease. 34.5% of the patients stated that they received psychological counseling after their diagnosis. No significant relationship was found between family problems, social activities, age and educational level.
Conclusions: Systemic lupus erythematosus is a connective tissue disease affecting various organ systems and leading to various comorbidities. Our results suggest that family and social relations detoriate in lupus patients due to their illness independent of their age and educational level. Over one third of the patients received psychological counseling after diagnosis. Moreover, results of this study suggest that having a diagnosis of lupus has substantial impact on the marital considerations.
References:
[1] Hochberg, Marc C. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis & Rheumatology 40.9 (1997): 1725–1725.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6127

AB0473 ANTI CCP AND ANTI MCV ANTIBODIES ARE MARKER OF ARTHRITIS IN SYSTEMIC LUPUS ERYTHEMATOUS & SCLERODERMA

A.M. Elsayed[1], S.A. ElBakry[1], N.O. El-Azizi[1], S.I. Ibrahim[1], A. Abdelzaher[1], N.M. Lotfy[2], F.M. Badr[1]. *[1]Internal Medicine & Rheumatology; [2]Clinical pathology, Facilty of Medicine- Ain Shams University, Cairo, Egypt*

Background: Anti-citrullinated protein antibodies (ACPA) have been reported as more specific serological markers of rheumatoid arthritis (RA). They provide a superior alternative to the rheumatoid factor (RF) test in laboratory diagnostics of RA (1). Different studies suggest that the enzymatic citrullination and the production of ACPAs may also be associated with other inflammatory arthritis-associated autoimmune diseases (2).
Objectives: Is to detect the presence of anti CCP and anti CMV antibodies in SLE & SSc and its correlation to radiological findings and disease activity.
Methods: Our study was included 70 SLE patients and 30 systemic sclerosis (SSc) patients diagnosed according to ACR classification criteria. After informed consent, all patients were subjected to detailed history taking, full clinical examination including rheumatological examination, laboratory investigations: included CBC, ESR, CRP with titer, urine analysis, renal & liver function, serum uric acid, Anti CCP antibodies & Anti MCV antibodies by ELISA. X- ray and U/S on both hands and knees and disease activity score using SLEDAI score for SLE patients and SSc disease activity score (Medsgar score) for SSc patients.
Results: In our study, anti CCP antibodies were found in 8 (11.4%) of SLE patients and 4 (13.3%) SSc patients, while anti MCV antibodies were found in 14 (20%) SLE patients and 8 (26.7%) of SSc patients.There is association between presence of anti CCP Abs and anti MCV Abs and a clinically evident arthritis in both SLE and SSc. Strong relationship between high CRP level and a severe arthritis and joint erosions was noticed in SLE patients. A significant radiological evident in the form of synovial hypertrophy and bony erosions were found using ultrasonography and plain X-ray with seropositive anti CCP and anti MCV Abs in both SLE and SSc patients.In our study, cut off value of anti CCP which was >12, with sensitivity of 70.42%, specificity of 60% positive predictive value of 80.6%, negative predictive value of 46.2% with diagnostic accuracy of 61.7%, and best cut off value of Anti MCV which was >11, with sensitivity of 98.46%, specificity of 30%, positive predictive value of 75.3%, negative predictive value of 90% with diagnostic accuracy of 60.2% in SLE & SSc.
Conclusions: There is a significant association between presence of anti CCP antibodies and anti MCV antibodies and the presence of evident arthritis either clinical or radiologically by using both x-ray and U/S on both hands and knees in SLE and SSc patients.
References:
[1] Xia L, Rulin J, Jinxia Z, et al. The Role of Anti-Mutated Citrullinated Vimentin Antibodies in the Diagnosis of Early Rheumatoid Arthritis. The Journal of Rheumatology 2009; 36:46.
[2] Szodoray P, Szabó Z, Kapitány A., et al. Anti-citrullinated protein/peptide autoantibodies in association with genetic and environmental factors as indicators of disease outcome in rheumatoid arthritis. 22 Autoimmunity Reviews 2010; 9: 140–3.
Acknowledgements: We thanks all the participating patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2489

AB0474 THYROID DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS: ITS IMPACT AS A CARDIOVASCULAR RISK FACTOR

A. Mabrook, M.I. Abd elkareem, M.M. Rayan. *Rheumatology, Alazhr University, Assuit, Egypt*

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease caused by immune system–mediated tissue damage Thyroid function abnormalities and thyroid autoantibodies have been frequently described in patients with rheumatologic autoimmune diseases, such as SLE
Objectives: The aim of the study Was to assess thyroid function and anti-thyroid antibodies in SLE patients and evaulate the effects of the thyroid dysfunction on the clinical parameters, disease activity and assess its impact as a cardiovascular risk factor.
Methods: A total number of Fifty SLE female patients were selected, Triglycerides (TG), total cholesterol (TC), LDL and high density lipoprotein (HDL).Thyroid Stimulating Hormone (TSH),serum freeT3 (FT3), freeT4 (FT4).Serum thyroid peroxidase antibodies (TPOab) and serum thyroglobulin antibodies (TGab) erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), IMT (intima-media thickness) of the carotid arteries and Echocardiography was done for all patients
Results: There is a statistically significant correlation between SLE and thyroid disorder p. value<0.05.clinical hypothyroidism was the most common abnormality presented followed by subclinical hypothyrodism.There is a statistically significant correlation between IMT and thyroid disorder p. value<0.05.There is a statistically significant correlation between cardiac valves disorder and thyroid disorderT, we found a statistically significant correlation between pericardial effusion and thyroid disorder p. value<0.05.
Conclusions: we conclude that thyroid disorder is more common in lupus patients especially those in exacerbation and +ve for antithyroid Ab and Those with thyroid dysfunction had increased cardiovascular risk. These patients should be investigated for Lipid profile echocardiography and neck US for detection of early atherosclerosis and other CVD Those with thyroid dysfunction had increased cardiovascular risk.
References:
[1] Nakisa R, Mesbah Sh, Eskandar K-S, and Nazarinia M.A,(2015).
[2] The Prevalence of Thyroid Dysfunction in Patients With Systemic Lupus Erythematosus. Iran Red Crescent Med J. 2015 December; 17(12): e17298.

[3] Tektonidou MG, Anapliotou M, Vlachoyiannopoulos P, Moutsopoulos HM. (2004) Presence of systemic autoimmune disorders in patients with autoimmune thyroid diseases. Ann Rheum Dis. 2004;63(9):1159–61. doi: 10.1136/ard.2004.022624.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6752

AB0475 CHANGES IN HEART RATE VARIABILITY REFLECT CHANGES IN CLINICAL STATUS AND PATIENT REPORTED OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS: A LONGITUDINAL ANALYSIS

A. Thanou[1], S. Stavrakis[2], J.C. Reynolds[2], S. Kamp[1], P. Kamp[1], J.A. James[1,2], J.T. Merrill[1]. *[1]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation; [2]University of Oklahoma Health Sciences Center, Oklahoma City, United States*

Background: We previously observed an association between systemic lupus erythematosus (SLE) disease activity and heart rate variability (HRV) with a preliminary observation of consistency between these two measures when disease activity changed between two timepoints (1).
Objectives: To prospectively test the hypothesis that HRV reflect longitudinal changes in clinical status and patient reported outcomes.
Methods: The current project evaluated HRV measurements using a 5 min ECG in SLE patients who completed a minimum of 2 visits in an ongoing clinical trial. HRV parameters were calculated in the time domain (RMSSD and pNN50) and the frequency domain [high frequency (HF) as well as low frequency to high frequency (LF/HF) ratio]. A mixed effects linear model, with generalized estimating equations to account for clustering of visits for each patient, was used to compare changes in HRV between paired visits and to examine linear associations between HRV parameters and clinical scores. All models were adjusted for baseline values of each HRV parameter.
Results: Forty nine patients (age 44.9±11.7, 46 female), followed in a total of 413 paired visits (median time between visits 1 month), were included. Global BILAG score was inversely associated with RMSSD (regression coefficient β=-1.39±0.01; $p<0.0001$). BILAG, SLEDAI and PGA were directly associated with the LF/HF ratio (β=0.96±0.02; $p<0.0001$, 0.42±0.10; $p<0.0001$ and 0.83±0.09; $p<0.0001$, respectively). Changes in BILAG were inversely associated with changes in RMSSD and pNN50 (β=-7.0±1.9; p=0.003 and -1.6±0.04; $p<0.0001$, respectively). BILAG changes were also directly associated with changes in the LF/HF ratio (β=0.78±0.05; $p<0.0001$). Categorical improvement, defined as $\geq$1 letter grade improvement in BILAG and no new BILAG A or B scores, occurred in 77 (19%) visit pairs (group 1) and either no improvement or worsening in 335 (81%) group 2. RMSSD and HF increased in group 1 compared to group 2 (group difference=-33.3±10.1; p=0.001 and -30.9±4.1; $p<0.0001$, respectively), and the LF/HF ratio decreased in group 1 compared to group 2 (group difference=3.1±0.8; p=0.002). Changes in Physical Component Summary (PCS) of SF36v2 were inversely related to changes in SLEDAI and PGA (β=-0.39±0.14; p=0.006 and -0.19±0.02; $p<0.0001$, respectively). Changes in Mental Component Summary (MCS) were inversely related to changes in BILAG, SLEDAI and PGA (β=-0.23±0.07; p=0.0001, -0.31±0.10; p=0.002 and -0.08±0.03; p=0.008, respectively). PCS was related to HF (β=0.67±0.28, p=0.01) whereas MCS was inversely related to the LF/HF ratio (β=-0.11±0.03, p=0.0001). Changes in PCS were related to changes in pNN50 (β=0.21±0.05, p=0.0001) and changes in MCS were related to changes in HF (β=1.57±0.18; $p<0.0001$).
Conclusions: Changes in HRV reflect changes in clinical status and patient reported outcomes in patients with SLE. These data suggest that HRV may be a simple non-invasive tool used to gage or predict clinical improvement in SLE. Further studies are warranted.
References:
[1] Thanou A, Stavrakis S, Dyer JW, Munroe ME, James JA, Merrill JT. Impact of heart rate variability, a marker for cardiac health, on lupus disease activity. Arthritis Res Ther. 2016 Sep 2;18:197.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5425

AB0476 INNER EAR INVOLVEMENT IN SYSTEMIC RHEUMATIC DISEASES

G. Tsirves[1], P.V. Voulgari[2], D. Archimandriti[2], E. Pelechas[2], D. Asimakopoulos[1], A.A. Drosos[2]. *[1]Otorhinolaryngology Clinic; [2]Rheumatology Clinic, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece*

Background: Patients with systemic rheumatic diseases have increased prevalence of sensorineural hearing loss (SNHL). Detection of cochlin specific antibodies has been reported in patients with idiopatic sensorineural hearing loss. Interestingly, cochlin has been shown a stronger link to autoimmune hearing loss.
Objectives: Objective of this cross-sectional study was to calculate the prevalence of SNHL in patients with systemic rheumatic diseases and to detect human cochlin antibodies in their sera.
Methods: This was a prospective study. Patients older that 18 year old who gave informed consent and fulfilled the criteria of American College of Rheumatology for rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjogren's syndrome (SS) and systemic sclerosis (SSc) were included. Complete head and neck clinical examination was performed, including otoscopy, nasendoscopy and hearing investigation with pure tone audiometry (250Hz -8000Hz). All medical treatments as well as Disease activity score (DAS) 28 for RA and SLE disease activity index (SLEDAI) for SLE were documented. An average tone loss was calculated, taking as a starting point the loss in dB at various frequencies according the American Committee on Hearing and Equilibrium Guidelines for Meniere's disease and also recommendation 02/1 of "Bureau International d' Audiophonologie" (BIAP). Blood samples of the patients were tested for the presence of IgG anti-cochline antibodies (COCH-IgG). The results were compared with those of sex and age-matched healthy subjects.
Results: We studied 133 patients (60 with RA, 41 with SLE, 24 with SS and 8 with SSc) and 133 healthy subjects.61.4% of patients reported vertigo, 41% hyperacousis, 39% hearing loss, 38% tinnitus, 37.9% headache and 2.1% sensation of ear pressure with unremarkable otoscopy. The prevalence of SNL was increased in patients affected by RA, SLE, SS and SSc in comparison to healthy controls (66.6%, 31.71%, 54.17% and 75% respectively). The average hearing thresholds (AHT) calculated using BIAP recommendation 02/1 were significantly increased in RA compared to SLE. AHT were also increased in patients with RA and secondary SS but without statistical significance compared to RA patients. There was a statistically significant correlation between AHT and DAS28 in RA. No correlation observed between AHT and SLEDAI. COCH-IgG were detected in two samples (one patient with RA and one with RA and SS).
Conclusions: Cochlin has been shown to have a stronger link to autoimmune hearing loss, but our study concluded no correlation of hearing loss with human cochlin IgG (COCH). Additional prospective studies are needed to elucidate its pathogenesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4805

AB0477 VITAMIN D STATUS, SYSTEMIC LUPUS ERYTHEMATOSUS ACTIVITY AND ENDOTHELIAL DYSFUNCTION

A. Caraba, V. Crisan. *Internal Medicine-Rheumatology, University of Medicine and Pharmacy "Victor Babes" Timisoara, Romania, Timisoara, Romania*

Background: Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease, in which cardiovascular complications due to premature and accelerated atherosclerosis represent a serious problem. Endothelial dysfunction is the first step in the atherosclerosis development. Low levels of vitamin D have a high prevalence in lupus patients, correlating with high prevalence of cardiovascular diseases in these patients.
Objectives: The aim of this study was represented by the assessment of endothelial dysfunction in patients with active systemic lupus erythematosus, and correlations of this with SLE activity and vitamin D status.
Methods: The study was performed on a group of 35 female patients with active systemic lupus erythematosus. In all the patients were assessed: SLE activity using SLEDAI (SLE Disease Activity Index), vitamin D status and endothelial dysfunction by means of flow-mediated dilation (FMD). Data were presented as mean ± standard deviation. The statistically analysis was performed using Pearson's test, $p<0.05$ was considered statistically significant.
Results: The mean age of the studied patients was 33.68±8.55 years, and the average duration of SLE was 8.91±5.29 years. The assessed parameters had the values: SLEDAI 9.02±4.51, vitamin D 12.79±2.45 μg/l (4 patients had vitamin D deficiency, and 31 patients had vitamin D insufficiency), and FMD 9.26±2.34%. There were significant correlations between vitamin D levels and FMD (r =0.4517, p=0.003), and between vitamin D levels and SLEDAI (r = -0.6297, p=0.00025).
Conclusions: Low values of vitamin D levels were present in all the studied patients, correlating with the systemic lupus erythematosus activity, and endothelial dysfunction.
References:
[1] Reynolds JA, Bruce IN. Vitamin D in systemic lupus erythematosus: potential beyond bone health. Int J Clin Rheumatol 2009; 4(3): 297–309.
[2] Emam FE, Abd El-Wahab TM, Mohammed MS, et al. Assessment of serum vitamin D level in patients with systemic lupus erythematosus. Egypt Rheumatol Rehabil 2014; 41:71–78.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3282

AB0478 COMPARATIVE STUDY BETWEEN PATIENTS WITH NORMAL AND OVERWEIGHT IN A COHORT OF SYSTEMIC LUPUS ERITEMATHOSUS FROM ARGENTINA

A.M. Beron, S. Sapag Duran, M. Garcia Carrasco, A.M. Sapag Duran, G. Medina, G. Nasswetter, D. Dubinsky. *Rheumatology, Clinical Hospital "Jose de San Martin", University of Buenos Aires., CABA, Argentina*

Background: Systemic lupus erythematous (SLE) have an increase cardiovascular risk, worsened by overweight and obesity. Increased BMI is associated with other severe complications and comorbidities as lupus nephritis, hypertension, insulin resistance and dyslipemia. Body weight is a modifiable risk factor.
Objectives: To determine the frequency of overweight and obesity in patients with SLE and their impact on this disease

Methods: Descriptive, cross-sectional study. We reviewed the medical records of outpatients with SLE (ACR 1997) who were seen since 2014 to 2016 in the Clinical Hospital of Buenos Aires, Argentina.
We evaluated sex, age, disease duration, obstetric history, use and doses of oral corticosteroids, BMI, 25 OH vitamin D and educational level. Disease activity was scored by SLEDAI. Scores ≥4 were classified as active.
The patients were classified into 2 groups, according to BMI: normal weight (NW) (19–25), overweight and obesity (≥25).
Results: One hundred and sixty two of 230 were evaluated. Sixty-eight patients were excluded due to lack of data. 157 (97%) were women. Mean age for both sexes was 40.6±14.3 years (p 0.70). Means of: SLEDAI 4.3±4.47 (54.9% had SLEDAI ≥4), IMC: 27.04±5.22 (56% had a BMI ≥25) and 25-hidroxivitamin D was 25.15±9.0.
Relation between 2 groups, according to BMI: 84.5% whom were in NW group have received steroids at some point vs 95.6% in BMI≥25 group (p 0.02). Mean steroids doses: BMI ≥25: 9.53±10.98 vs 5.0±7.2 in NW group (p 0.04). Multivariate analysis showed that BMI ≥25 continued significantly associated with SLE duration, independently of the steroids use and other variables.
25 OH vitamin D tended to be lower in BMI ≥25 vs NW, but no significant differences (24.53±9.91 vs 25.50±9.85) (p=0.071)

Table 1. In the multivariate analysis, Number of pregnancies was the only one variable remained significant (OR: 0.78, IC 95%: 0.63–0.98) (p=0.03)

Variable	IMC ? 25 (n: 71)	IMC ≥25 (n: 91)	P
Duration (months) Median (rank)	60 (1–384)	84 (2–480)	0,02
Pregnancies mean (SD)	1,20±1,62	2,64±2,84	0,0
Menopause (%)	27 (38,5)	51 (58,6)	0,009
Abdominal perimeter mean (SD)	88±8,3	99±11,9	0,0
Depression (%)	9 (12,5)	24 (26,6)	0,02
Chronic renal failure (%)	2 (2,7)	9 (10)	0,03
SLEDAI ≥4 (%)	33 (45,8)	56 (62,2)	0,02
SLICC mean (SD)	0,30±0.55	1,3±1,3	0,0
SLICC ≥1 (%)	18 (25)	64 (71,1)	0,0
Arterial hypertension (%)	12 (16,6)	32 (35,5)	0,003
Grade and University Studies (%)	32 (45)	19 (20)	0,004

Conclusions: Over a half of our cohort had BMI ≥25 and was characterized by older age, more frequent menopause, longer course of the disease, increased steroid use and lower educational level. Depression and hypertension were the statistically more frequent comorbidities found. Obesity was associated with more activity and accrual damage including chronic renal disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2766

AB0479 THE ROLE OF ANTIBODIES TO XANTHINE OXIDASE AND ADENOSINE DEAMINASE IN THE DEVELOPMENT OF ANTI-PHOSPHOLIPID SYNDROME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

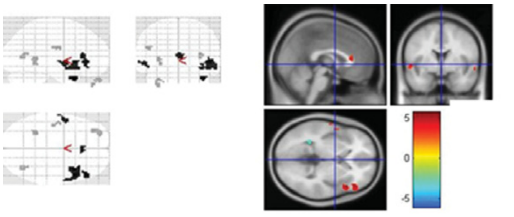
A.V. Aleksandrov, I.Y. Alekhina, N.V. Aleksandrova, N.V. Nenasheva, V.A. Aleksandrov. *Federal State Budgetary Science Institution Research Institute for Clinical and Experimental Rheumatology, Volgograd, Russian Federation*

Objectives: The aim of the research was to study the processes of formation of antibodies to the enzyme purine metabolism (PM) - xanthine oxidase (XO) and adenosine deaminase (ADA) - in patients with systemic lupus erythematosus (SLE) with laboratory indicants of secondary antiphospholipid syndrome (APS).
Methods: 30 healthy people and 60 SLE patients with different clinical manifestations were included in this research. Antibodies to the investigated enzymes were determined in the procedure of an indirect ELISA-test using immobilized form of the corresponding enzyme as antigen array (We have developed this technique). The results of the detection of antibodies to the XO (anti-XO), antibodies to ADA (anti-ADA) and antibodies to the ADC (anti-ADC) were recorded on a spectrophotometer at a wavelength of 450 nm. b_2-glycoprotein-I-dependent (b_2GP-I) to the phospholipid antibodies (aPL) class IgM and IgG were determined by using a commercial test kit “Anti-Phospholipid Screen IgG/IgM” (Orgentec). The levels of IgG aPL/IgM did not exceed 10 GPL/MPL-U/ml in the group of healthy individuals.
Results: According to the survey the number of SLE patients with elevated levels of anti-ADA was 51.6%, the anti-XO - 53.3%. There has been a number of statistically significant correlations between the presence of anti-XO with clinical and laboratory parameters: the level of circulating immune complexes (r=0.297, p=0.024), with a hemoglobin level (r= -0.286, p=0.042), the number of lymphocytes (r= -0.29, p=0.033), and platelets (r= -0,308, p=0.028). In 25 (41.7%) patients with SLE aPL IgG class were detected, in 19 (31.7%) - aPL IgM were detected. As a result of multivariate dispersive analysis leading role of aPL in the development of APS has been established (F=52,5, p<0,001).
In positive for the presence of anti-ADA patients with SLE aPL IgG class (but not aPL class IgM) were detected more frequently and at higher titer than in SLE patients, without this type of antibodies (p=0.029). Joint detection of anti-ADA and aPL in patients with SLE manifestations was associated with cytopenia (p=0.019, Fisher’s exact test). It was also noted that elevated levels of anti-XO were significantly more frequently detected in patients which were also positive for the presence of aPL IgG class (p=0.036) and aPL IgM class (p=0.044). Comparison of the groups of patients with SLE, the positive and negative for the presence of anti-XO, demonstrated a statistically significant increase in the frequency of signs of vasculopathy (chi-square=4.4, p=0.042).
Considering a direct link between the level of anti-XO and the level of the CIC we can assume that the anti-XO in the composition of the CIC have some impact on the transformation of “xanthine oxidase ↔ xanthine dehydrogenase” in the direction of increasing the formation of XO and, as a consequence, a significant increase of generation of superoxide radicals, release of calcium ions into the extracellular space, and, in addition, platelet aggregation and increased blood viscosity.
Conclusions: Antibodies to enzymes PM may be a factor in the development and maintenance of vascular disorders in patients with SLE, and their detection can be used as an additional test in the complex diagnosis of SLE with symptoms of APS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4728

AB0480 A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY ON THE PSYCHOPATHOLOGY OF PATIENTS WITH PRIMARY SJOGREN’S SYNDROME AND ANXIETY DISORDER

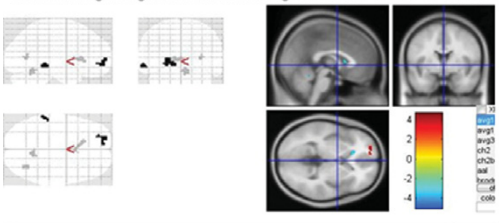
B. Cui, Y. Liu. *West China Hospital, Chengdu, China*

Background: Sjogren syndrome (SS) is a chronic systemic autoimmune disease characterized by exocrine gland inflammation and symptoms of oral and ocular dryness. Anxiety affects as many as 50–70% of persons living with SS. While anxiety is commonly experienced, very little is known concerning the mechanisms of cognitive dysfuction in SS.
Objectives: To reveal the psychopathology of patients with Sjogren’s syndrome and anxiety disorder.
Methods: 12 patients with pSS and anxiety disorder (SAS≥50), 11 patients with pSS, and 10 healthy controls were recruited. (1) Self-rating Anxiety Scale (SAS) were used to assess anxiety level of participations. All the subjects went through functional magnetic resonance imaging (fMRI) while listening actively to neutral words, negative words and negative words alternating with neutral ones.
Results: When subjects listened to neutral words alternating with no words, prefrontal cortex and BA21 were active in patients with pSS and anxiety disorder. When subjects listened to negative words alternating with no words, patients showed increased activity in prefrontal cortex, BA21, anterior cingulate and fusiform. Furthermore, when subjects listen to negative words alternating with neutral words, patients with pSS and anxiety disorder showed more increased



BRODMANN	Pixels	Max t value	P value	coordinates		
32	9	3.80	0.001	43	-21	6
21	34	3.15	0.001	63	-24	-6
47	103	3.11	0.000	31	18	-3
47	41	3.85	0.004	51	38	12

Fig.1 The results of comparison between pSS with anxiety group and pSS group, while listening to negative words alternating with neutral words. （P<0.005）



BRODMANN	Pixals	Max t value	P value	coordinates		
10	40	3.78	0.004	-24	51	-3
	39	3.72	0.004	-9	18	6
47	15	4.39	0.004	-31	27	0

Fig.2 The results of comparison between pSS with anxiety group and health controls, while listening to negative words alternating with neutral words. （P<0.005）

activity in prefrontal cortex, anterior cingulate, and caudate nucleus than that of other two groups.

Conclusions: Anxiety disorder commonly exists in patients with pSS. The pathology of this psychological symptom is poorly understood, which may be one of manifestation of nervous system involvement. fMRI may provide a novel insight into the pathological process accompanying subtle psychiatric disorders commonly experienced by patients with pSS.

References:

[1] Massara A, Bonazza S, Castellino G, et al. Central nervous system involvement in Sjögren's syndrome: unusual, but not unremarkable–clinical, serological characteristics and outcomes in a large cohort of Italian patients. Rheumatology (Oxford). 2010;49:1540–9.

[2] Martinez S, Cáceres C, Mataro M, et al. Is there progressive cognitive dysfunction in Sjögren Syndrome? A preliminary study. Acta Neurol Scand. 2010;122:182–8.

[3] Barbara M. Segal, Bryon A. Mueller,et al. Disruption of brain white matter microstructure in primary Sjogren's syndrome: evidence from diffusion tensor imaging. Rheumatology 2010;49:1530–1539.

[4] Liu LJ, Zhang XY, He N1, et al. Genetic variation in WDR1 is associated with gout risk and gout-related metabolic indices in the Han Chinese population. Genet Mol Res. 2016 Apr 28;15(2). doi: 10.4238/gmr.15027381.

Acknowledgements: Thanks are due to Dr. Gong for assistance with the experiments and to YQ. Wang for valuable discussion.There is no financial support or other benefits from commercial sources for the work reported on in the manuscript, or no other financial interests that any of the authors may have, which could create a potential conflict of interest or the appearance of a conflict of interest with regard to the work.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6103

AB0481 SUBCLINICAL NEUROPSYCHIATRIC DYSFUNCTIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS -A HOSPITAL BASED STUDY

C.S. Morad[1], H.E. Mansour[1], K.A. Ahmed[2], S.G. Arafa[1]. *[1]Internal medicine and Rheumatology; [2]Radiodiagnosis, Faculty of Medicine, Ain Shams University, Cairo, Egypt*

Background: Up to 50% of systemic lupus erythematosus (SLE) patients experience neuropsychiatric manifestations (NP) during the disease course but many might have subclinical neuropsychiatric lupus (NPL), causing significant increase in morbidity and mortality. The pathogenesis of NPL is multifactorial and involves various inflammatory cytokines, autoantibodies and immune complexes[1].

Objectives: To examine for the presence of subclinical NPL, cerebral atherosclerosis and their correlation - if any to brain magnetic resonance imaging (MRI/MRA) findings and SLE disease activity.

Methods: This is a cross sectional observational study that included thirty adult female SLE patients fulfilling the updated ACR classification criteria for SLE[2]. All were subjected to: detailed history taking, thorough clinical examination, assessment of SLE disease activity using Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score, psychometric evaluations using the Modified Mini-Mental State Examination (MMSE) to assess for cognitive dysfunction, Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Scale (HAM-A) to assess for the presence of depression and anxiety respectively. CBC, ESR, full blood chemistry, urine analysis, protein/creatinine ratio, brain MRI/MRA.

Results: The mean age was 31.7 years (22 to 40 years). 12 patients (40%) had positive antiphospholipid (APL) antibodies with or without clinically evident antiphospholipid syndrome (APS). 22/30 (73.33%) had different NP manifestations, 13 had depression (43.3%), 15 had anxiety (50%) and 16 had cognitive impairment (53.3%). All patients with depression and anxiety, 87.5% of patients with dementia had MRI abnormalities. All SLE patients with positive aPL were found to have MRI abnormalities, while MRI abnormalities were found in only 8 SLE patients with negative aPL (100% vs. 44.4%) ($p<0.001$). There was a statistically significant correlation between SLE disease activity and both NP manifestations and MRI/MRA abnormalities. aPL antibodies also had a significant correlation with NP manifestations. MRI abnormalities included discrete white matter lesions (60%), cortical atrophy (25%) and gross infarctions (15%). MRA revealed atherosclerotic changes of one or more of the large intracranial vessels in (27.27%) of NPSL patients.

Conclusions: Significant number of SLE patients without overt neuropsychiatric manifestations were found to have subclinical cerebrovascular and cognitive dysfunctions, depression and anxiety by simple bedside questionnaires. SLE disease activity positively correlates with neuropsychiatric manifestations. The presence of APL antibodies is a strong risk factor for developing NPSL. Several distinct brain MRI patterns were observed in patients with active NPSL, suggestive of different pathogenetic mechanisms.

References:

[1] Popescu A and Kao A. Neuropsychiatric systemic lupus erythematosus. Current neuropharmacology, 2011, 9(3):449.

[2] Petri M, Orbai A, Alarcón G, Gordon C, Merrill J, Fortin P, Weisman M. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis & Rheumatism, 2012, 64(8):2677–86.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4601

AB0482 ELEVATION OF SERUM PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 (PCSK9) CONCENTRATIONS AND ITS CORRELATION WITH C-REACTIVE PROTEIN, BUT NOT ATHEROGENIC LIPIDS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C. Fang[1], L. Huang[2], T. Luo[3], X. Chen[1], L. Lin[1]. *[1]Rheumatism Department; [2]Nuclear Medicine Department; [3]Ultrasonic Cardiogram Department, Second affiliated hosptial of Fujian Medical University, Quanzhou, China*

Background: Patients with systemic lupus erythematosus (SLE) have a tendency of accelerated atherosclerosis with controversial benefits from statin. This phenomenon can only partly be explained by traditional risk factors for cardiovascular disease. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a serine protease associated with cardiovascular risk that not only regulates cholesterol metabolism, but acts as a critical regulator of inflammatory reaction. PCSK9 inhibitors were also highly promising drugs bringing added cardiovascular benefit when administered with statin [1] [2].

Objectives: The present study firstly aimed to compare serum PCSK9 levels in SLE patients and healthy controls. The association between PCSK9 concentrations with atherogenic lipids and C-reactive protein (CRP) in SLE patients was also analyzed.

Methods: 77 individuals encompassed; 47 patients with SLE and 30 age- and sex-matched controls. Serum PCSK9, lipoproteins concentrations and CRP levels were assessed in patients and controls. Individuals with history of smoking, diabetes, infection, tumor and statin use were excluded.

Results: Serum PCSK9 levels were significantly elevated in patients with SLE, compared with healthy controls ($p=0.034$). PCSK9 positively correlated with serum levels of CRP ($r_s=0.351$, $p=0.016$); The tendency seemed more significant in female patients ($r_s=0.487$, $p=0.001$); No correlation with statistical significance between PCSK9 levels with disease activity (SLEDAI) or serum lipids parameter was found ($p>0.05$, all) (Table 1).

Table 1. Characteristics of patients and controls and correlational analysis of PCSK9 levels and disease parameters in SLE patients. Data are shown as number or median (interquartile range), respectively

Variables	Healthy controls	SLE	r_s, p-value
Number	30	47	NA
Female/Male	24/6	42/5	NA
Age (years)	30.5 (26–39.5)	33 (28–42)	-0.014, 0.927
PCSK9 (ng/ml)	292.44 (199.87–499.93)	390.53 (305.37–525.92)	NA
SLEDAI	NA	6 (4–8)	0.092, 0.539
Cholesterol (mmol/l)	NA	4.50 (3.90–5.40)	-0.012, 0.935
LDL cholesterol (mmol/l)	NA	2.38 (1.74–3.19)	0.002, 0.989
ApoA1 (g/l)	NA	1.30 (0.97–1.59)	0.011, 0.943
ApoB (g/l)	NA	0.79 (0.63–0.94)	0.181, 0.223
Triglycerides (mmol/l)	NA	1.26 (0.79–1.64)	-0.020, 0.896
HDL cholesterol (mmol/l)	NA	1.49 (1.22–1.86)	-0.112, 0.453
CRP (mg/l)	NA	1.31 (0.50–3.60)	0.351, 0.016
CRP (mg/l) in female patients	NA	1.195 (0.500–3.568)	0.487, 0.001

Conclusions: Elevation of PCSK9 was observed in patients with SLE and correlated with CRP but not atherogenic lipids, particularly in female patients. The result was indicative of pathogenic role of PCSK9 in the low-grade inflammation which promotes the atherogenic process in SLE patients.

References:

[1] Giugliano RP, Sabatine MS. Are PCSK9 Inhibitors the Next Breakthrough in the Cardiovascular Field?. J Am Coll Cardiol. 2015 Jun 23;65(24):2638–51.

[2] Walley KR, Thain KR, Russell JA, et al. PCSK9 is a critical regulator of the innate immune response and septic shock outcome.Sci Transl Med. 2014 Oct 15;6(258):258ra143.

Acknowledgements: The authors thank Qiulan Li for the excellent technical assistance.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1487

AB0483 RESPONSIVENESS OF LUPUS IMPACT TRACKER AMONG CHINESE PATIENTS WITH LUPUS

C.C. Mok[1], J. Block[2], M. Jolly[2]. *[1]Medicine, Tuen Mun Hospital, HK, Hong Kong; [2]Medicine and Behavioral Sciences, Rush University Medical Center, Chicago, United States*

Background: Lupus Impact Tracker (LIT), a 10 item, patient reported outcome tool for patients with systemic lupus erythematosus (SLE) has undergone psychometric validation and responsiveness studies in the US and Europe.

Objectives: To report results on responsiveness of Lupus Impact Tracker among Chinese patients with SLE.

Methods: 430 patients with SLE meeting the ACR classification criteria were recruited in Hong Kong, China at a single center. LIT scores from two visits one year apart were analyzed for responsiveness and Minimal Clinically Important

Difference (MCID) against patient report and physician assessed anchors of changes in health. Two patient reported anchors were used (Global change in health and item 2 of Short Form 36 form). Physician assessed anchors of change in health were disease activity (Physician global assessment-PGA, SELENA-SLEDAI) and damage (SLICC-SDI/ACR). Change in PGA of ≥0.3 and SELENA-SLEDAI of ≥4 in either direction was used to define worsening in disease activity. Analysis of variance was used to compare changes in LIT score against the anchors.

Results: Mean (SD) age of participants was 42 (14) years. Ninety five percent were women. Mean (SD) PGA, SELENA-SLEDAI and SDI at baseline were 0.5 (0.5), 2.9 (3.0) and 0.7 (1.2) respectively. Mean (SD) LIT score at baseline was 27.8 (18.2). Mean changes in LIT scores in response to worsening, no change or improvement based on patient report and physician assessments are shown in Table 1. MCID for "some worsening" were -4.0 and -3.9 on patient reported health question and SF36 question 2 respectively.

Table 1: Responsiveness of LIT to patient and physician based anchors in SLE.

Anchor	Change	N	Mean Change In LIT	p-value
Patient Reported Change				
SF36-Q2	Worse	118	-4.7	<0.001
	No Change	155	0.3	
	Much Better	157	2.5	
Global Change In Health Status	Worse	118	-4.7	<0.001
	No Change	155	0.3	
	Better	157	2.5	
Patient Assessed Change				
PGA	Increase of ≥0.3	72	-2.8	0.02
	Stable	251	-1.0	
	Decrease of ≥0.3	104	2.7	
SELENA- SLEDAI	Increase of ≥4	49	-3.5	0.005
	Stable	340	-0.6	
	Decrease of ≥4	41	6.0	
SDI	Unchanged	405	0.1	0.005
	Increase of ≥ 1.0	21	-8.7	

Conclusions: LIT shows responsiveness to changes in both patient-reported and physician assessed changes in health status among Chinese SLE patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3941

AB0484 LUPUS NEHRITIS AND PREGNANCY: MATERNAL AND FETAL OUTCOME

P.B. Alba [1], C. Otaduy [1], C.A. Gobbi [1], A. Alvarez [2], A. Albiero [3], E.H. Albiero [1], M.L. Propato [2], M.A. Yorio [1]. *[1] Rheumatology, Córdoba State University; [2] Rheumatology, Hospital Materno Neonatal; [3] Rheumatology, Hospital Córdoba, Córdoba, Argentina*

Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that primarily affects women during their reproductive years. The presence of Lupus nephritis (LN) may result in an increased risk of disease flare and adverse maternal and fetal outcomes, such as preeclampsia, fetal loss, and preterm delivery

Objectives: The purpose of this work is to evaluate pregnancy outcome in SLE patients with previous diagnosis of LN.

Methods: We retrospectively studied SLE patients according 1997 ACR criteria with previous diagnosis of LN by renal biopsy who attended to Materno Neonatal Hospital during the last 5 years. We evaluated demographic, clinical, laboratory and obstetric data. Renal biopsies were classified according ISN/RNP 2004. Lupus activity was evaluated by modified pregnancy SELENA SLEDAI score at the conception and during pregnancy. Maternal complications were evaluated: Preeclampsia, HELLP, Gestational Diabetes, Premature Rupture of the membranes, arterial and venous thrombosis, and others. Fetal outcome was evaluated as live birth, gestational age and weight at birth.

Results: 44 pregnancies in 32 patients were included. Maternal mean age was 22,68 years old, mean duration SLE was 7.8 years and 22% had antiphospholipid syndrome (APS), 62.5% were from Córdoba city, 84.3% did not have health insurance, and they have mean previous pregnancies of 2 with 1 live birth. Maternal complications were: Pre eclampsia in 22.7% of patients, Preterm delivery in 20.45% of patients, Premature rupture of the membranes in 6.8%, Gestational Diabetes in 2.27% of patients. 14 patients had normal labour, 29 cesarean section and 1 abortion. 97% (n=42) of patiens have live birth with mean gestational age of 36 weeks with mean weight at birth of 2.399 g. and there was no maternal mortality.

Table 1. Maternal Complications

Preeclampsia	10 (22,7%)
Pre term delivery	9 (20,4%)
Premature rupture of the membranes	3 (6,8%)
Gestacional diabetes	1 (2,3%)
Mortality	0
Renal relapse	8 (18,1)
Renal Insufficiency	2 (4,5%)

Conclusions: SLE patients with previous LN had a good maternal and fetal outcome in this study.

References:

[1] Moroni G, Doria A, Giglio E, Tani C, Zen M, Strigini F, Zaina B, Tincani A, de Liso F, Matinato C, Grossi C, Gatto M, Castellana P, Limardo M, Meroni PL, Messa P, Ravani P, Mosca M. Fetal outcome and recommendations of pregnancies in lupus nephritis in the 21st century. A prospective multicenter study. J Autoimmun. 2016 Nov;74:6–12. doi: 10.1016/j.jaut.2016.07.010. Epub 2016 Aug 2.

[2] Lazzaroni MG, Dall'Ara F, Fredi M, Nalli C, Reggia R, Lojacono A, Ramazzotto F, Zatti S, Andreoli L, Tincani A. A comprehensive review of the clinical approach to pregnancy and systemic lupus erythematosus. J Autoimmun. 2016 Nov;74:106–117. doi: 10.1016/j.jaut.2016.06.016. Epub 2016 Jul 2.

[3] Moroni G, Doria A, Giglio E, Imbasciati E, Tani C, Zen M, Strigini F, Zaina B, Tincani A, Gatto M, de Liso F, Grossi C, Meroni PL, Cabiddu G, Messa P, Ravani P, Mosca M. Maternal outcome in pregnant women with lupus nephritis. A prospective multicenter study. J Autoimmun. 2016 Nov;74:194–200. doi: 10.1016/j.jaut.2016.06.012. Epub 2016 Jun 30.

Acknowledgements: We are grateful whit Secyt subsidy UNC.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6675

AB0485 PRIMARY ANTIPHOSPHOLIPID SYNDROME: MATERNAL AND FETAL OUTCOME

C. Otaduy [1], P.B. Alba [1], C.A. Gobbi [1], A. Alvarez [2], A. Albiero [3], E.H. Albiero [1], M.L. Propato [2], M.A. Yorio [1]. *[1] Rheumatology, Córdoba State University; [2] Rheumatology, Hospital Materno Neonatal; [3] Rheumatology, Hospital Córdoba, Córdoba, Argentina*

Background: Antiphospholipid antibodies (APLAs) have been associated with pregnancy loss and other obstetric complications, such as pre-eclampsia, fetal growth restriction and preterm delivery.

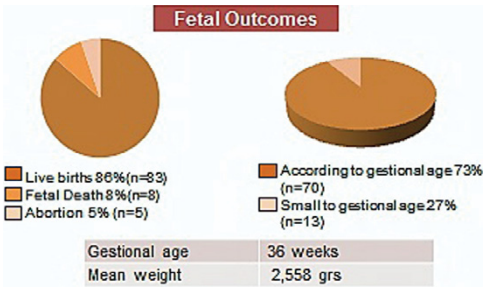
Objectives: The purpose of this work is to evaluate maternal and fetal pregnancy outcome in Primary Antiphospholipid Syndrome (PAPS).

Methods: We retrospectively studied PAPS patients according to Sydney Criteria who are attended to Materno Neonatal Hospital during the last 8 years. We evaluated demographic, obstetric and thrombotic clinical data. Maternal complications were evaluated: Preeclampsia, HELLP, Gestational Diabetes, Premature rupture of fetal membranes, arterial and venous thrombosis, mortality, the way of end of pregnancy, and others. Fetal outcome was evaluated as live birth, gestational age and weight at birth.

Results: 96 pregnancies in 68 patients were included. Maternal mean age was 30,75 years old, 84% were from Córdoba city, 70.5% did not have health insurance, and they have mean previous pregnancies of 4 with 1 live birth. Maternal complications were: Pre eclampsia in 12 patients (12.5%), Preterm delivery in 6 patients (6.25%), Premature rupture of fetal membranes in 8 (8.33%), Gestational Diabetes in 7 (7.29%), Arterial Thrombosis in 2 (2.08%), Venous thrombosis in 3 (3.12%). 33,69% have normal labour and 66,33% cesarean section. 86% of patients have live birth with mean gestational age of 36 weeks with mean weight at birth of 2.558 g and 73% of patients according to gestational age.

Table 1. Maternal Complications

Pre Eclampsia	12 (12,5%)
Pre term delivery	6 (6,2%)
Premature rupture of fetal membranes	8 (8,2%)
Gestacional Diabetes	7 (7,3%)
Arterial Thrombosis	2 (2%)
Venous Thrombosis	3 (3,1%)
Notch	10 (10%)
Mortality	0



Conclusions: PAPS pregnancies patients had a good maternal and fetal outcome in this study.

References:

[1] Bertolaccini ML, Sanna G2 Recent advances in understanding antiphospholipid syndrome. F1000Res. 2016 Dec 22;5:2908. doi: 10.12688/f1000research.9717.1. eCollection 2016.

[2] Pelusa HF, Pezzarini E, Basiglio CL, Musuruana J, Bearzotti M, Svetaz MJ, Daniele SM, Bottai H, Arriaga SM. Antiphospholipid and antioangiogenic activity in females with recurrent miscarriage and antiphospholipid syndrome.Ann Clin Biochem. 2016 Sep 16. pii: 0004563216672248. [Epub ahead of print.

[3] Moroni G, Doria A, Giglio E, Tani C, Zen M, Strigini F, Zaina B, Tincani A, de Liso F, Matinato C, Grossi C, Gatto M, Castellana P, Limardo M, Meroni

PL, Messa P, Ravani P, Mosca M. Fetal outcome and recommendations of pregnancies in lupus nephritis in the 21st century. A prospective multicenter study.J Autoimmun. 2016 Nov;74:6–12. doi: 10.1016/j.jaut.2016.07.010. Epub 2016 Aug 2.
Acknowledgements: We are grateful whit Secyt subsidy UNC.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5621

AB0486 INCIDENCE OF VERTEBRAL FRACTURES: 8 YEARS FOLLOW-UP STUDY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

C. Mendoza Pinto [1,2], M.D.L.L. Leon Vazquez [3], A. Montiel Jarquin [4], H. Sandoval-Cruz [5], M.A. Buendía Luca [1], M. García-Carrasco [1,6]. *[1]Medicine School, BUAP; [2]Systemic Autoimmune Diseases Research, Hgr36-Cibior, IMSS; [3]Systemic Autoimmune Diseases Research, Hgr-36 Imss; [4]Hospital de Traumatología y Ortopedia, IMSS; [5]Radiology Unit, Hgr-36 Imss; [6]Systemic Autoimmune Disease Research Unit, Hgr36-Cibior, IMSS, Puebla, Mexico*

Background: Vertebral fractures (VF) are the hallmark of bone fragility. Patients with systemic lupus erythematosus (SLE) are at high risk of developing prevalent VF. Although several risk factors for VF in patients with SLE have been suggested, there is limited longitudinal supporting data in the literature.
Objectives: The aims of this study are to determine the incidence of VF and to evaluate possible associations between potential risk factors and the occurrence of VF in women with SLE.
Methods: Consecutive patients with SLE were enrolled in a prospective, observational study from 2006 to 2015. Information on potential risk factors, including demographics, clinical data and bone mineral density (BMD) at the lumbar spine and hip on dual-energy X-ray absorptiometry was collected at baseline and follow-up. Semi-quantitative analysis was used to determine incident VF on lateral thoracic and lumbar radiographs, defined as any vertebral body graded normal at baseline and at least mildly deformed (20–25% reduction or more in any vertebral height) during follow-up. Differences in baseline characteristics were assessed in patients with and without radiographic VF.
Statistical analysis: The Chi-square or Fisher's exact test, independent samples t-test, and Mann-Whitney U-test were used as appropriate to compare baseline characteristics of patients with and without prevalent or incident VF. Possible risk factors for incident VF were assessed by multivariate logistic regression analysis.
Results: Of 110 SLE patients included, with a median follow-up of 8 (IQR 8–9) years, 22 (20%) had radiographic VF at baseline; 35 (32%) patients had a new VF. The annual incidence rate of new morphometric VF was 3.5 (95% CI 2.4–4.91) per 100 patient/years. Most fractures were located in the mid-thoracic and thoracolumbar region of the spine. Table 1 shows sociodemographic and clinical differences between patients with and without VF. In the multivariable analysis, VF were significantly associated with baseline BMD at the total hip and longer disease duration. Cumulative glucocorticoid dose, postmenopausal status and previous prevalent VF were not associated with VF.

	Vertebral fractures		
	Yes (n= 35)	No (n=105)	p
Age, years, mean (SD)	44.1 ± 11.0	41.4 ± 11.8	0.272
BMI, kg/m^2, mean (SD)	27.1 ± 5.3	27.3 ± 3.9	0.871
Postmenopausal at baseline, n (%)	**22 (63)**	**30 (40)**	**0.021**
Disease duration, years, median (IQR)	**9.0 (5-14)**	**5.0 (3-12)**	**0.005**
Vertebral deformity at baseline, n (%)	9 (26)	13 (17)	0.317
25OHvitD levels, ng/mL, mean (SD)	20.8 ± 6.6	19.1 ± 7.0	0.407
SLICC/ACR DI, ≥1 n (%)	**21 (60)**	**29 (39)**	**0.042**
Cumulative dose of GCT, gram, median (IQR)	**16.2 (7-41)**	**9.9 (6-24)**	**0.037**
BMD lumbar spine, g/cm^2, mean (SD)	0.981 ± 0.222	1.039 ± 0.217	0.205
BMD total hip, g/cm^2, median (IQR)	**0.884 (0.844-1.025)**	**0.981 (0.914-1.055)**	**0.011**
Use of bisphosphonates during follow-up,	15 (43)	24 (32)	0.185

Conclusions: In this SLE cohort in daily clinical practice, radiographic VF were frequently present in SLE patients, especially those with longer disease duration and low hip BMD.
References:
[1] Borba VZC, Matos PG, da Silva Viana PR, et al. High prevalence of vertebral deformity in premenopausal systemic lupus erythematosus patients. Lupus. 2005;14(7):529–33.
[2] Mendoza-Pinto C, García-Carrasco M, Sandoval-Cruz H, et al. Risk factors of vertebral fractures in women with systemic lupus erythematosus. Clin Rheumatol. 2009;28(5):579–85.
[3] Bultink IEM, Lems WF, Kostense PJ, et al. Prevalence of and risk factors for low bone mineral density and vertebral fractures in patients with systemic lupus erythematosus. Arthritis Rheum. 2005;52(7):2044–50.
Acknowledgements: This work was supported in part by grant from FIS/IMSS/PROT/MD15/1500.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1238

AB0487 NEUROLOGIC MANIFESTATIONS AND THEIR IMPACT ON CHRONIC DAMAGE IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME: RESULT FROM A MONOCENTRIC COHORT

D. Mazilu [1], D. Potarniche [2], I. Saulescu [1], A. Borangiu [1], L. Groseanu [1], C. Constantinescu [1], V. Vlad [2], F. Berghea [1], V. Bojinca [1], D. Opris-Belinski [1], A. Balanescu [1], D. Predeteanu [1], R. Ionescu [1]. *[1]"Sfanta Maria" Clinical Hospital, "Carol Davila" University of Medicine, Bucharest, Romania; [2]"Sfanta Maria" Clinical Hospital, Bucharest, Romania*

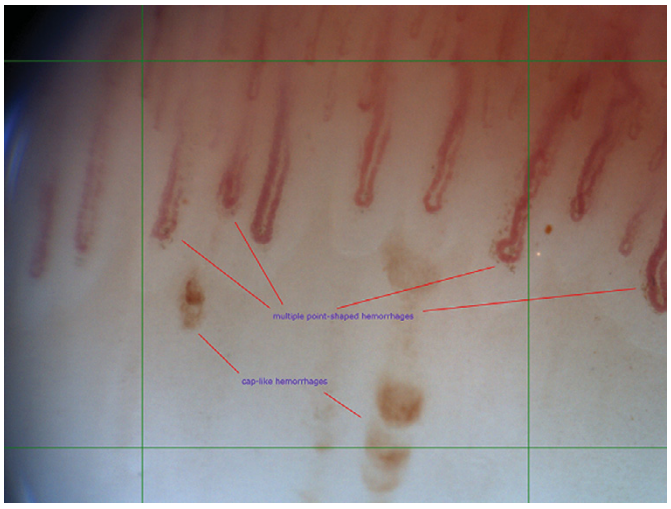
Background: Antiphospholipid syndrome (APS) is an autoimmune disease with wide clinical features and cumulative damage. The nervous system involvement is very broad and severe.
Objectives: The aim of this study is to analyze the impact of neurologic manifestations on Damage Index in Patients with APS (DIAPS).
Methods: All consecutive patients known with APS were included in our monocentric cohort. Data on medical history, clinical manifestations, aPL profile and medication were collected. DIAPS score was used to measure damage in each patient.
Results: Seventy six patients with APS were included: 11 patients with primary APS and 65 patients with secondary APS, with mean disease duration of 9.59±7.39years. Overall,35 patients (46.1%) had neurologic manifestations. Their mean disease duration was 9.2±5.76 years. Seven patients had primary APS and 28 patients had secondary APS. Six patients were on chronic oral anticoagulant therapy and low dose aspirin, 12 patients on oral anticoagulant alone and 15 patients on low dose aspirin. Transient ischemic attack was the first manifestation of APS in 4 patients (11.42%) at mean age of 29.5±10.96 years. Their mean DIAPS value was 7.75±4.19. Ischemic stroke was the first APS manifestation in 12 patients (34.28%) at mean age of 40.08±16.31years, with DIAPS mean value of 7.41±3.67. All of these patients have neurological sequelaes. The DIAPS value was higher in patients with neurologic manifestations (3±2.9 vs 5.71±3.62, p=0.001) and DIAPS value correlated significantly to neurologic manifestations (R=0.416, p<0.000) reflecting it's impact on cumulative damage in APS patients.
Conclusions: Neurologic manifestations in APS patients have a great impact on cumulative damage especially in patients presenting with ischemic stroke or transient ischemic attack as the first manifestation of APS.
References:
[1] M-C Amigo et al. Development and initial validation of a damage index (DIAPS) in patients with thrombotic antiphospholipid syndrome (APS). Lupus (2015) 24, 927–934.
[2] L.A. Martinez-Martinez et al. Damage Index in Patients with Thrombotic Antiphospholipid Syndrome: Retrospective Cohort Study. Ann Rheum Dis 2016;75:1065.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4370

AB0488 CAPILLAROSCOPY FINDINGS IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS, A DUTCH EXPERIENCE OF 20 CHILDREN AND ADOLESCENTS

D. Schonenberg-Meinema [1], M. vd Berg [1], A. Nassar-Sheikh-Rashid [1], G. de Bree [2], L. Hak [3], M. van Onna [3], K. Melsens [4,5], M. Cutolo [6], T. Kuijpers [1], V. Smith [4,5]. *[1]Department of Pediatric Hematology, Immunology, Rheumatology and Infectious Diseases; [2]Department of Infectious Diseases; [3]Department of Clinical Immunology and Rheumatology, AMC Amsterdam, Amsterdam, Netherlands; [4]Department of Rheumatology; [5]Department of Internal Medicine, Ghent University Hospital, Ghent, Belgium; [6]Research Laboratory and Academic Unit of Clinical Rheumatology, University of Genova, Genova, Italy*

Background: Capillaroscopy findings can be qualitatively described as: normal, microangiopathy (non-specific abnormalities) or scleroderma pattern (1). Capillary abnormalities, described in varying prevalence in patients with systemic lupus erythematosus (SLE), are mainly described as microangiopathy (2–4)
Objectives: To describe capillary characteristics in a cross-sectional cohort of patients with childhood-onset SLE (cSLE) by quantitative and qualitative assessment
Methods: Nailfold videocapillaroscopy (NVC) was performed in cSLE-patients (onset <18 years) with a x200 magnification lens (Optilia). The following capillaroscopic characteristics were evaluated per millimeter: density (compared to mean density known for age, sex and ethnicity) (5), number of abnormal shapes (as defined by the EULAR study group on microcirculation in Rheumatic Diseases (6)), giant capillaries (defined as apical diameter >50 mcm), maximum apical diameter (dilatations defined as apical diameter 20–50mcm) and microbleedings (large hemorrhages and small multiple point-shaped hemorrhages surrounding the capillary loop [image])
Results: 4063 capillaries from 20 patients with cSLE, were analyzed. All patients showed capillary abnormalities, 15% (n=3) showed a scleroderma-pattern. A lower mean density (mean 6.7, range 1.9–9.5) was seen in 55% (n=11), multiple

(>8 per patient) abnormal shapes in 60% (n=12), apical dilatations in 90% (n=18). Total count of large/small point shaped hemorrhages was 109/855, with a mean of 0.2/1.6 per analyzed image/per patient. These were detected in 85/85% of patients (n=17)



Conclusions: In this pilot (n=20) of cSLE patients, all showed capillary abnormalities. The most striking finding was the point-shaped bleeding surrounding the capillary, observed in 85% (n=17) of our patients. Prospective longitudinal cohort studies in children through the EULAR study group on microcirculation in Rheumatic diseases will elucidate whether specific findings can be found in child rheumatic diseases

References:

[1] Cutolo M. Atlas of capillaroscopy in rheumatic diseases. Milan: Elsevier; 2010.
[2] Ingegnoli F. Capillaroscopy abnormalities in relation to disease activity in juvenile systemic lupus erythematosus. Microvascular research. 2013;87:92–4.
[3] Dolezalova P, Young SP, Bacon PA, Southwood TR. Nailfold capillary microscopy in healthy children and in childhood rheumatic diseases: a prospective single blind observational study. Ann Rheum Dis. 2003;62(5):444–9.
[4] Shenavandeh S, Habibi S. Nailfold capillaroscopic changes in patients with systemic lupus erythematosus: correlations with disease activity, skin manifestation and nephritis. Lupus 2017:961203316686702.
[5] Terreri MT, Andrade LE, Puccinelli ML, Hilario MO, Goldenberg J. Nail fold capillaroscopy: normal findings in children and adolescents. Seminars in arthritis and rheumatism. 1999;29(1):36–42.
[6] Smith V, Beeckman S, Herrick AL, Decuman S, Deschepper E, De Keyser F, et al. An EULAR study group pilot study on reliability of simple capillaroscopic definitions to describe capillary morphology in rheumatic diseases. Rheumatology (Oxford). 2016;55(5):883–90.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4704

AB0489 THE SLE-KEY® RULE-OUT TEST PERFORMS WELL AS AN AID IN CLINICAL PRACTICE

D. Massenburg, J. Oldenberg, A. Sell, T. Krause, A.F. Wells. *Rheumatology and Immunotherapy Center, Franklin, WI, United States*

Background: The SLE-key® test was developed by ImmunArray and was validated to rule out SLE with 94% sensitivity, 75% specificity and a negative predictive value (NPV) of 93%[1]. We reported earlier that the SLE-key® RuleOut test could aid in the diagnosis and disposition of a cohort of 55 patients in our clinical practice[2].
Objectives: We have now expanded this cohort and report here the usefulness of the SLE-key® test in aiding the management of a cohort of challenging and suspected SLE patients in a large clinical practice.
Methods: In patients referred to the Rheumatology and Immunotherapy Center, in Franklin, WI, results from the SLE-key® RuleOut test were included as part of the clinical evaluation. Serum samples were collected from individual subjects with informed consent and tested at VERACIS (Richmond, VA), using the SLE-Key® iCHIP®[1].
Results: We reviewed the diagnoses and clinical disposition of patients both before and after SLE-key® testing. In particular, we looked at the ability of the SLE-key® test to enhance our ability to reach a definitive diagnosis across the full cohort of patients, at the disposition of patients who were referred with a suspicion of SLE as part of the differential diagnosis, at the impact of SLE-key® testing on the diagnosis of the subset of patients who presented with minimal symptoms, and at the group of patients who had been referred following an ANA test. Results are summarized in Table 1. In the cases where SLE was ruled out, patients were treated for a variety of disorders including fibromyalgia, joint pain, MCTD, Sjogren's disease and others.

Table 1

Patient Subgroup	Status post SLE-key	Clinical Outcomes
Patients with uncertain diagnosis in our clinic prior to SLE-key® testing.	79% had an actionable diagnosis following SLE-key® test	57% were diagnosed to have SLE. 43% not SLE. Patients treated for a variety of disorders other than SLE
Patients referred to our clinic with SLE as part of differential diagnosis	62% confirmed SLE 32% Ruled Out	> 50% of those RuledOut were diagnosed with myalgia/ fibromyalgia and treated accordingly
Minimally symptomatic patients	65% Ruled Out for SLE	Patients treated for a variety of disorders other than SLE
Patients referred following ANA testing	44% Ruled Out for SLE	Patients treated for a variety of disorders other than SLE

Conclusions: The diagnosis of patients referred in the clinical rheumatology setting remains an ongoing challenge. The SLE-key® RuleOut test provides a laboratory aid to improve the diagnostic and dispositive efficiency saving undue concern, time and resources both to the patient and to the healthcare system. A retrospective analysis of our practices prior to the introduction of SLE-key® is warranted.

References:

[1] Putterman et al., Journal of Immunological Methods, 2016.
[2] Massenburg et al., Arthritis Rheumatol. 2016; 68 (suppl 10).

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5779

AB0490 ANALYSIS OF COMMON GRAM-NEGATIVE BACTERIA AND THEIR DRUG RESISTANCE IN HOSPITALIZED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

D. Chen, Z. Zhan. *Rheumatology, The first affiliated hospital of SUN YAT-SEN UNIVERSITY, Guangzhou, China*

Background: Infection is an important cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). The spectrum of infectious agents in SLE patients varies significantly among different ethnic groups. The national surveillance study from the China showed that Gram-negative bacteria (GNB) was the most the common bacterial infection in China, while Gram-positive bacteria (GPB) was predominant in European countries.
Objectives: To identify the spectrum and drug resistant pattern of infection caused by GNB in patients hospitalized with SLE.
Methods: The clinical and microbiological data from hospitalized SLE patients with bacterial infection between June 2005 and June 2015 was collected and then analyzed retrospectively.
Results: Two hundred and sixty-eight episodes of bacteria had been identified from 3815 hospitalized patients. In terms of isolated microorganisms, gram-negative bacteria (GNB) were predominant over gram-positive bacteria (GPB) (178 isolates vs. 90 isolates). In the GNB, *Escherichia coli* (66/178, 37.1%) was the most common isolate, followed by *Acinetobacter baumannii* (36/178, 20.2%), *Klebsiella pneumoniae* (24/178, 13.5%), *Pseudomonas aeruginosa* (20/178, 11.2%), *Haemophilus influenzae* (10/178,5.6%), *Salmonella sp.* (7/178, 3.9%), *Enterobacter aerogenes* (5/178, 2.8%), *Stenotrophomonas maltophilia* (5/178, 2.8%), *Citrobacter freundii* (3/178,1.7%), *Proteus mirabilis* (2/178,1.1%). Resistant isolates (53/178, 30.0%) were more common documented in GNB, mostly extended-spectrum beta-lactamase (ESBL) producing *Escherichia coli* (30/66, 45.5%) and *Klebsiella pneumonia* (6/24, 25%), and multi-drug resistant *acinetobacter baumannii* (36.1%). Susceptibility tests showed that the ESBL-producing strains were highly sensitive to carbapenems, β-lactamase inhibitor compound families, and certain cefalosporin (Cefepime and Ceftazidime) *in vitro*. (the resistance rate <20%), whereas it was highly resistant to ampicillin and Gentamicin. Besides carbapenems and Cefoperazone/sulbactam, *Acinetobacter baumannii* was resistant to most antibiotics.
Conclusions: GNB was predominant in Chinese hospitalized patients with SLE. The drug resistance of GNB has increased significantly. It was necessary to rational use of antibiotics in patients with SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1951

AB0491 THE ASSOCIATION OF BASELINE HYPERURICEMIA IN PREMENOPAUSAL WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND DEVELOPMENT OF NEPHRITIS

D.H. Lim[1], S. Hong[2], J.S. Oh[3], Y.-G. Kim[2], C.-K. Lee[2], S.W. Choi[1], B. Yoo[2]. *[1]Division of rheumatology, Department of Internal Medicine, Ulsan university hospital, Ulsan; [2]Division of rheumatology, Department of Internal Medicine, Asan Medical Center; [3]Division of rheumatology, Department of Internal Medicine, National Medical Center, Seoul, Korea, Republic Of*

Background: Renal involvement is a common and serious manifestation of SLE. Hyperuricemia may be associated with lupus nephritis as a result of renal

damage. However, it is not yet well known whether hyperuricemia is independently associated with renal involvement even in patients without known predisposing factors for hyperuricemia such as decreased renal function, old age, male gender, menopause, and drugs.

Objectives: The aim of this study was to evaluate the association of baseline serum uric acid level and development of nephritis in patients diagnosed with SLE.

Methods: We retrospectively reviewed electronic medical records of 101 female SLE patients whose ages at the time of diagnosis (baseline) were 45 years old or below in a tertiary medical center from January 2000 to March 2015. SLE with renal involvement was diagnosed when patients met the renal disorder of the 1997 ACR criteria for SLE. We compared baseline serum uric acid levels of the SLE patients who had nephritis at the time of diagnosis or later (nephritis group) with the patients who had not developed nephritis (non-nephritis group) during follow-up period.

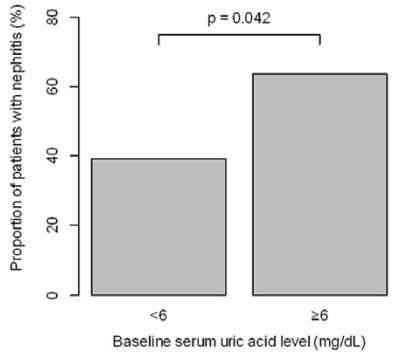
Results: Among 101 patients, 22 (22%) had hyperuricemia (serum uric acid ≥6 mg/dL) at baseline and 45 (45%) had developed nephritis during follow-up period (median 6.1 years). There were significant differences in baseline serum uric acid level, glomerular filtration rate (GFR), anti-dsDNA antibody and complement level between non-nephritis group and nephritis group (Table). Interestingly, among 59 patients with normal renal function (baseline GFR ≥90 mL/min/1.73m^2), baseline serum uric acid level was also significantly higher in the nephritis group than non-nephritis group (Table). Moreover, the patients with hyperuricemia at baseline were more likely to develop nephritis than those without hyperuricemia during follow-up period (64% vs. 39%, p =0.042) (Figure).

Table 1. Baseline Characteristics of Study Patients with Systemic Lupus Erythematosus

	Non-nephritis group	Lupus nephritis group	*p*
All patients (%)	56 (55)	45 (45)	
Sex, Female (%)	56 (100)	45 (100)	
Age, years	28.2±8.3	28.9±7.6	0.680
Body Mass Index, kg/m^2	21.2±3.8	22.0±3.0	0.105
Follow-up, years	6.0±4.3	7.5±4.3	0.068
Serum Uric Acid, mg/dL	4.5±1.6	5.5±1.5	**0.003**
GFR, mL/min/1.73m^2	103.1±24.9	85.6±27.0	**0.001**
Anti-dsDNA, IU/mL	56.4±107.9	141.8±163.4	**0.001**
C3, mg/dL	80.1±32.3	48.6±30.2	**0.000**
C4, mg/dL	14.0±8.3	9.8±8.2	**0.005**
Drugs that may increase serum uric acid level[1] (%)	5 (8.9)	2 (4.4)	0.626
Drugs that may decrease serum uric acid level[2](%)	1 (1.8)	0 (0.0)	1.000
Patients with normal renal function (baseline GFR≥90) (%)	39 (66)	20 (34)	
Serum Uric Acid, mg/dL	4.3±1.4	5.1±1.4	**0.047**
GFR, mL/min/1.73m^2	113.0±15.6	106.2±11.7	0.095
Anti-dsDNA, IU/mL	56.2±111.0	135.0±185.2	0.060
C3, mg/dL	76.3±35.0	47.3±30.6	**0.003**
C4, mg/d	13.3±7.8	8.8±7.2	**0.028**

Values are mean ± SD or number (%). [1]Diuretics, aspirin, pyrazinamide, or cyclosporine. [2]Allopurinol, febuxostat, benzbromarone, losartan, fenofibrate, or atorvastatin.

Figure. Proportion of patients who had developed nephritis according to serum uric acid levels at the time of diagnosis with SLE



Conclusions: These findings suggest that high serum uric acid level at the time of diagnosis in premenopausal women with SLE may be independently associated with nephritis. More careful evaluation would be required for development of nephritis in such patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4751

AB0492 NUCLEIC ACIDS OXIDATIVE STRESS STATUS IN SJÖGREN'S SYNDROME

D. Tecer[1], R. Tural[2,3], A. Sepici Dincel[2], F. Gogus[1]. [1]*Physical Medicine and Rehabilitation, Division of Rheumatology;* [2]*Medical Biochemistry, Gazi University, Faculty of Medicine, ankara;* [3]*Vocational School of Health Services, Sinop University, Sinop, Turkey*

Background: Although there are many defence systems that protect cellular macromolecules against oxidation, oxidative DNA and RNA damage still occurs. Oxidative damage to nucleic acids has been found to be associated with etiopathogenesis and disease activity of inflammatory disorders. Oxidised guanine species have been recognized as a biomarker of oxidative DNA and RNA damage by endogenously generated oxygen radicals. Sjögren's syndrome (SS) is an autoimmune disorder and associated with overexpression of proinflammatory cytokines. Related to excess expression of proinflammatory cytokines, a prooxidant state could be postulated in SS.

Objectives: We aimed to evaluate levels of nucleic acids oxidative stress products in patients with SS.

Methods: 11 patients with SS diagnosed according to 2012 American College of Rheumatology (ACR) Classification Criteria for Sjögren's Syndrome, 19 patients with psoriatic arthritis (PsA), diagnosed according to Classification Criteria for Psoriatic Arthritis (PSARC), 9 patients with rheumatoid arthritis (RA), diagnosed according to 2010 Rheumatoid Arthritis Classification Criteria, and 12 healthy controls were included. All SS patients were on hydroxychloroquine sulphate 400mg/day. All PsA and RA patients were on methotrexate 15–20mg/week and folic acid 5 mg/week. The serum samples were collected from participants and stored at -30 C until assayed. Three oxidised guanine species, 8-hydroxy-2'-deoxyguanosine as a DNA oxidation marker, 8-hydroxyguanosine as a RNA oxidation marker, and 8-hydroxyguanine as a DNA and RNA oxidation marker, were measured using DNA/RNA Oxidative Damage ELISA Kit (Cayman Chemicals, USA).

Statistics: All data are presented as mean and standard deviation (SD). Differences between groups were examined using Kruskal- Wallis tests. The Mann-Whitney U test was performed to test the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons. A p-value less than 0.05 were considered as statistically significant. Statistical analysis of correlation was performed by using the Spearman rank test.

Results: There was no statistically significant difference between the groups in terms of age and gender. The average level of serum oxidised guanine species in the PsA, RA, SS and healthy control groups were 2871.77±336.20, 2672.20±292.04, 3375.57±344.21, 2777.55±237.05 pg/mL respectively. Oxidised guanine species levels were significantly higher in patients with SS and positively correlated with CRP levels (p:0.011, r: 0.726) (table 2).

Table 1. Demographic characteristics of individuals

	Psoriatic arthritis	Rheumatoid arthritis	Sjögren's syndrome	Healthy controls	p value
Age	41.05 ± 11.61	51.56 ± 11.17	48.25 ± 10.31	41.17 ± 6.50	0.076
Female/male	8/11	8/1	11/1	5/7	0.096

Table 2. Correlation between oxidised guanine species level and ESR, CRP, IgG, IgA, IgM, C3, C4

		ESR	CRP	IgG	IgA	IgM	C3	C4
oxidised guanine species level	p	0.428	0.01	0.721	0.556	0.04	0.745	0.704
	r	0.253	0.726	0.226	0.189	-0.595	0.105	0.123

ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, Ig: Immunoglobulin, C: Complement

Conclusions: A marked increase in DNA damage leading to oxidative stress may contribute to tissue damage in SS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3286

AB0493 BLYS UPREGULATION IS RELATED TO LYMPHOPENIA IN SYSTEMIC ERYTHEMATOUS LUPUS PATIENTS

E. Grau Garcia[1], C.M. Feced Olmos[1], E. Labrador Sánchez[1], F.M. Ortiz-Sanjuan[1], M. Fernandez Matilla[2], N. Fernández-Llanio[2], I. Chalmeta Verdejo[1], K. Arévalo Ruales[1], R. Negueroles Albuixech[1], J. Ivorra Cortes[1], J.J. Fragio Gil[1], I. Martínez Cordellat[1], R. González Mazarío[1], L. Gonzalez Puig[1], C. Alcañiz Escandell[1], C. Nájera Herranz[1], I. Cánovas Olmos[1], E. Vicens Bernabeu[1], J.E. Oller Rodriguez[1], J.A. Castellano Cuesta[2], V. Fornés Ferrer[3], D. Hervás Marín[3], J.A. Román Ivorra[1]. [1]*Rheumatology Department, HUP la Fe;* [2]*Rheumatology Section, Hospital Arnau de Vilanova;* [3]*Biostatistics Unit, IIS la Fe, Valencia, Spain*

Background: B lymphocyte stimulator factor (BLyS) is produced by wide range of cells of the immune system, and has proven to be a key factor in the selection and survival of B cells. BLyS is an important factor in the pathology of Systemic Lupus Erythematosus; elevated serum levels (≥20ng/mL) of soluble BlyS are at increased risk of flare.

Objectives: Analyze the association among BLyS levels and clinical manifestations, as well as with SLE clinical activity.

Methods: A cross-sectional and observational study was performed in patients diagnosed of SLE according to SLICC 2012 criteria and healthy controls. The study included a complete blood-test and clinical data collected by personal interview. Disease activity assessment was made by SLEDAI index and for the evaluation of chronic damage we used the validated SLICC damage index. Serum concentration of BLyS was analyzed by colorimetric methods. Lupus patients were dichotomized as high and low BLyS levels based on BLyS levels above 2 SD of the mean in healthy controls. Biostatistical analysis with R (3.3.2.) was performed.

Results: Two hundred forty-two SLE patients were evaluated; 94.4% of them were female. Mean values were as follow: age at diagnosis 33.29±13.53 years, disease duration 15.82±10.56 years, SLEDAI 5.91±5.06, SLICC score 1.06±1.42, BLyS levels 1.811±1.757 ng/mL. The 22.5% of patients displayed increased BLyS levels. The 29.6% of total patients exhibit SLEDAI values up to 6, and only the 7% of them showed SLEDAI values up to 6 and high BLyS levels simultaneously. Higher BLyS levels were significantly correlated to the ANAs positivity (p=0.0006) and lymphopenia (p=0.01) but showed no correlation with hypocomplementemia neither anti-dsDNA. The statistical analysis did not yield differences in the clinical activity or accumulated damage between patients with lower and higher BLyS levels.
Conclusions: In our series we observed a 22.5% of patients with high levels of BLyS, and the 7% of cases had BLyS high levels and SLEDAI>6. BLyS upregulation is related to ANAs positivity and lymphopenia. We have found no statistical evidences on the relationship of BLyS levels and clinical activity in our series of patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4186

AB0494 INCREASED LEVELS OF INTERFERON ALPHA AND INTERLEUKIN-10 AS CLINICAL ACTIVITY BIOMARKERS IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS

E. Grau Garcia[1], M. Fernandez Matilla[2], C.M. Feced Olmos[1], E. Labrador Sánchez[1], F.M. Ortiz-Sanjuan[1], N. Fernández-Llanio[2], E. Tovar Sugreñes[3], K. Arévalo Ruales[1], R. Negueroles Albuixech[1], J. Ivorra Cortes[1], J.J. Fragio Gil[1], I. Martínez Cordellat[1], R. González Mazarío[1], I. Chalmeta Verdejo[1], L. Gonzalez Puig[1], C. Alcañiz Escandell[1], C. Nájera Herranz[1], I. Cánovas Olmos[1], E. Vicens Bernabeu[1], J.E. Oller Rodriguez[1], J.A. Castellano Cuesta[2], V. Fornés Ferrer[4], D. Hervás Marín[4], J.A. Román Ivorra[1,3]. *[1]Rheumatology Department, HUP la Fe; [2]Rheumatology Section, Hospital Arnau de Vilanova; [3]Medical School, UCV; [4]Biostatistics Unit, IIS la Fe, Valencia, Spain*

Background: Systemic lupus erythematous (SLE) is an autoimmune disease characterized by immune system disruption, including deregulation of cytokine production. Interferon alpha (INF1A) is considered a key molecule in SLE etiopathogenesis, being responsible of the differentiation of dendritic cells from monocytes, and indirectly of interleukin 10 (IL10) upregulation. The B lymphocyte stimulating factor (BLyS) is involved in autoantibodies production and clinical activity, and is regulated by other cytokines as IL10 and INF1A.
Objectives: To analyze the association among INF1A, IL10 and BLyS levels and clinical activity in SLE.
Methods: A cross-sectional, observational study of 142 patients diagnosed of SLE according to SLICC 2012 criteria and 34 healthy controls was performed. A complete blood-test was made, and clinical data by personal interview was collected. We analyzed serum concentration of IL10, BLyS and INF1A by colorimetric methods. Patients were dichotomized as high and low levels for each cytokine based on the cytokine level above 2 SD of the mean in healthy controls. Biostatistical analysis with R (3.3.2.) was performed.
Results: In our SLE patients we observed higher values of IL10, BLyS and INF1A than controls ($P<0.001$, P=0.005 and P=0.043 respectively), showing an average values in patients of 13.39±27.73 pg/mL INF1A, 9.99±15.84 pg/mL IL10 and 1811.31±1757.81 pg/mL BLyS. The mean clinical activity measured by SLEDAI was 5.91±5.06.
Statistical analysis indicate that INF1A levels are correlated to IL10 levels (P=0.001) and BLyS levels (P=0,034). Due to this finding, we categorized SLE patients by low or high level of the three cytokines: 44 INF1A(-)IL10(-)BLyS(-); 61 INF1A(+)IL10(-)BLyS(-); 5 INF1A(+)IL10(-)BLyS(+); 18 INF1A(+)IL10(+)BLyS(-) and 14 INF1A(+)IL10(+)BLyS(+). There is a high association of increased IL10-INF1A levels and the increased of clinical activity by SLEDAI score ($P<0.001$), and to a lesser extent with increased IL10-INF1A-BLyS levels. Patients with high IL10-INF1A and IL10-INF1A-BLyS showed a significant rise in C3-C4 consumption ($P<0.001$ and P=0.001 respectively) and high anti-dsDNA (P=0.001 and P=0.002 respectively). Patients with increased INF1A-BLyS exhibited high anti-dsDNA (P=0.004) and ENA positivity ($P<0.001$). In addition, patients with increased levels of IL10-INF1A-BLyS showed ANAs ($P<0.001$) and antiphospholipid autoantibody positivity (P=0.004).
Conclusions: The 69% of our SLE patients displayed almost one cytokine increased, being the INF1A the cytokine that mainly is increased. However, increased IL10 levels, irrespective of whether there is also increased levels of BLyS and/or INF1A, is the cytokine which best fits to clinical activity in SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4180

AB0495 ASSESSMENT OF FRACTURE RISK IN A COHORT OF EGYPTIAN FEMALE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

E.A. Hafez[1], S.A. El Bakry[1], S.I. Ibrahim[1], C.S. Morad[1,1], S.A. Hamza[2], D.M. Abd El-Khalik[1]. *[1]Internal medicine and Rheumatology; [2]Geriatric Medicine, Faculty of Medicine, Ain Shams University, Cairo, Egypt*

Background: Survival of systemic lupus erythematosus (SLE) patients has improved dramatically due to improved treatment, and the morbidity pattern has shifted towards long-term complications as osteoporosis. SLE occurs in women during child-bearing years and the disease often persists to the postmenopausal period[1]. Assessment of fracture risk in SLE patients is important as fractures may occur while bone mineral density (BMD) is above the osteoporotic threshold or at the normal range[2]. Osteocalcin measurement helps to assess fracture risk and select patients for treatment.
Objectives: To assess the fracture risk in a cohort of Egyptian female SLE patients by using BMD and osteocalcin level with correlation to disease activity, damage index and drugs in use.
Methods: 70 females with SLE ≥40 years old satisfying the SLICC classification criteria were enrolled with detailed history taking including disease duration, drugs in use, traditional risk factors, regular exercise, history of previous fractures and menstrual history. Assessment of disease activity using Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and disease damage using the Systemic Lupus International Collaborative Clinics/ American College of Rheumatology Damage Index (SLICC/ACR DI). Serum calcium, phosphorus and alkaline phosphatise were measured. BMD measured by dual energy X-ray absorpiometry (DEXA) scans at lumbar spine (LS) (L2-L4) and femoral neck (FN), serum osteocalcin level and World Health Organization fracture risk assessment tool (FRAX®).
Results: 14//70 (20%) patients had LS osteoporosis, 25//70 (35.7%) had LS osteopenia and 6/70 (8.6%) had FN osteoporosis, 30/70 (42.9%) had FN osteopenia. FRAX-Major ≥20% was observed in 10% of patients, FRAX-HIP ≥3% was seen in 27.1% of patients. Serum osteocalcin level was significantly decreased in SLE patients with lower BMD than those with normal BMD, and significantly decreased in patients with osteoporosis than those with osteopenia. A significant negative correlation was found between osteocalcin level and age of patients, disease duration, SLEDAI and SLICC scores, current, IV pulse and cumulative steroids, immunosuppressants, anticoagulants, but there was a positive correlation with antimalarials and calcium supplements.
Conclusions: SLE patients are at greater risk for developing osteoporosis and osteopenia. Ten-year risk of major and hip fractures was high in SLE patients. Increasing age, disease duration, high anti-DNA titres, SLEDAI and SLICC were associated with a higher 10-year probability of major osteoporotic fracture. FRAX predicted incident hip and major osteoporotic fractures among SLE patients with normal and low bone mass not just those with frank osteoporosis. Physicians should be alerted to the higher risk of future fractures in SLE patients for periodic monitoring.
References:
[1] Furukawa M, Kiyohara C, Horiuchi T, Tsukamoto H, Mitoma H, Kimoto Y et al. Prevalence and risk factors of vertebral fracture in female Japanese patients with systemic lupus erythematosus. Mod Rheumatol, 2013; 4:765–73.
[2] Van den Bergh J, Van Geel T, Lems W and Geusens P. Assessment of individual fracture risk: FRAX and beyond. Curr Osteoporos Rep, 2010; 8:131–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3907

AB0496 VENOUS THROMBOSIS IS MORE PREVALENT IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME (APS) ACCOMPANYING SYSTEMIC LUPUS ERYTHEMATOSUS, WHILE LIVEDO RETICULARIS IN PRIMARY APS

E.N. Hałady, A. Wieczorek, M. Olesińska. *Connective Tissue Diseases, Institute of Geriatrics, Rheumatology and Rehabilitation, WARSAW, POLAND, Warsaw, Poland*

Background:
APS more often overlaps with other systemic autoimmune diseases like systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) than occur as a distinct disease. Our purpose was to evaluate what are the differences between patients with primary APS and APS accompanying SLE.
Objectives: The objective of this study was to compare patients with primary APS and APS/SLE group whther we can find find any clinical or laboratory parameters that can distinguish them from each other.
Methods: 112 patients with APS were included to the study, 57 of them with primary APS and 55 with coexisting SLE. These patients were followed at the Department of Connective Tissue Diseases, NIGRiR, Warsaw, Poland. At inclusion a full medical history and physical examination data were recorded.
Results: Both groups were similar in age, gender and duration of disease. Among all the clinical manifestations of APS, venous thrombosis was more frequent in patients with concomitant SLE. Skin involvement was significantly more prevalent in primary APS and it was caused mainly by livedo reticularis presence. From neurological manifestations, the occurrence of epilepsy was comparable, when EEG changes were more frequent in APS/SLE group. From laboratory measures, leucopenia, low complement concentrations and proteinuria were more prevalent in APS/SLE group. No differences were observed in thrombocytopenia and elongation of APTT as well as antiphospholipid antibody profile.
Conclusions: In conclusion, arterial thrombosis is more characteristic for primary APS. We found that livedo reticularis is very characteristic feature for primary APS. Although epilepsy occurrence is comparable in APS and APS/SLE, higher frequency of EEG changes in APS/SLE group suggests that the mechanisms

Table 1. Main differences in both groups

	Total N=112	APS N=57 (50,9%)	TRU+APS N=55 (49,1%)	P
Age	48,3±13,7	46,9±14,3	49,7±13,2	0,2187
Gender	96 (85,7%)	45 (78,9%)	51 (92,7%)	0,0698
APS duration (months)	72 [24–144]	48 [13–120]	80 [31–156]	0,2329
Venous thrombosis	61 (54,5%)	25 (43,9%)	36 (65,4%)	**0,0218**
Arterial thrombosis	63 (56,2%)	30 (52,6%)	33 (60,0%)	0,4320
Thrombosis all	97 (86,6%)	47 (82,5%)	50 (90,9%)	0,1891
livedo reticularis	53 (47,3%)	41 (71,9%)	12 (21,8%)	**<0,0001**
EEG changes	18 (16,1%)	5 (8,8%)	13 (23,6%)	0,0323
Epilepsy	20 (17,9%)	8 (14,0%)	12 (21,8%)	0,2823

leading to this feature can be distinct between this two conditions. Additionally, it appears to be more reasonable to add thrombocytopenia to clinical criteria of APS, because its frequency does not depend on SLE presence.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1736

AB0497 SIX CASES OF MACROPHAGE ACTIVATION SYNDROME AS PRESENTING MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

F. Dall'ara[1], I. Cavazzana[2], M. Frassi[2], M. Taraborelli[2], M. Fredi[2], F. Franceschini[2], L. Andreoli[1], A. Tincani[1], P. Airò[2]. *[1]Rheumatology and Clinical Immunology, University of Brescia - Dscs; [2]Rheumatology and Clinical Immunology, Spedali Civili of Brescia, Brescia, Italy*

Background: Macrophage Activation Syndrome (MAS) is a life-threatening syndrome characterized by excessive immune activation. It can be triggered by conditions affecting immune homeostasis, such as infections, malignancies and rheumatologic disorders, including Systemic Lupus Erythematosus (SLE). In previous studies, prevalence of MAS among SLE patients ranged from 0.9% to 4.6%.

Objectives: To describe the presentation and treatment of both MAS and SLE in patients with both syndromes.

Methods: Monocentric retrospective evaluation: patients with MAS according to HLH classification criteria were identified in our cohort of SLE patients (classified according to ACR and SLICC criteria)followed for at least 1 year between 1972 and 2014.

Results: Among 511 patients with SLE (mean age at diagnosis:31 years ±2),6 patients (1.2%)with MAS were identified (all female). Their main clinical and laboratory features are reported in table 1.Median HLH score was 226.5 (IQR 204–254),with a probability of having MAS of 96%.In all cases MAS happened simultaneously to the onset of SLE.Median age at diagnosis was 31.5 years, median SLEDAI was 12.All patients had fever above 38°C,lymphadenopathy,hematological involvement,and high titer ANA positivity. Workup for infections and malignancies was negative in all cases.All patients were treated with corticosteroids (100% received intravenous immunoglobulin pulse of methylprednisolone);concomitant medications were: cyclosporin A in 83%, IVIG in 67%, granulocyte colony-stimulating factor in 17%, mycophenolate mofetil in 17%, etoposide in 17% and plasma exchange in 17%. Two patients required haemotransfusion.All cases required hospital admission, and 2 were admitted in intensive care unit. No death from MAS was observed (median follow up: 34.5 months;IQR25–48).One patient died 44 months after after MAS for pulmonary adenocarcinoma.Table 1:main clinical and laboratory features at diagnosis of SLE and MAS

Table 1: main clinical and laboratory features at diagnosis of SLE and MAS

Clinical features of MAS n (%)		SLE ACR classification criteria	
Fever	6 (100%)	§Malar rash/Oral ulcers/Photosensitivity/ LED	5 (83%)
Hemorrhages	1 (17%)		
CNS dysfunction	0 (0%)		
Lymphadenopathy	6 (100%)		
Hepatomegaly	4 (67%)	Arthritis	2 (33%)
Splenomegaly	4 (67%)	Nephritis	0
		Serositis	3 (50%)
		CNS disease	1 (17%)
		Haematological involvement	6 (100%)
MAS Laboratory Parameters median (IQR)		Autoantibodies n (%)	
WBC (x10³/uL)	2.1 (1.8-2.3)	ANA	6 (100%)
Neutrophils (x10³/uL)	1.5 (0.87-1.8)	anti-ds DNA	5 (83%)
HGB (g/dL)	7.6 (7-8,2)	anti-RNP	2 (33%)
PLT (x10³/uL)	134 (72-142)	anti-Ro	1 (17%)
AST (U/L)	250 (166-402)	anti-Sm	1 (17%)
ALT (U/L)	111 (92-135)	antiphospholipid Ab/LA	3 (50%)
LDH (U/L)	769 (535-915)		
Ferritin (µg /L)	4607 (1897-31533)	*Direct Coombs Test +	5 (100%)
Fibrinogen (mg/dL)	97 (35-170)	C3 mg/dl (n.v 80-160)	34 (28-70)
Triglycerides (mg/dl)	511 (317-605)	C4 mg/dl (n.v 10-40)	13 (7-17)
ESR (mm)	17.5 (9-24)		
CRP (mg/dl)	37 (10-49)		

* this test was available only for 5 patients

§at least one of these criteria: malar rash; Oral ulcers; Photosensitivity; LED: Discoid Lupus Erythematosus

CNS: central nervous system; WBC white blood cells; HGB: hemoglobin; PLT: plateletAST: aspartate aminotrasferase; ALT: alanine aminotrasferase; LDH: lactate dehydrogenase; ESR: erytrocyte sedimentation rate; CRP: C-reactive protein; ANA antinuclear antibodies; anti-ds DNA: anti double stranded DNA antibodies; anti-RNP: anti-ribonucleoprotein antibodies; LA: Lupus anticoagulant: n.v.: normal values

Conclusions: MAS is a rare complication in our SLE cohort and can complicate the onset of SLE, but it seems to be a very uncommon manifestation during the course of the disease.Fever may be a red flag for possible MAS, particularly if temperature is persistently above 38° in absence of signs and symptoms of underlying infection.In our series, all cases were treated successfully with immunosuppressive drugs and cytotoxic agents such as etoposide were used only in one case.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6692

AB0498 SOLUBLE CD14 (PRESEPSIN) AS A POTENTIAL BIOMARKER TO DISCRIMINATE INFECTION VS. ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

I. Posso-Osorio[1], A. Echeverry[1], D. Aguirre-Valencia[1], G. Castaño[2], G. Tobón[1]. *[1]Rheumatology; [2]Laboratory of inmunology, Fundación Valle del Lili, CALI, Colombia*

Background: Differentiation of Systemic Lupus Erythematosus (SLE) activity and infection in a febrile SLE patient become difficult, since initial clinical presentation may be similar. Several biological markers (including procalcitonin and CRP) have been evaluated, with discordant results. Soluble CD14 (sCD14), also called presepsin, is the receptor for lipopolysaccharide - lipopolysaccharide binding protein (LPS-LBP) complexes. CD14 could activate a series of signal transduction pathways and inflammatory cascades, and lead to systemic inflammatory responses.(1)

Objectives: The aim of this study is to evaluate the utility of sCD14 as a biomarker to differentiate infection *vs.* activity in SLE patients admitted with systemic inflammatory response (SIRS).

Methods: We included 11 patients with SLE (ACR criteria 1997) and SIRS (International conference 2001) admitted to the ER and/or ICU. The measurement of sCD14 in plasma by enzymatic immunoassay of chemiluminescence *in vitro* was performed to differentiate active SLE *vs.* infection. Infection was considered if a positive culture/PCR was obtained. Mann-Whitney test was used to evaluate the association of variables with infection.

Results: All patients were female; mean age 37.9 years. An infectious disease was confirmed in 5 cases (3 bacterial including urinary tract infection, pneumonia and bacteremia; 1 viral infection by Chikungunya virus and 1 fungal by *histoplasma capsulatum*). sCD14 was elevated in the infected SLE patients (median: 1005 pg/mL- RIC: 533–1415-) vs patients with lupus flare (median: 431.5 pg/mL - RIC: 369–579-) (p=0,04).

Conclusions: High values of sCD14 levels seem to be useful to differentiate infections from activity in SLE patients with SIRS. More patients and further analysis are necessary to define the clinical use of this biomarker.

References:

[1] Zou Q, Wen W, Zhang X. Presepsin as a novel sepsis biomarker. World J Emerg Med [Internet]. Second Affiliated Hospital of Zhejiang University School of Medicine; 2014 Aug 22;5(1):16–9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4129857.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2495

AB0499 TOTAL BODY WATER AND ITS CORRELATION WITH SICCA SYMPTOMS IN PRIMARY SJÖGREN'S SYNDROME

G. Hernandez-Molina[1], P. Almeda-Valdés[2], G. López-Carrasco[2], M. Astudillo-Angel[1], M. González-Acevedo[2], V. Zamora-Legoff[1], P. Sánchez-Fernández[2], C. Aguilar-Salinas[2], I. Cruz Bautista[2]. *[1]Immunology and Rheumatology; [2]Endocrinology Department, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico*

Background: Patients with primary Sjögrens' syndrome (PSS) suffer from severe alterations in both the quality and quantity of saliva and tears. Body water represents around 50–55% of the body weight. Tears contain 98% of water and saliva 99.5%.

Objectives: To evaluate the percentage of total body water (TBW) among patients with PSS and to assess its correlation with sicca symptoms.

Methods: We included 85 patients with PSS and 85 historical non diabetic controls matched by gender, age (±3 years) and body mass index (±1kg/m^2) (BMI). We assessed the presence of sicca symptoms, Schirmer-I test, non-stimulated whole salivary flow (NSWSF) and ocular staining. We also evaluated the ocular and oral domains of the ESSPRI, a validated scale for symptoms (a higher score implies worst symptoms). We obtained the TBW percentage with a bioelectric impedance analysis (BIA-SECA-514, Hamburgo).

Results: 80% were women, mean age 54.8±13.7 years and mean disease duration 11.5±7.52 years. The percentage of TBW was similar among patients and controls (PSS 46.85±4.6 vs. 46.9±4.5, p=0.88). Among the patients, the

TBW negatively correlated with age (ρ=-0.25, p=0.02), disease duration (ρ=-0.30, p=0.005), BMI (ρ=-0.78, p=0.001) and the ocular component of the ESSPRI (ρ=-0.28, p=0.01), but not with the NSWSF or the ESSPRI oral component. When we compared the patients in the 25% percentile (group with the lowest % of water) vs. the remaining patients, the former group was older (56.6±8.1 vs. 54±14.2, p=0.02), with longer disease duration (12.4±5.9 vs. 10.8±7.12, p=0.03), lower scores at the Schirmer test (1 (range 0–8) vs. 2 (range 0–9), p=0.01), higher BMI (31.1±5.1 vs. 23.7±2.9, p=0.001) as well as with higher ESSPRI ocular domain scores (8.3±1.4 vs. 6.7±2.5, p=0.007). With the linear regression analysis, the variables that remained associated with the TBW were disease duration (β -0.22, p=0.001), BMI (β-0.76, p<0.001) and the ocular domain of the ESSPRI (β-0.15, p<0.001).

Conclusions: Patients with PSS had similar TBW percentage than controls. However among patients with PSS, the TBW had a negative correlation with the intensity of ocular symptoms independently of disease duration, age and BMI.

References:

[1] Guyton, Arthur C. (2006). Textbook of Medical Physiology (11th ed.). Philadelphia: W.B. Elsevier Saunders. p. 295. ISBN 0–7216–0240–1.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2388

AB0500 TOLERABILITY, EFFICACY AND IMMUNOGENICITY OF 23-VALENT PNEUMOCOCCAL VACCINE IN SLE PATIENTS

G.M. Tarasova, B.S. Belov, M.S. Sergeeva, S.K. Soloviev, E.A. Aseeva, N.G. Klukvina, T.V. Popkova, E.N. Alexandrova, A.A. Novikov, M.V. Cherkasova. *V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Concurrent infections turn out to be the second leading cause of death in systemic lupus erythematosus (SLE) pts after SLE per se. Immunization of SLE pts with pneumococcal vaccine is an important prophylactic approach to prevent severe lower respiratory tract (LRT) infections in SLE pts.

Objectives: To study the relevance of 23-valent pneumococcal vaccine for immunization of SLE pts.

Methods: The study included 30 SLE pts, 27 females, 3 males, aged 19 - 62 y. Duration of follow up (FUP) was 12 months in 24 pts, and 7–10 months – in 6 pts. High disease activity at the time of immunization was documented in 1 patient, low activity – in 20 pts, moderate – in 4 pts, and remission – in 5. 29 pts were treated with glucocorticosteroids (GCs), 23 – with hydroxychloroquine, 14 pts – with cytostatic (CS) agents. Twelve pts were on biological disease-modifying antirheumatic drugs (bDMARDs). One dose (0,5 ml) of 23-valent polysaccharide pneumococcal vaccine was administered subcutaneously. The duration of FUP was 7–12 months. Control visits were scheduled as follows: at baseline (Visit 1), at 1st, 3rd, and 12th months (Visit 4) after immunization. Standard clinical examination and lab tests, including blood immunology, were performed at each visit. Vaccine immunogenicity was evaluated based on the level of serum antibodies (AT) to Streptococcus pneumoniae capsular polysaccharide (VaccZymeTM PCP Ig 2 panels (The Binding Site Ltd, Birmingham, UK)) – 4 times during 1 year.

Results: No post-immunization complications were seen in 11 (36,7%) pts, local reactions of varying intensity lasting from 2 to 7 days were documented in 18 (60%) pts. One patient (3,3%) developed the local *type* III hypersensitivity reaction known as Arthus phenomenon. All symptoms subsided within 7 days after administration of antihistaminic agents and local GCs. Not a single vaccination-related SLE exacerbation episode was documented in 24 pts during the FUP. Significant (≥2-fold vs baseline) increase of serum AT levels to S. pneumoniae polysaccharide was observed during the FUP (Table).

In 10 (41,7%) out of 24 pts ("non-responders") more than 2-fold increase of anti-S. pneumoniae ATs was not achieved by 12th month of FUP. Among them 7 (70%) pts were receiving bDMARDs. 4 (28,6%) out of 14 "responders " were also treated with bDMARDs.

Non-severe pneumonia was documented in 2 out of 24 pts within1 year after vaccination; both cases successfully resolved after 7- and 5-days of oral antibiotic treatment in an out-patient setting. Both pts had episodes of pneumonia in past medical history. One of them had SLE-induced interstitial lung disease. This patient was treated with GCs, mycophenolate mofetil, and rituximab, no post-vaccination response was documented. The second patient had two previous pneumonia episodes, she demonstrated 4–5-fold increase in anti- S. pneumoniae AT titre; her therapy included GCs (10 mg/day) and hydroxychloroquine. There were no clinical or radiological symptoms of pneumonia in remaining 22 pts during the whole FUP.

Table. Anti-pneumococcal AT concentrations in SLE pts, Me (25,75 percentiles), n=24.

Visit	Visit 1 (baseline)	Visit 2 (1 mo)	Visit 3(3 mo)	Visit 4 (12 mo)
AT concentration Mg/L	**97,4[a]** (68,0; 128,1)	**407,8[b]** (231,2; 488,8)	**301,8[c]** (164,3; 424,6)	**265,5[d]** (120,0; 438,7)
		b-a, p =0,00006	c-a, p =0,00008	d-a, p =0,002

Conclusions: Obtained results are indicative of good tolerability, safety and immunogenicity of 23-valent pneumococcal vaccine in SLE pts. Further studies are necessary for more comprehensive evaluation of vaccine clinical efficacy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2347

AB0501 THE ASSOCIATION BETWEEN GLUCOCORTICOIDS AND DAMAGE ACCRUAL IN PATIENTS WITH SLE USING GLUCOCORTICOID FOR LONG-TERM

G. Wang, X. Li, Z. Dou, W. Wang, R. Liu. *Rheumatology and Immunology, Anhui Provincial Hospital Affiliated to Anhui Medical University, Hefei, China*

Background: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease characterized by a relapsing-remitting course. Long-term prognosis of SLE patients remains poor [1]. Due to the effect of potent anti-inflammatory and immunosuppressive, glucocorticoids (GCs) remain the cornerstone of treatment in SLE. However, GCs produce several adverse reactions, most are time and dose dependent, limiting their clinical usefulness. Increased longevity with prolonged exposure to GCs and inflammatory insults might contribute to organ damage accrual, which retards further improvement of survival in these patients [2]. Assessment the extent of organ damage caused by SLE has been considered an important part of the assessment of prognosis. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index (SDI) is a validated instrument designed to measure irreversible damage resulting from SLE disease activity and its treatment. The study of damage accrual in patients with SLE caused by the long-term treatment of GCs is still not clear.In a large SLE cohort, followed prospectively, we determined to investigate the association between damage accrual with GCs, both cumulative prednisone dose and high-dose prednisone. The results of our study could shed more light on the risk/benefit ratio of GCs in long-term maintenance treatment with SLE patients.

Objectives: To evaluate the association between long-term glucocorticoids use and damage accrual in patients with systemic lupus erythematosus.

Methods: Medical records of 535 SLE patients from Department of Rheumatology and immunology of Anhui Provincial Hospital were reviewed. 512 patients were femal. The cohort's mean age was 38.27±12.84 years with mean disease duration of 7.33±5.75 years. Their Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) scores were noted. (1) Univariate analysis and multivariable regression analysis were performed to determine factors associated with SDI. (2) Analysis were also performed to determine damage associated with cumulative prednisone dose and high-dose of prednisone (exposure to prednisone at a dosage of 60 mg/day for 1 month).

Results: (1) Among 535 patients in our cohort only 5 paitents (0.9%) had never been treated with glucocorticoids. A total of 192 patients (35.9%) had been treated with high dose of prednisone. In addition, 86.9% of patients had been treated with hydroxychloroquine. (2) The highest organ damage was musculoskeletal (n=79, 14.8%), followed by skin damage (n=35, 6.5%) and renal (n=28, 5.2%). Ninety patients were diagnosed with hypertension. (3) SDI scores were associated with age of onset, exposure to high-dose prednisone, hypertension.(4) Cumulative prednisone dose was associated with osteoporosis, osteonecrosis and hypertension; exposure to high-dose prednisone was associated with osteonecrosis, lupus nephritis and hypertension.

Conclusions: Long-term taking prednisone predicted damage accrual. The most common damage was osteoporosis, osteonecrosis and hypertension.

References:

[1] Lopez R, Davidson JE, Beeby MD, et al. Lupus disease activity and the risk of subsequent organ damage and mortality in a large lupus cohort[J]. Rheumatology. 2012,51(3):491–8.

[2] Mak A, Isenberg DA, Lau CS. Global trends, potential mechanisms and early detection of organ damage in SLE[J]. Nature reviews Rheumatology. 2013,9(5):301–10.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3931

AB0502 STRONG REDUCTION OF ANTI-MÜLLERIAN HORMONE IN SYSTEMIC LUPUS ERYTHEMATOSUS WOMAN OF REPRODUCTIVE AGE

C. Li, J. Xie, X. Wang, X. Liu, G. Chen. *Division of Rheumatology and Clinical Immunology, the First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China*

Background: Systemic lupus erythematosus (SLE) is a clinically autoimmune disease characterized by production of autoantibodies and immune complex deposition. That induces multiple organ damages such as nephritis, pneumonitis and central nervous system (CNS) lupus et al. Moreover, SLE which mainly occurs in reproductive woman could threaten ovarian function. In recent years, ovarian reserve dysfunction in SLE are attracting increasing attentions. Especially cyclophosphamide (CYC) therapy was already well known as a higher risk to result in premature ovarian failure (POF) 1,2. However, few research has been performed in association between SLE itself and ovarian reserve. POF which is a critical cause of secondary amenorrhea and infertility still has not been treated effectively until now. Accordingly, an early precaution is important to make an informed decision about impaired ovarian reserve in SLE.

Objectives: To study the association between systemic lupus erythematosus (SLE) itself and strongly reduced Anti-Müllerian Hormone (AMH) values.

Methods: SLE women during reproductive ages 18–40 years were recruited compared with age-matched healthy controls (HC). AMH Levels and its relationship to clinical parameters and disease activity were investigated.

Results: Totally 91 SLE patients were enrolled (means ± SD age 28.38±5.80 years; SLE duration 47.15±44.70 months; SLE-2k scores 6.48±7.02). There were 73 subjects without cyclophosphamide therapy (SLE-CYCfree), 18 subjects previously exposed to CYC (SLE-CYC) and 79 HC. AMH values in SLE-CYC cases decreased significantly than HC and SLE-CYCfree (1.38±1.93 versus 4.10±3.40, *P*=0.002; 1.38±1.93 versus 3.62±3.61, *P*=0.013). No different was found between SLE-CYCfree and HC groups (*P*=0.377). Strong reduced AMH values (<0.5 μg/L) were identified in 12 of 73 (16.4%) SLE-CYCfree patients and 1 of 79 (1.3%) HC (*P*=0.001, OR=15.344). Furthermore, 10 (31.2%) SLE-CYCfree women aged ≥30 years had low AMH levels compared with 2 (4.9%) patients less than 30 years (*P*=0.004, OR=8.86). 29.6% (8/27) SLE populations over 3 year-duration of illness and 8.7% (4/46) in cases with less than 3 years were observed (*P*=0.046, OR=4.42). No difference reached statistical significance in SLEDAI-2K, Complement C3 and C4, IgG and IgM between SLE-CYCfree and SLE-CYC groups.

Conclusions: SLE was confirmed to be closely associated with low AMH levels. SLE could play a critical role in development of abnormal ovarian reserve. And moreover, over 3-year disease duration and ages over 30 years in reproductive-aged SLE women might enhance the risk of impaired ovarian reserve.

References:

[1] Warne GL, Fairley KF, Hobbs JB, Martin FI. Cyclophosphamide-induced ovarian failure. N Engl J Med 1973; 22:1159–62.
[2] McDermott EM, Powell RJ. Incidence of ovarian failure in systemic lupus erythematosus after treatment with pulse cyclophosphamide. Ann Rheum Dis 1996;4:224–9.
[3] Cui L, Qin Y, Gao X, Lu J, Geng L, Ding L, et al. Antimüllerian hormone: correlation with age and androgenic and metabolic factors in women from birth to postmenopause. Fertil Steril 2016;105: 481–5.
[4] Visser JA, de Jong FH, Laven JS, Themmen AP. Anti-Müllerian hormone: a new marker for ovarian function. Reproduction 2006;131: 1–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1489

AB0503 THE OUTCOME OF SYSTEMIC LUPUS ERYTHEMATOUS IN KYRGYZ PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOUS UNDER LONG-TERM OBSERVATION

G. Koilubaeva, E. Karimova, M. Dzhetybaeva, K. Dzhailobaeva, A. Dzhumakadyrova. *Rheumatology, National Center of Cardiology and Internal Medicine Named After Academician M. Mirrahimov, Bishkek, Kyrgyztan*

Background: Systemic lupus erythematosus (SLE) is a devastating disease affecting different organs, ultimately leading to organ failure and death. To date, there are no data regarding the real-life picture of SLE in Kyrgyzstan.

Objectives: Analysis of SLE outcome in Kyrgyz patients under long-term observation.

Methods: The study involved 50 patients under prospective study treated in the NCCIM from January 2012 to August 2016 with SLE at the age of 27 years (median - 27 [23; 36])., with disease duration about 1 year (median - 1 [0.3, 3.0]), including 45 women and 5 men. The outcome of SLE was estimated as the number of exacerbations based on the SFI index (moderate or severe), irreversible organ damage by SDI, death, remission (complete or drug related). Remission was defined as complete if for the patients, who were not receiving any treatment, no clinical and immunological SLE activity was recorded. Drug remission was registered when clinical and immunological disease activity was absent in patients receiving supporting doses of prednisolone (from 5 mg to 10 mg) and receiving the following cytostatic drugs: 200 - 400 mg per day of PLQ or 100 - 150 mg per day of AZA or 7.5 mg of MTX per week.

Results: During the 3-year-long dynamic monitoring, in 50 patients observed 2 years after the initial examination 62 cases of exacerbation of SLE were registered (median, 2.0 [1.5, 2.5]). Out of these there were 36 severe (58%) and 26 moderate outbreaks (42%). Severe exacerbations were mainly related to kidneys - in 42 patients (84%), 7 out of which experienced simultaneous exacerbation of articular syndrome, 5 lupus dermatitis, 2 patients had CNS damage in the form of visual and audial hallucinatory syndrome with encephalopathy and bilateral pyramidal insufficiency (1) and encephalopathy with anxiety disorders (1). Moderate exacerbations were mainly caused by the lesions of skin and joints (20), myositis (1), in one case there was a necrotizing vasculitis of the lower extremities. The main causes of SLE breakouts were: for 33 patients (66%) - low compliance (when the patients themselves stop taking GC and cytostatics), for the remaining 17 patients (34%) - exacerbation of the SLE process.

Towards the end of monitoring the development SDI was the result of accumulation of organ damage caused by the disease itself (61%) as a result of: ischemic stroke (3), reduced GFR less than 50 ml per minute (4) due to heavy lupus nephritis, paresis of the right motor oculi (1), changes in the retina (1), pulmonary fibrosis (1), and pulmonary arterial hypertension (1). Over the entire period of careful dynamic study of the 50 patients no fatalities were recorded. Remission was achieved in 10 patients (20%) out of 50. The majority of patients had drug remission (9), except for one patient with baseline nephritis, dermatitis, arthritis, which was in complete remission during three years.

Conclusions: During the three years of medical observations remission was achieved in 20% of patients, most of them with drug remission (90%). 62 cases of SLE exacerbation were registered, with a predominance of severe outbreaks (58%), mainly caused by low compliance (53.2%). Development SDI was mainly due to the accumulation of organ damage caused by the disease itself (61%).

References:

[1] It is necessary to improve the rheumatology service in the regions of the country.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5174

AB0504 PREGNANCY OUTCOME AND ITS RELEVANT FACTORS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

H. Takei[1], Y. Kaneko[2], T. Takeuchi[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine; [2]Division of Rheumatology, Department of Internal Medicine, Department of Internal Medicine, Keio University, Tokyo, Japan*

Background: Pregnancy outcome is one of the major concerns to manage systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) since they often affect women in reproductive ages. However, the predictive factors of poor pregnancy outcome and disease flare during pregnancy have not fully investigated.

Objectives: To elucidate the factors affecting the pregnancy outcome in patients with systemic erythematosus (SLE) and rheumatoid arthritis (RA).

Methods: Patients with SLE and RA in our university between 2012 and 2016 who experienced pregnancy were retrospectively reviewed. Medical information was collected from their chart.

Results: Thirty six pregnancies in 26 SLE patients and 26 pregnancies in 21 RA patients were identified. Among SLE pregnancies, the mean age, disease duration and prednisolone dose were 32.7±4.6, 8.9±7.7 years and 5.6±4.1 mg/day, respectively. The disease activity was well controlled (the mean SLEDAI, 2.4±2.1). Live birth pregnancies were 31 (86.1%) and fetal loss occurred in 5 pregnancies (3 spontaneous abortions, 1 ectopic gestation and 1 hydatidiform mole). The mean dose of prednisolone was significantly lower in the pregnancies with live birth than those with fetal loss (4.9±3.4 vs 11.3±3.3mg/day, p=0.02), while proteinuria, SLEDAI, history of lupus nephritis, positivity of antiphospholipid antibodies and anti-SSA/Ro antibodies were not significantly different between the two groups. Maternal lupus flare occurred in 6 (16.7%) during pregnancy or after the delivery and was significantly associated with proteinuria at the time of conception (p=0.02). Low body birth occurred in 9 (29.0%) and was also significantly associated with proteinuria at the time of conception (p=0.002). Among RA patients, the mean age and disease duration were 33.5±5.6 and 9.9±7.4 years. The mean DAS28-ESR, CDAI and HAQ were 2.18±0.88, 3.07±4.10 and 0.30±0.50, respectively and 14 achieved DAS28-ESR remission (<2.6). Seven (26.9%) discontinued biological agents before conception while 8 (34.6%) continued to use biological agents. Although 5 (19.2%) experienced the disease flare during pregnancy, all 26 pregnancies were live birth. The patients who discontinued biological agents more frequently experienced the disease flare than those who continued, during pregnancy or postpartum within 1 year after delivery (85.7% vs 25%, p=0.04).

Conclusions: High live birth rates were observed in both SLE and RA pregnancies on the condition of well-controlled disease activity. In SLE pregnancies, less prednisolone dose at the time of conception may be associated with live birth. SLE pregnancies with proteinuria and RA pregnancies with discontinuation of biological agents are associated with disease flare and should be cautiously monitored.

References:

[1] Arthritis Rheum. 2005;52(2):514–21.
[2] Rheumatology (Oxford). 2002;41(6):643–50.
[3] J Rheumatol. 2015;42(8):1376–82.

Disclosure of Interest: H. Takei: None declared, Y. Kaneko Consultant for: AbbVie, Astellas Pharma, Chugai Pharmaceutical, Bristol-Myers K.K., Eisai, Mitsubishi Tanabe Pharma, Pfizer Japan, and Takeda Pharmaceutical, Speakers bureau: AbbVie, Astellas Pharma, Chugai Pharmaceutical, Bristol-Myers K.K., Eisai, Mitsubishi Tanabe Pharma, Pfizer Japan, and Takeda Pharmaceutical, T. Takeuchi Grant/research support from: Pfizer Japan, Mitsubishi Tanabe Pharma, Eisai, Astellas Pharma, UCB, Chugai Pharmaceutical, Bristol-Myers K.K., Daiichi Sankyo, AbbVie, Janssen Pharmaceutical K.K., Pfizer Japan, Asahi Kasei Pharma, Takeda Pharmaceutical, AstraZeneca K.K., Eli Lilly Japan K.K., and Novartis Pharma K.K., Consultant for: Pfizer Japan, Mitsubishi Tanabe Pharma, Eisai, Astellas Pharma, UCB, Chugai Pharmaceutical, Bristol-Myers K.K., Daiichi Sankyo, AbbVie, Janssen Pharmaceutical K.K., Pfizer Japan, Asahi Kasei Pharma, Takeda Pharmaceutical, AstraZeneca K.K., Eli Lilly Japan K.K., and Novartis Pharma K.K., Speakers bureau: Pfizer Japan, Mitsubishi Tanabe Pharma, Eisai, Astellas Pharma, UCB, Chugai Pharmaceutical, Bristol-Myers K.K., Daiichi Sankyo, AbbVie, Janssen Pharmaceutical K.K., Pfizer Japan, Asahi Kasei Pharma, Takeda Pharmaceutical, AstraZeneca K.K., Eli Lilly Japan K.K., and Novartis Pharma K.K.

DOI: 10.1136/annrheumdis-2017-eular.3626

AB0505 DOES VITAMIN D DEFICIENCY CONTRIBUTE TO COGNITIVE DYSFUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS?

H.A. Hussein[1], N.A. Fouad[2], L. Daker[3], A. Elamir[4], S.R. Mohamad[4]. *[1]Internal Medicine, Fayoum University, Cairo; [2]Rheumatology; [3]Neurology; [4]Medical Biochemistry, Fayoum University, Fayoum, Egypt*

Background: Neurocognitive impairment is one of the most common SLE manifestations. However, its pathophysiology remains poorly understood [1]. Vitamin D deficiency is a potential risk factor for cognitive impairment [2,3].
Objectives: Our aim is to evaluate the relationship between 25(OH)D3 level and cognitive performance in patients with SLE.
Methods: Thirty Egyptian patients diagnosed as systemic lupus erythematosus and their age and sex matched controls were subjected to a battery of neuropsychological evaluation by California Verbal Learning Test (CVLT-II), Controlled Oral Word Association Test (COWAT) and Trail making test and evaluation of depression by using Beck Depression Inventory (BDI). Serum level of 25(OH)D3 was measured in cases and controls.
Results: Patients with SLE had a worse performance than controls in verbal memory total recall, executive function and phonemic verbal fluency as there was a statistically significant difference in CVLT-II total recall, Trail making test and phonemic-COWAT respectively. There was no significant difference between the patients and controls in Beck Depression Inventory (BDI). There was a significant positive correlation between the vitamin D level and executive function assessed by trail making test (r =0.399, p=0.03).

Table 1. Comparison of psychometric tests between the patients and controls

Psychometric tests	Patients (n=30)	Controls (n=20)	p value
CVLT- II total recall	39.65±7.43	53.05±11.89	**<0.0001***
CVLT-II –II short term free recall	8.823±2.87	9.94±3.17	0.2
CVLT-II –II short term cued recall	2.04±1.58	2.41±2.52	0.6
CVLT-II –II long term free recall	9.96±3.36	10.52±2.76	0.5
CVLT-II –II long term cued recall	1.47±1.16	2.23±2.79	0.3
Trail Making Test	178.04±86.76	80.53±28.24	**<0.0001***
COWAT- phonemic	17.96±7.63	30.82±7.23	**<0.0001***
COWAT- semantic	11.47±3.16	14.17±4.84	0.05

Table 2. Correlations between vitamin D level and measures of cognitive among cases

	Vitamin D level	
	r	P-value
cvlt-total recall	0.040	0.843
cvlt-short term free recall	0.000	0.999
Cvlt short cued recall	0.219	0.273
Cvlt free long term recall	0.281	0.155
cvlt cued delayed	-0.079	0.695
Trail making test	0.399	0.039*
COWAT semantic	0.024	0.906
COWAT phenomic	-0.198	0.333

Conclusions: Vitamin D deficiency in patients with SLE could have a significant impact on their cognitive performance.
References:
[1] Carbotte R. M., Denburg S. D. and Denburg J. A., "Cognitive Dysfunction and Systemic Lupus Erythematosus," In: R. G. Lahit, Ed., Systemic Lupus Erythematosus, Churchill Livingstone, New York, 1992, pp. 865–881.
[2] Etgen T, Sander D, Bickel H, Sander K, Forstl H. Vitamin D deficiency, cognitive impairment and dementia: a systematic review and meta-analysis. Dement Geriatr Cogn Disord. 2012; 33:297–305.
[3] Balion C, Griffith LE, Strifler L, Henderson M, Patterson C, Heckman G, et al. Vitamin D, cognition, and dementia: a systematic review and meta-analysis. Neurology. 2012; 79:1397–405.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5713

AB0506 PREGNANCY OUTCOMES IN WOMEN WITH RHEUMATIC DISEASES: A SINGLE CENTER-STUDY

I. Añón Oñate, I. Notario Ferreira, P. Morales Garrido, M.Á. Ferrer González, C. Caro Hernández, L. Pérez Albaladejo, M.J. Soto Pino, A. González Utrilla, E. Raya Álvarez, R. Cáliz Cáliz. *Rheumatology, Complejo Hospitalario Universitario de Granada, Granada, Spain*

Background: Systemic Lupus Erythematosus (SLE), Antiphospholipid Syndrome (APS) and Thrombophilia are associated with considerable pregnancy-related morbidity. Multidisciplinary teams allows the application of an experienced protocol to monitor and treat them during pregnancy in order to reduce adverse pregnancy outcomes and this way improve the prognosis of the pregnancy.
Objectives: To investigate pregnancy outcomes in women with rheumatic diseases and thrombophilia from a Spanish cohort.
Methods: A population of 93 patients diagnosed with SLE, APS and Thrombophilia atended in a specialized multidisciplinary unit of Rheumatic Diseases and pregnancy from the Complejo Hospitalario Universitario de Granada, Spain from January 2012 to December 2016. The following variables were collected: age, presence of antiphospholipid antibodies and anti Ro, thrombotic episodes and prior abortions, treatment during pregnancy, obstetric outcomes births/abortion and pregnancy length. The statistical analysis was done using the McNemar Test.
Results: 93 pregnant women were included in the study. 26 were diagnosed with SLE, 32 with APS and 35 with Thrombophilia (mostly, Heterozygotes for MTHFR gene). 47.3% were younger than 35 years and 52.7% were elder than 35 years. 66.7% had one or more prior abortions, meaning a total record of 159 abortions and an average of 1.71±1.76 abortions per patient. The treatment received by the patients is specified in table 1. 9 patients (3 APS and 6 thrombophilia) received a treatment with intravenous gammaglobulin with doses of 400 mg/kg, apart from Low-Molecular-Weight Heparin (LMWH) and Acetylsalicylic Acid (ASA), two days in a row at the beginning and then every three weeks during the whole pregnancy. 90 (96.8%) pregnancies were developed. 6 of them were preterm pregnancies and 84 were term pregnancies. Only 3 abortions (3.2%) occurred in the patients monitored in our unit. The reduction in the number of abortions was statistically significant ($p<0.001$). Regarding those 3 registered abortions, 2 were patients diagnosed with SLE, with no records of previous abortions and they occurred during the second trimester of pregnancy. 1 was diagnosed with APS and she had records of 2 previous abortions and occurred during the first trimester of pregnancy. Those patients who received treatment with gammaglobulin iv showed an mean of 4.88±1.85 previous abortions per patient and all had a term delivery (100%).

Table 1. The treatment received by the patients

	SLE (n=26)*	APS (n=32)*	Thrombophilia (n=35)
Patients treated with LMWH, n*	2	2	23
Patients treated with ASA, n*	9	1	3
Patients treated with LMWH + ASA, n*	5	29	8
Patients without prophylactic treatment, n	10	0	1

*Systemic Lupus Erythematosus (SLE), Antiphospholipid Syndrome (APS), Low-Molecular-Weight Heparin (LMWH), Acetylsalicylic Acid (ASA).

Conclusions: Our results demonstrate a decrease in the number of abortions and a larger number of term pregnancies since the inclusion of patients with high risk pregnancies in our unit. Prophylactic treatment is effective for the prevention of abortions, reaching higher rate live birth pregnancies. The multidisciplinary evaluation is essential to prevent complications in women diagnosed with rheumatic diseases with high obstetric risk.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6549

AB0507 COBALAMIN (VITAMIN B12) STATUS IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME (APS), ITS ASSOCIATION WITH ATHEROSCLEROTIC VASCULAR LESIONS

I. Segeda[1], S. Shevchuk[1], I. Kuvikova[1], O. Shevchuk[2], I. Segeda[3], S. Shevchuk[3], I. Kuvikova[3], O. Shevchuk[3]. *[1]Rheumatology, Institute of Invalid Rehabilitation; [2]Rheumatology, Vinnitsya National Medical University, Vinnitsya, Ukraine; [3]Affiliation not provided*

Background: Cobalamin (vitamin B12) insufficienty is associated with the development of many diseases. It is known that the growth of clinical and subclinical manifestations of atherosclerotic vascular lesions are often associated with low cobalamin level. Cobalamin status is unknown in patients with antiphospholipid syndrome (APS). There are no data about the role of folic acid in the development of atherosclerotic vascular lesions in patients with APS
Objectives: To evaluate vitamin B12 status in patients with APS and to explore its relationship with atherosclerotic vascular lesion.
Methods: We observed 82 patients with APS and 37 healthy individuals. Content of cobalamin (vitamin B12) in serum were determined by immunochemical detection (ECLIA). Cobalamin level above 200 pg/ml was considered as normal within 200–300 pg/mL - both extremely low, below 200 pg/ml - insufficienty. All patients were underwent detection of endothelial dysfunction - dilatation of brachial artery endothelium, investigation of "intima-media" thickness of common carotid artery (IMT) and the presence of atherosclerotic plaques (AP).
Results: In patients with APS we recorded a significant reduction of cobalamin in the serum (351±14,3 pg/mL (95% CI: 148–562 pg/mL) compared to control group (445±18,1 pg/mL (95% CI: 272–622 pg/mL). Indicators of cobalamin status in patients with secondary APS were significantly worse than patients with primary APS. Thus, in patients with secondary APS cobalamin content was on 26.7% lower (95% CI: 140–559 pg/ml) than in the control group. In patients with primary APS cobalamin content was on 13.0% lower (95% CI: 202–565 pg/ml) than in controls, but 18.7% higher than in patients with secondary APS. Cobalamin (vitamin B12) insufficienty is accompanied by significant thickening of the walls of the common carotid artery. Thus, in patients with cobalamin deficiency IMT was on 17% higher than that in patients with optimal levels of the vitamin. Cobalamin deficiency is also associated with endothelial dysfunction. Thus, in patients with vitamin deficiency dilatation of brachial artery was significantly, by 48.6% less than in people with normal vitamin B12 status. The share of people with the presence of atherosclerotic plaques, transient ischemic attack (TIA), stroke, myocardial infarction (MI) and angina in patients with cobalamin deficiency was also higher.
Conclusions: Thus, in patients with APS low cobalamin status is associated with subclinical manifestations of atherosclerotic vascular lesions.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3006

AB0508 EFFECT OF ALCOHOL CONSUMPTION AND SMOKING ON DISEASE DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS: DATA FROM KOREAN LUPUS NETWORK (KORNET) REGISTRY

J.N. Kim, S.-K. Kim, J.-Y. Choe, C.U. Lee. *Division of Rheumatology, Department of Internal Medicine, Catholic University of Daegu School of Medicine, Daegu, Korea, Republic Of*

Objectives: We assessed correlations of smoking habits and alcohol consumption with disease activity or damage in patients with systemic lupus erythematosus (SLE).
Methods: A total of 505 patients with SLE were enrolled in the KORean lupus Network (KORNET) SLE registry from January 2014 to January 2016. Disease activity and organ damage were measured by the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index, respectively. Multivariate logistic regression analysis was used to analyze associations with cutaneous lesions.
Results: There are no differences in SLEDAI-2K and SLICC/ACR damage indexes according to either smoking status or alcohol consumption. More frequent cutaneous damage was observed in current alcohol drinkers compared to non-current alcohol drinkers (p=0.020). Cutaneous damage was significantly associated with alcohol consumption [Odds ratio (OR) 4.048, 95% confidence interval (CI) 1.251 – 12.102, p=0.020]. Both low (1–5 glasses/week) and high (≥6 glasses/week) amounts of alcohol consumption had a significant impact on cutaneous damage compared to the absence of current alcohol consumption (p=0.033 and p=0.027, respectively). Pairwise comparison of alcohol consumption and smoking status with cutaneous damage showed that only alcohol consumption was significantly associated with the presence of cutaneous damage, compared to non-current alcohol consumption and non-current smoking (OR 3.513, 95% CI 1.130 – 10.920, p=0.030).
Conclusions: Current alcohol consumption, but not smoking, might influence the development of cutaneous damage in patients with SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3070

AB0509 IDENTIFICATION OF NOVEL BIOMARKERS ASSOCIATED WITH DISEASE ACTIVITY OF PRIMARY SJÖGREN'S SYNDROME AND CLINICAL RESPONSE TO VAY736

J. Doucet[1], R. Kazma[1], M. Cabanski[1], E. Kamphausen[1], P. Maguire[1], A. Avrameas[1], M.-A. Valentin[1], Y. Li[2], A. Auger-Sarrazin[1], S. Kaiser[1], P. Follet[1], S. Oliver[3], A. Vitaliti[1]. *[1]Translational Medicine/Biomarker Development, Novartis Institutes for Biomedical Research; [2]Global Development NPH, Novartis AG; [3]Translational Medicine, Novartis Institutes for Biomedical Research, Basel, Switzerland*

Background: Overexpression of B cell activating factor (BAFF) contributes to the pathogenesis of primary Sjögren's syndrome (pSS) [1]. Treatment of pSS patients with VAY736, an anti-human BAFF receptor mAb, appears promising and was associated with a positive therapeutic effect [2]. Given the complexity and heterogeneity of pSS, there is a need to further identify molecular mechanisms involved in pSS and in response to new therapeutics.
Objectives: To address this question, we assessed a panel of biomarkers in 27 patients from a clinical trial and tested their associations with pSS activity and clinical response to VAY736.
Methods: This study comprised 27 pSS patients treated with a single intravenous dose of VAY736 at 10 mg/kg (n=12), 3 mg/kg (n=6), or placebo (n=9). The disease activity scores included EULAR Sjogren's Syndrome Disease Activity Index (ESSDAI) and Patient Reported Index (ESSPRI), patient's and physician's reported visual analog scales (VAS), Short-Form 36 and Multidimensional Fatigue Inventory (MFI). BAFF and a panel of chemokines in serum and saliva were assessed using immunoassays. Circulating B cells and B cell subsets were measured by flow cytometry. High frequency ultrasound (US) of the parotid and sub-mandibular glands measured gland thickness and quality using a 4 point scoring (de Vita) [3]. Shear wave elastography of the parotid glands was also measured. All biomarkers were measured at baseline (BL) and post-treatment w6, w12, w24. The effect of VAY736 on biomarker levels was assessed by descriptive statistics. Correlations between biomarkers and disease activity scores were calculated at BL and w6, w12, and w24 using levels and relative changes from BL.
Results: In addition to B cell depletion, serum BAFF increase, and improvements in US and elastography measures [2], a subset of serum chemokine tended to be reduced nine weeks after VAY736 treatment. Pooling all 27 patients, salivary BAFF levels correlated with parotid De Vita scores at BL (left: r=0.75, right: r=0.72, $p<10^{-4}$ for both) and w6 (left: r=0.72,; right: r=0.78, $p<10^{-4}$ for both) but not at later time points. Pooling the 18 VAY736 treated patients, increase in salivary BAFF correlated with decrease in MFI at w6 (r=-0.83, $p=3\times10^{-4}$) and high levels of one of the serum chemokines at BL correlated with decrease in ESSPRI at w24 (r=-0.76, $p=3\times10^{-4}$). In the same patients, the B cell count at BL correlated with changes in several clinical outcomes at w12: ESSPRI (r=-0.65, p=0.01), Physician's VAS (r=-0.6, p=0.01), shear wave (r=-0.63, p=0.02), and parotid thickness (r=-0.6, p=0.03).
Conclusions: We identified a set of markers correlated with clinical outcomes in pSS after treatment with VAY736, which have the potential to provide additional insight in pSS and treatment-modifying effects. Further large-scale studies are necessary to confirm the value of these markers.
References:
[1] Varin MM et al. Autoimmun Rev 2010;9(9):604–8.
[2] Dörner T et al. Arthritis Rheum 2016; 68(suppl S10):4051.
[3] De Vita S, et al. Clin Exp Rheumatol 1992;10:351–6.
Disclosure of Interest: J. Doucet Employee of: Novartis AG, R. Kazma Employee of: Novartis AG, M. Cabanski Employee of: Novartis AG, E. Kamphausen Employee of: Novartis AG, P. Maguire Employee of: Novartis AG, A. Avrameas Employee of: Novartis AG, M.-A. Valentin: None declared, Y. Li Employee of: Novartis AG, A. Auger-Sarrazin Employee of: Novartis AG, S. Kaiser Employee of: Novartis AG, P. Follet Employee of: Novartis AG, S. Oliver Employee of: Novartis AG, A. Vitaliti Employee of: Novartis AG
DOI: 10.1136/annrheumdis-2017-eular.4736

AB0510 NEUROPSYCHIATRIC MANIFESTATIONS AND DISEASE ACTIVITY IN POLISH COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

K. Pawlak-Bus, M. Spalek, P. Leszczynski. *Department of Rheumatology and Rehabilitation, University of Medical Sciences, Poznan, Poland*

Background: Neuropsychiatric systemic lupus erythematosus (NPSLE) is defined as wide range of neurological and psychiatric symptoms due to inflammation and ischemic processes. It is difficult to recognize primary NPSLE because of multiple central and peripheral symptoms.
Objectives: The aim of the study was to identified and classified the group of NPSLE patients with evaluation of disease activity.
Methods: We observed clinical neuropsychiatric (NP) manifestations in the cohort of 128 Polish patients with SLE. All patients with suspicion of NP symptoms had neuropsychological and imaging examinations. Symptoms of NPSLE were observed in 38 (30%) patients (34 female and 4 male) with average age 38±6 years (range 18–61 yrs), average disease duration 6,6±5,6 years (range 1,0 - 18,0 yrs). Patients were treated with oral and pulse glucocorticoids (GC) and 89% of them standard immunosuppressive drugs (CYC, MMF, AZA,MTX, CsA). As a background therapy 82% of these patients were on chloroquine or hydroksychloroquine (CQ/HCQ). All patients were assessed according to Systemic Lupus Erythematosus Disease Activity Index by SLEDAI (version 2000), Physical Global Assessment (PGA) and damage index (SDI).
Results: Central and peripheral NPSLE symptoms were recognized and categorized (Tab 1). All NPSLE patients had symptoms from central nervous system, but only 16% (n=6) of them had peripheral lupus manifestations. Mean SLEDAI score at NP event was very high 29±9,6, but mean SLEDAI score without NP symptoms was 15±8,3 and was connected with musculoskeletal, mucocutaneous, renal and hematological domains respectively n=29, 76%; n=23, 60%; n=11, 29%; n=8, 21%. Low disease activity was estimated at 3% of patients examined.Most of lupus patients (n=37, 97%) had moderate or high disease activity regardless of NP symptoms. In our study group lupus patients during NPSLE symptoms were immunologically active with increased anti-dsDNA antibodies (n=30, 78%) and/or lower complements C3 and/or C4 levels (n=21, 55%).
Conclusions: In Polish lupus cohort we observed more frequently lupus-related primary neuropsychiatric symptoms from central nervous system, especially cognitive dysfunctions, mood disorders, cerebrovascular events. Clinical activity of NPSLE patients was rather high and definitely most of patients were immunologically active despite aggressive immunosuppressive treatment and with standard background therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4265

AB0511 VITAMIN D: POTENTIAL ROLE IN ANTIPHOSPHOLIPID SYNDROME

L. Riancho-Zarrabeitia[1], M. Cubería[2], S. García-Canale[2], G. Daroca[2], M. García-Unzueta[3], J.L. Hernández[4], M. López-Hoyos[5], P. Muñoz[2], M. Agudo[1], V. Martínez-Taboada[1]. *[1]Rheumatology; [2]Hospital Universitario Marqués de Valdecilla, Santander, Spain; [3]Biochemistry; [4]Internal Medicine; [5]Immunology, Hospital Universitario Marqués de Valdecilla, Santander, Spain*

Background: Vitamin D, due to its immunoregulatory properties, has been implicated in the pathogenesis of autoimmune diseases, such as antiphospholipid syndrome (APS).
Objectives: A) To determine vitamin D levels in patients with primary APS and to compare them with patients with positive antiphospholipid antibodies (aPL), not meeting clinical criteria for APS, and with healthy controls. B) To analyze the association of the vitamin D levels with both the clinical manifestations and the immunological profile of patients with primary APS.
Methods: We conducted a retrospective study including patients attended at the rheumatology clinic from a tertiary facility in Northern Spain. We included 74

patients with primary APS, 54 patients with positive aPL serology not meeting clinical criteria for APS and 326 healthy controls adjusted by the month of vitamin D analysis. We considered 30 ng/ml and 10 ng/ml as the thresholds for vitamin D insufficiency and deficiency, respectively.
Results: Median levels of vitamin D were similar in the three groups: 21 (range 5–69) in primary APS, 25 (4–50) in the aPL-positive group, and 21 (4–105) in controls. Overall, 53.9% of measurements were performed during the sunny season (April to September). Ten percent of patients with primary APS were males, versus 16% in the aPL serology group and 26% among healthy controls (p=0.007). Mean age was 46±15 in primary APS, 49±17 in the aPL-positive group and 53±10 in the control group (p<0.001). Regarding vitamin D insufficiency, 82% of APS patients had levels of vitamin D (<30 ng/ml) versus 70% and 72% of patients with aPL serology and controls, respectively (p=0.168). When analyzing the prevalence of vitamin D deficiency (<10 ng/ml), we found significant differences across the groups: 16.2% in patients with primary APS, 11.1% in patients with positive serology and only 4.9% in healthy controls (p=0.002). There was no significant association between insufficient levels of vitamin D and the presence of thrombotic or obstetric events. Nevertheless, we found a trend for the presence of more thrombotic events in patients with vitamin D deficiency (p=0.097). Regarding the immunological profile, we found no association between vitamin D and either the number of positive antibodies or their serological evolution. However, we found an association between insufficient levels of vitamin D and the presence of lupus anticoagulant (54.7% vs 18.2%, p=0.047)
Conclusions: More than 80% of patients with primary APS have insufficient levels of vitamin D and 16% of them have very low levels of vitamin D.
Primary APS patients show a higher frequency of vitamin D deficiency than healthy controls.
Patients with vitamin D insufficiency have more commonly positivity for lupus anticoagulant.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5129

AB0512 EPIDEMIOLOGICAL, CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS OF ANTIPHOSPHOLIPID SYNDROME: STUDY OF 170 PATIENTS

L. Riancho-Zarrabeitia, S. García-Canale, M. Cubería, G. Daroca, M. López-Hoyos, P. Muñoz, M. Agudo, V. Martínez-Taboada. *Hospital Universitario Marqués de Valdecilla, Santander, Spain*

Background: Antiphospholipid syndrome (APS) is an autoimmune disease defined by the presence of antiphospholipid antibodies (aPL) and thrombosis and/or pregnancy morbidity. Although thrombotic and obstetric APS are considered the same disorder, there are pathogenetic and clinical differences between them.
Objectives: To describe the epidemiological, clinical and immunological characteristics of a cohort of APS patients from a defined population and to study the differences between thrombotic, obstetric and mixed APS.
Methods: Retrospective study including patients attending the rheumatology and the obstetric clinics of a tertiary facility in Northern Spain. All patients met APS classification criteria.
Results: We included 84 patients with thrombotic APS, 76 with obstetric APS and 10 with mixed APS. Main demographical characteristics are showed in table. There were differences in the age of discovery a positive serology (46±15 yr in thrombotic APS, 36±8 yr in obstetric, and 36±14 in mixed APS). Moreover, the prevalence of systemic lupus erythematosus (SLE) was higher in patients with thrombotic and mixed APS (26% and 30% vs 5% in obstetric APS, p=0.001). Anticardiolipin antibodies were, overall, the most frequently positive. Lupus anticoagulant was significantly more common in patients with thrombotic and mixed APS (70% and 71% vs 30% in obstetric APS, p=0.002). We found no differences in the load of antibodies between the three groups. Regarding traditional cardiovascular risk factors (CVRF), tobacco use was the most common, followed by hypertension and dyslipidemia. The last two factors were more frequent in patients with thrombotic and mixed APS than in those with obstetric APS (p<0.001). As expected, treatment with heparin was more frequent in obstetric and mixed APS, while oral anticoagulants were more frequently used in thrombotic APS. Antimalarial drugs were less frequently used in obstetric APS (17% vs 37% and 30%, p=0.020), probably due to a lower prevalence of lupus in this group.

	Total 170	Thrombotic APS 84	Obstetric APS 76	Mixed APS 10	P
Age (yr), mean ± SD	41,2±13,7	46.5±15.5	35.9±8.1	36.5±14.4	<0.001
SLE, n (%)	29 (17)	22 (26)	4 (5)	3 (30)	0.001
Load of antibodies				0.201	
– 1	63 (37)	24 (29)	34 (45)	5 (50)	
– 2	68 (40)	37 (44)	28 (37)	3 (30)	
– 3	38 (22)	23 (27)	13 (17)	2 (20)	
aCL	130 (77)	67 (80)	54 (72)	9 (90)	0.306
aB2Gp1	108 (64)	56 (67)	49 (65)	3 (30)	0.070
LA	53 (58)	40 (70)	8 (30)	5 (71)	0.002
Family history of thrombosis, n (%)	21 (19)	14 (29)	4 (7)	3 (50)	0.011
Traditional CV risk factors, n (%)					
Tobacco use	69 (41)	37 (44)	28 (37)	4 (40)	0.650
Hypertension	55 (32)	41 (49)	10 (13)	4 (40)	<0.001
Dyslipidemia	48 (28)	39 (46)	5 (7)	4 (40)	<0.001
Diabetes mellitas	8 (5)	4 (5)	4 (5)	0	0.761
Previous treatment, n (%)					
Heparin	88 (52)	28 (33)	54 (72)	6 (60)	<0.001
Oral anticoagulants	71 (42)	62 (74)	3 (4)	6 (60)	<0.001
Antiplatelet therapy	145 (86)	63 (76)	74 (97)	8 (80)	<0.001
Corticoids	5 (3)	5 (6)	0	0	0.072
Antimalarials	47 (28)	31 (37)	13 (17)	3 (30)	0.020
Immunosuppressants	5 (3)	4 (5)	1 (1)	0	0.371

Conclusions: In our cohort, patients with thrombotic or mixed APS have a higher frequency of SLE than patients with obstetric APS. Positivity for lupus anticoagulant is more common in patients with thrombotic or mixed APS. Regarding traditional CVRF, hypertension and dislypidemia are more common in patients with thrombotic or mixed APS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4338

AB0513 FATIGUE IN CHINESE PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A CROSS SECTIONAL STUDY

L. Li[1], Y. Cui[1], S. Chen[1], Q. Zhao[1], L. Li[2], Z. Gu[1]. *[1]Department of Rheumatology, Affiliated Hospital of Nantong University; [2]School of Nursing of Nantong University, Nantong, China*

Background: Primary Sjögren's syndrome (pSS) is the second most common systemic autoimmune disease, with a female-male ratio of 9:1, and characterized by sicca symptoms of the eyes and mouth, including joint pains and multi-system involvement. pSS affects patients' health-related quality of life (QoL), mental status and relationships with family. In pSS patients, symptoms such as fatigue, depression, arthralgia, fibromyalgia and general loss of well-being are commonly reported. Among them, fatigue is the most common problem that includes physical and mental fatigue, it can be as disabling as pain, which is difficult to manage and has a notable impact on QoL. Fatigue is a tiredness which may be mental, physical, or both, and that results in an inability to function at normal performance levels. However, the underlying pathophysiological mechanisms of fatigue remain unclear. A number of studies have reported the association of fatigue with Primary Sjögren's syndrome (pSS), whereas, because of the small sample size of pSS patients, we still lack large sample studies to find the relationship between pSS and fatigue.
Objectives: To investigate the relationship of fatigue severity to other clinical features in primary Sjögren's syndrome (pSS) and to identify factors contributing to the physical and mental aspects of fatigue in Chinese patients.
Methods: Sixty-seven consecutive patients with PSS according to the American-European Consensus group (AEGG) criteria were included. Demographic, clinical and biological characteristics for all patients were collected. The Fatigue Severity Scale (FSS), Profile of Fatigue (ProF), Visual analogue scale, Hospital Anxiety and Depression Scale (HADS), OHIP-14 Scale, MDADI Scale and PSQI Scale were adopted to assess fatigue, depression, anxiety, xerostomia, xerophthalmia and sleep disturbances. Associations with fatigue were compared using multivariate regression.
Results: 94% of our patients were women. The mean age of patients was 51.13±13.23 years, and the mean disease duration was 4.12±4.49 years. The mean oral dryness was 51±17.82, and the mean ocular dryness was 33.56±26.3. Abnormal fatigue, defined as an FSS score >or=4, was present in 64% of the patients. Dry symptoms, low educational level, Pain and depression had a negative impact on fatigue scores. The regression models explained that Pain and depression were the strongest predictors of fatigue according to the FSS.
Conclusions: Fatigue is a tiredness which may be mental, physical, or both, and that results in an inability to function at normal performance levels. However, the underlying pathophysiological mechanisms of fatigue remain unclear. From our study, we found that psychosocial variables are determinants of fatigue, and fatigue is associated with depression, but depression is not the primary cause of fatigue in primary SS. Therefore, the investigation of the pathophysiologic correlates of physical and mental aspects of fatigue is needed to guide the development of more effective interventions.
Acknowledgements: This study was supported by National Natural Science Foundation of China (81401124);the Collaborative Innovation Program of Affiliated Hospital of Nantong University; College graduate research and innovation of Jiangsu Province (KYZZ16–0358, KYZZ15–0353).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3076

AB0514 THE RELATIONSHIP BETWEEN SERUM LEVEL OF C-TERMINAL TELOPEPTIDE OF TYPE I COLLAGEN WITH COURSE OF SYSTEMIC LUPUS ERYTHEMATOSUS AND STRUCTURAL AND FUNCTIONAL STATE OF BONE TISSUE

S. Shevchuk, L. Denyschych, L. Marynych. *National Pirogov Memorial Medical University, Vinnytsya, Ukraine, Vinnytsya, Ukraine*

Background: It is well known, that the incidence of osteoporosis in patients with systemic lupus erythematosus (SLE) is higher compared to the population level. Its severity in patients with SLE is associated with a number of factors: female gender, disease activity, damage index, glucocorticoid therapy etc. One of metabolic factors indicating the reducing bone mineral density (BMD) is the level

of C-terminal telopeptide of type I collagen (CTX). Its place in the formation of osteoporosis in SLE patients is poorly understood, as well as its relationship with the course of the disease.
Objectives: The aim of study was to determine serum level of CTX in the SLE patients and its relationship with structural and functional state of bone tissue, course of the disease.
Methods: The study involved 58 SLE women (study group) and 29 healthy individuals (control group) representative by age and gender. The mean age of patients was 45,11±1,03 years. For every patient data were recorded on age, body mass index (BMI), chronic SLE damage (SLICC/ACR DI) and disease activity score (SLEDAI), cumulative glucocorticoid dose, serum concentrations of interleukin-6 (IL-6) and C-reactive protein (CRP), bone resorption marker (CTX). Serum concentration of CTX was determined using ELISA test system "Nordic Bioscience Diagnostics A/S". Changes in BMD of the lumbar spine and proximal hip were determined by Dual-energy X-ray absorptiometry.
Results: It was established, that in patients with SLE serum level of C-terminal telopeptide of type I collagen was 1,15±0,03 ng/ml, while in the control group – 0,83±0,03 ng/ml, or was higher more than 19,0%. Violation of bone remodeling in patients with SLE was associated with reduced BMD, increased incidence of osteopenia and osteoporosis. Thus, the mean concentration of CTX in patients with osteoporosis was 1,63±0,04 ng/ml, while in patients with normal bone – 1,0±0,03 ng/ml. In SLE patients with osteopenia the level of C-terminal telopeptide of type I collagen was 1,23±0,04 ng/ml (higher more than 23% compared with the control group). Increased CTX practically had no correlation with age, duration of the disease, smoking and BMI. At the same time the serum CTX was associated with chronic SLE damage index (r =0,51), SLEDAI disease activity (r =0,41), concentration of IL-6 (r =0,45) and CRP (r =0,44)
Conclusions: Alterations of bone metabolism were found in 19% female SLE patients in the form of increasing serum CTX and closely associated with the severity and activity of the disease, high levels of CRP and IL-6 and did not depend on the age, disease duration, smoking and body mass index.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5770

AB0515 SKIN MANIFESTATIONS AS INDEPENDENT PREDICTORS AND THE INITIAL RISK FAKTORS FOR SYSTEMIC ANTIPHOSPHOLIPID EVENTS

L. Stojanovich, A. Djokovic, N. Stanisavljevic, M. Zdravkovic. *Internal Medicine Department, University Hospital Center Bezanijska Kosa, Belgrade, Serbia*

Background: Antiphospholipid syndrome (APS) patients express skin manifestations with the presence of various levels of antiphospholipid antibodies (aPL).Several studies have shown the frequency of dermatological manifestations with APS[1,2,3], including livedo reticularis, cutaneous ulcers, acrocyanosis, and other.
Objectives: Dermatological manifestations can be the initial clue in the diagnosis of this disease.
Methods: Our study includes a total of 508 APS patients; 360 were PAPS patients (283 female and 77 male, mean age 44.0±12.9 years),148 had APS associated with SLE/SAPS (133 female and 15 male,mean age 47.7±14.8 years).aPL analysis included:LA, aCL (IgG/IgM), β_2GPI (IgG/IgM).In all patients, we collected data considering frequently occured skin lesions.
Results: Our results showed prevalence of skin manifestations in SAPS group of patinenst regading to PAPS (Table 1). Patients with skin manifestations overall had higher prevalence of thrombosis (Table 2).

Table 1. Prevalence of skin manifestations analyzed in PAPS and SAPS group

	PAPS (N=360)	SAPS (N=148)	p
Livedo	46 (12.8%)	86 (58.1%)	**0.0001**
Skin ulcerations	31 (8.6%)	47 (31.8%)	**0.0001**
Pseudovasculitis lesions	34 (9.4%)	72 (48.6%)	**0.0001**
Superfitial cutaneous necrosis	9 (2.5%)	25 (16.9%)	**0.0001**
Digital gangrene	3 (0.8%)	14 (9.5%)	**0.0001**
Skin manifestations overall	98 (27.2%)	113 (76.4%)	**0.0001**

Table 2. Skin manifestations and thrombosis

	PAPS (p values)	SAPS (p values)
Livedo	0.038	0.062
Skin ulcerations	0.024	**0.004**
Pseudovasculitis lesions	0.007	**0.019**
Superfitial cutaneous necrosis	0.005	0.380
Digital gangrene	1.000	**0.008**
Skin manifestations overall	0.0001	**0.076**

Conclusions: Dermatological manifestations can be very often the initial symptoms of severe manifestations of APS.Our study showed that patients with secondary APS had higher prevalence of skin lesions, and that some aPL types were risk factors for thrombotic manifestations in APS patients
References:
[1] Toubi E, Krause I, Fraser A, Lev S, Stojanovich L, Rovensky J, et al. Livedo reticularis is a marker for predicting multi-system thrombosis in antiphospholipid syndrome. Clin Exp Rheumatol 2005;23:499–504.
[2] Weinstein S, Piette W. Cutaneous manifestations of antiphospholipid antibody syndrome. Hematol Oncol Clin North Am 2008;22:67–77.
[3] Asherson RA, Cervera R, Klumb E, Stojanovich L. et all.: Amputation of Digits or Limbs in Patients with Antiphospholipid Syndrome. 21 January 2008. Seminars in Arthritis and Rheumatism. 2008; 38: 124–31.
[4] Stojanovich L, Markovic O, Marisavljevic D et all. Influence of antiphospholipid antibody levels and type on thrombotic manifestations: results from the Serbian National cohort study. Lupus 2011;0: 1–8.
[5] Stojanovich L, Kontic M, Djokovic Aet all. Association between Systemic Non-criteria APS Manifestations and Antibody Type and Level: Results from the Serbian National Cohort Study. Clinical and Experimental Rheumatology, 2013,31(5):756–60.
Acknowledgements: This work was supported by research grant number 175041 for 2011 - 2017, issued by the Ministry of Science of the Republic of Serbia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2759

AB0516 INCIDENCE OF CANCER IN A COHORT OF PATIENTS WITH PRIMARY SJÖGREN SYNDROME

M. Brom, S. Moyano, M. Scolnik, L.E. Pompermayer, I.J. Gandino, E.R. Soriano. *Rheumatology, Hospital Italiano de Buenos Aires, Ciudad Autónoma de Buenos Aires, Argentina*

Background: The most severe complication of Sjögren Syndrome is the development of lymphoproliferative processes. Several neoplasia have been associated with the disease, being non-Hodgkin lymphoma the most frequent one.
Objectives: Our objective was to evaluate incidence of cancer in a cohort of patients with primary Sjögren Syndrome.
Methods: A retrospective descriptive study was performed in a university hospital with its own health insurance and captive population. Using electronic medical records and laboratory database were review the entries performed between 01/01/2000 and 12/31/2015. We analyzed those patients with either diagnosis of Sjögren Syndrome, complain of dry mouth/eyes, or positive antibodies anti-Ro/SSA and anti-LA/SSB.
Among these patients, we included those fulfilling either ACR 2012 or EULAR 2002 Sjögren criteria, or those who were diagnosed as Primary Sjögren Syndrome by the treating rheumatologist even if they did not fulfill criteria.
We then proceeded to register and analyze demographic, clinical and histopathologic information available on their clinical records.
Results: One hundred fifty-seven patients with Primary Sjögren Syndrome were identified. Female accounted for 95.5% of the cohort; mean age at diagnosis was 49.4 years (SD 19). Median follow-up time was 7.7 years (IQR 8). The development rate and type of neoplasia was the following:

- Lymphomas: Three (Two MALT lymphomas of the parotid and one disseminated non-Hodgkin lymphoma). Density of Incidence 260/100,000 person/year (CI 95%: 50 – 750/100,000 person/year)
- Multiple Myeloma: One
- Skin (non-melanoma) neoplasia: Four
- Solid organ Neoplasia: Seven (Four breast cancer, one lung cancer, one uterus cancer, one tongue cancer). Density of Incidence 600/100,000 person/year (CI 95% 240 – 1240/100,000 person/year)

Univariate analysis showed association between lymphoma and cryoglobulinemia (p=0.01; OR=5,8), low C4 fraction of complement (p=0.01; OR=5,1), anemia (p=0.02; OR=1,96) and leucopenia (p=0.03; OR=1,67)
Conclusions: Development of cancer is a known complication of Primary Sjögren Syndrome. The association between lymphoma and cryoglobulinemia, low C4 fraction of complement, anemia and leucopenia enhances the importance of periodic screening for neoplasms among this subgroup of patients with Primary Sjögren Syndrome.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3195

AB0517 PREDICTIVE FACTORS FOR INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

M. Kechida[1], N. Lorenzo[2], R. Klii[1], S. Hammami[1], I. Khochtali[1]. *[1]Internal Medicine and Endocrinology Department, Fattouma Bourguiba Hospital, Monastir, Tunisia; [2]Internal Medicine and cancerology Department, Saint-Cyr Hospital, Lyon, France*

Background: it's known that infection could complicate the course of systemic lupus erythematosus (SLE) because of the immune status or the long term steroids and immunosuppressors.
Objectives: This study was aiming at determining the prevalence of infectious complications during SLE and their predictive factors.
Methods: A retrospective bi-centric analyzes of 289 patients diagnosed as SLE between January 2004 and December 2016 according to the ARA criteria of 1997 was conducted. A descriptive analysis of infectious complications was first made, then a comparative study between patients with (group 1) and without (group 2) infectious complications was performed to detect predictive factors.
Results: Mean age was 84.6±13 years (14–72 years) with a sex ratio F/M=6.

Cardiac involvement and lupus nephritis (LN) were developed in 20% of patients. About 13.75% of patients had neurological manifestations, 26.5% articular complications, 16% vascular involvement and 10% of them developed infectious complications. Eight percent of these infections were diagnosed concomitantly with the diagnosis of SLE and 92% of them after the diagnosis of lupus with an average of 25 months. About 52.9% of the patients developed more than 2 episodes of infection. The spectrum of infectious complications was: pulmonary in 33.3%, urinary in 22.2% and cutaneous in 13.9%. Tuberculosis was the most frequent infection 12.5%. Lupus flare complicated the infection in 28.6% of patients with mean SLEDAI score at 10. Comparative study between group 1 and group 2 revealed that LN, corticosteroids and immunosuppressors were associated with a high risk of infection (p=0.002, p=0.017 and p=0.034 respectively). In multivariate analysis only LN was an independent predictive factor (OR=3.5, 95% CI=1.06-12.87, p=0.049).

Conclusions: Infections may complicate the course of SLE with flares presenting in 1/3 of cases. Half of the patients had more than 2 episodes of infection during their follow up. The presence of LN represents a predictive factor of such complication.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3009

AB0518 NEW 2016 ACR/EULAR CLASSIFICATION CRITERIA FOR SJÖGREN SYNDROME: USEFULNESS AND APPLICABILITY IN CLINICAL PRACTICE

M. Retuerto Guerrero[1], L. Sierra Herranz[2], C. Moriano Morales[1], C. Iñiguez Ubiaga[1], M. Garijo Bufort[1], A. Crespo Golmar[1], C. Álvarez Castro[1], E. Díez Álvarez[1], A. López Robles[1], M. Martín Martínez[1], T. Perez Sandoval[1]. *[1]Rheumatology Department; [2]Pneumology Department, University Health Care Complex of León, Leon, Spain*

Background: The Sjögren syndrome (SS) is an autoimmune disease where the cellular and humoral mechanisms affect the exocrine glands. In 2016, new classification criteria validated by ACR and EULAR were established.

Objectives: To compare the new criteria with those used so far in our hospital, as well as to assess the need for changes in the current diagnostic strategy.

Methods: Retrospective observational study in which 65 patients diagnosed with SS at the Hospital of León were randomly included. We reviewed the diagnostic tests performed and the fulfilment of the different classification criteria developed since 1993. Other variables studied were: sex; age at the time of diagnosis and the months from the onset of symptoms; xerostomia and xerophthalmia; extraglandular involvement, ESSDAI; immunosuppression; Raynaud; lymphoma development; and analytical alterations.

Results: The mean age at the time of diagnosis was 54.9 years ±14 | 23–82 |, with an average of months from the onset of symptoms to the diagnosis of 10.2±9.5 | 0–36|. 90.8% were women. 87.7% presented xerostomia; and 91% showed xerophthalmia, being severe in 43.1%. 64.6% had extraglandular manifestations; being the most prevalent the joint manifestation (60%) and the cutaneous one (18.4%). Over the past year, 37% developed haematological alterations in the form of cytopenias, and 73% biological alterations. At the time of the study, 32.8% presented low activity, 38.5% moderate activity and 9.2% high activity, measured by ESSDAI; being higher in anti-Ro positive patients (p=0.011). There was no association between ESSDAI and other antibodies, Raynaud or severe ocular involvement. 10.8% required systemic immunosuppression (RTX 5, AZA 2) and 18.5% needed ocular immunosuppression (topical cyclosporine). Only one patient developed lymphoma.

A Schirmer's test (ST) was performed in 92.3% (positive in 89.2%), saving the Van Bijsterveld test for patients with severe ocular involvement. The Ocular Staining Score (OSS) was not performed in any patient.

The scintigraphy of the salivary glands was positive in 70.8% of the patients and was not performed in 21.5%. The parotid sialography was only performed in two patients and the study of the salivary flow was not stimulated in none of them.

Regarding the autoimmunity, 80% presented positive antiRo; 61.5% antiLa; 89% ANA; 61.5% RF; 43% quadruple positivity.

Labial gland biopsy was performed only in 18.4%, with a positive result in 75%.

All patients met the 1993 European Criteria; 86.2% met the European-American criteria of 2002; and only 10.8% met the SICCA-ACR Criteria. The new criteria validated by ACR and EULAR were verified in 80%. Four patients who fulfilled the European criteria did not meet the new criteria, coinciding with those patients with negative ST, but positive scintigraphy.

Conclusions: In our hospital, the method for electing the xerostomia study was the salivary scintigraphy; therefore, we cannot establish direct comparisons with the new criteria.

The incorporation of non-stimulated salivary flow in our diagnostic strategy is necessary.

We should consider conducting a lip biopsy more systematically for histological confirmation since there are no validated diagnostic criteria.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5255

AB0519 LABORATORY ABNORMALITIES IN PATIENTS WITH PRIMARY SJOGREN'S SYNDROME

M. Fernandez Castro[1], J.L. Andreu[2], C. Sanchez-Piedra[3], V. Martínez Taboada[4], A. Olive[5], J. Rosas[6] on behalf of SJOGRENSER group, part of the Spanish Society of Rheumatology Systemic Autoimmune Diseases Study Group (EASSER). *[1]Rheumatology, Hospital Infanta Sofía; [2]Rheumatology, Hospital Puerta de Hierro Majadahonda; [3]Research unit, Spanish Society of Rheumatology; [4]Rheumatology, Hospital Marqués de Valdecilla, Madrid; [5]Rheumatology, Hospital Hospital Germans Trias i Pujol, Barcelona; [6]Rheumatology, Hospital Hospital Marina Baixa, Alicante, Spain*

Background: Primary Sjögren's syndrome (pSS) is a chronic systemic autoimmune disease often accompanied by analytical abnormalities. Altered levels in serum protein concentration, blood cell count and autoantibodies contribute to the broad spectrum of biological manifestations that characterize pSS.

Objectives: The objective of this study is to evaluate the presence of laboratory abnormalities in patients with pSS from the SjogrenSER registry.

Methods: We conducted a multicentre transversal study of a cohort of pSS patients fulfilling 2002 European/American criteria, from 33 Spanish rheumatology departments. Every patient was interviewed for data collection and signed an informed consent. Data were also collected by reviewing medical records. Local ethics committees approved the study. Variables were analysed by descriptive statistical methods, using means, medians and rates. Chi-square was used to establish the statistical associations. A $p<0.05$ was considered significant.

Results: Four hundred and thirty-seven patients were included. Ninety-five percent of them were women. The median age of the cohort was 58 years. AntiRo antibodies were present in 93.6% of patients and AntiLa antibodies in 67.3% of patients. All patients were ANA+. Rheumatoid factor (RF) was positive in 64.8% of patients. Low levels of C3 and C4 were observed in 14.87% and 14.19% of patients, respectively. Polyclonal hypergammaglobulinemia (HGG) was present in 53% of patients. Thirteen patients had cryoglobulins (2.97%). An increase in β2microglobulin was observed in 22.2% of patients. Fifty-six percent of the patients had hematological involvement: 29% of the patients had anemia, 38% had leukopenia (38% lymphopenia, 10.5% had neutropenia), and 9% had thrombocytopenia. The median ESR was 25 mm. Age at diagnosis and age at onset of symptoms were significantly lower in patients presenting RF+ vs RF- (48.71 vs 53.73, $p<0.001$ and 44.76 vs 49.53, p=0.001, respectively), decreased C3 vs normal C3 (45.66 vs 51.18, p=0.004 and 42.2 vs 46.99, p=0.018, respectively), decreased C4 vs normal C4 (47.02 vs. 50.89, P=0.042, for age at diagnosis) and HGG (47.59 vs 54, $p<0.001$, and 43.44 vs 50.16, $p<0.001$, respectively). ESR was significantly higher in patients with hematological involvement (35.94 vs 26.24, $p<0.001$), RF+ (36.39 vs 22.91, $p<0.001$), decreased C3 (37.8 vs 30.53, p=0.026) and C4 (38.71 vs. 30.42, p=0.04)), HGG (36.21 vs 26.03, $p<0.001$) and increased β2microglobulin (38.80 vs 29.71, p=0.009). ESSDAI (Eular Sjögren Syndrome Disease Activity Index) was significantly higher in patients with haematological involvement (5.58 vs 3.69, $p<0.001$), RF+ (5.40 vs 3.53, $p<0.001$) and HGG (5.31 vs 3.93, P=0.011). The median ESSDAI score was 2 (P25-P75, 0–4).

Conclusions: in SjogrenSER registry all patients were serologically positive. More than half of the patients presented abnormalities in serum proteins and 14% had hipocomplementemia. More than half of the patients had abnormalities, mostly leucopenia and lymphopenia. Patients with analytical alterations were younger at the time of diagnosis and had more often elevated ESR and higher ESSDAI score.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2603

AB0520 THE ROLE OF LEPTIN IN SJOGREN'S DISEASE

M. Erdoğan[1], M.E. Tezcan[2], K. Başak[3]. *[1]Internal medicine division of Rheumatology, Cerrahpaşa Medical Faculty; [2]Internal medicine division of Rheumatology; [3]Pathology, Dr. Lürfi Kırdar Kartal Training and Research Hospital, Istanbul, Turkey*

Background: Sjogren's disease (SD) is a multisystemic disease mostly manifest with sicca symptoms. Lympocytic infiltration of the glandular and extra glanduler organs is the dominant pathologic feature of the disease. Multiple stimulators were accused in the pathogenesis of SD. Leptin, an endogenous peptide, involves in various metabolic processes as well as influence immune system (1). Increased serum leptin level is observed in patients with autoimmune diseases such as SD, systemic lupus erythematosus and rheumatoid arthritis when compared to healthy controls (2).

Objectives: Even if serum leptin level increases in the patient with SD, there is no data about its effect on exocrine glands. We aimed to compare density of leptin in the salivary gland of SD patients with control group. Furthermore we evaluted the relation between intensity of lympocytic infiltration and density of leptin in the salivary glands of SD patients

Methods: We applied leptin immunostain to minor salivary glands samples of 24 SD patientss,who were fullfilled American College of Rheumatology Sjögren's Disease Classification Criteria (ACR-SDCC) and 19 patients who undergo minor salivary gland biopsy due to clinically on suspicion of SD but not fullfilling the ACR-SDCC and had no lymphocytic focus on biopsy. Herein,leptin density in acinar and ductal structures of the salivary glands were evaluated in both groups.Moreover,

minor salivary gland samples of SD patients were also assessed for relationship between focus score, disease progression (evaluated with SSDAI) and leptin immunostaining.

Results: Demographic features of both group were similar. Furhermore, there were no difference in leptin staining features of both group.Additionally, we found that higher focus score (>2) was associated with more diffuse leptin staining and higher SSDAI scores related with diffuse acinar staining.

Figure 1. Total leptin Satining in Different Focus Score Groups

		Total Leptin Staining			
		≤2	3-4	≥5	Total
Focus Score	Focus 1	2	1	3	6
	Focus 2	0	9	3	12
	Focus Score >2	0	0	6	6
	Total	2	10	12	24

*p=0.02

Figure 2. Stromal Leptin Staining in Different Focus Groups

		Stromal staining				
		No Staining	Focal	Modest	Wide	Total
Focus Score	Focus 1	1	3	2	0	6
	Focus_2	0	9	1	2	12
	Focus >2	0	0	0	6	6
	Total	1	12	3	8	24

*p=0.001

Conclusions: Different leptin staining features in higher focus score and higher disease activity might indicate the role of leptin especially in more significant disease. Leptin may locally stimulate chemotaxis and activate infiltration of glands with inflammatory cells. We suggested further studies aimed to understand autocrine effect of leptin and evalute its role in SD pathogenesis

References:

[1] Stofkova, A. Leptin and adiponectin: from energy and metabolic dysbalance to inflammation and autoimmunity. Endocrine regulations, 2009, 43.4: 157–168.
[2] Vadacca, Marta, et al. Leptin in immuno-rheumatological diseases. Cellular & molecular immunology, 2011, 8.3: 203–212.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5407

AB0521 ANTIPHOSPHOLIPID SYNDROME - ATHEROSCLEROSIS AND CLINICAL-IMUNOLOGICAL CORRELATIONS

N. Stoilov[1], V. Boyadzhieva[2], R. Rashkov[1]. *[1]Clinic of Rheumatology; [2]Clinic of Rheumatolog, UMBAL "Sv. Ivan Rilski", Sofia, Bulgaria*

Background: Antiphospholipid syndrome (APS) is an autoimmune, multisystem disease characterized by thrombocytopenia, venous and/or arterial thrombosis, pathological course of pregnancy in women (preeclampsia, eclampsia, miscarriage) and the presence of a heterogeneous group of antibodies - antiphospholipid antibodies. Recent studies show that in the pathogenesis of atherosclerotic process relevant inflammatory component of the immune response, as well as elements of autoimmunity (autoantibodies and autoantigens autoreactive lymphocytes). A number of autoimmune rheumatic diseases, including RA, SLE and API are characterized by accelerated atherosclerosis and therefore an increased risk of cardiovascular morbidity and mortality.

Objectives: The aim of the study was to investigate the incidence of cardiovascular events and atherosclerosis in patients with primary and secondary antiphospholipid syndrome, spyamo healthy subjects and patients with systemic lupus erythematosus without antiphospholipid antibodies.

Objectives of the study:

- To compare the damage to aa. Carotes in patients with APS compared to healthy subjects and patients with SLE without antifosfolipindi antibodies.
- To compare Are score in patients with APS compared to healthy individuals without antifosfolipindi antibodies.
- To compare atherosclerosis of aorta in patients with APS compared to healthy subjects and patients with SLE without antifosfolipindi antibodies.
- To compare cutaneous vascular lesions (Raynaud, Livedo reticularis, periungual vasculitis, son pulp gangrene, asphyxia, vasculitis lesions) on the limbs and body in patients with API spyamo healthy subjects and patients with SLE without antifosfolipindi antibodies.

Methods: For the purpose of this study examined 127 patients, 18 men (14%) and 109 women (86%), positive antiphospholipid antibodies. Patients were selected from the Department of Rheumatology, University Hospital "St. Ivan Rilski" – Sofia.

All the patients were tested for: ANA, aPL, standart laboratory tests.

Instrumental methods:

- calcium score of a. coronaria sinister, a. anterior descendens sinister, a. circumflexa sinister, a. coronaria dexter, Aorta, Valva aorte.
- Ultrasonographic examination of aa. Carotes to measure the Intima-media thickness.

Results: It is proved strong, statistically significant correlation between aCL antibodies and the presence of plaques in the left common carotid artery (p=0.041). Absent the dependence between the antibody titers and incidence of carotid plaques.

In the group with APS, 33,3% (14) establishes a positive calcium score of coronary arerii, 11.9% (5) plozhitelnite for aorta. Aortic valve Absent deposits. In the control group positive calcium score is when one person (5.88%).

Conclusions: We found that patients with antiphospholipid syndrome suffer from early developmentof atherosclerosis. In the process of atherogenesis involved inflammatory componentof immune response. Atherosclerosis can be viewed as an inflammatory autoimmune disease.

It is proved strong, statistically significant correlation between aCL antibodies and the presence of plaques in the left common carotid artery (p=0.041). Absent the dependence between the antibody titers and incidence of carotid plaques.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6615

AB0522 CLINICAL FINDINGS AND THEIR RELATIONSHIP WITH THE PROFILE OF ANTIPHOSPHOLIPID ANTIBODIES IN DOMINICAN PATIENTS

R. Vasquez-Colon[1], P. Gottschalk[1], C. Tineo[1], P. Lopez[1], R. Tejada[2], E. Loyo[1]. *[1]Reumatologia, Hospital Regional Universitario Jose Maria Cabral y Baez; [2]Investigaciones Clinicas, Pontificia Universidad Catolica Madre y Maestra, Santiago, Dominican Republic*

Background: There is an increased risk of thrombotic events and obstetric morbidities in individuals with antiphospholipid antibodies (APAs) compared with the general population. The risk of complications is further increased in those patients who have a rheumatic diseases and antibody positivity.

Objectives: The purpose of this study is to determine the clinical findings and their relationship with the profile of antiphospholipid antibodies in patients with rheumatic disease, of the Division of Rheumatology of the Hospital Regional Universitario José Ma. Cabral y Baez, Dominican Republic.

Methods: Patients with 18 years of age and above, with a confirmed rheumatic disease was eligible for enrollment; those with positive titers for APAs, that met the inclusion and exclusion criteria, were included in our study. The institutional review board approved the protocol.

This is a transverse study, with retro-prospective data gathering from patients and their medical records. Demographic information at the time of APA measurement and medical information regarding the rheumatic disease and clinical course were collected from the patient's medical record, with a follow-up of 10 years.

Results: 40 patients were included in this study. The male to female ratio was 19:1; mean age was 36±10 years. A large number of patients (13 patients, 32.5%) were asymptomatic for antiphospholipid syndrome (APS) at the time of this study; eight patients (20%) were carriers without defining manifestations. Ten patients (25%) were categorized as vascular APS and five patients (12.5%) as obstetric APS; three patients (7.5%) had vascular and obstetric APS. One patient presented with catastrophic APS. In evaluating such specific profile of antiphospholipid antibodies, aCL was observed that corresponded to the antibody most frequently identified with IgG isotypes (52.5%) and IgM 47.5%. The lupus anticoagulant (LA) corresponded to the second most common (37.5%). The isotypes of the anti-B2GP-I were identified in less proportion. We report 89 pregnancies during the follow, with 29 abortions and 60 live births, of which 12 were premature and 11 born with intrauterine growth restrictions.

Conclusions: The most frequent clinical manifestations were livedo reticularis, vascular thrombosis in lower extremities, Raynaud's phenomenon, migraine, cerebrovascular disease, thrombocytopenia, leukopenia, and alteration of urine sediment.

References:

[1] Hughes GR. Antiphospholipid Syndrome Hughes Syndrome: 10 Clinical Topics. Lupus 2010; 19:343–6.
[2] Musial J. Antiphospholipid Antibodies and Thrombosis. Thromb Res 2012; 129:345–7.
[3] Erkan D, Barbhaiya M, George D et al. Moderate Versus High-Titer Persistently Anticardiolipin Antibody Positive Patients: Are They Clinically Different and Does High-Titer Anti-Beta 2-Glycoprotein-I Antibody Positivity Offer Additional Predictive Information? Lupus 2010; 19:613–9.
[4] Petri M. Update on Anti-Phospholipid Antibodies in SLE: The Hopkins' Lupus Cohort. Lupus 2010; 19:419–23.
[5] Tarr T, Lakos G, Bhattoa HP et al. Analysis of Risk Factors for the Development of Thrombotic Complications in Antiphospholipid Antibody Positive Lupus Patients. Lupus 2007; 16: 39–45.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4135

AB0523 AN ANALYSIS OF THE FACTORS INFLUENCING THE BODY IMAGE DISTURBANCE WITH SYSTEMIC LUPUS ERYTHEMATOSUS LIVING IN CHINA

Q. Zhao, Y. Cui, L. Li, S. Chen, C. Zhou, Z. Gu. *Department of Rheumatology, Affiliated Hospital of Nantong University, Nantong, China*

Background: Systemic Lupus Erythematosus (SLE) is a chronic, autoimmune rheumatic disease that can affect multiple systems/organs in the body and is characterized by relapses and remission, usually affects women in the reproductive age group. SLE may cause inflammation activity and damage in any of the organs, often resulting in decreased physical, emotional and social abilities, depression, pain, fatigue, visible or invisible changes in appearance. Recent studies have indicated that body image disturbance (BID) can lead to a variety of cognitive, emotional and behavioral changes. BID will cause the individual having a negative perception of the body, negative emotional experience and the corresponding behavior disorders.
Objectives: To explore the relationship between social and economic status, disease activity, mental state, self-esteem, quality of life and the essential BID with Systemic Lupus Erythematosus Living in China.
Methods: The investigation is from in October 2015 to December 2016 at the Affiliated Hospital of Nantong University. There are 109 cases of hospitalized patients, including 8 cases of male, female 101 cases, mean age is 35.3±12.2. Scale including body image disorder scale (BID), respectively. Body image was assessed using the Body Image Disturbance Questionnaire (BIDQ) which contains seven scaled items scored from 0 (not affected) to 8 (extremely affected) pertaining to appearance-related concerns (BIDQ1); mental preoccupation (BIDQ2); emotional distress (BIDQ3); social, occupational, or functional impairment (BIDQ4); social life interference (BIDQ5) and educational, occupational, or other functional interferences (BIDQ6); and behavioural avoidance (BIDQ7). Systemic lupus erythematosus disease activity index (SLEDAI); the hospital anxiety and Depression Scale (HADS) in systemic lupus erythematosus; disease-specific HRQOL measure for adults with SLE (Lupus QOL), including health (PH), pain (PN), planning (PL), intimate relationship (IR), a burden to others (BV), emotional Health (EH), body image (BI), fatigue (F). Spearman's coefficient for nonparametric and Pearson's coefficient for parametric data were computed. Variables that were significant in univariate analysis were included in a multivariate linear regression model. All p-values less than 0.05 were considered statistically significant.
Results: SLE patients were most concerned about their body size (33.38%) and skin (32.23%), 55.34% SLE patients were more concerned about the change of body shape caused by disease. There was significant correlation between BID and disease status, psychological status and quality of life in patients with SLE. Physical health is correlated with BD1, Pain is correlated with BID1, BID4–7, Planning is correlated with BID2, BID4–7, Intimate relationships is correlated with BID4–7, Burden to others is correlated with BID3–7, Emotional health, fatigue are associated with BID3–7. Anxiety and depression also affect BID, anxiety is an important predictor of BIDQ1, BIDQ3–6, depression is a predictor of BIDQ2, BIDQ 3–6.
Conclusions: Patients with Systemic Lupus Erythematosus Living in China are much easier bear with BID, anxiety, depression, less quality of life will lead to BID, in view of the body image perspective, this study will help explore the influence factors of BID in patients with SLE.
Acknowledgements: The study was supported by The Natural Science Foundation of China (81401124).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5284

AB0524 TRANSLATION AND VALIDATION OF THE FATIGUE SEVERITY SCALE, THE PITTSBURGH SLEEP QUALITY INDEX AND THE MODIFIED HEALTH ASSESSMENT QUESTIONNAIRE INTO THE MALTESE LANGUAGE, IN A COHORT OF MALTESE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

R. Magro[1], A.A. Borg[1], L. Camilleri[2]. *[1]Rheumatology, Mater Dei Hospital; [2]Statistics and Operations Research Department, University of Malta, Msida, Malta*

Background: The Fatigue Severity Scale (FSS), Pittsburgh Sleep Quality Index (PSQI) and Modified Health Assessment Questionnaire (mHAQ) are validated questionnaires that measure fatigue, sleep quality and function respectively. Research in the Maltese population, on systemic lupus erythematosus (SLE) requiring the use of these questionnaires, necessitates their translation and validation into the Maltese language.
Objectives: The aim of the study is to translate, validate and perform cross-cultural adaptation of the FSS, PSQI and mHAQ into the Maltese language, according to the recommended methodology.[1]
Methods: The original instruments were translated into Maltese by two translators whose mother language is Maltese. One of the translators had a medical background and was knowledgeable on the concepts being examined in the questionnaires; while the other did not. The two translated versions of the instruments were then compared and the discrepancies were resolved by reaching a consensus on the best Maltese version that reflects the underlying meaning of the original English version. The preliminary initial Maltese translations were then given to two other translators for back translation into English. English was the native language of these translators and they were totally blind to the original versions. The back translated English versions were then compared to the original English questionnaires and any discrepancies were highlighted. The equivalent statements in the Maltese translations were discussed and changes were made to reflect the original English versions more accurately. The pre-final Maltese translations were produced and pilot tested in a sample of 20 bilingual SLE patients to evaluate the clarity of the questionnaires. These 20 patients were also asked to fill in the original English version of the FSS, PSQI and mHAQ, seven days after filling in the Maltese versions. Psychometric testing was carried out to assess reliability of the translation, internal consistency and validity.
Results: Reliability of the translation of the FSS, PSQI and mHAQ into Maltese was analysed by using Kendall's tau test for statements having an ordinal scale and Pearson's correlation test for variables having a metric scale. The *p* value for each statement in the FSS, PSQI and mHAQ was less than 0.05 showing that the reliability of the translated versions was satisfactory. Internal consistency of the Maltese translations was demonstrated using Cronbach's alpha. This was calculated to be 0.877 for the FSS, 0.859 for the PSQI, and 0.897 for the mHAQ. Validity of the Maltese translation of the FSS was assessed by its correlation with the visual analogue scale for fatigue using Pearson's Correlation test. Pearson's R value was 0.809 and the *p* value was <0.001 confirming a positive significant correlation.
Conclusions: This study has confirmed the reliability and internal consistency of the translated English versions of the FSS, PSQI and mHAQ into Maltese. Moreover the validity of the Maltese version of the FSS has been shown. The Maltese translations can be finalised and used for research purposes.
References:
[1] Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine. 2000; 25(24): 3186–3191.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2201

AB0525 CLINICAL AND RENAL HISTOLOGIAL CHARACTERISTICS OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH ANTI-SS-A AND ANTI-SS-B ANTIBODIES COMPARED TO THOSE WITHOUT

R. Anan, Y. Kaneko, J. Kikuchi, M. Ushikubo, S. Saito, T. Takeuchi. *Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan*

Background: Systemic lupus erythematosus (SLE) is a chronic condition with a broad clinical spectrum, which can affect multiple organs and systems. Although the most featuristic autoantibodies are anti-DNA and anti-Sm antibodies, anti-SS-A antibody and anti-SS-B antibody are detected in 30–40% and 7–45% of SLE patients, respectively. However, the clinical features of those positive patients are unclear.
Objectives: The aim of this study was to clarify the associations of anti-SS-A and anti-SS-B antibodies with the clinical features of SLE and histological findings of lupus nephritis (LN).
Methods: We enrolled consecutive Japanese patients with SLE who had visited Keio University Hospital from 2013 to 2015 and whose anti-SSA and anti-SSB antibodies were measured. The patients were divided according to the presence or absence of anti-SS-A and anti-SS-B antibodies, and their associations of the clinical features and renal biopsy histological findings were examined.
Results: A total of 253 patients were enrolled, 215 (84%) were female, and the mean age was 55.2 years. Anti-SS-A antibody was detected in 152 cases (69%), and anti-SS-B antibody in 40 cases (18%). No difference was found in sex, age, the rates of anti-DNA and anti-Sm positivity between both the anti-SS-A positive group and the anti-SS-A negative group, and between the anti-SS-B positive group and the anti-SS-B negative group. While the frequencies of oral ulcers (38% vs. 37%, p=0.83), arthritis (82% vs. 79%, p=0.58), serositis (23% vs. 22%, p=0.94), neuropsychiatric involvement (14% vs. 10%, p=0.35), LN (51% vs. 63%, p=0.07), leukopenia (74% vs. 69%, p=0.44), and thrombocytopenia (26% vs. 31%, p=0.44) were not different between the anti-SS-A positive group and the anti-SS-A negative group,.mucocutaneous involvement (84% vs. 63%, p=0.002), alopecia (37% vs. 19%, p=0.002), lymphopenia (97% vs. 89%, p=0.020) were significantly higher in the anti-SS-A positive group than the anti-SS-A negative group. The frequencies of neuropsychiatric involvement (24% vs. 10%, p=0.015) was significantly higher in the anti-SS-B positive group than the anti-SS-B negative group. The period from the SLE onset to the LN onset was significantly shorter in the anti-SS-A positive group than the anti-SS-A negative group (4.0 years vs. 9.0 years, p=0.005), and in the anti-SS-B positive group than the anti-SS-B negative group (0.4 years vs. 6.8 years, p=0.008). Focusing on the histological findings of LN patients, the anti-SS-A positive group had significantly lower rate of renal tubular atrophy (8.0% vs. 16%, p=0.042) and interstitial fibrosis (7.6% vs. 16%, p=0.031) than the anti-SS-A negative group. The anti-SS-B positive group had also significantly lower rate of renal tubular atrophy (3.3% vs. 13%, p=0.048) and interstitial fibrosis (2.1% vs. 13%, p=0.016). Finally, chronicity Index was significantly lower in the anti-SS-A positive group (2.37 vs. 4.14, p=0.002) and in the anti-SS-B positive group (1.17 vs. 3.33, p=0.008).
Conclusions: SLE patients positive for anti-SS-A and anti-SS-B antibodies had

characteristics with frequent mucocutaneous involvement, alopecia, neuropsychiatric involvement, and lymphopenia. They should be followed carefully for early onset of LN.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3964

AB0526 B1 CD5+ LYMPHOCYTES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: RELATION TO DISEASE ACTIVITY

S.I. Nasef[1], H.H. Omar[2], H.H. Omar[3], M.S. Ghaly[1]. *[1]Physical Medicine, Rheumatology and Rehabilitation; [2]Clinical Pathology; [3]Internal Medicine, Faculty of Medicine, Suez Canal University, Ismailia, Egypt*

Background: B cells are essential players in the pathogenesis of Systemic lupus erythematosus (SLE). Membrane CD5 elevates the threshold of B cell receptor mediated responses, and thus prevents the release of antibodies. So, misguided signalling through CD5 could lead to autoimmunity. Hence, $CD5^+$ B cells were considered to play a paradoxical role in preventing rather than inducing autoimmunity. This challenging view differs from the old interpretation that elevated levels of B1 $CD5^+$ cells in SLE patients represent a direct source of autoantibodies responsible for organ damage.

The clinical implications of this new concept for the role of B1 $CD5^+$ cells in SLE have not been fully addressed yet and there is no consensus agreement about the proportions of B1 CD5+ cells in SLE patients. Moreover, the relation of B1 $CD5^+$ cells to disease activity and organ damage is not sufficiently studied.

Objectives: To assess the expression of B1 $CD5^+$ cells in SLE patients and to evaluate their relationship with disease activity and organ damage.

Methods: We recruited 100 SLE patients and 100 healthy control subjects. Based on SLE disease activity index (SLEDAI), patients were divided into two groups; active SLE (n=50) and inactive SLE (n=50). SLE was active when SLEDAI was $\geq$4. The expression of ($CD5^+CD20^+$) B1 cells was evaluated using flow cytometry. Lymphocytes were gated depending on both side and forward scatter. From the gated lymphocytes, B1a cells were identified double positive cells for CD20 and CD5. Percentage and absolute numbers of $CD20^+CD5^+$ (B1a cells) and their mean fluorescence intensity (MFI) were measured. The histogram of CD5 expression was used to assess its expression on CD20 cells (figure 1).

Laboratory work included CBC, ESR, CRP, Serum creatinine, Protein/creatinine ratio, Urine analysis, 24 hour protein collection in urine, Complement levels, (Anti-dsDNA) and (ANA).

Results: Mean age of patients was 31.3±8.8 years. Females constituted 94% (n=94) of patients. Mean disease duration was 5.28±4.8 years. Mean SLEDAI was 10.28±5.16.

The proportions of ($CD5^+CD20^+$) B1 cells were significantly lower in SLE patients versus controls (5.9±4.4% vs 20.2±4%, $p\leq0.001$). Similarly, the absolute numbers of ($CD5^+CD20^+$) B1 cells (cell/mm^3) were significantly lower in SLE patients versus controls (100.2±103.4 vs 557.6±163.3, $p\leq0.001$).

The expression of ($CD5^+CD20^+$) B1 cells was decreased in active SLE patients (4.5±3.8%) in comparison to inactive patients (7.3±4.7%) (p=0.027). B1 ($CD5^+CD20^+$) absolute cell number (cell/mm^3) was significantly lower in active SLE patients (71.4±82.9) compared to inactive ones (129.0±115.1) (P=0.047).

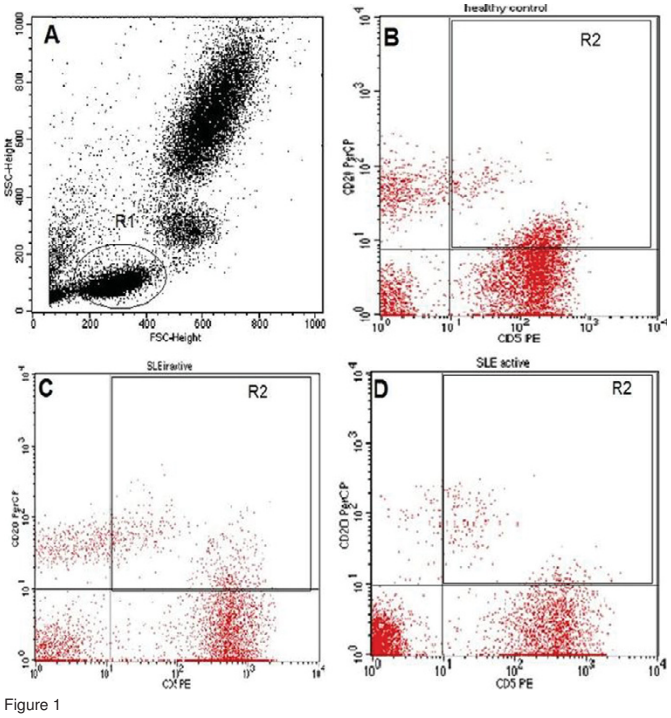


Figure 1

MFI of $CD5^+/CD20^+$ was significantly decreased in SLE patients compared to healthy control (146.9±109 vs 196±48, P=0.033). B1 cells ($CD5^+CD20^+$) correlated positively with C3 (r=0.322, p=0.022) and C4 (r=0.307, p=0.030). No correlation was found between ($CD5^+CD20^+$) B1 cells and disease duration, autoantibodies or any specific system or organ damage.

Conclusions: Expression of B1 $CD5^+$ cells was significantly decreased in SLE patients. Decreased B1 $CD5^+$ cells expression was associated with higher disease activity. B1 $CD5^+$ correlated positively with complement levels. These findings denote that CD5 expression on B cells may play a regulatory role in SLE pathogenesis and decrease occurrence of flares.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2006

AB0527 PROGRANULIN AND INSULIN-LIKE GROWTH FACTOR-2 AS BIOMARKERS FOR DISEASE ACTIVITY AND PATHOLOGICAL CHANGES IN LUPUS NEPHRITIS

S. Goma, M. Abdelaziz, E. El-Hakeim, M. El Zohri, S. Sayed. *Assiut University, Egypt, Assiut, Egypt*

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease (1), characterized by the production of autoantibodies, and formation of immune complexes due to the polyclonal activation of T and B lymphocytes that result in tissue and organ damage (2). During inflammation, neutrophils and macrophages release serine proteases to cleave progranulin (PGRN) into granulin (GRN), which exert their pro-inflammatory effects that counteract the anti-inflammatory effects of intact PGRN (3). Insulin-like growth factor-2 (ILGF-2) binds to insulin-like growth factors (IGFs) with high affinity (4). Although reports suggest that IGFBP-2 is a reliable biomarker of renal deterioration, it is still needed to confirm that it has high sensitivity and specificity in discriminating kidney disease caused by SLE from other origins.

Objectives: The aim of this study was to explore whether PGRN and ILGF-2 can be used as useful markers not only for accurate diagnosis of patients with active lupus nephritis (LN) but also for prediction of the disease activity in these patients.

Methods: Twenty-five patients with systemic lupus erythematosus, twenty-five patients with chronic renal failure and twenty-five age- and sex-matched healthy volunteers were enrolled in the study. Routine laboratory investigations and measurement of serum PRGN and IGFBP-2 levels were done.

Results: Our results showed that the mean age of SLE, CRF and control groups 31.12±12.34, 38.7±9.4 and 32.96±13.66 respectively with no significant difference between the three groups. There was female predominance in the three groups. Disease duration was 4.78±4.26 in SLE patients.The mean of SLEDAI score was 15.04±7.54. All renal biopsy results were class 2, 3, and 5 with a percentage of 32%, 24%, and 44% respectively.

Table 1. Levels of PRGN and ILGF-2 in SLE, CRF and control groups

	SLE	CRF	Control	P	P1	P2	P3
PRGN, pg/ml	2558.92±1170.77	1814.6±330.28	1052±276	<0.001**	<0.001**	<0.001**	<0.001**
ILGF-2, ng/ml	26.44±11.55	6.14±2.25	3.3±1.7	<0.001**	<0.001**	<0.001**	0.148

P: Comparison between all groups. P1: comparison between SLE and CRF. P2: comparison between SLE and control. P3: comparison between CRF and control. Table 2. Levels of PRGN and ILGF-2 in relation to SLEDAI score, renal SLEDAI, and Renal biopsy

	PRGN pg/ml	ILGF-2 ng/ml
SLEDAI score		
Moderate	1945.6±300	26.8±11.7
High	2072.1±545.5	20.1±5
Very high	4269.2±1106.8	37.6±12.6
P value	0.002**	0.006**
Renal SLEDAI		
Inactive	2251.2±841	23.3±8.9
Active	2764.1±1335	28.6±12.9
P value	0.311	0.196
Renal biopsy		
Class 2	2199.31±854.85	24.38±13.31
Class 3	2244.17±767.97	23.75±7.01
Class 4	2992.14±1453.93	29.41±12.41
P value	0.270	0.540

SLEDAI: Systemic Lupus Erythematosus Disease Activity Index. *Statistically significant difference ($p<0.05$) **Statistically significant difference ($p<0.01$).

Conclusions: PGRN and ILGF-2 are significantly elevated in SLE than CRF and control and were associated with SLEDAI. Hence they are considered specific to LN.

References:

[1] Rahman A, Isenberg DA. (2008) Systemic lupus erythematosus. N Engl J Med 358:929–939.
[2] Kotzin BL. (1996) Systemic lupus erythematosus. Cell 85: 303–306.
[3] Park B, Buti L, Lee S et al. (2011) Granulin is a soluble cofactor for toll-like receptor 9 signaling. Immunity 34(4):505–513.
[4] Firth SM, Baxter RC. (2002) Cellular actions of the insulin-like growth factor binding proteins. Endocr Rev 23(6):824–54.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2082

AB0528 PATIENT ACTIVATION AND THE FACTORS AFFECTING IT IN PRIMARY SJÖGREN'S SYNDROME

S.T. Souter[1], B. Hargreaves[2], K.L. Hackett[3], W.-F. Ng[3]. *[1]Newcastle University; [2]Freeman Hospital; [3]Institute of Cellular Medicine & NIHR Newcastle Biomedical Science Research Centre, Newcastle upon Tyne, United Kingdom*

Background: Increased patient activation has been associated with reduced costs of treatment[1] and improved patient outcomes[2]. The effect of primary Sjögren's syndrome (pSS) on patient activation however has not been established.
Objectives: This study aims to identify how activated patients with pSS are, and to ascertain whether factors such as ESSPRI score, EULAR dryness score and self-reported quality of life influence this.
Methods: Patient activation in 170 pSS patients was assessed using the 13-item Patient Activation Measure (PAM-13). A PAM-13 score from 0–100 was obtained using the PAM-13 Scoring Spreadsheet, which also gave a corresponding activation level ranging from 1–4. Descriptive statistics of the PAM-13 scores was performed, and frequency analysis of the corresponding activation level. Demographic, clinical and self-reported measures such as age, gender, ESSPRI score and EQ5D-3L score were linked to each patients' PAM-13 scores. Spearman's correlation analysis was performed to assess the relationship between the continuous variables and PAM-13 score, and Fisher's exact test was used to assess the relationship between activation level and the categorical variables.
Results: The mean PAM-13 score of the 170 patients studied was 59.5 (SD 13.5). 17.6% of patients were in level 1 of activation, 26.5% in level 2, 40.0% in level 3, and 15.9% in level 4. The mean age of the sample was 59.6 (SD 13.1), and 83.5% were female.
EQ5D-3L score had the strongest correlation with increased PAM score (r_s 0.405, p 0.000). Increasing self-reported pain in the ESSPRI questionnaire was correlated with a decreasing PAM score (r_s -0.355, p 0.000), as was increasing ESSPRI score (r_s -0.337, p 0.000). Increasing abnormal fatigue (r_s -0.189, p 0.016) and EULAR dryness (r_s -0.190, p 0.013) score were only weakly correlated with a decrease in PAM-13 score. Decreases in patients self-reported mobility (p 0.000), self-care (p 0.002), and ability to perform daily activities (p 0.018) were also associated with differences in activation score.
Conclusions: Factors such as a patients self-reported health and pain have a moderate correlation with activation in pSS patients, while dryness and fatigue are only weakly correlated with changes in activation. This should be considered in the future when devising treatment plans and clinical trials.
References:
[1] Hibbard JH, Greene J, Overton V. Patients With Lower Activation Associated With Higher Costs; Delivery Systems Should Know Their Patients' 'Scores'. Health Affairs. 2013;32(2):216–222.
[2] Hibbard JH, Greene J, Shi Y, Mittler J, Scanlon D. Taking the Long View: How Well Do Patient Activation Scores Predict Outcomes Four Years Later? Medical Care Research and Review. 2015;72(3):324–337.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6933

AB0529 ROLE OF THE ANTI-RO52 AND RO60 ANTIBODIES QUANTIFICATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

S. Heredia[1], M. Martinez-Morillo[1], A. Riveros[1], L. Gifre[1], A. Teniente-Serra[2], B. Quirant[2], S. Holgado[1], L. Mateo[1], A. Prior[1], Y. Garcia[1], J. Camins[1], E. Martínez-Cáceres[2], A. Olivé[1]. *[1]Rheumatology; [2]Immunology, Hospital Universitari Germans Trias i Pujol, Badalona, Spain*

Background: Anti-Ro antibodies (Ab) are especially directed against two antigens, Ro52 and Ro60, with different structure and function. Studies in systemic lupus erythematosus (SLE) have been described a relationship between the presence of anti-Ro Ab and dry syndrome, subacute cutaneous lupus, myocardial involvement or minor renal involvement. However, studies about the clinical usefulness of determining the 2 specificities of anti-Ro Ab in SLE are not conclusive. It seems that anti-Ro52 could be associated with joint involvement and lung disease, while anti-Ro60 could be related to late-onset SLE. In this paper we evaluate the clinical usefullness of anti-Ro52 and Ro60 Ab chemiluminescence quantification in patients with SLE.
Objectives: To analyze the presence of anti-Ro52 and Ro60 Ab in a cohort of patients with SLE and evaluate its correlation with clinical, analytical and immunological parameters.
Methods: 152 patients with SLE (according to the SLICC criteria 2013) attended in an university hospital were included. Qualitative immunoblot analysis of anti-Ro Ab was performed on all of them; those with positive values were also assessed by a chemiluminescence quantification of anti-Ro52 and Ro60 Ac (normality <19.9 CU). Other LES specific Ab were also analyzed by immunoblot, indirect immunofluorescence and ELISA. Clinical variables (age, oral ulcers, alopecia, synovitis, serositis, antiphospholipid syndrome (APS), Sjögren's syndrome, cutaneous, neurological and renal involvement), analytical (complement, cytopenia and coombs test) and activity and damage index of SLE (SLEDAI and SLICC) were also evaluated. The study was approved by the Clinical Research Ethics Committee of the center, and all patients signed informed consent.
Results: 91% (138) were women with a mean age of 46±12 years (range, 20–75) and an average SLE evolution of 12±7 years (range, 1–40). 32% (49/138) of the patients had anti-Ro positive determination by immunoblot: 36 were anti-Ro52 positive (mean value 696±726 CU) and 48 anti-Ro60 positive (mean value 504±696 CU) by chemiluminescence. Only one anti-Ro52 positive patient was anti-Ro60 negative. 10.5% had late-onset SLE. The mean SLEDAI was 1.84±2.48 while the SLICC was 0.32±0.7, with a mean anti(ds)DNA Ac values about 207.87±357.15 IU/ml. 37.5% had hypocomplementemia. Anti-Ro positive patients by immunoblot had a higher value of anti(ds)DNA compared to the patients without Ro positive values and patients with both positivity by chemiluminescence had lower prevalence of APS, however the quantitative values of anti-Ro52 and anti-Ro60 were not related with clinical, analytical or immunological parameters.
Conclusions: 32% of patients in the cohort were anti-Ro positive being mostly anti-Ro60 positive. The presence of anti-Ro Ab was associated with higher value of antiDNAds and lower prevalence of APS. However, the quantitative values of anti-Ro52 and anti-Ro60 Ab by chemiluminescence were not related to the different parameters analyzed in the study. These results indicate the need to assess the quantification of anti-Ro Ab in a larger cohort of patients with SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5057

AB0530 PREVALANCE OF OSTEONECROSIS OF BONE IN PATIENTS OF SLE IN A NEWLY ESTABLISHED RHEUMATOLOGY CLINIC IN CENTRAL INDIA

S. Malviya[1], N. Gupta[2], R. Gupta[3]. *[1]Department of Rheumatology, Indore, India, Medanta Superspeciality Hospital; [2]Department of Anaesthesia, SAIMS, Indore, Indore; [3]Department of Rheumatology, Indore, India, MEDANTA Medicity, Gurugram, India*

Background: Osteonecrosis (OCN) is a well recognized complication of SLE. The prevalence rate of AVN in SLE ranges from 8–25% in various studies. It is always debatable if corticosteroids or disease itself causes OCN. Although long term corticosteroids use can cause OCN, but in few cases and studies it has shown disease itself can be the causative event.
Objectives: To study the prevalance of Osteonecrosis of bone among patients of SLE attending the newly established Rheumatology clinic over 2 years time.
Methods: All the patients of SLE with OCN attending the newly established Rheumatology clinic of the town were included in the study.OCN was diagnosed on the basis of MRI after screening with X-ray.Serological data collected. Routine investigations done were collected. Details of patients were included in a set proforma and details noted in the same.
Results: Among 180 patients of SLE were included in the study. Among those, 9 patients (5%) were diagnosed with OCN. Seven patients of OCN had been on steroids but 2 patients never received any drugs, both were male. All the patients were AN A positive (Homegenous pattern in 6 and Speckled in 3), Anti-ds-DNA was positive in 7 and Anti-Smith in 2. Most common site of OCN was Femur head (n=6), Lower femoral condyles in 2 patinets of OCN and head of Talus in 1. Anti-phospholipid antibodies were found in 3 patients.
Conclusions: Osteonecrosis was found in 5% of patients of SLE. Most of the patients had active disease with OCN occurred very early during the course of disease. This suggest OCN can be seen due to disease itself as 2 patients never received any drugs. Most common antibodies associated was anti ds-DNA antibody. So among patients of SLE with hip or pain in joints/bone not explaining active arthritis, OCN should be ruled out.
References:
[1] Lam G.K.W, Petri M. Assessment of Systemic Lupus Erythematosus. Clin Exp Rheumatol 2005;23 (Suppl. 39): S120–132.
[2] Mont MA, Glueck CJ, Pacheco IH, Wang P, Hungerford DS, Petri M. Risk factors for osteonecrosis in systemic lupus erythematosus. J Rheumatol 1997;24:654–62.
[3] Petri M. Musculoskeletal complications of systemic lupus erythematosus in the Hopkins Lupus Cohort: an update. Arthritis Care Res 1995;8:137–45.
[4] Dubois EL, Cozen L. Avascular (aseptic) bone necrosis associated with systemic lupus erythematosus. JAMA 1960;174:966–71.
[5] Harrington KD, Murray WR, Kountz SL, Belzer FD. Avascular necrosis of bone after renal transplantation. J Bone Joint Surg Am 1971;53:203–15.
[6] Murray WR. Hip problems associated with organ transplants. Clin Orthop 1973;90:57–69.
[7] Heimann WG, Freiberger RH. Avascular necrosis of the femoral and humeral heads after high dosage corticosteroid therapy. N Engl J Med 1960;263:672–5.
[8] Abeles M, Urman JD, Rothfield NF. Aseptic necrosis of bone in systemic lupus erythematosus. Relationship to corticosteroid therapy. Arch Intern Med 1978;138:750–4.
Acknowledgements: Dr Arvind Rawal: Orthopaedician.
Dr Mallika Kwatra- Pathologist
Dr Sandeep Shrivastava- Director
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4634

AB0531 ANTI-CENTROMERE POSITIVE PRIMARY SJÖGREN'S SYNDROME – CHALLENGE TO CLASSIFICATION CRITERIA

S. Palshina[1], V. Vasiliev[1], E. Sokol[1], B. Chaltsev[1], E. Rodionova[1], T. Safonova[2]. *[1]Nasonova research institute or rheumatology; [2]Research Institute of Ophthalmic diseases, Moscow, Russian Federation*

Background: The prevalence of anti-centromere antibodies (ACA) among patients with primary Sjögren's syndrome (pSS) varies from 3,7% till 10,9% [1;2]. They have special course of the disease: 1) with some features of systemic sclerosis (SSc), but rarely evolve to it, 2) higher prevalence of hepatitis and primary biliary cholangitis - PBC.
Objectives: to describe the peculiarities of this subgroup; to evaluate it's conformity to the latest classification criteria for pSS (2012, 2016) [3;4] and prevalence of SSc with ACR2013 criteria [5].
Methods: From 2012 to 2016 in a single rheumatic center 50 ACA positive patients (47 female; 3 male) national (Russian) criteria (1987) and in 68%cases - AECG 2002 criteria for pSS (SSc excluded) [Tabl.1]. The mean age was 59,2±9,6 yrs. All diagnostics methods are listed in the table 1, lymphomas were verified pathomorphologicaly with immunohystochemical staining.
Results: In our study 2/3 (64%) ACA+pts with pSS did't fulfill ACR2012 criteria, because of the lack of aRo or aLa or combination of RF+ANA. According to the criteria, 2016 [4] also just 60–68% pts will have ≥4scores for diagnosing pSS. SSc (limited form) due to new criteria [5] might be revealed in 11/50 (22%) cases. MALT lymphoma of salivary glands arised in 5/6 pts with visible enlargement of parotid glands.

Table 1. Characteristics of pSS patients with positive ACA

Parameters	Value (n, %)
Sialography of parotid gland: sialectasis	47/50 (94%)
Xerostomia (grade I-III) stimulated parotid saliva flow rate <0,5ml/5min (III)	27/43 (62,8%)
Keratoconjunctivitis sicca with ocular staining score ≥5	31/50 (62%)
Schirmer's test ≤5 mm/5 minutes	29/48 (60,4%)
Focal lymphocytic sialadenitis ≥1 foci/4 mm^2	28/30 (92%)
Non-Hodgkin lymphoma (incl. MALT lymphoma)	6 (5) =12% (10%)
aRo/SS-A ≥50 IU/ml	16/50 (32%)
aLa/SS-B ≥50 IU/ml	3/50 (6%)
IgM RF positive ≥2UNL (>30 IU/ml)	9/50 (18%)
AMA positive >10 IU/ml	13/31 (41,9%)

Conclusions: pSS with positive ACA is challenging for diagnostics with comprehensive classification criteria (32–64% doesn't meet it [3;4]). These patients overlaps SSc, some PBC. PBC is not rare among, but biliary tract lesions (AMA+(rarely absent, 2% in our study) with slightly elevated liver enzymes, esp.GGT, and stage 1 typical to PBC without progression) are more common.
References:
[1] Bournia VK et al. Anticentromere antibody positive Sjögren's Syndrome: a retrospective descriptive analysis. Arthritis Res Ther. 2010;12(2): R47.
[2] Nakamura H et al. Anti-centromere antibody-seropositive Sjögren's syndrome differs from conventional subgroup in clinical and pathological study. BMC Musculoskelet Disord. 2010 Jul 1;11:140.
[3] Shiboski SC et al. American College of Rheumatology Classification Criteria for Sjögren's Syndrome: A Data-Driven, Expert Consensus Approach in the SICCA Cohort. Arthritis Care Res (Hoboken). 2012; 64(4): 475–487.
[4] Shiboski SC et al. 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjögren's Syndrome. ARTHRITIS & RHEUMATOLOGY. 2016; Vol. 00 (00): p 00–00.
[5] van den Hoogen F et al. 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism collaborative initiative. Arthritis Rheum. 2013 Nov;65(11):2737–47.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6974

AB0532 VITAMIN D IN A MALAYSIAN LUPUS COHORT AND ITS CORRELATIONS WITH CLINICAL AND IMMUNOLOGICAL PARAMETERS

S.G. Ong, H.J. Ding. *Medicine, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia*

Background: Numerous studies have demonstrated that inadequate vitamin D levels are common in systemic lupus erythematosus (SLE) patients and they correlate inversely with disease activity. To date, there is paucity of data on the prevalence of vitamin D status, as well as its clinical and immunological associations in Malaysian SLE patients.
Objectives: Our study aimed to determine the prevalence of vitamin D deficiency and insufficiency in SLE patients, and to examine the associations between vitamin D status with gender, ethnic groups, clinical manifestations of SLE, Schirmer's test, cardiovascular risk factors, bone mineral density and autoantibodies.
Methods: This retrospective study included 216 SLE patients who attended the Rheumatology Clinic of Kuala Lumpur Hospital between January 2013 and December 2015. Data was obtained from patients' medical records. All patients fulfilled the 1997 American College of Rheumatology revised classification criteria for SLE. Serum 25(OH)D concentrations were measured by electrochemiluminescence immunoassay.
Results: A total of 216 SLE patients were included in this study. Eleven (5.1%) were males and 205 (94.9%) were females. There were 141 (65.3%) Malay, 53 (24.5%) Chinese, 19 (8.8%) Indian and 3 (1.4%) of other ethnic group. This corresponded with the pattern of ethnic distribution in the Malaysian population. Their ages ranged from 14 to 75 years, with a mean age of 35.9±7.1 years. Mean duration of SLE at the time of 25(OH)D analysis was 6.9 years (range from 0 to 39 years), and mean age was 35.1±6.4 years (range from 14 to 75 years). Mean 25(OH)D concentration was 51.3±14.8 nmol/L (range from 7.5 to 156.1 nmol/L). Fifty (23.1%) patients had vitamin D deficiency, 120 (55.6%) had vitamin D insufficiency, while 46 (21.3%) had adequate vitamin D levels.
Our study showed statistically significant association between vitamin D status and ethnic group ($p<0.001$). The Chinese ethnic group had the lowest proportion of patients with vitamin D deficiency and insufficiency (60.4%), while Malay had the highest proportion at 86.5%. Mean levels of serum 25(OH)D in Chinese, Indian and Malay SLE patients were 66.3±36.7 nmol/L, 54.9±36.4 nmol/L, and 45.0±27.5nmol/L, respectively. Among the clinical manifestations of SLE, only lupus nephritis showed a statistically significant association with vitamin D status ($p<0.001$). In terms of cardiovascular risk factors, hypertension demonstrated significant correlation with vitamin D status ($p=0.032$).
No significant association was found between vitamin D status and gender. Nonetheless, male SLE patients had higher mean 25(OH)D concentrations at 69.4±36.9 nmol/L, compared to female at 50.2±31.6 nmol/L. There were no significant correlations between vitamin D status and clinical features of lupus such as cutaneous lesions, arthritis and NPSLE; positive Schirmer's test; cardiovascular risk factors, that are, dyslipidemia and diabetes mellitus; osteoporosis; and autoantibodies which included anti-dsDNA antibody, anti-Ro antibody, anticardiolipin antibody and rheumatoid factor.
Conclusions: Sub-optimal vitamin D levels are prevalent among SLE patients in a tropical country and are associated with ethnic group, lupus nephritis and hypertension. It is essential to include vitamin D supplementation in the management of SLE patients.
References:
[1] Toloza SMA, Cole DEC, Gladman DD, et al. Vitamin D insufficiency in a large female SLE cohort. Lupus 2010;19: 13–19.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1100

AB0533 JUVENILE AND JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: CLINICAL CHARACTERISTICS, DISEASE ACTIVITY AND DAMAGE

T.A. Gheita[1], R.E. Gheith[1], H.S. El-Fishawy[2], D.M.R. Bahgat[3], A.M. Nour El-Din[4]. *[1]Rheumatology and Clinical Immunology; [2]Internal Medicine; [3]Clinical and Chemical Pathology, Faculty of Medicine - Kasr Al-Ainy School of Medicine - Cairo University, Cairo; [4]Pediatrics, National Research Centre (NRC), Giza, Egypt*

Background: The diagnosis of systemic lupus erythematosus (SLE) in children is challenging as the heterogeneous manifestations and disease impact on the child's growth highlighted the importance of timely diagnosis and management.
Objectives: The aim of the present study was to assess and compare the clinical characteristics, disease activity and damage between juvenile (JSLE) and juvenile-onset (JO-SLE) Egyptian patients.
Methods: Seventy-eight SLE patients (26 JSLE and 52 JO-SLE) were included in this study. Disease activity was assessed using the SLE Disease Activity Index (SLEDAI) and organ damage using the Systemic Lupus International Collaborating Clinics (SLICC) index.
Results: The mean age of the JSLE children was 13.25±2.09 years and 23.17±4.26 years for JO-SLE cases. JO-SLE cases were older at disease onset with a higher female-to-male ratio. There were no noticeable gender differences. There was a significantly higher frequency of serositis, nephritis and hematological involvement in the JO-SLE (57.7%, 76.9% and 73.1%) compared to the JSLE cases (15.4%; 30.8% and 30.8%) ($p<0.001$ for all). The erythrocyte sedimentation rate, creatinine and proteinuria were significantly increased in JO-SLE while alkaline phosphatase was higher in JSLE cases. In JO-SLE cases, SLEDAI significantly increased (5.96±6.18 *vs* 3.12±1.97; $p=0.003$) and the SLICC tended to increase compared to the JSLE children. More JO-SLE cases received hydroxychloroquine and azathioprine.
Conclusions: The existence of differences in clinical phenotype has been confirmed, between JSLE and JO-SLE especially as regards serositis, nephritis and heamatological affection. The disease damage was comparable which denotes that the maximum organ involvement occurs in childhood with an almost stationary course. Rheumatologists caring for children with SLE must be aware of the greater risk of major haematological and renal involvement as well as important long-term morbidity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2993

AB0534 THROMBOTIC MICROANGIOPATHY IN PREGNANT WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: CHARACTERICTICS AND OUTCOMES

T. Kirsanova[1], M. Vinogradova[1], A. Kolyvanova[2], N. Klimenchenko[1]. *[1]Federal State Budget Institution "Research Center for Obstetrics, Gynecology and Perinatology" MoH, Russian Federation; [2]Moscow State University, Moscow, Russian Federation*

Objectives: to evaluate the impact of thrombotic microangiopathy (TMA) on perinatal and maternal outcomes in patients with systemic lupus erythematosus (SLE).
Methods: This study included 21 SLE patients with pregnancy, who developed TMA signs during pregnancy. Patients underwent general survey, clinical and laboratory assessment for disease activity and APL-antibodies. All of them had low SLE-activity indices.
Results:

Table 1. Laboratory features of pregnant patients with SLE

	TMA (n=7)	Without TMA (n=14)
Hb,g/l	89,8	95,8
LDH, Ed/l	716,39	331,2
ALT, Ed/l	110,9	21,3
AST,Ed/l	69,1	24,3
Creatinine, mkmol/l	113,3	77,3
GFR, ml/min	50,5	81,1
Proteinuria, g/24h	0,65	0,28
Thrombocytes, x10^9	135,5	213,8
sFLT/PLGF	66,6	18,9

Table 2. Perinatal outcomes in pregnant women with SLE

	TMA (n=7)	Without TMA (n=14)
– Livebirth	4	12
– Stillbirth	3	1
Weigh	1363,3	3047,3
Mean gestational age	29,1	36,2

TMA signs were found in 7/21 SLE patients (33%). Patients with TMA had significantly higher systolic and diastolic blood pressure ($P \leq 0.05$), higher serum creatinine and lower estimated glomerular filtration rate ($P \leq 0.05$) than that of those without TMA lesions (tabl.1). APLA positivity was significantly more frequent in patients with TMA (3/7 vs 0/14). TMA onset in 2 patients occurred before 20 gestational weeks, 5/7 have developed PE signs (23–38 weeks), only 3/7 had classical HELLP syndrome. There was no PE in patients without TMA. There was a significant association between the detection of TMA and adverse perinatal outcomes (tabl.2).
Patient with TMA and SLE had a poor outcome and most severe course: 5/7 had a PE (3/7 developed HELLP),3/7 had antenatal fetal death, 3/7had signs of heart damage,5/7 a variety of neurological manifestations. Despite of PE signs in 5/7 with TMA the blood sFlt1/PLGF levels were slightly above normal (average sFlt/PLGF levels in preeclampsia without SLE in our another study is 404,47)
Conclusions: TMA is not an uncommon disorder in pregnant patients with SLE. It is associated with APLA positivity only in 1/3 cases. TMA was significantly associated with renal impairment, systemic hypertension and adverse perinatal outcomes. Less increased ratio of sFlt-1/PlGF in TMA patients than "pure" PE may confirm that PE in patients with TMA is not a condition due to angiogenic factors imbalance. Circulating concentrations of angiogenic factors appear not to be suitable markers to assess the severity of PE and adverse outcomes in SLE patients. Thus, TMA may be an important cause of renal injury and renal dysfunction in a subset of pregnant patients with SLE and associated with worse renal and perinatal prognosis. Complement over-activation via both classical (SLE+APS) and alternative pathways might play an important role in the pathogenesis of TMA in SLE.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6589

AB0535 FATIGUE IS ASSOCIATED WITH HS-CRP IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

T. Aung, L. Sahakian, B. Skaggs, J. Grossman, M. McMahon. *Rheumatology, UCLA, Los Angeles, California, United States*

Background: Fatigue is highly prevalent and has a negative impact on quality of life in patients with Systemic Lupus Erythematosus.[1,2] The 9-item Fatigue Severity Scale (FSS) is one of the commonly used self-report questionnaires to measure fatigue in patients with chronic disease.[3] Although fatigue is one of the most commonly reported symptoms in SLE, previous studies have not consistently found any clear association between disease activity (as measured by the SLEDAI)[4] or with laboratory measures of disease activity.[1]
Objectives: To determine whether fatigue is associated with any laboratory measures of disease activity or inflammation in patients with SLE.
Methods: SLE patients and age-matched controls participating in our longitudinal "Biomarkers of Cardiovascular Disease in SLE" completed FSS questionnaires at study entry. Laboratory measures of cardiovascular risk assessment and lupus disease activity assessments were performed in plasma, including high sensitivity C-reactive protein (hs-CRP), myeloperoxidase (MPO), homocysteine, fasting lipid panels, erythrocyte sedimentation rate (ESR), C3, C4, dsDNA, and urine protein/creatinine ratio (UPCR).
Results: 54 patients and 37 control individuals participated. FSS scores were higher in patients with SLE (4.79±1.63 (mean ± SD) compared to healthy subjects (3.17±1.83, $P<0.001$). There were no significant correlations between FSS and age, gender, or SLE disease duration.
In SLE patients, there was significant correlation between FSS scores and hs-CRP (r=0.56, p=0.004), and an inverse correlation with myeloperoxidase (-0.37, p=0.045). No associations between FSS and C3, C4, dsDNA, ESR, UPCR, fasting lipid levels, or homocysteine were seen in the SLE group. No associations between FSS and laboratory measures of cardiovascular risk assessment were seen in the control group.
Conclusions: Although fatigue is not correlated with traditional laboratory measures of disease activity in SLE patients, we did find significant associations between fatigue, hs-CRP, and myeloperoxidase in our cohort. Future longitudinal studies are underway to determine whether these associations also reflect the risk for progression of cardiovascular disease in patients with high fatigue.
References:
[1] Krupp L B, LaRocca N G MJ et al. A study of fatigue in systemic lupus erythematosus. J Rheumatol. 1990;17(11):1450–1452.
[2] Tench CM, McCurdie I, White PD, D'Cruz DP. The prevalence and associations of fatigue in systemic lupus erythematosus. Rheumatology (Oxford). 2000;39(11):1249–1254. doi:10.1093/rheumatology/39.11.1249.
[3] Hjollund NH, Andersen JH, Bech P. Assessment of fatigue in chronic disease: a bibliographic study of fatigue measurement scales. Health Qual Life Outcomes. 2007;5:12. doi:10.1186/1477–7525–5-.
[4] Wang B, Gladman DD, Urowitz MB. Fatigue in lupus is not correlated with disease activity. J Rheumatol. 1998;25(5):892–895.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2175

AB0536 ANTICARDIOLIPIN ANTIBODIES IN SYSTEMIC LUPUS ERYTHEMATOSUS

T. Ben Salem, I. Naceur, M. Tougorti, M. Lamloum, I. Ben Ghorbel, M.H. Houman. *Internal Medicine, Rabta university hospital, Tunis, Tunisia*

Background: Anticardiolipin (ACL) antibodies have been independently associated with high incidence of thrombotic diseases and pregnancy associated disorders in patients with systemic lupus erythematosus (SLE).
Objectives: This study aims to assess influence of ACL antibodies in SLE and their association with clinical, biological and immunological features.
Methods: A retrospective study of 246 patients with systemic lupus erythematous (revised ACR criteria) conduced in an internal medicine department over a period time of 14 years. Two groups were compared according to the positivity of ACL antibodies (group1: positive ACL/ group2: negative ACL).
Results: ACL antibodies were positive in 48.8% of SLE patients (screened in 168 patients). This prevalence was similar in female and male. Poor general state at diagnosis was more frequent in the ACL positive group (55.7% vs 38.6%; p=0.02). The following data were comparable in the two groups: joint involvement (91.8% vs 90.8%; p=0.7), pericarditis (33.8% vs 37.8%; p=0.6) and pleural effusion (24.1% vs 29.5%; p=0.44). Alopecia (38.6% vs 27.9%; p=0.2), central nervous system involvement (12.5% vs 18.8%; p=) and peripheral neuropathy (6.4% vs 11.1%; p=) were more frequent in the group 2 without significant difference. Prevalence of lupus nephritis was more important in the group 1 (52.8% vs 38.8%; p=0.07). Thromboembolic complications: deep venous thrombosis (13.8% vs 11.9%; p=0.72) and pulmonary embolism (10.8% vs 7.1%; p=0.51) were more frequent in patients with ACL antibodies without significant difference. Obstetrical complications were more frequent in group 1 but differences were not statistically significant; spontaneous abortions (29.5% vs 20.4%; p=0.29), intra-uterin death (13.6% vs 9.3%; p=0.5), premature birth (6.8% vs 1.9%; p=0.3).
There were no associations between hematologic disorders and ACL antibodies; leucopenia (51.3% vs 39.5%; p=0.13) and), lymphopenia (81% vs 80.2%; p=0.9), anemia (77.2% vs 74.4; p=0.6) and thrombopenia (22.8% vs 23.5%; p=0.9) were comparable in the two groups. Frequencies of anti-ds DNA antibody and of antibodies to extractable nuclear antigens were similar in the two groups. Only anti-B2GP1 antibodies were significantly associated to ACL antibodies (51.3% vs 17.2%; $p<0.001$).
Conclusions: ACL antibodies were found in 30–40% of patients with SLE, this is comparable to our group.
No significant associations of ACL antibodies.to thrombotic events or obstetrical complications were found in our patients
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3909

AB0537 ACUTE ACALCULOUS CHOLECYSTITIS: A RARE MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

T. Ben Salem, A. Kefi, M. Jedidi, M. Lamloum, I. Ben Ghorbel, M.H. Houman.
Internal Medicine, Rabta university hospital, Tunis, Tunisia

Background: Acute acalculous cholecystitis (AAC) is a rare complication of systemic lupus erythematosus (SLE) but should be recognized
Objectives: The aim was to describe clinical, biological and radiological features of AAC in SLE patients.
Methods: We report four cases of AAC complicating SLE among 246 patients.
Results: Case 1: A 37-year-old woman with one year history of arthralgia and Raynaud's phenomenon was admitted for fever, cutaneous lesions, nausea and abdominal pain. The right upper quadrant of the abdomen was tender and we noted oral ulcerations and wrist synovitis. Laboratory data showed lymphopenia, hemolytic anemia and an inflammatory syndrome. There was no cholestasis or cytolysis. Antinuclear antibodies (ANA), anti-nucleosome, anti-Sm and anti-ribosome antibodies were positive. Abdominal sonography revealed ascites and gallbladder wall was thick and irregular. The diagnosis of AAC complicating a SLE was made and patient was treated with antibiotics and corticosteroids. Two weeks later, she was asymptomatic and abdominal sonography was normal.
Case 2: A 32-year-old woman had SLE with arthralgia, cutaneous manifestations, hematological involvements and pulmonary hypertension; she was treated with corticosteroids and cyclophosphamide. Six month later, at time of the second pulse of cyclophosphamide, she presented with jaundice and tender hepatomegaly without abdominal pain. Liver enzymes rates were normal except bilirubin which was high at 47 UI. Her abdominal sonography showed gallbladder wall thickness without bile ducts enlargement or gallstones. Patient was continued on steroids and cyclophosphamide but she died because of heart failure.
Case 3: A 40-year-old patient with 12-year-history of SLE was admitted for fever and dyspnea. On physical examination, there was tenderness on right upper quadrant of her abdomen. Cholestasis and cytolysis were found. Abdominal sonography showed a striated and thick gallbladder wall (17 mm). Computer tomography confirmed the gallbladder wall thickness and note pericholecystic edema. Patient was also diagnosed with myocarditis and seritis. A new SLE relapse was obvious and she was treated with prednisone 1 mg/kg/day and azathioprine. The outcome was good and she still is asymptomatic.
Case 4: A 56-year-old-woman was admitted with abdominal pain and fever, limbs paresthesia. Abdominal examination was normal. Biological data showed anemia, thrombopenia and cholestasis. ANA, anti-DNA and anti-Sm were positive. Abdominal sonography showed gallbladder wall thickness and pericholecystic edema. SLE diagnosis with peripheral neuropathy, lupus nephritis, hematological manifestations and ACC was made. Patient was given corticosteroids and cyclophosphamide with good outcome.
Conclusions: Only few cases of AAC complicating SLE are reported. Cholecystitis can be an initial manifestation of SLE and reveal the disease or can occur at any time of the disease course. ACC is always associated to other disease manifestations. Patients present with abdominal pain, vomiting and fever. Ultrasonography and computed tomography confirm the diagnosis. The outcome is good with steroids. Sometimes patients are given antibiotics and/or underwent cholecystectomy because of infectious cholecystisis suspicion. None of our patients had surgery.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2785

AB0538 URINARY LEVELS OF VCAM-1 AND TWEAK AS BIOMARKERS OF LUPUS NEPHRITIS

T. Urrego[1], B. Ortiz-Reyes[1], G. Aroca[2], A.L. Vanegas-García[3,4], A.A. Cadena Bonfanti[2], L. Almendrales[2], C.H. Muñoz[3,4], L.A. González[3], A. Iglesias[2], G. Vásquez[1,3], J.A. Gómez-Puerta[1,3]. *[1]Grupo de Inmunología Celular e Inmunogenética, Universidad de Antioquia, Medellín; [2]Grupo investigación Nefrología, Universidad Simón Bolivar, Baranquilla; [3]Grupo de Reumatología, Universidad de Antioquia; [4]Grupo de Reumatología, Hospital San Vicente Fundación, Medellín, Colombia*

Background: TNF-like WEAK inducer of apoptosis (TWEAK) is able to increase the expression of various molecules involved in the inflammatory response with relevant effects also in angiogenesis. The pathological functions of TWEAK are primarily attributed to its ability to induce the expression of several pro-inflammatory cytokines, chemokines and cell adhesion molecules, including vascular cell adhesion molecule-1 (VCAM-1) (1). Some previous studies (most of them in Caucasic, Afro-American and Asiatic cohorts) have demonstrated clinical utility of VCAM-1 and TWEAK as biomarkers in patients with systemic lupus erythematosus SLE (2).
Objectives: To evaluate the diagnostic value of urinary VCAM-1 and TWEAK in a cohort of Latin-American patients with SLE.
Methods: Patients meeting the revised ACR criteria for SLE were recruited from 2 different centers at Medellín and Baranquilla, Colombia. Urinary levels of VCAM-1 (uVCAM-1) and TWEAK (uTWEAK) were measured using an ELISA kit (R&D system, USA). SLE activity was measured with SLEDAI. Inactive LN was defined by the presence of: 24 hours proteinuria $\leq$500 mg/dl, inactive urine sediments and stable serum creatinine. Mann-Whitney tests were used to compare data and Spearman's rank correlations were used to examine associations.
Results: One hundred and fifty eight SLE patients were recruited (89% female) with median age of 32.8±12.1 years and median disease duration of 7.27±6.6 years. Mestizo (77%) and African Latin-American patients (20%) were majority. Mean SLEDAI score was 8.5±8.7. One hundred and four patients (64%) had lupus nephritis (LN). 76 out of 104 patients had biopsy proven LN, in 62% of cases with proliferative forms. uVCAM-1 and uTWEAK were significantly higher in patients with LN than without LN. At the same time, uVCAM-1 and uTWEAK were significantly higher in patients with active vs inactive LN (Figure). uVCAM-1 (581±1197 vs 189±256 ng/ml, p<0.001) and uTWEAK levels (3202±3778 vs 1123±1873 pg/ml, p=0.038) were significantly higher in patients with Class V LN in comparison with other LN classes. uVCAM-1 and uTWEAK levels had a mild positive correlation with SLEDAI (r=0.22 and r=0.16, respectively). In addition, uTWEAK correlated with 24 hours proteinuria (r=0.28). No significant correlation was found between uVCAM-1 and uTWEAK.

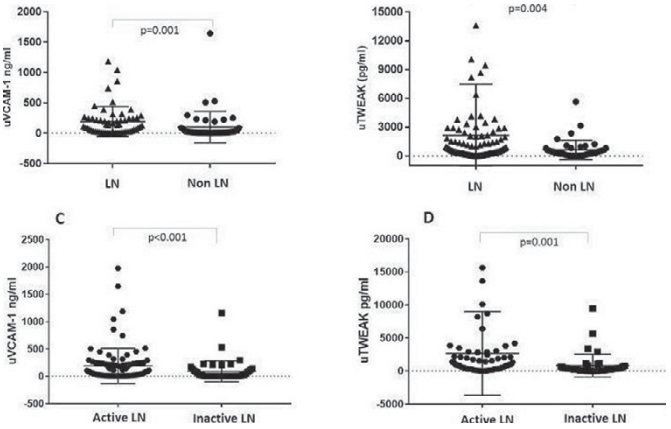


Figure 1. Urinary levels of VCAM-1 and TWEAK in patients with and without LN (A and B) and in patients with active vs inactive LN (C and D).

Conclusions: uVCAM-1 and uTWEAK are useful biomarkers in Latin-American patients with SLE for the identification of patients with LN and active LN. In addition, urinary levels of VCAM-1 and TWEAK were significantly more elevated in patient with membranous LN.
References:
[1] González-Sánchez DA, Álvarez CM, Vásquez G, Gómez-Puerta JA. Role of TWEAK/Fn14 signalling pathway in lupus nephritis and other clinical settings. Nefrologia. 2016. pii: S0211–6995(16)30084–4.
[2] Skeoch S, Haque S, Pemberton P, Bruce IN. Cell adhesion molecules as potential biomarkers of nephritis, damage and accelerated atherosclerosis in patients with SLE. Lupus. 2014;23:819–24.
Acknowledgements: JA Gómez-Puerta was supported by Colciencias (conv. 656 de 2014).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4071

AB0539 DOES ERYTHROCYTE SEDIMENTATION RATE REFLECT DISEASE ACTIVITY IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATODES? CORRELATION WITH ACUTE PHASE REACTANTS, IMMUNOLOGICAL PARAMETERS AND PROTEINURIA

V.S. Schäfer, K. Weiß, A. Krause, W.A. Schmidt. *Medical Center for Rheumatology and Clinical Immunology Berlin-Buch, Immanuel Krankenhaus Berlin, Berlin, Germany*

Background: Patients with active systemic lupus erythematosus (SLE) are considered to have raised erythrocyte sedimentation rate (ESR) rather than raised C-reactive protein (CRP). Yet published evidence is low for this statement. DsDNA-antibodies, C3 complement, ferritin and proteinuria are also commonly applied to assess SLE.
Objectives: Firstly, to assess how ESR correlates with above mentioned laboratory parameters: in general, in the presence of clinical activity and/or infection or in the absence of both. Secondly, to determine if these parameters are associated with disease flare or infections.
Methods: A retrospective analysis of patients of a tertiary referral centre with SLE who underwent inpatient treatment between 2006 and 2015. Data on laboratory parameters, infection and disease flare, judged by the treating physician, were extracted. Patients were divided in four SLE groups: flare only (n=147), infection only (n=48), both (n=23), and neither infection nor flare (n=153). ESR was correlated to CRP, ferritin, proteinuria, C3-reduction and raised dsDNA-antibodies for the whole cohort and within each SLE group. Further, the association between all laboratory parameters and a) disease activity with and without infection, b) the presence of infection with and without disease activity, was tested.
Results: We identified 203 SLE patients, 26 males, with a total of 371 visits. Mean age was 45.6 years (SD± 16.5 years). Table 1 (top part) shows the correlation

coefficients of ESR with the other laboratory parameters. ESR correlated moderately with CRP amongst all groups (r=0.47–0.58); weakly with ferritin in the general and the flare group (r=0.26); and very weakly with C3-reduction and raised dsDNA-antibodies (r<0.2) in each group. Concerning proteinuria, the correlation was weak for all, for flaring and for silent patients (r=0.22 – 0.35), moderate for patients with both infection and activity (r=0.56). There was no correlation in infected patients (r <0.06). Table 1 (bottom part) displays the p-values for the association of parameters with disease activity or infection, respectively. ESR, reduction of C3, proteinuria and raised dsDNA-antibodies were all associated with disease activity in the whole cohort and in the non-infected group; CRP only in non-infected patients. In the infected group, raised dsDNA-antibodies and proteinuria were the only parameters showing significant relation to disease activity. ESR and CRP were significantly associated with infections when looking at all or at inactive patients, but not in active patients.

Table 1: Correlation of laboratory parameters to ESR and association with disease flare and infection

Parameters	ESR	CRP	Ferritin	C3-reduction	Raised dsDNA-antibodies	Proteinuria
Coefficients for correlation to ESR						
all patients (n=371)		0.498*	0.256*	0.165*	0.134*	0.349*
flare only (n=147)		0.549*	0.268*	0.064	0.101	0.222*
Infection only (n=48)		0.468*	0.109	0.172	0.12	0.056
both (n=23)		0.575*	0.266	0.037	0.205	0.556*
silent (n=153)		0.556*	0.25	0.032	0.082	0.341*
P-value for the association with disease activity						
all patients (n=371)	<0.001 *	0.692	0.405	<0.001*	<0.001*	<0.001*
without infection (n=300)	<0.001*	<0.001*	0.318	<0.001*	<0.001*	<0.001*
with infection (n=71)	0.186	0.321	0.713	0.268	<0.001*	0.007*
P-value for the association with infections						
all patients (n=371)	<0.001*	<0.001*	0.797	0.384	0.023*	0.059
without activity (n=201)	<0.001*	<0.001*	0.642	0.281	0.068	0.088
with activity (n=170)	0.039	0.213	0.576	0.255	1	0.057

Conclusions: Both, ESR and CRP are elevated in patients with SLE flare and are weakly correlated with other laboratory activity parameters. Thus, while normal CRP argues against infection elevation of ESR and CRP is not sufficient to distinguish between SLE flare and infection.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5123

AB0540 ORGAN DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

V. Zivkovic[1], B. Mitic[2], B. Stamenkovic[1], S. Milenkovic[1], J. Jovanovic[1], I. Aleksic[1]. *[1]Institute for Treatment and Rehabilitation "Niška Banja", Niska Banja; [2]Clinic of nephrology Clinical centre Nis, Nis, Serbia*

Background: Organ damage in patients with systemic lupus erythematosus (SLE) occurs as the consequence of the disease itself, administered therapy, primarily corticosteroid and cytostatic, as well as the accompanying diseases and complications.

Objectives: Our aim in this paper was to examine the degree of irreversible organ changes in SLE patients using the SLICC/ACR Damage Index (SDI) and to establish the correlation of organ damage with disease activity, quality of life, and severity of fatigue, as well as with the immunological parameters – anti-dsDNA antibodies, anti-nucleosome, anti-C1q antibodies, and MCP1 in the serum and urine.

Methods: The study involved 83 SLE patients (77 women and 6 men), aged 45.8±9.2 years on the average, with average disease duration of 10.6±7.9 years, hospitalized at the Clinic of Rheumatology of the "Niška Banja" Institute, in whom the diagnosis was made based on the revised 1997 ACR criteria. The disease activity was evaluated using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and a physician's global assessment. The degree of organ damage was evaluated using the SDI. The quality of life was assessed based on The Medical Outcome Survey Short Form 36 (SF-36), and the severity of fatigue was measured using the Fatigue Severity Scale (FSS). The level of antibodies was determined using the ELISA test, and serum and urine MCP1 with the sandwich enzyme immunosorbent assay method according to the manufacturer's instructions (R&D Systems, Inc. Minneapolis, USA).

Results: The mean value of organ damage index in all SLE patients was 1.8±2.0 (median 1, min 0, max 9). Twenty-five (30.1%) patients did not have any organ damage (SDI=0); 21 (25.3%) had SDI=1; SDI=2 or 3 was found in 20 patients (24.1%), and 17 patients (20.5%) had SDI≥4. Neuropsychic and musculoskeletal changes were the most common organ damage manifestations, present in 23 (27.7%) of patients. In 21 patients (25.3%), cardiovascular changes were seen, and ocular lesions in 14 patients (16.9%). Renal and pulmonary changes were found in 13 patients (15.7%), cutaneous changes in 3 patients (3.6%), and gastrointestinal changes in 2 patients (2.4%). In 5 cases (6.0%) malignancies were detected, and diabetes mellitus in 2 patients (2.4%). A statistically significant positive correlation of SDI was established with age (r=0,348, p=0,001), disease duration (r=0,412, p<0,001), SLEDAI (r=0,359, p=0,001), global physician's assessment (r=0,357, p=0,001) and fatigue (r=0,296, p=0,007), and a negative correlation with quality of life (r=-0,386, p<0,001). There were no correlations of SDI with the level of anti-dsDNA, anti-nucleosome, anti-C1q antibodies, nor with serum and urine MCP1 levels.

Conclusions: Musculoskeletal, neuropsychic, and cardiovascular changes were the ones most commonly seen. Organ damage positively correlated with age and disease duration, a higher disease activity, poorer quality of life, and more severe fatigue.

References:

[1] Roberts AL, Rizzolo D. Systemic lupus erythematosus: an update on treat-to-target. JAAPA. 2015;28(9):22–8.

[2] Yee CS, Su L, Toescu V, et al. Birmingham SLE cohort: outcomes of a large inception cohort followed for up to 21 years. Rheumatology (Oxford).2015;54(5):836–43.

[3] Cervera R, Doria A, Amoura Z et al. Patterns of systemic lupus erythematosus expression in Europe. Autoimmun Rev. 2014;13(6):621–9.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5140

AB0541 CO-MORBIDITY STATUS IN SYSTEM LUPUS ERYTHEMATOSUS PATIENTS

V. Dostanko[1], V. Yagur[2], N. Dostanko[2], K. Chizh[2]. *[1]Infomed; [2]2-d Department of Internal Medicine, BSMU, Minsk, Belarus*

Background: The improved survival of patients with Systemic Lupus Erythematosus (SLE) over the past decades highlighted the problem of co-morbidity (several different chronic pathologies presence) in SLE patients because many of them reach the age when the burden of concomitant diseases could increase and become ordinary.

Objectives: To evaluate the frequency of concomitant diseases and to estimate the total co-morbidity status in SLE patients.

Methods: The retrospective study of co-morbidity in SLE patients was conducted on the database of Byelorussian Republican Rheumatologic Center. It included 212 patients: 192 women and 20 men at the age of 16.1 to 68.3 (mean ± SD: 33.2±12.3 years) at the baseline (first visit). The diagnosis of SLE was in conformance with 1997 ACR modified classification criteria for SLE [1]. The comprehensive assessment of patient co-morbidities was performed by Kaplan-Feinstein co-morbidity index (KFI) [2] which includes twelve pathology categories: arterial hypertension (HT), heart disease (HD) presence, nervous system (ND) involvement, respiratory system (RD) pathology, vascular (VD), kidney (KD), liver (LD) gastrointestinal (GID) and musculoskeletal (MSD) diseases, other pathology (OD), malignancies and alcoholism. A co-morbidity score of 1 indicates low level of co-morbidity, 2 - moderate and 3 - high level of co-morbidity for corresponding pathology. The possible grade of co-morbidity is calculated as a sum score for all categories and varies from 0 to 36 points.

Results: KFI in SLE patients at the first visit varied from 0 to 7 points (Me: 2; 25–75% range: 0–3) and had minor differences in age and sex groups (NS, Fisher's exact test). One-third of patients (n=68) had no co-morbidities.

One of the most common pathology was HT which was diagnosed in 39 patients (18.4%, 95% CI 5.6–26.7%): 34 women and 5 men (p=0.591, NS, Fisher's exact test). Over the 13-year follow-up period the frequency of HT dramatically increased to 52.9% (95% CI 37.0–68.0%) i.e. 2.9 times vs baseline (p<0,001). Prognostic odds ratios (pOR) of HT were 7.6 (95% CI 3.1–18.2) and 3.2 (1.4–7.6) for lupus nephritis presence and signs of glucucorticoid disease ("cushingoid"), correspondingly.

Other common co-morbidities were GID and HD. Coronary HD and congestive heart failure were revealed in 43 (20.3%) patients. GID were registered in 44 (20.8%) patients, among them 9 (4.2%) patients had gastric/duodenal ulcer. VD, ND and RD were revealed in 7 (3.3%) patients for each category, KD and LD frequency was 6 (2.8%) for both pathology. MSD were registered in 8 (3.8%) and OD, including different infections, anemia, diabetes etc. were registered in 39 (18.4%) patients. There were no cases of malignancies or alcoholism in our patients.

Conclusions: Total co-morbidity status revealed in SLE patients at baseline varied up to the 20 percent of the maximal possible level for all age and sex groups. Arterial hypertension was one of the most common pathology which demonstrated significant and predictable growth over the 13-year follow-up period.

References:

[1] Hochberg, M.C. Updating the American College of Rheumatology Revised Criteria for the classification of Systemic Lupus Erythematosus // Arthritis Rheum. 1997; 40: p.1725.

[2] Kaplan M. H., Feinstein A. R. The importance of classifying initial comorbidity in evaluating the outcome of diabetes mellitus // Journal Chronic Disease. 1974; 27: p.387–404.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6520

AB0542 PRESENTATION AND OUTCOME OF LUPUS NEPHRITIS IN THE MULTICULTURAL SOCIETY OF WESTERN AUSTRALIA – A SINGLE CENTRE EXPERIENCE

W.D. Raymond[1], K. Minas[2], L. Tyack[2], B. Wong[2], A. Douglas[2], A. Kang[3], D. Wong[3], A. Chakera[1,2], J. Nossent[1,4]. *[1]School of Medicine & Pharmacology, University of Western Australia; [2]Renal Medicine; [3]Pathology; [4]Rheumatology, Sir Charles Gairdner Hospital, Perth, Australia*

Background: Lupus Nephritis (LN) is one of the most severe complications that can occur in patients with Systemic Lupus Erythematosus (SLE) as it increases the risk of renal failure, comorbidity and death. As with SLE, there is a significant impact of ethnicity on LN severity and outcome.
Objectives: To investigate the impact of ethnicity of LN presentation and health outcomes in a tertiary referral centre in Western Australia.
Methods: Single centre retrospective cohort study of 104 patients with biopsy confirmed lupus nephritis (LN) collating clinical characteristics, renal histopathology, serology, medication use, disease activity (Systemic Lupus Erythematosus Disease Activity Index - 2K (SLEDAI-2K)), organ damage (SLICC-Damage Index (SDI)), and clinical outcomes from index biopsy event to the last visit. Outcomes included the high serum creatinine ($\geq$150 umol/L), low eGFR ($<$50%), the need for renal replacement therapy (RRT), and death. Outcomes were assessed across ethnicity with comparative statistics, Chi-square, and survival analysis.
Results: Asian (n=17, 16.3%), Caucasian (n=79, 76.0%) and Indigenous (n=8, 7.7%) patients were similar for age (p=0.149), gender (p=0.309) and SLEDAI-2K (8.5 vs. 9.0 vs. 13.0, p=0.897), non-renal SLEDAI-2K (10.5 vs 2 vs. 1, p=0.528). Time to biopsy from the initial SLE diagnosis was shorter in Asian and Indigenous patients (p=0.055). At the index biopsy, ethnic groups were similar for WHO Class distribution (predominantly Classes 3 and 4, p=0.345) and clinical signs of renal disease (the presence of haematuria, proteinuria, pyuria and/or red cell casts) (p=0.874). Indigenous patients trended towards higher creatinine (66.0 vs 71.0 vs. 101.5, p=0.214), lower eGFR (60% vs. 60% vs. 32.5%, p=0.076), lower C3 (0.67 vs. 0.65 vs. 0.47g/L, p=0.375) and C4 (0.15 vs 0.12 vs 0.03g/L, p=0.272), and higher anti-dsDNA antibody levels (16.0 vs 26.5 vs 520.0, p=0.81), albeit non-significantly (due to low numbers).
At the last follow-up, 6.4 years (IQR 3.8, 12.4) after the index biopsy, 10%, 30% and 12.5% of Asian, Caucasian and Indigenous patients had high serum creatinine levels ($\geq$150 umol/L) (p=0.434) and 10%, 28.9% and 25.0% had low eGFR ($<$50%) respectively. Chronic renal replacement therapy (RRT) was needed in 0%, 5.1%, and 12.5%, respectively (p=0.386), while death occurred in 0%, 8.7% and 25.0%, respectively (p=0.115). Indigenous patients had the poorest survival rates at 1, 5 and 10 years compared to Caucasian patients (p=0.002).
Conclusions: This interim analysis demonstrated that Asian patients had a better prognosis regarding serum creatinine, eGFR, commencement of RRT and mortality, compared to Caucasian and Indigenous patients. Indigenous patients were both over-represented in this cohort and showed poorer prognosis in terms of RRT and mortality rates compared to Asian or Caucasian patients in WA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5854

AB0543 ANXIETY AND DEPRESSION IN CHINESE PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

Y. Cui[1], L. Li[1], Q. Zhao[1], S. Chen[1], L. Li[2], Z. Gu[1]. *[1]Department of Rheumatology, Affiliated Hospital of Nantong University; [2]School of Nursing, nantong University, Nantong, China*

Background: Primary Sjögren's syndrome (pSS) is a multisystem autoimmune disorder characterised by lymphocytic infiltration and exocrine failure of salivary and lacrimal glands, resulting in the classical symptoms of the disease including xerostomia (dry mouth) and keratoconjuctivitis sicca (dry eyes). pSS has the potential to impair both psychological state and the health-related quality of life (HR-QOL). A common mental health problem among adults with pSS is anxiety and depression. In addition, depression is more common in pSS than in the general population and has been associated with enhanced fatigue, reduced health-related quality of life, increased levels of physical disability and increased health care costs. Besides, depressed pSS patients have poorer long-term outcomes, including more complications. Anxiety was more common than depression in pSS. The most affected domains were vitality in the SF-36 and general/physical fatigue in the MFI. Extraglandular systemic involvement was not a major determinant of QoL alteration in patients with pSS.
Objectives: Prevalence of anxiety and depression are high in women with Primary Sjögren's syndrome (pSS). Our aim was to compare anxiety and depression in pSS patients and healthy controls and evaluate its relationship with the disease activity, sleep and quality of life; as well as to analyze potential determinants of anxiety and depression.
Methods: Sixty-seven patients fulfilling the American-European Consensus Group criteria for pSS (mean age 52.76 years (s.d. 13.16)) and 42 age-matched healthy controls were included. Participants completed self-administered questionnaires, namely Hospital Anxiety and Depression Scale (HADS), Short Form 36 (SF-36) scores and the Pittsburgh Sleep Quality Index (PSQI). In addition, the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI); Patient Reported Index (ESSPRI) and systemic inflammation (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level) were recorded in patients. Independent samples t-tests, $\chi 2$ analyses and logistic regression modeling were used to analyze the data.
Results: pSS patients experienced greater anxiety and depression than controls (HADS-A scores: mean± SD 6.5±3.4 for pSS versus 3.8±3.4 for controls; P =0.002. HADS-D scores: mean± SD 6.7±4.1 for pSS versus 4.2±3.5 for controls; P =0.012). And there were significant correlations among fatigue, pain, disease activity, dryness, sleep, quality of life and anxiety/depression. Meanwhile, logistic regression analysis revealed that poor quality of life and ESSPRI were significantly associated with anxiety/depression in pSS patients.
Conclusions: The study suggests that optimal care of pSS patients may include the detection and management of anxiety and depression. Early recognition and appropriate intervention is therefore essential to reduce the negative impact of anxiety and depression on the patient's quality of life and outcome of their disease.
Acknowledgements: This research was supported by grants from the National Natural Science Foundation of China (81471603, 81172841); "Top Six Types of Talents" Financial Assistance of Jiangsu Province (Grant no. 10.WSN016).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3069

AB0544 LEVELS OF VITAMIN D IN A COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERITHEMATOSUS. RELATIONSHIP WITH DISEASE ACTIVITY AND BONE MASS

Y. Garcia-Mira, S. Heredia, M. Martínez-Morillo, L. Gifre, A. Prior-Español, J. Camins, J. Cañellas, S. Holgado, L. Mateo, A. Olivé. *Hospital Universitari Germans Trias i Pujol, Badalona, Spain*

Background: Vitamin D (vit D) is an immunoregulatory hormone which seems to mediate immune tolerance. Several studies have suggested that vit D deficiency may be related to increased disease activity in patients with systemic lupus erythematosus (SLE).
Objectives: To analyze 25-hydroxyvitamin D (25-OHD) levels in a cohort of patients with SLE and to investigate their relationship with clinical, analytical, immunological and densitometric parameters.
Methods: Prospective study including patients with SLE (according to SLICC criteria 2013) performed in an Academic Hospital with a referral area of 800.000 inhabitants. 152 patients with SLE were included (138 women [46 postmenopausal]/14 men) with a mean age of 46±12 years (range: 20–75). Clinical parameters (including risk factors for osteoporosis, presence of skeletal fractures, treatment with glucocorticoids (GCC) as well as SLE involvement including haematologic, renal, neurological and skin), biochemical determinations (including 25-OHD, parathormone (PTH)), immunological (ANA, DNA and complement) and SLE activity and severity (assessed by SLEDAI and SLICC index) were assessed in all patients. Bone mineral density was performed by DXA (at lumbar spine and proximal femur). Vit D deficiency was defined as 25-OHD values under 20 ng/mL. Low bone mass was considered as T or Z scale $<$-1 SD; and osteoporosis as T $<$-2.5 SD [age$>$50 years] or Z $<$-2 SD [age $<$50 years]. The study was approved by the Clinical Research Ethics Committee and all patients provided informed consent to participate. Statistical analysis was performed by SPSS.20.
Results: The mean values of 25-OHD were 19.8±11.4 (range, 4.2–66.6). 87.5% of patients had 25-OHD levels below 30 ng/mL, 61.2% below 20 ng/mL and 15.1% below 10 ng/mL. The lowest values were in winter (80%) and spring (64.3%). 42.8% of patients received vitamin D supplements. 56.5% of patients had low bone mass (T or Z scale $<$ -1 SD), and 15.8% had osteoporosis. Levels of 25-OHD showed no correlation with SLE disease activity (complement, Ac antiDNAds, SLICC/SLEDAI) neither with bone mass by DXA. Patients with low bone mass (T or Z $<$-1 SD scale) were older (at the time of inclusion and age of SLE diagnosis), had higher SLICC and lower complement levels whereas no differences were observed in SLEDAI and 25-OHD values. 37.5% of the patients were treated with GCC. Patients without GCC treatment had higher prevalence of vit D deficiency (73.9% vs. 55.6%, p=0.034) compared to patients with GCC treatment.
Conclusions: 61.2% of patients with SLE have 25-OHD deficiency, which is more frequent in winter and spring, and mostly in those patients without GCC treatment. 25-OHD values showed no correlation with the disease activity and damage. However, patients with low bone mass had higher SLICC and hypocomplementemia. Thus, our results suggest the need to perform clinical guidelines to assess bone mass and bone metabolism in this clinical condition. Additionally, we recommend quantifying vit D levels in winter/spring and don't forget to assess those patients without GCC treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5349

AB0545 EFFECT OF EMPATHY NURSING ON THE LIFE QUALITY OF THEPATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Y. Wen[1], L. Yan[1], L. LiMin[2]. *[1]Department of Rheumatology; [2]Nursing department, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: The patients with Systemic Lupus Erythematosus always had sub-health status in psychology and been troubled by the chronicity of the disease. Empathy nursing is an effective treatment for chronic disease such as cancer or terminal patients.

Objectives: To investigate the effect of empathy nursing on the life quality of patients with Systemic Lupus Erythematosus (SLE).
Methods: 120hospitalized patients with SLE admitted from January 2014 to December 2016 were divided into the control group and the experimental group for 60 people in each randomly. The control group was given routine care and the experimental group was given additional empathy care for 6 months. The World Health Organization Quality of Life (WHOQOL-BREF) Chinese version was evaluated on the 2nd day of hospitalization and 6 months after discharge respectively.
Results: Before intervention, the life quality of the two groups was poor. The scores of the control group and the experimental group in each field had no statistic difference (44.13±16.72 vs 44.08±17.33 in physiology, 51.13±14.38 vs 52.01±13.87 in psychology, 58.12±15.33vs 56.71±8.12in social relation, 54.93±13.2 vs 55.33±11.78 in environment and 52.52±15.6vs 52.03±13.44 overall), ($P>0.05$). After the intervention, the scores of the WHOQOL-BREF scale in the two groups were improved to different extents ($P<0.05$) (59.33±13.76 vs 66.77±16.21 in physiology, 57.43±7.88 vs 64.55±11.76 in psychology, 65.22±13.34 vs 72.11±8.12 in social relation and the overall scores were 59.95±14.32 vs 67.89±6.42).The scores of the four dimensions in physiology, psychology, social relations and environment were significantly different from those before the intervention ($P<0.05$). The improvement of the scores in physiology, psychology, social relations in the experimental group was more obvious than the control group ($P<0.05$).
Conclusions: Empathy nursing can obviously improve the life quality of SLE patients, and it is worthy to be popularized.
References:
[1] Empathy - can it be taught? Jeffrey D, Downie R.J R Coll Physicians Edinb. 2016 Jun;46(2):107–112.
[2] Communication Needs of Patients with Breast Cancer: A Qualitative Study. Khoshnazar TA, Rassouli M, Akbari ME, Lotfi-Kashani F, Momenzadeh S, Rejeh N, Mohseny M. Indian J Palliat Care. 2016 Oct-Dec;22(4):402–409.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3096

AB0546 CLINICOPATHOLOGICAL CHARACTERISTICS OF SJÖGREN'S SYNDROME IN THE PRESENCE OR ABSENCE OF OBJECTIVE SICCA SYMPTOMS

Y. Suzuki[1,2], H. Fujii[1], K. Yamada[1], M. Kawano[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Kanazawa University Graduate School of Medicine; [2]Division of Nephrology and Rheumatology, Department of Internal Medicine, Ishikawa Prefectural Central Hospital, Kanazawa, Japan*

Background: Sjögren's syndrome (SS) is generally diagnosed on the basis of objective criteria, including xerophthalmia, xerostomia, autoantibodies, and labial salivary gland biopsy. Patients without objective sicca symptoms (non-sicca SS) require a biopsy. For such patients, we should evaluate pretest probability using parameters other than sicca symptoms before performing an invasive biopsy. To assess pretest probability, data on clinicopathological characteristics of non-sicca SS are needed.
Objectives: This study aimed to analyze the clinicopathological features of non-sicca SS. Epidemiological data, antibody profiles, organ involvement, and labial salivary gland biopsy results in non-sicca SS patients were compared with those in SS patients with objective sicca symptoms (sicca SS).
Methods: We selected 103 patients with primary SS who met Japanese or American College of Rheumatology criteria; those whose results exceeded the focus score by 1 underwent salivary gland biopsy. Objective xerophthalmia was evaluated with the Schirmer's test, and objective xerostomia with the Saxon's test. Seventeen patients were excluded because neither test was performed. Sicca SS was defined as a positive Schirmer's and/or Saxon's test result. Clinical and laboratory data were compared in 70 sicca SS and 16 non-sicca SS patients.
Results: Non-sicca SS patients were younger at diagnosis (45.9±14.8 vs. 61.4±15.1 years, $p<0.001$), had a shorter disease duration (1.1±1.5 vs. 6.9±8.9 years, $p<0.001$), and had a higher rate of positive anti-SS-A/Ro antibody (100 vs. 74.3%, p=0.023), and a lower rate of positive anti-centromere antibody (6.3 vs. 44.3%, p=0.005). Subjective xerophthalmia and xerostomia rates were similar between the groups, but fewer non-sicca SS patients had sicca symptoms as chief complaints (18.8 vs. 58.6%, p=0.004). There were no significant differences in focus score, leukocyte and lymphocyte counts, serum IgG levels, and positive rheumatoid factor and antinuclear antibody levels. The maximum European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI) score during follow-up showed no significant difference (3.34±4.27 in non-sicca SS vs. 3.83±4.68 in sicca SS, p=0.30). However, more non-sicca SS patients had ESSDAI scores ≥ 1 (100 vs. 71.4%, p=0.015), a positive correlation with the biological domain of the ESSDAI (87.5 vs 58.6%, p=0.03), and articular symptoms (37.5 vs 8.6%, p=0.003).
Conclusions: Non-sicca SS patients were younger, had shorter disease duration, and a higher rate of positive correlation with the biological and articular domains of the ESSDAI. Moreover, all non-sicca SS patients had ESSDAI scores ≥ 1. When we diagnose SS patients without objective sicca symptoms, we should assess age, disease duration, and extraglandular organ involvement before performing labial salivary gland biopsy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5177

AB0547 THE PREVALENCE AND THE RISK FACTOR OF HYPERTENSION AND DYSLIPIDEMIA IN SYSTEMATIC LUPUS ERYTHEMATOSUS PATIENTS: EXPLORATORY RESEARCH

Y. Miura[1], M. Saito[1], K.-E. Sada[2], N. Yajima[1]. *[1]Division of Rheumatology, Department of Internal Medicine, Showa University School of Medicine, Shinagawa-ku, Tokyo; [2]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama City, Japan*

Background: Hypertension (HT) and dyslipidemia (DL) are the risk factors for all-cause mortality, cardiovascular and cerebrovascular disease, and end-stage renal disease in SLE patients [1)]. Neither disease activity nor chronic damage were associated with the metabolic syndrome in SLE patients [2)] and there were few reports about the risk factors of HT and DL in Japanese SLE patients.
Objectives: We aimed to describe a prevalence of HT and DL and to identify the risk factor of HT and DL in Japanese SLE patients.
Methods: All SLE patients visited at Showa University Hospital and Okayama University Hospital from January 2016 to September 2016, were enrolled in a cross-sectional study. SLE patients who satisfied American College of Rheumatology (ACR) criteria were included. HT was defined as usage of anti-HT drugs and DL was defined as usage of anti-DL drugs. We performed descriptive statistics and binomial logistic regression analysis to identify the risk factors of HT and DL. Variables considered possible risk factors were BMI, drinking status, smoking status (current smoking), current daily dose of glucocorticoids, past maximum dose of glucocorticoids, lupus nephritis, Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), and Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR-DI).
Results: In total, 244 participants were enrolled. The mean age was 46.2±15.3 years, and 222 (91%) were female. The mean current daily dosage of glucocorticoids was 6.7±5.9 mg, and the mean SLEDAI-2K was 5.0±5.2 and the mean SLICC/ACR-DI was 1.3±1.7. The prevalence of HT and DL were 29.1% (71/244) and 22.1% (54/244). Both HT and DL were confirmed in 11.9% (29/244) patients. On binomial logistic regression analysis, BMI (regression coefficients (β)= -0.095; 95% confidential interval (CI) = -0.173 to -0.020), drinking status (β =0.443; 95% CI =0.000 to 0.879), past maximum dosage of glucocorticoids (β= -0.018; 95% CI = -0.036 to -0.004) and lupus nephritis (β= -0.727; 95% CI =0.230 to 1.241) were identified as the significant independent risk factors of HT. On the other hand, only age (β= -0.030; 95% CI = -0.055 to -0.006) was identified as the independent risk factor of DL. There was no independent risk factor of having both DL and HT.
Conclusions: Our results could help to identify patients at higher risk of HT and DL.
References:
[1] Hsin-Hui Yu. et al. Statin reduces mortality and morbidity in systemic lupus erythematosus patients with hyperlipidemia: A nationwide population-based cohort study. Atherosclerosis. 2015;243:11–18.
[2] Cecilia P Chung. Et al. High prevalence of the metabolic syndrome in patients with systemic lupus erythematosus: association with disease characteristics and cardiovascular risk factors. Ann Rheum Dis. 2007;66:208–214.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2875

AB0548 CIRCULATING PROLACTIN LEVEL IN SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH DISEASE ACTIVITY: A META-ANALYSIS

Y.H. Lee, Y.H. Seo. *Rheumatology, Korea University Medicial Center, Seoul, Korea, Republic Of*

Background: Prolactin has an immune stimulatory effect and may promote autoimmunity by encouraging the development of antigen presenting cells expressing MHC class II and co-stimulatory molecules and modulating IFN-γ secretion.
Objectives: This study aimed to evaluate the relationship between circulating prolactin level and systemic lupus erythematosus (SLE), and to establish a correlation between plasma/serum prolactin levels and SLE activity.
Methods: We performed a literature search for studies that examined prolactin status in SLE patients and controls, and the relationship between circulating (serum or plasma) prolactin levels and SLE using PUBMED, EMBASE, and Cochrane databases. We conducted a meta-analysis comparing the plasma/serum prolactin levels in patients with SLE to controls, and examined correlation coefficients between circulating prolactin level and SLE disease activity.
Results: Twenty-five studies with a total of 1,056 SLE patients and 426 controls were included. Prolactin levels were significantly higher overall in the SLE group than in the control group (SMD =0.987, 95% CI =0.512 – 1.463, $p=4.7\text{x}10^{-5}$). Stratification by ethnicity showed significantly elevated prolactin levels in the SLE group in Asian, Latin American, and mixed populations (SMD =0.813, 95% CI =0.137 – 1.490, p =0.018; SMD =0.981, 95% CI =0.307 – 1.655, p =0.004; SMD =1.469, 95% CI =0.443 – 2.495, p =0.005, respectively), but not in the European population. Meta-analysis of correlation coefficients showed

a significantly positive correlation between circulating prolactin level and SLE activity (Correlation coefficient =0.379, 95% CI =0.026–0.487, p=4.0x10^{-9}).
Conclusions: Our meta-analysis demonstrated that circulating prolactin levels are higher in patients with SLE and that a significantly positive correlation exists between prolactin levels and SLE activity.
Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1243

Vasculitis

AB0549 DEMOGRAPHIC FEATURES AND CLINICAL ASPECTS OF BEHÇET'S DISEASE IN OMANI PATIENTS

A.S. Al Ghafri, H. Al Wahshi. *Rheumatology, Royal Hospital, Muscat, Oman*

Background: Behçet's disease (BD) is a chronic, relapsing, multi-system vasculitis of unknown aetiology. Few reports support the hypothesis that BD has a primarily hereditary basis. It complicated diversified clinical features predominantly involving oral and genital ulcers, ocular and cutaneous lesions. The clinical features of this disease have been described to be different according to geographical areas and gender.
Objectives: The objective of the study is to explore the demographic features and clinical aspects of BD in Omani patients.
Methods: 56 BD patients were recruited and clinical data parameters were recorded including age, sex, age at diagnosis, duration of symptoms till diagnosis, disease characteristics such as oral and genital ulcers, ocular manifestations, the presence of arthritis and cutaneous lesions such as papulopustular lesions and erythema nodosum. Furthermore, other systemic involvement was studied including gastrointestinal, neurological & vascular manifestations. Laboratory tests of BD and treatment used were recorded in each patient.
Results: The onset was between 6–74 years with a male predominance. Oral ulcers were the most common manifestation, followed by genital ulcers, ocular lesions and arthritis. Vascular lesions and GI manifestations were less common. Cutaneous manifestations were rare in patients with BD. The frequency of neurological involvement was significantly high. There were no reported cardiac or urogenital manifestations.
Conclusions: There are quite significant clinical geographical and gender differences among BD patients in which genetic and immunological factors might participate it's aetiopathogenesis.
Acknowledgements: The authors thank Department of research, Oman Medical Specialty Board, Muscat, Oman, for their excellent technical assistance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1202

AB0550 AN AUDIT OF BEHCET'S SYNDROME RESEARCH: RECENT 6 YEARS

A. Murt[1], A. Ercaliskan[1], H. Yazici[2]. *[1]Internal Medicine, Cerrahpasa Medical Faculty; [2]Rheumatology, Academic Hospital, Istanbul, Turkey*

Background: A previous audit by our group of Behçet's syndrome (BS) research, published in 2011 (1) had revealed a list of problems related to research methodology. They were mainly the relative lack of prospective studies, proper use of control groups, a marked under utilization of power calculations where needed and a paucity of studies reporting negative results.
Objectives: We have reassesed the same items as in the previous survey in articles about BS since published. An additional item looked at was self criticism in manuscript preparation (2).
Methods: Original articles from 15 highest impact factor journals of internal medicine, rheumatology, dermatology and ophtalmology between January 2010 and February 2016 were analyzed by two observers. Study designs, presence of necessary control groups, power calculations and reporting of negative outcomes were tabulated. Presence of self-criticism was assessed both by reading and specific word scanning. Discrepansies between the observers was reconciled in a joint session of all 3 authors.
Results: A total of 188 articles, 149 (79%) clinical and 39 (21%) basic, were analyzed. Of 94 studies in which a time-element classification was appropriate; 14% were prospective, 57% cross-sectional and 29% retrospective studies. There were only 3/188 controlled trials. Out of 71 studies in which the study design necessitated control groups, 69 (97%) had healthy and 30% had diseased while 2 did not have any control groups. 50 of the same 71 studies were about genetic association and 13 (26%) had diseased controls in addition to the usual healthy controls. Out of 107 studies in which power calculations were necessary, only18 (16%) gave power calculations. Of these 13 were belonged to 50 (26%) of the genetic association studies and 3/3 to the controlled drug trials. Among 107 studies in which a negative outcome could be expected only 12 studies (11%) reported scuh outcomes. Finally, by electronic scannnig, a limitation acknowledgement was present in 92/188 (49%) of articles [76/149 (51) for clinical and 16/39 (41%) for basic]. When self critique was assesed by text reading these percentages increased to 113 (60%) for total, 93 (62%) clinical and 20 (51%) for basic science studies.
Conclusions: Similar methodological problems seem to exist in current BS research as compared to what we had noted 6 years ago. The relative lack of basic science articles (21%) in a condition with a yet unknown cause (s) and the paucity of controlled clinical trials with the recent much increased avaliability of biologics are particularly worrisome. On the other hand; there was an increased inclusion of diseased controls in genetic association studies, 26% in the current and 13% in the former surveys. Similarly, an optimistic note might be that the currrent survey showed basic research in BS included more self-criticism (41–51%) as compared to what was noted among the general rheumatology manuscripts (15–20%) (2).
References:
[1] Esen F, et al. An Audit of Behcet's Syndrome Research: A 10 year Survey. J Rheumatol 2011;38:99–103.
[2] Yazici H, et al. There was self critique among basic than in clinical Science articles in three rheumatology journals. J Clin Epid 2014;67: 654–657.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5691

AB0551 THE IMPACT OF TEMPORAL ARTERY BIOPSY ON DIAGNOSIS OF GIANT CELL ARTERITIS IN CLINICAL PRACTICE

E. Kaltsonoudis[1], D. Kirochristos[2], A. Bai-Papoudou[3], P. Voulgari[3], A.A. Drosos[3]. *[1]Rheumatology Clinic, Department of Internal Medicine, Medical School, University of Ioannina; [2]Department of Surgery, University Hospitasl of Ioannina, Department of Surgery; [3]Rheumatology Clinic, Department of Internal Medicine, Medical School, University of Ioannina, Medical School, University of Ioannina, Ioannina, Greece*

Background: Temporal artery biopsy (TAB) is the current gold standard for diagnosis of giant cell arteritis (GCA). Clinical manifestations of GCA include cranial symptoms, features of polymyalgia rheumatica (PMR), fever of unknown origin (FUO) and large vessel involvement, following by elevation of C- reactive protein (CRP) and erythrocyte sedimentation rate (ESR). In these patients TAB confirms diagnosis.
Objectives: In the current study the impact of TAB on diagnosis of GCA in a large number of patients is presented.
Methods: 245 patients who had undergo TAB were evaluated. All patients were more than 50 years old and were admitted in a tertiary University Hospital during the period 2006–2016. More specifically 164 were admitted in the division of internal medicine (DIM), 53 in the rheumatology clinic (RC), 6 in the eye clinic (EC) and 3 in the neurology clinic (NC). All the clinical and laboratory data were recorded and analyzed appropriately.
Results: The mean age of the patients was 68,6±5,6 year and 61,5% were women. 49/245 patients had positive TAB (21,17%). More specifically 5/6 positive TAB (83,3%) were ordered by the EC with signs of visual disturbances, mainly visual loss, diplopia and headache. 12/56 positive TAB (22,6%) were ordered by the RC with clinical features of headache and PMR. 31/164 (18,9%) with positive TAB were ordered by DIM with clinical signs of PMR, FUO and anemia of chronic disease and finally 1/3 with positive TAB (33,3) were ordered by the NC with clinical features of severe headache. All patients with positive TAB had elevated levels of CRP and ESR.
Conclusions: In elderly patients with cranial symptoms, visual disturbances, PMR, FUO and raised acute phase reactants, the possibility of GCA is very high and TAB is necessary to confirm diagnosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4749

AB0552 ANTIPHOSPHOLIPID ANTIBODIES IN GIANT CELL ARTERITIS

A. Hocevar, R. Jese, Z. Rotar, P. Zigon, S. Cucnik, M. Tomsic. *Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia*

Objectives: The aim of our prospective study was to evaluate the role of antiphospholipid antibodies (aPL) on the clinical presentation of giant cell arteritis (GCA).
Methods: GCA patients diagnosed for the first time between 1. September 2011 and 31. December 2016 at our secondary/tertiary rheumatology center and in whom aPL-Abs were determined at presentation were included. We studied four types of aPL-Abs in patient's sera: lupus anticoagulants (LA), IgG and IgM isotype of anticardiolipin antibodies (aCL), of antibodies to β2-glycoprotein 1 (aβ2GP1) and of antibodies to phosphatidylserine-prothrombin complex (aPS/PT). LA activity was determined only in patients not receiving anticoagulant therapy. A dilute Russell viper venom time test was used and a ratio above 1.2 was considered positive. aCL, aβ2GPI and aPS/PT were measured using an in-house ELISA. A value above the 99th percentile of healthy control population was taken as positive.
Results: During the 64-month observation period we performed all aPL-Abs tests in 121 GCA patients (81 females (66.9%); median (IQR) age 73.8 (66.4; 78.7) years). We found LA, aCL, aβ2GP1 and aPS/PT in 59 (48.8%), 55 (45.5%), 15 (12.4%) and 18 (14.9%) cases, respectively. Fifty-four patients (44.6%) were single, 25 (20.7%) double, 13 (10.7%) triple and 1 (0.8%) quadruple aPL-Abs positive. 28 patients (23.1%) were aPL-Abs negative. Clinical characteristics of individual aPL-Ab type groups are presented in Table 1. There was one case of

concurrent venous thrombotic event in our group (in a patient without aPL-Abs). The presence of aCL was associated with extracranial large vessel vasculitis (RR 1.8 (95% CI 1.1–2.9)). Double- or triple-positivity for any combination of "classic" aPL (LA and/or aCL and/or abeta2GP1) emerged as a marker of severe visual manifestations (RR of 2.1 (95% CI 1.1–4.3) for permanent or transient visual loss in case of double or triple aPL positivity vs. LA, aCL and aβ2GP1 negative cases). At least 1 year follow-up data (median (IQR) of 103 (54; 105) weeks) were available for 73 patients. 32 patients (43.8%) relapsed, most frequently those with positive aβ2GP1 (62.5%).

Table 1. GCA and aPL

	All GCA	aPL	aCL positive	aB2GPI positive	aPS/PT e positive	LA positive
Number of cases	121	28	55	15	18	59
Female (%)	66.9	67.9	72.7	60.0	66.7	66.1
General symptoms (%)	76.0	67.9	78.2	66.7	66.7	81.4
Headache (%)	69.4	82.1	61.8	66.7	61.1	71.2
Jaw claudication (%)	42.1	46.4	43.6	33.3	22.2	44.1
Visual symptoms (%)	24.0	35.7	20.0	13.3	22.2	16.9
PVL or TVL (%)	12.4	14.3	16.4	13.3	5.6	11.9
PMR (%)	14.0	14.3	16.4	6.7	22.2	11.9
Stroke (%)	2.5	3.6	3.6	0	0	0
Venous thrombosis (%)	0.8	3.6	0	0	0	0
LVV (CDS) (%)	38.8	38.5	50.9	33.3	17.6	31.0
TA CDS (%)	80.2	78.6	74.5	80.0	88.9	79.7
TAB (%)	83.0	86.4	92.5	76.9	84.6	76.6
ESR (mm/h)#	86 (65; 110)	75 (61; 95)	83 (64; 107)	108 (94; 115)	88 (71; 118)	94 (73; 116)
CRP (mg/l)#	73 (45; 134)	62 (36; 124)	69 (44; 106)	95 (66; 164)	65 (52; 117)	113 (65; 170)
Relapse during follow up (%)	43.8	47.1	38.2	62.5	30.0	45.5

Legend: aPL antiphospholipid antibodies; TVL transient visual loss (amaurosis fugax); PVL permanent visual loss; TA temporal artery; TAB temporal artery biopsy; CDS color Doppler sonography; LVV large vessel vasculitis; ESR erythrocyte sedimentation rate; CRP C-reactive protein; #median (IQR).

Conclusions: Our results indicate that aCL could identify GCA patients with extracranial large vessel disease. The double- or triple-positivity for any combination of LA and/or aCL and/or aβ2GP1 seems to be a marker of severe visual manifestations.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2508

AB0553 UPDATED SYSTEMATIC REVIEW 2016: EFFICACY AND SAFETY OF BIOLOGICAL THERAPY COMPARED TO SYNTHETIC IMMUNOSUPPRESSANTS OR PLACEBO IN THE TREATMENT OF UVEITIS ASSOCIATED WITH BEHÇET'S DISEASE

A. Urruticoechea-Arana[1], T. Cobo-Ibáñez[2], V. Villaverde García[3], M. Santos Gómez[1], K. Vargas-Osorio[4], L. Fariñas-Padrón[4], F. Díaz-González[5], V. Calvo-Río[6], R. Blanco-Alonso[6]. *[1]Rheumatology, Can Misses Hospital, Ibiza; [2]Rheumatology, University Hospital Infanta Sofía, Madrid; [3]Rheumatology, University Hospital of Móstoles, Móstoles; [4]Family and Community Medicine, Can Misses Hospital, Ibiza; [5]Rheumatology, Hospital of the Canary Islands, Islas Canarias; [6]Rheumatology, University Hospital of Marqués de Valdecilla., Santander, Spain*

Background: Systematic treatment used in ocular involvement of Behçet's disease are corticosteroids, synthetic and biological immunosuppressants. The possible irreversible ophthalmological complications make it a priority to know the efficacy of these drugs.

Objectives: To analyze the efficacy and safety of biological therapy vs. Cyclosporin A (CsA), azathioprine (AZA), or placebo in reducing the number of uveitis relapses and improving visual prognosis in patients with Behçet.

Methods: Systematic search of the literature in MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials from its inception until August 22, 2016. In additional manual search in international conferences and in the references of included studies. Selection criteria: 1) adults with Behçet's disease and uveitis, 2) Biological therapies, 3) placebo or active comparator with CsA or AZA, 4) outcome measures to evaluate efficacy: number of recurrence of uveitis, visual prognosis, cystic macular edema, retinal vasculitis, vitritis, hypopyon and or adverse events. Meta-analyses, systematic reviews, clinical trials, and observational studies of >10 control patients were included. The selection, review and evaluation of the quality of the articles was carried out by 2 independent reviewers. The Oxford scale was used to determine the quality of studies.

Results: Of 256 articles, 9 met the inclusion criteria: 3 retrospective observational and 6 randomized clinical trials in 378 patients with Behçet and refractory uveitis to synthetic corticosteroids and/or immunosuppressants. The age range was 9–63 years, with male dominance and a follow-up period of 6–36 months. The different treatments: 3 observational studies compared infliximab (IFX) with CsA and IFX with CsA associated with AZA or methotrexate (MTX) and IFNα2a with AZA associated with CsA; 2 clinical trial (CT) compared adalimumab (ADA) with placebo; 1 CT RTX associated with MTX with ciclofosfamide (CFM) associated with AZA; 1 CT secukinumab (SECUK) with placebo; Another daclizumab (DACL) with placebo and the last pegIFN-α-2b with systemic and/or immunosuppressive corticosteroids. Adverse events were recorded as secondary outcomes in the 9 studies.

Conclusions: With variable evidence, IFX appears to be safe and more effective than CsA in reducing short-term uveitis relapse and the number of severe long term complications and retinal vasculitis flares. RTX is similar to CYA associated with AZA in improving short term inflammatory activity. ADA is more effective than placebo as a corticosteroid sparing, achieving early and sustained control in patients with intermediate, posterior, or active uveitis. PegIFNα-2b significantly reduced the dose of corticosteroids, and improved the quality of life. Treatment with IFNα-2a reduces the uveitis/year relapse rate and improves visual acuity. SECUK and DACL, are not effective in reducing uveitis flares but could have an effect on immunosuppressants sparing. The results of this review support the benefit of performing more well-designed comparative studies with IFX, ADA, RTX and IFN-α.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3309

AB0554 RELATIONSHIP BETWEEN DISEASE ACTIVITY AND NEUTROPHIL-LYMPHOCYTE RATIO, PLATELET-LYMPHOCYTE RATIO AND MEAN PLATELET VOLUME IN BEHÇET'S DISEASE

I.E. Okatan, M. Torgutalp, A. Ateş, E. Uslu Yurteri, M.E. Yayla, A.B. Keleşoğlu Dinçer, T.M. Turgay, G. Kınıklı. *Department of Internal Medicine, Division of Rheumatology, Ankara University Faculty of Medicine, Ankara, Turkey*

Objectives: Behcet's syndrome (BS) is an autoimmune disease characterized by chronic inflammation and endothelial dysfunction. There are only a few studies examining the relationship between neutrophil-lymphocyte ratio (NLR), mean platelet volume (MPV), platelet-lymphocyte ratio (PLR) and BS. The aim of this study was to determine NLR, PLR and MPV levels and their association with disease activation in BS patients with mucocutaneous, ocular and vascular involvement.

Methods: The study included 259 patients with BS and 41 healthy individuals. Age, sex, total white blood counts, neutrophil, platelet, mean platelet volume and lymphocyte counts of the patients were recorded. Patients with inflammatory bowel, hematological, infectious, cardiovascular diseases, hyperlipidemia, chronic liver, chronic kidney disease, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, malignancy and corticosteroid use were excluded from the study. Of 259 patients, 163 had active disease (75 active mucocutaneous (MC), 40 active ocular, 48 active vascular involvement) and 96 had inactive disease. MPV, NLR and PLR values of the patients were compared between the groups. P value <0.05 was considered significant.

Results: Age and sex were similar between the groups. We compared the MPV, NLR and PLR values of patients with active and inactive disease. NLR and PLR were significantly higher while MPV was lower in the active group than the inactive and control groups (Table 1). Statistically significant higher PLR and NLR were found in the active MC and vascular groups, significantly lower MPV was seen only in vascular active group. This significance was not seen in active ocular group (Table 2). We also evaluated the same patient's active and inactive periods of the disease, lower MPV, higher NLR and PLR values were seen MC and vascular groups (for all groups $p<0,05$). When the active 3 groups were compared within themselves, the MPV value was significantly lower and NLR and PLR values were significantly higher in vascular group than active ocular and active mucocutaneous groups (p=0.033, <0.001, 0.001, respectively).

Table 1. Demografic and laboratoary, characteristics

Baseline characteristics	Active BD n=163	Inactive BD n=96	Control n=41	p
Age, y (IQR)	35,7 (16,2)	31,3 (13,2)	38,4 (11,8)	0,143
Male, n (%)	69 (%42,3)	36 (%37,5)	10 (%24,4)	0,105
CRP, mg/L (IQR)	4,8 (20,9)	2,7 (5,1)	1 (2,9)	**<0,001**
ESR, mm/h (IQR)	24 (30)	12 (16)	11,5 (9)	**<0,001**
MPV (f/L)	8,5±1,1	8,9±1	8,8±0,9	**0,011**
NLR (IQR)	2,4 (1,7)	1,9 (1,0)	1,8 (0,8)	**<0,001**
PLR (IQR)	134 (63)	116 (44)	130 (65)	**0,012**

Table 2. MPV, NLR and PLR values

		MPV	NLR	PLR
Mucocutaneous Involvement	active (n=75)	8,6±1,0	2,4 (1,4)	134 (54)
	inactive (n=96)	8,8±1,1	1,9 (0,9)	118 (51)
	P	0,168	**0,009**	**0,006**
Ocular Involvement	active (n=40)	8,8±1,5	1,9 (1,3)	117 (43)
	inactive (n=96)	8,8±1,1	1,9 (0,9)	118 (51)
	P	0,807	0,716	0,386
Vascular Involvement	active (n=48)	8,1±0,9	3,2 (2)	161 (98)
	inactive (n=96)	8,9±1,1	1,9 (1,0)	116 (44)
	P	**<0,001**	**<0,001**	**<0,001**

Conclusions: The low MPV and the high NLR and PLR are found in the active disease, which is especially significant in vascular and mucocutaneous groups. In the light of our findings, NLR and PLR were associated with the activity of BS especially with vascular involvement. The low MPV and the high NLR and PLR. The low MPV and the high NLR and PLR may be useful disease activity markers in behcet's disease.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4807

AB0555 ANCA VASCULITIS AND CLASSIC CARDIOVASCULAR RISK FACTORS: COINCIDENCE OR CAUSALITY?

C. Busca, J.J. Ríos, Á. Robles, A. Noblejas, E. Martínez, C. Soto, I. Vives, J.A. Troncoso, L. Bailón, F. Arnalich. *Internal Medicine, la Paz Hospital, Madrid, Spain*

Background: Unlike other systemic autoimmune diseases (rheumatoid arthritis or systemic lupus erythematosus), the mechanisms involved and the association between ANCA vasculitis with cardiovascular risk factors (CVRF) or cardiovascular events (CVE) are unknown. There may be a phenomenon of "early" atherosclerosis that contributes to an increased cardiovascular risk. This process would not be explained only by the co-existence of the classics CVRF.
Objectives: We reviewed the prevalence of classical CVRF and CVE in a cohort of patients diagnosed with ANCA vasculitis. We analyzed whether the appearance of these factors was prior to or subsequent to the diagnosis of the disease or during its evolution.
Methods: A descriptive cross-sectional analysis of the classic CVRF and CVE was analyzed in a cohort of patients with ANCA positive vasculitis in follow-up in the Autoimmune Diseases Division of a Spanish hospital. The main demographic characteristics, type of vasculitis and the presence of arterial hypertension, type 2 diabetes mellitus (T2DM), dyslipemia, smoking and obesity were reviewed. Likewise we analyzed CVE (heart failure -HF-, acute coronary syndrome -ACS-, stroke or transient ischemic attack -TIA- and peripheral arteriopathy –PA-) and if each factor was presented at the diagnosis of the disease or they appeared during the evolution after starting immunosuppressive treatment.
Results: A total of 35 patients were studied: 21 women (60%) and the average age was 53 years old. A number of 15 were microscopic polyangiitis, 9 granulomatosis with polyangiitis and 11 allergic granulomatous angiitis. Twenty one patients presented hypertension, 9 of them (42.9%) developed it after the diagnosis of vasculitis. From 7 patients with diabetes mellitus, 5 of them were before diagnosed with vasculitis. Nineteen presented dyslipemia and 9 of them (47.4%) presented lipid alteration during the evolution of vasculitis. Overweight/obesity was evident in 4 of the 11 cases after the diagnosis of vasculitis. Only 5 patients did not have a cardiovascular event. ACS was observed in 3 patients, HF in 2 and PA in 1 patient. There were no cases of TIA or ischemic stroke. Four of them had dyslipidemia (3 after diagnosis of vasculitis) (p=0.18) and 3 had hypertension (2 after diagnosis of vasculitis, p=0.66). Three patients were overweight or obese (p=0.3) and two had T2DM (p=0.2), both of them appeared after the diagnosis. Previous history of smoking was observed in 4 of the 5 patients (p=0.06). In 3 patients (71.4%) the cardiovascular event was recorded prior to vasculitis diagnosis and only in 2 cases it occurred during the evolution.
Conclusions: This study shows that a high percentage of patients with ANCA vasculitis also presents some type of classic CVRF despite of CVE were not elevated. The diagnosis and treatment of ANCA-positive vasculitis did not statiscally correlate with a greater number of CVE, therefore it would be necessary to carry out studies with a larger number of patients in order to establish conclusions. It is not well defined that weight may have these factors in the prognosis of patients with ANCA vasculitis. These data suggest the need to maintain a close monitoring and therapeutic approach of classic CVRF in this relatively young group of patients.
References:
[1] Cohen Tervaert JW. Best Pract Res Clin Rheumatol. 2013 Feb;27 (1):33–44.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5262

AB0556 INCIDENCE AND RISK FACTORS OF INFECTIONS IN SYSTEMIC NECROTIZING VASCULITIS

C.E. Pena, M. Pera, C. Costi, G. Lucila, P. Castellani, Y. Nuccetelli, M. Garcia. *HIGA San Martin la Plata, la Plata, Argentina*

Background: Infections in patients with systemic vasculitis represent one of the main causes of mortality. Risk factors of infection such as corticosteroid use, intensity of immunosuppressive therapy, age, presence of leucopenia, lymphopenia,hypogammaglobulinemia,associated organic involvement, and dialysis dependence have been identified
Objectives: a)To determine the incidence of infection in patients diagnosed with:Polyangeitis with Granulomatosis (GPA), Eosinophilic Polyangiitis with Granulomatosis (EGPA), Microscopic Polyangeitis (PAM) and Panarteritis Nodosa (PAN), b) clinical characteristics and associated risks factors.
Methods: Analytical, observational,retrospective study. Data source:clinical records of patients diagnosed with ANCA associated vasculitis and Panarteritis Nodosa, evaluated in a center of rheumatology (2000–2016). Variables:Demographic data, clinical manifestations, laboratory data, infectious events serious (requiring hospitalization or prolonged antibiotic/antiviral treatment, recurrences of herpes zoster virus or opportunistic infections), sites of infection, isolated microorganisms, mortality related to the infectious event
Results: 80 patients, 61.25% women. Mean age at diagnosis: 49.2 years (range 18–77). Types of vasculitis: 41.2% GPA, 18.7% EPGA, 26.25% PAM, 3.73% PAN not associated with HBV and 10% ANCA-associated vasculitis that did not met classification criteria. Systemic involvement (68%), pulmonary (59%), renal (58%) and otorhinolaryngology (43.6%) were the most frequent. 36 infectious events were recorded in 28 patients. Follow-up time: Median 22 m (IQR6–64). Incidence of infection:38.4%, with a median of 3 m (IQR 1–18 m) from diagnosis of vasculitis. Low respiratory infections (40.7%), sepsis (39.3%), and urinary tract infections (15%) were the most common. 25% of these patients presented a second infectious event, being low respiratory tract the most frequent site (47%). Two patients had a 3rd event (soft tissue infection, septic shock). Bacterial etiology was the most prevalent (45%).Mortality at the 1st event was 14.3% (n: 4). 71.4% of patients were in the induction phase of treatment. Immunosuppressants used prior to infectious event: cyclophosphamide (48.1%), azathioprine (11.1%), methotrexate (7.4%), mofetil mycophenolate (3.7%), none (22.2%). Corticosteroids $\geq$30 mg/d were observed in 35.7% patients, ranging from 7.5–30 mg/d (10.7%), and $\leq$7.5 mg /d in 35.7%. Presence of leukopenia (26%), lymphopenia (44%), hypoalbuminemia (24%), renal insufficiency (63%) and dialysis dependency (37%) were identified in patients with infectious events. Renal involvement (p0.01) and dialysis dependence (p0.001) were significantly associated with infection.
Conclusions: The incidencia of infection was 38.4%.Lower airway infections, septicemia and urinary tract infections are the most commonly implicated sites. Most infections occurred in the induction phases of the disease. Dialysis dependence and presence of renal involvement were significantly associated with the presence of infection.
References:
[1] Debouverie O.Infections Events During the Course of Systemic Necrotizing Vasculitis A retrospective study of 82 cases. La Revue de Medicine Interne 2010; 35: 636–642.
[2] Kronbickler A. Frecuency, risk factors and prophylaxis of infection in ANCA-associated vasculitis. Eur J Clin Invest 2015; 45 (3): 346- 368.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1758

AB0557 HEART LESSON IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

D. Rednic[1], R. Rancea[2], F. Cozma[1], L. Damian[1], L. Muntean[1,3], M.M. Tamas[1,3], S.-P. Simon[1,3], I. Felea[1], S. Rednic[1,3]. *[1]Rheumatology, Clinical County Emergency Hospital; [2]Cardiology, Heart Institute "Niculae Stancioiu"; [3]"Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania*

Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a disorder characterised by systemic small vessel vasculitis, that occurs typical in patients with a positive history of late-onset asthma and allergic rhinitis. Cardiac involvement is the major cause of mortality. There is required a standardised method to assess cardiac involvement in EGPA.
Objectives: To assess the clinical and imagistic caracteristics of EGPA patients with cardiac involvement in a tertiary referral hospital.
Methods: Fourteen patients (pts) with EGPA were retrospectively analysed between 2010–2016, in Rheumathology Departament in Cluj-Napoca. All patients were screened for cardiac involvement by electrocardiogram (ECG) and cardiac ultrasonography (CUS). Cardiac involvement was defined as follows: ventricular hypertrophy, kinetic abnormalities, valvulopathy, pericardial effusion or diastolic dysfunction. Cardiac magnetic resonance (CMR) and coronarographie was assessed in 4 pts with ECG or CUS abnormalities.
Results: Characteristics of EGPA patients is detailed in table 1. Six out of 14 pts had cardiac involvement (table 2). Only one patient was symptomatic. CMR abnormalities were: endocardial fibrosis in 2 pts, subepicardial inflammation

Table 1. Demographic caracteristic of EGPA patients. EGPA, eosinophilic granulomatosis with polyangiitis; Cardiac, patients with cardiac involvement, Non cardiac, pacients without cardiac involvement; ANCA, anti-neutrophil cytoplasmatic antibody

Characteristics of EGPA Patients	n=14	Cardiac (n=6)	Non cardiac (n=8)
Age at onset, yr ± SD	54.57±9.7	53±12.19	55.75±8.04
Female, n	8	4	4
History of astm, n	7	3	4
ANCA (+), n	5	3	2
Organ involvement, n			
Renal	1	1	0
Pulmonary	9	4	5
Neurologic	10	5	5
Ophtalmic	1	0	1
Skin	6	1	5

Table 2. Electrocardiographic and echocardiographic findings in EGPA patients with cardiac involvement

Electrocardiographic and echocardiographic findings	n=6
Conduction disorders	2
Ischemia in inferior leads, n	1
Pericardial effusion, n	4
Kinetic abnormalities, n	3
Septal thickening, n	3
Mitral insufficiency, n	1
Diastolic dysfunction, n	4

and fibrosis in 1 patient, ventricular hypoperfusion in 2 pts and hypertrophic cardiomyopathy (HCM) in 2 pts. The pts with subepicardial inflamation and HCM had a more severe outcome. Three out of the 6 pts with cardiac involvement were pANCA (+). Hypereosinophilia was singnificantly higher in the group with cardiac involvement ($p<0.012$). None of the patients had positive coronarography.
Conclusions: Cardiac involvement is frecvent and is associated with hypereosinophilia. Absence of pANCA was not associated with the cardiac involvement, in contrast with other publications. CMR makes the difference between inflamatory and noninflamatory lesions, beeing useful in clinical assessment and in treatment decisions, therfore this examination could avoid a fatal outcome. Furthermore, in the future, CMR may replace cardiac byopsy.
References:
[1] Thomas Neumann Cardiac Involvement in Churg-Strauss Syndrome Impact of Endomyocarditis. Medicine (Baltimore). 2009 Jul;88(4):236–43.
[2] Nir Pillar, MD Hypereosinophilic Syndrome With Cardiac Involvement: Early Diagnosis by Cardiac Magnetic Resonance Imaging. Canadian Journal of Cardiology 28 (2012) 515.e11–515.e13.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6383

AB0558 BIOSIMILAR INFLIXIMAB FOR BEHÇET'S SYNDROME

E. Dinçses[1], S.N. Esatoğlu[1], E. Seyahi[1], M. Melikoğlu[1], I. Fresko[1], V. Hamuryudan[1], D. Uçar[2], Y. Özyazgan[2], Z. Kutlubay[3], C. Mat[3], S. Yurdakul[1], G. Hatemi[1]. *[1]Internal Medicine, Division of Rheumatology; [2]Department of Ophtalmology; [3]Department of Dermatology, Istanbul University, Cerrahpasa Medical School, Istanbul, Turkey*

Background: The efficacy and safety of biosimilar infliximab has been studied in several inflammatory conditions and biosimilar was approved for all indications of the reference product in several countries. However, to the best of our knowledge, there was no published reports on its use in Behçet's syndrome (BS).
Objectives: We aimed to report our experience with biosimilar infliximab for the treatment of 3 different types of organ involvements in BS.
Methods: We reviewed the charts of all BS patients who were prescribed infliximab in our multidisciplinary BS clinic. Among the 88 patients who were prescribed infliximab, 4 had used biosimilar infliximab (5 mg/kg) due to refractory disease despite conventional immunosuppressives.
Results: *Case 1:* The first patient was a 28-year-old man who had received azathioprine (AZA), cyclosporine-A and methotrexate for 6 years for ocular involvement. Six months after the immunosuppressives were stopped due to sustained remission he had a stroke with right hemiparesis. Cranial MRI revealed venous infarct extending from posterior limb of left internal capsule to pons and mesencephalon, involving corpus callosum. Cervical MRI revealed a hyperintense lesion between C3-C8 segments. His cranial MR venography excluded sinus thrombosis. He received intravenous pulse corticosteroid followed by biosimilar infliximab. He achieved clinical remission and his MRI at month 3 showed almost total regression of the lesions. He is still in remission at 7th month of therapy. *Case 2:* The second patient was a 24-year-old man using AZA 2,5 mg/kg/day for refractory skin lesions when he developed bilateral external iliac vein and right common iliac vein thrombosis. Biosimilar infliximab was added to AZA. His abdominal superficial collateral vein distension regressed and Doppler ultrasonography at month 4 showed recanalization in bilateral external iliac veins and residual thrombosis only in the right common iliac vein. *Case 3:* The third patient was a 41-year-old man who had used colchicine, AZA, sulfasalazine, interferon-alpha and adalimumab for refractory arthritis. Biosimilar infliximab was started, with only a partial response. After one year treatment was switched to etanercept 50 mg/week and is attack-free for the last 7 months. *Case 4:* The fourth one was a 26-year-old man who was prescribed infliximab for panuveitis refractory to AZA, cyclosporine-A and interferon-alpha. The first infusion was biosimilar infliximab, but the following infusions were reference infliximab due to reimbursement policy of the hospital. There were no adverse events after switching to reference infliximab and the patient is doing well at 8 months of therapy.
Conclusions: Our limited experience showed that biosimilar infliximab may be effective for BS patients refractory to conventional immunosuppressives.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6019

AB0559 IMPROVING THE MANAGEMENT OF GIANT CELL ARTERITIS: A REVIEW OF CARE PATHWAY FOR PATIENTS WITH SUSPECTED GIANT CELL ARTERITIS IN A DISTRICT GENERAL HOSPITAL

F.E. Sin[1], M. Ragheb[2], R. Shah[2], A. Hunter[2], W. Shattles[2], U. Davies[2], R. Makadsi[2], S. Griffith[2]. *[1]Rheumatology Department, Brighton and Sussex University Hospitals NHS Trust, Brighton; [2]Rheumatology Department, East Surrey Hospital, Redhill, United Kingdom*

Background: Giant cell arteritis (GCA) requires prompt diagnosis and treatment to prevent irreversible neuro-ophthalmic complications. Conversely, misdiagnosis leads to unnecessary treatment with high dose glucocorticosteroids (GC) and their associated complications. The British Society of Rheumatologists (BSR) Guideline emphasises early recognition of symptoms and prompt treatment when index of clinical suspicion is high.
At East Surrey Hospital (ESH), we noted that some patients were not managed in accordance with BSR guidelines. Additionally, there is no existing care pathway for patients with suspected GCA to be referred to Rheumatology and for Temporal Artery Biopsy (TAB), often resulting in delayed care provision, or unnecessary use of healthcare resources.
Objectives: This study aims to audit the management of patients with suspected GCA against BSR guidelines. It also aims to evaluate patients' journey, to identify inefficiencies within the management pathway, in order to initiate improvements in service.
Methods: Case notes of patients seen in ESH with suspected GCA between March 2015 and December 2016 were reviewed retrospectively. Cases were identified through keyword search on hospital discharge letters and Rheumatology clinic letters.
Results: Case notes of 67 patients (21M, 46F) were analysed. Of those presenting with suspected GCA, 31% fulfilled ACR classification criteria. 28% had documented visual symptoms at presentation.
Concordance with BSR guidelines: 79% of patients were started on GC at presentation. Of these 15% had a TAB within 7 days of starting GC. 34% were seen by a Rheumatologist within a week of presentation. Of those referred for a TAB 47% were performed within a week of referral.
Care Pathway: The majority of patients (78%) first presented to GPs. Despite this, only 64% of referrals to rheumatology were by GPs. Other referral sources included the Acute Medical Unit (27%) and ophthalmology (5%). 49% were seen by a Rheumatologist within 7 days from referral. 25% had a final diagnosis of GCA.
Conclusions: The small proportion of patients with a final diagnosis of GCA highlighted that early Rheumatology assessment is important to minimise unnecessary TAB and high dose GC. Additionally, the lack of a structured care pathway and a standardised referral system for GCA meant that a large proportion of patients had delay in the diagnosis, inappropriate treatment with GC, and unnecessary TAB. These added to the burden of other already stretched medical specialities.
In light of this; a GCA pathway was implemented to enable rapid access to Rheumatology in patients with suspected GCA. The on-call team was advised to redirect any GP or A&E referrals with suspected GCA to the rheumatology on-call bleep. Patients will be assessed and managed by the rheumatology on-call Registrar or Consultant within 24 hours. The impact of these new implementations will be reaudited in 2017.
References:
[1] Bhaskar Dasgupta, Frances A. Borg, Nada Hassan, Leslie Alexander, Kevin Barraclough, Brian Bourke, Joan Fulcher, Jane Hollywood, Andrew Hutchings, Pat James, Valerie Kyle, Jennifer Nott, Michael Power, Ash Samanta; BSR and BHPR guidelines for the management of giant cell arteritis. Rheumatology 2010;49(8):1594–1597.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5463

AB0560 STUDY ON STREPTOCOCCAL INFECTION RELATIONSHIP WITH HENOCH-SCHONLEIN PURPURA IN CHILDREN

F. Li[1], H. Zeng[2]. *[1]Department of Pediatric Allergy, Immunology and Rheumatolog; [2]Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: To study hemolytic Streptococcus infection relationship with Henoch-Schonlein Purpura in children.
Methods: 42 cases in children with Henoch-Schonlein Purpura (Observer Group) and healthy children in 40 cases of physical examination (the control group) for blood antistreptolysin O (ASO) detection, observation group at the same time children are divided into (belly-non-abdominal Purpura and Purpura group set and repeatedly attacks groups and the Group of non-recurrent) for statistical analysis.
Results: Observation group in the blood ASO detection positive 22 cases, accounted for 52.4%; normal control group children 40 cases, blood ASO detection positive 2 cases, accounted for 5%, both comparison differences has significantly significance ($\chi^2=22.22$, $p<0.01$); abdominal type Purpura children with 23 cases, blood ASO detection positive 17 cases, accounted for 73.9%; non-abdominal type Purpura children with 19 cases, blood ASO detection positive 5 cases, accounted for 26.3%, both comparison differences has significantly significance ($\chi^2=9.45$, $p<0.01$); 14 cases in children with recurrent Henoch-Schonlein Purpura, ASO blood test positive in 12 cases, 85.7%, non-recurrent attacks of 28 cases of children with Henoch-Schonlein Purpura, ASO blood test positive in 10 cases, 35.7%, comparing the two differences are significant ($\chi^2=9.35$, $p<0.01$).
Conclusions: Streptococcal infections may be the important factor relatated to Henoch-Schonlein Purpura in children.Purpura and Purpura of abdominal type recurrence is related with streptococcal infection, which is the great value to treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2136

AB0561 B CELL THERAPY IN REFRACTORY/ RELAPSED ANCA ASSOCIATED VASCULITIS- A SINGLE CENTRE PROSPECTIVE OBSERVATIONAL STUDY

G.G. Ekbote, R. Gupta, N. Mendiratta, N. Negalur, M. Bindroo, V. Singal.
Rheumatology, MEDANTA, the Medicity, Gurgaon, India

Background: Rituximab (Rtx), a novel biological, having B cell depletion mechanism is an anti- CD 20 antibody and is found to be useful in patients of ANCA associated vasculitis. In AAV the disease activity correlates with increased circulating B cells. Rituximab has been found to be useful in depleting these B cells. According to the RAVE study, Rituximab was shown to be non-inferior to Cyclophosphamide in inducing remission. It also showed that the regimen (Rtx) may be superior to the standard regimen of Cyclophosphamide and glucocorticoids for remission induction in severe relapsing ANCA-associated vasculitis.
In our study, B cell therapy was given in those patients only who had persistent disease activity or relapse.
Objectives: To assess response of Rtx in relapsed /refractory cases of AAV and show that it is a good therapeutic stratergy in such cases.
Methods: In our cohort there were 49 patients of ANCA associated vasculitis, diagnosed by clinical and serological criteria, (by both ELISA and IFA) classified according to ACR criteria and supported, wherever possible, by biopsy. In this prospective study, patients were seen during January 2012 to January 2017. A total of 15 patients received Rituximab for various reasons. Rituximab (Rtx) was given as 1 gram infusion on day 1 and day 15 as induction therapy and subsequently 6 monthly maintenance doses of 500 mg were administered. No other immunosuppression other than steroids were given.
Results: Median follow up was 22 months. All patients had recieved Cyclophosphamide (median dose 6 grams) and 1mg/kg glucorticoids at onset. Among the patients who received Rituximab, all had anti PR3 antibody positive & all were GPA clinically. 14 patients (93.33%) had lung involvement, renal involvement was seen in 7 (46.6%) patients, 13 (86.6%) patients had upper respiratory tract involvement, 6 (40%) had ophthalmic involvement. Nervous system involvement was seen in 5 (33.3%) and myocarditis was seen in 3 (20%) each. 3 (20%) patients had gangrene.
Indications for receiving Rtx were heterogenous. It was given for involvement of lung, renal, ophthalmic, upper respiratory and nervous system in 6 (40%), 3 (20%), 3 (20%), 1 (6.66%) and 1 (6.66%) respectively. Whereas 1 (6.66%) patient received Rtx for persistent disease activity.
12 out of 15 patients (80%) achieved remission at mean follow up of 3 months while one achieved at 6 months follow up & all maintained continued remission. 1 patient was due for 3-month follow up. 1 patient died due to lung infection during the course. 4 patients had permanent morbidities/organ damage which they already had before starting Rtx. Only one patient had infusion reaction at the end of 1st induction however she remained in remission after the first dose itself.
Conclusions: 86.6% patients achieved remission after Rtx and remained in continous remission at median follow up of 22 months. Rtx is a very good therapeutic strategy for refractory/relapsed especially PR3+ AAV also it can be used as a maintenance regimen for long term.
References:
[1] Stone JH, Merkel PA, Spiera R, Seo et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. N Engl J Med. 2010;363:221–23.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5596

AB0562 CLASSIFICATION OF ANCA ASSOCIATED VASCULITIS BASED ON PR3 AND MPO SEROLOGY & THEIR OUTCOME: A SINGLE CENTRE PROSPECTIVE STUDY

G.G. Ekbote, R. Gupta, N. Mendiratta, N. Negalur, M. Bindroo, V. Singal.
Rheumatology, MEDANTA, the Medicity, Gurgaon, India

Background: It is often difficult to classify small vessel vasculitis, especially AAV, as Granulomatosis polyangitis [GPA], Microscopic polyangitis [MPA], Eosinophilic granulomatosis polyangitis [EGPA] & Idiopathic cresentic glomerulonephritis. But with the discovery of ANCA, rheumatologists divide this as ANCA positive or negative vasculitis.
Objectives: To classify AAV as anti-proteinase 3 (PR3) antibody+ or anti-myeloperoxidase (MPO) antibody + & compare their clinical presentation & outcome.
Methods: 49 patients were included in our study from August 2011 till January 2017. Patients were classified according to PR3 and MPO serology [based on ELISA].
Results: Median follow up was 18 months. PR3 + were 38 and 11 patients were MPO+. GPA was significantly higher in PR3 Group vs MPO group [36 (94.7%) vs 1 (9.1%) p<0.0001*] while MPA was significantly lower in PR3 group as compared to MPO (2 [5.3%] vs 5 [45.45%] p=0.001*). All EGPAs were MP0+ (4 [36.35%]). 48 fulfilled ACR clinical criteria for GPA/MPA or EGPA. 1 patient with arteritic anterior ischemic optic neuropathy without any other major organ involvement had significantly higher titres of MPO antibodies & was sorted as unclassified AAV. None were idiopathic crescentic glomerulonephritis in our cohort. 18 were biopsy proven [15 PR3+vs 3 MPO+]. Lung involvement was significantly higher in PR3 group than MPO group (32 [84.2%] vs 6 [54.5%] p=0.037*).Kidney involvement was also more in PR3 group but was not statistically significant (20 [52.6%] vs 4 [36.4%] p=0.341). Upper respiratory involvement was significantly higher in PR3 group (26 [68.4%] vs 3 [27.3%] p=0.014*).
Comparision between manifestations of ophthalmic, cardiac, peripheral vascular system & nervous systems of PR3+ & MPO+ groups was not statistically significant.
Complete remission without permanent organ damage was seen in 16 (42%) vs 6 (54.5%) in PR3 and MPO groups respectively (p=0.465). Frequency of relapse/refractory disease, though higher in PR3 group, was not statistically significant (PR3 vs MPO, 10 [26.3%] vs 1 [9.1%] p=0.228). Rates of morbidity & mortality were not significant statistically between PR3 & MPO groups (11 [28.9%] vs 2 [18.2%] p=0.476 & 3 [7.9%] vs 1 [9.1%] p=0.899 respectively). Similar comparisons were made between those who were classified clinically as GPA, MPA & EGPA with respect to remission, relapse, morbidity and mortality. All EGPAs achieved remission. Comparison between groups when divided as GPA & PR3 and MPA & MPO did not show statistical significance. 15 patients (all clinically GPA & PR3+) of the cohort [39.5%] received rituximab for relapse/refractory disease during/after initial induction therapy with cyclophosphamide & steroids.
Conclusions: In this study, we did not find any advantage of clinical classification over serological. Wrongly diagnosing patients when disease is still evolving & inter-clinician bias are eliminated when classifying patients according to serology. Classification as PR3 & MPO is simpler and universal.
References:
[1] Hunder, G. G. et al. The American College of Rheumatology 1990 criteria for the classification of vasculitis. Introduction. Arthritis Rheum. 33,1065–1067 (1990).
[2] Houben E, Bax WA, van Dam B, et al.Diagnosing ANCA-associated vasculitis in ANCA positive patients: A retrospective analysis on the role of clinical symptoms and the ANCA titre. Carubbi. F, ed. Medicine. 2016;95(40):e5096.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4878

AB0563 RITUXIMAB IN PATIENTS WITH TAKAYASU ARTERITIS: A SEVEN PATIENTS EXPERIENCE

G. Pazzola[1], F. Muratore[1], N. Pipitone[1], F. Crescentini[1], P. Cacoub[2], L. Boiardi[1], L. Spaggiari[3], C. Comarmond[2], S. Croci[4], D. Saadoun[2], C. Salvarani[1]. *[1]Rheumatology, Arcispedale S Maria Nuova, Reggio Emilia, Italy; [2]Internal Medicine and Clinical Immunology, Groupe Hospitalier Pitie-Salpetriere, Paris, France; [3]Radiology; [4]Inflammation Laboratory, Clinical Immunology, Allergology and Advanced Biotechnologies Unit, Arcispedale S Maria Nuova, Reggio Emilia, Italy*

Background: Takayasu arteritis (TAK) is a large vessel vasculitis involving the aorta and its major branches in patients younger than 40 years. Glucocorticoids (GCs) are the mainstay of treatment for TAK, but relapses and GC dependence are seen in more than two-thirds of patients. Increasing evidence supports a role for B cells in the pathogenesis of TAK. Circulating plasmablasts and memory B cells are increased, while naive B cells are decreased in patients with active TAK as compared with inactive and control patients [1]. These findings suggest a potential role for B cell depleting therapy in TAK.
Objectives: Our aim was to assess the efficacy and safety of Rituximab (RTX) in a series of 7 patients with TAK.
Methods: We conducted an open-label study on 7 TAK patients (5 followed prospectively, 2 retrospective cases) treated with RTX. All patients satisfied the American college of Rheumatology classification criteria for TAK. Six of the 7 patients had a disease refractory to high dose GCs and conventional immunosuppressive (IS) and/or biologic agents. One newly diagnosed, treatment naïve TAK patient refused GCs and received RTX alone. RTX was administered according to rheumatoid arthritis scheme (2 infusions of 1.000 mg, 15 days apart). Clinical evaluation, laboratory tests (full blood count, ESR, CRP) and imaging modalities (CTA or MRA, and PET/CT) were performed at first RTX administration and every 6 months thereafter. Disease activity was assessed using Kerr index. Radiographic disease progression was defined as new or worsening lesions at follow-up CTA or MRA. PET/CT was considered positive for active disease if two or more large vessels showed grade 2 FDG uptake or higher.
Results: Seven patients (6 females) were included in the study. Mean (SD) age was 32.4 (±16.1) years. At first RTX administration, all patients had active disease

Table 1. Parameters of disease activity before and after Rituximab treatment

Case	Age/Sex	Disease duration (yr)	Previous therapy	ESR/CRP at first RTX (mm/h, mg/dl)	PDN dose at first RTX (mg/day)	Concomitant IS therapy	RTX cycles	ESR/CRP 6 months after last RTX (mm/h, mg/dl)	Imaging (CTA/MRA) 6 months after last RTX	PET/CT 6 months after last RTX	Kerr index 6 months after last RTX	Outcome 6 months after last RTX	PDN 6 months after last RTX	Therapeutic changes	Follow-up (m)
1	20/F	2y	MTX	38/6.2	25g	MTX 20 mg weekly	2g	6/4.7	No disease progression	Positive	Positive	Active disease	5g	Stop RTX, start ADA	12g
2	32/F	0m	None	48/4.6	0m	None	1g	6/3.4	Disease progression	Positive	Positive	Disease progression	12.5g	Stop RTX, start PDN+TCZ	12g
3	21/F	1y	MMF	12/2.7	50g	MMF 2 gr day	1g	16/2.8	Disease progression	Positive	Positive	Disease progression	5g	Stop RTX, start ADA	12g
4	60/M	20y	MTX, MMF, ADA, IFX	66/2.0	25g	MMF 2 gr day	2g	18/0.5	No disease progression	Negative	Negative	Remission	7.5g	PDN tapering, No changes	36g
5	19/F	3y	MTX, AZA, TCZ, IFX, ADA	98/11.5	50g	None	2g	78/4.0	Disease progression	Positive	Positive	Disease progression	10.75g	Stop RTX, start MMF	24g
6	22/F	1y	AZA, MTX	MD/4.5	10g	None	1g	MD/0.3	No disease progression	ND	Negative	Remission	2.5g	No changes	72g
7	54/F	3y	MTX, AZA, TCZ	MD/1.10	15g	None	3g	MD/0.20	No disease progression	ND	Negative	Remission	10g	PDN tapering, No changes	60g

ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; RTX = rituximab; PDN = prednisone; IS = immunosuppressive; CTA = Computerized Tomography Angiography; MRA = Magnetic Resonance Angiography; PET/CT = positron emission tomography/computerized tomography; MTX = methotrexate; ADA = adalimumab; TCZ = tocilizumab; MMF = mycophenolate mofetil; IFX = infliximab; AZA = azathioprine; MD = missing data; ND = not done.

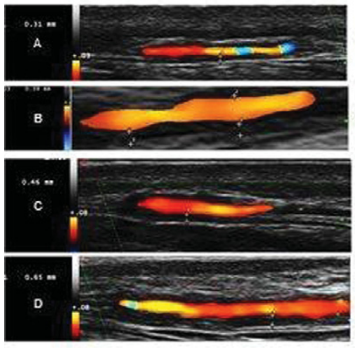
according to Kerr index (≥2), and had also evidence of active disease at PET/CT. Table 1 summarizes the main results of our study.
Despite RTX treatment, 4 of the 7 patients had evidence of persistent disease activity and/or radiographic disease progression during follow-up.
Three out of 7 patients in whom RTX was employed as rescue therapy achieved complete remission.
Conclusions: Our data do not support a role for RTX as first line biologic therapy in TAK patients, but it may have a role in some patients as second/third line biological therapy.
References:
[1] Hoyer BF et al. Takayasu arteritis is characterised by disturbances of B cell homeostasis and responds to B cell depletion therapy with rituximab. Ann Rheum Dis 2012;71:75–9. doi:10.1136/ard.2011.153007.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5158

AB0564 TEMPORAL ARTERITIS: IS THERE ANY CORRELATION BETWEEN ULTRASONOGRAPHIC ARTERIAL WALL INVOLVEMENT AND THE INFLAMMATORY CELLULAR INFILTRATE AT HISTOLOGICAL EXAMINATION?

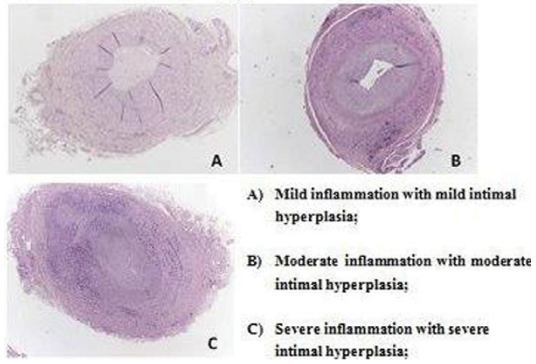
G. Germano[1], P.L. Macchioni[1], A. Cavazza[2], L. Cimino[3], F. Muratore[1], C. Salvarani[1]. [1]*Rheumatology Unit;* [2]*Pathology Unit;* [3]*Ophthalmology Unit, IRCCS Arcispedale Reggio Emilia, Reggio Emilia, Italy*

Background: Ultrasonographic alterations such as the halo sign and the compression test are now accepted as surrogate markers of artery inflammation. No data have yet been published on the correlation between the ultrasonographic grading of arterial wall inflammation and the grading of cellular infiltrate.
Objectives: To compare a semiquantitative ultrasonographic grading (USG) of TA involvement (halo sign and media-intima thickness) with a semiquantitative grading of the inflammatory burden in patients with giant cell (temporal) arteritis (GCA).
Methods: Fiftheen consecutive patients with new onset clinical symptoms and satisfiing ACR criteria for GCA, with positive halo sign in the frontal branch and positive temporal artery biopsy have been enrolled. For each patients we performed power Doppler ultrasonography of temporal artery with a 18–6 MHz linear probe (Esaote MyLab 70) and measured the maximum halo thickness of TA frontal branch in a quantitative and semiquantitave (0–3) grade of involvement (0 = <0.37 mm, 1 = in between 0.38–0.44, 2 = 0.45–0.6 mm, 3 = >0.6). TA biopsy was done in the same frontal branch evalutaed with US. Then we compared the ultrasonographic data with a semiquantitative (0: absent, 1: mild, 2: moderate, 3: severe) grading of the trasmural cellular inflammatory infiltrate and with the intima-media thickness of the TA biopsy specimen. Moreover US results were correlated with the other patterns of histological alterations (giant cells, calcifications, laminar necrosis). Correlation between variables was done by Rho of Spearman method.

Ultrasonography of temporal artery: grading of Halo thickness



Grading of the trasmural cellular inflammatory infiltrate and intima-media thickness of the TA biopsy.



Results: 15 patients, 6 males and 9 females (mean age 71.6±7 years – duration symptoms at onset 1.7±1.3 months – mean ESR 60 mm/h ±29 – mean CRP 8 mg/dl ± 5.2) entered the study. US halo sign was bilateral in 10/15 (66,7%). The mean halo thickness was 0.53 mm ± 0.12. Five patients had USG =1, six patients =2 and four patients =3. The hystological inflammatory grade 1 was present in seven pts, grade 2 in four and grade 3 in four pts. No significant correlation were found between USG and histological inflammatory grade, nor with the presence of giant cells, calcifications, laminar necrosis and intima-media thickness.
Conclusions: No correlation has been found between the size of the halo sign and the hystological inflammatory grading.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5093

AB0565 INSUFFICIENT INFLUENZA VACCINATION COVERAGE IN GIANT CELL ARTERITIS. A FRENCH POPULATION-BASED STUDY

G. Pugnet[1], M. Lapeyre-Mestre[2], M. Mounie[2], G. Moulis[1], L. Sailler[1]. [1]*Service de Médecine Interne, CHU Toulouse Purpan;* [2]*INSERM UMR 1027, Toulouse, France*

Background: French general health insurance scheme has implemented a national influenza vaccination program, including full refund for those 65 years old or more. Despite this program, only 62.6 to 71% of people aged over 65 years are vaccinated and no data are available regarding influenza vaccination coverage (IVC) in GCA.
Objectives: To evaluate the rate and the factors associated with seasonal influenza vaccination coverage in incident giant cell arteritis (GCA) patients compared with controls.
Methods: Using the French National Health Insurance system (SNIIRAM), we included patients with incident GCA from the Midi-Pyrenees region, southern France, and randomly selected 6 controls matched by sex and age at calendar date from January 2005 to December 2008 and followed them till April 2011. The vaccination rate was estimated from vaccine dispensation registered in the SNIIRAM. IVC was compared between GCA and their controls using longitudinal multivariate Poisson regression.
Results: Eighty-seven incident GCA patients over 65 years of age and 509 in the control group were included. Mean follow-up was 4.4±1.2 and 4.2±1.2 years, respectively. During the yearly influenza campaigns from 2005–2006 to 2010–2011, the IVC rates in the GCA group and the control group ranged from 60.8 to 74.7% vs 56.6 to 70.4%, respectively. Incident GCA influenza vaccination rate was 20% higher than controls (RR=1.20; IC 1.09 to 1.32, P<0.001) (Table 1).

Table 1. Associated factors with recommended influenza vaccination (Multivariate longitudinal Poisson analysis)

		Adjusted RR	IC 95%	P
GCA	GCA	1.20	1.09 - 1.32	< 0.001
Comorbidity at baseline				
- High blood pressure		1.13	1.04 - 1.24	0.006
Age, *years*	] 64.4 ; 71.5]	1		
	] 71.5 ; 80]	1.15	1 - 1.32	0.048
	] 80 ; 91.9]	1.13	0.99 - 1.29	0.079
Gender	Female	1.05	0.96 - 1.16	0.259
Time, *Influenza campaigns*	[2005 : 2008]	1		
	[2008 : 2010]	1.11	1.08 - 1.14	< 0.001
	[2010 : 2011]	1.05	1.02 - 1.08	0.002
GCA*Time	GCA * [2008 : 2010]	0.90	0.87 - 0.92	< 0.001
	GCA * [2010 : 2011]	0.77	0.72 - 0.83	< 0.001

GCA: giant cell arteritis, RR: Relative Risk, CI: Confidence Interval. GCA *Time: the interaction term between to have GCA and time variable,

Conclusions: Rates of recommended influenza vaccinations are insufficient in GCA patients over 65 years. More attention should be paid for appropriate vaccination during GCA course.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1814

AB0566 18F-FDG-PET-POSITIVE TEMPORAL ARTERY IN GIANT CELL ARTERITIS: A POSSIBLE CORRELATION WITH HISTOPATHOLOGICAL FINDINGS

H. Kono[1], Y. Okada[1], K. Asako[1], H. Kikuchi[1], Y. Oguchi[1], Z.-I. Honda[1], A. Takeuchi[1], T. Tokairin[2], K. Saito[2]. [1]*Department of Internal Medicine;* [2]*Department of Pathology, Teikyo University School of Medicine, Tokyo, Japan*

Background: Giant cell arteritis (GCA) a form of vasculitis in persons older than 50 years, in which cranial and systemic large vessels can be involved. ^{18}F-fluorodeoxyglucose positron emission tomography - computed tomography (^{18}F-FDG-PET-CT) is increasingly used to diagnose inflammation of the large arteries in GCA. But it is very rare to observe an inflammation of temporal arteries of GCA using ^{18}F-FDG-PET.

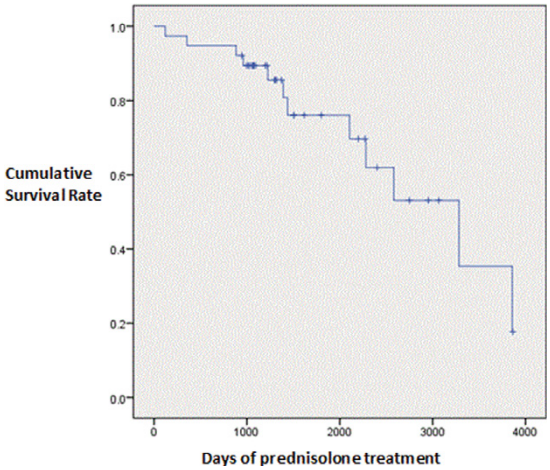
Objectives: To understand the mechanism and frequency of the positive temporal artery of GCA in ^{18}F-FDG-PET.
Methods: This was a retrospective chart review of 3 patients with giant cell arteritis who underwent all of ^{18}F-FDG-PET, MRI, CT angiogram, ultrasound and histopathologic evaluation of temporal arteries. To investigate the cases of FDG-PET positive temporal arteries in GCA, a systematic literature review was done in Pubmed using ^{18}F-FDG-PET AND ("temporal arteritis" OR "giant cell arteritis").
Results: A case report: An 85-year-old male presented with muscle weakness. Three years before admission, he experienced pain in his neck and both extremities. Rheumatoid arthritis was diagnosed at another hospital, and the patient was treated with methotrexate and prednisolone, which resolved his symptoms. The medication was discontinued after 2 years. Two months before admission he began coughing due to interstitial pneumonitis, and later developed muscle weakness and difficulty walking. On admission a physical examination revealed swelling of the bilateral temporal arteries. A blood test showed accelerated ESR at 54mm/h and a CRP of 4.6 mg/dL. Ultrasound showed an increased diameter, hypoechoic wall thickening (halo), stenosis, and calcification of the arterial wall of the temporal artery. A contrast CT showed wall thickening in the affected segments, calcification, stenosis and enhancement of the soft tissue around the temporal artery. An ^{18}F-FDG-PET scan indicated increased uptake of ^{18}F-FDG at the temporal arteries whereas no uptake was found in the other arteries including the aorta and carotid arteries. A biopsy of the temporal artery revealed necrotizing vasculitis with a few giant cells and the formation of a microscopic neutrophilic abscess. When compared with 2 other cases of temporal arteritis with a negative ^{18}F-FDG uptake, the severity of inflammation and the number of giant cells in the present case were not remarkably high. A systematic literature review identified 4 cases of ^{18}F-FDG-PET positive temporal arteries in 454 cases of GCA of 82 papers. Of note, large arteries were positive for ^{18}F-FDG-PET in 253 cases of GCA in the same series.
Conclusions: The hierarchy for FDG uptake by resting inflammatory cells is neutrophil > macrophage = lymphocyte in vitro, indicating that the sites where neutrophils dominate are more likely to be visualized by ^{18}F-FDG PET in vivo. In addition to the known usefulness of ^{18}F-FDG-PET in visualizing inflammation in large vessels, the increased uptake of ^{18}F-FDG to the temporal artery may help to identify the neutrophilic inflammation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4171

AB0567 THE LONG TERM HEALTH RELATED QUALITY OF LIFE (HRQOL) IMPACT ON GIANT CELL ARTHRITIS (GCA) PATIENT

H. Horiuchi. *General Medicine, Kurashiki Central Hospital, Okayama, Japan*

Background: Health related quality of life (HRQOL) of Giant cell Arthritis (GCA) patients is improtant because it adds depth to our understanding of how a disease and its treatments affect them. Though only one previous study has addressed the short term impact of GCA on HRQOL, the long term impact has not fully been investigated.
Objectives: The aim of our study is to assess the long term HRQOL outcomes of GCA patients using the Japanese version of EuroQol 5 Dimention (EQ-5D).
Methods: 40 GCA patients who admitted to our hospital from November 2004 to June 2014 were enrolled. All patients were received prednisolone over 2 years. Patients who had lost their eyesight were excluded because vision concern for HRQOL nor it is difficult to mesure by using EQ-5D. This is a retrospective study and deta were collected by telephone interview. Patients evluated their health status using five dimensions. The EQ-5D score were calculated based on the Japanese version of the value set. Primary outcome is the mortality rate and the norm of EQ-5D score. As a secondary analysis, we classified the patients as follows and compare the mortality rate and EQ-5D score between two groups.

Figure1: Kaplan Meier survival estimate



Group 1: GCA patients who received prednisolone over 5 years.
Group 2: GCA patients who received prdnisolone less than 5 years.
Results: There were 16 male (40%) and 24 female (60%). The median age was 83.5 (95% CI 79.24–87.76). The mortality rate was 37.5% (15 patients). Kaplan-Meier curve is shown in Figure1. The median EQ-5D score was 0.746 (95% confidence interval [CI] 0.852–0.640) and it is lower than Japanese norm (0.853 in male and 0.808 in female). In the secondary analysis, the mortality rate was 56.0% (14 patients) in Group1 and 6.6% (1 patient) in Group2. It was significantly higher in Group 1 ($P<0.05$). The median EQ-5D score was 0.764 (95% CI 0.579–0.870) in Group1 versus 0.768 (95% CI 0.621–0.915) in Group2. There was no statistically significant difference between them ($P=0.813$).
Conclusions: This study focused on GCA patients with prednisolone therapy over 2 years. It showed that EQ-5D was decreased compared with the Japanese norm but it didn't clearly decrease after 2 years of treatment. These findings suggest the value of measuring health status in GCA patients by EQ-5D at least first 2 years of treatment, because it would allow comprehensive evaluation of the patient's health condition and add another dimension to the subjective symptoms and laboratory data.
References:
[1] Arthritis and Rheumatism Vol.49,No6, December 15,2003,pp819–825.
[2] J Neuroophthalmol. 2001 Dec;21(4):266–73.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3691

AB0568 APPLICATION OF OZONATED WATER IN ORAL ULCER PATIENTS WITH BEHCET'S DISEASE

H. Miao, L. Zhang, G. Zhang, K. Xu. *Rheumatology, Shanxi Dayi Hospital, Taiyuan, China*

Background: Behcet's disease is a systemic vasculitis disease of unknown etiology. Oral ulcer is the most common symptoms, the ulcer is various, the swelling and pain is obvious, and it is easy to recurrent, these symptoms affected the patient's diet and life seriously.Therefore, it is important to care the patients with Behcet's disease of oral ulcer.The ozonated water had many functions such as immune activation and immune regulation, it can induce the production of many cytokines,promote the repairment of oral epithelium.At the same time,the ozonated water had a direct effect on the nerve endings,it played a better analgesic effect, it was widely used in oral mucositis which induced by chemotherapy.But there were few studies about application ozonated water in the patients with Behcet's disease of oral ulcer, it was not widely used in clinical practice.
Objectives: Apply the ozonated water in patients with Behcet's disease,observe the effectiveness in patients with Behcet's disease of oral ulcer.
Methods: From June 2014 to June 2016,82 cases of hospitalized patients with Behcet's disease were randomly divided into study group and control group (n=41), the control group used nursing method of gentamycin sulfate solution and nystatin solution gargle alternatively,the research group using ozonated water gargle,observe and evaluate the healing effect of two groups of patients.
Results: The research group had significant improvement in healing oral ulcer and relieving pain ($P<0.05$).
Conclusions: Ozonated water had a perfect effect in patients with Behcet's disease of oral ulcer.
References:
[1] Wainstein J, Feldbrin Z, Boaz, M et al. Defficacy of ozone-oxygen therapy for the treatment of diabetic foot ulcers[J].Diabetes Technol Ther 2011;31(12):1255–1260.
[2] Kim KI, Kim JW, Lee HJ, et al. Recombinant human epidermal growth factor on oral mucositis induced by intensive chemotherapy with stem cell transplantation [J]. Am J Hematol 2013;88(2):107–112.
[3] Xiaotong Yi.The effect of ozonated water on the anti-inflammatory and wound healing of infected wound [J]. Asia Pacific Traditional Chinese medicine, 2012;8(4):331–350.
[4] Xia Wu. Effect of different nursing methods in patients with Behcet's disease of oral ulcer [J]. Southwest Military 2010;12(3):571–572.
[5] Yuan Li, Zeju Yu, Shuling Yang, et al. Effect of ozone water treatment in oral ulcer which induced by radiotherapy[J]. Chinese Journal of nursing, 2012;18(24):2956–2957.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3371

AB0569 CHANGE IN SERUM LEVEL OF SOLUBLE E-SELECTIN AND MMP-9 IN CHILDREN WITH KAWASAKI DISEASE

H. Zeng. *Department of Pediatric Allergy, Immunology and Rheumatolog, Guangzhou Women and Children's Medical Center, Guangzhou, China*

Objectives: Kawasaki disease (KD)is a kind of febrile disorder without definite etiology. Coronary artery aneurysms are the major complication of Kawasaki disease (KD). r11le pathogenesis of the vascular damage remains unknown.This study Wfl8 conducted to explore the pathophysiological role of E-selectin (ES), CMatrix metalloproteinase 9 (MMP-9) in KD.and to look for the evidenee of direct relationship between the plasma levels of ES,MMP-9 and the incidence of the coronary artery lesion (CAL).

Methods: Soluble ES and MMP-9,were measured in 68 patients with KD,20 patients with febrile disease and 20 healthy children by using double antibody sandwich enzyme linked immunosorbent assay (ELISA).Patients with KD were separated into acute phase group, subacute phase group, recovery phase group. coronary artery lesion group (CAL), non-coronary artery lesion group (NCAL).
Results: KS and MMP-9 levels in the acute phase group,subacute phase group were significantly higher than those in the healthy group. Plasma ES and MMP-9 levels of CAL group were significanfly higher than those of NCAL group in acute phase. ne peak level of ES and MMP-9 appeared in the acute phase.There Was a significant correlation between KS and MMP-9 levels in KD patients ($r=0.643$, $P<0.01$).
Conclusions: the increase of plasma PS and ES levels in KD acute phase and subacute phase might play an important role in the pathophysiology of the VasCUlax damage.KS and MMP-9 may potentially be a predictor of CAL in patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2123

AB0570 CLASSIFICATION, EPIDEMIOLOGY, AND CLINICAL PHENOTYPES OF PRIMARY VASCULITIDES IN COLOMBIA

J.E. Barahona-Correa[1,2], Ó.E. Gómez-Cárdenas[3], J.C. Sarmiento Monroy[1,2], R.D. Mantilla[1,2]. *[1]Rheumatology, Center of Dermatology and Rheumatology (FUNINDERMA); [2]Center for Autoimmune Diseases Research (CREA), Universidad del Rosario; [3]Department of physiological sciences, School of Medicine, Pontifical Xavierian University, Bogotá, Colombia*

Background: Primary vasculitides usually pose a diagnostic challenge. They represent a wide spectrum of heterogeneous vascular disorders characterized by variable target vessel involvement, vascular abnormalities, and end organ damage [1]. Several studies about primary vasculitides expose epidemiologic data, mainly from North America and Europe. Nevertheless, data in Latin America is scarce [2].
Objectives: To describe the prevalence and clinical presentation of primary vasculitides.
Methods: This was an observational cross-sectional study in which well-characterized patients were assessed from 2001 to 2016. Each patient was evaluated by the same rheumatologist in a single rheumatology outpatient center in Bogota, Colombia. Patients were classified either according to ACR 1990 criteria (Granulomatosis with polyangiitis, Eosinophilic granulomatosis with polyangiitis, Henoch-Schönlein purpura, Polyarteritis nodosa, Takayasu arteritis, Giant cell arteritis), EMA algorythm (Microscopic polyangiitis) or 2012 revised Chapell Hill nomenclature criteria (Variable Vessel Vasculitis, Single-Organ Vasculitis). ANCA-Associated Vasculitis (AAV) was used to define Small Vessel Vasculitis (SVV) not fulfilling either ACR 1990 criteria or EMA algorythm.
Results: A total of 56 patients were included. Baseline characteristics of patients were as follows: female gender 75%, mean age 56±15.7 years, and median disease duration 3 (IQR 6) years. Most of patients (73%) were diagnosed at first year of disease onset, and fulfilled international classification criteria (63%). SVV was the most frequent phenotype (55%), and C-ANCA/anti-PR3 were the most frequently identified auto-antibodies (40%). Musculoskeletal manifestations (arthralgia, arthritis, and myalgia), mucocutaneous disorders (including vasculitic/necrotic lesions, mucosal ulcers, and purpura), neurological compromise (peripheral and central), and renal involvement (acute renal failure, glomerulonephritis, and lung-kidney syndrome) were the most frequently reported onset symptoms in 29%, 29%, 23%, and 21%, respectively. Interestingly, most of patients did not develop organic compromise other than the onset manifestation form. Thirteen percent of patients fulfilled polyautoimmunity criteria and 9% presented with multiple autoimmune syndrome. Antiphospholipid syndrome was the most common associated autoimmune disease described. Corticosteroids were the most common treatment used in 93% of patients, followed by azathioprine in 57%, cyclophosphamide, methotrexate, and rituximab in 29%, and antimalarials in 27% (Tab.1). No deaths occurred during follow-up.

Table 1. Demographic and immunologic characteristics.

Female gender, n [%]	42 [75]
Mean age at onset, years	51 ± 16.7
Mean age at diagnosis, years	53 ± 15.9
Polyautoimmunity*	7 [13]
Multiple Autoimmune Syndrome **	6 [9]
AAV ANCA distribution	n [%]
C-ANCA/PR3*	12 [40]
P-ANCA/MPO	11 [37]
Both ANCA	3 [10]
No data	4 [13]
Type of vasculitis	n [%]
Small Vessel	31 [55]
AAV	19 [34]
Granulomatosis with polyangiitis	8 [14]
Eosinophilic granulomatosis with polyangiitis	2 [4]
Microscopic polyangiitis	1 [2]
Henoch-Schönlein purpura	1 [2]
Medium Vessel	4 [7]
Polyarteritis nodosa	4 [7]
Large Vessel	13 [23]
Takayasu arteritis	5 [9]
Giant cell arteritis	8 [14]
Other	8 [14]
Behçet	3 [5]
Aortitis	1 [2]
Skin-limited	3 [5]
Cogan syndrome	1 [2]

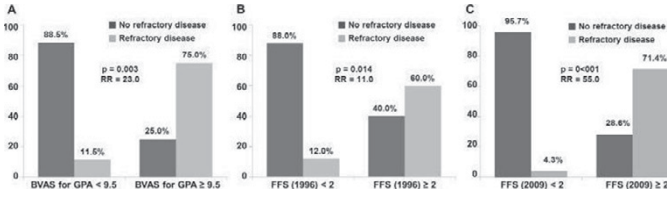
* The presence of more than one autoimmune disease in a single patient. Distribution of autoimmune comorbidities were as follows: antiphospholipid syndrome, systemic lupus erythematosus-SLE like (3 each); autoimmune hepatitis, autoimmune thyroid disease, myasthenia gravis, pyoderma gangrenosum, rheumatoid arthritis, Sjögren's syndrome, and vitiligo (1 each).
** Multiple Autoimmune Syndrome: The presence of three or more well-characterized autoimmune diseases in the same patient.
* A case of TAK with positive C-ANCA was excluded.

Conclusions: Vasculitides are conditions with several subphenotypes, being ANCA-associated the most frequently reported. Onset symptoms seem to be the main drivers of disease evolution. Appropriate and prompt diagnosis is critical to enable timely intervention, aimed to prevent end organ damage and reduce morbidity in these patients. Controlling disease activity and preventing progression is the milestone of treatment. Characterization of Latin America population is pivotal to raise awareness of health-care workers, and policy makers.
References:
[1] Khosla A, et al. Radiol Clin North Am. 2016;54(3):613–28.
[2] Iglesias Gamarra A, et al. Med Sci Monit. 2010;16(3):RA58–72.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6766

AB0571 BIRMINGHAM VASCULITIS ACTIVITY SCORE MORE THAN 9.5 AT DIAGNOSIS IS AN INDEPENDENT PREDICTOR OF REFRACTORY DISEASE OF GRANULOMATOSIS WITH POLYANGITIS

J. You, H.J. Kim, S.-W. Lee. *Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, Seoul, Korea, Republic Of*

Background: Granulomatosis with polyangiitis (GPA), that is identical to what has been called Wegener's granulomatosis, is one of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV). GPA is characterized by necrotising granulomatous inflammation usually affecting small to medium vessels, and it often involves the upper and lower respiratory tracts and commonly provokes necrotising glomerulonephritis. It has been reported that the mortality rate in untreated patients increased up to 90% within 2 years after diagnosis, and the overall mortality rates were ranging from 12% to 44% within 4 to 10 years. The major causes of death are known as cardiovascular disease, adverse events of immunosuppressive agents and major organ involvement of GPA. If there might be predictors of relapse or refractory disease of GPA during the follow-up duration, they can help physicians to select the induction therapeutic regimens, decide the duration of the maintenance therapeutic regimens and adjust the follow-up interval in order to improve the disease course of GPA.
Objectives: We investigated whether clinical manifestations, anti-neutrophil cytoplasmic antibodies (ANCAs), Birmingham vasculitis activity score (BVAS) for granulomatosis with polyangiitis (GPA) and five factor score (FFS) at diagnosis can predict relapse or refractory disease in 30 histology-proven GPA patients with the follow-up duration ≥12 weeks.
Methods: We reviewed the medical records of 30 GPA patients. We collected clinical data, ANCAs, BVAS for GPA, FFSs at diagnosis, and we compared variables between the two groups based on relapse or refractory disease. The optimal cut-offs were extrapolated. Multivariate logistic regression and Cox hazard model analyses were conducted to identify predictors of refractory disease.
Results: The mean age and follow-up duration of patients were 63.3 years old and 45.2 months. The mean initial BVAS for GPA, FFS (1996) and FFS (2009) were 5.4, 0.6 and 1.0. There were no significant predictors of relapse. The mean BVAS for GPA, FFS (1996) and FFS (2009) of patients with refractory disease were higher than those without ($p<0.05$ for all). Patients having BVAS for GPA ≥9.5, FFS (1996) ≥2 and FFS (2009) ≥2 exhibited significantly enhanced risk of refractory disease than those having not (RR 23.0, RR 11.0, and RR 55.0, respectively), and low cumulative refractory disease free survival rates. Multivariate Cox hazard model analysis proved BVAS for GPA ≥9.5 was an independent predictor of refractory disease during the follow-up duration (OR 12.892).



Conclusions: BVAS for GPA ≥9.5 was an independent predictor of refractory disease during the follow-up duration ≥12 weeks.

References:
[1] Jennette JC, Falk RJ, Bacon PA, et al. (2013) 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 65(1), 1–11.
Acknowledgements: This study was supported by a faculty research grant of Yonsei University College of Medicine (6–2016–0145) and by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute, funded by the Ministry of Health and Welfare, Republic of Korea (HI14C1324).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4573

AB0572 EFFICACY AND SAFETY OF RITUXIMAB FOR ANCA ASSOCIATED VASCULITIS

K. Fujita[1], M. Hirata[1], S. Oguni[2], Y. Nakashima[2], Y. Nomura[2], Y. Yamamura[3], K. Nonaka[2], N. Shibutou[1,2], N. Momoki[2], A. Ueno[1], T. Ombe[2], K. Maruyama[2], M. Hiramatsu[2], M. Yamamura[1]. *[1]Centre for Rheumatology; [2]Centre for Kidney Diseases, Okayama Saiseikai General Hospital; [3]Okayama University Hospital, Okayama, Japan*

Background: In Japan, rituximab (RTX) has become one of the dominant alternatives for ANCA associated vasculitis (AAV) even for elderly patients.
Objectives: The efficacy and safety of RTX for AAV patients was determined at our hospital.
Methods: Nineteen patients with AAV, including 14 newly diagnosed patients and 6 relapsed patients, had been treated with RTX. There were 10 males and 9 females. They were all MPO-ANCA positive; 16 were diagnosed with microscopic polyangiitis (MPA), 2 with granulomatosis with polyangiitis (GPA), and 1 with undifferentiated, according to the EMA classification of AAV. The mean age at RTX induction was 71.3 years (range: 40 – 82 years). The efficacy was evaluated by the BVAS score at the time of first induction and after 6 month treatment. Adverse events were recorded during the 6-month treatment.
Results: The mean of BVAS decreased from 17.3 (range: 7–35) at the first induction to 1.2 (0–4) at 6 month of RTX treatment. Of the 10 patients who could be followed-up for over 6 months, 7 patients achieved remission (BVAS=0) (remission rate: 70.0%). The titer of mean MPO-ANCA decreased 136.1 IU/mL (9.9–300 IU/mL) to 44.4 IU/mL (1.0–114.0 IU/mL) at 6 month. The dose of prednisolone decreased from 34.4mg/day (5–60mg/day) at baseline to 5.5mg/day (0–10 mg/day) at 6 month. The adverse events were as follows: 3 patients experienced reactivation of cytomegalovirus (CMV) with a CMV colitis, one patient with sepsis following urinary-tract infection, and one patient with bacterial pneumonia. One patient with PMA died of exacerbation of the disease itself.
Conclusions: In Japan, AAV, mostly MPO-ANCA-positive PMA, affects elderly persons. The results suggest that RTX may provide a therapeutic option for elderly patients at the age of over 70 years with severe MPA, with an acceptable safety profile and rapid glucocorticoid tapering. However, careful monitoring for infectious diseases will be needed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2568

AB0573 AUTOLOGOUS STEM CELL TRANSPLANTATION IN THE MANAGEMENT OF REFRACTORY BEHÇET'S SYNDROME: A CASE SERIES FROM A SINGLE CENTRE OF EXCELLENCE

L. Chadwick[1,2], D. Thong[2], J. Nair[1], N. Goodson[1,2], R. Moots[1,2]. *[1]Aintree University Hospital; [2]Institute of Ageing and CHRonic Disease, University of Liverpool, Liverpool, United Kingdom*

Background: Evidence regarding haematopoietic stem cell transplantation (HSCT) in refractory Behçet's Syndrome (BS) is limited. A systematic review in 2014 identified 20 patients with BS who had undergone HSCT, from which 9 patients underwent HSCT with refractory BS as the primary indication. Of these 20 patients: 15 achieved complete remission, 1 patient achieved partial remission, 2 patients relapsed, 1 patient died and 1 had no outcome reported. Nine patients had reported complications, 5 patients had no complications and 6 patients were missing data. All data was sourced from single case studies (1).
Objectives: Outline the indications, outcomes and complications of HSCT in a case series of 4 patients with BS managed at a single centre of excellence.
Methods: Case notes were reviewed for 4 patients from the Liverpool Behçet's Centre of Excellence (LBCE) who have undergone HSCT.
Results: The primary indication for 3 of the 4 patients who have undergone autologous HSCT at LBCE was refractory BS. Patient 1 underwent HSCT for multiple myeloma, but suffered from severe BS with neurological and venous involvement and is now in partial remission with occasional mild muco-cutaneous ulceration, not requiring systemic immunosuppression. Patient 2 underwent HSCT for severe refractory neuro-Behçet's. This patient is now in complete remission after commencing azathioprine for oral ulceration. The indications for HSCT in patients 3 and 4 were severe muco-cutaneous ulceration and dermatological involvement refractory to numerous biologic agents with high ongoing steroid dependency. Patient 3 also had previous thrombophlebitis and patient 4 had previous gastro-intestinal ulceration. They are both currently in complete remission but follow up time is limited. Patient 3 had a post-HSCT complication of pneumonia and mucositis which resolved without persistent morbidity, patient 4 had an upper limb deep vein thrombosis (DVT) as an inpatient.
Conclusions: HSCT is an effective treatment modality for severe refractory BS and can result in medication free remission. However, the associated risks should be considered and alternative treatment options deliberated or exhausted before opting for this treatment modality.
References:
[1] Soysal T, Salihoğlu A, Esatoğlu SN, Gültürk E, Eşkazan AE, Hatemi G, et al. Bone marrow transplantation for Behçet's disease: a case report and systematic review of the literature. Rheumatology. 2014; 53(6):1136–41.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4745

Abstract AB0573 – Table 1

Patient	Age at HSCT (years)	Sex	Disease duration at HSCT (years)	BS manifestations	Treatment pre-HSCT	HSCT Indication	Follow up (months)	Complications	Outcome	Treatment post-HSCT
1	47	M	6	OU GU S MSK V N	Tacrolimus	Multiple Myeloma	135	Nil	OU GU (minor)	Pred 4mg
2	29	M	5	OU GU S Ocular N	MMF Tacrolimus IFX ETN CYCP ALN	Neuro-Behçets	80	Nil	1x flare 2013 (OU)	AZA
3	51	M	4	OU GU S V N	AZA MMF ETN ADA Certolizumab Interferon	Refractory, severe OU & GU	1	DVT	Remission	nil
4	42	F	Unknown	OU GU S MSK Gastro	AZA Leflunomide MTX Thalidomide IFX ADA ETN ALN	Refractory, severe OU & GU	8	Pneumonia & Mucositis	Remission	Pred 40mg

OU = oral ulceration, GU = genital ulceration, MSK = musculoskeletal, S = skin, N = neurological, V = vascular. AZA = azathioprine, CYCP = cyclophosphamide, MMF = mycophenolate motefil, MTX = methotrexate. ADA = adalimumab, IFX = Infliximab, ETN = Etanercept, ALN = Alentuzumab.

AB0574 VENOUS INVOLVEMENT IN BEHCET'S DISEASE: A RETROSPECTIVE ANALYSIS OF 75 CASES

L. Belhadj, A. Hariz, I. Boukhris, I. Kechaou, S. Azzabi, L. Ben Hassine, E. Cherif, N. Khalfallah. *Internal medecine B, Charles Nicolle Hospital, Tunis, Tunisia*

Objectives: Behcet's disease (BD) is a chronic multisystem inflammatory disease characterized by recurrent mouth and genital ulcerations. The vascular involvement varies from 7, 7 to 43% depending on ethnicity. Venous lesions are

the most frequent vascular manifestation in BD. In this study, we looked at the pattern and outcome of venous events in BD.
Methods: Seventy five patients, who fulfilled the criteria of the International Study Group for diagnosis of BD, were recruited. We studied the characteristics of patients with thrombotic venous events. Clinical data parameters were recorded, including age at onset, the vascular and extra-vascular manifestations of the disease.
Results: Twenty six from 75 patients had vascular event. Twenty three of these patients had a venous event. The mean age of the patients at the first venous event was 32 years. There were 22 males and 4 females. The first venous event occurred before BD diagnosis in one case and in the same time of onset of the disease in two cases. In the other cases, venous event occurred in patients followed for BD and the mean disease duration was 5, 82 years. The mean number of recurrence of venous events was 1, 46. Deep vein thrombosis was the most frequent single vascular event (76, 92%). The most frequent localizations were in legs (23 cases). Four patients had cerebral vein thrombosis. A pulmonary venousinvolvement, a Budd-Chiari syndrome,an inferior and superior vena cava syndrome and arms thrombosis were found in only one case each one. An arterial event was associated in 2 cases. An association with ocular manifestations was observed in 26, 9% patients and neurologic manifestations in 11, 53%.
Conclusions: Although there is no agreement on the frequency rate of the vascular lesions in the littérature, most the vascular lesions in the litterature, most of the reported series indicate that the venous lesions are by far, more common than the arterial lesions. Kabbaj et al. reported 85% venous, 10% arterial and 5% mixed arterial and venous involvment which is similar to the reported frequency in our patients.
In conclusion, the frequency of vascular complications of BD in our patients is similar to those reported around the world.
References:
[1] Seyahi E. BehÃ§et's disease: How to diagnose and treat vascular involvement.
[2] Best Pract Res Clin Rheumatol. 2016 Apr;30(2):279–295.
[3] Seyahi E. BehÃ§et's disease: How to diagnose and treat vascular involvement.Best Pract Res Clin Rheumatol. 2016 Apr;30(2):279–295.
[4] Balta S, Balta I, Ozturk C, Celik T, Iyisoy A. BehÃ§et's disease and risk of vascular events. Curr Opin Cardiol. 2016 Jul;31(4):451–7.
[5] Seyahi E, Cakmak OS, Tutar B, Arslan C, Dikici AS, Sut N, Kantarci F, Tuzun H, Melikoglu M, Yazici H. Clinical and Ultrasonographic Evaluation of Lower-extremity Vein Thrombosis in Behcet Syndrome: An Observational Study. Medicine (Baltimore). 2015 Nov;94(44):e1899.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6850

AB0575 RETROSPECTIVE SURVEY OF CONCOMITANT AUTOIMMUNE DISEASES AND AUTOANTIBODIES IN A COHORT OF PATIENTS WITH ANCA-ASSOCIATED VASCULITIS (AAV)

M. Casal Moura[1,2,3], S. Prieto-González[3], G. Espígol-Frigolé[3], G. Murgia[3,4], M. Alba[3], J. Hernández-Rodríguez[3], M. Cid[3]. *[1]Department of Internal Medicine, São João Hospital Center; [2]Department of Medicine, Porto Medical School, Porto, Portugal; [3]Department of Autoimmune Diseases, Hospital Clínic. University of Barcelona. IDIBAPS, Vasculitis Research Unit, Barcelona, Spain; [4]University Clinic for Visceral Surgery and Medicine, Bauchzentrum Bern, Bern, Switzerland*

Background: Anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV) – granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA) have heterogenous clinic and biologic phenotypes. Sporadic reports indicate that some AAV patients may have other autoimmune diseases but the frequency of the association is unknown.
Objectives: Our purpose was to assess the frequency of other autoimmune diseases or autoantibodies in a well-defined cohort of AAV patients.
Methods: Retrospective survey of a cohort of patients regularly controlled at outpatient facility of an Autoimmune Disease Department in a 5-year period (2011–2016). Clinical and immunologic data were retrieved from electronic records. All patients were diagnosed and treated by the authors.
Results: We included 110 AAV patients – 36 (32.7%) GPA, 45 (40.9%) MPA and 29 (26.4%) EGPA. Regarding to ANCA specificity – 23 (20.9%) against proteinase 3 (PR3)-ANCA, 68 (61.8%) against myeloperoxidase (MPO)-ANCA and 19 (17.3%) were ANCA negative. Organ-specific auto-immune diseases was actively searched in 73 (81.1%) patients and was present in 43 (58.9%) patients. More prevalent autoimmune diseases diagnosed were: hypothyroidism (15,34.9%), pernicious anemia (12,27.9%), Sjögren syndrome (8,18.6%), hyperthyroidism (4,9.3%) and primary biliar cholangitis (3,7.0%). Autoantibodies more frequently positive were: ANAs 29 (67.4%), ASMA 27 (62.8%), anti-parietal cells 20 (46.5%), anti-thyreoglobulin 6 (14.0%), anti-peroxidase 12 (27.9%), anti-SSa 5 (11.6%), anti-SSb 3 (7.0%) and RF 14 (32.6%). Prevalence of organ-specific autoimmune disease was higher in MPA (67.4vs.32.6%,p=0.001) and ANCA-MPO carriers (81.4vs.18.6%,p<0.001). Pernicious anemia was more prevalent in MPA (41.4vs.0%,p=0.027) and in ANCA-MPO (34.3vs.0%,p=0.054) and myositis was more prevalent in ANCA-PR3 (12.5vs.0%,p=0.037). ANAs positivity was more prevalent in ANCA-MPO carriers (74.3%vs.36.5%,p=0.048). Predictive factors for development of organ-specific autoimmune disease identified were: female gender (OR 2.710,95% CI 1.034–7.099,p=0.043), MPA syndrome (OR 3.578, 95% CI 1.334–9.523,p=0.011) and MPO carriers (OR 3.346, 95% CI 1.166-9.601,p=0.025).
Conclusions: A substantial percentage of AAV patients, particularly MPA and anti MPO carriers, have associated autoimmune diseases and autoantibodies. The limitations of our study (retrospective assessment and lack of comparator) do not allow accurate estimation of prevalence. The severity of AAV and difficulties in management, may lead to overlooking of associated autoimmune diseases which appear to be frequent. Associated autoimmune disease may contribute to additional burden in AAV patients. (Supported by SAF 2014 57708-R).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1537

AB0576 ANTINEUTROPHILIC CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS: IS HYPOCOMPLEMENTEMIA A PREDICTOR OF POOR PROGNOSIS?

M. Estévez, A. Argibay, L. Rodriguez, R. Lorenzo, M. Freire, C. Vázquez-Triñanes, I. Villaverde, B. Gimena, J. Fernández-Martín, A. Rivera. *Systemic Autoimmune diseases and Thrombosis Unit, University Hospital Complex of Vigo, Vigo, Spain*

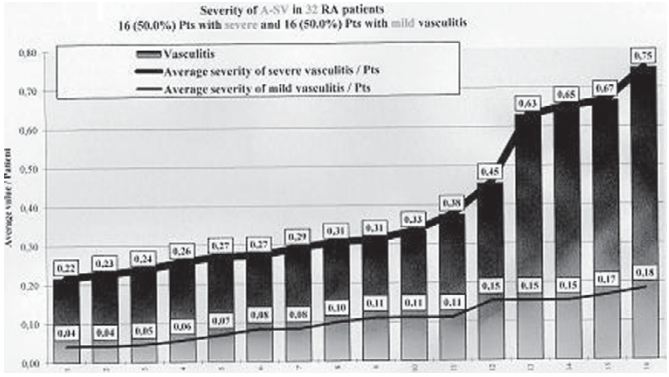
Background: Antineutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV) is a necrotizing vasculitis that predominantly affects small vessels and is associated with ANCA specific for myeloperoxidase (MPO-ANCA) or proteinase 3 (PR3-ANCA). The major clinicopathologic variants of AAV include microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis (EGPA). Recent studies have demonstrated the crucial role of complement activation in the pathogenesis of AAV. However, the clinical characteristics of AAV with hypocomplementemia (HC) still remain unclear.
Objectives: The aim of our study was to anlyze the demographic, laboratory, treatment and clinical characteristics of AAV using medical records. To compare the AAV patients with and without HC.
Methods: Retrospective study of patients with AAV diagnosed and followed in a specific Systemic Autoimmune Diseases and Thrombosis Unit. We defined HC as the state in which at least one of the following was lower than the lower limit of the normal range: Complement 3 (C3), Complement 4 (C4). Demographic, clinical, treatment and evolution data were recorded and analyzed using SPSS 22.0.
Results: Thirty-six patients with AAV were included (94,4% MPO-ANCA, 5,6% PR3-ANCA). 8 patients were diagnosed of GPA, 21 of MPA and 3 of EGPA. 61,1% of the patients were males and the mean age at the onset of the disease was 63,11±14,38 years [30–85]. 75% of patients had any vascular risk factors. Renal involvement occurred in 32 patients (88,9%): hematuria in 96,9%, proteinuria in 90,6% (>1 gr 68,7%) and glomerular filtration decreased in 81,25%. Biopsy was performed in 22 patients and a focal and segmental necrotizing glomerulonephritis with extracapillary proliferation was the finding more common. Pulmonary disease (61,1%) included interstitial disease 40,9%, alveolar hemorrhage 22,7% and nodules 18,2%. Other clinical manifestations were constitutional syndrome 36,1% (the main symptom was asthenia); ear, nose, and throat manifestations 33.3%; neurologic involvement 27.8% (the main finding was polyneuropathy); articular manifestations 33.3% and skin lesions 16,7%. All the patients received prednisone in combination with cyclophosphamide (69.4%) or rituximab (13.9%). Azathioprine was used as glucocorticoid-sparing agent (41.7%). 83.3% of the patients needed hospital admission and 6 died (16.7%). Eleven patients (30,6%) had HC at their diagnosis of AAV. Compared to the AAV patients without HC (n=25), we found no significant differences in the outcome or severity of the manifestations (evaluated by Five factor score). The small sample size could in part explain these results.
Conclusions: Our patients with HC at diagnosis of AAV did not have different characteristics than those without HC. More studies are needed to determinate if HC is a predictor of poor prognosis in AAV patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5924

AB0577 SYSTEMIC AUTOIMMUNE VASCULITIS IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS

M. Bély[1], Á. Apáthy[2]. *[1]Department of Pathology, Policlinic of the Order of the Brothers of Saint John of God; [2]Department of Rheumatology, St. Margaret Clinic Budapest, Budapest, Hungary*

Background: Systemic vasculitis of autoimmune origin (A-SV) may be regarded as a basic histological manifestation of rheumatoid arthritis (RA) [1,2].
Objectives: The aim of this study was to characterize the severity of systemic autoimmune vasculitis at death in RA patients.
Methods: A randomized autopsy population of 161 in-patients with RA was studied.
A-SV complicated RA in 32 (19.88%) patients [3].
RA was confirmed clinically according to the criteria of the ACR [4].
The severity of vasculitis was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale in12 organs (heart, lung, liver, spleen, kidney, pancreas, gastrointestinal tract, adrenal gland, skeletal muscle, peripheral nerve, skin and brain) at death) [1]. ("0": no vasculitis, "1": sporadically (scattered) located

vasculitis, "2": less than five, "3": five or more involved blood vessels/microscopic field with a x20 objective)
The age at death, and the onset and duration of RA with mild (<0.2/patient), or severe (0.2A-SV, were compared by Student (Welch) t-probe.
Results: 16 (50.0%) of 32 patients had a "mild" degree of A-SV (females 11, avg age of 70.91 years, range 80 – 63, onset of RA: 62.55, avg disease duration: 8.36 years at death; males 5, avg age of 71.6 years, range 83–58, onset of RA: 57.2, avg disease duration: 14.4 years).
16 (50.0%) of 32 patients had "severe A-SV" (females 8, age of 60.88 years, range 82–32,onset of RA: 52.67, avg disease duration: 13.5 years at death; males 8, avg age of 65.0 years, range 78–53, onset of RA: 53.25, avg disease duration: 11.75 years).
Four (12.5%) of 32 patients had "extremely severe A-SV" (with an average cumulative value of severity/RA patient with SV >0.630) (females 1, age of 82.0 years, onset of RA: 62.0, average disease duration: 20.0 years at death; males 3, average age of 69.7 years, range 78 – 59, onset of RA: 60.7, average disease duration: 9.0 years)
Severity of SV in 32 RA patients with A-SV – according to increasing average values of vasculitis/patient – is summarized in Figure.



Conclusions: A-SV is caused by circulating immune complexes in RA. Immune complexes spread via the bloodstream and provoke vasculitis throughout the body.
We found no differences in the linear and basically parallel development of A-SV between patient groups with mild and severe vasculitis.
The progression of vasculits was the same in both patient groups suggesting differences in production of circulating immune complexes.
Quantitative differences in the production of circulating immune complexes may be related to a "benign" or "aggressive" clinical course of RA, which may be due to genetical and other factors.
In 4 of 32 RA patients the severity of vasculitis showed a "step-wise" growth curve with "extreme severe" A-SV (0.630 or <) according to increasing average values of vasculitis/patient (Figure 1). There was no gradual transition between the "extremely severe" and "severe" degrees A-SV. This profile of "step-wise" general severity in patients with vasculitis may represent a subgroup of patients with a different genetic-immunologic background.
References:
[1] Bély M, Apáthy Ágnes: Clinical pathology of rheumatoid arthritis. 1–440 pp. Akadémiai Kiadó, Budapest 2012 http://www.akkrt.hu.
[2] Bywaters EGL, Scott JT: J chron Dis, 1963; 18 (8):905–912.
[3] Bély M, Apáthy Á: Ann Rheum Dis, 2003; 62 (Suppl. II):449.
[4] Arnett FC et al: Arthritis Rheum. 1988; 31(3):315–24. PMID: 3358796.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1223

AB0578 ARTERIAL ANEURYSMS MOROCCAN EXPERIENCE STUDY OF 37 CASES

M. Moudatir[1], M. Moudatir[2]. [1]*Internal medicine;* [2]*12 rue la saone, Polo, University hospital ibn rochd, Casablanca, Morocco*

Background: Behcet's disease is a systemic vasculitis with a tropism for the venous system. Arterial involvement is uncommon (1%) and mainly represented by aneurysms that can be life-threatening.
Objectives: This retrospective study was conduced in the internal medicine department of the University Hospital Ibn Rochd of Casablanca, over a period of thirty-five years between 1980 and 2016. Where included all the cases of Behcet's disease diagnosed in our service (1618 case).
Methods: We aimed to determine the epidemiological profile, the different possible clinical manifestations and to discuss both prognosis and treatment in such cases.
Results: 37 patients – 32 men and 5 women – presented arterial involvement in type of arterial aneurysm, which represents a rate of 2.35%.
Mean age at diagnosis was 32 years old (ranges 17–54). This complication was the revealing event for Behcet's disease in 2 cases, concomitant in 3 cases and occurring after an average of 6-year-period evolution of the disease in 32 cases.
The aneurysm affected: the pulmonary artery (22 cases), the abdominal aorta (5 cases), the femoral artery (5 cases), the internal carotid artery (2 cases), the iliac artery (2 cases) and the middle cerebral artery (1 case). The aneurysm was associated with venous disease (18 cases), pulmonary embolism (2 cases) and intracardiac thrombus (1 case).
The medical treatment has relying on anticoagulants (6 cases), anti-aggregating agents (9 cases), corticosteroids (36 cases), immunosuppressive drugs – cyclophosphamide (23 cases) and azathioprine (12 cases), while 7 patients underwent surgical intervention.
Evolution was favorable in 23 patients and with negative outcome in 14 patients (9 relapses and 5 deaths).
Conclusions: Arterial aneurysms are the most common arterial complications in the context of Behcet's disease, while the prognosis remains poor in the absence of early and appropriate management (corticosteroids, immunosuppressive agents, surgery).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7012

AB0579 IMMUNE RELATED DIFFUSE ALVEOLAR HAEMORRHAGE: SINGLE CENTER EXPERIENCE AND LONG TERM OUTCOME – RHEUMATOLOGICAL PERSPECTIVE

M.A. Bindroo, R. Gupta, N. Mendiratta, D. Raval, G. Ekbote, V. Singal.
Rheumatology and Clinical Immunology, Medanat the Medicity, gurgaon, India

Background: Diffuse alveolar haemorrhage (DAH) is a feature of several immune and nonimmune disorders. Failure to diagnose and treat DAH syndromes in their early stages may lead to acute respiratory failure, CKD and death. Prognosis is poor with in-hospital mortality ranging from 20% to 100%. Immune related DAH is monophasic and if treated early and achieved remission, long term outcome is good.
Objectives: To evaluate the therapeutic response and long term outcome in patients with Immune related (AAV & SLE) DAH.
Methods: A retrospective review of medical records of patients admitted under Rheumatology and Clinical immunology department with Immune related DAH was made with regards to their presentation, treatment & response, mortality, morbidity and long term outcome. Study was performed after approval and ethical clearence from IRB.
Results: From June 2012 to Augst 2016, 18 patients (15 were AAV related & 3 as SLE related) were admitted. Amongst AAV patients, PR3 positive were 11 & MPO positive were 4. Fourteen patients were females and 4 males, age ranged from 14 – 68 yrs (median=54.5 yrs). Mean duration of disease before onset of DAH was 3 months. Nine (50%) patients had associated kidney and musculoskeletal involvement. Eleven (61.11%) patients were admitted under ICU care requiring artificial ventilation. Pulse methylprednisolone injections were given in 15 (83.33%), Cyclophosphamide in 13 (72.22%), IVIg in 2 (11.11%), plasmapheresis in 7 (38.88%) patients. Time from first consultation to pulse methylprednisolone was in range from 1 to 5 days. Out of 18, 11 patients achieved remission. In hospital mortality was seen in 5 (27.77%) patients, all were AAV (MPO+=3, PR3+=2), all were complicated with sepsis with MODS before death. Out of 7 who received plasmapheresis, 2 patients (28.4%) died, 2 patients developed CKD (dialysis independent). Duration of ICU& hospital stay in days ranged from 3 to 28 days & 2 to 40 days respectively. Mean follow up was 16 months (range 11–42 months) on OPD visits. Two had relapse on follow up (1 nephritis, 1 persistant cavities with episcleritis) who were given Rituximab. Total 5 (38.46%) received Rituximab out of which 2 were refractory to Cyclophosphamide, 2 had relapse & 1 concomitantly. Eight patients (44.44%) developed morbidity in the form of dialysis independent-CKD in 4 (PR3+ in 2, MPO+ in 1 and Lupus nephritis in 1) with concomitant cataract in 1, ILD in 2, hearing loss in 1 and finger amputation in 1). All 13 patients who survived are in remission. Ongoing maintenance treatment is Azatjioprine in 5, Mycophenolate mofetil in 3 and Rituximab in 3 patients.
Conclusions: High index of suspicion with early diagnosis and treatment results in low mortality and better long term outcome. All mortality was because of delay in diagnosis. Rituximab is effective in achieving remission in refractory as well as relapsed cases
References:
[1] Yi Lin, MD, et al. J Clin Rheumatol. 2009 Oct;15(7):341–4.
[2] Diffuse alveolar hemorrhage in systemic lupus erythematosus: risk factors and clinical outcome: results from affiliated hospitals of Catholic University of Korea2011 Jan;20(1):102–7.
[3] Alveolar haemorrhage in ANCA-associated vasculitides: 80 patients' features and prognostic factors. Kostianovsky A1.Clin Exp Rheumatol 2012 Jan-Feb;30(1 Suppl 70):S77–82.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4064

AB0580 CLINICAL CHARACTERISTICS AND RISK FACTORS OF BEHCET'S PATIENTS WITH CONDUCTION DISTURBANCES-DATA FROM A CARDIOVASCULAR CLINICAL CENTER IN CHINA

R. Bai, N. Gao. *Anzhen Hospital, Capital Medical University, Beijing, China*

Background: Behcet's disease is a kind of systemic vasculitis affecting multiple systems. Although symptomatic cardiac involvement in Behcet's disease is uncommon, the fatality rate may reach up to 29%. Conduction disturbances might lead to poor outcome and often need permanent pacemaker implanted. The characteristics of conduction disturbances in Behcet's disease were rarely reported before.
Objectives: To investigate the clinical characteristics of Behcet's patients with conduction disturbances and explore the underlying risk factors.
Methods: We reviewed 57 medical records of Behcet's disease with cardiovascular lesions in Anzhen Hospital, Capital Medical University between January 2002 and July 2015, and analyzed the clinical characteristics.
Results: (1) There were 13 patients with conduction disturbances out of a total of 57 Behcet's disease cases (22.8%) in our research: three patients with first-degree atrioventricular block; one patient with Mobtizs type I second- degree atrioventricular block; four patients with third-degree atrioventricular block; one patient with the left anterior branch block; one patient with complete right bundle branch block; three patients with first-degree atrioventricular block combined with the left anterior branch block or complete right bundle branch block. One patient (7.7%) died from infectious endocarditis and aortic root abscess during hospital stay.
(2) Hemoglobin level was significantly lower in cases than controls (111.23±23.06 vs. 127.16±19.86 g/L, P=0.017); The median of albumin level in cases was higher than controls [34.5 (14.2) vs. 38.5 (9.9) g/L, P=0.032] (Table 1); C reactive protein level was higher in cases than controls [26.12 (21.3) vs. 6.7 (16.4) mg/L, P=0.045] (Table 1).
(3) The aortic valvular insufficiency presented more frequently in patients in the case group than the control group (92.3% vs. 47.7%, respectively; P=0.004).Heart reconstruction can be seen in Behcet'patients with cardiac involvement. The echocardiography showed the following parameters were significantly different between two groups: left ventricular end-diastolic diameter (64.85±10.96 vs. 52.55±10.13 mm, P=0.001); left ventricular end-contraction diameter [48 (15) vs. 31 (13) mm, P=0.001]; left atrial diameter [50 (17) vs. 35.85 (13) mm, P=0.003]; outflow tract of right ventricle [26 (7) vs. 27 (6) mm, P=0.045]
(4) Aortic valvular insufficiency was an independent risk factor for Behcet's disease with conduction disturbances (OR =1.157, 95% CI 1.034, 1.293, P=0.011).
Conclusions: Behcet's disease is one of the unusual etiologies of atrioventricular block. The evaluation of conduction disturbance should be kept in mind when diagnosing BD's patient.
References:
[1] Desbois A C, Wechsler B, Cluzel P, et al.: Cardiovascular involvement in Behcet's disease.Rev Med Interne 2014; 35(2):103–111.
[2] Braunwald E,Fauci A.S, Kasper D, et al.: Harrison's principles of international medicine. New York: McGraw-Hill 2001,1287.
[3] Butt SU, McNeil J.: Complete heart block in a Caucasian woman with Behçet's disease: a case report. J Med Case Rep 2016;19;10:102.
[4] Gao N, Han W, Ci WP,et al.: Clinical data analysis of cardiovascular involvement in Behcet's disease. Zhonghua Yi Xue Za Zhi 2016,24;96(19):1523–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1240

AB0581 TWO YEARS EXISTENCE OF REUMA.PT/VASCULITIS – THE PORTUGUESE REGISTRY OF VASCULITIS

N. Khmelinskii[1], C. Ponte[1], D. Peixoto[2], M. Rodrigues[3], L. Teixeira[4], S. Sousa[4], J. Aleixo[5], T. Pedrosa[6], S. Serra[6], W. Castelão[6], A. Cordeiro[4], I. Cordeiro[4], S. Fernandes[1], C. Macieira[1], P. Madureira[5], A. Malcata[3], V. Teixeira[1], R. Vieira[5], M. Eusébio[7], F. Martins[7], G. Sequeira[8], J. Branco[6], L. Costa[5], J. Canas da Silva[4], J.A. Pereira da Silva[3], C. Afonso[2], J.E. Fonseca[1], H. Canhão[7], R.A. Luqmani[9], M.J. Santos[4,7]. *[1]Hospital Santa Maria-CHLN, Lisboa; [2]Unidade Local de Saúde Alto Minho, Ponte de Lima; [3]Centro Hospitalar Universitário de Coimbra, Coimbra; [4]Hospital Garcia de Orta, Almada; [5]Centro Hospitalar São João, Porto; [6]Hospital Egas Moniz-CHLO; [7]Sociedade Portuguesa de Reumatologia, Lisboa; [8]Hospital de Faro-CHA, Faro, Portugal; [9]NDORMS, University of Oxford, Oxford, United Kingdom*

Background: The vasculitides are a group of relatively rare diseases with different manifestations and outcomes. New therapeutic options have led to the need for long-term registries. The Rheumatic Diseases Portuguese Register, Reuma.pt, is an electronic clinical record, created in 2008, which currently includes specific protocols for 11 diseases and >16000 patients registered from 79 national and international rheumatology centres. Since October 2014, a dedicated protocol to vasculitis has been created as part of the European Vasculitis Society initiative of having compatible European registries.
Objectives: To describe the structure of Reuma.pt/Vasculitis and characterize the patients registered over the last two years.
Methods: We developed a dedicated web-based software to enable prospective collection and central storage of anonymised data from patients with vasculitis. All Portuguese rheumatology centres were invited to participate. Data regarding demographics, diagnosis, classification criteria, imaging and laboratory tests, outcome measures of prognosis, damage, disease activity and quality of life, and treatment were collected. We performed a cross-sectional descriptive analysis of all patients registered up to January 2017.
Results: A total of 492 patients, with 1114 visits, from 11 centres were registered in Reuma.pt/Vasculitis. The mean age was 53±20 years at last visit; 68% were females. The diagnoses followed the 2012 Chapel Hill Consensus nomenclature (Table 1). The most common diagnoses were Behçet's disease (BD) (39%) and giant cell arteritis (GCA) (20%). Patients with BD met the International Study Group 1990 criteria, the International Criteria for BD 2006 and 2013 in 84%, 95% and 95% of cases, respectively. Patients with GCA met the 1990 American College of Rheumatology criteria in 95% of cases. Data on vascular ultrasound was available in 74% of patients; 73% compatible with the diagnosis. Assessment of the Birmingham Vasculitis Activity Score (BVAS) and Vasculitis Damage Index (VDI) was available for all vasculitides and the Five Factor Score calculation of survival rate for ANCA associated vasculitis (AAV) and polyarteritis nodosa (PAN). The mean BVAS at first visit was 18±7 for AAV and 15±9 for PAN; the mean VDI at last visit was 3±2 for AAV and 2±2 for PAN. Health related quality of life assessments (SF-36, EQD5, FACIT and HADS) were also collected. Treatment registry with the disease assessment variables shown in graphics was available for all patients; only 6% were under biologic treatment.

Table 1. Diagnosis, demographics and organ involvement of the vasculitis patients registered in Reuma.pt/Vasculitis.

		Total	TAK	GCA	PAN	MPA	GPA	EGPA	CV	IgAV	BD	CS
Demographics	Number of patients (% of total)	492 (100)	19 (3.8)	99 (20.1)	22 (4.4)	13 (2.6)	31 (6.3)	22 (4.4)	14 (2.8)	11 (2.2)	191 (38.8)	12 (2.4)
	Female/male ratio	2.2	8.5	1.7	1.2	2.3	1.1	2.7	2.8	0.6	2.8	1.4
	Mean age at diagnosis in years (SD)	44.3 (22.9)	31.4 (11.8)	73.7 (7.9)	38.1 (20.9)	60.1 (15.8)	49.1 (11.6)	47.1 (16.3)	53.2 (12.2)	30.0 (19.6)	27.6 (13.4)	28.4 (11.6)
Organ involvement	Generalsymptoms	35%	75%	54%	56%	71%	73%	57%	50%	29%	14%	44%
	Musculoskeletal	53%	43%	55%	67%	71%	76%	57%	75%	63%	50%	44%
	Skin	55%	0%	2%	78%	17%	40%	69%	57%	88%	76%	33%
	Eyes	41%	14%	47%	25%	17%	41%	14%	13%	0%	48%	100%
	ENT	25%	0%	48%	13%	33%	90%	71%	0%	0%	1%	100%
	Chest / pulmonary	13%	0%	0%	38%	43%	61%	100%	0%	0%	4%	11%
	Cardiovascular	42%	90%	87%	63%	33%	13%	31%	13%	0%	23%	0%
	Gastrointestinal	60%	13%	5%	43%	17%	13%	17%	25%	75%	98%	88%
	Genitourinary	55%	44%	6%	33%	71%	69%	29%	0%	63%	83%	17%
	Neurologic	48%	71%	90%	55%	50%	47%	81%	50%	0%	25%	33%

The patients with single-organ vasculitis, vasculitis associated with systemic disease, vasculitis associated with probable etiology, not-classifiable vasculitis or missing diagnosis are excluded.
BD – Behçet's disease; CS – Cogan syndrome; CV – cryoglobulinemic vasculitis; EGPA – eosinophilic granulomatosis with polyangiitis; ENT – ear nose and throat; GCA – giant cell arteritis; GPA – granulomatosis with polyangiitis; IgAV – immunoglobulin A vasculitis; MPA – microscopic polyangiitis; PAN – polyarteritis nodosa; SD– standard deviation; TAK – Takayasu arteritis

Conclusions: Reuma.pt/Vasculitis is a registry adapted for routine care, allowing an efficient data repository at a national level with the potential to link with other international databases. It facilitates research, trials recruitment, service planning and benchmarking.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1815

AB0582 ATHEROSCLEROTIC RISK FACTORS AND UPPER RESPIRATORY INFLAMMATIONS OF MPO-ANCA POSITIVE ANCA ASSOCIATED VASCULITIS

N. Ono[1], T. Miyamura[2], Y. Inoue[3], N. Ueki[4], K. Miyake[4], S. Nagano[5], H. Inoue[6], N. Ueda[7], K. Oryoji[8], T. Sawabe[9], S. Yoshizawa[10], Y. Takemoto[11], Y. Kimoto[12], S. Ohta[13], H. Nishizaka[14], I. Furugo[15], S. Yoshizawa[2], H. Niiro[16], T. Horiuchi[12], H. Nakashima[4], Y. Tada[1]. *[1]Rheumatology, Saga University, Saga; [2]Rheumatology, National Fukuoka Hospital; [3]Rheumatology, Fukuoka Red Cross Hospital; [4]Rheumatology, Fukuoka University, Fukuoka; [5]Rheumatology, Iizuka Hospital, Iizuka; [6]Rheumatology, Saiseikai Fukuoka Hospital, Fukuoka; [7]Rheumatology, Miyazaki Prefectural Miyazaki Hosipital, Miyazaki; [8]Rheumatology, Matsuyama Red Cross Hospital, Matsuyama; [9]Rheumatology, Hiroshima Red Cross Hospital, Hiroshima; [10]Rheumatology, Hamanomachi Hospital, Fukuoka; [11]Rheumatology, Saiseikai Karatsu Hospital, Karatsu; [12]Rheumatology, Kyushu University Beppu Hospital, Beppu; [13]Rheumatology, Shimonoseki City Hospital, Shimonoseki; [14]Rheumatology, Kitakyushu Municipal Medical Center; [15]Rheumatology, JR Kyushu Hospital, Kitakyushu; [16]Rheumatology, Kyushu University, Fukuoka, Japan*

Background: Recent studies had proven that the genetic backgrounds of ANCA associated vasculitis (AAV) were dependent on ANCAs. We and other groups had shown the differences between MPO-ANCA positive Granulomatosis with polyangitis (MPO-GPA) and Microscopic polyangitis (MPA) (1–3). It is not clear what determine these two phenotypes.
Objectives: To elucidate the etiologies of two phenotypes, we compared the backgrounds and comorbidities between MPO-GPA and MPA.
Methods: Retrospectively we recruited MPO-GPA and MPA patients through the two multi-center cohorts (Cohort A: 2001–2012, Cohort B: 2012–2016). We classified patients with EMEA classification and ANCA. We found 40 MPO-GPA and 126 MPA cases without overlaps. We compared those backgrounds, comorbidities, organ involvements and outcomes.
Results: The average age of MPO-GPA group was similar to that of MPA (69.1 years old vs 72.1 years old). But MPO-GPA preferentially affected female patients (80.0% vs 52.8%) with lower creatinine levels (1.03mg/dl vs 2.7mg/dl). Two year survivals of MPO-GPA were significantly better than MPA (95.8% vs 73.2%, p=0.0424). Interestingly MPO-GPA patients had less atherosclerotic risk

factors, i.e. smoking history (6.3% vs 38.4%), hypertension (10.4% vs 30.5%) and diabetes (12.5% vs 17.9%). Instead these patients had more upper respiratory inflammations (chronic sinusitis, chronic otitis media and allergic rhinitis, 33.3% vs 6.6%) before the disease onset.

Conclusions: We found that MPA had more atherosclerotic risk factors, and MPO-GPA had more upper respiratory inflammations. These factors may determine MPA or GPA phenotypes in MPO-ANCA positive AAV.

References:

[1] Ono N at al. Characteristics of MPO-ANCA-positive granulomatosis with polyangiitis: a retrospective multi-center study in Japan. Rheumatol Int. 2015 Mar;35(3):555–9.

[2] Miloslavsky EM et al. MPO-ANCA-Positive and ANCA-Negative Patients With Granulomatosis With Polyangiitis (Wegener's): Distinct Patient Subsets. Arthritis Rheumatol. 2016 Dec;68(12):2945–2952.

[3] Schirmer JH at al. MPO-ANCA-Positive Granulomatosis With Polyangiitis (Wegener's) Is a Clinically Distinct Subset of ANCA-Associated Vasculitis: A Retrospective Analysis of 315 Patients From a German Vasculitis Referral Center. Arthritis Rheumatol. 2016 Dec;68(12):2953–2963.

Acknowledgements: We gratefully acknowledge the work of people who helped to correct patients data.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2839

AB0583 DIFFERENCES BETWEEN ISOLATED AORTITIS AND NON-INFECTIOUS AORTITIS SECONDARY TO OTHER ENTITIES. STUDY OF 93 PATIENTS FROM A SINGLE CENTER

N. Vegas-Revenga[1], J. Loricera[1], D. Prieto-Peña[1], J.L. Hernández[2], I. Martínez-Rodríguez[3], J.I. Banzo[3], M. Calderón-Goercke[1], V. Calvo-Río[1], L.C. Domínguez-Casas[1], C. González-Vela[4], P. Fuentevilla[1], M.Á. González-Gay[1], R. Blanco[1]. *[1]Rheumatology; [2]Internal Medicine; [3]Nuclear Medicine; [4]Pathology, Hospital Universitario Marqués de Valdecilla. IDIVAL, Santander, Spain*

Background: Non-infectious aortitis is an inflammation of aortic wall which may be isolated or associated with a cluster of diseases.

Objectives: Our aim was to compare the clinical and laboratory findings of patients with isolated aortitis and patients with aortitis secondary to other underlying conditions.

Methods: Retrospective study of 93 patients with non-infectious aortitis diagnosed by PET/CT scan from a referral center from January 2010 to December 2016. We have considered two groups: *group a)* isolated aortitis; and *group b)* secondary aortitis. Distributions of *categorical variables were* compared by the Pearson Chi^2 or Fisher exact test. Quantitative variables were analyzing using the Student t test or Mann-Whitney U test as appropriate.

Results: Ninety-three patients were diagnosed with non-infectious aortitis. One patient was excluded due to missing data. Group a) was composed by 54 patients (34 women/ 20 men) with a mean age of 67±11 years; group b) comprised 38 patients (28 women/ 10 men) with a mean age of 68±11 years. In this group, the underlying conditions we found were: giant cell arteritis (n=24), Takayasu arteritis (n=3), spondiloarthropathy (n=3), Sjögren's syndrome (n=3), ulcerative colitis (n=2), sarcoidosis (n=1), rheumatoid arthritis (n=1), polyarteritis nodosa (n=1). The comparative study between both groups is shown in the TABLE. Only inflammatory low back pain and polymyalgic syndrome yielded statistical signification.

Variables	Group a (isolated aortitis) n= 54	Group b (secondary aortitis) n= 38	p
Age (years), *mean±SD*	67.2 ± 11.1	68.0 ± 11.2	0.73
Age ≥ 70 years, *n (%)*	21 (38.9)	18 (47.4)	0.42
Sex *(M/W), n*	20/34	10/28	0.28
Time from symptoms onset to PET date, *median [IQR]*	12.5 [3-36]	19.5 [6-75.5]	0.29
Symptoms at the time of requesting PET			
- Constitutional symptoms, *n (%)*	15 (27.8)	14 (36.8)	0.24
- Fever, *n (%)*	7 (13.0)	11 (28.9)	0.06
- Inflammatory low back pain, *n (%)*	23 (42.6)	7 (18.4)	**0.015**
- Lower limb pain, *n (%)*	29 (53.7)	13 (34.2)	0.07
- Polymyalgic syndrome, *n (%)*	40 (74.1)	18 (47.4)	**0.016**
- Headache, *n (%)*	7 (13.0)	11 (28.9)	0.06
Laboratory values at the time of requesting PET			
- Anaemia, *n (%)*	8 (14.8)	10 (26.3)	0.16
- ESR (mm/1sth), *mean±SD*	44.7 ± 31.6	42.1 ± 38.3	0.42
- CRP (mg/dl), *median [IQR]*	0.9 [0.6-2.3]	0.9 [0.2-2.6]	0.76
Treatment at the time of requesting PET			
- Patients on corticosteroids, *n (%)*	25 (46.3)	23 (60.5)	0.18
- Prednisone dose (mg), *median [IQR]*	10 [5-10]	10 [7.5-16.9]	0.05
- Patients on traditional IS agents, *n (%)*	4 (7.4)	7 (18.4)	0.11

Conclusions: In this study, we observed that both the presence of inflammatory low back pain and polymyalgic syndrome might have clinical relevance in the clinical suspicion of primary aortitis. However, larger studies are needed to corroborate these findings.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3233

AB0584 UTILITY OF PET/CT SCAN FOR THE DIAGNOSIS OF AORTITIS. A STUDY OF 170 PATIENTS FROM A SINGLE CENTER IN A 6-YEAR PERIOD

N. Vegas-Revenga[1], J. Loricera[1], D. Prieto-Peña[1], I. Martínez-Rodríguez[2], J.I. Banzo[2], M. Calderón-Goercke[1], V. Calvo-Río[1], C. González-Vela[3], J. González-Vela[1], M.Á. González-Gay[1], J.L. Hernández[4], R. Blanco[1]. *[1]Rheumatology; [2]Nuclear Medicine; [3]Pathology; [4]Internal Medicine, Hospital Universitario Marqués de Valdecilla. IDIVAL, Santander, Spain*

Background: Aortitis is the inflammation of the aortic wall. This entity is often under-recognised due to its frequent presentation with non-specific symptoms. PET/CT scan represent a major breakthrough to establish an early diagnosis, but this is an expensive technique.

Objectives: Our aim was to compare the baseline characteristics of patients with a suspicion of aortitis and positive results on PET/CT scan, and those with a negative result, in order to search for predictive factors, that improve the clinical probability of diagnosis aortitis by this imaging technique.

Methods: Retrospective study on 170 patients and PET/CT scans ordered by suspicion of aortitis from a referral center from January 2010 to December 2016. According to a pre-specified protocol, the baseline epidemiological and clinical variables of patients with positive and negative PET/CT scans results for aortitis were reviewed. Distributions of *categorical variables were* compared by the Pearson Chi^2 or Fisher exact test. Quantitative variables were analyzing using the Student t test or Mann-Whitney U test as appropriate.

Results: In 170 patients, PET/CT scans were performed due to clinical suspicion of aortitis, and were positive in 93 (54.7%) cases. Patients (113 women/57 men) had a mean age of 67.7±13.1 years (range, 20–90 years). One patient was excluded because missing clinical or laboratory data.

The underlying diseases at the moment of ordering the PET/CT scan were: giant cell arteritis (GCA) (n=28), spondiloarthropaties (n=7), conectivopaties (n=6), Takayasu arteritis (n=3), ulcerative colitis (n=3), other condition (n=11). The remaining 111 patients did not have any underlying condition suggestive of aortitis. Two out of 170 patients suspected an infectious aortitis (*Brucella* and *Salmonella*); however, PET/CT was negative in both cases.

Characteristics of patients with positive and negative PET/CT scans were summarized in the Table. Patients with GCA had a higher percentage of positive PET/CT scans, whereas they were negative more frequently in patients who did not have any condition suggestive of underlying aortitis. Only inflammatory low back pain and polymyalgic syndrome were significantly more frequent in patients with positive PET/CT scans. The remaining clinical and laboratory variables did not show differences between both groups.

TABLE

	Positive PET n= 92	Negative PET n= 77	p
Age (years), mean±SD	67.4± 11.1	68.1±15.2	0.73
Age ≥ 70 years, n (%)	39 (41.9)	41 (53.2)	0.14
Sex (women), n (%)	62 (67.4)	54 (70.1)	0.63
Underlying condition			
- *Giant cell arteritis, n (%)*	24 (26.1)	4 (5.2)	**0.0002**
- *Takayasu arteritis, n (%)*	3 (3.3)	0 (0)	0.31
- *Ulcerative colitis, n (%)*	2 (2.2)	1 (1.3)	0.87
- *Conectivopaties, n (%)*	3 (3.3)	3 (3.9)	0.86
- *Spondiloarthropaties, n (%)*	3 (3.3)	4 (5.2)	0.79
- *None, n (%)*	54 (58.7)	57 (74.0)	**0.03**
- *Other, n (%)*	3 (3.3)	8 (10.4)	0.11
Symptoms at the time of requesting PET			
- *Constitutional syndrome, n (%)*	30 (32.6)	36 (46.8)	0.06
- *Fever, n (%)*	18 (19.6)	15 (19.5)	0.98
- *Inflammatory low back pain, n (%)*	30 (32.6)	14 (18.2)	**0.03**
- *Diffuse lower limbs pain, n (%)*	42 (45.7)	28 (36.4)	0.22
- *Atypical polymyalgia rheumatica, n (%)*	30 (53.6)	13 (38.2)	0.15
- *Headache, n (%)*	18 (19.6)	9 (11.7)	0.16
- *Polymialgic syndrome, n (%)*	56 (60.9)	34 (44.2)	**0.03**
Laboratory markers at the time of requesting PET			
- *Anaemia, n (%)*	18 (20.2)	22 (28.9)	0.19
- *ESR (mm/1sth), mean±SD*	43.3±34.3	43.5±31.1	0.72
- *CRP (mg/dl), median [IQR]*	0.9 [0.3-2.6]	0.9 [0.3-2.5]	0.54
Treatment at the time of requesting PET			
- *Patients with corticosteroids, n (%)*	48 (51.6)	36 (46.8)	0.48
- *Dosage of prednisone (mg), median [IQR]*	10 [5-15]	10 [7.5-15]	0.80
- *Patients with traditional immunosuppressants, n (%)*	11 (12.0)	5 (6.5)	0.21

Conclusions: In this study, we have found that the presence of inflammatory low back pain and polymyalgic syndrome, especially in GCA patients, may have clinical relevance in ordering a PET/CT scan when aortitis was suspected.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3368

AB0585 VASCULITIS DAMAGE INDEX IN LIMITED AND SYSTEMIC GRANULOMATOSIS WITH POLIANGIITIS IN MEXICAN PATIENTS

O. Vera-Lastra, A.G. Angulo-Gonzalez, J. Sepulveda-Delgado. *Internal Medicine, Hospital Especialidades CMN la Raza. Instituto Mexicano Seguro Social, Mexico City, Mexico*

Background: Granulomatosis with polyangiitis (GPA) has been transformed

from life-threatening conditions to chronic relapsing long-term diseases as a result of significant advances in immunosuppressive therapy. Structured clinical assessment using Vasculitis Damage Index (DVI) should form the basis of a treatment plan and be used to document progress.

Objectives: To investigate the Vasculitis Damage Index and clinical manifestations in localized and systemic granulomatosis with poliangiitis in Mexican patients

Methods: We enrolled 61 patients with GPA according to The American College of Rheumatology (ACR) criteria at a referral hospital during the period from 2005 to 2015. Clinical and laboratory data, organ involvement and the Vasculitis Damage Index (VDI) were recorded at baseline. Patients were divide into systemic and localized form for their analysis.

Results: They were 61 GPA (34 men and 27 women) mean age 42 years old at diagnosis. Systemic form was observed in 53% and localized form 47%. Chronic sinusitis was the most frequent manifestation in 33% followed by otologic in 26%. Subglottic stenosis 4 patients, alveolar hemorrhage 1%. Of the patients with the systemic form 22 presented focal and segmental glomerulonephritis and 10 patients (32%) rapidly progressive glomerulonephritis. Distal-symmetric polyneuropathy and cranial neuropathy were present in 24%; scleritis 24.5% and proptosis in 18%, palpable purpura 26.2% and ulcers in 9 patients (14.8%). The VDI score in the systemic form was 3.8 and in the localized 2.6, p= NS. The disease related damage was pronounced in kidneys and upper airways. The majority of patients in the induction to remission phase received steroids plus cyclophosphamide, 7 patients also received plasmapheresis and in maintenance phase they were treated with methotrexate or azathioprine.

Conclusions: In this cohort of patients with GPA, a high chronic damage was found which was similar in both systemic and localized forms of this vasculitis. The VDI was more prominent in kidneys and upper airways in GPA patients

References:

[1] Bhamra K, et al. Damage assessment in ANCA-associated vasculitis. Curr Rheumatol Rep. 2012; 14:494–50.
[2] Kamali S, et al. Predictors of damage and survival in patients with Wegener's granulomatosis: analysis of 50 patients, J Rheumatol 2010;37:374–78.
[3] Luqmani R, et al. State of the art in the treatment of systemic vasculitides. Front Immunol 2014;5:471.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5690

AB0586 EVALUATION OF ASSSOCIATION BETWEEN ANTIPHOSPHOLIPID ANTIBODIES OR LUPUS ANTICOAGULANT POSITIVITY AND SEVERITY OF VASCULAR INVOLVEMENT IN TAKAYASU ARTERITIS PATIENTS

E. Fırat[1], A. Erden[2], A. Sari[2], B. Armagan[2], L. Kilic[2], O. Karadag[2], A. Akdogan[2]. [1]*Internal Medicine, Hacettepe University Faculty of Medicine;* [2]*Rheumatology, Hacettepe University of Medicine, Ankara, Turkey*

Background: Takayasu Arteritis is a rare large-vessel vasculitis variant that affects the aorta and its main branches and the pulmonary arteries. Antiphospholipid syndrome is characterized by obstetric and thrombotic complications in the presence of antiphospholipid antibodies, which consist of anticardiolipin antibody, lupus anticoagulant and anti -β2 glycoprotein I. The association of antiphospholipid antibodies and Takayasu arteritis is very rare and few cases decumented it, while others argued aganist such association.

Objectives: This study was planned to find out the prevelance of immunoglobulin-IgM/G anti-cardiolipinantibodies, anti beta 2 glycoprotein- 1antibodies and lupus anticogulant and evaluate the relationship between these antibodies and disease severity/complications in Takayasu arteritis patients.

Methods: 53 patients with Takayasu arteritis patients were enrolled in this study. We obtained blood samples to detectIgM/G anti-cardiolipin antibodies, anti beta 2 glycoprotein 1 antibodies and lupus anticogulant (LA) levels from all patients during their routine control. ImmunoglobulinIgM/G anti-cardiolipin antibody, anti beta 2 glycoprotein 1 antibodies were measured by using a standardized enzyme-linked immunosorbent assay (ELISA) and lupus anticogulant was measured using the diluteRussell's viper venom time (dRVVT).

Results: No patients was positive forIgM/G anti-cardiolipin antibody. Seven were positive immunoglobulin IgM anti beta 2 glycoprotein 1 antibodies, three were positive immunoglobulin IgG anti beta 2 glycoprotein 1 antibodies, one waspositive LA. All of the antibody titters were low. TA patients who had antibody positivity had longer disease duration ($p<0.05$). Antibody and LA positive patients had superior mesenteric artery and celiac artery involvement more frequently then the antibody negative patients ($p<0.05$).

Conclusions: In this study that there were no association between the antibodies positivity and vascular involvement or disease complications and severity in TA patients. In conclusion we can not suggest the routine evaluation of antiphospholipid antibodies or lupus anticoagulant test during the follow-upTakayasu arteritis patients. These antibodies may only be measured in the presence of clinical suspicion.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3529

AB0587 ANTINEUTROPHILIC CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS AND HYPOCOMPLEMENTEMIA: CLINICAL IMPACT AND OUTCOME

S. Deshayes[1], A. Aouba[1], K. Khoy[2], D. Mariotte[2], T. Lobbedez[3], N. Martin Silva[1]. [1]*Department of Internal Medicine;* [2]*Department of Immunology;* [3]*Department of Nephrology, CHU Côte de Nacre, Caen, France*

Background: Although their pathophysiology are still largely unknown, there are growing evidences that complement (C) alternative pathway activation is implicated in antineutrophilic cytoplasmic antibody-associated vasculitis (AAV) pathogenesis.

Objectives: The aim of our study was to evaluate the clinical characteristics and outcome of AAV patients, according to their serum C levels at diagnosis.

Methods: A retrospective monocentric study carried out in Caen University Hospital led to identify proteinase-3 (PR3) or myeloperoxidase (MPO)-ANCA AAV patients (via an ELISA technique). All patients with available C3 and C4 levels (by nephelemetry) at diagnosis were included, except for eosinophilic granulomatosis with polyangiitis (EGPA), which has a different pathophysiology. AAV were classified between granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA), and limited or severe forms according to respectively European Medicines Agency vasculitis algorithm and WGET group. Patients were categorized in the hypocomplementemia group if the C3 or C4 level at diagnosis was below the lower limit of the normal range (respectively 750–1400 mg/l and 100–340 mg/l). Categorical variables were reported as percentages and compared using Fisher's tests. Continuous variables were expressed as means and analyzed using Student's t-test. Associations between survival, renal survival and relapse-free survival, and low serum C levels were evaluated by the log-rank test. A p-value <0.05 was considered to be statistically significant.

Results: Among the 157 AAV patients identified, 81 were excluded (8 EGPA, 73 without C3 and C4 determinations before treatment initiation). On the 76 AAV included (43 GPA, 33 MPA), median age at diagnosis was 65 years (M/F, 38/38). Clinical presentations included constitutional symptoms (56, 73.7%), pulmonary (52, 68.4%), renal (50, 65.8%), rheumatologic (43, 56.6%), and ear, nose or throat (37, 48.7%) involvements, without statistical differences between groups. Twelve (15.8%) deaths and 41 relapses in 25 (32.9%) patients were noted (median follow-up: 38 months). Four patients (5.3%) had hypocomplementemia: 1 patient had isolated low C3 level, 1 had isolated low C4 level, and 2 had both low C levels. All 4 patients had renal involvement. The C level, controlled in 1 patient, became normal 1 month later. No thrombotic microangiopathy (TMA) features were found on the 2 performed kidney biopsies.

	Hypocomplementemia group (n=4)	Normal complement level group (n=72)	p value
Male %	50	50	1
Age at diagnosis (years), median ± SD	71±9	65±16	0.18
BVAS, median ± SD	21±8	18±7	0.26
Granulomatosis with polyangiitis %	75	57	0.64
PR3-ANCA %	50	60	1
Limited vasculitis %	0	28	0.57
End-stage renal disease %	75	15	0.02
Death %	50	14	0.12
Relapse %	25	36	1

Survival and renal survival were significantly lower in the hypocomplementemia group ($p=0.0011$ and $p<0.001$, respectively), but relapse-free survival was similar ($p=0.1$).

Conclusions: Hypocomplementemia at AAV diagnosis may be responsible for worse survival and renal prognosis. This particular phenotype may confer resistance to common immunosuppressive approaches as in thrombotic microangiopathy caused by abnormalities in the regulation of the C system. These results also argue for larger studies and for investigating C pathway targeting.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1293

AB0588 CONCOMITANT ASSOCIATION OF GIANT CELL ARTERITIS AND MALIGNANCY: A MULTICENTER RETROSPECTIVE CASE-CONTROL STUDY

S. Deshayes[1], N. Chanson[2], K. Sacré[2], C. Blanchard-Delaunay[3], O. Espitia[4], T. Le Gallou[5], M. Groh[6], J.-E. Kahn[7], V. Grobost[8], S. Humbert[9], M. Samson[10], R. Mourot Cottet[11], K. Mazodier[12], A. Dartevel[13], M. Versini[14], A. Dumont[1], B. Bienvenu[1], A. Aouba[1], H. de Boysson[1] on behalf of French Study Group for Large Vessel Vasculitis (GEFA). [1]*Department of Internal Medicine, CHU Côte de Nacre, Caen;* [2]*Department of Internal Medicine, Hôpital Bichat, Paris;* [3]*Department of Internal Medicine, Centre Hospitalier de Niort, Niort;* [4]*Department of Internal Medicine, CHU Hotel Dieu, Nantes;* [5]*Internal Medicine, CHU Rennes, Rennes;* [6]*Department of Internal Medicine, Hôpital Cochin, Paris;* [7]*Department of Internal Medicine, Hôpital Foch, Suresnes;* [8]*Department of Internal Medicine, CHU Estaing, Clermont-Ferrand;* [9]*Department of Internal Medicine, CHU de Besançon, Besançon;* [10]*Department of Internal Medicine, Hôpital François-Mitterrand, Dijon;* [11]*Department of Internal Medicine, Hôpital Civil, Strasbourg;* [12]*Department of Internal Medicine, Hôpital de la Conception,*

Marseille; [13]Department of Internal Medicine, CHU Grenoble, Grenoble; [14]Department of Internal Medicine, Hôpital Archet 1, Nice, France

Background: Giant cell arteritis (GCA) is a large-vessel vasculitis affecting elderly people, and most frequently women (sex-ratio of 2.3). Some studies suggest an increased risk of malignancies in GCA.
Objectives: We aimed to describe the clinical, paraclinical characteristics and outcomes of GCA patients with concomitant malignancy and compare them to a control group without malignancy.
Methods: Patients with a diagnosis of GCA and of solid neoplasm or malignant blood disease, within one year before or after the diagnosis of vasculitis, were included. A random group of age-matched (3:1) control patients from our monocentric inception cohort of GCA patients from Caen University Hospital was constituted.
Results: Twenty-four observations were collected (median age 75.5 years). All fulfilled ≥3/5 ACR criteria. Temporal artery biopsy was positive in 17 cases (70.8%). There were 1 active (4.2%) and 9 former (37.5%) smokers. Only 1 patient had a previous prostate cancer. Malignancies were 10 malignant blood diseases (41.7%, 3 chronic lymphoid leukemias, 3 essential thrombocythemias, 1 myeloma, 1 chronic myelomonocytic leukemia, 1 MALT lymphoma, 1 Waldenström's macroglobulinemia) and 14 solid neoplasms (58.3%, 3 lung, 3 breast, 2 prostate, 1 thyroid, 1 colon, 1 pleural cancers, 1 melanoma, 1 Kaposi's sarcoma and 1 Merkel cell carcinoma). Malignancy was diagnosed at a median of 1 month after GCA diagnosis in 21 patients and before in the other 3. Diagnosis of malignancy was made in consultation in 5 patients (3 skin cancers and 2 breast cancers), on lab tests in 13 (thrombocytosis, anemia or increased prostate specific antigen) and on imaging in 6. Treatments of malignancy included chemotherapy alone in 8 patients (33.3%), simple monitoring in 6 patients (25%), surgery alone in 4 patients (16.7%), surgery and radiotherapy and/or chemotherapy in 4 patients (16.7%), decrease of corticosteroids in 1 patient, and 1 patient was lost to follow-up. Two patients (8.3%) died from infectious complications, 8 patients (33.3%) had a GCA relapse, including one with concomitant malignancy relapse. After a median follow-up of 16 months [0–134], 5 patients (20.8%) were weaned from steroids, all considered in malignancy remission. Seven patients (29.1%) were still under chemotherapy, 9 patients (37.5%) were considered to be in malignancy remission. There were more males in patients with concomitant malignancy, compared to the control group (respectively 15/24 and 21/72, p<0.005).
Conclusions: Our study shows an over-representation of male gender in GCA with concomitant malignancy. Vasculitis outcomes were not influenced by the malignancy treatment. The diversity of malignancies encountered in this study raises the issue of an incidental association. Initial clinical and paraclinical follow-up dictated by vasculitis may have led to an early identification of associated malignancy, and thus represent a lead time bias.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1291

AB0589 THE ROLE OF ANCA SPECIFICITY IN THE CLINICAL MANIFESTATIONS AT DISEASE ONSET: COMPARISON BETWEEN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS AND MICROSCOPIC POLYANGIITIS

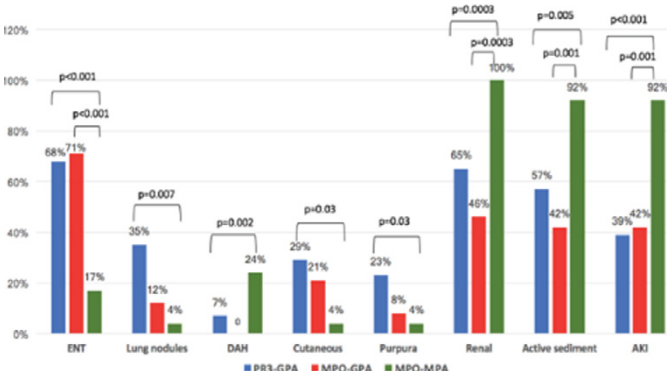
S. Monti[1], M. Felicetti[2,3], S. Balduzzi[1], R. Padoan[2], A. Berti[3], G. Paolazzi[3], G. Brunori[3], F. Schiavon[2], R. Caporali[1]. *[1]Rheumatology, University of Pavia, IRCCS Policlinico San Matteo Foundation, Pavia; [2]Rheumatology, Department of Medicine DIMED, University of Padova, Padova; [3]Rheumatology, Santa Chiara Hospital, Trento, Italy*

Background: ANCA specificity, rather than clinical diagnosis, has been suggested to influence the phenotype and clinical course of ANCA associated vasculitis (AAV) (1,2).
Objectives: To investigate differences in clinical presentation at disease onset between MPO-ANCA-positive granulomatosis with polyangiitis patients (MPO-GPA), PR3-ANCA-positive-GPA (PR3-GPA), and MPO-ANCA-positive microscopic polyangiitis (MPO-MPA).
Methods: Clinical records of AAV patients from three third level rheumatologic centers in Northern Italy were retrospectively analyzed.
Results: Of the 133 AAV patients included, 84 were PR3-GPA, 24 MPO-GPA, and 25 MPO-MPA. Patients with MPO-MPA were significantly older at diagnosis compared to both PR3-GPA and MPO-GPA (average age 63±10, 49±15, 55±29, respectively) (Table 1).
Patients with MPO-GPA experienced a significant diagnostic delay compared to PR3-GPA (17±30 vs 7±14, p=0.02). ENT involvement was equally frequent in both GPA groups despite ANCA specificity, and significantly more represented than the MPO-MPA group (68%, 71% and 17% respectively; p<0.001). Figure 1. Renal involvement was significantly more frequent in MPO-MPA patients (100%) compared to GPA (p<0.001), without differences between MPO-GPA (46%) and PR3-GPA (65%). Alveolar haemorrhage (DAH) was an onset manifestation mainly in MPO-MPA compared to the other two groups (24% vs 7% in PR3-GPA; p=0.02). Cutenous manifestations, mainly purpura, were significantly more reported in PR3-GPA compared to MPO-MPA (29% vs 4%; p=0.03).
Conclusions: Clinical phenotype of GPA at disease onset did not seem to be influenced by ANCA specificity. Despite ANCA positivity (PR3 or MPO), GPA patients were significantly different from MPA.

Table 1. Clinical characteristics of patients with GPA and MPA at disease onset according to ANCA specificity

	GPA-PR3 (A) (n=84)	GPA-MPO (B) (n=24)	MPA-MPO (C) (n=25)	p
Male/female n (%)	46 (55%)/38 (45%)	10 (42%)/14 (58%)	10 (40%)/15 (60%)	0.29
Age at disease onset (average ± SD)	49±15	55±19	63±10	**p<0.001** A vs C p<0.001 B vs C p=0.03
Diagnostic delay (months ± SD)	7±14	17±30	10±19	0.07
Systemic symptoms	54 (65%)	16 (67%)	19 (76%)	0.59
ENT	55 (68%)	17 (71%)	4 (17%)	**<0.001**
Pulmonary	57 (69%)	16 (67%)	16 (64%)	0.86
Cutaneous	24 (29%)	5 (21%)	1 (4%)	**0.03**
Ocular	16 (20%)	3 (12%)	2 (8%)	0.34
Cardiovascular	4 (5%)	2 (9%)	1 (4%)	0.77
Gastrointestinal	2 (3%)	0	0	0.56
Renal	53 (65%)	11 (46%)	25 (100%)	**<0.001**
Nervous system	26 (31%)	8 (33%)	8 (35%)	0.94

Figure 1. Differences in onset clinical manifestations among PR3-GPA, MPO-GPA and MPO-MPA



References:
[1] Schirmer JH, Wright MN, Herrmann K, et al. Myeloperoxidase-Antineutrophil Cytoplasmic Antibody (ANCA)-Positive Granulomatosis With Polyangiitis (Wegener's) Is a Clinically Distinct Subset of ANCA-Associated Vasculitis: A Retrospective Analysis of 315 Patients From a German Vasculitis Referral Center. Arthritis Rheumatol Hoboken NJ 2016;68:2953–63.
[2] Miloslavsky EM, Lu N, Unizony S, et al. Myeloperoxidase-Antineutrophil Cytoplasmic Antibody (ANCA)-Positive and ANCA-Negative Patients With Granulomatosis With Polyangiitis (Wegener's): Distinct Patient Subsets. Arthritis Rheumatol 2016;68:2945–2952.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4760

AB0590 PERFORMANCE OF 2017 ACR/EULAR PROVISIONAL CLASSIFICATION CRITERIA FOR GRANULOMATOSIS WITH POLYANGIITIS IN CHILEAN POPULATION

S.F. Elgueta, L. Ricci Larrea, D. Vargas, P. Wurmann, I. Goecke. *Hospital Clínico Universidad de Chile, Santiago, Chile*

Background: Anca Associated Vasculitis (AAV), are a group of necrotizing primary vascultitis, whith multisistemic manifestation, of unknown etiology. The variants are: Microscopic Polyangiitis (MPA), Granulomatosis with polyangiitis (GPA), Granulomatosis whith Polyangiitis and Eosinophilia (GPE) and AAV limited to one organ. Until now, there are no diagnostic criteria for AAV. Therefore definitions, as Chapell Hill consensus Conference Nomenclature, classification criteria and the physician judgement are used for diagnosis. Currently the DCVAS (Diagnosis and Classification Criteria in Vasculitis) proyect is developing diagnostic criteria for AAV, using data-driven methods. The preliminary DCVAS classification criteria for granulomatosis whith polyangiitis has been recently realesead.
Objectives: To evaluate and compare the acuraccy of ACR/EULAR 2017 provisional Classification Criteria for GPA whith the ACR 1990 Classification Criteria In Chilean patients with AAV.
Methods: All adult patients (>18 yo) with diagnoses of AAV according to their rheumatologist judgment, from 2000–2016 at the University of Chile, Clinical Hospital (UCCH), were included. Clinical variables of interest were extracted form medical chart and AAV database, wich is kept for these patients at the Rheumatology Section of UCCH. Based on that data, the Classification criteria ACR 1990 and 2017preliminary ACR/EULAR (DCVAS) classification criteria for GPA were applied to each individual. Sensibility, especifity, Likehood ratio (LR +/-), predictive values (PPV/NPV) and accuracy were calculated for both sets of Criteria as compared to Clinical diagnosis
Results: 93 patient were included in the study. 59 patients with GPA, 33 with

MPA and 1 with GPE (Patients characteristics are described in Table 1). From the 59 patients with GPA according to clinical judgment, 34 fullfilled the ACR 1990 criteria (57,63%) whereas 51 (86,44%) fullfilled the ACR/EULAR 2007 criteria. From the 33 patients diagnosed as having MPA 9 (27,27%) and and 3 (9.09%) fulfilled classification criteria for GPA according to ACR 1990 criteria and 2017 ACR/EULAR preliminary criteria, respectively.The patient with GPE did no classify as GPA by either set of criteria.The values for Sensibility, Espicifity, LR+ LR-, PPV and NPV in our population for both Criteria sets, are described in table 2.

Table 1. Patient characteristics

	N	Gender (F)	Age, Av (S.D.)	ACR 1990 + for GPA	ACR/ EULAR 2017 + for GPA
GPA	59 (63.44%)	30 (50.85%)	46.54 (13.32)	34 (57,63%)	51 (86,44%)
MPA	33 (35.48%)	23 (69.7%)	62,72 (2.11)	9 (27,27%)	3 (9,09%)
GPE	1 (1.08%)	1	62	0	0
Total	93	39 (41.94%)	52,45 (14.97)	43 (46,24 %)	54 (58,06 %)

Table 2.- Performance of ACR 1999 and ACR/EULAR preliminary Criteria for GPA in Chilean Patients

GPA Clasification Criteria	ACR 1990	ACR/EULAR 2017, preliminary Criteria
Sensitivity	57,6%	91,5%
Especificity	70,6%	91,2%
Positive Predictive Value	77,3%	94%
Negative Predictive Value	49%	86%
Positive Likelihood Ratio	1,96	10,3
Negative Likelihood Ratio	0,6	0,9
accuracy	0,62	0,91

Conclusions: In our population, provisional 2017 ACR/EULAR criteria for classificatión of GPA have better acurracy than ACR 1990 classification criteria.

References:

[1] -Leavitt RY, Fauci AS, Bloch DA, Michel BA, Hunder GG, Arend WP, Calabrese LH, Fries JF, Lie JT, Lightfoot RW Jr, et al.The American College of Rheumatology 1990 criteria for the classification of Wegener's Granulomatosis. Arthritis Rheum 1990;33:1101–7.

[2] -Luqmani, R, Merkel, P. New Clasification Criteria for ANCA-Associated Vasculitis: Implication for Clinical Practice. Lecture, 2016 ACR/ARHP Annual Metting.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6732

AB0591 EFFICACY AND SAFETY PROFILE OF INTRAVENOUS CYCLOPHOSPHAMIDE TREATMENT IN ELDERLY PATIENTS WITH SYSTEMIC VASCULITIS

S. Shimoyama[1], T. Kurita[1], S. Fukaya[2], M. Kanda[2] on behalf of Japanese Red Cross Kitami Hospital, Hokkaido P.W.F.A.C. Obihiro Kosei Hospital. *[1]Internal medicine/ General medicine, Japanese Red Cross Kitami Hospital, Kitami; [2]3rd Department of Internal medicine, Hokkaido P.W.F.A.C. Obihiro-Kosei General Hospital, Obihiro, Japan*

Background: Intravenous cyclophosphamide is mainstay of remission induction and dose reduction of glucocorticoid in patients with systemic vasculitis. However, little evidence has yet shown the safety profile of intravenous cyclophosphamide, especially in elderly patients.

Objectives: To evaluate efficacy and safety of patients diagnosed as systemic vasculitis and treated with intravenous cyclophosphamide.

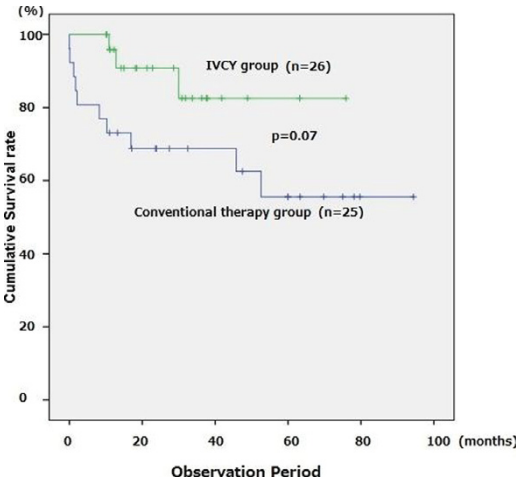
Methods: This retrospective study comprised the patients with active systemic vasculitis who were admitted to Kitami Red Cross Hospital and Obihiro-Kosei General Hospital from April 2009 to March 2016. These patients were treated with intravenous cyclophosphamide plus conventional therapy (IVCY group) or only with conventional therapy (glucocorticoid/azathioprine/tacrolimus and methotrexate) (conventional therapy group). The patients treated with oral cyclophosphamide or rituximab were excluded. Primary endpoint was defined as death or serious infections. Prognostic factors in IVCY group were analyzed by multivariate Cox regression methods.

Results: This study comprised 90 patients with active systemic vasculitis (61 microscopic polyangiitis, 9 eosinophilic granulomatosis with polyangiitis, 10 granulomatosis with polyangiitis, and 10 polyarteritis nodosa). Fifty-one patients were over 70-year-old (26 patients in IVCY group). The mean observation period was 30.1 months. IVCY group had a trend for higher event-free survival rate as compared with conventional therapy group (p=0.19). IVCY group had significantly higher cumulative survival rate as well (p=0.04). Age (HR=1.07, 95% CI 1.01–1.14, p=0.03), five factor score (FFS, HR=3.39, 95% CI 1.36–8.44, p=0.01) and glucocorticoid dose at 24 weeks (GC24, HR=1.14, 95% CI 1.05–1.22, p=0.001) were identified as risk factors for events. In patients over 70-year-old, IVCY group had a trend for higher cumulative survival rate as well (p=0.07, Figure1). FFS (HR=3.30, 95% CI 1.19–9.15, p=0.02) and GC24 (HR=1.10, 95% CI 1.02–1.20, p=0.01) were identified as risk factors for events.

Table 1. Background of patients with IVCY group and conventional therapy group

	IVCY group (n=54)	conventional therapy group (n=36)	P value
MPA,n (%)	36 (67%)	25 (69%)	0.95
EGPA,n (%)	6 (11%)	3 (8%)	0.56
GPA,n (%)	8 (15%)	2 (6%)	0.36
PN,n (%)	4 (7%)	6 (17%)	0.19
age (y)	66.4±15.5	72.3±15.9	0.09
Male,n (%)	19 (35%)	13 (36%)	0.93
FFS (d=0)	0.6±0.7	0.7±0.8	0.40
BVAS (d=0)	10.9±5.5	10.5±6.4	0.71
PSL (mg, d=0)	50±11	38±13	0.39
PSL pulse,n (%)	18 (33%)	22 (61%)	0.01
AZA,n (%)	13 (24%)	14 (39%)	0.10
MTX,n (%)	2 (4%)	4 (11%)	0.17

Abbreviation: MPA (microscopic polyangiitis), EGPA (eosinophilic granulomatosis with polyangiitis), GPA (granulomatosis with polyangiitis), PN (polyarteritis nodosa), BVAS (Birmingham Vasculitis Activity Score), AZA (azathioprine), MTX (methotrexate), d = 0 means day 0; the start of the treatment.



Conclusions: Intravenous cyclophosphamide treatment had acceptable safety profile even in elderly patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3338

AB0592 PULMONARY ARTERY ANEURYSM IN BEHÇET'S DISEASE: RETROSPECTIVE MONOCENTRIC TUNISIAN STUDY

S. Hammami, A. Sondes, R. Klii, M. Kechida, M. Ben Nasr, I. Kochtali. *Internal medicine, University Hospital F Bourguiba Monastir, Monastir, Tunisia*

Background: Behcet's disease (BD) is a chronic inflammatory disorder. Arterial inflammatory involvement includes predominantly aortic and pulmonary aneurysmal lesions, affects about 10% of patients with BD. They account for the severity of the disease and are a leading cause of death

Objectives: To investigate the frequency of Behcet's disease with pulmonary artery aneurysm (PAA). We aimed to review PAA and other systemic involvements associated with PAA in BD and to provide a review of diagnostic techniques, treatment and prognosis

Methods: 243 BD patients were recruited for this study (152 men, 91 women, mean age 31.7±7 years. Diagnosis of BD was made according to the international study group for Behçet's disease [International Study Group for Behçet's Disease, lancet 1990; 335: 1078–80]. All patients underwent full clinical examination, routine laboratory investigations. Chest X-rays and pulmonary CT angiography were performed on all patients with pulmonary involvement.

Results: Eight of the patients have pulmonary aneurysm, all of them are male, mean age 32.6±13, The mean disease duration until PAA appear was 2.8±3.5 years. The main pulmonary symptoms were as follows: dyspnea 87%, cough 50%, hemoptosis: 75%, fever 37%. Other systemic involvements associated PAA are as follows: buccal (100%) and genital (75%) ophthalmic 25%, neurological 50%, cardiac 25%. 3 patients presented with Hughes Stovin syndrome. The treatment includes corticosteroids, colchicine and immunosuppressant agents (Cyclophosphamid or azathioprine), only two patients reveive coil embolization. At follow up for a median of 4 years (1 to 25 years), three patients died because they stopped their medication.

Conclusions: The prognosis of PAA is poorer than other lesions involved in BD, treatment (immunosuppressant agents, colchicine) seems to improve the prognosis. It is important to maintain the immunosuppressive therapy and a regular follow-up to prevent these complications

References:
[1] Desbois AC et al Aortic inflammatory lesions in Behçet's disease Rev Med Interne. 2016 Apr;37(4):230–8.
[2] Celik S et al. Pulmonary artery aneurysms in Behçet's syndrome: a review of the literature with emphasis on geographical differences. Clin Exp Rheumatol. 2015 Nov-Dec;33(6 Suppl 94):S54–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6671

AB0593 ANCA-ASSOCIATED VASCULITIS WITH BOTH MPO-ANCA AND PR3-ANCA SHARES CHARACTERISTICS OF ANCA-ASSOCIATED VASCULITIS WITH SINGLE ANCA

S.M. Kim[1], J. Kim[2], S.W. Kang[2], S.-C. Shim[2], S.-J. Yoo[3]. *[1]Internal Medicine, Chungbuk National University Hospital, Cheong-ju; [2]Internal Medicine, School of Medicine Chungnam National University; [3]Internal Medicine, Chungnam National University Hospital, Daejeon, Korea, Republic Of*

Background: The anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides are heterogeneous group of necrotizing inflammation of small vessel and the presence of the ANCA. ANCAs are defined according to the target antigens, leukocyte proteinase 3 (PR3) and myeloperoxidase (MPO). Recently, the ANCA specificity could be better for classification of ANCA-associated vasculitides than the clinical diagnosis. A few patients have both MPO- and PR3 ANCA. However, the clinical characteristics of these patients were not known in detail.
Objectives: To analyze organ involvement of patients with ANCA-associated vasculitis according to ANCA type focusing both MPO- and PR3-ANCA (both-ANCA) positive vasculitis
Methods: The medical records of the patients with positive ANCA and clinical diagnosis or the patients with positive ANCA and vasculitis diagnosis confirmed by biopsy were reviewed at two regional tertiary hospitals. The age at diagnosis, sex, and the organ involvement of kidney, lung, upper airway (nose/sinus/ear), skin, peripheral nervous system, central nervous system, and gastrointestinal tract were collected. The clinical variables were analyzed by ANCA type.
Results: Total 82 patients with positive ANCA and clinical diagnosis or histologic diagnosis of vasculitis were searched. MPO-ANCA positive patients was 63 (76.8%), PR3-ANCA 9 (11.0%), and both MPO- and PR3-ANCA was 10 (12.2%). The age at diagnosis of patients with PR3-ANCA was younger than patients with MPO-ANCA or both-ANCA (PR3-ANCA, 49.6 vs. MPO-ANCA, 66.1 vs. both-ANCA, 62.1, $p<0.05$). Moreover, kidney involvement were MPO-ANCA was 77.8%, PR3-ANCA 22.2%, and both-ANCA 80% ($p<0.05$). Upper airway involvement was also significantly associated with ANCA type (PR3-ANCA, 66.7% vs. MPO-ANCA, 23.8% vs. both-ANCA, 50.0%, $p<0.05$). The involvement of skin, central or peripheral nervous system, gastrointestinal tract or the presence of lung fibrosis and lung nodule or mass did not differ according to ANCA type.
Conclusions: ANCA-associated vasculitis with both MPO-ANCA and PR3-ANCA has more kidney involvement than ANCA-associated vasculitis with PR3-ANCA and more upper airway involvement than ANCA-associated vasculitis with MPO-ANCA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6476

AB0594 RELATION OF CERTAIN BLOOD PICTURE PARAMETERS AND VASCULAR ENDOTHELIAL GROWTH FACTOR TO CLINICAL MANIFESTATIONS AND DISEASE ACTIVITY IN BEHÇET'S DISEASE PATIENTS

T.A. Gheita[1], R.E. Rabea[1], B.R. Sakr[1], S.M. Abd ElHamid[2]. *[1]Rheumatology and Clinical Immunology; [2]Clinical Pathology, Faculty of Medicine - Kasr Al-Ainy School of Medicine - Cairo University, Cairo, Egypt*

Background: Behçet's disease (BD) is a systemic inflammatory condition sharing the clinical features of both auto- inflammatory diseases and variable vessel vasculitis. Endothelial dysfunction (ED) plays an important role in the pathogenesis of BD. Several markers can be used to evaluate ED as mean platelet volume (MPV), red cell distribution width (RDW), neutrophil-lymphocyte ratio (NLR) and vascular endothelial growth factor (VEGF).
Objectives: The aim of the present study was to measure the MPV, RDW, NLR and serum level of VEGF in BD patients and to study their relation with disease manifestations and activity.
Methods: Ninety six BD patients and 60 matched controls were enrolled in this study. The MPV, NLR, RDW and serum VEGF level were measured. Disease activity was assessed by the BD Current Activity Form (BDCAF). The influence of an associated metabolic syndrome (MetS) was also considered.
Results: The mean age of the 96 patients was 34.9±10.1 years (18–73 years), male:female 4.7:1 and the disease duration was 9±7 years (0.6–40 years). MetS was present in 13.7%. Two patients were siblings and 5 had juvenile-onset BD. The RDW and NLR were significantly higher in patients (15.5±2% and 2.7±2.9) than controls (14.3±1.03% and 1.5±0.8) ($p<0.001$ each), while the MPV and VEGF were comparable. The MPV was significantly decreased in patients with vascular involvement (p=0.04) and increased in those with psychiatric disorders (p=0.02). The RDW was significantly higher in patients with vascular involvement (p=0.04) especially those with venous thrombosis and in those with neurological manifestations (p=0.03). The NLR was higher in males (p=0.01) and in those with retinal vasculitis (p=0.03) and vein occlusion (p=0.02). None of the parameters significantly correlated with the BDCAF. However, the NLR was the most valuable parameter to predict disease activity at a cut-off level of 1.69 ng/L (sensitivity 75%, specificity 55.6%). The MPV significantly correlated with the body mass index (BMI) (p=0.008), cholesterol (p=0.01) and low density lipoprotein (LDL) ($p<0.001$); the RDW correlated with the erythrocyte sedimentation rate (ESR) (p=0.003) and total leucocytic count (TLC) (p=0.04); the NLR with TLC (p=0.001) and blood urea (p=0.001) and VEGF with the TLC (p=0.048) and high density lipoprotein (HDL) (p=0.02). None of the parameters was significantly different according to the presence of MetS. Regarding the medications received, the RDW was significantly higher in patients who received cyclophosphamide and warfarin than those who did not (p=0.003 and $p<0.001$ respectively) and the level of VEGF tended to be lower in patients who received colchicine (p=0.06).
Conclusions: In BD, only the RDW and NLR were significantly increased raising the possibility of a potential role in the disease susceptibility and pathogenesis with no obvious relation to the disease activity or to an associated MetS. Together with the serum VEGF, they may all serve as useful markers to reveal the pattern of organ involvement while the NLR was the most valuable cost effective parameter to signify the disease activity. The influence of medications warrants further studies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2242

AB0595 NOVEL APPROACHS BASED IN CURRENT EVIDENCE IN ANCA-ASSOCIATED VASCULITIS WITH RENAL INVOLVEMENT TREATMENT

V. Vazquez[1], G. Gonzalez[2], J. Robaina Sindin[2]. *[1]Nephrology, Hospital Simplemente Evita, Gonzalez Catan, Pcia Buenos Aires; [2]Nephrology, Hospital de Clínicas José de San Martín, Universidad de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina*

Background: ANCA-associated vasculits (AAV) are a group of multi-system autoinmune diseases characterized by inflamation and necrosis in small and medium vessels.AAV could respond to diferent therapeutics protocols depends on diverse levels of clinical severity and early treatment could improve the outcome of the disease.In spite of recognized efficay of regimens consisting of cyclophosphamide and high-dose corticosteroids to control the AAV,efforts to minimize drugs-related toxicity led to consider targeted therapies.
Objectives: Considering the currently quality evidence in therapies novely proposed to AAV and the severity of renal disease presentation,we suggest new rational approaches emphasizing targeting B-cells therapy and preventing disease relapse
Methods: We identified the latest quality evidence using methodological search filters,assessed the evidence quality with Cochrane Renal Goup check list and determinated the strenght of recommendations by Levels of Evidence (Oxford Centre for Evidence-based Medicine)
Results: Rituximab (RTX), a monoclonal anti-CD 20antibody, has emerged as the biologic agent more using in AAV patients in current publications and unlike latest Guides and Recommendations published,RTX would be recommended in induction and maintenance AAV with renal involvement treatment (Table 1).

Table 1

AAV Induction Therapy	Early systemic (GF>60 ml'):MTX + GC (Ib,B) Severe generalised (Cr>5.68 mg/dl):CFM IV/PO + MPS (Ia,A) Generalised with contraindication to CFM:RTX + GC (Ib,B) Prophylaxis against *Pneumocystis jirovecii* (in CFM or RTX therapy):Cotrimoxazol PO (IIb,B) Severe with RPGN: Plasma Exchange-adjuvant therapy (Ia, B)
AAV Maintenance Therapy	Low-dose GC + AZA up 18 months (IIb,B) Low-dose GC + LF (less safer) (Ib,B) Low-dose GC + MTX with GF >60 ml/'(Ib,B) Avoid use CFM long-term (higher relapse risk) (Ia,A) In GPA:RTX + GC low-dose each 6 months up18 months (Ib, B)
AAV Relapse	Minor Relapse:increase GC dose (IIb,C) Major Relapse:RTX + GC (Ia,A) Major Relapse with CFM cumulative dose <36 gr:CFM + GC (Ib,B) Plasma Exchange and/or MPS (IIb,C)
VAA Refractaria	RTX + GC,specially patients whose never recived RTX (II,B) Plasma Exchange in RPGN and/or dialysis-dependen (Ia,B)

GF: glomerular filtrate, MTX:metotrexate, GV: glucocorticoids, Cr: creatinine, CFM: ciclophosphamide, IV: intravenous, PO: oral, MPS: metilprednisolone, RTX: rituximab, RPGN: rapidly progressive glomerulonephritis, AZA: azathioprine, LF: leflunomide, GPA: granulomatosis with polyangiitis.

Conclusions: Current therapeutical protocols for AVV with renal involvement show that emerging therapies like RTX could improve rates of relapses and treatment-related toxicity. Further studies would provide target-therapeutical options
References:
[1] Vazquez V et al. Clinical practice guideline for ANCA-associated vasculitis with renal involvement. Medicina (Buenos Aires). 2015;75 Suppl 1:1–38
[2] Mukhtyar C et al. EULAR recommendations for the management of primary small and medium vesselvasculitis. Ann Rheum Dis 2009;68:310–317.

[3] Guillevin L et al. Rituximab versus Azathioprine for Maintenance in ANCA-Associated Vasculitis. N Engl J Med 2014;371:1771–80.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2302

AB0596 INTERFERON-Γ RELEASE ASSAY (T-SPOT.TB) IN THE DIAGNOSIS OF TUBERCULOSIS INFECTION IN PATIENTS WITH BEHCET'S DISEASE: A SINGLE CENTER EXPERIENCE IN CHINA

W. Zheng[1], X. Wu[2], P. Chen[3], L. Zhao[1], J. Liu[1], L. Zhang[4], X. Liu[4], Y. Zhao[1], X. Zeng[1]. *[1]Rheumatology, Peking Union Medical College Hospital, BEIJING; [2]Rheumatology, General Hospital of Tianjin Medical University, Tianjing; [3]Rheumatology, Affiliated Mindong Hospital of Fujian Medical University, Fujian; [4]Infectious Diseases, Peking Union Medical College Hospital, BEIJING, China*

Background: In many aspects Behcet's disease (BD) is correlated with tuberculosis (TB). They may mimic each other on clinical manifestations. For example erythema nodosa, arthritis, gut lesions could be occurred in both disease and it is difficult for differential diagnosis. Some patients with newly-diagnosed BD were found to have active or latent or old TB and anti-TB therapy could relieve some of the symptoms. In etiology, it has been postulated that tubercle bacilli may act as a trigger of BD through the mechanism of molecular mimicking. Vice versa, defective cell-mediated immunity in BD patients may increase individual susceptibility of TB.It is extremely important to clarify TB existence or not in BD patients. Since BD patients commonly need glucocorticoid and immunosuppressant or even biologic agent such as anti-TNFa. And these medications may increase the risk of occurrence or flare of TB. But positive result of PPD shows little value in this special population due to acupuncture reaction in BD patients.In this pilot study, the values of interferon-γ release assay (T-SPOT-TB) in diagnosing active TB in BD patients were explored.
Objectives: To investigate the diagnostic value of the T-SPOT.TB in BD patients complicated with tuberculosis infection.
Methods: The clinical, radiology and laboratory data were collected and analyzed in 175 hospitalized BD patients from the Peking Union Medical College Hospital between January 2010 and March 2015. Statistical analysis was carried out using IBM SPSS version 20.
Results: Of the 175 BD patients, the positive rate of tuberculosis infection in BD patients was 34.3%. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the T-SPOT.TB test for the diagnosis of ATB were 87.5%, 73%, 36.8%, 98.3%, respectively. Positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were 3.24 and 0.17. The median number of SFCs in the BD-ATB group was higher than that in the BD-LTB group and BD-OTB ($p<0.001$ and p=0.012). By ROC method, it was suggested that 70 SFCs act as a cutoff for diagnosing BD-ATB with the sensitivity, specificity, PPV, NPV, PLR and NLR were 87.5%, 85%, 24.6%, 98.5%, 5.79 and 0.15, respectively. The rates of LTB infection had no significant difference between BD patients and healthy controls. Agreement between T-SPOT.TB and TST in BD patients measured by the kappa coefficient was poor (kappa =0.37).Multiple logistic regression analysis revealed that BD patients with positive T-SPOT.TB had the highest likelihood of ATB (OR 11.93, 95% CI 2.108–67.508, p=0.005).
Conclusions: T-SPOT.TB is a promising test in the diagnosis of BD complicated with tuberculosis infection, and higher number of SFCs may has a higher risk of ATB.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4149

AB0597 LOW-DOSE RITUXIMAB AS INDUCTION THERAPY FOR JAPANESE PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

Y. Takakuwa, H. Hanaoka, T. Kiyokawa, K. Ishimori, H. Iida, H. Nagafuchi, T. Okazaki, S. Ozaki. *Division of Rheumatology and Allergy, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan*

Background: Four times of once-weekly doses of 375 mg/m^2 rituximab (RTX) are frequently used as remission induction therapy for ANCA-associated vasculitis (AAV). Since this regimen has been basically generated from experience of B-cell non-Hodgkins' lymphoma in the Europe and North America, appropriate dose and interval for patients with AAV in other population have been poorly investigated. Here we comprehensively analyzed the efficacy and tolerability of high or low dose regimen of RTX in Japanese patients with AAV.
Objectives: We investigated the efficacy and safety issue of low dose RTX for Japanese patients with AAV.
Methods: We retrospectively examined AAV patients who met the 2012 Chapel Hill classification from 2006 to 2016. We divided them into 2 groups, those treated with high-dose (HD) and low-dose (LD) RTX. HD RTX was the original regimen and LD RTX consisted of twice of one-weekly dose of 375 mg/m^2. We evaluated cumulative complete remission (CR) rate and relapse-free rate for 1.5 years. CR was defined as BVAS=0 and relapse was defined as BVAS$\geqq$1.
Results: We evaluated 17 patients with HD and 11 patients with LD RTX. Higher percentage of elderly patients was observed in LD group ($p<0.01$). No significant difference was found in BVAS (p=0.49) and VDI (p=0.15) before treatment. No significant difference was found in cumulative CR rate (p=0.90) (Fig. 1A), relapse-free rate (p=0.48) (Fig. 1B), B cells counts and serious adverse events. We found patients with nasal involvement and pulmonary nodule/cavity formation had higher relapse rate in LD group than those with HD group (p=0.05,and p=0.09 respectively).

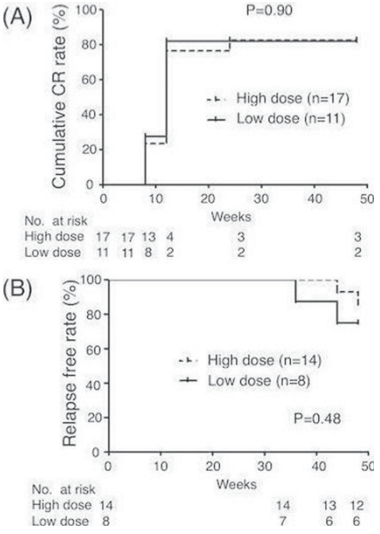


Figure 1

Conclusions: LD regimen of RTX, especially in elderly patients, might be effective in remission induction therapy in AAV.
References:
[1] Ozaki S, et al. Mod Rheumatol 2012; 22: 394–404.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5410

Scleroderma, myositis and related syndromes

AB0598 SERUM DEFENSIN LEVEL IN SYSTEMIC SCLEROSIS PATIENTS

T. Emiroglu[1], H. Küçük[2], B. Goker[2], S. Haznedaroglu[2], H. Pasaoglu[3], Ö. Varan[2], M.A. Öztürk[2], O.T. Pasaoglu[3], A. Tufan[2]. *[1]Department of Internal Medicine; [2]Department of Internal Medicine, Division of Rheumatology; [3]Department of Biochemistry, Gazi University Faculty of Medicine, Ankara, Turkey*

Background: Skleroderma is an autoimmune disease characterized by fibrosis of skin and lung as well as involvement of kidney, gastrointestinal system and heart (1). Etiology and exact mechanism of disease is poorly understood. A small number of studies have examined the role of AMPs on autoimmune diseases. It has been demonstrated that the amount of alfa- and beta-2 defensin serum levels are increased in systemic lupus erythematosus patients (2.3). Likewise, the association between AMPs and other diseases such as idiopathic pulmonary fibrosis, diffuse panbronchiolitis, pulmoner alveolar proteinosis and psoriasis has been reported (4).
Objectives: No study investigated the role of AMPs on scleroderma patients. Hence, we aimed to investigate AMP serum levels and their possible association in these patients.
Methods: There were 42 patients (40 female, mean age 42 years) and 38 healthy subjects (32 female, mean age 38 years) in the study. For SSc patients, the following data were recorded at enrollment: disease subset (limited/diffuse), autoantibodies (antinuclear, anti-centromere (ACA), and anti-scl), blood tests, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), modified Rodnan skin score, presence and history of digital ulcers, presence and history of involvement kidney and gastrointestinal system, interstitial lung disease detected by chest HRCT and pulmonary function tests, estimated pulmonary arterial systolic pressure at echocardiography.
Results: There were 42 patients (40 female, mean age 42 years) and 38 healthy subjects (32 female, mean age 38 years) in the study. Twenty-nine of the patients had diffuse systemic sclerosis and thirteen of the patients had limited systemic sclerosis. Average disease duration is 5.5 years. Pulmonary involvement was detected in twenty patients. The levels of beta 1 and beta 2 defensin that are epitelyal defensins were higher than control group but it has not reached statistical significance. (beta-1 defensin 235±178 vs 185±24 pg/ml, p=0.08 and beta2 defensin 253±453 vs 152±101 pg/ml, p=0,1). Alpha defensin levels in scleroderma patients were significantly higher than control group (563±415 vs 377±269 ng/mL,p=0.02). In sub-group analysis patients with interstitial lung disease had a higher level of alpha defensive than those without involvement (684±473 vs430±299 ng/ml, p=0.04). There was an negative correlation between alfa defensin and Rodnan score (r=0.30) and CRP (r=0.34).
Conclusions: Alpha defensin levels in scleroderma patients were significantly higher than control group, There may be an increase in the level of alpha defensin in a cause of vasulopathy in scleroderma patients

References:
[1] Almeida, C., I. Almeida, and C. Vasconcelos, Quality of life in systemic sclerosis. Autoimmunity reviews, 2015. 14(12): p. 1087–1096.
[2] Vordenbäumen, S., et al., Elevated levels of human beta-defensin 2 and human neutrophil peptides in systemic lupus erythematosus. Lupus, 2010. 19(14): p. 1648–1653.
[3] Sthoeger, Z.M., et al., High α-defensin levels in patients with systemic lupus erythematosus. Immunology, 2009. 127(1): p. 116–122.
[4] Jansen, P.A., et al., β-Defensin-2 protein is a serum biomarker for disease activity in psoriasis and reaches biologically relevant concentrations in lesional skin. PloS one, 2009. 4(3): p. e4725.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2627

AB0599 COMBINATION OF CAPILLAROSCOPIC AND ULTRASONOGRAPHIC EVALUATIONS OF THE HAND TO DETECT SEVERE VASCULOPATHY IN SYSTEMIC SCLEROSIS: RESULTS OF A CROSS-SECTIONAL STUDY

A. Lescoat[1], G. Coiffier[2], M. de Carlan[1], C. Droitcourt[3], C. Cazalets[1], A. Perdriger[2], P. Jégo[1]. *[1]Internal Medicine; [2]Rheumatology; [3]Dermatology, CHU, Rennes, France*

Background: Although micro-vessel alterations have been largely described, macrovascular involvement is also frequent in Systemic Sclerosis (SSc). Macrovascular damages specifically involve narrowing or occlusions of proper palmar digital arteries and ulnar artery. On the contrary, radial artery is rarely concerned. Ulnar artery occlusion (UAO) assessed by power doppler ultrasonography (PDUS) has proven to be predictive of the onset of new ischaemic DUs in longitudinal studies (1). PDUS could also be a reliable tool to evaluate finger pulp blood flow (FPBF). Only few studies have explored the association between macrovascular damages evaluated by PDUS and microvascular involvement assessed by nailfold capillaroscopy (NC) (2). The association between macrovascular disease and calcinosis or Acro-osteolysis is still to be determined in SSc.
Objectives: to confront microvascular damages on NC with macrovascular manifestations evaluated by PDUS in SSc patients. Micro and macro-vascular damages were confronted with the main digital manifestations of the disease: digital ulcers (DU), Acro-osteolysis and Calcinosis.
Methods: NC, hand X-Rays and PDUS were systematically performed in 64 unselected SSc patients. PDUS evaluation with assessment of Ulnar Artery Occlusion (UAO) and finger pulp blood flow (FPBF) was performed blinded for the results of X-Rays and NC.
Results: UAO and pathologic FPBF were associated with severe capillary loss (<4 capillaries/mm) on NC (respectively OR=4.04 (1.23–13.29); $p<0.05$ and OR=3.38 (1.03–11.05); $p<0.05$). UAO was significantly associated with Cutolo's late NC pattern (OR=3.80 (1.31–11.01); $p<0.05$). A DU history was associated with UAO (OR=10.71 (3.36–34.13); $p<0.0001$), pathologic FPBF (OR=7.67 (2.52–23.28); $p<0.0001$), late pattern (OR=6.33 (2.03–19.68) and severe capillary loss (OR=8.52 (2.15–33.78); p=0.001). Acro-osteolysis was also associated with UAO (OR=15.83 (3.95–63.54); $p<0.001$), pathologic FPBF (5.52 (1.71–17.90) p=0.003), late NC pattern (OR=6.86 (2.18–21.53); p=0.001) and severe capillary loss (OR=7.20 (2.16–24.02), p=0.001). Calcinosis on X-rays were associated with late NC pattern (5.41 (1.82–16.12); p=0.002), severe capillary loss (OR=12.69 (3.14–51.26); $p<0.0001$) and UAO (3.19 (1.14–8.92); 0.025) but not with pathologic FPBF. Combination of UAO and severe capillary loss in a same patient was especially associated with DU history (OR=18.60 (2.24–154.34); p=0.001) and Acro-osteolysis (OR=10.83 (2.56–45.88); p=0.001).
Conclusions: The combination of macro and microvascular evaluations by PDUS and NC may help to detect patients with a more severe vasculopathy.
References:
[1] Lescoat A, Coiffier G, Rouil A, Droitcourt C, Cazalets C, de Carlan M et al. Vascular evaluation of the hand by Power Doppler Ultrasonography provides new predictive markers of ischemic digital ulcers in systemic sclerosis. Arthritis Care Res (Hoboken). 2016 Jul 7.
[2] Rosato E, Gigante A, Barbano B, Cianci R, Molinaro I, Pisarri S, et al. In systemic sclerosis macrovascular damage of hands digital arteries correlates with microvascular damage. Microvasc Res. nov 2011;82(3):410–5.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4278

AB0600 CLINICAL RELEVANCE OF AUTOANTIBODY PROFILES IN SYSTEMIC SCLEROSIS

A. Burlui[1,2], A. Cardoneanu[1,2], E. Rezus[1,2]. *[1]Rheumatology, "Grigore T. Popa" University of Medicine and Pharmacy; [2]Rheumatology, Clinical Rehabilitation Hospital, Iasi, Romania*

Background: Systemic sclerosis (SSc) is a connective tissue disease accompanied by immune abnormalities. A number of autoantibodies such as anti-centromere, anti-topoisomerase I, anti-RNA polymerase III and anti-U3 (fibrillarin) antibodies were proven to be of great diagnostic and prognostic factors in patients with scleroderma. Certain studies have reported the presence of antinuclear, anti-SSA (Ro) and/or anti-SSB (La), anti-Pm/Scl, anti-endothelial cell and anti-nucleosome antibodies in patients with systemic sclerosis. However, the clinical relevance of these autoantibodies is yet to be fully elucidated.
Objectives: Our aim was to assess clinical features, capillaroscopic abnormalities and autoantibody titers in patients with systemic sclerosis as well as analyze relationships between these parameters.
Methods: We conducted a prospective observational study on 36 adult patients who satisfied ACR/EULAR 2013 criteria for systemic sclerosis.We recorded disease duration. current symptoms and classified patients as limited cutaneous (lc) SSc and diffuse cutaneous (dc) SSc. Skin involvement was assessed using the modified Rodnan skin score (mRSS). We performed nailfold videocapillaroscopy using a FEDMED Digitale 100N at a magnification of 200X. Thoracic Xrays were done to establish the presence of pulmonary fibrosis. Ultrasounds were performed by a single examiner to evaluate pulmonary artery pressure. Blood samples were drawn to measure anti-topoisomerase 1, anti-centromere, anti-SSA (Ro), anti-SSB (La), anti-U1RNP and anti-nucleosome antibody titers (ELISA). Patient characteristics were included in a database and analyzed using IBM SPSS Statistics v20.
Results: Our study group was composed of 20 dc SSc (55.6%) and 16 lc SSc (44.4%) patients. Severity of capillary changes correlated with mRSS values (p,0.01), anti-topoisomerase I (p=0.006), anti-SSA (p=0.01) and anti-nucleosome antibodies (p=0.02). We found positive associations between the presence of dysphagia, anti-centromere (p=0.009) and anti-SSA ($p<0.01$) titers in patients with lc SSc. Anti-centromere antibody positivity also correlated with pulmonary hypertension (p=0,011) and pulmonary fibrosis (p=0,04) in these patients. Anti-SSA antibodies correlated with pulmonary hypertension ($p<0.01$) and capillaroscopic changes (p=0.024) in dc SSc.
Conclusions: Our findings support the relationship between autoantibody titers, systemic involvement and microvascular changes in scleroderma patients. Non-specific autoantibodies such as anti-nucleosome and anti-SSA antibodies were associated with microvascular changes in our study group. Further studies in this field may provide new information on SSc pathogenesis and possibly novel targets for treatment in scleroderma patients.
References:
[1] Fuschiotti P. Current perspectives on the immunopathogenesis of systemic sclerosis. ImmunoTargets and Therapy. 2016;5:21–35. doi: 10.2147/ITT.S82037.
[2] Choi MY, Fritzler MJ. Progress in understanding the diagnostic and pathogenic role of autoantibodies associated with systemic sclerosis. Current Opinion in Rheumatology. 2016;28(6):586–594. doi: 10.1097/BOR.0000000000000325.
[3] Rezus E. Reumatologie, "Gr. T. Popa", UMF. Iasi, 2014, 162–183.
[4] Rezus E. Sclerodermia Sistemica in Reumatologie, "Gr. T. Popa", UMFIasi, 2014, 162–183. ISBN: 978-606-544-255-9.
[5] Pattanaik D, Brown M, Postlethwaite BC, Postlethwaite AE. Pathogenesis of Systemic Sclerosis. Frontiers in Immunology. 2015;6:272. doi: 10.3389/fimmu.2015.00272.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2577

AB0601 ANATOMIC AND FUNCTIONAL ASSESSMENT OF PERIPHERAL PERFUSION IN PATIENTS WITH SYSTEMIC SCLEROSIS. IS THERE ANY CORRELATION BETWEEN CAPILLAROSCOPIC FINDINGS AND ERGOSPIROMETRY?

A. Sarantopoulos[1], I. Gkougkourelas[1], A. Pataka[2], I. Stanopoulos[2], I. Koulas[1], P. Boura[1]. *[1]Clinical Immunology Unit, 2nd Dpt of Internal Medicine; [2]Pulmonary Department, "G. Papanikolaou" General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece*

Background: Microvasculopathy of systemic circulation in patients with Systemic Sclerosis (SS) is widely assessed by digital capillaroscopy (DC), a method that evaluates the architecture of capillary network and reveals changes of vascular anatomy. On the other hand, ergospirometry (ERG) reveals functional impairment of microcirculation by assessing indirect measures of peripheral tissue ischemia (most suitable VE/VCO2). Since today, there have been studies correlating DC findings with spirometric parameters (respiratory volumes)[1,2]; nevertheless, no reports have been published correlating the same DC findings with ERG parameters (functional microvascular perfusion).
Objectives: To propose the use of DC as a screening tool for impaired functional microvasculopathy by investigating correlations between patterns of capillaroscopic findings with ergospirometric values of peripheral tissue blood perfusion.
Methods: 11 patients (11 women mean age 43+/- 12 ys) with SS were evaluated contemporary with High Resolution Computed Tomography of the chest, ERG, and DC. Parameters were correlated with multiple regression analysis. Statistic significance was considered $p<0.05$.
Results: Patient data are shown in the table.
Patients with late pattern in capillaroscopy had less endurance in exercise test ($P<0.05$) but no correlation was found between capillaroscopic pattern and VE/VCO2 ($P>0.05$). Age was a crucial confounding factor.
Conclusions: The correlation of late pattern capillaroscopy findings with reduced ergospirometric endurance in 11 patients indicates that in a larger cohort, specific parameter associations between DC and ERG are probable to emerge.

Diffuse scleroderma	6/11
Limited scleroderma	5/11
Pulmonary hypertension	4/11
History of digital ulcers	5/11
Time of endurance in minutes (ergospirometry)	5':32" (±65")
Diffusion capacity (%pred)	82±15
Pulmonary fibrosis	7/11
VE/VCO2 (mean values ± sd)	32±5
Patterns of capillaroscopy	1/11 normal 1/11 early 4/11 active 5/11 late

References:
[1] Ghizzoni C, Sebastiani M, Manfredi A, et al. Prevalence and evolution of scleroderma pattern at nailfold videocapillaroscopy in systemic sclerosis patients: Clinical and prognostic implications. Microvasc Res. 2015 May; 99: 92–5.
[2] Castellví I, Simeón-Aznar CP, Sarmiento M, et al. Association Between Nailfold Capillaroscopy Findings and Pulmonary Function Tests in Patients with Systemic Sclerosis. J Rheumatol. 2015 Feb; 42(2): 222–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6599

AB0602 CAROTID ATHEROESCLEROTIC PLAQUES DETECTED BY ULTRASOUND IN SYSTEMIC SCLEROSIS PATIENTS UNDER 55 YEARS OLD

I. Sanz Pérez[1], F. Martínez Valle[1], A. Guillén del Castillo[1], N. Pizzi[2], R. Solans Laque[1], E. Callejas Moragas[1], I. Gonzalez Nieto[1], V. Fonollosa Pla[1], C.P. Simeón Aznar[1]. *[1]Internal Medicine; [2]Nuclear cardiology, Hospital Universitari Vall d'Hebron, Barcelona, Spain*

Background: In Systemic sclerosis (SSc), as in other autoimmune diseases such as rheumatoid arthritis or systemic lupus erythematosus, cardiovascular events are one of the most frequent causes of mortality not attributed to the disease itself.
Objectives: The aim of this study was to assess the presence of subclinical atherosclerosis by carotid Doppler ultrasound in SSc patients under 55 years.
Methods: We conducted a cross-sectional study that included 78 SSc patients without cardiovascular events from H. Vall d'Hebron cohort (Barcelona). Carotid Doppler ultrasound was performed to measure the Carotid Intima Media Thickness (CIMT) of common carotid artery (CCA) and detection of cholesterol plaques in CCA, bulb and internal and external carotid arteries, according to Mannheim consensus criteria. The results were compared to a healthy cohort from Barcelona, adjusted to age and sex[1]. We used SCORE for populations with low risk and REGICOR as cardiovascular risk assessment charts.
Results: Risk factors and SSc related features are described in table 1. Twenty three patients (29.5%) had carotid plaques (CP) being the presence of CP statistically significant compared to the healthy cohort (29.5% vs 15.6%; $p<0.05$; IC 0.04–0.24). None of the patients were catalogued as high risk according to SCORE chart. According to REGICOR chart, 4 patients (5.1%) were catalogued as intermediate risk and none as high risk. The four intermediate risk patients had CP. Carotid Intima Media Thickness mean (CIMTm) and maximum (CIMTmax), were statistically significant increased compared to the healthy cohort (CIMTm 0,57 vs 0,53; $p<0,05$ and CIMTmax 0,74 vs 0,61; $p<0,05$).
We performed multivariate regression analysis. Age, CIMTmax, low High Density Lipid (HDL), the presence of pulmonary hypertension, and Diffuse cutaneous SSc patients were independent factors for the presence of CP.

Female	62 (79.5%)
Age	44 (20–55)
Disease duration	14 (0–38)
Limited cutaneous SSc	41 (57.7%)
Diffuse cutaneous SSc	17 (23.9%)
Sine Scleroderma SSc	8 (11.3%)
Initial Scleroderma	5 (7%)
Arterial Hypertension	18 (23.1%)
Diabetes mellitus	2 (2.8%)
Statin treatment	14 (17.9%)
Smokers	15 (19.2%)
Digital ulcers	30 (42.3%)
Pulmonary Hypertension*	4 (5.1%)
Interstitial lung disease	32 (41%)

*Mean pulmonary artery pressure >25 mm Hg at right heart catheterization.

Conclusions: SSc patients under 55 years old often have subclinical atheromatous disease which could be detected by carotid ultrasound. Risk charts do not correlate with the presence of subclinical atheromatous disease. The presence of carotid plaque is more frequent in SSc patients with pulmonary hypertension, diffuse cutaneous subtype and patients with low HDL. CIMT could be useful although it is currently not recommended in cardiovascular risk guidelines.
References:
[1] Junyent M, Gilabert R, Núñez I, Corbella E, Vela M, Zambón D, et al. Carotid ultrasound in the assessment of preclinical atherosclerosis. Distribution of intima-media thickness values and plaque frequency in a Spanish community cohort. Med Clin (Barc). 2005;125(20):770–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6471

AB0603 QUANTITATIVE VIDEOCAPILAROSCOPY STUDY IN SYSTEMIC SCLEROSIS

A. Guillén-Del Castillo, C.P. Simeón-Aznar, E.L. Callejas-Moraga, S. Alonso-Vila, V. Fonollosa-Pla, A. Selva-O'Callaghan. *Department of Systemic Autoimmune Diseases, Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain*

Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by immunological features, microvascular disturbances and fibrosis as a consequence of a massive production of extracellular matrix.
Objectives: The aim of this study was to analyse the alterations of the capillary nailfold bed and describe their correlation with clinical variables.
Methods: 134 patients were selected with SSc according to LeRoy and Medsger diagnostic criteria from the Hospital Universitari Vall d'Hebron cohort. Patients underwent an echocardiogram, pulmonary function test and nailfold videocapillaroscopy (NVC) within a 3 months period. NVC was performed from 2nd to 5th finger of both hands. NVC features were quantitatively measured. Informed consent was obtained by all the participants. SPSS 20.0 were used for statistical analysis. A P-value <0.05 was considered as significant.
Results: Female was the predominant gender (113, 84.3%). The most common cutaneous subtypes were limited SSc, diffused SSc (88, 65.7% and 28, 20.9%, respectively). Almost 80% of patients met the ACR/EULAR 2013 classification criteria. The age (± standard deviation) at NVC was 38.5 (± 15.7) years, and the interval from the first SSc symptom and NVC was 16 (± 12.6) years. Anticentromere antibodies (ACA) were the most frequent in 36.6% of patients, followed by anti-topoisomerase I in 23.1%. Regarding organ involvement, 62 (46.3%) patients suffered from digital ulcers, 58 (43.3%) interstitial lung disease (ILD), 11 (8.2%) pulmonary hypertension, 110 (82.1%) gastrointestinal disturbances and 103 (76.9%) some cardiac alterations. The forced vital capacity was 80.8 (± 20.1) % and diffusion capacity for carbon monoxide (DLCO) was 66.2 (± 23.7) %. Regarding echocardiography results, the tricuspid regurgitation velocity (TRV) was 2.8 (± 0.3) m/s and the right ventricular systolic pressure 30.7 (± 12.0) mmHg. NVC findings were described as follows: the median of number of capillaries was 5.4 /mm, enlarged capillaries 0.8/mm, giant capillaries 0.2 /mm, microhemorragies 0.1 /mm, ramified capillaries 0.3 /mm, tortuous capillaries 0.6 /mm and disorganized capillaries 0.0 /mm. SSc-ILD patients presented lower capillary density 4.8 /mm compared with 5.8 /mm in the other group (P=0.005), and also more frequent ramified capillaries 0.3 /mm compared with 0.2 /mm (P=0.013). With respect to the correlations, the number of capillaries was related with the DLCO (rho =0.26, P=0.003) but negatively with the RVSP (rho = - 0.21, P=0.03). Giant capillaries were correlated with LVEF (rho =0.27, P=0.001) and greater tricuspid annular plane systolic excursion (TAPSE) (rho =0.21, P=0.01). Microhemorraghies were associated with LVEF (rho =0.29, P=0.001) although negatively with age at NVC (rho = - 0.25, P=0.003) and time from first symptom (rho = - 0.25, P=0.003). Disorganized capillaries were related with age at NVC (rho =0.17, P=0.04) but negatively with DLCO (rho = - 0.18, P=0.035).
Conclusions: The existence of a correlation between NVC features and clinical variables suggests that microvascular alterations may play a role as a pathogenic link with the cardiopulmonary SSc manifestations.
Acknowledgements: Guillen-Del Castillo A. is a researcher supported by the Contratos Predoctorales de Formación en Investigación (PFIS) grant from Instituto de Salud Carlos III [FI14/00643].
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4612

AB0604 RITUXIMAB EXPERIENCE IN PATIENTS WITH LONGSTANDING SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: A SERIES OF 14 PATIENTS

A. Sari[1], D. Guven[2], B. Armagan[1], L. Kilic[1], A. Erden[1], A. Akdogan[1]. *[1]Rheumatology; [2]Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey*

Background: Interstitial lung disease (ILD) is the leading cause of mortality in systemic sclerosis (SSc) patients. Treatment options are rather limited in SSc associated ILD (SSc-ILD).
Objectives: Objective of this study was to report the experience of RTX treatment in a series of patients with longstanding SSc-ILD in whom unsatisfactory response in lung functions was noted under conventional treatments.
Methods: We retrospectively reviewed charts of 197 SSc patients evaluated between April 2015 and November 2016. 14 patients who received rituximab (RTX) for SSc-ILD participated in this analysis. The severity of ILD based on PFTs was defined as follows; mild (FVC between 71% and 80% of predicted), moderate (FVC between 51% and 70% of predicted) and severe (FVC $\leq$50%). The extent of skin disease was clinically measured by using Modified Rodnan Skin Score (mRSS) tool. End of follow-up was considered as six months after the last RTX dose.
Results: Median (IQR, interquartile range) age was 53.2 (46.8–55.5) and median disease duration was 9.1 (5.1–13.6) years. Median FVC was 52.5 (41.5–64.0)

prior to RTX. At the end of follow-up, no significant change was revealed in FVC when compared with pre-RTX values [58.0 (44.7–58.7), p=0.065]. FVC was improved in four patients and stabilized remaining ten patients. All of the patients with improvement of PFTs had moderate or severe restrictive lung disease. High resolution thorax computed tomography (HRCT) findings remained stable in 7 and showed progression of ILD in 3 patients. In total, mRSS remained stable at the end of follow-up when compared with baseline [8.0 (5.2–12.2) vs. 6.0 (4.0–12.2),p=0,026].

Table 1. Demographic, clinical and laboratory data of patients

Age/ Sex	Disease duration, years	Cutaneous subset	Auto-antibodies	Previous immuno-supresive treatment	RTX cycles	Follow-up after RTX, months	FVC (predicted%)	
							Before RTX	After RTX
52/F	7.0	Diffuse	ANA, Scl-70	CYC, MMF	2	12	44	44
39/M	10.1	Diffuse	ANA, Scl-70	MMF	4	24	75	79
55/F	5.0	Diffuse	ANA, Scl-70	MMF	4	24	75	70
43/F	16.6	Limited	ANA, Scl-70	CYC, MMF	1	6	38	47
50/F	4.6	Limited	ANA, Scl-70	CYC, MMF	4	24	52	57
65/F	13,0	Diffuse	ANA, Scl-70	CYC, MMF	1	6	42	41
48/F	5.7	Limited	ANA, Scl-70	CYC	4	24	67	64
54/F	18.9	Diffuse	ANA, Scl-70	CYC, MMF	2	12	39	57
53/F	15.0	Limited	ANA, Scl-70	CYC, MMF	5	30	53	44
56/F	5,1	Limited	ANA, Scl-70	CYC	1	6	40	45
52/F	8.2	Limited	ANA	–	3	12	59	59
18/F	11.2	Diffuse	ANA, Scl-70	MMF	1	6	63	73
62/F	4.6	Limited	ANA, Scl-70	CYC, MMF	3	18	51	61
54/F	13.1	Limited	ANA, Scl-70	CYC, MMF	5	30	54	67

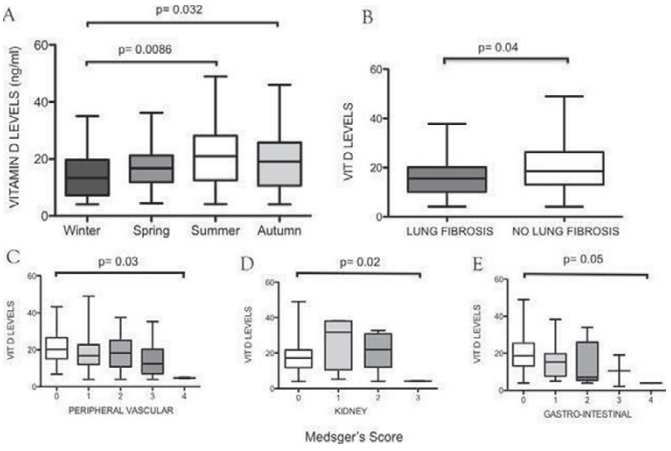
FVC, forced vital capacity; ANA, antinuclear antibody; Scl-70, antitopoisomerase-1 antibody; CYC, cyclophosphamide; MMF,mycophenolate mofetil; RTX, rituximab.

Conclusions: In this case series of SSc patients treated with RTX, improvement or stabilization of pulmonary functions was observed in most of SSc patients. RTX may be useful in SSc-ILD patients with longer disease duration and resistant to conventional immunsupresive therapies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5501

AB0605 VITAMIN D SERUM CONCENTRATION IN EUROPEAN SYSTEMIC SCLEROSIS PATIENTS: CORRELATIONS WITH SEASONALITY, ORGAN INVOLVEMENT AND STANDARD ORAL SUPPLEMENTATION

A.C. Trombetta [1], V. Smith [2], E. Gotelli [1], M. Ghio [1], S. Paolino [1], C. Pizzorni [1], A. Sulli [1], M. Cutolo [1]. *[1]Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genoa, Genoa, Italy; [2]Department of Internal Medicine, Faculty of Medicine and Health Sciences; Department of Rheumatology, Ghent University Hospital, Ghent University, Ghent, Belgium*

Background: Vitamin D deficiency is reported to interfere with immune responses and to correlate with course and outcome in several autoimmune diseases. In systemic sclerosis (SSc), low 25-hydroxyvitamin D (25(OH)D) serum concentration has been recognized.
Objectives: To investigate relations between 25(OH)D serum concentration and seasonality, clinical parameters as well as standard oral supplementation, in SSc patients.
Methods: 154 SSc patients (mean age 59±15 years, 24.7% diffuse form and 75.3% limited form) were evaluated, at any time of the year, in a retrospective survey. Serum 25(OH)D quantification was performed using the LIAISON 25-OH vitamin D assay (Diasorin, Italy). Pulmonary function test, chest x-ray, lung CT scan, electrocardiography, Doppler echocardiography, renal artery resistive index by eco color Doppler, Dual X-ray absorptiometry, were performed at the time of sample collection. Disease severity scale (DSS) was performed according to Medsger. Drug assumption (glucocorticoids, calcium channel blockers, cyclic intravenous iloprost, endothelin receptor antagonists) and supplementation with vitamin D analogues, were recorded. Non-parametric tests were used for statistical analysis.
Results: Average 25(OH)D serum concentration was found to be 18.7±9 ng/ml (<20 classified as deficiency). A significant difference was observed among seasonal 25(OH)D serum concentration (winter: 14.6±7.8 ng/ml, spring: 17.2±7.9 ng/ml, summer 21.43±10 ng/ml, autumn 20.2±10; p=*0.032*) (Figure 1). A significant correlation was found between 25(OH)D serum concentration and presence/absence of bi-basal fibrotic changes at lung computed tomography (CT) scan (average values: 16.1±8 ng/ml and 20±10 ng/ml, respectively, *p=0.04*). Peripheral vascular *(p=0.03*), kidney (*p=0.02*), gastrointestinal (*p=0.05*) Medsger's DSS parameters also were found to correlate with 25(OH)D serum concentration (Figure 1). Interestingly, no influence of treatment with vitamin D analogues (1,000 UI daily) was found regarding 25(OH)D serum concentration in treated (18.8±10 ng/ml) and in not treated (18.7±9 ng/ml) SSc patients (p=0.81).
Conclusions: In SSc is confirmed a serum 25(OH)D deficiency that we report to be associated with lung involvement, peripheral vascular, kidney and gastrointestinal Medsger's DSS parameters, as well as with seasonality. Supplementation with vitamin D analogues did not influence present results.



Therefore, for successful replacement, supra-physiological oral vitamin D3 doses or programmed UVB light exposure should be considered.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4919

AB0606 MORTALITY ASSOCIATED FACTORS TO IDIOPATHIC INFLAMMATORY MYOPATHIES (IIMS)

A.C. Costi [1], P. Sansinanea [1], C. Pena [1], A. Testi [1], A. Salas [1], J. Marcos [1], V. Arturi [1], A. Vulcano [1], M. Pera [1], R. García Salinas [2], R. Aguila Maldonado [1], L. García Var [1], V. Nagua [1], M.A. García [1]. *[1]Rheumatology, HIGA San Martín; [2]Rheumatology, Hospital Italiano, la Plata, Argentina*

Background: Idiopathic inflammatory myopathies (IIMs) include a group of muscular diseases characterized by the presence of muscle inflammation. The mortality of the IIMs has been estimated between 13 and 50%.
Objectives: To evaluate mortality rate and associated factors in patients with IIMs.
Methods: Retrospective, observational study, where patients with IIMs (Bohan & Peter 1975) were included. Data were obtained from medical records from patients with myopathy (Increase CK, muscle weakness, cutaneous involvement, interstitial lung involvement) evaluated in a reference rheumatology center of Argentina (1992–2016). Descriptive statistics were performed. Chi2 test, Student's test or Mann Whitney as appropriate multivariate logistic regression analysis.
Results: From 102 patients evaluated 89 enter the study, 73% were female. Mean age at diagnosis 48±14 years. Clinical Manifestations: Skin involvement 77% (erythema Heliotrope 51%, rash on the neck and V-sign 60%, back and shoulders 50%, photosensitivity 60%, Gottron's papules 50%, pruritus 33%, erythema peri nail 21%), pulmonary involvement 19% Raynaud 28%, muscle weakness 86%, muscle weakness of the neck 33%, respiratory muscles 13%, myalgias 60% and dysphagia 53%.
Muscle biopsy: performed in 36/89 with pathological findings in 83%, electromyogram performed in 35%. Intensive care unit admission 14/89 (16%). Laboratory: raised CPK 68% with an mean value 3527 IU/ml, raised Transaminase 60%, ANA positive 65%, SSA/RO 25%, Jo1 4.4%, RNP 7%, increased CRP 28% and ERA 59%.
Clinical Subtypes IIMs: Dermatomyositis (DM): 61%, Antisynthetic syndrome (AS): 6%, Myopathy associated with connective tissue disease: 19%, Associated with statins: 4, 4%, Polimyositis: 10%. Association with neoplasia was observed in 15%. Treatments: Corticoids pulses 21%, corticoids 97% (mean starting dose 45 mg meprednisone), methotrexate 77%, hydroxychloroquine 36%, azathioprine 30%, cyclophosphamide 16%, intravenous immunoglobulin 15%, biological 10% and cyclosporine 3%.

Univariate analysis

Variables	Mortality (Odds Ratio)	95% IC	
Male sex	3	1,03–8,4	P<0,039
Respiratory muscle weakness	5,47	IC: 1,4–20,59	p<0,007
ANA positive	6	1,27–27	P<0,01
Neoplasms	3,8	1,1–1,3p	P<0,026
Glucocorticoid pulses	5,7	1,81–17,8	P<0,001
Intravenous immunoglobulin	3,67	1,06–12,6	P<0,03
Serious infections	17	4,6–61,5	P<0, 0000012

Multivariate analysis of logistic regression

Variable	OR	IC (95,0%)		p
Malignant neoplasm	8,785	1,229	62,797	**0.03**
Serious infections	69,168	10,079	474,666	**0.0001**
Glucocorticoid pulses	3,745	0,635	22,092	0.145
Male sex	5,899	1,141	30,504	**0.034**
Intravenous immunoglobulin	0,906	0,100	8,217	0.93
Respiratory muscle weakness	0,524	0,050	5,527	0.59
ANA positive	4,247	0,638	28,259	0.135

Mortality was 22.5% (20/89 patients), CI95 (14.3–32.5). Mean time from diagnosis to the event was 18 months. The primary cause of death was sepsis 14/20 (70%).
Conclusions: Mortality of patients with inflammatory myopathies was 22%, and the primary cause was infectious. In the analysis of multiple variables, male sex, presence of neoplasms and serious infectious complications were significantly factors associated with mortality.
References:
[1] J Clin Rheumatol 2016; 22: 51–56.
[2] Med Clin 1999; 112:521–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5243

AB0607 PULMONARY EMBOLISM IN SYSTEMIC SCLEROSIS – ONE YEAR FOLLOW UP

A.C. Duarte[1], I. Cordeiro[1], M. Ferreira[2], T. Judas[2], M.J. Loureiro[3], J. Santos[4], S. Carmona[4], M.J. Santos[1], A. Cordeiro[1]. *[1]Rheumatology; [2]Internal Medicine; [3]Cardiology; [4]Nuclear Medicine, Hospital Garcia de Orta, Almada, Portugal*

Background: Risk of pulmonary embolism (PE) in systemic sclerosis (SSc) has been estimated between 2.51–3.47 fold higher when compared to non-SSc patients (pts). Proinflammatory state, vasculopathy and vascular injury may contribute to a prothrombotic state in SSc and increased risk for venous thromboembolism.
Objectives: Calculate frequency and identify possible risk factors for PE among SSc pts;analyse efficacy of longterm anticoagulation (ACO) in these pts.
Methods: We conducted a retrospective analysis of 110 pts with SSc followed in our Rheumatology department and selected those who performed lung ventilation/perfusion scintigraphy (V/Q scan) or CT pulmonary angiography due to worsening dyspnea/fatigue or isolated reduction of the carbon monoxide diffusing capacity (DLCO). We collected demographic features, comorbidities, age at SSc diagnosis, anti-nuclear antibody specificities, dyspnea according to New York Heart Association (NYHA) classes and results of cardiopulmonary exams. PE and related variables were assessed at baseline and after 12 months of ACO.
Results: PE was diagnosed in 12 out of 29 (41.4%) SSc pts that met inclusion criteria, with the majority presenting bilateral peripheral multisegmental defects. Most were females (91.7%), mean age of 59.4 (±12.7) years (yrs). Two thirds were diagnosed with limited SSc with mean disease duration of 13.3 (±12.9) yrs. Mean time between SSc and PE diagnosis was 8.5±8.2 yrs, although one third of the pts was diagnosed within the first year of SSc diagnosis. One patient was taking oral contraceptives and none had thrombophilia, previous surgery or cancer.
One third was classified as having NYHA class≥3, with a mean N-terminal pro-brain natriuretic peptide (NTproBNP) of 1108pg/mL (19 to 8069). Six pts had concomitant interstitial lung disease (ILD) and 8 had an estimated pulmonary artery systolic pressure (PASP)≥35 mmHg (6 of them had concomitant ILD). From these only 2 had pulmonary hypertension confirmed by right heart catheterization and 1 died.
When comparing SSc pts with and without PE, Scl70 positivity was more common in pts with PE (p=0.041). No significant associations were found between PE and several cardiovascular risk factors.
From the 12 pts with PE, 10 were on longterm ACO:5 on rivaroxaban, 4 on warfarin and 1 on apixaban. Clinical reassessment after 12 months of ACO is shown in figure 1.

Patient	Anticoagulant	Symptoms*	NT-pro BNP	V/Q scan	PASP (mmHg)	DLCO
1	Warfarin	Discrete improvement	Reduction (>100 pg/mL)	Not available	Not available	Identic
2	Rivaroxaban	Identic	Identic	Identic	Identic	Identic
3	Non-pplicable§					
4	Rivaroxaban	anticoagulated for < 6 months				
5	Warfarin	Identic	Identic	Identic	Identic	Discrete improvement (29»36)
6	Apixaban	Discrete improvement	Discrete raise (±100 pg/mL)	Decrease in perfusion defects	Worsening (28»40)¥	Identic
7	Warfarin	Discrete improvement	Identic	Identic	Improvement (51»30)	Not available
8	Warfarin	Identic	Marked raise (>5000 pg/mL)¥	Not available	Not available	Not available
9	Non-pplicable§					
10	Rivaroxaban	Identic	Raise (±200 pg/mL)	Identic	Not available	Identic
11	Rivaroxaban	Discrete improvement	Identic	Identic	Not available	Not available
12	Rivaroxaban	anticoagulated for < 6 months				

*Symptoms evaluated were fatigue and dyspnea; § V/Q scan defects are too subtle and the risk is considered to outweigh the benefit of anticoagulation; ¤ Cardiac catheterization demonstrated important coronary disease; ¥ In relation with worsening of ILD
Figure 1 – Patients' reassessment after 12 months of ACO

Conclusions: Our results suggest that PE is frequent in SSc and must be considered in the differential diagnosis of worsening fatigue and dyspnea and/or reduction of DLCO/PASP increase. PE may occur more frequently in Scl70 positive pts and early in disease course, probably due to vasculopathy and vascular injury being more prominent in the early phase of the disease. Although there is no consensus regarding the optimal ACO, the disease's vasculopathy seems to be an important contributor, potentially preventing improvement in perfusion defects, regardless of the anticoagulant used.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5214

AB0608 PREDICTIVE FACTORS FOR LONG-TERM SURVIVAL AND DISEASE PROGRESSION OF SYSTEMIC SCLEROSIS – A LONGITUDINAL ANALYSIS

A.M. Gheorghiu[1,2], A. Radu[1,2], R. Oneata[1,2], A. Soare[1,2], R. Dobrota[1,2], S. Magda[2,3], T. Constantinescu[2,4], R. Jurcut[2,5], R. Sfrenţ-Cornăţeanu[2,6], M. Bojincă[1,2], V. Stoica[1,2], C. Mihai[1,2]. *[1]Internal Medicine and Rheumatology, Cantacuzino Hospital; [2]Carol Davila University of Medicine and Pharmacy; [3]Emergency University Hospital; [4]Marius Nasta Institute of Pneumology; [5]C.C. Iliescu Institute for Cardiovascular Diseases; [6]Physiopathology and Immunology Department, Bucharest, Romania*

Background: Systemic sclerosis (ScS) has unpredictable course and high mortality. Generalised Estimating Equations (GEE) is a technique useful for longitudinal data analysis, using data from all time points and adjusting for within-patient correlation,i.e. correlation between time points within the same patient. GEE does not require a normal distribution of dependent variables, making it attractive for analyzing SSc data.
Objectives: To identify predictive factors for death and unfavorable outcomes.
Methods: Data of SSc patients with ≥2 visits in our EUSTAR centre in 2004–2016 were analyzed. GEE investigated the relationship over time between outcomes (death, digital ulcers (DUs), forced vital capacity (FVC), modified Rodnan skin score (mRSS)) and potential predictors (age, gender, disease duration, cutaneous subset, mRSS at baseline, DUs history, DLCO, left ventricle ejection fraction (LVEF), proteinuria), separately for each predictor and in combined models.
Results: 89 patients (12.4%males, mean±SD age 49.2±12.2years, disease duration 4.1±7.5years) were included, with a follow-up of up to 13years. There were 14deaths, most due to lung involvement (7/14). In multivariable GEE analysis (Table 1), predictors of death were a shorter disease duration, DUs history, and a lower LVEF. Predictors for FVC decrease over time were difuse cutaneous subset (dcSSc), younger age and lower DLCO. Younger age, shorter disease duration and higher baseline mRSS were the most important predictors for higher mRSS at follow-up. The only predictor for the development of new DUs was a history of DUs.

Table 1. Prediction factors for death and for evolution over time of parameters reflecting disease severity in SSc

Predictors	Death	DUs	FVC	mRSS
	OR (95% CI)	OR (95% CI)	B (95% CI)	B (95% CI)
Age	1.1 (0.9, 1.3)	0.9 (0.9, 1.0)	0.3 (0.1, 0.6)*	-0.1 (-0.2, -0.01)*
Disease duration	0.8 (0.7, 0.9)***	1.0 (0.9, 1.1)	-0.0 (-0.3, 0. 3)	-0.1 (-0.3, -0.03)**
mRSS baseline	0.9 (0.9, 1.1)	1.1 (0.9, 1.1)	0.2 (-0.2,0.7)	0.4 (0.3, 0.6)***
DLCO	0.9 (0.9, 1.0)	1.0 (0.9, 1.0)	0.5 (0.3, 0.6)***	0.1 (-0.0, 0.0)
LVEF	0.9 (0.90, 0.98)**	0.9 (0.9, 1.1)	0.2 (-0.2, 0.7)	0.0 (-0.2, 0.2)
Male gender	1.9 (0.3, 11.2)	0.5 (0.1, 1.9)	0.7 (-9.3, 10.7)	-1.2 (-3.9, 1.5)
dcSSc	6.8 (0.6, 81.7)	0.7 (0.2, 2.9)	-16.5 (-28.9, -4.9)**	1.7 (-0.1, 3.4)
DUs history	13.1 (3.1, 55.8)***	28.4 (2.3, 356.4)**	3.2 (-2.1, 8.4)	0.2 (-1.4, 1.7)
Proteinuria	1.1 (0.6, 1.8)	0.9 (0.4, 1.9)	2.2 (-2.5, 6.8)	1.7 (-0.1, 3.5)

*p<0.05, **p<0.01, ***p<0.001.

Conclusions: Patients with shorter disease duration, dcSSc, higher mRSS, lower DLCO and LVEF and a history of DUs had a more unfavorable course. GEE is a robust technique for longitudinal data analysis, excellent for identifying prediction factors in SSc.
Acknowledgements: *This abstract is part of the QUANTICAP project, UEFIS-CDI PN-II- PT-PCCA-2013–4-1589 grant.*
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5783

AB0609 CORRELATION OF PSYCHOLOGICAL PROFILE (MMPI-II A BDII TESTS) OF SCLERODERMA PATIENTS WITH ORGAN MANIFESTATION AND IMMUNOLOGICAL PROFILE

A. Smržová[1], L. Hubáčková[2], S. Kreiselová[2], J. Zapletalová[3], P. Horák[4]. *[1]3Rd Department of Internal Medicine – Nephrology, Rheumatology and Endocrinology; [2]Department of Psychology; [3]Department of Medical Biophysics; [4]Faculty of Medicine and Dentistry, Palacký University Olomouc, Olomouc, Czech Republic*

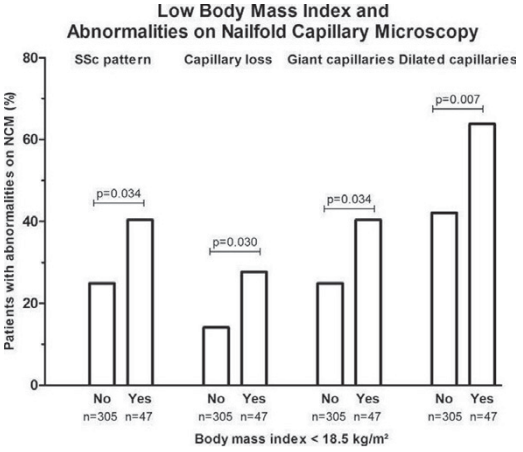
Background: There is high prevalence of mood disorders in patients with systemic scleroderma. Psychical distress can influent some of clinical manifestations and can worse the course of the disease and socioeconomicall status of patients.
Objectives: The aim of study is detection of correlations of depression and psychological profile measures by MMPI-II (The Minnesota Multiphasic Personality Inventory) and BDI-II (The Beck Depression Inventory-II) and organ manifestation and immunological profile of patients with systemic sclerosis.

Methods: From March 2015 to July 2017 we examined 42 patients with scleroderma, from which 37 filled the valorisation criteria of MMPI-II test. The data of MMPI-II scales and BDI-II was correlated with antropometric data, form of disease, disease duration, duration of RP, organ major manifestation, comorbidities, use of medication and immunological profile.
Results: In this study 37 patient were included (6 men, 31 women, mean of age – 58.8±10.6y., duration of disease 8,9±9.1y, duration of RP 13.9±13.4y.), 10 patient have diffuse, 27 patient limited form. Subjective perceived depression detected by BDI II test was present in 11 patients (35%, mild 6, moderate 3 and 2 severe). Total BDI-II score correlated with anticentromer Abs (p=0.05), total cholesterol (p=0.008), LDL (p=0.05) and gastrointestinal manifestation (p=0.002). Positivity in domain - Hypochondria, Depression, Hysteria, Psychastenia and Social introversion was highly prevalent (47–13%). This results of MMPI-II suggest a specific psychological profile of SSc patients. There was no correlation for age, subset of disease, cardiovascular manifestation, valvular damage and myositis. Smokers are much more introvert (p=0.012). Positivity of anti Scl70 Ab correlated with incredulity (p=0.038), schizophrenia, hypomania and family disharmony (p=0.046). Positivity of anticentromer antibodies was connected with incredulity (p=0.038), hypomania, alienation to family, egocentrism (p=0.042), psychotic thinking, psychomotoric retardation (p=0.037) and subscales of BDI-II test (Loss of pleasure, Self-Criticism, Self-Dislike). From organ manifestation, pulmonary hypertension correlated with himself degradation (p=0.037). Gastrointestinal manifestation has the same correlation and BDI-II subscale-Guilt Feelings (p=0.042). It is interesting, that absence of lung damage demonstrated with alienation self and family (p=0.049), posttraumatic stress disorder (p=0.025), problems in family (in more scales, p=0.028,0.03,0.029), schizophrenia (p=0.03). Patients without digital ulceration have much more neurologic symptoms (p=0.023). Using of antidepressant and anxiolitic medication correlated with a lot of scales in domain of depression, anxiety, social introversion, family distress and self devaluation. Disease duration and duration of RP correlated with psychomotoric retardation.
Conclusions: Patients with scleroderma may have special psychological profile. MMPI-II test shows specific psychologic abnormalities of scleroderma patients. Psychiatric and psychologic intervention can be very useful in complex care of these patients.
Acknowledgements: MZ CR VES15–28659A.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6528

AB0610 NAILFOLD CAPILLARY MICROSCOPY AND LOW BODY MASS INDEX IN RAYNAUD'S PHENOMENON PATIENTS

A.M. Van Roon[1], A. Eman Abdulle[1], A.M. van Roon[1], A.J. Stel[2], A.J. Smit[1], H. Bootsma[2], D.J. Mulder[1]. [1]*Internal Medicine - Vascular Medicine;* [2]*Rheumatology and Clinical Immunology, University of Groningen - University Medical Center Groningen, Groningen, Netherlands*

Background: Underweight patients develop Raynaud's phenomenon (RP) more frequently. [1] In a small study, skin temperature and perfusion in RP patients was positively associated with body mass index (BMI). [2] In clinical practice, we frequently observe an abnormal nailfold capillary microscopy (NCM) in underweight subjects with presumably primary RP, from which the implications are unknown.
Objectives: The aim is to study whether being underweight is associated with the presence of more abnormalities on NCM.
Methods: NCM, assessed by widefield videocapillaroscopy, was retrospectively assessed in consecutive patients with suspected RP. Patients were included when they had negative serology and did not develop any definite connective tissue disease or organ involvement after a maximum of 5 years follow-up. NCM pattern was classified as normal, non-specific, early, active or late, based on the Cutolo patterns. Weight and height were measured for clinical practice and patients were divided by BMI category: underweight (BMI$<$18.5 kg/m^2), normal weight (BMI 18.5–25 kg/m^2), and overweight (BMI $>$25 kg/m^2). Dilated and giant capillaries were counted as well as the total number of capillaries.
Results: A total of 352 patients were included (median age 40.6 years (24.9–52.9), male/female: 111/241), of which 47 were underweight, 220 normal weight and 85 overweight. Patients who were underweight presented more abnormalities (dilated capillaries, capillary loss or giant capillaries) on NCM, as shown in figure 1. BMI was negatively associated with NCM pattern, number of dilated capillaries and number of giant capillaries (r=-0.247, r=-0.225 and r=-0.221 respectively, all p$<$0.001) and positively with the total number of capillaries (r=0.260, p$<$0.001).
Conclusions: In addition to well-known thermoregulatory abnormalities, clear NCM pattern abnormalities are more frequently observed in underweight patients with primary RP. BMI was negatively associated with the number of dilated capillaries and positively with capillary density. These data potentially suggest that damage to the microvasculature in underweight patients with primary RP may occur independently of the presence or development of a CTD and may be explained by other mechanisms.
References:
[1] Roquelaure Y, Ha C, Le Manac'h AP, Bodin J, Bodere A, Bosseau C, et al. Risk factors for Raynaud's phenomenon in the workforce. Arthritis Care Res (Hoboken) 2012 Jun;64(6):898–904.
[2] Giurgea GA, Mlekusch W, Charwat-Resl S, Mueller M, Hammer A, Gschwandtner ME, et al. Relationship of age and body mass index to skin temperature and skin perfusion in primary Raynaud's phenomenon. Arthritis Rheumatol 2015 Jan;67(1):238–242.



Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3243

AB0611 MYCOPHENOLATE MOFETIL FOR THE TREATMENT OF INFLAMMATORY MYOPATHY RELATED INTERSTITIAL LUNG DISEASE: A SYSTEMATIC REVIEW

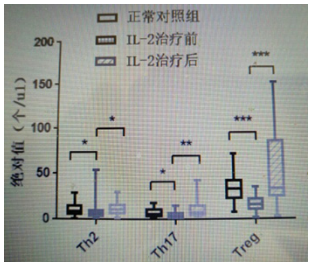
B. Lopez[1], D.A. Isenberg[2], P.A. Gordon[1]. [1]*Rheumatology, King's College Hospital;* [2]*Rheumatology, UCL, London, United Kingdom*

Background: Inflammatory myopathies (IIM) are a heterogeneous group of rare autoimmune rheumatic diseases in which extramuscular manifestations, especially interstitial lung disease (ILD), are common and may occur in the absence of muscle symptoms. ILD has been identified as a marker of poorer prognosis, with sparse, mainly observational evidence, supporting the use of immunosuppressant therapies.
Despite the lack of clinical trial evidence, corticosteroids are considered first-line therapy. Cyclophosphamide is frequently used for severe disease and Azathioprine as maintenance therapy. Mycophenolate Mofetil (MMF) has emerged as a promising treatment, encouraged by data published from a randomised controlled trial comparing Cyclophosphamide with MMF in patients with systemic sclerosis and ILD, which showed similar efficacy and better tolerability in the MMF group (1).
Objectives: To examine the evidence supporting the use of MMF in patients with IIM associated ILD.
Methods: An electronic literature search was performed using the Ovid platform. Population: Adults diagnosed with IIM according to validated criteria (2, 3) or antisynthetase syndrome (defined by the presence of anti-synthetase antibodies), with ILD demonstrated by HRCT or lung biopsy and treated with MMF, with extractable outcomes regarding ILD. Outcomes were recorded as positive (improvement/stabilisation) and negative (deterioration) as defined by the American Thoracic Society consensus guidelines (4).
Results: 506 initial citations were identified, with 23 studies included in the review comprising a total of 82 patients. Median follow up was 12 months, median age 55 years. There was sufficient data to apply America Thoracic Society criteria in 37 patients: improvement/stabilisation n=29, deterioration n=8. Although the criteria could not be applied in 45 patients, improvement/stabilisation was reported in 44 with deterioration in one patient. A non-significant trend to better outcomes was observed when MMF was prescribed as first line therapy, in Jo-1 positive patients and non-Usual Interstitial Pneumonia pattern. Mean Prednisolone dose reduced from 40 mg/day to 10.1 mg/day. No significant toxicity was reported.
Conclusions: Mycophenolate Mofetil is a promising drug with encouraging results, but randomised controlled clinical trials are needed to prove its efficacy.
References:
[1] Tashkin DP, Roth MD, Clements PJ, Furst DE, Khanna D, Kleerup EC, et al. Mycophenolate mofetil versus oral cyclophosphamide in scleroderma-related interstitial lung disease (SLS II): a randomised controlled, double-blind, parallel group trial. Lancet Respir Med. 2016;4(9):708–19.
[2] Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med. 1975;292(7):344–7.
[3] Sontheimer RD. Would a new name hasten the acceptance of amyopathic dermatomyositis (dermatomyositis siné myositis) as a distinctive subset within the idiopathic inflammatory dermatomyopathies spectrum of clinical illness? J Am Acad Dermatol. 2002;46(4):626–36.
[4] American Thoracic Society. Idiopathic pulmonary fibrosis: diagnosis and treatment. International consensus statement. American Thoracic Society (ATS), and the European Respiratory Society (ERS). Am J Respir Crit Care Med. 2000;161(2 Pt 1):646–64.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6327

AB0612 EFFICACY OF LOW DOSE AND SHORT-TERM IL-2 TREATMENT TO EXPAND ENDOGENOUS REGULATORY T CELLS IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE

B. Zhang[1], L.L. Shang[1], J.P. Cao[2], H.Y. Gao[2], C. Gao[3], X.F. Li[2]. *[1]The Second Hospital of Shanxi Medical University, Taiyuan, China; [2]Rheumatology, The Second Hospital of Shanxi Medical University, Taiyuan, China; [3]Brigham and Women's Hospital/Children's Hospital Boston, Harvard Medical School, Boston, American Samoa*

Background: The concept of Mixed Connective Tissue Disease (MCTD) was first proposed by Sharp and his colleagues in 1972.[1] MCTD has overlapping features between at least two autoimmune diseases, such as SLE, SSc, PM/DM and RA. Regulatory T cells (Treg cells) play a critical role in the maintenance of immune tolerance and the regulation of immune responses. Treg cell dysfunction contributes to the initiation of pathogenesis and the maintenance of high disease activity in RA and SLE.[2] Recently, some studies have indicated that the proportion of Treg cells was different from healthy controls in SSc patients.[3] Therefore, MCTD may be associated with Treg cells.
Objectives: To explore the status of CD4+T cells in peripheral blood of patients with MCTD; to explore the effect of low dose interleukin -2 (IL-2) treatment on the balance of Treg cells and Th17 cells in patients with MCTD, and to observe the short-term curative effect.
Methods: CD4+T cells in the peripheral blood of 58 MCTD patients and 33 healthy controls were analyzed by flow cytometry. All of 58 cases were treated with standard therapy, including corticosteroids, NSAIDs, immunosuppressants, or combination therapy. Among them, 26 cases of MCTD without using immunosuppressant (CYC, MTX, LEF, MMF), were as untreated group, another 32 cases were as treated group. Then we compared the difference of CD4+T cells between two groups. In 58 patients with MCTD, a total of 27 patients were treated with low-dose IL-2 (50WIU) on the basis of standard treatment for 5 days. The difference of CD4+T cells before and after treatment with IL-2 was compared.
Results: The absolute count of CD4+CD25+FOXP3+Treg cells in peripheral blood of patients with MCTD was significantly lower than those in healthy controls. There was no significant difference in the absolute count of CD4+CD25+FOXP3+Treg cells in the peripheral blood between the treated group and the untreated group. The absolute count of CD4+CD25+FOXP3+Treg cells was significantly higher than those before treatment with IL-2.

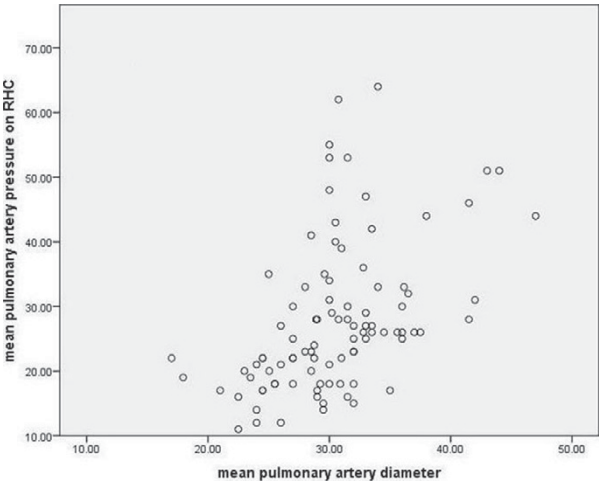


Conclusions: The absolute count of CD4+CD25+FOXP3+Treg cells in peripheral blood of patients with MCTD were significantly reduced, which may be the mechanism of immune imbalance in MCTD patients. The decrease of the absolute count of CD4+CD25+FOXP3+Treg cells in peripheral blood of patients with MCTD was not associated with the use of immunosuppressive agents. Low dose and short-term IL-2 treatment may increase the absolute count of CD4+CD25+FOXP3+Treg cells in the peripheral blood in patients with MCTD, so as to restore the immune balance in patients with MCTD.
References:
[1] Sharp GC, Irvin WS, Tan EM, et al. Mixed connective tissue disease – an apparently distinct rheumatic disease syndrome associated with a specifi c antibody to an extractable nuclear antigen (ENA). Am J Med 1972; 52: 148–159.
[2] Vila J, Isaacs JD, Anderson AE. Regulatory T cells and autoimmunity. Curr Opin Hematol, 2009, 16(4):274–279.
[3] Cordiali-Fei P, Mussi A, D'Agosto G, et al. Assessment of T regulatory cells and expanded profiling of autoantibodies may offer novel biomarkers for the clinical management of systemic sclerosis and undifferentiated connective tissue disease. Clin Dev Immunol, 2013, 2013:390563.
Acknowledgements: Thanks to my supervisor, my colleagues and superiors.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4017

AB0613 PULMONARY ARTERY DIAMETER AND PULMONARY HYPERTENSION IN SYSTEMIC SCLEROSIS

B.E. Schreiber[1], C.P. Denton[2], G. Robinson[3], A.U. Wells[4], G. Keir[4], N. Sverzelatti[5], J. Suntharalingam[3], G. Coghlan[1]. *[1]Royal Free Hampstead NHS Trust; [2]University College London, London; [3]Royal United Hospital, Bath; [4]Royal Brompton Hospital, London, United Kingdom; [5]Parma University Hospital, Parma, Italy*

Background: Systemic sclerosis may be complicated by pulmonary hypertension. CT-determined pulmonary artery diameter has been shown to correlate with presence of pulmonary hypertension in idiopathic patients and in interstitial lung disease but not in scleroderma.
Objectives: To determine the utility of CT-determined main pulmonary artery diameter (MPAD) for predicting pulmonary hypertension (PH) in 97 patients with systemic sclerosis who had CT chest within six months of right heart catheterisation.
Methods: Retrospective review of right heart catheter and CT data done within six months in 97 patients. The CT scans were blindly scored by two radiologists.
Results: 97 patients (75 female, 22 male) with systemic sclerosis who underwent CT scan and right heart catheterization were analysed. About 2/3 had the limited subtype (64 limited, 24 diffuse, 6 undefined).
Pulmonary hypertension was present in 55 patients (57%) and interstitial lung disease affecting 20% of the lung or more was present in 42 patients (43%).
Survival was worse in those with pulmonary hypertension. Median survival was 9.3 years in those without pulmonary hypertension (8.1–10.5) and 4.4 years in those with pulmonary hypertension (2.6–6.2). Presence of interstitial lung disease and pulmonary hypertension were independent predictors of survival.
An ROC curve shows area under the curve of 0.864. MPAD threshold of 25 mm or greater has a sensitivity of 98% and a specificity of 33% for the presence of pulmonary hypertension; 30 mm has a sensitivity of 73% and a specificity of 81% for the presence of pulmonary hypertension; 32 mm has a sensitivity of 56% and a specificity of 88% for the presence of pulmonary hypertension and 34 mm has a sensitivity of 35% and a specificity of 98% for the presence of pulmonary hypertension.
Survival was worse in those with a MPAD of 30mm or greater, with median survival of 5.5 years (3.8–7.2) compared to survival of 9.3 years (7.9–10.7) in those with MPAD smaller than 30mm. It was not a significant predictor of survival after adjustment for presence of pulmonary hypertension and interstitial lung disease.



Conclusions: The CT determined MPAD correlates strongly with the presence of pulmonary hypertension in patients with systemic sclerosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1872

AB0614 ANTISYNTHETASE SYNDROME: AUTOANTIBODIES, CLINICAL PATTERN AND MANAGEMENT OF 17 SPANISH PATIENTS

C. Busca, Á. Robles, I. Vives, J.A. Troncoso, L. Bailón, J.J. Ríos, A. Noblejas, F. Arnalich. *Internal Medicine, la Paz Hospital, Madrid, Spain*

Background: Antisynthethase syndrome (ASS) is a heterogeneous rare inflammatory condition characterized by myopathy, intersticial lung disease (ILD), arthritis, mechanic hands and Raynaud phenomenon (RP). The hallmark of ASS is the presence of antibodies against aminoacyl-transfer RNA synthetases (anti-ARS). Eight different anti-ARS have been described: anti-Jo1, anti-PL7, anti-PL12, anti-EJ, anti-OJ, anti-KS, anti-Zo, anti-Tyr/YRS. Despite recent publications, correlation between autoantibodies clinical pattern and management in ASS is not entirely well-known.
Objectives: The aim of this study was to define clinical features, autoantibodies and outcomes of a series of ASS patients.
Methods: We retrospectively analyzed the epidemiology, clinical data, lung function parameters, muscle enzymes, electromyogram (EMG) and autoantibodies pattern and its relationship with clinical manifestations, treatment management and outcomes of 17 patients recruited between 2005 and 2016 from the Autoimmune Diseases Division of a Spanish hospital.
Results: A total of 17 patients were reviewed (15 female). Mean age at diagnosis was 55 years. Median time delay to diagnosis was 5 months. Median follow-up was 65 months. Main clinical symptoms were dyspnea (76.5%), polyartrhitis (58.6%), muscle weakness and myalgias (52.9%), RP (41.1%) and mechanic

hands (23.5%). Lung involvement was defined by HRCT compatible with ILD (64.7%) and abnormal functional exploration (47.1%): restrictive pattern (87.5%) and diminished DLCO (61%). Muscle involvement was defined by elevated CK (52.9%) with a median maximum value of 517 IU/L, myopathic pattern on 8 of 13 performed EMG (61.1%) with myositis found in 4 of them (50%), and inflammatory myositis in 5 of 8 performed biopsies (62.5%). Anti-ARS findings were anti-Jo1 (11), PL12 (2), PL7 (1), anti-EJ (2) and one patient with both PL7 and PL12. Anti-Jo1 predominant clinical pattern was ILD (72.7%), followed by myopathy (63.6%) and concomitant myopathy and ILD (45.5%). Anti-PL12 was associated with ILD, RP, and esophageal involvement and no myopathy. Anti-PL7 patient showed mild myopathy and cutaneous association alone. A combination of anti-PL12 and PL7 was described in one patient who developed ILD with severe myopathy. Anti-EJ patients had pulmonary involvement but no evidence of muscle disease. There was no evidence of cancer in any of our patients. Corticosteroids therapy was administered in most of them (88.2%), and corticodependence was highlighted, being necessary at times to associate one or more immunosuppressants.

Conclusions: Regardless of ASS being a rare disease, 17 patients were collected. Anti-Jo1 was the most described antibody. It is important to note that one patient was found to be positive for both anti-PL7 and PL12 meanwhile they were described as exclusive, showing overlap of clinical pattern with severe muscle injury. This finding suggests that positive results for more than one ASS antibody infer more severity. In contrast with previous literature, pulmonary was more frequent than muscle involvement. The coexistence of both was observed in a small group (35.3%), mostly in anti-Jo1 patients (45.5%). Therefore, we suggest the need to request ASS antibodies in patients with pulmonary or/and muscle involvement at onset although classic clinical pattern is missing.

References:

[1] Mirrakhimov AE. Curr Med Chem. 2015;22 (16):1963–75.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5218

AB0615 PERSISTENCE OF HUMAN PAPILLOMAVIRUS IN THE CERVIX OF WOMEN WITH SYSTEMIC SCLEROSIS

C. Vacchi, M. Colaci, G. Cassone, C. Esposito, F. Lumetti, D. Giuggioli, C. Ferri.
Rheumatology Unit, University of Modena and Reggio Emilia, Modena, Italy

Background: Persistent infection by high-risk oncogenic Human Papillomavirus (HPV) is the main cause of the development of dysplastic or malignant lesions of the cervix. Furthermore, a few life habits, such as smoking, sexual habits and hormonal contraception, are known risk factors for cervical HPV infection. In addition, increased frequency of persistent HPV infection or high-grade intra-epithelial lesions rates was anecdotally described in patients affected by immune-mediated diseases, such as systemic lupus erythematosus, rheumatoid arthritis and systemic sclerosis (SSc), in comparison with the general population.

Objectives: To determine the prevalence of persistent HPV infection in an SSc patients series and its possible correlation with the disease clinical features.

Methods: The study retrospectively evaluated 52 consecutive female SSc patients (age 56.7±11.2SD years, disease duration 12.1±7.4SD years), classified according to the ACR/EULAR 2013 criteria, referring to our university-based Rheumatology Unit. Detection of HPV DNA and viral genotyping in cervical swabs were carried out. Moreover, abnormal Papanicolau test smears were classified using the Bethesda system.

Results: Fourteen(26.9%) patients presented a cervical swab positive for HPV infection,including12 infected by high risk or probable-high risk HPV types. Six (11.5%) patients presented multiple infection ($\geq$2 HPV types), including one case with high-grade intra-epithelial lesion.

Only tabagism was significantly correlated to HPV infection; namely,smoking habit was observed in 41.6% of SSc patients with and in 21.7% of those without HPV infection, respectively; p=0.006); moreoverimmunesuppressive therapies, namely mofetil mycophenolate, cyclophosphamide or rituximab, tended to be associated withHPV infection (presence/absence 21.4 vs 21.7%; p=0.055).

More interestingly, amongSSc patients over 50, HPV infection was found in 9/38 (23.7%) individuals, a frequency markedly higher than that expected in age-matched general population from the same geographical area (5%).

Conclusions: Persistent HPV infection was observed in over a quarter of SSc patients, notably in women over 50. The HPV positivity was not related to SSc clinical features, while a significant association with tabagism and immunesuppressive therapies was evidenced. Considering the possible clinico-prognostic implication on the overall disease outcome, routinely gynaecological screening of SSc female patients ishighly recommendable.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5356

AB0616 COST ANALYSIS RELATED TO SUBCUTANEOUS IMMUNOGLOBULINS IN PATIENTS WITH INFLAMMATORY MYOPATHIES AND IMMUNE-MEDIATED CHRONIC NEUROPATHIES. RESULTS OF AN OPEN LABEL STUDY

C. Vacchi, M. Sebastiani, A. Manfredi, G. Cassone, F. Campomori, C. Ferri.
Rheumatology Unit, Universita di Modena e Reggio Emilia, Modena, Italy

Background: Intravenous Immunoglobulins (IVIg) represent a relevant treatment option in various immune-mediated disorders such as idiopathic inflammatory muscle diseases (IIMD), immune-mediated chronic neuropathies (IMCN), hematologic autoimmune diseases, Still disease, Felty syndrome, systemic lupus erythematosus, vasculitis, some organ-specific autoimmune disease, and atopic diseases. The IVIg treatment is expensive and need of hospital-based assistance for administration; the recent avaibility of home-therapy with subcutaneous immunoglobulins (SCIg) may significantly reduce costs and improve the patient's quality of life.

Objectives: The primary objective was to perform an analysis of costs of SCIg administration in patients affected by IIMD or IMCN compared to that of previous IVIg treatments.

Methods: We prospectively evaluated 6 consecutive patients (3 males and 3 females, mean age 65,3 years, range 63 - 77), 2 affected by IIMD in the context of polymiositis and 4 by IMCN, 3 in the context of vasculitis and 1 in the context of undifferentiated connective tissue disease. All patients were previously treated with IVIg at the dosage of 2g/Kg monthly, (mean monthly dosage 143 g, range 98 – 160, average patient weight 71,5 kg, range 49 - 80), with good clinical and humoral response. After a mean therapy duration of 49.8 months (range 12 – 125) all patients were shifted to SCIg at the dosage of 10 g twice a week (80 g monthly). Each patient was followed-up by humoral and clinical evaluation, including Medical Research Council (MRC) score to quantify muscle strength and INCAT Sensory Score to evaluate sensory symptoms. The costs of the two therapeutic strategies were also compared, excluding indirect costs (absences from work and productivity losses, transport and parking, health care sector costs).

Results: In 5/6 patients, we observed the maintenance of clinical and humoral status after a mean follow-up of 21 months (range 4 - 51), in particular we observed a stability in MRC score in patients presenting loss of strenght and INCAT score in patients presenting sensory symptoms. Furthermore, the treatment with SCIg was well-accepted and preferred to IVIg by all patients. In one patient SCIg were discontinued after 2 weeks, because of the appearance of a haemorrhagic lesions nearby the injection site (in the same patient IVIg have been stopped because of a hypertensive crisis during the infusion). Direct cost associated to IVIg amount to 252€ for 5 g of immunoglobulins (7,056€ monthly, considering a protocol of 2 g/kg/monthly and a patient-weight of 70kg), while direct costs associated to SCIg (20g weekly) amount to 6,400€/monthly, with a saving of 656€/monthly and 7,872€/yearly. In our case-series the annual saving was 9,686.40€/patient (from 86,486.40€ to 76,800€, for IVIg and SCIg, respectively).

Conclusions: Our experience suggests that the shift to SCIg from IVIg in patients affected by IIMD and IMCN is feasible, cost-effective, safe and well-accepted by patients. Further studies are needed to evaluate the effectiveness of SCIg in first-line therapy of these diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4336

AB0617 CLINICAL CHARACTERISTICS OF DIABETES MELLITUS PATIENTS WITH AND WITHOUT SCLEREDEMA BUSCHKE SKIN DISORDER

C. Varjú [1], D. Kovács [1], B. Gábris [1], E. Kálmán [2], L. Czirják [1], B. Bódis [3], V. Csonka [1]. *[1]Department of Rheumatology and Immunology; [2]Department of Pathology; [3]1st Department of Internal Medicine, University of Pécs, Pécs, Hungary*

Background: Scleredema adultorum of Buschke is a rare disorder characterized by non-pitting hardening of the skin around the neck, shoulders, occasionally the face and the trunk. The most frequent form of scleredema is associated with diabetes mellitus (DM). The histopathologic features of scleredema are characterized by thickened collagen bundles within the reticular dermis that are separated by mucopolysaccharides (mainly mucin) containing fenestrations.

Objectives: To compare clinical data of patients with Buschke-scleredema-DM to diabetic patients without skin involvement patients (Control-DM) with a focus on the late vascular and neurological complications.

Methods: Clinical data of 105 diabetic patients were investigated based on their medical histories and physical examinations. All subjects met the following inclusion criteria: each of their disease duration time of DM had to be more than three years. Twenty-eight patients with Scleredema-DM were collected (three of type 1 and 25 of type 2 diabetes, 19 female, nine male; their mean age (±SD) was 63.0±9.3 and mean DM-duration time was 17.9±9.6 years). Seventy-seven consecutive, age and DM-duration matched patients without skin involvement were investigated as controls (nine patients with type 1 and 68 with type 2 M, 50 female, 27 male, their mean age was 63.3±11.9 and mean DM-duration time was 17.4±10.7 years). For statistical analysis Pearson's Chi-squared, Fisher and Mann-Whitney U tests were used.

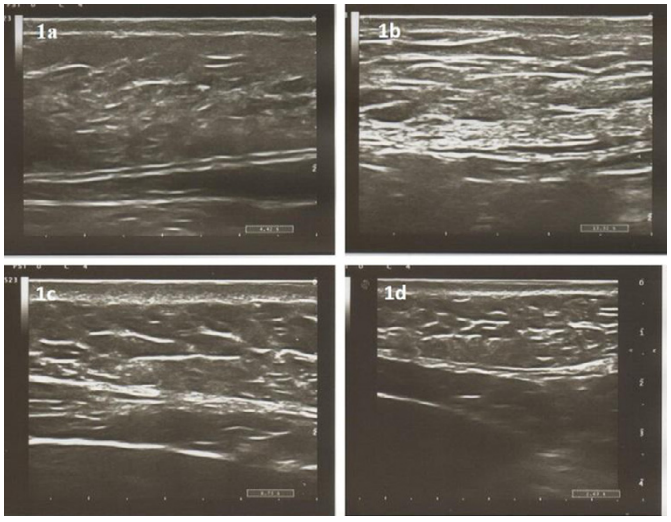
Results: In the medical history of the Scleredema-DM group stroke occurred more frequently (8 of 28 cases, 28.6%) compared to the Control-DM group (5/77, 6.5%, /$p<0.01$/). There were no significant differences in the occurrence of myocardial infarction (5/28, 17.9% vs. 10/77 cases, 13.0%), nephropathy (5/28, 17.9% vs. 10/77 cases, 13.0%), retinopathy (13/28 cases 46.4% vs. 28/77, 36.3%) and of peripheral neuropathy (21/28 patients, 75.0% vs. 49/77, 63.6%) respectively. Higher level of cholesterol and triglycerides was present in the Scleredema-DM group compared to the Control-DM cases (mean cholesterol was: 5.7±1.5 mmol/l vs. 4.6±1.2 mmol/l, /$p<0.01$/; triglyceride: 2.3±1.1 mmol/l vs. 1.84±1.6 mmol/l

/p<0.01/), though there were no significant differences in the mean actual level of hemoglobin A1c in the sera, or comparing the body mass index (BMI) between the two investigated groups.
Cholesterol levels were significantly higher in both Scleredema-DM patients group taking /p<0.01/ or not taking /p<0.05/ statins compared to similar control diabetic patient groups. Concerning the triglyceride, also a higher levels of triglyceride were found in Scleredema-DM patients who were taking statins /p<0.05/, compared Control-DM patients who were also taking statins, but no difference were shown in triglyceride levels between the Scleredema-DM group and the Control-DM group both who were not treated by statins.
Conclusions: Scleredema can be assessed by a simple skin-examination and might be a risk factor for stroke in patients with DM. Patients with scleredema are associated with increased cholesterol and triglyceride levels and a higher incidence of stroke compared to matched DM control population.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2553

AB0618 A UNIQUE ULTRASOUND PATTERN OF ADIPOSE TISSUE IN SYSTEMIC SCLEROSIS PATIENTS: A COMPARISON WITH RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY CONTROLS. TWO SIDES OF ADIPOSE TISSUE INVOLVEMENT IN SYSTEMIC CHRONIC INFLAMMATORY DISEASES

C. Rotondo[1], R. Fanizzi[1], A. Chialà[2], M.G. Anelli[1], G. Righetti[1], M. Nivuori[1], E. Praino[1], L. Dinoia[1], S. Lopriore[1], G. Laselva[1], C. Scioscia[1], F. Cacciapaglia[1], G. Lapadula[1], F. Iannone[1]. [1]*Deto - Rheumatology Unit, Bari University, Bari;* [2]*Internal Medicine Unit, P.O. Valle d'Itria, Martina Franca (TA), Italy*

Background: Systemic sclerosis (SSc) and rheumatoid arthritis (RA) are both chronic and systemic inflammatory diseases, involving connective tissue. The adipose tissue is acknowledged as an immune organ that secretes numerous inflammatory signals and it is supposed playing an important role in up-regulation of inflammatory status. A few data are published on altered white adipose tissue (WFT) distribution in patients (pts) with RA. None data are available about WFT distribution in SSc pts
Objectives: We aimed to characterize the subcutaneous adipose tissue (total (sWFT); superficial (SsWFT); inner (IsWFT)) and visceral adipose tissue (vWTF) thickness, evaluated by ultrasound (US) of abdominal adipose tissue, in SSc pts, with different body mass index classes (BMI), comparing with RA pts and healthy controls (HC).
Methods: 42 SSc pts, 57 RA pts and 12 HC were recruited in this study. WFT measurements were assessed, using US (7.5 MHz probe), along the xiphoumbilican line: sWFT thickness (distance between the inner edge of the skin at the outer edge of the alba line (AL)), SsWFT (lobular upper zone of sWFT), IsWFT (sWFT- SsWFT); vWFT thickness (distance between the inner edge of the AL and the peritoneal line).
Results: No subject enrolled had metabolic syndrome. RA pts had thicker vWFT (15.6±7.6mm) than SSc pts (10.8±5.8mm) or HC (10.1±3.8mm) (p=0.001). In particular, the upper-weigh RA pts had vWFT 88% thicker than upper-weight HC and the RA obese pts had vWFT 87% thicker than obese HC. While, the upper-weight SSc pts had vWFT 22% thicker than upper-weight HC, and the SSc obese pts had vWFT 16% thicker than obese HC. Positive correlations were found between all WFT measures and BMI in RA pts and HC (p≤0,05). In SSc pts we found lack of correlation between SsWFT and BMI (r=0.232; p=0.145). Of note, only in SSc pts we observed different US WFT patterns (fig. 1a, fig. 1b) characterized by rearrangement of normal sWFT structure (HC fig. 1c and RA pts fig. 1d). These structural rearrangements consisted in the absence of adipose lobules, replaced by hypoechoic – anechoic areas (fig.1a) (attributable to edema), or by hyperechoic lines and spots (fig.1b) (attributable to fibrotic replacement of subcutaneous abdominal fat), independently by SSc diffuse or SSc limited skin subset.



Conclusions: In SSc and RA the WFT is abnormal. The WFT in RA seems be altered just for dimension and distribution, in particular the vWFT is overexpressed; it might be due to vWFT hyperactivity induced by inflammatory status. In SSc, the WFT is altered in the structure of sWFT. A direct involvement of sWFT in pathologic mechanism of SSc is supposed. An edema phase and a fibrotic phase of abdominal sWFT can be hypothesized, independently by skin involvement. If these findings will be confirmed by fat histological analysis, the US of WFT might be an important tool for the clinicians to identified the earlier stage and/or the active phase (edema) of SSc, in order to support physicians in the decision making about the treatment management.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5228

AB0619 CONNECTIVE TISSUE DISEASE-ASSOCIATED INTERSTITIAL LUNG DISEASE TREATED WITH CYCLOPHOSPHAMIDE OR RITUXIMAB: A UNICENTRE, OPEN-LABEL AND COMPARATIVE STUDY

C. LóPez-Medina[1], F.J. Godoy-Navarrete[2], P. Peinado-Villén[2], P. Font-Ugalde[1], M.C. Castro-Villegas[1], R. Ortega-Castro[1], J. Calvo-Gutiérrez[1], L. Ladehesa-Pineda[1], L. Bautista-Aguilar[1], A. Escudero-Contreras[1], E. Collantes-Estévez[1]. [1]*Rheumatology, Hospital Universitario Reina Sofía de Córdoba/ Imibic/ Universidad de Córdoba;* [2]*Universidad de Córdoba, Córdoba, Spain*

Background: To date, rheumatologists do not have curative treatments for connective tissue disease-associated interstitial lung disease (CTD-ILD) (1), therefore an stabilization of the disease is considered as a therapeutic success. One of the most frequent drugs used for achieving this goal is Cyclophosphamide (CYC); however, in the last years there has been an increasing interest in the use of Rituximab (RTX) as a treatment for CTD-ILD.
Objectives: To compare long-term effectiveness of CYC vs. RTX as a treatment in patients with CTD-ILD.
Methods: Unicentre and retrospective study in which it was analyzed clinical and image data of 26 CTD-ILD patients treated with CYC or RTX between June 2004 and December 2016.
Previously, we checked that baseline characteristics and baseline levels of Pulmonary Function Tests (PFTs) in both groups were similar by using Fisher and T-student tests.
The primary outcome of the study was the stabilization of PFTs or HRTC (High Resolution Tomography Computed Tomography) considering as relapse: a) a deterioration ≥10% in FVC (Forced Vital Capacity), or b) a decrement ≥15% in DLCO (diffusing capacity of carbon monoxide), or c) a worsening in HRCT. The prognostic effect of each treatment on stabilization was evaluated using the Kaplan-Meier method and Long Rank test.
Subsequently, values of FEV1 (forced expiratory volume in one second), FVC, DLCO and DLCO/VA were compared 12 months after the beginning of the treatment with their corresponding baseline levels in both groups, using paired T-test. Finally, direct comparison between the CYC and the RTX groups was performed at the 12-months time point using T-test.
Results: The study includes 20 women and 6 men with an average age of 58.9±14.2 years. 14 patients had a diagnosis of Systemic Sclerosis whereas 12 had other types of CTD.
From the 26 patients, 15 received CYC and 11 RTX, according to the physician's decision. Both groups presented similar baseline characteristics and levels in PFTs.
The Kaplan-Meier method showed that the treatment had an influence on the stabilization of CTD-ILD, although long Rank test was non-significative. The average of months without relapse in CYC and RTX group was 59.79±9.50 and 79.27±7.81 respectively.
Patients in the CYC group did not present any changes in FEV1, FVC, DLCO and DLCO/VA levels during the first year of treatment. In contrast, patients in RTX group showed an increase of all PFTs levels during the first year of monitoring, although these differences were non-significatives. A direct comparison between both treatment groups after 12 months showed lower levels of all PFTs in CYC vs RTX, been DLCO/VA (67.30±10.69 and 86.25±4.59, respectively) statistically significative.
Conclusions: This study suggests, in patients with ILD-CTD, that CYC treatment stabilizes the lung function, whereas RTX shows a tendency to improve it. Also, patients with RTX treatment shows a larger mean time of stabilization than CYC group. However, large scale randomized controlled trials are needed to confirm these results.
References:
[1] Fischer A, du Bois A. Interstitial lung disease in connective tissue disorders. Lancet 2012;380:689–98.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2072

AB0620 ORAL HEALTH IN PATIENTS WITH SYSTEMIC SCLEROSIS: AN EUSTAR CENTER EXPERIENCE

C. Ancuta[1,2], M. Antohe[2], E. Ancuta[3], R. Chirieac[4], C. Iordache[2].
[1]Rheumatology 2, Clinical Rehabilitation Hospital; [2]University of Medicine and Pharmacy Grigore T Popa Iasi; [3]Research Department, Elena Doamna Clinical Hospital; [4]Sanocare Medical and Research Center, IASI, Romania

Background: Although the orofacial manifestations are commonly reported among patients with systemic sclerosis (SSc), only few studies have adequately addressed the issue of oral health-related quality of life (QoL) in such pathobiological settings.
Objectives: The aim was to characterize the oral health status (OHS) of adults with SSc and to compare with the general population.
Methods: A cross-sectional prospective observational study in 37 consecutive SSc in a EUSTAR cohort (EUSTAR 162 center) and 37 gender and age-matched controls without SSc.
A standardized oral exam meaning OHS (periodontal, dental, mucosal and microbial), oral health-related behaviors and oral HRQoL (Oral Health Impact Profile, OHIP) were evaluated in all recruited individuals, while oral manifestations such as size of oral aperture, oral dryness, manual dexterity for oral hygiene and HRQoL only in SSc.
Multivariable regression analysis was done to evaluate association between SSc, oral abnormalities, oral health status and QoL.
Results: Overall, SSc had significantly reduced oral HRQoL compared with controls ($p<0.05$).
We demonstrated lower resting salivary flow rates ($p<0.05$) and pH ($p<0.05$), reduced maximal mouth opening ($p<0.05$), smaller interincisal distance ($p<0.05$) in SSc group as compared to their controls. Moreover, despite comparable oral health-related behaviors (e.g. same level of daily tooth-brushing), the majority of SSc experienced caries ($p<0.05$) and presented with more periodontal disease ($p<0.05$) comprising periodontal pockets (pocket depth PD>3 mm) ($p<0.05$), clinical attachment level (CAL) $\geq$5.5 mm ($p<0.05$).
Finally, SSc was documented as a significant independent predictor of OHIP, missing teeth, periodontal disease, interincisal distances as shown by multivariate regression ($p<0.05$).
Conclusions: SSc patients are at risk to develop impaired oral health and oral HRQoL compared with the general population.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4115

AB0621 DEVELOPMENT OF SYSTEMIC SCLEROSIS IN TRANSGENDERED FEMALES: A CASE SERIES

C. Campochiaro, C. Fonseca, E. Derrett-Smith, V.H. Ong, C.P. Denton. *Centre for Rheumatology and Connective Tissue Diseases, Royal Free Hospital and UCL Division of Medicine, London, United Kingdom*

Background: Scleroderma (SSc) is an autoimmune connective tissue disease with a female preponderance (female to male ratio of 9.7:1) [1]. Sex hormones are thought to play a role in the susceptibility to autoimmune diseases [2].
Objectives: We report 3 cases of SSc in male-to-female transsexuals diagnosed following their male-to-female transition
Methods: Medical records of 3 patients diagnosed with SSc after male-to-female transition were reviewed. Disease features, hormonal therapies and surgical interventions related to gender reassignment were collected.
Results: At our tertiary University Hospital clinical service, 3 male-to-female transsexual patients were diagnosed with SSc following their surgery between May 1997 and October 2016. All 3 patients had started their transition before the onset of the disease and had not been diagnosed with any autoimmune disease before either starting the hormonal therapy required for the transition or before undergoing plastic surgery interventions. The first case was diagnosed with anti-RNA pol III +ve diffuse cutaneous SSc at the age of 35 yearsa year after the first surgical intervention for infected silicone buttock implants and approximately 5 years of hormonal therapy with combination of mestranol and norethisterone (Norinyl-1®). She experienced scleroderma renal crisis 2 years after the diagnosis and severe vascular involvement with frequent and severe digital ulcers (DU), Raynaud's phenomenon (RP), gastroesophageal reflux disease (GERD), pulmonary arterial hypertension and telangiectasiae. She required chronic dialysis and was treated with mycophenolate mofetil (MMF), rapamycin, bosentan and proton-pump inhibitors (PPI). She eventually died 8 years after the diagnosis. The second case was diagnosed at the of 49 years, approximately 6 months following her gender reassignmentand 5 years after having started hormonal therapy initially with conjugated estrogen isolated from pregnant mares (Premarin®) and later with ethinylestradiol and gestodene (Femodene®). She developed ANA –ve, antiCCP antibody and rheumatoid factor positive limited cutaneous SSc/rheumatoid arthritis overlap syndrome and experienced severe DUs, RP, GERD, inflammatory arthritis and pulmonary fibrosis (PF). She was treated with MMF, PPI, calcium-channel blocker (CCB) and low-dose steroid therapy with good response. The third case was diagnosed at the age of 43 years, 2 years after having started triptorelin (Decapeptyl®) and oestradiol valerate. She had not undergone any surgical intervention prior to her diagnosis. She developed anti-PM/Scl +ve limited cutaneous SSc/myositis overlap syndrome and experienced RP, GERD and PF. She has only been treated with PPI and CCB prior to her reconstructive surgery.
Conclusions: Although still debated, the role of sex hormones in triggering autoimmunity has been suggested in animal models and human studies [2]. The development of SSc in our case series supports the notion that altered profile of sex hormones may modulate autoimmunity in genetically susceptible individuals with distinct clinical and laboratory characteristics.
References:
[1] Barnes J et al. Epidemiology of systemic sclerosis: incidence, prevalence, survival, risk factors, malignancy, and environmental triggers. Curr Opin Rheumatol 2012.
[2] Pennell LM et al. Sex affects immunity. J autoimmun 2012.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2912

AB0622 RENAL RESISTIVE INDEX (RRI): PROPOSAL FOR AGE-ADJUSTED CUT-OFF VALUES IN SYSTEMIC SCLEROSIS PATIENTS

C. Bruni[1], V. Maestripieri[2], G. Tesei[1], M. Chiostri[3], C. Sambalino[3], S. Guiducci[1], S. Bellando-Randone[1], M. Boddi[3], M. Matucci-Cerinic[1].
[1]Department of Experimental and Clinical Medicine, Division of Rheumatology; [2]Department of Internal Medicine, Division of Medicine for Care Complexity III, University of Florence; [3]Department of Heart and Vessels, Division of Cardiology I, Azienda Ospedaliera Universitaria Careggi, Firenze, Italy

Background: Renal resistive index (RRI) by Doppler ultrasound, reflects changes in both renal vascular and tubular-interstitial compartments and systemic vascular compliance related to physiological (age) and pathological conditions among which hypertension, diabetes mellitus, hyperuricaemia, dyslipidaemia and chronic kidney disease play a major role [1]. Because of the age-related changes in RRI reported in literature [2,3] the use of a 0.70 cut-off to detect renal damage, as proposed [4], was questioned: renal injury in younger decades (<60yrs) may occur also for RRI value <0.70 and be underestimated. In systemic sclerosis (SSc), RRI was previously correlated with disease duration, glomerular filtration rate and nailfold-videocapillaroscopy pattern [5–7], although tested on small samples and not investigating the possible confounding role of age-related RRI values.
Objectives: to describe RRI in a larger scleroderma population and to test both the fixed 0.70 RRI cut-off and age-adjusted cut-offs in reflecting renal and other disease-related organ damage.
Methods: SSc patients attending classified according to ACR/EULAR 2013 criteria were enrolled. Data on renal arteries Doppler ultrasound (RRI), autoantibodies status and biochemical tests for renal function/damage, subset and extent of skin fibrosis, instrumental assessment for internal organ involvement were collected and analysed as appropriate with SPSS vers 20.0. Considering that age-adjusted mean values were higher in the SSc population compared to literature values for the general population, we created SSc-specific age-adjusted pathologic cut-offs dividing our SSc population in quartiles and considering RRI values above the 75th percentile as pathologic (Table 1).
Results: 190 SSc patients (age 56.3±15.0 years, disease duration 6±8,20 men) were eligible for the study. In the SSc population significant positive correlations between RRI and age, as well as significant associations between RRI and above mentioned general population comorbidities [1], were confirmed. When considering absolute value of RRI, the 0.70 pathologic cut-off and age-adjusted cut-offs validated in the general population [1], only renal function, systolic PAP, DLCO and late nailfold scleroderma pattern were associated with RRI (Figure 1). Pathologic RRI identified according to age cut-offs could not detect early renal damage, but was significantly associated with various fibrotic [interstitial lung disease (p=0.015), tendon friction rubs (p=0.032), skin fibrosis vs no skin involvement ($p<0.001$),

Age	Proposed SSc age-adjusted pathologic cutoff
1st quartile, ≤48 years	≥0,68
2nd quartile, 49–58 years	≥0,69
3rd quartile, 59–67 years	≥0,75
4th quartile, ≥68 years	≥0,77

		RRI basal value			RRI general population cutoff 0,70			proposed SSc age-adjusted pathologic cutoffs		
Variables	value				RRI≥0,70 (85pts)	RRI<0,70 (105 pts)		yes (61pts)	no (129 pts)	
Creatinine Clearance	86,63±31.34		p=-0,352	p<0.001	77,85±28.33	94.16±3.87	P<0.001			N.S.
Proteinuria/24h	84.46±65.66			N.S.			N.S.			N.S.
classification (Very early SSc vs Early SSc+SSc)	41 vs 159 (21,7 vs 78,3%)	0,67±0,06	0,69±0,07	p=0,051	13 (15%)	28 (26%)	p=0,052	6 (9,8%)	35 (27%)	p=0,007
classification (SSc vs Very early SSc+ Early SSc)	125 vs 65 (65,6% vs 34,4%)	0,70±0,07	0,66±0,06	p=0,002	61 (72%)	64 (61%)	p=0,014	51 (83.6%)	74 (57,4%)	p<0,001
dcSSc+lcSSc	134 (70,5%)	0,70±0,07	0,67±0,06	p=0,019			N.S.	55 (41)	79 (59)	p<0,001
mRSS	2 (0-35)			N.S.			N.S.	7,70±8,68	3,59±6,66	p=0,001
sPAP	27,93±10,7		ρ=0,336	p<0,001	31,08±13,00	25,55±6,05	p=0,001			N.S.
ILD	72 (37,9%)			N.S.			N.S.	31 (50,8%)	39 (30,2)	p=0,015
FVC	104±22,1			N.S.			N.S.	99,09±22,14	106,12±21,76	p=0,0141
DLCO	72,2±20,5		ρ=-0,207	p=0,005	68,66±21,14	75,23±19,79	p=0,032	67,07±22,57	74,72±18,44	p=0,020
DLCO/VA	81,8±20,0			N.S.			N.S.			N.S.
DU	65 (34,2%)			N.S.			N.S.	30 (49,2%)	35 (28,2%)	p=0,006
Late Scleroderma Pattern on NVC	41 (21,5%)	0,71±0,06	0,68±0,07	p=0,004	24 (28%)	17 (16%)	p=0,024	21 (34,4)	20 (15,5)	p=0,002
Tendon friction rubs	9 (4,7%)			N.S.			N.S.	6 (9,8)	3 (2,3)	p=0,032
Scl70	59 (31,1%)			N.S.			N.S.	25 (40,9)	34 (26,3)	p=0,044
RNApolIII	3 (1,6%)			N.S.			N.S.	3 (4,9%)	0 (0%)	p=0,033

higher mRSS (p=0.001)] and vasculopathic manifestations [late scleroderma pattern (p=0.002) and digital ulcers (p=0.006)] of the disease (Figure 1).
Conclusions: in clinical practice, different age-related or non-related RRI cut-offs must be used when looking for renal or extrarenal SSc-induced damages.
References:
[1] Boddi, Intern Emerg Med 2015;2)Boddi, Am J Hypertens 1996;3)Ponte, Hypertension 2014;4)Platt, Am J Roentgenol 1989;5)Rivolta,Arthritis Rheum 1996;6)Rosato, Seminar ARthritis Rheum 2012;7)Rosato, Arthritis Care Res 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6420

AB0623 PROGNOSTIC VALUE OF RENAL RESISTIVE INDEX (RRI) IN SYSTEMIC SCLEROSIS: PRELIMINARY DATA FROM A SINGLE CENTRE

C. Bruni[1], V. Maestripieri[2], G. Tesei[1], M. Chiostri[3], C. Sambalino[3], S. Guiducci[1], S. Bellando-Randone[1], M. Boddi[3], M. Matucci-Cerinic[1].
[1]Department of Experimental and Clinical Medicine, Division of Rheumatology; [2]Department of Internal Medicine, Division of Medicine for Care Complexity III, University of Florence; [3]Department of Heart and Vessels, Division of Cardiology I, Azienda Ospedaliera Universitaria Careggi, Firenze, Italy

Background: Renal Resistive Index (RRI- measured with Renal arteries Doppler ultrasound) is a useful technique to evaluate vascular and tubular-interstitial damage in both general and systemic sclerosis (SSc) population, where increased RRI values correlates with longer disease duration [1], lower glomerular filtration rate and more advanced nailfold-videocapillaroscopy pattern [2]. Moreover, higher RRI values were seen in SSc patients with new occurrence of digital ulcers [3].
Objectives: to test the prognostic value of RRI [absolute, ≥0.70 and SSc age-adjusted pathologic value (Table1)] and RRI delta change in predicting general and organ-specific worsening in scleroderma patients.
Methods: SSc patients classified according to ACR/EULAR 2013 criteria were enrolled. Demographics data and renal ultrasound data were collected. Data on clinical worsening had been collected as herewith specified: a) Skin worsening as an increase of mRSS≥5 units, b) Peripheral vascular worsening as the appearance of new digital ulcers or the worsening of nailfold videocapillaroscopy scleroderma pattern, c) Lung worsening as decline of FVC≥15% or FVC<80% with new detection of ILD on chest HRCT or worsening of HRCT-ILD extent, d) Cardiac worsening as new onset of left ventricular failure requiring treatments or new onset of PAH confirmed on RHC or detection of severe ventricular arrhythmias on 24h EKG, e) Renal worsening as a new scleroderma renal crisis or reduction of creatinine clearance ≤30 ml/min. General worsening was recorded in case of death due to SSc or for any of the above organ-specific worsening. Data were analysed as appropriate with SPSS vers. 20.0.
Results: 190 SSc patients (age 56.3±15.0 yrs, 170 women, disease duration 6±8yrs, 65 with a follow up RRI measurement after 2.8±0.9 years) were enrolled. After a mean clinical follow-up of 3.6±2.6 years, 89 (46.8%) pts showed general worsening. Skin, peripheral vascular, cardiac, lung and renal worsening were detected in 14 (7.4%), 40 (21%), 32 (16.8%), 38 (20%) and 11 (5.8%) patients respectively. We registered 10 (5.2%) deaths and 43 (22.6%) patients with multiple organ worsening. Both absolute value of RRI and ≥0.70 RRI cut-off showed no significant association with organ or global clinical worsening, At the opposite, RRI cut-offs adjusted for age were associated with cardiac worsening (p=0.065 =- Figure 1). When in 65 patients the pattern of delta RRI and clinical worsening were analysed (Table 1), wider RRI changes were associated with general worsening (p=0.029) and cardiac worsening (p=0.006). The significance of these associations increased when sub-analyse was repeated focused on patients with normal SSc age-adjusted RRI values at baseline evaluation (p=0.017 and p<0.001 respectively, Figure 1).

Age	Proposed SSc age-adjusted pathologic cutoff
1st quartile, ≤48 years	≥0,68
2nd quartile, 49–58 years	≥0,69
3rd quartile, 59–67 years	≥0,75
4th quartile, ≥68 years	≥0,77

	RRI basal value (190 pts)		RRI>0,70 (85 pts)		SSc age-adjusted pathologic (61 pts)		ΔRRI (available 65 pts)		ΔRRI in baseline SSc age-adjusted normal RRI (45 patients)	
	n (%)	p value	n (%)	p value	n (%)	p value	(n) mean±SD	p value	(n) mean±SD	p value
General Worsening	89 (46,8)	N.S.	37 (43,5)	N.S.	31 (50,8)	N.S.	(33)+0,03±0,05 vs (42) 0,00±0,04	0,029	(24)+0,04±0,04 vs (21) +0,01±0,03	0,017
Cardiac Worsening	32 (16,8)	N.S.	16 (18,8)	N.S.	15 (24,5)	p<0,001	(13)+0,05±0,05 vs (52) +0,01±0,04	p=0,006	(7)+0,08±0,03 vs (38) +0,02±0,04	p<0,001

Conclusions: increase in RRI could be used as a sentinel sign for general and cardiac worsening in SSc patients, especially when age-related RRI variations are taken into account.
References:
[1] Rivolta R, Arthritis Rheum. 1996.
[2] Rosato E, Semin Arthritis Rheum. 2012.
[3] Rosato E, Arthritis Care Res (Hoboken). 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6533

AB0624 INTERSTICTIAL LUNG DISEASE IN SCLERODERMA: SEVERITY ASSOCIATED FACTORS. OBJETIVES

D. Sanchez Cano[1], N. Ortego Centeno[2], M.T. Cruces Moreno[1], L. Sáez Comet[3], M. Freire[4], J.A. Todlí Parra[5], M. Rodríguez Caballeira[6], C. Simeón Aznar[7] on behalf of RESCLE. *[1]Internal Medicine; [2]Sistemic Autoimmune Diseases Unit, Hospital Campus de la Salud, GRANADA; [3]Internal Medicine, Hospital Universitario Miguel Servet, Zaragoza; [4]Unidad Trombosis y Vasculitis, Hospital Xeral de Vigo, VIGO; [5]Internal Medicine, Hospital Universitario la Fe, Valencia; [6]Internal Medicine, Hospital Universitari Mútua de Terrassa, Terrassa; [7]Sistemic Autoimmune Diseases Unit, H. Universitari General de la Vall D'hebron., Barcelona, Spain*

Background: Systemic sclerosis (SSc) can virtually affect any organ system (such as lungs, kidneys, gastrointestinal tract, and heart). However, it is the pulmonary manifestations that account for the majority of deaths, especially interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH).
Objectives: Our aim was to assess the differences between severe and mild-to-moderate ILD in SSc.
Methods: A descriptive study was performed, using the available data from the Spanish Scleroderma Study Group (RESCLE). ILD was deemed as serious when forced vital capacity (FVC) was <50%. Patients were classified attending the modified classification criteria proposed by LeRoy and Megdsger.
Results: Fourteen referral centers for SSc participated in the registry. By April 2014, 1374 patients with SSc had been enrolled, 541 of whom (39.4%) had ILD, which was severe in 72 of them (13.2%). There were no significant differences as far as sex and age at onset is concerned. Patients with diffuse SSc presented with severe ILD more frequently than those with limited SSc (57% vs. 35%, p=0.002), as well as those who had tested positive for ATA (51% vs. 33%, p=0.005). Additionally, prevalence of FVC<50% was higher in patients with myopathy (32% vs. 15%, p=0.002). Mean FVC was 40.2±6.4 in the severe ILD group, whilst it was 80.3±18.9 in the mild-to-moderate one (p<0.001), and mean DLco was 36.7±15.2 and 62.9±34.5, respectively (p<0.001). Likewise, DLco<70% was also more frequent among patients with severe ILD (100% vs. 69%, p<0.001), as well as mean DLco/VA (56.2±24.2 vs. 74.2±42.0, p=0.002). PAPs was equally higher when FVC<50% (42.2±18.2 vs. 35.1±13.4, p=0.034), and so was the frequency of PAPs>40mmHg (66% vs. 29%, p<0.001) and PAH by right heart catheterism (19% vs. 11%, p=0.050). Finally, by means of a multiple logistic regression, both ATA positivity [OR 0.17 (0.05–0.58), p=0.005] and low DLco [0.93 (0.91–0.95), p=0.000] were found to be related with FVC<50%
Conclusions: Patients with ACA positivity and with a limited variant of SSc seem to be at lower risk of severe interstitial lung involvement. Furthermore, the presence of myopathy may contribute to explain the decrease of FVC in SSc patients.
References:
[1] Steen VD, Medsger TA. Changes in causes of death in systemic sclerosis, 1972–2002. Ann Rheum Dis 2007; 66: 940–4.
[2] LeRoy EC, Medsger TA, Jr. Criteria for the classification of early systemic sclerosis. J Rheumatol 2001; 28: 1573–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2545

AB0625 AUTOANTIBODY PROFILE IN PATIENTS DIAGNOSED WITH IDIOPATHIC INFLAMMATORY MYOPATHY: MULTICENTER REGISTRY ON INFLAMMATORY MYOSITIS FROM THE RHEUMATOLOGY SOCIETY IN MADRID, SPAIN

D.C. Hernández Flórez[1], L. Valor[1], J. Martinez[1], B. Joven[2], L. Nuno[3], C. Larena[4], I. Llorente[5], C. Barbadillo[6], P. Garcia de la Pena[7], L. Ruiz[8], H. Moruno[9], T. Cobo[10], R. Almodovar[11], L. Lojo[12], M. Garcia[13], F. Lopez-Longo[1]. *[1]H. Gregorio Maranon; [2]H.12 de Octubre; [3]H.La Paz; [4]H.Ramon y cajal; [5]H.La Princesa; [6]H.Puerta de Hierro; [7]H.Norte Sanchinarro; [8]H.Nino Jesus; [9]H.Principe de Asturias, Madrid; [10]H.Infanta Sofia, Asturias; [11]H.F.Alcorcon; [12]H.Infanta Leonor; [13]InMusc, Madrid, Spain*

Background: Inflammatory myopathies (IIM) are a heterogeneous group of autoimmune rheumatic diseases characterized by muscle inflammation and progressive weakness. They include any kind of primary inflammatory muscle disease that is not otherwise better explained by metabolic, toxic, infectious, neurologic or inherited causes. The presence of autoantibodies (AA) in IIM is variable and they can recognize nuclear and cytoplasmic cellular components.
Objectives: To evaluate the AA profile in patients diagnosed with IIM.
Methods: We evaluated 479 patients that included 12 hospitals belonging to the IIM registry of the Rheumatology Society in Madrid (SORCOM-REMICAM) with diagnosis from January 1980 to December 2014. All patients were diagnosed of IIM according to Bohan and Peter criteria. The AAs evaluated were ANA (n=476), anti-Jo1 (n=457), anti-RNP (n=427), anti-MI2 (n=159) and ACA (n=293), according to the standard techniques in the respective laboratories. The presence of ANA was considered valid with at least two positive determinations. The AAs were compared according to the classification I) as dermatomyositis (primary

and secondary dermatomiositis) (DM) and polymyositis (PM) including the rest of the patients. Also, IIM were classified (II) as primary polimiositis (PPM), primary dermatomyositis (PDM), overlap syndrome (OSd), juvenile myopathies (JM), cancer-associated myopathies (CAM), autoimmune necrotizing myopathy and inclusion body myositis (these were grouped as other myositis; OM).
Results: In the PM and DM groups 250 and 229 (52.2% and 47.8%) patients were included respectively. Positive ANA, anti-Jo1 and anti-RNP were higher in the PM than in the DM group (67, 22 and 19% vs. 56, 11 and 6%) (p=0.21, p=0.002, p=0.0001, respectively). The presence of anti-MI2 was higher in the DM group (p=0.024), according to the classification II, we found statistically significant differences in ANA, anti-Jo1, anti-RNP and anti-ACA. The OSd group had the highest proportion of ANA, anti-RNP and ACA positive AA and the JM group had the lowest frequency of Anti-Jo1 (see Table 1).

Table 1. Autoantibodies profile in IIM according to classification II

AA	Comparison between groups		Frequency	P
ANA	OSd vs.	PPM	91% vs. 54%	0,0001
		PDM	91% vs. 63%	
		JM	91% vs. 40%	
		CAM	91% vs. 63%	
	PDM vs.	JM	63% vs. 54%	
Anti-Jo1	JM vs.	PPM	3% vs. 25%	0,0001
		PDM	3% vs. 19%	
		OM	3% vs. 36%	
Anti-RNP	OSd vs.	PPM	40% vs. 6%	0,0001
		PDM	40% vs. 3%	
		JM	40% vs. 7%	
		CAM	40% vs. 5%	
ACA	OSd vs.	PDM	18% vs. 3%	0,002

Conclusions: The AA associated with the IIM subtypes is consistent with published scientific evidence on other cohorts for ANA, anti-Jo1, anti-RNP and anti-MI2, in spite of the small sample size. The OSd group showed higher ANA and anti-RNP frequencies which might be explained by the coexistence of SLE and MCTD patients. It could be interesting to follow up those PPM patients with positive AA because they could be in the future diagnosed with a connective tissue disease. Carrying out longitudinal studies that include a greater proportion of patients may help to evaluate and predict the clinical course of IIM.
References:
[1] Bohan A, Peter JB. N Engl J Med 1975 Feb 13;292(7):344–7.
Acknowledgements:.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7050

AB0626 EPITOPE PROFILING OF ANTI-RO52 ANTIBODIES IN PATIENTS WITH SYSTEMIC SCLEROSIS, SYSTEMIC SCLEROSIS-ASSOCIATED PRIMARY BILIARY CIRRHOSIS, AND PRIMARY BILIARY CIRRHOSIS ALONE

C. Liaskos[1], A. Gkoutzourelas[1], T. Simopoulou[1], E. Marou[1], T. Scheper[2], W. Meyer[2], L. Sakkas[1], D.P. Bogdanos[1]. [1]*Rheumatology and Clinical Immunology, University of Thessaly, School of Health Sciences, Larisa, Thessaly, Greece;* [2]*Institute of Immunology, Euroimmun AG, Lubeck, Germany*

Background: Anti-Ro52 antibodies are detected in patients with Sjogren's syndrome (SjS), systemic sclerosis (SSc) and other autoimmune rheumatic diseases. Epitope mapping studies of anti-Ro52 in autoimmune rheumatic diseases have failed to find any difference on epitope recognition suggesting a common stimulus for the loss of tolerance to Ro52. Such epitope differences, however, were noted between SjS and non-rheumatic diseases and in particular, SjS-associated primary biliary cirrhosis (SjS-PBC) or PBC alone (1).
Objectives: To assess whether or not the Ro52 epitope profile in anti-Ro52+ SSc patients differs from that of SSc-associated PBC (SSc-PBC) or PBC.
Methods: Serum samples were obtained from 63 anti-Ro52-positive (by ELISA) patients (33 SSc, 10 SSc-PBC, 20 PBC alone). Antibody reactivity to full length recombinant Ro52 and 5 baculovirus expressed Ro52 fragments spanning the whole sequence [Ro52–1 (aa 1–129), Ro52–2 (aa 125–268), Ro52–3 (aa 269–475), Ro52–4 (aa 57–180, partly overlapping with Ro52–1 and Ro52–2), and Ro52–5 (aa 181–320, partly overlapping with Ro52–2 and Ro52–3)] were tested by a line immunoassay.
Results: Reactivity was present to: full length Ro52 in all anti-Ro52 positive SSc, PBC-SSc, or PBC patients by line immunoassay; Ro52–1 in 6/33 (18.2%) SSc, 3/10 (30%) SSc-PBC, and 3/20 (15%) PBC; Ro52–2 in 33/33 (100%) SSc, 10/10 (100%) SSc-PBC and 20/20 (100%) PBC; Ro52–3 in 0/33 (0%) SSc, 0/10 (0%) SSc-PBC and 0/20 (0%) PBC; Ro52–4 in 4/33 (12.1%) SSc, 2/10 (20%) SSc-PBC, and 4/20 (20%) PBC and Ro52–5 in 11/33 (33.3%) SSc 4/10 (40%) SSc-PBC, and 9/20 (45%) PBC respectively ($p>0.05$ for all epitopes amongst the 3 cohorts). No statistically significant correlation was found.
Conclusions: The major epitope of anti-Ro52 does not differ among SSc, PBC-SSc and PBC and is localized on aa125–268, the major epitopic region of anti-Ro52 antibodies in SjS and other rheumatic diseases. Our epitope mapping data suggest that the mechanisms responsible for the loss of tolerance to Ro52 is common amongst diseases.
References:
[1] Mytilinaiou, Maria G.; Meyer Wolfgang; Komorowski, Lars; Probst, Christian; Davies, Edward T.; Vergani, Diego; Bogdanos, Dimitrios P. B-cell epitope mapping of anti-Ro52 responses in patients with primary biliary cirrhosis., Hepatology, Vol. 52 (4), 2010, 489.
Disclosure of Interest: C. Liaskos: None declared, A. Gkoutzourelas: None declared, T. Simopoulou: None declared, E. Marou: None declared, T. Scheper Employee of: Euroimmun AG, W. Meyer Employee of: Euroimmun AG, L. Sakkas: None declared, D. Bogdanos: None declared
DOI: 10.1136/annrheumdis-2017-eular.5299

AB0627 RISE-SSC: A DOUBLE-BLIND, RANDOMISED STUDY EVALUATING THE EFFICACY AND SAFETY OF RIOCIGUAT FOR THE TREATMENT OF PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

D. Khanna[1], Y. Allanore[2], C. Denton[3], M. Matucci-Cerinic[4], J. Pope[5], Z. Yao[6], J. Curram[7], J. de Oliveira Pena[8], O. Distler[9]. [1]*University of Michigan, Ann Arbor, United States;* [2]*Paris Descartes University, Paris, France;* [3]*University College London, London, United Kingdom;* [4]*University of Florence, Florence, Italy;* [5]*University of Western Ontario, Ontario, Canada;* [6]*Bayer AG, Beijing, China;* [7]*Bayer plc, Newbury, United Kingdom;* [8]*Bayer AG, Whippany, New Jersey, United States;* [9]*University Hospital of Zürich, Zürich, Switzerland*

Background: Diffuse cutaneous systemic sclerosis (dcSSc) is a severe subtype of SSc, a rare, chronic autoimmune connective tissue disease associated with significant morbidity and mortality, and with reduced quality of life. Currently, there are no approved disease-modifying therapies to treat the vascular and fibrotic damage in patients with dcSSc. Soluble guanylate cyclase stimulators, such as riociguat, target the transforming growth factor beta pathway, inhibiting signalling through non-SMAD pathways. They have been shown to inhibit dermal fibrosis in several animal models and to ameliorate fibrosis of the skin and intestine in bleomycin-induced fibrosis and experimental chronic graft-versus-host disease.[1] These preclinical data suggest that riociguat has vascular and antifibrotic properties that may be beneficial in dcSSc, potentially delaying disease progression.
Objectives: RISE-SSc (NCT02283762) is an international, multicentre, randomised, double-blind, placebo-controlled, parallel-group, Phase II study to assess the efficacy and safety of treatment with riociguat versus placebo in patients with dcSSc. The primary efficacy endpoint is change in modified Rodnan skin score (mRSS) from baseline to Week 52.
Methods: Eligibility criteria include a disease duration of ≤18 months and mRSS of 10–22, parameters identified to be predictors of progression of skin fibrosis.[2] Patients were randomised (1:1) to treatment with riociguat (adjusted up to 2.5 mg tid over the first 10 weeks) or placebo for a total of 52 weeks. The double-blind phase will be followed by an open-label extension phase for up to 6 years where all patients receive riociguat.
Results: Study recruitment was completed on 30 Dec 2016 and 121 patients have been randomised. Mean±SD age at inclusion was 50.7±12.3 years (range 18–79) and 76% (n=92) were female. At baseline the mean±SD mRSS was 16.8±3.7 (range 10–22) and disease duration was 8.8±5.5 months (range 0.5–18.5). Almost 70% of the patients tested positive for either anti-SCL-70 (43%) or anti-RNA polymerase III (25%) antibodies, while 32% of patients tested negative for these two antibodies. Swollen and tender joint counts were present in 38 (31.4%) and 51 (42.1%) patients, respectively, while 35 patients (28.9%) had tendon friction rubs. Digital ulcers were present in 15 patients (12.4%) at baseline.
Conclusions: RISE-SSc has a unique trial design with a cohort enriched for disease progressors,[2] which is reflected in the baseline characteristics of the randomised patients. Results of the RISE-SSc study will provide data to inform not only the efficacy, safety and tolerability of riociguat treatment in patients with dcSSc, but also the feasibility of a new trial design based on cohort enrichment.
References:
[1] Khanna D, et al. J Scleroderma Relat Disord 2016;1:186–93.
[2] Maurer B, et al. Ann Rheum Dis 2015;74:1124–31.
Disclosure of Interest: D. Khanna Grant/research support from: Bayer, BMS, Genentech/Roche, Sanofi-Aventis, NIH K24AR063120, Consultant for: Actelion, Bayer, Covis, Cytori, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis, Y. Allanore Grant/research support from: BMS, Genentech-Roche, Inventiva, Pfizer, Sanofi, Consultant for: Actelion, Bayer, Biogen, Genentech-Roche, Galapagos, Medac, Pfizer, Sanofi, Servier, UCB, C. Denton Grant/research support from: CSL Behring, Bayer, GSK, Inventiva, Consultant for: Actelion, Bayer, GSK, Merck-Serono, Genentech-Roche, Inventiva, Sanofi-Aventis, Boehringer Ingelheim, M. Matucci-Cerinic Grant/research support from: BMS, Pfizer, Actelion, MSD, Lilly, Speakers bureau: Pfizer, BMS, Actelion, Lilly, J. Pope Grant/research support from: Bayer, Merck, Consultant for: BMS, Roche, Bayer, Merck, Z. Yao Employee of: Bayer Healthcare Company Ltd, Beijing, China, J. Curram Shareholder of: Bayer AG, Employee of: Bayer plc, J. de Oliveira Pena Employee of: Bayer US LLC, O. Distler Grant/research support from: Actelion, Bayer, Boehringer Ingelheim, Pfizer, Sanofi, Consultant for: 4 D Science, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm, Sinoxa, Speakers bureau: AbbVie, iQone Healthcare, Mepha

DOI: 10.1136/annrheumdis-2017-eular.3718

AB0628 MACROVASCULAR DYSFUNCTION OF UPPER AND LOWER LIMBS CORRELATES WITH DIGITAL ULCERATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS

E. Moradkhan[1], S. AleSaeidi[2], F. Gharibdoost[3]. *[1]Shahid Beheshti University of Medical Siences; [2]Rheumatology, Internal medicine, Tehran university of medical sciences, Medical Faculty; [3]Tehran university of medical siences, Tehran, Iran, Islamic Republic Of*

Background: Systemic sclerosis (SSc) is a chronic connective tissue disorder of unknown etiology characterized by tissue fibrosis and vascular damage [1]. Digital ulcerations (DUs) are common manifestations of vascular involvement [2]. Althoughthe vascular dysfunction of SSc has been considered mainly to affect microvasculature [3], there is recent evidence showing that SSc is associated with the prevalence of large vessel disease [4]. However, only a few studies investigated the relationship between macrovascular disease and its role in the clinical manifestations of SSc such as ulcers.
Objectives: To assess the relationship between the Macrovascular dysfunction of upper and lower limbs with digital ulcerations in patients with systemic sclerosis.
Methods: Ninety patients with SSc (45 cases with DUs and 45 cases without DUs) enrolled in this study. Patients with other rheumatologic diseases and diabetics patients were excluded from the study. Data which were collected from the patients, included, age, past medical history of cardiovascular disease and dyslipidemia, SSc disease duration, type of SSc (lcSSc or dcSSc), Raynaud's phenomenon (RP), RP duration and digital ulcerations (DUs), Body weight (BW), Height, Waist circumference (WC), Body mass index (BMI), Blood pressure (BP), serum levels of SCL-70 antibody and Anti β2 microglobulin antibody. Then Doppler sonographies were performed. The outcome variables were the peak systolic velocity (PSV) and resistance index (RI) of ulnar, radial, popliteal, dorsalis pedis and tibia artery.
Results: The SSc patients with DUs have significantly lower PSV and higher RI in the ulnar (PSV:52.1±7.9 vs 55.7±4.1, p=0.006 and RI: 0.58±0.15 vs 0.52±0.06, p=0.003), dorsalis pedis (PSV: 33.9±1.9 vs 34.5±0.4, p=0.027 and RI: 0.54±0.11 vs 0.50±0.04, p=0.045) and tibial artery (PSV: 32.6±3.1 vs 34.4±0.9, p<0.001 and RI: 0.62±0.16 vs 0.51±0.07, p<0.001) in comparison to SSc patients without DUs. PSV and RI of ulnar artery were significantly correlated with age (p=0.012 and p=0.019), disease duration (p=0.001and p=0.001) and Raynaud's phenomenon (RP) duration (p=0.048 and p=0.028). PSV and RI of tibial artery had significant correlation with age (p=0.038 and p=0.009), systolic blood pressure (p=0.022 and p=0.037) and diastolic blood pressure (p=0.015 and p=0.010).
Conclusions: We concluded that digital ulceration in patients with SSc might be frequently related to the macrovascular dysfunction in below the elbow and knee.
References:
[1] Walmsley D, Goodfield MJ. Evidence for an abnormal peripherally mediated vascular response to temperature in Raynaud's phenomenon. Br J Rheumatol 1990;29:181–4.
[2] Chung L, Fiorentino D. Digital ulcers in patients with systemic sclerosis. Autoimmun Rev 2006;5:125–28.
[3] Ho M, Veale D, Eastmond C, Nuki G, Belch J. Macrovascular disease and systemic sclerosis. Ann Rheum Dis 2000;59:39–43.
[4] Veale DJ, Collidge TA, Belch JJ. Increased prevalence of symptomatic macrovascular disease in systemic sclerosis. Ann Rheum Dis 1995;54:853–5.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1041

AB0629 FROM LOCALIZED SCLERODERMA TO SYSTEMIC SCLEROSIS: A POSSIBLE EVOLUTION

E. Cocchiara, C. Esposito, V. Raimondo, A. Spinella, F. Lumetti, M. Colaci, D. Giuggioli, C. Ferri on behalf of Rheumatology Unit, University of Modena and Reggio Emilia, Modena, Italy. *Ospedale Policlinico di Modena, Modena, Italy*

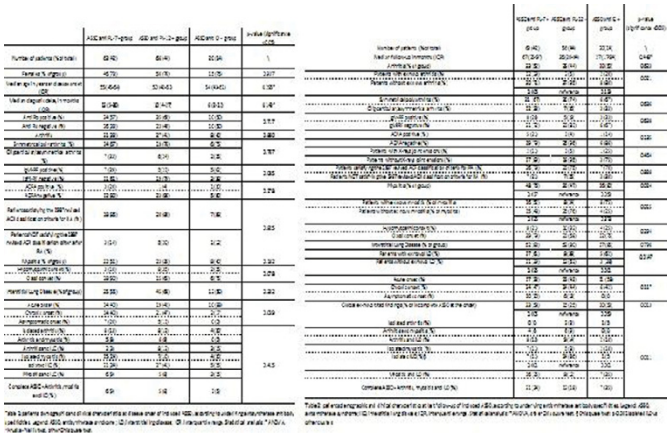
Background: Systemic Sclerosis (SSc) is a connective tissue disease characterized by skin fibrosis and visceral organ involvement. Localized Scleroderma (LoS), also known as morphea, is a fibrosing condition limited to the skin, subcutaneous tissue, underlying bone, and rarely central nervous system if present on face and head. SSc and LoS may share some aspects, such as histopathological findings, presence of autoantibodies and systemic symptoms, especially Raynaud phenomenon (RP). In this perspective they may represent two ends of a spectrum of disease.
Objectives: The aim of our study is to evaluate the evolution from LoS to SSc in our case series of SSc patients.
Methods: We retrospectively investigated 330 patients fulfilling the SSc-ACR/EULAR criteria referred to our University-based Rheumatology Unit. The occurrence of LoS preceding the SSc diagnosis was evaluated for each patient on the basis of medical records; clinical, laboratory, and instrumental features were analyzed, from the presenting symptoms at the disease onset to the first visit and during the follow-up, with particular attention to very early cutaneous manifestations.
Results: Five SSc patients (1.5% of our SSc series) had a clinical history of LoS prior to SSc diagnosis. All were women with mean age at time of LoS onset of 39±16.1SD years and time interval between LoS and SSc diagnosis of 19.2±16SD months. Skin biopsy was performed in 4/5 patients showing nonspecific inflammatory infiltrate, collagen fiber deposition and dermis sclerosis. In all patients RP was the first extra-dermal symptom, preceding LoS in 2/5 patients. Cutaneous involvement was represented by patches of skin sclerosis localized in limbs, trunk and face; while scleroderma was classified as cutaneous limited SSc in 4/5 patients and sine scleroderma in one. Following the SSc onset 2/5 patients had a history of digital ulcers, 1/5 esophagopathy, 1/5 interstitial lung disease; while capillaroscopy evidenced a SSc pattern in 4/5 patients. ANA were detected in all patients with anti-ENA positivity in 3/5 (1 ACA, 1 anti-Scl70, 1 anti-U1RNP); the presence of autoantibodies was observed in 3/5 individuals before SSc onset. None referred exposure to toxics or cigarettes smoke, while autoimmune thyropathy was the most frequent comorbidity. No local treatments had been employed for LoS but only low dosage of systemic steroids.
Conclusions: LoS and SSc are two distinct clinical entities that may share some clinical features; however, LoS is characterized by the absence of sclerodactyly, RP, digital ulcers, and typical SSc capillaroscopic changes; while possible internal organs involvement is much less frequently observed and the transition to SSc is exceptional and reported in only pediatric population. At our knowledge, this is the first observation of well-documented evolution from LoS to SSc in adult population as shown by updated review of the literature. The presence of RP and ANA positivity observed before the SSc onset can be considered as red flags of LoS evolution towards SSc, as reported in literature in pediatric population. SSc following LoS seems to be characterized by higher prevalence of vasculopatic symptoms compared to fibrotic complications. Finally, a careful clinical and laboratory monitoring of patients with LoS is recommendable to early identify the possible evolution to overt SSc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5120

AB0630 CLINICAL SPECTRUM TIME COURSE COMPARISON BETWEEN PL-7, PL-12 AND EJ POSITIVE ANTISYNTHETASE SYNDROME

E. Trallero Araguas[1], A. Selva O'Callaghan[1], C.A. Scire[2], V. Codullo[3], S. Castaneda[4], N. Ortego Centeno[5], J.A. Pereira da Silva[6], C. Fiehn[7], A. Schwarting[8], A. Manfredi[9], G. Emmi[10], S. Barsotti[11], O. Molberg[12], A. Doria[13], S. Parisi[14], S. Scarpato[15], N. Pipitone[16], M. Piga[17], I. Cavazzana[18], F.J. Lopez-Longo[19], J. Bachiller-Corral[20], M. Benucci[21], J. Rojas-Serrano[22], K. Triantafyllias[23], N. Perez-Gomez[24], G. Cagnotto[25], F. Maurier[26], L. Quartuccio[27], E. Bartoloni Bocci[28], P. Tomietto[29], R. Caporali[3], F. Iannone[30], M.A. Gonzalez-Gay[31], L. Cavagna[3] on behalf of AENEAS collaborative group. *[1]Internal Medicine, Vall d'Hebron General Hospital, Barcelona, Spain; [2]Reumatology, UOC Reumatologia, Azienda Ospedaliero Universitaria S. Anna, Ferrara; [3]Rheumatology, University and Irccs Foundation Policlinico S. Matteo, Pavia, Italy; [4]Rheumatology, Hospital Universitario de la Princesa, IIS-IP, Madrid; [5]Systemic Autoimmune Diseases Unit, Hospital Clínico San Cecilio, Granada, Spain; [6]Rheumatology, Centro Hospitalar e Universitário, Coimbra, Portugal; [7]Rheumatology, ACURA Centre, Baden Baden; [8]Rheumatology, University Hospital Johannes-Gutenberg, Mainz, Germany; [9]Rheumatology, Azienda Ospedaliero-Universitaria Policlinico, Modena; [10]Experimental and Clinical Medicine, University, Florence; [11]Rheumatology, AOU Pisana, Pisa, Italy; [12]Rheumatology, University Hospital, Oslo, Norway; [13]Rheumatology, University, Padua; [14]Rheumatology, Città della salute e della scienza, Torino; [15]Rheumatology, ASL Salerno, Scafati; [16]Rheumatology, S.Maria Hospital –IRCCS, Reggio Emilia; [17]Rheumatology, University, Cagliari; [18]Rheumatology, University and AO Spedali Civili, Brescia; [19]Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Italy; [20]Rheumatology, University Hospital Ramón y Cajal, Madrid, Spain; [21]Rheumatology, Azienda Sanitaria di Firenze, S. Giovanni di Dio Hospital, Firenze, Italy; [22]Rheumatology, Instituto Nacional de Enfermedades Respiratorias, Ismael Cosío Villegas, Mexico city, Mexico; [23]Rheumatology, ACURA Centre, Bad Kreuznach, Germany; [24]Rheumatology, Hospital Clinico Universitario, Santiago de Compostela, Spain; [25]Rheumatology, Skane University Hospital, Lund, Sweden; [26]Medicine, HPMetz, Metz, France; [27]Rheumatology, Santa Maria della Misericordia Hospital, Udine; [28]Rheumatology, University, Perugia; [29]Rheumatology, Cattnara Hospital, Trieste; [30]Rheumatology, University, Bari, Italy; [31]Rheumatology, Hospital Universitario Marqués de Valdecilla, IDIVAL, University of Cantabria, Santander, Spain*

Background: Arthritis, myositis and Interstital lung disease (ILD) represent the classic clinical triad of antisynthetase syndrome (ASSD). In anti Jo-1 positive patients, these findings may appear also during the follow-up. Even if a similar cumulative trend has been showed also in non anti Jo-1 positive ASSD, a head to head comparison of clinical spectrum time course in these patients is still lacking
Objectives: To assess the clinical spectrum time course in non anti Jo-1 positive ASSD, according to different underlying non anti Jo-1 specificities
Methods: Clinical, laboratory and instrumental data collection of anti PL-7, PL-12, and EJ positive patients from an international database of ASSD
Results: We identified 63 (42%) anti PL-7, 66 (44%) anti PL-12 and 20 (14%) anti EJ positive patients, reporting their characteristics in table 1 (disease onset) and 2 (last follow-up). At disease onset, no substantial differences were observed. At the end of follow-up, we observed some differences between anti PL-12 and both anti PL-7 and anti-EJ positive patients. In particular, anti PL-12 positive patients presented less frequently ex-novo triad findings and had a reduced prevalence of

myositis. From the clinical point of view, the main pattern of disease presentation was an isolated ILD in all groups at the onset and only in anti-PL12 positive ASSD at last follow-up.



Conclusions: Our study seems to indicate that clinical spectrum time course of anti PL-12 positive ASSD is different from that of anti PL7 and of anti EJ positive ASSD. The clinical pattern associated with these two latter antibodies was very similar. Furthermore, anti PL-12 positive patients seems to have a more stable disease, with a less common occurrence of ex-novo triad findings during the follow-up

References:

[1] Cavagna L. Medicine 2015.
[2] Cavagna L. CRAI 2016.
[3] Cavagna L. ARD 2016 (Abstract).
[4] Trallero Araguas E. Scand J Rheumatol 2016.

Acknowledgements: To all members of the AENEAS collaborative group.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2592

AB0631 THE CLINICAL CONSEQUENCES PRESENCE OF ANTI-PM/SCL ANTIBODIES IN SYSTEMIC SCLEROSIS

E. Wielosz, M. Dryglewska, M. Majdan. *Department of Rheumatology and Connective Tissue Diseases, Medical University of Lublin, Lublin, Poland*

Background: Anti-PM/Scl (a-PM/Scl) antibodies are found in different systemic autoimmune disease such as polymyositis, dermatomyositis, systemic sclerosis (SSc), and overlap syndromes. According to literature they are detected in about 2% of patients with SSc, but their presence are more common in SSc with myositis overlap. Features positively associated with the presence of a-PM/Scl antibodies included younger age at disease onset, skeletal muscle involvement, calcinosis, inflammatory arthritis, and overlap disease. On the other hand interstitial lung disease and gastrointestinal symptoms were less frequent in SSc patients with a-PM/Scl.

Objectives: The aim of the study was to assess the clinical consequences presence of a-PM/Scl antibodies in patients with SSc.

Methods: The study was performed in 126 European Caucasian SSc patients (98-female and 28-male) hospitalized consecutively in the Department of Rheumatology and Connective Tissue Diseases. Patients fulfilled the ACR classification criteria of SSc (59 have diffuse cutaneous SSc and 67 limited SSc). The study group were studied according to the presence of a-PM/Scl antibodies applying commercial test – EUROLINE Systemic Sclerosis Profile. Detection and interpretation of results was carried out electronically using the specific program Euroimmun– EUROLINEScan. The subtype of SSc, incidence of internal organ involvement and serological profile were determined in the whole group. Due to the presence of a-PM/Scl antibodies, patients were divided into two groups a-PM/Scl (+) SSc - 22 pts and a-PM/Scl (-) SSc- 104 pts.

Results: a-PM/Scl antibodies were detected in 22/126 patients with SSc (17,5.%) We showed a significant positive association with a-PM/Scl antibodies and myalgia or myosistis (p=0,0379), contractures (p=0,0002) and prevalence of overlap syndrome (p=0,0142). There were no relationship between the presence of a-PM/Scl antibodies and subtypes of SSc, other organ involvement, digital ulcers or calcinosis.

Conclusions: In SSc anti-PM/Scl antibodies are frequently associated with myalgia or myositis, contractures and overlap syndrome.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4393

AB0632 ASSESSMENT OF VEGF AND OTHER CYTOKINES IN THE TEAR OF PATIENTS WITH SYSTEMIC SCLEROSIS

A. Rentka[1], J. Hársfalvi[2], K. Köröskényi[3], G. Szücs[4], Z. Szekanecz[4], P. Szodoray[5], A. Berta[1], Á. Kemény-Beke[1]. *[1]Department of Ophthalmology, University of Debrecen, Faculty of Medicine, Debrecen; [2]Department of Biopsysics and Radiation Biology, Semmelweis University, Budapest; [3]Department of Biochemistry and Molecular Biology; [4]Department of Rheumatology, University of Debrecen, Faculty of Medicine, Debrecen, Hungary; [5]Institute of Immunology, Rikshospitalet, Oslo, Norway*

Background: Systemic sclerosis (SSc) is an autoimmune disease, characterized by widespread small vessel vasculopathy, immune dysregulation with production of autoantibodies, and progressive fibrosis. SSc may be associated with sicca syndrome. Changes in levels of proangiogenic and proinflammatory cytokines had already been determined largely in serum, however, the local inflammatory and cytokine milieu in the tear of SSc patients has not yet been evaluated.

Objectives: We wished to determine VEGF and other cytokine and chemokine levels in tear samples of SSc patients.

Methods: First, forty-three patients (40 female and 3 men, mean (SD) age 61 (48–74) years) with SSc and 27 healthy controls were enrolled in the VEGF study. Basal tear sample collection and tear velocity investigations were carried out followed by an ophthalmological examination. Total protein concentrations and VEGF levels were determined in tear samples. In the multiple cytokine study, unstimulated tear samples were collected from nine patients with SSc and 12 age- and gender-matched healthy controls. The relative levels of 102 different cytokines were determined by a cytokine array, and then absolute levels of four key cytokines were determined by a magnetic bead assay.

Results: In the first study, the mean collected tear fluid volume developed 10.4 L (1.6–31.2) in patients and 15.63 L (3.68–34.5) in control subjects. The mean total protein level was 6.9 g/L (1.8–12.3) and 4.1 g/L (0.1–14.1) in tear samples of SSc patients and controls, respectively. In patients with SSc, the mean VEGF tear concentration was 4.9 pg/L (3.5–8.1) compared to 6.15 pg/L (3.84–12.3) in healthy samples. Multicytokine-array studies revealed shifted cytokine profile characterized by predominance of proinflammatory mediators in the tear samples of SSc patients. Out of the 102 analyzed proteins, nine were significantly increased in tears of patients with SSc. Based on the multiplex bead results, CRP, interferon-inducible protein 10 (IP-10) and monocyte chemoattractant protein-1 (mcp-1) levels were significantly higher in tears of patients with SSc compared to controls.

Conclusions: Impaired angiogenesis has been found by other investigators in SSc. This is reflected by lower VEGF levels in the tear samples of SSc patients compared to controls. The multi-cytokine array study revealed increased production of CRP and two important pro-inflammatory chemokines in the tear of SSc patients. Our current data depict a group of inflammatory mediators, which may play a significant role in ocular pathology of SSc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3218

AB0633 RITUXIMAB IN SCLERODERMA RELATED INTERSTITIAL LUNG DISEASE: A SINGLE CENTRE EXPERIENCE FROM NORTH INDIA

G. Naidu, S.K. Sharma, V. Dhir, S. Jain. *Internal Medicine, PGIMER, Chandigarh, India*

Background: Pulmonary involvement is one of the major causes of morbidity and mortality in patients with progressive systemic sclerosis (PSS). Clinically significant interstitial lung disease (ILD) is noted in 25% of patients and accounts for 33% of deaths in PSS patients [1, 2]. Cyclophosphamide (CYC) and mycophenolate mofetil (MMF) have been shown to retard progression of ILD [3, 4]. The limited data on rituximab indicate that rituximab might be effective in PSS related ILD [5].

Objectives: To study the efficacy of rituximab in patients with PSS related ILD.

Methods: The clinical details of all patients of PSS related ILD who were treated with rituximab were noted retrospectively from the case files. Forced vital capacity (FVC) value before and 1 year after administration of rituximab were noted. Increase in FVC by 10% from baseline was considered as improvement and fall in FVC by 10% or absolute value less than 40% of predicted was considered as worsening. Patients with FVC ±10% from baseline were considered to have stabilized lung functions.

Results: A total of 11 patients received rituximab between 2013 and 2016. Six (54.5%) patients were females. Median age of the subjects was 44 years (range: 31–75 years). All patients received intravenous CYC at least 1 year before rituximab administration and had either not responded to CYC or worsened after initial response to CYC. All patients received 2 doses of rituximab (1gram each) at 2 weeks interval. Median FVC before rituximab was 57% of predicted. Two patients did not have post rituximab FVC values. Median FVC 1 year after rituximab was 54% predicted. Out of the remaining 9 patients, 2 (22.2%) patients had improvement in FVC, 6 (66.7%) patients had stabilization of FVC and 1 patient worsened. One patient, who had stabilization of FVC with rituximab expired after 2 years of receiving rituximab.

Conclusions: Rituximab was effective in stabilization of lung functions in patients of PSS with ILD who did not have favourable outcome with intravenous CYC.

Efficacy of rituximab in treatment naive PSS related ILD patients needs to be studied.

References:

[1] Tyndal AJ, Banert B, Vonk M, Airo P, Cozzi F, Carreira PE et al. Causes and risk factors for death in systemic sclerosis: a study from the EULAR Scleroderma Trials and Research (EUSTAR) database. Ann Rheum Dis. 2010; 69: 1809–152.
[2] McNearney TA, Reveille JD, Fischbach M, Friedman AW, Lisse JR, Goel N et al. Pulmonary involvement in systemic sclerosis: associations with genetic, serologic, sociodemographic and behavioral factors. Arthritis Rheum. 2007; 57: 318–26.
[3] Tashkin DP, Elashoff R, Clements PJ,Goldin J, Roth MD, Furst DEet al. Cyclophosphamide versus placebo in scleroderma lung disease. N Engl J Med. 2006;354: 2655–66.
[4] Tashkin DP, Roth MD, Clements PJ, Furst DE, Khanna D, Kleerup EC et al. Mycophenolate mofetil versus oral cyclophosphamide in scleroderma-related interstitial ling disease (SLS II): a randomised controlled, double blind, paralle group trial. Lancet Respir Med. 2016; 4: 708–19.
[5] Daoussis D, Melissaropoulos K, Sakellaropoulos G, Antonopoulos I, Markatseli TE, Simopoulou T et al. A multicenter, open-label, comparative study of B-cell depletion therapy with Rituximab for systemic sclerosis-associated interstitial lung disease. Semin Arthritis Rheum. 2016; pii: S0049–0172(16)30344–4.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5384

AB0634 RITUXIMAB IN SYSTEMIC SCLEROSIS-INTERSTITIAL LUNG DISEASE, A CASE SERIES OF 18 PATIENTS

G. Guzelant[1], M. Melikoglu[1], B. Musellim[2], D.D. Yilmaz[2], I. Fresko[1], E. Seyahi[1], G. Hatemi[1], S. Ugurlu[1], V. Hamuryudan[1]. *[1]Cerrahpasa Medical Faculty Department of Internal Medicine Division of Rheumatology; [2]Cerrahpasa Medical Faculty Department of Pulmonology, Istanbul University, Istanbul, Turkey*

Background: Interstitial lung disease (ILD) is a severe complication of systemic sclerosis (SSc). Immunosuppressives such as cyclophosphamide (CYC) and mycophenolate mophetil (MMF) are used in its treatment with no proven efficacy (1). Rituximab (RTX) appears to be an emerging agent according to case series.

Objectives: This retrospective study aims to evaluate the efficacy of RTX on SSc-ILD in a group of patients followed in our center.

Methods: A chart review revealed 18 patients (16 women, 2 men; mean age 50.3±12.1 SD years (range 30–72), mean disease duration 8.3±9.3 SD years) with SSc who have been diagnosed as having ILD (confirmed by high-resolution thorax computed tomography and pulmonary function tests) and have been treated with one or more cycles of RTX. Efficacy was evaluated according to the criteria of the American Thoracic Society: improvement= an increase in FVC≥10% or DLCO≥15%; worsening= a decrease in FVC≥10% or DLCO≥15%; stabilization= changes in FVC less than 10% or DLCO less then 15% (2).

Results:

Table 1 Demographic findings of the patients and their response to RTX treatment

	Group 1 (ILD with short duration and naive to treatment)	Group 2 (ILD with long duration and previous IS therapy)	All patients
Number of patients	4 (22.2%)	14 (77.7%)	18
Sex (F/M)	3/1	13/1	16/2
Mean disease duration	2±0.8 SD years	10.2±9.8 SD years	8.3±9.3 SD years
Follow-up time after initiation of RTX	12.2±6.8 SD months	21±12.4 SD months	19±11.8 SD months
Baseline FVC%	69.2±20.9	65.1±14	
Last FVC%	66.7±13	61.6±19.6	
Baseline DLCO%	57.7±24.1	43.5±12.2	
Last DLCO%	52±18	41.2±21.8	
Outcome: Stable/ Improvement (n)	2	7	9
Worsening (n)	2	5	7
Death	0	1	1
Unable to do PFT (n)	0	1	1

Four patients were treatment naive for ILD when they received RTX (Group 1). The mean duration between the diagnosis of ILD and RTX treatment in Group 1 was 3.5 months (range 0–14 months). The average RTX cycle in this group was 2 with 1 patient also receiving mycophenolate mophetil in combination with RTX. The mean follow-up time after the initiation of RTX in this group was 12.2±6.8 SD months (range 7–22 months). FVC/DLCO was stable or improved in 2/4 compared to baseline and worsened in 2/4 at the end of follow-up at group 1.

Fourteen patients had a 10.2 years-history of SSc and have been treated with immunosuppressives (cyclophosphamide, azathioprine, methotrexate, MMF) for ILD before RTX (Group 2). The mean duration between the diagnosis of ILD and RTX treatment in Group 2 was 71.2 months (range 5–246 months). These patients received a mean of 3 cycles of RTX with 5 receiving MMF (n=3) or AZA (n=2) in addition to RTX. One patient died after 3 months following the first RTX cycle (unknown reason) and 1 was unsuitable for spirometry because of microstomia. Of the remaining 12 patients in Group 2, improvement or stabilisation was seen in 7 and worsening was seen in the remaining 5 patients.

Conclusions: RTX appears to be modestly effective for ILD of SSc. The duration of ILD as well as the presence or absence of previous immunosuppressive therapy do not appear as playing a role in response.

References:

[1] Avouac J et al. EULAR Scleroderma Trials and Research group (EUSTAR) recommendations for the treatment of systemic sclerosis. Ann Rheum Dis 2009.
[2] An Official ATS/ERS/JRS/ALAT Statement: IPF: Evidence-based Guidelines for Diagnosis and Management.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4908

AB0635 THE CLINICAL FEATURES AND PROGNOSIS OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SCLERODERMA AND OTHER CONNECTIVE TISSUE DISEASE DURING THE MODERN MEDICAL ERA IN JAPAN

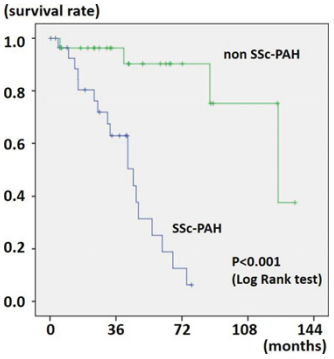
H. Maki[1], M. Hatano[2], S. Minatsuki[1], T. Inaba[1], I. Komuro[1], Y. Asano[3], S. Sato[3]. *[1]Cardiovascular Medicine; [2]Therapeutic Strategy for Heart Failure; [3]Dermatology, The University of Tokyo, Tokyo, Japan*

Background: Due to the recent progress of vasodilators for pulmonary arterial hypertension (PAH), the prognosis of PAH has been getting better for the past 10 years. Among them, idiopathic PAH (IPAH) well improved but PAH associated with connective tissue disease (CTD-PAH) especially scleroderma (SSc-PAH) have poorer prognosis than IPAH.

Objectives: This study intended to clarify the clinical features and prognosis of CTD-PAH in modern era when multiple PAH drugs are available, in addition, compare between SSc-PAH and PAH associated with other CTD-PAH (non SSc-PAH).

Methods: Fifty-seven consecutive CTD-PAH patients were enrolled to this study, who received hemodynamic examination with right heart catheterization between 2004 and 2016. Thirty of 57 patients were SSc-PAH patients and other 27 patients were non SSc-PAH patients (11 mixed connective tissue disease, 8 systemic lupus erythematosus, 5 primary sjogren syndrome, 1 polymyositis, 1 rheumatoid arthritis and 1 Still's disease were included). We retrospectively analyzed the relationship between clinical parameters at baseline and the prognosis of CTD-PAH patients.

Results: Mean age at entry were 65.3±10.3 and 48.3±15.5 years old each other (SSc-PAH vs non SSc-PAH $P<0.001$). Twenty-eight SSc-PAH (93%) and 26 non SSc-PAH patients (96%) took at least one vasodilator, among them, 18 SSc-PAH (60%) and 13 non-SSc-PAH (48%) patients took multiple vasodilators at the end of follow-up period. Comparing the baseline clinical parameters between two groups, vital capacity and diffusing capacity of the lung for carbon monoxide (DLCO) were significantly lower in SSc-PAH patients than non SSc-PAH patients and brain natriuretic peptide and creatinine level were higher in SSc-PAH patients than non SSc-PAH patients ($P<0.05$). However, there were no significant differences in hemodynamic indices between two groups. During a mean follow-up period of 42.5±31.5 months, 22 patients (18 SSc-PAH and 4 non SSc-PAH) died or received lung transplantation. The SSc-PAH patients had worse prognosis than non SSc-PAH patients (figure: $P<0.001$). Only 6 of 18 SSc-PAH patients and 1 of 4 non SSc-PAH patient died of PH related cardiovascular event and other principal causes of death included interstitial lung disease (ILD), neoplasm and infection. Applying multivariate Cox-proportional hazard regression, mean pulmonary arterial pressure, right atrial pressure, creatinine level and %DLCO were extracted as the independent risk for all-cause mortality.



Conclusions: SSc-PAH patients had poor prognosis among CTD-PAH patients despite the progression of PAH drugs. As well as the report from REVEAL registry, not only PAH severity but also respiratory dysfunction may predict the prognosis of CTD-PAH patient. Scleroderma is multiorgan disease affected by complex pathology of vasoconstriction (ischemia), proliferation, inflammation, autoimmune disorder and fibrosis. Our data suggest that vasodilator alone is not enough to improve the prognosis of CTD-PAH patients. Comprehensive therapeutic strategy for scleroderma is needed.

References:

[1] Chung L.et al. Unique predictors of mortality in patients with pulmonary arterial hypertension associated with systemic sclerosis in the REVEAL registry. Chest 2014;146(6):1494–1504.

Disclosure of Interest: H. Maki: None declared, M. Hatano Grant/research support from: Ministry of Health, Labour and Welfare, Bayer Japan, Nippon Shinyaku Co,.Ltd, GlaxoSmithKline K.K., Speakers bureau: Actelion pharmaceuticals Japan Ltd, Bayer Japan, S. Minatsuki: None declared, T. Inaba: None declared, I. Komuro Grant/research support from: Actelion pharmaceuticals Japan Ltd, Y. Asano Grant/research support from: Ministry of Health, Labour and Welfare, S. Sato Grant/research support from: Ministry of Health, Labour and Welfare
DOI: 10.1136/annrheumdis-2017-eular.4271

AB0636 A COMPARISON STUDY OF PREVALENCE OF TRADITIONAL CARDIOVASCULAR RISK FACTORS AND FRAMINGHAM RISK SCORE IN SYSTEMIC SCLEROSIS PATIENTS AND MATCHED CONTROLS

J. Sousa-Neves, M. Cerqueira, D. Santos-Faria, J. Leite Silva, C. Afonso, F. Teixeira. *Rheumatology, Hospital Conde de Bertiandos, ULSAM, Ponte de Lima, Portugal*

Background: In Systemic Sclerosis (SSc), data on prevalence of traditional cardiovascular (CV) disease risk factors is scarce and conflicting (1). Therefore, SSc patients CV risk attributed to traditional CV risk factors remains an issue of debate.
Objectives: To evaluate if patients with SSc have a higher prevalence of traditional CV disease risk factors and a higher risk of long-term CV events based on the risk prediction tool of the Framingham risk score (FRS) in comparison with age, race and sex matched control subjects.
Methods: The study comprised patients diagnosed with SSc, fulfilling both the 1980 ACR and the 2013 ACR/EULAR criteria for the disease, and followed-up at our Rheumatology Department and a group of age, race and sex-matched controls. Inclusion criteria were age 30 to 74 and no history of CV events in order to calculate FRS. In total, 46 out of 62 patients were eligible for the study. Traditional CV disease risk factors (diabetes, arterial hypertension and smoking) were compared among the 46 patients with SSc and 51 matched controls. Systolic blood pressure (SBP) values and total and high-density lipoprotein (HDL) cholesterol levels were also collected. The 10-year risk for CV events according to FRS was calculated and means of patients and controls were compared. Subjects' distribution into 3 categories of risk – low (<10% risk), medium (10–20% risk) and high (>20% risk) was also compared. Parametric and nonparametric tests were used for comparison between groups. P value <0.05 was defined as statistically significant.
Results: Mean risk for CV events in 10-years assessed by FRS was 10.00%±8.61 for SSc patients and 7.76%±8.30 for matched controls. Differences were not statistically significant (p=0.196). Additionally, prevalence of diabetes, arterial hypertension and smoking did not differ significantly between the two groups (p=0.890, p=0.443, p=0.651, respectively). Total and HDL cholesterol levels were also similar between groups (p=0.963 and p=0.506, respectively). Only SBP values (mmHg) of SSc patients were significantly higher (128.50 mmHg [113.5 to 139.3]) (median [interquartile range]) compared with controls (120.00 [110 to 130]), p=0.031. Subjects' distribution into the 3 groups of risk defined was similar for both groups (p=0.205).
Conclusions: In our study, prevalence of traditional CV disease risk factors and 10-year risk for CV events based on FRS assessment tool did not differ significantly between SSc patients and age, sex and race matched controls.
References:
[1] Psarras A, Soulaidopoulos S, Garyfallos A, Kitas G and Dimitroulas T. A critical view on cardiovascular risk in systemic sclerosis. Rheumatol Int. 2017 Jan;37(1):85–95.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4528

AB0637 SUBCLINICAL ATHEROMATOSIS AND VITAMIN D DEFICIENCY IN PATIENTS WITH SCLERODERMA

J.J. Gonzalez Martin[1], O. Carrion[2], A. Abdelkader[2], E. Calvo[1], F. Aramburu[1], F. Sainz[2], P. García de la Peña[1]. *[1]Rheumatology; [2]Angiology and Vascular Surgery, Hospital Universitario HM Sanchinarro, Madrid, Spain*

Objectives:
To study whether patients with systemic sclerosis (SSc) have an increased cardiovascular risk (CVR), measured on the basis of analytical, angiodinamic and/or vascular lesions on carotid ultrasound.
The carotid IMT is a marker of cardiovascular morbidity and mortality, allowing measurement and monitoring of atherosclerosis in asymptomatic individuals, being surrogate markers of future coronary disease, stroke and general death in the general population and in inflammatory rheumatologic diseases.
Methods: Epidemiological and analytical data were collected, including the determination of the RCV SCORE index.
Vascular ultrasound protocol included assessment of carotid intima-media thickness (IMT), presence of atheromatous plaques, and exploration of peripheral arteriopathy using the ankle arm index (ABI).
Results: Seventy adult patients with ES diagnosis (ACR-EULAT 2013 criteria) were included.
94% of the women had a mean age of 50.2±12.5 years, and an average evolution time of 3.0±4.4 years.
The distribution by subgroups was: limited SSc (48%), diffuse SSc (34%), pre-SSc (4'2%), sine SSc (2.8%), MCTD (5'7%) and overlap syndrome 4'2%). The mean SSRm was 9.3±7.0 (range 0–42).
The ANA were positive in 91.4%, ACA (51.4%), ATA (10%), RNA polymerase (4'2%).
4% were DM, 7% were obese, 11% were active smokers, 13% were HTN, and 28% were ex-smokers.
28% had hypercholesterolemia with a mean total cholesterol of 192.5 (SD ± 31.9) and LDL of 102.4 (SD ± 29.4 mg/dL).
57% received vasodilators, most of them ARA-II. 10% bosentan, 4.2% sildenafil, and a 2.8% combination therapy.
The percentage of immunosuppressive drugs was corticoid (50%), MTX (34%), mycophenolate (3%), AZA (11%), HCQ (14%), CP %).
The IMT presented pathological values (>0.9 mm) in 39% of the sample, 23% had atheroma plaques (being bilateral in 40%). Subclinical atheromatosis affected 41.4% (patients without cardiovascular events, pathological IMT and/or atheroma plaques). The ABI had pathological values (<0.9) in 17% of the patients.
In the bivariate analysis, the pathological GIM was related to the presence of ACA antibodies (OR =3.80, 95% CI: 1.15–12.52, p=0.028) and with the SCORE index of CVR (OR =2.93, 95% CI: 1.12–7, 64, p=0.028); And the presence of atherosclerotic plaques was associated with increased SSRm score (OR 1.09, 95% CI 1.00–1.19, p=0.046), and the highest CVR SCORE index (OR 3.90, 95% CI: 1.31–11.56, p=0.014.
In the multivariate analysis, the serum vitamin D concentration showed a protective effect on IMT (OR =0.94, 95% CI 0.89–0.99, p value =0.025); And the main determinant of atheromatous plaques is the SCORE index, since the increase of one unit in SCORE index multiplies by 4 the probability of presenting plaques (OR =4.06, 95% CI: 1.31–12.60; P=0.015), once the effect of SSRm was controlled.
Conclusions:
- 40% of the patients had pathological IMT values, showing association with the presence of positive AAC and the SCORE risk index.
- The serum concentration of 25-OH-vitamin D showed a protective effect on IMT. Sixty percent of the sample had vitamin D deficiency.
- The presence of atheromatous plaques (23% of patients) was associated with higher SSRm indexes and SCORE cardiovascular risk.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6995

AB0638 CARDIAC TRANSPLANT IN SYSTEMIC SCLEROSIS-ASSOCIATED CARDIOMYOPATHY: MONOCENTRIC EXPERIENCE OF 3 CASES

J. Lenaerts[1], J. Lenaerts[2], R. Westhovens[2], W. Droogne[3], A. Ciarka[3], J. Van Cleemput[3], E. De Langhe[2]. *[1]Internal Medicine; [2]Rheumatology; [3]Cardiology, UZ Leuven, Leuven, Belgium*

Background: Cardiac involvement in systemic sclerosis (SSc) is a frequent complication, but end-stage cardiac failure remains uncommon and represents a poor prognosis. Heart-lung and lung transplant is an established treatment option for SSc-related pulmonary disease. Due to the limited published data, no recommendations exist for cardiac transplant in the context of SSc.
Objectives: We present our monocentric experience of 3 patients with SSc who underwent cardiac transplant for SSc-related end-stage heart disease (multiple hospitalisations due to failure of medical therapy and life-threatening complications).
Results: *Case 1* is a 59-year-old male with limited cutaneous SSc. Antinuclear antibody (ANA) was negative. He had vascular (digital ulcers) and cardiac (heart failure (left ventricular ejection fraction (LVEF) 20%, NYHA class IV)) involvement, without major gastrointestinal or pulmonary involvement (no interstitial lung disease (ILD) or pulmonary arterial hypertension (PAH: assessed by right heart catheterization (RHC))). He underwent a cardiac transplant at the age of 51, after a disease duration of 6 years. Post-transplantation immunosuppressant therapy consists of tacrolimus and mycophenolic acid, initially associated with methylprednisolon, which is the standard immunosuppression protocol at our institution.
Case 2 is a 55-year-old male with limited cutaneous SSc. ANA was positive,

	Case 1	Case 2	Case 3
Sex, age	Male, 59 years	Male, 55 years	Male, 50 years
Type of SSc	Limited	Limited	Diffuse
Disease duration at Tx	6 years	7 years	4 years
ANA	Negative	1/320, speckled, no SSc-specific antibody	Negative
Pre-Tx			
NYHA class	IV	III	III
LVEF	20%	40%	40%
RHC: mPAP in mmHg	26	20	31
RHC: PCWP in mmHg	20	14	28
Post-Tx			
NYHA class	I	I	I
LVEF	60%	55%	60%
RHC: mPAP in mmHg	19	13	21
RHC: PCWP in mmHg	12	8	12

Tx: Transplant; mPAP: Mean pulmonary artery pressure; PCWP: Pulmonary capillary wedge pressure.

1/320, speckled pattern, but no SSc-related autoantibody has been identified. He had gastrointestinal (upper gastrointestinal tract dysmotility), muscular (myositis) and cardiac (heart failure with secondary cardiac cirrhosis (LVEF 40%, NYHA class III)) involvement, without major pulmonary involvement (no ILD or PAH). He underwent a cardiac transplant at the age of 54, after a disease duration of 7 years. Standard immunosuppressants were initiated.

Case 3 is a 50-year-old male with diffuse cutaneous SSc. ANA was negative. He had vascular (digital ulcers), gastrointestinal (upper gastrointestinal tract dysmotility) and cardiac (heart failure with secondary cardiac cirrhosis (LVEF 40%, NYHA class III)) involvement, without major pulmonary involvement (no ILD or PAH). He underwent a cardiac transplant at the age of 49, after a disease duration of 4 years. Standard immunosuppressants were initiated.

At present, 1,5 years (case 2 and 3) and 8 years (case 1) after transplant, the donor hearts are still functioning well. No other SSc-related organ manifestations have occurred.

Conclusions: We present 3 patients with SSc who successfully underwent cardiac transplant for SSc-related end-stage heart disease. None had other major SSc-related organ involvement. This supports the limited published data that cardiac transplant is feasible and can be considered in end-stage SSc-related cardiomyopathy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4251

AB0639 SUPERIOR TREATMENT RESPONSE OF INTERSTITIAL LUNG DISEASE IN INFLAMMATORY MYOPATHIES COMPARED TO OTHER CONNECTIVE TISSUE DISEASES – A PROSPECTIVE COHORT STUDY

J.J. Maya[1], A. Borja[2], A. Abril[1], I. Mira-Avendaño[2]. [1]*Rheumatology;* [2]*Pulmonary, Mayo Clinic Florida, Jacksonville, United States*

Background: Interstitial Lung Disease (ILD) associated to Connective Tissue Disease (CTD) represent a challenge for clinicians and researchers because of their significant morbidity and mortality. Although the different types of ILD associated to CTD are often studied and managed as one because of their autoimmune background, there are considerable differences in their etiopathogenesis and therefore it can be assumed that there are differences in their response to treatment (1). Even though previous studies have analyzed the impact of immunosupipression in ILD secondary to sclerodema, additional studies are needed in order to determine the response to treatment of the different forms of ILD associated to CTD (2–3).

Objectives: To characterize and analyze the response to treatment of different types of ILD associated to CTD. The primary endpoint is the Functional Vital Capacity (FVC) change at 6 months and 1 year, and secondary endpoints arere the change in Diffusion Capacity of the Lung for Carbon Monoxide and in a 6 Minute Walk Test.

Methods: A prospective cohort study is being carried out where all patients who present to the Mayo Clinic Florida pulmonary clinic, age 18 to 80, with established CTD and diagnosed with ILD, and all patients with ILD who meet the criteria for immunologic mediated process, are being followed for a year in order to evaluate the clinical and functional outcomes to treatment. Patients with moderate to severe Pulmonary Hypertension, and active smokers with bronchiolitis pattern are being excluded. Exploratory analysis were performed on the first group of patients enrolled in the study, continuous variables were described with central tendency measures and the mean absolute difference in adjusted 12-month FVC was analyzed between the different types of CTDs using student's t test.

Results: Thirteen patients with ILD were enrolled in the study's initial phase. Five of the patients had been diagnosed with an Inflammatory Myopathy (IM), 2 with Rheumatoid Arthritis, 1 with an Undifferentiated Connective Tissue Disease, 1 with Churg-Strauss Syndrome, and one with Systemic Sclerosis. One patient was treated with Rituximab only; 2 with Rituximab and a steroid; 3 with Mycophenolate Mofetil (MMF) only; 2 with steroids, MMF, and Rituximab; 1 with a TNF inhibitor and MMF; 1 with MMF and steroids; 1 with Azathioprine and steroids; and 1 received only steroids. IMs were compared to the rest. At 1 year follow-up FVC mean absolute difference for the IMs demonstrated and improvement of 0.43 while the other CTDs had worsen by a mean of 0.04 (p=0.01). There were no statistical differences at 6 months for all outcomes or at 1 year for DLCO and 6MWT.

Conclusions: To our knowledge, this is the first time that a cohort of ILD associated to CTD patients is followed and analyzed after 1 year of treatment. Our results suggest that there is a difference in the response to treatment of ILD depending on the underlying CTD. Specific types of ILD associated to CTD likely benefit from early and aggressive treatment, but longer follow ups and larger studies are needed in order to be able to validate and further understand these pathologies.

References:

[1] Chest 2013; 143 (3): 814–824.
[2] Lancet Respir Med. 2016 Sep;4(9):708–19.
[3] Semin Arthritis Rheum. 2016 Oct 13.[Epub ahead of print].

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5653

AB0640 DOES MIXED CONNECTIVE TISSUE DISEASE WITHOUT ANTI-U1RNP EXIST?

J. Martínez-Barrio[1,2], E. Estrada[3,4], J.G. Ovalles-Bonilla[1], L. Valor[1], D. Hernández-Flórez[1], T. del Río[1], I. Janta[1], J.C. Nieto Gonzalez[1], B. Serrano[1], R. González Benítez[1], C. Sáenz Tenorio[1], L. García-Montoya[1], M. Correyero[1], A. Silva[1], A. López-Cerón[1], C. Gonzalez[1], I. Monteagudo[1], F.J. López-Longo[1]. [1]*Department of Rheumatology, Hospital General Universitario Gregorio Marañón;* [2]*Universidad Complutense de Madrid;* [3]*Facultad de Salud, Universidad Camilo José Cela;* [4]*Facultad de Psicología, Universidad Autónoma de Madrid, Madrid, Spain*

Background: Mixed Connective Tissue Disease (MCTD) is a systemic autoimmune rheumatic disease (SARD) characterized by clinical manifestations of systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and polymyositis (PM) and the presence of anti-U1-RNP antibodies.

Objectives: To determine whether there are patients with symptoms of MCTD in the absence of anti-U1-RNP antibodies.

Methods: This was a monocentric, prospective, observational study of patients with SARD. All patients diagnosed of MCTD according to Kasukawa and/or Alarcón-Segovia's criteria, SLE, SSc, PM, overlap syndromes (simultaneous or sequential criteria of 2 or more SARD), Sjögren's syndrome, Antiphospholipid syndrome, systemic vasculitis and undifferentiated or incomplete SARD (at least one clinical criterion of the classification criteria and a related antibody of any of the SARD) were included in the "Autoimmune Systemic Rheumatic Diseases Registry" of the Hospital General Universitario Gregorio Marañon Rheumatology Department from 1986 to 2012. The registry includes 2406 patients diagnosed with SARD. Patients with rheumatoid arthritis were excluded. Patients with clinical MCTD criteria were divided into seropositive (MCTD, with anti-U1RNP) and seronegative (possible MCTD, without anti-U1RNP). The registry counts with the local Institutional Ethics Board approval.

Results: A total of 692 patients were recruited, 608 women (87.9%). Seventy (70, 10.1%) patients were classified as seropositive and 75 (10.8%) as seronegative by Kasukawa's criteria. Sixty-two (62, 8.9%) patients were classified as seropositive and 54 (7.8%) as seronegative according to Alarcón-Segovia's criteria. There were no significant differences in age at disease onset, age at diagnosis or disease duration ($p>0.05$) between seropositive and seronegative patients. Seropositive patients with Kasukawa's criteria presented more frequently: lymphadenopathy, malar rash, leukopenia, Raynaud's phenomenon, muscle weakness and increase of muscle enzymes (Table 1). By Alarcón-Segovia's criteria, patients who developed myositis were more frequent in the seropositive group (p=0.007, OR 3.25, 95% CI, 1.44–7.32).

Kasukawa criteria	Seropositive MCTD		Seronegative MCTD		*P*	OR	95% CI OR	
	n	%	*N*	%			Inf	Sup
Lymphadenopathy	28	40%	17	23%	0.038	2.275	1.105	4.681
Malar rash	25	36%	8	11%	0.001	4.653	1.928	11.231
Leucopenia	41	59%	17	23%	<0.001	4.824	2.348	9.909
Muscle weakness	32	50%	24	32%	0.042	2.125	1.083	4.171
Increase of muscle enzymes	45	64%	35	47%	0.049	2.057	1.056	4.008

Conclusions: Some patients with SARD manifestations fulfill MCTD clinical criteria, both Kasukawa's and Alarcón-Segovia's, in the absence of anti-U1-RNP antibodies from the onset of the disease and throughout its evolution (seronegative MCTD). The frequency of seronegative MCTD was similar to the frequency of seropositive MCTD. Patients with seropositive MCTD presented more frequently manifestations of SLE (lymphadenopathy, malar rash and leukopenia) when using Kasukawa's criteria and of PM when using both criteria.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5192

AB0641 ARTERIAL STIFFNESS AND CLINICAL ASSOCIATION IN PATIENTS WITH SYSTEMIC SCLEROSIS

K. De La Cruz Rodríguez[1], G. Martínez Bonilla[2], V. González Díaz[2], K. García Osuna[2], J. Reyes Rueda[2], C. Gómez López[2], J. Polanco Cruz[2], A. Bernard Medina[2], E. Cardona[3], A. Macías Chumacera[4], C. Ramos Becerra[4], S. Gutiérrez Ureña[2], S. Cerpa Cruz[2]. [1]*Rheumatology Service;* [2]*Hospital Civil Fray Antonio Alcalde;* [3]*Mechanical Vascular Service;* [4]*CUCS, Guadalajara, Jalisco, Mexico*

Background: Systemic sclerosis is an autoimmune disease characterized by microvascular damage and fibrosis. There are several studies that shown macrovascular damage with arterial stiffness (AS) and the risk of cardiovascular complications. Carotid-femoral pulse wave velocity (CF-PWV) and augmentation index (AIx) are two competent methods to determine AS and predictors of cardiovascular disease. Association between AS and microvascular damage is unknown in systemic sclerosis patients.

Objectives: To determine the frequency of arterial stiffness in patients with systemic sclerosis and its association with clinical manifestations.

Methods: We performed a cross-sectional study; patients with diagnosis of systemic sclerosis according to ACR/EULAR 2013 criteria were included and the control group was selected from a database of mechanical vascular service. AS

was non-invasively assessed by Pulse pen device and AIx was evaluated by tonometry. Statistical analysis was done with SPSS v22 software, we calculated mean and standard deviation, for continuous variables we used Student t test, categorical variables were analyzed by using chi-square or Fisher's exact test. The correlation of AS and clinical variables was assessed with Spearman's correlation.

Results: Forty seven patients were included and compared with 39 healthy subjects; mean age of study group was 48±14. vs control group 47±13.7 (p=0.08) 93% were female. Prevalence of AS was 11% vs 3% p=0.039. AS was more frequent in limited systemic sclerosis sub-group and we found correlation with abnormal capillaroscopy, Rho 0.292 p=0.04.

Conclusions: Arterial stiffness is more prevalent in patients with limited systemic sclerosis and association with abnormal caillaroscopy suggest that both macro and microvascular damage is present in these patients and could explain the presence of early atherosclerosis and increased risk of cardiovascular disease.

References:

[1] Vargas John, Lafyatis Robert. Etiology and pathogenesis of systemic sclerosis. Marc Hochberg. Texbook of Rheumatology (Sixth Edit). Elsevier, 2015. 1177–1245.
[2] Ngian G.-S., Sahhar J., Wicks I., Van Doornum, S. Arterial stiffness is increased in systemic sclerosis: A cross-sectional comparison with matched controls. Arthritis and Rheumatism 2012. 64, S301.
[3] Colaci M., Giuggioli D., Manfredi A., Sebastiani M. Aortic pulse wave velocity measurement in systemic sclerosis patients, Rheumatism 2012. 64(6), 360–367.
[4] Man A., Zhu Y., Zhang Y., Dubreuil M., Rho Y. H., Peloquin C. Choi, H. K. The risk of cardiovascular disease in systemic sclerosis: a population-based cohort study. Annals of the Rheumatic Diseases 2013. 72(7), 1188–93.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3345

AB0642 THICKNESS OF THE INTIMA-MEDIA COMPLEX AND DOPPLER VELOCITY PARAMETERS IN SCLERODERMA PATIENTS

K. Rutka[1], E. Gindzienska-Sieskiewicz[2], R. Milewski[3], S. Sierakowski[2], U. Lebkowska[1]. *[1]Radiology; [2]Rheumatology; [3]Statistics and Medical Informatics, Medical University of Bialystok, Bialystok, Poland*

Background: Systemic sclerosis (Ssc) is a chronic inflammatory autoimmune disease, that involves various tissues and organs, including the cardiovascular system. Ssc patients might suffer from a number of complications – including cardiovascular system diseases. Diagnostic imaging is an important tool in assessment of vascular lesions, and ultrasound (including Doppler ultrasound) is one of the most important examinations, which allow to scan for presence of atherotic lesions, assess the intima-media complex thickness as well as provide measurements of the blood flow parameters.

Objectives: The aim of study was to determine if there is any difference in the intima-media complex thickness as well as in blood flow parameters measured using Doppler ultrasound examination in scleroderma patients and the general population.

Methods: 35 patients, aged 19–75, with diagnosed systemic scleroderma were examined using a Doppler ultrasound examination. Thickness of intima-media complex (IMT) approximately 2 centimeters from the carotid bulb was assessed for both right and left common carotid artery (CCA). The standard parameters of blood flow were measured – including peak systolic velocity (PSV), end diastolic velocity (EDV), as well as resistive index (RI), pulsative index (PI) and standard deviation (SD) was measured in the common carotid arteries, internal carotid arteries (ICA) as well as in the vertebral arteries (VA).

Results: The mean IMT value in CCA was approximately 0.63mm (0.35 – 0.9mm).

The mean, minimal and maximal values measured in CCA equalled respectively: PSV – 68.7 cm/s (22.4–94 cm/s), EDV – 19,7 cm/s (4.7–30.35 cm/s), PI – 1.95 (0.41–2,09) and RI – 0.68 (0.28–0.81). In ICA the measured values were as follows: PSV – 68.4 cm/s (38.65–96.9 cm/s); EDV – 23.6 cm/s (9,05–38.6 cm/s), PI – 1.16 (0.76–1.71) and RI – 0.65 (0.37–0.79); in VA PSV – 46.5 cm/s (26.75–75.35 cm/s); EDV – 12.4 cm/s (6.1–22 cm/s), PI – 1.38 (0.6–2.28) and RI – 0.73 (0.34–1.33).

A positive correlation between the age of examined subjects and the IMT was found (p=0.002; R=0.49). Additionaly, a negative correlation between the IMT and the EDV was found (p=0.008, R=-0.44).

Conclusions: The mean thickness of intima-media complex in the examined group of SSc patients is within the values that were established for a healthy population, however a further investigation, including a control group study will allow to evaluate whether there is no correlation between systemic sclerosis and increased IMT.

A negative correlation between IMT and EDV was shown, which is an interesting finding, and could be confirmed in a control group study and on a larger group of patiens.

References:

[1] Kochanowicz J. et al Normal reference values of ratios of blood flow velocities in internal carotid artery to those in common carotid artery using Doppler sonography. J Clin Ultrasound. 2009 May;37(4):208–11.
[2] Buljan K et al. Relationship between Age and Thickness of Carotid Arteries in a Population without Risk Factors for Atherosclerosis. Coll Antropol. 2015 Sep;39(3):779–84.
[3] Yazici B. et al. Cerebral blood flow measurements of the extracranial carotid and vertebral arteries with Doppler ultrasonography in healthy adults. Diagn Interv Radiol. 2005 Dec;11(4):195–8.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6296

AB0643 MALIGNANCY SCREENING IN AUTOIMMUNE MYOSITIS AMONGST AUSTRALIAN RHEUMATOLOGISTS

K. Dutton[1], M. Soden[2]. *[1]Rheumatology, RBWH, Brisbane; [2]Rheumatology, Townsville Hospital, Douglas, Australia*

Background: The association between cancer and autoimmune myositis is well established and has lead to the common practice of malignancy screening in asymptomatic individuals. The international literature advocates widely for cancer screening in autoimmune myositis however no consensus or guideline has been published to set forth a process for screening standardisation (1). Malignancy screening is a complicated topic and recommendations in favour of screening should in principle be based on a judicious assessment of the evidence in terms of the benefits, risks and costs. In inflammatory myositis there is currently insufficient evidence to support any recommendation with respect to cancer screening. In the absence of clinical guideline and quality evidence, our study aimed to establish the current trends in malignancy screening amongst Australian Rheumatologists.

Objectives: To explore the current trends in malignancy screening in autoimmune myositis amongst Australian Rheumatologists using an online questionnaire.

Methods: Research approval was granted by The Townsville Hospital. An invitation email containing the survey weblink was sent twice to 386 Australian Rheumatologists between August 2015 and August 2016. Voluntary participation and anonymity were guaranteed. The questionnaire contained a fixed set of multiple choice questions that requested data on respondent demographics, practice setting and screening preference, practice and concerns. Open entry comment was an option throughout the questionnaire. Fifty-eight Rheumatologists, 1 Immunologist and 1 Paediatric Rheumatologist responded (16% response rate). There were 3 survey dropouts. The data was pooled, coded and analysed using statistical software. All data was included in the analysis.

Results: Most respondents (N=58) were in private (67%) and/or public practice (68%), in practice for >10 years (70%), conducted cancer screening (93%) and were "very" or "somewhat" confident in their screening practice (90%). The majority (72%) performed cancer screening independent of patient characteristics. Determinants that triggered screening (in descending order of popularity) were: tobacco use (N=11), history of cancer (N=10), age >40 (N=7), cancer family history (N=7), age >50 (N=3) and age >60 (N=1). Most respondents indicated preference to order screening tests (in descending order of popularity): mammogram (81%); CT chest & abdomen (78%); myeloma screen (70%); chest x-ray (69%), serum PSA (67%), PAP smear (54%), colonoscope (44%), LDH (41%), pelvic USS (33%), gastroscope (33%), FOBT (33%), tumour markers (28%), CT neck (17%), nuclear bone scan (15%), PET CT (4%) & testicular USS (2%). Respondents (N=57) indicated that cancer screening was problematic due to a lack of clinical practice consensus & guideline (77%), test selection knowledge (37%) and knowledge regarding repeated screening (53%). The potential for harm in conducting screening was identified to be a problem by most respondents (62%).

Conclusions: The practice of malignancy screening in autoimmune myositis amongst Australian Rheumatologists is highly variable. Practice is driven by patient factors and clinician preferences. The cancer screening process is felt on several fronts to have inherent problems. Guideline, consensus and further research is needed in this area to address the challenges and evidence gap.

References:

[1] Masiak, A et al. (2016). Clinical characteristics of patients with anti-TIF1-y Abs. Reumatologia. 54(1): 14–18.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1148

AB0644 FINGERPRINT ABNORMALITIES IN SYSTEMIC SCLEROSIS: A SINGLE CENTER SURVEY FROM INDIA

K. Chanakya, P.K. Devarasetti, R.V.P. Irlapati, L. Rajasekhar. *Rheumatology, Nizams institute of medical sciences, Hyderabad, India*

Background: Fingerprint [FP] abnormalities are known in patients with Systemic Sclerosis [SSc]. Little has been described about their frequency, systemic associations and social impact in literature.

Objectives: To study the fingerprint abnormalities in Systemic Sclerosis patients

Methods: Raynaud's phenomenon [RP] was taken as the inclusion criteria. Patients with SSc [limited LcSSc and diffuse DcSSc], SSc overlap with other Connective Tissue Diseases [CTDs] and other CTDs with RP were screened for FP abnormalities using a Standardization Testing and Quality Certification (STQC) Directorate certified biometric FP scanner. FP quality assessment was done by recording The National Institute of Standards and Technology [NIST] finger print image quality [NFIQ] scores[1]. NFIQ's 5 levels of quality are intended to be predictive of fingerprint matching. NFIQ=1 indicates high quality samples and NFIQ=5 indicates poor quality samples. Other associated systemic features of

the disease were noted. Also the social difficulties due to fingerprint abnormalities were noted. Healthy controls with no RP were included for comparison.
Results: 40 consecutive patients with RP attending Rheumatology outpatient services of our institute were screened for FP abnormalities. 29 with SSc [20-DcSSc, 9-LcSSc], 8 with overlap syndromes and 1 each of SLE, Undifferentiated Vasculitis and Undifferentiated CTD. It was noted prior to screening that 19 patients experienced some difficulty in the past with biometric recognition of their FPs at various times. On screening with biometric scanner, 15 of 40 [37.5%] had FP abnormalities in the form of non recognition of at least one finger with a median of 2 [range 1–6 fingers]. Of these 15, seven had DcSSc, six had LcSSc and two with overlap syndromes. The mean NFIQ score of these 15 patients was 4.5 [poor] and the mean NFIQ scores in SSc was 3.8. Eleven [27.5%] patients could not get government Identity cards based of FP scanning, four could not avail various government benefit schemes which needed their fingerprints as identity. Sixteen [40%] had history of digital vasculopathy in the form of digital pits, digital ischemia or ulcers. PAH was found in one and eight had Interstitial lung disease. Among the 10 controls all FPs were recognized and the mean NFIQ score was 2.2 indicating a better quality of FPs.
Conclusions: Fingerprint abnormalities occur frequently in patients with systemic sclerosis causing social disabilities in few. The quality of FPs in SSc patients is poor. Raynaud's phenomenon and vasculopathy are frequently associated. Documentation of this abnormality should allow the use of other biometric tools for personal identification.
References:
[1] E. Tabassi, C. Wilson, C. Watson, "Fingerprint Image Quality", NIST Internal Report 7151, National Institute for Standards and Technology, 2004.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3860

AB0645 LYMPHOCYTE SUBSETS T, B AND NK CELLS IN SYSTEMIC SCLEROSIS

L. Schneider[1], V. Hax[1], N. Marcondes[1], R.M. Xavier[2], R. Chakr[1].
[1]Rheumatology; [2]Rheumatologi, HCPA, Porto Alegre, Brazil

Background: Systemic sclerosis (SSc) is a rare multisystem disease with underlying immune mechanisms, whose pathogenesis remains unclear. Few previous reports have evaluated lymphocyte subpopulations in SSc and your results are conflicting.
Objectives: The present study aimed to analyze the lymphocyte subsets in SSc patients in comparison to healthy individuals.
Methods: Peripheral blood (PB) samples to analyze lymphocyte subsets were obtained from a non-random convenience sample of 20 SSc patients. Twenty healthy individuals recruited from the blood bank were used as sex and age-matched controls. Blood samples were analyzed by flow cytometry for total T cells, CD4+ and CD8+ T cells subsets, CD19+ B cells and total NK cells. Statistical analyses were performed using the IBM Statistical Package for Social Sciences (SPSS 18.0). Data are expressed as mean ± SD and median and range. Non-parametric Mann–Whitney U test was used for analyses of the flow cytometry. A probability $p<0.05$ was considered statistically significant.
Results: The mean (SD) age of SSc patients was 57.9 (14.2) years, 95% were female and 31.6% presented diffuse cutaneous SSc (dcSSc). Patients presented a lower mean total lymphocyte count compared to healthy controls (23.7% vs. 29.6%, p=0.026) (Table 1.). No statistically significant differences were found in the percentages or the absolute numbers of T, B or NK cells.

		Patients	Controls	p[a]
Leukocytes		8.02±1.51	6.79±3.39	0.108
Lymphocytes	%	23.53±14.06	29.97±15.08	0.026*
	Absolute	1.70±1.59	2.06±0.03	0.512
CD45	%	99.79±0.11	99.71±0.11	0.165
CD3	%	71.20±3.57	75.11±1.79	0.398
	Absolute	1.35±1.20	1.60±0.07	0.478
CD4	%	48.59±4.09	47.76±8.78	0.289
	Absolute	0.85±0.94	0.99±0.12	0.620
CD8	%	25.10±0.04	28.38±1.19	0.277
	Absolute	0.48±0.29	0.51±0.03	0.301
CD19	%	8.89±11.57	10.44±2.07	0.478
	Absolute	0.20±0.02	0.17±0.03	0.512
NK	%	6.73±8.39	6.71±5.40	0.883
	Absolute	0.14±0.35	0.14±0.09	0.947
Ratio	T/B	8.54±4.11	7.31±2.3	0.383
	CD4/CD8	1.93±0.23	1.73±0.33	0.157

Conclusions: Our data support previous reports indicating that depletion of lymphocyte in the PB of SSc patients. However, we found no significant difference in relation to lymphocyte subtypes, which differs from the literature data.
References:
[1] T and NK Cell Phenotypic Abnormalities in Systemic Sclerosis: a Cohort Study and a Comprehensive Literature Review. Almeida et al, 2015.
[2] Liu M, Wu W, Sun X, Yang J, Xu J, Fu W, Li M. New insights into CD4+ T cell abnormalities in systemic sclerosis. Cytokine & Growth Factor Reviews, 2016; 28:31–36.
[3] Gambichler T, Tigges C, Burkert B, Höxtermann S, Altmeyer P, Kreuter A. Absolute count of T and B lymphocyte subsets is decreased in systemic sclerosis. Eur J Med Res 2010; 15:44–46.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7032

AB0646 DETERMINANTS OF QUALITY OF LIFE IN SYSTEMIC SCLEROSIS AND PATIENT'S PERCEPTION OF THEIR ILLNESS

L. Groseanu[1,2], A. Balanescu[1,2], D. Predeteanu[1,2], D. Opris-Belinski[1,2], V. Bojinca[1,2], I. Saulescu[1,2], A. Borangiu[1,2], D. Mazilu[1,2], C. Constantinescu[1,2], F. Berghea[1,2], R. Ionescu[1,2]. *[1]Internal Medicine and Rheumatology, Sf Maria Clinical Hospital; [2]Department 5- Internal Medicine, University of Medicine and Pharmacy Carol Davila, Bucharest, Romania*

Background: Systemic sclerosis (SSc) is a chronic multi-system autoimmune disease associated with disability and reduced quality of life.
Objectives: The purpose of this study was to assess health-related quality of life and disease perception in a group of SSc patients.
Methods: We performed a case-control study on 50 SSc patients from EUSTAR cohort 096. Socio-demographic data, disease characteristics and self-assessment questionnaires: Health assesment questionnaire (HAQ), EuroQol-5D (EQ5D) and the Brief Illness Perception Questionnaire were collected.
Results: The group included 41 females,31 limited SSc subsets.
Medium HAQ value was 0.9 (0.6). Patients with higher Rodnan score (p=0.002), synovitis (p=0.02), late capillaroscopic pattern (p=0.02), muscle weakness (p=0.001), gastrointestinal involvement (p=0.01) and those on immunosuppressants (p=0.02) have a poor life quality.
According to EQ-5D, the quality of life was related to specific organ involvement. 48% of the patients had some mobility problems, 6% were confined to bed; mobility was influenced by lung involvement (p=0.008), digital ulcers (p=0.03) and Medsger score (p=0.01). 48% of the patients had some self-care problems and 8% were not able to wash/dry themselves; self-care was influenced by the Rodnan score (p=0.02), diffuse subset (p=0.02), muscle weakness (p=0.03) and gastrointestinal involvement (p=0.021). 64% of the patients had some problems in performing usual activities and 16% were not able to perform them; the performance was influenced by disease subset (p=0.01), Medsger score (p=0.02), cardiac involvement (p=0.02) and the use of immunosuppressants (p=0.01). 52% of the patients had some and 38% had extreme pain/disconfort; 66% of the patients were moderately and 20% were extremly anxious/depressed. Both were related to digital ulcers (p=0.01, respectively p=0.045)
The illness had a great impact on patients life 7.3 (2.5)/10. The main determinant was pulmonary fibrosis (p=0.04). The patients consider that their disease will continue for quite a long time 8.7 (2.6)/10. Most of the patiens do not feel to have a good control on their disease 6.3 (3.3)/10 and unfortunately they do not think that the treatment is very helpful 7.9 (2.7)/10. The intensity of the symptoms is quite severe 7.5 (2.7)/10,related to digital ulcers (p=0.04) and gastrointestinal involvement (p=0.02). Patients are very concerned about their disease 9.1 (2.3)/10, most of them being emotionally affected 7.6 (2.6).
Conclusions: This study confirms the presence and magnitude of impaired life quality in patients with SSc with impact on mobility, self-care, usual activities. The major determinants were the extend of skin involvement, musculoarticular, gastrointestinal involvement and digital ulcers. Often patients are anxious/depressed, had a high pain intensity and the perception of this illness is pessimistic.
References:
[1] Hudson M, Canadian Scleroderma Research Group Health-related quality of life in systemic sclerosis: a systematic review. Arthritis Rheum. 2009;61(8):1112–2.
[2] Frantz C et al. Impaired quality of life in systemic sclerosis and patient perception of the disease: A large international survey. Semin Arthritis Rheum. 2016;46(1):115–23.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4178

AB0647 DIAGNOSIS OF SYSTEMIC SCLEROSIS – "A TANGLED STORY"

L. Groseanu[1,2], A. Dima[1], T. Gudu[1], A. Balanescu[1,2], D. Predeteanu[1,2], D. Opris-Belinski[1,2], I. Saulescu[1,2], A. Borangiu[1,2], C. Constantinescu[1,2], D. Mazilu[1,2], M.M. Negru[1,2], F. Berghea[1,2], V. Vlad[1], C. Cobilinschi[2], M. Abobului[1,2], R. Ionescu[1,2]. *[1]Internal Medicine and Rheumatology, Sf Maria Clinical Hospital; [2]Department 5 - Internal Medicine, University of Medicine and Pharmacy Carol Davila, Bucharest, Romania*

Background: Proper diagnosis of scleroderma is often long and difficult, since it is such a rare disease, and one which few doctors or patients are familiar with.
Objectives: To establish the interval between the symptoms' onset of systemic sclerosis (SSc) and what type of investigations are performed until the patients reach the final diagnosis of a rheumatologist
Methods: This is a cross-sectional study that included randomly selected patients with a a diagnosis of SSc which were evaluated based on a questionnaire about symptoms at onset, specific consults and investigations. Descriptive statistics were used.
Results: The study group included 47 patients, of which only 5 were males and 17 from rural areas.The medium age was 53 (14.4) years.

First symptom of onset was Raynaud phenomena 91.3% of the cases, followed by skin changes (56.5%), puffy fingers (52,2%), gastrointestinal and musculoarticular symptoms (23.9% each).
The medium duration between the first symptom and a medical consult was 6 (63.5) months. The first medical consult was done by a internal medicine specialist -38.3%, by a rheumatologist-29.8%, a gastroenterologist-12.8%, a dermatologist-8.5%, a nephrologist and a pneumologist-4.2% and neurologist 2.1%
The first suspected diagnosis was SSc in 14 cases, Raynaud syndrome in 8, connective tissue disease in 5, rheumatoid arthritis in 4, cancer, autoimmune hepatitis, idiopathic pulmonary fibrosis each in 2 cases and none in 10 cases.
The medium number of consults until final diagnosis was 3.4 (1.7). The medium duration from the first symptom until the correct diagnosis was 39.2 (74) months.
The first investigations recommended were blood tests in almost all of the patients (95.7%), but only a third of them included specific scleroderma autoantibodies. Capillaroscopy was performed as an initial diagnostic test in only 6 patients (12.8%). The mean interval from disease onset until the patient was referred to the first capillaroscopy was 13.5 (28.8) months, to specific autoantibodies was 40.17 (61.3) month, to echocardiography was 36.38 (54) months, to lung function tests and lung CT – 41.76 (65.8) months.
There were no significant statistical differences between patients coming from rural environment and those coming from urban environment. The only significant statistical difference between diffuse and limited subset was the time the patient was referred to echocardiography (19.8 (47.6) months for the diffuse subset, 66.8 (94.6) months for the limited subset, p=0.04).
The only statistical difference between males and females was related to the interval that capillaroscopy was performed (14 (20.5)months in females, 4.8 (5) months in males, p=0.02).
Conclusions: Scleroderma is a less well-known disease. This lack of awareness contributes to delayed diagnosis and delayed onset of therapy. Often such diagnostic uncertainty and frustration takes a huge toll on the psychological well-being of these patients, who describe their journey to diagnosis as being one of the most difficult part of their illness. One of our missions as rheumatologist is to increase recognition of this disorder.
References:
[1] https://www.sclero.org/scleroderma/diagnosis/difficult.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3954

AB0648 DISEASE-RELATED AUTOANTIBODY PROFILE IN SYSTEMIC SCLEROSIS IN GREECE

C. Liaskos[1], E. Marou[1], T. Simopoulou[1], M. Barmakoudi[1], G. Efthymiou[1], T. Scheper[2], W. Meyer[2], D.P. Bogdanos[1], L. Sakkas[1]. *[1]Rheumatology and Clinical Immunology, University of Thessaly, School of Health Sciences, LARISSA, Greece; [2]Institute of Immunology, Euroimmun AG, Lubeck, Germany*

Background: Autoantibodies (autoAbs) help in diagnosis and predicting clinical phenotypes in systemic sclerosis (SSc).
Objectives: To determine the clinical utility of 13 SSc-related autoAbs in SSc patients in Greece.
Methods: 131 consecutive patients with SSc (111 female, mean age 58.1±14 years; 49 with diffused cutaneous SSc [dcSSc] and 82 with limited cutaneous SSc [lcSSc]) were analyzed by a multiplex line immunoassay (Euroimmun) for autoAbs against 13 SSc-related antigens. Twenty two patients with primary Raynaud phenomenon (RP), and 22 healthy controls were also analyzed
Results: ANA by indirect immunofluorescence was present in 128 (97.7%) patients with SSc. Excluding anti-Ro52, 113 (89.3%) SSc patients were positive for at least one autoAb: anti-Topo I abs in 54 (41.2%), anti-CENPA in 37 (28.2%, all reactive with CENPB), anti-RNA polymerase III (RP11) in 19 (14.5%), anti-RNA polymerase III (RP155) in 13 (9.9%), anti-fibrillarin in 4 (3.1%), anti-Ku in 6 (4.6%), anti-NOR90 in 8 (6.1%), anti-PM/Scl100 in 2 (1.5%), and anti-PM/Scl75 in 4 (3.1%). There was no immunoreactivity for Th/To or PDGFR. Overall, 102 (77.9%) SSc patients had autoAbs against Topo I, CENPA or CENPB, RP11 or RP155. Anti-Topo I abs were strongly associated with dcSSc, interstitial lung disease (ILD) ($p<0.001$), and pulmonary arterial hypertension (PAH) (p=0.019). Anti-CENB abs were associated with lcSSc, and negatively associated with ILD. Anti-RP11 and anti-NOR90 abs were associated with male gender, and anti-NOR90 associated with ILD. In PR individuals and healthy individuals anti-Ro52 immunoreactivity was found in 9.1% and 13.6%, respectively, but no other immunoreactivity was detected.
Conclusions: Anti-Scl70, anti-CENP and anti-RNA pol III are the most prevalent autoAbs in SSc. Anti-Topo I and anti-NOR90 abs are associated with ILD and/or PAH.
Disclosure of Interest: C. Liaskos: None declared, E. Marou: None declared, T. Simopoulou: None declared, M. Barmakoudi: None declared, G. Efthymiou: None declared, T. Scheper Employee of: Euroimmun AG, W. Meyer Employee of: Euroimmun AG, D. Bogdanos: None declared, L. Sakkas: None declared
DOI: 10.1136/annrheumdis-2017-eular.4641

AB0649 SYSTEMIC SCLEROSIS IN ARGENTINA: EVALUATION OF A SINGLE CENTER COHORT AND COMPARISON WITH INTERNATIONAL SERIES

M. Garcia Carrasco[1], L.O. Roa Prerez[1,2], R. Gomez[1,2], S. Leal[1,2], F. Paniego[1], N. Perez[1], G.G. Nasswetter[1], D. Diana[1]. *[1]Rheumatology Division; [2]Hospital de Clinicas José de San Martín, Buenos Aires, Argentina*

Background: Systemic sclerosis (SS) is an autoimmune disease with generalized vascular dysfunction and a myriad of clinical and laboratory manifestations. Spreading of thickening of the skin, serological characteristics and the pattern of compromise of the internal organs help to classify them as diffuse scleroderma, localized sclerosis and systemic sinus scleroderma. Reports of Latin American cohorts published to date are scarce.
Objectives: To describe the clinical and serological data for a single center cohort and to compare those with national and international cohorts.
Methods: Descriptive, observational, cross-sectional study. We analyzed our SS database. Patients were evaluated since 01/15 to 05/2016 and fulfilled SS classification criteria (ACR 1980/ACR-EULAR 2013).Patients were classified according to Le Roy criteria in Limited Systemic Sclerosis (lSS), Diffuse Systemic Sclerosis (dSS), Systemic Sclerosis sine scleroderma (SsnS) and pre-systemic sclerosis (pSS). Organic compromise was defined as follows: Gastrointestinal (GI): esophagic dismotility by manometry or esophagitis by endoscopy; Lung: Pulmonary hypertension (PH): PSAP>25 mmHg by right heart catheterization; Intersticial Lung Disease (ILD): compatible HRCT or <70% predicted FVC or<80% predicted DLCO; Heart: Left ventricle dysfunction without PH or arterial hypertension, pericardial effusion; Digital ulcers and pitting scars; History of sclerodermic renal crisis (RSC); calcinosis. Anti-Scl-70 was determined by ELISA and anti-Centromere (ACA) by IIF.
Results: 123 patients were included.74% with lSS,24% dSS and 2% SsnS; age at diagnosis (years): 49.7 (18–79 DS: 12.27) and 48.7 (27–79 DS: 13.01) in lSS and dSS respectively. Raynaud's phenomenon previous to diagnosis (years) 7,7 (0–54 DS: 12.81) in lSS and 4.03 (0–22 DS: 5.5) in dSS. 49.5% lSS were ACA positive vs 17% in dSS as well also 41,4% had Scl-70 positive ($p<0.05$). Lung:58.6% of dSS presented ILD and 3,4% RSC, according to published reports. No statistically significant differences were found about the presence of calcinosis, digital tip ulcers or PH between dSS and lSS. GI: was studied in only 39/123 patients with 84,6% affected among those.

Table 1. Comparison of main variables among different cohorts

	Diffuse				Limited systemic sclerosis					
	US, n		EUSTAR, n		Spain, n		Germany, n		Argentina*, n	
	119	128	2838	4481	243	568	484	674	29	91
Oesophageal dysmotility (%)	67	67	70	66	71	57	69	59	31.5	38.5
ILD (%)	63	37	52	11	70	39	56	21	59	22
PH (%)	2	31	6	ND	14	9	19	15	3.4	3.3
RSC (%)	17	2	4	1	8	1	16	9	3	0
Digital ulcers (%)	ND	ND	20	33	64	39	34	24	10.3	5.5
Calcinosis (%)	23	42	ND	ND	24	20	ND	ND	14	19

*HCJSM.

Conclusions: Our data showed similar results to the local and european cohorts. We found fewer calcinosis and digital tip ulcers in both lSS and dSS than international cohorts. A lower prevalence of PH was reported in lSS respect to other series, and it might be atributed to the method wich it was measured. (right heart catheterism).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3520

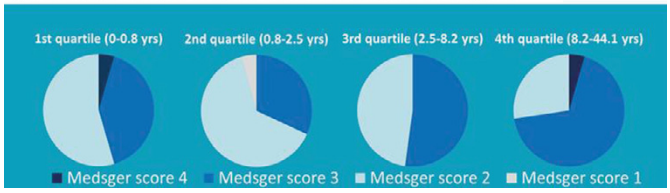
AB0650 ANTI-TOPOISOMERASE POSITIVE SYSTEMIC SCLEROSIS PROGNOSIS INFAUST?

M. Boonstra, G.A. Beerends, H.U. Scherer, J.K. de Vries-Bouwstra.
Rheumatology, LUMC, Leiden, Netherlands

Background: Anti-topoisomerase antibodies (ATA) in systemic sclerosis (SSc) have been associated with poorer prognosis including diffuse skin involvement, pulmonary fibrosis, cardiac involvement and increased mortality. However, 30–60% of ATA-positive SSc patients demonstrate only limited skin involvement and some have only mild disease course. In SSc, optimal risk stratification is of utmost importance for tailored clinical management at the patient level.
Objectives: We aimed to determine the prevalence of mild disease among ATA positive patients and to investigate which readily available clinical parameters best identify patients with highest disease severity.
Methods: Clinical baseline data from SSc patients included in the Combined Care In Systemic Sclerosis (CCIS) cohort of the Leiden University Medical Center were extracted. Patients fulfilling ACR 2013 criteria and ATA positive were included. Descriptive statistics were used to summarize sociodemographic, clinical and serological features. Patients with grade 3 or 4 disease on any of the Medsger severity subscales were considered to be severely diseased. We compared presence of diffuse cutaneous involvement, Raynaud's, pitting scars, calcinosis, proximal muscle weakness, >10% weight loss, interstitial lung disease and pro-BNP between the severity groups and corrected for confounding by disease duration (time since non-Raynaud) by stratifying into quartiles.

Results: Of 422 SSc patients in the database, 344 patients had SSc meeting ACR criteria. 89 patients were exclusively ATA-positive, of which n=42 with mild disease and n=47 with severe disease. Patients with severe disease appeared to be younger (mean age 50 vs 55 yr), more often non-caucasian (51 vs 12%), with a longer time since non-Raynaud (median 4 vs 2 yr) and more often diffuse skin involvement (dcSSc;62 vs 41%), calcinosis (6 vs 0%) and weight loss (23 vs 7%). Stratification by disease duration, however revealed there are no real differences between mild en severe disease. Overall 47% of ATA+ patients in our cohort presented with mild SSc. When stratifying patients according to time of non-Raynaud, 55% of ATA+ patients presented with mild disease in the first disease duration quartile (median follow-up 0.5 years, range 0–0.8 years). In the forth disease duration quartile, according non-Raynaud time (median follow-up 12.7 years, range 8.2–44.1) the percentage with mild disease was still 27% (Figure 1).

Figure 1. Medsger scores of ATA patients stratified by duration non-Raynaud



Conclusions: In our cohort, 47% of ATA-positive patients presented with mild systemic sclerosis, which could not be explained by disease duration. This suggests that solely the presence of ATA is of limited clinical relevance. Readily available sociodemographic and clinical parameters including type of skin involvement seem to have only limited value in identifying ATA patients with more severe SSc. More complex serological findings as antibody titers and fine-specifity of ATA should be defined for optimal serological subsetting.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6414

AB0651 THE EFFECT OF CYCLOPHOSPHAMIDE ON PULMONARY FUNCTION AND DEPENDENCE ON DISEASE ACTIVITY OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH SYSTEMIC SCLEROSIS

M. Vonk[1], W. van den Hombergh[1], H. Knaapen[1], S. Simons[2], J. Fransen[1], F. van den Hoogen[1]. *[1]department of Rheumatology; [2]department of Pulmonology, Radboud University Nijmegen, Nijmegen, Netherlands*

Background: The pathogenesis of interstitial lung disease associated with systemic sclerosis (SSc-ILD) is not completely elucidated, although it is believed that chronic alveolar inflammation leads to increasing fibrosis. Treatment strategies using cyclophosphamide (CYC) have been focusing on the inflammatory pathway of SSc-ILD. We hypothesized that CYC is more effective in patients that are in the early, inflammatory phase.

Objectives: The objectives of this study are to analyze the effects of intravenously CYC pulses (750mg/m^2) on pulmonary function (FVC, DLCO) in SSc-ILD after 12, 24 and 36 months, and whether this effect is dependent on the extent of ILD, the proportion of ground glass compared to fibrosis, SSc disease duration or baseline DLCO <60%.

Methods: Patients with SSc-ILD receiving CYC pulses between 2003 and 2015 were classified by the Goh (2008) criteria in either limited or extensive ILD, using HRCT at baseline independently judged by two raters. Pulmonary function tests were performed at 0, 6, 12, 24 and 36 months. Missing outcome data due to drop-out were replaced by last observation carried forward, except in case of death.

Results: Seventy-five patients were included, 33 with limited ILD, 42 with extensive ILD. There were no baseline differences in age, gender, SSc subtype classification, disease duration or autoantibody status. Mean FVC and DLCO were stable after 12, 24 and 36 months of follow-up (figure 1).

There was no effect in the degree of change in mean FVC and DLCO for the different effect modifiers (table 2): the extent of ILD, proportion of ground glass compared to fibrosis, short SSc disease duration or baseline DLCO <60%.

Conclusions: Mean FVC and DLCO in SSc-related ILD was stable during 36 months of follow-up after cyclophosphamide pulse therapy. The extent of ILD, proportion of ground glass, SSc disease duration and baseline DLCO <60% did not influence the effect of CYC on pulmonary function. CYC did not appeare to be more effective in the early phase of SSc-ILD.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3441

AB0652 EARLY ORGAN INVOLVEMENT, SURVIVAL AND CAUSES OF DEATH IN AN UNSELECTED COHORT OF DUTCH PATIENTS WITH SYSTEMIC SCLEROSIS

M. Vonk, W. van den Hombergh, H. Knaapen, F. van den Hoogen, J. Fransen. *Department of Rheumatology, Radboud University Nijmegen, Nijmegen, Netherlands*

Background: Systemic sclerosis (SSc) patients are at risk for organ involvement and premature death. The occurrence of organ involvement that is reported differs widely between various long term cohort studies; ILD 25–90%, PAH 8–32%, CI 5–30%, and SRC 4–12%. Differences in findings also apply to survival, the 5- and 10-year survival rates between studies vary from 80% to 90% and from 60% to 85% respectively (1–3).

Objectives: To assess the occurrence of organ involvement and death in a large, unselected cohort of Dutch SSc patients at the moment of diagnosis and during 5 years of follow-up, stratified by disease subtype and auto-antibodies.

Methods: Up to 2015, 690 SSc patients were included in the Nijmegen SSc cohort. Occurrence of interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), cardiac involvement (CI), scleroderma renal crisis (SRC) and occurrence of death were determined using survival analysis, stratified by disease subtype (limited cutaneous SSc and diffuse cutaneous SSc) and auto-antibodies (ACA, ATA, anti-RNP).

Results: Organ involvement was already present at SSc diagnosis in 32% of patients. In 25%, organ involvement developed during follow-up, mostly ILD (22%). Significant differences between lcSSc and dcSSc were found in SRC at baseline and ILD, PAH and SRC during follow-up. Between the autoantibody subgroups, the occurrence of ILD, PAH and SRC at baseline and ILD during follow-up differed. There were no differences in survival between subtypes and auto-antibodies. The overall 5-year survival rate was 89%. Patients without organ involvement at SSc diagnosis had a better 5-year survival rate than patients with organ involvement at SSc diagnosis: 95% versus 73% respectively ($p<0.001$). (figure 1)

Conclusions: In many SSc patients, organ involvement is already present at diagnosis or develops in the first 5 years after diagnosis.

Survival is significantly worse in patients who already have involvement at the moment of SSc diagnosis.

References:

[1] Muangchan C, Canadian Scleroderma Research G, Baron M, Pope J. The 15% rule in scleroderma: the frequency of severe organ complications in systemic sclerosis. A systematic review. The Journal of rheumatology. 2013;40(9):1545–56.

[2] Vonk MC, Broers BM, Heijdra YF, Ton E, Snijders R, van Dijk AP, et al. Systemic sclerosis and its pulmonary complications in the Netherlands An epidemiological study. AnnRheumDis. 2008.

[3] Nihtyanova SI, Schreiber BE, Ong VH, Rosenberg D, Moinzadeh P, Coghlan JG, et al. Prediction of pulmonary complications and long-term survival in systemic sclerosis. Arthritis & rheumatology. 2014;66(6):1625–35.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3426

AB0653 EFFICACY OF AN INTENSIVE 24-WEEK PHYSIOTHERAPY PROGRAMME IN MYOSITIS PATIENTS - PRELIMINARY DATA FROM A SINGLE-CENTER CONTROLLED STUDY

M. Spiritovic[1,2], S. Oreska[1], H. Storkanova[1], P. Cesak[2], A. Rathouska[1], K. Kubinova[1], M. Klein[1], L. Vernerova[1], O. Ruzickova[1], R. Becvar[1], H. Mann[1], K. Pavelka[1], L. Senolt[1], J. Vencovsky[1], M. Tomcik[1]. *[1]Department of Rheumatology, 1st Medical Faculty, Charles University, Institute of Rheumatology; [2]Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic*

Background: Involvement of musculoskeletal system (inflammatation, atrophy and permanent damage to the muscle) in idiopathic inflammatory myopathies (IIM) leads to impaired function and reduced muscle strength, endurance, aerobic capacity and decreased quality of life. Data on efficacy of non-pharmacologic care in IIM is very limited due to variety in studied interventions/outcomes.

Objectives: To address the limitations of existing studies, and evaluate the effect of a controlled, long-term (24-week intervention, 24-week follow-up), intensive (1h physiotherapy twice weekly, and home-exercise for 1h 5x weekly), tailored physiotherapy program to improve muscle strength, endurance and deep stabilizer system, and quality of life/disability in cohorts with a substantial number of IIM patients.

Methods: All patients fulfilled the Bohan and Peter 1975 diagnostic criteria for dermatomyositis (DM) or polymyositis (PM), had skeletal muscle involvement, and were consecutively recruited from 2014 to 2016 at the Institute of Rheumatology in Prague. Both groups received educational materials and instructions for home exercise at baseline, however, only intervention group underwent the intensive physiotherapy programme. At months 0,3,6,12 all patients were assessed by a physician [physical examination, Myositis intention to treat index (MITAX), Myositis disease activity assessment visual analogue scale (MYOACT), and Myositis damage index (MDI)], and a physiotherapist blinded to intervention [standardized tests evaluating the level of muscle strength [Manual muscle test-8 (MMT-8)], and endurance [Functional index-2 (FI-2)], patients filled out patient reported outcomes (PRO)/questionnaires [HAQ, SF-36, Beck's depression inventory-II

(BDI-II), PROs assessing nutrition and fatigue], body composition was analyzed using densitometry (iDXA Lunar) and bioelectric impedance (BIA2000-M), and patients provided blood for routine laboratory analysis and biobanking. Normality of data was tested and inter-group analysis performed with 2-way ANOVA and intra-group analysis by Friedmann's test with Dunn's post hoc test.
Results: 27 IIM patients (22 female/5 male, 10 DM/12 PM/5 IMNM (immune mediated necrotizing myopathy), median of age 58.0 and disease duration 7.0 years) were recruited into the intervention group (IG) and 27 patients into the control group (CG) (24 female/3 male, 13 DM/12 PM/2 IMNM, median of age 56.5 and disease duration 4.7 years). Compared to observed statistically significant deterioration in CG over the period of months 0–6, we found statistically significant improvement in FI-2, MMT8, HAQ, BDI-II (Table 1). Only numerical improvement in IG compared to numerical deterioration in CG, which has not reached statistical significance, was observed in SF-36 and fatigue PROs.

Parameter (unit)	Intervention group Mean ± SEM	Control group Mean ± SEM	Intra-group analysis (Friedmann+Dunn)		Inter-group analysis (2WA)
			Interevention gr.	Control group	
MMT-8	m0: 54.7 ± 2.6	m0: 64.2 ± 2.3	m0-m3: p<0.001	m0-m3: p<0.01	p<0.0001
	m3: 60.7 ± 2.4	m3: 58.4 ± 2.0	m3-m6: p<0.01	m3-m6: p=NS	
	m6: 69.1 ± 1.9	m6: 55.3 ± 2.0	m0-m6: p<0.001	m0-m6: p<0.001	
FI-2 (%)	m0: 30.0 ± 4.4	m0: 40.2 ± 5.9	m0-m3: p<0.001	m0-m3: p=NS	p<0.0001
	m3: 46.9 ± 4.7	m3: 30.8 ± 4.9	m3-m6: p<0.001	m3-m6: p=NS	
	m6: 70.6 ± 4.9	m6: 28.7 ± 4.5	m0-m6: p<0.001	m0-m6: p<0.01	
HAQ	m0: 0.91 ± 0.16	m0: 1.25 ± 0.17	m0-m3: p=NS	m0-m3: p=NS	p=0.0012
	m3: 0.69 ± 0.14	m3: 1.33 ± 0.18	m3-m6: p=NS	m3-m6: p=NS	
	m6: 0.56 ± 0.11	m6: 1.27 ± 0.19	m0-m6: p<0.001	m0-m6: p=NS	
BDI-II	m0: 11.9 ± 2.1	m0: 13.3 ± 1.5	m0-m3: p=NS	m0-m3: p=NS	p=0.0186
	m3: 10.7 ± 1.7	m3: 15.2 ± 1.8	m3-m6: p=NS	m3-m6: p=NS	
	m6: 8.9 ± 1.5	m6: 14.6 ± 1.4	m0-m6: p<0.05	m0-m6: p=NS	

Acronyms: SEM, standard error of the mean; Friedmann, Friedmann's test; Dunn, Dunn's post hoc test; 2WA, two way ANOVA, MMT-8, Manual muscle test-8; FI-2, Functional index-2; HAQ, Health assessment questionnaire'BDI-II, Beck's depression inventory-II; m0, month 0 (= at the baseline); m3, month 3 (= in the middle of intervention period); m6, month 6 (= at the end of intervention); p, p-value; NS, not significant

Conclusions: Our intensive 24-week physiotherapy programme led to a significant improvement in muscle strength, endurance, function and depression, which was clinically meaningful in a substantial proportion of patients.
Acknowledgements: Supported by AZV-16–33574A.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4910

AB0654 AN ULTRASOUND ASSESSMENT OF THE HAND AND WRIST IN EGYPTIAN PATIENTS WITH SYSTEMIC SCLEROSIS

M. Hassanien, S. Rashad, A. Aljohee. *Rheumatology Department, assuit, Egypt*

Background: Systemic sclerosis (SSc, scleroderma) is a systemic disease characterized by fibrosis, progressive vascular obliteration and the production of autoantibodies.Ultrasound (US) imaging has advantages of simplicity, low cost, noninvasiveness, real-time capability and portability compared with traditional EDX. US imaging also offers high temporal and spatial resolutions, and can potentially provide dynamic anatomical information regarding local structures and kinesiology, few studies evaluate joint and tendons involvement in SSc by US the incidence and abnormality are differs among studies
Objectives: describe and determine possible correlations between US abnormalities of hand and wrist and clinical findings in SSc Egyptian patients
Methods: Randomly selected 50 Egyptian SSc patients were enrolled in the study in outpatient clinic Rheumatology department, Assuit university hospital. Clinical examination and US evaluation (Gray Scale and Power Doppler (PD)) of the tendons and joints of hands and wrists, were performed bilaterally on both dorsal and palmar sides. Joint assessment was performed on all MCP and PIP joints as well as the wrist and tendon assessment included finger flexors and extensors, wrist extensors and flexors. The scoring for synovitis was based on the EULAR/ OMERACT scoring system
Results: Within the cohort, 100% of the patients were female; mean age and range disease duration were 40.93±11.71 (20–61) years and 8.13±5.56 (0.5–25)years, respectively. Modified Rodnan Skin Score mean and range were 23.17±9.14 (13–43), 22 patients were diffuse type (44%) and 28 patients were limited type (56%), 67% had inflammatory arthralgia as reported by patients. US examination revealed abnormalities in 76% of all cases. Synovitis was present in 74% of patients (22% wrist; 15% MCP/PIP, 63% both); with a grade 2 and 3 synovitis in 29% cases. The grade 2 or 3 synovitis was associated with a higher age ($p<0.05$) and disease duration ($p<0.03$) but not with inflammatory markers (CRP, ESR) and C3 nor with anti-CCP antibodies.
Furthermore, patients with US proven grade 2 or 3 synovitis had interstitial lung disease involvement (ILD) (74%) and elevated systolic pulmonary artery pressure >35 mmHg in (46%). Grade 1 synovitis did not correlate with tenderness or joint swelling. Synovitis using PD abnormalities were present in 20% patients, but only a 25% had concomitant clinical synovitis. Bone erosions (>1mm) were observed in 15%, which located at the second and third MC heads and at the styloid process of the ulna. The presence of bone erosions was associated with the presence of grade 2 or 3 synovitis. US identified tenosynovitis in 40% of patients, involving the wrist extensors in the vast majority of cases (70%), especially of the 2nd extensor compartment.
Conclusions: US examination detects significant synovitis of the hand and wrist in the absence of clinical findings, and reveals structural damage in a number of patients. The grade 2 or 3 synovitis was associated with a higher age, and ILD involvement. Tendon involvement is frequent with specific pattern of wrist extensors. Thus, US seems to be a valuable tool to identify subclinical joint manifestations in Egyptian SSc patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1101

AB0655 ULTRASOUND B-LINES IN THE EVALUATION OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS: CUT-OFF POINT DEFINITION FOR THE PRESENCE OF PULMONARY FIBROSIS

M. Tardella[1], M. Di Carlo[1], M. Carotti[2], E. Filippucci[1], W. Grassi[1], F. Salaffi[1].
[1]*Rheumatology Department, Università Politecnica delle Marche, Jesi;*
[2]*Radiology Department, Università Politecnica delle Marche, Ancona, Italy*

Background: Although in Systemic Sclerosis (SSc) the cutaneous manifestations are the most noticeable features, lung involvement guides the disease prognosis. High resolution computed tomography (HRCT) is the mainstay for the detection of the interstitial lung disease (ILD). However, exposure to ionising radiation is a major limitation for the repetition of this examination. Over the last years, lung ultrasound (US) gained an intriguing potential in the evaluation of several pulmonary condition, and in previous studies was found a significant correlation between US score and HRCT score [1].
Objectives: To establish the cut-off point of the US B-lines number for detecting the presence of SSc-ILD.
Methods: Patients with SSc-ILD underwent chest HRCT, lung US, pulmonary function test, and clinical assessment. Exclusion criteria were represented by the presence of a coexisting congestive heart failure and other lung or pleural diseases (i.e., pneumonia, pleural effusion). HRCT were scored for the presence of ILD by an experienced radiologist, in accordance with the Warrick method. US assessment was performed by a US skilled rheumatologist, blinded to the HRCT results, and included the bilateral evaluation of 14 lung intercostal spaces (LIS) [2]. In each LIS the number of B-lines was recorded and summed. To test discriminant validity we used the receiver operating characteristic (ROC) curve analysis applying a Warrick score of 7 as external criterion for the presence of SSc-ILD.
Results: Forty patients completed the study. The US B-lines number and the Warrick score confirmed an excellent correlation (Spearman's rho: 0.819, $p<0.001$). The ROC curve analysis revealed that the presence of 10 US B-lines is the cut-off point with the greatest positive likelihood ratio (12.52) for the presence of SSc-ILD (Table).

US B-lines number	Sensitivity	95% CI	Specificity	95% CI	+LR	95% CI	–LR	95% CI
≥2	100.00	87.2–100.0	0.00	0.0–24.7	1.00			
>2	100.00	87.2–100.0	15.38	1.9–45.4	1.18	0.3–4.2	0.00	
>3	100.00	87.2–100.0	46.15	19.2–74.9	1.86	1.0–3.3	0.00	
>4	100.00	87.2–100.0	61.54	31.6–86.1	2.60	1.7–4.0	0.00	
>5	100.00	87.2–100.0	69.23	38.6–90.9	3.25	2.3–4.7	0.00	
>8	100.00	87.2–100.0	76.92	46.2–95.0	4.33	3.2–5.8	0.00	
>9	96.30	81.0–99.9	84.62	54.6–98.1	6.26	4.9–8.0	0.044	0.004–0.4
>10	**96.30**	**81.0–99.9**	**92.31**	**64.0–99.8**	**12.52**	**10.5–14.9**	**0.040**	**0.003–0.6**
>11	92.59	75.7–99.1	92.31	64.0–99.8	12.04	10.0–14.6	0.080	0.008–0.8
>14	88.89	70.8–97.6	92.31	64.0–99.8	11.56	9.4–14.2	0.12	0.01–1.0
>15	85.19	66.3–95.8	92.31	64.0–99.8	11.07	8.9–13.8	0.16	0.02–1.3
>16	81.48	61.9–93.7	92.31	64.0–99.8	10.59	8.3–13.4	0.20	0.03–1.5
>19	70.37	49.8–86.2	92.31	64.0–99.8	9.15	6.8–12.2	0.32	0.04–2.3
>20	59.26	38.8–77.6	92.31	64.0–99.8	7.70	5.4–10.9	0.44	0.06–3.1
>21	55.56	35.3–74.5	92.31	64.0–99.8	7.22	5.0–10.5	0.48	0.07–3.3
>22	51.85	31.9–71.3	92.31	64.0–99.8	6.74	4.5–10.0	0.52	0.08–3.6

Conclusions: The detection of 10 B-lines is highly predictive for the HRCT presence of SSc-ILD. In SSc patients, a lung US follow-up can optimize the employment of chest HRCT.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6828

AB0656 NAILFOLD VIDEOCAPILLAROSCOPY FEATURES OF PATIENTS WITH ANTISYNTHETASE SYNDROME

M. Sebastiani[1], V. Codullo[2], A. Manfredi[1], A. Selva O'Callaghan[3], F. Furini[4], A. Iuliano[5], A. Schwarting[6,7], L. Cavagna[2], K. Triantafyllias[7] on behalf of NASCAR Study Group. [1]*Policlinico di Modena, University of Modena and Reggio Emilia, Modena;* [2]*University of Pavia, Pavia, Italy;* [3]*Universidad Autonoma de Barcelona, Barcelona, Spain;* [4]*University of Ferrara, Ferrara;* [5]*Azienda Ospedaliera San Camillo-Forlanini, Roma, Italy;* [6]*University Mainz, Mainz;* [7]*ACURA Rheumatology Clinics, Bad Kreuznach, Germany*

Background: Antisynthetase syndrome (ASSD) is an autoimmune disease characterized by the clinical triad arthritis, myositis, and interstitial lung disease (ILD). As in inflammatory myopathies, nailfold videocapillaroscopy (NVC) alterations have been sporadically described also in ASSD patients, but no elucidating data are available.
Objectives: To investigate the possible specific NVC features of ASSD patients.
Methods: Within the framework of a multicenter study, we retrospectively analyzed NVC images of ASSD patients, after excluding patients with overlap syndrome with systemic sclerosis. Two operators in a blind manner re-evaluated all

patients with at least one image per finger. For each patient, we examined number of capillaries (mean number of capillaries per mm in the distal row), enlarged and giant capillaries, micro-hemorrhages, avascular areas, ramified capillaries, and the presence of a scleroderma (SSc)-like pattern, according to Manfredi et al. Finally, we correlated NVC features with clinical and serological findings of ASSD patients.
Results: The NVC of 54 ASSD patients were analyzed (males/females 1/6.8, mean age 55.79, CI95% 51.9–59.9 years, mean disease duration 59.4, CI95% 27.9–90.9 months). Raynaud's phenomenon (RP) was recorded in 51.9% of patients, arthritis in 79.6%, myositis in 53.7%, and ILD in 92.6%. NVC alterations were observed in 53.7% of AASD patients. Nineteen patients (35.2%) showed a SSc-like pattern; the main features were disarrangement of hairpin and angiogenetic aspects (42.6%), avascular areas (38.9%), giant capillaries (27.6%), and microhemorrhages (20.4%). Finally, the mean number of capillaries was reduced (7.8±2/mm). No significant association was recorded between SSc-like pattern and the presence of arthritis, myositis, and ILD, nor with RP. Among other NVC features, angiogenesis was significantly associated to female gender (p=0.031), while microhemorrhages were inversely associated to the presence of arthritis (0.033). No association was observed between NVC features and autoantibodies profile. Of interest, in 58% of patients with ILD we observed at least a NVC alteration vs no patients without ILD (p=0.04). Finally, in patients with RP NVC alterations were recorded in 15/28 patients (53.6%) and a SSc-like pattern in 11/28 (39.3%), while only 57.9% of patients with SSc-like pattern had a clinically manifest Raynaud's phenomenon.
Conclusions: Despite preliminary, the present is the first study concerning NVC in AASD patients. Regardless of the presence of Raynaud's phenomenon, NVC alterations are frequently observed; in particular, a SSc-like pattern is recorded in more than 1/3 of patients. NVC should be performed in all ASSD patients at diagnosis regardless of the presence of RP in the patient history and during follow-up. ASSD should be always considered in the screening of RP. A prospective multicenter study has been planned to identify specific patterns and possible associations between NVC findings and clinical and serological features of ASSD.
References:
[1] Manfredi A, et al. 2015.
[2] Sebastiani M, et al. 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5376

AB0657 SMALL INTESTINAL BACTERIAL OVERGROWTH IN RELATION TO GASTROINTESTINAL SYMPTOMS IN SYSTEMIC SCLEROSIS

M.D.P. Cruz-Dominguez[1], G. Garcia-Collinot[1], E.O. Madrigal-Santillan[2], A. Carranza-Muleiro[1], L.J. Jara[3], D.H. Montes-Cortes[4], G. Medina-Garcia[1], O. Vera-Lastra[5]. *[1]Research Division, Instituto Mexicano del Seguro Social, Hospital de Especialidades CMN la Raza; [2]Posgrade, IPN, ESM; [3]Research and Education Direction, Instituto Mexicano del Seguro Social, Hospital de Especialidades CMN la Raza; [4]Emergency Room, Hospital General CMN la Raza; [5]Internal Medicine, Instituto Mexicano del Seguro Social, Hospital de Especialidades CMN la Raza, Mexico, Mexico*

Background: Autonomic dysfunction, smooth muscle fibrosis and vascular damage lead to small intestinal bacterial overgrowth (SIBO) in Systemic Sclerosis (SSc). SIBO is characterized by diarrhea, abdominal pain, bloating, malabsorption and malnutrition.
Objectives: To evaluate by NIH PROMIS® gastrointestinal symptoms scales and SIBO by hydrogen breath test (HBT) in patients with SSc.
Methods: We include 68 patients with SSc (ACR-EULAR 2015) who signed informed consent. NIH PROMIS®questionarie was applied to evaluated gastrointestinal symptoms and classified in not symptomatic, least, mildy, moderately and most symptomatic. Glucose HBT was applied after 14 hours fast, oral hygiene and 30 days free of antibiotics. Patients who has a negative HBT with symptoms associated to glucose ingestion we repeat test with lactulose.
Results: We applied questionnaire to 58 SSc patients, age 52 (26–75)years, 65 (96%) female and 3 (4%) males, disease duration 13 (1–40) years, limited SSc 41 (59%) and diffuse 27 (41%), body mass index 24 (12–39).
They are using prednisone (28%), micofenolate (14%), methotrexate (19%), azatioprin (5%), amlodipine or nifedipine (33%). Patients had continuous and very high increase of parts per millon (ppm) of exhaled Hydrogen: min0: 13 ppm (5–21), min15:17 ppm (5–43), min30:17 (3–49), min45:18ppm (7–103), min 60:22ppm (8–145), min90:18ppm (2–250), min120:25ppm (3–212), min150:71ppm (3–235). Normal values: <10 ppm during total test (Figure1).
Frequency of gastrointestinal symptoms were flatulence (87.5vs81.2%), nausea/vomiting (72.7vs37.6%), constipation (65.6vs40%), diarrhea (45.2vs33.4%), abdominal pain %) and incontinence (39.4vs31.3%) respectively between SCB (+) positive and negative.
Hyperproduction of hydrogen in breath had a direct correlation to severity of their symptoms ($p \leq 0.05$). The severity of diarrhea was in close relation to the severity of its rectal incontinence (r=0.73,p=0.001), and greater abdominal pain with flatulence (r=72, p=0.001).
Conclusions: Gastrointestinal symptoms are common in SSc regardless of whether they have SIBO. However, a higher Row Score SGI or moderate severe status (NIH PROMIS) correlates with high H scores from the 30th minute, therefore, the questionnaire is useful within the SSc assessment.

Spearman Correlation Row Score(NIH PROMIS) with ppm H+ Test of SIBO		overgrowth (SIBO)				
		Negative		Positive		
		n=24	%	n=44	%	p
Nausea and vomiting r=0.28*min45,0.29*min60,0.43*min90,0.49*min120,0.46*min150	Asymptomatic	5	9.8%	2	3.9%	
	Least	2	3.9%	2	3.9%	
	Mild	3	5.9%	6	11.8%	0.13
	Moderate	3	5.9%	7	13.7%	
	Severe	4	7.8%	17	33.3%	
Diarrhea, r=0.43*min120	Asymptomatic	3	5.9%	10	19.6%	
	Least	3	5.9%	3	5.9%	
	Mild	5	9.8%	6	11.8%	0.34
	Moderate	5	9.8%	7	13.7%	
	Severe	1	2.0%	8	15.7%	
Constipation r=0.41*min90, 0.47*min120, 0.043*min150	Asymptomatic	0	0.0%	4	8.2%	
	Least	2	4.1%	1	2.0%	
	Mild	8	16.3%	6	12.2%	0.05
	Moderate	2	4.1%	11	22.4%	
	Severe	4	8.2%	11	22.4%	
Abdominal pain r=0.32*m120	Asymptomatic	1	2.0%	0	0.0%	
	Least	7	13.7%	9	17.6%	
	Mild	6	11.8%	8	15.7%	0.16
	Moderate	1	2.0%	4	7.8%	
	Severe	2	3.9%	13	25.5%	
Distension r=0.36*m0,0.35*min15, 0.3*min45,0.37*min60, 0.386*min90,0.36*min120	Asymptomatic	1	2.0%	1	2.0%	
	Least	2	4.0%	1	2.0%	
	Mild	1	2.0%	2	4.0%	0.08
	Moderate	8	16.0%	6	12.0%	
	Severe	5	10.0%	23	46.0%	
Incontinence r=0.28*min45, 0.37*min120	Asymptomatic	8	15.7%	17	33.3%	
	Least	0	0.0%	0	0.0%	
	Mild	5	9.8%	3	5.9%	0.24
	Moderate	2	3.9%	8	15.7%	
	Severe	2	3.9%	6	11.8%	
* p<0.05						

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6824

AB0658 FACTORS INFLUENCING ELAPSED TIME TO A DEFINITIVE DIAGNOSIS OF SYSTEMIC SCLEROSIS AND THEIR RELATIONSHIP WITH THE NUMBER OF ATTENDING PHYSICIANS AND THEIR MEDICAL SPECIALIZATION

Y. Erez[1], H. Yarkan Tugsal[2], G. Kenar[2], B. Zengin[2], D. Solmaz[3], M. Ozmen[3], G. Can[2], N. Akkoc[2], F. Onen[2], M. Birlik[2]. *[1]Internal Medicine; [2]Rheumatology, Dokuz Eylul University School of Medicine; [3]Rheumatology, Katip Celebi University School of Medicine, Izmir, Turkey*

Background: The diagnosis of Systemic Sclerosis (SSc) can be difficult due to its rarity and heterogeneity. In addition, not all physicians are expert in the identification of patients with early SSc features.
Objectives: The aim of this study was to investigate factors influencing the time elapsed since a proper diagnosis of SSc and their relationship with the number of attending physicians and their specialization, among Turkish patients. In Turkish healthcare system,each patient may directly go to the hospitals and choose appropriate care facility and physician.
Methods: The study covers 240 SSc patients who were diagnosed according to 1980 ACR criteria in the rheumatology database at the University of Dokuz Eylul, Izmir. Data included demographics, SSc duration, SSc subtype, physical examinations (mRodnan Score-mRS), and a face-to-face structured interview. Cases were excluded if they couldn't recall date of initial symptoms and all the prior attending physicians including their specialization until a definitive diagnosis of SSc. As clinical characteristics are different than pure SSc patients, overlap syndromes were excluded. Mann-Whitney U test was used to assess the difference between dependent and independent variables. The association between mRS and dependent variables was evaluated by Spearman correlation test.
Results: Remaining 135 patients (F:88.8%), mean age±SD (52.14±11.58 years) identified. 55 (41%) patients had diffuse and 80 (59%) patients had limited disease. 119 (88%) patients SSc diagnosed by a rheumatologist however, 48 patients (35%) were first seen by an internist. Median time to diagnosis was 36 months (1–588) from the onset of Raynaud Phenomenon (RF) and 11 months (0–397) from the onset of the first non-RF symptom for our cases. Relation between some parameters and time to diagnosis were shown in Table.1. Mean number of attending physicians until SSc diagnosis was calculated as 3,54 (SD±1,66). None of the demographic and clinical parameteres (SSc subtype, mRS, symptom duration) were related with the number of attending physician. There was no correlation detected between mRS and time to diagnosis and number of attending physicians. Nevertheless it was established that median number of physicians was less for patients who were referred to a proper clinician by their familier healthcare practitioners (p: 0,019).

Table 1. Time to diagnosis from Raynaud's and first non-Raynaud's symptom onset stratified clinical and demographic parametres

	Time to diagnosis from RF median-months	p	Time to diagnosis from first non-RF median-months	p
Sex				
Female	19 (4-299)	>0,05	11 (0-397)	>0,05
Male	39 (1-588)		15 (0-277)	
Education situation				
Less than highschool	44(0-588)	>0,05	11(0-397)	>0,05
Highschool and more	20(0-288)		14(0-297)	
Scl subtype				
Diffuse	23 (1-299)	***0.013****	11(0-297)	>0,05
Limited	45 (1-588)		11.5(0-397)	
Referred by healthcare practitioner				
Positive	24 (1-349)	>0,05	11(0-191)	>0,05
Negative	42 (1-588)		11(0-397)	
Initial symptom				
RF	49 (0-588)	***0.001***		
RF-non-RF together	21 (0-470)			

RF-non-RF together: less than one year between onset of RF and first non-RF symptom

Conclusions: Time to diagnosis from onset of RF is significantly shorter in diffuse SSc. Although mRS is typically higher in diffuse SSc, no correlation has been found between mRS and time to diagnosis. Therefore, duration of diagnosis may be influenced by internal organ involvement and other complications rather than skin changes due to lack of awareness of physicians about SSc related early skin changes. Referral to a proper physician by a familier healthcare practitioner decreased the number of physicians attending till the diagnosis, although it did not affect the time to diagnosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4645

AB0659 ASSOCIATION BETWEEN -12518A/G GENE POLYMORPHISM ENCODING MONOCYTE CHEMOATTRACTANT PROTEIN 1 (MCP-1) AND SERUM LEVEL OF C-REACTIVE PROTEIN IN DIFFERENT CLINICAL AND SEROLOGICAL PHENOTYPES OF SYSTEMIC SCLEROSIS IN THE RUSSIAN COHORT OF PATIENTS

M. Krylov, L. Ananieva, O. Koneva, M. Starovoytova, O. Desinova, O. Ovsaynnikova, E. Samarkina, A. Novikov, E. Aleksandrova. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Immune system activation with associated up-regulation in the production of extra-cellular matrix proteins by fibroblasts are known specific features in the pathogenesis of systemic scleroderma (SSc). Most recent data indicate that MCP-1 and MCP-3 chemokines from the family of monocyte chemoattractant proteins are also involved into SSc pathogenetic process. C-reactive protein (CRP) is known as the marker of acute-phase inflammation. The association between increased CRP levels and SSc clinical and serological parameters has been reported recently.

Objectives: To study the association between -2518 A/G gene polymorphism, encoding *MCP-1*, and CRP levels in different clinical SSc phenotypes in the Russian cohort of pts.

Methods: PCR-RFLP method was used to identify *MCP-1* genotype in 81 SSc pts aged 49,4±12,6 years, with mean SSc duration 11,1±9,0 years. CRP concentrations were measured with highly sensitive immunoturbidimertry method.

Results: CRP levels were correlated with *MCP-1* genotypes in pts with limited (lcSSc) and diffuse (dcSSc) phenotypes, with interstitial lung disease (ILD+), with SSc duration >3 years, with increased CRP level (>5 mg/L), with positive antibody titers to DNA topoisomerase I (ATA+) and antibody to centromeres (ACA+). A total cohort analysis showed that carriers of -2518AA genotype had higher mean CRP level versus G allele carriers (12,6±7,5 mg/L vs 4,9±4,8 mg/L, respectively, p=0,009), although similar trend was found in dcSSc phenotype (16,4±19,5 mg/L vs 6,1±4,4 mg/L, respectively, p=0,040). In pts with -2518AA genotype and SSc duration >3 years mean CRP level was significantly higher than in G allele carriers (1,1±16,7 mg/L vs 4,5±4,4 mg/L, respectively, p=0,025). In (ILD+) and (ATA+) subgroup pts with -2518AA genotype demonstrated higher mean CRP levels as compared to G allele carriers (12,4±15,6 mg/L vs 5,5±5,1 mg/L, respectively, p=0,018; and 17,6±20,9 mg/L vs 5,5±5,5 mg/L, respectively, p=0,010). CRP levels (>5 mg/L) were found in 31 (38%) pts and were significantly different between AA genotype carriers and G allele carriers (27,4±19,2 mg/L vs 10,4±3,8 mg/L, respectively, p=0,003). No associations between genetic variations in the *MCP-1* gene and CRP levels in lcSSc phenotype, SSc duration <3 years, CRP levels <5mg/L and (ACA+) pts were established.

Conclusions: Our data demonstrate that -2518A/G *MCP-1* gene polymorphism is closely associated with CRP levels, thus, it can be considered as a new marker, reflecting the severity of the disease and unfavorable SSc prognosis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3130

AB0660 CHARACTERISTICS OF AL-I LIGHT-CHAIN AND AMYLOID A DEPOSITION IN PROGRESSIVE SYSTEMIC SCLEROSIS – A COMPARATIVE POSTMORTEM CLINICOPATHOLOGIC STUDY OF 12 PATIENTS

M. Bély[1], Á. Apáthy[2]. *[1]epartment of Pathology, Policlinic of the Order of the Brothers of Saint John of God; [2]Department of Rheumatology, St. Margaret Clinic Budapest, Budapest, Hungary*

Background: Different types of amyloid deposits may be present in systemic sclerosis (SSc), as consequences (complications) of basic or associated diseases.

Objectives: The aim of this study was to determine the type, prevalence and extent of amyloid deposits on different tissue structures in various organs in SSc.

Methods: We studied histopathologically 12 SSc patients (females 11, average age: 54.82 years, range 66–32, onset of SSc: 48.86, average disease duration: 6.43 years; one male, age 65.0 years at death, onset of SSc and average disease duration not known, who died at the National Institute of Rheumatology. SSc was diagnosed clinically according to the criteria of the ACR [1]. In 1 (8.0% of 12) 67 year old female patient (onset of SSc: 66 years, disease duration: 1 year) SSc was accompanied by B-cell lymphoma and complicated by systemic AL-l light-chain amyloidosis. In 1 (8.0% of 12) 53 year old female patient (onset of SSc: 41 years, disease duration: 12 years) SSc was complicated by systemic amyloid A (aA) deposition.

Amyloid deposits on different tissue structures [arteriole, small artery, medium size artery, venule, small vein, medium size vein, interstitial collagen fiber, reticulin fiber (collagen IV), and nerve] of 6 organs [heart, lungs, kidney, gastrointestinal tract, skin and brain] were determined histologically. The extent of amyloid deposition was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale, based on the number of involved tissue structures per light microscopic field [2].

The prevalence and extent of amyloid-l light-chain and amyloid A deposits on different tissue structures were compared by Student (Welch) t-probe.

Results: The involvement of different tissue structures (prevalence in %) and the average extent of AL-l light-chain and amyloid A deposits (absolute value) are summarized in Table 1.

Table 1

Tissue structures	SSc-l Prevalence in %	SSc-aA Prevalence in %	p<	SSc-l Average extent	SSc-aA Average extent	p<
Arteriole	83,33	66,67	0,2749	2,00	1,33	0,1709
Small artery	83,33	66,67	0,1709	2,17	1,00	0,0414
Medium size artery	83,33	66,67	0,1520	2,33	0,67	0,0090
Interstitial collagen	66,67	50,00	0,2998	0,83	0,83	0,5000
Medium size vein	50,00	50,00	0,2735	1,17	0,50	0,1476
Small vein	50,00	50,00	0,5000	0,58	0,50	0,4088
Venule	33,33	33,33	0,5000	0,33	0,33	0,5000
Collagen IV	33,33	16,67	0,2749	0,50	0,33	0,3671
Nerve	0,00	0,00		0,00	0,00	
Average/Structure	53,70	44,44	0,232	1,10	0,61	0,075

Conclusions: In SSc patients the prevalence and extent of l light-chain and amyloid A deposits on different tissue structures changed parallel.

The higher prevalence and extent of l light-chain deposits in contrast to amyloid A may be explained with qualitative differences of l light-chain and amyloid A; l light-chain seems to have greater affinity for tissues than amyloid A protein.

Infiltration of the vessel walls – regarding the amount of l light-chain and amyloid A deposits in arterioles and arteries in contrast to the veins – showed a converse tendency in SSc patients with AL-l or AAa. This may be related to sluggish blood flow or stasis (backward congestion and accumulation of circulating precursors) in both diseases.

References:

[1] van den Hoogen F et al: Ann Rheum Dis 2013; 72:1747–1755 doi: 10.1136/annrheumdis-2013-204424.

[2] Bély M, Apáthy Ágnes: Clinical pathology of rheumatoid arthritis. 1–440 pp. Akadémiai Kiadó, Budapest 2012 http://www.akkrt.hu.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1222

AB0661 ORAL HEALTH-RELATED QUALITY OF LIFE MEASURED WITH OHIP 49 HIGHLY CORRELATES WITH DISEASE ACTIVITY AND SEVERITY IN SYSTEMIC SCLEROSIS PATIENTS

K. Parat[1], M. Radić[2], K. Borić[2], D. Perković[2], D. Biočina Lukenda[1], D. Martinović Kaliterna[2]. *[1]Department of Oral Medicine and Periodontology, Study of Dental Medicine, School of Medicine, University of Split; [2]Division of Rheumatology and Clinical Immunology, Center of excellence for Systemic Sclerosis in Croatia, University Hospital Split, Split, Croatia*

Background: Systemic sclerosis (SSc) is associated with decreased saliva production and interincisal distance, more missing teeth, and periodontal disease. Orofacial manifestations of SSc contribute greatly to overall disease burden and still are regularly overlooked and under-treated. Previous studies did not confirm correlation between disease severity and oral health-related quality of life in SSc patients.

Objectives: The aim of this study was to determine possible correlation of the SSc clinical parameters with oral health-related quality of life measured with the Oral Health Impact Profile 49 (OHIP 49).
Methods: Subjects were recruited from the Center of excellency for systemic sclerosis in Croatia cohort. Detailed dental by the same dentist and clinical examinations were performed according to standardized protocols. Associations between oral health-related quality of life and disease charachteristics were examined. We evaluated the disease severity using clinical and laboratory parameters according to the Medsger Severity Scale. The level of SSc activity was evaluated according to Valentini activity score. Oral quality of life was measured using the OHIP 49, which consists of 49 questions on the frequency of adverse oral conditions such as toothache, mouth pain, difficulty chewing or pronouncing words and discomfort related to appearance (higher scores indicating worse oral health-related quality of life). The study was approved by the University Hospital Split Ethics Committee.
Results: Thirty-one SSc patients (29 women and 2 men, mean age 56.45±13.60 years, median disease duration 7 years with minimum–maximum range 1–28 years) were consecutively enrolled for this study between January 2014 and December 2015. All patients fulfilled the ACR criteria for the diagnosis of SSc. The distinction between limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc) was made according to the Leroy et al. criteria (28 dcSSc, 3 lcSSc). OHIP 49 scores highly positively correlated with disease activity (p=0.005, r=0.4872, Spearman's rank coefficient) and severity (p=0.016, r=0.4303, Spearman's rank coefficient). Furthermore, oral health-related quality of life positively correlated with the skin involvement evaluated by modified Rodnan skin score (p=0.003, r=0. 5207, Spearman's rank coefficient). Impaired quality of oral health positively correlated with the severity of general involvement, skin, gastrointestinal and joint/tendon involvement (p=0.003, r=0.506 for general involvement, p=0.003, r=0.511; $p<0.001$, r=0.591 and p=0.02, r=0.391 for skin, gastrointestinal and joint/tendon involvement, respectively, Spearman's rank coefficient). OHIP 49 score was highly variable between anti-topoisomerase I antibodies positive or negative SSc patients ($p<0.001$, Fisher's exact test).
Conclusions: Contrary to previous studies in our study disease severity and activity were related to OHIP 49 scores. Our data suggest that OHIP scores correlate with severity of general involvement, skin, gastrointestinal, and joint/tendon involvement in SSc patients. Disease subset and autoantibodies profil could play a role in the oral manifestation of SSc. Better collaboration between rheumatologists and the dental team is required to improve access to dental care and oral health outcomes for SSc patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6267

AB0662 SYSTEMIC SCLEROSIS (SSC) COHORT IN ABU DHABI: FOCUS ON DIGITAL ULCERS (DU)

M. Al-Maini[1], H. Al-Mashari[1], T. Khan[1], N. Abutaha[1], R. Aneja[1], A. Las Alas[1], S. Gonuguntla[1], M. Cerinic[2], K. Khawaja[1]. *[1]Adult and Pediatric Rheumatology, Allergy and Immunology, Al-Mafraq Hospital, Abu Dhabi, United Arab Emirates; [2]Rheumatology, University of Florence, Florence, Italy*

Background: DU are a significant burden for SSc patients affecting approximately 40–50% of patients (1). No data are available on the frequency of DU on SSC patients living in the United Arab Emirates.
Objectives: To identify the frequency of DU in a cohort of SSC in Abu Dhabi which is the capital city of the United Arab Emirates (UAE).
Methods: SSC patients identified according to ACR EULAR criteria through the hospital electronic medical records system, which was implemented from January 2011 for medical documentation in all public hospitals in Abu- Dhabi and districts. Using the International statistical classification of diseases and related health problems, usually called by the short form name international classification of Diseases (ICD), version 9 (710.1) from 1st of January 2011 to 31st of December 2016. Retrospective review of electronic medical records and paper case notes was performed on patients who presented during this period. The frequency of DU was searched. DU were defined (1) and categorised (2) (no digital ulcers, episodic (rarely recurrent), recurrent (frequently recurrent) and chronic ($\geq$1 DU at every follow up). Results and the incidence of gangrene were compared to data from DUO registry (3).
Results: 47 SSc patients (Male to female ratio 12 (25.5%) to 35 (74.5%) (Duration of disease from 2 to 24 years with peak age for ulcers between 40–50 years) were identified. No ulcers were detected in 34 patients (72.3%) while DU were found in 13 patients (27.7%): they were episodic in 9 patients (19%) and chronic in 4 patients (8.5%) of the total patients. No recurrent ulcers were found. Only one patient (2%) evolved to gangrene (she was a smoker). The other 12 patients with DU were non-smokers and three of them were under 16 years of age.
Conclusions: In Abu Dhabi SSc population, the incidence of DU is 27.7%. This differs from the incidence in the western literature where it peaks from 40 to 50% (3). Our patients had episodic (19%) and chronic DU (8.5%) of the total patients. The incidence of gangrene in our cohort was lower when compared to the data reported in the DUO registry (20%) (2). Although patients live in a very warm climate, DU are still experienced in SSc in Abu Dhabi. Likely, the chronic exposure to air conditioning may explain this paradox.
References:
[1] Suliman Y et al. Preliminary musculoskeletal ultrasound (MSUS) ulcer definition does not correlate with visual observation in systemic sclerosis (SSc) patients. J. scleroderma relat. disord. 2017 (in press).
[2] Matucci-Cerinic M et al. Elucidating the burden of recurrent and chronic digital ulcers in systemic sclerosis: long-term results from the DUO Registry. Ann Rheum Dis. 2016;75:1770–6.
[3] Allanore Y, Denton CP, Krieg T, etal.Clinical characteristics and predictosof gangrene in patients with systemic sclerosis and digital ulcers in Digital Ulcer Outcome Registry: a prospective, observational cohort. Ann Rheumatic Dis 2016;75:1736–1740.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4828

AB0663 THE RELATIONSHIP OF SERUM LEVEL OF ANTICCP ANTIBODY WITH SEVERITY OF SKIN INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS REFERRED TO TOHID HOSPITAL

N. Moghimy[1], A. Saeidi[2]. *[1]Liver and Digestive Research Center; [2]Master of clinical Psychologist, Kordestan Medical Scienses, Sanandaj, Iran, Islamic Republic Of*

Background: Systemic sclerosis is a chronic systemic disease of unknown etiology. There are a number of autoantibodies that correlated with disease severity and severity of skin involvement (1). Various studies have shown that AntiCCP Ab can also be seen in other autoimmune diseases such as systemic sclerosis (2–4). Results Polimen et al (4) and Morita et al (3) studies showed no relationship was found between AntiCCP Ab with skin Rodnon score.
Objectives: This study aimed to determine the relationship between serum levels of AntiCCP Ab with severity of skin involvement in systemic sclerosis patients referred to Tohid Hospital.
Methods: This study is a cross - sectional study, in the study population included all patients diagnosed with systemic sclerosis according to ACR 1980 criteria and subtypes according to Le Roy, that between 2013 and 2014 referred to Tohid hospital. We used from MRSS index to determine the extent of skin involvement. Sampling was available and we used to determine this association from chi-square statistics and to determine the amount of the connection from Phi statistics. Serum antibodies directed against CCP were assessed by ELISA.
Results: The results showed that the patients who were evaluated at the end of study were 50 patients, of whom 48 were women (96%) and (2%) 2 were male. The mean age of subjects is 38±10 years. The subtype of systemic sclerosis in 15 (%30 percent) of the patients were diffuse systemic sclerosis and 35 patients (%70 percent) have limited systemic sclerosis. Serum Anti CCP Abntibody was positive in 10% (5 patients). Also, there is no statistically significant relationship between the severity of skin involvement with Anticcp Ab (p=0.164).Severity of skin involvement in both groups was more severe form, and there is no statistically significant relationship between the severity of skin involvement and subtypes of systemic sclerosis (p=0.233). Also we didn't find no association between levels AntiCCP and joint symptoms and other symptoms.
Conclusions: In this study wasn't observed a significant correlation between serum levels of Anti CCP Antibody with severity of skin involvement in patients with systemic sclerosis (p=0.164),also serum level of AntiCCP Antibody couldn't as a predict factor to determine the severity of the disease. It seems that the relationship between other symptoms of systemic sclerosis and serum level of AntiCCP Antibody may be result from overlapping with RA.
References:
[1] Shand L, Lunt M, Nihtianovas, Hoseini M, Silman A, Blake M "Relationship between Change in skine score and disease outcome in diffuse cutaneous scleroderma" arthritis rheum 2007 jul:56(7):2422–31.
[2] Marrone M, Chiala A, Tampoia M, Iannone F et al, Prevalence of anti-CCP antibodies in systemic sclerosis, Reumatismo. 2007 Jan-Mar;59(1):20–4.
[3] Morita Y, Moro Y, Sugiura K, Tomita Y "Anti cyclic citrollinated Peptide in Systemic Sclerosis". 2008 jul:26(4):542–7.
[4] Polimeni M, Feniman D, Skare Ts, Nishihara Km "Anti cyclic citrollinated Peptide antibodies in scleroderma patints".clin rheumatal 2012 may;31(5):877–80.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1159

AB0664 LEVEL OF SATISFACTION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

N. Loghin-Oprea[1], S. Vetrila[2], L. Mazur-Nicorici[2], M. Cebanu[3], V. Salaru[4], M. Mazur[1]. *[1]Internal Medicine; [2]Cardiology; [3]Emergency Medicine; [4]Family Medicine, PI SUMPh Nicolae Testemitanu, Chisinau, Moldova, Republic of*

Background: Idiopathic Inflammatory Myopathies (IIM) are the group of rare diseases that carry a significant impact on patient's quality of life, influenced by the level of patient's satisfaction regarding medical services.
Objectives: To assess the patient's satisfaction and quality of life.
Methods: A cross-sectional study was performed from December 2015 to December 2016. There were included consecutive patients that fulfilled the Bohan and Peter[1] criteria for IIM. The collected information was about demographic data, clinical and laboratory findings. The patient's satisfaction was assessed by self-administered Patient Satisfaction Questionnaire (PSQ III)[2], which is a 50-item tool, covering 7 domains: general satisfaction, technical quality,

interpersonal aspects, communication, financial aspects, time spent with doctor, access/availability/convenience. To estimate the quality of life we applied Short Form-8 questionnaire with 8 items for 8 domains and two components: mental and physical.

Results: There were 32 patients enrolled in the study, including 23 females and 9 males, mean age 52.5±14.26 (range 25–78), the disease duration was 8.3±5.3 (range 0.5–12) years. The physical component was lower 37.49±8.49, than the mental component 44.96±6.24 points, we determined that the quality of patient's life was reduced. The PSQ III results were: general satisfaction 20±2.93, technical quality 36.8±5.93, interpersonal aspects 26.50±4.92, communication 19.7±3.25 and access/availability/convenience indicated 44.75±6.29 score. The time spent with doctor was 7±1.15, a border score. The average result in the financial aspects domain was 21.6±6.6, lower than the midpoint scoring (24). We identified correlation between the quality of life and the access/availability/convenience PSQ III domain. For the mental compound the correlation was moderate ($r=0.5$ $p<0.005$) and for physical domain it was weak ($r=0.27$ $p<0.005$), these results can be explained by the fact that patients got accustomed with the disease, but they are more interested in access to care and require increasement of the duration of medical consultation.

Conclusions: Patients with idiopathic inflammatory myopathies have reduced quality of life; however they are satisfied of the medical attendance. The dissatisfaction was with the financial aspect, due to the long-term disease course and high indirect costs.

References:

[1] Bohan A, Peter JB. N Engl J Med 1975 Feb 13;292(7):344–7.
[2] Ware J.Jr. et al. Defining and measuring patient satisfaction with medical care. Eval Program Plann. 1983; 6(3–4): 247–63.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4844

AB0665 ASSOCIATION BETWEEN MICROVACULATURE CHANGES AND PULMONARY INVOLVEMENT IN SYSTEMIC SCLEROSIS: A FOLLOW-UP STUDY

R. Bečvář[1], M. Tomčík[2], J. Štork[3], A. Slováková[4]. *[1]Department of Rheumatology; [2]Institute of Rheumatology; [3]Department of Dermatovenerology; [4]Department of Pneumology, General Teaching Hospital, Praha 2, Czech Republic*

Background: Lung involvement is the major cause of mortality in patients with systemic sclerosis (SSc). Gas transfer (DLCO) and FVC levels have traditionally been used as measures of disease severity and reductions of both parameters have been associated with increased mortality. In SSc repeated attacks of Raynaud's phenomenon lead to the reduced capillary density leads with reduced blood flow and tissue ischemia. Raynaud's phenomenon can occur also in the lungs. Tissue hypoxia usually initiates the formation of new blood vessels from the pre-existing microvasculature. Nailfold capillaroscopy is a safe, noninvasive routine way for the microvascular investigation.

Objectives: The aim of this study was to assess the correlation between capillaroscopic abnormalities and parameters of interstitial lung involvement at baseline and after one year follow-up in patients with SSc.

Methods: All patients underwent routine clinical examination (dyspnea, cough, crepitus), pulmonary function tests, DLCO (alveolitis grade and fibrosis), blood gases and HRCT scan of chest (1). Microvasculature changes were assessed using nailfold videocapillaroscopy (NVC) which was performed by two independent examiners. The obtained images were analysed anonymously by two investigators blinded for the clinical and serum status of SSc patients and classified as early, active and late pattern, non specific or normal picture (2). For statistical evaluation Poisson's correlation coefficient and T-test were used. All examinations were performed at baseline and after 12 months.

Results: Total 42 patients (38 females) were investigated: 30 individuals with limited form, 7 with diffuse form, 3 patients with scleroderma sine scleroderma, 1 with overlap syndrome and 1 with undifferentiated connective tissue disease. The mean age ± standard deviation (SD) of the whole cohort was 51±22 years and the mean disease duration ± SD was 10±7 years. 3 patients (7.5%) had early NVC pattern, 12 patients (30%) had active, 10 (58%) late pattern, and 17 (37.5%) had nonspecific changes or normal picture. The patients with late NVC pattern exhibited more often mild to moderate alveolitis, decreased FEV1 and FVC and DLCO. When correlating NVC patterns with clinical findings, pulmonary function test and HRCT scans we found only an association of low significance with dyspnea and alveolitis grade (both $p<0.1$). After one year follow-up similar results were obtained ($p<0,001$ and $p<0,01$, respectively).

Conclusions: In our study NVC patterns did not seem to correlate with severity of interstitial lung disease in SSc patients even after one year follow-up.

References:

[1] Corrado A et al. Joint Bone Spine. 2010.
[2] Cutolo M et al. J Rheumatol. 2000.

Acknowledgements: This study was performed with support of CMH Research Projects No 00000023728.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2421

AB0666 MYOPATHIES ASSOCIATED WITH SYSTEMIC SCLEROSIS: CLINICAL AND IMMUNOLOGICAL FEATURES FROM A TERTIARY CENTRE COHORT

R. Nichitean, A. Mociran, I. Szabo, L. Damian, I. Felea, S. Siao-Pin, S. Rednic. *Rheumatology, Scju Cluj Napoca, Cluj Napoca, Romania*

Background: Systemic sclerosis (SSc) is a connective tissue disease characterized by skin and internal organ fibrosis due to immune activation, vascular damage and excessive synthesis of collagen [1]. Muscle involvement is still a variable feature, with prevalence from 14% to 79% due to the lack of diagnostic consensus criteria [2].

Objectives: The aim of this study was to characterize the clinical, biochemical and immunological features of SSc patients with muscle involvement and to find any correlations amongst them.

Methods: We retrospectively analysed data for 18 SSc patients with myopathy out of 254 SSc patients followed between 2000 and 2016 in a Romanian academic hospital centre. All patients fulfilled the ACR/EULAR criteria for the diagnosis of SSc and had a history of myopathy. Myopathy was defined as the presence of muscle weakness, myalgia, with creatine kinase (CK) and/or lactate dehydrogenase (LDH) level >2N (two times the upper normal range). Clinical, biochemical and immunological parameters were assessed by descriptive statistics, logistic regression and Chi-square test.

Results: The prevalence of myopathy was 7.0%. General features in myopathy-SSc patients are detailed in Table 1. Male sex represents a risk factor for muscle involvement (OR=38.2, p-value<0.001). The ratio of diffuse subtype to the limited subtype was 0.8. The major organ involvement associated with myopathy was lung fibrosis (55.5%). Most prevalent autoantibody was anti-Scl70 (44.4%). The onset of muscle symptoms occurred within a median of 1.6 years (range 0–12 years) after SSc diagnosis. Among the studied patients, 12 (66.6%) had muscle weakness, and 13 (72.2%) had myalgia. CK and LDH levels were elevated in 16 (88.88%) and 18 (100%) cases, respectively. AST level values were found to be slightly higher than ALT ones but not statistically significant (p-value=0.15). A positive correlation was found between levels of LDH and AST (Pearson coefficient=0.72) and between CK and LDH (Pearson coefficient=0.66). No association was identified with inflammatory parameters.

Table 1.

SSc general data and associated features		Number out of 18 (total) and %
Female sex		12 (66.6%)
Diffuse SSc form		8 (44.4%)
Age at SSc diagnosis		43 ye ars
Digital ulcers		3 (16.6%)
Calcinosis		6 (33.3%)
Autoantibodies	Anti-nuclear	16 (88.8%)
	Anti-Scl70	8 (44.4%)
	Anti-centromere	0
	Anti-RNP	2 (11.1%)
	Anti-PM/Scl	1 (5.5%)
Heart involvement		2 (11.1%)
Lung fibrosis		10 (55.5%)
Scleroderma renal crisis		2 (11.1%)
Arthritis		4 (22.2%)
Oesophagus involvement		6 (33.3%)
Motor weakness		12 (66.6%)
Myalgia		13 (72.2%)

Conclusions: This study emphasizes the fact that male SSc patients are at increased risk of developing myopathy. Although the prevalence of muscle involvement was quite low than reported in other cohort series, the results are similar to the more recent publications [3]. We showed that myopathy occurred more often in anti-Scl70 positive patients and that anti-centromere wasn't present at all. All patients should be carefully assessed for muscle involvement in the first years of SSc diagnosis and screened for lung fibrosis, regardless of cutaneous subtype of the disease.

References:

[1] Systemic sclerosis: current pathogenetic concepts and future prospects for targeted therapy. Lancet 1996; 347:1453.
[2] Paik, J., Mammen, A., Wigley, F. and Gelber A. Myopathy in scleroderma, its identification, prevalence, and treatment: lessons learned from cohort studies. Curr Opin Rheumatol 26: 124–130.
[3] RaB Ranque, A Bérezné, V Le-Guern, C Pagnoux et al. Myopathies related to systemic sclerosis: a case–control study of associated clinical and immunological features. Scand J Rheumatol 2010;39:498–505.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1579

AB0667 CLINICAL AND THERAPEUTIC DIFFERENCES BETWEEN POLYMYOSITIS AND DERMATOMYOSITIS IN A COLOMBIAN COHORT WITH IDIOPATHIC INFLAMMATORY MYOPATHY

R. Fuentes[1], F. Vargas[1], M.A. Alzate[2], D. Hernandez-Parra[2], J.C. Salazar-Uribe[3], P. Ortiz-Salazar[2], R. Pineda[2] on behalf of Artmedica IPS, Medellin, Colombia. *[1]Rheumatology division; [2]Clinical information group, Artmedica IPS; [3]School of Statistics, Faculty of Sciences, National University of Colombia, Medellin, Colombia*

Background: The idiopathic inflammatory myopathies (IIM) are a group of immune-mediated systemic conditions characterized by chronic muscle inflammation, resulting in muscle weakness (1).
Objectives: To characterize the disease in a Colombian cohort with idiopathic inflammatory myopathy, assessing differences in its classification, cutaneous and systemic manifestations, laboratory results, and therapeutic approach, according to the type of myopathy.
Methods: A cross-sectional study was conducted in 112 patients, in whom sociodemographic, clinical and therapeutic characteristics were analyzed based on the type of myopathy. Statistical association was examined by means of Chi-square tests, Mann-Whitney test, and logistic regression analyses.
Results: From the 112 patients recruited, 59 had polymyositis (PM) and 53 had dermatomyositis (DM). The patients were classified with Peter & Bohan criteria as: "definite" diagnosis 67 (60%), "probable" 35 (31%) and "possible" 9 (10%). A high proportion of males were found in this cohort. Our most notable findings are listed in Table 1, noticing for this population a high rate of polyautoimmunity associated to PM (OR 3.81 95%IC 1,003–14,53) and an association between ANAs antibodies positivity and DM (OR 7.03 95%IC 2,16–22,9). Patients with PM presented higher values of CK, LD and transaminases. Also, according to the therapeutic approach, PM was positively associated with the use of azathioprine and immunoglobulins (OR 2,59 95%IC 1,18–5,69 and OR 3,21 95%IC 1,19–8,19, respectively), while chloroquine and hydroxychloroquine were mainly used in DM patients.

Table 1. Sociodemographic and clinical characteristics of Colombian patients with idiopathic inflammatory myopathy

	Polymyositis N=59		Dermatomyositis N=53		p-value
	N	%	N	%	
Female	41	69,5	35	66	0,69
Age (mean)	54,3		49,4		0,09
Clinical characteristics					
Symmetrical muscle weakness	59	100	51	96,2	0,13
Gottron's papules	0	–	49	92,4	**<0.0001**
Heliotrope rash	0	–	35	66	**<0.0001**
Shawl sign/ V sign	0	–	29	54,7	**<0.0001**
Polyautoimmunity	11	18,6	3	5,6	**0,03**
Muscle enzymes in serum					
CK (median)	3825		1012		**0,006**
LD (median)	554		433		**0,003**
ALT (median)	87		46,3		**0,01**
AST (median)	72		38		**0,005**
Aldolase	8	13,5	5	9,4	0,43
Autoantibodies					
ANA (+)	27	45,7	38	71,7	**0,0006**
Anti-Jo1 (+)	2	3,4	2	3,8	0,74
EMG					
Myophatic changes	41	69,5	27	50,9	0,34
Biopsy-proven myopathy					
Positive	30	50,8	16	30,2	0,7

SES, socioeconomic status; CK, creatine phosphokinase; LD, lactate dehydrogenase; AST, aspartate transaminase; ALT, alanine transaminase; EMG, electromyogram.

Conclusions: In this Colombian sample, a high proportion of patients were classified as definite diagnosis, high frequency of male-gender compromise, low association with cancer, and low prevalence of articular, pulmonary and cardiac involvements were found.
References:
[1] Rosa J, Garrot LF, Navarta DA, Saucedo C, Scolnik M, Bedran Z, et al. Incidence and prevalence of polymyositis and dermatomyositis in a health management organization in Buenos Aires. J Clin Rheumatol. 2013;19(6):303–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2966

AB0668 CALCINOSIS CUTIS AND ITS ASSOCIATION OF SERUM LEVELS OF OSTEONECTIN, OSTEONECTIN, NITRIC OXIDE AND TGF-B IN SYSTEMIC SCLEROSIS

R.A. Carranza Muleiro[1,2], M.D.P. Cruz-Domínguez[2], L.M. Apolinar[3], A.A. Reséndiz-Albor[2], A.L. Vázquez-Martínez[3], G. García-Collinot[2], L.J. Jara-Quezada[4], I.M. Arciniega[1]. *[1]Sección de Estudios de Posgrado e Investigación, Escuela Superior de Medicina Instituto Politécnico Nacional; [2]División de Investigación en Salud, Instituto Mexicano del Seguro Social Hospital de Especialidades Centro Medico la Raza; [3]Hospital de Especialidades Centro Medico Siglo XXI Laboratorio de Enfermedades Endocrinológicas, Instituto Méxicano del Segúro Social; [4]Jefatura de Investigación en Salud, Instituto Mexicano del Seguro Social Hospital de Especialidades Centro Medico la Raza, México city, Mexico*

Background: Systemic sclerosis (SSc) is characterized by fibrosis, autoimmunity and vasculopathy. ES is classified subtypes: diffuse (dSSc) and limited (ISSc). More than 35% develop calcinosis. Calcium, phosphorus, parathormone, vitamin D, TGF-β, nitric oxide and osteonectin and osteopontin involved in bone mineralization.
Objectives: The aim was to compare osteonectin (ON), osteopontin (OP), TGF-β, nitric oxide (NO), Paratohormone (PTH), Vitamin D and minerals concentrations in ES with and without calcinosis.
Methods: Cross-sectional study in ES patients (ACR criteria). We quantified OP, ON, TGF-β, ON, Calcium, Phosphorus, PTH and vitamin D in serum by ELISA. We performed descriptive statistics, Student t, Pearson correlation (significance $p<0.05$) in SPSSv21 program.
Results: We included 71 patients, age 52.94 (± 11.47); 28 (40%) with calcinosis (18 dSSc/10 ISSc), and 43 (60%) without calcinosis (13 dSSc/30 ISSc). Biochemical parameters between two groups. In the whole population the higher PCR had moderate positive correlation (r =0.41, p=0.042), and serum calcium level had a moderate negative correlation (r = -0.47, p=0.021); ON increased in direct relation to OP (r =0.3, p=0.014) and the serum levels of VitD had lower indirect relation with the evolution time of SSc (r = -0.28, P=0.025) and the ON increase in direct relation to serum creatinine (r =0.039, p=0.006).
Conclusions: Patients with a longer time evolution of SSc have less serum levels of VitD and those with higher inflammation (PCR) have a higher TGF-β than a potent inducer of fibrosis. PCR and TGF-B have a moderate direct correlation, PCR and Calcium have moderate indirect correlation, ON and OP have a low direct correlation, VitD and evolution of diseases (years) had a low indirect correlation and NO and creatinine had a very low direct correlation.
References:
[1] Fueki H, Hino R, Yoshioka M, Nakamura M, Tokura Y.Calcinosis cutis associated with primary Sjogren's syndrome: strong expression of osteonectin and matrix Gla protein.Rheumatology (Oxford) 2011; 50(12):2318–20.
[2] Kim SY, Choi HY, Myung KB, Choi YW.The expression of molecular mediators in the idiopathic cutaneous calcification and ossification. J Cutan Pathol 2008; 35(9):826–31.
[3] Ahmed S, O'Neill KD, Hood AF, Evan AP, Moe SM. Calciphylaxis is associated with hyperphosphatemia and increased osteopontin expression by vascular smooth muscle cells. Am J Kidney Dis 2001;37(6):1267–76.
[4] Kawakami T, Soma Y, Mizoguchi M, Saito R. Immunohistochemical expression of transforming growth factor beta3 in calcinosis in a patient with systemic sclerosis and CREST syndrome. Br J Dermatol. 2000;143(5):1098–100.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5603

AB0669 THE EULAR SYSTEMIC SCLEROSIS IMPACT OF DISEASE (SCLEROID) SCORE – A NEW PATIENT-REPORTED OUTCOME MEASURE FOR PATIENTS WITH SYSTEMIC SCLEROSIS – PRELIMINARY RESULTS FROM THE ONGOING VALIDATION STUDY

R. Dobrota[1], M. Becker[1], K. Fligelstone[2], J. Fransen[3], A. Kennedy[4], Y. Allanore[5], P. Carreira[6], L. Czirjak[7], C. Denton[8], R. Hesselstrand[9], G. Sandqvist[9], O. Kowal-Bielecka[10], M. Matucci Cerinic[11], C. Mihai[12], A. Gheorghiu[12], U. Müller-Ladner[13], M. Vonk[3], T. Heiberg[14], O. Distler[1]. *[1]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [2]FESCA, London, United Kingdom; [3]Department of Rheumatology, Radboud University Medical Center, Nijmegen, Netherlands; [4]FESCA, Dublin, Ireland; [5]Department of Rheumatology, University Paris Descartes and Cochin Hospital, Paris, France; [6]Division of Rheumatology, Hospital 12 de Octubre, Madrid, Spain; [7]Department of Immunology and Rheumatology, Faculty of Medicine, University of Pécs, Pécs, Hungary; [8]Centre for Rheumatology, Royal Free and University College London Medical School, Royal Free Campus, London, United Kingdom; [9]Department of Rheumatology, Lund University, Lund, Sweden; [10]Department of Rheumatology and Internal Medicine, Medical University of Bialystok, Bialystok, Poland; [11]Department of Rheumatology, University of Florence, Florence, Italy; [12]Department of Internal Medicine and Rheumatology, Cantacuzino Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [13]Department of Rheumatology and Clinical Immunology, Justus-Liebig University Giessen, Kerckhoff-Klinik Bad Nauheim, Bad Nauheim, Germany; [14]Department of Health and Social Sciences, Oestfold University College, Oslo, Norway*

Background: Patient reported outcome measures (PROM) are required as key outcomes in therapeutic trials in systemic sclerosis (SSc). Given the unmet need of a validated, comprehensive PROM in SSc, the ScleroID questionnaire was developed by a team of patients with SSc and medical experts in the field. This is intended as a brief, disease-specific, patient-derived, disease impact score for scientific and clinical use in SSc.
Objectives: To present a preliminary analysis from the ongoing ScleroID validation study.
Methods: This EULAR-endorsed project involves 11 European centers special-

Abstract AB0669 – Table 1

ScleroID weighting (out of a total of 100 points)	Raynaud phenomenon	Hand function	Upper gastrointestinal tract symptoms	Pain	Fatigue	Lower gastrointestinal tract symptoms	Limitations of life choices and activities
Median (IQR)	15 (20)	10 (15)	6 (10)	10 (10)	10 (10)	5 (10)	5 (10)

ized in SSc. Patients fullfilling the ACR/EULAR 2013 criteria were prospectively included since 05/16 in the ongoing observational cohort study. Patients filled in the ScleroID questionnaire (Figure 1), as well as selected comparators SHAQ, EQ5D, SF36. Additionally, they weighted the 10 dimensions of the ScleroID by distributing 100 points according to the perceived impact on their health. The final score calculation will be based on the ranking of the weights. The study includes a reliability arm (follow-up questionnaire 7–10 days from baseline), as well as a longitudinal arm, looking at sensitivity to change at follow-up visits after 6 and 12 months from baseline.

Results: As of 01/2017 the study cohort included 224 patients with valid baseline data, 44 also had a reliability visit and 6 a 6-months follow-up visit. 84.4% of patients were female, 54.4% had limited SSc, median age 58, and median disease duration 8 years. The highest preliminary median weights for ScleroID domains were for Raynaud, impaired hand function, fatigue and pain (Table 1). Except for pain, these dimensions were also scored most highly in the ScleroID questionnaire at baseline.

The EULAR Scleroderma Impact of Disease Score (ScleroID)

How much have the different aspects of systemic sclerosis affected you during the last week? Please mark your responses on the scale by choosing the appropriate number for each of the following dimensions:

Raynaud's phenomenon:
Circle the number that best describes the severity of your Raynaud's phenomenon during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Hand function:
Circle the number that best describes your hand function limitations due to your systemic sclerosis during the last week:
No limitation 0 1 2 3 4 5 6 7 8 9 10 Extreme limitation

Upper gastrointestinal tract symptoms (e.g. swallowing difficulties, reflux, vomiting):
Circle the number that best describes the severity of your upper gastrointestinal tract symptoms due to your systemic sclerosis during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Pain:
Circle the number that best describes the pain you felt due to your systemic sclerosis during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Fatigue:
Circle the number that best describes the impact of overall fatigue due to your systemic sclerosis during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Lower gastrointestinal tract symptoms (e.g. bloating, diarrhea, constipation, anal incontinence):
Circle the number that best describes the severity of lower gastrointestinal tract symptoms during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Limitations of life choices and activities (e.g. social life, personal care, work):
Circle the number that best describes how severe the limitations of life choices and activities due to your systemic sclerosis were during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Body mobility:
Circle the number that best describes how much your body mobility was affected due to your systemic sclerosis during the last week:
Not affected 0 1 2 3 4 5 6 7 8 9 10 Extremely affected

Breathlessness:
Circle the number that best describes how severe your breathlessness due to systemic sclerosis was during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Digital ulcers:
Circle the number that best describes how much your digital ulcers affected you overall during the last week:
None 0 1 2 3 4 5 6 7 8 9 10 Extreme

Conclusions: The EULAR ScleroID score is a novel tool designed for use in clinical practice and clinical trials to display the disease impact of SSc. In this preliminary analysis, Raynaud syndrome, impaired hand function, and fatigue were the main patient reported drivers of disease impact, however, further recruitment and validation of this new instrument is ongoing.

Disclosure of Interest: R. Dobrota: None declared, M. Becker: None declared, K. Fligelstone: None declared, J. Fransen: None declared, A. Kennedy: None declared, Y. Allanore Grant/research support from: Grant/research support from: Bristol-Myers Squibb, Roche/Genentech, Inventiva, Pfizer, Sanofi, and Servier, Consultant for: Actelion, Bayer, Roche/Genentech, Inventiva, Medac, Pfizer, Sanofi, Servier, and UCB, P. Carreira: None declared, L. Czirjak: None declared, C. Denton: None declared, R. Hesselstrand: None declared, G. Sandqvist: None declared, O. Kowal-Bielecka: None declared, M. Matucci Cerinic: None declared, C. Mihai: None declared, A. Gheorghiu: None declared, U. Müller-Ladner: None declared, M. Vonk: None declared, T. Heiberg: None declared, O. Distler Grant/research support from: 4 D Science, AbbVie, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, iQone Healthcare, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm and Sinoxa, Consultant for: 4 D Science, AbbVie, Actelion, Active Biotec, Bayer, BiogenIdec, BMS, Boehringer Ingelheim, ChemomAb, EpiPharm, espeRare foundation, Genentech/Roche, GSK, Inventiva, iQone Healthcare, Lilly, medac, Mepha, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Pfizer, Sanofi, Serodapharm and Sinoxa

DOI: 10.1136/annrheumdis-2017-eular.4975

AB0670 CLINICAL AND LABORATORY MANIFESTATIONS OF RNP-POSITIVE PATIENTS WITH SYSTEMIC SCLEROSIS

L.P. Ananyeva, R.U. Shayakhmetova, O.A. Koneva, M.N. Starovoitova, O.V. Desinova, O.B. Ovsyannikova. *Department of vasculopathy, V.A.NASONOVA Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Among patients, who meet the classification criteria for systemic sclerosis (SSc), there are the patients without specific SSc anti-nuclear antibodies and who are positive for antibodies to ribonucleoprotein (RNP). The clinical significance of the RNP antibodies in SSc is not clear.

Objectives: To investigate clinical and laboratory characteristics of SSc patients positive for antibodies to RNP.

Methods: The study included 52 patients (49 women and 3 men, mean age 44.2±15 years, median disease duration from the beginning of Raynaud's phenomenon 11.2±7years) who met the classification criteria of SSc (ACR/EULAR 2013) and have high level (>200 U/ml) of antibodies to RNP-70 (determined by ELISA, range 0–25 U/ml). Clinical, laboratory, and immunologic data were collected on all patients.

Results: All the patients met the criteria for classification of SSc ACR/EULAR 2013 (table 1). Other prevalent clinical manifestations were gastroesophageal reflux in 63, 5% of patients, joints involvement in 58%, myositis in 30, 7%, serositis in 27.5% (including 23% of pericarditis). All patients were positive for antinuclear factor (Hep-2) and in some cases RF, anti-SS-A, anti-SS-B, anti-Sm and anti-dsDNA antibodies were identified. The increased levels of CRP and/or ESR were found in 56% of cases. Among the SSc patients, there were 38 (73%) who satisfied for the classification criteria for mixed connective tissue disease (MCTD) proposed by Kasukawa et al. (1987).

Table 1. Frequency of items of SSc classification criteria (ACR/EULAR 2013) in the group under study

Items	52 patients
Skin thickening of the fingers extending proximal to the metacarpophalangeal joints	9 (17,3%)
Skin thickening of the fingers:	41 (78,8%)
puffy fingers	29 (55,7%)
sclerodactily	14 (27%)
Fingertip lesions	22 (42,3%)
Telangiectasia	25 (48%)
Abnormal nailfold capillaries	45 (86,5%)
Lung involvement:	37 (72%)
Pulmonary arterial hypertension	2 (4%)
Interstitial lung disease	35 (68%)
Raynaud's phenomenon	52 (100%)
SSc-related autoantibodies:	12 (23%)
ACA	4 (7,7%)
Anti-Scl-70	8 (15,4%)

Conclusions: In the group under study the limited form of SSc dominated, with high frequency of the different manifestations of vasculopathy, esophagus, joint and muscle disorders symptoms. A subtype of RNP-positive SSc patients often met the criteria for MCTD. This fact makes it reasonable to discuss the possibility of overlap-syndrome between these two diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6297

AB0671 INCREASED BODY FAT BUT DECREASED LEAN BODY MASS AND BONE MINERAL DENSITY IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES ARE ASSOCIATED WITH DISEASE DURATION, INFLAMMATORY STATUS, SKELETAL MUSCLE INVOLVEMENT AND PHYSICAL ACTIVITY

S. Oreska[1], M. Spiritovic[1,2], P. Cesak[2], O. Marecek[2], H. Storkanova[1], K. Kubinova[1], M. Klein[1], L. Vernerova[1], O. Ruzickova[1], R. Becvar[1], K. Pavelka[1], L. Senolt[1], H. Mann[1], J. Vencovsky[1], M. Tomcik[1]. *[1]Department of Rheumatology, 1st Medical Faculty, Charles University, Institute of Rheumatology; [2]Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic*

Background: Idiopathic inflammatory myopathies (IIM) are characterized by inflammation and atrophy of skeletal muscles, pulmonary and articular involvement, which limit the mobility/self-sufficiency of patients, and can have a negative impact on body composition.

Objectives: To assess body composition and physical activity of IIM patients and healthy controls (HC).

Methods: 54 patients with IIM (45 females/9 males; mean age 57.3; disease duration 5.8 years; polymyositis (PM,22)/dermatomyositis (DM,25)/necrotizing

myopathy (IMNM,7)) and 30 age-/sex-matched HC (25 females/5 males, mean age 54.9) without rheumatic/tumor diseases or manifest cardiovascular event were included. PM/DM patients fulfilled Bohan/Peter criteria for PM/DM. Anthropometric parameters and body composition were assessed (by densitometry-iDXA Lunar, and by bioelectric impedance-BIA2000-M), and physical activity was evaluated using Human Activity Profile (HAP) questionnaire. Routine biochemistry analysis was performed after 8 hours of fasting. Muscle involvement was evaluated by manual muscle test (MMT)-8. Data are presented as mean±SD.

Results: Compared to HC, patients with IIM had significantly increased body fat % as assessed by iDXA (BF%: 38.7±6.7 vs. 42.5±7.1%, p=0.015), but decreased lean body mass as assessed both by iDXA (LBM: 45.7±6.6 vs. 40.3±7.0 kg, p=0.0005) and BIA (LBM: 53.2±8.5 vs. 48.7±9.0 kg, p=0.0295), and increased ECM/BCM ratio (extracellular mass/body cell mass: 1.00±0.12 vs. 1.43±0.42, p<0.0001), which reflects worse muscle predispositions for physical exercise, aerobic fitness/performance, and also increases with deteriorating nutritional status. Compared to HC, IIM patients had significantly lower bone mineral density (BMD: 1.16±0.10 vs. 1.05±0.11 g/cm^2, p=0.0010), and were currently able to perform less energetically demanding physical activities according to HAP score (86.3±5.9 vs. 49.0±20.2, p<0.0001). Disease duration negatively correlated with BMD (r=-0.392, p=0.004) and LBM-BIA (r=-0.272, p=0.047). CRP was positively associated with BF% assessed both by DEXA (r=0.276, p=0.035) and BIA (r=0.306, p=0.025). MMT-8 score negatively correlated with ECM/BCM ratio (r=-0.385, p=0.006), and physical activity (HAP) negatively correlated with BF%>DEXA (r=-0.292, p=0.032).

Conclusions: Compared to healthy age-/sex-matched individuals we found significant negative changes in body composition of our IIM patients, which are associated with their disease duration, inflammatory status, skeletal muscle involvement, and physical activity, and could reflect their impaired nutritional status and predispositions for physical exercise, aerobic fitness and performance.

Acknowledgements: Supported by AZV-16–33574A, GAUK-214615.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4824

AB0672 RISK FACTORS AND TREATMENT OF RECURRENT DERMATOMYOSITIS AND POLYMYOSITIS

S. Yamada, H. Yamashita, Y. Takahashi, H. Kaneko. *Division of Rheumatic Diseases, National Center for Global Health and Medicine, Tokyo, Japan*

Background: Patients with polymyositis (PM) and dermatomyositis (DM) often have repeated exacerbations of myositis. Sometimes immunosuppressive agents are added to induce remission in steroid-resistant cases, with steroid reduction in maintenance therapy, and to prevent exacerbations. However, comparative clinical studies are difficult to conduct and the appropriate immunosuppressive agents are not known [1–2]. There are also no studies of the treatment in recurrent cases with repeated relapses.

Objectives: In this study, we defined myositis that relapses more than once as recurrent myositis and examined its risk factors and re-induction treatments.

Methods: Patients from our PM and DM database who were hospitalised between January 1991 and September 2016 were reviewed. We included only patients who had been followed for more than 1 year.

Results: There were 14 cases (13.1%) with recurrent myositis. The average observation period was 11.3 and 8.0 years in the relapsing and non-relapsing groups, respectively (P =0.18), and the average ages at onset were 46.2 and 55.0 years (P =0.17). The myositis relapse rate was significantly higher in the anti-aminoacyl-tRNA synthetase (ARS) antibody-positive group than in the group with other antibodies [8/24 (33.3%) *vs.* 0/14 (0.0%) cases; P =0.02]. The myositis relapse rate was significantly lower in the group in which one more immunosuppressive agent was combined in the initial treatment than in the group without any [3/53 (5.7%) *vs.* 11/48 (22.9%) cases; P =0.02]. The myositis relapse rate did not differ significantly between DM and PM, men and women, the groups with or without malignancy, the groups with or without interstitial pneumonia (IP), and groups with or without the following initial findings: fever, joint pain, dysphagia, constipation, bedridden, muscle pain, distal muscle weakness, cutaneous symptoms (*e.g.*, heliotrope rash, Gottron's sign, V signs, Raynaud's phenomenon, skin ulcers and necrosis, and itching sensation), cardiac complications, hypertension, diabetes, and smoking history. There was no significant difference in the serum creatine kinase and C-reactive protein between the relapse and no-relapse groups. Only 3 of 14 cases (21.4%) had successful re-remission induced and were on maintenance therapy. In two of these cases, two immunosuppressive agents other than glucocorticoid were added: tacrolimus and methotrexate in one and tacrolimus and mycophenolate mofetil in the other. The other 11 patients were treatment-resistant.

Conclusions: The presence of anti-ARS-antibody and initial treatment with glucocorticoid only (without any other immunosuppressive agent) were the only two risk factors for recurrent myositis; none of the other factors examined were significant. Recurrent myositis is often treatment-resistant; if one immunosuppressive agent cannot introduce remission, it is worth trying two agents.

References:

[1] Gordon PA, et al: Immunosuppressant of relapses and immunomodulatory treatment for dermatomyositis and polymyositis. Cochrane Database Syst Rev 2012; 15(8):CD003643.

[2] Dalakas MC, et al: A controlled trial of high-dose intravenous immune globulin infusions as treatment for dermatomyositis. N Engl J Med. 1993 Dec 30;329(27):1993–2000.

Acknowledgements:.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2529

AB0673 TESTING FOR ANTIBODIES SPECIFIC TO FIBRILLARIN (U3 RNP) SHOWS ADDED VALUE FOR DIAGNOSIS OF SYSTEMIC SCLEROSIS

I. Gehring[1], S. Sjölander[2], P. Höpfl[1], S. Swiniarski[1], L. Vinderslev Iversen[3], G. Gallo[4]. *[1]Thermo Fisher Scientific, Freiburg, Germany; [2]Thermo Fisher Scientific, Uppsala, Sweden; [3]Department of Dermatology, Aarhus University Hospital, Aarhus, Denmark; [4]Thermo Fisher Scientific, Milano, Italy*

Background: Systemic sclerosis (SSc) is a heterogeneous and often systemic autoimmune disorder characterised by specific autoantibody subsets. The disease is associated with anti-nuclear antibodies (ANA) and the detection of each of the autoantibodies is useful during diagnosis. Most SSc patients are positive for anti-centromere or anti-Scl70 antibodies. The presence of more rare antibodies to, e.g. Fibrillarin (U3 RNP), RNA-polymerase III and PM-Scl are often indicative of a systemic or a limited skin involvement.

Objectives: In this in-house study the prevalence, and clinical sensitivity and /specificity of anti-Fibrillarin antibodies in a subset of patients diagnosed with SSc was investigated. The major aim was to find out whether Fibrillarin testing would identify patients which are negative for standard parameters and therefore add value forin the diagnosticis workup for patients with suspected SSc.

Methods: Sera from 187 SSc patients, 53 blood donors and 177 disease controls were analysed for the presence of antibodies to CENP, Scl-70s, PM-Scl, RNA Pol III and Fibrillarin using the EliA platform (Thermo Fisher Scientific, Freiburg, Germany).

Results: In 149 out of the 187 patients one or more of the tested parameters were detected. Fibrillarin was identified in 7 out of the 149 patients including 6 solely positive for Fibrillarin. Overall sensitivity within this study is 79,68% with an overall specificity of 92,17%; for Fibrillarin sensitivity of 3,74% and specificity of 98,70% was shown within this cohort.

Conclusions: Increased diagnostic sensitivity was shown in this cohort of 187 patients with SSc by adding the analysis of antibodies against Fibrillarin. Testing allowed additional identification of 6 SSc patients which correlates to an increase of 3,74% in sensitivity.

References:

[1] Arthritis Res Ther 2003, 5:80–93.

[2] Rheumatology 2001;40:1157–1162.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4685

AB0674 YKL-40 IS THE BIOMARKER FOR THE PRESENCE OF INTERSTITIAL PNEUMONIA AND PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS

T. Furukawa, K. Matsui, M. Kitano, Y. Yokoyama, M. Sekiguti, N. Azuma, H. Sano. *Division of Rheumatology, Department of Internal Medicine, Hyogo College of Medicine, Nishinomiya, Japan*

Background: SSc is a refractory of connective tissue disease that causes fibrosis of the skin and various organs. Recently, it is attention to 2013 ACR/EULAR classification criteria because can diagnose early phase before causing skin involvement in SSc. Thus, we considered that YKL-40 which is known to be involved in inflammation, tissue fibrosis and remodeling, is useful marker for evaluating early diagnosis and complications in SSc. YKL-40 is a chitinase-like protein and expressed in the synovial membrane and cartilage fibroblast cells in Rheumatoid Arthritis. Several cases of relationship between SSc and YKL-40 have been reported overseas, but it is unclear. Our report is the first in Japan.

Objectives: We investigated serum YKL-40 levels and examined immunohistochemistry (IHC) with YKL-40 of cutaneous tissue in SSc patients. To clarify YKL-40 is useful biomarker in early diagnosis in the presence or absence of complications in Japanese SSc patients.

Methods: Between August 2014 and March 2016, we treated 57 SSc patients in our department. We excluded infection, malignant disease, and other active complication may be a factor that increases YKL-40 levels. The patients were divided into 4 groups depending on whether suffered IP or PAH, which can affect the prognosis. Group1 (n=30) did not suffer from either IP or PAH, Group2 (n=12) suffered from IP, Group3 (n=7) suffered from PAH, and Group4 (n=8) suffered from both IP and PAH. YKL-40 levels in 4 groups and a control group of healthy individuals (n=13) were measured by ELISA. And age percentile strata of YKL-40 were calculated because serum YKL-40 levels have reported to rise with age; YKL-40 age percentile = $100/(1 + (\text{Serum YKL-40 levels}^{-3}) \times (1.062^{\text{age}}) \times 5000)$. IHC with YKL-40 of skin biopsy tissue from patients and controls was performed to investigate YKL-40 expression.

Results: YKL-40 age percentile were elevated in Group1 compared to controls (42.0±24.5 vs 21.8±15.6), and were elevated due to complications (Group2, 3, 4: 61.8±21.4, 88.9±8.2, 94.4±8.7), with a tendency for PAH to cause greater elevation. There was no significant difference between Group3 and Group4, and

a significant difference was found between the other groups ($p<0.05$). IHC with YKL-40 revealed staining of the vessels in the superficial dermis in SSc and normal skin remained unstained. The ROC curve for PAH showed an AUC=0.959, and the most valid cut-off levels of YKL-40 age percentile was 85.2 (sensitivity 86.7% and specificity 92.8%).

Conclusions: Our report is the first report of IHC with YKL-40 in SSc. IHC suggest that YKL-40 may be further elevated by angiogenesis caused by microcirculatory damage in SSc. Our results suggest that YKL-40 may be very useful biomarker for diagnosing SSc and complications associated with microvascular lesions.

References:

[1] Cross-sectional evaluation of *YKL-40* serum concentrations in patients with systemic sclerosis. Relationship with clinical and serological aspects of disease. La Montagna G, D'Angelo S, Valentini G. J Rheumatol. 2003;30(10): 2147–51.

[2] High serum levels of *YKL-40* in patients with systemic sclerosis are associated with pulmonary involvement. Nordenbaek C, Johansen JS, Halberg P, et al. Scand J Rheumatol. 2005;34(4):293–7.

[3] Plasma *YKL-40* levels in healthy subjects from the general population. Bojesen SE, Johansen JS, Nordestgaard BG. Clin Chim Acta 2011; 412(9–10): 709–12.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5684

AB0675 ANTI-MDA5 POSITIVE DERMATOMYOSITIS: AN EMERGING ENTITY

V. Ortiz-Santamaria, A. Ponce, N. Busquets, N. Del Castillo, X. Surís.
Rheumatology Unit, Granollers General Hospital, Granollers. Barcelona, Spain

Background: Hypo or amyopathic dermatomyositis (DM) represent about 20% of the classic DM. Melanoma differentiation-associated gene 5 antibody or anti-MDA5 antibody, formerly known as anti-CADM140 antibody, has been reported in the last decade. This antibody is detected in more than 50% of patients with hypo or amyopathic DM and it has specific features such as the presence of ulcerative vascular lesions and rapid progression of the interstitial lung disease.

Objectives: To report anti-MDA5 positive DM cases diagnosed at a university county hospital, between 2012 and 2016.

Methods: Design: Retrospective descriptive study. Location: University county hospital. Reference area: ?350.000 inhabitants. Clinical manifestations, analytical results, diagnostic approach, treatment administered and follow-up have been exposed.

Results: We report four anti-MDA5 positive DM with a mean age at diagnosis of 54 years (35–77). Caucasian origin in 2 men and Maghreb origin in 2 women. They had no relevant medical history neither neoproliferative process was detected.

ANA were negative and CK values were normal in all the cases. Nailfold capillaroscopy was characteristic of DM pattern. Case B did not present cutaneous manifestations and he was diagnosed as anti-MDA5 DM after his death.

Discussion: B and C cases showed abnormal heart rhythm that could be related to myocardial involvement, as suggested in a recent publication of anti-MDA5 DM (1). In case C, sinus tachycardia was resolved with the clinical response to treatment.

In the literature reviewed, anti-MDA5 positive DM has been reported as a dermato-pulmonary syndrome, but probably the clinical profile of these patients remains to be defined. In our cases, one of them did not present skin lesions and another case did not develop pulmonary involvement 18 months after the diagnosis.

Conclusions: Keep in mind anti-MDA5 antibody in patients with cutaneous manifestations of DM with vasculopathy lesions, minimal or absent muscular disease, heart rhythm abnormalities not explained by other causes and/or rapidly progressive pulmonary involvement.

Anti-MDA5 positive DM may have a poor response to treatment and fatal outcome. It remains to be seen if early diagnosis could improve the life expectancy of these patients.

Abstract AB0675 – Table 1

	A	B	C	D
Sex	Female	Male	Female	Male
Age at disease onset	43	77	35	62
Fever	Yes	No	No	No
Heliotrope rash	Yes	No	Yes	No
Gottron papules	Yes	No	No	No
Skin ulceration	No	No	No	Yes
Joint disease (J)	No	No	**RA like**	**Palindromic like**
Raynaud's disease	No	No	No	No
Muscular disease (M)	No	No	**Yes**	No
Pulmonary disease (P)	**Bronchiolitis**	**Interstitial lung disease**	No	**Interstitial lung disease**
Cardiac disease (Card)	No	**Arrhythmias**	**Sinus tachycardia**	No
Aldolase (N<7)	Normal	NA	**11**	**14,6**
ESR/CRP mg/dL	**30/4,5**	**41/13,7**	**102/8,1**	**50/1,8**
Ferritin (30–400 ng/ml)	**1253**	NA	225	**2437**
Electromyography	NA	NA	Normal	NA
Muscle biopsy	NA	NA	**Miopathy**	NA
Skin biopsy	**DM**	NA	Nonspecific	**DM**
Treatment	CC + CPM + TACR + IVIG	CC	CC + MTX + HCQ	CC + CPM + TACR
Outcome (months)	Death	Death	Clinical response (18 m)	Alive (16 m)

RA = Rheumatoid Arthritis; NA = Not Avalaible; ANA = Antinuclear Antibodies; DM = Dermatomyositis; CC = Corticosteroids; CPM = Cyclophosphamide; TACR = Tacrolimus; IVIG = Intravenous Immunoglobulins; MTX = Methotrexate; HCQ = Hydroxychloroquine.

References:

[1] J Eur Acad Dermatol Venereol 2014; 28: 1097–102.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1475

AB0676 RELATIONSHIP BETWEEN BIOLOGICAL BIOMARKERS AND CHANGES IN RIGHT VENTRICLE THAT PRECEDE PULMONARY HYPERTENSION IN PATIENTS WITH SYSTEMIC SCLEROSIS

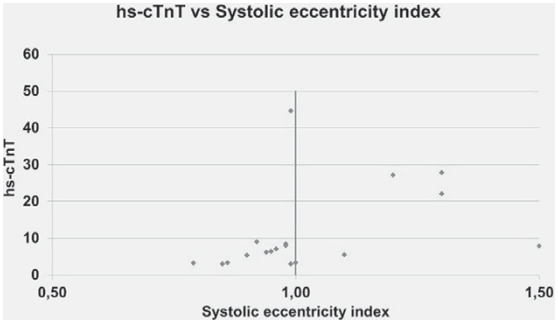
V. Márquez Fernández [1], C. Soto [1], A. Robles [1], A. Noblejas [1], E. Mártínez [1], G. Gúzman [2], C. Busca [1], F. Arnalich [1], J.J. Ríos [1]. *[1] Internal Medicine; [2] Cardiology, Hospital Universitario la Paz, Madrid, Spain*

Background: A higher prevalence of Pulmonary Hypertension (HP) has been described in patients with Systemic Sclerosis (ES) diagnosis, so this fact significantly overshadows the prognosis, since it leads to the failure of the right ventricle (RV). In this context, it could be very useful to identify ES patients who are at greater risk of developing PH in the future to make an early diagnosis of this complication, and prescribing an early theraphy to improve their prognosis.

Objectives: The purpose of this study is to investigate if certain fibrosis, inflammation and vasculopathy biomarkers could be associated to early functional changes in RV, assessed by echocardiography and cardiac nuclear magnetic resonance (MRI) in ES patients.

Methods: A cross-sectional study was performed on a cohort of ES patients diagnosed according to the LeRoy modified criteria, who were being following-up in the Systemic Autoimmune Diseases Unit of the Internal Medicine Service of La Paz Universitary Hospital. Serum levels of inflammation (IL-13, IL-6, TNF alpha), vasculopathy (VEGF), fibrosis biological markers (endoglin, PDRFR, TGFB1, TGFB2, TGFB3) and cardiac biomarkers (NT-proBNP, High sensitivity T troponin) were determinated as well as hemodynamic and cardiac morphological variables, were mesured by transthoracic echocardiography (systolic and diastolic eccentricity index, E/E' ratio, E/A, pulmonary artery systolic pressure, RV thickness) and cardiac MRI (Mean pulmonary artery velocity). We investigated how many patients had these markers elevated and how many of them had hemodynamic and morphological cardiac alterated measurements.

Results: Twenty patients with a diagnosis of ES (18 females/2 males) aged between 41 and 77 years, with a mean of 56 years, were included. A control group of 9 patients with similar demographic characteristics was included. ES subjets had higher levels of PDGFR (fibrosis marke) compared to the control group. In addition, in the group of ES patients, two statistically significant associations were observed: troponin T levels (hs-cTnT), endoglin and TGFB2 had higher leves in pacients with a systolic eccentricity index >1; a negative correlation was evidenciated between levels of NT-proBNP and the mean pulmonary artery velocity measurement (VELAP).



Conclusions: Hs-cTnT, Endoglin and TGF beta are biomarkers that could appear

elevated in patients with systolic eccentricity index >1. NT-proBNP is elevated in patients with decreased VELAP. This study demonstrates the association between certain cardiac biomarkers, fibrosis and vasculopathy peptids and early finding suggesting cardiac remodeling that occurs in some ES patients, which may help to predict the development of PH in those patients.

References:
[1] Mathai SC, Hassoun PM. N-terminal brain natriuretic peptide in scleroderma-associated pulmonary arterial hypertension. Eur Heart J 2007; 28: 140–141.
[2] Jinin M, Makino T, Kahjihara I, et al. Serum levels of soluble vascular endotelial grouth factor receptor-2 in patients with systemic sclerosis. Br. J. Dermatol. 2010; 162: 751–758.
[3] Roy AK, McCullagh BN, Segurado R et al. Detection of high-sensitivity troponin in outpatients with stable pulmonary hypertension identifies a subgroup at higher risk of adverse outcomes. J Card Fail 2014; 20 (1): 31–37.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4123

AB0677 INDIVIDUAL IMMUNOLOGICAL PREDICTORSOF THE RISK OF LUNG DAMAGE IN PATIENTS WITH SYSTEMIC SCLEROSIS

V. Hayevska, V. Chopyak, V. Hayevskyy on behalf of Chopyak Valentyna, Hayevskyy Volodymyr. *Department of clinical immunology and allergology, Lviv National Medical University named by Danylo Halytskyy, Lviv, Ukraine*

Background: A significant role in the formation and development of systemic sclerosis (SSc) belongs to immunogenetic factors and immunopathological mechanisms, so nowadays become important to find immunological predictors of early diagnosis of the disease. An urgent task is timely diagnosing the pulmonary complications as the main causes of high mortality and appointment of adequate therapy and objective assessment of its effectiveness.
Objectives: The main purpose was to develop a personal way of forecasting the risk of damage of the lungs, including its subtype – pneumofibrosis (PF) and pulmonary hypertension (PH) in patients with SSc.
Methods: To address this goal, the following studies performed: clinical, general laboratory, instrumental, immunological, molecular genetics, statistical methods. Adequacy and reliability of the results of mathematical model of the risk of damage the lungs were using criteria Wald and Xi-square. The results show that our model is correct with a probability of error less than 1% (p=0.001).
Results: We found that among the analyzed complex interrelated factors in the development of lung damage in patients with SSc significantly influenced: the duration of the disease, miRNA29b, expression levels in the blood concentration of IL17 in serum and blood, neutrophil phagocytic index t that we include in the predictive model.
We know that the most significant complications associated with damage to their lungs are pneumofibrosis and pulmonary hypertension, which threatened the rapid development of respiratory failure and a high mortality of these patients. In this regard analyzed immunological and molecular genetic parameters of patients with SSc depending on the development of PF and LH.
We found that among the complex of interrelated factors of the development of PF in patients with SSc significantly influenced the following factors: patient age, miRNA 29b, MCP-1, IFN-γ, TGF-β in serum, oxidative indicator “explosion” of neutrophils, which we have included in the predictive model.
At the same time, the development of PH in patients with SSc significantly affected other clinical and immunological factors: patient age, levels of endothelin-1, IL17 in serum, the number of CD4 + CD25 + Fox P3 + -lymphocytes, CD3 +/CDHLA-DR + -lymphocytes, CD4 + IL17 + -lymphocytes in peripheral blood, which we have included the following predictive model.
Conclusions: The application withdrawn prognostic clinical and immunological and molecular genetic criteria of lungs damage (pulmonary hypertension and pneumofibrosis) will enable medical practitioners to verify early visceral lesions in patients with SSc in time and justified the appointment of basic therapy.

References:
[1] Stern EP, Denton CP The Pathogenesis of Systemic Sclerosis. Rheum Dis Clin North Am. 2015 Aug;41(3):367–82.
[2] Meijs J, Anne A Schouffoer, et all A prediction model for progressive disease in systemic sclerosisRMD Open. 2015; 1(1) Published online.
[3] Peter A. Ward, M.D. Risk Prediction in Idiopathic Pulmonary Fibrosis American journal of respiratory and critical Care Medicine 2012 Vol 185: 6–7.
[4] Hanna M., Minna K. Et all Are risk predicting models useful for estimating survival of patients with rheumatoid arthritis-associated interstitial lung disease? BMC Pulmonary Medicine (2017), Published online.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6580

AB0678 ACCELERATED ACTIVATION OF 25-HYDROXYVITAMIN D TO 1,25-DIHYDROXYVITAMIN D IN SYSTEMIC SCLEROSIS PATIENTS- A RETROSPECTIVE STUDY

V.R. Mehta[1], J.F. Farrell[2], R. Peredo[1], L.S. Shapiro[3]. *[1]Rheumatology, Albany Medical Center; [2]Rheumatology, Albany College of Pharmacy and Health Sciences; [3]Rheumatology, Steffens Scleroderma Center, Albany, United States*

Background: There have been multiple reports of low vitamin D in Systemic Sclerosis (1, 2). The majority of these reports only measured 25-hydroxyvitamin D (calcifediol) and not 1,25-dihydroxyvitamin D (calcitriol). In our clinical observation, we noted that there may be a population of patients with low calcifediol but normal or high calcitriol.
Objectives: We aim to evaluate the frequency of normal or high calcitriol level in systemic sclerosis patient with low calcifediol levels.
Methods: We performed a retrospective analysis using data collected from a large private practice. We collected data from systemic sclerosis patients who had calcifediol and calcitriol levels ordered between January 2014 and January 2017, patients with sarcoidosis overlap were excluded.
Results: We identified 90 scleroderma patients with documented calcifediol and calcitriol levels and no history of sarcoidosis. Mean calcifediol level was 32.7 ng/mL (SD 20.2) and mean calcitriol level was 60.9 pg/mL (SD 27.6). Total of 42 patients were identified as having calcifediol level of less than 30 (normal >30), only 1 of these patients had calcitriol levels below 10 pg/mL (normal >10) and 6 patients had calcitriol levels above 75 pg/mL. Twenty-three out of 41 patients who had low calcifediol but high calcitriol level also had a CT chest with no diagnostic findings suggestive of sarcoidosis.
Conclusions: Our study suggests that while low calcifediol levels are common in systemic sclerosis patients, not all patients are truly vitamin D deficient and a calcitriol level should be checked before supplementation is initiated. There is some documented evidence of sarcoid and scleroderma overlap at greater than expected frequency which is under recognized and elevated calcitriol level in a systemic sclerosis patient should prompt further evaluation for sarcoidosis (3). We have identified a population of scleroderma patients with low calcifediol, elevated calcitriol level, but no evidence of sarcoidosis. Based on this observation we are planning a prospective study to investigate this further.

References:
[1] Caramaschi P, Dalla Gassa A, Ruzzenente O, Volpe A, Ravagnani V, Tinazzi I, et al. Very low levels of vitamin D in systemic sclerosis patients. Clinical rheumatology. 2010;29(12):1419–25.
[2] Sampaio-Barros MM, Takayama L, Sampaio-Barros PD, Bonfá E, Pereira RMR. Low vitamin D serum levels in diffuse systemic sclerosis: a correlation with worst quality of life and severe capillaroscopic findings. Revista brasileira de reumatologia. 2016;56(4):337–44.
[3] Judson MA, Shapiro L, Freitas S, Polychronopoulos VS, Highland KB. Concomitant sarcoidosis and a connective tissue disease: review of the clinical findings and postulations concerning their association. Respiratory medicine. 2013;107(9):1453–9.

Acknowledgements: Steven Obrzut, Heather Sickler and Tricia Bartel assisted with data collection.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5613

AB0679 THE CLINICAL VALUE OF NAILFOLD CAPILLAROSCOPY IN THE EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS

W. Gao, G. Zhang, L. Zhang, K. Xu, B. Li, Y. Yang, M. Yan. *Rheumatology, Shanxi Dayi Hospital, Shanxi Academy of Medical Sciences, taiyuan, China*

Background: Vascular changes was early pathological changes of SSc, gradually appearing with irreversible fibrosis of the skin and internal organs. Early diagnosis and assessment of the development and efficacy timely, could improve survival in patients with SSc.
Objectives: To assess the value of nailfold capillaroscopy in the early diagnosis of systemic sclerosis (SSc).
Methods: 60 patients with SSc and 55 patients with other connective tissue diseases.Data were extracted on clinical and laboratory parameters.2013 ACR/EULAR classification criteria and 1980 ACR criteria for SSc were evaluated.
Results: The sensitivity of the 2013 criteria was 91.7% compared to 56.7% for the 1980 criteria ($P<0.001$). The specifiity of two criteria was no significant difference. This sensitivity of the 2013 criteria was higher compared to the 1980 criteria among those with lcSSc (95.5% versus 50%).The pattern was consistent among those with disease duration <3 years (90.5% versus 57.1%,$P<0.05$),and disease duration ≥3 years (92.3% versus 56.4%, $P<0.05$). The sensitivity and specificity of nailfold capillaroscopy to determine SSc were 86.7% and 43.6%. Patients not fulfilling the two classification criteria were met the very early diagnosis of systemic sclerosishe, and often suffering from RP, and had an SSc pattern on nailfold capillaroscopy.
Conclusions: The sensitivity of 2013 ACR/ EULAR classification criteria was higher compared with 1980 ACR classification criteria.The specificity of two classification criteria was no significant difference. This sensitivity of two criteria was higher among those with lcSSc and short disease duration.Scleroderma pattern were significantly associated with the development of systemic sclerosis.

References:
[1] van den Hoogen F, Khanna D, Fransen J, et al.2013 classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative[J]. Ann Rheum Dis, 2013, 72(11):1747–1755.
[2] Alhajeri H, Hudson M, Fritzler M, et al. The 2013 ACR/EULAR Classification Criteria for Systemic Sclerosis Out-perform the 1980 Criteria: Data from the Canadian Scleroderma Research Group[J]. Arthritis Care &Research, 2015, 67(4):582–587.

[3] Maricq HR. Wide-field capillary microscopy[J]. Arthritis Rheum, 1981, 24(9): 1159–1165.
[4] Pavlov-Dolijanovic S, Damjanov NS, Stojanovic RM, et al.Scleroderma pattern of nailfold capillary changes as predictive value for the development of a connective tissue disease:a follow-up study of 3,029 patients with primary Raynaud's phenomenon[J]. Rheumatol Int, 2012,32(10):3039–3045.
[5] Marino Claverie L, Knobel E, Takashima L, et al.Organ involvement in Argentinian systemic sclerosis patients with "late" pattern as compared to patients with "early/active" pattern by nailfold capillaroscopy[J]. Clin Rheumatol, 2013, 32(6):839–843.
[6] Cutolo M, Grassi W, Matucci Cerinic M. Raynaud's phenomenon and the role of capillaroscopy[J]. Arthritis Rheum,2003, 48(11):3023–3030.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3449

AB0680 ANALYSIS THE CAUSES AND COUNTERMEASURES OF IGNORING SWALLOWING DYSFUNCTION IN PATIENTS WITH POLYMYOSITIS AND DERMATOMYOSITIS

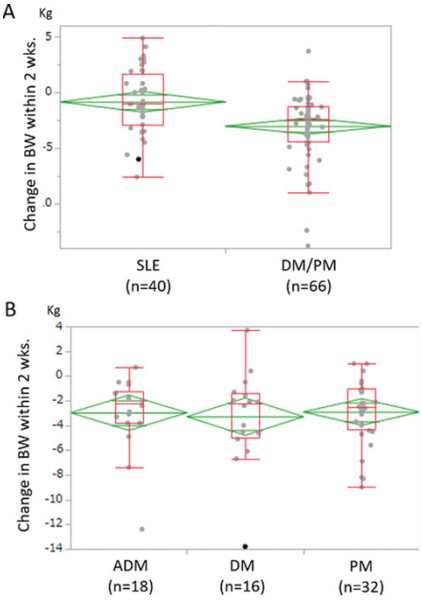
Y. Wen, Q. MinLi, L. Yan. *Department of Rheumatology, Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: The patients with Polymyositis and Dermatomyositis always ignored swallowing dysfunction and most of them eventually had no enough knowledge of this. For this situation, to find out the reasons and take appropriate measures was necessary.
Objectives: To analyze the causes of ignoring swallowing dysfunction in patients with Polymyositis and Dermatomyositis and to explore the corresponding preventive measures.
Methods: The clinical data of 47 patients with Polymyositis and Dermatomyositis in hospital from September 2012 to December 2013 was analyzed retrospectively. The swallowing function was evaluated by the water swallow test, and the patients' knowledge of swallowing dysfunction was surveyed.
Results: Only 2 patients complained of choking during swallowing, with ignorance rate of 95.74%. Positive rate was 40.43% in water swallow test, of which grade II dysphagia proposition was 58%, III grade was 32%, IV grade was 10%. 100% of patients believed that sternal obstruction or dysphagia as swallowing dysfunction. 89.36% of patients didn't think drinking water with bucking as swallowing dysfunction.
Conclusions: The symptoms of limb weakness in patients with Polymyositis and Dermatomyositis may obscure the presence of dysphagia. In addition, the patients do not have enough knowledge about dysphagia that to neglect the swallowing dysfunction. To improve detection rate of swallowing dysfunction in patients with Polymyositis and Dermatomyositis, earching detailed history by listing dysphagia performance and providing water swallow test is necessary.
References:
[1] Comparison between swallowing-related and limb muscle involvement in dermatomyositispatients. Kim SJ, Han TR, Jeong SJ, Beom JW. Scand J Rheumatol. 2010 Aug;39(4):336–40.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3125

AB0681 HIDDEN GENERALIZED EDEMA IN INFLAMMATORY MYOPATHY; GENERALIZED EDEMA IS AN UNRECOGNIZED CLINICAL FEATURE OF MYOSITIS?

Y. Namiki[1], K. Kurasawa[2], A. Tanaka[2], R. Yamazaki[1], H. Okada[2], S. Arai[2], T. Owada[1], R. Maezawa[1], M. Arima[1]. *[1]Department of Rheumatology, Dokkyo Medical University, Mibu, Tochigi; [2]Department of Rheumatology, Dokkyo Medical University, Mibu, Tochigi, Japan*

Background: Dermatomyositis (DM)/ polymyoitis (PM) are systemic diseases characterized by muscle inflammation, which shows varieties of clinical symptoms and signs. We have experienced cases of DM/PM with generalized edema as reported previously by others (1). Moreover, we found that there were many myositis patients who lost their body weight (BW) after starting of high dose glucocorticoid (GC) therapy. Thus, we hypothesized that hidden generalized edema is a characteristic clinical feature of myositis.
Objectives: To determine whether generalized edema is a hidden clinical feature of myositis. If so, what myositis patients have the feature.
Methods: The study was a retrospective observation study. The subjects were consecutive 67 of DM/PM and 53 of SLE patients who diseases for the first time, admitted our department from April 2007 to September 2016 and received immunosuppressive therapy including over 30mg/day GC. The patients were excluded who had cardiogenic or nephrogenic edema or whose BW data was not available. To detect hidden generalized edema caused by inflammation, we examined the change in BW within 2 weeks after starting immunosuppressive therapy. The clinical features of DM/PM patients with/without BW change were examined through reviewing medical record.
Results: The included subjects were DM/PM 66 patients (M/F; 18/48 with a mean age of 59.4 y.) and SLE 40 patients (M/F;14/26 with a mean age of 49.8 y.). The body weight of DM/PM and SLE were 56.4±14.0 and 54.7±10.9 kg, respectively. Decrease in BW within 2weeks after starting the therapy were 3.02±2.99kg of DM/PM and 0.85±2.87 kg of SLE, which was larger in DM/PM compared to SLE (Fig A). The numbers of patients who lost BW more than 2kg within the 2 weeks were 42 in DM/PM (64%) and 14 in SLE (35%).
Serum albumin levels were slightly decreased by 0.18 g/ dl (0.06 to 0.30; 95% CI) in DM/PM, while no significant change was detected in SLE.
In myositis, change in BW was similar among DM, amyopathic DM (ADM) and PM (Fig.B). Moreover, no differences were found in the change of BW between patients with and without male sex, malignancy, interstitial pneumonia, anti-ARS Ab and anti-MDA5Ab. Additionally, between patients with and without BW loss more than 2kg, no differences were found in age, serum TP, Alb and CRP levels before and after treatment and prognosis.



Conclusions: DM/PM patients lose BW by immunosuppressive therapy including GC, which indicates the existence of hidden generalized edema that might be a characteristic clinical feature in inflammatory myopathy.
References:
[1] Tu J1, McLean-Tooke A, Junckerstorff R. Increasing recognition of dermatomyositis with subcutaneous edema - is this a poorer prognostic marker? Dermatol Online J. 2014;20:21244.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4822

AB0682 THE INCIDENCE RATE OF INFLAMMATORY MYOPATHIES IN SLOVENIA

Ž. Rotar[1], A. Hočevar[1], M. Krošel[1], S. Praprotnik[1], M. Tomšič[1,2]. *[1]Department of Rheumatology, University Medical Centre Ljubljana; [2]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia*

Background: Annual incidence rates of inflammatory myopathies (IM) vary widely from 1.16–19.0 per 10^6 of adults.1 Our aim was to, for the first time, determine the incidence rate of IM in our population.
Objectives: To determine the incidence rate of IM in our population.
Methods: We retrospectively collected incident cases of IM from 1 January 2005 to 31 December 2016 at our department of rheumatology which is a part of an integrated secondary/tertiary university teaching hospital that is the only referral center for two well defined regions representing roughly a third of the national adult population. Tertiary cases are referred to our department from the entire country. We identified the cases by searching the electronic patient records (PRs) for ICD-10 codes M05, M33–35, M60, G73.7, G72.4. The paper and electronic PRs were scrutinized to assess clinical, laboratory and histopathological data. Descriptive statistics was used to describe our group of patients. The adult population size of the two regions served by our department was obtained from the national statistics institute database. The annual incidence rate for IM was then calculated.
Results: During the 12-year observation period we identified 117 new cases of IM from a well-defined adult white Caucasian population aged 18 or above. 38 cases were excluded from analyses since they were referred to our department from outside the two regions we serve on the secondary and tertiary level. Thus, we analyzed 79 cases of IM (63% female; median (IQR) age 67 (55–75) years; 44% ever smokers). The median time to diagnosis was 5 (IQR 3–12) months. We diagnosed 29% patients with dermatomyositis, 25% with anti-synthetase syndrome, 18% with polymyositis, 9% with statin induced necrotizing autoimmune myopathy, 9% with concomitant myositis as a part of connective tissue disease, 6% with paraneoplastic myositis, and 4% with undifferentiated myositis. The IM cases were most often diagnosed in the summer months (32.9%), followed

by spring (24.1%), fall (22.8%), and winter (20.3%). The clinical and laboratory characteristics at presentation are shown in Table 1. Muscle biopsy was performed in 93% of patients. Notably, patients with swallowing difficulties had more commonly had Raynaud phenomenon (RR 3.7 (95% CI 1.4–9.4), p=0.008).

Table 1. The clinical and laboratory characteristics at presentation

	# (%)
Myositis	72 (91)
Skin rash	42 (53)
Weight loss	35 (44)
Interstitial lung disease	29 (37)
Swallowing difficulties	31 (39)
Arthritis	20 (25)
Raynaud phenomenon	14 (18)
Fever	9 (11)
median ESR	27 (16-45)
MEDIAN CRP	7 (1-22)
Hep-2 test: ANA (≥1:160)	41 (52)
Hep-2 test: nonspecific cytoplasmic IF	20 (25)
Anti-ENAs	43 (54)
aJo-1	17 (22)
aPL-12	3 (4)
aMI-2	2 (2.5)
aPM/Scl	5 (6)
aKu	1 (1.3)
aU1-RNP	1 (1.3)
ACA	1 (1.3)
aRo	6 (8)
aSRP	1 (1.3)
aSAE	1 (1.3)
3HHMGCoaR	3 (4)
RTE/HSE	19 (24)
Histopathologically proven IM	86.5%

Legend: ACA – anti-centromere antibodies, ANA – anti-nuclear antibodies, anti-ENAs – autoantibodies against extractable nuclear antigens, CRP – C-reactive protein, EMG – electromyogram, ESR – erythrocyte sedimentation rate, RTE/HSE – rabbit thymus extract/human spleen extract used in the in-house anti-ENA counter-immuno-diffusion assay, IF – immunofluorescence, IM – inflammatory myopathy.

Conclusions: The averaged 12-year annual incidence of IM in the population under study was 9.4 (95% CI 7.5–11.8) per 10^6 adults.

References:
[1] Meyer A, et al. Rheumatology 2015.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2688

Spondyloarthritis - treatment

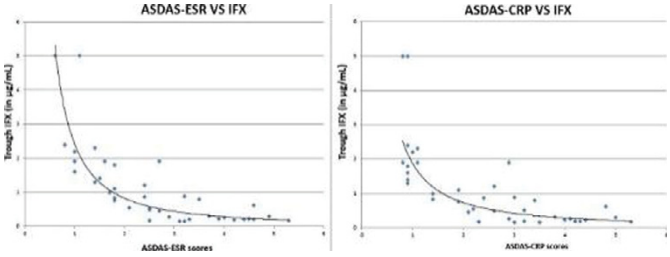
AB0683 TROUGH INFLIXIMAB LEVELS AND ANTI-INFLIXIMAB ANTIBODIES IN SPONDYLOARTHRITIS PATIENTS ON TREATMENT WITH LOW DOSE INFLIXIMAB: A SINGLE CENTRE CROSS-SECTIONAL STUDY

A. Patil[1], S.K. Upadhyaya[1], R. Dawar[2], B. Vaishnav[1], N. Dadhaniya[1], S.J. Gupta[1], R. Handa[1]. *[1]Rheumatology; [2]Microbiology, Indraprastha Apollo Hospitals, Delhi, India*

Background: Infliximab (IFX) is an anti-TNF, chimeric, monoclonal antibody approved for use in refractory spondyloarthritis (SpA). Studies done in patients with Rheumatoid arthritis[1] and Inflammatory bowel disease[2] have demonstrated the clinical utility of the measurement of serum trough IFX and antibodies to IFX (ATI). In India, many centres including ours use IFX at lower doses of 3–5 mg/kg and on demand IFX treatment without the use of the loading dose IFX in SpA patients[3]. Data on the utility of measuring trough IFX and ATI levels and their correlation with disease activity in such group of patients is lacking.
Objectives: To evaluate the co-relation between trough Infliximab levels and disease activity measures, viz ASDAS ESR and ASDAS CRP in SpA patients on low dose IFX therapy
To compare the mean ASDAS- ESR/CRP scores between ATI positive and ATI negative patients
Methods: Thirty-nine adult spondyloarthrtitis patients in the age group of 18–70 years, meeting the ASAAS classification criteria for peripheral and/or axial spondyloarthritis were recruited into the study. The inclusion criteria required the patients to have had received three or more infusions of IFX at 3–5 mg/kg/dose over the past 6 to 9 months. Blood samples were collected between two to three months after the previous IFX infusion for the measurement of the ATI and the trough IFX levels using the Matriks Biotek Shikari Q-ATI ELISA and Q-IFLIXI ELISA kits respectively. At the same time, disease activity of the patients was quantitated using ASDAS ESR and ASDAS CRP scores.
Correlation between the ASDAS scores and the trough IFX levels was analysed by Pearson's product moment correlation assay. The difference in mean trough IFX and ASDAS scores between the ATI positive and ATI negative patients were assessed using Welch two sample t-test.
Results: There was a moderately significant negative correlation between the trough IFX levels and the ASDAS-ESR ($r = -0.69$, $p<0.001$), ASDAS-CRP scores ($r = -0.67$, $p<0.001$) (Fig 1). ATI positive patients in comparison to ATI negative, had significantly higher ASDAS ESR and ASDAS CRP scores (Table 1).

Table 1. Table showing differences in ASDAS scores between ATI positive and negative patients

	ATI +ve patients	ATI –ve patients	P value
Mean ASDAS ESR	3.13	1.56	<0.001
Mean ASDAS CRP	3.06	1.45	<0.001



Conclusions: SpA patients from India on low dose, on demand IFX therapy, have both the trough IFX and ATI correlate significantly with the measures of disease activity. Therefore, these may be used in addition to clinical activity scores for a more cost effective on demand IFX therapy in SpA patients, especially in an expense constrained country like India.

References:
[1] Laine J, JokirantaT, Eklund K, Vakevainen M, Puolakka K. Cost effectiveness of routine measuring of serum drug concentrations and anti-drug antibodies in treatment of rheumatoid arthritis patients with TNFα blockers. Biologicals: Targets and therapy.2016;10:67–73.
[2] Pallagi Kunstar E, Farkas K, Szepes Z et al. Utility of serum TNFα, infliximab trough level and antibody titres in inflammatory bowel disease. World J Gastroenterol. 2014;20:5031–5.
[3] Kumar A. Experience with anti-tumour necorsis factor-α therapy in India. APLAR journal of Rheumatology. 2006;9:136–41.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2690

AB0684 CLINICAL RESPONSE AND RADIOGRAPHIC PROGRESSION IN ANKYLOSING SPONDYLITIS PATIENTS UNDER ANTI-TNF THERAPY: IMPACT OF HIP INVOLVEMENT

A.Y. Shimabuco[1], F.M. Milanez[1], J.C.B. Moraes[1], G.V. Perico[2], C.R. Gonçalves[1], M.G. Waisberg[1], P.D. Sampaio-barros[1], C.G.S. Saad[1]. *[1]Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, São Paulo; [2]Unidade Radiológica Criciúma, Criciuma, Brazil*

Background: Hip involvement is considered an important prognostic factor associated with radiographic progression in ankylosing spondylitis (AS) patients. However, there are no studies regarding hip involvement impact on clinical response and radiographic progression in AS patients under anti-TNF therapy.
Objectives: Compare clinical and radiographic progression in AS patients receiving anti-TNF therapy with and without moderate-severe hip involvement.
Methods: Forty-seven AS patients referred to receive anti-TNF treatment were included and classified according to baseline hip involvement based on Bath Ankylosing Spondylitis Radiology Hip Index (BASRI-Hip): none-minimal hip disease (hip grade <3) or moderate-severe disease (hip grade ≥3). Demographic data, presence of HLA-B27, extra-articular involvement, DMARD and NSAID use, clinical and laboratorial disease parameters (BASDAI, BASMI, BASFI, ASQol, mSASSS and inflammatory markers) were assessed at baseline and two years after anti-TNF treatment.
Results: Thirty-four (72.3%) patients were classified as none-minimal hip disease and 13 (27.7%) as moderate-severe hip involvement. Both groups were similar at baseline considering age, HLA-B27, extra-articular involvement and comedication use. Laboratorial markers (ESR, CRP) and disease parameters (BASDAI, BASFI and mSASSS) showed no difference at baseline. Moderate-severe group had longer disease (10.0±7.6 vs. 14.9±8.6, P=0.002, years), higher BASMI (3.8±2.4 vs. 6.5±2.5, P=0.002) and lower ASQoL (13.7±4.4 vs. 9.9±4.9, P=0.007). After two-years of anti-TNF therapy, both groups presented similar BASDAI response (delta BASDAI, p=0.134; final BASDAI, p=0.324) and an increase in mSASSS [no-minimal involvement: 13.6±18.3 vs. 16.1±19.4, P<0.001); moderate-severe involvement: 21.7±19.9 vs. 28.6±18.5, P=0.003]. At final evaluation patients with moderate-severe hip involvement presented higher mSASSS (28.6±18.5 vs. 16.1±19.4, P=0.02), despite similar delta BASDAI and final BASDAI.
Conclusions: Our study provides evidence that hip involvement did not impact on clinical response in AS patients under anti-TNF therapy but may have an effect on radiographic progression of these patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5970

AB0685 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN WORK PRODUCTIVITY AND HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS: LONG-TERM RESULTS FROM MEASURE 1 AND MEASURE 2

A. Deodhar[1], P.G. Conaghan[2], V. Strand[3], A. Boonen[4], G. Ferraccioli[5], F. Van den Bosch[6], V. Bhosekar[7], B. Porter[7], K. Gandhi[7], S. Jugl[8]. [1]*Oregon Health & Science University, Portland, Oregon, United States;* [2]*University of Leeds, Leeds, United Kingdom;* [3]*Stanford University School of Medicine, Palo Alto, CA, United States;* [4]*Maastricht University Medical Centre, Maastricht, Netherlands;* [5]*Catholic University of the Sacred Heart, Rome, Italy;* [6]*Ghent University Hospital, Ghent, Belgium;* [7]*Novartis Pharmaceuticals Corporation, East Hanover, United States;* [8]*Novartis Pharma AG, Basel, Switzerland*

Background: Patients (pts) with ankylosing spondylitis (AS) experience significant restrictions in work productivity and health-related quality of life (HRQoL). Secukinumab (SEC) demonstrated rapid improvements in signs, symptoms and physical functioning in pts with AS.[1]
Objectives: To assess whether the beneficial effects of SEC on AS signs and symptoms were reflected in improvements in work productivity and HRQoL in the overall population and in TNF inhibitor (TNF)-naïve pts and pts with an inadequate response or intolerance to TNF inhibitors (TNF-IR) for up to 52 weeks (wks) in MEASURE 2 and 104 wks in MEASURE 1.
Methods: 371 and 219 pts were randomized to SEC or placebo (PBO) in MEASURE 1 (10 mg/kg IV followed by 150 or 75 mg SC) and MEASURE 2 (150 or 75 mg SC), respectively. At Wk 16, PBO pts were re-randomized to SEC 150 or 75 mg SC (PBO pts with ASAS20 response at Wk 16 were switched to SEC at Wk 24 in MEASURE 1). Productivity was measured using the Work Productivity and Activity Impairment-General Health (WPAI-GH) questionnaire, which includes questions to assess absenteeism, presenteeism and overall work productivity impairment in employed pts, and general activity impairment in all pts during the preceding 7 days (0–100%). HRQoL was assessed with the ASQoL questionnaire (0–18 points). Across both studies, approximately 69% of pts were TNF-naïve and 31% were TNF-IR. Observed data are presented from the full analysis set and in subgroups stratified by prior TNF exposure. Only data with the approved dose (SEC 150 mg) are shown.

Table. WPAI-GH and ASQoL outcomes in MEASURE 1 and MEASURE 2 through Week 104

	MEASURE 1			MEASURE 2[a]		
	Overall	TNF-naive	TNF-IR	Overall	TNF-naive	TNF-IR
WPAI GH[b] (change from BL)						
Absenteeism (% work time missed due to health)[c]						
Wk 52	−2.1 (n=60)	−3.5 (n=47)	3.0 (n=13)	−4.9 (n=38)	−12.8 (n=23)	7.1 (n=15)
Wk 104	1.3 (n=49)	0.2 (n=41)	6.8 (n=8)	–	–	–
Presenteeism (% impairment while working due to health)[c]						
Wk 52	−20.2 (n=57)	−21.6 (n=45)	−14.9 (n=12)	−19.2 (n=37)	−25.5 (n=22)	−10.0 (n=15)
Wk 104	−25.1 (n=49)	−27.8 (n=41)	−11.3 (n=8)	–	–	–
Work Productivity (% overall work impairment due to health)[c]						
Wk 52	−21.2 (n=57)	−23.2 (n=45)	−13.8 (n=12)	−21.3 (n=37)	−29.5 (n=23)	−7.9 (n=14)
Wk 104	−23.0 (n=49)	−26.1 (n=41)	−6.9 (n=8)	–	–	–
Activity Impairment (% activity impairment due to health)[d]						
Wk 52	−25.4 (n=107)	−26.7 (n=83)	−20.8 (n=24)	−26.4 (n=61)	−30.5 (n=40)	−18.6 (n=21)
Wk 104	−27.3 (n=85)	−27.5 (n=67)	−26.7 (n=18)	–	–	–
ASQoL (change from BL)[c,e]						
Wk 52	−4.7 (n=109)	−5.0 (n=85)	−3.4 (n=24)	−5.2 (n=61)	−6.0 (n=40)	−3.7 (n=21)
Wk 104	−4.8 (n=86)	−5.0 (n=68)	−4.1 (n=18)	–	–	–

[a] WPAI-GH and ASQoL were not assessed at Week 104 of MEASURE 2; [b] In all categories, higher scores indicate higher impact on patients, employers, and society; a decrease from baseline represents improvement; [c] Assessed in 'employed' subjects only; [d] Assessed regardless of subject's employment status; [e] Higher scores represent greater impact on patients' QoL. A decrease from baseline represents improvement

BL, baseline; n, number of patients with sufficient data for evaluation; s, number of responders; SEC, secukinumab

Results: At baseline (BL), 77 of 125 and 45 of 72 randomized pts were employed and working in the SEC groups in MEASURE 1 and 2, respectively. Improvements in all WPAI domains were observed with SEC in the overall, TNF-naïve and TNF-IR populations at Wk 16 in both studies, and effects were generally sustained through Wks 52 and 104 (Table). In MEASURE 1, activity impairment in the total group improved by 49% and overall work productivity in those employed improved by 45% from BL at Wk 104. Improvements were 51%/49% in TNF-naïve and 42%/19% in TNF-IR pts, respectively. In MEASURE 2, activity impairment and work productivity improved by 43% and 40% vs BL, respectively at Wk 52; improvements in activity impairment/work productivity in TNF-naïve and TNF-IR pts were 49%/54% and 32%/16%, respectively. Similar responses were seen in the other WPAI scores across both studies. Early improvements in ASQoL were sustained through Wk 104 in MEASURE 1 and Wk 52 in MEASURE 2. At Wk 104 of MEASURE 1, ASQoL scores had improved by 48% vs. BL with SEC; improvements were 50% and 39% in TNF-naïve and TNF-IR pts, respectively.
Conclusions: SEC provides sustained improvements in work productivity and ASQoL for up to 104 wks among AS pts, regardless of prior TNF exposure.
References:
[1] Baeten. NEJM 2015;373:2534–48.
Disclosure of Interest: A. Deodhar Grant/research support from: Amgen, Abbvie, GSK, Eli Lilly, Janssen, Novartis, Pfizer, UCB, Speakers bureau: Eli Lilly, Janssen, Novartis, Pfizer, UCB, P. Conaghan Consultant for: Abbvie, BMS, Lilly, Novartis, Pfizer, Roche, Speakers bureau: Abbvie, BMS, Lilly, Novartis, Pfizer, Roche, V. Strand Consultant for: AbbVie, Amgen, BMS, Celgene, Celltrion, CORRONA, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi, and UCB, A. Boonen Grant/research support from: Merck, Pfizer, Abbvie and Amgen, Speakers bureau: Sandoz, Janssen, Lilly, G. Ferraccioli Grant/research support from: BMS, Roche, MSD, Speakers bureau: AbbVie, Pfizer, UCB.Roche, MSD, Eli Lilly, GSK, Novartis, F. Van den Bosch Consultant for: Abbvie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, UCB, V. Bhosekar Employee of: Novartis, B. Porter Shareholder of: Novartis, Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1856

AB0686 ASSOCIATION BETWEEN DRUG SERUM LEVELS AND DISEASE ACTIVITY IN ESPONDILOARTHRITIS PATIENTS TREATED WITH GOLIMUMAB

C. Redondo[1], A. Martínez[2], C. Plasencia[1], A. Jochems[2], D. Pascual-Salcedo[2], V. Navarro-Compán[1], M.G. Bonilla[1], I. Monjo[1], A. Balsa[1]. [1]*Rheumatology;* [2]*Immunology Unit, la Paz University Hospital, Madrid, Spain*

Background: Efficacy and safety of Golimumab (Glm) has been demonstrated for spondiloarthritis (SpA). Nonetheless, there is little data determining an association between an optimal drug levels concentration and the maintenance of a good control of disease activity. In Spa-Paz cohort we defined previously an optimal Glm levels concentration associated with a good clinical response.
Objectives: To investigate the association between serum levels of Glm, based on the optimal concentration defined previously in Spa-Paz cohort, and disease activity in a larger cohort of SpA.
Methods: Observational prospective SpA-Paz cohort study treated with Glm. Disease activity was measured by ASDAS and clinical improvement using Delta-ASDAS at baseline, 6 and 12 months of biologic therapy. ASDAS$<$2.1 was considered as low activity and clinically important improvement as Delta-ASDAS$\geq$1.1. Drug levels were measured by ELISA at 6 and 12 months of therapy and classified in 3 groups based on the optimal concentration range previously defined in our cohort: Group 1:$<$0.7 mg/L, group 2: 0.7–1.4 mg/L, group 3: $>$1.4 mg/L. At 12 months we made a LOCF analysis to include patient data (11 patients) with less than 12 months of treatment. We used the software Graph-Pad Prism 6 for statistical analysis.
Results: 46 patients of 79 with SpA treated with Glm were included in this study. The average age was 49 years old (age range 22–72 years old), 31 men (67%) and 15 women (33%). 22 patients (48%) were non-smokers and 13 (28%) active smokers. 25 (54%) were HLA-B27 positive. In total, 17 patients (37%) were classified in group 1, 16 (35%) in group 2 and 13 (28%) in group 3. At 12 months of therapy, most patients in low disease activity were in groups 2 and 3 but nevertheless, the majority of high disease activity patients were in group 3 (76% in groups 2 and 3 vs. 41% in group 1 with ASDAS$<$2.1; 24% in group 2 and 3 vs. 53% in group 1 with ASDAS$\geq$2.1; $p<0.0001$). Likewise, clinical improvement was significantly higher in groups 2 and 3 patients (62% in groups 2 and 3 vs. 35% in group 1, $p>0.0002$). There were no differences in clinical improvement between group 2 and 3. 11 patients (24%) discontinued the treatment, 1 for adverse effect and 10 for inefficacy, 50% of which (5 patients) were in group 1 at the suspension moment.
Conclusions: In our Glm treated SpA cohort, the majority of low activity patients and higher clinical improvement were classified in optimal or supraoptimal concentration group. Overoptimal concentration drug levels do not seem to contribute to major benefit in clinical improvement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5881

AB0687 ASSOCIATION BETWEEN GOLIMUMAB TAPERING STRATEGY AND DRUG SERUM LEVELS IN SPA-PAZ SPONDILOARTHRITIS COHORT

C. Redondo[1], A. Martínez[2], C. Plasencia[1], V. Navarro-Compán[1], L. Nuño[1], D. Peiteado[1], A. Villalba[1], A. Jochems[2], D. Pascual-Salcedo[2], A. Balsa[1].
[1]Rheumatology; [2]Immunology Unit, la Paz University Hospital, Madrid, Spain

Background: Golimumab (Glm) is a tumour necrosis factor (TNF) inhibitor used as Spondiloarthritis (SpA) treatment. There is more and more evidence of tapering therapies used in maintained low disease activity patients, avoiding overtreatments and adverse effects. Up to now, there are no studies concerning SpA patients with Glm tapering therapy and serum drug levels measured prior to tapering strategy.
Objectives: To analyze clinical and analytical course of SpA patients with Glm interval prolongation in SpA-Paz cohort. Associate pre-tapering Glm serum levels with flare occurrence along tapering treatment.
Methods: Observational prospective SpA-Paz cohort study of 22 patients treated with Glm that remained with low disease activity, so they started tapering strategy (Tap-S). We measured clinical activity with ASDAS and ∆ASDAS at baseline, pre-tapering visit (v-pre)and at 6, 12, 18 and 24 months after tapering starting (v-end). All of them had a clinically important improvement determined as ∆ASDAS≥1'1. We registered flares, defined as clinical worsening based on patient anamnesis and physical examination and on diverse activity indexes made from the beginning until the last visit. Drug serum levels in v-pre were measured by ELISA and classified following optimal concentration previously defined in our laboratory: <0'7 mg/L, 0'7–1'4 mg/L, >1'4 mg/L. We used the software Graph-Pad Prism 6 for statistical analysis.
Results: 22 of 79 patients from our cohort (28%) initiated Tap-S. The age range was between 25 and 70 years, 73% men and 27% women. 52% were non-smokers. 5 patients (23%) received another antiTNF drug previously (4 Infliximab, 1 Etanercept). All of them had a 6 months visit prior to tapering, 18 patients had 12 months visit, 8 had 18 months visit and 5 had 24 months visit. ASDAS and ∆ASDAS were similar in v-pre and v-end (ASDAS: 1'3±0'4 v-pre vs 1'2±0'7 v-fin, p=0'3; ∆ASDAS: 2'3±0'7 v-pre vs 2'4±0'9 v-end, p=0'6). 13 patients (59%) had 1 or 2 flares along tapering therapy. The occurrence of flare average was 14 months. In all the patients with flares, disease activity was controlled returning to previous tapering dose (4/13, 31%), to monthly schedule (6/13, 46%) or remaining tapering dose with symptomatic treatment adjustments (3/13, 23%). None of them discontinued the treatment. At v-end, ASDAS and ∆ASDAS were similar between patients with and without flares along Tap-S (ASDAS v-end: 1±0'7 in patients without flares vs 1'3±0'7 in patients with flares, p=0'4, ∆ASDAS v-fin: 2'7±0'7 in patients without flares vs 2'2±1 in patients with flares, p=0'3). All the patients (4/4, 100%) that were under optimal drug concentration (<0'7mg/L) had at least one flare along Tap-S; however, only 23% (3/9) of those who were in optimal drug concentration in v-pre (0'7–1'4 mg/L) had flares.
Conclusions: The tapering strategy in our SpA cohort treated with Glm results in similar disease activity control after 24 months of monitoring. The activity disease in patients with flares was controlled with symptomatic or biologic treatment adjustments avoiding therapy discontinuation. Flares incidence was more frequent in patients under optimal drug concentration in v-pre.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5911

AB0688 EFFECT OF TREATMENT WITH NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON DISEASE ACTIVITY IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS BASE ON DATA FROM 2 YEARS FOLLOW UP OF CORSAR COHORT

D. Rumiantceva, T. Dubinina, O. Rumyantseva, A. Demina, E. Agafonova, S. Erdes, S. Krasnenko. *Laboratory of spondyloarthritis, Nasonova Research Institute of Rheumatology, Moscow, Russia, Moscow, Russian Federation*

Background: Currently non-steroidal anti-inflammatory drugs (NSAIDs) are the first-line drugs for treatment of axial spondyloarthritis (axSpA) and much discussed question of influence frequency of intake NSAIDs on axSpA disease activity.
Objectives: To compare the frequency of intake NSAIDs with early axSpA disease activity.
Methods: The research included 65 patients (pts) with axSpA (criteria ASAS 2009) with disease duration <5 years and age at onset <45 years. Pts at least 2 years follow up, 32 (49,2%) males, pts mean age was 28,5 (5,8) y., average disease duration - 24,1 (15,4) mo, 60 (92,3%) pts were HLA-B27 positive. At baseline all pts were NSAID-naïve, DMARD-naïve, anti-TNF-naïve. For 2 years pts taking NSAIDs at therapeutic doses. The dosages of NSAIDs accounted by the ASAS NSAID index. 1 year after baseline – 9 (13,8%) pts started treatment with anti – TNF because of high activity of the disease and absence of effect from 2 NSAIDs. 2 years after baseline number of pts with anti-TNF equal - 15 (23,0%).
Results: Compared with baseline characteristic after 2 years have significantly reduced disease activity and increased the number of ASAS partial remission (PR) in patients with axSpA (Table 1).
There were no statistical differences between the frequency of NSAIDs intake and early axSpA disease activity (Table 2).

Table 1. Outcome parameters at baseline and after 2 years of NSAID treatment

	Baseline, NSAID naïve (n=65)	2 years after baseline with NSAIDs (n=50)	p
BASDAI, mean (s.d)	3,6 (1,9)	2,4 (1,9)	0,6
BASDAI≥4, % pts	29 (44,6%)	10 (20,0%)	0,05
BASDAI <3, % pts	26 (40,0%)	46 (92,0%)	0,01
ASDAS-CRP, mean (s.d)	2,4 (1,1)	1,7 (1,1)	0,0009
ASDAS-CRP≥2,1, % pts	39 (62,9%)	22 (44,0%)	0,4
ASDAS<1,3, % pts	11 (16,9%)	27 (54,0%)	0,004

Table 2. Outcome parameters at 1 and 2 years after baseline depend on NSAID index >50 or NSAID index <50

	1 year after baseline (n=56)			2 years after baseline (n=50)		
	NSAID index >50 n=40 (61,5%)	NSAID index <50 n=16 (23,0%)	P	>50 n=28 (56,0%)	NSAID index <50 n=22 (44,0%)	p
BASDAI, mean (s.d)	2,3 (1,5)	1,9 (1,8)	0,4	2,3 (1,5)	1,8 (1,3)	0,6
BASDAI≥4, % pts	3 (7,5%)	1 (6,2%)	1,0	4 (14,2%)	2 (9,1%)	0,8
BASDAI <3, % pts	28 (70,0%)	12 (75,0%)	0,8	20 (71,4%)	21 (95,4%)	0,5
ASDAS-CRP, mean (s.d)	1,6 (0,7)	1,3 (0,8)	0,4	1,7 (0,9)	1,4 (0,7)	0,2
ASDAS-CRP≥2,1, % pts	12 (30,0%)	3 (18,7%)	0,7	9 (32,1%)	8 (36,3%)	0,7
ASDAS<1,3, % pts	15 (37,5%)	6 (37,5%)	0,8	13 (46,4%)	10 (45,4%)	0,9
ASAS PR, % pts	15 (37.5%)	8 (50,0%)	0,6	12 (42,8%)	9 (40,9%)	1,0

Conclusions: Long reception of NSAIDs in patients with early axSpA reduces disease activity, however, the receive frequency does not affect the activity of the disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3646

AB0689 METABOLIC SYNDROME IN ANKYLOSING SPONDYLITIS AND THE EFFECT OF ANTI-TNF THERAPY

F. Atzeni[1], L. Gianturco[2], I.F. Masala[3], S. Bongiovanni[1], L. Boccassini[1], P. Sarzi-Puttini[1], M. Turiel[1]. *[1]Rheumatology Unit, L.Sacco University Hospital; [2]Cardiology Unit, Department of Biomedical Sciences for Health, IRCCS Galeazzi Orthopedic Institute, Milan; [3]Orthopedic and Trauma, Santissima Trinità Hospital, Cagliari, Italy*

Background: Metabolic syndrome (MeS) is a cluster of cardiovascular (CV) risk factors (obesity, dyslipidemia, hypertension, alterations in glucose metabolism, and insulin resistance) whose prevalence is increasing particularly in devoloped countries. In comparison with the general population, patients with ankylosing spondylitis (AS) are at increased risk of cardiovascular (CV) disease, which is one of the main causes of mortality among them.
Objectives: The aim of this study was to identify the relationship between MeS and disease activity in AS patients, and evaluate the the effect of anti-tumour necrosis factor (TNF) therapy.
Methods: The study involved 30 outpatients who met the New York diagnostic criteria for AS: 14 males and 16 females; mean age 53.07±10.73 years; mean disease duration 5.03±4.06 years. All of the patients were being treated with DMARDs and anti-inflammatory drugs, but none had received any biological agents or steroids at baseline. The patients underwent laboratory tests (lipid profile and glucose levels), a clinical and standard echocardiographic examination, carotid ultrasonography (including the assessment of intima-media thickness and pulse wave velocity), and speckle tracking echocardiography (STE) of the left ventricle (LV) using Philips QLAB software to evaluate their CV risk profiles. Functional impairment and disease activity were assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Bath Ankylosing Spondylitis Functional Index (BASFI). All of the patients were evaluated at baseline and after 12 months of anti-TNF treatment. The data were statistically analysis using non-parametric chi-squared and Mc-Nemar tests, and the Wilcoxon-Mann-Whitney test.
Results: Before starting anti-TNF therapy, the cohort was divided into two groups: those with MeS (25%) and those without. The patients with MeS higher BASDAI scores (chi-squared test: 4.85; p=0.03). After 12 months of follow-up, there was a statistically significant improvement in global longitudinal strain (GLS) in both groups: from a baseline median of 19.94 (IQR 18.66–20.78) to a median of 21.46 (IQR 20.37–22.69) (p=0.02) in the non-MeS group, and from a baseline median of 18.88 (IQR 16.00–19.35) to 19.54 (IQR 18.21–19.98) (p=0.04) in the MeS group. No other changes in CV parameters were observed. The improvement in BASDAI scores was greater in the MeS group, but the difference was not statistically significant. The prevalence of MeS decreased after 12 months of anti-TNF therapy, although the McNemar test showed that the decrease was of borderline significance (p=0.048).
Conclusions: AS patients are affected by MeS. The effects of anti-TNF drugs on MeS are still controversial, but our findings suggest that they improve CV markers such as GLS as well as disease activity. The main limitation of this study is its small sample size and short follow-up; further studies are required in order to clarify the influence of MeS on clinical therapeutic outcomes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1792

AB0690 CLINICAL EXPERIENCE WITH INFLIXIMAB BIOSIMILAR (BOW015) IN ANKYLOSING SPONDYLITIS- EFFICACY AND SAFETY ANALYSIS FROM AN INDIAN PERSPECTIVE

I. Agrawal[1], A.N. Roy[2], R. Kiran[3], V.K. Rao[4], R.N. Sarkar[5], S. Naorem[6], A. Ray[7], M. Shamil[8]. *[1]Department of Rheumatology, Paras Hospital, Delhi; [2]Department of Rheumatology, Yashoda Hospital; [3]Department of Rheumatology, Star Hospital, Hyderabad; [4]Department of Rheumatology, Manipal Hospital, Bengaluru; [5]Department of Rheumatology, Medical college of Kolkata, Kolkata; [6]Department of Medicine, Regional Institute of Medical Sciences, Imphal; [7]Department of Rheumatology, Radiant Medical Centre, Kolkata; [8]Medical Affairs Manager, Sun Pharma Laboratories Ltd, Mumbai, India*

Background: The regulatory phase III trial supporting the approval of biosimilar infliximab (BOW015) in India included only rheumatoid arthritis patients. Consequently there is paucity of data on the effectiveness of BOW015 in Ankylosing Spondylitis (AS).[1,2,3] Hence, we decided to objectively quantify the effectiveness and safety of BOW015 in AS patients.
Objectives: To determine safety, efficacy and tolerability of BOW015 in Indian AS patients.
Methods: We retrospectively collected data from seven centres to get a comprehensive picture of the Indian population. The protocol along with data collection form was designed by the investigators and ethics committee approval was obtained. Biologic naïve patients diagnosed with AS as per Assessment of Spondylo Arthritis International Society criteria who were having six months of follow up data during January-November 2016 were included in the study. Percentage of patients achieving major clinical improvement (Ankylosing Spondylitis Disease Activity Score C-reactive protein ($ASDAS_{CRP}$) >2 from the baseline to six months of follow up) was the primary variable. Secondary variables included; clinical improvement criteria ($ASDAS_{CRP}$>1.1 from the baseline to six months of follow up), change in $ASDAS_{CRP}$, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), CRP and Erythrocyte Sedimentation Rate (ESR) from the baseline to six months. Variables were reported as mean ± Standard Deviation (SD), absolute change in variable were reported along with their Confidence Interval (CI) and data was analyzed using Statistical Package for the Social Science V-22.
Results: A total of 68 patients treated with BOW015 having follow-up data for six months were analyzed. Mean age of patients was 32.63±11.73 (SD) years with mean body mass index of 25.72±7.48 (SD) kg/m^2 and about 32 (47%) patients had peripheral arthritis. Of the treated patients, 52 (76%) patients were administered four doses while 6 (9%) patients administered three doses, 3 (5%) patients administered two doses and 7 (10%) patients administered single dose as they were loss to follow up. As per the primary variable, 67.9% patients achieved major clinical improvement, 9.4% patients achieved clinical improvement and 22.6% were non-responders. There was an absolute change of -2.54 (95% CI -1.92, -3.17) in BASDAI and -1.77 (95% CI -1.43, -2.11) in $ASDAS_{CRP}$ right from first follow up corresponding to post 1st dose visit which was statistically significant (see Table-1). This trend was observed in the subsequent visits in BASDAI, $ASDAS_{CRP}$, ESR and CRP which continued till the end of six months. One patient developed pulmonary tuberculosis and marginally elevated liver enzymes were seen in two patients.

Table 1: Change in the primary and secondary variables

	Baseline (mean±SD)	Δ Baseline to 1st follow up (Mean Difference; 95% CI)	Δ Baseline to 2nd follow up (Mean Difference; 95% CI)	Δ Baseline to 6 months follow up (Mean Difference; 95% CI)	p value compared to previous visit and baseline vs. 6 months FU
BASDAI	5.83±1.90	-2.54 (95% CI -1.92, -3.17)	-3.44 (95% CI -2.79, -4.09)	-3.77 (95% CI -3.05, -4.48)	<0.05
$ASDAS_{CRP}$	3.88±0.80	-1.77 (95% CI -1.43, -2.11)	-2.212 (95% CI -1.86, -2.55)	-2.13 (95% CI -1.78, -2.47)	<0.05
ESR (mm/h)	39.45±27.04	-20.82 (95% CI -14.08, 27.55)	-26.137 (95% CI -19.05, -33.22)	-26.087 (95% CI - 17.89, 34.28)	<0.05
CRP(mg/L)	25.06±22.84	-18.408 (95% CI -12.01, 24.80)	-18.918 (95% CI -12.69, -25.14)	-15.702 (95% CI -9.38, 22.02)	<0.05

Conclusions: BOW015 showed significant improvement in $ASDAS_{CRP}$ and BASDAI in patients with AS on a six month follow up period and the clinical benefits were apparent as early as first dose of BOW015.
References:
[1] Kay J et al. Ann Rheum Dis 2014; 73(Suppl2):64.
[2] Kay J et al. Arthritis Rheumatol. 2014; 66(12):3538.
[3] Dörner T, Kay J. Biosimilars in rheumatology: current perspectives and lessons learnt. Nat Rev Rheumatol. 2015 Dec;11(12):713–24.
Disclosure of Interest: I. Agrawal: None declared, A. Roy: None declared, R. Kiran: None declared, V. Rao: None declared, R. Sarkar: None declared, S. Naorem: None declared, A. Ray: None declared, M. Shamil Employee of: Sun Pharma Laboratories Ltd, Mumbai, India
DOI: 10.1136/annrheumdis-2017-eular.5865

AB0691 METFORMIN THERAPY CAN RESTORE THE BALANCE OF TH17 AND TREG CELLS IN PATIENTS WITH SPONDYLOARTHRIT

J. He[1], J. Xie[1], H. Niu[1], R. Jia[1], J. Cao[1], Y. Liu[1], J. Li[1], J. Luo[1], X. Sun[1], X. Li[1], C. Lu[2], C. Gao[3]. *[1]Rheumatology, The Second Hospital of Shanxi Medical University, Taiyuan; [2]Rheumatology, West China Hospital of Sichuan Universit, Sichuan, China; [3]Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, United States*

Background: Spondyloarthrit (SpA) is a chronic autoimmune disease and is associated with immunological function disorder. Previous studies have observed that increased number of T17 cells and decreased number of Regulatory T (Treg) cell in patients with S [1,2]. However, the current therapy for SpA, focusedon NSAID, biological agents and glucocorticoid, can't correct the imbalance of Th17 and Treg cells. Metformin has been demonstrated a reducing effect on Th17 cells but an increasing effect on Treg cells, regulating the Thl7/Treg ratio [3].
Objectives: The study is to explore the effect of metformin therapy on the balance of Th17 and Treg cells in patients with SpA.
Methods: SpA patients (n=27) (from August 1st to November 30th in 2016, both outpatients and inpatients in our department, according to American-European Consensus Group criteria for SpA), who were given metformin (750mg/day for 6 weeks). Laboratory indicators were compared before and after metformin treatment.
Results: The number of Treg cells [25.37 (18.31,45.78) vs.34.43 (25.91,50.31), P=0.015] significantly increased after the treatment. At the same time, there was a significantly decrease in the ratio of Th17/Treg cells [0.26 (0.15,0.48) vs. 0.22 (0.1,0.33), P+0.037]. Besides, Th17 cells were also decreased [7.85 (4.95,10.65) vs. 6.42 (3.7,10.63)].
Conclusions: Metformin can restore and maintain the balance of Th17 and Treg cells in the patients with SpA. And it may be a potential therapy for SpA.
References:
[1] Jandus C, Bioley G, Rivals JP, Dudler J, Speiser D, Romero P. Increased numbers of circulating polyfunctional Th17 memory cells in patients with seronegative spondylarthritides.Arthritis Rheum. 2008;58:2307–17.
[2] Shen H, Goodall JC, Hill Gaston JS. Frequency and phenotype of peripheral blood Th17 cells in ankylosing spondylitis and rheumatoid arthritis.Arthritis Rheum. 2009;60:1647–56.
[3] Son HJ, Lee J. Metformin attenuates experimental autoimmune arthritis through reciprocal regulation of Th17/Treg balance and osteoclastogenesis. Mediators Inflamm.2014,2014:973986.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4554

AB0692 EFFECTS OF INTRAVENOUS GOLIMUMAB ON PATIENT-REPORTED OUTCOMES IN ACTIVE ANKYLOSING SPONDYLITIS: 28-WEEK RESULTS OF THE PHASE III GO-ALIVE TRIAL

J.D. Reveille[1], A. Deodhar[2], E.K. Chan[3], S. Peterson[4], N. Li[4], E. Hsia[4,5], L. Kim[4], K.H. Lo[4], D.D. Harrison[4], C. Han[6]. *[1]University of Texas Health Sciences Center, Houston; [2]Oregon Health & Science University, Portland; [3]Janssen Global Services, LLC, Raritan; [4]Janssen R&D, LLC, Spring House; [5]University of Pennsylvania School of Medicine, Philadelphia; [6]Janssen Global Services, LLC, Malvern, United States*

Objectives: To evaluate patient-reported outcomes (PRO) of physical functioning, mental health functioning, health state, and health-related quality of life (HRQoL) in patients (pts) w/active Ankylosing Spondylitis (AS) treated w/intravenously administered (IV) golimumab (GLM), an anti-TNFα monoclonal antibody.
Methods: GO-ALIVE is a Phase 3, multicenter, randomized, double-blind, placebo-controlled trial. Pts (aged ≥18 years) had a diagnosis of definite AS (per modified New York criteria) and BASDAI ≥4, total back pain visual analogue scale ≥4, and CRP ≥0.3mg/dL. At baseline, 208 pts were randomized either to IV GLM 2mg/kg (N=105) at Wks 0, 4, and every 8 wks or placebo (PBO, N=103) at Wks 0, 4, and 12, w/crossover to GLM at Wk 16.
Three PRO instruments were included: 1) SF-36, a generic instrument designed to measure physical & mental health functioning, 2) EQ-5D visual analogue scale (VAS), a generic measure of current health state & 3) Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire, a disease-specific instrument designed to measure the impact of AS on HRQoL. The scores for SF-36 range from 0–100 w/higher scores indicating better functioning. It has Physical (PCS) and Mental Component Summary (MCS) and eight subscales (physical functioning, role-physical, body pain, general health, vitality, social functioning, role-emotional, & mental health). EQ-5D has a scale of 0–100 (0=worst health you can imagine to 100=best health you can imagine). ASQoL assesses sleep, mood, motivation, ability to cope, activities of daily living, independence, relationships, & social life in pts w/AS. The scores range from 0–18 w/higher scores indicating worse HRQoL. Unadjusted p-values of least square mean differences (LSMD) between treatment groups were based on analysis of covariance (ANCOVA) controlling for prior anti-TNF therapy.
Results: Table 1 summarizes the mean changes from baseline at Wks 8, 16, & 28. Improvements from baseline in SF-36 PCS & MCS were greater in the GLM group than PBO at Wk 8 (6.83 vs. 2.07, p<0.001; 5.56 vs. 1.67, p=0.006, respectively) and maintained through Wk 16 (8.52 vs. 2.87, p<0.001; 6.47 vs.

0.84, p<0.001, respectively). Improvements in all SF-36 subscales were observed in the GLM group at Wks 8 & 16 compared to PBO (p<0.01, with the exception of the role-emotional subscale [p=0.058]). The percentage of pts achieving clinically meaningful change (5 points or greater) in SF-36 PCS & MCS were higher in GLM than PBO in Wks 8 & 16 (PCS: 58.1 vs. 27.2, 67.6 vs. 35.9, respectively; MCS: 48.6 vs. 34.0, 54.3 vs. 29.1, respectively; p<0.05 for all). Mean EQ-5D VAS improvements were greater (p<0.001) in GLM than PBO at Wks 8 & 16 (17.61 vs. 6.63, 20.32 vs. 4.79, respectively). Greater improvements in ASQoL were observed in GLM compared to PBO at Wks 8 & 16 (-4.5 vs. -1.5, p<0.001, -5.4 vs. -1.8, p<0.001, respectively). By Wk 28, after PBO crossed-over to GLM, improvement in PCS, MCS, EQ-5D VAS, & ASQoL were similar between the two treatment arms.

Table: Summary of mean (standard deviation) changes in SF-36, EQ-5D, and ASQoL.

		IV GOLIMUMAB 2mg/kg	PLACEBO
Patients		105	103
Mean (SD) change from baseline in SF-36 PCS:	Week 8	6.83 (6.90) (p<0.001)	2.07 (5.66)
	Week 16	8.52 (7.54) (p<0.001)	2.87 (6.11)
	Week 28	9.08 (8.02)	9.29 (7.09)
Mean (SD) change from baseline in SF-36 MCS:	Week 8	5.56 (9.26) (p=0.006)	1.67 (8.80)
	Week 16	6.47 (9.12) (p<0.001)	0.84 (9.82)
	Week 28	6.16 (10.91)	5.60 (9.70)
Mean (SD) change from baseline in EQ-5D VAS:	Week 8	17.61 (24.02) (p<0.001)	6.63 (19.881)
	Week 16	20.32 (24.59) (p<0.001)	4.79 (23.47)
	Week 28	20.52 (27.86)	22.45 (23.08)
Mean (SD) change from baseline in ASQoL:	Week 8	-4.5 (4.71) (p<0.001)	-1.5 (3.90)
	Week 16	-5.4 (5.01) (p<0.001)	-1.8 (4.50)
	Week 28	-5.3 (5.24)	-5.3 (4.84)

Conclusions: Adult pts w/active AS treated w/IV GLM showed marked improvements in physical functioning, mental health functioning, health state, & HRQoL.

Disclosure of Interest: J. Reveille Grant/research support from: Janssen Scientific Affairs, LLC., A. Deodhar Grant/research support from: Janssen, Amgen, Abbvie, GSK, Eli Lilly, Novartis, Pfizer, UCB, Consultant for: Janssen, Eli Lilly, Novartis, Pfizer, UCB, E. Chan Employee of: Janssen Global Services, LLC, S. Peterson Employee of: Janssen R&D, LLC, N. Li Employee of: Janssen R&D, LLC, E. Hsia Employee of: Janssen R&D, LLC, L. Kim Employee of: Janssen R&D, LLC, K. H. Lo Employee of: Janssen R&D, LLC, D. Harrison Employee of: Janssen R&D, LLC, C. Han Employee of: Janssen Global Services, LLC

DOI: 10.1136/annrheumdis-2017-eular.6145

AB0693 PATIENTS WITH CHRONIC INFLAMMATORY ARTHROPATHIES TREATED WITH GOLIMUMAB ACHIEVE A HIGHER SERUM LEVEL OF DRUG IF USED AS THE FIRST OR SECOND BIOLOGICAL DRUG

J. Rosas[1], M. Marco-Mingot[2], J.M. Senabre-Gallego[1], F. Llinares-Tello[2], A. Pons[1], X. Barber[3], G. Santos-Soler[1], E. Salas[1], C. Cano[1], M. Lorente[1], M. Sanchís-Selfa[3], J. Molina[2], M. García-Carrasco[4] on behalf of AIRE-MB Group. *[1]Rheumatology Department; [2]Laboratory Department, Hospital Marina Baixa, Villajoyosa (Alicante); [3]CIO, Universidad Miguel Hernández, Elche, Spain; [4]Rheumatology Department, Universidad Autómoma de Puebla, Puebla, Mexico*

Objectives: To know the influence of the order of introduction of Golimumab (GLM), on clinical efficacy in ankylosing spondylitis (AS), psoriatic arthritis (PSA) and rheumatoid arthritis (RA).

Methods: A prospective, observational study, in 46 consecutive patients with AS, APS and RA, treated with GLM. Data: epidemiological, concomitant DMARD, time of disease evolution, HLA-B27, RF and ACPA; from GLM: order of introduction, time in treatment, serum level and anti-GLM Ab. The clinical response was assessed in AS patients using BASDAI, BASFI, ASDAS-VSG. In patients with RA or peripheral APS, DAS28-VSG, DAS28-PCR and SDAI. Serum levels of GLM and anti-GLM Ab were determined by ELISA (Progenika, Grifols SA, Spain). Serum cutoff levels for serum GLM levels: 36 ng/mL and for anti-GLM Ab: UA>20 AU/mL. Samples were extracted just prior GLM administration (trough level) and stored frozen at -80ºC until analysis.

Results: Of 33 (72%) AS patients: 52% were males, mean age 53±12 years, mean BMI 28±4, disease mean evolution 16±12 years and in GLM: 1.3±1.1 years, 30% received DMARD, being GLM the first anti-TNF in 25%, second 37%, third 25% and fourth in 13%. The mean GLM level was 0.77±0.62 mg/mL and the prevalence of anti-GLM antibodies was 6%. In the 5 patients with RA and 8 with APS: 23% were men, mean age of 55±11 years, mean BMI 28±6, mean disease evolution of 10.5±8 years and in GLM of 2±1.5 years, the 85% of patients received DMARD, being GLM the first anti-TNF in 31%, second 15%, third 31% and fourth 23%. The mean GLM level was 0.703±0.53 mg/L. No anti-GLM Ab were detected.

Table 1. Characteristics of patients with receiving GLM, according to the order of introduction

Golimumab (GLM) RA-APS (n: 13)	1°–2° anti-TNF (n: 7)	3°–4° Anti-TNF (n: 6)	p
BMI, kg/m^2: mean (SD)	28,72 (6,62)	28,93 (6,66)	0,95
Disease evolution (years): mean (SD)	10,1 (7,64)	11,53 (10)	0,78
DMARD, n (%)	7 (100)	4 (67)	0,13
Years on GLM: mean (SD)	2,27 (1,86)	2,5 (2,04)	0,84
anti-GLM Ab, U/L, n (%)	0	0	–
DAS28-VSG, mean (SD)	1,74 (0,83)	2,12 (0,94)	0,47
DAS28-PCR, mean (SD)	1,82 (0,85)	2,28 (0,93)	0,39
SDAI, mean (SD)	3,92 (5,17)	7,67 (6,58)	0,30
Golimumab (GLM) AS (n: 33)	**1°–2° anti-TNF (n: 21)**	**3°–4° anti-TNF (n: 12)**	**p**
BMI, kg/m^2: mean (SD)	27,46 (4,20)	29,26 (3,09)	0,16
Disease evolution (years): mean (SD)	14,25 (10,55)	20,65 (14,27)	0,21
DMARD, n (%)	8 (38%)	2 (17)	0,57
Years on GLM: mean (SD)	1,75 (1,47)	1,13 (0,89)	0,14
GLM level, mg/dL: mean (SD)	0,919 (0,63)	0,448 (0,47)	**0,025**
anti-GLM Ab, U/L, n (%)	0	2 (17)	–
BASDAI: mean (SD)	5,96 (2,48)	6,10 (2,23)	0,86
ASDAS: mean (SD)	2,92 (0,87)	3,79 (2,68)	0,64

Conclusions: 1. The overall prevalence of anti-GLM Ab was 6% and 17% in AS patients. Not detecting in patients with RA or PSA. 2. Serum GLM level was higher among the patients receiving it as the 1st or 2nd anti-TNF. 3. In AS GLM as 3rd or 4th anti-TNF were able to achieve clinical remission, similar to that achieved as 1st or 2nd drug.

Acknowledgements: The study was supported by a grant from the Fundación Española de Reumatología (FVR/2012) and the Asociación para la Investigación en Reumatología de la Marina Baixa (AIRE-MB).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4308

AB0694 RHEUMATOLOGISTS' ATTRIBUTION OF PATIENT-REPORTED SYMPTOMS IN AXIAL SPONDYLOARTHRITIS (AXSPA): IMPACT ON RESPONSE TO TNF-INHIBITORS (TNFI) IN 508 PATIENTS

L. Gossec, A. Moltó, A. Etcheto, N. Boudersa, P. Claudepierre, N. Roux, F. Berenbaum, A. Martin, L. Sparsa, P. Coquerelle, M. Soubrier, S. Perrot, M. Dougados. *Predict-SpA Study Group, Paris, France*

Background: In axSpA, treatment decisions are mainly based on patient-reported symptoms: recommendations are to initiate TNFi in patients with active disease and with physician conviction that treatment is needed (ref). However, the attribution of symptoms to inflammation is difficult to establish in axSpA.

Objectives: The objective of the present analysis was to explore the link between physician-attributed causality for symptoms and treatment response to TNFi.

Methods: The PredictSpA study (ClinicalTrials.gov: NCT03039088) was a longitudinal observational multicenter study in France in 2015. Patients with physician-defined definite axSpA and starting a TNFi treatment were included, a TNFi was prescribed according to usual practice and efficacy was assessed at 12 weeks by BASDAI50 response. At baseline, symptoms levels including BASDAI and ASDAS were collected and the physician evaluated the causality of symptoms by answering the following 3 questions: how convinced are you that the symptoms of this patient are due to (A) inflammatory axSpA activity (B) to axSpA severity (eg syndesmophytes, kyphosis) and NOT to disease activity and (C) to other diseases and NOT axSpA. Each question was assessed 0–10 (not convinced at all to absolutely convinced). The link between a score ≥4/10 on each of the 3 questions and BASDAI50 response was assessed by univariate logistic regression. Patients interrupting the TNFi before 3 months were considered as non-responders and missing data were imputed using non-responder imputation.

Results: In all, 519 patients were included and 508 had data over 3 months: mean age 41.3 (SD 11.6) years, mean disease duration 6.1 (SD 8.4) years, 237 (46.7%) were women, 424 (83.5%) satisfied the ASAS criteria for axSpA of whom 379 (74.6%) were in the imaging arm and 45 (8.9%) in the clinical arm. Symptom levels were high: mean BASDAI was 5.7 (SD 1.8) and mean ASDAS-CRP was 3.3 (SD 0.9) with only 6 (1.2%) patients in inactive disease state according to ASDAS. The physician-attributed causality of symptoms was mostly related to inflammatory activity: mean scores for (A), (B) and (C) were respectively, 7.4 (SD 2.0), 2.3 (SD 2.5) and 2.1 (SD 2.2). When physicians attributed causality to non-axSpA (score (C) ≥4/10), BASDAI50 response was less frequent: 45/118 (38.4%) vs 213/390 (54.6%), odds ratio 0.5 [95% CI 0.3, 0.8].

Conclusions: In axSpA patients starting a TNFi with high symptom levels, physician-attributed causality of symptoms was mainly related to inflammatory activity of the axSpA. When physician-attributed causality was more oriented towards non-axSpA causes, BASDAI50 response after 3 months of a TNFi was lower. This confirms the validity of the ASAS-EULAR recommendations for starting a TNFi which rest on a level of symptoms but associated to physician conviction of the indication.

References:

[1] van der Heijde D, et al. 2016 update of the ASAS-EULAR management

recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017 [Epub ahead of print].
Acknowledgements: This study was conducted thanks to an unrestricted grant from MSD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4730

AB0695 DOSE TAPERING OF INFIXIMAB IN PATIENTS WITH SPONDYLOARTHRITIS

M. Correyero, J.C. Nieto, C.M. González, A. López, R. González, C. Saenz, L. García-Montoya, F.J.L. Longo, I. Monteagudo. *Rheumatology Department, Hospital General Universitario Gregorio Marañon, Madrid, Spain*

Background: Infliximab have proven to be effective in spondyloarthritis. Previous studies suggest that patients in clinical remission may benefit from dose reduction or pharmacological tapering without relapse.
Objectives: To study the evolution of clinical activity and physical function in patients with spondyloarthritis, ankylosing spondylitis (AS) and psoriatic arthritis (PsA) under Infliximab (IFX) tapering strategy.
Methods: This is a prospective single-centre observational study of patients diagnosed with AS and PsA treated with IFX (5 mg/kg/infusion) between January 1, 2012 and December 31, 2015. We included patients who achieved clinical remission or low activity index (expressed with BASDAI and BASFI) and decided to lower the dose of 5 to 4 mg/kg/infusion, maintaining the periodicity of the treatment in each patient. Demographic data (age, gender, time with IFX) daily activities, physical activity (BASDAI and BASFI) and laboratory data (ESR and CPR) were collected at the baseline visit prior to tapering, at the next infusion following dose reduction and the last infusion (between November 1st 2014 and December 31st, 2016).
Results: We included 18 patients (16 men) on IFX treatment with EA (16) or axial APs (2). The medians of age and time of evolution were 50.79 years (41.8–55.1) and 9.5 years (7.2–11.5), respectively. Table 1 shows the clinical and laboratory data obtained at the baseline visit, the next infusion and the last infusion. Fourteen patients (87.9%) continued with the dose of 4 mg/kg/infusion and are maintained in clinical remission. Four patients returned to the dose of 5 mg/kg/infusion due to loss of efficacy at dose reduction, with a mean follow-up of 17.6 months (17.0–19.1). Clinical remission was again achieved in the 4 patients, although one of them changed biological therapy due to loss of efficacy of IFX after 3 infusions with 5 mg/kg/infusion.

Table 1. Clinical and laboratory data during follow-up

	Baseline	Next Infusion	Last Infusion
BASDAI median (RI)	3,1 (1,45–4,45	4 (1,4–4,25)	4,1 (1,65–6,15)
BASFI median (RI)	2,8 (1,1–4,5)	3,6 (1,8–4,25)	2,8 (1–5)
ESR (mm/h) median (RI)	6,5 (3–11,25)	4,5 (3–11,5)	12,5 (6,5–16,75)
CPR (mg/dl) median (RI)	0,2 (0,2–0,55)	0,3 (0,1–0,4)	0,2 (0,1–0,72)

Conclusions: In our patients with spondyloarthritis dose reduction of IFX was well tolerated and safe, maintaining the clinical response measured by BASDAI and BASFI. In 3 out of 4 patients who worsened upon dose reduction, the 5 mg/kg/infusion dose recovered clinical remission.
References:
[1] Janta I et al. Clin Rheumatol. 2015;34: 935–42.
[2] Baraliakos X et al. RMD Open. 2016;2: e000272.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6554

AB0696 RETENTION RATES OF ADALIMUMAB, ETANERCEPT, AND INFLIXIMAB AS FIRST- OR SECOND-LINE BIOTHERAPIES FOR SPONDYLOARTHRITIS PATIENTS IN DAILY PRACTICE IN AUVERGNE (FRANCE)

M. Soubrier[1], B. Castagné[1], B. Pereira[2], A. Fan[1], T. Frayssac[1], M. Couderc[3], S. Malochet-Guinamand[1], S. Mathieu[1], Z. Tatar[1], A. Tournadre[3], J.-J. Dubost[1]. *[1]Rheumatology, C.H.U. HÔPITAL GABRIEL MONTPIED; [2]DRCI, CHU Gabriel Montpied; [3]Rheumatology, CHU Hopital Gabriel Montpied, Clermont-Ferrand, France*

Background: The use of tumour necrosis factor alpha (TNF-α) inhibitors – or anti-TNFs – has considerably improved the treatment of spondyloarthritis (SpA). The first three of these available anti-TNFs (infliximab, adalimumab, and etanercept) are the most widely used in the treatment of SpA. Their efficacy and safety have been demonstrated in extensive randomised controlled trials (RCTs).Nevertheless, the randomized studies were of short duration and included a selected population that differed from patients treated in daily practice
Objectives: To compare, in real-life settings, the retention rates of the initial anti-TNF treatment (etanercept [ETN], adalimumab [ADA],and infliximab [IFX]) used as first-line biotherapy for spondyloarthritis (SpA), and to evaluate treatment switches to another anti-TNF inhibitor in the event of treatment failure.
Methods: Monocentric retrospective cohort including all SpA patients starting an initial anti-TNF therapy between 2001 and 2015.
Results: Of the 249 SpA patients analysed (135 radiographic cases, 114 non-radiographic), 102 were given ETN, 62 ADA, and 85 IFX. In total, 103 discontinued treatment. The median retention duration was 69.7 months (17–∞) (ETN: 55.4 [17.6–94.6], ADA 57.6 [13.9–∞], and IFX: not reached). Retention was longer for IFX compared with ETN (HR=0.62 [0.39–0.99]) but non-significant compared with ADA (HR: 0.91 [0.56–1.48]). The percentage of patients continuing treatment after 5 years was 47% for ETN, 46% for ADA, and 62% for IFX. In multivariate analysis, the predictive factors for retention were a low BASDAI score (HR: 1.02 [1.01–1.04]), high CRP levels (HR 0.98 [0.97–0.99]), the concomitant use of disease-modifying therapy (HR: 0.4 [0.21–0.75]), and radiographic SpA (HR: 1.5 [1.0–2.52]). In total, 61 patients switched to another anti-TNF therapy. No difference was observed among the three anti-TNF therapies with regard to the median retention duration, but the retention rate was higher in the event of treatment switches from one monoclonal antibody to another.
Conclusions: The retention rate in SpA patients proved high, and retention for IFX was superior to that of ETN.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3699

AB0697 IMPACT OF THE BASELINE BATH ANKYLOSING SPONDYLITIS RADIOLOGY HIP INDEX ON THE STRUCTURAL HIP JOINT PROGRESSION AFTER TNFα BLOCKING THERAPY IN SPONDYLOARTHRITIES PATIENTS

K. Maatallah[1], M. Sahli[1], I. Mahmoud[2], W. Hamdi[1], O. Saidane[2], M. Kchir[1], R. Tekaya[2], L. Abdelmoula[2]. *[1]Rheumatology, Kassab university hospital; [2]Rheumatology, Charles Nicolle university hospital, Tunis, Tunisia*

Background: One of the major goals of treatment of spondyloarthrites (SpA) is to prevent or slow the radiographic damage.The results of clinical trials raised expectations that TNFi are effective not only on clinical and biological parameters of the disease but may also have structural effect.
Objectives: We assessed whether the baseline Bath Ankylosing Spondylitis Radiology (BASRI) hip index had effect on structural hip progression under TNFα blockers in SpA patients with hip disease.
Methods: This was a multicentric longitudinal study including SpA patients (ASAS2009) with hip disease under TNF α blockers. Anteroposterior X-rays of the pelvis obtained at baseline were compared with X-rays obtained after 5 years [3–10] of continuous TNF α blockers treatment. Radiographic progression of the hip was evaluated by the Bath Ankylosing Spondylitis Radiology Hip Index (BASRI-h), scoring system (min 0 = no change, 1 = focal joint space narrowing, 2 = circumferential joint space narrowing >2 mm, 3 = circumferential joint space narrowing ≤2 mm or bone-on-bone apposition of <2 cm and max 4 = bone deformity or bone-on-bone apposition of ≥2 cm) and the hip joint space width (assessed by the average of measurements at three distinct sites between the acetabulum and femoral head)[1]. The median progression of the hip joint space was chosen as cut-off to define the structural evolution, it was 0.3mm. A good response of the hip was defined by a stabilization or a decrease of the hip joint space less than 0.3 mm (RH+).A poor response was defined by a decrease of the hip joint space >0.3mm (RH-).
Results: 48 patients were included (81% male). The average age was 40.7±11years. The mean age at the onset of the disease was 25.8±10 years. Hip involvement was bilateral in 77% of cases. At baseline, the mean BASRI hip index was 2±0.8. The BASRI hip score was 1 in 26%, 2 in 51%, 3 in 18% and 4 in 5% of patients. The average of hip joint space width at baseline was 3.4±1.2mm. Infliximab was the most prescribed TNFα blocker (48%) followed by Etanercept (37.5%) and Adalimumab (14.5%).After 5years, the mean BASRI hip index remained stable 2±0.8, the BASRI hip score was 1 in 23%, 2 in 50%, 3 in 14% and 4 in 13% (p=ns). The variation of hip joint space width was-0.294 mm (p=ns). 29 patients were RH+. The BASRI hip index 2±0.8 and 2.1±0.9 in RH+ and RH- patients respectively with no statistically significant difference.
Conclusions: According to our study the structural hip joint progression under TNFα blockers is not influenced by the baseline BASRI hip index.
References:
[1] Konsta M,Sfikakis PP, Bournia VK, Karras D, Iliopoulos A.Clin Rheumatol (2013) 32:1229–1232.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6459

AB0698 COMPLEMENTARY AND ALTERNATIVE MEDICINE USAGE AND ASSOCIATED FACTORS IN ANKYLOSING SPONDYLITIS: PRELIMINARY RESULTS OF A CROSS-SECTIONAL STUDY

F.I. Cinar[1], O. Ozdemir[2], S. Yilmaz[3], N. Ozen[4], G. Bagcivan[5], I. Aydoğan[6], A.G. Yalcin[6], E. Tekgoz[3], M. Cinar[3]. *[1]Gulhane School of Nursing, University of Health Sciences; [2]Department of Nursing, Ankara Yildirim Beyazit University, Faculty of Health Sciences; [3]Department of Internal Medicine, Division of Rheumatology, University of Health Sciences, Gulhane Medical Faculty, Ankara; [4]University of Health Sciences, Okmeydani Training and Research Hospital, Kasimpasa Building, Istanbul; [5]Department of Internal Medicine; [6]Division of Rheumatology, Gulhane Training and Research Hospital, Ankara, Turkey*

Background: Several surveys indicate that the complementary and alternative medicine (CAM) use is especially prevalent in patients with chronic painful

conditions like ankylosing spondylitis (AS). Despite good treatment options such as tumor necrosis factor alpha (TNFα) inhibitors in AS, it is seen that patients have applied for CAM use for many reasons including local regulatory funding requirements, potential risks and accessibility of biological treatments. Few studies have examined the frequency of CAM use, and associations between demographic and disease-related factors of it in AS.

Objectives: To investigate the CAM usage of patients with AS and to determine the associated factors.

Methods: Total of 123 patients with AS, who were being followed in a tertiary rheumatology outpatient clinic, were included to the study. The demographic and clinical features along with the behaviors about the CAM usage of the patients agreeing to participate were recorded to the "Patient Assessment Form". The activity of the disease were determined with doctor global assessment (numeric visual analog scale (nVAS; 0–10), and Routine Assessment of Patient Index Data (RAPID)-3 score. The treatment adherence of the patients was assessed with the Morisky Green Levine Scale.

Results: One hundred eleven patients (%90.2) were male, and mean age was 36.5±8.8 years. The mean disease duration and mean delay in diagnosis were 10.9±6.4, and 3.7±3.9 years, respectively. The mean RAPID3 score, doctor and patient global assessment were; 9.9±5.3, 2.8±1.9, and 4.6±2.7, respectively. While 79 patients (%64.2) were on anti-TNF treatment, 76 patients were receiving NSAIDs, and 35 patients (%28.5) reported an adverse event related with the treatment. Forty-five patients (%36.6) reported to use any CAM (previous or current) (Table1). The reasons reported by the patients for the usage of CAM; media in %13, recommendations from family members or relatives in %10.6. It has been found that in married patients, the ones with lower the Morisky Green Levine Scale score (high adherence), CAM usage was statistically high ($p<0.05$). Receiving NSAIDs or anti-TNF agents was not statistically associated with CAM usage. The underlying expectations for the usage of CAM were; considering it might be helpful in %27.6; considering it might heal in %17.9; to relieve the pain in %14.6; and preventing to deteriorate the disease status in %12.2.

Table 1. Types of CAM use

CAM Type	n*	%
Plants and herbs	31	25.2
Massage	13	10.6
Spa	10	8.1
Praying/spiritual approach	6	4.9
Cupping	3	2.4
Imagining	2	1.6
Naturapati	2	1.6
Acupuncture	1	0.8

CAM, complementary and alternative medicine. *There are patients marked the method more than one.

Conclusions: In our study, we found that approximately one third of our AS patients were using CAM. When compared with the literature related with other diseases, CAM usage in AS patients was somewhat lower. Our results have demonstrated that treatment adherence was higher in those using concomitantly CAM in their therapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4196

AB0699 EFFECTS OF GLOBAL POSTURAL REEDUCATİON EXERCISE AND ANTI-TNF TREATMENTS ON DISEASE ACTIVITY, FATİGUE, MOBİLİTY, SLEEP QUALİTY AND DEPRESSİON IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS (PROSPECTIVE-CONTROLLED TRIAL)

N.H. Coksevim, D. Durmus, O. Kuru. *Physical Therapy and Rehabilitation, 19 Mayis University Medical Faculty, Samsun, Turkey*

Background: Ankylosing spondylitis (AS) is chronic inflammatory disease that affects primarily the spine and the sacroiliac joints. ASAS/EULAR guidelines describe regular exercise as the cornerstone of non-pharmacological treatment and pharmacological treatments including non-steroidal anti-inflammatory drugs as first-line therapy, and a tumour necrosis factor (TNF) alpha inhibitor (anti-TNFα) as second-line medication in patients with persistently high disease activity despite conventional pharmacological treatment in patients with AS.

Objectives: The purpose of this study was to investigate the effects of combination therapy with global postural reeducation exercise (GPR) and Anti-TNF treatments on pain, disease activity, mobility, fatigue, sleep quality, and depression in patients with active AS.

Methods: 60 active AS patients who meet the criteria of Modified New York and/or ASAS axial spondyloarthropathy were included in the study. Patients were divided into 3 groups. The first group was given anti-TNF therapy plus GPR exercise program. The 2nd group was given anti-TNF and conventional exercise therapy. The 3rd group was given routine exercise program along with their existing treatments (NSAIDs and/or SLZ). Following inventories are used for clinical evaluation: for disease activity – Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), for functionality – Bath Ankylosing Spondylitis Functional Index (BASFI), for mobility – lumbar Schober, chest expansion, hand-finger to floor distance, for fatigue – fatigue Multidimensional Assessment Questionnaire (MAF), for sleep quality – Pittsburgh sleep quality index (PSQI), for depression – Beck depression Inventory (BDI). All patients were evaluated before treatment and at 3 months.

Results: The demographic characteristics of the patients were compared and there was no significant difference between the groups. The improvements in all parameters were better in both groups receiving exercise and anti-TNF therapy than in the control group after treatment compared with baseline. The Anti-TNF + GPR exercise therapy resulted in greater improvements than the anti TNF+ conventional exercise therapy in pain, and mobility parameters.

Conclusions: Anti-TNF therapy and exercise were efficient in both groups on improving pain, disease activity, fatigue, sleep quality, and depression. However, the improvements in pain and mobility were greater in the active AS patients with GPR exercise method. Therefore motivated patients should be encouraged to perform this exercise program.

References:

[1] Lubrano E, Spadaro A, Amato S, et al. Tumour necrosis factor alpha inhibitor therapy and rehabilitation for the treatment of ankylosing spondylitis: A systematic review. Seminars in Arthritis and Rheumatism. 44(2015)542–550.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6379

AB0700 EFFICACY AND DRUG SURVIVAL OF ANTI-TUMOUR NECROSIS FACTOR-ALPHA THERAPIES IN PATIENTS WITH SPONDYLO-ARTHRITIS: ANALYSIS FROM THE THAI RHEUMATIC DISEASE PRIOR AUTHORIZATION (RDPA) REGISTER

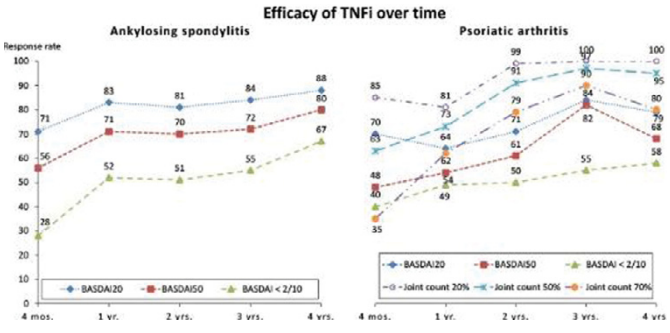
P. Chiowchanwisawakit [1], W. Katchamart [1], P. Chevaisrakul [1], P. Narongroeknawin [2], W. Louthrenoo [3], M. Osiri [4] on behalf of the Thai Rheumatism Association. *[1]Mahidol University; [2]Phramongkutklao Hospital and College of Medicine, Bangkok; [3]Chiang Mai University, Chiang Mai; [4]Chulalongkorn University, Bangkok, Thailand*

Background: Treatment recommendations for patients with spondyloarthritis (SpA) who inadequately respond to non-steroidal anti-inflammatory drugs (NSAIDs) and/or traditional disease-modifying antirheumatic drugs (DMARDs) are anti-tumour necrosis factor-alpha therapy (TNFi). There has been no data on the long-term efficacy and safety of TNFi in Thai patients with SpA.

Objectives: To evaluate the long-term efficacy and safety of the first TNFi in real-life practice and to identify the risk factors related to drug discontinuation in Thai patients with SpA from the RDPA registry.

Methods: Patients who fulfilled the 1984 Modified New York criteria for ankylosing spondylitis (AS), CASPAR criteria or Moll and Wright criteria for psoriatic arthritis (PsA) and the European Spondyloarthropathy Study Group Criteria or Modified Amor criteria for undifferentiated SpA (uSpA), and were prescribed the first TNFi between December 2009 and October 2014 in the RDPA registry were enrolled. Baseline demographic and clinical data were retrieved. A Cox proportional hazard model was used to identify the factors associated with discontinuation. The P-value of <0.05, two-sided was considered statistically significant.

Results: Of the 142 patients included, 97 had AS, 41 had PsA, and 4 had uSpA. Most AS patients were male (54.6%) with mean (SD) age of 44.6 (10.6) years, median (P_{25}–P_{75}) baseline BASDAI was 6.5 (5.6, 8.2) [from a 10-cm visual analog scale (VAS)], and median baseline patient global assessment (bPGA) was 7.2 (P_{25}–P_{75} 6.0, 8.0) (from a 10-cm VAS). For PsA patients, most were female (68.3%) with mean age of 52.6 (SD 12.2) years, median baseline BASDAI was 6.6 (P_{25}–P_{75} 4.9, 7.4) in patients with active axial involvement and median baseline number of joint involvement was 13.5 (P_{25}–P_{75} 6, 18.3) joints per patient with active peripheral joint involvement. The Efficacy of the TNFi treatment was good and it was increased over time in AS and PsA patients (figure 1). During the 5-year follow-up, AS, PsA, and uSpA patients had comparable discontinuation rate of their first TNFi treatment [25 (26%) in AS, 14 (34%) in PsA, and 1 (25%) in uSpA; p=0.82]. In univariate analysis, leflunomide use, and bPGA <3 comparing to >6 (from a 10-cm VAS) were associated with the discontinuation of TNFi in AS patients with hazard ratio (HR) (95% CI) of 2.56 (1.13, 5.81) and 8.59 (1.82, 40.65), respectively. For the patients with PsA, only infliximab use was associated with TNFi discontinuation with HR of 4.79 (95% CI 1.33, 17.20) in univariate analysis. The reasons for TNFi discontinuation were good response (38%), serious adverse effects (SAE) (30%), non-adherence (20%), and lack of efficacy (13%). Among SAE, 58% was infectious causes (57% tuberculosis and 43% non-mycobacterium infections). The others were non-infectious causes.



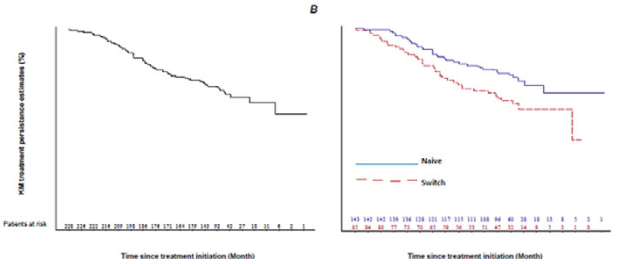
Conclusions: During the 5-year follow-up period, patients with SpA responded well to TNFi and the response rate increased over time. Tuberculosis was the most common SAE in this registry therefore surveillance of TB should be done.
Disclosure of Interest: P. Chiowchanwisawakit Grant/research support from: The Thai Rheumatism Association, W. Katchamart: None declared, P. Chevaisrakul: None declared, P. Narongroeknawin: None declared, W. Louthrenoo: None declared, M. Osiri: None declared
DOI: 10.1136/annrheumdis-2017-eular.5694

AB0701 THE REAL-LIFE USE OF GOLIMUMAB IN PATIENTS WITH IMMUNE-MEDIATED RHEUMATIC DISEASES: ONE YEAR RESULTS OF THE GO-PRACTICE STUDY

R.-M. Flipo[1], F. Tubach[2], J. Ouaniche[3], P. Goupille[4], E. Lespesailles[5], N. Gouyette[6], P. Bertin[7], B. Fautrel[8]. *[1]Rheumatology, CHU Roger Salengro, Lille, Lille; [2]Epidemiology Departement & Clinical Research, CHU Pitié Salpêtrière, Paris; [3]Private practice, Private practice, Toulon, France, Toulon; [4]Rheumatology, CHU Tours, Tours; [5]Rheumatology, CHR Orléans, Orléans, France; [6]Rheumatology, Msd France, Courbevoie Cedex; [7]Rheumatology, CHU Limoges, Limoges; [8]Rheumatology, CHU Pitié Salpêtrière, Paris, Paris, France*

Background: The GO-PRACTICE study was initiated to describe the use of Golimumab (GLM), a human anti-TNFα monoclonal antibody, in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) in French clinical practice.
Objectives: The primary objective of this interim analysis was to assess the persistence of GLM at 1-year.
Methods: Observational, multicenter, prospective, national study. Adult patients with RA, PsA and AS were included consecutively at GLM after the decision for GLM therapy has been taken or at least after GLM initiation, and followed-up for 2 years. We present here baseline characteristics for overall population (n=754) and interim results for patients with 1-year follow-up (n=228 patients with available data regarding persistence of GLM)
Results: A total of 754 patients (134 sites) were included between January 2015 and March 2016. Most of them had AS (64%), and 22% and 13% had RA and PsA, respectively. Mean age was 46±13 years and 61% were female. Almost 37% had received prior biotherapy.
Nearly all patients (99%) were prescribed GLM as 50 mg-monthly injections. GLM was mostly co-prescribed with other antirheumatic treatments (84%).
Of the 163 patients with available data at strictly 1-year, 56.4% were still treated with GLM; (61.9% in biotherapy-naïve patients); the persistence rate was similar across the three groups. The Kaplan-Meier duration curves of GLM are presented in figure 1. The main reason for GLM discontinuation was primary non-response, reported in 42% of patients.
Among patients who continued GLM treatment, a meaningful improvement in disease activity was observed at 1-year in 71.9% of RA, 63.2% of PsA and 68.0% of AS patients. Patients-reported outcomes, including pain and functional disability, also showed improvement

Figure 1: Kaplan–Meier duration curve of treatment with golimumab for A) the global population (n=228) and B) by prior biotherapy: biotherapy naïve patients (n=143, blue line) and biotherapy experienced patients (n=85, red dotted line).



Conclusions: In real-life practice in France, GLM was prescribed according to recommendations in terms of dosage and therapeutic strategy. One-year interim analysis, performed in one third of the cohort, suggests that GLM treatment is associated with clinical improvements leading to persistence of treatment. These results need to be confirmed in the final overall analysis planned in 2018.
Disclosure of Interest: R.-M. Flipo: None declared, F. Tubach: None declared, J. Ouaniche: None declared, P. Goupille: None declared, E. Lespesailles: None declared, N. Gouyette Employee of: MSD, P. Bertin: None declared, B. Fautrel: None declared
DOI: 10.1136/annrheumdis-2017-eular.4073

AB0702 IMPROVEMENT OF FATIGUE IN PATIENTS WITH SPONDYLOARTHRITIS TREATED WITH ANTI-TNF THERAPY: A PROSPECTIVE STUDY IN A REAL-LIFE SETTING

S. Desouches, E. Gaigneux, K. Louati, L. Lemeunier, C. Beauvais, J. Sellam, F. Berenbaum. *Rheumatology, APHP Saint-Antoine, paris, France*

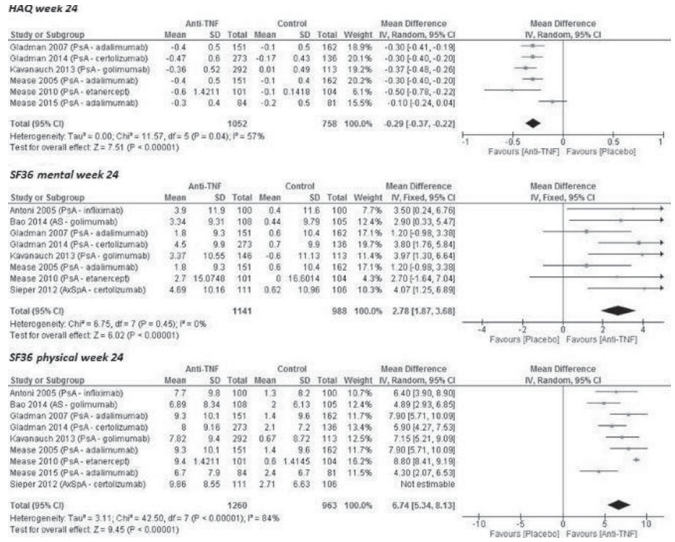
Background: Besides randomized controlled trials evaluating biologic agents on fatigue, the impact of anti-TNF therapy on this crucial symptom has been poorly assessed in a real-life setting (1).
Objectives: To assess the early effect of etanercept (ETN) on fatigue-related outcomes in spondyloarthritis (SpA) patients in a real-life setting.
Methods: This prospective study included patients with active SpA fulfilling ASAS 2009 axial or peripheral criteria requiring an anti-TNF. All patients were treated with ETN 50mg weekly. BASDAI, BASFI, functional assessment of chronic illness therapy-fatigue (FACIT-F) (0 maximum and 52 the minimum of fatigue) and visual analogic scale of fatigue (VAS-F) (0 the minimum -100 maximum of fatigue) were assessed at inclusion at the time of ETN beginning (M0) and 4±1 months later (M4).
The primary outcome was the M0-M4 change of VAS-F. The secondary outcomes were i) the M0-M4 change of FACIT-F ii) the frequency of patients who met improvement according to FACIT-F (defined as the minimal clinically important difference of FACIT-F corresponding to a 4-points decrease (FACIT-F responders). To determine whether fatigue change was related to disease activity improvement, a correlation between M0-M4 changes of BASDAI and VAS-F or FACIT-F was determined.
Results: 30 SpA patients were enrolled (60% women, mean age ± standard deviation 39±8 years-old, axial SpA 83%, mean BMI 26±4, 80% ETN as a 1st line). Mean BASDAI improved at M4 (M0 48±20 versus M4 36.5±22; p=0.04) as well as VAS-F (M0 69±18 vs M4 52±24; p=0.01). The frequency of patients having VAS-F>50/100 was 86% at M0 and decreased at 36% at M4. Conversely, no significant change was observed concerning FACIT-F (M0 24.5±24 versus M4 28.8±11: p=0.36). At M4, 64% patients were FACIT-F responders. FACIT-F and VAS-F M0-M4 changes were highly correlated (r=0.78, p<0.0001).
Despite no correlation between BASDAI and FACIT-F M0-M4 changes (r=0.36, p=0.1), a trend was observed for BASDAI and VAS-F M0-M4 changes in the same fashion (r=0.36, p=0.07). Interestingly, there was no baseline clinical characteristic associated with subsequent better fatigue improvement.
Conclusions: This real-life study investigating the early effect of etanercept therapy on fatigue in SpA patients showed that fatigue (according to VAS-F) significantly improved while effect on FACIT-F was less pronounced. This improvement was explained, only in part, by disease activity improvement.
References:
[1] Chauffier K, et al Clin Exp Rheumatol. 2013;31:864–70.
Acknowledgements: Grant from Pfizer.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2735

AB0703 IMPACT OF ANTI-TNF AGENTS ON PATIENT-REPORTED OUTCOMES IN SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW OF THE LITERATURE AND META-ANALYSIS

S. Laclau[1], A. Constantin[1,2], A. Cantagrel[1,2], T. Barnetche[3], A. Ruyssen-Witrand[1,4], Y. Degboe[1,2]. *[1]Rheumatology Center, Hospital Pierre Paul Riquet, Toulouse University Hospital; [2]CPTP, INSERM UMR 1043, Toulouse; [3]Rheumatology Department, Fhu Acronim, Bordeaux University Hospital, Bordeaux; [4]Pharmaco-épidémiologie, Evaluation de l'utilisation et du risque médicamenteux, INSERM UMR 1027, Toulouse, France*

Background: Disability, alteration in quality of life and fatigue are frequently reported in spondyloarthritis (SpA). Anti-TNF demonstrated clinical efficacy in SpA. However efficacy on patient-reported outcomes (PROs) may differ from medical assessment.
Objectives: To assess the impact of anti-TNF on quality of life, disability and fatigue reported by SpA patients.
Methods: *Design:* systematic review and meta-analysis of the literature. *Data sources:* two authors (SL and YD) independently screened PubMed-Medline, Cochrane library and EMBASE databases until November 2016. *Key words:* ("Patient reported" OR "quality of life" OR fatigue OR FACIT) AND (spondyloarthritis OR "psoriatic arthritis" OR "ankylosing spondylitis") AND (anti-TNF OR certolizumab OR etanercept OR adalimumab OR infliximab OR golimumab). *Articles selection:* randomized controlled trials (RCTs), published in English, assessing efficacy of anti-TNF on PROs, in ankylosing spondylitis (AS), psoriatic arthritis (PsA) or SpA according to the ASAS criteria. *Data collected:* fatigue assessed by FACIT score, quality of life assessed by Short Form 36 (SF36) mental and physical component or by Health AssessementQuestionnary Disability Index (HAQ). *Data analysis:* Article quality was evaluated by the JADAD scale. For SF36 and HAQ outcomes, pooled variations at 12 and 24 weeks were computed by meta-analysis. Heterogeneity was measured by I^2 index.
Results: Of the 604 articles identified, 37 references were eligible for systematic review and 13 for meta-analysis. Our systematic review identified 10 RCTs concerning AS, 20 concerning PsA and 7 concerning axial SpA. However due to the heterogeneity in available statistical data, references eligible for meta-analysis were mainly related to PsA.
HAQ assessment was available for a meta-analysis in 8 studies. HAQ was significantly improved at 12 and 24 weeks with anti-TNF. The impact on HAQ variation at week 24 was -0.29 points [95% CI: -0.37, -0.22]. Heterogeneity was important (I^2 =57%; see figure).
Ten studieswere eligible for a meta-analysis of anti-TNF effect on SF36 mental form. An improvement was observed at 12 and 24 weeks, although superior at 24 weeks. The effect at week 24 was 2.78 [95% CI: 1.87 - 3.68], without heterogeneity (I^2 =0%; see figure).

Twelve studies were eligible for a meta-analysis of anti-TNF effect on SF36 physical form. We observed a similar and significant improvement at 12 and 24 weeks. The effect at week 24 was 6.74 [95% CI: 5.34 – 8.13], with an important heterogeneity (I^2 =84%; see figure)
Fatigue was evaluated in 3 studies. Adalimumab induced a significant improvement in FACIT score at 12 and 24 weeks in one study. Two studies using different scores (Fatigue Assessment Scale, BASDAI fatigue item) to assess certolizumab effect highlighted similar findings: an early improvement in fatigue at week 12, remaining significant and stable at week 24.



Conclusions: Anti-TNFs agents significantly improve disability, quality of life and fatigue in patients with PsA.
Acknowledgements: Abbvie France pharmaceutical company provided logistic support by organizing a meta-analysis methods workshop, but played no further role in the project.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5268

AB0704 HIP ARTHROPLASTY IN PATIENTS WITH ANKYLOSING SPONDYLITIS - CLINICAL AND FUNCTIONAL EFFICIENCY

S. Lapshina[1,1], I. Akhtyamov[1,2], I. Gilmutdinov[2], L. Myasoutova[1]. *[1]Kazan State Medical University; [2]Republic Clinical Hospital, Kazan, Russian Federation*

Objectives: To evaluate the results of the hip joints replacement in patients with SpA under the dynamic supervision of a rheumatologist and orthopedic within the first year after the operation.
Methods: As part of special program for rheumatology patients hip endoprosthesis was done in 12 patients (mean age - 44,2±15,3 years) with SpA, 8 of them with ankylosing spondylitis (AS) and 4 with psoriatic arthritis (PsA). Duration of the disease - 13,3±7,9 years, positive for HLA B27 in 9 (75%) patients. High activity for ASDAS was at 58.3% of the patients. Took NSAIDs at the time of the operation - 11 (91.6%) patients, sulfasalazine 5 (41.6%), methotrexate- 2 (16.7%). 1 (8.3%) patient received etanercept,1 (8.3%) patient - infliximab. Dynamic observation of rheumatologist and orthopedic was carried out before, just after surgery, after 6 and 12 months, with the assessment of VAS, BASDAI, ASDAS, BASFI.
Results: The reduction of pain intensity on the VAS was observed in the first month after the surgery (47,3±18,6 mm), initially it was 74,0±24,1 mm, 42.5±9 after 6 months ($p<0.05$), after 12 months - up to 22,5±9,9 mm ($p<0.05$). ASDAS significantly ($p<0.05$) reduced from 2,94±2,01 to 1,68±1,35 - in 6 months and 1,26±0,88 - 12 months after operation; BASDAI: from 6,24±3,91 to 2,75±2,20 - 6 months, 2,65±1,53 at 1 year follow-up. BASFI index before surgery - 5,48±3,29, 6 months - 2,78±2,31, 1 year - 2,32±1,60 points. No complications after surgery were registered.
Conclusions: Hip joints endoprosthesis in patients with SpA is effective not only in improving functional ability and pain relief, but also a reduction of disease activity. Dynamic rheumatologist observation in perioperative period leads to positive dynamics in relation to the activity of SpA and quality of life of patients during the first year after surgery
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3966

AB0705 CONTINUED EFFECTIVENESS OF A BIOSIMILAR ADALIMUMAB AFTER STOPPAGE OF INITIAL TREATMENT IN PATIENTS WITH ANKYLOSING SPONDYLITIS

S. Bandyopadhyay[1], A. Ray[2], R.N. Sarkar[3], S. Dash[1], S. Mondal[1]. *[1]Medicine, Apollo Gleneagles Hospital; [2]Medicine, Fortis Hospital, Kolkata; [3]Medicine, Calcutta Medical College, Kolkata,, India*

Background: Adalimumab, an anti TNF-α agent, has been proven to be safe and effective in treatment of ankylosing spondylitis (AS). A biosimilar adalimumab was approved for use by Indian regulators in 2014. It is a "fingerprint match" of the reference adalimumab in terms of purity, potency, safety and clinical efficacy.[1,2] In the absence of availability of adalimumab in India, this biosimilar adalimumab currently serves as an accessible, cost-effective option for treatment of AS patients.
Objectives: This retrospective analysis evaluates effectiveness of biosimilar adalimumab (bADA), in terms of disease activity, safety and outcomes in real-life Indian AS patients treated for initial 24 weeks and then followed for next 24 weeks off biologic treatment.
Methods: Medical records of AS patients with Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) >4, who were prescribed bADA therapy between January to December 2015 were analysed. For patients, who stopped bADA treatment after 24 weeks, standard AS outcome-measurement scores including ESR, CRP, BASDAI, BASFI, and Health Assessment Questionnaire (HAQ) at baseline, week 24 and at week 48 were measured to evaluate ongoing efficacy, were compared using paired Student's T-test. Patients were allowed to continue methotrexate and salazopyrin as part of routine medical care.
Results: During the study period, 52 AS patients were prescribed bADA 40 mg s/c; 24 of these patients, who had stopped treatment after 6 months, were considered for this analysis. Mean age for this group was 36.57±10.81 years; 10 females. At the end of 24 weeks' treatment, there were significant reductions in levels of inflammatory markers ESR, CRP, as well as in BASDAI, BASFI and HAQ scores. Eight patients continued to receive methotrexate and 8 patients sulfasalazine as concomitant medications. After week 48 (24 weeks post stoppage), BASDAI and BASFI scores did not deteriorate despite discontinuation of bADA treatment. The patients' HAQ scores were also indicative of similar trends of continuing improved health status post the therapy.

Table 1. Disease activity scores and patient outcomes at 24 weeks after completion of biosimilar adalimumab therapy

Parameters	Baseline	Week 24 (last dose)	P value (baseline – week 24)	Week 48 (24 weeks bADA free period)*	P value (baseline – week 48)
BASFI	8.35±0.72	2.87±0.77	p<0.001	2.55±0.65	p<0.001
BASDAI	7.70±0.84	2.45±0.58	p<0.001	2.41±0.58	p<0.001
ESR	49.50±28.78	13.97±11.19	p<0.001	30.33±26.23^	p=0.02
CRP	19.71±12.24	3.58±3.6	p<0.001	6.13±9.41	p<0.001
HAQ (Pain)	67.71±7.22	27.08±8.2	p<0.001	28.13±9.42	p<0.001
HAQ (Health)	60.83±8.43	28.13±8.45	p<0.001	25.63±10.56	p<0.001

Data presented as Mean±standard deviation. *p = not significant for any parameter when compared for changes from week 24 to week 48. ^p=0.006 as compared to week 24 for rise in ESR during the bADA free period.

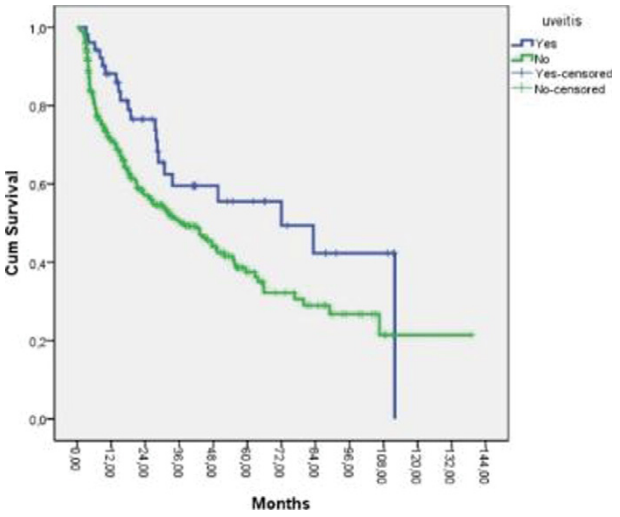
Conclusions: Biosimilar adalimumab therapy was effective in treating AS patients. The disease activity and health assessment scores continued to remain stable with no worsening after the stoppage of treatment for 6 months, indicating a post-therapy effectiveness in these patients with no reported adverse event.
References:
[1] Bandyopadhyay S, et al. Biosimilars. 2015;5:1–18.
[2] Jani RH et al. int J Rheum Dis. 2015 Jul 14.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3825

AB0706 ANKYLOSING SPONDYLITIS PATIENTS WITH UVEITIS HAD BETTER ADALIMUMAB RETENTION RATE: HUR-BIO REAL LIFE RESULTS

B. Armagan[1], A. Sari[1], A. Erden[1], L. Kilic[1], D.C. Guven[2], T. Pashayev[2], E. Bilgin[2], C. Simsek[2], E.C. Erdat[2], O. Karadag[1], A. Akdogan[1], S. Apras Bilgen[1], S. Kiraz[1], I. Ertenli[1], U. Kalyoncu[1]. *[1]Hacettepe University, Department of Internal Medicine, Division of Rheumatology; [2]Department of Internal Medicine Hacettepe University, Ankara, Turkey*

Background: Retention of biological drugs in inflammatory arthritis may be affected from different obvious and unknown factors. It can be related with patient characteritics or disease features. In ankylosing spondylitis (AS), retention rate of biological drugs may be related with extra-articular presentation of AS such as uveitis, as well.
Objectives: The objective of this study was to assess whether uveitis affected retention of adalimumab in AS patients in our single center biological cohort.
Methods: Hacettepe University Biological registry is single-center biological registry since 2005. HURBIO had 2165 spondyloarthritis patients of which 1190 patients had AS according to NY criteria. Until now, in 510 of 1190 patients have used adalimumab and 350 of 510 patients had available for uveitis. Patients

were assessed for demographic characteristics, disease duration, HLA-B27, DMARD and biological usage, biological switch ratio. Baseline disease activity was assessed with BASDAI, BASFI VAS (pain, fatigue and patients global assessment), ESR and CRP. Patients were compared according to having uveitis or not. Retention rate of adalimumab assessed by Kaplan-Meier survival analysis.
Results: Total 350 (59.4% male) AS patients analyzed. Mean age was 43 (12), mean disease duration and symptom duration were 10.5 (7.8) and 14.8 (9.6) years, respectively. 52 patients (14.8%) had uveitis. Median adalimumab survival time according to having uveitis were 71.9 (95% CI 25.4–118.6) months vs 36.4 (95% CI 23.3–49.4) months (log-rank p=0.014) (figure). Patients with uveitis were more frequently male (18.2% vs 9.8%, p=0.03), HLA-B27 positive (75.0% vs 49.5%, p=0.022). Patients with uveitis had more frequently SpA family history, as well (23.1% vs 10.8%, p=0.003). Age (49 (11) vs 41 (11) years, p<0.001), disease duration (14.4 (10.1) vs 9.8 (7.1) years, p<0.001), and symptom duration (22 (12) vs 14 (8) years, p<0.001) were higher in patients with uveitis. Baseline and last visit disease activities were similar regarding to uveitis.

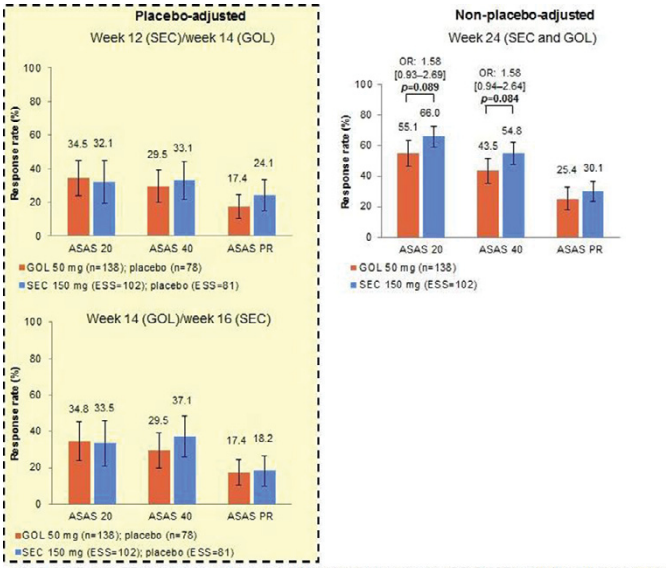


Conclusions: Determination of possible risk factors for retention of TNFi drugs is an important clinical problem for routine practise. It is well known that adalimumab is one of the treatment option for uveitis whether uveitis related with SpA or not. Our biological cohort supported that AS patients with uveitis had better adalimumab survival. For routine practise, adalimumab could be considered for AS patients with uveitis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4367

AB0707 COMPARATIVE EFFECTIVENESS OF SECUKINUMAB AND GOLIMUMAB IN ANKYLOSING SPONDYLITIS ASSESSED BY MATCHING-ADJUSTED INDIRECT COMPARISON USING PIVOTAL PHASE 3 CLINICAL TRIAL DATA

W. Maksymowych[1], E. Choy[2], Y. Yazici[3], J. Walsh[4], H. Thom[5], C. Kalyvas[6], T. Fox[7], K. Gandhi[8], S. Jugl[7]. *[1]University of Alberta, Edmonton, Canada; [2]University of Cardiff, Cardiff, United Kingdom; [3]New York University School of Medicine, New York; [4]University of Utah, Salt Lake City, United States; [5]University of Bristol, Bristol, United Kingdom; [6]MAPI Group, Houten, Netherlands; [7]Novartis Pharma AG, Basel, Switzerland; [8]Novartis Pharmaceuticals Corporation, East Hanover, United States*

Background: No data are available from head-to-head RCTs between secukinumab 150 mg (SEC; an anti-IL-17A) and golimumab 50 mg (GOL; a TNFi) in patients with active ankylosing spondylitis (AS). Matching-Adjusted Indirect Comparison (MAIC) can be used to estimate comparative effectiveness and enables treatment outcomes to be compared across effectively balanced trial populations. MAIC is an established method in health technology assessments and NICE have published guidance on appropriate methodology, and especially for addressing imbalances in observed covariates between trials.[1]
Objectives: To assess the comparative effectiveness of SEC and GOL up to week 24 using MAIC with pooled individual patient data (IPD) from the RCTs MEASURE 1 (M1) and MEASURE 2 (M2) and published aggregate data from the RCT GO-RAISE.
Methods: Pooled M1 and M2 data were used to maximize the effective sample size (ESS) for SEC. IPD from the SEC arms of M1 and M2 (n=197) were weighted to match the published baseline characteristics of the GOL arm of GO-RAISE (n=138). Placebo arms were matched in the same way; placebo-adjusted comparisons were possible only until week 16 because patients could receive active treatment from this time onwards. Logistic regression was used to determine weights for age, sex, BASFI, disease duration, CRP and previous TNFi therapy. Recalculated outcomes from M1 and M2 (SEC, ESS=102; placebo, ESS=81) were compared with data from GO-RAISE (GOL, n=138; placebo, n=78). Pairwise comparisons – reported as odds ratios (ORs [95% CIs]) – were performed for ASAS 20, ASAS 40 and ASAS PR responses at nearest-equivalent time points across trials: week 12 (SEC)/14 (GOL), week 14 (GOL)/16 (SEC) and week 24 (SEC and GOL). Non-responder imputation (NRI) was available for all binary outcome data. Strict thresholds were avoided when interpreting *p* values, in line with American Statistical Association 2016 guidance.
Results: There was no evidence of differences in ASAS 20 and ASAS 40 responses between SEC and GOL at weeks 12/14 and 14/16 (both placebo-adjusted). At week 24, non-placebo-adjusted ASAS 20 and ASAS 40 responses using NRI were higher with SEC than GOL (OR [95% CI]: 1.58 [0.93–2.69], *p*=0.089 and 1.58 [0.94–2.64], *p*=0.084, respectively). There was no evidence of differences in ASAS PR responses between SEC and GOL at weeks 12/14, 14/16 and 24. A sensitivity analysis conducted after adding BASDAI score to the matching parameters yielded similar results.



ASAS 20/40 and PR responses are the absolute mean response rate (GO-RAISE) and the predicted mean response rates (MEASURE 1 and MEASURE 2). Error bars shown are 95% CIs.
ASAS, Assessment of SpondyloArthritis International Society; ASAS 20/40, at least a 20%/40% improvement according to ASAS response criteria; ASAS PR, ASAS partial remission; CI, confidence interval; ESS, effective sample size; GOL, golimumab; OR, odds ratio; SEC, secukinumab.

Conclusions: There was no evidence of differences in ASAS responses between SEC and GOL in placebo-adjusted analyses. In non-placebo-adjusted analyses, SEC showed higher ASAS 20 and ASAS 40 responses than GOL at week 24.
References:
[1] Phillippo DM et al. (2016) NICE DSU Technical Support Document 18. Available from: http://www.nicedsu.org.uk.
Disclosure of Interest: W. Maksymowych Grant/research support from: AbbVie, Pfizer and Sanofi, Consultant for: AbbVie, Amgen, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sanofi and UCB, E. Choy Grant/research support from: Pfizer, Roche and UCB, Consultant for: Chugai Pharma, Eli Lilly, Janssen, Novartis, Pfizer, Regeneron, Roche, R-Pharm and Sanofi, Y. Yazici Grant/research support from: Celgene, BMS and Genentech, Consultant for: Celgene, BMS and Novartis, J. Walsh Consultant for: Novartis, H. Thom Consultant for: Eli Lilly, F Hoffman-La Roche, Novartis Pharma AG and Pfizer, C. Kalyvas Employee of: Paid employee of the Mapi Group. The Mapi Group received funding from Novartis Pharma AG for this study, T. Fox Employee of: Novartis employee with stock, K. Gandhi Employee of: Novartis employee with stock, S. Jugl Employee of: Novartis employee with stock
DOI: 10.1136/annrheumdis-2017-eular.5850

AB0708 TRANSITION FROM ONGOING INFLIXIMAB REFERENCE PRODUCT TO ITS BIOSIMILAR: CAN WE TALK ABOUT A FAILURE?

W. Akrout[1], A. Bosycot[1], R. Levet-Labry[1], E. Gazaix-Fontaine[2], M. Paul[1], P. Claudepierre[2]. *[1]Clinical Pharmacy Department; [2]Rheumatology Department, Henri Mondor University Hospital AP-HP, Créteil, France*

Background: Some recent publications support the fact that there is no clinically meaningful difference between infliximab biosimilar and the originator in naïve patients, but sole a few of them actually assessed the transition itself. Since May 2016, according to the European guidelines, the French Health Authorities have allowed interchangeability between a biotherapy reference product and its biosimilar. According to the last studies focusing on the safety and efficacy issues, avoiding the transition to biosimilar looks no longer justified.
Objectives: This work aimed to understand to which extent the use of infliximab biosimilar may result in the failure of the switch strategy in spondyloarthritis patients.
Methods: This is a retrospective study conducted from June to December

2016. Only were included the adult patients with rheumatoid arthritis (RA), spondyloarthritis (SpA) or psoriatic arthritis (PsA) having accepted the transition from Infliximab reference product (IFX^R) to its biosimilar (IFX^B). For SpA patients, transition monitoring was based on the end-of-dose "wearing off" (WO) phenomenon assessment before and after the switch, disease activity score BASDAI and also the inflammatory marker CRP. Transition was considered as unsuccessful after 2 IFX^B infusions with patient complain. In this case, the drug level was determined using ELISA before switching back to IFX^R, and any spacing infusions because a concomitant health disorder was sought.

Results: Of the 99 patients treated with IFX^R for more than 2 years, 91% (90/99) accepted the transition: 53 SpA, 23 RA and 14 PsA. Fourteen patients (12 SpA, 2 RA) didn't reach the 3rd IFX^B administration. SpA patients reported the occurrence of arthralgia (12/12) and a partial (8/12) or total (4/12) efficacy loss. Only 5 patients reported a 2 point-increase or more regarding the BASDAI score, and only 3 patients had an increase in the CRP level (*Cf.*Table 1). Except for P1, the efficacy loss was associated in each case with WO phenomenon already reported before the transition (8/12) or undetectable IFX level (3/12). For these 3 last patients, the IFX^B drug administration rate was increased by at least 2 weeks than usual because of a concomitant infection.

Table 1: SpA patients discontinued IFXB outcomes

SpA patients	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12
Arthralgia	+	+	+	+	+	+	+	+	+	+	+	+
Partial or total efficacy loss	+	+	+	+	+	+	+	+	+	+	+	+
↗BASDAI	-	+	+	+	-	-	-	+	-	-	-	+
↗ CRP	+	-	-	-	-	+	-	+	-	-	-	-
Existing WO	-	+	+	-	+	+	+	-	+	+	-	+
Undetectable IFX level	-	-	-	+	-	-	-	+	-	-	+	-
Spacing infusions	-	-	-	+	-	-	-	+	-	-	+	-

+: Yes: - : No

Conclusions: This observational study showed a transition failure rate at 16% (76/90) in global, which reached 23% (12/53) if limited to SpA. All SpA patients with supposed transition failure reported either a disease escape beforehand or a concomitant infection requiring to spacing infusions. In order to complete these results, an anti-IFX antibodies monitoring is in progress so to highlight any IFX activity loss. Any failure observed with the transition would be actually more complex than the presumably inefficacy of the biosimilar IFX^B especially for SpA patients. So, it seems difficult to assess robustly the inefficacy of the transition to IFXB in SpA patients only according to patient complain.

References:
[1] Park W et al. Arthritis Res Ther. 2016 Jan 20;18:25.
[2] Fiorino G et al. Expert Rev Clin Immunol. 2016;12(4):361–3.
[3] Jacobs I et al. BioDrugs. 2016 Dec;30(6):525–570.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4823

Spondyloarthritis - clinical aspects (other than treatment)

AB0709 THE RELATIONSHIPS BETWEEN THORACIC REGION INVOLVEMENT AND FUNCTIONS OF UPPER EXTREMITY, SCAPULAR KINEMATICS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: PILOT STUDY

O. Mete[1], D. Oskay[1], A. Tufan[2]. [1]*Physiotherapy and Rehabilitation;* [2]*Internal Medicine, Division of Rheumatology, Gazi University, Ankara, Turkey*

Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that mainly affects the axial skeleton. As the disease progresses, increased thoracic kyphosis can be seen in these patients. Because of increase in thoracic kyphosis, the orientation of the scapula on the thorax and thus the functions of upper extremity may change.

Objectives: The aim of the study is to investigate the relationships between thoracic region involvement and functions of upper extremity, scapular kinematics in patients with AS.

Methods: Fifteen (15) patients with AS and eleven (11) healthy control were participated in the study. Thoracic kyphosis angle and shoulder range of motions were assessed by using digital inclinometer, scapular and shoulder muscle strength were assessed by using digital dynamometer, three dimensional (3D) scapular kinematics were assessed by using electromagnetic tracking system, disability level of upper extremity were assessed by Turkish Version of Disability of Arm, Shoulder and Hand Questionnaire (DASH-T). Spearman correlation coefficient, Pearson correlation coefficient, Mann-Whitney U Test and Independent Sample T-test were used for statistical analysis.

Results: DASH-T, thoracic kyphosis angle, shoulder abduction, internal rotation, external rotation of dominant side, shoulder abduction, internal rotation of non-dominant side, anterior deltoid, middle deltoid, serratus anterior, downward trapezius muscle strengths of dominant and non-dominant side, upward rotation of scapula during 30,60,90 degrees humerothoracic elevations at sagital plane of dominant and non-dominant side showed significantly differences between two groups. Thoracic kyphosis angle showed correlations with DASH-T ($p<0,05$,r:0,619), shoulder flexion, abduction, internal rotation, external rotation of dominant side ($p<0,05$,r:-0,867), ($p<0,05$,r:-0,580), ($p<0,05$,r:-0,657), ($p<0,05$,r:-0,599) and shoulder flexion, abduction, internal rotation of non-dominant side ($p<0,05$,r:-0,813), ($p<0,05$,r:-0,665), ($p<0,05$,r:-0,741), respectively. Thoracic kyphosis angle showed correlations with anterior deltoid, middle deltoid, serratus anterior, middle trapezius, downward trapezius muscle strengths of dominant side and non-dominant side, respectively ($p<0,05$,r: -0,899), ($p<0,05$,r:-0,854), ($p<0,05$,r:-0,805), ($p<0,05$,r:-0,791), ($p<0,05$,r:-0,633), ($p<0,05$,r:-0,877), ($p<0,05$,r:-0,796), ($p<0,05$,r:-0,884), ($p<0,05$,r:-0,724), ($p<0,05$,r:-0,673). Correlations between thoracic kyphosis angle and anterior tilt of scapula during 90 degree humerothoracic elevations at sagital plane of dominant side were obtained ($p<0,05$, r:0,522).

Conclusions: Scapulothoracic joint biomechanics and functions of upper extremity were affected by kyphotic posture in patients with AS. One of the most important causes of biomechanical impairment in AS patients is the deterioration of scapular kinematics with kyphosis. For preventing functional impairment, treatment programs should be supplemented with scapular kinematic exercises.

References:
[1] Braun (2007). Ankylosing spondylitis. The Lancet.
[2] Kebaetse (1999). Thoracic position effect on shoulder range of motion, strength, and three-dimensional scapular kinematics. Archives of physical medicine and rehabilitation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5869

AB0710 REVIEW OF PREGNANCY OUTCOMES IN SPONDYLOARTHROPATHY IN A UNIVERSITY TEACHING HOSPITAL

A. Shajpal[1], M. Khare[2], A. Moorthy[3]. [1]*Obstetrics;* [2]*Maternal Fetal Medicine;* [3]*Rheumatology, University Hospitals of Leicester, Leicester, United Kingdom*

Background: Spondyloarthropathy (SpA) is a chronic inflammatory condition of the spine affecting mainly the male population however the incidence amongst the female population is increasing. The peak incidence of SpA is in the reproductive age group. There has been a lack of focus on pregnancy in SpA as compared to other autoimmune condition such as Lupus and Rheumatoid arthritis, but this is changing. There is a paucity of information (1) on fertility and pregnancy outcomes in this condition compared to other diseases and this may lead to inequality in healthcare delivery.

Objectives:
- To review the pregnancy outcomes in women with SpA in our unit
- To review ankylosing spondylitis activity during pregnancy
- To improve the quality of care in this group of patients by developing local pathways and appropriate MDT involvement

Methods: This is a retrospective case review of pregnancies in women with SpA booked at a large tertiary teaching hospital over three years between January 2014 and December 2016. We have an annual delivery rate of 11,000 maternities. The maternity electronic database and clinic diaries were used to identify the cases. A standardised proforma was used to collect and collate the data for demographics, pre pregnancy counselling, disease activity and pregnancy outcome.

Results: Six pregnancies were identified in the study period. All patients were under the care of a Rheumatologist. The maternal age range was between 28 and 35 years. The BMI ranged between18 and 37. Ethnicity included 5 caucasian and one Asian woman. Five women had previous pregnancies and one was in her first pregnancy. Two of the multiparous women had previously delivered by caesarean section. Three of the six women suffered from anxiety and/or depression and one had fibromyalgia. Two of the six patients were not on any medication at the start of pregnancy and didn't require any during pregnancy. Four women needed various analgesics and one patient was on sulfasalazine but stopped this at 5 weeks' gestation. NSAIDs was stopped in 3 women after confirmation of pregnancy. One patient who was on Anti TNF therapy discontinued the drug preconception. We observed 50% attended specialist maternal-fetal medicine and anaesthetic services. One patient saw a physiotherapist and accessed hydrotherapy during pregnancy.

Two of six patients delivered preterm (<37 weeks) and 4 delivered at term (>37 weeks). Of the preterm deliveries, 1 went into spontaneous labour not related to disease flare and the other was delivered electively for fetal concerns. All the women delivered by caesarean section. One was planned as an elective caesarean for maternal request due to difficulty abducting legs. All the remaining caesarean deliveries were for obstetric indications not related to SpA.

Conclusions: This small observational case series did not highlight any worsening SpA disease activity or poor pregnancy outcome. Further larger studies are required. However a care pathway for managing this group of patients would help to standardise the care during pregnancy. A multidisciplinary approach is essential to optimise the quality of care for these patients.

References:
[1] Pregnancy outcomes in patients with ankylosing spondylitis: a nationwide register study Gustav L Jacobson, Olof Stephansson, Johan Askling and Lennart T H Jacobsson Ann Rheum Dis 2016 75: 1838–1842.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3842

AB0711 REVIEW OF MANAGEMENT OF HLA B27 POSITIVE UVEITIS PATIENT ATTENDING A TERTIARY HOSPITAL – HOW GOOD ARE WE?

B. Kapoor[1], K. Periyasamy[1], M. Babbington[1], A. Moorthy[2]. [1]*Ophthalmology;* [2]*Rheumatology, Leicester Royal Infirmary, Leicester, United Kingdom*

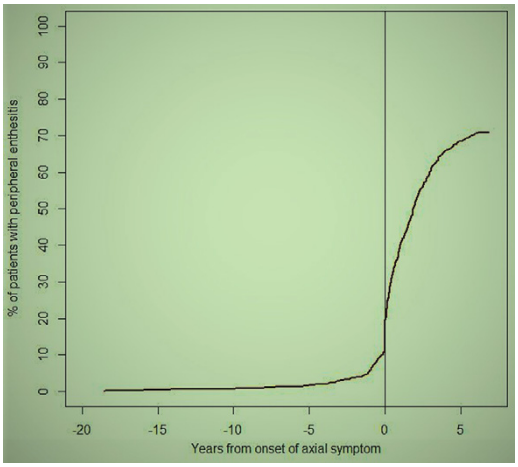
Background: Delay in diagnosing Spondyloarthroapthy is well documented. One of the reasons for the delay is the presentation of these group of patients to different specialties due to variety of extra articular manifestations. Acute anterior uveitis (AAU) is the most common extra-articular manifestation in HLA B27 positive spondyloarthropathies, occurring in 30–50% of cases [1]. It can occur before the onset of rheumatologic symptoms [2,3]. However quite often this group of patients is not routinely referred to or seen by the rheumatologist for further evaluation.
Objectives:
- To assess the ophthalmologist practice in evaluating patients with AAU for inflammatory back pain or other Rheumatological diagnoses.
- To identify the number of HLA B27 requests made for uveitis patients.
- To identify the referral rate of HLA B27 uveitis patients to Rheumatologists for evaluation.

Methods: We conducted a retrospective pilot study to assess all patients with AAU presenting over a period of one-week to our busy teaching hospital eye casualty which serves over one million population. All patients with Iritis were identified from eye causality records and medical case notes were obtained. A standard proforma was designed and piloted with few case notes initially. Modified proforma was subsequently used to collect the data which was collated and analysed using EXCEL spread sheet.
Results: A total of 62 patients (n=62) with AAU presented to eye casualty over a one-week period. Case notes of 49 patients could be procured. Majority of the patients were Caucasians (n=35) while the rest were Asians (n=12) and blacks (n=2). Sex ratio was nearly equal with 25 patients being males and the rest females. Most of our patients' age ranged between 20 to 60 years. 60% patients had a history of recurrent iritis. Out of these 9 patients had bilateral uveitis and 14 were unilateral. In 6 patients, the laterality was not documented. A history for spondyloarthropathy was elicited in only 14 patients by the ophthalmologist at the time of initial assessment. Out of these 14 patients Inflammatory back pain history was positive in 10 patients. Only 17 out of 62 (27%) patients had HLA B27 checked and it was noted to be positive in 5. Amongst the 5 HLA B27 positive patients 2 patients were referred to rheumatology whereas 2 patients were already under rheumatology.
Conclusions: We observed that there is a clear lack of understanding in eliciting effective rheumatology history in patients with recurrent anterior uveitis and requesting HLA B27 appropriately. Therefore, a need for a clear pathway for managing patient presenting with recurrent uveitis and HLA B27 positivity for evaluation of Inflammatory back pain. Clear local guidelines and pathway need to be developed to provide effective care. Good communication between the Ophthalmologist and Rheumatologist is key in early diagnosis and effective management of this deforming condition.
References:
[1] Khan AK. A worldwide overview: the epidemiology of HLA-B27 and associated spondyloarthritides. In: Calin A, Taurog JD, eds. The Spondylarthritides. Oxford: Oxford University Press, 1998: 17–26.
[2] Careless DJ, Inman RD. Acute anterior uveitis: clinical and experimental aspects. Semin Arthritis Rheum. 1995 Jun. 24(6):432–41.
[3] Chang JH, McCluskey PJ, Wakefield D. Acute anterior uveitis and HLA-B27. Surv Ophthalmol. 2005 Jul-Aug. 50(4):364–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4511

AB0712 CLINICAL CHARACTERISTICS OF SPONDYLARTHRITIS (SPA) WITH AND WITHOUT PERIPHERAL ENTHESITIS – DATA FROM THE DESIR COHORT

V. Nadon[1], A. Molto[2], A. Etcheto[2], L. Bessette[3], L. Michou[3], P. Claudepierre[4], D. Wendling[5], C. Tkaczyk[6], B. Haraoui[1], M. Dougados[2]. [1]*Institut de Rhumatologie de Montreal, Montreal, Canada;* [2]*Hôpital Cochin, Paris, France;* [3]*CHUL, Quebec, Canada;* [4]*Hôpital Henri Mondor, Créteil;* [5]*CHRU, Besançon, France;* [6]*Janssen, Montreal, Canada*

Background: Peripheral enthesitis, mostly in the lower limbs, is a major feature of spondyloarthritis (SpA). Its prevalence is highly variable depending on the population studied, estimated between 10% and 70%. The probability to develop a peripheral enthesitis over time and the factors associated with it are mostly unknown.
Objectives: The aims of the present study were: 1) To describe the prevalence and characteristics of peripheral enthesitis in early axial SpA population, at the inclusion in the DESIR cohort; 2) to estimate the incidence of peripheral enthesitis over time; 3) to determine the factors associated with the presence of peripheral enthesitis.
Methods: We used data from the DESIR cohort, a prospective multi-center, longitudinal French cohort of 708 patients with inflammatory back pain suggestive of early axial SpA (<3 years since axial symptoms onset). We performed a descriptive analysis to evaluate the prevalence and characteristics of the peripheral enthesitis at time of inclusion (location, number of enthesitis, and mean time between first enthesitis and axial symptoms). We also estimated the incidence of peripheral enthesitis over a follow up period of 60 months, using Kaplan-Meier curves. Finally, we determined the baseline characteristics associated with the presence of a peripheral enthesitis by multivariable analysis (logistic regression, including the variables significantly associated in the univariable analysis).
Results: At inclusion, 395 patients (55.8%) had peripheral enthesitis in their past medical history. The locations were mainly the plantar fascia (212/395, 53.7%) and the Achilles tendon (152/395, 38.5%). Seventy-seven (19.4%) of these patients developed peripheral enthesitis before their axial symptoms, with a mean time interval of 773 days. During the 5-year follow-up period, 109/708 (15.4%) patients developed new peripheral enthesitic symptoms, resulting in 504/708 (71.2%) patients who had presented with at least one episode of peripheral enthesitis at 5 years. Variables associated to peripheral enthesitis according to the univariable analysis were: older age, male gender, HLA B27 positivity, MRI sacroiliitis, Modified NY criteria fulfilled, presence of either anterior chest wall pain, peripheral arthritis, dactylitis or psoriasis, high BASDAI, BASFI or mean score ASAS-NSAID. Only the history of anterior chest wall pain and of peripheral arthritis were significantly and independently associated with the presence of peripheral enthesitis in the multivariable analysis (Odds Ratio (OR) =1.6 [95% Confidence interval (1.6 [1.1–2.3], and OR=2.1 [1.4–3.0], respectively)



Conclusions: This prospective study highlights the high prevalence of peripheral enthesitis in early axial SpA and stresses the importance of researching any signs and symptoms of enthesitis, especially in those patients with anterior chest wall pain and peripheral arthritis.
References:
[1] Sampaio-Barros, PERCIVAL DEGRAVA, et al. Primary ankylosing spondylitis: patterns of disease in a Brazilian population of 147 patients. The Journal of rheumatology 28.3 (2001): 560–565.
Disclosure of Interest: V. Nadon: None declared, A. Molto: None declared, A. Etcheto: None declared, L. Bessette: None declared, L. Michou: None declared, P. Claudepierre: None declared, D. Wendling: None declared, C. Tkaczyk Grant/research support from: This projet was partly supported by an unrestricted grant from Janssen Canada, B. Haraoui: None declared, M. Dougados: None declared
DOI: 10.1136/annrheumdis-2017-eular.5087

AB0713 UVEITIS SECONDARY TO SPONDYLARTHRITIS IN AN OCULAR INFLAMMATION INTERDISCIPLINARY UNIT

D. Peiteado[1], A. Pieren[1], A. Schlinker[2], V. Hidalgo[2], C. Millán[1], E. De Miguel[1], A. Balsa[1]. [1]*Rheumatology;* [2]*Ophthalmology, Hospital Universitario la Paz, Madrid, Spain*

Objectives: To describe the characteristics of ocular involvement in spondyloarthritis in an ocular inflammation interdisciplinary unit.
Methods: This descriptive study include the patients with uveitis secondary to spondyloarthritis or inflammatory bowel disease (IBD) treated by the rheumatologist from January 2012 to December 2016 in an ocular inflammation multidisciplinary unit. Demographic characteristics, aetiology, ocular involvement pattern, and systemic therapy data were collected and analysed.
Results: From 276 patients evaluated by the rheumatologist, 111 (40.2%) were uveitis secondary to systemic inflammatory diseases. Within this group, the uveitis

associated with spondyloarthritis (including also IBD) were the most frequent (68 patients, 61%). Focusing on this group, 57.4% were male with a mean age of 49±15.8 years. 73.5% were HLAB27 positive and 76% had radiologic sacroiliitis. In 24 patients (35.3%) the diagnosis of spondyloarthritis was made after the anamnesis in the uveitis unit. The diagnosis was already known in the other cases. The spondyloarthritis subtypes are described in the table.

Diagnosis	n (%)
Ankylosing spondylitis	33 (48.5)
Non radiographic axial spondyloarthritis	13 (19.1)
Psoriatic arthritis	5 (7.4)
IBD spondyloarthritis	5 (7.4)
Peripheral spondyloarthritis	4 (5.9)
Juvenile idiopathic arthritis	4 (5.9)
IBD (without Joint involvement)	3 (4.4)
Reactive arthritis	1 (1.5)
Total	68 (100)

According to the anatomical distribution, 95.6% were anterior uveitis (AU), followed by the intermediate and posterior ones (1,5% both). 85.3% has unilateral involvement and 10.3% bilateral. Relapsing acute AU was the most frequent pattern (73.5%), followed by non-relapsing acute AU (16.2%) and chronic AU (7.4%).

24 patients (35.3%) required treatment with DMARD to achieve uveitis control. The most commonly used drugs were salazopyrine (7 patients), methotrexate (6 patients), mycophenolate (1), and in another 6 patients anti-TNF treatment was started or the previous dose of the biological was adjusted.

The visual acuity (VA) was not perfect (VA≠1 in both eyes) in 35% in the first collected visit. 28% (19 patients) had cataract, and 19% (13) had ocular hypertension. Only 1 patient had bilateral cystoid macular edema. Follow-up data were available for 43 patients and VA was stable in 47%, worsening in 23% and improving in 30% (median follow-up time 23 months, IQR: 6–41)

Conclusions: Our work confirms that in spondyloarthritis the most frequent pattern of ocular involvement is relapsing acute AU. Spondyloarthritis diagnosis was made at the uveitis unit in 35% of patients. More than one-third of patients required systemic therapy for ocular involvement control. Thirty-five percent of the patients had a reduced VA, remaining stable or improving in most, during the follow-up.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6521

AB0714 DIFFERENTIATING CHARACTERISTICS IN PATIENTS WITH SPONDYLOARTHRITIS WHO HAVE RECEIVED DIFFERENTS ANTI-TNF THERAPIES

E. Moral[1], C. Plasencia[1], D. Pascual Salcedo[2], C. Tornero[1], P. Bogas[1], V. Navarro[1], A. Villalba[1], D. Peiteado[1], I. Monjo[1], A. Balsa[1]. *[1]Rheumatology; [2]Inmunology, la Paz University Hospital, Madrid, Spain*

Background: The term spondyloarthritis (SpA) encompass a group of crhonic inflammatory disease with predominant axial involvement. Anti-TNF therapy (AT) has stirred up the management of these diseases. Nevertheless, according to nationwide registries of the drug continuation rate in several countries, the rate of treatment failure is considerable. Nowdays there are insufficient data to evaluate the differences between responders (Resp-AT) and non-responders (Nonresp-AT) to anti-TNF therapy.

Objectives: To compare the main sociodemographic, clinical and analytical features at baseline, after 6 months of treatment and at the end of the first anti-TNF therapy of responders to a first anti-TNF therapy and non-responders to several anti-TNF therapies form our cohort of patients diagnosed with SpA. We also analized the association between drug levels (DL) and antidrug antibody (ADA) in non-responders to several anti-TNF.

Methods: 181 patients were included, 155 (85%) kept receiving their first AT therapy (responders) and 26 (15%) had discontinued at least two different AT therapies. The main demographic features, disease activity (BASDAI, ASDAS, CRP and ESR) were measured at baseline, after 6 months (v-6) and when the first AT was discontinued. Serum drug levels and/or ADA were measured at drug discontinuation of anti-TNF treatment and last visit in non-responders and responders respectively.

Results: The mean age was 55.3±15 and 50±10.8 in the resp-AT and nonresp-AT groups, respectively. The demographic and clinical characteristics of both groups are shown in Table 1. At baseline, a lower BMI was observed in the resp-AT group (25.6±5 resp-AT, 28.7±5 nonresp-AT, p=0.013); 59% and 35% were in concomitant treatment with DMARDS at baseline in the resp-AT and nonresp-AT groups respectively (p=0.032); 33% of the resp-AT were in monotherapy in the last visit compared to 62% of the nonresp-AT when discontinued the 1st AT (p=0.008). There were no differences in BASDAI (5.6±2 resp-AT, 6.1±1.9 nonresp-AT, p=0.2) and ASDAS (3.3±1.1 resp-AT, 3.4±1.1 nonresp-AT, p=0.8) at baseline. In v-6, the resp-AT group had a better clinical response in terms of BASDAI (3.2±2.3 in resp-AT, 4.7±2.4 in nonresp-AT, p=0.004) and ASDAS (1.7±0.9 in resp-AT, 2.7±1.2 in nonresp-AT, p=0.00), as well as in the delta-ASDAS (ΔASDAS) (1.56±1.2 resp -AT, 0.7±0.9 nonresp-AT, p=0.04). However, delta-BASDAI (ΔBASDAI) showed no difference between the two groups (2.3±2.3 resp-AT, 1.5±1.6 nonresp-AT, p=0.1).

Table 1. DEMOGRAPHIC CHARACTERISTICS

Population=181	Controls (n=155)	Cases (n=26)	p
Baseline			
Age	55.3±15	50±10.8	0,009
Sex (male)	104 (67%)	16 (62%)	0,6
B27+	93 (74%)	15 (62%)	0,3
BMI	25,5±5,3	28,7±5	0,013
Smokers	26	8	0,056
Disease duration (years)	9,5 ±12	7,6±9,3	0,4
RX (133): Sacroiliitis	65	14	0,6
MRI (37): Sacroiliitis	16	2	1
Uveitis	27	6	0,5
Enthesitis	53	16	0,015
Dactylitis	8	0	0,6
Peripheral	88	11	0,2
Psoriasis	16	5	
CRP baseline	16,7±23,7	12,3±21,3	0,4
ESR baseline	25,6±23,5	22±16	0,5
BASDAI baseline	5,6±2	6,1±1,9	0,2
ASDAS baseline	3,3±1,1	3,3±1,1	0,8
FAMES baseline	91	9	0,03
At 6 months			
BASDAI	3,2±2,3	4,7±2,4	0,004
ASDAS	1,7±0,9	2,7±1,2	0,00
ΔBASDAI	2,3±2,3	1,5±1,6	0,1
ΔASDAS	1,5±1,2	0,7±0,9	0,004
At drug discontinuation			
Monoterapia	51	16	0.08
Drug levels	138	13	0,02
ADA	1	4	0,00

24% of the nonresp-AT were ADA + at drug discontinuation, while only 0.7% of the AT-resp (AT) were ADA + (p=0.00) at last visit.

Conclusions: In our cohort of patients with axial SpA, a significant improvement in BASDAI, ASDAS and ΔASDAS after 6 months of treatment is associated with a lower frequency of drop-out of the first AT. Moreover a lower BMI, DMARDS at baseline and absence of ADA determine a better response to AT treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6566

AB0715 DIFFERENCES IN THE CO-MORBIDITIES DESCRIBED FROM SPONDYLOARTHRITIS PATIENTS WITH OR WITHOUT CONCOMITANT FIBROMYALGIA

E. Roussou, M. Karela, A. Georgiou. *Rheumatology, Barking, Havering and Redbridge University Hospitals NHS Trust, London, United Kingdom*

Objectives: To assess the differences in the occurrence of co-morbidities from cardiovascular, respiratory, renal/urological and Central nervous systems (CNS) between patients with spondyloarthritis (SpA) not having headache as presenting symptom and those having headache assuming that those describing headache represent secondary (s) fibromyalgia (FM). (previous submitted abstract provides justification on headache as presenting symptom associated with secondary sFM).

Methods: Data obtained through a questionnaire from 776 patients seen in clinic with SpA was analysed with reference to headache as symptom at presentation. From the total 776 patients 13 patients did not record an answer to the question and were hence excluded. The remaining 763 patients were divided in 2 groups: Those having headache at presentation (n=117) considered having sFM, and those not having headache at presentation (n=656).

	Headache at presentation (n=117)	No headache at presentation (n=656)	Statistical significance (p)	CI
Age (mean ± SD)	47.7 (13.16)	48.3 (14.3)	0.1	-5.757 to 0.912
Gender (M:F) ratio	28:89 1:3.1	219:419 1:1.9	0.3	-0.025 to 0.077
Disease duration	11.4 (12.1)	10.9 (10.8)	0.4	-1.905 to 4.470
Delay in diagnosis	6.43 (8.9)	6.3 (8.1)	0.7	-3.151 to 2.151
ESR	15.5 (14.8)	18.2 (18)	0.07	-11.064 to 0.582
CRP	10.4 (36)	8.2 (9.8)	0.4	-6.106 to 12.536
BASDAI score	7.31 (3.7)	6.06 (2.08)	0.000 (<0.005)	0.783 to 2.624
BASFI score	5.6 (2.7)	5.04 (2.7)	0.09	-0.143 to 1.626
Main problem				
Fatigue	77/116 (66.4%)	340/608 (55.9%)	0.018	0.029 to 0.299
Pain with pressure	71/117 (61.2%)	257/807 (42.4%)	0.000	0.122 to 0.378
Co-morbidities				
Heart	16/100 (16%)	59/479 (12.3%)	0.002	0.44 to 0.196
Lungs	11/99 (11.1%)	52/475 (10.9%)	0.1	-.014 to 0.135
Dizziness	50 (104) 48.1%	147/408 (30.1%)	0.000	0.220 to 0.453
Numbness	58 (105) 55.2%	199/505 (39.4%)	0.000	0.188 to 0.441
Kidneys/urology	23 (102) 22.5%	100/479 (20.9%)	0.1	-0.31 to 0.188

The data of patients with sFM were compared with the data of patients who did not report headache as a presentation symptom therefore not having FM with regards to age, disease duration, delay in diagnosis, disease activity (BASDAI) functional ability (BASFI), ESR, CRP and associated co morbidities from cardiovascular, respiratory, renal/urinary, and CNS systems. Central nervous system was evaluated by symptoms of dizziness and numbness.
Independent sample T test was used to explore differences between the 2 groups and confidence intervals obtained.
Results: Table shows demographics and disease characteristics as well as differences between SpA patients presenting with headache (indicating secondary FM), and those not presenting with headache. A greater proportion of patients with SpA and headache (sFM) report cardiovascular and CNS co-morbidities. There was no significant difference noted in the respiratory or renal/ urological co-morbidities amongst the 2 sub-groups.
Conclusions: A significantly higher proportion of patients described cardiovascular and CNS co-morbidities in the sFM group of SpA. No significant difference was noted in the 2 sub-groups with regards to the respiratory or renal systems.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5474

AB0716 PREVALENCE OF STRUCTURAL LESIONS TYPICAL FOR AXIAL SPONDYLOARTHRITIS IN YOUNG MILITARY RECRUITS BEFORE AND AFTER MECHANICAL STRESS

G. Varkas[1,2], M. de Hooge[1], T. Renson[1], P. Carron[1,2], S. De Mits[3], G. Souverijns[4], D. Elewaut[1,2], F. Van den Bosch[1,2]. *[1]Department of Rheumatology, Ghent University Hospital; [2]VIB Inflammation Research Centre; [3]Department of Rehabilitation Sciences and Physical Therapy, Ghent University, Gent; [4]Department of Radiology, Jessa Ziekenhuis, Hasselt, Belgium*

Background: Magnetic resonance imaging (MRI) has become the imaging modality of choice in early SpA. Not only has this imaging technique proven useful in the identification of inflammatory lesions on T2 FS/STIR sequences, also structural lesions such as erosions, sclerosis, fat infiltration and ankylosis can be seen on T1 sequences. There is still ongoing debate concerning the possible inclusion of any structural lesion in the definition of a positive MRI in order to improve specificity. However, erosions and fat infiltration have also been found in respectively more than 10% and 17% of non-SpA patients on MRI of the sacroiliac joints. [1]
Objectives: To evaluate the presence of structural lesions on MRI of the sacroiliac joints (MRI-SIJ) in young, asymptomatic subjects.
Methods: Twenty-five military recruits volunteered to perform a MRI-SIJ before and after 6 week of intense physical training, of which 22 recruits underwent imaging at both time points. The MRIs were scored for structural lesions by 3 trained readers MdH, GV and TR, blinded for time sequence and clinical findings. Regarding the number of lesions a consensus was made by agreement of 2 out of 3 readers.
Results: At baseline, structural lesions were present in 36.4% (8/22) of subjects of which 5 subjects presented with at least 1 erosion, one subject with sclerosis and 3 subjects presented fatty lesions. This increased to 50% subjects (11/22) with structural lesions on MRI-SIJ after 6 weeks of mechanical stress, of which 8 subjects with at least 1 erosion, one subject with sclerosis and 3 subjects with fatty lesions (P=0.453). The change scores for sclerosis, erosions and fatty lesions were respectively 0.0 (±0.0), 0.2 (±0.1) and 0.3 (±0.2). None of the subjects displayed ankylosis. The lesion distribution is visualized in Table1.

Table 1. Number of structural lesions in young military recruits before and after intensive training

N=22	Baseline	Week 6	P-value
Sclerosis			
Mean (±SD)	0.05 (±0.05)	0.05 (±0.05)	1.00
Median (25, 75 percentile)	0.0 (0.0, 0.0)	0.0 (0.0,0.0)	
Erosions			
Mean (±SD)	0.32 (±0.14)	0.55 (±0.17)	0.096
Median (25, 75 percentile)	0.0 (0.0, 0.25)	0.0 (0.0, 1.0)	
Fatty lesions			
Mean (±SD)	1.0 (±0.86)	1.3 (±1.0)	0.285
Median (25, 75 percentile)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	

Conclusions: Although not prevalent, structural lesions such as erosions, sclerosis and fatty lesions can be found in young asymptomatic subjects. However, these lesions do not seem to increase after 6 week of intense physical training.
References:
[1] Weber U, Lambert RG, Ostergaard M, Hodler J, Pedersen SJ, Maksymowych WP. The diagnostic utility of magnetic resonance imaging in spondylarthritis: an international multicenter evaluation of one hundred eighty-seven subjects. Arthritis Rheum. 2010;62(10):3048–58.
Acknowledgements: ASAS research grant 2017.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5967

AB0717 CONDUCTION DISTURBANCES IN A GROUP OF PATIENTS WITH AXIAL SPONDYLOARTHROPATHY

H.S. Park[1], A. Laiz[1], C. Alonso[2], A. Garcia-Guillén[1], M. Millán[1], B. Magallares[1], P. Moya[1], I. Castellví[1], C. Díaz-Torné[1], J.M. De Llobet[1]. *[1]Rheumatology; [2]Cardiology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*

Background: Cardiac conductance disturbances are known to be one of the many extra-articular manifestations of Ankylosing Spondilitis but not as well related to axial spondyloarthropathies.
Objectives: Description of conduction disturbances found in a group of patients with Axial Spondyloarthropathy (AxSpa) that met ASAS criteria.
Methods: Clinical and demographic variables of 78 patients with AxSpa were registered. It included cardiovascular risk factors as well as cardiacvascular adverse events. All of them had a routine electrocardiogram done which were analized by a cardiologist.
Results: 48 of the 78 patients were men, with a mean age of 61 with standard deviation (SD) of 14. The mean time of evolution of the disease was 23 years (SD ±16). HLA-B27 was prevalent in 54 (69.2%). The sacroileitis was found in radiologic examination of 72 (92.2%), and 6 (7.7%) of them presented edema in magnetic resonance imaging. Other clinical traits were: 43 (55.1%) peripheric arthritis 43, 8 (10.3%) dactilitis, 33 (42.3%) enthesitis, 16 uveitis (20.5%), 2 (2.6%) inflammatory bowel disease and psoriasis 34 (43.3%). The following cardiovascular risk factors were registered: 25 (32%) smokers, 42 (53%) hypertension, 32 (41%) dislipemia, 9 (12%) diabetes, 9 (12%) hyperuricemia and 20 (20%) obesity. 14 patients had structural cardiopathy (11 ischemic cardiopathy and 3 aortic valvulopathy). The electrocardiographic register showed conductance disorders in 20 patients (25.6%). The details of these findings are specified in table 1.

First grade auriculoventricular block	5
Second and third grade auriculoventricular block	2
Left anterior fascicular block	1
Right bundle branch block	2
Unspecific intraventricular conduction disorder	4
Bachmann interatrial conduction disorder	1

Conclusions: A quarter of our series of presented conduction disturbances in electrocardiography. The relation with disease evolution, as in Ankylosing Spondilitis remains yet to be analized.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4140

AB0718 PREVALENCE OF RISK FACTORS FOR FRACTURES IN AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW

J. Ramírez García[1], R. Curbelo[2], J.C. Nieto[3], S. Castañeda[4], L. Carmona[2]. *[1]Rheumatology, Hospital Clínic, Barcelona; [2]Instituto de Salud Músculoesquelética; [3]Rheumatology, Hospital G.U. Gregorio Marañón; [4]Rheumatology, Hospital de la Princesa, Madrid, Spain*

Background: Spinal fractures occur more than expected in axial spondyloarthritis (Ax-Sp). However, it is not totally clear whether fracture risk depends solely on biomechanical problems of the spondyloarthritic spine or whether the prevalence of risk factors for fracture is larger than expected in these patients.
Objectives: To describe the prevalence of risk factors for osteoporotic fractures (both axial and peripheral) in Ax-Sp.
Methods: A systematic literature search was conducted. Medline, Embase and Cochrane Library databases were searched with a sensitive strategy including type of study and synonyms of Ax-Sp. All contemporary cross sectional studies or baseline results from representative cohorts of Ax-Sp published between January 2006 and 2016 were selected for detailed review. Only studies that fulfilled a minimum quality for survey data were included. Data on bone mineral density, prevalence of osteoporosis, and risk factor for fractures in Ax-Sp patients were collected.
Results: After screening 3597 titles and abstracts, only 43 studies (34 cross-sectional, 3 prospective and 6 retrospective) were reviewed in detail. Of these, 20 studies compared Ax-Sp patients with a control group, either healthy individuals (17 studies) or subjects with other diseases (6 studies). Reported prevalence of osteoporosis varied from 2% to 39.6%. Alcohol intake (58–61%), use of corticosteroids (11.7–67%), and 25-OH vitamin D deficit (26–76%) were unexpectedly high in Ax-Sp patients. All other factors were within expected frequencies for a not too old population.
Conclusions: Our systematic review found that alcohol intake, steroid use and 25-OH-vitamin D deficit should be taken into account when assessing comorbidity in Ax-Sp in order to avoid excess fractures.
Acknowledgements: this project was funded by Merck Sharp & Dohme of Spain.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3539

AB0719 BASELINE CHARACTERISTIC OF NEWLY DIAGNOSED PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS FROM THE SINGLE CENTRE LITHUANIAN COHORT

J. Sabaliauskiene[1], A. Baranauskaite[2]. [1]*Rheumatology;* [2]*Lithuanian University of Health Sciences, Kaunas, Lithuania*

Background: The prevalence rates for spondyloarthropathies has been investigated in an epidemiological study in Lithuania (1), but no studies are analysing the demographics, clinical characteristics of SpA in Lithuania. Changes in spondyloarthritis (SpA) concept and application of the new criteria for classification should improve spondyloarthritis diagnostic standards in routine clinical practice.
Objectives: To assess demographics and clinical manifestations of firstly diagnosed axial spondyloarthritis, to compare ankylosing spondylitis (AS) with non-radiographic axial spondyloarthritis (nr-axSpA) using standardized clinical assessment tools.
Methods: In September 2014 our centre began to collect a cohort of patients with newly diagnosed axial spondyloarthritis, according to ASAS criteria. Statistical analysis was performed with SPSS 20.0. A $p<0,05$ was considered statistically significant.
Results: 97 patients (60 men, 37 women) have been included. All of them (100%) suffered from chronic back pain. Inflammatory back pain (according to ASAS criteria) was present in 77%. 34 (35,1%) patients already had definite radiographic changes in the sacroiliac joints (SIJ), therefore AS (based on modified New York criteria) was diagnosed. The mean age at first visit was similar: 34,3 (±10,0) in nr-axSpA and 36,1 (±11,0) in AS group. Duration of symptoms was significantly longer in AS group (mean 106,6 months in AS versus 44,8 months in nr-axSpA). The prevalence of HLA-B27 was similar: 74,6% vs 91.2% for nr-axSpA and AS, respectively. There were more males in AS group (76,5% vs 54,0%, p 0,03). The frequency of clinical features (peripheral arthritis, dactylitis) and extra-articular manifestations (enthesitis, uveitis, psoriasis, inflammatory bowel disease, preceding infection) was similar between the two subgroups ($p>0,05$). Mobility was slightly more impaired in AS patients, but it did not reach a significant level. No differences in the level of global pain, patient's global assessment were found. BASDAI did not show the significant difference between AS and nr-axSpA (mean 4,5±2,1 vs 3,9±2,0), as well CRP (mean CRP 17,33 mg/l vs 17,75 mg/l (p 0,2) and ESR.
Conclusions: Diagnosis of axial SpA in Lithuania remains delayed. The proportion of patients with AS among newly diagnosed axial SpA is high.There are more women in the nr-axSpA group. Both groups do not differ regarding clinical features, disease activity.
References:
[1] Adomaviciute D, Pileckyte M, Baranauskaite A, Morvan J, Dadoniene J, Guillemin F.Scand J Rheumatol. 2008 Mar-Apr;37(2):113–9 Prevalence survey of rheumatoid arthritis and spondyloarthropathy in Lithuania.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6944

AB0720 CHARACTERISTICS OF TUNISIEN SPONDYLOARTHRITIS PATIENTS WITH HIP DISEASE

K. Maatallah[1], F. Essafi[1], I. Mahmoud[2], K. Ben Abdelghani[3], O. Saidane[2], W. Hamdi[1], M.M. Kchir[1], R. Tekaya[2], L. Abdelmoula[2]. [1]*Rheumatology, MOHAMED KASSAB Orthopedics National Institute, manouba;* [2]*Rheumatology, Charles Nicolle hospital;* [3]*Rheumatology, Monji Slim hospital, tunis, Tunisia*

Background: spondyloarthritis (SpA) is characterized by inflammation of spine and sacroiliac joints. Hip involvement is the most frequent extra spinal arthritic manifestation of SpA and may lead to a worse functional outcome.
Objectives: The objective of this study was to assess clinical, biological and radiological characteristics of SpA patients with hip disease.
Methods: This is a transversal multicenter study, including SpAs patients (satisfying ASAS criteria2009) with hip disease Demographic, clinical, radiographic, and laboratory data were collected and analyzed. Radiographic forms of hip disease were assessed according to Netter classification (early, condensing, destructive, combined and synostosante forms). Radiographic severity was assessed by the modified Stokes Ankylosing Spondylitis Spine Score (mSASSS) and BASRI (Bath Ankylosing Spondylitis Radiologic Index).
Results: ninety four patients were evaluated (77men). The mean age was 41.53±11.97 years. The median age at disease onset was 26.23±10.29 years.The mean diagnostic delay was 6.48 years. 46% of patients were smoker. HLA B27 was positive in 50% of cases. A peripheral joint involvement was found in 33% of cases. Extra-articular manifestation was seen in 57% of patients: osteoporosis (16 patients), uveitis (15 patients), psoraisis (10 patients), chronic inflammatory bowel disease (12 patients). 78 patients had bilateral hip involvement and 147 hips were evaluated. The median BASDAI and BASFI scores were respectively 5,4 and 5,5. The mean index of severity for osteoarthritis for the hip (ISH) was 12.24 (±6.84). Patients had an early form of hip disease in 22% of cases, Condensing form in 3% of cases, combined forms in 22% of cases and destructive form in 53% of cases. BASRI-hip score was 1 in 24%, 2 in 49%, 3 in 19% and 4 in 8% of hips. Sacoiliac joint grade was 2 in 17%, 3 in 37% and 4 in 46% of cases. The mean mSASSS score was 15.34±16.22.
TNF inhibitors were indicated in 49% of patients (infliximab 23, Adalimumab 7 and Etanercept 18).31 patients received csDMARDs and 46 NSAID.
Conclusions: Our finding confirm previous observation that clinical and radiological hip involvement is associated with a more severe disease with a high activity and pronounced functional impairments.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5099

AB0721 THE EVALUATION OF ULTRASONOGRAPHIC AND CLINICAL ENTHESOPATHY IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES

E. Suleyman[1], H. Harman[2], K. Nas[1]. [1]*Division of Rheumatology and Immunology, Department of Physical Medicine and Rehabilitation, Sakarya University, Faculty of Medicine, Sakarya;* [2]*Rheumatology Clinic, Bolu İzzet Baysal State Hospital, Bolu, Turkey*

Background: Enthesitis is considered as the primary anatomical lesion in spondyloarthropathy (SpA) but it can be seen in other rheumatologic diseases. Its locations and clinical relationships have not been studied well in the literature.
Objectives: We aimed to investigate the frequency of ultrasonographic, clinical enthesopathy and the relationship between enthesopathy and disease activity, functional status in patients with rheumatoid arthritis (RA) and axial SpA.
Methods: Thirty three axial SpA, 21 RA patients and 30 healthy subjects were included in the study. The clinical and functional evaluations relied on the BASDAI, BASFI, ASQoL, DAS28, and HAQ, and on a VAS for entheseal pain, as well as on the MASEI. Knee, ankle and elbow were examined with US bilaterally in 172 joint regions.
Results: The physical examination scores for enthesitis were 1.97±2.68, 2.43±1.80, 0.23±0.12 in axial SpA, RA and healthy subjects, respectively. There was no statistically significant difference between axial SpA and RA about enthesitis physical examination scores (p=0.123). A statistically significant difference was not found between axial SpA and RA in quadriceps tendon enthesitis and distal patellar ligament enthesitis according to MASEI index (MASEI 3,4,5) (p=0.993, p=0.124, p=0.652). Other MASEI enthesit scores were statistically higher in axial SpA group than RA and healthy subjects (p=0.008). Positive correlations were found between BASDAI scores and enthesitis pyhsical examination scores, MASEI total scores (r=0.739, p=0.0001, r=0.516, p=0.002). There was moderately positive correlation between ASQoL total scores and MASEI total scores (r=0.466, p=0.006). HAQ total scores were not correlated with MASEI total scores (r=0.213, p=0.065).
Conclusions: Ultrasonographic enthesitis was associated with impaired quality of life in axial SpA. MASEI 1 and 2 was spesific entheseal regions in MASEI index for axial SpA. Different from RA, the calcaneal enthesitis region for clinical investigation and ultrasonographic enthesopathy should be focused on in axial SpA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6834

AB0722 THE IMPACT OF A REFERRAL STRATEGY FOR AXIAL SPONDYLOARTHRITIS IN YOUNG PATIENTS WITH CHRONIC LOW BACK PAIN: SHORT TERM OUTCOMES OF THE IMPACT STUDY

L. Van Hoeven[1,2], A. Korver[1,2], C. Appels[3], J. Hazes[1], F. van den Hoogen[4], M. van Oosterhout[5], J. Oostveen[6], J. Spoorenberg[7], I. Tchetverikov[8], T. Kuijper[2], B. Koes[9], A. Weel[1,2]. [1]*Rheumatology, Erasmus University Rotterdam;* [2]*Rheumatology, Maasstad Hospital, Rotterdam;* [3]*Rheumatology, Amphia Hospital, Breda;* [4]*Rheumatology, Sint Maartenskliniek, Ubbergen;* [5]*Rheumatology, Groene Hart Hospital, Gouda;* [6]*Rheumatology, ZGT, Almelo;* [7]*Rheumatology, UMCG, Groningen;* [8]*Rheumatology, Albert Schweitzer Hospital, Dordrecht;* [9]*Primary Care, Erasmus University Rotterdam, Rotterdam, Netherlands*

Background: A substantial amount of young patients with chronic low back pain (CLBP) have axial spondyloarthritis (axSpA), but early recognition of these patients is difficult for general practitioners (GPs). Recently, the CaFaSpA referral rule has been published and externally validated. It is an easy to use referral strategy that has shown to be able to identify patients with CLBP at high risk for axSpA in a primary care setting. The CaFaSpA referral rule consists of 4 items: inflammatory back pain, family history of axSpA or related disease, good reaction to NSAIDs and duration of back pain $\geq$5 years. If at least 2 out of 4 items are present, the referral rule is positive and a referral to a rheumatologist is advised.
Objectives: To assess the effect of the CaFaSpA referral rule on disability in young CBPP patients by comparing it with usual care, using the format of an impact analysis.
Methods: A cluster randomized controlled trial with GP practices as clusters. GP practices were randomized to either the intervention (use of the referral strategy) or control (usual care) group. Within these GP practices, patients aged 18–45 years with current CLBP were recruited. The primary outcome was disability caused by low back pain, measured with the Roland Morris Disability Questionnaire (RMDQ) scale 0–24. RMDQ score was obtained at baseline and 4 months after a referral advice was made. A higher RMDQ score means more disability. For statistical analysis a linear mixed effects regression model was used.

Results: 92 primary care practices were randomized, 679 patients participated (64% women, mean age 36.2 years (SD7.5) and median CLBP duration 9 years (IQR 4–15 years). 333 patients were randomized to the intervention group, both groups had similar characteristics at baseline. Sixty percent of participants had a positive referral rule. RMDQ scores are shown in table 1. Sub scores are shown for patients with a positive outcome of the referral rule (PRR) and a negative outcome of the referral rule (NRR). The change in RMDQ score after 4 months in the intervention group was -0.74 (95% confidence interval (CI) -1.31 – -0.18) and in the control group -0.46 (95% CI -0.98 – 0.05). There was no significant difference between groups.

Table 1. Estimated RMDQ scores with linear mixed effects regression model in young chronic low back pain patients by application of the CaFaSpA referral rule versus usual care*

	RMDQ at baseline	RMDQ after 4 months
Use of referral rule, mean (95% CI)	8.38 (7.58 - 9.18)	7.64 (6.78 - 8.49)
PRR^, mean (95% CI)	8.51 (7.56 - 9.45)	7.77 (6.74 - 8.79)
NRR±, mean (95% CI)	8.19 (7.02 - 9.35)	7.44 (6.18 - 8.69)
Usual care, mean (95% CI)	8.61 (7.82 - 9.39)	8.14 (7.33 - 8.96)
PRR^, mean (95% CI)	8.58 (7.65 - 9.50)	7.83 (6.87 - 8.79)
NRR±, mean (95% CI)	8.65 (7.55 - 9.76)	8.74 (7.54 - 9.93)

*= There were no significant differences between use of the referral rule and usual care; RMDQ=Roland Morris Disability Questionnaire; ^PRR=positive referral rule; ±NRR= negative referral rule

Conclusions: Compared with usual care, use of the CaFaSpA referral rule in CLBP patients in a primary care setting did not significantly impact disability in these patients, 4 months after a referral advice was made. Results after 12 and 24 months should be awaited before definitive conclusions about the impact of the CaFaSpA referral rule for axSpA in CLBP patients can be made.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6041

AB0723 TECHNICAL AIDS AGREED AMONG SPECIALISTS FOR THE MANAGEMENT OF COMORBIDITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: THE GECOAX PROJECT

C. González[1], R. Curbelo[2], J.C. Torre-Alonso[3], E. Collantes[4], S. Castañeda[5], M.V. Hernández[6], A. Urruticoechea-Arana[7], J.C. Nieto[1], J. García[8], M.Á. Abad[9], J. Ramírez[6], C. Suárez[10], R. Dalmau[11], M.D. Martín-Arranz[12], L. León[13], J.C. Hermosa[14], J.C. Obaya[15], T. Otón[2], L. Carmona[2].
[1]Rheumatology, HU Gregorio Marañón; [2]InMusc, Madrid; [3]Rheumatology, HU Monte Naranco, Oviedo; [4]Rheumatology, HU Reina Sofía, Córdoba; [5]Rheumatology, HU la Princesa, IIS-IP, Madrid; [6]Rheumatology, HU Clinic i Provincial, Barcelona; [7]Rheumatology, H Can Misses, Ibiza; [8]Rheumatology, HU 12 de Octubre, Madrid; [9]Rheumatology, H de Plasencia, Plasencia; [10]Internal Medicine, HU la Princesa, IIS-IP; [11]Cardiology; [12]Gastroenterology, HU la Paz; [13]Psychology, UCJC, Madrid; [14]Centro de Salud Ciudades, Getafe; [15]Centro de Salud Alcobendas, Alcobendas, Spain

Background: The management of comorbidity in patients with axial spondyloarthritis (Ax-SpA) needs improvement; the implementation of clinical practice guidelines is still deficient and heterogeneous.
Objectives: To prioritise comorbidities in Ax-SpA and to elaborate practical aids for their identification and follow-up.
Methods: A multidisciplinary panel [10 rheumatologists (6 experts in Ax-SpA), 2 family doctors, 1 internist, 1 cardiologist, 1 gastroenterologist, 1 psychologist and 3 methodologists] prioritised, in a discussion group, a list of comorbidities based on frequency and impact. Each comorbidity was discussed largely and systematic reviews were performed to support or discard items. In a second meeting, items to be included were presented, discussed, and those with lower priority disregarded.
Results: The panel produced a checklist for health professionals and another for patients. Each item is supported by arguments and references. Table 1 shows, schematically, the items included in the checklists.

Table 1. Items included in the checklist

Usual treatment	Of note: oral anticoagulants, antihypertensive drugs, ASA, steroids and NSAIDs.
Specific comorbidities	Hypertension, heart failure, renal failure, liver cirrhosis, gastric ulcer, infections, tuberculosis, neurological disease, and fracture risk.
Vaccine schedule and dental hygiene	Patient's vaccination status; prevention of infections.
Life-style	Physical activity (amount and type). Alcohol consumption. Detect possible abuses; important risk factor for other comorbidities.
Depression, quality of sleep and sexual life	The impact of Ax-SpA in the psychosocial sphere is relevant and should be carefully evaluated. Specific questionnaires are recommended.
Non-preventable diseases	Frequent association with uveitis, inflammatory bowel disease and cardiac pathology; systematise questions

Conclusions: These checklists are intended to facilitate the systematic evaluation of co-morbidity associated with Ax-SpA, thus allowing an earlier detection and better control and management of these patients by the rheumatologist.

Acknowledgements: This project was funded by Merck Sharp & Dohme Spain. Merck Sharp & Dohme had no influence on either the development of the project or the final content of the abstract.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4795

AB0724 HIGHER LIKELIHOOD OF ANTI-TNF PRESCRIPTION IN MEN VS WOMEN WITH ANKYLOSING SPONDYLITIS DESPITE SIMILAR DISEASE BURDEN: RESULTS FROM ROUTINE CARE AT TWO ACADEMIC RHEUMATOLOGY CENTERS OF USA AND SPAIN

M. Blasco-Blasco[1], I. Castrejón[2], M. Ruiz-Cantero[1], V. Joaní[3], E. Pascual[4], J. Block[2], T. Pincus[2]. *[1]Public Health, University of Alicante, Alicante, Spain; [2]Rheumatology, Rush University Medical Center, Chicago, United States; [3]Rheumatology, Alicante University General Hospital; [4]Rheumatology, Miguel Hernandez University, Alicante, Spain*

Background: Ankylosing spondylitis (AS) has been considered to be more prevalent in men compared to women. Besides, the clinical presentation in women is thought to be milder and more peripheral than in men. Some studies have suggested a higher burden of disease in women[1,2] but others not confirm these differences[3,4].
Objectives: To evaluate possible gender differences in men and women with AS seen in routine care at two academic rheumatology centers of the USA and Spain.
Methods: Sixty one men and 30 women with AS in Spain and 61 men and 31 women in the USA completed a Multidimensional Health Assessment Questionnaire (MDHAQ). The MDHAQ includes (0–10 scores) for physical function, pain, patient global estimate (PATGL), compiled into a 0–30 RAPID3, and fatigue scores. Furthermore, demographic data, biological (anti-TNFα) and DMARD therapies, were obtained from the medical records. A comparative analysis of men and women was performed by Mann-Whitney U tests for non-parametric quantitative data (median/interquartile range), and Chi square tests for qualitative data (frequencies/percentajes).
Results: We have not detected significant differences in men and women for function, pain, PATGL, or fatigue although a trend towards higher RAPID3 values was seen in females in both sites (Table). Anti-TNFα medications were prescribed more often in men than in women (81.2% vs 65.6%, in all patients p=0.02), statistically significant in Spain (82% vs 60%, p=0.02), and numerically higher in the USA (80.3% vs 71%, p=0.31). DMARD medications tend to be more prescribed in women than men in all patients (17.2% vs 23%, p=0.35) although no statistically significant.

Table 1. Health status and treatment of patients with SpA at two academic centers (*p<0.05)

	USA		Spain	
	Men (N=61)	Women (N=31)	Men (N=61)	Women (N=30)
Age, years	41.5 (31.7–56.9)	36.2 (31.7–56.8)	52.0 (46.0–65.4)	54.6 (43.3–61.4)
Education, years	16 (12–17)	16 (11–18)	9 (8–12)	8 (8–12)
White	31 (51%)	17 (55%)	56 (92%)	30 (100%)
Duration disease, years	12.1 (6.1–21.5)	6.3 (4–16.6)	22 (12.1–34.8)	21.4 (12.1–30.1)
HLA-B27+	26 (68%)	21 (88%)	49 (86%)	20 (69%)
MDHAQ				
Function, (0–10)	2 (0.3–4)	2.3 (0.3–4)	1.2 (0–2.7)	0.8 (0–2.3)
Pain, (0–10)	4 (1–7)	5 (2–7.5)	3 (1.5–6)	4 (1–5)
PATGL, (0–10)	3 (1.5–6.3)	5 (2–6.5)	4 (2–5.5)	3.5 (1–5.5)
RAPID3, (0–30)	8.5 (4.2–15.3)	11.8 (4–16.8)	6.8 (3.5–14.2)	8.1 (3.3–12.7)
Fatigue, (0–10)	3 (0–6.5)	5 (3–8)	3 (1–4.5)	2.8 (1–5.5)
Treatment				
Anti-TNFα	49 (80%)	22 (71%)	50 (82%)	18 (60%)*
DMARD	9 (15%)	7 (23%)	13 (21%)	7 (23%)

Conclusions: Men with SpA receive anti-TNFα more likely than women; although disease burden appears somewhat higher in women. This pattern is similar in both Spain and the USA, though statistically significant only in the Spanish population. Other parameters may be having weight in the management of SpA, such as radiographic signs versus peripheral manifestations.
References:
[1] van der Horst-Bruinsma IE, et al. Ann Rheum Dis 2013.
[2] Ortega Castro R, et al. Reumatol Clin 2013.
[3] Gremese E, et al. Rheumatology (Oxford) 2014.
[4] Shahlaee A, et al. Clin Rheumatol 2015.
Acknowledgements: University Institute for Gender Studies (University of Alicante) supported MBB.
Disclosure of Interest: M. Blasco-Blasco: None declared, I. Castrejón: None declared, M. Ruiz-Cantero: None declared, V. Joaní: None declared, E. Pascual: None declared, J. Block: None declared, T. Pincus Shareholder of: Health Report Services, Inc.
DOI: 10.1136/annrheumdis-2017-eular.3525

AB0725 USING A REDUCED JOINT COUNT IN MEASURING DISEASE ACTIVITY IN PSORIATIC ARTHRITIS, IS IT LEGIT?

M. Vis[1], K. Wervers[2], I. Tchetverikov[3], A. Gerards[4], M. Kok[5], C. Appels[6], L.-A. Korswagen[7], M. Hazes[1], J. Veris[8], H. van Groenendaal[9], J. Luime[1] on behalf of DEPAR. *[1]Rheumatology; [2]Erasmus MC; [3]Rheumatology, Alber Schweitzer hospital; [4]Vlietland ziekenhuis; [5]Rheumatology, Maasstad ziekenhuis, Rotterdam; [6]Rheumatology, Amphia ziekenhuis, Breda; [7]Rheumatology, Sint Franciscus Gasthuis, Rotterdam; [8]Rheumatology, RZWN, Goes; [9]Rheumatology, RZWN, Roosendaal, Netherlands*

Background: In Psoriatic arthritis (PsA) the pattern of joint involvement seems to be more heterogenic than Rheumatoid Arthritis (RA). Therefor the 66/68 joint count is frequently used in PsA scores. In this study we would like to investigate whether using less extensive joint counts influences PsA disease activity measures
Objectives: To evaluate the effect of using a 28, 44 or 66/68 joint count on Minimal Disease Activity (MDA).
Methods: Newly diagnosed PsA patients were included in the Dutch Early south-west Psoriatic Arthritis Registry (DEPAR) study between August 2013 and January 2017. Joint scores at baseline and 6 months were calculated using a 28, 44 and 66/68 joint count. Consecutively MDA was calculated using each of these joint counts. MDA is defined as minimal disease activity in 5 out of 7 domains (swollen joints, tender joints, PASI, patient vas pain, patient vas global, HAQ, enthesitis)
Results: In total, 413 patients were included into the study, of which 320 had reached 6 months follow-up at the time of this abstract. Half of the patients were male (49%), and mean age was 50 years (SD 13.8).
The percentage of patients with at least one involved joint (swollen or tender) at baseline decreased from 91% using the 66/68 score to 88% with 44 joints and then to 80% with a 28 joint count (Table 1). At 6 month these scores were 66% 63% and finally 56% respectively for the 66/68, 44 and 28 joint count. After 6 months, 96 patients (30%) had achieved MDA using the original 66/68 joint count. Using a 28 joint count, 10 more patients (10% of the MDA population) were classified as having achieved MDA.

Table 1. Joint scores and MDA at baseline (n=421) and 6 months (n=320) using 66/68, 44 and 28 joint counts in a population of newly diagnosed PsA patients

	Joints		
T0	66/68	44	28
Swollen joint score, median	2	1	1
Tender joint score, median	3	2	2
Swollen joint score >0, n (%)	311 (75)	298 (72)	256 (62)
Tender joint score >0, n (%)	346 (84)	331 (80)	290 (70)
Involved joint >0 (swollen and/or tender), n (%)	375 (91)	363 (88)	329 (80)
MDA, n (%)	56 (14)	65 (16)	70 (17)
T6	66/68	44	28
Swollen joint score, median	0	0	0
Tender joint score, median	1	1	0
Swollen joint score >0, n (%)	125 (41)	117 (38)	100 (32)
Tender joint score >0, n (%)	183 (59)	175 (57)	149 (48)
Involved joint >0 (swollen and/or tender), n (%)	204 (66)	195 (63)	171 (56)
MDA, n (%)	96 (30)	98 (31)	106 (33)

Conclusions: Using reduced joint count joints in PsA misclassifies around 10% of patients as having no joint involvement. It also misclassifies about 10% of the MDA population of having achieved MDA while they have not. Full 66/68 joint counts remain recommended for measuring disease activity in PsA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6851

AB0726 SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

M. Ismail, A. Mosallam, M. Abdelaziz, A. Moshrif. *Rheumatology, Faculty of Medicine, Al Azhar University, Assiut, Egypt*

Background: Systemic inflammatory response of various autoimmune diseases has been reported as a cause of accelerated atherosclerosis which is a risk factor for cardiovascular complications.
Objectives: This study aimed to evaluate atherosclerosis in patients with ankylosing spondylitis (AS) and its relation to disease activity.
Methods: The study was carried out on thirty AS patients, who fulfilled the modified New York criteria. Thirty apparently healthy normal volunteers, age and sex matched served as control. Complete History taking, General and systemic examination, Body mass index (BMI), Bath AS disease activity index (BASDAI), Bath AS functional index (BASFI), lipid profile, inflammatory markers and serum glucose level were done. Based on BASADI score, patients were then classified to active and inactive groups comprised 11 patients (37%) and 19 patients (63%) respectively. Carotid intima-media thickness (CIMT) was measured using real-time gray-scale sonography. The intima-media thickness (IMT) of common carotid artery, carotid bulb and internal carotid artery was determined.
Results: 25 males (83.3%) and 5 females (16.7%) with mean age 39.1±12.38, their mean disease duration 13.13±8.03 while controls were 21 males (70%) and 9 females (30%) with mean age 39.7±12.6.
While IMT was found significantly increased in patients (0.87±0.49) versus controls (0.5±0.12) ($P<0.001$), there was no significant difference regarding the presence of plaques and there was no stenosis found in cases or controls. No significant difference was found between active and inactive cases as regard to components of lipid profile. The mean IMT in active and inactive cases was 0.74±0.11 and 0.72±0.17 respectively with no significant difference. we found no significant correlation between IMT and different disease scores, ESR or CRP.
Conclusions: AS patients have a higher risk for developing atherosclerosis. IMT of common carotid artery could be added as a further investigation for detection and follow up of atherosclerosis in AS patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4502

AB0727 HIP OSTEOPOROSIS AND VERTEBRAL FRACTURES ARE ASSOCIATED WITH YOUNGER AGE AT DIAGNOSIS OF SPONDYLOARTHRITIS: RESULTS FROM THE COMOSPA STUDY

M.H. Derakhshan[1], N.J. Goodson[2], J. Packham[3], R. Sengupta[4], H. Marzo-Ortega[5], A. Molto[6], S. Siebert[1] on behalf of BRITSpA and COMOSPA investigators. *[1]Institute of Infection, Immunity & Inflammation, University of Glasgow, Glasgow; [2]Academic Rheumatology Department, University of Liverpool, Liverpool; [3]Haywood Rheumatology Centre, Keele University, Keele; [4]Royal National Hospital for Rheumatic Diseases, Bath; [5]NIHR, Leeds Teaching Hospitals Trust and LIRMM, University of Leeds, Leeds, United Kingdom; [6]Paris Descartes University, Hôpital Cochin, Paris, France*

Background: Spondyloarthritis (SpA) is associated with adverse bone health outcomes. It is not known whether age at disease diagnosis is associated with osteoporosis and fracture in later life.
Objectives: To examine the relationship between "younger age at SpA diagnosis" and risk of osteoporosis and fractures (vertebral and low-trauma peripheral).
Methods: COMOSPA is a large global cross-sectional study comprising 3984 patients with SpA from 23 countries1. We evaluated the association between "younger age at SpA diagnosis" (categorised into 5-year blocks) and vertebral fracture, low-trauma peripheral fracture, and osteoporosis (t<-2.5 on bone densitometry) using logistic regression. Models were adjusted for age, sex, BMI, smoking, alcohol, NSAIDs, DMARDs, biologics, steroids and vitamin D level. Subgroup analysis was performed, stratified by peripheral and/or axial joint involvement.
Results: Data were available for 3923 participants (64% male). Median age at SpA diagnosis was 33 (IQR 25–43) years. Younger age at SpA diagnosis was not associated with the risk of vertebral fractures in the entire cohort (OR=1.11, p=0.143) nor in the subgroup with axial SpA involvement, but was increased in those with peripheral arthritis (OR=1.26, p=0.014) indicating 26% excess risk for each 5-year younger age at time of SpA diagnosis.
There was no significant association between younger age at diagnosis and the risk of low trauma peripheral fractures or spinal osteoporosis in the entire cohort or any subgroups. Younger age at SpA diagnosis was associated with higher risk of hip osteoporosis in the entire cohort (OR=1.34, p=0.004) and both subgroups. Femoral neck osteoporosis demonstrated similar associations (Table).

Table 1. Association between "younger age at SpA diagnosis" and the risk of fractures and osteoporosis (multivariable)

	OR	95% CI for OR	*p* value
Vertebral Fractures (All)	1.11	0.96–1.29	0.143
Peripheral arthritis* subgroup	1.26	1.05–1.51	0.014
Axial disease* subgroup	1.07	0.92–1.24	0.370
Low trauma peripheral fracture (All)	1.01	0.85–1.20	0.924
Spinal Osteoporosis (All)	1.07	0.93–1.22	0.362
Peripheral arthritis* subgroup	1.09	0.92–1.28	0.338
Axial disease* subgroup	1.04	0.90–1.20	0.611
Hip Osteoporosis (All)	1.34	1.10–1.64	0.004
Peripheral arthritis* subgroup	1.30	1.02–1.64	0.031
Axial disease* subgroup	1.41	1.14–1.75	0.002
Femoral neck Osteoporosis (All)	1.32	1.12–1.54	0.001

*Subgroups overlap as many patients will have both axial and peripheral arthritis.

Conclusions: Younger age of SpA diagnosis was associated with higher risk of vertebral fracture in patients with peripheral arthritis but not axial disease in this study. Lack of association with vertebral fracture and spinal osteoporosis in axial disease may reflect difficulty in detecting spinal disease and osteoporosis in the presence of spinal pain and syndesmophytes. An association between hip osteoporosis and younger age at SpA diagnosis was noted.
References:
[1] Ann Rheum Dis 2016;75:1016–23.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3439

AB0728 RHEUMATIC MANIFESTATIONS OF INFLAMMATORY BOWEL DISEASES, STUDY FROM MIDDLE EAST

M. Hammoudeh[1], S. Alkaabi[1], M. Sharma[1], E. Al-Sayed[1], P. Chandra[2], M. Elbadri[1], S. Hammoudeh[3], N. Abu Nahya[2]. *[1]Medicine; [2]Research center, HMC; [3]Research center, Weill Cornell College-Qatar, Doha, Qatar*

Background: Musculoskeletal symptoms accompanying the diagnoses of Inflammatory bowel diseases (IBD), are seen in 6 -46% of cases1. There are very limited data about prevalence of rheumatic manifestations of IBD from the Middle East 2.

Objectives: The goal of this study is to examine the prevalence of rheumatic manifestations among patients diagnosed with IBD.

Methods: Between 1/2/2015 and 30/7/2016 all consecutive IBD patients were approached. A total of 127 adult patients signed the consent form. The diagnosis and extent of IBD (ulcerative colitis or Crohn's disease) had to be confirmed by a colonoscopy and histopathology. Patients were then interviewed and examined by one of two expert rheumatologists. A set of questions were used, complete rheumatological examination, X-rays of the lumbosacral and SI joints, and HLA-B27 test were done.

Results: Among our sample; 66% were Arabs and 34% are Asians, 58.3% were males, 52% fell in the age category of 30–49 years, 83.1% were married, 25.6% had a graduate degree, 36.5% had a history of smoking, and 15.2% had a family history of IBD.

The sample had 36%% with Crohn's disease, and 64% with ulcerative colitis. Any type of rheumatic manifestations were present in of 57.5% with no significant differences between the the two types of IBD diseases ($p>0.05$). The majority of these patients had peripheral manifestations (arthralgia, arthritis, enthesitis) (43.3%), while only 3.1% had axial alone, and 11% had both types. Among those with peripheral manifestations; 7.2% had type 1 arthritis (Pauciarticular), while 1.4% had type 2 arthritis (polyarticular). There were no significant differences between the two types of IBD diseases in regards to the presence of peripheral manifestations ($p>0.05$). However, the two diseases were significantly different in the presence of axial manifestations as more people with Crohn's have axial manifestations (19.6%) compared with Ulcerative colitis (12.3%). Those with Crohn's had more people with rheumatic manifestations 4–7 years before the diagnosis of IBD. HLA-B27 was positive in 5 patients 3 with Crohn's and 2 with ulcerative colitis. Logistic regression analysis of the data did not reveal any significant predictor or potential risk (type of IBD, gender, age group, BMI, smoking, family history, duration or extent) for the development of musculoskeletal manifestations in our patients.

Conclusions: In this study of musculoskeletal manifestations of patients with IBD from the Middle East 57.7% of them have any rheumatic manifestations.Peripheral manifesations occurred in 43%, axial alone in 3.1%, axial and peripheral manifestations in 11.5%, type I arthritis in 7.2% and type II in 1.4%. More patients with Crohn's has axial spondyloarthropathy (19.6%) compared with patients with ulcerative colitis (12.3%).

References:

[1] Atzeni F et al: Rheumatic manifestations in IBD. Autoimmunity reviews: 2014 pp 20–23.
[2] Al-Jarallah K, et al. Rheumatic complications of IBD among Arabs. Int J of rheum Dis 2013:16:134–138.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1495

AB0729 BENEFITS OF ADDITIONAL SPINAL MAGNETIC RESONANCE IMAGING COMPARED TO SACROILIAC JOINTS IMAGING ALONE IN THE DIAGNOSIS OF SPONDYLOARTHROPATHY

N. Ahmad[1], A. Khan[1], P. Yoong[2], J. Kitchen[1]. *[1]Department of Rheumatology; [2]Department of Radiology, Royal Berkshire NHS Foundation Trust, Reading, United Kingdom*

Background: Axial spondyloarthritis (AxSpA) is a chronic inflammatory condition predominantly involving the axial skeleton including the spine and sacroiliac joints. Magnetic resonance imaging (MRI) demonstrates inflammatory and structural changes in patients with both ankylosing spondylitis and non-radiographic (nrAxSpA) forms of SpA and has become widely used in diagnosing SpA.

Sacroiliitis is a prominent feature of SpA but up to 24% of patients with clinically active SpA can have normal MRI of their sacroiliac joints (SIJ).[1] Spinal inflammation is well recognized in SpA and studies have shown that 49% of clinically active nr-AxSpA patients have spinal lesions alone but no lesions in SIJ.[2] Thoracic spinal lesions are as common as SIJ lesions.[3] Therefore using spinal in addition to SIJ MRI should improve the overall sensitivity and specificity for the detection of the disease.

Prior to publication of the 2015 EULAR recommendations,[4] an evidence-based MRI protocol had been adopted in our hospital, using STIR and T1-weighted sequences of the whole spine and SIJs in patients with suspected SpA.

Objectives: To determine the additional diagnostic benefit of including limited sequence whole spine imaging with SIJ MRI to SIJ MRI alone in patients with suspected SpA.

Methods: MRI scans performed for suspected SpA over twelve months from November 2015 to November 2016 were reviewed retrospectively (n=203). Reports were analysed for presence and location of lesions suggestive of SpA. HLA-B27 status of the patients and the presence of SpA associated clinical features as defined by ASAS criteria were recorded.

Results: MRI scans from 203 patients with suspected SpA were reviewed. 81 (40%) were male and 122 (60%) were female. The age range was 13 to 78 years (mean =41). 130 (64%) were less than 45 years of age. 157/203 (77%) patients had been tested for HLA B-27 alleles of whom 46 (29%) were HLA-B27 positive. All patients had inflammatory back pain and 76 (37%) had one or more additional SpA features as per ASAS criteria.

Overall 43 (21%) patients had a positive MRI spine and/or SIJs for inflammatory or structural changes. 21/43 (49%) patients had inflammatory lesions in their sacroiliac joints only. 18/43 (42%) patients had inflammatory changes involving both SIJ and Spine and 4/43 (9%) had spinal inflammatory changes only with normal SIJs (Table 1). In these four patients the thoraco-lumbar spine was involved. In HLA-B27 positive patients (n=46), 25 (54%) had a positive MRI.

Positive Imaging Findings	Number of patients	Percentage of patients
SIJ & Spine	18	42
SIJ lesions alone	21	49
Spinal lesions alone	4	9
Total	43	–

Conclusions: The majority of patients with SpA can have their diagnosis confirmed on SIJ MRI. However a proportion of patients (9%) had spinal changes only. Additional spinal MRI has been shown to increase the diagnostic yield for axial spondyloarthropathy in our cohort.

References:

[1] Bennett AN, et al Arthritis&Rheumatism 2009;60(5):1331–41.
[2] Rudwaleit M, et al.Ann Rhem Dis 2008;67:1276–81.
[3] Van der Heijde D et al. Arthritis Rheumatol 2014;66(3):667–73.
[4] Mandl P, et al. Ann Rheum Dis 2015;0:1–13. doi:10.1136/annrheumdis-2014–206971.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4851

AB0730 CELL CHOLESTEROL TRANSPORT IN SPONDYLOARTHRITIDES AND ITS RESPONSE TO ANTI-RHEUMATIC DRUGS

N. Ronda[1], I. Hokstad[2], G. Deyab[3], D. Greco[1], S. Agewall[4,5], G. Hjeltnes[6], J.E. Whist[3], F. Bernini[1], I. Hollan[2,7,8,9]. *[1]Department of Food and Drug, University of Parma, Parma, Italy; [2]Lillehammer Hospital for Rheumatic Diseases; [3]Department of Medical Biochemistry, Innlandet Hospital Trust, Lillehammer; [4]Oslo University Hospital, Ullevål; [5]Institute of Clinical Sciences, University of Oslo, Olso; [6]Department of Medicine; [7]Innlandet Hospital Trust, Lillehammer, Norway; [8]Department of Medicine, Brigham and Women's Hospital; [9]Harvard Medical School, Boston, United States*

Background: Spondyloarthritis is associated to accelerated atherosclerosis, possibly due to chronic inflammation and lipid metabolism disturbances. Circulating lipoprotein function may be more important than concentration. In particular, cholesterol efflux capacity (CEC) of high density lipoproteins (HDL) opposes to foam cell formation and correlates inversely with cardiovascular risk[1]. Instead, the capacity of low density lipoproteins (LDL) to load cells with cholesterol (CLC) favors atherosclerosis. CEC and CLC may be altered independently from lipoprotein serum levels, *e.g.* due to chronic autoimmune inflammation or to medical therapies[2].

Objectives: Our aim was to compare CEC and CLC in patients with ankylosing spondylitis (AS) and psoriatic arthritis (PsA). We also aimed to evaluate CEC and CLC modification upon anti-rheumatic therapy and their relationship to lipoprotein levels.

Methods: Patients with AS (n=24) and PsA (n=36) were from the observational PSARA study. Treatment was: anti-TNF agents for AS; MTX alone or in combination with an anti-TNF agent for PsA.

Serum was drawn before, after 6 weeks and after 6 months of anti-rheumatic therapy to measure CEC with a validated cell model (radioisotopic technique to measure % cholesterol efflux on total cell cholesterol[3]) and CLC (with a macrophage model and fluorimetric measurement of cell cholesterol[2]).

Results: At baseline serum LDL and total cholesterol were higher in PsA than in AS patients. LDL, total cholesterol and HDL increased after treatment in AS, but not in PsA.

In AS, CEC increased after 6 weeks of treatment (4.9±0.3 vs. 5.5±0.3, 95% CI: -1.09 to -0.03, $p<0.05$), in parallel with HDL serum levels. In PsA, CEC did not differ between any of the time points.

CLC did not change with treatment in AS nor in PsA, but was overall higher in PsA than in AS patients. Despite the LDL serum level increase in AS, after 6 months of treatment the difference between CLC in PsA and AS was the most significant (34.0±1.8 in PsA vs 27.8±1.5 in AS, CI 95%: 3.28 to 6.67, $p<0.05$). In addition, after 6 months of therapy the correlation of CLC with LDL levels, present before treatment, was lost in the AS group. In the PSA group CLC did not correlate with LDL serum levels at any time point.

Conclusions: Our novel data indicate that pro-atherogenic lipoprotein dysfunction is more marked, and less responsive to anti-rheumatic treatment, in PsA than AS patients.

In AS, CEC improved significantly during anti-TNF therapy, probably due to increase in anti-atherogenic HDL. Despite the LDL increase associated with the anti-TNF therapy in AS patients, CLC stayed constant, standing against a hypothetical pro-atherogenic effect of such LDL increase.
These data may be useful for atherosclerosis prevention and treatment with tailored strategies for AS and PsA patients.
References:
[1] Khera AV, et al. N Engl J Med 364(2):127–35, 2011.
[2] Ronda N et al. Arthritis Rheumatol 67(5):1155–64, 2015.
[3] Zanotti I et al. Curr Pharm Biotechnol 13(2):292–302, 2012.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5776

AB0731 OVERCOMING THE PROBLEMS OF UNTRANSLATABILITY: A MOBILE PHONE APPLICATION IN THE EXAMPLE OF TURKISH VERSION OF BASDAI

Y. Özmen[1], E. Mammadov[1], Y. Yalçınkaya[1], A.U. Ünal[1], Z. Ertürk[1], Ü.G. Gazel[1], S. Kaymaz[1], A. Aksoy[1], F. Alibaz-Öner[1], N. İnanç[1], H. Direskeneli[1], A. Gökduman[2], P. Atagündüz[1]. *[1]Rheumatology, Marmara University Faculty of Medicine, Istanbil; [2]Pleksus Information Technologies Inc., Ankara, Turkey*

Background: Patient-reported outcomes (PROs) are important in monitoring and making treatment decisions.Recently,we reported that the translation of"tender points" in the fourth question of the Turkish version of BASDAI was not correctly understood,and replacing this question with an entheses examination (BASDAI-Q4) decreased the score (∆BASDAI:0.99,p<0.0001,95% CI0.54–1.44).[1]
Objectives: We report here the results of an investigator initiated clinical trial using a self-developed mobile phone application (MPA)[2] to overcome the problem of untranslability.
Methods: Out of 135 invited 95 axSpA patients participated.Initially,BASDAI self-report forms (BSRF) were administered.Thereafter,patients were randomized into two groups (2:1).GroupA completed a second set of BSRF after using the MPA with embedded videos defining terms and grading for each domain.GroupB completed a second set of BSRF under guidance of an inexperienced family physician (FP).A third set of BSRFs were completed by GroupB with the same FP after he went through the MPA.Afterwards,an entheses examination (EE) was performed by a blinded rheumatolgist and patients graded enthesis pain between 0–10.StandartQ4 was replaced with the EE scoring (BASDAI-Q4).Patients older than 45 years of age were excluded.
Results: Fifththree male (%55.7) and 42 female (%44.3)patients,with a mean disease duration of 13 years (SD=8.7)were studied.Sixtyfour and 31 patients were randomized to Groups A and B, respectively.Nine patients reported the Q4 as"not understood".32 patients had no enthesitis on EE,but of those only 21 scored"0" for Q4 during the unassisted-PRO.Eleven reporting no enthesitis had so on EE.In GroupA,out of six"not understood" responders forQ4,five reported enthesitis after MPA assistance and four had enthesitis at the final EE.Nineteen patients had no enthesitis on physical examination,but of those only 12 scored"0" for Q4 during the unassisted PRO,and an additional nine scored"0" forQ4 after MPA assistance.Six out of seven patients reporting no enthesitis,but with enthesitis on EE reported,enthesitis after MPA assistance.In GroupB,scoring forQ4 was similar after both the unassisted- and FP's first assistance PRO.Out of four "not understood" responders for Q4,two reported enthesitis after the second assistance of FP and both had enthesitis at the final EE.Six patients had no enthesitis on EE,but of those only4 scored"0" for Q4 during the unassisted-PRO,and an additional two scored"0" for Q4 after second FP-assistance.Two out of four patients reporting no enthesitis,but with enthesitis on EE,reported enthesitis after second FP-assistance.Mean BASDAI was significantly higher in both groups then BASDAI-Q4 (Group A=3.97±1.95 vs. 2.84±1.98, p<0.0001,95% CI0.58–1.52, Group B=3.81±2.05 vs. 2.98±2.25, p<0.0001,95% CI0.48–1.31). In both groups, MPA for both, patients and FPs resulted in more reliable overall BASDAI scores with BASDAI-Q4 as the gold standard (Group A=3.05±2.25 vs. 2.84±1.98, p=0.081, 95% CI0.71–1.45, Group B=3.21±1.87 vs 2.98±2.25, p=0.075,95% CI0.71–1.63).
Conclusions: Mobile applications may improve the quality of collected data in cases of untranslability even in previously validated PROs.
References:
[1] AtagunduzP,et-al.Arthritis Rheumatol.2015;67(suppl10).
[2] https://secure.yonetimislemleri.com/asasistan/.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4231

AB0732 SPONDYLOARTHRITIS IN THE DEMOCRATIC REPUBLIC OF CONGO

P. Lebughe[1], K. de Vlam[2], R. Westhovens[3], J.-M. Mbuyi-Muamba[1], J.-J. Malemba[1]. *[1]Rheumatology, University Hospital of Kinshasa, Kinshasa, Congo, The Democratic Republic of the; [2]Rheumatology; [3]Department of Development and Regeneration, Skeletal Biology and Engineering Research Center, Division of Rheumatology, University Hospitals Leuven, Leuven, Belgium*

Background: While spondyloarthritis (SpA) is intensively studied in the Western world, data are scarce in sub-Saharan Africa.
Objectives: To determine the spectrum of SpA in outpatients with rheumatological complaints attending two rheumatology practices in Kinshasa, Democratic Republic of Congo.
Methods: A descriptive cross-sectional study over six months (December 1st, 2012 till May 31th, 2013) in consecutive patients attending the two rheumatology practices of Kinshasa; diagnosis was based on Amor or the ESSG criteria, and a clinical evaluation by a rheumatologist. Sacroiliac joint radiographic lesions were scored with the modified New York criteria. BASDAI and BASFI were evaluated in axial SpA.
Results: One hundred five patients (10.7%) were diagnosed among 984 rheumatologic outpatients with a sex ratio (male to female) of 1.4. The average age at the onset of the disease was 41.3±12.4 years. Non-radiographical axial spondyloarthritis was the most frequent subtype (4.98%) followed by reactive arthritis (4.27%). Other subtypes were: ankylosing spondylitis (1.02%), psoriatic arthritis (0.1%), SAPHO syndrome (0.1%) and IBD associated arthritis (0.1%). Mean BASDAI and BASFI in axial SpA were 42.7/100 and 46.4/100 respectively. Peripheral enthesitis was found in 43% of SpA patients and uveitis (10.4%) was the most frequent extra-articular manifestation. We did not detect any family history. Median erythrocyte sedimentation rate and C reactive protein were 37 (range: 7–110) mm/h and 22 (range: 4–48) mg/l respectively.

Subtypes of SpA	*N* (Rf)	Sex distribution			P	Mean age (years) ±SD
		M	F	Ratio		
Nr-axSpA	49 (46.7)	27	22	1:0.8	0.23	40.5±7.5
ReA	42 (40.0)	20	22	1:1.1	0.47	40.2±13.1
AS	10 (9.5)	6	4	1:0.7	0.45	46.2±4.7
PsA	1 (0.95)	0	1			32
SAPHO Syndrome	1 (0.95)	1	0			35
Enteropathic arthritis	1 (0.95)	0	1			25
Juvenile SpA	1 (0.95)	1	0			13

Conclusions: This hospital-based study suggests a substantial occurrence of some subtypes of SpA in central Africa. A population-based study is needed.
References:
[1] Malemba JJ, Mbuyi-Muamba JM. Clinical and epidemiological features of rheumatic diseases in patients attending the university hospital in Kinshasa. Clin Rheumatol. 2008;27:47–54.
[2] Stolwijk C, van Onna M, Boonen A, van Tubergen A. Global Prevalence of Spondyloarthritis: A Systematic Review and Meta-Regression Analysis. Arthritis Care Res (Hoboken). 2015 Dec 29.
Acknowledgements: The authors would like to thank Dr Thierry Lusiense for helping with acquisition of data from the Rheumatology unit at Provincial General Hospital Kinshasa.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4642

AB0733 ASSOCIATIONS OF SERUM OSTEOPROTEGERIN AND IL-18 CONCENTRATIONS WITH CARDIOVASCULAR RISK IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS PATIENTS

E. Kontny[1], K. Bonek[2], P. Gluszko[2]. *[1]Department of Pathophysiology and Immunology; [2]Department of Rheumatology, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warszawa, Poland*

Background: Inflammatory spondyloarthropathies (SpAs), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are associated with cardiovascular (CV) disorders. In both diseases cytokines of IL-17/IL-23 axis are thought to play a pathogenic role. PsA, but not AS, is usually preceded by psoriasis, suggesting contribution of skin inflammation-related cytokines to disease manifestation and CV risk.
Objectives: To search in AS and PsA patients for the association between CV risk and serum concentrations of select cytokines, i.e. of IL-17/IL-23 axis, IL-18 and osteoprotegerin (OPG) related to skin inflammation and/or cardiovascular disease (CVD) pathogenesis, respectively.
Methods: Twenty patients with AS (15M/5F) and 18 patients with PsA (10M/8F) of similar age (mean±SD, 42±7 vs 46±10 years) and disease duration (6.5±10 vs 6.1±7 years) were evaluated. A group of 38 sex and age-matched healthy volunteers was used as a control. Routine laboratory tests, i.a. measurement of serum C-reactive protein (CRP) concentrations were performed. Clinical data, including evaluation of disease activity by $ASDAS_{CRP}$ and BASDAI indices, calculation of SCORE (Systemic Coronary Risk Evaluation) index and atherogenic index (AI=total cholesterol/HDL) were collected. Serum concentrations of IL-17AF, IL-21, IL-23, IL-27, IL-18 and OPG were measured by specific commercially available enzyme-linked immunosorbent assays (ELISA) and were expressed in pg/ml. The Mann-Whitney U-test was applied for intergroup comparison, and correlation was assessed using a Spearman's Rank two-tailed test (*R* value is shown).
Results: Compared with control, total group of SpAs patients was characterized by significantly elevated serum concentrations of OPG (1757±852 vs 1062±406 pg/ml), IL-18 (273±235 vs 164±195 pg/ml) and IL-21 (68±127 vs 20±49 pg/ml). Interestingly, while up-regulation of OPG (1517±387) and IL-18 (324±291)

was attributed to PsA, IL-21 increase (90.6±158) was found in AS group. Nevertheless, there was no significant difference between patients' groups in the tested cytokines concentrations. Despite of less active disease in PsA than in AS patients ($ASDAS_{CRP}$ 2.76±1 vs 3.44±0.89), PsA patients had higher AI (4.44±1.3 vs 3.37±1). Importantly, in both AS and PsA groups, OPG concentration positively correlated with SCORE values (*R*=0.613 and 0.792, respectively). However, in PsA patients also IL-18 concentration showed similar noxious associations, correlating positively with AI (*R*=0.705), and triglycerides level (*R*=0.679) but inversely with HDL level (*R*= - 0.525) and HDL/LDL ratio (*R*= -0.623). On the other hand, neither in AS nor in PsA patients the cytokines of IL-17/IL-23 axis were significantly related to CV risk.

Conclusions: By showing positive correlation of serum OPG with CV risk expressed by SCORE in AS and PsA patients we support opinion of an important role of OPG in CVD pathogenesis. Our results may also suggest that in PsA patients IL-18, up-regulated owing to skin inflammation, contributes to dyslipidemia and thus further increases CV risk.

Acknowledgements: Supported by the NIGRiR, Warsaw, Poland (grants No S/16 and S/2).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3475

AB0734 EVALUATION OF CARDIOVASCULAR RISK PROFILES IN A POPULATION OF PATIENTS WITH ANKYLOSING SPONDYLITIS: A CROSS-SECTIONAL STUDY

A. Ghrbel[1], M. Turki[1], A. Feki[2], B. Belhasan[3], R. Akrout[2], M. Chtourou[1], M. Neifar[1], H. Fourati[2], S. Baklouti[2], F. Ayedi[1]. *[1]Unit of Research "Molecular Bases of Human Diseases", 12ES17, Sfax Medicine University Biochemistry laboratory Habib Bourguiba Hospital; [2]Hedi Chaker Hospital; [3]Unit of Research "Molecular Bases of Human Diseases", 12ES17, Sfax Medicine University, Sfax, Tunisia*

Background: ankylosing spondylitis (AS), like the other chronic inflammatory rheumatic diseases, is considered to have higher cardiovascular (CV) risk (1). The Etiopathogenesis is not clearly defined.

Objectives: assess the early biological markers of atherosclerosis in Tunisian patients with AS compared with healthy controls and evaluate the relationship between Systematic Coronary Risk Evaluation (SCORE) for CV-related mortality and biological markers (2).

Methods: This was a cross-sectional study conducted since June 2015 until October 2016 including patients with AS in the South of Tunisia and matched controls with sex, age, body mass index (BMI) and smoking. Patients diagnosed with AS should fulfill the modified New York criteria. For patients and controls, we measured total cholesterol (TC), high density lipoprotein (HDL) cholesterol, triglycerides, apolipoprotein (Apo) AI, ApoB, lipoprotein (a) [Lp(a)] and C-Reactive Protein (CRP). Low-density lipoprotein (LDL) cholesterol was calculated with the Friedewald formula. SCORE was calculated through the use of sex, age, systolic pressure, smoking and TC. Comparisons were performed using two sample t-tests for parametric values and Wilcoxon Mann-Whitney Test for non-parametric values. Correlation analyses were performed with Spearman rank.

Results: Overall 79 patients with AS and 79 controls were included. The mean age was (43.81±14.29 vs 44,27±14 years). The sex ratio (M/F) was 2/1 and the mean BMI was (25.9±5.3 vs 25.76±3.5 kg/m^2). AS patients had significantly lower levels of HDL and TC and a higher level of CRP and atherogenic index (TC/HDL, ApoB/ApoA). AS patients had higher CV mortality than controls (1.1±1.8 vs 0,51±1.13%, p=0.01). The frequency of high cardiovascular risk was higher in AS patients (5 vs 2, p=0.4). The correlation between SCORE's risk and biological markers were positive with TC, LDL, Lp (a), TC/HDL ratio and LDL/HDL ratio.

Conclusions: AS patients are at a greater cardiovascular risk due to a higher CRP rate, atherogenic index and 10-year risk SCOREs of CV mortality. So, the dyslipidaemia and inflammation could be the aetiology of cardiovascular risk.

References:

[1] Mathieu S, Soubrier M. Le risque cardiovasculaire dans la spondyloarthrite axiale. Presse Med. 2015;44(9):907–11.

[2] Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J. 2003 Jun;24(11):987–1003.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6936

AB0735 EVALUATION OF PSYCHOLOGICAL STATE OF PATIENTS WITH ANKYLOSING SPONDYLITIS: REGIONAL REGISTRY AS A TOOL FOR IMPROVEMENT OF MANAGEMENT

S. Lapshina, D. Abdulganieva, L. Myasoutova. *Kazan State Medical University, Kazan, Russian Federation*

Background:
According to modern conception "T2T" a patient with ankylosing spondylitis (AS) takes an active part in the disease treatment that determines the importance of his psychological state.

Objectives: To evaluate interconnection between the psychological state of the patient with AS and the disease course.

Methods: Within the regional registry which is a part of epidemiological study of clinical diversity of AS in Russian population, 40 patients (32 males and 8 females) at the age of 21 to 56 years (average age 40,3±10,0) were examined. The average disease duration on the day of examination was 12,7±9,9 years, BASDAI - 5,54±1,8, BASFI – 5,34±2,48. Functional status (range of motion) was evaluated by means of BASMI. EQ-5D questionnaire was used for psychological state evaluation.

Results: A total of 17 (42,5%) patients had anxiety and depression: moderate – 15 (88,2%), severe – 2 (11,8%) responders. With the disease duration of less than 5 years propensity for depression and anxiety was noted by 6 out of 11 (54,5%) patients, 5 to 10 years – 2 out of 12 (16,7%), more than 10 years – 9 out of 17 (52,9%).

In patients with mild disease activity anxious and depressive states were not observed, with moderate disease activity they were revealed in 3 out of 7 patients (42,8%), with severe activity – in 9 out of 21 (42,8%), with very severe activity – in 5 out of 10 (50%) responders.

Among the patients without limitation of motion (BASFI) anxiety and depression was revealed in 2 out of 11 (18,2%), with moderate limitation –6 out of 18 (33,3%), with severe limitation –9 out of 11 (81,8%) patients. According to BASMI 1 out of 2 patients without limitation of motion had anxiety and depression, 6 out of 19 (31,5%) – with moderate limitation and 10 out of 19 (52,6%) with severe limitation.

The direct correlation was revealed between EQ-5D score and BASFI (r=0,996) and between EQ-5D and BASDAI (r=0,855), concurrently such correlation was absent between BASMI and EQ-5D.

Among the patients without anxious and depressive states 14 out of 23 (60,8%) patients take NSAIDs regularly while among the patients who noted propensity for anxiety and depression only 7 out of 17 (41,17%) take NSAIDs regularly.

Conclusions: Patients with short (less than 5 years) and long (more than 10 years) AS duration, severe disease activity and functional limitation are more prone to anxiety and depression. Patients with anxious and depressive states are less compliant with therapy which influences its efficacy. These data should be considered when the programs of AS patients' management are developed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3959

AB0736 THE DATA OF CENTRAL AORTIC PRESSURE AND PULSE WAVE VELOCITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

T. Aksenova[1,2], N. Ivashhenko[1,2], S. Tsarenok[1], V. Gorbunov[1], P. Gromov[2]. *[1]therapy, Chita State Medical Academy; [2]The hospital within the Russian Railroad Network, Chita, Russian Federation*

Background: Pulse Wave Velocity (PWV) is the main determinant of arterial stiffness. In recent years the increased arterial stiffness in Ankylosing Spondylitis was shown [1]. The most of investigations of arterial stiffness in ankylosing spondylitis were performed on the treatment by anti TNF-therapy [2]. However, today this issue has not been adequately studied.

Objectives: To evaluate the data of central aortic pressure and PWV and their relationship with Ankylosing Spondylitis.

Methods: 49 patients with Ankylosing Spondylitis aged between 19 and 60 (mean age 39.6±10.6) were examined. This group (group 1) included 38 men, 11 woman. Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) was 3.11±0.55. Duration of Ankylosing Spondylitis was from 0.5 to 20 years (mean 5.87±4.76 years). X-ray stage sacroiliac joints (according Modified New York Criteria) was 2.59±1.42. The control group included 33 healthy individuals. The groups were similar in age and sex. 10 patients with ankylosing spondylitis have history of arterial hypotension, however, at the time of inclusion in this study their blood pressure was stabilized. The groups did not differ by office blood pressure parameters and heart rate. Indicators of central aortic pressure and PWV were determined by applanation tonometry by SphygmoCor, Australia. For statistical analysis we used Mann-Whitney criteria and Spirmen correlation method. The study was based on GCP principles.

Results: Increased levels of central systolic blood pressure (118.02±14.02 vs 101.1±10.2, p=0.00001), central diastolic blood pressure (80.23±11.86 vs 71.8±7.3, p=0,001) were determined in patients with Ankylosing Spondylitis.

Patients with Ankylosing Spondylitis demonstrated the increase in central mean pressure compared to control groop on 17.2% (108.5±13.6 vs 92.6±9.4 p=0.0001). Pulse Wave Velocity (PWV) in the carotid-femoral segment in patients with ankylosing spondylitis was 6.5±1.3 m/sec vs 5.2±0.96 m/sec (p=0.0001) in the control group. The levels of augmentation pressure and Subendocardial viability ratio (SERV) were similar in the examined groups.

PWV was directly correlated with trangulus-to-wall (r=0,41; p=0,005) and with X-ray stage of sacroiliitis (r=0,31; p=0,043) and negative correlated with Lumbar flexion (Shober test) (r= - 0,38; p=0,009).

Conclusions: Increasing indicators of arterial stiffness, such as, PWV, central systolic blood pressure, central diastolic blood pressure, central mean pressure were determined in patients with Ankylosing Spondylitis. The relationship between clinical data, X-ray stage and PWV was demonstrated.

References:

[1] Berg I., Van der Heijde D., Dagfinrud H., Seljeflot I., Olsen I. C., Kvien T., Semb A., Provan S. Disease activity in ankylosing spondylitis and associations to markers of vascular pathology and traditional cardiovascular disease risk

factors: a cross-sectional study. The Journal of Rheumatology. 2015; 42 (4) 645–653. doi: 10.3899/jrheum.141018.
[2] Tam L.-S., Shang Q., Kun E. W., Lee K.-L., Yip M.-L., Li M., Li T.K., Zhu T.Y., Pui M.O., Li E.K., Yu C.-M. The effects of golimumab on subclinical atherosclerosis and arterial stiffness in ankylosing spondylitis – a randomized, placebo-controlled pilot trial. Rheumatology. 2014;53(6):1065–1074. doi:10.1093/rheumatology/ket469.
Disclosure of Interest: T. Aksenova Shareholder of: nothing to declare, Grant/research support from: nothing to declare, Consultant for: nothing to declare, Employee of: nothing to declare, Paid instructor for: nothing to declare, Speakers bureau: nothing to declare, N. Ivashhenko Shareholder of: nothing to declare, Grant/research support from: nothing to declare, Consultant for: nothing to declare, Employee of: nothing to declare, Paid instructor for: nothing to declare, Speakers bureau: nothing to declare, S. Tsarenok Shareholder of: nothing to declare, Grant/research support from: nothing to declare, Consultant for: nothing to declare, Employee of: nothing to declare, Paid instructor for: nothing to declare, Speakers bureau: nothing to declare, V. Gorbunov Shareholder of: nothing to declare, Grant/research support from: nothing to declare, Consultant for: nothing to declare, Employee of: nothing to declare, Paid instructor for: nothing to declare, Speakers bureau: nothing to declare, P. Gromov Shareholder of: nothing to declare, Grant/research support from: nothing to declare, Consultant for: nothing to declare, Employee of: nothing to declare, Paid instructor for: nothing to declare, Speakers bureau: nothing to declare
DOI: 10.1136/annrheumdis-2017-eular.2914

Psoriatic arthritis

AB0737 AA AMYLOIDOSIS IN RHEUMATOID ARTHRITIS AND IN PSORIATIC ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 173 PATIENTS

Á. Apáthy[1], M. Bély[2]. [1]*Department of Rheumatology, St. Margaret Clinic Budapest;* [2]*Department of Pathology, Hospital of the Order of the Brothers of Saint John of God, Budapest, Hungary*

Background: Rheumatoid arthritis (RA) and psoriatic arthritis (PsA), like all chronic autoimmune arthritides, may be complicated by AA amyloidosis (AAa).
Objectives: The aim of this study was to determine the prevalence and extent of AAa in RA and PsA patients, furthermore appraise the extent of amyloid A deposits in various organs.
Methods: At the National Institute of Rheumatology 11860 patients died between 1968 and 1998; among them 161 patients with RA and 12 with PsA. All of them were autopsied. RA and PsA were diagnosed clinically according to the criteria of the ACR [1,2].
Amyloid deposits on different tissue structures [arteriole, small artery, medium size artery, venule, small vein, medium size vein, interstitial collagen fiber, reticulin fiber (collagen IV), basal laminas, nerve, renal glomerulus] of 6 organs [heart, lungs, liver, kidney, skin and brain] were determined histologically.
The extent of amyloid A deposition was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale, based on the number of involved tissue structures per light microscopic field [3]. ("0": no amyloid deposits, "1": Sporadic, minimal amyloid deposits on different tissue structures, "2": less than five, "3": five or more involved tissue structures per microscopic field at objective magnification of x20)
The average prevalence and extent of amyloid A deposits of RA and PsA patients and the average prevalence and extent of amyloid A deposits in various organs were compared by Student (Welch) t-probe.
Results: The prevalence (in %) and the average extent of amyloid A deposits (absolute value) in various organs of RA and PsA patients are summarized in Table 1.

Table 1

Organs	RA-AAa Prevalence in %	PsA-AAa Prevalence in %	p<	RA-AAa Average extent	PsA-AAa Average extent	p<
Kidney	48,49	68,18	0,0611	0,99	1,41	0,0706
Heart	56,97	38,89	0,0651	0,97	0,67	0,1065
Liver	29,17	38,89	0,3014	0,60	0,67	0,3945
Lung	29,80	15,00	0,0852	0,44	0,13	**0,0002**
Skin	10,83	50,00	**0,0000**	0,18	1,00	**0,0027**
Brain	0,00	0,00	–	0,00	0,00	–
Average/Organ	29,21	35,16	0,332	0,529	0,645	0,341
Average/Patient	32,27	36,21	0,244	0,585	0,668	0,198

Conclusions: Based on the nearly same 0,585 versus 0.668, significantly not different: $p<0.198$) average amount of amyloid A deposits/patient, the immune processes (producing amyloid A deposition) of our RA and PsA patients may be similar.
The more prominent amyloid deposition in the lungs of RA patients (in contrast with PsA patients) may be associated with more frequent and pronounced pulmonary complications of RA (vasculitis, interstitial pneumonitis and fibrosis, etc.), than by PsA.
Extreme severe amyloid deposition in the skin of PsA patients may be due to local factors, namely severe systemic dystrophic changes of the skin in psoriasis. A diverse affinity of amyloid A to qualitative changed collagens cannot be ruled out in PsA in comparison with RA. In systemic sclerosis patients such change of collagens has been demonstrated [4].
References:
[1] Arnett FC et al: Arthritis Rheum. 1988; 31(3):315–24. PMID: 3358796.
[2] Helliwell PS, Taylor WJ: Classification and diagnostic criteria for psoriatic arthritis. Ann Rheum Dis 2005;64:ii3-ii8 doi:10.1136/ard.2004.032318.
[3] Bély M, Apáthy Á: Clinical pathology of rheumatoid arthritis: Cause of death, lethal complications and associated diseases in rheumatoid arthritis. 1–440 pp. Akadémiai Kiadó, Budapest 2012.
[4] Istok R, Bély M, Stancikova M, Svik K, Rovensky J: Annals Rheum Dis 1999; 58(Suppl. 1):192.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1224

AB0738 PRECLINICAL IMPAIRMENT OF MYOCARDIAL FUNCTION AND ENDOTHELIAL VASCULAR MARKERS IN EARLY PSORIATIC ARTHRITIS: ASSOCIATION WITH VITAMIN D LEVELS AND INFLAMMATION

A. Lo Gullo[1], G. Mandraffino[2], C.O. Aragona[2], V. Cairo[2], A. Saitta[1]. [1]*Clinical and Experimental Medicine;* [2]*Policlinico G Martino, Messina, Italy*

Background: Patients with psoriatic arthritis (PsA) have an increased prevalence of cardiovascular risk factors such as hypertension, myocardial dysfunction, and type 2 diabetes mellitus, and cardiovascular diseases (CVD) are the leading cause of death in these patients.
Furthermore, PsA patients have a high prevalence of vitamin D (vit-D) deficiency, considered an independent predictor of cardiovascular diseases and all-cause mortality in several clinical settings.
Objectives: We aimed to evaluate left ventricular (LV) mechanics in patients diagnosed with PsA and no clinical evidence for cardiovascular disease (CVD) using a more sensitive technique, which evaluates myocardial deformation in multidimensional planes for the detection of impaired LV function. Furthermore we evaluated carotid intima media thickness (cIMT) and pulse wave velocity (PWV), circulating proangiogenic haematopoietic cells (PHCs),as markers of endothelial dysfunction. We investigated the association between vitamin D levels, inflammatory mediators, markers of endothelial and myocardial dysfunction in patients with PsA.
Methods: The study enrolled 19 PsA patients and 16 sex- -age matched healthy controls. All participants underwent conventional echocardiography and 2-dimensional speckle tracking echocardiography (STE). Global longitudinal, circumferential, and radial strain were measured. PHCs,Vitamin D levels, C-reactive protein (CRP), fibrinogen, (PWV), (cIMT) were also evaluated.
Results: PHCs count and vitamin D levels were lower in PsA patients as compared to controls, while fibrinogen, CRP, PWV and cIMT were higher in PsA patients. STE analysis showed that PsA patients had significantly lower global longitudinal strain (-16.11±2.89% and -19.15±1.9%, respectively, p=0.05) and global circumferential strain (-14.21±2.7% and -20.22±4.13%, respectively, $p<0.01$) versus control group.
No correlation was found between longitudinal and circumferential strains and disease-related risk factors.
Vitamin D levels was found to correlate with longitudinal strain, ejection fraction, PHCs, diseases activity markers, and fibrinogen levels.
Conclusions: Subclinical impaired myocardial deformation and endothelial dysfunction were common in patients with PsA even when there is no clinical evidence for CVD. Furthermore, vitamin D seems to may have a role in the endothelial homeostasis and myocardial function.
Further studies on larger sample sizes could clarify whether a supplementation of Vitamin D could modify PHCs levels inflammatory indices, myocardial function and arterial stiffness in patients affected by PsA, therefore contributing to reduce cardiovascular risk in this patients.
References:
[1] Gladman DD, Ang M, Su L, et al. Cardiovascular morbidity in psoriatic arthritis.Ann Rheum Dis 2009;68:1131–5.
[2] Han C et al. Cardiovascular disease and risk factors in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis.J Rheumatol 2006;33:2167–72.
[3] Lo Gullo A al. Vitamin D Status in Rheumatoid Arthritis: Inflammation, Arterial Stiffness and Circulating Progenitor Cell Number. PLoS One. 2015 Aug 4;10(8):e0134602.
[4] Assalin HB, Rafacho BP, dos Santos PP, et al. Impact of the length of vitamin D deficiency on cardiac remodeling. Circ Heart Fail. 2013;6:809–16.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5189

AB0739 MHAQ RESPONSE AMONG PATIENTS WITH PSORIATIC ARTHRITIS INITIATING A TNFI

A. Ogdie[1], L. Palmer[2], D. Solomon[3], A. Kavanaugh[4], J. Greenberg[2,5], J. Curtis[6], L. Harrold[2,7], J. Kremer[2,8], P. Mease[9]. *[1]University of Pennsylvania, Philadelphia, Pa; [2]Corrona Research Foundation, Albany, NY; [3]Brigham and Women's Hospital, Boston, MA; [4]University of California San Diego, San Diego, CA; [5]New York University, New York, NY; [6]University of Alabama, Birmingham, AL; [7]University of Massachusetts, Worcester, MA; [8]Albany Medical College, Albany, NY; [9]Swedish Medical Center, Seattle, WA, United States*

Background: Improved functional ability is among the most relevant outcomes for patients with psoriatic arthritis (PsA).[1] The modified health assessment questionnaire (mHAQ) is one of the most commonly used patient reported outcome measures used in PsA and addresses the domains of disability and physical function.

Objectives: We examined the change in mHAQ over one year among patients with PsA initiating a TNFi and examined predictors of a clinically meaningful improvement in disability and physical function, as measured by the mHAQ.

Methods: Patients with PsA enrolled in the Corrona Registry between 2005–2013 were followed from initiation of a TNFi (etanercept, adalimumab, infliximab, certolizumab, or golimumab) to the visit closest to 12 months. Patients were required to have at least three tender or swollen joints for inclusion for this study (this is not an inclusion criteria for Corrona), mHAQ within six months prior to TNFi initiation date, and at least one follow up visit 5–13 months after TNFi initiation with mHAQ. The primary outcome was the proportion of patients with a decrease of 0.35 or more in the mHAQ score, the minimal clinically important improvement in PsA[2]. Predictors of mHAQ response were measured in the six months before TNFi initiation. Covariates with p-value $\leq$0.10 in univariable logistic regression models and $\leq$5% missing values were included in a multivariable model and removed individually until all remaining variables were significant ($p<0.05$).

Results: Among 1742 TNFi initiations, 721 initiations (623 patients) met inclusion criteria. Mean age at initiation was 51.5 years (SD 12.3), 56% were female, median PsA duration was 5 years (IQR 2–11), and median baseline mHAQ was 0.375 (IQR 0.125–0.875). The mean change in mHAQ was -0.098 (SD 0.38) and median change in mHAQ was 0 (IQR: -0.25 to 0.125); 23% had a mHAQ decrease of 0.35 of more. In univariable models, college education and being married or partnered were inversely associated with mHAQ response (baseline scores were lower in patients with these characteristics) while patient global, patient pain, baseline clinical disease activity index (CDAI) and swollen joint count were positively associated with the outcome. However, in a multivariable model, only age (0.96 per year, 0.94–0.98) and baseline mHAQ score (17.7 per one point, 10.6–29.4) were associated with a decrease of 0.35 or more in the mHAQ.

Table: Predictors of modified Health Assessment Questionnaire (mHAQ) decrease of 0.35 or greater at follow up visit closest to one year*

	Univariable			Multivariable		
Predictor	OR	95% CI	p	OR	95% CI	p
Female Gender	0.90	0.63-1.28	0.64			
Age at Initiation	0.97	0.96-0.98	<0.0001	0.96	0.94, 0.98	<0.0001
BMI >30 (versus =30)	0.83	0.58-1.17	0.35			
Baseline mHAQ	16.24	9.91-26.61	<0.0001	17.7	10.6, 29.4	<0.0001
Hypertension	0.71	0.48-1.04	0.09			
Cardiovascular disease	0.72	0.34-1.51	0.36			
Work Full Time	0.91	0.64-1.29	0.50			
Smoker (Prev/Current)	1.10	0.77-1.56	0.60			
Alcohol	0.86	0.61-1.23	0.45			
Previous biologic use	1.06	0.75-1.51	0.65			
College Education	0.68	0.47-0.97	0.03			
Married/Partnered	0.58	0.40-0.84	0.005			
Prednisone	1.59	0.998-2.52	0.06			
Patient Global	1.02	1.01-1.03	<0.0001			
Patient Pain	1.02	1.01-1.03	<0.0001			
Baseline CDAI	1.03	1.01-1.05	0.0002			
Tender joint count	1.02	0.995-1.05	0.13			
Swollen joint count	1.04	1.004-1.07	0.03			

Conclusions: A clinically meaningful change in mHAQ occurred in 23% of patients and was strongly associated with age and baseline mHAQ score. In this real world population, there was little change in mHAQ scores over one year, despite treatment. These analyses are limited by the floor effect of the mHAQ among patients with established PsA. Despite having at least 3 tender and 3 swollen joints, many patients in this cohort had a low mHAQ at baseline which did not allow for sufficient change to meet the MCII.

References:
[1] Mease PJ et al. J Rheumatol 2011; 38:2461–5.
[2] Orbai AM et al. Ann Rheum Dis 2016; Epub.

Acknowledgements: This work was funded by the Corrona Research Foundation.

Disclosure of Interest: A. Ogdie Grant/research support from: Pfizer (co-investigator), Consultant for: Pfizer, Novartis, L. Palmer: None declared, D. Solomon Grant/research support from: Grants to BWH from amgen, lilly, bristol myers squibb, and pfizer, Consultant for: Corrona, LLC, A. Kavanaugh: None declared, J. Greenberg Shareholder of: Corrona, LLC, Consultant for: Genentech, Janssen, Novartis and Pfizer, Eli Lilly, Employee of: Corrona, LLC, J. Curtis: None declared, L. Harrold Shareholder of: Corrona LLC, Grant/research support from: Pfizer (to UMass), Consultant for: Roche, Employee of: Corrona LLC, UMass Medical School, J. Kremer Shareholder of: Corrona, LLC, Employee of: Corrona, LLC, P. Mease: None declared

DOI: 10.1136/annrheumdis-2017-eular.3547

AB0740 SECUKINUMAB IN PSORIATIC ARTHRITIS: HIGH DISEASE BURDEN OBSERVED IN THE CORRONA PSORIASIS REGISTRY

A.B. Gottlieb[1], V. Strand[2], C. Karki[3], M. Mason[3], J. Greenberg[3], S. Jugl[4], K.K. Gandhi[5], P.J. Mease[6]. *[1]NY Medical College, New York; [2]Stanford University School of Medicine, Stanford; [3]Corrona LLC, Southborough, United States; [4]Novartis Pharma AG, Basel, Switzerland; [5]Novartis Pharmaceuticals Corp., East Hanover; [6]Swedish Medical Center and University of Washington, Seattle, United States*

Background: Secukinumab (SEC), a fully human anti–IL-17A monoclonal antibody, has significant efficacy in the treatment of moderate-to-severe psoriasis (Ps) and psoriatic arthritis (PsA), with a favourable safety profile. The Corrona Psoriasis Registry is an independent observational registry of Ps patients (pts) receiving FDA-approved systemic treatments (TNFis, anti–IL-17s and IL-12/23 and non-biologics) in the United States.

Objectives: To assess demographics, clinical features and pt reported outcomes (PROs) of Ps pts with concomitant PsA receiving systemic treatments at registry enrolment.

Methods: Adult Ps pts who initiated a systemic therapy at enrolment or in the previous 12 months, and concomitant PsA reported by a dermatologist, were included. Demographics (e.g. age, gender, BMI), disease activity (body surface area, investigator global assessment, psoriasis area severity index) and PROs (pain, fatigue, itch, EQ-VAS 0–100, work productivity and activity impairment and dermatology life quality index) were evaluated at enrolment and stratified by therapy: SEC, etanercept (ETN), adalimumab (ADA), ustekinumab (UST), and non-biologics (Non-B).

Results: As of October-2016, 2073 Ps pts were enrolled in the registry; 823 (39.7%) had a PsA diagnosis (mean disease duration 7.6 years) of which 37% were biologic naïve. Of the 823 pts with PsA, 25.4% received SEC, 6.2% ETN, 21.5% ADA, 17.6% UST, and 24.8% Non-B. Pts on SEC had a mean age 53.2 years, mean BMI 32.4; 45% were female; all comparable across the treatment groups. PsA pts treated with SEC had higher Ps disease activity than other treated groups (Table). A higher proportion of SEC treated PsA pts had diabetes and cardiovascular disease (25% and 19% respectively). Mean pain scores were higher in the SEC group; however other PROs assessed at enrolment were similar across treatment groups (Table).

Table 1. Pt characteristics at enrolment[1]

Mean ± SD	SEC N=209	ETN N=51	ADA N=177	UST N=145	Non-B* N=204	Overall N=823
PASI,(0–72)#	7.7±9.4	4.0±4.0	4.6±6.6	5.0±5.9	4.6±6.6	5.5±7.4
IGA, (0–4)#	2.5±1.2	2.4±0.9	2.0±1.2	2.1±1.2	2.3±1.1	2.2±1.2
BSA, (0–100%)#	14.4±20.9	6.8±9.9	8.0±13.3	8.8±15.0	7.8±12.0	9.9±15.8
Pain, (VAS 0–100)	33.2±33.2	20.3±24.8	22.9±30.6	21.9±28.0	23.7±30.4	25.6±30.8
Fatigue, (VAS 0–100)	39.4±29.7	36.3±33.1	34.6±29.9	33.4±27.5	39.1±30.6	37.0±29.9
Itch, (VAS 0–100)	41.6±34.7	34.6±31.4	32.9±34.5	33.5±32.8	37.7±33.7	36.7±33.9
EQ-VAS, (VAS 0–100)	69.0±22.8	68.5±23.4	71.1±22.2	71.0±20.3	66.3±24.1	69.0±22.7
DLQI (0–30)	7.6±6.2	5.6±5.5	6.6±6.1	7.4±7.1	6.2±5.4	6.8±6.1
WPAI - % overall work affected by Ps^	16.8±22.8	19.8±23.8	15.3±25.9	12.8±21.5	14.8±23.5	15.5±23.8

[1]Data on infliximab and ixekizumab not presented due to small sample sizes; #Mean scores were higher in incident users compared to prevalent users; *Non-biologics include: apremilast, cyclosporine, MTX; ^Assessed only in employed: n=124 (SEC); 37 (ETN); 121 (ADA); 98 (UST); 105 (Non-B); 510 (Overall).

Conclusions: These data show that Ps pts with concomitant PsA who initiated SEC in the Corrona Psoriasis Registry had higher disease activity, more comorbidities and suffered from more severe pain at enrolment. These differences need to be factored in for future analyses between treatment groups as data mature in this registry.

Disclosure of Interest: A. Gottlieb Grant/research support from: (Paid to Tufts Medical Center until 5/11/16, thereafter: None): Centocor (Janssen) Inc., Amgen, Abbott (AbbVie), Novartis, Celgene, Pfizer, Lilly, Levia, Merck, Xenoport, Dermira, Baxalta, Consultant for: Amgen Inc., Astellas, Akros, Centocor (Janssen) Inc., Celgene Corp., Bristol Myers Squibb Co., Beiersdorf Inc., Abbott Labs. (AbbVie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dermipsor Ltd., Incyte, Pfizer, Canfite, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, Glaxo SmithKline, Xenoport, Catabasis, Meiji Seika Pharma Co. Ltd, Takeda, Mitsubishi, Tanabe Pharma Development America Inc., Genentech, Baxalta, Kineta One, KPI Therapeutics, Crescendo Bioscience, Aclaris, Amicus and Reddy Labs, V. Strand Consultant for: AbbVie, Amgen, BMS, Celgene, Celltrion, Corrona, Crescendo, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi and UCB, C. Karki Employee of: Corrona, LLC., M. Mason Employee of: Corrona, LLC., J. Greenberg Shareholder of: Corrona, LLC., Consultant for: AstraZeneca, Celgene, Genentech, Janssen, Novartis and Pfizer, Employee of: Corrona, LLC., S. Jugl Shareholder of: Novartis, Employee of: Novartis, K. Gandhi Shareholder of: Novartis, Employee of: Novartis, P. Mease Grant/research support from: AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Consultant for: Abbvie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer, and UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Crescendo Bioscience, Genentech, Janssen, Lilly, Merck, Novartis, Pfizer and UCB

DOI: 10.1136/annrheumdis-2017-eular.2948

AB0741 PSORIATIC ARTHRITIS QUALITY OF LIFE QUESTIONNAIRE: TRANSLATION, CULTURAL ADAPTATION AND VALIDATION INTO PORTUGUESE LANGUAGE

A. Barcelos[1], C. Ambrósio[1], J. da Silva[2,3], S. McKenna[4], J. Wilburn[4], P.L. Ferreira[5,6]. *[1]Rheumatology Department, Centro Hospitalar Baixo Vouga, Aveiro; [2]Rheumatology Department, CHUC; [3]Faculdade de Medicina, Universidade de Coimbra, Coimbra, Portugal; [4]Galen Research, Manchester, United Kingdom; [5]Faculdade Economia, Universidade de Coimbra; [6]Centro de Estudos e Investigação em Saúde, Faculdade Economia - Universidade de Coimbra, Coimbra, Portugal*

Background: Psoriatic Arthritis (PsA) has a strong negative impact in the quality of life of patients, through pain, stiffness, functional disability, deformity and a variety of other dimensions. The Psoriatic Arthritis Quality of Life (PsAQoL) questionnaire is a disease-specific instrument developed to measure quality of life in patients with PsA.

Objectives: The aims of this study were to culturally adapt the questionnaire for Portugal, and evaluate its reliability and validity in patients with PsA.

Methods: The original UK English version of PsAQoL was translated into Portuguese by a bilingual translation panel. An independent lay panel reviewed the instrument's item phrasing to ensure appropriateness in colloquial European Portuguese. Structured cognitive debriefing interviews were conducted with ten PsA patients to assess the acceptability, the understanding and the redundancy or ambiguity of the questionnaire. The Portuguese PsAQoL was subsequently applied to PsA patients followed at the Rheumatology Department of Centro Hospitalar do Baixo Vouga, E.P.E. To assess reproducibility, thirty patients with PsA completed the Portuguese PsAQoL on two occasions, two weeks apart. A larger sample was recruited to determine internal consistency and construct validity. Descriptive statistical analysis was used to characterize the data. The Nottingham Health Profile (NHP) was used as a comparator instrument.

Results: Translation and adaptation were successful. The validation sample included 104 patients, 67% of whom were men. Their median age was 50.2 (SD=12.1) years and most were married. Cronbach's alpha for the Portuguese version of the PsAQoL was 0.91 and the test-retest reliability was 0.92, indicating that the measure has good internal consistency and produces low random measurement error. The PsAQoL could distinguish between groups of patients defined by self-reported general health status, self-reported severity of PsA and flare of arthritis. Duration of arthritis did not influence PsAQoL scores. There was a positive correlation between the total score of APsQoL and each of the dimensions of the NHP.

Conclusions: The Portuguese version on the PsAQoL was found to be relevant, understandable and easy to complete, reliable and valid. It should be considered for use in clinical practice and research settings to asses PsA-specific QoL.

References:

[1] McKenna S, Doward LC, Whalley D, et al. Development of the PsAQoL: a quality of life instrument specific to psoriatic arthritis. Ann Rheum Dis 2014; 63(2): 162–169.

[2] Wink F, Arends S, McKenna S, et al. Validity and reliability of the Dutch adaptation of the Psoriatic Arthritis Quality of Life (PsAQoL) Questionnaire. PloS One 2013; 8(2): e55912.

[3] Billing E, McKenna S, Staun M & Lindqvist U. Adaptation of the Psoriatic Arthritis Quality of Life (PsAQoL) instrument for Sweden. Scand J Rheumatol 2010; 39: 223–228.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3297

AB0742 ULTRASONOGRAPHY OF THE NAIL UNIT IN PSORIASIS AND PSORIATIC ARTHRITIS: A QUALITATIVE AND QUANTITATIVE ANALYSIS

A. Fassio[1], L. Idolazzi[1], A. Zabotti[2], E. Vantaggiato[1], C. Benini[1], O. Viapiana[1], M. Rossini[1], D. Gatti[1]. *[1]Rheumatology, Aoui Verona Reumatologia, Verona; [2]Rheumatology, University Hospital "Santa Maria della Misericordia", Udine, Italy*

Background: the nail unit is a shared topic of interest both for dermatologist and rheumatologist [1]. It is easy to study using imaging techniques such as ultrasonography. The nail was considered one of the possible target of assessment for the disease, especially when ultrasonography is performed. Ultrasound imaging of nails is a quite new technique, available since high frequencies probes were introduced in musculoskeletal examination and nail was considered one of the possible target for assessing the disease and defining its prognosis [2,3].

Objectives: to evaluate the presence of the nail involvement and subclinical alterations using ultrasonography in psoriasis and psoriatic arthritis.

Methods: the study sample included 82 patients affected by psoriasis and/or psoriatic arthritis and 50 healthy controls (HC). The patients were consecutively enrolled during their routine visit in the outpatient clinic and they performed clinical and ultrasonographic evaluation of the nail. Activity indexes (DAPSA, PASI, NAPSI) and other clinimetric parameters were considered.

Results: multivariate analysis of variance (mANOVA) was performed between groups and the nail plate and nail bed thickness, PASI, NAPSI, age and BMI were considered (table 1). Post hoc analysis underlined the differences between groups, in particular between healthy and affected. The lesions for nail plate and nail bed in the PASI score were analyzed using Pearson's chi square test and, secondary, odd ratios for significant results were calculated. Nail plate thickness and nail bed thickness were correlated with PASI, NAPSI, BMI and DAPSA. ROC curves were calculated obtaining also quantitative cut offs for nail plate and nail bed thickness in the affected vs healthy ones.

Table 1. patient groups and ANOVA results

	HC N=50 (M/F 22/28)	PSOs N=31 (M/F 22/9)	PsAs) N=51 (M/F 26/25)
	Mean ± SD	Mean ± SD	Mean ± SD
Eta	48.44±13.95	48.22±14.7	50.92±13.9
BMI	24.61±3.92	28.61±4.95*	28.64±5.84*
Thickness NAIL PLATE	0.051±0.006	0.063±0.011*	0.065±0.014+
Thickness NAIL BED	0.22±0.02	0.25±0.05*	0.25±0.04*

Conclusions: the application of ultrasonography is of potential advantages supported by the data of this study and strengthens the information available in literature, also adding quantitative parameters for the ultrasonography of the nail.

References:

[1] Ash ZR, Tinazzi I, Gallego CC, et al. Psoriasis patients with nail disease have a greater magnitude of underlying systemic subclinical enthesopathy than those with normal nails. Ann Rheum Dis 2012;71:553–6. doi: 10.1136/annrheumdis-2011–200478.

[2] Raposo I, Torres T. Nail psoriasis as a predictor of the development of psoriatic arthritis. Actas Dermo-Sifiliográficas Engl Ed 2015;106:452–7. doi: 10.1016/j.adengl.2015.02.001.

[3] Gutierrez M, Filippucci E, De Angelis R, et al. A sonographic spectrum of psoriatic arthritis: "the five targets." Clin Rheumatol 2010;29:133–42. doi: 10.1007/s10067-009-1292-y.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2723

AB0743 LOW RATES OF MAJOR ADVERSE CARDIAC EVENTS, MALIGNANCIES, AND SERIOUS INFECTIONS IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS TREATED WITH APREMILAST FOR ≥156 WEEKS: POOLED ANALYSIS FROM THE ESTEEM AND PALACE 1-3 PHASE 3 TRIALS

A. Kavanaugh[1], M. Augustin[2], E. Lespessailles[3], K.A. Papp[4], M. Paris[5], R. Chen[5], D.D. Gladman[6], D.M. Pariser[7], K. Peris[8]. *[1]University of California, San Diego, School of Medicine, la Jolla, United States; [2]Institute for Health Care Research in Dermatology and Nursing (IVDP), University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [3]University of Orléans, Orléans, France; [4]Probity Medical Research, Waterloo, Canada; [5]Celgene Corporation, Summit, United States; [6]Toronto Western Hospital, Toronto, Canada; [7]Eastern Virginia Medical School and Virginia Clinical Research, Inc., Norfolk, United States; [8]Catholic University of Rome, Rome, Italy*

Background: Apremilast (APR), an oral PDE4 inhibitor, was effective in phase 3, randomized, placebo (PBO)-controlled trials assessing treatment of moderate to severe plaque psoriasis (ESTEEM 1 and 2) and psoriatic arthritis (PsA; PALACE 1–3).

Objectives: We report incidence of MACE, malignancies, and serious infections (SIs; opportunistic and non-opportunistic) in pts receiving APR 30 mg BID (APR30) for ≥156 wks in a pooled analysis of these studies.

Methods: Incidence rates and exposure-adjusted incidence rates (EAIR)/100 pt-yrs of MACE, malignancies, SIs, and serious opportunistic infections (SOIs) are reported for 0 to 16 wks, 0 to ≤52 wks, and the APR-exposure period (0 to ≥156 wks) for pts receiving APR30 any time during the studies, through February 2015; ~30% (n=575) of pts received >3 yrs (>156 wks) of APR exposure.

Results: 2,242 pts were included in the safety analysis for 0 to 16 wks (PBO n=913, pt-yrs exposure [py]=260.2; APR30 n=1,329, py=377.8); 1,905 pts received APR30 during the APR-exposure period, representing 3,527.5 py; exposure during 0 to ≤52 wks was 1,524.5 py. At baseline 64.2% of PsA pts (PALACE 1–3) in the APR30 group were receiving concomitant DMARDs (including methotrexate). Incidence of MACE with APR30 was low and comparable to PBO during 0 to 16 wks. During 0 to ≤52 wks and the APR-exposure period, incidence of MACE (EAIR/100 pt-yrs) remained low (Table). Incidence rates (EAIR/100 pt-yrs) of hematologic malignancies, non-melanoma skin cancers, and solid tumors were similar with PBO (0.0, 1.2, 0.4) and APR30 (0.0, 1.3, 0.3) during 0 to 16 wks; incidence rates remained low during 0 to ≤52 wks and the APR-exposure period (Table). During 0 to 16 wks, the overall rate of infections (serious and non-serious) was low and comparable between pts receiving PBO (20.6%) and APR30 (24.8%). The overall rate of infections (serious and non-serious) was 42% during 0 to ≤52 wks and comparable to rates during the PBO-controlled period (0 to 16 wks); the majority of reported infections (URTI, nasopharyngitis, sinusitis) were not serious. During the PBO-controlled period (0 to 16 wks), rates of SIs with APR30 were low and comparable to PBO; no SOIs were reported. During 0 to ≤52 wks, the overall rate of SIs was low (0.6%; EAIR/100 pt-yrs: 0.7). The rate of SIs remained low (1.8%; EAIR/100 pt-yrs: 1.0) during the long-term cumulative APR-exposure period (0 to ≥156 wks) (Table). No clustering of any particular event was noted with respect to SIs; most events occurred in only 1 pt. No clinical reactivation of tuberculosis was reported with long-term APR30 exposure (0 to ≥156 wks). The rate of marked hematologic abnormalities remained low with long-term APR exposure.

	Treatment Period	
	0 to ≤52 Weeks	APR-Exposure Period 0 to ≥156 Weeks Cumulative Events*
	APR30 n=1,905 Pt-Yrs=1,524.5	APR30 n=1,905 Pt-Yrs=3,527.5
	EAIR/100 Pt-Yrs	EAIR/100 Pt-Yrs
Major adverse cardiac events§		
Acute myocardial infarction	0.1	0.1
Myocardial infarction	0.1	0.1
Subarachnoid hemorrhage	0.1	0.1
Cardiac arrest	0.0	0.1
Cerebral infarction	0.0	0.1
Malignancies		
Hematologic	0.0	0.1
Non-melanoma skin cancer	0.9	0.5
Solid tumors‡	0.3	0.4
Serious infections	0.7ǂ	1.0#
Pneumonia	0.1	0.1
Urinary tract infection	0.1	0.1
Appendicitis	0.1	0.1
Diverticulitis	0.1	0.1
Sepsis	0.0	0.1
Bronchitis	0.0	0.1

*Each patient's total exposure is defined as the time interval between the date of the first and last dose of APR30, regardless of when treatment was initiated, through February 2015.
§No adjudication of major adverse cardiac events for the APR-exposure period.
‡Including malignant melanoma.
ǂSerious infections occurring in patients included pneumonia (n=2), urinary tract infection (n=2), appendicitis (n=1), and diverticulitis (n=1).
#Serious infections occurring in ≥2 patients included pneumonia (n=5), appendicitis (n =3), bronchitis (n=3), diverticulitis (n=2), sepsis (n=2), and urinary tract infection (n=2).
APR30=apremilast 30 mg BID; EAIR=exposure-adjusted incidence rate; PBO=placebo; Pt-Yrs=patient-years.

Conclusions: Incidence of MACE, malignancies, and SIs was low in pts with psoriasis and PsA receiving APR30 for ≥156 wks. No new safety signals or SOIs were observed over time with APR30.

Disclosure of Interest: A. Kavanaugh Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, and UCB, M. Augustin Consultant for: AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene Corporation, Centocor, Eli Lilly, GSK, Janssen-Cilag, LEO Pharma, Medac, Merck, MSD, Novartis, Pfizer, UCB, and XenoPort, Speakers bureau: AbbVie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Celgene Corporation, Centocor, Eli Lilly, GSK, Janssen-Cilag, LEO Pharma, Medac, Merck, MSD, Novartis, Pfizer, UCB, and XenoPort, E. Lespessailles Grant/research support from: Amgen, Celgene Corporation, Eli Lilly, and Novartis, Speakers bureau: Amgen, Celgene Corporation, Eli Lilly, and Novartis, K. Papp Grant/research support from: AbbVie, Allergan, Amgen, Anacor, Astellas, Baxalta, Biogen-Idec, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene Corporation, Dermira, Dow Pharma, Eli Lilly, Galderma, Genentech, Glenmark, GSK, Janssen, Kyowa Hakko Kirin, LEO Pharma, MedImmune, Merck, Merck Serono, Mylan, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, Stiefel, Takeda, UCB, and Valeant, Consultant for: AbbVie, Akros, Allergan, Amgen, Anacor, Astellas, AstraZeneca, Baxalta, Baxter, Biogen-Idec, Boehringer Ingelheim, Bristol-Myers Squibb, Can-Fite BioPharma, Celgene Corporation, Celtic, Cipher, Dermira, Dow Pharma, Eli Lilly, Formycon, Forward Pharma, Funxional Therapeutics, Galderma, Genentech, Genexion, Glenmark, GSK, Janssen, Kyowa Hakko Kirin, LEO Pharma, Lypanosys, MedImmune, Merck, Merck Serono, Mitsubishi Pharma, Mylan, Novartis, Novommune, Pan Genetics, Pfizer, Regeneron, Roche, Sanofi-Aventis, Stiefel, Sun Pharma, Takeda, UCB, Valeant, Vertex, and Xoma, M. Paris Employee of: Celgene Corporation, R. Chen Employee of: Celgene Corporation, D. Gladman Grant/research support from: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, and UCB, D. Pariser Grant/research support from: Abbott Laboratories, Amgen, Astellas Pharma US, Asubio Pharmaceuticals, Basilea Pharmaceutical, Celgene Corporation, Dow Pharmaceutical Sciences, Eli Lilly, Galderma Laboratories, Graceway Pharmaceuticals, Intendis, Johnson & Johnson, Novartis Pharmaceuticals, Novo Nordisk A/S, Ortho Dermatologics, Photocure ASA, Stiefel Laboratories, and Valeant Pharmaceuticals, K. Peris Consultant for: Eli Lilly, LEO Pharma, MEDA, and Roche

DOI: 10.1136/annrheumdis-2017-eular.5065

AB0744 DOES TIMING OF INITIATION OF ANTI-TNF AGENTS AFFECT THE QUALITY OF LIFE OUTCOMES IN PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS?

P.W. Barnes[1], N. Rich-Garg[2], D. Choi[3], A. Deodhar[2]. *[1]School of Medicine; [2]Division of Arthritis & Rheumatic Diseases; [3]Public Health & Preventative Medicine, Oregon Health and Science University, Portland, United States*

Background: Psoriatic Arthritis (PsA) affects up to 30% of people with psoriasis[1]. While Tumor Necrosis Factor inhibitors (TNFi) are effective agents for PsA, the relationship between early treatment and patient reported outcomes in a real world setting has not been reported previously.

Objectives: To assess whether timely treatment with TNFi leads to better improvement in quality of life outcomes than delayed treatment.

Methods: This was a retrospective analysis of patients with PsA and/or Psoriasis (PsO) using TNFi with or without methotrexate, and who had a minimum of 2 visits at the Center of Excellence for Psoriasis and Psoriatic Arthritis at our university. Detailed demographic and clinical characteristics of this cohort have been published previously[2]. Demographics, quality of life measures (e.g. Routine Assessment of Patient Index Data – RAPID3, Psoriasis Quality of Life – PQoL12, Short Form 12 – SF-12), and clinical data (percent of body surface area involved with PsO – BSA%) were collected from patient-reported questionnaires and electronic medical records. Only those patients who had a chronological overlap of treatment exposure and QoL measures such as RAPID3, BSA, SF12 and PQOL were included. To ascertain treatment effects, a mixed-effects model was fitted to estimate the trend of each QoL outcome of a patient separately. Then, for all estimated trends of an outcome, a linear regression model was employed to explore the association between the magnitude of estimated trends and timeliness of TNFi treatments.

Results: The quality of life measures were not affected by how early after the disease onset TNFi treatment was started (in other words, no statistically significant associations between the effectiveness of TNFi treatment and disease duration) for RAPID3 (p=0.285), SF-12 (p=0.674), or BSA (p=0.078). For PQoL, there was a significant association between the trend of treatment effects and timeliness of treatment. A day of delay into treatment was resulted in a reduction of 4.4×10^{-4}/day in the trend of PQoL scores (p=0.007).

Conclusions: In this sample of PsA & PsO patients, timing of starting TNFi in patients with PsA had significant impact on improvements in the PQoL but not other quality of life measures such as RAPID3, SF-12 and BSA. A relatively short treatment history might have led to the negative correlations.

References:

[1] McLaughlin M, et.al. Early treatment of psoriatic arthritis improves prognosis. Practitioner 2014 258 (1777) 21–24.
[2] Truong B et.al. Demographics, clinical disease characteristics and quality of life in a large cohost of psoriasis patients with and without psoriatic arthritis. Clin, Cosm and Inv Dermatology 2015: 8: 563–569.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1535

AB0745 SUBCLINICAL ATHEROSCLEROSIS EVOLUTION IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH ANTI-TNF ALPHA: 5 YEARS FOLLOW UP

A. Ortolan[1], M. Puato[2], G. Boschetti[3], M. Lorenzin[1], A. Hoxha[1], L. Punzi[1], R. Ramonda[1]. *[1]Rheumatology Unit, Department of Medicine DIMED, University of Padova; [2]Clinica Medica III, Department of Medicine DIMED, Universityof Padova; [3]Clinica Medica III, Department of Medicine DIMED, University of Padova, Padova, Italy*

Background: Psoriatic arthritis (PsA) is associated with increased morbility and mortality and an accelerated atherosclerosis. Influence of anti-TNFalpha treatment (a widely used therapy in PsA) in subclinical atherosclerosis is still unclear.

Objectives: The aim of this study was to evaluate subclinical atherosclerosis progression before, during and after 5 years of anti-TNFalpha treatment.

Methods: Twenty-seven consecutive PsA patients were evaluated before TNF blockers therapy (T0), after 2 years (T1) and after 5 years (T2) of treatment. Subclinical atherosclerosis was evaluated through carotid duplex scanning, analyzing intima-media thickness (IMT) and flow-mediated dilation (FMD). IMT values were expressed as IMT mean (cumulative mean of all the IMT mean in every analyzed carotid segment) and M-MAX (cumulative mean of all the higher IMT in every analyzed carotid segment). Response to therapy was studied by the evaluation of tender and swollen joints (Tj and Sj), DAS 28 (disease activity score), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Metrologic and metabolic data were collected. For the statistical evaluation of parameters over time (T0 vs T1, T1 vs T2) Student's T test for paired data was used.

Results: From T0 to T1 a deterioration in IMT-mean and M-MAX ($p<0.01$) was

Table

	T0	T1	T2
IMT-mean	0.72±0.15	0.91±0.37*	0.92± 0,34
M-MAX	0.89±0.18	1.06±0.39*	1.10±0.35**
FMD	5.40±1.93	5.37±1.66	5.40±1.89
Tender joints (n)	8.10±5.56	2.09±2.32*	1.72± 2.05
Swollen joints (n)	3.85±3.84	0.25±0.72*	0.50±0.92
CRP	11.25±9.16	2.91±1.72*	2.73 ±2.51
DAS28	4,16±0.67	2.30±0.82*	2.40±0,9

Legend: IMT= intima-media thickness; M-MAX= cumulative mean of all the higher IMT in every analyzed carotid segment; FMD= flow-mediated dilation; CRP= C Reactive Protein; DAS28=Disease Activity Score 28joints; *= p<0.01 with respect to the previous determination; **=p<0.05 with respect to the previous determination

noted. At T2 IMT-mean remained stable, M-MAX worsened further ($p<0.05$). No significant variation in FMD was observed (Table). Noteworthy, from T0 to T2 systolic blood pressure and Body Mass Index remained stable (p=ns), while diastolic blood pressure decreased (p=0,001). A good response to PsA treatment was confirmed by a significant decrease (T0 vs T1) in Tj, Sj, DAS 28 and CRP ($p<0.01$); treatment efficacy was preserved from T1 to T2 (p=ns) (Table).

Conclusions: Our data revealed that in patients with PsA, despite treatment with TNF blockers, there is still a gradual, albeit slight progression of subclinical atherosclerosis assessed by ultrasonography. Other inflammatory mechanisms not related to TNF may be responsible of the progression in atherosclerotic disease.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5545

AB0746 PRELIMINARY RESULTS OF A TWO-YEAR FOLLOW UP OF SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH PSORIATIC ARTHRITIS

C. Vergara-Dangond[1], M. Robustillo-Villarino[1], V. Núñez-Monje[1], M. Aguilar-Zamora[1], L. Montolio-Chiva[1], E. Valls-Pascual[2], A. Ybáñez-García[1], Á. Martínez-Ferrer[2], J.J. Alegre-Sancho[1]. [1]*Rheumatology;* [2]*Hospital Universitario Dr. Peset, Valencia, Spain*

Background: Psoriatic arthritis (PsA) is a disease associated with an increased cardiovascular (CV) risk, due to early atherosclerosis, which is comparable to a rheumatoid arthritis population. However, there is a lack of studies that evaluate the progression of subclinical atherosclerosis over a year in these patients.

Objectives: To explore the progression of the vascular damage by different techniques in patients with PsA and the factors related with these changes.

Methods: Pre-post study with analytical components. 44 patients with PsA (CASPAR criteria) and peripheral joint involvement of more than one year since diagnosis were consecutively included. We gathered demographic (age, gender, BMI), clinical (traditional CV risk factors, previous CV event), and analytical variables (atherogenic index [AI], GFR [MDRD], fibrinogen, glycated hemoglobin, CRP, ESR, ultrasensitive CRP, apoB/apoA1 ratio) and basal CV risk was estimated with SCORE tool. Other variables were collected retrospectively from patients electronic medical record. The extracranial branches of carotid artery were explored by ultrasonography (US) using an Esaote MyLab70XVG with a 7–12 MHz linear transducer and an automated program measuring intima-media thickness (IMT) through radiofrequency (^{RF}QIMT), and the presence of atheroma plaques, as per the Mannheim consensus, was registered. Pulse wave velocity (PWV) was determined, as an arterial stiffness marker, by a validated MobilOGraph® device. Patients were followed during a 2-year period between may 2014 until december 2016. All of the tests were repeated after 2 years. Statistical analysis was performed using SPSS 17.0 software.

Results: We analyzed 38 patients, excluding those with high CV risk (previous CV event, GFR<60mg/dl, and/or type II or type I diabetes with organ affection) and followed during 2 years. At baseline, the mean and median of age was 59,2 and 60,5 years (39–88), respectively, mostly women (65,8%). The median BMI was 28 (17–35). 28,9% were smokers and 36,8% had hypertension. 26,3% received glucocorticoids, 57,9% NSAIDs, 84,2% DMARDs and 31,6% biologic therapies. The median CRP, ESR and DAS 28 were 5mg/L (1–19,1), 7mm/h (2–28) and 2,17 (1,24–3,7), respectively. The median SCORE was 1 (0–7), the PWV was 8 m/s (5,6–13,5) and basal IMT was 728 μ(462–1087); the presence of atheroma plaques was detected in 35,1% of the patients.

After 2 years, plaque appearance was seen in 15% more of patients, as well as worsening of PWV and IMT in 56,8% and 38,9% of patients, respectively.These changes were not significant. No patient developed a CV event.

In the bivariate analysis, PWV progression at 2 years related with advanced age ($p<0,002$), and with elevated SCORE ($p<0,044$), and showed a tendency with higher arterial systolic pressure (ASP). We also observed a tendency to an association between plaque appearance, age and ASP; as well as lower apolipoprotein A1 levels with IMT.

Conclusions: The progression over time of the vascular damage in patients with PsA relates with traditional CV risk factors. These preliminary results must be confirmed in a posterior analysis with a greater number of patients.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3002

AB0747 THE EFFECT OF CERTOLIZUMAB PEGOL ON RADIOGRAPHIC PROGRESSION OVER 4 YEARS OF TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS

D. van der Heijde[1], R. Fleischmann[2], J. Wollenhaupt[3], A. Deodhar[4], L. Bauer[5], B. Hoepken[5], L. Peterson[6], P.J. Mease[7]. [1]*Leiden University Medical Center, Leiden, Netherlands;* [2]*UT Southwestern Medical Center and Dallas Metroplex Clinical Research Center, Dallas, United States;* [3]*Schön Klinik, Hamburg, Germany;* [4]*Oregon Health and Science University, Portland, United States;* [5]*UCB Pharma, Monheim, Germany;* [6]*UCB Pharma, Raleigh;* [7]*Swedish Medical Center and University of Washington, Seattle, United States*

Background: The RAPID-PsA trial (NCT01087788) investigated the efficacy and safety of certolizumab pegol (CZP) in patients (pts) with psoriatic arthritis (PsA). It demonstrated that CZP treatment inhibits radiographic progression over 96 weeks (wks).[1]

Objectives: We report the long-term effect of CZP treatment on radiographic progression in pts with PsA over 4 years.

Methods: The RAPID-PsA phase 3 trial was double-blind and placebo-controlled to Wk24, dose-blind to Wk48, and open-label (OL) to Wk216. Pts had active PsA and had failed ≥1 DMARD. Pts randomized to CZP (200mg Q2W or 400mg Q4W, following 400mg loading dose at Wks0, 2, 4) continued their assigned dose in the OL period. Radiographs taken at baseline (BL), and at Wks96, 168, 216, were read in a single reading campaign using the modified Total Sharp Score (mTSS) for PsA by 2 readers, blinded to patient information and time point sequence. The mean of the scores of the 2 readers was used. Outcomes reported are the least squares (LS) mean mTSS score, change from BL (CFB) in mTSS score, and the percentage of pts assessed for radiographic damage who achieved mTSS non-progression (defined either as CFB in mTSS score ≤0.5 or ≤0), for all Wk0 CZP-treated pts, irrespective of dose regimen. mTSS score and CFB were estimated using Mixed Model Repeated Measures (MMRM) estimates; proportions of pts with radiographic non-progression are presented as observed case.

Results: 409 PsA pts were randomized, of whom 273 received CZP from Wk0. The LS mean BL mTSS score was 16.0 and there was little increase from BL in mTSS score to Wk216 (Table). Amongst those who completed the study to Wk216, the majority of CZP-treated pts achieved radiographic non-progression to Wk216, both with non-progression defined as CFB in mTSS score ≤0.5 or ≤0 (Table). The change in LS mean mTSS score over time for Wk0 CZP-treated pts was consistently low throughout the trial: 0.14 (95% CI: 0.02–0.26) per 48 wks from BL to Wk96, and 0.18 (95% CI: 0.08–0.28) per 48 wks from Wk96 to Wk216.

Table: mTSS score and radiographic non-progression to Week 216 for patients treated with CZP from Week 0

	Week 0 CZP dose combined (N=273)			
	Week 0	**Week 96**	**Week 168**	**Week 216**
mTSS score, LS mean (SE) [95% CI] [a]	16.0 (2.2) [11.6–20.4]	16.2 (2.2) [11.8–20.6]	16.6 (2.3) [12.1–21.0]	16.7 (2.3) [12.2–21.1]
CFB in mTSS score, LS mean (SE) [95% CI] [a]	–	0.3 (0.1) [0.0–0.5]	0.6 (0.2) [0.3–1.0]	0.7 (0.2) [0.3–1.1]
Non-progression rate, n (%) [b]				
Patients with CFB in mTSS ≤0.5, n/N (%)	–	180/214 (84.1)	158/196 (80.6)	145/186 (78.0)
Patients with CFB in mTSS ≤0, n/N (%)	–	157/214 (73.4)	131/196 (66.8)	121/186 (65.1)

[a] Mixed Model Repeated Measures (MMRM) estimates; [b] Observed case; percentage of patients with non-progression, as a proportion of the number assessed for progression. CFB: change from baseline; LS: least squares; SE: standard error.

Conclusions: There was little radiographic progression in CZP-treated PsA pts, as measured by mTSS, throughout the 4-year RAPID-PsA trial.

References:

[1] Mease P. RMD Open 2015;1:e000119;doi:10.1136/rmdopen-2015–000119.

Acknowledgements: This study was funded by UCB Pharma. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: D. van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Daiichi, Eli Lilly, Galapagos, Gilead, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, UCB Pharma, Employee of: Director of Imaging Rheumatology B.V., R. Fleischmann Grant/research support from: Genentech Inc, Roche, Abbott, Amgen, UCB Pharma, Pfizer, Bristol-Myers Squibb, Eli Lilly, Sanofi-Aventis, MSD Pharmaceuticals, Novartis, AstraZeneca, Janssen, Consultant for: Roche, Abbott, Amgen, UCB Pharma, Pfizer, Bristol-Myers Squibb, Eli Lilly, Sanofi-Aventis, Novartis, AstraZeneca, Janssen, J. Wollenhaupt Grant/research support from: UCB Pharma, Consultant for: UCB Pharma, A. Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GlaxoSmithKline, Janssen, Novartis, Pfizer, UCB Pharma, Consultant for: Eli Lilly, Janssen, Novartis, Pfizer, UCB Pharma, L. Bauer Employee of: UCB Pharma, B. Hoepken Employee of: UCB Pharma, L. Peterson Employee of: UCB Pharma, P. Mease Grant/research support from: (Abbott) AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Novartis, Pfizer, Sun, UCB Pharma, Consultant for: (Abbott) AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Corrona, Dermira, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Sun, UCB Pharma, Zynerba, Speakers bureau: (Abbott) AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Genentech Inc, Janssen, Novartis, Pfizer, UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.1961

AB0748 HYPERURICEMIA IN PSORIATIC ARTHRITIS: A NEW LOOK AS A RISK FACTOR FOR CARDIOVASCULAR EVENTS

D.S. Bublikov. *Altay State Medical University, Barnaul, Russian Federation*

Background: According to various authors, the prevalence of hyperuricemia in patients with psoriatic arthritis constitutes up to 35% of the total patient population. Thus, seronegative spondylarthritis patients, as it is known, possess a higher incidence of cardiovascular mortality than the population in general, in particular due to life-threatening cardiac arrhythmias.
Objectives: To study the effect of hyperuricemia on the development of ventricular extrasystole in patients with psoriatic arthritis and the interrelation of uric acid levels and gradation of ventricular extrasystole.
Methods: The study involved patients with psoriatic arthritis, confirmed by CASPAR criteria (2006), n=59. The average age – 57.15±12.11 years. All patients underwent the study of myocardial contractility and treadmill test. Inclusion criteria - the presence of psoriatic arthritis for the period of at least one year, uric acid levels over 360 mkmol/L for women and more than 420 mkmol/L for men. The exclusion criteria included the presence of coronary heart disease, myocardial contractility disorders and decreased ejection fraction according to Simpson less than 55%. For all patients was recorded Holter ECG for the period of 24 hours on an outpatient basis. The level of uric acid was measured by means of the standard method of biochemical analyzer.
Results: The prevalence of ventricular extrasystole in patients with psoriatic arthritis and grading are shown in Table 1.
Moreover, there has been discovered a direct correlation of medium strength between the uric acid levels and frequency and Lown-Wolf gradation of ventricular extrasystole (Table 1).

Table 1

Lown-Wolf gradation of ventricular extrasystoles	Percentage of patients with with psoriatic arthritis	Average level of uric acid	Coefficient of correlation, r
I	25,40%	546,52+12,24	0,54
II	22,03%	622,15+28,11	0,47
III	1,69% (1 patient)	511,21	Small sample
IV a	20,34%	784,22+55,16	0,68
IV b	25,42%	774,13+22,60	0,33
V	5,08%	894,23+13,90	0,57

Conclusions: 1. Hyperuricemia in patients with psoriatic arthritis by exclusion of cardiogenic causes of cardiac extrasystole is an independent risk factor for ventricular extrasystole.
2. The level of hyperuricemia correlates directly with the Lown-Wolf gradation of ventricular extrasystole.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7042

AB0749 AXIAL INVOLVEMENT IN THE RUSSIAN COHORT OF EARLY PERIFERAL PSORIATIC ARTHRITIS PATIENTS AND ITS ASSOCIATION WITH ARTHRITIS ACTIVITY, PATIENT'S ASSESSMENT AND SEVERITY OF SKIN LESION

E.E. Gubar, E.Y. Loginova, L.N. Denisov, A.V. Smirnov, S.I. Glukhova, T.V. Korotaeva. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: The association of axial involvement with peripheral arthritis activity and skin lesion severity in early psoriatic arthritis (ePsA) patients (pts) has not been studied properly.
Objectives: to study the prevalence of axial involvement detected by magnetic resonance imaging (MRI) and X-ray of sacroiliac joints (SIJs) and its correlation with peripheral arthritis activity and skin lesion severity in peripheral ePsA pts.
Methods: 89 pts (M/F–42 /47) with peripheral ePsA according to CASPAR criteria were included; mean age 36.5±10.9 yrs, disease duration 12.1±10.1 mo., disease activity index (DAS)28 8.8±1.7, patient's pain VAS 55.0±17.9, patient's global disease activity VAS 56.9±17.1, C-RP16.1 [6.6; 31.0] mg/l, ESR 22.5±19.2 mm/h. All patients were evaluated for the presence of inflammatory back pain (IBP) by ASAS criteria. In pts having IBP disease activity was measured by BASDAI. The examination included X-ray of sacroiliac joints (SIJs), HLA B27 antigen, MRI of SIJs was performed in 79 pts, both with and without IBP, on Signa Ovation 0,35T. Bone marrow edema on MRI (STIR), considered as active MRI sacroiliitis (MRI-SI), was evaluated by an independent reader. Radiographic sacroiliitis (R-SI) was defined at 2 grade changes, at least in one SIJ, while definite radiographic SI (dR-SI) was considered according to New York criteria (unilateral grade $\geq$3 or bilateral grade $\geq$2). Skin lesion area was measured according to BSA. BSA $>$10% was defined as extensive.
Results: IBP was found in 58 out of 89 (65.1%) pts, 35 (60.3%) of them had short-term (episodic) IBP, and 23 (39.7%) pts had long-term IBP. MRI-SI was observed in 28 out of 79 (35.4%) pts. R-SI was determined in 42 out of 89 (47.2%) pts, while dR-SI was found in 27 out of 89 (30.3%) pts. 34 (38. 2%) pts were HLA-B27 positive. In pts having IBP disease activity by BASDAI was 4.5±1.6. An association was detected between the presence of MRI-SI and activity of peripheral arthritis by DAS28 (r=0.25; p=0.03). Correlation was detected between the presence of MRI-SI and the value of patient's global disease activity (r=0.23; p=0.047) as well as patient's pain (r=0.31; p=0.007). An association was found between the presence of MRI-SI and the skin lesion area. Among the group of 28 pts with MRI-SI, 6 (21.0%) pts had an extensive skin lesion area, while out of the group of 51 pts without MRI-SI only 2 (4.0%) pts had an extensive skin lesion area (p=0.033). A positive trend has been found between the presence of R-SI and erosive arthritis of hands and feet. Among the 42 pts having R-SI erosive arthritis was found in 18 (43.2%) pts while in 47 pts without R-SI–in 11 (23.9%) pts (p=0.06).
Conclusions: in the Russian cohort of early peripheral PsA pts, careful examination quite often revealed high prevalence of axial involvement. Active inflammation of the SIJ detected by MRI (in 35% of pts) is more often found in pts with higher peripheral arthritis activity measured by DAS28, with higher values of patient's pain /patient's global disease activity, with more extensive skin lesion area. There is a tendency that pts with more severe (erosive) peripheral arthritis more often develop R-SI.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3047

AB0750 THE GO-DACT PROTOCOL: A RANDOMIZED CONTROLLED TRIAL TO COMPARE THE EFFICACY OF GOLIMUMAB IN COMBINATION WITH METHOTREXATE (MTX) VERSUS MTX MONOTHERAPY, IN IMPROVING DACTYLITIS AND ENTHESITIS, IN MTX NAÏVE PSORIATIC ARTHRITIS PATIENTS

E. Vieira-Sousa[1], H. Canhão[2], J.E. Fonseca[1] on behalf of GO-DACT research team. *[1]Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa and Rheumatology Department, Hospital de Santa Maria, Lisbon Academic Medical Centre; [2]CEDOC, NOVA Medical School, Universidade Nova de Lisboa, Lisbon, Portugal*

Background: Dactylitis is a hallmark manifestation of psoriatic arthritis (PsA) and a key feature for PsA diagnosis. Active dactylitis is associated with a higher risk of erosions and can severely impact function. The therapeutic strategies for dactylitis are however largely empirical, with a profound absence of knowledge regarding efficacy, as primary endpoint, and impact on disease progression. The use of biologic disease modifying anti-rheumatic drugs (DMARDs) in patients with dactylitis, refractory to non-steroidal anti-inflammatory drugs (NSAIDs) or local corticosteroids, is recommended by EULAR guidelines, over the use of conventional DMARDs, based in the scarcity of evidence and properly designed studies in this field.
Methods: GO-DACT is an investigator initiated ongoing multicentric trial, involving 13 national Rheumatology departments. Patients older than 18 years, with the diagnosis of PsA and active dactylitis (tenderness score$\geq$1), refractory to NSAIDs, for 3 months, were included. Patients were randomized on a 1:1 ratio, to either MTX in combination with golimumab or placebo, for a period of 24 weeks. The primary aim of this trial is to determine differences of efficacy between the two treatment arms, in improving dactylitis (and enthesitis), as assessed by the dactylitis severity score (DSS) at 24 weeks. Key secondary outcomes include: Leeds dactylitis index (LDI), Leeds enthesitis index (LEI), joint counts, psoriasis area and severity index (PASI) and nail psoriasis severity index (NAPSI), health assessment questionnaire (HAQ), Dermatology life quality index (DLQI) and composite indexes for disease activity. The effect of treatment arms, on different tissue compartments, will be analysed by contrast-enhanced magnetic resonance imaging (MRI), with high resolution images for dactylitis, at baseline and 24 weeks.
Results: The results from GO-DACT are expected to have implications in clinical practice, bringing robust and valid data for the definition of dactylitis treatment stratification and algorithm.GO-DACT will also contribute to understand dactylitis pathogenesis through the assessment of treatment efficacy, namely in distinct tissue compartments as defined by MRI. https://www.clinicaltrials.gov (NCT02065713)
Acknowledgements:
Acknowledgments: This investigator initiated trial was supported by a research grant from Merck Sharp and Dohme
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5462

AB0751 THE DIFFERENCES AND SIMILARITIES BETWEEN PATIENTS AND PHYSICIAN GLOBAL ASSESSMENT IN PATIENTS WITH PSORIATIC ARTHRITIS

K. Nas[1], E. Kilic[2], R. Cevik[3], A.Z. Dagli[3], G. Kilic[4], S. Sag[1], A. Kamanli[1], I. Tekeoglu[1]. *[1]Div. of Rheumatology and Immunology, Dept of PM&R, Sakarya University Faculty of Medicine, Sakarya; [2]Rheumatology Clinic, Afyonkarahisar State Hospital, Afyon; [3]Div. of Rheumatology, Dept of PM&R, Dicle University Faculty of Medicine, Diyarbakir; [4]Dept. of PM&R, Afyon Kocatepe University Faculty of Medicine, Afyon, Turkey*

Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis, axial involvement, enthesitis, dactylitis and uveitis. The differences and similarities between patient's global assessment (PtGA) and physician's global assessment (PhGA) were not assessed clearly in PsA.
Objectives: The aim of this study was to assess differences and similarities between patient's and physician's perspective of global assessment in patients with PsA.

Methods: Patients with PsA over the age of 18-year-old who met the CASPAR classification criteria were underwent clinical and laboratory evaluation by using standardized protocol and case report form, from two universities outpatient's clinics. PtGA and PhGA, VAS-pain, fatigue, BASDAI, BASFI, health-related QoL were recorded at baseline visit. Pearson correlation coefficient were calculated for PtGA and PhGA. Linear regression model were used to asses relationship between global assessments and clinical finding.
Results: A total 144 patients with PsA (male 51, female 93) were included. Symptom duration (7.8±7.5 vs 11.3±11.2), VAS-pain (4.4±2.6 vs 4.9±2.6), PtGA (4.7±2.5 vs 5.0±2.4) and PhGA (4.0±2.2 vs 4.4±2.2) were similar between male and female patients with PsA ($p>0.05$). VAS-fatigue was higher in female patients with PsA than male ones (5.9±2.7 vs 4.4±2.8, p=0.001). Disease activity measurements such as, tender and swollen joint count, DAS28, BASDAI and acute phase reactant were similar for both sex. Correlation coefficient of Physician's global assessment was higher than PtGA in various clinical findings. The highest correlation coefficient was observed in VAS-pain (r=0.784) and followed by SF36-bodily pain (r=-0.613), BASDAI (r=0.587), NHP-physical activity (r=0.584), VAS-fatigue (r=0.555), BASFI question 5 (r=0.551) for PhGA ($p<0.0001$). However the highest correlation coefficient was observed in VAS-pain (r=0.690) and followed by NHP-physical activity (r=0.536), BASFI question 10 (r=0.512), BASDAI (r=0.499), SF36 (r=-0.490) and BASFI total score (r=0.484) for PtGA ($p<0.0001$). Statistically significant positive linear relation was observed between global assessment and clinical parameters (VAS-pain, fatigue, BASDAI, BASFI, DAS28, NHP-physical activity) by using simple linear regression model. VAS-pain and BASDAI question 1 explained 83.3% of PtGA as a predictor in multiple linear regression model. However, VAS-pain and DAS28 explained 68.4% of PhGA as a predictor in multiple linear regression model (table 1).

Table 1. Results of multiple linear regression of PtGA and PhGA

	R^2	B	SE	t	p
Patient's global assessment					
Constant	0.833	0.597	0.311	1.920	0.060
VAS-pain		0.665	0.061	10.939	?0.0001
BASDAI-1 How would you describe the overall level of fatigue/tiredness you have experienced in the past week?		0.205	0.063	3.243	0.002
Physician's global assessment					
Constant	0.684	0.399	0.310	1.285	0.201
VAS-pain		0.587	0.050	11.846	?0.0001
DAS 28		0.332	0.096	3.453	0.001

Conclusions: Assessment of disease activity as well as clinical parameters is considered to be complex in PsA. Patient's and physician's have different perspective of disease activity. Severity of pain and fatigue may be predictor of PtGA whereas; pain and objective disease activity measurement may be predictor of PhGA in patient with PsA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5396

AB0752 CONSENSUS STATEMENT ON THE USE OF METHOTREXATE IN PSORIATIC ARTHRITIS PATIENTS

J. Tornero[1], E. Loza[2], J.D.D. Cañete[3]. *[1]Rheumatology, Hospital de Guadalajara, Guadalajara; [2]Instituto de Salud Musculoesquelética, InMusc, Madrid; [3]Rheumatology, Hospital Clínic e IDIBAPS, Barcelona, Spain*

Background: Methotrexate (MTX) is the cornerstone in rheumatic diseases, including psoriatic arthritis (PsA), but the complexity of PsA and the paucity of randomised controlled studies and strategic trials need a clear analysis.
Objectives: To develop recommendations for the management of MTX in PsA (musculoskeletal manifestations) based on best evidence and experience
Methods: The coordinators formulated 14 questions about MTX use (indications, efficacy, safety) in patients with PsA. A systematic literature review was performed to answer these questions. Using this information, inclusion and exclusion criteria were stablished as well as the search strategies (Medline, Embase and the Cochrane Library), that were designed by an expert librarian. Two different reviewers selected the articles, first by title and abstract, then by detailed review, and collected data independently. Evidence tables were produced. With this evidence the coordinators proposed 12 preliminary recommendations that will be discussed and voted in a nominal group of expert meeting. The level of evidence and grade of recommendation will be defined using the Oxford Center for Evidence Based Medicine. Agreement will be stablished if at least 80% of the experts voted yes (yes/no).
Results: A total of 12 preliminary recommendations on the use of MTX in PsA were proposed (see table).
Conclusions: This document aims to help to answer usual clinical questions and facilitate decision making when treating PsA patients with MTX.
Disclosure of Interest: J. Tornero: None declared, E. Loza Grant/research support from: Abbie, Pfizer, Roche, Gebro, BMS, UCB, J. Cañete: None declared
DOI: 10.1136/annrheumdis-2017-eular.1395

Abstract AB0752 – Table 1

#	Recommendation	LE; GR
1	In patients with active peripheral disease (oligo-polyarthritis), the use of a csDMARD is recommended, MTX preferred, principally in cases of relevant skin involvement	1b; A
2	A starting dose of at least 10–15 mg/w is recommended, taking into account disease severity and patients prognostic factors	5; C
3	In case of insufficient response to MTX starting dose, a quick dose increase should be performed up to 25–30 mg/w in approximately 8 w	5; C
4	Oral MTX is recommended, but parenteral MTX should be considered in patients with high disease activity, those needing >15 mg oral/week, in those with low adherence to oral MTX, polypharmacy, obese patients, in order to avoid dosing errors, and always taking into account patients preferences	5; C
5	When the treatment target is reached for at least 6 months, then a dose adjustment is recommended in order to maintain the treatment target with the minimal MTX dose	5; D
6	Despite of lack of well designed clinical trials to demonstrate the efficacy of MTX in PsA, data coming from clinical trials using MTX as placebo, treat to target studies and years of rheumatologist accumulated clinical experience, all are in favor of MTX efficacy in peripheral PsA	1b; A
7	In patients with peripheral PsA and enthesitis/dactylitis, MTX could be an option along with steroids injections (if needed)	2a; B
8	In general, combined therapy with MTX and other csDMARD is not recommended	2a; B
9	If a biologic therapy is indicated, MTX continuation should be individually evaluated in each patient	1b; A
10	MTX improves anti-TNFα survival (monoclonal antibodies, mainly chimeric antibodies)	2a; B
11	No special safety problems, regarding to rheumatoid arthritis patients, have been reported with MTX in PsA patients	1b; A
12	PsA is a chronic disease in which MTX discontinuation is not recommended if there is maintained efficacy and the drug is well tolerated	3a; C

AB0753 ARTERIAL STIFFNESS INCREASE IN THE EARLY PHASE OF ARTHROPATHY RELATED WITH PSORIATIC ARTHRITIS IS NOT FURTHER MODIFIED BY STABLE PROLONGED RETENTION OF A MINIMAL DISEASE ACTIVITY CONDITION

F. Fischetti, F. Bozzao, M. Rovina, G. Simon, M. Bardelli, R. Carretta. *University of Trieste Italy, Trieste, Italy*

Background: Increased large arteries wall stiffness (AS) is a well known independent morbidity and mortality cardiovascular risk factor, not only related to hypertension and diabetets, but also induced by long standing systemic inflammation, as observed in inflammatory rheumatic or gut chronic diseases. Psoriatic arthritis (PsA) was also shown to increase cadiovascular morbidity, but this observation was commonly related with the associated occurrence of long term arthritis, disease activity and CV traditional risk factors
Objectives: To assess whether in a selected group of PsA patients, affected by recent onset (4–12 months) arthritis, not suffering from CV disease risk factors, evidence could be obtained of an early alteration of arterial wall function as expressed by an increased arterial pulse wave velocity (aPWV) and secondary reduced tonometric subendocardial viability ratio (tSEVR).
Further, we evaluated if a 18 months (Mth) treatment with synthetic disease modifying antirheumatic drugs (sDMARD) other than cyclosporine, leading to a demonstrable target of clinical "minimal disease activity"(MDA) could modify such possible modifications
Methods: Conclusive data were obtained in a selected goup of 12 PsA patients (Pts) (CASPAR criteria classified) (M/F, 6/5; mean age, 50.8; range, 40–65) not suffering from axial spondylitis who firsly underwent (without any previous treatment) aPWV measurement (PulsePen, Diatecne Srl, Milan) and tSEVR calculation, and then were re-evaluated for the same calculations after a 18 Mth time of sDMARD treatment. Each of the PsA Pts had a 3–4 Mth follow up and showed to reach the target of stable MDA (with also ultrasound confirmed remission of active synovitis) after a 4–8 Mth treatment. Before treatment, the group of PsA Pts was compared with an age, body weight, CV parameters and risk factors–matched control group of voluntary 22 healthy subjects (M/F, 11/11; mean age, 51.3; range, 41–67)
Results: Before any treatment, aPWV was higher in the group of patients with PsA than in control subjects (median, 8.667 m/s vs 6.963 m/s, $p<0.02$) while tSEVR was decreased (median, 1.44 vs 1.50, $p<0.05$). Aortic PWV was not modified after the sDMARD treatment (median m/s, before=8.691, after=8.048, p=0.55), despite statistically significant improvements of the disease activity scores (DAS28; modified CPDAI; DAPSA) as well as cutaneous PASI, and stable retention of a MDA condition. A direct correlation (Spearman rank) between aPWV and DAS28 (rho=0,70; p-value=0,04), BASDAI (rho=0,77; p-value=0,01), and HAQ (rho=0,66; p-value=0,05) was found, not instead between aPWV and ESR or CRP. Pts with PsA, at the end of the follow up, had increased levels of systolic (134,1±14,3 vs 122±11,2, $p<0,05$) and diastolic (82±7,4 vs 73,5±6,6, $p<0,05$) blood pressure, with unmodified heart rate
Conclusions: Early onset of PsA seems to be associated with already established and stable increase of AS. Subclinical previous phase of inflammation and length of psoriatic disease could be addressed as possible causes
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5528

AB0754 COMPARISON OF COMPOSITE INDICES TAILORED FOR PSORIATIC ARTHRITIS TREATED WITH CSDMARDS AND BDMARDS: A LONGITUDINAL OBSERVATIONAL STUDY

F.M. Perrotta, A. De Socio, E. Lubrano. *Medicina e scienze della salute, Università degli studi del Molise, Campobasso, Italy*

Background: Remission or low disease activity should be the target of therapy in chronic inflammatory arthritis as well as in Psoariatic arthritis (PsA). In a complex disease such as PsA, several methods are available to define remission that comprise the assessment of different clinical features.
Objectives: The aim of this study was to compare the composite indices tailored for PsA in both patients treated with csDMARDs and bDMARDs.
Methods: Adult PsA patients classified with CASPAR criteria and with >6 months follow up treated with first csDMARDs and bDMARDs were consecutively enrolled in our outpatient clinic. To assess disease activity, composite indices tailored for PsA namely DAPSA, cDAPSA, PASDAS, MDA (5/7) and MDA (7/7) were used. DAPSA and cDAPSA score ≤4, MDA 7/7 and PASDAS ≤1.9 identified remission while MDA 5/7and PASDAS <3.2 the minimal disease activity and inactive disease criterion[1–5].
Results: One hundred nine PsA patients were enrolled. Of this, 79 patients were in stable treatment with bDMARDs and 30 with csDMARDs. Overall, 28 (25.6%), 23 (21.1%), 19 (17.4%), 54 (49.5%), 13 (11.9%) and 35 (32.1%) PsA patients were in cDAPSA remission, DAPSA remission, MDA 7/7, MDA 5/7, PASDAS ≤1.9 and PASDAS <3.2. Patients in bDMARDs had a significantly low median DAPSA, cDAPSA and PASDAS score than patients treated with csDMARDs (table 1). Overall, the concordance between the indices ranging from slight to good.

Table 1. Demographic and clinical disease activity characteristics in patients treated with bDMARDs and csDMARDs

	bDMARDs (n=79)	csDMARDs (n=30)	P value
Female/male	38/41	16/14	ns
Mean age (SD), years	52.7 (12.4)	51.6 (12.3)	ns
Disease duration (SD), years	7.8 (9.3)	6.6 (8.2)	ns
PASI, median (25th-75th percentile)	0.3 (0–0.6)	1.5 (0–3.2)	0.02
Enthesitis (LEI) median (25th-75th percentile)	0 (0–1)	1 (0–3)	<0.01
CRP, mg/dl (25th-75th percentile)	0.3 (0.16–0.49)	0.3 (0.2–0.76)	ns
PASDAS, median (25th-75th percentile)	3.28 (2.69–3.72)	4.43 (3.73–4.76)	<0.01
MDA 5/7, n (%)	49 (62)	5 (16.6)	<0.01
MDA 7/7, n (%)	16 (20.2)	3 (10)	ns
DAPSA, median (25th-75th percentile)	6.8 (3.7–9.57)	18.1 (16.5–31.5)	<0.01
cDAPSA, median (25th-75th percentile)	6.5 (3.5–9.5)	17.5 (11.2–26.9)	<0.01

PASI: psoriasis area severity index; LEI: Leeds enthesitis index; CRP: C-reactive protein; PASDAS: psoriatic arthritis disease activity score; MDA: minimal disease activity, DAPSA: disease activity index for psoriatic arthritis.

Conclusions: PsA patients in bDMARD are more likely to reach a status of MDA and remission in respect to csDMARDs. PASDAS ≤1.9 and MDA 7/7 seem to be stringent remission criteria.
References:
[1] Coates LC et al. Defining disease activity in psoriatic arthritis: a proposed objective target for treatment. Ann Rheum Dis 2010;69:48–53.
[2] Coates LC et al. Defining low disease activity states in psoriatic arthritis using novel composite disease instruments. J Rheumatol 2016;43:371–5.
[3] Helliwell PS et al. The development of candidate composite disease activity and responder indices for psoriatic arthritis (GRACE project). Ann Rheum Dis 2013;72:986–91.
[4] Schoels MM et al. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. Ann Rheum Dis 2016;75:811–8.
[5] Nell-Duxneuner VP et al. Evaluation of the appropriateness of composite disease activity measures for assessment of psoriatic arthritis. Ann Rheum Dis 2010;69:546–49.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4359

AB0755 DEPRESSION AND ANXIETY MAY CONTRIBUTE TO HIGHER DISEASE ACTIVITY AND WORSE QUALITY OF LIFE IN PSORIATIC ARTHRITIS

F. Farkas[1], N. Ikumi[1], A. Szentpetery[1], B. Kirby[2], O. FitzGerald[1]. *[1]Department of Rheumatology; [2]Department of Dermatology, St. Vincent's University Hospital, Dublin, Ireland, Dublin, Ireland*

Background: Psoriatic arthritis (PsA) is a heterogeneous disease with variable types of joint involvement, extra-articular features, including skin psoriasis, and with well-known comorbidities such as depression and anxiety[1]. Composite Psoriatic Disease Activity Index (CPDAI) adequately assesses disease activity in this complex condition[2]. To date, no study has evaluated the relationship between depression/anxiety scores and CPDAI in PsA.
Objectives: The aim of this study was to compare 1) depression/anxiety scores; 2) physician-assessed and patient-reported outcome measures (PROMs) between patients with CPDAI≤4 suggesting low disease activity versus with CPDAI>4 reflecting moderate or severe disease activity in PsA.
Methods: PsA patients fulfilling the CASPAR criteria were recruited. Patients underwent musculoskeletal and skin assessments (TCJ68, SJC66, Leeds enthesitis index, dactylitis digit score and PASI) and they have completed questionnaires on physical function and health-related quality of life (HAQ, PsAQoL, DLQI, EQ-5D, BASDAI, BASFI, ASQoL, BRAF-NRS, pain and general health VAS). Patients were assessed for depression/anxiety using the Hospital Anxiety and Depression Scale (HADS-A and HADS-D) and Penn State Worry Questionnaire (PSWQ). Data were analyzed using Mann Whitney, Chi-square tests and linear regression model.
Results: 100 PsA patients were recruited; 57 presented with CPDAI≤4 (age 52.7±9.46 years) and 43 with CPDAI>4 (age 52±11.82 years). Patients with CPDAI>4 had significantly higher TCJ68 (p<0.001), Leeds enthesitis index (p=0.015) and significantly worse HAQ, BASDAI and ASQoL scores. There was no significant difference in other items of CPDAI between the two groups. Patients with CPDAI>4 had significantly higher HADS-D, HADS-A and PSWQ scores (p<0.001; p<0.001; p=0.001, respectively) and significantly worse PROMs, including PsAQoL, EQ-5D score, BASFI, BRAF-NRS, pain and general health VAS (Table 1). Multiple regression analysis revealed significant relationship between PsAQoL, BASFI and CPDAI (B=0.311, p=0.0093; B=0.568, p<0.0001, respectively).

Table 1. Comparison of patient-reported outcome measures between CPDAI ≤4 and CPDAI >4 groups

PROMs	CPDAI <4 n=57	CPDAI >4 n=43	p value
HADS-D	2.32±2.53	5.27±3.13	**<0.0001**
HADS-A	3.44±2.74	5.98±2.81	**<0.0001**
PSWQ	38.7±13.23	46.95±12.22	**0.001**
PAIN VAS	2.07±2.02	4.41±2.07	**<0.0001**
ghVAS	76.73±20.95	66.6±20.15	**0.005**
BRAF-NRS	12.35±4.51	16.41±4.76	**<0.0001**
PsAQoL	1.68±2.47	6.17±5.15	**<0.0001**
EQ-5D SCORE	0.82±0.15	0.66±0.19	**<0.0001**
BASFI	1.53±1.33	4.26±1.74	**<0.0001**

Mann-Whitney test. Results are presented as mean ± SD.

Conclusions: This is the first study assessing the relationship betweeen depression/anxiety and CPDAI in PsA. We have found significantly higher HADS-D, HADS-A, PSWQ scores and worse PROMs in patients with CPDAI>4 compared to those with CPDAI≤4. Based on our results there is significant relationship between depression/anxiety, physical function, quality of life and disease activity in psoriatic arthritis.
References:
[1] Haroon M. Expert Rev Clin Immunol. 2016.
[2] Mumtaz A. Ann Rheum Dis. 2011.
Disclosure of Interest: F. Farkas: None declared, N. Ikumi: None declared, A. Szentpetery: None declared, B. Kirby Grant/research support from: Abbvie, O. FitzGerald Grant/research support from: Abbvie, Pfizer, BMS, Consultant for: Abbvie, Pfizer, BMS, Novartis, Celgene, Janssen, UCB, Eli Lilly
DOI: 10.1136/annrheumdis-2017-eular.6825

AB0756 PRIMARY EFFICACY AND SAFETY OF ADALIMUMAB IN NAIL PSORIASIS FROM THE FIRST 26 WEEKS OF A PHASE-3, RANDOMIZED, PLACEBO-CONTROLLED TRIAL WITH SUBANALYSIS IN PATIENTS WITH AND WITHOUT PSORIATIC ARTHRITIS

B.E. Elewski[1], P.A. Rich[2], F. Behrens[3], G. Guillet[4], Z. Geng[5], O. Reyes Servin[5]. *[1]University of Alabama at Birmingham, School of Medicine, Birmingham; [2]Oregon Health and Science University Hospital, Portland, United States; [3]Goethe University Medical Center, Frankfurt, Germany; [4]Hopital la Miletrie, Service de Dermatologie, CHU Poitiers, France; [5]AbbVie Inc., North Chicago, United States*

Background: Psoriasis (Ps) disease burden for patients (pts) with psoriasis (Ps) and concomitant fingernail Ps plus psoriatic arthritis (PsA) is higher compared with pts with Ps alone.
Objectives: We report safety and efficacy of originator adalimumab (ADA) in pts with fingernail Ps, and also for pts with or without concomitant PsA.
Methods: Results are reported from the double-blind PBO-controlled, Period A in which 217 pts with moderate to severe plaque Ps and fingernail Ps were included and randomized 1:1 to receive 40 mg ADA every other week (eow) from wk 1 (initial 80 mg dose at wk 0), or matching PBO, for 26 wks. The primary endpoints were the proportion of pts with ≥75% improvement in modified Nail Ps Severity Index (mNAPSI 75) and the proportion of pts with Physician's Global Assessment of Fingernail Psoriasis (PGA-F) of clear (0) or minimal (1) with ≥2-grade reduction from baseline (primary in US only; for regulatory purposes). Missing data were handled by multiple imputation. Safety was assessed using treatment-emergent adverse events (AEs).
Results: Of the 217 randomized pts (108 PBO, 109 ADA), 84.3% were male; mean age was 46.7 years; 188 (86.6%) completed 26 wks of treatment or early escaped to Period B according to protocol. Both primary endpoints were met: total fingernail mNAPSI 75 was achieved by 3.4% PBO vs 46.6% ADA (p<0.001), and PGA-F 0 or 1 with ≥2 grades improvement was achieved by 6.9% vs 48.9% (p<0.001). At baseline, 28.6% had PsA (29.6% PBO, 27.5% ADA) with mean

duration 7.91 years [SD 8.314]. Total fingernail mNAPSI 75 was achieved by 0.5% PBO vs 61.5% ADA of pts with PsA and 4.6% PBO vs 40.9% ADA without PsA ($p<0.001$ for both groups). PGA-F 0 or 1 with $\geq$2-grade reduction was achieved by 4.4% PBO vs 59.3% ADA with PsA and 7.9% PBO vs 44.9% ADA without PsA ($p<0.001$ for both groups). Adverse events (AEs) in Period A were reported by 55.6% PBO vs 56.9% ADA (with PsA: 56.3% PBO vs 56.7% ADA; without PsA: 55.3% PBO vs 57.0% ADA without PsA); serious AEs by 4.6% PBO vs 7.3% ADA (with PsA: 9.4% PBO vs 10.0% ADA; without PsA: 2.6% PBO vs 6.3% ADA).

Conclusions: The primary results demonstrated that in this population, ADA was more effective than PBO for the treatment of fingernail Ps, and significantly improved signs and symptoms, both overall and regardless of the presence or abscense of PsA; no new safety risks were identified with ADA eow treatment for 26 wks.

Acknowledgements: AbbVie Inc. funded this study and participated in the study design; study research; collection, analysis and interpretation of data; and writing, reviewing and approving of this publication. All authors had access to the data, and participated in the development, review, and approval, and in the decision to submit this publication.

The authors would like to acknowledge Yihua Gu for statistical support, and Jody Bennett, for medical writing support in the production of this abstract; both are employed by AbbVie.

Disclosure of Interest: B. E. Elewski Grant/research support from: Abbvie, Amgen, Boehringer Ingelheim, Celgene, Incyte, Lilly, Merck, Novan, Novartis, Pfizer, Valeant, and Viamet, Consultant for: Anacor, Celgene, Lilly, Novartis, Pfizer, and Valeant, P. A. Rich Grant/research support from: AbbVie, Allergan, Amgen, Anacor, Cassiopea, Dusa, Eli Lilly, Galderma, Janssen, Leo, Meiji, Merck, Novartis, Pfizer, Psolar, Ranbaxy,Sandoz, and Viamet, Consultant for: AbbVie, Eli Lilly, Novartis, Sandoz, Polichem and Valeant, F. Behrens Grant/research support from: AbbVie, Amgen, Celgene, Janssen, Lilly, Novartis, Pfizer, Sandoz, and Sanofi, Consultant for: Abbvie, Chugai, Celgene, Genzyme, Lilly, Novartis, Pfizer, Roche, and Sanofi, G. Guillet Grant/research support from: AbbVie, Z. Geng Shareholder of: AbbVie, Employee of: AbbVie, O. Reyes Servin Shareholder of: AbbVie, Employee of: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.2148

AB0757 IMPACT OF DISEASE ACTIVITY ON PHYSICAL FUNCTION AND HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PSORIATIC ARTHRITIS

K. Nas[1], G. Kilic[2], R. Cevik[3], A.Z. Dagli[3], E. Kilic[4], S. Sag[1], U. Erkorkmaz[5], A. Kamanli[1], I. Tekeoglu[1]. *[1]Division of Rheumatology and Immunology, Department of Physical Medicine and Rehabilitation, Sakarya University Faculty of Medicine, Sakarya; [2]Physical Medicine and Rehabilitation, Afyon Kocatepe University Faculty of Medicine, Afyon; [3]Division of Rheumatology, Department of Physical Medicine and Rehabilitation, Dicle University Faculty of Medicine, Diyarbakir; [4]Rheumatology Clinic, Afyonkarahisar State Hospital, Afyon; [5]Department of Biostatistic, Sakarya University Faculty of Medicine, Sakarya, Turkey*

Background: Psoriatic arthritis (PsA) is a chronic progressive inflammatory disease characterized by peripheral arthritis, dactylitis, axial joint involvement and extraarticular features. Disease consequences such as chronic pain, severe joint damage and fatigue may adversely effect on a patient's physical function and health-related quality of life (QoL) to perform daily activities.

Objectives: The aim of this study was to investigate the potential relationship between physical function and health-related QoL and disease activity measures in patients with PsA.

Methods: For all participating patients, quality of life, functional and disease activity measures were measured by different ways: Nottingham Health Profile (NHP), psoriatic arthritis quality of life (PsAQoL), Ankylosing Spondylitis Quality of Life (ASQoL), SF36 health survey, Health Assessment Questionnaire (HAQ), BASFI, VAS pain, DAS28, BASDAI and acute phase markers including ESR and CRP.Patients with PsA were discriminated into low and high disease activity according to BASDAI ($\geq$6 vs $\leq$4).

Results: A total of 186 patients with PsA (116 female, 70 male, mean age 43,9±12,6) who met CASPAR criteria were included. Their mean symptom duration was 7.9±9.1 years. Patients with higher BASDAI score ($\geq$6) had significantly higher scores on all important items including health related QoL, fatigue, pain, and functional status. Correlation coefficients between disease activity and various health related QoL measurements were given in Table1. SF36 physical component score was significantly correlated with VAS-pain, BASDAI and DAS28 compared to SF36 mental component. Also, physical activity subscore of NHP was found higher correlated with disease activity indices for PsA in all NHP sections. Other quality of life measurements including PsQoL, HAQ and ASQoL were also significantly correlated with disease activity measurements.

Conclusions: Psoriatic arthritis has a major impact on patients' lives. Variable disease activity measurements were found correlated with all important QoL measurementss including NHP, SF36, PsQoL, HAQ and ASQoL. In patients with PsA, high disease activity may lead to severe impairments in daily activities and influence on participation in society.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6639

AB0758 AUDIT ON USTEKINUMAB DRUG SURVIVAL IN A DISTRICT GENERAL HOSPITAL VERSUS PSUMMIT 1 TRIAL RESULTS

G. Tracey, S. Webber. *Rheumatology, Weston General, Bristol, United Kingdom*

Background: Psoriatic arthritis (PsA) is an immune mediated inflammatory disorder that affects 10–30% of patients with psoriasis. Ustekinumab, a monoclonal anti–IL-12/23p40 antibody, is approved for the treatment of PsA and plaque psoriasis[1] PSUMMIT 1 was one of two phase 3 trials of ustekinumab in adults with active PsA[2]In England, use of medication is subject to guidance from National Institute for Health and Care Excellence (NICE). [TA340] recommend that Ustekinumab is a possible treatment, alone or with methotrexate, for adults with active psoriatic arthritis when treatment with non-biological disease-modifying antirheumatic drugs has not worked well enough if: treatment with tumour necrosis factor (TNF) alpha inhibitors is not suitable for them, or the person has had a TNF alpha inhibitor before[3] We audited the survival data from our cohort of patients in district general hospital (DGH) against data from PSUMMIT trial.

Objectives: Our objectives were to evaluate drug survival of Ustekinumab in PsA, to compare real world data with that from PSUMMIT trial.

Methods: Our biologics database was searched for patients currently receiving Ustekinumab treatment for Psoriatic Arthritis and those who have had treatment failures. Length of treatment was recorded and any adverse effects which caused the treatment to be stopped. Analysis of treatment non-responders was performed including previous biologics/drug use. We then compared our results to those in the treatment arms (Ustekinumab 45mg or 90mg)of the PSUMMIT trial at week 24 and 52.

Results:

Table 1

	Ustekinumab 45mg	Ustekinumab 90mg
DGH (n=20)	15	5
PSUMMIT (n=409)	205	204

Table 2

	DGH		PSUMMIT	
	(Ust 45mg)	(Ust 90mg)	(Ust 45mg)	(Ust 90mg)
Week 24 withdrawal	4/15	0/5	8/205	7/204
Reasons:				
Adverse effects	3		4	3
Inefficacy	1		2	1
Other (consent, lost follow up)			4	3
Week 52 withdrawal	0/8	0/3	17/197	15/197
Reasons:				
Adverse effects			2	5
Inefficacy			7	3
Other (consent, lost follow up)			8	7

Treatment Failure group (DGH): All patients had had at least one anti-TNF agent prior to Ustekinumab therapy. One patient had trialled 3, two had two, one had one. They had been stopped either due to inefficacy or intolerance.

Conclusions: Ustekinumab has been shown to be a generally well tolerated drug. Our treatment group had proportionally more treatment failures than the PSUMMIT trial (4/20 20% vs 24/409 5.8%). There is the obvious criticism that our patient numbers are very small. For eligibility in PSUMMIT trial the patients had to be anti-TNF naïve. In NHS ENgland, Ustekinumab is not NICE approved as a first line agent except in certain circumstances.Therefore, our patients have had

Abstract AB0757 – Table 1. Correlation coefficients between disease activity and various health related QoL measurements in patients with PsA [r (p)]

	VAS –pain	DAS 28	BASDAI	ESR	CRP
NHP-pain	0.571 (**<0.001**)	0.326 (**<0.001**)	0.644 (**<0.001**)	0.250 (**0.003**)	0.187 (**0.027**)
NHP-physical activity	0.599 (**<0.001**)	0.335 (**<0.001**)	0.652 (**<0.001**)	0.277 (**<0.001**)	0.111 (0.191)
NHP-fatigue	0.425 (**<0.001**)	0.324 (**<0.001**)	0.530 (**<0.001**)	0.287 (**<0.001**)	0.082 (0.337)
NHP-sleep	0.236 (**0.003**)	0.118 (0.162)	0.308 (**<0.001**)	0.113 (0.181)	-0.026 (0.764)
NHP-social isolation	0.214 (**0.008**)	0.299 (**<0.001**)	0.272 (**<0.001**)	0.080 (0.345)	-0.019 (0.824)
NHP-emotional reaction	0.315 (**<0.001**)	0.281 (**<0.001**)	0.326 (**<0.001**)	0.085 (0.315)	-0.023 (0.790)
SF36 physical component	-0.581 (**<0.001**)	-0.333 (**0.005**)	-0.449 (**<0.001**)	-0.346 (**0.004**)	-0.336 (**0.005**)
SF36 mental component	-0.439 (**<0.001**)	-0.232 (0.057)	-0.366 (**<0.001**)	-0.250 (**0.038**)	-0.198 (0.102)
PsAQoL	0.451 (**<0.001**)	0.285 (**<0.001**)	0.484 (**<0.001**)	0.103.(0.223)	-0.005 (0.955)
HAQ	0.428 (**<0.001**)	0.294 (**<0.001**)	0.386 (**<0.001**)	0.097 (0.246)	0.134 (0.107)
ASQoL	0.459 (**<0.001**)	0.459 (**<0.001**)	0.489 (**<0.001**)	0.220 (0.081)	0.068 (0.593)

previous exposure to anti-TNF agents to which they have either been intolerant or found ineffective. More research into drug survival and persistence should be considered as real world data may not reflect RCT results.

References:
[1] Stelara: package insert. Horsham (PA): Janssen Biotech; 2014.
[2] McInnes IB, Kavanaugh A, Gottlieb AB, Puig L, Rahman P, Ritchlin C, et al. Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1 year results of the phase 3, multicentre, double-blind, placebo-controlled PSUMMIT 1 trial. Lancet 2013;382:780–9.
[3] Ustekinumab for treating active psoriatic arthritis.NICE, Technology appraisal guidance [TA340] Published date: 04 June 2015.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4003

AB0759 NEUROPATHIC PAIN PREVALENCE IN PSORIATIC ARTHRITIS AND ITS CORRELATION WITH DISEASE ACTIVITY

H.E. Öz[1], S. Tuna[1], Ü. Gürbüz Uçar[2], N. Vedin Balcı[1]. *[1]Physical Therapy and Rehabilitation, Akdeniz University, Antalya; [2]Rheumatology, Izmir Bozyaka Training and Research Hospital, Izmir, Turkey*

Background: Psoriatic arthritis (PsA) is a systemic chronic inflammatory disease associated with psoriasis. Neuropathic pain is defined as pain which is produced by a primary lesion or dysfunction of peripheral or central nervous system.
Objectives: The aim of this study is to investigate the neuropathic pain component of chronic joint pain in psoriatic arthritis and to detect its correlation with disease activity and functional capacity.
Methods: During the patients' routine outpatient clinic visit, we gain information about patients' demographics. We used Pain Detect questionnaire to detect neuropathic pain component, Visual Analogue Scale for joint pain, Disease Activity Score 28-Joint (DAS28) for disease activity evaluation and Health Assessment Questionnaire (HAQ) for functional capacity evaluation.
Results: There were 48 PsA patients and 34 control patients in this study. Mean age was 52 (21–79), mean BMI is 27.5 kg/m^2 (20.8–53) and mean disease duration was 5 year in PsA group. Mean age was 54 (20.8–53), mean BMI was 27.6 kg/m^2 (20.8–53) in control group. Neuropathic pain component was positive in 22.9% of PsA and negative in 45.8% of PsA and unclear in 31.2% of PsA group. In control group, neuropathic pain component was positive in 35.3% of patients and negative in 41.2% of patients and unclear in 23.5% of patients. Mean pain detects score was 13 in PsA and 14 in control group. There was no statistically important difference between the PsA and control group's neuropathic pain prevalence (p=0.601) and mean PD score (p=0.24). Mean DAS 28 score was 3.5 (1–3.56) and mean HAQ score was 0.65 (0–2.05) in PsA group. There was a statistically important positive correlation between the PD score and HAQ score in PsA patients (Ro=0.460, p=0.001). In addition, there was a statistically unimportant positive correlation between the PD score and DAS28 score in PsA patients. There was a statistically unimportant positive correlation between the PD score and HAQ score in control group (Ro=0.411, p=0.016).
Conclusions: We detected neuropathic pain component in 22.9% of PsA patients but there was no difference between the PsA group and control group. Diagnosis of concomitant neuropathic pain by Pain Detect Questionnaire may be useful for pain management in PsA patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3711

AB0760 EFFICACY OF USTEKINUMAB IN A COHORT OF PATIENTS AFFECTED BY PSORIATIC ARTHRITIS IN REAL-LIFE

I. Notario Ferreira, M. Ferrer González, P. Morales Garrido, I. Añón Oñate, L. Perez Albaladejo, C. Caro Hernández, A. González Utrilla, E. Raya Álvarez, R. Cáliz Cáliz. *Rheumatology, Complejo Hospitalario Universitario de Granada, Granada, Spain*

Background: Psoriatic arthritis (APs) is a chronic inflammatory joint disease, that can be treated effectively with synthetic disease modifying anti-rheumatic drugs (DMARDs) and biological agents. Ustekinumab is a monoclonal antibody that inhibits IL-12 and 23 that has recently demonstrated efficacy and safety for the treatment of patients with APs in the PSUMMIT 1 and PSUMMIT 2 studies.
Objectives: To evaluate the efficacy of Ustekinumab in our patients with psoriatic arthritis with peripheral involvement in clinical practice conditions.
Methods: Descriptive, prospective, longitudinal and open study including patients diagnosed with psoriatic arthritis with peripheral involvement. All patients were given ustekinumab at an initial dose of 45 mg administered subcutaneously followed by another 45 mg dose 4 weeks later and then every 12 weeks. Clinimetric scores (DAS28, MASES, Pain VAS, Clinicians VAS) were assessed and CRP was measured al baseline and after 6 months of treatment.
Results: 52 patients were included, 25 were female (48.1%) and 27 male (51.9%). They had a mean age of 46.96±11.39 years, a disease duration of 5.03±5.08 years, and moderate disease activity (DAS 28 of 3.95±0.87), the number of tender and swollen joints were 6.24±4.9 and 2.82±2.36, respectively. The patients had received an average of 1.42±1.75 biological therapies previously. Ustekinumab was prescribed as a first line treatment in 42.3% of patients, 19% after failure of a TNF inhibitor and 38% of patients had received 2 or more biological therapies previously. Ustekinumab was administered alone in 51% of the patients, 36.5% in combination with methotrexate and 11.5% in combination with leflunomide. 23.1% of the patients had dactylitis and 36.5% had enthesitis (mean MASES 1.31±0.86). At 6 months of treatment, there were improvements in the number of tender and swollen joints (mean NAD 4.84±6.4 and NAT 2±3.4 at 6 months, respectively) and MASES index (mean at 6 months, 0.35±0.96). 15 patients had completed at least 6 months of treatment. Improvements in DAS28-CRP scores were observed at 6 months of treatment (3.26±1.62), with a mean DAS28 change after 6 months (∆DAS28) of -0.65±1.88. At month 6, 71.4% of the patients had low disease activity, and 35.7% were in clinical remission according to the DAS28 index.
Conclusions: Ustekinumab is effective in patients with psoriatic arthritis with peripheral involvement in routine clinical practice.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3675

AB0761 THE BIOLOGIC THERAPY USE FOR ENTHESITIS AS A PREDICTOR OF PSORIATIC ARTHRITIS IN PSORIATIC PATIENTS

I. Litovchenko[1], O. Golovchenko[2]. *[1]Medical Clinical Investigational Center of Medical Center "Health Clinic", Medical Center Health Clinic; [2]Medical Clinical Investigational Center of Medical Center "Health Clinic", Medical Center "Health Clinic", Vinnytsia, Ukraine*

Background: According to ACR data 15–20% patients (PTN) with psoriasis are developed with psoriatic arthritis (PsA). Herewith the enthesitis (ETS) as usual is the first signs of PsA manifestations. It is usually asymptomatic at the beginning of the disease, however it is successfully diagnosed with Doppler ultrasound (DU). In average, it takes about 2 years from beginning of the disease till diagnosis PsA is established. PsA treatment is low effective with DMARD, and middle effective with biologic therapy. Wherein no treatment restores the articular changes that have occurred. Thus the actual is to find some resolution to the effective therapy for PTN with psoriasis and also to identify the factors preceding the development of the PsA.
Objectives: Consider the application of biologic therapy before the articular changes in PTN with psoriasis and predictors of psoriatic arthritis.
Methods: Observed 82 PTN with pustural psoriasis without clinical manifestations of PsA. A physical examination (including PASI), a series of laboratory tests (hematology, CRP, RF, anti -ccp, HLA-B27, uric acid), DU to identify the PsA, its activity, as well as to the exclusion of other types of arthritis were used.
Results: 3,7% PTN were diagnosed with PsA with articular changes. 23,1% PTN were founded with enthesitis. The remaining 73,2% PTN had no signs of enthesitis during physical examination and DU. PTN with enthesitis were divided into 2 groups. I – 47% PTN (22% of them had clinical manifestations of enthesitis; the average group PASI– 42,4±8,2) received a 52-weeks course of ustekinumab (45 mg administered subcutaneously initially and 4 weeks later, followed by 45 mg administered subcutaneously every 12 weeks). II group – 53% people (20% PTN had clinical manifestations of enthesitis; the average group PASI– 43,6±9,0) did not receive biological therapy, but only standart treatment for psoriasis. After 1 year follow-up after completion of the treatment course – 11% PTN from group I developed PsA with articular changes. From the group II in 80% PTN developed PsA with articular changes. The average group I PASI– 7,6±1,5; the average group PASI– 6,2±1,3. ($p < 0,05$)
Conclusions: Thus, the ustekinumab use in psoriatic PTN with enthesitis possibly may be reasonable and will hinder the development of PsA. Ustekinumab is also high effective for the improving of the psoriasis skin symptoms.
DU is the high effective diagnostic method for detecting enthesitis without clinical manifestations.
Frequency of screening DU in PTN with psoriasis, for the early detection of enthesitis is the perspective for further study.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6153

AB0762 THE RELATIONSHIP BETWEEN SERUM PENTRAXIN-3 LEVELS, CARDIOVASCULAR DISEASE RISK AND DISEASE ACTIVITY IN PSORIATIC ARTHRITIS PATIENTS

I. Sunar[1], A.E. Ozdemirel[2], Z.S. Sürmeli[3], G. Yilmaz[1], E. Üstüner[4], H. Tutkak[5], A.P. Yalçin[1], S. Ataman[1]. *[1]Rheumatology, Ankara University Faculty of Medicine Physical Medicine and Rehabilitation, Rheumatology Division; [2]Rheumatology, Health Ministry Ankara Dışkapı Trainig and Research Hospital, Rheumatology Clinic, Ankara; [3]3. Health Ministry Istanbil Trainig and Research Hospital, Rheumatology Clinic, Istanbul; [4]Radiology, Ankara University Faculty of Medicine; [5]Immunology and Allergy, Ankara University Faculty of Medicine, Immunology an Allergy Department, Ankara, Turkey*

Background: Psoriatic arthritis (PsA) is an immune-mediated disease affecting skin, joints, entheses, spine, and the vasculature [1,2]. Increased inflammatory mediators are held responsible for impacts on the skin and musculoskeletal system as well as comorbid situations including cardiovascular disease (CVD) and metabolic syndrome [3]. PTX 3 is an acute phase reactant that has prognostic value for rheumatoid arthritis (RA), vasculitis, and psoriasis that also stands out as a novel biomarker for CVD in new researches [4].

Objectives: This study aims to assess the association between PTX 3 levels, disease activity and CVD risk in patients with PsA.
Methods: A total of 38 PsA patients applying to Ankara University Faculty of Medicine, Rheumatology Polyclinic and 32 age and sex-matched controls were enrolled in the study. tender and swollen joint counts, patient's and doctor's global assesment on VAS, ESR, CRP, fasting insulin, fasting glucose, total cholesterol, HDL, and LDL were noted. Also body mass index (BMI) and HOMA-IR score were calculated. Carotid intima media thickness (cIMT) was bilaterally assessed by Doppler ultrasound.
Results: The mean age was 49.5 in patients and 48.9 in controls. Sixty percent of the patients and 50% of controls were female. Of the patients, 15 (39%) used DMARD monotherapy, 8 (21%) used DMARD combination therapies, and 15 (39%) used anti TNF therapies. There was no statistically significant difference between groups in terms of hypertension, LDL levels, and smoking status (p:0.775, p:0.228, p:0.136 respectively). PsA patients had significantly higher BMI scores (p:0.03). Insulin levels and HOMA-IR scores were significantly higher among PsA patients compared to controls (p:0.001, p:0.005). There was statistically significant difference between groups in terms of PTX 3 ($p<0.001$). PTX 3 was significantly correlated with HOMA-IR and cIMT (r:0.243 p:0.043 and r:0.421 p:0.001 respectively). However no correlation between PTX 3 and disease activity parameters such as ESR, CRP, SJC, TJC, and VAS-pain was detected (p:0.824, 0.662, 0.922, 0.924, 0.410 respectively). There was not significant difference in terms of PTX-3 levels between PsA patients on biologic treatment or other treatment strategies (p:0.27).
Conclusions: Elevated levels of PTX 3 may be associated with cardiovascular involvement in PsA patients independent from the disease activity. This marker might be used for risk prediction for CVD or may represent a target for new therapies.
References:
[1] Braun J. New targets in psoriatic arthritis. Rheumatology (Oxford). 2016 Dec;55(suppl 2).
[2] Egeberg A. Psoriasis and comorbidities. Epidemiological studies. Dan Med J.2016 Feb;63(2).
[3] Rutter MK, Kane K, Lunt M, et al. Primary care based screening for cardiovascular risk factors in patients with psoriasis. Br J Dermatol. 2016 Mar 1.
[4] Inoue K, Kodama T, Daida H. Pentraxin 3: a novel biomarker for inflammatory cardiovascular disease Int J Vasc Med. 2012;2012:657025.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3757

AB0763 USTEKINUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS – RESULTS OF THE FIRST INTERIM ANALYSIS OF THE NON-INTERVENTIONAL STUDY SUSTAIN

J. Wendler[1], I. Schwarze[2], H. Schwenke[3], J. Behrens[4], T. Gruppe[4], F. Behrens[5]. *[1]Rheumatologische Schwerpunktpraxis, Erlangen; [2]Praxis für Internistische Rheumatologie, Leipzig; [3]Rheumatologisches MVZ Dresden, Dresden; [4]Janssen-Cilag GmbH, Neuss; [5]CIRI/Rheumatology & Fraunhofer TMP, Frankfurt, Germany*

Objectives: SUSTAIN is a prospective, multi-center non-interventional study in Germany to observe long term efficacy and safety, quality of life and further patient reported outcomes in patients with active psoriatic arthritis under treatment with Ustekinumab in routine clinical care.
Methods: In this study treatment with Ustekinumab is according to the label (Stelara®). It is planned to observe 400 patients at 75 centers for 160 weeks with documentation intervals at week 0 and 4 and then every 12 weeks. Besides demographic data, the following data will be documented: Amount of swollen and tender joints, tender entheses, skin symptoms (BSA and PASI), patient reported outcome concerning disease activity and pain, Health Assessment Questionnaire (HAQ), quality of life (SF-12), sleep quality (VAS), satisfaction with therapy of patient and physician, safety (adverse events [AE]/serious adverse events [SAE]), pharmacoeconomic aspects, number of patients with "Minimal Disease Activity" (MDA), number of patients with MDA at week 28 und 52.
Results: Overall, there have been 189 patients (56% women) at 59 centers documented after 11 months. At week 4 154 patients and at week 16 112 patients. At baseline, the patients had a mean age of 56 years (29–85), body weight 87 kg (50–147), BMI 30 (19–47), showed arthritis at small (68.8%) and/or big (51.3%) joints, skeletal involvement (19%), enthesitis (13.2%). The number of tender joints improved from a mean of 8,6 (CI 95% 7.1/10.2) to 4.7 (3.1/6.3) at week 16, number of swollen joints from 3,4 (2,6/4,2) to 1,4 (0.9/1.9). The patient reported global disease activity (0–100) decreased from 55.1 to 38.6 at week 16. Further improvements were documented for enthesitis, PSA, BSA, PASI, and pain. Efficacy of the therapy with Ustekinumab after 16 weeks was assessed as "very good" by 32.3% and as "good" by 44.8% of the treating physicians and by 34% and 40.2%, respectively, of the patients. In total, 60 adverse events were reported, of which four were serious. All in all safety of therapy with Ustekinumab after 16 weeks was assessed as "very good" by 51% and as "good" by 43.8% of the treating physicians, and by 55% and 37%, respectively, of the patients.
Conclusions: The non-interventional study SUSTAIN showed relevant improvements with elevated therapy satisfaction and good safety in patients with active psoriatic arthritis after 16 weeks under real world condition.
Disclosure of Interest: J. Wendler Consultant for: Janssen-Cilag GmbH, Speakers bureau: Janssen-Cilag GmbH, I. Schwarze: None declared, H. Schwenke: None declared, J. Behrens Employee of: Janssen-Cilag GmbH, T. Gruppe Employee of: Janssen-Cilag GmbH, F. Behrens Consultant for: Janssen-Cilag GmbH, Speakers bureau: Janssen-Cilag GmbH
DOI: 10.1136/annrheumdis-2017-eular.3764

AB0764 MALIGNANCY AND SERIOUS INFECTIONS AMONG PSORIATIC ARTHRITIS PATIENTS TREATED WITH BIOLOGICAL DRUGS IN A REGIONAL REGISTRY IN THE NORTHWEST OF SPAIN

J. Pinto-Tasende[1], F.J. Maceiras-Pan[2], L. Guerra-Vazquez[3], L. Fernandez-Dominguez[4], J.A. Mosquera-Martínez[5], C. García-Porrúa[6]. *[1]INIBIC-Rheumatology, Complejo Hospitalario Universitario A Coruña, A Coruña; [2]Rheumatology, Complejo Hospitalario Universitario de Vigo, Vigo; [3]Rheumatology, Complejo Hospitalario Universitario de Ferrol, Ferrol; [4]Rheumatology, Complejo Hospitalario Universitario de Ourense, Ourense; [5]Rheumatology, Complejo Hospitalario Universitario de Pontevedra, Pontevedra; [6]Rheumatology, Hospital Universitario de Lugo, Lugo, Spain*

Background: Biological treatments have provided new opportunities for disease control for patients with psoriatic arthritis. However, it is important to evaluate their safety, since they expose them to an increased risk of developing malignant tumors and serious infections.
Objectives: To examine the rate of solid tumors and serious infections among patients diagnosed with psoriatic arthritis (PsA) treated with biological drugs (BD) in 2011–2015.
Methods: We included all PsA patients (CASPAR criteria) under treatment with BD followed in our regional registry (reference population 2.055.000) between January 2011 and December 2015. In order to capture the incidence of new malignancy we excluded patients with a prior history of malignancy. Medical records were fulfilled for patients and were recorded solid tumors diagnosed (date of diagnosis and histology information) and all serious infections (requiring hospitalization or intravenous antibiotics) in this time. Incidence rates (IRs) were calculated per 1000 Person-year (py). We used for this analysis sex, age, disease duration, current BD with or without current DMARD associated. Continuous variables were reported as mean ± standard deviation (SD). Categorical variables were reported as percentages and frequencies. Differences were considered statistically significant if $p<0.05$ (two-tailed).
Results: Among 604 patients 329 (54.5%) of whom were men, with a mean age of 53.3±12.6 years and a time since the diagnosis of PsA of 12.4±8.7 years. There were 14 cancers diagnosed during treatment (2.3%), with an IR of 0.48 cases per 1000 patient-years. Patients who developed cancer had a higher age, 63.4±10.0 years vs 53.1±12.6, than those who did not developed (p=0.010). Etanercept was the most used (42%) and no differences were observed among BDs (p=0.214) or between naïve and non-naïve to BD (p=0.384). Current DMARD associated (56.2%) had not differences in tumors (p=0.429). Prostate tumor was the most frequent (21.4%). There were 42 had serious infection (6.2%), with an IR of 13.9 cases per 1000 patient-years, and was more common in men (4.7% vs 8.8%, p=0.049). Severe infections were more frequent in patients non-naïve to BD (10.4% vs 5.4%, p=0.026). Pneumonia (28.6%), varicella-zoster virus infection (16.6%) and soft tissue infections (14.3%) were most frequent. Latent tuberculosis infection was positive in 133 patients (22.0%) and 3 developed tuberculosis.
Conclusions: Patients older than 60 years with psoriatic arthritis treated with BDs had a higher incidence of tumor development. Most of patients were men and prostate tumor was the most frequent. Pneumonia was the most frequent serious infection and non-naïve to BD patients had a higher IR of serious infections.
References:
[1] Malignancy incidence in patients with psoriatic arthritis: a comparison cohort-based incidence study. Wilton KM, Crowson CS, Matteson EL.Clin Rheumatol. 2016 Oct; 35(10):2603–7.
Acknowledgements: The authors are grateful for the support of the members of the Galician Society of Rheumatology (SOGARE).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3300

AB0765 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENT IN FUNCTION, QUALITY OF LIFE AND FATIGUE OVER 2 YEARS IN PATIENTS WHO ACHIEVED DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS (DAPSA) REMISSION

J.S. Smolen[1], I.B. McInnes[2], L. Gossec[3], V. Strand[4], L. Pricop[5], T. Fox[6], S. Jugl[6], C. Gaillez[6] on behalf of the FUTURE 2 Study Group. *[1]Medical University of Vienna, Vienna, Austria; [2]University of Glasgow, Glasgow, United Kingdom; [3]UPMC Université Paris 06, Paris, France; [4]Stanford University School of Medicine, Stanford; [5]Novartis Pharmaceuticals Corp., East Hanover, United States; [6]Novartis Pharma AG, Basel, Switzerland*

Background: Disease Activity index for Psoriatic Arthritis (DAPSA) states are associated with functional impairment levels in patients (pts) with psoriatic arthritis (PsA).[1] Secukinumab demonstrated sustained improvements in disease activity assessed with DAS28-CRP, physical function and pt-reported outcomes (PROs) among active PsA pts over 104 weeks (wks) in the FUTURE 2 study.[2]

Abstract AB0765 – Table 1. Core components by DAPSA states with secukinumab or placebo at Wk 16

Mean ± SD	SJC (66)		TJC (68)		PtGA (cm)		PP (cm)		CRP (mg/dl)	
	300mg/150mg	PBO	300mg/150mg	PBO	300mg/150mg	PBO	300mg/150mg	PBO	300mg/150mg	PBO
REM*	0.4±0.7/0.2±0.4	1.0±1.4	0.2±0.4/0.3±0.5	0.5±1.0	0.6±0.5/0.6±0.5	0.6±0.6	0.7±0.7/0.7±0.4	0.8±0.6	0.3±0.3/0.5±0.4	0.2±0.2
LDA^	1.7±2.3/1.4±1.6	1.6±2.0	2.5±1.9/1.8±2.2	2.3±2.7	2.3±1.6/2.1±1.2	2.3±1.8	2.3±1.3/2.3±1.3	2.6±1.8	0.4±0.4/0.4±0.7	0.2±0.3
MDA#	4.5±3.8/4.9±3.0	4.9±3.4	6.0±4.1/7.0±2.8	7.5±4.1	3.8±2.3/3.9±1.9	3.9±1.8	4.1±2.0/3.8±1.8	4.5±1.8	0.4±0.4/0.9±1.0	0.7±1.2
HDA$	10.7±7.5/14.4±11.1	10.4±7.2	24.6±12.4/29.2±19.0	26.6±15.2	4.9±1.7/5.6±2.0	5.9±1.8	5.2±1.9/5.6±1.8	6.1±1.5	0.4±0.4/0.6±0.7	1.2±1.7

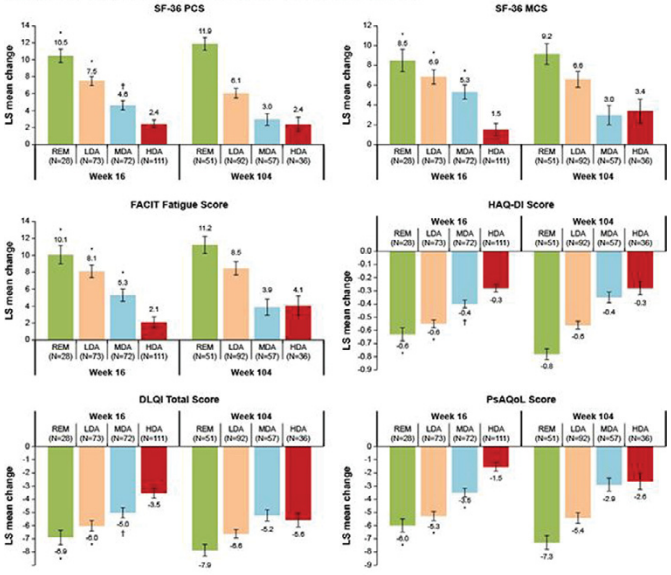
*n=14 (300mg), 10 (150mg) and 4 (PBO); ^n=27 (300mg), 34 (150mg) and 12 (PBO); #n=26 (300mg), 24 (150mg) and 22 (PBO); $n=30 (300mg), 32 (150mg) and 49 (PBO).

Objectives: To explore the relationship between DAPSA states and function, health-related quality of life and PROs, and the individual DAPSA components in the different states in pts treated with secukinumab through 104 wks using *post-hoc* analysis.

Methods: FUTURE 2 study design has been reported.[3] DAPSA was derived as sum of five core components: tender joint and swollen joint counts (TJC 68, SJC 66), pt global assessment (PtGA) and pain (PP) assessed by a 10cm VAS and CRP (mg/dl). Four DAPSA states were: remission (REM:≤4), low (LDA:>4–≤14), moderate (MDA:>14–≤28) or high disease activity (HDA:>28). Mean±SD of each core component of DAPSA were analysed at Wks 16, 24, 52 and 104 using observed data. The relationship between HAQ-DI, SF-36 PCS and MCS, PsAQoL, DLQI and FACIT-Fatigue with DAPSA states was assessed in the pooled treatment arms at each time point using a mixed-effect model for repeated measures (MMRM) analyses.

Results: Baseline characteristics were similar across treatment groups.[3] DAPSA scores at baseline (mean±SD) were 42.0±17.4, 46.8±24.3 and 44.9±25.3 in the secukinumab 300mg, 150mg and placebo groups, respectively. Mean scores of each component by DAPSA states at Wk 16 are shown in table and were sustained through Wk 104. Significant differences were observed among secukinumab treated pts between REM vs. HDA and LDA vs. HDA states for PRO scores through Wk104 (Figure).

Figure: Mean change in PRO scores by DAPSA states at Wks 16 and 104



*P <0.0001; †P <0.001; ‡P <0.01; §P <0.05 versus HDA. P-values are from a mixed-effects model for repeated measures (MMRM) analysis.
DLQI, Dermatology Life Quality Index; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire Disability Index; HDA, high disease activity; LDA, low disease activity; LS, least squares; PsA QoL, PsA-specific quality of life; MDA, moderate disease activity; REM, remission; SF-36 MCS, Short Form-36 Mental Component Summary; SF-36 PCS, Physical Component Summary

Conclusions: In pts treated with secukinumab 300 or 150mg, the five individual components related to DAPSA REM were <1 in contrast with other disease states and were sustained through Wk 104. DAPSA REM was associated with significantly greater improvement in physical function, health related quality of life and fatigue indicating that it is an important target to be achieved and sustained in PsA pts.

References:

[1] Schoels MM, et al. Ann Rheum Dis 2016;75:811–8.
[2] McInnes IB, et al. Arthritis Rheumatol 2016;68(suppl 10).
[3] McInnes IB, et al. Lancet 2015;386:1137–46.

Disclosure of Interest: J. Smolen Grant/research support from: AbbVie, Janssen, Eli Lilly, MSD, Pfizer, Roche, Amgen, AstraZeneca, Astro, Celgene, Celltrion, GSK, ILTOO, Medimmune, Novartis-Sandoz, Pfizer, Samsung, Sanofi and UCB., Consultant for: AbbVie, Janssen, Eli Lilly, MSD, Pfizer, Roche, Amgen, AstraZeneca, Astro, Celgene, Celltrion, GSK, ILTOO, Medimmune, Novartis-Sandoz, Pfizer, Samsung, Sanofi and UCB., I. McInnes Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer and UCB, L. Gossec Grant/research support from: UCB, Eli Lilly and Pfizer; Consultant for AbbVie, BMS, Celgene, Janssen, Novartis, Pfizer and Roche, V. Strand Consultant for: AbbVie, Amgen, BMS, Celgene, Celltrion, Corrona, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sanofi and UCB, L. Pricop Shareholder of: Novartis, Employee of: Novartis, T. Fox Shareholder of: Novartis, Employee of: Novartis, S. Jugl Shareholder of: Novartis, Employee of: Novartis, C. Gaillez Shareholder of: Novartis and BMS, Employee of: Novartis

DOI: 10.1136/annrheumdis-2017-eular.3648

AB0766 SECUKINUMAB PROVIDES SUSTAINED REMISSION AND LOW DISEASE ACTIVITY RELATED TO DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS (DAPSA): 2 YEAR RESULTS FROM THE FUTURE 2 STUDY

J.S. Smolen[1], I.B. McInnes[2], T.K. Kvien[3], L. Pricop[4], T. Fox[5], L. Rasouliyan[6], S. Jugl[5], C. Gaillez[5] on behalf of the FUTURE 2 Study group. *[1]Medical University of Vienna, Vienna, Austria; [2]University of Glasgow, Gasgow, United Kingdom; [3]Diakonhjemmet Hospital, Oslo, Norway; [4]Novartis Pharmaceuticals Corp., East Hanover, United States; [5]Novartis Pharma AG, Basel, Switzerland; [6]RTI Health Solutions, Barcelona, Spain*

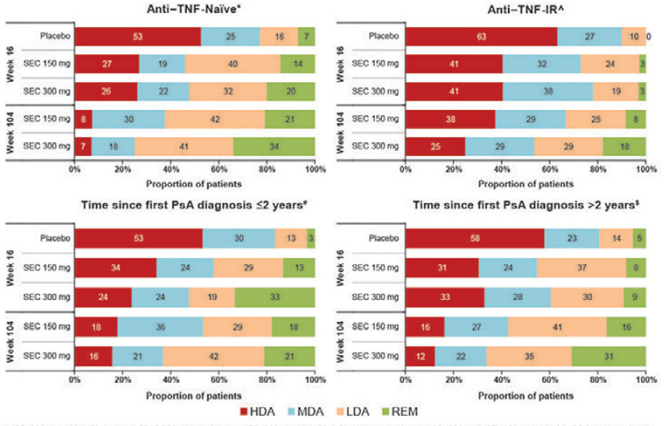
Background: Disease Activity Index for Psoriatic Arthritis (DAPSA) is a validated tool to measure disease activity states, focussing on peripheral joint involvement in psoriatic arthritis (PsA), and can be used to assess targets such as remission (REM) or low disease activity (LDA).[1]

Objectives: Secukinumab, a fully human anti–interleukin-17A monoclonal antibody, significantly improved American College of Rheumatology responses vs. placebo at Week (Wk) 24 that were sustained through Wk 104 in active PsA patients (pts) in the FUTURE 2 study[2]. This *post-hoc* exploratory analysis assessed DAPSA states through Wk 104.

Methods: In total, 397 active PsA pts were randomised to subcutaneous (s.c) secukinumab (300, 150 or 75mg) or placebo at baseline and Wks 1, 2, 3 and 4, and every 4 wks (q4w) thereafter. Placebo pts were re-randomised to secukinumab 300 or 150mg s.c q4w from Wk 16 or 24, depending on Wk 16 clinical response. DAPSA was derived as the sum of five variables: tender joint and swollen joint counts (TJC 68 and SJC 66); pt global and pain assessed on a 10cm visual analogue scale; and C-reactive protein levels (mg/dl) with validated cut-offs to indicate REM (≤4), LDA (>4 and ≤14), moderate disease activity (MDA; >14 and ≤28) and high disease activity (HDA; >28). DAPSA was assessed in the overall population and in pts stratified by prior anti-tumour necrosis factor (anti-TNF) therapy use (anti–TNF-naïve vs. inadequate response/intolerance to these agents [anti–TNF-IR]) and time since first PsA diagnosis (≤2 vs. >2 years) using observed data. Only data for secukinumab 300 and 150mg (approved doses) are reported.

Results: Baseline demographics and clinical characteristics were similar across treatment groups and previously reported.[3] DAPSA score at baseline (mean [SD]) was 42.0 (17.4), 46.8 (24.3) and 44.9 (25.3) in the secukinumab 300mg, 150mg and placebo groups, respectively. In the overall population, at Wk 16, REM was achieved in 14/97 (14.4%) with secukinumab 300mg and 10/100 (10%) with secukinumab 150mg vs. placebo 4/87 (4.6%); LDA in 27/97 (27.8%) and 34/100 (34%) vs. 12/87 (13.8%), respectively. REM or LDA were sustained through Wk 104 with secukinumab 300 and 150mg (55/84 [65.5%; REM + LDA] and 41/ 77 [53.2%; REM + LDA], respectively). The proportion of pts achieving each DAPSA state at Wks 16 and 104 by anti-TNF status (anti–TNF-naïve vs. anti–TNF-IR)

Figure. DAPSA at Wks 16 and 104 by anti-TNF status and Disease duration



*n= 65 (300 mg), 63 (150 mg) and 57 (PBO) at Wk 16 and n= 56 (300 mg) and 53 (150 mg) at Wk 104; ^n= 32 (300 mg), 37 (150 mg) and 30 (PBO) at Wk 16 and n= 28 (300 mg) and 24 (150 mg) at Wk 104; #n= 21 (300 mg), 38 (150 mg) and 30 (PBO) at Wk 16 and n= 19 (300 mg) and 28 (150 mg) at Wk 104; $n= 76 (300 mg) 62 (150 mg) and 57 (PBO) at Wk 16 and n= 65 (300 mg) and 49 (150 mg) at Wk 104

and by time since diagnosis (≤2 vs. >2 years) for secukinumab 300 and 150mg is presented in the figure.
Conclusions: In the overall population, a higher proportion of pts treated with secukinumab at Wk 16 achieved DAPSA REM than those treated with placebo, with REM and LDA sustaining through Wk 104. At Wk 16, a higher proportion of anti–TNF-naïve pts treated with secukinumab achieved and sustained DAPSA REM than anti–TNF-IR pts and a higher proportion of pts with early diagnosis (≤2 years) achieved DAPSA REM vs. pts diagnosed later (>2 years).
References:
[1] Schoels MM, et al. Ann Rheum Dis 2016;75:811–8.
[2] McInnes IB, et al. Arthritis Rheumatol 2016;68 (suppl 10).
[3] McInnes, et al. Lancet 2015;386:1137–46.
Disclosure of Interest: J. Smolen Grant/research support from: AbbVie, Janssen, Eli Lilly, MSD, Pfizer, Roche, Amgen, AstraZeneca, Astro, Celgene, Celltrion, GSK, ILTOO, Medimmune, Novartis-Sandoz, Pfizer, Samsung, Sanofi and UCB., Consultant for: AbbVie, Janssen, Eli Lilly, MSD, Pfizer, Roche, Amgen, AstraZeneca, Astro, Celgene, Celltrion, GSK, ILTOO, Medimmune, Novartis-Sandoz, Pfizer, Samsung, Sanofi and UCB., I. McInnes Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB., Consultant for: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB., Speakers bureau: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, and UCB., T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB., Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB., L. Pricop Shareholder of: Novartis, Employee of: Novartis, T. Fox Shareholder of: Novartis, Employee of: Novartis, L. Rasouliyan Consultant for: Novartis through employment at RTI, Employee of: RTI Health Solutions, S. Jugl Shareholder of: Novartis, Employee of: Novartis, C. Gaillez Shareholder of: Novartis and BMS, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.4666

AB0767 IL-17-22-23 PATHWAYS IN PSORIATIC ARTHRITIS AND PSORIASIS

K. Nas[1], R. Cevik[2], I. Yildiz[3], J. Rech[4], G. Schett[4]. *[1]Division of Rheumatology and Immunology, Department of Physical Medicine and Rehabilitation, Sakarya University, Faculty of Medicine, Sakarya; [2]Division of Rheumatology, Department of Physical Medicine and Rehabilitation; [3]Department of Biostatistic, Dicle University, Faculty of Medicine, Diyarbakir, Turkey; [4]Department of Internal Medicine and Institute for Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Germany*

Background: Psoriatic arthritis (PsA) is an immune-mediated chronic inflammatory arthropathy-associated with psoriasis. T helper 17 pathway has been shown to play an important role in PsA.
Objectives: In this study, we aimed to investigate concentrations of TH17 pathway cytokines such as IL-17, IL-22 and IL-23 in psoriasis (PsO) with/and without structural bone damage and psoriatic arthritis (PsA), and their relationship with disease activity and clinical findings.
Methods: A total number of 74 patients, 24 patients with PsA (mean age 57.5±11.37; 13 women, 11 men) and 25 patients with PsO and structural bone damage (mean age 49±13.92; 11 women, 14 men) and 25 patients with PsO and no structural bone damage (mean age 41±16.77; 7 women, 18 men), were recruited from the Department Internal Medicine 3 of the University of Erlangen-Numberg. Both PsO and PsA patients were evaluated according to the CASPAR criteria. Demographic and disease specific variables were recorded. Bone architecture of the metacarpal heads II and III were assessed by high-resolution peripheral quantitative computed tomography (HR-pQCT, XtremeCT, Scanco, Switzerland). Disease activity was assessed with Disease Activity Score (DAS28). Psoriatic skin and nail disease activity were measured by the PASI.
Results: The ages of the patients in the three groups were similar. *IL-17A concentrations were significantly differed between the* groups (p=0.000). However, for other cytokines there was no difference between PsA and PsO groups. Serum levels of IL-17A were significantly correlated to patient pain of VAS (r=-0.318, p=0.06), VAS patient global assessment (r=0.272, p=0.021), DAS28 (r=-0.394, p=0.001) and PASI (r=0.519, p=0.000) in PsA and PSO. PASI score were also positively correlated with IL23 (r=-0.286, p=0.015) and S100A8 (r=0.298, p=0.011).
Conclusions: IL-17A seems to play an important role in development of PsA and bone damage in PsO. This role should be elucidated by further and larger clinical studies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6768

AB0768 CLINICAL FEATURES OF RHEUMATOID FACTOR- OR ANTI-CYCLIC CITRULLINATED PEPTIDES-POSITIVE PATIENTS WITH PSORIATIC ARTHRITIS

K. Inui[1], T. Okano[1], H. Yoshimura[1], Y. Sugioka[2], K. Mamoto[1], T. Koike[2,3], M. Tada[4], H. Nakamura[1]. *[1]Orthopaedic Surgery; [2]Center for Senile Degenerative Disorders, Osaka City University Graduate School of Medicine, Osaka; [3]Search Institute for Bone and Arthritis Disease, Shirahama Foundation for Health and Welfare, Shirahama Cho; [4]Orthopaedic Surgery, Osaka City General Hospital, Osaka, Japan*

Background: Although rheumatoid factor (RF) negativity is among the Classification Criteria for Psoriatic Arthritis (CASPAR) for the diagnosis of psoriatic arthritis (PsA), not all patients with PsA are seronegative. Measurement of anti-cyclic citrullinated peptides (ACPA) is another key test for rheumatoid arthritis and PsA; however, the prevalence of ACPA in patients with PsA is unclear.
Objectives: We analyzed the clinical features of RF- or ACPA-seropositive patients with PsA in comparison with seronegative patients with PsA using the ISLAND registry (UMIN000024292).
Methods: One hundred patients with psoriasis referred from dermatologists for assessment of synovitis or enthesitis from July 2015 to August 2016 were enrolled. PsA was diagnosed by CASPAR, and synovitis or enthesitis was confirmed by ultrasound assessment. Factors compared between seropositive and seronegative patients included age, sex, comorbidities, use of disease-modifying antirheumatic drugs, prevalence of enthesopathy, eye symptoms, duration between skin onset and musculoskeletal onset, psoriasis area severity index, composite psoriatic disease activity (CPDAI), psoriatic arthritis screening and evaluation (PASE), disease activity score-28 (DAS-28), and laboratory data.
Results: In total, 52 patients had PsA and 48 patients had psoriasis without any musculoskeletal manifestations. Significant differences were observed in the age at onset of psoriasis (37.4 vs. 47.9 y, respectively; $p<0.01$) and several clinical parameters (CPDAI: 14.60 vs. 4.55, respectively [$p<0.01$], PASE: 50.8 vs. 32.0, respectively [$p<0.01$], DAS-28: 3.77 vs. 2.72, respectively [$p=0.009$]). ACPA positivity was observed in 15.9% of patients with PsA and in 0.0% of patients with psoriasis (p=0.04). Among 44 of the 52 patients with PsA whose ACPA data were available, the duration from skin onset to joint onset was shorter in the 7 ACPA-positive patients (54.3±52.8 months) than in the 37 ACPA-negative patients (147.8±158.0 months), although the difference was not statistically significant (p=0.30). There were no statistically significant differences in the PASE, DAS-28, C-reactive protein concentration, or matrix metalloproteinase-3 concentration. The differences between RF positive and negative patients were not also statistically significant.

Table 1

	ACPA Positive (n=7)	ACPA Negative (n=37)	p value
PASE	45.8±16.1	51.1±13.4	0.42
IBP positivity	28.6	40.5	0.69
DAS28-ESR	4.24±0.93	3.76±1.56	0.45
DAS28-CRP	3.78±0.73	3.67±1.39	0.84
CRP (mg/dl)	0.56 [0.02–20.39]	0.48 [0.00–16.05]	0.79
MMP-3 (ng/ml)	133.6 [42.8–184.2]	69.1 [13.5–245.1]	0.14
Duration (skin/SpA) (mo)	54.3±52.8	147.8±158.0	0.26

Data are presented as mean ± standard deviation or median [range] unless otherwise indicated.

Conclusions: Among the patients with PsA in this series, ACPA positivity occurred in 15.9% and RF positivity occurred in 12.8%. Seropositive patients with PsA tended to have a shorter duration between skin onset and joint onset. Clinical and laboratory findings were not significantly different between ACPA-positive and -negative patients. One possible explanation for this is that 40.4% of patients with PsA received biological disease-modifying antirheumatic drugs; therefore, their disease activity was stable.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1898

AB0769 SONOGRAPHIC SIGNS OF ENTHESITIS IN ESTABLISHED PSORIATIC ARTHRITIS AND HEALTHY VOLUNTEERS

K. Werversr[1], I. Herrings[1], J.J. Luime[1], M. Moed[1], I. Tchetverikov[2], A.H. Gerards[3], J.M.W. Hazes[1], M. Vis[1]. *[1]Rheumatology, Erasmus MC, Rotterdam; [2]Rheumatology, Albert Schweitzer Hospital, Dordrecht; [3]Rheumatology, Vlietland Hospital, Schiedam, Netherlands*

Background: Previous research in our group showed that sonographic signs of enthesitis are present in early and established PsA, but in young healthy volunteers as well. The Madrid Sonographic Enthesitis Index (MASEI) was only able to differentiate between patients and healthy volunteers after excluding knee enthesis thickness from the score and semi-quantitative scoring of Power Doppler (PD) signal (1).
Objectives: We aim to validate the modified MASEI in a larger cohort of established PsA patients and healthy volunteers.
Methods: Established PsA patients and healthy volunteers aged 35–55 were asked to participate in this cross-sectional study, irrespective of presence of enthesitis complaints. The triceps, quadriceps, proximal and distal patellar and Achilles tendon and plantar fascia (i.e. the locations of the MASEI) and the common extensor insertion at the lateral epicondyle of the elbow were evaluated sonographically for structural changes (i.e. erosions, calcifications and structure) and active inflammation (thickness, bursitis and PD).
Results: 84 established PsA patients and 25 healthy volunteers participated. Sonographic structural changes and one or two spots of PD signal were common in both groups. The modified MASEI was significantly higher in PsA patients

(median 12 (IQR 7.25–17) vs. 7.5 (5–9), P<0.001), while the original MASEI did not differ significantly (Table 1). Confluent PD over a larger area was only seen in 8% of the established PsA patients. Structural damage on ultrasound was more pronounced in the patients compared to the healthy volunteers. Number of PD locations and PD score did not distinguish the two groups.

Table 1. Participant characteristics and sonographic enthesitis scores

	PsA patients (n=84)	Healthy Volunteers (n=25)
Male, n (%)	45 (54)	12 (48)
Age, mean (SD)	55 (11)	47 (6)*
Disease duration, median years (IQR)	8.0 (4.9–12.3)	
LEI, median (IQR)	0.5 (0–2)	0 (0–0)**
Ultrasound		
MASEI, median (IQR)	15.5 (11–22)	13 (9–18)
Modified MASEI, median (IQR)	12 (7.25–17)	7.5 (5–9)**
structural components	7 (3–10)	3 (1–6)**
inflammatory components	6 (3.5–8.5)	3.5 (2–5.5)
Power Doppler		
in any enthesis, n (%)	74 (88)	22 (88)
score 3, n (%)	7 (8%)	0 (0%)
locations, median (IQR)	2 (1–3)	2 (1–3)
if positive, median (IQR)	1.5 (1.25–1.75)	1.5 (1.25–1.5)

PsA: Psoriatic Arthritis; SD: standard deviation, IQR: interquartile range; LEI: Leeds Enthesitis Index; MASEI: Madrid Sonographic Enthesitis Score; modified MASEI: MASEI with new PD scoring method (1: one spot of PD, 1.5: some spots of PD, 2: confluent signal, 3: severe signal) and without knee entheses thickness. Structural components: erosions, calcifications, structure. Inflammatory components: bursitis, thickness and PD signal. PD: Power Doppler. *P<0.01, **P<0.001 (Wilcoxon rank sum test).

Conclusions: Inflammatory and structural changes of the enthesis measured with ultrasound are common in both unselected PsA patients and healthy volunteers, but more pronounced in established PsA patients.

References:

[1] Wervers K, Rasappu N, Vis M, Tchetverikov I, Kok MR, Gerards AH, et al. AB0733 Masei Shows Substantial Changes in The Entheses of Young Healthy Volunteers – Amending Its PD Score and Excluding Knee Entheses Thickness Provides Better Discrimination of Enthesitis in Psoriatic Arthritis Patients. Ann Rheum Dis 2016;75:1155.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3431

AB0770 CHANGE OF PSORIATIC ARTHRITIS IMPACT OF DISEASE (PSAID12) QUESTIONNAIRE RELATED TO CHANGE IN DISEASE ACTIVITY IN EARLY PSORIATIC ARTHRITIS

K. Wervers[1], J.J. Luime[1], I. Tchetverikov[2], A.H. Gerards[3], M.R. Kok[4], C.W.Y. Appels[5], W. van der Graaff[6], J.H.L.M. van Groenendael[7], L.-A. Korswagen[8], J.J. Veris-van Dieren[9], J.M.W. Hazes[1], M. Vis[1] on behalf of Cicero. *[1]Rheumatology, Erasmus MC, Rotterdam; [2]Rheumatology, Albert Schweitzer Hospital, Dordrecht; [3]Rheumatology, Vlietland Hospital, Schiedam; [4]Rheumatology, Maasstad Hospital, Rotterdam; [5]Rheumatology, Amphia Hospital, Breda; [6]Rheumatology, Rivas Hospital, Gorinchem; [7]Rheumatology, Reumazorg Zuid West Nederland, Roosendaal; [8]Rheumatology, Sint Franciscus Gasthuis, Rotterdam; [9]Rheumatology, Reumazorg Zuid West Nederland, Goes, Netherlands*

Background: The Psoriatic Arthritis Impact of Disease 12-item questionnaire (PsAID12) has been developed to measure impact of Psoriatic Arthritis (PsA) for purposes of monitoring and clinical management. Although validated in patients with longstanding disease, data on validity and sensitivity to change in early PsA is lacking.

Objectives: We aim to relate change in disease activity to change in PsAID12 score in early PsA and evaluate which PsAID domains are more likely to change.

Methods: Patients with a new diagnosis of PsA were included in the Dutch southwest Early Psoriatic Arthritis cohoRt (DEPAR). For this analysis, patients that have PsAID12 (range 0–10) and Composite Psoriatic Disease Activity Index (CPDAI, range 0–15) data at two consecutive visits (i.e. 3 months apart) within the first year were included. In case multiple periods per patients were available, the first time period was chosen. The change in PsAID is compared to the change in disease activity over this period, measured with the CPDAI using Spearman's correlation coefficient. Change in score on individual domains of the PsAID was analysed in subgroups of patients that perceived improvement in health and those that perceived worsening. The SF-36 question on self-perceived change in health was used to determine these subgroups.

Results: 143 unique patients had at least one period with two PsAID and CPDAI measurements (67 from baseline-3 months, 26 3–6 months, 25 6- 9 months and 25 9–12 months). Mean age was 51 (SD 13.7) and 70 (49%) were male. The initial median PsAID was 3.35 (IQR 1.4–5.1) and the subsequent score was 2.25 (0.95–4.8 with a mean delta of 0.52 (P<0.01). Median first CDPAI score was 4 (2–7) and 3 (1–5) for the second with a mean delta of 0.45 (P<0.05). The difference in PsAID score was significantly but moderately correlated with the difference in CPDAI (Spearman's rho 0.267, P=0.0013). 58 patients (41%) report a better health status compared to 3 months ago. Figure 1 shows that patients with self-perceived improvement of health have the highest improvement in pain and only domains of skin problems and embarrassment/shame did not improve significantly. Patients reporting worsening of health (n=29) only have significantly lower scores in fatigue, discomfort and social domains.

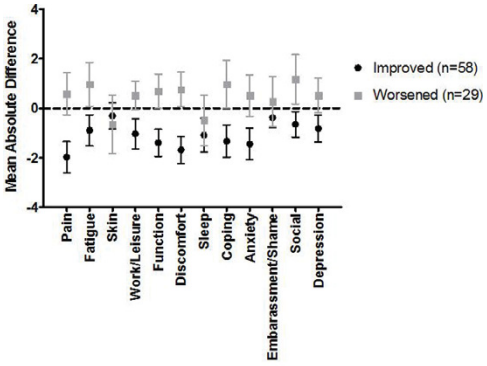


Figure 1. Mean absolute differences in PsAID12 domains in patients with self-perceived improvement of health (n=58, black) and patients reporting worsening of health (n=29, grey). Shown as mean value and 95%-Confidence Interval

Conclusions: Improvement in CPDAI disease activity is significantly but moderately associated with improvement in PsAID score, with the biggest improvement in the pain domain in patients with a self-reported improvement of health.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3817

AB0771 SAFETY AND EFFICACY OF APREMILAST THROUGH 104 WEEKS IN PATIENTS WITH MODERATE TO SEVERE PSORIASIS WHO CONTINUED ON APREMILAST OR SWITCHED FROM ETANERCEPT TREATMENT IN THE LIBERATE STUDY

K. Reich[1], M. Goodfield[2], L. Green[3], K. Nograles[4], R. Chen[4], E. Levi[4], R.G.B. Langley[5]. *[1]Dermatologikum Hamburg, Hamburg, Germany; [2]Leeds General Infirmary, Leeds, United Kingdom; [3]George Washington University School of Medicine, Washington, DC; [4]Celgene Corporation, Summit, United States; [5]Dalhousie University, Halifax, Canada*

Background: Many patients (pts) with chronic plaque psoriasis exhibit nail and scalp involvement that can markedly affect quality of life and be difficult to treat.

Objectives: The phase 3b LIBERATE (Evaluation in a Placebo-Controlled Study of Oral Apremilast and Etanercept in Plaque Psoriasis) study (NCT01690299) evaluated the efficacy and safety of apremilast or etanercept vs. placebo in biologic-naive pts with moderate to severe plaque psoriasis. Efficacy assessments included effects on preexisting nail and scalp disease and skin lesions.

Methods: In this double-blind, double-dummy study, pts were randomized (1:1:1) to placebo (PBO), apremilast 30 mg BID (APR), or etanercept 50 mg QW (ETN) through Week 16; thereafter, all pts switched to or continued APR (PBO/APR, ETN/APR, APR/APR) through Week 104. The primary end point was achievement of a ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI) score (PASI-75) at Week 16 with APR vs. PBO; the secondary end point was PASI-75 achievement at Week 16 with ETN vs. PBO. Physician assessments were also conducted for overall disease activity (static Physician's Global Assessment [sPGA]); scalp disease activity (Scalp Physician Global Assessment [ScPGA], limited to patients with score ≥3 at baseline, indicating moderate to very severe scalp disease); and nail disease (Nail Psoriasis Severity Index [NAPSI], limited to patients with active disease [NAPSI ≥1] in the target nail at baseline). Responses were assessed at Week 104 using the last-observation-carried-forward (LOCF) methodology.

Results: The APR extension phase (Weeks 16 to 104) included 226 pts (PBO/APR n=73; APR/APR n=74; ETN/APR n=79). At Week 16, PASI-75 scores vs. PBO were significant for both APR and ETN; long-term treatment with APR maintained both PASI-75 and sPGA 0 or 1 response levels (Table). Improvements were seen in nail and scalp disease at Week 16, and responses continued to improve with APR treatment over 104 weeks and in pts who switched from ETN to APR (Table). ScPGA 0 or 1 was achieved by 50.0% to 59.2% of pts across treatment arms, and mean percent improvement from baseline NAPSI score ranged from –48.1% to –51.1% (Table); the proportion of pts achieving NAPSI-50 response ranged from 48.6% to 65.2%. Adverse events (AEs) occurring in ≥5% of pts during Weeks 0 to 16 were diarrhea, nausea, nasopharyngitis, upper respiratory tract infection, and headache; long-term assessment by exposure-adjusted incidence rates (EAIR)/100 pt-yrs showed no increase with longer-term APR exposure. No increase in EAIR/100 pt-yrs of serious AEs occurred during the APR extension phase (3.45 to 5.49, across groups) vs. Weeks 0 to 16 (PBO 0.0; ETN 7.91; APR 12.57). Changes in laboratory parameters were infrequent and transient; EAIR/100 pt-yrs remained low across groups through 104 weeks.

Conclusions: APR demonstrated efficacy through Week 104 in pts who continued APR and pts who switched from PBO or ETN to APR at Week 16. The AE profile remained consistent with prolonged APR exposure, and no new safety or tolerability issues were observed through Week 104 in pts with moderate to severe plaque psoriasis.

Table. LIBERATE Efficacy Outcomes

Pts Achieving Response, % (LOCF)	PBO n=84	APR n=83	ETN n=83
Week 16			
PASI-75	11.9	39.8*	48.2*
sPGA 0 or 1§	3.6	21.7‡	28.9*
ScPGA 0 or 1¶	25.9	44.4**	50.0†
NAPSI-50§§	10.9	25.0##	48.0*
Percent change from BL in NAPSI¶¶	−10.1	−18.7	−37.7
Week 104	**PBO/APR n=73**	**APR/APR n=74**	**ETN/APR n=79**
PASI-75	50.7	45.9	51.9
sPGA 0 or 1§	27.4	18.9	26.6
ScPGA 0 or 1¶	50.0	59.2	56.6
NAPSI-50§§	48.6	60.4	65.2
Percent change from BL in NAPSI¶¶	−48.1	−48.2	−51.1

APR=apremilast 30 mg BID; ETN=etanercept 50 mg QW; LOCF=last observation carried forward. NAPSI=Nail Psoriasis Severity Index; NAPSI-50=50% or greater reduction from baseline in NAPSI score; PASI=Psoriasis Area and Severity Index; PASI-75=75% or greater reduction from baseline in PASI score; PBO=placebo; ScPGA=Scalp Physician Global Assessment; sPGA=static Physician's Global Assessment.
*$P<0.0001$; ‡$P=0.0005$; #$P\leq 0.0021$; **$P=0.0458$; †$P=0.0083$; ##$P=0.0701$ vs. PBO (LOCF). Italics indicate values are nominally significant due to hierarchical testing of study end points.
§With ≥2-point reduction from baseline.
¶In pts with ScPGA ≥3 (moderate to very severe) at baseline (exploratory): PBO n=58; APR n=54; ETN n=54 at Week 16 and PBO/APR n=50; APR/APR n=49; ETN/APR n=53 at Week 104.
§§In pts with NAPSI ≥1 at baseline: PBO n=46; APR n=52; ETN n=50 at Week 16 and PBO/APR n=37; APR/APR n=48; ETN/APR n=46 at Week 104.
¶¶PBO n=42; APR n=50; ETN n=50 at Week 16; PBO/APR n=33; APR/APR n=48; ETN/APR n=45 at Week 104.

Disclosure of Interest: K. Reich Consultant for: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celgene Corporation, Centocor, Covagen, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, Merck Sharp & Dohme, Novartis, Ocean Pharma, Pfizer (Wyeth), Regeneron, Takeda, UCB Pharma, and XenoPort, Speakers bureau: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celgene Corporation, Centocor, Covagen, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, LEO Pharma, Medac, Merck Sharp & Dohme, Novartis, Ocean Pharma, Pfizer (Wyeth), Regeneron, Takeda, UCB Pharma, and XenoPort, M. Goodfield: None declared, L. Green Consultant for: AbbVie, Amgen, Celgene Corporation, LEO Pharma, Novartis, Pfizer, and Valeant, Speakers bureau: AbbVie, Amgen, Celgene Corporation, LEO Pharma, Novartis, Pfizer, and Valeant, K. Nograles Employee of: Celgene Corporation, R. Chen Employee of: Celgene Corporation, E. Levi Employee of: Celgene Corporation, R. Langley Speakers bureau: AbbVie, Amgen, Celgene Corporation, Eli Lilly, LEO Pharma, Merck, Novartis, and Pfizer
DOI: 10.1136/annrheumdis-2017-eular.5163

AB0772 SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENT IN FUNCTION, QUALITY OF LIFE AND FATIGUE OVER 2 YEARS IN PATIENTS WHO ACHIEVED LOW DISEASE ACTIVITY RELATED TO PSORIATIC ARTHRITIS DISEASE ACTIVITY SCORE (PASDAS)

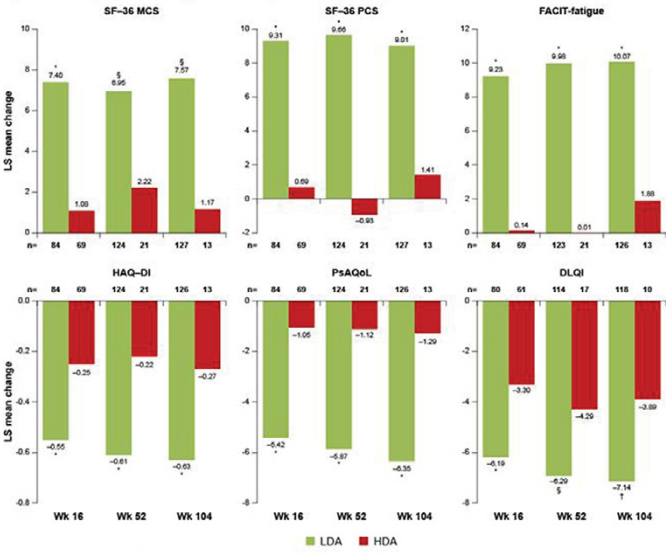
L.C. Coates[1,2], T.K. Kvien[3], P. Nash[4], L. Gossec[5], V. Strand[6], L. Pricop[7], L. Rasouliyan[8], K. Ding[7], S. Jugl[9], C. Gaillez[9] on behalf of the FUTURE 2 study group. *[1]University of Leeds; [2]Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; [3]Diakonhjemmet Hospital, Oslo, Norway; [4]University of Queensland, Brisbane, Australia; [5]UPMC Université Paris 06, Paris, France; [6]Stanford University School of Medicine, Palo Alto; [7]Novartis Pharmaceuticals Corporation, East Hanover, United States; [8]RTI Health Solutions, Barcelona, Spain; [9]Novartis Pharma AG, Basel, Switzerland*

Background: PASDAS is a composite index measuring disease activity in psoriatic arthritis (PsA), well correlated with HAQ and health related quality of life[1].
Objectives: To report the impact of secukinumab on individual core components of PASDAS and its relationship with function (HAQ-DI), health related quality of life (SF36-PCS and MCS, DLQI, PsAQoL) and fatigue in patients (pts) who achieved PASDAS low disease activity (LDA) vs. high disease activity (HDA) through Week (Wk) 104 using *post-hoc* analysis from FUTURE 2 trial.
Methods: 397 pts with active PsA were randomised to s.c. secukinumab (300, 150, or 75mg) or placebo in FUTURE 2 study.[2] PASDAS is derived from physician's global VAS, pts global VAS, SF-36 PCS, tender and swollen joints (TJC68 and SJC66), Leeds enthesitis count, dactylitis count and CRP level and has cut-points for HDA (≥5.4), LDA (<3.2) and remission (REM≤1.9).[3] PASDAS was assessed at Wks 16, 52 and 104 and reported as observed using non-mutually exclusive categories at group level. Additionally, the SF-36 PCS, SF-36 MCS, HAQ-DI, FACIT-Fatigue, PsAQoL, and DLQI were assessed by PASDAS LDA and HDA at Wks 16, 52 and 104 using MMRM analyses.
Results: Pts presented similar baseline characteristics. Mean±SD score of each PASDAS component among pts reaching LDA and HDA at Wk 16 for each treatment group are shown in table and were similar at Wk 104. Secukinumab treated pts achieving PASDAS LDA had significantly greater improvements in function, physical and mental health quality of life and fatigue compared to HDA through Wk 104 (Figure).
Conclusions: In pts treated with secukinumab, the most improved individual components with PASDAS LDA were related to dactylitis, enthesitis, SF36-PCS, Physician global VAS and SJC at Wk 16 and Wk 104. PASDAS LDA was associated with better improvement in function, quality of life and fatigue than HDA confirming the importance to reach stringent target in a PsA pts with multifaceted disease.

Table 1. Scores of PASDAS components at Wk 16

Core components, Mean ± SD	Secukinumab/PBO (s.c.), mg	LDA 300mg: n=37; 150mg: n=34; PBO: n=14	HDA 300mg: n=12; 150mg: n=23; PBO: N=34
Physician/Pt Global VAS	300	7.3±7.2/14.6±10.3	43.2±10.2/65.7±21.6
	150	8.3±8.7/13.2±10.3	55.7±16.2/67.8±14.9
	PBO	11.4±9.8/16.7±13.4	56.7±12.8/64.8±15.6
SF-36 PCS	300	51.5±5.8	34.9±6.0
	150	51.8±5.5	34.2±6.5
	PBO	49.4±6.6	33.5±8.2
SJC 66/TJC 68	300	2.2±3.0/2.3±3.4	12.3±10.0/27.9±16.1
	150	1.9±3.6/2.6±5.0	15.9±11.1/32.3±21.7
	PBO	1.7±2.0/3.4±4.7	10.1±6.1/25.4±14.0
Leeds Enthesitis Score	300	0.3±0.8	3.0±2.5
	150	0.1±0.3	3.0±2.5
	PBO	0.2±0.6	2.4±1.8
Tender Dactylitis count	300	0.03±0.2	0.9±2.6
	150	0	1.4±3.1
	PBO	0.1±0.5	1.3±2.4
CRP (mg/L)	300	3.3±3.5	5.0±4.5
	150	3.3±3.5	8.1±11.6
	PBO	5.8±15.2	14.7±19.5

Figure: Mean Change in PRO scores by PASDAS states (LDA vs. HDA) at Wks 16, 52 and 104



*P < 0.0001; †P < 0.001; ‡P < 0.01 versus HDA.
DLQI, Dermatology Life Quality Index; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire Disability Index; HDA, high disease activity; LDA, low disease activity; LS, least squares; n, number of pts with measurements; N, number of pts in each group of the specified analysis set; PsAQoL, PsA-specific quality of life; SF-36 MCS, Short Form-36 Mental Component Summary; SF-36 PCS, Short Form-36 Physical Component Summary
Wk 16: N= 85 (LDA) and N= 69 (HDA); Wk 52: N= 125 (LDA) and N= 21 (HDA); Wk 104: N= 128 (LDA) and N= 13 (HDA)
Analysis data were pooled across treatment arms; Placebo group not reported at Wk 16

References:
[1] Helliwell PS and Kavanaugh A. Arth Care and Res. 2014;66:749–56.
[2] McInnes IB et al. Arthritis Rheumatol.2016;68 (suppl 10).
[3] Coates LC & Helliwell PS. J Rheumatol. 2016;43:371–5.
Disclosure of Interest: L. Coates Grant/research support from: Abbvie, Janssen, Consultant for: Abbvie, BMS, Celgene, Pfizer, UCB, MSD, Sun Pharma, Novartis, Lilly, Janssen, T. Kvien Consultant for: bbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, Speakers bureau: bbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, P. Nash Grant/research support from: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, Consultant for: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, Speakers bureau: Novartis, Abbvie, Roche, Pfizer, BMS, Janssen, and Celgene, L. Gossec Grant/research support from: AbbVie, BMS, Celgene, Janssen, Novartis, MSD, Roche and UCB, V. Strand Consultant for: AbbVie, Amgen, BMS, Celgene, Celltrion, CORRONA, Genentech/Roche, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi, and UCB, L. Pricop Shareholder of: Novartis, Employee of: Novartis, L. Rasouliyan Consultant for: Novartis through employment at RTI Health Solutions, Employee of: RTI Health Solutions, K. Ding Shareholder of: Novartis, Employee of: Novartis, S. Jugl Employee of: Novartis, C. Gaillez Shareholder of: Novartis, BMS, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1482

AB0773 EFFECTIVENESS OF GOLIMUMAB IN TNF-INHIBITOR INADEQUATE RESPONDER PATIENTS WITH SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS

L. Santo[1], F. D'Onofrio[2], M.G. Anelli[3], N. Maruotti[2], R. Bucci[4], A. Semeraro[5], C. Zuccaro[6], G. Carlino[7], A. Marsico[5], L. Quarta[8], O. Casilli[8], P.C.F. Falappone[9], F. Iannone[3]. *[1]O.U. of Rheumatology, ASL Barletta, Bari; [2]UOC Reumatologia Universitaria, University of Foggia, Foggia; [3]DETO - Rheumatoly Unit, University of Bari, Bari; [4]Rheumatology Hospital Unit, AOU Foggia, Foggia; [5]O.U. of Rheumatology, ASL Taranto, Taranto; [6]Ambulatorio Reumatologia, Ospedale "Perrino", Brindisi; [7]ASL LECCE - DSS Casarano and Gallipoli, Rheumatology Service, Casarano; [8]OU of Rheumatology, "V.Fazzi" Hospital, Lecce; [9]Ambulatorio Reumatologia, Ospedale di Mesagne, Mesagne, Italy*

Background: In real-life world settings, failure of a first TNF-inhibitor (TNFi) put rheumatologists against a crossroad to choose a further TNFi or a biologic drug with a different mechanism of action.
Objectives: Aim of this study was to assess effectiveness of golimumab (GOL) as second line drug after failure of a first TNFi as treatment of patients affected with rheumatoid arthritis (RA), psoriatic arthritis (PsA), or axial-spondyloarthritis (Ax-SpA).
Methods: GOAREL is a prospective cohort of patients starting GOL in community-based care rheumatology centers in Apulia (south Italy) since 2013. Of 494, we selected 368 patients (RA n.73, PsA n.168, and n. Ax-SpA 127) commencing GOL as first ever biological (n.206, 56%) or second treatment (n.161, 44%) after inadequate response to a first TNFi (adalimumab (ADA, n.51), etanercept (ETA, n.81), or infliximab (IFX, n.29). Three patients failing certolizumab were excluded. Primary endpoint was to compare the drug retention rate of biological naïve and TNFi inadequate responders (TNFi-IR) patients on treatment with GOL. In addition, drug retention of second line GOL patients according to the firs TNFi was assessed. Drug survival was estimated by Kaplan-Meier life table analysis. Estimates hazard ratios (HRs) of 2- years drug discontinuation adjusted for demographics, type of disease, disease characteristics, body mass index, co-therapy with glucocorticoids or methotrexate, and prior TNFi were computed by backward selection Cox-regression model.
Results: 2-year drug survival on GOL of naïve and TNF-IR patients was not significantly different (Figure 1). Mean survival time was 20.0 months (95% CI 18.9–21.0) for naïve and 20.4 months (95% CI 19.3–21.6) for TNFi-IR patients. Likewise, drug retention rates on GOL of TNFi-IR patients subdivided by previous TNFi was not significantly different and similar to naïve patients (Figure 1). Mean survival time was 19.0 months (95% CI 16.7–21.4) for prior-ADA, 20.5 months (95% CI 18.9–22.1) for prior-ETA, and 22.0 months (95% CI 19.6–24.3) for prior-IFX. Multiple Cox-regression model showed gender female as the only independent factor positively associated to the risk of GOL discontinuation (HR 2.5, 95% CI 1.5–4.2, p 0.0001).

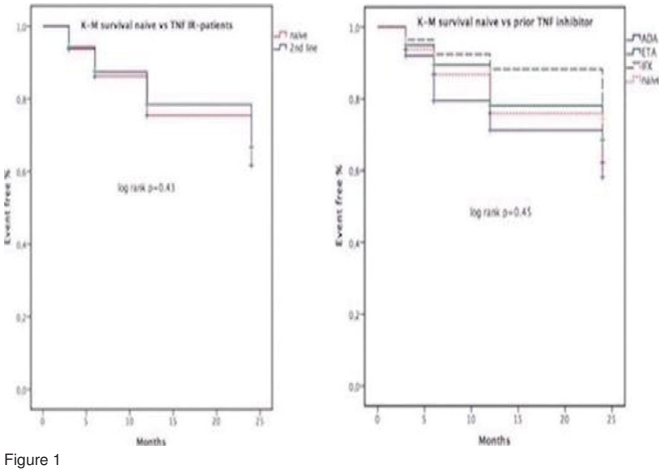


Figure 1

Conclusions: In real-life setting effectiveness of GOL seems to be similar in naïve or TNFi-IR patients with RA, PsA, and Ax-Spa. Furthermore, clinical outcomes were not influenced by the previous TNFi.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3610

AB0774 PREVALENCE, CLINICAL AND RADIOGRAPHIC CHARACTERISTICS OF SACROILITIS IN PATIENTS WITH PSORIASIS

L. Stefanović[1], D. Veljković[2], E. Mahmutović[3], V. Skakić[4]. *[1]Dom zdravlja Kraljevo; [2]Odsek za sanitetsko obezbeenje, Odred Žandarmerije, Kraljevo; [3]Državni Univerzitet Novi Pazar, Departman za biomedicinske nauke, Novi Pazar; [4]Institute Niska Banja, Nis, Serbia*

Background: Psoriasis is a skin disorder that is associated with arthritis. Sacroiliac joint involvement is considered to be less frequent than the other types of psoriatic arthritis.
Objectives: im of the study was to investigate the prevalence of sacroilitis in patients with psoriasis (Ps) in region of Kraljevo, Novi Pazar and Niška banja.
Methods: A multicenter, noninterventional, retrospective, cross-sectional study was conducted at 3 care centers in region of Kraljevo, Novi Pazar and Niška banja. Diagnosis of sacroilitis was based on clinical and antero-posterior pelvic X-rays Prevalence of sacroilitis and its clinical and radiologic characteristics were examined.
Results: Sacroilitis was documented in 24/100 (24%) patients with Ps. There was no significant difference in average age between Ps patients without sacroilitis (47,83) and Ps patients with sacroilitis (49,9). Sacroiliitis appeared to be unilateral in 12,5% and bilateral in 87.5% of patients. Ps preceded sacroilitis in 62,50% and sacroilitis preceded Ps in 29,17% of cases; concomitant onset of Ps and sacroilitis was present in 8,33%. Peripheral arthritis was found in 67,89% patients with sacroilitis.
Conclusions: The prevalence of sacroilitis and related spondylitis is high in patient with Ps. We found predominantly bilateral sacroilitis which is characteristic of ankylosing spondylitis. This is in contrast to present knowledge about the association of psoriasis and sacroiliitis. In 68% sacroilitis patients we found associated peripheral arthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6737

AB0775 UNDERESTIMATED AXIAL AND ENTHESIAL INVOLVEMENT IN PATIENTS WITH PSORIATIC ARTHRITIS IN A RUSSIAN DERMATOLOGICAL DAILY PRACTICE: COMPARED WITH RHEUMATOLOGICAL PRACTICE

M. Chamurlieva, E. Loginova, T. Korotaeva. *Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Psoriatic arthritis (PsA) is frequently underdiagnosed by dermatologists due to it's heterogeneous clinical manifestations such as peripheral arthritis, dactylitis, spondylitis and enthesitis. For the correct early diagnosis, choice of treatment and for better outcomes proper evaluation of all symptoms is required.
Objectives: to compare the definition of the main clinical symptoms of PsA by dermatologists and rheumatologists in daily clinical practice.
Methods: 103 pts (male-47/female-56) with different forms of plaque psoriasis (PsO), mean age 44±13.69 years (yrs.), mean psoriasis duration 10.7±10.2 yrs., mean PASI 5.05±1.23 were included. In dermatological clinic, all pts completed a PEST questionnaire and underwent clinical evaluation by a dermatologists in order to identify the main clinical symptoms of PsA such as peripheral arthritis, dactylitis, spondylitis and enthesitis. Later all pts were subsequently evaluated by rheumatologists to confirm/exclude the diagnosis of PsA based on CASPAR criteria and underwent standard clinical examination to identify the same symptoms - peripheral arthritis, dactylitis, spondylitis (based on inflammatory back pain (IBP) ASAS criteria) and enthesitis (based on Leeds Enthesial Index (LEI) plus Plantar Fascia (PF). M±m, %, t-test were peformed. All $p<0.05$ were considered to indicate statistical significance.
Results: 61 out of 103 pts with PsO (59.2%) had PsA based on rheumatological evaluation and CASPSR criteria. Dermatologists diagnosed peripheral arthritis in significantly less cases compared to rheumatologists: in 15 (24.6%) and in 35 (57.4%) out of 61 pts ($p<0.001$) accordingly. No significant difference was seen in clinical evaluation of dactylitis by dermatologists or rheumatologists - in 37 (60.7%) and in 40 (65.6%) out of 61 pts accordingly (p=0.32). Heel pain was noted by dermatologists in 32 out of 61 pts (52.5%) according to PEST questionnaire. Dermatologists could not find enthesitis according to LEI. Rheumatological examination based on LEI scale identified lateral epicondyles in 11 out of 61 pts (18%), enthesitis of medial femoral condyles in 8 out of 61 pts (13.1%), enthesitis of Achilles tendon insertions – in 25 out of 61 pts (41%). Enthesitis of PF were observed in 15 out of 61 pts (24.6%). Dermatologists noted back pain using PEST questionnaire in 30 out of 61 pts (49.2%). IBP based on ASAS criteria was not detected by a dermatologists in any case. In these 30 pts having back pain IBP was diagnosed by a rheumatologists in 21 (70%) cases; and in the rest 9 out of 30 pts (30%) mechanical back pain was observed. On the basis of clinical examination tendinitis was not noted by dermatologists, while rheumatologists found hand tendinitis in 13 out of 61 pts (21.3%).
Conclusions: Perypheral arthrtitis, axial and enthesial involvement were underestimated by dermatologists using PEST screening questionnaire, because it does not cover these symptoms in detail. ASAS criteria for IBP and standard enthesitis assessment should be implemented into Russian dermatological clinical practice. In order to improve early PsA diagnosis in dermatological practice, interdisciplinary educational training programmes and collaboration with rheumatologists are needed.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2771

AB0776 THE EFFECT OF PREGNANCY ON DISEASE ACTIVITY OUTCOMES IN PSORIATIC ARTHRITIS PATIENTS

M. Berman[1], D. Paran[1], D. Zisman[2], J. Wollman[1], D. Levartovsky[1], O. Elkayam[1]. [1]*Rheumatology, Tel Aviv Sourasky Medical Center, Tel Aviv;* [2]*Rheumatology, Carmel Medical Center, Haifa, Israel*

Background: Psoriatic arthritis often affects patients at a childbearing age. The relationship between pregnancy and psoriatic arthritis, in terms of pregnancy outcomes and its effect on disease activity, has not been well studied
Objectives: To evaluate the effect of pregnancy on disease activity in psoriatic arthritis
Methods: A retrospective review of files of female patients followed at Psoriatic arthritis clinic at the Tel Aviv Medical center was performed, patients with at least 1 pregnancy during follow up and one visit during or soon after pregnancy were included. A review of files was performed which included the following data: age, disease duration, pattern of PsA, disease activity before during and after pregnancy, record of treatment, including IA injections. Postpartum period was defined as up to 1 year after pregnancy. PsA activity was defined as follow: no disease activity (no active synovitis), mild disease (up to 1 joint involved), moderate to severe disease (more than 2 joints involved). The follow-up during and after pregnancy was classified as: improvement, worsening or stable
Results: 25 PsA women and 35 pregnancies were identified. 33 resulted in live healthy babies. One pregnancy was interrupted on week 23, so partial follow up was available. The mean age at pregnancy was 32.5 years. Table 1 summarizes status of disease activity before, throughout pregnancy and during the postpartum period in the whole group. No significant change in disease activity was noticed throughout pregnancy while significant proportion of patients flared at postpartum. Before 21 pregnancies patients were treated with biologic agents. In 15, biologic treatment was discontinued close to pregnancy or during the first trimester. In this group, 5 (33%) of patients were classified as mild to severe activity prior to pregnancy. This number increased up to 8 (53%), 7 (47%) and 14 (93%) during the 1st, 2nd trimester and postpartum period respectively. In 6 patients in whom biologics were continued beyond first trimester, no significant change in degree of disease activity was noticed. Interestingly, in the group of non-biologics treated patients, an improvement in disease activity was observed – the proportion of patients with mild to severe disease activity decreased from 85% close to pregnancy to 69% in the 1st and 2nd trimester and 58% in the 3rd one while an increase to 83% was observed after pregnancy. During 6 pregnancies, corticosteroids were initiated or the dosage increased- 83% in pregnancies where biologics were stopped before pregnancy.

Table 1. Disease activity during pregnancy

N (%)	Before	1st trimester	2ndtrimester	3rd trimester	Postpartum
No	15 (44%)	14 (41%)	13 (38%)	16 (48%)	6 (18%)
Mild	9 (26%)	10 (29%)	10 (29%)	9 (27%)	9 (27%)
Moderate to severe	10 (29%)	10 (29%)	11 (32%)	8 (24%)	18 (55%)

Conclusions: Patients with PsA definitively flare after pregnancy. Our results suggest that stopping treatment with biologic agents before pregnancy is associated with flare during pregnancy and the postpartum period. It seems that in terms of PsA disease activity, it may be recommended to continue treatment with biologic agents throughout pregnancy
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1810

AB0777 CHARACTERISTICS OF AMYLOID A DEPOSITION IN PSORIATIC ARTHROPATHY AND IN RHEUMATOID ARTHRITIS – A COMPARATIVE POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 RHEUMATOID AND 12 PSORIATIC ARTHRITIS PATIENTS

M. Bély[1], Á. Apáthy[2]. [1]*Department of Pathology, Policlinic of the Order of the Brothers of Saint John of God;* [2]*Department of Rheumatology, St. Margaret Clinic Budapest, Budapest, Hungary*

Background: The aim of this study was to determine the prevalence and extent of amyloid A deposition on different tissue structures in various organs of rheumatoid arthritis (RA) and psoriatic arthritis (PsA) patients.
Methods: AAa was detected in 34 (21.1%) (females: 29, average age: 64.3 years, range: 83–32, onset of RA: 48.6, average disease duration: 15.7 years; males: 5, average age: 51.2 years at death, range: 88–19, onset of RA: 41.3, average disease duration: 14.8 years) of 161 RA, and in 2 (16%) female: 2, average age: 57.5 years, range: 63–52, onset of PsA: 47.5, average disease duration: 11.0 years) of 12 PsA patients.
RA and PsA were diagnosed clinically according to the criteria of the American College of Rheumatology (ACR) [1,2].
Amyloid deposits on different tissue structures [arteriole, small artery, medium size artery, venule, small vein, medium size vein, interstitial collagen fiber, reticulin fiber (collagen IV), basal laminas, nerve, renal glomerulus] of 6 organs [heart, lungs, liver, kidney, skin and brain] were determined histologically. The extent of amyloid A deposits was evaluated by semi-quantitative, visual estimation on a 0 to 3 plus scale, based on the number of involved tissue structures per light microscopic field [3].
The prevalence and extent of amyloid A deposits on different tissue structures were compared by Student (Welch) t-probe.
Results: The average prevalence (in %) and the average extent of amyloid A deposits (absolute value) on different tissue structures of analyzed 6 organs in RA and PsA patients are summarized in Table.

Tissue structure	RA-AAa Prevalence in %	PsA-AAa Prevalence in %	p<	RA-AAa Average extent	PsA-AAa Average extent	p<
Arteriole	61,33	58,33	**0,28**	1,34	1,33	**0,49**
Small artery	50,28	58,33	**0,46**	0,94	1,21	**0,25**
Collagen IV	30,39	**41,67**	**0,36**	0,56	**0,83**	**0,21**
Interstitial collagen	**45,86**	33,33	**0,22**	**0,78**	0,58	**0,24**
Small vein	26,52	33,33	**0,42**	0,39	0,42	**0,44**
Medium size vein	21,55	25,00	**0,47**	0,37	0,33	**0,43**
Medium size artery	24,86	25,00	**0,42**	0,34	0,25	**0,27**
Venule	22,10	16,67	**0,32**	0,32	0,25	**0,35**
Nerve	4,97	16,67	**0,17**	0,08	0,17	**0,24**
Average/Structure	**31,98**	**34,26**	**0,388**	**0,57**	**0,60**	**0,444**
Average/Patient	**32,27**	**36,21**	**0,244**	**0,585**	**0,668**	**0,198**

Conclusions: The difference between average prevalence ($p<0.388$) and average amount ($p<0.444$) of amyloid A deposits/structures in RA and PsA patients was not significant.
The prevalence and extent of amyloiod A deposits on different tissue structures of analyzed organs changed parallel in RA or PsA patients except for collagen IV and interstitial collagen.
The reverse prevalence and extent of amyloid A deposits on collagen IV and interstitial collagen fibers between RA or PsA patients may be due to structural (qualitative) changes of collagen IV resulting in its increased affinity of amyloid A in PsA patients. Qualitative change of collagens in systemic sclerosis patients has been demonstrated [4].
References:
[1] Arnett FC et al: Arthritis Rheum. 1988; 31(3):315–24. PMID: 3358796.
[2] Helliwell PS, Taylor WJ: Classification and diagnostic criteria for psoriatic arthritis. Ann Rheum Dis 2005;64:ii3-ii8 doi:10.1136/ard.2004.032318.
[3] Bély M, Apáthy Ágnes: Clinical pathology of rheumatoid arthritis. 1–440 pp. Akadémiai Kiadó, Budapest 2012 http://www.akkrt.hu.
[4] Istok R et al: Pyridinoline in fibrotized tissues of patients with systemic sclerosis. Annals Rheum Dis 1999; 58(Suppl. 1):192.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1221

AB0778 PATIENT AND PHYSICIAN GLOBAL ASSESSMENTS ARE POORLY CONNECTED IN INDIVIDUAL PATIENTS WITH PSORIATIC ARTHRITIS AND ONLY POORLY EXPLAINED BY OTHER CLINICAL MARKERS OF DISEASE ACTIVITY

E.M. Egsmose[1,2], O.R. Madsen[1,2]. [1]*Department of Rheumatology, Copenhagen University Hospital Rigshospitalet Gentofte, Hellerup;* [2]*The DANBIO registry, Copenhagen University Hospital Rigshospitalet Glostrup, Glostrup, Denmark*

Background: Assessment of disease activity is important in the evaluation and monitoring of patients with psoriatic arthritis (PsA) in clinical care and research. As there is no single “gold standard” variable for assessment of disease activity several markers of disease activity are used, among these “global assessment” by the patient (PaGl) and by the physician (PhGl). The agreement and interplay between PaGl and PhGl are not well clarified in patients with PsA, however.
Objectives: The objective of the study was to examine associations on the group level and agreements on the individual patient level between PaGl and PhGl as scored on visual analogue scales (VAS) in the daily clinic by patients with active PsA and their rheumatologists.
Methods: Traditional disease activity data on 76 PsA patients with active disease planned to initiate biological treatment were extracted from the Danish DANBIO registry. Data comprised swollen joint count (SJC), tender joint count (TJC), CRP, patient and physician global assessment (PaGl and PhGl) and pain (VAS), HAQ-DI and DAS28-CRP (4v). Parametric statistics was used. The predictability of PaGl and PhGl, respectively, by all other disease markers mentioned and by age and sex was examined using stepwise multiple regression analysis. Agreement between the VAS scores was expressed as the bias (mean difference between intra-individual scores) and the 95% lower and upper limits of agreement (LLoA;ULoA) according to the Bland-Altman method.
Results: Mean age was 52.2±11.1 years and mean DAS28-CRP 4.7±1.1. 59.2% were of the patients were women. Mean PaGl was 63.7±23.2 and PhGl 39.9±19.8 ($p<0.0001$). PaGl was significantly but weakly correlated with PhGl ($r=0.42$, $p<0.0001$) with a high standard error of estimation (SEE) =21.2. PaGl was independently predicted by pain (beta =0.76, $p<0.0001$) and HAQ-DI (beta =0.19, $p<0.01$) and was not predicted by PhGl (p=0.61) (R =0.78, SEE =10.5, $p<0.0001$). PhGl was independently predicted by SJC (beta =0.43, $p<0.0001$) followed by pain (beta =0.41, $p<0.0001$) and CRP (beta =0.20, $p<0.05$) (R =0.70, SEE =14.4, $p<0.0001$) with no significantly contribution by PaGl (p=0.49). Differences between the patient-reported VAS-scores were small on the group level but on the individual level they were pronounced: LLoA;ULoA [bias] for PaGl

vs. PhGl was -21.9;69.5 [23.8], for PaGl vs. pain -17.1;22.0 [4.9], and for PhGl vs pain -60.8;23.0 [-18.9].
Conclusions: In patients with PsA, PaGl was in general scored considerably higher than PhGl. The two scores were poorly connected not only on the individual level but also on group level with no systematic differences between the scores. PaGl was best predicted by pain, and PhGl by SCJ reflecting patients and physicians diverging attitudes to the importance of the different disease manifestations. The findings highlight the challenge of understanding and dealing with discrepancies between assessments and attitudes by physicians and patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4092

AB0779 CLINICAL MANIFESTATIONS AND PARAMETERS AFFECTING THERAPEUTIC RESPONSE IN A COHORT OF 411 PSORIATIC ARTHRITIS PATIENTS

M.P. Migkos, T.-E. Memi, T.E. Markatseli, A.A. Drosos, P.V. Voulgari.
Rheumatology Clinic, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece

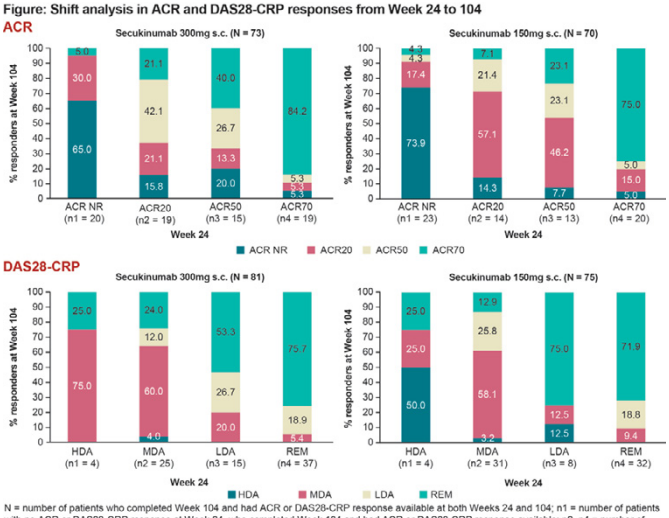
Background: Psoriatic arthritis (PsA) has various clinical manifestations. The therapeutic response of patients may be affected by epidemiological parameters such as body mass index (BMI), disease duration, sex and the choice of therapy.
Objectives: To illustrate the clinical manifestations of psoriatic arthritis and to assess the impact of epidemiological features and treatment choice on therapeutic response.
Methods: We retrospectively studied 411 patients diagnosed with PsA and we recorded the clinical manifestations of the disease. Data of 254 out of 411 patients were analyzed to examine the possible effect of BMI, disease activity, sex and treatment choice on therapeutic response. Patients were followed up at predefined time points [baseline, 12 weeks (wks), 24 wks, 48 and 240 wks after initiation of therapy]. The treatment response was assessed using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), disease activity score-28 (DAS) -C-Reactive Protein (CRP), DAS28-erythrocyte sedimentation rate (ESR) and Health Assessment Questionnaire (HAQ). Patients were categorized in three groups: patients treated with biological synthetic disease modifying anti-rheumatic drugs (DMARDs) (anti-tumor necrosis factor alpha (TNFa) agents), patients treated with synthetic DMARDs and combined therapy (biological and synthetic DMARDs).
Results: The interval between psoriasis and PsA in women is shorter (p=0,041). PsA presented predominantly as asymmetric oligoarthritis (41,60%), followed by symmetric polyarthritis (24,57%). Arthritis of distal phalangeal joints was established in 3,16%, while 4,37% showed only enthesitis or dactylitis. Axial involvement was recorded in 26,27%7.Twenty-eight patients had only axial disease and 80 had axial and peripheral joint involvement. 23/411 patients (5,60%),had eye involvement, 8/411 (1,95%) and 6/411 (1,46%) had involvement of the urogenital and gastrointestinal system, respectively. Eleven patients had pulmonary fibrosis. In the subgroup analysis of 254 patients, disease duration was positively correlated in all time points (p<0,005) with all disease activity scores. Statistical significant differences with respect to gender was observed for DAS28-CRP (3,93–2,96, 3,54–2,64 p<0,001) and DAS28-ESR (3,37 – 2,82 p=0,001, 3,06–2,62 p=0,023) at 12 and 24 wks respectively. More specifically women showed higher disease activity than males the first 6 months after treatment. BMI was not significantly correlated with the disease activity. Treatment with biological DMARD showed a statistically significant difference in all disease activity scores early in the disease course (p<0,05) in comparison with those receiving conventional DMARD. After the first 12 wks all disease activity scores were rather stable with no differences between the treatment groups.
Conclusions: PsA manifests predominantly as asymmetric oligoarthritis. Extraarticular manifestations are less frequent. Higher disease duration was associated with higher disease activity. Women early on disease course had higher DAS-28 scores. Treatment with biological DMARD showed better response in PsA patients compared with synthetic early in the disease course. However, after the first 12 wks there were no significant differences in treatment response with respect to treatment choice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4784

AB0780 SECUKINUMAB SUSTAINS INDIVIDUAL CLINICAL RESPONSES OVER TIME IN PATIENTS WITH PSORIATIC ARTHRITIS: 2-YEAR RESULTS FROM A PHASE 3 TRIAL, FUTURE 2

P. Emery[1], I.B. McInnes[2], P.J. Mease[3], M. Schiff[4], L. Pricop[5], S. Shen[5], Z. Wang[5], C. Gaillez[6] on behalf of the FUTURE 2 study group. *[1]University of Leeds, Leeds; [2]University of Glasgow, Glasgow, United Kingdom; [3]Swedish Medical Centre and University of Washington, Seattle; [4]University of Colorado, Denver; [5]Novartis Pharmaceuticals Corporation, East Hanover, United States; [6]Novartis Pharma AG, Basel, Switzerland*

Background: Achieving sustained clinical response to biologics is part of treat-to-target recommendations in psoriatic arthritis (PsA) and is aimed at optimising treatment goals.[1]
Objectives: To evaluate patient (pt)-level secukinumab data and report the likelihood of improving, sustaining or worsening of American College of Rheumatology (ACR) response and disease status (disease activity score 28 based on C-reactive protein [DAS28-CRP]) from Week (Wk) 24 to 104 in pts with active PsA from the FUTURE 2 trial.[2,3]
Methods: The findings of the FUTURE 2 trial through Wk 104 have been previously reported.[3] *Post-hoc* shift analyses were performed on ACR response between Wks 24 and 104 for subgroups of secukinumab-treated pts, based on their higher response rate at an earlier time point in 1 out of 4 categories (ACR non-responders [NR], ACR20, 50 or 70) by evaluating whether the response improved, sustained or worsened at a later time point using exclusive categories and as observed analyses. Similar shift analysis on DAS28-CRP derived criteria were performed in 4 exclusive categories extrapolated from rheumatoid arthritis: high, moderate, low disease activity (HDA, MDA, LDA) or remission (REM) only.[4]
Results: In total, 86/100 (86%) and 76/100 (76%) pts in the secukinumab 300 and 150mg groups, respectively, completed the 104-wk treatment. Of which, 73/70 and 81/75 pts in secukinumab 300/150mg were eligible for ACR and DAS28-CRP shift analysis, respectively, from Wk 24 to 104. Baseline demographics and clinical characteristics were balanced across the two dose groups.[2,3] Most secukinumab-treated pts who achieved at least an ACR20, 50 or 70 response and Psoriasis Area and Severity Index (PASI) 75 or 90 response at Wk 24, improved or sustained their response at Wk 104 (Figure, data not shown for PASI response). Similarly, a majority of pts who were in the MDA, LDA or REM category at Wk 24 sustained or improved their disease status related to DAS28-CRP score at Wk 104 (Figure).

Figure: Shift analysis in ACR and DAS28-CRP responses from Week 24 to 104



N = number of patients who completed Week 104 and had ACR or DAS28-CRP response available at both Weeks 24 and 104; n1 = number of patients with no ACR or DAS28-CRP response at Week 24, who completed Week 104 and had ACR or DAS28-CRP response available; n2–n4 = number of patients with ACR or DAS28-CRP response at Week 24, who completed Week 104 and had ACR or DAS28-CRP response available.

Conclusions: In this *post-hoc* analysis, a majority of secukinumab-treated pts who achieved at least ACR20 and PASI 75 response or at least MDA at Wk 24 sustained or improved their ACR and PASI responses or sustained or reduced their disease status at Wk 104. Numerically higher sustained response and LDA or REM rate was observed for secukinumab 300mg, thereby extending the sustainability of response and lowering the disease activity that has been previously reported at group level.[2,3]
References:
[1] Gossec L, et al. Ann Rheum Dis 2016;75:499–510.
[2] McInnes IB, et al. Lancet 2015;386:1137–46.
[3] McInnes IB, et al. Arthritis Rheumatol 2016;68;abstract: 2757.
[4] Wells G, et al. Ann Rheum Dis 2009;68:954–60.
Disclosure of Interest: P. Emery Consultant for: AbbVie, BMS, Merck, Novartis, Pfizer, Roche, UCB, I. McInnes Consultant for: Novartis, Amgen, Janssen, BMS, Pfizer, UCB, Abbvie, Celgene, Lilly, P. Mease Grant/research support from: AbbVie, Amgen, Biogen Idec, BMS, Celgene, Crescendo, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, Biogen Idec, BMS, Celgene, Covagen, Crescendo, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Amgen, Biogen Idec, BMS, Crescendo, Janssen, Lilly, Pfizer, UCB, M. Schiff Consultant for: Abbvie, BMS, Lilly, J&J, Speakers bureau: Abbvie, L. Pricop Shareholder of: Novartis, Employee of: Novartis, S. Shen Employee of: Novartis, Z. Wang Employee of: Novartis, C. Gaillez Shareholder of: Novartis, BMS, Employee of: Novartis
DOI: 10.1136/annrheumdis-2017-eular.1228

AB0781 PSORIATIC ARTHRITIS IN PSORIASIS PATIENTS: RESULTS OF A FRENCH SURVEY

P. Claudepierre[1], P. Richebé[2], S. Benkhalifa[3], D. Sid Mohand[4], B. Charles[4], Y. Braults[3], M. Lahfa[5]. *[1]Department of Rheumatology, Université Paris Est Créteil, Chenevier-Mondor Hospital, Créteil; [2]Department of Rheumatology, Université Paris Est Créteil, Chenevier-Mondor Hospital; [3]Pfizer; [4]France Psoriasis, Paris; [5]Private dermatology practice, Biarritz, France*

Background: Early detection of psoriatic arthritis (PsA) in patients with skin psoriasis (Pso) is critical to reduce the risk of joint damage, disability, and comorbidities. However PsA is mostly under-diagnosed in patients with Pso.
Objectives: first to compare characteristics of patients with Pso without PsA with those of patients with Pso and PsA, then to compare patients with Pso and potential but undiagnosed PsA (puPsA) to the other patients.
Methods: 817 patients completed an online questionnaire published by the French Psoriasis Patients Association, including multiple-choice questions regarding in particular past and current symptoms. For analysis, a first comparison was performed between patients with Pso without known PsA and patients with Pso and PsA, then between patients with symptoms suggestive of PsA (puPsA group), i.e., patients with past or current joint or back pain accompanied by waking up at night and/or morning stiffness, with PsA patients on the one hand, and with patients without known PsA and without symptoms suggestive of puPsA, on the other hand.
Results: 746 patients reported having Pso of which 192 (25.7%) had also PsA. Among the 554 patients without known PsA, 190 (34.3%) had symptoms suggestive of PsA, 101 (18.2%) had rheumatologic symptoms not suggestive of PsA, and 263 (47.5%) had no rheumatologic symptoms. The comparison, in multivariate analysis, between patients with Pso and PsA and patients with Pso without known PsA showed significant differences ($p<0.05$): Pso and PsA patients had more often current bone or joint pain at any time (OR=7.8), joint pain during the day (OR =2.45), stiff back or joints on waking (OR=1.77), painful and swollen fingers and toes (OR=3.15), past joint pain during the day (OR=3.05), and drug in tablet form (OR=2.07), biotherapy alone (OR=5.45) or with DMARDs (OR=16.06); conversely they had less often guttate psoriasis (OR=0.54). Results of the multivariate analysis comparing patients with puPsA to the other patients are shown in Tables 1 and 2 (comparison with patients with Pso and PsA in Table 1; comparison with patients with Pso without known PsA in Table 2).

Table 1. Multivariate analysis, patients with puPsA and Pso compared with patients with Pso and PsA

Covariates ($p<0.05$ for all OR)	OR [95% CI]
Current skin pain	OR=1.85 [1.12; 3.08]
Current bone or joint pain	OR=0.25 [0.15; 0.44]
Current joint pain during the day	OR=0.49 [0.29; 0.84]
Current back pain	OR=2.55 [1.52; 4.29]
Current painful and swollen fingers and toes	OR=0.29 [0.17; 0.51]
Past joint pain during the day	OR=0.39 [0.19; 0.79]
Biotherapy/Neither biotherapy nor DMARD	OR=0.28 [0.12; 0.67]
Biotherapy + DMARD/Neither biotherapy nor DMARD	OR=0.15 [0.04; 0.55]

Table 2. multivariate analysis, patients with Pso without known PsA compared with patients with puPsA

Covariates ($p<0.05$ for all OR)	OR [95% CI]
Current nail changes	OR=1.53 [1.02 ; 2.29]
Current fatigue	OR=2.53 [1.72 ; 3.72]
Other current symptoms	OR=0.33 [0.18 ; 0.60]
Hydration	OR=1.48 [1.01 ; 2.18]

Conclusions: That survey on Pso patients showed that a fourth of them also had PsA, but more importantly that about another fourth had puPsA, highlighting the underdiagnosis of PsA. It suggests that presence of fatigue and nail changes might raise suspicion of PsA in Pso patients.
Disclosure of Interest: P. Claudepierre Grant/research support from: AbbVie, MSD, Roche, Pfizer, Consultant for: AbbVie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche, UCB, P. Richebé: None declared, S. Benkhalifa: None declared, D. Sid Mohand: None declared, B. Charles: None declared, Y. Braults: None declared, M. Lahfa Consultant for: investigator or speaker for AbbVie, MSD, Celgene, Janssen, Novartis, Pfizer, Roche, Takeda, UCB, Lilly, Leo Pharma, Galderma, Astellas, Pierre Fabre. Dermatology.
DOI: 10.1136/annrheumdis-2017-eular.2397

AB0782 PSORIATIC ARTHRITIS EARLY ULTRASONOGRAPHIC CHANGES IN PATIENTS WITH PSORIASIS AND NAIL PSORIASIS. A COMPARATIVE STUDY WITH SUBJECTS WITHOUT PSORIASIS

P. Rodriguez Henriquez[1], M.L. Cardenas-Hernandez[2], L. Lammoglia-Ordiales[2], L.T. Becerril-Mendoza[3], R.M. Lacy-Niebla[2]. *[1]Rheumatology; [2]Dermatology, Hospital General Dr. Manuel Gea González; [3]Rheumatology, Hospital Juarez de Mexico, Mexico, Mexico*

Background: Psoriatic Arthritis (PsA) has a prevalence of 30% amongst Psoriasis (Ps)patients. However in patients with ungueal Ps the prevalence has been reported in up to 68% of cases. In muskuloskeletal ultrasound (MSUS) studies the lesion most frequently reported is enthesitis followed by synovitis in early PsA patients.
Objectives: To determine the presence of psoriatic arthritis early ultrasonographic changes in patients with psoriasis, nail psoriasis, and subjects without psoriasis.
Methods: Analytic, comparative, prospective and transversal study, in which patients with psoriasis, nail psoriasis, and subjects without psoriasis paired by age, were recruited. Each group underwent a skin and joint checkup, which included demographic data, comorbidities, psoriasis severity and joint signs and symptoms. The ultrasonographic evaluation consisted in a gray scale detection and classification according to severity scales, of synovitis, enthesitis, synovial effusion and bone erosions in the distal interphalangeal joints of both hands.
Results: A total of 16 patients, 8 with psoriasis and 8 with nail psoriasis, as well as 9 subjects without psoriasis, were recruited. The psoriasis group included mostly men (87.5%), unlike the subjects without psoriasis (44.4%) and the nail psoriasis group (37.5%) (p=0.09). The mean age for the study population was 55.16 + 8.09 years. There was no statistical significance between groups (p=0.430). The greatest prevalence of comorbidities was found in both groups with psoriasis. The mean time of disease duration in the nail psoriasis group was 20.12 + 14.54 years, vs 13.37 + 14.45 years in the psoriasis group (p=0.247). Synovitis was found in 100% of patients in the psoriasis group, vs 37.5% in the nail psoriasis group, and 62.5% in the subjects without psoriasis group (p=0.028). No enthesitis was observed in any group

Prevalence of synovitis

	Synovitis	Grade 1	Grade 2	Grade 3
Control group	62.5 %	12.5 %	37.5 %	12.5 %
Ungueal Psoriasis	37.5 %	62.5 %	25 %	12.5 %
Psoriasis	100 %	25 %	50 %	12.5 %

Chi-square test for synovitis between groups p= 0.28.
Chi-square test for synovitis grading p=0.269

Conclusions: Synovitis was more frequent than enthesitis in our population as an ultrasonographic finding of psoriatic arthritis. No association was found between other variables with synovitis, such as age, sex, disease duration and comorbidities.
References:
[1] Raposo I, Torres T. Nail psoriasis as a predictor of the development of psoriatic arthritis. Actas Dermosifiliogr 2015;106(6):452–457.
[2] Busse K, Liao W. Which Psoriasis Patients Develop Psoriatic Arthritis? Psoriasis Forum 2010;16(4):17–25.
[3] Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis 2005;64(2):ii14-ii17.
[4] Ibrahim G, Waxman R, Helliwell PS. The Prevalence of Psoriatic Arthritis in People With Psoriasis. Arthritis & Rheumatism (Arthritis Care & Research) 2009;61(10):1373–1378.
[5] Naredo E, Möller I, De Miguel E, et al. High prevalence of ultrasonographic synovitis and enthesopathy in patients with psoriasis without psoriatic arthritis: a prospective case-control study. Rheumatology (Oxford) 2011;50 (10):1838–1848.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5552

AB0783 THE RELATIONSHIP BETWEEN THE DEGREE OF SKIN INVOLVEMENT AND JOINT ACTIVITY IN PATIENTS WITH PSA: EXPERIENCE FROM THE CORRONA REGISTRY

P.J. Mease[1], C.J. Etzel[2,3], J.R. Lisse[4], A.W. Armstrong[5], W.J. Huster[4], S. Rebello[2], R. Dodge[2], T. Muram[4], S. Al Sawah-Folian[4], M.J. Murage[4], J.D. Greenberg[2,6], W. Malatestinic[4]. *[1]Swedish Medical Center, University of Washington School of Medicine, Seattle; [2]Corrona, LLC, Southborough; [3]UT MD Anderson, Houston; [4]Eli Lilly and Company, Indianapolis; [5]University of Southern California, Los Angeles; [6]NYU School of Medicine, New York, United States*

Background: Prior studies have shown inconsistent relationships between skin and joint symptoms in patients with comorbid psoriasis (PsO) and psoriatic arthritis (PsA)[1–3].
Objectives: To characterize the relationship between skin severity and joint activity in patients with comorbid PsA and PsO at enrollment.
Methods: Data from the U.S. Corrona PsA/spondyloarthritis (PsA/SpA) registry were obtained from the period 3/21/2013– 9/30/2016. Inclusion criteria included a diagnosis of PsA, a history of PsO, and age greater than 18 years. PsA patients were evaluated for skin severity as defined by Body Surface Area (BSA) and joint activity as defined by the level of clinical disease activity index (CDAI). Patient characteristics, including current and prior PsA medication use, were obtained during the enrollment visit. We evaluated the relationship of skin severity (BSA) and joint activity (CDAI) with multi-variable linear regression.
Results: 1,542 patients met inclusion criteria: 52.9% were women with mean (SD) age 53.7 (13.2) years, with median 9.0 years PsA disease duration, and 71 (4.6%) with fibromyalgia. 266 (18%) patients were on no DMARD therapy, 430 (29%)

were on csDMARDs only, 616 (42%) were on first line biologic/targeted synthetic (ts)DMARD therapy, and 172 (12%) were on second line biologic/tsDMARD therapy. The relationship between skin severity and joint activity was statistically significant ($p<0.0001$) with a correlation of 0.183. Results were similar when adjusting separately for treatment and for duration of PsA and PsO. Greater age, female gender, higher dactylitis count, not achievement of MDA, higher HAQ, and patient reported pain and fatigue affected the relationship.

Conclusions: The relationship between skin severity and joint activity is statistically significant and varies by age, gender, MDA, HAQ, and patient reported pain and fatigue. This suggests degree of skin involvement is important to take into account when evaluating PsA patients.

References:

[1] Gottlieb AB, Mease PJ, Mark Jackson J, Eisen D, Amy Xia H, Asare C, Stevens SR: Clinical characteristics of psoriatic arthritis and psoriasis in dermatologists' offices. J Dermatolog Treat 2006;17:279–287.

[2] Jones SM, Armas JB, Cohen MG, Lovell CR, Evison G, McHugh NJ: Psoriatic arthritis: outcome of disease subsets and relationship of joint disease to nail and skin disease. Br J Rheumatol 1994;33:834–839.

[3] Cohen MR, Reda DJ, Clegg DO: Baseline relationships between psoriasis and psoriatic arthritis: analysis of 221 patients with active psoriatic arthritis. Department of Veterans Affairs Cooperative Study Group on Seronegative Spondyloarthropathies. J Rheumatol 1999;26:1752–1756.

Acknowledgements: Corrona, LLC has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, AstraZeneca, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB.

Disclosure of Interest: P. Mease Grant/research support from: Celgene, Novartis, Abbvie, Amgen, BMS, Janssen, Lilly, Pfizer, Sun, UCB, Consultant for: AbbVie, Amgen, BMS, Crescendo, Celgene, Corrona, Demira, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Sun, Zynerba, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Crescendo, Genentech, Janssen, Novartis, Pfizer, UCB, C. Etzel Consultant for: Merk, Employee of: Corrona, LLC, J. Lisse Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, A. Armstrong Grant/research support from: AbbVie, Janssen, Lilly; speaker's bureau: AbbVie, Lilly, Consultant for: AbbVie, Amgen, Janssen, Merck, Lilly, Celgene, Novartis, and Pfizer, W. Huster Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Rebello Employee of: Corrona, LLC, R. Dodge Employee of: Corrona, LLC, T. Muram Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, S. Al Sawah-Folian Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, M. Murage Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, J. Greenberg Shareholder of: Corrona, LLC, Consultant for: Genentech, Janssen, Novartis and Pfizer, Eli Lilly, Employee of: Corrona, LLC, W. Malatestinic Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company

DOI: 10.1136/annrheumdis-2017-eular.1938

AB0784 EFFECTIVENESS OF ANTI-TNFS ON DACTYLITIS AND ENTHESITIS IN PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM THE CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS REGISTRY

P.J. Mease[1,2], R. Singh[3], K. Douglas[3], D. Hua[4], H.J. Litman[4], C. Karki[4], J. Griffith[3]. *[1]Swedish Medical Center; [2]University of Washington, Seattle; [3]AbbVie, Inc., Abbott Park; [4]Corrona, LLC, Southborough, United States*

Background: Dactylitis and enthesitis are common disease manifestations encountered in nearly 10–30% of patients with psoriatic arthritis (PsA). Previous clinical trial data suggests that anti-tumor necrosis factors (aTNFs) are effective in controlling dactylitis and enthesitis among PsA patients, however there are limited data from real world studies.

Objectives: To evaluate the effectiveness of aTNFs on dactylitis and enthesitis in patients with PsA enrolled in Corrona, a large US observational cohort of patients with PsA and spondyloarthritis.

Methods: Adult PsA patients who initiated or were currently on an aTNF at registry enrollment (baseline) between 3/2013–9/2016 and had a 12 month follow-up visit were included. Dactylitis was defined as a non-zero total dactylitis score on a scale 0–20 and enthesitis was defined by a non-zero score on the SPARCC enthesitis index, 0–16. The primary outcome was change in dactylitis and enthesitis scores at 12 months from baseline. Descriptive analysis of patient characteristics at baseline was examined and change in outcomes was evaluated using t-tests.

Results: There were 28 patients with dactylitis and 77 patients with enthesitis who met the inclusion criteria. Patients with dactylitis and enthesitis had a mean (SD): age of 48.2 (14.8) and 53.5 (11.5) years, body mass index of 30.8 (6.6) and 31.4 (7.6), disease duration of 9.3 (9.1) and 8.1 (7.7) years, and 28.6% and 45.5% were on methotrexate combination therapy respectively. Patients had a mean clinical disease activity index of 15.1 in both groups, 40.0% and 17.1% were in minimal disease activity, mean (SD): body surface area was 4.4 (4.4) and 5.2 (9.7), pain was 33.1 (29.5) and 43.3 (27.5) on a visual analogue scale (VAS) of 0–100, and more than 80% and 90% of patients had some morning stiffness in the dactylitis and enthesitis groups, respectively. At 12 months from baseline, there were significant improvements in both dactylitis and enthesitis scores in patients with PsA treated with aTNFs (Table).

Table: Primary outcomes in PsA patients on aTNFs at 12 months from baseline

	At enrollment	At 12 month visit	Change in score (enrollment – 12 month visit	p-value*
Dactylitis Count (0-20)	n=28	n=28	n=28	
Mean (± SD)	2.1 (±1.5)	0.5 (±1.1)	-1.6 (±1.8)	0.001
SPARCC Enthesitis Count (0-16)	n=77	n=77	n=77	
Mean (± SD)	4.1 (±3.2)	1.9 (±2.8)	-2.2 (±3.2)	<0.001

SPARCC: Spondyloarthritis Research Consortium of Canada; *Calculated based on a t test assessing whether the change in counts differs from 0.

Conclusions: In this clinical registry, aTNF therapy significantly improved both dactylitis and enthesitis at 12 months. Further evaluation of secondary outcomes and larger studies with comparator cohorts will further validate the effectiveness of aTNFs in improving the outcomes in PsA patients.

Acknowledgements: This study is sponsored by Corrona, LLC. The Corrona, LLC has been supported through contracted subscriptions in the last two years by AbbVie, Amgen, BMS, Crescendo, Eli Lilly and Company, Genentech, GSK, Horizon Pharma USA, Janssen, Momenta Pharmaceuticals, Novartis, Pfizer, Roche and UCB. The design, study conduct, and financial support for the study was provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the abstract.

Disclosure of Interest: P. Mease Grant/research support from: Celgene, Novartis, Abbvie, Amgen, BMS, Janssen, Lilly, Pfizer, UCB, Consultant for: Celgene, Corrona, Merck, Novartis, Abbvie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Merck, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Crescendo, Genentech, Janssen, Lilly, Novartis, Pfizer, UCB, R. Singh Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc, K. Douglas Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc, D. Hua Employee of: Corrona, LLC, H. Litman Employee of: Corrona, LLC, C. Karki Employee of: Corrona, LLC, J. Griffith Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc

DOI: 10.1136/annrheumdis-2017-eular.1532

AB0785 CONSISTENT SAFETY PROFILE WITH UP TO 4 YEARS OF APREMILAST TREATMENT: ANALYSIS OF DATA FROM 1493 PATIENTS WITH PSORIATIC ARTHRITIS IN 3 LARGE, PHASE III, LONG-TERM STUDIES

P.J. Mease[1], D.D. Gladman[2], J.J. Gomez-Reino[3], S. Hall[4], A. Kavanaugh[5], E. Lespessailles[6], G. Schett[7], M. Paris[8], L. Teng[8], J. Wollenhaupt[9]. *[1]Swedish Medical Center and University of Washington School of Medicine, Seattle, United States; [2]Toronto Western Research Institute, Toronto, Canada; [3]Hospital Clínico Universitario, Santiago, Spain; [4]Monash University, CabriniHealth, Melbourne, Australia; [5]University of California, San Diego, School of Medicine, la Jolla, United States; [6]University of Orléans, Orléans, France; [7]University of Erlangen-Nuremberg, Erlangen, Germany; [8]Celgene Corporation, Summit, United States; [9]Schön Klinik Hamburg Eilbek, Hamburg, Germany*

Background: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, regulates immune activity in psoriatic arthritis (PsA) patients. Safety data were pooled from the phase 3 PALACE 1, 2, and 3 studies.

Objectives: Evaluate the long-term safety of APR treatment for up to 4 years in patients with active PsA despite prior conventional DMARDs and/or biologics.

Methods: Patients were randomized at baseline (1:1:1) to placebo (PBO), APR 30 mg BID (APR30), or APR 20 mg BID (APR20). PBO patients were re-randomized

	APR-Exposure Period*			
	Weeks 0 to ≤52	Weeks >52 to ≤104	Weeks >104 to ≤156	Weeks >156 to ≤208
	APR30 n=721	APR30 n=520	APR30 n=443	APR30 n=401
Patients, n (%)				
≥1 AE	524 (72.7)	316 (60.8)	284 (64.1)	234 (58.4)
≥1 SAE	47(6.5)	35 (6.7)	40 (9.0)	28 (7.0)
AE leading to drug withdrawal	56 (7.8)	13 (2.5)	7 (1.6)	7 (1.7)
Death	0 (0.0)	1§ (0.2)	0 (0.0)	2‡‖ (0.5)
AEs in ≥5% of patients, n (%)				
Diarrhea	112 (15.5)	20 (3.8)	12 (2.7)	4 (1.0)
Nausea	108 (15.0)	11 (2.1)	10 (2.3)	3 (0.7)
Headache	75 (10.4)	17 (3.3)	12 (2.7)	7 (1.7)
Upper respiratory tract infection	60 (8.3)	27 (5.2)	24 (5.4)	21 (5.2)
Nasopharyngitis	41 (5.7)	31 (6.0)	20 (4.5)	26 (6.5)
Select marked abnormalities in clinical laboratory parameters, n/m (%)				
Alanine aminotransferase >3× ULN	9/713 (1.3)	2/518 (0.4)	2/442 (0.5)	1/401 (0.2)
Creatinine >1.7× ULN	1/713 (0.1)	0/518 (0.0)	0/442 (0.0)	1/401 (0.2)
Leukocytes <1.5, 10^9/L	0/713 (0.0)	0/517 (0.0)	0/442 (0.0)	0/401 (0.0)
Neutrophils <1, 10^9/L	2/713 (0.3)	3/517 (0.6)	2/442 (0.5)	2/401 (0.5)
Platelets <75, 10^9/L	0/713 (0.0)	0/517 (0.0)	1/441 (0.2)	0/399 (0.0)
Hemoglobin, male <10.5 g/dL, female <8.5 g/dL	5/713 (0.7)	4/517 (0.8)	5/442 (1.1)	5/401 (1.2)

*Includes all patients who received APR during the time interval relative to the start of APR treatment. §Motor vehicle accident on Day 489. ‡Cerebrovascular accident on Day 1330 in a 69-year-old man, considered unrelated to study drug; patient had history of myocardial infarction, atrial fibrillation, and cerebrovascular accident. ‖Stroke on Day 1224 in a 58-year-old woman, considered unrelated to study drug; patient had a history of chronic ischemic heart disease, hypertension, alcoholism, and atrial fibrillation. APR30=apremilast 30 mg BID; AE=adverse event; n/m=number of patients with ≥1 occurrence of the abnormality at any time point/number of patients with ≥1 post-baseline value; ULN=upper limit of normal.

to APR30 or APR20 at Week 16 (early escape) or Week 24. Double-blind APR treatment continued to Week 52; patients could continue APR during an open-label, long-term treatment phase for up to 5 years treatment. Visits in years 2, 3, and 4 were scheduled at 13-week intervals. Safety was assessed at each visit throughout the study, and results are summarized here by exposure.

Results: A total of 1493 patients were randomized and received ≥1 dose of study medication (PBO: n=495; APR30: n=497; APR20: n=501). At the 4-year data cut, the numbers of patients receiving APR30 and APR20 in each exposure period were 1441 in Weeks 0 to ≤52, 1028 in Weeks >52 to ≤104, 865 in Weeks >104 to ≤156, and 767 in Weeks >156 to ≤208. During the 0- to ≤52-week APR-exposure period, adverse events (AEs) occurring in ≥5% of APR30-exposed patients were diarrhea, nausea, headache, upper respiratory tract infection, and nasopharyngitis (Table). Most diarrhea and nausea AEs were reported within the first 2 weeks of treatment and usually resolved within 4 weeks; the frequency of gastrointestinal AEs decreased with longer APR30 exposure, and the frequency of other common AEs either decreased or remained stable with prolonged exposure (Table). Most AEs were mild/moderate in severity. During Weeks >156 to ≤208 of APR exposure, the discontinuation rate due to AEs was 1.7% with APR30, and the rate of serious AEs (SAEs) was 7.0%, consistent with earlier periods; most SAEs occurred in 1 patient each. Rates were very low for major cardiac events, malignant neoplasms, and serious opportunistic infections, comparable to the first year of treatment. Rates of depression remained very low in Weeks >156 to ≤208. Marked laboratory abnormalities were infrequent, and most returned to baseline with continued treatment.

Conclusions: APR30 demonstrated a favorable safety profile and was well tolerated for up to 208 weeks, marked by the lack of accumulation of immunosuppression or need for specific laboratory monitoring. The incidence of AEs remained stable or decreased with long-term exposure to APR30.

Disclosure of Interest: P. Mease Grant/research support from: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Consultant for: Abbott, Amgen, Biogen Idec, BMS, Celgene Corporation, Genentech, Janssen, Eli Lilly, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbott, Amgen, Biogen Idec, BMS, Genentech, Janssen, Eli Lilly, Pfizer, UCB, D. Gladman Grant/research support from: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB, Consultant for: AbbVie, Amgen, BMS, Celgene Corporation, Janssen, Novartis, Pfizer, UCB, J. Gomez-Reino Grant/research support from: Roche and Schering-Plough, Consultant for: BMS, Pfizer, Roche, Schering-Plough, UCB, S. Hall Consultant for: Boehringer Ingelheim, MSD, Roche, Schering-Plough, Servier, Wyeth, Paid instructor for: Amgen, AstraZeneca, Boehringer Ingelheim, Centocor, GSK, MSD, Pfizer, Sanofi Aventis, Sanofi Pasteur, Schering-Plough, Serono, Wyeth, Speakers bureau: Boehringer Ingelheim, GSK, MSD, Pfizer, Roche, Sanofi Aventis, Schering-Plough, Wyeth, A. Kavanaugh Grant/research support from: Abbott, Amgen, AstraZeneca, BMS, Celgene Corporation, Centocor-Janssen, Pfizer, Roche, UCB, E. Lespessailles Grant/research support from: Amgen, Eli Lilly, Novartis, Servier, Speakers bureau: Amgen, Eli Lilly, Novartis, Servier, G. Schett Grant/research support from: Abbott, Celgene Corporation, Roche, UCB, Consultant for: Abbott, Celgene Corporation, Roche, UCB, M. Paris Employee of: Celgene Corporation, L. Teng Employee of: Celgene Corporation, J. Wollenhaupt Grant/research support from: Abbott, BMS, MSD, Pfizer, UCB, Consultant for: Abbott, BMS, MSD, Pfizer, UCB

DOI: 10.1136/annrheumdis-2017-eular.3840

AB0786 SYSTEMATIC REVIEW OF MEASUREMENT PROPERTIES OF PATIENT REPORTED OUTCOME MEASURES IN PSORIATIC ARTHRITIS: A GRAPPA-OMERACT INITIATIVE

P. Højgaard[1,2], L. Klokker[1], A.-M. Orbai[2], K. Holmsted[1], E.M. Bartels[1], Y.Y. Leung[2], N. Goel[2], M. de Wit[2], D. Gladman[2], P. Mease[2], L. Dreyer[1], L.E. Kristensen[1], O. FitzGerald[2], W. Tillett[2], L. Gossec[2], P. Helliwell[2], V. Strand[2], A. Ogdie[2], C. Terwee[2], R. Christensen[1,2] on behalf of GRAPPA-OMERACT PsA Core Set Working Group. *[1]The Parker Institute, Frederiksberg and Bisbebjerg Hospital, Copenhagen, Denmark, Frederiksberg, Denmark; [2]GRAPPA-OMERACT PsA Core Set Working Group, International organisation, -*

Background: An updated psoriatic arthritis (PsA) core domain set (COS) for randomized controlled trials (RCTs) was endorsed at the Outcome Measures in Rheumatology (OMERACT) meeting in 2016 and reflects the patient and physician perspectives.[1]

Objectives: To synthesise the evidence on measurement properties of Patient Reported Outcome Measures (PROMs) in PsA in order to contribute to the development of a PsA core outcome measurement set (COMS) for RCTs adhering to the OMERACT filter 2.0 Framework.[2]

Methods: A systematic literature search was performed in EMBASE, MEDLINE and PsycINFO to identify studies published in English on PROM measurement properties in PsA. Two independent reviewers rated the quality of studies according to COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) guidelines,[3] extracted data on measurement properties and performed a qualitative evidence synthesis.

Results: Of 4703 identified references, 162 were read in full-text and 44 included in the systematic review (SR). Thirty-nine instruments, consisting of one or more scales, were analysed. PROMs measuring core set domains with at least fair quality evidence for good validity and reliability (and without evidence for inadequate measurement properties) were: Stockerau Activity Score for PsA (German) for the *Musculoskeletal Disease Activity* domain; the Psoriatic Symptom Inventory for *Skin Disease Activity*; the 36-Item Short Form Health Survey Physical Function scale and to a lesser extent the Health Assessment Questionnaire Disability Index and Bath Ankylosing Spondylitis Functional Index for *Physical Function*; the Psoriatic Arthritis Quality of Life Questionnaire, the Psoriatic Arthritis Impact of Disease questionnaire and VITACORA-19 (Spanish) for *Health related Quality of Life/Life Impact;* the Functional Assessment of Chronic Illness Therapy-Fatigue Scale for *Fatigue*, and the Social Role Participation Questionnaire for *Participation*. Evidence for content validity was lacking for most of these PROMs.

Conclusions: At least one PROM with some evidence for good validity and reliability was available for five out of eight inner circle domains of the PsA COS. Lack of content validity evidence constitutes a critical barrier for application to the PsA COS per the OMERACT Filter 2.0 Instrument Selection Algorithm [2]. This SR serves as a guide for additional research to increase knowledge of PROM measurement properties in PsA followed by stakeholder consensus for developing a PsA COMS.

PROSPERO:CRD42016032546

References:

[1] Orbai AM, de WM, Mease P et al. International patient and physician consensus on a psoriatic arthritis core outcome set for clinical trials. Ann Rheum Dis 2016. doi: 10.1136.

[2] Martin Boers, John Richard Kirwan, Peter Tugwell et al. The OMERACT handbook. Updated May 2016, http://www.omeract.org.

[3] Terwee CB, Mokkink LB, Knol DL et al. Rating the methodological quality in systematic reviews of studies on measurement properties: a scoring system for the COSMIN checklist. Qual Life Res 2012;21:651–7.

Disclosure of Interest: P. Højgaard Speakers bureau: Received speaking fees once from Celgene and UCB not related to the current work, L. Klokker: None declared, A.-M. Orbai: None declared, K. Holmsted: None declared, E. Bartels: None declared, Y. Y. Leung: None declared, N. Goel Employee of: QuintilesIMS, M. de Wit: None declared, D. Gladman: None declared, P. Mease: None declared, L. Dreyer: None declared, L. Kristensen: None declared, O. FitzGerald: None declared, W. Tillett: None declared, L. Gossec: None declared, P. Helliwell: None declared, V. Strand: None declared, A. Ogdie: None declared, C. Terwee: None declared, R. Christensen: None declared

DOI: 10.1136/annrheumdis-2017-eular.4631

AB0787 STUDY OF SERUM SCLEROSTIN LEVELS IN ASSOCIATION TO ENTHESIAL ULTRASONOGRAPHY IN EGYPTIAN PSORIATIC ARTHRITIS PATIENTS

R. Elmallah[1], E. EL Attar[1], D. Farrag[1], D. Samaha[2] on behalf of responsible for part of clinical measuring of sclerostin level. *[1]Rheumatology & Rehabilitation; [2]Clinical & Chemical Pathology, Faculty of Medicine Ainshams University, Cairo, Egypt*

Background: Psoriatic arthritis (PsA) is characterized by focal bone erosions and new bone formation, suggesting an uncoupling of osteoblast–osteoclast homeostasis [1]. Serum sclerostin is a protein inhibitor of wnt signaling pathway of bone formation implicated in the suppression of bone repair in inflammatory arthritis. The role of sclerostin in osteoimmunology and inflammatory arthritides is still controversial [2].

Objectives: This study aimed at measuring serum sclerostin in psoriatic arthritis men and to correlate its levels with disease activity scores, ultrasonographic findings and bone mineral density in those patients

Methods: This study included 30 male patients diagnosed with Psoriatic arthritis (PsA), 15 healthy age and sex matched volunteers as control group. Patients disease activity index measured. Clinical assessment by Leed's enthesitis Index (LEI) [3], Spinal manifestations scored according to Bath Ankylosing Spondylitis Activity Index [4], Serum sclerostin measured using enzyme linked immunosorbent assay. Ultrasonography of enthesis at Leeds enthesitis sites [5] and dual energy x-ray absorbiometry (DEXA) at the lumbar spine.

Results: The study included 30 PsA male patients with a mean age of 43.33±8.33 mean, body mass index (BMI) of 26.87±2.63 and 15 healthy age and sex matched

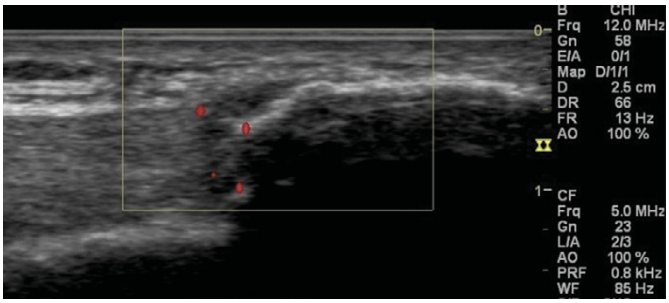


Figure 1. Ultrasonographic longitudinal scan of the tendoachillis showing hypoechoic area of edema & power Doppler signal at insertion.

controls with a mean age of 42.12±7.22 mean BMI of 25.87±3.51 with an unsignificant difference between two groups.
Serum sclerostin level significantly higher in PsA patients compared to controls with a mean of (0.64 and 0.37ng/ml) respectively, positive significant correlation with patients' age, disease activity scores, ultrasonographic findings of inflammation and damage at the enthesis as well as negative correlation with DEXA at lumbar spine. A positive though non-significant correlation detected between serum sclerostin and Leeds clinical enthesitis index (LEI) and CRP.
Conclusions: sclerostin plays important role in pathogenesis of psoriatic arthritis and associated with bone damage either systemic or localized. Further studies for the effect of treatment on serum sclerostin, ultrasonographic and bone mineral density findings is recommended
References:
[1] Homaira Rahimi & Christopher T. Ritchlin. Altered Bone Biology in Psoriatic Arthritis. Curr Rheumatol Rep (2012) 14:349–357.
[2] Matzelle MM, Gallant M, Condon KW, et al. Resolution of inflammation induces osteoblast function and regulates the Wnt signaling pathway. Arthritis Rheum 2012; 64:1540–1550.
[3] Healy PJ and Helliwell PS: "Measuring clinical enthesitis in psoriatic arthritis: assessment of existing measures anddevelopment of an instrument specific to psoriatic arthritis." Arthritis Care and Research 2008; 59(5):686–691.
[4] Garrett S, Jenkinson T, Kennedy LG et al. A new approach to defining disease status in ankylosing spondylitis: the Bath ankylosing spondylitis disease activity index. J Rheumatol (1994); 21 (12): 2286–2291.
[5] Ibrahim G, Groves C, Chandramohan M, Beltran A, Valle R, Reyes B, Healy P, Harrison A and Helliwell P S. Clinical and Ultrasound Examination of the Leeds Enthesitis Index in Psoriatic Arthritis and Rheumatoid Arthritis. ISRN Rheumatology Volume 2011(2011), Article ID 731917, http://dx.doi.org/10.5402/2011/731917.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1317

AB0788 DIFFERENCES IN THE PHENOTYPIC EXPRESSION OF RECENT ONSET PSORIATIC ARTHRITIS AMONG MEN AND WOMEN: BASELINE DATA FROM THE REAPSER STUDY

R. Queiro, A. Laiz Alonso, H.S. Park, C. Montilla Morales, E. Galíndez Agirregoikoa, J.J. Bethencourt Baute, S. Bustabad Reyes, P. Tejón Menéndez, M.Á. Belmonte, J.A. Pinto Tasende, E. Alonso Blanco Morales, J. Ramír. *Rheumatology, Hospital Universitario Central de Asturias (Coordinating Center), Oviedo, Spain*

Background: The natural history of psoriatic arthritis (PsA) according to gender of patients is an aspect of the disease only partially studied. In prospective PsA cohorts such information is barely known.
Objectives: To analyze baseline gender differences in the REAPSER cohort (Psoriatic Arthritis Registry of the Spanish Society of Rheumatology).
Methods: Observational, multicenter study (34 centers), with consecutive inclusion. We included adults of both sexes 18 years of age or older with PsA that met CASPAR criteria, and duration of less than two years since the appearance of symptoms attributed to PsA. Annual follow-up visits will be carried out for 5 years. Measurements: socio-demographic data; employment status and impact of the disease; family history of PsA and other inflammatory diseases; comorbidities and treatment; lifestyle; use of health services; clinical status at the time of diagnosis of PsA; anthropometric data; clinical evaluation of PsA manifestations; radiographic evaluation; analytical determinations; treatment of PsA. The study has been approved by the Ethical committees of the participating centers. Comparative statistical analysis: for qualitative variables, the χ-square or the Fisher exact statistic were used. For non-normal quantitative variables, non-parametric tests were used and for normal quantitative variables, Student's t-test was used.

Parameter	Men (N=142)	Women (N=68)	P values
Age (years)	50.2 (13.8)	49.6 (14.1)	NS
University studies	18.3%	16.2%	NS
Active worker	65%	49.3%	<0.001
BMI	27.3 (4.8)	28.5 (6)	NS
Waist-hip index	0.94 (0.1)	0.87 (0.1)	<0.001
Smoker	29.6%	32.4%	NS
Alcohol consumption	45.1%	16.2%	<0.001
Psoriasis family history	40.1%	45.6%	NS
PsA family history	8.5%	10.3%	NS
Charlson's CI (>3)	18.3%	17.6%	NS
Depression	7.7%	19.4%	0.014
Common Psoriasis	81%	61.8%	0.003
Pustular Psoriasis	2.1%	11.8%	0.006
Onicopathy	59%	49%	NS
PASI	1.5 (0.6–4.4)	1.2 (0.6–3)	NS
Peripheral pattern	80.3%	83.8%	NS
Axial pattern	7%	1.5%	NS
Mixed Pattern	12.7%	14.7%	NS
BASDAI (0–10)	4.1 (2.2–6)	4.8 (2.4–7.3)	0.008
BASFI (0–10)	1.8 (0.4–4.5)	2.9 (1.4–4.7)	0.065
Dactylitis	31.4%	47.1%	0.028
Pain (0–10)	4.5 (2–7)	6 (4–7.5)	0.021
PGA (0–10)	5 (3–7)	6 (3.5–8)	0.042
ESR (mm/h)	12 (5–20)	21 (10–29.5)	0.001

CI: comorbidity index. PASI: Psoriasis Area and Severity Index. PGA: Patient's Global Assessment. Data are expressed in percentages, means with SD (Standard Deviation), medians and IQR (Interquartile Range). There were no significant differences in SJC, TJC or PsAID (Psoriatic Arthritis Impact of Disease).

Results: The results are expressed in the table.
Conclusions: The baseline data from this prospective cohort point to significant differences in the phenotypic expression of PsA between men and women. Thus, in women, the prevalence of dactylitis and pustular psoriasis was higher, there were higher rates of depression and a perception of higher disease activity. Women scored higher on the pain linked to their arthritis and the activity of axial disease. They also had biological activity parameters (ESR) higher than that of men. It is necessary to determine if these differences are maintained or change over time.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5039

AB0789 THE PSORIATIC ARTHRITIS PATIENT'S JOURNEY: SPECIAL EMPHASIS ON DIAGNOSIS AND TREATMENT DELAYS

S. Moyano, M. Brom, F.B. Mollerach, L.E. Pompermayer, M.L. Acosta Felquer, M. Scolnik, J. Marin, L.G. Ferreyra Garrott, L.J. Catoggio, J.E. Rosa, E.R. Soriano. *Rheumatology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina*

Background: A delay in diagnosis and treatment of Psoriatic Arthritis (PsA) is associated with increased disability and damage in the long term. There is currently scarce data available about diagnosis delay, referrals delays, and time to first treatment in patients with PsA in developing countries.
Objectives: To describe the journey of patients with psoriatic arthritis, with special emphasis on diagnosis and treatment delays.
Methods: All patients with PsA registered in the Rheumatology Unit data base (between 2000–2016), with complete data, were included. Electronic medical records were manually revised, and the following data were obtained: date of first visit to a Dermatologists due to Psoriasis (PsO) symptoms, date of PsO diagnosis, date and type of first musculoskeletal symptom, specialty of physician seen at first visit for musculoskeletal symptoms, date of PsA diagnosis, date and reason for prescription of first Disease Modifying anti-Rheumatic Drug (DMARD). Primary outcome variable was mean lag time between first musculoskeletal symptom and diagnosis of PsA. Other variables calculated were: mean lag time between first musculoskeletal symptom and first physician encounter because of those symptoms, mean lag time to first DMARD and mean lag time between PsO diagnosis and PsA diagnosis. Variables associated with a delay in PsA diagnosis (more than one year delay) were analyzed in multivariable analysis (logistic regression).
Results: 93 patients were included, mean age 60.8 years (SD: 15.3), 61% males. Mean age at time of PsA diagnosis was 52 years (SD: 14.8). The most common musculoskeletal symptom was arthralgia (46%), followed by arthritis (37%), enthesitis (6%), low back pain (6%), and dactylitis (4%). Mean lag time between first musculoskeletal symptoms and visit to a physician because of those symptoms was 16,8 months (SD: 44,4) (median: 1,92 (IQR: 0,35–11,6). In Only 33% of the cases the first specialist seen was a Rheumatologist. Mean lag time between first musculoskeletal symptom and diagnosis of PsA was 19,2 (SD: 28,8) months (Median: 7,2 (IQR: 2,4–21,6 months). In 90 patients (97%), the diagnosis of PsO preceded the diagnosis of PsA, a mean time of 15.1 years (SD: 14.4). 83 patients (89%) received traditional DMARDs, 82% because of the musculoskeletal symptoms, with a mean lag time between PsA diagnosis and initiation of DMARDs of 11,4 months (SD: 31,2) (Median: 0,48 (IQR: 0–4,3) months). Forty-three patients (46.2%) had a delay on PsA diagnosis equal or greater than 1 year. In logistic regression analysis, including age, sex, first specialist seen and type of musculoskeletal symptom, none was independently associated with a delay equal or greater than 1 year in PsA diagnosis.
Conclusions: Mean time between symptoms' onset and PsA diagnosis was relatively short. However, a delay greater that one year was observed in almost half of patients. As none of the variables studied was associated with a delay in diagnosis, more studies are needed to identify potential actions that would help reducing this delay.
References:
[1] Kane D, et al. Rheumatology 2003;42:1469–1476.
[2] Haroon M, et al. Ann Rheum Dis 2014;0:1–6.
[3] Gladman DD, et al. Arthritis Rheum 1998;41:1103–1110.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2231

AB0790 HYPERURICEMIA IN PSORIATIC ARTHRITIS: PREVALENCE AND ASSOCIATED FACTORS

T. Gudu, A. Peltea, A. Balanescu, V. Bojinca, D. Opris, D. Predeteanu, R. Ionescu. *Rheumatology, Sf Maria Hospital, UMF Carol Davila, Bucharest, Bucharest, Romania*

Background: Hyperuricemia is frequent in psoriatic arthritis (PsA) and it seems to be related to metabolic syndrome rather than to extensive psoriatic skin disease [1].

Objectives: The objective of this study was to evaluate the prevalence of hyperuricemia in PsA patients and to identify the associated factors.
Methods: Design: cross-sectional study, including consecutive, unselected, adult PsA patients. Data collection: demographic variables (age, gender, disease duration), clinical variables (affected joints, current moderate/severe psoriasis, nail disease, axial involvement, enthesitis, dactylitis), biological factors (acute phase reactants), treatment-related variables (non-steroidal antiinflamatory drugs, corticosteroids, synthetic and biologic disease modifying drugs) and comorbidities [2]. Hyperuricemia was defined as uric acid level above 6.8 mg/dl [3]. Statistical analysis: the factors that were potentially associated with hyperuricemia were assessed by Spearman correlation and uni- and multivariate logistic regressions.
Results: In all, 120 PsA patients were included in the study: 69 (57.5%) women, mean age±standard deviation 54±11.8 years, mean disease duration 7±7.4 years; 24 (20%) had moderate/severe psoriasis and 30 (25%) were taking a biologic. A high percentage of patients had cardiovascular comorbidities, i.e., dyslipidemia 80%, hypertension 51.7%, obesity 34.2% and cardiovascular events 34.2%. Around a quarter of patients had hyperuricemia (33; 27.5%). Hyperuricemia was significantly associated with obesity, diabetes, ischemic heart disease and hypertension, but there was no correlation with current skin psoriasis. In the multivariate analysis, it was best explained by diabetes (odds ratio: 4.95, [95% confidence intervals: 1.47; 16.67]), ischemic heart disease (3.61 [1.00; 12.98]) and obesity (1.86 [1.04; 3.32]).
Conclusions: Hyperuricemia in PsA is associated with metabolic syndrome rather than skin psoriasis, but further longitudinal studies are needed to identify causal relationships.
References:
[1] Bruce IN, Schentag CT, Gladman DD. Hyperuricemia in psoriatic arthritis: prevalence and associated features. J Clin Rheumatol 2000;6(1):6–9.
[2] Baillet A, Gossec L, Carmona L, et al. Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. Ann Rheum Dis 2016;75(6):965–73.
[3] Campion EW, Glynn RJ, DeLabry LO. Asymptomatic hyperuricemia. Risks and consequences in the Normative Aging Study. Am J Med 1987;82(3):421–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5744

AB0791 HIGH PREVALENCE OF METABOLIC DISORDERS AND OBESITY IN PSORIATIC ARTHRITIS COMPARED TO PSORIASIS ALONE: A RETROSPECTIVE DERMATOLOGICAL CLINIC-BASED STUDY

N. Batkaeva[1], T. Korotaeva[2], E. Batkaev[1]. [1]*Department of dermatology, RUDN University;* [2]*V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: An association between increased adiposity, obesity (Obs), and psoriasis has emerged. In addition to obesity, patients with psoriasis are more likely to have metabolic syndrome.
Objectives: to evaluate the prevalence of endocrine diseases, nutritional and metabolic disorder (ENMD) comorbidity in patients (pts) with PsA and Psoriasis (PsO) patients without arthritis in the dermatological hospital cohort.
Methods: 889 pts (Male-516/Female-329) with moderate-to-severy plaque PsO, mean age 50.4±17.6 years, mean PsO duration 21.5±14.7 were included. PsO pts with Endocrine, nutritional and metabolic diseases (E00-E90) (ENMD), including Disorders of thyroid gland (E00–E07), Obesity and other hyperalimentation (E65-E68), Diabetes mellitus (E10-E14) (DM) were identify in the hospital Database reporting and coding by International Statistical Classification of Disease and Related Health Problems (ICD-10) between 2010 - 2015 years. M±m, t-test, χ^2, (%) were calculated. All $p<0.05$ were considered to indicate statistical significance.
Results: 302 out of 889 pts (33.9%) had PsA and 587 out of 889 pts (66.1%) had PsO alone. PsA pts were older then PsO pts – 55.3±13.7 and 50.4±17.6 ($p<0.001$). 155 out of 889 pts (17.4%) had ENMD. In PsA pts ENMD were found in significantly more cases than in PsO pts – in 76 out of 302 pts (25.2%) and in 79 out of 587 pts (13.5%) accordingly (χ^2=18.986, df=2, $p<0.00001$). In PsA pts ENMD coding as E00–E07 were found in significantly more cases than in PsO pts – in 25 out of 302 pts (8.3%) and in 23 out of 587 pts (3.9%) accordingly (χ^2=7.4211, df=2, p=0.00645). Obs coding as E65-E68 were found in significantly more cases in PsA pts compare to PsO pts - in 54 out of 302 pts (17.9%) and in 64 out of 587 pts (10.9%) accordingly (χ^2=8.4345, df=2, p=0.00368).
DM coding as E10-E14 were found in more cases in PsA pts compare to PsO pts - in 54 out of 302 pts (17.9%) and in 83 out of 587 pts (14.1%) accordingly (χ^2=2.1410, df=2, p=0.14341).
Conclusions: ENMD comorbidities are common for PsA and PsO without arthritis pts. Obs and disorders of thyroid gland were found in significantly more cases in PsA pts compare to PsO pts. Obesity and PsA are an unhealthy combination. Obesity may represent an additive cardio-metabolic risk factor in PsA subjects. High frequency of ENMD in PsA than PsO could be due to share inflammation pathways with insulin resistance and age. Patients with more severe psoriasis are at higher odds of endocrine, nutritional and metabolic diseases compared with those with mild psoriasis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2969

AB0792 CURRENT STATUS AND UNMET NEEDS IN THE MANAGEMENT OF PSORIATIC ARTHRITIS WITH CONVENTIONAL SYNTHETIC AND BIOLOGICAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS: TAIWANESE NATIONWIDE PHYSICIANS' PERSPECTIVES

T.-H. Li[1], C.-C. Lai[2], C.-Y.T. Tsai[2]. [1]*Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Chiayi Branch, Taichung Veteran General Hospital, Chiayi City;* [2]*Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Taipei Veteran General Hospital, Taipei City, Taiwan, Province of China*

Background: Psoriatic arthritis (PsA) contributes to enormous burden of disease and thus early correct diagnosis and adequate therapeutic management are essential for physicians in practice; however, There have been several studies highlighting the inadequate diagnosis and suboptimal therapies for PsA worldwide and physicians generally report difficulties in managing psoriasis.
Objectives: To analyze the real-world clinical practice of PsA in Taiwan, and assess physicians' adopted methods and difficulties of diagnosis, therapeutic consideration and strategy, in addition to rationales for biologic agents and unmet needs.
Methods: A nationwide cross-sectional observational study in Taiwan was conducted by means of the face-to-face in depth interviews with the 80 physicians, composed of 50 rheumatologists and 30 dermatologists, from November 2014 to January 2015.
Results: The major adopted diagnostic examinations for PsA are arthritis performance, psoriasis and nail dystrophy, roentgenological studies, personal and family history; however, more dermatologists rely on RF for initial diagnosis ($p<0.05$). The difficulties for diagnosis, considerations on therapeutic management and current prescription were reported and displayed some interdisciplinary difference. Rationales for biological agent selection were investigated and physicians generally favored etanercept in terms of milder symptoms or more conservative treatment. The main unmet needs for current biologic therapies for PsA included the aspects of better efficacy, safety, sustainability and oral administration.
Conclusions: The nationwide study is the first survey for real-world clinical practice of PsA in Asia and provides detailed messages about the diagnostic difficulties and therapeutic consideration, especially rationales and unmet needs on current biologic therapies, which may offer possible directions for new drug development. We also made interdisciplinary comparison, hence in order to improve comprehensive care.
References:
[1] Liu JT, Yeh HM, Liu SY, Chen KT. Psoriatic arthritis: Epidemiology, diagnosis, and treatment. World J Orthop 2014;5:537–43.
[2] van de Kerkhof PC, Reich K, Kavanaugh A, et al. Physician perspectives in the management of psoriasis and psoriatic arthritis: results from the population-based Multinational Assessment of Psoriasis and Psoriatic Arthritis survey. J Eur Acad Dermatol Venereol 2015;29:2002–10.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1360

AB0793 EFFICACY OF IXEKIZUMAB IMPROVING SF-36 SCORES IN BIOLOGIC DMARD-NAIVE PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM A PHASE 3 STUDY (SPIRIT-P1)

V. Strand[1], A.B. Gottlieb[2], T.K. Kvien[3], A. Naegeli[4], C.-Y. Lin[4], O. Benichou[4], J. Birt[4]. [1]*Stanford University School of Medicine, Palo Alto;* [2]*New York Medical College, Valhalla, United States;* [3]*Diakonhjemmet Hospital, Oslo, Norway;* [4]*Eli Lilly and Company, Indianapolis, United States*

Background: In a phase 3 randomized controlled trial (RCT), ixekizumab (IXE), a high affinity mAb that selectively targets interleukin-17A, significantly improved signs and symptoms of psoriatic arthritis (PSA)and health status vs placebo (PBO)[1].
Objectives: To evaluate the efficacy of IXE improving patient (pt)-reported health status, assessed by Short Form Survey (SF-36) physical and mental component summary (PCS and MCS) and domain scores in pts with active PSA vs PBO, compared with age-and gender (A/G)-matched population normative scores[2].
Methods: In phase 3 RCT (SPIRIT-P1; NCT01695239), bDMARD-naive pts with active PSA (N=417) randomly received IXE 80 mg either once every 4 Wks (Q4W) or 2 Wks (Q2W) after a 160 mg starting dose, or 40 mg adalimumab (ADA) Q2W, or PBO (all subcutaneous). Health status was assessed by SF-36 at baseline, Wk 12, and Wk 24. Treatment comparisons were by mixed model for repeated measures for continuous data and logistic regression for categorical data. Missing values were imputed by nonresponder imputation.
Results: Baseline SF-36 scores were similar across treatment groups. At Wk 24, significant improvements vs PBO were observed with ADA and IXEQ2W for PCS, and 5/8 domains (PF, RP, BP, GH, and RE), and with IXEQ4W for PCS and 6/8 domains (except VT and MH) (Figure) (post hoc for individual domains). In pts with baseline scores <A/G norms, significant improvements vs PBO were observed with ADA and IXEQ4W for PCS, MCS, and 5/8 domain scores (PF, RP,

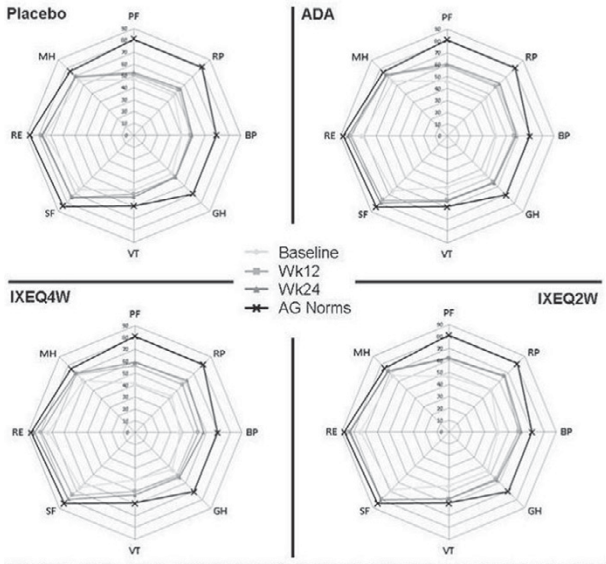
BP, VT and RE) and with IXE Q2W for PCS, MCS, and 7/8 domains (except MH) (post hoc). Within the same subgroup, a greater percentage of pts in each of the 3 active groups reported SF-36 scores ≥normative values at Wk 24 vs PBO, with statistical significance for PCS, MCS, and majority of the individual domains (Table) (post hoc).

Table 1. Percentage of patients with SF-36 scores ≥normative values at week 24 (n) among the patients reporting SF-36 scores <normative values at baseline (N) (nonresponder imputation)

SF-36 Scores, n/N (%)	PBO	ADA	IXEQ4W	IXEQ2W
Physical Component Summary	4/101 (4.0)	20/93 (21.5†)	12/98 (12.2*)	19/95 (20.0**)
Mental Component Summary	10/53 (18.9)	21/52 (40.4*)	21/58 (36.2*)	21/55 (38.2*)
Physical Functioning Domain	5/94 (5.3)	22/91 (24.2†)	14/97 (14.4*)	19/87 (21.8**)
Role Physical Domain	5/98 (5.1)	19/91 (20.9**)	16/93 (17.2*)	19/86 (22.1**)
Bodily Pain Domain	12/95 (12.6)	28/87 (32.2**)	27/96 (28.1*)	28/93 (30.1**)
General Health Domain	8/97 (8.2)	14/88 (15.9)	16/92 (17.4)	21/91 (23.1*)
Vitality Domain	11/73 (15.1)	22/71 (31.0*)	28/87 (32.2*)	22/74 (29.7*)
Social Functioning Domain	15/72 (20.8)	22/66 (33.3)	21/68 (30.9)	28/68 (41.2*)
Role Emotional Domain	7/54 (13.0)	17/59 (28.8*)	23/66 (34.8*)	27/64 (42.2†)
Mental Health Domain	17/69 (24.6)	19/62 (30.6)	18/69 (26.1)	24/68 (35.3)

*p<0.05; **p<0.005; †p≤0.001.

Figure: SF-36 domain scores at baseline, Weeks 12 and 24, compared with age- and gender-matched normative scores



PF, Physical Functioning; RP, Role Physical; BP, Bodily Pain; GH, General Health; VT, Vitality; SF, Social Functioning; RE, Role Emotional; MH, Mental Health; PCS, Physical Component Score; MCS, Mental Component Score; AG norms, age-and gender-normalized; ADA, adalimumab; BL, baseline; IXE, ixekizumab; PBO, placebo; Wk, week

Conclusions: In pts with active PSA, both IXE and ADA treatment groups reported significant improvements in pt-reported health status as assessed by SF-36 and the majority of its individual domains, both in the general trial population, and in the subgroup of pts with baseline scores <A/G norms.

References:

[1] Mease PJ et al. ARD, 2017, 76(1):79–87.

[2] Ware J, et al. How to score version 2 of the SF-36 health survey. Lincoln, RI: QualityMetric Inc.; 2000.

Disclosure of Interest: V. Strand Consultant for: Eli Lilly and Company, Abbvie, Amgen, BMS, Boehringer Ingelheim, Celltrion Corrona, EMDSerono, GSK, Janssen, Merck, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, UCB, A. Gottlieb Grant/research support from: Centocor (Janssen), Amgen, Abbott (Abbvie), Novartis, Celgene, Pfizer, Lilly, Levia, Merck, Xenoport, Dermira, Baxalta, Consultant for: Amgen Inc.; Astellas, Akros, Centocor (Janssen), Inc.; Celgene Corp., Bristol Myers Squibb Co., Beiersdorf, Inc., Abbott Labs. (Abbvie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dermipsor Ltd., Incyte, Pfizer, Canfite, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, Glaxo Smith Kline, Xenoport, Catabasis, Meiji Seika Pharma Co., Ltd, Takeda, Mitsubishi,Tanabe Pharma Development America, Inc, Genentech, Baxalta, Kineta One, KPI Therapeutics, Crescendo Bioscience, Aclaris, Amicus, Reddy Labs, T. Kvien Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celltrion, Eli Lilly, Epirus, Janssen, Merck-Serono, MSD, Mundipharma, Novartis, Oktal, Orion Pharma, Hospira/Pfizer, Roche, Sandoz and UCB, A. Naegeli Employee of: Eli Lilly and Company, C.-Y. Lin Employee of: Eli Lilly and Company, O. Benichou Employee of: Eli Lilly and Company, J. Birt Employee of: Eli Lilly and Company

DOI: 10.1136/annrheumdis-2017-eular.2331

AB0794 **EFFECT OF TOFACITINIB ON PATIENT-REPORTED OUTCOMES IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: RESULTS FROM TWO PHASE 3 STUDIES**

V. Strand[1], K. de Vlam[2], J.A. Covarrubias-Cobos[3], P.J. Mease[4], D.D. Gladman[5], T. Hendrikx[6], E. Kudlacz[7], D. Graham[7], J. Wu[7], L. Chen[8].

[1]Division of Immunology/Rheumatology, Stanford University, Palo Alto, CA, United States; [2]UZ Leuven, Leuven, Belgium; [3]Unidad Reumatologica Las Americas S.C.P., Mérida, Yucatán, Mexico; [4]Swedish Medical Center and University of Washington, Seattle, WA, United States; [5]Department of Medicine, University of Toronto, Toronto Western Hospital, Toronto, ON, Canada; [6]Pfizer Inc, Collegeville, PA; [7]Pfizer Inc, Groton, CT; [8]Pfizer Inc, New York, NY, United States

Background: Tofacitinib is an oral Janus kinase inhibitor under investigation for treatment of psoriatic arthritis (PsA). The safety and efficacy of tofacitinib for the treatment of PsA has been investigated in two Phase 3 randomised controlled trials (RCTs: OPAL Broaden [12 months; NCT01877668]; OPAL Beyond [6 months; NCT01882439]).

Objectives: To evaluate patient-reported outcomes (PROs) in patients (pts) with active PsA enrolled in OPAL Broaden (N=422) and OPAL Beyond (N=394). OPAL Broaden pts had an inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug and were naïve to tumour necrosis factor inhibitors (TNFi) whilst OPAL Beyond pts had an IR to ≥1 TNFi.

Methods: Pts were randomised to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, placebo (PBO)→ tofacitinib 5 mg BID, PBO→ tofacitinib 10 mg BID and, in OPAL Broaden, also to adalimumab 40 mg subcutaneously every two weeks (active comparator). Pts receiving PBO advanced to either tofacitinib 5 mg BID or 10 mg BID at month 3 (M3) in both RCTs. Least squares mean changes from baseline in: Patient's Global Assessment of Arthritis (PtGA; Visual Analogue Scale [VAS]); Arthritis Pain (Pain; VAS); Short Form-36 Health Survey (SF-36); Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F); Dermatology Life Quality Index (DLQI) and Ankylosing Spondylitis Quality of Life (ASQOL) questionnaires are reported. Nominal p values are reported without adjustments for multiple comparisons.

Results: Patients with active PsA in OPAL Broaden and OPAL Beyond RCTs receiving tofacitinib 5 mg and 10 mg BID reported improved PROs compared with PBO (Table 1). Greater improvements in PtGA and Arthritis Pain were observed as early as Week 2 through M3 with both tofacitinib doses compared with PBO in both studies (p≤0.05). Greater improvements were also reported in SF-36 Physical Component Summary, DLQI and ASQOL scores at M1 and M3 with both tofacitinib doses compared with PBO (p≤0.05). There were greater improvements in SF-36 physical functioning, bodily pain and vitality domains with both tofacitinib doses compared with PBO in both studies (p≤0.05) at M3. SF-36 social functioning domain showed greater improvement with tofacitinib 5 mg BID in OPAL Broaden and both tofacitinib doses in OPAL Beyond compared with PBO at M3 (p≤0.05). SF-36 role-physical domain showed greater improvement with tofacitinib 10 mg BID in OPAL Beyond at M3 compared with PBO (p≤0.05). FACIT-F showed a greater improvement in both studies at M3 with both tofacitinib doses compared with PBO (p≤0.05). In OPAL Broaden, improvements in PROs were similar between tofacitinib and adalimumab.

Table 1. PROs at Baseline and Change from Baseline (Δ) at Month 3

		OPAL Broaden				OPAL Beyond		
		Tofacitinib 5 mg BID N=107	Tofacitinib 10 mg BID N=104	Adalimumab 40 mg SC Q2W N=106	Placebo N=105	Tofacitinib 5 mg BID N=131	Tofacitinib 10 mg BID N=132	Placebo N=131
PtGA-VAS (mm)	Baseline, mean (SD)	54.67 (22.13)	53.60 (22.87)	50.56 (22.99)	53.90 (22.65)	57.42 (22.89)	58.52 (22.26)	55.76 (23.73)
	Δ, M3, LSM (SE)	-20.08 (2.28) *	-25.50 (2.29) ***	-21.47 (2.33) **	-11.40 (2.44)	-21.59 (2.23) ***	-19.88 (2.25) ***	-7.14 (2.25)
Arthritis Pain-VAS (mm)	Baseline, mean (SD)	55.74 (22.85)	54.42 (21.63)	50.68 (21.70)	53.15 (23.44)	56.35 (24.13)	59.45 (22.30)	54.91 (25.27)
	Δ, M3, LSM (SE)	-21.49 (2.33) ***	-27.10 (2.34) ***	-21.87 (2.39) **	-10.22 (2.50)	-21.66 (2.16) ***	-20.88 (2.19) ***	-7.72 (2.18)
SF-36 PCS	Baseline, mean (SD)	35.35 (7.87)	36.37 (7.58)	35.94 (8.57)	36.01 (7.43)	33.57 (8.46)	31.73 (8.93)	34.70 (9.55)
	Δ, M3, LSM (SE)	5.51 (0.73) *	5.69 (0.74) *	6.23 (0.75) **	2.68 (0.79)	5.18 (0.68) **	5.34 (0.69) **	1.77 (0.69)
SF-36 physical functioning	Baseline, mean (SD)	34.45 (10.01)	36.73 (9.53)	36.55 (9.80)	36.53 (9.09)	33.45 (10.43)	32.12 (9.87)	34.03 (10.99)
	Δ, M3, LSM (SE)	5.17 (0.85) *	5.23 (0.85) *	5.22 (0.86) *	2.06 (0.91)	5.00 (0.72) *	4.08 (0.73) *	1.69 (0.73)
SF-36 role-physical	Baseline, mean (SD)	37.38 (8.93)	38.08 (9.20)	37.94 (9.76)	36.38 (8.71)	34.63 (10.34)	32.69 (9.25)	35.86 (10.69)
	Δ, M3, LSM (SE)	4.45 (0.80)	4.79 (0.80)	5.21 (0.82)	3.63 (0.86)	4.99 (0.81)	5.44 (0.81) *	2.85 (0.81)
SF-36 bodily pain	Baseline, mean (SD)	34.62 (7.44)	34.91 (8.38)	36.03 (7.88)	35.10 (7.23)	33.24 (7.88)	32.63 (6.94)	35.42 (8.73)
	Δ, M3, LSM (SE)	7.75 (0.84) **	8.05 (0.84) **	7.52 (0.86) **	3.77 (0.90)	7.00 (0.79) ***	7.59 (0.80) ***	2.10 (0.80)
SF-36 general health	Baseline, mean (SD)	35.94 (7.59)	35.61 (8.51)	35.54 (8.23)	34.57 (7.92)	34.71 (8.71)	33.53 (9.39)	35.60 (10.09)
	Δ, M3, LSM (SE)	4.09 (0.70)	3.95 (0.70)	4.73 (0.71) *	2.64 (0.75)	3.67 (0.64)	3.92 (0.65)	2.45 (0.65)
SF-36 vitality	Baseline, mean (SD)	41.75 (9.16)	39.87 (9.92)	42.80 (10.29)	41.35 (8.86)	39.70 (10.22)	38.51 (9.02)	40.25 (10.75)
	Δ, M3, LSM (SE)	5.50 (0.89) *	5.90 (0.89) *	4.93 (0.91)	3.05 (0.95)	4.95 (0.83) *	4.75 (0.84) *	2.41 (0.84)
SF-36 social functioning	Baseline, mean (SD)	38.26 (10.30)	39.55 (11.32)	40.12 (10.61)	37.97 (9.72)	36.46 (11.47)	35.26 (11.12)	37.56 (11.81)
	Δ, M3, LSM (SE)	5.95 (0.90) *	5.22 (0.90) *	5.26 (0.92) *	3.63 (0.96)	6.25 (0.84) *	5.46 (0.86) *	2.89 (0.86)
FACIT-F total score	Baseline, mean (SD)	28.0 (10.46)	28.2 (10.63)	30.0 (11.23)	28.5 (9.52)	26.1 (12.15)	26.1 (10.27)	27.5 (11.58)
	Δ, M3, LSM (SE)	7.0 (0.85) *	6.0 (0.85) *	6.0 (0.87) *	3.3 (0.91)	7.0 (0.81) **	5.8 (0.82) *	3.0 (0.82)
DLQI	Baseline, mean (SD)	8.8 (7.27)	9.0 (7.66)	7.7 (7.10)	9.4 (7.64)	7.8 (7.05)	10.2 (8.20)	8.4 (7.71)
	Δ, M3, LSM (SE)	-4.7 (0.47) *	-5.4 (0.47) ***	-4.4 (0.48) *	-2.8 (0.50) *	-3.2 (0.43) ***	-5.4 (0.44) ***	-1.2 (0.43)
ASQOL	Baseline, mean (SD)	11.2 (5.00)	10.5 (4.91)	10.6 (5.26)	10.4 (4.82)	11.4 (4.83)	12.2 (4.45)	10.7 (5.20)
	Δ, M3, LSM (SE)	-4.0 (0.45) *	-3.9 (0.46) *	-4.0 (0.46) *	-2.1 (0.49)	-3.8 (0.38) ***	-3.5 (0.39) **	-1.5 (0.40)

*Nominal p≤0.05; ** p<0.001; *** p<0.0001. Other variables assessed as not achieving p≤0.05 at M3 were SF-36 Mental Component Summary (MCS), mental health and role-emotional domain scores

N is the number of patients who were randomised and received at least one dose of study medication. A subject was excluded from an analysis for an endpoint if the baseline was missing or there was no post-baseline observation

Δ, change from baseline; ASQOL, Ankylosing Spondylitis Quality of Life; BID, twice daily; DLQI, Dermatology Life Quality Index; FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue; LSM, least squares mean; M3, Month 3; PCS, Physical Component Summary; PRO, patient-reported outcome; PtGA, Patient's Global Assessment of Arthritis; Q2W, every two weeks; SC, subcutaneously; SD, standard deviation; SE, standard error; SF-36, Short Form-36 Health Survey; VAS, Visual Analogue Scale

Conclusions: Pts with active PsA receiving tofacitinib reported greater improve-

ments in PROs compared with PBO at M3 that were maintained throughout both RCTs.

Acknowledgements: To be presented at AAD 2017 and reproduced with permission. This study was sponsored by Pfizer Inc. Editorial support was provided by S. Morgan of CMC and was funded by Pfizer Inc.

Disclosure of Interest: V. Strand Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, CORRONA, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, K. de Vlam Consultant for: Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, UCB, Speakers bureau: Celgene, Eli Lilly, Janssen, J. Covarrubias-Cobos Grant/research support from: Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer Inc, P. Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis, Pfizer Inc, Sun, UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, CORRONA, Dermira, Janssen, Eli Lilly, Merck, Novartis, Pfizer Inc, Sun, UCB, Zynerba, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, Genentech, Janssen, Novartis, Pfizer Inc, UCB, D. D. Gladman Grant/research support from: Amgen, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer Inc, Novartis, UCB, Consultant for: Amgen, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, Eli Lilly, Pfizer Inc, Novartis, UCB, Speakers bureau: Amgen; AbbVie; Bristol-Myers Squibb; Celgene; Janssen; Eli Lilly; Pfizer Inc; Novartis; UCB, T. Hendrikx Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, E. Kudlacz Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, D. Graham Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, J. Wu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, L. Chen Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

DOI: 10.1136/annrheumdis-2017-eular.2445

Osteoarthritis

AB0795 OSTEOARTHRITIS AND COMORBIDITY: ASSOCIATION BETWEEN MENTAL FEATURES AND CYTOKINES LEVELS

E. Trifonova, O. Sazonova, E. Zonova. *Novosibirsk State Medical University, Novosibirsk, Russian Federation*

Background: Studies of mental health in patients with osteoarthritis (OA) are topical at the present time. This applies especially to OA patients with such comorbidity as obesity, metabolic syndrome (MS) and type 2 diabetes mellitus (T2DM). Psychological features, quality of life (QoL) and depression degree also can be linked with immunopathogenesis of OA with obesity, MS, T2DM.

Objectives: To explore the mental health in knee OA patients with obesity, MS, T2DM and to estimate association between psychological and immunological features.

Methods: Patients (n=128) with bilateral knee OA according to ACR criteria were divided into four groups. Group 1 (n=17) had obesity, group 2 (n=17) had MS, group 3 (n=56) had T2DM and group 4 (n=38) had only knee OA without comorbidity. All patients were comparable by age, sex and duration of OA. We assessed serum cytokine levels (IL-1b, IL-6, IL-10, IL-18), NO and adipokines (adiponectin, leptin) using ELISA. The parameters of QoL, mental health and depression degree were measured by short form 36 (SF-36), Knee injury and Osteoarthritis Outcome Score – (KOOS) and with patient health questionnaire-9 (PHQ-9). We also studied coping strategies to overcome pain by Coping Strategy Questionnaire (CSQ). U-Mann-Whitney test was applied to detect differences between groups. Correlation was assessed using Spearman correlation coefficient (r_s).

Results: During comparative analysis, we found many statistically significant differences in such indexes and questionnaires as SF-36, KOOS, PHQ-9, CSQ between groups knee OA patients with comorbidity and group knee OA patients without concomitant diseases. Patients with OA and obesity were characterized by low values of mental health (SF-MH) (median (Me) 52; interquartile range (IQR) 38–64; p=0.01). Patients from group 2 (MS) and 3 (T2DM) had significant impairment of QoL parameters, mental health values. Patients of these groups also had the higher degree of depression and built coping strategies to overcome pain of OA worse than patients of OA group. Differences in serum cytokine levels were found in patients with OA and T2DM (IL-6 p=0.0018; IL-18 p=0.0006; NO p<0.001). Significant high leptin level had OA patients with obesity (p=0.03) and OA patients with T2DM (p=0.0002). Correlation analysis identified the association between mental health and cytokines in OA patients with obesity and OA patients with T2DM. Some data are presented (Table).

Table. Correlations between mental parameters and serum cytokine levels in studied groups.

Cytokines	OA patients with obesity n=17	OA patients with T2DM n=56		
	Social Functioning (SF36-SF)	Vitality (SF36- VT)	Social Functioning (SF36-SF)	Coping Strategy Questionnaire (CSQ)
IL-1ß (pg/ml)	-0.51	-0.06	0.08	-0.15
IL-6 (pg/ml)	**-0.89***	**-0.33***	**-0.27***	-0.03
IL-10 (pg/ml)	-0.75	-0.18	-0.09	**-0.41***
NO (pg/ml)	-0.39	0.10	0.14	0.11
Leptin (ng/ml)	-0.27	**-0.28***	-0.22	**0.43***

Table legend: * r - p<0.005;

Conclusions: This study suggests that OA patients with obesity, MS and T2DM have special mental features which may be linked with immunological parameters. This data should be verified by larger studies and can be the part for an integrated program of treatment and rehabilitation of OA patients with comorbidity.

References:

[1] Perruccio, A.V. Cross-Sectional Contrast Between Individuals With Foot/Ankle vs Knee Osteoarthritis for Obesity and Low Education on Health-Related Quality of Life/A.V. Perruccio et al. // Foot & Ankle Int. – 2016.– Vol. 36, N 1. – P. 24–32.

[2] Siervo, M. Metabolic syndrome and longitudinal changes in cognitive function: a systematic review and meta-analysis/M. Siervo et al. // J. Alzheimers Dis. – 2014. – Vol. 41, N 1. – P. 151–161.

[3] Berge, L.I. Comorbidity between Type 2 Diabetes and Depression in the Adult Population: Directions of the Association and Its Possible Pathophysiological Mechanisms/L.I. Berge, T. Riise // Int. J. Endocrinol. – 2015. – Vol. 2015.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5896

AB0796 THE PREDICTIVE ROLE OF INTERLEIKINE 6 AND 10 IN IMPAIRMENT OF MENTAL HEALTH IN PATIENTS WITH KNEE OSTEOARTHRITIS AND UNCONTROLLED TYPE 2 DIABETES MELLITUS

E. Trifonova, O. Sazonova, E. Zonova. *Novosibirsk State Medical University, Novosibirsk, Russian Federation*

Background: The influence of different interleukins on development and progression of osteoarthritis (OA) has been proved. However, there is lack of data on relationship between mental health and immunological features in OA patient with type 2 diabetes mellitus (T2DM).

Objectives: To estimate the relationship between mental health and the proinflammatory serum cytokine levels in patients with knee OA and T2DM depending on glycemic control.

Methods: A study was performed on 45 persons who had bilateral knee OA according to the ACR criteria and T2DM. Then patients were divided into two groups according to the compensation degree T2DM taking into account parameters of glycated hemoglobin concentrations (HbA1c) which were assessed using liquid chromatography. Group 1 (n=26) had controlled T2DM. Group 2 (n=19) had uncontrolled T2DM. All patients were comparable by age, sex and duration of OA. Serum cytokine levels (IL-1b, IL-6, IL-10, IL-18), NO, and adypokines (adiponectin, leptin) using ELISA were measured. Blood glucose level was also estimated. The parameters of QoL, mental health, depression degree and coping strategies to overcome pain were measured by short form 36 (SF-36), Knee injury and Osteoarthritis Outcome Score – (KOOS) and with patient health questionnaire-9 (PHQ-9), Coping Strategy Questionnaire (CSQ). We used U-Mann-Whitney tests to detect differences between selected groups. Correlation was assessed using Spearman correlation coefficient (r_s).

Results: Patients with OA and uncontrolled T2DM had significant low values of role limitations due to emotional problems (SF-RE) (median (Me) 38; interquartile range (IQR) 25–52.3; p=0.02). Serum cytokines levels were not different between studied groups. Correlation analysis identified the relationships between parameters of mental health and serum cytokine levels in OA patients with uncontrolled T2DM. Certain data are presented (Table).

Table. Correlations between clinical parameters and serum cytokine levels in studied groups.

Cytokines	OA patients with uncontrolled T2DM n=19						
	Vitality (SF36-VT)	Social Functioning (SF36-SF)	Mental Health (SF36-MH)	Role Emotional (SF36-RE)	General Mental Health (SF36-MH)	Patient Health Questionnaire (PHQ-9)	Coping Strategy Questionnaire (CSQ)
IL-6 (pg/ml)	**-0.60***	**-0.62***	**-0.54***	-0.25	**-0.51***	**0.43***	-0.20
IL-10 (pg/ml)	**-0.48***	**-0.42***	**-0.64***	-0.25	**-0.56***	0.29	**-0.53***
NO (pg/ml)	0.12	0.08	0.12	**0.42***	0.31	0.15	-0.02
Leptin (ng/ml)	-0.31	**-0.42***	-0.14	-0.19	-0.15	0.28	0.35

Table legend: * r - p<0.005;

Conclusions: It follows from these results mental and immunology parameters of OA patients with uncontrolled T2DM can be linked. Such interleukins as IL-6 and IL-10 may play a role of potential biomarkers of mental impairment in this category of patients. These data should be verified by larger studies and may allow in future to develop programs of treatment and rehabilitation of OA patients with uncontrolled T2DM within personalized medicine.

References:

[1] Kapoor, M. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis/M. Kapoor, J. Martel-Pelletier, D. Lajeunesse et al. Nat. Rev. Rheumatol. 2011;7(1):33–42.

[2] Stannus, O. Circulating levels of IL-6 and TNF-alpha are associated with knee radiographic osteoarthritis and knee cartilage loss in older adults/O. Stannus, G. Jones, F. Cicuttini et al. Osteoarthr. Cartil. 2010:18(11):1441–1447.
[3] Louati K. et al. Association between diabetes mellitus and osteoarthritis: systematic literature review and meta-analysis. RMD open. 2015;1(1).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5940

AB0797 LONG TERM PROSPECTIVE MULTICENTER RANDOMIZED PLACEBO-CONTROLLED STUDY OF HYALURONIC ACID IN SMALL JOINTS OSTEOARTHRITIS (SJOA)

E. Tsvetkova[1], L. Denisov[1], E. Panasyuk[1], E. Nasonov[2]. *[1]Clinical Research laboratory; [2]Scientific Leader, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia, Moscow, Russian Federation*

Objectives: Assessment of the efficacy, tolerability and period of aftereffect of the single administration into 1st carpometacarpal and 1st metatarsophalangeal OA joints of 1.0 ml (20mg) of hyaluronic acid (Durolane) as compared with placebo.
Methods: The study included 120 pts with OA of small hand joints or feet, pain intensity >40 mm by VAS and consisted of two phases: "blind" phase up to 24 weeks, period of assessment of long term efficacy results – 48 weeks. The efficacy was assessed by 40% pain subsiding, index AUSCAN (for the hand), dose of NSAID, total effect assessment.
Results: Both groups were comparable by basic clinical criteria, 40% pain subsiding by VAS (mm) was noted in experimental group to 24th week in 79.7%, in the placebo group – 30% (chi-square: $p<10^{-5}$), relation of chances (OR) equal to 9.1 (3.9–21.1). Dispersion analysis of pain, stiffness and function of AUSCAN index revealed reliable differences between Durolane and placebo. Statistically significant difference ($p<0.0001$) according to assessment of general condition by the doctor and patient were found out in experimental group from the 4th week and were stable till 48th week. Adverse effects related to the therapy were not found. NSAID dose was decreased in 45.7% in experimental group and in 30% in placebo group.
Conclusions: efficacy and considerable duration of aftereffect of single administration of Durolane SJ (small joints) as compared with placebo was demonstrated in 24 and 48 weeks.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5740

AB0798 AMTOLMETIN GUACIL-EFFECTIVE AND GOOD SAFE NONSTEROIDAL ANTI-INFLAMMATORY DRUG IN KNEE OSTEOARTHRITIS PATIENTS WITH DYSPEPSIA

E. Tsvetkova[1], L. Denisov[1], E. Nasonov[2] on behalf of AGATA group. *[1]Clinical Research laboratory; [2]Scientific Leader, V.A.Nasonova Research Institute of Rheumatology, Moscow, Russia, Moscow, Russian Federation*

Objectives: To investigate the efficacy and tolerability of amtolmetin guacil (AMG; Niselat®, Dr. Reddy's Laboratories Ltd, India) versus previous therapy with nonsteroidal anti-inflammatory drugs (NSAIDs) in patients with knee osteoarthritis (OA) and signs of dyspepsia.
Methods: The open-label observational study included 220 patients aged 30–65 years who suffered from knee OA and intense pain during NSAID intake and had symptoms of dyspepsia in the absence of contraindications to the use of AMG. Among the comorbidities that generally occurred in 68% of the patients, there was a preponderance of hypertension (42%), lower extremity varicose veins (6.4%), and diabetes mellitus (6%).
Treatment efficacy was evaluated using three domains of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), by also taking into account pain intensity and general health assessment on the visual analogue scale. A Severity of Dyspepsia Assessment (SODA) scale was used to rate dyspepsia.
Results: AMG had a marked analgesic effect confirmed by 40% or more pain reduction thatoccurred in 72.5% of the patients. The high analgesic effect of AMG was confirmed by a statistically significant ($p<0.001$) reduction in the WOMAC index (pain and stiffness) and by an increase in functional activity. Therewas a significant decrease in painless and painful signs of dyspepsia, as well as positive changes in the measures"overall assessment of dyspepsia severity" ($p<0.001$) and "satisfaction with treatment". Overall assessment ofAMG tolerability was only positive: excellent (33%), good (56%), and satisfactory (11%). There were no seriousadverse events (AE). AE were graded as moderate and mild in 8 and 82% of cases, respectively. AE were recordedin 7.7% of the patients.
AMG had a marked analgesic effect confirmed by 40% or more pain reduction that occurred in 72.5% of the patients. The high analgesic effect of AMG was confirmed by a statistically significant ($p<0.001$) reduction in the WOMAC index (pain and stiffness) and by an increase in functional activity. There was a significant decrease in painless and painful signs of dyspepsia, as well as positive changes in the measures "overall assessment of dyspepsia severity" ($p<0.001$) and "satisfaction with treatment". Overall assessment ofAMG tolerability was only positive: excellent (33%), good (56%), and satisfactory (11%). There were no serious adverse events (AE). AE were graded as moderate and mild in 8 and 82% of cases, respectively. AE were recorded in 7.7% of the patients.
Conclusions: The findings suggest that AMG offers good prospects for knee OA treatment.
Acknowledgements: Otteva A.N., Dubikov A.I., Yakupova S.P., Ivanova O.N., Korshunov N.I., Vaisberg A.R., Abyshev R.A., Tartynov A.V.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5253

AB0799 DECREASED RATIO OF TIMP1/MMP-9 IS ASSOCIATED WITH HIGHER PAIN SENSITIVITY IN A SUBSET OF OSTEOARTHRITIC PATIENTS WITH LOW MECHANISTIC TARGET OF RAPAMICIN GENE EXPRESSION IN THE PERIPHERAL BLOOD

E.V. Tchetina[1], G.A. Markova[1], E.A. Taskina[2], N.G. Kashevarova[2], E.P. Sharapova[2], L.I. Alekseeva[2]. *[1]Immunology & Molecular Biology; [2]Osteoarthritis, Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Progression of osteoarthritis (OA) produces loss of articular cartilage that may culminate in pain, loss of joint function, and disability. Osteoarthritic changes in articular cartilage are associated with progressive proteolytic degradation of the extracellular matrix due to excessive expression of metalloproteinases (MMPs) over their tissue inhibitors (TIMPs). At the same time, decrease in TIMP concentration versus MMP has been previously associated with an increase in pain sensitivity.
Objectives: Here we hypothesized that imbalance in TIMP1 and MMP-9 gene and protein expressions in the peripheral blood might contribute to pain perception in OA patients.
Methods: We examined whole blood of 65 OA outpatients and 27 healthy subjects. Clinical testing comprised physical examination, radiographic and WOMAC scoring, and ultrasonography. Total RNA isolated from the whole blood was used for gene expression examination of mTOR, mechanistic target of rapamycin, a major regulator of cell growth and proliferation, metalloproteinase MMP-9, and tissue inhibitor of metalloproteinase, TIMP1 using quantitative Real-time RT-PCR. p70-S6K (mTOR read-out), MMP-9, and TIMP1 protein levels were quantified by ELISA.
Results: 23 OA outpatients exhibited significant downregulation of mTOR gene expression (subset "Low mTOR") while other 42 OA outpatients have demonstrated upregulation of mTOR gene expression (subset "High mTOR") in the peripheral blood compared to healthy controls. Although both OA outpatient subsets had comparable radiographic severity according to Kellgren-Lawrence grading, similar age, disease duration, and body mass index, "Low mTOR" patients experienced significantly higher pain at joint function versus "High mTOR" subset. This was associated with a significant upregulation of MMP-9 gene expression in "Low mTOR" patients versus healthy subjects while TIMP1 expression remained equal to controls. In a "High mTOR" subset, both gene expressions were significantly upregulated. p70-S6K and TIMP1 protein concentrations measured in the peripheral blood mononuclear cells were significantly lower in "Low mTOR" patients versus that in "High mTOR" while MMP-9 protein expression was significantly higher compared to healthy subjects in both examined OA subsets.
Conclusions: Our results show that TIMP1 and MMP-9 gene expressions measured in the peripheral blood might be associated with pain sensitivity in OA outpatients while low level of TIMP1/MMP-9 ratio indicates increased pain perception.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2254

AB0800 KNEE OSTEOARTHRITIS PATIENTS' USE OF AND COMPLIANCE TO AN ORTHOTIC INTERVENTIONS

E. Mauricio, M. Sliepen, D. Rosenbaum. *Universitätsklinikum Münster, Münster, Germany*

Background: Knee osteoarthritis (KOA) is the most common form of arthritis with an estimated lifetime prevalence of 44.7% (1). The use of orthotic devices (knee braces, insoles, wedged shoes) is a generally accepted conservative therapy for KOA patients (2). However, it is suggested that their effectiveness is detrimentally affected by poor patient compliance due to discomfort while wearing these devices (3).
Objectives: The aim of this study is to objectively establish the compliance to an orthotic intervention using a thermal sensor (TS) and comparing it to patients' self-reported wear time.
Methods: Ten medial KOA patients (mean±SD age 57.6±13.4 years, BMI 27.3±3.2 kg/m^2), clinically diagnosed according to the ACR Guidelines, were recruited for this study. A small, light-weight TS with the size of an average lithium battery (0.5℃ resolution) was placed in a newly developed ankle-foot-orthosis (AFO) that patients were asked to wear as often as possible during a period of six weeks. The TS measured the temperature every 5 minutes for 4 weeks. Patients rated the comfort of the orthosis during the first visit using a scale from 1 to 5 (1 being the most comfortable).
Additionally, the patients reported during these six weeks how many hours per day they had worn the orthosis and rated which amount of pain they felt each day (from 0=no pain to 10=most painful). To determine the patients' compliance, the AFO wear time, derived from the TS, was compared to the wear time per day recorded in the patients' diaries. The threshold to differentiate the wear

and non-wear times was set at 25℃. Timeframes during which the temperature rose above 25℃ were classified as wear time. A Wilcoxon signed-rank test was performed between the different wear times and Spearman's correlations between pain, comfort and wear time were determined.

Results: On average, patients wore the device for 143±80 h according to the form they filled out, whereas the TS measured only 83±86 h, leading to an overestimation of 72%. Patients reported an average pain level of 3±1.4 during the six weeks period and the AFO's comfort was rated with 1.9±0.3.

Statistical differences were found between the wear time reported by the patients and the wear time derived from the TS (p=0.005). Additionally, a significant correlation between the AFO comfort and the wear time derived from the TS was found (r = -0.81; p=0.001). No significant correlation was found between pain and wear time.

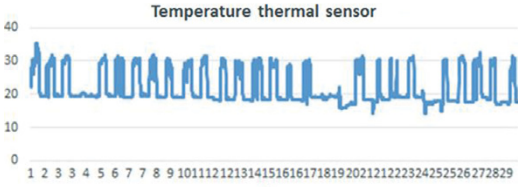


Figure 1: Data set from one of the patients.

Conclusions: As can be expected, patients who found the AFO more comfortable were the ones who wore the orthosis for longer periods. The wear time recorded by the TS was significantly lower compared to the self-reports. This might be due to a social desire bias, overestimating the amount of hours of wearing the AFO as we asked the patients to wear it as often as possible. Secondly, patients might have trouble to accurately recall the amount of wear hours, thereby inducing an overestimation of wear time. As the reliability of self-reported measures seems to be questionable, such data should be interpreted with care.

References:

[1] Lee S et al. Int J Rheum Dis, 2015.
[2] Duivenvoorden T et al. The Cochrane Library, 2015.
[3] Brouwer RW et al. Cochrane Database Syst Rev, 2005.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1415

AB0801 EVALUATION OF EFFECTIVITY OF RADIOTHERAPY FOR PAIN CONTROL IN OSTEOARTHRITIS AND SOFT TISSUE PATHOLOGY

F. Aramburu, Á. Montero, R. Silvia, J. González, E. Calvo, M. Valero, C. Rubio, P. Garcia de la Peña on behalf of Rheumatology and Radiotherapy services.
Rheumatology, HM hospitales, Madrid, Spain

Background: Osteoarthritis and soft tissue pathology are diseases that produce important pain and disability in many patients. Some studies support that the low-dose radiotherapy may be effective in refractory diseases.

Objectives: The main objective of this study is to evaluate whether the treatment with radiotherapy is long-term effective to reduce the pain in osteoarthritis and soft tissue pathology. The secondary objective is to evaluate the analgesic requirements before and after the treatment.

Methods: A prospective and observational study was designed. 38 patients were included. 53 different pathologies were treated including knee osteoarthritis, trochanteric bursitis, calcinosis, rizartrosis, pyramidal syndrome, rotatory cuff pathology and shoulder osteoarthritis, plantar fasciitis, epicondylitis, hand osteoarthritis, tibialis posterior tendonitis, ankle osteoarthritis, hip osteoarthritis and hand tendonitis. All these pathologies did not respond to conventional therapy (non steroidal antiinflamatory drugs, rehabilitation or infiltrations). Initially, the patients received a treatment of radiotherapy with a dose of 6 Gray divided in 6 sessions during 2 weeks. The patients that did not respond after 6 weeks received a second treatment with the same characteristics. The modification in Visual Analogic Scale (VAS) of pain was evaluated as well as analgesic intake before and after the treatment.

Results: No side effects were observed. 92% were women and 8% men. Mean age was 66,82, standard deviation (SD): 12,97 (42–89). 44 locations responded to one treatment and 19 needed a second one.

The mean VAS prior treatment was 7,38, SD: 1,49, (10–4). Mean VAS after the first treatment was 3,81 SD: 2,84 (9–0).

The mean VAS after the first treatment in locations that received 2 treatments was 6,65 SD: 1,46 (9–5), and mean VAS after the second one was 4,56 DE: 2,66 (8–1).

By pathology, the difference in means was: 4,8 in knee osteoarthritis (N=11), 4,78 in trochanteric bursitis (N=10), 5 in calcinosis (N=3), 5,33 rizartrosis (N=8), 4 in pyramidal syndrome (N=2), 3,87 in rotatory cuff pathology and shoulder osteoarthritis (N=6), 6 in plantar fasciitis (N=1), 7 in epicondylitis (N=1), 3,22 in hand osteoarthritis (N=11), 6 in tibialis posterior tendonitis (N=2), 4 in ankle osteoarthritis (N=2), 2 in hip osteoarthritis (N=1) and 2,2 in hand tendonitis (N=5).

Until November 2016, 12 patients (17 pathologies) were followed-up for 6 months. The mean VAS before treatment of these pathologies was 7,29 SD: 1,21; (9–4). After 6 months mean VAS reduced to 1,47 SD: 1,42; (5–0).

The analgesic intake was reduced in 37,98% of patients, 10,34% used the same amount and 34,48% was not known. 17,24% did not take analgesic drugs at all after treatment.

Conclusions: The treatment with low dose radiotherapy was long-term effective for reducing the pain level in our study.

References:

[1] Minten MJ, Mahler E, den Broeder AA et al. The efficacy and safety of low-dose radiotherapy on pain and functioning in patients with osteoarthritis: a systematic review. Rheumatol Int. 2016 Jan; 36(1):133–42.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4256

AB0802 EFFECTS OF DIETARY MAGNESIUM SUPPLEMENTATION AND INTRA-ARTICULAR MAGNESIUM SULFATE ON EXPERIMENTAL OSTEOARTHRITIS AND POTENTIAL MOLECULAR MECHANISMS BY MRNA AND LNCRNA EXPRESSION PROFILES SCREENING

G. Lei[1], C. Zeng[1], H. Li[1], J. Wei[2], T. Yang[1], B. Wise[3], X. Ding[1], Y. Zhang[1], Y. Yang[1], Z. Deng[1], J. Li[4], Y. Cui[5]. *[1]Department of Orthopaedics; [2]Health Management Center, Xiangya Hospital of Central South University, Changsha, Hunan Province, China; [3]Department of Internal Medicine and Department of Orthopaedics, University of California, Davis School of Medicine, Sacramento, CA; [4]Division of Rheumatology, Department of Internal Medicine, Rush University Medical Center, Chicago, IL, United States; [5]International Medical Center, Xiangya Hospital, Central South University, Changsha, Hunan Province, China*

Background: Epidemiological studies of ours and other groups have reported an inverse association between dietary and serum Mg with knee radiographic osteoarthritis (OA) [1–4].

Objectives: To investigate the effects of dietary magnesium supplementation and intra-articular $MgSO_4$ on the development of experimental rat osteoarthritis, and explore the underlying potential molecular mechanisms by mRNA and lncRNA expression profiles screening.

Methods: Rat osteoarthritis model was induced by surgery. Articular cartilage damage was evaluated by modified Mankin score system after intervention of dietary magnesium supplementation or intra-articular $MgSO_4$ injection. Microarray was performed to reveal alteration of expression profiles of mRNA and lncRNA after intervention of $MgSO_4$ on human osteoarthritis chondrocytes. Bioinformatics analyses including gene ontology analysis, pathway analysis, target gene predictions and network analysis were used.

Results: Comparing with normal diet, dietary Mg supplementation showed significantly ameliorated cartilage damage at the medial femoral condyle, lateral tibial plateau and medial tibial plateau ($P \leq 0.05$), and approaching significance at the lateral femoral condyle (P=0.06). All four locations exhibited mitigated cartilage damage in the intra-articular $MgSO_4$ group compared with intra-articular saline ($P \leq 0.05$). 1767 lncRNAs and 2558 mRNAs were upregulated while 994 lncRNAs and 1512 mRNAs were downregulated in chondrocytes with intervention of 50mM MgSO4 compared with control group (fold change ≥ 2.0). The top 6 lncRNAs which showed the largest difference were ENST00000425914.2, ENST00000419881.1, ENST00000561231.1, ENST00000609062.1, TCONS_00029212 and ENST00000429530.1. Bioinformatics analyses indicated that the differentially expressed lncRNA target genes of chondrocyte after intervention of 50mM $MgSO_4$ are enriched in negative regulation of phosphatidylinositol 3-kinase signaling.

Conclusions: Both dietary magnesium supplementation and intra-articular $MgSO_4$ injection may exert cartilage protective effects by causing widespread changes in the profile of lncRNAs and mRNAs of chondrocytes.

References:

[1] Hunter DJ. Evidence of altered bone turnover, vitamin D and calcium regulation with knee osteoarthritis in female twins. Rheumatology 2003;42(11):1311–6.
[2] Zeng C, Wei J, Li H, Yang T, Zhang FJ, Pan D, et al. Relationship between Serum Magnesium Concentration and Radiographic Knee Osteoarthritis. J Rheumatol 2015;42(7):1231–6.
[3] Qin B, Shi X, Samai PS, Renner JB, Jordan JM, He K. Association of dietary magnesium intake with radiographic knee osteoarthritis: Results from a population-based study. Arthritis Care & Research 2012;64(9):1306–11.
[4] Zeng C, Li H, Wei J, Yang T, Deng Z, Yang Y, et al. Association between Dietary Magnesium Intake and Radiographic Knee Osteoarthritis. PLOS ONE 2015;10(5):e127666.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4647

AB0803 DOES INTRA-ARTICULAR INJECTION OF PLATELET-RICH PLASMA PROVIDE CLINICALLY PREFERABLE OUTCOMES IN THE KNEE OSTEOARTHRITIS? A DOUBLE-BLIND, RANDOMIZED CONTROLLED PILOT STUDY

J. Moghimi[1,2], R. Ghorbani[1], H. Beiki[1]. *[1]Social Determinants of Health Research Center; [2]Department of Internal Medicine, Semnan university of medical sciences, Semnan, Iran, Islamic Republic Of*

Background: Knee osteoarthritis (OA) symptoms Improvements with platelet-

rich plasma (PRP) have been ascribed to its ability to rectify intra-articular inflammatory processes.
Objectives: The aim of this study was to determine the safety, feasibility and changes in symptom severity, sports activity, lower limb function, and function in daily living activities following intra-articular injections of PRP in mild to moderate knee OA.
Methods: In this double-blind randomized controlled pilot study, 34 patients with knee OA grade 2 or 3, from March 2013 to February 2016 were selected. Participants were randomly assigned one knee as the case and other knee was considered as control to receive three injections of either PRP or placebo. The administering doctor and the patients were blinded to group allocation. Outcomes included safety and recruitment data, 100 mm the EuroQol-visual analogue scales (EQ-VAS), the international knee documentation committee (IKDC), the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and the Tegner Activity Score (TAS) at three and six months.
Results: Twenty four (100%) participants met the inclusion criteria. No treatment-related major adverse events were reported. The PRP group demonstrated significant improvements at all follow up time points in the WOMAC (3 months: p=0.017; 6 months: p=0.029, ETA=0.601). For the PRP group, the 11.47 mm reduction in EQ-VAS at 6 months (p=0.040) and the 7.35 mm at 3 months (p=0.035) was statistically significant improvement from baseline. The PRP group also significantly improved IKDC (p=0.039, ETA =0.619) and TAS (p=0.028, ETA =0.641) at three months. The placebo group showed improvements on only the IKDC Function at 3 months (p=0.019, ETA =0.591). There were no significant between-group differences for any of the self-reported measures at either time-point.
Conclusions: The study provides proof-of-concept evidence about the safety and feasibility of intra-articular injections of PRP necessary to appraise a larger clinical trial knee OA. Our preliminary findings also suggest PRP improves self-reported symptom severity, sports activity, and function in daily living activities, however no between-group differences were found. PRP may provide an effective and safe novel treatment for knee OA.
Acknowledgements: This study was supported by Semnan University of Medical Sciences, Semnan, Iran.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1387

AB0804 SINGLE-NUCLEOTIDE POLYMORPHISM (SNP) RS143383 GROWTH AND DIFFERENTIATION FACTOR 5 (GDF5) IN KNEE OSTEOARTHRITIS IN EGYPTIAN POPULATION

M. Hassanien[1], N.A. Mohamed[2], S.A. Mahran[1]. *[1]Rheumatology Department; [2]Medical Biochemistry, Assuit University, assuit, Egypt*

Background: Osteoarthritis (OA), is an age-related common polygenic disease characterized by the thinning and loss of the articular cartilage in synovial joints such as knees. The etiology and pathogenesis of OA is largely unknown, the single-nucleotide polymorphism (SNP) rs143383 (C/T) influencing OA susceptibility across a range of ethnic groups.
Objectives: The present study investigated to identify the association of polymorphism in GDF-5 gene with osteoarthritis in Egyptian population.
Methods: This Case control study of 100 women and 100 male $\geq$40 years that fulfilled American College of Rheumatology (ACR) for Knee OA and 100 controls recruited from the outpatient clinic of Department of Rheumatology, Asyut university, Egypt. Clinical symptoms were assessed with WOMAC index and VAS for knee pain. The severity of disease was determined by radiological grades (Kellgren Lawren). Body Mass Index (BMI) was recorded. DNA isolation and genotype analysis the method of (Southam *et al.*, 2007) was followed for determining the GDF-5 gene (T/C; rs143383) polymorphism. Amplification was performed.
Results: There were weak but significant associations present between the GDF5 polymorphism and knee OA at the allele level (C vs. T: 0.85, 95% CI =0.78–0.93) and genotype level (CC vs. TT: 0.72; CT vs. TT: 0.81; CC/CT vs. TT: 0.83; CC vs. CT/TT: 0.78) in the overall population. A stronger significant association was observed for CC vs. TT (OR =0.83, P$<$0.001) in comparison with other models. In males we identified a second polymorphism, located in the 3'-UTR of *GDF5*, that influenced allelic expression of the gene independent of rs143383.
Conclusions: GDF5 is an OA susceptibility gene with association between the GDF5 polymorphism and clinical symptoms of knee OA in Egyptian population.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1273

AB0805 PANLAR CONSENSUS. RECOMMENDATIONS FOR THE MANAGEMENT OF OSTEOARTHRITIS OF THE HAND, HIP AND KNEE. SHORT TITLE: PAN-AMERICAN LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY (PANLAR) OSTEOARTHRITIS (OA) STUDY GROUP

M.J. Quintero[1], H. Riera[2], R. Espinosa[3], R. Souto[4], C. Rossi[5], J.F. Molina[6], J. Salas[7], F. Radrigan[8], G. Reyes[9], L. Urioste[10], S. Papasidero[11], A. Garcia[12], I. Iraheta[13], E. Nieto[2], R. Arape[14], O. Castaneda[15], J. Angulo[16], I. Coimbra[17], L.M. Franco[18], C. Acosta[19], V. Liendo[20], R. Chacón-Díaz[2], M. Vera[2], A. Reginato[21], C.V. Caballero[22], O. Rillo[23] on behalf of (PANLAR) Osteoarthritis (OA) Study Group. *[1]ReumatologíA; [2]Universidad de Los Andes, Mérida, Venezuela, Bolivarian Reoublic of, Mérida, Venezuela, Bolivarian Republic Of; [3]Reumatología, Instituto Nacional de Rehabilitación, Ciudad de México, Mexico; [4]Cátedra de Reumatología de la Facultad de Medicina de la Universidad de la Republica; [5]Cátedra de Reumatología de la Facultad de Medicina de la Universidad de la Republica, Montevideo, Uruguay; [6]Rheumatology and the Arthritis Clinical Research Unit at Medicarte, Medellin; [7]Grupo de Reumatólogos del Caribe, Barranquilla, Colombia; [8]Universidad Católica de Chile, Santiago, Chile; [9]Servicio de Reumatología, Hospital Quirúrgico 10 de Octubre, Cerro, la Habana, Cuba; [10]Universidad Católica San Pablo, Bolivia, Bolivia, Plurinational State Of; [11]Servicio de Reumatología del Hospital General de Agudos Dr. E. Tornú, Buenos Aires, Argentina; [12]Facultad de Medicina, Universidad Francisco Marroquín; [13]Facultad de Medicina, Universidad Francisco Marroquín, Ciudad de Guatemala, Guatemala; [14]Centro Clínico la Isabelica, Carabobo, Venezuela, Bolivarian Republic Of; [15]Universidad Peruana de Ciencias Aplicadas; [16]Universidad Nacional Mayor de San Marcos, Peru, Peru; [17]Universidade Estadual de Campinas, Brasil, Brazil; [18]Instituto de Urología, Valencia; [19]Complejo Hospitalario Universitario "Ruiz y Páez", Ciudad Bolívar; [20]Unidad de investigación Reumatológica. Clínica Félix Boada., Caracas, Venezuela, Bolivarian Republic Of; [21]División of Rheumatology, The Warren Alpert School of Medecine., Providence, United States; [22]Universidad de la Sabana, Barranquilla, Colombia; [23]Hospital Pirovano, Buenos Aires, Argentina*

Background: This consensus derives from a previous study of Demographic and Clinical Characteristics by the PANLAR OA study group, reporting significant differences in handling these patients and in which it was evident the need of reaching an agreement in the management of hand, hip and knee OA in Latin America (2)
Objectives: The aim is to update the recommendations for the treatment of hand, hip and knee OA by agreeing on key propositions relating to the management of hand, hip and knee OA,identifying and critically appraising research evidence for the effectiveness of the treatments and by generating recommendations based on the available evidence and expert opinion.
Methods: Recommendations were developed by a group of 40 specialists made up of rheumatologists and members of other medical disciplines. A systematic review of articles, meta-analyses and guidelines for the management of hand, hip and knee OA published from 2008 and January 2014 was done. The level of evidence and strength of recommendation were classified according to the Jadad scale (3).The level of agreement was established through a Delphi technique.
Results: Both "strong" and "conditional" recommendations are given for management of hand, hip and knee OA and non-pharmacological, pharmacological and surgical modalities of treatment are presented according to the different levels of agreement.
Conclusions: These recommendations are based on the consensus of clinical experts from a wide range of disciplines considering the available evidence, while balancing the benefits and risks of non-pharmacological, pharmacological and surgical treatment modalities. It is hoped that these recommendations will be utilized by healthcare providers involved in the management of patients with hand, hip and knee OA.
References:
[1] Reginato, Anthony M. et al. Osteoarthritis in Latin America: Study of Demographic and Clinical Characteristics in 3040 Patients. JCR: Journal of Clinical Rheumatology 21.8(2015):391–397.
[2] Jadad, A.R.; Moore R.A.; Carroll D.; Jenkinson C.; Reynolds D.J.M.; Gavaghan D.J.; McQuay H.J.(1996). Assessing the quality of reports of randomized clinical trials: Is blinding necessary? Controlled Clinical Trials 17:1–12. doi: 10.1016/0197-2456(95)00134-4. PMID 8721797.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6001

AB0806 THE EFFECT OF REPETITIVE ACTIVE RANGE OF MOTION VERSUS CONTINUOUS PASSIVE MOTION ON EARLY FUNCTIONAL OUTCOMES AFTER PRIMARY TOTAL KNEE REPLACEMENT

M. Erduran[1], M. Eymir[2], B. Ünver[2]. *[1]Faculty of Medicine Surgery Medicine Department of Orthopaedics and Traumatology, Dokuz Eylül University, Izmir, Turkey; [2]School of Physical Therapy and Rehabilitation, Dokuz Eylül University, Izmir, Turkey, Izmir, Turkey*

Background: Continuous passive motion (CPM) is a common procedure in total knee replacement (TKR), but its effectiveness is controversial at early stage after TKR. Some studies have claimed that CPM promoting rapid postoperative recovery and the range of motion (ROM). However, some studies have demonstrated that CPM have any benefit on ROM, length stay of hospital and postoperative recovery (1, 2). Several studies have examined the use of CPM, but there is not any study that compared the effect of repetitive active range of motion (AROM) vs. CPM on early functional outcomes after TKR.
Objectives: The aim of this study was to compare the effect of AROM vs. CPM on early functional outcomes after TKR.
Methods: The study group consisted of 71 patients, who underwent primary TKR because of arthrosis were consecutively allocated to a AROM group (n=40, with

median age; 70.8±7.9 years), and were allocated to a CPM group (n=31, with median age; 69.7±8.4 years). Patients were evaluated regarding knee function score (Hospital for Special Surgery (HSS) score), pain (Numeric Pain Rating Scale (NPRS)), knee circumference, knee range of motion, length of hospital stay, the day of knee flexion angle achieved 70 degrees and quality of life (Short-Form 12 Health Survey (SF-12). Functional activities were evaluated using the Iowa Level of Assistance Scale and walking speed was evaluated using the Iowa Ambulation Velocity Scale. Also functional outcomes were evaluated with timed up and go (TUG) test and 10-meter walk test (10 MWT). Patients were evaluated preoperatively and at discharge.
Results: At baseline, demographic and anthropometric characteristics were similar in groups and there was no statistically difference between groups ($p>0.05$). It was determined that; the AROM group had better results in terms of reduction of pain severity ($p<0.001$). When the HSS knee scores were compared there was statistically difference between groups ($p<0.001$) and the HSS knee scores were lower in CPM group after surgery. There were no statistical differences in knee circumference, knee range of motion, the day of achieved active straight leg raise, length of hospital stay, the day of knee flexion angle achieved 70 degrees, quality of life, the IOWA help level score, IOWA walking speed score, 10 MWT score and TUG test score between groups after TKR ($p>0.05$).
Conclusions: In patients with TKR, application of repetitive AROM has better results than CPM to decrease pain severity, improve the HSS knee score. However, AROM has no effect on the early functional outcomes and the other early patients' outcomes. The current results suggest that application of AROM might be an effective method to decrease pain severity, improve the HSS knee score.
References:
[1] Maniar RN, Baviskar JV, Singhi T, et al. To use or not to use continuous passive motion post–total knee arthroplasty: Presenting functional assessment results in early recovery. The Journal of Arthroplasty. 2012;27(2),193–200.
[2] Bruun-Olsen V, Heiberg KE, Mengshoel AM. Continuous passive motion as an adjunct to active exercises in early rehabilitation following total knee arthroplasty–a randomized controlled trial. Disability and Rehabilitation. 2009;31(4), 277–283.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5851

AB0807 VALIDITY OF THE QUADRICEPS ANGLE MEASUREMENT IN PATIENTS WITH VARUS KNEE OSTEOARTHRITIS: COMPARE THE GONIOMETRIC AND PHOTOGRAMMETRY METHOD TO RADIOGRAPHY METHOD

M. Erduran[1], M. Eymir[2], B. Ünver[2], N.D. Demirkıran[3]. *[1]Faculty of Medicine Surgery Medicine Department of Orthopaedics and Traumatology, Dokuz Eylül University, Izmir, Turkey; [2]School of Physical Therapy and Rehabilitation, Dokuz Eylül University, Izmir, Turkey; [3]Department of Orthopaedics and Traumatology, Dokuz Eylül University, Izmir, Turkey, Izmir, Turkey*

Background: Various measurement methods have been defined to assess the alignment of the lower extremities. The Q-angle measurement is reported to be associated with knee injury and patellofemoral dysfunction. The Q-angle has been assessed using radiography scans, goniometer and photogrammetry methods in supine and standing positions. The radiography method is accepted to be the most accurate and valid measurement technique in measurement the Q-angle. But as a result of being expensive and time-consuming, this invasive method is not mostly preferred in research and clinics. The goniometric measurement of Q-angle is practical because it is simple, requires inexpensive equipment (only a goniometer), and can be applied in a short time. Photogrammetry measurement technique is also an advantageous method for reducing measurement errors caused by goniometers and reduction of investigator errors.
Objectives: The aim of the present study, was to compare the clinical assessment of the Q-angle (goniometric and photogrammetric measurement methods) to a radiological assessment using radiograph (criterion validity) in patients with varus knee osteoarthritis.
Methods: The study group consisted of 15 (median age 68.6±11.9 years) patients with unilateral and bilateral varus knee osteoarthritis. Q-angle measurements were assessed on both lower extremities with three different goniometric methods (goniometric measurement method in standing position with quadriceps muscle relaxed; goniometric measurement method in supine position with quadriceps muscle relaxed; and contracted) using a 360° universal goniometer. After the goniometric measurements, photographs were taken with quadriceps muscle relaxed in standing position. For radiographic assessment, we used patients' lower extremity scanograms, which had been taken to determine the diagnosis and treatment from the Computer Patient Archiving System database.
Results: There was a good correlation between the radiographic assessment and photogrammetric measurement ($r=0.623$, $p<0.001$). Also a good correlation was observed between radiographic assessment and goniometric measurement (in standing position with quadriceps muscle relaxed; in supine position with quadriceps muscle relaxed; and contracted) ($r=0.676$, $p<0.001$, $r=0.616$, $p<0.001$, $r=0.676$, $p<0.001$, respectively).
Conclusions: According to our result, the photogrammetric measurement and the goniometric measurement appear to be valid alternatives to the radiographic measurement for determining the Q-angle. These alternative measures might be used by clinicians and researchers to measure the Q-angle of patients with varus knee osteoarthritis in orthopaedic clinics.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6827

AB0808 COMPARING THE EFFECTS OF PHYSICAL THERAPY AND NON-STEROIDAL ANTI-INFLAMMATORY TREATMENT ON SLEEP QUALITY, QUALITY OF LIFE AND CLINICAL STATUS IN KNEE OSTEOARTHRITIS

M. Sezgin[1,1], E. Yeşildal[1], H. Ankaralı[2], G. Sahin[1]. *[1]Department of Physical Medicine and Rehabilitation, Mersin University Medical Faculty, Mersin; [2]Department of Biostatistics and Medical Informatics, Duzce University Medical Faculty, Düzce, Turkey*

Objectives: We aimed to compare the effectiveness of physical therapy (PT) and non-steroidal anti-inflammatory drug (NSAID) therapy on sleep quality, quality of life and clinical status in patients with knee osteoarthritis (OA).
Methods: Demographic characteristics of the participants were recorded. MOS sleep scale, Nottingham Health Profile (NHP) and Western Ontario ve McMaster Universities Osteoarthritis Index (WOMAC) were used to evaluate sleep quality, quality of life and clinical status of patients before and after the treatment.All patients were divided into two groups as PT (57 patients) and NSAID (43) groups. The patients in the drug group were administered oral dexketoprofen (50 mg/day, for two week) and the patients in the PT group were administered five times a week, total 15 seances hot-pack, ultrasound and transcutaneous electrical nerve stimulation therapy.
Results: Demographic characteristics, MOS sleep scale and NHP were similar at baseline in both groups ($p>0.05$). WOMAC pain, stiffness, and physical function scores before treatment were significantly poorer in the PT group than the NSAID group ($P<0.05$). There were statistically significant improvements on the MOS sleep scale (except snoring subscore, $p=0.05$, table 1), NHP (except social isolation, $p=0.209$) and and WOMAC pain, stiffness, physical function and total scores of both groups after the treatments ($p<0.05$). Improvement was also similar when both groups were compared after the treatment ($p>0.05$). After the two treatment, significantly side effect was not observed.
Conclusions: PT and NSAID therapy has good effectiveness on sleep quality, quality of life and clinical status in knee OA.
References:
[1] Wilcox S, Brenes GA, Levine D, et al. Factors related to sleep disturbance in older adults experiencing knee pain or knee pain with radiographic evidence of knee osteoarthritis. J Am Geriatr Soc 2000; 48:1241.
[2] Vivien CA, Priscilla SA, Christian G. Sleep and rheumatologic disorders. Sleep medicine reviews 2008;12: 211–228.
[3] Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. Lancet 2005; 365:965–973.54.
[4] Fielden JM, Gander PH, Horne JG, et al. An assessment of sleep disturbance in patients before and after total hip arthroplasty. J Arthroplasty 2003; 18:371–6.
[5] Hunter DJ, Lo GH. The management of osteoarthritis: an overwiev and call to appropriate conservative treatment. Rheum Dis Clin N Am 2008; 34:689–712.99.
[6] Hays RD, Martin SA, Sesti AM, Spritzer KL. Psychometric properties of the Medical Outcomes Study Sleep measure. Sleep Med 2005; 6:41–44.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3910

AB0809 FALL RISK AND RELATED FACTORS IN KNEE OSTEOARTHRITIS

M. Alkan Melikoglu[1], A. Kul[2]. *[1]Rheumatology; [2]Physical Medicine and Rehabilitation, Ataturk University Faculty of Medicine, Erzurum, Turkey*

Background: Balance, as a complex task, may be affected in knee osteoarthritis (KOA) and this may cause postural instability and fall risk.
Objectives: The aim of this study was to determine the fall risk in patients with KOA with an objective computerized technique and to evaluate the potential risk factors for falls in these patients.
Methods: Patients with KOA and controls were included in this cross-sectional study. Gender, age, and body mass index (BMI) were recorded. Pain was evaluated with a visual analog scale (VAS). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess the patients and the Falls Efficacy Scale International (FES-I) was used for the evaluation of fall efficacy. Knee radiographs were recorded with the Kellgren–Lawrence grading scale. Fall risk analysis was performed by using the Tetrax Interactive Balance System, which is a computerized posturography device.
Results: One hundred patients with KOA and 30 controls were included. The age, gender, and BMI scores were similar between the groups. FES-I scores were significantly higher in the cases than in the controls ($p<0.000$). Using a computerized system, significantly higher fall risk results ($p<0.000$) and significantly low, moderate, and high fall risk distribution were recorded in the cases than in the controls ($p<0.000$). Fall risk was significantly related to age, pain, and the WOMAC scores of the patients.

Conclusions: Using an objective computerized technique, our study demonstrated a higher fall risk in patients with KOA than in healthy individuals. This higher risk was shown even in the early radiographic phases of the disease related to age, pain, and dysfunction. An understanding of factors on postural control seems to be critical in successful fall prevention in these patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3072

AB0810 CORRELATION BETWEEN KNEE EXTENSOR MUSCLE STRENGTH AND GAIT ENDURANCE AFTER TOTAL KNEE ARTHROPLASTY

M.J. Suh, B.R. Kim. *Jeju National University Hospital, Jeju, Korea, Republic Of*

Objectives: This study was undertaken to identify the relationship of objective physical performance and gait endurance after 1 month after total knee arthroplasty.
Methods: One-hundred ninety-five patients (32 males and 163 females; average age 72.6±6.1 years) who underwent a primary total knee arthroplasty (TKA). Patients completed 6-minute walk test (6MWT) to assess gait endurance. Additional physical performance test including timed up and go (TUG) test, timed Stair Climbing Test (SCT), instrumental gait analysis for spatio-temporal parameters, and isometric knee flexor and extensor strength of the surgical and nonsurgical knees 1 month after TKA were measured. To evaluate self-reported physical function, self-reported disease-specific physical function measured by using the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) and self-reported quality of life measured by using EuroQOL five dimensions (EQ-5D) questionnaire. Visual analog scale (VAS) of post-operative knee pain was recorded each patient.
Results: In the bivariate analyses, the postoperative gait endurance had a significant positive correlation with the postoperative gait speed ($r=0.48$, $p<0.001$), cadence ($r=0.40$, $p<0.001$), stride length ($r=0.58$, $p<0.001$), postoperative peak torque (PT) extensor of surgical knee ($r=0.36$, $p<0.001$), postoperative peak torque (PT) flexor of surgical knee ($r=0.25$, $p<0.001$), postoperative peak torque (PT) extensor of non-surgical knee ($r=0.49$, $p<0.001$), postoperative peak torque (PT) flexor of non-surgical knee ($r=0.34$, $p<0.001$), EQ5D ($r=0.33$, $p<0.001$) and a significant negative correlation with TUG ($r=-0.46$, $p<0.001$), SCT-ascent ($r=-0.63$, $p<0.001$), SCT-descent ($r=-0.68$, $p<0.001$), WOMAC pain score ($r=-0.29$, $p<0.001$), WOMAC stiffness score ($r=-0.35$, $p<0.001$), WOMAC function score ($r=-0.43$, $p<0.001$).
In the linear regression analyses, the postoperative Visual analog scale (VAS) ($\beta=-6.91$, $p=0.03$), peak torque (PT) extensor of surgical knee ($\beta=0.56$, $p=0.04$) and peak torque (PT) extensor of non-surgical knee ($\beta=0.77$, $p<0.001$) were a factors predictive of the postoperative 6MWT.

	Correlation coefficients (r)
	6MWT
TUG (sec)	-0.46*
SCT (sec)	
Ascent (sec)	-0.63*
Descent (sec)	-0.68*
Gait parameter	
Gait Speed (m/sec)	0.48*
Cadence (steps/min)	0.38*
Stride length (cm)	0.23*
Gait cycle duration (sec)	-0.03
Stance phase duration (% of gait cycle)	-0.11
Swing phase duration (% of gait cycle)	0.11
Double support duration (% of gait cycle)	-0.02
Single support duration (% of gait cycle)	-0.01
Strength $_{\text{score (NM)}}$	
PT extensor of surgical knee ($N{\cdot}m{\cdot}kg^{-1}BW$)	0.36*
PT flexor of surgical knee ($N{\cdot}m{\cdot}kg^{-1}BW$)	0.25*
PT extensor of non-surgical knee ($N{\cdot}m{\cdot}kg^{-1}BW$)	0.49*
PT flexor of non-surgical knee ($N{\cdot}m{\cdot}kg^{-1}BW$)	0.34*
Deficit of extensor (%)	0.12
Deficit of flexor (%)	0.13
ROM (degrees)	
Knee flexion (°)	0.08
EQ-5D	0.33*
WOMAC	
Pain	-0.29*
Stiffness	-0.35*
Function	-0.43*

Values represent correlation coefficients (r)

*p<0.05, †p<0.01

Abbreviations: 6MWT, 6-minute walk test, TUG, timed up and go, SCT, timed stair climbing test, PT, peak torque, ROM, range of motion, VAS, Visual Analog Scale, WOMAC, Western Ontario McMaster Universities Osteoarthritis Index, EQ-5D, EuroQOL five dimensions,

Conclusions: This study demonstrated that quadriceps muscle strength significantly influenced on gait endurance 1 month after TKA. Using variables measured after surgery, it may be possible to predict with good accuracy for postoperative gait speed. In addition, these results could be of importance in determining effective rehabilitation strategies focusing on resistance training for improvement of gait speed early after TKA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1043

AB0811 HYALURONIC ACID INTRA-ARTICULAR INJECTION VERSUS ORAL ATORVASTATIN IN THE TREATMENT OF KNEE OSTEOARTHRITIS

M. Jokar, Z. Mirfeizi, K. Hashemzadeh, H. Zarei. *Mashhad University of Medical Sciences, Mashhad, Iran, Islamic Republic Of*

Background: Osteoarthritis is a degenerative joint disorder of articular cartilage and is the most common type of arthritis in the elderly. Some studies have suggested that Hyaluronic acid[1] and atorvastatin[2] may have a role in the treatment of osteoarthritis.
Objectives: The purpose of the present study was to investigate and compare the potential effects of Hyaluronic acid and Atorvastatin on the symptoms of knee osteoarthritis.
Methods: We conducted an open, randomized, parallel study on patients with knee osteoarthritis. Eligible patients were those who met the ACR criteria of primary knee osteoarthritis, radiologically ascertained grade I or II of knee osteoarthritis on the Kellgren-Lawrence scale, had a pain score≥60 (maximum 100) and age 50–70 years. Patients are not eligible if they had secondary osteoarthritis, systemic disease like diabetes, history of inflammatory arthritis, sever knee deformity (varus or valgus >50 degree), history of coagolopathy, sever cardiovascular disease, and active infections. Patients were enrolled from outpatient clinic of Imam Reza Hospital, Mashhad, Iran. We divided them randomly into two groups; Group 1 (n=35) received intra-articular Hyaluronic acid each week for three weeks, and group 2 (n=35) received oral atorvastatin 40 mg/day orally for six months. Symptoms were assessed by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at baseline and every month up to 6 months.
Results: Twenty eight patients (40%) were male and 42 patients (60%) were female. There was not a significant difference between 2 groups regard to sex (P=0.626). Mean age of patients was 57.9±1.1 years. Groups mean age did not differ significantly (P=0.710). The pain and function scores were significantly decreased only in the Hyaluronic acid group in the second month (P<0.001). There was not any significant improvement in any group in the next months (figure 1).

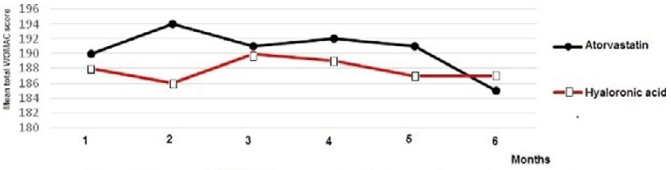


Figure 1 Mean total WOMAC score during the interventions in the studied patients

Conclusions: Intra articular Hyaluronic acid improved the pain and function of patients with knee osteoarthritis in the second months after injection. Atorvastatin did not have any effect on the knee osteoarthritis symptoms during 6 months.
References:
[1] Petrella RJ, Petrella M. A prospective, randomized, double-blind, placebo controlled study to evaluate the efficacy of intraarticular hyaluronic acid for osteoarthritis of the knee. J Rheumatol 2006; 33:951.
[2] Pathak NN, Lingaraju MC, Balaganur V, Kant V, More AS, Kumar D, Kumar D, Tandan SK. Anti-inflammatory and chondroprotective effects of atorvastatin in a cartilage explant model of osteoarthritis. Inflamm Res. 2015 Apr;64(3–4):161–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2042

AB0812 DIFFERENTIATED APPROACH TO THE TREATMENT OF OSTEOARTHRITIS WITH COMORBIDITIES

N. Shuba, A. Krylova, T. Khambir, A. Pilipenko, T. Voronova. *Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine*

Background: A significant prevalence of osteoarthritis (OA), the most disability joint disease in the world, which is important in the search for the new treatment. Analysis of modern therapy of OA was the reason for research efficacy of NSAIDs and SYSADOA on biochemical, inflammatory and immunological signs in the treatment of OA.
Objectives: Differentiated approach to the treatment of OA depending of presence of hyperuricemia.
Methods: 176 patients (144 women, 32 men) was exanimated, aged (59,71±0,86) years with confirmed radiographic OA according to Kellgren and Lawrence scale. Division into groups was performed depending on treatment. For 14 days group 1 (n=30) received nimesulide 100 mg twice daily, and group 2 (n=30) - meloxicam

15 mg 1 per day. For 6 months 3rd group (n=54) received diacerein 50 mg twice a day and the 4th group (n=32) - chondroitine sulfate (CS) 500 mg twice daily. 5th group (n=30) received glucosamine sulfate (GS) 400 mg 3 times per week for 1.5 months. It was estimated dynamics of VAS, WOMAC, Lequesne, uric acid (UA), CRP, IL-1β, IGF-1, NO, ESR, biochemical indicators. Statistical analysis - SPSS Statistics.

Results: Nimesulide compared to meloxicam found more effective for WOMAC index, the reduction of pain, stiffness and functional failure 53.93% vs 37.3%, 29.7% vs 13.5%, 41.6% vs 26.6% respectively. Only nimesulide decreased NO by 40.2%, and showed a decrease trend of UA from 375,33±24,6 to 321,57±19,6 mkmol/l while meloxicam had no effect on their levels. In 60% of patients with OA was found hyperuricemia with nephrolithiasis. Was showed the relation between the severity of OA and the presence of hyperuricemia by VAS, Lequesne, WOMAC, lesions more number joints, higher stage of X-ray progress. Diacerein, CS and GS showed clinical effect on pain reduction by VAS, Lequesne, WOMAC ($p<0.05$), respectively. Was showed lower levels of CRP, IL-1, NO during treatment by diacerein (CRP from 5,6 (IQR: 3,6–8,0) to 3,0 (IQR: 1,95–4,3) mg/l, IL-1 from 19,47 (IQR: 15,22–23,81) to 12,0 (IQR: 9,0–16,2) pg/ml, NO of 4,09 (IQR: 3,0–4,19) to 2,2 (IQR: 1,0–3,44) mmol/l), CS (CRP from 6,0 (IQR: 3,25–9,0) to 3,10 (IQR: 1,81–6,0) mg/l, IL-1 20,0 (IQR: 11,5–26,52) pg/ml to 16,7 (IQR: 9,80–18,62) pg/ml, NO of 3,0 (IQR: 2,05–4,00) to 2,0 (IQR: 2,0–3,0) mmol/l) and GS (CRP from 6,0 (IQR: 4,0–8,45) to 4,0 (IQR: 4,0–6,0) mg/l, IL-1 from 4,69 (IQR: 2,5–7,59) to 2,52 (IQR: 1,75–3,94) pg/ml, NO 3,28 (IQR: 2,02–4,79) to 2,37 (IQR: 1,59–3,03) mmol/l) ($p<0,05$). Diacerein reduced UA from 415,5 (IQR: 347,0–452,5) to 374,0 (IQR: 318,75–423,5) mkmol/l ($p=0.001$) and glucose from 5,1 (IQR: 4,8–5,8) mmol/l to 4,88 (IQR: 4,00–5,40) mmol/l ($p=0.0001$). CS in patients with hyperuricemia ($p=0.001$) increased the level of UA, which reduced the efficacy of CS, but without hyperuricemia didn't influence the level of UA and efficacy of CS.

Conclusions: Was showed that nimesulide is more effective than meloxicam during first 14 days, and reduces NO, an important proinflammatory factor. The presence of hyperuricemia in 60% patients with OA, resulted in a more severe OA. Diacerein decreases UA and glucose, given an advantage in treatment these patients, which isn't presented with CS (which increased UA).

References:

[1] National Clinical Guideline Centre. Osteoarthritis. Clinical guideline CG177; 2014.

[2] Hyperuricemia and the risk for subclinical coronary atherosclerosis – data from a prospective observational cohort study. Krishnan E. et al. Arthritis Res. Ther. 2011;13(2):66.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3407

AB0813 PROPOSAL FOR THE CONSTITUTION IMPLEMENTATION AND DEVELOPMENT OF THE PROGRAM OF CENTERS OF EXCELLENCE IN OSTEOARTHRITIS IN LATIN AMERICA

P. Santos-Moreno[1], R. Arape[2], R. Chacon[2], L. Franco[2], H. Riera[2], C. Caballero[3], M. Quintero[2]. *[1]Rheumatology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia; [2]Rheumatology, Center for Osteoarthritis, Caracas, Caracas, Venezuela, Bolivarian Republic Of; [3]Rheumatology, Universidad del Norte, Barranquilla, Colombia*

Background: Osteoarthritis (OA) is the most prevalent disease in the Americas, with an estimated prevalence of 5–10% of the population. These patients have difficulties accessing the clinic, as well as poorly successful therapeutic programs. We plan to develop a program of Centers of Excellence (CoE) in OA, to meet and respond to these needs, generate data and local research applicable to our health systems.

Objectives: In a first phase: To create OA pilot centers in Venezuela and Colombia under the CoE scheme, defined in REAL-PANLAR project (Panamerican league of associations for rheumatology project for implementation of CoE in Rheumatoid Arthritis). In a second phase under the auspices of PANLAR to create the Pan American Network of Centers of Excellence in OA (CEOA).

Methods: A systematic review of the literature in global and regional databases (Pubmed, Medline, Scopus, Lilacs) was conducted and through a Delphi-modified methodology and a consensus of experts, naming a coordinator by subject, we established the conceptual bases and defined OA Center of Excellence.

Results: The group proposes: 1. Clinical detection and early diagnosis of OA, discarding false positives and diagnosing early OA; 2. Model of patient-centered and multidisciplinary care: frequency of care are to be established according to the conditions of the patient and the multidisciplinary team. 3. Implementation of a specific clinical register of OA with indexes such as WOMAC, Lequesne and also EuroQol and definition of socioeconomic characteristics. 4. Paraclinics and Imaging: Each patient will be given a general laboratory study at admission and then every two years including a metabolic profile. Conventional Rx of hands, hips, knees or lumbosacral column depending on the location and then annual or depending on the evolution. Ultrasound, upon admission to the program, six month later, if synovitis was detected, for redefining the treatment and then annually for evaluation of the articulatory damage; CT and MRI when deemed necessary (OMERACT) 5. Definition of the disease management program in axes: treatment protocol of pain with sequential treatment lines, DMOADs, viscosupplementation, Glucosamine + Chondroitin, Strontium Ranelate, Piascledin; Alternative Medicine and Surgical Treatment 6. Establishment of a management program that includes Structure, Process and Outcome Indicators to define the CEOA as Standard, Optimal and Model. 7. Education modules for patients and families; Continuing Medical Education for all members of the multidisciplinary team; Generation of research in the areas above mentioned.

Conclusions: The unmet needs in OA determine the implementation of units of CEOAs, to promote management knowledge, and define T2T strategies, in order to improve clinical outcomes, reducing disability and consequently economic and social costs.

References:

[1] REAL-PANLAR Project for the Implementation and Accreditation of Centers of Excellence in Rheumatoid Arthritis in Latin America: A Paper From REAL-PANLAR Group on Improvement of Rheumatoid Arthritis Care in Latin America Establishing Centers of Excellence. Santos-Moreno P, Galarza-Maldonado C, Caballero-Uribe CV, et al. J Clin Rheumatol. 2015 Jun;21(4):175–80.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4557

AB0814 MEDIAL SHIFT OF THE TIBIAL ARTICULAR SURFACE SHOULD BE TAKEN INTO ACCOUNT FOR ONE FACTOR OF MEDIAL OSTEOARTHRITIS OF THE KNEE

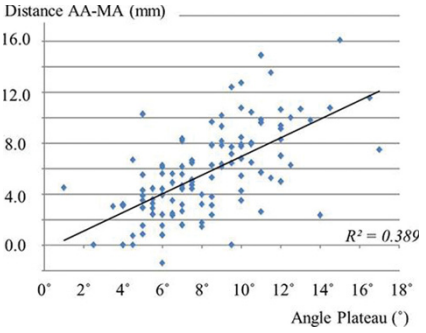
R. Nagamine. *Center of Artificial Joint and Rheumatism, Fukuoka Tokushukai Medical Center, Kasuga, Japan*

Background: Varus knee is one factor of medial osteoarthritis of the knee. According to the concept of the constitutional varus[1)], the bone growth disturbance at the growth plate in the medial proximal metaphysis of the tibia results in proximal tibia vara. In this situation, the tibia is bent at the proximal metaphysis and the tibial articular surface (TAS) may be shift medially. The medial shift of the TAS will increase the mechanical loading in the medial side of the knee. The medial shift of TAS will also influence the value of the Hip-knee-ankle (HKA) angle because the tibial plafond that is the end point of the mechanical axis (MA) of the tibia will shift laterally.

Objectives: The purpose of this study was to assess the extent of the medial shift of TAS in knees with medial osteoarthritis, and to assess the effect of this medial shift of TAS on the value of HKA angle.

Methods: This study consists of 116 knees with medial osteoarthritis. The mean age was 75.3 years old. The mean standing femorotibial angle (FTA: lateral angle between femoral and tibial anatomical axes) was 183.6°. The anatomical axis (AA) was the central line of the femoral and the tibial shaft. On the anteroposterior view radiograph of the tibia, AA, MA and tibial plateau tangent were drawn. MA is the line between the center of the tibial spines notch and the center of the tibial plafond. Two angle parameters and two distance parameters were measured. Those are angle between AA and MA (Angle AA-MA) (the value was positive when MA located medial to AA), angle between the tibial plateau tangent and the line perpendicular to AA (Angle plateau), distance from AA to the center of the tibial spines notch on the tibial plateau (Distance AA-MA) (the value was positive when Point M located medial to AA), and the length of MA.

Results: The mean (±SD) Angle AA-MA and Angle plateau was 1.0° ± 0.6° and 8.2° ± 2.9°, respectively. The mean Distance AA-MA and length of MA was 5.6±3.4mm and 347.3±3.4mm, respectively. Figure 1 shows the relationship between Angle Plateau and Distance AA-MA. The correlation coefficient between two parameters was 0.62. The more proximal tibia had varus deformity, the more the tibial articular surface shifted medially. The maximum Distance AA-MA was 16.1mm. In this case, HKA angle underestimated varus deformity up to 3°.



Conclusions: The knees with proximal tibia vara have medial shift of the tibial articular surface. There are three factors to influence the evaluations of the medial osteoarthritis of the knees. Firstly, varus knees have higher loading condition in medial compartment because of proximal tibia vara and medial shift of the tibial articular surface. Secondly, HKA angle under-estimates varus deformity in knees with medial shift of the tibial articular surface. Thirdly, FTA cannot reveal the exact loading condition, either. Even with the same FTA, it is clear that loading in the medial compartment is larger in knees with medial shift of the tibial articular surface compared with knees with simple medial osteoarthritis. The medial shift of the tibial articular surface should be taken into account for one factor of medial osteoarthritis of the knee.

References:
[1] Bellemans J, et al. The Chitranjan Ranawat award: is neutral mechanical alignment normal for all patients? The concept of constitutional varus. Clin Orthop Relat Res. 2012;470(1):45–53.
Acknowledgements: none.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4521

AB0815 PREVALENCE OF DORSAL AND LUMBAR VERTEBRAL OSTEOARTHRITIS IN WOMEN OVER 50 YEARS OF AGE EVALUATED USING THE LANE RADIOGRAPHIC SCORE IN FIVE LATIN-AMERICAN COUNTRIES

S.M. Carrillo[1], D.X. Xibillé[2], E. Granados-Sandoval[3], D. Curiel-Quiroz[4], E. Denova-Gutierrez[4], M.G. Olvera-Soto[5], P. Clark[4]. *[1]Rheumatology, Hospital Regional 1ro de Octubre ISSSTE, CDMX; [2]SEIC-Investigación, Servicios de Salud de Morelos, Cuernavaca; [3]Radiology Unit, Hospital Regional 1ro de Octubre ISSSTE; [4]Unidad de Epidemiologia Clinica, Hospital Infantil Federico Gómez Facultad de Medicina UNAM; [5]Unidad de Investigación, Colegio Mexicano de Reumatologia, CDMX, Mexico*

Background: Osteoarthritis is the most common musculoskeletal disease worldwide. Spinal osteoarthritis (OA) is a frequent cause of back pain and disability in patients over 60. The frequency of radiographically-evident dorsal and lumbar OA in Latin America is unknown
Objectives: To determine the prevalence of dorsal and lumbar vertebral OA in a database-driven random sample of women 50 years of age and older from the Latin-American Vertebral Osteoporosis Study (LAVOS) in 5 LA countries (México, Brazil, Argentina, Colombia and Puerto Rico)
Methods: Lumbar and Dorsal X-rays were performed per a standardized protocol and analyzed independently by two trained radiologists and a general practitioner using the Lane score to establish diagnosis and degree of vertebral OA severity. Inter and intra observer agreement was determined to be $k>0.6$. Descriptive statistics were used to analyze demographic variables. Prevalence was determined using means and standard deviations for quantitative variables and simple frequencies and percentages for qualitative variables. Bivariate analysis was performed to associate age, BMI and other variables with the presence of OA, using c^2 and the magnitude of association through OR and 95% CI, carrying out a multivariate analysis to adjust the frequency of OA to other variables
Results: 405 women, mean age 69.4 (58–80), median weight 64 kg (56.9–73.4) mean height 151.8 cm (±7.6) were analyzed. 5.65% were underweight, 21% had normal weight, 41.6% were overweight and 31.5% were obese. Argentina contributed 19% of the sample, Brazil 14.8%, Colombia 20.1%, México 33.3% and Puerto Rico 12.8%. OA prevalence per age group was 76.3% (95% CI 68.4–84.2) in those 50–59, 83.8% (95% CI76.6–91.2) in those 60–69, 84.3% (95% CI 76.7–91.7) in those 70–79 and 94.9% (95% CI 90.4–99.3) in those 80 or older (p=0.003). Prevalence per country was as follows: Brazil 93%, Colombia 90%, México 85%, Puerto Rico 79% and Argentina 74%. Prevalence per BMI was 80% in normal weight, 82.5% in overweight and 87.5% in obese. 72.6% of sampled women had dorsal OA (Argentina 48.1%, Brazil 65%, Puerto Rico 73.1%, México 79.3%, Colombia 90.1%). Obesity was a risk factor for the development of dorsal OA (OR 2.46) when compared to normal BMI (p=0.01). Lumbar OA was found in 44.9% of the sampled women (Argentina 68.8%, Brazil 65%, Colombia and Puerto Rico 42.3% each, México 37%). Adjusting for age, BMI, height loss, steroid use and physical activity, the OR for presenting OA is 6.45 ($p<0.001$) in women over 80 compared to those 50–59
Conclusions: Radiographic OA is highly prevalent in Latin American women over 50 and associated with progressing age and BMI. Brazil has the highest prevalence of OA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3612

AB0816 COMPREHENSIVE ANALYSIS OF A NEW CHEMICAL COMPOUND FOR THE TREATMENT OF OSTEOARTHRITIS BY A PROTEOMIC APPROACH IN HUMAN CHONDROCYTES

S. Cheleschi[1], V. Calamia[2], M. Fernandez-Moreno[3], A. De Palma[1], M. Galeazzi[1], M. Anzini[4], A. Fioravanti[1], F.J. Blanco[5]. *[1]Department of Medicine, Surgery and Neuroscience, Rheumatology Unit, University of Siena, Policlinico le Scotte, Siena, Italy; [2]2Servicio de Reumatología, Grupo de Proteómica; [3]2Servicio de Reumatología, Grupo de Genomica, INIBIC-Hospital Universitario A Coruña, A Coruña, Spain; [4]3Department of Biotechnology, Chemistry and Pharmacy, Università di Siena, Siena, Italy; [5]2Servicio de Reumatología, Grupo de Proteómica y Genomica, INIBIC-Hospital Universitario A Coruña, A Coruña, Spain*

Background: Selective cyclooxigenase (COX)-2 inhibitors were developed to prevent NSAIDs gastro-intestinal adverse effects. VA692, a new hydroxyetyl selective COX-2 inhibitor, showed anti-inflammatory, anti-nociceptive and chondroprotective properties. Proteomics is being applied for the study of drug mode of action, toxicity and to identify new drugs targets.
Objectives: The aim of this study was to analyze the anti-inflammatory effect of VA692, in comparison with celecoxib. By iTRAQ methodology, we quantitatively analyzed the different expressed profiles in T/C-28a2 cell line treated with the studied drugs in presence of IL-1β.
Methods: Human T/C-28a2 chondrocytes cell line were generated by Goldring group. Human articular cartilage was obtained from femoral heads of five OA patients. Cells were incubated with VA692 and celecoxib (1, 0.5 and 0.2μM) in presence of Interleukin (IL)-1β (5ng/ml) for 48h. The expression of inflammatory cytokines and anti-oxidant enzymes was evaluated by quantitative qRT-PCR, PGE_2 release by ELISA, and apoptosis and ROS production by flow cytometry. T/C-28a2 cell line was also processed to carry out western blot tests and finally employed for the iTRAQ analysis. Statistical analysis was performed by ANOVA and Bonferroni multiple comparison tests.
Results: IL-1β-stimulated chondrocytes showed a significant increase ($p<0.001$) of COX-2, IL-1β, IL-6, IL-8, superoxide dismutase (SOD)-2 and catalase (CAT) gene expression, as well as of PGE2 levels. The tested drugs significantly counteracted the effect of IL-1β, with a better modulation by VA692 1μM in T/C-28a2 cell line ($p<0.01$ for COX-2, IL-1β, IL-8, CAT; $p<0.001$ for IL-6, SOD-2). Regarding apoptosis and ROS production, the new drug was able to significantly reduce ($p<0.05$) their increase induced by IL-1β ($p<0.05$). Proteomic analysis led to identification of 797 proteins in T/C28a2 cell line, 123 of which were significantly modulated by VA692 in presence of IL-1β ($p<0.001$), and 34 by IL-1β alone ($p<0.05$). 22 proteins were commonly modulated in both groups, thus indicating that 101 proteins were regulated by VA692 in a specific manner. Among the proteins down-regulated by VA692, some with structural function were detected, responsible for cytoskeleton riorganization, as well as chaperones (heat shock proteins) and glycolitic enzymes. Proteins involved in calcium metabolism and in ribosome biogenesis resulted up-regulated instead, as well as SOD-2 as confirmed by western blot analysis.
Conclusions: Our data demonstrated the anti-inflammatory effect of VA692, suggesting also its anti-apoptotic and anti-oxidant role. The proteomic profile showed that VA692 induced not only an anti-inflammatory effect in chondrocytes but, interestingly, this compound also seemed to regulate their anabolic response.
References:
[1] Hochberg MC et al.Arthritis Care Res 2012.
[2] McAlindon TE et al. Osteoarthritis Cartilage 2014.
[3] Bingham CO III. Cleve Clin J Med 2002.
[4] Anzini M et al. J Med Chem 2013.
[5] Calamia V et al.Arthritis Res Ther 2010.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6441

AB0817 IMPROVING CARE FOR PATIENTS WITH OSTEOARTHRITIS IN FIVE EUROPEAN COUNTRIES: THE JIGSAW-E PATIENT PANEL

S. Blackburn[1], J. Meesters[2], M. De Wit[3], L. Campbell[1], C. Rhodes[1], D. Schiphof[2], T. Vliet Vlieland[2], S. Bierma-Zeinstra[4], N. Østerås[5], S. Pais[6], E. Roos[7], N. Evans[1], K. Dziedzic[1]. *[1]Keele University, Keele, United Kingdom; [2]Leiden University Medical Center (LUMC), Leiden; [3]VU University Medical Centre, Amsterdam; [4]Erasmus MC - University Medical Centre Rotterdam, Rotterdam, Netherlands; [5]Diakonhjemmet Hospital, Oslo, Norway; [6]University of Algarve, Algarve, Portugal; [7]University of Southern Denmark, Odense, Denmark*

Background: EULAR guidelines for osteoarthritis (OA) endorse high quality care and support to self-manage with core recommended treatments such as exercise, weight loss and the provision of written information and education. An EU-funded project, Joint Implementation of Guidelines for oSteoArthritis in Western Europe (JIGSAW-E)[1], aims to improve the management of OA across five European countries (UK, Netherlands, Norway, Denmark, Portugal) by implementing an intervention to enhance the OA consultation.
Coordinated, cross-border Patient and Public Involvement and Engagement (PPIE), working in active partnership with the project team, is an essential component of JIGSAW-E.
Objectives: To describe the PPIE in the JIGSAW-E project.
Methods: A two-day international workshop established the JIGSAW-E Patient Panel to act as the voice of patients and the public in the project and to co-develop clear information and resources for patients. Panel members meet regularly with the project teams in each country. The Patient Panel is coordinated and supported by dedicated PPIE teams in the UK and Netherlands.
Results: The JIGSAW-E Patient Panel consists of Patient Champions and patient representatives from newly established or existing patient groups in each of the five countries. The Patient Champions form a core group of seven patient representatives who work closely with the Patient Panel and the JIGSAW-E team. PPIE activities have included:
- One Patient Champion sits on the JIGSAW-E project steering committee.
- In the Netherlands, Patient Panel members substantially contributed to the translation and cultural adaptation of a guidebook for patients with OA. This process will continue as JIGSAW-E is rolled out in each of the five countries.
- Patient Panel members in the UK have helped refine an OA Quality Indicator questionnaire[2] for use in JIGSAW-E.

A glossary of terms has been developed to support the involvement of Patient Panel members throughout the project.
Conclusions: Effective and meaningful PPIE is a central component to delivery and success of raising awareness and implementing the OA management

recommendations on a national level. The Patient Panel represents a step forward in international collaboration of PPIE within implementation projects. The Patient Panel is producing culturally appropriate and relevant information and resources for patients in five European countries. Future activities may include the development of patient stories to support increased adoption of JIGSAW-E, providing the patient perspective during training of health care professionals, and the digitisation of patient resources into Smartphone or tablet Apps.

References:
[1] https://goo.gl/a4xYUV.
[2] Blackburn et al. Res. Involvement and Engagement (2016) 2:5. doi: 10.1186/s40900-016-0019-x.

Acknowledgements: JIGSAW-E is funded via the West Midlands AHSN by EITHealth. Funding from the WM AHSN, the Regional Innovation Fund NHS England and Shropshire CCG. KD is part funded by a Knowledge Mobilisation Research Fellowship (KMRF201403002) from the NIHR.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2711

AB0818 PERSONALIZED ARTICULATING JOINT DISTRACTION FOR TREATMENT OF TIBIOFEMORAL OSTEOARTHRITIS: CLINICAL FEASIBILITY

T. Struik[1], R.J. Custers[2], N.J. Besselink[1], J.E. Jaspers[3], A.K. Marijnissen[1], F.P. Lafeber[1], S.C. Mastbergen[1]. *[1]Rheumatology & Clinical Immunology; [2]Orthopedics; [3]Medical Technology & Clinical Physics, University Medical Center Utrecht, Utrecht, Netherlands*

Background: Osteoarthritis (OA) patients encounter progressive pain and functional disabilities, including joint stiffness, due to degeneration of the joint tissues. For knee OA, the most prevalent form, available treatment strategies are limited in number and focus primarily on minimizing the functional disability, inflammation, and pain in a conservative manner since still no unambiguously proven effective disease modifying approaches are available. Progress in the development of joint sparing procedures however, has demonstrated the regenerative capacity of the osteoarthritic knee and with that the delay for conventional last resort therapy such as total knee arthroplasty (TKA). Knee Joint Distraction (KJD) is a joint preserving procedure that can postpone knee arthroplasty in case of knee osteoarthritis for over 5 years [1]. Distraction is applied with an external fixator for 6–8 weeks.
Objectives: To reduce the burden on patients during treatment originating from a restriction in joint flexion during KJD, we evaluated an articulating frame. A personalized articulating KJD-device was developed, biomechanically tested, and technical feasibility was evaluated in cadaveric legs. Reproduction of joint specific motion was demonstrated and articulating KJD was concluded to be technically feasible. In this study, clinical feasibility was tested in 3 patients.
Methods: Patients received rigid knee joint distraction treatment in general practice. After 2–4 weeks, the frame was removed in the outpatient clinic and the joint was flexed in a continuous passive motion (CPM) device until 30° flexion was reached, or motion became painful. Subsequently, the articulating frame was attached to the bone pins (figure 1), followed by computerized personalization of the hinge from a non-invasive motion measurement. After assembling the custom parts, weight-bearing and non-weight-bearing radiographs were taken at 0, 15, and 30° flexion for joint space width measurements. Finally, the articulating device was replaced by the rigid frame and treatment was continued according to clinical practice.
Results: For none of the three patients, the articulating distractor could be personalized. In the first patient, 15° flexion was achieved on the CPM, but pin positions did not allow for positioning of the frame. In the other patients, 8° and 15° flexion was measured, which was too little motion for the custom software to generate personalized hinge parts. Pain at the pin sites during motion was reported by all patients.

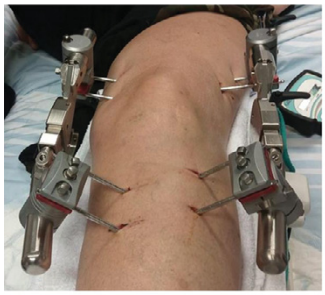


Figure 1 *The articulating frame assembled to the same bone pins and bone pin clamps as used for rigid joint distraction in clinical practice, and previous to measurement of joint-specific motion and customization of joint specific hinge parts.*

Conclusions: Despite confirmation of joint-specific articulating distraction on cadaveric legs, clinical feasibility could not be demonstrated, mainly due to painful motion of soft tissues along the bone pins.

References:
[1] Woude J-TAD van der, Wiegant K, Roermund PM van, Intema F, Custers RJH, Eckstein F, et al. Five-Year Follow-up of Knee Joint Distraction Clinical Benefit and Cartilaginous Tissue Repair in an Open Uncontrolled Prospective Study. Cartilage. 2016 Aug 26;1947603516665442.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1724

AB0819 IS INCREASING THE TREND OF PRIMARY TOTAL HIP ARTHROPLASTIES FOR THE PATIENTS WITH OSTEOARTHRITIS, BUT DECREASING THE RATE OF WOMEN IN SUPER-AGING AREA OF JAPAN IN LAST TWELVE YEARS?

Y. Takakubo[1], K. Sasaki[1], H. Oki[1], Y. Naganuma[1], A. Narita[1], J. Ito[1], H. Kawaji[2], M. Ishii[2], M. Takagi[1]. *[1]Department of Orthopaedic Surgery, Yamagata University Faculty of Medicine; [2]Department of Orthopaedic Surgery, Yamagata Saisei Hospital, Yamagata, Japan*

Background: Elderly people over 65 year-old have increased year by year in many countries[1]. Because their rate was from 19.5% at 2004 to 26.8% at 2015 in Japan and 30.8% at 2015 in our super-aging area, the numbers of total joint arthroplasties have increased too[2]. In fact, the numbers of total hip arthroplasty predicted increasing from six hundred fifty-six thousand cases at 2010 to one million three hundred seventy-six thousand cases at 2020 in USA[3]. The rate of total joint arthroplasty, including primary total hip arthroplasty, may reflect trends in management and health outcomes of elderly people with osteoarthritis (OA) in our super-aging area of Japan[1,4].
Objectives: The aim of this study was to analyze the trend of primary total hip arthroplasties for the patients with OA in our institutes in the last twelve years.
Methods: We surveyed the number and rate of orthopaedic surgeries and primary total hip arthroplasties in our two institutes from 2004 to 2015.
Results: We had 19,862 cases of orthopaedic surgeries, including 3,782 primary total hip arthroplasties in the last twelve years. They have increased year by year ($r=0.92$, $p<0.05$, Fig. 1). Mean age was 64.5 old-year (62.4–66.8) in last twelve years, had become older year by year ($r=0.78$, $p<0.05$), 62.4 old-year at 2004 vs 66.8 old-year at 2015. Mean rate of female was 87% (85–91) in last twelve years, had gradually decreased year by year ($r= -0.68$, $p<0.05$), 91% at 2004 vs 85% at 2015.

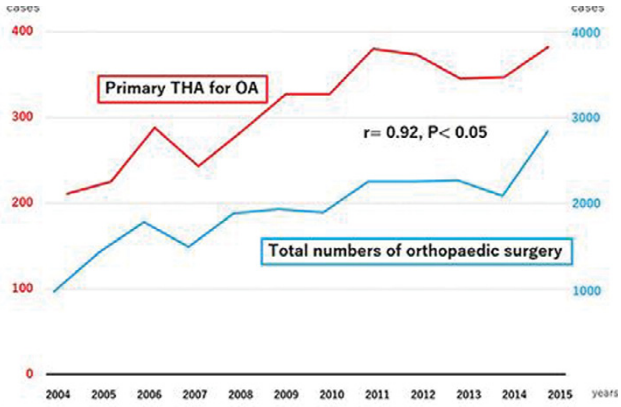


Fig. 1

Conclusions: The rate of total joint arthroplasties including primary total hip arthroplasty increased year by year, and related to total numbers of orthopaedic surgeries in our super-aging area of Japan. Mean age at receiving primary total hip arthroplasty was older annually but mean rate of women had gradually decreased year by year. Although majority of OA hip consist of female which have secondary dysplastic acetabulum in our country[2], it might increase gradually the patients of man with OA hip in super-aging time in Japan.

References:
[1] National Institute of Population and Social Security Research. Japanese Mortality Database, 2014. http://www.ipss.go.jp/.
[2] Jingushi S, et al. J Orthop Sci. 15:626–31, 2010.
[3] Kurtz SM, et al. J Bone Joint Surg Am. 96: 624–30, 2014.
[4] Yamagata prefecture, Health and longevity Promotion Section. Rate of elderly people in Yamagata prefecture, 2014. http://www.pref.yamagata.jp/ou/kikakushinko/020052/tokei/jinkel.html.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2181

Osteoporosis

AB0820 FREQUENCY OF OSTEOPOROSIS AND ASSOCIATED RISK FACTORS IN MEXICAN PATIENTS WITH RHEUMATOID ARTHRITIS

A.N. Rangel-Botello[1,2], A. Gallegos-Posada[2], F. Jasso-Ávila[2], D. Ramos-Bello[1,2], C. Villa-Calderón[3], M.U. Martínez-Martínez[1,2], C. Abud-Mendoza[1,2]. *[1]Rheumatology, Hospital Central "Dr. Ignacio Morones Prieto"; [2]Faculty of Medicine, Autonomous University of San Luis Potosí, San Luis Potosí; [3]Faculty of Medicine, Autonomous University of Aguascalientes, Aguascalientes, Mexico*

Background: The risk of osteoporosis in patients with rheumatoid arthritis (RA) is well described and may be associated with genetic and environmental factors. The frequency of generalized osteoporosis in different studies is variable.
Objectives: The aim of the study was to investigate the frequency of osteoporosis as well as to describe the risk factors in RA population.
Methods: Retrospective study, including patients with RA who had at least 2 densitometries in their follow up. We collected demographic characteristics, use of glucocorticoids (GC), other medications and antibody profile. Variables were compared between groups with or without osteoporosis. The frequency of osteoporosis was calculated according to the T-score and logistic regression was performed to explore the association of osteoporosis and relevant variables. Statistical analysis was performed using R software version 3.2.1. Baseline characteristics were compared between groups of patients (osteoporosis in the lumbar spine, femoral neck and hip) defined according to the T-score results. We used x^2 or Fisher test for categorical variables as appropriate and Wilcoxon test for continuous variables. A logistic regression model was used to explore the relationship between osteoporosis and variables that could contribute as risk factors.
Results: One hundred and five patients were included, 96.2% were women, RA evolution of 7 (IQR 8) years. The frequency of osteoporosis was: lumbar spine 55.2%, hip 12%, and femoral neck 25.7%. Patients with lumbar spine osteoporosis had higher age (62 vs 58 years, p=0.13), lower weight (57 vs 63.8 kg, p=0.00004) and higher FRAX scores (26.5 vs 11.5, p=0.004; 8.5 vs 2.4, p=0.02). The associated risk factors were: weight (OR 1.09, 95% IC 1.03–1.15, p=0.001), GC use (OR 4.36, 95% IC 1.0–19.89, p=0.049), menopause (OR 22.78, 95% IC 2.73–190.12, p=0.003). There was no association with disease activity (DAS28-ESR) (OR 0.64, 95% IC 0.42–0.96, p=0.049).

Multivariate logistic regression analysis of osteoporosis associated factors

	OR	95% IC	P value
Age	1.01	0.96–1.07	0.553
Weight	1.09	1.03–1.15	0.001
DAS28-ESR	0.64	0.42–0.96	0.034
Glucocorticoids	4.36	1.00–18.89	0.049
Menopause	22.78	2.73–190.12	0.003
ACCP	2.00	0.38–10.47	0.409

OR: odds ratio, IC: confidence interval, DAS28-ESR: Disease Activity Score, ESR: erithrosedimentation rate.

Conclusions: The frequency of lumbar spine osteoporosis in our population was similar to that reported in previous studies (38.9%>50%). In our study only significant association with weight, GC use and menopause was observed
References:
[1] Deodhar AA, Woolf AD. Bone mass measurement and bone metabolism in rheumatoid arthritis: a review. Br J Rheumatol. 1996;35:309–22.
[2] Haugeberg G, et al. Bone mineral density and frequency of osteoporosis in female patients with rheumatoid arthritis: results from 394 patients in the Oslo County Rheumatoid Arthritis register. Arthritis Rheum. 2000;43:522–30.
[3] Guler-Yuksel M, et al. Bone mineral density in patients with recently diagnosed, active rheumatoid arthritis. Ann Rheum Dis. 2007;66:1508–12.
[4] Peng J, et al.Bone Mineral Density in Patients With Rheumatoid Arthritis and 4-Year Follow-up Results.J Clin Rheumatol 2016;22: 71–74.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5678

AB0821 HIGH PREVALENCE OF VITAMIN D3 DEFICIENCY IN PATIENTS WITH RHEUMATIC DISEASES AND MUSCULOSKELETAL DISORDERS IN CYPRUS

A. Tsirogianni[1], P. Hadjicostas[2]. *[1]General Hospital of Larnaca, LARNACA; [2]Agios Panteleimon Orthopedic Clinic, NICOSIA, Cyprus*

Background: Vitamin D3 (vitD) deficiency has been associated with an increased risk of a wide range of acute and chronic diseases including rheumatic diseases. Low serum 25(OH)D levels has been reported in mediterranean countries but little is known about the sunny island of Cyprus.[1,2]
Objectives: To assess vitamin D status among Cypriot patients with various rheumatic diseases (RD) and non-inflammatory musculoskeletal disorders (MSD).
Methods: Serum levels of 25(OH)D were randomly measured in 277 Cypriot patients with RD and MSD who attended the rheumatology outpatient clinics at the General hospitals of Larnaca and Ammochostos in 2016. 84/277 patients were receiving vitD supplements and excluded from analysis. From the rest 193 patients (female/male [F/M]:151/42, mean age:58, rage:21–89), 69 had rheumatoid arthritis (RA) (F/M:54/15, mean age:62, range 27–83), 31 seronegative spondyloarthropathies (SpA) (F/M:13/18, mean age:54, rage:21–73), 65 MSD (e.g. osteoarthritis, back pain, neck pain, arthralgia) (F/M:61/4, mean age 56, range 21–82), 16 autoimmune diseases (lupus, sjogren's, scleroderma) (F/M:15/1, mean age:61, rage:45–79)) and 12 various other RD (F/M:8/4, mean age 55, rage 21–89). 20 patients had additionally Hashimoto's thyroiditis (F/M:18/2, mean age:56, rage:28–73).
Results: The mean serum vitD levels in all patients were 20.4 ng/ml (range 3.2–56.8 ng/ml). VitD deficiency (<20 ng/ml) was found in 122/193 patients (63%), insufficiency (21 to 29 ng/ml) in 49/193 patients (25%) and sufficiency (>30 ng/ml) in 22/193 patients (11%).[3] The mean values (range) of vitD levels and the percentage of patients that had vitD deficiency, insufficiency and sufficiency per disease category were; RA: 19.8 ng/mL (8.1–53.3 ng/ml), 64%, 28% and 9% respectively, spa: 21.9 ng/ml (7.2–54.0 ng/mL), 48%, 35% and 16% respectively, MSD: 20.3 ng/ml (6.6–48.0 ng/ml), 63%, 28% and 9% respectively, autoimmune diseases: 17.9 ng/ml (3.20–37.00 ng/ml), 81%, 6% and 13% respectively, other RD: 22.7 ng/ml (9.0–56.8 ng/ml), 75%, 0%, 25% respectively and Hashimoto's thyroiditis: 18.8 ng/ml (7.2–37.0 ng/ml), 80%, 5% and 15% respectively. Analysis of the total number of patients showed significant differences in vitD levels and rates of vitD deficiency among females and males (19.3 ng/mL, [range 3.2–54.0 ng/mL], vs 23.7ng/mL, [range 7.2–56.8 ng/mL] [p=0.009] and 70% vs 43% respectively). Seasonal variations or age-related differences in vitD levels were not observed in this study.
Conclusions: High rates of vitD deficiency were observed in patients with RD and MSD in the island of Cyprus despite the sunny climate. Avoidance of sun exposure is presumed to be the main reason. Further studies are needed.
References:
[1] Kolokotroni et al. Public Health Nutr. 2015;18(1):112–21.
[2] González-Gross et al. Br J Nutr. 2012;107(5):755–64.
[3] Hossein-nezhad et al.Mayo Clin Proc. 2013;88(7):720–755.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6647

AB0822 CLINICAL FEATURES AND PREDICTIVE FACTORS OF ORAL BISPHOSPHONATE-RELATED OSTEONECROSIS OF THE JAW: AN ANALYSIS OF 8 CASES IN A SINGLE INSTITUTION

A. Suzuki[1], M. Yoshida[1], M. Mori[2], Y. Sakamoto[3]. *[1]Department of Rheumatology; [2]Department of Pathology; [3]Department of Oral Surgery, Mitsui Memorial Hospital, Tokyo, Japan*

Background: Oral bisphosphonates (BPs) have been increasingly prescribed for the treatment of and prophylaxis for osteoporosis over the past decade. More than 190 million prescriptions for oral BPs have been dispensed worldwide, and, thus, the number of patients that develop oral BP-related osteonecrosis of the jaw (BRONJ) is expected to increase in the future. Although previous studies have investigated oral BRONJ, predictive factors have not yet been identified [1].
Objectives: The aim of the present study was to clarify the clinical features and predictive factors of oral BRONJ.
Methods: We included 8 patients who had taken oral BPs and were diagnosed with BRONJ at Mitsui Memorial Hospital (Tokyo, Japan) between 2011 and 2016. The following details were collected for each patient from a review of medical charts: sex, age, type of BP used, duration of BP administration, co-morbidities, laboratory values at presentation including hemoglobin, albumin, and serum creatinine values, clinical stage of the lesion, site affected, and pathological findings. Laboratory values of patients with BRONJ were compared with those of 242 patients (as a control group) who were prescribed BPs in October 2016 at our hospital. The Mann-Whitney U-test and chi-squared test were used for statistical comparisons between the oral BRONJ and control groups. Risk factors for BRONJ were assessed using multivariate analyses with a logistic regression analysis. All analyses were performed using SPSS ver. 21.
Results: The mean age and female ratio in the oral BRONJ and control groups were 74.5±13.8 years and 75.0%, and 71.1±12.7 years and 66.1%, respectively (p=0.26, p=0.61). The mean interval between the initiation of BP therapy and a confirmed diagnosis was 45.9±35.5 months. Seven patients had lesions in the mandibular bones and alendronate was used in six cases. Oral BPs were administered to three patients with rheumatoid arthritis or multiple sclerosis, all of whom were given a maintenance dose of corticosteroids. The remaining three out of 5 oral BP users developed BRONJ after dental extraction. Regarding laboratory results, serum albumin values were significantly lower in the oral BRONJ group than in the control group (3.7±0.3 g/dl and 4.2±0.4 g/dl, respectively, p<0.01). Serum hemoglobin levels were slightly lower in the oral BRONJ group than in the control group (11.3±1.3 g/dl and 12.4±1.7 g/dl, respectively, p =0.06). A multiple logistic regression analysis identified serum albumin levels as the only significant predictive factor for oral BRONJ (OR=0.14; 95% CI 0.03–0.71, p<0.05). A pathological examination was available in six patients, with Actinomycetes being identified as the causative species in 4.
Conclusions: Oral BRONJ mainly developed in patients with long-term corticosteroid use for an underlying illness or those who underwent dental extraction, and hypoalbuminemia was the only laboratory marker identified as a predictive factor for BRONJ.

References:
[1] Diniz-Freitas M et al., Oral bisphosphonate-related osteonecrosis of the jaws: Clinical characteristics of a series of 20 cases in Spain. Med Oral Pathol Oral Cir Bucal 2012;17:e751.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2506

AB0823 EVALUATION OF OSTEOPOROSIS AND FRACTURES IN PATIENTS WITH DIABETES MELLITUS TYPE 2: RESULTS OF A 5-YEAR FOLLOW-UP

V.L. Masenko[1], A.N. Kokov[1], S.E. Semenov[1], T.A. Raskina[2], O.L. Barbarash[1]. *[1]Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases; [2]Kemerovo state medical academy of Federal Agency of Healthcare and Social Development, Kemerovo, Russian Federation*

Objectives: The aim of the study is to determine the characteristics of bone mineral density (BMD) and the the prevalence of fractures of the vertebral fractures and long bones in men with diabetes mellitus type 2 on the basis of 5-year prospective study.
Methods: 251 males (60.56±8.7years) were examined. The patients were divided into 2 groups: patients with type 2 diabetes mellitus (n=65) and patients without disorder of carbohydrate metabolism (n=186). All patients underwent DXA-definition of BMD (g/cm^2), T-score of the spine and bones of the femur. Dynamic observation for 5 years and the determination of vertebral fractures and long bones.
Results: BMD measured in lumbar spine and proximal femur were analyzed. According DXA BMD of femur in patients with diabetes is significantly higher than that of non-diabetics (0,928 [0,847;1,029]; 0,858 [0,779 0,928]; p=0,000005). T-score is also higher in diabetics (-1,47 [-2,12;-0,63]; -2,01 [-2,71;-1,49]; p=0,000020). BMD and T-score of the lumbar vertebrae in diabetic patients was also is significantly higher: BMD (Group I =1,002 [0,902;1,182]; Group II =0,969 [0,879;1,106]; p=0,008). T-score (-0,94 [-1,43; -0,05]; -1,07 [-1,54; -0,40]; p=0,014). After 5 years, spine or long bones fractures marked in 12 patients (18%) from I group. In Group II was observed only 5 episodes of bone fracture (2.6%).
Conclusions: BMD in men with diabetes are higher, but they often develop bone fractures. Perhaps this is due to pathological remodeling of bone tissue on a background of metabolic disorders, when bone is more dense, but fragile.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1124

AB0824 THE METHOD OF CALCULATING THE PROBABILITY OF OSTEOPENIA IN PATIENTS WITH MULTIFOCAL ATHEROSCLEROSIS

A.N. Kokov[1], V.L. Masenko[1], S.E. Semenov[1], T.A. Raskina[2], O.L. Barbarash[1]. *[1]Federal State Budgetary Scientific Institution Research Institute for Complex Issues of Cardiovascular Diseases; [2]Kemerovo state medical academy of Federal Agency of Healthcare and Social Development, Kemerovo, Russian Federation*

Objectives: To determine probability of the presence of osteopenic syndrome in patients with multifocal atherosclerosis based on the multislice computed tomography (MSCT) evaluation of vascular calcification.
Methods: 186 male (60±6,7 years) with multifocal atherosclerosis. All the patients underwent the measurement of BMD with X-ray absorptiometry. Moreover, calcium scores (CS) of coronary and brachiocephalic arteries were obtained using Agatston method.
Results: Among the patients had a high prevalence of osteopenia syndrome (87.1%). According to X-ray absorptiometry T-score values of lumbar vertebrae -1.07 [-1.54; -0.40], T-score of the proximal femur -2.01 [-2.71; -1.49]. We also found a large amount of calcification of the coronary arteries according MSCT: calcium score (CS) 471.8 [118.2; 916,8]. Calcification of the carotid arteries in patients of the study group was less pronounced: CS 113.9 [44.5; 300.8], but noted significant direct relationship between the degree of calcification of different vascular beds (r=0,35, p<0,05). We have data on the significant inverse association between bone density and a coronary artery calcification (r=-0,29, p<0,05), and the carotid artery (r=-0,22, p<0,05) by using Spearman rank correlations. Factors that affect the probability of osteopenic syndrome (according X-ray absorptiometry) in patients with known rates of calcification of the coronary and carotid arteries were obtained by regression analysis. These factors were coronary CS (p=0.012), carotid CS (p=0.034), the mass of calcifications of the carotid arteries (p=0.025) and the presence of a stenosis of the carotid arteries (p=0.026). The predictive model for estimating the probability of the presence of osteopenia in patients with multifocal atherosclerosis has been is designed using regression coefficients of each of the factors. As a result, ROC-analysis of the area under the ROC-curve for this prediction model was 0.792 (p=0.0001). The model was tested in the study sample. The specificity of the model was 72.1%, sensitivity of the model was 80.2%.
Conclusions: The study results suggest that indicators of calcification of the carotid and coronary arteries resulting from a routine examination by MSCT of patients with multifocal atherosclerosis have a high predictive capacity for assessing the probability of the presence of osteopenic syndrome in this category of patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1125

AB0825 COMPARISON OF BONE DENSITY CHANGES ONE YEAR AFTER TREATMENT WITH ZOLEDRONIC ACID VERSES DAILY TERIPARATIDE

A.K. Aggarwal, D. Jain, N. Aggarwal. *Rheumatology, Institute of Rheumatology & Pain, Ghaziabad, India*

Background: The treatment of Osteoporosis is difficult to monitor and so usually incomplete resulting in inadequate response.[1]
Objectives: To evaluate the minimum period of treatment required with Bisphosphonates and Parathyroid hormone in order to see a significant change in serial Bone Mineral Density analysis (BMD).
Methods: Low BMD patients were subjected to yearly infusion of Zoledronic Acid 5mg (ZA) verses daily Subcutaneous injections of Teriparatide 20 μg (PTH). A single center pencil beam bone densitometer was used to measure serial BMD at baseline and yearly. Average BMD measures from the Spine L2, L3 and L4 (BS) and Total Hip (BH) were evaluated. The percentage change in the mean BS and BH readings was calculated to look for the least significant change (LSC) in the density scores.
Results: Significant change of 4.65% was seen (LSC=2.6%)[2] in the Spine in the PTH group after one year of treatment while it took two years in the ZA group for a 2.77% change. There was no significant change (LSC=3.6%)[2] in both groups in the BH. A p>0.05 was considered statistically significant. The finding is summarized in Table 1.

Table 1

Study group of 100 patients					Percentage Change in BMD			
Treatment Group	N	Gender		Age range	BS*		BH**	
		Males	Female	Years	After 1 yr	After 2 yrs	After 1 yr	After 2 yrs
ZA - Zoledronic Acid	50	12	38	42–79	2.19	2.77	0.02	2.47
PTH -Teriparatide	50	10	40	40–75	4.651	X	2.272	X
LSC - Least Significant Change for single DXA machine					2.50%		3.60%	

*Average of L2,3,4 Spine; **Total Hip.

Conclusions: Significant result of treatment with PTH requires a period of one year of therapy while with ZA it needs two years. The LSC in BMD is seen in the Spine and not in the Total Hip BMD.
References:
[1] Glen M. Blake, Ignac Fogelman. Role of Dual-Energy X-Ray Absorptiometry in the Diagnosis and Treatment of Osteoporosis.
[2] Shepherd JA1, Lu Y. A generalized least significant change for individuals measured on different DXA systems.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3198

AB0826 RESULTS OF BONE MINERAL DENSITY IN COELIAC DISEASE: ABOUT 30 CASES

H. Kchir[1], D. Kaffel[2], R. Zgolii[1], D. Issaoui[1], H. Chaabouni[1], H. Sahli[3], N. Maamouri[1], M. Elleuch[3], M.M. Kchir[2], N. Ben Mami[1]. *[1]gastroenterology B, Rabta hospital, Tunis; [2]Rheumatology, Kassab institute, Manouba; [3]Rheumatology, Rabta hospital, Tunis, Tunisia*

Background: The link between Coeliac disease (CD) and low bone mass has been established in several large international studies.
Objectives: To determinate the prevalence and risk factors of osteopenia and osteoporosis in a Tunisian population of coeliac patients.
Methods: We carried a retrospective study from January 1991 to December 2015 including all cases of CD diagnosed in the departement of Gastroenterology B in Rabta's Hospital. We retained all patients having a bone mineral density (BMD). We used the WHO criteria for the diagnosis of osteoporosis and osteopenia.
Results: During the period of the study, 78 cases of CD were included. Thirty among them, performed a BMD: 25 women and 5 men with an average age of 35.8 years. Malnutrtion was found in 14 patients with a BMI <20Kg /m^2. Smoking was found in one case. Among women, 2 were menopaused. BMD showed a low bone mass in 76,3% of patients: osteoporosis in 43.3% and osteopenia in 33.3%. The mean T score was -2.08 DS in the lumabr spine (LS) and -1DS in the Femur (F). The mean Z score was -1.66DS in LS and -0.73DS in femur. Osteoporosis was found in 13 patients: 3 men and 10 women (2 among them were menopaused). The research of risk factors of osteoporosis found a smoking (N=1), and an associated autoimmune disease in 5cases: A diabetes Mellitus in 3 patients, and an autoimmune hepatitis an Sjogren Syndrome in 1 case. Finally, a marked villous atrophy was associated to osteoporosis in 9 cases.
Conclusions: Our study showed that approximately ¾ of coeliac patients had a low bone mass. Osteoporosis was found in 33% of our patients and was associated to a marked villous atrophy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6923

AB0827 COMPARISON OF THE CAPABILITY OF RADIAL BONE MINERAL DENSITY AND CALCANEAL QUANTITATIVE ULTRASOUND VARIABLES IN THE IDENTIFICATION OF MEN WITH OSTEOPOROSIS

A. Oral, D. Sindel, A. Yaliman, S. Asghari Kaleibar, S. Esmaeilzadeh. *Physical Medicine and Rehabilitation, Istanbul University Istanbul Faculty of Medicine, Istanbul, Turkey*

Background: Bone mineral density (BMD) as measured by dual-energy X-ray absorptiometry (DXA) is considered the gold standard for the management of osteoporosis. Recently, quantitative ultrasound (QUS), which is easy to use, inexpensive, portable, does not use ionizing radiation, and has also been shown to provide information about bone quality and to predict fracture risk, has gained growing interest in this area.
Objectives: The aim of this study was to compare the capability of one-third radius (33% radius) DXA BMD measurements and calcaneal QUS (cQUS) variables for identifying axial osteoporosis as measured by DXA in men.
Methods: Axial BMD measurements at the lumbar spine and at the hip (femoral neck and total hip), 1/3 radius BMD of the non-dominant forearm were made using DXA and cQUS variables at both sides as measured twice were obtained in 179 men aged between 24 and 85 years. Osteoporosis was defined based on the WHO criteria in men aged 50 and over, a man having been considered as osteoporotic in the presence of a T-score $\leq$-2.5 in any of the axial regions measured. For defining axial osteoporosis or BMD below the expected range for age, Z-scores of $\leq$-2.0 were used in men younger than the age of 50 years. Receiver operating characteristic (ROC) analysis was used to assess the osteoporosis identification capability of measurements.
Results: The areas under ROC curves (AUCs) for 1/3 radius BMD, its T-score, the lowest means (as calculated as the mean of the two calcaneal QUS measurements for each heel) of quantitative ultrasound index (QUI), QUI T-score, broadband ultrasound attenuation (BUA), speed of sound (SOS), and estimated heel BMD (eBMD) for identifying axial osteoporosis or BMD below the expected range were found as 0.755, 0.767, 0.760, 0.758, 0.717, 0.768, and 0.764 ($p<0.001$ for all), respectively.
Conclusions: In conclusion, AUCs pointed to similar (for QUI, QUI T-score, and eBMD) or even better (for SOS) osteoporosis discriminative capability of cQUS variables in comparison to radial DXA BMD variables. These findings may have implications that cQUS variables, particularly SOS, may be used for the identification of osteoporosis in men whose axial BMD cannot be measured by DXA due to certain circumstances as well as in circumstances where DXA is not available.
References:

[1] Marín F, González-Macías J, Díez-Pérez A, Palma S, Delgado-Rodríguez M. Relationship between bone quantitative ultrasound and fractures: a meta-analysis. J Bone Miner Res 2006;21:1126–35.
[2] Moayyeri A, Adams JE, Adler RA, Krieg MA, Hans D, Compston J, Lewiecki EM. Quantitative ultrasound of the heel and fracture risk assessment: an updated meta-analysis. Osteoporos Int 2012;23:143–53.
[3] Kilappa V, Moilanen P, Xu L, Nicholson PH, Timonen J, Cheng S. Low-frequency axial ultrasound velocity correlates with bone mineral density and cortical thickness in the radius and tibia in pre- and postmenopausal women. Osteoporos Int 2011;22:1103–1113.

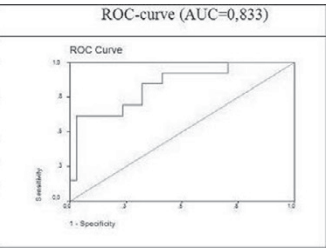
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6686

AB0828 MAJOR RISK FACTORS OF OSTEOPOROSIS IN RA FEMALE PATIENTS WITH NORMAL MENSTRUAL CYCLE

E.A. Taskina, L.I. Alekseeva, I.S. Dydykina, M.M. Podvorotova, A.V. Smirnov, S.I. Glukhova, E.L. Nasonov. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russia, Moscow, Russian Federation*

Background: Only postmenopausal women were in the researcher's focus in the majority of publications on osteoporosis (OP) risk factors (RF) in RA female patients (pts). Meanwhile the data on OP RF in menstruating women presented in the rare available papers are not consistent.
Objectives: To identify the major OP RF in RA female pts with normal menstrual cycle.
Methods: 51 RA (based on ACR criteria) female pts with normal menstrual cycle aged 20 to 51 years (mean age 41,1±7,9) were examined. The following info was included in each individual pts' files: anthropometric parameters, social and demographic data, case history, clinical examination and lab findings, traditional OP RF, pts' joint status, comorbidities status, pain intensity assessments and VAS evaluation of pts' general health status. Axial bone mineral density (BMD) was measured with DEXA scan using Z-score calculator. Based on the OP status all pts were divided into 2 groups:pts with OP–16 (31,4%), and pts without OP–35 (68,6%).
Results: Comparative analyses of the groups showed that: OP pts were younger vs the pts without OP (36,9±10 vs 42,8±6,3 years, p=0,02). Disease duration was comparable in both groups. Clinical manifestations of inflammation activity (mean DAS 28 score and hsCRP) were statistically significantly more pronounced in the OP group vs the pts without OP (4,91±1,39 vs 4,19±1,06, p=0,049; 27,8 (10,8–43,5) vs 7,4 (1,4–22,7) mg/L, p=0,02, respectively). High DAS 28 (50 vs 20,6%, RR=2,43, 95% CI 1,07–5,53, p=0,03) scores were more often documented in the OP pts. Pronounced feet and hand bone destruction based on the radiographic findings was documented in the majority of pts in both groups, although in the OP pts the joint space narrowing counts (97 (62,5–121) vs 73,5 (53–87), p=0,02) and the total Sharp score (98 (64,5–183) vs 89,0 (63–112), p=0,03) were statistically significantly higher. The OP pts were more often administered oral GCs (81,3 vs 37,1%, RR=2,19, 95% CI 1,34–3,57, p=0,004), as well as GCs -pulse therapy (56,3 vs 25,7%, RR=2,18, 95% CI 1,08–4,45, p=0,04), had higher GCs cumulative dose (18,8 (8,1–30,7) vs 6,4 (0,8–14,1)g, $p<0,01$), higher GC daily dose at the time of examination (8,8 (6,3–10) vs 5 (3,8–6,3)mg/day, p=0,01) and higher average daily dose in the previous year (8,8 (5–10) vs 3,8 (2,5–6,3)mg/day, p=0,01) versus the pts without OP. Analysis of traditional RF (low body weight/BMI, long immobilization periods, smoking, family history of OP and others) showed no difference between the two groups. Discriminant analysis revealed the following major OP RF in the RA female pts before menopause: RA activity (based on the Das 28 score) and GCs dose at the time of examination (given GCs therapy lasts $\geq$3 months). Meanwhile the patient's body weight and age at the onset of RA were identified as protective factors for BMD. Based on the abovementioned risk and protective factors and the derived coefficients the authors designed a formula allowing to predict of OP in female RA pts before menopause with high accuracy (area under the ROC-curve=0,833). The model accuracy is 85,1%.

Factors	Discriminant function coefficients
RA activity (DAS 28)	0,667
GCs dose at the time of examination	0,257
Age at RA onset	-0,09
Body weight	-0,034
Constant	1,319



Conclusions: RA activity and GCs dose (GCs therapy duration $\geq$3 months) were identified as the major OP RF in young RA female pts before menopause, thus adequate and timely therapy aimed at obtaining RA control and achieving remission should be considered as key OP prevention strategy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2312

AB0829 BONE METABOLISM IN LIVER TRANSPLANT PATIENTS TWO-YEAR STUDY. INFLUENCE OF MEDICAL INTERVENTION PRIOR TO SURGERY AND ANTIRESORPTIVE TREATMENT

E. Labrador Sánchez [1], E. Grau Garcia [1], K. Arévalo Ruales [1], J.J. Fragio Gil [1], R. González Mazarío [1], C. Alcañiz Escandell [1], I. Cánovas Olmos [1], I. Chalmeta Verdejo [1], C.M. Feced Olmos [1], L. Gonzalez Puig [1], J. Ivorra Cortes [1], I. Martínez Cordellat [1], C. Nájera Herranz [1], R. Negueroles Albuixech [1], J.E. Oller Rodriguez [1], F.M. Ortiz-Sanjuan [1], E. Vicens Bernabeu [1], A. Villota Bello [2], V. Fornés Ferrer [3], D. Hervás Marín [3], D. Moya Nájera [4], A. Moya Herraiz [5], J.A. Román Ivorra [1,2]. *[1]Rheumatology Department, HUP la Fe; [2]Medical School, UCV; [3]Biostatistic Unit, IIS la Fe; [4]Health and Sport Group, UV; [5]Hepatology Department, HUP la Fe, Valencia, Spain*

Background: Osteoporosis is a frequent complication in patients with chronic liver diseases, mainly in advanced stages or with evidence of cholestasis. During the first few months after liver transplant (LT) it seems that there is an accelerated bone mass loss and greater fracture risk.
Objectives: To study the antiresorptive treatment effect in bone metabolism in patients undergoing LT and to evaluate whether medical intervention prior to LT decreases the risk of osteoporosis
Methods: We recruited patients from the LT Protocol of Osteoporotic Risk Assessment. The patients were evaluated 3–6 months before surgery, shortly after transplant (month 0) and 6–12–18–24 months after surgery. Data of bone metabolism biomarkers, densitometric values and antiresorptive treatment was collected. Biostatistical analysis with R (3.3.2.) was performed.
Results: We selected 163 LT patients of which 86 completed 24 months follow-up. From the total cohort, 77.8% were men and the mean age at transplantation 54.53±9.4 years old. 92.6% of patients were supplemented with vitamin D after surgery and 19.6% initiated antiresorptive treatment. We observed that 25-OHVitamin D, PTH, beta-CTX and P1NP levels were corrected through the follow-up. T-score during the first year of follow-up decreased slightly and at 24 months the tendency was towards increase. This pattern was stronger in lumbar spine (t-score -1.48±1.34 after surgery and -1.28±1.06 at 24 months). Statistical analysis showed that antiresorptive treatment significantly influence lumbar and hip densitometric values ($P<0.001$ and $P<0.001$ respectively) as well as P1NP levels (P=0.003 and P=0.012 respectively). Moreover, obesity (P=0.0004), as well as beta-CTX (P=0.029) and 25-OHVitamin D (P=0.024) standardization improved hip densitometric values. Finally, LT patients evaluated before surgery showed better lumbar densitometric values than those evaluated after the transplant (P=0.007).

Conclusions: We observed 25-OHVitamin D levels and bone metabolism biomarkers correction during the first two years after LT. Medical intervention prior to LT as well as antiresorptive treatment seem to play a decisive role in bone mineral density improvement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5855

AB0830 BONE MINERAL DENSITY IN MULTIPLE MYELOMA: 39 CASES

Z. Saoussen, H. Mouanaa, A. Arfa, M. Jguirim, B. Ismaiel, M. Touzi, N. Bergaoui.
Rheumatology departement of Monastir University Hospital, Monastir, Tunisia

Background: In multiple myeloma (MM), osteolysis affects more than 80% of patients. This leads to bone pain, pathological fractures and hypercalcemia. These lesions result from an alteration of bone remodeling by increased osteoclast activity and decreased osteoblasts one. The real impact of this osteolysis on bone mineral density remains largely understudied. To the best of our knowledge the impact of MM on bone mineralization was studied worldwide only for 6 times where our study is the second biggest one.
Objectives: The aim of the study was to evaluate bone mineralization in the patients with multiple myeloma according to the criteria of diagnostic (IMWG: International Myeloma Working Group 2014, during a period of 5 years (2011–2016).
Methods: This is a transverse and descriptive study. The bone mineral density was measured by dual-energy X-ray absorptiometry with Lunar Prodigy in spine (L2-L4) and femoral neck.
Results: Thirty-nine patients were collected. The average age was 63±10 years [50 years, 86 years] upon them 26 men and 13 women. The sex-ratio is equal to 2. 11 patients were smoking (35%), 9 of them had diabetes and only 2 were alcoholic (6%). The Body Mass Index (BMI) average was 29 kg/m^2. Only one case was underweight (3%). The reason of seeking health carewas poor general state in 14 cases (49%), bone pain in 22 cases (78%),5 cases among them of generalized bone pain (23%) and 12 cases of rachialgia (4.5%) and only 4 cases of pathological fracture (15%). The distribution of patients according to the Durie and Salmon Classification was as follows: 25 cases (84%) in stage III, 3 cases (10%) in stage II, 2 cases (7%) in stage I, and 27 cases (90%) Type A and 3 cases (10%) type B. The average of the monoclonal spike was 34g/L [2.5g/L, 88g/L] The heavy chains antibodies were IgG type in 19 cases (64%), IgA type in 7 cases (24%), IgM type in only one case (4%) and IgD type in only one case (4%). The light chains were Kappa type in 19 cases (64%) and Lambda type in 11 cases (37%). The ISS score was equal to 1 in 6 cases (23%), equal to 2 in 13 cases (34%) and equal to 3 in 8 cases (30%).The average bone mass in the spine was 0.998±0.254g/cm^2 [0.632g/cm^2; 1.892g/cm^2] and in the femoral neck 0.869±0.254g/cm^2 [0.632g/cm^2; 1.892g/cm^2]. The average of the Z-score in the spine was -0.762±1.895 [-4.4; 5.7] and in the femur -0.438±0.962 [-2.8; 1.4]. The mean T-score in the spine was -1.626±2.025 [-4.9; 5.6] and in the level of the femur -1.567±1.178 [-3.7; 1]. There was a decrease of bone mineral density noticed in 15 patients (39%) in at least one place (T-score more than 2.5 SD below normal of young healthy persons. Seventeen patients (58%) were candidates for *autogenous bone graft*. They had *induction chemotherapy* (Dexamethasone-thalidomide). Others was treated by MPT protocol (Prednisone-Thalidomide-Dexamethasone) in 8 cases (28%), CDT protocol (Cyclophosphamide-Thalidomide-Dexamethasone) in one case (4%) and MP protocol (Melphalan -Prednisone) for the remaining (10%).
Conclusions: BMD analysis suggests that MM is associated with systemic bone disease with progressive loss of bone mass at both the spinal and lumbar levels. In order to better study the impact of multiple myeloma and chemotherapy on bone densitometry, a densitometry controlin about 5 years is favorable.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6754

AB0831 FRAX SCORE: AN INTERESTING WAY FOR GASTROENTEROLOGISTS TO ASSESS FRACTURE RISK IN PATIENTS WITH LONG-TERM PROTON PUMP INHIBITORS

H. Romdhane[1], M. Cheikh[1], K. Abdelghani[2], R. Ennaifer[1], N. Bel Hadj[1], A. Laatar[2]. *[1]Gastroenterology and hepatology; [2]Rhumatology, Mongi Slim Hospital, TUNIS, Tunisia*

Background: Proton pump inhibitors (PPI) are effective in many indications. Nevertheless, some serious adverse effects associated with prolonged exposure, including an increase in fracture risk, have occurred. This would be explained by two main mechanisms: decreased absorption of calcium secondary to decreased gastric acidity and inhibition of proton pump of osteoclasts reducing bone resorption.
The Frax score assess the 10-year probability of osteoporotic fracture or hip fracture in subjects older than 40 years.
Objectives: The aim of our study was to evaluate the usefulness in our practice of this score in patients under long-term PPI.
Methods: We included patients who had been taking PPI for at least one year. In all patients, we specified the indication and duration of PPI. We then looked for the main personal or family risk factors for osteoporosis. Bone mineral density (BMD) was performed in all patients and frax score was calculated for those older than 40 years.
Results: Fifty-two patients were included in our study. The mean age was 49.5±14.55 years [21 - 84 years] with a sex ratio of 0.48. Long-term PPI were indicated in 75% (n=39) of patients for gastroesophageal reflux, in 11.5% (n=6) for chronic gastritis with failure of Helicobacter Pylori eradication, in 3.8% (n=2) for persistent epigastralgia, in 5.7% (n=3) for functional dyspepsia and finally in 3.8% (n=2) of patients in prophylaxis of gastroduodenal lesions in chronic use of NSAIDs. The mean duration of intake was 45.4 months [12–240 months]. The main osteoporotic risk factors were tobacco in 25%, alcohol in 12%, physical inactivity in 42% and dysthyroidism in 6% of cases. In our study, 20 women among the 35 included (57% of cases) were already menopausal. An osteoporotic fracture in a first-degree relative was noted in 23% of cases, including one parent reporting two fractures. A history of fragility fracture was observed in 11 patients (21%) including 3 men and 8 women. The mean daily calcium intake was 567.2±327.6 mg /d [230 -2315 mg /d]. Calcium intake was insufficient in 94% of patients. BMD was normal in 15 patients (29% of cases) while 71% (n=37) had low BMD. In our population, age (p=0.02), calcium intake (p=0.029) and menopause ($p<0.0001$) were significantly related to low BMD. The duration of PPI intake was negatively correlated with BMD. Patients taking PPI for at least 30 months were 6.5 times more likely to have low BMD (95% CI [1.5–27.4]). The mean FRAX score for major osteoporotic fractures in 37 patients older than 40 years was 1.08±0.84% [0.3–3.3%]. For hip fractures, the mean score was 0.26±0.29% [0–1.4%]. There was a significant correlation between mean Frax score and BMD ($p<0.0001$). None patient had a patent or subclinical fracture during the follow-up period.
Conclusions: Our study shows an increased risk of fracture in patients under long-term PPI, especially if they have other osteoporotic risk factors. In this context, Frax score is a simple and non-invasive tool for assessing fracture risk in these patients and to adapt screening strategy for sub-clinical fractures.
References:
[1] none.
Acknowledgements: none.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5399

AB0832 EFFECT OF LONG-TERM PROTON PUMP INHIBITORS ON BONE MINERAL DENSITY

H. Romdhane, M. Cheikh, H. Ben Nejma, R. Ennaifer, N. Bel Hadj.
Gastroenterology and hepatology, Mongi Slim Hospital, TUNIS, Tunisia

Background: Proton pump inhibitors (PPI) are widespread nowadays. Recent concerns have emerged about possible bone complications of long-term use of PPIs, such as low bone mineral density (BMD) and an increased risk of fractures.
Objectives: The aim of our study was to evaluate the effect of long-term use of PPIs on bone by measuring the BMD in order to estimate the frequency of osteopenia and osteoporosis, and to determine the risk factors associated to this complication.
Methods: It was a prospective study including consecutive patients who where taking proton pump inhibitors for at least one year. In all patients we realized a bone densitometry in order to evaluate the bone strength and we calculated the FRAX score to estimate the risk of osteoporotic fracture at ten years.
Results: We included 52 patients. The mean age was 49,5 years old. The male-female ratio M/F was 0,48. At least three risk factors were found in more than 50% of the population. The calculated daily calcium intake was insufficient in 94% of the patients. The mean duration of PPIs intake was 45 months. The most frequent indication was gastro esophageal reflux disease (75%). The PPI prescription was appropriate in 94% of the cases. The prevalence of osteopenia and osteoporosis was respectively 52% and 19%. The predictive factors of low BMD were an age $\geq$50 years old (p=0,03), the menopause ($p<0,0001$), a calcium intake $\leq$550 mg/day ($p<0,038$), and a PPI use duration $\geq$30 months ($p<0,006$). The multivariate study could not be undertaken because of co linearity of the factors.
Conclusions: The long term PPI use is associated to the risk of bone complications, especially among patients at risk for osteoporosis. It seems reasonable to be more vigilant in prescribing PPIs and use lowest effective dose for patients with appropriate indications, and to screen these complications if necessary.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5281

AB0833 BONE MINERAL DENSITY IN TUNISIAN PATIENTS WITH AUTOIMMUNE HEPATITIS

M. Cheikh, H. Romdhane, H. Bennejma, R. Ennaifer, N. Bel Hadj.
Gastroenterology and hepatology, Mongi Slim Hospital, TUNIS, Tunisia

Background: Bone loss in autoimmune hepatitis (AIH) is scanty and conflicting. The pathogenic mechanisms are not completely elucidated.
Objectives: This study aimed to assess the prevalence and risk factors for bone loss in patients with AIH.
Methods: Bone mineral density (BMD) using X-ray absorptiometry at both lumbar spine and femoral neck sites was measured in patients with AIH. Were excluded patients with diseases disturbing the bone density. Osteopenia was considered if T-score <-1.5 DS and osteoporosis if T-score <-2.5 DS.

Results: Twenty eight patients were enrolled in the study. They were 19 women (sex-ration M/F=0.6), with a mean age of 54 years [extremes: 13 - 73 years]. Most patients had type 1 AIH (89.2%). Seventeen patients were diagnosed at stage of cirrhosis (60.7%). Associated auto-immune manifestations were observed in 42.8% of cases. Overlap syndrome with primary biliary cirrhosis was noted in 21.4% of cases. Fifty five percent of patients were on steroid treatment with or without azathioprine. BMD was low in 9 patients (32%) as fellow: osteopenia in 6 cases and osteoporosis in 3 cases. There was a correlation between bone loss and use of steroid treatment but it wasn't statistically significant (p=0.07).
Conclusions: In our series, the prevalence of bone loss in AIH is high (45%). This data suggests that bone status should be assessed routinely in patients with AIH, especially in those on steroid treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6442

AB0834 RISK FACTORS FOR DECREASED BONE MINERAL DENSITY IN INFLAMMATORY BOWEL DISEASE IN A TUNISIAN COHORTE

H. Romdhane[1], M. Cheikh[1], K. Abdelghani[2], R. Ennaifer[1], N. Bel Hadj[1], A. Laatar[2]. [1]*Gastroenterology and hepatology;* [2]*Rhumatology, Mongi Slim Hospital, TUNIS, Tunisia*

Background: Patients with inflammatory bowel disease [IBD] are at risk for metabolic bone disease. Many studies have identified various risk factors but most of them have involved western patients.
Objectives: The aim of this study was to investigate the prevalence and the risk factors for metabolic bone disease in Tunisian IBD patients.
Methods: Retrospective study including patients with IBD admitted in our department between January 2011 and December 2015. Demographic and clinical characteristics of patients were analysed. Bone mineral density of the femoral neck, total femur and lumbar spine was quantified by dual-energy X-ray absorptiometry.
Results: Among 82 patients followed for IBD (70.7% with Crohn's disease; 29.3% with Ulcerative colitis), a bone densitometry was performed in 56% of cases (n=46). 16 patients have osteopenia and 7 had osteoporosis, as assessed by T-score. Univariate analysis showed that Crohn'n disease in particular ileal disease, high steroid dose and the presence of extra-intestinal manifestations were significantly associated with a low bone mineral density (for all $p<0.05$). In the other hand, IBD duration since diagnosis, sexe, tabagism were not associated with bone loss.
In multivariate regression analysis, risk factors for decreased bone mineral density were IBD duration since diagnosis, high steroid dose, ileal crohn's disease and extra-intestinal manifestations.
Conclusions: In our Tunisian cohort of IBD patients, Crohn's disease, high steroid dose and extra-intestinal manifestations were associated with increased risk for metabolic bone disease. High risk patients should be identified and appropriate therapies should be started early to improve long term quality of life.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5301

AB0835 DENOSUMAB AS A FIRST CHOICE DRUG FOR GLUCOCORTICOID INDUCED OSTEOPOROSIS TREATMENT INSTEAD OF BISPHOSPHONATE

I. Yoshii[1], T. Chijiwa[2]. [1]*Orthopaedic Surgery, Yoshii Hospital, Shimanto City;* [2]*Rheumatology, Kochi Memorial Hopsital, Kochi, Japan*

Background: Glucocorticoid induced osteoporosis (GIO) is serious problem for raising risk of bone fragile fracture. In general, first choice drug for GIO is bisphosphonate (BPH), however, denosumab (dMAB), a monoclonal antibody of receptor activator of nuclear factor kappa-B ligand, is closed up as a alternative selection for GIO recently.
Objectives: The aim of this study is to evaluate effectiveness of dMAB in bone mineral density (BMD) for GIO treatment compared to BPH.
Methods: In the patients in whom glucocorticoid steroid (GCs) have been administered for more than three months, who met indication criteria for GIO what was determined by the Japanese Society for Bone and Mineral Research in 2014, that is matrix calculated in adding points of past fracture history, age, dosage of GCs, and BMD value (1), were enrolled. Before March 2013, data was lacking, so patients who have been administrated GCs after April 2013 were picked up. Patients BMD at GCs administration, at 6 months after initial treatment, if drug was changed, also at 6 months after second treatment, for minimum lumbar spine (LS), femoral neck (FN), and greater trochanter (GT) were measured with dual-energy X-ray absorptiometry (DEXA). Patients were classified by drug for initial treatment and second drug if administered. Patients age, initial, average, and total dose of GCs, term length of administration, and BMD and its gain for each chance were compared with Mann-Whitney U-test and Student's paired T-test.
Results: 149 patients in whom 48 with no drug administrated (N), 24 for BPH naïve and continued (BB), 22 for BPH naïve and changed to dMAB (BD), 21 for dMAB naïve and continued (DD), 34 for dMAB naïve and changed to BPH (DB) were counted. In these, sex distribution was 26 for men and 123 for women. Underlying disease for administration of GCs were rheumatoid arthritis for 114, polymyalgia rheumatica for 12, idiopathic thrombocytopenic purpura for 9, systemic lupus erythematosus for 6, and others for 8. For groups, age at baseline, initial, average, and total dose, and term length of administration of GCs demonstrated no significant difference between any pairs of the groups. BMD at baseline for Group N demonstrated significant greater per-cent of young adult mean (%YAM) than Group DD ($p<0.01$) in all parts, yet greater than the other groups but not statistically significant. In Group N, BMD had significantly decreased from the baseline to 6 months later in all parts ($p<0.01$). In the other groups, BMD had shown gain at 6 months after drug administration in all part, however, in Group DB showed mean %YAM loss for GT after first and second drug administration compared to Group BD had shown %YAM loss after first but gain after second drug for FN (Table 1).

First Drug (FD)	none	bisphosphonate		denosumab	
Second Drug (SD)	none	none	denosumab	none	bisphosphonate
Cases	48	24	22	21	34
age at baseline	69.7±10.8	73.7±16.5	81.8±12.2	72.5±11.5	71.5±10.8
initial dose of GCs	6.78±8.98	6.88±8.25	5.58±6.95	5.21±3.47	6.95±2.25
average dose of GCs	3.77±2.13	5.49±3.76	5.06±1.61	3.49±1.49	5.12±2.06
term length of administration	53.6±45.3	84.7±44.9	38.2±46.4	51.9±58.7	65.2±46.0
total dose of GCs	3836.6±4444.3	7170.2±10923.8	2447.1±6365.9	5017.1±9057.3	7898.2±772.9
BMD of lumbar spine at baseline	89.1±16.9	78.1±17.7	80.2±12.4	70.9±9.3	75.9±12.4
BMD of LS at six months after administration of FD	86.5±19.1	79.3±10.5	81.8±15.2	72.9±13.5	75.9±15.5
BMD of LS at six months after administration of SD			81.2±12.8		77.3±9.2
BMD of FN at baseline	90.8±12.8	77.3±9.3	70.6±12.9	66.8±7.6	72.1±8.8
BMD of FN at six months after administration of FD	87.8±15.4	80.0±14.6	69.1±12.2	65.9±12.4	74.3±11.4
BMD of FN at six months after administration of SD			71.2±11.3		74.4±15.3
BMD of GT at baseline	85.8±9.8	80.8±10.1	71.2±12.7	67.1±12.6	75.2±9.4
BMD of GT at six months after administration of FD	83.5±14.5	80.1±12.9	71.2±12.7	68.9±12.6	75±9.3
BMD of GT at six months after administration of SD			74.2±13.3		74.2±10.3

Table 1: Results of glucocorticoid induced osteoporosis (GIO) patients for each group classified by used drugs. GCs : glucocorticoids, BMD : bonemineral density, LS : lumbar spine, FN : femoral neck, GT : greater trochanter. Unit in BMD is per cent of young adult mean (%YAM).

Conclusions: From these results, dMAB is effective role in raising BMD for GIO as a initial drug, and a second drug even after inadequate response to BPH. dMAB could be possible to be chosen as a first choice drug for GIO treatment.
References:
[1] Suzuki, Y., Nawata, H., Soen, S. et al. J Bone Miner Metab (2014) 32: 337. doi:10.1007/s00774–014–0586–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3106

AB0836 PERFORMANCE OF QUANTITATIVE ULTRASOUND AND SIX OSTEOPOROSIS RISK INDEXES IN MENOPAUSAL WOMEN: VALIDATION AND COMPARATIVE EVALUATION STUDY

I. Ghozlani[1], A. El Maataoui[2], M. Ghazi[3], A. Kherrab[3], R. Niamane[3]. [1]*Rheumatology Department, Military Hospital;* [2]*Chemistry-Biochemistry Department, Faculty of Medicine and Pharmacy, Ibn Zohr University, Agadir;* [3]*Rheumatology Department, Military Hospital Avicenne, Marrakech, Morocco*

Background: A number of questionnaire-based systems and the use of portable quantitative ultrasound scanners (QUS) have been devised in an attempt to produce a cost-effective method of screening for osteoporosis.
Objectives: to assess the sensitivity and specificity of different techniques and their ability to act as screening tools in relation to dual energy X-ray absorptiometry (DXA).
Methods: 295 white postmenopausal women aged over 60 were enrolled. Each subject completed a standardized questionnaire which permits the measure of six osteoporosis indexes and had bone mineral density (BMD) measured using QUS and DXA. Sensitivity and specificity of the different techniques in relation to DXA were plotted as receiver-operating characteristic (ROC) curves at DXA T-score total hip $\leq$ -2.5 (osteoporosis).
Results: BUA sensitivity and specificity values were respectively 76.8% and 51.2% at the total hip. The optimal cut-off T-score for QUS was -2 at the total hip. The osteoporosis self-assessment tool (OST) provided consistently the highest AUC (0.80) among the clinical tools and had the best sensitivity and specificity balance (90.2%>44.5%). OST negative likelihood ratio was 0.22.
Conclusions: OST (based only on the weight and the age) performed slightly better than QUS and other risk questionnaires in predicting low BMD at the total hip.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1449

AB0837 BONE METABOLISM AND OSTEOPOROSIS RISK FACTORS ANALYSIS IN SPINAL CORD INJURY PATIENTS AT TWELVE MONTHS FOLLOW UP

I. Martínez Cordellat[1], F. Torralba Collados[2], C. Grao Castellote[2], E. Grau García[1], V. Fornes Ferrer[3], E. Labrador Sánchez[1], K. Arévalo Ruales[1], J. Fragio Gil[1], R. González Mazarío[1], C. Alcañiz Escandell[1], I. Chalmeta Verdejo[1], C. Feced Olmos[1], L. González Puig[1], J. Ivorra Cortés[1], R. Negueroles Albuixec[1], J.E. Oller Rodríguez[1], F. Ortiz Sanjuán[1], E. Bernabeu Vicens[1], C. Nájera Herranz[1], I. Cánovas Olmos[1], J.A. Román Ivorra[1]. [1]*Rheumatology Department;* [2]*Spinal Cord Injury Unit;* [3]*Biostatistics Unit IIS la Fe, Hup la Fe, Valencia, Spain*

Background: The spinal cord injury associated with the immobilization of the

patient leads to a decrease in bone mass. The bone loss greater is observed in the 6 months after the spinal cord injury, and stabilizing between 12–16 months after the same. The incidence of fractures oscillates between 1.5% and 6%.
Objectives: To assess bone metabolism and bone fracture incidence in SPI patients.
Methods: Prospective study of SPI patients from the Spinal Cord Injury Unit of La Fe Hospital. In all cases densitometry, x-ray image, bone metabolism biomarkers and clinical evaluation have been performed according protocol. Statistical techniques was carried out using R software 3.2.3, using mixed linear regression models.
Results: We studied 40 patients with SCI, 54% of them men and 46% women, with a mean age of 59.5 years (57.3- 63.5). The 58% of patients showed thoracic injuries, 48.6% paraparesis and 46.7% presented level C in Asia scale. The baseline study was performed in 100% of patients (n=40), 65% in month 6 (n=26), 30% in month 12 (n=12), and in 22.5% in month 18 (n=9). The 32.4% of patients received supplementation with calcium and vitamin D at month 0, 66.7% at month 6 and 100% at month 12.
In month 6, the 11.1% was treated with antiresorptive drugs.
An increase in vitamin D values can be observed in the population with follow-up (values of 16.82 in month 0 to 39.33 in month 12), justified by the supplementation, and there is an increase in Calcium and a decrease in phosphorum values.
There was also a decrease in PTH levels in month 12 (32.3) compared to month 0 (34.08), as well as a decrease in bctx levels. Probably related to the increase of vitamin D.
Despite a decrease in the densitometric parameters at month 6, a slight recovery in bone mineral density at month 12 was observed. No bone fractures were seen during Follow-up in none of the patients.
Results from biochemical markers and densitometry are showed in the table

Parameter	Month 0	Month 6	Month 12
	Mean (SD)	Mean (SD)	Mean (SD)
Calcium	9.04 (0.47)	9.57 (0.36)***	9.39 (0.34)***
Phosphorus	3.83 (0.62)	3.42 (0.45)***	3.4 (19.94)***
25OH Vitamin D	16.82 (10.4)	37.27 (15.52)***	39.33 (19.94)***
PTH	34.08 (21.74)	36.16 (19.46)	32.3 (12.6)
P1NP	76.1 (79.18)	64.27 (28.11)	65.87 (25.76)
BCTX	0.94 (0.46)	0.62 (0.87)**	0.34 (0.21)***
Lumbar spine tscore	-0.24 (1.58)	-0.25 (1.11)	-0.3 (1.27)
Femoral neck tscore	-0.73 (1.34)	-1.35 (1.03)**	-1.26 (1.25)**
Hip bone tscore	-0.74 (1.25)	-1.56 (1.29)***	-1.52 (1.4)***

*p<0,05, **p<0,01,***p<0,001.

Conclusions: A high percentage of our patients with spinal cord injury has a vitamin D deficiency. In addition, the lower levels are associated with cases where the mobility limitation is higher. As patients increase vitamin D values, a decrease in the bctx and PTH parameters is observed.
No fractures were detected during follow-up.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5487

AB0838 EPIDEMIOLOGY AND ANALYSIS OF FALLS IN PATIENTS DURING BALNEOTHERAPY IN DANUBIUS HEALTH SPA PIESTANY

I. Rybar[1], V. Kolnikova[2], T. Zimanova[2], R. Gaspar[2]. *[1]Department of Rheumatology, National Institute of Rheumatic Diseases; [2]Department of Physiotherapy, Danubius Health Spa, Piestany, Slovakia*

Background: Patients falls in hospitals are frequent and undesirable complications that may lead to negative outcomes such as injuries, prolonged hospitalization and legal liability.
Objectives: To investigate the incidence and characteristics of patients hospitalized in the Health Spa Piestany.
Methods: Prospective analysis of falls in the group of in-patients of health spa during a year since 01.01.2015 to 31.12.2015.
Results: Overall there were hospitalized in the health spa 25 774 in-patients. The mean age of patients was 64,02±13,16 years. There were women - 15 301, mean age (63,61±11,57 years) and men 10 473, with mean age (64,43±9,22 years). Falls were confirmed in 131 patients (women 94, mean age 68,55±10,22 years and men 37 males, mean age 70,39±7,62 years. Fractures have been confirmed in 19 patients, all of them non-vertebral. The ankle distortion were in 11 patients and lacerated wounds in 10 patients. There were collapse status in 8 and commotio cerebri in 1 patient. Spa therapy had to be discontinued only in 5 from 131 patiens due to falls. The annual incidence of falls reached 5,08 cases/1000 patients. In women there were - 6,14 cases/1000 women a year and in men 3,53 cases/1000 men a year. The annually incidence of fractures reached 0,69/1000 pacients. The most common locations of falls were hotel rooms, especially bathtub in the bathroom (49%), slightly less facilities for balneotherapy (22%), the area outside the spa (21%) and at least in the park area of health spa 8%. Women and men who have suffered falls had significantly higher age and had also high rate of cardio-vascular morbidity (87%).
Conclusions: The annual incidence of falls among patients in a balneotherapy reached to 5.08 cases per 1,000 patients per year. Incidence of falls in women was almost twice as high compared to men. The age of women and men with falls was significantly higher (p<0,001) compared to other patients and they also had higher rate of cardiovascular morbidity. The most common locations of falls were bathtubs in the bathroom.
References:
[1] Gazibara T. et al.: Psychogeriatrics. 2017 Jan 27. doi: 10.1111/psyg.12217.
[2] Cockayne S. et al.: PLoS One. 2017 Jan 20;12(1):e0168712.
[3] Tsonga T. et al.: Clin Orthop Surg. 2015 Dec;7(4):449–56.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5278

AB0839 THE EFFICACY AND SAFETY OF DENOSUMAB LOCAL EXPERIENCE)

J. Al-Saleh, N. Salah, A.S. Hasan, S. Mohamad, F.A. ElBadawi, M. Khamashta. *Rheumatology Department, Dubai Hospital, Dubai, United Arab Emirates*

Background: Denosumab was introduce to the United Arab Emirates Market in 2013.Given the limited experience in using Denosumab in the region we have explored it efficacy and safety in daily practice.
Objectives: To assess the efficacy and safety of Denosumab in our practice.
Methods: *Inclusion criteria:* All patients received Denosumab in a dose of 60mg every six months. Underwent DEXA scan in Dubai Health Authority. *Exclusion from analysis:* Other Doses of Denosumab, who received less than 3 doses, and those with no follow up DEXA scan. *Outcome measures:* 1) Efficacy: Proposed Criteria for Assessing Clinical Response [1,2]. a) "inadequate": incident fracture and significant BMD decrease. b) "possible inadequate": incident fracture or significant BMD decrease. c) "appropriate": no fracture and stability or increase in BMD. 2) Safety: Reviewing the medical records and conduct patients interview for occurrence of the following adverse events. *Statistical analysis:* Descriptive statistical analysis, Graphpad Prism 6 was used.
Results: 143 patient identified. Out 139 patients 86 were eligible for analysis (See table 1). At baseline 39% had normal vitamin D level, 57% had insufficiency and 4% had deficiency. 20 of 86 did not undergo repeated DEXA scan. 9% had osteopenia and 91% had osteoporosis before initiating Denosumab in comparison 8% had normal bone mineral density, 45% had osteopenia and 47% post four injections of Denosumab. Table 2 summarize the comparison between the responders and non-responders. There was a significant positive correlation in the increase in bone mineral density among the responders at the femoral neck and the lumbar spine, (r=0.56, 95% confidence interval: 0.31–0.74, P-value <0.0001 No report of any of the adverse events 86 patients who completed 2 years or more on treatment.

Table 1. Patients characteristics at baseline

Variables	Number	Percentage
Age (yrs) median, (1st Quartile- 3rd Quartile)	65, (58–67)	
51- 65	48	35%
>65	76	55%
Female	126	91%
UAE	121	87%
Comorbidities	72	52%
Received 4 Denosumab doses or more	86	62%
DEXA scan in DHA at Baseline	136	98%
Osteopenia	12	9%
Osteoporosis	124	91%
Fractures	12	9%

Table 2. Comparison between the appropriate Response group "Responders" and inadequate response group "Non-responders"

Variables	Responders	Non-responders	Odds Ratio	P-value	95% CI
Number	52	14			
Rheumatic Diseases	6	36	0.1	0.0001	0.05–0.2
Fracture	0	3	0.2	NS	
Pre-treatment fractures	9	1	9.5	0.02	2.0–70

Conclusions: Denosumab was effective and safe in our patients. Long-term follow up is required to verify these findings in our population.
References:
[1] Diez-Perez and Gonzalez-Macias. Inadequate responders to osteoporosis treatment: proposal for an operational definition. Osteoporos Int. 2008 Nov;19(11):1511–6.
[2] E. M. Lewiecki & N. B. Watts. Assessing response to osteoporosis therapy Osteoporos Int (2008) 19:1363–1368.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6791

AB0840 LOCAL FRACTURE LIAISON SERVICE (FLS): CHARACTERISTICS AND FIRST 6 MONTHS OF EVOLUTION IN PATIENTS AFTER HIP FRACTURE: PRELIMINARY RESULTS

J. Rosas[1], C. Cano[1], M. Lorente[1], A. Pons[1], E. Salas[1], T. Llinares[2], M. Hernández[3], J.M. Senabre-Gallego[1], M. Marco-Mingot[4], J.D. Alvarado[3], G. Santos-Soler[1], H. Arcos[3], A. García[3], J.I. Hernández[3], J.J. Jiménez[3], X. Barber[5], C. López[3], M.D. López[3], A.M. Molinos[3], B. Statti[3], M. Sanchís-Selfa[5] on behalf of FLS-HMB and AIRE-MB Groups. *[1]Rheumatology Department; [2]Traumatology Department; [3]Radiology Derpartment; [4]Laboratory Department, Hospital Marina Baixa, Villajoyosa (Alicante); [5]CIO, Universidad Miguel Hernández, Elche, Spain*

Background: Hip fracture has great impact on morbi-mortality, but a large percentage of patients do not receive treatment.
Objectives: To know the characteristics of patients whith hip fracture and its evolution in the first 6 months.
Methods: A prospective, 6-month follow-up study of patients over 60 years old admitted for hip fracture, evaluated in a local FLS. At 3 months after discharge, patients are evaluated for: epidemiological data, fracture income (days of admission, prior and discharge of osteoporosis (OP) drugs, general biochemistry and vitamin D), OP records and possible diseases or osteopenizing drugs, lumbar spine and hip Bone densitometry (BMD) lateral dorsal and lumbar spine radiology and the treatment was decided. The electronic history before and after 6 months of the fracture were reviewed.
Results: Of 152 patients >60 years old, admitted in 2016 due hip fracture, 77 (51%) were during the first 6 months. However, radiology or BMD data were not available for 30 (39%) patients, 16 (21%) for death and 14 (18%) for loss of follow-up. Mean BMI was 26.02±6.2. The mean age of menopause was 49±5 years. 1% of the patients received corticosteroids and 2% of patients an osteopenizing disease (COPD) was found. Mean time of admission was 7.57±2.51 days. In 3% of the patients, before the fracture were receiving OP treatment, which continued to discharge. The mean level of calcium, phosphorus and alkaline phosphatase was normal. However, the mean level of 25OH vitamin D was 13.55±8.63 ng/ml (median: 12 ng/ml, range: <4 to 29 ng/ml).
In 11 of the 27 (41%) patients, in whom radiology was available, the presence of vertebral fracture was demonstrated. The mean T-score for lumbar BMD was 1.8±1.65 DE (32%: the result was normal, 36% osteopenia, 32% OP), femoral neck 2.59±0.77 DE (27%: osteopenia, 77% OP) and in total hip: 2.56±0.86 DE (56%:osteopenia and 44% OPand In Ward of 3.2 DE. 100% of patients evaluated in Rheumatology, initiated treatment for OP: zoledronate: 40%, alendronate: 20%, denosumab: 25%, PTH: 15%.
Conclusions: In patients with hip fracture: 1) Mortality is high (21%), in the first 6 months after fracture. 2) The prevalence of vertebral fracture is 40%. 3) It is accompanied by very low blood levels of vitamin D. 4) In a high percentage the result of BMD is normal or osteopenia. 5) A minimum number of patients receive specific treatment for osteoporosis after fracture. 6) Evaluation in a FLS, ensures the evaluation and treatment of patients.
Acknowledgements: The study was supported by a research grant from the Asociación para la Investigación en Reumatología de la Marina Baixa (AIREMB).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4234

AB0841 MEDICAL AND SOCIAL CONSEQUENCES IN HIP FRACTURES DEPENDING ON THE METHOD OF TREATMENT

J.V. Averkieva, T. Raskina. *State Medical University Kemerovo, Kemerovo, Russian Federation*

Background: medical and social significance of osteoporosis is determined by its consequences - fractures of the vertebrae and the bones of the peripheral skeleton leading to high rates of mortality and disability among older adults. Purpose: to follow basic health and social consequences among the surviving patients with hip fractures aged 50 years or older at 6, 24 months.
Objectives: The study included 432 patients (328 women and 104 men) with radiographic evidence of hip fractures that occurred with minimal trauma.
Methods: Surgical treatment was performed in 171 (40,04%) patients, conservative treatment-261(59.96%).
Results: tracked mortality in hip fractures in 432 patients. It was found that in the first 6 months in the surgical treatment of deaths registered in 11 (6,43%) patients and in 84 (32.18%) - the conservative ($p<0.0001$). After 12 months after fracture increased mortality rate after the surgical treatment and after conservative (12.9% and 44.81%, respectively, $p<0.0001$). It was revealed that in the first 6 months in patients with surgical treatments bedridden were 10 (8.0%) men and 78 - a group with conservative treatment (66.67%) ($p<0.0001$).
Restriction of physical activity within the room was observed in 86 (68.8%) patients with surgery, and in 30 (25.64%) patients - with conservative treatment ($p<0.0001$). Aids used after surgical treatment of 105 (84.0%) patients after conservative - 34 (29.0%) ($p<0.0001$). Social impact showed that after 6 months of observation revealed a low proportion of patients with complete recovery of function after a surgery, or after conservative treatment (8.0% and 5.13%, respectively; p=0.5). After 24 months from the time of the fracture using surgical methods bedridden stayed only 1 (0.4%) and 16 patients (13.68%) - with conservative methods (χ^2 =18,3; $p<0.0001$). There was a significant decrease in the number of patients with limited motion activity within the room in the group with surgery and in the group with conservative (10.4% and 26.5%, respectively, p=0.002). When surgical treatment aids continued to use 38.4% (48 patients) under conservative treatment - 58.97% (69 people) (χ^2=10,24; p=0.002). Full restoration of function was observed in 72 (57.6%) and 32 (27.35%) patients who received surgical and conservative treatment, respectively (χ^2 =4,62; $p<0.0001$).
Conclusions: the obtained during this study data suggest that the immediate and long-term consequences in patients with a fracture of the proximal femur depends on the method of treatment. Surgical treatment is the method of choice for the treatment of patients with this type of fracture.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5716

AB0842 SARCOPENIA AND OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Aminov. *Medical Radiology, Tashknet Institute for Postgraduate Medical Education, Tashkent, Uzbekistan*

Background: Musculoskeletal disorders in RA are characterized by lesions of the peripheral joints, the development of local and systemic osteoporosis (OP), as well as a decrease in muscle mass and strength, which are currently being considered within the framework associated with chronic diseases syndrome sarcopenia and cachexia.
Objectives: To determine the prevalence and the relationship between sarcopenia and OP in patients with RA.
Methods: 156 RA patients were examined, of whom 83 postmenopausal women (mean age-61.7 years) and 73 males (mean age, 59 years). The control group consisted of 35 healthy subjects matched for age and sex. Exclusion criteria were: other rheumatic and endocrine diseases, severe somatic diseases, cancers, etc. The states of bone mineral density (BMD) at the lumbar spine (L1-L4) and femoral bone were assessed by dual-energy X-ray absorptiometry (DXA).
Results: Most RA patients (83% women and 63% men) were observed to decrease in BMD of osteopenia/OP level. BMD were negatively correlated with radiographic stage of RA, the DAS 28 and HAQ. IPC also revealed significant correlations with laboratory parameters such as creatinine, total protein, albumin, rheumatoid factor, and 1,25 (OH) D. Investigation of body composition showed a statistically significant reduction ITM RA patients compared to the control group, with no differences between the groups for fat mass. Sarcopenia had 25% of women and 55% men with RA, whereas the control groups, 8.7% and 0%, respectively. The majority of patients of both sexes sarcopenia observed on the background of the normal range of body fat index. Status of TM in patients with RA was statistically significant ($p<0,05$) associated with femoral BMD and lumbar spine (r=0,3), BMI (r=0,5), force brush compression (r=0,4) RA radiographic stage (r= -0,4), indicators of total protein (r=0,5).
Conclusions: Patients with RA, together with OP/osteopenia have a significant reduction in muscle (lean) mass. Sarcopenia in patients with RA was observed in the majority of men (55%) and 25% of women, significantly more than the control groups. Implementation of the DRA with the program “whole body” will allow time to identify not only bone, but also muscle loss in RA patients, which will help to intensify targeted therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3165

AB0843 RELATIONSHIP BETWEEN THE HISTOLOGICAL CLASSIFICATION OF MARSH AND THE AFFECTATION OF THE BONE METABOLISM IN PATIENTS WITH A RECENT DIAGNOSIS OF CELIAC DISEASE

L. López[1], M. Larrea[2], A. Erra[1]. *[1]Rheumatology; [2]Gastroenterology, Hospital San Rafael, Barcelona, Spain*

Background: Celiac disease is a chronic autoimmune pathology that affects people with genetic predisposition, caused by a permanent intolerance to gluten. Its prevalence has been estimated at around 1% but about 30% of patients are diagnosed after age 60.Its diagnosis is made through clinical data, serological markers, study of duodenal biopsy (BD) and response to the gluten-free diet. The histological study (Marsh classification) remains the gold standard to the diagnosis and allows classification of the disease in 4 types: grade I (less histological lesion) to grade IV (total duodenal mucosal atrophy).In these patients the deficiency of 25-OH vitamin D (vit D) is very frequent and is one of the causes of osteomalacia associated with malabsorption.
Objectives: To evaluate if there is a relation between the histological classification of Marsh and the bone metabolism in patients with a recent diagnosis of celiac disease.
Methods: Prospective study, which included all patients with a recent diagnosis of celiac disease by the Digestive Service during the period 2014–2016. This diagnosis was made through a clinical, serological (anti-transglutaminase IgA, anti-endomysium IgA), histological BD and genetic study (HLA DQ2 and HLA DQ8).
All patients underwent a study of phospho-calcium metabolism including: calcemia, phosphataemia, vit D, PTH, alkaline phosphatases, 24-hour calciuria and a densitometric study (BMD). We present the inclusion data of these patients

Results: 15 patients were included: 11 women and 4 men, with a mean age of 42.2 years (SD+/-16)
The genetic study was performed in 12 patients: 75% were positive for HLA DQ2 and 25% for HLA DQ8.
The determination of antibodies was positive in 12 patients (73%) and negative in 3 (27%). These 3 were positive for the genetic study (2 HLA DQ2 and 1 HLA DQ8).
The study of BD showed: type I in 4 patients; Type IIIa in 2 patients; Type IIIb in 6 patients; Type IIIC in 3 patients.
BMD showed normal values in 33%, osteopenia in 47% and osteoporosis (OP) in 20% of patients. Thus, 67% had an alteration in BMD at the time of diagnosis.
100% had a Vit D deficit, with a mean value of 14.3 ng/mL (range 4.15–26.8). 75% of them had values below 20 ng/mL (40% less than 10 ng/mL).
40% had secondary hyperparathyroidism (SHP), 83% of which had an alteration in BMD (67% osteopenia and 16% OP). The BD of the patients with SHP and alteration of the BMD showed a histological pattern type Marsh III.
No patient presented an alteration in the values of calcemia, phosphataemia or calciuria.
The relationship between the degree of alteration in BMD and the Marsh classification (table) was studied.
72% of patients with a Marsh III had an alteration in BMD (3 OP and 5 osteopenia vs 3 normal).

DMO	Marsh I	Marsh IIIa	Marsh IIIB	Marsh IIIc	Total
Osteoporosi	0	0	2	1	3
Osteopenia	2	2	1	2	7
Normal	2	0	3	0	5
Total	4	2	6	3	15

Conclusions: Most patients with celiac disease have an alteration in BMD.
In our study, all patients with celiac disease had a Vit D deficiency with no alteration of calcemia or calciuria.
Only in patients with SHP, there is a correlation between alterations in BMD and a higher degree of Marsh.
Most patients with a histological Marsh III have abnormalities in BMD.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3114

AB0844 FALLS: RISK AND PREVENTION IN PRIVATE RHEUMATOLOGY PRACTICE

L. Poulain[1], V. Strotz[2], X. Grapton[3], P. Lemesle[4] on behalf of Groupe CREER. *[1]Private Rheumatology Practice, la Garenne-Colombes; [2]Private Rheumatology Practice, Antony; [3]Private Rheumatology Practice, Colombes; [4]Private Rheumatology Practice, Bois-Colombes, France*

Background: Menopaused and osteoporotic women have a higher risk of fractures when falling. Fall prevention is important when taking care of those women.
Objectives: After identifying fall risk factors, defining the % of fractured fallers and the part of osteoporotic women in this population, we want to evaluate the relevance of balance tests and to favor prevention measures for those patients.
Methods: 110 patients, 60 years and older (including 24 controls), having falled within a year, have seen 28 private practice rheumatologists in the larger Paris area and were subject of our multicentre retrospective study.
Results: Fallers mean age was 75 years.
37% of the fallers within a year fractured after falling. Among them, 95% were post-menopausal fractures versus 64% when including the control group.
Post-fall or post menopausal fracture sites are identical. In order: spine 26%, wrist 18%, ribs 6%.
The circumstances of the falls are: 1) lack of attention 2) slipping 3) stumbling.
61% of the fallers have at least one physical activity, among them 71% a weight-bearing physical activity. The most common physical activity was walking (46%).
Among the fractured, 32% had physical activity, 42% hadn't.
72% of the fallers had at least one fall risk factor: 94% had intrinsic risk factors, 28% extrinsic, and an average of 2 risk factors within the older than 80 years.
Intrinsic factors: 1) osteo-articular 2) eye-vision 3) postural 4) drugs, out of 13 items.
Extrinsic: 1) obstacles 2) footwear out of 7 items.
45% of the fallers within a year had at least one osteoporosis risk factor: 1) low body mass index
2) cortico-steroids 3) early menopausis 4) smoking, out of 9 items.
70% of our patients had vitamin D level>30 ng/l (as recommanded)
69% of the patients had recent bone density measures: bone density was lower only at femoral neck of fractured fallers versus non fractured fallers.
The unipodal balance test (positive when standing less than 5 seconds) was relevant in 42% of the patients with or without fractures. Get up and go test was not relevant in our study population.
94% of the rheumatologists participating in the study recommend at least 2 fall prevention measures: 1) correct vitamin D levels 2) physical activity 3) reeducation 4) eye vision correction, out of 12 items.
Conclusions: A significant part of menopaused women with anteriority of falls and fractures will refracture after falling again. Beside treating osteoporosis, we should identify potential fallers by doing unipodal tests, consider and correct fall risk factors, encourage those patients to keep on physical activity and prescribe reeducation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1540

AB0845 TECHNETIUM-99 CONJUGATED WITH METHYLENE DIPHOSPHONATE AMELIORATES GLUCOCORTICOID INDUCED OSTEOPOROSIS IN RATS

L. Shi[1], Y. Ning[2], J. Li[1], F. Hu[2], X. Zhang[2]. *[1]Peking University International Hospital; [2]Peking University People's Hospital, Beijing, China*

Background: ^{99}Tc-MDP has been used in Chinese RA patients for over 15 years and many more studies have focused on this agent in RA. However, the previous studies limited in its effect on the effects of anti-inflammation. As a special form of bisphosphonate, the anti-osteoporotic effect of ^{99}Tc-MDP is unclear.
Objectives: To systematically investigate the effect of technetium-99 conjugated with methylene diphosphonate (^{99}Tc-MDP), an anti-inflammatory drug effective in treating rheumatoid arthritis (RA), on cortical and cancellous bones in glucocorticoid-induced osteoporotic (GIO) rats, as well as comparing the effect of ^{99}Tc-MDP with that of methylene diphosphonate (MDP).
Methods: Forty-eight Sprague-Dawley rats were randomly divided into six groups: blank, negative control, high dose, medium dose, low dose, and positive control groups. After dexamethasone was given to all groups except the blank group to induce osteoporosis, the rats in different groups were treated with saline, MDP, or different doses of
Results: Micro-CT analyses showed that: (1) ^{99}Tc-MDP reversed glucocorticoid induced bone microarchitecture destruction by increasing vBMD, BV/TV, Tb.Th, Tb.N and decreasing BS/BV, Tb.Sp and TBPf; (2) effect of ^{99}Tc-MDP increased as its dosage increased; and (3) ^{99}Tc-MDP could improve cortical bone thickness while MDP failed to do so. Micro-CT spatial structure analysis and histology also yielded consistent results, indicating ^{99}Tc-MDP increased trabecular number and connectivity morphologically. Finally, biomechanics revealed ^{99}Tc-MDP can enhance the extrinsic stiffness of bone by changing bone geometry.
Conclusions: ^{99}Tc-MDP has anti-osteoporotic effect by improving both cancellous and cortical bone, as well as increasing extrinsic bone stiffness. The dual effect of ^{99}Tc-MDP, anti-inflammatory and anti-osteoporotic, may suggest a potential clinical application for patients with both GIO and RA.
References:
[1] Hoes JN, Jacobs JW, Buttgereit F, et al. Current view of glucocorticoid co-therapy with DMARDs in rheumatoid arthritis. Nature reviews Rheumatology 2010;6:693–702.
[2] Bijlsma JW. Disease control with glucocorticoid therapy in rheumatoid arthritis. Rheumatology 2012;51 Suppl 4:iv9–13.
Acknowledgements: We thank Mr. Kai Gao for providing the rats and Dr. Min Feng for assistance in histological processing of the rats. This work was supported by grants from the Natural Science Foundation of China (81501396 to Dr. Lianjie Shi, and 81302554 to Dr. Fanlei Hu).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6240

AB0846 OSTEOPOROSIS AND ATHEROSCLEROSIS - ALTERNATIVE OR COEXISTENCE

L. Lagvilava. *Rheumatology, Clinic " Consilium Medulla", Tiblisi, Georgia*

Background: The majority of scientific research data promote the idea that OP and Atherosclerosis are inter-connected via OPG system. Scientists have speculation that OPG is the molecular bond between artery hardening and bone resorbtion. Thus the mechanism explained above makes obvious the co-existence of two: Artery hardening and Osteoporosis.
Objectives: There are number of ongoing Clinical trials on Denosumab therapy in patients with diagnosis of Osteoporosis and Atherosclerosis. The increase of Bone mineral density is associated with less intensive hardening of arteries. This fact inspired us to study bone mass in patients with cardiovascular events and atherosclerosis.
Methods: 1675 men, age range 38–78 years, mean age 59±4.3 Disease duration 6,4±1,75 with the diagnosis of Atherosclerosis (revealed on coronarography, assessed lipid profile).At the moment of research Stabile Angina Pectoris (Stable Angina) found in 20% (335); unstable angina non S-T elevation in 48% (804); -Myocardial Infarction 32% (536) Bone Mass was assessed by DXA Absorbtiometry technique (Hologic 1000) using T and Z Scores (WHO 1994). As a control group 680 healthy Georgian men 40–70 age range were assessed.
Results: Men having atherosclerosis are rather predisposed to Osteoporosis than health individuals.In Atherosclerosis subgroup normal bone mass was measured in 23% (385.25 patients) of patients; Osteopenia was diagnosed in 19% (315.25 patients), Osteoporosis was detected in 58% (971.5%) according to T-Score SD BMD records are shown in table 1.
Conclusions: 1.According to our research more than 50% of men with verified Atherosclerosis are diagnosed to have Osteoporosis 2.The lowest BMD values were observed in Lumbar Spine L1-L4, indicating that trabecular bone is more

Table 1

	Stable Angina n=335	Unstable angina nont S-T n=804	Myocardial Infarction n=536	Healthy N=680
L2- L4	-2.6±11 *	-2.9±1.4 **	-3.1±1.1 **	-0.6±0.2
Prox. Femur Neck	-1.8±0.5*	-2.6±1.4**	-2.5±1.6**	-1.14±0.26
Prox. Femur Total	-2.7±1.48**	-2.7±0.2**	-2.7±1.25**	-1.05±0.5

*p<0.01 **p<0.001.

deteriorated than cortical 3.Correlation between T Score values and clinical forms of Atherosclerosis were not observed 4. The best understanding of interrelations of mechanisms could point out the right direction for the simultaneous therapy against both targets – Osteoporosis and Atherosclerosis 5. Therefore the expectation of establishing novelty direction among other subtypes of the Medical Specialties as a Preventive Gerontology can be realistic

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1110

AB0847 ACCURATE ASSESSMENT OF FEMORAL ECHOSOUND APPROACH PERFORMANCE THROUGH DXA ERROR ANALYSIS

M. Muratore[1], F. Conversano[2], P. Pisani[2], M. Peccarisi[3], A. Greco[3], T. De Marco[3], E. Quarta[1], L. Quarta[1], A. Grimaldi[1], S. Casciaro[2]. *[1]OU of Rheumatology Galateo Hospital, San Cesario di Lecce, ASL-LE; [2]National Research Council, Institute of Clinical Physiology; [3]Echolight Spa, LECCE, Italy*

Background: Currently, the accepted "gold standard" method for bone mineral density (BMD) measurement and osteoporosis diagnosis related to the reference axial anatomical sites is dual-energy X-ray absorptiometry (DXA). However, actual DXA effectiveness is limited by several factors, including intrinsic accuracy uncertainties and specific errors in patient positioning, image segmentation, and post-acquisition data analysis, as documented by very recent literature [1]. This may affect the comparative evaluation of the effectiveness of novel diagnostic methods whose validation studies adopt DXA outcomes as standard reference to assess diagnostic performance.

Objectives: To assess the impact of DXA errors on the performance of an innovative ultrasound parameter for osteoporosis diagnosis on the femoral site, known as Osteoporosis Score (OS).

Methods: 202 patients aged in 46–75 years underwent two diagnostic investigations on the femoral neck: a conventional femoral DXA and an echographic scan performed by employing the innovative EchoSound technology [2]. Initially, the performance of the OS parameter was evaluated considering all the available DXA reports as reference in the data analysis, and calculating the corresponding accuracy in patient classification (osteoporotic, osteopenic, or healthy) and the correlation coefficient between the DXA-measured BMDs and the OS-derived BMD values. At a later stage, the DXA errors were taken into account by performing a strict quality control on DXA reports: all those cases affected by a typical inaccuracy [1] were excluded from the analysis and the actual diagnostic accuracy of the EchoSound technology was re-assessed by analysing only the reliable DXA reports. Intra- and inter-operator repeatability of OS-derived BMD values were also measured in a group of patients.

Results: A diagnostic accuracy of 84.4% (r =0.78, p<0.001) was obtained for the EchoSound approach when all the DXA reports were included in the analysis. In the second part of the study, 61 out of the initial 202 (30.4%) patients were excluded from the analysis because their DXA reports were affected by specific errors. An actual diagnostic accuracy of 94.2% was then obtained on the remaining 141 patients, together with a high correlation between DXA-measured BMDs and OS-derived BMD values (r =0.88, p<0.001). Intra- and inter-operator repeatability of OS-derived BMD values, expressed in terms of the root mean square coefficient of variation (RMS-CV), resulted equal to 0.29% and 0.34% for intra- and inter-operator variability, respectively, therefore documenting a very good measurement repeatability.

Conclusions: Undetected DXA errors had an impact on the accuracy evaluation of EchoSound femoral neck densitometry, causing an underestimation of OS performance in osteoporosis diagnosis. The quality control analysis on DXA reports can be useful to study the actual performance of different ultrasonic methods that considered routine DXA reports as the gold standard reference.

References:

[1] Eur Radiol 2015;25:1504.
[2] UMB 2015;41:281.

Acknowledgements: Work partially funded by FESR PO Apulia Region 2007–13 – Action 1.2.4 (grant n. 3Q5AX31: ECHOLIGHT Project).

Disclosure of Interest: M. Muratore: None declared, F. Conversano Shareholder of: Echolight spa, a National Research Council spin-off that may or may not benefit from results of this study, P. Pisani: None declared, M. Peccarisi Employee of: Echolight Spa, A. Greco Employee of: Echolight Spa, T. De Marco Employee of: Echolight Spa, E. Quarta: None declared, L. Quarta: None declared, A. Grimaldi: None declared, S. Casciaro Shareholder of: Echolight spa, a National Research Council spin-off that may or may not benefit from results of this study

DOI: 10.1136/annrheumdis-2017-eular.4843

AB0848 DENTAL PANORAMIC RADIOGRAPHY AS A TOOL FOR IDENTIFICATION OF OSTEOPOROSIS: AMONG TUNISIAN WOMEN

M. Brahem[1], M. Jguirim[1], M. Khemiss[2], I. Chaabani[2], E. Chebil[3], M. Younes[4], T. Ben Alaya[2], M. Ben Khelifa[2], I. Bejia[1], M. Touzi[1], S. Zrour[1], N. Bergaoui[1]. *[1]Rheumatology; [2]Stomatology, Fattouma Bourguiba Hospital Monastir, Monastir; [3]Maxilla-Facial; [4]Rheumatology, Taher Sfar Mahdia, mahdia, Tunisia*

Background: Osteoporosis is defined as a skeletal disorder characterized by low-bone mass predisposing to an increased risk of fracture. At present, the evaluation of bone mineral density (BMD) is the main diagnostic tool in osteoporosis, and it is the most effective and accurate measurement for identifying and monitoring the disease. However, several studies have been conducted with the object of detecting whether these skeletal changes in the mandible are specific to the osteoporotic stage.

Objectives: The purpose of this study was to determine whether the madibular indices on panoramic radiographs are useful for identifying women with osteoporosis or osteopenia (low BMD).

Methods: Tunisian women aged from 30 to 60 years,who consulted the Rheumatology department of Fattouma Bourguiba university hospital in2017.The measure the BMD using the dual-energy X-ray absorptiometry (DEXA), were recruited to participate in this case-control study.Among the 60 women selected, 30 were diagnosed with osteoporosis or osteopenia (T-score <-1; cases) and 30 with normal T-score (T-score >-1; controls). The mandibular cortical index (MCI), the mental index (MI), the panoramic mandibular index (PMI) and the alveolar crest resorption degree (M/M ratio)were measured from digital panoramic radiographs in the right and left mandibles and the mean was calculated for each subject.The MI, PMI and M/M ratio values were evaluated using the Z test, and MCI values were analysed using the Chi^2 test.

Results: The mean age of patients with osteoporosis/osteopenia was 58.61±8.11and 56.07±9.72 in the control group.The mean bone miniral density (BMD)in vertebral site was 0.856±0.090g/cm^2 and 1.216±0.185g/cm^2 in control group.In femoral site,it was 0.877±0.221g/cm^2 and 1.061±0.142g/cm^2 respectively.The mean T-score in vertebral site was -2.38±0.81DS in osteoporosis/ osteopenia group and 0.64±1.58DS in control group.In femoral site,it was -1.57±0.97DS and 0.21±1.16 respectively.

The analysis of the panoramic radiography showed that in the osteoporosis/osteopenia group: the mean value of MI was 3.56±0.89, the mean PMI was 0.25±0.06 and the mean M/Mratio was 0.71±0.14; concerning the MCI: 46.7% were classified C2 stage and 53.3% were classified C3 stage.

In the control group, the mean MI was 4.42±0.98, the mean PMI was 0.30±0.07 and the mean M/Mratio was 0.77±0.11; 30.1% were classified C1 stage, 53.3% were classified C2 stage and only 16.6% were classified C1 stage.

This study showed that the MI and the PMI were significantly smaller in the group with osteoporosis/osteopenia. However, the M/M ratio was not significantly different.Therefore, the MCI was significantly more affected in the osteoporosis/osteopenia group.

Conclusions: In our study, we proved that the MI, PMI and MCI values were affected in women with osteoporosis/osteopenia, compared with normal patients. Therefore, these indices could be used as an ancillary method in the diagnosis of osteoporosis in women.

References:

[1] C S Valerio et al, Dentomaxillofacial Radiology (2013) 42, 20120059.
[2] André Ferreira Leite, et al, Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:648–656.
[3] Vlasiadis Z. Konstantinos, et al, Maturitas 58 (2007) 226–235.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3558

AB0849 ASSOCIATION BETWEEN PERIODONTITIS AND OSTEOPOROSIS

M. Brahem[1], M. Jguirim[1], M. Khemis[2], E. Chebil[3], D. Chaabouni[2], M. Younes[4], T. Ben Alaya[2], M. Ben Khelifa[2], I. Bejia[1], M. Touzi[1], S. Zrour[1], N. Bergaoui[1]. *[1]Rheumatology; [2]Stomatology; [3]E.N.T. Head Neck Surgery, Fattouma Bourguiba Hospital Monastir, Monastir; [4]Rheumatology, Taher Sfar Mahdia, mahdia, Tunisia*

Background: Both periodontitis and osteoporosis have similar sign of bone resorption in nature and have multifactorial etiologic factors, although the mediator factors or mechanism may be different. How to prevent and treat these two bone-loss diseases is always an important issue in public health. However, the relationship of them is still uncertain.

Objectives: The aim of our study is to evaluate the relationship between periodentitis and osteoporosis.

Methods: Tunisian women aged from 30 to 60 years, who consulted the Rheumatology department of Fattouma Bourguiba university hospital between Febrary to December 2017. The measure the bone mineral density (BMD) using the dual-energy X-ray absorptiometry (DEXA), were recruited to participate in this case-control study. Among the 60 women selected, 30 were diagnosed with osteoporosis or osteopenia (T-score< -1; cases) and 30 with normal T-score (T-score> -1; controls). The oral examination was done by a dentist in the stomatology department in the same hospital.

Results: The mean age of patients with osteoporosis/osteopenia was 58.61±8.11

[51–81 and 56.07±9.72 [40–76] in the control group.the mean bone miniral density (BMD)in vertebral site was 0.856±0.090g/cm^2 and 1.216±0.185g/cm^2 in control group. In femoral site, it was 0.877±0.221g/cm^2 and 1.061±0.142g/cm^2 respectively. The mean T-score in vertebral site was -2.387±0.814 DS in osteoporosis/ osteopenia group and 0.643±1.587 DS in control group. In femoral site, it was -1.577±0.970 DS and 0.213±1.162 respectively.The oral examination showed an excessive tooth mobility in 60% and 36.7% of controls without a significant difference, a gingival recession in 50% and 30% of controls, the presence of periodontal pockets in 23.3% and 16.7% of controls without a significant difference, a plaque index $\geq$2 in 53,3% of osteoporosis/osteopenia patients and 63,3% of controls and a non rectilinear trajectory of mouth opening in 13,3% and 3,3% of controls.

Conclusions: Our study showed that patients with osteoporosis or osteopenia have a poor oral hygiene, but without significant difference with control group.However, patients who were diagnosed as osteoporosis must pay more attention to their periodontal health. Good oral hygiene maintenance might be a crucial factor for preventing the deterioration of osteoporosis progressing.

References:

[1] Yi-Fang Huang et al, The Impact of Oral Hygiene Maintenance on the Association Between Periodontitis and Osteoporosis; Medicine; Volume 95, Number 6, February 2016.

[2] Reddy MS. Osteoporosis and periodontitis: discussion, conclusions, and recommendations. Ann Periodontol. 2001;6:214–217.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5184

AB0850 HELICOBACTER PYLORI INFECTION AND OSTEOPOROSIS IN POST MONOPAUSAL WOMEN

N. Abdolahi, M. Aghaei, M. Naghdi. *Golestan Rheumatology Research Center, Golestan University of Medical Sciences, Gorgan, Iran, Islamic Republic Of*

Background: Osteoprosis is a health problem that if is left untreated,can lead to serious health & economical complications.It is also very common in postmenopausal women. Mineral deficiency, smoking, low BMI, some certain diseases and some medications can also cause osteoprosis. H.Pylori infection can also increase levels of inflammatory cytokines and bone turn over regulatory cytokines,as a result, it is likely that H. pylori infected patients are at increased risk for osteoprosis.

Objectives: the present study was done to understanding the association between H.Pylori seropositivity and osteoprosis in postmenopausal women.

Methods: The study population consisted of 34 osteoporotic patients and 73 healthy controls. Serum levels of h.pylori antibody (IgA,IgG) were measured by ELISA method.

Results: There was no difference in levels of IgA and IgG h.pylori antibody between patients and healthy controls

IgA seropositivity was 70.6% in osteoporotic women and 54.8% in healty women (p value: 0.1). Also H. pylori IgG seropositivity was 82% in osteoporotic women and 75.3% in healthy women (p value: 0.4). We didnot find any correlation between H. pylori seropositivity and bone mineral density in post menopausal women.

Conclusions: In this study, we found that Helicobacter pylori infection does not increase the osteoporotic chance and is not a reliable risk factor for osteoporosis. greater sampele size, gastric biopsy to detect atrophic gastritis, bone turn over factors and Cag detection is recommended in order to achieve more accurate results

References:

[1] Shih-Chun Lin, Malcolm Koo, and Kun-Wei Tsai. Association between Helicobacter pylori Infection and Risk of Osteoporosis in Elderly Taiwanese Women with Upper Gastrointestinal Diseases: A Retrospective Patient Record Review, Gastroenterology Research and Practice, 2014;2014:814756.

[2] Kakehasi A.M, Mendes C.M.C, Coelho L.G.V, et al "The presence of Helicobacter pylori in postmenopausal women is not a factor to the decrease of bone mineral density," Arquivos de Gastroenterologia, vol. 44, no. 3, pp. 2007,266–270.

[3] Figura N, Gennari.L, Merlotti et al., "Prevalence of Helicobacter pylori infection in male patients with osteoporosis and controls," Digestive Diseases and Sciences, vol. 50, no. 5, pp. 2005, 847–852.

[4] Asaoka D, Nagahara A, Hojo M, Sasaki H, Shimada Y, Yoshizawa T, Osada T, Watanabe S. The Relationship between H. pylori Infection and Osteoporosis in Japan. Gastroenterol Res Pract. 2014;2014:340765.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6445

AB0851 ZOLEDRONATE AUDIT – ARE WE MEETING EUROPEAN GUIDELINES?

N. Begum[1], A. Khan[1], A. Nandagudi[2]. *[1]Rheumatology/General Medicine; [2]Rheumatology, Basildon & Thurrock NHS Foundation Trust, Basildon, United Kingdom*

Background: Zoledronate is recommended by European guidelines for the treatment of osteoporosis particularly where first-line oral drugs are ineffective or contraindicated. EULAR's guidelines are complimented by UK organisations including the National Institute of Health and Care Excellence (NICE), National Osteoporosis Guidelines Group (NOGG), British Society of Rheumatology (BSR) and the National Osteoporosis Society (NOS).

Objectives: The aim of our audit was to ascertain whether our use of zoledronate was compliant with current guidelines and review the real life experience.

Methods: We performed a retrospective audit of fifty patients who were commenced on zoledronate for the treatment of osteoporosis during 2012–2016 in our Trust. Data gathered included the reasons for commencement, whether patients had appropriate monitoring and the effect it had on DEXA and FRAX scores.

Results: The age ranged from 44–88 years; 67% were between 60–80 years with 80% females. Vertebral fragility fractures were the most common type of fracture (42%). Zoledronate was commenced primarily because of either intolerance or inefficacy to oral anti-osteoporotic treatment (Table 1). It was commenced as first line in 20% because of contraindications to oral drugs. Almost 70% of our patients received zoledronate for two or three years. There was an improvement by 43% and 38% in the DEXA t-score for the spine and hip respectively. Stable t-scores were recorded for the spine and hip in 49% and 54% respectively, whereas 8% deteriorated. Three patients sustained a fragility fracture and a further 11 experienced side effects (Table 2); five patients consequently stopped treatment. Only 3% had recorded FRAX scores pre- or post-zoledronate treatment. All of our patients had their calcium and renal function measured before each zoledronate infusion whilst over 80% had their vitamin D checked. All of our patients had dental checks prior to treatment. Following post-treatment DEXA scans 46% continued zoledronate and 16% were on a drug-free holiday. A third were switched to denosumab due to ineffectiveness, side effects or contraindications.

Table 1. Rationale for Zoledronate Commencement

Rationale	Number	%
Intolerance	24	38%
GI Contraindication	11	17%
Inefficacy	24	38%
Other Contraindication	4	7%

Table 2. Side Effects of Zoledronate

Side Effect	Number	%
Bony Pain	1	9%
Flu-Like Symptoms	5	46%
Aches	1	9%
Acid-Reflux	1	9%
Rash	1	9%
Other	2	18%

Conclusions: The majority of our patients had improvements or stability in bone mineral density T-scores with only 20% experiencing side effects. Our results show that the vast majority of our patients are treated with zoledronate in concordance with guidelines. Nonetheless we can make improvements in recording FRAX scores and monitoring vitamin D levels. This has been highlighted to the multidisciplinary osteoporosis team and changes have been instigated. We plan to re-audit in due course.

References:

[1] Kanis JA, McCloskey EV, Johansson H, Cooper C, Rizzoli R, Reginster JY. European guidance for the diagnosis and management of osteoporosis in postmenopausal women J. ESCEO & IOF. Osteoporos Int. 2013; 24: 23–57.

[2] Osteoporosis: Clinical guideline for prevention and treatment. NOGG. 2013.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5015

AB0852 INCREASED INFECTION RATE WITH CONCOMITANT RANK LIGAND INHIBITOR DENOSUMAB AND BIOLOGIC THERAPIES FOR RHEUMATIC DISEASES: REALITY OR ILLUSION? EXPERIENCE WITH 40 PATIENTS OVER 66 MONTHS AT THE UNIVERSITY OF SOUTHERN CALIFORNIA

P.S. Chhibar, G. Ehresmann. *Rheumatology, University of Southern California, Los Angeles, United States*

Background: Patients with autoimmune diseases are at increased risk of early onset osteoporosis due to multiple reasons including prolonged exposure to corticosteroids and the disease process itself in RA patients. Same patients are more likely to be on TNF inhibitors or other biologics, which causes them to be at an increased risk of infections. Denosumab, an anti-RANK ligand inhibitor, itself a biologic, used to treat osteoporosis, is associated with increased infection risk as Receptor activator of nuclear factor kappa B ligand (RANKL) is also expressed on activated T and B lymphocytes (1). It is unknown if there is an added risk of infections when TNF inhibitors/biologic agents and denosumab are used concomitantly.

Objectives: To determine if denosumab and biologics are associated with increased infection risk.

Methods: Data was collected and analyzed on 40 patients in the rheumatology clinic who had been on denosumab and TNF inhibitor/ other biologic for 66 months at the Keck Medical Center of USC.

Results: Patient characteristics: Mean age: 70±9.8 SD years, Gender: 98% were females, 2% Males. 75% had RA, 10% SLE, 15% had other rheumatic diseases. 70% on TNF inhibitors, 30% on other biologics. Before Denosumab (over 2 years): cumulative infection rate 17.5%, which is 8.75 cases per 100 person-years. 9% hospitalization rate. Post Denosumab: After 12 months: No infections within the first year. After 60 months: incidence rate of infections=12.5 cases/100 person-years. After 66 months, incidence rate of infections=15.9 cases/100 person-years. Urinary tract infection (UTI) accounted for the most common infection (17.5%). No opportunistic infections, and no reactivation of latent TB found in our patients.
Conclusions: No infections developed within the first year, suggesting a cumulative effect of increased infection risk, if any. We cannot attribute the overall infection rate solely to the combination of denosumab and biologics as patients who developed infections either had Diabetes Mellitus, urinary incontinence, recent surgery, underlying pulmonary disease. Patients did not develop infections beyond what would be expected for their comorbidities and medications. Whether prophylactic antibiotics are indicated in patients with recurrent infections PRIOR to denosumab is uncertain, but may be a consideration in certain patients.
References:
[1] Cummings SR, San Martin J, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. N Engl J Med. 2009;361:756–765. doi: 10.1056/NEJMoa0809493.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1140

AB0853 DENOSUMAB: CLINICAL PERSPECTIVE AND DRUG SURVIVAL IN A SECONDAY CARE SET UP IN UK

R. Laxminarayan, U. Dissanayake, N. Sayed, K. Narangoda. *Rheumatology, Queen's Hospital, Burton on Trent, United Kingdom*

Background: Denosumab has become a useful parental therapy for the treatment of osteoporosis. FREEDOM extension study has shown safety and effectiveness of denosumab beyond 8 years. Real life data on the efficacy and safety of denosumab is lacking. There are no studies looking at the drug survival in the osteoporosis population either. Observational data from clinical practice can provide unique clinical perspective for novel therapies like denosumab.
Objectives: 1. To look at the baseline characters of patients receiving denosumab in a secondary care unit in UK.
2. To study the drug survival rate, analyse the reasons for discontinuation of therapy.
3. To assess fractures during the course of denosumab therapy.
Methods: We looked at the case records retrospectively of all the patients receiving denosumab therapy from 01/01/2011 to 31/12/2016. A database to record baseline characters, indications and previous fracture was prepared. Renal function, calcium, alkaline phosphatase (ALP), vitamin D levels at baseline and renal function, calium and ALP levels for each injection visit were noted. Vitamin D status was assessed at least once a year. Reasons to stop therapy were recorded.
Results: 237 patients were offered the treatment. One patient declined the treatment at the beginning.
5 (2.1%) patients had fracture on treatment. 2 had a hip fracture and one of them had a previous fracture (humerus). Other fracture sites were ankle, humerus and metatarsal. None of them had any further fractures during the follow up period.
61 patients discontinued therapy during the course of treatment over 3 years. 8 (4.2%) had infections, 7 (3.6%) due to declining eGFR and 9 (4.7%) were lost to follow up. 1 patient had jaw necrosis after the first injection. 1 developed hepatitis after the first injection which resolved on withdrawal of therapy. 6 (3.1%) patients withdrew consent for therapy. 19 (8%) patients died causes unrelated to denosumab therapy. 23 (9.7%) patients moved away. Treatment was stopped due to other side effects in 3 patients (2 had rash and 1 headache). There were no episodes of hypocalcaemia.
Conclusions: 1. Majority patients were elderly and female. Majority were high risk and had received osteoporosis treatments previously.
2. Denosumab therapy was well tolerated and nearly 2/3rd were stll receiving therapy at 3 years. Treatment was withdrawn due to an adverse event in only 14 (6%) patients.
3. Fracture rate was very low and there were no repeat or multiple fractures.
References:
[1] Pappapoulos S et al. The effect of 8 or 5 years of denosumab treatment in postmenopausal women with osteoporosis: results from the FREEDOM Extension study. Osteoporosis Int. 2015 Dec;26(12):2773–83.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5290

Abstract AB0853 – Table 1. Baseline characters

Total no of patients	Gender F (%)/M (%)	Age (in years) Mean (range)		eGFR Mean (range)		Prior fracture (%)		Baseline bone density (data for 99 patients)	
236	210 (89%)/ 26 (11%)	76 (45–95)		37.9 (17.7–90)		93 (39.4%)			
		>75	142 (60%)	<30	7 (3%)	Vertebral	37 (39.8%)	Osteoporosis	61 (61.6%)
		65–74	65 (27.4%)	30–59.9	88 (37.2%)	Wrist	12 (13%)	Osteopenia	30 (30.3%)
		55–64	22 (8.8%)	>60	141 (59.3%)	Hip	8 (8.6%)	Normal	8 (8.1%)
		<55	9 (3.8%)			Multiple	4 (4.3%)		

AB0854 THE BMD CHANGE AFTER IBANDRONATE (BONVIVA®) TREATMENT IN OSTEOPENIC POSTMENOPAUSAL WOMEN

S.E. Park, K. Choi. *Orthopaedic Surgery, Dongguk University International Hospital, Seoul, Korea, Republic Of*

Background: Ibandronate (Bonviva®) is effective in the treatment of postmenopausal women with osteoporosis. But, there were few datas about Ibandronate (Bonviva®) treatment in Korea. We evaluated the effect of Ibandronate (Bonviva®) therapy on bone mass and compared the effectivity on bone mineral density (BMD) in 1-year treatment group
Objectives: The aim of the study is to assess the effect of 1-year treatment with Ibandronate (Bonviva®) on bone mineral density (BMD) in postmenopausal women with osteopenia or osteoporosis.
Methods: The BMD was assessed in 118 postmenopausal women with osteopenia or osteoporosis from March 2007 to January 2011, 42 patents who treated with 2.5 mg per day of Ibandronate (Bonviva®) were enrolled to study. BMD of lumbar spine (L2-L4) and femur was assessed by dual energy absortiometry at baseline, 12 months after treatment.
Results: The annual BMD of the lumbar spine showed a 9.11% increase, while also positive changes were noted in the proximal femur as a 1.89% increase. The BMD changes were 11% (L: Lumbar spine) and 1.1% (F: Femur) for the T-scores <-4.0, 6.3% (L) and 0.9% (F) for the T-scores -3.0∼-4.0, and 3.8% (L) and 0.5% (F) for the T-scores >-3.0 respectively.
Conclusions: This study suggests that Ibandronate (Bonviva®) treatment in postmenopausal women with osteopenia or osteoposis is effective in terms of improving BMD.
References:
[1] Llewellyn-Jones D. Osteoporosis. In: Burger H, Boulet M editors. A portrait of the menopause: expert reports on medical and therapeutic strategies for the 1990s. Lancs: The Parthenon Publishing Group 83–103, 1991.
[2] Kanis JA, Melton LJ III, Chistiansen C, Johnston CC, KhaltaevN. The diagnosis of osteoporosis. J Bone Miner Res 9:1137–1141, 1994.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1036

AB0855 THE DISPARITIES BETWEEN FRACTURE RISK ASSESSMENT (FRAX) WITH BMD AND WITHOUT BMD IN KOREAN PATIENTS WITH ANKYLOSING SPONDYLITIS- MULTICENTER TRIAL

S.-R. Kwon[1], S.T. Choi[2], C.-H. Suh[3], H.-A. Kim[3], J.-Y. Jung[3], S.-S. Kim[4], S.-H. Kim[5], J.-M. Kim[5], S.-Y. Lee[1]. *[1]Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Inha University, INCHEON; [2]Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Chung-Ang University, Seoul; [3]Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Ajou University, Suwon; [4]Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Ulsan University, Gangneung Asan Hospital, Gangneung; [5]Division of Rheumatology/Dept. of Internal Medicine, College of Medicine, Keimyung University, Daegu, Korea, Republic Of*

Objectives: The aims of this study are to determine the proportion of patients with ankylosing spondylitis (AS) at high risk for major osteoporotic and hip fractures of Fracture risk assessment (FRAX) in Korean and to determine if a care gap exists for high risk.
Methods: This study is a multicenter study including 163 AS patients in 5. All of the AS patients fulfilled the modified New York criteria. The classification of osteoporosis according to WHO criteria was based on T-score ≤ -2.5. The FRAX criteria for high risk of osteoporotic fracture, which is 10-year probability of ≥20% for major osteoporotic fracture or ≥3% for hip fracture, were calculated by the FRAX tool including the bone mineral density (BMD) values. We assessed various demographic factors, clinical and laboratory findings of AS, and medication use for AS and osteoporosis, and then evaluated the risk factors for osteoporotic fracture.
Results: The mean age of AS patients was 44.3 years, and 42 patients were female (25.2%) with 23 postmenopausal women 56.1%. Osteoporotic fracture was detected in 16 (9.8%) patients with AS. Among the 16 patients ≥65 years of age, 2 (12.5%) and 8 (50%) were at high risk for a major osteoporotic fracture (10-year probability >20%) and hip fracture (>3%), respectively.
Among patients with BMD measurements (n=106), the 10-year risk of a major osteoporotic fracture and hip fracture calculated with BMD was significantly higher than in those without BMD measurements (P=0.001, P=0.002) respectively. The 10-year risk of a major osteoporotic and hip fracture fracture calculated with BMD was significantly higher than in those without BMD measurements (P<0.001, P=0.003) respectively among male patients with BMD measurements (n=74). There is no statistic difference of the 10-year risk of a major osteoporotic fracture

and hip fracture between those calculated with BMD and those without BMD measurements (P>0.05) respectively among female patients (n=32).
Conclusions: A substantial gap exists between FRAX with BMD and without BMD in Korean patients with AS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5575

AB0856 T-SCORE OF THE SPINE AS PREDICTOR OF THE FEMORAL NECK FRACTURE

S.D. Jandric. *Department for FRM, Faculty of Medicine, University of Banjaluka, Banja Luka, Republic of Srpska, Bosnia and Herzegovina*

Background: Osteoporosis is defined as a progressive, systemic skeletal disorder characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture. There are numerous hip fracture risks. Bone mineral density (BMD) and T-score measured by dual-energy X-ray absorptiometry (DXA) are the main determinants of the clinical evaluation of hip fracture risk. World Health Organization classification defined osteoporosis as T-score below –2.5 SD.
Objectives: The aim of this study was to estimate differences in DXA measurements (BMD and T-score of the spine) and potential predictors of the femoral neck fracture in the patients with osteoporosis.
Methods: This study included 181 patients with osteoporosis (165 female and 16 male), average age of the 65, 6±8.5 years (range of 44.1 to 87.3 years). Eighty one patients had fracture of the femoral neck. All patients in this group were managed operatively by hip arthroplasty, after clinical and radiological diagnostic procedures. DXA measurement was performed on Advanced Prodigy Lunar device for these patients postoperatively. BMD of the femoral neck was measured on the no operated side. Age, sex, height, weight, BMI, BMD and T-score of the spine at the level of L1-L4, BMD of the right and left femoral neck were estimated. The control group included 100 patients with osteoporosis (93 female and 7 male), average age of the 65.1±8, 5 years. Student's t-test and Logistic regression were used for statistical analysis. Dependent variable was presence of the fracture of the femoral neck and independent variables were age, sex, height, weight, BMI, BMD and T-score of the spine and BMD of the femoral neck.
Results: Results of our study showed statistically significant difference between T-score of the spine (t=-2,973, p<0.01) as well as between BMD of the spine (t=-12,376, p<0.001) of patients with and without fracture of the femoral neck. T-score of the spine was significant predictor of fracture of the femoral neck (p<0, 01) when controlled by age, sex, height, weight, BMI, BMD of the spine, BMD of the femoral neck.
Conclusions: T-score and BMD of the spine were statistically significantly lower in patients with fracture of the femoral neck than in patients with osteoporosis without fracture. T-score of the lumbar spine was significant predictor of fracture of the femoral neck in patients with osteoporosis. Probability of femur neck fractures increased with the decrease of T-score of lumbar spine in patients with osteoporosis. These results can help in predicting femur neck fractures.
References:
[1] British National Formulary. September 2005; 385–9.
[2] Vid KS JA, Thien A, Hill R. Ann R. Implementation of and compliance with NICE guidelines in the secondary prevention of osteoporotic fractures in postmenopausal women. Coll Surg Engl 2008; 90: 213–5.
[3] Del Rio LM, et al. Is bone microarchitecture status of the lumbar spine assessed by TBS related to femoral neck fracture? A Spanish case-control study. Osteoporos Int. 2013; 24(3):991–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2768

AB0857 PROBLEMS OF DIAGNOSTICS AND PROPHYLAXIS OF GLUCOCORTICOID-INDUCED OSTEOPOROSIS IN REAL CLINICAL PRACTICE

S. Yakupova, R. Demidov. *Kazan State Medical University, Kazan, Russian Federation*

Background: Oral glucocorticoids (GC) are used in different medicine fields and appear as risk factors of glucocorticoid-induced osteoporosis (GIO).
Objectives: The aim is to estimate the frequency of use of prophylaxis of OP, use drugs that are approved for GIO and also an awareness of GIO of patients with prolonged intake of GC.
Methods: 50 patients (10 men and 40 women), taking GC, took part in research. 30 patients (60%) were from rheumatology department, 5 patients (10%) from pulmonology department, 5 patients (10%) from gastroenterology department, 10 patients (20%) from nephrology department of Republic Clinical Hospital. Mean age of patients - 48,84±14,03 years (from 26 to 73). The following signs were estimated: clinical data, osteoporosis risk factors, instrumental tests (X-ray, densitometry). FRAX assessment of fracture risk was performed, the questionnaires of patients' awareness of GIO was completed.
Results: The duration of intake GC – 5,93±4,86 years. Minimal dose of GC per day (if receiving prednisone) – 7.5 mg; maximal dose – 60 mg. 10-year risk of major osteoporotic fractures by FRAX, adjusted according to GC dose - 18,11±11,01. 32 patients (64%) were given recommendations for changing lifestyle and diet for GIO prophylaxis, 40 patients (80%) - recommendations for intake of calcium and vitamin D medications, but only 31 patients (62%) followed recommendations and started the intake of calcium medications. From the said number of patients only 14 patients (45,2%) used appropriate daily dose of calcium and vitamin D.
Drugs that are approved for GIO were have to be prescribed for 18 patients, but only 6 patients (33,3%) underwent treatment, principally bisphosphonates. Only half of them underwent densitometry after starting the therapy. 72,2% patients with GIO used calcium and 30,7% were taking appropriate daily dose of calcium and vitamin D. 70% rheumatologic patients knew about GIO and in 90% cases calcium and vitamin D drugs were recommended. Only 50% of patients from non-rheumatologic departments knew about GIO and in 65% cases calcium and vitamin D drugs were recommended.
Conclusions: Clinical recommendations in real clinical practice are rarely fulfilled. Less than 60% patients were taking calcium and vitamin D, which are recommended for all patients, who started the GC therapy; only 33% of patients received osteoporosis therapy, only half of them underwent densitometry. Patients are insufficiently informed about necessity of changing lifestyle and diet for GIO prophylaxis. Education for patients taking GC and training for rheumatologic and non-rheumatologic specialties are necessary.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6867

AB0858 ASSOCIATION OF BONE MINERAL DENSITY WITH DEVELOPMENT OF HEART FAILURE IN DIABETIC PATIENTS

V. Vasilkova[1], T. Mokhort[2], E. Naumenko[3], M. Zmailik[4]. *[1]Endocrinology, Gomel State Medical University, Gomel; [2]Endocrinology, Belarusian State Medical University, Minsk; [3]Functional Diagnostics; [4]Endocrinology, The Republican Research Center for Radiation Medicine and Human Ecology, Gomel, Belarus*

Background: Diabetes mellitus has shown to be a significant risk factor for the development and prognosis of heart failure (HF) and associated with an increased risk of fractures [1]. Osteoporosis and heart failure are generally considered two distinct diseases, but recent evidence suggests a link between both diseases.
Objectives: The aim of the study was to investigate the association of bone mineral density with the risk of developing heart failure in diabetic patients.
Methods: 85 patients both sexes with type 2 diabetes aged 58.69±9.07 years were studied. Besides standard laboratory parameters, the echocardiographic and BMD measurements were performed. Estimated glomerular filtration rate was measured.
Results: Among diabetic subjects, 8 patients (9.4%) had osteoporosis, 21 (24.8%) had osteopenia and 56 (65.8%) had a normal BMD. Increased serum NT-proBNP (p<0.001) and decreased left ventricular ejection fraction (EF) (p=0.03) were significantly correlated with low T-score L1-L4 cutoff points between groups (normal, osteopenia, and osteoporosis). Multivariate stepwise linear regression analysis of the significant variables revealed that NT-proBNP, EF were independent predictors of lumbar BMD among female patients with diabetes mellitus. After adjusting for age, gender, and related comorbidities, the osteoporosis group was associated with a significantly higher risk of coronary artery disease in women with diabetes. However, no association between BMD and HF was found in men.
Conclusions: Osteoporosis may be an independent factor for HF in women with diabetes mellitus. Our data suggested that early detection of abnormal BMD should warrant for early search of undetected HF in diabetic women. A further study is needed to elucidate the effects of BMD on cardiac function in diabetic patients.
References:
[1] Heart failure is a risk factor for orthopedic fracture: a population-based analysis of 16,294 patients. van Diepen S, Majumdar SR, Bakal JA, McAlister FA, Ezekowitz JA Circulation. 2008 Nov 4; 118(19):1946–52.
Acknowledgements: We acknowledged the help from the Republican Research Center for Radiation Medicine and Human Ecology for the technical assistance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3867

AB0859 CAN ZOLENDRONIC ACID USE LEAD TO IMPAIR RENAL FUNCTION IN OSTEOPOROSIS PATIENTS?

Y.-C. Chen, C.-H. Ko. *Rheumatology, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, Province of China*

Background: Bisphosphonates are recommended in patients with osteoporosis patients. clinical concerns had been considered in kidney safety.
Objectives: This study investigated the safety of bisphosphonate effects on renal function in patients with magnetic resonance imaging (MRI)-proven acute osteoporotic vertebral fractures after vertebroplasty.
Methods: This retrospective study was conducted in osteoporotic patients with acute vertebral fractures treated with vertebroplasty between January 2001 and December 2015. Their gender, age, body mass index (BMI, kg/m^2), co-morbidities were recorded, as well as their use of zolendronic acid. Those with increase in creatinine was defined as progress of renal function. Logistical regression was used to adjust the variables.
Results: There were 989 patients (783 females; mean age, 74.08±9.26 years).

71patients accepted zolendronic acid, the others accept other anti-osteoporotic agents. 35 (49.3%) of zolendronic acid had increased creatinine, while 379 (41.3%) of non-zolendronic acid had creatinine changes (p=0.117). After adjust variables, zolendronic acid did not increase creatinine (*p*=0.291; OR: 0.750; 95% CI: 0.440–1.279).(Table 1)

Table 1. Risk of increase in renal function in zolendronic acid after adjust variables

	Regression coefficient	S.E.	Wald	P value	OR	95% C.I.for OR	
						Lower	Upper
Zoledronic acid	-0.288	0.273	1.116	0.291	0.750	0.440	1.279
Smoking	0.250	0.343	0.533	0.465	1.284	0.656	2.513
Alcohol	0.025	0.065	0.147	0.702	1.025	0.903	1.164
BMI	0.007	0.017	0.160	0.689	1.007	0.974	1.040
DM	-0.165	0.164	1.022	0.312	0.848	0.615	1.168
HTN	-0.418	0.149	7.856	0.005	0.658	0.491	0.882

Conclusions: Zolendronic acid use did not lead to increase in creatinine as compared with the control group. However it need more cases to confirm this findings.

References:

[1] Miller PD Bone. 2011 Jul;49(1):77–81.

Acknowledgements: We thanks Chang Gang Memorial Hospital for data support.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3087

AB0860 THE PREDICTORS FOR 24 MONTHS EFFICACY OF DENOSUMAB, AN ANTI-RANKL ANTIBODY, ON OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM MULTICENTER STUDY (TBCR-BONE)

Y. Hirano [1], Y. Kanayama [2], N. Takahashi [3], N. Ishiguro [3], T. Kojima [3].
[1] Rheumatology, Toyohashi Municipal Hospital, Toyohashi; [2] Orthopaedic Surgery and Rheumatology, Toyota Kosei Hospital, Toyota; [3] Orthopaedic Surgery and Rheumatology, Nagoya University Graduate School of Medicine, Nagoya, Japan

Background: Although medication of rheumatoid arthritis (RA) has been improved by early intensive treatment using csDMARDs, tsDMARDs and bDMARDs for decades, treatment of concomitant disease in RA patients, such as osteoporosis (OP), will be more important to improve activity of daily living of RA patients. Although denosumab (DMB), an anti-RANKL antibody, was approved for treatment of OP in Japan in 2013, clinical data in real world is lacking in patients with RA. We reported 12 months efficacy of denosumab on osteoporosis in patients with RA at EULAR 2016 in London [1]. Here we report results for 24 months.

Objectives: To investigate the 24 months efficacy of denosumab (DMB) on osteoporosis in patients with rheumatoid arthritis (RA-OP) and to explore predictors of efficacy from multicenter study (TBCR-BONE).

Methods: 59 female cases with RA-OP treated with DMB for 24 months were included in this study. Bone mineral density (BMD) of lumbar spine (LS-BMD) and total hip (TH-BMD) and serum bone turnover markers (P1NP and TRACP-5b) were measured at baseline and every 6 month until 24 months. Spearman's rank correlation coefficient was calculated between %increase of BMD at 24 months and various data (baseline patients' characteristics, parameters of RA disease activity [DAS28-CRP, SDAI, CRP, MMP-3] and bone turnover markers (BTMs) [P1NP and TRACP-5b]). Time averaged data (ta-data) which was averaged data of every 6 month was utilized for analysis with respect to data of RA disease activity and BTMs besides baseline data.

Results: Mean age was 59 years old. Mean RA duration was 16 years. Rates of concomitant prednisolone use was 33.9%. Mean DAS28-CRP was 2.7. 44% of cases had the past history of fracture. Mean FRAX was 28%. Daly teriparatide was used in 11 cases before DMB treatment. %increase of LSBMD at every 6 month was significantly increased (4.7%>6.7%>7.7%>8.3%) and %increase of THBMD at every 6 month was significantly increased (2.9%>3.3%>4.9%>4.9%) (Fig1). %decrease of P1NP and TRACP-5b was 37.4%>33.8%>25.5%>26.0% and 33.3%>29.8%>26.1%>23.1%, respectively (Fig2). Fig3 showed that parameters (correlation coefficient) which were correlated with %increase of LSBMD at 24 months were %increase of LSBMD at 6 months (0.61), baseline P1NP (0.33) and time averaged %decrease of TRACP-5b (0.30). Parameters (correlation coefficient) which were correlated with %increase of THBMD at 24 months were %increase of LSBMD at 6 months (0.42), %increase of THBMD at 6 months (0.69), baseline P1NP (0.36), time averaged %decrease of P1NP (0.37), baseline TRACP-5b (0.29) and time averaged %decrease of TRACP-5b (0.29). Although %increase of BMD at 24 months was not correlated with disease activity of RA, taCRP was significantly correlated with taP1NP (0.57) and taTRACP-5b (0.45).

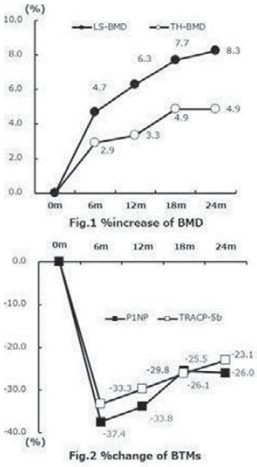
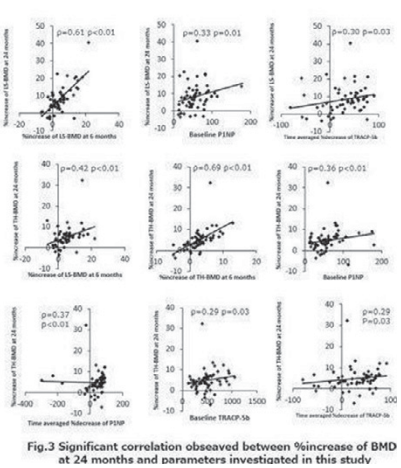


Fig.1 %increase of BMD

Fig.2 %change of BTMs


Fig.3 Significant correlation obseaved between %increase of BMD at 24 months and parameters investigated in this study

Conclusions: DMB was effective in RA-OP. Early response of BMD, baseline values of BTMs and response of BTMs were suggested to be the predictors of the efficacy of DMB in RA-OP. Inflamation of RA was correlated with not BMD but BTMs.

References:

[1] Hirano Y et al. The predictors for 12 months efficacy of denosumab, an anti-RANKL antibody, on osteoporosis in patients with rheumatoid arthritis from multicenter study (TBCR-BONE). Ann Rheum Dis2016; 75(Suppl2): 94.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3938

Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis

AB0861 EXPRESSION CONTROL BY METHYLATION OF THE TLR1, TLR2, TLR4, IL1B, ALPK1 SLC2A9 AND SLC22A12 GENES IN MONOCYTES OF PATIENTS WITH GOUT

N. Paniagua Díaz [1], E.G. Tranquilino Batres [1], A.P. López Flores [2], A. Lozano Cardenas [2], E. Vallarino Reyes [2], A.L. Alvarez Grijalva [2], L. Sanchez Chapul [1], C. Hernández Díaz [3], L. Ventura Ríos [3], A. Lopez Macay [1]. *[1] Enfermedades Neuromusculares, Instituto Nacional de Rehabilitacion; [2] Ciencias de la vida, Instituto de Estudios Superiores Monterrey; [3] LUMA, Instituto Nacional de Rehabilitacion, Mexico City, Mexico*

Background: The gout is an inflammatory multifactorial disorder where the diet, age, sex, absorption regulation of uric acid in kidney and genetic, contribute to the onset of the disease. The balance of uric acid concentration not only depends on metabolism of purines but also on the clearance of uric acid, in which many proteins participate in the reabsorption and transport of urate. Is unknown if the peripheral blood leukocyte cells can change their expression and regulation mechanism of the urate transporters by the presence of uric acid in gout patients [1–4].

Objectives: Analyze changes in gene expression and the methylation pattern of the TLR2, TLR4, SLC2A9, SLC22A12, SLC22A3 and ABCG2 in neutrophils and peripheral blood monocytes from patients with gout and controls

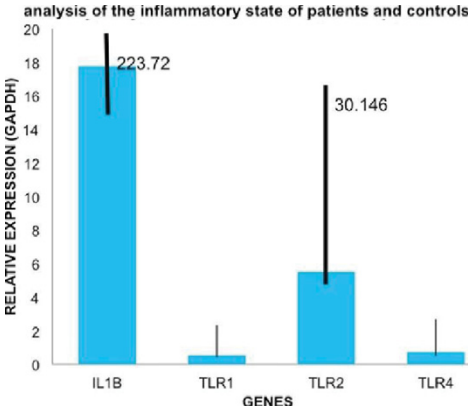
Methods: The isolation of peripheral blood neutrophils and monocytes cells was performed by negative immunomagnetic selection (MACxpress kit, EUA). By flow citometry were analyzed the previously separate cell populations, mononuclear (MN), polymorphonuclear (PMN) cells and neutrophils (N) (CD15, CD16, CD14). The DNA and RNA extraction was realized with a without columns kit and with Trizol technique. The gene expression analysis will be performed from total RNA by RT-PCR kit (Promega). Methylation analysis will be carried out the bisulfite conversion (ABCAM) from total DNA and HRM-PCR. For both studies, gene expression and methylation analysis are designed specific primers

Results: The biggest difference between asymptomatic gout patients (n=12) and controls (n=12), in the biochemical parameters (Table 1), is in the higher levels of uric acid and triglycerides that the patient presents. Actually, we've already evaluated the genetic expression of TLR1, TLR2, TLR4 and IL1b in mononuclear cells of 5 asymptomatic gout patients and 5 controls (Plot 1). Interestingly, IL1b is UP-regulated in sample group bye a mean factor of 16.350 and TLR2 is UP-regulated in sample group in comparison to control group by a mean factor of 3.686.

Table 1. Characteristics of patients and controls

	Patients	Controls
Participants (n)	12	12
Age (years)	40.75	29.75
BMI (kg/m^2)	29.27	24.05
SM n (%)	8.33	0
Hypertension, n (%)	58.33	0
Urate (mg/dL)	8.35	4.87
Glucose (mg/dL)	84.83	81.33
Cholesterol (mg/dL)	196.33	175.25
Tryglicerides (mg/dL)	276.67	109.42
Creatinine (mg/dL)	1.02	0.79

Conclusions: The asymptomatic patients with a higher mean of uric acid (8mg/dL) and tryglicerides (145.60 mg/dL) had a higher expression of IL1b and TLR2 compared to controls.



References:
[1] Neogi T., et al. Gout Classification. Criteria An American College of Rheumatology/European League Against Rheumatism. Arthritis & Rheumatology. 2015.
[2] Busso N., et al. Review Mechanisms of inflammation in gout. Arthritis Research & Therapy 2010.
[3] Mitroulis I., et al. Review, Neutrophils, IL-1β, and gout: is there a link. Semin Immunopathology. 2013.
[4] Partial HPRT. Deficiency with a Novel Mutation of the HPRT Gene in Combination with Four Previously Reported Variants Associated with Hyperuricemia. International Medicine. 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3594

AB0862 THE SENSITIVITY OF THE DOUBLE CONTOUR SIGN IN HAND JOINTS WOULD BE BETTER BY THE DORSAL SURFACE EXAMINATION

A.M. Mahdi [1,2], H. Rkain [1], M. Erraoui [1], R. Watfeh [3], S. Aktaou [3], L. Tahiri [1], R. Bahiri [1], F. Allali [1], N. Hajjaj-Hassouni [1]. *[1]Rheumatology, Faculty of Medicine and Pharmacy; [2]University Mohamed V, Rabat; [3]Faculty of Medicine and Pharmacy, Rabat, Morocco*

Objectives: To compare the prevalence of ultrasonographic gout specific sign double contour between the dorsal and palmar surfaces of the hand joints.
Methods: This is a cross-sectional study which includes 15 patients with chronic gout, defined according to the American College of Rheumatology criteria (ACR 1977). Ultrasound (US) examination was performed using a high-frequency linear probe (Toshiba Xario®, frequency (8–14 MHz)) in B and Doppler modes. 560 articular sites were studied at their dorsal and palmar surfaces. We compared the prevalence of the hyperechoic band over the superficial margin of the articular cartilage described as a double contour (DC) between the dorsal and palmar surfaces at each site studied.
Results: The mean age at onset was 54.7±12,6 years, and the median diagnosis duration was 0 (0.3) years).
The results of the US examination are summarized in Table 1

Table 1. comparison of double contour prevalence between the dorsal and palmar surfaces of wrist, MCP, PIP and DIP joints in the studied population

Joints (N=540)	Dorsal surface (%)	Palmar surface (%)	P
Wrist joints (N=120)	12,6	7,3	**<0.001**
Radiocarpal (N=30)	20	6,7	0,6
Ulnocarpal (N=30)	13,3	6,7	**0,01**
Scaphotrapezial (N=30)	3,3	13,3	0,8
Trapeziometacarpal (N=30)	13,3	3,3	0,1
MCP (N=150)	8	6,6	**<0.001**
MCP 1 (N=30)	3,3	10	0,1
MCP 2 (N=30)	13,3	6,7	**0,014**
MCP 3 (N=30)	6,7	6,7	**0,002**
MCP 4 (N=30)	6,7	0	**<0.001**
MCP 5 (N=30)	10	10	**<0.001**
PIP (N=150)	4	7,3	**<0.001**
IP (N=30)	3,3	10	0,1
PIP 2 (N=30)	6,7	3,3	0,9
PIP 3 (N=30)	6,7	13,3	**0,01**
PIP 4 (N=30)	3,3	10	0,1
PIP 5 (N=30)	0	0	**<0.001**
DIP (N=120)	0,8	3,3	**0,033**
DIP 2 (N=30)	0	0	**<0.001**
DIP 3 (N=30)	3,3	3,3	**0,002**
DIP 4 (N=30)	0	3,3	**<0.001**
DIP 5 (N=30)	0	6,7	**<0.001**

Conclusions: Our study suggests that globally, DC predilect significatily in dorsal than in palmar surfaces of hand joints. These results should be verified on a larger population.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3881

AB0863 THE POPLITEUS GROOVE IN THE LATERAL FEMORAL CONDYLE: A SHELTER FOR MONOSODIUM URATE CRYSTALS?

A. Di Matteo, E. Cipolletta, M. Ausili, E. Filippucci, W. Grassi. *Clinica Reumatologica, Università Politecnica delle Marche, Jesi (AN), Italy*

Background: Gout is a crystal related arthropathy characterized by deposition of monosodium urate (MSU) crystals at articular and periarticular structures. Ultrasound (US) has gained an important role in the diagnosis of gout due to its capability to clearly detect various expressions of MSU crystal depositions in joints, tendons and bursae [1]. The popliteus tendon inserts in a depression on the outer side of the lateral femoral condyle. It has a close connection to the lateral meniscus and is surrounded by the popliteal recess which is in direct communication with the knee joint cavity [2].
Objectives: To evaluate the prevalence of US findings indicative of MSU crystal deposition at the popliteus groove in patients with gout.
Methods: Consecutive patients with gout, diagnosed according to the 2015 ACR/EULAR criteria, and disease controls diagnosed according to the corresponding diagnostic/classification criteria were enrolled. All the patients underwent a bilateral US examination (carried out using a Logiq 9 US system working with a linear probe operating at 15 MHz) at the popliteus groove level. The US examination was performed with the patient lying supine on the examination bed. A knee flexion of approximately 45° was necessary to visualize the popliteus groove in the lateral aspect of the femoral condyle just deep to the proximal part of the lateral collateral ligament. The following US abnormalities indicative of MSU crystal depositions were evaluated: isolated shining dots, aggregates (heterogeneous hyperechoic foci that maintain their persistent high degree of reflectivity which occasionally may generate posterior acoustic shadow) and tophi (inhomogeneous hyperechoic/hypoechic material surrounded by a small anechoic rim which may generate posterior acoustic shadows).
Results: We enrolled 17 patients with gout and 22 disease controls: 9 calcium pyrophosphate deposition disease (CPPD), 8 rheumatoid arthritis and 5 psoriatic arthritis. A total 78 popliteus groove were examined by US. US findings indicative of MSU crystal deposition were detected in at least one knee in 13 out of 17 gout patients (76.5%) and in 7 out of 22 controls (31.8%). Table 1 shows the prevalence of the US abnormalities indicative of MSU crystal deposition in the two groups. Six out of the 10 US abnormalities (60%) found in controls were detected in CPPD patients.

Table 1

	Gout	Controls
Patients	17	22
Popliteus grooves assessed by US	34	44
Popliteus grooves "positive" for US findings indicative of MSU crystal deposits	23 out of 34 (67.6%)	10 of out 44 (22.7%)
Isolated shining dots	9 out of 23 (39.1%)	8 out of 10 (80%)
Aggregates	8 out of 23 (34.8%)	2 out of 10 (20%)
Tophi	6 out of 23 (26.1%)	0 (0%)

Conclusions: These preliminary results suggest that the popliteus groove could be regarded as a sentinel area for detecting MSU crystals. These findings should lead to further investigations aimed at identifying the factors and associated with MSU crystals deposition at popliteus groove level.

References:
[1] Neogi T, Jansen TLTA, Dalbeth N, et al. 2015 Gout Classification Criteria: An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative. Arthritis Rheumatol 2015;67:2557–68.
[2] Jadhav SP, More SR, Riascos RF, et al. Comprehensive review of the anatomy, function, and imaging of the popliteus and associated pathologic conditions. Radiographics. 2014 Mar-Apr;34(2):496–513.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4462

AB0864 SENSITIVITY AND SPECIFICITY OF SONOGRAPHIC DETECTION OF URATE CRYSTAL DEPOSITS IN HYALINE CARTILAGE IN PATIENTS WITH GOUT IN YEARLY STAGE

A. Petrov, V. Fursova, A. Petrov. *Medical Academy named after Georgievsky, Crimean Federal university named after V.I. Vernadsky, Simferopol, Russian Federation*

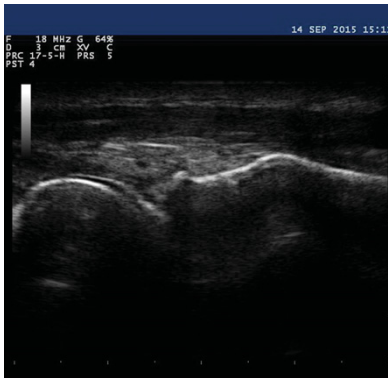
Background: In some cases differential diagnosis between yearly gouty arthritis and other types of arthritis is very difficult. In 2015 the sonographic detection of urate crystal deposits in hyaline cartilage as a new criterion was included in set of classification criteria of gout [1]. But diagnostic value of that ultrasound marker in first month of disease is underinvestigated.
Objectives: To investigate sensitivity and specificity of sonographic detection of gouty hyperechoic deposits in hyaline cartilage in patients with gout in comparison with other signs of gout in debut of arthritis.
Methods: The 104 patients with yearly arthritis (duration of symptoms less

than 6 month) was examined by clinical, laboratory, X-Ray and ultrasonography. After investigation the following diagnoses were made: Gout in 32 patients, Osteoarthritis in 28 patients, Rheumatoid arthritis in 28 patients, Psoriatic arthritis in 16 patients. Ultrasound investigation of affected joints was performed in all subjects by linear probe 18 MHz. Urate crystal deposits were seen on the surface of the hyaline cartilage as a hyperechoic thin line or dots on the cartilage, wich sometimes imitate double contour of bones [2, 3]. Sensitivity and specificity of ultrasound sign were compared with subcutaneous tophi, bone cysts (X-Ray sign) and hyperuricemia.

Results: The urate crystal deposits in gyalinic cartilage of at least one of affected joints were revealed in 28 of 32 (87,5%) patients with Gout, in 3 of 28 (10,7%) patients with Osteoarthritis and 1of 16 (6,3%) patients with Psoriatic arthritis. Comparative data of sensitivity and specificity of crystal deposits, bone cysts, subcutaneous tophi and hyperuricemia are represented in table below.

Table 1. Sensitivity and specificity of different diagnostic markers in yearly stage of gout

Diagnostic marker	Sensitivity, %	Specificity, %
Hyperechoic lineal urate deposits in gyalinic cartilage	87,5	94,4
Bone cysts	21,7	88,8
Subcutaneous tophi	25,0	98,6
Uric acid level from 360 mkmol/l up to 480 mkmol/l	46,9	86,1
Uric acid level more than 480 mkmol/l	34,4	97,2



Conclusions: Ultrasound detection of urate crystal deposits in hyaline cartilage in patients with gout in yearly stage has a high sensitivity and comparable level of specificity with other diagnostic markers of Gout.

References:

[1] Neogi T et al. Gout classification criteria: an American College of Rheumatology European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2015;74(10):1789–1798.
[2] Filippucci E., Di Geso L, Grassi W. Tips and tricks to recognize microcrystalline arthritis. Rheumatology 2012;51(7):18–21.
[3] Naredo E et al. Ultrasound-detected musculoskeletal urate crystal deposition: which joints and what findings should be assessed for diagnosing gout? Ann Rheum Dis. 2014;73(10):1522–1528.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1292

AB0865 SERUM URATE AND ITS ASSOCIATION WITH RACE IN YOUNG ADULTS: BASELINE ANALYSIS FROM A RANDOMIZED CLINICAL TRIAL

M.B. Saddekni[1,1], A.L. Gaffo[2], P.J. Foster[1], S.R. Biggers[2], E.J. Rahn[2], P. Li[3], K.G. Saag[1]. *[1]UAB School of Medicine, Division of Clinical Immunology and Rheumatology; [2]Department of Medicine, Division of Rheumatology and Immunology; [3]UAB School of Public Health, Department of Biostatistics, University of Alabama at Birmingham, Bimringham, United States*

Background: Increased levels of serum urate (sUA) have been reported in association with hypertension, chronic kidney disease and obesity. All these conditions are over-represented in US African Americans, who also have greater environmental risk factors for hyperuricemia development including elevated fructose intake. Our group has previously reported that young African Americans have lower sUA concentrations than Caucasians after adjustment for clinical and demographic factors.

Objectives: To determine whether there is a differential association between sUA and race in young adults.

Methods: We examined baseline data on consecutively enrolled individuals (age 18 – 40 years) in an interventional study aimed at lower blood pressure (BP) through the administration of urate-lowering therapy. African Americans were over-represented in the sample by study-design. Inclusion criteria included a sUA of $\geq$5.0 mg/dL for men or $\geq$4.0 mg/dL for women. After means comparisons between races, we performed multivariable adjustments for age, gender, BP, and body mass index (BMI) a multiple linear regression model. Data reported are mean ±standard deviation.

Results: 86 participants recruited from Birmingham, AL were included in the analysis. Participants had a mean age of 28.5±6.9 years, 36% were female, 41% were African Americans (AAs), and the mean BMI was 29.2±6.8 kg/m^2. The mean sUA was 5.9±1.2 mg/dL (n=77, range: 3.9 to 8.5 mg/dL). We found a significantly lower sUA for African Americans compared to persons of other races (5.4±1.2 mg/dL vs 6.2±1.1 mg/dL, p=0.005). After multivariable analysis the difference in sUA between AAs and other races was attenuated to non-significance (p=0.33) due to the effects of BMI and gender. As expected, the association between sUA and gender was significant (Table).

Table 1. Multivariable regression model on the association between serum urate and race among young adults (n=86)

Variable	Estimate (95% confidence interval)	p
Race (African-Americans versus other races)	-0.34 (-0.82 , 0.15)	0.18
Age (per year)	0.02 (-0.02, 0.05)	0.34
Gender (men versus female)	1.36 (0.87, 1.85)	$<$0.001
BMI (per unit of kg/m^2)	0.04 (0.00, 0.07)	0.035

BMI = Body-mass index.

Conclusions: In this cross-sectional analysis of young adults, AAs had lower sUA concentrations than other races. However, this difference is explained by the effect of gender differences in sUA and BMI. A potential limitation is that participants were enrolled after they met a sUA threshold so not all the ranges of sUA in a normal population are represented in this analysis. Larger studies will be needed to fully address this question.

References:

[1] Feig, D.I., JAMA, 2008. 300(8): p. 924–32.
[2] Fang, J. JAMA, 2000. 283(18): p. 2404–10.
[3] Gaffo, A.L. Arthritis Res Ther. 2012 Jan 6; 14(1):R4.

Acknowledgements: National Institute of Arthritis and Musculoskeletal and Skin Diseases P50AR060772, K24AR052361 (to KGS).

Disclosure of Interest: M. Saddekni: None declared, A. Gaffo Grant/research support from: Amgen, AstraZeneca, Consultant for: Cymabay, Ardea, Employee of: US Government, P. Foster: None declared, S. Biggers: None declared, E. Rahn: None declared, P. Li: None declared, K. Saag Grant/research support from: AstraZeneca, Crealta, Takeda, Consultant for: Ardea/AstraZeneca, Crealta, Takeda

DOI: 10.1136/annrheumdis-2017-eular.5390

AB0866 EVALUATION OF THE ACHIEVEMENT OF A THERAPEUTIC TARGET OF<6 MG/DL IN ALGERIAN PATIENTS TREATED FOR GOUT

B. Bengana[1], S. Slimani[2], K. Testas[3], F. Rahal[4], M. Makhloufi[5], A. Ladjouze[4], S. Lefkir-Tafiani[1]. *[1]Rheumatology, Derpartement of Rheumatology -University Medical Centre Beni Messous, ALGIERS; [2]Rheumatology, University of Batna, Batna; [3]Rheumatology, El kherroub Hospital, Constantine; [4]Rheumatology, Ben Aknoune Hospital, ALGIERS; [5]Medicine, University of Batna, Batna, Algeria*

Background: Gout is one of the most prevalent rheumatic conditions in the developing world, due of the aging of the population and the modifications in the life style. The 2014 EULAR recommendations for the management of gout have defined the therapeutic target of 60 mg/L for gouty patients (recommendation 8). The aim of the study was to assess the adherence of Algerian patients with gout to these recommendations.

Methods: We have retrospectively analyzed patients files aged 18 and more, followed in a rheumatology setting for gout, in 4 centers in Algeria. Demographic, clinical and lab data were collected. We have excluded files with missing data. Were noted the used therapeutics and serum uric acid in every patient through time. Tolerance was noted.

Results: We have analyzed 145 complete files: 98 men (68%), with a mean age of 65.4±11.4 years. All patients except two had rheumatic manifestations, 20 patients had renal insufficiency and 15 had tophi. Main comorbidities were hypertension (40 patients) and diabetes (25 patients). The mean serum uric acid level was 96±14 mg/L. Concerning symptomatic drugs, 81 patients have taken colchicine and 15 NSAIDs, the remaining patients have taken other drugs or combination therapy. All patients but one have received serum uric acid lowering therapy (allopurinol in majority of cases), with a median dosage of 200 mg/day, and only 5 patients taking more than 300mg/day. The mean serum uric acid level at 6 months was 58±14 mg/L, with 58% of patients achieving a level of $<$60 mg/L.

Conclusions: In rheumatology settings in Algeria, more than 93% of gouty patients received allopurinol, with an excellent tolerance. However, it seems that dosage is insufficient, with only 58% of patients achieving the EULAR recommendation 8. More efforts have to be provided to optimize this therapy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4031

AB0867 PEGLOTICASE RE-TREATMENT AFTER A GAP IN THERAPY: DATA FROM TWO PHASE III TRIALS AND AN OPEN-LABEL EXTENSION STUDY

H.S. Baraf[1], A. Morton[2], B. LaMoreaux[3], J. Kent[3]. [1]*Medicine, George Washington University, Washington DC;* [2]*Internal Medicine, Michigan State University School of Osteopathic Medicine, East Lansing;* [3]*Medical Affairs, Horizon Pharma, Lake Forest, United States*

Background: Pegloticase is a PEGylated recombinant uricase approved in the US for treating adult patients with chronic refractory gout. As a biologic medication, pegloticase is administered intravenously every 2 weeks. It is currently not known whether a gap in the standard biweekly regimen can be tolerated or would be associated with a loss of efficacy. During the pivotal trial testing of pegloticase, some patients experienced a delay between participation in the randomized controlled trial (RCT) and the open-label extension (OLE) that followed. Analysis of the clinical impact of this gap was carried out to understand whether therapeutic benefit would be affected.
Objectives: The objective of this analysis was to determine, among pegloticase responders, the effect of a 28 or more day gap between doses of pegloticase on the subsequent urate lowering response and frequency of infusion reactions.
Methods: These analyses utilized results from two RCTs of pegloticase and a 2-year OLE. In the RCTs, 36 of 85 patients, who were dosed with pegloticase every two weeks, were classified as responders (persistent urate lowering during intensive monitoring at 3 and 6 months of the RCT), and went on to enroll in the OLE and receive additional doses of pegloticase. Of these 36 patients, 14 had a gap between pegloticase doses of more than 28 days.
Results: Among the 14 patients with a gap of more than 28 days between doses of pegloticase therapy the length of the gap ranged from 34 to 167 days (mean =72.5 days, median =59.5 days). Of these 14 patients, 8 received pegloticase on an every-4-week dosing schedule in the OLE and 6 remained on every-2-week dosing. Ten of the 14 patients maintained their serum urate level <6mg/dL in the OLE. Five of 6 that remained on every 2 week dosing and 5 of 8 that went to every 4 week dosing continued to have serum urate <6mg/dL. (see table 1). By logistic regression analysis, the length of the gap had no significant effect on the subsequent urate lowering effect of pegloticase. Of the fourteen patients with a gap in pegloticase therapy, 2 (14%) had infusion reactions during a total of 632 infusions in the OLE yielding a re-treatment IR rate of 0.32%.

Table 1. Continued responder proportions and infusion reaction rates by OLE dosing group

Dosing Group	Total	Continued Responders	Percentage	Infusion Reaction Rate
Combined	14	10	71%	0.32
Every 2 weeks	6	5	83%	0.30
Every 4 weeks	8	5	62.5%	0.34

Conclusions: The majority of patients in this limited dataset who were previously responders to pegloticase dosed every 2 weeks continued to maintain a serum urate lowering response to pegloticase after a gap in therapy. Infusion reactions during re-treatment occurred in 2 patients with a re-treatment infusion reaction rate of 0.32%.
References:
[1] Sundy, J.S., Baraf, H.S.B., Yood, R.A., et al. Efficacy and tolerability of pegloticase for the treatment of chronic gout in patients refractory to conventional treatment, JAMA, 2011;306(7):711–720.
[2] Becker, M.A., Baraf, H.S.B., Yood, R.A., et al. Long-term safety of pegloticase in chronic gout refractory to conventional treatment, Ann Rheum Dis, 2013;72:1469–1474.
[3] Lipsky, P.E., Calabrese, L.H., Kavanaugh, A., et al. Pegloticase immunogenicity: the relationship between efficacy and antibody development in patients treated for refractory chronic gout, Arthritis Research & Therapy, 2014;16:R60.
Disclosure of Interest: H. Baraf Consultant for: Horizon Pharma, Takeda, Ironwood, A. Morton Consultant for: Pfizer, Sanofi Regeneron, Ironwood, Horizon, Speakers bureau: Prizer, Amgen, Abbvie, Janssen, Celgene, Horizon, Novartis, Ironwood, B. LaMoreaux Employee of: Horizon Pharma, J. Kent Employee of: Horizon Pharma
DOI: 10.1136/annrheumdis-2017-eular.5365

AB0868 IS IT APPROPRIATE TO DISCONTINUE COLCHICINE THERAPY IN GOUT PATIENTS IN REMISSION?

Y. Özdem İnan[1], N. Alpay Kanıtez[2], S. Çelik[2], S. Yılmaz Öner[2], C. Bes[2]. [1]*Bakırköy Dr Sadi Konuk Training and Research Hospital, Istanbul, Turkey;* [2]*Rheumatology, Bakırköy Dr Sadi Konuk Training and Research Hospital, Istanbul, Turkey*

Background: Colchicine can reduce the risk of recurrent attacks and it is an appropriate first-line gout attack prophylaxis therapy. There is limited data in the literature about duration of colchicine treatment in patients with gout disease.
Objectives: In this study, we aimed to investigate the frequency of gout attacks between patients with colchicine treatment and patients who are colchicine terminated.
Methods: 54 gout patients under colchicine treatment were enrolled to the study. The subjects were divided into 2 groups. Group 1 (n=19) was consisted of patients whom colchicine therapy was terminated because of remission for three months; group 2 (n=35) was consisted of patients on colchicine treatment. Groups were compared according to the existing of newly gout attacks after the 3rd month. Baseline and the third months of the uric acid levels were also analyzed in each group.
Results: The body mass indexes, the disease intervals, the number of the attacks, and the duration of the attacks were not significantly different ($p>0.05$ for all) (Table 1). Compared to the group 2, the newly gout attacks were not found to be different in group 1 for 3 months ($p>0.05$) (Table 1). The uric acid levels were significantly decreased both in two groups (both $p<0.05$) (Table 2).

Table 1. Demographical and clinical characteristics of patients

Patient variables	Group 1 (n=19)	Group 2 (n=35)	p
Gender, F/M	0/19	12/23	0.040
Age, years	53.36±14.06	62.11±12.72	0.024
BMI	28.22±3.57	30.29±5.63	0.153
Uric acid, mg/dL	7.40±1.30	8.21±1.92	0.108
Disease age, months	111.63±172.70	53.48±59.75	0.170
Number of the attacks, one year	2.68±2.35	3.37±3.75	0.413
Duration of the attacks, days	16.73±16.32	10.91±14.50	0.202
Newly attacks in 3 months	5/14	7/28	0.734

Table 2. Before and after treatment comparisons of the uric acid levels

Variables	Baseline	3rd month	p
Group1	7.40±1.30	6.47±1.19	0.008
Group 2	8.21±1.92	6.74±1.70	<0.001

Conclusions: The colchicine is the mainstay treatment for gout disease. It not only prevents the attacks of the gouts also prevents the development of uric acid nephropathy that exaggerates the kidney disease in gout patients. This study showed that, in gout patients in remission, termination of the colchicine treatment does not affect the development of the new attacks as shown similar attacks were also observed in non-terminated patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1423

AB0869 STRESS FRACTURES, A RETROSPECTIVE STUDY OF 325 FRACTURES IN 227 PATIENTS IN RHEUMATOLOGY PRACTICE BETWEEN 2000 AND 2015

C. Nourisson, J.-J. Dubost, B. Pereira, A. Tournadre, S. Malochet-Guinamand, M. Soubrier. *CHU Clermont Ferrand, Clermont-Ferrand, France*

Background: Stress fractures are common in both young and active patients (fatigue fracture) as well as in elderly osteoporotic patients (insufficiency fractures).
Objectives: The aim of this study was to describe characteristics of stress fractures treated in rheumatology at the Clermont-Ferrand University Hospital, to compare them according to their anatomic location (pelvis, lower limb or feet/ankle) and their diaphyseal or metaphyseal/epiphyseal location.
Results: Between 01/01/2000 and 12/31/2015, 325 fractures were identified in 227 patients divided in 176 women (including 116 postmenopausal women) and 51 men. Population averaged age was 65.2 years [15–99 years]. 142 (43.7%) fractures occurred at pelvis, 93 (28.6%) at lower limbs and 87 (26.8%) at feet and ankles. The fracture was spontaneous in 63.6% of cases. History of pain was recorded in 92.3% with more frequently (90.3%) mechanical pain. Diagnostic delay was on average 70 days.
In 51 patients (22.5%) an orthopedic factor could have promoted stress fracture. 54 patients (23.8%) had a history of chronic inflammatory rheumatism, 28 (12.3%) of cancer, and 20 (8.8%) had chronic renal failure.
Among the possible iatrogenic factors, 51 patients (23.4%) received oral corticosteroid therapy, 20 (9.2%) methotrexate, 59 (27%) proton pump inhibitor and 17 (7.8%) serotonin reuptake inhibitor. 49 patients (22.5%) already had vitamin-calcium supplementation, 37 (17%) received biphosphonate therapy. 56.6% were osteoporotic and 29.5% were osteopenic.
First-line medical imaging was in 87% conventional radiography, positive in 37%. 106 patients (46.7%) performed bone scan with a sensibility of 99%. MRI sensibility (n=65, 28.7%) was 88% and CT-scan sensibility (n=47, 20.7%) 65.2%. Compared to other sites, pelvic fractures were more frequent ($p<0.001$) and occurred more frequently in postmenopausal women ($p=0.03$). These patients were older ($p<0.001$) and had more fracture history ($p=0.006$). Hip bone mineral density ($p=0.03$) was lower, and osteoporosis prevalence higher ($p=0.004$).
Pelvic fractures occurred more frequently after fall ($p<0.001$), lower limb fractures spontaneously ($p=0.03$) and those of the feet-ankles group after an unusual activity ($p<0.001$). Patients from metaphyseal-epiphyseal fracture group were older ($p=0.05$) than those from the diaphyseal fractures group and delay in completing complementary examinations was longer ($p=0.04$).
Conclusions: In conclusion, pelvic stress fractures are more frequent in a rheumatology department and suggest insufficiency fracture. Stress fracture should be more often suspected when mechanical pain of the pelvis and lower limbs occurs, even spontaneously. Regardless of the site, an assessment of fracture risk factors and bone mineral density evaluation seems necessary.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6741

AB0870 METABOLIC AND CARDIOVASCULAR GOUT ARE THE MOST FREQUENT CLINICAL VARIANTS OF THE DEBUTING GOUT

E. Mikhnevich[1], T. Pavlovich[1], E. Mytnik[2]. [1]*Department of Internal Medicine, University of Medicine;* [2]*Diagnostic Center, Rheumatology Clinic, Minsk, Belarus*

Background: Gout is phenotypically and genotypically heterogeneous. In most cases, renal mechanism plays an important role in the development of gout. At the same time, gout, as a rule, occurs on the basis of pre-existing comorbid pathology.
Objectives: To determine clinic-pathogenetic variants of gout depending on a leading comorbid pathology at the gout onset.
Methods: We included 604 patients with confirmed gout from our Center database. During 2010–2016, comorbidities were registered before the gout onset, at its appearance, during and at the last examination. Metabolic syndrome (MS) was defined by 5 components. CVD included CHD, atrial fibrillation, CHF and stroke. Patients after organ transplantation and with terminal renal failure observed in specialized centers were not recruited.
Results: In 67,1% (n=405) of patients, the gout developed on the basis of pre-existing MS, thus, this variant may be called a metabolic gout (MG) and considered as a component of MS. The patients with MG were younger, the mean age of symptoms onset was 42 (35–48) years. At the first gout attack, all patients had BMI≥25 kg/m^2, 8,2% (n=33) had pre-existing HTN, and in 14,3% (n=58) of cases the diagnosis of HTN was firstly made. No one patient had diabetes mellitus (DM). Frequent regular or single abundant alcohol intake together with overeating as factors more often favoring gout attack were revealed in all patients. At the last examination, only 38,1% (n=230) of patients had MS without any CVD, the mean age was 50 (45–55) years; 98,7% (n=227) had BMI≥25 kg/m^2; 73,9% (n=170) presented with HTN; 59,1% (n=136) showed dyslipidemia; 6,5% (n=15) had DM. In 8,3% (n=19) of patients, changing the lifestyle and normalizing the weight resulted not only in decreased hyperuricemia but lower attacks rate or even their total disappearance during a 5 year follow-up. The second variant of gout onset developing in patients with pre-existing CVD, can be called a CV gout or cardiorenovascular (CRV) gout. This type of gout was revealed in 28,5% (n=172) of patients, the disease debuted later, at the age of 60 (55–64) years (p<0,001). 97,7% (n=163) had HTN (χ^2=30,1, p<0,001) and 27,3% (n=47) – DM (χ^2=32,65, p<0,001), both features were more common in CV gout. 85,5% (n=147) had BMI≥25 kg/m^2 (F=0,066, p<0,001). Regular alcohol intake was considerably lower – 33,7% (n=58) (χ^2=167,4, p<0,001), but medication use was higher – diuretics in 14,5% (n=25) (χ^2=21,77, p<0,001) and low-dose aspirin in 37,2% (n=64) of patients (F=0,24, p<0,001). At the last examination, the mean age of patients was 63 (59–69) years (p<0,001), chronic GFR <60 ml/min was observed in 47,7% (n=82) of patients (F=0,34, p<0,001).
The secondary gout developed in 4,4% (n=27) of patients with various diseases: myelo-, lymphoproliferative and other blood diseases - 6 cases, renal gout - 13, gut gout after partial gut resection - 2, and anorexic gout - 2. Alcoholic gout without MS was diagnosed in 4 patients, all men with body mass deficiency.
Conclusions: In our opinion, there are two main clinic-pathogenetic variants of debuting gout – metabolic and cardiovascular, the both with different conditions of occurrence, progression and prognosis. In clinical practice, it is reasonable to differentiate these variants, that is determined by the need to simplify complex multimodal diagnostic and therapeutic approach to the patients with gout.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3524

AB0871 NSAIDS AND LIVER FUNCTION IN PATIENTS WITH GOUTY ARTHRITIS

E. Mikhnevich[1], T. Rayeuneva[1], K. Leonchik[1], E. Mytnik[2]. [1]*University of Medicine;* [2]*Rheumatology Clinic, Diagnostic Center, Minsk, Belarus*

Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) have been associated with hepatotoxicity. Drug-induced liver injury (DILI) in patients under NSAIDs is more frequently presented by hepatocellular damage with elevated serum alanine aminotransferase (ALT) levels (1).
Objectives: To evaluate the hepatocellular toxicity due to NSAIDs on the basis of changes in serum ALT levels in patients with gouty arthritis (GA).
Methods: 376 patients with GA registered in our database were included in our retrospective study. Males made 92,8% (n=349). Mean age was 57 (50–62) years; mean duration of gout – 7 (3–10) years. NSAIDs were prescribed to the patients with gouty attack by generalists, and then all patients were addressed to the Rheumatology Clinics. Serum ALT levels were determined at the onset of gout attack and 3–10 days after starting NSAIDs therapy. All NSAIDs used were generics. The hepatotoxicity was considered when ALT level was 2 times (or more) upper limits of normal values (42 U/l for men and 35 U/l for women) according to DILI criteria. ALT level at baseline was within the normal limits in 80,8% (n=304) of cases, its elevation was identified in 19,2% (n=72).
Results: We divided the patients into 3 groups according to the type of changes in serum ALT levels after receiving NSAIDs:
Group 1: 69,4% (n=261) of patients with normal ALT 24 (17–30) U/l before and 24 (18–32) U/l after treatment (p>0,05).
Group 2: 11,4% (n=43) of patients with normal basal ALT 26 (21–35) U/l and its elevation to 77 (72–88) U/l (p<0,001) after NSAIDs therapy.
Group 3: 19,2% (n=72) of patients with elevated basal ALT 57 (46–91) U/l, who had different type of ALT response to NSAIDs therapy. We identified 3 subgroups within the third group:
Subgroup A: 7% (n=5) of patients with elevated ALT level at the beginning of gout attack – 92 (62–123,5) U/l and higher value after treatment – 151 (129–215) U/l (p<0,001). Subgroup B: 23,6% (n=17) of patients with elevated ALT before treatment – 53 (47,5–62) U/l and non-significant changes after therapy – 51 (44,5–63,5) U/l (p >0,05). Subgroup C: 69,4% (n=50) of patients with elevated ALT before treatment – 59 (49–89) U/l and reduced and/or normal ALT level after therapy – 42 (29–57) U/l (p<0,001). While the patients from subgroup A have demonstrated supplementary hepatotoxicity due to NSAIDs on the basis of pre-existing liver injury, the absence of changes in ALT levels in subgroup B has been suggested in favor of a chronic liver injury. Subgroup C has reflected the effect of NSAIDs to decrease and even normalize the elevated basal ALT value. This may be linked to a hepatic inflammation, which is likely associated with alcohol intake, but hyperuricemia could also be involved.
Conclusions: 69,4% (261 from 376) of patients with GA having normal basal ALT values did not demonstrate any changes in ALT level after NSAIDs treatment; in 11,4% of patients, hepatocellular NSAIDs–induced hepatotoxicity was revealed. In the group of patients with elevated basal ALT level, the response of ALT to NSAIDs treatment was as follows: no significant changes – 23,6%, elevated value – 7%, reduced or normalized value – 69,4%. The last subgroup (C) requires more detailed study.
References:
[1] Schmeltzer P. A., Kosinski A. S., Kleiner D. E. et al. Liver injury from nonsteroidal anti-inflammatory drugs in the United States. Liver International 2016;36(4): 603–609.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3542

AB0872 DIAGNOSTIC EFFICIENCY OF DETERMINING THE PURINE METABOLISM ENZYMES ACTIVITY IN THE DIFFERENTIATION OF GOUT

E. Mozgovaya, A. Trofimenko, S. Bedina, I. Zborovskaya. *Federal State Budgetary Institution " Research Institute of Clinical and Experimental Rheumatology", Volgograd, Russian Federation*

Background: Serum uric acid (UA) level is the most important risk factor for gout. At the same time many people with hyperuricemia do not suffer from gout, and UA level can return to normal during gout exacerbation.
Objectives: to improve the diagnostics of the gout.
Methods: 53 gout patients were the target group. The mixed control group was consisted of 150 rheumatoid arthritis patients, 95 osteoarthritis patients, 55 ankylosing spondylitis patients. The diseases were diagnosed in accordance with the international standards. Adenine deaminase, Adenosine deaminase (ADA), AMP-deaminase (AMPDA), Guanine deaminase, Guanosine deaminase, Guanosine phosphorylase, 5'-nucleotidase, Xanthin dehydrogenase (XDG), Xanthin Oxidase, Purine nucleoside phosphorylase activities were determined in blood serum with subsequent evaluation of sensitivity (Se), specificity (Sp), likelihood ratio of positive (LRP) and, likelihood ratio of negative (LRN) result, predictive value of positive and negative results.
Results: The AMFDA and ADA activities were defined as a screening marker to diagnose of the gout from a joint syndrome another genesis. Threshold AMPDA activity 1,67 IU was characterized with the predictive value of negative results (without taking into account the prevalence) near 100%, Se 98%, Sp 62,45%.
Cutoff value (CV) of ADA activity (9,57 IU) was characterized with LRN 0,104, Se 92,45%, Sp 72,65%, the sum (Se+Sp 165,10%), which was maximum not only for this test but for all the studied enzymes. The predictive value of negative results (without taking into account the prevalence) was 98,20%. The clinically significant CV of positive result for the ADA activity definition was identified also: LRP was 6,93 (Se 22,64%, Sp 96,73%) for the range of 12.58 IU and above. This fact allows the use of this test not only for the screening, but also, in some cases, for the verification of gout with significant pretest probability of this disease.
Two CV were selected for the XDG activity: 7,49 μM/l×min (Se 47,17%, Sp 97,14%) and 8,39 μM /l×min (Se 39,62%, Sp 99,59%). The result of XDG activity determining in the range of 7.49 - 8.39 μM /l×min is an important argument in favor of the gout presence, but this may be useful for differential diagnosis only at high pretest probability of the gout.
Conclusions: Determination of the ADA activity was gave way to AMPDA activity determination at the gout screening and to XDG activity determination at gout verification. However, the ADA multifunctionality, evidenced clinically significant presence of the second CV (positive results) and a small proportion of the cases, which covered a "grey area" between CV (27.48%), provided the ability to use this marker as a backup in the absence of diagnostically relevant AMPDA and XDG activities.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2304

AB0873 CHARACTERISTICS OF ADHERENCE, PERSISTENCE AND THERAPEUTIC ALLIANCE IN PATIENTS WITH GOUT

E. Alvarez-Hernandez[1], L.D. Upegui-Arango[2], J. Vazquez-Mellado[1], E. Aranda-Arreola[1], R. Burgos-Vargas[1], I. Pelaez-Ballestas[1]. *[1]Rheumatology, Hospital General de Mexico, Mexico DF, Mexico; [2]Rheumatology, 2.Universidad Industrial de Santander, Bucaramanga, Colombia*

Background: Adherence is the extent to which the patient takes their medications and follow the directions prescribed by their doctor. It has two components: compliance (the degree or extent of conformity to the recommendations about day-to-day treatment by the provider with respect to the timing, dosage, and frequency) and persistence (the duration of time from initiation to discontinuation of therapy). The therapeutic alliance is the patient physician relationship that allows the patient to participate actively in their treatment. The reported adherence varies from 43 to 78% in patients with chronic diseases. In gout, the adherence varies from 10 to 46%.
Objectives: To evaluate the characteristics of adhesion in patients with gout.
Methods: Patients with gout from the GRESGO cohort were included. Sociodemographic, clinical, and treatment data were collected and the HAQ-DI, EuroQol-5d and a specific questionnaire of adherence and therapeutic alliance were applied.
Results: The study included 238 patients (97.1% male), whit a mean age of 47.7±12.7 years, educational level 9.2±4.2 years. The adherence index (prescribed doses/doses taken) was 86%. Only 28.6% never stopped treatment. 4.6% took the doses at the correct time. Most frequent causes of suspension were lack of supply (37%) and forgetfulness (30%). Only 5% buy all of their medications, 10% follow the lifestyle changes. 49.6% do not take the medication when they disagree with their doctor.
Conclusions: Despite having a good adherence index there are discrepancies with the qualitative answers, since more than 70% did not have good persistence and more than 90% did not comply with the schedule.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6680

AB0874 CHARACTERISTICS OF GOUT IN CAMEROON, CENTRAL AFRICA: A HOSPITAL-BASED STUDY

M.S. Doualla, F. Kamdem, F. Kemta Lekpa. *Service de Médecine Interne, Douala General Hospital, Douala, Cameroon*

Background: Few data are available on the characteristics of gout in sub-Saharan Africa (1).
Objectives: We performed this study with the aim to present the clinical, laboratory and imaging characteristics of gout at the time of diagnosis in Cameroon.
The results obtained will be compared with data from the Western literature.
Methods: We performed a cross-sectional study among the 10,186 out patients seen at the Rheumatology unit of Douala General Hospital, Douala, Cameroon, between 2004 and 2014. We included patients with gout diagnosis (ACR criteria 1977). The main socio-demographic and clinical data on gout at the time of diagnosis were collected.
A $p<0.05$ was significant.
Results: We included 511 patients (5.02%) including 415 men and 96 women. The mean age was 55.9±10.8 years.
Joint pain (n=508, 99.4%), joint effusion (n=198, 38.7%) and fever (n=20, 3.9%) were the main reasons for consultation at diagnosis. Knees (n=300, 62.6), ankles (n=187, 39.0%) and MTP1 joints (n=128, 26.7%) were the most affected joints. Tophi were mainly located at the elbows (n=72, 66.0%), MTP1 (n=20, 18.3%), and ears (n=18, 16.5%) [Table 1].
Gout was as acute (n=255, 49.9%) as it was chronic (n=256, 50.1%). The clinical presentation was oligoarticular in 195 patients (38.7%), monoarticular in 172 patients (34.1%), and polyarticular in 137 patients (27.2%).
The mean uric acid level was 82.4±22.3 mg/L, with hyperuricemia found in 401 patients (78.4%). Elevated acute phase reactants was present in 81.9% of patients. Structural involvements related to gout were present in 181 (74.8%) of the 241 patients who had performed an X-ray.
Comorbidities were present in 344 patients (67.3%), hypertension (n=208, 40.7%), obesity (n=151, 29.5%), osteoarthritis (n=111, 21.7%), oesogastroduodenal complaints (n=74, 14.5%), diabetes (n=52, 10.2%), and chronic kidney diseases (n=42.8.2%).
Associated factors ($p<0.05$) in the occurrence of gout were obesity, alcohol intake, diuretics intake, and menopause (in women).
Conclusions: Gout has the same clinical, laboratory and imaging characteristics in Cameroon than in Western countries. The main difference comes from the place of the knee as the main joint involved by gouty arthritis at the time of diagnosis in our study.
References:
[1] Usenbo A, et al. PLoS One. 2015 Aug 4;10(8):e0133858.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6990

Table 1. Localization of gouty arthritis and tophi

Joint stiffness and/or tenderness		Tophi location	
	n (%)		n (%)
Knee	300 (62.6)	Elbow	72 (66.0)
Ankle	187 (39.0)	MTP1	20 (18.3)
MTP1	128 (26.7)	Ear	18 (16.5)
Wrist	93 (19.4)	Wrist	10 (9.2)
Elbow	81 (16.9)	PIP	9 (8.2)
PIP	56 (11.7)	Foot	9 (8.2)
MCP	53 (11.1)	IDP	8 (7.3)
Foot	50 (10.4)	Ankle	8 (7.3)
Shoulder	49 (10.2)	Knee	8 (7.3)
Others MTP	24 (5.0)	Others MTP	6 (5.5)
DIP	15 (3.1)	MCP	5 (4.6)
Others	30 (6.3)	Achille tendon	1 (0.9)
		Imprecises location	18 (16.5)

AB0875 DO WE CONTROL GOUT IN PRIMARY CARE FOLLOWING EULAR RECOMMENDATIONS?

F. Leon Vazquez[1], C. Sanz Rodrigo[2], C. Muñoz Martínez de Salinas[2], M. Ferruelo Magán[2], M. Metola Gómez[2], A. Del Caño Garrido[1], C. González Fernández[2]. *[1]CS San Juan de la Cruz, Servicio Madrileño de Salud, Pozuelo de Alarcón (Madrid); [2]CS Puerta Bonita, Servicio Madrileño de Salud, Madrid, Spain*

Background: Inadequate control of hyperuricaemia in gout patients can lead to more arthritis, activity limitations and higher gout-related treatment costs. General Practitioners can use well tolerated urate-lowering drugs, but some patients are inadequately controlled. European League against Rheumatism (EULAR) has published new guidelines[1] in 2016 with similar serum Uric Acid (sUA) goals.
Objectives: To evaluate sUA control in patients diagnosed with gout who were attended in primary care and to compare them to EULAR 2016 guidelines[1].
Methods: Retrospective analysis, carried out in 2 primary care health centres (8 family doctors) in Spain. We selected patients that have consulted in the last year diagnosed with gout at any time. Demographic variables, gout-related drugs and last sUA level were collected. Adequate control was defined as sUA level <6 mg/dL.
Limitations: We used only one isolated sUA value. No drug doses were analyzed. We did not distinguish severe from mild gout.
Ethical-legal aspects: We did not identify the patients. There was no intervention.
Results: We analyzed 231 patients diagnosed with gout, mean 70.1 years-old (Confidence Interval $CI_{95\%}$ 68.3–72.0), 189 (81.8%) were men. The mean sUA was 6.55 mg/dL ($CI_{95\%}$ 6.31–6.79 mg/dL).
39% were adequately controlled according to EULAR (sUA <6 mg/dL), 25.5% were close to the objective (6–7mg/dL) and clearly inadequate (>7mg/dL) in 35.5%. 10% had really bad control (sUA >9 mg/dL).
There was no difference between control in male 6.58 mg/dL ($IC_{95\%}$ 6.33–6.83) and female 6.40 mg/dL ($CI_{95\%}$ 5.73–7.07). Control improves in elder people: <60 years 7.01 mg/dL ($CI_{95\%}$ 6.60–7.42) vs.>70 years 6.30 mg/dL ($CI_{95\%}$ 6.00–6.60)
The only 14 patients receiving febuxostat achieved similar control using allopurinol (6.5 versus 6.7 mg/dL).
Conclusions: The degree of control of sUA in primary care patients in our area is mostly between optimal and acceptable, but it can be optimized in more than half of the cases. In a few patients the control is lousy. The worst-controlled patients were the youngest.
References:
[1] Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castañeda-Sanabria J, Coyfish M, Guillo S, Jansen TL, Janssens H, Lioté F, Mallen C, Nuki G, Perez-Ruiz F, Pimentao J, Punzi L, Pywell T, So A, Tausche AK, Uhlig T, Zavada J, Zhang W, Tubach F, Bardin T. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2017 Jan;76(1):29–42. http://ard.bmj.com/content/76/1/29.abstract.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6961

AB0876 OSTEOMALACIA: MODALITIES OF PRESENTATION AND ETIOLOGY OF 20 CASES

H. Mouanaa, Z. Saoussen, A. Arfa, M. Jguirim, I. Bejia, M. Touzi, N. Bergaoui. *Rheumatology Unit of the Monastir University Hospital, Monastir, Tunisia*

Background: Osteomalacia is a defect of mineralization of the protein framework of the skeleton.
Objectives: We try through our series to determine the presentation modalities and the various causes of this fragile benign osteopathy.
Methods: It is a descriptive retrospective study of cases collected in our rheumatology department between 2001 and 2016, concerning patients with osteomalacia
Results: Twenty patients were collected: 13 women and 7 men with an average age of 53±19 years [22 years, 80 years]. The mean duration of the disease is 45 months [5–172]. The findings were: bone pain in 55% of cases, pelvic pain in 45% of cases, a waddling gait in 5 cases (25%), fractures with low energy in 40% of cases, Functional impotence of the lower limbs in 35% of cases and a biological discovery in 2 cases (10%). Hypocalcemia, phosphorus deficiency and hypocalciuria were found in 14 cases, ie 70%. Alkaline phosphatases were elevated in 12 cases, with a variable rate of 2 to 7 times normal.The PTH, performed in 17 cases, was elevated in 53% of the cases. In our series, all

patients had hypovitaminosis D. In addition, an associated iron deficiency anemia was detected in 50% of the cases, biological stigma of digestive malabsorption in 40% of the cases and renal insufficiency in 15% of the cases. Standard radiographs showed diffuse demineralization in 90% of cases, Looser-Milkman streaks in 40% of cases and fractures in 30% of cases. Bone scintigraphy among 8 patients revealed diffuse hyperfixation in 4 cases (50%), localized hyperfixation in 3 cases (37%) and non conclusive images in only one case (12.5%). Bone densitometry performed in 5 patients showed secondary osteoporosis in 80% of cases. The diagnosis of osteomalacia was retained in 2 cases, celiac disease in 5 cases, renal insufficiency in 1 case, phosphate diabetes in 3 cases including Fanconi syndrome, hypophosphatasia in one case and tubular involvement as part of ankylosing spondylitis In one case. Etiology was a neoplastic cause in 4 cases including multiple myeloma. All the patients had a vitamin-calcium treatment (calcium intake between 500mg and 2g per day with an average of 2.5 cp/d, phosphorus in 3 cases and an etiological treatment in 3 cases. The resection of the tumor was the reason behind a clinical-biological improvement in the case of thyroid tumors. The outcome was favorable in the short term for all cases.

Conclusions: Osteomalacia is a generalized benign osteopathy, essentially linked to a deficiency in vitamin D often unrecognized. The diagnosis is simple and the treatment is easy, but the ignorance of the etiological forms can be responsible for an unfavorable evolution.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6986

AB0877 APPLICATION OF GOUT DIARY IN HEALTH EDUCATION OF GOUT PATIENTS

H. Miao, L. Zhang, G. Zhang, K. Xu. *Rheumatology, Shanxi dayi hospital, Taiyuan, China*

Background: Gout is a heterogeneous disease characterized by increased levels of blood uric acid. It is difficult to achieve a comprehensive and effective control of gout only by drugs, drug therapy must be combined with health education, diet and lifestyle changes. However, most of the gout patients had wrong thinking about their disease, diet and drug therapy.The status of China's health education in gout patients:the research teams were dispersed and unstable, the content of health education needed to be further refined, the models of health education were very simple.Based on the traditional models of health education,the purpose of this study is to explore the effect of gout diary in gout patients, by recording gout diary in order to improve their daily life behaviors and related laboratory indexes,aim to provide a new method for health education of gout patients.

Objectives: In order to explore the effect of gout diary,we applied the gout diary in gout patients.

Methods: From January 2015 to December 2015,110 cases of gout hospitalized patients were randomly divided into study group and control group (n=55).The control group used traditional education models:patient education forum,gout handbook,patient group discussion,etc.Based on the control group,the research group used not only the traditional education models,but also added gout diary,the patient can record the diary by themselves.In order to evaluate the effect of gout diary,we used questionnaires and related laboratory indexes.

Results: The research group had significant improvement in laboratory indexes,healthy behaviors and life style ($P<0.05$),such as quit smoking, quit drinking, according to the doctors' suggestions, pay more attention to their blood uric acid and other laboratory indexes, see the doctor regularly, maintain ideal body weight,exercise regularly,working and resting regularly,keeping happy mood.

Conclusions: Apply the gout diary in gout patients, we can achieve a perfect effect.

References:

[1] Li Yun Zhang, MD, H. Ralph Schumacher, Hou Heng Su, et al.Development and Evaluation of a Survey of Gout Patients Concerning Their Knowledge About Gout. Journal of Clinical Rheumatology[J]. 2011, 8,17(5):1–7.
[2] Glazebrook KN, Guimaraes LS, Murthy NS, et al. Identification of Intraarticular and Periarticular Uric Acid Crystals with Dual-Energy CT[J]. Initial Evaluation Radiology. 2011, 261(2):516–524.
[3] Roddy E, Doherty M. Epidemiology of gout[J]. Arthritis Res Ther, 2010,12(6):223.
[4] Zhu Y, Pandya BJ, Choi HK. Comorbidities of gout and hyperuricemia in the US general population: NHANES 2007–2008[J]. The American Journal of Medicine, 125(7), 2012:679–687.
[5] Choi HK, Curhan G. Independent impact of gout on mortality and risk for coronary heart disease. Circulation, 2007,116(8):894–900.
[6] Rees F, Jenkins W, Doherty M. Patients with gout adhere to curative treatment if informed appropriately:proof-of-concept observational study[J]. Ann Rheum Dis, 2013,72(6):826–830.
[7] Pullen C, Walker SN, Fiandt K. Determinants of health-promoting lifestyle behaviors in rural older women[J]. Fam Community Health, 2001,24(2):49–72.

Acknowledgements: -.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3370

AB0878 EFFECT OF DIALYSIS AND LOW DOSE URATE-LOWERING ON SERUM URATE LEVELS IN PATIENTS WITH GOUT

I. Urionagüena[1,2], S.P. Chinchilla[2,3], G. Garcia Erauzkin[4], M.L. Muñiz-Gomez[4], F. Pérez-Ruiz[1,2,3]. *[1]Rheumatology Division, Cruces University Hospital; [2]BioCruces Health Research Institute, Barakaldo, Biscay; [3]University of the Basque Country, Basque Country; [4]Nephrology Division, Cruces University Hospital, Barakaldo, Biscay, Spain*

Background: The effect of dialysis on urate levels (sUA) in patients with gout has not been well characterized. No prospective series are available from the literature, and no recommendation has yet been made by either EULAR or ACR on the topic.

Methods: Exploratory, observational, prospective study. Patients with crystal-proven gout and at least one flare the previous year to entrance into dialysis program, either hemodialysis (HD) or home peritoneal dialysis (PD), were followed-up. No urate-lowering drug was prescribed for the first 3-month period, but low-dose allopurinol (50 mg/day) was to be prescribed from 6-month visit onwards if tophi (any subcutaneous or ultrasonographic >10 mm longest diameter) were present or febuxostat in case allopurinol was not clinically suitable. sUA levels previous to the first dialysis procedure were recorded, along with sUA levels pre-dialysis (pre-sUA) and immediately post-dialysis (for patients on hemodialysis) sUA (post-sUA) were obtained during follow-up at 3, 6, and 12 months of follow-up. No prophylaxis was prescribed, and only adrenocorticotropic hormone (ACTH) analogue or corticosteroids were to be used for the treatment of flares.

Results: 17 patients studied to date: 12 men, mean age 69 (IQ range 62–78). Time from onset of gout was 7years (IQR 1–10) pre-dialysis, and 2 patients entered into dialysis due to prolonged use of NSAIDs because recurrent, longstanding gout over 20 years. Allopurinol (n=6) and febuxostat (n=2) had been prescribed previously to dialysis procedures. ULT was prescribed to 10 patients: 4/4 patients on PD and 6/13 on HD as per in methods; patients treated were prescribed allopurinol 50 mg/day but one who showed HLA-B58 antigen and was treated with febuxostat 80 mg every 3 days. After 12 months 5 patients were lost for follow-up: 2 underwent a renal transplant, 3 were dialyzed at private centers. Follow-up ranged from 12 to 30 months.

There was a significant reduction in sUA at 3-month (Δ - 2.6 mg/dl), compared to baseline sUA. Reduction of sUA from 3–6-month and 3–12 month was greater in patients treated with ULT (Table).

The rate of flares at 3-month was similar in patients on HD (5/13) than in patients on PD (2/4), only one flare was reported at 6 month follow-up visits, none afterwards. No serious side effect was observed.

Table 1. Change in pre-sUA and post-sUA (mg/dl) globally and with interventions

Patients/sUA	0 month	3rd month	PostHD-3rd month	6th month	PostHD-6th month	12th	PostHD-12th month
All (N=17)	9.8	7.2	2.8	5.8	3.1	5.5	1.2
Not treated (N=10)	9.4	6.2	3.1	5.7	3.2	5.8	1.2
Treated from 6-month (N=7)	10.0	7.7	2.7	5.8	3.0	5.3	1.2
PD	10.2	8.0		6.0		5.0	
HD	9.7	6.9	2.8	5.7	3.0	5.7	1.2

Conclusions: In this exploratory study, dialysis is effective in reducing sUA levels. In hemodialysis, both sUa and postHD-sUA may be needed to better estimate the effect of interventions on sUA. Low dose ULT seems to be effective and may be considered to properly control sUA, but only to be considered in patients with severe (tophaceous) gout.

Disclosure of Interest: I. Urionagüena: None declared, S. P. Chinchilla: None declared, G. Garcia Erauzkin: None declared, M. L. Muñiz-Gomez: None declared, F. Pérez-Ruiz Consultant for: Amgen, Ardea, AstraZeneca, Gruenenthal, Menarini, Speakers bureau: AstraZeneca, Gruenenthal, Menarini

DOI: 10.1136/annrheumdis-2017-eular.2980

AB0879 AN INTERNET TRIAL OF CHERRY EXTRACT VS. DIET MODIFICATION: PATIENT CHARACTERISTICS, GOUT SEVERITY AND DIET CHARACTERISTICS

J. Singh[1], G. Mcgwin[2]. *[1]Rheumatology; [2]Biostatistics, University of Alabama at Birmingham, Birimingham, United States*

Background: Gout is often treated with life-long pharmacological therapies. Patients are interested in non-pharmacological interventions as adjunct to these therapies. To our knowledge, non-pharmacological have not been studied in detail.

Objectives: To describe the baseline characteristics of patients with gout enrolled in an Internet pilot study comparing the benefits and harms of diet modification to cherry extract intake.

Methods: Patients were enrolled over an 8-month period using the Internet. Diagnosis of gout was confirmed by contacting their health care provider. We describe the baseline characteristics of patients with physician-confirmed gout, who were randomized in the Internet gout study.

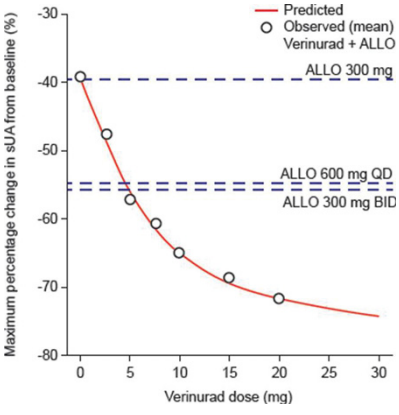
Results: We randomized 83 participants in an Internet gout pilot study, randomized to diet modification (n=43) or cherry extract (n=40); 3 patients withdrew before receiving intervention. The mean age of study participants was 56 years, (SD,

16), mean body mass index was 33 kg/m^2 (SD, 10), 73% were male; 67% were white Americans, 25% were African Americans and 7% other/mixed race/ethnicity. Participants took a median of 35 minutes to complete study assessment.
Almost half of the participants were taking medications for the treatment of gout: allopurinol, 42%; febuxostat, 1%, probenecid, 0%; colchicine, 29%. Forty-five percent participant were taking none of these medications. 41% smoked ever, 27% were using a special diet and participants had alcohol use an average of 2 days in the last week. Average number of gout flares were four in the last year. Dietary assessments showed that average daily intakes were as follows: calories, 2005; carbohydrate, 221 gm; fat, 82 gm; fiber, 19 gm; caffeine, 197 ml. The HEI2010 score of 64 was comparable to what was observed with NHANES for people in the average age range of this study.
Conclusions: Patients recruited in an Internet gout study, successfully responded to assessments, and had patient characteristics similar to gout populations described previously. The dietary assessments in this provide may provide a unique insight to design interventions to improve diet to improve gout outcomes.
References:
[1] Singh JA, Bharat A, Edwards NL. An internet survey of common treatments used by patients with gout including cherry extract and juice and other dietary supplements. J Clin Rheumatol. 2015;21(4):225–226. doi:10.1097/RHU.0000000000000246. PubMed PMID: 26010189.
Acknowledgements: This work was supported by a grant from UAB COERE nad UAB MHRC centers.
Disclosure of Interest: J. Singh Grant/research support from: Savient, Takeda, Consultant for: Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology, G. MCGWIN: None declared
DOI: 10.1136/annrheumdis-2017-eular.2762

AB0880 PHARMACODYNAMIC EFFECTS AND SAFETY OF VERINURAD (RDEA3170) IN COMBINATION WITH ALLOPURINOL VERSUS ALLOPURINOL ALONE IN ADULTS WITH GOUT: A PHASE 2A, OPEN-LABEL STUDY

R. Fleischmann[1], P. Winkle[2], J.N. Miner[3], X. Yan[3], L. Hicks[3], S. Valdez[3], J. Hall[3], M. Hernandez-Illas[4]. *[1]University of Texas, Southwestern Medical Center, Metroplex Clinical Research Center, Dallas, TX; [2]Anaheim Clinical Trials, Anaheim, CA; [3]Ardea Biosciences, Inc., San Diego, CA; [4]QPS MRA (Miami Clinical Research), Miami, FL, United States*

Background: Verinurad (RDEA3170) is a high-affinity, selective URAT1 inhibitor in development for the treatment of gout and asymptomatic hyperuricemia.
Objectives: This Phase 2a, randomized, open-label, multicenter study investigated the multiple-dose pharmacodynamics (PD), pharmacokinetics (PK), and safety of oral verinurad in combination with allopurinol versus allopurinol alone in adults with gout (NCT02498652).
Methods: Patients aged ≥18 and ≤75 years with gout and serum uric acid (sUA) ≥8 mg/dL were randomized to 1 of 2 cohorts to receive allopurinol (300 mg) in combination with verinurad (dose range 2.5 mg to 20 mg) and allopurinol 300 mg or 600 mg alone (each treatment period was 7 days). Medications were administered once daily ~30 min after breakfast (for allopurinol 300 mg b.i.d. group, the second allopurinol dose was in the evening). Colchicine 0.6 mg for gout flare prophylaxis was initiated at approximately Day -14 (start of urate-lowering therapy [ULT]) washout) or Day -7 if not on ULT. Serial blood and urine samples were measured on Days -1, 1, 7, 14, 21, 28, and 35 for PD and PK endpoints. Safety assessments included adverse events (AEs) and laboratory, electrocardiogram, and vital sign parameters.
Results: Forty-one patients were randomized (n=20–21 per cohort). Serum PD data pooled across cohorts demonstrated maximal % decrease in sUA from baseline (Emax)at 6–10 h after verinurad and allopurinol combination treatment. Addition of verinurad (2.5 mg to 20 mg) to allopurinol decreased sUA in dose-dependent manner (Figure). Greater sUA reductions were observed for dose combinations of verinurad ≥5 mg with allopurinol 300 mg versus allopurinol 600 mg alone, while allopurinol 600 mg once daily was equivalent to allopurinol 300 b.i.d. Emax was 46.9%, 58.9%, 59.9%, 67.1%, 68.4%, and 74.3% for verinurad at doses of 2.5, 5, 7.5, 10, 15, and 20 mg in combination with allopurinol 300 mg, versus 39.7%, 53.8%, and 54.4% with allopurinol 300 mg, allopurinol 600 mg, and allopurinol 300 mg b.i.d. alone. No drug-drug interaction on verinurad and allopurinol plasma PK parameters was observed.

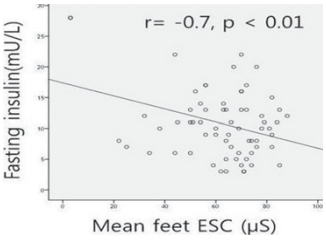


Conclusions: Verinurad coadministered with allopurinol dose-dependently decreased sUA. All dose combinations of verinurad and allopurinol in this study were generally well tolerated with no serious AEs or renal-related events during combination treatment.
Disclosure of Interest: R. Fleischmann Grant/research support from: Ardea Biosciences, Inc., P. Winkle Employee of: Anaheim Clinical Trials, J. Miner Employee of: Ardea Biosciences, Inc., X. Yan Employee of: Ardea Biosciences, Inc., L. Hicks Employee of: Ardea Biosciences, Inc., S. Valdez Employee of: Ardea Biosciences, Inc., J. Hall Employee of: Ardea Biosciences, Inc., M. Hernandez-Illas: None declared
DOI: 10.1136/annrheumdis-2017-eular.5429

AB0881 ASSESSMENT OF SUDOMOTOR FUNCTION IN PATIENT WITH GOUT

J.W. Lee[1], H.O. Kim[2], S. Lee[3], G. Kim[4]. *[1]Busan St. Mary's Hospital, Busan; [2]KyungSang University, ChangWon; [3]Busan National University; [4]Gosin univeristy, Busan, Korea, Republic Of*

Background: Sodorimetry is a non-invasive device measures sweat gland dysfunction using electrochemical skin conductance (ESC) of hands and feet and is useful for assessing peripheral small fiber nerve function. Little is known about the dysfunction of peripheral small fiber nerve in patients with gout.
Objectives: To evaluate the prevalence and characteristics of small fiber neuropath (SFN) in patients with gout compared with a healty control group and to identify factors associated with SFN in gout.
Methods: 80 male patients with well symtom controlled gout (age: 58±12) and 80 healthy controls were enrolled. Each patient was required to fast over 8 hours before blood samples. Serum fasting glucose, fasting insulin, uric acid, serum 25-(OH) D, lipid profiles, Creatinine (Cr) and r-GTP were measured. Body mass index (BMI) and Homeostatic model assessment insulin resistance (HOMA IR) were calculated. Patients already diagnosed with hypertension and diabetes were excluded.
Results: The mean feet and hands ESC were significantly lower in the gout group than the control group. Mean Hands ESC was irrelevant to age, BMI, fasting glucose and insulin, HOMA-IR, vit D, uric acid, Cr, and lipids. However, mean feet ESC showed significant correlation with fasting glucose (r=-0.7, p<0.01) and HOMA-IR (r=-0.25, p=0.03).



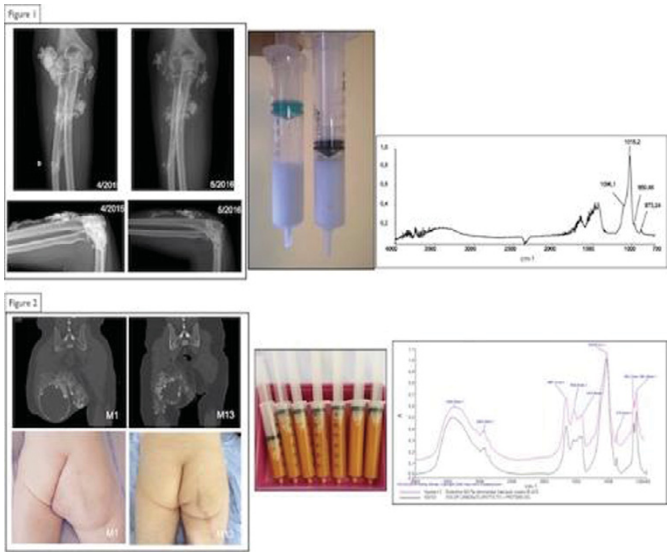
Conclusions: Sudomotor function was significantly lower in patients with gout than the control group. Mean feet ESC was correlated with fasting glucose and insulin resistance in patients with gout. These results suggest that dysfunction of SFN in gout patients is associated with insulin resistance and impaired fasting glucose.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5789

AB0882 EFFICACY OF INTRALESIONNAL SODIUM THIOSULFATE IN DISABLING TUMORAL CALCINOSIS: ABOUT TWO CASES

J. Goossens[1], M. Courbebaisse[2], V. Ratsimbazafy[3], D. Bazin[4], M. Daudon[5], V. Frochot[5], P. Richette[1], F. Lioté[1], H.-K. Ea[1], V. Guigonis[6]. *[1]Rheumatology department, LARIBOISIÈRE Hospital; [2]Physiology Department, Georges Pompidou European hospital, Paris; [3]Pharmacy department, Mother and Child hospital, Limoges; [4]Functional explorations department, TENON Hospital; [5]Laboratoire Chimie de la Matière Condensée de Paris, UMPC, Paris; [6]Pediatric Department, Mother and Child hospital, Limoges, France*

Background: Tumoral Calcinosis (TC) is a difficult-to-treat complication that can occur during the course of several diseases such as dermatomyositis or genetic hyperphosphatemia. It is a painful and disabling condition that can give rise to local complications including joint mobility reduction, cutaneous ulceration and superinfection. Until now, many treatments have been used with inconstant efficacy.
Objectives: Intravenous sodium thiosulfate gives promising results in calciphylaxis and ectopic calcifications, and intra-lesional injections could be effective for tumoral calcinosis.

Methods: We report two cases of successful intra-lesional injections of sodium thiosulfate (STS).
Results: Case 1: A 44-years old woman, with history of dermatomyositis developed in 2009 several TC involving the extensor surfaces of the right elbow and forearm, the two ischiatic regions, fingers and lumbar back. As TC kept growing despite successive treatments, including intravenous STS, we proposed weekly intra-lesional injections of 10% STS in the elbow's lesion. The injected volume varied from 10 to 30 mL at each session. Fourrier transform infrared spectroscopy (FTIR) of the aspirations confirmed that TC was composed of carbonated-apatite crystals. After 6-month treatment, we observed clinical and radiological regression of elbow TC whereas bottom TC and finger calcifications were unchanged (Fig 1). No side effect was observed except a subcutaneous infection occurring after an injection during the fifth month. This infection resolved with anti-staphycoccal antibiotics. Calcium, bicarbonate and chlorus serum levels, anion gap and eGFR remained unchanged during STS treatment.
Case 2: A 42-year old male presented with a prolonged history of hyperphosphatemic familial TC, confirmed by genetic analysis revealing homozygous mutations in the gene encoding the fibroblast growth factor 23. The extraosseous calcifications comprised a plain lesion on the right side of the left tibia and a massive heterogeneous lesion in the right buttock, making it the sitting position impossible. Treatment with maximal dose of phosphate binders, diet prescription and an attempt to surgically remove of the buttock's lesion were unsuccessful. Topical application of STS led to a near complete disappearance of the tibial lesion but was inefficient to treat the TC at the buttock. Considering the potential efficacy of STS in this patient, local injections of 25% STS (12 mL every week) were performed. The calcified material aspiration's analysis confirmed that TC was composed of carbonated-apatite crystals. Calcium and bicarbonate serum levels, anion gap and eGFR remained unchanged. After a 12-month treatment of STS injections, the lesion had significantly regressed (Fig 2), allowing the patient to sit again with no pain.



Conclusions: Intra-lesional injection of STS seems to be a promising treatment for TC. More studies are needed to confirm these results, and to understand the mechanisms implicated in the calcinosis resorption.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2809

AB0883 THE SENSITIVITY OF GOUT SPECIFIC ULTRASOUND SIGNS AT METATARSOPHALANGEAL JOINTS WOULD BE BETTER BY THE DORSAL SURFACE EXAMINATION

M.A. Mahdi[1], H. Rkain[1], M. Erraoui[1], R. Watfeh[2], S. Aktaou[1], L. Tahiri[1], R. Bahiri[1], F. Allali[1], N. Hajjaj-Hassouni[1]. *[1]Rheumatology; [2]Faculty of Medicine and Pharmacy, University Mohamed V, Rabat, Morocco*

Objectives: To compare the prevalence of ultrasonographic gout specific signs at the dorsal and plantar surfaces of the metatarsophalangeal joints (MTP).
Methods: This is a cross-sectional study which includes 15 patients with chronic gout, defined according to the American College of Rheumatology criteria (ACR 1977). Ultrasound (US) examination was performed using a high-frequency linear probe (Toshiba Xario®, frequency (8–14 MHz)) in B mode. 150 articular sites were studied at their dorsal and plantar surfaces. The ultrasound has objectified the presence of two signs: hyperechoic band over the superficial margin of the articular cartilage described as a double contour (DC) and the tophaceous deposits at the joint cavity. We compared the prevalence of the two signs between the dorsal and palmar surfaces at each site studied.
Results: The mean age at onset was 54.7±12,6 years, and the median diagnosis duration was 0 (0.3) years).
The results of the US examination are summarized in Table 1.

Table 1. Prevalence comparison of DC and tophaceous deposits between dorsal and plantar surfaces at MTP joints

Joints (N=150)	Double contour (%)			Tophaceous deposits (%)		
	Dorsal surface	Plantar surface	P	Dorsal surface	Plantar surface	P
MTP 1 (N=30)	33,3	10	0,03	56,7	6,7	0,01
MTP 2 (N=30)	13,3	0	<0.001	13,3	0	<0.001
MTP 3 (N=30)	6,7	0	<0.001	3,3	0	<0.001
MTP 4 (N=30)	0	0	<0.001	6,7	0	<0.001
MTP 5 (N=30)	3,3	0	<0.001	10	0	<0.001

Conclusions: Our study suggests that globally, DC predilect significatily in dorsal than in plantar surfaces of MTP joints. These results should be verified on a larger population.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3773

AB0884 PREVALENCE OF ULTRASONOGRAPHIC GOUT SPECIFIC SIGNS OF HAND AND FINGERS JOINTS

M.A. Mahdi[1], H. Rkain[1], M. Erraoui[1], R. Watfeh[2], S. Aktaou[1], L. Tahiri[1], R. Bahiri[1], F. Allali[1], N. Hajjaj-Hassouni[1]. *[1]Rheumatology; [2]Faculty of Medicine and Pharmacy, University Mohamed V, Rabat, Morocco*

Objectives: To evaluate the prevalence of ultrasonographic gout specific signs of hand and fingers joints.
Methods: This is a cross-sectional study which includes 15 patients with chronic gout, defined according to the American College of Rheumatology criteria (ACR 1977). Ultrasound (US) examination was performed using a high-frequency linear probe (Toshiba Xario®, frequency (8–14 MHz)) in B mode. 540 articular sites were studied at their dorsal surface. The ultrasound has objectified the presence of two signs: hyperechoic band over the superficial margin of the articular cartilage described as a double contour (DC) and the tophaceous deposits at the joint cavity.
Results: The mean age at onset was 54.7±12,6 years, and the median diagnosis duration was 0 (0.3) years).
The results of the US examination are summarized in Table 1.

Table 1. Prevalence of ultrasonographic gout specific signs of the wrist, MCP, PIP and DIP joints in the studied population

Joints (N=540)	Double contour (%)	Tophaceous deposits (%)
Wrist joints (N=120)	12,6	36
Radiocarpal (N=30)	20	43,3
Ulnocarpal (N=30)	13,3	50
Scaphotrapezial (N=30)	3,3	16,7
Trapeziometacarpal (N=30	13,3	43,3
MCP (N=150)	8	18
MCP 1 (N=30)	3,3	16,7
MCP 2 (N=30)	13,3	33,3
MCP 3 (N=30)	6,7	16,7
MCP 4 (N=30)	6,7	3,3
MCP 5 (N=30)	10	20
PIP (N=150)	4	16,6
IP (N=30)	3,3	30
PIP 2 (N=30)	6,7	16,7
PIP 3 (N=30)	6,7	20
PIP 4 (N=30)	3,3	10
PIP 5 (N=30)	0	6,7
DIP (N=120)	0,8	10
DIP 2 (N=30)	0	13,3
DIP 3 (N=30)	3,3	13,3
DIP 4 (N=30)	0	6,7
DIP 5 (N=30)	0	6,7

Conclusions: This study showed a predilection for the gout specific ultrasound signs (DC and tophaceous deposits) of the wrist and MCP joints. The contribution of musculoskeletal ultrasound seems to be very interesting to objectify the presence of gout specific signs in the hand and fingers joints.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3877

AB0885 PREVALENCE OF ULTRASONOGRAPHIC GOUT SPECIFIC SIGNS OF FOOT JOINTS

M.A. Mahdi[1], H. Rkain[1], M. Erraoui[1], R. Watfeh[2], S. Aktaou[1], L. Tahiri[1], R. Bahiri[1], F. Allali[1], N. Hajjaj-Hassouni[1]. *[1]Rheumatology; [2]Faculty of Medicine and Pharmacy, University Mohamed V, Rabat, Morocco*

Objectives: To evaluate the prevalence of ultrasonographic gout specific signs of foot joints.
Methods: This is a cross-sectional study which includes 15 patients with chronic gout, defined according to the American College of Rheumatology criteria (ACR 1977). Ultrasound (US) examination was performed using a high-frequency linear probe (Toshiba Xario®, frequency (8–14 MHz)) in B mode. 330 articular sites were

studied at their dorsal surface. The ultrasound has objectified the presence of two signs: hyperechoic band over the superficial margin of the articular cartilage described as a double contour (DC) and tophaceous deposits at the joint cavity.
Results: The mean age at onset was 54.7±12,6 years, and the median diagnosis duration was 0 (0.3) years).
The results of the US examination are summarized in Table 1.

Table 1. Prevalence of ultrasonographic gout specific signs of hind-foot, mid-foot and Metatarsophalangeal joints in the studied population

Joints (N=330)	Double contour (%)	Tophaceous deposits (%)
Hind-foot	8,8	10
Talocrural (N=30)	13,3	13,3
Subtalar:		
Lateral (N=30)	3,3	10
Medial (N=30)	10	6,7
Mid-foot	14,4	32,2
Talonavicular (N=30)	13,3	13,3
Intertarsal (N=30)	6,7	43,3
Tarsometatarsal (N=30)	23,3	40
MTP (N=150)	11,3	18
MTP 1 (N=30)	33,3	56,7
MTP 2 (N=30)	13,3	13,3
MTP 3 (N=30)	6,7	3,3
MTP 4 (N=30)	0	6,7
MTP 5 (N=30)	3,3	10

Conclusions: This study showed a predilection for the gout specific ultrasound signs (DC and tophaceous deposits) in the tarsometatarsal and metatarsophalangeal joints, especially in the first MTP. The contribution of musculoskeletal ultrasound seems to be very interesting to objectify the presence of gout specific signs of the foot joints.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2468

AB0886 PHARMACOKINETICS, PHARMACODYNAMICS, AND TOLERABILITY OF VERINURAD (RDEA3170), A SELECTIVE URIC ACID REABSORPTION INHIBITOR, IN HEALTHY ADULT MALE SUBJECTS

M. Gillen[1], Z. Shen[2], J.N. Miner[2]. *[1]AstraZeneca, Gaithersburg, MD; [2]Ardea Biosciences, Inc., San Diego, CA, United States*

Background: Verinurad (RDEA3170) is a selective uric acid reabsorption inhibitor in clinical development for the treatment of gout and asymptomatic hyperuricemia.
Objectives: The aim of this study was to evaluate the pharmacokinetics, pharmacodynamics, and tolerability of verinurad following single and multiple doses in healthy adult males.
Methods: This was a Phase 1, randomized, double-blind, placebo-controlled, single- and multiple-ascending dose study. Panels of 8 male subjects (6 active, 2 placebo) received a single oral dose of verinurad or placebo in either a fasted (2 mg, 5 mg, 20 mg, 40 mg) or fed (5 mg, 20 mg) state and panels of 12 male subjects (9 active, 3 placebo) received ascending doses of once-daily verinurad (1 mg, 5 mg, and 10 mg) or placebo in a fasted state for up to 10 days. Verinurad was administered as an oral solution for 1 and 2 mg doses and in tablet form for doses >2 mg. Serial plasma/serum and urine samples were assayed for verinurad and uric acid at predetermined time points. Safety was assessed by adverse event (AE) reports, laboratory tests, vital signs, and electrocardiograms (ECGs).
Results: A total of 81 adult males aged 18–54 years enrolled and completed the study. Following single oral doses of verinurad, absorption was rapid and exposure (maximum plasma concentration [C_{max}] and area under the plasma concentration-time curve [AUC]) increased in a dose-proportional manner up to the maximum dose tested; C_{max} was achieved at 0.5–0.75 hours post-dose in the fasted state, and was slightly delayed to 1.25 hours post-dose in the fed state. Food appeared to decrease AUC by about 23% and C_{max} by about 50%. Following multiple daily doses, there was modest accumulation of verinurad. Urinary excretion of verinurad accounted for approximately 2% of the administered dose, suggesting that renal excretion is a minor elimination pathway for unchanged verinurad. Reductions in serum uric acid (sUA) correlated with dose. Under fasted conditions, single-dose administration of verinurad 2, 5, 20, or 40 mg reduced sUA levels by 16%, 24%, 48%, and 62%, respectively. Following multiple once-daily dosing for 10 days, verinurad reduced sUA levels by 22%, 44%, and 61% for the 1, 5, and 10 mg doses, respectively. A persistent pharmacologic effect (>15% fractional excretion of uric acid relative to baseline) was evident for at least 24 hours after dosing for verinurad doses of 2 mg or above. Verinurad was well tolerated at all doses. No serious AEs, severe AEs, discontinuations due to AEs or clinically significant laboratory or ECG abnormalities were reported.
Conclusions: Single and multiple doses of verinurad were well tolerated, absorption was rapid and exposure was dose-proportional. Verinurad increased urinary uric acid elimination and resulted in sustained reductions in sUA. These data support further clinical evaluation of once-daily verinurad as a treatment for gout.
Acknowledgements: The authors thank Caroline Lee of Ardea Biosciences, Inc. for critical review of the abstract.
Disclosure of Interest: M. Gillen Employee of: AstraZeneca, Z. Shen Employee of: Ardea Biosciences, Inc., J. Miner Employee of: Ardea Biosciences, Inc.
DOI: 10.1136/annrheumdis-2017-eular.5133

AB0887 PHARMACOKINETICS, PHARMACODYNAMICS, AND TOLERABILITY OF VERINURAD (RDEA3170), A SELECTIVE URIC ACID REABSORPTION INHIBITOR, IN HEALTHY JAPANESE MALE SUBJECTS

M. Gillen[1], J.N. Miner[2], S. Valdez[2]. *[1]AstraZeneca, Gaithersburg, MD; [2]Ardea Biosciences, Inc., San Diego, CA, United States*

Background: Chronic gout is a significant clinical problem in Asia, including Japan, where many patients remain suboptimally treated with currently available therapies. Verinurad (RDEA3170) is a selective uric acid reabsorption inhibitor in clinical development for the treatment of gout and asymptomatic hyperuricemia.
Objectives: The aim of this study was to evaluate the pharmacokinetics, pharmacodynamics, and tolerability of verinurad in healthy Japanese and non-Asian adult male subjects.
Methods: This was a Phase 1, randomized, single-blind, placebo-controlled study (NCT01872832). Panels of 8 Japanese male subjects were randomized in a 3:1 ratio to receive a modified-release formulation of oral verinurad (2.5 mg, 5 mg, 10 mg, 15 mg) or placebo administered as a single dose in a fasted state and as multiple once-daily doses in a fed state for 7 days. A panel of 8 non-Asian male subjects received single and multiple doses of oral verinurad (10 mg) or placebo. Serial plasma/serum and urine samples were assayed for verinurad and uric acid at predetermined time points. Safety was assessed by adverse event (AE) reports, laboratory tests, vital signs, and electrocardiograms (ECGs).
Results: Of 48 randomized subjects, 46 (Japanese: 39, non-Asian: 7) completed the study. Treatment groups were generally well balanced; however, mean body weight and body mass index were approximately 14% and 7% lower, respectively, in Japanese than non-Asian subjects. Following single- or multiple-oral doses of verinurad in Japanese subjects, exposure (maximum plasma concentration [C_{max}] and area under the plasma concentration-time curve [AUC]) increased in a near dose-proportional manner under fasted or fed conditions. The time to C_{max} (T_{max}) was approximately 1.25–2.0 hours post-dose under fasted conditions. A moderate-fat meal delayed T_{max} up to 5 hours post-dose and increased plasma verinurad exposures up to 109%. Following once-daily multiple doses, there was modest accumulation of verinurad. C_{max} and AUC were 38% and 23% higher, respectively, in Japanese versus non-Asian subjects, largely due to the difference in body weight. Mean reductions in serum uric acid following once-daily multiple dosing of verinurad 10 mg were 62% and 58% at maximum reduction and 46% and 44% at 24 hours post-dose in Japanese and non-Asian subjects, respectively. Verinurad was well tolerated at all doses. One Japanese subject discontinued verinurad due to an AE of urticaria that resolved after 11 days. No serious AEs, Grade 3 or 4 AEs, or clinically significant laboratory or ECG abnormalities were noted.
Conclusions: Verinurad significantly lowered serum uric acid and was well tolerated in both healthy Japanese and non-Asian males, despite small differences in plasma pharmacokinetics. These data support further evaluation of once-daily verinurad as a treatment for hyperuricemia with or without gout in the Japanese population.
Acknowledgements: The authors thank Caroline Lee and Zancong Shen of Ardea Biosciences, Inc., for critical review of the abstract.
Disclosure of Interest: M. Gillen Employee of: AstraZeneca, J. Miner Employee of: Ardea Biosciences, Inc., S. Valdez Employee of: Ardea Biosciences, Inc.
DOI: 10.1136/annrheumdis-2017-eular.5200

AB0888 TENOFOVIR INDUCED OSTEOMALACIA: A PROFILE BASED ON THREE PATIENTS WITH LOW PHOSPHORUS AND NORMAL LEVELS OF VITAMIN D AND PARATHYROID HORMONE

M. Lovy. *Desert Oasis Healthcare, Palm Springs, California, United States*

Background: Tenofovir can induce proximal renal tubular changes that result in varying expression of Fanconi syndrome[1,2]. Less commonly, osteomalacia related to hypophosphatemia[2,3] can occur and has been documented with bone biopsy[3]. The clinical details of 28 reported cases of tenofovir induced osteomalacia, some of whom had vitamin D deficiency and secondary hyperparathyroidism, was recently summarized[3].
Objectives: To describe the clinical presentation and course of three HIV patients with tenofovir induced hypophosphatemic osteomalacia and compare to cases previously reported.
Methods: The clinical, laboratory, and radiologic features of three HIV patients referred for evaluation of pain and osteoporosis were reviewed.
Results: All three patients were male, had diffuse pain, suffered multiple clinical fractures, and were on combination long and short acting opioids at the time of presentation. Two were in wheelchairs and two had neuropathy.
All patients had hypogonadism and proteinuria and case 1 had glycosuria. All patients had normal 25-OH vitamin D, vitamin B12, PTH, serum protein electrophoresis, magnesium, CBC, calcium, CPK, sedimentation rate, TSH. Case 1 had fractures of the hip, sacrum, and humerus; case 2 hip and ribs; and case 3 ribs, pelvis and knee. The technetium bone scan showed a similar pattern of increased uptake in multiple ribs, calcaneus, metatarsal bones, knees, and

Case	Age	HIV, Y	TN, Y	Sx	VAS	BMI	alkphos	PO4	Cr	K+	NTX	FemN	LS
1	49	10	4	8	80	20.4	309	2.2	1.80	2.9	128	-3.5	-4.2
2	69	32	10	8	70	18.0	245	1.5	1.33	4.2	57	-2.6	-2.3
3	61	30	7	36	84	20.0	576	1.2	1.18	3.3	98	-3.2	-3.8

Y = years, Sx = symptoms in months, VAS = visual analogue scale, alkphos = alkaline phosphatase (39–117 IU/L), PO4 = phosphorus (2.5–4.5mg/dL), Cr = creatinine (0.76–1.27mg/dL), K+ = potassium (3.5–5.2mml/L), FemN = femoral neck T-score, LS = lumbar spine T-score.

sacrum in all three patients. A MRI of the knee showed bone marrow edema in case 2 and an atypical longitudinal fracture of the femur in case 3. Tenofovir was withdrawn, oral phosphates given, and resolution of pain and biochemical changes occurred in 4–8 months. Bone mineral density in case 1 repeated 1 year after presentation increased 16% in the femoral neck and 19% in the lumbar spine.

The laboratory and clinical features in our cases shared with those previously reported include long duration of HIV and tenofovir treamtent, severe pain and disability, low BMI, neuropathy, hypogonadism in men, elevation of alkaline phoshatase and varying degrees of renal tubular dysfunction.

Conclusions: Long term tenofovir therapy in HIV patients can induce a devastating disabling osteomalacia caused by hypophosphatemia with features of Fanconi syndrome with or without vitamin D deficiency. A long standing history of HIV infection, low BMI, neuropathy, and hypogonadism in male patients may predispose or be associated with this complication. A serum phosphorus, alkaline phosphatase, and urinalysis should be followed regularly in all tenofovir treated patients to avoid the consequences of osteomalacia.

References:

[1] Karras A, et al, Clin Infect Dis 2003; 36:1070–1072.
[2] Earle KE, et al, J Bone Miner Dis 2004; 19:714–721.
[3] Mateo L, et al, Clin Rheumatol 2016; 35:1271–1279.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2644

AB0889 FACTORS CONTRIBUTING TO LENGTH OF INPATIENT HOSPITAL STAY FOR PATIENTS WITH ACUTE GOUT ARTHROPATHY AT THE NORTHERN HOSPITAL: AN OBSERVATIONAL STUDY

M. Mian [1,2], M.N. Hossain [3], M. Omair [1], D. Liew [1,2], C.E. Owen [1,4], A.M. Foote [1,2], R.R.C. Buchanan [1,2,4]. *[1]Department of Medicine, Austin Health; [2]Department of Medicine, Northern Health; [3]School of Public Health and Preventive Medicine, Monash University; [4]Department of Medicine, University of Melbourne, Melbourne, Australia*

Background: Gout is a common inflammatory arthropathy with a reported prevalence ranging from 1.7% to 4% within Australia – one of the highest in the world, second only to New Zealand.[1] Epidemiological studies have established that its prevalence has increased steadily over recent years, with the impact of the disease on the rise.[2]

Gout has painful and debilitating effects on patients leading to impact on their quality of life. Even though usually managed in the primary care setting, many patients are ultimately admitted as inpatients to hospital with the associated increased resource utilisation and cost. There is a growing recognition of the economic burden of gout.[3] A Canadian study estimated 5-year total health costs of patients with gout at $10,332 more than comparable gout free patients.[4]

Objectives: To identify factors potentially contributing to increased length of inpatient hospital stay for acute exacerbations of gout in a teaching hospital in Melbourne, Australia.

Methods: Patients admitted to The Northern Hospital, Melbourne, Australia with a discharge diagnosis of gout as their only acute medical problem between 1st July 2014 and 30th June 2016 were identified using ICD-10 disease coding from institutional compensation reports. Retrospective chart review was performed identifying length of stay and for variables which may potentially affect it.

Results: 121 patients were discharged with an acute gout flare over the 2 years with a mean age of 66±15 years. The vast majority of patients in this cohort were male (86%). The mean length of stay was 2.3 days (95% CI 1.83–2.78 days), with a median of 1 day. The median length of hospital stay was increased by 2 days if patients lived alone (p=0.042) and 1 extra day if the C-Reactive Protein (CRP) measured at admission was >100 mg/L (p=0.001). Hospital stay was similarly prolonged by a single day if more than one joint was involved in the flare (p=0.003).

Conclusions: Gout without antecedent acute medical comorbidity is a common acute medical presentation to hospital with a large corresponding economic burden. Factors affecting length of inpatient stay include social status, marked elevation of CRP and polyarticular involvement. This study identifies factors which warrant further investigation as to how they may be ameliorated in order to improve health resource utilisation.

References:

[1] Smit E, Hoy D, Cross M et al. Burden of disability due to musculoskeletal (MSK) disorders. Ann Rheum Dis 2014; 73: 1470–1476.
[2] Becker MA. Recent developments in the management of gout. Rheumatology 2012;51:i1.
[3] Shields GE, Beard SM. A systematic review of the economic and humanistic burden of gout. PharmacoEconomics 2015;33: 1029–1047.
[4] Fischer A, Cloutier M, Goodfield J, Borrelli R, Marvin D, Dziarmaga A. The direct economic burden of gout in an elderly Canadian population. J Rheumatol 2017;44(1):95–101.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5632

AB0890 SYSTEMIC LUPUS ERYTHEMATOSUS AND GOUT: REALLY AN UNUSUAL ASSOCIATION?

N. Quilis [1], M. Andrés [2,3]. *[1]Seccion de Reumatologia, Hospital Universitario Vinalopó, Elche; [2]Seccion de Reumatologia, Hospital General Universitario de Alicante; [3]Departamento de Medicina Clínica, Universidad Miguel Hernández, Alicante, Spain*

Background: Patients with systemic lupus erythematosus (SLE) often suffer from cardiovascular comorbidity such as hypertension, dyslipidemia or coronary heart disease. However, the association with gout – an independent cardiovascular risk factor – is considered unusual - it is not reported in the EULAR textbook (1)-, and might not be taken into account when acute arthritis occurs in SLE patients, also due to the predominance of women in this disease.

Objectives: To review our experience regarding SLE patients who developed gout, and to perform a literature review of reported cases to date.

Methods: Retrospective review of patients with SLE and crystal-proven gout in our Rheumatology Unit, a tertiary care center. We recorded clinical and laboratory variables related to both diseases. Then, we performed a bibliographical review in Pubmed (1965 – 2016) to identify reported cases of coexistence of both diseases.

Results: Out 189 SLE patients seen in our Unit, we have identified two cases with crystal-proven gout: 1) A 68 years-old woman with SLE and nephritis diagnosed 30 years ago, who developed polyarthritis affecting her hands. 2) A 47 years-old man with lupus for 22 years with nephritis and renal failure, who developed acute arthritis involving right knee and ankle. In both cases, urate crystals were demonstrated at synovial fluid. The table shows the results of the literature review together with our two cases. To date, 36 cases with coexistent SLE and gout have been reported. Median age at time of gout diagnosis was 43.5 years (p25–75 32.5–52.0), being 26 females (72%). SUA levels were found notably high (median 13.5mg/dL), and tophi, a marker of gout severity, were demonstrated in almost half of cases (44.4%). The majority of patients (91%) were on glucocorticoids at time of gout diagnosis. According to common factors leading to hyperuricemia, lupus-related renal damage (86%) and use of diuretics (83%) predominated in the series.

Ref.	Sex & Age (years)	Lupus Nephritis	Diuretics	Corticoids	Time between SLE and gout diagnoses (years)	Acute arthritis	Tophi	SUA at diagnosis (mg/dL)	Other crystals in synovial fluid
Quilis 2017	F 65	Yes	No	No	30	Yes	No	11.1	No
	M 47	Yes	No	No	22	Yes	No	12.2	No
Moidel 1981	M 48	Yes	Yes	Yes	11	Yes	No	10.8	No
	F 39	Yes	Yes	?	10	?	Yes	12	No
Wall 1982	M 45	Yes	Yes	Yes	10	Yes	No	8.8	No
Rose 1982	F 34	No	No	Yes	1,5	Yes	No	?	CPP, hydroxyapatite
Helliwell 1982	M 39	Yes	?	Yes	12	Yes	Yes	14.8	No
Lally 1982	F 29	Yes	Yes	Yes	9	Yes	No	10.2	No
Bradley 1983	F 31	Yes	Yes	Yes	4	Yes	Yes	16.5	No
	F 57	Yes	?	Yes	20	Yes	Yes	9.5	No
Rodríguez 1984	F 17	Yes	Yes	Yes	5	No	Yes	12	CPP, hydroxyapatite, cholesterol
Greenfield 1985	F 56	Yes	Yes	Yes	12	Yes	No	13-18	No
	M 41	Yes	Yes	Yes	14	Yes	No	9	No
Tsuboi 1986	F 25	Yes	Yes	Yes	7	No	Yes	12.2	No
Frocht 1987	F 37	Yes	Yes	Yes	7	Yes	No	12.9	No
McDonald 1988	M 43	Yes	Yes	Yes	10	No	Yes	8.3-10.8	No
Kalmar 1982	F 47	Yes	Yes	Yes	6	No	Yes	16.1	No
Alarcon 1983	F 52	No	?	?	14	Yes	No	18	No
Kurita 1989	F 37	Yes	Yes	Yes	15	No	Yes	11.4	No
Veerapen 1993	F 31	Yes	?	Yes	11	Yes	Yes	11.5	No
	M 24	Yes	Yes	Yes	6	Yes	Yes	15	No
	M 22	Yes	Yes	Yes	4	Yes	Yes	10.1	No
McMillen 1994	F 52	Yes	?	Yes	7	Yes	No	6.9	No
Ho 2003	F 61	No	Yes	Yes	6	Yes	Yes	17.3	No
	F 37	Yes	Yes	Yes	5	Yes	Yes	17.5	No
	F 30	No	Yes	Yes	8	Yes	No	12.9	No
	F 50	Yes	Yes	Yes	13	Yes	Yes	10.3	No
	F 68	Yes	Yes	Yes	4	Yes	No	9.9	No
	F 77	No	Yes	Yes	14	Yes	Yes	9.2	No
	F 33	Yes	Yes	Yes	7	Yes	No	11.2	No
Bajaj 2004	F 22	Yes	No	Yes	9	?	?	18.4	No
	F 44	Yes	Yes	Yes	10	?	?	15.1	No
	M 46	Yes	Yes	Yes	9	?	?	15.1	No
	M 47	Yes	No	Yes	31	?	?	13.4	No
	F 53	Yes	Yes	No	4	?	?	15.1	No
	F 55	Yes	Yes	Yes	21	?	?	6.7	No

Conclusions: Data supports including gout into the differential diagnosis of episodes of acute arthritis in SLE patients. This makes crucial the routine analysis of all synovial fluid samples, but especially in patients with long-term disease, renal impairment, and diuretic use.

References:

[1] EULAR Textbook on Rheumatic Diseases. BMJ, 2015.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5292

AB0891 HIGH FREQUENCIES OF CVD RISK FACTORS, OBESITY, METABOLIC SYNDROME, AND VITAMIN DEFICIENCIES IN A DANISH COHORT OF GOUT PATIENTS

O. Slot. *Copenhagen Center for Arthritis Research, Rheumatology, Copenhagen University Rigshospitalet Glostrup, Glostrup, Denmark*

Background: Gout is associated with increased risk of Cardio-Vascular Disease and death.
Objectives: To measure the frequencies of a number of potentially modifiable CVD risk factors in gout patients.
Methods: Comorbidities and CVD risk factors were measured and registered in a cohort of 100 consecutive new crystal proven gout patients.
Results: 88 males (62.1±13.6 years) and 12 females (74.1±6.9 years) were included. See table for results.

Comorbidities	
Previous CVD (n=36/100)	36%
Hypertension (BT>140/90 mmHg) (n=80/100)	80%
Hypertension without antihypertensive treatment (n=22/100)	22%
Diabetes (n=28/100)	28%
Nephropathy (eGFR<60 ml/min) (n=29/99)	29%
One or more comorbidities	86%
Comorbidity risk factors	
BMI, mean±SD (n=95)	29.6±5.3
BMI ≥30 (n=44/95)	46%
Metabolic Syndrome (Int Diab Fed 2006) (n=68/95)	72%
P-High Density Lipoprotein <1.00 mmol/l (n=30/96)	32%
P-Low Density Lipoprotein >3.0 mmol/l (n=39/91)	43%
P-Triglyceride >2.00 mmol/l (n=48/96)	50%
Homocysteine >15 μmol/l (n=28/71)	40%
Homocysteine ≥20 μmol/l (n=17/71)	24%
Cobalamine <200 pmol/l (n=14/90)	16%
Folate ≤9 nmol/l (n=22/86)	26%
25 (OH)-vitamin D3 <50 nmol/l (n=45/94)	48%
25 (OH)-vitamin D3 <20 nmol/l (n=18/94)	19%

Conclusions: Nephropathy, obesity, and dyslipidemia are known to correlate to hyperuricemia and gout. Reciprocally hyperuricemia and gout may lead to development of comorbidities, i.e. hypertension, CVD, and nephropathy.
Almost half the patients in this study were obese emphasizing the correlation between hyperuricemia and gout and obesity. Weight reduction is beneficial for control of hyperuricemia and gout, and is an important lifestyle factor that may be addressed in the treatment of hyperuricemia.
Metabolic Syndrome is characterized by abdominal obesity and at least two of the following criteria: hypertension, diabetes, hypertriglyceridemia, and low blood levels of high-density-lipoprotein. Metabolic Syndrome is associated with a two-fold risk of CVD and was present in 72% of the gout patients.
High homocysteine levels are correlated to endothelial dysfunction and increased risk of CVD. In this study the majority of patients had levels of homocysteine in the upper normal range, and a quarter had hyper-homocysteinemia. Elevated homocysteine has previously been reported in gout correlated to impaired renal function, but hyper-homocysteinmia can also be induced by low blood levels of cobalamin, which was present in 16%, and low levels of folate, which was found in 26%. In addition, low folate has been associated with endothelial dysfunction and CVD independently of homocysteine.
Low levels of 25(OH)-vitamin D3 were observed in nearly half of the gout patients and deficiency were found in 19%. Obesity is known to be associated with low levels of vitamin D. Negative correlation between uric acid and Vitamin D has though been reported after correction for weight. Uric acid suppresses 1-alpha hydroxylase leading to low levels of 1,25(OH)2-vitamin D3 which is correlated to dyslipidemia and Metabolic Syndrome. Urate Lowering Therapy has been shown to counteract suppression of 1-alpha hydroxylase.
Due to the increased risk of CVD and death associated with gout and the high prevalence of comorbidities and CVD risk factors in gout patients - comprehensive evaluation, information, and treatment of reversible co-morbidities and risk factors is recommended to be a part of the clinical management of gout.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3701

AB0892 PROGRESSIVE CLINICAL BENEFIT IN CHRONIC REFRACTORY GOUT PATIENTS ACHIEVING A PERSISTENT URATE LOWERING EFFECT FROM PEGLOTICASE TREATMENT

P. Khanna[1], B. Mandell[2], R. Fleischmann[3], J. Kay[4], A. Yeo[5], P. Lipsky[6]. *[1]Rheumatology, University of Michigan, Ann Arbor, MI; [2]Dept. of Medicine, Cleveland Clinic, Cleveland, OH; [3]Metroplex Clinical Research Center, Dallas, TX; [4]U Mass Memorial Medical Center, Worcester, MA; [5]Horizon Pharma, Lake Forest, IL; [6]AMPEL BioSolutions, LLC, Charlottesville, VA, United States*

Background: Pegloticase is a recombinant uricase conjugated to polyethylene glycol approved for treatment of patients with chronic refractory gout. It profoundly decreases serum uric acid (UA) and resolves tophi, but the quality of the clinical benefit in patients achieving long-term UA lowering has not been assessed.
Objectives: To assess the clinical benefit of long-term UA-lowering with pegloticase in patients with gout.
Methods: This analysis used results from two randomized controlled trials (RCTs) of 6- months duration and the 2-year open-label extension (OLE) of these studies.[1,2] Efficacy was assessed in responders to the approved treatment regimen (8 mg pegloticase every 2 weeks [q2w]) in the RCTs (i.e., patients with plasma UA <6.0 mg/dL for ≥80% of the assessments around the 3 and 6 month time periods.) Clinical assessments included serum UA, frequency of gout flares, Patient Global Assessment (PGA), tender and swollen joints (TJC and SJC), pain measured with a 100-mm visual analog scale (VAS), Health Assessment Questionnaire Disability Index, bodily pain and the Arthritis-Specific Health Index from the Medical Outcomes Study Short Form 36 item, and reduction of target tophi.
Results: 33 patients who responded to pegloticase in the RCTs were followed throughout the OLE. Of these, 20 received 8 mg pegloticase q2w and 13 q4w. Both groups maintained markedly decreased serum UA levels during the OLE. Results for patients who received pegloticase q2w indicated significant improvements between RCT baseline and the final OLE evaluation for serum UA (P<0.0001), PGA (P=0.02), TJC (P=0.04), SJC (P=0.01), and pain VAS (P=0.01); 61.5% of patients in this group had complete target tophus resolution (P<0.0001). Results for those treated q4w indicated significant improvements between RCT baseline and the final OLE evaluation for serum UA (P<0.001), PGA (P=0.004), TJC (P=0.004), SJC (P=0.012), and pain VAS (P=0.01); 100% of patients in this group had complete tophus resolution (P<0.001). After an initial increase in gout flares during the initial 3 months of the RCT, there was a persistent decrease throughout the OLE. Maximal target tophus reduction was observed after 13–25 weeks of the OLE. Two of 20 (10%) patients receiving pegloticase q2w and 4 of 13 (31%) treated q4w lost the persistent UA-lowering effect during the OLE.
Conclusions: There were significant sustained clinical benefits with long-term pegloticase treatment in patients with chronic refractory gout achieving a UA lowering effect during the first 6 months of therapy. Significant decreases in TJC, SJC, and pain were noted along with significant improvements in PGA, suppression of gout flares, and resolution of tophi. In most patients, maximal benefit was noted after 6–12 months of pegloticase therapy, with many patients meeting newly proposed criteria for gout remission.[3]
References:
[1] Sundy JS, et al. JAMA. 2011;306:711–720.
[2] Becker MA, et al. Ann Rheum Dis. 2013;72:1469–1474.
[3] de Lautour H, et al. Arthritis Care Res. 2016;68:667–672.
Disclosure of Interest: P. Khanna Grant/research support from: AstraZeneca, Consultant for: Horizon, Ironwood, Selecta Bio, B. Mandell Grant/research support from: Horizon, Consultant for: Horizon, Ironwood, R. Fleischmann Consultant for: Horizon, J. Kay: None declared, A. Yeo Consultant for: Horizon Pharma, P. Lipsky Consultant for: AstraZeneca, Celgene, EMD Serono, GSK, Horizon Pharma, Janssen, Medimmune, Pfizer, Roche, Sanofi, UCB
DOI: 10.1136/annrheumdis-2017-eular.4119

AB0893 DISEASE RELATED KNOWLEDGE IN GOUT PATIENTS AND THE RELATIONSHIP WITH ADHERENCE TO URATE-LOWERING THERAPY IN EAST CHINA

R. Yin[1], T. Fu[1], Q. Zhang[1], L. Zhang[1], L. Li[2], Z. Gu[1]. *[1]Department of Rheumatology, Affiliated Hospital of Nantong University; [2]School of Nursing, Nantong University, Nantong, China*

Background: Gout is a chronic rheumatic disease caused by deposition of monosodium urate crystals in and around the joint, with a reported prevalence of 1.1% in mainland China and 6.24% in Taiwan, making it the most common form of inflammatory arthritis. With the disease progression, gout can cause permanent joint destruction, bone erosion, and organ damage. Urate-lowering therapy (ULT) is necessary to lower and maintain serum urate (sUA) levels at a therapeutic target of <360 μmol/L as this is associated with fewer gout flares, reduction of tophus size, and depletion of urate crystal stores in synovial tissues, making gout the only chronic arthritis that can be "cured". Disease related knowledge of gout patients should be assessed before attempting to improve health education.To date, except one study from south China, all other published papers about gout knowledge and medication adherence are from other countries. To our knowledge, there is no survey from east China.
Objectives: The current study aimed to investigate knowledge related to gout and it's risk factors, and the relationship with adherence to urate-lowering therapy in patients with gout in east China.
Methods: A cross-sectional study of 229 gout patients recruited from the Affiliated Hospital of Nantong University between August 2015 and November 2016 was conducted with two questionnaire, Gout Knowledge Questionnaire (GKQ) and Compliance Questionnaire on Rheumatology (CQR). Chi-square analysis, t-test, rank sum test, as well as logistic regression analysis were used to analyze data.
Results: 21.5% (49/228) of gout patients in east China had knowledge of gout, and 9.1% (13/143) adhered to ULT. Age, employment, income, alcohol use, family history, acute flares in preceding 1 year, and colchicine use were associated with awareness of gout-related knowledge, and age, income, alcohol use, and colchicine use were the predictors. Among patients with ULT, patients adherent to ULT tended to have gout-related knowledge, compared with non-adherent patients. Awareness of the cause of gout attack, flare prevention induced by ULT and comorbidity were correlated with medication adherence, and the cause of gout attack as well as flare prevention induced by ULT were predictors of adherence to ULT in gout patients in east China.

Conclusions: In this study, 78.5% of patients in east China didn't have gout-related knowledge. Patients' knowledge on gout is a significant independent determinant of adherence to ULT.

Acknowledgements: This study was supported by grants from the Cultivative Distinguished Young Scholars Project of Nantong University (2nd);the 2015 Graduate Innovation Project of Nantong University (YKC15075); and College graduate research and innovation of Jiangsu Province (KYZZ15–0353).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3071

AB0894 TREATMENT ADHERENCE TO URATE-LOWERING THERAPY IN CHINESE GOUT PATIENTS

R. Yin[1], H. Cao[1], T. Fu[1], Q. Zhang[1], L. Zhang[1], L. Li[2], Z. Gu[1]. *[1]Department of Rheumatology, Affiliated Hospital of Nantong University; [2]School of Nursing, Nantong University, Nantong, China*

Background: Gout, which is characterised by deposition of monosodium urate monohydrate (MSU) in synovial fluid and other tissues, is the most common form of inflammatory arthritis in man and older women. In addition to recurrent acute arthritis, subcutaneous tophi and chronic painful arthritis, gout also affects morbidity and premature mortality. Previous studies have reported that effective ULT can decrease sUA levels enough to prevent further crystal formation, dissolve existing urate crystals and eliminate the causative agent, thus reducing the frequency of acute gout attacks and preventing urate nephropathy, uric acid nephrolithiasis, and the deposition of tophi: a common cause of progressive joint damage, deformity and functional impairment, making gout the only chronic arthritis that can be "cured". However, gout patents' adherence rate to ULT is low, ranged from 10 to 46%. Emerging data suggest that poor adherence to long-term ULT use may be an important contributor to the suboptimal outcomes seen in gout and nonadherence may be worse in gout than in any other chronic disease. This suggests that there is a strong need to make a further study on drug adherence and its risk factors.

Objectives: Non-adherence in gout patients using urate-lowering therapy (ULT) may lead to joint destruction and permanent disability. Purpose of this cross-section survey was to explore Chinese gout patients' adherence rates and investigate potential risk factors for medication non-adherence.

Methods: A total of 129 gout patients were recruited from the Affiliated Hospital of Nantong University from August 2015 to September 2016. Patients were asked to complete a standardized self-report questionnaires (Compliance Questionnaire on Rheumatology, Treatment Satisfaction Questionnaire for Medication version II, Health Assessment Questionnaire, Confidence in gout treatment questionnaire, Gout Knowledge Questionnaire, Patient Health Questionnaire-9, Generalized Anxiety Disorder-7, and 36-Item Short Form Health Survey). Data was analyzed by independent sample t-test, rank sum test, chi-square analysis as well as logistic regression modeling.

Results: Based on CQR, 9.6% of gout patients were adherent to ULT. Adherence was associated with HAQ, GKQ, treatment satisfaction for medication, confidence in gout treatment and MCS. Other demographic, clinical and psychological characteristics were not related to adherence. Logistic regression models identified HAQ, GKQ and MCS as predictors of medication non-adherence.

Conclusions: In the current study, 90.4% of gout patients didn't adhere to their ULT prescription. HAQ, GKQ, treatment satisfaction for medication, confidence in gout treatment and MCS were relevant to medication adherence, and HAQ, GKQ and MCS were independent predictors of medication non-adherence in patients with gout. These findings could help medical personnel develop useful interventions to improve gout patients' medication adherence and quality of life.

Acknowledgements: This study was supported by grants from the Cultivative Distinguished Young Scholars Project of Nantong University (2nd); the 2015 Graduate Innovation Project of Nantong University (YKC15075); and College graduate research and innovation of Jiangsu Province (KYZZ15–0353).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3075

AB0895 OSTEOPOROSIS RISK FACTORS IN PATIENTS WITH CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION DISEASE (CPPD)

S. Vladimirov, M. Eliseev, O. Zhelyabina, A. Smirnov, S. Glukhova. *V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Osteoporosis (OP) risk factors (RF) in CPPD patients are not sufficiently studied, although some of these RFs may be more prevalent in CPPD pts than in general population [1]

Objectives: To identify the input of individual RFs into OP development in pts with *CPPD*

Methods: 64 patients with CPPD (35 males and 29 females), but without OP were included into open prospective study. CPPD was confirmed based on McCarty criteria (detection of calcium pyrophosphate crystals in the synovial fluid using polarized light microscopy and detection of chondrocalcinosis based on joint radiography or US examination). 40 pts of those had acute and/or chronic arthritis, and 24 pts had osteoarthritis with CPP crystal depositions. Mean age was 57.6±10.2 years, mean follow up – 4.85±0.96 years. Bone mass density (BMD) was measured by dual energy X-ray absorptiometry (DXA) at the forearm, lumbar spine and total hip was performed in all pts at baseline. OP was diagnosed by BMD (T-criterion $\leq$2,5). The following OP risk factors were evaluated in this study: sex, age $>$55 years for females and $>$65 years for males, smoking, alcohol, fractures in past medical history, fractures in parents, BMI $\leq$20 kg/m^2, BMI $\leq$25 kg/m^2, serum levels of calcium, magnesium, vitamin D, hypoparathyroidism (HPT), chronic kidney disease (GFR $\leq$60 mL/min), intake of diuretics and glucocorticosteroids (GCs), Erythrocyte sedimentation rate (ESR) $>$20 mm/h, C-reactive protein (CRP) $>$5,0 mg/L. Odds ratio (OR) (95% confidence interval, CI) was estimated for each risk factor and logistic regression analysis was performed. Statistical analysis was made using SPSS v. 11 package, *p* values of $<$0.05 were considered statistically significant.

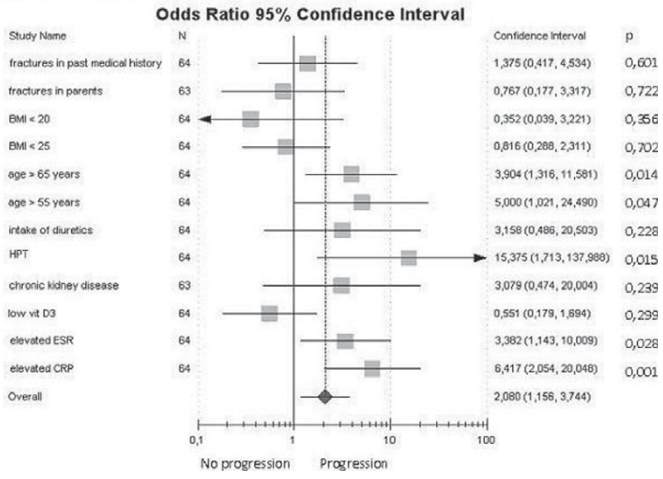
Results: OP was identified in 22 (34%) out of 64 pts with CPPD (13 males and 9 females) by the end of the study. The following factors were associated with OP: age $>$55 years in females (odds ratio (OR) 5.0, 95% CI; 1.021–24,49; *p*=0.047), age $>$65 years in males (OR 3.9, 95% CI 1.3–11.5; *p*=0.014), HPT (OR 15.38, 95% CI 1.7–137.9; *p*=0.015), elevated ESR (OR 3.38, 95% CI 1.14–10.0; *p* =0.028) and CRP (OR 6.42, 95% CI 2.05–20.05; *p*=.001) (Fig.1).

Only hypoparathyroidism was identified by logistic regression analysis (sensitivity-71%, specificity -82%) as OP-associated risk factor (OR 14.24, 95% CI 1.05–194.05; *p*=0.046) (Table 1).

Table 1. Data from multiple logistic regression analysis

Study	OR	Lower	Upper	p
sex	1,215	0,259	5,709	0,805
BMI$<$25kg/m^2	1,483	0,325	6,774	0,611
Age$>$65	1,293	0,274	6,093	0,745
Diuretics intake	2,771	0,189	40,617	0,457
HPT	14,245	1,046	194,055	0,046
CKD	1.025	0.082	12.876	0.985
lower vit.D3	0,503	0,116	2,173	0,357
elevated ESR	3,830	0,764	19,214	0,101
elevated CRP	3,855	0,608	24,44	0,152

Fig 1. Risk factors for osteoporosis (forest plot).



Conclusions: Hypoparathyroidism is the key risk factor for OP in CPPD pts. Among other risk factors chronic inflammation (ESR and CRP levels) is of highest importance.

References:

[1] Ross P.D. Osteoporosis: frequency, consequences, and risk factors. Archives Internal Med.1996; 156:1399–141.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3755

AB0896 THE EFFECT OF SERUM URIC ACID LEVELS ON TOPHUS STATUS AND FLARES IN PATIENTS WITH GOUT: A SYSTEMATIC REVIEW

S. Mitchell[1], L. Manounah[1], H. Liedgens[2], E. Johannes[3]. *[1]Decision Resources Group, Bicester, United Kingdom; [2]Head Health Economics and Outcomes Research, Market Access, SBU Europe?; [3]Head Market Access Europe, Grünenthal GmbH, Aachen, Germany*

Background: Gout is a chronic, progressive, inflammatory disease characterised by elevated serum uric acid (sUA) levels. sUA levels above its saturation point result in the deposition of monosodium urate crystals, which lead to gout flares and tophi (1). Multiple studies support the use of sUA levels as a marker for clinical improvements; hence the therapeutic goal is to lower sUA levels ($<$6.0 mg/dL) to improve the symptoms of gout and reduce the risk of associated comorbidities (2,3).

Objectives: To conduct a systematic review to identify studies reporting the effect of sUA levels on the incidence of gout flares and tophus status in adult patients with gout/hyperuricaemia, with a focus on publications reporting a correlation between the parameters.

Methods: Publications were identified by interrogating electronic databases; Medline & MEDLINE In-Process, EMBASE and the Cochrane Library (accessed 6 Sept 2016). Eligibility criteria included adult patients with a diagnosis of acute/chronic gout or hyperuricemia, with no restriction on publication date, study design or geography.
Results: In total, 59 studies met the pre-defined inclusion criteria and were reviewed; of these, 17 reported the relationship between sUA levels and flares (n=12) and/or tophus status (n=11). Two studies were multinational (North America), and 15 were single country (US [n=10]; Spain [n=2]; New Zealand [n=1]; Germany [n=1]; Japan [n=1]). The majority of studies had a follow-up period of ≤1 year, with one reporting 10 years' follow-up. All 12 studies evaluating flares reported that achieving sUA levels ≤6 mg/dL was associated with a decreased risk of gout flares, compared with sUA levels >6 mg/dL ($p<0.05$ in 8 studies). All 11 studies evaluating tophus status reported that achieving sUA levels ≤6 mg/dL was associated with improvements in tophus status, compared with sUA levels >6 mg/dL ($p<0.05$ in 4 studies). The remaining 42 studies reported the impact of urate lowering therapy on sUA levels and gout flares or tophus status, but not the correlation between the parameters. The qualitative results in these studies indicated that increases in sUA levels were associated with an increased risk of gout flares and worsening of tophus status.
Conclusions: Maintenance of sUA levels <6 mg/dL is associated with improvements in tophi resolution and flare reduction in adult patients with gout/hyperuricaemia. Whilst longer-term follow up studies (>5 years) are warranted, this review further supports that decreases in sUA levels are a marker for clinical improvements.
References:
[1] Keenan R, et al. Etiology and pathogenesis of hyperuricemia and gout. Elsevier Saunders. 2013;94:1533–53.
[2] Richette P, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2016:annrheumdis-2016–209707.
[3] Shoji A, et al. A retrospective study of the relationship between serum urate level and recurrent attacks of gouty arthritis: evidence for reduction of recurrent gouty arthritis with antihyperuricemic therapy. Arthritis Care Res. 2004;51(3):321–5.
Disclosure of Interest: S. Mitchell: None declared, L. Manounah: None declared, H. Liedgens Employee of: Grünenthal GmbH, E. Johannes Employee of: Grünenthal GmbH
DOI: 10.1136/annrheumdis-2017-eular.6023

AB0897 FUNCTIONAL DISABILITY AND HEALTH-RELATED QUALITY OF LIFE IN CHINESE PATIENTS WITH GOUT: A CROSS-SECTIONAL STUDY

T. Fu[1], R. Yin[1], L. Zhang[1], Q. Zhang[1], Y. Xia[1], J. Ji[1], Z. Da[1], X. Zhu[1], L. Li[2], Z. Gu[1]. [1]*Department of Rheumatology, Affiliated Hospital of Nantong University;* [2]*School of Nursing of Nantong University, Nantong, China*

Background: As the most common arthritis in adults, gout is a painful, inflammatory disease that may cause functional disability and decreased health-related quality of life (HRQoL). However, there are currently no known reported studies related to functional disability and HRQoL of gout patients from China.
Objectives: This cross-sectional study aims to investigate the effect of demographic variables, disease parameters, and psychological status on functional disability and HRQoL of Chinese gout patients.
Methods: A self-report survey was administered to 226 gout patients and 232 healthy individuals using the Short Form 36 health survey (SF-36) for HRQoL and the Health Assessment Questionnaire-Disability Index (HAQ-DI) for functional disability. Gout patients were asked to complete the 10 cm Visual Analog Scale (VAS) for total pain, the Patient Health Questionnaire (PHQ-9) for depression, and the Generalized Anxiety Disorder (GAD-7) questionnaire for anxiety. Blood samples were taken to examine the level of uric acid (UA). Independent samples t-tests, Chi square tests, spearman and/or pearson correlation and multiple linear regression were used to analyze the data.
Results: Our results found that individuals with gout have poorer HRQoL compared to healthy controls and the mean disability score was 0.32 (SD 0.54), representing mild disability. SF-36 and almost all components of the SF-36 score were associated with place of residence, hypertension, DM, cardiovascular disease, disease duration, number of flares/last year, total pain, number of tophi, presence of tender joints, colchicines use, corticosteroids use, depression, and anxiety ($p<0.05$). This variable was also significantly related to the HAQ-DI score ($p<0.05$). Additionally, there were significant relationships among age, income/year, allopurinol use and HAQ-DI ($p<0.05$). Stepwise multiple linear regression identified number of flares/last year, place of residence, depression and DM as predictors of functional disability. Disease status (total pain, number of flares/last year, presence of tender joints, cardiovascular disease, colchicine and corticosteroids use) and psychological disorders (depression and anxiety) were significantly accounted for poor HRQoL.
Conclusions: Chinese gout patients experienced mild disability and poor HRQoL. Disease status and psychological status were important risk factors linked to functional disability and HRQoL in Chinese gout population. These data suggest medical personnel should pay more attention to functional disability and HRQoL of gout patients and make suitable interventions to relieve their psychological disorders and finally to reduce their functional ability and improve their HRQoL.
Acknowledgements: This study was supported by Grants from the Chinese National Natural Science Foundation (no. 81671616 and 81471603).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3078

AB0898 SLEEP QUALITY IS ASSOCIATED WITH ALCOHOL USE AND FUNCTIONAL CAPACITY IN CHINESE PATIENTS WITH GOUT: A CROSS-SECTIONAL STUDY

T. Fu[1], R. Yin[1], L. Zhang[1], Q. Zhang[1], Y. Xia[1], J. Ji[1], Z. Da[1], X. Zhu[1], L. Li[2], Z. Gu[1]. [1]*Department of Rheumatology, Affiliated Hospital of Nantong University;* [2]*School of Nursing of Nantong University, Nantong, China*

Background: Poor sleep quality is common in patients with chronic diseases and may lead to disease aggravation and decreased quality of life. The increasing prevalence of poor sleep in individuals with chronic medical conditions is associated with adverse demographic, clinical, and psychological characteristics. However, there are currently no known reported studies related to the sleep quality of gout patients.
Objectives: This study aims to evaluate the prevalence of poor sleep quality and investigate the contributors of poor sleep in Chinese gout patients.
Methods: A self-report survey was administered to 226 gout patients and 232 healthy individuals using the Pittsburgh Sleep Quality Index (PSQI) for sleep quality, the Patient Health Questionnaire (PHQ-9) for depression, and the Generalized Anxiety Disorder (GAD-7) questionnaire for anxiety. Gout patients completed the 10 cm Visual Analog Scale (VAS) for total pain, and the Health Assessment Questionnaire-Disability Index (HAQ-DI) for functional capacity. Blood samples were taken to examine the level of uric acid (UA). Independent samples t-tests, Chi square analyses, and logistic regression were used to analyze the data.
Results: Our results found that the prevalence of poor sleep (PSQI≥5) was 55.3% and the mean global score of PSQI was 6.69 (SD 3.48) in patients, which were significantly higher than the controls (17.7% and 3.83 (SD 1.88), respectively). There were significant correlations among alcohol use, HAQ-DI, PHQ-9, GAD-7 and sleep quality in gout patients. Patients with yellow rice wine and wine use preferred to have better sleep quality. While, disease stage was associated with hypertension, total pain, number of tophi, presence of tender joints and swollen joints. Meanwhile, logistic regression models identified alcohol use and depression as predictors of poor sleep quality.
Conclusions: More than half of Chinese gout population suffered from poor sleep, which significantly higher than healthy individuals. These findings suggested medical personnel should pay more attention to the sleep quality of gout patients, especially those with depression. Additionally, it is beneficial for the patients with normal UA level to take moderate yellow rice wine and wine to improve their sleep quality.
Acknowledgements: This study was supported by Grants from the Chinese National Natural Science Foundation (no. 81671616 and 81471603).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3081

AB0899 DEPRESSION AND ANXIETY CORRELATE WITH DISEASE-RELATED CHARACTERISTICS AND QUALITY OF LIFE IN CHINESE PATIENTS WITH GOUT: A CROSS-SECTIONAL STUDY

T. Fu[1], H. Cao[1], R. Yin[1], L. Zhang[1], Q. Zhang[1], L. Li[2], X. Feng[3], Z. Gu[1]. [1]*Department of Rheumatology, Affiliated Hospital of Nantong University;* [2]*School of Nursing of Nantong University;* [3]*Department of Stomatology, Affiliated Hospital of Nantong University, Nantong, China*

Background: Depression and anxiety are common worldwide and may lead to disease aggravation and decreased health-related quality of life (HRQoL). The increasing prevalence of depression and anxiety in gout patients is associated with demographic and gout characteristics. However, there are currently no known reported studies related to the association between HRQoL and depression/anxiety.
Objectives: This cross-sectional study aims to evaluate the prevalence of depression and anxiety and investigate the potential risk factors for depression and anxiety in Chinese gout patients.
Methods: A self-report survey was administered to 193 gout patients and 208 healthy individuals from September 2015 to September 2016. Patients were asked to complete a set of standardized self-report questionnaires [Visual Analog Scale (VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI), Patient Health Questionnaire (PHQ-9), Generalized Anxiety Disorder (GAD-7) questionnaire, Short Form 36 health survey (SF-36)]. Independent samples t-tests, χ^2 analyses, and logistic regression were used to analyze the data.
Results: We found 15% of gout patients had depression, and 5.2% had anxiety, which were significantly higher than the healthy controls (1.4 and 1.0%, respectively). There were significant correlations among education, pain, disease duration, stage of gout, disability, number of tophi, presence of tender joints, HRQoL, and psychological status. Meanwhile, logistic regression analysis identified number of tophi, HAQ-DI, and MH scale as predictors of depression in gout patients. Education, GH, and VT domains were significantly accounted for anxiety.

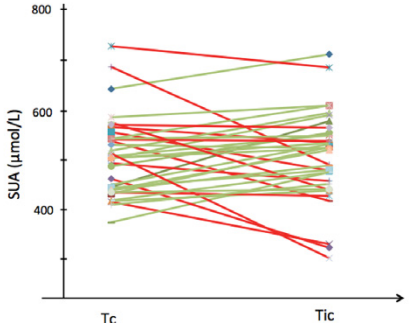
Conclusions: The prevalence of depressive and anxious symptoms among gout patients was higher than healthy individuals. Education, disability, tophi and HRQoL were important risk factors linked to this disorder in Chinese gout population. These findings suggested medical personnel should pay more attention to the psychological health of gout patients and make objective interventions to relieve their depression and anxiety, especially those with low education level, more than two tophi, severe disability, and poor HRQoL.
Acknowledgements: This study was supported by Grants from the Chinese National Natural Science Foundation (no. 81671616 and 81471603).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3082

AB0900 SERUM URIC ACID LEVEL VARIATIONS DURING GOUT ATTACKS ARE LINKED NEITHER TO INFLAMMATION NOR TO URIC ACID FRACTIONAL EXCRETION: A PROSPECTIVE STUDY OF 35 PATIENTS

V. Masson Behar[1], C. Desthieux[1], C. Aparicio[2], P. Manivet[3], T. Bardin[1], P. Richette[1], F. Lioté[1], A. Ostertag[1], H.-K. Ea[1]. *[1]Service de rhumatologie, hôpital Lariboisière, AP-HP, centre Viggo Petersen, University Paris Diderot, INSERM UMR 1132, Bioscar; [2]Policlinique, hôpital Lariboisière, AP-HP; [3]Crb Bb-0033–00064, BioBanking and Analytics Systems, APHP, Paris, France*

Background: Acute gout is usually associated with a decrease in serum uric acid (SUA) level but the mechanism responsible for this phenomenon remains unclear.
Objectives: We aimed to investigate relationships between changes in SUA level, urinary excretion of uric acid and biochemical markers during gout attack.
Methods: SUA, eGFR (estimated glomerular filtration rate), serum CRP level and urinary excretion of UA, expressed as fractional excretion of UA (FeUA), from 35 ULT (urate-lowering therapy)-free and diuretic-free gout patients were prospectively measured during acute gout attack (Tc) and intercritical (Tic) phase. In 11 patients, data were available after achievement of SUA target (Tt) (<360 μmol/l) under ULT. Demographics data and waist circumference (WC) were collected. Data are expressed as mean ± SD.
Results: There were 32 men, mean age 57.9 years, mean body mass index 28.6 kg/m^2, and mean waist circumference 104 cm. Overall 17.1% had type 2 diabetes, 37.1% dyslipidemia, 54.3% hypertension, 34.4% obesity, 74.3% abdominal obesity and 51.4% chronic kidney disease (CKD, 31.4% CKD 2 and 20% CKD 3–5). Gout duration was 3.9±6.7 years, 28.6% of patients had tophus and 31.4% gout arthropathy. SUA, eGFR and FeUA values were similar between Tc and Tic phases: SUA: 504.9±79.9 and 507.6±89.7 μmol/l; eGFR: 78.1±28.8 and 81.4±33.8 ml/min/1.73m^2; FeUA: 4.90±2.3 and 4.45±3.3%, respectively. Moreover, the FeUA values were identical between Tt, Tic and Tc in 11 patients who achieved SUA target (296.0±37.8 μmol/l) under ULT. CRP levels were higher at Tc (44.8±69.4 mg/dL) than Tic (5.2±3.3 mg/dl) and Tt (4.6±1.2 mg/dl). While mean SUA levels were similar between Tc and Tic, SUA levels were lower in Tc than Tic in 21 patients (mean difference: 56.9±33.7 μmol/l) (figure1). In contrast, 14 patients had a SUA level higher in Tc than in Tic (mean difference: 78.6±71.5 μmol/L) (figure 1). SUA variations between Tc and Tic were not correlated with FeUA modifications in these two groups (p=0.15). Similarly, SUA and FeUA variations were not correlated with CRP variations between Tc and Tic (p=0.29 and p=0.30, respectively).

Figure 1. Variations of SUA between gout attack (Tc) and intercritical (Tic) phases (Green color: patients (N=21) with lower SUA level at Tc than at Tic; red color: patients (N=14) with higher SUA level at Tc than at Tic)



Conclusions: SUA levels during gout attack can be either higher or lower than SUA during intercritical phase. These variations are linked neither to inflammation level nor to FeUA. It would be interesting to assess the intestinal excretion of uric acid, xanthine oxidase activity and diet intake during these different gout phases.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4808

AB0901 CLINICAL SIGNIFICANCE OF URATE DEPOSITION IN TENDON: A DUAL-ENERGY CT STUDY

Y. Eun[1], I.Y. Kim[1], H. Jeong[1], E.-J. Park[2], H. Kim[1], J. Lee[1], E.-M. Koh[1], H.-S. Cha[1]. *[1]Department of Medicine, Samsung Medical Center, Seoul; [2]Department of Medicine, Jeju National University Hospital, Jeju, Korea, Republic Of*

Background: Dual-energy computed tomography (DECT) is advanced imaging modality that shows the deposition of monosodium urate (MSU) crystal in tissue as a color signal. The MSU crystal deposit around the symptomatic joint is considered as positive finding, but the clinical significance of urate deposition around the tendon is still unclear.
Objectives: The aim of this study was to compare the clinical characteristics and DECT findings in people with MSU crystal deposition in the joints and people with urate deposition in the tendons.
Methods: DECT was performed in 71 patients who complained of recurrent painful swelling of the joints, and 35 of them showed MSU crystal deposition in the joints on DECT. Clinical manifestation and serum uric acid level data were collected.
Results: Most of the included patients were middle-aged (mean age 50 years, SD 15) and 67 patients (94%) were male. All patients who had MSU crystal deposition in joints on DECT had a history of typical gout attacks, and 29 patients (81%) had a history of gout attacks among patients with urate deposition only in tendons (p=0.011). The mean uric acid level of patients included in the study was as high as 7.5±2.2 mg/dL. In the highest uric acid level, the absolute value was higher in patients with urate deposition in joints, but there was no statistical significance. The correlation between the gout attack site and the urate deposit sites was 91% in patients with joint involvement, but only 6% in patients without joint involvement (p<0.001). There were 4 patients (11%) who showed gouty erosion without MSU crystal deposition in joints on DECT.
Conclusions: The MSU crystal deposition in the tendon was not correlated well with clinical features, suggesting that it is more likely to be associated with artifact or asymptomatic hyperuricemia. However, in some patients, MSU crystal deposition may be observed only in the tendon, even with gouty erosion. Therefore, careful interpretation of the DECT results is necessary.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6331

Infection-related rheumatic diseases

AB0902 TUBERCULOSIS SCREENING IN PATIENTS RECEIVING BIOLOGIC THERAPY

S. Bouden, A. Fazaa, K. Oueniche, S. Saidi, S. Kassab, S. Chekili, K. Ben Abdelghani, A. Laatar. *Rheumatology, Hopital Mongi Slim, la Marsa, Tunisia*

Background: The advent of biological treatments has greatly improved the management of chronic inflammatory diseases (CID). However, these biologics increase the risk of infection including the possible development of tuberculosis (TB). Screening of latent tuberculosis infection (LTBI) is therefore necessary prior to their initiation, especially in Tunisia, which is considered as a high-incidence area of TB.
Objectives: The aims of this study were to identify the prevalence of LTBI among patients candidate to initiate biologics, to analyze the tolerance of preventive therapy and to detect active TB or conversions of immunodiagnostic tests under biologics.
Methods: A retrospective study was conducted, over a period of 14 years (2002–2016). Patients with CID, candidate to initiate biological treatment, were included. The screening of LTBI was performed according to the national Tunisian guidelines. Clinical data, screening and follow-up information on biological therapy were assessed.
Results: A total of 76 patients were enrolled in the study, 32 men and 44 women with a mean age of 66 years [17–80]. Rheumatoid arthritis (RA) was the most common CID (44%). The diagnosis of LTBI was established in 16 cases (21%). Among them, 3 had a Tuberculin Skin Test (TST) more than 10mm associated with a positive Interferon Gamma Release Assay (IGRA), 11 had only a positive TST, and 2 had only a positive IGRA. One of them had a history of pulmonary TB but adequately treated. All patients with positive screening were considered for preventive treatment. Thirteen (81%) received an association of isoniazid-rifampicin for 3–6 months, and 3 (19%) received isoniazid for 6 months. Toxicity was reported in 4 cases (25%): hepatotoxicity (n=1), dermatologic toxicity (n=1), fever (n=1) and stomachache (n=1). During the follow-up period, no case of reactivation has been reported among patients with LTBI. Out of the 60 patients with negative baseline screening, only 4 have been re-screened (6%) and none had conversions in immunodiagnostic tests. However, among patients who screened negative, one case of active pulmonary TB has been reported in a woman who had an ankylosing spondylitis (AS) and who was receiving infliximab during 22 weeks. She hadn't previous TB history or new TB exposure.
Conclusions: Our study showed that the Tunisian recommendations allowed detecting a LTBI in 21% of biologic therapy candidates. The initial screening and the prophylactic treatment improve the safety of these treatments. However, we noted a low rate of re-screening, as the Tunisian guidelines do not recommend

annual screening. Wide studies should be designed in order to evaluate the efficacy of re-screening.

References:
[1] He D, Bai F, Zhang S et al. High incidence of tuberculosis infection in rheumatic diseases and impact for chemoprophylactic prevention of tuberculosis activation during biologics therapy. Clin Vaccine Immunol 2013; 20:842–847.
[2] Carmona L, Gómez-Reino JJ, Rodríguez-Valverde V, et al. Effectiveness of recommendations to prevent reactivation of latent tuberculosis infection in patients treated with tumor necrosis factor antagonists. Arthritis Rheum 2005;52:1766–72.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6727

AB0903 LABORATORY FINDINGS IN PATIENTS WITH CHIKUNGUNYA FEVER AND CHRONIC JOINT SYMPTOMS – A LONGITUDINAL ASSESSMENT

A. Ranzolin[1,2], R.M. Correia[2], H.D. de Lima[2], M.R.D.A. Freitas[2], A.F.R. de Oliveira[2], A.L.B.P. Duarte[1], C.D.L. Marques[1], P.R.S. de Melo[2], L.F. da Rocha Jr[1,2]. *[1]Hospital Das Clínicas of Pernambuco; [2]Instituto de Medicina Integral Professor Fernando Figueira, Recife, Brazil*

Background: Chikungunya Fever (CF) is an arbovirosis with a high attack rate, affecting large proportion of the population in its outbreaks (85%>90% of infected are symptomatic). In general, it is recommended to carry out laboratory tests when patients reach subacute phase or show signs of severity at the beginning of the disease. There are few studies showing which laboratory results are relevant and their clinical applicability.
Objectives: To recognize the most frequent findings of laboratory tests in a cohort of patients with CF and chronic joint symptoms and to correlate laboratory results with clinical data.
Methods: Patients with diagnosis of CF (clinical and epidemiological criteria) were followed in a cohort study. Clinical data and laboratory tests were collected in a regular schedule in the first months of the disease.
Results: A total of 54 patients were enrolled during 10 months, persistent changes in some patients were recorded (table).

Table 1. Persistent laboratory findings in patients with Chikungunya Fever in subacute/chronic phases

> 50%	Decreased vitamin D (53.8%)
40%>50%	Increased CRP (43.3%)
30%>40%	Decreased: HDL cholesterol (36.5%), eosinophil (37.3%),
20%>30%	Increased: glucose (28.3%), GGT (27.4%), γ globulin (27.4%), glycated hemoglobin (26.4%), calcium (25.4%), alkaline phosphatase (24.5%), β globulin (23.5%), cholesterol (23.0%) Decreased: total bilirubin (20.0%)
10%>20%	Increased: triglycerides (17.6%), LDH (17.3%), ferritin (13.7%), ALT (13.2%), direct bilirubin (12.0%), α2 globulin (11.7%) Monocytosis (11.1%), Limphocytosis (10.0%)
5%>10%	Hyperchloremia (8.0%) Increased: neutrophils (7.54%), LDL (5.88%), folic acid (5.88%), uric acid (5.76%), platelets (7.54%) Decreased: CPK (7.54%), albumin (5.88%), neutrophils (9.43%) Hyponatremia (5.88%),

CRP = C reactive protein, GGT = gamma glutamyl transferase, LDH = lactate dehydrogenase, ALT = alanine aminotransferase, CPK = creatine phosphokinase.

In the subacute phase, the ESR (erythrocyte sedimentation rate) correlated with number of swollen joints (r=0.45, p=0.03), VAS (visual analogue scale) of pain (r=0.72, p=0.0002), VAS patient's general health (r=0.50 p=0.02), VAS by physician (r=0.45, p=0.03) and with HAQ (r=0.51, p=0.01). In subacute phase the VAS of morning stiffness correlated with CRP (r=0.46, p=0.02). In chronic phase, CRP correlated with VAS of pain (r=0.47, p=0.02) and there was a reversal in the correlations between ESR and VAS of general health of the patient (r=-0.54, p=0.03), VAS of physician (r=-0.52, p=0.02), swollen joints (r=-0.46 p=0.03) and HAQ (r=-0.56, p=0.01). ESR and SF-12 (mental component) were correlated (r=0.61, p=0.01).
Conclusions: Levels of ESR correlated with measures of pain and worsening of functional capacity in subacute phase. In chronic phase, there was reversal of this correlation, indicating that ESR does not reflect clinical worsening of patients at this stage. Further clinical studies are needed to better analize other alterations.

References:
[1] Weaver SC, Lecuit M. Chikungunya virus and the global spread of a mosquito-borne disease. N Engl J Med 2015 Mar 26;372(13):1231–9.
[2] Brito CA, Sohsten AK, Leitão CC et al. Pharmacologic management of pain in patients with Chikungunya: a guideline. Rev Soc Bras Med Trop. 2016; 49(6):668–679.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5599

AB0904 FUSOBACTERIUM NECROPHORUM MASQUERADING AS NEISSERIA IN SEPTIC ARTHRITIS

C.H. O'neill[1], H. McCormick[2], M. Leith[1], L. McCorry[3], J. McKenna[2], A. Pendleton[3], Y. Protaschik[3], A. Loughrey[2], P.V. Coyle[2], D. Fairley[2]. *[1]Rheumatology; [2]Microbiology; [3]Belfast Health and Social Care Trust, Belfast, United Kingdom*

Background: Infective arthritis with fusobacterium is rare and difficult to diagnose & initially can be misidentified as Neisseria arthritis based on microscopy results. It is associated with Lemierre's Disease & is important to recognise.
Objectives: To demonstrate that a "linked up" approach between culture and PCR in the analysis of joint fluids will provide timely identification of the organism and allow for appropriate antibiotic use & to show the utility of bacterial 16S rRNA PCR in sterile site fluid analysis.
Methods: This is a case study of a pyogenic wrist infection with *Fusobacterium necrophorum* in the rheumatology department
Results: Our report follows a 17 year old caucasian female presenting with a history of left wrist pain, swelling and flu-like symptoms. Microscopy of joint aspirate revealed gram negative diplococci. Empirical antibiotic therapy, Ceftriaxone, was used to cover for potential gonococcus. Real-time PCR testing was negative for both gonococcus and meningococcus. However a real-time PCR assay targeting the bacterial 16S ribosomal RNA gene detected bacterial DNA[1]. The patient did not clinically improve and further aspirate remained positive for the 16S rRNA gene target. As all joint aspirates and other specimens remained culture negative, the decision was taken to attempt bacterial 16S rRNA PCR and sequencing on DNA extracted directly from the joint aspirate. The sequences recovered were identified as *F necrophorum.* This was eventually confirmed by anaerobic culture of the initial joint aspirate. A suspicion of Lemierre's disease (thrombophlebitis of the internal jugular vein and/or bacteraemia) was raised, however jugular venous dopplers were normal.
The outcome was favourable following guided antibiotic treatment.
Conclusions: This case illustrates that *F. necrophorum* infection may occur with unusual or disseminated presentation, but in the absence of the classical features of Lemierre's syndrome. The possibility of Neisseria was recognised early & appropriate empirical antibiotic cover was used. This is important given the emergence of virulent meningococcal serogroup W ST11 strains causing infections with unusual presentation (including septic arthritis) in the UK[2]. Reliance on microscopy findings alone could have led to an incorrect diagnosis of gonococcal septic arthritis – a condition with very low complication rates and excellent prognosis. In contrast, non-gonococcal septic arthritis is a medical emergency with significant morbidity and mortality[3]. The *F. necrophorum* infection in this case could have had fatal complications if it had been managed as a gonococcal infection. Secondly this case highlights the utility of bacterial 16S PCR and sequencing directly from a normally sterile site, allowing accurate diagnosis and appropriate treatment.

References:
[1] Yang S et al (2002)Quantitative Multiprobe PCR Assay for Simultaneous Detection and Identification to Species Level of Bacterial Pathogens J Clin Micro 40(9):3449–3454.
[2] Ladhani SN, et al(2014) Increase in Endemic Neisseria meningitidis Capsular Group W Sequence Type 11 Complex Associated With Severe Invasive Disease in England and Wales. Clinical Infectious Disease 60:578–585.
[3] Shirtliff & Mader (2002) Acute septic arthritis. Clin Microbiol Rev. 15(4):527–44.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6272

AB0905 THE EFFICACY OF TRIMETHOPRIM/SULFAMETHOXAZOLE TO PREVENT ACUTE-ONSET DIFFUSE INTERSTITIAL LUNG DISEASES WITH CONNECTIVE TISSUE DISEASE PATIENTS

F.Y. Chen, K. Setoguchi, M. Ogawa, S. Kamei. *Systemic Immunological Disease, Tokyo Metropolitan Komagome Hospital, Tokyo, Japan*

Background: Acute-onset diffuse interstitial lung diseases (AoDILD) are highly mortal condition and their cause are often difficult to discriminate. Trimethoprim 80mg/sulfamethoxazole 400mg single strength (TMP-SMX SS) has been used for Pneumocystis Pneumonia (PCP) prophylaxis and highly effective but the dose was originally developed in pediatric cancer patient's study and there is possibility that in connective tissue disease (CTD) patients, less dose can be as effective.
Objectives: The aim of this study is to examine hypothesis that taking TMP-SMX for PCP prophylaxis with CTD also have prophylactic effect against AoDILD and how about those effect in under dose patients for some reason
Methods: We retrospectively investigated data from 621 patients with TMP-SMX for PCP prophylaxis during and 43 patients who admitted for either acute respiratory failure/acute interstitial pneumonia/PCP/drug induced pneumonitis during 2004–2016 in our department.
Results: There was no single case who admitted to hospital due to AoDILD with TMP-SMX for PCP prophylaxis. There were 34 cases admitted for AoDILD and 9 cases (26%) were dead. Among 25 cases, 5 cases developed AoDILD after TMP-SMX cessation. 70 cases ware taking under dose prophylaxis for some reasons but there was also no AoDILD case.
Conclusions: Taking TMP-SMX for PCP prophylaxis may also have prophylactic effect against AoDILD. And those effect may also exist even under dose.

References:
[1] Hughes WT, et al.: N Engl J Med 1977;297:1419–26.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4687

AB0906 PYOGENIC SEPTIC ARTHRITIS: IS THERE A DIFFERENCE WHEN GERM IS NOT IDENTIFIED?

H. Sahli[1], M. Sahli[1], R. Tekaya[2], O. Saidane[2], R. Khalfallah[1], I. Mahmoud[2], L. Abdelmoula[2]. *[1]Rheumatology Departement, Mohamed Taher Maamouri University Hospital, nabeul; [2]Rheumatology Departement, Charles Nicolle Hospital, tunis, Tunisia*

Background: Pyogenic septic arthritis (PSA), defined by the presence of living microorganisms in the affected joint, is a therapeutic emergency. Germ isolation is a primordial step in the diagnostic and therapeutic approach.
Objectives: The aim of this study was to study the differences between PSA with positive and negative bacteriology.
Methods: This is a retrospective study which included medical records of patients treated for PSA in a rheumatology department over seventeen years. The epidemioclinical and paraclinical data were recorded. We used the SPSS 11.5 for the statistical analysis to compare patients with (group 1) and without an isolated causative agent (group 2).
Results: We evaluated 49 patients with a diagnosis of PSA. They were 26 (53.1%) men and 23 (46.9%) women. The average age was 55+/-18.7 years (ranging from 15 to 95 years). Comorbidities were observed in 31 (63.3%) patients. The onset of symptoms was acute in 37 (75.5%) patients and progressive in 12 (24.5%) patients. The most common symptoms were joint pain and stiffness (100%) and functional impotence (87.8%). All patients were treated with double or triple antibiotics. Among the studied patients, 27 (55.1%) had negative culture results. Statistical analysis used to compare cases with an isolated pathogen to those cases without an isolated pathogen, noted female predominance in group 2 but there was no statistically significant difference (p=0.252). Patients in group 1 and group 2 had a comparable mean age (p=0.08). Patients in both groups had comparable risk factors for PSA (p=0.549). Acute onset was more common in group 2 (51.4% versus 48.6%) but without a significant difference (p=0.507). Biological inflammatory syndrome was more frequent in group 2 but with no statistically significant difference (p=0.235). The study of the appearance of the synovial fluid did not demonstrate a statistically significant difference between the two groups (p=0.125). The abnormalities of standard x-rays were similar in both groups (45.2% in group 1 versus 54.8% in group 2, (p=1)). The statistical study of all other variables didn't show differences between the two groups.
Conclusions: PSA was not associated with major differences if the germ was or not isolated.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6187

AB0907 CONTRIBUTION OF IMAGING IN THE DIAGNOSIS OF INFECTIOUS SPONDYLODISCITIS

H. Sahli[1], A. Bachali[1], R. Tekaya[2], I. Mahmoud[2], O. Saidane[2], L. Abdelmoula[2]. *[1]Rheumatology Department, Mohamed Taher Maamouri University Hospital, nabeul; [2]Rheumatology Department, Charles Nicolle hospital, tunis, Tunisia*

Background: Infectious spondylodiscitisis represents a diagnostic and therapeutic emergency. Imaging is fundamental in the management of the disease.
Objectives: The aim of this study is to analyze the contribution of imaging in the diagnosis of infectious spondylodiscitis.
Methods: This is a retrospective study which included medical records of patients treated for psoas abcess during the twelve past years [2006–2016]. Epidemiologic, clinical, and imaging data (Standard X ray, Computed tomography (CT), magnetic resonance imaging (MRI)) were recorded and analysed.
Results: Ninety patients were included in this study. The average age was 55 years [16–86] with an even distribution between males and females. Mean symptom duration was of 4 months. The most frequently isolated pathogen was Mycobacterium tuberculosis (63.3%), followed by pyogenic germs (21.2%) and Brucella (15.5%). Standard X ray were pathological in 89% of cases: showed narrowing of intervertebral space (72.2%), endplate destruction (42.2%), erosions of vertebra (13.3%), opacity (12.2%), vertebral fracture (10%), paravertebral spindle (5.5%) and posterior archlysis lesion (2.2%). Standard radiographswere normal in 12 cases and in 1 case, spinal CT showed vertebral destruction wirh " mirror-image ". Spinal MRI, performed in the remaining 11 cases, confirmed the diagnosis in all cases and showed paravertebral collections (n=3), epiduritis (n=3), psoas abscess (n=2), microabscess (n=1) and spinal compression (n=1). In case of posterior archlysis lesion and vertebral fracture, MRI confirmed the diagnosis by showing paravertebral collections.
Conclusions: Management of infectious spondylodiscitis has benefited from advancements in imaging allowing an early diagnosis and treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2770

AB0908 BIOLOGICAL AND RADIOGRAPHIC FINDINGS IMPACT ON GERM IDENTIFICATION DURING SEPTIC ARTHRITIS

H. Sahli[1], M. Sahli[2], R. Tekaya[2], R. Khalfallah[1], O. Saidane[2], I. Mahmoud[2], L. Abdelmoula[2]. *[1]Rheumatology Departement, Mohamed Taher Maamouri University Hospital, nabeul; [2]Rheumatology Departement, Charles Nicolle Hospital, tunis, Tunisia*

Background: Septic arthritis may cause damage and inflammation in short period of time. The germ determination must be the first objective to allow targeted treatment. Bacteriological tests remain negative in 7–35% of cases of septic arthritis.
Objectives: The aim of this study was to determine the impact of biological and radiographic findings on germ identification during septic arthritis.
Methods: This a retrospective study which included medical records of patients treated for septic arthritis during the seventeen past years. Epidemiologic, clinical, biologic, bacteriologic and therapeutic data were recorded and analysed. We made a comparison between patients who had a germ identified (Group 1) with whom who hadn't (Group 2).
Results: Fifty nine patients with septic arthritis were included in this study. The mean age of the patients was 54.6±19 years and a sex ratio (F/M) of 0.9. Causative agents were isolated in 27 patients (45.7%). Biological data showed leukocytosis in 25 (42.4%) patients. Mean leukocyte count was 10673±5003. Leukopenia was noted in 1 case. One patient had neutropenia. Lymphopenia was observed in 4 patients (6.7%). Two patients had hyperlymphocytosis. Anemia, mainly of the inflammatory type, was noted in 47 cases (79.66%). The mean Creactive protein (CRP) was 150.6±106, and the mean erythrocyte sedimentation rate (ESR) was 104.9. Twenty three patients (38.9%) had other perturbations of the biological balance: cholestasis (n=1), cytolysis (n=4) and renal perturbation (n=15). Radiological signs suggestive of septic arthritis were observed in 40 cases (67.8%): articular pinching (28.8%), geodes and erosions (14%), total destruction of the joint (0.67%) or thickening f the soft parts at the beginning (11.86%). Ultrasound exam, performed in 22 cases, showed articular effusion (n=15), synovial thickening (n=8), a soft tissue collection (n=3), and periarticular erosion (n=2). CT, performed in 6 patients, was normal in one case. The abnormalities noted were: collection of soft parts (n=2), joint effusion (n=2), bone demineralization (n=1), bone erosion (n=1) and osteochondritis (n=1). MRI, performed in 2 patients, was pathological in both cases and showed synovitis and cortical erosion with medullary edema. The comparison of the 2 groups according to germ identification showed that biological inflammatory syndrome was more frequent in group 2 (100% versus 96.8%) but without a statistically significant difference (p=0.346). Mean value of CRP and ESR were comparable in the two groups (p=0.65 and 0.19). The mean value of hemoglobin was comparable in the two groups (10.87 versus 10.54 g/dl) (p=0.566). It was similar about the blood count. Abnormalities of standard x-rays were similar in both groups (70.4% in group 1 versus 65.5% in group 2) (p=0.784). The most frequent radiological abnormality in the two groups was articular pinching (40.7% in group 1 and 46.8% in group 2).
Conclusions: In our study, the biological and radiological data had not shown any impact on the identification of the germ.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3835

AB0909 SEPTIC PSEUDARTHROSIS OF THE HUMERUS TREATMENT USING ORTHFIX EXTERNAL FIXATION

S. Daas[1], H. Sahli[2], M.A. Sbai[1], M. Souissi[1], A. Khorbi[1]. *[1]Orthopedic Departement; [2]Rheumatology Departement, Mohamed Taher Maamouri University Hospital, nabeul, Tunisia*

Background: The septic pseudarthrosis of the humerus is a very difficult process that poses a towfold challenge: the infection eradication while trying to get consolidation.
Objectives: The aim of this study was to analyze the results of the treatment of septic pseudarthritis of the humerus with Orthofix monolateral axial external fixator.
Methods: This is a retrospective study which included 17 medical records of patients treated for septic pseudarthritis of the humerus debridement and stabilization by Orthofix over a period of 7 years.
Results: They were 13 women and 4 men with a mean age 44 years. The fracture site was most often at the distal half of the humerus. The initial treatment of the fracture was pinning or intramedullar nailing. Surgical management of pseudoarthrosis was performed 3.5 months after the first surgical procedure. All cases had a bone debridement and stabilization with a monoplane Orthofix axial external side. Fifteen cases had also a bone graft. The mean period of stabilization was 7months. Patients were evaluated clinically and radiologically each month. At the mean of three years of follow-up, we obtain osseous consolidation for all patients in the average of seven months. All patients underwent rehabilitation of the shoulder and elbow after treatment. The functional result were excellent results in 47% of cases, good results in 35,3% of cases and poor results in 17,7%. The Quick DASH score average was 28±5. The average of the elbow motion was 109 ° of flexion with an average of 30 °of deficit in extension. The useful range of motion of the elbow was preserved in 14 patients. There was a shaft angulation under 20 ° in 3 cases and over 20 ° in 3 other cases. We noted

in four cases a bone shortening consolidations of 2 cm. We had a case of radial nerve neuraprexie which regressed spontaneously.
Conclusions: Orthofix is the method of choice for the treatment of septic pseudarthritis of the humerus.
Associate eradication of the germ antibiotic and steroid intake spongy it allows the consolidation of the bone. Furthermore, the monolateral axial external fixator is tolerated well and allows movement of the shoulder and elbow throughout the period of treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3852

AB0910 INFECTIOUS SPONDYLODISCITIS IN THE SANITARY AREA OF TORRELAVEGA BETWEEN 2000 AND 2016: 62 CASES

I. Morante Bolado[1], M. Santos-Gómez[1], I. Villa Blanco[1], E. Aurrecoechea Aguinaga[1], T. Ruiz Jimeno[1], J. Calvo Alén[2]. *[1]Rheumatology, Sierrallana Hospital, Torrelavega; [2]Rheumatology, University Hospital of Araba, Vitoria, Spain*

Objectives: To analyze the clinical characteristics, most frequent diagnostic methods and different treatments used in spondylodiscitis (SD) in our sanitary area.
Methods: Descriptive and retrospective study of patients with the diagnose of infectious SD (clinical or microbiological) from 2000 to 2016. In each case we studied the presence of underlying diseases, an episode of infection in the previous 6 months, way of presentation, location, diagnostic methods, treatment and evolution, comparing among different etiologies.
Results: 62 patients were diagnosed of spondylodiscitis. 41 men (24–90 years: mean 71,7). 58 were pyogenic, 3 tuberculous (TBC) SD, and 1 candida. The patients with TBC were younger (mean age: 45.3; $p<0.05$). An underlying disease was observed in 51 patients, specially Diabetes Mellitus (DM) (31% of SD). 4 patients were Rheumatoid Arthritis patients. A previous episode of bacteriemia or a primary source of infection was identify in a 33% of the cases, obtaining a microbiological isolation in 47/62 (75.8%) SD (43 bacterial, 3 TBC and 1 Candida). The most frequent pathogens were Gram +(G+) (50% of the total SD) being S. aureus and S epidermidis responsible of 21/62 cases (33.8%). In the 94% of SD caused by G+, hemocultures positive were obtained, in comparison to a 55% of SD caused by G- (p=0.016).
The most frequent presentation symptoms were: lumbar pain (95.1%), fever (50%) and neurological deficit (18%). Leucocytosis was present in only a third of the SD, observing an increase of ESR and CRP in the pyogen etiology (p no significative for low number of patients in SD group caused by TBC) and lower levels of hemoglobin, cholesterol and albumin. Lumbar area was affected in the 77% of SD (77% in G+ and 50% in G-). In a 13% of patients, more than one intersomatic space was affected, being visible the presence of an abscess in 44/62 cases (71%). It was necessary surgical treatment in 7/44 (16%). 5 patients died due to pathology related to SD (8%), without any correlation with a risk factor and other 5 presented a relapse in the subsequent months.
Conclusions:
- the bacterial SD are the predominant group, being DM the most frequent risk factor.
- The incidence of SD due to TBC and fungi is scarce in our environment, being absent the Brucella etiology.
- The G+ SD usually have a previous associated bacteriemia.
- The majority of the patients had pain in the presentation, but only half of them had associated fever.
- The most frequent location of SD was lumbar.
- We established a 8% of mortality rate in our sanitary area.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4007

AB0911 ACUTE RHEUMATIC FEVER CASE SERIES PRESENTING WITH ARTHRITIS IN ADULTS

I. Dogan[1], O.N. Koyun[2]. *[1]Rheumatology; [2]Internal medicine, Hitit University Corum, CORUM, Turkey*

Background: Acute rheumatic fever (ARF) is an inflammatory reaction to group A hemolytic streptococcus that emerging 2–3 weeks after infection; presenting with joint, cardiac, neurological and dermatological symptoms. The incidence is reported to be 0.5–3: 100.000 in developed countries and 20–100: 100.000 in developing countries.[1] ARF is a common disease in Turkey. It is most common between the ages of 6 and 20 years. It is rare in adults and arthritis is common with carditis in adults.[2]
Objectives: Due to the ARF is rarer at adulthood, ARF-associated arthritis at adults has been reported as a case report series.
Methods: Five patients who were admitted to our rheumatology policlinic in a tertiary medical center located in Corum province, with early arthritis between 2014 and 2016 were diagnosed with ARF associated arthritis.
Results: The age of ARF associated arthritis patients ranged from 35 to 56 years (Mean age 45.6 years). Two of these patients were male and three were female. One patient has atrial fibrillation and coronary artery disease in other one as a comorbidity. All of patients had tonsillitis in the last 15 days. Two of the patients had a previous ARF story.

The results of the laboratory and the clinical findings are given in table:

Patient	Age/ Gender	Previous ARF Diagnosis	Echocardiography Findings	Arthritis	Sydhenam chorea/ subcutaneous nodule/erythema marginatum	Anti-STREPTOLYSINO Antikoru (0–200 IU/ml)
1	35/F	–	2. MI	+	–/–/–	430
2	42/M	+	mild MS	+	–/–/–	472
3	42/F	–	1–2. AI	+	–/–/–	500
4	53/F	–	mild MS 2. AI, 2. TI	+	–/–/–	320
			2. AI, 2. TI	+		
5	56/M	+	1. AI	+	–/–/–	456

F: Female, M: Male, AI: Aortic valve insufficiency, MI: Mitral valve insufficiency, MS: Mitral valve stenosis, TI: Tiricuspit valve insufficiency.

Acute rheumatic fever associated arthritis was diagnosed according to Jones criteria due to migratory arthritis, carditis findings with Echocardiography, and ASO titer elevation. The ANA, anti-CCP, RF, and Brucella agglutination tests were negative. Non-steroidal anti-inflammatory drugs, oral methyl prednisolone 16 mg per day and benzathidine penicillin G 1.2 million units per month were initiated as treatments. Methyl prednisolone dose was taperde gradually. In one patient using warfarin, depo peniciline i.m. was not given because it could be risky for hematoma. In another patient with coronary artery disease, methylprednisolone 4 mg per day was started because coronary bypass was planned. Symptoms of all patients were improved after treatment.
Conclusions: Acute rheumatic fever associated arthritis is not a common condition in adult patients,and should be kept in mind with poststreptococcal reactive arthritis in arthritis developed after upper respiratory tract infections in adults.
References:
[1] Stollerman G.H. Rheumatogenic group A streptococci and the return of rheumatic fever, Adv. Intern. Med. 35 (1990) 1–25.
[2] Ben-Dov I. Acute rheumatic fever in adults over the age of 45 years: an analysis of 23 patients together with a review of the literature. Semin Arthritis Rheum. 1980 Nov; 10(2):100–10.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2630

AB0912 ASSESMENT OF CLINICAL AND RADIOLOGICAL PROGNOSTIC VARIABLES IN PATIENTS WITH SPONDYLODISCITIS

J.J. Fragio Gil[1], R. Gonzalez Mazarío[1], M. Tasias Pitarch[2], E. Calabuig Muñoz[2], J. Ivorra Cortes[1], C.M. Feced Olmos[1], F.M. Ortiz-Sanjuan[1], E. Labrador Sánchez[1], K. Arévalo Ruales[1], E. Grau Garcia[1], I. Chalmeta Verdejo[1], L. Gonzalez Puig[1], I. Martínez Cordellat[1], R. Negueroles Albuixech[1], C. Alcañiz Escandell[1], J.E. Oller Rodriguez[1], E. Vicens Bernabeu[1], C. Nájera Herranz[1], I. Cánovas Olmos[1], D. Hervás Marín[3], M. Salavert Lleti[2], J.A. Román Ivorra[1]. *[1]Rheumatology Department; [2]Infectious Disease Unit, HUP la Fe; [3]Biostatistic Unit, IIS la Fe, Valencia, Spain*

Background: Spondylodiscitis is an infectious disease of the intervertebral space, often caused by hematological spreading from a distance septic focus, especially Endocarditis. Because of its low incidence combined with an ambiguous symptoms, delay diagnosis and treatment of this condition, raising probability of an undesirable outcome.
Objectives: To identify poor prognosis variables in patients with Spondylodiscitis
Methods: Observational retrospective study with non-quirurgic spondylodiscitis patients from 2010 to 2016 was performed. Demographic information, clinical history, laboratory test and radiological data were compiled from the clinical history management software. Statistical analysis was performed with the software R (version 3.3.2).
Results: We included 55 patients, with a mean age of 63.47 (16.11) years old. Males predominated (69%). The average time with axial pain was 64.44 (80.63) days. Mean length of hospital stay was 64.44 (80.63) days and readmission rate was 32.7%. 20% of patients required further surgical procedures. Most of patients showed high CRP levels at their admission, with an average value of 112.97 (83.64) mg/L. Underlying endocarditis proportion was 16.4% and in this patients hospital stay was significative higher; nevertheless, it was not correlated with worse prognosis. 50% of patients showed vertebral destruction on MRI; 14.8% cord compression and 20.4% of patients developed neurological complications (7 of them paraparesis). Furthermore, vertebral destruction was statistically correlated with epidural abscess (P=0.026). Isolation and microbiological identification in blood cultures was possible in 83.6% of patients. Most frequent bacteria was Gram positive (50.09%), then Gram negative (18.2%), mycobacteria (10,9%) and fungi (3.6%).
Conclusions: Delay in diagnosis is an important issue in Spondylodiscitis patients. Higher complications rates are mainly in relation to greater vertebral destruction. Underlying infectious endocarditis was described in a small proportion of patients in contrast to other studies. Presence of epidural abscess was also correlated with vertebral destruction, for this reason, patients with this finding should be more carefully follow-up.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5891

AB0913 AGREEMENT STUDY AND EXPERT CONSENSUS FOR THE CLINICAL PICTURE OF CHIKV INFECTION

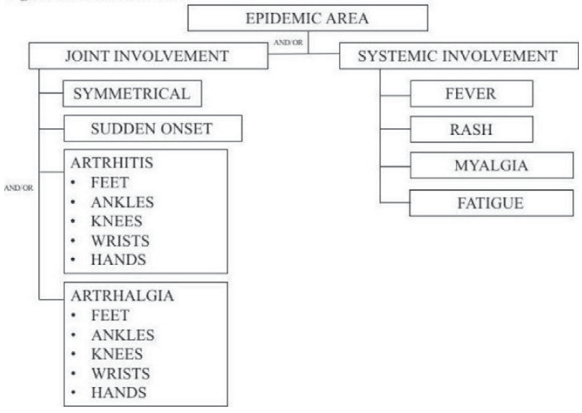
J.C. Rueda[1], J.-I. Angarita[1], C. Pinzon[2], A.M. Santos[1], E.-L. Saldarriaga[1], J.M. Rueda[3], D.L. Saaibi[4], E. Forero[5], I. Pelaez-Ballestas[6], P.X. Pavía[7], J. Londono[8]. *[1]Reumatología; [2]Departamento de Investigación Clínica, Facultad de Medicina, Universidad de la Sabana, Chia; [3]Unidad de Reumatología, Centro Médico Imbanaco, Cali; [4]Reumatología Ubit, Centro Médico Carlos Ardila Lulle, Bucaramanga; [5]Medicina Interna, Reumatología, Universidad del Norte, Barranquilla, Colombia; [6]Reumatología, Hospital General de México, México, Mexico; [7]Unidad de Investigación Científica, Hospital Militar Central; [8]Reumatología, Universidad de la Sabana-Hospital Militar Central, Bogotá, Colombia*

Background: World Health Organization suggested case definitions to suspect and diagnose chikungunya virus infection which are: possible case, probable case and confirmed case. Although useful, when applied in practice, its lack definition for specific joint involvement and absence of other systemic symptoms apart from fever, leads to a broad clinical spectrum which increases the need for laboratory tests.
Objectives: To establish agreement on clinical criteria of CHIKV infection based on clinical expertise of specialists from affected areas of Colombia and to develop a set of clinical criteria.
Methods: A group of specialists in rheumatology, epidemiology and bacteriology from different parts of Colombia with experience in diagnosis and treatment of CHIKV patients from the epidemic of 2014–2015 met to reach agreements on clinical characteristics of CHIKV infection. A series of questions were formulated and agreement in percentage was calculated on the following answers: totally agree, agree, not in agree or disagree, disagree and totally disagree. Agreement was set when the sum to the answers totally agree and agree or disagree and totally disagree of was ≥50%. When agreement was not reached, the moderator performed a discussion with the opinions of the confronting members of the group and after that reformulated the question. This procedure was made until agreement was reached. With the results a set of clinical criteria was proposed.
Results: The agreement percentage to the formulated questions are depicted in table 1. Disagreement was achieved with mucosal imvolvement (100%), G/I involvement (88%), and arthralgia and arthritis in shoulders (63% and 100%) and in elbows (100%).
Conclusions: Agreement was achieved in abrupt onset of symptoms, and the presence of fever, rash, myalgia, fatigue, and symmetrical arthritis or arthralgia of wrists, hands, knees, ankles and feet. A set of clinical criteria was proposed (figure 1).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1882

Table 1. Agreement Percentage to Formulated Questions on CHIKV Clinical Characteristics

Do you consider as clinical criteria:	Totally Agree	Agree	Not in Agree or Disagree	Disagree	Totally Disagree	Type of Agreement (Total)
Symmetrical joint involvement	100	0	0	0	0	Agree (100)
Abrupt onset of symptoms	100	0	0	0	0	Agree (100)
Fever	38	50	12	0	0	Agree (78)
Rash	13	75	0	12	0	Agree (88)
Myalgia	25	75	0	0	0	Agree (100)
Fatigue	63	25	12	0	0	Agree (88)
Arthralgia in wrists	50	25	13	0	12	Agree (75)
Arthritis in wrists	75	13	0	12	0	Agree (88)
Arthralgia in hands	88	12	0	0	0	Agree (100)
Arthritis in hands	88	12	0	0	0	Agree (100)
Arthralgia in knees	13	63	0	12	12	Agree (76)
Arthritis in knees	13	63	12	0	12	Agree (76)
Arthralgia in ankles	100	0	0	0	0	Agree (100)
Arthritis in ankles	100	0	0	0	0	Agree (100)
Arthralgia in feet	50	38	0	12	0	Agree (88)
Arthritis in feet	75	13	0	12	0	Agree (88)

Figure 1. Clinical Criteria



AB0914 CUTANEOUS LEISHMANIASIS IN PATIENTS TREATED WITH BIOLOGICAL THERAPY

J. Lluch[1], M. López de Recalde[1], X. Michelena[1], J. Marcoval[2], X. Juanola[1]. *[1]Department of Rheumatology; [2]Department of Dermatology, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*

Background: Leishmaniasis is a chronic protozoal disease endemic in several areas of the world. In the Mediterranean basin cutaneous leishmaniasis is caused by *Leishmania infantum* and usually produces localized skin lesions. Biological therapy (BT) may increase the risk of reactivation or development of infections such as tuberculosis, mycoses and protozoan diseases. However, there is scarce literature on *Leishmania* infections in patients treated with anti-TNF drugs. We have diagnosed five cases of cutaneous leishmaniasis in patients treated with anti-TNF drugs in the last four years.
Objectives: To show the clinical characteristics and the evolution of cutaneous leishmaniasis in patients treated with BT at a tertiary level hospital.
Methods: We reviewed the clinical characteristics, previous treatments, the complementary tests used for the diagnosis, the main disease, the therapy used for the treatment of the infection, the clinical evolution and the reintroduction of the BT.
Results: In the last four years we have diagnosed five cases of cutaneous leishmaniasis in patients treated with BT. Four of them were men and one a woman, the age range was 35 to 61 years old. In four of them the symptoms were only cutaneous, but one of them also had systemic impairment, basically hepatosplenomegaly. For the diagnosis skin biopsy, positive PCR for *Leishmania* DNA from skin samples, serology and response to treatment were all needed. Three cases were patients treated with adalimumab and two treated with infliximab. Three patients had Crohn's disease, one psoriatic arthritis and the other ankylosing spondylitis. The diagnostic delay was between 5 and 24 months. All patients were treated with EV liposomal amphotericin B, and two of them also received intralesional injections of meglumine antimoniate. In all cases resolution was achieved, and there have been no relapses to date after reintroduction of BT.



Conclusions: We have to consider cutaneous leishmaniasis in patients with BT who present compatible skin lesions, especially in endemic areas. It is important to be aware of this type of condition in order to make a fast and accurate diagnosis.
References:
[1] Alvar J, Vélez ID, Bern C, et al. WHO Leishmaniasis Control Team. Leishmaniasis worldwide and global estimates of its incidence. PLoS One 2012; 7:e35671.
[2] Dujardin JC, Campino L, Cañavate C et al. Spread of vector-borne diseases and neglect of Leishmaniasis, Europe. Emerg Infect Dis 2008; 14:1013–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4259

Abstract AB0914 – Table 1

Gender	Age	Disease	Biologic therapy	Time with BT	Affection	Evolution until diagnosis	Treatment	Evolution
Man	35	Crohn disease	Adalimumab	4 years	Cutaneous	12 months	Intralesional injections of meglumine antimoniate EV liposomal amphotericin B.	Resolution. Reintroduction of BT.
Woman	55	Crohn disease	Infliximab	3 years	Cutaneous	24 months	Intralesional injections of meglumine antimoniate EV liposomal amphotericin B.	Resolution. Reintroduction of BT.
Man	61	Crohn disease	Adalimumab	3 years	Cutaneous and hepatosplenomegaly	5 months	EV liposomal amphotericin B	Resolution. Reintroduction of BT.
Man	58	Psoriatic arthritis	Adalimumab	19 months	Cutaneous	8 months	EV liposomal amphotericin B	Resolution.
Man	51	Ankylosing spondylitis	Infliximab	12 years	Cutaneous	5 months	EV liposomal amphotericin B	Resolution. Reintroduction of BT.

AB0915 FREQUENT CONVERSION AND REVERSE CONVERSION OF TUBERCULIN SKIN TEST BUT NOT OF AN INTERFERON GAMMA RELEASE ASSAY (T-SPOT.TB) DURING LONG TERM BIOLOGIC TREATMENT OF RHEUMATIC PATIENTS

K. Thomas, A. Makris, C. Tsalapaki, A. Lazarini, K. Klavdianou, K. Antonatou, C. Koutsianas, C. Hatzara, E. Hadziyannis, D. Vassilopoulos. *Joint Rheumatology Program, Clinical Immunology-Rheumatology Unit, 2nd Department of Medicine and Laboratory, National and Kapodistrian University of Athens, Hippokration General Hospital, Athens, Greece*

Background: There are limited data regarding the value of tuberculosis (TB) rescreening in rheumatic patients on biologic (bDMARD) therapies who had a negative baseline TB screening.
Objectives: To examine the rates of conversion and reverse conversion at repeated TB screening testing with 2 available assays (tuberculin skin testing-TST and an interferon gamma release assay-IGRA: T-SPOT.TB) in rheumatic patients with negative baseline screening during long term bDMARD treatment.
Methods: Rheumatic patients with negative baseline screening (TST and T-SPOT.TB) were re-screened one year after TNF inhibitor (TNFi) therapy (1st rescreening) and ~6 years later on bDMARDs (2nd re-screening). The rate of conversion and reverse conversions of the 2 assays were recorded. Only patients who did not receive isoniazid (INH) therapy between the 1st and 2nd rescreening were analyzed.
Results: Among 70 patients with negative TB baseline screening, 21 patients with 2 re-screenings available were identified; one patient with TST conversion at the 1st rescreening who converted back to negative at the 2nd rescreening after INH treatment, was excluded from the study. 20 patients were finally included in the study (RA=7, PsA=6, AS=5, other diseases=2). 50% were women with a mean age of 57.1±12.4 years and mean disease duration at the last screening of 13.1±6.2 years. The mean interval between the 1st and 2nd rescreening was 68.6±13 months. At the last evaluation, 90% (18/20) were still on bDMARDs (TNFi=55%, non-TNFi=45%), 45% (9/20) on non-biologic DMARDs and only one patient (5%) on corticosteroids. None of the patients displayed conversion or reverse conversion with T-SPOT.TB compared to 6 (30%) with TST at the 2 rescreenings (p=0.02). At the 1st rescreening, 4/20 (25%) had converted their TST to positive; at the 2nd rescreening, 2 reverted back to negative (1 patient with PsA on etanercept and 1 with RA on steroids, methotrexate and golimumab) while the other 2 remained TST positive (1 with PsA on etanercept and 1 with Still's disease exposed to etanercept, tocilizumab and canakinumab). Among the 16 patients who remained TST and T-SPOT.TB negative at the 1st rescreening, 2 (12.5%) became TST positive at the 2nd rescreening (12 mm and 7 mm, respectively). Both patients were on long term infliximab treatment without history of TB exposure. After thorough evaluation, no evidence of active TB infection was found in any of the 6 patients who converted TST either in the 1st or 2nd rescreening.
Conclusions: Among rheumatic patients with negative baseline TB screening, conversion or reverse conversions were much more frequent with TST compared to an IGRA (T-SPOT.TB) at repeat testings during long term bDMARD therapy. These preliminary findings need to be taken into account while designing the appropriate repeat TB screening strategy for this group of patients.
Acknowledgements: Supported by research grants from the Special Account for Research Grants (S.A.R.G.), National and Kapodistrian University of Athens, Athens, Greece.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4582

AB0916 WHIPPLE DISEASE: A RARE DISEASE DIFFICULT TO DIAGNOSE

L. Ferrieres, L. Alric, M. Laroche, D. Bonnet, S. Thebault. *CHU Toulouse France, Toulouse, France*

Background: Whipple disease is a very rare disease needing a long term treatment. The most frequent symptoms are recurrent arthralgia or arthritis, chronic diarrhoea, abdominal pain and weight loss.
Objectives: In this work, we have highlighted the main clinical features and diagnostic procedures that lead to the diagnosis and comment on the clinical response, treatment, and the factors of relapse.
Methods: Subjects were recruited from the Internal Medicine and Rheumatologic Departments of an University Hospital from November 1997 to January 2016. Overall, 12 subjects were finally diagnosed.
Results: Mean age was 54.3 years (age range: 30–81), with more male patients (58.3%). Almost all patients had articular symptoms and impaired general condition (91.7%); and a majority had digestive symptoms (75%). Regardless of the symptoms, the most efficient diagnostic tools were the PCR screening on the gastrointestinal biopsies and saliva (83.3% and 72.7% positive results, respectively). More than half of the patients relapsed (55.6%). The relapsing patients were older (63.2 (44–81)) and mostly male with a majority (60%) of digestive symptoms and a delayed diagnosis.
Conclusions: In current practice, it is highly difficult to diagnose Whipple disease. In order to decrease the delay between the first symptoms and the diagnosis, effective tools such as saliva and stools PCR should be used since higher delays of diagnosis lead to a higher number of relapses.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6975

AB0917 SAFETEY AND EFFICACY OF DIRECT-ACTING ANTIVIRAL AGENTS FOR THE TREATMENT OF HCV IN RHEUMATIC DISEASES: CASE SERIES

M.C. Ditto[1], R. Talotta[1], S. Parisi[2], M.C. Gerardi[1], A. Batticciotto[1], F. Rigamonti[1], P. Sarzi Puttini[1], E. Fusaro[2], M. Antivalle[1]. *[1]Rheumatology Unit, Luigi Sacco Universitary Hospital, Milan; [2]Rheumatology Unit, Azienda Ospedaliera Universitaria Città della Salute e della Scienza di Torino, Turin, Italy*

Background: Until approximately 5 years ago interferon (IFN) associated with Ribavirina (RBV) was the gold standard of HCV therapy. Literature data shown that IFN could exacerbate symptoms related to the autoimmune diseases, and flares or intolerance are reported. Recent advances in antiviral therapy had completely modified the HCV infection approach. Direct acting antiviral agents (DAAs) are more efficacious, safer and more tolerable of IFN-HCV treatment.
Objectives: To show safety and efficacy of IFN-free HCV eradication in inflammatory arthritis patients with concomitant immunosuppressive treatment.
Methods: We evaluated 5 patients (M:F=4:1; median age 50±13.4), affected by inflammatory arthritis and concomitant HCV infection requiring eradication, treated with cDMARDs or bDMARDs (anti-TNFα) and DAAs. Demographic data and concomitant medications are showed in table 1.
Results: Patient 01 and 02 were affected by psoriatic arthritis with severe cutaneous and articular involvement. The first one was also under Lamivudina treatment because concomitant HBV infection and cirrhosis. Patient 03 was affected by enteropathic arthritis (RCU), treated with AZA 100 mg. Patient 04 was affected by rheumatoid arthritis and latent TBC under Nicizina 300 mg daily treatment. Patient 05 was affected by ankylosing spondylitis. Before starting DAAs he was treated with Telaprevir/Peg-IFN/RBV but during the treatment vulgar psoriasis with diffuse and severe involvement appeared. IFN-therapy was interrupted and DAAs therapy started with no flares or other adverse events.
Four patients (01, 02, 04, 05) were under anti-TNF-α treatment and 1 patient (03) was under Azatioprina treatment. During therapy with DAAS any flare of autoimmunity disease or adverse events were observed. HCV-RNA was undetectable after 3 months in 4 patients and after 6 months in 1 patient.
Conclusions: For all of patients IFN-free therapy was efficacious (blood-HCV-RNA undetectable after treatment) and safe (no adverse events). DAAs therapy could be the best choice to HCV eradication in patients affected by autoimmune rheumatic diseases treated with immunosuppressive drugs.
References:
[1] Kohtaro Ooka and Joseph K. Lim, Treatment of Hepatitis C in Patients Undergoing Immunosuppressive Drug Therapy, Journal of Clinical and Translational Hepatology 2016 vol. 4 | 206–227.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6641

Abstract AB0917 – Table 1. Demographic data and concomitant medications

Pts	Age	Diagnosis	Concomitant liver injury	Concomitant Therapy	HCV IFN-free treatment	HCV title Before	HCV title After	Duration of treatment (months)	AE/flare (n)
01	62	PA	HBV infection	INFLIXIMAB	+ Ribavirina + Declatasvir + Sofosbuvir	2110126 2110126	<12	6	0
02	52	PA	No	ADALIMUMAB	+ Ribavirina + Sofosbuvir	2235436	<12	3	0
03	61	EnA	HBV infection	AZATIOPRINA	+ Desabuvir + Ombitasvir + Paritaprevir + Ritonavir	7034701	<12	3	0
04	46	RA	No	ETANERCEPT	+R ibavirina + Sofosbuvir	2633651	<12	3	0
05	29	SA	No	ETANERCEPT	+ Ribavirina + Desabuvir + Ombitasvir + Paritaprevir + Ritonavir	2168665	<12	3	0

AB0918 REACTIVE ARTHRITIS POST VIRAL – AN UNUSUAL PRESENTATION IN AN EPIDEMIC IN NORTH INDIA

N. Mendiratta, R. Gupta, D. Rawal on behalf of Dr Dhiren Raval. *MEdanta, MEdcity, New Delhi, India*

Background: This study was performed at a Private hospital in New Delhi, India during the epidemic phase of Viral fever. The peak months of viral fever from mosquitoes (Aedes Aeygpti) like Dengue and Malaria (Anopheles)has been from July to October, till the holy festival of Diwali arrives. Chikungunya came like a wave this time along with dengue and Malaria.The worst epidemic since the last 6 years.A disease common in South India, took North India by a storm. 15–20 deaths were also reported due to Chikungunya virus. Apart from Chikungunya (serology negative) there were a lot of other viruses causing arthritis. Our study deals with post viral arthritis, a new variant which has never been described before.
Objectives: 1. To study the pattern of arthritis after viral fever. Is it reactive or a new variant
2. To observe for the evolution of Acute viral arthritis into chronic arthritis
3. The management of Post viral arthritis
Methods: It is a retrospective study conducted at the end of the epidemic. The patients are being followed up over next 3 months to observe for resolution of symptoms, persistent arthritis or evolution into chronic form. 100 patients are being included which were examined and independently assessed by 3 different consultants.
Inclusion criteria: 1. All patients who presented with complaints of persistent joint pains and swelling preceded by fever (Average duration 4–8 weeks). 2. Documented synovitis (Oligoarticular and polyarticular)
Exclusion criteria: 1. Known case of Rheumatoid Arthritis, Connective tissue disease, Vasculitis and Spondyloarthopathy 2. Arthalgia with no documented synovitis 3. Patients on DMARDS previously
Results: Detailed results are still under compilation as patients are under follow up (6 months) for further course.
No of patients: 100
Average Age: 47
Average Disease Duration: 6 weeks (after fever)
Average No of Joints involved: 3–4
Symmetry: All Asymmetrical (Large+ Small)
80% patients had asymmetrical joint involvement. Most common joints were: MCP followed by PIP and then the large joints: shoulders and ankles. It was associated with significant early morning stiffness (30 minutes) like other inflammatory arthritis. 60% had response to short course of NSAIDS and low dose steroids (Injection Depomedrol 80 mg intramuscular once a week) and recovered in 2 weeks, 30% had a prolonged course of 4–6 weeks, butdid not need any further medications. 5% developed into Chronic arthritis (Further follow up pending)
Conclusions: Reactive arthritis is a known entity and it has typical involvement of the lower limbs, usually preceded by urinary tract infection or GI infection. Even with Viral arthritis, the presentation of joint pains and swelling is usually during the acute fever episode. The pattern described here was different. All the patients had fever at presentation which lasted for 3–5 days and 4–6 weeks later they developed synovitis. There was characteristic involvement of Small joints of the hands (PIP and MCPS) (different from reactive).We are still in process of collecting follow up data which will give us a clue on prognosis of this arthritis and future prospects. So, what do we label it as ... Reactive arthritis-a new variant or a post viral arthritis.
References:
[1] Varache S, Narbonne V, Jousse-Joulin S, et al. Is routine viral screening useful in patients with recent-onset polyarthritis of a duration of at least 6 weeks? Results from a nationwide longitudinal prospective cohort study. Arthritis Care Res 2011;63:1565–70.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1168

AB0919 THE PROGNOSTIC FACTORS DURING OSTEOARTICULAR TUBERCULOSIS

O. Saidane [1], M. Sellami [1], S. Cheikhrouhou [2], I. Mahmoud [1], R. Tekaya [1], L. Abdelmoula [1]. *[1]Rheumathology; [2]Parasitology, Charles Nicolle Hospital, Tunis, Tunisia*

Background: Osteoarticular tuberculosis (OAT) is still common in Mediterranean countries such as Tunisia.The incidence of OAT is increasing, mainly related to expanding immunosuppressive factors and comorbidities.
Objectives: This study aimed to analyze the prognostic factors and therapeutic outcomes of OAT.
Methods: Over a period of 20 years [1996- 2016], patients with the diagnosis of OAT were retrospectively identified. Clinical, laboratory and radiology features in these patients were analyzed to identify the prognostic factors.
Results: Sixty patients (29 men) fulfilled the diagnostic criteria, admitted to the Rheumatology Service with an average of 54 years (range: 16 to 86).We did not find any significant association between prognosis and an advanced age (>60years) at the time of diagnosis, a long diagnostic delay or initial neurologic involvement.However, we found that cervical localization in tuberculous spondylodiscitis, classified as an only infection site or in multi-level vertebral damage, was significantly associated to a poor prognosis.Our study revealed that hyperleucocytosis higher than 11500 elements/mm^3 at the initial blood count constituted the only biological bad prognostic factor during OAT. Based on radiological findings, the presence of abscess or vertebral compression fractures on bone imaging (MRI)and the presence of vertebral deformity (kyphosis or kyphoscoliosis) were strongly linked to a bad outcome.The following table (Table1) summarizes the poor prognostic factors during OAT.

Table 1. The poor prognostic factors during OAT

PROGNOSTIC FACTOR	p	Odds Ratio
White blood cell counts >11500 elements/mm^3	0,041	22
Presence of abscess on MRI	0,024	13
Presence of vertebral compression fractures	0,018	Indefinite
Vertebral deformity	<0,001	Indefinite
Cervical localization	0,033	15
Age>60years	0,078	–
Long diagnostic delay	0,062	–
Initial neurologic damage	0,053	–

Conclusions: This study revealed that cervical localization in tuberculous spondylodiscitis, initial hyperleucocytosis, and the presence of abscess on MRI as well as vertebral compression fractures and vertebral deformity are associated with a bad outcome in OAT.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2997

AB0920 TUBERCULOSIS OSTEOMYELITIS OF THE PUBIC SYMPHYSIS: REPORT OF TWO CASES

R. Sonia, S. Boussaid, I. Abdelkafi, S. Hela, C. Ilhem, E. Mohamed. *Rheumatology, la Rabta, Tunis, Tunisia*

Background: Infection of the symphysis pubis is a rare complication for less than 1% of cases of osteomyelitis. The predisposing causes reported are pelvic surgery, trauma and intravenous drug abuse. We report cases of osteomyelitis of the pubic symphysisdue to mycobacterium tuberculosis which is extremely
Results: The two patients were 47 and 75 year-old women. They were admitted because of three month's history of progressive perineal pain and a hypogastric mass without fever in the first case, and bilateral inguinal pain with limited flexion and rotation of the right hip in the second one. Blood tests showed an elevated erythrocyte sedimentation rate (ESR) of 27 mm and 75 mm. The leucocytes rates were at 5580/mm^3 and 6000/mm^3. Plain X-ray revealed irregularity and widening of the symphysis pubis. Tuberculin skin test was positivein one case and negative in the other. Chest radiograph was normal. The bacteriological cultures for tubercule bacillus in sputum and urines negative. The typhic and brucellian serological diagnosis as well as blood cultures were negative. CT scan showed irregular destruction and erosion of the pubic bone with a soft tissue mass. A biopsy of the symphysis was performed. Histologic examination of the bone material revealed a granulomatous inflammation with caseous necrosis confirming the diagnosis of tuberculosis. Anti-tuberculous treatment was prescribed and led to full recovery.
Conclusions: Tuberculosis is a major health problem in mediterranean countries,including Tunisia. These two cases present a timely reminder that tuberculosis should always be considered as part of the differential diagnosis of treatment of tuberculosis osteomyelitis of the pubic symphysis. Radiological investigations with plain X-rays, CT, MRI and bone scan are hepful. Treatment of tuberculous osteomyelitis of the pubic symphysis is based mainly on anti-tuberculous drugs.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6940

AB0921 INFECTIOUS SPONDYLODISCITIS: EPIDEMIOLOGICAL, CLINICAL, PARACLINICAL AND THERAPEUTIC ASPECTS

A. Feki, R. Akrout, I. Sellami, M. Ezzeddine, H. Fourati, S. Baklouti. *Hedi Chaker Hospital, -Sfax, Tunisia*

Background: Spondylodiscitis is an infection of a disc and the two adjacent vertebrae due to the introduction of a pyogenic, usually by the haematogenous route. It's quite a rare disease accounting for 2–7% of all cases of septic osteomyelitis [1, 2].
Objectives: To study the clinical, microbiological, radiological, therapeutic and evolving of infectious spondylodiscitis
Methods: A retrospective descriptive study conducted over years in the department of rheumatology, including all patients with infectious spondylodiscitis. Clinical given were collected from paper patients records.
Results: We included 67 patients. There were 38 men and 29women. The mean age was 55 years. The male to female ratio was 38:29.Risk factors of spondylodiscitis were observed in 19 patients. The approximate time from onset of symptoms to diagnosis was from 3 to 365 days (median, 132 days). Back pain was the most common symptom. Spinal syndrome was found in all patients. The most frequent location of spondylodiscitis was lumbar spine. Signs of spinal cord compression including paraplegia or paraparesis of the lower limbs were observed in 31 patients. Pachymeningitis was associated in 1

case. The paravertebral abscess was associated to the disc involvement in 23 cases. Epiduritis was associated in 21 cases. Plain radiography, performed in in the majority of cases (63 cases, 94%), demonstrated pathological pictures in 56 (83.5%) patients. MRI, performed in 60 (89.5%) patients, disease was in all patients. Pathogens were isolated in 43 (64.1%) cases. Tuberculosis was the most common cause. The leading causative agents in non tuberculousspondylodiscitis were: Staphylococcus aureus (8 isolates, 11.9%), brucella (7 isolates, 10.4%), Escherichia coli (2 isolates, 2.9%) and streptococcus B (1 isolates, 1.4%).Two microorganisms combined (mycobacterium tuberculosis and a pyogenic) was found in one case. Medical treatment was adapted to the prescribed seed. Surgical treatment was performed in 6 patients. After therapy, 59 (88%) patients had regression of symptoms, two patients had a permanent neurological impairment (paraplegia), one patient had recurrence of infection and one patient was dead.

Conclusions: Infectious spondylodiscitis has been diagnosed with increasing frequency. It should be taken into consideration in differential diagnosis in patients with significant back pain and laboratory evidence of an acute inflammatory process, especially metastatic spinal disease or inflammatory spondyloarthritis

References:

[1] Zimmerli W. Clinical practice.Vertebralosteomyelitis. N Engl J Med 2010 Mar; 362(11):1022–9.

[2] Cottle L, Riordan T. Infectious spondylodiscitis. J Infect 2008 June;56(6): 401–12.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6916

AB0922 CLINICAL MANIFESTATIONS AND OUTCOMES OF ACUTE SEPTIC ARTHRITIS IN SONGKLANAGARIND HOSPITAL: A 10-YEAR RETROSPECTIVE STUDY

T. Yaowmaneerat, D. Aiewruengsurat. *Internal Medicine, Prince of Songkhla University, Hadyai, Songkhla, Thailand*

Background: Septic arthritis is a rheumatologic emergency. Its delayed diagnosis and treatment cause joint morbidity and mortality.[1] Cases involving antimicrobial-resistant bacteria have been reported.[2,3]

Objectives: To determine the clinical manifestations and outcomes of septic arthritis, find the factors associated with mortality, and discover the incidence of drug-resistant organisms in our institution

Methods: A retrospective study was performed. Septic arthritis was defined as the presence of acute inflammatory arthritis indicated by a positive synovial fluid or synovial tissue culture for bacteria. A total of 116 septic arthritis patients, who visited Songklanagarind Hospital from January 2005 to December 2014, were reviewed.

Results: The patient median age was 58 (IQR: 46, 72). Sixty-one patients (52%) were female. The median onset of symptoms and symptoms until diagnosis were 5 (IQR: 2, 7) and 6 (IQR: 3, 10) days, respectively. Eighty-eight cases (76.7%) had underlying diseases that might predispose to joint infection. Sixty-nine cases (59.5%) had pre-existing joint disease. Joint pain was the most common presenting symptom, and 58% of the cases had fever. The most common presentation was monoarthritis (87%), which was predominantly associated (78%) with knee joint involvement. The median synovial fluid leukocyte counts were 64,460 cells/μL (IQR: 30,300; 129,000). Blood cultures were positive in 53 patients (49.1%). Synovial fluid cultures commonly had *Streptococcus spp.* growth (41%). Seven cases (7%) involved drug-resistant organisms. All of them either were diagnosed with septic arthritis during hospitalization or had a history of previous surgery. Twenty-five percent of the cases obtained the empirical antibiotic, ceftriaxone, and 86 patients (80%) underwent arthrotomy drainage. The mortality rate was 12%, and its associated factors were cancer, liver disease and advanced age.

Conclusions: *Streptococcus spp.* is an emerging cause of septic arthritis in Southern Thai patients. Physicians should be aware of this in patients presenting with fever and acute monoarthritis, particularly those with comorbidities and underlying joint diseases. The proper empirical antibiotic of choice is ceftriaxone.

References:

[1] Garcia-Arias M, Balsa A, Mola EM. Septic arthritis. Best practice & research Clinical rheumatology. 2011;25(3):407–21.

[2] Frazee BW, Fee C, Lambert L. How common is MRSA in adult septic arthritis? Annals of emergency medicine. 2009;54(5):695–700.

[3] Chao CM, Lai CC, Hsueh PR. Bacteriology of septic arthritis at a regional hospital in Southern Taiwan. Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi. 2013;46(3):241–2.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1737

Fibromyalgia

AB0923 MEETING THE FIBROMYALGIA CRITERIA HAS A NEGATIVE IMPACT ON TNF INHIBITORS EFFICACY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

A. Dantu[1,2], J. Michaud[2], M. Gauthier Prieur[1], F. Da Silva[1], S. Pouplin[2], T. Lequerre[2], O. Vittecoq[2], M. Verdet[1]. *[1]Rheumatology, Elbeuf Louviers Val de Reuil Hospital, Saint Aubin les Elbeuf; [2]Rheumatology, Rouen University Hospital, Rouen, France*

Background: Fibromyalgia and spondyloarthritis can coexist and the overlap between the two diseases could have consequences on TNF inhibitors efficacy.

Objectives: To evaluate TNF inhibitors efficacy in patients with axial spondyloarthritis fullfilling or not fibromyalgia criteria.

Methods: Prospective observational bicentric study on 25 patients who met ASAS 2009 axial spondyloarthritis criteria. Fibromyalgia was defined by ACR 2010 fibromyalgia criteria or by a ≥5/6 score of the Fibromyalgia Rapid Screening Tool. Following items were recorded before and after a 6 months treatment with TNF inhibitors: Visual Analog Scale for pain and for patient global disease activity, values of ESR and CRP, number of tender joints, MASES score, number of Yunus tender points. All patients filled a self-questionnaire with BASDAI, BASFI, FiRST and ACR 2010 fibromyalgia scale items using SSS and WPI. Criterion of judgment: an ASAS partial remission state was compared in patients with or without fibromyalgia.

Results: Of the 25 patients enrolled, 15 (60%) fulfilled ACR 2010 fibromyalgia criteria and 9 (36%) had a ≥5/6 FiRST score. The proportion of patients fulfilling an ASAS partial remission state was significantly lower in patients with fibromyalgia according to the ACR 2010 criteria (20% vs 70%, p=0,034) or to the FiRST score (0% vs 62,5%, p=0,0028). These patients had more severe disease activity and physical fonction than the patients without fibromyalgia. In this study, some factors were related with absence of ASAS partial remission: female gender, prior TNF inhibitor failure, ACR 2010 fibromyalgia criteria positivity, to have more than 11 Yunus points and to have a ≥5/6 FiRST score.

Conclusions: Meeting the fibromyalgia criteria might have an impact on ASAS partial remission state and on efficacy of TNF inhibitors in patients with axial spondyloarthritis. The FiRST score was more specific to predict an absence of ASAS partial remission than the ACR 2010 fibromyalgia criteria. TNF inhibitors should be used with circumspection in case of FiRST score ≥5/6 in patients with axial spondyloarthritis.

References:

[1] Perrot S., Bouhassira D., Fermanian J., the CEDR (2010) Development and validation of the Fibromyalgia Rapid Screening Tool (FiRST). Pain 150(2):250–256.

[2] Wolfe F., Clauw DJ., et al. (2011) Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia. J Rheumatol 38:1113–1122.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4310

AB0924 THE ROLE OF SELF LIMITING BEHAVIOUR, DEPRESSION AND SLEEP IN THE SEVERITY OF FATIGUE IN PATIENTS WITH FIBROMYALGIA

M. Fernandes[1], M.P. Guzzo[2], C. Iannuccelli[2], L. Mallia[1], F. Lucidi[3], M. Di Franco[2], C. Violani[1]. *[1]Department of Psychology; [2]Department of Internal Medicine and Medical Specialties; [3]Department of Developmental and Social Psychology, "Sapienza" University, Rome, Italy*

Background: Fatigue and sleep disturbances are prominent symptoms in Fibromyalgia (FM) and significantly affect the level of the patients' impairment. Some studies reported a synergic interaction of depression and poor sleep quality associated with fatigue (e.g. [1]); while Marques et al. [2] showed a significant association of the fatigue severity with a limiting behaviour self-regulatory style of the patients, i.e. reducing daily activities and excessive resting.

Objectives: The purpose of this cross-sectional study was to analyse the predictors of severity of fatigue in Italian patients with FM.

Methods: Outpatients with a FM diagnosis who fulfilled both ACR/EULAR 1990 and 2010 criteria [3,4], after a medical visit at the Fibromyalgia center at Sapienza University Hospital "Umberto I", were invited to participate in a study on their cognitions and behaviours wearing for one week a wrist actigraph (AMI Motionlogger Watch). Actigraphic sleep parameters were averaged over six days. After 7 days the participants returned the actigraph and answered a structured interview conducted by a trained psychologist which included validated scales measuring depression (Brief Symptom Inventory [5]), perceived fatigue (Checklist of Individual Strength [6]), sleep habits (Sleep Disorder Questionnaire [7]) and behaviour regulation patterns (All-or-nothing and Limiting behaviour scales from Behavioural Responses to Illness Questionnaire [8]). In the previous month and during the study, pharmacological and non-pharmacological treatments were unchanged.

Results: Actigraphic monitoring and structured interview were completed by 39 female FM patients, with a mean age of 44.9 years (SD=8.55) and an illness mean duration of 6.5 years (SD=5.72). The majority of the patients reported insomnia complaints, and 29 (74.4%) met the DSM criteria for chronic insomnia. Fatigue severity resulted as the best subjective measure of fatigue, and was positively and significantly correlated with self-management through limiting behaviour, and with Total Time in Bed (TTB) measured through actigraphy. The correlation between TTB and Total Time Slept (TTS) and depression were not significant. Hierarchical regression considering TTB, Depression and Limiting behaviour, showed that all these variables give a significant independent contribution to the prediction

of perceived severity of fatigue (47% of variance): limiting behaviour (β=0.52, p<0.01), TTB (β=0.31, p<0.05), Depression (β=0.29, p<0.05).
Conclusions: These correlational findings suggest that self-regulation through limiting activity should be given priority attention in cognitive behavioural interventions aimed at reducing subjective fatigue.
References:
[1] Nicassio et al. Pain 2002;100:271–9.
[2] Marques et al. Int J Behav Med 2013;20:229–38.
[3] Wolfe et al. Arthritis Rheum 1990.
[4] Wolfe et al. Arthritis Care Res (Hoboken) 2010;62:600–10.
[5] Derogatis et al. Pearson; 1993.
[6] Beurskens et al. Occup Environ Med 2000;57:353–7.
[7] Violani et al. Brain Res Bull 2004;63:415–21.
[8] Spence et al. Psychol Med 2005;35:583–93.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5762

AB0925 GENDER DIFFERENCE IN FIBROMYALGIA: COMPARISON BETWEEN MALE AND FEMALE PATIENTS FROM AN ITALIAN MONOCENTRIC COHORT

M.P. Guzzo[1], C. Iannuccelli[1], M.C. Gerardi[2], B. Lucchino[1], G. Valesini[1], M. Di Franco[1]. *[1]Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Rome; [2]Unità di Reumatologia, ASST-Fatebenefratelli Sacco – Polo Universitario, Milan, Italy*

Background: Fibromyalgia (FM) is one of the main causes of chronic widespread pain (CWP). It is characterized by CWP, which is the cardinal symptom, and the presence of more than 11 tender points (hyperalgesia). [1] Other symptoms such as fatigue, sleep disturbances, difficulties with memory and concentration, irritable bowel syndrome, headache, depression are frequent. Worldwide mean prevalence of FM is 2,7% with female/male ratio of 4:1. In Italy the prevalence is 3,7% with the same female/male ratio. [2]
Objectives: The aim of the study is to analyze clinical features of a cohort of male patients with CWP and to evaluate gender differences in patients diagnosed as FM.
Methods: The study population consisted of 101 consecutive male subjects referred to the Clinic for the Diagnosis and Therapy of Fibromyalgia, in the period between January 2007 and October 2016, matched with a control group of 101 females with CWP referred to the clinic in the same period. Complete clinical evaluation was performed in all patients.
Results: Ninety-seven male subjects (96%) were referred to the clinic for a history of musculoskeletal pain, among these 53% reported fatigue and 60% complained about sleep disorders. A stressful trigger (work or family problems, bereavement, infections) at the onset of pain was reported by 42% of patients. Fifty-two percent of patients reported mood changes. Physical examination showed hyperalgesia in 15% of the subjects and a mean tender points' (TP) count was 4.6 (range 0–18). The diagnosis of FM was performed according to ACR 1990 criteria, since the enrollment included patients referred to the clinic before the publication of the latest ACR criteria [3, 4]. Only 18 male subjects (18%) fulfilled the classifying criteria. In the female group CWP was reported by 97%, fatigue by 65%, and sleep disorders by 72% of patients. Stressful events were reported by the 50% of female population. Mood changes were described by 54% of female subjects and were predominantly depressive. Physical examination revealed hyperalgesia in 48 subjects (47%) and the mean TP count was 11 (range 0–18). The diagnosis of FM was confirmed in 60% of subjects. Comparing the two cohorts of patients with FM, mean age at the time of the visit and mean age of onset of symptoms resulted significantly higher in females than in males (p=0.02 and p=0.04 respectively). There was no statistically significant difference in the number of TP, in fatigue, sleep and mood disorders and in the percentage of stressors considered as a trigger for the disease. Hyperalgesia was the only feature more common in females than in males (p=0.03).
Conclusions: The significant higher frequency of hyperalgesia in women suggests a different presentation of CPW, that is the cornerstone of FM, in the two sexes. Moreover, the prevalence of FM was higher in females than in males when 1990 ACR criteria were used. It can be assumed that further gender differences could be showed applying 2010 ACR criteria.
References:
[1] Wolfe et al,1990.
[2] Queiroz LP, 2013.
[3] Wolfe et al, 2010.
[4] Wolfe et al, 2011.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4839

AB0926 AUTONOMIC DYSFUNCTION IN FIBROMYALGIA MAY BE MEDIATED BY HYPERMOBILITY SYNDROME

D. Aslanyan[1], Z. Cipinova[2], N.A. Harrison[1], H.D. Critchley[1], K.A. Davies[1], J.A. Eccles[1]. *[1]BSMS; [2]BSUH, Brighton, United Kingdom*

Background: Neuropsychiatric symptoms are common in Fibromyalgia (FMS). FMS is associated with dysautonomia, particularly orthostatic intolerance, in which there is a phenomenological overlap with anxiety. FMS and dysautonomia are both associated with joint hypermobility (JHS).
Objectives: To investigate whether signs and symptoms of dysautonomia in FMS are mediated by JHS.
Methods: Eighteen patients with FMS (all female; mean age 41.06 years) and 19 controls (14 female; mean age 46.42 years) were recruited. JHS was assessed by Brighton Criteria. Multi-systemic symptoms suggestive of dysautonomia were quantified using Autonomic Symptoms and Quality of Life Scale (ASQoLS). Neuropsychiatric symptoms were formally quantified including anxiety level (BAI), depressive symptom level (BDI), panic disorder symptom severity (PDSS) and dissociative experiences (DES). All participants underwent autonomic function testing (9 minute tilt table with heart rate (HR) recording).
Statistical comparison between groups was performed using independent samples t test and chi squared as required, correlations were explored using pearson or spearman rho as appropriate. Formal mediation analysis was performed using the method of Baron and Kenny (1), which stipulates that a mediator variable must reduce the statistical relationship between the independent and dependent variable.
Results: FMS patients had significant objective features of dysautonomia including higher baseline HR (p=.001) and maximal HR during tilt (p=.002) compared to controls and reported significantly higher autonomic symptom burden (p=.001). Symptoms correlated with changes in physiology during autonomic challenge in patients (r=.536, p=.039), but not controls. Across the study anxiety score correlated with absolute change in pre-tilt and average HR during tilt (r=.483, p=.050) and symptoms of dysautonomia (r=.813, p=.001). Dysautonomia symptoms correlated with DES (r=.793, p=.001), PDSS (r=.742, p=.001), interoceptive sensibility (r=.627, p=.007) and BDI (r=.502, p=.040). There was a significant association between JHS and FMS (p=.001), but not generalized joint laxity. Across all participants, dysautonomia symptoms correlated with Beighton score (r=.353 p=.032) and JHS participants reported higher heart rates during autonomic challenge (p=.002) and greater symptom burden (p=.001). The significant relationship between autonomic symptoms and maximum HR during tilt was fully mediated by presence of JHS or FMS (Figure 1). JHS partially mediated the relationship between FMS and increased anxiety scores and fully mediated the relationship between FMS and maximum HR during tilt (Figure 2).

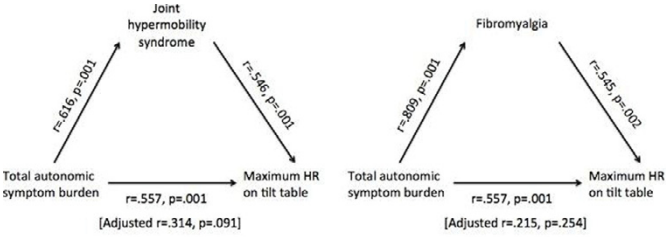


Figure 1: The significant relationship between autonomic symptoms and maximum HR during tilt was fully mediated by presence of JHS or FMS

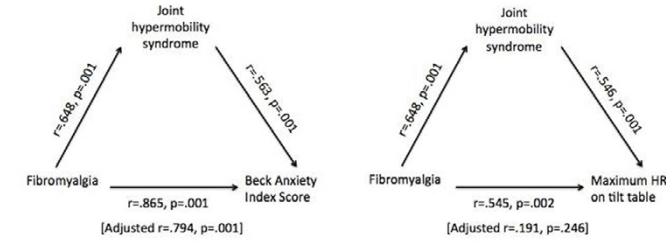


Figure 2: JHS partially mediated the relationship between FMS and increased anxiety scores and fully mediated the relationship between FMS and maximum HR during tilt

Conclusions: This study confirms that objective and subjective measures of dysautonomia are more common in FMS, and associated with JHS in this cohort, suggesting a common underlying mechanism which requires further exploration. We highlight the importance of assessing patients with FMS for both JHS and dysautonomia, which may inform further management of this often challenging condition.
References:
[1] Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. J Pers Soc Psychol. 1986 Dec;51(6):1173–82.
Acknowledgements: This work was supported by a MRC CRTF to JAE and supported by BSUH NHS Trust NIHR Clinical Research Facility.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5048

AB0927 RELIABILITY AND VALIDITY OF TURKISH VERSION OF FIBROMYALGIA PARTICIPATION QUESTIONNAIRE

L. Altan[1], R. Çeliker[2], I. Ercan[3], M. Birtane[4], K. Akgün[5], C. Zateri[6], N. Taştekin[7], A. Rezvani[8], I. Aktaş[9], S. Özdolap[10], E. Dursun[11], N. Dursun[11], S. Sarıkaya[10]. *[1]Physical Medicine and rehabilitation, Uludağ University Medical Faculty, Bursa; [2]Physical Medicine and rehabilitation, Acibadem University, Faculty of Medicine, Istanbil; [3]Uludağ University Medical Faculty, Bursa; [4]Trakya University, Faculty of Medicine, Edirne; [5]Istanbul University, Cerrahpaşa Faculty of Medicine, Istanbul; [6]Physical Medicine and rehabilitation, Canakkale Onsekiz Mart University, Faculty of Medicine, Çanakkale; [7]Physical Medicine and rehabilitation, Trakya University, Faculty of Medicine, Edirne; [8]Physical Medicine and rehabilitation, Bezmialem University, Faculty of Medicine; [9]Physical Medicine and rehabilitation, Fatih Sultan Mehmet Teaching and Research Hospital, Istanbul; [10]Physical Medicine and rehabilitation, Bulent Ecevit University, Faculty of Medicine, Zonguldak; [11]Physical Medicine and rehabilitation, Kocaeli University, Faculty of Medicine, Kocaeli, Turkey*

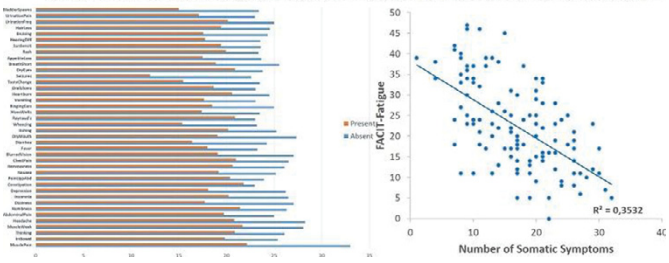
Background: Fibromyalgia (FMS) is a chronic health problem characterized by a wide range of physical and psychological symptoms. There are few high-quality instruments to evaluate the participation and social functioning of fibromyalgia patients. Farin et al. designed the Fibromyalgia Participation Questionnaire (FPQ) as an instrument for measuring the participation and social functioning of FMS patients. The original version of FPQ has been demonstrated to have acceptable internal consistency, reliability and criterion validity.
Objectives: To test reliability and validity of Turkish version of Fibromyalgia Participation Questionnaire (FPQ-T)
Methods: One hundred and eighty-four female fibromyalgia syndrome patients were included in the study. All patients filled FPQ-Turkish (FPQ-T) questionnaire which was obtained by translation from German according to the guideline for the cross-cultural adaptation process.
The patients filled the revised Fibromyalgia Impact Questionnaire (FIQ) and reevaluated FPQ-T two hours later. Internal consistency reliability of FPQ-T was assessed by calculating "if item deleted" using Cronbach alpha and "item-total correction" coefficient for each item of the questionnaire. Consistency of sub-scales and correlation of test-retest values were assessed. Test-retest values were compared using Wilcoxon test. Criterion validity was measured using FIQ scales by Spearman's rho correlation coefficient.
Results: For internal reliability, Cronbach alpha coefficient was calculated as 0.957 for non-working and 0.958 for working patients. Cronbach alpha values of 0.939, 0.871, and 0.914 were obtained for daily, social, and work life, respectively. Correlation coefficients were 0.888 for daily life, 0.859 for social life, and overall 0.901 in non-working group versus 0.896 in working group. Comparison of scores obtained from test-retest measurements showed no significant difference except for Item-3. Correlation of symptom severity score (SSS) and FPQ-T were r=0.385 ($p<0.001$) and r=0.390 ($p<0.001$) for the non-working and working sub-groups, respectively. Construct validity evaluation showed significant correlation between SSS and FPQ-T.
Conclusions: The results of our study showed that FPQ-T is reliable and valid for assessing participation and social functioning in fibromyalgia patients in our society.
References:
[1] Williams DA, Clauw DJ (2009) Understanding fibromyalgia: Lessons from the broader pain research community. J Pain 10:777–791.
[2] Farin E, Ullrich A, Hauer J (2013) Participation and social functioning in patients with fibromyalgia: development and testing of a new questionnaire. Health Qual Life Outcomes 11:135.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1710

AB0928 FATIGUE IN FIBROMYALGIA REFLECTS OVERALL BURDEN OF DISEASE

M. Antivalle, A. Batticciotto, F. Rigamonti, M.C. Ditto, M.C. Gerardi, R. Talotta, A. Mutti, P. Sarzi-Puttini. *Rheumatology, L. Sacco University Hospital, Milano, Italy*

Background: Fatigue in fibromyalgia is a very common and disabling symptom, being reported by over 75% of patients. However, the relationship between fatigue and the different manifestations of fibromyalgia has not been convincingly elucidated.
Objectives: Aim of the our work was to study the relationship between fatigue, pain, and somatic symptoms in fibromyalgia.
Methods: 123 patients with fibromyalgia classified according to 2010 criteria were studied, 113 Females and 10 Males, mean age 47.41±11.21 years, mean disease duration 6.83±6.52 years. Fatigue was assessed by FACIT-Fatigue questionnaire (13 items, score 0–52, higher values representing less fatigue), and results were correlated to the number of Tender points (TP), to Widespread Pain Index (WPI), to Symptom severity Scale (SSS), and to Polysymptomatic Distress Scale (PDS) values. Correlations were computed by parametric or non parametric methods as appropriate.
Results: Average FACIT-Fatigue score (22.51±10.6) was lower than the 25th percentile of the general population (35), and was not correlated to age or to disease duration ($p>0.05$). FACIT-Fatigue showed statistically significant inverse

Fig. 1. Left panel: FACIT-Fatigue score according to the presence or absence of individual somatic symptoms. Right panel: Correlation between FACIT-Fatigue score and the number of reported somatic symproms.



correlations with the number of tender points (r = -.303, p=0.001), WPI score (r=-0.329, $p<0.001$), SSS score (r=-0.651, $p<0.001$), PSD score (r=-0.522, $p<0.001$), and with the total number of somatic symptoms (r=-0.594, $p<0.000$) (Fig. 1, right panel). Furthermore, for each of the 40 somatic symptoms suggested by 2010 criteria, the presence of the symptoms was associated with higher levels of fatigue (Fig 1, left panel).
Conclusions: The results of our study confirm that fatigue is a prominent feature of fibromyalgia. Higher levels of fatigue reflect higher levels of widespread pain, and a higher burden of somatic symptoms.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6534

AB0929 BALANCE IN FIBROMYALGIA IS NOT RELATED WITH LOWER LIMB STRENGTH

P. Serra-Añó, M. Aguilar-Rodríguez, S. Cortés-Amador, G.V. Espí-lópez, N. Sempere-Rubio. *Physical Therapy, University of Valencia, Valencia, Spain*

Background: Postural control, that depends on many sensory contributors and motor skills, is altered in people with fibromyalgia (FM) [1–3]. Knowing those contributors that could be impaired in this population is important to design an appropriate balance therapy.
Objectives: Due to the fact that people with FM use to present a strength loss [7], our main goal was to explore the relation between postural control and lower limb strength in this population. Further, the sensory inputs contributors to the postural control were assessed.
Methods: A cross-sectional study was conducted in a sample of 40 FM patients. A force platform was used to assess postural control under five bipedal conditions: i) eyes-open (EO); ii) dual task (recalling a typical day in their life) (DT); iii) eyes-close (EC); iv) eyes-open over a foam (FEO); v. eyes-close over a foam (FEC). Three variables, "Ellipse", "RMS" and "Sample Entropy" (SampEn), were recorded (for both directions). Further, maximal quadriceps (qdc) and hamstring (hmsg) isometric strength were assessed using a dynamometer. Spearman correlations were conducted to establish the relationship between postural control and strength and a repeated-measures MANOVA, to analyze differences between conditions.
Results: When EO and DT (performed with eyes open) were compared, no significant differences were obtained. However when patients closed their eyes, an increase in ellipse and RMS_AP and a decrease in variability were obtained. The same was true when the tests were performed over a foam (altering proprioception), Table 1.

Table 1. Comparison of sensory inputs results

	Ellipse (mm^2)	RMS_AP (mm)	RMS_ML (mm)	SampEn_AP	SampEn_ML
EO	295.66 (460.93)	5.58 (3.66)	2.46 (2.30)	0.74 (0.14)	0.90 (0.10)
DT	388.92 (530.23)	5.77 (4.22)	2.79 (2.18)	0.67 (0.15)	0.86 (0.13)
EC	508.18 (801.69)[1]	6.77 (3.94)[12]	3.08 (2.04)	0.65 (0.15)[1]	0.85 (0.14)[1]
FEO	815.32 (981.44)[123]	7.63 (4.19)[12]	4.81 (3.04)[123]	0.61 (0.14)[12]	0.79 (0.10)[123]
FEC	1425.54 (1291.53)[1234]	10.87 (4.20)[1234]	6.48 (2.95)[1234]	0.53 (0.11)[1234]	0.69 (0.13)[1234]

EO: eyes-open; DT: dual task; EC: eyes-close; FEO: Eyes-open over a foam; FEC: Eyes-close over a foam; Superscript 1, 2, 3, 4: Significant differences with test 1, 2, 3 and 4, respectively ($p<0.05$).

Furthermore, no significant correlations ($p>0.05$) were observed between strength and balance except for a weak significant correlation between hmsg strength and RMS_AP ($r_s=-0.33$, $p<0.05$) in the EC test.
Conclusions: Postural control worsens in FM people when some sensory inputs are altered or missed. Further, there is no correlation between lower limb strength and balance in this population.
References:
[1] Akkaya N, Akkaya S, Atalay NS, Acar M, Catalbas N, Sahin F. Assessment of the relationship between postural stability and sleep quality in patients with fibromyalgia. Clin Rheumatol. 2013;32(3):325–331.
[2] Jones KD, King LA, Mist SD, Bennett RM, Horak FB. Postural control deficits in people with fibromyalgia: a pilot study. Arthritis Res Ther. 2011;13(4):R127.
[3] Russek LN, Fulk GD. Pilot study assessing balance in women with fibromyalgia syndrome. Physiother Theory Pract. 2009;25(8):555–565.
[4] Góes SM, Stefanello JM, Homann D, Lodovico A, Hubley-Kozey CL, Rodacki AL. Torque and muscle activation impairment along with insulin resistance are associated with falls in women with fibromyalgia. J Strength Cond Res Strength Cond Assoc. 2016; 30(11), 3155–3164.

Acknowledgements: Grant GV2016/140. Conselleria Educació Ciencia i esports. Valencia, Spain.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3433

AB0930 CROSS-SECTIONAL ANALYSIS OF THE AUTONOMIC NERVOUS SYSTEM (HEART RATE VARIABILITY): CORRELATIONS WITH PSYCHOLOGICAL DIMENSIONS IN WOMEN WITH FIBROMIALGIA, RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS

T.L. Santiago, D. Peixoto, C. Costa, J.A. Pereira da Silva. *Rheumatology, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal*

Background: Autonomic nervous system (ANS) dysfunction has been proposed to play a role in the pathophysiology and maintenance of rheumatic diseases, including fibromyalgia (FM) and rheumatoid arthritis (RA). Heart rate variability (HRV) analyses provide a quantitative marker of ANS activity. Some studies suggest an association between reduced HRV parameters and psychological dimensions, namely a negative emotional state. This led us to hypothesize an association between rheumatic diseases and higher sympathetic activity mediated by a negative emotional state.
Objectives: To establish correlates between HRV parameters with rheumatic disease groups and psychological dimensions.
Methods: Sixty women (FM, *n*=20; RA, *n*=20; healthy controls (Ct), *n*=20) completed a self-reported questionnaire addressing demographic characteristics, the Eysenck Personality Questionnaire, the Hospital Anxiety and Depression Scale, and the Beck Depression Inventory-II (BDI-II).
HRV analysis was performed by photopletismography between 8:00 and 10:00am, after an overnight fast, in a sitting position, for 5-minutes. We obtained the time and frequency-domain indices of HRV, including SDNN (standard deviation of the NN intervals), RMSSD (root-mean square differences of successive R-R intervals), high frequency power (HF), low frequency power (LF) and very low frequency (VLF). LF/HF ratio reflects sympathetic to parasympathetic balance.
Statistical analysis were performed considering: A) Rheumatic disease groups (FM/RA/Ct), and B) Psychological scores (irrespective of disease group): higher versus lower tertile in the personality questionnaires and score above (depression) versus below 20, in BDI-II. Between-groups comparisons were performed with Kruskal-Wallis test and analysis of covariance (age was adjusted during analyses), as appropriate.
Results: Neuroticism, anxiety and depression scores were significantly higher in FM and RA patients compared with controls ($p<0.05$). However, no statistically significant difference was observed in HRV parameters between disease groups. No statistically significant difference was observed in HRV parameters between tertile groups for psychological dimensions, except for depression. The values of HF power (parasympathetic activity) were lower in the high depression group compared to the low depression group ($p<0.05$). The ratio of LF/HF was higher among the depression group than the control group ($p<0.05$).
Conclusions: This study did not found significant differences in the HRV between the three rheumatic disease groups. The results confirm that depression is accompanied by dysfunction of the autonomic nervous system, specifically lower parasympathetic activity. These results suggest that psychological dimensions, namely depression, must be taken into account when evaluating the ANS and its impact in disease pathogenesis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5974

AB0931 EFFECTS OF MANUAL THERAPY ON PAIN, POSTURE, FLEXIBILITY, QUALITY OF SLEEP AND DEPRESSIVE SYMPTOMS IN FIBROMYALGIA SYNDROME

T. Duymaz[1], G. Sakınç Toprak[2]. *[1]Physiotherapy and Rehabilitation, Istanbul Bilim University, Şişli-Istanbil; [2]Physiotherapy and Rehabilitation, Acıbadem Hospital, Izmit-Kocaeli, Turkey*

Background: Fibromyalgia syndrome (FMS) is a chronic musculoskeletal pain condition characterized by widespread and a constellation of other symptoms.
Objectives: The purpose of this study was to investigate the therapeutic effects of a Manual Therapy (MT) protocol for improving pain, posture, flexibility, tender points, impact of FMS symptoms, sleep quality and depressive symptoms with FMS.
Methods: Patients completed demographic information, a number of self-report measures including Visual Analog Scale for assessing pain, Fibromyalgia Impact Questionnaire, the Pittsburgh Quality of Sleep Questionnaire Index and the Hospital of Anxiety and Depression Scale.The patients underwent a protocol of MT for a 60-minute session for 3 weeks (5/wk). The protocol was as the following release and mobilisation. All analyses were performed with the SPSS (version 22.0)statistical program
Results: 16 women,3 men patients who had FMS were treated with MT.Demographic variables of the participants are provided in Table 1.While there was a favorable change in all measurement parameters after treatment ($p<0.001$).There was a statistically significant difference between before and after the treatment measurement parameters (Table 2)

Table 1.Demographic variables of the participants

Variables	Mean ±SD (min-max)
Age (year)	36.05±8.16 (20–58)
BMI (kg/m^2)	24.19±4.16 (19.49–33.06)
Duration of symptoms (year)	4.81±2.41 (1–9)

Conclusions: This study found that the application of a MT protocol was effective for improving pain, posture, flexibility,tender points, impact of FMS symptoms, sleep quality and depressive symptoms in individuals with FMS.
References:
[1] Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. JAMA. 2004;292:2388–2395.
[2] Castro-Sa' nchez AM, Matara' n-Peñ arrocha GA, Arroyo-Morales M. Effects of myofascial release techniques on pain, physical function, and postural stability in patients with fibromyalgia: a randomized controlled trial. Clin Rehabil. 2011;25:800–813.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5833

AB0932 PREVALENCE OF TYPE D PERSONALITY IN TURKISH PATIENTS WITH FIBROMYALGIA SYNDROME

Y. Garip[1], T. Guler[1], O.B. Tuncer[2], S. Onen[3]. *[1]Physical Medicine and Rehabilitation, Ankara Numune Training and Research Hospital, Ankara; [2]Physical Medicine and Rehabilitation, Medipol University Medical School, Istanbul; [3]Psychiatry, Sevket Yılmaz Eğitim ve Araştırma Hastanesi, Bursa, Turkey*

Background: Type D personality is a distressed personality type involving two personality traits, namely negative affectivity and social inhibition, which are described as tendency to experience negative emotions and to inhibit self-expression in social relationships, respectively (1).
Objectives: The present study investigated the prevalence of type D personality in Turkish patients with fibromyalgia (FM) and evaluated the association between type D personality and clinical parameters of FM. Although there is adequate number of studies focusing on the relation between FM and psychological conditions such as depression and anxiety; this topic has been rarely addressed in the literature.
Methods: A total of 100 patients with FM fulfilling 1990 American College of Rheumatology (ACR) diagnostic criteria and 50 healthy controls were included. Type D personality was assessed by Type D Scale-14 (DS-14). FM disease severity was determined by Fibromyalgia Impact Questionnaire (FIQ), functional status by Stanford Health Assessment Questionnaire (HAQ), and health-related quality of life (HRQoL) by Nottingham Health Profile (NHP). Severity of pain and fatigue were measured by Visual Analog Scale (VAS).

Abstract AB0931 – Table 2. Comparison of before and after treatment in all measurement parameters

Variables	Before Treatment Mean ± SD (min–max)	After Treatment Mean ± SD (min–max)	z	p
Number of tender points	12.10±1.24 (10–15)	7.31±2.26 (2–11)	-3.840	0.000**
VAS at night	6.84±1.30 (3–9)	0.91±0.64 (0–2)	-3.843	0.000**
VAS in activity	7.31±1.24 (4–9)	1.11±0.81 (0–2.20)	-3.850	0.000**
VAS in rest	6.42±1.46 (3–9)	0.49±0.81 (0–2.40)	-3.834	0.000**
Distance of Tragus-Wall (cm)	12.08±1.95 (9–17)	10.72±1.90 (8.20–15.60)	-3.529	0.000**
Distance of processus spinosus-Skapula (cm) (R)	10.65±3.03 (6.50–17)	10.26±2.76 (7–15)	-2.007	0.045*
Distance of processus spinosus-Skapula (cm) (L)	11.21±3.17 (7–17)	10.26±2.76 (7–15)	-2.842	0.004**
Trunk Lateral Flexion (°) (R)	36.47±3.35 (30–41)	37.00±3.39 (30–41)	-1.821	0.069
Trunk Lateral Flexion (°) (L)	33.47±4.01 (27–41)	36.68±3.28 (30–41)	-3.534	0.000**
Distance of hand-floor (cm)	6.86±4.84 (0–17)	5.18±3.92 (0–14)	-3.219	0.001**
FIQ	56.25±18.74 (19.79–85.58)	46.39±17.99 (19.59–67.98)	-3.724	0.000**
HAD-A	10.89±3.91 (5–19)	4.73±3.49 (0–10)	-3.849	0.000**
HAD-D	9.78±3.29 (2–15)	5.05±2.06 (0–9)	-3.632	0.000**
PSQI	10.52±3.40 (5–15)	3.63±2.47 (0–8)	-3.830	0.000**

Wilcoxon Test. *p<0.05; **p<0.001.VAS: Visual Analog Scale;FIQ: Fibromyalgia Impact Questionnaire; HAD-A: Hospital Anxiety and Depression-Anxiety; HAD-D: Hospital Anxiety and Depression-Depression; PSQI: Pittsburgh Quality of Sleep Questionnaire Index.

Results: Prevalence of type D personality was 33% in FM patients, and 12% in controls. It was higher in the patients with FM (Odds ratio (OR) =3.612 confidence interval (CI) 95% (1.398–9.333)) ($p<0.01$) compared with controls. Type D FM patients scored higher in tender point count (TPC), FIQ, HAQ, VAS-pain and all NHP subgroups except energy ($p<0.01$) (Table 1). Type D personality was found as correlated with FIQ, TPC, HAQ, VAS-pain and NHP subgroups except energy ($p<0.01$).

Table 1. The comparison of clinical variables and HRQoL between type D and non-type D patients

	Type D FM patients (*n*=33) mean ± standard deviation	Non-type D FM patients (*n*=67) mean ± standard deviation	*p* value
Pain (VAS,10 cm)	8.55±0.75	5.80±1.19	<0.00001*
Fatigue (VAS,10 cm)	4.45±3.18	4.01±3.54	0.549
TPC	15.72±2.33	12.91±1.84	<0.00001*
FIQ	86.27±8.43	64.07±11.47	<0.00001*
HAQ	1.24±0.80	0.52±0.51	<0.00001*
NHP-pain	89.17±10.73	64.33±14.07	<0.00001*
NHP-physical mobility	53.41±16.91	22.57±21.01	<0.00001*
NHP-energy	45.45±42.13	37.31±41.14	0.358
NHP-sleep	80.00±19.36	56.23±22.55	<0.00001*
NHP-social isolation	60.60±37.24	15.52±25.06	<0.00001*
NHP-emotional reactions	83.71±14.14	51.52±25.06	<0.00001*

HRQoL: Health-related quality of life, FM: Fibromyalgia, VAS: Visual analog scale, TPC: Tender point count, FIQ: Fibromyalgia Impact Questionnaire, HAQ: Stanford Health Assessment Questionnaire, NHP: Nottingham Health Profile. *$p<0.01$ (significant).

Conclusions: Type D personality is prevalent among Turkish patients with FM, with a rate of 33%. It is associated with poor HRQoL regarding pain, physical mobility, sleep, and social and emotional functions. Based on our findings, assessment of personality characteristics of the patients with FM may hold the key for the treatment of the disease. Presence of type D personality should be taken into account in FM in order to develop new treatment strategies for the patients who have inadequate response to conventional therapies.

References:

[1] Denollet J. Type D personality: a potential risk factor refined. J Psychosom Res 2000;49:255–66.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1547

Back pain, mechanical musculoskeletal problems, local soft tissue disorders

AB0933 PREDICTIVE MODEL FOR SHOULDER PAIN USING CLINICAL AND EPIDEMIOLOGICAL VARIABLES

C. Feced Olmos [1], E. Labrador Sánchez [1], J. Ivorra Cortes [1], E. Grau Garcia [1], E. Vicens Bernabeu [1], J.J. Fragio Gil [1], R. González Mazarío [1], C. Alcañiz Escandell [1], I. Cánovas Olmos [1], I. Chalmeta Verdejo [1], L. Gonzalez Puig [1], I. Martínez Cordellat [1], C. Nájera Herranz [1], R. Negueroles Albuixech [1], J.E. Oller Rodriguez [1], F.M. Ortiz-Sanjuan [1], D. Hervás Marín [2], J.A. Román Ivorra [1,3].
[1] Rheumatology Department, HUP la Fe; [2] Biostatistics Unit, IIS la Fe; [3] Medical School, UCV, Valencia, Spain

Background: Shoulder pain is a very common complaint with poor prognosis and high recurrence. To evaluate the shoulder pain, anamnesis and physical examination are used, but a diagnosis of certainty is difficult. Clinical history and specific exploration maneuvers tend to be poorly correlated with the underlying problem. There are few studies that assess the predictability of shoulder pathology using patient characteristics and exploration.

Objectives: To assess if the combination of exploratory maneuvers and clinical data predicts the type of affection of the painful shoulder in a sensitive and specific way.

Methods: We conducted a prospective study with patients who attended to the Rheumatology Department of HUP La Fe by painful shoulder between February 2016 and January 2017, excluding those with known inflammatory diseases. A rheumatologist performed the anamnesis and the selected exploratory maneuvers: Jobe and Gerber test and palpation of the acromioclavicular joint. A second rheumatologist, blind to physical examination and medical history, performed the shoulder ultrasound scan. Biostatistic analysis was performed using software R version 3.3.2.

Results: 119 patients (66.4% women) with a mean age of 60±12.56 years and shoulder pain were collected. Time of pain evolution was 20.43±24.09 months and the right shoulder was the most affected one (71.4%). The association between the maneuvers of Jobe and the involvement of the supraspinatus (SE), as well as the Gerber maneuver with the affectation of the subscapular were statistically significant. However the sensitivity and specificity of both maneuvers are very low, so that alone is not suitable to identify the affected tendon or the type of alteration. Thus, a predictor model (nomogram) of the most common shoulder pathologies (subacromiodeltoid bursitis, tendinosis or SE tears) was developed using epidemiological and clinical examination variables.

Conclusions: Based on our results, the predictor model performed using epidemiological and clinical examination variables would be able to predict the most frequent pathologies of the shoulder. Imaging tests have a certain delay time, and by applying this predictor model, a diagnosis of presumption could be established in primary care, giving the opportunity to institute an early treatment. In addition, patients could be referred more efficiently to the appropriate specialty (rheumatology, traumatology or rehabilitation), avoiding delays.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6010

AB0934 TREATMENT OF LATERAL EPICONDYLITIS WITH ESWT: A SHAM-CONTROLLED DOUBLE BLINDED RANDOMISED STUDY

E.A. Gokmen [1], O. Karatas [2], E. Gilgil [3]. *[1] Physical Medicine and Rehabilitation, Antalya Training and Research Hospital; [2] Physical Medicine and Rehabilitation, Korkuteli Public Hospital; [3] Physical Medicine and Rehabilitation, Akdeniz University Hospital, Antalya, Turkey*

Background: Lateral epicondylitis is a term describing the clinical condition that causes pain and sensitivity in musculotendinous adhesion sites of the wrist extensor muscles originating from the lateral epicondyle of the humerus, resulting in repetitive stresses due to overuse (1,2).

Objectives: The aim of this study was to investigate the efficiency of extracorporeal shockwave therapy (ESWT) in the treatment of lateral epicondylitis as randomized, prospective, controlled and double blind.

Methods: 47 patients (35 women, 12 men) with lateral epicondylitis were included in the study. The mean age of patients was 45.94±10.46 years. Patients were randomized into two groups: active ESWT (n=22) and *sham* ESWT (n=25). Patients were randomly allocated to receive 1 session per week for 3 weeks of either sham or active ESWT.

Patients were evaluated before the treatment, and at the end of the first week, first month and third month after the last treatment session with Patient-rated Tennis Elbow Evaluation Questionnaire (PRTEE), Visual Analogue Scale (VAS) for pain assessment and physical examination of lateral epicondyle of the elbow with special clinical tests.

Results: Compared with pretreatment values in ESWT group, significant improvement was observed in all parameters after treatment. At the first week after the therapy significant improvement was observed in *sham* group but at the first and third month after the therapy no significant difference was found. In comparison of ESWT and *sham* over 3 months after the treatment, significant improvements were observed in ESWT group in all parameters.

Conclusions: there was a significant decrease in pain and a significant improvement in function following ESWT. Although there was a reduction in pain and improvement in function with sham treatment as well, this difference was not as significant as in active group.

References:

[1] Murrey PM, Ön Kol ve Dirsek. In: Weinstein SL, Buckwalter JA, Alpaslan M (Ç. Ed). Turek Ortopedi İlkeler ve Uygulamaları. Ankara, Güneş 2009; 401–15.
[2] Cordasco FA, Parkes JC II. Overuse Injuries of the Elbow. In: Nicholas JA, Hershman EB. The Upper Extremity In Sports Medicine. Missouri, Mosby-Year Book 1995; 317–30.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6508

AB0935 THE ROLE OF EPIDURAL INJECTIONS IN PATIENTS WITH CHRONIC SCIATICA: A REVIEW BASED ON THE EVIDENCE OVER THE PAST 5 YEARS

G. Ferreira Dos Santos, M. Amaral Silva, E. Marques, M. De Fátima Carvalho.
Physical and Rehabilitation Medicine Department, Hospital de Curry Cabral - Centro Hospitalar de Lisboa Central (CHLC), Lisbon, Portugal

Background: Among various modalities applied in the management of painful conditions of the spine, epidural injections (EI) are one of the most commonly utilized interventions. EI can be administered in the lumbar spine by either caudal (CEI), interlaminar (IEI), or transforaminal (TEI) approaches and various steroids have been used in these injections[1,2]. The purpose of EI is to provide analgesia for a varying duration, whilst making it easier for the patient to undergo a rehabilitation program during this time[1].

Objectives: The aim of this review is to evaluate the efficacy of the different types of EI in patients suffering from chronic sciatica, based on the evidence published over the past 5 years.

Methods: Relevant studies were retrieved by searching PubMed, Medline, The Cochrane Library and UpToDate. Publications from 2012 to 2016 which specified the use of EI to treat chronic sciatica were considered, and all the studies selected were written in the English language only.

A total of 11 articles were gathered, of which 5 were excluded after analysis of their title and abstract. Of the 6 papers included in this study, 5 are systematic reviews and 1 is a meta-analysis of 10 randomized controlled trials.

The outcomes measured were improvement in pain and functional status. The Numeric Rating Scale (NRS) and Visual Analogue Scale (VAS) were the most commonly used baseline scales for pain evaluation. The Oswestry Disability Index (ODI) was the most used scale for the functional disability scoring system in the literature.

Results: 4 of the 6 papers included in this review reported improvements in pain ranging from 30 to 83% and in functional status ranging from 26 to 86% from the pre-injection state, with follow-up periods lasting up to 2 years after the EI. 2 of these 4 studies showed Level II evidence for EI for long-term efficacy in managing chronic sciatica, with no significant difference among CEI, IEI or TEI.
The remaining 2 papers (out of the total 6) associated EI with immediate improvements in both pain and function, but found the benefits to be unsustained. 1 paper reported 1 serious adverse event in one of the trials analyzed and found the data on harms to be sparse on most trials. Another paper concluded that injecting local anesthetic alone might be preferable to injecting local anesthetic with steroid as omitting the steroid could lessen the risk of rare, but possibly fatal complications.
Conclusions: Despite variability in the studies included and methods used for data synthesis, most of the articles included in this review showed positive results for both pain relief and improvement in functional status with EI.
Although no studies found significant difference among CEI, IEI or TEI in terms of efficacy, each approach has its advantages and these should be taken into account when choosing the best approach for each patient.
As supporting evidence, this review shows that EI with or without steroids are a fast, safe and clinically effective treatment method for patients with chronic sciatica.
References:
[1] Bhatti A, Kim S. Role of Epidural Injections to Prevent Surgical Intervention in Patients with Chronic Sciatica: A Systematic Review and Meta-Analysis. Cureus. 2016, 8(8): e723.
[2] Pinto R, et al. Epidural Corticosteroid Injections in the Management of Sciatica: A Systematic Review and Meta-analysis. Ann Intern Med. 2012, 157:865–877.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2747

AB0936 FLEXIBILITY AND STRENGTH OF THE TRUNK IN CHRONIC LOW BACK PAIN TWO YEARS AFTER A FUNCTIONAL RESTORATION PROGRAM

R. Maaoui[1,1], S. Zrida[1], I. Ksibi[1], N. Mouhli[1], H. Rahali[1], M. Sghir[2], W. Kossomtini[2]. *[1]Physical and Rehabilitation Medicine, military hospital Tunis, tunis; [2]Physical and Rehabilitation Medicine, regional hospital Tahar Sfar of Mahdia, Mahdia, Tunisia*

Background: Low-back pain affects significatively the flexibility and the muscular strength of the trunk. It was demonstrated in literature the positive effect of restoration programs in these parameters at short-term evaluation.
Objectives: Evaluate the flexibility and the muscular strength and endurance of the trunk two years after a functional restoration program
Methods: Prospective study on patients with low back pain evaluated before, at the end of the restoration program and two years later. We have evaluated the following parameters: trunk flexibility by use of the Schöber index and the finger–ground distance test (FGD), hamstring flexibility by measurement of the thigh-leg (TL) angle, back flexor and back extensor endurance, assessed with the Shirado test and the Sorensen test, respectively.
Results: Thirty patients were evaluated. Initially, the results reported decreased flexibility: 53% with FGD >15.53 cm; 37% with the thigh-leg (TL) angle >15° and decreased muscle endurance: Schirado 30.26±29.662s; Sorensen 26.3860±18.5208s. The short-term efficacy of the program showed significatively improvement in all parameters (p=0,01). However, this improvement decreased 2 years later but it remains significant. This loss can be attributed to the fact that 70% of patients abandoned self-rehabilitation exercises
Conclusions: The restoration program seems to have good effect in short and long term evaluations in the flexibility and muscular strength of the trunk.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4954

AB0937 DUPUYTREN'S CONTRACTURE: 15 YEARS OF EXPERIENCE WITH 36 CASES

H. Mouanaa, M. Jguirim, A. Arfa, A. Farhat, M. Brahim, A. Mhenni, Z. Saoussen, I. Bejia, M. Touzi, N. Bergaoui. *Rheumatology Unit of the Monastir University Hospital, Monastir, Tunisia*

Background: Dupuytren's contracture is characterized by thickening and retraction of the palmar aponeurosis due to fibroblastic proliferation leading to progressive and irreducible fingers' flexion. Dupuytren's contracture appears to be a disease with poor clinical symptomatology and the therapeutic progress, in particular the needle aponeurotomy, continues to increase.
Objectives: We propose to describe the epidemiological, clinical and therapeutic characteristics- particularly the needle fasciotomy- of Dupuytren's contracture diagnosed and treated in our Rheumatology department.
Methods: This is a retrospective descriptive study that collected patients with Dupuytren's disease over a 15-year period from 2001 to 2016.
Results: Thirty-six patients were collected. The mean age was 63±10 years (46 years, 83 years) and the sex ratio was 5. 34% of the patients were manual workers, of whom 42% were masons, 25% were farmers and 17% were carpenters. 8% Of longshoremen and 8% of dressmakers. The personal history was diabetes in 63% of cases, of which 26% were unbalanced, hypertension in 31% of cases and hypercholesterolemia in 14% of cases. 6% of patients were epileptic. 23% of patients were ethyl and 13% were smokers. 6% had an associated Leddherhose disease. 9% of our patients had a family history of Dupuytren's disease. The mean time to diagnosis was 60 months [03 months to 180 months]. The clinical examination showed an exclusive involvement of the left hand in 22% of cases, right hand in 12% of cases and bilateral involvement in 66% of cases. The fingers affected were: 59% the ring finger, 49% the little finger, 23% the middle finger, 12% the index and 5.5% the inch, in order of frequency of mention. The stages of Dupuytren's disease at their discovery were as follows: stage 4 (25%), stage 3 (34%), stage 2 (24%) and stage 1 (17%). Skin examination showed that 58% of the skin was inflicted and 42% of the skin was soft. From a therapeutic point of view, 86% of the patients benefited from a needle aponevrotomy with a good progression in 97% and a recurrence in 8% of the cases. In all stages combined, the average postoperative therapeutic gain was 0.83 stage at the Left hand and 1.43 stage at the right.
Conclusions: The Dupuytren's contracture is the object of a scientific subject whose wealth grows exponentially. These range from the paternity of his first description, to the place of the last therapeutic modalities.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6967

AB0938 AN ATYPICAL CASE OF SARCOIDOSIS REVEALED BY A BILATERAL PREPATELLAR BURSITIS

J. Perrier-Cornet[1], R. Ouichka[1], S. Moawad[2], I. Chary-Valckenaere[1]. *[1]Rheumatology; [2]Dermatology, CHU Nancy, NANCY, France*

Background: Prepatellar bursitis is not very frequent in daily practice and the main causes are infections, crystal arthropathies or trauma.
We report the case of a 49-year-old man presented to our department with bilateral anterior knee pain. Pain started 3 months ago without any triggering factor. He denied any trauma or infection. The patient also denied any history of gout, rheumatoid arthritis or systemic lupus.
Objectives: On clinical exam, bilateral knee swellings were noticed consistent with prepatellar bursitis with no wound or abrasion, no fever, signs of arthritis or lymphadenopathy.
Methods: Knee ultrasonography and skeletal scintigraphy confirmed symmetrical prepatellar bursitis. Laboratory findings showed elevated ESR and CRP but no other abnormalities.
Few days later, the patient presented with subcutaneous painful nodules that appeared on his forearms. Biopsy was done and showed deep subcutaneous sarcoid nodules of Darier-Roussy, confirming the diagnosis of sarcoidosis.
Further work up revealed typical sarcoid pulmonary involvement. Bilateral hilar and mediastinal lymphadenopathy with beaded appearance of interlobular septa were noticed on CT-scan of the chest.
The Positron Emission Tomography showed abnormally high ^{18}F-fluorodeoxy glucose uptake in the thoracic lymph nodes.
Results: All the diagnostic work up confirmed the diagnosis of systemic sarcoidosis. The decision was to start oral corticosteroids. Few days after starting the systemic steroids, the skin lesions and the knees pain improved significantly.
Conclusions: The conclusion is that after excluding the main causes of bursitis (infection, trauma and inflammatory arthritis) (1), it's necessary to keep in mind sarcoidosis as possible diagnosis.
This clinical observation is important because involvement of the bursa is a rare musculoskeletal manifestation of sarcoidosis (2). Moreover, it's very uncommon to diagnose sarcoidosis presenting with just bilateral prepatellar bursitis with no other musculoskeletal or rheumatological symptoms (3).
The association of bursitis, inflammatory skin lesions and thoracic lymphadenopathy is uncommon but may suggest the diagnostic of sarcoidosis.
References:
[1] Mathieu S, Prati C, Bossert M, Toussirot E, Valnet M, Wendling D. Acute prepatellar and olecranon bursitis. Retrospective observational study in 46 patients. Joint Bone Spine. 2011;7:423–4.
[2] Fujimoto H, Shimofusa R, Shimoyama K, Nagashima R, Eguchi M. Sarcoidosis presenting as prepatellar bursitis. Skeletal Radiol. 2006;35:58–60.
[3] Ruangchaijatuporn T, Chang EY, Chung CB. Solitary subcutaneous sarcoidosis with massive chronic prepatellar bursal involvement. Skeletal Radiol. 2016;45:1741–5.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2753

AB0939 CHANGE IN THE SURGICAL TREATMENT FOR CERVICAL SPINE DISORDERS RELATED TO RHEUMATOID ARTHRITIS DURING RECENT 15 DECADES

K. Sakuraba, K. Kai, H. Miyahara. *National Hospital Organization Kyushu Medical Center, Fukuoka, Japan*

Background: Since the appearance of biological DMARDs in Japan, disease control of rheumatoid arthritis has been ameliorated. Inflamed synovitis and destructive arthritis declined dramatically, which resulted in a decrease in the number of synovectomy and joint prosthesis gradually. On the other hand,

surgeries for hand or foot disorders have been increasing. However, it is unclear about the surgery for cervical spine disorder.
Objectives: We clarified the change in the surgical treatments for cervical spine disorder related to RA patients at our institution.
Methods: From 2001 to 2015, we identified 71 RA patients with a cervical spine surgery. The mean age was 65.4 years (range, 44–90 years). The patients consisted 11 males and 60 females. The mean disease duration was 20 years (range, 0–52 years). They were classified into three subgroups according to the affected level: the upper lesions (UL) such as atlantoaxial subluxation, the middle and lower lesions (MLL) including subaxial subluxation, and the expanded lesions (EL) which have both features. Individual groups were assessed the change of the number of surgical treatment. In addition, we divided the period into first seven years (from 2001 to 2007) and last eight years (from 2008 to 2015), and compared each other.
Results: There were 38 patients in UL, 25 patients in MLL and 8 patients in EL. Most patients in UL were underwent atlantoaxial fixation by Magerl and Brooks procedure, and the number of them was constant throughout the entire period. Occipito-cervical fusion has been decreasing. Although there were much surgeries of MLL disorder in last 8 years than that in first 7 years, most of them did not have RA change such as endplate erosion and subluxation.
Conclusions: There was no significant change in EL throughout all periods. In conclusion, surgeries for cervical spine disorder of RA patients remained in our institute. However, disorders related to RA within them, especially MLL, were decreasing. it indicates that expansion of RA remission has led to the reduction of cervical spine surgeries with RA change.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1156

AB0940 EFFICACY AND SAFETY OF PLATELET RICH PLASMA PERI-NEURAL INJECTION IN TREATMENT OF DIABETIC NEUROPATHY: DOUBLE BLIND RANDOMIZED CONTROLLED TRIAL

M. Hassanien [1], Y. Saad [1], A. Alawamy [2], W.A. Khalifa [3], D. Abdelkarem [4].
[1] Rheumatology Department; [2] Anathesia department Assuit university; [3] Internal Medicine; [4] Clinical Pathology, Assuit University, assuit, Egypt

Background: Neuropathy is a common complication of diabetes mellitus (DM) not only leads to an impaired quality of life, but also to an increased morbidity and mortality.Autologous platelet-rich plasma is easy and cost-effective method. Platelet-derived angiogenesis factor capable of stimulating new capillary growth by inducing migration of endothelial cells, influence the process of angiogenesis and revascularisation.
Objectives: evaluate the clinical efficacy and safety of perineural PRP injection in the treatment of diabetic neuropathy (DN) compared to tradition medical treatment.
Methods: Sixty patients were selected from Endocrinology unit Department of Internal medicine, Assuit university Hospital, Egypt had type II diabetes mellitus neuropathy (DN) of at least 5 years duration of symptoms, regardless of age and gender double blindly divided into two groups, both groups had control blood glucose. Group I underwent PRP preineural injection under ultrasound guidance and group II underwent medical treatment. Baseline pain and nerve conduction study of upper and lower limb nerves and sural nerve conduction studies, F-wave. nerve conduction study were determined at 3 months after the procedure. Primary outcome was the total effective rate. The total effective rate = (the number of patients with significant effect+ the number of patients with effect)/total number of patients. A “significant effect” meant that limb pain, numbness, and fatigue were significantly reduced, nighttime sleep was improved, and NCV from electromyography increased $>$5 m/s or returned to normal. An “effect” meant that the symptoms mentioned above were relieved, and NCV compared with pre-treatment increased $<$5 m/s. “Failure” meant that the symptoms did not improve, and there were no changes in NCV electromyography
Results: We recruited 60 diabetic patients (type II) with peripheral neuropathy with a mean age 35.27±12.86 years with disease duration of 7.42±3.51 years. Of these, 56% cases with upper limb nerves neuropathy only while the rest 44% had sural nerve plus upper limb nerves neuropathy. Nerve conduction study showed axonal affection in only 26% and all had delayed distal latency and prolonged motor conduction velocities. generalized DN is found in 70% of total patients and 30% of had focal Entrapment of the nerve includes median neuropathy at the wrist 50%, ulnar neuropathy at the elbow 30% and peroneal neuropathy at the knee 20% and no patients had radiculoplexus neuropathies.

	Group I		P-value
	Baseline	3 months Post injection	
Mean motor NCV ± SD	35.6±12.67	46.38±10.68	$\leq$0.05*
Mean DL ± SD	9.19±8.16	4.55±5.66	0.09
Sural conduction velocity	17.00±10.86	34.00±6.84	$\leq$0.001**
	Group I	Group II	P-value
Effect	85.47±9.91%	79.38±12.40%	0.16
Significant effect	95.29±15.28%	81.00±9.64%	$\leq$0.001**
Total effective rate	22/30 (73.3%)	11/30 (36.6%)	$\leq$0.05*
Failure	7.00±2.86/30	18.00±2.84/30	$\leq$0.001**

Conclusions: Autologous platelet-rich plasma is an easy and cost-effective method as a treatment of diabetic peripheral neuropathy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1272

AB0941 PATIENTS PROFILE AT ORTHOGERIATRIC UNIT: NEW MODEL OF CARE

S. Hammami, A. Meziani, A. Ioana, C. Dumont, V. Latteur. *Geriatric, GHdC Belgium, Charleroi, Belgium*

Background: Fractures in elderly patients its a prevalent problem. Older patients due their characteristics requires a specific care. The orthogeriatric Unit has been shown to be one of the most beneficial units. It is important to evaluate the model of care
Objectives: Evaluate the main variables of fractures patients treated at a orthogeriatric Unit and their complications
Methods: This is a partially concurrent prospective study, taking place in a large urban academic hospital GHdC in Belgium. The participants were 87 consecutive elderly people, admitted directly to a geriatric-based orthogeriatric ward.
Results: A total of 87 patients were included. The average age was 85.2±5.2 years, 20 male, 67 female. Most of them (n=44,52%) were admitted for a hip fractures, 44% (n=38) were transferred from emergency department, ISAR score was 3.9±1.1, Preoperative stay was less than 24 h for 54% of our population, Mini nutritional assessment was 18.7±4.3, Mini mental state examination was 20.6±6.4, the Cumulative Illness Rating Scale was 17.1±4.5, the mean number of medicine was 6.8±3.3, Activity of Daily Living 15 days after admission was 12.2±5.5. Delirium was the principal complication 55% (n=44). Mean hospital stay between admission and discharge/transfer to convalescence unit was 23.8±12.9. In-hospital mortality was 11% (n=10)
Conclusions: Fractures is a frequent and disabling pathology among geriatric fragile population, its treatment requires an interdisciplinary approach. This must be managed by the collaboration between geriatrician and orthopedist. We believe that the orthogeriatric Unit providing subacute and acute care will improve the general outcome of fragile geriatric patients
References:
[1] González-Montalvo JI et al The orthogeriatric unit for acute patients: a new model of care that improves efficiency in the management of patients with hip fracture. Hip Int. 2010 Apr-Jun;20(2):229–35.
[2] Smith TO et al Factors predicting incidence of post-operative delirium in older people following hip fracture surgery: a systematic review and meta-analysis. Int J Geriatr Psychiatry. 2017 Jan 17.
Acknowledgements: Geriatric multidisciplinary team working in GHdC Charleroi Belgium.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5845

AB0942 EFFECT OF CORTICOSTEROID INFILTRATIONS ON DIABETES. A MONOCENTRIC RETROSPECTIVE STUDY

S. Mathieu, M. Couderc, Z. Tatar, J. Lopez, S. Malochet-Guinamand, J.-J. Dubost, A. Tournadre, M. Soubrier. *Rheumatology, CHU Gabriel Montpied, Clermont-Ferrand, France*

Background: Corticosteroid therapy can unbalance diabetes, particularly when administered orally, but also during articular infiltration. Corticosteroid infiltrations are an integral part of the therapeutic arsenal in rheumatology. They are utilized to treat congestive articular flare-ups of osteoarthritis or inflammatory rheumatic diseases. Periarticular or ductal pathologies, such as trochanteric bursitis, rotator cuff pathology and carpal-tunnel syndrome, may require the use of these infiltrations. Caution is often required when using corticosteroid infiltrations in diabetics.
Objectives: The purpose of our study was to evaluate whether or not diabetic patients undergoing a corticosteroid infiltration during hospitalization had a diabetes imbalance.
Methods: Diabetic patients having undergone a corticosteroid infiltration during hospitalization between 2009 and 2015 were sought. We collected data regarding their rheumatological pathology, glycated hemoglobin (HbA1c), and fasting glycemia on the day of the infiltration, the next day and after 48 hours.
Results: A total of 114 patients were included in our study. The average age was 72.1±9.4 years. All of them had Type 2 diabetes, and 35 of them were treated with insulin. Average HbA1c was 7.3±0.1%. Overall, 47 (41.2%) patients had an HbA1c below 7%. A total of 31 (27.2%) patients had a diabetes imbalance after infiltration, and 19 of these, who were taking oral antidiabetics, required 48 hours of rapid insulin to balance their glycemia. Overall, 12 patients increased their insulin dose. Out of the 47 patients with good HbA1c, 7 (14.9%) of them had a glycemia imbalance, versus 24 (35.8%) who were unbalanced out of the 67 patients whose HbA1c exceeded 7% (p=0.013).
Conclusions: Corticosteroid infiltrations can lead to a diabetes imbalance, thus making it necessary to administer a few days of rapid insulin or to increase the insulin dose. A patient whose HbA1c is below 7% has a low risk of unbalancing his/her diabetes after corticosteroid infiltration.
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2918

AB0943 SIGNIFICANCE OF MUSCLE VOLUME & FATTY DEGENERATION OF LUMBAR PARASPINAL MUSCLE IN SPINAL IMBALANCE

Y.-S. Park, J. Lee, J.-S. Park. *Department of Orthopaedic Surgery, Hanyang University Guri Hospital, Guri city, Korea, Republic Of*

Background: Spinal sagittal imbalance which is closely associated with low back pain is considered as a factor in a variety of spinal disorders.
Objectives: The present study was to determine the relationship between the sagittal imbalance and sarcopenia, especially cross sectional area (CSA) and fatty degeneration (FD) of muscle around the spine.
Methods: Overall, 165 patients are included in this study, classified by three groups according to the distance from sagittal vertical axis to posterior end of upper end plate of sacrum.
38 patients were classified as group 1 (distance ≥9cm), 50 and 53 patients as group 2 (distance 5–9cm) and group 3 (distance <5cm), respectively. For measurement of CSA and FI of paraspinal muscles, five transverse T1W images of S1-S5 were obtained from PACS and measured with Adobe Photoshop 7.0®, by counting the number of pixels included in each selected muscle area. A variance analysis on average muscle surface area of those five images was done with SPSS 19.0 Windows version (SPSS Inc., Chicago, IL, USA).
Results: The average age of total patients was 69.1, average BMI was 22.57 and bone density was -2.34 (T-score).
No significant differences were detected on ages, BMI, and bone density. Each correction coefficient of multifidus, erector spinae and psoas muscle was 0.80, 0.75 and 0.81, respectively.
CSA of paraspinal muscles has significant differences between group I and III, II and III. Psoas has significant differences between all groups. FI has significant differences between all groups in multifidus and between I and III, II and III in erector spinae. But, psoas has no significance between three groups.
Conclusions: Authors were able to detect significant muscle atrophy in the group with severe imbalance. And degeneration of paravertebral muscle has significant increased with sagittal imbalance. Effort for preventing weakness of muscle around spine might cause influence to alignment of spine.
References:
[1] Fortin M, Lazáry À, Varga PP, McCall I, Battié MC. Paraspinal muscle asymmetry and fat infiltration in patients with symptomatic disc herniation. Eur Spine J Off Publ Eur Spine Soc Eur Spinal Deform Soc Eur Sect Cerv Spine Res Soc 2016;25:1452–9. doi:10.1007/s00586–016–4503–7.
[2] Lee SH, Park SW, Kim YB, Nam TK, Lee YS. The fatty degeneration of lumbar paraspinal muscles on computed tomography scan according to age and disc level. Spine J Off J North Am Spine Soc 2016.
[1] doi:10.1016/j.spinee.2016.08.001.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4228

Paediatric rheumatology

AB0944 USE,SAFETY AND EFFICACY OF ETANERCEPT IN JIA–A SINGLE CENTRE RETROSPECTIVE STUDY FROM NORTH INDIA

A. Shivpuri[1], S. Mittal[1], M. Agarwal[2], S. Sawhney[2]. *[1]Fellow in Training, Pediatric Rheumatology; [2]Consultant, Sir Ganga Ram Hospital, New Delhi, India*

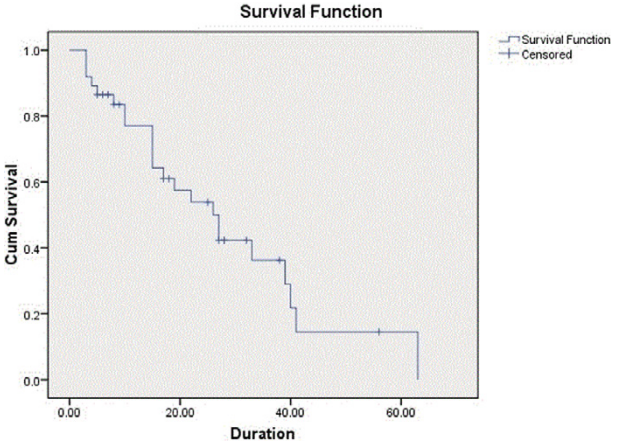
Background: The treatment paradigm for Juvenile Idiopathic Arthritis (JIA) has changed in last decade:Early diagnosis,objective assessment & appropriate use of biologic response modifiers (BRMs) are common place.Etanercept (Et) is available in India for 15yrs. BRM use in developing world is fraught with challenges: cost, high burden of Tuberculosis (TB) & retention. In view of the cost & safety concerns regarding TB, at our centre, full dose Et is used for 3–6 mths, followed by dose tapering as tolerated.
Objectives: 1. To determine the use, safety & efficacy of Et in JIA. 2. To determine the factors that determine responders vs non responders. 3. To determine the factors that determine disease free survival on stopping Et
Methods: This study was done from 15thJune'15 to15thDec'16 (18mths) at Sir GangaRam Hospital. *Inclusion criteria:* All JIA pts who took Et for min 12 wks & attended the outpatients during the study period. *Outcome:* All pts who achieved the Wallace criteria of inactive ds, clinical remission on (CRoM) or off medication within 4 months were termed as responders.
Results: *Use:* 46pts recd Et (29M,17F). Median (Md) age at JIA onset: 9.08yrs (1.16–16.5).Md delay to diagnosis: 4mths (0.5–63). Md age at initiation of Et: 11.6yrs (4.25–20.3). *Indications:* Partial response to Intraarticular steroids/bridging steroids & DMARD-32; Started upfront for high ds.burden: 14. *Diagnoses:* ERA30 (65%), Poly JIA8 (17%), OJIA 3 (7%), SOJIA 3 (7%) & UJIA 2 (4%). *Safety:* Screening: Mantoux +ve: 6, Quantiferon+ve: 2,antitubercular therapy for latent TB: 8. Side effects: 41 (88%) had no adverse event. 5 pts - 1 each had enteric fever, varicella, uveitis, hemolysis, malaria. *Follow up:* Md duration of follow up-47.5 mths (2–147). *Medications at last follow up:* Et ongoing in 20 (43.5%), 12 on 2nd BRM, 12 off BRM & 2 lost to follow up. *Status at last follow up:* Of 37 responders - 8 currently active.
Responders vs non responders: 37 responded (2 excluded duration <12 wks). In all responders drug was tapered/stopped. No demographic, clinical, lab criteria could predict responder from non responder (Table 1).

	Responders (37/44)	Non Responders (7/44)	p value
Md time to inactivity post Et	9wks (1–52)	–	
Md time to flare	15m (3–63)	–	
Md duration of taking Et	18m (3–56)	5.5 m (2–22)	0.01
Md Time to first taper Et	5m (1–34)	2m (1.5–16)	0.44
Median ESR	38 (4–125)	63 (22–125)	0.08
SJC ≤4 jts >4 jts	29 (78.4%) 8 (21.6%)	4 (57.1%) 3 (42.9%)	0.34
TJC ≤4 jts >4 jts	32 (86.5%) 5 (13.5%)	4 (57.1%) 3 (43%)	0.10

Of 37 responders, 15 (40.5%) did not show any flare (Table 2).

	Flared (22/37)	Never flared (15/37)	p value
Md time to inactivity post Et	11wks (1–36)	6 wks (2–52)	0.43
Md time to flare	15m (3–63)	18m (3–33)	0.74
Md duration of Et	17.5m (3–53)	25m (6–56)	0.64
Md Time to first taper	5.5m (1–12)	4m (2–34)	0.58
Md time to stop steroids	3m (1–12)	2m (1–4)	0.16
Median ESR	28 (4–120)	45 (15–125)	0.29
SJC≤4 jts >4jts	17 (77.3%) 5 (22.7%)	12 (80%) 3 (20%)	1
TJC≤4 jts >4jts	19 (86.4%) 3 (13.6%)	13 (86.7%) 2 (13.3%)	1

Disease free survival on Et: Of 37 responders, 22 flared. No factors could predict flare in pts who recd tapering Et dose or after stopping Et. Some needed repeat cycles of Et/2nd BRM. Kaplan Meier curve of responders confirmed that no pt would be flare free at 63mths of follow up.



Conclusions: Et is safe to use & had no adverse events in 89%. Needed most for ERA. Effective in 84%. On using shortterm Et, 59% flared either on tapering/stopping. These pts responded to reinitiation of Et/BRM. On long term follow up (63mth) there were no flare free pts.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4892

AB0945 COHORT STUDY OF 112 PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS DURING TRANSITION FROM PEDIATRIC TO ADULT CARE

A.-C. Debrach[1], A. Beaumel[2], A. Rougelot[2], J.-P. Larbre[2], M. Couret[1], F. Coury[2]. *[1]Rheumatology, CHUV, Lausanne, Switzerland; [2]Rheumatology, HEL, Lyon, France*

Background: Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory arthritis in children. The International League of Associations for Rheumatology 2001 (ILAR) classification includes 7 subgroups: systemic JIA, polyarticular JIA, oligoarticular JIA, enthesitis related arthritis (ERA), psoriatic arthritis and undifferentiated arthritis. Most paediatric inflammatory arthritides persist into adulthood. Therefore, a transition from paediatric to adult rheumatology is a necessary step. Transition is defined as an active process by which a young patient with a chronic disease develops skills and resources to gradually take control of their condition. The transition phase should be anticipated and structured because of the risk of failure in monitoring. However difference in classification criteria in paediatric and adult rheumatology can cause significant difficulty for adult rheumatologists.
Objectives: The aim of this study was to determine the characteristics of juvenile-onset arthritis seen during the transition period and to compare *paediatric* classification criteria to those of adults.
Methods: A retrospective *bi-centre* study was performed. Patients with JIA according to ILAR classification were included and had a consultation at transition. JIA classification criteria were compared to ACR/EULAR 2010 criteria

for rheumatoid arthritis (RA), Yamaguchi criteria for adult Still's disease and ASAS criteria for spondyloarthritis.
Results: 112 patients were included: 17 systemic JIA, 26 polyarticular JIA, 19 oligoarticular JIA, 41 ERA and 9 psoriatic arthritis. The median age of transition was 19 years old. Eight cases of uveitis were observed among patients with oligoarticular JIA and 7 with ERA. Radiographic structural damages were assessed and showed 15% of patients with erosions or carpitis, mainly in polyarticular and systemic JIA patients. 29% of patients with ERA displayed sacroiliitis. In comparison with adult rheumatism, 42% of patients with systemic JIA fulfilled Yamaguchi criteria and 23% of patients with polyarticular JIA fulfilled ACR/EULAR criteria for RA. 41% of patients with oligoarticular JIA, 73% with ERA and 100% with psoriatic arthritis fulfilled ASAS criteria for spondyloarthritis.
Conclusions: Our study confirmed the articular destructive potential of polyarticular and systemic JIA and an ocular risk in oligoarticular JIA. Comparison of JIA criteria to adult rheumatism criteria showed that polyarticular JIA with positive rheumatoid factor fulfilled ACR/EULAR criteria for RA. However, oligoarticular JIA and polyarticular JIA without rheumatoid factor did not fulfill any adult rheumatism criteria and seem to be paediatric entities. Finally, most patients with ERA and psoriatic arthritis fulfilled the ASAS criteria for spondyloarthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6205

AB0946 CALCINOSIS IN CHILDREN WITH JUVENILE DERMATOMYOSITIS FROM A SINGLE-CENTRE IN NORTH INDIA

A. Sharma, A. Jindal, A. Gupta, D. Suri, S. Singh. *Pediatrics, Post Graduate Institute of Medical Education and Research, Chandigarh, India, Chandigarh, India*

Background: Juvenile dermatomyositis (JDM) is a rare childhood autoimmune inflammatory muscle disorder that can result in severe disability or death. Calcinosis is a unique and a poorly understood long-term complication of JDM (1). Calcinosis can present in various forms like nodular calcinosis, tumoral deposits, calcinosis universalis.
Objectives: We present here the images of calcinosis in children with JDM
Methods: All children diagnosed to have JDM and registered in Pediatric Rheumatology Clinic at Post Graduate Institute of Medical Education and Research, Chandigarh, India, were evaluated for presence of calcinosis. Consent was taken from patients or caregivers
Results: A total of 36 patients were evaluated. Twelve (33.33%) patients had calcinosis (Fig 1). Interestingly, 4 children had calcinosis at the time of diagnosis



Figure 1. Calcinosis in children with JDM. Radiographs showing Calcinosis in children with JDM

Conclusions: Calcinosis is a distinct complication of JDM which is uncommon in inflammatory myopathies in adults (2). Calcinosis can be disabling and disfiguring. It may not be obviously visible in all patients and radiographs help reveal the extent of involvement.
References:
[1] Tansley SL, McHugh NJ, Wedderburn LR. Adult and juvenile dermatomyositis: are the distinct clinical features explained by our current understanding of serological subgroups and pathogenic mechanisms? Arthritis Res. Ther. 2013;15:211.
[2] Robinson AB, Reed AM. Clinical features, pathogenesis and treatment of juvenile and adult dermatomyositis. Nat. Rev. Rheumatol. 2011;7:664–75.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5992

AB0947 CHARACTERISTICS OF A TRANSITION CLINIC FOR YOUNG PEOPLE WITH RHEUMATIC DISEASES

B. Serrano-Benavente[1], J.C. López-Robledillo[2], D. Clemente[2], I. Monteagudo[1], J.C. Nieto-González[1]. *[1]Rheumatology, Hospital General Universitario Gregorio Marañón; [2]Paediatric Rheumatology, Hospital Niño Jesús, Madrid, Spain*

Background: Paediatric rheumatologic diseases can still be active in the adulthood. Transitional care units are very important for the transition from paediatric to adult health care system.
Objectives: To describe the demographic characteristics, paediatric rheumatologic diseases distribution and active treatments in a Rheumatologic Transitional Care Unit (RTCU).
Methods: We included all new patients who attended the RTCU of a tertiary level hospital from 1st September 2015 until 31st December 2016. These patients were remitted from the paediatric rheumatology unit of two tertiary level hospitals. We retrospectively analyzed their demographic, laboratory and treatment characteristics. The connective tissue diseases (CTD) group included systemic lupus erythematosus, Behçet disease, dermatomyositis and scleroderma. Patients were considered active according to the physician opinion.
Results: We attended 81 new patients. 59 were female (72.8%) and the median age (range) was 19 years (18.1–20.7). 65.43% were diagnosed with Juvenile Idiopathic Arthritis (JIA) and 12.35% with CTD. Table 1 shows the main baseline characteristics of the patients. In the first visit at the unit, half of the patients did not have any systemic treatment (41 patients [50.62%]). From the remaining 40 patients with systemic treatment, 16 patients (40%) were under biologic treatment, mostly anti-TNFα. In any of the two first appointments, 20 patients (24.7%) were active, most of them from the JIA group. Seven (35%) of these patients increased or changed the treatment, 6 of them initiating a biologic treatment.

Table 1. Demographic and treatment characteristics

	Total (n: 81)	Juvenile Idiopathic Arthritis (n: 53)	Connective Tissue Diseases (n: 10)
Gender, Women (%)	59 (72.83)	39 (73.58)	9 (90)
Age of disease onset - Median (IQR)	10.3 (4.5–14.2)	6.5 (2.1–12.9)	14.4 (11.5–15.6)
Arrival age at the unit - Median (IQR)	19 (18.1–20.7)	19.1 (18.1–21)	19 (18.4–20.5)
Active in the 2 first appointments N (%)	20 (24.69)	15 (28.30)	4 (40)
Antinuclear antibodies, N (%)	32 (39.50)	20 (37.73)	5 (50)
Uveitis at any time, N (%)	11 (13.58)	9 (16.98)	0
Without treatment at the arriving time, N (%)	41 (50.61)	23 (43.39)	5 (50)
sDMARD at arriving, N (%)	30 (37.03)	25 (47.17)	5 (50)
Biologic therapy at arriving, N (%)	16 (19.75)	13 (24.53)	0

sDMARD: synthetic disease-modifying antirheumatic drugs. IQR:Interquartile range.

Conclusions: Our RTCU received mostly JIA patients. Median age at arriving was slightly higher than expected. A fourth of patients were active in the transition moment. All this data highlights the need of an strict control of these patients in the transitional period.
References:
[1] Foster HE. Ann Rheum Dis 2016;0:1–8.
[2] Calvo I. Rheumatol Int (2015) 35:1615–1624.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5185

AB0948 INSUFFICIENT CALCIUM INTAKE IN PEDIATRIC POPULATION WITH RISK FACTORS FOR OSTEOPOROSIS

B. Magallares López[1], J. Betancourt[2], G. Fraga[2], N. Pardo[3], M. Torrent[2], A. Marin[4], S. Herrera[4], E. Carreras[2], J. Casademont[4], J. Malouf Sierra[4]. *[1]Rheumatology; [2]Pediatrics; [3]Hospital Santa Creu I Sant Pau, Barcelona, Spain; [4]Internal Medicine, Hospital Santa Creu I Sant Pau, Barcelona, Spain*

Background: Compliance with daily calcium requirements in paediatric and young age is necessary to acquire peak bone mass, especially in populations that meet one or more risk factors for fractures
Objectives: To study the characteristics of the pediatric population with at least one risk factor for developing low bone mass/osteoporosis and to measure their calcium intake
Methods: Demographic and clinical data were prospectively collected from patients aged 2 to 20 years that met at least 1 risk factors for bone fragility, including: inflammatory diseases, treatment with Immunosuppressants and/or

corticoesteroids, malabsortive disorders, chronic systemic disorders such as nephropathies or hematologic diseases, etc. The patients or their legal tutors signed the Informed Consent in order to participate in the study. The average daily calcium intake was collected through the Spanish INDICAD 2001 study survey, together with a comprehensive anamnesis. If patients or their family reported taking food not included in the survey, its calcium content were consulted in the Spanish Food Composition Database published by the BEDCA Network of the Ministry of Health Science and Innovation

Results: Data were collected from 50 patients, with a mean age of 9.2 years (2–20), 28 (56%) female, 86% Caucasian, 6% Arab, 2% Asian and 6% Latin. The most frequent diagnoses were: Food intolerances/malabsorption: 32%, nephropathies: 22%, JIA: 16%, vasculitis: 10%, other inflammatory diseases: 8%. 42% had received systemic corticosteroids at some point, and 16% were receiving corticosteroids at present. Average daily calcium intake was 718 mg/d. They were divided by age groups, attending to daily calcium needs per group. In Table 1 we can observe the Recommended Daily Amount (RDA) of calcium by the Spanish Association of Pediatrics and the consumption collected, by age group.

Age group	% Age group	RDA (mg/d)	Average intake (mg/d) ± SD	Range: min–max (mg/d)	% That reaches RDA
Pre-escholar (2–3 a)	14%	700	819±280	513–1346	57.1%
Escholar (4–9 a)	32%	1000	702±240	254–1075	18.8%
Teenagers (10–17a)	48%	1300	689±350	350–1925	8.3%
Young (18–20 a)	6%	1100	797±182	621–985	0%

Only 3 children with low calcium intake were taking supplements.A decrease in calcium RDA adherence was observed with increasing age, statistically significant (p=0.009). There was also a lower calcium intake in the non-Caucasians compared to Caucasians statistically significant (p=0.044), which was not associated with age.

Conclusions: Calcium intake in the population under 21 years old with at least 1 risk factor for developing low bone mass/osteoporosis is lower than recommended. In addition, recommendations are based on the physiological needs of the healthy population and it could be expected to be insufficient for those with chronic diseases. It should be noted that calcium intake in the groups with higher requirements (adolescents and young people) is lower, with a reduction in the proportion of patients who meet the compliance with the RDA as age increases. Studies with a larger population are needed to ratify these results together with serum calcidiol levels

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2049

AB0949 THE ANNUAL COST OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

B. Serpen[1], O. Altug-Gucenmez[1], C. Acari[1], M.K. Sozmen[2], B. Makay[1], S.E. Unsal[1]. [1]*Faculty of Medicine, Unit of Pediatric Rheumatology, Dokuz Eylul University;* [2]*Faculty of Medicine, Department of Public Health, Izmir Katip Celebi University, Izmir, Turkey*

Background: The management of juvenile idiopathic arthritis (JIA) includes various methods including such as medication, hospitalization, rehabilitation.

Objectives: To determine how much juvenile idiopathic arthritis cost; the components of this cost; how new treatments, i.e. biologics, improve the disease course and hospital expenditures.

Methods: This study was conducted in Dokuz Eylul University, Pediatric Rheumatology Unit between March 2015-March 2016. One-hundred six JIA patients who had a follow-up period of at least 1 year according to International Edmonton 2001 criteria were included. This retrospective cost study evaluated the data of these patients and calculated the direct cost for the follow-up period. Clinical data was collected from patient files that were in department's archive and cost data was gathered from Probel Hospital Information Management system. Patient data form covering sociodemographic and clinical information, patient drug form and annual medical cost form was filled out for each patient.

Results: 58.5% (n=62) of patients was female and 41.5% (n=44) was male. The mean age was 12.0±4.3 years. 34.0% (n=36) of patients was oligoarticular type, 28.3% (n=30) was poliarticular type, 22.6% (n=24) was enthesitis related arthritis (ERA), 8,5% (n=9) was psoriatic type and 6.6% (n=7) was systemic type. The cost of medication counted for 88.3% (453244.94 TL) of total direct annual cost. Total direct medical cost was highest for ERA (n=7742.55±9891 TL). While the annual cost was calculated as 10451 TL per person for biologic using patients, for the patients using non-biologic treatments it was determined as 1472 TL per person. 1 TL=0.32 € 1 TL =0.35 $

Conclusions: Medication is responsible for most of the total direct medical cost in patients with JIA. Our results showed concordance with previous studies on the subject. This situation could be attributed to biologic agents that are being used in treatment in recent years. More prospective studies on the effectiveness of cost of treatment, with greater amount of patient and more homogenous subgroups are needed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5743

AB0950 PREDICTORS OF RESPONSE TO ETANERCEPT TREATMENT DEPENDING ON JUVENILE IDIOPATHIC ARTHRITIS CATEGORY

E. Kashchenko[1], E. Alexeeva[1,2], T. Bzarova[1,2], S. Valieva[1], R. Denisova[1], O. Lomakina[1], K. Isaeva[1], M. Soloshenko[1], A. Karaseva[1]. [1]*Federal State Autonomous Institution "National Scientific and Practical Center of Children's Health" of the Ministry of Healthcare of the Russian Federation;* [2]*I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Background: Anti-TNF biologics are highly effective and widely used in clinical practice for the treatment of JIA. However, some children lack of response with few reliable predictors of a good or poor response to treatment found [1–3]. As clinical picture patterns are significantly differ for 7 JIA subclasses, we propose to found predictors of response to therapy for each of JIA category.

Objectives: To identify clinical and laboratory parameters associated with response to etanercept treatment in 12 months in patients with different JIA category.

Methods: Patients from four JIA categories (n=195) were divided to groups with excellent, intermediate and poor response after 12 month treatment with etanercept according to ACRPedi criteria, achieving inactive disease by Wallace criteria and JADAS-71 cut-off point. For each of JIA category univariate and multivariate logistic regression analysis was conducted to identify potential baseline factors associated with treatment response. Baseline factors included clinical, laboratory and anamnestic data.

Results: From total cohort 91/90/85/68.5 percent of patients achieved ACR30/50/70/90 in one year etanercept treatment; 45.5% patients were considered excellent responders, 30% - intermediate responders, and 24.5% - poor responders. Highest efficacy of therapy was shown in persistent oligoarthritis patient, lowest – in enthesitis-related arthritis and polyarthritis patients. Potential baseline predictors of excellent and poor response which were significant are described in the table.

JIA category	Predictors of excellent response	Predictors of poor response
Persistent oligoarthritis	smaller amount of DMARD	–
Extended oligoarthritis	shorter disease duration (DD)	–
Enthesitis-related arthritis	–	– longer DD
RF-negative polyarthritis	– smaller number of joints with limited range of motion (LOM) – lower CRP level at the baseline – younger age at disease onset (ADO)	– longer DD – older ADO

Analysis showed that poor response in all JIA categories was mainly associated with demographic data (longer DD and older ADO). However, factors associated with excellent response significantly differed depending on JIA category (anamnestic factors, number of involved joints, laboratory factors, and demographic factors).

Conclusions: Response to etanercept therapy is strongly associated with JIA category. Shorter disease duration and lower number of DMARDs used before start of etanercept, lower number of joints with LOM, and lower C-reactive protein at baseline are predictors of better response to etanercept.

References:

[1] Otten MH, et al. JAMA 2011;306:2340–7.
[2] Kearsley-Fleet L, et al. Rheumatology (Oxford) 2016;55:840–7.
[3] Solari N, et al. J Rheumatol 2013;40:192–200.

Disclosure of Interest: E. Kashchenko Grant/research support from: Novartis, E. Alexeeva Grant/research support from: Roche, Abbott, Pfizer, Bristol-Myers Squibb, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Bristol-Myers Squibb, Medac, Novartis, Pfizer, T. Bzarova Grant/research support from: Roche, Pfizer, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Pfizer, S. Valieva Grant/research support from: Roche, Bristol-Myers Squibb, Speakers bureau: Roche, Merck Sharp & Dohme, Bristol-Myers Squibb, Medac, Novartis, R. Denisova Grant/research support from: Roche, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Medac, O. Lomakina: None declared, K. Isaeva Grant/research support from: Roche, Novartis, M. Soloshenko: None declared, A. Karaseva: None declared

DOI: 10.1136/annrheumdis-2017-eular.3918

AB0951 FACTORS ASSOCIATED WITH RESPONSE TO ADALIMUMAB TREATMENT IN JUVENILE IDIOPATHIC ARTHRITIS

E. Kashchenko[1], E. Alexeeva[1,2], T. Bzarova[1,2], S. Valieva[1], R. Denisova[1], O. Lomakina[1], K. Isaeva[1], M. Soloshenko[1], A. Karaseva[1]. [1]*Federal State Autonomous Institution "National Scientific and Practical Center of Children's Health" of the Ministry of Healthcare of the Russian Federation;* [2]*I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Background: Tumor necrosis factor inhibitors are highly effective and safe in treatment of juvenile idiopathic arthritis (JIA). Nonetheless, to select the optimal therapy and to achieve maximum therapeutic effect it is necessary to consider the individual characteristics of the patient. Adalimumab (ADA) is widespread use for mild and severe polyarticular JIA especially in the presence of uveitis, but there is lack of data about clinical and laboratory predictors of response to ADA in different JIA categories.

Objectives: To identify clinical and laboratory parameters associated with

Abstract AB0951 – Table 1

Factors	Excellent response to ADA	Poor response to ADA
CHAQ score	lower at start of ADA (ExtOligo)	–
VAS disease activity by patient/parent	higher at start of ADA (ERA)	lower at start of ADA (ERA)
VAS disease activity by physician	–	lower at start of ADA (PersOligo)
Need for corticosteroid eye drops (for uveitis patients)	Absence in anamnesis (PersOligo)	–
Morning stiffness	Shorter at start of ADA (ERA), longer at start of ADA (PersOligo)	–
Joints with active arthritis	–	higher at start of ADA (PolyRF-)
erythrocyte sedimentation rate (ESR)	–	lower at start of ADA (PolyRF-)

response to adalimumab treatment in 12 months in patients with different JIA category.

Methods: Analysis include patients with enthesitis-related arthritis (ERA, n=56), RF-negative polyarthritis (polyRF-, n=50), extended oligoarthritis (extOligo, n=30), and persistent oligoarthritis (persOligo, n=62) with median age 10.5 (IQR 7–14) and median JADAS-71 19.5 (IQR 15–28). Patients were divided to response groups after 12 month treatment with ADA according to ACRPedi criteria, achieving inactive disease by Wallace criteria and JADAS-71 cut-off point as excellent, intermediate and poor responders. For each of JIA category univariate and multivariate logistic regression analysis was conducted to identify potential baseline factors associated with treatment response. Baseline factors included clinical, laboratory and anamnestic data.

Results: ADA was shown to be effective in all groups with 90%/89%/82%/63% children with ACR30/50/70/90 during one year therapy. The most significant factors ($p<0.05$) associated with response to ADA treatment are presented in summarized table.

Our findings demonstrated that different predictors corresponded with different JIA categories. Interestingly subjective scales of disease activity was shown to be strongly associated with response to therapy. At the same time VAS severity at baseline were inversely correlated with achievement of good response. Duration of morning stiffness correlated with excellent response in children with 2 different categories. However, for ERA patients shorter duration was associated with better response to treatment while vice versa for PersOligo patients.

Conclusions: Predictors of response to ADA treatment differ in JIA categories. Low disease activity parameters (clinical and laboratory) at baseline not always predict good response to therapy.

Disclosure of Interest: E. Kashchenko Grant/research support from: Novartis, E. Alexeeva Grant/research support from: Roche, Abbott, Pfizer, Bristol-Myers Squibb, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Bristol-Myers Squibb, Medac, Novartis, Pfizer, T. Bzarova Grant/research support from: Roche, Pfizer, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Pfizer, S. Valieva Grant/research support from: Roche, Bristol-Myers Squibb, Speakers bureau: Roche, Merck Sharp & Dohme, Bristol-Myers Squibb, Medac, Novartis, R. Denisova Grant/research support from: Roche, Centocor, Novartis, Speakers bureau: Roche, Merck Sharp & Dohme, Abbott, Medac, O. Lomakina: None declared, K. Isaeva Grant/research support from: Roche, Novartis, M. Soloshenko: None declared, A. Karaseva: None declared

DOI: 10.1136/annrheumdis-2017-eular.4011

AB0952 EXPERIENCE OF TOCILIZUMAB USE IN TREATMENT OF JUVENILE IDIOPATHIC ATRTRITIS IN CHELYABINSK REGIONAL CHILDREN HOSPITAL

G.A. Glazyrina[1], N.A. Kolyadina[2]. *[1]South Ural Governmental Medical University; [2]Chelyabinsk Regional Children Hospital, Chelyabinsk, Russian Federation*

Background: Recently due to application of interleukin (IL)-6 inhibitors prognosis for systemic juvenile idiopathic arthritis (sJIA) has significantly improved. 526 children with JIA are under monitoring in Chelyabinsk region, 42 children have sJIA. Tocilizumab is the drug of choice for sJIA treatment. It is registered within the Russian Federation for use in children older than 2 years. In Chelyabinsk Regional Children Hospital tocilizumab has been used for 5 years.

Methods: 18 children (12 boys, 6 girls) aged from 2 to 17 (mean age 10.7 years) diagnosed with sJIA were under monitoring. Disease duration was from 6 months to 15 years (mean duration 6 years). JIA was diagnosed based on ILAR diagnostic criteria. SJIA was diagnosed in 16 children, sero-negative polyarthritis was diagnosed in 2 children. Tocilizumab was introduced intravenously every 2 or 4 weeks in dose of 12 mg/kg for children <30 kg or 8 mg/kg for children ≥ 30 kg. Therapy duration was from 3 months to 5 years (average duration 23 months). Assessment of disease activity and therapy efficiency was conducted in accordance with ACR pedi criteria. Nonparametric statistical methods were used to compare results.

Results: Prior to tocilizumab use high disease activity was observed in all children. Average number of joints with active arthritis was 13,5 [6;15] (Me [25;75%]). Average number of joints with functional impairments – 12,5 [6;15]. Average ESR (according to Panchenkov) – 50 [40;60]mm/h, CRP 98,6 [55;139]g/L. Assessment of functional activity according to CHAQ questionnaire- 2,09 [2;2,5]. Activity assessment according to VAS by doctor – 82 [75;90]. Assessment of parents according to VAS 84 [80;90]. No eye lesions were found in children under monitoring. All 16 children with sJIA had fever, hepatosplenomegaly and lymphadenopathy, the rash had 11 children, polyserositis - 8. In 5 children there was a complication in the form of a syndrome of macrophage activation.

During the tocilizumab therapy a decrease in disease activity was observed in all patients. Mean number of joints with active arthritis was 1 [0;2] (Me [25;75%]) (P=0.0002). Mean number of joints with functional impairments – 3 [0;3] (P=0.0003). Average ESR was 4 [3;5]mm/h (P=0.00002), CRP 0,75 [0;1]g/L (P=0.0003). Assessment of functional activity according to CHAQ questionnaire was 0,25 [0;0.5] (P=0.0004). Activity assessment according to VAS by doctor – 16 [10;20] (P=0.0002). Assessment of parents according to VAS 18 [10;20] (P=0.0002).

Clinical disease remission (according to ACR pedi criteria– $\geq$90%) was observed in 11 patients after 6–9 months of treatment. Remission duration up to now is from 3 months to 4 years. Efficiency according to ACR pedi criteria is 70% in 6 children, 50% in 1.

The drug was well-tolerated. Undesirable effect such as allergic skin reactions were observed only in one child. In one child the lack of efficiency produced by switching to canakinumab. Drug was cancelled in 3 patients due to long-term remission (3–4 years), but 2 of them after a year needed the resumption of therapy in connection with the aggravation of the disease.

Conclusions: Tocilizumab therapy was highly effective and safe in patients with JIA. Clinical remission was achieved in 61,1% children. Decrease in disease activity was observed in 39,9% of children. No serious undesirable effects were reported.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3354

AB0953 ARTHRITIS FOLLOWING PARASITIC INFECTION IN THE DIFFERENTIAL DIAGNOSIS OF JUVENILE IDIOPATHIC ARTHRITIS

M. Maschio[1], S. Pieropan[2], F. Caldonazzi[1], G. Dallagiacoma[2], V. Ravagnani[3], D. Degani[1], G. Piacentini[1], D. Biasi[2], M. Rossini[2]. *[1]UOC pediatria; [2]UOC reumatologia, AOUI, Verona; [3]Reumatologia, Azienda Ospedaliera Carlo Poma, Mantova, Italy*

Background: According to literature arthritis is a rare complication following parasitic infection. In the italian pediatric population parasitic infection is manly caused by Enterobius Vermicularis; it is often asymptomatic but common symptoms can be anal nocturnal itching, insomnia, irritability, abdominal pain together with arthralgia

Objectives: To describe cases of mono or poliarthritis due to parasitic infection in young patients followed at the Verona's Pediatric Rheumathology Clinic from 2010 to 2016

Methods: Medical records of 8 patients followed at the Pediatric Rheumatology were analyzed. The mean age of 8 patients was 8 (F:M 3:5). The following data were evaluated: anamnesis data, clinical symptoms (anal itching, irritability, arthralgia, abdominal pain and arthritis), Blood test and scotch tape test. All patients underwent joint ultrasound (US). Physical symptoms of joint's involvement were evaluated in all children by an experienced rheumatologist.

Results: 6 patients had symmetrical poliathirtis, 2 patients had monoarthritis (knee and hand). Symptom's complaint were systemic (12,5%), abdominal (25%), and general pruritus (25%).Blood test confirmed high inflammation indices (25%) and hypereosinophilia (12,5%).Serological tests and stool investigations allowed to diagnose the following infections: Enterobius vermicularis (6 cases) giardia lamblia (1 case); dientaomeba fragilis (1 case).Joint US evidenced synovium hyperplasia in 75% of the cases and tenosynovitis in 50% of the cases.After appropriate antiparasitic treatment complete articular and systemic symptomatic remission was observed (100% cases); also joint US control normalized.2 cases, after about 6 months, were re-evaluated for arthritis relapse and in both cases a parasitic reinfection was confirmed.

Conclusions: Analysis of this series of patients underlines the following data: arthritis can be a manifestation of parasitic infection; treatment must be aimed against the parasite involved in order to achieve complete clinical and laboratory data remission; reinfection must always be considered in cases of relapse; differential diagnosis of this form of arthritis with other chronic polyarthritis is fundamental due to the risk of disseminated infection in case of immunosuppressive treatment

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4876

AB0954 RELATIONSHIP BETWEEN SERUM COMPLEMENT LEVELS AND RENAL PATHOLOGICAL CLASSIFICATION IN CHILDREN WITH SILENT LUPUS NEPHRITIS

H. Wakiguchi[1], T. Kubota[2], S. Takei[3]. *[1]Department of Pediatrics, Yamaguchi University Graduate School of Medicine, Ube; [2]Department of Pediatrics, Kagoshima University Graduate School of Medical and Dental Sciences; [3]School of Health Science, Faculty of Medicine, Kagoshima University, Kagoshima, Japan*

Background: Silent lupus nephritis is defined by some pathological evidence of lupus nephritis with normal urinary findings. It is therefore apparent only upon renal biopsy. Serum complement levels have been associated with overall lupus disease activity. Despite recent progress in understanding the pathogenesis of lupus nephritis, including complement, our understanding of silent lupus nephritis, especially in children, remains limited.
Objectives: To search whether serum complement levels are associated with renal pathological classification in children with silent lupus nephritis.
Methods: We determined serum C3 and C4 levels and International Society of Nephrology/Renal Pathology Society classification in 25 patients with paediatric silent lupus nephritis before initial therapy who were admitted to our hospital. Patients were classified as having silent lupus nephritis based on normal urinary findings at baseline renal biopsy in juvenile systemic lupus erythematosus.
Results: Serum C3 levels varied between International Society of Nephrology/Renal Pathology Society classes, with significantly lower levels for silent lupus nephritis patients in class III compared to class II, and for class II compared to class I. There was no significant difference in serum C4 levels between International Society of Nephrology/Renal Pathology Society classes in patients with silent lupus nephritis.
Conclusions: Our results suggest that serum C3 levels were associated with renal pathological classification in children with silent lupus nephritis. We propose that serum C3 levels would provide a useful tool for predicting latent severe nephritis in patients with juvenile systemic lupus erythematosus who have normal urinary findings before initial therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1012

AB0955 NEW ONSET OF UVEITIS, PSORIASIS OR IBD AS PARADOXICAL EFFECTS OF BIOLOGICS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: SINGLE CENTER EXPERIENCE

I. Nikishina, O. Kostareva, M. Kaleda, S. Rodionovskaya, S. Arsenyeva, D. Alekseev, E. Fedorov, A. Shapovalenko. *V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Biological agents (BA) are high efficacy options for current therapy for patients (pts) with juvenile idiopathic arthritis (JIA). They are successfully used not only for the arthritis but also for uveitis, psoriasis and inflammatory bowel disease (IBD). However, paradoxical induction of these conditions in pts treated with BA is a well-established phenomenon.
Objectives: To evaluate the frequency of new onset of uveitis, psoriasis or IBD occurring under BA therapy in JIA pts, to establish clinical features, which may be associated with development of such effects.
Methods: Retrospective cohort study involved all JIA pts (740) who were treated with BA in our clinic from 2004 to 2016. All cases of new onset (*no*)-uveitis/psoriasis/IBD collected; clinical features of disease onset and course, activity level, JIA category, exposure to Methotrexate (MTX) and BA, presence of ANA, HLA B27 were studied.
Results: We identified 20 (2.7%) pts (11 female/9 male) with *no*-uveitis under BA, mostly during etanercept (ETA) therapy (18 cases from 285 ETA courses, 6.3%), 1/112 - in abatacept (ABA) and 1/233 - in adalimumab (ADA); 2.46 events/100 patient-year (PY) vs 0.31 in ABA, and 0.15 in ADA), ETA exposure was 14.9±9.9 months (mo). JIA subtypes were as follows: RF-neg polyarthritis 5 (25%), persistent oligoarthritis 3 (15%), extended oligoarthritis 10 (50%) ERA - 2 (10%). JIA started in this group at the age of 4.5±3.9 yrs.18/20 patients had high laboratory activity (CRP 55±25 mg/l) and severe arthritis before BA initiation. Most of pts (16/20) achieved 90–100% ACRpedi-response by the uveitis development. 1 pt was treated by ADA for the 71 mo *and* switched to ABA. in 1 pt *no*-uveitis was obseved under ABA. 12/20 pts were ANA-positive, 10/20 pts had HLAB27, 1 pt did not have ANA or HLAB27. Uveitis was occurred earlier in ANA plus B27 positive pts (mean exposure - 10.7 mo vs 27.4 in ANA+ and 21.6 in B27+ pts). 17/20 (85%) of pts received MTX. In all cases of *no*-uveitis BA was switched. 5 pts from 740 (0.7%) developed *no*-psoriasis under BA: INF - 2 cases (0.62/100PY), ADA - 2 (0.15/100PY), ABA -1 (0.31/100PY). JIA subtypes were presented by RF-negative polyarthritis (1), extended oligoarthritis – 3. All received MTX. 1/5 pts was ANA+, 2/5 - HLAB27+. Average age of disease onset was 9.8±7.8 years; BA exposure before psoriasis was 25±11.5 mo. Therapy was continued in 3/5 pts; switched from INF to ADA in 2. Only 1 case of *no*-IBD was occurred in female patient fulfilled to systemic-onset JIA criteria years. She was treated by INF for the 62 months and switched to ADA due to secondary inefficiency presented by active polyarthritis and sacroiliitis (HLAB27neg), but 2 months later severe gastrointestinal symptoms appeared and diagnosis of Crohn's disease was established by endoscopy.
Conclusions: Our study suggested that new onset of uveitis, psoriasis and IBD is rare adverse event during BA therapy in JiA. It seemes to be as delayed implication of disease natura. but not therapy complication. Uveitis observed mostly in pts receiving ETA, unlike the psoriasis mainly developed during TNF-monoclonal antibodies using. High activity aggressive manifestations at disease onset and good initial response to BA are typical features for all pts, who developed paradoxical effects under BA therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6753

AB0956 INFLUENCE OF BIOLOGICAL THERAPY ON BONE MINERAL DENSITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

I. Chyzheuskaya[1], L. Byelyaeva[2], N. Vasiljeva[2], R. Filonovich[1], L. Zajtseva[1]. *[1]Department of pediatrics, 4th City Children's Clinical Hospital of Minsk; [2]Department of pediatrics, Belarusian Medical Academy of Postgraduate Education, Minsk, Belarus*

Background: Juvenile idiopathic arthritis (JIA) is one of the most common and most disabling rheumatic diseases in children. JIA is a systemic chronic inflammatory immunopathological disease, which leads to dysfunction of the joints, their deformation and limitations of life of the child, violates the child's growth and development. One of the complications of systemic JIA in children is osteoporosis. In the pathogenesis of osteoporosis important place is given to the use of glucocorticoids. In world Rheumatology successfully used drugs aimed at the major pro-inflammatory cytokines such as tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-6 (IL-6), and others.
Objectives: The purpose of research - to determine the influence of biological therapy on bone mineral density in children with JIA.
Methods: 15 children with systemic JIA (mean age 11,9±3,4 years) were examined in the rheumatological department of 4th city clinical hospital of Minsk. Bone mineral density was assessed by 2-energy X-ray absorptiometry (DEXA) at two points of the skeleton. The level of mineralization of skeletal mineral content was estimated in the bone tissue (BMC), bone mineral density (BMD) and the parameter Z-score. Z-score was used to determine the incidence of osteopenia and osteoporosis in children surveyed. In accordance with the WHO criteria for normal bone mineral density was diagnosed with the Z-score> -1 SD, osteopenia - at Z-score <-1 SD, but> - 2,5 SD, osteoporosis - with Z-score <-2,5 SD. Statistical data processing carried out using an integrated application package "Statistics 6 for Windows".
Results: In a study of children osteopenia was diagnosed in 9 patients with systemic JIA (mean Z-score -2,3 SD) Osteoporosis was diagnosed in 6 patients with systemic JIA (mean Z-score -2,7 SD). All children received a mean dose of methotrexate 12.7 mg/m^2 of body surface area, an average dose of methylprednisolone 0.34 mg/kg body weight per day and treatment of IL-6 inhibitor - tocilizumab 8 mg/kg body weight every 2–4 weeks. Bone mineral density was measured prior to initiating therapy tocilizumab and after 2 years of therapy.
During tocilizumab therapy achieved remission of the disease, all children was canceled methylprednisolone. After re densitometry of 2 years after the beginning of therapy improvement noted tocilizumab Z-score in children with osteopenia with Z-score -2.3 SD to Z-score -1.4 SD, in children with osteoporosis a Z-score -2 7 SD to Z-score - 2,1 SD.
Conclusions: The results indicate a positive influence tocilizumab therapy to bone mineral density in children with JIA.
Acknowledgements: This study would not have been possible without the collaboration of numerous Belarusian pediatric rheumatologists, patients and their parents.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6787

AB0957 IS THERE A DIFFERENCE IN THE CLINICAL PRESENTATION OF JUVENILE SYSTEMIC SCLERODERMA PATIENTS ACCORDING THE AGE OF ONSET: RESULTS FROM THE JUVENILE SCLERODERMA INCEPTION COHORT WWW.JUVENILE-SCLERODERMA.COM

I. Foeldvari[1], J. Klotsche[2], O. Kasapçopur[1], A. Adrovic[1], V. Stanevicha[1], M.T. Terreri[1], E. Alexeeva[1], M. Katsicas[1], V. Smith[1], R. Cimaz[1], M. Kostik[1], T. Lehman[1], J. Anton[1], W.-A. Sifuentes-Giraldo[1], F. Sztajnbok[1], T. Avcin[1], M. Janarthanan[1], M.J. Santos[1], M. Moll[1], D. Nemcova[1], C. Battagliotti[1], J. Brunner[1], D. Eleftheriou[1], L. Harel[1], T. Kallinich[1], K. Minden[2], S. Nielsen[1], K. Torok[1], Y. Uziel[1], A. Stevens[1], C. Pilkington[1], N. Helmus[1]. *[1]Hamburg Center for Pediatric Rheumatology, Hamburg; [2]DRFZ, Berlin, Germany*

Background: Juvenile systemic sclerosis (jSSc) is an orphan autoimmune disease. It was rarely looked at the differences between the clinical presentations of patients at different paediatric age groups. The juvenile scleroderma inception cohort (www.juvenile-scleroderma.com) is a prospective standardized register for patients with jSSc.
Objectives: Comparison of clinical characteristics of patients with different age range at the time of inclusion in the registry.
Methods: Patients with jSSc were included worldwide to the juvenile scleroderma inception cohort. We compared the demographics and clinical characteristics of

the patients at different age ranges. We created 3 cohorts with different age ranges at onset of disease. Patents aged less than 5 years (Group1), 5–10 years (Group2) and over 10 years (Group3) at the time of diagnosis of the first non-Raynaud involvement of jSSc.
Results: Up till now 88 patients were enrolled,14 patients (15%) in Group1, 22 (25%) in Group2 and 52 (59%) in Group3. Diffuse subtype occurred in 71% in Group1, in 82% in Group2 and in 65% in Group3. Most patients were Caucasian. Disease duration at time of inclusion into the cohort was 3.9 years in Group1, 4.9 years in Group2 and 2.2 years in Group3. ANA positivity was 57% in Group1, 77% in Group2 and 86% in Group3. Anti-scl 70 was around 30% in all groups. Anti-Centromere positivity was 7 to 10%. Mean modified skin score was 12.4 in Group1, 16.5 in Group2 and 15.9 in Group3. Raynaud Phenomenon occurred in 85 to 95% of the patients. History of active or inactive ulceration occurred in 57% in Group1, 62% in Group2 and 43% in Group3. Decreased FVC under 80% occurred in 43% in Group1, 32% in Group2 and 30% in Group3. Pulmonary hypertension occurred in 7% in Group1 and in 10% in Group3. No renal hypertension was observed. Urinary sedimentary changes occurred in 7% in Group1 and in 10% in Group3. Gastrointestinal involvement occurred in 21% in Group1, 45% in Group2 and 27% in Group3. Musculoskeletal involvement occurred in 58 to 64%. Patient global disease activity (VAS 0–100) was 42.8 to 47.9. Patient global disease damage (VAS 0–100) was 39.6- to 45.0. Physician global disease activity (VAS 0–100) was 35.4–40.0. Physician global disease damage (VAS 0–100) was 37.1 in Group1, 41.3 in Group2 and 27.7 in Group3.
Conclusions: It seems to be that patients, with onset of the disease in younger age have more severe disease as patients with disease onset after the age of 10 years. We need more patients in our cohort to gain more sufficient data to prove our preliminary observation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3419

AB0958 PROPOSAL FOR A JUVENILE SYSTEMIC SCLEROSIS RESPONSE INDEX (JSSCRI): RESULT OF THE CONSENSUS MEETING IN HAMBURG. GERMANY 11TH OF DECEMBER 2016

I. Foeldvari[1], D.F. Furst[2], J. Anton[3], E. Baildem[4], M. Blakley[5], T. Constantin[6], P. Costa Reis[7], M. Curran[8], M. Cutolo[9], C. Denton[10], K. Fligelstone[11], B. Hinrichs[12], F. Ingegnoli[13], A. Kienast[1], D. Němcova[14], C. Pain[4], C. Pilkington[15], V. Smith[16], D. Khanna[17]. *[1]Hamburg Center for Pediatric and Adolescent Rheumatology, Am Schön Klinik Eilbek, Hamburg, Germany; [2]UCLA, Los Angeles, United States; [3]Sant Joan de Déu Hospital, Barcelona, Spain; [4]Alder Hey Children's Foundation NHS Trust, Liverpool, United Kingdom; [5]Indiana University, Indianapolis, United States; [6]Semmelweis University, Budapest, Hungary; [7]Hospital de Santa Maria, Lisbon, Portugal; [8]Northwestern University, Chicago, United States; [9]University of Genova, Genova, Italy; [10]Royal Free Hospital; [11]FESCA, London, United Kingdom; [12]Practice Buchholz, AMS, Hamburg, Germany; [13]University of Milan, Milano, Italy; [14]Department of Pediatrics and Adolescent Medicine Charles University, Prague, Czech Republic; [15]GOSH, London, United Kingdom; [16]GU(H), Ghent, Belgium; [17]Univ Michigan, Michigan, United States*

Background: Juvenile Systemic Sclerosis (jSSc) is an orphan disease. There is increasing interest in testing novel therapies in the management of fibrotic diseases. Therefore, it is very important to develop a Response Index for jSSc (JSScRI) to distinguish effective therapies from placebo. In 2014 at the 1st JSScRI Consensus Meeting in Hamburg, following two rounds of a Delphi process, a proposal for domains and items for a JSScRI were made. In 2016, the 2nd JSScRI Consensus Meeting was held in Hamburg, Germany.
Objectives: To conduct a Nominal Group Technique (NGT) and select potential core data set items that could change as outcome measures) that will be incorporated in the development of a JSScRI.
Methods: Before the 2nd JSScRI Consensus Meeting, the items from the 1st JSScRI Consensus Meeting (2014) were scored via Email, in a Delphi by the participants of the current meeting. Participants included 14 experts in adult and juvenile SSc and a patient partner. During the subsequent face to face NGT meeting, moderated by DEF, and the items were scored anonymously by the participants after a nominal group discussion. The domains and items were scored regarding their importance for 1 year clinical trial from 1 (not relevant at all) to 9 (most relevant). A priori, it was agreed by the participants that the goal of the NGT was to exclude items that: 1. Are not feasible and 2. do not represent a changeable outcome measure even though they may represent the impact of disease on quality of life, vocational or recreational activity. Items with a median score of <4 in which greater than 1/3 of participants scored 1–3 [despite the item having a median score >3] were excluded.

Table 1. Assessment of the Activity of the Musculoskeletal domain

	Whole Group	1–3	4–6	7–9
1) Swollen joints	7	0	1	12
2) Limited range	7.5	1	1	10
3a) MMT	8	0	1	11
3b) CMAS	7	4	1	7
4) Presence of tendon friction rub	7	1	2	10
5a) CK	8	1	1	11
5b) Aldolase	7	3	3	7

Results: Seventy-one items in 13 domains were scored. Six items were not scored as they were felt to not represent an outcome measure or were non-feasible and six items received a median score less then 4.
Table 1 provides an example of the musculoskeletal domain with the median scores for different outcome measures.
Conclusions: In a rigorous, NGT consensus meeting, some item reduction for the JSScRI was achieved. Items will be tested in a prospective way in the patients of the inception cohort of juvenile SSc (www.juvenile-scleroderma.com).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2862

AB0959 EVALUATE THE CARDIOVASCULAR RISK THROUGH CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN THE YOUNG ADULT AGE

J.J. Bethencourt, L. Expósito, S. Bustabad. *Rheumatology, Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain*

Background: The relationship between inflammation and atherosclerosis has been demonstrated, so it is important to identify early markers of the disease. Ultrasound carotid intima-media thickness (CIMT) measurement is a non-invasive, consistent, validated technique used as a marker to identify subclinical arteriosclerotic disease.
The long-term risk of cardiovascular disease in young adult patients with juvenile idiopathic arthritis (JIA) is unclear and there are no risk management guidelines for these patients.
Objectives: To assess whether there is an increase in CIMT in the young adult with a history of JIA and to relate CIMT with classic cardiovascular risk factors in these patients.
Methods: Observational and cross-sectional study. Follow-up patients from transitional care between 18 and 36 years old, with JIA diagnosis by ILAR classification. Filiations data, anthropometric variables and activity disease scores were collected.
We performed, prior informed consent, CIMT measurement by radiofrequency with Esaote MyLab 70XVG. Three measurements were performed on each carotid artery, according to the protocol of the American Society of Echocardiography.
Results: Of the 20 patients, 17 (85%) women and 3 (15%) men. Subtype distribution was 8 (40%) oligoarticular, 1 of them ANA negative; 8 (40%) polyarticular being 4 seropositive and 4 seronegative; 1 systemic (5%); 2 (10%) psoriatic arthropathy and 1 (5%) HLA B27 positive arthritis. 66.7% are with disease modifying drugs (26.7% synthetic and 40% biological), while 33.3% do not have specific treatment.
The main variables studied are described in the attached table (Table 1).
In two previous independent studies conducted by Falaschi and Huang, CIMT was found to be 0.54±0.03 mm and 0.54±0.06 mm in 26 and 38 patients, respectively. From these results a mean and standard deviation of 0.54±0.05 mm were obtained. Using this last result as a control group, we compared it with the results of our series (0.466±0.068), with a significant difference ($p<0.001$).
In the statistical analysis, using the Rho Spearman, a significant correlation of the CIMT with the time of evolution of the disease in years ($r=0.579$) and systolic blood pressure ($r=0.621$) was observed at the level of 0.01 and with C Reactive Proteine ($r=0.524$) and BMI ($r=0.471$) at the 0.05 level.

	N	Minimum	Maximum	Media	Typical deviation
Age	20	18	36	24,75	5,350
Diagnosis age	20	1	16	9,70	5,048
Evolution time (years)	20	5	27	15,00	6,720
BMI (Kg/cm^2)	19	15,5	38,5	24,505	6,4347
Abdominal perimeter	20	58	126	81,33	19,392
Waist-hip index	20	44	135	90,40	26,009
Systolic blood pressure	20	96	130	114,05	7,258
Diastolic blood pressure	20	60	99	73,80	12,271
Left CIMT	20	394	634	464,15	54,788
Right CIMT	20	337	600	467,45	80,275
HAQ	17	,00	2,25	,3529	,59986
VAS pain (mm)	18	0	8	3,17	2,618
CRP (mg/L)	17	,3	57,7	9,419	14,6040
DAS28	16	,97	3,97	1,8856	,88204

Conclusions: The carotid intima-media thickness of patients with JIA were lower than the controls previously described in the literature, so we will complement this study with our population controls.
In addition to classic cardiovascular risk factors such as systolic blood pressure and BMI, there is correlation with the evolution time in years of the disease and CRP, so that in transitional care programs we must the activity of the disease and insist on identification, control and follow-up of the classics factors associated with cardiovascular risk.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4029

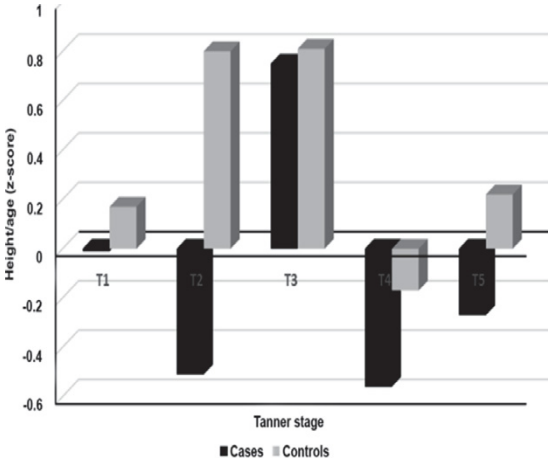
AB0960 GROWTH AND SEXUAL MATURATION IN GIRLS WITH JUVENILE IDIOPATHIC ARTHRITIS

L.M. Gonçalves[1], S.H. Machado[2], R.M. Xavier[3], P.J.C. Maróstica[4], P. Lora[5], L. Trindade[5]. *[1]student, PUCRS; [2]Rheumatology service, HCPA; [3]Rheumatology service, UFRGS; [4]Pediatrics service, UFRGS/Hcpa; [5]Unisinos, Porto Alegre, Brazil*

Background: Juvenile idiopathic arthritis (JIA) is a heterogeneous group of diseases with onset before the age of 16 years and joint inflammation as a main feature. Longitudinal growth is one of the main physical changes in childhood and adolescence. The etiology of delayed growth in children with JIA is multifactorial and strongly associated with prolonged inflammatory activity.
Objectives: To evaluate growth, sexual maturation, and the difference between final and expected height in girls with JIA and no glucocorticoid treatment for at least six months, as compared to a group of healthy girls.
Methods: This cross-sectional study involved 44 girls with JIA, diagnosed according to International League of Associations for Rheumatology (ILAR) criteria, and 59 healthy controls, aged between eight and 18 (incomplete) years with no comorbid chronic diseases. Demographic data were collected from all participants, and disease and treatment variables were compiled for the patient group. Anthropometric measurements were converted into z-scores based on WHO standards. Sexual maturation was classified according to Tanner stages.
Results: BMI and height z-scores were lower in girls with JIA as compared to control participants. These values differed significantly in Tanner stage II. Three (6.8%) girls with JIA had height-for-age z-scores <-2 (short stature). Girls with polyarticular JIA and higher cumulative glucocorticoid doses were significantly more likely to present with short stature. The percentage of prepubertal girls in the JIA group was significantly higher than that observed in the control group, (p=0.012). Age of menarche, adult height, and the difference between actual and expected height did not differ between groups.

Table 1. Comparison of pre- and postmenarcheal growth parameters between groups

Variables	Patients (n=44) Mean ± SD	Control participants (n=59) Mean ± SD	*p*
Menarche – n (%)	17 (38.6)	37 (62.7)	0.026
Age of menarche (years)	12.2±1.51	11.5±1.24	0,066
Menarche >2 years – n (%)	13/17 (76.5)	22/37 (59.5)	0.363
Δ Target height (father/mother)	-3.15±7.87 (n=8)	1.31±5.44 (n=16)	0.117
Nutritional data			
BMI z-score	-0.10±1.29	0.92±1.19	0.007
Height/age z-score	-0.14±1.24	0.27±1.17	0.253
Bone age z-score	-1.53±4.29	-1.42±2.17	0.928



Conclusions: These findings suggest that even six months after the suspension of glucocorticoid treatment, children with more severe forms of JIA and exposure to higher doses of glucocorticoids are still susceptible to growth impairment and delayed puberty.

References:

[1] PETTY RE, SOUTHWOOD TR, MANNERS P, et al.: International League of Associations for Rheumatology classificayion of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol 2004, 31:390–2.
[2] BECHTOLD S, SIMON D: Growth abnormalities in children and adolescents with juvenile idiopathic arthritis. Rheumatol int 2014; 34:1483–8.
[3] GIANNINI C, MOHN A, CHIARELLI F:Growth abnormalities in children with type 1 diabetes, juvenile chronic arthritis, and asthma. Int J Endocrinol 2014; 2014: 265954.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3016

AB0961 A COHORT OF PATIENTS WITH AUTOINFLAMATORY DISEASES FOLLOWED-UP IN A UNIT OF PAEDIATRIC AND TRANSITIONAL RHEUMATOLOGY: A DESCRIPTIVE STUDY

A. Boteanu, M. Llop Vilatella[1,1], M.A. Terán Tinedo, M.Á. Blázquez Cañamero, W.A. Sifuentes Giraldo, M. Vázquez Díaz, M.L. Gámir Gámir. *Rheumatology, Hospital Universitario Ramón y Cajal, Madrid, Spain*

Background: The autoinflammatory diseases (AD) are uncommon, most of them are presented as episodes of recurrent fever and may be accompanied by other inflammatory symptoms. This group of diseases includes polygenic entities (without a single known genetic mutation) such as Behçet's disease (BD), systemic-onset juvenile idiopathic arthritis (soJIA), Chronic recurrent multifocal osteomyelitis (CRMO) and PFAPA syndrome. On the other hand, we found the entities that present with specific monogenic mutations, such as Familial Mediterranean Fever (FMF), TNF receptor-associated periodic syndrome (TRAPS), hyper-IgD syndrome and periodic fever (HIDS), cryopyrinopathies (FCAS, MWS, CINCA), Blau's syndrome and PAPA. A group of patients who can not be classified into a specific diagnosis are clustered as recurrent fever without known genetic anomaly (RFW).
Objectives: To describe and compare the clinical features of monogenic and polygenic AD and RFW seen in a paediatric and transitional rheumatology unit of a Spanish tertiary care hospital.
Methods: We performed a retrospective study including 39 patients with AD followed-up in our center.
Results: The distribution of diagnoses was: soJIA 19 patients (48.72%), BD 5 (12.82%), PFAPA 6 (15.38%), CRMO 3 (7.69%), RFW 4 (10.26%), HIDS 1 (2.56%) and CINCA 1 (2.56%). Patients came from different regions of Spain, being 22 of them boys (56.41%) and 17 girls (43.59%). The genetic study was performed in 12 patients, being positive in 7 (17.95%). Mean age at onset of symptoms was 5±5.65 years in monogenic diseases, 7.96±4.84 years in polygenic disorders and 9.5±5.91 years RFW. Delay in diagnosis in monogenic diseases was higher than in polygenic diseases (67±69.29 months vs. 24.03±30.33 months, respectively). The clinical manifestations more frequently found were fever, followed by joint involvement, being more common in monogenic diseases than in polygenic disorders (table). Haemoglobin levels were lower in monogenic than in polygenic diseases 9.95 g/dL ± 0.63 vs. 11.69 g/dL ± 2, ESR and CRP was higher in monogenic diseases 106 mm/h ± 68.5 and 80.5 mg/L ± 84.14 vs. 56.1 mm/h ± 33.78 and 57.95 mg/L ± 57.95, unlike ferritin that was more elevated in polygenic disease 896 μg/dL ± 1788.34 than in monogenic diseases 183 μg/dL ± 195.7. During his follow up 84.62% of patients received corticosteroids, 51.8% methotrexate and 46.15% biological therapy.

	Monogenic	Polygenic	Recurrent fever
Fever	100%	81.25%	100%
Joint involvement	100%	62.5%	75%
Rash	100%	59.38%	0%
Lymphoadenopathy	50%	46.88%	25%
Splenomegaly	100%	12.5%	0%
Abdominal involvement	30%	21.88%	25%

Conclusions: soJIAs was the most frequent AD in our center. All the patients had a similar gender distribution. Delay in diagnosis was greater in monogenic diseases compared with polygenic disorders. Fever and joint involvement were the more common clinical manifestations, especially in monogenic diseases. Ferritin levels were higher in polygenic diseases, whereas CRP and ESR which were higher in monogenic diseases. During the follow-up most patients required treatment with corticosteroids and approximately half of them required biological therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6912

AB0962 CLINICAL AND LABORATORY CHARACTERISTICS OF NON-BACTERIAL OSTEOMYELITIS: DATA ANALYSIS OF 91 PATIENTS

M.M. Kostik[1], O. Kopchak[1,2], A. Mushkin[3]. *[1]Saint-Petersburg State Pediatric Medical University, Saint-Petersburg; [2]Kirov's regional children's hospital, Kirov; [3]Federal State Budget Institute "Science research Institute of Phthisiopulmonology", Saint-Petersburg, Russian Federation*

Background: Non-bacterial Osteomyelitis (NBO) is a sterile inflammatory bone disorder of unknown etiology. It typically affects children and most commonly presents with bone pain and/or swelling.
Objectives: The aim of study is to evaluate clinical and laboratory features of non-bacterial osteomyelitis in children.
Methods: Our retrospective – prospective study was included 91 patients with NBO. A routine blood test (WBC, platelets, ESR, C-reactive protein (CRP) and hemoglobin levels), a radiological examination and a bone biopsy with evaluation bacteriological and morphological data were performed in all patients.
Results: The mean age of onset NBO was 7.3 years (2.5; 10.6). We did not reveal any gender peculiarities in our study. Family history of immune-mediated diseases is found in 5/75 (6.7%) in prospective group. Concomitant immune-mediated diseases were noted in 62/89 (68.1%). Diagnostic delay was 6.3 (2.0; 17.8)

months. The radiological examination was performed in the following ratio: X-rays - 91 (100.0%), CT - 79 (86.8%), MRI - 66 (72.5), including MRI "whole body" with 15 pts, bone scintigraphy - 54 (59.3%). Monofocal form was registered in 1/3 cases. 2/3 cases was presented as a typical multifocal process with predominant involvement femur - 37 (40.7%), bone of foot - 36 (39.6%), tibia - 33 (36.3%), spine – 29 (31.9%). The number of foci is 3.0 (1.0; 6.0). We did not revealed any significant differences in quantity of WBC, platelets, hemoglobin level, ESR, CRP). Evidence confirming NBO was a negative bone biopsy in 100.0% cases. However, morphological data were as non-specific, as granulomatous inflammation.

Conclusions: NBO is determined as a primarily chronic multifocal process without specific clinical and laboratory peculiarities, associated with immune-mediated diseases. Diagnose must be established on morphological and bacteriological data bone biopsy.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1749

AB0963 LIPID ABNORMALITIES IN CHILDREN AND ADOLESCENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

L.F. Bogmat, N.S. Shevchenko, I.N. Bessonova, V.V. Nikonova. *Department of Cardiorheumatology, Institute of Children and Adolescents Health Care, Kharkiv, Ukraine*

Background: Systemic lupus erythematosus is an autoimmune disease that leads to the progressive destruction of the vital organs and systems, promotes early disability, premature mortality. The main reasons for the latest adult population of patients have complications of atherosclerotic vascular lesions stuch as the myocardial infarction and the stroke. The greatest effectiveness of preventive measures of the progression of atherosclerotic process and its associated cardiovascular complications determine the maximum early to start immediately after diagnosis in childhood and adolescence.

Objectives: To evaluate the lipid spectrum of the blood of children and adolescent patients with SLE.

Methods: It was been examined 26 persons 7–18 years with systemic lupus erythematosus, mostly female (88.46%), which were determined by the concentration of total cholesterol (total cholesterol), HDL cholesterol (HDL cholesterol), low density lipoprotein cholesterol (LDL), triglycerides (TG), calculated coefficient of the atherogenicity (CA = (total cholesterol - HDL cholesterol)/HDL cholesterol). Distribution groups conducted depending on the duration of the disease: the first consisted of 10 patients (38.46%) with a term of 1–3 years of the disease, the second - 16 people (61,54%) with duration of more than 3 years. The control group consisted of 10 healthy peers.

Results: Average lipid spectrum of the blood of patients did not exceed the reference values and had no statistical differences in the patients allocated to groups. However, in comparison with the control group the children with SLE had significant differences that reflect the peculiarities of formation of their metabolic disorders. Thus, total cholesterol and TG levels in both the first and the second groups were significantly higher than the control value and accounted for (5,02±0,26) mmol /L (5,24±0,26) mmol/L vs (3,39±0,20) mmol/L ($p<0$, 05) and (1,64±0,54) mmol/L (1,45±0,19) mmol/L vs (0,72±0,08) mg /L ($p<0.05$), respectively. Similar changes had occurred with parameters of LDL cholesterol, which significantly increased among patients with disease duration of 1–3 years ((3,08±0,26) mmol/L vs (1,73±0,03) mg/dL in the control group; $p<0.05$) and reached biggest values in patients with SLE over the course of 3 years ((3,57±0,82) mmol/l, $p<0.05$). In parallel, the concentration of HDL cholesterol patients of the second group decreased ((1,38±0,06) mmol/L vs (1,51±0,08) mg/dL healthy subjects, $p<0.1$), the consequence was significant increase in their spacecraft ((2,79±0,69) conv. units. against (1,24±0,17) conv. units. in comparison group, $p<0.05$).

In addition, patients with SLE found a direct correlation of total cholesterol blood of disease activity, confirmed a direct correlation ($r = 0,632$; $p<0.05$).

Conclusions: Thus, changes of blood lipid profile in the SLE patients occur in the early stages of the disease in childhood and adolescence, have the atherogenic focus, which compounded with increasing the duration and disease activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6569

AB0964 SOME PECULARITIES OF THE COURSE OF JUVENILE IDIOPATHIC ARTHRITIS IN PATIENTS TREATED WITH TOCILIZUMAB

O.A. Oshlyanska, A.G. Artsymovych. *Connective Tissue Disorders in Children, State Institute of Pediatrics, Obstetrics and Gynecology, Academy of Medical Sciences of Ukraine, Kyiv, Ukraine*

Background: The introduction of biological therapy drugs contributes to changing the natural course of the disease in cases of severe JIA.

Objectives: To clarify impact of tocilizumab on the course of JIA.

Methods: Of 117 children with JIA being under observation for the last five years 35% receive biologic therapy (3 etanercept, 21 adalimumab, 11 tocilizumab) during 1–5 years. Retrospective analysis of the data from clinical, laboratory and instrumental studies in the dynamics of the TCZ treatment of patients with JIA was made.

Results: Among children treated with TCZ 63,6% were sJIA cases, 63,6% were female. Age of onset 6,1±4,7y (6m–10,5y), all had acute onset, hyperthermia, severe pain syndrome, exudative arthritis in all pJIA cases and half of sJIA cases. ESR 39,7±11,2 mm/h, CRP 53,8±16,1 mg/L, all patients had anemia, leukocytosis and were seronegative for RF and anti-CCP, 3 of pJIA patients revealed ANA (1:1200–2400), IL-6 19,78±6,7 pg/ml. Before biological therapy has begun, SJIA courses were continuously relapsing in all cases with 4,7±2,1 exacerbations per y; during the 1st y of illness 8 cases run with coxitis, 7-cervical spine involvement, 9-wrists damage. All patients received CS therapy before initiating TCZ, 45,4% of them with pulse therapy, all marked by the inability to minimize the CS dose, all received 2–4 DMARDs in high doses. 2 patients received adalimumab before TCZ treatment. Elapsed time from the onset to biological agent prescription was 5,37±5,1 years. At the start of biological therapy JADAS was 19,6±5,7, stunted growth -1,88±0,3 σ, according to densitometry, osteoporosis took place in every case (Z=-2,7±1,1). After 6 month JADAS was 1,8±1,1, ESR and CRP normalized, IL-6 rate remained high in 36% cases. After 1 year the severity of osteoporosis decreased (Z = -1,17±0,8), bone deficiency depended on duration of TCZ exposure (r = -0,72) and on the elapsed time from onset of JIA before the start of biological therapy (r = -0,84). The mean increase in height was 7.73 cm/patient-year (+1±0,8 σ). Stunted growth depended on the duration of the TCZ course (r=-0,81) and the elapsed time from the onset of the disease to the start of biological therapy (r=-0,72). After 1 y of TCZ all children had normal weight and BMI for age (19,89±1,9). After 1–5 ys of treatment JADI was evaluated 2,1±2,9 (0–7), the degree of joint damage didn't depend on the duration of the biological therapy (r=0,24) and correlated with the time elapsed from the onset of the disease before treatment (r =0,59). During the treatment, exacerbations were marked only in 1 case, adverse events in 3 cases (skin infections, leukopenia). TCZ therapy allowed to completely discontinue CS in 63,6% cases, minimize them to 4 mg/day in others, DMARDs are discontinued in 9% cases.

Conclusions: Administration of TCZ is rather effective towards the drug induced remission even in long-time JIA process, but the least joint damage, osteoporosis and stunted growth can be obtained with earlier tocilizumab prescription. Reclassification of patients according to specific clinical and immunological features leads to optimization of the selection of targeted therapy.

References:

[1] While identifying in onset of JIA polyarticular destruction and systemic features (hyperthermia, anemia, leukocytosis, high laboratory activity and severity of osteoporosis) one should consider the feasibility of early administration of tocilizumab.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2715

AB0965 EVALUATION OF BONE MINERAL DENSITY IN CHILDREN WITH CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS AT DIAGNOSIS

Ö. Sert[1], E. Çomak[2], G. Kaya Aksoy[2], A. Gemici[2], M. Koyun[2], S. Akman[2]. *[1]Pediatrics; [2]Department of Pediatric Nephrology and Rheumatology, Akdeniz University School of Medicine, Antalya, Turkey*

Background: Chronic recurrent multifocal osteomyelitis (CRMO) is a rare autoinflammatory disorder that has sterile bone inflammation as a main phenotypic feature. Diagnosis of CRMO is based on typical clinical and radiologic findings and presence of some inflammatory markers. Plain radiographs, technetium bone scan and MRI may be used for diagnosis of children with suspected CRMO. Despite data for other imaging methods in chidren with CRMO, little information is available regarding the bone mineral density.

Objectives: The aim of the study was to evaluate bone mineral density (BMD) findings in children with CRMO at time of diagnosis.

Methods: The medical records of children with CRMO were reviewed retrospectively. Children who met Bristol diagnostic criteria were included in the study. Clinical and laboratory findings, bone scan and MRI features were analyzed. Bone mineral density was measured by DEXA technique at femoral neck and lumbar spine regions; a Z-score< -2 was considered as osteoporosis.

Results: A total of 6 patients, one girl and 5 boys, with a median age of 10 years (4 – 14 years) and a median follow-up period of 38.5 months (3 – 72 months) were included in the study. MRI and whole body technetium bone scan were performed at 6 and 4 children, respectively and detected at least two lesions MRI or bone scans. Osteoporosis was detected in 5 patients at diagnosis. Bone mineral density Z-scores were median -2.9 [-4.9±(-2,4)] and -2.9 [-4,1 – (-1,8)] at femoral neck and lumbar spine, respectively.

Conclusions: Osteoporosis is common in children with CRMO, it may be related with disease spectrum. Evaluation of bone mineral density abnormalities at time of diagnosis and during therapy may be a part of primary care in children with CRMO.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4452

AB0966 THE CLINICAL OBSERVATION OF IMMUNOADSORPTION IN TREATMENT OF CHILDREN WITH REFRACTORY AUTOIMMUNE DISEASES

P. Zeng[1], H. Zeng[2]. [1]*Department of Pediatric Allergy, Immunology and Rheumatolog, Guangzhou Women and Children's Medical Center, Guangzhou;* [2]*Department of Pediatric Allergy, Immunology and Rheumatology, Guangzhou Women and Children's Medical Center, Gungzhou, China*

Objectives: Explore the clinical efficacy and safety of the immunoadsorption assisted treatment of children with refractory autoimmune diseases.
Methods: Use HA280 type resin perfusion machine for four times of whole blood immunoadsorption treatment for one case of a 4-year-old child combined with severe dermatomyositis and pulmonary infection, one case of 9-year-old child with severe allergic purpura combined with gastrointestinal bleeding, intestinal perforation, after intestinal tract partial hepatectomy, one case of 11-year-old child with systemic juvenile idiopathic arthritis combined with head and facial cellulites and macrophage activation syndrome. Observe the improvement of its clinical manifestations, serum immunoglobulin, complement, liver and kidney function, myocardial enzymes, autoantibodies.
Results: The children's signs and symptoms improved significantly after treatment of whole blood immunoadsorption, the sensitivity of the adrenal cortex hormones increased, liver and kidney function, myocardial enzymes improved, the levels of serum IGG descended, complement (C3, C4) rose, anti-cyclic citrullinated peptide (CCP) was negative.
Conclusions: The whole blood perfusion immunity adsorption treatment is able to to reduce blood plasma IGG, improvement complement C3 and C4 level, eliminates anti-CCP immune body in vivo, reduce the cardiac muscle zymogram and the liver enzyme in a short time, increase sensitivity to the adrenal cortex hormone, alleviate immunological disease's symptom in active stage, have the affirmative function to make the baby pass the dangerous period safely. The child whole blood fills the class immunity adsorption not to present the untoward effect. No untoward effect happened.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2119

AB0967 CLINICAL, LABORATORY PROFILES AND LONG-TERM OUTCOME OF JUVENILE CUTANEOUS PAN: A SINGLE CENTER EXPERIENCE

R.A. Castellanos-Moreira[1], J.M. Mosquera[1], S.C. Rodriguez-Garcia[1], J. Calzada[1], A. Vicente[2], E. Iglesias[1], R. Bou[1], J. Anton[1]. [1]*Rheumatology;* [2]*Dermatology, Hospital Sant Joan de Déu, Barcelona, Spain*

Background: Cutaneous polyarteritis nodosa (cPAN) is an immune complex-mediated rare disease that affects small and medium sized vessels in the dermis and subcutaneous tissue.
The clinical course is characterized by periodic exacerbations and remissions that may persist for many years. Most patients respond to NSAIDs and glucocorticoids (GC), whereas some may require DMARDs and/or immunomodulatory therapy.
Objectives: To describe the diferrent clinical patterns, laboratory findings and long term outcomes of juvenile cPAN in a tertiary care hospital.
Methods: Retrospective observational study, including all patients diagnosed with cPAN between 2002–2016. Diagnosis relied on clinical features confirmed by histological study. Recorded data included clinical features, laboratory results and long-term outcomes.
Results: 10 children were included (7 female), mean age at onset was 9.9 years (r:4.1–16.3). Delay from symptoms onset to biopsy confirmed diagnosis was 2±2.3 months; 4 patients underwent a second biopsy due to inconclusive results in the first performed.
Clinical features included cutaneous (100%) and osteomuscular involvement (50%), fever (40%), neuropathy (10%) and weight loss (10%). Reported cutaneous symptoms were 8 patients with nodules, 4 livedo, 4 purpura, 1 ulcer and 1 necrosis. Most lesions were localized in the lower limbs (8), even though it was also reported in upper limbs (3) and trunk (3). Most cases exhibited raised CRP, ESR and leukocyte count with a mean of 26.4±47.9 (mg/L), 27.7±29.7 (mm/h), and 8.6±5.3 (x 10^9/L) respectively.
As first line therapy, all patients received GC and 6 NSAIDs. 8 were given a DMARD such as HCQ or MTX. Due to persistent activity or relapse, rescue treatment with pulse-GC (20%), MMF (10%) or IVIG (20%) was instituted. Only 1 patient received penicillin prophylaxis due to relapses associated with streptococcal infection.
Mean follow-up was 3.9 years (r: 1.1–10.4). 4 patients had a monophasic disease, six suffered ≥2 relapses. At last follow-up 9 patients were on remission, even though 3 were off-therapy. No complications were reported.
Conclusions: Clinical and laboratory findings in our series was similar to previous reports. However, our patients presented a greater number of relapses and DMARDs requirement.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4120

AB0968 HYPOVITAMINOSIS D IN JUVENILE IDIOPATHIC ARTHRITIS: PREVALENCE AND RELATED FACTORS

R. Galindo Zavala[1], L. Martín Pedraz[2], E. Núñez Cuadros[3], G. Díaz-Cordovés Rego[4], A.L. Urda Cardona[2]. [1]*Paediatric Rheumatology;* [2]*Paediatrics;* [3]*Universitary Regional Malaga Hospital, Malaga, Spain;* [4]*Rheumatology, Universitary Regional Malaga Hospital, Malaga, Spain*

Background: 25hydroxy-vitamin D not only plays a key role in calcium homeostasis, but also has antiinflammatory and immunomodulatory properties. Hypovitaminosis D prevalence in children suffering from Juvenile Idiopathic Arthritis (JIA) ranges from 6% to 30% according to different publications.
Objectives: Evaluate hypovitaminosis D prevalence in JIA pediatric patients in Spain and assess involved factors.
Methods: Observational cross-sectional study in JIA Spanish patients from 4 to 15 years, monitored by a Pediatric Rheumatology Unit. Monoarticular forms and patients with other chronic diseases or receiving different treatments from those indicated for JIA were excluded.
Anthropometric, clinical and treatment data were recorded. Bone metabolism parameters and validated diet (KIDMED) and exercise (PAQ-C/PAQ-A) questionnaires were obtained.
Hypovitaminosis D was defined as 25hydroxy-vitamin D plasma levels lower than 30 ng/ml
Results: 76 children participated. Their characteristics are included in table 1.
The population's prevalence estimation of hypovytaminosis D in children with JIA was 16 - 35% (CI 95%).
We found no relationship between 25 hydroxy-vitamin D levels and sex, JIA subtype neither duration or dose of systemic glucocorticoids.
In bivariate analysis we found direct association between hypovitaminosis D and Body Mass Index percentile (BMIp) (p=0,05), received dose of prednisone (p=0,03) and clinical activity duration (p=0,04); and an inverse relationship with physical activity level (p=0,04).
In multivariate analysis, relationship between hypovitaminosis D and BMIp (B 0,024; p 0,016) and with disease activity (B 0,015; p 0,01) were maintained. Moreover, we found an inverse association with biological disease-modifiying antirheumatic drugs (B-4,69; p 0,048), specifically with anti-tumoral necrosis factor α (antiTNFα) (B -4,7; p 0,042)

PATIENTS' CHARACTERITICS (N=76)		
Gender (Male), n (%)		23 (30,3)
Age (years), median (IR)		10,83 (8,52-13,54)
25OH-Vitamin D (ng/mL), mean (+/-SD)		34,04 ng/mL (8,90ng/mL)
DISEASE CHARACTERISTICS (N=76)		
JIA subtype, n (%)	Systemic	9 (11,8)
	Persistent oligoarticular	35 (46,1)
	Extended oligoarticular	12 (15,8)
	Positive RF polyarticular	1 (1,3)
	Negative RF Polyarticular	19 (25,0)
Duration disease (years), median (IR)		6,55 (3,29-9,45)
Inflammatory activity duration (days), median (IR)		385,0(246,75-761,25)
RECEIVED TREATMENTS (N=76)*		
Systemic GC, n (%)		61 (80,2)
GC treatment duration (days), median (IR) *(n=84)		125,00 (66,00-179,00)
Mean GC dose (mg/kg/day), median (IR)		0,276 (0,169-0,457)
Synthetic DMARDs treatment, n (%)		39 (51,3)
Biological DMARDs treatment,, n (%)		21(27,6)
Biological DMARDs treatment subtype, n(%)	Anti-TNFα	15 (19,7)
	Anti-IL1	4 (5,2)
	Anti-IL6	2 (2,6)

JIA: Juvenile idiopathic arthritis; RF: Rheumatic factor; GC: glucocorticoids; DMARD: Disease-modifying antirheumatic drug; Anti- TNFα: anti- tumoral necrosis factor α;Anti-IL1: anti-interleukin 1; Anti-IL6: anti-interleukin 6

Conclusions: Hypovitaminosis D prevalence in our population is similar to previously described.
JIA patients with higher BMIp have more hypovitaminosis D, as it has been reported in other inflammatory diseases.
A direct relationship exists between inflammatory activity and vitamin D, but we need more studies to asses if one is cause or consecuence of the other.
Patients treated with antiTNF have better plasma levels of 25 hydroxy-vitamin D, this can be explained because these drugs may increase 25 hydroxy-vitamin D

levels or due to a better response to antiTNF of those patient with higher plasma levels of 25 hydroxy-vitamin D.

References:
[1] Nisar MK, Masood F, Cookson P, Sansome A, Östör AJ. What do we know about juvenile idiopathic arthritis and vitamin D? A systematic literature review and meta-analysis of current evidence. Clin Rheumatol 2013; 32:729–734.
[2] Santos-Antunes J, Corte-Real Nunes A, Lopes S, Macedo G. The Relevance of Vitamin D and Antinuclear Antibodies in Patients with Inflammatory Bowel Disease Under Anti-TNF Treatment: A Prospective Study. Inflamm Bowel Dis 2016;22:1101–1106.
[3] Ham M, Longhi MS, Lahiff C, Cheifetz A, Robson S, Moss AC. Vitamin D levels in adults with Crohn's disease are responsive to disease activity and treatment. Inflamm Bowel Dis. 2014; 20(5):856–60.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6232

AB0969 IMPACT OF JUVENILE IDIOPATHIC ARTHRITIS ON SCHOOLING

S. Rahmouni, A. Fazaa, K. Ouenniche, S. Kassab, S. Chekili, K. Ben Abdelghani, A. Laater. *Rheumatology Department, Mongi SLim hospital, marsa, Tunisia*

Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children and is one of the major causes of morbidity and physical disability.Due to frequent absences,children with chronic health impairments are also often confronted with educational difficulties.
Objectives: The aims of this study were to assess the impact of JIA on children's schooling and to determine the factors that influence their school level.
Methods: This is a cross-sectional study including patients with JIA (ILAR criteria).A detailed questionnaire was completed for each participant by interviewing them or their parents as well as by information obtained from their medical records.Collected data included age,sex,subtype of JIA,disease duration,level of disability according to the Childhood Heath Assessment Questionnaire (CHAQ),visual analog scale for patient's overall assessment of disease activity,duration of morning stiffness, joint counts,erythrocyte sedimentation rate,C-Reactive Protein,Disease Activity Score (DAS28).Medications used for JIA treatment were also documented.
Data on the school performance of patients and their siblings were obtained using telephone interviews (educational level, absenteeism, school delay by repetition, drop-out).
The comparison of quantitative variables was performed with the Mann-Whitney test and the comparison of qualitative ones was performed with the Chi square test. The significance level was set at 0.05.
Results: A total of 38 patients with JIA were included, 23 female and 15 male, with a mean age of 26 years [12–51] and a mean disease duration of 237 months [5–496].The average age of the onset of the disease was 7.4 years [1.5–16].
The most common subtype was rheumatoid factor-positive polyarthritis (n=16) followed by systematic (n=7), oligoarticular (n=6), rheumatoid factor-negative polyarthritis (n=5) and Enthesitis-related arthritis (n=4). The mean DAS28 was 2.63 [0.76 - 5.55] and the median CHAQ was 0.528 [0–3].Twenty-seven of the children were receiving corticosteroid. Disease-modifying anti-rheumatic drugs were used by 34 of the 38 patients: methotrexate (n=23), sulfasalazine (n=8),leflunomide (n=7),biotherapies (n=14). Twenty patients had complications:*Hip arthritis (n=15),* growth stunting (n=12), uveitis (n=4). Joint replacement was required in 9 cases.
Four patients were illiterate,12 had dropped out of school,21 reported repeated absences due to illness.A year of schooling was repeated by 61.7% of patients.Ten out of 32 patients over the age of 20 had an university level.Almost 80% of patients were exempted of physical education.
There were no significant associations between the school-related problems,the socio-demographic characteristics and the various parameters of clinical and biological activity studied.School failure was similar among patients and their siblings (p=0.05).
Conclusions: Our study suggested that JIA negatively affects schooling of children.More studies with a larger sample are needed to identify the variables associated with school failure in order to ensure the proper management of these patients and to increase their academic performance.

References:
[1] Bouaddi et al. Impact of juvenile idiopathic arthritis on schooling. BMC Pediatrics 2013,13:2.
[2] Kamrul Laila et al. Impact of Juvenile Idiopathic Arthritis on School Attendance and Performance. American Journal of Clinical and Experimental Medicine 2016;4(6):185–190.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6037

AB0970 CLINICAL AND IMMUNOLOGICAL CHARACTERISTICS IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS TREATED WITH RITUXIMAB

S. Garrote, A. Alia Jimenez, A. Boteanu, M.A. Blazquez, M.L. Gamir. *Rheumatology, Ramon y Cajal Hospital, Madrid, Spain*

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that is more severe in pediatric population than in adults. Biological therapy with anti-CD20 (rituximab) is an option in patient that do not respond to conventional therapy.
Objectives: The aim of this study is to determine the clinical and immunological response in 9 patients with childhood-onset systemic lupus erythematosus (cSLE) that received treatment with rituximab in a third level hospital
Methods: This is a retrospective observational study. 9 patients treated with Rituximab between November 2007 and October 2016 were included and their medical records were reviewed. The response to treatment at 6 months and one year after the first infusion of Rituximab were assessed. Patients with overlap syndromes were excluded. All patients fulfilled four or more of the 1982 revised American College of Rheumatology criteria for the diagnosis of SLE (<16 years).
Results: Nine pediatric patients with SLE treated with rituximab were included, all of them were female. The age at diagnosis of SLE was a mean of 15,22 years. The mean time duration of disease was 87,55months (5–255m). 7 patients were caucasians. Rituximab was indicated in 6 patients with class IV of lupus nephritis (LN) 1/9 with class III LN, 1/9 with severe cutaneous lupus, and with severe hematological manifestations in 1 case (haemolytic anemia). In addition, 6/9 patients had mucocutaneous and articular manifestations. The disease activity of all patients was assessed using SELENA-SLEDAI index pre rituximab infusion, the mean was
17,11 (8–33). All patients had low level of complement C3 and C4 and 8/9 increased anti-DNA. In 8/9 patients Rituximab was used as a rescue treatment and in a single case as a first line.
3/6 patients with renal involvement were previously treated with cyclophosphamide (CF) iv and mycophenolate, 2/6 CF. In case of cutaneous involvement the previous treatment was methotrexate, azathioprine (AZA) and dapsone and in case of hemolytic anemia was AZA.
The treatment protocol was 1 gram x 2 (1 cycle) in 7/9 patients, 375mg/m^2 x 4 in 1/9 cases and 600mg monthly for 5 months in the case of hemolytic anemia. Five patients received more than 1 cycle. After the administration of Rituximab, the SELENA-SLEDAI activity index was 4.5 points. At 6 months a complete response was obtained in the case of hematological and cutaneous manifestations, in 2 cases of lupus nephritis (proteinuria <0.5 g/day) and partial response was obtained in 2 cases. Data were not analyzed in 2 patients (death and less than 6 months of the first dose of rituximab). Patients with partial response and lack of response achieved complete response at 12 months. 2/9 patients had side effects (Rituximab pneumonitis in 1 case and infections in 2 cases). Mortality was 11.11% (1/9 patients, per infection and lupus activity, SLEDAI pre rituximab =33)
Conclusions: In our study, although it consisted of few patients, it was objected that Rituximab therapy in patients with cSLE is effective, reduces lupus activity index, especially in cases of renal, cutaneous and hematologic involvement, that don't respond to conventional therapy. It may be consider in the future as an effective alternative treatment at first line treatment.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6846

AB0971 CHARACTERISATION OF THE PATIENTS AT THE TIME OF THE TRANSITION INTO THE ADULT RHEUMATOLOGY. 63% OF THE PATIENTS ARE IN REMISSION AT THE TIME OF THE TRANSITION

S. Tatsis[1], I. Foeldvari[2]. [1]*Department of Rheumatology, Marienkrankenhaus;* [2]*Hamburg Center for Pediatric and Adolescent Rheumatology, Am Schön Klinik Eilbek, Hamburg, Germany*

Background: The issue of transition from pediatric to adult rheumatology service is an emerging important topic. In 2012 a transition clinic was established according to the "Berliner Transitionsprogramm" [1] in cooperation of the Hamburger Zentrum für Kinder-und Jugendrheumatologie and the Rheumatology Unit of the Marien Hospital in Hamburg. The Berliner programm suggests three visits of the patient in transitionprocess, in the presence of the pedriatic and an adult rheumatologist together, and the fourth visit conducted by the adult rheumatologist alone. We present the characteristics of the patients at the time of the 4th visit.
Objectives: To characterize the patient population at the time of enrollment into the adult service in the frame of our transition programm.
Methods: We collected patient data starting 8/2012 to 11/2016. We summarized the patient population, who succesfully transitioned from pediatric to adult rheumatologic service, concerning diagnosis, sex, age at the time of diagnosis, disease duration at the time of transition, JADAS, HAQ, VAS globular assessment, VAS pain, medication and disease activity.
Results: 73 patients were transitioned. 65% of them female. Mean age at diagnosis of the patients was 12.5 years. Mean disease duration at time of transition ws 10.8 years. The mean JADAS Score was 3.18 and the mean HAQ Score was 0.136. The patients global activity score was, on a VAS of 0 to 100, 14.03 and the global pain score, on a VAS of 0 to 100, 12.33. 39.7% of the patients received synthetic DMARDS and 34% biologic DMARDS: Only 1 patient received steroids. 24.6% of the patients were off medication. 63% of the patients were in remission, 61% of them on medication and 39% off medication in remission.
Conclusions: In this monocenter cohort 63% of patients were in remission, and with the mean JADAS Score of 3.18 most of them have low disease activity under the current treatment. The mean HAQ Score with 0.136 reflects a score, which is expected in healthy controls. But 75.4% of the patients needed medication to

achieve this good condition. The amount of patients on medication emphasize the need of the structured transition.

References:

[1] Minden K, Niewerth M, Muther S: [Berlin transition program: from adolescents to adults in rheumatology treatment]. Z Rheumatol 2014, 73(6):526–531.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3171

AB0972 CHILDHOOD ONSET STROKE AND VASCULITIS ASSOCIATED WITH DEFICIENCY OF ADENOSINE DEAMINASE 2 (DADA2)

V. Paisal[1], E. Al-Abadi[1], T. Southwood[1], E. Wassmer[2]. [1]*Paediatric Rheumatology;* [2]*Paediatric Neurology, Birmingham Children's Hospital, Birmingham, United Kingdom*

Background: The deficiency of Adenosine Deaminase 2 (DADA2) is a rare autosomal recessive condition resulting from mutations in CECR1 (Cat Eye Syndrome Chromosome Region 1) gene, mapped to chromosome 22q11.1. It is a type of autoinflammatory disease, mainly characterised by early-onset polyarteritis, haemorrhagic, ischemic strokes and hypogammaglobulinemia (1). We report a case of 7-year boy presenting with haemorrhagic stroke and vasculitis responding to immunosuppression with Anti-TNF drug.

Objectives: A 7 year boy presented to the emergency department with reduced consciousness, headaches and nose bleeds. Initial imaging showed an intraparenchymal haemorrhage requiring frontal craniotomy and evacuation of the haematoma. This acute presentation was preceded by a history of recurrent fevers, weight loss, testicular pain, erythema nodosum and tender lymph nodes.

Methods: The laboratory findings revealed anaemia, ESR of up to 61mm/h, C-reactive protein 100, normal immunoglobulins, positive Anti nuclear antibody (ANA), mildly raised antibodies to double stranded DNA (dsDNA) and Proteinase 3 antibody. Skin biopsy confirmed panniculitis. CT imaging and angiography of the head at the time of acute presentation showed intraparenchymal haemorrhage and aneurysm of the left middle cerebral artery. Further CT angiography of the whole body revealed renal and liver microaneurysms. A provisional diagnosis of Polyarteris nodosa was made and started on steroids and cyclophosphamide. He had further genetic testing, showing mutation in CECR1, leading to Adenosine deaminase 2 deficiency. Patient responded to cyclophosphamide induction regime, which was followed by Etanercept.

Results: We report a case of ADA2 deficiency presenting initially with features of an autoinflammatory disorder, complicated by acute stroke secondary to haemorrhage. Our patient exhibited most of the clinical symptoms previously reported in ADA2 deficiency, including its association with polyarteritis nodosa (2). Although, he did not exhibit hypogammaglobulinaemia (3) which has been reported, interestingly, he was positive for markers of autoimmunity (ANA, ANCA) (4). It has been reported that treatment with anti-TNF and IL-6 (5) could lead to improvement, and our patients initial response to cyclophosphamide was excellent, followed by continued treatment with Etanercept.

Conclusions: Screening for adenosine deaminase 2 deficiency should be considered in all children presenting with neurological symptoms and features of vasculitis.

References:

[1] Roberta Caorsi, Federica Penco, Francesca Schena and Marco Gattorno. Monogenic polyarteritis: the lesson of ADA2 deficiency.Pediatric Rheumatology 2016. DOI: 10.1186/s12969–016–0111–7.

[2] Nanthapisal S, Murphy C, Omoyinmi E, Hong Y, Standing, A, Berg S, Ekelund M, Jolles S, Harper L, Youngstein T, Gilmour K, Klein N, Eleftheriou D, Brogan PA. Deficiency of adenosine deaminase type 2 (DADA2): a description of phenotype and genotype in 15 cases. Arthritis and Rheumatism.

[3] Segel R, King MC, Levy-Lahad E. Mutant ADA2 in vasculopathies. N Engl J Med 2014;371:481–2. doi:10.1056/NEJMc1407114.

[4] Zhou Q, Yang D, Ombrello AK et al. Early-onset stroke and vasculopathy associated with mutations in ADA2. N Engl J Med 2014;370:911–20. doi:10.1056/NEJMoa1307361.

[5] Van Eyck L, Liston A, Wouters C. Mutant ADA2 in vasculopathies. N Engl J Med 2014;371:480 doi:10.1056/NEJMc1405506#SA4.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5098

AB0973 ANTIPHOSPHOLIPID ANTIBODIES IN CHILDREN WITH SYSTEMIC LUPUS ERYTHMATOSUS AND JUVENILE IDIOPATHIC ARTHRITIS

W. Gouda[1], A. Mohamed[2]. [1]*Rheumatology, Aswan University, Aswan;* [2]*Pediatrics, Mansoura Univeristy, Mansoura, Egypt*

Background: Antiphospholipid antibodies (aPL) are a family of autoantibodies that present in a small percentage of the population but occur more commonly in patients with Antiphospholipid syndrome (APS) and Systemic lupus erythematosus (SLE).

Objectives: We aimed to determine of the level of anti-β2-glycoprotein I (anti-β2GPI) (IgG and IgM) isotypes and anticardiolipin antibodies (aCL) as inflammatory markers in children with SLE and Juvenile Idiopathic Arthritis (JIA) and figure out their relation to the clinical manifestations and activity of the disease.

Methods: This prospective study included one hundred twenty children, sixty five having SLE and fifty five having JIA, their ages range between 4.5 – 16 years (37 males and 83 females).In addition, twenty apparently healthy children of comparable age, sex and nutritional status were used as a control group. All patients and normal controls were subjected to full clinical and laboratory investigations included aCL and anti-β2GPI level (IgG and IgM) measured by a standardized ELISA.

Results: IgG isotype of anti-β2GPI was found to be positive in 27.7% and 14.5% for SLE and JIA groups respectively. However IgM isotype of anti-β2GPI was found to be positive in 24.6% and 7.25% for SLE and JIA groups respectively. The mean levels of both IgG and IgM isotypes of anti-β2GPI were found to be significantly increased in comparison to controls ($P<0.001$) in both SLE and JIA groups. IgG isotype of aCL was found to be positive in 23.1% and 18.2% for SLE and JIA groups respectively. However IgM isotype of aCL was found to be positive in 18.5% and 18.2% for SLE and JIA groups respectively. A significant positive correlation was found between IgM and IgG isotypes of anti-β2GPI and with their corresponding class of aCL in both SLE and JIA groups. A significant positive correlation was found between the elevation of anti-β2GPI (IgG) and thrombocytopenia together with neuropsychiatric disease in SLE. While in JIA elevation of anti-β2GPI was found to be correlated only with elevation of aCL irrespective to clinical or laboratory data.

Conclusions: The study reported a higher prevalence of aPL in children with SLE and JIA. Elevated levels of anti-β2GPI (IgG) correlated with thrombocytopenia together with neuropsychiatric disease in SLE.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1593

AB0974 ETANERCEPT TREATMENT FOR A PATIENT WITH REFRACTORY MACROPHAGE ACTIVATION SYNDROME IN JUVENILE SYSTEMIC LUPUS ERYTHEMATOUS

Y. Ramirez, T. Díaz, R. Maldonado, E. Faugier, A.V. Villarreal, N. Acevedo on behalf of Pediatric Rheumatology. *Hospital Infantil de México Federico Gómez, Mexico City, Mexico*

Background: Macrophage activation syndrome (MAS) is a serious, potentially fatal complication of childhood systemic inflammatory disorders, and it is most frequent in Systemic Juvenile Idiopthic Arthritis, for instance, it is increasingly reported in other pediatric rheumatic diseases as lupus erythematosus and Kawasaki disease.

Objectives: To describe clinical case report of a 16 year old girl with Juvenil Systemic Lupus Erythematosus and Macrophage Activation Syndrome refractory.

Methods: A 16-year-old woman with recent diagnosis of Systemic Lupus Erythematosus in November 2015. At admission with continuos fever lasting 2 months, with initial laboratory studies with Triglycerides 395 mg/dl, Ferritin 3.300 ug/l, soluble receptor IL-2 2.838 U/ml, fibrinogen 166 mg/dl, Hemophagocytos in bone marrow, presence of persistent cytopenias. Initial management with methylprednisolone 30 mg/kg/day (3 days) without clinical response was initiated. Management is added to Cyclosporin A (10 mg/kg/day), reporting subtherapeutic serum levels despite high doses without clinical response and improvement of laboratory controls. During the hospital stay complete 13 weeks of treatment with Etposide (180 mg/dose), with ferritin levels in 4,180 ug/l, triglycerides 438, Fibrinogen 455 mg/dl, WBC 5,000 ul^{-1} (3,400 neutrophils, lymphocytes 1,050), platelet count 78 x 103 ml^{-1}, hemoglobin 7.2 g/dl. After three months of treatment, she was given with Etanercept 0.4mg/kg/dose, 2 times a day. Currently in week 3 of treatment with WBC 6,500 ml^{-1}, hemoglobin 9.7 g/dl, platelet count 140 x $103ml^{-1}$ and ferritin 4,270 ng/ml. The patient remains disease with costicosteroid, cyclosporine, and etanercept, without adverse events.

Results: Patient treated with Etanercept during 5 weeks, presenting clinical response for MAS.

Conclusions: A general therapeutic protocol for MAS is not available: first line treatment is usually represented by parenteral administration of high dose corticosteroids. Mild forms are reported to respond to steroids alone in association with supportive medicaments. Steroid-resistant cases or the most severe forms of MAS require the addition of cyclosporine A, other therapeutic regimens have been studied such as high-dose intravenous immunoglobulins, antithymocyte globulins, etanercept, etoposide and plasmapheresis

References:

[1] Takahashi, N., Naniwa, T., & Banno, S. (2008). Successful use of etanercept in the treatment of acute lupus hemophagocytic syndrome. Modern Rheumatology, 18(1), 72–75.

[2] Cron, R. Q., Davi, S., Minoia, F., & Ravelli, A. (2015). Clinical features and correct diagnosis of macrophage activation syndrome. Expert review of clinical immunology, 11(9), 1043–1053.

[3] Bracaglia, C., Prencipe, G., & De Benedetti, F. (2017). Macrophage Activation Syndrome: different mechanisms leading to a one clinical syndrome. Pediatric Rheumatology, 15(1), 5.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5636

AB0975 **INCIDENCE OF INFECTIONS WITH BIOLOGICAL THERAPIES IN PARAGUAYAN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: BIOBADAGUAY (BIOLOGICAL THERAPIES ADVERSE EVENTS PARAGUAYAN-URUGUAYAN REGISTER)**

Z. Morel[1,2], P. De Abreu[3], I. Acosta[3], G. Avila[4], S. Cabrera[4] on behalf of BIOBADAGUAY Group. *[1]Cátedra de Pediatría, Universidad Nacional de Asunción; [2]Pediatría, Hospital Central del IPS; [3]Sociedad Paraguaya de Reumatología; [4]Hospital Central del IPS, Asunción, Paraguay*

Background: Biological Therapies (BT) are important in the therapeutic arsenal of rheumatic diseases; however there is an increased risk of infections with their use.
Objectives: To determine the frequency and type of infections in Paraguayan patients with Juvenile Idiopathic Arthritis (JIA), included in the BIOBADAGUAY Register.
Methods: A prospective observational study of patients with JIA treated with BT, included in the BIOBADAGUAY Register. Patients at the onset of BT were included. The change and/or discontinuation of BT and the occurrence of adverse events (AEs) were recorded. Infectious events as affected organ, type, severity, outcome and need of temporary or permanent suspension of the biological agent were analyzed.
Results: 59 patients with JIA and 69 BT were identified between May 2012 and December 2016. Female: 63% (37), Men: 37% (22). The mean age was 10 (3–18) years old. Mean disease progression of 2.8 (0.2–12) years from the diagnosis to BT beginning. JIA subtypes: poliarticular negative RF (27%), oligoarticular (27%: extended 22% and persistent 5%), enthesitis related arthritis (21%), systemic (12%), poliarticular positive RF (7%), psoriatic (3%), other (indeterminate) (3%). Biologic treatments: Adalimumab (ADM) 41 (59%), Etanercept (ETN) 19 (28%), Tolicizumab (TCZ) 9 (13%). There were 83 AEs of all treatments, 80 (96%) no serious and 3 (4%) severe with 1 death. Infections and infestations 54 (65%) of AEs were recorded. Of all TB infections: the 94% (51) were not serious and the 63% (34) required temporal discontinuation. Most infectious recovered without sequelae, except one death due to pneumonia (Table 1).

Type	Number AA	Agent	Suspension	Complete recovered
Respiratory Infection	33	18 ADM	21 Temporal	Yes
Infection		9 ETN		
		6 TCZ		
	1	1 TCZ	Yes	No (Death)
Pulmonary Tuberculosis	1	1 ETN	1 Temporal	Yes
Dengue	3	2 ADM	3 Temporal	Yes
		1 ETN		
Infectious Diarrea	3	1 ADM	3 Temporal	Yes
		1 TCZ		
		1 TCZ		
Urinary Infection	2	1 ETN	2 Temporal	Yes
		1 ADM		
Chickenpox	1	1 ADM	Temporal	Yes
Herpes	2	2 ADM	No	Yes
Toxoplasmosis	1	1 ADM	1 Temporal	Yes
Vulvovaginitis	1	1 ADM	No	Yes
Skin Infection	5	1 ADM	2 Temporal	Yes
		3 ETN		
		1 TCZ		
Scabies	1	1 TCZ	No	Yes
Total	54	28 ADM	34 Temporal	
		16 ETN		
		10 TCZ		

Conclusions: 1) Infections and infestations (65%) were the AEs more frequently observed. 2) Of al Infections, respiratory tract iwere the most frequently observed. 3) Most of the infections were not serious and recovered without sequela. 4) The most frequently agent involved in infectious events was ADM (52% of all infections); even so it is most frequently administered agent. 5) Increased number of patients, greater diversity of treatment as well as a longer data to corroborate the observation period is required.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3228

Other orphan diseases

AB0976 **REMISSION OF MULTICENTRIC RETICULOHISTIOCYTOSIS WITH COMBINATION TOCILIZUMAB AND ZOLEDRONATE**

A. Gough[1], B. Barber[2], H. Evennett[3], S. Hern[4], M. Lloyd[1]. *[1]Rheumatology; [2]Radiology; [3]Dermatology, Frimley Park Hospital, Frimley; [4]Dermatology, Spire Clare Park Hospital, Crondall, United Kingdom*

Background: Multicentric reticulohistiocytosis (MRH) is a rare non-Langerhans cell histiocytosis. It can affect any organ but predominantly skin and joints. Joint involvement usually precedes skin involvement and can be very destructive. Early diagnosis and treatment is therefore important but can be difficult.We describe a woman with MRH and severe erosive joint disease who responded to combination tocilizumab and zoledronate.
Objectives: A 43 yr old woman presented in 2012 with a 3 mth history of rash on her face, chest and ears and fingers, and arthralgia affecting shoulders, wrists, fingers and knees. On examination she had diffuse hand swelling, right knee effusion and erythematous eruption affecting her face, chest and ears with papules on the sides of her fingers.
Investigations: normal FBC, CRP, U+Es, LFTs. ESR 12 mm/hr. ANA +ve at 1:1280 (finely speckled). Ro +ve; ENA including Jo-1, ANCA and dsDNA antibodies -ve, C3/4, Igs all normal/-ve. Hand XR: periarticular DIP erosions. Skin biopsy: large multinucleate cells with abundant cytoplasm staining positive with CD68 (histiocytic marker); CD1a negative (Langerhans cell marker), consistent with MRH. PET-CT body: incidental finding of thymic remnant.
Methods: Initial Rx:prednisolone 20 mg od + HCQ 200mg bd with initial good response of joint and skin symptoms, but recurrence of symptoms on reducing steroid dose. Nov 2012: MTX up to 20mg /week added. Stopped after 4 mths because of a linear rise in P3NP levels to 11.2. Fibroscan showed slightly raised stiffness of 7.4kPa. AZA 75mg od introduced in Feb 2013, then etanercept 50mg weekly. This led to good control of symptoms for approximately 4 mths on single agent therapy. March 2014: relapse of joint and skin symptoms. June 2014: tocilizumab 8mg/kg iv 4 weekly started. After 5 infusions, her skin cleared for the first time. December 2014: relapse of joint and skin symptoms. Tocilizumab was adjusted to 650mg per mth from 620mg in view of slight weight gain. Annual iv zoledronate 5mg was started. She has had no further joint or skin exacerbations. July 2015: prednisolone was down to 1mg daily and stopped completely by May 2016. From July 2015 there appears to have been no progression in DIP joint erosions, and possibly some healing of the DIP changes. She has remained off any steroids.
Results: Picture shows X ray hands July 2015



Conclusions: The pathogenesis of MRH is poorly understood. The overexpression of cytokines including TNFα, IL-1 and IL-6 in inflammatory lesions gives a number of logical drug options, including tocilizumab. The observation that mononuclear cells in both skin nodules and synovium in MRH exhibit some properties of osteoclasts might explain the mechanism behind reported success using bisphosphonates. To our knowledge, this is only the second case to report success with using tocilizumab in the treatment of MRH and the first to report on concomitant treatment with a bisphosphonate. No adverse effects have been observed throughout treatment, and remission appears to be sustained. Without withdrawing treatment we cannot know if the remission is natural or drug induced, though the relatively short timescale suggests a drug effect.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4488

AB0977 **DETERMINATION OF A CUT-POINT BETWEEN LOW/HIGH ANTI RNP ANTIBODIES TITRES, IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE**

D.A. Botello Corzo[1], C. Bouroncle Alaluna[1], C. De la Puente Bujidos[1], A. Boteanu[1], G. Roy Ariño[2]. *[1]Rheumatology; [2]Immunology, Hospital Ramón y Cajal, Madrid, Spain*

Background: Sharp described Mixed Connective Tissue Disease (MCTD) in 1972[1]. MCTD is characterised by the presence of Raynaud phenomenon, puffy hands, synovitis, acrosclerosis, myositis and positive anti-ribonucleoprotein (RNP) antibodies. Classification criteria for MCTD except for Kasukawa's criteria demand the presence of high titres of anti-RNP antibodies (measured by hemagglutination). As a result, the cut-point between low and high anti-RNP titres must be well defined. In best of our knowledge, this cut-point have not been established for modern laboratory techniques.
Objectives: Determinate a cut-point between low/high anti-RNP titles measured by ELISA, for the diagnosis of Mixed Connective Tissue disease. Describe the clinical and immunological characteristics of patients with positive titres of anti-RNP antibodies.
Methods: It was a Retrospective cohort study of patients with positive anti-RNP antibodies (>10) measured by ELISA. We had identified all patients with positive antiRNP antibodies titres in the last five years, using our laboratory base date. Clinical histories were reviewed, we recollected clinical and paraclinical data. We performed descriptive analysis and ROC curves for diagnostic tests with STATA software.
Results: We detected 75 patients with positive antiRNP antibodies, we obtained 65 clinical records. 89,23% (58) of patients were women and 10,77% (7) men.

The mean age at diagnosis was 45,01 years (SD 16,71 ± years), The median of tracing was seven yeas (P25 de four years/P75 de 14 years). The mean initial antiRNP titre was 239,33 the median was 144 (P25 58/P75 400). The initial diagnosis were Mixed Connective Tissue Disease 6,25% (4), Undifferentiated Connective Tissue Disease 31,25% (20), systemic erythematosus lupus 45,31% (29) and Others 14,06% (9). MCTD diagnosis was made in 29,69% (19) of patients at the end of follow-up. Patients with MCTD as final diagnosis presented in their first visit Raynaud phenomenon 73,68% (14), puffy hands 31,58% (5), acrosclerosis 10,56% (2), myositis 21,05% (4), Arthralgias 68,42% (13), arthritis 57,89% (11), Pulmonary arterial hypertension 5,26% and Interstitial lung disease 10,53% (2). The initial RNP titre was evaluated using the number of times over the laboratory cut point. The area under the ROC curve for the initial RNP was 0,70. Looking for the highest specificity with and adequate sensitivity, we selected the cut-point with highest LR +. The selected cut-point was ≥24,4 times the laboratory cut-point, with s specificity of 77,78 and a sensitivity of 57,89.

Conclusions: The cut-point for low/high RNP titres measured by ELISA in our cohort of patients with MCTD as a final diagnosis was ≥24,4 times the laboratory cut-point.

References:

[1] Sharp GC, Irvin WS, Tan EM, Gould RG, Holman HR. Mixed connective tissue disease–an apparently distinct rheumatic disease syndrome associated with a specific antibody to an extractable nuclear antigen (ENA). Am J Med. 1972 Feb;52(2):148–59.

[2] Amigues JM1, Cantagrel A, Abbal M, Mazieres B. Comparative study of 4 diagnosis criteria sets for mixed connective tissue disease in patients with anti-RNP antibodies. Autoimmunity Group of the Hospitals of Toulouse. J Rheumatol. 1996 Dec;23(12):2055–62.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6914

AB0978 ASSOCIATION OF INFLAMMATORY ARTHRITIS WITH VOGT-KOYANAGI-HARADA SYNDROME (VKHS)

D. Ramos-Bello [1], G. Aguilera Barragán-Pickens [1], A.J. Pedro-Martínez [1], G. Martínez-Flores [1], T.A. Luna-Zúñiga [1], A.N. Rangel-Botello [1], P.L.R. Hernández-Briano [2], M.G. Rangel-Charqueño [2], E. Santillán-Guerrero [1], C. Abud-Mendoza [1]. *[1] Unidad regional de Reumatología y Osteoporosis; [2] Departamento de Oftalmología, Hospital Central "Dr. Ignacio Morones Prieto" y Facultad de Medicina de la Uaslp, SLP, Mexico*

Background: VKHS is a rare cause of granulomatous uveitis leading to significant visual loss in patients who develop it, usually accompanied with extraocular manifestations that include meningismus, vitiligo, poliosis, and hearing loss. In our country is responsible for 13% to 27% of all uveitis, affecting mainly young women.

Objectives: To describe the presence of inflammatory arthritis in patients with VKHS at a third level hospital.

Methods: A cross-sectional study of 4 patients with established VKHS that fulfilled the 2001 revised diagnostic criteria for Vogt-Koyanagi-Harada disease (1) was rolled out. Ultrasonography was performed to all patients by a trained rheumatologist in carpal, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints evaluating presence of power Doppler (PD) signal, bone erosions, and cartilage changes.

Results: We included 3 women and 1 man, mean age was 34.7±10.3 years, and they all had characteristics of complete VKHS. Mean disease duration (since first manifestation of ocular symptoms) was 5.2±3.5 months. One patient had synovitis on physical examination. Out of the 4 patients with PD signal, 4 had involvement of both wrist, MCP and PIP joints consistent with polyarthritis pattern, and bone erosions were detected in one patient (Table)

Table. Characteristics of patients with VKHS and inflammatory arthritis

	Sex	Age	Complete VKHS	Serous retinal detachment	PD in carpal joints	Number of MCP joints with PD	Number of PIP joints with PD	Number of erosions	ESR/CRP elevation	Reumatoid Factor/ACCP
Patient 1	F	21	Yes	Yes	Yes	4	3	0	Yes	No
Patient 2	F	36	Yes	Yes	Yes	7	3	0	Yes	No
Patient 3	M	36	Yes	Yes	Yes	6	4	0	Yes	No
Patient 4	F	46	Yes	Yes	Yes	7	1	2	Yes	No

VKHS: Vogt-Koyanagi-Harada syndrome; PD: power Doppler signal; MCP: metacarpophalangeal joint; PIP: proximal interphalangeal joints, ESR: erythrocyte sedimentation rate; CRP: C reactive protein; ACCP: anti-cyclic citrullinated peptide

Conclusions: The presence of inflammatory arthritis in patients with VKHS has only been described in one case (2). Despite the exceptionality, we propose that polyarthritis and probably erosive arthritis can represent part of the spectrum of the disease, processes that share some features of the genetic susceptibility with rheumatoid arthritis as HLA-DR4, CTLA-4 and STAT4.

References:

[1] Read RW, et al. Revised diagnostic criteria for Vogt- Koyanagi-Harada disease: report of an international committee on nomenclature. Am J Ophthalmol 2001; 131:647–652.

[2] Aydin T, et al. Association of Vogt Koyanagi Harada Syndrome and Seronegative Rheumatoid Arthritis. Ethiopian Journal of Health Sciences. 2016;26(2):193–196.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4483

AB0979 EOSINOPHILIC FASCITIS: CLINICAL EXPERIENCE IN A SERIES OF 21 PATIENTS

J.C. Quevedo [1], R. Lopez [1], M. Garcia-Bustuinduy [2], C. Rodriguez-Lozano [1], B. Rodriguez-Lozano [3], S. Bustabad [3], E. Trujillo [3]. *[1] Servicio de Reumatologia, Hospital Universitario de Gran Canaria Doctor Negrin, Las Palmas; [2] Servicio de Dermatologia; [3] Servicio de Reumatologia, Hospital Universitario de Canarias, la Laguna, Spain*

Background: The Eosinophilic fascitis (EF) is a uncommon sclerodermiforme síndrome with unknown etiology and poorly understood pathogenesis and natural evolution. The published series are short, with a total of 280 cases described in the literature from 1974.

There is neither clinical tests nor consensus on the EF treatment.

Objectives: To describe a series of 21 patients with EF.

Methods: Multicentric, retrospective Case Series Study.

We reviewed 21 patients diagnosed of EF (cutaneous induration+consistent biopsy) between January 1998 to January 2015. A total of 13 males and 8 females.

Results: The mean age at diagnosis was 41 years 8range between 28 and 66).

Trigger factor was suspected in 8 patients (intense exercise in 7).

The zones of cutaneous affectation were fundamentally the upper and low extremities.

The hyperesonophilia was present in 100% of the patients. The average of the % more high of hyperesosinophilia was 21.2% (range 4–45.4%).

11 patients presented artralgias and 5 patients presented arthritis (4 polyarticular/1 oligoarticular).

The MRI was used for diagnosis and/or follow-up in 8 patients, especially in the diagnosed ones in the last 5 years.

The average initial dose of prednisone was 40 mg/día, the average maximum dose of prednisone was 40 mg/dia and the mean steroid treatment duration was 22 months (range 9–47 months). Other immunomodulatory agents were: methotrexate 11, hydroxychloroquine 2, azatioprina 2 and D penicillamine 1.

5 years after follow-up, the evolution was the complete resolution in 13 patients and the partial improvement in 6.

Other clinical and analytical manifestations (N=21).	YES, n (%)	NO, n (%)
Hypergammaglobulinemia	13 (63)	8 (37)
Elevated ESR	4 (16)	17 (84)
Elevated CRP	8 (37)	13 (63)
Elevated CK	0	21 (100)
Systemic symptoms	7 (32)	14 (68)
Visceral affectation	3 (11)	18 (89)
Autoimmune thyroid	2 (5)	19 (95)
Peripheral neuropathy	4 (16)	17 (84)

Conclusions: In our series, the EF prevails in males, in the decade of the 40 and in the majority one did not find trigger factor. There was presence of arthritis in a significant percentage of patients. In the last years the use of the RMN has been added to the diagnosis and to the follow-up. Though there are no clinical tests that support it the use of the metotrexato has been generalized as adjuvant treatment to the steroids.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6444

AB0980 EPIDEMIOLOGICAL PROFILE OF THE PULMONARY DISEASES IN MIXED CONNECTIVE TISSUE DISEASE: ABOUT 55 CASES

R. Amri [1], I. Mejri [1], H. Sahli [2], A. Mahfoudhi [1], I. Ben Ahmed [1], R. Jazi [1]. *[1] Internal Departement; [2] Rheumatology Departement, Mohamed Taher Maamouri University Hospital, nabeul, Tunisia*

Background: Mixed connective tissue disease (MCTD) are a systematic autoimmune disease that the aetiopathogeny remains misunderstood. This disease is often associated with systemic involvement which sometimes is very serious, such as pulmonary diseases.

Objectives: To describe the characteristics of the pulmonary diseases among a sample of MCTD.

Methods: We conducted a retrospective study including patient's cases diagnosed with a MCTD between the period of 10 years in the departement of internal medicine. The demographic, clinical, treated in the immunological, biological and radiological data were collected then analysed.

Results: In total we had 55 patients. 87% of them were female. The mean age of the sample was 50, 64±15 years. Major types of MCTD were: Rheumatoid polyarthritis (45.5%), sarcoidosis (18.2%), scleroderma (12.7%), and the lupus erythematosus (10. 9%). These causes were diagnosed after a mean delay of 686, 18 days. A lung disease was found in 50.9% of the cases. It was either present without symptoms in 52.8% of the cases or revealed by dyspnoea (22.6%), a cough (18.9%)or hemoptysie isolated or associated to thoracic pains (1.9% each).The most frequent type of respiratory diseases were adenopathies (26.9%). Pleurisy, fibrosis, and interstitial lung diseases were described among 11.5% of the cases. Bronchiectasis, Lung arterial high blood pressure, pleural nodules, bronchi dilatation were reported in 7.7%. In only 3.8% we had patients with cancer and emphysema. Chest radiographs were normal in 65.5% of the

cases but we discovered interstitial lung diseases (12.7%), pleurisy (7.3%), pleural nodule and mediastinal enlargement (3.6%) and pneumopathy (1.8%). The same appearences were described in the CT scann normal in 18.5% but in different proportions: adenopathies (25.9%), interstitial lung abnormalities (14.8%), fibrosis (11.1%), bronchiectasis (7,4%) and bronchi dilatation, pleurisy, nodule and mediastinal enlargement (3.7%). Respiratory functional exploration were normal in 69.2% obstructive lung disease and restrictive pulmonary disease were found within 11.5% of the patients.
Conclusions: Improvement of the knowledge of these diseases will improve the care before the appearance of complications.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6207

AB0981 CLINICAL FEATURES OF 28 CASES OF LIMB RESTRICTED VASCULITIS AND FASCIITIS

H. Mukoyama, K. Nishimura, R. Saito, Y. Nakamura, T. Nagamoto, T. Yokota. *Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, Kurashiki, Okayama, Japan*

Background: We sometimes experience the cases with fever and muscle pain of lower limbs without any other specific features. There are sporadic case reports of eosinophilic fasciitis and limb restricted vasculitis. However, few reports compare and discuss such cases.
Objectives: To describe the clinical features, MRI findings, histopathology, diagnosis and response to treatment of these cases.
Methods: We retrospectively analyzed the clinical features of 28 patients who were admitted to our hospital because of fever and muscle pain of lower limbs from 2004 to 2016.
Results: Among the 28 patients, 17 were vasculitis syndrome; eleven were limb restricted small vessel vasculitis (LrSvv), six were microscopic polyangiitis (MPA). Seven were fasciitis; three were eosinophilic fasciitis, three were diffuse fasciitis without eosinophilia and one was tuberculous fasciitis. One was relapsing polychondritis, one was Behçet's disease and the other two were myalgia without specific diagnosis. In our study, average age was 57.5±19.9 years old and older than in previously reported cases of limb ristricted vasculitis[1,2]. Sixteen were female, twelve were male. Abnormal MRI findings in non-infectious fasciitis and vasculitis syndrome were bilateral. Tuberculous fasciitis showed specifically abnormal intensity and fluid collection in unilateral thigh. Unilateral lesion and fluid collection may indicate infectious disease and bilateral lesion may indicate autoimmune or autoinflammatory diseases. MRI of vasculitis syndrome and fasciitis showed hyperintense T2-weighted signals in muscles of either legs, or thighs, or both. (n=3), MPA (n=1) and fasciitis (n=3). On MRI scan, abnormal fascial signal intensity was seen in all the patients with fasciitis and 6 (40%) with vasculitis syndrome. It was difficult to differentiate between vasculitis and fasciitis by MRI findings. Muscle biopsy was performed in 25 patients. In most cases, we performed en bloc biopsy, including muscle, fascia, skin and subcutaneous tissue. MRI was useful to determine the location of biopsy. All patients were treated with glucocorticoids. Immunosuppressive agents (azathioprine, n=10; methotrexate, n=5; cyclophosphamide, n=1; tacrolimus, n=1) were added in 15 patients and anti-tuberculous drugs in one. None of the 11 patients with LrSvv showed positive blood tests of anti-neutrophil cytoplasmic antibody or developed any other organ involvement during follow-up period (median 96 months; range 3–125). They responded well to glucocorticoid therapy (oral prednisolone 0.5–0.6mg/kg/day or intravenous methylprednisolone at doses of 1g/day). Recurrence rate of LrSvv patients was 0%, although that of MPA patients was 50% (n=3). In four patients with LrSvv, treatment was ceased and they achieved drug-free remission. There were no apparent differences between the patients who achieved drug-free remission and who didn't.
Conclusions: MRI and muscle biopsy were useful for diagnosis of disease with fever and muscle pain of lower limbs.
References:
[1] Gallien S, et al. Ann Rheum Dis 2002;61:1107–9.
[2] Khellaf M, et al. Ann Rheum Dis 2007;66:554–556.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4169

AB0982 ANALYSIS OF THE TREATMENT EFFICACY FOR RETROPERITONEAL FIBROSIS - A CASE SERIES. SUSPICION OF ERDHEIM-CHESTER DISEASE IN A PATIENT WITH AN INITIAL DIAGNOSIS OF RETROPERITONEAL FIBROSIS, REFRACTORY TO STANDARD TREATMENT

J. Koblowski[1], A. Juszkiewicz[1], M. Kania-Pudło[2], W. Tlustochowicz[1]. *[1]Internal Medicine and Rheumatology; [2]Radiology, Military Institute of Medicine, Warsaw, Poland*

Background: Retroperitoneal fibrosis (RPF) is a rare disorder characterized by the development of fibrotic tissue in the retroperitoneum involving the abdominal aorta, iliac arteries and ureters. Erdheim-Chester disease (ECD) is a rare, non-Langerhans histiocytosis. Symptoms of ECD often resemble retroperitoneal fibrosis.
Objectives: Evaluation of standard treatment efficacy in 13 consecutive RPF patients. Revision of the diagnosis in patients unresponsive to standard therapy.
Methods: A retrospective analysis of 13 consecutive RPF patients (10 males and 3 females) treated in our department since 2008 was performed. All patients were treated with tapered dose of steroids combined with an immunosuppressive agent (cyclophosphamide in 4, azathioprine in 9, methotrexate in 6, hydroxychloroquine in 5 patients). Urologic interventions were undertaken as necessary.
Results: The treatment was effective in 10 patients: reduction of the retroperitoneal mass in computed tomography (CT) and normalization of the laboratory tests, including markers of inflammation and creatinine concentration. No improvement was found in 3 patients. However, in a further diagnostic work-up the diagnosis of RPF was maintained only in one of these 3 patients. In the second pateint an ANCA-asssotiated vasculitus was ultimately diagnosed. The third patient was treated with a combination of steroids and cyclophosphamide without any radiological improvement. However, the revision of CTs revealed the presence of changes typical of Erdheim-Chester disease.
Conclusions: The standard treatment (based on a combination of steroids and immunosuppressive drugs) is efficient in most partients with RPF. In refractory cases an alternative diagnosis, such as systemic vasculitis or Erdheim-Chester disease, should be taken into account.
References:
[1] Diamond El et al. Consensus guidelines for the diagnosis and clinical management of Erdheim-Chester disease. Blood. 2014 Jul 24;124(4):483–92.
[2] Kermani TA et al. Idiopathic retroperitoneal fibrosis: a retrospective review of clinical presentation, treatment, and outcomes. Mayo Clin Proc. 2011 Apr;86(4):297–303.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5960

AB0983 MEFV MUTATIONS IN ARMENIAN PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES

K. Ginosyan, A. Beglaryan[1,1], V. Vardanyan. *Internal Medicine, Yerevan State Medical University, Yerevan, Armenia*

Background: The systemic diseases of connective tissue have autoimmune mechanism in development. While autoimmunity involves adaptive immune activation, autoinflammation involves innate immune activation. The prototype of autoinflammatory diseases is familial Mediterranean fever (FMF), which is the global medical problem for Armenian ethnos on the whole, affecting 1–2% of population.
Objectives: The aim of this study was investigation of MEFV mutations and their possible influence on the systemic diseases in Armenian patients.
Methods: We have examined 183 patients with FMF. All patients with FMF fulfilled Tel-Hashomer FMF diagnostic criteria. Molecular-genetic detection of 12 MEFV mutations common for Armenians carried out in Medical Genetic Centre of Armenia. In 49 patients one of autoimmune systemic diseases was diagnosed: in 24 patients- seronegative spondyloarthropathy (SNSA), in 23 - systemic lupus erythematosus (SLE), 1 patient developed Sjogren's disease and 1- systemic sclerosis.
Results: In the SNSA group from 24 patients 16 were male, 8 were female, the mean age of patients was 35,4±12,2.The mean age at the beginning of the disease was 14,91±12,6. In all cases the symptoms of FMF were preceded symptoms of arthritis. Unilateral sacroiliitis was revealed in 6 patients, bilateral sacroiliitis-in 18 patients. The limitation of lumbar motion was assessed by Schober's test. 7 patients with Schober's test 1–2 cm had bilateral sacroiliits grade III-IV and fulfilled the modified New York criteria for ankylosing spondylitis. HLA B-27 was examined in 7 patients. In 5 cases it was negative, and in 2 cases –positive. MEFV gene analyses were carried out in 21 cases: 7 patients had one heterozygote mutations: 6-M694,1-M680I; 5 patients -M694V/M694V, 9 patients had compound heterozygote mutations: 5- M694V/V726A, 3 - M694V/E148Q, 1 - M680I/E148Q. So, the prevalent mutation was M694V.
In SLE group from 23 patients female were 21 (91.3%), male – 2 (8.7%). Mean age of patients was 37.4±2.5 years. The beginning of FMF was earlier than SLE. The activity of SLE estimated by SLEDAI index was significant lower than in SLE without FMF. SLE co-occurring with FMF had mild duration than classic lupus according to both clinical and laboratory findings including serological markers of SLE -ANA, anti-dsDNA. The prevalent mutation was M694V - 44.6%; V726A composed 21.7%, M680I-9.8%. Most common variations with M694V were followings:M694V/M694V,M694V/V726A,M694V/N.
Conclusions: A remarkable overlap was highlighted between FMF and SLE: both diseases have such common features as arthralgia, myalgia, arthritis, fever, skin involvement, serositis and renal involvement. It is likely, that the moderation in disease phenotype and peculiar disease characteristics observed in patients with both SLE and FMF are related to MEFV. MEFV mutations appear to modify SLE phenotype. Sacroilitis may be seen more frequently in FMF patients than expected. On the other hand, FMF must be kept in mind if patients not responding to the usual therapeutic interventions for sacroiliitis.
References:
[1] Doria Z., Zen M., Bettio S., et al. Autoinflammation and autoimmunity:bridging the divide. Autoimmune Rev.2012 Nov;12 (1): 22–30.
[2] Cattan D. MEFV Mutation Carriers and Diseases other than FMF;Proved and Non-proved Associations; Putative Biological Advantage. Curr. Drug Targets-Inflam.&Allergy, 2005;4:105–112.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5109

AB0984 TOCILIZUMAB MONOTHERAPY FOR POLYMYALGIA RHEUMATICA ~ RESULTS OF 52-WEEK TREATMENT OF A PROSPECTIVE, SINGLE-CENTER, OPEN, SINGLE-ARM TRIAL

K. Amano, K. Chino, Y. Okada, A. Shibata, A. Okuyama, T. Kurasawa, H. Takei, T. Kondo. *Rheumatology and clinical immunology, Saitama Medical Center, Saitama Medical University, Kawagoe, Japan*

Background: Polymyalgia rheumatic (PMR) is a chronic inflammatory rheumatic disease in the elderly people. Glucocorticoid (GC) is still definitely a mainstay for the treatment of PMR, but long-term GC therapy is a major risk factor of osteoporotic fractures, diabetes, hyperlipidemia, cardio-cerebral vascular events, glaucoma, etc. So GC-free treatment strategies for PMR are necessary for some patients with PMR. IL-6 is involved in the pathogenesis of PMR and quite a few case reports have already shown the efficacy of tocilizumab (TCZ) in PMR patients and some of them received TCZ monotherapy without GC.
Objectives: To assess the efficacy and safety of TCZ monotherapy for PMR
Methods: Thirteen PMR patients (male 3, female 10) who had been diagnosed by 2012 ACR/EULAR classification criteria from Jan 2013 to Feb 2015 were enrolled in our study (IRB application No. 638, UMIN registration No. 000008812) after obtaining the written informed consent. TCZ (8 mg/kg) was administered biweekly for the first 2 months (5 infusions) and every 4 weeks thereafter for 40 weeks (total 48 weeks). ESR, CRP, patient's global health assessed by visual analog scale (VAS), PMR activity score were evaluated every 4 week prospectively and were evaluated at week 52. Remission was defined as PMR activity score less than 1.5.
Results: Baseline patients' characteristics revealed various kinds of comorbidities in 11 patients; hypertension in 7, hyperlipidemia in 5, diabetes mellitus in 3, osteoporotic vertebral fractures in 2, history of angina pectoris in 1, history of brain infarction in 1, history of hematemesis due to NSAID ulcer in 1 and glaucoma in one patient. Nine patients could complete this 52-week trial and could achieve remission at week 52. Two patients discontinued TCZ because of no response at week 6 (No.1) and week 16 (No. 8) respectively. One patient (No.2), who were in clinical remission of PMR, dropped out from this study due to pemphigoid at week 50 and received GC therapy. Patient No. 12 abandoned TCZ at week 12 because of lung infiltrates although she was treated successfully with TCZ monotherapy, and she had been in remission without any treatment until week 52. The other 3 drop-out patients could obtain remission with GC therapy at week 52. There were no serious adverse events during 52-week treatment period.
Conclusions: TCZ mono-therapy was effective in most (9 out of 13) PMR patients although response was not so rapid as compared to GC. TCZ mono-therapy may be a good alternative therapy instead of GC for elderly patients with various comorbidities.
References:
[1] Unizony S, et al.: Arthritis Care Res 2012; 64(11):1720–1729.
[2] Macchioni P, et al.: Aemin Arthritis Rheum 2013; 43(1): 113–118.
[3] Toussirot E, et al.: J Rheumatol 2016 43(1): 249–251.
[4] Leeb BF, et al.: Arthritis Rheum 2007; 57(5): 810–815.
Acknowledgements: We will thank Izumi Oshima, Takashi Kukita for data collection and management of this study.
Disclosure of Interest: K. Amano Grant/research support from: Chugai Pharnmaceutical Co.Ltd., K. Chino: None declared, Y. Okada: None declared, A. Shibata: None declared, A. Okuyama: None declared, T. Kurasawa: None declared, H. Takei: None declared, T. Kondo: None declared
DOI: 10.1136/annrheumdis-2017-eular.4525

AB0985 METHOTREXATE AS INDUCTION OF REMISSION THERAPY FOR LOCALIZED MANIFESTATIONS OF IGG4-RELATED DISEASE

L. Rovati[1], E. Della-Torre[1], M. Lanzillotta[1], E. Bozzalla Cassione[1], E. Bozzolo[1], C. Canevari[2], M. Falconi[3,4], L. Dagna[1,4]. *[1]Unit of Immunology, Rheumatology, Allergy and Rare Diseases; [2]Unit of Nuclear Medicine; [3]Pancreatic Surgery Unit, San Raffaele Scientific Institute; [4]Università Vita-Salute San Raffaele, Milan, Italy*

Background: Medium to high dose glucocorticoids represents the treatment of choice for inducing remission in IgG4-related disease (IgG4-RD) patients[1]. However, clinicians might prefer alternative equally effective drugs in clinical settings where long-term corticosteroids treatment is contraindicated, such as diabetes or osteoporosis. We recently reported the efficacy of methotrexate in maintaining glucocorticoids induced IgG4-RD remission[2].
Objectives: To evaluate the efficacy of methotrexate as induction of remission therapy in selected cases of mild and localized IgG4-RD complicated by clinical scenarios that might advise against corticosteroids treatment.
Methods: Five patients with active untreated IgG4-RD were started on oral or subcutaneous methotrexate (up to 15–20 mg/week). Efficacy of methotrexate in inducing remission was assessed at 6 months by 18F-FDG PET/CT scan and by measuring the IgG4-RD Responder Index (RI)[3] and circulating plasmablasts[4]. Partial response (PR) corresponded to an improvement of the IgG4-RD RI >2 points. Complete response (CR) corresponded to an IgG4-RD RI score <3.
Results: All patients were males with a mean age of 67 years (range 53–78). Two had pancreatic involvement; one had lymph node enlargement; one had pancreatic and lymph node involvement; one had pancreatic, aortic, submandibular gland and lymph node involvement. Patients with pancreatic involvement presented with increased serum amylases or abdominal discomfort; none had obstructive jaundice; all had overt diabetes. The mean IgG4-RD RI, serum IgG4 concentration and plasmablasts counts at baseline were 8 (6–15), 483 mg/dL (136–983) and 3336/mL (330–9330 /mL), respectively. All patients had increased 18F-FDG uptake on PET/CT scan within the affected organs. After 6 months of methotrexate, Patients 1, 2, and 3 were on CR with improved or normalized PET/CT findings, serum IgG4 and plasmablasts levels. Patient 5 achieved PR, showing improved 18F-FDG-PET/CT findings, normal plasmablasts level, but stable serum IgG4 concentration; after 10 months of methotrexate, persistence of disease activity prompted the introduction of glucocorticoids. Methotrexate was stopped in Patient 4 after 5 months because of nausea and vomiting; at 6 months he showed persistently increased plasmablasts count and 18F-FDG uptake on PET/CT, thus requiring a rescue therapy with glucocorticoids. (Table 1)

	Patient #1 (M, 78) Type 1 AIP, aortic, submandibular gland, lymph node involvement		Patient #2 (M, 67) Type 1 AIP		Patient #3 (M, 70) Type 1 AIP, lymph node involvement	
	Pre-Treatment	6 months (MTX 20 mg/week)	Pre-Treatment	6 months (MTX 15 mg/week)	Pre-Treatment	6 months (MTX 15 mg/week)
IgG4-RD RI	15	2 (CR)	6	2 (CR)	9	1 (CR)
IgG4 (mg/dL)	498	313	586	324	221	157
PBs/mL	2520	250	940	470	3560	130
18F-FDG-PET/CT	Increased FDG activity in all affected organs except pancreas	Decreased FDG activity in submandibular glands; negative in all the other organs	Increased FDG activity in pancreatic head and tail	Partial reduction in pancreatic FDG activity	Increased FDG activity in pancreas and hilar lymph nodes	Negative in all the involved organs

	Patient #4 (M, 61) Type 1 AIP		Patient #5 (M, 53) Lymph node involvement	
	Pre-Treatment	6 months (MTX 15 mg/week)	Pre-Treatment	6 months (MTX 20 mg/week)
IgG4-RD RI	6	NA	6	3 (PR)
IgG4 (mg/dL)	136	NA	973	819
PBs/mL	330	880	9330	0
18F-FDG-PET/CT	Increased FDG activity in pancreatic head and body	Markedly increased FDG activity in pancreatic head and body	Increased nodal FDG activity	Decreased nodal FDG activity, but not dimensional reduction of the lymph nodes

Abbreviations: M, male; AIP, autoimmune pancreatitis; MTX, methotrexate; PDN, prednisone; IgG4-RD RI, IgG4-related disease responder index; PBs, plasmablasts; 18F-FDG, fluorodeoxyglucose; PET/CT, positron emission tomography/CT scan; CR, complete response; PR, partial response; NA, not available.

Conclusions: In localized forms of IgG4-RD with mild manifestations, methotrexate represents a promising alternative strategy for inducing disease remission, especially in the presence of contraindications to glucocorticoids.
References:
[1] Khosroshahi A, et al. International Consensus Guidance Statement on the Management and Treatment of IgG4-Related Disease. Arthritis Rheumatol. 2015.
[2] Della-Torre E, et al. Methotrexate for maintenance of remission in IgG4-related disease. Rheumatology (Oxford). 2015.
[3] Carruthers MN, et al. Development of an IgG4-RD Responder Index. Int J Rheumatol. 2012.
[4] Wallace ZS, et al. Plasmablasts as a biomarker for IgG4-related disease, independent of serum IgG4 concentrations. Ann Rheum Dis. 2015.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4499

AB0986 FAMILY MEDITERRANEAN FEVER GENE MUTATIONS: A POORLY STUDIED CAUSE OF INTERMITTENT HYDRARTROSIS

M. Espinosa Malpartida[1], C. Barbadillo Mateos[1], C. Ramos Giraldez[1], B.J. Flores Robles[1], E. González Vioque[2], C. Merino Argumanez[1], M. Jimenez Palop[1], J. Sanz Sanz[1], H. Godoy Tundidor[1], J. Campos Esteban[1], J.L. Andreu Sanchez[1], L.F. Villa Alcazar[1], J. Mulero Mendoza[1]. *[1]Rheumatology; [2]Biochemistry, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain*

Background: Familial Mediterranean Fever (FMF) is an inherited autoinflammatory disorder caused by *mutations in the MEFV gene* encoding pyrine, characterized by recurrent episodes of fever and serositis. Some patients with FMF present *incomplete penetrance* of the disease and may manifest only as *intermittent arthritis*.
Objectives: Characterization of *musculoskeletal clinical manifestations* in patients with mutations of the MEFV gene in our hospital.
Methods: We retrospectively reviewed clinical records of patients with mutations detected in the Family Mediterranean Fever MEFV gene in our hospital from January 1, 2008 to October 1, 2016. We collected parameters such as age at diagnosis, age of onset Of the symptoms, sex, affected joints, other extra-articular manifestations and type of MEFV gene mutation.

Abstract AB0986 – Table 1

Patient	Sex	Diagnostic age	Onset age	Arthritis	Location	Other musculoskeletal manifestations	Extra-articular manifestations	MEFV Mutation	Homo/ Heterocytosis
1	M	47	40	Yes	Knee	No	No	p Glu148Gln	Heterocytosis
2	M	14	13	Yes	Knee	No	No	R202Q	Homocytosis
3	M	22	22	No		No	Lymphocytic myocarditis	p Glu148Gln	Heterocytosis
4	M	52	47	No		Arthralgias	Abdominal pain. Pleuritis	R202Q	Heterocytosis
5	M	39	20	Yes	PIPs	Arthralgias	Abdominal pain	R202Q	Heterocytosis
6	M	61	54	No		Tendinopathy	Recurrent pericarditis	R202Q	Homocytosis
7	M	17	16	No		No	Abdominal pain	R202Q	Heterocytosis

Results: Seven patients with MEFV gene mutations were reviewed, all of them were women, ranging in age from 14 to 61 years old. Two of them had *recurrent knee monoarthritis*, one had a history of *arthritis* in the hands and erratic *arthralgias*, one had erratic arthralgias and two had no musculoskeletal manifestations. The 2 patients with intermittent hydrartrosis responded satisfactorily to *colchicine*, but not the other patients with other musculoskeletal manifestations.
Conclusions: *Genetic testing* of the common *mutations of the MEFV gene* should be considered in patients with *recurrent episodes of monoarthritis* without justifying cause (palindromic rheumatism, intermittent hydrartrosis, etc.)
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3429

AB0987 THE RELATIONSHIP BETWEEN ANTI-INTERLEUKIN-1 THERAPIES AND MEFV GENE MUTATIONS IN FAMILIAL MEDITERRANEAN FEVER PATIENTS: A SINGLE CENTER EXPERIENCE

M.E. Derin[1], S. Gültekin[2], M. Şahin[3], A. Şahin[1]. *[1]Rheumatology - Internal Medicine; [2]Internal Medicine; [3]Biochemistry, Cumhuriyet University Medical Faculty, Sivas, Turkey*

Background: Familial Mediterranean fever (FMF) is an autoinflammatory disease characterizing recurrent self-limiting attacks of inflammation mainly placed in serosal surfaces of the body with fever (1). Colchicine is an important weapon of the humanity in FMF treatment yet. However, the puzzle of inflammation was solved, and so, inflammasome complex and interleukin-1 were discovered. Eventually, new era started with anti-interleukin-1 agents in colchicine resistant and/or intolerant FMF patients (2).
Objectives: The aim of this study is to evaluate the effectiveness of anti-interleukin-1 (anti-IL-1) agents on the characteristics of attacks, the adverse effects associated with anti-IL-1 treatment, and relation between therapy and MEFV gene mutations in 23 FMF patients with resistant and/or intolerant to colchicine.
Methods: Between January 2015 and December 2016, twenty-three-FMF patients that following-up at Cumhuriyet University Medical Faculty Rheumatology-Internal Medicine Department were included in to the study. Anakinra (69,6%), and canacinumab (30,4%)] were used in 23 FMF patients. 20 cases were resistant to colchicine, 3 were intolerant to colchicine.
Results: The median age of the patients was 28 years,(18–54) and the median age at diagnosis was 20 years (3–50). Of the FMF patients, nine (39.1%) were female and fourteen (60.9%) were male. The distribution of MEFV gene mutation frequencies in the FMF patients was no mutation in one (4,3.%) patient, M694V heterozygous in nine (39,1%), M694V homozygous in 7 (30,4%), E148Q heterozygous in one (4,3%), and compound heterozygous mutation in 3. (13%) patients. 16 patients used anakinra (100mg/day) for 6 mounths (median) and 7 used canacinumab (150mg/2 months) for 3 mounths (median). Four of 7 patiens were resistant to anakinra. After a median follow up 6 months overall clinical response [no attack (18 patients) or decreased frequency of attacks (5 patients)] was %100. In an FMF patient with no mutation, his brother and mother had FMF with no mutations on MEFV gene. We achieved good clinical and laboratory responses in the patient by canacinumab.
Conclusions: Anti-IL-1 agents can be got involved in a new place safely and effectively in FMF patients along with colchicine. In addition, whole gene analysis should be done in refractory FMF patients with no mutations in order to could investigate new mutations, epigenetic mechanisms or other unexplained reasons.
References:
[1] Ben-Chetrit E, Touitou I. Familial Mediterranean Fever in the world. Arthritis Rheum 2009; 61:1447–1453.
[2] Özdoğan H, Ugurlu S. The emerging treatments in Familial Mediterranean fever. In: Gattorno M, editor. Familial Mediterranean Fever, 1st edition, Switzerland: Springer; 2015:137–157.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6487

AB0988 BEHÇET'S DISEASE IN A DEFINED AREA OF NORTHWESTERN SPAIN

M. Estévez, A. Argibay, R. Lorenzo, M. Freire, J. Fernandez-Martín, B. Gimena, C. Vázquez-Triñanes, A. Rivera. *Systemic Autoimmune diseases and Thrombosis Unit, University Hospital Complex of Vigo, Vigo, Spain*

Background: Behçet's disease (BD) is a multisystemic inflammatory chronic disease. There is a wide variation in the clinical features of BD among geographical groups.
Objectives: To determine the demographic and clinical characteristics of BD in a defined area of northwestern Spain (Vigo).
Methods: Patients with BD (International Criteria BD) and seen in the University Hospital of Vigo in Spain, from 1994 to 2016, were retrospectively enrolled. Demographic, clinical, treatment and evolution data were recorded and analyzed using SPSS 22.0.
Results: Our patients were 26 male and 25 female. The mean age at the onset of the disease was 33±11.95 years (11–62). Oral and genital ulcers were seen in 100% and 84.3% respectively and skin lesions in 88.2%. Ocular involvement occurred in 35.3%, neurological disease in 39.2% and gastrointestinal involvement in 29.4% (the area worst affected was colon and small bowel). Vascular disease was present in 33.3%. See table 1. Pathergy test was performed in 18 patients (35.29%) and 10 (55.5%) were positives. HLA B51 was studied in only 13 patients (25.5%) and 8 (61.5%) were positives. 62.7% of patients had no cardiovascular risk factors (CVRF), 27.4% were smokers, 7.8% were hypertensive and 3.9% were hyperlipidemic and diabetic respectively. CVRF were not related to thrombotic events ($p>0.05$). In regard to gender influence, only pseudofolliculitis was significantly more frequent in men ($p<0.001$). There was a trend for increased prevalence of ocular disease and elevated erythrocyte sedimentation rate/serum C-reactive protein in men, and anemia in women, which, however, did not reach statistical significance. Treatment consisted of corticosteroids (92.2%), colchicine (68.6.%) and another immunosuppressive agent (35.3%). During the disease course 78.4% of the patients had an outbreak, 45.1% initiated or changed to immunosuppressive agent and 19.6% used biological drugs. Most of our patients (92.1%) were admitted to hospital and these constitute an evident bias. Two patients died during the followup period, but only one in relation of BD (upper gastrointestinal bleeding and seizures).
Conclusions: Our series has some particular aspects especially the high frequency of gastrointestinal lesions and neurologic involvement. CVRF do not seem to play a role in the development of thrombotic events. Our results confirm the ethnic and geographic variation of BD expression.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3983

Abstract AB0988 – Table 1. Clinical manifestation of our BD patients

Skin lesions 41/55 (88.2%)	Ocular disease 18/51 (35.3%)	Neurologic disease 20/51 (39.2%)	Vascular disease 17/51 (33.3%)	Gastrointestinal involvement 15/51 (29.4%)
Pseudofolliculitis 58.8%	Uveitis 23.5%	Aseptic meningitis 11.7%	Venous thrombosis 21.6%	Pain 11.7%
Erythema nodosum 39.2%	Retinal vasculitis 5.9%	Seizures 7.8%	Arterial thrombosis 7.8%	Bleeding 9.8%
Leukocytoclastic vasculitis 5.9%	Episcleritis 3.9%	Cerebral venous thrombosis 5.9%	Mixed thrombosis 2%	Diarrhea 5.9%
	Vascular occlusion 2%	White matter lesions 5.9%	Aneurysm 2%	Fever 2%
		Stroke 3.9%		
		Paresthesias 3.9%		
		Others 5.9%		

AB0989 RHEUMATOLOGIC COMPLICATIONS OF THALASSEMIA: SHOULD RHEUMATOLOGISTS JOIN THE MANAGEMENT TEAM?

M.H.A. Noureldine[1], A.T. Taher[2], A.A. Haydar[3], A. Berjawi[2], M.A. Khamashta[4,5], I. Uthman[2]. *[1]Department of Neurosurgery, Lebanese American University; [2]Department of Internal Medicine, American University of Beirut; [3]Gilbert and Rose-Marie Chagoury School of Medicine, Lebanese American University, Beirut, Lebanon; [4]Lupus Research Unit, St Thomas Hospital, London, United Kingdom; [5]Department of Rheumatology, Dubai Hospital, Dubai, United Arab Emirates*

Background: Beta-thalassemia major is accompanied by progressive multiple organ systems involvement due to the disease pathophysiology as well as iron overload from blood transfusions on a regular basis. Rheumatologists are not frequently involved in the multidisciplinary management of the disease, in which rheumatologic complications are relatively common.

Objectives: To highlight the rheumatologic complications of beta-thalassemia, which include musculoskeletal manifestations such as arthritis and arthropathies, joint effusions, osteoporosis, bone fractures, and arthralgias as well as connective tissue diseases such as pseuoxanthoma elasticum (PXE).
Methods: We searched the literature through GoogleScholar and PubMed for all publications reporting on rheumatologic manifestations in beta-thalassemia. The following keywords were used: thalassemia, rheumatoid arthritis, osteoarthritis, iron-overload, septic arthritis, deferiprone-related arthropathy, crystal arthritis, effusions, osteoporosis, fractures, bone marrow hyperplasia, scoliosis, aseptic necrosis, arthralgia, myalgia, and pseudoxanthoma elasticum. All reports published between 1970 and 2016 were included.
Results: Arthralgia and low back pain are among the most common musculoskeletal manifestations of thalassemia. Many studies are reporting an increased rate of RA in hemoglobinopathies such as thalassemia, the association of which may be attributed to genetic factors. Arthritis may develop secondary to iron deposition in the synovial tissue or due to iron chelators such as deferiprone, which may provoke a self-limited arthritis due to synovial destruction sustained by free radicals production during iron interchange. Several studies reported increased incidence (16%>30%) of arthropathy in beta-thalassemia patients on deferiprone therapy. Multiple etiologies contribute to osteoarthritis in thalassemia patients such as bone marrow expansion, iron deposition within the joint, and hypoparathyroidism. Only few cases of Salmonella enteriditis septic arthritis were described in thalassemia patients. The associations between osteoporosis and hypogonadism, diabetes, and vitamin D and calcium deficiency were found significant. Skin lesions of PXE were reported in up to 16% in beta-thalassemics.
Conclusions: The pathophysiology of thalassemia and subsequent blood transfusions affect almost every organ system. Rheumatologic manifestations ranging from musculoskeletal complications to connective tissue diseases are common among thalassemia patients. Rheumatologists are highly encouraged to be involved in the multidisciplinary approach for the management of beta-thalassemia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3332

AB0990 PERI-ARTERITIS AS A NOVEL PARANEOPLASTIC PRESENTATION OF MYELODYSPLASTIC SYNDROME: A CASE SERIES AND REVIEW OF THE LITERATURE

N. Droz, C. Gota. *Rheumatology, Cleveland Clinic Foundation, Cleveland, United States*

Background: Myelodysplastic syndromes (MDS) are characterized by ineffective and dysplastic hematopoiesis resulting in peripheral blood cytopenias with varying risk for progression to acute myelogenous leukemia (AML)[1].
Autoimmune manifestations have been well described in association with MDS[2]. Peri-arteritis has rarely been reported.
Objectives: Here, we present a novel association of MDS with peri-arteritis.
Methods: Three patients within our institution and one in the literature were identified. Patients were diagnosed with MDS according to 2008 World Health Organization classification with concomitant occurrence of peri-arteritis on imaging[3].
Results: See Table 1.
Conclusions: Autoimmune manifestations associated with MDS occur in 7–25% of patients. The most commonly reported conditions include vasculitis, inflammatory arthritis and connective tissue disease. There is a paucity of literature describing peri-arteritis associated with MDS[2]. Review of the literature revealed only one other case of peri-arteritis associated with MDS outside of those identified at our facility[4].
With this case series, we report peri-arteritis as a novel presentation of MDS. Peri-vascular inflammation may mimic idiopathic retroperitoneal fibrosis, however, persistent cytopenias, lack of response to immunosuppressive therapy and persistence of elevated inflammatory markers should prompt the physician to evaluate for an underlying diagnosis of MDS.

References:
[1] Ades L, Itzykson R, Fenaux P. Myelodysplastic Syndromes. Lancet. 2014;383(9936):2239–52.
[2] Mekinian A, Grignano E, Braun T et al. Systemic inflammatory and autoimmune manifestations associated with MDS. Rheumatology.2016;55(2):291–300.
[3] Swerdlow S, Campo E, Harris N et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Lyon, France: IARC Press; 2008.
[4] Inoue M, Kano T, Ozaki T et al. Rheumatic manifestations and an epipharyngeal mass accompanied by MDS. Mod Rheumatol. 2015;25(4):653–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1557

AB0991 PREVALENCE OF FIBROMYALGIA AND DEPRESSION IN PATIENTS WITH AUTOIMMUNE /INFLAMMATORY SYNDROME INDUCED BY ADJUVANTS COMPARED TO PATIENTS WITH SYSTEMIC SCLEROSIS

O. Vera-Lastra, P. Blas Hernadez, A. Sánchez-Rodríguez, L.J. Jara. *Internal Medicine, Hospital Especialidades CMN la Raza. Instituto Mexicano Seguro Social, Mexico City, Mexico*

Background: Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) has been associated with previous exposure to various agents such as mineral oil, silicone and vaccines, which act as adjuvants eliciting chronic stimulation of the immune system and manifestation of autoimmune diseases. There is little information about fibromyalgia (FM), depression and the deterioration of the quality of life in ASIA patients.
Objectives: To determine the prevalence of FM, depression and both in ASIA patients associated to mineral oil versus systemic sclerosis (SSc) patients.
Methods: A comparative cross-sectional study was performed in patients with ASIA according to Shoenfeld's criteria associated to injection of mineral oil with cosmetic purposes. The prevalence of fibromyalgia according to criteria of ACR, depression by Beck questionnaire and quality of life with FS-36 in patients with ASIA versus patients with systemic sclerosis matched by age were evaluated.
Results: There were 100 women, 50 ASIA patients (mean age 49±9.7 years) compared to 50 SSc patients (mean age 49±10 years). Of patients with ASIA, 40 patients had non-specific rheumatic disease and 10 met ACR criteria for SSc in 4 patients, SLE 3 and overlap syndrome 1 (SLE plus SSc) and rheumatoid arthritis 2. In ASIA vs. SSc we found depression in 72% vs 46% respectively, $p<0.005$, fibromyalgia in 66 vs 48%, $p<0.008$ and fibromyalgia plus depression in 56% vs. 28, $p<0.005$. Patients with ASIA had a worse quality of life than SSc by SF36 and the most affected parameter was the emotional one.
Conclusions: ASIA patients associated to injection of mineral oild had higher prevalence of depression, fibromyalgia and greater deterioration of quality of life compared to SSc patients. There is a possible link between ASIA, depression and FM.

References:
[1] Agmon-Levin N et al. Chronic fatigue syndrome and fibromyalgia following immunization with hepatitis Bvaccine:another angle of autpimmune (auto-inflammatory)syndrome induced by adjuvants (ASIA). Immunol Res 2014;60:376–82.
[2] Vera Lastra o, et al. Autoimmune /Inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome):clinical and immunological spectrum. Expert Rev Clibn Immunol 2013;9:361–73.
[3] Jara LJ; et al. Severe manifestation of autoimmune syndrome induced by adjuvants (shoenfeld's syndrome. Immunol Res 2016 Jul 13.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6263

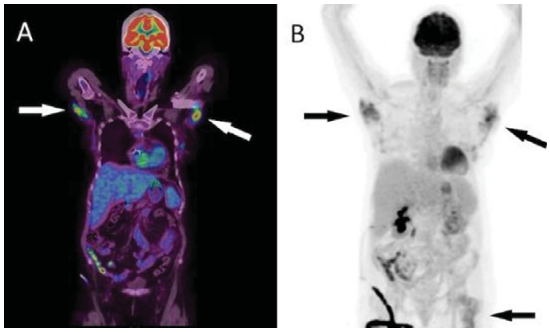
Abstract AB0990 – Table 1

Patient	1	2	3	4[4]
Age	67	37	67	70
Sex	Female	Female	Female	Male
MDS type	CMML-1	MDS with multi-lineage dysplasia; progression to AML	MDS Unclassifiable	MDS with multi-lineage dysplasia
Presenting Symptoms	Hydronephrosis, abdominal pain, weight loss	Serositis, dyspnea, fevers, rash	Rapidly evolving peri-arteritis, adominal pain	Organizing pneumonia, fever, arthralgias
Bone Marrow Biopsy	Hypercellular, features of CMML-1	Normocellular, multilineage dysplasia, 4%blasts, 20q deletion	Hypercellular, granulocytic hyperplasia, 2% blasts	Normocellular, multilineage dysplasia
ANCA and ANA	Negative	Negative	Negative	Negative
ESR (0–15mm/hr)	21	76	57	
CRP (<0.9mg/dL)	5.4	31.2	4.9	9
Radiographic extent of peri-arteritis	Infra-renal abdominal aorta and common iliac arteries	Thoracic aorta and branch vessels	Carotid arteries, thoracic and abdominal aorta, femoral vessels	Internal carotid artery
Treatment	Corticosteroids	Corticosteroids, anakinra, methotrexate, IVIG	Corticosteroids	Corticosteroids
Clinical Course	Ureteral stenting and nephrostomy tube placement improved symptoms. Inflammatory markers remained elevated despite treatment.	Multiple treatment modalities failed to improve symptoms or inflammatory markers. MDS transformed to AML requiring stem cell transplant. Her disease was then quiescent.	Despite treatment, disease was complicated by aortic dissection which was managed non-operatively. Azacitidine was initiated but she died of infectious complications.	Epipharyngeal mass improved with corticosteroids. Disease course was complicated by infection.

AB0992 A DIFFICULT DISTINCTION – ERDHEIM-CHESTER DISEASE MIMICKING IGG4-RELATED DISEASE

P. Korsten[1], C.O. Sahlmann[2], S. Hakroush[3]. *[1]Department of Nephrology and Rheumatology; [2]Department of Nuclear Medicine; [3]Institute of Pathology, University Medical Center Göttingen, Göttingen, Germany*

Background: Rheumatologists are often confronted with systematic and rare diseases. Even among the rare diseases, clinical features may overlap, but treatment options for different diseases may differ.
Objectives: To illustrate the diagnostic challenges the clinician is confronted with when facing rare and systemic diseases in clinical practice with a case report where clinical features were overlapping.
Methods: A 64-year-old woman was presented to our institution after suffering from two ischemic strokes. Cerebral imaging was suggestive of large-vessel vasculitis. Additionally, imaging also revealed a left-sided retro-orbital mass. Her past medical history was notable for retroperitoneal fibrosis with ureteral obstruction requiring percutaneous drainage six months before presentation and placement of a cardiac pacemaker several years ago. Treatment with high-dose prednisone had been initiated but showed no clinical or laboratory improvement.
Results: Clinical examination revealed mild persistent facial hemiparesis and difficulty with ambulation. Mild exophthalmos was present on her left side. On palpation, there were palpable axillary masses bilaterally. Otherwise, her physical examination was normal. Laboratory analysis revealed elevated soluble interleukin-2 receptor levels at 2800 IU/mL (N: 230–770 IU/mL) and mildly increased C-reactive protein at 10 mg/L (N: <5 mg/L). Autoantibodies, including rheumatoid factor, IgG4, ANCA, ANA, and ENA were all within normal range. Plasma cells were normal on flow cytometric analysis. A PET-CT was performed which revealed signs of alveolitis, retroperitoneal fibrosis, axillary masses with strong tracer uptake (figure 1) as well as tracer uptake of the left femur and periaortic sheathing. We performed a biopsy of the left-sided axillary mass. Histopathologic analysis showed Touton giant cells and septal fibrosis. Staining was negative for CD1a and S100 but positive for CD68. Molecular pathologic analysis revealed the presence of the BRAFV600E mutation, findings that are consistent with the diagnosis of Erdheim-Chester disease. We initiated treatment with the BRAF-inhibitor vemurafenib and will follow the patient closely. Staining for IgG4 was negative.



Conclusions: Erdheim-Chester disease (ECD) and IgG4-related disease are very rare disorders and can present with similar clinical findings, such as retroperitoneal fibrosis, alveolitis or lymph node enlargement. About 500 cases of ECD worldwide have been reported. ECD is a non-Langerhans cell histiocytosis with a reported five-year survival rate of about 68%. Roughly 50% of patients show a BRAF mutation. Various treatment options have been reported and are recommended by the recently published consensus guidelines (1). These include interferon-alpha, vemurafenib and also TNF-alpha inhibitors, such as infliximab, but also interleukin-antagonists, such as anakinra (IL-1) or tocilizumab (IL-6). Rheumatologists have to consider non-Langerhans cell histiocytoses in the differential of systemic diseases because the distinction can be difficult and imaging, as well as meticulous histopathologic analyses, are necessary to correctly diagnose these patients because treatment differs.
References:
[1] Diamond EL et al. Consensus guidelines for the diagnosis and clinical management of Erdheim-Chester disease. Blood 2014 Jul 24;124(4):483–92.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6903

AB0993 ELDERLY - ONSET SARCOIDOSIS: A SINGLE CENTER COMPARATIVE STUDY

S. Kobak[1], F. Sever[2], H. Semiz[3], M. Orman[4]. *[1]Rheumatology, Istinye University Faculty of Medicine, LIV Hospital, Istanbul; [2]Chest Diseases, Medicalpark Hospital; [3]Internal Medicine; [4]Statistics, Ege University Faculty of Medicine, Izmir, Turkey*

Background: Sarcoidosis is a chronic granulomatous inflamatory disease characterized with non-caseified granuloma formation. It is rarely affects patients older than 65 years old.
Objectives: The purpose of this study is to compare and evaluate the demografic, clinical and laboratory features of elderly-onset (EOS) and young-onset sarcoidosis (YOS) patients.
Methods: One hundred and thirty one patients diagnosed with sarcoidosis according to clinical, radiologic and histopathological evaluation were included in this study.The patients with initial symptoms started after age 65 were accepted as EOS. Demografic, clinic, radiologic, and laboratory data and the medication which the patients recieved were recorded and retrospectively evaluated.
Results: Twenty (15.3%)of 131 patients were diagnosed as EOS, and 111 (84.7%) patients were evaluated as YOS. Fifteen of 20 EOS patients were female and 5 of them were male. Average duration of the disease was determined as 38.4months for YOS and 22.5months for EOS (p=0.556).Delay of the diagnosis was 12months for YOS while it was 3months for EOS (p=0.001).Higher rates of fatique, comorbid diseases and more Hydroxychloroquine (HQ) use were detected in EOS patients comparing to YOS (p=0.010, p=0.003 and p=0.039 respectively).There was obviously more disease modifying anti-rheumatic drugs (DMARDs) use by YOS group but statistical difference wasn't significant. The 3-year survival rate after diagnosis of sarcoidosis was %95 in the EOS group, compared with %100 in the YOS group.
Conclusions: In this study we showed that YOS and EOS patients may be presented with different clinical, and laboratory features. EOS patients are characterized with higher rates of fatique and comorbid diseases, less inflammatory sign and delayed diagnosis, and less DMARDs usage.
References:
[1] Newman LS, Rose CS, Maier LA. Sarcoidosis. N Engl J Med 1997; 336: 1224±1234.
[2] Chen ES, Moller DR. Etiology of sarcoidosis. Clin Chest Med. 2008; 29:365–377.
[3] Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med. 2007;357:2153–65.
[4] Iannuzzi MC, Fontana JR. Sarcoidosis: clinical presentation, immunopathogenesis, and therapeutics. J Am Med Assoc. 2011;305:391–9.
[5] Baughman RP, Teirstein AS, Judson MA, Rossman MD, Yeager H Jr, Bresnitz EA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med.2001;164:1885–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1377

AB0994 ANTI TNF-ALPHA THERAPY WOULD BE LIFESAVING IN DEFICIENCY OF ADENOSINE DEAMINASE-2

S. Sahin[1], A. Adrovic[1], K. Barut[1], S. Ugurlu[2], E.T. Turanli[3], H. Ozdogan[2], O. Kasapcopur[1]. *[1]Department of Pediatric Rheumatology; [2]Department of Rheumatology, Istanbul University, Cerrahpasa Medical Faculty; [3]Department of Molecular Biology and Genetics, Istanbul Technical University, Faculty of Science and Letters, Istanbul, Turkey*

Background: Deficiency of adenosine deaminase-2 (DADA2) is a rare form of autoinflammatory disorder with limited reported cases.
Objectives: In this study, we have characterized the clinico-immunological, radiological and genetic characteristics of eight childhood-onset DADA2 patients. We aimed to compare these features between surviving and deceased patients.
Methods: Demographic features, clinical characteristics, imaging findings, mutations and pharmacological treatments compared between surviving and deceased DADA2 patients.
Results: Eight patients from seven families were enrolled. While five of them were still surviving, three of them had died due to various reasons. Median age of the patients at disease onset and diagnosis were 7 years (range 0.5–13 years) and 14 years (range 5–27years), respectively. The main clinical manifestations were cutaneous manifestations (7/8), recurrent low-grade fever (6/8), neurological involvement (6/8) and gastrointestinal involvement (5/8). All patients had increased acute phase reactants at presentation and also during flares. Until the diagnosis of DADA2, five patients have been followed-up with the diagnosis of PAN; two patients both with PAN and FMF, and one patient with CAPS and vasculitis.

Abstract AB0994 – Table 1. Clinical features and imaging results of DADA2 patients

Age at disease onset	7	0.5	1	9	7	7	1.5	13
Previous diagnosis	PAN	PAN	PAN	PAN	PAN-FMF	PAN-FMF	CAPS, Vasculitis	PAN
GIS involvement	Yes	Yes	No	Yes	Yes	Yes	No	No
Cutaneous findings	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Neurologic involvement	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Neuroimaging findings	Ischemic stroke	Hemorrhagic stroke	Periventricular leucomalasia	Normal	Normal	Cerebral atrophy	İschemic stroke	İschemic stroke
CECR1	p.Gly47Arg	p.Gly47Arg	p.Gly47Arg	p.Gly47Val and p.Trp264Ser	p.Gly47Arg	p.Gly47Arg	p.Gly47Arg and p.Arg306Ter	p.Gly47Arg

Demographic, clinical, neurological features and genetic mutations did not differ in surviving and deceased DADA2 patients. Deceased and surviving subjects differed in terms of medication usage after the diagnosis of DADA2. Anti-TNF alpha treatment has been initiated in 5 surviving patients soon after the diagnosis of DADA2. However, unfortunately three patients who have died, were able to use either a few doses of anti-TNF alpha treatment or none; one patient due to reluctance of patient and two patients due to establishment of a definite diagnosis with genetic analysis after the patients had died.

Conclusions: Although this study includes limited number of patient, to our knowledge this study for the first time compares the phenotypic, genotypic and medication differences between surviving and deceased DADA2 patients. Anti-TNF alpha treatment seems to be very efficient and lifesaving in DADA2 patients.

References:

[1] Zhou Q, Yang D, Ombrello AK, et al. Early-onset stroke and vasculopathy associated with mutations in ADA2. N Engl J Med 2014;370(10):911–20.
[2] Navon Elkan P, Pierce SB, Segel R, et al. Mutant adenosine deaminase 2 in a polyarteritis nodosa vasculopathy. N Engl J Med 2014;370(10):921–31.
[3] Garg N, Kasapcopur O, Foster J, et al. Novel adenosine deaminase 2 mutations in a child with a fatal vasculopathy. Eur J Pediatr 2014;173:827–30.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4254

AB0995 CLINICAL, THERAPEUTIC, AND GENETIC ANALYSES IN A PATIENT WITH PAPA SYNDROME COMPLICATED WITH INFLAMMATORY BOWEL DISEASE

T. Koga[1], Y. Hidaka[1], K. Fujimoto[1], S. Kaieda[1], K. Mitsuyama[2], K. Iwamoto[3], K. Fujita[4], R. Nishikomori[5], T. Hoshino[1], H. Ida[1]. *[1]Division of Rheumatology, Department of Medicine, Kurume University School of Medicine; [2]Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume University School of Medicine; [3]Coloproctology Center, Kurume Hospital, Kurume, Fukuoka; [4]Department of Pathology, Tenri Hospital, Tenri, Nara; [5]Department of Pediatrics, Kyoto University Graduate School of Medicine, Kyoto, Japan*

Background: PAPA syndrome is an autoinflammatory disease linked to mutations in the *PSTPIP1* gene [1]. These mutations produce a hyper-phosphorylated PSTPIP1 protein and alter its participation in the activation of the "inflammasome" [2]. PAPA syndrome is characterized by pyogenic arthritis with pyoderma gangrenosum and acne, and ususally treated with corticosteroids. Reports from the literature suggest that patients with poorly controlled PAPA syndrome may benefit from IL-1 blockade [2]; however, we cannot use these biologics for PAPA syndrome in our country.

Objectives: To elucidate the pathogenesis of PAPA syndrome, we examined the clinical status and complications before and after treatment and also analyzed the *PSTPIP1* gene.

Methods: We herein report a 25-year-old Japanese male who suffered from recurrent arthritis in his knee and ankle joints, pyoderma gangrenosum, and acne. He had experienced melena and multiple colonic ulcers had been detected by colonfiberscopy. His ulcerations resembled ulcers associated with Crohn's disease. A histological examination was then performed for the synovium of this knee joints, skin lesions of pyoderma gangrenosum, and the colon. The genomic DNA of *PSTPIP1* were analysed in both the patient and his family. We also examined the serum level of IL-1, IL-6, and TNF-α before and after treatment of biologics (adalimumab and infliximab) in this patient.

Results: 1) A histological analysis revealed that a large number of neutrophils had accumulated in the skin lesions; however, very few neutrophils were detected in the pathological lesions of the knee joints and colon. 2) According to a gene analysis, we detected a novel heterozygous mutation (E101G) in the *PSTPIP1* gene; however, his healthy father also had the same mutation, thus suggesting that this mutation of *PSTPIP1* might not be related to his phenotype. We are searching for other affected genes besides the *PSTPIP1* gene for PAPA syndrome in this case. 3) After treatment of biologics (infliximab), the clinical symptoms, such as arthritis and multiple colonic ulcers were considerably improved and the serum level of IL-6 and TNF-α were decreased in this patient.

Conclusions: We herein reported a Japanese PAPA syndrome patient who was complicated with inflammatory bowel disease and had a good response to biologics. A genetic analysis suggested that this particular phenotype might not have been affected by a mutation of the *PSTPIP1* gene.

References:

[1] Smith EJ, Allantaz F, Bennett L, et al. Clinical, molecular, and genetic characteristics of PAPA syndrome: a review. Curr Genomica 11:519–27, 2010.
[2] Ter Haar N, Lachmann H, Özen S, et al. Treatment of autoinflammatory diseases: results rom the Eurofever Registry and a literature review. Ann Rheum Dis. 72:678–85, 2013.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3986

AB0996 FREQUENCY OF HLA-B*51 AND THE ASSOCIATION WITH CLINICAL MANIFESTATIONS IN ARMENIAN PATIENTS WITH BEHÇET DISEASE

V.N. Mukuchyan, A. Haroyan. *Erebuni Medical Center, Yerevan, Armenia*

Background: Behçet disease (BD) is a system inflammatory disease mostly characterized by oral and genital ulcers and variable manifestations affecting other organs, mainly skin and eye. The HLA class I molecule HLA-B*51 allele is strongly associated with BD in many different ethnic groups and appears to be a significant risk factor for BD in the ancient Silk Route areas in contrast with Western and Northern Europe and U.S.[1–4]

Objectives: Our purpose was to show the frequency of presence of HLA-B*51 allele in Armenian patients with BD and estimate any correlation with common symptoms of disease depended on presence of HLA-B*51.

Methods: Forty-seven patients of Armenian origin (28 males 59.6% and 19 females 40.4%) fulfilling the International Criteria for BD (ICBD) with mean age 29.7±11.3 years; disease duration – 5.3±12.4 years were enrolled. We observed the clinical manifestations of BD of both HLA-B*51 carriers and non-carriers.

Results: HLA-B*51 was detected in 38 (80.8%) patients, of whom 25 male and 13 female (65.8% and 34.2%, respectively). Arthritis, erythema nodosum and genital ulcers were significantly more common in HLA-B*51-positive patients (83.3%, 83.3% and 80.6% respectively) than in HLA-B*51-negative ones (16.7%, p=0.032, 16.7% p=0.032 and 19.4% p=0.023 respectively).

Conclusions: In this ever first estimation of HLA-B*51 gene frequency in patients with BD in Armenia, our results indicated that the frequency of HLA-B*51 allele in BD is 80.8% which is higher than elsewhere (in Japan 58.9%, Iran 61.9%, Turkey 75%, Saudi Arabia 76.9% Greece 78.9%)[5]. Furthermore, this investigation revealed HLA-B*51 carriage much more often in male than in female BD patients. In addition HLA-B*51 carriers are in significant higher risk of development of arthritis, erythema nodosum and genital ulcers.

References:

[1] Ohno S, Aoki K, Sugiura S at al (1973) Letter. HLA 5and Behçet disease. Lancet 2:1383 – 1384.
[2] Ohno S, Ohguchi M, Hirose S et al (1982) Close association of HLA Bw51 with Behçet disease. Arch Ophthalmol 100:1455–1458.
[3] de Menthon M, Lavalley MP, Maldini C et al (2009) HLA-B51/B5 and the risk of Behçet disease: A systemic review and meta-analysis of case-control genetic association studies. Arthritis Rheum 61:1287–1296.
[4] Gul A, Ohno S (2012) HLA-B*51and Behçet disease. Ocul Immunol Inflamm 20:37–43.
[5] Yoshiaki Ishigatsubo. Behçet disease: from Genetics to Therapies. Springer 2015: 42–43.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4715

Diagnostics and imaging procedures

AB0997 ULTRASONOGRAPHIC EVALUATION OF ANTERIOR KNEE PAIN IN YOUNG ADULTS

A.A. Negm, M. Khairy, A. Hasseb, K. Abbas. *Rheumatology, Al-Azhar University, Cairo, Egypt*

Objectives: The Primary outcome of the present work is to detect type and frequency of Ultrasonographic changes in patients with anterior knee pain. Secondary outcome is to determine the role of MSUS in early detection of causes of anterior knee pain (AKP).

Methods: Sixty patients with AKP and 20 sex and age matched healthy control were included in this study obtained from the outpatient of Physical Medicine and Rheumatology Department of El Hussein and Bab El-Sharia university hospitals. Inclusion criteria: age between 20–40. Exclusion criteria: Trauma, Crystal induced arthritis, connective tissue diseases (RA, SLE, SpA), chronic liver or kidney disease and previous surgery. Full medical history and clinical examination as well as WOMAC, knee Conventional Radiography and Musculoskeletal Ultrasonography (MSUS) were done to all patients. Bilateral MSUS examination of the following common sites: Insertion of quadriceps tendon, Ligamentum patellae and Anterior aspect of the knee from medial to lateral. According to EULAR guide lines for musculoskeletal ultrasonography.

Results: The mean duration of knee pain in patients group was 11.42±9.134 months. ESR, CRP and WOMAC were higher in patients group ($p<0.01$). MSUS showed significantly more frequent Supra-patellar and Infra-patellar bursitis in patients than control group (p=0.000). patients had higher frequency of cartilage clarity loss (p=0.039) as well as lower cartilage thickness than control, 2.28±0.258 vs 2.73±0.261 mm respectively (P=0.000, 95% CI: 0.31 to 0.58)

Conclusions: The degree of Knee pain, measured by WOMAC, is positively correlated with inflammatory biomarkers (ESR and CRP) in patients with Anterior knee pain. MSUS revealed a positive correlation between Femoral Articular Cartilage thickness and the periarticular tendon- thickness, namely Patellar origin, patellar insertion and Quadriceps insertion. Interestingly, our data present an evidence of the negative impact of the duration of knee pain over Femoral Articular Cartilage thickness as well as Patellar origin thickness. (FAC thickness get worse with longer duration of pain)

References:
[1] Backhaus, M., et al. Guidelines for musculoskeletal ultrasound in rheumatology. Annals of the rheumatic diseases 60.7 (2001): 641–649.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4490

AB0998 DIAGNOSTIC VALUE OF 14-3-3 (ETA) IN RHEUMATOID ARTHRITIS

A. Novikov, E. Aleksandrova, M. Cherkasova, T. Popkova, E. Luchihina, D. Novikova, D. Karateev. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Protein 14-3-3η (eta) involved in the upregulation of inflammatory and joint damage factors [1]. 14-3-3η is the candidate biomarker of rheumatoid arthritis (RA) [2].
Objectives: To evaluate the clinical utility of 14-3-3η for diagnosis of RA.
Methods: We studied 44 patients (pts) with RA, 5 man and 39 women, median (25–75 percentile) of age 45 (33–59) years; disease duration is 10 (5–20) months, DAS28 5,2 (4,4–6,2); 5 pts with systemic lupus erythematosus, 4 – ankylosing spondylitis, 5 – OVERLAP, 4 with psoriatic arthritis and 20 healthy individuals. 14-3-3η, anti-cyclic citrullinated peptide autoantibody (anti-CCP) was measured in serum by commercial enzyme-linked immunosorbent assays, IgM rheumatoid factor (IgM RF) measured – by immunonephelometry.
Results: The diagnostic sensitivity of 14-3-3η for RA (cut off 0,19 ng/ml) is 70,5%, specificity – 83,7%; positive likelihood ratio – 4,33, negative likelihood ratio – 0,35; positive predictive value – 81,6%, negative predictive value – 73,5%; AUC – 0,78 (CI 0,68–0,88). Concomitant presence of 14-3-3η and IgM RF, anti-CCP was determined in 68%, 73% of the patients with RA respectively. 14–3-3η had correlation with IgM RF ($r=0,7$, $p<0,05$).
Conclusions: Serum 14-3-3η are helpful for the diagnosis of RA.
References:
[1] van Beers-Tas MH, et al. A prospective cohort study of 14-3-3η in ACPA and/or RF-positive patients with arthralgia. Arthritis Res Ther. 2016 Apr 1;18:76. doi: 10.1186/s13075–016–0975–4.
[2] Maksymowych WP, et al. 14-3-3η Autoantibodies: Diagnostic Use in Early Rheumatoid Arthritis. J Rheumatol. 2015 Sep;42(9):1587–94. doi: 10.3899/jrheum.141385. Epub 2015 Jul 15.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3997

AB0999 FINNISH COHORT OF PATIENTS WITH RAYNAUD'S PHENOMENON-NAILFOLD VIDEOKAPILLAROSKOPY FINDINGS AND AUTOANTIBODY VALUES

A. Häme[1], K.-L. Vidqvist[2], P. Parmanne[1], A. Puhakka[3], T. Hasan[4], H. Mäkinen[2], J. Panelius[4], R. Peltomaa[1], M. Perovaara[2], R. Luosujärvi[1]. *[1]Rheumatology, Helsinki University Hospital, Helsinki; [2]Rheumatology, Tampere University Hospital, Tampere; [3]Actelion Pharmaceuticals, Espoo; [4]Dermatology, Helsinki University Hospital, Helsinki, Finland*

Background: Raynaud'n phenomenon (RP) is very common all around the world, especially in cold climates (from 3 to 22%) (1). Nailfold capillaroscopy and autoantibodies have a pivotal role in diagnosing of different diseases in the context of RP (2).This is a first study of patients with RP in Finnish tertiary care hospitals.
Objectives: Aim is to investigate nailfold videokapillaroskopy (NVC) findings and autoantibody-values in patients with Raynaud's phenomenon first time in Finnish prospective multicenter study cohort.
Methods: We enrolled consecutive 160 patients with Raynaud's phenomenon who underwent NVC 9/2012–4/2013. Nailfold capillaries of II-V fingers of both hands were examined by using an optical probe videokapillaroskope mounted with x200 magnification lens. Images where analyzed with Videocapt software (DS Medigroup, Milan, Italy). NVC findings were classified with qualitative scoring, and early, active and late patterns were classified as"scleroderma pattern". Serum levels of antinuclear antibodies (ANA), antitopoisomerase I antibodies (anti-Scl-70) and anticentromere antibodies (ACA) were analyzed. Clinical and epidemiological features were reviewed.
Results: The mean age of the patients was 50, 4 years (±14, 8 SD), range 19–81 years, and 79, 4% were female. 15, 6% of patients were smokers and 3 had diabetes. Reasons for performing of NVC can be divided into three categories: (i) assessment of disease activity in previously diagnosed scleroderma (n=26), (ii) differential diagnosis of Raynaud's phenomenon (n=98), and (iii) assessment of Raynaud's phenomenon in other rheumatic diseases (n=36).
In group ii mean age was 48, 6 years (±14, 6 SD), 77, 6% were female and 17,3% were smokers. In this group 26, 5% (n=26) were diagnosed with scleroderma or there was strong suspicion of scleroderma at the first consultation of this study, 52% (n=51) were diagnosed with primary Raynaud's phenomenon and 21, 5% (n=21) were diagnosed with some other rheumatic disease (MCTD (n=2), Sjögren's syndrome (n=3), SLE (n=4), UCTD (n=8) and rheumatic arthritis (n=4)). Among those patients who was diagnosed with scleroderma, only 4% (n=1) had normal NVC pattern, 76,0% had scleroderma pattern (n=19) and 20,0% (n=5) had other non-specific changes. 19,2% (n=5) had low titers of ANA, 7,7% (n=2) had medium titers of ANA and 76,0% (n=19) had high titers of ANA. 69, 2% (n=18) had anticentromere antibodies (ACA) and 3, 8% (n=1) had antitopoisomerase I antibodies (anti-Scl-70). Those patients who had positive ACA or anti-Scl-70 also had a NVC scleroderma-pattern.
Conclusions: The main reason for NVC in this cohort was differential diagnosis of Raynaud's phenomenon, and in most patients in diagnostic group primary Raynaud's phenomenon was diagnosed. NVC is useful method for differential diagnosis of Raynaud's phenomenon.
References:
[1] Spencer-Green, George. Outcomes in primary Raynaud phenomenon: a meta-analysis of the frequency, rates, and predictors of transition to secondary diseases. Archives of internal medicine 158.6 (1998): 595–600.
[2] Ingegnoli, Francesca, et al. Improving outcome prediction of systemic sclerosis from isolated Raynaud's phenomenon: role of autoantibodies and nail-fold capillaroscopy. Rheumatology (2010): kep447.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1431

AB1000 EVALUATION OF NEUROPATHIC FOOT AND ANKLE PAIN IN RHEUMATOID ARTHRITIS PATIENTS: ELECTROPHYIOLOGICAL AND ULTRASOUND STUDIES

A.E.-S.I. El-Hewala[1], S.G. Soliman[2], A.A.E.-A. Labeeb[2], A.A. Zytoon[3], A.T. Elshanawany[2]. *[1]Rheumatology and Rehabilitation, Zagazig University, Sharqeya; [2]Rheumatology and Rehabilitation; [3]Radiodiagnosis, Menoufia University, Menoufia, Egypt*

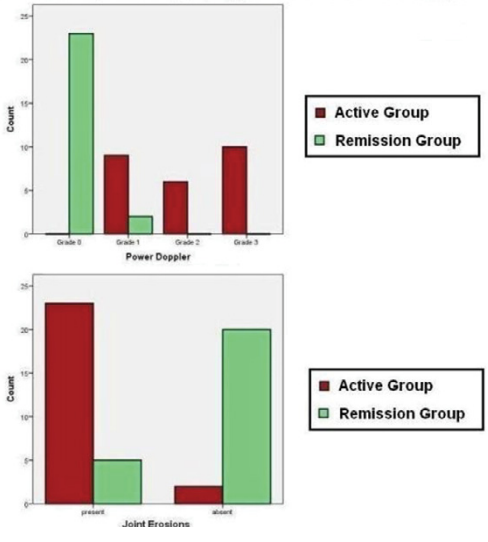
Background: The majority of rheumatoid arthritis (RA) patients develop symptoms related to their foot or ankle.[1] Extraarticular manifestations occur in 10–20% of patients. Symptoms of neuropathy may be overlooked or overestimated in case of severe joint disease, restriction, pain and deformities.[2]
Objectives: This study aimed to evaluate neuropathic foot and ankle pain in RA patients using electrophysiology and musculoskeletal ultrasound (MSUS) to address the association between these findings and disease activity.
Methods: Fifty patients fulfilling the 2010 ACR/EULAR classification criteria and having neuropathic foot and/or ankle pain, were recruited. According to DAS28 system, patients were divided into two equal groups (25 patients each); active and remission. Twenty five healthy subjects were included as controls. Routine tibial and peroneal nerve conduction studies, as well as electromyography of tibialis anterior and abductor hallucis muscles, were performed.[3,4] MSUS assessment of the ankle joint and extra-articular portion of the foot was also performed.[5]
Results: Thirty nine (78%) patients showed the electrophysiological findings of foot neuropathy, irrespective of the disease activity level. In total, 48% of the patients had demyelinating mononeuropathies (entrapment neuropathies), whereas the other 30% had symmetrical axonal neuropathies (Table 1).

Table 1. Electrophysiological Findings (n=50)

	N (%)
Posterior tibial entrapment at ankle	10 (20%)
Peroneal entrapment at fibular neck	6 (12%)
Combined entrapments of posterior tibial nerve at ankle & peroneal nerve at fibular neck	8 (16%)
Pure sensory axonal neuropathy	12 (24%)
Sensorimotor axonal neuropathy	3 (6%)

Ultrasound diagnosis of posterior tibial entrapment at the ankle was encountered in 20 (40%) patients. In addition, a positive power Doppler (PD) signal and

Figure (1): Distribution of power Doppler signals and erosions among patients (n=50)



erosions of the ankle joint were prevalent among the active group in comparison with patients in remission ($p \leq 0.001$), as shown in figure (1).
Conclusions: Peripheral nerve affection is common in the rheumatoid foot, irrespective of the disease activity level. The most common foot neuropathies are; posterior tibial entrapment at the ankle, peroneal entrapment at the fibular neck and pure sensory axonal neuropathy. MSUS is valuable for diagnosis of posterior tibial entrapment at the ankle. In addition, a positive PD signal and erosions of the ankle joint are associated with disease activity.
References:
[1] Loveday DT, Jackson GE, Geary NP. The rheumatoid foot and ankle:current evidence. Foot Ankle Surg 2012; 18:94–102.
[2] Ibrahim I, Medani S, El-Hameed M, Imam M, Shaaban M. Tarsal tunnel syndrome in patients with rheumatoid arthritis, electrophysiological and ultrasound study. Alexandria J Med 2013; 49:95–104.
[3] Preston D, Shapiro B. Routine lower extremity nerve conduction. In:Preston D, Shapiro B, editors. Electromyography and neuromuscular disorders. 3rd ed. Philadelphia: Elsevier; 2013.115–124.
[4] Preston D, Shapiro B. Anatomy for needle electromyography. In:Preston D, Shapiro B, editors. Electromyography and neuromuscular disorders. 3rd ed. Philadelphia: Elsevier; 2013. 174–190.
[5] Riente L, Delle Sedie A, Iagnocco A, Filippucci E, Meenagh G, Valesini G et al. Ultrasound imaging for the rheumatologist V. ultrasonography of the ankle and foot. Clin Exp Rheumatol 2006; 24:493–498.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1984

AB1001 CLINICAL VERSUS ULTRASOUND EVALUATION OF PERIPHERAL ENTHESITES IN A COHORT OF SPONDYLOARTHRITIS

A. Haddouche, S. Haid, S. Bencheikh, S. Slimani, A. Abdessemed, N. Brahimi, A. Ladjouze. *Medicine, University of Algiers 1, Algiers, Algeria*

Objectives: Clinical versus ultrasound evaluation of peripheral enthesites in a cohort of spondyloarthritis
Methods: A monocenter prospective study of all SpAs ≥18 years meting the ASAS criteria for SpA followed in a rheumatology center over a period from January 2015 to April 2016. Demographic, clinical, lab and ultrasound characteristics were noted. Fifteen entheseal sites were investigated bilaterally: insertions of supra-spinatus, sub-scapular, medial and lateral epicondylar tendons, triceps brachialis, gluteus medius, quadriceps proximal and distal insertion (patellar ligament, medial and lateral collateral ligament), Achilles tendon, plantar aponeurosis. These sites were assessed clinically and with US during the same visit and then results were compared between the clinical and the US examination.
Results: A total of 208 patients were included, mainly men (63.5%). The mean age was 40.2±11.7 years and the mean duration of the SpA was 11.8±8.7 years. Axial radiographic SpA was the most frequent phenotype (69.2%) and ankylosing spondylarthritis was the most frequent sub-group (57.7%). At examination, 88.9% had an active disease (ASDAS-ESR and/or ASDAS-CRP>1.3) and 64.4% of SpAs were taking NSAID. Clinical examination and US revealed at least one abnormal enthesis in 55.3% and 86.1%, respectively. Overall, 6240 entheses were examined, 44.2% were considered abnormal by clinical examination and 83.2% by US. The US abnormalities were entesophytes (69.5%), erosions (54.8%), hypochogenicity (49%), thickening (46.4%), bursitis (30.5%), calcifications (20.9%) and finally Doppler signal near the cortical bone in 20% of the examined entheses. The evidence of entheseal abnormalities by clinical examination has a poor likehood ratio (LR) for the presence of any US abnormality (LR + =1.4, LR- =0.8), for the acute US abnormalities (LR + =1.25, LR-=0,8), for the chronic US abnormalities (LR + =1.3, LR =0.8) as well as for the presence of the Doppler signal (LR + =1.1, LR- =0.9) at all sites.
Conclusions: US is useful to detect structural and inflammatory abnormalities of the enthesis in the SpA and can complete physical examination in order to better evaluate enthesitis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1978

AB1002 CLINICAL AND ULTRASOUND PREVALENCE OF PERIPHERAL ENTHESITIS IN AN ALGERIAN COHORT OF SPONDYLOARTHRITIS

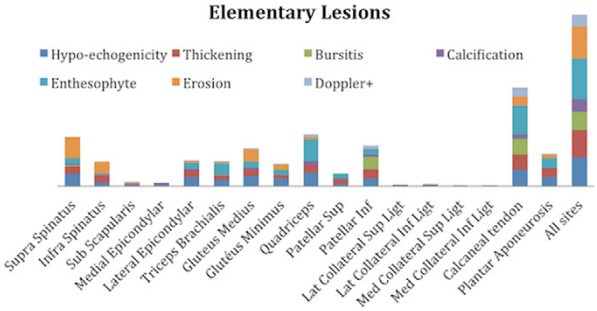
A. Haddouche, S. Haid, S. Bencheikh, S. Slimani, A. Abdessemed, N. Brahimi, A. Ladjouze. *Medicine, University of Algiers 2, Algiers, Algeria*

Background: Algerian Spondyloarthritis (SpA) is characterized by a high prevalence and more severe axial and articular lesions compared to the caucasian population, What about enthesitis involvement?
Objectives: To estimate the global and site-specific clinical and ultrasound prevalence of peripheral enthesitis in an Algerian cohort of SpA
Methods: AA monocenter prospective study of all SpA ≥18 years meting the ASA criteria for SpA followed in a rheumatology center at EHS Ben Aknoun over a period from January 2015 to April 2016 Demographic, clinical, lab and ultrasound characteristics were noted. Fifteen enthesic sites were investigated: insertions of supra-spinatus, sub-scapular, medial and lateral epicondylar tendons, triceps brachialis, gluteus medius, quadriceps proximal and distal insertion (patellar ligament, medial and lateral collateral ligament), Achilles tendon, plantar aponeurosis. These sites were assessed clinically and ultrasonographically during the same consultation to determine the global and site-specific clinical and ultrasound prevalence of peripheral enthesitis. Elementary ultrasonographic lesions were noted. The comparison between clinical and ultrasound prevalence was performed using the Mac Nemar test using the SPSS software.
Results: A total of 208 patients were included, mainly men (63.5%). The mean age was 40.2±11.7 years. The mean duration of the SpA was 11.8±8.7 years. Axial radiographic SpA was the most frequent phenotype (69.2%) and ankylosing spondylarthritis was the most frequent sub-group (57.7%). At examination, 88.9% had an active disease (ASDAS-vs and/or ASDAS-crp>1.3) and 64.4% of SpAs were taking NSAID 6240 entheses were assessed clinically and 7072 entheses examined with ultrasound

Table 1. The global and site-specific clinical and ultrasound prevalence of peripheral enthesitis

	Clinical%	Ultrasound%	P
Calcaneal tendon	13,9	68,8	<0,001
Quadricipital	9,9	49	<0,001
Supra Spinatus	17,8	45,7	<0,001
Gluteus Medius	11,3	34,6	<0,001
Patellar Inf	8,9	32,5	<0,001
Plantar Aponeurosis	14,7	32,2	<0,001
Triceps Brachialis	10,3	26,7	<0,001
Lateral Epicondylar	23,8	24,5	NS
Infra Spinatus	–	24	–
Gluteal Minimus	–	22,6	–
Patellar Sup	10,6	14,9	NS
Sub Scapularis	18,5	5	<0,001
Medial Epicondylar	12,7	3,8	<0,001
Inf Collateral Lat Ligt	6,5	2,6	0,009
Sup Collateral Lat Ligt	5,8	1,9	0,007
Collateral Med Sup Ligt	5,8	0,7	<0,001
Collateral Med Inf Ligt	5	0,5	<0,001
All sites	44,2	83,2	<0,001

Figure 1 summarizes the prevalence of elementary ultrasound lesions per site.



Conclusions: In this cohort and as expected, ultrasound (with at least one elementary lesion) was superior to clinical examination for the detection of peripheral enthesitis (83.2 vs. 44.2%, P<0.001). Interesting sites to explore according to the prevalence and to the presence of a Doppler signal (<2mm/cortical) would be insertions of the calcaneal, quadricipital, patellar, gluteal, plantar aponeurosis and triceps brachialis tendons.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1572

AB1003 MEDIAN AND ULNAR NERVE CROSS-SECTIONAL AREA IN CARPAL TUNNEL SYNDROME WITH EXTRATERRITORIAL SPREAD OF SENSORY SYMPTOMS

B. Mansiz Kaplan[1], M. Akdeniz Leblebicier[2], I. Yagci[3]. *[1]Department of Physical Medicine and Rehabilitation, University of Health Sciences, Ankara Training and Research Hospital, Ankara; [2]Department of Physical Medicine and Rehabilitation, Gumushane State Hospital, Gumushane; [3]Department of Physical Medicine and Rehabilitation, School of Medicine, Marmara University, Training and Research Hospital, Istanbul, Turkey*

Objectives: To evaluate the relationship between extramedian spreading of sensorial symptoms and median and ulnar nerve cross-sectional area in patient with carpal tunnel syndrome (CTS), to compare the ultrasonographic and electrophysiological findings in patients with CTS whose sensorial symptoms are extramedian spreading or median distribution only.
Methods: Patients with CTS were divided into two groups as with and without extramedian symptoms and were assessed clinically, electrophysiologically and ultrasonographically by three blind investigators. In electrophysiological tests, median and ulnar nerve conduction studies were performed. Nerve cross-sectional areas were measured at hamatum hook, psiform bone, radio-ulnar joint, one-third distal part of forearm, and medial epicondyle for median nerve; radio-ulnar joint, psiform bone, one-third distal part of forearm, and medial epicondyle for ulnar nerve by ultrasonography.

Results: The study was completed with 61 patients (108 hands). Extramedian symptoms were present in 31 patients (54 hands). Finger grip strength was lower, pain values evaluated with visual analogue scale were higher in these patients ($p<0.05$). There was no statistically significant difference in electrophysiological and ultrasonographic parameters between two groups.
Conclusions: These results suggest that extramedian spread in CTS patients is more related to central and peripheral sensitization than peripheral causes.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6551

AB1004 NOMENCLATURE ON MEDICAL, DIAGNOSTIC, AND THERAPEUTIC PROCEDURES IN RHEUMATOLOGY

B. Yoldi[1], M.A. Martin[2], C. Plana[3], A. Gómez[4], M. Valero[5], J.L. Andreu[6], J.V. Moreno[7]. *[1]Rheumatolgy, Hospital Universitari Dexeus, Barcelona; [2]Sociedad Española de Reumatología, Madrid; [3]Rheumatology, Hospital Clínic Provincial, Barcelona; [4]Rheumatology, Hospital Parc Taulí, Sabadell; [5]Rheumatology, HM Hospitales; [6]Rheumatology, Hospital Universitario Puerta del Hierro, Madrid; [7]Rheumatology, Hospital Vall d'Hebron, Barcelona, Spain*

Background: One of the missions of the Spanish Society of Rheumatology (SER) is to provide professionals involved with the necessary tools to ensure a better care for patients suffering from a rheumatic disease. Up to now, there is no benchmark that quantifies the complexity of medical acts in this specialty. Therefore, there is a need to adopt a physician activity scale that would allow assessment of their professional activity and skills regarding patient care.
Objectives: To compile a nomeclature of medical, diagnostic, and therapeutic procedures in the field of rheumatology; and to establish a hierarchical classification system according to a complexity index.
Methods: A list of care, diagnostic, and therapeutic acts was compiled based on the nomenclature created by Drs Fernandez and Olive. The hierarchical classification system was based on the construction of a complexity index which was calculated by two factors: time of completion and degree of complexity of each act. Time of completion was stated according to the document "Standards of Process Time and Patient Care Quality" by Dr Alonso. The degree of complexity of each rheumatologic act was agreed thanks to a panel of experts using a Delphi technique in two rounds. Subsequently, it was validated against a questionnaire which was sent to the 1144 partners of SER via its web.
Results: The total of included acts was 54. The results obtained with the Delphi method tended to show a consensus of opinion (media $\sigma 2$ - $\sigma 1$=0.75–1.43=-0.68, media IQR2 – IQR1=0.8–1.9=-1.1). Furthermore, a validation of these results was carried out through a massive survey among the partners of SER. The survey results showed a high degree of agreement (at least 70.0 per cent of the partners agreed or strongly agreed with the complexity of each act).
The degree of complexity in successive visits was 100. In the query section for consultations, the highest scores were obtained by first visit to hospitalized patient (366) and home visit (369). Regarding diagnostic techniques, the highest scores were obtained with biopsies: bone (465), sural nerve (416), and synovial (380). Also worth mentionioning the scores obtained by ultrasound scan (204), capillarioscopy (113) and densitometry (112). Regarding therapeutic techniques, intra-articular injection under sedation in children obtained a score of 388; while intra-articular injection with ultrasound control obtained a score of 163. The clinical report of disability was agreed to have a score of 323, and the expert report obtained a score of 370.
Conclusions: This work has made it possible to create a nomenclature of 54 acts in Rheumatology where biopsies (bone, sural nerve, synovial), visits to hospitalized patients, home visits, infiltration under sedation in children, and expert reports are identified as the most complex acts. Musculoskeletal ultrasound is considered twice as complex as a successive visit, capillaroscopy, or bone densitometry. These results will make it possible to improve patient care and establish a solid and agreed foundation to negotiate the provision of public and private services.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4353

AB1005 HYPOTHYROID AND HYPERTHYROID STATUS WAS STRONGLY ASSOCIATED WITH MUSCULOSKELETAL ULTRASONOGRAPHIC ABNORMALITIES WITH ARTHRALGIA

B.Y. Kim[1], S.S. Kim[2], J.R. Choi[3], H.-S. Kim[1]. *[1]Department of Internal Medicine, Soonchunhyang University college of Medicine, Seoul; [2]Department of Internal Medicine, Gangneung Asan Medical Center, Gangneung; [3]Department of Internal Medicine, Pohang Saint Mary's Hospital, Pohang, Korea, Republic Of*

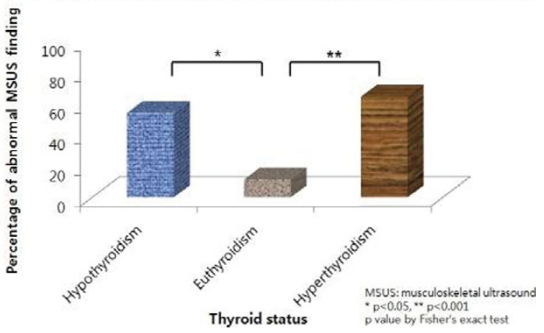
Background: Thyroid dysfunction can cause musculoskeletal symptoms and sign. Ultrasonography is a useful tool for the evaluation of synovitis and is more accurate than clinical examination.
Objectives: The purpose of the study was to determine whether musculoskeletal ultrasonographic (MSUS) abnormalities were observed according to the state of thyroid disease.
Methods: Patients with thyroid disease were categorized as euthyroid, hypothyroid, or hyperthyroid status according to thyroid hormone levels and evaluated the association with MSUS abnormalities. In addition, the association of the presence of thyroid autoantibodies with MSUS abnormalities was also studied. In MSUS, an experienced rheumatologist examined the presence of synovial fluid, synovial hypertrophy, and grade of power doppler in the knee joint.
Results:

Table 1. Patient characteristics

	Patients (n=109)
Age – mean ± SD (years)	58.2±13.0
Sex – n (%)	
Male	13 (11.9)
Female	96 (88.1)
Thyroid diseases duration – median (range), (years)	4 (0–13)
Distribution of thyroid diseases - n (%)	
Euthyroid status	61 (56)
Hypothyroid status	11 (10.1)
Hyperthyroid status	37 (33.9)
Positive thyroid autoantibodies – n (%)	68 (62.4)
Taking thyroid medication – n (%)	100 (91.7)
Patient's Knee VAS (100mm) – median (range)	10 (0–80)
MSUS finding – n (%)	
Normal	72 (66.1)
Abnormal	37 (33.9)

109 consecutive patients who visited the endocrinology outpatient clinic and had thyroid disease with normal or abnormal thyroid function tests participated in the study. MSUS abnormalities were statistically significantly higher in hyperthyroid or hypothyroid status than in euthyroid status ($p<0.001$). However, there was no statistically significant difference between hypothyroid status and hyperthyroid status. The presence of MSUS abnormalities with abnormal thyroid function was corrected according to the presence of radiological Knee osteoarthritis. Both hypothyroid and hyperthyroid status was still associated with MSUS abnormalities regardless of knee osteoarthritis. Visual analogue scale for knee pain was higher in patients with MSUS abnormalities ($p<0.001$). But, there was no statistically difference of MGUS abnormalities with presence of thyroid autoantibodies.

Figure 1. It shows frequency of Abnormal MSUS finding according to thyroid status



Conclusions: Both hypothyroid and hyperthyroid status was significantly associated with MSUS abnormalities with knee arthralgia. MSUS is a useful tool to detect clinically early joint abnormalities. We suggest that patients with diagnosed thyroid dysfunction and who remain uncontrolled, should assess the MSUS examination in patients with arthralgia. Moreover a thyroid function test for unexplained arthritis maybe warranted.
References:
[1] Cakir M, Samanci N, Balci N, et al. Musculoskeletal manifestations in patients with thyroid disease. Clin Endocrinol 2003;59:162–7.
[2] Wakefield RJ, Green MJ, Marzo-Ortega H, et al. Should oligoarthritis be reclassified? Ultrasound reveals a high prevalence of subclinical disease. Ann Rheum Dis 2004;63:382–5.
[3] Magni-Manzoni S, Epis O, Ravelli A, et al. Comparison of clinical versus ultrasound-determined synovitis in juvenile idiopathic arthritis. Arthritis Rheum 2009;61:1497–504.
[4] Karim Z, Wakefield RJ, Quinn M, et al. Validation and reproducibility of ultrasonography in the detection of synovitis in the knee: a comparison with arthroscopy and clinical examination. Arthritis Rheum 2004:50:387–94.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3054

AB1006 POWER-DOPPLER TECHNIQUE IN PAGET'S DISEASE OF BONE: A NEW MONITORING TOOL OF THERAPEUTIC RESPONSE. STUDY ON 43 PATIENTS

C. Artusi[1], C. Mastaglio[2], C. Arnoldi[2], V. Galbiati[2], P.L. Meroni[1]. *[1]Chair and Division of Rheumatology, Gaetano Pini Institute, University of Milan, Milan; [2]Unit of Rheumatology, Ospedale Moriggia-Pelascini, Gravedona (CO), Italy*

Background: To date the evaluation of the disease activity and the monitoring of the therapeutic response of patients affected by Paget's disease of bone is based only on clinical and hematological data. However, in clinical practice the management of these patients is still challenging. Previous angiographic

and histological studies have revealed that the accelerated bone turnover is associated with an increased blood flow and hypervascularity, suggesting a role of high-resolution sonography with power-Doppler (PD) and color- Doppler (CD) in Paget's disease. Our preliminary data demonstrated that this technique shows not only the alterations of the pagetic bone profile, but also the hypervascularization of the osteoperiosteal-layer, both at the diagnosis and during follow-up.

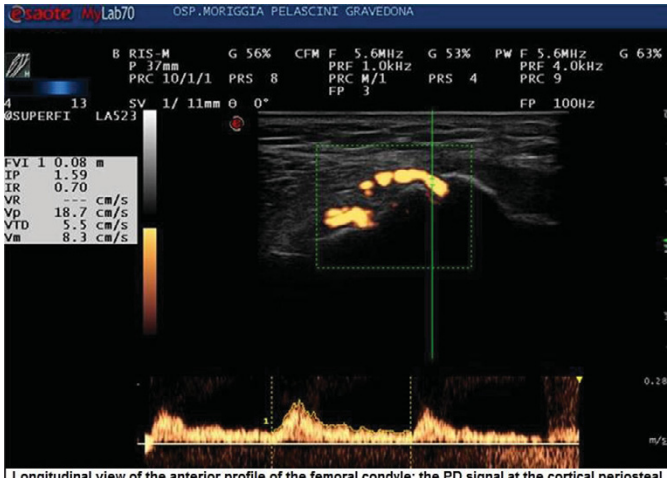
Objectives: To validate the PD technique as a useful tool not only for the diagnosis of Paget's disease of bone but also for the evaluation of the disease activity and for the monitoring of the therapeutic response.

Methods: Forty-three consecutive patients affected by Paget's disease of bone and treated with neridronate were followed up over the last ten years. Patients were classified in eight clinical patterns defined by the presence of bone alkaline phosphatase elevation over the normal range (BAP+), bone pagetic pain as visual analogue scale ≥30 (VAS+) and PD alterations of osteoperiosteal vascularization (PD+). Data were analyzed by Fisher exact test (two tails) to assess the associations between BAP+, VAS+ and PD+ at different times during follow up: before the start of the therapy, after the first, the second and the third neridronate cycle of therapy, and at the end of all cycles.

Results: At any time BAP+ and VAS+ were not associated. A trend of association between VAS+ and PD+ could be observed only after the first neridronate cycle. In contrast, the association between BAP+ and PD+ was statistically significant before the therapy, at the end of all cycles of therapy and after the second one, but not after the first one.

Table 1. Associations between BAP elevation over the normal range, VAS and PD alterations of osteoperiosteal vascularization, p<0.05

	BAP+/VAS+		BAP+/PD+		VAS+/PD+	
	n	P value	n	P value	n	P value
Before therapy	40	1.000	35	0.0063	35	0.5620
After first therapy cycle	40	0.6225	35	0.6176	35	0.0751
After second therapy cycle	22	0.4701	21	0.0263	21	1.000
After third therapy cycle	9	1.000	9	1.000	9	1.000
At the end of all therapy cycles	40	1.000	35	0.0290	35	1.000



Longitudinal view of the anterior profile of the femoral condyle: the PD signal at the cortical periosteal layer shows a systolic peak and a continuous diastolic flow with low-resistance index.

Conclusions: The lack of association between VAS+ and PD+ or BAP+ may be due to the difficulty of the patients in identifying and quantifying the pagetic pain, and suggests the weakness of the clinical criteria in defining the disease activity. Otherwise, PD technique proves to be a fast, reliable and not expensive tool, which is also very useful for monitoring/achieving better control of Paget's disease of bone.

References:

[1] Adami S., et al. Italian guidelines for the diagnosis and treatment of Paget's disease of bone. Reumatismo, 2007; 59(2):153–168.
[2] Singer F.R., et al. Paget's Disease of Bone: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, 2014; 99(12):4408–4422.
[3] Mastaglio C., et al. Characterization of Osteocortical-Periosteal Layers by High-Resolution Sonography Using a Doppler Technique in Paget's Disease of Bone. JDMS, 2008; 24(3):136–144.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4272

AB1007 THE SLE-KEY® TEST DETECTS AN SLE SEROLOGIC SIGNATURE THAT PERSISTS OVER TIME AND IS INDEPENDENT OF DISEASE ACTIVITY

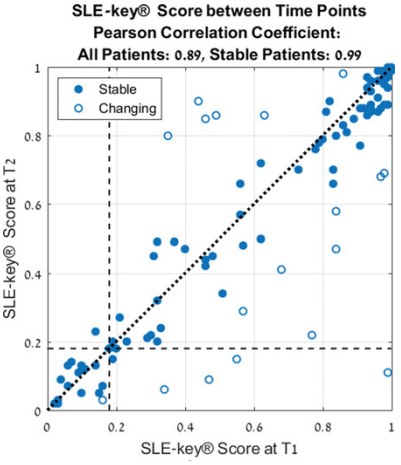
C. Putterman[1], M. Petri[2], R. Caricchio[3], P. Safer[4], K. Jakobi[4], R. Sorek[4], I. Gluzman[4], S. Wallace[5], I.R. Cohen[6]. *[1]Division of Rheumatology, Albert Einstein School of Medicine, NY; [2]Division of Rheumatology, Johns Hopkins University School of Medicine, MD; [3]Temple Lupus Clinic, Temple University, Philadelphia, PA, United States; [4]ImmunArray LTD, Rehovot, Israel; [5]ImmunArray Inc, VA, United States; [6]Weizmann Institute of Science, Rehovot, Israel*

Background: We previously described the SLE-key® RuleOut test[1,2] to rule out the presence of systemic lupus erythematosus (SLE) with 94% sensitivity, 75% specificity, and 93% negative predictive value. We also reported that the SLE-key® signature appeared to be independent of disease activity or duration[3] suggesting[4] that that the SLE-key® signature might persist over time in the same subject.

Objectives: Here we report that the SLE-key® signature remains stable over time in paired samples drawn from most individual subjects, regardless of disease activity.

Methods: We determined the SLE-key® RuleOut scores for 113 paired serum samples submitted by clinics specializing in SLE. SLEDAI scores at the time of the blood draw ranged from 0 to 22. The mean SLEDAI difference within the pairs was 2.7±6.3. Samples were collected from subjects with a T1-T2 time difference that ranged from 0 to 11.5 years (mean =2±2.6 years).

Results: The SLE-Key® RuleOut test identifies an SLE-specific signature based on a profile of autoantibodies to a combination of nucleic acids (complex ssDNA and a defined oligonucleotide) and protein biomarkers. Patients with an SLE-key® score of >0.18 are considered not ruled out for a diagnosis of SLE. In 84% of paired samples, patients' SLE-key® scores remained essentially the same (Figure 1, closed circles). The scores for these subjects were stable, persistent, and independent of SLEDAI score or time between sampling. Significant changes in the SLE-key® scores of 18/113 patient pairs (open circles) appear to be independent of time between blood draws and change in SLEDAI score. In 7 cases there was a change in Rule Out status of the patients. In 3 cases, both scores were close to the 0.18 threshold and the change was deemed not significant. In 4 cases, patients' status changed from RuledOut to Not Ruled Out, but with no correlation to change in SLEDAI score or time between sampling dates. Records of patients with changing SLE-key® scores are being studied to determine the reasons and the clinical implications of the change.



Conclusions: The SLE-key® RuleOut test detects a serologic signature which remains stable between sampling dates and over a long period of time after diagnosis in 84% of subjects. Subjects who were ruled out at T1 were generally ruled out at T2. Patients not ruled out at T1 remained not ruled out at T2. The clinical implications of a changing SLE-key® RuleOut score in the remaining 16% of patients may be meaningful, and are currently being carefully investigated.

References:

[1] Fattal et al; Immunology 2010.
[2] Putterman et al., J Immunol Methods, 2016.
[3] Putterman et al., Lupus 2016.
[4] Cohen IR, Lupus Open Access 2016.

Acknowledgements: The authors wish to acknowledge the invaluable contributions of Cohen-Gindi O, Lerner M, Tarnapolski O, Blumenstein Y, Javaherian A, Pitts J, Barton M and Wong E and Innovative Medicines Initiative Joint Undertaking under grant agreement n° 115308 BIOVACSAFE.

Disclosure of Interest: C. Putterman Consultant for: ImmunArray, M. Petri: None declared, R. Caricchio: None declared, P. Safer Employee of: ImmunArray, K. Jakobi Employee of: ImmunArray, R. Sorek Employee of: ImmunArray, I. Gluzman Employee of: ImmunArray, S. Wallace Employee of: ImmunArray, I. Cohen Shareholder of: ImmunArray, Consultant for: ImmunArray

DOI: 10.1136/annrheumdis-2017-eular.5963

AB1008 DISTRIBUTIONS OF ANTIBODIES IN SLE PATIENTS IN DIFFERENT ETHNIC GROUPS IN XINJIANG

C. Xiaomei, W. Lijun. *Department of Rheumatology and Immunology, People's Hospital of Xinjiang Uyghur Autonomous Region, urumqi, China*

Objectives: The aim of this study was to explore distributions of antibodies in SLE patients in different ethnic groups in xinjiang.

Methods: Data were obtained from 670 patients with SLE from Department of Rheumatology and immunology in our hospital between January 2012 and October 2016.All patients fulfilled the 1997 ACR SLE classification criteria. Data about their gender, age, ethnic groups and result of antibodies test were collected.
Results: Totally 670 completed data were collected.there are 438 (65.37%) of these patients (68.22%) were Han population,136 (20.29%)were Uighur, 43 (6.42%) were Kazakh, 30 (4.48%) were hui people and 23 were other minorities live in xinjiang. The titer of ANA was higher in minorities than Han population (Z=-3.516, P<0.01). As compared with Han population, the positive rate of anti-Smith antibaodies and anti-SSA antibodies in SLE patients, significantly higher than han population (χ^2=5.902, P<0.017; χ^2=42.787, P<0.001, respectively). However, there are no significant different of the positive rate ofanti-SSA antibodies, anti-Scl-70 antibodies, anti-Jo-1 antibodies,anti-ds-DNA antibodies between Han population and minorities.
Conclusions: Distributions of antibodies in SLE patients were different between Han population and minorities.the positive rate of anti-Smith antibaodies and anti-SSA antibodies in SLE patients were significantly higher than han population.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6291

AB1009 MRI CONTRIBUTES TO ACCURATE DIAGNOSIS OF NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH SERUM NEGATIVE HLA-B27

C.-C. Lu[1,2], G.-S. Huang[3], H.-C. Chen[1], T.S.-H. Lee[4], F.-C. Liu[1], S.-Y. Kao[1], S.-J. Chu[1], T.-Y. Ho[1], C.-H. Chen[5], S.-Y. Lyu[6]. *[1]Division of Rheumatology, Department of Internal Medicine, Tri-Service General Hopsital, National Defense Medical Center, Taipei City, Taiwan, Province of China; [2]Department of Pathology, University of Washington, Seattle, United States; [3]Department of Radiology, Tri-Service General Hopsital, National Defense Medical Center; [4]Department of Health Promotion and Health Education, National Taiwan Normal University, Taipei City; [5]Division of Rheumatology, Department of Internal Medicine, Taipei Tzu Chi Hospital, New Taipei City; [6]Division of Radiology, Taoyuan General Hospital, Ministry of Health and Welfare, Taoyuan City, Taiwan, Province of China*

Background: Based on ASAS axial spondyloarthritis (SpA) criteria, the presence of structural changes of sacroiliac (SI) joints such as sclerosis, bone erosion, joint space widening or ankyloses dose not meet the definition of active sacroiliitis on magnetic resonance imaging (MRI), if there is no bone marrow edema (BME). However only less than half Asian patients with SpA were characterized by BME. Neither serum inflammatory markers such as c reactive protein (CRP) nor erythrocyte sedimentation rate (ESR) is able to be useful as diagnostic markers in the early phase of SpA. HLA-B27 is associated with early diagnosis of SpA and axial inflammation of SI joints on MRI. Nonetheless, HLA-B27 is not associated with structural lesions of SI joints. All factors contribute to difficult defining early Asian SpA patients in the absence of serum HLA-B27 and active imaging inflammation.
Objectives: The aim of this study is to evaluate the prevalence of structure changes of SI joints on MRI in Taiwanese SpA patients in the absence of serum HLA-B27.
Methods: Thirty-three patients with inflammatory back pain and morning stiffness (disease duration more than 3 months) and high disease activity (BASDAI$\geq$4) who had to be either serum HLA-B27 positive (10 patients) with $\geq$1 SpA-feature or HLA-B27 negative with $\geq$2 SpA-features (22 patients) were included in this prospective study. All patients did not meet the definition for a positive radiograph according to the modified New York criteria. MRI was performed with multiple sequence (Coronal and axial T1-weighted spin echo, coronal and axial short-tau inversion recovery). SI joints were evaluated for the prevalence of subchondral BME and structure changes (sclerosis, bone erosion, joint space widening and ankylosis). All patients were tested for X-rays of the pelvis and serum levels of ESR and CRP. Correlation analysis was performed among the different collected variables.
Results: Subchondral BME was only present in 8 of 23 patients with SpA in the absence of serum HLA-B27 (34.8%), while 7 of 10 (70%) HLA-B27 serum positive SpA patients had active BME on MRI. Structural changes of SI joints, including sclerosis, bone erosion and joint space widening were identified in 8 (80%), 10 (100%) and 5 (50%) SpA patients with positive serum HLA-B27, respectively. Nevertheless, these structural changes of SI joints on MRI were more common in HLA-B27 serum negative patients, as 15 (65.2%), 20 (87.0%) and 7 (30.4%) of 23 serum negative patients, respectively.
Conclusions: MRI contributes to detect structural changes of SI joints for patients with nonradiographic axial SpA in the absence of serum HLA-B27.
References:
[1] Rudwaleit, M. & Sieper, J. Nat. Rev. Rheumatol. 2012;8, 262–268.
[2] van Tubergen, A. & Weber, U. Nat. Rev. Rheumatol. 2012;8, 253–261.
[3] van der Heijde D, et al. Ann Rheum Dis 2017;0:1–14.
[4] Turina MC, et al. RMD Open 2017;2:e000319.
[5] Baraliakos, X. & Braun, J. Nat. Rev. Rheumatol. 2013;9, 498–502.
[6] Navallas M, et al. Radiographics. 2013;33:933–56.
[7] Lambert RGW, et al. Ann Rheum Dis 2016;75:1958–1963.
[8] Chung HY, et al. Ann Rheum Dis. 2011;70:1930–6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6069

AB1010 ULTRASOUND MORPHOSTRUCTURAL PATTERN OF THE TIBIOFIBULAR JOINT. PRELIMINARY RESULTS

C. Hernández-Díaz[1], L. Ventura-Rios[1], M. Maldonado[2], G. Sanchez-Bringas[3]. *[1]Laboratorio de Ultrasonido Musculoesquelético y Articular, Instituto Nacional de Rehabilitación, Mexico City, Mexico; [2]Reumatologa, Cuzco, Peru; [3]Departamento de Embriologia, Facultad de Medicina, UNAM, Mexico City, Mexico*

Background: The anatomy of the proximal tibiofibular (TF) joint is directly related to its ability to withstand stress applied in either a longitudinal or axial fashion. It is traditionally evaluated by CT scan, however, in certain conditions, it could be evaluated by ultrasound (US) conveniently; so far US has not been using to evaluate the TF joint. US is an innocuous, accessible and cheap image technique, that has demonstrated its utility for evaluating joints in several pathologic conditions, and might have an important role in the early diagnosis of inflammatory, degenerative or even tumoral lesions at the level of the TF joint; there are no studies that have evaluated the morpho- structural pattern of the TF joint.
Objectives: To describe the morphostructural pattern of the tibiofibular joint in healthy subjects.
Methods: Subjects older than 18 yrs old, with no history of past/present lesion of the knee, without any joint or neurovascular disease were included. A short questionnaire related to physical activity applied, and clinical evaluation to discard instability performed. US of both knees in extension done, using an Esaote ® MyLab 70 ultrasound equipment with a 7.5 - 12 MHz linear transducer. Descriptive statistics done
Results: Thirty-six patients (27 women, 75%) included, mean age 41.2±8.9 years, mean weight 71±12.46 kg, mean height 1.61±0.09 ms and BMI 71.07±12.40. 69% of the subjects practice mild exercise activities. By US mean distance between tibia and fibula were 3.2±1.17 cm; the mean thickness of the ligaments (superior and inferior) was 3.2±0.99 cm and 3.2±0.89 respectively, and in the superior e inferior fibular ligaments were 3.2±0.99 cm and 3.2±0.89 cm respectively. Ligaments were hyperechoic in 61.1%, a well-defined border was seen only in 48.6%. Inside of joints a hypoechoic tissue was observed
Conclusions: These preliminary results suggest that US can be a useful tool for evaluating the tibiofibular joint.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6840

AB1011 RELIABILITY OF SONOGRAPHIC PERITENON EXTENSOR TENDON INFLAMMATION PATTERN IN PSORIATIC ARTHRITIS

C. Macía[1], H.B. Hammer[2], S. Falcao[3], J. Medina[4], M. Gutierrez[5], E. De Miguel[6]. *[1]Rheumatology, Hospital Universitario Severo Ochoa, Madrid, Spain; [2]Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; [3]Rheumatology, Chronic Diseases Study Center (CEDOC), NOVA Medical School, UNL, Lisboa, Portugal; [4]Rheumatology, Hospital Clínico Universitario, Valladolid, Spain; [5]Rheumatology, Division of Musculoskeletal and Rheumatic Disorders. Instituto Nacional de Rehabilitación, Mexico City, Mexico; [6]Rheumatology, Hospital Universitario la Paz, Madrid, Spain*

Background: Preliminary results demonstrate that the peritenon inflammation of the extensor digitorum tendon (PTI) is a specific ultrasound (US) pattern of Psoriatic Arthritis (PsA) at metacarpophalangeal joint (MCPj) level. It was suggested as a pattern playing a key role in the differential diagnosis between Rheumatoid Arthritis and PsA [(1,2)].
Objectives: In spite of PTI's clinical impact, there are no data regarding the reliability of US PTI evaluation. The present study addressed this topic by testing the reliability of US on evaluation of PTI.
Methods: 27 consecutive non selected PsA patients with clinical involvement of at least one 2nd to 5th MCPj were included. A rheumatologist trained in PTI assessments obtained the US images exploring the dorsal aspect of MCPj from 2nd to 5th of both hands using a MyLab 70 XVG machine, Esaote, Genova, Italy, with a greyscale (GS) 13 MHz probe and a 7.1 MHz power Doppler (PD) frequency, PRF 750 Hz and a 60 Gain. 3–5 seconds videos of each MCPj were obtained in transversal and longitudinal views for further reliability analysis. In the inter-reader reliability analysis, performed by five readers from five different hospitals and four countries, it was scored as present or absent 1) PTI (defined as an hypoechoic swelling of the soft tissue surrounding the extensor tendon at MCPj level with or without PD) and 2) intra-articular synovitis (IAS, OMERACT definition), both in PD and GS. The consensus of true US results for every joint and lesion was achieved when at least three readers had the same opinion. Cohen's Kappa test was used for statistical analysis.
Results: Clinical MCPj involvement was present in 60 (27.7%) of the 216 joints whereas US detected IAS and/or PTI in 75 (34.7%). US showed GS PTI in 41 (19%) and PD in 38 (17.6%) of the joints, while GS IAS was found in 63 (29.2%) with PD activity in 41 (19%) of the joints. The inter-reader reliability is shown in the Table. Intra-reader reliability results expressed as mean Kappa were 0.826 for PTI PD, 0.784 for PTI GS, 0.743 for IAS PD and 0.637 for IAS GS.
Conclusions: US examination of MCPj shows that PTI is near as frequent as IAS in PsA with reliability of its scoring at least as good as for joint synovitis. This opens the possibility of introducing US scoring of PTI, which may be of importance for the diagnosis and follow-up of PsA patients.
References:
[1] Gutierrez M et al. Ann Rheum Dis 2011; 70: 1111–4.

Table 1. Inter-reader reliability

PTI PD	Reader 2	Reader 3	Reader 4	Reader 5	Mean Kappa 0.685
Reader 1	0.755	0.887	0.772	0.641	
Reader 2		0.705	0.666	0.534	
Reader 3			0.722	0.644	
Reader 4				0.525	
PTI GS	Reader 2	Reader 3	Reader 4	Reader 5	Mean Kappa 0.590
Reader 1	0.682	0.778	0.739	0.535	
Reader 2		0.608	0.603	0.456	
Reader 3			0.614	0.445	
Reader 4				0.440	
IAS PD	Reader 2	Reader 3	Reader 4	Reader 5	Mean Kappa 0.680
Reader 1	0.562	0.733	0.685	0.763	
Reader 2		0.597	0.590	0.714	
Reader 3			0.640	0.806	
Reader 4				0.706	
IAS GS	Reader 2	Reader 3	Reader 4	Reader 5	Mean Kappa 0.567
Reader 1	0.593	0.593	0.511	0.727	
Reader 2		0.583	0.478	0.615	
Reader 3			0.423	0.579	
Reader 4				0.564	

[2] Zabotti A et al. Clinical and Experimental Rheumatology 2016; 34: 459–465.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1438

AB1012 CLINICAL UTILITY OF ANTIHISTONE ANTIBODIES: A DESCRIPTIVE STUDY

D. Boveda-Ruiz[1], B. Vilas-Pio[2], M. Freire-Dapena[2], R. Lorenzo-Castro[2], A. Soto-Peleteiro[2], S. Mirete-Bachiller[3], A. Rivera-Gallego[2]. *[1]Internal Medicine, Hospital Clínico Universitario de Valladolid (SACYL), Valladolid; [2]Internal Medicine; [3]Immunology, Complexo Hospitalario Universitario de Vigo, Vigo, Spain*

Background: Antihistone antibodies (AHA) have been linked to Drug-Induced Lupus Erythematosus (DILE) for decades[1]. However, for some authors this relationship is not so clear and sugest that the presence of these autoantibodies is related to other autoimmune diseases more frequently[2,3,4].
Objectives: The main objetive of this work was to study the association of AHA with different autoimmune entities (including DILE) and secondarily, look into which clinical manifestations and which autoantibodies are more frequently related to AHA.
Methods: We performed a descriptive study. A database was constituted using all patients with AHA+ in any blood analysis between years 2000 and 2016 in the University Hospital Complex of Vigo. The variables of the study were: presence of autoimmune disease, clinical manifestations and related autoantibodies.
Results:

Variable	Men	Women	All	% Total
Age	50	45	46	
Gender	15	58	73	100
SLE	8	27	35	48
DILE	0	0	0	0
Scleroderma	0	4	4	5
Sjögren	1	8	9	12
Rheumatoid Arthritis	0	3	3	4
No diagnosis	5	19	24	33
Malar rash	1	11	12	16
Photosensitivity	2	11	13	18
Oral ulcers	1	10	11	15
Arthritis	6	31	37	51
Lupic nephropathy	4	13	17	23
Raynaud	1	11	12	16
Hematological abnormalities	5	20	25	34
AntiRo+	4	12	16	22
AntiLa+	2	5	7	10
AntiSm+	3	8	11	15
AntiDNAds+	3	25	28	38

None of the 73 patients AHA+ developed DILE while almost the 50% of them suffer any other autoimmune disease. We found a high percentage of AHA+ patients with lupus erythematous complications such as arthritis and hematological abnormalities. AntiDNAds antibody was the more frequent coexpressed autoantibody.
Conclusions:
- AHA detection is not useful as DILE screening.
- AHA+ sugest the presence of other autoimmune disease rather than DILE.
- AHA+ may be related to lupus erythematous systemic complications.

References:
[1] Fritzler MJ, Tan EM. Antibodies to histone in drug-induced and idiopathic lupus erythematosus. J Clin Invest. 1978;62:560–567.
[2] Peng SL, Craft J. Antinuclear antibodies. In: Ruddy S, Harris ED, Sledge CB, eds. Kelley's Textbook of Rheumatology. 6th ed. Philadelphia, Pa: WB Saunders; 2001:166.
[3] Kubo M, Ihn H, Yasawa N, et al. Prevalence and antigen specificity of antihistone antibodies in patients with polymyositis/dermatomyositis. J Invest Dermatol. 1999;112:711–715.
[4] Zirwas MJ, Kress DW, Deng JS. The Utility of Antihistone Antibody Screening in the Diagnosis of Drug-Induced Lupus Erythematosus. Arch Dermatol Apr 2004; VOL 140: 494–495.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3005

AB1013 DEVELOPMENT AND VALIDATION OF A FLOURESCENCE OPTICAL IMAGING RHEUMATOID ARTHRITIS SCORING SYSTEM FOR SYNOVITIS IN THE WRIST AND HAND

D. Glinatsi[1], M. Østergaard[1,2], L. Terslev[3], S. Ohrndorf[4], M. Ammitsbøll-Danielsen[3]. *[1]Copenhagen Center for Arthritis research, COPECARE, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup; [2]Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copehangen; [3]Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark; [4]Department of Rheumatology and Clinical Immunology, Charité – University Medicine, Berlin, Germany*

Background: Fluorescence optical imaging (FOI) has been suggested as an imaging modality for assessment of inflammation (i.e. synovitis) in the hands, and has in several studies been compared to US and MRI, using different, but not validated scoring systems.
Objectives: To develop and validate a semi-quantitative FOI RA scoring system for synovitis in the wrist and hand.
Methods: 46 RA patients, eligible for induction or intensification of disease modifying anti-rheumatic drug and with ≥1 clinically swollen joint in the hand were included. FOI image-sets of both wrists and hands were obtained at baseline, and after 3 and 6 months' follow-up using a Xiralite system unit (nanoPET Pharma GmbH, Berlin, Germany). The patients received a bolus of i.v. indocyanine green (ICG) pulsion (1mg/kg body weight) 10 seconds after starting the examination, which obtained 1 image/second over 6 minutes. The image-sets were anonymized and randomized and were assessed for synovitis at the wrist, 1st-5th metacarpophalangeal, 1st interphalangeal and 2nd-4th proximal interphalangeal joint levels in both hands by two readers blinded to patient data but not chronology. 23 image-sets were re-anonymized and re-read for intra-reader agreement analysis. The scoring system for synovitis was based on the assumption that inflamed tissue would demonstrate a more rapid enhancement than surrounding tissues. For each joint, the images were assessed sequentially from start of the injection of ICG-pulsion to peak enhancement. At the peak enhancement, the color index was adjusted in order to increase the discrepancy between colors. Synovitis was defined as a sharply marginated enhancement with clear delineation from surrounding tissues and correct anatomical location lasting ≥3 seconds. The thickness of the pathology fulfilling these criteria was compared to the width of the joint in the transverse plane at the 3rd second of enhancement and the following semi quantitative scoring system (0–3) was applied: grade 0: no enhancement, grade 1: <1/3, grade 2: ≥1/3 but ?2/3, grade 3: ≥2/3 of joint thickness (range 0–66). Descriptive statistics and the Wilcoxon signed-rank test were used to assess change in score over time. Intra-/inter-reader for status and change scores were assessed using single measure intra-class correlation coefficients (ICC) and smallest detectable change (SDC, change scores only). Responsiveness was assessed using standardized response mean (SRM).
Results: Median (IQR) total synovitis score at baseline was 9.5 (4.0;16.5) and improved with -5.0 (-10.0;-1.0) and -8.0 (-13.5;-3.0) at 3 and 6 months' follow up, respectively ($p<0.01$). Intra- and inter-reader ICCs were good to very good for total scores (Table 1). The SDCs were generally low and for the inter-reader SDCs, 56% and 60% of the patients had a change >SDC between baseline and 3 and 6 months, respectively. The mean SRM for total change scores at 3 at 6 months' follow-up were moderate to good (0.7 and 0.8).

Table 1

	ICC Baseline	ICC 3 months' follow-up	ICC 6 months' follow-up	ICC Change, baseline to 3 months	ICC Change, baseline to 6 months	SDC Change, baseline to 3 months	SDC Change, baseline to 6 months
	Intra-reader agreement, reader 1						
Total scores	0.90	0.86	0.83	0.87	0.92	6.2	4.9
Wrist	0.82	0.92	0.62	0.88	0.91	1.4	1.4
MCP joints	0.86	0.72	0.93	0.76	0.85	4.8	3.6
PIP joints	0.95	0.96	0.86	0.90	0.90	2.9	3.3
	Intra-reader agreement, reader 2						
Total scores	0.95	0.97	0.90	0.90	0.90	6.2	6.5
Wrist	0.92	0.88	0.81	0.78	0.80	1.6	1.6
MCP joints	0.96	0.96	0.92	0.92	0.89	3.3	3.4
PIP joints	0.94	0.95	0.80	0.88	0.90	3.8	3.9
	Inter-reader agreement						
Total scores	0.88	0.84	0.60	0.81	0.70	4.8	6.2
Wrist	0.76	0.72	0.58	0.67	0.65	1.1	1.3
MCP joints	0.86	0.80	0.76	0.81	0.66	3.1	3.7
PIP joints	0.91	0.82	0.39	0.79	0.71	2.6	3.6

Intra-and inter-reader intra-class correlation coefficients (ICC) were interpreted as follows: good: ICC≥0.60, very good: ICC≥0.80. Abbreviations: SDC: smallest detectable change, MCP: metacarpophalangeal, PIP: proximal interphalangeal.

Conclusions: The novel FOI RA synovitis scoring system showed high reliability and moderate to good responsiveness in the wrist and hand. Future studies should focus on assessing the sensitivity and specificity of the FOI synovitis score with ultrasound and magnetic resonance imaging as gold standard.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4633

AB1014 SAFETY OF OUTPATIENT PERCUTANEOUS NATIVE RENAL BIOPSY IN PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES: RESULTS FROM A MONOCENTRIC COHORT

D. Roccatello, S. Sciascia, D. Rossi, C. Naretto, M. Bazzan, L. Solfietti, M. Radin, S. Baldovino, E. Menegatti. *Department of Rare and Immunologic Diseases, G. Bosco Hospital and University of Turin, TOrino, Italy*

Background: Renal involvement is common in patients with systemic autoimmune conditions, mainly systemic lupus erythematosus (SLE) and vasculitis, including cryoglobulinemia. Despite the advances in percutaneous kidney biopsy (PKB) techniques and overall improved safety of the procedure, clinically significant bleeding complications do occur.
Objectives: to investigate the safety of performing percutaneous native kidney biopsy (PKB) as an outpatient procedure (implying an observation period of 6 hrs) compared to the traditional inpatient policy in patients with systemic autoimmune conditions.
Methods: Group I, in whom PKB was performed in the outpatient department (2012–2016) and followed by 6 hours' observation period and then by regular outpatient visits and group II, in whom PKB was performed and followed by at least 1-day hospital admission. Group II included retrospectively retrieved patients who underwent PKB in our Institution between January 2000 and November 2012 as in patient procedure. All biopsies were performed by a single nephrologist following a structured protocol.
Results: A total of 81 biopsies (group I and group II) were included in this study, 44 (54%) of patients were female and the mean age was 49.9±17.6 years. Twenty-six per cent of biopsies were performed for the diagnostic workup of nephrotic range proteinuria, 21% for rapidly progressive renal insufficiency, and the remaining 53% for non-nephrotic proteinuria and/or hematuria. No patient suffered for a major complication and only 3 (3.7%) patients (one with cryoglobulinemic vasculitis and 2 with ANCA associated vasculits) developed a minor complication, including gross hematuria in one case and sub-capsular perinephric hematoma on sonography not requiring intervention in 2 patients
Conclusions: The lack of major complications and the very limited rate of minor bleeding support that outpatient biopsy could be a valuable, safe, and perhaps cost-effective method of obtaining diagnostic renal tissue in the majority of patients with systemic autoimmune diseases.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2162

AB1015 AUTOMATED SQUEEZE TEST (GAENSLEN'S COMPRESSION MANEUVER) IN RHEUMATOID ARTHRITIS PATIENTS. EXPLORATORY STUDY

D. Vega-Morales, J.A. Esquivel-Valerio, A.C. Arana-Guajardo, M.A. Garza-Elizondo. *Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Monterrey, Mexico*

Background: The squeeze test (a.k.a Gaenslen's Compression Maneuver) consists on the compression of the metacarpal-phalangeal (MCP) joints to elicit pain in a patient with active synovitis. The squeeze test has three main purposes: Screening of inflammatory arthritis, as a predictor of rheumatoid arthritis in arthralgia patients, and as a quick and practical evaluation of the presence/absence of synovitis in patients already diagnosed with RA. The force and the way to perform the squeeze test had been evaluated in rheumatologists on a biomechanical device, with conflicting results. We developed a biomechanical device to perform the squeeze test.
Objectives: Our aim is to determine the force whether the automated squeeze test discriminate patients with active RA from inactive ones. And the force that differentiates a healthy patient from a RA patient.
Methods: Observational study in RA (ACR/EULAR 2010) patients and healthy persons. We perform 3-squeeze test on the device in the MCP joints and record the force enough to elicit pain. And then compare them with the joint counts by the clinician
Results: Two hundred MCP joints from 50 hands were tested. From 25 RA patients with a mean age of 54.6 years (SD 11.22), with a mean disease latency of 1.2 years (SD 2.7). The total swollen joint count was 16 (7 right joints + 9 left joints) and 70 total tender joint count (30 right joints and 40 left joints). The median of force that caused pain in the RA patient's right hand was 3.07 kg (IQR 2.4) and the left hand was 2.78 kg (IQR 3.8). The cut-off for the force to detect a tender right hand joint was 1,020 grams with a sensitivity of 100% and specificity of 10%; for a swollen right hand joint was 1,400 with a sensitivity of 100% and specificity of 28.6%. For a tender left hand joint was 1620 grams with a sensitivity 70% and specificity of 6.7%; and for a swollen left joint was 1990 grams with a sensitivity of 100% and specificity of 27.3%.
In the second phase, 560 MCP joints of 140 hands from 70 healthy volunteers were compressed. The median force to elicit pain in the right hand was 4.2 kg (IQR 9.5) vs. 3.07 kg (IQR 8.7) from RA patients (p=0.003). And for left hand 4.6 kg (IQR 9.7) vs. 2.78 kg (IQR 9.2) from RA (p=0.014).
Conclusions: It is necessary to continue the exploration of the maneuver in different clinical settings. Validate the strength in patients with different arthropathies, activity levels and different clinical stages (screening, activity, prediction) and also with imaging methods for evidence of inflammation (US, MRI)
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3318

AB1016 ANTI-DFS70, A TOOL IN USUAL CLINICAL PRACTICE: A CASE SERIES

D. Ybáñez-García [1], E. Valls-Pascual [1], C. Vergara-Dangond [1], M. Aguilar-Zamora [1], L. Montolio-Chiva [1], Á. Martínez-Ferrer [1], J.M. López-Ortega [2], J.J. Alegre-Sancho [1]. *[1]Rheumatology; [2]Clinical Analysis Laboratory Service, Hospital Universitario Dr. Peset, Valencia, Spain*

Background: The presence of anti-nuclear antibodies (ANA) has been considered a characteristic of systemic autoimmune diseases (SAD). Patients are frequently referred for study because they have ANA and are followed because of the possibility to develop SAD. Approximately, 20% of healthy individuals with ANA detected by indirect immunofluorescence (IFI), especially at low titers, have a dense, fine speckled pattern (DFS) that frequently corresponds to the presence of anti-DFS70 antibodies. The importance of this antibody is due to its low prevalence in subjects with ASD (<1%) compared to its presence in 33.1% of healthy subjects with ANA.
Objectives: To describe the usefulness of Anti-DFS70 in a series of patients presenting ANA.
Methods: We collected prospectively throughout the year 2016 all the patients referred to a tertiary hospital for ANA study and in whom the presence of anti-DFS70 antibodies was confirmed. All patients underwent a thorough medical history, physical examination, and relevant follow-up tests were performed according to the clinical presentation. The IFI was performed in a Menarini Zenit-Up/GSight system, as well as ANA screening in Hep-2000 (Fluorescent IgG ANA-Ro Test System-immunoconcepts) and the detection of anti-DFS70 antibodies by immunoblot (ANA + DFS70 Dot Blot-Alphadia).
Results: We collected in a period of 12 months a total of 7 patients with anti-DFS70 antibodies. Most of them (6/7) were referred because of non-specific symptoms such as arthralgia, fatigue, thrush, edema, ... and the presence of ANA. The findings are detailed in Table 1.

Abstract AB1016 – Table 1

Case	1	2	3	4	5	6	7
Symptoms	Polyarthralgias Arthritis 4th interphalangeal joint	General pain Dry eye and dry mouth	Polyarthralgias Back pain Inflammatory markers +	Arthromyalgias Fatigue Fever Anti-TNF-a	Polyarthralgias Back pain Fatigue, oral aphthosis	Hand pain and deformity of 2nd PIPs	Left foot edema
Gender	♀	♀	♀	♂	♀	♀	♀
Age	45	47	37	48	39	56	55
Hemogram/Renal/liver function	N	N	N	N	N	N	N
RF/ACPA	(–)	(–)	(–)	(–)	(–)	(–)	(–)
ANA (IFI)/ENAs	+1/160/–	+1/160/–	+1/320/–	+1/160/–	+1/160/–	+1/320/–	+1/80/–
C3, C4	NP	N	NP	NP	NP	NP	NP
Schirmer/Ss	NP	N	NP	NP	NP	NP	NP
CRP/ESR	N	N	21/17	N	N	N	N
Comorbidities	Type 2 DM	Graves Basedow	Hand angioedema	PsA	Graves Basedow	Dyslipidemia	No
RX /MRI	CPPD	Degeneration of left TMC and dorsal spine	L4-L5, L5-S1 Retrolistesis			Mild degenerative signs in PIP and TMCs	Synovial fluid in talo-navicular and tarsal joints
Axial/joint	Degenerative axial and joint signs		C5-C6-C7 Protrusions				
Diagnosis	OA CPPD	OA	OA Discopathy	PsA	Fibromyalgia Chronic fatigue	OA	Resolved foot arthritis

NP: not performed, N: normal, OA: osteoarthritis, PsA: psoriatic arthritis, CPPD: chondrocalcinosis.

Conclusions: Anti-DFS70 is a valuable biomarker, with a very low prevalence in SAD, which gives it a role as a negative predictive marker of developing SAD when it is appears alone. Its detection in serum with a dense fine speckled pattern ANA (IFI) should be part of the protocol of the immunology laboratory. It is a cost-effective determination, as demonstrated in a recent study, by avoiding the costs associated with the follow-up of these patients. In our case, its finding allowed us to reassure the patient and avoid the accomplishment of further complementary tests, as well as an unnecessary monitoring.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3410

AB1017 THE DEFEAT OF THE HIP JOINT IN ANKYLOSING SPONDYLITIS BY MAGNETIC RESONANCE IMAGING

E. Agafonova[1,1], T. Dubinina, A. Dyomina, O. Rumiantceva, D. Rumiantceva, M. Podryadnova, A. Starkova, S. Krasnenko, M. Urumova, S. Erdes. *Laboratory seronegative spondyloarthritis, Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: According to the carried out epidemiological studies in Russia of patients with ankylosing spondylitis (AS) defeat of the hip joints was impairment in 46% of cases, but was the reason for the replacement in 7% of cases. i
Objectives: To compare the clinical manifestations of hip arthritis (coxitis) with the results of magnetic resonance imaging (MRI) of the hip joints (HJ) in patients with ankylosing spondylitis (AS).
Methods: Examined 117 patients (mean age 31,7±12.7 y meeting modified N-Y criteria), with complaints of pain in the hip joints. The average age of onset of disease was 26.3±20.3 years, HLA-B27 identified in 93% of patients. The median duration of AS – 57 [2–384] months. BASDAI 5,7±3,1. Diagnosis of hip septic arthritis were made based on clinical signs - the presence of pain in hips and/or restriction of movements in HJ at the time of patient admission to the clinic. In addition to clinical and radiographic examination all patients were performed MRI modes T1 and STIR.
Results: The Median duration of clinical manifestations of coxitis by the time of the study was 60 months. [25‰; 75‰], evaluation of pain in HJ for numeric rating scaler (NRS) – 4 [2; 8]. According to MRI identified the following inflammatory changes (IC): synovitis-71 (83%) patients, bone marrow edema (BME)- 44 (31,6%) patients (BME acetabulum 36%, BME heads 63%), a combination of synovitis and BME were 7 patients (9%). Depending on radiological stage (estimated by BASRI hip), patients were divided into two groups (table 1).
Results:

Table 1

Parameters	Group (1) BASRI hip 0-I (n=48)	Group (2) BASRI hip II-IV (n=60)	P
Gender (w/m), n	20/28	33/36	0,04*
AS duration,mo, Me [25‰, 75‰]	43 [19;80]	102 [24;120]	0,006*
BASDAI, Me [25‰, 75‰]	4,1 [2,6; 5,5]	5,6 [4,2; 6,7]	0,003*
BASFI, Me [25‰, 75‰]	2,8 [2,0; 3,8]	3,3 [2,0; 5,4]	0,2*
HLA-B27, n (%)	96 (91%)	84 (91%)	0,7*
ASDAS (CRP) Me [25‰, 75‰]	2,8 [2,0; 3,8]	3,5 [2,6; 3,8]	0,002*
ESR, mm/h, Me [25‰, 75‰]	10 [5; 25]	25 [8; 35]	0,001*
CRP, mg/mL, Me [25‰, 75‰]	10,5 [3,8; 28,5]	23,0 [4,9; 43,5]	0,06*
NRS, Me [25‰, 75‰]	5 [3;6]	6 [4;7]	0,01*
MRI Synovitis n (%)	44 (92%)	27 (45%)	0,003*
Osteitis n (%)	6 (12,5%)	38 (64%)	0,0001*

Conclusions: MRI allows to clarify the cause of the pain and limitations of movement in HJ with AS, determine the patient has inflammatory changes, including in the absence of radiographic changes in these joints. Patients with severe radiological change (BASRI II-IV), have a greater duration of the disease, severe functional abnormalities in the BASFI index. With increasing radiological stage (BASRI hip II-IV) increased the detection rate of osteitis by MRI. Further research to clarify the relationship of clinical manifestations of coxitis (pain level) from MRI data.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4985

AB1018 DETECTION OF ANTI-DFS70 ANTIBODIES BY INDIRECT IMMUNOFLUORESCENCE (IIF) ON NOVEL HEP-2/DFS70-KO SUBSTRATE FOR DISCRIMINATING ANTINUCLEAR ANTIBODIES (ANA) – POSITIVE HEALTHY INDIVIDUALS (HI) AND PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

E. Aleksandrova, Z. Verizhnikova, A. Novikov, T. Panafidina, T. Popkova. *V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation*

Background: Autoantibodies against intracellular antigens are a serological hallmark of ANA-associated systemic autoimmune rheumatic diseases (AARD) such as SLE. IIF on HEp-2 cells for ANA remains the "gold standard" but it has very low positive predictive value. Up to 20% of serum samples from HI have been reported to have a positive ANA IIF test, the majority of them due to the presence of anti-dense fine speckled 70 (anti-DFS70) antibodies. Monospecific anti-DFS70 antibodies represent a biomarker that can be used to discriminate AARD patients (pts) from HI in ANA IIF positive subjects. Recognition of the DFS70 ANA IIF pattern can be challenging. The DFS-KO Hep-2 cells inhibit anti-DFS70 antibodies reactions, providing clear differentiation of the DFS pattern from classical ANA patterns.
Objectives: To evaluate the utility of a novel HEp-2/DFS70-KO IIF substrate for the detection of anti-DFS70 antibodies in HI and SLE pts.
Methods: We studied 45 HI (36 F/9 M; age 50.4 [24.0–72.0] years, median [interquartile range 25–75%]) and 12 pts with SLE (ACR criteria, 1997) (10 F/2M, age 38.9 [17.0–65.0] years; disease duration 100.3 [4.0–432.0] months; SLEDAI 2K score 11.7 [2–30]; SLICC damage index score 1.28 [0–4]). Serum samples were tested for classical ANA and anti-DFS70 antibodies by IIF technique with a mixture of standard HEp-2 cells and DFS70-KO HEp-2 cells ("Trinity Biotech", Bray, Ireland) as a substrate. Fluorescence titers $\geq$1: 160 were considered as positive for ANA patterns.
Results: ANA were present in 7/45 (15.6%) of HI and in 12/12 (100%) of SLE pts. All SLE pts and 3/45 (6.7%) of HI showed classic ANA patterns (homogeneous, speckled, and mixed) in the absence of DFS70 pattern. 4/45 (8.9%) of HI had classic ANA negative/anti-DFS70 antibodies positive IIF results. Isolated anti-DFS70 antibodies were found in 57% of ANA IIF positive HI. Among HI classic ANA and anti-DFS70 antibodies were detected in the low- to medium-titer range (1:160–1:320). The frequency of anti-DFS70 antibodies did not correlated with age.
Conclusions: The detection of isolated anti-DFS70 antibodies may be regarded as an exclusion criterion for the diagnosis of SLE. The testing for anti-DFS70 antibodies in a single step by HEp-2/DFS70-KO IIF method should be included into a modified ANA diagnostic algorithm. Additional investigations are required to evaluate the clinical relevance of anti-DFS70 autoantibodies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4008

AB1019 ASSOCIATION OF INFLAMMATORY DISEASES – A CURRENT TOPIC FOR THE PRACTITIONER

A. Cardoneanu[1,2], A. Burlui[1,2], C. Cijevschi Prelipcean[3], E. Rezus[1,2]. *[1]Rheumatology, University of Medicine and Pharmacy "Gr.T.Popa"; [2]Rheumatology Clinic, Rehabilitation Hospital; [3]Gastroenterology, University of Medicine and Pharmacy "Gr.T.Popa", iasi, Romania*

Background: Autoimmune, infectious, traumatic or neoplastic inflammation represents a warning for the practitioner. Numerous clinical specialties face daily with the presence of inflammation. The efforts of medical staff aim to establish the pathogenesis, the expansion and to find the most effective ways of treatment.
Objectives: Our study objective is to highlight the correlations between Spondylarthropathies (SpA) and intestinal manifestations, the link between the antigen HLA B27 and joint and intestinal inflammatory changes and also the relationship between the presence of sacroiliitis and bowel disorders.
Methods: The study included 42 patients (28 men, 14 women). Of the 42 patients, 31 were diagnosed with ankylosing spondylitis (AS) (according to modified New York criteria), 8 with psoriatic arthritis (PsA) (using CASPAR diagnosis criteria) and 3 patients had had reactive arthritis (ReA) (according to ASAS criteria). All subjects enrolled in the study were screened for the presence of the antigen HLA-B27. Sacroiliitis was highlighted through pelvis X-ray centered on the SI joints. All patients diagnosed with AS presented radiological sacroiliitis, only 5 cases in the group of PsA and 1 patient diagnosed with ReA. To investigate the presence of intestinal inflammation, a colonoscopy with biopsy was performed to all subjects included in the study. Among patients with AS, 5 of them had inflammatory changes suggestive of Crohn's disease (CD) and 2 for ulcerative colitis (UC). Subclinical intestinal inflammation was evidenced in 15 cases: 12 of SA group and 3 of PsA group. We also highlighted 7 cases of irritable bowel syndrome: 1 patient with PsA and 6 patients with SA.
Results: After the statistical analysis of the collected data, the following statistically significant correlations were found ($p<0.05$): radiological sacroiliitis correlated with AS and PsA; the antigen HLA-B27 is in close relation with all 3 forms of spondylarthritis; subclinical intestinal inflammation was positively correlated with AS and PsA. No associations were found between the presence of intestinal inflammation and sacroiliitis.
Conclusions: This study points the link between intestinal and joint inflammation, primarily due to a common pathogenic mechanisms. A careful monitoring and a close collaboration between gastroenterologists and rheumatologists contributes to an optimal management of these patients.
References:

[1] Baeten D, de Keyser F, Mielants H, Veys EM. Ankylosing spondylitis and bowel disease. Best Pract Res Clin Rheumatol Sep 2002;16(4):537–549.
[2] Salmi M, Jalkanen S. Human leukocyte subpopulations from inflamed gut bind to joint vasculature using distinct sets of adhesion molecules. J Immunol 2001;166:4650–4657.
[3] May E, Marker-Hermann E, Wittig BM, Zeitz M, Meyer zum Buschenfelde KH, Duchmann R. Identical T-cell expansions in the colon mucosa and the synovium of a patient with enterogenic spondyloarthropathy. Gastroenterology 2000;119:1745–1755.
[4] Peeters H, vanderCruyssen B, vander Cruyssen B, Mielants H, de Vlam K, Vermeire S, et al. Clinical and genetic factors associated with sacroiliitis in Crohn's disease. J Gastroenterol Hepatol Jan 2008;23(1):132–137.

[5] de Vlam K, Mielants H, Cuvelier C, de Keyser F, Veys EM, de Vos M. Spondyloarthropathy is underestimated in inflammatory bowel disease: prevalence and HLA association. J Rheumatol Dec 2000;27(12):2860–2865.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2228

AB1020 MULTIFREQUENCY BIOIMPEDANCE COMBINED WITH ACOUSTIC MYOGRAPHY – A NON-INVASIVE PAIN-FREE ASSESSMENT OF MUSCLE USE

E.M. Bartels, J. Kvistgaard Olsen, H. Bliddal, L.E. Kristensen, B. Danneskiold-Samsøe. *The Parker Institute, Department of Rheumatology, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Frederiksberg, Denmark*

Background: Musculoskeletal diseases may involve muscle function, which often deteriorates due to a combination of pain and lack of exercise. Possible correction of this by training, or at least achievement of optimal efficiency of involved muscles with therapy, taking age and affecting disease into account, is an area which needs easily applicable and non-invasive pain-free assessment methods capable of monitoring daily living tasks outside a strict laboratory setting. Multi-frequency bioimpedance (mfBIA), assessing muscle health prior to exercise, in combination with Acoustic Myography (AMG), which allows real-time tests while e.g. walking or bicycling, may be such a method.
Objectives: To validate AMG combined with mfBIA for muscle-use assessment during a series of daily activity movements and exercise with the aim of introducing the method in the clinic.
Methods: 10 healthy subjects aged 25–68 years were assessed with mfBIA (Impedimed, Brisbane, Australia) prior to and following exercise of m. gastrocnemius during walking, stair climbing and descending, and cycling with increasing load. AMG was recorded with a CURO unit (MyoDynamik ApS, Frederiksberg, Denmark), and data handling was carried out with the software belonging to the devices. The mfBIA parameters considered were resistance (R), internal (Ri) and external (Re) resistance and centre frequency (fc), and the AMG parameters were Efficiency (E) – synchronization of motoric units, Temporal summation (T) – how frequently do you use a particular muscle fibre, and Spatial summation (S) – how many fibres in use at a given time, all given as Median; Min,Max.
Results: The mfBIA data, showing the health state of the muscle, showed changes in R, Ri, Re and fc as expected for a healthy muscle as an effect of exercise. The AMG data showed good reproducibility with repeated measurements. Walking on flat ground was less synchronized (E 2; 1,4) as were walking up (E 4; 1,6) and down stairs (E 3; 1,6), than cycling (E 8.5; 5,9). With increasing load during cycling, E decreased with the higher demand to E 5.5 range 1–7. The T-score was similar around 7 for all types of walking, while overall decreasing with increasing load during cycling from 6.5 to 5.5. The S-score was low during the three types of walk, indicating use of many fibres (S around 3), which is in line with the low E-score. For cycling the S-score decreased slightly with increasing load, from 8 to 7.5.
Conclusions: The combined method of mf-BIA and AMG shows good reproducibility. This method has the potential to assess training possibilities in patients with musculoskeletal diseases by testing directly on muscles during the movements of daily function. The method is applicable in real life settings outside the laboratory.
Acknowledgements: The Parker Institute is supported by the OAK Foundation
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3369

AB1021 VIDEOCAPILLAROSCOPIC FINDINGS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH OR WITHOUT JACCOUD'S ARTHROPATHY

C. Lins[1], E.P.D. Fonseca[2], D.L.D.S. Ribeiro[2], W.G.D. Santos[2], G. Rosa[2], V. Machicado[2], A.L. Pedreira[2], A.P.M.D. Souza[2], C. Baleeiro[2], L.G.D.S. Ferreira[2], I.S.D. Oliveira[3], J.P.C.G.D. Silva[3], A.M. Atta[3], M.B. Santiago[2]. *[1]EBMSP - Escola Bahiana de Medicina e Saude Publica; [2]EBMSP - Escola Bahiana de Medicina e Saude Publica; [3]HUPES - Hospital Universitario Edgard Santos, Salvador, Bahia, Brazil*

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that can present, as other collagen vascular disorders, changes in blood vessels. It can be evaluated by a non-invasive technique called periungual nailfold videocapillaroscopy (VCP). This technique is helpful in the diagnosis of systemic sclerosis (SSc), being part of the new classification criteria, and identifies individuals with Raynaud's phenomenon who are at a higher risk for developing SSc.
Objectives: This study aims to describe the videocapillaroscopic profile of a series of SLE patients and investigate if the VCP pattern is different among those with Jaccoud's arthropathy (JA) compared to the patients without this complication.
Methods: The patients were submitted to VCP, clinical evaluation, and laboratory tests. The capillaroscopic patterns were defined as minor, major and scleroderma (SD). The presence of capillaroscopic findings such as elongated capillaries, increased tortuosity, ectasia, prominent venous plexus, neoangiogenesis, hemorrhage and megacapillaries was also observed.
Results: In a population of 113 female patients with SLE (67 without JA and 46 with JA), at least one alteration was observed in VCP in 89.40% of patients, and the "nonspecific changes" were the most prevalent. Minor changes were seen in 39 (58.2%) and 26 (56.5%) patients, and major changes were seen in 21 (31.3%) and 11 (23.9%) patients without and with JA, respectively. The SD patterns were observed in 02 (3.0%) and 03 (6.5%) patients without and with JA, respectively ($p>0.05$).
Conclusions: The majority of patients of SLE present changes in the VCP exam, but such a tool does not allow distinguish those with or without JA.
References:
[1] Lambova SN, Muller-Ladner U. Capillaroscopic pattern in systemic lupus erythematosus and undifferentiated connective tissue disease: what we still have to learn? Rheumatology international. 2013;33(3):689–95.
[2] Ingegnoli F. Capillaroscopy abnormalities in relation to disease activity in juvenile systemic lupus erythematosus. Microvascular research. 2013;87:92–4. Santiago MB, Galvao V. Jaccoud arthropathy in systemic lupus erythematosus: analysis of clinical characteristics and review of the literature. Medicine. 2008;87(1):37–44.
[3] Ingegnoli F, Zeni S, Meani L, Soldi A, Lurati A, Fantini F. Evaluation of nailfold videocapillaroscopic abnormalities in patients with systemic lupus erythematosus. Journal of clinical rheumatology: practical reports on rheumatic & musculoskeletal diseases. 2005;11(6):295–8.
[4] Ragab O, Ashmawy A, Abdo A, Mokbel A. Nailfold capilloroscopy in systemic lupus erythematosus. The Egyptian Rheumatologist. 2011;33:61–7.
Acknowledgements: M. B.S. has received a scholar ship from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6627

AB1022 THE RECALL SURVEY: THE RELATIONSHIP BETWEEN ULTRASOUND SYNOVITIS AND BONE EROSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

E. Filippucci[1], C. Bonali[2], P. Macchioni[3], A. Iagnocco[4], A. Delle Sedie[5], S. Tropea[6], O. Epis[7], M. Canzoni[8]. *[1]Clinica Reumatologica, Università Politecnica delle Marche, Ancona; [2]Rheumatology Unit, Ospedale San Paolo, Bari; [3]Rheumatology Unit, Reggio Emilia Hospital, Reggio Emilia; [4]Academic Rheumatology Unit, Università degli Studi di Torino, Torino; [5]Rheumatology Unit, Università di Pisa, Pisa; [6]ASP7, Busacca Hospital, Ragusa; [7]Rheumatology Unit, Ospedale Niguarda Milano, Milano; [8]Local Health Unit (ASL) Rome-1, Rome, Italy*

Background: Ultrasound (US) has shown to be a sensitive imaging tool for the detection of subclinical signs of synovitis in patients (pts) with rheumatoid arthritis (RA); further studies are still required to delineate the impact of US findings in the management of RA pts in daily clinical practice.
Objectives: To investigate the relationship between US findings indicative of joint inflammation and US bone erosions at joint level in pts with RA.
Methods: In 2015 an educational event focused on the added value of US in RA pts was held in 22 rheumatology centers in Italy. In every center, the local rheumatologists provided RA pts to be examined by US. Pts signed an informed consent and a brief history of them was collected by the local rheumatologists (previous and current therapy, DAS28, HAQ score). Bilateral US examinations of wrists, metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints were performed by rheumatologists expert in US, to assess synovitis (joint effusion, synovial proliferation, and power Doppler (PD) signal), and bone erosions, using a Logiq E R7, General Electrics, with a 4.2–13 MHz linear probe. All US findings were scored using a 4 degree semiquantitative scoring system.
Results: In 465 RA pts, a total of 10.230 joints were scanned. Of these joints, 3.969 (39%) showed joint effusion and/or synovial proliferation and 1.784 (17%) were found positive for PD signal. The most frequently involved joints were the wrists followed by the second MCP joints and first MTP joints. In 749 joints US detected at least one bone erosion. The most frequently eroded joints were the wrists, the second and fifth MCP joints and the first and fifth MTP joints. A total of 226 RA pts showed at least one bone erosions and in 181 (80%) of these pts the eroded joints were found positive for PD signal.
Conclusions: A high prevalence of PD signal was found in the joints found eroded by US. This is the first study providing such an evidence using a portable US equipment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4286

AB1023 QUANTIFERON®-TB GOLD IN-TUBE ASSAY CAN BE USED FOR LATENT TUBERCULOSIS SCREENING BEFORE BIOLOGICAL DRUG TREATMENT IN A BCG VACCINATED COUNTRY: HUR-BIO SINGLE CENTER REAL LIFE RESULTS

E. Şeyhoğlu[1], O.A. Uyaroğlu[1], A. Erden[2], L. Kılıç[2], B. Armağan[2], A. Sarı[2], M. Baykal[2], S. Ak[2], Ö. Karadağ[2], A. Akdoğan[2], S. Apraş Bilgen[2], S. Kiraz[2], I. Ertenli[2], U. Kalyoncu[2]. *[1]Department of Internal Medicine; [2]Division of Rheumatology, Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey*

Background: Patients treated with biologic agents have increased risk of

developing active tuberculosis (TB). It is essential to screen patients for latent TB before starting a biologic drug. Population is vaccinated with BCG in Turkey and BCG vaccination decreases the specifity of tuberculin skin test. QuantiFERON-TB Gold In-Tube Assay (QFT) is an another good option to screen latent TB.
Objectives: The objective of this study was to assess reliability of QFT test for latent TB before biological treatment.
Methods: Hacettepe University Rheumatology Biologic Registry (HUR-BIO) is a single center biological registry since 2005. Between Nov 2011 and July 2015, 1347 patients were assessed by QFT for latent TB. All consecutive patients were evaluated by a standard questionnaire between July 2015 and October 2016. This questionnaire included demographic characteristics, medical and treatment history, symptoms of active TB. 671 patients were assessed by the physicians. TB status of other 676 patients were checked from Turkish national tuberculosis registery records. It's an obligatory disposition for physicians to inform health ministery about TB cases and all TB patients must be recorded in those regitry. The mean TB incidance per year was calculated for every anti-TNF agents and non-TNF biological agents.
Results: Total 1347 (58.1% female) patients were recruited to study. Mean age was 42±12 years. Diagnosis were followed; RA 436 (32.4%), SpA 844 (62.5%), others 67 (5.1%). Total biological drug exposure was 2329 patient-years; adalimumab (660 years), etanercept (630 years), infliximab (426 years), golimumab (283 years), certolizumab (78 years), and total anti-TNF duration (2071 years). Non-TNFi exposure was 258 patient-years. Positive and indeterminate QFT results were found in 267 (19.8%) and 20 (1.5%) patients, respectively and those patients were prescribed INH prophylaxis. In addition, INH was prescribed to 37 (2.7%) patients according to chest X-Ray and physician decision. Pulmonary TB found in 3 of 1347 (0.22%) patients. TB was developed 38, 28 and 21 months after TNFi. The mean TB incidance per year was 128.8/100.000 for all biological drugs. The mean TB incidance per year according to QFT positive and negative patients were 181.8/100.000 vs 112.4/100.000.
Conclusions: According to QFT screening for latent TB, INH was started almost 20% of patients. However, if we used TST for latent TB test in BCG vaccinated countries, INH would started almost 70–80% of patients. Therefore QFT was a good tool for latent TB screening in BCG vaccinated countries. Consequently, QFT test seems acceptable to determinate latent TB during biological drug usage. In addition, TB incidance has increased almost 7 times of our national TB incidance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4080

AB1024 ULTRASOUND IN GIANT CELL ARTERITIS: CUT-OFF AND PITFALLS IN THE HALO SIGN

E. De Miguel[1], L.M. Beltran[2], I. Monjo[1], F. Deodati[2], W.A. Schmidt[3], J. García-Puig[2]. *[1]Rheumatology; [2]Internal Medicine, Hospital Universitario la Paz, Madrid, Spain; [3]Rheumatology, Immanuel Krankenhaus, Berlin, Germany*

Background: At the age of presentation of Giant Cell Arteritis (GCA) atherosclerosis is common. The ultrasonographic (US) appearance of athermanous plaque is usually easily differentiated from the hypoechoic halo of GCA. However, the US appearance of the increased of the intima-media-thickness (IMT) in an atherosclerotic carotid artery may have similar image appearance as the halo sign. We hypothesize that atherosclerosis could produce an increase of temporal artery (TA) IMT and cause false-positives halo sign.
Objectives: The aim of this study was to explore the better cut-off in the IMT of TA to minimise the number of false-positive GCA diagnosis caused by atherosclerosis.
Methods: Consecutive non selected patients, ≥50 years-old with high vascular risk according to European Guidelines on cardiovascular disease prevention, and without signs or symptoms of GCA, were included.
Ultrasonography of carotid artery: Carotid US examinations were performed on a Mylab Seven (Esaote Medical Systems, Italy) with a 4–13 MHz linear-array. The system employed dedicated software radiofrequency-tracking technology to obtain IMT (QIMT®).
Ultrasonography of temporal superficial artery: A color Doppler ultrasound (CDU) and grey scale measure of the IMT/halo sign in both TA and its branches was performed by a second experienced sonographer. A Mylab Twice equipment (Esaote, Geneve, Italy) was used, with a 22 MHz frequency for grey scale and a 12.5 MHz for CDU (color gain of 51, PRF of 2 kHz). The sonographer was blind to the clinical and carotid ultrasound IMT data.
Results: Forty patients were studied, 28 men (70%), with a mean age of 70,6±6,9 years. Three patients were active smokers and 27 ex-smokers. Arterial hypertension was present in 39 (97.5%), dyslipidaemia in 34 (85%) and diabetes in 19 (47.5%). The mean erythrocyte sedimentation rate was 13.6±11.0. The table shows that an IMT >0.30 mm (halo sign) was seen in at least 1 TA branch of 18 patients (45%) with 33 TA branches affected (20.6%). An IMT cut-off >0.34 mm, was present in 4 patients (10%). When at least two affected branches with this measure were required to make the US diagnosis (criteria recommended to improve specificity) only one patient (2.5%) produced a false-positive halo sign.
Conclusions: To the best of our knowledge, this is the first communication indicating that atherosclerosis is a potential cause of false-positive halo sign. We propose a cut-off of AT IMT >0.34 mm in at least two branches to minimise the number of false positives in GCA diagnosis.
Disclosure of Interest: None declared

	Carotid IMT mm	Right		Left		Number of branches with halo	
		TA frontal	TA parietal	TA frontal	TA parietal	Cut-off IMT >0.3 mm	Cut-off IMT >0.34 mm
Patient 4	1.185	0.37	0.31	0.31	0.31	4	1
Patient 5	0.948	0.26	0.31	0.31	0.27	2	0
Patient 6	1.135	0.18	0.31	0.24	0.25	1	0
Patient 7	1.164	0.31	0.28	0.28	0.28	1	0
Patient 9	1.243	0.37	0.4	0.45	0.35	4	4
Patient 10	1.196	0.28	0.28	0.34	0.28	1	0
Patient 11	1.21	0.31	0.31	0.25	0.28	2	0
Patient 12	1.165	0.29	0.28	0.28	0.31	1	0
Patient 14	1.37	0.29	0.22	0.31	0.31	2	0
Patient 16	1.33	0.25	0.28	0.23	0.34	1	
Patient 17	1.027	0.28	0.32	0.37	0.34	3	1
Patient 18	0.989	0.25	0.31	0.28	0.28	1	0
Patient 19	1.017	0.19	0.28	0.25	0.31	1	0
Patient 25	0.802	0.29	0.27	0.31	0.25	1	0
Patient 30	1.200	0.31	0.29	0.21	0.24	1	0
Patient 32	0.978	0.31	0.3	0.36	0.25	3	1
Patient 35	0.766	0.23	0.28	0.33	0.29	1	0
Patient 37	1.048	0.34	0.33	0.27	0.31	3	0

DOI: 10.1136/annrheumdis-2017-eular.1462

AB1025 THE SUPERB MICROVASCULAR IMAGING IS MORE SENSITIVE THAN CONVENTIONAL POWER DOPPLER IMAGING IN DETECTION OF ACTIVE SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS

G.Y. Lee[1], S. Kim[1], S.T. Choi[2], J.-S. Song[2]. *[1]Radiology; [2]Internal Medicine, CHUng-Ang University College of Medicine, Seoul, Korea, Republic Of*

Background: Precise evaluation of synovial inflammation and bony deformity is very important for the management of rheumatoid arthritis (RA). One of the most popular used methods to detect synovial inflammation and bony erosion is ultrasonography. Previous literatures revealed that US using power Doppler imaging (PDI) could detect more sensitive synovial inflammation than conventional radiography. However, there are still some limitations in ultrasonography. The superb microvascular imaging (SMI) is a new software technology introduced by Toshiba, which can detect a vascularity more sensitively without artifacts.
Objectives: In this prospective study, we evaluated the clinical usefulness of the SMI compared to PDI for the detection of active synovitis in patients with RA.
Methods: This prospective observational study includes 56 patients with RA (42 females; mean age,), from June 2015 to October 2016. The mean age of RA patients was 53.2±17.6 years, and 42 patients were female (75.0%). All the included patients underwent ultrasound about both wrists and hands (total 22 joints; wrist joints, metacarpophalangeal joints, and proximal interphalangeal joints). All the ultrasound examinations were performed at the volar side of the wrists and hands using both conventional PDI and SMI which use Aplio TM 500 Ultrasound (Toshiba Medical Systems Corporation). Their results were scored for each joint from grade 0 to grade 3 according to the vascularity (grade 0, no vascularity; grade 1, single vessel; grade 2, vascular flow less than 50% in field of view; grade 3, equal to 50% or more). The sum of grades for 22 joints was compared between PDI (PDI-sum) and SMI (SMI-sum). The correlation between the sum of grades values and inflammatory laboratory parameters including the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and disease activity score 28 (DAS28) were also evaluated.
Results: The mean values of ESR, CRP and DAS28 were 27.13±18.06 mm/hr, 6.78±9.14 mg/L, and 2.71±1.11 respectively. The positive rates of rheumatoid factor and anti-cyclic citrullinated antibody were 73.2% and 75.0%, respectively. The sum of grades for 22 joints was significantly higher in SMI-sum compared to PDI-sum (10.27±6.20 vs. 5.80±3.79, $p<0.001$). The SMI-sum was highly correlated with the PDI-sum score ($\gamma=0.800$, $p<0.001$). The SMI-sum showed positive correlation with DAS28, tender joint count, swollen joint count, visual analogue pain scale, and CRP level ($\gamma=0.486$, $p<0.001$; $\gamma=0.385$, $p=0.003$; $\gamma=0.467$, $p<0.001$; $\gamma=0.547$,$p<0.001$; $\gamma=0.351$, $p=0.008$, respectively). The number of clinical remission (DAS28 score below 2.6) was 28 (50.0%). The SMI-sum was significantly higher than PDI-sum in patients with clinical remission (7.96±5.39 vs. 4.64±3.03, $p<0.001$). All of the patients with clinical remission showed active synovitis at more than one joint in SMI.
Conclusions: SMI showed a more sensitive vascularity in RA patients than PDI. We could detect active synovitis through SMI in the RA patients with clinical remission. SMI could be a useful technology for the evaluation of synovitis in RA patients, especially for the detection of clinically subtle, but active synovitis in RA patients with remission.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4571

AB1026 AN ANA SCREENING ASSAY (ELIA® CTD SCREEN) CONTAINING MULTIPLE ANTIGENS INCREASES THE SENSITIVITY AND SPECIFICITY OF ANA TESTING BY INDIRECT IMMUNOFLUORESCENCE

G. Steiner[1], T. Perkmann[2], T. Horn[3], H.P. Kiener[1]. [1]*Internal Medicine III-Rheumatology;* [2]*Laboratory Medicine, Medical University Vienna;* [3]*Phadia Austria GmbH, Thermo Fisher Scientific, Vienna, Austria*

Background: Antinuclear antibodies (ANA) are the serological hallmark of connective tissue diseases (CTD) and indirect immunofluorescence (IIF) on Hep-2 cells is still considered the gold standard for ANA screening. While this method is sensitive it lacks specificity. Moreover, low-titer ANA subspecificities may escape detection by IIF.
Objectives: To investigate the usefulness of an ANA screening assay containing most of the diagnostically relevant antigens for CTD diagnostics.
Methods: Sera from 265 consecutive patients presenting with symptoms characteristic of connective tissue diseases (but without a clear diagnosis yet) were analysed by IIF and the EliA® CTD Screen (Thermo Fisher Scientific) containing the following antigens: dsDNA, U1-snRNP, Sm, Ro60, Ro52, La, Rib-P, topoisomerase I (Scl-70), centromere B, RNA polymerase III, fibrillarin, Jo-1, Mi-2, Pm/Scl. All positive sera were further analyzed by monospecific assays (Thermo Fisher Scientific).
Results: Among the 265 patients, 90 were positive by IIF and 78 by CTD Screen; 61 sera were positive in both systems, 17 only in the CTD Screen and 29 only in IIF. In all double positive patients at least one diagnostically relevant antibody was detected, with anti-Ro and anti-dsDNA antibodies being most frequently detected. Importantly, antibodies were also detected in 15 of the 17 patients who were exclusively positive in the CTD Screen: 7 patients had anti-dsDNA, 4 anti-Ro, 1 anti-La, 2 anti-U1snRNP, and 1 patient had anti-Jo-1 antibodies. In contrast, among the 29 sera exclusively positive by IIF only two contained a diagnostically relevant antibody. Clinical evaluation revealed that 16 out of the 17 CTD Screen pos/IIF negative patients presented with at least 1 clinical sign commonly associated with systemic rheumatic disease (sicca syndrome, 12 patients; arthritis/arthralgias, 13 patients; microangiopathy, 2 patients; myositis, 2 patients; leukocytopenia, 2 patients; Raynaud's phenomenon, 5 patients; pericarditis, 1 patient; thromboembolic events, 2 patients). These patients may be at higher risk for developing a CTD, or, alternatively, may be at an early stage of a CTD in which a definite diagnosis is not yet to be made. The combination of distinct autoantibodies with clinical signs of systemic rheumatic disease, however, warrants a careful follow up in these patients.
Conclusions: ANA screening assays containing multiple antigens such as the EliA® CTD Screen seem to be helpful diagnostic tools that should be used in addition to IIF for detection of disease-associated autoantibodies enabling the physician to substantially improve diagnostics of connective tissue diseases.
Disclosure of Interest: G. Steiner Consultant for: Phadia Austria GmbH, Thermo Fisher Scientific, T. Perkmann: None declared, T. Horn Employee of: Phadia Austria GmbH, Thermo Fisher Scientific, H. Kiener: None declared
DOI: 10.1136/annrheumdis-2017-eular.6053

AB1027 THE UTILITY OF LIP BIOPSY IN PATIENTS DIAGNOSED OF IPAF (INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES)

H.S. Park[1], P. Millan[2], D. Castillo[2], M. Millan[1], P. Moya[1], B. Magallares[1], A. Laiz[1], C. Diaz[1], J.M. De Llobet[1], I. Castellvi[1]. [1]*Rheumatology;* [2]*Pneumology, Hospital Universitari de la Santa Creu i Sant Pau, Barcelona, Spain*

Background: The European Respiratory Society/American Thoracic Society Task Force has defined a classification criteria for interstitial pneumonia with features of autoimmunity that does not accord to a specific systemic disease. This criteria combines clinical, serological and radiological domains. The clinical criteria does not include dry syndrome eventhough the serological criteria does include antiRo and antiLa antibodies. It is known that some patients with dry syndrome with antibodies negativity undertake lip biopsy to confirm Sjögren Syndrome (SS). Therefore lip biopsy could be useful to IPAF if SS is suspected.
Objectives: Determine the utility of lip biopsy in patients with interstitial pneumonia that present symptoms suggestive of an autoimmune disease.
Methods: Retrospective study of patients attended between june of 2010 and june of 2016 in a tertiary referral hospital was done. We included 23 Pneumology patients diagnosed of IPAF that were referred to Rheumatology clinic to rule out underlying connective disease. All patients had a complete immunologic study, two pulmonary function test including diffusion capacity of CO and a lip biopsy to confirm SS. The results of the lip biopsy was analysed with different variables.
Epidemiologic data, blood test, pulmonary function test and pattern of ILD by high definition CT or lung biopsy were analysed. Changes in therapeutic decisions and pulmonary function test a year after the lip biopsy were also registered. To compare qualitative variables we used Chi Square test or Fisher exact test when necessary. The statistical significance was set up to p-value inferior to 0.05.
Results: 16 of 23 patients with ILD met classification criteria of IPAF (69.6%). 12 were women (52.2%) with a median age of 77 (from 54 to 87 years). The findings of our group is summarised in table 1.
9 lip biopsies confirmed SS (39.1%) and 7 changed treatment according to result (30.4%). No variables such as sex, smoking, previous lung disease, dry syndrome or Schirmer test showed relation with lip biopsy result. Previous treatment with corticosteroids did not seem to influence the results of lip biopsy eventhough it was not statistically significant (p-value 0.059). No relation with antinuclear antibody or acute phase reactants was observed either. Lip biopsy was most useful to diagnose SS for those with Usual Interstitial Pattern ($p<0.02$) among other patterns of ILD.

Variable	Number (percentage %)
Sex	Women 12 (52.2), Men 11 (47.8%)
Exposition to toxic	3 (13%)
Dry syndrome	19 (82.6%)
Altered Schirmer test	11 (55%)
Antinuclear antibody (>1/160)	12 (52.2%)
Anti La/Ro52/Ro60	0 (0)
Rheumatoid Factor	6 (26.1%)
Previous corticosteroid therapy	7 (30.4%)
Diagnostic lip biopsy	9 (39.1%)
IPAF criteria	16 (69.6%)
ILD pattern	UIP 4 (17.4%), NSIP 13 (56.5%), LIP 1 (4.3%)

Conclusions: Lip biopsy is a complementary examination to consider for IPAF. In our group the results were significant for UIP. Corticosteroid therapy did not seem influential to the results of lip biopsy eventhough it was not statistically significant. In 39.1% SS was diagnosed and in 30.4% treatment was changed according to results.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5465

AB1028 PREVALENCE AND DISTRIBUTION OF SESAMOID BONES IN THE HAND DETERMINED USING DIGITAL TOMOSYNTHESIS

H.H. Kwon[1], B.S. Koo[2], Y. Song[3], Y.-K. Sung[1], S. Lee[3], J.-B. Jun[1]. [1]*Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases;* [2]*Department of Internal Medicine, Inje University Seoul Paik Hospital, Inje University College of Medicine;* [3]*Department of Radiology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic Of*

Background: Sesamoid bones are round or oval-shaped bones that are embedded in tendons. The prevalence and distribution of sesamoids in the hand varies between different populations. Conventional radiography (CR) is generally used to identify the sesamoid bones. However, there was no study using digital tomosynthesis (DTS).
Objectives: The aim of this study was to identify the prevalence and distribution of sesamoid bones in the hand using DTS in comparison to previous studies.
Methods: Using CR and DTS, hand images (81 left and 100 right) taken at a tertiary hospital were retrospectively reviewed. The sesamoid bones were identified in the distal interphalangeal (DIP), interphalangeal (IP), and metacarpophalangeal (MCP) of the thumb (I), index (II), long (III), ring (IV), and small (V) fingers. Differences in number of sesamoid bones detected on CR and DTS were analyzed.
Results: Sesamoid bones were observed in MCP I (100%), MCP II (46%), MCP III (2%), MCP IV (2%), MCP V (53%), and IP (53%) on CR. Using DTS, sesamoid bones were found more often in MCP I (100%), MCP II (54%), MCP III (2%), MCP IV (1%), MCP V (59%), and IP (75%). Differences in the mean number of sesamoid bones detected on CR and DTS were statistically significant. Sesamoid bones in DIP joints were frequently observed on DTS, but rarely found on CR.
Conclusions: Most sesamoid bones in the hand were detected in MCP I, II, V, and IP joints, and were more often detected on DTS than CR. DTS is a reliable tool to evaluate bony structures in the hand.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4553

AB1029 ULTRASOUND NAIL ASSESSMENT IN PSORIATIC ARTHRITIS AND PSORIASIS COMPARED WITH HEALTHY CONTROLS

I. Janta[1], O. Baniandres Rodriguez[2], L. Valor[1], J. Martinez Barrio[1], J.G. Ovalles[1], J.C. Nieto Gonzalez[1], C. Gonzalez[1], J. Lopez Longo[1], I. Monteagudo[1], E. Naredo[1,3]. [1]*Rheumatologist;* [2]*Dermatology, Hospital General Universitario Gregorio Marañón;* [3]*Rheumatology, Joint and Bone Research Unit, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain*

Background: Assessment of nail involvement is currently made by clinical assessment using nail psoriasis severity index (NAPSI). Whilst clinical assessment can detect superficial nail changes, the matrix and the extensor tendon region are not accessible for clinical assessment.
Musculoskeletal (MS) ultrasound (US) is playing an important role in the evaluation of psoriatic arthritis (PsA) patients. Recently, MSUS has been more used in the evaluation of nail involvement in psoriasis (Pso) and PsA patients.
Objectives: The primary objective of this observational, cross-sectional study was to assess the MSUS morphological and vascular abnormalities in nail in PsA and Pso patients compared with healthy controls. The secondary objective was to compare MSUS and clinical assessment of the nail in PsA and Pso patients.
Methods: We included patients with PsA (diagnosed according to CASPAR criteria) and patients with Pso without joint involvement (diagnosed by an experienced dermatologist according to clinical findings) and healthy controls.

Clinical evaluation consisted in the evaluation of the NAPSI and PASI scores. The MSUS evaluation consisted in the evaluation of 10 hand nails. In B-mode (BM) we evaluated the followings: thickness of the nail bed from the distal phalanx bone surface to the ventral plate (PB) according to Worstman X et al.; thickness of the nail from dorsal to ventral plate (IP); dorsal and ventral plate morphology, echogenicity and integrity. Additionally, we performed a color Doppler (CD) evaluation for the presence of CD signal at the nail bed and matrix level. A score for BM and different scores for CD were calculated for each nail and sums of all nails for BM and CD scores were calculated for each patient.

Results: We evaluated 60 patients with PsA, 23 with Pso and 20 controls. 52.4% were female. The mean age (SD; range) was 50.2 (13.6; 23–83). The age was higher in patients (Pso and PsA) than in controls ($p<0.001$). Patients with PsA were more treated with DMARD (81.7%) while patients with Pso were more treated with topics (73.9%) than DMARDs (13%), ($p<0.001$). The majority of the patients (96%) had a PASI score less than 12. The NAPSI was higher in Pso patients than in PsA patients ($p<0.001$); for all controls the NAPSI was 0.

US measurements of IP and PB were significantly higher in patients than in controls in the majority of the nail ($p<0.045$). Total US score for BM was significantly higher in patients than in controls ($p<0.001$). There were no significant differences for the majority of CD scores between patients and controls.

Overall we found weak to moderate positive correlations between NAPSI and US scores for BM, both for matrix and bed. For most of the nails we found no correlation between NAPSI and CDUS scores; for the rest of the nails the correlation was weak, both positive and negative.

References:

[1] The MSUS measurements and scores showed to be higher in patients with PsA and Pso compared with controls, while CD scores showed no differences.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4126

AB1030 IDENTIFICATION OF VERTEBRAL FRACTURES IN FRACTURE LIASION SERVICES ACROSS THE UNITED KINGDOM

J. Sayer, S. Stephenson. *Service Development, National Osteoporosis Society, Bath, United Kingdom*

Background: Fracture Liaison Services (FLS) can prevent secondary fracture through systematic identification of low trauma fractures using dedicated case finding, with assessment and treatment of osteoporosis where necessary. Services are now being measured for quality against *Clinical Standards for Fracture Liaison Services* published by the National Osteoporosis Society in 2015.[1] The first standard asserts that all patients over 50 years with a newly reported vertebral fracture will be systematically and proactively identified.

Objectives: To evaluate provision for systematic identification of newly reported vertebral fractures in patients aged over 50 at Fracture Liaison Services (FLS) across the UK.

Methods: A gap analysis tool was used to measure service provision against standard one of the *Clinical Standards for Fracture Liaison Services*, relating to the systematic and proactive identification of vertebral fractures. Data was collected at 78 sites in the UK.

Results: 63% (49) of sites had *no* systematic process in place to identify vertebral fractures. Only 10% (8) sites identified *all* newly reported vertebral fractures. 27% (21) had procedures in place to identify *some* vertebral fractures, i.e. those within certain cohorts. There was considerable disparity across the UK. Sites in Scotland were significantly more likely to have comprehensive processes in place (38%, 6/16) than in the rest of the UK (3%, 2/62).

Conclusions: Systematic identification of vertebral fractures poses a particular challenge to services due to a number of factors. Vertebral fractures are difficult to identify as they tend not to present or be admitted in acute settings where FLS are primarily based. In addition, services require support from Radiology, including a commitment to avoid ambiguous terminology when reporting vertebral fractures. Furthermore, as a category, vertebral fractures fall between departments (Rheumatology, Orthopaedic, Fracture Clinic, A&E, Spinal services) making systematic identification even more challenging. In the Fracture Liaison Service Database Facilities Audit (May 2016), the most frequently cited barrier to the identification of vertebral fractures was lack of a patient pathway.[2] Gap analysis shows a paucity of provision in the identification of vertebral fractures. This is the key driver for work underway in the NOS to develop a patient pathway for vertebral fractures, in conjunction with clinical experts, to promote best practice and best patient care.

References:

[1] https://www.nos.org.uk/health-professionals/fracture-liaison-services.
[2] https://www.rcplondon.ac.uk/projects/outputs/fls-db-facilities-audit-fls-breakpoint-opportunities-improving-patient-care.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3464

AB1031 ANTI-DRUG ANTIBODIES: ASSAY PERFORMANCE IN PATIENTS TREATED WITH ANTI-TNF BIODRUGS

B. Hock[1], J.L. O'donnell[2], J. Liu[2], P. Keating[2], M. Spellerberg[2], L. Stamp[3], M. Barclay[3]. *[1]Haematolgy Research Group, University of Otago; [2]Immunology Section, Canterbury Health Labs; [3]Medicine, University of Otago, Christchurch, New Zealand*

Background: Minimum biodrug concentrations of ~7mg/l are predictive of disease remission[1]. Very low/absent biodrug concentrations associate with loss of benefit which may be due to ADA[2] however the clinical utility of ADA is assay dependant. In rheumatoid arthritis the combination of low/absent drug concentration and the presence of ADA appears to have the greatest utility[3]. Canterbury Health Laboratories, New Zealand (CHL) has developed a competitive binding ELISA to detect neutralising antibodies whereas most commercial assays utilise a bridging methodology

Objectives: Compare performance of a competitive binding assay with two commercial bridging assays in the detection of ADA to anti-TNFα biodrugs in serum samples with low/absent biodrug concentration

Methods: Serum samples referred for anti TNF biodrug concentrations found to have very low/undetectable concentrations (<1mg/l) were tested for ADA using the competitive-bind assay and two bridging assays (TANI Medikal and GRIFOLS)

Results: Over a 22 month period (Jan 2014 – Oct 2016), 67% (331/497) of referred samples had biodrug concentrations below 7mg/l and 15% (n=79) had low/undetectable biodrug concentrations (adalimumab n=36 or infliximab n=43). ADAs were detected in 53% (42/79) of this latter group. The competitive binding assay detected ADAs in all samples testing positive for ADA by binding assay. In addition a further 8 samples were positive for ADA by the competitive assay: 53% (42/79) positive for ADA by the competitive assay and 33% positive by one or other of the commercial assays

Conclusions: The competitive binding ELISA was more sensitive in detecting biodrug ADAs in serum samples with very low/undetectable biodrug concentrations

References:

[1] Felice C, Marco M, Pugliese D,et al. Expert Opin Biol Ther 2015;15:1107–1117.
[2] Schaeverbeke T, Truchetet M, Kostine M, Barnetche T et al. Rheumatology 2016;55:210–220.
[3] Jani M,Chinoy, Warren R, et al. Arthritis and Rheumatology 2015;67:2011–2019.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1757

AB1032 COMPARISON OF DIFFERENT TECHNIQUES FOR DETECTING ANTI-DFS70 ANTIBODIES

J.M. López-Ortega[1], Á. Sánchez-Herrero[1], N. Estañ-Capell[1], D. Ybáñez-García[2], E. Valls-Pascual[2], C. Vergara-Dangond[2], M. Aguilar-Zamora[2], L. Montolio-Chiva[2], À. Martínez-Ferrer[2], J.J. Alegre-Sancho[2]. *[1]Laboratory; [2]Rheumatology, Hospital Universitario Doctor Peset, Valencia, Spain*

Background: Antinuclear antibodies (ANA) positivity with a dense fine speckled (DFS) pattern by indirect immunofluorescence (IIF), as per the definition of the International Consensus on ANA Patterns (ICAP), is not uncommon and is linked to the presence of anti-DFS70 antibodies. These antibodies, in the absence of others, are very valuable as biomarkers of exclusion of a systemic autoimmune disease (SAD).

Objectives: To evaluate anti-DFS70 antibody detection by two different laboratory techniques and its relation with different IIF patterns, including DFS pattern.

Methods: During three months, the serum of patients with positive ANA was consecutively collected. Three groups of patients were established according to their IIF pattern: a first group (D) with a DFS pattern as per ICAP; a second group (M) with other speckled with positive mitosis patterns; and a third group (C), as a control, with well defined homgeneous and speckled patterns.

In order to perform a preliminary analysis, 10 serum samples were randomly selected from each group. In each serum sample, an ANA screening by IIF on Hep-2000 cells (Fluorescent IgG ANA-Ro Test System – Immunoconcepts) using an AP-16 Elite/Zenit-Up/GSight system from Menarini, and an anti-DFS70 antibodies detection by two different laboratory techniques (IIF on Hep-2 cells [Hep-2/DFS70 Knock-out - Immco Diagnostics] and inmunoblot [ANA+DFS70 Dot Blot – Alphadia]) were performed. Simultaneously, antibodies against extractable nuclear antigens (ENA), nucleosomes (NUS) and histones (HIS) were tested.

Results: In group D, positivity for anti-DFS70 antibodies was confirmed in 7/10 cases, all of them being negative for other ANA. In group M, 2/10 serum samples were positive for anti-DFS70 and 2/10 were positive for anti- NUS antibodies, none of them being positive for anti-ENA. In group C, no sample was positive for anti-DFS70 antibodies, while all of them showed positivity for antibodies against ENA, NUS and HIS.

The detection of anti-DFS70 was found to be equal by the two methods in 8 of the 9 positive cases, being both negative in the others. In no case the presence of anti-DFS70 was associated with a diagnosis of SAD.

Conclusions: Both IIF and immunoblot are suitable methods for detecting anti-DFS70 antibodies. We propose to determine anti-DFS70 and to perform an ENA screening in case of finding a DFS pattern of ANA by IIF, and to investigate anti-DFS70 in other speckled patterns with positive mitosis if no other specificities have been previously found.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3848

AB1033 THE EXPRESSION OF IMMUNOGLOBULIN G AND IMMUNOGLOBULIN G4 IN LYMPHOMA

J. Li[1], Z. Zhang[2]. *[1]Rheumatology department, Shanxi Dayi Hospital, Shanxi; [2]Rheumatology department, Peking University First Hospital, Beijing, China*

Background: Although IgG4-related disease has been gradually recognized, its relationship with malignant diseases, especially lymphoma has been an eternal topic.
Objectives: To explore the expression of IgG4 positive cells in lymphoma.
Methods: Surgical excision specimens with definite diagnosis of lymphoma from January to December, 2013 were collected. Hematoxylin-eosin staining and immunohistochemical staining of IgG and IgG4 were then evaluated on dense lymphoplasmacytic infiltration, storiform fibrosis and obliterative phlebitis. For the quantification of IgG and IgG4 positive cells, the areas with the highest density of positive cells were evaluated. Three high-powered fields (hpf) in each section were analyzed, and the average number of positive cells per hpf was calculated.
Results: 16 patients with lymphoma were selected in our study. There were 9 males and 7 females with an average age of 51 years old. The pathologic type included 13 cases of non-Hodgkin lymphoma and 3 cases of Hodgkin lymphoma. Sub types of Non-Hodgkin lymphoma contained 8 cases of diffuse large B cell lymphoma, 2 cases of small B cell lymphoma, 1 case of mucosa accociated lymphoid tissue marginal zone B cell lymphoma (MALToma), follicular lymphoma, peripheral T-cell lymphoma and hepatosplenic T-cell lymphoma. The 16 specimens all manifested as dense lymphocytic infiltration, accompanied by atypical lymphocytes. Proliferation of fibrous tissue was only seen in one specimen. 14 cases were IgG positive with the highest cell count from 20–350/hpf. IgG can be expressed in both cytoplasm and cytomembrane. 2 cases of IgG4 positive were Hodgkin lymphoma and the highest cell counts were 11 and 12/hpf respectively.
Conclusions: IgG4 positive cell, fibrosis and obliterative phlebitis seldom appear in lymphoma. Added specific tumor signature molecules, it may not be difficult to distinguish lymphoma from IgG4-related disease.
References:
[1] Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med 2012 2012–02–09;366(6):539–51.
[2] Yamamoto M, Takahashi H, Tabeya T, Suzuki C, Naishiro Y, Ishigami K, et al. Risk of malignancies in IgG4-related disease. Mod Rheumatol 2012 2012–06–01;22(3):414–8.
[3] Takahashi N, Ghazale AH, Smyrk TC, Mandrekar JN, Chari ST. Possible association between IgG4-associated systemic disease with or without autoimmune pancreatitis and non-Hodgkin lymphoma. Pancreas 2009 2009–07–01;38(5):523–6.
[4] Choe JY, Go H, Jeon YK, Yun JY, Kim YA, Kim HJ, et al. Inflammatory pseudotumor-like follicular dendritic cell sarcoma of the spleen: a report of six cases with increased IgG4-positive plasma cells. Pathol Int 2013 2013–05–01;63(5):245–51.
[5] Koneval T, Applebaum E, Popovic D, Gill L, Sisson G, Wood GW, et al. Demonstration of immunoglobulin in tumor and marginal tissues of squamous cell carcinomas of the head and neck. J Natl Cancer Inst 1977 1977–10–01;59(4):1089–97.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3999

AB1034 SCORING SYSTEMS OF MUSCLE MRI IN IDIOPATHIC INFLAMMATORY MYOPATHIES

K. Kubinova, H. Mann, J. Vencovsky. *Institute of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic*

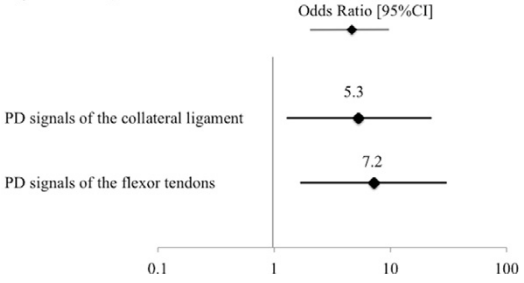
Background: MRI is a widely used radiological method for assessing muscle involvement in idiopathic inflammatory myopathies (IIM). There is still no universally accepted and validated scoring protocol for the quantification of pathological changes in muscles.
Objectives: To identify MRI scoring systems used in previous studies. To summarize the most frequently evaluated MRI features and to suggest parameters for a unified scoring system, that has to be validated in the future.
Methods: A detailed literature search was conducted in the standard medical databases. Information regarding individual MRI scoring systems were obtained from the methodological explanations and their parameters were compared.
Results: We identified different scoring systems with a large variability of assessed localizations and parameters (Table 1). Muscle oedema as a sign of active muscle inflammation was evaluated in all studies. There were some studies using modified Mercuri score for evaluation of the fatty infiltration as a marker of chronic muscle damage or the Goutallier grading (1, 2), developed originally for the assessment of inherited neuromuscular disorders or structural changes in orthopedics. Perifascicular oedema or soft-tissue oedema were also assessed in some cases. There was no concordance between evaluated muscle groups.
Conclusions: MRI plays a significant role in the evaluation of pathological changes in IIM. This search demonstrated, that there is no widely used, standardized method for assessment of a MRI finding. According to our results, a future concept of MRI scoring system should include evaluation of muscle oedema, fatty infiltration and possibly also the presence of perifascicular (-fascial) and subcutaneous tissue inflammation. Muscle groups most convenient for evaluation have to be determined as well.
References:
[1] Goutallier D, et al. Influence of cuff muscle fatty degeneration on anatomic and functional outcomes after simple suture of full-thickness tears. J Shoulder Elbow Surg, 2003;12(6):550–4.
[2] Zheng Y, et al. Magnetic resonance imaging changes of thigh muscles in myopathy with antibodies to signal recognition particle. Rheumatology, 2015;54(6):1017–1024.
Acknowledgements: Supported by the project (Ministry of Health, Czech Republic) for conceptual development of research organization 00023728 (Institute of Rheumatology).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3656

AB1035 EXAMINATION OF ULTRASOUND FINDINGS IN UNDIFFERENTIATED SPONDYLOARTHRITIS PATIENTS WITH DACTYLITIS

K. Fujikawa[1], Y. Endo[1], A. Mizokami[1], M. Mine[2], A. Kawakami[3]. *[1]Rheumatology, Japan Community Healthcare Organization, Isahaya General Hospital; [2]Rheumatology, Suga Orthopedic Hospital, Isahaya; [3]Immunology and Rheumatology, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan*

Objectives: To evaluate the ultrasound findings in undifferentiated spondyloarthritis (uSpA) patients with or without dactylitis.
Methods: Between April 2014 and December 2016, sixty-six patients with uSpA diagnosed at our center were consecutively enrolled. The diagnosis of uSpA was made by the Japan College of Rheumatology (JCR)-certified rheumatologists and dactylitis was defined as sausage-digit appearance. Ultrasound, clinical and laboratory findings at diagnosis in patients with dactylitis (dactylitis group; n=30) were compared to those without dactylitis (non-dactylitis group; n=36). Grey scale (GS) and power Doppler (PD) signals of the wrist and finger joints, PD signal of extensor and flexor tendon sheaths, and PD signals of the collateral ligament of the fingers in both hands were assessed by ultrasound. Ultrasound assessment was made by JCR-registered sonographers.
Results: There were no significant differences in clinical and laboratory findings, including inflammatory back pain, arthritis of the lower limbs, tenderness of the entheses, radiographic/MRI changes of sacroiliac joint and HLA-B27 allele frequency, between two groups. In ultrasound findings, the dactylitis group had significantly more PD signals of the flexor tendon sheaths (83% vs. 22%, $p<0.0001$), the collateral ligament (83% vs. 25%, $p<0.0001$), and the MCP joint (30% vs. 3%, $p<0.01$) as compared with the non-dactylitis group. In logistic

Figure 1. Logistic regression analysis of ultrasound findings for the contribution of diagnosis of dactylitis



Abstract AB1034 – Table 1. Muscle MRI scoring systems

Author	Muscle oedema	Fatty infiltration	Sequences	Muscle groups	Other aspects
Pipitone 2016	1 = present, 0 = absent	–	STIR	17 bilat.	–
Andersson 2015	1 = present, 0 = absent	0 - 4 Goutallier gr.	T1W, STIR	thigh, NS	–
Malattia 2014	0 = no abnormalities, 1 = mild-moderate <50%, 2 = high degree >50%	–	STIR	42 (whole body MRI)	perifascicular + subcutaneous tissue inflammation
Zheng 2014	0–5 scale from normal to moderate intrafascicular global oedema	0–5 modif. Mercuri score	T1W, STIR	12, thigh muscles bilat.	–
Davis 2011	0 = absent, 1 = mild, 2 = moderate, 3 = severe	–	STIR	4, thigh bilat.	soft-tissue + perifascicular oedema
Studynkova 2007	VAS 0–10	–	STIR	thigh muscles, NS	muscle oedema extent + total MRI affection

STIR = short-tau inversion recovery, NS = not specified, T1W = T1 weighted sequences, VAS = visual analogue scale.

regression analysis, the PD signals of the flexor tendons and collateral ligament were independent contributors to a diagnosis of dactylitis (Figure 1).
Conclusions: Development of active inflammation of enthesis organ determined by ultrasound is supposed to associate importantly with the judgment as dactylitis in patients with uSpA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3170

AB1036 PREDICTIVE VALUE OF BASAL REACTANTS IN AN EARLY ARTHRITIS CLINIC. DOES ESR ELEVATION CRITERIA MAKE A DIFFERENCE?

L. Mayordomo[1], M.L. Velloso[1], P. González-Moreno[2], C. Gómez-Cano[1], A. Gutiérrez-Leonard[3], J.L. Marenco[1]. *[1]Rheumatology Department, Hospital Universitario Valme; [2]Rheumatology Department, HVM; [3]Physioterapy, HVR, Sevilla, Spain*

Background: The presence of high acute phase reactants may help the diagnosis and classification of patients with rheumatoid arthritis, specially in seronegative patients.
Objectives: Our objective was to establish if the presence of high basal reactants in early arthritis may help to establish the diagnosis of rheumatoid arthritis following criteria of ACR 1987 (which does not include positive reactants in diagnostic criteria). at 12 months of follow-up.
Methods: The presence of acute phase reactants at the baseline visit (elevated CRP and elevated ESR according to two different criteria) was studied in a population of 70 patients referred to the arthritis clinic with criteria for suspicion of early arthritis to meet at least one of the Following criteria: a) Swelling in 2 or more joints b) Pain in MCFs, MTFs and/or wrists c) Morning stiffness greater than 30 minutes (* SERAP study criteria), with <12 months of evolution of symptoms. None of the patients had previous diagnosis of rheumatoid arthritis or other inflammatory joint disease nor had previous treatment with steroids or DMARDs. The presence of high VSG (mm/h) was considered according to two criteria: a) ESR 1: VSG>20 or b) ESR 2 (criterion according to age and sex) (1): Age ≥50 years ESR>20 in men and ESR>30 in women; Age <50 years of age, ESR>15 mm/h in men and>20 in women.Statistics: Chi-square or Fisher test (for any value <5), Odds ratio (OR) calculation.
Results: 70 patientes, 45 women (64,3%), x age 51,57±16,08 y (18–85) were included, x disease duration 3,47 meses ± 2,59 (0,53–11.73), 48/70 (68,5%) RF and ACPA negative. 49 patients meet ACR 1987 criteria, but 5 were finally classified in non-RA group because they meet criteria of other inflammatory chronic articular conditions (eg. psoriatic arthritis RA-like). 45/70 patients had high baseline CRP (64.3%), ESR 1 38/70 (54.3%) and ESR 2 35/70 (50%). Basal CRP>5 showed statistically significant differences for RA diagnosis (ACR 1987 criteria) p=0.003, OR =4,64 (1.62–13,24) but basal positive ESR 1 criteria did not (p=0.122). Basal positive ESR2 showed significant differences for diagnosis of RA, with p=0.036, OR =2,78 (0,99–7,47). In the subgroup of seronegative patients, basal CRP could predict ACR 1987 RA diagnosis at 12 months follow-up p=0,019, OR 4,2 (1,23–14,36), but ESR (both ESR1 and ESR2) not (p=1,000). If the 5 patients ACR 1987 meeting criteria RA-like but diagnosed ot other inflammatory conditions were included, the results are similar but ESR2 reached a better confidence interval p=0.036, OR 3,63 (1,20–10,94).

RA ACR 1987 CRITERIA 44 PT		RA YES	P univariate	OR	IC 95 %
CRP	YES	34/45 (75,5%)	0,003	4,64	(1,62-13,24)
	NO	10/25 (40%)			
ESR1	YES	30/38 (78,9%)	0,122 NS	-	-
	NO	19/32 (59,4%)			
ESR2	YES	26/35 (74,3%)	0,048	2,78	(0,99-7,47)
	NO	18/35 (51,4%)			
CRP	YES	18/28 (64,3%)	0,019	4,2	(1,23-14,36)
seronegative	NO	6/20(30%)			

ACR 1987 CRITERIA (AR+AR-LIKE) 49 PT		RA YES	P univariate	OR	IC 95 %
CRP	YES	37/45 (82,2%)	0,006	5,01	(1,67-14,98)
	NO	12/25 (48%)			
ESR1	YES	30/38 (78,9%)	0,116 NS	-	-
	NO	19/32 (59,4%)			
ESR2	YES	29/35 (82,8%)	0,036	3,63	(1,20-10,94)
	NO	20/35 (57,1%)			

Conclusions: The presence of elevated basal CRP>5 may be used as a factor that helps to predict the diagnosis of rheumatoid arthritis according to ACR 1987 criteria for RA. The baseline elevated ESR according to the sex and age criterion could be useful as a predictor factor for the diagnosis of rheumatoid arthritis, while the VSG criterion>20 in all patients does not demonstrate differences in the study between the two groups with final diagnosis AR and non-RA. In seronegative patientes, only CRP demostrated predictive value but ESR not.

References:
[1] Bottiger LE, Svedberg CA. Normal erythrocyte sedimentation rate and age. Br Med J 1967; 2:85–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6659

AB1037 INTEROBSERVER RELIABILITY OF KNEE OSTEOARTHRITIS LESIONS USING MUSCULOSKELETAL ULTRASOUND: DIFFERENCES BETWEEN STATIC VERSUS REAL TIME READING

M.J. Audisio[1], A.M. Bertoli[2], G.E. Py[1]. *[1]Reumatología, DHEG; [2]Reumatología, Instituto Strusberg, CORDOBA, Argentina*

Background: Musculoskeletal ultrasound (MSU) is an imaging technique proved to be valid in several musculoskeletal conditions. In osteoarthritis (OA) it allows the identification of inflammation and structural damage. However, MSU is an operator dependent method and its widespread use has been hampered by questions related to the reliability of both, image acquisition and image interpretation.
Objectives: The objective of this study was 1) to evaluate the interobserver reliability of knee OA according to the definitions used by the OMERACT reliability exercise of inflammatory and structural abnormalities in patients with knee osteoarthritis using ultrasound and 2) to compare the interobserver reliability on previous collected images (static reading, thereafter) versus after the acquisition and interpretation of images in real time (real time reading, thereafter).
Methods: A reliability exercise based on the reading of US images was conducted by two experienced rheumatologists in MSU. A set of 59 images of both, normal and OA knee lesions were collected for the static reading. A set of 20 knees were scanned by each rheumatologist for the real time reading. Dichotomous and semi-quantitative scoring (0–3) was performed for the presence of damage on the condrosynovial margin, osteochondral margin and matrix of the throchlear cartilage, osteophytes at the lateral and medial femoral condyle and proximal tibia, medial and lateral meniscal extrusion and Baker's cyst. Interobserver reliability was calculated by the Cohen's kappa coefficient.
Results: Interobserver reliability scores for the static reading were good for cartilage damage, meniscal extrusion and Baker's cyst, while they were excellent for the presence of osteophytes. The scores for the real time reading were poor to moderate for cartilage damage, osteophytes and Baker's cyst and good for meniscal extrusion. These results are shown in Table 1.

Table 1. Interobserver κ values for agreement of the static and real time reading of US abnormalities in knee osteoarthritis

Lesion	Static reading κ (SE)	Real time reading κ (SE)
Condrosynovial margin	0,588 (0,180)	0,588 (0,180)
Cartilage matrix	0,732 (0,118)	0,317 (0,143)
Osteochondral margin	0,658 (0,148)	0,251 (0,163)
Medial condyle osteophyte	0,538 (0,176)	0,412 (0,213)
Lateral condyle osteophyte	0,792 (0,194)	0,385 (0,228)
Medial tibial osteophyte	0,865 (0,129)	0,490 (0,96)
Lateral tibial osteophyte	0,744 (0,236)	0,432 (0,213)
Medial meniscal extrusion	0,673 (0,204)	0,704 (0,159)
Lateral meniscal extrusion	0,633 (0,234)	0,573 (0,185)
Baker's cyst	0,714 (0,256)	0,490 (0,960)

Conclusions: This exercise shows that the interobserver reliability of MSU for the detection of knee OA lesions is widely different depending on the type of reading (static versus real time). Although MSU seems to be reliable for the detection of knee OA lesions, caution needs to be taken in the interpretation of published data regarding the type of reading exercise performed.
References:
[1] Ann Rheum Dis 2016;75:842–846.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3863

AB1038 INFLUENCE OF AGE ON ENTHESIS IN TUNISIAN PEOPLE: AN ULTRASOUND STUDY

K. Ben Abdelghani[1], M. Chammakhi[1], A. Fazaa[1], S. Rejaibi[2], S. Kassab[1], S. Chekili[1], A. Laatar[1]. *[1]Rheumatology, Hopital Mongi Slim; [2]Epidemiology, Faculty of Medicine of Tunis, Tunis, Tunisia*

Background: By aging, many changes occur in the different components of the locomotor system, leading to a pathological situation such as osteoarthritis or remaining totally asymptomatic.
Objectives: The aim of the current study was to compare,via ultrasound, the entheseal changes in two groups of people having different ages by calculating a modified Madrid sonography enthesitis index.
Methods: The study was conducted in the rheumatology department of Mongi Slim hospital in Tunisia, between June 2015 and December 2016, including 17 healthy subjects. We indentified two groups: (G1) 9 persons aged >50 years [51–68] and (G2) 8 persons aged ≤50 years-old [37–50].
All the included persons underwent an enthesis ultrasound exploration (Esaote-MyLab 60 machine and a 13–18 MHz linear array transducer) by a rheumatogist

experimented in ultrasound. Five enthesis locations bilaterally (distal Achilles tendon, distal andproximal patellar ligaments, distal quadriceps, and brachial triceps tendons) in each person were explored.The following elemental lesions of enthesis were evaluated: thickness, presence of calcifications, erosions,enthesophyte, loss of fibrillar patternand power Doppler signal.
The calculated index was compared by Mann-Whitney U test between cases and controls. The significance level was set at 5%.
Results: In our study population, the median age was 51.8±2.3 years and the median body mass index was 30±1 kg/m^2. This last was similar between the two groups. All included subjects were female.
The total enthesitis index was higher in G1 (6.67±0.91)than G2 (3.50±0.73) with a statistically significant difference (p=0.01).
Considering each evaluated enthesis, the distal patellar ligament score was significantly higher in the G1 (1.67±0.55 vs 0.25±0.16 with p=0.03). For the other enthesis, there was no significantly difference between the 2 groups.
Conclusions: The distal patellar ligament enthesis changes shown in older persons may be the traduction of a silent-stage of knee osteoarthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6630

AB1039 RELATIONSHIPS BETWEEN SONOGRAPHIC AND ELECTROPHYSIOLOGICAL MEASURES IN PATIENTS WITH IDIOPATHIC CARPAL TUNNEL SYNDROME WAITING FOR SURGERY

M. Valls Roc[1], E. Junyent Vilanova[2], A. Grau Martin[3], O. Codina Guinó[1], M. Sala Gomez[1]. *[1]Rheumatology; [2]Traumatology; [3]Internal Medicine, HOSPITAL of FIGUERES, Girona, Spain*

Background: Sonography is a diagnostic tool with great development in diagnosing entrapment neuropathy. It's an easy, painless, fast, non-invasive technique and can explore how the nerve's morphology and pathologies are associated. An electroneurogram is used to assess the intensity of nerve involvement.
Objectives: To determine the relationship between the intensity of nerve involvement by electroneurogram and the measurement of the cross-sectional area (CSA) of the median nerve by sonography in patients with idiopathic carpal tunnel syndrome (CTS) waiting for surgery.
Methods: 56 wrists of 39 consecutive patients waiting for surgery were tested, however 5 were excluded because were found to have anatomic variants (4 bifid nerves, 2 median arteries) and 1 fybrolipoma. Therefore, the final sample was 51 wrists of 37 consecutive patients (11 male and 26 females), with a mean age of 59.2 years (26–85), all with electrophysiologically confirmed idiopathic CTS. Patients were classified by their electrophysiologic grade. The median nerve cross-sectional area at proximal and distal carpal tunnel was measured using high frequency ultrasound.
Relationships between CSA, the severity of the electrophysiologic grade and the duration of symptoms were analysed. Also, a median nerve morphological characteristics examination (hipoecogenicity, loss of fascicular structure, Power Doppler signal and anatomical variants) was undertaken.
A comparison between CSA and the severity of the electrophysiologic grade was made using an independent T test and the connection between CSA and the duration of symptoms was calculated using ANOVA test.
Results: Patients were classified by their electrophysiologic severity grade (8 mild, 13 moderate, 29 severe and 1 very severe). The mean ultrasound area of distal medial nerve was 8.7 mm^2 in mild-moderate and 9.2 mm^2 in severe-very severe cases (p=0.52). The average of proximal CSA was 11.6 mm^2 in mild-moderate and 14.1 mm^2 in severe-very severe cases with statistical signification differences (p=0.026). Relationship between CSA and symptom's duration wasn't identified. In 89.2% of the cases, hipoecogenicity and the loss of fascicular structure were observed but no cases were found to show positive Power Doppler signal.
Conclusions: The most valid and relevant parameter regarding the electroneurogram in the diagnosis of CTS is CSA at proximal carpal tunnel by sonography. A cross-sectional area measuring more than 9–10 mm^2 has been suggested to be pathologic and our study confirms these results. While the electroneurogram is the gold-standard method in the diagnosis of nerve involvement severity, a sonography could improve the diagnostic sensibility and give information about nerve's morphology and associated pathologies.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4214

AB1040 CLINICAL UTILITY OF BONE SCINTIGRAPHY FOR INFLAMMATORY ARTHRITIS

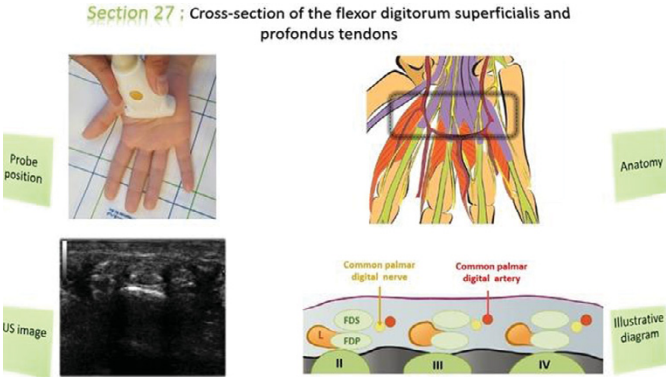
M. Jiang, K. Le Marshall, K. Lim. *Department of Rheumatology, Western Health, Footscray, Australia*

Background: Bone scintigraphy is often used in the workup of patients with rheumatological disease, in particular for the investigation of inflammatory arthritis. It also has a role in the investigation of malignancy and fractures. As an imaging technique, it is very sensitive but not specific for inflammation. The most common technique used is triple phase scintigraphy, with the 2nd phase (blood pool phase) being the most useful for identifying inflammation.
Objectives: To evaluate the clinical utility of bone scintigraphy in the workup of patients with rheumatological disease, in particular for inflammatory arthritis.
Methods: This was a retrospective study of patients seen in the rheumatology outpatients between January 2011 and July 2014, who had bone scintigraphy as part of their workup. Their clinical record was reviewed to obtain pre- and post-test clinical diagnoses, bone scintigraphy reports and investigations (ESR/CRP, rheumatoid factor/CCP antibodies). For patients who had followup at one year we recorded their clinical diagnosis at this time.
Results: A total of 226 patients had bone scintigraphy, with a median age of 54 years. 63% were female.
The main indication for bone scintigraphy was to assess for inflammation in 194 patients. For this group, the most common pre-test diagnosis of inflammatory arthritis (41%), followed by degenerative arthritis (36%), unclear diagnosis (20%) and mixed inflammatory and degenerative arthritis (3%).
Overall, 49% (n=95) of patients had their diagnosis changed after bone scintigraphy.
The pre-test diagnosis was compared to bone scintigraphy findings with the highest confirmatory rate for degenerative arthritis (67%), followed by inflammatory arthritis (49%) and mixed arthritis (40%).
Bone scintigraphy findings were also compared to post test diagnosis with the highest confirmatory rate for degenerative arthritis (91%), followed by inflammatory arthritis (70%) and mixed arthritis (14%).
There was no significant association between patient factors (age, gender, ESR/CRP, RF/CCP) and having confirmatory or conflicting bone scintigraphy findings.
The post test diagnosis was compared to the diagnosis at one year, with the diagnosis being unchanged in 84% for inflammatory arthritis and 45% for degenerative arthritis.
Conclusions: This study showed that bone scintigraphy lead to a change in diagnosis in a large proportion of patients and was better at confirming degenerative arthritis or ruling out inflammatory arthritis.
References:
[1] De Leonardis F, Orzincolo C, Prandini N, Trotta F. The role of conventional radiography and scintigraphy in the third millennium. Best practice & research Clinical rheumatology. 2008;22(6):961–79.
[2] Kim JY, Cho SK, Han M, Choi YY, Bae SC, Sung YK. The Role of Bone Scintigraphy in the Diagnosis of Rheumatoid Arthritis According to the 2010 ACR/EULAR Classification Criteria. Journal of Korean Medical Science. 2014;29(2):204–9.
[3] Sudoł-Szopińska I, Ćwikła JB. Current imaging techniques in rheumatology: MRI, scintigraphy and PET. Polish Journal of Radiology. 2013;78(3):48–56.
[4] Al-Janabi M. Imaging modalities of the painful wrist: the role of bone scintigraphy. Rheumatology (Oxford, England). 2002;41(10):1085–7.
Acknowledgements: I would like to acknowledge Sara Vogrin (University of Melbourne) for her assistance with statistical analysis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4591

AB1041 ULTRASONOGRAPHY OF NORMAL MUSCULOSKELETAL STRUCTURES IN 100 SECTIONS: A BOOKLET AND A CD-ROM

M.A. Mahdi, H. Rkain, M. Erraoui, S. Aktaou, L. Tahiri, R. Bahiri, F. Allali, N. Hajjaj-Hassouni. *Rheumatology, Faculty of Medicine and Pharmacy, University Mohamed V, Rabat, Morocco*

Objectives: To present a booklet and a CD-ROM with a mini-atlas including 100 sections illustrating the normal ultrasound musculoskeletal anatomy.
Methods: We performed an ultrasound examination of large and small joints of the medical staff not suffering from any musculoskeletal disorder. Ultrasound examination was performed using a high-frequency linear probe (Toshiba Xario®, frequency (8–14 MHz)) in B mode. Finally, for the sake of clarity of the presentation of this library, we presented each image accompanied with another showing the valid positioning of the probe and an annotated schema for each section made.
Results: We present in the form of CD-ROM and booklet a photo library of a mini-atlas.



The joints studied are:
- The wrist and hand
- The elbow
- The shoulder
- The ankle and foot
- The knee
- and the hip

100 sections were performed, we presented them together with images showing ther normal corresponding musculoskeletal anatomy, the valid positioning of the probe, and also an annotated schema corresponding to each section. We give here below the example of a section illustrating a cross-section of flexor digitorum superficialis and profondus tendons

Conclusions: We hope that we give to rheumatologists a simple tool to recall and standardize the practice of musculoskeletal ultrasound. We intend to enrich it, in the future, with the pathological images and interventional ultrasound videos.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4514

AB1042 DYNAMIC CONTRAST-ENHANCED MAGNETIC RESONANCE IMAGING IN A RANDOMIZED PLACEBO-CONTROLLED RHEUMATOID ARTHRITIS TRIAL – IMPACT OF APPLYING JOINT COVERAGE QUALITY CRITERIA

M.B. Axelsen[1], H. Bliddal[2], L.T.H. Jacobssen[3], M.S. Hansen[4], A. Dudek[5], M. Rell-Bakalarska[6], M. Boesen[7], J. Stefanek[8], B. Sundman-Engberg[9], M. Østergaard[1]. *[1]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Centre of Head and Orthopedics, Rigshospitalet; [2]The Parker Institute, Hospital Frederiksberg-Bispebjerg, Copenhagen, Denmark; [3]Department of Rheumatology and Inflammation Research, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden; [4]Center for Rheumatology and Spine Diseases, Rigshospitalet, Gentofte, Denmark; [5]Centrum Medyczne MEDENS S.C., Wojewodztwo slaskie; [6]Rheumatology, Rheumatology, Poland, Poland; [7]Department of Radiology, The Parker Institute, Hospital Frederiksberg-Bispebjerg, Copenhagen, Denmark; [8]UCB Biosciences GmbH, Monheim, Germany; [9]UCB Pharma AB, Stockholm, Sweden*

Background: Dynamic contrast-enhanced MRI (DCE-MRI) has been proposed for evaluating treatment response in RA. In a 16-week anti-TNF trial, DCE-MRI measures of inflammation analyzed for regions of interest (ROIs) covering MCP joints 2–5 and PIP joints 2–5 detected improvements at week 16, but not at earlier time point[1].

Objectives: To investigate if solely analyzing joints fulfilling predefined MRI quality criteria for joint visualization would increase the responsiveness and discrimination between treatments of DCE-MRI.

Methods: Patients with active RA despite stable DMARD therapy for ≥12 weeks were randomized 2:1 to certolizumab pegol (CZP) or 2 weeks of placebo (PBO) followed by CZP (CZP+PBO). MRIs were obtained at weeks 0 (baseline), 1, 2, 4, 8 and 16. Only joints fulfilling MRI joint quality criteria (≥3MCP/≥2PIP joint slices including the distal and/or the proximal bone of the joint and part of the joint cavity) were included in analyses. ROIs covering each joint were analyzed for number of enhancing voxels (Nvoxel), initial rate of enhancement (IRE) and maximum enhancement (ME) using the DYNAMIKA software (Image Analysis, UK).

Results: For 38 (CZP: 26; PBO+CZP: 12) of the 40 randomized patients, ≥1 joint fulfilled the quality criteria at baseline. 31 MCP2, 28 MCP3, 23 MCP4, 7 MCP5, 29 PIP2, 29 PIP3, 28 PIP4 and 12 PIP5 joints were included. No individual joints showed significant changes over time or differences between groups. Analyses by joint group (MCP2–4 and PIP2–4) had few data available. Nvoxel and ME decreased numerically, but not significantly, for PIP2–4.

Conclusions: There were no statistically significant changes in DCE-MRI on joint level or joint group level or between groups. Applying strict joint coverage quality criteria compromises the statistical power of the DCE-MRI analyses underlining the importance of standardization of the method.

References:

[1] Østergaard. Arthritis Rheum 2014;66(Suppl. 10):518.

Disclosure of Interest: M. B. Axelsen Grant/research support from: UCB Nordic funded the study, H. Bliddal Grant/research support from: UCB Nordic, L. T. H. Jacobssen Consultant for: Abbvie, Celegen, MSD, Novartis and UCB, M. Hansen: None declared, A. Dudek: None declared, M. Rell-Bakalarska: None declared, M. Boesen Consultant for: Chairman of the clinical advisory board Image Analysis, LTD London, J. Stefanek: None declared, B. Sundman-Engberg: None declared, M. Østergaard Grant/research support from: and/or speaking/consultant fees: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli-Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, and Wyeth

DOI: 10.1136/annrheumdis-2017-eular.1946

AB1043 RHEUMATOID FACTOR ISOTYPES – STILL AN USEFUL TOOL IN THE DIAGNOSIS OF RHEUMATOID ARTHRITIS?

M. Guerra[1], R. Vieira[1], A.P. Cruz[2], T. Videira[1], P. Pinto[1]. *[1]Department of Rheumatology; [2]Department of Clinical Pathology, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal*

Background: Rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) are key serologic markers in the diagnosis of Rheumatoid Arthritis (RA) included in the 2010 ACR/EULAR diagnostic criteria. Determination by enzyme-linked immunosorbent assay (ELISA) allows RF isotypes' quantification (IgG, IgA and IgM), improving diagnostic accuracy [1,2].

Objectives: To assess the clinical value of RF-IgG/IgA/IgM (ELISA) in the diagnosis of RA, in comparison to RF-IgM (nephelometry).

Methods: A population of RA outpatients fulfilling the 2010 ACR/EULAR diagnostic criteria was cross-sectionally evaluated. Data on demographic and clinical characteristics was collected. RF-IgG / IgA / IgM (ELISA, Orgentec®), RF-IgM (nephelometry, Siemens®) and ACPA-IgG (ELiA, ThermoFisher®) were measured. Values three times or more above the upper limit of normal were considered high-positive (in agreement to 2010 ACR/EULAR diagnostic criteria).

Results: A total of 87 patients (70.1% female) were included, with a mean (SD) age of 57.3 (12.29) years. Median time of disease evolution was 6 years, ranging from 0 to 37 years. Erosions were present in 50.6% (N=44). RF-ELISA was positive (at least one isotype increased) in 85.1% (N=74); the most frequent isotype was IgM (70.1%;N=61) and the most frequent combination was IgG, IgA and IgM positivity (46.0%;N=40) (table1). FR-nephelometry and ACPA were positive in 58.6% (N=51) and 47.1% (N=41), respectively.

Comparing the two RF methods, 56.3% (N=49) were both RF-nephelometry and RF-ELISA positive; 28.7% (N=25) were RF-ELISA positive and RF-nephelometry negative, and only 2.3% (N=2) verified the opposite (p=0.001). As for RF high-positivity, 4.6% (N=4) of the 87 patients were only RF-nephelometry high-positive, 9.2% (N=8) only RF-ELISA high-positive and 34.5% (N=30) both high-positive ($p<0.001$).

In the RF-nephelometry negative population (N=36), ACPA and RF-ELISA were both positive in 11.1% (N=4). Only 8.3% (N=3) were solely ACPA positive and 58.3% (N=21) solely RF-ELISA positive, however without statistical significance.

Considering the ACPA negative population (N=46), 32.6% (N=15) were both RF

Table 1. Frequencies of RF-ELISA isotypes' profiles

Profile	n	%
IgG–IgA–IgM–	13	14,9
IgG+IgA–IgM–	1	1,1
IgG+IgA+IgM–	4	4,6
IgG+IgA?IgM+	1	1,1
IgG+IgA–IgM+	12	13,8
IgG+IgA+IgM+	40	46,0
IgG–IgA+IgM+	5	5,7
IgG–IgA–IgM+	3	3,4
IgG–IgA+IgM–	8	9,2

Abstract AB1042 – Table 1. Baseline values of and changes in DCE-MRI parameters for MCP2–4 and PIP2–4

	Baseline	Change week 0–week 1	Change week 0–week 2	Change week 0–week 4	Change week 0–week 8	Change week 0–week 16
Median change [number]	PBO+CZP/CZP	PBO+CZP/CZP	PBO+CZP/CZP	PBO+CZP/CZP	PBO+CZP/CZP	PBO+CZP/CZP
Nvoxel						
MCP2–4	295/131	NA/-503	62/0	NA/0	90/53	NA/-473
	[5]/[12]	[1]/[4]		[1]/[5]	[2]/[4]	[1]/[5]
PIP2–4	108/144	-35/0	-56/-12	-80/-75	-69*/10	-32/-12
	[8]/[15] [3]/[6]	[5]/[7]	[5]/[4]	[7]/[10]	[5]/[8]	
IRE						
MCP2–4	0.000/0.004	NA/0.000	0.006/0.00	NA/0.000	0.273/-0.023	NA/0.002
	[4]/[9]	[0]/[3]	[2]/[2]	[0]/[4]	[2]/[2]	[0]/[5]
PIP2–4	0.013/0.006	-0.002/-0.001	0.000/0.001	0.003/0.000	0.014*/0.000	0.000/0.023
	[8]/[10]	[2]/[3]	[5]/[5]	[5]/[3]	[5]/[5]	[4]/[2]
ME						
PIP2–4	0.013/0.006	-0.002/-0.001	0.000/0.001	0.003/0.000	0.014*/0.000	0.000/0.023
	[8]/[10]	[2]/[3]	[5]/[5]	[5]/[3]	[5]/[5]	[4]/[2]
PIP2–4	1.76/1.99	-0.16/-0.30	-0.17/0.02	-0.23/0.03	-0.02/-0.01	-0.19/-0.12
	[8]/[10]	[2]/[3]	[5]/[5]	[5]/[3]	[5]/[5]	[4]/[2]

NA: Not applicable. Difference between time points: Wilcoxon Signed Ranks test: *$p<0.05$.

positive; 45.7% (N=21) were RF-ELISA positive and RF-nephelometry negative and 4.3% (N=2) the opposite, without a statistical significance.
Conclusions: ELISA is superior to nephelometry detecting RF in patients with RA, as also in quantifying high-positive values.
References:
[1] Routine measurement of IgM, IgG, and IgA rheumatoid factors: high sensitivity, specificity, and predictive value for rheumatoid arthritis. Swedler W, Wallman J, Froelich CJ, Teodorescu M. J Rheumatol, 1997 Jun;24(6):1037–44.
[2] Is rheumatoid factor still a superior test for the diagnosis of rheumatoid arthritis? Singh U, Vishwanath A, Verma PK et al. Rheumatol int, 2010 June; 30(8):1115–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2606

AB1044 EVALUATION OF A FLUOROENZYME IMMUNOASSAY (ELIA-CTD) IN THE SCREENING OF PATIENTS SUSPECTED FOR AUTOIMMUNE CONNECTIVE TISSUE DISEASES

M. Elkhalifa[1], R. Abdulhadi[1], H. Ramadan[1], S. Barrientos[1], S. Saleh[1], O. Alsaed[2], A.-W. Al-Allaf[2]. *[1]Laboratory Medicine and Pathology; [2]Medicine, Hamad Medical Corporation, Doha, Qatar*

Background: Detection of auto-antibodies directed against nuclear antigens (antinuclear antibodies or ANA) have important diagnostic and prognostic implications in connective tissue diseases (CTD). The conventional indirect immunofluorescence assay on HEp-2 cell line (ANA-IIF) is the most commonly used method to detect ANA. The ANA-IIF can be labor intensive and suffers from lack of specificity.
Objectives: To evaluate the utility of a new fluoroenzyme Immunoassay "EliA-CTD" as an alternative for screening patients suspected for autoimmune connective tissue diseases.
Methods: Sixteen Hundread (1600) consecutive patients' sera submitted for anti-nuclear antibodies were tested using the ANA-IIF (Diasorin S.P.A, Saluggia, Italy) and the new EliA-CTD screen (Phadia GmbH, Frieiburg, Germany). ANA testing was ordered by both primary and secondary care physicians. The EliA-CTD screening assay is a fluoroenzyme immunoassay which is performed on the Phadia-250 automated platform. The EliA–CTD assay contains ANA-targeted recombinant antigens including dsDNA, Sm-D, Rib-P, PCNA, U1-RNP (70, A, C), SS-A/Ro, SS-B/La, Centromere B, Scl-70, Fibrillarin, RNA Polymerase III, Jo-1, Mi-2, and PM-scl. The test results are expressed as ratio, with >1.0 considered positive. For ANA-IIF, the cut off for positive results was 1:40 or greater. Additionally, further testing for dsDNA and other extractable nuclear antigens (ENA) was undertaken on a subset of sera that were ANA-IIF+ or whenever there was discrepancy between the two methods.
Results: The overall agreement between the two methods was 84.2%. Three hundread and eight (308) out of 1600 (19.3%) samples tested positive by ANA-IIF positive as compared to 101/1600 (6.6%) for the EliA-CTD assay. Additional testing showed that 105 samples were positive for ENA including dsDNA. Of those, 101 were EliA-CTD positive and 81 were ANA-IIF positive. By incorporating the ENA results, the calculated sensitivity and specificity for the EliA-CTD were 97.1% and 99.7% respectively with positive and negative predictive values for the EliA-CTD assay of 96.1% and 99.8%, respectively. The corresponding sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the ANA-IIF assay at different dilutions is shown below:

Titer	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
≥1:40	77.7	84.8	26.0	98.2
≥1:80	60.3	95.3	32.4	98.4
≥1:160	57.4	97.4	41.3	98.4
≥1:320	46.5	98.7	48.8	98.5

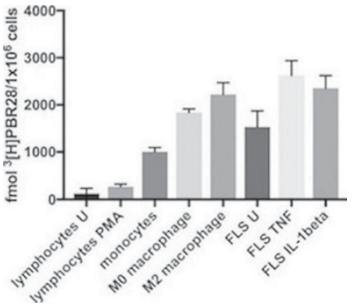
Conclusions: The new automated EliA-CTD assay shows superior sensitivity and specificity compared to the conventional labor intensive ANA-IIF. The EliA-CTD can be used as an upfront screening tool for connective tissue diseases. Depending on the clinical details, any EliA-CTD positive results could be reflexly followed by additional testing including ANA-IIF testing to elucidate the titer and pattern.
References:
[1] Hayashi N, Kawamoto T, Mukai M, Morinobu A, Koshiba M, Kondo S, Maekawa S, Kumagai S. Detection of Antinuclear Antibodies by Use of an Enzyme Immunoassay with Nuclear HEp-2 Cell Extract and Recombinant Antigens: Comparison with Immunofluorescence Assay in 307 Patients. Clinical Chemistry 2001; 47(9):1649–1959.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2679

AB1045 MACROPHAGE TARGETED POSITRON EMISSION TOMOGRAPHY (PET) FOR THE IMAGING OF INFLAMMATORY ARTHRITIS; AN IN VIVO AND IN VITRO INVESTIGATION OF TRANSLOCATOR PROTEIN (TSPO) TRACER UPTAKE

N. Narayan[1], H. Mandhair[1], C. Coello[2], A. Saleem[2], A. Sabokbar[1], P. Taylor[1]. *[1]Nuffield Dept of Orthopaedics, Rheumatology, Musculoskeletal Sciences, University of Oxford, Oxford; [2]Imanova Centre for Imaging Sciences, London, United Kingdom*

Background: TSPO targeted PET tracers are increasingly recognised as cellular imaging markers of macrophage infiltration, due to the high expression of TSPO on activated macrophages. Previous work demonstrated the ability of [^{11}C]PK11195 TSPO PET to detect subclinical inflammation in RA, and predict flare in both those with established RA and ACPA positive arthralgia. However, high background uptake of [^{11}C]PK11195 in bone, and inability of [^{11}C]PK11195 to detect lesions in AS has driven the investigation of newer TSPO tracers for the detection of inflammatory arthritis.
Objectives: Here, we present data confirming the ability of the TSPO tracer [^{11}C]PBR28 to detect and quantify synovitis in both RA and PsA, and in vitro work that assesses more fully what TSPO tracer accumulation in inflamed synovium actually reflects at a cellular level, especially considering TSPO is ubiquitously expressed.
Methods: 10 patients (5 with RA, 5 with PsA) with evidence of inflammation in one or both knees (as confirmed by clinical examination and US) and 4 healthy volunteers underwent PET/CT both knees using the TSPO tracer [^{11}C]PBR28. Arthritis patients underwent synovial biopsy of one knee within 7 days of scan. Healthy synovium was obtained from patients undergoing knee arthroscopy for ligamentous injury. Synovial tissue was stained for CD68, CD163 and TSPO. For in vitro work, human monocytes, lymphocytes and synovial FLS from RA patients were harvested, and macrophages differentiated from monocytes. RNA was extracted for PCR. Other cells underwent density centrifugation to extract the cytoplasmic cell fraction, and a radioligand binding assay with [^{3}H]PBR28 was undertaken, to assess tracer binding to TSPO in each cell type
Results: Tracer uptake correlated significantly with severity of inflammation on clinical examination and ultrasound, as did synovial sublining staining for CD68, TSPO and CD163 (see table 1). There was negligible staining for all stains in healthy control synovium. qPCR demonstrated highest TSPO mRNA in stimulated FLS (fold change 62.75±10.03) and M2 macrophages (60.69±2.38), with lymphocytes having the least TSPO expression. PBR28 saturation binding confirmed these findings at protein level (see graph 1).

Tissue marker	Clinical synovitis severity		
	1 (mild)	2 (moderate)	3 (severe)
TSPO	1.50±0.08	2.19±0.19	3.06±0.12
CD68	2.17±0.3	2.42±0.21	2.96±0.05
CD163	1.61±0.03	2.19±0.1	2.81±0.04



Conclusions: Our data demonstrates that the TSPO tracer PBR28 is capable of detecting and quantifying synovitis in RA and PsA. PBR28 tracer uptake correlates with macrophage marker staining, but not with fibroblast marker staining in our patient cohort. mRNA and protein data demonstrate, however, that there is a similar expression of TSPO in activated macrophages and activated FLS, hence TSPO tracer accumulation is as likely to represent FLS activation as it is macrophage activation.
References:
[1] Gent YY et al. Macrophage positron emission tomography imaging as a biomarker for preclinical rheumatoid arthritis: findings of a prospective pilot study. Arthritis Rheum 2012; 64:62–6.
[2] Gent YYJ et al. Subclinical synovitis detected by macrophage PET, but not MRI, is related to short-term flare of clinical disease activity in early RA patients: an exploratory study. Arthritis Res Ther 2015; 17:266.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1838

AB1046 COULD SERUM TWEAK LEVEL BE AN INDICATOR OF SUBCLINICAL ATHEROSCLEROSIS IN RHEUMATOID ARTHRITIS?

M. Ucer[1], N. Yilmaz[2], B. Cengiz Elcioglu[3], T. Sahin[3], P. Gun Atak[4], S. Yavuz[2]. *[1]Internal Medicine; [2]Rheumatology; [3]Cardiology; [4]Biochemistry, Istanbul Bilim University, Istanbul, Turkey*

Background: TWEAK is a type 2 transmembrane glycoprotein of TNF family that has multiple functions such as angiogenesis, regulation of tissue production-

destruction, proinflammatory cytokine release. TWEAK and Fn14 receptor interaction has an important role in pathogenesis of atherosclerosis. Our aim was to evaluate subclinical atherosclerosis and its association with serum sTWEAK, Fn14 and CD163 levels in RA patients.
Methods: One hundred Rheumatoid Arthritis (RA), 50 Spondyloarthritis (SpA) patients and 50 healthy controls (HC) were included in the study. Serum soluble TWEAK, CD163 and Fn14 levels were measured by ELISA tecnique. Subclinical atherosclerosis was evaluated by echocardiography, which includes carotis intima media thickness (cIMT), aortic strain, stiffness and elasticity.
Results: In RA group 73 (73%) patients were using DMARD's and 27 (27%) were biological drugs, the mean DAS28 score was 3.49±1.31. At the end of the study, TWEAK levels were found significantly lower (RA; 942.4±305.9, AS; 1087.2±311.0 and HC; 1061.3±402.8 pg/ml, p=0.05), and Fn14 levels were significantly higher (RA; 509.4±861.4, AS; 163.5±249.0 and HC; 91.5±67.9 pg/ml, $p<0.01$) in RA patients compare to both groups. In addition Fn14 levels were higher in RA patients using biological drugs and seropositive subgroups (1042±1363 vs. 312±451 pg/ml, $p<0.01$ and 674±101 vs. 188±236 pg/ml, respectively, $p<0.01$). Fn14 levels were correlated with disease duration (r=0.38, $p<0.01$). CD163 levels were similar in all groups. Although there was not any difference in cIMT measurements among groups, aortic stiffness was increased (p=0.03), aortic strain and elasticity were decreased (p=0.03, p=0.02) in RA patients compare to healthy controls. Multivariate analysis showed cardiovascular parameters were only associated with age.
Conclusions: In this study we observed impaired aortic parameters showing subclinic atherosclerosis in RA patients. At the same time, decreased levels of serum sTWEAK and elevated levels of serum sFn14, were also shown in RA group. The difference in levels of serum soluble form of these biomarkers may be related to vascular damage in our RA patients who have low disease activity. However, further studies are needed to demonstrate association between atherosclerosis and these biomarkers in RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2267

AB1047 CAN THE ACR/EULAR 2010 CLASSIFICATION CRITERIA BE USED AS DIAGNOSTIC TOOL FOR RHEUMATOID ARTHRITIS IN REAL LIFE?

N.F.L. Conijn[1], D. Lopes Barreto[1], T.M. Kuijper[1], M. van der Steen[2], J. van der Kooij[3], A.E.A.M. Weel[1], J.M.W. Hazes[4], M.R. KoK[1]. *[1]Rheumatology; [2]Business intelligence; [3]Planning and Control, Maasstad hospital; [4]Rheumatology, Erasmus Medical Center, Rotterdam, Netherlands*

Background: To date, due to the large variability in its clinical manifestations, early identification of rheumatoid arthritis (RA) relies on practice-based evidence. Moreover, this variation hampers the comparability and accurate stratification of the base population within and between RA trials. In 2010 the ACR/EULAR working group developed RA classification criteria that were primarily intended for research purposes. Despite its use in scientific settings, one can speculate on the effectiveness of these criteria when used in the routine clinical practice of diagnosing RA.
Objectives: In this study we aimed to investigate the degree of concordance between the diagnosis of RA in routine clinical practice and the ACR/EULAR 2010 classification criteria.
Methods: All patients who received a diagnosis of RA between 2010–2016 within our hospital were identified according to the financial diagnosis treatment combination (DTC) code, which corresponds to the ICD-10. Clinical and demographic data were extracted from our digital patient records of which 10% of the data were cross-checked by random selection. In retrospect we collected variables at time of RA diagnosis such as: number and type of swollen/painful joints, inflammatory markers, rheumatoid factor (RF), anti-citrullinated protein antibody (ACPA), disease duration and patients primary/secondary/tertiary diagnosis according to the rheumatologist. Additionally, all patients were classified according to the ACR/EULAR 2010 criteria for RA. The degree of concordance was determined by descriptive statistics.
Results: The database included 977 patients with a DTC RA of which 673 (69%) had RA according to the rheumatologist. From the patients who were clinically diagnosed with RA, 463 (69%) fulfilled the ACR/EULAR 2010 criteria (see figure 1), this is 47% of the total DTC RA patients. The majority of the population was female (72%) and the mean age was 59. A number of 161 (24%) patients were diagnosed with RA according to the rheumatologists, but did not fulfil the ACR criteria. These patients had less inflammation, were more often RF and/or ACPA negative, and had less involved joints. About 5% of the data were missing.
Conclusions: It can be concluded that the DTC codes are not the most reliable source of information in terms of the diagnosis. There is a discrepancy between the DTC code, the diagnosis according to the rheumatologist and the classification criteria. The degree of concordance between rheumatologist and the ACR criteria is comparable to the numbers described in literature. Since in our practice aspects of the ACR classification are used for diagnostic purposes, we will investigate factors that drive the specificity. Furthermore, reasons for the ICD-10/ DTC and final diagnostic mismatch is of great importance and will be studied as well. These factors will indicate opportunities on the use of the ACR/EULAR criteria in clinical practice.
Acknowledgements: None
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5790

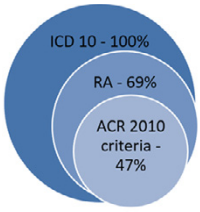


Fig. 1. Degree of concordance between RA identification and diagnosis, and classification criteria. RA refers to the diagnosis RA made by the rheumatologist. As some patients with RA may have been incorrectly classified by ICD 10, the circles are not completely overlapping.

AB1048 ULTRASOUND ASSESSMENT OF CARTILAGE THICKNESS IN PATIENTS WITH HAND OSTEOARTHRITIS

O. Balueva[1], A. Sarapulova[2], O. Teplyakova[2]. *[1]Ultrasound Diagnosis, Medical Association "New hospital"; [2]Urals State Medical University, Yekaterinburg, Russian Federation*

Background: The destruction of cartilage is one of the basic mechanisms of the progression of hand osteoarthritis (HOA). Radiographic study indicates the thickness of the cartilage indirectly based on the degree of joint space narrowing (JSN). At the same time, the ultrasound (US) method allows to measure it directly.
Objectives: To determine the thickness of the cartilage in the interphalangeal joints of patients with HOA and to correlate this rate with the degree of JSN, identified by radiologic imaging.c imaging.
Methods: 45 women at the age of 45 – 75 years were included in the research. All of them were diagnosed of HOA according to the criteria of American College of Rheumatology (ACR). For each patient 8 proximal interphalangeal joints (PIP) were surveyed. The conventional radiographs (CRs) of each hand were performed for all patient in the standard frontal projection and the radiological changes were assessed using Kallman's method. Next, US investigation was carried out. The thickness of the cartilage was measured in the central part of the 2–5 proximal phalanx heads of both hands in the dorsal longitudinal view in the static image in gray- scale with the flexion position no more than 90 degrees. The cartilage is defined as a thin hypoechoic smooth layer, paralleling the contours of the articular surface. The thickness of the cartilage was defined as the distance between the subchondral bone and the surface layer of cartilage, which was the border between the cartilage and the joint cavity. In the presence of synovitis measurement of joint cartilage was carried out before the border and hypertrophic synovial if they differed in the degree of intensity of the US signal. The measurement of cartilage thickness was carried out by a conventional line, which was an exact perpendicular to the surface of the subchondral bone and parallel to the direction of US waves. Measurement was not carried out if visualization of the surface layer of cartilage was not possible. The control group consisted of 45 women 45–75 years old without HOA, but with ultrasound investigation. Data were analyzed using Statistica 10.0 and are presented as mean (standard deviation), "odds ratio" coefficient (OR) and χ 2 Pearson's correlation coefficient.
Results: 360 joints of both hands were investigated with successful measurement of the cartilage thickness of 338 (94.7%) joints. The average value of the cartilage in all PIP was 0.31 (0.11) mm. The maximum thickness of the cartilage was obtained in the 2nd PIP joints - 0.34 (0.12) mm on the right hand and 0.36 (0.14) mm on the left hand. For the control group results were 0.38 (0.11) mm and 0.37 (0.13) mm respectively. We have found a reliable relationship between the degree of JSN and cartilage thickness with the OR 1.849 (95% confidence interval 1.198 – 2.855), $\chi 2 = 7.772$, p=0.0053.
Conclusions: US reduction of the cartilage thickness is a marker of cartilage loss which is correlated with the results of radiologic examination. This makes possible to use ultrasound as an alternative method of diagnosing HOA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6512

AB1049 CLINICAL UTILITY OF AUTOANTIBODIES AGAINST EXTRACTABLE NUCLEAR ANTIGENS IN ROUTINE CARE: FREQUENCY OF REPEATED TEST REQUESTS AND DIAGNOSTIC VALUE OF ANTI-JO-1 (ANTI-HISTIDYL-TRNA SYNTHETASE)

P. Jobanputra[1], F. Malik[2], E. Derrett-Smith[1], T. Plant[3], A. Richter[4]. *[1]Department of Rheumatology, Queen Elizabeth Hospital Birmingham, Birmingham; [2]Department of Rheumatology, Epsom & St. Helier University Hospitals NHS Trust, Carshalton; [3]Department of Immunology, University of Birmingham; [4]Department of Immunology, Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom*

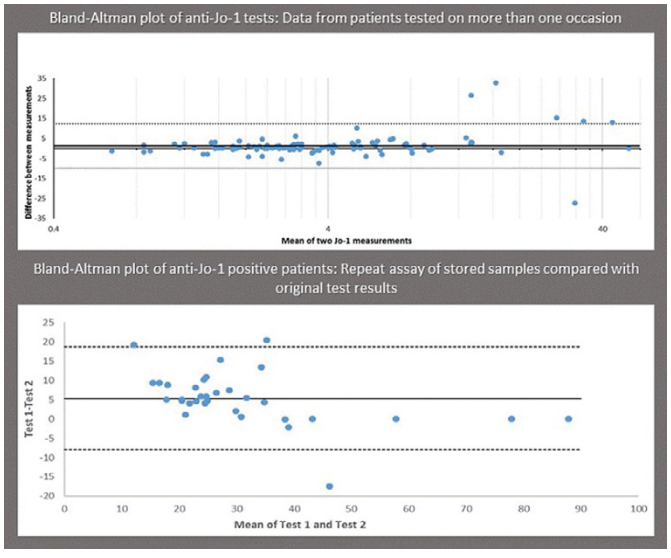
Background: High-throughput high-sensitivity ELISAs for autoantibodies associated with CTD, such as extractable nuclear antigens (ENA), are used widely. Anti-Jo-1 (anti-histidyl-tRNA synthetase), one of this panel, is believed to confer a poor prognosis due to an association with interstitial lung disease (ILD) and myositis.

Objectives: To describe: the pattern of anti-ENA positive tests; frequency of repeated requests; stability and repeatability of anti-Jo-1 tests; clinical characteristics of anti-Jo-1 +ves compared with controls; and diagnostic value of anti-Jo-1 for ILD.
Methods: All anti-ENA test requests, from any hospital department, between Jan 2013 and Dec 2014 were identified. Serum samples are screened for ENA (Quanta Lite® ENA profile, Inova Diagnostics) and positive samples have specific ENA antibodies levels quantified. Data from anti-Jo-1 positive patients and controls was extracted from electronic records allowing a minimum of 12 months after first test.
Results:

	Jo-1 Positive (n=40)	Controls (n=80)	P value*
Age, mean years (range)	53 (19–86)	52 (17–87)	–
Sex (% female)	70%	79%	0.37
Dead	13%	4%	0.12
Current or previous malignancy	10%	10%	1.0
Raynauds	17.5%	6.3%	0.10
Inflammatory arthritis	20%	19%	1.0
Clinical myositis diagnosis	5%	1.3%	0.26
CPK >1000 units/liter	5%	1.3%	0.26
Interstitial lung disease	12.5%	6%	0.30
CT chest done during study period	17/40	20/80	0.06
ANA (≥1:100)	18/38 (47.4%)	22/79 (27.8%)	0.06
RF	8/25 (32%)	12/44 (27.3%)	0.78
CCP	0/19 (0%)	3/33 (9.1%)	0.54
Anti-dsDNA (Crithidia +ve)	7.5%	1.3%	0.11
Scl70	7.5%	0%	**
SSA/Ro	10%	0%	**
SSB/La	10%	0%	**
RNP	10%	0%	**

*Fisher's exact test, two tailed. **Statistical analyses were not done on these comparisons as by definition controls were negative for ENA antibodies.

4009 samples from 3581 patients were tested. The first sample tested, chronologically, was designated test of interest. 616 (17.2%) patients were anti-ENA screen +ve, and 40 (1.1%) anti-Jo-1 +ve (>20 AU/mL). Anti-ENA tests were done more than once for 350/3581 (9.8%) patients (428/4009 (10.7%) samples) and for 7/40 (17.5%) of anti-Jo-1 +ve patients. The median interval between 1st and 2nd requests: 124 days (IQR 233 days). The Table shows data for anti-Jo-1 patients and randomly selected ENA -ve controls. The frequency of ILD, myositis and Raynaud's was comparable. Sensitivity and specificity of Jo-1 for ILD, a key feature of "anti-synthetase syndrome", were 50% (CI 19–81%) and 68% (CI 59–77%) respectively. Positive predictive value 12.5% (CI 4 to 27%) and negative predictive value 93.8% (CI 86–98%). Of patients with the highest anti-Jo1 titres (≥40 AU/mL, 10/40 patients, 25%): 3 had ILD, 1 myositis and 2 had a malignancy (disseminated melanoma and CML). Bland-Altman plots show that anti-Jo-1 values remained stable when patients were re-tested at another time but re-testing available stored samples from +ve patients showed important variation (Figure).



Conclusions: Anti-Jo-1 is uncommon in a heterogenous hospital population and is only weakly predictive for ILD. When tested repeatedly levels remain stable over many months. Repeated testing for anti-ENA is common and potentially unnecessary. Controls over repeated requests could yield cost savings.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2939

AB1050 COMPARATIVE STUDY BETWEEN ULTRASONOGRAPHIC ASSESSMENT AND CLINICAL EXAMINATION IN RHEUMATOID ARTHRITIS WITH OPTIMIZED BIOLOGICAL THERAPY AND NON BIOLOGICAL TREATMENT

R. Martínez[1], M. Fernández[1], E. Rubio[1], R. Menor Almagro[1], B. Hernández[2], J. Povedano[2]. *[1]Rheumatology, Hospital Universitario Virgen del Rocío; [2]Rheumatology, Hospital Universitario Virgen Macarena, Sevilla, Spain*

Background: In rheumatoid arthritis (RA), patients in low activity disease or clinical remission measured by disease activity indexs can present subclinical activity by ultrasound study. The ultrasonographic inflammation in examination of joints is an important predictive value of structural damage.
Objectives: The aim of our study was to describe subclinical ultrasonographics activity in patients with RA in low disease activity or clinical remission, with optimized biological therapy and non biological treatment.
Methods: Transversal and longitudinal study describing the ultrasonographic changes in gray scale and doppler in parallel with blind clinical evaluation. We included patients with RA according to ACR/EULAR classification criteria in low activity disease or remission measured by DAS28, under optimized biological therapy at least for 6 months and non biological treatment. They were sent by their usual clinician, making a random selection. They were evaluated in the same day by a rheumatologist and blind sonographer. VAS, VGP, VGM, HAQ, tender joints count, swollen joint count, CDAI, SDAI and DAS28 were evaluated. Regarding the ultrasound, were evaluated synovitis and doppler in 12 joints (wrists, second to fifth MCF and fifth bilateral MTF). The comparison between clinical examination and ultrasonography test was performed by the kappa index, with satisfactory value of >0,6.
Results: A total of 69 patients were included, 35 with optimized biological therapy and 34 non biological treatment. The median optimization time was 12 months. The baseline characteristics only offered stadistical significance in swollen joint count and average time of disease (table 1).
The concordance study between clinical joint exploration and ultrasonographic examination showed a higher kappa index in patients with optimized biological therapy: 0,52 in gray scale and 0,40 in doppler. In patients without biological therapy showed an index kappa =0.17 by the gray scale test, and kappa index =0.26 by doppler.

Table 1

Variable characteristics	Non biological treatment	Optimized biological therapy	p
Age: average ± DE (years)	53,8±10	54±11,7	0,834
Women (%)	73,5	65,7	0,498
Time of diseases progression: median (p25-p75) (months)	55 (34–116)	120 (84–139)	0,003
Rheumatoid factor + (%)	71,3	81,80%	0,544
Anti CCP + (%)	71,4	81,7	0,512
Metotrexate dose: average ± DE	9,0±1,3	8,1±1,4	0,658
Corticoids dose: average ± DE	1,7±0,4	1,5±0,4	0,856
HAQ: average ± DE	1,0±0,2	1,3±0,2	0,309
Tender joint count: median (p25-p75)	0 (0–1,5)	1 (0–2)	0,200
Swollen joint count: median (p25-p75)	0 (0–1)	1 (0–2)	0,013
CDAI: average ± DE	7,7±5,1	6,8±5	0,437
SDAI: average ± DE	10,0±5,6	10,0±6,5	0,588

Conclusions: Our results show the existing discrepancy between the clinical examination and ultrasonographic test in patients in low disease activity/remission by DAS28, even more with the use of doppler. In the comparison of both groups we observed an increase in the difference in those who did not receive biological therapy. In patients with optimized biological teraphy, with higher swollen joint count in physical examination, kappa index was near of normality in grayscale. The detection of subclinical joint damage is often undertreated, showing ultrasound as a noninvasive technique of great help reducing joint damage.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4406

AB1051 ULTRASONOGRAPHY AND POWER DOPPLER ULTRASONOGRAPHY OF KNEE JOINT IN PATIENTS WITH HEPATITIS C VIRUS RELATED ARTHRITIS

R. Elgohary[1], A. Khalil[2], G. Ragab[3]. *[1]Internal Medicine, Rheumatology & Clinical Immunology subspecialty, Kasr Alainy; [2]New Kasr El-Aini Teaching Hospital; [3]Internal Medicine, Rheumatology & Clinical Immunology subspecialty, Kasr Alainy, Cairo, Egypt*

Background: HCV is a hepato-lymphotropic virus. Chronic arthritis is one of its extrahepatic manifestations[1]. The high frequency of rheumatoid factor (RF) positivity in HCV patients makes it difficult to differentiate between rheumatoid arthritis (RA) and HCV-related arthritis (HCVrA). An accurate and early diagnosis of HCVrA is important to avoid unnecessary immunosuppressive therapy[2]. Ultrasonography provides safe and quick access for the diagnosis of many rheumatic diseases.
Objectives: To illustrate ultrasonographic findings obtained in knee joints of patients with HCVrA & to compare these findings with those obtained from knee joints of RA patients.

Methods: Fifteen patients with HCVrA & 15 RA patients were subjected to: full history, clinical examination, Ultrasonography assessment using a Philips HDI 5000 system with 12–5 MHz Broadband Linear Transducer. Both knees were examined by one ultrasonographer who was blind to clinical data.
Results: In HCVrA, synovial hypertrophy was detected in 10% of knees (3/30) of which 66% (2 knees) exhibited Doppler signals, while in RA it was detected in 70% (21/30) of which 95% (20 knees) exhibited Doppler signals. Significant difference was found between the two groups ($p<0.01$). Knee effusion was detected in 80% (24/30), & 86% (26/30), of patients with HCVrA & RA respectively, no significant difference was found. Cartilage degeneration was detected in 76% (23/30) & 83% (25/30), of patients with HCVrA & RA respectively. Bone erosions were detected in 20% (6/30) in the RA group. It was not detected in HCVrA patients. In HCVrA, there was no correlation between the presence of synovial hypertrophy with respect to cartilage degeneration and knee effusion.
Conclusions: We found no specific ultrasonographic feature specific for HCV related knee arthritis, the knee effusion is a predominant feature and the hypertrophied synovium is not frequently found. No destructive lesions were found to be related to the disease itself; however this should be confirmed by histopathological assessment.
References:
[1] Craxì Antonio, Laffi Giacomo & Zignego Anna Linda. Hepatitis C virus (HCV) infection: A systemic disease. Molecular Aspects of Medicine 2008;29:85.
[2] Rosner Itzhak, Rozenbaum Michael, Toubi Elias, Kessel Aharon, Naschitz Jochanan, and Zuckerman Eli. The Case for Hepatitis C Arthritis, Seminars in Arthritis and Rheumatism 2004;33:377–379,381–382.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4094

AB1052 QUALITATIVE SYSTEMATIC REVIEW: LACK OF CONSENSUS ON THE CLASSIFICATION CRITERIA FOR DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS

J.S. Kuperus[1], E.E. de Gendt[1], F.C. Oner[1], P.A. de Jong[2], S.C. Buckens[2], A.E. van der Merwe[3], G.J. Maat[4], E.A. Regan[5], D. Resnick[6], R. Mader[7], J.-J. Verlaan[1]. *[1]Orthopedics; [2]Radiology, University Medical Center Utrecht, Utrecht; [3]Anatomy, Academic Medical Center, Amsterdam; [4]Anatomy, Leiden University Medical Center, Leiden, Netherlands; [5]Medicine, National Jewish Health, Denver, Colorado; [6]Radiology, University of California San Diego, San Diego, California, United States; [7]Rheumatology, Ha'Emek Medical Center, Afula, Israel*

Background: Diffuse idiopathic skeletal hyperostosis (DISH) is a condition characterized by flowing ossifications of the spine with or without ossifications of entheses elsewhere in the body.[1,2] Studies on prevalence and pathogenesis of DISH use a variety of partially overlapping combinations of classification criteria, making meaningful comparisons across the literature difficult.[3,4]
Objectives: The aim of this study was to systematically summarize the criteria available to classify or diagnose DISH to aid in the development of a more uniform set of diagnostic and/or classification criteria.
Methods: A search was performed in Pubmed, Embase, Cochrane Library and Web of Science using the term DISH and its synonyms. Articles were included when two independent observers agreed that the articles proposed a new set of classification criteria for DISH. All retrieved articles were evaluated for methodological quality and the presented criteria were extracted. The criteria were placed into one of three groups being "descriptive studies", "sets of criteria for dichotomous diagnosis" or "sets of criteria with consecutive phases".
Results: A total of 24 articles met the inclusion criteria. Two articles were descriptive studies, 11 contained dichotomous classification criteria and 11 described a set of criteria with consecutive phases. In all articles spinal hyperostosis was required for the diagnosis of DISH. Peripheral, extraspinal manifestations were included as a (co-)requirement for the diagnosis DISH in five articles. Most discrepancies revolved around the threshold for the number of vertebral bodies affected and to defining different developmental phases of DISH. More than half of the retrieved articles described a dichotomous set of criteria and did not consider the progressive character of DISH.
Conclusions: In our systematic review we summarize the available different classification criteria for DISH and highlight the lack of consensus on the diagnosis of (early) DISH. Consensus criteria, including consecutive phases of new bone formation that characterize DISH can be developed based upon established diagnostic and/or classification criteria.
References:
[1] Resnick D, Niwayama G. Radiographic and pathologic features of spinal involvement in diffuse idiopathic skeletal hyperostosis (DISH). Radiology. 1976;119(3):559–568.
[2] Mader R, Verlaan J, Buskila D. Diffuse idiopathic skeletal hyperostosis: clinical features and pathogenic mechanisms. Nat Rev Rheumatol. 2013;9(12):741–750.
[3] Pillai S, Littlejohn G. Metabolic factors in diffuse idiopathic skeletal hyperostosis - a review of clinical data. Open Rheumatol J. 2014;8(1):116–128.
[4] Mader R, Buskila D, Verlaan J-J, et al. Developing new classification criteria for diffuse idiopathic skeletal hyperostosis: back to square one. Rheumatology (Oxford). 2013;52(2):326–330.
Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4656

AB1053 A NOVEL METHOD FOR IDENTIFYING RADIOGRAPHIC BASELINE RISK OF OSTEOARTHRITIS USING AN ANISOTROPY-BASED TEXTURE ANALYSIS ALGORITHM: DATA FROM THE OSTEOARTHRITIS INITIATIVE

R. Ljuhar[1], T. Haftner[2], Z. Bertalan[1], D. Ljuhar[3], A. Fahrleitner-Pammer[4], H.-P. Dimai[4], S. Nehrer[2] on behalf of Osteoarthritis. *[1]ImageBiopsy Lab, Vienna; [2]Department for Health Sciences and Biomedicine, Danube University Krems, Krems; [3]Braincon Technlogies, Vienna; [4]Division of Endocrinology and Diabetology, Medical University Graz, Graz, Austria*

Background: Osteoarthritis (OA) is the most common form of arthritis and affects disproportionately the knee. Recent developments in imaging techniques showed that OA is not just a joint disease but also involves progressive changes in the subchondral/subarticular bone area of the tibia. On top of the accepted method of measuring the joint space width, assessments of the trabecular bone structure in selected regions of interest (ROI) in conventional X-rays may be offering an alternative method for quantifying the risk and progression of this disease.
Objectives: The accepted method for assessing OA - Joint space width (JSW) and Joint Space Area (JSA) measurements - have limited capabilities in regard to early identification and reproducible follow-ups of the disease. The objective of this abstract is to evaluate the trabecular bone structure as an area for early identification of OA risk, applying texture anisotropy algorithms and subsequently comparing the results to standard JSW and JSA measurements.
Methods: This study was performed using data from the Osteoarthritis Initiative. The image data set was restricted to female, Caucasian, right knee exams recorded with the same modality. Furthermore we selected exams which had a KL grade of 0 at the baseline exam and a deteriorating KL grade $\geq$2 at the 96 month follow up. 22 cases fulfilled these criteria and we selected 22 matching controls with no signs of OA at the 96 month follow up. The selected region of interest (ROI) for the analysis of the radiographic texture consisted of four ROIs in the subchondral tibia and one additional ROI in each femur condyle – in total 6 ROIs. For each individual ROI, the degree of texture anisotropy was calculated and compared between case/control. In addition, JSW & JSA were calculated in both groups using a proprietary software-based method (ImageBiopsy Lab, Vienna, Austria).
Results: Whereas the JSW and the JSA measurements did not yield any significant differences with respect to their mean values (Cohen's d =0.139 and 0.028), the calculated texture parameters showed that differences in values between cases and controls can be found in two of the subchondral ROIs (ROI1&2) with Cohens'd values of 0.625 and 0.831, respectively. With respect to selected patient, the differences in anisotropy results were significant using these texture parameters.
Conclusions: Our results indicate that using the selected radiographic texture parameters, an early identification of patients at risk for developing OA using conventional X-rays can be achieved. This may offer an additional method for quantifying the risk of baseline OA. This is supported by the Cohen's d values that are by definition relatively large (0.625 and 0.831). Ongoing research focuses on larger sample set validation and the use of such algorithms for additional applications, such as the early identification of fracture risk.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5860

AB1054 QUANTITATIVE ULTRASOUND FOR ASSESSMENT OF DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RELIABILITY AND CONSTRUCT VALIDITY

R.P. Goswami, A. Ghosh, D. Lahiri, P. Ghosh. *Department of Rheumatology, IPGMER, KOLKATA, INDIA, Institute of Post Graduate Medical Education and Research, Kolkata, India*

Background: Joint ultrasound is an integral part of assessment of patients with rheumatoid arthritis (RA). Semi-quantitative grading of ultrasound is subjective whereas quantitative ultrasound (QUS) may be more objective.
Objectives: To evaluate the reliability and construct validity of QUS of wrist joints in patients with RA.
Methods: We studied 95 patients with RA. Following parameters were studied: swollen and tender joint counts (SJC and TJC), patient and evaluator global assessment (PGA, EGA) and disease activity score (DAS28). Patients were classified as active disease and disease in remission as per expert clinician opinion. Colour Doppler ultrasound (CDUS) of wrists was done to obtain semiquantitative grading. Scans were processed in image analysis software (Photoshop CS4) to obtain the following: colour fraction of intrasynovial (IS) vascular signals (CF(IS) = pixel area of IS vascular signals/pixel area of entire IS area (area(IS)), CF(total) (pixel area of both IS and extrasynovial vascular signals/area (IS)) and number of IS (N(IS)) and extrasynovial (N(ES)) vascular signals. Images were stored and independently rated for both CDUS and QUS by two different raters blinded to each other's rating.
Results: Demographics of patients were: mean age 48±16.7 years, mean disease duration 24 months (range 4–600), mean DAS28 of 2.98±1.18 and 40% (38/95)

had active disease. CDUS findings were: synovial proliferation: grade 1: 27.4%, grade 2: 54.7%, grade 3: 11.6%; vascularity: grade 1: 41.1%, grade 2: 32.6% and grade 3: 9.5%. Summary findings of QUS were: CF(IS): 8.6±10.63 (median 4.4), CF(total): 9.9±11 (median 5.2), median N(IS): 3 (0–26) and mean N(ES): 1.2 (0–19). Cohen's kappa for synovial proliferation was 0.402 ($p<0.001$) and vascularity was 0.605 ($p<0.001$). Intraclass correlation (ICC(1,2)) for CF(IS) was 0.996 (95% confidence interval (CI): 0.994–0.997) and ICC(1,2) for CF(total) was 0.995 (95% CI: 0.993–0.997). CF(IS) was correlated with SJC (r=0.22, p=0.029), TJC (r=0.39, $p<0.001$), PGA (r=0.5, $p<0.001$), EGA (r=0.583, $p<0.001$) and DAS28 (r=0.47, $p<0.001$); correlations for CF (total) were: SJC (r=0.25, p=0.013), TJC (r=0.41, $p<0.001$), PGA (r=0.525, $p<0.001$), EGA (r=0.515, $p<0.001$) and DAS28 (r=0.5, $p<0.001$). Significant correlations were also observed for N(IS) with SJC (r=0.282, p=0.006), TJC (r=0.411, $p<0.001$), PGA (r=0.48, $p<0.001$), EGA (r=0.514, $p<0.001$) and DAS28 (r=0.467, $p<0.001$). Spearman rank correlations of CDUS vascularity were: SJC (r=0.26, p=0.01), TJC (r=0.292, p=0.004), PGA (r=0.26, p=0.012), EGA (r=0.168, p=0.103) and DAS28 (r=0.275, p=0.007). Spearman rank correlations of CF(IS), CF(total) and N(IS) with CDUS vascularity were 0.828, 0.864 and 0.689 respectively ($p<0.001$). Cut-off values for CF(IS), CF(total) and N(IS) for distinguishing active RA from RA in remission were 4.78 (AUC: 0.82, 95% CI: 0.73–0.9), 5.75 (AUC: 0.89, 95% CI: 0.69–0.88) and 2.5 (AUC: 0.77, 95% CI: 0.68–0.86) respectively. There were 40 patients with CDUS vascularity $\geq$2 among which 62.5% (25/40) had active disease. In this group only CF(total) >5.75 could distinguish between patients with active disease from disease in remission (100% (25/25) vs., 80% (12/25), p=0.046).

Conclusions: CF(IS) and CF(total) had excellent inter-rater reliability and construct validity. Simple quantitative cutoff values could distinguish between active RA from remission.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6482

AB1055 LEUKOCYTE ESTERASE REAGENT STRIPS FOR RAPID DIAGNOSIS OF INFLAMMATORY SYNOVIAL FLUID

S. Rodríguez-Muguruza[1], S. Malumbres[2], A. Olive[3], O. Valero[4], S. Holgado[3], L. Mateo[3], M. Martínez-Morillo[3]. *[1]Rheumatology, Virgen de la Cinta Hospital, Tarragona, Spain; [2]Clinical Biochemistry Service, Germans Trias I Pujol Hospital, Barcelona, Belgium; [3]Rheumatology, Germans Trias I Pujol Hospital; [4]Department of Statistics, Automona de Barcelona University, Barcelona, Spain*

Background: The analysis of synovial fluid is an important tool for diagnosing joint disease. When synovial fluid is removed, the white cell count (WCC) decreases with time, and an inflammatory liquid could become a false non-inflammatory specimen. Reagent strip testing of urine is a valid tool for the diagnosis of urinary tract infection, via the detection of leukocyte esterase activity. It has been used for the analysis of others body fluids. Synovial fluid test at the site of arthrocentesis using reagent strips could have potential benefits as a screening tool.

Objectives: To evaluate the performance of leukocyte esterase reagent strips for diagnosis of inflammatory synovial fluid.

Methods: Prospective single center study. We analyzed synovial fluids samples collected from patients in a tertiary university Hospital (November 2015- December 2016). Synovial fluid samples were tested within 1 hour after collection. We analyzed: The presence of leukocyte esterase using the leukocyte esterase reagent strips test (originally designed for urine test, URI-Clip Test, Menarini Diagnostics). It was recorded semi quantitatively: negative, 1+ (>25 WBC/uL), 2+ (>75 WBC/uL) or 3 +(>500 WBC/uL) by comparison with a standard color chart found on the container's label. The WCC, formula, glucose level. The WCC was measured by manual leukocyte counting, using saline as diluents. Cultures were also collected. We consider + if leucocyte esterase pad was more or equal than 1+ positive. The cut-off for the WCC (>2000cells/mm^3) was used to differentiate between inflammatory and non-inflammatory specimens. We compared the WCC (reference standard diagnostic test) with the presence of leukocyte esterase using the leukocyte esterase reagent. Sensitivity (Se), specificity (Sp), PPV, NPV were determined. P-value smaller than 0.05 were considered significant.

Results: During the study period, 125 joint fluid specimens were analyzed: 56 (44.8%) mechanical and 69 (55.2%) inflammatory. Of the mechanical fluids 33 (58.9%) were negative by leukocyte esterase reagent and of the inflammatory fluids 67 (97.1%) were positive. The Se and Sp of leukocyte esterase reagent was 97.1% and 58.9% respectively. The PPV was 74.4% and NPV was 94.3%. The 2 false-negative results (negative by leukocyte esterase reagent but more than 2000 WBC/mm^3), showed a predominance of mononuclears (> =91%), the median WCC was 2 775/mm and median neutrophil percentage was 8.5%. For inflammatory fluids: semi-quantitative results (negative, 1+, 2+ and 3+) were significantly different regarding the main leukocyte, neutrophil and lymphocyte count (table).

	Negative	1+	2+	3+	p value
Total cell (cel/mm^3)	3025	18272.9	10553.5	56494.2	<0.0001
Leukocyte (cel/mm^3)	2775	12907.1	8528.8	30870.2	<0.0001
Lymphocyte (%)	91.5	50.4	21.61	6.4	<0.0001
Neutrophil (%)	8.5	49.6	83.7	91.7	<0.0001

Conclusions: Our results demonstrate that leukocyte esterase reagent strips are a rapid, cheap, and sensitive tool to identify inflammatory synovial fluid. Leukocyte esterase reagent strips had an excellent Se but a poor Sp, it could be used as a screening tool in primary care practice. A positive result may indicate an inflammatory process, then the patient should be referred to a rheumatologist.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2657

AB1056 RADIOGRAPHIC ANALYSIS OF METATARSUS PRIMUS ELEVATUS IN PATIENTS WITH RHEUMATOID FOREFOOT DEFORMITIES

S. Mizuki, D. Hiraoka, K. Kushimoto, H. Yamasaki, K. Yoshida, K. Oryoji, K. Kamada, E. Yokota. *The Center for Rheumatology, Matsuyama Red Cross Hospital, Matsuyama, Ehime, Japan*

Background: Metatarsus primus elevatus involves dorsal elevation of the first metatarsal relative to the lesser metatarsals. The role of metatarsus primus elevatus in rheumatoid forefoot deformity is yet to be elucidated. We hypothesize that metatarsus primus elevatus can be attributed to a different pathomechanism than typical rheumatoid forefoot deformities such as hallux valgus, splay foot, and flat foot.

Objectives: To clarify the radiographic characteristics of metatarsus primus elevatus in patients with rheumatoid forefoot deformities.

Methods: We retrospectively reviewed standing anteroposterior and lateral radiographs of 51 feet (37 patients; mean age 65.7±7.1 years) before toeplasty due to metatarsalgia at our hospital. The elevation of the first metatarsal relative to the second metatarsal (MPE), the hallux valgus angle (HVA), the intermetatarsal angle (IMA), talar pitch, and calcaneal pitch were measured. For statistical analyses, the Mann-Whitney U test was used.

Results: Median MPE was 1.7 mm (interquartile range: 0.7–4.5 mm). We compared the group with MPE >5 mm (N=12 feet) to the group with MPE $\leq$5 mm (N=39 feet). The group with higher MPE was significantly younger (p=0.011). There was no significant difference in HVA between the two groups (p=0.068), although IMA was significantly smaller in the group with higher MPE (p=0.033). In the group with higher MPE, calcaneal pitch was greater ($p<0.001$) and talar pitch was smaller (p=0.016).

Conclusions: In patients with metatarsus primus elevatus, other rheumatoid forefoot deformities such as spray foot and flat foot were not observed. There was a wide range of hallux valgus severity. Metatarsus primus elevatus may be attributed to greater hindfoot calcaneal pitch.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1945

AB1057 MULTIDISCIPLINARY APPROACH FOR DIAGNOSING CONNECTIVE TISSUE DISEASE-RELATED LUNG DISEASE: IS IT USEFUL FOR RHEUMATOLOGISTS?

S. Peña Montelongo[1], A. Monroy Calero[1], O. Acosta Fernández[2], S. García Hernández[3], L. Pérez Martín[2], A. Bonilla Arjona[4], H. Sánchez Pérez[1], S. Bustabad Reyes[1], B. Rodríguez-Lozano[1]. *[1]Rheumatology; [2]Pneumology; [3]Pathology; [4]Chest Section, Radiology, Hospital Universitario de Canarias, Tenerife, Spain*

Background: Many patients with idiopathic interstitial pneumonia (IP) have certain clinical, serological and/or pulmonary morphologic features suggesting an underlying autoimmune disease (AD), but without meeting established criteria for connective tissue disease (CTD), a situation labelled as "IP with autoimmune features" (IPAF)[1]. To identify an underlying aetiology is important because it may impact on treatment and prognosis, and could be optimised by multidisciplinary approach.

Objectives: 1.To identify prevalence of IPAF in routine practice. 2. To determine the value of lung biopsy to diagnose underlying AD.3. To describe the course of IPAF.

Methods: Observational, longitudinal retrospective study in a tertiary hospital specific outpatient clinic for IP patients with cough and dyspnea as dominant symptoms requiring co-evaluation by rheumatologists in 2010–2016. Variables included: clinical, serologic and morphological findings by High-Resolution Computed Tomography of lungs assessed by 2011 current guidelines[2] and open lung biopsy. Statistical analysis:SPSS 17.0.

Results: Of 410 patients evaluated for IP, 93 had rheumatologist assessment, 70 F (75.3%), mean age at diagnosis 62.6 years (SD12.13), of whose 48 had no previous diagnosis. Mean follow-up 3.54 (SD2.77)years in undiagnosed patients. The most frequent radiological patterns were: inconsistent with usual interstitial pneumonia (UIP) (67.7%), UIP (22.6%), Possible UIP (4.3%), others (4.3%). Lung biopsy was performed in 15 patients (16%),11 without previous diagnosis. Histopathology patterns: 8 non-specific interstitial pneumonia (NSIP) in whom final rheumathologic clinical diagnosis was IPAF in 6 and UCTD in 2; 1 UIP (Sjögren); 1 vasculitis (p-ANCA) and 1 lymphoid interstitial pneumonia (LIP) corresponding to IPAF. We found lymphoid aggregates in one patient diagnosed as a IPAF. Overall new diagnostics were: IPAF 43.8%, UCTD 4.2%, CTD 52.1%.14/93 (15%) patients died, of whom 6 had IPAF (43%).

Conclusions: 1. Of patients with IP referred for rheumatologist assessment, 31% has no established CTD, with IPAF as clinical diagnosis in 24.7% of overall patients. 2. Surgical lung biopsy allowed to diagnose AD in 23% of unlabelled

patients. 3. After a follow-up time of 3.5 years,43% of patients that died had been diagnosed as a IPAF.

References:
[1] Fischer A,et al. Er Respir J 2015.
[2] Raghu G, et al.Am J Respir Crit Care Med 2011.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5550

AB1058 SENSITIVE DETECTION OF DYNAMIC CHANGES OF BONE EROSIONS IN INFLAMMATORY ARTHRITIS BY MUSCULOSKELETAL ULTRASOUND: A COMPARATIVE ANALYSIS WITH HIGH-RESOLUTION PERIPHERAL QUANTITATVE COMPUTED TOMOGRAPHY

S. Finzel[1,2], G. Schett[2], S. Kraus[3], R. Voll[1], M. Backhaus[4]. *[1]Department of Rheumatology and Clinical Immunology, University Medical Center Freiburg, Freiburg; [2]Department of Internal Medicine III, Rheumatology and Immunology, University Clinic of Erlangen, Erlangen, Germany; [3]Department of Internal Medicine, Kontonsspital Baden, Baden, Switzerland; [4]Department of Internal Medicine, Rheumatology and Clinical Immunology, Park-Klinik Weissensee, Academic Hospital of Charité, Berlin, Germany*

Background: Bone erosion is a hallmark of inflammatory joint diseases. Its meticulous detection is highly important for correct diagnosis and monitoring of therapy response. Earlier studies showed that musculoskeletal ultrasound (MSUS) has a higher sensitivity than conventional radiography with regards to detection of bone erosions (1) making MSUS more and more popular. The OMERACT ultrasound working group is currently standardizing and validating MSUS as an imaging outcome tool.
Objectives: To investigate the ability of MSUS to sensitively and specifically detect bone erosions in a longitudinal setting using HR-pQCT as a gold standard.
Methods: This is a sequel study to our 2011 cross-sectional comparative analysis on MSUS and HR-pQCT (2). 4/6 healthy individuals, 6/6 psoriatic arthritis patients and of 10/14 rheumatoid arthritis patients were available for follow-up and received an MSUS and an HR-pQCT scan of the clinically dominant hand. Bone erosions at the radial, palmar, and dorsal sites of the second metacarpophalangeal (MCP) joint, as well as the palmar and dorsal sites of the third and forth MCP joints were assessed for prevalence and severity in MSUS and by HR-pQCT. Afterwards, data were compared to the 2011-dataset. MSUS was graded as described earlier (2).
Results: Datasets without follow-up from the baseline cohort were eliminated. Sensitivity of MSUS in comparison to HR-pQCT regarding correct detection of erosions was 95% and specificity was 75%. %. For this analysis, grade 1 lesions were included. At follow-up sensitivity was 86% and specificity 79%. At follow-up, 36 MSUS-lesions were no longer detectable in MSUS; 21/36 were false-positive lesions at baseline. Only one false-positive lesion was detected at both time points. One new lesion was detected by MSUS and confirmed by HR-pQCT. Overall severity of bone erosions regressed in MSUS; these findings were confirmed by HR-pQCT (p=0.04).
Conclusions: This is the first study on change of bone erosions over time comparing MSUS and HR-pQCT. MSUS was confirmed being a sensitive imaging tool able to detect changes of erosions over time. Thus, it may be an adept tool to monitor treatment response in inflammatory joint diseases. Correct identification of bone erosions and differentiation from physiological vessel channels requires knowledge of predilection sites of erosions and physiological cortical breaks; this might aid to further increase the diagnostic value of MSUS.

References:
[1] Wakefield RJ et al. The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis: a comparison with conventional radiography. Arthritis Rheum. 2000.
[2] Finzel S et al. A detailed comparative study of high-resolution ultrasound and micro-computed tomography for detection of arthritic bone erosions. Arthritis Rheum. 2011.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6969

AB1059 THE PREVALENCE OF DENSE FINE SPECKLED PATTERN IN ROUTINE SCREENING FOR SYSTEMIC AUTOIMMUNE DISEASES USING INDIRECT IMMUNOFLUORESCENCE-ANTINUCLEAR ANTIBODY TEST

S. Kim, Y.L. Jeon, M.H. Kim, W.I. Lee, S.Y. Kang. *Department of Laboratory Medicine, Kyung Hee University College of Medicine, Seoul, Korea, Republic Of*

Background: The nuclear dense fine speckled (DFS) pattern is one of the most commonly observed finding in indirect immunofluorescence-antinuclear antibody (IIF-ANA) assay on HEp-2 cells. Unlike other ANA, DFS pattern is not prevalent in ANA-associated rheumatic diseases (AARD). The antigen was initially named DFS70 (70kD protein) according to the IIF pattern and later known as the lens epithelium-derived growth factor p75 (LEDGF/p75). Autoantibodies showing a DFS pattern have been reported in interstitial cystitis, various chronic inflammatory conditions, autoimmune thyroiditis, atopic dermatitis, cancer, as well as in apparently healthy individuals. Among IIF-ANA tests referred to the laboratory from the Department of Dermatology, the most common IIF-ANA positive pattern is DFS.
Objectives: To compare the clinical significance of DFS pattern in dermatologic diseases (including alopecia) with other departments.
Methods: Between June and December 2016, IIF-ANA testing using HEp-2 cell line slide (Kallestad; Bio-Rad, USA) was performed on 4,130 samples referred as screening for systemic autoimmune diseases in Kyung Hee University Hospital. The identified patterns in IIF-ANA assays were analyzed according clinical department and diagnosis.
Results: The Department of Dermatology was the most requesting IIF-ANA assay (2579/4130, 62.4%) and the Department of Rheumatology and the remaining departments were 18.1% (749/4130) and 19.5% (802/4130), respectively. The prevalence of IIF-ANA positivity was 10.97% (453/4130) and those of the Department of Dermatology, the Department of Rheumatology, and the remaining departments were 8.5% (219/2579), 15.5% (116/749), and 14.7% (118/802), respectively. The DFS pattern was the most common IIF-ANA positive pattern (173/453, 38.2%) and the prevalence of DFS pattern in the Department of Dermatology, the Department of Rheumatology, and the remaining departments were 48.4% (106/219), 26.7% (31/116), and 30.5% (36/118), respectively.
Among 173 patients with ANA pattern of DFS, 168 patients were reviewed based on their medical chart. The most of patients were from Department of Dermatology and Rheumatology. 101 patients with positive DFS were from Department of Dermatology, the majority of 55 patients were diagnosed with alopecia. 31 patients of department of Rheumatology showed positive ANA pattern of DFS and a great part of patients were diagnosed with rheumatism.
Conclusions: According to previous studies, up to 20% of healthy individuals have been reported to have a positive IIF-ANA test and the DFS pattern has been reported in 33% of ANA positive healthy individuals, but not in ANA positive systemic autoimmune diseases. In this study the prevalence of DFS pattern of ANA positivity in patients with dermatologic diseases including alopecia was similar with prevalence reported in healthy individuals. The patients with alopecia appear to show higher prevalence of positive ANA pattern of DFS than other patients with dermatologic disorders. This study was performed with routinely IIF-ANA requested patients to screen for systemic autoimmune diseases. Therefore, further evaluations comparing healthy individuals and patient group with more various disease entities are needed to confirm our findings.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5665

AB1060 MEASURING AGREEMENT IN THE ULTRASONOGRAPHIC EVALUATION OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS. A LATIN-AMERICAN MULTICENTER EXERCISE ASSESSING THE INFLUENCE OF SONOGRAPHER EXPERIENCE AND EXPERTISE

T. Cazenave[1], M.V. Martire[2], C. Waimann[3], M. Rosemffet[1]. *[1]Instituto de rehabilitación psicofísica, Buenos Aires; [2]Hospital Italiano de la Plata, la Plata; [3]Hospital Dr. Hector Cura, Olavarria, Argentina*

Background: Ultrasonography (US) is an important tool in rheumatology practice but it depends on sonographer's experience.
Objectives: To evaluate the reliability of US assessment among observers across Latin American using a web tool.
Methods: Cross-sectional study. Fifty-one Latin American ultrasonographers took part in a web- based US exercise evaluating images from 20 RA patients. The 4 joints US score was calculated for each patient including bilateral radiocarpal, midcarpal and second metacarpophalangeal joints. PD and GS were graded from 0 to 3. US scores comes as the result of the addition of PD and GS score, being 36 the highest disease activity.
Five patients were evaluated twice in order to address intra – rater reliability. The inter and intra-rater reliability was assessed using a two-way random, absolute, individual and average-measures intra-class correlation coefficient (ICC). We stratified sonographers according to experience (defining High experience as: at least 5 years of experience and 80 US assessments/month).
Results: A total of 1020 US image assessments were performed. Mean 4-joints US score was 17±8. The ICC was in the excellent range for intra [(individual ICC = 0.945 (IC95% 0.905–0.965); average ICC =0.972 (IC95% 0.950–0.982)] and

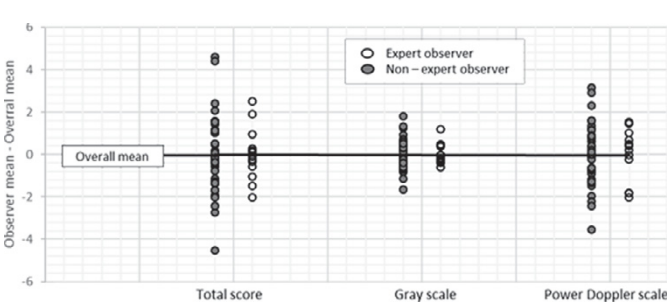


Figure 1, Agreement with the mean between multiple observers in total score, gray and power doppler subscale.

inter- reader reliability [(individual ICC =0.867 (IC95% 0.786–0.934); average ICC = 0.997 (IC95% 0.995–0.999)].
When comparing high with low experience sonographers, there was no significant differences in intra-class correlation coefficient. However, there was a greater variation between the means among low experience readers (13 to 22) and higher experience sonographers (14–18) (Figure 1).
Conclusions: US reliability is related to sonographer expertise and experience.
Acknowledgements: Edith Alarcón, Lucio Ventura, Walter J. Spindler, Christina Hernandez-Diaz, Javier Rosa, Santiago Ruta, Mara Guinsburg, Gustavo Rodriguez Gil, Cecilia Urquiola, Guillermo Py, Magalí Alva, Patricio Tate, Carmen Cerón, Lida Santiago, Ana Laura Alvarez del Castillo Araujo, Maria Jezabel Haye Salinas, Erika Catay, Maximiliano Bravo, Johana Zacariaz, Clarisa Sandobal, Gonzalo Pacheco, Mariana Benegas, David Navarta, Verónica Arturi, Ana Bertoli, Marcelo Audisio, Carlos Pineda, Natalia Estrella, Carla Airoldi, Paula Kohan, María Julia Santa Cruz, Lina Saldarriaga Rivera, Romulo Wong, Ignacio Carrillo, Hugo Najera, Julio García, Daniele Freitas Pereir, Fernanda Athayde Cardoso Linhares, José Alexandre Mendonça, Maritza Quintero, Anthony M. Reginato, Eliana Natalí Ayala Ledesma, Lorena Urioste, Eugenio De Miguel, María Soledad Gálvez Elkin, Carla Saucedo, Josefina Marin, Rodolfo Arape, Marwin Gutierrez.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5870

AB1061 THE HIGH DOSES GOLIMUMAB BRING BETTER SUPPRESSION OF ULTRASONOGRAPHIC SYNOVIAL INFLAMMATION IN PATIENTS WITH RHEUMATOID ARTHRITIS?

T. Okano[1], K. Inui[1], Y. Sugioka[2], K. Mamoto[1], T. Koike[2,3], H. Nakamura[1].
[1]Department of Orhopedic surgery; [2]Center for Senile Degenerative Disorders (CSDD), Osaka City University Graduate School of Medicine, Osaka; [3]Search Institute for Bone and Arthritis Disease (SINBAD), Shirahama Foundation for Health and Welfare, Wakayama, Japan

Background: Biologic diseasemodifying antirheumatic drugs (bDMARDs) that target cytokines and cytokine receptors such as tumor necrosis factor (TNF)alpha and interleukin (IL)6 have been established as a standard therapy of rheumatoid arthritis (RA) for patients with conventional systemic DMARDs, such as methotrexate (MTX), resistant disease. Golimumab, one of the bDMARDs, is an antibody targeting to TNF-alpha. In Japan, we can choose the dose of golimumab 50mg or 100mg according to the disease activity. Recent advance of ultrasound (US) equipment allows obtaining high-quality gray-scale (GS) imaging and sensitive power Doppler (PD) assessment, especially at small joints of the hands and feet. To date, US is the most sensitive imaging modality available in daily rheumatology practice for the assessment of residual synovitis.
Objectives: The aim of this study was to compare the ultrasound findings between patients with rheumatoid arthritis (RA) treated by golimumab 100mg and 50mg.
Methods: Patients with RA treated by golimumab were consecutively included. Ultrasound examination was performed at 52 synovial sites, bilateral first to fifth MCP, first IP and second to fifth PIP joints, first to fifth flexor tendon and wrists, 2nd and 6th compartment of extensor tendons and first to fifth MTP joints, by using HI VISION Ascendus (Hitachi Medical Corporation, Japan) with a multifrequency linear transducer (18–6 MHz). The GS and PD signals were scored in each synovial site using a semi-quantitative scale from 0 to 3.
Results: Fifty-five patients with RA (46 female, mean age: 64.2±12.1 years) were included and analyzed. In comparison between the dose of Golimumab at the time of ultrasound examination, disease activity (DAS28-CRP) was significantly higher in 100mg group (100mg, n=15: 3.6±1.0, 50mg, n=40: 2.3±0.9; $p<0.001$), but ultrasound findings were not significantly different between golimumab 100mg and 50mg groups. In patients achieving remission, ultrasound findings were not different between 100mg started and 50mg started groups.

Table 1. The comparison between golimumab 100mg and 50mg RA patients at the time of ultrasound examination

	Golimumab 100mg (n=15)	Golimumab 50mg (n=40)	*P* value
Age (years old)	60.3±12.2	65.6±12.0	0.161
Disease duration (years)	17.5±9.6	14.2±9.5	0.263
Duration of golimumab use (years)	1.8±0.9	2.1±1.5	0.542
DAS28-CRP	3.6±1.0	2.3±0.9	<0.001
SDAI	14.0±6.9	5.7±5.0	<0.001
Total GSUS score	16.9±12.6	14.8±12.7	0.572
Total PDUS score	11.3±9.07	6.5±6.0	0.076
Maximum PDUS grade	2.0±1.0	1.6±0.8	0.207

Conclusions: Even patients have high disease activity, golimumab 100mg suppress the synovitis and tenosynovitis very well. In the condition where disease activity was sufficiently controlled, there was no difference in the synovitis findings of ultrasound at the dose of golimumab.
Acknowledgements: We wish to thank Setsuko Takeda, Ayumi Hashimoto, Emi Yamashita, Rika Morinaka, Hatsue Ueda and Tomomi Iwahashi for their special efforts as a sonographer and collecting data.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1451

AB1062 PATTERNS OF MUSCULOSKELETAL SYSTEM INVOLVEMENT IN PATIENTS WITH TYPE I AND TYPE II DIABETES MELLITUS

T.I. Adrosy, M.I. Hanafy, H.S. Hamoud, A.A. Negm. *Rheumatology Department, Faculty of Medicine, Al-Azhar Univerist, Cairo, Egypt*

Background: Diabetes mellitus (DM) is a chronic disease, no known cure except in very specific situations. Musculoskeletal Utrasonography (MSUS) has a great sensitivity that can help clinical examination for the detection of peripheral enthesitis associated with DM
Objectives: To study the different patterns of musculoskeletal (MSK) system affection in both types of diabetes mellitus (DM).
Methods: We performed a retrospective single-center study on sixty five patients during the period from May 2014 to February 2015, to evaluate MSK manifestations in diabetic patients at Sayyed Galal University Hospital, Cairo, Egypt. Patients were identified as diabetics based on Diagnosis and Classification of Diabetes Mellitus diagnostic criteria (1997) (1). Clinical data, laboratory investigations, X-ray, musculoskeletal ultrasonography (MSUS) (2) and Bone mineral density was measured using Dual energy X-ray absorptiometry (DEXA) scan (3) were all collected from all patients.
Results: We included 65 diabetic patients; of these 21 patients (32.31%) had type I diabetes while 44 patients (67.69%) had type II diabetes. Age in type I was 24.5±10.5 years while in type II was 50.1±8.44 years (P=0.001). DM type II showed higher BMI (P=0.001), fatigue (P=0.005), shoulder periarthritis (frozen shoulder) (P=0.034), knee osteoarthritis (P=0.002), cheiroarthropathy (P=0.016), anserine bursitis (P=0.001) and plantar fasciitis (P=0.003) than type I. Osteoporosis was found in both types but type II showed more prevalence 13/44 patients (29.5%) while type I showed only 3/21 (14.2%). No statistically significant difference between both groups as regard t-score in the three sites. MSUS showed increased prevalence of quadriceps tendon enthesophytes in type I (P=0.033), while Infrapatellar (P=0.023) and retrocalcaneal bursitis (P=0.001) were more prevalent in type II DM.
Conclusions: Early evaluation of any diabetic patient regarding BMD by DEXA scan and soft tissue by MSUS seems to be beneficial for early detection of any abnormality and therefore early management and prevention of complications.
References:
[1] American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2013; 36.
[2] Blake GM and Fogelman I. DEXA scanning and its interpretation in osteoporosis. Hosp Med 2003; 64:521–5.
[3] Balint PV, Kane D, Wilson H, McInnes IB and Sturrock RD: Ultrasonography of entheseal insertions in the lower limb in spondyloarthropathy. Ann Rheum Dis 2002; 61:905–910.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2420

AB1063 ULTRASONOGRAPHIC ASSESSMENT OF SYNOVITIS IN PATIENTS WITH LESSOR TOE DEFORMITY DUE TO RHEUMATOID ARTHRITIS

T. Kashiwagura[1], Y. Kimura[2], I. Wakabayashi[3], M. Fujii[2], M. Kobayashi[4], M. Urayama[5], T. Aizawa[6], Y. Sugimura[7], H. Aonuma[8], N. Miyakoshi[9], Y. Shimada[10]. *[1]Department of Orthopedic Surgery, Akita City Hospital; [2]Department of Orthopedic Surgery; [3]Department of Rehabilitation Medicine, Akita City Hospital, Akita; [4]Department of Orthopedic Surgery, Hiraka General Hospital, Yokote; [5]Department of Orthopedic Surgery, Ogachi General Hospital, Yuzawa; [6]Department of Orthopedic Surgery, Kita Akita Municipal Hospital, Kita Akita; [7]Department of Orthopedic Surgery, Nakadori general hospital, Akita; [8]Kakunodate general hospital, Senboku; [9]Akita University Graduate school of Medicine, Akita, Japan; [10]Department of Orthopedic Surgery, Akita University Graduate school of Medicine, Akita, Japan*

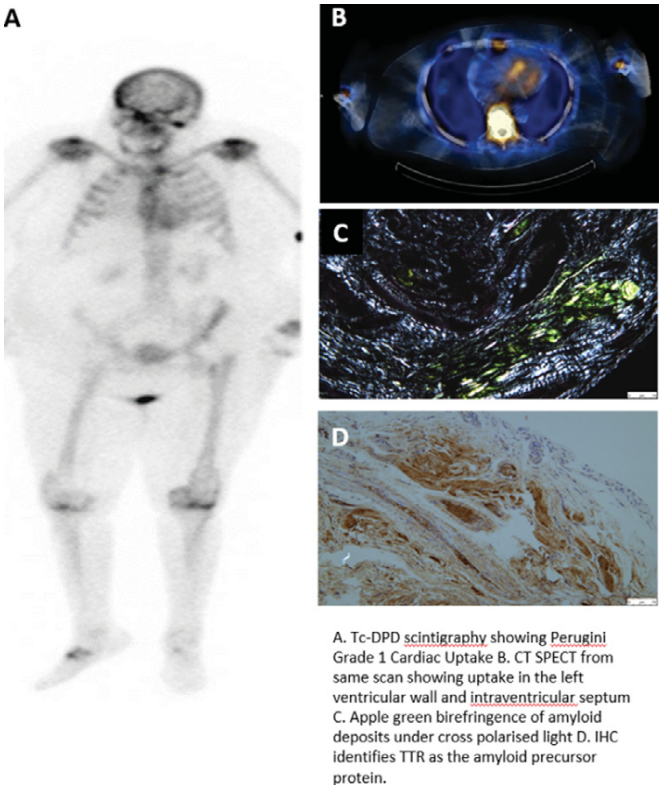
Background: In recent years, joint ultrasonography has been widely used for the diagnosis and treatment of rheumatoid arthritis (RA), allowing visualization of synovitis. Its clinical usefulness in early diagnosis and evaluation of disease activity has been reported. Continuous inflammation, osteochondral destruction, and soft tissue destruction due to synovitis in toe joints result in various clinical pictures of the foot. In the lateral toes in the forefoot, subluxation or luxation of the metatarsophalangeal (MTP) joints may occur, leading to painful callosities and resultant disturbance in activities of daily living. Few reports have addressed toe deformity and joint ultrasonographic findings of synovitis in the forefoot.
Objectives: In this study, lateral MTP joints were assessed using joint ultrasonography in RA patients to examine the correlation with deformity.
Methods: Seventy feet of 61 RA patients were examined in the outpatient clinic of our hospital. Patients who underwent surgery were excluded. The mean age of the patients was 66 years (24 to 92 years), and the mean duration of disease was 12 years and 9 months (1 month to 40 years). Biologic products were used for 23 feet. Joint ultrasonography was performed by the same examiner, using the same room and apparatus. Synovitis was defined as Grade 1 or more as determined by the power Doppler method. Based on foot radiographs in upright position obtained before and after ultrasonography, patients with luxation, subluxation, and joint fissure narrowing were classified into the deformity group, those with bone erosion and geode formation into the bone erosion group, and lack of abnormal findings into the normal group.

Results: Synovitis was found in MTP joints in 41 (14.6%) of 280 toes. The incidence rates of synovitis in the deformity group, the bone erosion group, and the normal group were 27.3%, 13.1%, and 6.7%, respectively. Synovitis was found in 21.7% of patients on therapy with biologic products and in 38.3% of those without such therapy. There were no significant differences in the mean duration of the disease, visual analogue scale score, erythrocyte sedimentation rate, matrix metallopeptidase 3 level, or health assessment questionnaire score among the 3 groups.
Conclusions: Synovitis was also found in patients who showed no changes on imaging of the toes. Synovitis persisted in some patients even after establishment of toe deformity. Drug therapy, intensification of conservative therapy, and synovectomy should be considered to prevent further deformation.
References:
[1] Wakefield RJ. Ann Rheum Dis 63; 382–5: 2004.
[2] Brown AK. Arthtitis Rheum 58(10); 2958–67: 2008.
Acknowledgements: The authors wish to acknowledge Miss Sasaki, for her help in interpreting the significance of the results of this study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1244

AB1064 CARPAL TUNNEL BIOPSY AND BONE SCINTIGRAPHY USING THE TECHNETIUM-3,3-DIPHOSPHONO-1,2-PROPANODICARBOXYLIC ACID (99M) (TC-DPD) TRACER CAN IDENTIFY CLINICALLY SILENT CARDIAC AMYLOIDOSIS AT A POTENTIALLY TREATABLE STAGE

T.A.-B. Youngstein[1], S. Tsamados[2], J.A. Gilbertson[1], L. Smith[1], D. Hutt[1], T. Lane[1], D. Rowczenio[1], T. Rezk[1], C.C. Quarta[1], R. Manwani[1], C. Whelan[1], M. Fontana[1], H.J. Lachmann[1], J.D. Gillmore[1], N. Goddard[2], P.N. Hawkins[1].
[1]National Amyloidosis Centre, UCL Division of Medicine; [2]Department of Orthopaedics, Royal Free London NHS Foundation Trust, London, United Kingdom

Background: Carpal tunnel syndrome (CTS) is the only known early clinical manifestation of wild-type transthyretin amyloidosis (ATTRwt; formerly known as senile systemic amyloidosis) which causes an amyloid cardiomyopathy. At the UK National Amyloidosis Centre 98% of those with proven ATTRwt have evidence of median nerve entrapment on neurophysiological studies and 48% have a history of carpal tunnel decompression as much as 12 years prior to heart failure symptoms. ATTRwt is diagnosed in approximately 150 individuals in the UK each year although post-mortem studies suggest presence of ATTwt amyloid deposits 30% of males over 80 years (yrs)[1]. A novel bone tracer, Technetium-3,3-diphosphono-1,2-propanodicarboxylic acid (99m) (Tc-DPD) largely abrogates the need for cardiac biopsy, identifying cardiac ATTR amyloidosis with a sensitivity of 98% and specificity of 70%[2]. Amyloid deposition can be readily identified by Congo red staining of carpal tunnel biopsies taken at routine decompression surgery. Immunohistochemistry (IHC) is usually able to determine the amyloid fibril protein (amyloid type). Rheumatologists are ideally placed to request CT biopsy. Developing this underused but diagnostic test is of particular importance in light of emerging therapies for ATTR amyloidosis.
Objectives: To determine the utility of CT biopsy as a diagnostic tool in systemic ATTR amyloidosis, and its utility in combination with Tc-DPD scintigraphy in identifying pre-clinical cardiac amyloidosis.
Methods: CT biopsies were taken at decompression surgery. Biopsies were stained with Congo red and viewed under cross polarised light. IHC was used to type amyloid deposits using standardised techniques.
Results: We analysed 37 CT biopsies, 73% female, median age 65.8 yrs (35–87 yrs). 5 biopsies contained amyloid deposits (13.5%) by Congo red staining. 3 were typed as ATTR amyloid using immunohistochemistry (8%), median age 80.35 yrs. The amyloid type could not be determined by IHC in two cases. No cases of proven ATTR amyloid had a history of heart failure symptoms. Of these, a 74 yr old male attended the NAC for diagnostic work up. He had a normal ECG and Echocardiogram, however, Tc-DPD scintigraphy was able to demonstrate low grade uptake.
Conclusions: Carpal tunnel biopsy can readily identify ATTR amyloid deposition and may identify those at risk of developing cardiac ATTR amyloidosis in the future, permitting earlier intervention with novel therapeutics aimed at preventing accumulation of amyloid. This ongoing study aims to identify the UK prevalence of ATTR amyloid in those with carpal tunnel syndrome and to create a cohort of those who may develop systemic ATTR amyloidosis to further elucidate the disease natural history.
References:
[1] Senile systemic amyloidosis: clinical features at presentation and outcome. Pinney JH et al., J Am Heart Assoc. 2013 Apr 22;2(2). doi: 10.1161/JAHA.113.000098.
[2] Nonbiopsy Diagnosis of Cardiac Transthyretin Amyloidosis. Gillmore JD et al., Circulation. 2016 Jun 14;133(24):2404–12. doi: 10.1161/CIRCULATIONAHA.116.021612.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5040

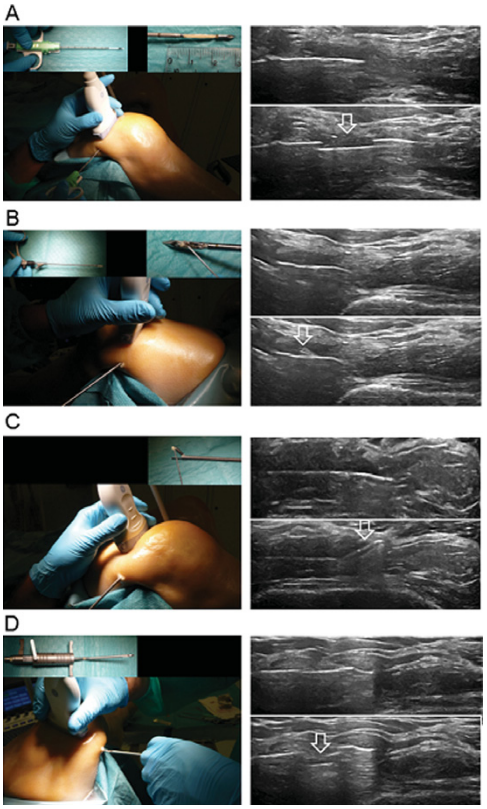


A. Tc-DPD scintigraphy showing Perugini Grade 1 Cardiac Uptake B. CT SPECT from same scan showing uptake in the left ventricular wall and intraventricular septum C. Apple green birefringence of amyloid deposits under cross polarised light D. IHC identifies TTR as the amyloid precursor protein.

AB1065 NEEDLE VERSUS FORCEPS TECHNIQUE IN ULTRASOUND-GUIDED SYNOVIAL BIOPSY OF THE KNEE JOINT

T. Hügle[1], P. Urbaniak[1], M. Müller-Gerbl[2], C. Marx[3], G. Tamborrini[3].
[1]Department of Rheumatology, University Hospital Basel; [2]Institute of Anatomy, University Basel; [3]Ultrasound Center Rheumatology, Basel, Switzerland

Background: Ultrasound-guided synovial biopsy is increasingly applied in rheumatology. Usually forceps- or needle-based techniques are used. So far there has been no direct comparison of different devices regarding their suitability in high resolution musculoskeletal ultrasound (hrMSUS)-guided synovial biopsy.



Objectives: To compare different forceps and needle-based instruments in hrMSUS-guided synovial biopsy in a cadaver study.
Methods: A core needle biopsy (A, Quickcore, Cook Medical, Bloomington, IN, USA), a retrograde forceps (B, Retroforce, Karl-Storz GmbH Tuttlingen, Germany), an anterograde arthroscopy forceps (C, Karl Storz GmbH, Tuttlingen, Germany) and an convexly shaped integrated core needle system (D, Synovex, Hipp Medical, Kolbingen, Germany) were tested for ultrasound-guided synovial biopsy of the suprapatellar recess in cadaver knee joints. Four senior rheumatologists scored each intervention from 0–5 regarding the following characteristics: visualization, handiness, accuracy, synovial tissue yield, invasiveness and overall suitability. Each intervention was recorded as static images and video clips.
Results: In all devices, enough representative synovial tissue was obtained and the instruments were all well visualized by hrMSUS. Core needle biopsy and the integrated needle system were best visualized due to their horizontally shaped closing mechanism. The core needle obtained a high yield of superficial synovial tissue and was the least invasive procedure. Despite handiness and accuracy were higher in the forceps instruments, overall suitability for hrMSUS-guided synovial biopsy was rated highest for the core biopsy needle.
Conclusions: Technically, all of the tested devices can be used for hrMSUS-guided synovial biopsy. Core needle biopsy seems to be most suitable for this intervention due to a low invasiveness, good visualisation and optimal yield of superficial synovial tissue.
References:
[1] Hügle T et al. Retrograde synovial biopsy of the knee joint using a novel biopsy forceps. Arthrosc Tech. 2014;3(3):e317–9.
[2] Hügle T et al. Development of a New Device for Synovial Biopsies. Surg Innov. 2015;22(5):496–9.
Disclosure of Interest: T. Hügle Shareholder of: Prof. Hügle contributed to the development of the Retroforce and Synovex instruments and receives royalties from Karl-Storz GmbH and Hipp Medical AG., P. Urbaniak: None declared, M. Müller-Gerbl: None declared, C. Marx: None declared, G. Tamborrini: None declared
DOI: 10.1136/annrheumdis-2017-eular.5933

AB1066 DIAGNOSTIC UTILITY OF THE MEDIAN/ULNAR NERVE CROSS-SECTIONAL AREA RATIO IN CARPAL TUNNEL SYNDROME

T. Atan[1], Z. Günendi[2]. *[1]Physical Medicine and Rehabilitation, Hitit University, Çorum Training and Research Hospital, Çorum; [2]Physical Medicine and Rehabilitation, Gazi University Faculty of Medicine, Ankara, Turkey*

Background: The most commonly used ultrasonographic measurements for the diagnosis of CTS are measurement of the median nerve cross-sectional area (m-CSA) at different levels of the carpal tunnel.[1] The cross-sectional area of a nerve may differ according to biometric characteristics such as age, sex, height, weight and wrist thickness.[2–4]
Objectives: The aim of this study was to assess the diagnostic utility of the ultrasonographic ratio of m-CSA to ulnar nerve cross-sectional area (u-CSA), the m-CSA/ u-CSA ratio, in carpal tunnel syndrome (CTS).
Methods: Patients (n=50) with positive symptoms and electromyography results of CTS and control subjects (n=50) with negative electromyography results of CTS were evaluated. The most symptomatic hand of each participant were included in the assesment. Ultrasonographic m-CSA and u-CSA measurements were made at the level of the pisiform bone, and m-CSA/u-CSA ratio was calculated.
Results: Using the m-CSA cut-off value of 9.95 mm^2 showed a sensitivity of 92% and a specificity of 42%. Conversely, the cut-off value 13.90 mm^2 showed a sensitivity of 56% and a specificity of 92%. Using the cut-off value 2.96 for the ratio of m-CSA/u-CSA showed a sensitivity of 86% and a specificity of 38% while using the cut-off value 3.71 showed a sensitivity of 52% and a specificity of 90% in the diagnosis of CTS.
Conclusions: The ratio of m-CSA/u-CSA at the level of the pisiform bone did not provide an additional benefit for the diagnosis of CTS. Ultrasonographic m-CSA measured at the same level was found to be more sensitive and specific method.
References:
[1] Mondelli M, Flippou G, Gallo A, Frediani B. Diagnostic utility of ultrasonography versus nerve conduction studies in mild carpal tunnel syndrome. Arthritis Rheum. 2008;59:357–66.
[2] Bathala L, Kumar P, Kumar K, Shaik A, Visser LH. Normal values of median nerve cross-sectional area obtained by ultrasound along its course in the arm with electrophysiological correlations, in 100 Asian subjects. Muscle Nerve. 2014;49:284–6.
[3] Qrimli M, Ebadi H, Breiner A, et al. Reference values for ultrasonograpy of peripheral nerves. Muscle Nerve. 2016;53:538–44.
[4] Won SJ, Kim BJ, Park KS, Yoon JS, Choi H. Reference values for nerve ultrasonography in the upper extremity. Muscle Nerve. 2013;47:864–71.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6550

AB1067 SUITABILITY OF CADAVER MODELS IN ULTRASOUND DIAGNOSTICS AND INTERVENTIONS IN RHEUMATOLOGY: FOOT AND ANKLE

V. Halász[1], Á. Nemeskéri[1], D. Bong[2], P. Mandl[3], I. Möller[2], E. Naredo[4], P.V. Bálint[5] on behalf of EULAR Anatomy for the Image Study Group. *[1]Department of Anatomy, Histology and Embriology, Semmelweis University, Budapest, Hungary; [2]Department of Rheumatology, Instituto Poal de Reumatologia, Barcelona, Spain; [3]Division of Rheumatology, Medical University of Vienna, Vienna, Austria; [4]Department of Rheumatology, Hospital Universitario Fundación Jiménez Díaz and Autónoma University, Madrid, Spain; [5]3rd Department of Rheumatology, National Institute of Rheumatology and Physiotherapy, Budapest, Hungary*

Background: Employment of cadaver specimens in ultrasonography provides a useful and safe model for education, enhances the anatomical knowledge of sonographers and may help determine the accuracy of ultrasound-guided interventions.
Objectives: In this systemic literature review (SLR) we assessed the role and use of cadaver specimens in sonographic studies of the foot and ankle in the field of rheumatology.
Methods: For our literature review we utilized the MEDLINE database, which were supplemented by searches in Google Scholar and Science Direct when the articles were not available through PubMed. Original studies in English language were included in the full paper review with an exception of three German language studies with English abstracts were also included. In the full paper review studies were selected for inclusion featured the sonographic study of cadaver specimens of the foot and ankle. Data were extracted on study characteristics and interventions.
Results: The search yielded 1241 articles, of which 130 were selected for detailed review. In the end, 23 full papers met inclusion criteria. The studies could be grouped as follows: description of detailed ultrasound anatomy (9), testing of accuracy of ultrasound guided interventional procedures (8), examination of artificial tears and lesions (4), foreign bodies (1) and joint effusions (1). The results that were obtained in the studies of the fully reviewed papers utilized a total of 294 cadaveric specimens, with an average of 12.78 (range: 1–48) cadaveric specimens included in each study.
Conclusions: The use of cadaver specimens of the foot and ankle may facilitate the validation of new sonographic methods which assess these joint regions, however the major disadvantage of these studies was the low number of cadaveric specimens.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4635

AB1068 ULTRASOUND OF SALIVARY GLANDS IN SJOGREN'S SYNDROME- WHICH SEMI-QUANTITATIVE SCORING SYSTEM IS THE BEST?

V.C. Iorgoveanu[1], V. Bojinca[2], V. Vlad[3], D. Mazilu[4], I. Saulescu[2], L. Groseanu[2], D. Opris[2], A. Balanescu[2], C. Constantinescu[2], D. Predeteanu[2], R. Ionescu[2]. *[1]Rheumatology, Carol Davila University of Medicine and Pharmacy; [2]Rheumatology, Saint Mary Clinical Hospital, UMF Carol Davila; [3]Rheumatology, Saint Mary Clinical Hospital; [4]Saint Mary Clinical Hospital, UMF Carol Davila, Bucharest, Romania*

Background: Sjogren Syndrome (SS) affects mainly exocrine glands. The latest diagnostic criteria designed for clinical studies are also used as guidance in clinical practice [1].
Ultrasonography (US) demonstrates specificity and sensibility in parotid and submandibular gland evaluation (SG). Parameters considered are echogenicity, homogeneity and margins regularity [1,2,3]. To standardize the assessment of B mode US of SG, different semi-quantitative scores were proposed.
Objectives: To apply and compare 9 US semi-quatitative scoring systems in B mode scanning of salivary glands in Sjogren Syndrome.
Methods: A research using keywords "salivary glands", "ultrasonograpy", "Sjogren Syndrome", "semi-quantitative score" in Medline/Pubmed was performed. There was a selection of most relevant articles. There were not considered relevant publications with impact factor <1. We performed the examination on SG in B mode US and applied these scores (De Vita, Niemela, Hocevar, Salaffi, Yukinori, Cornec,Theander) to our patients (primary and secondary SS).
Results: Eighty four SG in patients diagnosed with primary and secondary (57.15%) SS were assessed. In the group of patients with SSA/SSB presence (85.7%), mean score was De Vita 1.78+/-1.21, Niemela 2.56+/-2.17, Hocevar and Wernicke 2.39+/-2.14, Salaffi 2.83+/-2.52, Yukinori 2.39+/-2.14, Milic 3.39+/-2.14, Cornec 1.78+/-1.215, Theander 1.28+/-0.752. Schirmer test and the need for using the artificial tears was correlated to SG alterations in scoring systems proposed by Niemela (r 0.465, $p<0.05$) and Salaffi (r 0.496, $p<0.02$). All scoring systems were strongly correlated between them ($r>0.8$, $p<0.01$).
Conclusions: Inhomogeneity of parenchyma was considered in all scoring systems. Others considered relevant glandular dimension and margins regularity [2,3.4]. There was no difference between the scoring systems. Xeroftalmia valided through Schirmer test is correlated to SG parenchymal alterations. Our data is an update about semi-quantitative scoring systems in US of SG in SS.
References:
[1] Vitali C, Bombardieri S, Jonsson R et al. Classification criteria for Sjögren's

Syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. AnnRheum Dis 2002;61:554–8.
[2] Makula E, Pokorny G, Palkó A.The place of magnetic resonance and ultrasonographic examinations of the parotid gland in the diagnosis and follow-up of primary Sjögren's syndrome. Rheumatology (Oxford). 2000;39(1):97–104.
[3] Niemelä RK, Takalo R, Hakala M. Ultrasonography of salivary glands in primary Sjogren's syndrome. A comparison with magnetic resonance imaging and magnetic resonance sialography of parotid glands. Rheumatology (Oxford). 2004 Jul;43(7):875–9.
[4] El Miedany YM, Ahmed I, El Gafaary M. Quantitative ultrasonography and magnetic resonance imaging of the parotid gland: can they replace the histopathologic studies in patients with Sjogren's syndrome? Joint Bone Spine.2004;71(1):29–38.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5469

AB1069 SHOULDER ULTRASONOGRAPHY IN DIABETIC PATIENTS – IS THERE DAMAGE WITH NO CLINICAL SIGN?

V.C. Iorgoveanu[1], V. Bojinca[2], R. Malitchi[2], M. Gheorghe[2], C. Ionescu[2], R. Ionescu[2]. *[1]Rheumatology, Carol Davila University of Medicine and Pharmacy; [2]Rheumatology, Saint Mary Clinical Hospital, UMF Carol Davila, Bucharest, Romania*

Background: Degenerative lesions in shoulder rises exponentialy with age and diabetes was found to be associated with shoulder pain [1,2].
Objectives: To evaluate the prevalence and type of lesions of shoulder in diabetic patients with no pain using ultrasound (US).
Methods: We included consecutive patients with diabetes with no pain or clinical tumefaction in shoulder. US was performed in both shoulders using the standard scanning planes and dynamic maneuvers. Clinical data as fasting glycemia, BMI, treatment were recorded.
Results: Forty two shoulders were examined in 21 consecutive patients (mean age 67.92+/-7.35 years, weight 81.75 +/- 13.57 kg, BMI 25+/-2 kg/m^2, fasting glycemia 151.85+/-33.72mg/dl) with diabetes diagnosis mean 5.33 years +/- 5.99. Majority of patients were under treatment with oral antidiabetics (58.3%). Degenerative lesions were found in subscapular (SSc) 33.3% and supraspinatus (SpS) 8.3%) tendons as well as intratendinous micro ruptures with calcifications (33.3% bilateral calcifications in SSc, SpS). Impingement syndrome was objectified in 16.6% of examinations. Minimal inflammatory signs as: sub-acromion sub deltoidian bursitis in 50% (minimum in 33.3%, 8.3% bilateral) and long head biceps tenosynovitis in 58.33% (8.3% minimal Doppler signal). 83.3% showed humeral irregularities and also erosions were found (8.3%).
Conclusions: Degenerative and minimal inflammatory lesions in shoulder of diabetic patients exist with no clinical sign (pain, tumefaction). Ultrasonography might be an usefull technique to confirm these alterations before the appearance of symptoms.
References:
[1] Thomas SJ, McDougall C, Brown ID, et al. Prevalence of symptoms and signs of shoulder problems in people with diabetes mellitus. J Shoulder Elbow Surg. 2007;16:748–751.
[2] Abate M, Schiavone C, Salini V. Sonographic evaluation of the shoulder in asymptomatic elderly subjects with diabetes. BMC Musculoskelet Disord. 2010;11:278.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5482

AB1070 UNRAVELLING AUTOIMMUNE DISEASES THROUGH NAILFOLD CAPILLAROSCOPY

V.R. Bernardino[1,2], A.C. Rodrigues[1,2], A.C. Llado[1,2], M.A. Fernandes[1,2], M. Vicente[1,2], A.C. Grilo[2,3], A. Panarra[1,2], M.F. Moraes-Fontes[1,2]. *[1]Unidade de Doenças Auto-imunes/Medicina 7.2, Hospital de Curry Cabral, Centro Hospitalar de Lisboa Central; [2]NEDAI/SPMI – Núcleo de Estudos de Doenças Autoimunes, Sociedade Portuguesa de Medicina Interna, Lisbon; [3]Serviço de Medicina Interna, Hospital Beatriz Ângelo, Loures, Portugal*

Background: Nailfold capillaroscopy (NC) is non-invasive and used by clinicians as a diagnostic tool. It allows the distinction between primary and secondary Raynaud Phenomenon (RP), the latter usually associated to autoimmune diseases (AID).
Objectives: Characterize the utility of NC assessment for diagnosis of AID and to evaluate main differences in NC pattern, according to the presence of RP.
Methods: NC were performed with a Videocap biomicroscope using well established classification criteria [1]. NC images and reports from all patients evaluated from January 2011 to final December 2016 were retrospectively analysed. Comparisons were made using the Wilcoxon Rank Sum and Chi square tests, p values of $<$0,05 were considered statistically significant.
Results: In the last 6 years, 1100 NC were performed, 159 to man and 941 to women. Mean age was 42 [±19] years. NC requests came from 17 different hospital units. RP was present in 83% of patients (RP+, n=909) of whom 71% (n=641) had a prior diagnosis of AID, most frequently Systemic Sclerosis (SSc) (24%, n=143), Systemic Lupus Erythematosus (SLE) (21%, n=123), Sjögren's Syndrome (SS) (10%, n=62), Mixed Connective Tissue Disease (MCTD) (9%, n=52) and Antiphospholipid Syndrome (APS) (8%, n=48). NC patterns allowed for the classification of RP+ subjects into primary (3%) and secondary (81%); in 4% of subjects NC findings were abnormal but inconclusive. From secondary RP, scleroderma (37%) and non-scleroderma pattern (62%) were further separated; the former was later classified according to scleroderma-like (15,02%), early (33%), active (38%) and late (15%) scleroderma patterns.29% of RP+ patients did not have AID diagnosed; NC disclosed the diagnosis of SSc (n=24), APS (n=5), SS (n=4), SLE (n=2), MCTD (n=1), overlapping syndrome (n=1) and paraneoplastic syndrome (n=1).
In RP- patients, the main diagnosed AID were SLE (20%, n=17), SSc (14%, n=12) and SS (8%, n=7). NC results in RP- subjects were normal (24%) (including 92% of controls), inconclusive (22%) and suggestive of capillaritis (16%). Although RP-, some patients (38%) presented dysmorphic capillaries suggestive of secondary involvement (38%); NC findings in these patients included megacapillaries and microhemorrhages (scleroderma-like (26%), early (41%), active (30%) and late (7%)).
Demographic data was similar in both groups. Statistically significantly higher frequencies of AID ($p<0.0001$), SSc ($p=0.0006$), NC secondary non-SSc pattern ($p<0.0001$) and NC secondary active SSc pattern ($p=0.002$) were found in RP+ patients.
Conclusions: NC findings in RP+ were more pathological than in RP-subjects, probably due to pre-existing AID and more frequent positivity. Secondary non scleroderma pattern was more prevalent in RP+ patients. In RP- group, almost a quarter of NC assessments were normal, but capillary abnormalities were also revealed, suggesting this diagnostic approach can help to disclosure microvascular disease, even if RP is absent. NC further disclosed important leads to diagnose SSc, APS and MCTD in our population.
References:
[1] Cutolo M et al. Arthritis and Rheumatism. 2003 Nov; 48(11):3023–3030.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1242

AB1071 SIMPLIFIED ASSESSMENT IN NAILFOLD CAPILLAROSCOPY IN RHEUMATOLOGY

V. Durigan, G. Calizaya, A. Secco, F.E. Romanini, M.L. Sormani de Fonseca, V. Ortiz, M. Uemura, L. Takashima, M. Mamani. *Rivadavia, CABA, Argentina*

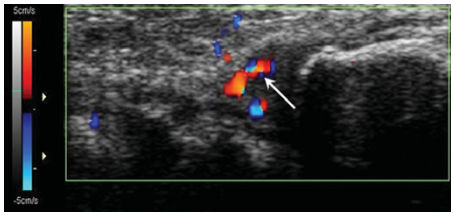
Background: Nailfold Capillaroscopy is a non-invasive diagnostic technique designed to evaluate small vessels of the microcirculation. The most important indication for capillaroscopy is Raynaud's phenomenon. The complexity and meticulous evaluation of the eight fingers is difficult to apply in daily practice given the limited availability of time to perform. For this reason it is necessary to develop simple and abbreviated techniques, to achieve an optimal and rapid evaluation of the patient.
Objectives: Determine the performance of the method of the 4° finger for the diagnosis of SD pattern in patients with Raynaud's Phenomenon taking the eight finger pattern as a gold standard.
Methods: Cross-sectional study with blinded and independent measurements. Nailfold Capillaroscopy was performed on the four fingers of each hand, except thumbs. Another observer evaluated the 4th finger of the hands. The interobserver agreement was made before carrying out the study and was 100%. The 8-finger method (gold standard) was considered positive when at least one finger has SD pattern and the 4° finger method was considered positive when at least one of them presents the SD pattern. We included patients older than 18 years with a diagnosis of Raynaud Phenomenon. Patients with thickening of the skin in the nailfold, digital lesion that made it difficult to assess (trauma, amputation, burns, etc.) and patients who did not consent to the procedure were excluded.
Results: We included 78 patients, 90% was female. The mean age was 53 years (DS +/- 13.5). Sixty-three patients had a score of eight fingers positive (cases) and 15 had a score of eight fingers negative (controls). The sensitivity of the 4° finger evaluation method was 89% (95% CI: 82–96%) and 93% specificity (95% CI: 88–99%). The positive predictive value of this method was 98% (95% CI: 95–100%) and the negative predictive value was 67% (95% CI: 56–77%). The positive likelihood ratio was 13 (95% CI: 2–89).
Conclusions: The simplified method of the 4° finger showed good performance for the diagnosis of SD pattern compared to the standard method of evaluation of the 8 fingers.
References:
[1] Sormani de Fonseca ML. Manual de Capilaroscopía. Buenos Aires: McDowell, 2000. Capítulo 1: 35.
[2] Cutolo M, Sulli A, Pizzorni C, Accordo S. Nailfold videocapillaroscopic assessment of microvascular damage in systemic sclerosis. J Rheumatol 2000; 27: 155–60.
[3] M. Cutolo et al. Nailfold videocapillaroscopic patterns and serum autoantibodies in systemic sclerosis. Rheumatology 2004; 43: 719–726.
[4] Ariane L. Herrick, Maurizio Cutolo. Clinical Implications From Capillaroscopic Analysis in Patients With Raynaud's Phenomenon and Systemic Sclerosis. Arthritis And Rheumatism 2010. Vol 62, No 9: 2595–2604.
[5] Sonsoles Piera –Velázquez et al. Patogénesis de la Esclerosis Sistémica. Rev Peruana de Reumatología 2004; 10(3): 34–42.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3815

AB1072 THE DEVELOPMENT OF ULTRASOUND SEMIOTICS OF DEFEATS OF THE JOINTS IN RHEUMATOID ARTHRITIS

V. Sirotka[1,1], U. Sirotka[2], A. Litvyakov[1]. [1]*Department of Internal Diseases No. 1;* [2]*Department of Traumatology, Vitebsk State Medical University, VITEBSK, Belarus*

Background: Differential diagnosis of rheumatoid arthritis today is challenging in cases of atypical clinical and laboratory picture arthritis [1]. Often the use of standard x-ray is not informative for the first two years of the disease. Erosive joint damage detected by the standard X-ray only after 2 years from the onset of the disease and only 36% of cases (M. Bukhari [et al., 2001), while the degree of articular destruction progresses with time and is correlated with a decrease in joint function.
Objectives: Development ultrasound semiotics for the diagnosis of rheumatoid arthritis using ultrasonic method of investigation of the joints.
Methods: We studied 113 patients with RA and 30 with no articular pathology – a control group (CG).
In the group of patients with RA - 88 people were women (79,7%), 35 people (20,3%) were men; the median age was 40.3 years (33–46), and the median duration of current RA – 4 years (1,75–10).
The diagnosis of RA was established according to modified ACR criteria of 1987. The activity of the inflammatory process of the I degree was 19 (27,5%) patients, II – 36 (52,2%), III in 14 (20.3%).
The control group was the patients medical history and clinically at the time of inspection there was no symptoms of the joints. Among them 15 men (50%) and 15 women (50%). The median age in the CG was 38.5 years (33–48).
All patients were multiplescale dynamic study II, V metacarpophalangeal and wrist joints by the ultrasonic device expert class using a sensor with a frequency of 12 MHz.
Results: Patients from the control group by ultrasound examination of the joints, we visualized the articular surfaces of the bones in the form of hyperechoic structures with clear smooth contours, homogeneous echostructure; the synovium is not visualised or she had homogeneous echostructure and a thickness of not more than 2.9 mm; the tendon was determined in the form of a hyperechogenic bundle, of a thickness not exceeding 1.5 mm.
Patients with RA identified the following ultrasound signs of lesions of the joints: focal pannus (96,6%) - area of pathologically altered synovial membrane thickness of more than 3 mm with a "tumor-like" invasive growth and the presence of pathological vascularization (indirect signs of neoangiogenesis) detected when using Doppler on the erosion pannus; thinning synovia outside erosion (99%); erosion, pannus (99%); combined erosion (96%); the erosion of inflammation: acute (45.6%) and chronic (89%); moderate synovitis (89,4%); swelling of periarticular soft tissues (88,4%); tenosynovitis (67,6%); periarticular effusion (66,9%); positive "pain test" in 6% of cases under ultrasound control.



Conclusions: Given the results obtained, we have developed ultrasonic diagnostic criteria of RA.
Diagnostic criteria for rheumatoid arthritis:
1. Pannus with pathological vascularization;
2. Thinning synovia outside of the pannus;
3. Erosion of the articular surface of the bone (pannus, associated erosion/erosion inflammation);
4. Moderate synovitis;
5. Tenosynovitis;
6. Periarticular swelling/effusion.

References:

[1] Raftery, G. Compresion of musculoskeletal ultrasound practices of a rheumatologist and a radiologist. G. Raftery, G. Hide, D. Kane. Rheumatology. 2007;232(3):519–522.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2068

AB1073 D-DIMER AS AN EARLY MARKER IN PATIENTS WITH LUPUS MESENTERIC VASCULITIS

X. Ma, X. Feng, H. Wang, B. Hua, L. Sun. *Rheumatology, Drum Tower Hospital, Nanjing University School of Medicine, Nanjing, China*

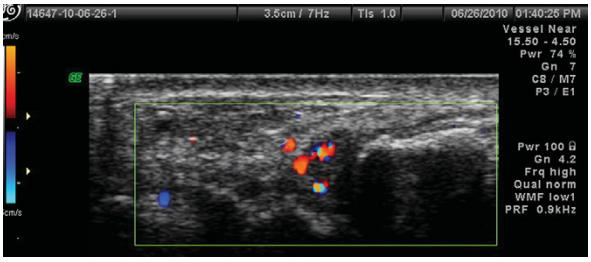
Background: Gastrointestinal manifestations are common in systemic lupus erythematosus (SLE) patients. Lupus mesenteric vasculitis (LMV) is a major cause of acute abdominal pain in SLE patients. No early serum marker contributes to the diagnosis of lupus mesenteric vasculitis.
Objectives: The aim of this study was to investigate clinical significance of serum D-dimer level as an early diagnosis marker of LMV patients.
Methods: The 57 systemic lupus erythematosus patients were retrospectively analyzed and classified into LMV group (n=19) and Non-LMV group (n=38) between May 2010 and January 2016. The serum D-dimer level was measured on the first day after SLE patients presented acute abdomen as well as imaging, other laboratory-testing parameters, and SLEDAI during the same period. The maximum and mean D-dimer values were analyzed and compared with other potential markers for diagnosis of LMV. The correlation of D-dimer level with other potential severity markers and inflammation parameters were also studied.
Results: Both maximum and mean D-dimer level on the first day of presentation of acute abdomen were significantly higher in LMV patients. The D-dimer level was correlated well with L-lactate and SLEDAI. In addition, D-dimer level was detected poor correlation with white blood cell count and C-reactive protein level.
Conclusions: D-dimer level could be an effective and early serum diagnosis marker of LMV.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3045

AB1074 THE TYPES OF EROSIVE LESIONS OF JOINTS IN RHEUMATOID ARTHRITIS

V. Sirotka[1], U. Sirotka[2], A. Litvyakov[1]. [1]*Dept. of Internal Diseases No. 1, Vitebsk State Medical University, VITEBSK;* [2]*Dept. of Traumatology, Orthopedics and Military Field Surgery, Vitesbek State Medical University, Vitesbek, Belarus*

Background: Early diagnosis of erosive lesions in rheumatoid arthritis (RA) remains today an important task, especially in the absence of specific laboratory markers. Promising research aimed at studying the informative instrumental diagnostic methods (ultrasound, Rg, MRI) to identify the characteristics of erosive joint damage in patients with RA [1].
Objectives: To study diagnostic possibilities of instrumental methods to identify the species of erosive joint damage in patients with RA.
Methods: We examined 104 patients with RA. Among patients of the 1st group were women 81 (77.9%), men - 23 (22,1%), average age was 38±12.1 years. Diagnosis of rheumatoid arthritis was exhibited with the EULAR diagnostic criteria [2] and the ACR [3]. All patients were Rg-graphy, ultrasound and MRI of the hands. Statistical processing of the information package.
Results: Erosive lesion of joints at RA is presented by the proliferation-caused erosion (erosion of the pannus) in combination with the development of the focal pannus with vascularization and inflammatory-destructive erosion (true erosion inflammation) outside the pannus (image 1). In the study the true erosion of inflammation of the articular surface of the bone ultrasound method identified at 87.9% of the joints in RA, significantly higher ($p<0,0001$) than in 34% of the joints in Rg-study; erosion pannus identified in 99.2% of the joints in patients with RA by means of ultrasonography, was significantly higher ($p<0,0001$) than 24.3% of the joints in the Rg-study. So erosion from the focal invasive growth of pannus, associated erosion, erosion, acute and chronic inflammation of the articular surface of the bone in patients with RA by ultrasonography were visualized significantly more often ($p<0,0001$) than in Rg, which allowed to define only the fact of presence of erosive lesions of the joints, but not allowed to determine the erosive lesions. The sensitivity of ultrasound accounted for 97.9% (95% CI: 97,7–98,1%); specificity - of 95.7% (95% CI: of 95.5–95.9 per cent). And in Rtg-graphy sensitivity accounted for 55.3% (95% CI: 54,8–55,8%); the specificity - of 87.7% (95% CI: 87,4–88%).



Conclusions: When comparing the results of a comprehensive study of joints in patients with RA despite the fact that Rg and MRI allow us to visualize and measure bone structure and pathology, ultrasound is only allowed to identify two types of erosive lesions of the joints: the true erosion inflammation and erosion of the pannus.

References:

[1] Sirotka V. Cliniko-tool differential diagnostics erosive lesions of joints at patients with rhematoid and reactive arthritis. V. Sirotka, A. Litvyakov. Vedecky Prumysl Evropskeno Kontinentu-2013: Materialy IX Mezinarodni Vedecko-Prakticka Conference, Praha, 27 Listopadu - 05 Prosincu 2013 rocu. Praha Publishing House "Education and Science". Praha, 2013. pp. 23–24.
[2] 2010 Rheumatoid Arthritis Classification Criteria: an American College of

Rheumatology/European League Against Rheumatism collaborative initiative/D. Aletaha et al. Ann. Rheum. Dis. 2010(69)1580–1588.
[3] The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis/F.C. Arnrett et al. Arthritis Rheum. 1988(31):315–324.

Acknowledgements: Gratitude my supervisor professor, PhD. Litvyakov A., for the help in conducting studies head of the Department of ultrasonic diagnosis PhD. Shilenok V. and my family (Sirotka and Seviaryn) for their support and understanding.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2024

Public health, health services research and health economics

AB1075 PHYSICIAN POSTGRADUATE EXPERIENCE HAS A PREDICTIVE ROLE FOR PHYSICIAN EFFICIENCY INDEX REGARDING PATIENTS WITH RHEUMATOID ARTHRITIS: A COHORT, EXPLORATORY STUDY

A. Emamifar[1], S.M. Mousavi[1], I.M. Jensen Hansen[1,2]. *[1]Rheumatology, Svendborg Hospital, Odense University Hospital, Svendborg; [2]DANBIO, Copenhagen, Denmark*

Background: Much effort has been made to improve the efficiency of health care system by delivering cost-effective, high-quality care.Nurse staffing's contribution to daily practice plays a significant role to reach this goal.[1]
Objectives: To elucidate the differences between ratios of nurse/physician consultation as well as physician efficiency index (PEI) of senior rheumatologists and junior physicians in rheumatology residency training regarding patients with Rheumatoid Arthritis (RA).In addition, to delineate the correlation of physician postgraduate experience and PEI.
Methods: The mean intervals between standard consultation by a physician or nurse for all senior rheumatologists and junior physicians as well as nurse/physician visits ratio and PEI (= nurse/physician visits ratio * mean interval), regrading RA patients seen during Nov 2013–2015, were calculated. Multiple linear regression analysis was performed to delineate the relationship between physician postgraduate experience and PEI. To monitor treatment outcome, Disease Activity Score in 28 joints-C-reactive Protein (DAS28-CRP) and Health Assessment Questionnaire (HAQ) were consecutively measured three times: first at physician consultation, second at following nurse consultation and third either at a nurse or physician consultation.

Table 1

Physicians	Number of patients**	DAS28 at baseline	Interval (day) ±SD	Nurse/Physician visits ratio	Physician efficiency index	Physician postgraduate experience (year)
P1*	244	4.8±1.2	126.9±85.1	(604/617)0.98	124.2	29
P2*	183	4.4±1.2	133.1±105.3	(207/384)0.54	71.7	20
P3*	129	4.5±1.3	114.5±85.2	(96/309)0.31	35.6	11
P4*	97	4.4±1.0	84.8±83.3	(133/252)0.53	44.8	10
P5	37	3.8±1.2	118.5±78.4	(15/52)0.29	34.2	9
P6	51	4.3±1.2	138±102	(5/68)0.07	10.1	8
P7	60	4.4±1.4	194.2±86.3	(14/103)0.14	26.4	8
P8	29	4.4±1.3	114.8±78.4	(14/41)0.34	39.2	7
P9	39	4.1±1.2	159.2±105.5	(14/53)0.26	42.0	7
P10	15	4.6±1.4	179.1±115.1	(1/16)0.06	11.2	6
P11	25	4.2±1.2	0	(0/24)0	–	3

P1–P4*: Specialists in rheumatology (n=4), P5–P11: junior physicians in rheumatology residency training (n=7). **Some of patients had consultation with more than one physician. DAS28:Disease Activity Score in 28 joints.

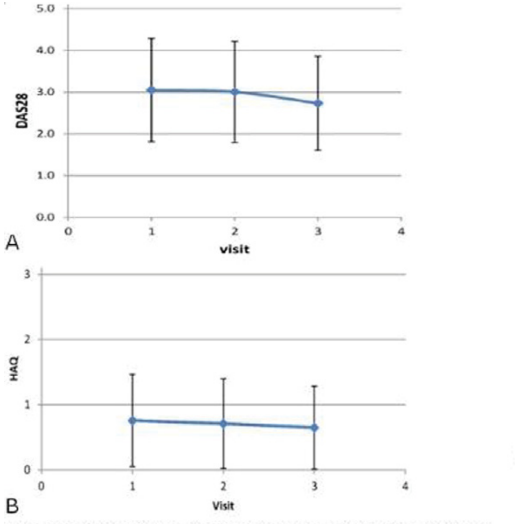


Fig 1. A: Curve of the means of Disease Activity Score in 28 joints ± Standard Deviation at first (by physicians, 3.05±1.24), second (by nurses, 3.01±1.21) and third (by physician or nurse, 2,73±1.13) visits and B: Curve of the means of Health Assessment Questionnaire scores ± Standard Deviation at first (by physicians, 0.759±0.707), second (by nurses, 0.709±0.686) and third (by physician or nurse, 0.649±0.634) visits.

Results: 3699 visits, belonged to 672 RA patients (64.1% female, the mean of age 64.9±14.1 and DAS28 at baseline 4.5±1.2), were included. There was a significant difference between the nurse/physician visits ratios of senior rheumatologists and junior physicians (P=0.01). Additionally, the mean PEI of senior rheumatologists was significantly higher than of junior physicians (P=0.04) (Table 1). A positive correlation was found between physician postgraduate experience and PEI adjusted for DAS28 at baseline and number of patients for each physician (Regression coefficient (95% Confidence Interval): 5.427 (1.068–9.787), P=0.022). DAS28 and HAQ score were significantly decreased if physician visits were followed by nurse visits (P=0.004 for DAS28 and P=0.025 for HAQ) (Fig.1), indicating a good treatment outcome at nurse consultations.
Conclusions: Junior physicians should be supervised to delegate responsibilities to nurse staffing. So, entire department operates more efficient, leading to prevent extra expenses (due to the differences in yearly salary of physicians and nurses). Quality of care should be monitored continuously by markers of disease activity and CRP.

References:
[1] Dall TM,et al.The economic value of professional nursing.Med Care2009;47:97–104.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2100

AB1076 LOW BACK PAIN IN TURKISH BUS DRIVERS: PILOT STUDY

Z.B. Karakoc[1], Z. Sarı[1], F. Koroglu[2], M. Aamir RashediBonab[3], S. Karakas[4], B. Kapşigay[1]. *[1]Physiotherapy and Rehabilitation, Marmara University Health Science Institute, Istanbul; [2]Physiotherapy and Rehabilitation, Yalova University, Termal Vocational School of Higher Education, Yalova; [3]Physiotherapy and Rehabilitation, Goztepe Medical Park Hospital; [4]Physiotherapy and Rehabilitation, Goztepe Training and ResearchHospital, Istanbul, Turkey*

Background: Lowback pain is a common problem whichincreasefinancialburden of government (1).The incidence of back pain that can be seen in every part of society is also high in drivers (2). We haven't seen any investigation about low back pain of Turkish drivers in literature. We thought that it should be research because of changeable ethnic differences.
Objectives: The aim of our study was to determine the rate of lowback pain and it'srelationshipbetweenquality of life in drivers.
Methods: Intercity and municipalitydriversof Istanbul and Yalova, participated in our study.Itwasdesigned as cross-sectional and complementarytype. Inclusion-criteriawerevolunteerforthis study and driving at least eight hours per day, being a driver for at least three years. Those with congenital deformities, having an accident history and doing an additional job were excluded from this study. After getting drivers' demographic data, "Oswestry Low Back Disability Questionnaire" forlowback pain and "Nottingham Health Profile" forhealthquality of life weresurveyedface to face. Chi-square and Spearman'scorelationnon-parametric test in the SPSS statistics programwereusedforstatistical analysis in this study.
Results: All of the 261 people who participated in this study were male. Their mean of age, weekly working hours and working year were 43±9.28, 50±13.09 and 18±1.04, respectively. %50 of participantshavelowback pain and those of 43%reported that jobsatisfactionwasaffecteddue to pain. Itwasdetermined that 10% of participants, whosejobsatisfactionwereaffected, didn't tapply the medical-doctor. While there was a significant relationship between low back pain and quality of life (p=0.000); there was no relationship between these two parameters and age and working year (p>0.05). It was determined that applying to medical doctor (p=0.02) and drug use rate (p=0.015) increased if the painful period lasted longer.
Conclusions: Low back pain affects quality of life related to health status. In this study, it was seen that the incidence of low back pain was high in long-distance drivers and affected job satisfaction in a great way. We think that the rates of drug use and medication usage can be reduced by increasing leisure time activity before increasing the severity of back pain and lengthening painful period. In addition, half of this occupation group is influenced by low back pain and once again it has been shown that waist schools should be expanded in our country.

References:
[1] Hoy, D.,Brooks, P., Blyth, F., andBuchbinder, R. The Epidemiology of LowBack Pain. Best Practice andResearchClinicalRheumatology. 2010; 24(6): 769–781.
[2] Anderson, Robert. The Back Pain of Bus Drivers: Prevalencein an Urban Area of California. Spine. 1992; 17(12); 1481–1488.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5931

AB1077 DOES PRECONSULT ELECTRONIC EXCHANGE AFFECT POSTCONSULT DIAGNOSIS?

G. Miller[1], B. Chou[1], N. Patel[2], G. Karpouzas[1]. [1]*Division of Rheumatology;* [2]*Department of Internal Medicine, Harbor UCLA Medical Center, Torrance, CA, United States*

Background: Harbor UCLA is an urban safety-net hospital in Los Angeles for underserved patients. In 2014, LA County Department of Health Services adopted an electronic consultation (E-consult) referral and dialogue system to improve access to subspecialists in the ambulatory care setting. The E-Consult system provides a platform for primary care providers to ask questions or engage in dialogue with specialists, request consultation, and track submitted requests. Back and forth messaging prior to acceptance for face-to-face consultation is termed a "preconsult exchange".
Prior studies of E-Consult systems have suggested benefits which include a reduction in wait times compared to paper referrals[1] and a perceived improvement in patient care[2]. We sought to further clarify the effect of a preconsult exchange versus immediate booking on a patient's diagnosis and wait time in an effort to provide some guidance on whether E-Consult should be used as a screening tool to reduce unnecessary visits or as a communication method to clarify details before a face-to-face visit.
Objectives: To determine whether preconsult exchange:
1. Influences the odds of arriving at a different diagnosis after face-to-face consultation compared to the requesting provider's original diagnosis
2. Influences the odds of arriving at a diagnosis of a different autoimmune condition versus a non-autoimmune condition (fibromyalgia, primary osteoarthritis, chronic pain, or other non-rheumatologic condition)
3. Results in a significant delay in face-to-face evaluation
Methods: We performed a retrospective chart review of all 238 new patient referrals between 11/2014 and 5/2016 to the Harbor UCLA Rheumatology clinic generated through the E-Consult system, reviewed by BC or GM, deemed appropriate, and seen for face-to-face evaluation. These patients were grouped by exposure (Preconsult exchange or not). Odds of change in diagnosis and confidence intervals were calculated using 2x2 contingency tables and Chi-Square tests. A student's T test was used to compare mean number of days between E-Consult initiation and face-to-face appointment.

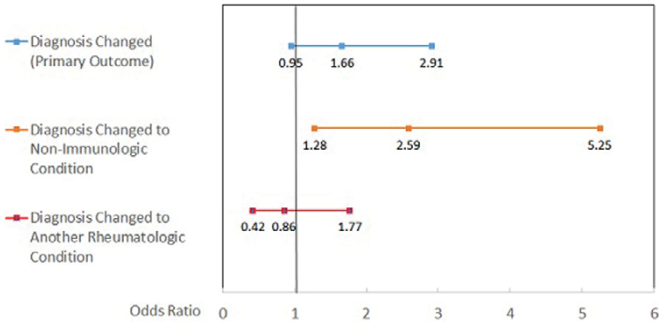


Figure 1. Odds of Change in Diagnosis Following a Preconsult Exchange

Conclusions: There was a trend towards a change in diagnosis overall among patients for whom there was a preconsult exchange, but a statistically significant increase in odds for change to non-immunologic diagnoses. This suggests that preconsult exchange highlights those patients for whom there is a higher likelihood of a non-immunologic diagnosis.
However, preconsult exchange was associated with a significant time cost - an additional 26 day delay for a face-to-face visit (due to the time needed for both submitter and reviewer to complete their dialogue) in comparison to an immediately booked patient.
References:
[1] Chen A et al. A Safety-Net System Gains Efficiencies Through 'eReferrals' To Specialists. Health Affairs 29, no.5 (2010):969–971.
[2] Scheibe MM et al. Efficiency Gains for Rheumatology Consultation Using a Novel Electronic Referral System in a Safety-Net Health Setting. Arthritis Care Res (Hoboken). 2015 Aug;67(8):1158–63.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5581

AB1078 IMPACT OF PRE-SCREENING ON RHEUMATOLOGY OUTPATIENT CLINIC PRACTICE

C. Orr, O. McElvaney, M. McQuillan, M. Hussein, S. Donnelly, G. McCarthy, C. McCarthy. *Rheumatology, Mater Misericordiae University Hospital, Dublin, Ireland*

Background: Chronic rheumatological diseases are predominantly managed in an outpatient setting, and these out patient clinics constitute a significant workload for rheumatolgy clinicicians. When unnecessary outpatient visits occur, service provision to those most in need of rheumatology review, both new referrals and those with established diagnoses in need of urgent review, is compromised. There is an evidence base for such screening in secondary care centres from other internal medicine disciplines (1).
Objectives: To determine the impact of introducing pre-clinic screening, and exploring the potential for follow up using telephone, by a physician extender (PE), on attendances at a rheumatology outpatient department.
Methods: A retrospective chart review of all patients attending a rheumatology outpatient clinic was performed over a 4-week period, 15/08/2016- 09/09/2016. Patients were categorized into new or follow-up attendees and the follow-up patients were further subcategorized into 1 of 4 groups:
A) Attending to receive results of investigations requiring no further treatment;
B) Attending with a chronic rheumatological disease requiring no active change in management;
C) Attending to receive results of investigations requiring further treatment;
D) Attending with a chronic rheumatological disease requiring active change in management.
Patients in categories A and B, may be safely managed by a phone call from a physician, or PE. Those in C and D would need to be reviewed in clinic, following triage by phone using a PE.
Results: 232 subjects were included (5 category A, 118 category B, 4 category C, 105 category D). 123 (53.0%) could be managed by phone utilizing a PE, thus obviating the need for review in clinic. The remaining patients could be triaged by telephone by a PE, and the schedule for review adjusted to prioritise those most in need of review. It is likely that such a strategy for reviewing patients would be more clinically efficient, have a greater impact on patient well-being, and be cost-saving.
Conclusions: Routine pre-screening for patients attending rheumatology clinics should be considered to improve effectiveness of the commodity rheumatology expertise.
References:
[1] Donnellan, F., Harewood, G.C., Cagney, D., Basri, F., Patchett, S.E. and Murray, F.E., 2010. Economic impact of prescreening on gastroenterology outpatient clinic practice. Journal of clinical gastroenterology, 44(4), pp.e76-e79.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6893

AB1079 FOLLOW UP OF PATIENTS WITH RHEUMATIC DISEASES BY MEANS OF A SMARTPHONE APPLICATION: SATISFACTION INDEX BASED ON A SURVEY AMONG USERS AND CARE PROVIDERS

C.A. Guillen-Astete[1], J.L. Alba-Barton[2]. [1]*Rheumatology Department, Ramon y Cajal University Hospital, Madrid, Spain;* [2]*Informatics, Surveys and Stata, Lima, Peru*

Background: Therapeutic adherence is the main variable in order to assess success or failure of any treatment. It is matter of interest to any clinician to get information enough about treatment response along time to reach a better understanding of any factor that conditions adherence failure or treatment interruptions. However, this kind of information is quite difficult to obtain in real scenarios due to lack of time or memory issues.
Objectives: The aim of present study is to assess the opinion of users of a smartphone application developed to improve the follow up of patients with different rheumatic diseases.
Methods: We conducted a survey to the users of REUMapp, an electronic form based on Google Form® software. REUMapp is an electronic interactive form developed for four different clinical scenarios: REUMapp-Esp (spondyloarthritis), REUMapp-Cristal (gout and othe microcrystalline arthropathies), REUMapp-AR (Rheumatoid arthritis) and REUMapp-MSK (soft tissues). All forms were developed over the basis of paper forms previously used for the same purposes and to be checked on follow up consultation. Forms were designed to gather information about daily treatment adherence (binomial), daily modifications (categorical), adverse effects (categorical) and therapeutic response in terms of visual analogical scale. REUMapp-ESP and REUMapp-AR include also specific joint recounts and indexes. All the forms could be completed in less than 3 minutes by the patient or his/her care provider. Every form contents became part of a database easily accessible during the follow up visit in a summarized way. Between 2014–2016, 419 apps were installed in patients or care provider's smartphones from two non public rheumatology clinics of Madrid with fully consentient of them. A survey was send to every user at the third to twelfth month after installation who have had one follow up consultation at least and who previously used the paper forms. Survey was developed using a multiple answer scheme using visual 7-level horizontal Likert scales. Topics of the survey were as follows: simplicity, time consumption and usefulness. Surveyed patients also were asked for the usefulness of the paper-based form.
Results: 205 Patients or care providers answered the survey. From them, 36 patients had diagnosed by rheumatoid arthritis, 23 by spondyloarthritis, 68 by gout or other microcrystalline arthritis and the rest by any other soft tissue rheumatisms. Following table shows the results of the survey. In the non parametric analysis of usefulness, the app was considered more useful than the paper format with a wilcoxon coefficient of contrast for paired data of -6.6589 ($p<0.0001$).
Conclusions: The smartphone applications described in this study have a good acceptance among patients of care providers in terms of usefulness, time consumption and simplicity and they are considered more useful than the printed models.

	Mean	Median	Mode	Variance	Standard deviation	Interquartile range	Curtosis (STD)
SIMPLICITY (1: Too difficult; 7: Very easy)	5.4927	5.0	7.0	2.2610	1.5037	2.0	0.8358
* The user is the patient	5.3453	5.0	6.0				
* The user is the care provider	5.5564	5.0	7.0				
*The user is the patient and the care provider.	5.6648	5.0	6.0				
TIME CONSUMPTION (1: Not significant ; 7: Too much)	3.4341	3.0	3.0	2.5911	1.6176	2.0	0.0678
USEFULNESS (1: None; 7: Very useful).	5.4585	6.0	7.0	2.1319	1.4601	2.0	1.5696
USEFULNESS OF THE PAPER MODEL (1: None; 7: Very useful).	4.3902	5.0	5.0	3.5626	1.8875	3.0	-0.9363

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5182

AB1080 RESULTS IN THE FOLLOW-UP OF THE NURSING CONSULTATION FOR THE MONITORING OF RHEUMATOLOGIC PATIENTS TREATED WITH INTRAVENOUS THERAPIES

C. Nájera Herranz[1], I. Cánovas Olmos[1], J. Ivorra Cortes[1], E. Grau Garcia[1], C. Alcañiz Escandell[1], K. Arévalo Ruales[1], I. Chalmeta Verdejo[1], C.M. Feced Olmos[1], J.J. Fragio Gil[1], R. González Mazarío[1], L. Gonzalez Puig[1], E. Labrador Sánchez[1], I. Martínez Cordellat[1], R. Negueroles Albuixech[1], J.E. Oller Rodriguez[1], F.M. Ortiz-Sanjuan[1], E. Vicens Bernabeu[1], D. Hervás Marín[2], J.A. Román Ivorra[1]. *[1]Rheumatology Department, HUP la Fe; [2]Biostatistics Unit, IIS la Fe, Valencia, Spain*

Background: In the management of rheumatologic patients treated with intravenous therapies, its regular monitoring is recommended in order to ensure its safety. The Nursing Consultation for monitoring rheumatologic patients treated with Intravenous Therapies (NCIT) represents a major support to patient caring for it provides patient monitoring before treatment administration and prior to rheumatologist consultation.
Objectives: To analyze number and types of incidents detected in the NCIT.
Methods: A cross-sectional longitudinal, observational study of data from patients followed-up in the NCIT (which was initiated in 2012) was performed. We have collected data of gender, diagnosis, drug administered, incidents detected previously to the drug administration, and if the incident was detected by telephone (one day before drug administration) or by personal interview. Biostatistical analysis with R (3.3.2.) was performed.
Results: We analyzed 7809 drug infusions corresponding to 545 patients (73% women). 48.25% of patients were diagnosed with osteoporosis (OP), 30.1% rheumatoid arthritis (RA), 5.7% ankylosing spondylitis (AS), 4.2% systemic lupus erythematous (SLE), 2.9% psoriatic arthritis (PsoA) and 8.3% had other diagnosis. The intravenous therapies were antiosteoporotic drug (7.8%) and biological and immunosuppressive treatment, being the most common drugs tocilizumab (38.89%), infliximab (31.9%) and abatacept (18.05%). In the 7809 treatment infusions, 477 incidents (4.1%) were registered, 33 of them related to the antiosteoporotic therapies and the other 444 incidents (93%) occurred in the biological therapies. The 63.7% of the incidents were detected by telephone one day before drug infusion. Statistical analysis showed that SLE patients exhibit higher tendency to incidents (4.8% of incidents in the 392 treatments for SLE patients; P=0.026) than other autoimmune diseases. On the other hand, RA and AS patients have incidents detected mainly by telephone ((P=0.047 y P=0.029 respectively). We also observed a high number of incidents in the intravenous administration of TCZ (P=0.009).
Conclusions: The NCIT has performed the follow-up of more than 5oo patients with only 6% of incidents, contributing to an improvement in the patients' health and in its caring. Moreover, the fact of identifying the incidents helps to reduce the number of personal consultations, avoids drug preparation in those cases where this infusion is suspended, and in summary it improves management of hospital resources.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5702

AB1081 INTEGRATING CASE FINDING AND INITIAL MANAGEMENT FOR OSTEOARTHRITIS, ANXIETY AND DEPRESSION INTO ROUTINE PRIMARY CARE NURSE-LED LONG-TERM CONDITION REVIEWS: RESULTS FROM THE ENHANCE PILOT TRIAL

C. Jinks[1], E. Nicholls[1,2], J. Liddle[1], E.L. Healey[1], A.L. Evans[1], C.A. Chew-Graham[1], K.S. Dziedzic[1], V.A. Tan[1], A.G. Finney[1], M. Porcheret[1], S. Lawton[2], V. Cooper[1], M. Lewis[1,2], C.D. Mallen[1] on behalf of ENHANCE team. *[1]Research Institute for Primary Care & Health Sciences; [2]Keele Clinical Trials Unit, Keele University, Keele, United Kingdom*

Background: Co-morbid osteoarthritis (OA), anxiety and depression are undermanaged in primary care yet have significant impact on pain, disability and outcomes of other long-term conditions (LTCs).
Objectives: To test the feasibility and acceptability of integrating case-finding and initial management for OA, anxiety and depression within extended primary care practice nurse (PN)-led LTC review consultations.
Methods: A stepped wedge pilot trial with process evaluation. PNs gave a study pack to patients age ≥45 years attending routine LTC reviews (asthma, COPD, hypertension, ischaemic heart disease, diabetes). The intervention included case finding questions (Generalized Anxiety Disorder (GAD2), Whooley 2-item depression, diagnosing OA clinically (hands, hips, knees or feet)) followed by further assessments (anxiety (GAD7), depression (PHQ9), joint examination). PNs completed an electronic patient record and initiated management. Predetermined success criteria were to recruit 4 practices; deliver training to 2 PNs per practice, recruit 50% of those invited, ensure 75% follow up (6 week, 6 month), and the satisfaction (GPAQ) of intervention patients to be at least as acceptable as that of control patients. 24 audio recorded consultations provided insight into fidelity of intervention delivery.
Results: Four practices were recruited. PNs were sequentially trained in practice prior to switching to intervention. Of the 474 people invited, 319 responded (207 control, 112 intervention) (67%). 83% and 79% of participants returned 6 week and 6 month questionnaires respectively. Demographic characteristics, general health, pain intensity, anxiety and depression scores were similar across arms. Overall, self-reported health (EQ5D5L) was high (median 0.84; IQR 0.72, 0.94). 14% of participants reported moderate to severe depression (PHQ9). Median GPAQ scores were similar (control 1.00 (IQR: 1.00, 1.29), intervention 1.00 (IQR: 1.00, 1.14)). 96% of those in the intervention arm reported being asked about joint pain, 93% reported being asked about mood. Audio recordings revealed that case finding questions were used as intended in most consultations (joint pain 20/24 consultations, anxiety 15/24, depression 6/24). One referral to physiotherapy and none to primary care mental health services were recorded by the PNs.
Conclusions: Recruitment and follow up were good. However, to target those who may benefit from the intervention, changes to the target population and eligibility criteria are required. There was reasonable delivery of the case finding questions, but limited referral and signposting, highlighting areas to optimise ahead of a main trial.
Acknowledgements: ELH, CJ, CCG, ALE and CDM are part funded by NIHR Collaborations for Leadership in Applied Health Research and Care West Midlands. CDM is funded by NIHR School for Primary Care Research, NIHR Research Professorship in General Practice (NIHR-RP-2014–04–026). KSD is part-funded by an NIHR Knowledge Mobilisation Research Fellowship (KMRF-2014–03–002). Views expressed in this paper are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2473

AB1082 IMPACT OF ANKYLOSING SPONDYLITIS VERSUS NON-RADIOGRAPHIC SPONDYLOARTHRITIS ON EARLY RETIREMENT

C. Cobilinschi, R. Ionescu, D. Opris-Belinski. *Sfanta Maria Clinical Hospital, Bucharest, Romania*

Background: Axial spondyloarthritis include non-radiographic SpA (nr-SpA) and ankylosing spondylitis (AS), suggesting the extent of sacroiliac involvement on imaging techniques (1). The influence of the two conditions on patients' physical function and their impact on work capacity should be regularly assessed so that we can better contribute to patients' social integration.
Objectives: The present study aims to assess the differences between AS and nr-SpA patients under anti-TNF therapy regarding disease related retirement (DR) and its contributing factors.
Methods: Over a period of eleven months 136 patients diagnosed with AS or nr-SpA on current biological therapy were included. Demographic data and working status were assessed. Statistical analysis was performed with SPSS 20.0.
Results: In the study cohort 69% of patients were males. The predominant age group was situated between 30 to 40 years old (29.8%), while 20.2% were over 50. Out of the study group, 66% confirm they are active in their work field with a minimum of seven hours per day, whereas 4.3% reached their retirement age. 29.8% of patients were granted a disability retirement and the majority (42.9%) belonged to the 40–50 age group. Surprisingly, 6.8% of early retired patients were under 30. Out of the DR category, 92.9% were diagnosed with AS, while the rest of 7.1% had nr-SpA. The interval from diagnosis to the initiation of biological therapy was 72.5±85.1 months for AS patients and 64.1±71.2 for nr-SpA. 23.2% of patients applied for early retirement before biological therapy and only 3.1% resumed work after anti-TNF introduction. Patient gender did not influence the working capacity. At the time of study inclusion, 12% of patients with AS and 4% of patients with nr-SpA still exhibited signs of highly active disease, according to ASDAS-CRP assessment.
Conclusions: Almost a third of patients in the study group were offered early retirement due to axial SpA. The vast majority of disease related retirement patients were known with AS, thus emphasizing the extent of disability brought on by this entity. However, a significant percentage of patients suffered from nr-SpA, raising doubts as to whether clinicians can promptly diagnose this entity and offer early, appropriate treatment so that inability no longer occurs.
References:
[1] Wendling D, Prati C, Claudepierre P, Guillot X, Breban M. Non-radiographic spondyloarthritis: A theoretical concept or a real entity? Jt Bone Spine. 2012.
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5352

AB1083 WORK IMPAIRMENT IN PATIENTS EXPERIENCING MUSCULOSKELETAL PAIN

N.M. Higgins[1], A. Cochrane[1], C.J. Rothwell[1], O. FitzGerald[2], P. Gallagher[3], J. Ashton[4], R. Breen[5], A. Brennan[6], O. Corcoran[7], D. Desmond[1]. *[1]Department of Psychology, Maynooth University, Maynooth; [2]School of Medicine and Medical Sciences, University College Dublin; [3]School of Nursing and Human Sciences, Dublin City University; [4]Physiotherapy Services, Beaumont Hospital; [5]Royal College of Physicians in Ireland; [6]Physiotherapy Services, AMNCH, Dublin; [7]Rheumatology Services, Waterford University Hospital, Waterford, Ireland*

Background: Many individuals with musculoskeletal disorders (MSD) continue to work. Little is known about those who remain occupationally active relative to those who are on sick leave, despite the clear potential for reduced productivity or work ability, and associated downstream effects.
Objectives: To assess self-reported work impairment and its associations with psychosocial risk factors amongst workers seeking care for musculoskeletal pain.
Methods: Recruitment took place in five Irish hospitals. Self-report questionnaires were used to assess risk of progressing to long-term sick leave and work disability (Örebro Musculoskeletal Pain Screening Questionnaire; ÖMPSQ), work ability, work impairment (WPAI) and work performance (WRFQ).
Results: 155 patients (53.5% female; mean age =46.50 years (range 20 to 71)) completed the questionnaire. 25.2% (n=39) were at high risk of progressing to long-term sick leave and work disability according to the ÖMPSQ. 62.6% (n=97) were classified as functioning poorly according to the WRFQ; 52.3% reported having poor work ability (n=81). Higher work role functioning was associated with higher pain self-efficacy (OR =1.514); better work ability was associated with older age (OR =1.063) and poorer function (OR =0.929); absenteeism was associated with lower pain self-efficacy (OR =0.650) and higher return to work expectancy (OR =1.179). Presenteeism was associated with higher pain intensity (β =0.259) and lower pain self-efficacy (β = - 0.385).
Conclusions: MSDs affect many individuals ability to work effectively. While all participants have managed to stay at work despite decreased levels of work ability and functioning, approximately a quarter are at high risk of progressing to long-term sickness absence. Interventions that attempt to improve mutable factors, such as pain self-efficacy, may help reduce the likelihood of work disability.
Acknowledgements: This research is funded by the Health Research Board [RCQPS-2014–2].
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5981

AB1084 CONTRIBUTION OF CLINICAL TRIALS TO THE EFFICIENCY OF ARTHRITIS RHEUMATOID MANAGEMENT

C. Alcañiz Escandell, E. Vicens Bernabeu, F.M. Ortiz-Sanjuan, J.E. Oller Rodriguez, C. Nájera Herranz, I. Cánovas Olmos, E. Grau Garcia, C.M. Feced Olmos, E. Labrador Sánchez, K. Arévalo Ruales, R. Negueroles Albuixech, J. Ivorra Cortes, J.J. Fragio Gil, I. Martínez Cordellat, R. González Mazarío, I. Chalmeta Verdejo, L. Gonzalez Puig, J.A. Román Ivorra. *Rheumatology Department, HUP la Fe, Valencia, Spain*

Background: Treatment and management of Rheumatoid Arthritis (RA) results in a high cost to the Health system such as the Spanish Health System. During the realization of clinical trials (CT) the sponsor is the one that pays for the direct healthcare costs of the patients, which leads to savings to the National Health System (NHS).
Objectives: To estimate the economic impact of conducting clinical trials (CT) for the NHS in terms of avoided costs.
Methods: A retrospective observational study was conducted using information from the clinical trials performed at the Clinical Research Rheumatology Department in the HUP la Fe from 2011 to 2015. Also a Cost-analysis was performed according Health System perspective. We calculated the length of stay in the CT in weeks for each patient included with RA diagnosis. Afterwards, we also calculated the total number of weeks of treatment for the total number of patients. In order to evaluate the economic impact in terms of avoided costs, economic evaluation included direct healthcare costs (rheumatologist visits, nurse care, laboratory tests and pharmacological treatment), and it was compared to the cost of the best alternative treatment in the market.
Results: A total of 35 CT were analyzed in this period, 14 of them focused on RA. Two observational studies and one CT (premature closure by the sponsor) were discarded. Therefore, 11 were considered in this study and a total of 76 patients with RA were analysed which add together 2609 weeks of treatment. This is approximately equivalent to treating 50 RA patients with biological therapy during one year. Evaluating the health savings that biological treatment would have cost during the 2609 weeks, we obtain a total amount of 699.176,88 €. This represents an annual saving of 139.835€ over the 5 years analyzed.
Conclusions: Our Clinical Research Unit managed to save a total amount of 13.935,30 € per patient in CT per year. Clinical Research Units should be considered as an efficient tool to the NHS.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6082

AB1085 MEASURING PATIENT SATISFACTION OF BIOLOGICAL TREATMENTS IN A REGIONAL HOSPITAL

D. Grados[1], A. Retamero[2], A. Riveros[1], C. Baliu[3], E. Nogues[3], D. Ferrandez[2], F. Bové[4], A.M. Colquechambi[5], M. Cucurell[3]. *[1]Rheumatology; [2]Pharmacy; [3]Dermatology; [4]Nursery; [5]Family medicine, Hospital d'Igualada (consorci sanitari Anoia), Igualada, Spain*

Objectives: To determine/measure the satisfaction degree of patients with rheumatologic (rheumatoid arthritis, spondyloarthropathies and other arthritis) and dermatological (psoriasis, psoriatic arthritis and suppurative hidrosadenitis) disease treated with a biological drug.
Methods: Descriptive prospective study conducted in a Regional Hospital with a reference area of 109,530 inhabitants.
A survey was conducted to all patients, thepatientswhocollectedtheir medication at the Pharmacy Service (self-administration treatment) and the patients who came for consultation (treatment administered by the nursing staff). The satisfaction degree before and after the biological treatmentwas evaluated.From 0 to 10, where 0 was the maximum dissatisfaction and 10 the maximum satisfaction; and improvement of pain, where 0 implied no improvement and 10 maximum improvement.
Clinical records were reviewed and a database was generated for exploitation with SPSS-vs 22. All patients received an information sheet from the study and signed an informed consent form.
Results: A total of 100 patients were analyzed: 45 men and 55 women. The mean age was 53 years (SD 14.9). 42% of patients were actively employed.
Distribution of patients by pathologies: 46 (46%) rheumatoid arthritis, 25 (25%) psoriasis, 16 (16%) psoriatic arthritis, 8 (8%) spondyloarthropathies, 2 (2%) suppurative hydrosadenitis and 1 (1%) juvenile idiopathic arthritis.
Distribution of biological drugs: 49 (49%) adalimumab, 20 (20%) ustekinumab, 18 (18%) etanercept, 6 (6%) golimumab, 3 (3%) tocilizumab, 2 (2%) secukinumab,1 (1%) certolizumab. The treatment was self-administered in 61 patients.
Only 30 (30%) patients had undergone previous biological treatment. At present, 43 patients had some additional treatment, 38 with methotrexate and 5 with leflunomide.

Satisfaction degree before biological treatment, n (DE)	2.8 (2.6)
Satisfaction degree after biological treatment, n (SD)	7.9 (1.6)
Pain improvement, n (SD)	7.8 (2.1)
Comfort with the route of administration, n	94
Comfort with frequency of administration, n	97
Degree of pain during administration, n (SD)	3.2 (3.2)
Patients who have missed doses, n	15
Patients who have controlled the disease with the biological treatment, n	93
Patients who have improved the quality of life with the biological treatment, n	93
The patient considers to have sufficient information of the drug, n	80
The patient considers to have sufficient information of the disease, n	87
They belong to a patient association, n	4

Conclusions: The satisfaction degree of patients with their biological treatment is very high regardless of the route of administration. Most of them are in monotherapy or with low doses of FAME. 61% of patients self-administer the drug at home. 93% of patients consider that there has been a change in their quality of life and that they can lead a normal life.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5483

AB1086 THE PREVALENCE AND THE REACTIVATION RATES OF HEPATITIS IN PATIENTS WHO ARE TAKING AN IMMUNESUPRESSIVE AGENT FOR TREATMENT OF A RHEUMATOLOGICAL DISEASE

B.N. Coskun[1], B. Yagız[1], S. Ermurat[1], E.S. Danaci[2], A.N. Tufan[1], E. Dalkilic[1]. *[1]Rheumatology; [2]Internal Medicine, Uludag University, Bursa, Turkey*

Background: Today, the immunosuppressive treatment agents became important for therapy of rheumatoid diseases. Theoretically, the use of these agents may result in reactivations be in patients that infected with Hepatitis B (HBV) and Hepatitis C (HCV) virus.
Objectives: We aimed to study the reactions during treatment and prevalence of HBV and HCV infections in rheumatology patients who are using immunosuppressive treatment.
Methods: The records of a total of 1146 patients who were taking an immunosuppressive treatment for a rheumatoid disease were reviewed retrospectively. The hepatitis serology, type of immunosuppressive treatment, the duration of treatment, liver function tests, complete blood count; HBV – DNA and HCV – DNA and antiviral agents and time of use (if patient is infected) were recorded.
Results: There were 682 (59.5%) women and 464 (40.5%) men, the mean age was 45.04±13.13. Ankylosing spondylitis (AS) was diagnosed in 453, rheumatoid arthritis (RA) in 365, psoriatic arthritis in 151, systemic lupus erythematosus in 43, vasculitis in 39, Behçet Disease in 26, systematic sclerosis in 18, myositis in 9, juvenile rheumatoid arthritis in 7, Sjögren Syndrome in 7, Still Disease in 3, familial mediterian fever in 6, retroperitoneal fibrosis in 1 and mixed connective tissue disease in 1 patient. The rate of HbsAg positivity was 1.8% in AS and 2.2% in RA; the rate of HCV positivity was 0.7% and 1.9% respectively. While

HBsAg, AntiHBs and anti-HBcIgG was tested for 898 patients, in 28 patients (2.4%) HBsAg and AntiHBs were negative and anti-HBcIgG was positive. The liver function tests were increased in two occult hepatitis patients, and lamivudine was administered for one and tenofovir for another patient. HCV-RNA was found negative in 12 of 18 patients that positive for HCV. Only one patient had ribavirin + interferon treatment and no reactivation was detected during follow up. The mean length of immunsuppressive treatment was 22.26±18.21 months for HBV positive patients, 19.43±21.40 months for HCV positive patients and 20.94±19.7 months for occult hepatitis. Furthermore, we 10.1% of the patients were vaccinated, 13.4% had natural immunity and 50.7% of patients has not encounter with virus.
Conclusions: HBV prevelance was 3.99% and HCV prevelance was 0.95% in general population, although there is difference according to geographical region in our country. HBV prevelance was the highest 9.9% in southeast region and the lowest 0.7 – 2.5% in west region. Low HBV prevelance could be associated with included patients that was young and stay in west region. Because hepatit virus can be reactivate under immunsupressive treatment, patients should be scanned and be careful for occult hepatitis in these scans.
References:
[1] Vassilopoulos D, Calabrese LH. Viral hepatitis: review of arthritic complications and therapy for arthritis in the presence of active HBV/HCV. Curr Rheumatol Rep. 2013 Apr;15(4):319.
[2] Chen YM, Chen HH, Chen YH, Hsieh TY, Hsieh CW, Hung WT, Lan JL, Chen DY. A comparison of safety profiles of tumour necrosis factor α inhibitors and rituximab therapy in patients with rheumatoid arthritis and chronic hepatitis C. Ann Rheum Dis. 2015 Mar;74(3):626–7.
Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6005

AB1087 POVERTY, POOR NEIGHBORHOODS, AND SLE OUTCOMES: THE PATIENT'S PERSPECTIVE

E. Yelin, J. Yazdany, L. Trupin. *University of California, San Francisco, San Francisco, United States*

Background: Studies have shown that persons in poverty experience worse outcomes of SLE and that the effect of poverty on outcomes is exacerbated for those living in neighborhoods with a high proportion of households in poverty. We report the results of a project to explore the viewpoint of SLE patients on how income and neighborhood affect disease outcomes.
Objectives: To explore the perspective of SLE patients with SLE on the effect of income, neighborhood, and stress on outcomes: 1) How does presence or absence of money affect care for SLE and in dealing with disease? 2) What role, positive or negative, does neighborhood play in SLE care and outcomes? 3) What are specific stresses that make dealing with SLE difficult?
Methods: We recruited SLE patients for qualitative interviews from a national longitudinal study of SLE conducted between 2003 and 2015. Subjects were selected to highlight the effects of income (those in the highest and lowest income quintiles), neighborhoods (living in neighborhoods with a high proportion of households in poverty vs. not), geographic diversity (four regions of the U.S.; urban, suburban, and rural residents), and range of SLE outcomes. An experienced interviewer conducted hour-long semi-structured interviews which were recorded, transcribed, and analyzed using grounded theory methods.
Results: 28 qualitative interviews were completed; 11 from the highest income group and 17 from the lowest (11 from poor neighborhoods).3 were men, 20 members of racial/ethnic minorities, and mean age was 49, range 22–70. Among the poor, none cited lack of money as limiting their access to care, but all stated that it necessitated choosing which pressing needs to focus on, with food and housing a higher priority than dealing with their SLE. Among the more affluent, financial resources were used to provide help in daily chores or to withdraw from work to reduce stress and allow for more time to manage their disease. Among the poor, none cited a positive benefit of neighborhood in finding health care resources or in mitigating how they dealt with disease but all cited a negative effect of being exposed to high rates of crime, the principal stress mentioned (F*rom a central city resident:* "A good neighborhood for someone with lupus is a place where you're not robbed twice in a year inside your apartment and not raped on way home from the bus". *From a rural resident:* "I don't worry about safety anymore. I sleep with a 357 Magnum"). Among the more affluent, local neighborhoods played no role in accessing care or in dealing with disease, with several stating they used professional networks not based in their neighborhood to find skilled providers or support (*From a resident of suburban Phoenix:* My physician's classmate in medical school was a rheumatologist at Mayo who knew someone here in Arizona").
Conclusions: Poverty forced choices in priorities, with SLE often having a lower priority than housing or food security. Exposure to crime was the stress repeatedly mentioned by the poor as exacerbating the disease. The affluent in this study indicated that they were able to reduce stress by paying for personal assistance, withdrawing from work, and using networks that extend beyond their neighborhoods to help gain access to resources. Mitigating poverty and reducing exposure to crime by helping the poor move to safer neighborhoods through housing vouchers may improve outcomes in SLE for the poor.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1524

AB1088 THE PATIENTS' VIEWPOINT ON A SPECIALISED BIOLOGIC SERVICE

E. Cefai, D. Balzan, C. Mercieca, A.A. Borg. *Rheumatology, Mater Dei Hospital, Msida, Malta*

Background: Biologic disease modifying anti-rheumatic drugs (DMARDs) have been a major breakthrough in the treatment of inflammatory arthritis. In clinical practice, providing timely monitoring to ensure continued efficacy and safety remains a challenge. The availability of a dedicated clinic for patients on biologics may help meet these standards.
Objectives: The aim of this study was to get the patients' perspective of our dedicated biologic clinic and identify any unmet needs.
Methods: Patients attending the biologic clinic between April and September 2016 and who were on a biologic for more than 2 years were interviewed by a trainee following their clinic visit. The patients were asked about their level of satisfaction on various aspects including waiting times, education, involvement in decision-making and duration of consultations.
Results: 44 patients (23 females, 21 males) participated in the survey, of whom 21 suffered from rheumatoid arthritis, 17 from ankylosing spondylitis and 6 from psoriatic arthritis. The mean age of participants was 55.1 (SD 12.62) years. The mean DAS28 was 2.26 (SD 1.03) and the mean BASDAI was 4.21 (SD 2.4). Disease duration was less than 5 years in 20%, 6 to 10 years in 30% and more than 10 years in 50%. Overall satisfaction with arthritis education before initiation of treatment was 91%, which then dropped to 76% after treatment initiation. Satisfaction with education regarding biologic therapy was more consistent at 84% and 81% before and after starting treatment, respectively. 84% of patients reported to be satisfied with their involvement in the decision to start and continue biologic therapy. 77% of patients were satisfied with a consultation lasting 15 to 20 minutes and 77% were also satisfied with 6-monthly visits. The most valued source of education was communication with the caring rheumatologist (n=32), followed by specialist nurse education (n=15), Internet resources (n=14) and use of leaflets (n=13). 95% of patients reported to have rarely or never missed an appointment. The rheumatology advice line was used by 54% of patients, whilst the rest reported that they did not need it since starting the biologic. The greater majority of advice line users were very satisfied with the service provided. Amongst the unmet needs mentioned, were better arthritis education and the introduction of telephone consultations.
Conclusions: Even though most patients were clinically well-controlled, continued education delivered by the caring rheumatologist and specialist nurse is still greatly valued. Patients attending this clinic highly valued the staff dedication and had good communication with their caring clinician. They were highly satisfied with the length and frequency of consultations. Nonetheless, a significant number suggested the need to introduce telephone consultations, which could be considered for those stable patients after receiving proper education.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3237

AB1089 USE OF NATURAL LANGUAGE PROCESSING TO ENHANCE RETRIEVAL OF RHEUMATOID ARTHRITIS DISEASE ACTIVITY OUTCOMES MEASURES IN US VETERANS

G.W. Cannon[1], S. Mehrotra[2], B.C. Sauer[2]. *[1]Rheumatology; [2]Salt Lake City Va Medical Center, Salt Lake City, United States*

Background: Rheumatoid arthritis (RA) disease activity measures in the Veterans Affairs RA (VARA) registry are extracted automatically through natural language processing (NLP). While this system is very effective at extracting data when templated notes are properly used, it lacked an error detection and feedback mechanism. Accuracy of the registry is essential for credible epidemiological research and patient care. We report a new automated approach with an active error monitoring and reporting system to alert providers of missing or potentially erroneous elements that can be easily corrected using standardized addendums available in the electronic medical record. The automated NLP system was revised to identify, extract, and integrate these updates to support the calculation of DAS28 and other composite outcome measures for the VARA database.
Objectives: 1. To describe the systems to identify needed corrections of VARA data.
2. To outline the procedures that allow providers to easily use addendums to enter corrections into the medical record to be automatically captured and loaded into the VARA database.
Methods: Procedures were developed and tested at a single pilot VARA site using data available in the Corporate Data Warehouse (CDW) from 01/01/2016 to 12/31/2016. A Java program was designed to retrieve Rheumatology notes, and corresponding addendums, based on "local" and "national" note titles. Notes were then processed to extract defined elements of RA disease activity listed in the table below. After each scheduled NLP run the system generates a log file that provides a summary, and patient-level report of completed and missing data elements. Providers receive the report and are asked to review the clinical notes of patient visits with missing data elements and follow simple procedures that leverage addendums to add or correct data elements when template violations occur. Addendums are also used to terminate the flag and request for review when the items are not available in the notes. Updating the VARA database from addendums occurs during the next NLP run.

Results: During the pilot testing phase the automated system processed 516 notes and identified 489/516 (94.8%) as successful loads, and 27/516 (5.2%) were flagged as problematic since one or more data elements were missing. Misapplication of the template occurred in 21/27 (77.8%) of notes flagged by the monitoring system and corrected with addendums. An additional NLP run produced 510/516 (98.8%) completed assessments with calculated DAS28 scores. Specific elements recovered using this process are presented in table below.

Total notes processed (n = 516)	Number (%)	
Elements investigated	Missing data elements	Elements Corrected
Tender Joint Count	1/516 (99.8%)	1/1 (100%)
Swollen Joint Count	2/516 (99.6%)	2/2 (100%)
Patient Global Assessment	11/516 (97.8%)	8/11 (72.7%)
Physician Global Assessment	9/516 (98.2%)	7/9 (77.8%)
Modified Health Assessment Questionnaire	15/516 (97.1%)	10/15 (66.7%)
Pain Score	11/516 (97.8%)	9/11 (81.8%)
Total notes with ≥1 missing elements	27/516 (94.8%)	21/27 (77.8%)

Conclusions: The addition of this error monitoring system provides an efficient data correction system and is expected to motivate and reinforce the use of RA templates. The implications of which may be profound as we transition from traditional epidemiological research to a more active learning healthcare enterprise. This pilot study established "proof of concept" and the next challenge is to adapt the technology to other VARA and non-VARA sites. This technology and framework could enable collaborative clinical research networks that are committed to large-scale pragmatic and observational effectiveness studies.

Acknowledgements: Work Sponsored by VA Specialty Care Centers of Innovation, VA Health Service Research and Development.

Disclosure of Interest: G. Cannon Grant/research support from: Amgen, S. Mehrotra Grant/research support from: Amgen, B. Sauer Grant/research support from: Amgen

DOI: 10.1136/annrheumdis-2017-eular.5620

AB1090 IS THERE AN ETHNIC VARIATION IN ACCEPTANCE OF BIOLOGIC THERAPY? A UNIVERSITY HOSPITAL EXPERIENCE

H. Selvaskandan, H. Al-Ani, A. Moorthy. *Department of Rheumatology, University Hospitals of Leicester, Leicester, United Kingdom*

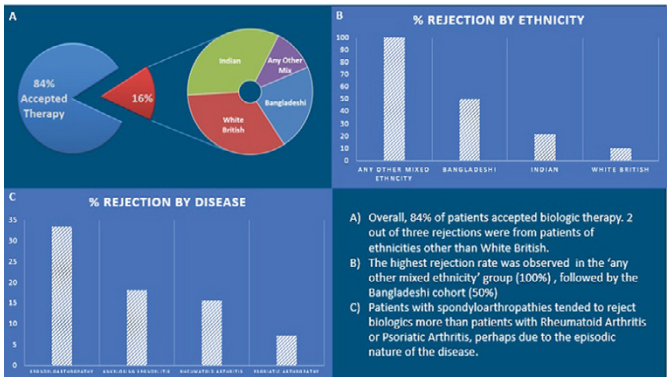
Background: Ethnic variation in drug adherence & preference is well documented (1). While usually a reflection of patient autonomy, the issue takes significance if it impedes the provision of effective evidence based care. Indeed, race affects rheumatological disease outcomes (2), likely for both biological & psychosocial reasons. Studies from United States of America found ethnic minorities were less likely to be on a biologic for a rheumatological disease compared to Caucasians, even after adjustment for education & insurance (3). Studies in the United Kingdom found similar results (4), although few investigated the disparity in the acceptance of biologics between ethnicities. Leicester, a midland UK city has an ethnically diverse population, where identifying and addressing such disparities is crucial in delivering effective & equal care.

Objectives: To determine any disparity in acceptance of biologic therapy, when offered in person, in a healthcare system free at the point of access, between White British and other ethnicities.

Methods: Data was collected from nurse led Biologics therapy clinics, from October 2016 to December 2016. All patients referred were deemed suitable for a biologic as per NICE guidlelines by a Rheumatologist, and were attending the clinic for counselling, assessment & consenting. Proformas were piloted, and improved proformas with information including demographic, disease & treatment details, as well the outcome of the consultation (biologic accepted or rejected) was used to collect data. The collated data were then analysed using EXCEL spread sheet.

Results: Data was collected from 55 patients. Interestingly, sex distribution was nearly equal (54% female). 57% of the total sample was White British (WB). The remaining 43% included; Indian, Bangladeshi, Pakistani, White Other, Asian other, African Caribbean & Any other mixed race. The most common disease necessitating referral for a biologic was rheumatoid arthritis (53%).

16% of patients rejected a biologic drug, of which 66% were ethnic minorities. The rejection rate among ethnic minorities was thus 24% compared to 10% in the WB cohort. The highest rejection rate was within the Any Other Mixed Ethnicity cohort (100%), followed by the Bangladeshi cohort (50%). Of note, all patients who rejected biologic therapy from an ethnic minority background did not speak English as their first language. Rejection rates were highest in the Spondyloarthropathies (21%).



Conclusions: Our results demonstrate a disparity between the White British population and other ethnicities in the acceptance of biologics, despite one to one counselling. This can have detrimental impacts on treat to target concept and disease progression, and thus will be further investigated & addressed.

References:

[1] Katz J. Patient Preferences and Health Disparities. JAMA. 2001;286(12):1506.
[2] Jordan J. Effect of race and ethnicity on outcomes in arthritis and rheumatic conditions. Current Opinion in Rheumatology. 1999;11(2):98–103.
[3] Lee at al. Treatment disparity related to race/ethnicity and education in rheumatoid arthritis patients: Comment on the article by Constantinescu et al. Arthritis Rheum. 2009;61(8):1141–1142.
[4] Kumar, K. et al. FRI0166 Ethnicity Is Associated With Biologic Treatment Persistence In Rheumatoid Arthritis. Annals of the Rheumatic Diseases 74.Suppl 2 (2015): 483.2–483. Web.

Acknowledgements: Administrators & Rheumaotlogy Nurses of University Hospitals of Leicester.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2944

AB1091 HIGH ACCEPTANCE RATE IN RA, AS AND PSA PATIENTS WHEN BEING STARTED ON BIOSIMILAR TNF OR BEING SWITCHED FROM THE ORIGINAL TNF MAB (REMICADE, ENBREL) - A SINGLE CENTER EXPERIENCE

H. Kellner. *Schwerpunktpraxis für Rheumatologie und Gastroenterologie, München, Germany*

Background: Biiosimilar TNF Mab (BioTNF) have become available in most of the European countries in the last few years. They are labeled to be used in the most common rheumatic diseases, like RA, AS and PsA. Controlled studies have shown comparable efficacy and safety of BioTNF and original TNF (Remicade, Enbrel). BioTNF are allowed to be used in TNF naive patients as well as in TNF pretreated patients (switchers). Prescriptions in different countries may vary due to local most often cost driven restrictions.

So far, little is known about the awareness, acceptance and possible obstacles which may influence patients willingness to accept therapy with BioTNF instead using the original compounds

Objectives: The study was conducted and designed to get a deeper insight in what may influence patients decision making and willingness to accept treatment with BioTNF firsthand or accept switching.

Methods: Between February 2015 and December 2016 41 patients (BioINF n=29, BioETA n=12) were introduced to BioTNF therapy. 9 Patients (Bio-INF n=3, Bio-ETA n=6) received TNF therapy the first time, in 32 patients (Remicade n=23, ETA n=8) werde switched from the originator TNF compound to BioTNF. All patients received comprrehensive information on BioTNF in verbal and written form.

A standardised questionaire was used to ask patients on their awareness, acceptance and about possible obstacles for the usage of BioiTNF Mab.

Results: 6 out of 9 TNF naive patients agreed after their first information on BioTNF to start therapy with BioINF (n=3) or BioETA (n=3). Another 2 patients accepted BioETA therapy on their second visite. Only one patients asked to be started on the originator TNF Remicade. In patients being ask to switch from Remicade to BioINF 19 patients accepted promptly to be switch and in patients with Enbrel therapy 6 out of 9. Finally only 1 patient on Remicade TNF therapy denied even after a third visit to be switched. Mayor concern to deny the use of BioTNF were possible lack of efficacy (30%), safety (32%) and missing longterm experience (35%). The main motivation to switch was patients believe to save money and that they were ask to switch to BioTNF Mab on short notice from their health care insurance company.

Conclusions: There is a high acceptance rate in patients with chronic inflammatory rheumatic disease to be started on or switched to BioTNF (>90%). Their are little concerns in patients accepting BioTNF with regard to safety or efficacy of BioTNF. Patients are aware of BioTNF as a less costly way to treat their rheumatic condition. Physicians should be aware of this willingness and offer BioTNF therapy were it is appropriate. Using BioTNF is a cost saving way to use biologics in rheumatic therapy with equal efficacy and safety compared to the originiator compounds.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4211

AB1092 SATISFACTION AND BELIEF REGARDING TREATMENT WITH INTERSTITIAL LUNG DISEASE AND RHEUMATIC DISEASES IN MULTIDISCIPLINARY OUTPATIENT CLINIC

J. Jung[1], S. Jung[1], S. Kim[2], J.R. Choi[3], H.-S. Kim[1]. *[1]Internal medicine, the Soonchunhyang University Seoul Hospital, Seoul; [2]Internal medicine, Gangneung Asan Medical Center, Gangneung; [3]Internal medicine, Pohang Saint Mary's Hospital, Pohang, Korea, Republic Of*

Background: Among rheumatic disease-related lung disease, interstitial lung disease (ILD) is the most prevalent and contributing to the mortality and morbidity. Increasing number of recent reports dealing with ILD of rheumatoid arthritis (RA), Sjögren's syndrome (pSS) and systemic sclerosis (SSc), multidisciplinary discussions (MDDs) have been growing interest for diagnostic accuracy with dedicated service. There was little evidence indicating that multidisciplinary outpatient clinic resulted in improvements in clinical outcomes including satisfaction and belief.
Objectives: We have designed validated a scale of evaluating coping strategies about satisfaction and belief in patient of ILD and rheumatic disease with multidisciplinary approach.
Methods: From December 2015 to September 2016, we evaluated 20 patients of rheumatoid disease with ILD and 20 patients of idiopathic pulmonary fibrosis. Patient perceptions of illness, treatment beliefs, and moods were measured via the multiple choice questionnaires presenting brief Illness perception questionnaire, beliefs about medicines questionnaire, and patient health questionnaire 2 for comparing the effectiveness of MDDs and routine ILD management.
Results: In univariate analysis, beliefs in necessity and concerns of medication differed significantly high in multidisciplinary outpatient clinic for people with ILD (intentional or unintentional). When controlling for other factors that may impact medication nonadherence, more belief in necessity of medication and greater positive emotional response to disease were presented in multidisciplinary outpatient clinic for people with ILD (OR 1.51, CI 1.01–1.82).
Conclusions: The MDD including rheumatologist and pulmonologist allows a satisfactory management comparing routine ILD management. It showed better coping improvements about the emotional distress, pain, and beliefs about treatment. Further research to investigate long-term clinical outcomes of multidisciplinary outpatient clinic for people with ILD is required, overlying the enhancement of mutual communication.
References:
[1] Vliet Vlieland TP. Multidisciplinary team care and outcomes in rheumatoid arthritis. Curr Opin Rheumatol 2004;16(2):153–6.
[2] Vliet Vlieland TP, Hazes JM. Efficacy of multidisciplinary team care programs in rheumatoid arthritis. Semin Arthritis Rheum 1997;27(2):110–22.
[3] Oberai B, Kirwan JR. Psychological factors in patients with chronic rheumatoid arthritis. Ann Rheum Dis 1988;47(12):969–71.
[4] Cramer JA, Roy A, Burrell A, et al. Medication compliance and persistence: terminology and definitions. Value Health 2008;11(1):44–7 doi: 10.1111/j.1524–4733.2007.00213.x [published Online First: Epub Date]|.
[5] Pakas I, Ioannidis JP, Malagari K, et al. Cyclophosphamide with low or high dose prednisolone for systemic sclerosis lung disease. J Rheumatol 2002;29(2):298–3046.
[6] Mouthon L, Berezne A, Guillevin L, et al. Therapeutic options for systemic sclerosis related interstitial lung diseases. Respir Med 2010;104 Suppl 1:S59–69 doi: 10.1016/j.rmed.2010.03.018 [published Online First: Epub Date]|.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4179

AB1093 BIOSIMILAR INFLIXIMAB IN RHEUMATOLOGY PRACTICE - THE CYPRUS EXPERIENCE

J. Joseph, M. Solonos, M. Michaelides, V. Hadjiroussos, V. Skoutellas, N. Zannettou, C. Christodoulou, E. Mina, A. Therapontos, D. Nikiforou, S. Psarellis, S. Symeonidou, A. Tsirogianni, M. Michaelidou. *Cyprus Rheumatology Association, Nicosia, Cyprus*

Background: Infliximab ('Remicade') has been authorized in the EU since 1999. It has a license for use in major rheumatic diseases and inflammatory bowel disease. The biosimilar 'Inflectra' received its license in Europe in September 2013. It was first launched in Central and Eastern Europe, and some smaller Western European markets due to earlier patent expiry. Inflectra was introduced to Cyprus in 2014 and soon after that, every patient with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis would receive this agent when a biologic agent was required. At first there was significant concern amongst the medical community regarding efficacy and safety of biosimilars. Careful observation and pharmacovigilance are therefore required to analyse the effectiveness and safety of biosimilar agents since the significant price difference means that they will be used extensively from now on.
Objectives: The aim of this study was to record statistics of use, effectiveness and safety of the first biosimilar 'Inflectra' following its introduction in Cyprus.
Methods: Cypriot rheumatologists completed an online form for every patient who was prescribed 'Inflectra' from the introduction of the biosimilar in 2014, until late 2016. Collected data included patient characteristics, diagnosis, whether the patient remains on the drug or not, reasons for discontinuation, side effects and physician impression of effectiveness.
Results: 160 patients were entered. Male: Female ratio was roughly equal and 90% were taking a biologic for the first time ('biologic naive'). Indications were Rheumatoid arthritis in 40%, Ankylosing spondylitis in 33%, psoriatic arthritis and other spondyloarthropathies in 20% and a few patients were treated for eye disease and other 'off-label' indications. At the time of recording, 25% of patients were on the drug for less than 3 months, 25% 3–6 months, 25% 6–12 months and 25% over a year. Overall 30% of patients had to discontinue and 70% remain on the drug. Of those who discontinued, 65% did so within 6 months of starting. Of all patients treated with Inflectra, 10% stopped due to side effects, 7% had immediate non-effectiveness and 3% had secondary lack of efficacy. 80% of patients experienced no adverse effect. Amongst the 160 patients, recorded adverse events included 8 infections, 8 skin rashes, 9 headaches and 5 severe allergic reactions. Amongst the infections were 2 respiratory, 2 herpes zoster, 1 sinusitis 1 cellulitis, 1 urinary and 1 gastroenteritis. 94% knew they were taking a biosimilar and 80% had no objection. Patient concerns included safety and effectiveness. The treating doctor was 'quite' or 'very' happy with achievement of the therapeutic target in 66% of cases and 'unhappy' in only 15%.
Conclusions: Despite understandable concerns with the introduction of biosimilars, the experience with our first 160 patients was good; numbers remaining on the drug and adverse effects were similar to previous large studies of infliximab. Rheumatologists feel happy the therapeutic target has been met in a significant majority of cases. Continuous observation and pharmacovigilance are required as with the introduction of any new agent.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4200

AB1094 ASSOCIATION BETWEEN USE OF TRADITIONAL CHINESE MEDICINE AND MEDICATION ADHERENCE AMONG CHINESE-AMERICAN RHEUMATOLOGY PATIENTS

K. Sun[1], H. Tian[2], Y.J. Chang[3], L. Lee[1], J.C. Leng[4], L.A. Mandl[1]. *[1]Hospital for Special Surgery; [2]New York University School of Medicine; [3]Mount Sinai Beth Israel; [4]Memorial Sloan Kettering Cancer Center, New York, United States*

Background: Chinese-Americans (CA) are a fast-growing US immigrant group with high utilization of Traditional Chinese Medicine (TCM) and worse SLE and RA outcomes than Caucasians (1,2). The effect of TCM use on adherence to prescribed western medications for systemic rheumatic diseases is unknown.
Objectives: To evaluate whether TCM use is associated with adherence to western medicines prescribed for systemic rheumatic diseases among CA patients.
Methods: Patients with systemic rheumatic diseases were recruited from 2 rheumatology clinics that serve a predominantly CA immigrant population. Inclusion criteria were speaking Mandarin or English and having medication(s) prescribed by the rheumatologist. TCM use, adherence, Patient-Reported Outcomes Measurement Information System (PROMIS) domains, and other variables were assessed using validated instruments available in English and Chinese. Adherence was classified as high or medium/low based on the 8-item Morisky Medication Adherence Scale (3). Medication complexity was assessed using the Medication Regimen Complexity Index (MRCI) (4); higher score indicates more complexity.
Results: 177 enrolled, mean age 54 (range 20–97), 62% female, 73% ≤high school education, 75% Medicaid (subsidized insurance), and only 18% spoke English. Diagnoses were RA (43%), SLE (17%), SpA (16%), Sjogren's (8%), gout/CPPD (6%), and other (10%). 49% reported TCM use in the past year, most commonly *tuina* massage (48%), acupuncture (47%), and herbs (39%). 27% reported high adherence. Table 1 shows significant univariate associations with high adherence. In multivariate analysis adjusting for all variables in Table 1, only TCM use (OR 2.6, p=0.027) and higher MRCI (OR 1.1, p=0.019) were associated with high adherence.

Table 1

	High adherence, n=48	Med/Low adherence, n=129	p-value
Age, years (SD)	63 (11)	52 (17)	<0.001
Employed, %	29	48	0.044
≥20 years in US, %	58	39	0.02
Age at immigration, years (SD)	44 (14)	35 (12)	<0.001
RA, %	56	38	0.029
MRCI, mean (SD)	15 (7)	11 (6)	0.001
TCM use, %	63	44	0.03
PROMIS Sleep disturbance, T-score (SD)*	47 (10)	52 (9)	0.005
PROMIS Anxiety, T-score (SD)*	46 (11)	49 (10)	0.04
PROMIS Fatigue, T-score (SD)*	49 (11)	52 (10)	0.03

*Lower score is better.

Conclusions: Among poorly integrated and low socioeconomic status CA rheumatology patients, TCM use was statistically significantly associated with high adherence to western medication, as was higher MRCI. TCM use does not appear to represent an alternate but rather complementary approach to disease management in these patients. Future studies should evaluate whether TCM use is associated with disease activity and outcomes over time.
References:
[1] Barton JL, et al. Racial and ethnic disparities in disease activity and function among persons with rheumatoid arthritis from university-affiliated clinics. Arthritis Care Res 2011;63:1238–1246.

[2] Mok MY, Li WL. Do Asian patients have worse lupus? Lupus 2010;19:1384–1390.
[3] Morisky DE, et al. Predictive Validity of a Medication Adherence Measure in an Outpatient Setting. J Clin Hypertens 2008;10:348–354.
[4] George J, et al. Developmennt and Validation of the Medication Regimen Complexity Index. Ann Pharmacoepidemiol 2004;38:1369–1376.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1819

AB1095 EARLY DIAGNOSIS AND TREATMENT OF CHRONIC DISEASES: NATIONAL REVIEW AND GUIDELINES - RA AS AN EXAMPLE

L. Euller Ziegler on behalf of the High Council for Public Health (HCSP).
Rheumatology Department, Academic Hospital and University of Nice, Nice, France

Background: Managing the increasing burden of chronic diseases is a major public health problem. Are early diagnosis and management a key point for their optimal care and outcome?
Objectives: Assessing early diagnosis and management of chronic diseases was the aim of a study carried out by the High Council for Public Health (HCSP), independent national body gathering experts nominated by the Minister of Health, to provide health authorities with expertise on development of national public health goals, assess their achievement and contribute to their monitoring
Methods: A multidisciplinary working party run within the HCSP a review of scientific data supporting early intervention benefits, as well as frequency, impact and mechanisms of delayed management on individuals and society, in order to produce national guidelines. A huge amount of data were analyzed:argued contributions from national Professional organizations and Patient associations, literature analysis, audition of national agencies representatives.
Results: Early stages of chronic diseases are less studied than later ones.Nevertheless, there is a strong evidence that delayed diagnosis and management are frequent and often adversely affect patients and society. The frequency, length and burden of delayed care were analyzed, varying with each disease, availability of efficient treatments and guidelines, socio-economic context. Optimal time for adequate management from symptom onset was reviewed, as well as medico-economic studies
Rheumatologic disorders appeared as models, notably Rheumatoid Arthritis (well-established window of opportunity, international guidelines for early diagnosis and management, including T2T and patient active implication). Evidence for early treatment benefit was also found for spondyloarthritis, osteoporosis, obstructive sleep apnea syndrome, chronic obstructive pulmonary disease, renal insufficiency, autism spectrum disorders, bipolar disorders, ... Ethical considerations may arise; in Alzheimer's disease, a diagnosis source of marked anxiety, there is no effective pharmacological treatment- but non pharmacological treatments are quite helpful for patients and family and therefore recommended by health authorities.
Obviously, the benefit of early intervention must be strongly assessed. When this benefit is proven, too many patients are facing delays, often long, with adverse consequences and increased burden for society. The mechanisms of such delayed management are multiple and often intricate; we analyzed the barriers to optimal care linked with professionals, patients, family, health system and society, in order to identify the ways to optimize the outcomes and therefore improve the global health status of the population.
Finally the HCSP established a set of guidelines, in 3 axis

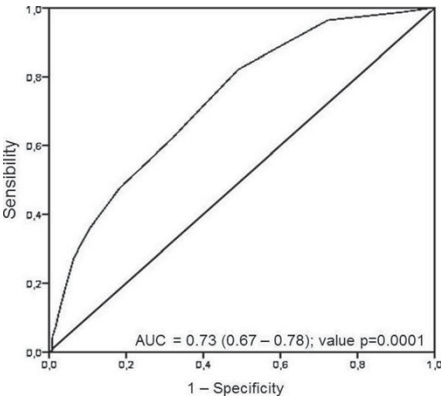
- disseminate widely the available knowledge among professionals, patients, the general public, taking into account the social poor perception of chronic diseases
- implement effectively change in practice toward early treatment, when appropriate:timely coordination between professionals and patient, fair diagnosis announcement, early patient implication, fight against social health inequalities
- develop research on early stages of chronic diseases, diagnosis, management and outcomes.

Conclusions: From a national public health perspective, early diagnosis and management, in the chronic diseases where their benefit is proven, should be better known and effectively implemented.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4038

AB1096 TIMED UP AND GO TEST (TUG) FOR SARCOPENIA SCREENING

L.I. Filippin[1], V.O.N. Teixeira[2], N.C. Oliviera[3], D.D. Berwanger[4], F. Miraglia[1].
[1]Program Post-graduat Saúde e Desenvolvimento Humano, Centro Universitário la Salle, Canoas/RS, Canoas; [2]Post-doctoral Fellow, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre; [3]Physiotherapy Graduate; [4]Physical Education Graduate, Centro Universitário la Salle, Canoas/RS, Canoas, Brazil

Background: Sarcopenia is a multifactorial syndrome characterized by a decrease of muscle mass and force together with functional performance impairment. Sarcopenia has been described as an independent predictor factor of health adverse outcomes such as falls, decreased quality of life, enhanced risk of death and higher treatment costs. However, there are just a few screening tolls of low cost and easy applicability to detect sarcopenia. In this context, a standard mobility assessment such as the TUG test has recently been described as a predictor of sarcopenia.
Objectives: To evaluate the performance of *timed up and go test* (TUG) as a screening toll for sarcopenia in the elderly.
Methods: This is a cross-sectional home study with 211 elderly participants of the South Region of Brazil. Sarcopenia diagnosis criteria was based on the European Working Group on Sarcopenia in Older People (EWGSOP). Individuals that presented low muscle mass (women: $\leq$6.37kg/m^2 and men: $\leq$8.90kg/m^2) added to decreased handgrip strength (women: $<$20kgf and men: $<$30kgf) and/or walking speed ($\leq$0.8m/s) were considered sarcopenic. TUG test quantifies functional mobility through the task of getting up from a chair, walking 3m and come back to sit on the chair.
Results: Based on EGWSOP criteria for sarcopenia, 17.1% (n=36) received the sarcopenia diagnosis. A ROC curve was constructed to evaluate the discriminatory power of TUG (AUC: 0.73 [IC 0.67 – 0.78; p=0.0001]). TUG test presented high sensibility (88.9%) and negative predictive values (93.2%), with a cutoff point of 7.5 seconds (figure 1).



Conclusions: Detecting the beginning of sarcopenia could allow for early interventions and slow the syndrome process, preventing further hospitalizations and economic burden. In this context, TUG is an easy, fast and low-cost test with high sensibility for sarcopenia detection that could be used as screening toll for this syndrome.
References:
[1] Barbosa-Silv TG, Bielemann RM, Gonzalez MC, et al. Journal of Cachexia, Sarcopenia and Muscle. 2016; 7:136–143.
[2] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Age Ageing. 2010;39(4):412–23.
[3] da Silva Alexandre T, de Oliveira Duarte YA, Ferreira Santos JL, Wong R, Lebrão ML. J Nutr Health Aging. 2014;18(8):751–6.
[4] Ishii S, Tanaka T, Shibasaki K, Ouchi Y, Kikutani T, Higashiguchi T, et al. Geriatr Gerontol Int. 2014;14 Suppl 1:93–101.
[5] Malmstrom TK, Morley JE. J Am Med Dir Assoc. 2013;14(8):531–2.
[6] Martinez BP, Gomes IB, Oliveira CS, Ramos IR, Rocha MD, Forgiarini Júnior LA, et al. Clinics (Sao Paulo). 2015;70(5):369–72.
Acknowledgements: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq); Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2385

AB1097 PATIENTS' EXPERIENCES OF REMOTE MONITORING OF RHEUMATOID ARTHRITIS USING A SMARTPHONE APP

L. Austin[1], C. Sanders[1], W. Dixon[2]. *[1]Centre for Primary Care, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre; [2]Arthritis UK Centre for Epidemiology, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom*

Background: The care of patients with Rheumatoid Arthritis (RA) is guided by monitoring changes in disease activity. However, whilst a number of patient-related outcome measures (PROMS) exist[1], they are not collected on an on-going basis. Consequently, there are few objective measurements of disease activity, between clinic visits, to inform treatment decisions. In response to this, the REMORA study (REmote MOnitoring of Rheumatoid Arthritis) is developing a smartphone app, to capture data on disease activity and integrate it directly into the electronic patient record. The project explores whether on-going collection of electronic patient-reported outcomes (ePROS) between clinic visits can enhance clinical care, support patient self-management, and provide a sustainable source of data for research.
Objectives: To describe patients' experiences of remote monitoring of their disease activity, and the perceived value in relation to clinical consultations and self-management.
Methods: A diverse sample of 20 patients with RA entered data into the app over

a three month period in response to daily, weekly and monthly question sets (table 1). An optional diary component was included, but not integrated into the EPR. The ePROS had been determined during earlier interviews with rheumatology patients, practitioners and researchers.
Qualitative interviews were conducted with patients at the end of the three month period. Interviews explored patients' views on the components of the app, and perceived implications for self-management and clinical care. Interviews were transcribed and analysed thematically.
Results: Qualitative analysis of the data identified a number of themes including; the benefits and limitations of using scales to reflect changes in symptoms experienced, the value of the diary for providing contextual information and an *"outlet"* for feelings, and the impact the data made to their clinical consultation and self-management.
Overall, the collection of longitudinal data was seen as useful by patients. Successful integration with the EPR allowed data to be displayed graphically during clinical consultations. Reviewing remote monitoring data detected changes which may otherwise have been missed such as flares in disease, or gradual improvements in response to new treatments. Data therefore facilitated "*a shared conversation*" and decision making around treatment plans.
Additionally, being able to self-reflect on data recorded enabled patients to identify triggers and alleviators in relation to their disease activity and take steps to self-manage their RA; for example, by recognising when they needed to rest as opposed to *"just carrying on"* when their symptoms were more severe.

Table 1. ePROS

Daily	Pain, difficulty with physical activities, fatigue, sleep difficulties, physical wellbeing, emotional wellbeing, coping
	Morning stiffness
Weekly	Number of tender & swollen joints
	Global assessment of wellbeing
	Employment status
	Impact on number of hours worked
	Experienced a flare
	Description of flare
Monthly	Health Assessment Questionnaire (HAQ) impact of disease on daily activities.

Conclusions: The app was well received by patients and feedback suggests that the ePROS recorded can capture changes in disease activity in a manner that is meaningful to patients and facilitates both clinical consultations and self-management.
References:
[1] http://oml.eular.org/Toolbox of Patient Reported Outcomes.
Acknowledgements:.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6552

AB1098 TEMPORARY WORK DISABILITY CAUSED BY MUSCULOSKELETAL DISEASES AT THE HOSPITAL CLÍNICO UNIVERSITARIO DE VALLADOLID: 6 MONTHS EXPERIENCE

M.D. Sánchez González [1], C.C. Macía Villa [2], C. González-Montagut Gómez [1], J. Medina Luezas [1]. *[1]Rheumatology, Hospital Clínico Universitario de Valladolid, Valladolid; [2]Rheumatology, Hospital Universitario Severo Ochoa, Leganés (Madrid), Spain*

Background: Musculoskeletal diseases are the leading cause of disability in the world and have a high impact on direct (health) and indirect (labor) costs. Labor casualties in Spain, when temporary, are known as temporary work disability (TWD). Since 2013, follow-up of patients with TWD (when the origin of the disease is a musculoskeletal condition) is being carried out in a monographic consultation within the external consultations of the Rheumatology Service of the Hospital Clínico Universitario de Valladolid.
Objectives: To describe the experience of the last 6 months in the consultation of temporary musculoskeletal incapacities (TWDMSDs) of the Hospital Clínico Universitario de Valladolid.
Methods: The TWDMSDs consultation is operational 2 days a week. The referral system is direct from Medical Inspection via email (1st part confirmatory work leave). The patients come from 7 Health Centers (population 82,000 people). The agenda is configured daily according to the emails sent, contacting the patients by telephone, excluding those with trauma, surgeries, pregnancies, non-localized, rejection or discharge. The assessment of the patients in consultation, according to usual clinical practice. A medical report is issued (medical history, physical examination, completed or requested tests, recommendations and treatment). The data are collected in SPSS, proceeding to its subsequent analysis.
Results: During the last six months of follow-up, 354 emails have been received. A total of 106 patients were evaluated, with the following characteristics: 54.3% women and 45.7% men, mean age 43.4 years, 95% performed physical work. Axial pathology was observed in 67.8% of cases and peripheral in 32.2%. The patients evaluated with some rheumatic pathology reached 96%. The average delay from the start of the work leave to the email was 12.2 days, and from the start of the work leave to the first consultation of 6.7 days (including weekends). 65.4% of the patients were discharged from the TWDMSDs agenda in the 1st consultation, without requiring interconsultations or requests for diagnostic tests, with an infiltration of 8% of the patients, arthrocentesis at 2%, ultrasound at 28% and Exercise guidelines were given to 76% of patients. The mean number of consultations up to discharge was 1.3. The mean time from onset of discharge to discharge was 21.1 days and from the first consultation until discharge by Rheumatology was 6.6 days.
Conclusions: The TWDMSDs consultation makes possible the early detection of rheumatologic musculoskeletal pathology, allowing an early action that minimizes the number of requested tests and interconsults generated and achieves an early diagnosis and treatment of patients, with the consequent benefits that this entails. The patients evaluated in consultation are mainly of average age, with physical work, mechanical pathology, resolution of the problem that causes the TWD and reincorporation to the working life of early form. In the discharge report, recommendations are included to minimize future casualties (work refocus, orthotics, exercises, treatment regimens in the event of a recurrence of symptoms) and explain the importance of being actively involved in their pathology to prevent progression.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2886

AB1099 COUNSELLING ON FAMILY PLANNING AND CONTRACEPTION, AND PREGNANCY OUTCOME IN WOMEN WITH RHEUMATIC DISEASES: A NATIONAL SURVEY OF 398 PATIENT-REPORTED QUESTIONNAIRES FROM 24 RHEUMATOLOGY CENTERS

M.G. Lazzaroni [1], F. Dall'Ara [1], L. Andreoli [1], C. Carini [1], M. Rodrigues [2], R. Reggia [1], E. Bartoloni-Bocci [3], R. Gerli [3], C.B. Chighizola [4], M. Gerosa [4], P.L. Meroni [4], L. Sinigaglia [4], P. Conigliaro [5], R. Perricone [5], A. Corrado [6], F.P. Cantatore [6], S. D'Angelo [7], I. Olivieri [7], M. Favaro [8], A. Doria [8], A. Ruffatti [8], E. Generali [4], C. Selmi [4], M. Meroni [9], M. Cutolo [9], M. Padovan [10], M. Govoni [10], G. Pazzola [11], C. Salvarani [11], S. Peccatori [12], G. Paolazzi [12], I. Prevete [5], G.D. Sebastiani [5], G. Minisola [5], A. Brucato [13], V. Ramoni [14], R. Caporali [14], C. Montecucco [14], C. Tani [15], M. Mosca [15], M. Trevisani [16], N. Malavolta [16], M. Vadacca [5], A. Afeltra [5], E. Vivaldelli [17], A. Maier [17], E. Baldissera [4], E. Visalli [18], R. Foti [18], L. Zuliani [19], A. Gabrielli [19], N. Romeo [20], A. Tincani [1]. *[1]Brescia, Italy; [2]Coimbra, Portugal; [3]Perugia; [4]Milano; [5]Roma; [6]Foggia; [7]Potenza; [8]Padova; [9]Genova; [10]Ferrara; [11]Reggio-Emilia; [12]Trento; [13]Bergamo; [14]Pavia; [15]Pisa; [16]Bologna; [17]Bolzano; [18]Catania; [19]Ancona; [20]Cuneo, Italy*

Background: Rheumatic diseases (RD) predominantly affect young women during reproductive age. Pregnancy, contraception and family planning (FP) are crucial for the quality of life of these patients.
Objectives: We aimed to investigate 'women's health' through a self-reported questionnaire. Answers from patients with connective tissue diseases (CTD) vs chronic arthritis (CA) were compared.
Methods: 24 centres distributed the questionnaire (65 multiple-choice and 12 open-answer questions) to women with RD (18–45years) regularly attending their outpatient clinics.
Results: Answers were collected from 249 CTD vs 149 CA patients. Their desire to have children was influenced by RD in 40% of cases: half of them reduced the number of children they wanted (Table 1). 39% CA vs 29% CTD were afraid of being mother because of disability.
24% CTD vs. 18% CA had at least one miscarriage; 21% CTD vs. 2% CA had more than one.
31% CTD and 34% CA were never asked about their desire to have children. 61% CTD vs 70% CA received counselling about contraception, given by a gynaecologist (G) (58% vs 64%), rheumatologist (R) (22% vs 14%) or both (7% vs 9%). 60% in both groups received a counselling before pregnancy: 34% vs 39% from R and G, 14% vs 22% by R. This positively changed family planning in 64% vs 59%. We created a Knowledge Index (based on the average of the normalized performed scores on 6 key questions for different sections): 55% CTD patients vs 44% CA had a medium-high score. A higher score directly correlated with the desire to became pregnant and with a multidisciplinary counselling.

The disease has reduced your desire to have children?

	CTD	CA
NO	36/91 (40%)	22/54 (41%)
YES	52/91 (57%)	28/54 (52%)
No Answer	3/91 (3%)	4/54 (7%)

If yes, I reduced the number of children that I wanted, because I was afraid...	CTD	CA
...of not being able to take care of them because of the disease	26/91 (29%)	21/54 (39%)
...that the child could have the same disease	15/91 (17%)	8/54 (15%)
...that drugs or disease could harm the baby	26/91 (29%)	20/54 (37%)

Table 1. Reasons for reduced family size in patients who declared that their RD had influenced their desire of having children

Conclusions: This survey suggested that CTD have a major impact on FP and family size, possibly mediated by the increased rate of miscarriages as compared to CA. Concerns about reproductive issues could be positively overcome by adequate counselling.
Rheumatologists should implement the discussion about FP and the compatibility of drugs with pregnancy in the management of young women with RD, especially those with CTD for whom contraception and pregnancy have particular implications.
Acknowledgements: Statistical analysis supported by an unrestricted grant by UCB Pharma
Thanks to Patients' Associations and Participants
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2268

AB1100 PATIENT SELF-MANAGEMENT APPS AS ONE MODULE OF AN INTEGRATED TIGHT-CONTROL CONCEPT BASED ON THE EXAMPLES OF THE DIGITAL APPLICATIONS RHEUMALIVE UND AXSPALIVE

M. Feuchtenberger[1], S. Kleinert[2], F. Schuch[2], S. Spähtling-Mestekemper[3], C. Kuhn[4], M. Welcker[5]. *[1]Rheumatologie, Schwerpunktpraxis für Rheumatologie, Burghausen; [2]Rheumatologie, Rheumatologische Schwerpunktpraxis, Erlangen; [3]Rheumatologie, Rheumapraxis München-Pasing, München; [4]Rheumatologie, internistische Schwerpunktpraxis am Ludwigsplatz, Karlsruhe; [5]Rheumatologie, MVZ für Rheumatologie Dr. Martin Welcker, Planegg, Germany*

Background: Medical Applications have the potential to support physicians and patients to document the course of the disease and optimize therapies. We describe the linkage and integration of patient reported outcomes (PROs) into existing medical office software and rheumatologic documentation systems by means of the digital applications RheumaLive and AxSpALive. RheumaLive is certified as medical product class I, and certification for AxSpALive is in preparation.
Methods: RheumaLive and AxSpALive are applications that can be downloaded free of charge from the common app-stores (Android, Apple) and installed on mobile devices (smartphones, tablets). A freeware version for PCs is also available (Windows- und Mac OS X-Version). A diary functionality allows to document the medication uptake (partially filed, memory-functionality for medication uptake available), validated scores like VAS, SJC, morning stiffness, FFBh (comparable to HAQ), BASDAI, RADAI, etc. and days of sick leave (+/- related to the rheumatic disease). All App-versions are password-protected, which is provided by the treating rheumatologist (relationship patient-physician).
The patient reported outcomes are stored locally on the respective device. For the subsequent visit, they can be printed or sent encrypted to the treating physician via internet in a prespecified interval. A specific software allows to integrate the data into the existing medical office software.
In daily practise, data entered by patients into RheumaLive can be screened and compared with collected clinical data and laboratory measures, because of it's certification as medical product. In case of an increasing disease activity the patient can be rapidly contacted and medication can be modified, if necessary. Regular F2F-appointments remain integral part of the medical care, even in case of good controlled disease activity. But in case of F2F-appointments, PROs can be delivered by patients, saving time and resources.
The PROs can be made available to rheumatologic documentation systems like RheumaDok via predefined interfaces.
Results: In a first pilot phase 54 patients in 4 rheumatologic specialised practices were documented. In the next phase the number of patients and participating practices/centres shall be increased.
Further studies are necessary to show if the integration of PROs which are collected via electronical application can lead to an improvement of rheumatologic diseases.
Conclusions: The integration of PROs collected with RheumaLive and AxSpALive into existing rheumalogic documentation systems allows a close monitoring of disease courses and therapies according to the "tight control" principle.
Acknowledgements: RheumaLive and AxSpALive werde developed by Starhealth GmbH on behalf of UCB Pharma GmbH.
Disclosure of Interest: M. Feuchtenberger Speakers bureau: UCB, S. Kleinert Speakers bureau: UCB, F. Schuch Speakers bureau: UCB, S. Spähtling-Mestekemper Speakers bureau: UCB, C. Kuhn: None declared, M. Welcker Speakers bureau: UCB
DOI: 10.1136/annrheumdis-2017-eular.5782

AB1101 QUALITY OF LIFE AND WORK IN PATIENTS WITH ANKYLOSING SPONDYLITIS OF WORKING AGE

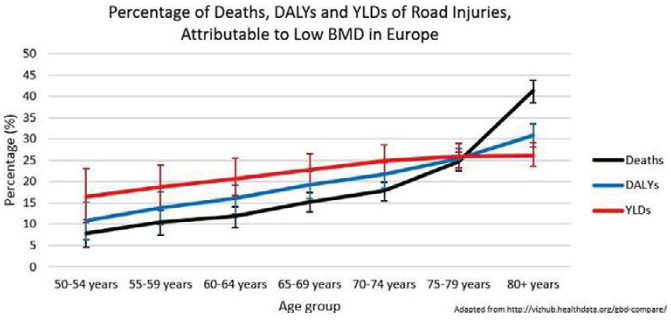
M. Parvu[1], G.M. Muresan[2], A.I. Cozos[3], I.A. Biro[1], H.V. Popoviciu[1], S. Szasz[1], S. Voidazan[4]. *[1]Rheumatology, Rehabilitation, University of Medicine and Pharmacy Tg.Mures, Emergency County Hospital; [2]Internal Medicine; [3]Rheumatology, Rehabilitation, Emergency County Hospital; [4]Epidemiology, University of Medicine and Pharmacy, Tg.Mures, Romania*

Background: The assessment of the quality of life is a current research issue in patients with ankylosis spondylitis[1,2]. The tools for assessing the life quality, come to complete the other methods of investigation, which assess in a subjective manner the negative impact of the disease on daily activities.
Objectives: The purpose of this study is to define the functional ability, the disease activity, to investigate the correlation between work and quality of life, and the impact of the quality of life in patients with AS.
Methods: The study is an observational prospective study, which includes a total of 91 patients defined with AS in according to the modified New York criteria, from the Rheumatology Clinic of Targu-Mures. Data were obtained by questionnaires including several generic and disease related Quality of life tools. It includes specific tools: BASDAI (Bath Ankylosing Spondylitis Disease Activity Index); BASFI (Bath Ankylosing Spondylitis Functional Index); ASQOL (Ankylosing Spondylitis Quality of Life); and generic tools:SF-36 (Short-Form 36), Eq 5D (European-Quality of life 5 Dimensions), HAQ (Health Assessment Questionnaire and VAS (Visual Analogue Scale).
Results: Out of 91 patients, 82% were males, 18% were females; mean age (years) 50,27±11,05SD; age at disease onset (years)36,20±13,51SD; duration of disease (years) 14,22±9,69SD; retiring mean age (years) 44,54±7,65SD. The mean values for BASDAI=4,23±2,21SD; BASFI=4,88±2,61SD; EQ-5D=5,71±0,20SD; EQ-VAS=64,26±18,938D; HAQ=0,747±0,51SD; SF-physical summary=33,53±8,33SD; SF-emotional summary=47,57±10,03SD; ASQOL=6,94±2,68SD. We found a positive correlation between the disease onset and retiring age $p<0,0001$, r=0,731a nd a negative significant correlation between BASFI and SFphysical summary ($p<0,0001$, r=-0,798), ASQOL and SF-emotional summary, $p<0,0001$, r=-0,595).
Conclusions: The results showed the invalidant potential of the AS, with major impact upon the quality of life.
References:
[1] Van der Heijde D, Landewe R. Assessment of disease activity, function and quality of life. In 1st edition Philadelfia:Mosby Elsevier;2006, 206–213.
[2] Dovard LC, McKenna SC, Meads MD et all. Translation and Validation of non English version of the ASQOL questionnaire. BioMed Central, Health and QOL outcomes, 2007, 5L7 doiL1.1186/1477–7525–5-7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6559

AB1102 LOW BONE MINERAL DENSITY IS A MAJOR CONTRIBUTOR IN THE EUROPEAN HEALTH BURDEN DUE TO ROAD TRAFFIC ACCIDENTS IN PEOPLE AGED 50 YEARS AND ABOVE

N. Wilson[1], L. Sanchez-Riera[2], D. Prieto-Alhambra[3], C. Cooper[4], K. Dreinhöfer[5], A. Woolf[6], L. March[1], P. Halbout[7]. *[1]Institute of Bone and Joint Research, University of Sydney, Sydney, Australia; [2]University Hospital Bristol NHS Foundation Trust, Bristol; [3]Oxford NIHR Musculoskeletal Biomedical Research Unit, University of Oxford, Oxford; [4]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, United Kingdom; [5]Center for Musculoskeletal Surgery, Charité Universitätsmedizin, Berlin, Germany; [6]Institute of Health Research, University of Exeter Medical School, Exeter, United Kingdom; [7]International Osteoporosis Foundation, Nyon, Switzerland*

Background: Road traffic accidents (RTAs) are the second leading injury health burden and cause of death in Europe, after falls (1). A significant but as yet unreported proportion of such burden is potentially due to low bone mineral density (BMD), especially among older people, through its relationship with fractures.
Objectives: To measure the percentage of deaths, disability-adjusted life years (DALYs) and years lived with disability (YLDs) due to RTA in people aged 50 years and above attributable to low BMD in the European population for the year 2015.
Methods: The estimates followed the Counterfactual Risk Assessment Methodology used in the GBD study (1). Systematic review was performed seeking population-based studies with femoral neck BMD (FNBMD) measured by Dual-X-Ray-Absorptiometry in people 50 years and over. Age- and sex- specific levels of mean +/-SD FNBMD (g/cm^2) were extracted from eligible studies, and this was used as the exposure variable. The age and sex-specific 99th percentile from non-Hispanic whites in National Health and Nutrition Examination Survey (NHANES) 2009–2010 was used as theoretical minimum risk factor exposure distribution, to estimate the potential impact fraction (PIF) of FNBMD for fractures. Relative risks of FNBMD for fractures were obtained from a previous meta-analysis (2). Attributable deaths due to RTA-related fractures were obtained through coded hospital data. Disability levels were established by applying disability weights to each type of fracture. Then, PIFs were applied to obtain attributable deaths and disability due to low BMD.
Results: In the European population aged 50–69 and 70 years and above, 10.8% (95% CI: 8.9–12.4%) and 30.9% (29.1–32.4%) of RTA-related deaths, respectively, were attributable to low BMD. In the age group 50–69 this was the second most important risk factor following alcohol use and in those 70 years and above became the most important risk factor, with double the weight of alcohol use. This represents 2,537 and 5,460 absolute deaths in those aged 50–69 and 70 years and above, respectively. The percentage of health burden and disability caused by RTAs attributable to low BMD grew steadily from the ages of 50 and onwards.
Conclusions: This data shows the non-previously reported important role of low BMD as a preventable risk factor for European RTAs' health burden in population 50 years and over, which requires urgent attention.



References:
[1] Forouzanfar et al. Lancet 2016.
[2] Johnell et al. JBMR 2005.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3278

AB1103 THE IMPORTANCE OF ADEQUATE SCREENING TO AVOID FALSE POSITIVES IN THE DIAGNOSIS OF RHEUMATOID ARTHRITIS

P. Santos-Moreno[1], D. Gomez[1], E. Castillo[1], R. Giraldo[1], G. Ballesteros[1], L. Villarreal[2], D. Buitrago-Garcia[3], J. Bello[3]. *[1]Rheumatology; [2]Psychology and processes; [3]Epidemiology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: The lack of expertise and skills in the diagnosis of in rheumatoid arthritis (RA) in primary level of Colombian medical centers can cause misdiagnosis of rheumatic diseases. Due to this issue in a specialized center in RA we stablished a multidisciplinary model and a strict disease management algorithm to diagnose properly our patients; as a consequence we have achieved the accurate diagnosis of great proportion of patients that were false positives diagnosed initially as RA.
Objectives: The aim of this study was to show effectiveness and accuracy of a screening method to avoid false-positive diagnosis of RA in a cohort of patients with supposed diagnosis of RA.
Methods: During two years we evaluated patients with presumptive diagnosis of RA. We conducted a cross-sectional study; we included patients who were referred from primary care centers to a RA specialized center in a 24 month period with presumptive diagnosis of (RA). Each patient was evaluated to confirm or rule-out diagnosis of RA as follows: a rheumatologist fulfilled a complete medical record, including joint counts; it was assessed rheumatoid factor and anti-citrullinated antibodies, and other laboratories depending on each case. Also were made x-rays of hands and feet, and in some cases of persistent doubt about the diagnosis was requested comparative MRI of hands or/and feet. Descriptive epidemiology was perfomed.
Results: Between 2015 and 2016 6813 patients were evaluated in our specialized center, in 76% of cases RA was confirmed, the remaining 1593 patients (24%) had a wrong diagnosis of RA; of these misdiagnosed patients, (87%) were female, and 205 (13%) male, with an average age of 62±12 years. Between differential diagnosis which were found in this cohort of misdiagnosed patients: osteoarthritis in 849 patients (63.3%), Sjögren syndrome (7%) Systemic lupus erythematosus (6%) the remaining 30% of patients had conditions such as gout, psoriasis, osteoporosis, myalgia, soft tissue diseases among others. The majority of patients with wrong diagnosis took DMARDs (23%), calcium (11%), biologics (10%) acetaminophen (9%), neuropathy medications (7%), acetaminophen plus opioids (5%), osteoporosis medications (5%), opioids (4%), glucosamine (4%), diacerein (3%), the remaining patients took medications such as NSAID, glucosamine, antigout agents, gastritis drugs, among others.
Conclusions: The results of this program show that almost 25% patients with presumptive RA diagnosis are misdiagnosed; this is evidence that can be extrapolated to primary care centers in Colombia. The most important cofounding diagnosis was osteoarthritis and many patients were receiving DMARDs for treatment. For this reason there is an urgent need of education strategies for primary care physicians and the implementation of centers of excellence in RA, in order to conduct a proper diagnose and avoid clinical and health economics consequences of misdiagnosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5249

AB1104 COST-EFFECTIVENES ANALYSIS OF TNF INHIBITORS USE COMPARED TO DMARDS IN THE FATAL AND NONFATAL ACUTE CORONARY ISCHEMIC EVENT

R.K.S. Gomes[1], J.Y.K. Viscondi[2], M.R.C. Nobre[2]. *[1]Center of specialty of the municipality of Blumenau and Brusque, Blumenau; [2]São Paulo University, São Paulo, Brazil*

Background: Epidemiological studies have established that rheumatoid arthritis is associated with an increase in cardiovascular disease[1,2]. The evaluation of tumour necrosis factor inhibitors (TNFi) on the reduction of the risk of acute myocardial infarction and death due to cardiovascular causes has shown promising results[3]. The economic evaluation for these outcomes are not established yet.
Objectives: To evaluate the cost-effectiveness of TNFi versus disease-modifying antirheumatic drugs (Dmards) to avoid a new case of acute ischemic heart disease and death in rheumatoid arthritis patients.
Methods: A cost-effectivenes analysis (CEA) was performed using a Markov model 6-month transition cycle, with time horizon of 30 years, under the Brazilian public healthcare system perspective. Costs are expressed in 2015 Reais and effectiveness measures are new cases of acute ischemic coronary disease and cardiovascular death.
Results: The average cost in 30 years of Dmards and TNFi was 14,291,105.28 and 96,151,873.86 Reais, respectively. The incremental effectiveness was 2.69 cases of coronary artery disease and consequent incremental cost-effectiveness ratio (ICER) of 30,527,502.27 Reais per new cases avoided, while for cardiovascular death, incremental effectiveness was 1.33 and an ICER of 61,634,231,69 Reais per new cases avoided. The univariate analysis identified that the most relevant parameter in the ICER on both outcomes was the TNFi drug. The sensitivity analysis established that, in order to, reach the amount of willingness to pay (WTP) per semester to avoid an acute myocardial infarction, the average cost of TNFi should be 1,337.47 Reais per case avoided and the average cost for the cardiovascular death avoidence sould be 954.22 Reais. All the analyzes performed establish an unfavorable relationship of the drug treatment strategy with TNFi.
Conclusions: The findings of the CEA among patients with rheumatoid arthritis for cardiovascular outcomes when compared to the strategy of TNFi drug treatment with the dominant strategy Dmards after the first 6 months of exposure point out an unfavorable relationship, surpassing the amount of expenses recommended by the Ministry of Health of Brazil in the year 2015.
References:
[1] Symmons DP, Gabriel SE. Epidemiology of CVD in rheumatic disease, with a focus on RA and SLE. Nat Rev Rheumatol. 2011;7(7):399–408.
[2] Bergström U, Jacobsson LT, Turesson C. Cardiovascular morbidity and mortality remain similar in two cohorts of patients with long-standing rheumatoid arthritis seen in 1978 and 1995 in Malmö, Sweden. Rheumatology (Oxford). 2009;48(12):1600–5.
[3] Dixon WG, Watson KD, Lunt M, Hyrich KL; British Society for Rheumatology Biologics Register Control Centre Consortium. Reduction in the incidence of myocardial infarction in patients with rheumatoid arthritis who respond to anti-tumor necrosis factor alpha therapy: results from the British Society for Rheumatology Biologics Register. Arthritis Rheum. 2007;56(9):2905–12.
Acknowledgements: Foundation for Research Support of the State of São Paulo, FAPESP 2013/12979–1.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2124

AB1105 FACTORS IMPACTING PATIENTS' DECISION TO START TREATMENT VARY BY RACE

R. Cozmuta[1], L. Fraenkel[2]. *[1]Rheumatology, Emory University, Atlanta; [2]Yale University, New Haven, United States*

Background: Previous research has found that young minority women tend to be more risk averse compared to their Caucasian counterparts. The reasons underlying these differences, however, are not understood.
Objectives: The objective of this study was to examine whether factors influencing perceived treatment importance vary by race.
Methods: Women between the ages of 20 and 45 completed a survey. The survey recorded sociodemographic data, trust in healthcare systems and beliefs in medications. It also included a hypothetical scenario in which subjects were asked to rate the importance of taking a medication for a patient with joint pain, migraines and fatigue that benefits 70% of people and is well tolerated except for the rare risk (1 per 100,000) of a neurologic disease that may cause weakness, trouble with vision and numbness. Associations between patient characteristics, medication beliefs, and trust with perceived importance of taking the medication were evaluated for each race. Variables found to be statistically significant were subsequently evaluated using multiple linear regression.
Results: 299 women completed the survey. Baseline characteristics by ethnicity are described in Table 1.Hispanic women had more negative medication beliefs than did Non-Hispanic Whites, and both Non-Hispanic Black and Hispanic

Table 1. Patient characteristics by race

Variable	Non-Hispanic White	Non-Hispanic Black	Hispanic	P value
Age (mean, SD)	34.1 (7.2)	35.2 (8.4)	32.8 (8.6)	0.1
Poor self-reported health (%)	12	14	12	0.9
Some college education (%)	75	61	43	**<0.01**
Income <12,000/year (%)	23	33	34	0.2
Difficulty paying for meds (%)	68	58	60	0.3
Medication beliefs (mean, SD)	20.6 (4.6)	21.6 (4.4)	22.3 (4.7)	**0.04**
Trust (mean, SD)	27.9 (5.5)	28.6 (5.7)	29.1 (5.5)	0.3
Hopeful (mean, SD)	4.2 (1.6)	3.5 (1.7)	3.6 (1.7)	**<0.01**
Worried (mean, SD)	4.6 (1.6)	4.8 (1.8)	5.1 (1.6)	0.2
Important (mean, SD)	5.3	5.6	5.5	0.3

Table 2. Association of subject characteristics with perceived importance by race

Variable	Non-Hispanic Whites	Non-Hispanic Blacks	Hispanics
Medication beliefs[1]	- 0.55 (**<0.01**)	-0.24 (**0.01**)	-0.08 (0.46)
Hopeful[1]	0.54 (**<0.01**)	0.16 (0.09)	0.37 (**<0.01**)
Worried[1]	- 0.27 (**0.01**)	-0.02 (0.87)	0.05 (0.66)
Trust[1]	0.22 (**0.02**)	0.33 (**0.01**)	0.17 (0.11)
Poor self-reported health[2]	1.66 (0.10)	1.19 (0.25)	-1.4 (0.16)
Some college education[2]	-1.16 (0.25)	1.9 (0.06)	0.65 (0.52)
Income <12,000/year[2]	0.38 (0.71)	1.65 (0.11)	0.06 (0.96)
Difficulty paying for meds[2]	0.00 (0.99)	-2.05 (**0.04**)	-0.42 (0.68)

[1]Correlation coefficient (p value); [2]T-test (p value).

subjects had lower levels of hope compared to Non-Hispanic White subjects (difference between means <0.05). Associations between subject characteristics and perceived importance of taking the medication are presented in Table 2. In a multilinear regression model (including education, difficulty paying for medications, medication beliefs, trust, hope and worry), hope was associated with perceived importance of taking the medication in all three ethnic groups. Additional findings differed by race, with medication beliefs in Non-Hispanic White subjects; difficulty paying for medications in Non-Hispanic Black subjects, and worry in Hispanic subjects being associated with perceived importance of taking the medication.

Conclusions: Our findings confirm the important influence of emotion on decision making, and suggest that while hope is universally associated with perceived importance of taking a medication, other factors differed, highlighting differences in the decision making process across ethnic groups.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2369

AB1106 VERBAL PATIENT EDUCATION ON VACCINATION IN ADULTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES: IS IT ENOUGH TO IMPROVE VACCINATION RATES?

R. Magro, M. Rogers, F. Camilleri. *Rheumatology, Mater Dei Hospital, Msida, Malta*

Background: Patients suffering from autoimmune inflammatory rheumatic diseases (AIIRD) are at increased risk of infections, due to the underlying condition and its treatment. A study on vaccination in AIIRD carried out at Mater Dei Hospital, Malta in 2015, showed that 37.9% of the patients received the influenza vaccine in the previous year and 8.3% had received the pneumococcal vaccine ever. Only 38.3% knew that they had an increased risk of infection because of their condition.

Objectives: The aim of the current study was to establish whether verbal education on vaccination, influenced patients' vaccination rates in the following year. A further aim was to determine whether the patients had a better understanding of their increased infection risk following verbal education.

Methods: The initial study carried out in 2015 consisted of a short face-to-face interview with 60 patients who suffered from autoimmune inflammatory rheumatic diseases. Following the interview, verbal information was given to the patients on their increased risk of infection, and the importance of vaccination, in particular the influenza and pneumococcal vaccine. After 1 year, the patients were contacted by means of a telephone call. They were interviewed with regards to their vaccination history and knowledge of their infection risk. Of the 60 patients, 2 had passed away. Therefore 58 patients were included in the study.

Results: The study included patients with a variety of AIIRD including rheumatoid arthrtitis, ankylosing spondylitis and psoriatic arthritis. 60.3% were females and the mean age was 63.1 years (range 25 to 82 years). Influenza vaccination rates in the previous year improved from 37.9% in 2015 to 41.4% in 2016 (p=0.704). Pneumococcal vaccination rates improved from 6.9% to 17.2% (p=0.086). On questioning the patients regarding their knowledge of increased infection risk, there was no improvement following the verbal education. In fact 37.9% of patients questioned in 2015, and 34.5% in 2016 knew that they were at increased risk of infection because of their condition. 33% of patients studied in 2016 could recall that they had been advised to take vaccination because of their underlying condition or treatment. This improved from 7% in 2015 (p<0.005). The proportion of patients who could recall the vaccination advice given was significantly higher in those below 61 years (p<0.005). However, there were no significant gender difference (p=0.147).

Conclusions: Verbal education resulted in more patients receiving the pneumococcal vaccination (although not statistically significant because of the small number involved). It also resulted in a significant increase in the number of patients who were able to recall that they were adviced to take vaccination because of their condition. However, only 33% could recall this after a year. Verbal education did not effect the number of patients who took the influenza vaccine and the patients' knowledge of their increased infection risk.

This study highlights that verbal education helps to improve vaccination rates in autoimmune inflammatory rheumatic diseases. However, the advice given tends to be forgotten by the majority of patients after one year. Thus repeated verbal education is necessary, particularly in elderly patients. Moreover other methods of education, such as written information in the form of leaflets, may be useful.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1962

AB1107 ASSESSMENT OF AGREEMENT BETWEEN SELF-REPORT INFLAMMATORY ARTHRITIS SYMPTOMS AND CORRESPONDING GP DIAGNOSIS IN PATIENTS WITH PMR

S.L. Hider[1,2], M. Blagojevic-Bucknall[2], S. Muller[2], K. Clarkson[2], C. Mallen[2]. *[1]Haywood Academic Rheumatology Centre, Haywood Hospital, Staffordshire; [2]Arthritis Research UK Primary Care Centre, Keele University, Keele, United Kingdom*

Background: Polymyalgia rheumatica (PMR) is the commonest inflammatory condition among those aged 50 years and over, with a lifetime risk of 2.4% in females and 1.7% in males. Seronegative rheumatoid arthritis is an important differential diagnosis. It is thought a proportion of PMR patients develop an inflammatory arthritis, although prevalence estimates vary.

Objectives: To determine the proportion of PMR patients (1) reporting symptoms of possible inflammatory arthritis using a validated self-report inflammatory arthritis algorithm; and (2) who subsequently receive a diagnosis of inflammatory arthritis in their primary care medical records.

Methods: A cross-sectional questionnaire study was developed to investigate impact of PMR in primary care patients. All eligible adults aged ≥50 years, registered with one of 150 participating practices with a first ever Read coded diagnosis of PMR in the last 3 years were mailed a questionnaire including items about socio-demographics, PMR characteristics, joint problems and comorbid conditions. Self-reported inflammatory arthritis (IA) was defined using a validated scoring algorithm (1) with positive responses coded as 1 and negative responses as -1; a score >0 is regarded as predictive of IA. IA score was calculated for those patients that had complete data on all required variables. A list of Read Codes relating to inflammatory arthritis, compiled by a rheumatologist and a GP, were searched for in primary care medical records of consenting respondents. Period of interest was from date of first ever PMR diagnosis in the medical records until survey mail-out.

Results: 704 eligible patients were identified and sent a questionnaire, with 550 (78%) responding. Responders and non-responders did not differ significantly by age or gender. Medical records could be obtained for 385 patients, of whom 310 completed the questionnaire fully and were included in the analysis. IA score ranged from -8.4 to 2.5, with 21 (7%) patients being classed as having a positive IA score. 8 out of 310 patients had at least one inflammatory arthritis Read code recorded from date of first diagnosis of PMR in their medical record, although only 2 of these also fulfilled the self-report IA criteria.

Conclusions: In this PMR cohort the proportion subsequently diagnosed with an inflammatory arthritis was low (2.5%) although more patients reported inflammatory symptoms. The agreement between self-reported inflammatory symptoms and Read Code diagnosed inflammatory arthritis was low.

References:

[1] Tavares R, Wells GA, Bykerk VP et al. A a parallel group cohort to determine the measurement properties of an early inflammatory arthritis detection tool. Rheumatology 2013;52:2077–2085.

Acknowledgements: This study represents independent research funded by the National Institute for Health Research (NIHR). CDM is funded by the National Institute for Health Research (NIHR) Collaborations for Leadership in Applied Health Research and Care West Midlands, the NIHR School for Primary Care Research and a NIHR Research Professorship in General Practice (NIHR-RP-2014–04–026). The views expressed are those of the authors and not necessarily those of the NHS, NIHR or the Department of Health.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5271

AB1108 HANDLING OF DE NOVO ARTHRITIS IN ADULTS BY GENERAL PRACTITIONERS: A SURVEY IN A FRENCH COHORT

S. Lecauchois[1], S. Gentile[2], P. Champsaur[3], J.-P. Mattei[4], L. Dillinger[5], V. Goeb[6], S. Guis[4,7]. *[1]Aix Marseille Université, AP-HM, Marseille Cedex 9, France; [2]Public Health; [3]Radiology; [4]Rheumatology, Aix Marseille Université, AP-HM, Marseille Cedex 9; [5]General Practitioner, Aix-en-Provence; [6]Rheumatology, CHU Amiens, Université de Picardie Jules Verne, Amiens; [7]Crmbm-Cemerem UMR 7339, CNRS, Aix Marseille Université, Marseille, France*

Background: A guide of good clinical practice regarding *de novo* arthritis in adults has been edited.

Objectives: The aim of this work is to identify whether the diagnostic and therapeutic tools proposed by general practitioners (GPs) to adults with a *de novo* arthritis is in line with the corresponding recommendations.

Methods: A questionnaire regarding the characteristics and the handling of *de novo* arthritis in adults has been submitted to 300 GPs chosen randomly from a French cohort database. The study period was from February 2015 to February 2016. Fifty seven GPs participated in the study (19%).

Results: No particular specificity was identified in the GP group. The age of patients ranged between 40 and 75 yo. The prevalence of arthritis was less than 5% among the GPs patients. The relative number of each category of arthritis was rheumatoid arthritis (29%), spondyloarthritis (14%), PPR (8%), other kinds of microcrystalline arthritis: chondrocalcinosis, (38.4%), gout (11,6%).

Joints with mechanic degenerative effusion related to osteo-arthritis might be misdiagnosed as an inflammatory arthritis.

The knee was the most frequently involved joint in arthritis. The initial paraclinical

survey was related to biology. Most of the patients were treated with NSAI as an initial intent. A corticoids-based therapy was proposed to 1.4% of the patients and the corresponding specialist was a rheumatologist (98%).
Conclusions: The *de novo* arthritis prevalence for GPs is less than 5% with the knee being the most affected joint. Most frequently, GP are faced with gout, rheumatoid arthritis and spondyloarthritis. The handling is in line with the corresponding guide of good clinical practice.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2521

AB1109 DOSE DE-ESCALATION IN A SPECIALIZED OUTPATIENT CLINIC ON BIOLOGICAL THERAPY: COST MINIMIZATION OBSERVATIONAL STUDY

S. Manrique-Arija, I. Ureña, F.G. Jimenez-Nuñez, N. Mena-Vazquez, V. Coret, L. Cano-García, M.C. Ordoñez-Cañizares, C.M. Romero-Barco, M. Rojas-Gimenez, C. Domic, C. Fuego, G. Diaz-Cordoves, A. Belmonte, M.V. Irigoyen, A. Ponce, M. Rodriguez-Perez, A. Fernandez-Nebro. *Department of Reumatology at the University Regional Hospital of Malaga (HRUM). Institute for Biomedical Research in Málaga (IBIMA). Malaga University., Malaga, Spain*

Objectives: To estimate the annual cost in the use of biological therapy (BT) in patients with different rheumatic diseases when dose modifications are undertaken in daily clinical practice in a specialized outpatient clinic during 2016 and to compare the results with data obtained in 2013.
Methods: *Design:* Cost minimization observational study under conditions of clinical practice. *Patients:* Patients with different rheumatic diseases who come to a specialized outpatient clinic on BT in the Rheumatologic department at a tertiary Spanish hospital (with a tight follow-up) that had been treated with BT under reduced doses during 2016 were collected. *Protocol:* Reductions in treatment dose or dose frequency were established empirically and were carried out by their rheumatologist in those patients who were in remission (DAS 28 <2,6) for at least 6 months without steroids. *Main outcome:* Reduction of annual average cost in euros in BT used in patients who are in dose reduction in clinical practice in 2016. Secondary outcome:Differences in annual costs reduction in 2016 compared with 2013. The cost reduction was calculated by comparing the actual expenditure (after modifying treatment dose in clinical practice) with the theoretical costs (official price) in case you had not made the adjustment. *Statistical analysis:* Sample descriptive analysis. Reducing annual absolute costs and by treatment after tapering down doses in clinical practice in 2016 and the differences found between 2013 were calculated.
Results: During 2016, the dose of the BT of 168 patients (94 Subcutaneous BT and 74 intravenous BT) were modified in clinical practice after reaching clinical remission:mean of DAS 28 (mean±SD)=2.31±0.76 or BASDAI (mean±SD)=2.15±1.39 without radiographic progression. Most patients were women (n=113;67%)and had rheumatoid arthritis (n=103;62%) and the rest were distributed among: spondyloarthritis (n=28;17%), psoriatic arthritis (n=22;13%), juvenile idiopathic arthritis (n=10;5%) and Systemic Lupus Erithematosus (n=5;3%). No patients treated with certolizumab or anakinra was modified treatment doses. During this period, 5 patients discontinued BT (3 remissions and 2 minor adverse events). Table 1 shows the number of patients by type of BT and costs. The BT dose reduction in clinical practice during 2016 represented a saving of *676,501.67*€ and a greater efficiency of treatments while in 2013, only 86 patients (30 etanercept, 15 adalimumab, 16 Infliximab (Remicade), 15 Tocilizumab IV and 55 Rituximab) had a modified dose of BT in clinical practice assuming a saving of 396,995.46€. The difference in the annual cost reductions in 2016 compared to 2013 meant a saving of 279.506,21€ more in the last year. Table 1.

Biological Therapy	Patients with reduced doses	Theoretical Annual costs (Label doses)	Real Annual Costs (Clinical practice doses)	Annual costs reduction 2016
Etanercept	53	582,453.04	317,649.69	264,803.35
Adalimumab	28	343,186.48	217,922.02	125,264.46
Golimumab	3	32,297.46	28,898.76	3,398.70
Tocilizumab sc	9	109,755.36	79,137.42	30,617,94
Tocilizumab iv	15	179,821.23	136,803.11	43,018.12
Abatacept	1	16,512.42	17,410.64	898.22
Infliximab (Remicade)	15	164,589.70	119,720.52	44,869.18
Rituximab	44	286,410.96	122,779.26	163,631.7
Total	168	**1,715,026.65**	**1,040,321.42**	**676,501.67**

Conclusions: In rheumatic diseases we may do a dose de-escalation of BT in patients who go into remission and therefore we could reduce the associated costs of BT and being more efficient with the treatments. We believe that it is important to create specialized outpatient clinics on BT where a tight-control management of these patients and an individualized treatment are carried out.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6220

AB1110 WHAT CAN GOOGLE TRENDS CAN TELL US ABOUT A DISEASE? BIG DATA TRENDS ANALYSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS

S. Sciascia, M. Radin. *Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Torino, Italy*

Background: "*Infodemiology*" and "*infoveillance*" are two recent terms created to describe a new developing approach for public health, based on Big Data monitoring and data mining, applicable to provide new insights into unmet needs, such as the epidemiology of an uncommon disease like Systemic Lupus Erythematosus (SLE)[1].
Analysing how people (including patients, researchers, physicians) search and navigate the Internet for health-related information, as well as how they communicate and share this information, can provide valuable insights into health-related behaviour of populations.
Objectives: In this study we aimed to investigate trends of Internet search volumes linked to SLE, on-going clinical trials and research developments associated to the disease, using Big Data monitoring and data mining. We also aimed to analyse peak-related information to investigate knowledge translation of novel therapies for SLE and the influence of media on health-related information seeking.
Methods: We performed a longitudinal analysis based on the large amount of data generated by Google Trends, scientific search tools (SCOPUS, Medline/Pubmed/ClinicalTrails.gov) considering "SLE", and "lupus" in a 5-year web-based research.
Results: We observed an overall higher distribution of search volumes from Google Trends in United States, South America, Canada, South Africa, Australia and Europe (mainly Italy, United Kingdom, Spain, France, Germany), showing a geographically heterogeneity in insight into health-related behaviour of the different populations towards SLE. Data from Medline/Pubmed, SCOPUS and ClinicalTrials.gov were also analysed in order to monitor public health relevant publications and on-going trials. When comparing these results to the distribution of search volumes of Google Trends, we observed an overall similar distribution of Big Data for United States and Europe, while South America, Canada, Australia and South Africa were less represented. We observed a misbalance between search volumes for Google Trends compared to Medline/Pubmed, SCOPUS and ClinicalTrials.gov in some areas, suggesting a recent and expanding interest on SLE-related health issues in some countries.

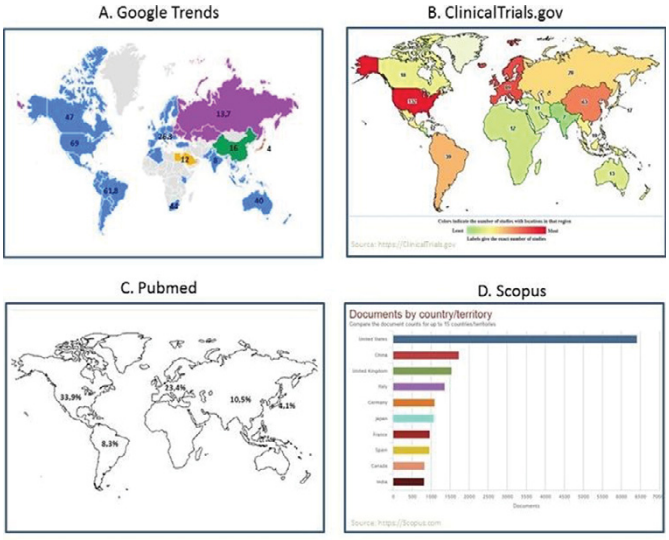


Figure1.: profile plots for relative search volumes. Profile plots show the relative search volumes, from January 2011 to January 2016, for 'Systemic Lupus Erythematosus' using Google Trends (Panel A), ClinicalTrials.gov (Panel B), PubMed (Panel C) and Scopus (Panel D). Date of search 16th October 2016.

Conclusions: We observed in some countries a misbalance between the search volumes generated by Google Trends and those analyzed through scientific search tools. This new approach, merging togheter informatics and epidemiology, is able to investigate health information seeking. In the near future it might give an estimate of the health-related demand and even of the health-related behaviour of patients with SLE.
References:
[1] Eysenbach G. Infodemiology and infoveillance: framework for an emerging set of public health informatics methods to analyze search, communication and publication behavior on the Internet. J Med Internet Res 2009;11:e11. doi:10.2196/jmir.1157.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1611

AB1111 A PROSPECTIVE COHORT STUDY MEASURING COST-BENEFIT ANALYSIS OF THE OTAGO EXERCISE PROGRAMME IN COMMUNITY DWELLING ADULTS WITH RHEUMATOID ARTHRITIS

S. Abdulrazaq[1], T. O'Neill[2], E.K. Stanmore[3], J. Oldham[1], D. Skelton[4], M. Pilling[5], B. Gannon[1], C. Todd[1]. [1]*School of Nursing, Midwifery and Social Work and MAHSC;* [2]*School of Medical Sciences;* [3]*School of Nursing, University of Manchester, Manchester;* [4]*University of Glasgow, Glasgow;* [5]*University of Manchester, Manchester, United Kingdom*

Background: Falls are one of the major health problems in adults with Rheumatoid Arthritis (RA). Interventions, such as the Otago Exercise Programme (OEP), can reduce falls in community dwelling adults by up to 35%. The cost-benefits of such a programme in adults with RA have not been studied
Objectives: To determine healthcare cost of falls in adults with RA, and estimate whether it may be cost efficient to roll out the OEP to improve function and prevent falls in adults living with RA.
Methods: Patients with Rheumatoid Arthritis aged ≥18 years were recruited from four rheumatology clinics across the Northwest of England. Participants were followed up for 1 year with monthly fall calendars, telephone calls and self-report questionnaires. Estimated medical cost of a fall-related injury incurred per-person were calculated and compared with OEP implemention costs to establish potential economic benefits.
Results: 535 patients were recruited and 598 falls were reported by 195 patients. Cumulative medical costs resulting from all injury leading to hospital services is £ 374,354 (US$540,485). Average estimated cost per fall is £ 1120 (US$1617). Estimated cost of implementing the OEP for 535 people is £ 116,479 (US$168,504) or £ 217.72 (US$314.34) per-person. Based on effectiveness of the OEP it can be estimated that out of the 598 falls, 209 falls would be prevented. This suggests that £ 234,583 (US$338,116) savings could be made, a net benefit of £ 118,104 (US$170,623).

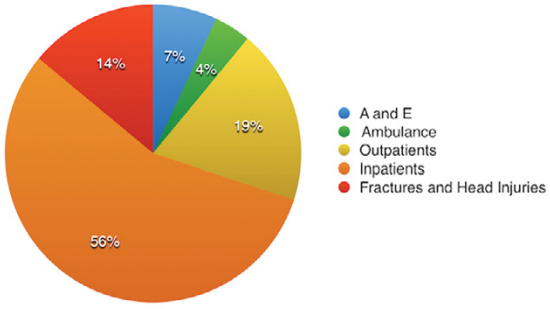


Figure 2. Chart showing spread of cost in health care costs

Conclusions: Implementation of the OEP programme for patients with RA has potentially significant economic benefits and should be considered for patients with the disease.
References:
[1] Stanmore EK, Oldham J, Skelton DA, O'Neill T, Pilling M, Campbell AJ, et al. Fall incidence and outcomes of falls in a prospective study of adults with rheumatoid arthritis. Arthritis Care Res (Hoboken). 2013;65(5):737–44.
[2] Stanmore EK, Oldham J, Skelton DA, O'Neill T, Pilling M, Campbell AJ, et al. Risk factors for falls in adults with rheumatoid arthritis: a prospective study. Arthritis Care Res (Hoboken). 2013;65(8):1251–8.
[3] Hayashibara M, Hagino H, Katagiri H, Okano T, Okada J, Teshima R. Incidence and risk factors of falling in ambulatory patients with rheumatoid arthritis: a prospective 1-year study. Osteoporos Int. 2010;21(11):1825–33.
[4] Gillespie LD, Robertson MC, Gillespie WJ, Sherrington C, Gates S, Clemson LM, et al. Interventions for preventing falls in older people living in the community. Cochrane Database Syst Rev. 2012;9:CD007146.
[5] Gardner MM, Robertson MC, Campbell AJ. Exercise in preventing falls and fall related injuries in older people: a review of randomised controlled trials. British Journal of Sports Medicine. 2000;34(1):7–17.
[6] Robertson MC, Campbell AJ, Gardner MM, Devlin N. Preventing injuries in older people by preventing falls: a meta-analysis of individual-level data. J Am Geriatr Soc. 2002;50(5):905–11.
Acknowledgements: Special thanks to all the participants involved in the research and also the nursing staff who supported the data collection phase of the study at Manchester Academic Health Science Centre (MAHSC).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1439

AB1112 DATANETWORK RHEUMA 4.0 – REAL WORLD DATA FROM PRIVATE PRACTICE

S. Kleinert[1], F. Schuch[1], S. Späthling-Mestekemper[2], M. Feuchtenberger[3], C. Kuhn[4], M. Welcker[5]. [1]*Rheumatologie, Rheumatologische Schwerpunktpraxis, Erlangen;* [2]*Rheumatologie, Rheumapraxis München-Pasing, München;* [3]*Rheumatologie, Schwerpunktpraxis für Rheumatologie, Burghausen;* [4]*Rheumatologie, Internistische Schwerpunktpraxis am Ludwigsplatz, Karlsruhe;* [5]*Rheumatologie, MVZ für Rheumatologie Dr. Martin Welcker, Planegg, Germany*

Background: The datanetwork Rheuma 4.0 (DNR_4.0) is a consortium of 5 internistic-rheumatologic specialized practices. Patient data that were collected routinely will be pooled pseudonymized (e.g. via RheumaDok) and will be made available to answer numerous healthcare- and scientific research questions.
Methods: The participating centres document the following data in specific rheumatologic data documentation systems (RheumaDok, Emil, DocuMed.rh). These data will be routed automatically to the data base of the DNR_4.0 via a prespecified interface and can be used for certain research areas:
Diagnosis (by rheumatologist (R), anamnesis (R), medication (R), morning stiffness (R, patient (P)), scores like RADAI (R, P), DAS28 (R), BASDAI (P), BASFI (P), quality of life (R, P). Also prespecified laboratory measures (R) like ESR, CRP etc. can be collected automatically.
Patient reported Outcomes (PROs) that were entered via mobile applications like RheumaLive and AxSpALive can be collected in certain intervalls and be sent encrypted into the medical office data base.
The data entered by patients will be screened by the rheumatologist or nurse and will be stored in the underlying data base. Clinical data that are collected during regular F2F-appointments will be stored together with the PROs according to a specific period of time.
Results: The datanetwork Rheuma 4.0 (DNR_4.0) is an association of 5 internistic-rheumatologic specialized practices.
By the automated documentation of PROs (patient) and medical measures (rheumatologist) in an underlying data base, scientific and health care real worl data can be collected without extra workload or time requirements. These data are specific and different from data collected by other centres. In principal, the extension of the group to increase the number of participating centres is easily possible because the interface is an "open system". This allows to build an automised collecting, big and representative data base.
Now pooled data sets of 18.000 patients are available in the data base. In a first step, quality and the completeness of the existing data sets will be evaluated and the daily documentation routines will be described. Anonymised statistical analysis of the pooled data sets of the rheumatologic centres will allow to gain knowledge in respect to health care research of the own working group and external interested parties like research groups, sick funds, insurance companies and companies.
Conclusions: The german biologic registry Rabbit and the "Core documentation" data base deliver valid data about the safety and efficacy of rheumatologic medication. The datanetwork Rheuma 4.0 will make a valuable contribution – especially in conjunction with apps of patient's self management like RheumaLive and AxSpALive – to health care research, therapeutic strategies and clinical questions from daily practice.
Acknowledgements: RheumaLive and AxSpALive werde developed by Starhealth GmbH on behalf of UCB Pharma GmbH.
Disclosure of Interest: S. Kleinert Speakers bureau: UCB, F. Schuch Speakers bureau: UCB, S. Späthling-Mestekemper Speakers bureau: UCB, M. Feuchtenberger Speakers bureau: UCB, C. Kuhn: None declared, M. Welcker Speakers bureau: UCB
DOI: 10.1136/annrheumdis-2017-eular.5674

AB1113 PATIENT PARTICIPATION IS CRUCIAL WHEN INTRODUCING NEW DEVICE TECHNOLOGIES IN THE MANAGEMENT OF CHRONIC ARTHRITIS: APPLYING THE PARKER MODEL, A QUALITATIVE 3-STEP APPROACH

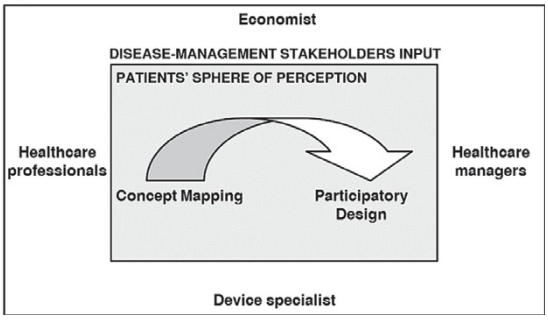
T.S. Jørgensen[1], L. Klokker[1], M. Skougaard[1], H. Asmussen[2,3], A. Lee[4], I. Mountian[5], H. Gudbergsen[1], L.E. Kristensen[1]. [1]*The Parker Institute, Copenhagen University Hospital, Bispebjerg and Frederiksberg, Copenhagen;* [2]*Communication IKH, Roskilde University, Roskilde;* [3]*NATiON, Copenhagen;* [4]*University of Southern Denmark, Odense, Denmark;* [5]*UCB Pharma, Brussels, Belgium*

Background: Patients' participation in design, development, and implementation of new device technologies is essential to ensure added value in patients' disease management.
Objectives: To explore the applicability and relevance of ava®, an electromechanical device (e-Device), as an alternative method for subcutaneous administration of certolizumab pegol.
Methods: The Parker Model is an innovative 3-step qualitative research approach, which combined concept mapping (CM), participatory design (PD), and stakeholder evaluation (SE) to evaluate the e-Device (Figure). CM was applied through workshops, with the participation of patients, using a structured group process focusing on relevant themes to identify issues and concerns with the e-Device. Patients used this information in a series of iterative PD sessions; patients participated in 3 interactive sessions to create a personal e-Device prototype in

cooperation with a designer and a medical expert. This was followed by a common group session. Finally, SE was performed based on semi-structured group and individual interviews with patients and disease-management stakeholders.

Results: The study included 9 rheumatoid arthritis (RA) patients, 4 psoriatic arthritis (PsA) patients, 1 ankylosing spondylitis (AS) patient, 2 doctors, 2 nurses, 1 medical secretary, and 4 key public servants involved in the disease management of the selected rheumatic diseases. Saturation was reached after 3 CM patient workshops, generating 121 statements, which were organized by the participants into themes. Through content analysis of the results from the 3 workshops, 4 concepts were generated: technical usability, physical design, concerns, and enthusiasm. These data were used in the iterative PD sessions, resulting in 4 new proposed prototypes. Finally, SE demonstrated that the identified concepts were pivotal for both facilitating and hampering device implementation, thus creating value when introducing the new e-Device.

Figure: The Parker Model



Conclusions: Patient participation in the 3-step qualitative Parker Model identified important aspects to consider when designing and implementing an innovative device for the treatment and management of RA, PsA, and AS. This is the first time a composite, qualitative research model has been applied when introducing a new device to support these disease areas. The responses from patients and disease-management stakeholders indicated that it is key to include patient input in the design and adaptation of devices alongside education and communication with stakeholders. These resources can help ensure added value when developing devices for the management of RA, PsA, and AS using biologic medicines.

Acknowledgements: This study was funded by UCB Pharma and the Oak Foundation. We thank the patients and their caregivers in addition to the investigators and their teams who contributed to this study. Editorial services were provided by Costello Medical Consulting.

Disclosure of Interest: T. Jørgensen Speakers bureau: Abbvie, Biogen, Novartis, Roche, UCB Pharma, L. Klokker: None declared, M. Skougaard: None declared, H. Asmussen Consultant for: The Parker Institute, UCB Pharma, A. Lee: None declared, I. Mountian Employee of: UCB Pharma, H. Gudbergsen: None declared, L. Kristensen Speakers bureau: AbbVie, Amgen, BMS, Celgene, Eli Lilly, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, UCB Pharma

DOI: 10.1136/annrheumdis-2017-eular.1770

AB1114 PATIENT'S SELF-MONITORING OF DISEASE ACTIVITY OF RHEUMATIC DISEASES VIA WEBAPP – STUDY DESIGN, PATIENT'S PERSPECTIVE AND RECRUITMENT IN THE FIRST 11 MONTHS OF THE SWISS MULTICENTRE, LONGITUDINAL COMPASS II STUDY

V.K. Jaeger[1], P. Schiffer[2], P. Zufferey[3], L. Pichler[1], A. Badaracco[4], M. Walder[5], J. Dudler[6], D. Frey[7], F. Müller[1], U.A. Walker[1]. *[1]University Hospital Basel, Basel; [2]Praxis beim Rathaus, Zofingen; [3]Lausanne University Hospital, Lausanne; [4]Studio Medico Badaracco Cattaneo, Lugano; [5]Praxis Walder, Dübendorf; [6]Hôpital Cantonal Fribourg, Fribourg; [7]Praxis Frey, Basel, Switzerland*

Background: The management of patients with rheumatic diseases is guided in part by asking patients about their medical history at each clinic visit. Patients often find it difficult to accurately remember the course of their symptoms between these appointments as they are often months apart. Regular app-based patients' self-monitoring of disease activity (with our without feedback to the rheumatologist) between clinic visits might provide a possible solution for this.

The COmPASS I study [1] demonstrated that RA patients' self-assessments of disease activity via App correlate strongly with rheumatologists' assessments. Following up on this, the Swiss based COmPASS II study is embedded in the Swiss rheumatology registry (SCQM) and hence allows the linkage of data obtained via the COmPASS II App from the patients with routine clinical data collected in the registry.

The main aims of the COmPASS II study are to assess if continuous self-monitoring of the disease by patients optimises disease management and outcome in rheumatic diseases, and to assess the fluctuation of disease activity between clinic visits.

Objectives: The objectives of this abstract are to describe the set-up and the recruitment of the COmPASS II study in the first 11 months.

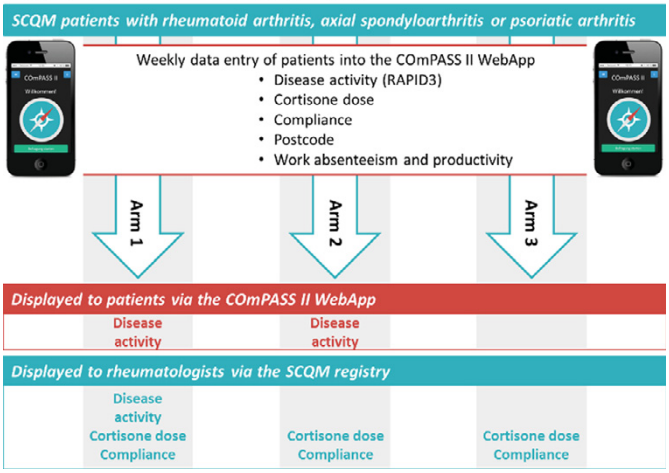
Methods: The COmPASS II App questionnaire consists of the RAPID3 score, a validated, commonly used PRO to self-assess disease activity. Additionally, patients are asked about their therapy compliance and cortisone dose.

At inclusion, interested patients with RA, axSpA and PsA are electronically randomized into 3 study arms (Figure 1). In arm 1 patients and rheumatologist are displayed the self-assessed disease activity over time, the patient directly via the App and the rheumatologist via the SCQM registry. In arm 2 only the patients are displayed their disease activity chart and in study arm 3 neither sees the recorded data. Patients are encouraged to fill in the App weekly.

Results: The COmPASS II App went online on the 15/02/2016. In the first 11 months of COmPASS II, 272 patients were enrolled by their rheumatologist. 64% of patients used the WebApp (32% in arm 1, 38% in arm 2 and 30% in arm 3); 82% of patients filled in the questionnaires for longer than a months, the longest follow-up was 11 months. On average patients use the App every 2 weeks.

Patients found the App easy to use "The COmPASS II WebApp is so easy to use. It doesn't even take me 2 min." and received feedback included "Now my rheumatologist sees how I was since the last appointment instead of me trying to remember how I was half a year ago.".

Figure 1. Design of the COmPASS II study.



Conclusions: The COmPASS II study will validate the utility of app-based patients' self-assessments in enhancing disease control in a treat to target approach and deliver numerous additional scientific data.

References:

[1] Mueller R et al. Patient's Self-Monitoring Via Smartphone: The Compass Study - COrrelation between PAtient self-ASSessment of rheumatoid arthritis disease activity via smartphone technology and physicians' validated scores [abstract]. Arthritis Rheumatol. 2014;66(S10).

Acknowledgements: COmPASS II is supported by an unrestricted grant from AbbVie.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3260

AB1115 THE FEASIBILITY OF UTILIZATION OF MOBILE DEVICES TO ENHANCE PATIENT REPORTED OUTCOMES MEASURES (PROMS) IN RHEUMATOLOGY PRACTICE

V. Ognenovski[1,2], K. Burger[3], K. Weiss[4], L. Esser[4], D. Khanna[1]. *[1]Division of Rheumatology, University of Michigan, Ann Arbor, United States; [2]Rheumatology Clinic, Ss Cyril and Methodius Faculty of Medicine, Skopje, Macedonia, The Former Yugoslav Republic Of; [3]Information Technology; [4]University of Michigan, Ann Arbor, United States*

Background: Patient reported outcome measures (PROMs) are accepted modalities of gathering patient-reported health status such as physical, mental and social well-being. In addition to research applications, in some countries such as the United States, some of these measures are being considered as metrics for quality of care. The advent and wide spread use of the electronic medical record (EMR) in the United States has enabled providers (and patients) to collect PROMs electronically via patient portals (1).

At the University of Michigan, the patient medical record is maintained by MiChart- an EPIC®software which interfaces with the Patient Reported Outcomes Measures System –PROMIS (2)- an NIH funded project for development of assessment tools for collecting and analyzing patient health status. Our initial effort focused on integrating the PROMIS questionnaires into the patient EMR for two domains: Adult Physical Function and Pain Intensity Scores into patient portals (electronic patient-physician communication tool), thus enabling patient to complete questionnaires from home computers. Our collection rate of completed PROMs questionnaires via patient portals was about 5–10%.

Objectives: The aim of our project was to examine/enhance collection rate of PROMs with the utilization of portable devices /tablet based PROMs at the time of check-in the clinic by the patient.

Methods: PROMs data was collected from all patients visiting one of the outpatient rheumatology clinics at the University of Michigan from July 1,2016 – Jan 31, 2017. An Android based tablet using Welcome ® software was handed to every patient with instructions to complete a questionnaire on Adult Physical Function and Pain Intensity Score – PROMIS based questionnaires on patient-reported outcome measures. The results were stored in the patients EMR.
Results: Between July 1st 2016 and Jan 31st, 2017, we collected PROMs on patients via patient portals (home computers) and in office mobile devices-tablets. Assisted completion was done by clinic staff on a clinic desk top computer. Total of 2059 out of 2554 patients invited to participate completed the PROMs questionnaires. Of those patients that answered the questionnaires, 82% were done on a mobile device, 10% of patients used the home portal, 8% of patients needed in office assistance. 20% of patients did not answer the questionnaires.

Mode for completion of PROMs	Number of patients
Mobile Device	1694
Portal Home PC	211
Assisted in clinic	154
Total questionnaires completed	2059

Conclusions: Mobile devices are being increaseinlgy used by the patients in the United States for capture of PROMs. Mobile devices increased the PROMs collection rate from approximately 10% to 80% when combining both home portal (home PC) and an office based mobile device (Tablet). Mobile devices alone accounted for >80% of the collection rate of PROMs. In an era of changing information technology, the utilization of mobile devices for PROMs should be explored as a preferred modality.
References:
[1] Wagner L, et al. Integrating the Patient-Reported Outcomes Measurement Information System(PROMIS) symptom assessment into routine cancer care. Cancer 2015 Mar 15;121(6):927–34.
[2] http://www.nihpromis.com/.
Disclosure of Interest: V. Ognenovski: None declared, K. Burger: None declared, K. Weiss: None declared, L. Esser: None declared, D. Khanna Grant/research support from: Bayer, BMS, Genentech/Roche, Sanofi-Aventis, NIH K24AR063120, Consultant for: Actelion, Bayer, Covis, Cytori, EMD Serono, Genentech/Roche, Gilead, GSK, Sanofi-Aventis
DOI: 10.1136/annrheumdis-2017-eular.6300

Epidemiology, risk factors for disease or disease progression

AB1116 PREVALENCE OF POLIAUTOIMMUNITY AND FAMILY AUTOIMMUNITY IN MEXICO

A. Arellano-Martinez, V. Gonzalez-Diaz, S. Cerpa-Cruz, S. Gutierrez-Ureña, J. Reyes-Rueda, K. Garcia-Osuna, G.E. Martinez-Bonilla. *Rheumatology Service, Hospital Civil Fray Antonio Alcalde, Guadalajara, Mexico*

Background: Autoimmune diseases share pathophysiological mechanisms, genetic factors and certain environmental triggers. Its frequency is reported up to 43% for poliautoimmunity and almost half of these have family autoimmunity, but this is unknown in our population.
Objectives: To identify the prevalence of poliautoimmunity and family autoimmunity in a Rheumatology Service of a third level hospital in Mexico.
Methods: Observational, descriptive, cross-sectional study. Consecutive outpatients who attended the Rheumatology Service of the Hospital Civil de Guadalajara "Fray Antonio Alcalde" during 2 months were applied a questionnaire to obtain demographic data, autoimmunity and risk factors. Descriptive statistical analysis was done.
Results: Of 1,208 patients, 484 (40%) had autoimmunity, of these 58 (12%) had polyautoimmunity and 6 (1%) with Multiple Autoimmune Syndrome (MAS). The most frequent of 35 autoimmune diseases registered were: RA 42%; SLE 17%; AS 6%; SSc 5%; SSj 4%; PsA 3%; JIA 3%; autoimmune hypothyroidism 3%; APS 2%; Dermatomyositis 2% and Psoriasis 1%. In the group with polyautoimmunity SLE was present in 26 (45%) patients, SSj in 13 (22%) and autoimmune thyroid disease in 14 (24%). In the MAS group autoimmune thyroid disease in 5 patients. Patients with polyautoimmunity developed first: SLE (14%) and RA (14%). In the patient with MAS autoimmune thyroid disease in 33%. Of the 58 patients with poliautoimmunity 31 (53%) have familial autoimmunity, of which SLE is the most frequent in (22%), followed by autoimmune thyroid disease (17%) and RA (16%). All 6 MAS patients had familial autoimmunity. Referent to risk factores: 154/484 reported active smoking. Of the 58 patients with poliautoimmunity, only 23 (40%) had or are current smokers. Of the 6 patients with MAS 50% presented this risk factor.158/484 (33%) patients had periodontal disease. In patients with autoimmune disease 54% were overweight (28%) or obese (26%). Of the 58 patients with poliautoimmunity 48% were overweight and 21% obese; of patients with MAS 50% were overweight or obese. Only one patient had ASIA syndrome with GCA diagnosed.
Conclusions: The search of polyautoimmunity is required in all patients with autoimmune disease and convenient to consider that these patients will have a higher frequency for familial autoimmunity. Smoking and periodontal disease are widely known risk factors that are no taken serious by patients.
References:
[1] Raza KeGD. Preclinical Inflammatory Rheumatic Diseases. An Overview and Relevant Nomenclature. Rheumatic Diseseas Clinic of North America. 2014;(40).
[2] Coelho Aec. Familial autoimmunity and polyautoimmunity in 60 Brazilian Midwest patients with systemic slcerosis. Revista Brasileira de Reumatologia. 2016;: p. 314–22.
[3] Anaya Jec. The kaleidoscope of autoimmunity: multiple autoimmune syndromes and familial autoimmunity. Expert Review of Clinical Inmunology. 2007;: p. 623–35.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6952

AB1117 LATENT TUBERCULOSIS INFECTION AND TUBERCULOSIS IN PATIENTS WITH RHEUMATIC DISEASES UNDER TREATMENT WITH ANTI-TUMOR NECROSIS FACTOR DRUGS

A.L.B. Morsch [1], G. Garziera [2], F. Otesbelgue [3], F.L. Staub [3], P.E. Palominos [1], C.V. Brenol [1,3], D.R. Silva [2,3,4]. *[1] Serviço de Reumatologia; [2] Programa de Pós-Graduação em Ciências Pneumológicas, Hospital de Clínicas de Porto Alegre; [3] Faculdade de Medicina, Universidade Federal do Rio Grande do Sul; [4] Serviço de Pneumologia, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil*

Background: The introduction of biological agents, especially the tumor necrosis factor inhibitors (anti-TNF) for the treatment of rheumatic diseases increased the risk of developing tuberculosis (TB). Screening for latent TB infection (LTBI) is strongly recommended before starting therapy with anti-TNF agents.
Objectives: This study aimed to identify the prevalence of LTBI and TB among patients with rheumatic diseases on anti-TNF drugs.
Methods: In a cross-sectional study, the electronic medical records of all adult patients (≥18 years old) undergoing anti-TNF treatment at Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil, were reviewed. Every patient underwent Tuberculin Skin Test (TST) before starting anti-TNF treatment.
Results: In total, 176 patients were included. The mean age was 51.9±12.4 years, 34.7% were males, and 90.9% were white. The underlying diseases were rheumatoid arthritis (RA) in 50.6% (N=89), ankylosing spondylitis (AS) in 27.8% (N=49) and psoriatic arthritis (PsA) in 17.6% (N=31). Anti-TNF agents started after TST were: infliximab (22.7%, N=40), adalimumab (48.9%, N=86), etanercept (27.3%, N=48), and golimumab (1.1%, N=2). The prevalence of positive TST was 29.5%. Household contact with TB was significantly associated with a positive TST (p=0.020). RA patients had lower TST reactions than AS patients (p=0.022). There were six cases of TB (3.4%) diagnosed during anti-TNF therapy.
Conclusions: We demonstrated a high prevalence of positive TST (29.5%) among patients with rheumatic diseases in a region with high TB prevalence. Our data corroborates the ACR's recommendation that patients who live in high TB incidence settings should be tested annually for LTBI.
References:
[1] Ishiguro T, Takayanagi N, Kagiyama N, Yanagisawa T, Sugita Y: Characteristics of tuberculosis in patients with rheumatoid arthritis: a retrospective single-center study. Intern Med 2014, 53: 1291–1298.
[2] Arkema EV, Jonsson J, Baecklund E, Bruchfeld J, Feltelius N, Askling J: Are patients with rheumatoid arthritis still at an increased risk of tuberculosis and what is the role of biological treatments? Ann Rheum Dis 2015, 74: 1212–1217.
[3] Singh JA, Furst DE, Bharat A, Curtis JR, Kavanaugh AF, Kremer JM et al.: 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res (Hoboken) 2012, 64: 625–639.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6340

AB1118 REVIEW OF METHODS FOR ASSESSING THE RELATIONSHIP BETWEEN WEATHER AND CHRONIC MUSCULOSKELETAL PAIN

A. Beukenhorst [1], J. McBeth [1], D. Schultz [2], J. Sergeant [1,3], W.G. Dixon [1]. *[1] Arthritis Research UK Centre for Epidemiology, Centre for Musculoskeletal Research; [2] Centre for Atmospheric Science, School of Earth and Environmental Scie nces, University of Manchester; [3] NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester University Hospitals NHS Foundation Trust, Manchester, United Kingdom*

Background: People with chronic pain commonly believe that their pain is affected by the weather. Despite a century's worth of research, there is no scientific consensus on the existence of a relationship between weather and chronic pain.
Objectives: A systematic literature review to (1) gain an overview of existing research on the weather-pain relationship, and (2) summarise the methodologies, methodological rigour and risk of bias in published studies of patients with musculoskeletal conditions.

Methods: Systematic search strategies were developed for 5 databases (Medline, Embase, PsycInfo, Scopus, Web of Science) to retrieve studies that investigated the relationship between weather conditions and chronic pain. Original articles describing observational studies that related chronic pain (primary outcome) to weather conditions (exposure), were included. Study characteristics, methodology (e.g. measurements of pain and weather, aspects of statistical analysis) and data on risk of bias (validation of participants' exposure and diagnosis, coverage of weather variation, correction for confounders) was extracted. Methodological rigour was summarised by mapping the methodological variability among studies and ranking these from least to most rigorous.
Results: The searches returned 16,081 articles. After removing 3090 duplicates and excluding 12726 articles during title screening, 265 abstracts were assessed for eligibility. Of 64 observational studies that met the inclusion criteria, 30 (47%) investigated pain associated with musculoskeletal conditions, 24 (38%) investigated headache and 10 (16%) investigated pain associated with other conditions such as sickle cell disease and dental pain. After full text assessment, 10 of 30 papers on musculoskeletal conditions were excluded because they investigated risk of acute pain episodes rather than chronic pain symptoms (n=6), or investigated multiple conditions (n=4). The 20 included studies investigated rheumatoid arthritis (6, 30%), osteoarthritis (6, 30%), fibromyalgia (6, 30%) and low back pain (2, 10%). A total of 15 studies (75%) reported some effect of weather on chronic pain, and this was clinically significant (consistent and sufficient size of effect) in 6. Participant numbers varied from 19 to 2491. 1 study was cross-sectional and 19 longitudinal with follow ups ranging from two weeks to 3.5 years, with participants scoring their pain once to daily for 12 months. Pain was measured with a Visual Analog Scale or Numeric Rating Scale in 17 (85%). Weather conditions were retrieved from local weather stations, with most studies assuming that participants stayed in the area/city (65%) or postcode area (20%) where they lived.
In 12 (60%) studies, participants were blinded to the study hypothesis. Methods for correcting for confounders were highly variable, with 7 studies not addressing any, and the remainder addressing one or more of 32 confounding variables.
Conclusions: Methodological variability of studies investigating the relationship between weather and chronic musculoskeletal pain is high. This methodological review will inform best research practice for those investigating the relationship between the weather and chronic pain.
Acknowledgements: Mary Ingram, librarian
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6571

AB1119 A DESCRIPTIVE STUDY OF GOUT PATIENTS IN A MULTI-ETHNIC SOCIETY

C. Chua[1], P. Cheung[2], A. Santosa[2], A. Lim[2], G.G. Teng[2]. *[1]Internal Medicine Residency; [2]Division of Rheumatology, University Medicine Cluster, National University Health System, Singapore, Singapore*

Background: Gout is a common inflammatory arthritis with rising global prevalence and health burden, especially in the Asia-pacific regions. Ethnicity may play a significant role suggesting lifestyle and/or genetic predisposition, but studies in Asia are limited[1,2].
Objectives: Our study sought to assess the demographic and clinical factors of gout in the multi-ethnic Singapore and describe the burden and treatment pattern in our patients.
Methods: 282 adults with rheumatologist-diagnosed gout were recruited from rheumatology clinics of an academic medical centre in Singapore. Data on demographic and lifestyle features, medical conditions, gout severity and treatment were obtained.
Results: 282 subjects were recruited and 92.6% were men. There were 77% Chinese, 18.8% Malays and 2.5% Indians, compared to Singapore's population makeup (74%, 13% and 9% respectively). Mean age at recruitment was 52.6 years (SD 16.1) while age at gout onset was 42.5 years (SD 16.7). 34.4% received primary or no education; 67.0% were employed and 20.7% retired. 22.7% were current alcohol drinkers while 50.7% were teetotalers. 23.4% were current smokers. Mean body mass index (BMI) was 28.1kg/m^2 (SD 6.0), 26.6% had BMI $\geq$30kg/m^2 while 69.9% had BMI $\geq$25kg/m^2. Prevalence of hypertension was 56.7%, diabetes mellitus 18.8%, dyslipidemia 48.2% and chronic kidney disease (CKD, defined as glomerular filtration rate $<$60ml/min/1.73m^2) 32.4%. Malays had significantly less alcohol intake (1.9%) but higher proportions of diabetes (32.1%), CKD (50.9%) and obesity (54.7%), compared with Chinese subjects (26.3%, 16.1%, 28.6% and 19.8% respectively, all Ps $<$0.05). Gout severity was rated moderate by 30.9% and severe in 50.4%; 69.3% suffered $\geq$3 attacks in 6 months. Mean SU was 477.8μmol/L (SD 130.8). 80.1% were on allopurinol. Subjects (22.3%) who achieved serum urate (SU) $\leq$360μmol/L, when compared to those with SU $>$360μmol/L, were more likely to be on urate lowering therapy (82.5% vs 60.7%, P=0.001), on higher mean allopurinol dose [337 mg/d (SD 166) vs 233 mg/d (SD 140), P$<$0.001] and statin (54.8% vs 33.3%, P=0.003). There were no significant differences amongst ethnicities for SU levels, gout severity and number of attacks.
Conclusions: Gout has substantial health burden in Singapore. Hypertension, dyslipidemia and obesity are more prevalent in our gout subjects compared to our population. Despite notably less alcohol intake compared with other cohorts[3–5], Singapore Malays seemed to suffer higher prevalence and comorbidities of gout. Majority of patients had moderate to severe disease but less than 25% achieved target SU levels highlighting suboptimal management of gout locally.
References:
[1] Kuo CF, et al. Global epidemiology of gout: prevalence, incidence and risk factors. Nat Rev Rheumatol 2015;11(11):649–62.
[2] Krishnan E, et al. Gout in ambulatory care settings in the United States. J Rheumatol 2008;35(3):498–501.
[3] Lee CH, et al. Factors associated with gout in South Koreans: analysis using the National Health Insurance Corporation and the National Health Screening Exam databases. Clin Rheumatol 2013;32(6):829–37.
[4] Cea Soriano L, et al. Contemporary epidemiology of gout in the UK general population. Arthritis Res Ther 2011;13(2):R39.
[5] Vázquez-Mellado J, et al. Metabolic Syndrome and Ischemic Heart Disease in Gout. J Clin Rheumatol 2004;10(3):105–09.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3950

AB1120 COMPARISON OF NON-RADIOGRAPHIC SPONDYLOARTHRITIS VERSUS ANKYLOSING SPONDYLITIS PATIENTS UNDERGOING BIOLOGICAL THERAPY

C. Cobilinschi, D. Opris-Belinski, R. Ionescu. *Sfanta Maria Clinical Hospital, Bucharest, Romania*

Background: Axial spondyloarthritis include non-radiographic spondyloarthritis (nr-SpA) and ankylosing spondylitis (AS); they reveal the extent of sacroiliitis assessed by conventional x-ray or MRI (1). The natural history of nr-SpA follows various evolution patterns; smoking, male gender, high levels of inflammatory markers or initial radiographic lesions are among predictor factors of progression to AS (2).
Objectives: The objective of the present study was to compare features related to progression of nr-SpA patients versus AS patients undergoing biological therapy with an anti-TNF agent.
Methods: This was an observational, cross-sectional study including 94 patients with nr-SpA and AS under continuous anti-TNF therapy for at least six months. SPSS 20.0 was used to analyze data with a P value of 0.05.
Results: Out of the selected study group, 69 patients were diagnosed with AS having a mean age of 44.8±10.8, while 25 patients had nr-SpA. Patients with nr-SpA were aged 32.1±6.6 years old and 40% of them were women, a rate significantly than in the AS group (P=0.05). Mean age at disease onset was 30.7 years for the AS subgroup versus only 23.8 years for patients with nr-SpA (P$<$0.001). AS patients presented a significantly higher value of the BMI compared to nr-SpA (27 versus 24.7 kg/m^{2,} P$<$0.001). 91% of patients had positive HLA B27 and 7.4% had a positive family history of SpA, with no significant differences between the two subgroups. A higher level of CRP was noticed in AS patients (P=0.038).In the study cohort the time interval from symptom onset to establishing a diagnosis was of 39.9±55.6 months, with a mean delay interval of 2.32 years for patients with nr-SpA and higher, of 3.5 for patients with AS (P=0.01).
Conclusions: The nr-SpA group had a considerably higher percentage of females compared to the AS subgroup. AS patients presented higher values of CRP at follow-up visits as opposed to nr-SpA patients. There were no significant differences between nr-SpA and AS patients regarding BASDAI or PtGA scores, smoking status or frequency of uveitis. The presence of HLA B27 did not differ between the two subgroups, thus it might not be a reliable predictive factor of progression.
References:
[1] Akgul O, Ozgocmen S. Classification criteria for spondyloarthropathies. World J Orthop. 2011;2(12):107–115.
[2] Wendling D, Non-radiographic spondyloarthritis: A theoretical concept or a real entity? Jt Bone Spine 2012;79(6):531–533. doi:10.1016/j.jbspin.2012.06.009.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5344

AB1121 TRABECULAR BONE SCORE COMBINED WITH CLINICAL RISK FACTORS CAN PREDICT INCIDENT FRACTURE IN RHEUMATOID ARTHRITIS PATIENTS

D. Kim[1], S.-K. Cho[1], H.-R. Park[1], Y.Y. Choi[2], Y.-K. Sung[1]. *[1]Rheumatology, Hanyang University Hospital for Rheumatic Diseases; [2]Nuclear medicine, Hanyang University Hospital, Seoul, Korea, Republic Of*

Background: Fracture is one of the most common and important comorbidities in rheumatoid arthritis (RA) patients, especially patients who use glucocorticoids (GC). However, bone mineral density (BMD) by dual-energy x-ray absorptiometry (DXA) which is the gold standard of diagnosing and monitoring osteoporosis is not a useful tool for predicting new fracture in RA patients. Previous studies suggested the possibility of trabecular bone score (TBS) as a useful predictor for incident fracture.
Objectives: We aimed to evaluate the accuracy of TBS combined with clinical risk factors or BMD for prediction of new fracture in patients with RA.
Methods: A total of 100 female RA patients were enrolled with assessment of TBS, BMD, and clinical risk factors for fracture. During follow-up period, we

calculated the incident rate of all fractures. After dividing the patients according to the use of GCs, we compared baseline characteristics and fracture-free survival between two groups. We compared accuracies of TBS, BMD, clinical risk factors for fracture and their combinations for predicting new fractures using areas under the receiver operator characteristic (ROC) curve (AUC).

Results: A total of 14 fractures in 12 patients were occurred among 100 patients during follow-up (428.8 person-years): 9 among the 44 in GC users and 5 in 56 GC non-users. Incidence of fracture was not different between two groups (log-rank test, p=0.27). AUC for incident fracture prediction of TBS alone [AUC 0.54, 95% confidence interval (CI) 0.35–0.72] was comparable with TBS combined with L-spine BMD (AUC 0.54, 95% CI 0.36–0.71) or with hip BMD (AUC 0.55, 95% CI 0.37–0.73). Accuracy for prediction of new fracture is increased when TBS was combined with age and history of previous fracture (AUC 0.74, 95% CI 0.62–0.85). In GC users, history of previous fracture alone (AUC 0.79, 95% CI 0.62–0.97) showed the best accuracy for predicting new fracture among TBS, BMD, clinical risk factors for fracture and their combinations.

Conclusions: TBS combined with age and previous history of fracture showed the highest accuracy for predicting new fracture compared to TBS or BMD alone or their combinations in RA patients. In GC users, history of previous fracture alone showed the highest accuracy for predicting new fracture.

References:

[1] Briot K, Paternotte S, Kolta S, Eastell R, Reid DM, Felsenberg D, et al. Added value of trabecular bone score to bone mineral density for prediction of osteoporotic fractures in postmenopausal women: the OPUS study. Bone 2013;57:232–6.

[2] McCloskey EV, Oden A, Harvey NC, Leslie WD, Hans D, Johansson H, et al. A Meta-Analysis of Trabecular Bone Score in Fracture Risk Prediction and Its Relationship to FRAX. J Bone Miner Res 2016;31:940–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5573

AB1122 ALL-CAUSE OF HOSPITAL MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND LUPUS ERYTHEMATOSUS IN A UNIVERSITY HOSPITAL DURING 1998 TO 2014

D. Vega-Morales, J.A. Esquivel Valerio, A.C. Arana-Guajardo. *Rheumatology Service, Hospital Universitario Dr. José Eleuterio González, Monterrey, Mexico*

Background: All-cause and cause-specific mortality is increased in patients with systemic lupus erythematosus (SLE) and Rheumatoid Arthritis (RA) when compared to the general population. Mortality can be attributed to the disease per se, side effects of drugs and effect of comorbidities. The survival of patients has improved over the past years when compared to historical controls

Objectives: The objective is to describe all-case of mortality in patients with SLE and RA in a university hospital.

Methods: This is an observational, descriptive, and cross-sectional study. We included all patients with SLE and RA hospitalized during 1998 to 2014. The cause of death was obtained from medical records and classified according to International Classification of Diseases (ICD)-10. We made a descriptive analysis of all-cause of mortality of both diseases.

Results: We analyzed 1,330 medical records, of which 215 died in hospital. The respiratory insufficiency was the most common mortality diagnosis in both diseases (RA 29%, SLE 24.1%), followed by sepsis (RA 25%, SLE 20.4%). The all-cause of mortality of SLE and RA are shown in Table 1. Of the 467 RA hospital admissions, the 5.1% died, and of the 863 SLE hospital admissions, the 22.1% died.

Table 1. Mortality of RA and SLE

Year	RA		SLE	
	Hospital admissions, n=467	Deaths, n=24	Hospital admissions, n=863	Deaths, n=191
1998–99	18 (3.9)	3 (25)	57 (6.6)	12 (47.4)
2000	22 (4.7)	0 (0)	21 (2.4)	4 (19)
2001	14 (3)	0 (0)	36 (4.2)	5 (13.9)
2002	17 (3.6)	0 (0)	22 (2.5)	2 (9.1)
2003	26 (5.6)	0 (0)	65 (7.5)	22 (33.8)
2004	33 (7.1)	1 (3.03)	40 (4.6)	9 (22.5)
2005	28 (6)	1 (3.57)	64 (7.4)	32 (50)
2006	27 (5.8)	0 (0)	39 (4.5)	7 (17.9)
2007	34 (7.3)	0 (0)	33 (3.8)	9 (27.3)
2008	40 (8.6)	2 (5)	49 (5.6)	19 (38.8)
2009	28 (6)	0 (0)	53 (6.1)	8 (15.1)
2010	24 (5.1)	7 (29.17)	60 (7)	10 (16.7)
2011	27 (5.8)	0 (0)	51 (5.9)	9 (17.6)
2012	31 (6.6)	2 (6.45)	80 (9.3)	9 (11.3)
2013	41 (8.8)	6 (14.63)	88 (10.2)	15 (17)
2014	40 (8.6)	2 (5)	66 (7.6)	16 (24.2)
2015	17 (3.6)	0 (0)	39 (4.5)	3 (7.7)

RA: Rheumatoid arthritis, SLE: Systemic Lupus Erythematosus.

Conclusions: Advances in the diagnosis and treatment of SLE and RA, have decreased the morbidity and mortality of the two diseases. Infectious and cardiovascular pathologies were the most frequent causes of death.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3316

AB1123 POOR ASSESSMENT OF RISK OF OSTEOPOROSIS AFTER A FOREARM FRACTURE IN WOMEN: A HEALTH INSURANCE DATABASE STUDY IN THE LOIRE VALLEY REGION (FRANCE)

E. Cattelain-Lopez[1,2], D. Chu Miow Lin[1], P. Goupille[1,2], A. Happe[3], E. Lespessailles[4], F. Jacquot[2], P. Tauveron[2], E. Rusch[5,6], E. Oger[3], D. Mulleman[1,2]. *[1]Rheumatology, Université François Rabelais de Tours; [2]Rheumatology, CHRU de Tours, Tours; [3]Pharmaco-epidemiology, Université de Rennes 1, Rennes; [4]Rheumatology, CHR d'Orléans, Orléans; [5]Health Economy, Université François Rabelais de Tours; [6]Health Economy, CHRU de Tours, Tours, France*

Background: Bone Mineral density (BMD) assessment is a useful tool to evaluate bone fragility and is largely recommended in patients at risk of osteoporosis. We have previously reported in 250 women aged 50 year-old or more that only ≈10% of them had a BMD after a forearm fracture (1).

Objectives: Herein, we evaluated BMD assessment and prescription of anti-osteoporotic drugs after a forearm fracture in women after 50 year-old in a large population database.

Methods: We identified all forearm fractures in women aged 50 years old or more in the "Centre-Val de Loire, France" area between 01/01/2011 and 31/12/2012, using the National Health Insurance database which cover both private and public sectors of the whole population. We analyzed the reimbursement and determinants of BMD assessment such as age, consumption of drugs inducing osteoporosis, anti-osteoporotics drugs and long term illnesses.

Results: We identified 4120 women with a forearm fracture during the study period. Among them, 546 (13.25%) had a BMD assessment performed at a median time of 4 months after the fracture. Women who had had a BMD were significantly yonger than those who had not (67.44 years versus 74.63 years: OR=0.941 CI95% (0.932–0.949)). Anti-aromatase treatment was positively associated with BMD assessment (OR=3.233 (CI95%: 1.976–5.290)) while corticosteroid were not (OR=0.866 (CI95%: 0.601–1.247)). Among the women who had a BMD assessment, 168/546 (30.77%) had an anti-osteoporotic drug initiated after the forearm fracture, versus 231/3574 (6.46%) in those who had no BMD performed ($p<0.05$).

Conclusions: In this large population, less than 15 percent of women over 50 year-old have a BMD assessment after a forearm fracture. BMD assessment was associated with anti-osteoporotic drugs initiation.

References:

[1] Erny F, Auvinet A, Chu Miow Lin D, et al (2015) Management of osteoporosis in women after forearm fracture: data from a French health insurance database. Joint Bone Spine: 82:52–55.

Acknowledgements: We thank Caroline Rault, department of Pharmaco-epidemiology, Rennes and Florence Erny, department of Rheumatology, Tours for their support and contribution in this project. This work would not have been possible without the help of Mehdi Gabbas "Caisse National d'assurance Maladie" (CNAM-TS), Valérie Edel, "Institut des données de Santé" (IDS), and the "Institut National de la Santé de de la Recherche Médicale" (Inserm). This study has been funded by the "groupe de recherche et d'investigation sur l'ostéoporose" (GRIO) and by the "Association Français de lutte anti-Rhumatismale" (AFLAR). This work is the result of the "Prevention of osteoporosis after distal forearm fracture – Prévention de l'Ostéoporose après fracture du Poignet (POP)" study group.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3982

AB1124 EFFECT OF SARCOPENIA, SUBCUTANEOUS ADIPOSE TISSUE AND ABDOMINAL VISCERAL FAT ON MORTALITY RISK OF COMMUNITY-DWELLING OLDER ADULTS: A POPULATION-BASED PROSPECTIVE COHORT STUDY IN BRAZIL

F.M. Santana, D. Domiciano, M. Gonçalves, L.G. Machado, C.P. Figueiredo, J.B. Lopes, V. Caparbo, L. Takayama, R.M.R. Pereira. *Department of Rheumatology, University of São Paulo, São Paulo, Brazil*

Background: Body composition changes resulting from ageing (decreased muscle mass and increased fat tissue) are frequently not accompanied by concomitant changes in body mass index (BMI). Thus, BMI has low accuracy to estimate death risk attributed to changes in body composition in the older adults[1]. Currently, the best method for body composition analysis in routine clinical practice is dual energy X-ray absorptiometry (DXA)[2]. However, the few studies on body composition by DXA and mortality risk in elderly have some limitations, such as analysis not compartmentalized (subcutaneous and visceral tissues) of body fat and appendicular muscle mass not adjusted for fat mass[3].

Objectives: We sought to investigate the association between body composition by DXA (including visceral fat measurement) and mortality in a longitudinal, prospective, population-based cohort of elderly subjects.

Methods: 839 community-dwelling subjects (516 women, 323 men), ≥65 years, were assessed by questionnaire on clinical data, laboratory exams and body composition by DXA using Hologic QDR 4500A equipment. DXA APEX software computes visceral adipose tissue (VAT) by subtracting the subcutaneous adipose tissue (SAT) from the total android fat. All analyses were performed at baseline. Total body fat was expressed by fat mass index (FMI) [(total body fat (kg)/height^2 (m)]. Sarcopenia was defined as low appendicular muscle mass adjusted for fat. Mortality was recorded during 4 year-follow-up. Multivariate logistic regression was used to compute odds ratios for all-cause and cardiovascular mortality.

Results: Over a mean 4.06±1.07 years of follow-up, there were 132 (15.7%) deaths. In men, after adjustment for age, BMI, smoking, physical activity, alcohol, diabetes, dyslipidemia, cardiovascular event, recurrent falls, 25OHD and PTH, the presence of sarcopenia (OR 11.36, 95% CI: 2.21–58.37, p=0.004) and visceral fat mass (OR 1.99 95% CI: 1.38–2.87, p<0.001, for each 100g-increase) significantly increased all-cause mortality risk, while FMI was associated with decreased mortality risk (OR 0.48, 95% CI: 0.33–0.71, p<0.001). Similar results were observed for cardiovascular mortality in men: sarcopenia (OR 14.84, 95% CI: 5.15–47.72, p<0.001), visceral fat mass (OR 1.66, 95% CI: 1.31–2.10, p<0.001) and FMI (OR 0.57,95% CI: 0.43–0.76, p<0.001). In women, only sarcopenia was predictor of all-cause (OR 62.88, 95% CI: 22.59–175.0, p<0.001) and cardiovascular death (OR 74.54, 95% CI: 9.72–571.46, p<0.001).
Conclusions: Sarcopenia and fat distribution are associated with all cause and cardiovascular mortality risk in elderly, and they are different according to sex. Visceral fat and subcutaneous fat have opposite roles on mortality risk in elderly men, and this is distinct from what is observed in young adults.These findings point to the risk of encouraging weight loss in the elderly aiming young adult goals. Furthermore, DXA seems to be a promising tool for evaluation risk of mortality in elderly, since it is easily applicable in clinical practice.
References:
[1] Thibault R, Pichard C. Ann Nutr Metab 2012.
[2] M Zamboni, G Mazzali, E Zoico, et al. International Journal of Obesity 2005.
[3] Yves Rolland, Adeline Gallini, Christelle Cristini, et al. Am J Clin Nutr 2014.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2224

AB1125 PREDICTION OF CHRONIC DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS BY USING MACHINE-LEARNING MODELS

F. Ceccarelli[1], M. Sciandrone[2], C. Perricone[1], G. Galvan[2], F. Morelli[2], L.N. Vicente[3], I. Leccese[1], L. Massaro[1], E. Cipriano[1], F.R. Spinelli[1], C. Alessandri[1], G. Valesini[1], F. Conti[1]. *[1]Lupus Clinic, Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Roma; [2]Dipartimento di Ingegneria dell'Informazione, Università di Firenze, Firenze, Italy; [3]Departemento de Matematica, Universidade de Coimbra, Coimbra, Portugal*

Background: The increased survival in Systemic Lupus Erythematosus (SLE) patients implies the development of chronic damage, occurring in up to 50% of cases after a follow-up of 10 years. Its prevention is a major goal in the SLE management. During the last years, it has been suggested that Artificial Neural Networks (ANNs) could be a useful prediction tool in medical *scenarios*, by using patients' data as inputs and the specific outcomes as outputs. The International Conference on Advanced Computing and Communication Systems in 2015 underlined the possible application of sophisticated data analysis tools, such as machine learning methods, in SLE patients, in the light of their potential application to diagnostic and prediction purposes.
Objectives: In the present study, we aimed at predicting chronic damage in a large monocentric SLE cohort by using neural networks.
Methods: For the present analysis, we used data from 413 SLE patients (1997 ACR criteria; M/F 30/383; mean age ± SD 46.3±11.9 years; mean disease duration ± SD 174.6±112.1 months, mean follow-up period ±SD 63.9±30.7 months). At each visit, the patients underwent a complete physical examination and clinical and laboratory data were collected in a standardized, computerized, and electronically filled form. All the patients were evaluated at least twice per year. Autoantibodies and complement serum levels were also registered. Chronic damage was assessed by the SLICC/ACR Damage Index (SDI). We applied Recurrent Neural Networks (RNNs) as a machine-learning model to predict the risk of chronic damage. The clinical data sequences registered for each patient during the follow-up were used for building and testing the RNNs. We used 27 clinical and laboratory items for the mathematical model.
Results: At the first visit, 35.8% of patients had an SDI≥1, with a mean±SD value of 1.7±1.1. For the RNN model, two groups of patients were analyzed: patients with SDI=0 at the baseline, developing damage during the follow-up (N=38), and patients without damage (SDI=0). In particular, in the first group, we used all the visits before the development of damage, and in the second group, we considered patients with at least 5 visits and a follow-up of 2 years. We created a mathematical model with an AUC value of 0.77, able to predict damage development. A threshold value of 0.35 (sensitivity 0.74, specificity 0.76) seems able to identify patients at risk to develop damage.
Conclusions: We applied RNNs to identify a prediction model for SLE chronic damage. By using longitudinal data, including laboratory and clinical items, we created a mathematical model able to identify patients at higher risk to develop chronic damage.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5331

AB1126 CITRULLINATION OF PROTEINS, SMOKING AND RHEUMATOID ARTHRITIS

G. Belakova[1], V. Manka[1], P. Racay[2], E. Zanova[3]. *[1]MEDMAN s.r.o; [2]Biochemistry Department/Commenius University, Martin; [3]Department of Rheumatology, Piestany, Slovakia*

Background: Rheumatoid arthritis (RA) is an inflammatory disease characterized by chronic synovitis and erosive destruction of articular cartilage and bone ultimately leading to joint deformities, disability, loss of quality of life and work loss. There are multiple risk factors, both environmental and genetic, that may predispose an individual to developing RA. Cigarette smoking is the most important risk factor. Citrulline contained within proteins is created post-translationally by the action of the enzyme peptidyl arginine deiminase on the aminoacid arginine. Citrullination takes place in several normal cellular processes, including inflammation, apoptosis, and cellular differentiation. Additionally, tissues involved in inflammation have increased levels of citrullinated proteins. Smoking may lead to increased formation of citrullinated proteins, which in the appropriate genetic background leads to autoimmunity to citrullinated proteins and subsequently the development of clinically apparent RA. This model of RA development is compelling at least in terms of anti-citrullinated peptides antiodies (ACPA) positive RA that occurs in smokers, although the specific anatomic sites and mechanisms by which smoking leads to ACPA generation and RA have yet to be elucidated.
Objectives: To evaluate the prevalence of tobacco smokers in different sub-groups of patients with RA. Sub-groups were formed according to the combination of positivity and negativity of ACPA and rheumatoid factor (RF).
Methods: We examined patients with rheumatoid arthritis. We performed examination of ACPA and RF at the baseline. We formed 4 sub-groups of patients with rheumatoid arthritis: ACPA positive and RF positive, ACPA positive and RF negative, ACPA negative and RF positive, ACPA negative and RF negative. We collected data from medical history concerning smoking status in each individual patient.
Results: The total number of 290 patients with rheumatoid arthritis was examined. There were 50 patients in the sub-group with ACPA positivity and RF positivity, 19 of them were smokers (38%, n=50). There were 13 patients in the sub-group with ACPA positivity and RF negativity, 5 of them were smokers (39%, n=13). There were 97 patients in the sub-group with ACPA negativity and RF positivity, 28 of them were smokers (29%, n=97). There were 130 patients in the sub-group with ACPA negativity and RF negativity, 28 of them were smokers (21%, n=130. The highest prevalence of smokers was in the sub-group of patients with ACPA and RF positive rheumatoid arthritis (39%) and ACPA positive and RF negative rheumatoid arthritis (38%). The prevalence of smokers in ACPA negative sub-groups of patients with rheumatoid arthritis is significantly lower.
Conclusions: We confirmed that prevalence of smokers is significantly higher in the sub-group of patients with ACPA positive rheumatoid arthritis than in the sub-group with ACPA negative rheumatoid arthritis. Quitting smoking is highly recommended especially to these patients in order to achieve a favorable effect on the course of the disease.
References:
[1] Maria J H de Hair, et al. Smoking and overweight determine the likehood of developing rheumatoid arthritis. Ann Rheum Dis 2013;72(10):1654–1658.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5405

AB1127 HEALTH LOCUS OF CONTROL IN SYSTEMIC LUPUS ERYTHEMATOSUS – A CROSS-SECTIONAL ANALYSIS OF THE LULA-COHORT IN GERMANY 2013

G. Chehab[1], J.G. Richter[1], R. Brinks[1], R. Fischer-Betz[1], B. Winkler-Rohlfing[2], M. Schneider[1]. *[1]Policlinic of Rheumatology and Hiller Research Unit Rheumatology, Medical Faculty, Heinrich-Heine-University, Duesseldorf; [2]German Lupus Self-Help Community, Wuppertal, Germany*

Background: Health Locus of Control (HLC) is the degree to which individuals believe that their health is controlled by internal (self-responsibility) or external factors (healthcare professionals or chance). This generalized expectancy might affect different disease aspects, especially in chronic diseases.
Objectives: Our objective was to assess the influence of HLC on different disease aspects in a representative sample of German systemic lupus erythematosus (SLE) patients.
Methods: The LuLa-Study is a longitudinal survey on a multitude of SLE associated factors that is being conducted annually by means of a self-reported questionnaire among members of the German LE self-help community since 2001 and is ongoing. Inclusion criteria are a diagnosis of SLE and returning the completed paper questionnaire. Amongst others medication, health-related quality of life (Short-Form-12), damage (Brief index of lupus damage) and disease activity (Systemic Lupus Activity Questionnaire) are surveyed. In 2013 we additionally inquired about the health locus of control (HLC) that distinguishes between the "internal" HLCint (self-responsibility) and the two external dimensions HLCdoc and HLCchance considering their doctor respectively chance responsible for personal health. A high HLC was assumed for values above the upper quartile of the specific scales. Accessory questions examined fatigue (Fatigue severity scale), medication adherence (Morisky medication adherence scale), and illness perception (Brief illness perception questionnaire).

Results: Patients with a high internal health locus of control (HLCint 13.1 vs. 9.1) had less pain (numeric rating scale 0–10), less flares, a better mental and physical health related quality of life, lower disease activity and less fatigue. Patients with a high external 'doctor'-related health locus of control (HLCdoc 10.7 vs. 7.2) were older, had more co-morbidities, more disease damage and received more frequently an immunosuppressive therapy. No significant differences were found between the patients with a high external 'chance'-related HLC compared to the lower scoring patients (HLCcha 11.1 vs. 6.3). Participants with a high external 'doctor'-related HLC had a more threatening view on their illness and a better adherence to medication (high adherence in 78.6% vs. 59.4%). Participants with a high internal HLC perceived their disease significantly less threatening. Higher education levels (school education, further education) went along with a decrease of external 'doctor'-related HLC (HLCdoc).
Conclusions: Health locus of control has a significant impact in patients with SLE. Depending on the HLC different disease characteristics, treatments, levels of medication adherence and illness perception were noticed. Holistic care needs to consider the impact different HLCs may have. The direction of causality cannot be proved beyond reasonable doubt in this cross-sectional analysis. Hence additional longitudinal studies are necessary.
Acknowledgements: The LuLa-study is supported by unrestricted grants from GlaxoSmithKline and UCB Pharma.
Disclosure of Interest: G. Chehab Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study, J. Richter Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study, R. Brinks: None declared, R. Fischer-Betz Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study, B. Winkler-Rohlfing: None declared, M. Schneider Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study
DOI: 10.1136/annrheumdis-2017-eular.3720

AB1128 HELICOBACTER PYLORI IN SYSTEMIC LUPUS ERYTHEMATOSUS ITS ASSOCIATION WITH ENDOSCOPIC AND HISTOPATHOLOGIC FINDINGS

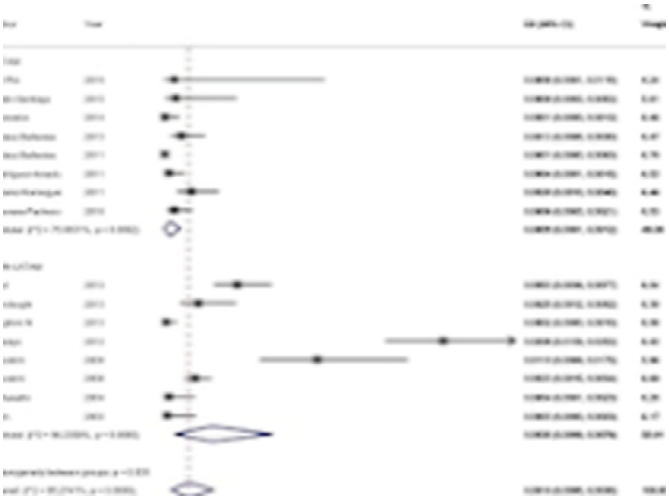
I. Arroyo Prado[1], J.A. Velarde Ruiz Velasco[2], C.E. Gomez Lopez[1], S. Gutierrez Ureña[1], G. Martinez Bonilla[1], V. Gonzalez Diaz[1], J.I. Espejo Pascencia[3], S. Cerpa Cruz[1]. *[1]Rheumatology; [2]Gastroenterology; [3]Pathology, Fray Antonio Alcalde Hospital, Guadalajara, jalisco, Mexico*

Background: Helicobacter pylori (Hp) is a Gram-negative bacteria and the cause of most of the chronic gastric infections and its prevalence is above 50% worldwide. This infection is a well-known risk factor to gastric MALT lymphoma but also could be the trigger of several autoimmune diseases such as immune thrombocytopenic purpura and systemic lupus erythematosus
Objectives: To determine the frequency of H pylori in systemic *lupus erythematosus patients* (SLE).
Methods: A cross-sectional study was done in patients who fulfilled the 2012 SLICC criteria for SLE and were willing to sign the informed consent to be subjected to endoscopic procedure. The tissue sample was analyzed by pathologist. We used mean and standard deviation to describe the data, to compare both groups Student t test was done and for continuous variables we used chi-square; the correlation analysis was performed with
Results: Twenty two SLE patients were included and we chose a control group from database of endoscopic clinic with diagnosis of functional dyspepsia. Mean age of study group was 31 vs 48 year-old, 95% were women, 32% with immunosuppressant and 95% were taking *antimarials*. The frequency of Hp in SLE patients was 60%, dsDNA and anti-Ro autoantibodies were associated with the presence of Hp; the study group had more frequency of nodular gastritis, metaplasia and dysplasia. Seventy per cent of patients had less than 5 years of diagnosis.
Conclusions: We found a high frequency of H pylori infection in patients with SLE. Metaplastic and dysplastic changes were also more prevalent in the SLE group. Our data suggest that Hp infection took place in early stages of disease.
References:
[1] Daniel S Smyk, Andreas L Koutsoumpas, Maria G Mytilinaiou, Eirini I Rigopoulou, Lazaros I Sakkas, Dimitrios P Bogdanos. Helicobacter pylori and autoimmune disease: Cause or bystander. World J Gastroenterol 2014 January.
[2] Sarfaraz Ahmed Hasni Role of helicobacter pylori infection in autoimmune diseases. Curr Opin Rheumatol. 2012 July; 24(4): 429–434.
Acknowledgements: no clinficts of interest.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4166

AB1129 A SYSTEMATIC REVIEW ON PREVALENCE OF BACK PAIN AND SPONDYLOARTHRITIS BASED ON COPCORD STUDIES

J. Moreno-Montoya[1], J. Rodriguez-Amado[2], R. Burgos-Vargas[3], I. Pelaez-Ballestas[3]. *[1]Universidad del Bosque, Bogota, Colombia; [2]Research Associate of South Florida, Miami, United States; [3]Rheumatology Unit, Hospital General de Mexico, Mexico, Mexico*

Objectives: To determine, through a systematic review and meta-analysis, the prevalence of back pain (BP) and spondyloarthritis (SpA) in the adult general population and explore the heterogeneity between studies in and out Latin America (LATAM).
Methods: MEDLINE, Embase, BIREME, LILLACS and Web of Science were searched using a strategy combining key words and related database-specific subject terms to identify relevant cross-sectional studies based on COPCORD methodology published since 2006. Included articles were assessed for risk of bias and quality based on the STROBE statement. Prevalence figures for BP and SpA (European Spondyloarthropathy Study Group criteria) were analyzed according to female percentage of sampled individuals, mean age and sample size. A mixed effect model was used to obtain the combined prevalence and a meta-regression to estimate the effects of these variables. Prevalence stratified values were obtained according to its geographical location.
Results: 44 out of 127 papers in English, Spanish or Portuguese were selected. Of them, 16 contained BP or SpA prevalence data. Estimates for any Spa prevalence ranged from 0,1% to 2%, with an average of 0,3% (95% CI: 0,01%>0,05%). The random-effects pooled prevalence was 0,18% (0,06%>0,36%). The prevalence of BP was 6.54% (3.8%>9.2%) with a pooled value of 5.24% (2.6%>8.7%). In both cases the heterogeneity was significant ($p<0.01$). No effect was associated to SpA heterogeneity, but an increase in the prevalence of BP was associated to sample size (random effect coefficient: 0,045, p=0.04). The stratified analysis did not show differences in terms of heterogeneity or prevalence for BP (Pooled prevalence for BP: 5.4%; 2.9%>8.5%, p=0.9); on the contrary, for Spa, for non-LATAM studies, the pooled proportion was significant bigger (prevalence in LATAM 0.05%, 0.01%>0.012%; non-LATAM: 0.35%, 0.09%>0.78%, p=0.03)



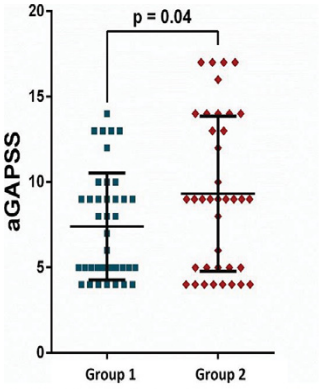
Conclusions: We found significant variations in prevalence across this review. In particular, they related to sample size of BP studies. Similarly, there was a significant variation between LATAM versus other latitudes respect to the prevalence of SpA. The limited number of studies included in this meta-analysis however, prevents clear explanations of the mechanisms underlying these results.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3916

AB1130 RELAPSE RISK ASSESSMENT IN YOUNG APS PATIENTS WITH PREVIOUS STROKE EVENT USING THE ADJUSTED GLOBAL ANTIPHOSPHOLIPID SYNDROME SCORE (AGAPSS)

I. Cecchi[1], M. Radin[1], K. Schreiber[2], M.J. Cuadrado[3], C. Perez-Sanchez[4], C. Lopez-Pedrera[4], D. Roccatello[5], S. Sciascia[5]. *[1]Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Turin, Italy; [2]Department of Thrombosis and Haemophilia, Guy's and St Thomas' Hospital; [3]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; [4]GC-5/Rheumatology, IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain; [5]Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases - Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Turin, Italy*

Background: The most frequent manifestation of arterial thrombosis in patients affected by Antiphospholipid syndrome (APS) is ischaemic stroke, especially in young adults (less than 50 years old) [1]. Young adults affected by APS are a group of patients at greater risk of developing serious stroke events and recurrences of thrombosis. Therefore, risk stratification in this particular group is crucial, especially in order to prevent a recurrence of ischaemic thrombotic event.
Objectives: With the present study we aimed to assess the clinical usefulness of the adjusted Global AntiphosPholipid Syndrome Score (aGAPSS) [3] for risk stratification of thrombosis relapse and/or progression of known ischaemic lesions dectected with Magnetic Resonance Imaging (MRI) in a cohort of young adult APS patients.

Methods: The analysis included 80 APS patients (≤50 years old) who presented a previous stroke event (patients who experienced cerebral venous sinus thrombosis were not included in the analysis). Clinical and laboratory data were retrospectively collected. Treatment was based on phisician's opinion according to clinical settings. The aGAPSS was calculated for each patient by adding the points corresponding to the risk factors, based on a linear transformation derived from the β regression coefficient as follows: 3 for hyperlipidaemia, 1 for arterial hypertension, 5 for aCL IgG/IgM, 4 for antiβ2glycoprotein I IgG/IgM and 4 for LA. Relapse was defined as the recurrence of thrombotic event and/or progression of known ischaemic lesions detected with MRI.
Results: Results pointed out that patients with relapse of thrombotic events and/or progression of known ischaemic lesions were 39 out of 80 (48.7%) and patients without relapse were 41 out of 80 (51.3%). Significantly higher aGAPSS values were observed in relapse group when compared to the non-relapse group [mean aGAPSS 9.08 (S.D. 4.7) Vs. mean aGAPSS 7.22 (S.D. 3.3); T test: $p<0.05$]. Distribution of aGAPPS values among the two groups is illustrated in Graph 1.



Graph 1.: Distribution of aGAPPS values among the two groups; Group 1: patients without relapse of thrombotic events and/or progression of known ischaemic lesions detected with MRI; Group 2: patients who presented relapse of thrombotic events and/or progression of ischaemic lesions.

Conclusions: Our analysis suggests that aGAPSS could represent an effective tool to stratify the risk of relapse of thrombosis and/or progression of ischaemic lesions in young APS patients with clinical history of stroke. These data could also aid developing different therapeutic approaches, especially for patients at higher risk of relapse.
References:
[1] Tektonidou MG, Varsou N, Kotoulas G, Antoniou A, Moutsopoulos HM. Cognitive deficits in patients with antiphospholipid syndrome: association with clinical, laboratory, and brain magnetic resonance imaging findings. Arch Intern Med 2006;166(20):2278–84.
[2] Meroni PL, Borghi MO, Raschi E, Tedesco F. Pathogenesis of antiphospholipid syndrome: understanding the antibodies. Nat Rev Rheumatol. 2011;7:330–9.
[3] Sciascia S, Sanna G, Murru V, Roccatello D, Khamashta MA, Bertolaccini ML. GAPSS: The Global Anti-Phospholipid Syndrome Score. Rheumatology (Oxford) 2013; 52:1397–403.
Acknowledgements: None.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6891

AB1131 RISK OF DEVELOPING ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

I. Starodubtseva. *Internal Diseases, Nn Burdenko Voronezh State Medical University, Voronezh, Russian Federation*

Background: Patients with chronic inflammatory diseases have an increased risk of developing atherosclerosis. Pro-inflammatory cytokines such as interleukin-(IL-)1beta and tumor necrosis factor-(TNF-)alpha, C-reactive protein (CRP) influence on the progression and development of both rheumatoid arthritis (RA) and atherosclerosis.
Methods: 620 patients with RA (diagnosis according to ACR /EULAR) from the rheumatology in-patient clinic with the mean age of 43.4±10; 95.4% ACCP – positive patients, activity on DAS (Disease Activity Score) 28 II, III; 85.4% female with the disease duration for about 3–15 years were enrolled in the trial. We assessed the level of IL-1 with the use of ELISA.
Results: The constructed model surfaces indicated the interdependence of IL-1, the activity of DAS 28 and the level of LDH in RA patients. The correlative and regressive analysis of the results showed the statistically significant correlation of TG, LDG and markers of inflammation IL-1, DAS 28: p=0.627 ($p<0.01$), p=0.527 ($p<0.01$), p=0.712 ($p<0.01$), p=0.776 ($p<0.01$) accordingly. The correlation coefficient between hs-CPR and the indicators of the lipid profile revealed similar interconnections.
Conclusions: According to the results of modeling, disease activity on DAS and markers of inflammation (IL-1 and hs-CRP) as a markers of the severity of inflammatory process in RA patients are risk factors for developing atherosclerosis. The analysis of inflammation indicators in RA patients allows to assess the risk of developing and progressing atherosclerosis. The data enables to select the best possible personified therapy for such patients at the early stage of the disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1677

AB1132 HIGHER RATES OF OBESITY AND ASSOCIATIONS WITH POORER CLINICAL STATUS IN PATIENTS WITH RA, OA AND SLE: A CROSS-SECTIONAL STUDY FROM ROUTINE CARE

I. Castrejon, N. Shakoor, J.A. Block, T. Pincus. *Rheumatology, Rush University Medical Center, Chicago, United States*

Background: Obesity is a risk factor for many chronic rheumatic diseases. In rheumatoid arthritis (RA), obesity is associated with increased comorbidities, higher medical costs, disease activity, and poorer physical function[1]. In OA, obesity is a risk factor for both incidence and progression, and has a negative impact on outcomes[2]. In systemic lupus erythematous (SLE), obesity is associated with more severe renal involvement, lower quality of life, and increased cardiovascular risk[3].
Objectives: To assess associations of obesity with patient self-report multidimensional health assessment questionnaire (MDHAQ) scores and physician global assessments in patients with RA, OA and SLE seen in routine care.
Methods: All patients at one academic center complete a MDHAQ, which includes a 0–10 scale for physical function (FN), 0–10 visual analogue scales (VAS) for pain (PN) and patient global assessment (PATGL), compiled into a 0–30 RAPID3, as well as scales for fatigue, depression, and demographic data. Physicians complete a VAS for patient global (DOCGL). Body Mass Index (BMI) was calculated from the medical record as weight (kg)/ height (meters)^2. Patients were classified by BMI as normal (18.5–25), overweight (25–30), or obese (>30) according to the WHO guidelines. Demographic and clinical MDHAQ data were compared in the 3 diagnostic groups according to BMI groups using ANOVA and chi-square tests.
Results: 396 patients with RA, 425 with OA, and 306 with SLE were studied. Obesity was reported by 40% of RA and SLE patients, and 59% of OA patients, a higher percentage than matched individuals in the general population in the same region (30.8%). Obesity was higher in African-American patients (48% in RA, 70% in OA, and 53% in SLE). Education level, gender, and age did not differ significantly across the groups. Obesity was associated with poorer physical function, poorer patient global and higher pain in all 3 diagnostic groups, with higher depression scores in OA and SLE (Table). DOCGL was significantly higher only in OA (data not shown).

Table 1. MDHAQ scores and physician global assessment according to BMI groups

MDHAQ scores	Normal (BMI=18.5–25)	Overweight (BMI=25–30)	Obesity (BMI>30)
RA (N=381)	110 (29%)	112 (30%)	154 (40%)
Function (0–10)	2.1 (2.2)	2.4 (2.2)	2.9 (2.0)*
Pain (0–10)	4.4 (2.8)	4.6 (3.0)	5.1 (3.1)*
Fatigue (0–10)	3.4 (2.9)	3.6 (3.1)	4.5 (3.2)*
PATGL (0–10)	3.8 (2.7)	4.1 (3.1)	4.8 (2.8)*
Depression (0–3.3)	0.5 (0.7)	0.5 (0.7)	0.6 (0.8)
OA (N=420)	60 (14%)	102 (24%)	247 (59%)
Function (0–10)	1.7 (1.5)	2.6 (1.8)	3.2 (2.0)*
Pain (0–10)	5.1 (2.9)	6.7 (2.5)	6.6 (2.6)*
Fatigue (0–10)	3.4 (2.9)	4.3 (2.9)	5.3 (3.1)*
PATGL (0–10)	4.5 (3.1)	5.7 (2.5)	5.9 (2.7)*
Depression (0–3.3)	0.4 (0.6)	0.6 (0.8)	0.7 (0.8)*
SLE (N=299)	84 (28%)	85 (28%)	121 (40%)
Function (0–10)	1.4 (1.5)	1.2 (1.6)	2.3 (2.1)*
Pain (0–10)	3.5 (3.2)	3.9 (3.1)	5.2 (3.3)*
Fatigue (0–10)	4.2 (3.3)	4.2 (3.4)	5.1 (3.2)
PATGL (0–10)	3.6 (2.9)	3.9 (3.1)	4.6 (3.2)*
Depression (0–3.3)	0.4 (0.6)	0.4 (0.6)	0.7 (0.8)*

*$p<0.01$.

Conclusions: Obesity is more prevalent in patients with rheumatic diseases compared with the general population. Obese patients had poorer status on most MDHAQ scores, particularly physical function and pain. Obesity is an important comorbidity in patients with rheumatic diseases.
References:
[1] J Rheumatol 2015, 42(12):2261–2269.
[2] Obes Rev 2014, 15(7):578–586.
[3] Autoimmunity Reviews 2014;13: 981–1000.
Disclosure of Interest: I. Castrejon: None declared, N. Shakoor: None declared, J. Block: None declared, T. Pincus Shareholder of: Health Report Services, Inc
DOI: 10.1136/annrheumdis-2017-eular.3812

AB1133 HIGH CONSUMPTION OF SEAFOODS OR VEGETABLES NEGATIVELY CORRELATES WITH DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS

I. Murakami[1], K. Murakami[1], M. Hashimoto[2], M. Torii[3], K. Ikeda[4], A. Kuwabara[5], K. Tanaka[6], A. Yoshida[1], T. Usui[1], N. Kuramoto[1], R. Nakashima[1], Y. Imura[1], H. Yoshifuji[1], M. Tanaka[2], K. Ohmura[1], T. Mimori[1]. *[1]Department of Rheumatology and Clinical immunology, Graduate School of Medicine; [2]Department of the Control for Rheumatic Diseases, Graduate School of Medicine; [3]Department of Human Health Sciences, Graduate School of Medicine; [4]Department of Diabetes, Endocrinology and Nutrition, Graduate School of Medicine, Kyoto University, Kyoto; [5]Department of Health and Nutrition, Osaka Shoin Women's University, Osaka; [6]Department of Food and Nutrition, Kyoto Women's University, Kyoto, Japan*

Background: Food intake is one of the important environmental factors of various diseases, and possibly influences the pathogenesis of RA. However, we have little knowledge about the impact of food intake on the pathogenesis of RA. Because each country has its own food culture, the study focused on the dietary habit in Japan is essential in order to clarify the clinical impact of food intake in Japanese RA patients.
Objectives: The aim of this study is to clarify the relationship between the dietary habit of RA patients and their disease status.
Methods: We took the questionnaire survey about dietary habit in 2015, in KURAMA (Kyoto University Rheumatoid Arthritis Management Alliance) cohort as single institute. Disease activity was also examined in this cohort. These data were combined and statistically analyzed.
Results: 563 RA patients were enrolled from KURAMA cohort; female: male 4:1, age 63 years old, disease duration 15.5 years, DAS28-ESR 2.8 on average. Multivariate analysis showed that the intake frequency of vegetables had statistically significant negative correlation with DAS28-ESR (β=–0.17, $p<0.01$), SDAI (β=–0.15, $p<0.01$), HAQ (β=–0.15, $p<0.01$) and MMP-3 (β=–0.13, $p<0.01$). The intake frequency of frozen foods had positive correlation with MMP-3 (β=0.12,$p<0.01$). The intake frequency of juice had positive correlation with DAS28-ESR (β=0.11,$p<0.01$) and SDAI (β=0.11,$p<0.01$). Factor analysis revealed five dietary patterns, which were labeled "seafoods", "meat and fried foods", "vegetables and fruits", "snacks" and "processed foods". The "seafoods" had statistically significant negative correlation with DAS28-ESR (β=–0.10, p=0.027), SDAI (β=–0.11, p=0.015), HAQ (β=–0.11, p=0.015) and MMP-3 (β=–0.11, p=0.013). The "vegetables and fruits" had also statistically significant negative correlation with DAS28-ESR (β=–0.13, $p<0.01$), SDAI (β=–0.14, p=0.015), HAQ (β=–0.17, $p<0.001$) and MMP-3 (β=–0.14, $p<0.01$).
Conclusions: This study implicates that the disease activity of RA may be alleviated by high consumption of vegetables and fruits, or seafoods.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1631

AB1134 CHARACTERISTICS OF AUTOIMMUNE FEATURED INTERSTITIAL LUNG DISEASE IN KOREAN PATIENTS

J.-H. Kim, J. Jae Hyun, Y.H. Seo, S.J. Choi, G.G. Song. *Inrernal medicine, Korea University Medical center, Seoul, Korea, Republic Of*

Background: Interstitial lung disease (ILD) includes a heterogeneous group of disorders that result in diffuse parenchymal lung disease, with overlapping clinical, radiographic, and physiologic manifestations. Several rheumatologic conditions are associated with the development of ILD. There are many patients who are not diagnosed as definite connective tissue disease (CTD). These patients may have an undifferentiated connective tissue disease (UCTD).
Objectives: The aim of this study was to compare the prevalence and characteristics of patients with CTD-ILD, UCTD-ILD and Idiopathic pulmonary fibrosis (IPF) in Korean patients.
Methods: We study compared the prevalence and characteristics of patients with connective tissue disease-associated interstitial lung disease (CTD-ILD), undifferentiated connective tissue disease-associated interstitial lung disease (UCTD-ILD), or idiopathic pulmonary fibrosis (IPF) between January 2015 and June 2016 in Korea university guro hospital. Clinical characteristics, laboratory tests, and high-resolution CT images were analyzed and compared among three groups.
Results: CTD-ILD was identified in 13.0%, UCTD-ILD in 18.2%, and IPF in 68.7% among 307 patients. Female and younger age patients were dominant in CTD-ILD group. Pulmonary symptoms were more common in IPF, while extra-pulmonary symptoms were more common in CTD-ILD and UCTD-ILD group. Patients with CTD-ILD had more abnormal antibody tests than those of UCTD-ILD and IPF. Usual interstitial pneumonia pattern was dominant in HRCT images among three groups.
Conclusions: CTD-ILD is not able to be diagnosed accurately in ILD patients. A systematic evaluation of extra-pulmonary symptoms and serologic tests in patients with ILD can identify CTD-ILD, UCTD-ILD, and IPF.
References:
[1] Vij R, Noth I, Strek ME. Autoimmune-featured interstitial lung disease: a distinct entity. Chest. 2011;140(5):1292–9.
[2] Castelino FV, Varga J. Interstitial lung disease in connective tissue diseases: evolving concepts of pathogenesis and management. Arthritis Res Ther. 2010;12(4):213.
[3] Kinder BW, Shariat C, Collard HR et al. Undifferentiated connective tissue disease-associated interstitial lung disease: changes in lung function. Lung. 2010;188(2):143–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5647

AB1135 ALLOPURINOL AND THE RISK OF INCIDENT PERIPHERAL ARTERIAL DISEASE IN THE ELDERLY AMERICANS: A U.S. MEDICARE CLAIMS DATA STUDY

J. Singh, J. Cleveland. *University of Alabama at Birmingham, Birmingham, United States*

Background: Recently we found that use of allopurinol, the most commonly used urate-lowering therapy (ULT), was associated with a reduction of the risk of myocardial infarction and stroke, acute manifestations of CAD. Given that both PAD and CAD are manifestations of atherosclerosis and a similarity of disease pathophysiology between them, an obvious question was whether allopurinol use would reduce PAD. To our knowledge, no previous studies have examined whether allopurinol use reduces the risk of PAD.
Objectives: To examine whether new allopurinol use is independently associated with a reduction of the risk of incident peripheral arterial disease (PAD) in the U.S. elderly.
Methods: We used the 5% random Medicare sample from 2006–2012 to examine the association of allopurinol use and its duration with risk/hazard of incident PAD, in a retrospective cohort study. Multivariable Cox regression models adjusted for demographics, comorbidity, cardiac medications and cardiac conditions. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated.
Results: We identified 26,985 episodes of incident allopurinol use in 25,282 beneficiaries, of which 3,167 allopurinol use episodes (12%) ended in incident PAD. In multivariable-adjusted analyses, allopurinol use was associated with HR of 0.88 (95% CI, 0.81, 0.95) for incident PAD, as was female gender, 0.84 (95% CI, 0.78, 0.90). In a separate multivariable-adjusted model, compared no allopurinol use, longer durations of allopurinol use were associated with lower HR of PAD: 181 days to 2 years, 0.88 (95% CI, 0.79, 0.97) and $>$2 years, 0.75 (95% CI, 0.63, 0.89). Other factors significantly associated with a higher hazard of PAD were age 75-$<$85 and $\geq$85, female gender, higher Charlson index score, and black race. Sensitivity analyses adjusting for cardiac conditions and medications, confirmed these findings with minimal to no attenuation of hazard ratios.
Conclusions: New allopurinol use was independently associated with a lower risk of PAD in the elderly. Longer allopurinol use durations seemed more protective. Mechanisms of protective effect need to be studied in future studies.
Disclosure of Interest: J. Singh Grant/research support from: Takeda and Savient, Consultant for: Savient, Takeda, Regeneron, Merz, Iroko, Bioiberica, Crealta and Allergan pharmaceuticals, WebMD, UBM LLC and the American College of Rheumatology, J. Cleveland: None declared
DOI: 10.1136/annrheumdis-2017-eular.6848

AB1136 THE AGE OF ONSET OF RHEUMATOID ARTHRITIS CORRELATES WITH AIR POLLUTION AND HEALTH EXPENDITURE: RESULTS FROM MULTINATIONAL DATABASES

J.D. Castillo-Ortiz[1], A. Barajas-Ochoa[1], I. Peláez-Ballestas[2], A. Ramirez-Gomez[1], F.J. Aceves-Avila[1,3], J.J. Castaneda-Sanchez[1], C. Ramos-Remus[4]. *[1]Unidad de Investigacion en Enfermedades Cronico-Degenerativas, Guadalajara; [2]Hospital General de Mexico, Ciudad de Mexico; [3]Hospital General Regional 46, IMSS; [4]Universidad Autonoma de Guadalajara, Guadalajara, Mexico*

Background: Environmental variables contribute up to half of the variation in the rheumatoid arthritis (RA) susceptibility. We have recently reported that the age of RA onset (RAo) varies across latitudes around the world, starting younger around the Tropic of Cancer (1). Latitude gradients have been used as a surrogate for studying the influence of the environment on the risks of disease in order to generate hypotheses for further investigation.
Objectives: This is an exploratory study to assess whether the age of RAo correlates with tropospheric pollutants (2), electromagnetic fields, Inequality-adjusted Human Development Index (I-HDI) and Health Expenditures as per national census of participating countries.
Methods: The age of RAo was obtained from the GEO-RA group database that involves 2,481 patients from 41 countries. Information of the tropospheric pollutant PM10 (particulate matter 10μ), the I-HDI, and Health Expenditures per capita was obtained from the World Health Organization's reports. The average of each country's electromagnetic fields (nanotesla, nT) from the past 50 years was calculated using geographic coordinates per country through the magnetic field calculator of The National Centers of Environmental Information. Pearson's correlation and linear regression were used to evaluate the correlation of these environmental variables with the age of RAo by country.
Results: Complete data sets were available in 35 of the 41 countries. Overall, the mean age of RAo was 44±4.8 years, the annual average of PM10 of 57.5±39.3 $\mu g/m^3$, the Health Expenditure per capita of US $2,212±2,742, and the electromagnetic fields of 41,900±8,720 nT. The age of RAo was younger in countries with high PM10 levels (r= -0.61, $p<0.01$), high inequality (I-HDI, r=0.59,

p<0.01), and low Health Expenditure per capita (r=0.61, p<0.01); the age of RAo did not correlate with nT. A significant linear regression equation was found [F(2,32)=13.61, p<0.01, R2=0.46] in the age of RAo, Health Expenses per capita (β=0.0007; CI 95% 0.00004 to 0.001) and PM10 levels (β=-0.044; CI 95% -0.085 to -0.002).

Conclusions: The tropospheric pollutant PM10 and the components of the Health Expenditure per capita such as the provision of health services, family planning activities and nutrition activities are variables worth to further study through hypothesis-testing designs.

References:

[1] GEO-RA Group. Latitude gradient influences the age of onset of rheumatoid arthritis: a worldwide survey. Clin Rheumatol 2016. DOI: 10.1007/s10067–016–3481–9.

[2] Essouma M, Noubiap JJ. Is air pollution a risk factor for rheumatoid arthritis? J Inflamm (Lond) 2015; 12:48. DOI: 10.1186/s12950–015–0092–1.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5509

AB1137 THE ROLE OF SOCIAL DETERMINANTS ON THE PREVALENCE OF RHEUMATIC DISEASES IN LATIN AMERICA. A MULTILEVEL COPCORD STUDY

J. Moreno-Montoya[1], C. Pacheco-Tena[2], Y. Granados[3], J. Londoño[4], S. Guevara-Pacheco[5], B. Pons-Estel[6], O. Vega-Hinojosa[7], M. Garza-Elizondo[8], M.V. Goycochea-Robles[9], R. Quintana[10], F. Julian-Santiago[11], J. Alvarez-Nemegyei[12], A.M. Santos-Granados[13], R. Burgos-Vargas[14], I. Pelaez-Ballestas[14] on behalf of GEEEMA/GLADERPO. *[1]Epidemiology, Universidad del Bosque, Bogota, Colombia; [2]Faculty of Medicine, Universidad Autonoma de Chihuahua, Chihuahua, Mexico; [3]Rheumatology Unit, Hospital Dr. Manuel Nuñez Tovar, Maturin, Venezuela, Bolivarian Republic Of; [4]Faculty of Medicine, Universidad de la Sabana, Bogota, Colombia; [5]Faculty of Medicine, Universidad de Cuenca, Cuenca, Ecuador; [6]Rheumalogy Unit, Hospital Provincial, Rosario, Argentina; [7]Research Unit, Clinica Reumacenter, Juliaca, Peru; [8]Rheumatology Dpt., Hospital Universitario, Monterrey; [9]Research Unit, IMSS, Mexico City, Mexico; [10]Rheumatology Dpt., Hospital Provicial, Rosario, Argentina; [11]UNAM, Mexico; [12]Research Unit, HARE, Merida, Mexico; [13]Universidad de la Sabana, Bogota, Colombia; [14]Rheumatology Unit, Hospital General de Mexico, Mexico, Mexico*

Objectives: To determine the impact of individual and regional variables on the geographic distribution of RD across six Latin-American countries

Methods: This is a secondary multilevel analysis of cross-sectional data of COPCORD studies that investigated the prevalence of RD in Argentina, Colombia, Ecuador, México, Peru, and Venezuela. Individual factors were sex, age, comorbidities, job status, and Health Assessment Questionnaire (HAQ) score. Contextual level variables were country and subject's identification as indigenous. RD predictors, including individual and regional variables, particularly indigenous status were identified with logistic regression models. The effect of contextual variables was estimated with median odds ratio's (OR) estimation.

Results: Most individuals included in this analysis came from urban areas (82.40%); their mean age was 43.12 years (95% CI 43.01–43.35); and 56.0% were women. Nearly all of them reported >1 comorbidity (94.70%) and 72.19% were economically active. The prevalence of any RD varied from 1.55% in Peru to 26.09% in Argentina. The mean prevalence of Rheumatoid Arthritis (RA) was 1.58 (range 0.64 to 2.47) (table 1). Aside comorbidities, individual level variables associated to any RD were sex (OR: 1.35; 95% CI 1.28–1.43), age (OR: 1.02; 95% CI 1.01 -1.03), and HAQ score (OR: 3.71; 95% CI 3.22–4.28). Crude comparisons showed significant variations among countries (p<0.01) and indigenous groups (OR: 1.69; 95% CI 1.58–1.81). These findings were confirmed by adjusted analysis (Median OR 1.26; 95% CI 1.14–1.38) (table 2).

Table 1. General prevalences and sample sizes across countries

Country	n	%	Prevalence %			
			Any RD	RA	OA	Fibromyalgia
Argentina	1656	3.94	26.09	2,42	3.86	0.06
Colombia	6734	16.01	6.53	0,64	5.18	0.25
Ecuador	4877	11.60	13.2	0,88	10.58	2.05
Mexico	22175	45.69	18.34	2,47	12.01	0.82
Peru	1095	2.60	1.55	0,65	0.55	0.09
Venezuela	5512	9.45	14.94	0,9	16.47	0.38
Total/General	42049	100.00	16.00	1,58	10.42	0.77

Table 2. Individual and contextual factors associated to any RD

Any rheumatic diseases	OR	p	95% IC	
Any comorbidities	1,676	<0,001	1,542	1,821
Age (yrs)	1,019	<0,001	1,017	1,022
HAQ	2,456	<0,001	2,240	2,693
Schooling level	0,970	<0,001	0,962	0,978
	MOR*	p	95% IC	
Indigenous vs. Non-indigenous	1,266	0,015	1,146	1,386

Conclusions: There common factors associated to the prevalence of RD in the region, however, the estimation of its impact varies in significant way across countries and related to the fact of belong to an indigenous group indicating an increase in the estimated ORs.

Acknowledgements: National Council for Science and Technology (CONACYT);Colegio Mexicano de Reumatologia (Mexico). EsSalud (Perú). Universidad de Cuenca (Ecuador).ASOREUMA (Colombia). Federico Wilhelm Agricola Foundation (Argentina). PDVSA East, SUELOPETROL and Bristol-Myers Laboratory (Venezuela)

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3305

AB1138 ENGAGEMENT IN A UK SMARTPHONE STUDY EXAMINING THE ASSOCATION BETWEEN WEATHER AND PAIN: PRELIMINARY RESULTS FROM CLOUDY WITH A CHANCE OF PAIN

K.L. Druce[1], J. McBeth[1,2], S.N. van der Veer[1], D.A. Selby[3], B. Vidgen[4], K. Georgatzis[5], A.M. Chowdry[1], R. Lakshminarayana[6], D.M. Schultz[7], C. Sanders[8], J.C. Sergeant[1,2], W.G. Dixon[1,2]. *[1]Arthritis Research UK Centre for Epidemiology, University of Manchester; [2]NIHR Manchester Musculoskeletal Biomedical Research Unit, Central Manchester University Hospitals NHS Foundation Trust, Manchester; [3]Department of Statistics, University of Warwick, Coventry; [4]Oxford Internet Institute, University of Oxford, Oxford; [5]School of Informatics, University of Edinburgh, Edinburgh; [6]uMotif, London; [7]Centre for Atmospheric Science, School of Earth and Environmental Sciences; [8]Medical Sociology, Division of Population Health, Health Services Research and Primary Care, University of Manchester, Manchester, United Kingdom*

Background: Smartphones can facilitate collection of temporally-rich self-reported data, and have proven to enable large recruitment. However, their viability to support epidemiological research is uncertain due to concerns about selection bias and unsustained engagement.

Objectives: To examine the characteristics and engagement of participants in the first six months of Cloudy with a Chance of Pain, a UK smartphone-based study investigating the link between the weather and chronic pain.

Methods: Between 20th of January and 29th of February 2016, we recruited UK residents 17 years or older with chronic pain (≥3 months) who owned a smartphone. Participants received prompts from an app developed by uMotif, which they used to daily report the severity of ten pain-related symptoms. Of those who enrolled, those eligible for analysis provided sufficient baseline data to confirm they were ≥17 years old, and at least one symptom. The characteristics of those who were eligible were examined. Engagement per day was defined based on whether participants had completed any of the ten symptoms. Participants were then clustered by their engagement over time using a first-order hidden Markov models. Participant characteristics were then compared between the clusters.

Results: Of 7972 people who registered to participate, 6370 were eligible. 81% of participants were female, with a mean age of 49 years (SD 12.9). The most common diagnosis was arthritis (40% type unspecified, 19% rheumatoid arthritis), followed by fibromyalgia/chronic widespread pain (24%) and "other pain diagnosis" (23%). We identified four clusters of engagement: high (14%), moderate (22%), low (39%) and tourists (25%). Median days of data entry ranged from 1 (1–1) to 175 (IQR: 152–177) for the tourist and high engagement clusters respectively. Those in the high and moderate clusters (n=2249, 35%) engaged on at least 50% of days in the study (high: 79%; moderate: 50%). Highly engaged participants were older (median 56 (47–63)) when compared to those who were low engagers (47 (39–57)) or tourists (49 (40–58)). A lower proportion of tourists were women (76% (95% CI: 74–78), than in any other cluster (high: 82% (80–85), moderate: 84% (82–86), low: 81% (79–82)).

Conclusions: Cloudy with a Chance of Pain recruited a large sample of people with chronic pain, of whom over one in three participants engaged in smartphone-based symptom reporting for at least 50% of days in the first six months. Smartphone studies enable quick mass participation with sustained daily data entry, providing unprecedented volumes of daily data. While there may be selection bias towards older females in our study, younger men are also less likely to participate in studies using traditional data collection methods. Our study suggests that smartphones could provide a viable alternative to traditional data collection methods.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2692

AB1139 AUTOANTIBODY AGAINST COMPLEMENT COMPONENT 1Q SUBCOMPONENT IS ASSOCIATED WITH THE PATHOGENESIS OF RECURRENT PREGNANCY LOSS

K. Ohmura[1], K. Oku[1], T. Kitaori[2], M. Kono[1], S. Tanimura[1], E. Sugawara[1], R. Hisada[1], H. Nakamura[1], S. Shimamura[1], Y. Fujieda[1], M. Kato[1], T. Bohgaki[1], O. Amengual[1], S. Yasuda[1], M. Sugiura-Ogasawara[2], T. Atsumi[1]. *[1]Division of Rheumatology, Endocrinology and Nephrology, Hokkaido University Graduate School of Medicine, Sapporo; [2]Department of Obstetrics and Gynecology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan*

Background: In recurrent pregnancy loss (RPL), the pathogenesis of the majority of cases remains to be explained. Antiphospholipid, syndrome (APS) is one

of the disorder responsible for causing RPL and its overwhelmed complement activation recognized as a major pathogenic mechanism. Autoantibodies against complement component 1q subcomponent (aC1q) have been shown to associate with complement activation in primary APS, but the relevance of aC1q in RPL is still unclear. We hypothesized that aC1q would be associated with the pathogenesis of RPL in patients with or without APS, especially in RPL of unknown etiology.
Objectives: The aim of this study was to explore the significance of aC1q in RPL.
Methods: As a clinical study, we conducted a retrospective cross-sectional study comprising a total of 134 patients with RPL of unknown etiology, 27 with obstetric APS (OAPS), 14 parous patients with connective tissue disease (CTD) without historical obstetric/thrombotic complications and 17 parous healthy controls (HC). Serum levels of aC1q were measured using a solid-phase ELISA (Buhlmann Laboratories AG, Switzerland) and defined as positive using cut-off value of more than 15 U/mL according to the manufacturer. In murine model, 8–12 week-old female BALB/c mice were mated with isolated males and the presence of vaginal plug was defined as day 1 of pregnancy. Mice were treated with intravenous injections of anti-mouse C1q monoclonal antibody (JL-1), isotype control IgG2b or PBS. To block C5a receptor (C5aR), mice were intravenously pre-treated with anti-C5aR antibody, 30 minutes before the injection of JL-1 on day 8. Mice were sacrificed on day 16 of pregnancy and fetal resorption ratios, weight of fetuses and placentas, serum levels of C3a and immunohistochemical staining of complement components on placental tissue were compared among each group.
Results: Among RPL, OAPS, CTD and HC, 47 (35%), 8 (30%), 3 (21%) and 2 (12%) were positive for aC1q, respectively. In RPL patients, aC1q was more prevalent ($p<0.05$) and its titer was significantly higher than in HC (median and interquartile range [IQR] 12 [8–21] vs. 0 [0–4.3], $p<0.0001$) (Figure 1). In murine model, fetal resorption ratio was higher ($p<0.01$), weight of fetuses and placentas lower ($p<0.05$), and serum levels of C3a higher ($p<0.01$) in mice treated with JL-1 than in control mice. Immunohistological findings showed that complement components were more deposited on placenta in JL-1 treated mice than in control mice. Furthermore, the additional blockade of C5aR cancelled the pathogenic changes in JL-1 treated mice.

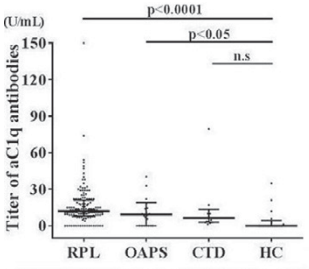


Figure 1. Titers of anti-C1q antibodies (aC1q) among recurrent pregnancy loss (RPL), obstetric antiphospholipid syndrome (OAPS), connective tissue disease (CTD) and healthy controls (HC) groups.
The titers of aC1q were significantly higher in RPL and OAPS compared to HC group (Dunn test). Horizontal bars show median and whiskers indicate the first and third quartiles.

Conclusions: Clinical findings showed that aC1q could be relevant to RPL. Moreover, we have established aC1q induced pregnancy loss model mice. Our study indicates that aC1q has a pathophysiologic role in RPL and that anticomplement therapy might be effective for at least some groups of patients with RPL for whom specific treatment remains to be established.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1008

AB1140 WHO DISABILITY ASSESSMENT SCHEDULE 2.0 IS RELATED TO UPPER AND LOWER EXTREMITY SPECIFIC QUALITY OF LIFE

K.S. Park, Y.-H. Cheon. *Gyeongsang National University, Jinju, Korea, Republic Of*

Background: Musculoskeletal complaints influence disability, but the relative contribution of concurrent upper and lower extremity health-related quality of life (HRQOL) on patient perceptions of disability is unclear.
Objectives: We evaluated whether two disease specific quality of life instruments (DASH and WOMAC) reflect a patient's perception of general disability using the WHO Disability Assessment Schedule 2.0 (WHODAS 2.0) and determined whether disability components are explained by upper and lower extremity HRQOL.
Methods: We recruited 421 randomly chosen participants 50 years or older without stroke, cancer, or history of surgery for musculoskeletal disease who participated in the Namgang Cohort. Upper extremity HRQOL was determined with the DASH score and lower extremity HRQOL with the WOMAC; as a measure of disability, we obtained WHODAS 2.0 component. Multiple regression modeling was used to assess the relative contributions made by upper and lower extremity HRQOL to disability.
Results: Most patients reported knee pain (61.0%), shoulder (17.1%), elbow (28.5%) and hand (56.1%). Mean WHODAS 2.0 total score was 28.06 (SD=14.2), corresponding to mild to moderate disability and WOMAC and DASH scores were 23.2 (SD=22.1) and 22.4 (SD=19.3). When adjusted for age, sex, level of education, spouse, self rated health, hypertention, DM and depression, the DASH total score was correlated with the getting around (β=0.137, p=0.032) and social participation (β=0.226, $p<0.001$) and the WOMAC total score was correlated with the getting around (β=0.362, $p<0.001$) and social participation (β=0.289, $p<0.001$)
Conclusions: We found that in a community-based population, perceived actibity limitation and social participation were associated with upper and lower extremity HQRQOL. Since the WHODAS 2.0 does not target a specific disease (as oppose to the DASH, WOMAC), it can be used to compare disabilities caused by different diseases.
References:
[1] Pösl M, Cieza A, Stucki G. Psychometric properties of the WHODASII in rehabilitation patients. Qual Life Res. 2007;16(9):1521–31.
[2] Silva C, Coleta I, Silva AG, Amaro A, Alvarelhão J, Queirós A, Rocha N. Adaptation and validation of WHODAS 2.0 in patients with musculoskeletal pain. Rev Saude Publica. 2013 Aug;47(4):752–8.
[3] Tazaki M, Yamaguchi T, Yatsunami M, Nakane Y. Measuring functional health among the elderly: development of the Japanese version of the World Health Organization Disability Assessment Schedule II. Int J Rehabil Res. 2014 Mar;37(1):48–53.
Acknowledgements: This work was supported from the Ministry of Agriculture Food and Rural Affairs in Korea.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4589

AB1141 PREVALENCE OF LONG-TERM STEROID THERAPY: FRENCH DATA

L. Couvaras, S. Trijau, G. De Lamotte, V. Pradel, T. Pham, P. Lafforgue. *APHM, Marseille, France*

Background: Corticosteroids are widely used for various diseases, from chronic respiratory conditions to auto-immune disorders. However, there are few epidemiological data about long-term steroid therapy in southern Europe (1, 2, 3).
Objectives: To describe chronic glucocorticoid prescriptions in a large cohort.
Methods: Information was collected from a national public health-insurance database that covers 4.1 million individuals and 83% of the population, in our geographic area of Provence-Alpes-Côte-d'Azur and Corsica, from September 1, 2009 through August 31, 2011. We identified subjects aged of 15 years and over starting glucocorticoid therapy. Chronic glucocorticoid therapy was defined as $\geq$7.5mg of prednisone equivalent per day during at least 90 days consecutive. We identified the incident cases of long-term glucocorticoid therapy, defined as those prevalent cases who did not fill glucocorticoid prescriptions during the first 6 months of the 24-month study period.
Results: We identified 32,812 patients who were prescribed glucocorticoid therapy, yielding 0.97% prevalence. Of these 32,812 patients, 14,205 (43.3%) met our definition of incident cases, yielding an incidence of 0.42% for 18 months in the overall population aged at least 15 years, corresponding to an incidence of long-term glucocorticoid therapy of 2.8/1000 inhabitants/year. Among these incident cases, the most currently prescribed glucocorticoids were prednisolone (64%) and prednisone (32%). Sixty-three per cent of patients received only one type of glucocorticoid while 33% received two and 5% received 3 or more of them. The average treatment duration was 270.9 days (CI 95% 267.7 – 274). Most prescriptions (55,4%) were initiated by general practitioners. The median prednisone-equivalent dose was 11mg/day (IQR, 8.8–17.8) and varied very little with age and sex.
Rheumatoid arthritis was the most common disease associated with chronic glucocorticoid prescriptions in this cohort (30%), followed by chronic respiratory failure (21%), internal medicine diseases such as connectivite tissue diseases, polymyalgia rheumatica or Giant-cell arteritis (21%), asthma (15%) and infammatory bowel diseases like ulcerative colitis or Crohn's disease (13%).
Conclusions: Long-term corticosteroid therapy is frequent in France, its description is close to what is already known in Europe.
References:
[1] Overman RA, Heh JY, Deal CL. Prevalence of oral glucocorticoid usage in the United States: a general population perspective. Arthritis Care Res (Hoboken) 2013;65:294–8.
[2] Gudbjornsson B, Juliusson UI, Gudjonsson FV. Prevalence of long term steroid treatment and the frequency of decision making to prevent steroid induced osteoporosis in daily clinical practice. Ann Rheum Dis 2002;61:32–6.
[3] Fardet L, Petersen I, Nazareth I. Prevalence of long-term oral glucocorticoid prescriptions in the UK over the past 20 years. Rheumatology 2011;50:1982–90.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6792

AB1142 VITAMIN D LEVELS AND ASSOCIATION WITH DISEASE ACTIVITY IN PARAGUAYAN SLE PATIENTS

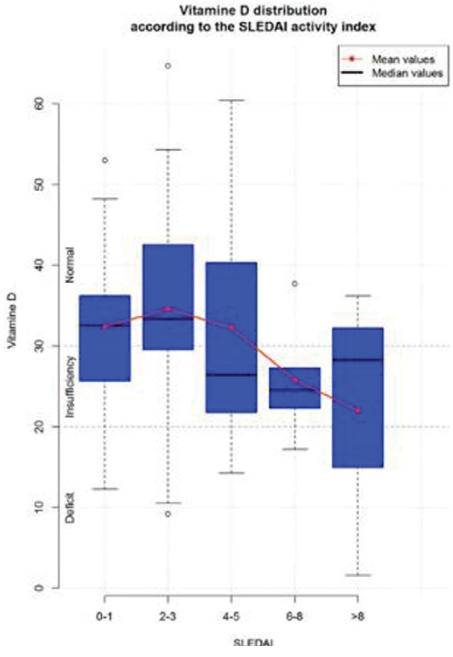
L. Román[1], G. Avila Pedretti[1], M.E. Acosta[2], M. Melo[1], M.T. Martinez[1], D. Margarita[1], I. Acosta Colman[1]. *[1]Facultad de Medicina- UNA; [2]Producción, Instituto de Investigación en Ciencias de la Salud, Asunción, Paraguay*

Background: Systemic Lupus Erythematosus (SLE) is a systemic inflammatory disease associated with genetic, environmental, hormonal and immunological factors. Vitamin D levels are nowadays considered as one possible factor associated with disease activity. Therefore, previous studies have analyzed vitamin D to the severity of SLE.
Objectives: To assess the Vitamin D status in paraguayan SLE patients and its association with disease activity.
Methods: An observational Trial has been performed on individuals diagnosed with SLE. Epidemiological, clinical and biochemical data have been recorded for each patient to study the association between vitamin D concentrations, the phospho-calcium metabolism parameters and disease activity. Quantitative determination of Vitamin D was perform using chemoluminescence ARCHITEC assay. Vitamin D status was interpreted as follows: deficiency ≤20 ng/ml and insufficiency 21–29 ng/ml. The statistical association tests were performed using linear (SLEDAI activity index) and logistic (Inactive/Mild vs Moderate/Severe) regressions. The epidemiological, clinical and biochemical variables were used as explanatory variables in these models.This study is a preliminary analysis of a trial supported by CONACYT (Paraguay) to investigate the role of vitamin D in patients diagnosed with SLE.
Results: We included 77 SLE patients, of whom 94.8% (73/77) were female. The average age of patients at the time of the study was 30.7±10.3 years. All patients received calcium supplements associated with vitamin D. The average vitamin D concentration was 32.2±12.10 ng /ml. 29.9% (23/77) of patients had vitamin D insufficiency and 13.0% had vitamin D deficiency. 94.8% (73/77) of the population had normal serum calcium and the total population had a normal phosphoremia. As for the dosage of PTH, it was found that 27.3% (21/77) have high values of PTH. 20.8% (16/77) of the patients had positive anti-DNA. Low C3 complement was observed in 30/77 (39%) and low C4 in 50/77 (64.9%) patients.
The mean value of SLEDAI at the time of the study was 2.32±2.83. When we study the distribution of vitamin D concentration according to the disease activity (SLEDAI) a clear pattern is observed linking lower vitamin D concentrations with higher disease activity (Figure 1). Patients with lower vitamin D concentrations are more likely to have higher disease activity (OR 0.93, 95% CI 0.88–0.99;P-Value=0.059. The means and standard deviations of vitamin D depending on the SLEDAI activity index are provided in Table 1.

Table 1. Mean and standard deviation of each patient group according to the ranges of SLEDAI activity index

SLEDAI	Mean	Standard deviation
0–1	32.41	9.61
2–3	34.59	13.37
4–5	32.28	14.38
6–8	25.8	7.61
>8	22.03	18.13

Figure 1. Distribution of vitamin D depending on the SLEDAI activity index



Conclusions: In this preliminary study of Paraguayan SLE patients, Vitamin D deficiency was frequent despite treatment with supplements. In addition, a clear association between SLEDAI and Vitamin D values was observed. The final analysis in a larger patient cohort will have to confirm these findings and clarify relation with disease activity.
References:
[1] Eloi M, Horvath DV, Ortega JC, Prado MS, Andrade LE, Szejnfeld VL, de Moura Castro CH. 25-Hydroxivitamin D Serum Concentration, Not Free and Bioavailable Vitamin D, Is Associated with Disease Activity in Systemic Lupus Erythematosus Patients. PLoS One. 2017 Jan 13;12(1).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3322

AB1143 THE IMPACT OF ANTI-CYCLIC CITRULLINATED PEPTIDE SEROPOSITIVITY ON EROSION PREVALENCE AMONG PATIENTS WITH RHEUMATOID ARTHRITIS OF VARYING DISEASE DURATION

L. Harrold[1], K. Price[2], H. Litman[3], S. Connolly[2], E. Alemao[2], S. Rebello[3], W. Hua[3], J. Kremer[4]. *[1]University of Massachusett, Worcester; [2]Bristol-Myers Squibb, Princeton; [3]Corrona, LLC, Southborough; [4]Albany Medical College and The Center for Rheumatology, Albany, United States*

Background: Little is known regarding the prevalence of erosive disease in a contemporary cohort of patients with RA and whether erosive disease prevalence differs by disease duration and seropositivity to anti-citrullinated protein antibodies (ACPA).
Objectives: To characterize the proportion of patients with RA with erosive disease by disease duration category and stratified by positive and negative serological status (anti-cyclic citrullinated peptide [anti-CCP], a surrogate for ACPA).
Methods: We identified patients with RA aged ≥18 years who were enrolled in the Corrona registry (October 2001–June 2016), with available disease duration, radiographic/MRI/ultrasound studies and serological status based on anti-CCP. Patients were grouped based on RA disease duration (0–2, 3–5, 6–10 and >10 years from diagnosis). Unadjusted prevalence erosion rates were calculated based on the proportion of patients with reports of erosions present on joint radiographs/MRIs/ultrasounds. Seropositivity was based on laboratory results (anti-CCP ≥20 U/mL) at enrolment in the Corrona registry. Chi-squared tests were used to assess differences in prevalence rates.
Results: There were 9759 patients who met inclusion criteria. Most were women (76%), middle-aged (mean [SD] 57 years [14]), with moderate disease activity (mean [SD] CDAI 14.7 [13.4]). Prior use of at least one biologic or targeted synthetic DMARD had occurred in 41% of patients. Overall, the prevalence of erosive disease was 28.6%, with higher prevalence among CCP+ (35.4%) vs CCP– (20.1%) patients ($p<0.001$, chi-squared test). The prevalence of erosions increased with increasing disease duration ($p<0.001$; Table). For each disease duration group, the prevalence of erosions was higher in patients who were CCP+ compared with those who were CCP–.

Table 1. Prevalence of Erosions According to Disease Duration and Serological Status

	Disease duration (years)			
	0–2	3–5	6–10	>10
Overall	19.3 (905/4699)	28.3 (475/1678)	33.4 (469/1404)	47.8 (946/1978)
Serological status				
CCP–	16.1 (359/2226)	22.7 (169/744)	21.8 (128/588)	28.1 (206/733)
CCP+	22.1 (546/2473)	32.8 (306/934)	41.8 (341/816)	59.4 (740/1245)

Data are % (n/N).

Conclusions: Erosions were common in this cohort of patients, and prevalence of erosions increased with longer disease duration. Patients who were CCP+ had higher rates of prevalent erosions than those who were CCP– with similar disease duration.
Disclosure of Interest: L. Harrold Shareholder of: Corrona LLC, Grant/research support from: Pfizer, AstraZeneca, Consultant for: Roche, Med IQ, K. Price Employee of: Bristol-Myers Squibb, H. Litman Employee of: Corrona LLC, S. Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, S. Rebello Employee of: Corrona LLC, W. Hua Employee of: Corrona LLC, J. Kremer Shareholder of: Corrona LLC, Grant/research support from: AbbVie, Bristol-Myers Squibb, Genentech, Lilly, Novartis, Pfizer, Employee of: Corrona LLC, Speakers bureau: Genentech
DOI: 10.1136/annrheumdis-2017-eular.1657

AB1144 GOOD THERAPEUTIC RESPONSE WITH BIOLOGICS: REMISSION IS REALITY. DATA FROM THE AUSTRIAN BIOREG REGISTRY

M. Herold[1,2], G. Eichbauer-Sturm[3], T. Nothnagl[4], R. Puchner[5], B. Rintelen[4], P. Spellitz[6], B.F. Leeb[4,7] on behalf of BioReg Austria. *[1]BioReg Austria, Vienna; [2]Department of Internal Medicine VI, Innsbruck Medical University, Innsbruck; [3]Rheumatologist in private practice, Linz; [4]2nd Department of Internal Medicine, Lower Austrian State Hospital, Stockerau; [5]Rheumatologist in private practice,*

Wels; [6]Rheumazentrum Wien-Oberlaa, Vienna; [7]Karl Landsteiner Institute of Clinical Rheumatology, Stockerau, Austria

Background: Remission or at last low disease activity is the aim of drug therapy in patients with chronic inflammatory rheumatic diseases. We evaluated disease activity in patients treated with biologics and using data of the Austrian biologic registry.
Objectives: The aim of this evaluation was to elucidate disease activity in patients with rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PsA) at baseline and at control-visits every six months after inclusion in BioReg.
Methods: Data were extracted from the Austrian BioReg registry (http://www.bioreg.at) which was initiated in 2009 to document patients treated with one of the biologics approved in Austria. Patients with ongoing biologic therapy as well as biologic-naïve patients starting biologic therapy can be included (baseline, BL). Further documentation is recommended about every six months (V1,V2 up to V11). Meanwhile, 1877 patients (rheumatoid arthritis (RA) n=1046, ankylosing spondylitis (SpA) n=446, psoriatic arthritis (PsA) n=322, other disease n=63) have been documented. Estimation of disease activity is done using DAS-28 as well as RADAI-5 in RA, SASPA in PsA, and BASDAI in SpA.
Results: DAS-28 (median values of BL; V1; V2; V9; V10) of patients with RA are 3,30; 2,51; 2,58; 2,52; 2,49, the respective RADAI-5 values are 3,2; 2,4; 2,2; 2.0; 2,3. BASDAI in patients with SpA were 3,60; 2,61; 2,45; 2,63; 2,20. Median values of inflammation's laboratory markers (ESR in mm/1st hour and CRP in mg/l) were always within the normal range (ESR and CRP in RA 15; 12; 12; 12,5; 14 and 2,0; 2,0; 2,0; 2,0; 2,0; in SpA: 8; 6; 7; 8; 8; and 2,0; 1,4; 1,4; 1,1; 1,0 in PsA 9; 8; 9; 7 (V7); 6 (V8); and 1,6; 1,5; 1,4; 1,9 (V7); 0,8 (V8)).
Conclusions: Our data confirm the efficiency of therapy with biologicals. During 5 years of continuous treatment more than half of patients with RA reach and keep remission with a DAS-28 below 2,6 and normal values of ESR and CRP. Also patients with SpA and PsA show similar successful therapeutic response.
Acknowledgements: BIOREG is supported by an unlimited industrial grant
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3898

AB1145 GENDER, AGE AND PULMONARY FUNCTION IN DOMINICAN PATIENTS WITH RHEUMATIC DISEASES

M.A. Santos [1], E. Tavera [2], C. Tineo [1], E. Loyo [1], J. Reyes [3]. *[1]Rheumatology, Hospital Regional Universitario Jose Maria Cabral y Baez; [2]Pneumologyst, Union Medica Clinic; [3]Investigation, Pontificia Universidad Catolica Madre y Maestra, Santiago, Dominican Republic*

Background: Interstitial lung disease (ILD) is a frequent entity in patients with rheumatic diseases, worsening the prognosis of those who suffer it (1). Previous studies have used the GAP (Gender, Age, Pulmonary function) model stage system to determine mortality at 1, 2 and 3 years (2). For stage I is 5.6% the first year, 10.9% second and 16.3% the third. GAP II has a mortality of 16.2%, 29.9% y 42.1% for the first, second and third year. For stage III, 39.2%, 62.1% and 76.8% respectively (3)
Objectives: To perform GAP model stage system in Dominican patients with Interstitial Lung Disease (ILD) related to Rheumatic Diseases (RD).
Methods: This is an observational, cross sectional study, with 42 patients who presented ILD related to RD. The GAP model stage system was determined by using demographic variables and pulmonary function tests such as spirometry and lung diffusion capacity (DLCO).
Results: 36 patients were female; the median age was 45±12 years. The mean value for Forced Vital Capacity (FVC) was 72%, Forced expiratory volume in 1 second (FEV1) 73%, and the ratio FEV1/FVC 99%. The DLCO mean value was 66±23 ml/min/mmHg. 35 patients (83.3%) were in stage I, 7 patients (16.6%) in stage II and none in stage III. The statistical significant variables were the time of diagnosis of the RD (p=0.013); with 4.9 years for those in stage I and 10.8 years for stage II; the time of the diagnosis of the ILD (p=0.003) with 2.1 years for patients in stage I and 4.8 years for stage II and smoking (p=0.063).
Conclusions: These findings suggest that the GAP model system is an useful tool to stage patients with interstitial lung disease related to rheumatic diseases. It can also help us make changes in treatment based on the stage. Special attention must be paid to those with a longer time of diagnosis of the RD, time of diagnosis of the ILD and/or smoking.
References:
[1] Vij R. Diagnosis and treatment of connective tissue disease-associated interstitial lung disease. CHEST 2013;143(3).
[2] Hoon S. Comparisons of prognosis between surgically and clinically diagnosed idiopathic pulmonary fibrosis using GAP model. Medicine Journal 2016; vol 95 (11).
[3] Ley B. A multidimensional index and staging system for idiopathic pulmonary fibrosis. Ann Intern Med. 2012, 156:684–691.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2152

AB1146 PHARMACOLOGICAL APPROACH OF KNEE OSTEOARTHRITIS TREATMENT IN PRIMARY CARE IN SPAIN

M. Herrero Barbero [1], S. Gimenez [2], J. Vergara [3], E. Viles I Lladó [4], H. Martinez [4], G. Rodríguez Roca [5], L. Sánchez [1], J.A. Díaz Muñoz [6], J.F. Frias [7], A. Castaño [8], J.J. Jiménez Díaz [9], Á. Rodríguez de Cossío [10], R. Belenguer [11], J.L. Llisterri [12], J. Vergés Milano [1,13] on behalf of EMARTRO. *[1]Bioiberica, Barcelona; [2]Unidad de Gestión Clínica el Limonar, Malaga; [3]Centro de Salud Huercal, Almería; [4]Bioiberica S.A., Barcelona; [5]Centro de Salud la Puebla de Montalbán, Toledo; [6]Centro de Salud Ávila Rural, Ávila; [7]Hospital Universitario Virgen de las Nieves, Granada; [8]Centro de Salud Corella, Navarra; [9]Centro de Salud Los Cubos, Burgos; [10]Centro de Salud San Martin de la Vega, Madrid; [11]Centro de Salud Algemesí; [12]Centro de Salud Ingeniero Joaquín Belloch, Valencia; [13]Osteoarthritis Fundation International, Barcelona, Spain*

Background: Osteoarthritis (OA) is the most prevalent joint disease and the leading cause of disability from 60 years onwards. In fact, 14,8% of the Spanish population has OA.
Objectives: This study aimed to analyze the indications and average doses prescribed in the treatment of knee osteoarthritis in Primary Care in Spain.
Methods: The EMARTRO study was designed as an observational, multicenter, transversal study to compare probability of suffering a comorbidities based on presence of symptomatic knee OA visited by GPs. Sociodemographic, anthropometric, clinical parameters and clinical variables of interest were recorded. The prescribed medications and doses indicated in syntomatic knee OA were analyzed in patients included in the EMARTRO study.
Results: A total of 1173 patients were included, of whom 646 had knee OA. Patients with OA had a mean (SD) BMI of 30.9 (5.1), systolic blood pressure 132.8 (14.5) and diastolic blood pressure 77.9 (9.1) mm Hg. They also had a mean of 4.3 (1.9) comorbidities, the most frequent were hypertension 358 (62.2%), dyslipidemia 336 (58.3%), diabetes mellitus II 126 (21.9%), and gastroesophageal reflux 110 (19.1%). As for the symptomatology, the patients presented a mean (SD) pain in Huskisson's VAS of 65.18 (15.27) mm and algofunctional Lequesne score of 11.35 (4.86).
Patients were treated with a mean of 2,2 medications. The 45.5% of osteoarthritic patients were treated as monotherapy, 35.5% were taking 2 medications for osteoarthritis, 15.3% 3 and 3.7% 4 or more medications. It should be noted, taking into account the high levels of pain, that 15% of the patients did not receive any treatment.
Regarding prescribed medications for knee OA, 378 (58.2%) patients were treated with paracetamol at a mean daily dose (SD) of 1,150.5 (1,815.5) mg; 232 (35.9%) received NSAIDs, with metamizole being the most prescribed at doses 1,092 (538) mg, ibuprofen at doses 1,136 (528,8) mg and naproxen at doses 941,8 (238,5) mg. Next, 131 (20.3%) patients were treated with opioids, tramadol being the most frequent at doses 102.7 (49.7) mg; 87 (13.3%) with SYSADOA being chondroitin sulphate the most frequent at doses 758.7 (247.7) mg. Finally, 87 (13.3%) of the patients were treated with COX-2, mainly with etoricoxib at doses of 69.3 (27.1) mg.
Conclusions: Although the patients presented many concomitant pathologies, it is frequent to approach osteoarthritis in polytherapy. In addition, despite the high symptomatology, patients are treated primarily with a mild analgesic such as paracetamol at doses lower than those recommended. It is paradoxical the high prescription of NSAIDs in a population with a high prevalence of cardiovascular and gastrointestinal pathologies as well as an increase in the prescription of opioids.
Disclosure of Interest: M. Herrero Barbero Employee of: Bioiberica, S. Gimenez: None declared, J. Vergara: None declared, E. Viles I Lladó Employee of: Bioiberica, H. Martinez Employee of: Bioiberica, G. Rodríguez Roca: None declared, L. Sánchez Employee of: Bioiberica, J. A. Díaz Muñoz: None declared, J. F. Frias: None declared, A. Castaño: None declared, J. J. Jiménez Díaz: None declared, Á. Rodríguez de Cossío: None declared, R. Belenguer: None declared, J. L. Llisterri: None declared, J. Vergés Milano Consultant for: Bioiberica, Employee of: Bioiberica
DOI: 10.1136/annrheumdis-2017-eular.3624

AB1147 COMORBIDITY PROFILE IN MEN AND WOMEN AFFECTED BY SYNTOMATIC KNEE OSTEOARTHRITIS AND IMPACT OF GENDER IN THE SYMPTOMATOLOGY AND PERCEPTION OF HEALTH STATUS

M. Herrero Barbero [1], S. Gimenez [2], J. Vergara [3], E. Viles I Lladó [4], H. Martinez [4], G. Rodríguez Roca [5], L. Sánchez [1], J.A. Díaz Muñoz [6], J.F. Frias [7], A. Castaño [8], J.J. Jiménez Díaz [9], Á. Rodríguez de Cossío [10], R. Belenguer [11], J. Vergés Milano [1,12], J.L. Llisterri [13] on behalf of EMARTRO. *[1]Bioiberica, Barcelona; [2]Unidad de Gestión Clínica el Limonar, Malaga; [3]Centro de Salud Huercal, Almería; [4]Bioiberica S.A., Barcelona; [5]Centro de Salud la Puebla de Montalbán, Toledo; [6]Centro de Salud Ávila Rural, Ávila; [7]Hospital Universitario Virgen de las Nieves, Granada; [8]Centro de Salud Corella, Navarra; [9]Centro de Salud Los Cubos, Burgos; [10]Centro de Salud San Martin de la Vega, Madrid; [11]Centro de Salud Algemesí, Valencia; [12]Osteoarthritis Fundation International, Barcelona; [13]Centro de Salud Ingeniero Joaquín Belloch, Valencia, Spain*

Background: Osteoarthritis (OA) is the most prevalent joint disease and the leading cause of disability from 60 years onwards. In fact, 14,8% of the Spanish

population has OA. This study aimed to analyze the indications and average doses prescribed in the treatment of knee osteoarthritis in Primary Care in Spain.

Objectives: This study aimed to analyze the comorbidity profile of men and women affected by symptomatic knee OA and the differences between genders in the perception of health status with regard to pain and loss of function due to their OA, quality of life and mental health.

Methods: The EMARTRO study was designed as an observational, multicenter, transversal study to compare probability of suffering a comorbidities based on presence of symptomatic knee OA visited by GPs. Sociodemographic, anthropometric, clinical parameters and clinical variables of interest were recorded. The probability of suffering comorbidities based on presence OA was estimated using the Odds Ratio estimation with conditioned logistic regression models. Depending on the variable, comparisons between groups were done using t-Student, Chi-square and Mann-Whitney.

Results: A total of 646 patients were included, 71% were women. Mean (SD) age was 67.9 (6.6) years.

Patients were obese without gender differences, with a BMI of 30.4 (4.4) and 31.2 (5.5) (p=0.0651) in men and women, respectively.

Men had a mean (SD) systolic blood pressure higher than women, 134.7 (15.0) vs 132.2 (14.5) mmHg (p=0.0453) and no differences were observed in diastolic pressure (p=0.5930).

As regards to the concomitant pathologies, no increase was detected in the likelihood of suffering comorbidities linked to the gender [OR=0.607 (95% CI: 0.260–1.418) p=0.2490]. Men with OA were more likely to have angina pectoris [OR=4.493 (95% CI: 1.299–15.536) p=0.0176] and underwent coronary bypass [OR=3.706 (95% CI: 1.389–9.890) p=0089].

Osteoarthritic women elicited more pain in Huskisson's VAS 62.8 (14.7) vs 66.8 (15.4) mm (p=0.0027) and worse function according to the Lequesne index 10.0 (4.9) vs 12.1 (4.7) ($p<0.0001$).

In terms of quality of life according to the EuroQol, women presented worse quality of life in dimesion of mobility (p=0.0001) and in the dimensions of daily activities, pain/discomfort and anxiety/depression ($p<0.0001$).

Finally, regarding mental health status, women had worse scores in the Goldberg scale to detect psychological disorders ($p<0.0001$) and more cases of anxiety and depression according to the HAD scale ($p<0.0001$).

Conclusions: The results of the present study indicate that women with osteoarthritis of the knee, despite having the same diagnosis and a similar comorbidity profile to men, have a worse perception of health status regarding the symptoms of their osteoarthritis, their quality of life and their mental health.

Disclosure of Interest: M. Herrero Barbero Employee of: Bioiberica, S. Gimenez: None declared, J. Vergara: None declared, E. Viles I Lladó Employee of: Bioiberica, H. Martinez Employee of: Bioiberica, G. Rodríguez Roca: None declared, L. Sánchez Employee of: Bioiberica, J. A. Díaz Muñoz: None declared, J. F. Frias: None declared, A. Castaño: None declared, J. J. Jiménez Díaz: None declared, Á. Rodríguez de Cossío: None declared, R. Belenguer: None declared, J. Vergés Milano Consultant for: Bioiberica, Employee of: Bioiberica, J. L. Llisterri: None declared

DOI: 10.1136/annrheumdis-2017-eular.3625

AB1148 INFODEMIOLOGY AND SEASONALITY OF SYSTEMIC LUPUS ERYTHEMATOUS USING GOOGLE TRENDS

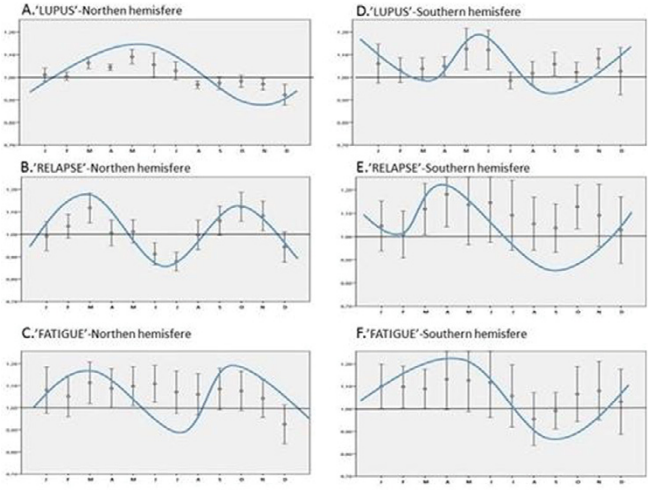
M. Radin, S. Sciascia. *Department of Clinical and Biological Sciences, Center of Research of Immunopathology and Rare Diseases- Coordinating Center of Piemonte and Valle d'Aosta Network for Rare Diseases, Torino, Italy*

Background: People affected by chronic rheumatic conditions, such as systemic lupus erythematosus (SLE), frequently rely on Internet and search engines to look for terms related to their disease, and its possible causes, symptoms and treatments. "Infodemiology" and "infoveillance" are two recent terms created to describe a new developing approach for public health, based on Big Data monitoring and data mining[1]. Different clinical and epidemiological studies have been conducted on seasonality of SLE, and focused on flare, fatigue and periodicity of onset of clinical manifestations. Overall, SLE disease activity has been associated with specific seasonal patterns in both, Northern and Southern hemispheres, possibly in relation to sun exposure, meteorological factors and vitamin D levels[2,3].

Objectives: In this study, we aimed to investigate trends of Internet research linked to SLE and symptoms associated to the disease seasonality by applying a Big Data monitoring approach.

Methods: We analyzed the large amount of data generated by Google Trends, considering "lupus", "relapse" and "fatigue" in a 10-year web-based research. Google Trends automatically normalized data for the overall number of searches, and presented them as relative search volumes, in order to compare variations of different search terms across regions and periods. The Menn-Kendall test was used to evaluate the overall seasonal trend of each search term and possible correlation between search terms.

Results: We observed a seasonality for Google search volumes for lupus-related terms (Figure 1). In Northern hemisphere, relative search volumes for "lupus" were correlated with "relapse" (τ=0.85; p=0.019) and with fatigue (τ=0.82; p=0.003), whereas in Southern hemisphere we observed a significant correlation between "fatigue" and "relapse" (τ=0.85; p=0.018). Similarly, a significant correlation between "fatigue" and "relapse" (τ=0.70; $p<0.001$) was seen also in the Northern hemisphere.



Profile plots for relative search volumes. Profile plots show the relative search volumes for 'lupus' (A and D), 'relapse' (B and E) and 'fatigue' (C and F), in the Northern and Southern hemispheres, respectively, for different months of the year, with estimates sinusoidal curves.

Conclusions: Despite the intrinsic limitations of this approach, the current study provides additional evidence for seasonality of lupus by using Google Trends. Internet-acquired data might represent a real-time surveillance tool and an alert for healthcare systems in order to plan the most appropriate resources in specific moments with higher disease burden

References:

[1] Eysenbach G. Infodemiology and infoveillance: framework for an emerging set of public health informatics methods to analyze search, communication and publication behavior on the Internet. J Med Internet Res. 2009;11:e11.

[2] Dall'Ara F, Andreoli L, Piva N, Piantoni S, Franceschini F, Tincani A. Winter lupus flares are associated with low vitamin D levels in a retrospective longitudinal study of Italian adult patients. Clin Exp Rheumatol. 33:153–8.

[3] Zhang H, Xu S, Tang D, Liang D, Liu H. Seasonal distribution of active systemic lupus erythematosus and its correlation with meteorological factors. 2011;66:1009–1013.

Acknowledgements: None.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1603

AB1149 THE ABILITY OF THE HEALTH SYSTEM TO IDENTIFY THE BURDEN OF RHEUMATOID ARTHRITIS IN SERBIA: A EULAR SURVEY

M.I. Zlatkovic-Svenda[1], R.M. Stojanovic[1], S.B. Sipetic-Grujicic[2], M.M. Radak-Perovic[1], N.S. Damjanov[1], F. Guillemin[3]. *[1]Institute of Rheumatology University of Belgrade School of Medicine; [2]Institute of Epidemiology University of Belgrade School of Medicine, Belgrade, Serbia; [3]INSERM – Cic-Ec 1433, University Hospital, and Université de Lorraine, Ea 4360 Apemac, Nancy, France*

Objectives: to estimate the rheumatoid arthritis (RA) prevalence in two urban regions of Serbia, covering the northern and the southern part, under the European League Against Rheumatism (EULAR) prevalence survey; to assess the ability of the health system to recognize and treat patients with RA.

Methods: The survey was conducted in four Serbian towns: Belgrade in the north and three towns in the south: Cacak (Moravicki region), Uzice (Zlatiborski region) and Krusevac (Rasinski region), covering 36.5% of the total Serbian population with more than 99% Caucasians, mostly orthodox Serbs (83%), <4% Hungarians, Roms and Bosnians and a minority of other nationalities. The first-detection phase of the study comprised previously translated and validated telephone Questionnaire usage with 33 items covering signs, symptoms, self-reported diagnosis and classification criteria for RA (ACR 1987) (1). Diagnoses were confirmed by rheumatologists in a second-confirmation phase. Prevalence results were standardized for age and sex with regard to Serbian population (national census 2002). Confirmed RA cases were asked two more questions: "How long had you had symptoms before you were given the diagnosis of RA" and "How had you been treated for that period of time".

Results: 6213 people were contacted and 63.6% answered the survey; joint pain was reported by 1,799 persons, and joint pain accompanied with joint swelling by 606 persons. A total of 23 RA cases were identified; 2 newly diagnosed. The standardized RA prevalence estimates were 0.30% (95% confidence interval [95% CI] 0.09;0.51) for the north, e.g. 0.09 (95% CI 0.08;0.26) for men and 0.49% (95% CI 0.19;0.79) for women. RA prevalence estimates were 0.42% (0.12;0.72) for the south; 0.28 (0.00;0.56) for men and 0.55% (0.09;1.00) for women, with

the female to male ratio 5,5:1 in the north and 2:1 in the south. Time period from the first symptoms occurence to the RA diagnosis was 17.7 (13.2) months for the northern part and 25.0 (16.9) for the southern; 20.6 (14.9) for Serbia; in that period patients were mostly treated with NSAIDS (82%) and physical therapy (30%); short-lasting corticosteroids were given to 13%, peroral corticosteroids to 4% and no patients were treated with DMARDS.

Conclusions: RA prevalence in the southern and northern part of Serbia is in line (0.42% [95% CI 0.12;0.72]) vs 0.30% [95% CI 0.09;0.51]), being more frequently presented in females as compared to males (five times more in the north and two times more in the south). Delay in diagnosis as compared to the first symptoms occurence was 21 months and during that time no patients were treated with DMARDS.

References:

[1] Zlatkovic-Svenda MI, Stojanovic RM, Milenkovic MP, Vlajinac HD, Le Bihan E, Guillemin F. Adaptation and validation of a telephone questionnaire – Serbian version for case detection of rheumatoid arthritis and spondyloarthropathy (multicentric Eular study). Clin Exp Rheumatol. 2007;25 (1): 75–84.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4899

AB1150 SLEEP HEALTH AND QUALITY OF LIFE IN PATIENTS WITH KNEE OSTEOARTHRITIS BEFORE AND AFTER TOTAL KNEE REPLACEMENT

M. Nuñez[1], E. Nuñez[2], J.M. Segur[3], L. Lozano[3], J. Montañana[3], V. Segura[3], M. Marti[4], A. Garcia-Cardó[4], S. Sastre[3], X. Alemany[3]. *[1]Rheumatology and IDIBAPS Area 1, Hospital Clinic; [2]SAP Suport al Diagnòstic i al Tractament, Institut Català de la Salut; [3]Orthopedic Surgery and IDIBAPS; [4]Rheumatology, Hospital Clinic, Barcelona, Spain*

Background: Studies report that sleep disturbances are often associated with chronic musculoskeletal disease. There is no agreed definition of sleep health, but some characteristics, such as sleep duration (number of hours daily) and sleep quality or satisfaction (subjective evaluation of good or poor sleep) are used to evaluate sleep health. In a previous study in patients with severe osteoarthritis awaiting total knee replacement (TKR), patients reporting good quality sleep had better health-related quality of life (HRQL) measured by the specific WOMAC and generic SF-36 questionnaires.

Objectives: To measure sleep health in patients included on a waiting list for TKR and 12 months after TKR.

Methods: Prospective study with a 12-month follow up. Sociodemographic and clinical variables were determined. Sleep health: hours of sleep and reparative sleep (RS) were examined using the question "How well do you usually sleep?" measured on a Likert scale (1=good [RS], 2=regular, 3=badly, 4=with medication/treatment (non-reparative sleep [NRS]). Function and pain were measured using the WOMAC and SF-36 questionnaires. Comparisons were made using t-tests (paired samples) and McNemar's test. Linear regression models were used to analyze associations. Dependent variables: WOMAC and SF-36 pain and function dimensions; independent variables: sleep quality, age, sex, BMI, number of comorbidities, depression/anxiety.

Results: 105 patients (79% female, mean age 69.39 years [SD 8.3]) were included. 80% had $\geq$2 comorbidities (mean 2.71 [SD 1.8]), mean BMI was 33.68 (SD 6.7), 32 had depression/anxiety, and mean sleep duration was 6.63 hours (SD 1.4). 12 months after TKF there were significant improvements in WOMAC dimension scores (mean $>$25 points, $p<0.001$) and SF-36 scores (mean $>$19). At study inclusion, 23% reported RS with a mean sleep duration of 7.5 hours (SD 1.1) vs. 6.24 hours (SD 1.5) in NRS patients (p=0.002). 12 months after TKR, 40% of patients had RS (p=0.029). Patients with RS had better scores in all quality of life dimensions ($<$10 points) than those with NRS ($p<0.05$) at baseline and at 12 months. Multivariate analysis showed RS was independently associated with pain and function (WOMAC and SF-36) ($p<0.007$).

Conclusions: Sleep health was associated with better HRQL before and after TKR. Although more patients had RS after TKR, 60% of patients continued not to have sleep health. Although often undervalued clinically, sleep health is closely associated with the health status.

Acknowledgements: This work was funded by project PI/13/00948, integrated in the Plan Nacional I+D+I and cofounded by ISCIII-Subdirección General de Evaluación and European Regional Development Fund (ERDF).

References:

[1] Buysse DJ. Sleep health: can we define it? Does it matter? Sleep. 2014 Jan 1;37(1):9–17. doi: 10.5665/sleep.3298.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1777

AB1151 MONTH OF BIRTH AFFECTS THE RISK OF RHEUMATIC DISEASES: A NATIONWIDE CASE-CONTROL STUDY

N. Koo, J. Lee, B.W. Lee, S.-K. Kwok, S.H. Park, J.H. Ju. *Division of Rheumatology, Department of Internal Medicine, School of Medicine, The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, Korea, Republic Of*

Background: There have been several studies which demonstrated the impact of birth on the risk of certain diseases such as asthma or cardiovascular diseases. However, rheumatic diseases have not yet been thoroughly investigated in terms of association with birth month.

Objectives: In this study, we sought to determine whether birth month or season could affect the risk of rheumatologic diseases.

Methods: The birth month patterns of patients with rheumatic diseases were compared with to those of general population. We utilized the claims data of Health Insurance Review and Assessment Service (HIRA) which covers nearly 90% of total population in Korea. The associations between birth month/season and 32 diseases were investigated using logistic regression.

Results: Our dataset included 17,247,458 (male 8,224,670; female 9,022,788) individuals from HIRA database from January, 1997 to August, 2015. Among 27 rheumatic diseases, 8 diseases including Crohn's disease (CD), ulcerative colitis (UC), rheumatoid arthritis (RA), systemic lupus erythematosus, polymyalgia rheumatica (PMR), ankylosing spondylitis (AS), multiple sclerosis, gout, fibromyalgia (FMS) were significantly associated with birth month ($P<0.05$). In terms of seasonality, CD, UC, RA, Sjogren's syndrome, PMR, AS, Gout, and FMS demonstrated significant difference. CD, UC and AS showed higher prevalence in individuals born in winter and lower prevalence in summer. On the other hand, people who were born in summer showed higher possibility to have gout and FMS compared to those born in winter. In consistent with previous reports, type 1 diabetes is more prevalent in those born in winter. Angina and myocardial infarction showed higher prevalence in patients born in spring and lower in fall. This consistency reflects the relevance of our dataset and methodology.

Conclusions: We found significant impacts of birth month/season on various rheumatic diseases. Seasonal variation of infective agents, sun exposure or food ingestion during gestation or early infancy may explain the association between birth month/season and certain disease development.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2891

AB1152 THE INCIDENCE OF HYPERSENSITIVITY TO NSAIDS IN THE GROUP OF PATIENTS WITH MUSCULOSKELETAL DISORDERS

O. Brzezińska-Pawłowska[1], A. Sztanka[2], K. Słodkowski[2], A. Lewandowska-Polak[2], J. Makowska[2]. *[1]Department of Rheumatology, Immunology and Allergy; [2]Department of Rheumatology, Medical Univercity of Lodz, Łódź, Poland*

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most common cause of drug hypersensitivity reactions (DHR). Recent studies show that the prevalence of hypersensitivity reaction to drug is particularly in Poland.

Objectives: To assess the frequency and the risk od developing NSAID hypersensitivity in patients with chronic disorders of the musculoskeletal system.

Methods: The study group consisted of 200 patients (age 19–88 years - 54,5±14, women-161, men-39) hospitalized in the Department of Rheumatology in 2015–2016. All patients filled questionnaire regarding symptoms of DHR after ingestion of non-steroidal anti-inflammatory drugs. The presence of DHR, clinical pattern of the reaction, frequency of NSAIDs administration and comorbidities have been studied. In statistical studies the main risk factors were defined.

Results: Seventy-seven patients from study group (38,5%) reported symptoms that occurred within 24 hours after NSAIDs ingestion. Symptoms characteristic for hypersensitivity reaction were reported by 40 patients (20%). Respiratory symptoms like dyspnea and/or cough were reported by 22 patients (11%). Cutaneous symptoms (urticaria/angioedema/dermal flush) were reported also by 29 patients (14,5%). Three patients experienced loss of consciousness. Thirty-seven patients reported isolated stomach cramps.

The symptoms developed usually between 2–12 hours after drug intake. In 37 patients oral administration caused DHR reaction, moreover in 14 patients also topical application led to adverse reaction. In most of patients reaction appeared due to COX-1 inhibitor and interestingly in 3 patients reaction was evoked by celecoxib which is perceived to be safe alternative for patients with NSAIDs hypersensitivity. Chronic urticaria, asthma and systematic drug intake occurs the main risk factors of hypersensitivity.

Conclusions: Drug hypersensitivity reactions are reported very frequently in population of patients with chronic musculoskeletal disorders. Our studies suggest that patients taking protractedly NSAIDs are in group with high risk of drug hypersensitivity development.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5408

AB1153 OSTEOPOROSIS RISK FACTORS IN PARTICIPANTS OF HEALTHY AGING ACADEMY

O. Brzezińska-Pawłowska[1], A. Łuczak[2], D. Stalmach[2], A. Lentas[2], M.L. Kowalski[1], J. Makowska[2]. *[1]Department of Immunology, Rheumatology and Allergy; [2]Department of Rheumatology, Medical Univercity of Lodz, Łódź, Poland*

Background: Osteoporosis is a major cause of morbidity and mortality in elderly population. It is known that the mortality rate in European population within 1 year of hip fracture is about 30%, and another 30% of patients need long term nursing for the rest of their life. However, the prevalence and associated risk factors in the Polish elderly population have not been well documented. The aim of the

study was to assess prevalence of osteoporosis in Polish elderly population and to assess risk factors related to osteoporotic fractures
Objectives: The study was based on questionnaires distributed among 645 students (61 men, 533 women and 51 not report mean age 69,42±5,88) attending the Healthy Aging Academy at Medical University.
Methods: Students were asked to answer 20 questions including information about endured fractures, osteoporosis risk factors, screening densitometry, treatment of osteoporosis, supplementation with vitamin D3 and calcium. Also, questions about classical risk factors for osteoporosis (loss of height (5 cm/year), family history, falls, loss of weight, treatment with steroids) were included to questionnaire.
Results: Fractures caused by fall from their own height were reported by 180 (27,91%). Moreover, 96 (14,88%) responders without fracture history declared more than 3cm decrease of height after their forties, what strongly suggest osteoporotic vertebral fractures. Forty three (24%) of the respondents had multiple fractures and single fractures were reported by 137 (76%) respondents. The most common localization of fractures was forearm (57%), shin bones (10,4%) and foot bones (9%). Among subjects who underwent densitometry after the fracture 32% had the diagnosis of osteopenia; 19,4% were diagnosed with osteoporosis and in 23,1% bone density was within normal limits. The strongest risk factors for osteoporotic fractures were numerous falls per year (p=0,000) and frequent drinking of alcohol (p=0,008). The risk factors of fractures (sum of risk factors for falls and osteoporosis) among people with previous fractures vs. those without fractures were statistically significant (p=0,037). Only 13% of patient with fracture and 15% of all patients with osteoporosis and osteopenia were treated by antiosteoporotic drugs (ibandronian/aledronian). Calcium supplementation was received by 30% of patients with fracture and 43% supplemented vitamin D3.
Conclusions: The prevalence of osteoporotic fractures in population of relatively well educated population of participants of Third Age University seems to be high. Patients with osteoporosis do not receive appropriate pharmacological prophylactic treatment, pointing at the need for education of primary care physicians and elderly population about burden and consequences of osteoporosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5452

AB1154 CHARACTERIZATION OF CHILEAN PATIENTS WITH PULMONARY DISEASE ASSOCIATED TO A RHEUMATOLOGIC DIAGNOSIS IN AN INTEGRATED POLYCLINIC. HOSPITAL PADRE HURTADO EXPERIENCE

O. Valenzuela[1], V. Agar[1], J.P. Leiva[2], I. Allende[2], G. Bozzano[2], G. Miranda[3], S.E. Ibáñez Vodnizza[1]. *[1]Rheumatology department, Clinica Alemana de Santiago/Hospital Padre Hurtado; [2]Facultad de Medicina Clinica Alemana de Santiago - Universidad del Desarrollo; [3]Hospital Padre Hurtado, Santiago, RM, Chile*

Background: Pulmonary diseases associated to a rheumatologic condition constitute a heterogeneous group of pathologies that are grouped according to their clinical and radiological similarity. There is a perception that the incidence of these diseases has been increasing, however, in Chile, there are no up-to-date publications regarding the characteristics of this group of patients.
Objectives: To describe and characterize patients with pulmonary disease associated to a rheumatologic diagnosis at Hospital Padre Hurtado, Chile, between the years 2014 and 2016.
Methods: Patients with suspected lung involvement associated to a connective tissue disease were evaluated by a bronchopulmonar specialist and a rheumatologist in a joint polyclinic. If the diagnosis was confirmed by the specialist the patient was included in the database. Data collected included age, gender, rheumatologic diagnosis and radiological pattern.
Results: 76 patients were included. 85.5% were female. The mean age was 58 years. Eighty-nine percent of the patients came from the Rheumatology department. These patients developed respiratory symptoms during the course of their disease. The remaining 11% were patients controlled in the Pulmonary diseases department, and the respiratory symptoms were the first manifestation of their conective tissue disease.The rheumatologic diagnoses that were concluded in this multidisciplinary polyclinic were distributed as described in Table 1.
69.7% of the patients have completed the radiological evaluation (Table 2).
Conclusions: Having a multidisciplinary clinical unit allowed us to order and protocolize the study, follow-up and treatment of the patients with lung involvement associated with a connective tissue disease. Currently, the multidisciplinary management of these patients is indispensable, as described in the literature.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4109

Table 1. Rheumatologic diagnosis of 76 patients

Rheumatoid Arthritis (%)	31 (40.8)
Scleroderma (%)	8 (10.5)
Inflammatory Myopathy (%)	5 (6.6)
Sjögren Syndrome (%)	5 (6.6)
Systemic Lupus Erythematosus (%)	4 (5.3)
Undifferentiated Connective Tissue Disease (%)	3 (3.9)
Mixed Connective Tissue Disease (%)	3 (3.9)
Recurrent Polychondritis (%)	2 (2.6)
Other diagnosis (%)	15 (19.7)

Table 2. Radiological evaluation of 53 patients

Interstitial Lung Disease pattern: Non Usual Interstitial Pneumonia (%)	26 (49.1)
Interstitial Lung Disease pattern: Usual Interstical Pneumonia (%)	8 (15.1)
Bronchiolitis (%)	6 (11.3)
Emphysema (%)	5 (9.4)
Nodules (%)	3 (5.7)
Pulmonary embolism (%)	2 (3.8)
Bronchiectasis (%)	1 (1.9)
Sarcoidosis (%)	1 (1.9)
Tracheal stenosis (%)	1 (1.9)

AB1155 DEPRESSION AND SUICIDALITY ARE COMMON IN PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS, AND RATES ARE COMPARABLE TO THOSE IN PSORIASIS

A. Sheahan[1], R. Suruki[1], P.C. Taylor[2], V.S. Sloan[1]. *[1]UCB Pharma, Raleigh, United States; [2]Kennedy Institute, Oxford, United Kingdom*

Background: Depression and suicidality are well-described comorbidities in psoriasis (PSO). The prevalence of these comorbidities in psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) is less well described.
Objectives: To assess the prevalence of depression and suicidality in PsA and axSpA in the recent literature, and compare rates to PSO.
Methods: For PsA and axSpA, we evaluated the recent English-language literature identified through a PubMed search; we used a recent review and performed a targeted review of the period since the publication in order to establish the rates for PSO for comparison.[1] Review articles were also examined to identify key publications.
Results: Rates of depression in PSO vary widely, depending on the outcome definition and method of ascertainment. Dowlatshahi et al. reported a pooled rate of 9.0–55.0%, with rates from the literature after the review period ranging from 9.0–39.8%. Rates for suicidality also varied widely, with 2.5–17.3% of patients (pts) reporting suicidal ideation. The limited data available provide ranges for depression in PsA of 3.4–28.6%, and in axSpA of 3.1–44.0%. The single study that differentiated between ankylosing spondylitis (AS) and non-radiographic (nr)-axSpA did not identify a difference between the two groups.[2] Very limited data existed on suicidality in PsA and axSpA. For PsA, the incidence rates (IR) of suicidal ideation, attempts, and suicide per 1000 person-years in the UK were 0.4, 1.3, and <0.001, respectively;[3] no prevalence data were identified. In a study in China, 2.5% of pts with axSpA reported a past suicide attempt,[4] while a study in Turkey found 9.6% of pts with AS had thoughts of suicide in the past year, but without plans.[5] Depending on the study, different definitions and tools were used to assess depression (eg. HADS, ICD9, antidepressant use), and even when the same tool was used, different cutoffs for defining depression were implemented (eg. cutoff for HADS ranged from $\geq$5 to $\geq$11), making comparisons across studies difficult. In a large observational study of AS with matched controls, the IR of depression per 1000 pt-years was 5.48 in AS versus 3.29 without AS, risk ratio 1.63.[6]
Conclusions: Although data are limited, rates of depression and suicidality in PsA and axSpA are comparable to those in PSO. Comparisons between studies and diseases are challenging due to a lack of standardized assessment tools and definitions of depression and suicidality. There are almost no data for nr-axSpA, which unlike AS has no gender predominance. Given that depression in PSO pts is more common in women,[7] understanding the relative prevalence in AS versus nr-axSpA would be important. Generating additional data regarding the impact of depression and suicidality in PsA and axSpA should increase awareness among treating physicians.
References:
[1] Dowlatshahi EA. J. Invest Dermatol 2014;134:1542–51.
[2] Klic GE. Medicine (Baltimore) 2014;93:e337.
[3] Hagberg KW. Mod Rheumatol 2016;26:774–9.
[4] Chan CY. Int J Rheum Dis 2014; doi:10.1111/1756-185X.12456.
[5] Saygin C. Clin Exp Rheumatol 2015;33(6 Suppl 94):S30–5.
[6] Shen CC. J Rheumatol 2016;43:625–31.
[7] Lamb RC. Br J Dermatol 2016; doi:10.1111/bjd.14833.
Disclosure of Interest: A. Sheahan Employee of: UCB Pharma, R. Suruki Employee of: UCB Pharma, P. Taylor: None declared, V. Sloan Employee of: UCB Pharma
DOI: 10.1136/annrheumdis-2017-eular.2455

AB1156 THE DESCRIPTIVE EPIDEMIOLOGY OF CUTANEOUS LUPUS ERYTHEMATOSUS IN THREE LARGE U.S. ADMINISTRATIVE DATABASES, 2010-2014

S.A. Hall[1], L. Li[2], S. Eaton[2], C. Musselli[2], A. Dilley[1]. *[1]Epidemiology; [2]Biogen, Cambridge, United States*

Background: Previous epidemiologic studies of cutaneous lupus erythematosus (CLE) have not described the pediatric burden, and have focused on specific geographic areas, limiting generalizability.
Objectives: To describe the demographics, comorbid conditions and pharmacy drug utilization of CLE patients, 3 large sources of U.S. administrative claims

data: 1) commercial insurance, 2) Medicaid insurance, and 3) Medicare insurance were utilized.
Methods: The data source was Truven Health MarketScan® Databases, containing medical service and prescription drug claims from commercial, Medicaid (11 states) and Medicare supplemental insurance plans for >80M US patients. CLE cases were identified by presence of ≥2 service dates with an ICD-9 code 695.4 on unique dates ≥28 days apart during the study period (Jan 1 2010-Dec 31 2014). For the most recent study year, the 5 most frequent comorbidity categories were reported using Clinical Classifications Software (CCS) Level 2 groupings. Similarly, the 5 most frequent pharmacy dispensings among CLE cases in 2014 were reported.
Results: In the Commercial, Medicaid, and Medicare claims data, 35,781, 7,361 and 5,594 CLE patients, respectively, were identified. CLE cases were >80% female with <6% aged <19 (Table). The most frequent CCS category (in all databases except Medicare) was CCS 13.7 (SLE and connective tissue disorders including systemic sclerosis, sicca syndrome, dermatomyositis, and polymyositis) where 63.1%, 76.6%, and 59.4% of CLE cases in the Commercial/Medicaid/Medicare data, respectively, had ≥1 claim. The most frequently-dispensed medication was corticosteroid hormone (62.5%, 72.1%, and 62.3% in the Commercial/Medicaid/Medicare data), while antimalarials were used by 58.3%, 55.9%, and 52.1% of CLE patients in the 3 databases, respectively.

Table 1. Demographics of CLE patients, by database, 2010–2014

	Commercial	Medicaid	Medicare
N	35,781	7,361	5,594
Mean (Median) Age	46.6 (49)	44.1 (44)	71.9 (71)
Age category			
≤18	2.2%	5.3%	0.0%
19–30	9.1%	15.1%	0.0%
31–45	29.5%	32.3%	0.1%
46–60	47.9%	33.1%	2.5%
61–64	10.7%	5.4%	1.9%
65+	0.7%	8.8%	95.5%
% Female	84.8%	89.7%	81.2%

Conclusions: Our results document a low relative burden of pediatric CLE. Notably, 23 to 41% of CLE patients did not have a claim for SLE or other connective tissue disease. Limitations include the inability of code 695.4 to distinguish between CLE subtypes, including discoid and subacute cutaneous lupus.
Disclosure of Interest: S. Hall Shareholder of: Biogen, Employee of: Biogen, L. Li Shareholder of: Biogen, Employee of: Biogen, S. Eaton Shareholder of: Biogen, Employee of: Biogen, C. Musselli Shareholder of: Biogen, Employee of: Biogen, A. Dilley Shareholder of: Biogen, Employee of: Biogen
DOI: 10.1136/annrheumdis-2017-eular.5402

AB1157 PREVALENCE OF MUSCULOSKELETAL DISORDERS AMONG GARMENT INDUSTRY WORKERS IN BANGLADESH

S.A. Haq, N. Shazzad, S. Ahmed, A.Z. Al-Qadir, A. Shahin. *Rheumatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh*

Background: Garments industry is flourishing in many developing countries. Attention is often not paid to ergonomics. It is plausible that the prevalence of musculoskeletal (MSK) pain may be high among garments workers.
Objectives: To estimate the prevalence of symptoms and disorders (MSD) among garment workers in Bangladesh.
Methods: This cross sectional study was carried out among 350 workers in two garment factories by face-to-face interview. The COPCORD (Community Oriented Program for Control of Rheumatic Disorders) methodology was adopted for the survey.The workers were classified into cutting, sewing, finishing and quality control operators. Trained interviewers identified subjects with musculoskeletal pain. Trained internists and rheumatologists examined the positive respondents.
Results: The point prevalence of musculoskeletal pain was 61.71%. The parts commonly affected during the preceding 7 days of interview in the whole group were shoulder (17.9%), lower back (15.2%), neck (13.8%) and knee (10.8%). The cutting operators suffered more from back (15.4%), neck (15.4%) and lower limb (11.5%); sewing operators from lower limb (12.4%), back (8.5%) and upper limb (7.7%); finishing operators from lower limb (50%) and quality control group from back pain (50%). Multiple regional pains were more frequent (n=155) among all operators.The sewing and cutting operators suffered from multiple regional pains more than other operators.The prevalence of Rheumatoid arthritis (RA) 0.9%, spondyloarthropathy (SpA) 1.42%, undifferentiated arthritis (UA) 1.1%, nonspecific low back pain (NSLBP) 4.6%, soft tissue rheumatism (STR) 3.7%, osteoarthritis (OA) 0.9% and lumbarspondylosis 1.1%.Nonspecific pain was the commonest condition (63.71%).
Conclusions: Rheumatic disorders are common causes of morbidity, disability, and work loss among the garment workers of Bangladesh where male and female workers are almost equally affected. Multiple regional involvementsare common in this occupational group. Mechanical disorders are the commonest.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1966

AB1158 PREVALENCE OF COMORBIDITIES IN PSORIATIC ARTHRITIS: A CROSS-SECTIONAL STUDY

T. Gudu, A. Peltea, M. Abobului, A. Balanescu, F. Berghea, V. Bojinca, A. Borangiu, C. Constantinescu, L. Groseanu, M.M. Negru, D. Opris-Belinski, D. Predeteanu, I. Saulescu, V. Vlad, R. Ionescu. *Rheumatology, Sf Maria Hospital, UMF Carol Davila, Bucharest, Bucharest, Romania*

Background: Psoriatic arthritis (PsA) is associated with important comorbidities: cardiovascular, gastro-intestinal, infectious, malignant, and psychiatric [1, 2]. However, they are less studied in PsA compared to other chronic inflammatory arthritis.
Objectives: The objective of this study was to calculate the prevalence of comorbidities and risk factors in a cohort of PsA patients.
Methods: This was an observational cross-sectional study, including consecutive, unselected adult patients, with a diagnosis of PsA according to their rheumatologist. Data collected: demographical, clinical (affected joints, current psoriasis, axial involvement, enthesitis, dactylitis), biological (acute phase reactants), and treatment related (nonsteroidal anti-inflammatory drugs, synthetic remissive drugs and biologics). Data on comorbidities and risk factors were collected according to the European League Against Rheumatism (EULAR) recommendations on reporting comorbidities in chronic inflammatory rheumatic diseases in daily practice [3].
Results: In all, 129 PsA patients were included: 77 (59.7%) women, mean age ± standard deviation 53.5±11.8 years, disease duration 7±7.4 years; 53 (41.1%) had axial involvement, 33 (25.6%) dactylitis, 18 (14%) enthesitis, and 24 (18.6%) current moderate/severe psoriasis. Most of them had low or moderate disease activity and almost a quarter of them (32; 24.8%) were taking a biologic.
The most prevalent comorbidities were: dyslipidaemia 103 patients (79.8%), hypertension 67 (51.9%), obesity 44 (34.1%), diabetes 21 (16.3%) and ischemic heart disease 15 (11.6%). Almost a third of patients (42, 32.6%) suffered a cardiovascular event after their PsA diagnosis, of which heart attack 2 patients, stroke 4, cardiac failure 4 and peripheral arterial disease one patient. Cardiovascular events correlated with smoking (r=0.893, p<0.001) and current moderate/severe psoriasis (r=0.218, p=0.013).
Regarding infectious comorbidities: 11 patients (8.5%) had a history of tuberculosis after being diagnosed with PsA, 7 (5.4%) chronic viral hepatitis, of which 4 with B virus and 3 with C virus, and 5 patients (3.9%) developed severe infections. Five patients (3.9%) were diagnosed with neoplasia, but no correlation was identified with any of the clinical, biological or treatment related included variables. Only 11 patients (8.5%) were diagnosed with depression, but the prevalence is probably underestimated, since not all patients were screened to this end.
Conclusions: PsA is associated with a high prevalence of comorbidities, especially cardiovascular diseases. This should be taken into consideration in the therapeutic and the global management of PsA patients.
References:
[1] Husni ME, Mease PJ. Managing comorbid disease in patients with psoriatic arthritis. Curr Rheumatol Rep 2010;12(4):281–7.
[2] Ogdie A, Yu Y, Haynes K, et al. Risk of major cardiovascular events in patients with psoriatic arthritis, psoriasis and rheumatoid arthritis: apopulation-based cohort study. Ann Rheum Dis 2015;74(2):326–32.
[3] Baillet A, Gossec L, Carmona L, et al. Points to consider for reporting, screening for and preventing selected comorbidities in chronic inflammatory rheumatic diseases in daily practice: a EULAR initiative. Ann Rheum Dis 2016;75(6):965–73.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5838

AB1159 HIGH DOSE GLUCOCORTICOIDS AS A RISK FACTOR OF SIGMOID DIVERTICULITIS PERFORATIONS IN AUTOIMMUNE DISEASES

T. Kuranobu, M. Ishitoku, T. Tokunaga, Y. Yoshida, S. Hirata, T. Nojima, E. Sugiyama. *Department Clinical Immunology and Rheumatology, Hiroshima university hospital, Hiroshima, Japan*

Background: It has been reported that glucocorticoids (GCs) and non-steroidal anti-inflammatory drugs (NSAIDs) might increase sigmoid diverticulitis perforations (SDPs) for rheumatoid arthritis patients, however, there are few previous reports referring to the relationship between SDPs and GCs in patients with systemic autoimmune diseases. We investigate relationship between SDPs and GCs in patients used GCs for not only rheumatic patients but also other autoimmune disease' sufferer.
SDPs and GCs
Objectives: To describe development of SDPs during high dose GC (over PSL 0.8mg/kg equivalent) therapy for systemic autoimmune diseases in our department, additionally reviewing previous reports with regard to the relationship between SDPs and GCs.
Methods: 187 patients hospitalized in our department from April 2015 to December 2016 were retrospectively reviewed.
Results: Among 187 patients, 61 took high dose GCs, 29 took moderate dose GCs (0.5–0.6mg/kg PSL equivalent), 53 took low dose (less than 0.5mg/kg PSL equivalent), and 29 didn't take GCs. Four patients out of 61 who took high dose GCs developed SDPs (table). Nobody developed SDPs in moderate, low and

not any dose GCs group. Case 1–3 took NSAIDs. Case 2 received mPSL pulse therapy (mPSL 1 g x 3 days). Case 1 and 2 developed SDPs within 3 months from initiating GCs. Case 1 recurred SDPs at 17 and 63 months from initiating GCs. Case 2 was prescribed Tacrolimus as a concurrent medication. All four patients were operated to remove the perforated segment, and case 2 and 4 were created artificial anus. Although they were clinically diagnosed as SDPs only case 4 clarified perforation in pathological findings.

case	age sex	target	age at onset (year)	period from GCs start to onset (mo)	maximum doses of GCs (mg)	doses at onset (mg)	cumulative doses of GCs (mg)
1	76 female	Dermatomyositis	70	3	60	32.5	2.5
2	72 male	Polymyositis	70	2	60	19	6
3	74 female	Rheumatoid vasculitis	74	94	50	9	30
4	73 male	Psoriatic arthritis	71	103	40	10	25

table – patients characteristics and GCs profile

Conclusions: We should take care of developing SDPs in patients described high dose GCs.

References:

[1] Mpofu S, Mpofu CM, Hutchinson D, Maier AE, Dodd SR, Moots RJ. Steroids, non-steroidal anti-inflammatory drugs, and sigmoid diverticular abscess perforation in rheu- matic conditions. Ann Rheum Dis 2004; 63: 588–590.

[2] Humes DJ, Fleming KM, Spiller RC, West J. Concurrent drug use and the risk of perforated colonic diverticular dis- ease: a population-based case-control study. Gut 2011; 60: 219–224.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3212

AB1160 EPIDEMIOLOGY AND CLINICAL PRESENTATION OF OCULAR INVOLVEMENT IN A POPULATION OF 278 PATIENTS WITH NON INFECTIOUS UVEITIS

V. Venerito[1], G. Lopalco[1], L. Cantarini[2], C. Fabiani[3], M. Fornaro[1], A. Vitale[2], S. Guerriero[4], R. Favale[4], M. Giannini[1], M. Nivuori[1], F. Cacciapaglia[1], G. Laselva[1], M. Galeazzi[2], G. Lapadula[1], F. Iannone[1]. *[1]Department of Emergency and Organ Transplantations, Rheumatology Unit, University of Bari "Aldo Moro", Bari; [2]Interdepartmental Research Center of Systemic Autoimmune and Autoinflammatory Diseases, Rheumatology Unit, Policlinico le Scotte, University of Siena, Siena; [3]Department of Ophthalmology, Humanitas Clinical and Research Hospital, Rozzano; [4]Department of Basic Medical Sciences, Neuroscience and Sense Organs, Ophthalmology Unit, University of Bari "Aldo Moro", Bari, Italy*

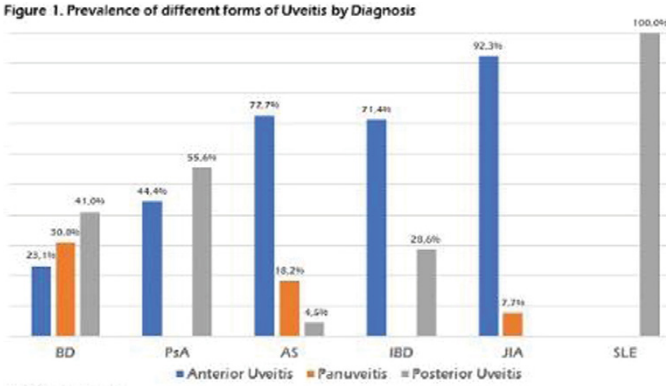
Background: Uveitis is a sight-threatening inflammation which may involve different anatomic parts inside the eye. Rheumatologists should be aware of the ocular clinical signs and of the frequency of uveitis because it may cause irreversible lesions to the eye that predominantly affect people in their most productive years, being one of the most common extra-articular manifestation in several rheumatic diseases.

Objectives: We aimed to describe the presentation of the clinical features of ocular involvement in a population of patients affected with newly diagnosed Non Infectious Uveitis (NIU).

Methods: 278 patients (mean age 42±18,18 years, range 4 - 87) from three specialized centres, all affected with uveitides, were enrolled; 158 were female, 120 male, all caucasian but one asiatic. Complete ophtalmologic examination was carried out in all of them, malignancy or infections of any kind were preventively ruled out. In addition blood tests, serum antibodies level evaluation and HLA haplotype typization were performed. Moreover instrumental tests were performed when a relation with systemic diseases was suspected. Uveitides were then classified according to the Standardization of Uveitis Nomenclature Working Group Criteria.

Results: 149 (53,6%) patients were affected with Anterior Uveitis (AU), 45 (16,2%) with Panuveitis, 16 (5,8%) with Intermediate Uveitis (IU) and 68 (24,5%) with Posterior Uveitis (PU). 110 (41,7%) patients were known to have a systemic disease at the moment of the uveitis onset. HLA-B27 positivity was found in 15,8% of patients, whereas HLA-B51 positivity was found in 21,9% of patients. Behçet's Disease (BD) was diagnosed in 39 (14%) patients: in particular AU was found in 9 out of 39 patients (23,1%), while PU in 16 out of 39 patients (41%). Ankylosing Spondylitis (AS) was recognized in 22 (7,9%) patients: AU was diagnosed in 16 out of 22 (72,7%) of them while 4 out of 22 (18,2%) where affected with Panuveitis. The cases of Psoriatic Arthritis (PsA) were 9 (3,2%); specifically, AU was recognized in 4 out of 9 (44,4%) of them while PU was found in 5 out of 9 (55,6%) of them. We also defined the most common form of uveitis in patients affected with either Juvenile Idiopathic Arthritis, or Systemic Lupus Erythematosus, or Sarcoidosis, or Vogt-Koyanagi-Harada disease or Inflammatory Bowel Diseases. The idiopathic form of uveitis, was diagnosed in 162 (58,3%) patients. Anti-nuclear antibodies (ANA) levels were assessed in 148 patients of whom 57 (38,5%) have been found ANA positive and 91 (61,5%) ANA negative. Notably 38 (66,7%) ANA positive patients were affected with AU.

Figure 1. Prevalence of different forms of Uveitis by Diagnosis



BD: Behçet's Disease
PsA: Psoriatic Arthritis
AS: Ankylosing Spondylitis
IBD: Inflammatory Bowel Diseases
JIA: Juvenile Idiopathic Arthritis
SLE: Systemic Lupus Erythematosus

Conclusions: Our study provides a depiction of clinical features and epidemiology of ocular involvement in a huge population of patients presenting newly diagnosed NIU. Notably, in our population, idiopathic uveitis was the most commonly diagnosed form; it took shape of AU in 56,6% of cases. The majority of HLA-B27 positive uveitides were also AU (68,2%), while, among HLA-B51 uveitides, PU (39,3%) and AU (37,7%) were recognized as the most common presentations.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2232

Validation of outcome measures and biomarkers

AB1161 PORTUGUESE ADAPTATION AND VALIDATION OF THE ANKYLOSING SPONDYLITIS QUALITY OF LIFE (ASQOL) QUESTIONNAIRE

A. Águeda[1], A. Heaney[2], S.P. McKenna[2], A. Barcelos[1]. *[1]Rheumatology, Centro Hospitalar do Baixo Vouga, E.P.E., Aveiro, Portugal; [2]Galen Research Ltd., Manchester, United Kingdom*

Background: Ankylosing Spondylitis (AS) is a chronic rheumatic disease that affects mainly the axial skeleton and entheses. If left untreated, AS evolves with limited spine mobility and irreversible structural changes, with severe repercussions in patients' quality of life. Throughout the years many instruments have been used in order to evaluate AS impact in patients' lives, focusing predominantly on symptoms and functioning however, these instruments do not inform on the impact of the condition on quality of life (QoL). The ASQoL is a patient reported outcome measure, specifically developed to evaluate QoL in AS patients. It has been adapted to several languages worldwide, though a Portuguese version hadn't been developed yet.

Objectives: Translation of the ASQoL questionnaire into Portuguese and ascertain its psychometric properties.

Methods: Translation of the original UK English ASQoL into Portuguese was performed by bilingual panel and then assessed by a lay panel. Cognitive debriefing interviews were performed with AS patients to assess face and content validity. Finally, a sample of AS patients were included in a test-retest postal survey, administered on two different occasions, two weeks apart, to investigate the reliability and construct validity of the new Portuguese adaptation of the ASQoL. Nottingham Health Profile (NHP) was used as a comparator measure.

Results: The Portuguese version of ASQoL proved to be relevant and easy to understand.

Validation of the ASQoL included fifty-eight AS patients, with a mean age of 51 years (Range 25.0 – 80.0), with 55.2% males. The Portuguese ASQoL had good internal consistency at Time 1 (α =0.93) and Time 2 (α =0.91). Test-retest reliability was excellent, with a strong positive correlation between scores at two time points ($r=0.92$, $p<0.001$). Correlation between ASQoL scores and NHP was moderately strong with Spearman's rank correlation coefficients between ASQoL and NHP section scores, including the distress scale embedded within, all $p<0.001$. These results suggest that patient's quality of life is influenced by many factors in addition to disease severity, including social skills and ability to adapt to physical limitations.

The Portuguese version of ASQoL was able to discriminate between patients who differed on their perception of general health and presence of comorbidity, although there were no significant differences according to self-perception of disease severity.

Conclusions: The Portuguese version of the ASQoL performed well, demonstrating good psychometric properties for use in clinical studies and trials of patients with AS. The lack of significance in the analysis by self-perceived disease severity may be due to the relatively small sample size.

References:

[1] LC Doward, A Spoorenberg, SA Cook, D Whalley, PS Helliwell, LJ Kay, SP McKenna, A Tennant, D Van der Heijde, MA Chamberlain; Development of the ASQoL: a quality of life instrument specific to ankylosing spondylitis; Ann Rheum Dis 2003;62:20–26.

[2] KL Haywood, AM Garratt, K Dziedzic, PT Dawes. Generic measures of health-related quality of life in ankylosing spondylitis: reliability, validity and responsiveness. Rheumatology 2002;41:1380–1387.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6807

AB1162 RAPID3 SCORE CAN PREDICT DISEASE ACTIVITY IN PRIMARY SJÖGREN'S SYNDROME

B. Öz[1], A. Karatas[1], Z. Ömercikoğlu[2], O. Catak[3], N. Gozel[2], S. Cur[2], E. Donder[2], S.S. Koca[1]. *[1]Rheumatology Department; [2]Department of Internal Medicine; [3]Department of Ophthalmology, Faculty of Medicine, Firat University, ELAZIG, Turkey*

Background: Sjögren's syndrome (SS) is a chronic autoimmune disease that causes salivary and lacrimal gland dysfunction, resulting in oral and ocular dryness. The European League Against Rheumatism (EULAR) SS disease activity index (ESSDAI) is a systemic disease activity index measuring disease activity in patients with SS. The ESSDAI includes 12 domains. EULAR SS patient-reported index (ESSPRI) is used to evaluate dryness, fatigue, and pain symptoms, and their impact on the disease. Routine Assessment of Patient Index Data 3 (RAPID3) is used to evaluate disease activity in patients with rheumatoid arthritis which is another inflammatory disorder.

Objectives: This study aims to evaluate whether RAPID3 is useful in primary SS.

Methods: 30 patients with primary SS were enrolled in the study. ESSDAI, ESSPRI and RAPID3 scores were recorded. Chi-square, Mann Whitney U test and Pearson correlation analysis were performed for the statistical analysis.

Results: Demographically and clinical data were shown in the Table-1. Mean ESSDAI, ESSPRI and RAPID3 scores were 3.8±3.6, 5.8±1.7, and 14.8±5.2, respectively. RAPID3 scores were positively correlated ESSPRI ($r=0.669$, $p<0.001$). In addition, when we set the cut-off value to 12 on the RAPID3 score (>12 accepted as active, and ≤ 12 accepted as inactive), ESSPRI score was significantly higher in active patients (6.4±1.4 vs. 4.1±1.4, p=0.002). However, there was no relationship between RAPID3 and ESSDAI scores.

Schirmer test was positively correlated with tear break up time (BUT) ($r=0.573$, $p=0.007$). Lissamine green score was negatively correlated with Schirmer test and BUT ($r=-0.484$, $p=0.007$, and $r=-0.507$, $p=0.004$, respectively). Despite there was high compliance among these three scales evaluating eye involvement, these scales did not appear to correlate with the ESSDAI, ESSPRI, and RAPID3 scores that assess global disease activity. The mean age was significantly higher in patients with Schirmer test ≤ 5 mm compared to the patients with >5 mm (55.6±6.9 vs. 47.6±8.5 years, p=0.044).

Table 1. Demographics and clinical variables

	SS (n=30)
Mean age, years	51.0±8.7
Disease duration, years	6.3±4.6
Sex, % females	100
WBC, $10^3/\mu l$	5.9±1.8
Hemoglobin, g/dl	13.3±1.5
ESR, mm/h	19.5±16.4
CRP, mg/dl	7.2±13.5
ANA positivity, %	83.3
Anti-Ro positivity, %	65.5
Anti-La positivity, %	46.2
HAQ	32.4±4.9
Schirmer test, mm	11.4±6.4
BUT, sec	3.2±1.8
Lissamine green score	2.2±1.1

SS; Sjögren's syndrome, WBC; white blood cell count, ESR; erythrocyte sedimentation rate, CRP; C-reactive protein, ANA; anti-nuclear antibody, HAQ; health assessment questionnaire, BUT; tear break up time.

Conclusions: In SS, it is not simple to detect disease activity. Comorbid psychosomatic diseases affect the set detecting global disease activity. On the other hand, the activity of glandular involvement and global disease activity are not with compliance. Therefore, new and easy tools are necessary in primary SS. In our study, RAPID3 score is corelated with ESSPRI. This result suggests that RAPID3 is useful to detect disease activity in primary SS.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6243

AB1163 ANTIBODIES BINDING SYNTHETIC OLIGONUCLEOTIDES DISTINGUISH LUPUS FROM RHEUMATOID ARTHRITIS, SCLERODERMA AND SJOGREN'S SYNDROME

C. Putterman[1], A. Gabrielli[2], A. Balbir-Gurman[3], P. Safer[4], K. Jakobi-Brook[4], R. Sorek[4], I. Gluzman[4], S. Wallace[5], I.R. Cohen[6]. *[1]Division of Rheumatology, Albert Einstein School of Medicine, NY, United States; [2]Istituto di Clinica Medica dell'Università di Ancona, Ancona, Italy; [3]Rheumatology Unit, Rambam Health Care Campus and Rappaport Faculty of Medicine, Technion, Haifa; [4]ImmunArray LTD, Rehovot, Israel; [5]ImmunArray Inc, VA, United States; [6]Weizmann Institute of Science, Rehovot, Israel*

Background: The SLE-key® RuleOut iCHIP® antigen microarray-based test rules out a diagnosis of SLE with a sensitivity of 94%[1].

Objectives: Here we report the use of the iCHIP® platform and a set of synthetic oligonucleotide antigens to distinguish between SLE subjects and those with a diagnosis of Rheumatoid Arthritis (RA), Scleroderma (SSc), Sjogren's syndrome (SS), or healthy individuals (HC).

Methods: We examined IgM and IgG antibody binding to 22 synthetic oligonucleotides (44 features) in the sera of HC subjects (N=40); SLE (N=30); SSc (N=40); SS (N=20); or RA (N=30) patients. Univariate analysis (FDR adjusted p-values) was used to determine the ability of each feature to separate between SLE and the different classes of subjects.

Results: Table 1 shows that multiple oligonucleotides successfully distinguished SLE patients from all other groups. All significant features were IgG antibodies, except for 1 IgM. Table 2 shows the impact of single nucleotide change on autoantibody binding. PolyG (G17) separates SLE from all but SS. T1G16 separates SLE from HC subjects, while G16T1 gave no significant separation. The addition of a G to the 5' and 3' end of T16 enhanced IgG antibody binding and improved separation between SLE and other autoimmune diseases with at least 10-fold improved significance as compared to T20. PolyG sequence length impacts the ability of the oligonucleotides to separate between SLE and the other groups (Fig. 1A). Unexpectedly, sequences either shorter or longer than G14 were effective in separating SLE from HC, RA, and SSc, while G14 was not effective. Furthermore, none of the polyG homopolymers could separate SLE from SS. Sequences rich in C or T were more effective at separating between SLE and SS patients (Fig. 1B).

Table 1

SLE Compared to:	Number of significant oligonucleotides Minimal FDR corrected p value: 0.003–4E-6	
	IgG	IgM
HC	17	0
RA	10	0
SSc	14	1
SS	2	0

Table 2

Class	Oligo	HC Vs SLE	RA Vs SLE	SSc Vs SLE	SS Vs SLE
PolyG ± 3' or 5' T	G17	0.04	**0.0006**	**0.007**	NS
	T1G16	0.03	NS	NS	NS
	G16T1	NS	NS	NS	NS
PolyT ± 3' & 5' G	GT16G	**0.000004**	**0.008**	**0.0001**	**0.003**
	T20	**0.001**	0.03	**0.007**	0.04

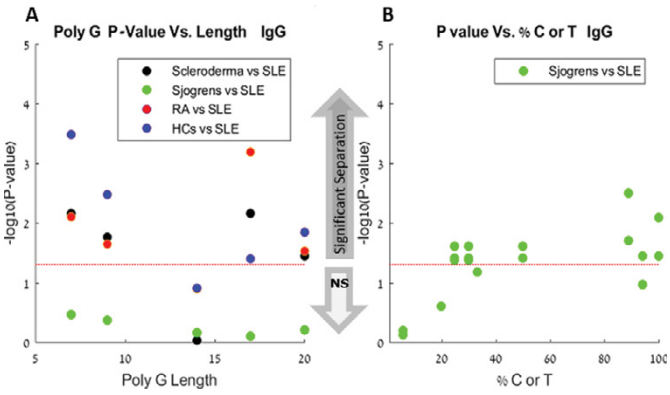


Figure 1

Conclusions:

- Autoantibody binding to oligonucleotides can be used to differentiate SLE from other autoimmune conditions and healthy subjects.
- The structural basis for the differences in binding of antibodies from disease sera to the various oligonucleotides is not yet understood, but may be due to immunologically unique conformations and secondary structures of oligonucleotides of defined length and sequence.
- SSc can be differentiated from SLE based on particular antibody binding to epitopes of oligonucleotides containing C and T.
- RA can be differentiated from SLE more significantly than the other autoimmune conditions.

- The iCHIP® microarray technology is being further developed to generate a clinically useful test to rule in a diagnosis of SLE relative to other related autoimmune diseases.

References:
[1] Putterman et al., J Immunol Methods 2016.
[2] Fattal et al., Immunology, 2010.
[3] Fattal et al., Immunology, 2015.

Acknowledgements: Authors wish to acknowledge Cohen-Gindi O, Lerner M, Tarnapolski O, Blumenstein Y, Javaherian A, Pitts J, Barton M and Wong E. and the Innovative Medicines Initiative Joint Undertaking under grant agreement n° 115308 BIOVACSAFE.

Disclosure of Interest: C. Putterman Consultant for: ImmunArray, A. Gabrielli: None declared, A. Balbir-Gurman: None declared, P. Safer Employee of: ImmunArray, K. Jakobi-Brook: None declared, R. Sorek Employee of: ImmunArray, I. Gluzman Employee of: ImmunArray, S. Wallace Employee of: ImmunArray, I. Cohen Shareholder of: ImmunArray, Consultant for: ImmunArray

DOI: 10.1136/annrheumdis-2017-eular.6129

AB1164 RABIOPRED, AN INNOVATIVE THERAGNOSTIC TOOL FOR PRECISION MEDICINE IN RHEUMATOID ARTHRITIS PATIENTS

E. Schordan[1], M. Mehdi[1], S. Danilin[1], M. Coq[1], M. Schumacher[1], T. Huizinga[2], H. Firat[1]. *[1]Firalis, Huningue, France; [2]Leiden University Medical Center, Leiden, Netherlands*

Background: Anti-TNF alpha biologicals are an important breakthrough in the treatment of Rheumatoid Arthritis (RA) patients. However, 30–40% of RA patients do not respond to these therapies. Therefore, there is an unmet need for a tool to predict treatment response that would help clinicians choose an optimal treatment for RA patients.

Objectives: Under the framework of Horizone2020 SME Instrument of European Commission, Firalis has identified and developed a panel of 2159 mRNA genes which can predict non-response to anti-TNF alpha therapy using the HTG EdgeSeq platform, an innovative combination of a nuclease protection assay & next generation sequencing (NGS).

Methods: RABIOPRED assay is a proprietary panel of Firalis signatures, which also includes targets selected by the *BTCure consortium*, to predict treatment response of anti-TNF alpha biologicals. In total 2175 targets were selected for the development and 2159 are successfully included in the panel. Each oligonucleotide is a 100-mer comprising a 25-mer "wing" at the 5' end and 3' end, and a 50-mer sequence in between that is complementary to the target mRNA. QC is checked for secondary structure and absence of homology with other sequences. Analytical parameters are assessed and repeatability of the RABIOPRED assay is validated on both Paxgene and purified RNA samples. Sample input is set at 32 µl for Paxgene RNA blood and 25 ng for extracted RNA.

Results: Mean correlation factor for 12 samples on 8 replicates for Paxgene and RNA samples are $R^2>0.97$ and $R^2>0.99$ respectively. First analysis and predictive modelling shows an AUC over 0.95 for the prediction of non-response to anti-TNF alpha. In the present work, we disclose the performance of the CE-IVD RABIOPRED assay based on more than 200 samples obtained from the prospective clinical studies, PRINT and RA-TNF. The algorithm will be further validated within the ongoing RABIOPRED Proof-of-Performance study (ClinicalTrials.gov Identifier: NCT03016260) in 720 patients treated by anti-TNF alpha biologicals (5 originators and 3 biosimilars) launched in December 2016. First version of the CE-IVD RABIOPRED assay will be available during Q2 2017 and open for testing.

Conclusions: We are showing that we can accurately measure mRNA expression with RABIOPRED assay using HTG-EdgeSeq NGS platform. Preliminary performance of the assay shows that it can efficiently predict treatment response to anti-TNF alpha biologicals. The algorithm will be later on validated in a multi-centric proof-of-performance clinical study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6417

AB1165 THE MINIMAL CLINICALLY IMPORTANT DIFFERENCE (MCID) RAISES THE SIGNIFICANCE OF OUTCOME EFFECTS ABOVE THE STATISTICAL LEVEL

F. Angst[1], A. Aeschlimann[1], J. Angst[2]. *[1]Research, Rehabilitation Clinic "REHACLINIC", Bad Zurzach; [2]Psychiatry, Psychotherapy and Psychosomatics, Psychiatric Hospital Burghölzli, University of Zurich, Zurich, Switzerland*

Background: In measurement of outcome effects, the patient's subjective perception to feel a change in health defines clinical effectiveness irrespective of statistical significance. Nevertheless, many – especially pharmacological – studies argue with statistical effects alone.

Objectives: To review, develop, illustrate, and discuss current and proposed new concepts of effect quantification and significance.

Methods: Different methods for determining minimal clinically important differences (MCIDs) were reviewed and further developed focusing on their characteristics and (dis)advantages. The concepts were illustrated by empiric rehabilitation effects (evaluation study) and a randomized controlled trial (investigative study) in knee osteoarthritis.

Results: In controlled studies, empirical score differences between verum and placebo become statistically significant if sample sizes are sufficiently large. For example, a score difference of 5 points (scale 0–100) between the verum and the placebo effect becomes statistically significant, if the sample sizes are $n\geq33$ for each of both groups at a standard deviation=10 of the score differences (baseline to follow-up). MCIDs by contrast, are defined by patients' perceptions, which led to "anchoring" of effects by the "transition" item, where patients rate their change of health between baseline and follow-up in an evaluation study. The MCID for improvement by the "mean change method" is the difference of the mean change experienced by the "slightly better" group minus that of the "almost equal" group. The MCID can be expressed as absolute or relative score, as effects size (ES), standardized response mean (SRM) and standardized mean difference (SMD) (bivariate). It can further be adjusted by multivariate regression modeling. In our example of knee osteoarthritis, the MCID for pain relief was 8.74 score points (scale 0–100), 17.15% of the baseline score, ES=0.407, SRM=0.413, SMD=0.469. This is consistent to the range of 0.30–0.50 for MCIDs reviewed in literature. After adjusting for potential confounders, the MCID was 7.09 score points or an increase of 2.9% per score point to feel better obtained by logistic regression.

Conclusions: Absolute and relative MCIDs are easy to interpret and apply to data of investigative studies. MCIDs expressed as ES/SRM/SMD reduce bias, which mainly results from dependency on the baseline score. Multivariate linear and logistic regression modeling further reduces bias by adjustment for possible confounders and increase validity. Anchor-based methods use clinical/subjective perception to define MCIDs and should be clearly differentiated from distribution-based methods that provide statistical effect significance only.

References:
[1] Angst F, Aeschlimann A, Angst J. The minimal clinically important difference (MCID) raised the significance of outcome effects above the statistical level, with methodological implications for future studies. J Clin Epidemiol 2016;epub 13/12/2016.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1820

AB1166 QUANTUM BLUE® ADALIMUMAB: EVALUATION OF A POINT OF CARE RAPID TEST FOR THERAPEUTIC DRUG MONITORING OF SERUM ADALIMUMAB LEVELS

F.I. Bantleon, S. Kräuchi, T.B. Schuster, M. Schneider, J.M. Weber. *Bühlmann Laboratories Ag, Schoenenbuch, Switzerland*

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease affecting approximately 1% of the population [1]. The pathogenesis of RA involves the overexpression of tumor necrosis factor alpha (TNFα) and other cytokines [2]. Adalimumab (ADA) is a human monoclonal antibody directed against TNFα and is highly effective in the treatment of RA. For efficient treatment trough levels of ADA need to be adjusted within a therapeutic window which is 5 to 10 µg/mL [3]. A rapid test allows faster reporting of trough levels, providing a great advantage over test formats that need samples to be sent to a central or service laboratory. Here we report on the technical performance evaluation of the Quantum Blue® Adalimumab lateral flow test.

Objectives: Development and performance evaluation of a rapid test for the monitoring of ADA trough levels in human serum at the point of care.

Methods: The sandwich lateral flow immunoassay uses a TNFα coated gold label and a highly specific monoclonal antibody immobilized on the test membrane to detect ADA in diluted human serum samples. Sensitivity of the assay was determined by calculating limit of detection (LoD) and limit of quantification (LoQ) according to CLSI EP17-A2 guideline. Moreover, the assay was evaluated regarding cross-reactivity with other therapeutic antibodies targeting TNFα, influence of rheumatoid factors (RF) and high dose hook effect. A method comparison was performed against a commercially available ELISA (RIDASCREEN® ADM Monitoring, R-Biopharm, Germany) to compare the trough level results of 40 patients treated with ADA. All statistical analyses were performed with Analyse-it for Excel.

Results: The Quantum Blue® Adalimumab test allowed analysis of serum samples within 15 minutes. The samples were diluted 1:20 in chase buffer before application onto a test cassette (volume 80 µL). The readout was performed with the Quantum Blue® Reader resulting in adalimumab concentration levels in the lower µg/mL range. The test exhibited a LoD of 0.2 µg/mL and a LoQ of 0.69 µg/mL. No high dose hook effect was detected for samples containing up to 1000 µg/mL ADA. The latter two data sets allowed a measuring range of 1 to 35 µg/mL of ADA in patient samples. Other therapeutic TNFα blockers, like infliximab and golimumab, showed no cross-reactivity with the Quantum Blue® Adalimumab test. RF showed no influence on correct measurement of ADA at all tested concentrations. The method comparison to a well-established commercial ELISA method revealed a slope of 1.12 and a regression coefficient (r^2) of 0.90 (by Passing-Bablok). A Bland-Altman analysis showed a bias of 1.9% confirming the overall excellent correlation of the two methods as well as the accuracy of our newly developed rapid test.

Conclusions: The BÜHLMANN Quantum Blue® Adalimumab assay enables the quantitative determination of ADA trough levels over the clinically relevant range in serum with a time to result of only 15 minutes. The assay exhibits an excellent accuracy and correlation to a well-established laboratory reference

method. Hence, it represents a valuable tool for the clinician to assess the trough levels during ADA treatment follow up at the point of care.

References:
[1] Tayar J.H. Int J Clin Rheumatol (2013);8(2):165.
[2] Smolen J.S. Lancet (2016);Dec 3;388(10061):2763.
[3] Moss A.C. Gastroenterol Report (2015);3(1):63.

Disclosure of Interest: F. Bantleon Employee of: Employee of BÜHLMANN Laboratories AG, S. Kräuchi Employee of: Employee of BÜHLMANN Laboratories AG, T. Schuster Employee of: Employee of BÜHLMANN Laboratories AG, M. Schneider Employee of: Employee of BÜHLMANN Laboratories AG, J. Weber Employee of: Employee of BÜHLMANN Laboratories AG

DOI: 10.1136/annrheumdis-2017-eular.4981

AB1167 AUTOREACTIVE T CELLS TO CITRULLINATED HSP90 IN INTERSTITIAL LUNG DISEASE IN RHEUMATOID ARTHRITIS

J. Chen[1], S. Song[2], Y. Liu[3], D. Liu[4], S. Ge[5], D. Ascherman[6]. *[1]Rheumatology, Xiamen University, Xiamen; [2]Rheumatology, The First Affiliated Hospital of Xiamen University; [3]State Key Laboratory of Molecular Vacinology and Molecular Diagnosis, Xiamen University; [4]Radiology, The First Affiliated Hospital of Xiamen University; [5]State key Laboratary of Melecular Vacinology and Molecular Diagnosis, Xiamen University, Xiamen, China; [6]Rheumatology, University of Miami Miller School of Medicine, Florida, United States*

Background: Previous studies have indicated that anti-citrullinated protein antibody (ACPAs) titers are associated with the presence and severity of interstitial lung disease (ILD) in RA. The lung might be a site of initiation of immunity to citrullinated proteins. Previous studying anti-citrullinated HSP90 (citHSP90β) profiles between bronchial veolarlavage fluid (BALF) and serum indicated the lung plays a direct role in shaping the immune repertoire of RA-ILD.
Objectives: Whether citHSP90β contributes to the initiation or perpetuation of autoimmune interstitial lung abnormalities (ILA) in RA remains to be clarified. To address this issue we investigated the spontaneous T cell responses to the putative autoantigen citrullinated HSP90β in different stages of RA-ILD.
Methods: In RA-no ILD (n=19), indeterminate ILD (ILA1) (n=24), subclinical RA-ILD (ILA 2) (n=20), clinical RA-ILD (ILA3) (n=4) and other connective tissue disease associated ILD (CTD-ILD) (n=14) patients. Cultures derived from whole blood were individually stimulated with HSP90β, citHSP90β, citrullinated BSA, or no antigen. The concentration of 13 cytokines and chemokines in the plasma supernatant were then measured using Luminex xMAP technology.
Results: CitHSP90β induced significantly higher levels of IFN-γ levels in RA-ILD (ILA=2+3) groups compared to the RA-no ILD group (p=0.002), but did not stimulate the production of other cytokines (p>0.05). Furthermore, citHSP90β did not stimulate the production of IFN-γ or other cytokines stimulated those individuals with non-RA CTD-ILD (p=0.1039, IFN-g).
Conclusions: The production of IFN-γ by T cells stimulated with citHSP90b demonstrates a bias toward TH1 immune responses that are likely involved in the pathogenesis of RA-ILD. The presence of autoreactive Th1-like cells in RA patients in conjunction with citrullinated autoantigens may indicate the involvement of this autoantigen in the pathogenesis of RA-ILD. Early targeting of the immune reactions in the lung might therefore be a new approach to modulate disease.

References:
[1] Chen J, Doyle TJ, Liu Y, Aggarwal R, Wang X, Shi Y, et al. Biomarkers of rheumatoid arthritis-associated interstitial lung disease. Arthritis & rheumatology. 2015; 67:28–38.
[2] Harlow L, Rosas IO, Gochuico BR, Mikuls TR, Dellaripa PF, Oddis CV, et al. Identification of citrullinated hsp90 isoforms as novel autoantigens in rheumatoid arthritis-associated interstitial lung disease. Arthritis and rheumatism. 2013; 65:869–79.
[3] Bongartz T, Cantaert T, Atkins SR, Harle P, Myers JL, Turesson C, et al. Citrullination in extra-articular manifestations of rheumatoid arthritis. Rheumatology (Oxford). 2007; 46:70–5.
[4] Nijenhuis S, Zendman AJ, Vossenaar ER, Pruijn GJ, vanVenrooij WJ. Autoantibodies to citrullinated proteins in rheumatoid arthritis: clinical performance and biochemical aspects of an RA-specific marker. Clinica chimica acta; international journal of clinical chemistry. 2004; 350:17–34.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2596

AB1168 TOUCH STUDY: TECHNOLOGY AND OUTCOMES USED IN CLINIC IN A DAY HOSPITAL

L. Cunha-Miranda[1], C. Miguel[1], C. Silva[1], F. Barcelos[1], R. Marques[1], R. Trinca[2], A. Cardoso[3], J. Borges[1], S. Fernandes[1], H. Santos[1], A. Faustino[1]. *[1]Rheumatology; [2]Nurse Day Hospital; [3]Nutrition, Instituto Português de Reumatologia, Lisboa, Portugal*

Background: Patient reported outcomes PRO are a key element in the global evaluation of patients, especially those followed in a day hospital. The use of touchscreen computers is one of the new features in the day hospital of Instituto Português de Reumatologia.
Objectives: to evaluate the transition from paper to touchscreen computers technology of the PRO in use in Reuma.pt
Methods: We considered a step up model of comparison with 2 months intervals one before the use of the touchscreen computers, one two months after the introduction of touchscreen computers and a third after an intermediate evaluation (comparison between interval 0 and 1) of the results.A specific formation to physicians and nurses to be aware of missing data from non-total completion of the questionnaires was introduced between the first and second evaluation. The percentage of questionnaires totally completed by number of patients were obtained for every period and diagnosis
Results: 631 day hospital appointments were evaluated according to diagnosis and interval and the percentage was obtained (Table 1)

Table 1. Results comparing questionnaires by diagnosis and intervals

	Paper interval 0 (Sept –Nov 15)			Interval 1 (Nov 15- Jan 16)			Interval 2 (Jan – Mar 16)		
AS	N	N Quest.	Pct.	N	N Quest.	Pct.	N	N Quest.	Pct.
BASDAI	95	95	100,00%	92	87	94,57%	93	92	98,92%
BASFI	95	94	98,95%	92	89	96,74%	93	92	98,92%
EQ5D	95	91	95,79%	92	85	92,39%	93	88	94,62%
AsQol	95	88	92,63%	92	83	90,22%	93	85	91,40%
SF-36	95	80	84,21%	92	72	78,26%	93	77	82,80%
HADS	95	27	28,42%	92	87	94,57%	93	91	97,85%
FACIT	95	93	97,89%	92	91	98,91%	93	92	98,92%
RA									
HAQ	112	111	99,11%	124	124	100,00%	115	114	99,13%
SF-36	112	96	85,71%	124	101	81,45%	115	98	85,22%
HADS	112	9	8,04%	124	111	89,52%	115	114	99,13%
FACIT	112	108	96,43%	124	122	98,39%	115	114	99,13%
EQ5D	112	105	93,75%	124	119	95,97%	115	113	98,26%

Only HADS had a significative (p<0.000) improvement for every disease, with the use of the touchscreen computers from interval 1 to 2. On our intermediate evaluation comparing paper to tablet we saw a lower percentage of questionnaires fully completed (although not statistical significative) and a formal awareness formation addressing the causes was made with all the physicians and nurses of the day hospital. The PRO from Reuma.pt was not developed for tablets and some issues regarding missing data associated with that was found
Conclusions: The use of technology can contribute for better data in Reuma.pt and other national registries by saving time (medical and nurse) for clinical evaluation, by integrating patients in their evaluations and by cost reduction, and carbon footprint. Issues regarding the adaptability of software to tablet technology have to be addressed to insure an overall improvement.

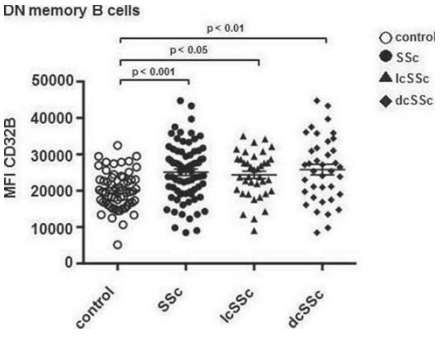
Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6897

AB1169 COMPENSATORY INCREASE IN FCΓRIIB EXPRESSION ON B CELLS IN PATIENTS WITH SYSTEMIC SCLEROSIS

N. Yagi, T. Matsushita, Y. Hamaguchi, K. Takehara. *Department of Dermatology, Faculty of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Kanazawa, Japan*

Background: Systemic sclerosis (SSc) is a systemic autoimmune disease that is characterized by excessive fibrosis and microvascular damage. The contribution of B cells to the pathology of SSc has been mainly recognized as polyclonal B cell activation and autoantibody production. The receptor for the Fc region of IgG (FcγRs) is member of the Ig superfamily, the members of which modulate the activation and inhibition of immune responses. FcγRIIB is the only FcγR that has an inhibitory function. Previous studies revealed that a decrease in the expression of FcγRIIB on B cells induced excessive immune responses and resulted in the development of autoimmunity. However, the expression levels of FcγRIIB on B cells in SSc currently remain unknown.
Objectives: We aimed to clarify how the abnormal activation of B cells involves inhibitory FcγRIIB on B cells in SSc patients.
Methods: Blood samples were collected from 76 SSc patients (38 limited cutaneous SSc [lcSSc], 38 diffuse cutaneous SSc [dcSSc]) and 59 healthy subjects. We evaluated the expression of FcγRIIB, CD80, CD86, and CD95 on B cell subsets. B cells were classified into five subsets depending on their surface molecular expression by flow cytometry: naïve B cells ($CD19^+IgD^+CD27^-$), preswitched memory B cells ($CD19^+IgD^+CD27^+$), double negative (DN) memory B cells ($CD19^+IgD^-CD27^-$), switched memory B cells ($CD19^+IgD^-CD27^{mid}$), and plasmablasts ($CD19^+IgD^-CD27^{high}$). The mRNA expression of FcγRIIB was measured using real-time PCR. We examined the relationship between FcγRIIB expression and clinical features.
Results: The expression of FcγRIIB on SSc naïve B cells and DN memory B cells was significantly stronger than that on the B cells of healthy subjects (Figure 1) (p<0.05 and p<0.001, respectively). FcγRIIB mRNA expression on SSc B cells was also significantly stronger than that on the B cells of healthy subjects (p<0.01). The expression of CD80, CD86, and CD95, activation markers on B cells, was stronger in all 5 B cell subsets, except for CD80 in switched memory B cells and plasmablasts. Patients with the stronger expression of FcγRIIB on DN memory B cells more frequently had interstitial lung disease than those with normal levels (p<0.05). Cyclophosphamide pulse therapy significantly reduced the expression of FcγRIIB on preswitched memory B cells and switched memory B cells (p<0.05 and p<0.05, respectively).



Conclusions: Our results suggest that SSc B cells exhibit compensatory increases in the expression of FcγRIIB in order to suppress the abnormal activation of B cells, and the expression of FcγRIIB may be an indicator of the clinical severity of SSc.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2064

AB1170 PREVALENCE OF ANTI-CARP ANTIBODIES IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: ASSOCIATION WITH CLINICAL, SEROLOGICAL AND HISTOLOGICAL ASPECTS

S. Colafrancesco [1], G. Piacarelli [1], A. Pecani [1], T. Colasanti [1], F. Spinelli [1], C. Alessandri [1], C. Barbati [1], M. Vomero [1], B. Cerbelli [2], R. Priori [1], G. Valesini [1]. *[1] Dipartimento di medicina interna e specialità mediche; [2] Dipartimento di radiologia, Oncologia e Scienze Patologiche, Sapienza Univeristy of Rome, Rome, Italy*

Background: The presence of antibodies against carbamylated peptides (anti-CarP) has been associated with increased disease activity and severe joint damage in rheumatoid arthritis. Our group has demonstrated their presence also in other inflammatory conditions with a high prevalence in Sjogren's Syndrome (SS) (14/45, 31.1%)[1]. There is only one study up to now investigating anti-CarP in SS demonstrating a prevalence of these antibodies in 27% of cases and an association with the presence of germinal centres (GCs)[2]. Thus, these antibodies have been proposed as a new tool for identifying SS patients with a more aggressive disease.
Objectives: To confirm the presence of anti-CarP antibodies in a large mono-centric cohort of patients with SS and investigate their association with clinical, serological and histological features.
Methods: Serum samples from consecutive patients with SS (AECC criteria) were collected and stored at -20°. Anti-CarP antibodies were detected by a modified solid-phase "home-made" ELISA[1]. The mean +3 times SD was used as cut-off. Minor paraffin embedded salivary glands were stained by H&E and IHC using lymphocytes T and B markers [anti-CD3, anti-CD20 (DAKO)]. GCs presence was defined by H&E and confirmed by identification of follicular dendritic cells (anti-CD21, DAKO). Images were analysed as follows: focus score (FS) calculation, mean foci area, presence of segregated foci (SF), GCs and lymphoepithelial lesions (LELs).
Results: Clinical and laboratory features of SS patients are shown in table. Serum anti-CarP were detected in 30/104 patients (28.8%) without association with any clinical or serological feature (Fisher's exact test). Positive patients were more likely to present SF (P=0.024). No association was found with the presence of GCs or LELs. Anti-CarP titre correlated with the FS (P=0.045, r=0.304), the number of foci (P=0.008, r=0.347), mean foci area (P=0.028, r=) and the percentage of SF (P=0.046, r=0.331) (Spearman's test). Prevalence of anti-CarP was higher in patients with arthritis [7/15 (46.6%)] than those without ([23/89 (25.8%)] (p>0.05).

Clinical features	Number (%)
Sex (M/F)	5/99
Age at diagnosis (mean±SD, years)	53±11.7
Xerophthalmia	93/104 (89.4)
Xerostomia	97/104 (93.2)
Glandular swelling	31/104 (29.8)
Arthritis	15/104 (14.4)
Lymphoma	3/104 (2.8)
Laboratory features	
ANA	88/104 (84.6)
Anti-Ro/SSA	54/104 (51.9)
Anti-La/SSB	42/104 (40.3)
Hypergammaglobulinemia	28/104 (26.9)
Rheumatoid factor	38/104 (36.5)
Leucopenia	21/104 (20.1)
Hypocomplementemia	9/104 (8.6)
Monoclonal component	8/104 (7.6)
Cryoglobulinemia	5/104 (4.8)

Mean anti-CarP titre was higher in patients with arthritis compared to those without (322.3±173.8 aU/ml vs 279.5±171.1, P=0.004, respectively).
Conclusions: This is the largest cohort of SS patients screened for anti-CarP so far. Our results show a prevalence of anti-Carp antibodies in agreement with the literature; however, no association was found with any clinical or serological aspect. Anti-CarP do not seem to be associated with histological features predictive of lymphoma, i.e. CGs and LELs. Nonetheless, considering the titre correlation with the FS, mean foci area and percentage of segregation, higher serum levels of anti-CarP may reflect a severe tissue inflammation more prone to form organized infiltrates. This finding, in association with the evidence of higher levels in patients with arthritis, may support the idea that these antibodies are useful to measure the severity of systemic inflammation.
References:
[1] Pecani A et al. Arthritis Res Ther. 2016 25;18(1):276.
[2] Bergum B et al. Ann Rheum Dis. 2016;75(8):1494–500.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5774

AB1171 ARTICULAR AND EXTRA-ARTICULAR DAMAGE INDEX ASSESSMENT IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

S.M. El-Gamal, E.A.K. Elewa, M.M. Ashour. *Rheumatology and Rehabilitation, Zagazig University Hospitals, Zagazig, Egypt*

Background: Juvenile Idiopathic Arthritis is a broad term used to describe several different forms of chronic arthritis in children. Variable assessment tools can be used for assessment of JIA disease activity. JADI is composed of 2 parts (Viola et al., 2005).
Objectives: Assessment of the articular and extraarticular damage index in juvenile idiopathic arthritis patients.
Methods: This study was carried out on 60 JIA patients. Patients who had inflamed synovia related to trauma or malignant disease, septic arthritis, bone diseases, as dysplasia or osteomyelitis were excluded. *Clinical assessment:* sex, age at disease onset, JIA category, educational level, loss of school years and previous use of systemic corticosteroid and second-line drug therapies. *Local examination:* Number of swollen joints, joints with pain on movement/tenderness, joints with limited range of motion, joints with active arthritis were recorded for every patient. *Disease activity:* was measured by using the (JADAS-27). *Functional ability:* was assessed by (CHAQ). *Laboratory assessment:* included ESR and CRP. *Radiographic assessment:* scored according to the adapted Sharp/van der Heijde score. *Damage assessment:* was assessed using the Juvenile Arthritis Damage Index.The (JADI-A) and (JADI-E).
Results: *Patient characteristics:* 6 had systemic onset, 29 had polyarthritis, 14 extended oligoarthritis, 11 had persistant oligoarthritis and none of them had psoriatic arthritis. 38 females and 22 males (56.7%) percent of patients lost some years of education ranging from 0–3 years. Patients in remession were very few 5 patients only. According to the C-HAQ score (13.3%) of patients had no disability (11.7%) mild disability (41.6%) moderate disability and (33.3%)severe disability. 60% patients had articular damage and 35% patients had extraarticular damage. The wrist was the most frequently damaged joint.The growth failure, pubertal delay and leg length discrepancy were the most frequently reported extraarticular items. *Correlation of JADI with other disease variables:* showed that JADI-A is correlated with physician's global assessment, CHAQ, radiological damage.
Conclusions: Ours is the first study that has used JADI to assess outcome in patients with JIA in Egypt. JADI has a good correlation with traditional outcome measures in JIA and may be a good tool to be used in clinical practice and is likely to increase current understanding of the natural history of the disease.
References:
[1] Singh G., Arthreya B.H., Fries J.F., et al. (1994): Measurement of health status in children with juvenile rheumatoid arthritis. Arthritis Rheum.; 37 (12) 1761–769.
[2] Viola S., Felici E., Magni-Manzoni S., et al. (2005): Development and validation of a clinical index for assessment of long term damage in juvenile idiopathic arthritis. Arthritis & Rheumatism ;52(7):2092–2102.
[3] Ravelli A. and Martini A. (2007): Juvenile idiopathic arthritis. Lancet 369:767–78.
[4] Boros C. (2010): Juvenile idiopathic arthritis. Australian family physician ;39(9):630–636.
[5] Tanner JM, Davies PS 1985.Clinical longitudinal standards for height and height velocity for North American children. J Pediatr 107:317–329.
Acknowledgements: First of all, thanks to Gracious Allah. I would like to express my profound gratitude and appreciation to Prof. Dr. Enass Abdel Kader Elewa and to Prof. Dr. Mahmoud Moustafa Ashour for support and supervision.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6707

AB1172 NEUROPATHIC PAIN SCREENING TOOLS IN RHEUMATOID ARTHRITIS: REAL WORLD DATA

T. Martins Rocha[1], S. Pimenta[1], M. Bernardes[1], A. Bernardo[1], M. Barbosa[2], R. Lucas[3], L. Costa[1]. *[1]Rheumatology; [2]Pain Unit, Centro Hospitalar de São João; [3]Clinical Epidemiology, Faculty of Medicine University of Porto (FMUP), Porto, Portugal*

Background: The Leeds Assessment of Neuropathic Symptoms (LANSS) and the painDETECT questionnaire (PDQ) are two validated screening tools for neuropathic pain (NP). Recent evidence reported a low level of agreement between these tests in knee Osteoarthritis. Several studies have recently applied the PDQ in Rheumatoid Arthritis (RA), suggesting a NP component in these patients, although the application and performance comparison with LANSS is yet to be studied.
Objectives: Evaluate PDQ and LANSS performance for NP classification and investigate its optimal cutoff points in a RA cohort.
Methods: Observational, cross-sectional study was designed including RA patients followed at our Rheumatology department. Patients with diagnosed neuropathy or non-RA risk factors for NP were excluded. Selected patients were evaluated in a medical visit where LANSS and PDQ were applied. Agreement between the two questionnaires was evaluated using kappa coefficient analysis. Receiver operating characteristic (ROC) analysis was performed using each tool as gold-standard and cutoff points to optimize agreement were investigated. Non-concordant patients were compared with concordant patients using parametric and non-parametric tests. Significance level was set as <0.05.
Results: 112 RA patients were included, 86 (77%) were females, with a mean (SD) age of 55.1 (10.8) years and median disease duration of 13 years (range: 2–41). 102 (91%) were treated with DMARDs and 42% with a biologic DMARD. 45 (40%) patients had NP applying the LANSS ($\geq$12) and 28% had NP in the PDQ (19 possible and 12 likely; no demographic or clinical significant differences were found between these two groups). 82 (73%) patients had concordant NP classification (59 negative, 23 positive) by the two tests. Concordant group had significantly superior median disease duration and inferior LANSS scores compared to non-concordant group (14 *vs* 12 years and 8 *vs* 13, respectively, $p<0.05$) with no other significant differences found. A moderate agreement (κ=0.41) and linear correlation (r=0.58, $p<0.001$) were observed between the two tests. In the ROC curve analysis, PDQ ($\geq$13) showed an area under the curve (AUC) of 0.80, 95% CI [0.72–0.88] with a sensitivity and specificity of 51% and 88%, respectively, using LANSS as gold standard. LANSS ($\geq$12) had an AUC of 0.80, 95% CI [0.71–0.90] and a sensitivity and specificity of 74% and 73%, respectively, using PDQ as gold standard. After ROC curve analysis, optimal cutoff for PDQ was 10, showing greater sensitivity (69%) but lower specificity (79%) with a slight increase in the agreement between the tests (κ=0.48). For the LANSS, the optimal cutoffs were the previous value or 13 (sensitivity 68% and specificity 78%) with a modest gain in the agreement (κ=0.42). Correction for both cutoff points resulted in a more substantial increase in agreement level (κ=0.51).
Conclusions: In this study, LANSS and PDQ had a moderate level of agreement, possibly because they capture different dimensions of NP. New possible cutoffs were studied to increase agreement between the tests. Further studies with other conditions and a validated gold-standard for NP are needed to confirm this data.
References:
[1] Cohen J. Educ Psychol Meas. 1960;20:37–46.
[2] Moreton B.J. et al Arthritis Care Res. 2015 Apr;67(4):519–28.
[3] AW Christensen et al. Scand J Rheumatol 2016;1–9.
Disclosure of Interest: T. Martins Rocha Grant/research support from: Portuguese Society of Rheumatology/Alfa Wassermann on May 2015, S. Pimenta: None declared, M. Bernardes: None declared, A. Bernardo: None declared, M. Barbosa: None declared, R. Lucas: None declared, L. Costa: None declared
DOI: 10.1136/annrheumdis-2017-eular.5127

AB1173 PHYSICIAN VISUAL ANALOG SCALE ESTIMATES FOR OVERALL GLOBAL ASSESSMENT, INFLAMMATION, DAMAGE, AND DISTRESS TO ASSESS PATIENTS AND SUPPORT CLINICAL DECISIONS IN ROUTINE RHEUMATOLOGY CARE: ANALYSIS OF INTER-RATER RELIABILITY

T. Pincus, I. Castrejon, J. Chua, A. Kugasia, J. Schmukler, S. Weinberg, J.A. Block. *Rheumatology, Rush University Medical Center, Chicago, United States*

Background: A physician global estimate of patient status (DOCGL) was developed to quantify inflammatory activity in rheumatoid arthritis (RA) clinical trials. However, DOCGL may be affected by joint damage and/or distress (in fibromyalgia, depression, etc). One approach to document the possible impact of these problems on DOCGL is to add 3 physician visual analog subscale (VAS) estimates for inflammation, damage, and distress. These subscales have been shown to be useful in patients with diagnoses other than RA (1) but inter-rater reliability has not been analyzed.
Objectives: To analyze inter-rater reliability between senior rheumatologists and trainees on 4 VAS estimates for overall DOCGL, inflammation (DOCINF), damage (DOCDAM) and distress (DOCSTR), in patients with various rheumatic diagnoses.
Methods: Patients seen in routine care were assigned 4 physician VAS estimates for overall DOCGL, and levels of inflammation or reversible symptoms (DOCINF), organ damage or irreversible symptoms (DOCDAM), and distress or symptoms not explained by inflammation or damage (DOCSTR). VAS estimates were assigned independently by a senior rheumatologist and a rheumatology trainee for the same patient at the same visit. Mean differences, correlations, and possible discordance of $\geq$2units/10 between estimates of the senior rheumatologist and the trainee were analyzed.
Results: VAS estimates by the 2 physicians were analyzed in 64 patients with different rheumatic diseases, including osteoarthritis (16%), RA (14%), fibromyalgia (14%), and systemic lupus erythematosus (13%). Mean differences of scores assigned by the senior rheumatologists versus trainees were <0.43/10, less than 5% of the total scales, slightly lower for DOCINF, and slightly higher for the 3 other subscales ($p<0.001$) (Table). Mean estimates of both physicians for damage and distress were higher than for inflammation by 1.1 to 1.6 units (Table). Correlations of all 4 VAS between rheumatologists and trainees were significant ($p<0.001$) (Table). More than 70% of the estimates were concordant for DOCGL (75%), DOCINF (78%), and DOCDAM (70%), while concordance was somewhat lower for DOCSTR (57%) (Table).
Conclusions: Good inter-rater agreement between two physicians is seen for 4 VAS estimates for overall global assessment, inflammation, damage, and distress. Mean scores for damage and distress were higher than for inflammation, indicating the complexity of rheumatology care. Quantitative scores can add to documentation of patient status and to support of clinical decisions for doctors, patients, and payers.
References:
[1] Bull Hosp Jt Dis (2013). 2015 Jul;73(3):178–84.
Disclosure of Interest: T. Pincus Shareholder of: Health Report Services, Inc, I. Castrejon: None declared, J. Chua: None declared, A. Kugasia: None declared, J. Schmukler: None declared, S. Weinberg: None declared, J. Block: None declared
DOI: 10.1136/annrheumdis-2017-eular.3526

AB1174 ORM2 AND APOA2 SERUM LEVELS CAN PREDICT OA PATIENT RESPONSE TO CHONDROITIN SULFATE/GLUCOSAMINE HYDROCHLORIDE: RESULTS FROM THE MOVES STUDY

V. Calamia[1], M. Camacho-Encina[1], L. González-Rodríguez[1], P. Fernández-Puente[1], I. Rego-Pérez[2], M. Herrero[3], H. Martínez[3], C. Ruiz-Romero[1], F.J. Blanco[1]. *[1]Grupo de Proteomica-PBR2-ProteoRed/ISCIII-Servicio de Reumatología; [2]Grupo de Genómica-Servicio de Reumatología., Instituto de Investigación Biomédica de A Coruña (INIBIC), Complexo Hospitalario Universitario de A Coruña (CHUAC), Sergas. Universidade da Coruña (UDC)., la Coruña; [3]Clinical R&D Area, Bioiberica S.A., Barcelona, Spain*

Background: A shotgun proteomic analysis performed on sera from patients enrolled in the Multicentre Osteoarthritis interVEntion trial with Sysadoa (MOVES) led to the discovery of a panel of putative predictive protein biomarkers useful to stratify osteoarthritis (OA) patients into responders and non-responders, either to Chondroitin sulfate/Glucosamine hydrochloride (Droglican®, Bioiberica S.A.,Barcelona,Spain) or Celecoxib.
Objectives: To validate the sensitivity and specificity of a panel of six serum proteins useful to predict the patient response to Droglican treatment, in order to optimize therapeutic outcomes in OA.
Methods: We analyzed the serum levels of a panel of six putative predictive protein biomarkers by enzyme-linked immunosorbent assays (ELISAs): APOA2, APOA4, APOH, C4BPa, ITIH1 and ORM2. All the subjects studied belonged to the MOVES cohort at baseline (Droglican sub-cohort, n=260). Non-parametric and multivariate analysis were performed to test the effects of the clinical variables, including gender, age, BMI, radiologic Kellgren/Lawrence (K/L) grade and WOMAC score at baseline, as well as the serum levels of each of the six mentioned proteins, on the response to Droglican treatment according to the OMERACT-OARSI criteria and the WOMAC pain score (20%, 30%, 50% and 70% reduction) recorded at the end of the trial (after 6 months of treatment).
Results: Non parametric analysis showed decreased serum levels of ORM2

Abstract AB1173 – Table 1. Mean and SD for the four physician estimates according to the rheumatologist (rheum) and the trainee, inter-rater reliability and levels of concordance and discordance for each estimate

VAS (0–10)	Rheum	Trainee	Mean Difference	Pearson r all $p<0.001$	Rheumatologist (Rheum) and trainee discordance groups by 2/10 units, no. (%)		
					Rheum > Trainee	Rheum = Trainee	Rheum < Trainee
Overall DOCGL	3.9 (1.9)	4.0 (2.2)	-0.05 (1.9)	0.61	11 (17%)	48 (75%)	5 (8%)
DOCINF	1.7 (1.6)	1.4 (1.6)	0.28 (1.6)	0.50	8 (13%)	50 (78%)	6 (9%)
DOCDAM	2.8 (2.2)	2.7 (2.2)	0.01 (2.0)	0.61	11 (17%)	45 (70%)	8 (12%)
DOCSTR	3.3 (2.9)	2.9 (2.4)	0.43 (2.8)	0.47	12 (19%)	36 (57%)	15 (24%)

at baseline in responders to Droglican according to the OMERACT-OARSI criteria compared to non-responders (76,11±53,25 vs 104,25±84,93; n=171 *vs* 46; *p*=0,047), meanwhile the values for APOA2 appeared statistically increased in responders with a 50% reduction in WOMAC pain score compared to non-responders (79,95±58,53 vs 66,05±46,49; n=129 *vs* 112; *p*=0,028). Patients with lower levels of ORM2 (median concentration=69,8 ug/mL) and/or higher level of APOA2 (median concentration=63,8 ug/mL) showed a markedly better response to pharmacotherapy. Statistical interactions between ORM2 and APOA2 levels and radiologic K/L grade were also detected (*p*=0,048 and *p*=0,002 respectively). No statistically significant differences were found for the other four proteins.
Conclusions: Our results show that ORM2 and APOA2 levels significantly correlates with patients response to Droglican suggesting the possibility of their use in predictive assays in order to optimize therapeutic outcomes in OA. Validation studies in different cohorts are needed to identify and validate a cut-off point for these biomarkers.
Disclosure of Interest: V. Calamia: None declared, M. Camacho-Encina: None declared, L. González-Rodríguez: None declared, P. Fernández-Puente: None declared, I. Rego-Pérez: None declared, M. Herrero Employee of: Bioiberica S.A., H. Martínez Employee of: Bioiberica S.A., C. Ruiz-Romero: None declared, F. J. Blanco: None declared
DOI: 10.1136/annrheumdis-2017-eular.6224

AB1175 DECREASED AUTOPHAGIC ACTIVITY IN T LYMPHOCYTES FROM PATIENTS WITH NEWLY DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS

X. Luo[1], Y. Liu[2], M. Yang[2]. *[1]Department of Rheumatology; [2]West China Hospital, Sichuan University, Chengdu, China*

Background: Alterations in T-lymphocyte homeostasis have been suggested to play a key role in the pathogenesis of SLE. Autophagy is now emerging as a core player in the development and the functioning of the immune system.
Objectives: we investigated the autophagic behavior of T cells from patients with SLE.
Methods: Thirty patients with SLE and twenty-five healthy subjects matched for gender and age were recruited. The levels of mRNA encoding ATG5, ATG7, Beclin-1 and LC3 was determined by quantitative real-time polymerase chain reaction (qPCR), and evaluate autophagy activity in T cells by flow cytometry. The number of autophagic structures was examined by TEM in T cells from SLE patients and healthy controls.
Results: We documented a decreased of mRNA expression of LC3 and Atg7 in T cells from patients with SLE (t=2.282, P=0.027; t=3.573, P=0.001).A decreased percentage of autophagic cells was comfirmed in T cells from patients with SLE, as compared to healthy donors by flow cytometry (t=2.034, P=0.047).no significant correlations between autophagy levels in T cells and the disease activity of patients were observed ($p>0.05$).
Conclusions: Our results indicate that autophagy activity in T cells from SLE patients is decreased, which may contribute to the development of SLE, and thus that resetting autophagic activity may be an important therapeutic goal in this autoimmune disease.
Acknowledgements: The authors thank Dr Liu Qinsong, and Mr Xia Yanhui for their technical assistance.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2558

AB1176 ANTI-MX1 ANTIBODY: A NEW POTENTIAL BIOMARKER EXPANDING THE CONCEPT OF INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES (IPAF)

Y. Hamano[1], H. Kida[1], A. Murakami[2], M. Yanagawa[3], K. Ueda[3], O. Honda[3], Y. Kato[1], H. Takamatsu[1], N. Tomiyama[3], A. Kumanogoh[1]. *[1]Department of Respiratory Medicine, Allergy and Rheumatic Diseases, Osaka University, Suita; [2]Medical & Biological Laboratories Co., Ltd., Ina Laboratory, Ina; [3]Department of Radiology, Osaka University, Suita, Japan*

Background: "Interstitial pneumonia with autoimmune features (IPAF)" is the updated concept instead of UCTD-ILD or lung-dominant CTD, classifying idiopathic interstitial pneumonias (IIPs) with underlying autoimmune processes by the presence of a combination of features from three domains; clinical, serologic, and morphologic domains. In IIPs, idiopathic non-specific interstitial pneumonia (INSIP) and idiopathic pulmonary fibrosis are often difficult to distinguish without surgical lung biopsy. We discovered autoantibody against myxovirus resistance protein-1 (MX1), type I interferon-inducible protein, as the biomarker specific for INSIP and associated with favorable prognosis [1]. We also reported that some of patients with collagen vascular diseases (CVDs) possess anti-MX1 antibody only when complicated with interstitial lung disease [2].
Objectives: This study was aimed to investigate the association of anti-MX1 antibody positivity with IPAF category in patients with IIPs and their clinical characteristics through a cross-sectional study. We also assessed the potential of anti-MX1 antibody to expand the concept of autoimmunity in IIPs.
Methods: Anti-MX1 antibodies in sera of consecutive Japanese patients with chronic fibrosing IIPs (n=114), who visited the outpatient office of Osaka University Hospital from February to October 2014, were measured using ELISA. IPAF patients were classified according to the IPAF criteria in 2015 ERS/ATS statement. Comparison of the patients' clinical characteristics and high-resolution computed tomography (HRCT) findings evaluated by three thoracic radiologists blinded to the clinical information were statistically analyzed. Serum IFNα was measured using ELISA.
Results: Among 114 patients with IIPs, 20 patients (17.5%) were positive for anti-MX1 antibody and 33 patients (28.9%) were classified as IPAF. When IPAF patients (n=33) were compared with non-IPAF patients (n=81), IPAF was associated with female, higher level of C-reactive protein (CRP), the presence of HRCT findings of "predominantly peribronchovascular distribution" and the absence of two HRCT findings of "honeycombing' and 'traction bronchiectasis". Of 81 non-IPAF patients, 13 patients (16.0%) were anti-MX1 antibody positive. Among them, if anti-MX1 autoantibody were included into the existent serological domain in the IPAF criteria, 8 patients (9.9%) would be classified as IPAF. Anti-MX1 antibody positivity did not correlate with IPAF category. In non-IPAF patients, anti-MX1 antibody-positive patients were associated with female and predominantly smaller 'spared area' when compared to anti-MX1 antibody-negative patients. Serum IFNα concentration was not associated with either anti-MX1 antibody positivity or IPAF category.
Conclusions: A substantial number of patients classified as non-IPAF were positive for anti-MX1 antibody, suggesting that this new autoantibody could have the potential expanding the definition of IPAF. The further studies for the clinical course and drug efficacy of anti-MX1 antibody-positive non-IPAF patients must be explored.
References:
[1] Hamano Y et al. Classification of idiopathic interstitial pneumonias using anti–myxovirus resistance-protein 1 autoantibody. Scientific Reports 2017 (in press).
[2] Ann Rheum Dis 2014;73(Suppl2): 1139.
Disclosure of Interest: Y. Hamano: None declared, H. Kida: None declared, A. Murakami Employee of: Medical & Biological Laboratories Co., Ltd., Ina Laboratory, M. Yanagawa: None declared, K. Ueda: None declared, O. Honda: None declared, Y. Kato: None declared, H. Takamatsu: None declared, N. Tomiyama: None declared, A. Kumanogoh: None declared
DOI: 10.1136/annrheumdis-2017-eular.4280

Rehabilitation

AB1177 THE COMBINATION OF PHYSIOTHERAPY AND BIOLOGICAL THERAPY FOR THE MANAGEMENT OF ANKYLOSING SPONDYLITIS

A. Sehimi, Y. Slimani, N. Messaoud, O. Bensaber. *Physical Medicine and Rehabilitation Department, University Hospital and Medicine Faculty of Sidi Bel Abbes, Sidi Bel Abbes, Algeria*

Background: The management of the ankylosing spondylitis (AS) aims at relieving patients'pain, restoring their joint mobility and preventing structural damage which results in progressive deformity, in order to improve the functional status and quality of life of these patients, using various pharmacological and non-pharmacological means. The importance of the physiotherapy in patients with AS under biological treatment was reported in some studies, but the literature on this topic is still scarce.
Objectives: Report the experience, of our department of Physical and Rehabilitation Medicine, in the management of the AS, especially the effect of the combination of physiotherapy and biological therapy on pain, disease activity, spinal mobility, functional capacity and quality of life.
Methods: Prospective study on 20 patients diagnosed with AS, treated with tumor necrosis factor alpha inhibitors (TNFa inhibitors) and placed under physiotherapy for 3 months. At baseline and at the end of 3 months, we evaluated Bath AS Disease Activity Index (BASDAI), occiput-wall distance, Hirtz index, Schober index, Bath AS Functional Index (BASFI) and Visual Analog Scale (VAS) of patient's quality of life.
Results: The 20 patients (9 females), aged 38.4 years±10.24 [range 19–55], treated with TNFa inhibitors (Etanercept in 35% and Adalimumab in 65%) and included in a physiotherapy program of 3 months (3 sessions/week), comprising muscle relaxation, flexibility exercises for cervical, thoracic and lumbar spine, range of motion exercises of coxofemoral joints, muscular strengthening, straight posture and respiratory exercises.
After 3 months, all outcome parameters showed statistically significant improvements ($P<0,05$), as shown in the folliwing table.

		Paired Diffrences	
		Mean	*P* value
Pair 1	BASDAIbaseline – BASDAImonth3	3,44615	0,000
Pair 2	BASFIbaseline – BASFImonth3	2,9654	0,000
Pair 3	OWIbaseline – OWImonth3	1,7125	0,023
Pair 4	SCHOBERbaseline – SCHOBERmonth3	-1,5667	0,000
Pair 5	HIRTZbaseline – HIRTZmonth3	-0,7273	0,001
Pair 6	VASpatient_baseline - VASpatient_month3	4,0833	0,000

Conclusions: According to our results, the combination of physiotherapy and

biological therapy is an effective mean in increasing functional capacity and joint mobility, decreasing disease activity, improving quality of life for AS patients. Currently available data do not adequately address what role physiotherapy may have on patients with AS receiving biological drugs [1]. There are a few studies evaluating the effects of exercises in patients with AS receiving TNFa inhibitors [2,3].

References:
[1] Elyan M, Khan MA (2008) Does physical therapy still have a place in the treatment of ankylosing spondylitis? Curr Opin Rheumatol 20:282–286.
[2] Dubey SG, Leeder J, Gaffney K (2008) Physical therapy in anti-TNF treated patients with ankylosing spondylitis. Rheumatology (Oxford) 47:1100–1101.
[3] Lubrano E, D'Angelo S, Parsons WJ, Serino F, Tanzillo AT,Olivieri I, Pappone N (2006) Effects of a combination treatment of an intensive rehabilitation program and etanercept in patients with ankylosing spondylitis: a pilot study. J Rheumatol 33:2029–2034.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5453

AB1178 A PROSPECTIVE STUDY ON THE EFFECTS OF 3-MONTH COURSES OF TRADITIONAL PHYSIOTERAPY AND YOGA IN PATIENTS WITH CHRONIC ARTHRITIS AND PRIMARY FIBROMYALGIA

C. Nalli[1], L. Andreoli[1], R. Avanzini[2], P. Tipa[2], M. Zanetti[2], C. Milini[3], S. Olivieri[4], E. Abrami[5], R. Furfari[5], R. Gorla[1], A. Tincani[1]. *[1]Rheumatology and Clinical Immunology Unit, Spedali Civili and University of Brescia; [2]Physical Therapy Student, University of Brescia; [3]Rehabilitation Unit, Spedali Civili; [4]Accademia Essse; [5]Associazione Bresciana Artrite Reumatoide (ABAR) Onlus, Brescia, Italy*

Background: Physical activity is of fundamental importance for people with rheumatic diseases (RD). The traditional approach of Physiotherapy (PT) has been placed side by side with other physical programs, such as Yoga (Y), aimed at reducing chronic pain and improving the quality of life.
Objectives: To evaluate the effects of PT and Y on patients with inflammatory and non-inflammatory RD: Chronic Arthritis (CA) and Primary Fibromyalgia (FM).
Methods: Patients were enrolled in a prospective study including 3 months of PT and 3 months of Y (with a specific focus on the control of breathing - *Ai-jutsu*). Each activity was performed bi-weekly in a dedicated facility. Patients were randomly allocated to either the group starting with PT or that starting with Y. After 3 months they switched to the other activity. At the beginning and at the end of each activity patients underwent a medical assessment of their physical status and were proposed questionnaires: 1) HAQ for disability in everyday life; 2) ZUNG self-rating depression scale; 3) Tampa scale for Kinesiophobia assessing the fear and avoidance of movement. Patients with FM compiled also the FIQ for the impact of FM in everyday life. All patients rated their physical pain by VAS (Visual Analogic Scale) from 0 to 10.
Results: Thirteen patients with CA (77% female, median age 62 years, median disease duration 19 years) and 8 with FM (100% female, 56 years, 9 years) participated in the study. At baseline, there were no differences between CA and FM patients in terms of ZUNG, HAQ and Tampa scores. After 3 and 6 months of activity, all items had a tendency toward improvement, with a statistically significant reduction for VAS in both groups (nearly -30%). By intra-group comparison between the beginning and the end of each activity, we observed that patients with CA had a significant reduction of ZUNG and HAQ scores (50 vs 40.5 and 0.600 vs 0.475, respectively) during PT activity, while FM patients had a trend toward the increase of Tampa score (24.5 vs 34.5). During Y activity, significant reductions were observed in VAS score for CA patients (5 vs 2.5) and in Tampa score for FM patients (34.5 vs 23.5). Overall, all items had a tendency toward improvement for FM patients during Y activity.
Conclusions: This pilot study involving both patients with inflammatory and non-inflammatory RD demonstrated benefit from an integrated program of sequential PT and Y and highlighted differences in patients' needs according to their disease type. Particularly, PT seemed to bring more benefit to CA patients, probably because of the individualized work on joint movement range and muscular strengthening, while FM patients may have had a negative impact by this approach, as seen by the increase in the fear of movement. Conversely, FM patients had a tendency toward improvement during Y activity.
Acknowledgements: We thank the Patients Association (ABAR) for promoting and supporting the activities of this study and Essse Accademia for gently introducing our patients to the world of Yoga.
Disclosure of Interest: C. Nalli: None declared, L. Andreoli: None declared, R. Avanzini: None declared, P. Tipa: None declared, M. Zanetti: None declared, C. Milini: None declared, S. Olivieri Employee of: Accademia Essse, E. Abrami: None declared, R. Furfari: None declared, R. Gorla: None declared, A. Tincani: None declared
DOI: 10.1136/annrheumdis-2017-eular.4376

AB1179 CAN THE PATIENTS WITH TOTAL KNEE ARTHROPLASTY ACHIEVE DISCHARGE CRITERIA FOR KNEE FLEXION

C. Sevinc, A. Arik, S. Onal, V. Bayrakci Tunay. *Hacettepe University, Ankara, Turkey*

Background: Knee range of motion (ROM) at discharge following total knee arthroplasty is used as a clinical indicator of performance. At least 90 degrees of flexion is standard discharge criteria for many hospitals.
Objectives: To investigate whether the discharge criteria is realistic in patients with TKA.
Methods: 13 patients (11=female, 2=male) who underwent unilateral TKA were included in this study. Mean age was 68.46±7.52 years, mean body mass index (BMI) was 30.14±5.6 kg/m^2. Hospitalization duration was recorded. Knee flexion and extension degree were measured actively with goniometer during heel sliding on discharge day. Oxford Knee Score (OKS) was used to evaluate physical function and pain before surgery. Overall scores ranges from 0 (worst) to 48 (best). Descriptive statistics were used to analyse the data using SPSS v22.
Results: Hospitalization duration was 5.07±1.25 days. Knee flexion degree and knee extension limitation were found 79.15±20.84° and 12.92±7.31°, respectively. Oxford Knee Score was calculated 19±8.30 point. Patients' results were given at Table 1.

Table 1. Patients' results

Patients	Knee flexion degree (°)	Extension limitation (°)	Oxford Knee Score
1	65	11	28
2	98	18	33
3	94	12	15
4	88	10	17
5	100	24	22
6	36	24	14
7	86	12	15
8	70	15	17
9	90	2	12
10	80	10	36
11	42	10	12
12	80	20	10
13	100	0	16

Conclusions: Patients have noticeable extension limitations at discharge. It should follow in the upcoming days. Nearly half of the patients flexed their knee less than expected. Due to the fact that discharge criteria for knee flexion is unrealistic. It should be investigate whether patients with less knee flexion degree can gain function as patients with more knee flexion degree.

References:
[1] Husted, Henrik, et al. Traditions and myths in hip and knee arthroplasty: A narrative review. Acta orthopaedica 85.6 (2014): 548–555.
[2] Naylor, Justine M., et al. Is discharge knee range of motion a useful and relevant clinical indicator after total knee replacement? Part 1. Journal of evaluation in clinical practice 18.3 (2012): 644–651.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6397

AB1180 THE INTENSIVE EXERCISE PROGRAMME FOR NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS AND FOR ANKYLOSING SPONDYLITIS MAY IMPROVED QUALITY OF LIFE AND DISEASE ACTIVITY

M. Husakova[1], K. Pavelka[1], M. Spiritovic[1,2], A. Levitova[1,2]. *[1]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague 2; [2]Charles University, Faculty of Physical Education and Sport, Prague, Czech Republic*

Background: The therapy for axial spondyloarthritis (axSpA) is complex. Although anti-inflammatory medication is necessary for axSpA treament, the exercise therapy is required to maintain mobility. The limited data are available to evaluate the effect of exercise therapy on quality of life in axSpA, particularly in patients with the non-radiographic form of the disease (nr-axSpA).
Objectives: To investigated the quality of life in axSpA subgroups, nr-axSpA and Ankylosing spondylitis (AS) in response to intensive rehabilitation programme
Methods: 46 patients with axSpA characterised according to criteria of Assessment of SpondyloArthritis international Society (ASAS) as nr-axSpA (n=23) and AS (n=23) with stable disease and treatment underwent 24 weeks long intervention. The intervention consisted in twice a week outpatient group physiotherapy as exercise units of 60 minutes and a daily home-based exercise programme. All outcomes, disease activity (Bath AS Disease Activity Index, BASDAI and AS Disease Activity Index, ASDAS-CRP) and quality of life (AS quality of life, ASQoL and European quality of life, EurQoL) as well as patients self-reported outcomes such as "patients global assessment" and "pain assessment" were measured at baseline and at the end of exercise program.
Results: Altogether, 41 axSpA patients (AS, n=22 and nr-axSpA, n=19) finished complete six months programme. The disease activity was improved in all axSpA patients (ASDAS-CRP 2.08±0.12 to 1.83±0.11, $p<0.01$), particularly in nr-axSpA subgroup, ASDAS-CRP (1.98±0.19 to 1.71±0.15, $p<0.05$). There were no differences in the changes in ASDAS-CRP and BASDAI over the exercise training between groups (data not shown). After exercise therapy, positive changes of "Patients global assessment", were evaluated by patients of both subgroups, nr-ax-SpA (33.42±5.13 to 23.68±4.11, $p<0.01$) and AS (35.22±3.94 to 25.2±2.92, $p<0.01$). The "assessment of pain during the last 7 days", however, was improved only by patients in the nr-axSpA subgroup (34.74±5.88 vs. 21.05±4.71, $p<0.05$). The quality of life, ASQoL was not changed after rehabilitation programme.

The EurQoL was changed in all axSpA (0.74±0.21 to 0.77±0.18 $p<0.05$), but significantly was improved only in nr-axSpA subgroup (0.72±0.23 to 0.78±0.18, $p<0.01$), not AS. Similarly, the improvement of the assessment of "hodiernal health status" was found after an intervention only in the nr-axSpA subgroup (65.81±21.80 to 78.00±13.77, $p<0.01$).

Conclusions: Our study demonstrated beneficial effect of intensive exercise programme on disease activity and patients self-reported outcomes in nr-axSpA and AS patients. The patients suffering from nr-axSpA can profit at least similarly from the rehabilitation care as those with radiographic form. The exercise programme should be recommended for both subtypes of axSpA.

References:

[1] Millner JR, et al. Exercise for ankylosing spondylitis: an evidence-based consensus statement. Semin Arthritis Rheum. 2016;45:411–27. doi: 10.1016/j.semarthrit.2015.08.003.

Acknowledgements: This study has been supported by the Project for Conceptual development for institution of Ministry of Health Czech Republic - Institute of Rheumatology (number 023728), by SVV for FTVS UK (number 2016–260346), GAUK (number 214615) and PRVOUK (number P38).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2589

AB1181 LOCAL STEIOD AND INSULIN INJECTION IN MANAGEMENT OF CARPAL TUNNEL SYNDROME; A COMPARATIVE STUDY

M.H. Abu-Zaid, S. El morsy, S.A. Hablas. *Rheumatology and Rehabilitation, Faculty of Medicine Tanta University Egypt, Tanta, Egypt*

Background: Carpal tunnel syndrome (CTS) is the most common focal nerve entrapment; local corticosteroid (CS) injection has been widely used to treat CTS. Recently; Local insulin Injection in CTS has been studied as insulin has anti-inflammatory anti-edematous effects.

Objectives: To compare the effectiveness of local steroid and insulin injections in management of CTS

Methods: Forty patients complaining of mild or moderate idiopathic CTS (diagnosed clinically & electrophysiologically and classified according to American association of neuromuscular diagnostic medicine monograph) divided into 2 equal groups.

Group I received two local injections of 10 IU NPH insulin into the affected carpal tunnel 2 weeks intervals. Group II: received single injection of triamcinolone acetonide (20 mg/0.5 ml) all procedures done after informed consent. Patients with severe or secondary type of CTS were excluded from this study. Evaluation of the patients was done at baseline, 2 and 4 months later clinically by measuring visual analogue scale (VAS), Phallen and compression tests and electrophysiologically by measuring motor and sensory nerve conduction studies of median and ulnar nerves using a standardized technique.

Results: There was significant improvement in all clinical parameters in both groups after 2 and 4 months from injection ($p<0.01$) including VAS, Phallen and compression tests with more improvement was noticed in group I. Also there was significant improvement in electrophysiological parameters such as distal motor latency (DML) and distal sensory velocity of median nerve 2 and 4 months after treatment ($p<0.01$).However the improvement was more in group I but the difference between results in both groups were statistically nonsignificant.

Table 1. clinical and electrophysiological results

	Before injection		After 2 months		After 4 months	
	Group I	Group II	Group I	Group II	Group I	Group II
VAS	7.1±1.03	7.25±1.377	4.05±1.23	5.107±1.57	3.2±1.39	3.75±1.878
Positive Phallentest %	100	95	60	60	30	35
Positive compression test%	100	100	60	65	30	30
DML (ms)	4.61±0.34	4.63±0.569	4.375±0.37	4.405±0.51	4.15±0.14	4.18±0.548
Distal median nerve sensory velocity (m/s)	32.9±5.32	32.8±4.78	36.9±6.21	36.05±5.3	39.9±5.39	39.11±6.146

Conclusions: Local insulin injection is as effective as (or even better than) local steroid injection in management of CTS

References:

[1] Sun Q, Li J, Gao F. New insights into insulin: The anti-inflammatory effect and its clinical relevance. World J Diabetes. 2014 Apr 15; 5(2): 89–96.

[2] Ginanneschi F, Filippou G, Bonifazi M, Frediani B, Rossi A. Effects of Local Corticosteroid Injection on Electrical Properties of Aβ-Fibers in Carpal Tunnel Syndrome. J Mol Neurosci, 2014; 52:525–530.

[3] Ashraf A, Yazdani A, Mirshams S. Evaluation of the effectiveness of local insulin injection in type 2 diabetic patients with CTS. Electromyogr Clin Neurophysiol. 2009 May-Jun;49(4):161–6.

Acknowledgements: Thanks a lot to Dr. Samar Abd Alhamed for her great efforts in completing statistical analysis in this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1215

AB1182 THE ROLE OF VITAMIN D AND EXERCISES IN CORRECTION OF AGE-RELATED SKELETAL MUSCLE CHANGES IN POSTMENOPAUSAL WOMEN

V. Povoroznyuk, N. Dzerovych, N. Balatska, A. Belinska, R. Povoroznyuk. *D.F. Chebotarev Institute of Gerontology Nams Ukraine, Kyiv, Ukraine*

Background: The aim of the study was to evaluate the role of vitamin D and exercises in correction of age-related skeletal muscle changes in postmenopausal women.

Objectives: 38 postmenopausal women aged 53–82 years (mean age – 67.00±7.08 yrs; mean height – 160.31±6.83 cm; mean weight – 63.25±8.59 kg, body mass index – 24.62±3.09 kg/m^2) were examined. All subjects were free of systemic disorders (endocrine, renal, hepatic etc.) and did not take any medications known to affect skeletal and muscle metabolism. The women were divided into the following groups: A – control group (n=10), B – women who took an individually-targeted vitamin D therapy (n=11), C – women who took an individually-targeted vitamin D therapy and OTAGO Exercise Programme (http://www.hfwcny.org/Tools/BroadCaster/Upload/Project13/Docs/Otago_Exercise_Programme.pdf) during 12 months.

Methods: The assessment of the examined women was conducted every 3 months at the medical center. We used the following questionnaires: SARC-F, IADL-questionnaire, frailty scale, Desmond fall risk questionnaire. For evaluation of skeletal muscle function and strength, we assessed the usual gait speed and used hand dynamometry. 25(OH)D total and iPTH levels were measured by electrochemiluminescent method i.e. Elecsys 2010 analytical system (Roche Diagnostics, Germany) and test-systems cobas. The lean mass was measured by the DXA method (Prodigy, GEHC Lunar, Madison, WI, USA). "Statistika 6.0" © StatSoft, Inc. was used for the data processing purposes.

Results: At the baseline, the groups of examined women did not differ in their age, anthropometric characteristics, 25(OH)D values, data of skeletal muscle mass, strength and function. In women of the control group, the mean 25(OH)D level significantly increased after 9 months of observation (9 months – $p=0.03$) purportedly due to the seasonal factors. In women of 2nd and 3rd groups, the 25(OH)D level significantly increased after 3, 6, 9 and 12 months of observations (2nd group: 3 months – $p=0.009$, 6 months – $p=0.007$, 9 months – $p=0.005$, 12 months – $p=0.003$; 3rd group: 3 months – $p<0.001$, 6 months – $p<0.001$, 9 months – $p<0.001$, 12 months – $p<0.001$). The data of SARC-F, IADL-questionnaires did not change during 12 months of observation in women of 1st and 2nd groups; however, in the 3rd group the SARC-F data significantly decreased after 12 months ($p=0,02$) while the IADL data – significantly increased after 9 ($p=0.04$) and 12 months ($p=0.05$). The data of frailty scale and Desmond fall risk questionnaire did not differ in all groups during 12 months. The muscle strength significantly increased after 9 months ($p=0.01$) in women of 3rd group while in women of 1st and 2nd group this parameter did not change. The usual gait speed and lean mass assessed by DXA did not change in all groups during 12 months. The fall frequency in women of 1st group significantly increased after 12 months, in women of 2nd group it did not change while in women of 3rd group the fall frequency significantly decreased.

Conclusions: Using individually-targeted vitamin D therapy and OTAGO Exercise Programme during 12 months significantly improves daily activity, muscle strength and decreases the fall frequency in postmenopausal women.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5898

Education

AB1183 PATIENT'S EDUCATION IN THE ADMINISTRATION OF SUBCUTANEOUS DRUGS IN THE RHEUMATOLOGY DAY-CARE HOSPITAL UNITS

A. Erra, A. Fagil, L. López. *Rheumatology, Hospital San Rafael, Barcelona, Spain*

Background: Rheumatology Day-Care Hospital Unit (DHU) is defined as a hospital care for a few hours with the objective to do diagnosis, clinical trials and/or multiple test, patient education and treatments that cannot be done in the outpatient clinic, but which do not justify the complete stay in the hospital

Objectives: Analyze the number of visits that one patient needs in the Rheumatology-DHU to learn the self-administration of a subcutaneous drug.

To evaluate if there are differences between the numbers of visits made in Rheumatology-DHU for the different drugs, and between the different age groups of the patients.

Methods: All patients who were prescribed a subcutaneous drug (except denosumab) during the period January 2015 - December 2016 were referred to Rheumatology-DHU. The nurse gave instructions, she supervised the patient's learning and she decided if the patients needed a new control in Rheumatology-DHU.

The following data were recorded: sex, age, diagnosis, drug, number of visits each patient made in Rheumatology-DHU, reason for new visit to Rheumatology-DHU in patients who had already been discharged and adherence to treatment.

Results: 101 patients were visited in Rheumatology-DHU (8 were referred twice for education of different drugs). 79 were women (78%) and 22 men (22%). Mean age (MA) of 65 +/- 17 years (SD).

Diagnosis MA/SD	MTX	PHT	GOL	ETA	ADA	CER	ABA	SECU	Total
Rheumatoid arthirits 62±16	30	0	2	4	2	1	2	0	41
Psoriatic arthritis 52±17	9	0	5	1	1	1	0	1	18
Anquilosing spondilytis 48±12	1	0	2	2	3	2	0	0	10
Osteoporosi 79±7	0	40	0	0	0	0	0	0	40
Total (%)	40 (37%)	40 (37%)	9 (8%)	7 (6%)	6 (6%)	4 (3%)	2 (2%)	1 (1%)	109

MTX: methotrexate PTH: teriparatide GOL: golimumab ETA: etanercept ADA: adalimumab CER: certolizumab ABA: abatacept SECU: secukimumab SD: standard deviation.

A total of 238 visits were made in Rheumatology-DHU.
Adherence to treatment was 98.2%.
Six patients (5.5%) required a new referral to Rheumatology-DHU: 1 for poor adherence to treatment (ADA), 3 for skin lesions (2 MTX and 1 GOL), 2 supervise the treatment (1 CER and 1 MTX).
In 9% of the patients, the education was done to a reference person and not to the patient himself.
The number of visits in the Rheumatology-DHU were: 1 in 26 patients (MS of 66 +/- 19.6 years), 2 in 59 patients (MS 65 +/- 18); 3 in 13 patients (MS 64 +/- 13); 4 in 6 patients (MS 67 +/- 14); 5 in 2 patients (MS 68 +/- 17), 6 in 2 patients (MS 70 +/- 22), 9 in 1 patient (47 years).
We analyzed PTH and MTX groups (because they had the highest number of patients) and we observed that in the PTH group 82% required ≤2 visits, 18%> of 2 visits. Patients in MTX group: 77% ≤2 visits and 23%>2 education visits. There weren't significant differences between the two groups (p=0.576).
Conclusions: Adherence to treatment in patients who are referred to Rheumatology-DHU to learn the self-administration of a subcutaneous drug is very high.
The new visits in Rheumatology-DHU for doubts or side effects were few.
Patients on PTH treatment, who were older, didn't require a higher number of visits or more new referrals to Rheumatology-DHU. Therefore, age is not a limiting factor for the right learning of patients.
The patient's education by nurse in Rheumatology-DHU is necessary for the right control of our patients
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3201

AB1184 EDUCATIONAL NEEDS OF PATIENTS WITH RHEUMATIC DISEASES RECEIVING BIOLOGICS

A.T. Kotulska[1], E.J. Kucharz[1], P. Wiland[2], M. Olesinska[3], A. Felis-Giemza[3], M. Kopec-Medrek[3], W. Romanowski[3], L. Szymczak-Bartz[3], M. Tlustochowicz[3], J. Lewandowicz[3], J. Kowalska-Majka[3], J. Bucka[3], M. Majdan[3], Z. Kielbik[3], M. Korkosz[3], A. Bielinska[3], P. Leszczynski[3], K. Pawlak-Bus[3], M. Puszczewicz[3], M. Majewski[3], K. Smolik[3], T. Migas-Kukla[3], M. Sochocka-Bykowska[3], M. Szarecka[3], B. Luberda[3], M. Falenta-Hitnarowicz[3], J. Swikszcz-Gniadek[3], W. Lepiarz-Rusek[3], G. Rozwadowski[3], B. Chara[3], J. Zajdel[3], Z. Zdrojewski[3], I. Rosmus-Kuczia[3] on behalf of Research Group of the Polish Society of Rheumatology. *[1]Internal Medicine and Rheumatology, Medical University of Silesia, Katowice; [2]Rheumatology and Internal Medicine, Medical University of Wroclaw, Wroclaw; [3]Research Group of the Polish Society of Rheumatology, Katowice, Poland*

Background: Biologics are still considered by patients as a new and partially enigmatic tool for management of rheumatic diseases.
Objectives: The study was designed to evaluate educational needs and sources of knowledge in patients with rheumatic diseases treated with biologics.
Methods: Anonymous questionnaires were distributed in 23 Polish rheumatological centers involved in the treatment, 1231 questionnaires were used for analysis. Responses were received from 606 patients with rheumatoid arthritis, 427 with ankylosing spondylitis, 117 psoriatic arthritis, and 62 adult patients with juvenile idiopathic arthritis (in whom administration of the drugs had been introduced before they were 18-year-old), as well as 19 ones receiving the drugs due to other musculoskeletal disorders. The investigated group constituted about one-fifth of all rheumatic patients on biologics in Poland.
Results: Almost all the patients had learnt for the first time on biologics from their rheumatologist (93%). Few only patients had got such data from internet or from other patients. Likewise, most of the patients got majority of educational data on treatment with biologics from rheumatologist who was supervising the therapy (82%). Remaining sources included internet (8%) and other patients (5%). Relative low number of patients was educated by nurses (2%). Most of the patients (87%) were looking for more details on biological treatment. The patients with rheumatic disease lasting less than 10 yrs. were more interested in the management than those suffering longer. Most of the patients (94%) considered their rheumatologist as the main person responsible for their education on biologics. There was no difference between patients with various rheumatic diseases as well as no difference was found between female and male patients. Biological treatment attracted more interest in younger than older patients.
Conclusions: Education is still a challenge in patients receiving biologics. Most of the patients represented traditional attitude to health education, expecting almost all educational data to be provided by their physician. We were surprised that role of the nurses was found to be rather low. An increase in role of nurses seems to be the future aim of the educational efforts in Polish rheumatology.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2999

AB1185 REAL-LIFE EXPERIENCE AND MUTUAL EXPECTATIONS OF PATIENTS AFFECTED WITH CHRONICAL INFLAMMATORY RHEUMATIC DISEASES AND THEIR RELATIVES; CONSEQUENCES IN PATIENT EDUCATION: A QUALITATIVE STUDY BY THE PROXYRIC GROUP OF THE PATIENT EDUCATION DIVISION OF FRENCH RHEUMATIC DISEASE SOCIETY

D. Poivret[1], A. Untas[2], E. Boujut[3], C. Vioulac[2], C. Delannoy[4], L. Carton[5], N. Legoupil[6], G. Hayem[7], S. Pouplin[8], A.-C. Rat[9], J.-S. Giraudet-Le Quintrec[6], C. Beauvais[10]. *[1]Chr Metz Thionville, Metz; [2]Institut psychologie Paris Descartes, Paris; [3]Institut psychopathologie et processus de santé, Versailles; [4]Cabinet Psychologie; [5]AFLAR; [6]Service Rhumatologie A, hôpital Cochin, Paris; [7]Service Rhumatologie, Hôpital Ambroise Paré, Boulogne Billancourt; [8]Service Rhumatologie, CHU, Rouen; [9]Service Rhumatologie, CHU Brabois, Nancy; [10]Service Rhumatologie, CHU Saint Antoine, Paris, France*

Background: Interaction with relatives has a significant role on patients' health, and can also impair relatives'health. Education processes need codification to enrole relatives in the programms.
Objectives: To create a patient education program for relatives and patient affected by rheumatic inflammatory desease
Methods: Individual semi-directed by 2 psychologists interviews, have been performed and their thematic content analysed with the QDA Miner program. A guide had been achieved by rheumatologists, psychologists et patient association representatives. The (patient/relative) dyad, has been first questioned together, and then individually.
Results: 20 patients, average age 59 years (27–79) affected with Rheumatoïd Arhritis (n=13), Spondyloarthritis (n=9) with an average disease duration of 12,8 years (1–39) and one of their relatives (being their spouse in 18 cases) have been recruited in 7 rheumatology departments in France. Common life duration was 27,5 years as an average (1,5–57). About 2/3 of patients and relatives have a common view on: relative's role in bringing an emotional support but needs a knowledge on disease and treatments; emotional distress experienced by both patient and relative; the worrries and reative's feelings of not knowing how to to do; the help brought by the relative in everyday's life and his participation to care management. Only a few relatives talked about concerns, regrets of past life, and burden feeling of patient. Relatives also express unfairness feelings. 2/3 of patients and relatives report will of independence of the patient, who wants to manage alone, and does not express his difficulties. 50% of relatives think they anticipate patient's needs, they are also directly resquested by the patients. On the other side, the patients often report that they watch over relative's health. 50% of patients and relatives mention the idea of complementarity and " team ", but also tensions or conflicts. Patient Education contribution would be sharing and exchanging between them, according to 2/3 of patients and relatives, who therefore would prefer group education (12/20). Relatives however more often mention a common education with patient, and patients prefer a separate education of relative. The main limit to of this study is that participation to study has favored harmoniously functioning dyads, what may explain the weak rate of abandonment feeling.
Conclusions: Expectations on relatives' role seem to be common in terms of practical and emotional support. Relatives sometimes mention the "positivation" of their role, but also emotional distress and helplessness feeling. Patients fear they are a burden and want to be independent. A specific educational management of relatives is more often suggested by patients than by relatives.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1682

AB1186 OPTIMISATION OF RHEUMATOLOGY UNDERGRADUATE TEACHING: SELF-DIRECTED DEVELOPMENT OF POWERPOINT PRESENTATIONS BASED ON THEORETICAL CLINICAL CASES

F.A.H. Cooles[1,2], R.L. Batten[1], J. Stewart[1], D. Coady[1]. *[1]City Hospitals Sunderland NHS Foundation Trust, Sunderland; [2]NIHR Newcastle Biomedical Research Centre based at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University, Newcastle Upon Tyne, United Kingdom*

Background: One element of rheumatology undergraduate teaching in City Hospital Sunderland, UK traditionally involves "paper cases" delivered via small group learning and discussion. Although popular it has had poor feedback from both the students and the tutors at times especially when the tutor to student ratio is high (>1:6). With limited numbers of tutors (Consultant Rheumatologists), this issue was becoming more frequent.
Objectives: We wished to explore alternative yet still interactive methods to highlight key learning points relating to common rheumatological conditions in a 60 minute teaching session and to make this fun and engaging.

Methods: 30 undergraduate medical students (January 2017) were given modified teaching material for a 60 minute teaching session a week later. This material involved a partially populated Microsoft Powerpoint slideshow including prompts about a theoretical patient's clinical case in the notes section. This guided development of a clinical case presentation which covered diverse aspects of clinical care, e.g. imaging, extra-articular disease, drug side effects and disease activity scores. Clinical cases addressed systemic lupus erythematous, early rheumatoid arthritis (RA), ankylosing spondylitis and established RA. Students (groups of 2–3) received one case each were encouraged to use images and online teaching repositories to enhance their presentation. This provided the framework for a 20 minute teaching presentation which was given to their student peers at a formal teaching day 1 week later. A tutor was also present during these sessions (with a ratio of 1:10) to ensure adequate understanding of topics had been achieved and to answer any questions. Feedback was sought from the students and compared with previous "paper case" (non-modified) sessions.
Results: Feedback obtained (n=9) showed 55% of students rated the modified teaching session as "excellent" with the remainder rating it as "good". Free-text comments included "good to have students to do the presentations so they cover relevant points" "very useful to have a quick 20 minute overview of different conditions & preparation was useful" and "lots of learning, interactive". Additional comments included the wish for more time to cover the points in even more depth. Informal feedback from the tutors of these events was also favourable with tutors believing students had a developed a greater depth of understanding. These findings compared favourably with the previous years "paper-case" feedback (March 2016, n=13) where only 23% (n=3) of students had rated the session as "excellent" as well as free text comments emphasising wishes for more time to read through cases and smaller group discussion.
Conclusions: Current "paper based" modalities can easily be utilized and "re-purposed" to optimize both self-directed and formal teaching components of undergraduate teaching. This can promote the understanding of complex rheumatological learning points in a relatively short period of time and allow students exposure to modalities, such as imaging, which may previously be excluded in a traditional "paper case" format.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6451

AB1187 SURVEY ON GENERIC DRUGS (GE) AND BIO-SIMILAR DRUGS (BIO-S) OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA) AND THEIR DOCTORS - COHORT STUDY OF THE JAPANESE CLINICIAN BIOLOGICS RESEARCH GROUP

K. Funahashi[1], T. Yoshitama[2], T. Tetsu Oyama[3], A. Sagawa[3], K. Katayama[3], T. Matsubara[3], N. Nishimoto[3], S. Kiyokawa[3], N. Miyake[3], A. Akihiko Nakamura[3], M. Oribe[3], T. Tomohiko Yoshida[3], T. Mitsuka[3] on behalf of Japanese Clinician Biologics Research Group. *[1]Clinical Research, Matsubara Mayflower Hospital, Kato, Japan; [2]Japanese Clinician Biologics Research Group, Kobe, Andorra; [3]Japanese Clinician Biologics Research Group, Kobe, Japan*

Background: In Japan in 2014 the market share for generic drugs was 50%, lower than that of Western nations, but the reasons why the patients themselves turn down the opportunity to switch to a generic drug when asked at the pharmacy are not clear. In addition, the use of bio-similar drugs became possible in Japan in 2015, but the degree of knowledge that patients have regarding them is unknown.
Objectives: Therefore we carried out a patient survey about generic and bio-similar drugs, and at the same time, we also conducted a questionnaire for doctors who prescribed them, and conducted a comparative study of patient's and doctor's awareness regarding these drugs.
Methods: The survey was carried out amongst 4151 patients being treated at 20 research group member facilities. It was an anonymous written survey. After the section on patient background (age, gender, disease history) was completed, patients were asked their impressions of generic drugs, their attitudes towards changing to a generic, whether or not they had ever experienced an adverse effect with a generic drug, what knowledge they had regarding bio-similar drugs, and if they had any interest in or experience with using bio-similar drugs.We also asked 32 physicians about permissions and restrictions on GE use, negative experience of GE, problems of GE, experience of BIO-S and future plans for use, conditions of BIO-S usage, etc.
Results: The group was 78% female, the majority of whom were in their 60's, and most had disease history of more than 10 years. Those with a good impression of GE drugs comprised 41%, those with a bad impression 9.4%. 34% of patients had switched to GE drugs, those who would not or could not were 24%. Those who reported a bad experience (lessening of effectiveness, or an adverse effect) were 8%.Meanwhile, in GE survey of doctors, about 65% partially restricted the use of GE, and about 70% had experiences of weakening of effects and occurrence of adverse events when using GE. Regarding patient knowledge of BIO-S, 13% knew of them, and 44% replied that they had no interest in them, even after being shown explanatory materials about the drugs. 63% of patients said they would rely on their physicians's judgement regarding choosing BIO-S drugs, with 10% stating they would choose BIO-S based on cost benefits. On the other hand, approximately 40% of physicians have experience using BIO - S, while about 60% have experience explaining them to patients. About 60% replied that they plan to use BIO-Ss to be released in the future but on the condition of regular and detailed provision of safety information.
Conclusions: Due to experience in using GE, physicians wish to receive detailed information on individual drugs, and desire it even more in the case of BIO-S drugs. RA patients with RA have received little information on BIO-S, and this can be thought to be a direct result of lack of information for prescribing physicians.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2288

AB1188 WHAT IS THE VALUE OF RHEUMATOLOGY ON-CALL SERVICE? AN EVALUATION OF ACUTE RHEUMATOLOGY ON-CALL SERVICE IN A TERTIARY CENTRE

L.H. Lee, A. Gupta. *Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom*

Background: Rheumatology is largely an outpatient specialty. Changes in healthcare structure in recent years have seen a trend for increased demand for specialty input in acute inpatient care. However, financial pressures on the other hand have led to calls to curtail specialty on-call service. Service provision apart, "being on-call" has traditionally been seen as an important educational experience, equipping registrars with valuable acute rheumatology skills. Despite all these, there is little published literature evaluating the contribution and workload of Rheumatology on-call service.
Objectives: This study sought to evaluate the contribution of Rheumatology on-call service as well as to assess the spectrum of conditions referred.
Methods: An electronic database was created to record details of on-call referrals received by one Rheumatology specialty registrar in a tertiary hospital. These included relevant clinical details, outcomes of referral and working diagnosis.
Results: A total of 40 referrals were recorded over 9 days in a 5-week period from December 2016 to January 2017. Seventeen referrals were reviewed on the same day by the rheumatology registrar. Referrals from medical wards comprised 10 out of 17 referrals reviewed. Other sources of referrals were Emergency Department, General Practitioners and Rheumatology advice phone line with 4, 2 and 1 referrals respectively.
Of the 17 patients reviewed on-call, 11 referrals (65%) could be classified in the category of "acute hot joint", 2 were in the category of vasculitis and connective tissue disorders, 2 were predominantly mechanical problems, 1 was referred with a painful limb while 1 had an elevated creatine kinase. Thirteen of these 17 patients required an arthrocentesis, 12 of which were either performed or supervised by the rheumatology team. Septic arthritis was diagnosed in only one patient. Three of the 17 patients had musculoskeletal ultrasound scan performed by the rheumatology team on the same day.
Conclusions: Rheumatology on-call service provides a significant contribution to acute care which cannot be substituted by other specialties. It also continues to provide rheumatology trainees with experience in acute rheumatology although it could be argued that the spread of conditions seen were skewed toward acute hot joints and that exposure to connective tissue disorders and vasculitis was limited. The results of this study have important implications for planning and delivery of postgraduate Rheumatology training curriculum and delivery of on-call Rheumatology service.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5537

AB1189 "GO TRANS": OUTCOME OF THE PROGRAM OF WORKSHOPS FOR ADOLESCENTS WITH RHEUMATOLOGICAL DISEASES

M.A. Blázquez[1], A. Boteanu[1], L. León[2], S. Lerma[3], M. Vázquez[1]. *[1]Hospital Universitario Ramón y Cajal; [2]2 Idissc, Hospital Universitario Clínico San Carlos Madrid; [3]Hospital Niño Jesús, Madrid, Spain*

Background: Transition is the process by which a young patient with a chronic disease is able to develop skills and have access to resources to ensure that physical, psychological, educational and vocational needs are covered during the stage from youth to adulthood. According to SERPE and EULAR/PReS recommendations, the goal of transition programs is to improve the support to patients during this process, mainly working in multidisciplinary teams.
Objectives: Our main purpose was to accomplish self-care, illness awareness, stress management and negative emotions workshops focused in improving their life quality.
Methods: Workshops are conducted by a psychologist, a pediatric physiotherapist, two rheumatologists and a rheumatology nurse at our center. It consists of a total of 7 workshops (first six for patients and the last for parents). Five of these workshops are based on HEADSS system (home, education, activities, drugs, sexual activity, and emotions) and the two others are focused on disease and treatment consciousness. Parents signed an informed consent document. Workshops lasted 90 minutes in sessions outside of the consultation hours. At baseline, several questionnaires were completed, VAS pain (parents and patients), VAS general (parents and patients), JAMAR (parents and patients), PedsQL 4.0, those questionnaires were also completed after 3 months together with a satisfaction survey.
Results: A total of 12 patients were included, with ages between 11 to 16 years old, with an average of 14 years old. A total of 10 patients completed 100% of the program (6 girls and 4 boys). 6 patients had AIJ (oligoarticular, enthesitis-related arthritis, psoriatic arthritis), 3 suffered from LES and 1 had Behçet. All patients

were under immunosuppressive therapy and 60% of them received biological treatment. 20% of patients had clinical activity data. The average of global VAS was 12 (0–100) and the average of VAS pain was 0.9 (0–100). The average of initial PEDSQL 4.0 was 80.7 (0–100) and the PEDSQL 4.0 at three months was 74.4. At the end of the workshops, 100% of parents and patients would recommend other patients to attend it, more than 50% of patients think that they would be able to go to medical visits without their parents and 90% of them would take responsibility for their treatments. A 90% of patients think that workshops have helped to improve their relationship with their rheumatologist and 60% of them have improved their knowledge about the disease. Regarding to physical activity leves, 30% of the patients have increased it compared to baseline. More than 50% of parents have observed a positive attitude change towards the disease after the program.

Conclusions: Transition programs are important for the transfer to be effective throughout the involvement of adolescent, who takes responsibility for his/her disease and also to ensure their psychosocial needs are met. Rheumatologists must be ready to cover these needs with the support of other specialists. Our experience with the program was very positive since most of the patients improved their knowledge about the disease and its autonomy concerning their medical consultations and treatments, being very satisfied with the contents of the workshops.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6525

AB1190 BEHAVIOR AND TRENDS IN COLOMBIAN PATIENTS WITH RHEUMATIC DISEASES RELATED TO THE TECHNOLOGICAL TOOLS IN CONSULTATION OF RHEUMATOLOGY

M.C. Latorre [1], A.M. Ocaña [2]. *[1]Reumatologia, Country Medical Center; [2]Electronic Engineering, Octesoft, Bogota, Colombia*

Background: In the last decades the internet has changed the way of communication with patients using email, social media and other technological tools, as a complement to the consultation. The development of websites and electronic history are part of these tools that have come to change communication with the patient.

Objectives: To analyze the behavior and trends of Colombian patients with rheumatic diseases related to use electronic tools.

Methods: We analyzed 425 patients between September 2015 and December 2016, who attended to consultation at Country Medical Center. Everyone was provided the website http://www.dra-mconstanzalatorre-reumatologa.com/. This website was developed by Octesoft (http://www.octesoft.com/), company specialized in development website and software. In this website have general information the clinic, access, schedules, glossary, news, medical information and can request online appointment

Results: We included 425 patients with rheumatic diseases, 85.5% female, with an average age of 52.5 years old. 95% lived in urban areas. 92% had internet access. 80% had smart phone. They were stratified by educational level, finding that 70% had college level. And by age groups it was found that patients between 30 and 50 years old in 72% of cases used the electronic way to request the appointment or ask questions. Patients between 18 to 29 years old prefer social media. Patients over 60 years of age preferred to use the telephone. The reasons for using the online appointment were: easy access at any time 84% tool speed 10%. Difficulty for the use of the telephone at work 2%. Others 4%. When patients communicate via email 90% of the questions are related to requesting the appointment.

During this period the website had 3860 views. With a progressive increase from 60 to 538, with an average of 227, with the highest number of visits between November and December. The patients showed satisfaction with the use of technological tools by 89%.

There is no relationship with the use of technological tools with other factors such as gender, rheumatic disease, other diseases or job.

Conclusions: In this study we find that patients gradually and progressively adopt the use of other tools for communication different from conventional, such as web site or email in the request of their appointments and in the communication with rheumatologist. We found that the main factors for adopting these changes are the group of age, especially between 30 to 50 years old and the level of education, when the level of study is university, tend to use on-line communication. It is important to give different alternatives of communication to patients according to their characteristics.

References:

[1] Bujnowska-Fedak BMC Public Health 2015; 15:194.
[2] González ME, Quesada G, Urrutia I, Gavidia JV. Int J Health Care Quality Assurance. 2006;19(2):146–57.
[3] Khoury,V. Kourilovitch,M. Massardo,L. Clin Rheumatol 2015; 34 (Suppl 1):S45–S49.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6085

AB1191 ANALYSIS OF FACTORS RELATED TO THE LEARNING OF RHEUMATOLOGY BY TRAINING DOCTORS OF OTHER SPECIALTIES

M.A. Belmonte-Serrano [1], P. Tejón-Menendez [2], J.A. Castellano-Cuesta [3], N. Fernandez-Llanio [3], P. Bernabeu [4], V. Jovaní-Casado [5], J. Rosas Gomez-Salazar [6], F. Navarro-Blasco [7], A. Ybañez-Garcia [8], A. Lozano-Saez [9] on behalf of Reumeval working group. *[1]Reumatología; [2]Hospital General de Castellón, Castellón de la Plana; [3]Reumatología, Hospital Arnau de Vilanova, Valencia; [4]Reumatología, Hosp San Juan; [5]Reumatología, Hosp General; [6]Reumatología, Hosp Marina Baixa, Alicante; [7]Reumatología, Hosp General, Elx; [8]Reumatología, Hosp Peset, Valencia; [9]Reumatología, Hospital General, Castellón de la Plana, Spain*

Background: Many doctors in training of other specialities make a monthly rotation in the rheumatology unit, but usually no formal assessment of the skills and knowledge acquired is performed.

Objectives: To know which factors are related to learning of Rheumatology skills by training doctors (MIR) of other specialties rotating in spanish Rheumatology units.

Methods: An online platform for the evaluation of the knowledge of Rheumatology has been developed (REUMEVAL, see www.reumeval.com). It contains a set (DB) of 300 multiple-choice questions developed by staff rheumatologists on 10 topics of general interest. The set questions passed a Delphi round and 15% of them were replaced by more appropriate ones.

Each MIR that goes to perform a rotation in a teaching Rheumatology Unit (REU) is offered to participate with two tests of 30 questions randomly extracted from the DB. The first test is done just arriving at REU, assessing the basic knowledge that was obtained in the university. At the end of the rotation in REU, usually 30 days, a second test is performed, assessing the increase of knowledge achieved.

Results: As of December 2016, 384 tests were carried out by 216 physicians training in 14 hospitals of the Valencian region in Spain Of these, 166 (77%) completed both tests. 74% were in training for family medicine (MFC). The mean score of the 1st test was 5.59 (out of 10 points), and the second test was 6.55 points, with an average increase of scorings of 22.4% ($p<0.001$). Men showed higher scorings than women in their 1st test (5.92 vs 5.56), but the difference was lost in the 2nd test (6.79 vs 6.47). Younger residents (ages 20–30 years) had a 1st higher score than those aged 30–40 or$>$40 years (5.8 vs 5.2 vs 5.1 respectively) but were similar in the 2nd test (6.6 Vs 6.3 vs. 6.8). By nationality, Spaniards had higher initial scores than foreigners (5.78 vs 4.91, $p<0.01$) but there were no differences in the second test (6.55 vs 6.49). For specialties, dermatology, internal medicine and RHB had initial scores higher than MFC (7.3 - 6.1 - 6.3 vs. 5.4), but in the second test there were no significant differences.

Conclusions: The level of knowledge in Rheumatology of the residents who start a training rotation in this specialty is moderate, with an average of 5.59 points out of 10 possible. At the end of the rotation their scores increased an average of 22%, which shows a significant improvement but still not very high. Several factors were related to basic knowledge scores but lost significance in the final test, reflecting appropriate improvements in knowledge in all subgroups.

Acknowledgements: To Fundacion Valenciana de Reumatologia and to MSD laboratories for an unrestricted grant.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4498

AB1192 NATIONAL BAROMETER TO ASSESS THE EMOTIONAL ASPECTS OF PATIENTS WITH RHEUMATOID ARTHRITIS. OPINAR PROJECT

S. Castañeda Sanz [1], M.A. Gonzalez-Gay [2], E.F. Vicente [1], C. Alegre de Miguel [3], M. De la Hera [4], V. Torrente-Segarra [5], L. Merino-Meléndez [6], A. Juan-Mas [7], L. Alcaide [8,9], A.I. Torralba [9], J.L. Baquero [10]. *[1]Rheumatology, Hospital de la Princesa, Madrid; [2]Rheumatology, H. Marques de Valdecilla, Santander; [3]Rheumatology, H U Quirón-Dexeus, Barcelona; [4]Rheumatology, Clínica Mompía, Cantabria; [5]Rheumatology, H U Hospitalet-Moisès Broggi, Barcelona; [6]Rheumatology, H General San Pedro, Logroño; [7]Rheumatology, H U Son Llatzer, Palma de Mallorca; [8]Rheumatology, ConArtritis; [9]Rheumatology, Coordinadora Nacional de Artritis; [10]Scientia Salus, Madrid, Spain*

Background: The WHO defines health as the state of physical, psychic and social well-being. In contrast, patients with rheumatoid arthritis (RA) frequently report that treatment is directed mainly at combating physical affection and hardly anything to emotional and social aspects.

Objectives: To assess the emotional impact and degree of satisfaction with the medical care received in the patient with poor prognosis RA.

Methods: National, structured and anonymous survey of 26 questions conducted between March and July 2016. Responses were counted as percentages or as means/medians of the score given on a Likert scale from 1 to 10 (minimum and maximum, respectively). Analyzes were performed using Microsoft 2012: mean (m), standard deviation (SD), median (M), interquartile range (IQR) and statistical significance of differences (Student *t* test). The study was approved by the National Coordinator ConArtritis and the CEIC of the reference hospital.

Results: The survey was completed by 100 of 122 enrollees, 75 by telephone and 25 via email; 83 women and 17 men, with a mean age of 49.4 years (SD 12.1); from all the Spanish Autonomous Communities. 52% were considered of poor

prognosis (participant's own perception). 66.7% of self-perceived high-activity RA by patients exceeded the physician's impression; and 31.03% of the intermediate-activity. The degree of knowledge and the importance given to certain aspects of the disease in relation to the poor prognosis ranged from 8 to 9/10 in the different items analyzed. The awareness of their seropositivity against FR and ACPA was 77% and 17%, respectively. 63% consider the physical aspect more disabling, but 52% gave more value to feeling good emotionally. The mean treatment score for physical aspects was 7.07 (SD 2.52), whereas for emotional aspects was 3.39 (SD 2.57). 51.9% of self-considered poor prognosis patients believed that biological treatment was delayed and 50% related that to poorer outcome. 97% wanted to participate in the doctor's decisions, but 38% declared they had no choice. There were no statistically significant differences between the prognostic groups.

Conclusions: More than half of the patients self-reported poor prognosis. Two-thirds estimated poorer health status than physicians if their RA was of high activity; 1/3 if it was intermediate. Patients considered all assessed aspects as determinants of poor prognosis (m>8). The degree of knowledge of their condition was high, being lower for joint damage and activity and prognostic markers. The beginning of treatment with biologicals was perceived as delayed in more than half of those who declared themselves with poor prognosis and half of them related it to a worse evolution. A high percentage of patients showed low satisfaction with the emotional attention received. Most claim to be more involved in medical decisions, although more than 1/3 does not seem to be able to do so.

Acknowledgements: Coordinadora Nacional de Artritis (ConArtritis)

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5336

AB1193 DEVELOPING THE KOREAN EDUCATIONAL NEEDS ASSESSMENT TOOL (KOREAN-ENAT) IN RHEUMATOID ARTHRITIS: A CROSS-CULTURAL VALIDATION USING RASCH ANALYSIS

Y.-K. Sung[1], D. Kim[1], S.J. Cha[1], D. Yoo[1], S.-H. Kim[2], M. Ndosi[3], S.-K. Cho[1]. *[1]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul; [2]Department of Measurement and Evaluation of Physical Education, Chungbuk National University, Cheongju, Korea, Republic Of; [3]Centre for Health and Clinical Research, University of the West of England, Bristol, United Kingdom*

Background: The Educational Needs Assessment Tool (ENAT) is a 39-item patient-completed questionnaire designed to help patients identify and prioritize their educational needs. It was originally developed in the UK and validated in 7 rheumatic diseases including rheumatoid arthritis (RA).[1]

Objectives: This study aimed to undertake cross-cultural adaptation and validation of the ENAT in RA for use in Korea.

Methods: The study involved two main phases: (1) Cross-cultural adaptation of the ENAT from English into Korean and (2) validation of the Korean-ENAT. The first phase followed an established process of cross-cultural adaptation of self-report measures.[2] For the second phase, patients with RA completed the Korean-ENAT at the outpatient clinic of a university hospital and Rasch measurement computer program, WINSTEPS, was used to analyze the data. Fit to the model was determined by the observed data Infit and Outfit statistics (≥0.50 and ≤1.50); where a value of 1.00 suggests a perfect fit to the model expectations. The unidimensionality of the scale was determined by item (and person) separation index ≥2.00 and reliability ≥0.80.

Results: An adequate conceptual equivalence was achieved following the adaptation process. A total of 123 patients completed the Korean-ENAT. Their mean ± SD age was 46.7±12.3, disease duration 53.7±71.2 months and the majority (81.3%) were female. Thirty-five of the 39 items displayed good fit to the model. The 4 items deviating from the model had Infit and Outfit >1.50. The item separation index (5.26) and item reliability index (0.97) provided evidence for good reliability of items. All the 7 domains of the Korean-ENAT were found to fit the Rasch model. The internal consistency of the Korean-ENAT was high and unidimensionality was confirmed (Person separation index =3.41 reliability index =0.92; item separation index =16.82 and reliability index =1.00).

Table 1. Fit statistics for the Korean ENAT subscales

	Infit		Outfit		Point-biserical correlation
Subscales	MNSQ	ZSTD	MNSQ	ZSTD	PTMEA CORR.
Pain	1.31	2.30	1.40	2.80	0.75
Movement	1.00	0.10	1.01	0.10	0.85
Feelings	0.77	-1.90	0.80	-1.60	0.84
Disease	1.27	2.00	1.15	1.00	0.84
Treatments	1.30	2.20	1.21	1.40	0.85
Self-help	1.05	0.50	1.08	0.70	0.84
Support	0.75	-2.10	0.75	-2.10	0.83

MNSQ = mean-square; ZSTD = z-standardized; MNSQ between ≥0.50 and ≤1.50 for model fit.

Conclusions: Using a standard process in cross-cultural adaptation, the ENAT was adapted into Korean and Rasch analysis confirmed that the construct validity, reliability, and unidimensionality of the Korean-ENAT. The Korean-ENAT provides valid and reliable estimates of educational needs of people with RA in Korea.

References:

[1] Ndosi M, et al. Validation of the educational needs assessment tool as a generic instrument for rheumatic diseases in seven European countries. Ann Rheum Dis 2014; 73: 2122–9.

[2] Beaton DE, et al. Guidelines for the process of cross-cultural adaptation of self-report measures. Spine 2000; 25: 3186–91.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4549

AB1194 ANTINUCLEAR ANTIBODIES ALGORITHM FOR THE PRIMARY HEALTH CARE PHYSICIANS IN CYPRUS

V. Scoutellas[1], G. Mitis[2], G. Achniotou[3]. *[1]Rheumatology Department; [2]Immunology Department, Nicosia General Hospital; [3]Health Insurance Organization, Nicosia, Cyprus*

Background: due to our daily clinical and laboratory practice, we realized that primary care physicians of Cyprus (public & private sector), as well as other medical specialties, are not familiar with the clinical significance of autoantibodies used to diagnose autoimmune rheumatological diseases. This resulted to an increasing number of orders for autoantibodies, which were irrelevant to the person's condition, leading to a high expenditure for tests not clinically needed, whereas the laboratory was not able to respond to the demand with the available resources (human, hardware, economic).

Objectives: (a) to persuade, through education, all the primary care physicians of Cyprus to order autoantibodies up to the point of the primary healthcare level and (b) to minimize the number of unneeded orders, as well as the expenditure, and save resources. To accomplish this target, we created an algorithm for ordering antinuclear antibodies (ANA). Mainly the primary care physicians should use the algorithm as a protocol.

Methods: we searched the literature to find (a) existing algorithms for ordering the ANA, as well as other autoantibodies that should be performed if ANA is found positive and (b) the relevant scientific evidence to guide primary care physicians while ordering ANA. In addition, we planned educational lectures for all the primary care physicians (public & private sector). Our scope was to develop an algorithm that guides the primary care physician to order antinuclear antibodies only if the person's symptoms are relevant to an autoimmune rheumatological disease.

Results: we found algorithms from different sources (university clinics, scientific societies [medical and laboratory], commercial companies producing autoantibody kits). Most of the algorithms found were focusing on the suspected disease, for which the relevant autoantibodies should be ordered. We established an algorithm targeting the primary care physicians: they should only order antinuclear antibodies if an autoimmune rheumatology disease is suspected; if ANA is negative, then an autoimmune disease does not exist and the test should never be repeated (unless there is an important reason); if ANA is positive, then the person should be sent for a consultation to a rheumatologist, who is responsible to take the medical history, examine clinically the person and decide if there is a need or not to order for any other autoantibodies, if an autoimmune rheumatology condition is still suspected. The developed algorithm was communicated (year 2014) to the primary care physicians through lectures in small teams (it was repeated in seven different teams, and captured almost all). The Cyprus Rheumatology Society acknowledged the algorithm, whereas the Health Insurance Organization, with the Ministry of Health, organized the educational part.

Conclusions: the development and establishment (years 2015–2016) of the algorithm for the ordering of antinuclear antibodies by the primary care physicians, changed their attitude towards ordering nowadays with more scientific and evidenced based criteria. This was seen on the lower numbers of orders of antinuclear antibodies within these two years.

References:

[1] the developed algorithm, with the associated text and lecture (all in pdf format), can be viewed (greek language only) and/or downloaded from http://www.hio.org.cy/gr/kko_ergkon_eksetaseon_pfy.html.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2033

Health Professionals in Rheumatology Abstracts

Poster Presentations

THURSDAY, 15 JUNE 2017

HPR interventions (educational, physical, social and psychological)

THU0720-HPR PHYSICAL ACTIVITY IN PATIENTS WITH INFLAMMATORY ARTHROPATHIES

A. López Esteban, I. Janta, J.C. Nieto Gonzalez, F. García, C. Garaballu, T. del Rio, C. Barbero, C. Gonzalez, J. Lopez Longo, I. Monteagudo. *Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain*

Background: Inflammatory arthropathies are a group of diseases that have common characteristics, like unknown etiology, autoimmune or autoinflammatory pathogenesis, genetic predisposition and chronicity. These affect people of all ages and can cause physical, psychic, and social disability. Physical activity is essential to decrease symptoms of pain, fatigue and weakness, improving joint mobility, increasing muscle mass, flexibility and psychosocial health.
Objectives: To describe the physical activity in patients with inflammatory arthropathies.
Methods: In this transversal, observational study we evaluated all patients with inflammatory arthropathies treated with intravenous biologic therapy in a Day Hospital Unit (DHU) of a tertiary hospital. We collected the following data: demographics, indexes of disease activity according to each disease, fatigue questionnaire (FACIT), health questionnaire SF-12, physical activity questionnaire (IPAQ), and fibromyalgia questionnaire (FIRST). This represents a cohort of patients that initiate an educational program on the importance of physical activity in the management of the disease.
Results: We included 222 patients (60.8% female), with a median age (SD; range) of 56.19 (12.89; 25–82) and a median disease duration (SD) of 16.54 (9.6). Of all included patients, 54.1% had rheumatoid arthritis, 39.2% had spondyloarthropathy and 6.8% has psoriatic arthritis; 26.8% were in remission, 39.2% presented moderate activity disease and 13.5% had high disease activity. Forty five (20.3%) patients had fibromyalgia according to FIRST questionnaire. According to the IPAQ questionnaire, 19.8% performed high physical activity, 24.8% moderate physical activity and 55.4% low physical activity. The FACIT score was significantly greater in patients with low physical activity ($p<0.05$). 73% of patients considered that their diseases affect the performance of physical activity. 67% of the patients had none or very low daily physical activity, 80% would like to do more exercise. Among sports or physical activities performed by the patients, the most common was walking (65%), then swimming (12%), cycling and gym (8%) and running (6%). Of the patients who perform physical activity, 43% practice more than one sport.
In a multivariate regression logistic, only the gender and the age related with the physical activity, and not the disease; males (p=0.024; Exp(B) 2,389; IC 95% 1,124- 5,059) and younger persons (p=0,004; Exp (B) 0,959; IC 95%: 0,943–0,987) performed more physical activity.
Conclusions: Patients with inflammatory joint diseases perform low physical activity. The nurse plays a very important role in educating and informing the patients about their illness, and helping them in changing their lifestyle, encouraging increased physical activity with appropriate programs depending on the alterations that produce each disease, in order to improve their quality of life.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4938

THU0721-HPR MULTIDISCIPLINARY EDUCATIONAL PROGRAM FOR PATIENTS WITH HIP- OR KNEE-OA: RESULTS OF A PILOT STUDY

A. Claassen[1], H. Schers[2], S. Koëter[3], J. Botman[4], W. Rijnen[5], W. Noort-van der Laan[1], C. van den Ende[1] on behalf of projectteam "Towards a regional approach of osteoarthritis". *[1]Rheumatology, Sint Maartenskliniek; [2]Primary and Community Care, Radboud University Medical Center; [3]Orthopaedic Surgery, Canisius Wilhelmina Hospital; [4]Stichting Gezondheidscentrum de Kroonsteen - de Vuursteen; [5]Orthopaedic Surgery, Radboud University Medical Center, Nijmegen, Netherlands*

Background: Providing relevant disease-related and self-management related information helps patients to timely seek contact with care providers and become actively involved in their own care process. A problem recognized in the area of Nijmegen, the Netherlands is the conflicting information about OA which is disseminated by different health professionals and health organizations. Therefore, health professionals from primary care, multiple hospitals and health organisations decided to work together and develop an educational program based on a structured inventory of informational needs and on consensus-based information addressing those needs.
Objectives: To determine preliminary effects of a multidisciplinary patient educational program on health care utilization (primary outcome) and on body mass index (BMI), self-efficacy, knowledge on OA and treatment, illness perceptions, pain and functioning and physical activity.
Methods: A total of 146 participants attended 11 organized courses. The educational program consisted of 2 meetings, provided by a physiotherapist, a general practitioner (GP) and an orthopaedic surgeon or specialized nurse. The program comprised education on OA, treatment options and self-management, tips, practical assignments and aphorisms on OA which are repeated by the different course leaders. At baseline and at 3 months follow-up, the following outcome measures were assessed: contacts with different health care providers in the past 3 months, BMI (kg/m^2), self-efficacy (10–40), knowledge on OA and treatment (0–22), illness perceptions (0–100), pain and functioning (0–100) and physical activity (min/week). Paired-sample t-tests and McNemar's test were used to estimate the preliminary effects of the program on primary and secondary outcomes.
Results: A total of 144 participants agreed to participate in this study, 108 (75%) participants filled out both questionnaires. The mean (SD) age of the participants was 69.1 (10.2) years with 62.5% being female. Fifty-six percent of the participants had experienced their OA symptoms for less than 5 years. We found a significant decrease in proportion of patients who had visited their GP in the past 3 months (40.7% to 25.0%, p-value 0.02). Also, we observed a statistically significant decrease in proportion of patients who visited the physiotherapist in the past 3 months, (36.1% to 25.0%). Illness perceptions changed positively (95% CI: 0.4 – 3.4), and knowledge on OA and treatment options improved (95% CI: -3.0 - -1.6). No changes in pain, functioning and self-efficacy were found. However, a trend towards a decrease in BMI and an increase in physical activity was seen.
Conclusions: Results of this study show that collaborating with multiple health professionals to provide patients with clear information on OA, treatment and self-management options in a multidisciplinary educational program, can result in differences in health care utilization and have positive effects on illness perceptions and knowledge on OA. A randomized controlled trial is needed to confirm these results.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2382

THU0722-HPR THE EFFECTS OF KINESİO TAPING ON PAIN, JOINT RANGE OF MOTION, MUSCLE STRENGTH AND DISABILITY IN IMPINGEMENT SYNDROME

A. Yildiz[1], Y. Buyuktepe[2]. *[1]Physiotherapy and Rehabilitation, Marmara University Health Sciences Faculty; [2]Istanbul Education and Research Hospital, Istanbul, Turkey*

Background: The impingement syndrome is common cause of shoulder pain. Physical therapy includes manual therapy techniques, electrotherapy modalities and exercises in this problem. The Kinesio Taping application is a definitive rehabilitative taping technique that is designed to facilitate body's natural healing process while providing support and stability to muscles and joints without restricting the body's range of motion
Objectives: The purpose of this study was to determine the efficacy of kinesio taping (KT) on subjects' pain, joint range of motion, muscle strength and level of disability in treatment of impingement syndrome (IS).
Methods: The study was conducted patients with IS. The subjects were divided into two groups randomly as general physical therapy applications group (GPTG) and kinesio taping group (KTG). GPTG was treated transcutaneous electrical nerve stimulation (TENS), hotpack and ultrasound for ten session. KTG's therapy was contained shoulder kinesio taping application in addition to TENS, hotpack and ultrasound. KT was applied as "Y strip" to deltoid and supraspinatus muscles and was "I strip" to muscle of teres minor. The groups were evaluated before and after treatment in terms of pain, range of motion (ROM), muscle strength and scores of shoulder disability. Visual analog scale was used to assess of pain (night pain, rest pain, pain with motion and general pain), goniometer measurements was used to assess of shoulder ROM, Shoulder Disability Questionnaire and Disabilities of the Arm Shoulder and Hand were used to assess of shoulder disability.
Results: 54 patients with IS aged 18 to 65 years were recruited to the study. Demographic data were similar in the groups. When compared before and after treatment, the level of pain (night pain, rest pain, pain with motion and pain in functional use) was significantly decreased in both groups ($p<0,05$) (Table 1), also an improvement was seen in muscle strength ($p<0,05$), ROM ($p<0,05$) and in the scores of disability of shoulder ($p<0,05$) in both groups. In terms of overall pain relief the KTG scores better than GPTG. Internal and external rotation muscle

forces increase in the KTG; flexion, extension, internal and external rotation muscle forces increased in the GPTG ($p<0,05$ for all). But there was no significant difference between the two groups.

Table 1. The level of pain in GPTG and KTG

	GPTG (mean ± sd)			KTG (mean ± sd)		
	Before Therapy	After Therapy	p	Before Therapy	After Therapy	p
Night pain severity	6,69±3,4	3,62±2,9	<0,001	5,28±3,18	2,32±2,23	<0,001
Rest pain severity	3,97±3,31	2,45±2,78	0,005	2,96±3,29	1,08±1,75	0,031
Pain severity with motion	8,07±1,81	5,14±2,47	<0,001	7,72±2,03	4,36±2,21	<0,001
Severity of general pain	7,76±4,54	4,66±3,99	<0,001	8,40±3,13	4,8±2,69	0,005

Active internal and external rotation ROM increased in KTG ($p<0,05$). Functionality and disability scores were improved in two groups. It was detected that while there was no difference between the groups in terms of the values of muscle strength, functionality and disability scores.

Conclusions: The kinesiologic band can be used as an supportive therapy method in the early shoulder treatment program because of it provides painless shoulder motion to clinicians. We consider that KT applications in addition to general physical therapy applications may have positive effects in the treatment of impingement syndrome.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4613

THU0723-HPR A PHYSIOTHERAPY-LED IN-PATIENT INTENSIVE REHABILITATION PROGRAMME FOR ANKYLOSING SPONDYLITIS: FOLLOW-UP OUTCOMES

C. Clarke[1], P. Taggart[1], J. Monaghan[1], J. McKnight[2], A. Cairns[2]. *[1]Physiotherapy; [2]Rheumatology, Musgrave Park Hospital, Belfast, United Kingdom*

Background: Physiotherapy and exercise are highly important in the management of Ankylosing Spondylitis (AS). Physiotherapy is delivered to patients with AS in either in-patient or out-patient settings. Knowledge of the effectiveness of an in-patient delivered programme is useful for physiotherapists in assisting patients to achieve their goals.

Objectives: To assess the short-term effectiveness of an intensive rehabilitation programme using BASMI and EASI-QOL outcomes, and long-term patient satisfaction and physical activity behaviour and adherence to exercise plan.

Methods: Thirty-two AS patients (25 males and 7 females) admitted to an in-patient rheumatology ward underwent a 1 to 2-week physiotherapy-led intensive rehabilitation programme and were then discharged with a home exercise programme. Pre/post rehabilitation BASMI scores were available for 26 patients. The primary outcome measure was the proportion of patients achieving an improvement on BASMI scores at discharge. Secondary outcome measures included improvements in physical activity levels and adherence to home exercise plan for longer than 3 months which was obtained via a postal patient satisfaction and physical activity questionnaire achieving a response rate of 50% (n=16).

Results: Improvements in BASMI scores was achieved in 69% of patients (n=18) at the end of the in-patient rehabilitation period. Improvements in EASI-QOL were achieved in 83% of patients (n=15) at the end of the in-patient rehabilitation period. Ninety- four percent of patients (n=15) increased their physical activity levels after discharge, with 81% (n=13) of patients maintaining their home exercise programme for 3 months or more. Thirty-seven percent (n=7) of patients carry out at least 150 minutes of physical activity per week (National Recommended Physical Activity Guidelines is 150 minutes/week of moderate intensity).

Conclusions: This recent audit shows the effectiveness of an intensive physiotherapy-led in-patient rehabilitation programme for Ankylosing Spondylitis improving BASMI scores in the short-term and increasing physical activity behaviour over the long-term. Future work will aim to compare demographics and medical treatment differences between improvers and non-improvers.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3799

THU0724-HPR SELF-MANAGEMENT EXERCISE PROGRAM ASSOCIATED TO SPA THERAPY INCREASED THE PHYSICAL ACTIVITY LEVEL OF PEOPLE WITH SYMPTOMATIC KNEE OSTEOARTHRITIS: A QUASI-RANDOMIZED CONTROLLED TRIAL

C. Gay[1], C. Auclair[2], N. Boisseau[3], L. Gerbaud[4], E. Coudeyre[1]. *[1]Physical and Rehabilitation Medicine Department, Clermont-Ferrand University Hospital, Clermont Auvergne University, INRA, Human Nutrition Unit UMR1019, Clermont Ferrand; [2]Public Health Department, Clermont-Ferrand University Hospital, Clermont Auvergne University, PEPRADE, EA 4681; [3]Laboratory of the Metabolic Adaptations to Exercise under Physiological and Pathological condition (AME2P), Clermont Auvergne University, EA 3533, Clermont-Ferrand; [4]Public Health Department, Clermont-Ferrand University Hospital, Clermont Auvergne University, PEPRADE, EA 4681, Clermont Ferrand, France*

Background: Treating knee osteoarthritis (OA) in the medical phase is today well standardized. Guideline orientated approaches aiming at increasing physical activity (PA), improving pain and disability.

Objectives: To assess effectiveness of self-management exercise program associated to spa therapy at 3 month on the improvement of physical activity (PA) level, disability, pain, anxiety, fears and believes in symptomatic knee osteoarthritis people.

Methods: Prospective, multicentric, quasi-randomized controlled trial with alternate month design method (one month periods). People with symptomatic knee OA people (stage I-IV, Kelgren and Lawrence scale) with low and moderate PA level were included in 3 spa therapy resorts. Intervention group (IG) received 5 self-management exercise sessions (1h30; education, aerobic, strength training, range of motion) + information booklet + 18 sessions (1h) of conventional spa therapy (STC). Control group (CG) received information booklet + 18 sessions of STC. The primary outcome was changes at 3 months in PA level (IPAQ short form score) and secondary outcomes were WOMAC function, pain (VAS), HAD anxiety/depression, KOFBeQ fears and believes changes.

Results: 131 subjects were included. The mean age was 65.6 years [± 6.7]. WOMAC function score was 22.1/68 [±11.3] and pain was 4.6/10 [± 1.9] at inclusion. Both groups significantly increased PA level measured with continuous IPAQ total score (MET-minutes/weeks), with superiority for IG (+77.8%; p=0.0062) than CG (+50.7%; p=0.0099). There was no change in setting time. Disability (-11.3%; p=0.0370) and pain (-15.2%; p=0.0032) also decreased significantly for both groups. Anxiety (-11.6%; p=0.0195) and fears and believes (-18.2%; p=0.0146) decreased significantly only in intervention group. Other data will be presented later.

Conclusions: This study confirms the impact of STC on disability and pain and gives news data's on physical activity level. Self-management exercise program improve anxiety, fears and believes. Complex educational strategies comprising information booklet with or without self-management exercise program can be proposed and adapted to OA phenotypes.

References:

[1] Fernandes, Linda, Kåre B. Hagen, Johannes W. J. Bijlsma, Oyvor Andreassen, Pia Christensen, Philip G. Conaghan, Michael Doherty, et al. EULAR Recommendations for the Non-Pharmacological Core Management of Hip and Knee Osteoarthritis. Annals of the Rheumatic Diseases 72, no. 7 (July 2013): 1125–35.

[2] Gay, C., A. Chabaud, E. Guilley, and E. Coudeyre. Educating Patients about the Benefits of Physical Activity and Exercise for Their Hip and Knee Osteoarthritis. Systematic Literature Review. Annals of Physical and Rehabilitation Medicine 59, no. 3 (June 2016): 174–83.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1929

THU0725-HPR COST EFFECTIVENESS ANALYSIS OF ABATACEPT COMPARED WITH TNF INHIBITORS IN PATIENTS WHO ARE POSITIVE FOR ANTI-CITRULLINATED PROTEIN ANTIBODIES BASED ON RESULTS FROM AN OBSERVATIONAL TRIAL

S. Johal[1], E. Alemao[2]. *[1]PAREXEL International, London, United Kingdom; [2]Bristol-Myers Squibb, Princeton, United States*

Background: Anti-citrullinated protein antibodies (ACPA) are highly specific to RA and patients (pts) who are ACPA positive (+) tend to develop more severe, erosive disease than ACPA-negative pts.[1] In an observational study exploring the status of ACPA on RA treatment response to abatacept (ABA) or a TNF inhibitor (TNFi), mean (SE) changes from baseline in CDAI at 6 months was –8.8 for ABA and –5.6 for TNFi initiators.[2]

Objectives: To evaluate the costs and benefits of treating pts with RA who are ACPA+ with ABA vs TNFi on background MTX.

Methods: An economic analysis was carried out estimating lifetime direct costs and quality-adjusted life years (QALYs) of ACPA+ pts with RA treated with ABA or TNFi from a UK National Health Service (NHS) perspective. QALYs are a measure of disease burden, adjusted to reflect quality of life lived. As data for the economic analysis were derived from a real-world study, an "average" pt was modelled, whose baseline characteristics were based on the observational study. CDAI changes at 6 months for each treatment were converted to HAQ changes, and disease progression was based on HAQ score changes over a lifetime. Continuation of therapy was based on rates from the real-world study. Mean long-term survival on treatment with ABA or TNFi was derived from the literature.[3] In the base case, pts discontinuing ABA or TNFi moved to palliative care (MTX). Direct medical costs and quality of life scores were correlated to HAQ scores.[3,4] Costs included hospitalizations, joint replacements and treatment costs. Estimates of differences in costs and QALYs between ABA and TNFi initiators were used to calculate an incremental cost-effectiveness ratio (ICER; cost per QALY gained). The annual cost of TNFi was calculated as an average of TNFi drugs in the UK (£ 9113). For ABA, an average cost of five biologics was used (£ 9244) to reflect a realistic cost to NHS UK. A sensitivity analysis examined the effect of varying the input parameters of efficacy, cost and utilities on costs and outcomes.

Results: Based on an "average" pt from the observational study, the total estimated QALYs for ABA and TNFi initiators were 6.4 and 6.27, respectively. Total lifetime costs were £ 41,378 and £ 40,627, respectively. The lifetime cost for

ABA initiators was higher than for TNFi initiators due to the higher proportion of pts continuing ABA after 6 months. ABA treatment resulted in lower hospitalization costs. The cost per QALY for ABA (vs TNFi) was £ 8667. An intervention with an ICER of less than £ 30,000 per QALY gained is generally considered to be cost effective in the UK. In a sensitivity analysis, in which the annual cost of TNFi was assumed to be the same as a biosimilar agent (£ 7829), the ICER increased to £ 25,660.

Conclusions: Based on real-world data, abatacept is a cost-effective alternative to TNFi in an ACPA+ pt with RA. The increased treatment costs of abatacept are offset by the gain in benefits (QALYs) from higher CDAI reductions with abatacept.

References:
[1] van der Helm-van Mil AHM, et al. Arthritis Res Ther 2005;7:R949–58.
[2] Harrold LR, et al. Ann Rheum Dis 2016;75(Suppl 2):505–6.
[3] Malottki K, et al. Health Technol Assess 2011;15:1–278.
[4] Stevenson MD, et al. Health Technol Assess 2016;20:1–610.

Disclosure of Interest: S. Johal Consultant for: PAREXEL Access Consulting received a Consultancy fee to support the analysis, Employee of: HERON Commercialization, E. Alemao Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

DOI: 10.1136/annrheumdis-2017-eular.3436

THU0726-HPR WHAT CHARACTERISES PATIENTS REFERRED FOR SURGICAL CONSULTATION DUE TO CARPOMETACARPAL OSTEOARTHRITIS?

E.M.H. Gravas[1], R. Nossum[2], R.E.M. Eide[3], A. Klokkereide[4], K.H. Matre[3], M. Olsen[4], S. Darre[2], O. Andreassen[1], N. Osteras[1], I. Kjeken[1].
[1]Diakonhjemmet Hospital, Oslo; [2]St.Olavs Hospital, Trondheim; [3]Haukeland University Hospital, Bergen; [4]Haugesund Rheumatism Hospital, Haugesund, Norway

Background: Carpometacarpal osteoarthritis (CMC-OA) is a common joint condition, with a prevalence of 13% in people aged 41 to 50 years, increasing to 68% in people between 71 and 80 years. In the absence of disease-modifying interventions, non-pharmacological approaches are considered as core treatments for hand OA, while surgery is recommended for those with severe CMC-OA.

Objectives: To describe function and previous treatment in patients referred for surgical consultation due to CMC-OA.

Methods: Individuals referred for surgical consultation due to their CMC-OA at three Norwegian departments of rheumatology were invited to participate. Those who agreed attended a clinical assessment and reported their symptoms, disability and function using validated outcome measures including the Quick-Dash (0–100, 0=no disability) and the MAPHand (1–4, 1=no limitations).

Results: A total of 180 patients (mean age 63, range: 45 to 82; 79% women) were included. Thirty-six percent were referred for right hand, 43% for left hand, and 21% for bilateral surgery. Concerning previous treatment for hand OA, 21% (78% women) had received hand surgery, 22% (81% women) physical or occupational therapy, and 11% (95% women) had consulted a rheumatologist. Women consistently reported higher pain levels compared to men, had more finger joints with bony enlargements and significantly lower grip and pinch strength in both hands (Table). They also reported significantly more disability and activity limitations at Quick Dash; 38.6 versus 30.4, (p=0.006) and MAPHand; 2.0 versus 1.7 ($p<0.001$), for women and men, respectively. However, for finger range of motion, men had slightly more flexion deficit and less palmar abduction in their left hand compared to women.

Conclusions: Among patients referred for surgical consultation due to CMC-OA, women self-reported lower hand function and scored poorer than men in observer based assessments. Even if conservative treatment is recommended before referral for surgery, only a few participants had received such treatment for their hand OA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3662

Abstract THU0726-HPR – Table 1. Hand function

	Right hand		p-value	Left hand		p-value
	Women	Men		Women	Men	
No. of joints with bony enlargements, mean (SD)	1,9 (2,3)	1,2 (2,9)	0,10	1,6 (2,3)	1,3 (2,8)	0,46
Proportion with normal max grip strength[a], % (SD)	65,7 (27,6)	90,9 (26,1)	<0,001	64,0 (26,3)	83,5 (21,2)	<0,001
Proportion with normal max pinch strength[a], % (SD)	66,2 (28,8)	73,6 (28,3)	<0,001	66,8 (25,8)	71,5 (29,0)	<0,001
Number of painful joints, mean (SD)	4,2 (3,3)	2,0 (2,1)	<0,001	3,8 (3,0)	1,8 (1,7)	<0,001
Pain at rest[b], mean (SD)	2,3 (2,2)	1,7 (1,8)	0,10	2,8 (2,6)	2,3 (2,1)	0,23
Pain following grip strength assessment[b],mean (SD)	2,7 (2,5)	2,4 (2,9)	0,60	2,6 (2,3)	2,5 (2,4)	0,92
Pain following pinch strength assessment[b], mean (SD)	2,9 (2,7)	2,7 (3,0)	0,67	3,1 (2,8)	3,1 (2,7)	0,98
Total flexion deficit (mm), mean (SD)	11,2 (30,5)	8,0 (24,4)	0,56	10,4 (27,8)	10,7 (33,6)	0,96
Palmar abduction thumb[c], mean degrees (SD)	50,9 (11,7)	51,5 (12,5)	0,77	50,0 (11,9)	48,5 (10,6)	0,49
Abduction CMC[c] , mean degrees (SD)	37,9 (9,6)	40,3 (12,0)	0,20	37,9 (9,9)	38,1 (10,6)	0,92

[a]Measured in Newton using the Grippit. [b]Numeric rating scale (NRS): 0–10, 0= no pain. [c]Measured in degrees using the Pollexograph.

THU0727-HPR BLENDED INTERVENTIONS FOR FATIGUE SELF-MANAGEMENT: IS THIS THE WAY PATIENTS AND PROFESSIONALS LIKE TO GO?

C. Bode[1], E. Taal[1], H. Vonkeman[2], F. Ben Allouch[1], K. Hohl[1]. *[1]Psychology, Health & Technology, University Twente; [2]Rheumatology, Medisch Spectrum Twente, Enschede, Netherlands*

Background: Blended care, the integration of online and face-to-face care, promises to combine the best of two worlds.

Objectives: To explore the attitudes and needs concerning blended care of two key stakeholders: health professionals and patients.

Methods: Rheumatologists (8) and specialized nurses (5) were recruited in a Dutch hospital and patients with an inflammatory rheumatic disease (10) were recruited via flyers in hospitals and patient organizations in Germany. A semi-structured interview scheme was used to explore knowledge, experiences, needs and perceived (dis)advantages of a blended care format for fatigue self-management. Transcribed verbal data were coded with hierarchical coding schemes.

Results: Perspective of professionals: Blended care matches needs for psychosocial interventions in medical settings, has a patient-friendly and flexible format, reflects the active role of patients and can easily be imbedded in standard care. Reported barriers were low education and skills in technology use in patients, the lack of proven and safe interventions and costs for development/ implementation. Patient perspective: Patients expected better communication, time saving and improvement of autonomy in self-management. They were concerned about loss of personal contact and in general, patients were very critical regarding online activities, privacy risks and guaranteed quality of eHealth products.

Conclusions: Health professionals and patients differ in their attitudes towards blended care. Professionals are better informed and have a more positive attitude, whereas patients' attitudes towards blended care are mainly driven by their reservations towards the reliability and safety of the internet in general. Results will be discussed on the background of attitudes towards eHealth in different countries.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6838

THU0728-HPR COMPARISON OF THE EFFECTIVENESS OF FUNCTIONAL AND NIGHT SPLINT FOR RHIZARTHROSIS: ONE-YEAR FOLLOW-UP OF A CONTROLLED, RANDOMIZED, BLINDED CLINICAL TRIAL

F.C. Silva, S.M.M. Adolph, R.V.T. da Silva, J. Natour. *Department of rheumatology, Federal university of São Paulo, São Paulo, Brazil*

Background: Rhizarthrosis is an inflammatory degenerative joint disease affecting the trapeziometacarpal joint. The main symptom is pain, leading to difficulty with hand functions and reduced quality of life. Two randomized controlled trials found in the literature reported similar findings in terms of pain reduction and improved hand function with the use of a short orthosis for rhizarthrosis; one of the trials showed the benefits when the device was used for daytime function while the other showed the benefits when the orthosis was used during nighttime rest.

Objectives: To compare the effectiveness of functional (daytime) and night splint (Figure 1) in reducing pain and improving functionality in patients with rhizarthrosis.

Methods: A controlled, randomized, blinded clinical trial with sixty patients diagnosed with rhizarthrosis. The patients were assessed by a blinded assessor at the beginning of the treatment and after 45, 90, 180 and 360 days the following variables were evaluated: pain at the base of the thumb using a a numerical pain scale; thumb range of motion measured using a goniometer; grip strength evaluated by a hydraulic hand dynamometer; pinch strength using the pinch gage; hand dexterity evaluated with the pick-up test; function evaluated by the Brazilian version of the AUSCAN LK 3.01 Hand Osteoarthritis Index, the Cochin Hand Function Scale, the Michigan Hand Outcomes Questionnaire and a Likert-type scale. The Hand Outcomes Questionnaire, Cochin Scale and Michigan Questionnaire were used to assess hand function and patient satisfaction using a Likert scale.

Results: Most of the variables analyzed, including patient characteristics such

as age, gender, disease duration and hand dominance, were homogeneous at the beginning of the study. In both groups there was a reduction in hand pain with time (intragroup analysis). Pain in the functional group, expressed as mean ± standard deviation, was 6.82±1.72 and 4.77±2.45 at the beginning and end of the treatment, respectively, and the corresponding figures for the nighttime group were 7.20±1.63 and 4.83±2.68. The p values for both groups were $p<0.001$. There were no statistically significant differences in the majority of the parameters assessed between the groups, including the outcome pain. Three measures considered to be occasional, presented a significant difference between the groups: right palmar abduction p=0.023 and right tripod pinch strength p=0.006 with better results for the group that used the night splint; and time execution of the pick-up test with eyes closed to the right hand p=0.048 with more representative results for the functional (daytime) splint use.



Figure 1: Splint for rhizarthrosis

Conclusions: There was no statistically significant difference between functional and night splint in terms of pain, function or any of the other parameters assessed in rhizarthrosis patients after one year of treatment.

References:

[1] Carreira ACG, Jones A, Natour J. Assessment of the effectiveness of a functional splint for osteoarthritis of the trapeziometacarpal joint of the dominant hand: a randomized controlled study. J Rehabil Med 2010;42(5): 469– 74;

[2] Rannou F, Dimet J, Boutron I, et al. Splint for Base-of-Thumb Osteoarthritis. A randomized trial. Annals of Internal Medicine 2009;150(10):661–9; osteoarthritis: systematic review and meta-analysis. Disabil. Rehabil, Early Online 2015: 1–19.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5590

THU0729-HPR PATIENTS AND CAREGIVERS PREFERENCES RELATED WITH THE USE OF INFORMATIC TECHNOLOGY TOOLS FOR EDUCATION IN RHEUMATOID ARTHRITIS

S. Henao[1], F. Rodriguez[2], L. Villarreal[3], P. Santos-Moreno[4], M. Cabrera[5], D. Buitrago-Garcia[6], C. Caicedo[7]. *[1]Patient service; [2]Patient Program; [3]Psychology and processes; [4]Rheumatology; [5]Engineer and processes; [6]Epidemiology, Biomab, Center for Rheumatoid Arthritis, Bogota; [7]Public Health, Universidad Nacional de Colombia, Bogota, Colombia*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease of the joints affecting more than 1% of global population, it is a long term condition that causes pain, disability and affects the quality of life (1). It has been demonstrated that patient's involvement with its treatment and disease management can be more effective than information-only given by the physician or a health care professional (2).

Objectives: To describe patient's preferences regarding information technology tools for education and RA management in a specialized center in Bogotá Colombia.

Methods: We conducted a descriptive study where a survey was applied to a group of patients or care-givers attending to a patient-focused symposium in Bogotá Colombia. Descriptive epidemiology was done; percentages and averages were calculated for qualitative variables.

Results: We included 452 participants, 80% were patients and 20% caregivers, only 25% referred to assist to informative activities regarding disease management, 41% reported to have information regarding RA, also between 29% and 45% of patients acknowledged the role of the health-care team in the disease activity management. Regarding technology information tools patients considered that WhatsApp was the most important tool to received messages to disease management (40%) followed by YouTube and websites. 70% reported to have a computer or a mobile phone with internet connection, 60% reported to use Facebook while only 30% reported to use easily websites and twitter.

Conclusions: It is important to know the preferences and access that patients and caregivers have to informatics technology in order to create self-care programs that really are going to be used in this population. This survey is evidence not only to start an educational program in our specialized center but to the health care professionals and stakeholders in Colombia.

References:

[1] Prothero L, Georgopoulou S, de Souza S. Patient involvement in the development of a handbook for moderate rheumatoid arthritis. 2016.

[2] Vermaak V, Briffa NK, Langlands B, Inderjeeth C, McQuade J. Evaluation of a disease specific rheumatoid arthritis self-management education program, a single group repeated measures study. BMC musculoskeletal disorders. 2015;16:214.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5450

THU0730-HPR CONTENT AND SUPERVISION OF GROUP EXERCISE THERAPY (GET) FOR AXIAL SPONDYLOARTHRITIS (AXSPA) IN THE NETHERLANDS; A NATION WIDE SURVEY

F. Van Der Giesen[1,2], S. Van Weely[2], N. Lopuhaa[3], T. Vliet Vlieland[2]. *[1]Rheumatology, Haga Teaching Hospital, The Hague; [2]Orthopedics, Leiden University Medical Center, Leiden; [3]Dutch Arthritis Foundation, Amsterdam, Netherlands*

Background: For axSpA patients exercise therapy is recommended in (inter)national treatment guidelines. Apart from mobility exercises, muscle strengthening and cardio vascular training are recommended therapeutic modalities [1,2]. In the Netherlands 45 therapy groups (land based exercises; 1, hydrotherapy; 13, combination groups; 31) are organized by 17 local patient organizations exclusively for AxSpA patients. It is unclear if the treatment recommendations are followed and what the nature of the supervision in these exercise programs is.

Objectives: To describe the therapeutic modalities used and characteristics of the supervision in GET for patients with axSpA in the Netherlands.

Methods: A questionnaire was sent to the coordinating supervisors of GET from the17 local patient organisations involved in GET for axSpA with questions regarding the frequency and duration of group exercise programs and treatment modalities (mobility, stregthening and/or cardio-vascular exercises) used in land-based and hydrotherapy parts of the programs. In addition the questionnaire included questions regarding the number of supervisors involved in the supervision of GET, their professional background (physical therapist, other), years of experience with GET (<1yr, 1–5 yrs, >5yrs) additional education related to rheumatic diseases (yes/no) and rheumatology network membership (yes/no).

Results: All 17 coordinating supervisors of GET for axSpA returned the questionnaire. All exercise groups were performed once a week with a median (range) duration of 30 minutes (30–60) for the hydrotherapy and 105 minutes (45–180) for the combination therapy groups. Regarding land-based treatment modalities, active joint range of motion exercises and muscle strengthening exercises were used as stated by 15/17 and 14/16 coordinators respectively. In hydrotherapy this was 17/17 both. 13/16 coordinators stated that cardio-vascular training was used in land-based parts and in hydrotherapy parts in 14/17. Only 1/17 coordinator stated that hart rate monitoring (land-based) was used. A total of 64 supervisors were involved in GET for axSpA of whom 54/60 were physical therapists. 35/59 were involved for more than 5 years, 21/55 had post graduate rheumatology education and 10/54 were rheumatology network members.

Conclusions: Mobility and strengthening exercises are used in the majority of GET programs, but hart rate monitoring is almost never used raising questions regarding the intensity of these programs. The duration of exercise sessions showed a wide variety, as did the program composition (water based/land and water based) identifying considerable practice variation. The majority of the supervisors were physical therapists with long standing experience but only a minority had postgraduate rheumatology education. To ensure the quality of GET for patients with axSpA, reducing practice variation is a future challenge. Education of GET supervisors might be important aspects and target of priority.

References:

[1] Van der Heijde D, Ramiro S, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Annals of the rheumatic diseases. 2017.

[2] Dutch Arthritis Association, Guidelines for diagnostics and treatment in axial spondylitis. 2014.

Acknowledgements: This study was funded by the Dutch Arthritis Foundation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4192

THU0731-HPR CAN A THREE WEEKS PROGRAM IN A REHABILITATION CENTER IMPROVE SYMPTOMS AND EXERCISE-FREQUENCY FOR RHEUMATIC PATIENTS?

G. Jarret, A. Orpana. *Skogli Helse- og Rehabiliteringsenter AS, Lillehammer, Norway*

Background: Rehabilitation for people with rheumatic disorders (15% of worldwide population) is a long term project (Stoffer et al. 2015). Rheumatic patients do not exercise as often as recommended (Holm et al. 2015). Intensive multidisciplinary interventions in rehabilitation-centers are in some countries an option – of which there is little effect knowledge. Perhaps data from a quality-management report can shed some preliminary light on this subject.

Objectives: Primarily to observe short and long term effects of a three weeks intensive multidisciplinary program for people with rheumatic disorders, and secondary to see if a correlation can be found between level of training frequency and levels of pain, stiffness, and self rated health.

Methods: 738 patients (age 62.0+11.1, 84% women), followed a three weeks multidisciplinary program of individual and group sessions - with physiotherapy as main focus - during the period of August 2010 to September 2016 at Skogli Health- and Rehabilitation Center, Lillehammer, Norway.
3-month follow-up: N=252 and 12-month follow-up: N=118. Data from self-reported questionnaires at T1-T4 was gathered. Paired sampled T-tests and Pearson product-moment correlation coefficients was used to analyze the data obtained, using IBM SPSS Statistics v.23.
Instruments:

- NRS-11 for pain and stiffness at baseline (T1), at discharge (T2), and at 3- (T3) and 12 months (T4) after discharge.
- Likert scale (1–6) for self-rated level of health at T1, T2, T3 and T4.
- Self-reported level of training frequency at T1, T3 and T4

Results: There was a clear mean improvement ($p<0.0001$) on all factors at T2 of moderate/large effect-size. At T3 there was a mean improvement ($p<0.05$) on all factors, except pain, of small/moderate effect size. There was a mean improvement ($p<0.05$) on self-rated level of health and training frequency at T4 of a small effect size. Worth noting is that the degree of stiffness and pain at T4 is back to T1-level.
There was a correlation ($p<0.05$) between level of training frequency and self-rated level of health (small at T1/T3, medium at T4), but no correlation between level of training frequency and level of pain or stiffness, at any time. This suggests that a higher training frequency is associated with a higher sense of health – regardless of symptom levels.
Conclusions: People with rheumatic disorders seem to have a very positive short term effect on all aspects after a three week intensive multidisciplinary program, but gradually return to pre-rehab levels during the following year – especially regarding symptoms like stiffness and pain. At the same time there seems to be a much slower decline in self-rated level of health – especially for those who regularly exercise. Properly randomized controlled trials are however needed to be able to draw any clear conclusions.
Implications: There might be a need for intensive multidisciplinary programs for rheumatic patients at intervals of less than a year, to be able to better keep the general health and function gained. Another possible implication is to implement a stronger focus on teaching rheumatic patients the necessity for an active lifestyle – including regular exercises – for them to be able to maintain their sense of general health, regardless of symptom levels.
References:
[1] Stoffer MA, Smolen JS, et al. Ann Rheum Dis 2015; 74: 1145–1149.
[2] Holm I, Tveter AT, et al. Physiotherapy 2015; 101 (3): 273–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1258

THU0732-HPR ENHANCED MANAGEMENT OF ANKYLOSING SPONDYLITIES THROUGH GUANGDONG INTERNET HOSPITAL IN CHINA:A RANDOMIZED, CONTROLLED TRIAL

H. Zhengping[1], L. Tianwang[1], H. Zhixiang[1], P. Xia[1], Z. Lihua[2], H. Yukai[1], Y. Xiaoyan[1], L. Meng[1], H. Xuechan[1], W. Yunqing[1], L. Xumian[1], T. Yao[1].
[1]Department of Rheumatology and Clinical Immunology; [2]Nursing Department, Guangdong NO.2 Provincial People's Hospital, Guangzhou, China

Background: Ankylosing Spondylitis (AS) is a kind of common chronic disease.Guangdong Internet Hospital is China's first officially recognized network hospital and the government encourage development of telemedicine in the country. Increasing research evidences support the efficacy of telemedicine in management of chronic diseases. However, There are still few researches about AS management by using telemedicine.
Objectives: We here conducted a 6-month randomized, controlled trial to evaluate the feasibility and efficacy of Guangdong Internet Hospital in AS management.
Methods: A total of 102 AS patients were randomly divided into two groups: standard care (ST) group or standard care with Network-Enhanced Management (ST-NEM) group. NEM enhanced disease management including cognition of the disease, medication monitoring, behavioral management and psychotherapy. Individuals were assessed by using several tools at baseline and 6 months later: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for the disease acticity, Ankylosing Spondylitis Functional Index (BASFI) for the functional limitation, the Zung Self-Rating Anxiety Scale (SAS) and the Zung Self-Rating Depression Scale Zung (SDS) for the psychological status, Pittsburgh sleep quality index (PSQI) for the sleep quality, and SF-36 for the general health status. In addition, we made a satisfaction survey about the network platform in the management of the disease. Both group received the same medications during the period. There were no significant differences in baseline demographic and clinical characteristics between the two groups.
Results: After 6 month, 91 patients completed the trial. BASFI (1.75±0.73 vs. 2.04±0.69, P=0.026), SAS (28.12±3.22 vs. 39.56±4.61, P=0.022), SDS (26.51±6.34 vs. 32.12±6.34, P=0.031), PSQI (3.31±0.46 vs. 4.79±0.54, P=0.019) and SF-36 (SF-36M: 54.24±9.66 vs. 61.41±8.56, P=0.014; SF-36P: 63.42±11.08 vs. 68.98±10.46, P=0.032) were significantly lower in ST-NEM group than ST group after 6 months. There was no significant difference in BASDAI (2.66±0.91 vs. 2.75±0.75, P=0.068) between the two groups. Individuals assigned to the ST-NEM group reported significantly improvement in functional limitation, psychological status, sleep quality and the general health status. In addition, Guangdong Internet Hospital were widely accepted by the AS patients in disease management.
Conclusions: Guangdong Internet Hospital showed potential feasibility and efficacy in AS management. AS patients may receive disease management through the netwrok platform conveniently and effectively, especially those in the remote areas of the country. The results may be important for clinical practice in disease management of AS by using telemedicine.
References:
[1] Sinclair. 2015. Effectiveness and User Acceptance of Online Chronic Disease Management Interventions in Rural and Remote Settings: Systematic Review and Narrative Synthesis. Clinical Medicine Insights: Therapeutics: 43.
[2] Tu J, Wang C, Wu S. 2015. The internet hospital: an emerging innovation in China. The Lancet Global Health 3: e445-e6.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2963

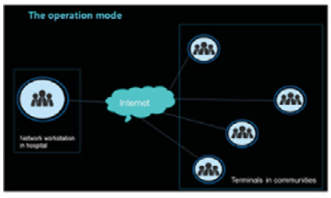


Figure.1 The operation mode of Guangdong Internet Hospital

Table 1.Baseline Demographic and Clinical Characteristics of AS patients

Characteristic	ST-NEM (n=47)	ST (n=44)	Total(n=91)
Male(n)	43	41	84
Age(y)			
Mean(SD)	27.69(5.31)	28.53(5.72)	28.10(5.49)
Disease duration(y)			
Mean(SD)	4.16(6.91)	4.58(7.08)	4.36(6.94)
B27positive (n)	41	39	80(88.9%)
Education Status(n)			
Junior high school	3	5	8(8.8%)
Senior high school	23	22	45(49.5%)
College Graduate	19	15	34(37.4%)
Post Graduate	2	2	4(4.4%)

n:number of cases, y:years, %:percentage, SD:standard deviation

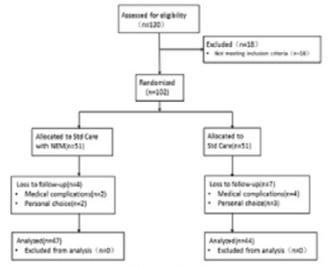


Figure 2.CORT Study Flow diagram

Table 2. The primary outcomes in two groups at baseline and 6 months later

Assessme	Baseline			6 months later		
nt Tool	ST-NEM	ST	P value	ST-NEM	ST	P value
BASDAI	5.22± 1.26	5.41 ± 1.58	0.32	2.66± 0.91	2.75± 0.75	0.068
BASFI	4.71± 1.49	4.86 ± 1.37	0.20	2.75± 0.72	2.04± 0.69	0.026
SDS	52.62± 5.12	54.52± 6.34	0.61	26.51± 6.34	32.12± 6.34	0.031
SAS	47.32± 6.41	48.58± 5.32	0.38	28.12± 3.22	39.56± 4.61	0.022
PSQI	0.71± 1.13	0.63± 0.96	0.44	3.31± 0.46	4.79± 0.54	0.019
SF-36M	44.06±6.06	46.08±9.18	0.58	54.24± 9.66	61.41± 8.56	0.014
SF-36P	50.43±9.15	52.61±10.48	0.31	63.42± 11.08	68.98± 10.46	0.032

SF-36M: SF-36 Mental Component Summary score
SF-36P: SF-36 Physical Component Summary score

Table 3. Result of patients' satisfaction survey

Contents	Strongly agree	Agree	Not agree
It was convenient and quick to achieve disease management	40	7	0
The nurse's explanations were easily understood	40	7	0
Problems could be solved with this network platform in time	36	8	3
It was useful to my disease recovery	42	5	0
My privacy was protected	43	4	0
I will keep using the network hospital in future	40	5	2
I will recommended to my family and friends	43	3	1

THU0733-HPR REHABILITATION IN WARM CLIMATE FOR YOUNG ADULTS WITH INFLAMMATORY RHEUMATIC DISEASE. A 12 MONTHS RANDOMIZED CONTROLLED TRIAL

I.R. Nilssen[1,2], H. Koksvik[2], K. Grønning[1], A. Steinsbekk[1]. *[1]Department of Public Health and Nursing, Norwegian University of Science and Technology; [2]Norwegian National Advisory Unit on Pregnancy and Rheumatic Diseases, Department of Rheumatology, ST.OLAVS Hospital, Trondheim, Norway*

Background: Rehabilitation in warm climate has long been an established non-pharmacological treatment for patients with inflammatory rheumatic disease (IRD) in Norway. It has however not been tailored to the needs of young adults, who often have different challenges than older adults with IRD.
Objectives: The aim of this study was to investigate if a rehabilitation program in warm climate tailored to young adults from 20 to 35 years had effect on physical function and self-management/coping, 12 months after completed intervention.
Methods: This was an open randomized controlled pilot trial, with a 2-group parallel design and a 1:1 allocation ratio. Patients were recruited from three different rheumatology outpatient clinics in central Norway. The intervention group received a 17 day long rehabilitation stay in Spain. The main component of the tailored intervention was intensive exercise (2–3 times per/day), individual physiotherapy (daily) and patient education. The control group received treatment as usual. The primary outcome measure was physical function assessed by the "30 second Sit to Stand test" (30sSTS, number of sit and stand during 30 seconds, higher score is better) and self-management/coping measured by the "Effective Musculoskeletal Consumer Scale" (EC17, higher score is better).
Results: Forty patients (mean age 27.5, 65% female) with IRD (intervention/control: 3/2 rheumatoid arthritis, 3/9 juvenile idiopathic arthritis, 4/5 psoriatic arthritis, 8/3 ankylosing spondylitis and 2/1 polyarthritis) were randomized. 19 out of 20 patients completed the intervention. At twelve months follow up there were 3 patients lost to follow up from the intervention group, and 2 in the control group. Patients in the intervention group had a significant improvement in the 30sSTS test 3, 6 and 12 months after completed intervention, compared to the control group (Table 1). The within group analysis showed that both groups improved at 6 and 12 months. The EC17 showed no difference between the two groups at 3, 6 or 12 months.
Conclusions: The results indicate that the intervention group significantly improved their physical function one year after the intervention compared to the control group, but there was no effect on self-management/coping. These results

Abstract THU0733-HPR – Table 1

Outcome measures	Baseline values	Change from baseline to					
		3 months		6 months		12 months	
	Mean (SD)	Mean (95% CI)	p-value	Mean (95% CI)	p-value	Mean (95% CI)	p-value
30sSTS							
Within group							
Intervention	12.75 (3.2)	8.7 (5.7–11.8)	**<0.001**	8.5 (5.1–11.9)	**<0.001**	10.6 (7.3–14.0)	**<0.001**
Control	13.15 (2.7)	1.1 (-0.5–2.7)	0.169	3.7 (1.2–6.2)	**0.006**	3.8 (0.6–7.1)	**0.024**
Between groups		7.6 (4.3–10.9)	**<0.001**	4.7 (0.7–8.8)	**0.024**	6.8 (2.3–11.3)	**0.004**
EC17							
Within group							
Intervention	64.5 (19.1)	0.9 (-4.0 -5.7)	0.709	2.2 (-3.4–7.8)	0.427	4.0 (-3.7–11.7)	0.291
Control	64.4 (10.3)	2.2 (-2.1–6.5)	0.295	6.8 (1.9–11.7)	**0.009**	4.2 (-1.2–9.5)	0.119
Between groups		-1.3 (-7.6–4.9)	0.670	-4.6 (-11.8–2.6)	0.2	-0.2 (-9.0–8.7)	0.966

might reflect that the focus of the intervention was mainly intensive exercise, and less on self-management /coping. This was a small study and the results should be interpreted with caution.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2256

THU0734-HPR ASSESSMENT OF LOCAL DISEASE ACTIVITY AFTER AN INTENSIVE HAND EXERCISE PROGRAM IN PATIENTS WITH RHEUMATOID ARTHRITIS MEASURED BY ULTRASOUND IMAGING: AN EXPLORATORY RANDOMIZED CONTROLLED TRAIL

C. Bartholdy, M. Henriksen, E. Wæhrens, K. Ellegaard[1,1]. *The Parker Institute, Frederiksberg, Denmark*

Background: In 90% of patients with rheumatoid arthritis (RA) the joints of the hand are affected, causing impaired hand function. In general, reduced strength and range of motion of the hand are seen in patients with RA.

Studies have shown positive effect on pain and function after exercise intervention for the hand in patients with RA. However, it is unclear if the disease activity in the joints of the hand is influenced by an exercise program.

Ultrasound imaging (US) is shown to correlate with other markers of disease activity in RA and can be used as a surrogate measure for inflammation in the joint, as US visualizes synovial hypertrophy and increased blood flow.

Objectives: To investigate if intensive hand exercise combined with joint protection education for the hand in women with RA can be conducted without a negative effect on the disease activity in the wrist and metacarpal (MCP) joints.

Methods: This is a sub-study of a randomised clinical trial investigating hand exercise therapy as add on to education in joint protection during activities of daily living (ADL) performance. The intervention group (IG) had both ADL education and exercise therapy and the control group (CG) had only ADL education.

The participants were women with RA involving the hand who had been on stable medication for at least three month.

At baseline all participants were examined by a rheumatologist. The joints were examined, blood samples collected and pain and strength of the hand were measured. Patient's functional ability was assessed using the Assessment of Motor and Process Skills (AMPS). US examination of the wrist and MCP 2–5 dorsal and volar in both hands was made. In the US examination both the amount of synovial hypertrophy and increased blood flow (Doppler activity) was evaluated. The evaluated was made according to a validated scoring system sum. (1)

After baseline examination the patients were randomised to either IG or CG.

The hand exercise program contained both range of motion and strengthening exercises for the finger, wrist, elbow and shoulder joints. The exercise program was conducted four times a week for eight weeks, once a week supervised by a physiotherapist, to avoid overload of the joints and to progress the exercises if possible.

After eight weeks all baseline measures were repeated and change from baseline was calculated using the per protocol approach.

Results: Fifty five women with RA were included in the study (IG: 28; CG 27).

US score and CRP change from baseline:

	Intervention group (n=22) Mean (SD)	Control group (n=25) Mean (SD)	Difference Between groups Mean (95%CI)	P value
Baseline US synovial hypertrophy	18.38 (16.25)	21.68 (23.66)		
Baseline US Doppler	6.57 (12.48)	7.24 (13.15)		
Baseline US sum score	23.82 (27.18)	28.92 (35.97)		
Baseline CRP	4.95 (6.96)	3.71 (3.70)		
Change US synovial hypertrophy	0.57 (3.93)	1.8 (7.16)	-1.23 (-4.74-2.28)	0,36
Change US Doppler	-0.33 (4.62)	0.92 (8.20)	-1.25 (-4.28-1.77)	0,52
Change US sum score	0.23 (6.90)	2.72 (13.63)	-2.50 (-7.74-2.76)	0,43
Change CRP	-0.86 (6.13)	1.86 (3.71)	-2.71 (-5.67-0.23)	0.10

Eight withdraw during the study period, six from the IG and two from the CG. Thus, 22 from the IG and 25 in the CG were included in the final analysis. The mean age 63.6 (12.6) years and mean disease duration was 12.7 (11.3) years, baseline mean tender and swollen joint were 4.8 (4.7) and 1.3 (1.7), respectively. No differences in change from baseline in tender joint count, hand pain and strength and functional ability was seen between the two groups (data not shown). The mean score and change from baseline in US score and inflammatory marker (CRP) in the blood are seen in table below.

Conclusions: Women with RA of the hand experience no negative effect on the disease activity in the joints of the hand after eight weeks combined hand exercise and joint protection education.

References:

[1] Hammer HB et al. Ann Rheum Dis 2011 Nov;70(11):1995–8.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5193

THU0735-HPR SHARED CARE OF RHEUMATOLOGIST AND NURSE CONSULTATIONS IN FOLLOW UP OF RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS OUTPATIENTS WITH LOW DISEASE ACTIVITY: A MONOCENTRIC, RANDOMIZED CONTROLLED TRIAL

K. Claes[1], A. Van Hecke[2], P. Jacques[1]. *[1]Rheumatology; [2]Centre of nursery and midwifery, University Ghent, Ghent, Belgium*

Background: Due to national regulations, the role of nurses in the management of arthritis patients differs significantly in all European countries (1). In Belgium, regularized consultations conducted by a rheumatology nurse do not exist.

Objectives: The study investigated whether rheumatology nurse consultations alternating with rheumatologist consultations for RA or AS patients with low disease activity is non-inferior compared to the usual care by the rheumatologist. Primary outcomes were safety and disease activity. Secondary outcomes were fatigue, pain, functional index, patient satisfaction, the level of self-management and self-efficacy.

Methods: This is a monocentric randomized controlled trial. The intervention group received a consultation conducted by a rheumatologist alternating with a nurse consultation, every 8 weeks. Patients in the control group received usual care: consultations performed by a rheumatologist every 8 weeks.

Results: Mixed method analyzes were performed. No statistical significant between-group effects were found nor in the RA group nor in the AS group, although there was a clinical relevance towards disease activity by AS patient in the intervention group. DAS 28 dropped with a mean difference of 0,4 (-1,1 – -0,2, SD 0,30). The ASDAS and BASDAI both decreased with 1.1 (-1,4 – -1,3, SD 0,1 and -1,7 – -1,4, SD 0,1 respectively). No safety signals from biochemical parameters such as SGOT, GOT and creatinine were detected. Inflammatory markers (ESR and CRP) remained stable in both groups. The secondary outcomes showed no significant between-group effects for both diseases. The self-efficacy outcome noticed a positive in-between-group effect by patients with RA in the intervention group.

Conclusions: In the follow-up of patients with RA or AS and low disease activity, outcome is not different when rheumatology nurse consultations alternating with rheumatologist consultations are compared to usual care. Implementing nurse consultations can positively influence the disease activity and patient self-efficacy.

References:

[1] van Eijk-Hustings Y et al. (2014) EULAR recommendations for the role of the nurse in the management of chronic inflammatory arthritis. Annals of Rheumatic Diseases 73:429–509.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2341

THU0736-HPR EFFICACY OF DIFFERENT TYPES OF EXERCISE PROGRAMS IN OSTEOPOROSIS WITH HIGH RISK OF FALLS

K. Kazár-Tóth[1], C.K. Karóczi[1], B. Monek[1], C. Gácserné[1], É. Kovács[2], G. Poór[1], I. Mikó[1]. *[1]National Institute of Rheumatology and Physiotherapy; [2]Semmelweis University, Institute for Applied Health Sciences, Budapest, Hungary*

Background: While ageing the frequency of osteoporosis increases. The most frequent risk factor is falling and consequently bone fractures which in this population is associated with high mortality. According to WHO data, 28–35% of elderly over 65 years falls at least once per year, which increases to 32–47% over 70 years.
Objectives: The purpose of this randomized control study was to investigate the efficacy of a land-based and water-based exercise program specifically targeting balance to reduce fall risk in patients over 65 years with osteoporosis. We assumed that water-based training program would develop balance efficiently even at elderly people with severe degenerative diseases. Coordination in water is possible to be developed efficiently.
Methods: The study was carried out in the National Institute of Rheumatology and Physiotherapy. 61 participants were randomized [n=20 sensorimotor training group, n=20 control group (CG)] in the land-based sensorimotor training program (SMT) and 21 people [n=7 Ai Chi group (AC), n=7 water adapted sensorimotor training group (WASM), n=7 control group] in the water-based training program (WBT). The control group did not participate in any training program. The exclusion criteria were neurological, cardiovascular and musculoskeletal diseases, which contraindicated the participation in the training program. Functional Reach Test (FRC), Timed Up and Go Test (TUG), Star Excursion Balance Test (SEBT) and coordination test by stabilometer were used to measure static and dynamic balance. The measurements were performed before and after the training period. The results of the SMT were analyzed with two-sample t-test, and the results of the WBT with non-parametrical methods. The results were defined with $p<0,05$ statistical margin by SPSS program.
Results: After 18-weeks of the SMT program significant improvement was experienced in the SMT group compared to the CG with the following parameters: FRC ($p<0.001$), TUG ($p=0.01$). In the coordination test no significant difference was found between the SMT and the CG ($p=0.09$). After 8-weeks of the WBT programs significant improvement in the mediolateral direction of SEBT was detected in the WASM ($p=0.028$) and in the AC group ($p=0.043$) compared to the CG. FRC test was shown marginal significance ($p=0.075$) in the WASM group, while at the AC group remarkable improvement ($p=0.043$) was recognised compared to the CG. In the TUG test significant improvement was found in the CG and the WASM ($p=0.028$, $p=0.043$) compared to the CG.
Conclusions: The findings from this study support the efficacy of the land- and water-based exercise programs in improving balance in this sample. Our results pointed out that balance improved efficiently even at degenerative joint diseases. Limitations of our research was the small number of the participants and the short duration of the program. In the light of the promising outcome we will continue our research that would result in an efficient fall prevention in this population with high risk of falling.
References:
[1] Sherrington C, Tiedemann A, Fairhall N, Close JC, Lord SR. (2011). Exercise to prevent falls in older adults: an updated meta-analysis and best practice recommendations. NSW Public Health Bulletin, Vol. 22(3–4): 78–83.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3783

THU0737-HPR EXPERIENCES AND APPRECIATION OF SHARED MEDICAL APPOINTMENT OF YOUNG ADULTS WITH A RHEUMATIC DISEASE, IN TRANSITION FROM CHILD TO ADULT CARE

L. Gossens[1], J. Ammerlaan[1], L. Cazemier[1], H. Bouwens[2], B. Formsma[2], J. van Laar[1], A. Kruize[1]. *[1]Rheumatology and Clinical Immunology; [2]Patient partner, UMC Utrecht, Utrecht, Netherlands*

Background: Young adults with rheumatic diseases deal with questions and uncertainties since their disease and treatment affect both physical and socio-emotional development[1,2]. As part of the transition from child to adult care, the UMC Utrecht offers a shared medical appointment (SMA). During a SMA, four to six patients are seen together in the presence of a doctor and nurse specialist. Compared to an individual consultation with a doctor or nurse, a SMA is offering extensive exchange of information and shared experiences focussed on everyday life, as sport, study, work and treatment[3]. During a SMA, patients learn from each other, which supports self-management. In practice, the care providers notice that young adults are reluctant to join a SMA, they hesitate to have a consultation in presence of their peers. When invited, most patients, however, do attend a SMA, and it is unknown how these young adults experience and appreciate the SMA. This evaluation is a first step of a larger project. The results will be deepened and supplemented with the findings on interviews with young adults and professionals, in order to give an advice for further development of the SMA in our clinic.
Objectives: Evaluating experiences and appreciation of SMA in transition patients in order to further develop the SMA in our clinic.
Methods: In the period of January 2014 till December 2016, patients in transition who participated in SMA were asked to fill in an evaluation questionnaire. This questionnaire focussed on expectations, quality of medical care compared to an individual consultation, information about disease and treatment during a SMA and the presence of other young adults. Data was analysed by the researchers and patient partners using SPSS and thematic analysis.
Results: Forty-five patients filled in the evaluation questionnaire, among them 35 women, with an average age of 19.6 years. The majority had a form of juvenile idiopathic arthritis (n=39); with average disease duration of 9,4 years and most were using a DMARD and/or biological (n=35). The results showed that participating patients were just as satisfied with the medical care in a SMA compared to a regular consultation; they indicate that more information was given in a SMA and the presence of peers was experienced as pleasant. Most appreciated were sharing experiences, individual stories and tips. Personal attention and lack of privacy were perceived as less pleasant, moreover young adults expressed to find it difficult to discuss personal issues.
Conclusions: Although it is difficult to motivate the young adults to attend the SMA, whenever they do attend, they appreciate a SMA in positive way, especially on benefits of sharing information and meeting peers, when offered in addition to individual consultations with doctor and nurse.
References:
[1] Ammerlaan JW, Scholtus LW, Bijlsma JWJ, Prakken ABJ, Kruize AA. An urge for change: Transitional care for young adults with juvenile idiopathic arthritis. Patient Education and Counseling 2013;92:127–129.
[2] Foster HE, Minden K, Clemente D, Leon L, McDonagh JE, et al. EULAR/PReS standards and recommendations for the transitional care of young people with juvenile-onset rheumatic diseases. Ann Rheum Dis 2016;0:1–8.
[3] Noffsinger E. Running group visits in your practice. New York: Springer, 2009.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3257

THU0738-HPR PROMOTING PHYSICAL ACTIVITY IN RHEUMATOID ARTHRITIS: DEVELOPING A THEORY-BASED BEHAVIOUR CHANGE INTERVENTION

L. Larkin[1], A. Fraser[2], S. Gallagher[3], N. Kennedy[1]. *[1]Department of Clinical Therapies, University of Limerick; [2]Department of Rheumatology, University Hospitals Limerick; [3]Department of Psychology, University of Limerick, Limerick, Ireland*

Background: Physical activity has numerous benefits for people who have RA, however interventions targeting physical activity behaviour in people who have RA have had limited efficacy [1].
Objectives: To develop a theory-based behaviour change intervention to promote physical activity in people who have RA.
Methods: Development was guided by the UK's Medical Research Council Complex Interventions framework [2] and consisted of three components;
1. Narrative review which explored the use of behaviour change theory in previous interventions
2. Systematic review which examined the content and structure of previous interventions
3. Qualitative study which explored the preferences of key stakeholders (people who have RA and health professionals) about the design of the intervention.
Results: Previous interventions lacked consideration of behaviour change theory in design and delivery, and there was a large degree of variance in content, structure and delivery. Lack of knowledge of current physical activity

Intervention	Overview	Detail
Aim	Promote physical activity	Time spent in moderate-intensity aerobic activity
Participants	Adults (18 years+), diagnosis of RA	Newly-diagnosed
Outcome measures	Physical activity (time spent in moderate-intensity ADLs)	ActivPAL™ activity monitor
	Physical activity beliefs, Self-efficacy, Quality of life, Pain, Fatigue	To be determined at protocol stage
Mode	Face-to-face	Initial 1:1 session, follow-up in group sessions
Location	Community location	Local health or community centres
Deliverer	Health professional (credible source)	Physiotherapist
*Content	Education	4.1 Instruction on how to perform a behaviour, 5.1 Information about health consequences, 5.2 Salience of consequences, 1.1 Goal setting (behaviour), 1.2 Problem solving
	Enablement	1.4 Action planning, 1.5 Review behaviour goals, 2.2 Feedback on behaviour, 2.3 Self-monitoring of behaviour, 6.1 Demonstration of behaviour, 6.2 Social comparison
	Modeling	8.1 Behavioural practice/rehearsal
Control	Education	1 group information session on physical activity

ADL = activities of daily living; RA = Rheumatoid arthritis
*As per Behaviour Change Wheel (Michie et al 2014)

recommendations for people who have RA was highlighted in the qualitative study, and delivery preferences were identified. Intervention development was mapped to the Behaviour Change Wheel [3] and employed the Theory of Planned Behaviour as it's theoretical basis. The proposed intervention is outlined in Table 1.

Conclusions: We have developed a theory-based intervention which considers the preferences of key stakeholders. Future research will determine the feasibility and effectiveness of this intervention.

References:
[1] Larkin et al (2015) Behaviour change interventions to promote physical activity in rheumatoid arthritis: a systematic review. Rheum Intl 35(10):1631–40.
[2] Craig et al (2008) Developing and evaluating complex interventions: new guidance, BMJ (Clinical research ed.), 337, a1655.
[3] Michie et al (2014) The Behaviour Change Wheel: A Guide to Designing Interventions., Silverback Publishing: Great Britain.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1374

THU0739-HPR THE PHENOMENON OF ALEXITHYMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

M. Ramkhelawon, R.A. Grekhoff, G. Suleymanova. *Rheumatology, Research Institute for Clinical and Experimental Rheumatology, Volgograd, Russian Federation*

Background: Alexithymia as a radical in the structure of premorbid personality is attracting the attention of researchers as one of the possible psychological risk factors in the development of psychosomatic disorders in rheumatic diseases. Clinical experience supports the evidence of the relevance of alexithymia conception in relation to the many somatic patients, who show a limited ability to describe and differentiate emotion and create fantasies, and hence indicate the role of alexithymia phenomenon in the pathogenesis of psychosomatic disorders in SLE.

Objectives: To study the relationship of the levels of alexithymia with other clinico-psychological characteristics.

Methods: 87 patients with systemic lupus erythematosus (SLE) was surveyed with the Toronto Alexithymia Scale (TAS).

Results: According to the results obtained, SLE patients demonstrated a high level of alexithymia (73,86±2,6 points). The results of the research showed that the level of alexithymia, on one hand, does not depend upon gender, age, character and activity of the pathological process ($p>0.05$). On the other hand, there was a significant inverse correlation between alexithymia and the level of the patient's education ($r = -0,42$ $p=0.031$). Moreover, internality in interpersonal interaction ($r = -0,44$ $p=0.028$), and significant direct correlation with indicators such as, the disease duration ($r = -0,46$ at $p=0.01$), the intensity of neurotic disorders (asthenia ($r = -0,42$ $p=0.033$), depression ($r = -0,52$ $p=0.006$), anxiety ($r =0.43$ $p=0.028$), hypochondriasis ($r = -0,48$ $p=0.01$), as well as psychological defense mechanism "Regression" ($r =0,42$ $p=0,022$).

Conclusions: Therefore, between the development of alexithymia in SLE patients and certain clinico-psychological characteristics, a particular association exists which provides a definite step for psychotherapeutic interventions aimed at correcting alexithymia personality traits of SLE patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2615

THU0740-HPR INFLUENCE OF BIOFEEDBACK THERAPY ON THE MICRO-CIRCULATION IN SYSTEMIC SCLEROSIS

M. Ramkhelawon, R.A. Grekhoff, G. Suleymanova, S.A. Kharchenko. *Rheumatology, Research Institute for Clinical and Experimental Rheumatology, Volgograd, Russian Federation*

Background: Microcirculatory disorders are one of the most important clinical symptoms of systemic sclerosis (SSc), therefore we found it feasible to evaluate the clinical efficacy of biofeedback (BFB) in the complex therapy of patients with SSc based upon analysis of nailfold capillaroscopy.

Objectives: To study the impact of the method of biofeedback therapy on microcirculation disturbances in patients with SSc.

Methods: The study included 40 patients with SSc under observation. Among the patients examined, 95% were women and 5% were men. The average age of the patients - 38±3,3 years, duration of illness - 14±2,6 years. Raynaud's phenomenon (RP) was observed in all the patients. A severe form of RP was seen in 80% of the patients. The effectiveness of biofeedback therapy was analyzed by studying the dynamics of the measures from the nailfold capillaroscopy and comparing the data obtained of patients from the main and control groups.

Results: It was found that, patients who were under biofeedback therapy, showed significant positive dynamics in the following signs of capillaroscopic picture: dilation of the capillaries ($c2 =9,643$ $p=0,026$), morphological changes of the capillaries ($c2 =4,90$ $p=0,027$), and hemorrhage ($c 2 =4,514$ $p=0,034$). In the control group of patients, in only one indicator of capillaroscopy that a significant change was noted, particularly by the presence of dilated capillaries ($c2 =5,833$ with $p=0,016$). These findings suggest that treatment results were significantly better in the main study group of patients with SSc.

Conclusions: The implementation of biofeedback therapy favors a decrease in reflex musculo-tonic syndromes, improvement of microcirculation and peripheral blood flow and significantly allows an amelioration in the results of SSc therapy.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2616

THU0741-HPR PLACEBO AND NOCEBO EFFECTS INDUCED BY CONTEXTUAL FACTORS. A SURVEY ON BELIEFS AND ATTITUDES OF ITALIAN MUSCULOSKELETAL PHYSIOTHERAPISTS

G. Rossettini[1], T. Geri[1], A. Palese[2], M. Fiorio[3], A. Viceconti[1], M. Testa[1]. *[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova, Savona; [2]Department Biological and Medical Science, University of Udine, Udine; [3]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy*

Background: Context effects are well known and were described as integral part of the clinical setting (1). The conscious use of contextual factors (CF) has been recently proposed as an effective modality capable to influence the physiotherapy outcome by facilitation of placebo responses. (2) To date, the knowledge about CF adoption in clinical practice of physical therapists is absent.

Objectives: The aim of this study was to investigate frequency of use, beliefs and attitudes about contextual factors among Italian physical therapists specialized in manual therapy (OMTs)

Methods: An invitation to participate in an online survey was sent to 906 OMTs through the database of the Master in Musculoskeletal Rehabilitation (MRDM) of University of Genova by SurveyMonkey Software®. These likely correspond to more than 85% of the whole OMTs population in Italy. A 17 items questionnaire and two clinical scenarios assessed behaviour, beliefs and attitudes of OMTs about CF adoption in clinical practice and data were analysed by descriptive statistic.

Results: 906 OMTs were invited to participate in the survey and 558 responded (62%). The majority of OMTs uses CF in their practice frequently (52%). They believe that an actual effect of CF can occur in acute pain (57%), chronic pain (78%) and rheumatologic disorders (56%). OMTs consider the use of CF ethically acceptable when it exerts beneficial psychological effects and their effectiveness was shown during clinical experience (31%). They disagree on the adoption of CF when they are based on deception, undermine the trust between OMT and patients, create legal problems or produce side effects (17%). 38% of respondents do not communicate the use of CF to their patients and they adopt CF as addition to other physical therapy interventions with the aim of optimizing clinical responses (20%). Expectation and psychological mechanisms are believed to be the main aspects behind placebo and nocebo effects induced by CF (7%).

Conclusions: The use of CF is quite common among Italian OMTs and they mostly had positive attitudes towards their use and effectiveness.

References:
[1] Di Blasi Z, Harkness E, Ernst E, Georgiou A, Kleijnen J. Influence of context effects on health outcomes: a systematic review. Lancet. 2001 Mar 10;357(9258):757–62.
[2] Testa M, Rossettini G. Enhance placebo, avoid nocebo: How contextual factors affect physiotherapy outcomes. Man Ther. 2016;24:65–74.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4361

THU0743-HPR A NEW AND ALTERNATIVE TREATMENT IN SCLERODERMIC DIGITAL ULCERS

M. Muratore[1], D. Carati[2], L. Quarta[1], A. Grimaldi[1], E. Quarta[1], M. Garzya[1], D. Longo[1], O. Casilli[1], F. Calcagnile[1]. *[1]U.O. Reumatologia- P.O. "V. Fazzi" Lecce, LECCE; [2]Research & development, Ekuberg Pharma, MARTANO, Italy*

Background: Digital ulcers (DUs) are a major clinical problem for patients with systemic sclerosis (SSc). Patients with DUs may suffer from severe pain and often undergo a limitation of daily life activities, thus resulting in a functional impairment with a significant impact on the patient's health-related quality of life. Prevention of further complications and lesions is possible if the initial evaluation is performed early and correctly and if a treatment is started promptly.

Objectives: The primary objective is to demonstrate the effect of Lecoxen cream (Ekuberg Pharma, Italy) in comparison with another cream (Fitostimoline cream, DAMOR SpA, Italy) on the reduction of the number and size of DUs in patients with systemic sclerosis evaluating in addiction the reduction of pain dealing with DUs and quality of life.

Methods: In this single-blind randomized progressive trial 39 women, with confirmed digital ulcers present for at least 4 weeks with a surface area greater than 0.5 cm^2 but smaller than 2,5 cm^2, that follow Iloprost therapy (0,05mg/2 times/month), afferent to the Operative Unit (O.U.) of Rheumatology of the Local Health Unit (LHU) of San Cesario di Lecce, were randomized to receive the topical application of Lecoxen cream (group I: 20 women) or Fitostimoline cream (group II: 19 women). We took digital photographs to measure ulcer surface area and to draw the periwound area before the first cream application and after 30 days. Then an evaluation of DUs diameter and number was carried out. A

tailored questionnaire was administered as Visual Analogue Scale (VAS) during monitoring visits, to evaluate intensity of pain. Furthermore quality of life was monitored through Short Form (36) Health Survey.
Results: Mean age was similar in the two study groups with values of 45.4±5.6 years and 46.1±4.1 respectively. In the patients treated with Lecoxen cream, the reduction of lesion size was significantly higher (70%–75%) ($p<0,001$) in comparison with those registered in group II (40–45%) ($p<0,05$); a significant improvement was observed in levels of pain in Group I (30 days: $p<0,001$), while in group II the results of reduction were not significant. The analysis of SF36 survey showed highly significant reduction ($p<0,001$) of indexes in group I. At last visit, 32 ulcers were healed: 17 in the group I ($p<0,001$), 11 in the Group II ($p<0,01$). Two-way analysis of variance (ANOVA) test was used to examine differences. Intragroup changes were evaluated with the paired Student t-test. A p-value of <0.05 was considered to be significant.
Conclusions: Lecoxen cream showed the greatest effect on the mean reduction of the lesion size and pain levels. In the patients treated with Lecoxen cream the reduction of lesion size was 70%–75%; the reduction was smaller in the group II. At last visit, 32 ulcers were healed: 17 in the group I, 11 in the Group II. Data collected from SF36 surveys are very interesting, because they show a clear improvement in quality of life of scleroderma patients, who underwent three different treatments. In particular, a better subjective perception of tactile sensation and minor discomfort in the pathological skin have been reported. On the basis of the results, it could be argued that the medical device Lecoxen cream may be useful in the treatment of DUs in patients suffering from systemic sclerosis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6225

THU0744-HPR ASSESSMENT OF ADALIMUMAB SUBCUTANEOUS INJECTION RELATED PAIN AND EFFECTIVENESS OF NURSE SUPPORT FOR PATIENTS WITH RHEUMATOID ARTHRITIS

M. Fusama[1], M. Suzaki[2], T. Hirasawa[3], M. Takemoto[4], Y. Asano[4], K. Higashi[1], T. Tsuru[2], K. Tanimura[5], M. Natsumeda[6], H. Nakahara[7]. *[1]Division of Nursing, NTT West Osaka Hospital, Osaka; [2]PS Clinic, Fukuoka; [3]Division of Nursing, Hokkaido Medical Center for Rheumatic Diseases, Sapporo; [4]Division of Nursing, Sweet Hospital, Kurashiki; [5]Hokkaido Medical Center for Rheumatic Diseases, Sapporo; [6]Sweet Hospital, Kurashiki; [7]NTT West Osaka Hospital, Osaka, Japan*

Background: Subcutaneous injection of biologic agents gives more freedom and independence for patients with rheumatoid arthritis (RA) than intravenous injection. Despite this, patients with RA sometimes select intravenous injections due to concerns over self-injection, such as injection anxiety, including pain, and lack of confidence in giving a self-injection [1]. It is reported that one in five people are estimated to experience injection anxiety [2]. Therefore, an understanding of subcutaneous injection pain and anxiety and support for anxiety of patients with RA are important for appropriate usage of subcutaneous biologics.
Objectives: The aim is to evaluate pain and anxiety caused by adalimumab (ADA) subcutaneous injection and assess the effectiveness of nurses' care.
Methods: Patients with RA using ADA self-injections were enrolled. Pain was assessed in 4 categories: general, needle insertion, drug injection, needle removal. Pain was evaluated using Visual Analogue Scale (VAS) scale. Effectiveness of support by nurses was also assessed using self-questionnaires and free-format comments. Statistical analyses were performed utilizing Wilcoxon's signed rank test and Spearman's rank correlation coefficient.
Results: Twenty patients (Male: Female, 4: 16) completed the questionnaire. Average age and disease duration were 68 and 12.6 years, respectively. Mean ± SD of Pain VAS were 34.9±28.1 mm (General), 30.3±30.6 mm (needle insert), 42.5±35.6mm (drug injection) and 11.8±18.4mm (needle removal). There were no statistically significant differences between general pain and needle insertion ($p=0.631$), or general pain and drug injection ($p=0.121$). However, statistically significant differences were found between general pain and needle removal ($p=0.001$). Moreover, there were statistically significant differences between needle insertion and removal ($p=0.003$), and drug injection and needle removal ($p=0.00048$). General pain showed statistically significant correlation with needle insertion pain ($r=0.653$, $p=0.0018$) and drug injection pain ($r=0.615$, $p=0.004$). However, general pain was not correlated with needle removal pain ($r=0.137$, $p=0.565$).
Patients with RA answered that support by nurses was effective for relieving pain (30%), reduction of anxiety (35%) and improving treatment motivation (50%). According to the patients, nurses helped raise motivation by explaining that treatment prevents the progression of RA and allows many patients to feel better and have less pain. Interaction with nurses appears to be effective in reducing injection pain and anxiety and improving motivation for self-injection treatment.
Conclusions: These data indicate that needle insertion and drug injection pain have great influences on general pain. Support by nurses is likely to reduce injection anxiety and pain, resulting in higher motivation toward self-injection treatment.
References:
[1] Keininger D, et al. Health Qual Life Outcomes. 2011 Jan 13; 9:2.
[2] Nir Y, et al. Am J Trop Med Hyg 2003, 68: 341–4.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5000

THU0745-HPR A COMPARİSON THE EFFECTİVENESS OF WHOLEBODY VİBRATİON, PROGRESSİVE RESİSTİVE EXERCİSE AND HOME-BASED EXERCİSE İN PATİENTS WİTH KNEE OSTEOARTHRİTİS

M. Pekesen Kurtça[1], U. Baş Aslan[1], E. Kuyucu[2]. *[1]Physical Therapy and Rehabilitation, Pamukkale University, Denizli; [2]Orthopedics and Traumatology, Medipol University, Istanbul, Turkey*

Background: Knee osteoarthritis (OA) is the most common type of lower extremity OA. Systematic reviews of randomized controlled trials (RCTs) indicate that exercise therapy reduces pain and patient-reported disability in patients with knee osteoarthritis (OA), but to date, type and the optimal exercise regimen has not been identified.
Objectives: The aim of our study was to determine the effects of whole body vibration training exercise, progressive resistive exercise, home-based exercise used in osteoarthritis treatment on pain, muscle strength, functional status and quality of life.
Methods: Fourty five patients (mean age=53,86±5,33 years, 43 female, 2 male) diagnosed with bilateral knee osteoarthritis (Grade II-III, Kellgren &Lawrence) were included in this study. The assesments were performed at baseline, after third months when they completed the exercise programme and sixth months. Whole body vibration exercise training in Group-1; progressive resistive exercise training in Group-2; home-based exercise training in Group-3; were applied for three days per week, three months, totally 36 sessions. All the groups were included patient education programme at baseline. The pain was assesed according to Visual Analog Scale (VAS) and quadriceps muscle strength was evaluated by using Handheld dynamometry. The functional status of the patients was evaluated by WOMAC (Western Ontario and McMaster Universities) index and health related quality of life was evaluated by Nottingham Health Profile (NHP).
Results: Significant improvement was found after treatment on pain, quadriceps muscle strength, functional status and quality of life in all groups ($p<0.05$). When the groups compared by ANOVA it was found that outcome measures were not significantly different between Group-1, Group-2 and Group-3 ($p>0.05$).
Conclusions: Supervised resistive exercises and whole body vibration exercises were more effective in strengthening lower extremity muscles when compared to home exercise training in patients with knee OA. However, the increase in muscle strength was not observed at long- term follow- up in both groups. Neither whole body vibration exercise training programme nor progressive resistive exercise and home-based exercise programme were found to be superior for the treatment of osteoarthritis. All types of exercise training programmes were beneficial for pain, functional status, quadriceps muscle strength and quality of life. Further studies with long-term follow-up are warrented.
References:
[1] Vincent KR, Vincent HK. Resistance exercise for knee osteoarthritis. Am J Phys Med Rehabil 2012; 4 (5 0):45–52.
[2] Thomas KS, Muir KR, Doherty M, Jones AC, O'Reilly SC, Bassey EJ. Home based exercise programme for knee pain and knee osteoarthritis: randomised controlled trial. BMJ 2002; 325–752.
[3] Jordan KM, Arden NK, Doherty M, et al. EULAR Recommendations 2003: an evidence based approach to the management of kneeosteoarthritis: Report of a task force of the standing committe for international clinical studies including therapeutic trials (ESCISIT). Ann Rheum Dis 2003;62:1145–55.
[4] Li X, Wang X, Chen B, Huang L, Liu Y. Whole –body vibration exercise for knee osteoarthritis:a systematic review and meta-analysis. Evidence-Based Complementary and Alternative Medicine 2015; 1:1–11.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6854

THU0746-HPR RHEUMATOLOGY NURSE SPECIALISTS AND DMARD PRESCRIPTION - WHERE ARE WE NOW?

M.K. Nisar[1], J. Begum[2]. *[1]Rheumatology, Luton & Dunstable University Hospital; [2]Rheumatology, Luton, Luton, United Kingdom*

Background: It is widely acknowledged that a multidisciplinary team approach is the best way to care for rheumatology patient group. The rheumatology nurse specialist (RNS) is an integral part of this multidisciplinary team. EULAR has published recommendations for their role in the management of chronic inflammatory arthritis (van Eijk-Hustings Y et al, 2012). The Department of Health also highlights the need for providing different models of care in a more cost effective way. It recognises that the nurse specialists' role is the bedrock of an effective care providing team and can contribute to answering the challenge of health provision in a financially difficult environment (Department of Health, 2008).
Objectives: We undertook a pilot survey to understand the present climate of rheumatology practitioners' prescribing of methotrexate in their practice.
Methods: "Learning Rheum" is a national initiative with an aim to establish a core curriculum for rheumatology nursing. Prior to its national meeting, the steering committee organised a focus group discussion of an ideal training structure to be able to successfully deliver DMARD education for patients. Methotrexate was accepted as index DMARD for the purpose of the exercise. A questionnaire

was created based on the discussion and all participants of the meeting were surveyed. Replies were compiled to ascertain the current picture of service delivery and educational training.
Results: 25 rheumatology specialist nurses participated in the exercise. Their job experience ranged from one week to 25 years (median 7 years). 21/25 (84%) ran independent clinics. 16/25 (64%) were employed at band 6. Five (20%) did not feel confident in counseling patients initiating methotrexate. Apart from two, no one had any formal training in delivering DMARD education. 10/25 (40%) had never been supervised whilst undertaking an educational session for patients. Six (24%) did not feel confident to teach or supervise their peers.
Conclusions: This is a pioneering survey mapping the training of rheumatology practitioners and nurse specialists to service delivery. This initiative highlights a wide variation in the training structure of a key job provision. There is lack of formal induction programme. Despite most participants running independent clinics and providing DMARD education for years, they confessed to have no formal education and little supervision. Over a fifth did not feel confident in counseling patients commencing methotrexate despite being in the job for a median of 18 months. Though most centres are delivering contemporary services, these are not being used effectively for developing key team members. A quarter of the cohort felt unprepared to impart the skills to peers (median experience 1 year).
In conclusion, there is wide variation in the training of rheumatology nurse specialists. This can potentially have a negative impact on a relatively young workforce. There is a need for improving training standards to help deliver good quality rheumatology professionals of the future.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2783

THU0747-HPR EFFECT OF DIFFERENT PHYSICAL THERAPY PROGRAMS ON PAIN, STRENGTH AND FUNCTIONAL SITUATIONS ON KNEE OSTEOARTHRITIS

Ö.E. Günaydın, V. Bayrakcı Tunay. *Sports Physiotherapy, Hacettepe University, Ankara, Turkey*

Background: Knee Osteoarthritis (OA) is one of the most common causes of disability with an increasing prevalence and incidence with age. Although there are studies in the literature that examine the efficacy of ESWT, Kinesio taping and exercise on knee OA, there is no study to compare these methods with each other.
Objectives: The purpose of this study is to compare the effects of Extracorporeal Shockwave Therapy (ESWT), Kinesio taping and exercise therapy on pain, knee strength and functional situations of patients with knee osteoarthritis (OA).
Methods: Forty eight female patients aged between 50–65 and previously diagnosed with a grade 1–3 (Kellgren-Lawrence scale) knee OA included in this study. Patients were assessed before treatment and after treatment at 6 weeks and at 12 weeks. Visual Analog Scale, (VAS), (ISOMED®2000 D&R GmbH, Germany) isokinetic device, Timed Up and Go test (TUG) and WOMAC scale were carried out for assessing patients' pain, knee strength and functional situations. After randomising the patients into 3 different groups, the first group received 1 session of ESWT per 6 weeks, the second group received 2 sessions of Kinesio tape per 6 weeks and the third group was prescribed with an exercise program only.
Results: The between-groups results showed a significant improvement for the pain during night, pain during resting,and WOMAC test in the exercise group ($p<0,05$), while no difference was found for the other measurements ($p>0,05$). The inter-groups results showed significant improvements in 3 of the groups ($p<0,05$), while there was no difference in 60 degrees/sec isokinetic quadriceps strength test in the Kinesio taping group and TUG test in the ESWT group.
Conclusions: The results of this study showed that; ESWT, Kinesio tape and exercise therapies are all effective in decreasing pain intensity, improving knee strength and functional status levels of patients with knee OA and can be used as alternative approaches to treat symptoms of knee OA.
References:
[1] Plotnikoff, R., Karunamuni, N., Lytvyak, E., Penfold, C., Schopflocher, D., Imayama, I. ve diğerleri. (2015) Osteoarthritis prevalence and modifiable factors: a population study. BMC Public Health, 15, 1195.
[2] Sarzi-Puttini, P., Cimmino, M.A., Scarpa, R., Caporali, R., Parazzini, F., Zaninelli, A. ve diğerleri. (2005). Osteoarthritis: an overview of the disease and its treatment strategies [Bildiri].Seminars in arthritis and rheumatism.
[3] De Oliveira Melo, M., Aragão, F.A.,Vaz, M.A. (2013) Neuromuscular electrical stimulation for muscle strengthening in elderly with knee osteoarthritis–a systematic review. Complementary therapies in clinical practice, 19 (1), 27–31.
[4] Zhao, Z., Jing, R., Shi, Z., Zhao, B., Ai, Q.,Xing, G. (2013) Efficacy of extracorporeal shockwave therapy for knee osteoarthritis: a randomized controlled trial. Journal of surgical research, 185 (2), 661–666.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5437

THU0748-HPR RECOMMENDATIONS ON PHYSICAL THERAPY PRESCRIPTION FOR AXIAL SPONDYLOARTHRITIS IN THE NETHERLANDS

S. van Weely[1], F. van der Giesen[1], N. Lopuhaa[2], F. van Gaalen[3], T. Vliet Vlieland[1]. *[1]Orthopaedics, Rehabilitation and Physical Therapy, Leiden University Medical Center, Leiden; [2]Dutch Arthritis Foundation, Amsterdam; [3]Rheumatology, Leiden University Medical Center, Leiden, Netherlands*

Background: In national and international guidelines physical therapy, comprising exercise interventions and education, is recommended as a required treatment modality for the optimal treatment of axial spondyloarthritis (axSpA). [1–3]. However, specific details regarding referral for physical therapy and optimal content and dose of exercise interventions are lacking. Research showed large variation in the content of exercise therapy in axSpA patients, which reflects suboptimal care [4].
Objectives: To develop practice recommendations on indications for referral, content, dose and safety aspects of exercise therapy for axSpA patients based on scientific evidence, expert opinion and patient values. The ultimate aim is improving the quality of exercise therapy care for people with axSpA.
Methods: The recommendations are based on scientific evidence, expert opinion and patient values and were formulated following a combination of literature review and three expert-group meetings (consisting of patients, rheumatologists, physical and exercise therapists, policy makers, scientists and special interest groups). In three consecutive expert-meetings clinically relevant questions, draft recommendations based on systematic literature reviews, and final recommendations including level of agreement were generated. Lastly, a field consultation among physical and exercise therapists, rheumatologists, scientists and special interest groups will be scheduled and an implementation strategy, comprising of an information intervention and directives, will be developed.
Results: In the first expert-group meeting 18 clinically relevant questions were formulated, on: indication and referral, assessment, content of treatment, evaluation and safety. In addition to recently published systematic reviews, additional literature reviews concerned assessment, safety and the dosage of exercise therapy. Related to the clinical questions, a framework for the therapeutic process and 12 draft recommendations were developed and discussed in the second meeting. In the third and last meeting the 12 recommendations regarding the delivery of physical therapy and exercise interventions were set and the level of agreement was determined.
Conclusions: The expert-meetings and literature searches led to 12 practice recommendations and a clear starting point for the development of the implementation strategy. Twelve practice recommendations regarding the delivery of physical therapy for patients with axSpA were developed, based on scientific evidence, expert opinion patient values. The field testing and development and execution of a dissemination and implementation strategy will be done in 2017.
References:
[1] Dagfinrud H, et al. Physiotherapy interventions for ankylosing spondylitis. Cochrane Database Syst Rev. 2008.
[2] van der Heijde D, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017.
[3] Steeringgroup recommendations Spondyloartritis, Dutch Rheumatology Association, Guidelines for diagnosis and treatment of axial Spondyloartrtis, 2014.
[4] Van der Giesen et al. Use and content of physical and (group)exercise therapy for people with axial spondylarthritis, NVR congress, posterpresentation, 2016.
Acknowledgements: The Dutch Arthritis Foundation financially supported this project.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4432

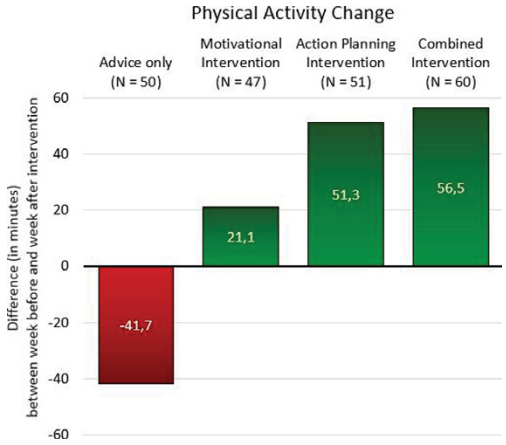
THU0749-HPR INCREASING PHYSICAL ACTIVITY IN PEOPLE WITH A CHRONIC DISEASE: EXAMINING THE EFFECTIVENESS OF A MOTIVATIONAL AND A PLANNING INTERVENTION, THEIR INTERACTION AND VARIOUS POTENTIAL MODERATORS AND MEDIATORS

S. Hilberdink[1], G.-J.Y. Peters[2]. *[1]Allied Healthcare Centre for Rheumatology and Rehabilitation, Groningen; [2]Psychology and Education Science, Open University of the Netherlands, Heerlen, Netherlands*

Background: Physical activity has many health benefits, especially in people with a chronic disease. Behaviour change interventions appear more effective than just advice when increasing physical activity. However, most studies that compare different interventions overlook interaction effects between methods and their parameters for effectiveness.
Objectives: Present study examined the effectiveness of a motivational and an action planning intervention for increasing physical activity in patients with a chronic disease. Their interaction as well as various potential moderators and mediators were studied in order to identify which intervention is effective in which patients.
Methods: In a healthcare centre specialised in the treatment of people with a chronic disease, participants whose physiotherapist would advise them to be more physically active were randomly assigned to one of four interventions in a factorial design: 1) a control condition with only advice, 2) a motivational intervention

with information about health benefits and selecting personally relevant motives and social support sources regarding physical activity, 3) an action planning intervention in which participants specified which physical activities they would do, when, where and for how long and 4) a combination of these interventions. Prior to the intervention, participants' leisure time physical activity in the past week was measured with items from the SQUASH. Also behavioural intentions, expected social support and planning behaviour with regard to leisure time physical activity were measured. Directly after the intervention, positive outcome expectations and self-efficacy were measured. After a week, physical activity measures were administered again.

Results: 208 Participants (71% female; mean age 62 years; 40% with a rheumatic disease) completed the study. Figure 1 displays the average change in physical activity for each intervention. Multiple regression analyses showed that both the motivational intervention (β=0.22) and action planning (β=0.31) significantly predicted a positive physical activity change and that these effects appeared additive as opposed to catalytic. The effects were not moderated by intention, expected social support or planning behaviour, nor mediated by outcome expectations or self-efficacy. The motivational intervention's effectiveness was weakly correlated with the number of personally relevant exercise motives identified (r=0.22) and the action planning's effectiveness was weakly related to the number of plans made (r=0.19) and to one's outcome expectations after the intervention (r=0.21).



Conclusions: These data suggest that using a motivational or action planning intervention seems beneficial for increasing physical activity in patients with a chronic disease, independent of one's intentions, expected social support and planning behaviour. The data also suggest that action planning is preferable over a motivational intervention and that the added value of a motivational intervention is minimal if action planning is used.

This study was limited by only measuring physical activity after a week and by using self-report. Future studies should investigate longer term effects, other potential moderators and mediators and interaction effects between other promising behavioural change methods.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2137

THU0750-HPR THE EFFECTIVENESS OF THERAPEUTIC FOOTWEAR IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

M. Tenten-Diepenmaat[1], M. Leeden van der[1,2], T. Vliet Vlieland[3], L.D. Roorda[1], J. Dekker[2,4]. *[1]Amsterdam Rehabilitation Research Center, Reade; [2]Department of Rehabilitation Medicine, VU University Medical Center, Amsterdam; [3]Department of Orthopaedics, Rehabilitation and Physical Therapy, Leiden University Medical Center, Leiden; [4]Department of Epidemiology and Biostatistics, Amsterdam Public Health research institute, VU University Medical Center, Amsterdam, Netherlands*

Background: Therapeutic footwear is recommended in guidelines for the treatment of foot problems in patients with rheumatoid arthritis (RA) and commonly prescribed and frequently used, especially in patients with established RA, foot deformities or erosions in foot joints.

Objectives: The objectives of this study were to summarize the effectiveness of therapeutic footwear on foot function, pain, physical functioning, health-related quality of life, adherence, adverse events and patient satisfaction in patients with RA.

Methods: All randomized controlled trials, randomized controlled cross-over trials, (quasi-experimental) clinical trials, and uncontrolled studies investigating the effect of therapeutic footwear in patients with RA related foot problems were included. Therapeutic footwear consists of custom-made or ready-made shoes. A literature search was conducted in The Cochrane Central Registry for Controlled Trials (CENTRAL), PubMed, EMBASE and PEDro up to January 19, 2017. Selection and inclusion of articles, data extraction (using a standardized template) and assessment of methodological quality (using a checklist for between-group and within-group comparisons) was conducted by two independent reviewers. Quantitative data analyses was conducted, when quantitative data analysis was not possible qualitative data analysis was performed.

Results: Thirteen studies were identified. In five studies, one of which was of high quality, between-group differences were reported. In twelve studies, of which two were of high quality, within-group differences were reported. Qualitative data-syntheses for the within-group differences of custom-made therapeutic footwear resulted in weak evidence for the reduction of foot pain and improvement of physical functioning. Quantitative data-analyses of the within-group differences of ready-made therapeutic footwear resulted in a medium to large effect for the reduction of foot pain (SMD -0.68, 95% CI -1.00 to -0.37; P=0.0001; 162 participants), and a small to medium effect for the improvement of physical functioning (SMD -0.32, 95% CI -0.62 to -0.02; P=0.04; 128 participants). Qualitative data-analyses of the between-group differences of ready-made therapeutic footwear resulted in inconclusive evidence for foot pain and physical functioning.

Conclusions: In within-group designs, there is weak evidence for the reduction of foot pain and improvement of physical functioning after wearing custom-made therapeutic footwear. Furthermore, in within-group designs there is a medium to large effect of ready-made therapeutic footwear on the reduction of foot pain, and a small to medium effect on the improvement of physical function. Controlled, between-group designs resulted in inconclusive evidence. A definite RCT is necessary to investigate the between-group effectiveness of therapeutic footwear in patients with RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5809

THU0751-HPR EFFECTIVENESS OF FOOT ORTHOSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS RELATED TO QUALITY OF LIFE AND PAIN. A SYSTEMATIC REVIEW AND META-ANALYSIS

G. Gijon-Nogueron, L. Ramos-Petersen, S. Garcia-Mayor, J.M. Morales-Asencio. *Nursing and Podiatry, University of Malaga, Malaga, Spain*

Background: Foot pain and deformity is almost ubiquitous in RA and results in considerable physical and psychosocial impairment [1]. Epidemiological studies consistently suggest a 90% prevalence of foot pain despite advances in pharmacological therapy [2]. Mechanical and other non-pharmacological interventions such as orthoses and footwear, have an important role in managing foot pathology in patients with their systemic disease controlled [1,3]. The effectiveness of treatment with insoles, especially in early periods, was studied in a randomized controlled trial, which results suggested an immediate clinical improvement, reducing foot pain, disability and limited functionality.[1]

Objectives: The aim of this study is the effectiveness of foot orthosis in patients with rheumatoid arthritis in terms of quality of life and pain.

Methods: A systematic review and meta-analysis was conducted of randomized controlled trials.

Participants: Patients with rheumatoid arthritis were included. The criteria of exclusion were Juvenile Rheumatoid Arthritis, analysis of gait,

Intervention: Studies had to compare foot orthosis

Comparison: Other type of treatments, other type of foot orthosis, sham

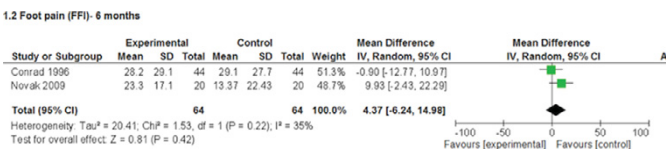
Outcomes: Evaluation of Pain or Quality of life with any tool that measure this outcomes

The search was conducted in Cochrane, CINAHL, PubMed, EMBASE, LILACS, and Cuiden. An independent peer review was carried out. The Mesh term and fields used were foot, ankle, joint, rheumatoid arthritis, foot, orthosis, insole, foot orthosis.

Results: After the analysis of 71 studies, 4 were included for the systematic review. The 4 studies enrolled 285 participants. Follow-up periods varied from 6 to 30 months.

Only two studies were included in the meta-analysis [4,5], both of them with pain (measured with Foot Function Index) as the selected outcome.

A meta-analysis of the two trials showed that use of FO resulted in a non-significant improvement in disability compared with control (MD (95% CI): 4.37 (-6.24, 14.98); N=64) (Figure 1).



Conclusions: Foot orthoses showed improvements in pain and disability/quality of life, but no significant differences between groups were found.Future research needs to increase the number of RCTs in this topic because results are not conclusive.

References:

[1] Woodburn J, Barker S, Helliwell PS. A randomized controlled trial of foot orthoses in rheumatoid arthritis. J Rheumatol. 2002;29:1377–83.

[2] Otter SJ, Lucas K, Springett K, Moore A, Davies K, Young A, et al. Comparison

of foot pain and foot care among rheumatoid arthritis patients taking and not taking anti-TNFalpha therapy: an epidemiological study. Rheumatol Int. 2011;31:1515–9.
[3] Hennessy K, Woodburn J, Steultjens MPM. Custom foot orthoses for rheumatoid arthritis: A systematic review. Arthritis Care Res (Hoboken). 2012;64:311–20.
[4] Conrad KJ, Budiman-Mak E, Roach KE, Hedeker D, Caraballada R, Burks D, Moore H. Impacts of foot orthoses on pain and disability in rheumatoid arthritics. J Clin Epidemiol. 1996 Jan;49(1):1–7.
[5] Novak P, Burger H, Tomsic M, Marincek C, Vidmar G. Influence of foot orthoses on plantar pressures, foot pain and walking ability of rheumatoid arthritis patients–a randomised controlled study. Disabil Rehabil. 2009;31(8):638–45.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2739

THURSDAY, 15 JUNE 2017

HPR measuring health (development and measurement properties of PROs, tests, devices)

THU0752-HPR DEVELOPMENT OF THE "TREATMENT BELIEFS IN KNEE AND HIP OSTEOARTHRITIS (TOA)" QUESTIONNAIRE

E.M. Selten[1], J.E. Vriezekolk[1], H.J. Schers[2], M.W. Nijhof[3], W.H. van der Laan[4], R.G. van der Meulen-Dilling[5], R. Geenen[6], C.H. van den Ende[1].
[1]Rheumatology, Sint Maartenskliniek; [2]Primary and Community Care, Radboud University Nijmegen Medical Centre; [3]Orthopaedics, Sint Maartenskliniek, Nijmegen; [4]Rheumatology, Sint Maartenskliniek, Woerden; [5]Physical Therapy and Manual Therapy, Partnership Velperweg, Arnhem; [6]Psychology, Utrecht University, Utrecht, Netherlands

Background: Use of non-surgical treatment modalities in osteoarthritis (OA) is suboptimal[1], which might be influenced by patients' beliefs about treatments. An instrument for measuring treatment beliefs in OA is not available yet.
Objectives: To develop a questionnaire assessing patients' beliefs about treatment modalities of hip and knee OA: the "Treatment beliefs in OA (TOA) questionnaire" and to evaluate its clinimetric properties.
Methods: The item pool, drawn from two previous qualitative studies, comprised beliefs regarding 5 treatment modalities: physical activity, pain medication, physiotherapy, injections and arthroplasty. A draft questionnaire comprising beliefs on these 5 treatment modalities was developed (200 items, Table 1). Two samples of patients with knee or hip OA (N=840, N=700) were recruited from our hospital to test the clinimetric properties of the TOA questionnaire. Descriptive analyses, explorative factor analyses (EFA; sample 1) and confirmatory factor analyses (CFA; sample 2) were conducted for each treatment module separately. Internal consistency was assessed with Cronbach's Alpha (both samples). In order to examine test-retest reliability a subsample of sample 2 (N=67) was asked to fill out the final TOA questionnaire again after two weeks.
Results: 351 patients filled out the draft TOA questionnaire (sample 1), 289 patients filled out the final TOA questionnaire (sample 2), with a subsample (N=50) who filled out the final questionnaire twice. EFA yielded a two factor solution for each treatment modality. The factors were labeled "positive treatment beliefs" and "negative treatment beliefs". The final TOA questionnaire comprised 60 items; items per treatment modality ranged from 9 to 14. CFA showed adequate fit indices for physical activities and physical therapy, while fit indices for the treatment modalities pain medication, injections and arthroplasty just failed to reach adequate cut-off values. Internal consistency was good to excellent for the subscale positive treatment beliefs (Cronbach's α between 0.84 and 0.90), and mediocre to acceptable for the subscale negative treatment beliefs (Cronbach's α between 0.66 and -0.79). Test-retest reliability was satisfactorily to good with ICCs from 0.66 to 0.88 and SEMs from 0.17 to 0.52.

Table 1: Example items in the TOA questionnaire

Items TOA-questionnaire	Disagree				Agree
I think *[doing physical activities]* leads to risks	1	2	3	4	5
My quality of life improves through *[using pain medication]*	1	2	3	4	5
I think *[physiotherapy]* causes pain	1	2	3	4	5
I can do household chores more easily through *[an injection]*	1	2	3	4	5
I think *[a joint replacement]* is pervasive	1	2	3	4	5

Conclusions: The TOA questionnaire is the first questionnaire assessing positive and negative beliefs regarding five treatment modalities for knee and hip OA. The TOA questionnaire showed moderate structural validity and good internal consistency and test-retest reliability. The TOA questionnaire is useful for a better understanding of patients' treatment beliefs. Future research will examine how treatment beliefs, in interaction with other variables, influence treatment choices.
References:
[1] Churchill 2016. The development and validation of a multivariable model to predict whether patients referred for total knee replacement are suitable surgical candidates at the time of initial consultation. Can J Surg, Vol. 59, No. 6, pp. 407–414.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4815

THURSDAY, 15 JUNE 2017

HPR epidemiology and public health (including prevention)

THU0753-HPR PREDICTING THE FUTURE DEVELOPMENT OF SPONDYLOARTHRITIS AMONG PATIENTS WITH IDIOPATHIC ACUTE ANTERIOR UVEITIS USING REAL-WORLD DATA

M. Haroon[1], K.A. Betts[2], F. Mu[2], M. Skup[3], J.K. Anderson[3], A.D. Joshi[3].
[1]Division of Rheumatology, University Hospital Kerry, Tralee, Ireland; [2]Analysis Group, Boston; [3]AbbVie Inc., North Chicago, United States

Background: Previous studies have suggested an association between idiopathic acute anterior uveitis (AAU) and spondyloarthritis (SpA), including showing that at least 40% of AAU patients have undiagnosed SpA. However, the clinical factors to predict the incident diagnosis or future development of SpA remain poorly recognized.
Objectives: The objectives of this study were: 1) to describe the patient characteristics of AAU patients with and without SpA diagnosis, and 2) to identify the predictive factors of SpA diagnosis among AAU patients using real-world data.
Methods: Adult patients with at least one diagnosis of AAU (ICD-9-CM: 364.01 or 364.02) were selected from a large US insurance claims database (01/01/2008–06/30/2015). The first AAU diagnosis was defined as the index date. Patients were required to have at least 6 months of continuous data availability before the index date. Patients with intraocular surgery, penetrating or blunt eye trauma, or a diagnosis of rheumatoid arthritis or SpA on or prior to the index date were excluded. Potential predictive factors for subsequesnt diagnosis of SpA included demographic characteristics, type of AAU (primary [first diagnosis] vs. recurrent), SpA-related comorbidities, and healthcare resource utilization prior to the index date. Factors predictive of SpA diagnosis were selected into a multivariable Cox proportional hazards model based on statistical significance and clinical relevance. Hazards ratios (HR) and p-values were estimated for each factor.
Results: A total of 48,822 patients with AAU were included, and among them, 1,032 patients were newly diagnosed with SpA during the follow-up period which was 24 months on average. Patients with SpA were younger (45.7 vs. 50.4 years), more likely to be male (52% vs. 42%), more likely to have recurrent AAU (44% vs. 29%), back pain (21% vs. 13%), SpA-related comorbidities including inflammatory bowel disease (IBD) (4% vs. 1%) and psoriasis (3% vs. 1%), and more likely to use corticosteroids (45% vs 40%). Predictive factors in the final Cox model were: male vs. female (HR=1.55; p-value$<$0.01), age$<$45 vs. $\geq$45 years old (1.65; $<$0.01), recurrent vs. primary AAU (1.94; $<$0.01), back pain under age 45 vs. no back pain (1.90; $<$0.01), back pain above age 45 vs. no back pain (1.46; $<$0.01), psoriasis (5.16; $<$0.01), IBD (2.50; $<$0.01), chiropractor/physical therapist visits (1.29; 0.01), conjunctivitis (1.23; 0.02), nonsteroidal anti-inflammatory drugs use (1.44; $<$0.01), use of conventional synthetic disease-modifying anti-rheumatic drugs (1.32; 0.05), joint pain (1.14; 0.19), imaging test use (1.03; 0.74), corticosteroids use (1.07; 0.33), and enthesitis/heel pain (1.13; 0.36). When sacroiliitis was included in the model, results remained largely similar.
Conclusions: There are significant differences among isolated AAU patients and AAU patients that developed SpA later. The most predictive factors of SpA diagnosis were male, age$<$45 years, recurrent AAU, back pain, and other extra-articular manifestations of SpA such as IBD and psoriasis. Since delayed diagnosis is common among SpA patients, identifying such predictive factors can help inform risk stratification.
Disclosure of Interest: M. Haroon Grant/research support from: AbbVie and Pfizer, K. Betts Consultant for: AbbVie, F. Mu Consultant for: AbbVie, M. Skup Employee of: AbbVie, J. Anderson Employee of: AbbVie, A. Joshi Employee of: AbbVie
DOI: 10.1136/annrheumdis-2017-eular.3028

THU0754-HPR WORK STATUS IN WOMEN WITH FIBROMYALGIA – A 12-YEAR FOLLOW UP STUDY

S. Johannesson[1], L. Nordeman[2,3], M. Joelsson[1], K. Mannerkorpi[2], A. Bergenheim[1,2,3]. *[1]Närhälsan rehabilitation centre, Region Västra Götaland; [2]Institute of Neuroscience and Physiology/Physiotherapy, Sahlgrenska Academy, University of Gothenburg, Gothenburg; [3]Närhälsan Research and Development Primary Health Care, Region Västra Götaland, Sweden*

Background: Fibromyalgia (FM) affects approximately 1–3% of the general population in the Western world and about 10% have been found to report Chronic Widespread Pain (CWP). The work ability is often affected in persons with FM and CWP. Previous research has shown a small improvement of symptoms over time in patient with FM and CWP. Sustain in work has been

shown to predict improvement in pain, pressure tenderness, fatigue, stiffness, depression, disturbed sleep, disease specific health, physical aspects and quality of life in persons with FM/CWP. There is lack of research about long-term follow-up of work status in FM and CWP. To enable patients with FM or CWP to sustain in work or return to work it is crucial to gain knowledge about which factors that can affect their work status in the long-term.
Objectives: To investigate change in work status and possible predictors of work status after 12 years in a cohort of women with FM and CWP.
Methods: In 2004, 166 women with FM and CWP participated in a randomized controlled trial in Sweden investigating effects of patient education and pool exercise. The 166 women were invited to participate in a follow-up study in 2016 in which long-term effects on work status, aspects of health and physical function were investigated. 126 participated in the follow-up study of which 98 were <65 years of age (age of retirement in Sweden) and included in the present study of work status. Data was collected by a standardized interview, a battery of questionnaires and an examination including tests of physical function. Work status refers to percentage of full-time work divided into four categories; 0%/1–49%/50–79%/80–100%. Wilcoxon's signed-rank test was used for comparisons of work status over time within the group.
Multivariable forward stepwise logistic regression was used for analyses of predictors of work status after 12 years. The dependent variable was work status dichotomized into <50%/≥50% work. Independent variables were baseline values of age, work status, symptoms of stress, pain intensity, overall health status, leisure time physical activity, walking capacity, health related quality of life and depression.
Results: The 98 women showed a significant increase in work status ($p<0.001$) at the 12 years follow-up. Proportions of work status in category 1–4 at baseline were 56%/10%/22%/10% and at follow-up it was 36%/11%/23%/28%. The participants' age, overall health assessed with Fibromyalgia Impact Questionnaire (FIQ) and health related quality of life assessed with SF-36 Physical component summary (PCS) at baseline predicted work status 10–12 years later. Age (years): OR 0.90 (95% CI 0.84–0.97), p=0.004. FIQ total score (0–100): OR 0.94 (95% CI 0.91–0.97), $p<0.001$. SF-36 PCS (0–100): OR 1.1 (95% CI 1.0–1.2), p=0.019.
Conclusions: Women with FM or CWP appear to improve their work status on group-level over time. Lower age, better overall health and higher health related quality of life at baseline were found to predict higher probability of working 50–100% after 12 years.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4782

THU0755-HPR DIETARY PROTEIN INTAKE AND UPPER LEG MUSCLE STRENGTH IN PATIENTS WITH KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

A.H. de Zwart[1], M. van der Leeden[1,2], L.D. Roorda[1], M. Visser[3], M. van der Esch[1], W.F. Lems[1,4,5], J. Dekker[2,6]. *[1]Amsterdam Rehabilitation Research Center, Reade; [2]Dept of Rehabilitation Medicine, VU University Medical Center (VUmc); [3]Dept. of Health Scienses, section Nutrition and Health, VU university Amsterdam; [4]Dept of rheumatology, VU University Medical Center (VUmc); [5]Jan van Breemen Research Institute; [6]Dept of Psychiatry, VU University Medical Center (VUmc), Amsterdam, Netherlands*

Background: In patients with knee osteoarthritis (OA) muscle weakness is common and is strongly related to more pain and activity limitations. Therefore, conservative treatment focuses on optimizing muscle strength in patients with knee OA. Determinants of muscle strength such as muscle quantity and quality, level of pain and physical activity are widely studied in knee OA. Only a limited number of studies have focused on the relation between nutrition and muscle strength in patients knee OA.
Protein is an essential building block for muscle tissue. Adequate dietary protein intake is needed to preserve muscle tissue. In a part of the general older population lower intakes than the recommended daily protein intake are observed [1,2]. Higher levels of dietary protein intake have been linked to greater muscle mass and strength in older adults[3,4]. Whether there is an independent association between lower dietary protein intake and lower muscle strength in knee OA patients in unknown.
Objectives: To determine whether lower dietary protein intake is associated with lower muscle strength in patients with knee OA.
Methods: In this cross-sectional study, baseline data of patients with symptomatic and radiographic knee OA from the progression subcohort of the Osteoarthritis Initiative (OAI) were used. Protein intake was measured by the Block Brief 2000 food frequency questionnaire and expressed as g per day/ kg bodyweight. Knee muscle strength was measured in the index knee by the Good Strength chair test, and expressed as the sum of both flexion and extension strength (N/kg bodyweight). Linear regression analysis was used to test the association, adjusting for relevant demographic, clinical and behavioral confounders.
Results: Data from 1128 patients (mean age 61.7±SD 9.1 y., 60.4% female) were used. A Kellgren and Lawrence grade of 2, 3 or 4 was scored in 25.7%, 44.7% and 30.0% of the patients, respectively.The mean daily protein intake was 0.68±SD 0.26 g/kg bodyweight, and the mean muscle strength was 5.33±SD 1.96 N/ kg bodyweight. In the unadjusted model, lower protein intake was associated with lower muscle strength (B = -0.804, 95% CI -0.336 to -1.272, p=0.001). After adjusting for age and gender, lower protein intake was still associated with lower muscle strength (B = -1.102, 95% CI -0.680 to -1.524, $p<0.001$) and was maintained after controlling for other relevant confounders.
Conclusions: Lower protein intake is independently associated with lower muscle strength in patients with knee OA. To confirm this relationship, future research is needed to test this association in longitudinal and interventional studies in patients with knee OA.
References:
[1] Fulgoni VL, 2008, Am J Clin Nutr 87:1554S–1557S.
[2] Kerstetter et al., 2003 J Nutr 133:855S–861S.
[3] Houston et al., 2008 Am J Clin Nutr. 2008 Jan; 87(1):150–5.
[4] Beasley et al., 2013 J Am Geriatr Soc. 2013;61(11):1863–71.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3386

THURSDAY, 15 JUNE 2017

HPR patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

THU0756-HPR PREDICTORS OF FEAR OF MOVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

G.I. Kinikli[1], H. Guney[1], S. Karahan[2], A. Ates[3], M. Turgay[3], G. Kinikli[3]. *[1]Department of Physiotherapy and Rehabilitation, Hacettepe University Faculty of Health Sciences; [2]Department of Biostatistics, Hacettepe University Faculty of Medicine; [3]Department of Rheumatology, Ankara University Faculty of Medicine, Ankara, Turkey*

Background: Rheumatoid arthritis (RA) is a systemic chronic autoimmune inflammatory disease characterized by synovial joint inflammation that results in functional limitations accompanied by social and psychological outcomes.
Objectives: The aim of this study was to investigate the association between fear of movement and age, upper and lower extremity functions and functional disability in patients with Rheumatoid Arthritis (RA).
Methods: A total of 88 patients with RA participated to the study. Disease activity was assessed using the Disease Activity Score in 28 joints (DAS28). Functional disability was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI). The Disabilities of the Arm, Shoulder and Hand Score (QuickDASH) was used to assess the upper extremity function. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess the lower extremity function. The Tampa Scale for Kinesiophobia (TSK) was used to assess pain-related fear of movement. The multiple stepwise linear regression model with R-square (R^2) was used to compare across the models and explain the total variance.
Results: Eight independent variables namely, age (r=0.215; p=0.044), QuickDASH (r=0.504; $p<0.001$), HAQ-DI (r=0.315; p=0.003), WOMAC Pain (r=0.512; $p<0.001$), WOMAC Stiffness (r=0.419; $p<0.001$), WOMAC Function (r=0.398; $p<0.001$), WOMAC Total (r=0.429; $p<0.001$), WOMAC range (r=0.419; $p<0.001$), demonstrated significant correlations with TSK. There were correlations between two independent variables (QuickDASH, p=0.013; WOMAC Pain, p=0.034) and TSK (R^2=0.293).
Conclusions: Health professionals should keep in mind that fear of movement were likely to cause poorer upper extremity functional disability and lower extremity pain levels in spite of varied drug therapies in patients with RA.
References:
[1] Wan, S. W., He, H.-G., Mak, A., Lahiri, M., Luo, N., Cheung, P. P., & Wang, W. (2016). Health-related quality of life and its predictors among patients with rheumatoid arthritis. Applied Nursing Research, 30, 176–183.
[2] Doury-Panchout, F., Metivier, J., & Fouquet, B. (2015). Kinesiophobia negatively influences recovery of joint function following total knee arthroplasty. European journal of physical and rehabilitation medicine, 51(2), 155–161.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2817

THU0757-HPR EUROPEAN QUALITATIVE RESEARCH PROJECT ON PATIENT-PREFERRED OUTCOMES IN EARLY RHEUMATOID ARTHRITIS (EQPERA): RATIONALE, DESIGN AND METHODS OF AN ONGOING MULTI-COUNTRY, MULTI-CENTER, MULTI-LANGUAGE, LONGITUDINAL QUALITATIVE STUDY

K. Van der Elst[1], A. Bremander[2], A. De Groef[1], I. Larsson[3], E. Mathijssen[4], J. Vriezekolk[4], R. Westhovens[1], Y. van Eijk-Hustings[5]. *[1]Rheumatology, University Hospitals Leuven, Leuven, Belgium; [2]Research and Development Center; [3]Spenshult Research and Development Center, Spenshult Hospital, Halmstad, Sweden; [4]Department of Rheumatology, Sint-Maartenskliniek, Nijmegen; [5]Department of Patient & Care/Rheumatology, Maastricht University Medical Center, Maastricht, Netherlands*

Background: Ample studies exist on outcome assessment from the patient perspective in Rheumatoid Arthritis (RA), but little is known about health and

treatment preferences of recently diagnosed patients, and how these evolve over time. A Belgian qualitative study has set the scene (1), but knowledge on cross-cultural nuances in patient-preferred outcomes is lacking. To this end, EQPERA – European Qualitative research collaboration on Patient-preferred outcomes in Early Rheumatoid Arthritis– was founded.
Objectives: EQPERA aims to unravel longitudinally preferences for treatment and health outcomes among patients with early RA across Belgium, the Netherlands and Sweden. To yield sound results, specific preparations for this cross-country qualitative study are reported here.
Methods: Several steps have been undertaken to ensure trustworthiness of findings and consistency across countries in sampling, interviewing, analysis and project management: a detailed research protocol has been written; the interview guides have been translated following a structured forward-backward linguistic validation process; templates for data collection and a quality assurance reporting tool have been developed; and local staff has been trained and supervised by the project leader in implementing the study protocol. Each country will document changes with sufficient detail in their research logbook.
Results: EQPERA will be a qualitative, explorative, longitudinal study with active involvement of patient researchers. In each country, a purposive sample of patients with early RA will be individually interviewed 3–6 months after start of the initial RA treatment and subsequently, the same participants will be invited back to take part in a focus group 12–18 months after RA treatment initiation. Data collection and analysis will be independently conducted by the local research teams in their native language. The local teams will analyze their interview data using the constant comparison method as detailed in Qualitative analysis guide of Leuven, after which Saldana's guiding questions will be adopted for analyzing change over time. Afterwards, a meta-synthesis of all locally gathered and interpreted data will be conducted to explore and describe patterns, similarities and differences across countries.
Conclusions: This European project is a first step in gathering contextual findings on patient-preferred outcomes in early RA. Such knowledge is of crucial importance for tailoring therapeutic approaches in a timely and meaningful way. Our innovative, qualitative, longitudinal research design goes beyond the abilities of the frequently used cross-sectional designs in qualitative research. Large, multi-national qualitative projects are scarce in rheumatology research, thus applied data management and quality assurance strategies could be of interest to other researchers.
References:
[1] Van der Elst K, et al. Unraveling Patient-Preferred Health and Treatment Outcomes in Early Rheumatoid Arthritis: A Longitudinal Qualitative Study. Arthritis Care Res (Hoboken). Arthritis Care Res (Hoboken). 2016;68(9):1278–87.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6747

THURSDAY, 15 JUNE 2017

HPR professional education, training and competencies

THU0758-HPR APPLICATION OF THE EULAR RECOMMENDATIONS FOR PATIENT EDUCATION FOR PEOPLE WITH INFLAMMATORY ARTHRITIS IN SWITZERLAND

K. Niedermann[1], C. Madelaine-Bonjour[2], M. Roffler[3], A. Kocher[4] on behalf of Health Professionals in Rheumatology Switzerland. *[1]School of Health Professions, Zurich University of Applied Sciences, Winterthur; [2]Rheumatology, University Hospital, Lausanne; [3]Swiss League Against Rheumatism, Zurich; [4]Rheumatology, University Hospital, Bern, Switzerland*

Background: The recently published EULAR recommendations for patient education (PE) in people with inflammatory Arthritis (IA) encompass two overarching principles and eight recommendations (1). The average overall agreement of PE experts with the recommendations is usually high (at least 8.8 (SD+/-0.5) on a 1–10 Numeric Rating Scale NRS) (1, 2). The recommendations ought to be disseminated and implemented to establish a core standard for delivering PE and training for health professionals (HPs) in delivering PE across Europe.
Objectives: The Swiss HPs in rheumatology organisation, hpr Switzerland, aimed to evaluate the current standard of PE as well as the agreement with and application of the EULAR PE recommendations in Switzerland, in order to develop further implementation steps.
Methods: An online survey was conducted among HPs and rheumatologists in the major rheumatology clinics (n=28) of the German and French part in Switzerland. The current knowledge and skills in PE and the performance of PE in clinical practice were assessed by multiple choice questions. The agreement with the PE recommendations was assessed on a 1–10 NRS and their application in the rheumatology clinics on a 4-point scale ("applied"/"rather applied"/"rather not applied"/"not applied").
Results: A total of 57 HPs, among them 12 rheumatologists, 21 nurses, 15 physiotherapists, 6 occupational therapists, 2 medical assistants) from 12 rheumatology clinics participated. Of these HPs, 31 (55%) worked for more than 6 years in rheumatology and 15 (27%) indicated to have a formal training in PE. They perceived that PE formed a substantial part of their work (33.5% on average), the most important element being "providing information" (48%), compared to 27% counselling and 25% behavioural interventions.
The average overall agreement with the PE recommendations was 7.0 (SD+/-2.25). Recommendations 3 and 7 were well applied (72%) in the rheumatology clinics. Least applied were the recommendations 4 and 6 with 21% and 24% respectively. Recommendations 1, 2, 5 and 8 reached between 40–50% application rates.
Image/graph shows Agreement with and Application of the PE Recommendations in Switzerland

Overarching principles
1. Patient education is a planned interactive learning process designed to support and enable people to manage their life with inflammatory arthritis and optimise their health and well being
2. Communication and shared decision making between people with inflammatory arthritis and their health care professionals are essential for effective patient education

Recommendations	Agreement mean (SD)	Application '(rather) applied')
1. PE should be provided for people with IA as an integral part of standard care in order to increase patient involvement in disease management and health promotion	7.03 (2.39)	42.4%
2. All people with IA should have access to and be offered PE throughout the course of their disease including as a minimum; at diagnosis, at pharmacological treatment change and when required by the patient's physical or psychological condition	6.79 (2.22)	48.5%
3. The content and delivery of PE should be individually tailored and needs-based for people with IA	6.68 (2.35)	72.7%
4. PE in IA should include individual and/or group sessions, which can be provided through face-to-face or online interactions, and supplemented by phone calls, written or multimedia material	7.08 (2.08)	21.2%
5. PE programmes in IA should have a theoretical framework and be evidence-based, such as self-management, cognitive behavioural therapy, or stress-management	7.08 (2.20)	48.5%
6. The effectiveness of PE in IA should be evaluated and outcomes used must reflect the objectives of the PE programme	7.05 (2.44)	24.2%
7. PE in IA should be delivered by competent HPs and/or by trained patients, if appropriate, in a multidisciplinary team	7.26 (2.26)	72.7%
8. Providers of PE in IA should have access to and undertake specific training in order to obtain and maintain knowledge and skills	6.82 (2.08)	42.3%

Conclusions: The overall agreement with the recommendations was high, although lower than the overall agreement of PE experts (1,2). The application of most recommendations was found to be moderate to low in Swiss rheumatology institutions; however no comparisons with other countries are available. "Providing information" was reported as the most important PE element. This emphasises the need to implement the PE recommendations as well as to improve HPs' knowledge on delivering and evaluating effective PE, in order to provide beneficial PE interventions for people with IA in Switzerland.
References:
[1] Zangi, HA.; Ndosi, M; Adams, J; Andersen, L; Bode, C; Boström, C; van Eijk-Hustings, Y; Gossec, L; Korandová, J; Mendes, G; Niedermann K; Primdahl, J; Stoffer, M; Voshaar, M; van Tubergen, A, (2015). EULAR recommendations for patient education for people with inflammatory arthritis. Ann Rheum Dis, 6, 74. 954–62.
[2] Patermann J, Ehlebracht-König I, Lind-Albrecht G, Genth E, Reusch A, Küffner R, Müller-Ladner U, Braun J. EULAR recommendations for patient education of people with inflammatory arthritis. Translation and evaluation in Germany. Z Rheumatol. 2016 Mar;75(2):187–99.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6038

THURSDAY, 15 JUNE 2017

HPR interventions (educational, physical, social and psychological)

THU0759-HPR DOES PHYSIOTHERAPY AND REHABILITATION PROGRAM IMPROVE MOBILITY AND DAILY LIVING ACTIVITIES IN ELDERLY INPATIENT WITH OSTEOPOROSIS?

M. Karapinar[1], T. Firat[2], N. Kirdi[2]. *[1]Department of Physiotherapy and Rehabilitation; [2]Hacettepe University, Ankara, Turkey*

Background: Osteoporosis (OP) is a generalized skeletal disorder characterized by compromised bone strength and deterioration of bone quality, often leading to fragility. Elderly osteoporosis is being public health problem that highly affects people especially above 65 years. Physiotheraphy and rehabilitation programs are

important in the prevention and management of osteoporosis. Exercises improve mobility in elder inpatient by increasing activity, muscular strength, flexibility, and reducing the risk of falls and length of stay in hospital.

Objectives: The aim of our study was to investigate the effects of physiotherapy and rehabilitation program on mobility, physical activity and quality of life in elderly inpatient.

Methods: A hundred and twenty four patient with OP (mean age: 73,03±5,9) participated in this study. A total of patients who were randomized as study and control group followed by Hacettepe University Faculty of Medicine Department of Internal Medicine, Division of Geriatric Medicine Department of Physiotheraphy and Rehabiltation, Geriatric Rehabilitation Unit were, were included to the study. Assessment for cognitive function (Mini Mental State Test), functional mobility (De Morton Mobility Index), activities of daily living (Katz Index of Independence in Activities of Daily Living), quality of life (EuroQol-5D) were used at admission and discharge in hospital. Thirty minutes physiotherapy and rehabilitation program including breathing, balance and coordination and strengthening exercises was performed by the intervention group under supervision of physiotherapist during the stay in hospital. Control group did not special exercise, they continued their activities of daily living. exercise. Length of stay in hospital of all participant was recorded.

Results: Sixty two patients were randomly assigned to the each group.The groups were similar in sociodemographical feature ($p>0.05$). Improvements in mobility, quality of life and daily physical activity levels were found in the study group ($p<0.05$). There were no significant differences between control and intervention group in length of stay in hospital ($p>0.05$).

TABLE I. Results of the 3 primary outcome measures at admission and disharge for the two groups

		X± SD Admission	X± SD Discharge	p
DEMI	Intervention Group	50,64±20,59	57,82±22,35	**0,000***
	Control Group	47,91±22,01	48,56±21,72	0,346
Katz ADL	Intervention Group	14,30±3,13	15,98±2,91	**0,001***
	Control Group	14,35±2,42	14,61±2,44	0,769
EQ-5D	Intervention Group	9,87±4,74	9,58±4,65	**0,019***
	Control Group	9,50±2,24	9,51±2,17	0,776

X±SD : Mean ± Standart Deviations, DEMI : De Morton Mobility Index, KATZ : The Katz Index of Independence in Activities of Daily Living , EQ5D : The EuroQol

Conclusions: These results revealed the necessity of physiotherapy and rehabilitation program to prevent negative effects of the hospitalization process of the geriatric patients with osteoporosis.

References:

[1] Muche, J., McCarty, S., & Kishner, S. (2015). Geriatric Rehabilitation.
[2] Curran, E., Clifford, S., Forman, S., & Power, D. (2014, September). Screening of Osteoporosis Treatment in Patients Presenting with Fragility Fractures in a Geriatric Active Rehab Unit. In Irish Journal Of Medical Science (Vol. 183, Pp. S334-S335). 236 Grays Inn Rd, 6th Floor, London Wc1x 8hl, England: Springer London Ltd.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3884

THURSDAY, 15 JUNE 2017

HPR service developments, innovation and economics in healthcare

THU0760-HPR PATIENT ADVICE LINE - THE POTENTIAL CLINICAL AND FINANCIAL BENEFITS TO A RHEUMATOLOGY DEPARTMENT

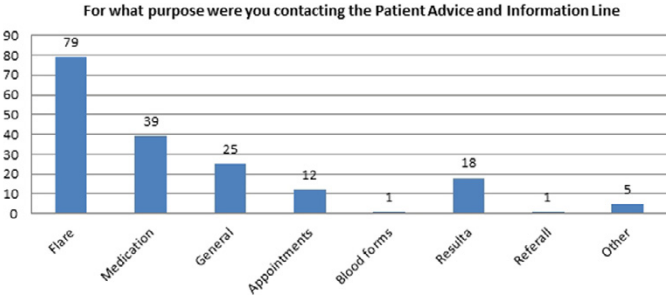
A. Mason, C. Beevor, J. Ledingham. *Portsmouth Hospitals Trust, Portsmouth, United Kingdom*

Background: EULAR recommendation 3 for the role of the nurse in the management of chronic inflammatory arthritis states that patients should have access to nurse-led telephone services to enhance continuity of care and to provide ongoing support (1). In the UK quality standard 6 of the National Institute for Health and Care Excellence guidelines for the care of rheumatoid arthritis (RA) recommends that people with RA and disease flares, or possible drug related side effects should receive advice within 1 working day of contacting the rheumatology service. In 2016 audit data from England and Wales show that 96% of trusts report being able to provide patients with a telephone advice line but no further detail on these services was available (2).

Objectives: Data from our patient advice line were collected over a 6 month period. The objective was to understand who was using the helpline, the speed of our response, how much of the workload could be managed by nursing staff and the clinical and financial impact.

Methods: All patient calls made to our patient helpline were recorded and data were collected prospectively on patient demographics, disease, purpose of call, response time and the cost and revenue produced. Patient feedback was collected via a questionnaire. Data were collected from April 2016 to November 2016.

Results: 150 patient calls were responded to. 108 calls were from females and were 42 from males. The majority of patients had RA (75/150). Other conditions are displayed in the graph below. The majority of calls were regarding a flare of their condition or medication queries (79/180 and 39/180 respectively) with some patients calling for more than one reason. 83% of calls were answered within 24 hours. A clinical nurse specialist is available to respond to calls over weekends. Income generated from responding to calls by the department was £ 1900 per month. Expenditure was £ 1650 per month. Patient satisfaction was high with 130/150 stating the main reason for the call was answered to their satisfaction (7 stating no, 13 not stated).



Conclusions: Our advice line gives patients easy access to specialist advice. Patient satisfaction is high. Responses are timely and fast. Multiple concerns are commonly addressed, such as advice regarding flare of disease and medication queries. This service will be

References:

[1] Van Eijk-Hustings et al. EULAR recommendations fo the role of the nurse in the management of chronic inflammatory arthritis. Ann Rheum Dis 2012;71:13–19.
[2] BSR Rheumatoid and Early Arthritis 2nd Annual Report 2016. Available http://www.hqip.org.uk/resources/rheumatoid-and-early-inflammatory-arthritis-2016/.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2160

THU0761-HPR BIOLOGICAL THERAPY SURVIVAL: MULTI-CENTRIC ANALYSIS IN REAL CLINICAL PRACTICE CONDITIONS

D. Ybáñez García[1], J.J. Alegre-Sancho[1], A. Martínez-Cristóbal[2], J.A. Castellano Cuesta[3], M. Fernández Matilla[3], N. Fernández-Llanio Comella[3], I. Ríos-Martin[4], A.M. Martinez-Arroyo[4]. *[1]Rheumatology, H Doctor Peset, Valencia; [2]Rheumatology, H de la Ribera, Alzira, Valencia; [3]Rheumatology, H Arnau de Vilanova, Valencia; [4]I+D, PORIB GES, Paterna, Valencia, Spain*

Background: Biological treatment (BT) has changed the evolution of rheumatic diseases. A way to evaluate the effectiveness of BTs is considering therapeutic survival as an effectiveness subrogate marker

Objectives: To describe BT use; To evaluate BT survival in indications according to product label, in clinical practice, in 3 Spanish hospitals

Methods: Observational retrospective study, based on clinical history (CH) revisions of patients with Rheumatoid arthritis (RA), Psoriasic Arthritis (PA), and Espondiloarthiritis (EA) treated with BT.

CH standardization was performed by data collected since 2013 by rheumatologists thought MEDiadd® RHEUMA tool.

Variables: age, gender, indication (RA, PA, EA) TB: Etanercept (ETN), adalimumab (ADA), certolizumab (CRT), golimumab (GOLI), infliximab (IFX), abatacept (ABA), tocilizumab (TCZ), rituximab (RTX). Start and end date from 2002 to 2016

Exclusion criteria: Patients and/or treatment lines with incomplete data (lack data or $n<15$) were also excluded.

Descriptive statistics and Kaplan-Meier survival analysis were performed with r-project.com

Results: From initial 1155 patients, 76 were excluded because of incomplete data. Almost half of the patients (42.35%) were diagnosed with RA, 30.03% have EA and 18.07% PA. 10% were excluded because of other indications. 79.46% of patients with RA are women, as 36.36% of EA and 50.96% of PA; Most of the patients are over 55y. In all indications, the range of 36–54y is the one that present a higher percentage of patients.

For the Kaplan-Meier survival analysis, the complete set of BT that each patient had received was analyze independently, considering 1206 cases. Table 1 shows average time and percentage survival at 1st year

After 1 year, ETN showed the higher rates of survival in RA (98.5%); IFX (100%), and ETN (99%) in PA; and GOLI (100%) followed by ETN (95.8%) in EA. Those BT were used to compare survival curves, finding differences in all cases (α=0.05) except in IFXvsETN in RA; ETNvsIFX in PA; and IFXvs GOLI in EA. Analysis after 5 years showed that the higher survival rates were for IFX in RA (94.4%) and PA (94.7%) and for ETN in EA (89.4%)

Conclusions: BTs with highest survival rates are ETN and IFX for RA and Aps; In EA, GOLI presents a higher rate at 1-year, but at 5-year is overcome by ETN

Standardized information is crucial to assess the global impact of BT. CH analysis reveals clinical practices which describe the effectiveness of treatments in the world, which can help in the decision-making process

Acknowledgements: By their collaboration: Dr Casado; Dr Valls; Dr Martinez; Dr Aguilar; Dr Vergara; Dr Begazo

Abstract THU0761-HPR – Table 1

Indication	Time (months)	ABA	ADA	CERTO	ETN	GOLI	IFX	RTX	TCZ
RA	x̄	29,7	58,6	28,8	57,4	24,6	27,3	60,5	35,7
	ED	22	42,5	17,7	39,7	20,4	25	32,8	27,1
	1-year (%)	98	93	89,6	**98,5**	77,8	94,4	97,8	88,4
	1-year CI95%	0,942–1	0,881–0,981	0,805–0,998	0,968–1	0,6076–0,996	0,844–1	0,937–1	0,812–0,963
	p-value	<0,001*	0,011*	<0,001*		<0,001*	**0,115**	0,005*	<0,001*
PA	x̄		43,4		59,6	37,3	51,8		
	ED		33,7		46,6	19,1	27,5		
	1-year (%)		87,8		99	91,7	**100**		
	1-yaer CI95%		0,802–0,961		0,971–1	0,831–1			
	p-value		0,025*		**0,894**	0,007*			
EA	x̄		43,1		54,2	33,7	51,4		
	ED		32,2		37,1	16,7	47,6		
	1-year (%)		95,6		95,8	**100**	93,5		
	1-year CI95		0,921–0,991		0,923–0,995		0,853–1		
	p-value		0,04*		0,008*		**0,06**		

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5810

THU0762-HPR ONLINE CONSULTATION FOR CHINESE PATIENTS WITH RHEUMATIC DISEASES BASED ON SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOLS: A STUDY OF MEDICAL ECONOMICS

F. Xiao[1], Z. Guo[2], Z. Zhang[3], W. Min[4], Y. Tang[5], X. Duan[6], L. Mo[7], H. Wu[8], X. Xu[9], Y. Zhao[10], F. Jiang[11], H. Xiao[1], Y. Zhao[1], Y. Jia[1], F. Zhang[12]. *[1]Medical Department, Shanghai Gothic Internet Technology Co., Ltd., Shanghai; [2]Department of Rheumatology, The First People's Hospital of Huainan City, Huaian; [3]Department of Rheumatology and Immunology, Linyi people's Hospital, Linyi; [4]Department of Rheumatology and Immunology, Heze Municiple Hospital, Heze; [5]Department of Rheumatology and Immunology, Yantai YuHuangDing Hospital, Yantai; [6]Department of Rheumatology and Immunology, The Second Affiliated Hospital of Nanchang University, Nanchang; [7]Department of Rheumatology, The First Affiliated Hospital of Xi'an Jiao Tong University, Xi'an; [8]Department of Rheumatology and Immunology, Dongguan People's Hospital, Dongguan; [9]Department of Rheumatology and Immunology, Changhai Hospital, Shanghai; [10]Department of Rheumatology and Immunology, First Affiliated Hospital of Harbin Medical University, Harbin; [11]Department of Rheumatology and Immunology, Huzhou Third People's Hospital, Huzhou; [12]Department of Rheumatology and Immunology, Peking Union Medical College Hospital, Beijing, China*

Background: China doesn't have efficient primary medical care and referral system. Patients can choose any hospitals or any doctors they like to seek medical care. As a result, most patients with rheumatic diseases rushed to a few large cities. Survey shows that more than 40% of the rheumatic disease patients are unnecessary to go to hospital and they only need advices from specialist. Smart System of Disease Management (SSDM) is a series of applications for chronic diseases management, which develop the interaction between doctors and patients. Our previous study showed that rheumatoid arthritis (RA) patients can master the SSDM and perform self-management after training, including disease activity score with 28 joints (DAS28) and health assessment questionnaire (HAQ) evaluations, as well as medication and lab test data entries.
Objectives: To evaluate the feasibility and benefit of the medical economics of online consultation based on SSDM by rheumatologist.
Methods: The rheumatologists implemented the education and training programs on patients in using SSDM and assist the patients in downloading SSDM mobile application. The SSDM includes doctors' and patients' applications. After data entry, patients can synchronize data to their authorized doctor. On the basis of these data, the rheumatologists can accept the request from their follow-up patients through SSDM and practice consultation in the form of text or telephone call.
Results: From February 2015 to January 2017, 333 rheumatologists supplied 3,119 patients (RA 46%, systemic lupus erythematosus 22%, ankylosing spondylitis 12%, Gout 11%, osteoarthritis 4%, other rheumatic diseases 5%) with 136 times free and 3,556 paid consultations. Paid consulting included 3,537 times text Q&A and 19 telephone consultations. The consulting fee ranged from RMB 10 to 500 yuan (EUR: RMB =1: 7.33) each in average of 121.3±55.19 yuan, which rate match the registration fee in hospital. The total collection of fee for consultations was 399,320 yuan RMB. 35.9% patients receiving online consultation lived in different city with the rheumatologists. If patients seek medical in hospital, in addition to the registration fees and medical expenses, the mean cost of transportation, accommodation, meals and lost wages was 552.68±477.51 (200 - 2,800) yuan. The total of cost for all patients would have been 2, 509,920 yuan RMB, which is 6.29 times compare with the cost of online. Through the SSDM system for online consultations, patients can save 84.09% of the cost. Survey shows all patients were satisfied and 60.28% of them were "very satisfied" with the consultations.
Conclusions: Using SSDM system to obtain online consultation, Chinese patients with rheumatic disease can enjoy reduced cost with high satisfaction. In the era lack of primary care system in China, SSDM may serve a complimentary platform to control medical care cost, as well as relieve the tensions between health care professionals and patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5072

THU0763-HPR ADDRESSING THE ELEPHANT IN THE ROOM: A POSSIBLE NEW AND EFFECTIVE WAY TO INCREASE PATIENT ADHERENCE TO MEDICAL ADVICE

G. Grønhaug[1], S. Arnesen[2]. *[1]Department of Public Health and General Practice, Norwegian University of Science and Technology, Trondheim; [2]Department of Comparative Politics, University of Bergen, Bergen, Norway*

Background: Lack of Patient adherence to medical advice (PAMA) are recognized as an era of interest for the last decades [1]. There have been several initiatives to improve PAMA such as patient centred care, shared decision-making, introduction of e-health and m-health. Although they are proven better than usual care, neither of these initiatives is proven successful. Outcome of medical interventions depends on complex psychological and sociocultural factors of which many are uncontrolled by health professionals.
Objectives: In the present study we assess beliefs about priorities in public health care, and adherence to medical advice to establish a novel approach to increase PAMA.
Methods: The Norwegian Citizen Panel (NCP) [2] is an experimental survey. Respondents are randomized to answer similar questions with slightly different wording. NCP is currently about 5000 respondents based on random selection performed by the Norwegian people register. The present study is based on responses to two question experiments from NCP adressing beliefs about priorities in public health care, and adherence to medical advice. The question on priorities in health care is divided in six groups (two control group, four experimental). The question on adherence is divided in three groups (one control group, two experimental). All questions are answered with a seven point Likert scale.

Table 1

Question nr	Question phrases	Result	Confidence Intervall 95%		n=
			Lower bound	Upper bound	
1	Prioritising waiting lists for surgery				
1a	Patients with severe illness are treated first	0,7442	0,7169	0,7714	271
1b	Patients with severe illness are treated first resulting in longer waiting for one in your family	0,7596	0,7329	0,7864	285
1c	Patients with severe illness are treated first, resulting in longer waiting for yourself	0,7600	0,7341	0,7860	266
1d	Those who benefit most from treatment are prioritised	0,5226	0,4877	0,5576	265
1e	Those who benefit most from treatment are prioritised, resulting in longer waiting for one in your family	0,5560	0,5208	0,5912	277
1f	Those who benefit most from treatment are prioritised, resulting in longer waiting for yourself	0,5818	0,5465	0,6171	273
2	Treatment rejection				
2a	Medical doctor denies treatment	0,5009	0,4774	0,5245	539
2b	Medical expertise does not approve the treatment.*	0,5361	0,5117	0,5604	564
2c	Medical expertise and patient organisation agree on not approving the treatment.*	0,5730	0,5478	0,5982	523

Question 1 a-f is used to assess beliefs on health care systems priorities. Question 2 assesses aspects of potential new ways to increase patient adherence.
All questions are answered using a 7 point likert scale. Result is based on positive attitude regarding wording in the question
* Question phrases refer to how the physician explains to the patient why the treatment is rejected.

Conclusions: This study is the first to use experimental survey to assess PAMA. The result indicates that healthcare priorities form a base of trust between health care providers and patients. It further indicates that PAMA might increase if the healthcare provider refers to national expertise and patient organisations beliefs of a given treatment. This finding is supported by psychological theories of meaning-making[3].
Informing the patient about the views of the patient organisations and national expertise in the reasoning for a given treatment, may improve patient adherence to medical advices.

References:
[1] Costa E, Giardini A, Savin M, et al. Interventional tools to improve medication adherence: review of literature. Patient preference and adherence 2015;9:1303–14. doi: http://dx.doi.org/10.2147/PPA.S87551 [published Online First: 14.9.2015].
[2] Ivarsflaten E. Norwegian citizen panel Wave 2, 2014. First NSD edition, Bergen 2014 ed. University of bergen, 2014.
[3] Lewis J. From culturalism to transculturalism. Iowa journal of cultural studies 2002;1:14–32.

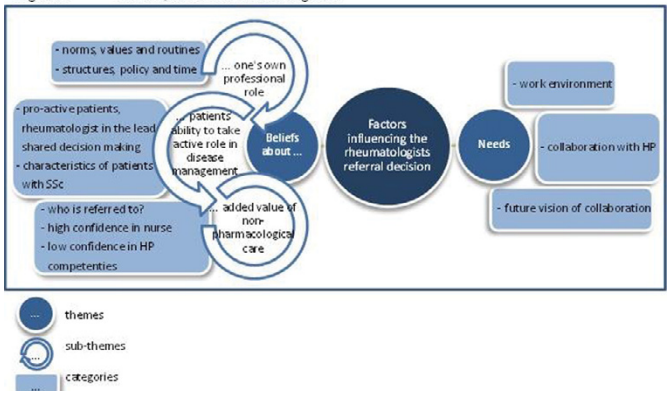
Acknowledgements: Siv Mørkved for the suport and encouragement to do the study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1914

THU0764-HPR WHAT MOVES THE RHEUMATOLOGIST? UNRAVELLING DECISION MAKING IN SSC REFERRAL – A QUALITATIVE STUDY

J.K. Stöcker[1,2], E. Cup[3], R. Nijhuis-van der Sanden[3], B. Staal[2,3], M. Vonk[3], F. van den Hoogen[1,3], E. van den Ende[1]. *[1]Sint Maartenskliniek; [2]Research group Musculoskeletal Rehabilitation, HAN University of Applied Sciences; [3]Radboud university medical center, Nijmegen, Netherlands*

Background: Well-coordinated multidisciplinary non-pharmacological care is considered to be a cornerstone in the management of patients with systemic sclerosis (SSc). However, unmet information and healthcare needs are found to be common in patients with SSc [1]. In addition, referrals by rheumatologists' do not always correspond with potential treatment goals as identified by health professionals (HP)[2].
Objectives: The aim of this study was to gain insight in the perspective of rheumatologists about the referral process of SSc patients to non-pharmacological care and to identify starting points for its optimisation.
Methods: Semi structured in-depth interviews were held with 13 out of 24 rheumatologists, specialised in SSc management, from different Dutch university and regional medical centres. The qualitative data analysis used an inductive thematic analysis by moving through a process of coding in layers of abstraction and interpretation: familiarization with data, generating initial codes, grouping similar codes in categories, discussing categories, searching for themes among categories, reviewing themes, defining and naming themes, and producing the final report.
Results: One major theme was identified as influencing decision making: "beliefs" and its three sub themes: a) beliefs about one's own professional role; b) beliefs about the patients' ability to take an active role in managing the disease and c) beliefs about the added value of non-pharmacological care. We also found an additional theme reflecting the "needs" of the rheumatologists regarding professional multidisciplinary collaboration (Figure 1). Another remarkable finding to be further explored was the discrepancy we found between the reliance of rheumatologists on established routines with regard to when and to whom to refer and the low confidence in HPs competencies on the other hand.

Figure 1. Themes, sub-themes and categories



Conclusions: The results of our study give insight that rheumatologists base their referral decisions on complex reasoning mindlines and beliefs about their own professional role, the patient's role and HP competencies.

References:
[1] Willems, L. M., Kwakkenbos, L., Leite, C. C., Thombs, B. D., van den Hoogen, F. J., Maia, A. C., & van den Ende, C. M. (2014). Frequency and impact of disease symptoms experienced by patients with systemic sclerosis from five European countries. Clinical And Experimental Rheumatology, 32(6 Suppl 86), S-88–93.
[2] Schouffoer, A., Zirkzee, E., Henquet, S., Caljouw, M., Steup-Beekman, G., Laar, J., & Vlieland, T. (2011). Needs and preferences regarding health care delivery as perceived by patients with systemic sclerosis. Clinical Rheumatology, 30(6), 815–824. doi:10.1007/s10067–010–1645–6.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5886

THU0765-HPR PATIENT SATISFACTION AND SELF-MONITORING OF CHRONIC INFLAMMATORY ARTHRITIS

K. Grønning[1,2], E.K. Lyngvær[2], A.S. Magnussen[2], E. Rødevand[2]. *[1]Department of Public Health and Nursing, Norwegian University of Science and Technology; [2]Rheumatology, University Hospital in Trondheim, Trondheim, Norway*

Background: Effective drug treatment for patients with inflammatory arthritis have brought a major proportion of patients in clinical remission. The need for regular follow-up intervals in specialized care is less; patients take greater responsibility for their own care, and patients request access to more flexible health care services. As a result of this development, the University Hospital, St.Olavs Hospital, Department of Rheumatology, has developed a on-demand pathway (PORS) for patients with inflammatory arthritis (RA, PsA and AS) in clinical remission or low disease-activity aiming for increased patient responsibility and flexibility.
Objectives: The aim of this study was to investigate patients' satisfaction with PORS regarding disease status, treatment, knowledge, responsibility, and cooperation with health care professionals.
Methods: We conducted a quest-back survey for patients included in PORS for $\geq$1 year in the period from June 2016 to October 2016. The survey contained 10 questions about the pathway. The response alternatives and scoring were: not at all =1, to a small extent =2, to some extent =3, to a large extent =4, to a very large extent =5, and not relevant =0.
Results: We identified 1048 eligible patients, 10 invitations were returned (unknown address), and 312 responded (30%). The descriptive analyses (see table) showed that the patients in general considered their disease activity to be in a stable phase. The cooperation with their general practitioner was good, they had to some or large extent sufficient knowledge to take responsibility for the blood test controls and adhere to prescribed medication. The patients were to some extent satisfied with the renewals of prescriptions and access to health professionals. The patients were less satisfied with the "promise" of getting outpatient appointments within 14 days if needed. Finally, the patients would largely recommend PORS to other patients.

PORS Questions	Mean (SD)	Median	Not relevant
Is the disease activity in a stable phase now?	3.70 (0.95)	4	–
Has the disease activity been in a stable phase since you became included in PORS?	3.62 (0.96)	4	1%
Do you have sufficient knowledge to take responsibility and carry out the routine blood test controls?	4.21 (0.94)	4	1%
Do you have sufficient knowledge and confidence to take your medications as prescribed?	4.26 (0.91)	4	1%
Do the renewals of medications prescriptions work okay?	3.16 (2.1)	4	26,6%
Do you get in touch with the Health Professionals at the Rheumatology Department by phone when you need to?	3.61 (1.6)	4	11,5%
Was the waiting time for an appointment at the department too long before you became included in PORS?	2.50 (1.33)	2	6,7%
Do you get the outpatient appointment within 14 days if you need one?	2.28 (2.06)	2	40,7%
Do you have a good cooperation with your general practitioner?	4.05 (1.07)	4	1,3%
Would you recommend PORS to other patients?	3.91 (1.33)	4	0,3%

Conclusions: We found that patients with inflammatory arthritis in general were satisfied with a management pathway encouraging greater responsibility for managing their own care and the possibility for more flexible contacts with the health care services. However, fullfilling the promise of outpatient appointments within 14 days were not always possible to achieve.
Acknowledgements: We would like to thank the local Rheumatology fund for financing the project.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3223

THU0766-HPR REFERRAL TO TELECARE. A NEW MODEL OF RHEUMATIC PATIENT FOLLOW-UP

L. Cano Garcia, N. Mena-Vazquez, S. Manrique-Arija, F.G. Jiménez-Núñez, I. Ureña-Garnica, C. Domic-Bueno, M. Rojas-Gimenez, C. Fuegos-Varela, M.V. Irigoyen-Oyarzabal, E. Vilchez-Ocaña, A. Fernández-Nebro. *Rheumatology, Hospital Regional Universitario de Málaga, Málaga, Spain*

Objectives: To analyze the medical ramifications that are made to the consultation

of telecare of Rheumatology Nursing (CTCER) of our hospital and health care activity generated by this.
Methods: Design: Observational study cross.
Patients: 301 patients for follow-up were derived to CTCER in a hospital of third level of January - November 2016. Our hospital serves a population of 600,000 people.
Protocol: We have a specific document for referral to CTCER where the rheumatologist specifies the reason for referral, the nurse review period and diagnosis. Nurse appointment the patient in its agenda for the telephone follow-up on the date indicated and recorded in the history of the patient efforts made the day of the appointment. The most common medical efforts making the nurse are preset by consensus with rheumatologists. Coming out than expected are reviewed with responsible for the patient's rheumatologist.
Variables analyzed: diagnosis, reason shunt type of FAME, adverse events, appearance of Comorbidities, nurse management, new problems after telephone consultation.
Statistical analysis: descriptive analysis of the main variables.
Results: Of the 301 patients, 68.4% were women. The diagnoses were: rheumatoid arthritis (RA) 116 (38.5%), spondyloarthropathy (SpA) 34 (11.3%), psoriatic arthritis (PsA) 45 (15%), systemic lupus erythematosus (SLE) (18.9%), vasculitis 1 (0.3%), arthritis juvenile idiopathic (AJI) 5 (1.7%), Still's disease adult 3 (1%), osteoporosis 4 (1.3%), 4 undifferentiated arthritis (1.3%). Them reasons of referral were: control to the month of home of FAME synthetic 120 (39.9%), Control to the home of FAME biological 28 (9.3%), review consultations 110 (36.5%), control toxicity hepatic 17 (5.6%), control alteration hematologic 7 (2.3%), control alteration renal 1 (0.3%), control of security of treatment Mycophenolate 4 (1.3%), control of safety of Teriparatide 6 (2%), wish gestational 1 (0.3%), analytical control not performed in consultation 13 (4.3%) (Table1). The most derived synthetic FAME was methotrexate 174 (57.5%) and the most derived biological FAME was etanercept 16 (5.3%) (table2). Nurse managed bypass autonomously 298 (99%) referrals, need help of the rheumatologist in 2 (0.7%) referrals and having only 1 shunt derived to 2017. 17 (5.6%) leads new problems with the call appeared: intolerance digestive 11 (3.7%), headache 3 (1%), worsening 1 (0.3%), moderate 1 infection (0.3%), poor adhesion 3 (1%), new comorbidity 3 (1%).
Conclusions: The inquiry of telecare is a form of collaborative work rheumatologist-nurse. The nurse can manage leads independently without having to go to your rheumatologist. This type of nurse call brings improvements in patient care, prevents displacement, decreased on-site visits and improves the safety of patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1674

THU0767-HPR ADVANCED PRACTICE MUSCULOSKELETAL PHYSIOTHERAPY SERVICES: A NATIONAL EVALUATION

O. Fennelly[1], C. Blake[1], O. Fitzgerald[2,3], R. Breen[2,4], A. Brennan[2,5], J. Ashton[2,6], C. Cunningham[1] on behalf of The National Clinical Programmes for Rheumatology and Orthopaedics. *[1]School of Public Health, Physiotherapy and Sports Science, University College Dublin; [2]National Clinical Programme for Rheumatology, Royal College of Physicians; [3]Department of Rheumatology, St. Vincent's University Hospital; [4]Health Service Executive, HSE; [5]Physiotherapy, AMNCH; [6]Physiotherapy, Beaumont Hospital, Dublin, Ireland*

Background: Patients with musculoskeletal (MSK) disorders may remain on lengthy hospital outpatient waiting lists to be reviewed by a consultant doctor, although medical or surgical intervention may not be required (1,2). In 2012, a waiting list initiative saw the introduction of Advanced Practice Physiotherapists (APPs) across 16 hospitals in Ireland. APPs triage and manage patients awaiting a consultant doctor appointment, who are deemed non-urgent or unlikely to require surgery on screening of referral letters. APP scope of practice generally involves some traditionally medical-controlled acts such as: administering injections, ordering investigations/imaging, surgical listing and onward referral to hospital specialities; and depending on consultant doctor availability, their input may be sought on clinical decisions if required.
Objectives:
- Profile the national APP patient caseload
- Establish the clinical outcomes of APP consultations

Methods: A national database was established with all APPs (n=22) submitting patient data for 2014. These data were analysed using descriptive statistics.

Table 1. Outcomes of APP Consultations

Clinical Outcome	Service Users (n=16,577) n (%)
Physiotherapy*	6,715 (41)
Clinical Investigations	4,833 (29)
Clinical Imaging[a]	1,865 (27)
Orthopaedic/Rheumatology Services[†]	2,818 (18)
Other Hospital Speciality[†]	563 (4)
MSK Injection	685 (4)
Surgical listing	404 (2)

Note: Other clinical outcomes included discharge. Clinical Imaging was added to the database from August to December inclusive. Valid data: [a]n=7,009, *n=16,194, [†]n=15,557.

Results: Data showed that APPs assessed 13,981 new patients, who presented most commonly with MSK disorders of the knee (n=3,096), lumbar spine (n=2,926) and shoulder (n=1,945) (Fig. 1) and the median wait time was 167 days (IQR 91–316). Including an additional 2,596 return appointments, the most common clinical outcomes were physiotherapy and/or clinical investigations (Table 1), and clinical decisions were made independently by the APP in 77% (n=11,728) of recorded cases (n=15,189).

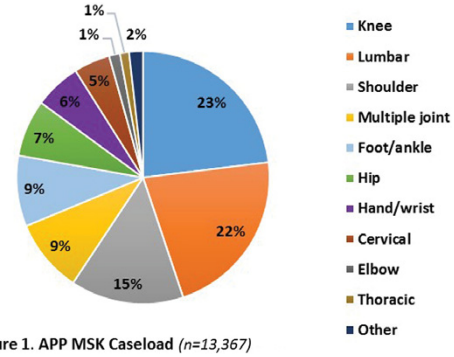


Figure 1. APP MSK Caseload *(n=13,367)*

Conclusions: APP services provide a more efficient MSK clinical pathway and reduce demands on the Consultant Doctor services. Collection of National Data enables ongoing service evaluation and monitoring of key performance indicators.
References:
[1] Wood, L., Hendrick, P., Boszczyk, B. & Dunstan, E. 2016. A review of the surgical conversion rate and independent management of spinal extended scope practitioners in a secondary care setting. Ann R Coll Surg Engl, 1–5.
[2] Desmeules, F., Toliopoulos, P., Roy, J. S., Woodhouse, L.J., Lacelle, M., Leroux, M., Girard, S., Feldman, D.E. & Fernandes, J. C. 2013. Validation of an advanced practice physiotherapy model of care in an orthopaedic outpatient clinic. BMC Musculoskelet Disorders, 14, 162.
Acknowledgements: I would like to thank the National Clinical Programmes and Health Service Executive for their funding and support of this project.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4300

THU0768-HPR PHONE FOLLOW-UP PROGRAM ENHANCES TREATMENT SAFETY AND DRUG CONCORDANCE ON DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS) THERAPY FOR RHEUMATOLOGY PATIENTS

P.F. Lee, Y.S. Cheung, C.K. Lam, M.C. Leung, C.M. Chan, W.L. Ng. *United Christian Hospital, Hospital Authority, Hong Kong, Hong Kong*

Background: DMARDs are beneficial for a number of rheumatic conditions. However, treatment effect may take a few weeks. On the other hand, patients may experience adverse effects (AEs) early on and they may not be able to follow complicated dosage titration regimen. In order to enhance treatment safety and empower self-management, rheumatic disease patients requiring initiation or change of DMARDs were recruited to a rheumatology nurse phone follow-up program.
Objectives: (1) To evaluate the service outcomes of Rheumatology Nurse Phone follow-up Program and (2) explore the factors that may influence treatment adherence
Methods: Upon initiation of DMARDs therapy at out-patient clinic or before hospital discharge, patients and/or their caregivers will be counseled for the new treatment plan and self-management knowledge by rheumatology nurse. A telephone follow-up by rheumatology nurse will be arranged within 4 weeks to monitor patients' condition. Treatment responses, AEs, drug concordance of patients and advice given in each phone consultation (PC) were recorded. Retrospective case review was performed.
Results: There were 1230 episodes of PC performed by rheumatology nurse in 2015. 180 episodes of PC involved 76 patients (56 female) were randomly selected. The average number of PC was 2.4 times per case. The mean age of patient was 58 (24–85) years. Disease categories mainly involved rheumatoid arthritis (60.5%), systemic lupus erythematosus (7.9%), spondyloarthritis (5.3%) and gout (3.9%). The most common DMARDs prescribed were methotrexate (40.8%), hydroxychloroquine (27.6%), sulphasalazine (22.4%) and 39.5% of the study cases have received steroid courses. Among the 76 patients, 8 (10.5%) have taken wrong dosage and another 4 (5.3%) patients have not started therapy due to worries about potential AEs. Altogether 40 patients (52.6%) reported AEs after starting DMARDs. The most common AEs were rash, itchiness, dizziness, alopecia and oral ulcers. For non-adherence behaviour, 8 patients (10.5%) have self-stopped their medication and another 7 patients (9.2%) have self-adjusted the medication respectively. Eventually 90% of the cases were able to continue therapy with or without adjustment of regimes. Only 7 cases (9.2%) required interruption of current treatment or switching to other DMARDs due to AEs within the study period.

Conclusions: Rheumatology nurse phone follow-up program provided a timely and convenient platform to increase patient understanding of disease and treatment, improve their self-efficacy and enhance safety and concordance with DMARDs treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4421

THU0769-HPR SCOPE FOR BIOLOGIC PRESCRIBING COST SAVING INITIATIVES WITHIN THE RHEUMATOLOGY DEPARTMENT

R. Heaton[1], J. Nasralla[1], A. Ismail[1], A. Brooks[2], L. Mercer[1], C. Filer[1].
[1]Rheumatology; [2]Pharmacy, Stepping Hill Hospital, Stockport, United Kingdom

Background: The rheumatology department at Stepping Hill Hospital prescribes biologic treatment for 400 inflammatory arthritis patients via external Homecare services. Significant resultant drug waste in the event of drug discontinuation is anticipated.[1] The initiation of a pro-active telephone call at three months, to capture and act upon primary inefficacy and non-tolerance has been considered as a potential alternative method for waste reduction.
Objectives: Establish the baseline level of biologic drug waste (via Homecare) following cessation of biologic treatment. Review whether a proactive phone call (and subsequent limitation of supply if appropriate) prior to the three month review at the start of biologic therapy can help reduce biologic waste. Establish whether there is scope to implement other initiatives to reduce waste in the department.
Methods: Patients who had stopped or switched biologic treatments delivered through Homecare providers were identified using the trust's biologic database and clinic records. Information on biologic delivery quantities and schedule were provided by Homecare companies. Data was analysed used Microsoft Excel®; number (and cost in accordance with pharmacy tariffs) of doses "wasted" was calculated by referring the date of treatment cessation with the date and quantity of last biologics deliveries and patient stock levels as reported by the homecare company. Doses obtained free of charge were excluded. Baseline data was captured over a six month period. Four costs were calculated; (1) Total waste. (2) Wasted supply exceeding two months to assess whether an increase in delivery frequency to two monthly could reduce waste. (3) Waste from unopened deliveries to establish whether waste could be reduced by improved patient education around refusing deliveries in the event of treatment failure or intolerance. (4) Waste from the second biologic prescription issued as a result of stopping biologic at the three month review to assess viability of the proactive phone. A proactive patient phone call was then initiated and waste data captured for a three month period following this intervention.
Results: 27 patients stopped treatment during the 6 months baseline data collection. 23 patients had drug waste totalling £ 32,140.80. The total value of wasted stock exceeding two months supply was £ 5,414.36. Three patients accepted deliveries for further supply and stopped treatment before opening final deliveries, creating a waste total of £ 5,509.09. Four patients stopped treatment at their three month review, £ 4,572.22 of additional biologic was supplied and then wasted as a result. Following the pro-active phone call intervention, 21 patients were contacted before their second supply was due and supply subsequently limited for 8 patients, four of whom stopped treatment at their next consultant review. Limiting supply in the four patients saved £ 6,682.
Conclusions: Initiating a proactive phone call at three months following biologic initiation can reduce drug waste. Other initiatives such as patient education to refuse deliveries and increasing delivery frequency also appear viable waste reduction initiatives.
References:
[1] Whiteman J, McVeigh O, Watters M. Hospital Pharmacy and the Pharmaceutical Industry Collaborate to Reduce Waste of Biologic Medicine. Rheumatology. 2016 Apr 1;55.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6333

THU0770-HPR COST SAVINGS BY FAVOURING INFLIXIMAB BIOSIMILARS IN THE EASTERN REGION OF AUSTRIA

B. Reichardt[1], G. Reiter[1], T. Stamm[2], V. Nell-Duxneuner[3].
[1]Behandlungsökonomie, BGKK, Eisenstadt; [2]Section for Outcomes Research, Center for Medical Statistics, Informatics, and Intelligent Systems, Vienna; [3]3Klinikum Peterhof and Ludwig Boltzmann Department for Epidemiology of rheumatic diseases, Nögkk, Baden, Austria

Objectives: Since April 2015, the availability of Infliximab biosimilars offered a new potential for cost savings in limited financial resources of the healthcare system. In Austria, there is currently no open tendering for drugs dispensed at charge of sickness funds and biosimilars take a long time to gain an appreciable market share overall. A contract made between the public hospital operator and the regionale sickness fund of the Eastern Austrian county Burgenland (BGKK) offered a new opportunity regarding the interface problems due to the dually financed (inpatient and outpatient care is separately financed in Austria) health system. Only outpatient care is covered by regional sickness funds.
Methods: With reference to the NOR-SWITCH study (1), confirming the interchangeability of the branded Infiximab and infliximab biosimilar, and the large price advantage of the latter, the BGKK agreed as an exception in the Austrian health system on direct reimbursement of infliximab to the public hospital operator (inpatient care).
The cost savings were calculated based on the monthly invoices of the hospitals. Instead of € 477.19 for 100 mg of branded infliximab, the price for biosimilar infliximab does not exceed € 300.–. The 23 patients on biosimilar were infused with 9,400 mg infliximab overall.
Results: After signing the agreement in December 2016, 23 consecutive patients, representing 82% of all patients on infliximab in Eastern Austrian county Burgenland, switched to or were incident users of an infliximab biosimilar, the 18% have not yet switched due to remaining stocks of branded infliximab or were adolescents where switching is not forced because of lacking data. According to the individual dosing and a price benefit of about 37%, monthly cost savings of about € 16,650.00 could be generated.
Conclusions: Despite availability of cost-effective infliximab biosimilars in Austria, the drugs did not gain significant market share, in contrast to the Scandinavian healthcare systems, $<$4% vs. $>$90% in the first half year of 2016. Further research is needed including clinical data to strengthen the results of this pilot study.
References:
[1] Jørgensen, K. et al. Biosimilar infliximab is not inferior to originator infliximab: Results from the 52-week randomized NOR-SWITCH trial. United European Gastroenterology Week 2016; LB15.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6202

THU0771-HPR INCORPORATING SENIOR PHARMACIST INPUT IN TERIPARATIDE PATHWAY ENSURES ADHERENCE TO PRESCRIBING GUIDANCE - AUDIT/QUALITY IMPROVEMENT RESULTS FROM A DISTRICT RHEUMATOLOGY UNIT

W. Gan, L. Bromilow, S. Vasireddy. *Bolton NHS Foundation Trust, Bolton, UK*

Background: Teriparatide is licensed for upto two years to treat severe osteoporosis. It is the most expensive osteoporosis treatment available (around £ 3500 per year). Hence a locally adapted national NICE guidance is used for prescribing in our department, but the previous level adherence was uncertain. In 2011, a directory of services was agreed for our metabolic bone clinic. At the time a Rheumatology senior pharmacist review with the prescribing senior clinician was agreed on our teriparatide treatment pathway, including pre-treatment DXA, and a specified bone profile screen before treatment and for repeat prescribing at specified intervals. The agreement also incorporated access for our patients to senior pharmacist advice if needed via the department's secreterial team.
Objectives: Our objective was to assess the impact of the senior pharmacist input on our adherence to the agreed guidelines in our Teriparatide pathway, including assessing treatment completion and response.
Methods: Patients with osteoporosis who were started on Teriparatide between 2011–2015 were identified from pharmacy prescribing spreadsheets. A retrospective review of case notes of all patients were carried out. Data including age, gender, prior agents tried, pre-treatment bone profile, pre and post treatment DXA, and treatment completion were collected on a Microsoft Excel 2010 spreadsheet for processing and descriptive statistics.
Results: 33 patients who were started on teriparatide treatment between 2011–2015 were identified (29 female and 4 male). Mean age was 76.2 (range 63–92). All had pre-treatment DXA, and 32 (97%) were compliant with recommendations for initiation of teriparatide treatment with respect to DXA (one patient borderline). All 33 patients had a pre-treatment bone profile within acceptable limits before start of treatment (adjusted Calcium, Serum Parathyroid Hormone, Vitamin D level, e-gfr). 28 (84.8%) patients tried one agent before initiation of Teriparatide treatment and 5 (15.2%) patients tried 2 agents. 24 (72.7%) patients completed the full course of recommended treatment. 11 out of 24 patients who completed Teriparatide treatment have had post-treatment DXA. 3 out of 24 patients who completed Teriparatide treatment had a fragility fracture after treatment.
Conclusions: This audit confirms the benefit of incorporating Rheumatology senior pharmacist review in the pathway from the excellent compliance with guidelines in initiating and managing Teriparatide noted in the results. This is likely to have also contributed to the high completion rate of the treatment course. However, only 11 out of 24 had post treatment DXA, and this needs improvement by the next audit cycle, through input of senior clinicians who are in charge of requesting DXA. We would, therefore, recommend incorporating senior pharmacist input for review in teriparatide treatment pathways routinely.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.7031

THU0772-HPR VARIATION IN RHEUMATOLOGY NURSING CARE IN THE NETHERLANDS: A SURVEY AMONG NURSES

Y. Van Eijk-Hustings on behalf of Working Group Rheumatology Nursing Research. *Clinical epidemiology and medical technology assessment/Patient & Care, Maastricht University Medical Centre, Maastricht, Netherlands*

Background: EULAR recommendations for the role of nurse aim at guaranteeing a certain standard of care for people with rheumatic musculoskeletal diseases

(RMDs) and at optimising the use of nursing competencies [1]. In the Netherlands, these recommendations seem well implemented. There are specialised nurses (SNs); nurses trained at a secondary vocational or Bachelor level, followed by a one-year educational program in rheumatology, and nurse practitioners (NPs), trained on a Master Level. SNs provide information, education and (psychosocial) support, but also monitoring of disease, supervised by a rheumatologist. NPs are trained and legally authorised to provide integral medical (e.g. prescribing) and nursing care independently. Informal discussions among rheumatology nurses suggest a variation in roles, and tasks of SNs and NPs, and of care organisation in rheumatology practices.

Objectives: The objective of this study was to explore current roles and tasks of SNs and NPs, and care organisation in order to visualise potential variation.

Methods: A web-based questionnaire, based on literature [2] and existing task descriptions was disseminated among all members of the Dutch Nurses Association, unit Rheumatology (n=257). The questions were in closed-ended, multiple choice, likert-scales and open-ended format as appropriate. Data were analysed descriptively. Subgroup analyses were carried out for SNs and NPs.

Results: In total 84 nurses, 75 SNs and 9 NPs responded. Characteristics, roles and main tasks are presented in Table 1.The majority of the SNs, 96.4%, and 100% of the NPs work at the outpatient clinic, providing individual face-to-face consultations or telephone support.

Table 1

	SN (n=75)	NP (n=9)
Age, mean years (sd)	47.6 (9.5)	46.7 (10.2)
Female (%)	98.7	88.9
Appointed, mean hours/week (sd)	24.8 (6.0)	33.1 (4.1)
Days/week, median (IQR)	3 (3.4)	4 (4,4)
Role (%)		
SN	85.3	33.3
NP	0	55.6
Other (e.g.combination with research or infusion)	14.7	11.1
Tasks (% always/often)		
Information and education about disease	89.3	100
Information and education about treatment	90.7	88.9
Metrology	78.7	100
Joint examinations 57.3	100	
Make diagnosis new patients	1.3	22.2
Manage patients with RMDs	54.6	88.9
Administrate medication	45.4	22.2
Give intra-articular injections	1.3	22.2
Independent prescribing	2.7	77.8
Screen for comorbidities	29.3	44.4
Manage patients on biologic therapy	54.7	100
Provide psychosocial support	82.7	77.8
Refer to other health professionals	58.7	77.8
Monitor patients on DMARD	70.7	88.9
Self-management support	77.3	33.3
Time for consultations, median (IQR) minutes		
New patient (diagnosing)	27.5 (0,30)	42.5 (32.5, 45)
Newly diagnosed patients	45 (30,60)	30 (17.5, 60)
Follow-up patients	30 (20,30)	17.5 (15, 20)

Conclusions: Differences in roles, tasks and available time for consultations visualise variation in care organisation and in the content of rheumatology nursing care, also within the SN and NP group respectively. Further research on these differences is necessary but they show inequity of care for people with RMDs in the Netherlands and also suggests suboptimal use of nursing competencies.

References:

[1] van Eijk-Hustings Y, et al. EULAR recommendations for the role of the nurse in the management of chronic infl ammatory arthritis. Ann Rheum Dis. 2012;71:13–19.

[2] Ryan S, et al. Characterizing the clinical practice and professional behaviour of rheumatology nurse specialists: a pilot study. Musculoskelet. 2010;8(3):136–42.

Acknowledgements: Funded by Dutch Rheumatology Nurses Association, unit Rheumatology.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2928

FRIDAY, 16 JUNE 2017

HPR measuring health (development and measurement properties of PROs, tests, devices) —

FRI0732-HPR THE PSS-QOL: DEVELOPMENT AND FIRST PSYCHOMETRIC TESTING OF A NEW PATIENT-REPORTED OUTCOME MEASURE FOR PSS PATIENTS

A. Lackner[1], J. Hermann[1], J. Unger[2], T. Stamm[3], M. Stradner[1], W. Graninger[1], C. Dejaco[1]. *[1]Dept. of Rheumatology & Immunology, Medical University of Graz, Graz; [2]Dept. of Health Studies, University of Applied Sciences, Bad Gleichenberg; [3]Institute of Outcomes Research, Medical University Vienna, Vienna, Austria*

Background: Patients with primary Sjögren Syndrome (PSS) are affected by glandular and extraglandular manifestations leading to physical and psychological impairment. To what extent these factors affect the health related quality of life (HRQL) of these patients is largely unexplored. Disease activity scores for PSS have been developed but there is no disease-specific HRQL questionnaire available so far.

Objectives: To develop a questionnaire for the assessment of HRQL in PSS.

Methods: In a previous qualitative study, concepts related to HRQL in PSS were identified by focus-group interviews with PSS patients. Based on these concepts, a questionnaire (PSS-QoL) was developed focusing on two main topics: physical (pain and dryness) and psychosocial dimension. The first draft of this questionnaire was evaluated by semi-structured interviews with PSS patients (n=6) and rheumatologists (n=4). Based on their feedback, a revised questionnaire was constructed and re-evaluated by the patients and physicians. Subsequently, psychometric testing of PSS-QoL was performed in 75 PSS patients of the outpatient clinic of the Medical University Graz. For testing of internal consistency Crohnbach's α was used. Convergent construct validity was tested by correlating the scores with the ESSPRI and the EQ-5D. Reliability was examined by asking patients who considered themselves to be in a stable disease to complete the questionnaire 1–2 weeks apart. In addition, an English version of PSS-QoL was was developed using a standard methodology for translation.

Results: Out of the 75 PSS patients, 91% were female, disease duration was 4.8±4.08 years and age of patients was 58.5±12.5 years.The internal consistency of the PSS-QoL showed a Crohnbach's α of 0.892 and we found a moderate correlation of the PSS-QoL with the ESSPRI ($Corr_{coeff}$=0.625) and the EQ-5D (EQ5D-pain/discomfort; $corr_{coeff}$=0.531). A second assessment was performed after 1–2 weeks in 21 patients with stable disease. The ICC for PSS-QoL was 0.958 (95% CI 0.926 to 0.981). In comparison, the ICC for EQ-5D in this population was 0.854 (95% CI 0.735 to 0.933). Subsequently, the final German version of PSS-QoL was translated forward and back into English by native speakers.

Conclusions: A questionnaire to assess the HRQL in PSS patients has been developed and tested for its psychometric properties. The PSS-QoL should allow for a better and more comprehensive assessment on patients' HRQL in PSS. Multicentre studies for further validation are needed.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3372

FRI0733-HPR THE EDUCATIONAL NEEDS OF PATIENTS WITH UNDIFFERENTIATED SPONDYLOARTHRITIS

A. Bremander[1,2,3], E. Haglund[2,3], S. Bergman[1,3,4], M. Ndosi[5]. *[1]Department of Clinical Sciences, Section of Rheumatology, Lund; [2]School of Business, Engineering and Science; [3]Spenshult Research and Development Center, Halmstad; [4]Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Primary Health Care Unit, Department of Public Health and Companionship Medicine, Gothenburg, Sweden; [5]Department of Nursing and Midwifery, University of the West of England, Faculty of Health and Applied Sciences, Bristol, United Kingdom*

Background: The educational needs of people with undifferentiated spondyloarthritis (USpA) have not been well studied. The educational needs assessment tool (ENAT) has been translated into Swedish and validated in other rheumatic diseases but not USpA.[1]

Objectives: To validate the educational needs assessment tool (ENAT) in people with USpA and use it to study their educational needs.

Methods: A cross-sectional study recruiting a random sample of patients with USpA from a hospital register. USpA was diagnosed according to the International Classification of Disease, ICD-10 (M46.0, M46.1, M46.8, and M46.9).[1] The study was approved by the Regional Ethics Board and all included patients signed an informed consent. We used a postal survey to collect data on disease activity (BASDAI) and educational needs (Swedish version of the ENAT).[2] The data was then utilized to assess the construct validity, internal consistency, unidimensionality and response bias of the ENAT using Rash analysis. Given fit to the Rasch model, we transformed the ENAT ordinal scores into interval logit-based scores before deploying descriptive and inferential statistics. Total ENAT Score ranges between 0 (no needs) and 156 (the highest level of needs), and comprises seven subscales (pain 0–24, movement 0–20, feelings 0–16, disease 0–28, treatments 0–28, self-help 0–24 and support 0–16). Finally, we categorised the data by gender, age (median split) and disease activity (BASDAI split at 4) and assessed differences between patient subgroups using the student's t-test.

Results: Complete responses were derived from 77 patients (48 women), mean (SD) age 50 (12) years, disease duration was 16 (11) years, BASDAI 4.9 (1.9) and BASFI 3.1 (2.3). When used as a 7-subscale questionnaire, the ENAT satisfied the requirements of Rasch model (c^2=11.488; p=0.119) including strict unidimensionality.

Overall, the mean (SD) ENAT scores for patients with USpA was 86 (32). Women reported higher needs than men in the domains of pain, mean (SD) 13.1 (6.8) vs. 10.1 (6.0), p=0.05; movement mean (SD) 13.0 (5.5) vs. 9.9 (5.7), p=0.02 and self-help, mean (SD) 17.0 (5.8) vs. 14.1 (5.0), p=0.03). Higher disease activity (BASDAI >4) was associated with higher educational needs, mean (SD) 92.6 (31.9) vs. 73.7 (29.4), p=0.02. There was no significant difference in educational needs between age groups.

Conclusions: The Swedish ENAT has been validated in USpA thus enabling an accurate estimation of the educational needs of people with USpA in Sweden.

Our data suggest that women and patients with higher disease activity are likely to have high levels of educational needs and these groups should be targeted in educational interventions for people with USpA.

References:
[1] Classification of diseases, WHO, http://www.who.int/classifications/icd/en/ acessed 170103.
[2] Ndosi M, Bremander A, Hamnes B, et al. Validation of the Educational Needs Assessment Tool as a Generic Instrument for Rheumatic Diseases in 7 European Countries. Ann Rheum Dis 2014;73:2122–2129.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2989

FRI0734-HPR EFFECTS OF VIRTUAL REHABILITATION ON SHOULDER PERIARTHRITIS

B. Kapşigay[1], Z. Sari[1], B. Kavlak[1], I. Aras[2], A. Tanhan[1]. *[1]Physiotherapy and Rehabilitation, Marmara University Health Science Institute; [2]Physiotherapy and Rehabilitation, Special Kızılay Medical Center, Istanbul, Turkey*

Background: The virtual rehabilitation (Nintendo Wii) program works with a 3-dimensional, computer-assisted, virtual reality creation system.The system creates a mirror effect and provides the smoothness of the movement of the adult. It keeps visual and sensory feedback during exercise.The avatar that appears on the screen detects motion and displays the result thanks to the control commander. The use of virtual reality practice in the exercise program is a new way of improving participation and motivation of participants.
Objectives: The aim our study is to investigate the effect of virtual rehabilitation on kinesophobia and clinical fragility in patients with shoulder periathritis.
Methods: Fifteen cases diagnosed with shoulder periarthritis were included in the study. In our study, we used Tampa Kinesophobia Scale for kinesophobia, VAS for pain severity, manual muscle test for muscle strength and goniometer for ROM. In addition to Clinical fragility Scale for fragility and 4-item Quality of Life Questionnaire were used to assess quality of life. Finally, Shoulder Pain and Disability Index (SPADI) was used for shoulder disability. Eight of 15 patients were included in the control group (CG) and 7 in the virtual rehabilitation group (VRG). Both groups were treated with Therapeutic US, TENS and Cold Pack. In addition to these, the control group consisted of 15 sessions of active stretching and strengthening exercises for 20 minutes each session; the VRG was given a total of 15 sessions of the virtual rehabilitation program for 45 minutes each session, with 3 sessions per week. Intra-group pretreatment and post-treatment differences were analyzed by Wilcoxon test, and inter-group comparisons were analyzed by Mann-Whitney U test.
Results: Statistically significant reductions in Frajilite, Kinesophobia, SPADI and VAS values were observed in the VRG analyzes; A statistically significant increase in the 4-item quality of life questionnaire, range of motion and muscle strength values was assessed ($p<0.05$). In the CG, there was a statistically significant decrease in kinesophobia, VAS and SPADI values; There was a statistically significant increase in joint range of motion and muscle strength evaluations ($p<0,05$). There was no statistically significant difference in the fragility evaluation of the CG ($p>0,05$).
Fragility and kinesophobia decreased in both groups after treatment compared to before treatment, but this decrease was found to be higher in VRG ($p<0.05$).
Conclusions: As a result of our study, virtual rehabilitation in the treatment of kinesophobia and fragility in shoulder periarthritis patients was game-focused and it was found to be an effective method for increasing participation and biofeedback. Virtual rehabilitation was considered as an alternative to conventional physiotherapy and rehabilitation programs.

References:
[1] Cherniack EP, Florez HJ, Troen BR. Emerging therapies to treat frailty syndrome in the elderly. Altern Med Rev 2007;12:246–58.
[2] Topinková E. Aging, disability and frailty. Ann Nutr Metab 2008;52:6–11.
[3] Bal, A. Ekşioğlu, E. Gürçay, E. Karaahmet, Ö. Küçük, S. ve Çakcı, A. (2008). Subakromiyal sıkışma sendromlu hastalarda omuz dizabilitesinde etkili faktörlerin değerlendirilmesi. Turkiye Klinikleri Journal of MedicalSciences, 28, 468–472.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5772

FRI0735-HPR ANALYSIS OF LEFT VENTRICULAR FUNCTION WITH ECHOCARDIOGRAM IN PATIENTS WITH PSORIATIC ARTHRITIS AND NOT DIAGNOSED CARDIOVASCULAR DISEASE

P. Egea-Serrano[1], A.C. Haro-Martínez[2], A. Vidal[1], D. Palma-Sánchez[2]. *[1]Cardiology; [2]Rheumatology, Hospital Rafael Mendez, Lorca, Spain*

Background: It is known that some rheumatologic disorders may affect the cardiovascular system. In the last years, psoriatic arthritis (PsA) has been pointed out as one of those.
Objectives: The aim of this study was to analyze if there was any subclinical dysfunction sign in patients with PsA of whom no cardiovascular disease had been diagnosed.
Methods: Forty three patients with PsA were studied. A comprehensive echocardiogram was performed. Variables recorded for each patient were: left ventricular (LV) dimensions, LV and right ventricular (RV) systolic function, valve morphology and function, LV diastolic function assessment, and longitudinal strain (LS) assessment with speckle tracking imaging. Information on age, sex, cardiovascular risk factors (hypertension, diabetes, dyslipemia, renal disease and smoking), and evolution time of PsA was also recorded. An electrocardiogram was also carried out for each patient.
Results: There were 23 men and 20 women. The mean age was 52±12 years old. The PsA mean evolution time was 6.8±5.3 years. Most of patients had at least one cardiovascular risk factor. All patients were in synusal rhythm. The LV end-diastolic diameter and ejection fraction, left atrium, and RV function were within normal limits. Men had overall a thicker interventricular septum (12±1.7 mm) when compared to women (9.7±1.6mm). 86% patients had a normal mitral valve function, as so 91% with aortic valve. None of them had findings suggesting pulmonary hypertension, or pericardial effusion. The diastolic function assessment in the general population revealed normal average of septal and lateral A' and S waves peak velocities, and E/E' ratio. Men had lower septal E' and S waves values and higher septal A' wave velocity. Nearly 50% of patients had a low septal E' or lateral E' wave peak velocity. 13 patients (30%) had impaired both septal E' and lateral E' waves, who were older and mainly men. The strain analysis showed an average of global LS - 17.9%±3%, two-chambers general LS -17.2%±5%, three-chambers general LS -19%±5.2%, and four-chambers general LS -17.3%±3.5%; without any significant difference between sex. 26 patients (60.5%) had global LS above normal limits; these were younger and with less PsA evolution time. Longitudinal strain values tended to be less negative at the basal level.
Conclusions: Half of the patients with PsA were found to have some feature of diastolic dysfunction and more than the half of them had a slightly impaired global longitudinal strain value. Further studies could be of value to determine whether these findings would have a specific impact on the follow-up in this kind of patients.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2990

FRI0736-HPR VALIDITY AND RELIABILITY OF PERFORMANCE TESTS ASSESSING BALANCE AND FALL RISK IN PATIENTS WITH TOTAL KNEE ARTHROPLASTY

D.C. Sarac[1], B. Unver[2], S. Cekmece[2], V. Karatosun[3]. *[1]Division of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Izmir Katip Celebi University; [2]School of Physiotherapy and Rehabilitation; [3]School of Medicine, Department of Orthopaedics, Dokuz Eylul University, Izmir, Turkey*

Background: Total knee arthroplasty (TKA) is a common surgical intervention that is performed with an aim to treat severe osteoarthritis (OA) of knee. Even though there is a rapid improvement in knee pain, functional improvement is limited in the following year after the surgery. Increased fall risk due to impairments in balance is one of the most common limitations after TKA. Therefore, balance and fall risk evaluation is an essential part of the assessment.
Objectives: The aim of this study was to determine the validity and reliability of various performance tests that are used for evaluating balance and fall risk in patients with TKA.
Methods: This study included 32 OA patients (27 F, 5 M) who undergone TKA surgery 6 months prior to the study. Mean age and BMI of the patients were 64±10,58 and 30,49±5,87, respectively. Participants performed the Timed Up and Go Test (TUG), 10 Meter Walk Test (10MWT), Single Leg Stance Test (SLST), Functional Reach Test (FRT), 2 Minute Walk Test (2MWT), Five Times Sit to Stand Test (5x SST) as performance tests. Each of the tests was performed twice, with a

Table 1. Test-Retest Reliability analysis of the performance tests

	Day 1 Mean (SD)	Day 2 Mean (SD)	ICC (95% CI)	SEM	MDC_{95}
TUG (sec)	10.67±4.53	10.61±5.05	0.95 (0.90–0.97)	1.01	2.79
10 MWT (sec)	9.89±3.37	9.72±3.03	0.97 (0.94–0.98)	0.58	1.6
SLST (sec)	14.96±14.90	18.97±19.15	0.74 (0.48–0.87)	7.59	21.02
FRT (cm)	26.19±7.33	26.60±6.63	0.94 (0.88–0.97)	1.79	4.95
2 MWT (m)	145.25±37.63	145.32±38.06	0.98 (0.96—0.99)	5.32	14.73
5x SST (sec)	13.54±6.26	13.04±5.03	0.96 (0.91–0.98)	1.25	3.46

Unit: Mean ± SD, ICC: Intraclass Correlation Coefficient CI: Confidence Interval, SEM: Standard Error of Measurement, MDC: Minimal Detectable Change at 95% Confidence Interval, sec: seconds, cm: Centimeters, m: meters, TUG: Timed Up and Go Test, 10 MWT: 10 Meter Walk Test, SLST: Single Leg Stance Test, FRT: Functional Reach Test, 2 MWT: 2 Minute Walk Test, 5x SST: Five Times Sit to Stand Test.

Table 2. Concurrent Validity of Performance Tests

	r value	*p**
TUG (sec)	-0.713	$p<0.01$
10 MWT (sec)	-0.736	$p<0.01$
SLST (sec)	0.754	$p<0.01$
FRT (cm)	0.695	$p<0.01$
2 MWT (m)	0.792	$p<0.01$
5x SST (sec)	-0.766	$p<0.01$

*Spearman Correlation Test; sec: seconds, cm: Centimeters, m: meters, TUG: Timed Up and Go Test, 10 MWT: 10 Meter Walk Test, SLST: Single Leg Stance Test, FRT: Functional Reach Test, 2 MWT: 2 Minute Walk Test, 5x SST: Five Times Sit to Stand Test.

1-day interval. ICC models were used to determine the test-retest reliability. Berg Balace Scale (BBS) was used as the reference standard to establish concurrent validity.

Results: All tests showed good to excellent reliability (ICC >0.94) except SLST which showed moderate to good reliability (ICC=0.74). Three of the tests (SLST, 10 MWT, 5x SST) found to have good to excellent validity (r>0.75) and three (2 MWT, TUG, FRT) found to have moderate to good reliability (r>0.69). Results are presented in details at Table 1 and Table 2.

Conclusions: TUG, 10MWT, SLST, FRT, 5x SST and 2 MWT are reliable and valid outcome measures, and could be used to assess balance and fall risk in patients with TKA. MDC scores presented in this study can be used to evaluate change in performance over time or effectiveness of interventions. 2 MWT and 5x SST were determined as the most reliable and valid methods among the investigated tests.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5918

FRI0737-HPR THE SOURCES OF PAIN IN ABDOMEN IN PATIENTS WITH RHEUMATOID ARTHRITIS

H. Palhuyeva[1], A. Litviakov[1], V. Shynkovski[2], N. Podolinskay[2]. *[1]Internal diseases; [2]Vitebsk State Order of Peoples' Friendship Medical Universityon, Vitebsk, Belarus*

Background: Systemic diseases of connective tissue associated with the early development of atherosclerosis [1,2]. It is well-known that the main cause of decrease the quality of life patients with rheumatoid arthritis (RA) is a chronic pain syndrome. The cause of pain can be joint inflammatory process, systemic manifestations of RA (vasculitis, pericarditis, pleurisy, polyneuropathy), complications of drug therapy, comorbid conditions. Pain in the stomach area may be associated with NSAID-gastropathy, problems with spinal discs, and perhaps with atherosclerotic lesions of the abdominal aorta.

Objectives: To estimate atherosclerotic changes of arteries in patients with RA and determine possible sources of pain in the abdomen by ultrasound-control palpation.

Methods: We included 75 patients with RA (age 38,7±7,4, males 93,3%) and 29 healthy subjects, matched for age and gender, without a history of cardiovascular diseases. An ultrasound investigation of the arterial vassal with measurement of the intima-media thickness (IMT) of carotids was performed. To determine the source of pain in the abdominal cavity ultrasound-control palpation of duodenal bulb, gallbladder, lumbar discs, and abdominal aorta was done. Severity of pain was assessed using the VAS.

Results: It has been determined, that in RA group IMT was 0.8 mm (0.7–0.9), compared with 0,6 mm (0,6–0,7) in control group. IMT positively correlate with the age, duration of disease, Ritchie index, C-reactive protein level. In 22 (29,3%) patients with RA we found atherosclerotic plaques lesion in carotids, aorta, and vessels of the lower extremities. Present of atherosclerotic plaques associated with disease durations (12 years (10–15) in group with plaques and 5 years (3–8) in group without plaques). The presence of atherosclerotic plaques is associated with rheumatoid factor (c^2=1,02, p>0,05), and systemic manifestations of RA (c^2=15,89, p<0,001).

In RA group 36 (48%) patients had indicated the presence of pain in the abdomen while performing ultrasound control palpation. In 15 (20%) cases was detected pain during palpation of the lumbar spine, VAS 48 (36–59). In 21 (28%) cases, patients indicated pain during palpation of the abdominal aorta, VAS 42 (31–65). In this group of patients we found signs of the atherosclerotic lesions of aorta: change in the contour of the vessel, the heterogeneous structure of the vascular wall. Atherosclerotic plaques in the abdominal aorta are founded in 21 (28%) cases.

Conclusions: Patients with RA had an increase thickness of IMT and atherosclerotic plaques, which appear in various vascular regions. During performing ultrasound-control palpation in 36 (48%) patients was detected pain, associated with vertebral changes 15 (20%), and with atherosclerotic changes of abdominal aorta – 21 (28%).

References:

[1] High incidence of cardiovascular events in a rheumatoid arthritis cohort not explained by traditional cardiac risk factors. I.D. del Rincon et al. Arthritis Rheum. 2001;44:2737–2745.

[2] Cardiovascular disease and risk factors in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. C. Han et al. J. Rheumatol. 2006;33(11):2105–2107.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5921

FRI0738-HPR QUALITY IN REHABILITATION FOR RHEUMATIC AND MUSCULOSKELETAL DISEASES (RMDS): DEVELOPMENT AND TESTING OF A RMD REHABILITATION QUALITY INDICATOR SET

I. Johansen[1], M. Klokkerud[1], T. Glott[2], M. Larsen[3], K. Lande[4], K.B. Hagen[1], I. Kjeken[1]. *[1]National Advisory Unit on Rehabilitation in Rheumatology, Diakonhjemmet Hospital; [2]Sunnaas Hospital; [3]National Rheumatism Association, Oslo; [4]Haugesund Rheumatism Hospital, Haugesund, Norway*

Background: Rehabilitation in Norway is characterized by a lack of coordination across levels of care, and by large variations in content and quality. A means to monitor the quality of care is to use quality indicators (QI), which are related to structure (the settings in which care is given), process (what is actually being done) or outcome of health care.

Objectives: To develop and test a set of quality indicators for rehabilitation of people with RMDs.

Methods: The QI set was developed following the Rand/UCLA Method and pilot-tested for validity and feasibility in 29 specialist and primary care rehabilitation units. Pass rates were recorded in telephone interviews with managers of the rehabilitation units (structure QIs (yes/no)), or patients (process and outcome QIs (yes/no)). Time use and participants rating of face validity on a numeric rating scale (0–10, 10=high validity) were recorded. Separate QI pass rates and summary QI pass rates were calculated.

Results: A total of 164 patients (mean (SD) age 58.5 (16.5) years and 76% women) participated. Mean (range) validity score for managers/patients was 8.3 (8)/7.9 (9), and mean answering time was 6.0/5.5 minutes.

A 100% summary pass rate was reached by only two of the rehabilitation units and 4% of the patients.

Conclusions: To our knowledge this is the first QI set developed to measure QI pass rates for rehabilitation of RMDs. The results indicate that the QI set is acceptable to respondents, and it's validity and feasible format make it suitable for monitoring quality of rehabilitation. The large variety in pass rates suggests a high potential for quality improvement in rehabilitation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1809

FRI0739-HPR A RHEUMATOLOGY PATIENTPANEL: THE PATIENT IS THE EXPERT, WE ARE THE SPECIALIST

J.E. Voorneveld-Nieuwenhuis, M.D. Kok, N. Basoski, M. Holtrop, D. Lopes Barreto. *Rheumatology, Maasstad Hospital Rotterdam, Rotterdam, Netherlands*

Background: Patient participation is known in the field of rheumatology research and is becoming more customary. The patient perspective can improve the care and line specific needs of the patient to the delivered care.Recently, ourRheumatology department within the Maasstad Hospital introduced the Value Based Health Care principle in order to optimize the current healthcare system.

Abstract FRI0738-HPR – Table 1. Structure, process and outcome Quality indicators (QI) with Pass rates (PR) in %

STRUCTURE QI (answered by unit managers)	**PR**	**PROCESS QI (answered by patients)**	**PR**
Has a defined patient target group	96		
Procedures for		Had an initial bio-psycho-social assessment	85
Developing an individual rehabilitation plan	76	Received a written rehabilitation plan	77
Regular team meetings with patients	72	Participated in minimum 2 team meetings	69
Meetings with possibility to participate for next of kin and external HPs*	65	It was possible for next of kin and external HPs to participate in the team meetings	19
Individual plans for follow-up after discharge	52	Received an individual plan for follow-up	65
		External HPs* were involved in follow-up	22
Procedures for involving patients in		**Participated in**	
Setting goals	93	Setting goals	91
Planning the intervention	93	Planning the intervention	71
Evaluating the intervention	89	Planning follow-up	74
Use of validated assessment instruments	69	**OUTCOME QI (answered by patients)**	**PR**
Assessment of		Satisfied or very satisfied with rehabilitation	88
Goal attainment at discharge	41	Reached important goals	89
Goal attainment 3–6 months after discharge	21		
Function at admission and discharge e	79	Had important improvement in physical, psychological or social function	86
Function 3–6 months after discharge	24		
HRQoL at admission and discharge	29	Had improvement in quality of life	77
HRQoL 3–6 months after discharge	17		
Registration of adverse events	96	Experienced negative events	12

*External HPs are health professionals from other health care settings, such as primary care.

We thought to measure the value for patients we should let them participate in the project and asked them about what is of value for them and what are there goals. A good reason to start with a patient panel.
Objectives: For this reason we aimed to create a patient panel of rheumatology patients that are well informed and prepared to actively cooperate and participate in research, and co-design novel healthcare strategies.
Methods: Staff members (e.g. doctors and nurses) were asked to nominate patients that are expected to actively participate in the panel. Nominated patients were verbally approached and asked to participate. After mutual agreement a contract was signed were patients discretion was warranted, the capacity to handle confidential information was assessed and equality between members of the panel and staff was ensured. Enlargement of the panel is primarily staff-driven, but panel members are also invited to actively recruit other rheumatology patients.
Results: The initial enrolment period lasted for six months. Thereafter, meetings were organized were discussion were held on various themes such as goals and value for rheumatology patients. Additionally, a focus group of rheumatoid arthritis (RA) patients was assembled to evaluate a PROMs measurement tool. To date, a number of four panel discussion have been held. Currently, our patient panel consists of 54 patients with all kinds of rheumatic diseases. Their demographic and clinical data are presented in Table 1.

Table 1

	Value
Patients (n)	54
Gender (%male)	17
Age (yrs)	51 (20–77)
Disease duration (yrs)	9 (0–30)
Diagnosis (%)	
– Rheumatoid Artrithis	54
– Arthrosis	15
– Fibromyalgia	10
– SpA (including APs and SA)	12
– Other	9

Our panel has been asked to participate in other (hospital-wide) programmes including the development and evaluation of a patient portal. We organize about three meetings for the whole panel every year and arrange focus group meetings to discuss specific subjects.
Conclusions: Panel members are very open and enthusiastic. Some quotes: "I'm happy to do something in return for the good care I receive.", and "I want to promote participation in scientific research". Deployment of patient participation for co-creating innovations alongside research is an asset these days to connect changes to patients perception.
In real live involving patient as an expert is not an effortless action for both patients and the expert care takers, it leads to satisfaction and an effective treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3454

FRI0740-HPR ONLINE REMOTE MONITORING OF PATIENTS WITH RHEUMATOID ARTHRITIS: FIRST RESULTS OF A PILOT STUDY

L. Renskers[1], S.A.A. Rongen[1,2], S. Teerenstra[3], M.E.J.L. Hulscher[1], P.L.C.M. van Riel[1,2]. *[1]IQ Healthcare, Radboud Institute for Health Sciences, Radboud university medical center, Nijmegen; [2]Rheumatology, Bernhoven, Uden; [3]Department for Health Evidence, Radboud Institute for Health Sciences, Radboud university medical center, Nijmegen, Netherlands*

Background: Since the disease activity of patients with RA tends to fluctuate between visits and disease flares are easily missed during regular visits, patients might benefit from a more closely spaced determination of disease activity, which could be realised by iMonitor[1]. iMonitor is a Software Medical Device developed and funded by Pfizer. This online system allows patients to complete three kinds of patient-reported outcome measures (PROMs): the Health Assessment Questionnaire (HAQ), Rheumatoid Arthritis Impact of Disease (RAID) and Rheumatoid Arthritis Disease Activity Index-5 (RADAI-5). iMonitor might contribute to identification of patients who need additional medical attention in between visits and reduction of visits for patients with stable disease activity.
Objectives: To determine the degree to which the PROM-scores in iMonitor are associated with DAS28. Moreover, PROM preferences and completion rates were studied.
Methods: Patients were recruited at Bernhoven (Uden, the Netherlands) by an announcement on the hospital website, leaflets and meetings. Instruction classes were organised in which researchers assisted patients in using iMonitor. Patients indicated which PROM(s) they want to complete in iMonitor and chose reminder email frequency (weekly, two-, four, six, or eight-weekly). Descriptive analyses were used to describe characteristics of the study population. Scatter plots with regression equations were performed with DAS28 as dependent and PROM as independent variable to determine the association between DAS28 and PROMs. Moreover, Pearson's correlations were calculated. PROM-scores within the fourteen day window before and after DAS28 assessment were included.
Results: In total 33 patients with RA were included, seventeen of them were female (52%). Mean (±SD) age was 56±11 years. Seventeen patients (52%) attended the instruction classes. Majority of patients (n=10) chose all three PROMs to complete, nine patients chose RAID+RADAI-5, seven chose HAQ+RAID, three chose RAID, two chose RADAI-5 and two chose HAQ+RADAI-5. From March 2016 until December 2016, 435 RAID-values, 329 RADAI-5-values and 222 HAQ-values were gathered. When taking PROM-values within the fourteen day window before and after DAS28 assessment, 159 DAS28-values could be coupled to 320 PROM-values. Regression analysis showed the following proportions of explained variance (R^2): 0.17 for HAQ, 0.32 for RAID and 0.29 for RADAI-5. Pearson's correlation coefficients were 0.41 for HAQ, 0.57 for RAID and 0.54 for RADAI-5. Most chosen reminder email frequency was four weeks (n=21). Completion rates (measured until December 31, 2016) were 65% for patients with one week PROM-frequency and for patients with two, four, six and eight week frequency completion rates were 39%, 24%, 30% and 0%, respectively.
Conclusions: RAID and RADAI-5 were moderately associated with DAS28 and showed highest proportions of explained variance. The association between HAQ and DAS28 was weaker. Patients receiving a weekly reminder email showed highest completion rates. This pilot study is a first step towards personalised healthcare and patient involvement in online remote monitoring.
References:
[1] Medical and Educational Goods and Services (MEGS): iMonitor. 2014 Available from: http://www.pfizer.co.uk/content/medical-and-educational-goods-and-services-megs-imonitor.
Disclosure of Interest: L. Renskers Grant/research support from: Pfizer, S. Rongen: None declared, S. Teerenstra: None declared, M. Hulscher: None declared, P. van Riel Grant/research support from: Pfizer
DOI: 10.1136/annrheumdis-2017-eular.5801

FRI0741-HPR SCREENING FOR DEPRESSION AND ANXIETY IN AN OUTPATIENT RHEUMATOLOGY CLINIC USING VALIDATED SELF-APPLIED QUESTIONNAIRES

L.F. Perez, A. Martinez, M. Moreno, L. Silveira. *Reumatologia, Instituto Nacional de Cardiologia Ignacio Chavez, Mexico City, Mexico*

Background: Anxiety and depression are often present in chronic rheumatic diseases. Recognition of these psychological disorders is fundamental for proper patient management. The absence of screening leaves more than >50% of patients with depression unidentified. Patient Help Questionnaire-9 (PHQ-9) and General Anxiety Disorder-7 (GAD-7) are two validated self-applied questionnaires that are appropriate to assess the presence of, depression and anxiety, respectively.
Objectives: 1) To assess the prevalence of depression and anxiety in a hospital based outpatient Rheumatology clinic and 2) To provide the attending physician with appropriate instruments that allow a rapid orientation on the psychological status of her/his patient.
Methods: Consecutive patients that attended our outpatient Rheumatology clinic from March to June 2016 were invited to participate in this crosssectional study. Participants filled out PHQ-9 and GAD-7 in the waiting room. The prevalence and severity of anxiety and depression were calculated for the most prevalent diagnoses.
Results: A total of 410 patients were recruited; 339 (82.8%) were female. Overall, 191 (46.6%) patients reported depressive symptoms (PHQ-9>5). Of them, 87 (21.2%) were classified as having moderate depression or higher (PHQ-9 >10). Prevalence of depression and anxiety among study participants according to each rheumatic disease is depicted in Table 1. Prevalence of moderate or severe depression was significantly different among various rheumatic diseases (p=0.001). Regarding anxiety symptoms, they were reported in 168 (40.7%); 67 (16.2%) of them had moderate or severe anxiety.

Disease	N	Moderate or severe depression	Moderate or severe anxiety
SLE	99 (24.1 %)	16 (16.2 %)	12 (12.1 %)
RA	107 (26.1 %)	26 (24.3%)	17 (15.9%)
FM	87 (21.3 %)	**30 (34.5 %) p= 0.001**	**27 (31 %) p=0.001**
OA	69 (16.8 %)	**25 (36.2 %) p= 0.001**	**22 (31.9 %) p=0.001**
SSc	18 (4.4 %)	13 (26 %)	8 (16 %)
Inflammatory myopathies	14 (3.4 %)	4 (28.6 %)	2 (14.3 %)
Osteoporosis	49 (12 %)	14 (28.6 %)	9 (18.4 %)
APS	42 (10.2 %)	**1 (2.4 %) p= 0.001**	3 (7.1 %)

Table 1. Prevalence of depression and anxiety among study participants according to each rheumatic disease. (SLE – Systemic lupus erythematosus, RA – Rheumatoid Arthritis, FM – Fibromyalgia, OA – Osteoarthritis, SSc – Systemic sclerosis, APS – Antiphospholipid syndrome.

Conclusions: This cross-sectional study shows that anxiety and depression are frequent in the Rheumatology clinic. We demonstrated that the use of a self-applied screening tool can help clinicians to properly detect depression and anxiety associated with diverse rheumatic diseases. Specia attention should be paid to patients with fibromyalgia and osteoarthritis.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6765

FRI0742-HPR DOES THE USE OF TECHNOLOGICAL DEVICES IMPROVE THE RELIABILITY OF MEASURING THE ACTIVE CERVICAL RANGE OF MOTION IN PATIENTS WITH NECK PAIN? A SYSTEMATIC REVIEW WITH META-REGRESSION

A. Rondoni[1], G. Rossettini[1], M. Strobe[1], F. Gallo[2], D. Ristori[1], M. Testa[1]. *[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova, Savona; [2]Department of Health Sciences, University of Genova, Genova, Italy*

Background: Economic impact of neck pain shows an increasing trend. In order to limit the costs of spine disorders management, it is important to assess clinical efficacy and the cost-worthiness of new technological devices, recently introduced in physical therapist's clinical practice
Objectives: This systematic review compares, in patients with non-specific neck pain, the reliability of measures of Active Cervical Range of Motion (ACROM) detected with technological devices with those assessed with low cost, common-use devices. As secondary outcomes, it was investigated if ACROM reliability depends on the plane on which the measured movement is performed
Methods: The literature search was carried out in Medline, Scopus, Embase, The Cochrane Library, CINHAL, PEDro and grey literature until August 2016. Inclusion criteria were: reliability design, population of adults with nonspecific neck pain, examiners of any level of experience, measures repeated at least twice and statistics indexes on reliability. Exclusion criteria were: other study designs, asymptomatic population or mixed population, single or none ACROM measure, inadequate statistics. The risk of bias was assessed by QAREL. It was considered inexpensive a device that costs at maximum 500 euros. A Univariate, and a Multivariate Analysis, were performed by using the Linear Mixed-Effect Model
Results: Searching the databases yielded 35,151 records. Nine studies met all eligibility criteria. The QAREL mean score of the selected studies was 3.7 out of 11. No significant effect of the type of device (inexpensive versus expensive) on ICC was observed for intra-rater (ICC=0.93vs0.91 p-value>0.99) and inter-rater reliability (ICC=0.80vs0.87 p-value>0.99) [Table 1]. The plane of movement did not affect inter-rater reliability (p-value=0.11) while significantly influenced the intra-rater reliability (p-value=0.0001) assessed with low-cost devices. Intra-rater reliability significantly decreases (p-value=0.0129) in frontal plane movements (side bending) compared with movement on the sagittal plane (flexion-extension).

Table 1. Comparison of intra and inter-rater reliability between tool types

Characteristics	ICC Descriptive statistics	Mixed effect model	
	Mean (SD)	β (95% CI)	p-value
Intra-rater reliability			
Tool Type			0.99
Expensive	0.91 (0.07)	0	
Inexpensive	0.93 (0.02)	0.01 (-0.04 : 0.06)	
Direction			0.56
Flexion & Extension	0.91 (0.07)	0	
Rotation	0.95 (0.02)	0.03 (-0.01 : 0.07)	
Side Bending	0.92 (0.01)	0.01 (-0.02 : 0.04)	
Age	rho =0.29	0.00 (-0.01 : 0.01)	0.79
Inter-rater reliability			
Tool Type			0.99
Expensive	0.87 (0.09)	0	
Inexpensive	0.80 (0.12)	0.03 (-0.15 : 0.21)	
Direction			0.06
Flexion & Extension	0.82 (0.09)	0	
Rotation	0.86 (0.11)	0.04 (-0.02 : 0.11)	
Side Bending	0.77 (0.13)	-0.04 (-0.10 : 0.01)	
Age	rho =0.58	0.01 (-0.01 : 0.03)	0.43

Conclusions: The use of expensive devices to measure ACROM in adults with nonspecific neck pain does not seem to improve the reliability of the assessment. The assessment of side bending showed the lowest level of inter-raters reliability. Since the quality of the analysed studies is low, the conclusion of the present study should be taken cautiously
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3991

FRI0743-HPR THE ASSOCIATION OF PHYSICAL FITNESS COMPONENTS WITH SLEEP QUALITY IN WOMEN WITH FIBROMYALGIA: THE AL-ÁNDALUS PROJECT

M. Borges-Cosic[1], V. Segura-Jiménez[2], F. Estévez-López[1,3], I.C. Álvarez-Gallardo[2], V.A. Aparicio[4], P. Acosta-Manzano[1], B. Gavilán-Carrera[1], M. Delgado-Fernández[1]. *[1]Physical education and sport, University of Granada, Granada; [2]Physical Education, University of Cádiz, Cádiz, Spain; [3]Department of Psychology, University of Utrecht, Utrecht, Netherlands; [4]Department of Physiology, University of Granada, Granada, Spain*

Background: Fibromyalgia women report poorer sleep quality, fewer hours of sleep, greater nighttime awakenings, and non-restorative sleep compared with healthy people and other clinical populations (Diaz-Piedra et al., 2015). Previous literature has shown a positive effect of exercise training on sleep quality in women with fibromyalgia (Munguía-Izquierdo et al., 2008). Given the close relationship between exercising and physical fitness improvement, it is important to ascertain the individual influence of physical fitness components on sleep quality in this population.
Objectives: To examine the individual association of physical fitness components with sleep quality in women with fibromyalgia.
Methods: A total of 444 women with fibromyalgia (means±sd =51.3±7.5 years old) from Andalusia (southern Spain) were included in this cross-sectional study. The Senior Fitness test battery was used to assess physical fitness. This battery consists of the chair sit-and-reach, back scratch, 30-second chair stand, arm curl, 8-foot up-and-go (lower score indicates better performance) and 6-minute walk tests, which assess lower body flexibility, upper body flexibility, lower body strength, upper body strength, speed agility and cardiorespiratory fitness, respectively. Sleep quality was measured using the total score of the Pittsburgh Sleep Quality Index (PSQI) questionnaire (greater score indicates worse sleep quality). Linear regression was used to explore the association of each physical fitness component with global sleep quality. Analyses were controlled for age, total body fat percentage, marital status, educational level, medication for relaxation/sleep and regular menstruation.
Results: Lower body flexibility (b=-0.033, β=-0.103), upper body flexibility (b=-0.031, β=-0.096), lower body strength (b=-0.191, β=-0.157), upper body strength (b=-0.111, β=-0.142) and cardiorespiratory fitness (b=-0.008, β=-0.154) were inversely associated with greater scores in the PSQI questionnaire (all, $p<0.05$). Speed-agility (b=0.282, β=0.128) was positively associated with the score in the PSQI ($p<0.01$).
Conclusions: The current study showed that higher physical fitness is generally associated with better sleep quality in women with fibromyalgia. It is important to mention that all the physical fitness components seem to be associated with sleep quality. Lower body strength and aerobic capacity were the components that showed the strongest associations with sleep quality. Future studies are warranted to elucidate the causality of these relationships.
References:
[1] Diaz-Piedra, Carolina et al. 2015. Sleep Disturbances of Adult Women Suffering from Fibromyalgia: Asystematic Review of Observational Studies. Sleep Medicine Reviews 21:86–99.
[2] Munguía-Izquierdo, D. & Legaz-Arrese, A. Assessment of the effects of aquatic therapy on global symptomatology in patients with fibromialgia síndrome: a randomized controlled trial. Arch. Phys. Med. Rehabil. 2008, 89:2250–2257.
Acknowledgements: This study was supported by the Spanish Ministry of Economy and Competitiveness (I+D+I DEP2010–15639; DEP2013–40908-R).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4801

FRI0744-HPR THE EFFECTIVENESS OF THE LOWER DOSE OF LASER TREATMENT ON KNEE OSTEOARTHRİTİS

E. Ekiz[1], K. Capaci[2], M. Korkmaz[3]. *[1]Physical therapy and rehabilitation, Alaşehir State Hospital, Manisa; [2]Physical therapy and rehabilitation, Ege University, Izmir; [3]Physical therapy and rehabilitation, Afyonkarahisar State Hospital, Afyonkarahisar, Turkey*

Background: During knee osteoarthritis (OA) therapy; medications, physical therapy modalities, exercises and surgical procedures are used. In previous studies, the benefits of low level laser therapy (LLLT) for pain in the low back, shoulder, elbow, and hand have reported.
Objectives: In this study we aimed to investigate the effectiveness of LLLT on pain, functional status, and quality of life in patients with knee osteoarthritis.
Methods: Patients with Kellgren-Lawrence stage 2–3 knee osteoarthritis were enrolled. It was planned as a prospective, randomized and double-blind study. Group 1 received active laser therapy and group 2 placebo laser therapy. Patients have been provided active/placebo laser therapy for two weeks (5 days a week, a total of 10 sessions). Patients were evaluated before, immediately after and 1 or 3 months after treatment. Outcome measurements included pain intensity at rest and at movement on visual analog scale, knee function using Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) scale, active/passive joint range of movement, quality of life using Short form 36 (SF-36), and 15-meter walking distance, painless walking distance.
Results: In this study, we observed improvements in knee pain, 15-meter walking distance, WOMAC pain, stiffness and function scores, Lequesne index, and SF-36 physical function and social function ($p<0.05$) in active LLLT group. Also, significant improvements were detected in SF-36 physical role, mental health, vitality and emotional role parameters compared with placebo laser group ($p>0.05$).
Conclusions: The present study demonstrated that LLLT is safe and effective upon pain and functional parameters on knee osteoarthritis. However, we think further long-term studies which will include more patients in order to determine the priority and effectiviness are required.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5187

FRI0745-HPR **INVESTIGATION OF ASSOCIATION BETWEEN WRIST PAIN, FUNCTIONAL PERFORMANCE, GRIP AND PINCH STRENGTH IN CHILDREN AND ADOLESCENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: CROSS-SECTIONAL STUDY**

S.N. Arman[1], E. Tarakci[2], O. Kasapcopur[3]. *[1]Department of Physiotherapy and Rehabilitation, Faculty of Health Science; [2]Department of Physiotherapy and Rehabilitation, Faculty of Health Science; [3]Medical Faculty of Cerrahpasa, Department of Pediatric Rheumatology, Istanbul University, Istanbil, Turkey*

Background: Juvenile idiopathic arthritis (JIA), among the most common chronic diseases of childhood, can be associated with pain. reduced range of motion, decreased muscle strength and functionality (1).
Objectives: The aim of this study was to assess the relationships between wrist pain and functional performance, grip and pinch strength in children and adolescents with JIA.
Methods: Cross-sectional study design was included 42 (36 female. 6 male) children and adolescents with JIA aged between 8 and 18 years. Patients who have at least one affected wrist included in the study. Sociodemographic data and clinical features were assessed by physical therapists. Hand grip strength was assessed with Jamar dynamometer Lateral, tip and palmar pinch strengths were assessed with Baseline pinchmeter. Wrist pain during the activity was evaluated with Numeric Rating Scale (NRS). A score of 0 indicated "no pain" and 10 indicated "extreme pain" for NRS. Functional performance of hand was assessed with "Jebson Taylor Hand Functional Test" (JTHFT). JTHFT consists 7 subtests: writing a 24-letter. card turning, picking up small common objects and placing them in a container, stacking checkers, stimulated feeding, moving light objects and moving heavy objects. All tests except writing performed on both right and left hand for JTHFT.
Results: The mean age and duration of disease was 13.05±3.04 (age range 8–18) and 6.55±3.78 years. respectively. Patient population consisted of 28 patients with polyarticular arthritis. 14 patients with oligoarticular arthritis. 39 of 42 patient's wrists were affected bilaterally. Significant relationships were found between writing and right palmar pinch strength (r= -0.34 p=0.023), right hand grip strength and right stimulated feeding (r=-0.32 p=0.039), left hand grip strength and left moving heavy objects (r=-0.33 p=0.028). Also, significant relationships were found between right lateral pinch strength and stimulated feeding (r=-0.33 p=0.028) and right stacking checkers (r=-0.31 p=0.039). For right side, significant relationships were found between palmar pinch and moving light objects (r=-0.35 p=0.020), moving heavy objects (r=-0.32 p=0.039), stimulated feeding (r=-0.36 p=0.017), stacking checkers (r=-0.36 p=0.017), card turning (r=-0.34 p=0.026) and JTHFT-total (r=-0.40 p=0.008).
Conclusions: The results of our study showed that hand grip and pinch strengths considerably decreased in children and adolescents with JIA, according to the normal means of the grip strengths of healthy children and adolescents reported in the literature (2). Our study suggested that decreased hand grip and pinch strengths may result impairment daily functions but wrist pain does not effect grip strengths or functional performance in children and adolescents with JIA. Therefore, we conclude that the grip training program will be effective in improving the functional performance of children and adolescents with JIA.
References:
[1] Ravelli A, Martini A (2007) Juvenile idiopatic arthritis. Lancet 369 (9563):767–778.
[2] Mathiowetz, Virgil, Diana M. Wiemer, and Susan M. Federman. Grip and pinch strength: norms for 6-to 19-year-olds. American Journal of Occupational Therapy 40.10 (1986): 705–711.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4896

FRI0746-HPR **THE FACTORS AFFECTING STAIR CLIMBING IN PATIENTS WHO HAVE AN AFFECTED KNEE JOINT WITH OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS**

S.N. Arman[1], E. Tarakci[1], O. Kasapcopur[2]. *[1]Division of Physiotherapy and Rehabilitation, Faculty of Health Science; [2]Department of Pediatric Rheumatology, Medical Faculty of Cerrahpasa, Istanbul University, Istanbil, Turkey*

Background: Juvenile idiopathic arthritis (JIA) encompasses a complex group of disorders with arthritis as a common feature. Patients with JIA may experience significant disability owing to muscular weakness, joint pain, contracture, and reduced mobility. Stair climbing performance is frequently used as a measure of lower extremity funtions in patients with chronic disease.
Objectives: The aim of this study was to investigating the factors affecting stair climbing in patients who have an affected knee joint with oligoarticular JIA.
Methods: 30 patients (aged 6–18 years) who have an affected knee joint with oligoarticular JIA were included in this study. Active range of motion (AROM) of knee was evaluated with universal goniometer. Muscular strength was estimated at maximal isometric force for the muscles of the lower extremities by using a portable handheld dynamometer (Lafayette, LA). Postural balance control was evaluated by using the Flamingo Balance Test (FBT). Static balance was measured by using the Functional Reach Test (FRT). Stair climbing performance was assessed with 10-stair climbing test (10SCT). All tests were performed thrice and the mean values of all were recorded. Relations between the factors affecting stair climbing in JIA were assessed by multiple linear regression analysis.
Results: The mean age was 9.63±2.76 and the mean disease duration was 4.41±2.16 years. Significant relationships were found between 10SCT and hip flexion muscle strength (r=-0.45 p=0.013), hip external rotation muscle strength (r=-0.48 p=0.007), knee extension muscle strength (r=-0.45 p=0.015) and dorsiflexion muscle strength (r=-0.37 p=0.044). According to linear regression analysis, stair climbing performance was affected by only hip flexion muscle strength (β=-0.40 p=0.026). However, it was not found relationships between AROM, FRT, FBT and 10SCT ($p>0.05$).
Conclusions: Stair climbing is a biomechanically complex activity of daily life for children. In current study, it was found that stair climbing performance was related with lower extremity muscle strengths in patients with JIA. Althought patients with JIA had only one affected knee joint, hip flexion muscle strength was primary predictor of stair climbing performance. We suggested that stair climbing performance should be considered in patients with juvenile idiopathic arthritis. Thus, not only affected joint, but also all lower extremity joints should be assessed multidimensionally.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4937

FRI0747-HPR **FEASIBILITY OF FOUR QUESTIONNAIRES TO EVALUATE PATIENT EDUCATION FOR PEOPLE WITH INFLAMMATORY ARTHRITIS**

R. Røe[1], K. Gronning[2], L.R. Eriksson[1], H.A. Zangi[3] on behalf of the Norwegian patient education expert panel. *[1]Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo; [2]Department of Public Health and Nursing, Center for Health Promotion Research, Norwegian University of Science and Technology, Trondheim; [3]National Advisory Unit on Rehabilitation in Rheumatology, Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway*

Background: No core set of outcomes to evaluate patient education (PE) programmes exists. Evaluation of existing outcome measures is recommended[1]. A Norwegian expert panel comprising patients and health professionals experienced in patient education (PE) participated in a 3-round Delphi-process. The aim of the process was to obtain consensus about outcome domains that might be influenced by PE for people with inflammatory arthritis (IA). Six domains were identified: Understanding disease and treatment, knowledge about healthy life style, coping strategies, self-efficacy, empowerment and communication with health professionals. Through a systematic literature search and further Delphi-rounds, the expert panel identified four patient-reported outcome measures (PROMs) that might capture these outcome domains.
Objectives: To test the feasibility of four identified PROMs suitable to evaluate patient education programmes.
Methods: Arthritis Self-Efficacy Scales (ASES) for pain and symptoms, Effective Consumer Scale (EC-17), Health Education Questionnaire (heiQ) and Patient Activation Measure (PAM) were tested in 13 PE programmes for people with IA at six rheumatology departments in Norway. The PROMs were divided into two test-sets, set A (ASES, EC-17 and PAM) and set B (ASES and heiQ). Data were collected before, immediately after and 3 months after PE programmes. The instruments were tested for missing values, internal consistency (Cronbach's α) and ability to detect change. Floor and ceiling effects were considered to be present if more than 15% of the patients achieved the lowest or highest possible score on each item.
Results: 104 patients answered the questionnaires before participation in a PE programme, 63 in group A and 41 in group B, respectively. 96 (92%) answered the questionnaires after intervention and 78 (75%) responded at 3-month follow-up. Missing values were few in all PROMs (range 0–1.7%). Cronbach's α was acceptable in ASES pain (0.75) and ASES symptoms (0.81), EC-17 (0.91) and PAM (0.78). HeiQ comprises eight separate subcategories; seven categories had acceptable Cronbach's α (0.72–0.86). All PROMs showed statistically significant improvements after the PE programmes. At 3-month follow-up statistically significant changes were found only in EC-17 (p=0.01, SRM 0.4) and three heiQ subcategories; emotional distress (p=0.01, SRM 0.5), skill and technique acquisition (p=0.02, SRM 0.5) and health service navigation (p=0.02, SRM 0.5). There were ceiling effects in all PROMs at baseline, 10/13 items in PAM, 5/17 in EC-17, 3/11 in ASES and 14/40 in heiQ. No floor effects were detected in any of the PROMs.
Conclusions: Based on this pilot study in patients with IA, EC-17 and three of the heiQ subcategories were the most feasible PROMs in terms of internal consistency and ability to detect change. Although ASES did not exhibit significant changes at 3-month follow-up, it should be considered as an outcome measure, because it is the only instrument to measure self-efficacy.
References:
[1] Zangi, H.A. et.al. EULAR recommendations for patient education for people with inflammatory arthritis. Ann Rheum Dis 2015;74:954–962.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1706

FRI0748-HPR CROSS-CULTURAL VALIDATION OF THE PORTUGUESE "RHEUMATOID ARTHRITIS IMPACT OF DISEASE" SCORE: CROSS-SECTIONAL STUDY

R.J.O. Ferreira[1,2], L. Gossec[3], S. Hewlett[4], C. Duarte[1,5], J.K. Nicklin[4], J.A.P. da Silva[1,5], M. Ndosi[4]. *[1]Centro Hospitalar e Universitário de Coimbra; [2]UICiSA:E, Escola Superior Enfermagem de Coimbra, Coimbra, Portugal; [3]Paris 06 University, Paris, France; [4]University of the West of England, Bristol, United Kingdom; [5]Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal*

Background: The Rheumatoid Arthritis Impact of Disease (RAID) score[1] assesses 7 impact domains of interest for people with rheumatoid arthritis (RA). Its use in research and clinical practice has been growing, and it is already translated into over 70 languages[2] but the cross-cultural validity of the Portuguese RAID has not been well established.
Objectives: To validate the Portuguese RAID for use in Portugal.
Methods: This was a single centre, cross-sectional validation study involving 2 phases: (i) cognitive debriefing with 38 patients to determine comprehension of the existing[2] Portuguese RAID (ii) cross-cultural validation using data from adult patients who were willing and able to complete the Portuguese RAID unaided. Analyses included fit to the Rasch model (implying construct validity, reliability and statistical sufficiency), tests for unidimensionality and invariance across different patient subgroups i.e. age, gender, education background, disease duration, function and culture. To test invariance to culture, the Portugal dataset was compared with datasets from France (n=195) and the UK (n=205).[3] RUMM2030 software was used in all analyses.
Results: Phase I led to minor changes in phrasing 3 items to enhance understanding and conceptual equivalence between the original RAID and the Portuguese version. In Phase II, 288 patients were included: mean (SD) age=60 (12) years, 82% females, 76% with disease duration ≥5 years, 30% on biologics. The Portuguese RAID was shown to have adequate fit to the Rasch model and high internal consistency (Table 1). Unidimensionality and invariance to age, gender, disease duration and function were confirmed (data not shown). The scale was well targeted for patients with different levels of disease impact (Figure 1). Pooling the datasets from Portugal, France and the UK revealed no cultural response bias (Table 1). RAID was then calibrated into logit-based scores to enable parametric analyses and bias-free cross-cultural comparisons if desired (data not shown).

Table 1. Results of Rasch analysis from pooled data

Country	N	RAID (n items)	Fit Residual Mean (SD)		Chi² Interaction		Person Separation Index
			Item	Person	Value (DF)	p-value	
Portugal	288	7	-0.13 (2.53)	-0.67 (1.60)	40.50 (35)	0.24	0.94
UK	205	7	0.22 (1.72)	-0.44 (1.37)	40.50 (35)	0.17	0.93
France	195	7	0.19 (1.99)	-0.71 (1.57)	25.69 (21)	0.22	0.91
Pooled	688	7	-0.06 (3.48)	-0.65 (1.55)	94.88 (63)	0.01	0.93
		6*	-0.34 (3.88)	-0.63 (1.44)	66.04 (54)	0.13	0.93
Expected values for perfect fi			0 (1)	0 (1)		>0.05	>0.85

DF, degrees of freedom; *6 items for cross-cultural comparisons (items 2 "Function" and 5 "Physical well-being" combined).

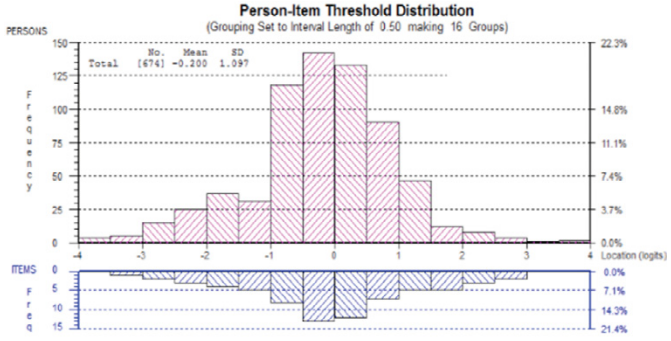


Figure 1. Distribution of items and persons along the same scale (logit score) confirming good targeting of the RAID.
The x-axis is the logit score and represents the interval scaling of the items according to the Rasch model, with –4 being no impact and 4 being high impact of disease.

Conclusions: This study confirms the Portuguese RAID as a robust unidimensional tool for use in Portugal. The raw scores of the 7-item RAID can be used with confidence in clinical practice. Conversion charts are available to enable accurate cross-cultural comparisons across Portugal, France and the UK.
References:
[1] Gossec L, et al. Ann Rheum Dis, 2011;70:935–42.
[2] EULAR RAID and PsAID Questionnaires. Available from http://www.eular.org/tools_products_.cfm Accessed 25th Jan. 2017.
[3] Hewlett S, et al. Ann Rheum Dis, 2015;74:Suppl 2:559.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2754

FRI0749-HPR THE EFFECT OF A SUPPORTED OSTEOARTHRITIS SELF-MANAGEMENT PROGRAM ON PHYSICAL ACTIVITY, PAIN, QUALITY OF LIFE AND SELF-EFFICACY. AN INTERVENTION STUDY WITH A REFERENCE GROUP

T.S.J. Jönsson[1], C.A. Thorstensson[2], E. Ekvall Hansson[3], L. Dahlberg[4]. *[1]Department of orthopaedics, Institute of Clinical Sciences, Lund; [2]Department of Clinical Neuroscience and Rehabilitation, Institute of Neuroscience and Physiology, Gothenburg; [3]Department of Health Sciences, Division of Physiotherapy; [4]Department of Orthopedics, Institute of Clinical Sciences, Lund, Sweden*

Background: People with osteoarthritis are less physical active than others and a large part are sedentary. It is unclear how to increase the physical activity level for patients with osteoarthritis.
Objectives: The primary aim of this study was to evaluate the effects from an evidence based supported osteoarthritis self-management program in patients with knee or hip osteoarthritis on physical activity. Secondary aim were to evaluate the effect on pain, quality of life and self-efficacy.
Methods: An intervention study with a reference group in which 104 patients (29–75 years) with knee (n=84) or hip (n=20) osteoarthritis participated in the intervention. Patients were referred to a supported osteoarthritis self-management program that include physical therapist delivered information and individually adapted exercise. The reference group comprised 28 patients (49–75 years) with knee (n=16) or hip (n=12) osteoarthritis from the waiting list at an orthopedic university clinic. Outcome measurements were made at baseline, 3 and 12 months. Physical activity were objective measured with an accelerometer. The secondary outcomes were patient reported, Visual Analog Scale (VAS) were used to measure pain, EQ-5D to measure quality of life and Arthritis Self Efficacy Scale to measure self-efficacy.
Results: The supported osteoarthritis self-management program did not improve physical activity *(p=0,77)* between baseline and 3 month follow up compared to the reference group. But it did improve pain (*p=0,02*), quality of life (*p=0,002*), self-efficacy-other (*p=0,015*) and self-efficacy-pain (*p=0,033*) between baseline and 3 month follow up compared to the reference group. The improvements in pain and quality of life in the intervention group persisted at 12 month follow-up.
Conclusions: The supported osteoarthritis self-management program delivering information and individualized exercise according to the national program BOA in Sweden improved pain, quality of life and self-efficacy. Despite these results, the physical activity level were not improved. More research on how to improve the physical activity in patients with osteoarthritis is needed.
References:
[1] Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis. 2014;73(7):1323–30.
[2] Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage. 2010; 18(4):476–99.
[3] Thorstensson CA, Garellick G, Rystedt H, Dahlberg LE. Better Management of Patients with Osteoarthritis: Development and Nationwide Implementation of an Evidence-Based Supported Osteoarthritis Self-Management Programme. Musculoskeletal care. 2014.
[4] Wallis JA, Webster KE, Levinger P, Taylor NF. What proportion of people with hip and knee osteoarthritis meet physical activity guidelines? A systematic review and meta-analysis. Osteoarthritis Cartilage. 2013;21(11):1648–59.
Acknowledgements: Grants were received from The Academy of Caring Sciences, Skåne University Hospital and The Swedish Rheumatism Association in Gothenburg.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5711

FRI0750-HPR CONSTRUCT VALIDITY OF THE INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE – LONG FORM IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

T.W. Swinnen[1,2,3], S. Willemijns[2], W. Dankaerts[1], R. Westhovens[2,3], K. de Vlam[2,3]. *[1]Research Group for Musculoskeletal Rehabilitation; [2]Skeletal Biology and Engineering Research Center, KU Leuven; [3]Division of Rheumatology, University Hospitals Leuven, Leuven, Belgium*

Background: Physical activity (PA) is increasingly recognized as an important outcome measure in patients with axial spondyloarthritis (axSpA). Indeed, PA interventions in axSpA have shown to improve clinical status and to reduce comorbidity. The International Physical Activity Questionnaire-Long Form (IPAQ-LF) may be a feasible self-reported PA measurement tool, but its validity is unknown in axSpA.
Objectives: To establish the convergent construct validity of the IPAQ-LF in axSpA.
Methods: Forty patients with axSpA (Male/Female: 24/16; Mean±SD, Age:44.38±11.30 yrs, BMI: 26.27±5.11 kg/m^2, disease duration: 11.40±9.50 yrs, disease activity (BASDAI): 3.69±2.59) completed the IPAQ-LF and wore the SenseWear Pro3 Multisensor Armband during five consecutive days (three weekdays and two weekend days). A priori, significant directional associations

evidenced by Spearman correlation coefficients of ≥.50 were hypothesized between IPAQ-LF total or its subscales and the armband to conform convergent construct validity (p<.05).
Results: IPAQ-LF total PA (Median (IQR): 16.71 (5.91–45.15) MET.hrs/day) was associated with Physical Activity Level (r=.434, p<.01), moderate to (very)vigorous PA (MET≥3, r=.439, p<.01), moderate PA (MET ≥3<6, r=.432, p<.01) and inactive time (MET≤1.8, r=-.382, p<.05) obtained with the armband. Similar, IPAQ-LF moderate PA (Median (IQR): 10.39 (2.41–23.71) MET.hrs/day) was related with PAL (r=.492, p<.01), moderate to (very)vigorous PA (r=.456, p<.01), moderate PA (r=.444, p<.01) and inactive time (r=-.491, p<.05). Also, IPAQ sitting (Median (IQR): 14.91 (10.89–20.80) hrs/day) was correlated to PAL (r=-.461, p<.01), moderate to (very)vigorous PA (r=-.391, p<.05), moderate PA (r=-.386, p<.05) and inactive time (r=.496, p<.01). No relevant nor significant correlations were found for the other IPAQ-LF subscales. Taken together, no hypothesis could be confirmed.
Conclusions: Even at a group level, the convergent construct validity of IPAQ-LF in axSpA was not confirmed. Self-reported PA outcomes may provide important contextual information on PA, but perform poor at quantifying PA levels in axSpA. Future research on a feasible self-reported PA measurement tool for these patients is required.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6932

FRIDAY, 16 JUNE 2017

HPR epidemiology and public health (including prevention)

FRI0751-HPR SAFETY PROFILE OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS - A REAL WORLD EXPERIENCE WITH GOOD RESULTS

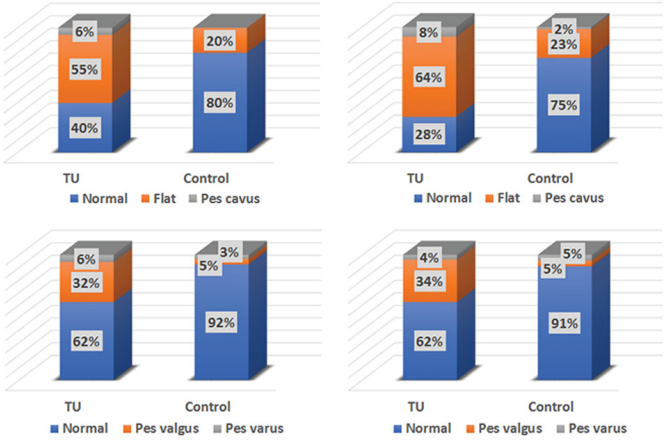
A. Malpica[1], P. Santos-Moreno[2], K. Mendez[3], D. Buitrago-Garcia[1].
[1]Epidemiology; [2]Rheumatology; [3]Pharmaceutical chemist, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia

Background: Tofacinitib is an oral Janus Kinase for the treatment for rheumatoid arthritis (RA). The efficacy and safety of tofacitinib in monotherapy or in combination with other DMARDs has been demonstrated in clinical trials. However previous studies had report hematological changes and infections associated to the use of this medication (1, 2); in the European Union (EU) Tofacitinib is an investigational medicine and has not been approved for use because concernings regarding its safety.
Objectives: We aim to describe the safety profile of Tofacitinib in patients with RA in in a real-life setting in Bogotá, Colombia.
Methods: During 2015- 2016 we followed patients from a RA specialized center in Colombia receiving Tofacinitib. Patients were treated with therapeutic goals T2T and a multidisciplinary approach. Adverse events were classified according the Common Terminology Criteria for Adverse Events (CTCAE) of the World Health Organization. Descriptive epidemiology for continuous variables, measure of central tendency and dispersion for qualitative and categorical variables through percentages and averages were calculated.
Results: We included 56 patients receiving tofacitinib, 80% were woman, 20% men. Mean age was 60±11 years. The mean time with RA was 17 months ± 12. 70% of patients had comorbidities; the most frequent comorbidity was hypertension 30%, followed by osteoporosis 25%, 7.5% Sjogren's syndrome, 7.5% diabetes mellitus among others. 70% of patients received some Anti-TNF drugs before using Tofacitinib; average time receiving tofacitinib was 33±32 weeks, mean DAS28 was 3.7±1.6. Regarding safety profile 10 of 56 patients presented any adverse event. 5 were mild, 4 moderate and 1 severe (1.7%). Diarrhea 1, Infections 1, Abdominal discomfort 3, Mouth papules 1, Rash 1, Sinusitis 1, Headache 1, Folliculitis 1 and Pancreatitis 1.
Conclusions: Tofacitinib is a safe and effective medication for patients with AR; regarding safety the proportion of patients with any AE is lower compared to previous studies, but the type of events were similar to clinical trials (1); none of our patients presented hematological changes; none of our patients presented Herpes Zoster infection.
References:
[1] Wollenhaupt J, Silverfield J, Lee EB, Curtis JR, Wood SP, Soma K, et al. Safety and efficacy of tofacitinib, an oral janus kinase inhibitor, for the treatment of rheumatoid arthritis in open-label, longterm extension studies. The Journal of rheumatology. 2014;41(5):837–52.
[2] He Y, Wong AY, Chan EW, Lau WC, Man KK, Chui CS, et al. Efficacy and safety of tofacitinib in the treatment of rheumatoid arthritis: a systematic review and meta-analysis. BMC musculoskeletal disorders. 2013;14:298.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3048

FRI0752-HPR COMPUTER PODOMETRIC MEASURING SYSTEM IN ASSESSMENT OF FLAT FEET AND LOWER LIMBS DEFORMITIES IN PATIENTS WITH SYSTEMIC SCLEROSIS

R. Michalik[1], A.J. Owczarek[1], P. Kotyla[2], J. Chudek[3], P. Antończak[4], E. Kucharz[2]. *[1]Department of Statistics, SPLMS in Sosnowiec, Medical University of Silesia in Katowice, Sosnowiec; [2]Department of Internal Medicine and Rheumatology; [3]Department of Pathophysiology, SMK in Katowice, Medical University of Silesia in Katowice, Katowice; [4]Department of Cosmetology, SPLMS in Sosnowiec, Medical University of Silesia in Katowice, Sosnowiec, Poland*

Background: Systemic sclerosis (SSc) is a connective tissue disease characterized by an excessive collagen production, fibrotic changes in the skin, internal organs, and vascular involvement. Patients with SSc may have pathological changes in their joints, especially in feet that enclosed: flat feet, valgus or varus foot, hallux valgus, tendinopathy, foot ulcers, joint space narrowing, joint subluxation and degenerative changes [1, 2].
Objectives: The aim of the study was to assess occurrence and the severity of lesions and deformities of spine and joints of lower limbs, especially of feet, in patients with SSc, in comparison to the healthy volunteers.
Methods: All subject have anamnesis, anthropometric tests, and feet assessment with the computer podometric measuring system.
Results: The study enclosed 53 patients with SSc (69.8% female) in mean age 55±12 and 65 healthy volunteers (53.8% female) in mean age 45±15. Disease duration median was 3 years (IQR =6). In comparison to healthy volunteers, patients with SSc have more frequent flat feet and pes valgus (p<0.001) – Figure 1. No significant differences (p=0.96) were observed in round back (8% both groups) and round-concave back (28% vs. 30%) occurrence. Patients with SSc have diminished spine mobility (15.06±5.52 vs. 26.09±6.52 [cm]; p<0.001), to small knee-joint and ankle flexion/extension regardless of body side, more often hallux valgus and longitudinal flat foot. No differences were observed in transverse flat foot and heel varus/valgus occurrence.



Abstract FRI0752-HPR – Table 1. Results of ANOVA with repeated measurements in SSc and control group with comparison between feet

Group	TU		Control		ANOVA		
Variable	Right	Left	Right	Left	p_{group}	p_{foot}	$p_{group*foot}$
Knee-joint flexion (°)	108.7±11.9	107.4±12.6	136.2±6.8	136.2±6.7	**<0.001**	0.61	0.63
Knee-joint extension (°)	0.13±3.86	-0.68±4.22	-1.29±1.63	-1.28±1.74	**<0.05**	0.34	0.32
Ankle flexion (°)	8.7±4.8	9±5.4	18.9±2.2	18.8±2.2	**<0.001**	0.82	0.73
Ankle extension (°)	32.8±10.9	31.6±10	45±4.3	44.9±4.5	**<0.001**	0.53	0.58
Computer podometric measuring system							
Hallux valgus angle α (°)	10.5±7.2	12.0±8.8	7.7±5.6	7.8±6.4	**<0.01**	0.22	0.26
Hallux varus angle β (°)	15.9±5.1	15.6±5.9	15.3±4.1	16.1±4.4	0.98	0.39	0.09
Heel angle γ (°)	14.3±1.6	14.4±1.8	14.3±1.4	14.7±1.4	0.59	0.06	0.15
Godunov- Sztriter Index (KY)	0.45±0.12	0.46±0.16	0.42±0.06	0.43±0.08	**<0.05**	0.46	0.68
Chippaux-Smirak Index (CSI)	0.38±0.09	0.40±0.11	0.29±0.09	0.30±0.09	**<0.001**	**<0.01**	0.06
WGWP	24.9±4.3	24.4±6.4	28.4±2.7	28.1±3.9	**<0.001**	0.48	0.82
Wejsflog Index	2.56±0.1	2.57±0.1	2.58±0.08	2.58±0.09	0.35	0.80	0.48

WGWP - The index of depth of the longitudinal arch of the foot.

Conclusions: Patients with SSc have a relatively high prevalence of feet pathological deformities and a smaller range of flexion of the joints than the lowest normal range, but mostly normal curvature of the spine.

References:

[1] La Montagna G, Baruffo A, Tirri R, Buono G, Valentini G: Foot involvement in systemic sclerosis: A longitudinal study of 100 patients. Semin Arthritis Rheum 2002, 31(4): 248–255.

[2] Sari-Kouzel H, Hutchinson CE, Middleton A, Webb F, Moore T, Griffin K, Herrick AL: Foot problems in patients with systemic sclerosis. Br Soc for Rheumatol 2001, 40: 410–413.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2525

FRI0753-HPR PAIN SPREAD AND PAIN INTENSITY IMPROVE OVER TIME IN WOMEN WITH FIBROMYALGIA AND CHRONIC WIDESPREAD PAIN. A 12 YEAR FOLLOW UP STUDY

A. Bergenheim[1,2,3], S. Johannesson[3], L. Nordeman[1,2], M. Joelsson[3], K. Mannerkorpi[2]. *[1]Närhälsan Research and Development Primary Health Care, Region Västra Götaland; [2]Institute of Neuroscience and Physiology/Physiotherapy, Sahlgrenska Academy, University of Gothenburg, Göteborg; [3]Närhälsan Rehabilitation Centres, Region Västra Götaland, Sweden*

Background: In the Western world, the prevalence of chronic widespread pain (CWP) is about 10–15% while Fibromyalgia (FM) affects approximately 1–3% of the population. The ACR 1990 criteria define CWP as pain ≥3 months on the right and left side of the body, above and below the waist and axial skeletal pain. The 1990 criteria for FM are CWP in combination with pain in ≥11 of 18 tender points on manual palpation. Previous studies indicate that some patients with FM or CWP improve over time and the key to improvement is an important question in research and clinical practice.

Objectives: The primary objective was to investigate the change of pain intensity and pain distribution after 12 years in 166 women with FM or CWP.

The secondary objective was to compare baseline values of health related variables between patients who fulfilled the criteria for FM/CWP at the 12 year follow-up and patients who did not.

Methods: In 2004, 166 women with FM or CWP participated in a randomized controlled trial in Sweden aiming to investigate effects of patient education and pool exercise. All 166 were invited to the present study in 2016 and 126 women (75%) participated. Data was collected by a standardized interview, questionnaires of health related aspects and a physical examination.

Primary, within-group changes were calculated for pain distribution (Bergman's pain drawing 0–18) and the subscale for pain intensity (0–100 mm) included in the Fibromyalgia Impact Questionnaire (FIQ).

Secondary, the group who fulfilled criteria for FM or CWP at follow-up were compared with the group who did not fulfil the criteria for FM or CWP, in overall health status (FIQ total), symptoms of stress (Stress and Crisis Inventory – SCI-93), walking capacity (6 min walk test), hand grip force (the Grippit) and self-reported physical activity (Leisure time physical activity instrument).

Results: Primary: The 126 women with FM or CWP improved in pain distribution: mean values at baseline 12.9 (SD 3.4) vs follow-up 11.4 (SD 4.7), $p<0.001$ and pain intensity: mean values at baseline 69 mm (SD 18.5) vs follow-up 59 mm (SD 22), $p<0.001$.

Secondary: 18% (n=23) of the 126 women did not fulfil the 1990 criteria for FM or CWP at follow-up, and they showed significantly better health status, lower symptoms of stress and higher walking capacity in 2004, than the women who still had FM or CWP at follow-up. Baseline mean values FM/CWP (n=123) vs Not FM/CWP (n=23): FIQ total 66 (SD 16) vs 55 (SD 15), p=0.006; SCI-93 80 (SD 23) vs 59 (SD 22), $p<0.001$; 6 min walk test 502 m (SD 86) vs 542 m (SD 80), p=0.028. No significant differences were found between the groups for baseline values of hand grip force and level of physical activity.

Conclusions: This study showed that distribution and severity of pain improved during 12 years in women with FM or CWP. The group that improved most (18%), reported better health status, lower stress and had better walking capacity 12 years earlier. This knowledge is important for health care professionals to motivate the patients to apply a variety of strategies, including physical activity, to improve their health and symptoms.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1257

FRI0754-HPR IMPACT OF CORTICOSTEROID UTILIZATION ON BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUG INITIATION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

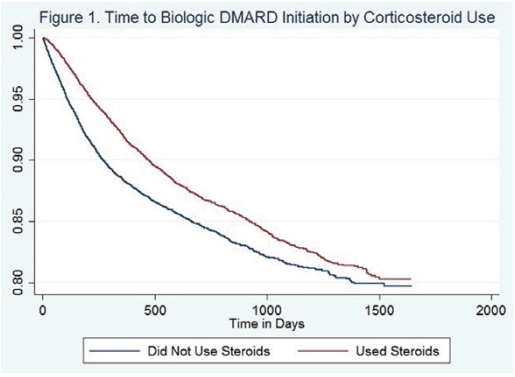
C.A. Spivey[1], J. Griffith[2], C. Kaplan[1], A. Postlethwaite[1], A. Ganguli[2], J. Wang[1]. *[1]University of Tennessee, Memphis; [2]AbbVie, North Chicago, United States*

Background: Treatment guidelines recommend low dose corticosteroids (steroids) as an effective short-term (<3 months) therapy among rheumatoid arthritis (RA) patients to "bridge" patients until benefits of disease modifying anti-rheumatic drugs (DMARDs) are observed and in flare management.[1] Physician quality reporting system (PQRS) measures in the US require a documented management plan for patients on steroids >10 mg/day and this may be a prompt to advance RA therapy. Understanding steroid treatment patterns and associated burden prior to biologic DMARD initiation can inform clinical and policy decision-makers on the appropriate use of these two drug classes in RA management.

Objectives: To examine effects of steroid treatment patterns on initiation of biologic DMARDs and adverse effects of steroid utilization before biologic DMARD initiation among patients with RA.

Methods: A retrospective analysis was conducted of adult RA patients (18 and older) in the US MarketScan Database (2011- 2015). The earliest date a patient was diagnosed with RA was the index date. The following patterns of oral and injectable steroid utilization were analyzed: whether steroids were used; duration of steroid use (short/long duration defined as < or ≥3 months); and steroid dosage (low as <2.5 mg/day, medium as 2.5-<7.5 and high as ≥7.5 mg/day). Kaplan-Meier survival analysis was used to compare time to initiation of first biologic DMARD across groups of steroid utilization. The effects of steroid use on initiation of biologic DMARDs were examined using Cox proportional hazards models. Likelihood and number of adverse events were examined using logistic and negative binomial regression models. Independent variables in all models included patient demographics and health characteristics.

Results: A total of 25,537 patients were included (40.82% used steroids). Based on Kaplan-Meier survival analysis, steroid users (Figure 1), those with longer duration, and in lower dosage categories had delayed time to initiation of a biologic DMARD than their counterparts (nonusers, those with shorter duration and higher dosages, respectively) ($P<0.001$). According to Cox proportional hazards model, lower hazard of biologic DMARD initiation was associated with steroid use ([HR]=0.89, 95% Confidence Interval [CI]=0.83–0.96, compared to nonusers), longer steroid duration (HR=0.73, 95% CI=0.60–0.89 compared to short duration) and lower dosages (HR=1.10, 95% CI=0.99–1.23 for medium dose and HR=1.93, 95% CI=1.59–2.34 for high dose compared to low dose). Higher likelihood of adverse events was associated with steroid use (Odds Ratio [OR]=1.13, 95% CI=1.06–1.20), and longer duration (OR=1.75, 95% CI=1.47–2.09) than their counterparts. Likelihood of adverse events did not significantly differ across dosages. Similar effects of steroid utilization were found on the number of adverse events.



Conclusions: The findings indicate that RA patients who use steroids, those with longer duration and lower dosages have delayed initiation of biologic DMARDS than their counterparts. RA patients who use steroids and those with longer duration have higher likelihood/number of adverse events prior to initiating biologic DMARDS.

References:

[1] Singh JA, et al. doi: 10.1002/acr.22783.

Disclosure of Interest: C. Spivey Grant/research support from: AbbVie, J. Griffith Shareholder of: AbbVie, Employee of: AbbVie, C. Kaplan Grant/research support from: AbbVie, A. Postlethwaite Grant/research support from: AbbVie, A. Ganguli Shareholder of: AbbVie, Employee of: AbbVie, J. Wang Grant/research support from: AbbVie

DOI: 10.1136/annrheumdis-2017-eular.1322

FRI0755-HPR POTENTIAL BENEFITS OF BIOLOGICS ON CARDIOVASCULAR DISEASES AND ORTHOPEDIC SURGERIES IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE POPULATION-BASED COHORT STUDY IN TAIWAN

D.-Y. Chen[1], C.-H. Tang[2], F. Yu[3], C.-Y. Huang[4]. *[1]Division of Allergy, Immunology and Rheumatology, Taichung Veterans General Hospital, Taichung; [2]School of Health Care Administration, Taipei Medical University, Taipei; [3]Pfizer Ltd., New Taipei City; [4]Formosa Biomedical Technology Corp., Taipei, Taiwan, Province of China*

Background: Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder, precipitating chronic inflammation of the joints, and also affects organs throughout the body, and even results in joint deterioration/disability. RA-related inflammation that is responsible for synovial lesions may be implicated in

the development of accelerated atherosclerosis, leading to increased risk of cardiovascular disease (CVD), and increased mortality.
Objectives: This study aimed at examining changes in the risk of deaths, CVD and RA-related orthopedic surgeries between the patients treated with conventional synthetic and biologic disease modifying antirheumatic drugs (csDMARD and bDMARD) for RA during 1997–2011.
Methods: Two cohorts of severe RA patients and their matched controls were identified from National Health Insurance claims database. The csDMARD cohort was patients who had medication claim for cyclosporine ≥50 mg/day with concomitant use of ≥2 csDMARDs for ≥28 days within 56 days after cyclosporine use during 1997–2003 (N=1,569). After csDMARD cohort was determined, the bDMARD cohort was selected if patients had ≥1 claim for bDMARD during 2003–2011 (N=1,530). Adjusted hazard ratios (aHRs) for the risk of death, myocardial infarction (MI), stroke, and RA-related orthopedic surgeries were assessed between the two cohorts and their controls, respectively, using Kaplan-Meier survival curves and Cox proportional hazards models.
Results: RA patients using bDMARD showed a markedly decreased risk of death (aHR:1.05; 95% CIs=0.84–1.33) compared with RA patients using csDMARD (aHR:8.75; CIs=7.43–10.31). Also, bDMARD was associated with a reduced risk of stroke (aHR:0.37; CIs=0.22–0.62) compared with csDMARD (aHR:0.73; CIs=0.51–1.05). For RA-related orthopedic surgeries, risks were slightly lower for bDMARD (aHR:4.14; CIs=3.30–5.20) compared with csMARD (aHR:5.77;CIs=4.88–6.81).
Conclusions: The introduction of biologics in the treatment of RA has showed to have beneficial impact on improving clinical outcomes, including decreased risks of death, stroke and RA-related orthopedic surgeries.
References:
[1] Avina-Zubieta JA, et al. Ann Rheum Dis. 2012 Sep;71(9):1524–1529.
[2] Maradit-Kremers H, et al. Arthritis Rheum. 2005 Feb;52(2):402–411.
Acknowledgements: NA.
Disclosure of Interest: D.-Y. Chen: None declared, C.-H. Tang: None declared, F. Yu Employee of: Pfizer Ltd., C.-Y. Huang: None declared
DOI: 10.1136/annrheumdis-2017-eular.1630

FRI0756-HPR EVALUATION OF MUSCULOSKELETAL COMPLAINTS ASSOCIATED WITH SMARTPHONE USE AMONG UNIVERSITY STUDENTS AND RELATED RISK FACTORS

E. Tonga, B. Özgül, E. Timurtas, M. Can, Y. Hasırcı, M.G. Polat. *Marmara University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Marmara University, Istanbul, Turkey*

Background: Smartphone use for long periods in a static and unsupported arm position could bring about abnormal alignment of upper limb and could cause postural problems and musculoskeletal pain. There are very few studies in the literature that examine the effect of smartphone use on musculoskeletal problems and related factors.
Objectives: The primary aim of our study was to determine the musculoskeletal complaint associated with smartphone use among university students. other purpose of the study was to investigate the relationships with smartphone type, smartphone use frequency, smartphone use posture, smartphone use addiction level and psychological stress.
Methods: 349 university students (240 women, 109 men; mean age 20.79±1,35) were included to our study. We conducted a survey that contains questions about students' smartphone usage patterns and habits. Nordic musculoskeletal Questionnaire was used to determine the musculoskeletal complaint associated with smartphone use. Working posture while using smartphone were evaluated with Rapid Upper Limb Assessment (RULA). Smartphone addiction level were determined with Smartphone Addiction Scale (SAS). Also we use the Beck Depression İnventory (BDI) to determine the psychological distress. Pearson correlation analysis were used to associations between parameters.
Results: Our results showed that university students had a high frequency of smartphone use and that the frequency was related to the level of addiction (r=0.199 p=0.00). %43 of students were use their smartphones extremely more than 4 hours. Students specified that they use their smartphones often for messaging with smartphone applications (%86.5). the most frequent symptoms were found in the neck (%59.6), shoulder (%51.82) and upper back (%54.4) regions. Statistically significant relationship was found between daily frequency of smartphone use and RULA neck posture score (r=0.170, p=0.001). Also there were statistically significant relationships found between BDI score and upper limb (r=0.15, p=0.005) and upper back (r=0.152, p=0.004) postures while using smartphone.
Conclusions: Smartphone users complain at least one area (neck, upper extremity, upper back. The frequency of smartphone use and addiction level is associated with abnormal postures while using smartphones which associated physiological distress. Consequently, musculoskeletal rehabilitation programs should include an analysis of preventive strategies which should be multifactorial with the team work of all health professionals.
References:
[1] Seong-Yeol Kim et al. Effect of duration of smartphone use on muscle fatigue and pain caused by forward head posture in adults. J Phys Ther Sci 2016;28:6.
[2] Junhyuk Park et al. The effects of heavy smartphone use on the cervical angle, pain threshold of neck muscles and depression Advanced Science and Technology Letters Vol.91.
[3] Shang-Yu-Yang et.al. Association between Smartphone use and Musculoskeletal Discomfort in Adolescent students. J Community Health 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6607

FRI0757-HPR NATURE OF JOINT INVOLVEMENT IN OSTEOARTHRITIS IN THE POPULATION: MULTI-JOINT OSTEOARTHRITIS, THE RULE NOT THE EXCEPTION?

E.M. Badley, D. Millstone, A.V. Perruccio. *Division of Health Care and Outcomes Research, Krembil Research Institute, Toronto, Canada*

Background: While population studies usually consider undifferentiated osteoarthritis (OA), cohort and other studies of OA typically focus on OA characterized by a primary joint involved, most frequently the knee, hip or hand. Relatively little attention has been paid to the involvement of other joints.
Objectives: To investigate the extent of multi-joint involvement in a representative sample of the population with OA.
Methods: Analysis of data from the Survey on Living with Chronic Diseases in Canada, Arthritis Component. This was based on a nationally representative sample of people aged 20 or older reporting arthritis as a long term health problem, diagnosed by a health professional, in the parent Canadian Community Health Survey, 2008. Respondents were asked about their type of arthritis, extent of pain on a 0–10 scale, and the extent to which arthritis affected their life (not at all; a little; moderately; quite a bit; extremely). Participants were also asked to indicate which joints were painful. The joints asked about were the right and left hands, wrists, elbows, shoulders, hips, knees, ankles, feet, back and neck. Data on other reported chronic health conditions (heart disease, respiratory, high blood pressure, migraines, mood disorders, bowel disorder/ulcers, stroke, cancer, and diabetes) and body mass index (BMI) were obtained from the parent survey. Analysis was restricted to people reporting OA (n=1749).
Results: The mean age of the sample was 65 years, with 44% aged less than 65; 74% were women. Ninety-three percent reported joint pain in the previous month. The mean "average" pain score was 5.2/10 with very little variation by age and gender. Overall, 92% reported that their arthritis affected their life at least a little, with 24% reporting quite a bit or worse, similarly with little variation by age and gender. The most frequently reported joint sites (e.g. one or both knees) were the knee (58%), hands (49%), back (47%), and hips (42%). Overall the sample was characterized by multi-joint involvement: only 10% reported only one troublesome joint, and 17% only one site. The mean number of painful joints was 5.6 (ranging from 1 to 18: median 5), and the mean number of joint sites was 3.9 (median 3). Women reported more joints than men (mean 5.9 vs 4.8) but there was no significant trend by age. There was no significant trend in number of joints by BMI, although the number of co-occurring conditions was higher in people with more painful joints; 25% of those with only 1–2 joints had a 2 or more co-occurring conditions, compared to 43% of those with 5 or more joints.
Conclusions: Although the most frequently reported painful joints were the knee, hip or hand, few people reporting OA in this representative population-based sample had joint symptoms in that joint alone, suggesting that studies that focus only on a primary joint may be missing the point. The lack of association of mean number of joints with obesity was surprising given a postulated metabolic contribution to OA. The association with co-occurring conditions needs further investigation. A reappraisal of our understanding of OA appears to be warranted given that multi-joint involvement appeared to be the rule not the exception.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6374

FRI0758-HPR CO-MORBIDITY PROFILE IN PATIENTS WITH RHEUMATOID ARTHRITIS. DATA FROM RHEUMATOID ARTHRITIS REGISTRY IN QATAR

F. Alam, M. Hammoudeh, S. Al Emadi. *Rheumatology section Internal Medicine, Hmc Doha, Doha, Qatar*

Background: Comorbid conditions are frequently associated with rheumatoid arthritis (RA) which not only increase morbidity but also has impact on treatment and may shorten the life span of those patients.
Objectives: To study the prevalence of different comorbid conditions among patients with RA.
Methods: Data was collected from rheumatoid arthritis Registry in Qatar. Patients fulfilling 2010 ACR/EULAR criteria for RA were included in this observational study from period of June 2013 to November 2015. Data about Baseline demographics, treatment pattern, disease scores and details of comorbid conditions were recorded in this observational study
Results: Data of 496 patients was analyzed. Demographic and disease characteristic of our RA cohort was as follows: 75.8% were female, 74.9% were positive for rheumatoid factor, 79.8% were positive for anti CCP and 31.3% have erosion at the time of data collection. One hundred thirty patients (26.4%) were receiving biologic drugs, 71.8 were on synthetic DMARDS (either as monotherapy or different combination) and 39.7% were receiving concomitant steroid.
The most commonly associated comorbid conditions were hypertension (24.2%) followed by diabetes mellitus (20.6%), dyslipidemia 10.9%, hypothyroidism 10.9%, asthma and chronic obstructive disease 1.4%.

Steroid was used by 39.2% of patients with diabetes and hypertension.
Cardiovascular events (Ischemic heart disease and ischemic stroke) occurred in 2.2% of patients and 45.5% of patients with cardiovascular events were receiving concomitant steroid. Infections requiring hospital visit were recorded in 1.8% of patients; 77.8% of patients with infection were on biologic DMARD and 33.3% were receiving concomitant steroid.
Out of Two hundred seventy six patients who underwent DXA scanning for estimation of bone mineral density, 48.6% were having decrease bone density (37% osteopenia, 11.6% osteoporosis).
Steroid use was significantly associated with decrease bone density.
Conclusions: Comorbid conditions are frequently associated with Rheumatoid arthritis as observed in our cohort of patients. Patient care should not be focused only on arthritis care. All RA patients should be screened for comorbidities and treated accordingly in order to avoid their deleterious effect on patient health.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1899

FRI0759-HPR COLLABORATION BETWEEN GENERAL PRACTITIONERS AND RHEUMATOLOGISTS TO MANAGE CARDIOVASCULAR RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS PATIENTS

J. Weijers [1], S. Rongen-van Dartel [1,2], M. Hulscher [1], P. van Riel [1,2]. *[1]IQ healthcare, Scientific Institute for Quality of Healthcare, Radboud university medical center, Nijmegen; [2]Department of Rheumatology, Bernhoven, Uden, Netherlands*

Background: To reduce the risk of cardiovascular disease in rheumatoid arthritis (RA) patients, adequate cardiovascular risk management (CVRM) is necessary. CVRM implies assessment, treatment and monitoring of cardiovascular risk factors[1]. The updated EULAR guideline states that cardiovascular risk assessment should be considered at least once every five years in all patients with RA[2]. A few studies show suboptimal risk management in daily practice in selected groups of patients.
Objectives: This study aims to describe current performance of the CVRM recommendation in a hospital based RA population in the South of the Netherlands. In this region, general practitioners (GPs) and rheumatologists closely collaborate into manage RA patients' cardiovascular risk.
Methods: Due to the collaboration, CVRM is performed as a part of a transmural care program. The rheumatologist informs the GP when a patient has been diagnosed with RA. The patient is placed on a list for CVRM to be screened by a specialised nurse practitioner. As a part of the collaboration, laboratory results requested by the GPs and rheumatologists are collected in one digital patient record system. This system is used to check whether the RA patient's lipid profile was determined in the previous five years. If not, a letter with the listed patient is sent to the GP a reminder for screening the patient. In this study, we checked six months later whether lipid testing was ultimately performed.
Results: In 70% (n=475) of all 679 RA patients (mean age 63 (SD 9 years), 68% women and median disease duration of 7 years (IQR 3–11)) a lipid profile was determined in the previous five years.
Of the 204 non-screened RA patients, 98 had been screened after sending the letter to their GP (+48%), see Figure 1. No differences in gender and disease duration were found between the screened and non-screened patients (p=.46 and p=.25 respectively). By contrast screened patients were 10 years older compared to the non-screened patients (66 year (SD12) vs 56 (SD 15) year, $p<0.0001$).

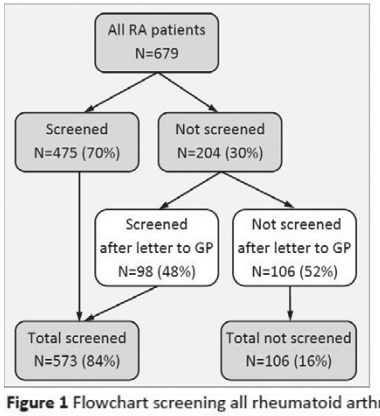


Figure 1 Flowchart screening all rheumatoid arthritis (RA) patients for their cardiovascular risk; results of sending a letter to general practitioners (GP).

Conclusions: As a result of the collaboration between GPs and rheumatologists, 70% of all RA patients was screened for CVRM. A small intervention, sending a reminding letter to the GP, increased this percentage even further, to 84%. This collaboration can be seen as a good practice to provide care in line with the EULAR guideline.
References:
[1] Barber CE et al. Best practices for cardiovascular disease prevention in rheumatoid arthritis: a systematic review of guideline recommendations and quality indicators. Arthritis care & research. 2015;67(2):169–79.
[2] Agca R et al. EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Annals of the rheumatic diseases. 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2423

FRI0760-HPR BIOSIMILAR USE AMONG EUROPEAN RHEUMATOID ARTHRITIS PATIENTS AND IMPACT ON PATIENT OUTCOMES

L. Chanroux, F. Mboge, A. Wadiwalla. *Therapy Watch, Research Partnership, London, United Kingdom*

Background: Biologic agents have been shown to help control disease progression in rheumatoid arthritis (RA) and significant reduce joint damage. However, their considerable cost has limited their widespread use.
Objectives: Biosimilars offers the opportunity for significant cost savings for national health services and the aim of this research is to better understand their use among European rheumatologists and their potential impact on patient outcomes.
Methods: We used data collected as part of an online treatment survey conducted among a panel of 261 rheumatologists between January and December 2016 across 5 European markets (France, Germany, Italy, Spain and the UK). Physicians were sampled to provide a representative mix of practice types and regions. Our record form sample included 9,650 patient currently treated with a bDMARD, 297 of which received a biosimilar. We split the sample into 2 groups, biosimilar patients = those treated with Benepali (etanercept), Remsima (infliximab), Inflectra (infliximab) and Flixabi (infliximab) and originator patients = those treated with Enbrel (etanercept) or Remicade (infliximab). We analysed patient demographic data along with current DAS, joint count, HAQ score and perceived disease severity to assess response to therapy over time.
Results: Biosimilars accounted for a total of 2.4% of our biologic sample with the greatest uptake of these agents reported in the UK (3.8%) and the lowest in France (1.6%). Use of biosimilars increased in patients who started their current biologic in 2016 (8.1%), with a marginally higher use seen in patients on their 2nd or higher line of bDMARD therapy vs. those on their 1st bDMARD (9.4% vs. 7.5%, respectively).
We saw no significant difference in the distribution of biosimilar and originator patients by age and gender although biosimilar patients appeared to have more severe disease. While a smaller proportion of biosimilar patients were perceived to have moderate/severe RA at diagnosis (79.1% vs. 88.4%) a greater proportion were thought to have moderate/severe disease at their latest visit (64.3% vs. 44.2%). The average DAS28 of biosimilar patients was higher at a directional level but their average HAQ score and tender/swollen joint count were non-significantly lower. Biosimilar patients were more likely to suffer from a comorbid condition (87.2% vs. 74.1%) and a autoimmune condition beyond their RA (17.2% vs. 11.6%). There were no significant differences in the proportion of patients unable to work due to their disease (4.3% on average from the total sample).
We analysed the data focusing solely on 1st line patients to reduce any bias introduced by previous lines of therapy but observed similar trends. A higher proportion of biosimilar patients were considered to have moderate to severe RA at their latest visit (67.9% vs. 43.0%) and a greater proportion of patients had a DAS28 >5.1 (23.3% vs.3.0%).
Conclusions: Our research suggests that biosimilar uptake remains limited amongst European rheumatologists with a directional trend towards 2nd line use. Our data did not clearly show any significant differences in the profile of biosimilar patients or their outcomes. Increased governance from healthcare regulators and additional clinical data may be needed to further establish the efficacy and safety of these agents and drive their wider use, ensuring greater cost efficiency and the potential for wider access to biologic therapies for RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6598

FRI0761-HPR CHRONIC WIDESPREAD PAIN PREVALENCE IN THE GENERAL POPULATION: A SYSTEMATIC REVIEW & META-ANALYSIS

P. Andrews, M. Steultjens, J. Riskowski. *Health and Life Sciences, Glasgow Caledonian University, Glasgow, United Kingdom*

Background: Chronic widespread pain (CWP) is a worldwide health problem and a significant contributor to disability. Understanding the impact of individual-dependent (e.g., gender) and contextual-dependent (e.g., survey method, latitude) factors have on CWP prevalence may provide a foundation population-based strategy for addressing CWP.
Objectives: To determine a general population worldwide estimate of CWP prevalence and to examine the individual and contextual-dependent factors related to CWP prevalence.
Methods: A systematic review was undertaken using seven databases. Along with data extracted from the manuscripts, additional contextual data including WHO development status and region, human development index (HDI; measure

Abstract FRI0761-HPR – Table 1. Individual- and contextual-dependent variables

		Random Effects Pooled Prevalence					Univariate Meta-regression	
		Studies	Estimates	Pooled Estimate	95% CI	I^2	I^2	p-value
Gender	Males (n=242808)	11	11	6.7	4.5–8.8	98.6	98.8	<0.01
	Females (n=290395)	11	11	10.9	8.1–13.7	98.7		
WHO Geographical Region	Europe (n=595876)	17	21	9.1	7.1–11.2	99.8	99.7	0.208
	Americans (n=16611)	6	6	10.9	5.1–16.7	99.4		
Latitude	<37° (n=6651)	6	6	10.5	4.5–16.5	98.9	99.8	0.622
	>37° (n=612233)	19	23	9.2	7.3–11.1	99.8		
Survey Type	Personal (n=551483)	18	22	10.0	7.7–12.3	99.5	99.5	0.746
	Non-Personal (n=67401)	7	7	7.8	4.8–10.7	99.4		
WHO Development Status	Developed (n=611999)	21	25	8.7	7.0–10.5	99.7	99.7	0.084
	Developing (n=6885)	4	4	13.9	6.4–21.4	98.5		
Socioeconomic Measures	GINI Index (n=618884)	25	29				99.5	0.258
	HDI (n=618884)	25	29				99.4	0.002
Reporting Quality	High (n=583819)	17	21	10.0	7.5–12.5	99.8	99.7	0.237
	Low (n=583819)	8	8	8.0	5.8–10.2	98.4		

Key: "Studies" refer to number of manuscripts, while "Estimates" relate to the number of countries within a manuscript that provided CWP prevalence estimates.

of socioeconomic position), GINI coefficient (measure of inequality), and latitude were added. Methodological reporting quality was assessed using the STROBE checklist [1]. Meta-analyses were conducted to determine global CWP prevalence, and individual- and contextual-dependent factors were evaluated using meta-regression analyses.

Results: Thirty studies across 20 countries (630,654 participants) met the inclusion criteria. Studies varied in CWP diagnostic criteria, survey method, and reporting quality. Study CWP sample prevalence ranged from 1.4–24.0%, with CWP in men ranging from 1.1–15.3%, while in women it ranged from 1.7–22.1%. Estimated overall CWP prevalence was 9.4% (7.6–11.3%). By gender, the global CWP prevalence estimate in women was significantly higher than for men (10.9% [8.1–13.7%] v 6.7% [4.5–8.8%], $p \leq 0.01$; Table). A meta-regression of the contextual factors showed the HDI was related to CWP prevalence (p=0.002), while other measures such as survey type, methodological reporting quality and GINI index showed no significant effect.

Conclusions: Globally CWP affects one in ten individuals within the general population, with women more likely to experience CWP than men. HDI was noted to be the socioeconomic factor related to CWP prevalence, with those in more developed countries having a lower CWP prevalence than those in less developed countries. There was a lack of data from countries with a lower socioeconomic position, and further CWP data in these areas can help determine if there are socioeconomic effects associated with CWP prevalence and can refine the CWP prevalence estimate.

References:

[1] Poorolajal, J., et al., Epidemiology and health, 2011. 33.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3638

FRI0762-HPR PREVALENCE OF TOBACCO USE IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES (AIRDS): EFFICACY OF COUNSELING IN QUITTING TOBACCO USE

S.S. Baghel, R. Rawat, R.D. Thakran, C. Messi, S. Kapoor, S. Garg, V. Kashyap, Q. Zaheer, A.N. Malaviya. *Rheumatology, Indian Spinal Injuries Centre, New Delhi, India*

Background: Autoimmune inflammatory rheumatic diseases (AIRDs) are chronic in nature and common presentation involves the musculoskeletal system. Off lately, the researches have proved the strong association of tobacco in the development of the disease and increasing severity as well as reducing treatment efficacy. Therefore, awareness about the deleterious effect of tobacco and counselling to quit the same should be an imperative part of the patient education.

Objectives: To assess the prevalence of tobacco use among patients with AIRDs and the effect of counselling on quitting tobacco.

Methods: AIRDs patients attending the rheumatology clinic, willing to participate in the survey were enrolled in this study. Tobacco use was categorized as active [smoking or oral tobacco use] or passive (when the patient was exposed to tobacco smoke).All the information collected in pre-design form, which included demographic information and current status of tobacco use. They were also counselled about the methods of quitting tobacco and its importance and short-term follow-up details were recorded.

Results: 361 patients were enrolled in this study, out of them 162 (44.87%) were tobacco-naive and 199 patients (55.12%) were either active or passive tobacco users, among them active tobacco user 113 (56.78%), and passive user 86 (43.21%).Active tobacco users were further classified into mild 53 (47%), moderate 50 (44%) and severe 10 (9%) users. Other characteristics were as follows; Female: Male ratio1.02:1 [F: M (183:178)], Rheumatoid arthritis 268 (74.2%) [F: M (171:97)], Spondyloarthropathy 93 (25.8%) [M: F (81:12)]. Residential details were: urban 284 (79%) and rural 79 (21%). Educational status: 28 (8%) illiterate, 148 (41%) basic education, 106 (29%) graduate, 79 (22%) postgraduate. Co-morbidities status: 123 (34%) having multiple co-morbidities and 238 (66%) have no co-morbidities.

276 (75%) patients were unaware of the ill effects of tobacco use in AIRDs whereas, remaining 85 (25%) were having little knowledge about it.

The results of persistent counselling and creating awareness with the help of audio-visual aids were 49/113 (43.4%) quit from the active user's category, whereas, 64/113 (56.6%) were unable to quit. Among passive users, 9/86 (10.46%) could able to quit whereas in a large significant number of patients follow-up information could not be obtained.

Conclusions: The use of tobacco was significantly higher in males (61.80%) than females (38.19%).But females were mainly passively exposed to tobacco. By an intense and regular counselling by the specialist rheumatology nurses; 43.4% of active and 10.4%, passive users were able to quit tobacco.

References:

[1] Aimer P, Treharne GJ, Stebbings S, Frampton C, Cameron V, Kirby S et al. Efficacy of a Rheumatoid Arthritis –Specific Smoking Cessation Program: A Randomized Controlled Pilot Trial. Arthritis Care Res 2017; 69:28–37.

[2] Naranjo A, Khan NA, Cutolo M, Lee SS, Lazovskis J, Pandya S, et.al. Smoking cessation advice by rheumatologist: results of an international survey on behalf of the QUEST-RA group.Rheumatology (oxford) 2014; 53:1825–29.

Acknowledgements: The author also wants to thanks, Mr Himanshu Negi (Data Entry help).

Disclosure of Interest: S. Baghel: None declared, R. Rawat: None declared, R. Thakran: None declared, C. Messi: None declared, S. Kapoor Consultant for: Advisory board of Novartis,Pfizer, S. Garg Consultant for: Advisory board of Intas, V. Kashyap: None declared, Q. Zaheer: None declared, A. Malaviya Consultant for: Advisory board of IPCA, Janssen, Pfizer, Roche, BMS,Dr. Reddy's, Zydus

DOI: 10.1136/annrheumdis-2017-eular.2089

FRI0763-HPR INVESTIGATING THE CLINICAL AND COST BURDEN OF PRIMARY SJÖGREN'S SYNDROME: A DESCRIPTIVE ANALYSIS FROM A US ADMINISTRATIVE CLAIMS DATABASE

S. Perera[1], L. Ma[2], R. Punwaney[3], S. Ramachandran[4]. *[1]GSK, London, United Kingdom; [2]GSK, Pennsylvania; [3]GSK, New York; [4]GSK, King of Prussia, United States*

Background: There is limited information available describing the disease burden of primary Sjögren's Syndrome (pSS).

Objectives: This retrospective cohort study aimed to provide a descriptive analysis of the clinical characteristics and disease burden of patients with pSS and describe their healthcare resource use and associated costs.

Methods: This retrospective cohort study (HO-15–16077) was conducted in the US Truven MarketScan® Commercial database. This database reports descriptive data from employees and their families, as covered by employer-sponsored private health insurance. The primary cohort comprised patients with ≥1 diagnosis of sicca syndrome prior to 1 January 2013, and continued enrolment for ≥24 months (1 January 2012 to 31 December 2013). Patients with any conditions mimicking sicca symptoms not due to SS were excluded, as were those with connective tissue disease that may suggest secondary SS. The 1:1 matched comparator population comprised subjects without a previous diagnosis of sicca syndrome (sicca-free). The primary objective was to describe the clinical characteristics and demographics of patients with pSS, including the proportion of patients with glandular versus extra-glandular disease. The secondary objective was to describe their healthcare costs and resource utilisation compared with sicca-free subjects.

Results: There were 12,717 eligible patients in the primary cohort: the majority (86%) were female and the mean age was 51 years. Overall, 61% of patients had claims associated with extra-glandular disease manifestations. These patients experienced a higher disease burden with 41% reporting pain, fatigue and/or insomnia, compared with 12% of patients with glandular disease only who reported pain, fatigue and/or insomnia. Patients in the primary cohort incurred greater annual healthcare service costs (1.6 times greater for all causes and 1.5 times greater for pSS-related causes) and healthcare resource utilisation compared with the sicca-free comparator cohort. The largest difference in SS-related resource utilisation was in the number of office visits (primary cohort: 5.8 visits per patient; comparator cohort: 4.7 visits per patient). Patients with extra-glandular disease also incurred greater average annual costs and used more healthcare resources than patients with glandular disease only.

Conclusions: Despite treatment, patients with pSS still experience a high disease burden. Here we have provided novel insights into the higher treatment cost and increased healthcare utilisation burden of pSS compared with the sicca-free cohort, in particular for patients with extra-glandular disease manifestations.
Acknowledgements: Study funded by GSK. Jennie Frain, PhD, Fishawack Indicia Ltd, UK, provided editorial assistance funded by GSK
Disclosure of Interest: S. Perera Shareholder of: GSK, Employee of: GSK, L. Ma Shareholder of: GSK, Employee of: GSK, R. Punwaney Shareholder of: GSK, Employee of: GSK, S. Ramachandran Shareholder of: GSK, Employee of: GSK
DOI: 10.1136/annrheumdis-2017-eular.2352

FRI0764-HPR MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND END STAGE RENAL DISEASE

S. Paudyal[1], J. Waller[2], A. Oliver[3], B. Le[3], N. Zleik[3], N.S. Nahman[3,4], L. Carbone[3,4]. *[1]Internal Medicine, School of Medicine, University of South Carolina, Columbia; [2]Biostatistics; [3]Medical College of Georgia, Augusta University; [4]Charlie Norwood Veterans Affairs Medical Center, Augusta, United States*

Background: Cardiovascular related mortality is higher in patients with rheumatoid arthritis (RA) compared to the general population, and accounts for more than half of all deaths in end stage renal disease (ESRD). The prevalence of ESRD is increasing and there are an increasing number of older patients with RA. Our recent study demonstrated approximately 1% of patients with ESRD have RA. The implications of ESRD on RA relative to the burdens of cardiovascular diseases, cardiovascular and all-cause mortality are not known.
Objectives: To determine whether patients with RA who have ESRD are at increased risk for cardiovascular disease (CVD) events, cardiovascular mortality and all-cause mortality compared to the general population of patients with ESRD.
Methods: Retrospective cohort study of adult patients (age 18 and older) with ESRD receiving renal replacement therapy (hemodialysis or peritoneal dialysis) in the United States Renal Data System (USRDS) who initiated dialysis between 2005 and 2008 followed for up to five years. Patients with an ICD-9 diagnostic code for RA on or before the start of dialysis and a 5% random sample of those without RA were included. Incident cardiovascular events, cardiovascular related mortality and all-cause mortality was determined in those with RA compared to those without RA.
Results: There were 2,824 subjects including 407 with RA and 2,417 without RA included in the analyses. There was no significant difference in the total number of incident CVD events by RA status (n=311 (76.4% RA) vs. n=1936 (80.1% without RA) (p=0.09). 76 patients with RA (18.7%) died from a CVD related cause compared to 403 without RA (16.7%), (p=0.32). Overall mortality was significantly higher in those with RA (n=226 (55.5%) vs. n=970 (40.1%) ($p<0.01$). Compared to those without RA, those with RA had a significantly shorter mean time in months from start of dialysis to any incident CVD event (17.5 (12.4)) vs. 21.2 (14.1) ($p<0.01$), CVD death, (34.2 (12.5) vs.37.9 (12.6) p=0.02), or all-cause mortality (33.1 (13.0) vs. 37.8 (12.6) ($p<0.01$). In final adjusted models, RA was associated with an increased risk for both CVD related mortality (aHR=1.23 (95% CI 1.05–1.43)) and all-cause mortality (aHR=1.22 (1.05 – 1.42) within five years. Risk factors for CVD and overall mortality included older age, a higher Charlson comorbidity index, tobacco use, needing assistance with ADLs and living in a nursing home. Black race and Hispanic ethnicity was associated with significantly less CVD and all cause-related mortality.
Conclusions: Physicians treating patients with RA and ESRD should be aware that these patients are at increased risk for cardiovascular related mortality and all-cause mortality compared with the general population of ESRD patients. Patients with ESRD and RA at higher risk for mortality can be identified by both demographic risk factors as well as overall health status.
Acknowledgements: Funding for this work was supported by the Translational Research Program (TRP) at the Medical College of Georgia and the Medical and Graduate Student Preceptorship award from the Rheumatology Research Foundation, Atlanta, Georgia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1152

FRI0765-HPR PREVALANCE OF SARCOPENIA IN ELDERLY WITH OSTEOARTHRITIS OF LARGE JOINTS

Y. Safonova[1], V. Tsurko[2]. *[1]Northwestern State Medical University named after II Mechnikov, Department of gerontology, Geriatrics and Nursing, St. Petersburg; [2]First Moscow State University named after IM Setchenov Department of Hematology and Geriatrics, Moscow, Russian Federation*

Background: Lean muscle mass and strength decline starting approximately at 40 years of age to become 25% of body weight at 75–80 years old [1]. Within the existing literature, sarcopenia is a highly prevalent condition in older people. The prevalence of sarcopenia increases considerably with age ranging from 5% to 13% in 60 to 70 years, from 11% to 50% for the population aged 80 years and older. In older persons, sarcopenia is related to falls and physical disability leading to reduced quality of life [2]. The prevalence of osteoarthritis increases with age so that 30 to 50% of adults over the age of 65 years suffer from this condition [3]. Age-related factor that contributes includes to the development of OA include a decline in muscle strength. People with lower extremity OA had a two to five times increased incidence of falls than age-matched healthy controls [4].
Objectives: Conduct analysis of condition of muscle strength and muscle functioning in older persons with osteoarthritis.
Methods: Prospective study of 159 patients aged 74±13,3 years was held. Condition of sarcopenia was estimated by lean body mass (LBM) in accordance with criteria of sarcopenia EWGSOP. Muscle strength was estimated by a hand dynamometer and muscle functioning was estimated on the basis of SPPB tests. Amount of pain was estimated by VAS.
Results: Sarcopenia was revealed in 31,45% of older persons with osteoarthritis. Cases of falls were observed in 28,30% (95% CI 21,5 - 36,0) in patients with osteoartritis with sarcopenia (average number of falls – 1,93) and in 16,98% of patients without sarcopenia (95% CI 11,5 – 23,7) (average number of falls – 0,48). Level of pain in patients with osteoartritis with sarcopenia amounted 3,16 points, in patients without sarcopenia – 3,49 points ($p>0,05$). Muscle strength in patients with sarcopenia was 14,36 kg, in patients without sarcopenia was significantly higher – 18,53 kg ($p<0,05$). Common point of SPPB tests in patients with sarcopenia was 6,9, in patients without sarcopenia significantly higher – 7,85 ($p<0,05$).
Conclusions: Patients with sarcopenia in the presence of osteoarthritis were observed to have significant decrease of muscle strength and muscle functioning, increase of frequency of falls which raises risk of repeated falls and their frequency, and consequently, deteriorates condition of musculoskeletal system in older persons.
References:
[1] Ferrucci L., Baroni M., Ranchelli A. et al. Interaction Between Bone and Muscle in Older Persons with Mobility Limitations. Curr Pharm Des. 2014; 20(19): 3178–3197.
[2] Morley JE. Sarcopenia: diagnosis and treatment. J Nutr Health Aging. 2008; 12:452–456.
[3] Felson DT. Risk factors for osteoarthritis: understanding joint vulnerability. Clinical orthopaedics and related research 2004;(427 Suppl):S16–21.
[4] Hoops ML, Rosenblatt NJ, Hurt CP, Crenshaw J, Grabiner MD. Does lower extremity osteoarthritis exacerbate risk factors for falls in older adults? Womens Health (Lond Engl). 2012;8(6):685–96.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3097

FRIDAY, 16 JUNE 2017

HPR professional education, training and competencies

FRI0766-HPR DOWN'S ARTHROPATHY - CLINICAL AND RADIOLOGICAL FEATURES OF ARTHRITIS IN CHILDREN WITH TRISOMY 21

C. Foley, E.J. MacDermott, O.G. Killeen. *OLCHC, Dublin, Ireland*

Background: Down's Arthropathy (DA) was first reported in the literature in 1984. Crude estimates suggest higher incidence and prevalence rates of DA compared with Juvenile Idiopathic Arthritis (JIA), (JIA prevalence 1/1000, estimated DA prevalence 8.7/1000). Despite this fact, there remains a paucity of data on this condition. DA is rarely recognised at onset, & remains under-diagnosed. As a direct consequence children with DA are presenting with significant joint damage and disability at diagnosis.
Objectives: Perform a musculoskeletal examination on children with Trisomy 21 (T21) aged 0–20 years
Methods: Children with T21 were invited to attend a screening clinic. Screening involved completion of a health questionnaire & a comprehensive musculoskeletal examination. DA cases detected were investigated & managed as per normal clinical practice. Data on a convenience sample of 33 newly diagnosed children with JIA was collected to create a comparison group.
Results: 503 children with T21 have been screened for DA, 22 new cases have been diagnosed. All of these children had poor language skills or were non-verbal. Only 11% of the parents suspected that their child may have arthritis prior to attending our screening clinics, and this was only after reading our recruitment literature. In total, we now have 33 children attending our centre with DA (combining cases attending pre-dating the start date of the study). This suggests the prevalence of DA in Ireland is 18–21/1000.
The majority of children presented with a polyarticular pattern of disease. No cases of uveitis have been observed to date. 88% of the DA cohort had small joint involvement of the hands, significantly higher than that observed in the JIA comparison group. Erosive changes were reported on X-Ray in 29.2% of the DA cohort (9.5% in the JIA Cohort). Methotrexate-associated nausea was a significant barrier to treatment with this DMARD in DA. There was a significant delay in diagnosis of DA, 1.7 years v 0.7 years in the JIA cohort.
Conclusions: Children with T21 are at increased risk of developing arthritis. There is a lack of awareness of this risk among health care professionals & the general public at large. This almost certainly contributes to poor recognition of the disease and a delay in diagnosis. The predominant pattern of disease is polyarticular small joint arthritis. Treatment with standard protocols used in JIA

is complicated by drug-associated side effects in children with T21. However, a good response to treatment with steroid intra-articular joint injections has been observed. Our study has raised a number of questions. Future research to accurately define this disease & identify best practice with regards to treatment would be invaluable. We advocate that all children with T21 should have annual musculoskeletal examination as part of their health surveillance programme.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.7020

FRI0767-HPR PARTICIPATING IN A MUSCULOSKELETAL RANDOMISED CONTROLLED TRIAL: IDENTIFICATION OF EDUCATION TRAINING NEEDS BY OCCUPATIONAL THERAPISTS AND PHYSIOTHERAPISTS IN THE UK

J. Adams[1,2], P. Barratt[2], S. Bradley[3], S. Barbosa-Bouças[4], K. Hislop Lennie[5], P. White[2] on behalf of OTTER II Trial working group. *[1]Arthritis Research UK, Centre of Excellence Sport, Ex & OA; [2]Faculty of Health Sciences, University of Southampton, Southampton; [3]Occupational Therapy, Poole General Hospital, Poole; [4]Department of Psychology, Buckinghamshire New University, High Wycombe; [5]Health Sciences, University of Southampton, Southampton, United Kingdom*

Background: There is an association between clinical teams engaging with research and improvement in the delivery of health services[1]. Randomised controlled trials (RCTs) provide strong evidence to influence practice in musculoskeletal services. For occupational therapists (OTs) and physiotherapists (PTs) implementing RCTs is not yet commonplace. As part of a multi-centred clinical effectiveness and efficacy RCT of splints for thumb base osteoarthritis (OTTER II Trial) we established an education training programme to support clinical therapists deliver the trial across 15 UK hospitals.

Objectives: To evaluate the content of trial training to educate and support OTTER II Trial clinicians in undertaking clinical research roles.

Methods: Two trial training days were run in the North and South of England. Therapists provided details of their clinical trial experience. They were asked to identify one area in which they felt confident and one in which they were not confident in participating in a RCT. These perceived facilitators and barriers were summarised using descriptive statistics and content analysis.

Results: Thirty five clinicians (20 OTs,15 PTs) attended a training day, 13 (37%) had no previous experience with clinical trials; 19 (54%) had been involved with at least one previous clinical trial. Clinicians considered they were already confident in; delivering the trial standardised assessment and treatment to patients n=21 (60%); trusting the OTTER II trial team and their own hospital research departments to support their research role n=11 (31%); understanding the trial protocol and what needed to be delivered n=6 (17%) and, being convinced that the trial asked a relevant question 3 (9%). Areas in which clinicians considered they did not have confidence included; the logistics and time management of delivering a RCT in their own hospital n=18 (51%); the associated trial paperwork to be completed n=8 (23%); NHS computer access/wifi access for randomisation procedure n=7 (20%); recruiting participants to time and target n=6 (17%) and staff capacity to deliver a RCT in the NHS alongside clinical commitments n=5 (14%).

Conclusions: Well documented trial protocols and support from a trusted research team and local hospital research departments were identified as key areas that help clinicians become confident to engage with a national clinical RCT. Clinicians are less confident about managing the practical logistics, staff time and trial paperwork involved in delivering a national RCT. Clinicians identify that they possess core clinical assessment and treatment skills that already equip them to recruit and treat patients as part of a national trial. The logistics of delivering a trial requires ongoing negotiation and support from clinical service managers and the clinical trial teams to ensure clinicians are supported to deliver the RCT to time and target.

References:

[1] Boaz et al 2015 BMJ Open 5:e009415 doi:10.1136/bmjopen-2015-009415.

Acknowledgements: The OTTER II Trial is funded by Arthritis Research UK (Grant Ref number 21019).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1095

FRI0768-HPR MUSCLE WASTING IN OSTEOARTHRITIS MODEL INDUCED BY ANTERIOR CRUCIATE LIGAMENT TRANSECTION

J.M.D.S. Silva, P.V.G. Alabarse, V.D.O.N. Teixeira, E.C. Freitas, F.H. de Oliveira, R.M.D.S. Chakr, R.M. Xavier. *Faculdade de Medicina, UFRGS, Porto Alegre, Brazil*

Background: Osteoarthritis (OA) is a chronic joint disease characterized by progressive loss of articular cartilage and abnormal bone formation. Furthermore, there are changes in periarticular muscles, such as loss of muscle mass, strength and function. These features may contribute to functional impairment among patients.

Objectives: This study aimed to investigate the molecular pathways involved in muscle wasting in an animal model of OA induced by anterior cruciate ligament (ACL) transection in rats.

Methods: Female Wistar rats were allocated into two groups: OA (submitted to the ACL transection; n=9) and SHAM (submitted to surgical procedures without ACL transection; n=8) [1]. Spontaneous exploratory locomotion, nociception and body weight of animals were evaluated weekly. Twelve weeks after the disease induction, animals were euthanized and the right knee joints were collected for further confirmation of the disease by histopathology, accordingly to OARSI histologic scoring system [2]. Gastrocnemius muscle from the right hind paw were dissected and weighed. Gastrocnemius was used for evaluation of muscle atrophy [3] and protein expression of myostatin, MuRF-1, MyoD and myogenin. Data were compared by Student's t test or ANOVA followed by Tukey's test or ANOVA followed by Mann–Whitney's U-test. The results are expressed as mean values ± standard deviation (SD) for symmetric variables and as medians with interquartile range for asymmetric variables. Significance was accepted at $P<0.05$.

Results: Histopathology of the right knee joints confirmed the development of the disease in animals from OA group. Gastrocnemius area of animals from OA group had a reduction of about 10% compared to animals from SHAM group. Protein expression of myostatin was increased in OA group, while myogenin expression was decreased. MuRF-1 and MyoD expression was similar in both OA and SHAM groups. Spontaneous exploratory locomotion, nociception, body weight and weight of gastrocnemius showed no difference between OA and SHAM groups.

Conclusions: Gastrocnemius atrophy in OA induced by ACL transection involves increased protein expression of myostatin and decreased protein expression of myogenin. In this model, muscle wasting may be linked to myostatin-induced deficits in satellite-cell differentiation due to decreased expression of myogenin.

References:

[1] Elsaid KA, Machan JT, Waller K, Fleming BC, Jay GD. The Impact of Anterior Cruciate Ligament Injury on Lubricin Metabolism and the Effect of Inhibiting Tumor Necrosis Factor alpha on Chondroprotection in an Animal Model. Arthritis and Rheumatism. 2009;60(10):2997–3006.

[2] Gerwin N, Bendele AM, Glasson S, Carlson CS. The OARSI histopathology initiative - recommendations for histological assessments of osteoarthritis in the rat. Osteoarthritis and Cartilage. 2010;18:S24-S34.

[3] Filippin LI, Teixeira VN, Viacava PR, Lora PS, Xavier LL, Xavier RM. Temporal development of muscle atrophy in murine model of arthritis is related to disease severity. Journal of Cachexia Sarcopenia and Muscle. 2013;4(3):231–8.

[4] de Oliveira Nunes Teixeira V, Filippin LI, Viacava PR, de Oliveira PG, Xavier RM. Muscle wasting in collagen-induced arthritis and disuse atrophy. Exp Biol Med (Maywood). 2013;238(12):1421–30.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4856

FRI0769-HPR EVALUATION OF THE EFFECTIVENESS OF DEEP WATER RUNNING FOR THE TREATMENT OF CHRONIC NONSPECIFIC LOW BACK PAIN

J.S. Arakaki, F.M. Jennings, S.R. Toffolo, J.C. Tamashiro, J. Natour. *Rheumatology, Universidade federal de São Paulo- UNIFESP, São Paulo, Brazil*

Background: Low back pain (LBP) is one of the most common musculoskeletal conditions and can lead to disability. Aerobic fitness exercises have recently been suggested as important in the management of pain and physical disability of LBP patients, but there are still no studies that prove the best exercise modality for this condition. One proposed modality is the Deep Water Running (DWR) which are aquatic conditioning exercises that simulates normal running on soil.

Objectives: To evaluate the effectiveness of Deep Water Running in the treatment of chronic nonspecific low back pain.

Methods: It was a randomized controlled trial with a duration of 16 weeks with evaluations performed before the intervention and 8 and 16 weeks after the beginning of the training. The population was composed of 60 patients aged over 18 years with diagnosis of chronic nonspecific low back pain. The intervention group performed aerobic conditioning exercise (Deep Water Running) in a heated pool. The sessions had duration of 50 minutes and frequency of 3 times a week for 16 weeks and with 70% of the maximum heart rate, with 10 bpm less for the difference in the behavior of HR in aquatic environment. The control group underwent aerobic conditioning by treadmill exercise for 50 minutes, 3 times a week for 16 weeks, and also with 70% of maximal heart rate. *Evaluation instruments:* Visual analog pain scale (EVA) in cm; Likert Scale of pain improvement and worsening according to the patient and according to the evaluator; Functional capacity through the Roland-Morris questionnaire and 6-minute walk test; SF-36 for general quality of life; And amount of anti-inflammatories used during the study period. Evaluations were performed by an evaluator who was unaware of the patient allocation group.

Results: The two groups were homogeneous regarding most clinical demographic characteristics in the initial evaluation. The two groups showed statistically significant improvement in the variables Roland Morris, EVA for pain and Time up and go, but no statistically significant differences were found between groups. At the Likert scale, the 6-minute walk test and the amount of anti-inflammatories used during the study, no significant differences were found, the two groups remained unchanged. No adverse events were observed in either group during the exercise program.

Conclusions: Deep water running aerobic exercise is as effective as treadmill walking in improving pain and functional capacity in patients with chronic nonspecific low back pain.

References:
[1] Abenhaim L, Rossignol M, Nordin M, Avouac B, Blotman F, Charlot J. The role of activity in the therapeutic management of back pain. Report of the International Paris Task Force on Back Pain.
[2] Brendon J, Bloess K, Oppermann J, Boese CK, Lohrer L, Eysel P. Conservative treatment of nonspecific, chronic low back pain: Evidence of the efficacy- a systematic literature review. Orthopade. 2016 jul;45 (7): 573–8.
[3] Cuesta-Vargasai, Adams N, Salazar JA, Belles. sPINE 2000; 25 (4SUPPLI): 1S-33S. A, Hazanas S, Arroyo Morales. Deep water running and general practice in primary care for non- specific low back pain versus geeneral practice alone: randomized controlled trial. Clin Rheumatol. 2012 jul; 31 (7): 1073–8.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1648

FRI0770-HPR A BETTER WAY TO DECREASE KNEE SWELLING IN PATIENTS WITH KNEE OSTEOARTHRITIS: INTERMITTENT PNEUMATIC COMPRESSION – A RANDOMIZED CONTROLLED CLINICAL TRIAL

Z. Sarı, O. Aydoğdu, I. Demirbüken, U.S. Yurdalan, G.M. Polat. *Physiotherapy and Rehabilitation, Marmara University, Health Sciences Faculty, Istanbul, Turkey*

Background: One of the most common symptoms of knee OA is swelling. Knee swelling negatively affects knee mechanics and muscle activity in patients with OA. Thus, knee swelling should be eliminated in the early period of rehabilitation. The utility of cold therapy for musculoskeletal injuries has been clearly established (1). It was shown that cold therapy may not be a statistically effective modality in improving range of motion and decreasing knee swelling (2).
Intermittent pneumatic compression (IPC), which has been used to treat limb swelling, is a common option for patients with lymphedema and venous leg ulcers. Currently, IPC is primarily used in the prevention of deep venous thrombosis. It is also used for venous insufficiency, arterial occlusive disease, prevention of hematoma, etc (3). However, despite its widely accepted use, the literature on IPC in musculoskeletal injuries is limited. In particular, there is no report on whether IPC, which is known to have positive effects on circulatory problems, affects the knee swelling in OA.
Objectives: In this study, we hypothesized that IPC may have better outcomes on knee swelling. We also investigated whether IPC may contribute to better short-term patient outcomes in patients with knee OA rather than cold therapy.
Methods: This was a randomized, prospective, comparative clinical study. The study included 81 patients aged 18–65, who were admitted to the Or – Ahayim Balat Hospital. The patients were randomly divided into two groups. One group (n=36) received ultrasound, transcutaneous electrical nerve stimulation, electrical stimulation, exercise, and cold packs. The second group (n=45) received ultrasound, transcutaneous electrical nerve stimulation, electrical stimulation, exercise, and IPC. The primary outcome on pre- and post – treatment follow – up was knee swelling. Secondary outcome measures included range of motion, muscle strength, pain intensity and disability.
Results: Intermittent pneumatic compression significantly decreased knee swelling in patients with osteoarthritis ($p<0.001$). A significant difference between the groups was found in knee swelling in favour of the intermittent pneumatic compression group (p=0.028). We also found significant improvements in range of motion, muscle strength, pain intensity and disability in both groups ($p<0.05$). No significant differences in any of secondary outcome variables between the groups ($p>0.05$).
Conclusions: The mechanism of our hypothesis was that in opposite of cold therapy which has local effects, IPC may affect circulatory of all lower extremity in patients with swollen knee. This randomized - controlled trial confirmed the hypothesized advantage of intermittent pneumatic compression over cold - pack on knee swelling in patients with knee osteoarthritis.
References:
[1] Rutherford DJ, Hubley-Kozey CL, Stanish WD: Knee effusion affects knee mechanics and muscle activity during gait in individuals with knee osteoarthritis. Osteoarthr. Cartil. 2012;20(9):974–81.
[2] Markert SE. The use of cryotherapy after a total knee replacement: a literature review. Orthopaedic Nursing. 2011:30(1):29–36.
[3] Chen AH, Frangos SG, Kilaru S, et al.: Intermittent pneumatic compression devices – Physiological mechanisms of action. Eur J Vasc Endovasc Surg. 2001;21(5):383–92.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5696

FRI0771-HPR WORK – RELATED LUMBAR PAIN IN PHYSIOTHERAPISTS WHO WORK IN DIFFERENT FIELDS – A PILOT STUDY

B. Karakoç, Z. Sarı, O. Aydoğdu, U.S. Yurdalan. *Physiotherapy and Rehabilitation, Marmara University, Health Sciences Faculty, Istanbul, Turkey*

Background: Having a job exposing the load on the lumbar region increases lumbar pain risk. Lumbar pain takes first place in musculoskeletal disorders among health care workers. A survey which investigated musculoskeletal disorders in physiotherapists indicated that the most common musculoskeletal disorders have seen in the lumbar region.
Objectives: The aim of this study was to determine the work – related lumbar pain in physiotherapists who work in different fields and differences in terms of occupational and personal variables.
Methods: This was a prospective, comparative and multi – central study. Physiotherapists who accepted to participate in this study voluntarily and work at any of paediatric, orthopaedic and neurological fields were received. Eighty – eight physiotherapists were taken first assessment. Their demographic information were taken and they filled out the Oswestry Low Back Disability Questionnaire. Twenty – nine cases who had any orthopaedic disease, surgical history and did not fill the entire of the Oswestry Low Back Disability Questionnaire excluded from the study. Twenty – eight women and 31 men met the criteria for inclusion.
Physiotherapists were divided into three groups as paediatric (n=21), orthopaedic (n=24) and neurological (n=14). Lumbar pain level, the number of daily patient transfer, daily working hours and daily standing working hours in three groups were compared. One – way ANOVA was used to compare the groups. SPSS v11.5 was used for the statistical analysis.
Results: There were no significant differences in lumbar pain levels between groups (p=0.342). Daily standing working hours of paediatric group were significantly less than orthopaedic group (p=0.021) and the number of daily patient transfer were significantly higher in paediatric group according to orthopaedic group (p=0.028). Daily standing working hours and the number of daily patient transfer of neurological group had no differences between other groups (p=0.173).
Conclusions: We think that the reason why no differences between the pain level of paediatric and orthopaedic group may be due to more daily transfers in paediatric group and more daily standing working hours in orthopaedic group. The cause why no differences between neurological field and others, might be because of another working factors which we did not assessed. There is a need for research examining in detail on working conditions and trials including more cases.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6858

FRI0772-HPR FORMAL RHEUMATOLOGY TRAINING FOR GENERAL PRACTITIONERS

S. Khan [1], A. Mohammad [1], K.P. O'Rourke [1], C. Sheeehy [2]. *[1]Rheumatology, Rheumatology, Midland Regional Hospital, Tullamore, Tullamore; [2]Rheumatology, University Hospital Waterford, Waterford, Ireland*

Background: Formal post graduate training in rheumatology is limited for primary care physicians or general practitioners. General practitioners (GPs) have extraordinary wide knowledge base, and deal with all age groups, from minor ailments to serious illnesses, thus it's not possible to expect them to have a strong hold of specialised conditions like inflammatory arthritis (IA) (2). General practitioners can be trained to manage these conditions in order to break the disconnect between the flow of knowledge and the burden of care in rheumatic conditions.
Objectives: The Rheumatology department in Midlands Regional Hospital and University Hospital Waterford facilitates GPs teaching in rheumatology outpatients clinics. Every year six GP trainees are trained by consultant rheumatologist. Each trainee receives one on one education in managing rheumatologic conditions including joints and soft tissue injections. This survey was done to evaluate whether GP trainees benefited from it in diagnosing and treating rheumatologic diseases when compared to non rheumatology trainees.
Methods: This is a cross sectional study of a convenience cohort. GP trainees who received rheumatology training as part of their hospital rotation were included as "cases", and compared to those who didn't have any formal rheumatology exposure during their training g as "control". The cases attended supervised rheumatology outpatients for one year, and. A questionnaire was emailed as well as distributed to the GP trainees, it included questions on trainees' ability and comfort level in diagnosing, assessing and managing inflammatory and non inflammatory conditions, along with joint and soft tissue injections.
Results: There were 60 participants in the study, 30 cases and controls each. Majority (94%) didn't have formal rheumatology teaching in the medical school, but had rheumatology experience post graduation, 30 being GP trainee in rheumatology and 7 as senior house officers attached to rheumatology team. The GP trainees had an average of 7 months exposure to rheumatology. The GP trainees who attended the rheumatology clinics were confident in: examining joints, differentiating musculoskeletal/ mechanical from inflammatory conditions, educating patients and commencing them on DMARDs, interpreting serological tests (RF, CCP, ANA etc), managing osteoarthritis, tennis elbow, and soft tissue and intra-articular Knee and shoulder injections, as compared to the trainees who didn't have any formal rheumatology training ($P<0.001$).
Conclusions: Rheumatology teaching for the GP trainees is certainly beneficial, and helps them in managing rheumatologic conditions in primary care settings.
Acknowledgements: Dr Declan Brennan, General Practicioners Coordinator, Midlands, Tullamore.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4917

SATURDAY, 17 JUNE 2017

HPR patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

SAT0717-HPR **PREGNANCY AND DELIVERY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS**

A. Zbinden[1], S. van den Brandt[2], P.M. Villiger[1], M. Østensen[1], F. Förger[1].
[1]Department of Rheumatology, Immunology and Allergology, Inselspital, University of Bern, Berne, Switzerland; [2]Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands

Background: Inflammatory rheumatic disease do have an influence on pregnancy course and outcome. There is little knowledge about the comparison between two rheumatic diseases.
Objectives: To analyze pregnancy complications, pregnancy outcome and delivery mode in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA).
Methods: Patients with RA and SpA were compared with those of matched healthy controls (HC) with respect to pregnancy complications, pregnancy outcome and delivery mode. Patients and controls were prospectively followed at the University of Bern.
Results: We analyzed 244 pregnancies, of which 96 pregnancies occurred in 86 RA patients, 78 in 70 SpA patients and 70 in 70 healthy women.
Pregnancy complications (gestational diabetes, preeclampsia, infection, premature rupture of membranes) were more frequent in RA patients (11.5%) and in SpA patients (17.9%) than in HC (1.4%).
Pregnancy outcome of 174 pregnancies in RA and SpA patients resulted in 178 live born infants, 6 sets of twins, one stillbirth and one induced fetal demise. The induced fetal demise was performed in a twin pregnancy on a fetus with a congenital anomaly. Congenital anomalies occurred in 6 infants (3 in RA and 3 in SpA patients). All HC had live births. Median birth weight was lower in patients compared with HC (RA: 3100g, SpA: 3245g, HC: 3455g). RA and SpA patients had more often small for gestational age infants (birth weight <10th percentile; RA: 16.2%, SpA: 11.4%, HC: 1.4%) and preterm deliveries (RA: 18.8%, SpA: 11.5%, HC: 1.4%).
With regard to delivery mode, most women had vaginal deliveries (RA: 51.0%, SpA: 57.7%, HC: 72.9%). Birth by caesarean section (elective and emergency), was more frequent in RA and SpA patients than in the healthy controls (RA: 44.8%, SpA: 39.7%, HC: 27.2%). Emergency caesarean sections were indicated in 22.9% of pregnancies among RA patients, in 21.8% of SpA patients and in 14.3% of healthy women.
Conclusions: Pregnancy complications, caesarean section, and adverse child outcomes were more frequent in patients with RA and SpA compared to healthy women. However, no significant differences in pregnancy outcomes were observed between RA and SpA patients indicating comparable risks induced by the autoimmune inflammatory process.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6086

SATURDAY, 17 JUNE 2017

HPR measuring health (development and measurement properties of PROs, tests, devices)

SAT0718-HPR **INFLUENCE OF PATIENT GLOBAL ASSESSMENT ON THE DISEASE ACTIVITY ASSESSMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: A METEOR CROSS-SECTIONAL STUDY**

R.J.O. Ferreira[1], M. Ndosi[2], C. Duarte[1], P. Carvalho[1], A. Chopra[3], K. Salomon-Escoto[4], D. Vega[5], D. van der Heijde[6], P. Machado[7], J.A.P. da Silva[1] on behalf of METEOR investigators. *[1]CHUC, Coimbra, Portugal; [2]UWE, Bristol, United Kingdom; [3]CRD, Pune, India; [4]UMMMC, Worcester, United States; [5]HU/UANL, Monterrey, Mexico; [6]LUMC, Leiden, Netherlands; [7]UCL, London, United Kingdom*

Background: Disease activity indices (DAI) are used to guide immunosuppressive therapy in rheumatoid arthritis (RA). The inclusion of patient global assessment (PGA) in these indices has been questioned as it conveys mainly disease impact rather than disease activity.
Objectives: To determine the influence of PGA on patient disease states and to determine PGA correlations with inflammatory parameters, disease impact, demographic, clinical and contextual factors.
Methods: The METEOR international database was used, namely data from patients' first available visit with no missing values on PGA, tender and swollen joint counts (TJC28, SJC28) and C-reactive protein (CRP). Remission rates were compared according to the DAS28CRP3v vs 4v and ACR/EULAR Boolean remission vs near-remission (failing 1 of the 4 criteria) definition. We assessed the correlation of PGA with (predominantly) inflammatory (TJC28, SJC28, CRP) and disease impact (pain and HAQ) factors. We used hierarchical modelling to explain PGA by 4 blocks (B) of independent variables (B1: gender, age, disease duration; B2: biologic DMARD, Gross National Income; B3: pain, HAQ; and B4: TJC28, SJC28, CRP).
Results: Among the 18280 patients analysed, 1930 (10.6%) were in DAS28CRP4v remission, and 2197 (12.0%) in DAS28CRP3v remission. According to the Boolean definition, 1207 (6.6%) patients were in remission. PGA was the main obstacle to Boolean remission: 2090 (79.0%) of the 2645 near-remission patients (Table 1). A considerable proportion of patients with low inflammation perceived high PGA (Figure 1).
PGA correlated better with Pain (r_p=.79) and HAQ (r_p=.55) than with TJC28 (r_p=.45), SJC28 (r_p=.36) or CRP (r_p=.25).
In the entire dataset, 60.2% of PGA variance was explained by Pain and HAQ, 1.8% by B1 and B2 of covariates and only 1.3% by B4 (TJC28, SJC28, CRP) (Table 2). In near-remission patients, B4 did not contribute significantly to changes in the model.

Table 1. Remission and near-remission rates (n=18280)

Disease Activity	3v	4v
DAS28CRP#, n (%)		
Remission (≤1.9)	2197 (12.0)	1930 (10.6)
Low (≤2.2)	3855 (21.1)	3485 (19.1)
Moderate to High (>2.2)	1228 (66.9)	12865 (70.3)
ACR/EULAR Boolean, n (%)		
Remission	1207 (6.6)	
Near-rem. PGA	2090 (11.4)	
Near-rem. CRP	214 (1.2)	
Near-rem. SJC28	165 (0.9)	
Near-Rem. TJC28	176 (1.0)	
Non-Remission	14428 (78.9)	

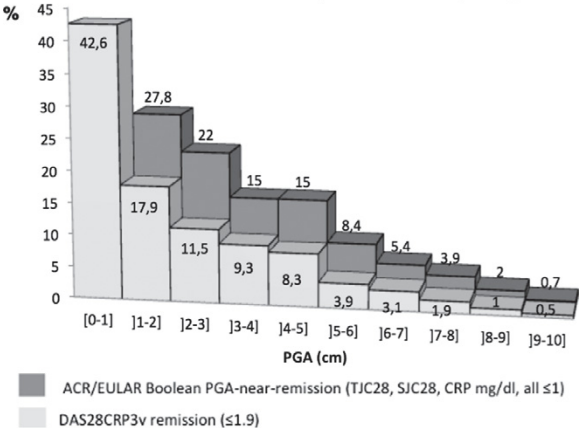
#Fleischmann 2015 (PMID:25143522).

Table 2. Hierarchical multivariable regression analysis to explain PGA

Model Block	All patients (n=6388)			Patients in Near-Remission (n=831)		
	Adj. R^2	R^2 change	sig. F Change	Adj. R^2	R^2 change	sig F Change
B1	0.008	0.008	<0.001	0.015	0.018	0.002
B2	0.018	0.010	<0.001	0.024	0.012	0.007
B3	0.620	0.602	<0.001	0.423	0.398	<0.001
B4	0.633	0.013	<0.001	0.426	0.004	0.092

Legend: B1 = Gender + Age + Dis. duration; B2 = B1 + Gross Nat. Income + bDMARD; B3 = B1 + B2 + Pain + HAQ; B4 = B1 + B2 + B3 + TJC28, SJC28, CRP.

Figure 1 - PGA distribution in patients in remission by DAS28CRP3v (n=2197) and in PGA-near-remission by Boolean definition (n=2090).



Conclusions: Two thirds of patients that achieve TJC28, SJC28, and CRP≤1 still perceive high PGA despite disease "inflammatory" control. The weight of PGA in DAI could lead to immunosuppressive overtreatment. In these patients, disease impact management, including non-pharmacological treatments delivered by Health Care Professionals, are more likely to be effective.
Disclosure of Interest: R. Ferreira Grant/research support from: MERIT foundation, M. Ndosi: None declared, C. Duarte: None declared, P. Carvalho: None declared, A. Chopra: None declared, K. Salomon-Escoto: None declared, D. Vega: None declared, D. van der Heijde: None declared, P. Machado: None declared, J. da Silva: None declared
DOI: 10.1136/annrheumdis-2017-eular.4695

SATURDAY, 17 JUNE 2017

HPR patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

SAT0719-HPR **"AND SUDDENLY YOU ARE A PERSON AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS!" DIFFERENT PERSPECTIVES OF INDIVIDUALS ON PREDICTIVE TESTING – RESULTS OF AN INTERNATIONAL QUALITATIVE INTERVIEW STUDY**

E. Mosor[1,2], M. Stoffer[2], G. Steiner[2], K. Raza[3], R.J. Stack[3], G. Simons[3], M. Falahee[3], G. Schett[4], A. Hueber[4], M. Engelbrecht[4], J. Smolen[2], T. Stamm[1]. *[1]Section for Outcomes Research, CeMSIIS - Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna; [2]Division of Rheumatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria; [3]Department of Rheumatology, University of Birmingham and Sandwell & West Birmingham Hospitals NHS Trust, Birmingham, United Kingdom; [4]Rheumatology and Immunology, Department of Internal Medicine 3, Universitätsklinikum Erlangen, Erlangen, Germany*

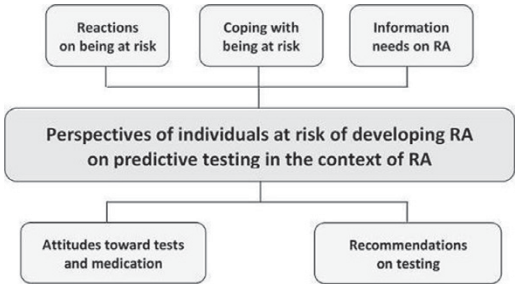
Background: People at risk of developing rheumatoid arthritis (RA) may be candidates for interventions aimed at preventing RA development [1]. The identification of such "at risk" populations includes testing for genetic and other (e.g. autoantibody) biomarkers. However, little is known about the people's perspectives on these tests, how they react and cope when identified as being a person "at risk" and what their unmet needs are.

Objectives: To expore the perceptions about RA and predictive testing and to understand the various reactions and coping strategies used when identified as being at risk of developing RA from the perspective of those directly concerned.

Methods: As part of the EuroTEAM project, a qualitative interview study with people who were informed of being at risk of developing RA was conducted. An interview schedule was developed and pilot-tested. Interviews were audio-recorded, transcribed verbatim and analyzed using thematic analysis.

Results: A total of 34 individuals (with rheumatoid factor and/or ACPA positive) already informed of being at risk of developing RA participated in the study, from Austria (n=15), Germany (n=15), and the UK (n=4). In Vienna, people who had been tested within an expanded health exam participated in this study. In Birmingham and Erlangen, people with arthralgia were recruited from the outpatient clinics. Analysis of the interview data revealed five overarching themes related to predictive testing in the context of RA (Figure).

There were differences between the perceptions of althralgia patients and asymptomatic individuals. People suffering from pain were much more frightened and worried when informed of being at risk of developing RA. As a consequence, they modified their lives in a larger extent and had greater knowledge about RA than those without any symptoms who were rather surprised, kept calm and hardly changed their lifestyle after being tested positive. Allmost all participants in this study would appreciate precise predictive tests in the context of RA. However, more than half of them would refuse synovial biopsy (even if this could help quantify risk more accurately) or preventive medication. Recommendations for an improved procedure of predictive testing in the field of RA were given, which could promote uptake of preventive strategies.



Conclusions: Participants showed large differences in views about predictive testing in the context of RA risk and offered specific suggestions that should be incorporated into service design and delivery in the context of future predictive testing programmes. These findings may also be relevant to prediction and prevention in the context of other diseases where multiple genetic risk factors interact with environmental risk factors to drive disease development.

References:

[1] van Steenbergen, H.W., T.W. Huizinga, and A.H. van der Helm-van Mil, The preclinical phase of rheumatoid arthritis: what is acknowledged and what needs to be assessed? Arthritis Rheum, 2013. 65(9): p. 2219–32.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4705

SATURDAY, 17 JUNE 2017

HPR service developments, innovation and economics in healthcare

SAT0720-HPR **LONGITUDINAL ANALYSIS OF RESPONSE, COSTS AND RESOURCE USE OF PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (BDMARDS) IN TAIWAN USING THE NATIONAL HEALTH INSURANCE RESEARCH DATABASE**

Q. Shi[1], T. Treuer[2], B.C. Wang[3], C.L. Gaich[4], C.-H. Lee[5], W.-S. Wu[5], W. Furnback[3], K.-J. Li[6], C.-H. Tang[7]. *[1]Eli Lilly & Co., Shanghai, China; [2]Eli Lilly & Co., Budapest, Hungary; [3]Elysia Group Ltd., Taipei, Taiwan, Province of China; [4]Eli Lilly & Co., Indianapolis, United States; [5]Eli Lilly & Co; [6]National Taiwan University; [7]Taipei Medical University, Taipei, Taiwan, Province of China*

Background: Rheumatoid arthritis (RA) is an inflammatory disorder associated with a significant physical and psychological burden. Patients with RA experience a lower quality of life than patients without RA. This study utilizes Taiwan's National Health Insurance Database (NHIRD) which is a claims-based database recording all interactions with the National Health Insurance (NHI) system.

Objectives: The objective of this study was to use the NHIRD to estimate the percentage of newly treated patients with inadequate response (IR) to biologic disease-modifying antirheumatic drugs (bDMARDs) as well as the costs and resources.

Methods: Data were from the catastrophic illness file within the NHIRD from 1/1/2009 to 12/31/2013. The index period spanned 2010 with a pre-index period consisting of the index date – 365 days, and patient follow-up was index date to 365 days post-index. Patients with a catastrophic illness card for RA were included in the study. Biologically-naïve patients included those who did not have a claim for a bDMARD or exclusion diagnoses in the pre-index period. Biologically-naïve patients with a bDMARD claim were indexed upon their first claim for a bDMARD during the index year. A validated algorithm was used to examine the rate of inadequate response in the biologically-naïve cohort of patients. Inadequate responders met one or more of the following criteria during their year of follow-up: low adherence (proportion of days covered <0.80); switched to or added a second bDMARD; added a new conventional synthetic DMARD (csDMARD); received ≥ 1 glucocorticoid injection; or increased oral glucocorticoid dosing. All-cause mean annual direct costs and resource use were measured in the year of follow-up. Costs were converted from NT$ to EUR using 1 NT$ =0.03 EUR.

Results: A total of 818 biologically-naïve patients initiated a bDMARD and were included in the study. At 1 year of follow-up, 66.01% (n=540) were classified as bDMARD-IR, 31.54% (n=258) were classified as confirmed stable, and 2.44% (n=20) were of unknown response status. Mean annual total direct costs in the follow-up year were €14,669 and €12,867 for the confirmed stable and inadequate responder cohorts, respectively. Mean annual non-medication costs were 40.4% (€578) higher for the IR cohort, and mean annual medication costs were 17.2% (€2,379) higher for the confirmed stable cohort. IR patients had higher mean annual resource utilization in the follow-up year with increases in hospital admissions (0.46 vs. 0.1), hospital days (3.4 vs. 0.49), outpatient visits (42.50 vs. 37.66), and emergency department visits (0.51 vs. 0.3).

Conclusions: A significant proportion of patients with RA initiating a bDMARD for the first time showed an IR to their treatment within a year. Patients with an IR had increased resource utilization and higher non-medication costs than those with stable disease. This level of IR suggests an unmet need in the RA treatment paradigm.

Disclosure of Interest: Q. Shi Employee of: Eli Lilly & Co., T. Treuer Employee of: Eli Lilly & Co., B. Wang Consultant for: Eli Lilly & Co., C. Gaich Employee of: Eli Lilly & Co., C.-H. Lee Employee of: Eli Lilly & Co., W.-S. Wu Employee of: Eli Lilly & Co., W. Furnback Consultant for: Eli Lilly & Co., K.-J. Li: None declared, C.-H. Tang: None declared

DOI: 10.1136/annrheumdis-2017-eular.5315

SATURDAY, 17 JUNE 2017

HPR epidemiology and public health (including prevention)

SAT0721-HPR **EXPOSURE TO PASSIVE SMOKING AND RA RISK; RESULTS FROM THE SWEDISH EIRA STUDY**

A.K. Hedström[1], L. Klareskog[2], L. Alfredsson[1]. *[1]Institute of Environmental Medicine; [2]Department of Medicine, Karolinska Institutet, Stockholm, Sweden*

Background: Smoking has consistently been associated with increased risk of developing rheumatoid arthritis (RA). However, no studies have been performed investigating the effect of exposure to environmental tobacco smoke (i.e. passive smoking) on RA risk.

Objectives: The aim of this study was to estimate the influence of passive smoking on the risk of developing the two major subsets of RA, defined by anti-citrullinated protein antibodies (ACPA) status.

Methods: A population-based case-control study using incident cases of RA was performed in Sweden, and the study population in this report was restricted to include never smokers (589 cases, 1764 controls). The incidence of RA among never smokers who had been exposed to passive smoking was compared with that of never smokers who had never been exposed, by calculating the odds ratio with a 95% confidence interval employing logistic regression.
Results: No association was observed between exposure to passive smoking and RA risk (OR 1.0, 95% CI 0.8–1.2 for ACPA positive RA, and OR 0.9, 95% CI 0.7–1.2 for ACPA negative RA). No suggestion of a trend between duration of passive smoking and RA risk was observed.
Conclusions: No association was observed between exposure to passive smoking and RA risk, which may be explained by a threshold below which no association between smoke exposure and RA occurs.
Acknowledgements: The EIRA study was supported by grants from the Swedish Medical Research Council, the Swedish Council for Health, Working life and Welfare, King Gustaf V:s 80-year foundation, the Swedish Rheumatism Foundation, Stockholm County Council, the insurance company AFA, the EU-supported AutoCure and BeTheCure projects, and from the COMBINE (Controlling chronic inflammatory diseases with combined efforts) project.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3389

SAT0722-HPR FAMILIAL RISKS OF RHEUMATOID ARTHRITIS: EVIDENCE FROM THE MALAYSIAN EPIDEMIOLOGICAL INVESTIGATION OF RHEUMATOID ARTHRITIS CASE-CONTROL STUDY

C.L. Too[1,2], L.K. Tan[3], A.F. Nurul Aain[3], S. Salsabil[3], H. Heselynn[4], S. Wahinuddin[5], I.S. Lau[6], S.C. Gun[7], S. Nor-Shuhaila[4], M. Eashwary[4], M.S. Mohd-Shahrir[8], M.-M. Ainon[9], R. Azmillah[6], O. Muhaini[10], C. Bengtsson[11], L. Padyukov[2], L. Alfredsson[11], L. Klareskog[2], M. Shahnaz[12].
[1]Allergy and Immunology Research Center, Institute for Medical Research, Kuala Lumpur, Malaysia; [2]Department of Medicine. Rheumatology Unit, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden; [3]Institute for Medical Research, Kuala Lumpur; [4]Department of Medicine, Putrajaya Hospital, Putrajaya; [5]Faculty of Medicine, Universiti Kuala Lumpur Royal College of Medicine Perak, Ipoh; [6]Department of Medicine, Selayang Hospital, Selayang; [7]Department of Medicine, Hospital Tunku Ja'afar Seremban, Seremban; [8]Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Center, Kuala Lumpur; [9]Department of Medicine, Tengku Ampuan Afzan Hospital, Kuantan, Pahang; [10]Department of Medicine, Hospital Raja Perempuan Bainun, Ipoh, Perak, Malaysia; [11]Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; [12]Ministry of Health. Level 12th, Block E7, Parcel E, Federal Government Administrative Center, Putrajaya, Malaysia

Background: Family history of rheumatoid arthritis (RA) is a surrogate for an individual's genetic and partly environmental risk of developing RA. It is assessed daily in clinical practice and its magnitude and pattern of distribution may provide information on the RA etiology.
Objectives: We investigated the association between family history of RA and the risk of anti-citrullinated peptide antibody (ACPA)-positive and ACPA-negative RA in the Malaysian population.
Methods: Data from the Malaysian Epidemiological Investigation of Rheumatoid Arthritis (MyEIRA) population-based case-control study involving 1,055 early RA cases and 1,055 age, sex and residential area-matched controls were analyzed. Information from interview-reported family history of RA or rheumatic stiff back among first degree relatives was used to estimate the risk of developing ACPA-positive and ACPA negative RA. The odds ratio (OR) with 95% confidence interval (CI) was calculated.
Results: In this study, 64% of the RA patients were ACPA-positive and 40% of the overall RA carried HLA-DRB1 shared epitope (SE) alleles. Family history of RA was significantly associated with an increased risk of developing RA in the Malaysian population (RA versus controls, 17.0% vs. 7.7%, OR 2.4, 95% CI 1.8–3.2, $p<0.0001$). The association between positive family history and risk of RA was uniformly observed for the ACPA-positive RA (OR 2.5, 95% CI 1.8–3.3, $p<0.0001$) and ACPA-negative RA (OR 2.3, 95% CI 1.6–3.2, $p<0.0001$) subsets, respectively. A dramatically increased risk for ACPA-positive RA was seen in individuals who both were having positive family history of RA and carried HLA-DRB1 SE alleles (OR 14.7, 95% CI 7.7–27.8). We also observed a lesser risk magnitude in the ACPA-negative RA patients (OR 5.7, 95% CI 2.7–11.9).
Conclusions: Our data demonstrate that family history of RA remains an important clinical risk factor for RA. In addition, positive family history of RA was associated with an increased risk of developing both the ACPA-positive and ACPA-negative RA in the Malaysian population, suggesting that the two RA subsets are similar in genetic risk factors that overlap with these diseases.
References:
[1] Frisell T, Saevarsdottir S, Askling J. Family history of rheumatoid arthritis: an old concept with new developments. Nat Rev Rheumatol. 2016 Jun;12(6):335–43.
[2] Frisell T, Hellgren K, Alfredsson L, Raychaudhuri S, Klareskog L, Askling J. Familial aggregation of arthritis-related diseases in seropositive and seronegative rheumatoid arthritis: a register-based case-control study in Sweden. Ann Rheum Dis. 2016 Jan;75(1):183–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4714

SATURDAY, 17 JUNE 2017

HPR patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

SAT0723-HPR GENDER DIFFERENCES IN COPING STRATEGIES AND ILLNESS ACCEPTANCE IN PATIENTS WITH INFLAMMATORY ARTHRITIS – A NATIONWIDE CROSS-SECTIONAL STUDY

B.A. Esbensen[1,2], C. Flurey[3], K.V. Jensen[1], L. Andersen[1], N.M. Hammer[1].
[1]Rigshospitalet - Glostrup, COPECARE, Centre for Rheumatology and Spine Diseases & Research Unit, Glostrup; [2]Department of Clinical Medicine, Faculty of Health and Medical, University of Copenhagen, Copenhagen, Denmark; [3]Rheumatology Unit, Bristol Royal Infirmary, West England, Bristol, United Kingdom

Background: There is an increasing focus on how patients with inflammatory arthritis (IA) manage living with arthritis. There are a preponderance of women with RA (70%), thus previous research has overall focused on female patients and their management. Research in other long term conditions suggests men need their own health strategy[1], thus it is important to investigate whether there are gender differences in coping strategies and illness acceptance within chronic IA.
Objectives: To explore gender differences in IA as reflected by coping strategies and illness acceptance. Furthermore, to identify factors associated with high degree of illness acceptance.
Methods: The study was conducted as a nationwide cross-sectional study using online survey during 2016. Patients >18 with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) were invited to contribute through: The Danish Rheumatism Organization, local arthritis networks, diagnosis networks, and rheumatology departments across the country. The self-report online questionnaire comprised Socio-demographics, Diagnosis, Symptoms (pain, fatigue, global), Medications, Disease Activity, Functional Status, Coping (i.e. confrontation, avoidance and acceptance-resignation) and Illness Acceptance. As recommended by EULAR 2 patients with RA (KVJ & LA; male and female, respectively), were included as equal research partners in all phases of the study. Descriptive statistics were applied to explore gender differences, and logistic regression analyses were performed to test for factors associated with illness acceptance.
Results: In total, 664 (85% women) were included in the study; RA 53%, PsA 27% and axSpA 20%. More men (40%) than women (30%) were treated with biological DMARDS (p=0.048). No significant gender differences were found in disease activity, symptoms and functional status. Overall, the total sample had high degree of illness acceptance and no significant difference was found between males and females. Regarding illness coping, women with IA tend to use avoidance as a coping strategy significantly more than men (p=0.015). In the final multivariable regression model, higher education (OR=1.46; 1.02–2.11), longer time diagnosed (OR=1.21 per 1-yr. increase; 1.01.-1.05), lower physical disability (OR=0.76; 0.69–0.85), better coping with fatigue (OR=1.13; 1.05–1.22), less avoidance (OR=0.93; 0.87–0.99) and acceptance-resignation (OR=0.62; 0.62–0.75) as coping strategies were significantly associated with high degree of illness acceptance.
Conclusions: No significant differences were found in illness acceptance among women and men with IA. However, women tended to use avoidance as a coping strategy more than men. High levels of illness acceptance may be explained by high education, longer disease duration, and better physical function, better coping of fatigue and less use of passive coping strategies.
References:
[1] White A, McKee M, Richardson N, et al. Europe's men need their own health strategy. BMJ 2011;343:d7397.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5027

SAT0724-HPR GOTHENBURG NURSE LED TIGHT CONTROL STUDY – GOTNET. PATIENTS' EXPERIENCES OF NURSE-LED CARE AND TIGHT CONTROL. A QUALITATIVE STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS

U. Bergsten[1,2], A.-S. Sjö[1]. *[1]Rheumatology Department, Sahlgrenska University Hospital, Gothenburg; [2]Department of Research, Development and Education, Region Halland, Varberg, Sweden*

Background: Rheumatoid arthritis (RA) is a chronic inflammatory illness, using both pharmacological and non-pharmacological therapies. Some patients experience good treatment, knowledge about their illness and situation. For other patients, it might look different depending on how much they know about their illness. Earlier research has primary focused on patients in remission. In order to strengthen and support patients with RA that are not feeling well, to give them more knowledge about their situation, one strategy could be that they have access to a nurse-led rheumatology clinic with person-centered care (PCC).

Objectives: The aim of this study was to describe patients' experiences of nurse-led care tight control.
Methods: Qualitative design was used in order to receive deeper understanding of the phenomenon. Interviews were conducted with 12 informants (with strategic sample) that participated in the intervention group of a randomized controlled trial exploring the effect of patient centered care, the Got-Net study. The interviews were analyzed using phenomenography approach.
Results: The informants' experiences of nurse-led care tight control emerged in three categories. The three categories describe the process, the relationship between the concepts. The first step describes the *Meeting of competence*, the next step that the informant experienced was *Relationship building* and the last step to have *Made a personal journey*.
Conclusions: Patients with RA who got the opportunity of nurse-led care and tight control became strengthen, got extended knowledge about their illness. Patients have been treated on their own level, knowledge and needs, by using a person-centered approach.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4675

SATURDAY, 17 JUNE 2017

HPR interventions (educational, physical, social and psychological)

SAT0725-HPR GOTHENBURG NURSE LED TIGHT CONTROL STUDY - GOTNET. A STUDY COMPARING "CARE AS USUAL" WITH NURSE LED CLINIC, TIGHT CONTROL AND PERSON CENTRED CARE IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) AND WITH MODERATE/HIGH DISEASE ACTIVITY

U. Bergsten[1,2], K. Almehed[2], L. Jacobsson[3]. [1]*Department of Research, Development and Education, Region Halland, Varberg;* [2]*Rheumatology Department, Sahlgrenska University Hospital, Gothenburg;* [3]*Department of Rheumatology a Inflammation Research, Institute of Medicine, Gothenborg, Sweden*

Background: The treatment guidelines of EULAR recommend treatment according to "tight control" (TC), clear treatment goals (Treat-to-Target, T2T) and patient involvement. Despite this, the care for patients with RA needs to be improved as demonstrated by the fact that as many as that 45% of patients with RA in Sweden (according to the Swedish Rheumatology Quality Register in 2015) do not reach the level of low disease activity. One way to overcome this could be nurse led clinics of RA patients, which for patients in remission have shown positive effects on patient's pain, knowledge and self-efficacy. We hypothesized that a nurse-led clinic based on the above principles of TC, T2T and Person-centered care would result in better outcome compared to care as usual.
Objectives: The aim of the study was to compare the effect of such nurse-led clinic with frequent visits and person-centered care with regular care of patients with established RA and a moderate to high disease activity.
Methods: This was a randomized, controlled, blinded assessor study that aimed to compare the effect of nurse-led clinic with regular care of patients with the established RA. Inclusion criteria were; duration of RA >2 yrs., DAS28>3.8, age <85 yrs. and not having experience with all available csDMARDs and bDMARDS. Patient with any severe current comorbidity were excluded. Intervention Group (IG): intervention included two elements; 1) disease activity control every 6th week, with clear treatment goals (DAS28 <2.6)and escalation of pharmacological therapy according to existing Swedish guidelines, 2) a written person-centered care health plan with shared goal setting and decision making between patient and nurse. Control Group (CG): Patients in the control group were followed by a physician once every 3 to 6 month. Evaluation was done at w 26 both per protocol (shown) and according to intention to treat (ITT) with LOCF. Primary outcome was change in DAS28 at week 26 and secondary outcome the proportions of good/moderate EULAR response. Pre study power calculations estimated group sizes to 60 patients in each group. Due to difficulties in the recruiting process the study was stopped preterm
Results: The study included 70 patients of which (IG: 36 and CG: 34) with similar baseline characteristics as a result of the randomization. Sixty-two patients completed the study at w 26 (IG: 29 and CG: 33). Both groups improved significantly in DAS 28 (Table 1). The change in DAS 28 was not significantly different between groups, although the numerical improvement was larger in the IG compared to CG (Table 1). Furthermore, significantly more patients in the IG improved according to EULAR Good or Moderate response (Table 1). Results were similar when analyzing according to ITT with LOCF.

Table 1. Primary outcome (delta DAS 28) and secondary outcome (good/moderate EULAR response)

	IG	CG	Difference (95% CI)
ΔDAS 28 (95% CI)	1.5 (-2.0,-1.0)	1.1 (-1.6,-0.6)	- 0.43 (-1.13,0.27)
EULAR Good/Moderate (%)	22/29 (76%)	16/33 (48%)	27% (3–51%)

Conclusions: This controlled trial suggest that a nurse-led clinic for RA patients with moderate/high disease activity may be effective. Although not shown, it likely to be cost-effective and possible to implement in clinical care.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2659

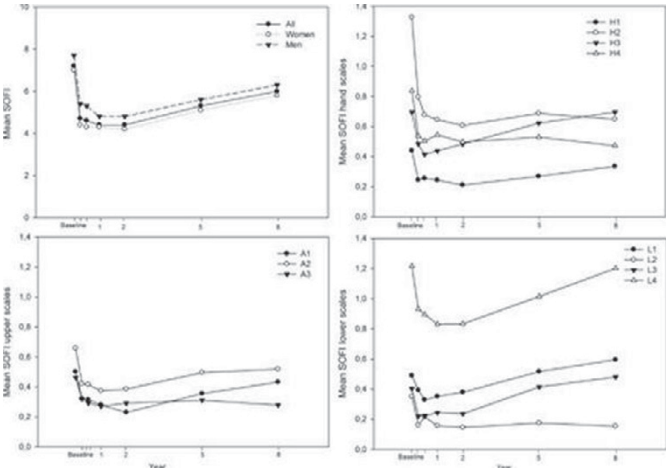
SATURDAY, 17 JUNE 2017

HPR patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

SAT0726-HPR FUNCTIONAL IMPAIRMENT IN PATIENTS WITH RA IN AN EIGHT YEAR PERSPECTIVE

A. Bremander[1,2,3], K. Forslind[4,5], K. Eberhardt[1], M. Andersson[1,3]. [1]*Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund;* [2]*School of Business, Engineering and Science, Halmstad University;* [3]*Spenshult Research and Devlopment Centre, Halmstad;* [4]*Department of Clinical Sciences, Section of Rheumatology, Lund University, Lund and Helsingborg;* [5]*Department of Research and Education, Helsingborg's hospital, Helsingborg, Sweden*

Background: In people with Rheumatoid arthritis (RA) impaired physical functioning is an acute as well as long term effect of the disease. Observational performance tests reflecting range of motion in upper as well as in lower extremities should be easy to perform in the clinic as well as in research as a complement to self-reported measures of physical functioning. The Signal Of Functional Impairment (SOFI)[1] is a performance test which so far has been applied only in Sweden but commonly used in the clinic and in long term follow-up clinical studies.
Objectives: The aim was to study performance-based function assessed with SOFI over 8 years and, secondly, to study which items included in SOFI that were associated with change in functioning over time.
Methods: An inception cohort of 1 052 patients with early RA, from the BARFOT-study, recruited 1992–2006 was investigated, mean (SD) age was 54 years (14), 70% were women. The patients were followed by a structured protocol at baseline, 3 and 6 months and at 1, 2, 5, and 8 years. SOFI consists of 3 parts measuring hand, arm (upper), and leg (lower) function (1). Hand function is tested by 4 movements; cylinder grip (H1), pen grip (H2), pincer grip (H3) and opposition of the thumb (H4). Arm function is assessed by 3 movements; hand behind the head and the ability to touch the cervical spine processes with fingers (A1), elbow supination (A2) and elbow extension (A3). Leg function is tested by 4 movements; the ability to touch the opposite knee with the heel while sitting (L1), knee extension in supine position (L2), dorsiflexion of the foot standing on a balance board (L3), and the ability to stand on tip toes without shoes (L4). An assessor scores the patient's ability to perform the different tests on an ordinal scale (0=normal, 1= partly impaired and 2= unable to perform). The range of SOFI scores is 0–44 (best to worst).
Results: At baseline the mean (SD) SOFI was 7.2 (5.8), and at 1 year follow-up the improvement was 2.75 (5.65), p<0.001. From 1 year to 8 year follow-up the deterioration was 1.5 (4.6), p<0.001. When studying hand, upper and lower function separately, the pen grip and the ability to stand on tip toes improves most during the first year. From 1 to 8 year the pincer grip and the ability to stand on tip toes are the items that deteriorate most (Figure). Assessment of the pen grip, the pincer grip and the ability to stand on tip toes explain 58% to 70% of the SOFI score over time, with the highest rate at 5 (65%) and 8 years follow-up (70%).



Conclusions: Functioning as assessed by SOFI improved during the first year in patients with early RA and then deteriorated slowly. Over a longer period, pincer grip and the ability to stand on tip toes seemed to be the two most important items to measure when assessing functional impairment over time.
References:
[1] Kerstin B. Eberhardt, B. Svensson and U. Moritz. Functional assessment of early rheumatoid arthritis British Journal of Rheumatology 1988;27:364–371.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4316

SAT0727-HPR THE EFFECT OF INSPIRATORY MUSCLE TRAINING ON AEROBIC CAPACITY, PULMONARY FUNCTION AND FUNCTIONAL STATUS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: A RANDOMIZED CONTROLLED STUDY

B. Basakci Calik, E. Gür Kabul, H. Taskın, O. Telli Atalay, U. Bas Aslan, M. Tascı, F. Bıcakcı, A.I. Yıldız. *Pamukkale University, Denizli, Turkey*

Background: In ankylosing spondylitis (AS) the chronic inflammatory process mainly affects the axial skeleton with ensuing pain and limitation of thoracic and spinal mobility. Most of the AS patients have the complaint of reduced exercise capacity. Pulmonary function impairment, chest wall restriction, weak respiratory muscle performance, peripheral muscle weakness and deconditioning have been reported as the hypotheses for reduced exercise capacity.
Objectives: The aim of this study was to evaluate the effects of inspiratory muscle training on aerobic capacity, pulmonary function and functional status in patients with AS.
Methods: A total of 32 patients (18 female, 16 male; mean age: 37.3±10.4 years) were included in this study. The patients were randomized as two groups; Group I consisted of 16 patients, received inspiratory muscle training (IMT) in addition to conventional exercise (CE), Group II consisted of 16 patients, received only CE. All assessments were done before and after the training (8 weeks) for every patient. Standard pulmonary function tests were applied for pulmonary volumes. Maximum inspiratory pressure (PImax), maximum expiratory pressure (PEmax) were also measured as respiratory muscle strength. Six-minute walk test (6MWT) was used for the assessment of aerobic capacity. For the evaluation of functional status, the Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI) were used. CE training program consisted of 20 exercises: motion and flexibility exercises of the cervical, thoracic, and lumbar spine; stretching of the hamstring muscles, erector spine muscle, and shoulder muscles. IMT training load was based on 50% of the patient's sustained maximum inspiratory pressure. The patients started by performing ten loaded inspiration with a 60 second rest period between each inspiration for three sets in each session. Four sessions of IMT was applied in a day. The exercises were performed as home program for five days per week, 40 minutes per session. Wilcoxan test was used to compare groups.
Results: After eight weeks follow-up, patients in Group I had a significant increase in PImax (p=0,000), PEmax (p=0,05), and 6MWT (p=0,041) compared with Group II (p=0,134, p=0,020, p=0,281, respectively). There were no significant differences of spirometric measurements. Comparison of the groups showed significantly superior results for group I in BASDAI (p=0,049).
Conclusions: Ankylosing spondylitis patients who performed eight weeks of inspiratory muscle training in addition to conventional exercise training, had an increased respiratory muscle strength, a better aerobic capacity, and disease activity than those who performed conventional exercise only. Inspiratory muscle training should be disseminated with these patients due to advantages.
References:
[1] Dragoi GR, Amaricai E, Dragoi M, Popoviciu H, Avram C. Inspiratory muscle training improves aerobic capacity and pulmonary function in patients with ankylosing spondylitis: A randomized controlled study. 2015 Clinical Rehabilitation, doi: 10.1177/0269215515578292.
Acknowledgements: Inspiratory muscle training should be disseminated with these patients due to advantages.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6076

SAT0728-HPR A PATIENT SATISFACTION SURVEY: PATIENTS' PERCEPTIONS OF BIOLOGIC DOSE TAPERING

C. Jones, H. Robinson, D. Rees, V. Jolliffe, J. Trickey, J. Wood, S. Andrews, S. Capillas, A. Peall. *Rheumatology, Wye Valley NHS Trust, Hereford, UK*

Background: Evidence shows that remission can be maintained in selected patients whose biologic medication is dose tapered[1]. In June 2015 we began tapering the doses of selected rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis patients in disease remission. The process was agreed with the local commissioners and a protocol[2] was devised to guide safe and evidence based biologic dose tapering. Benefits include reduced medication burden for patients, fewer day-case infusions and financial savings. However, there is a lack of knowledge of patients' perceptions of the process.
Objectives: Our department proposed to investigate patients' perceptions of their experience of dose tapering. We wanted to assess patients' understanding and acceptance of the process and ensure they felt included in decision making. Patient feedback enables reflection and improved practice.
Methods: An anonymous, tick-box, patient satisfaction survey was devised. It requested that patients stated the extent to which they agreed with a statement, also allowing free-text comments. The survey was posted to relevant patients after their identification from our biologics database. A stamped addressed envelope was provided for return of the completed survey.
Results: 56 surveys were posted, 46 (82%) were returned. 31 (67%) of patients were pleased to taper their medication, 35 (76%) felt fully included in decision making and 36 (78%) agreed that they had the opportunity to ask questions. Of the 13 patients whose disease flared post-taper, 8 (62%) agreed that they were promptly reviewed in clinic, 1 patient (8%) disagreed.
Some admitted to anxiety prior to dose tapering, however once established on their new dose, continuing disease remission was reassuring. Patients felt that they could contact the rheumatology helpline if required. Some also expressed that their quality of life had improved due to the decreased medication burden.
6 (37.5%) of the 16 rituximab patients who replied, disagreed that they were included in the decision to dose taper. Therefore, clinicians must ensure information provided is clear, that a full discussion occurs and the patient has an opportunity to ask questions. On review, it was evident that the wording of the survey may have caused confusion for rituximab patients. The term "dose reduction" may have suggested that the dose of medication in their infusion was reduced. In practice, the patient decreased from two infusions to one.
Conclusions: The majority of patients expressed that they were content with the biologic dose tapering process and felt sufficiently included in decision making. Importantly, a large proportion of patients were of the opinion that they were reviewed quickly when their disease flared.
Practice can be improved from the knowledge that some patients would appreciate more communication regarding the decision to dose taper. Also, when undertaking further patient surveys, questions must be clear and unambiguous.
References:
[1] JS Smolen, R Landewé, FC Breedveld, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis 2014;73:492–509.
[2] C Holloway. Wye Valley NHS Trust: Biologics in Rheumatology: Dose Tapering Protocol. Sept. 2015.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1862

SAT0729-HPR PSYCHOLOGICAL PROFILE OF PATIENTS WITH FIBROMYALGIA SYNDROME

D. Xhaxho[1], J. Lauri[2], M.A. Lauri[3], J. Fleri Soler[1], A. Borg[1], C. Mercieca[1]. *[1]Rheumatology, Mater Dei Hospital; [2]Mathematics; [3]Psychology, University of Malta, Swatar, Malta*

Background: Fibromyalgia (FM) is a chronic non inflammatory condition characterized by pain and fatigue as well as physical and psychological symptoms. Management can be particularly challenging and a combination of pharmacological and non pharmacological treatments are recommended.
Objectives: The aim was to study the level of anxiety and depression in fibromyalgia patients and whether these were associated with symptom severity, functional status, social or demographic factors.
Methods: A cross sectional survey of 155 consecutive patients attending the nurse-led fibromyalgia clinic was carried out. Patients were diagnosed using the 2010 ACR diagnostic criteria. Demographic data, Widespread Pain Index (WPI), Symptom Severity Score (SSS), VAS pain and VAS fatigue were recorded. Patients filled in the self-administered questionnaires including the Revised fibromyalgia impact questionnaire (FIQR), Hospital Anxiety and Depression Scale (HADS). Patients were classified as suffering from high anxiety or depression if HADS was $\geq$11, moderate if 8–10 and low $\leq$7 for each scale respectively.
Cross tabs and chi squared were used to study associations between anxiety and depression and social and demographic factors. Logistic regression analysis was performed to identify whether WPI, SSS, FIQR, VAS pain and VAS fatigue were predictors of severe anxiety and depression.
Results: One hundred fifty five patients (92% female) participated in the survey. The average age was 50.3 years (SD 11.5) and mean duration of symptoms 13.4 years (SD 11.3). The mean HADS-A (anxiety) was 11.8 (SD 4.13), HADS-D (depression) 9.1 (SD 3.8) and FIQR 60.3 (SD 17.6).
High levels of depression were reported by 31.5%, moderate 32.1% and low 30.3%. High levels of anxiety were reported by 60%, moderate 21.2% and low 13.3%. Both high levels of anxiety and depression were found in 25.2% of patients.
SSS was the single best predictor for anxiety (p=0.001) while disease duration (p=0.01), SSS (p=0.02) and FIQR (0.04) predicted depression. VAS pain and VAS fatigue were not good predictors of severe anxiety and depression. When patients with high levels of anxiety and depression were compared with those with moderate and lower levels no association was found with age or social factors including occupation, marital status, level of education and family support.
Conclusions: Both severe anxiety and depression were highly prevalent in our FM cohort, particularly anxiety. All FM patients need to be screened for anxiety and depression particularly those with high SSS and FIQR scores and longer disease duration.
A psychiatrist and psychotherapist with a special interest in FM are essential members of the multidisciplinary team to ensure that anxiety and depression are addressed early prior to starting further interventions for FM.
References:
[1] Jensen KB, Fransson P, Marcus HM, Williams SCR, Choy E, Mainguy Y, Gracely R, Ingvar M, Kosek E (2010) anxiety and depression in fibromyalgia

are related to poor perception of health but not to pain sensitivity or cerebral processing of pain. Arthritis & Rheumatology Journal 62(11).
[2] Ugar M, Sarp U, Karaaslan O, Tanik N, Arik HO (2015) Health anxiety and depression in patients with fibromyalgia syndrome. Journal of Inernational Medical Research 45(3):679–685.
Acknowledgements: NIL.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1445

SAT0730-HPR DIFFERENCES IN PERCEPTION OF THE DISEASE CONSTRAINTS BETWEEN THE CHILD AND PARENTS IN JIA

E. Ünal[1], P. Kısacık[1], G. Arin[1], N.B. Karaca[1], E.D. Batu[2], Z.S. Arıcı[2], E. Sönmez[2], Y. Bilginer[2], S. Özen[2]. *[1]Department of Physiotherapy and Rehabilitation, Hacettepe University Faculty of Health Science; [2]Pediatric Rheumatology, Hacettepe University Faculty of Medicine, Ankara, Turkey*

Background: Studies suggest that the perception of the child and family differ in juvenile idiopathic arthritis. This may pose a problem for the clinician's assessment (1,2).
Objectives: The aim of this study was to evaluate the differences in perception of the disease constraints between child and parent in JIA.
Methods: 129 children with JIA were included in the study.The main complaint about the illness was requested to be expressed in writing by both the child and the family. Individuals' expressions and demographic data were recorded. The main complaints were considered nominal. The correlation between the parent's and child's expressions were examined. The types of complaints were classified as none, functional, symptomatic, and both functional and symptomatic.
Results: The age range of children ranged from 6 to 21 (mean±SD; 12,86±3,68). When the complaints of the 129 children and the parents were compared, 45,7% were different, 20,2% were partially similar and 34,1% were perfectly similar complaints.When the answers of the 59 children and parents who differ in their complaints were examined; 67.8% of the children expressed a milder disease than their parents (Table1). While the family mostly concentrated on the symptoms, the children were worried on functional complaints (Table1).

Table 1. Results of the evaluations

	Child + Parent (n=129)	Differing perception of problems in the child and parent (n=59)
Group of complaint - Child		
None n (%)	49 (38)	16 (27,1)
Function n (%)	43 (33,3)	23 (39)
Symptom n (%)	20 (15,5)	9 (15,3)
Function + Symptom n (%)	17 (13,2)	11 (18,6)
Group of complaint - Parent		
None n (%)	50 (38,8)	16 (27,1)
Function n (%)	10 (7,8)	4 (6,8)
Symptom n (%)	57 (44,2)	36 (61)
Function + Symptom n (%)	12 (9,3)	3 (5,1)

Conclusions: As a result of this study, there was a difference between parent's and child's perception of the disease. While children report functional complaints, parents focus on symptomatic complaints. Exercise approaches should focus on the child's functional complaints and identify common goals with the family. Families should be educated about the importance of the complaints that the child expresses.
References:
[1] Manczak, M. Rutkowska-Sak, L. Raciborski, F. Health-related quality of life in children with juvenile idiopathic arthritis – child's and parent's point of view. Reumatologia 2016; 54(5):243–250.
[2] Consolaro, A. Negro, G. Lanni, S. et al. Toward a treat-to-target approach in the management of juvenile idiopathic arthritis. Clin Exp Rheumatol 2012; 30(4 Suppl 73): 157–162.
Acknowledgements: The author declare that they have no conflict of interest.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5749

SAT0731-HPR SYMPTOMS OF PAIN, FATIGUE AND SELF-EFFICACY IN YOUNG PATIENTS WITH SPONDYLOARTHRITIS – A COMPARISON BETWEEN WOMEN AND MEN

A. Torell[1], A. Bremander[2,3,4], S. Bergman[3,4,5], E. Haglund[2,4]. *[1]Department of physiotherapy, Ängelholms sjukhus, Ängelholm; [2]School of Business, Engineering and Science, Halmstad Univeristy, Halmstad; [3]Department of clinical Sciences, Lund, Section of rheumatology, Lund University, Lund; [4]Spenshult R&D center, Sweden, Halmstad; [5]Primary Health Care Unit, Department of Public Health and Community Medicine, Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*

Background: Spondyloarthritis (SpA) often has an early disease onset with inflammatory back pain debuting already in young adulthood. Studies have shown gender differences in disease specific areas but few studies have focused only on the younger subjects. Extended knowledge based on self-reported information can help to better understand the characteristics of these younger women and men with SpA.
Objectives: To study the differences between young women and men with SpA with regard to self-reported pain measures, disease activity, fatigue, self-efficacy and health status.
Methods: A cross-sectional population based cohort of 201 patients age 18–36 years with SpA identified through a health care register by searching for ICD-10 codes for SpA between the years 2003–2007. They all responded to a questionnaire survey in 2009. 29% were diagnosed with ankylosing spondylitis, 39% with psoriatic arthritis, and 32% with undifferentiated spondyloarthritis. The survey included questions concerning pain (NRS 0–10 and a pain mannequin), fatigue (NRS 0–10), self-efficacy (ASES 10–100, low-high). The pain mannequin was used to categorize patients into groups; no chronic pain (NCP), chronic regional pain (CRP)or chronic widespread pain (CWP). Self-reported disease activity (BASDAI 0–10) and health status (EQ5D, 0–1) were used to describe the group. Characteristic symptoms are reported as mean, standard deviation (SD) and frequencies. T-test and Chi2 test were used to study gender differences.
Results: The mean age (SD) was, 30 (5) years, 60% were women. The group reported disease activity scores (BASDAI) of 3.8 (2.3), health status 0.75 (0.16), and a disease duration of 7 (5) years. One third were smokers or former smokers, and 69% reached WHO's recommended level of health enhancing physical activity. 21% reported CRP, 41% CWP and the remaining 38% reported NCP. More women reported CWP pain than men, (48% vs. 30%, p=0.026). Women also reported worse pain compared to men, (3.9 (2.4) vs. 2.9 (2.1), p=0.001), worse fatigue (5.0 (2.6) vs. 3.9 (2.7), p=0.003), less self-efficacy for pain (53 (20) vs. 59 (21), p=0.040) and also for symptoms (59 (19) vs. 65 (20), p=0.038).
Conclusions: A significant proportion of both women and men reported symptoms consistent with chronic widespread pain already at young age. Women reported in general worse health compared to men, including pain distribution, pain intensity and pain management. This information could be valuable for clinicians in the care of young patients with SpA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4624

SAT0732-HPR RESILIENCE AND POSITIVE AFFECT ARE RELATED TO THE EXPERIENCE OF FATIGUE IN PATIENTS WITH A RHEUMATIC DISEASE

E. Taal[1], K. Schreurs[1], L. Guddorf[1], C. Bode[1], M. van de Laar[2]. *[1]Psychology, Health & Technology, University Twente; [2]Rheumatology, Medisch Spectrum Twente, Enschede, Netherlands*

Background: Fatigue is a common symptom in patients with a rheumatic disease. Resilience, the ability to bounce back or recover from stress, has been found to be related to lower fatigue in patients with cancer, traumatic brain injury, cardiac disease and fibromyalgia (see e.g. [1])
Objectives: To study the relationships of resilience and the resilience related factors positive affect, acceptance and engaged living with fatigue in patients with rheumatic diseases.
Methods: 57 patients with a rheumatic disease (rheumatoid arthritis, 70%; osteoarthritis, 11%; others, 9%) completed an online questionnaire. Fatigue was assessed with SF-36 vitality scale; pain with a VAS; Resilience with BRS and resilience related factors with PANAS (positive affect), AAQ-II (Acceptance) and ELS (engaged living). Data were analysed with hierarchical multiple regression analyses.
Results: Resilience, positive affect, acceptance and engaged living were multivariate significantly related to fatigue (R^2 =0.54; $P \leq 0.001$). Resilience (β=0.29; $P \leq 0.05$) and positive affect (β=0.39; $P \leq 0.01$) were significant individual predictors of lower fatigue in multiple regression analysis. Acceptance and engaged living were not significantly related with fatigue in the multivariate model. The relationship between resilience and fatigue was partially mediated by positive affect. When pain was included in the model the relations of resilience (β=0.27; $P \leq 0.05$) and positive affect (β=0.34; $P \leq 0.05$) with fatigue remained significant.
Conclusions: Resilience and positive affect may be predictors of decreased fatigue in rheumatic patients. Further longitudinal studies are needed to examine the causality of these relationships.
References:
[1] Smith BW, Dalen J, Wiggins K, Tooley E, Christopher P, Bernard J. The brief resilience scale: Assessing the ability to bounce back. Int J Behav Med 2008;15(3):194–200.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6378

SAT0733-HPR A QUALITATIVE STUDY ON OBSTACLES AND MOTIVATIONS TO VACCINATIONS IN RHEUMATOID ARTHRITIS

F. Fayet, C. Savel, M. Rodere, M. Soubrier, S. Mathieu. *Rheumatology department, CHU Clermont-Ferrand, Clermont-Ferrand, France*

Background: Rheumatoid arthritis (RA) is characterized by an increased risk of infection, which is further enhanced by the associated treatments like corticosteroid therapy or biologicals. To diminish this risk, influenza and

pneumococcal vaccinations have been recommended prior to initiating treatment with biological agents. The COMEDRA trial, conducted in France, revealed the usefulness of a nurse-led consultation in the management of RA-associated comorbidities. Despite this, however, only 40% of patients were shown to be appropriately vaccinated (1).
Objectives: This study sought to better understand the obstacles encountered in RA patients as to influenza and pneumococcal vaccinations, along with their motivations.
Methods: This qualitative study was conducted at the rheumatology department by means of semi-directed nurse-led interviews lasting about 45 minutes, between July and November 2015. Four topics were analyzed: obstacles and motivations to influenza vaccination, obstacles and motivations to pneumococcal vaccination, post-vaccination follow-up, and information sources. The interviews were registered and transcribed within 45 hours post-interview, and were pursued until data saturation. Transversal data analysis was carried out by the nurse in charge of the interview, then by a second nurse, with the two analyses assembled according to the traditional concept of double reading. Differences between both analyses were thoroughly discussed, with a consensus sought by a third researcher, namely a rheumatologist, as necessary.
Results: Overall, 15 interviews were conducted involving 11 women and 4 men, with a mean age of 63 years (29–83). All patients were suffering from RA and undergoing at least one immunosuppressant therapy. Most (80%) were vaccinated against pneumococcus, but only 33% against influenza, with eight patients declaring having been affected by influenza and one by pneumococcus-related pulmonary disease.
The obstacles to vaccinations, revealed during the interviews, primarily concerned fears of unwanted effects in relation with the vaccinations, particularly concerning the influenza vaccination. The patients also reported anxieties in relation with the vaccines' excipients, with overdoses, or with disease reactivation. Moreover, media impact, contradictory information, the fact that vaccinations were not always proposed, and the lack of traceability may also be considered obstacles against vaccinations. Influenza is often considered a benign disease, and the vaccine poorly efficacious. Patients with prior influenza were more motivated towards vaccination. The primary motivation reported by the patients, and especially as to the pneumococcal vaccination, was the protection provided by the vaccine. The perception of frailty and increased infection risk associated with the disease and its treatments were other sources of motivation, and particularly when vaccination was highly recommended by the physicians, and when there had been no public controversy.
Conclusions: The fears and motivations associated with these two vaccinations are not identical. Influenza vaccination appears to be poorer perceived, patients reporting more fears related to it. With respect to pneumococcus vaccination, we only collected a few comments, given that the vaccine is less well know, and thus better accepted.
References:
[1] Gossec L. Arthritis Rheumatol 2016; 68 (suppl 10).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4994

SAT0734-HPR THE EFFECT OF RHEUMATIC DISEASES ON WORK ABILITY: A STUDY OF SELF-ASSESSMENT OF SF-36 IN PATIENTS WITH SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

H. Song[1], J. Gu[2], H. Wu[3], S. Li[4], Y. Zhao[5], H. Sun[6], J. Huang[7], X. Li[8], R. Wu[9], B. Wu[10], C. Xiao[11], L. Qian[12], F. Xiao[13], H. Xiao[13], M. Wang[13], Y. Jia[13], Z. Zhang[5]. *[1]Department of Rheumatology and Immunology, Department of Rheumatology and Immunology, Beijing; [2]The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou; [3]Department of Rheumatology and Immunology, Dongguan People's Hospital, Dongguan; [4]The First Affiliated Hospital of PLA General Hospital, Beijing; [5]Department of Rheumatology and Immunology, The First Affiliated Hospital of Harbin Medical University, Harbin; [6]Shandong Provincial Hospital, Jinan; [7]The sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou; [8]Anhui Medical University Affiliated Provincial Hospital, Hefei; [9]The First Affiliated Hospital of Nanchang University, Nanchang; [10]The First People's Hospital of Jingzhou, Jingzhou; [11]TCM-Integrated Hospital of Southern Medical University, Guangzhou; [12]The Second Affiliated Hospital of Medical University of Anhui, Hefei; [13]Medical Department, Shanghai Gothic Internet Technology Co., Ltd., Shanghai, China*

Background: A variety of rheumatic diseases can significantly affect the patient's quality of life and work ability. SF-36 is a commonly used tool to assess the quality of life and work ability in patients with chronic disease. In the past, most patients were guided by doctors/nurses to assess SF-36 in a paper form. At present, there is a lack of research on the quality of life in patients with rheumatic diseases by using new mobile tools in the real world.
Objectives: To explore the effect to the life ability of rheumatic disease and the potential association between the disease activity and SF-36 in patients with rheumatoid arthritis (RA) using SSDM.
Methods: SSDM is a new smart disease management mobile tool, which includes physicians' and patients' application system. After entering the results of SF-36 assessment by patients, all data can be synchronized automatically to the mobile terminal of authorized rheumatologist. According to the scores of SF-36 ($<$12.5, 12.5–50 and $>$50), the quality of life was divided into three levels: poor, moderate and good.
Results: From June 2016 January 2017, data were extracted online from the mobile terminals of 839 adult patients (284 male and 555 female) in 62 hospitals across China. All patients performed self-assessment of SF-36 for a total of 1,065 times. The mean age was 38.12±13.87 (18 to 81) years and the median disease duration was 20.60 (0 to 573) months. There are 25 kinds of rheumatic diseases involved, including RA (23%), ankylosing spondylitis (AS, 19%), systemic lupus erythematosus (SLE, 13%), osteoarthritis (OA, 11%), Sjogren syndrome (SS, 10%), polymyositis/dermatomyositis (PM/DM, 6%), mixed connective tissue disease (MCTD, 6%) and others (12%).
The 8 items of SF-36 index were averaged between 49.07 (General Health perceptions, GH) to 74.12 (Physical Functioning, PF). The overall mean score of patients with different rheumatic diseases was higher than 50. However, there were 5 kinds of rheumatic diseases with average score of 5 items less than 50, including: MCTD, SS, PM/DM, AS and SLE in patients with GH score: 44.24, 44.60, 47.87, 47.93 and 49.16, PM/DM in patients with the Emotional Role functioning (RE): 47.52, Physical Role functioning (RP): 44.68 and AS patients with Reported Health Transition (HT): 49.64, respectively. In RA patients, 38% and 37% of patients reported that their ability to work were affected by disease and mood changes respectively. Bivariate correlation analysis showed that DAS28 was negatively correlated with the two item scores (RP and RE) of SF-36 index in RA patients, $p<0.01$.
Conclusions: SSDM can be used to assess SF-36 in patients with rheumatic disease. The Quality of life scores in patients with MCTD, SS, PM/DM, AS, and SLE were more likely to be affected by rheumatic disease. The disease activity (DAS28) of RA patients was negatively correlated with the work ability (RP and RE of SF-36 score).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4990

SAT0735-HPR PATIENTS' ASSESSMENT OF THE APPLICABILITY OF THE ULTRASOUND IMAGE METHOD

J.A. Mendonça[1], W.H. Rodrigues Ferreira[2], I.M.M. Laurindo[3]. *[1]Rheumatology, Pontifical Catholic University of Campinas, Campinas; [2]Rheumatology, Gruparj Petrópolis, Petrópolis; [3]Rheumatology, Universidade Nove de Julho, São Paulo, Brazil*

Background: The applicability of ultrasonography in diagnosis and monitoring of rheumatic diseases has been steadily growing but little is known about the patient's perspective.
Objectives: To assess the patient's knowledge of the ultrasound (US) method and its clinical applicability as well as to evaluate how much was learned after a lecture.
Methods: Patients with rheumatic diseases were invited to an educational meeting that included an US lecture. They were asked to fill out a questionnaire before and after the 35-minute lecture about US and its clinical uses. The questionnaire included questions about their disease and treatment, their educational background (years of study) and ten questions about US and its clinical uses (table).These ten questions had to be answered with *"yes"*, *"no"*, or *"I am not sure"*.
Results: A total of 70 patients attended the lecture and answered the questionnaires. Their demographic characteristics were as follows: Mean ± SD: age 63±12 years, disease duration: 9.6±0.8 years, the most frequent self- reported diagnosis was rheumatoid arthritis (57,2%), while osteoarthritis accounted for another 20%. Most patients had only eight years of study (64.3%) and a university degree was reported by 14%. The questionnaire responses of 66 patients with rheumatic diseases were analysed. There was a noticeable increase in the positive responses to these questions: 1, 2, 3 and 7, after the lecture, 44%

Table - Questions :

1)Do you know what arthritis is?

2)Do you know what an ultrasound exam is?

3) Do you believe that an ultrasound exam could help in the diagnosis of your disease?

4) Do you believe that an ultrasound exam could help in monitoring your treatment?

5)Have you ever had one of your joints examined by ultrasound ?

6)Has the exam changed your treatment?

7) Do you think that an ultrasound exam would help you to better understand what is happening to your joints?

8)Do you think that an ultrasound exam would help you follow the treatment ?

9) Do you believe that an ultrasound exam can detect inflammation in your joints even when it is not clinically diagnosable by your doctor?

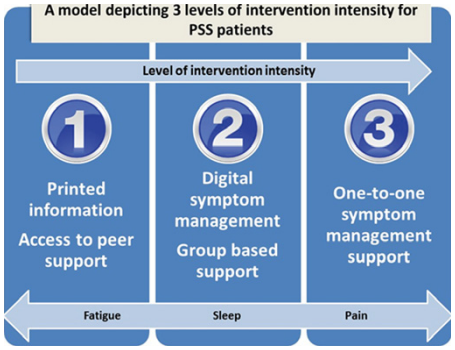
10) Do you think that an ultrasound exam would help you to understand your illness better?

(p=0.001); 29% (p=0.001); 10% (p=0.06); 27% (p=0.009), respectively. Although only 26% of the patients have had an articular US, in 65% it led to a change in treatment. Positive answers to some questions, which were perhaps too complex, showed a discrete increase, less than 10%, conceivably due to the surprisingly high background of positive answers.
Conclusions: As expected, the US image method was familiar to most but not its applicability in articular diseases. After the lecture there was an increase in understanding of the positive impact of US in rheumatic diseases, implying that short and focused lectures are a useful tool in educational programs for patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1426

SAT0736-HPR "LIKE A BAG OF LIQUORICE ALLSORTS – EVERYBODY'S GOT DIFFERENT FLAVOURS": A QUALITATIVE FOCUS GROUP STUDY TO EXPLORE SYMPTOMS OF FATIGUE, SLEEP DISTURBANCES AND PAIN IN PRIMARY SJÖGREN'S SYNDROME PATIENTS AND TO DEVELOP A FUTURE MODEL OF CARE

K.L. Hackett[1,2], V. Deary[2,3], K. Deane[4], J.L. Newton[1,2], W.-F. Ng[1,2], T. Rapley[1]. *[1]Newcastle University; [2]Newcastle upon Tyne NHS Foundation Trust; [3]Northumbria University, Newcastle upon Tyne; [4]University of East Anglia, Norwich, United Kingdom*

Background: Fatigue, sleep disturbances and pain, are symptoms of primary Sjögren's syndrome (PSS). However, current clinical interventions predominantly focus on treating patients' dryness symptoms.
Objectives: To explore the experience of fatigue, sleep disturbances and discomfort in people with PSS, to investigate the impact of these symptoms on patients' daily lives and to develop an intervention strategy to address them.
Methods: Qualitative focus groups with open-ended questions allowed participants to explore ideas together and focus on issues they perceived as being important. PSS patients (n=10) and spouses (n=3) took part in three focus groups divided into six sessions which were facilitated by two clinician researchers using a topic guide. Discussion topics included; the symptoms, strategies used by patients used to manage their symptoms, possible future intervention components proposed from the literature and possible modes of delivering future interventions. The meetings were audio-recorded, transcribed verbatim and analysed using thematic analysis[1].
Results: Patient participants all experienced these symptoms. Symptom severity varied within individuals and flares occurred unpredictably. Fatigue, sleep disturbances and discomfort, all affected patients' lives and those around them and sometimes felt overwhelming. Discomfort symptoms included oral and ocular dryness, tingling, nausea and difficulties tolerating light and noise. The invisible nature of these features meant patients often struggled to meet others' expectations, which affected their mood and resulted in social withdrawal. Fatigue was a major barrier to engaging in work, productivity and leisure activities. Sleep disturbances further compounded the fatigue. Patients employed a range of strategies to self-manage their symptoms to varying degrees of success.
Participants expressed a need for tailored support from health care professionals which included information provision, access to peer support and professional support to apply symptom management information. A three stepped model of care was proposed. The model includes different modes of delivering intervention content, including written information, education groups, peer support, digital self-management and one-to-one therapy. Intervention intensity increased with each step in the model.



Conclusions: Symptoms of fatigue, sleep disturbances and discomfort all impact on PSS patients' daily lives and individualised interventions are needed to support self-management. Care needs to be tailored as different patients require variable levels of support. A stepped model of future symptom management delivery is proposed.
References:
[1] Braun V and Clarke V (2006) Using thematic analysis in psychology. Qualitative Research in Psychology, 3(4), 77–101.
Acknowledgements: This project was funded by Arthritis Research UK (grant 20169) and the United Kingdom Occupational Therapy Research Foundation.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2823

SAT0737-HPR FACILITATORS AND BARRIERS FOR PARTICIPATION IN PHYSICAL ACTIVITIES IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS AND HEALTHY CONTROLS

K. Risum[1], A.M. Selvaag[1], Ø. Molberg[1], H. Dagfinrud[2], H. Sanner[1]. *[1]Oslo University Hospital; [2]Diakonhjemmet Hospital, Oslo, Norway*

Background: Knowledge is sparse regarding facilitators and barriers for participation in physical activity (PA) in patients with juvenile idiopathic arthritis (JIA) and whether they differ from controls. Furthermore, knowledge about preferences for leisure time physical activities and participation in physical education (PE) in school in JIA patients is limited.
Objectives: To explore participation in PA and PE in JIA patients, and to explore facilitators and barriers for PA participation in JIA and matched controls.
Methods: The study cohort included 60 JIA patients (50 girls, 10 boys) and 60 controls individually matched for age and sex randomly selected from the Norwegian Population Registry. Of the JIA patients, 30 had persistent oligoarthritis and 30 had polyarticular disease (extended oligoarthritis and polyarticular RF +/-). The patients were aged 10–16 years and recruited consecutively at Oslo University Hospital in 2015. Participation in PA and facilitators and barriers for PA participation, were explored with structured interviews. The interview guide was developed for this study based on literature review and clinical experience. Differences between the study groups were analyzed using the McNemar test.
Results: Participation in physical activities was not significantly different between JIA patients and controls (Table 1). The most commonly practiced organized physical activities in both groups were dancing and soccer, and the most commonly practiced unorganized physical activities were jogging, training at fitness center and strength exercising at home. Participation in PE is shown in Table 1. Fun was the most reported facilitator for participation in PA both in patients and controls, 40 (67%) vs 45 (75%), respectively, p=0.32. Becoming fit was an often reported facilitator in patients and controls, 12 (20%) vs 21 (35%) respectively, p=0.07. Being with friends was a facilitator more often reported by controls than patients, 13 (22%) in controls vs 1 (2%) patient (p<0.001). Less pain was a facilitator in 4 patients, but not in any controls (p=0.06). 26 (43%) patients and 19 (32%) controls reported barriers for participating in PA (p=0.46). More controls reported time as a PA barrier, 11 (18%) vs 3 (5%) (p=0.02), while more patients reported pain as a barrier; 18 (30%) vs 8 (13%) (p=0.03). Disease activity was a barrier in 4 (7%) patients.

Table 1. Participation in physical activity (PA) and physical education (PE)

	JIA (n=60)	Controls (n=60)	p-value
Participation in PA (organized/unorganized)	51 (85)	56 (93)	0.14
Participation in organized PA	38 (63)	47 (78)	0.11
Participation in unorganized PA	41 (68)	42 (70)	1.00
Participation in PE			<0.001
Always	42 (70)	59 (98)	
Always (sometimes with modification)	16 (27)	0 (0)	
Sometimes	2 (3)	1 (2)	

Numbers are n (%),

Conclusions: The majority of JIA patients and controls participated in organized or unorganized PA. Fun was the most reported facilitator in patients, followed by becoming fit and having less pain. Pain was the dominant PA barrier in patients, while time was the most frequently reported barrier in controls. Some patients experienced disease activity as a barrier. Nearly all the patients (97%) participated regularly in PE, but ¼ needed some modifications. These results are reassuring, and highlight the importance of enjoyment for participation in PA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6063

SAT0738-HPR EXPERIENCES OF TELE-HEALTH FOLLOW-UP IN PATIENTS WITH RHEUMATOID ARTHRITIS: A QUALITATIVE INTERVIEW STUDY

L.R. Knudsen[1], A. de Thurah[1,2], K. Lomborg[2,3]. *[1]Department of Rheumatology, Aarhus University Hospital; [2]Department of Clinical Medicine, Aarhus University; [3]The Research Programme in Patient Involvement, Aarhus University Hospital, Aarhus, Denmark*

Background: Recently, the effectiveness of monitoring disease activity in rheumatoid arthritis (RA) through patient reported outcome (PRO) based tele-health follow-up was tested in a randomized controlled trail, TeRA (1). The TeRA study evaluated the effectiveness of the tele-health follow-up but did not study how patients grasp this new form of disease control. Many studies on tele-medicine focus on the over-all patient satisfaction with tele-medicine follow-up, but gives limited insight into what drives patient satisfaction (2).
Objectives: To explore the experiences of a PRO based tele-health follow-up from the perspective of patients with RA with a special attention on experiences of taking a more active role and assuming more responsibility in the disease control.
Methods: The qualitative research strategy was Interpretive Description (3). From October 2015 to January 2016 we conducted individual semi-structured interviews

with 15 patients with RA who had taken part of the tele-health follow-up. The selection of participants was purposive and participants with different sex, age, disease duration and severity were included. Age ranged from 28 – 77 years and disease duration from 4 – 41 years. The analysis of the interview transcripts was inductive with a constant comparative approach. First, we identified the main themes that could describe the participants' experiences. Subsequently, we constructed patient types that could explain different perspectives on the tele-health follow-up.

Results: Five themes covered the participants' experiences with PRO based tele-health follow-up: "A flexible solution", "Responsibility", "Knowledge of RA", "Communication and involvement" and "Continuity". Two different types of personalities: "the keen patient" and "the reluctant patient", represented opposite perspectives and preferences regarding the core value of and approach to the tele-health follow-up compared to usual out-patient care.

Conclusions: In general, the participants had positive perceptions towards the PRO based tele-health follow-up and saw this as a flexible, time and resource saving solution. Disadvantages were mainly related to the missing face-to-face contact with health professionals. The two types of personalities, 'the keen patient' and 'the reluctant patient', contribute to the understanding of patients' different needs, wishes and abilities to take part in tele-health follow-up. Thus, our findings call for more insight of how tele-health follow-up could be integrated in routine clinical practice with a special attention on how to support "the reluctant" patient types.

References:

[1] De Thurah A, Stengaard-Pedersen K, Maribo T et al. A Tele-health Treatment Strategy for Tight Control of Disease Activity in Rheumatoid Arthritis: Results of the Non-inferiority Randomised Controlled Trail (the TeRA study). ClinicalTrials.gov Id: NCT02155894. Submitted 22.01.17. EULAR abstract number: EULAR17–2995.

[2] LeRouge MC, Garfield JM, Hevner RA. Patient perspectives of telemedicine quality. Patient Preference and Adherence 2015; 9:25 – 40.

[3] Thorne SE. Interpretive description. Left Coast Press, Inc. Walnut Creek. 2008. 1. edition.

Acknowledgements: We are grateful to the participants who shared their experiences. We also thank an internal research foundation at Aarhus University Hospital for supporting this study.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2903

SAT0739-HPR PATIENTS' PREFERENCES TOWARD CHARACTERISTICS OF TREATMENT WITH BIOLOGICAL AGENTS DIFFER ACCORDING TO EXPERIENCE WITH THEIR RHEUMATIC DISEASE AND TREATMENT RECEIVED OR PRESCRIBED: RESULTS FROM THE CARA STUDY

L. Sinigaglia[1], P. Sarzi-Puttini[2], L. Scalone[3,4], C.M. Montecucco[5], R. Giacomelli[6], G. Lapadula[7], I. Olivieri[8], A. Giardino[9], P. Cortesi[3,4], L.G. Mantovani[3,4], M. Mecchia[9] on behalf of CARA Study. *[1]Rheumatology Unit, G. Pini Hospital; [2]Rheumatology Unit, L. Sacco University Hospital, Milano; [3]University of Milano Bicocca, Monza; [4]CHARTA Foundation, Milano; [5]University of Pavia School of Medicine, IRCCS Policlinico San Matteo Foundation, Pavia; [6]Rheumatology Unit School of Medicine, University of L'Aquila, L'Aquila; [7]Rheumatology Unit, University of Bari, Bari; [8]Rheumatology Institute of Lucania (IRel), the Rheumatology Department of Lucania, San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, Potenza and Matera, and the Basilicata Ricerca Biomedica (BRB) Foundation, Italy, Potenza and Matera; [9]MSD Italia, Roma, Italy*

Background: The development of biologic therapies has created a more complex decision-making process to select the treatment option for patients. In order to optimize the appropriateness of the decisions, it is necessary to be informed and aware of the preferences of the interested parties and the influence of their experiences on their preferences for the different treatments.

Objectives: To estimate preferences of relevant treatment characteristics valued by the different subjects involved in the management of patients with rheumatic diseases. This abstract focuses on patients' preferences.

Methods: We involved patients with rheumatoid arthritis (*RA*), ankylosing spondylitis (*AS*) or psoriatic arthritis (*PsA*), who according to clinical practice, at the time of data collection had for the first time a prescription of (*naïve*), or received treatment with (*experienced*) biological drugs for at least 3 months in the last 12 months. Through a Discrete-Choice-Experiment, the participants valued 16 possible scenarios in which pairs of similarly effective treatments were described with 6 characteristics including 2–4 possible levels each: (1) frequency of administration; (2) mode and place of administration; (3) hospitality, service, efficiency and courtesy of health personnel; (4) frequency of reactions at the site of drug administration; (5) generalized undesired reactions or allergic reactions involving the whole body; (6) additional contribution added as healthcare taxes to be paid by all the citizens to make available the treatment to target patients.

Results: 513 patients from 30 centres through Italy participated, balanced for diagnosis and treatment experience (around 20% of each subgroup). Characteristics 4, 3 and 6 were the first, second and third most important ones for every subgroup, the fourth most important characteristic was 1 (*experienced RA*), 5 (*naïve AS*), and 2 for the other subgroups. Across all the subgroups, patients generally preferred very satisfactory levels of (3), infrequent (4), mild (5), and no (6). Instead, for characteristics (1) and (2) the patients generally preferred the frequency, mode and place of administration that were closer to those actually experienced or prescribed.

Conclusions: Taking into account the different opinions of patients on at least some treatment characteristics could guide the conduction of good choices aimed to optimize benefits and to allocate efficiently resources.

Disclosure of Interest: L. Sinigaglia: None declared, P. Sarzi-Puttini: None declared, L. Scalone: None declared, C. Montecucco: None declared, R. Giacomelli Grant/research support from: MSD, G. Lapadula: None declared, I. Olivieri: None declared, A. Giardino Employee of: MSD Italia, P. Cortesi Grant/research support from: Gilead, L. Mantovani: None declared, M. Mecchia Employee of: MSD Italia

DOI: 10.1136/annrheumdis-2017-eular.4889

SAT0740-HPR SIGNIFICANT OTHERS AS BOTH BARRIERS AND FACILITATORS FOR PARTICIPATION IN DAILY ACTIVITIES IN PERSONS WITH EARLY RHEUMATOID ARTHRITIS – AN INTERVIEW STUDY WITHIN THE SWEDISH TIRA PROJECT

M. Bergström[1], A. Sverker[1,2,3,4], Å. Larsson Ranada[1], E. Valtersson[2,3], I. Thyberg[5,6], G. Östlund[7], M. Björk[1,5]. *[1]Department of Social and Welfare Studies, Linköping University, Norrköping; [2]Department of Activity and Health; [3]Department of Medical and Health Sciences; [4]Department of Rehabilitation Medicine; [5]Department of Rheumatology; [6]Department of Clinical and Experimental Medicine, Linköping University, Linköping; [7]School of Health Care and Social Welfare, Mälardalen University, Eskilstuna, Sweden*

Background: Restrictions in participation in persons with rheumatoid arthritis (RA) have been reported to be closely connected with more pain, fatigue and difficulties in performing daily activities. In addition, support and positive interactions with others have been considered important. We therefore need to understand how significant others of persons with RA can be facilitators or barriers, in participation in daily activities. This becomes of even greater importance in the sensitive and adapting phase of early RA.

Objectives: To describe the meaning of significant others in relation to participation in daily activities in persons with early RA.

Methods: This interview study is part of the multicenter project TIRA. Fifty-nine persons (58% women) participated. Inclusion criteria were a diagnosis of RA during three years and being in working age, <64 years of age. Semi-structured interviews were conducted using Critical Incidence Technique (CIT) [1] and the material was analyzed using content analysis [2]. The study was approved by the Regional Ethics Committee.

Results: Four categories were revealed: *(1) Feelings and thoughts related to significant others*, where participants would feel like being someone's burden, taking out aggression on others, and express anxiety about how relationships and activities would function in the future. *(2) The importance of physical contact*, referring to both the problematic and manageable impact RA could have on intimate life, as well as body contact in the form of hugging. *(3) Getting the support you want*, where participants distinguished getting help they had not asked for, from helping each other out. The first being experienced as degrading, and the latter as feeling more involved in the activity. *(4) Adaption of daily activities*, referring to how the person and significant others consciously modified their activities and activity choices when needed.

Conclusions: Significant others can be either a barrier or facilitator for participation in daily activities, for persons with early RA. From a clinical point of view it is important to further involve significant others in the rehabilitation process, in order to enhance participation in daily activities for persons with RA.

References:

[1] Flanagan, C. The critical incidence technique. Psychol Bull 1954;51(4):327–58.

[2] Graneheim, UH. & Lundman, B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Educ Today 2004;24(2): 105–12.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2780

SAT0741-HPR PHYSICAL PERFORMANCE AND GAIT SPEED OF FALLER AND NON-FALLER ELDERLY PEOPLE WITH KNEE OSTEOARTHRITIS LIVING IN THE COMMUNITY

M. Karapinar, A. Abit Kocaman, N. Kirdi. *Department of Physiotherapy and Rehabilitation, Hacettepe University, Ankara, Turkey*

Background: Osteoarthritis (OA) is the most prevalent chronic degenerative joint disease in the elderly population. The main signs and clinical symptoms of this disease are pain, edema, stiffness, and articular instability. OA is considered to be an intrinsic risk factor for the occurrence of falls. Falls constitute as one of the major public health concerns. They frequently have a negative impact on the daily life of elderly people and could lead an increase of dependence, fear of new falls, fractures, immobility and death.

Objectives: The purpose of this study was to compare physical performance and gait speed among older people with knee osteoarthritis with and without a history of falls.

Methods: The community-dwelling older people (65 and older) were recruited from different social senior groups and from the Hacettepe University Hospital Geriatric Outpatient Clinic. 102 patients were screened and 62 subjects with unilateral knee OA were evaluated. We used a standardized questionnaire, consisting of sociodemographic datas, cognitive function, and history of falls during the previous year. Thirty one elderly with a history of falls and also 31 without a history of falls were studied. Physical performance was evaluated with Short Physical Performance Test (SPPT). Walking speeds were measured with Six Metre Walk Test. Fear of falling (FOF) was assessed by a question (Do you have fear of falling? yes/no)
Results: There were no differences between faller and non-faller elderly people in terms of age (76±8,4 years) and BMI (30,4±3,1 kg/m^2). A statistically significant difference was found in terms of walking speeds and short physical performance test ($p<0,005$, $p<0,005$).
Conclusions: As a result of this study, it was shown that the elderly people with knee OA and who have history of falls present worse performance in functional mobility and require a longer period of time to walking.
References:
[1] Huang MH, Lin YS, Yang RC, Lee CL. A comparison of various therapeutic exercises on the functional status of patients with knee osteoarthritis. Semin Arthritis Rheum 2003; 32: 398–406.
[2] Hinman RS, Bennell KL, Metcalf BR, Crossley KM. Balance impairments in individuals with symptomatic knee osteoarthritis: a comparison with matched controls using clinical tests. Rheumatology 2002; 41: 1388–1394.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3885

SAT0742-HPR THE EFFECT OF A NEOPRENE KNEE SLEEVES ON KNEE JOINT PROPRIOCEPTION IN PATIENTS WITH TOTAL KNEE PROSTHESIS

M. Eymir[1], S. Narin[1], V. Karatosun[2]. *[1]School of Physical Therapy and Rehabilitation; [2]Faculty of Medicine Surgery Medicine Department of Orthopaedics and Traumatology, Dokuz Eylül University, Izmir, Turkey, izmir, Turkey*

Background: Proprioception has been defined as the perceived sense of knee joint position (joint position sense) and movement (kinesthesis) (1). The sensory input from the joint capsule, muscles, ligaments, skin improve proprioceptive acuity. With total knee arthroplasty (TKA) surgery articular cartilage, meniscuses, articular ligaments are removed. Also articular effusion and hematoma formation increase following surgery. Therefore, proprioceptive acuity decrease after TKA surgery (2). The proprioceptive improvement might prevent patients with TKA from falling down and increase their sense of security during physical activities. The clinical effect of neoprene knee sleeves on knee proprioception has been evaluated by studies in both injured and uninjured populations (3). But there is not any study research on the effect of neoprene knee sleeves on knee proprioception in patients with TKA.
Objectives: The aim of this study was to determine the effect of the neoprene knee sleeves on knee joint proprioception in patients with TKA.
Methods: Sixty patients (50 female/10 male) with a median age 64.95±8.84 years were included in the study. Knee joint proprioception of all the patients was evaluated with and without a neoprene knee sleeves preoperatively and at discharge. Patients attempted to replicate target angles (in knee joint angle 15°, 30°, 60°) using active knee extension movements in sitting position. The average of the 3 repetitions of active joint repositioning test was recorded position sense score. The angular displacements from the target angles (in knee joint angle 15°, 30°, 60°) at the end of the active reproduction tests were recorded as position sense deficit scores.
Results: Preoperatively ($p<0.001$) and after surgery ($p<0.001$) patients' proprioceptive acuity measured with neoprene knee sleeves in knee joint angle 15°, 30°, 60°, had a significant improvement. When the proprioceptive acuity measured without neoprene knee sleeves before and after surgery were compared, had a significant decrease in proprioceptive acuity ($p<0.001$) in early stage after TKA surgery. Also when the proprioceptive acuity measured with neoprene knee sleeves in knee joint angle 15°, 30°, 60° before and after surgery were compared, no significant statistical differences were observed ($p>0.05$).
Conclusions: In patients with TKA due to osteoarthritis, application of neoprene knee sleeves has increased the proprioceptive acuity. The current results suggest that neoprene knee sleeves might be used for improving proprioception in early stage of patients with TKA.
References:
[1] Herrington L, Simmonds C, Hatcher J. The effect of a neoprene sleeve on knee joint position sense. Research in Sports Medicine. 2005; 13(1):37–46.
[2] Pap G, Meyer M, Weiler H-T, et al. Proprioception after total knee arthroplasty: a comparison with clinical outcome. Acta Orthopaedica Scandinavica. 2000;71(2):153–9.
[3] Chuang S-H, Huang M-H, Chen T-W, et al. Effect of knee sleeve on static and dynamic balance in patients with knee osteoarthritis. The Kaohsiung Journal of Medical Sciences. 2007;23(8):405–11.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4399

SAT0743-HPR RISK FACTORS FOR FEAR OF FALLING IN PATIENTS WITH KNEE OSTEOARTHRITIS

O. Aydoğdu, Z. Sarı, U.S. Yurdalan, G.M. Polat. *Physiotherapy and Rehabilitation, Marmara University, Health Sciences Faculty, Istanbul, Turkey*

Background: Severe knee osteoarthritis (OA) is characterized by stiffness, pain, and disability of the knee joint. Severe pain negatively affects muscle strength, coordination, postural stability, proprioception, mobility, and increases fall risk and possibly fear of falling. Individuals with severe knee OA experience loss of self-efficacy, activity avoidance, loss of self-confidence, and finally fear of falling without actually experiencing a fall (1). Despite the high prevalence of falls in patients with OA, few studies have investigated fear of falling in patients with knee OA (2).
Objectives: The present study was conducted to determine the risk factors affecting fear of falling and to investigate the relationship between fear of falling and age, gender, body mass index, pain level, range of motion, muscle strength, knee swelling, postural stability, and functional status in patients with knee OA.
The purpose of our study was to evaluate the regression of fear of falling and identify its risk factors in patients with severe knee OA.
Methods: A total of 71 patients who were diagnosed with knee OA according to the American College of Rheumatology (ACR) and who were accepted as stage 2 and 3 based on the Kellgren-Lawrence criteria, were included in the study.
Outcome measures included fear of falling, pain intensity, and range of motion, quadriceps and hamstring muscle strength, knee swelling, postural stability, and functional status.
Pearson correlation and multiple logistic regression test was used to determine the risk factors of fear of falling and relationships between fear of falling and age, body mass index, pain intensity, range of motion, muscle strength, knee swelling, postural stability, and functional status.
Results: Multiple logistic regression analysis showed that age (odds ratio=12.5, p=0.011), body mass index (odds ratio=14.5, p=0.030), pain intensity (odds ratio=3.5, p=0.045), range of motion (odds ratio=9.8, p=0.012), and knee swelling (odds ratio=8.4, p=0.019) were independent risk factors for fear of falling among patients with knee OA.
Conclusions: We conclude that age, body mass index, pain intensity, range of motion and knee swelling influence the fear of falling. They are viewed as an important predictor of fear of falling in knee OA. Our results could be used to help select knee OA patients who should be enrolled in fall prevention programmes.
References:
[1] Tsonga T, Michalopoulou M, Kapetanakis S, et al. Risk factors for fear of falling in elderly patients with severe knee osteoarthritis before and one year after total knee arthroplasty. J Orthop Surg (Hong Kong). 2016 Dec;24(3):302–306.
[2] Levinger P, Menz HB, Wee E, Feller JA, Bartlett JR, Bergman NR. Physiological risk factors for falls in people with knee osteoarthritis before and early after knee replacement surgery. Knee Surg Sports Traumatol Arthrosc. 2011 Jul;19(7):1082–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5714

SAT0744-HPR THE USE OF HEALTH ASSESSMENT QUESTIONNAIRE (HAQ) IN GIVING A PICTURE OF PATIENT EVERYDAY LIFE WITH RHEUMATOID ARTHRITIS

P. Toftegaard, I.M.J. Hansen. *Department of Rheumatology, Svendborg Hospital, Svendborg, Denmark*

Background: HAQ is used to monitor physical disability in patients with Rheumatoid arthritis (RA). At our department patients are planned to answer HAQ at every visit. The suitability for use in connection with ordinary clinical controls are questioned (1, 2) and furthermore we have the impression that the patients fill in the HAQ questionnaire because the staff wants it, and not because it make sense to the patients themselves.
Objectives: Evaluation of the HAQ from the patient perspective
Methods: A survey where all patients with RA who visited the outpatient clinic over a period of 3 weeks were invited to participate. Patients were asked to fill in a questionnaire to evaluate each question (20) in the HAQ on a scale from 1 – 10, 1 = no meaning and 10 = most meaningful. Values less or equal to five were evaluated as "no meaning". Furthermore a literature review was done, afterwards a Critical Appraisal Skills programme (CASP) was performed on publications found
Results: 100 patients were asked to participate, in total 67 questionnaires were returned, twelve patients were excluded because of incomplete answers, twenty-one did not return the questionnaires or did not want to participate. Depending on which of the 20 questions, different fractions of the patients did not find any meaning in the questions: 18.6% (are you able to shampoo and wash your hair?) up to 40.4% (are you able to use the bathtub?)
In the literature (3, 4) we found several themes of importance for everyday life with RA seen from the patients' perspective. Pain and impaired physical performance is of great significance for patients living with rheumatoid arthritis. It affects patients both physically, mentally and socially, as it may be necessary to cut back on social activities, to ask for help for ordinary everyday chores, changing or dropping work etc. This has implications for the role of the patient in the family. Powerlessness, frustration and uncertainty about the future affect the mood in form of anger and depressive thoughts.

Overall, it affects the patients' self-image and the patients' independence may be lost.

Conclusions: HAQ questionnaire is relevant in the term of defining the areas in everyday life, where the patients have problems. But the questionnaire does not contribute to elucidate the implications for the patient, which probably is the reason why many patients do not find the meaning with the questions. To evaluate the everyday living with and treatment of arthritis embedding the patient values, patient involvement in designing questionnaires is vital

References:

[1] Kvien TK. Epidemiology of disability in Rheumatoid arthritis. Rheumatology 2002;41:121–123.
[2] Seror R et al. Measure of function in rheumatoid arthritis: individualised or classical scales? Ann Rheum Dis. 2010;69: 97–101.
[3] Lütze U, Archenholtz B. The impact of arthritis on daily life with the patient perspective in focus. Scand J Caring Sci 2007;21(1):64.
[4] Hughes JG. Exploring the impact of rheumatoid arthritis on patients' lives. International journal of therapy and rehabilitation 2009 -11–01;16(11):594; 594–601; 601.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2153

SAT0745-HPR IMPACT OF AN INTERDISCIPLINARY INTERVENTION ON RA PATIENTS

I. Fortin[1], H. Sylvain[2], F. Banville[3], B. Lovisi[4], S.V. Rochefort[1]. *[1]Research, CISSS du Bas-Saint-Laurent/Hôpital Régional de Rimouski; [2]Sciences infirmières; [3]Research, Université du Québec à Rimouski, Rimouski; [4]Rheumatology, CISSS du Saguenay-Lac-St-Jean/Hôpital de Chicoutimi, Chicoutimi, Canada*

Background: Rheumatoid arthritis (RA) impairs patient function and quality of life (QoL) which, in turn, may lead to invalidity and chronicity of pain1. Even though a variety of effective treatments are available, there is still a significant portion of patients not attaining remission, of whom many continue to report moderate to high pain and fatigue despite low levels of inflammation1. Interdisciplinary interventions are promising approaches that may complement the medication effect on patient well-being and disease control, however previous studies on the effectiveness of interdisciplinary interventions seem conflicting.

Objectives: The primary objective is to compare the DAS28 response between patients receiving an interdisciplinary intervention (Intervention group) and patients followed under standard rheumatologic practice (Control group). Secondary objectives are to compare patient-reported outcomes such as pain, fatigue, general health, and patient empowerment between the two groups.

Methods: Prospective quasi-experimental, matched cohort (age, gender) study. Adult patients with a diagnosis of RA and DAS28 (CRP)$>$2.6 are eligible for the study. The Intervention group (n=28) benefits from interdisciplinary team intervention with the following professionals: rheumatologist, nurse, physiotherapist, social worker, kinesiologist, occupational therapist, and nutritionist. The Control group (n=32) receives a conventional rheumatologist-nurse intervention. Both groups see the rheumatologist approximately three times over 12 months. Interdisciplinary meetings take place in the hospital setting with the patients at Month 0 and Month 12 and without them at Month 6. The following outcome measures are used at each visit to the rheumatologist: patient pain, fatigue (Multidimensional Assessment of Fatigue; MAF), disability (HAQ), quality of life (SF-36), patient empowerment (Patient Activation Measure; PAM13), and patient satisfaction (QSC-F; only in Intervention group at Month 12).

Results: A total of 28 patients were enrolled in the Intervention group and 32 in the Control group without any significant differences in demographics or disease parameters with the exception of disease duration which was significantly higher in the Intervention group (10.9 vs. 5.8 years; p=0.021). Within 6 months of treatment, clinically important and statistically significant ($p<0.01$) improvements in DAS28 were observed in both groups which were maintained until 12 months. Overall, at 12 months, DAS28 response was comparable between groups (68% vs. 63%; p=0.140). However, when looking at patients with established RA (75% vs. 66.7%; p=0.039) and patients with low to moderate disease activity at baseline (73.9% vs. 56.5%; p=0.035), a higher response rate was observed in the Intervention group. No statistical differences were observed in the remaining outcomes between groups.

Conclusions: The results of the current study suggest that interdisciplinary interventions may be useful in conferring benefits on patient well-being and disease control that are above and beyond those resulting from medications. This seems to be particularly true among patients with established disease. Additional analyses looking into the exact mechanism of action of such interventions are required.

Disclosure of Interest: I. Fortin Grant/research support from: grant UCB, H. Sylvain Grant/research support from: Grant UCB, F. Banville Grant/research support from: UCB, B. Lovisi: None declared, S. V. Rochefort Grant/research support from: UCB

DOI: 10.1136/annrheumdis-2017-eular.6332

SAT0746-HPR TOWARDS MEASUREMENT OF PERSON-CENTERED CARE OUTCOMES IN OUTPATIENT NURSE-LED CLINICS

V. Bala[1,2], B. Fridlund[3], K. Forslind[4,5], B. Svensson[6], P. Hagell[7]. *[1]Department of Medicine, Section of Rheumatology, Helsingborg; [2]Department of Health Science, Lund University, Lund; [3]School of Health and Welfare, Jönköping University, Jönköping; [4]Department of Clinical Science, Section of Rheumatology, Lund University; [5]Department of Research and Education, Helsingborg's Hospital, Helsingborg; [6]Section of Rheumatology at the Institution of Clinical Science, Lund University, Lund; [7]The PRO-CARE Group, School of Health and Society, Kristianstad University, Kristianstad, Sweden*

Background: Person-centered care (PCC) is increasingly emphasized as a key component of effective illness management and of developing high quality of care. Despite considerable progress of PCC in many areas of care there is currently a gap and a need for means to assess PCC practice in outpatient care. In rheumatology, PCC is considered an unmet need and further development and evaluation of this approach to care is thus of high priority.

Objectives: To develop an instrument for measuring person-centered care from the perspective of the person with rheumatoid arthritis (RA) in nurse-led outpatient clinics.

Methods: A conceptual framework of PCC in the outpatient context and focusing on the meeting between the person with RA and the nurse and on the patient as an active care partner was undertaken. Based on this framework, qualitative interviews (1,2) and a literature review, a 35-item questionnaire was proposed and qualitatively tested regarding acceptability and content validity among 50 persons with RA attending a nurse-led outpatient clinic. Two versions of the questionnaire were tested: one using four response categories (0 = Totally disagree; 3 = Completely agree), and one using two response categories (0 = Disagree; 1 = Agree). Content validity was estimated by calculating Content Validity Index of the individual items (I-CVI) and of the overall instrument (S-CVI).

Results: Respondents found the items easy to understand (77%) and relevant (93%). Seventy-three percent of the respondents preferred the questionnaire version with four response categories. This version took a mean (SD) of 5.3 (2.5) minutes to complete. I-CVI values ranged from 0.87 to 1.00 and S-CVI was 0.94. About 80% of the respondents considered some items to be redundant. This resulted in a reduced 24-item draft questionnaire that yield a total score between 0–72.

Conclusions: A preliminary 24-item patient-reported PCC questionnaire was developed. Psychometric testing is needed for validation of this tool before implementation.

References:

[1] Bala SV, Samuelson K, Hagell P, Svensson B, Fridlund B, Hesselgard K (2012). The experience of care at nurse-led rheumatology clinics. Musculoskeletal Care 10: 202–211.
[2] Bala SV, Samuelson K, Hagell P, Fridlund B, Forslind K, Svensson B, Thomé B (2016). Journal of Clinical Nursing; doi: 10.1111/ jocn.13691.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6530

SAT0747-HPR CAN ACHIEVING SUSTAINED DAS REMISSION PREVENT PROGRESSION OF SUB- CLINICAL ATHEROSCLEROSIS? A PROSPECTIVE COHORT STUDY IN EARLY RHEUMATOID ARTHRITIS (ERA)

W.Y. Mak[1], Q. Shang[1], X.S.L. Lau[1], A.P.-W. Lee[1], C.M. Yu[1], E.K.-M. Li[1], P.C.H. Wong[2], L.H.P. Tam[2], K.Y. Kwok[3], M.L. Yip[4], H.T. Pang[5], V.W.-N. Lao[5], I.C.-W. Yim[6], L.S. Tam[1]. *[1]Dept of Medicine and Therapeutics, The Chinese University of Hong Kong; [2]Dept of Medicine and Therapeutics, Prince of Wales Hospital; [3]Dept of Medicine, Queen Elizabeth Hospital; [4]Kwong Wah Hospital, Hong Kong, Hong Kong; [5]Dept of Medicine and Geriatrics, Kwong Wah Hospital; [6]Dept of Medicine, Tseung Kwan O Hospital, Hong Kong, Hong Kong*

Background: Patients with rheumatoid arthritis (RA) have higher incidence of cardiovascular disease (CVD) and prevalence of arterial stiffness (AS) due to underlying inflammation. Effective immunosuppression using anti-TNF was shown to improve AS in early RA (ERA) patients.Whether it is a specific effect by blocking the TNFα pathway or suppression of inflammation remains uncertain. While achieving Disease Activity Score in 28joints (DAS) remission was associated with significant benefits in articular disease, its effect on co-morbidities such as CVD risk is uncertain.

Objectives: To investigate the effect of achieving sustained DAS remission on AS.

Methods: This randomized control trial investigates the effect of 2 tight-control treatment strategies aiming 1.Simplified disease activity score [SDAI$\leq$3.3]or 2.minimal disease activity [DAS$<$2.6] on AS in ERA patients.120 patients with active disease (DAS$\geq$3.2), symptoms onset $<$2years and bDMARDs naive were recruited and received 1-year treatment.Treatment are adjusted based on the standardized protocol every 3month aiming at either 1 of the 2 targets. AS is measured by branchial-ankle pulse wave velocity (baPWV) using a dedicated tonometry system (Omron VP-2000).

Results: In the interim analysis, results of 100 patients [male (23.0%); 52.8±13 years] completed 1year follow-up were analyzed. No significant differences between groups in clinical features, DMARD use and baPWV at month12

(M12) was observed yet significant improvement in disease activity was found in both groups.Hence,results from the 2 groups were combined to ascertain if achieving sustained DAS remission can prevent AS progression.The disease activity improved significantly [DAS: 4.8 (4.2,5.6) at baseline (BL) vs 2.38 (1.6,3.0) at M12, $p<0.001$]. 57% patients achieved DAS remission at M12 and 36% patients achieved DAS remission over 3 consecutive visits (sustained remission). No significant differences were found in disease activity, cardiovascular risk factors (CRF) and baPWV at BL between groups who can (CA) or cannot achieve (NA) sustained remission. At M12, no significant differences in CRF and baPWV were found between groups.However, the change in baPWV was significantly different between CA and NA group [-65.5 (-147.25, 44.0) cm/s vs 39 (-65.25, 124.75) cm/s, $p=0.005$]. The differences remained significant in the %change of baPWV [-4.4 (-9.67–2.84)% vs 2.51 (-4.34–10.28)%, $p=0.006$].I n univariate analysis,assocation of change in baPWV and potential predictors included BL baPWV, blood pressure (systolic & diastolic) and sustained DAS remission was found.By multivariate analysis,achieving sustained DAS remission was an independent predictor for baPWV reduction.

Table 1 – Changes in baPWV over a period of 12 months in patients who can or cannot achieve sustained DAS remission in 3 consecutive visits

	Sustained DAS remission in 3 consecutive visits			
	No (n=64)	Yes (n=36)	*p*	*p**
Baseline characteristics				
Female (n ,%)	47 (73.4%)	30 (83.3%)	0.259	
Age (year)	51.6 ± 12.8	54.9 ± 13.2	0.232	
DAS 28	5.01 ± 1.04	4.81 ± 0.92	0.327	
SDAI	27.4 (20.02, 41.08)	26.55 (18.95, 33.5)	0.343	
Diabetes (n ,%)	5 (7.8%)	3 (8.3%)	0.927	
Mean baPWV (cm/s)				
Baseline	1422.5 (1207.5,1581)	1478.5 (1286.3,1624)	0.166	
Month 12	1436 (1264, 1636.3)	1394.3 (1244.5, 1567.3)	0.698	
Changes in PWV (cm/s)	39(-65.25, 124.75)	-65.5 (-147.25, 44)	*0.005*	*0.02*
Percentage change in PWV, %	2.51 (-4.34, 10.28)	-4.4(-9.67, 2.84)	*0.006*	*0.012*

* Adjusted for baseline blood pressure and baPWV

Conclusions: Effective suppression of inflammation by achieving sustained DAS remission may prevent progression of AS in ERA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3367

SAT0748-HPR WORKING WITH A MUSCULOSKELETAL DISORDER – A QUALITATIVE STUDY OF WORKERS' EXPERIENCES

A. Cochrane[1], C.J. Rothwell[1], O. FitzGerald[2], P. Gallagher[3], J. Ashton[4], R. Breen[5], A. Brennan[6], O. Corcoran[7], D. Desmond[1]. *[1]Department of Psychology, Maynooth University, Maynooth; [2]School of Medicine and Medical Sciences, University College Dublin; [3]School of Nursing and Human Sciences, Dublin City University; [4]Physiotherapy Services, Beaumont Hospital; [5]Royal College of Physicians in Ireland; [6]Physiotherapy Services, AMNCH, Dublin; [7]Rheumatology Services, Waterford University Hospital, Waterford, Ireland*

Background: Musculoskeletal disorders (MSDs) are the leading cause of temporary and permanent work related disability across Europe, yet many people are able to remain at work.
Objectives: To explore perceived facilitators and barriers to staying at work amongst people experiencing MSD.
Methods: Semi-structured interviews conducted with 19 individuals who had attended musculoskeletal assessment clinics in three Irish hospitals within the preceding year with a confirmed diagnosis of non-inflammatory musculoskeletal disorder. Participants were only included if they had been in paid employment continuously for at least six of the previous 12 months. The interviews were audio-recorded and transcribed. Data were analysed using thematic analysis.
Results: Participants ranged in age from 21 to 50 years, most were female (n=16). Fifteen participants were continuing to work, while experiencing pain and some functional limitations. Job control emerged as a key factor in continued work participation, specifically, being able to organise workload and make modifications to work practices enabled participants to maintain an acceptable level of work performance. The value of work, both personal and financial, motivated people to continue to work. While some co-workers and supervisors were considered to be helpful, interviewees were concerned that they could lose their job if they asked for assistance or took time off work. Fatigue had a considerable impact on life outside of work, with interviewees reporting effects on family life and reduced participation in social activities.
Conclusions: While continuing to work was beneficial, negative spillover effects on life outside of work were commonly reported. Workers with MSD may benefit from interventions that focus on coping with pain and fatigue management, as well as those that raise awareness amongst employers.
Acknowledgements: This research is funded by the Health Research Board [RCQPS-2014–2].
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2909

SAT0749-HPR THE RELATIONSHIP BETWEEN SPINAL MOBILITY AND STATIC AND DYNAMIC BALANCE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

B. Unver, H. Yilmaz, F. Unver. *Dokuz Eylul University, School of Physical Therapy and Rehabilitation, Department of Orthopaedic Physiotherapy, Izmir, Turkey*

Background: Ankylosing spondylitis (AS) is a major chronic rheumatic disease that predominantly affects axial joints, determining a rigid spine from the occiput to the sacrum. The disease can lead to permanent spinal deformity and postural disorder during the later stages. Changes in axial mobility may lead to impaired postural control, with altered postural control being associated with increased fall risk and lower quality of life. The population with AS has been rarely studied regarding postural control, both dynamic and static.
Objectives: The aim was to investigate the relationship between spinal mobility and static and dynamic balance of patients with mild to moderate AS.
Methods: The study included 137 (74 male and 63 female) patients with a mean age of 51.19±10.72 (20–78) years who were diagnosed with AS according to the modified New York criteria. Patients were divided into two groups as tragus to the wall distance (TWD) <15 cm (Group I = mild AS, n=51) and TWD ≥15 (Group II = moderate AS, n=84). The mean duration of disease in Group I was 17.83±11.3 (1 - 50) years and the mean duration of disease in Group II was 20.78±9.67 (2 - 43) years. Spinal mobility measurements [TWD, cervical rotation (CR), modified Schober test (MST), lumbar lateral flexion (LLF), intermalleolar distance (IMM), thoracic expansion (TE) tests] were compared with static and dynamic balance tests in the groups. Static balance was assessed with one-foot standing with eyes open and closed. Dynamic balance was assessed with timed up and go test and Berg balance scale.
Results: A statistically significant difference was found between spinal mobility measurements and Berg balance scale scores between the groups. Spinal mobility values of Group II were worse than Group I ($p<0.05$). Berg balance scale scores were better in Group I than Group II ($p=0.028$). No statistically significant difference was found between the two groups in terms of static balance and timed up and go test ($p>0.05$). There was a weak and significant correlation between spinal mobility measurements [CR, MST, LLF, IMM, and TE] and static and dynamic balance in the positive direction ($r=0.177–0.284$, $p<0.05$). There was no significant correlation between TWD and static and dynamic balance ($p>0.05$).
Conclusions: In patients with AS, as the severity of the disease progresses, spinal mobility and dynamic balance worsen; however, the static balance does not change. These changes in the posture and balance can negatively affect patients' participation levels in daily life and increase their risk of falling. For this reason, we think that detailed evaluation of balance, balance training and fall preventing approaches should be included in the rehabilitation programs for the patients with AS.
References:
[1] Demontis A, et al. Rheumatol Int. 2016;36(3):333–9.
[2] Çınar E, et al. Eur J Rheumatol. 2016;3(1):5–9.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2278

SAT0750-HPR "IS THIS REALLY THE WAY WE SHOULD GO?" – PATIENT PERSPECTIVES ON RHEUMATOID ARTHRITIS MANAGEMENT

C.A. Lemay[1], K. Mazor[2], J. Kremer[3], W.B. Nowell[4], C. Bingham III[5], J. Curtis[6], E. Ruderman[7], L. Harrold[8]. *[1]Orthopedics, University of Massachusetts Medical School; [2]Meyers Primary Care Institute, Worcester; [3]Albany Medical College, Albany; [4]Global Healthy Living Foundation, Upper Nyack; [5]Johns Hopkins University, Baltimore; [6]The University of Alabama at Birmingham, Birmingham; [7]Northwestern University Feinberg School of Medicine, Chicago; [8]University of Massachusetts Medical School, Worcester, United States*

Background: Current rheumatoid arthritis (RA) treatment guidelines suggest aggressive management in order to minimize disease activity. To achieve this goal, clinicians will need to engage patients in shared decision making. Currently little is known regarding patient's preferences and goals for treatment.
Objectives: To understand patient perspectives on their goals with regard to RA disease and flare management and the barriers to, and facilitators of achieving those goals.
Methods: Participants were interviewed utilizing open-ended questions focused on understanding their goals of managing their disease (both disease flares and longstanding disease) as well as the barriers and facilitators of achieving those goals. We explored the following: disease impact; disease beliefs and behaviors; medication use; provider relationship and communication; availability of insurance coverage; and community resources. Interviews were recorded and transcribed. Data were categorized using content analysis techniques. Convenience sample of persons living with rheumatologist-diagnosed RA was recruited from rheumatology practices in 4 states to participate in telephone interviews.
Results: Twenty-seven participants completed an interview from March-August 2015. Mean age was 63 years; 82% were female and 82% Non-Hispanic White. Participants reported living with RA for an average of 12 years and 44% reported

that their RA was not well controlled. The most common participant goal was to improve or maintain physical function. Barriers to RA and flare management included: 1) Patient Level- lack of knowledge of how to manage flares and a reluctance to change or use medications, related to concerns about potential side effects, and limited understanding of the potential benefits; 2) Provider Level- inadequate communication between patient and provider, specifically in relation to flare management and; 3) Health System Level- difficulty navigating insurance, handling coverage gaps, affording high medication costs. Facilitators of RA and Flare management included: 1) Patient Level- successful use of non-medication approaches to disease management and the willingness to initiate conversation with their provider about changing medications and; 2) Provider Level- a positive relationship with their provider, including having trust in the provider, easy access to the provider, and positive communication.

Conclusions: We identified patient-, provider and health system-barriers and facilitators experienced by RA patients achieving their treatment goals. A common theme that emerged was inadequate shared decision making between patients and their providers related to lack of patient knowledge, inadequate communication, and mistrust.

Disclosure of Interest: C. Lemay Grant/research support from: Pfizer Inc, K. Mazor Grant/research support from: Pfizer Inc, J. Kremer Shareholder of: Corrona, Grant/research support from: Abbvie, Genentech, Lilly, Novartis, Pfizer, Employee of: Corrona, Speakers bureau: Genentech (non-promotional only, W. B. Nowell: None declared, C. Bingham III Consultant for: Bristol-Myers Squibb, J. Curtis Grant/research support from: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, AbbVie, Consultant for: Roche/Genentech, UCB, Janssen, Corrona, Amgen, Pfizer, BMS, Crescendo, AbbVie, E. Ruderman Grant/research support from: Pfizer Inc, Amgen, Consultant for: AbbVie, Amgen, Lilly, Novartis Pharmaceutical Corporation, Pfizer Inc., Janssen Pharmaceutica Product, L.P., L. Harrold Shareholder of: Corrona, Grant/research support from: Pfizer Inc, Consultant for: Roche Pharmaceuticals, Employee of: Corrona

DOI: 10.1136/annrheumdis-2017-eular.3930

SAT0751-HPR THE RELATIONSHIP BETWEEN ANAEROBIC EXERCISE CAPACITY AND ISOMETRIC LOWER EXTREMITY MUSCLE STRENGTH IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

D. Bayraktar[1], S. Savci[2], E. Manci[3], O. Altug-Gucenmez[4], B. Makay[4], N. İlcin[2], S.E. Unsal[4]. *[1]Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Izmir Katip Celebi University; [2]School of Physical Therapy and Rehabilitation; [3]Institute of Health Sciences; [4]Faculty of Medicine, Division of Pediatric Rheumatology, Dokuz Eylul University, Izmir, Turkey*

Background: Juvenile idiopathic arthritis (JIA) is a chronic disease that occurs before the age of 16 years. It was shown that anaerobic exercise capacity, which is important for most daily activities in children such as jumping, hoping and climbing was diminished in JIA. Previous studies showed that anaerobic exercise capacity was related to well-being level, functional status, and aerobic exercise capacity in JIA. However, no data is available about the relationship between lower extremity muscle power and anaerobic exercise capacity in children with JIA.

Objectives: To determine the possible relationships between lower extremity muscle strength and anaerobic capacity.

Methods: Forty-six children with JIA (14 F, 32 M), with a mean age of 13.74±2.29 years (min-max: 9–17 years) were included in the study. Isometric lower extremity muscle strength was assessed with a hand-held dynamometer at the end points of knee flexion, knee extension, hip flexion and hip extension movements, which are generated from gross lower extremity muscles and important for anaerobic power. All the muscle testing was performed on the right leg. Anaerobic exercise capacity was measured performing a 30-second Wingate test. Both absolute and per kilogram values for peak power and average power were noted. The relationships between the parameters were determined with Pearson's correlation coefficient. (Relationship levels were interpreted as 0.05–0.30: low correlation; 0.30–0.40: low-moderate correlation; 0.40–0.60: moderate correlation; 0.60–0.75: good correlation; 0.75–1.00: good-excellent correlation.

Results: All children completed the assessments without any adverse effects. Demographics, average isometric lower extremity muscle strengths and parameters related to the anaerobic exercise capacity testing were shown at Table 1. Moderate to good correlations were determined between isometric muscle strength and anaerobic exercise capacity parameters $p<0.001$ (Table 2).

Table 1. Demographics, isometric lower extremity muscle strength and anaerobic exercise capacity parameters

	Mean±SD
Age (years)	13.74±2.29
Height (cm)	159.72±11.08
Weight (kg)	53.76±14.95
BMI (kg/m^2)	20.76±3.92
Hip Flexion (kg)	16.81±5.47
Hip Extension (kg)	13.57±4.50
Knee Flexion (kg)	17.72±5.83
Knee Extension (kg)	22.08±6.94
Peak Power (W)	386.26±184.08
Peak Power (W/kg)	6.99±2.33
Average Power (W)	287.69±129.53
Average Power (W/kg)	5.22±1.60

SD: Standard Deviation; cm: centimeters; kg: kilogram; m: meter; W: watt; W/kg: watt/kilogram.

Table 2. The relationships between isometric muscle strength and anaerobic exercise capacity parameters

	Peak Power (W)	Peak Power) (W/kg)	Average Power (W)	Average Power (W/kg)
Hip Flexion (kg)	0.688*	0.629*	0.636*	0.552*
Hip Extension (kg)	0.618*	0.532*	0.581*	0.458*
Knee Flexion (kg)	0.642*	0.530*	0.630*	0.494*
Knee Extension (kg)	0.647*	0.465*	0.670*	0.469*

Pearson Correlation Test; kg: kilogram; W: watt; W/kg: watt/kilogram. *Significance at level <0.001.

Conclusions: The results of this study suggested that lower extremity muscle strength might influence the anaerobic exercise capacity. Exercise regimes including lower extremity strengthening might help improving anaerobic exercise capacity in children with JIA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5697

SAT0752-HPR THE MEASUREMENT OF PATIENTS' EXPECTATIONS OF A MULTIDISCIPLINARY AND DEDICATED FIBROMYALGIA PROGRAM

D. Xhaxho, A.A. Borg, C. Mercieca. *Rheumatology, Mater Dei Hospital, Swatar, Malta*

Background: Fibromyalgia (FM) is a chronic and multidimensional condition impacting the physical health and psychosocial state of the individuals. In addition to performing clinical and psychological assessments, evaluating patients' expectations may help address their specific needs and improve outcomes.

Objectives: The aim of this study was to assess the expectations of a cohort of FM patients participating in a multidisciplinary, dedicated fibromyalgia program.

Methods: This was a survey of 86 consecutive FM patients who were initiating a multidisciplinary program delivered by a rheumatologist, nurse, physiotherapist, occupational therapist, psychotherapist and GP with a special interest in FM. Patients were diagnosed using the 2010 ACR diagnostic criteria. Demographic data, Widespread Pain Index (WPI), Symptom Severity Score (SSS) were recorded. Patients filled in the self-administered questionnaires including the Revised fibromyalgia impact questionnaire (FIQR), Hospital Anxiety and Depression Scale (HADS) and a patients' expectations questionnaire. The latter consisted of both open ended and closed questions using a five- point Likert scale (1=strongly agree to 5=strongly disagree) about the following domains; physical, psychological, coping and social aspects.

Results: Eighty six patients (92% females) participated in the survey. The average age was 51.2 years (SD 10.60) and mean duration of symptoms 13.3 years (SD 11.17). The mean HADS-A was 11.6 (SD 4.37), HADS-D 8.67 (SD 3.47) and FIQR 55.9 (SD 21.64). In response to an open question about what was their main expectation from this program, just over half of the patients (52.3%) reported improvement of pain and fatigue as their most important outcome. This was followed by improved quality of life (19.3%), being able to cope better with ADLs, family and work (17.4%), obtain more knowledge about the condition (5.8%), while 15.1% did not have any expectations. When asked to rate their expectations for each specific domain: 64% expected significant improvement of physical symptoms, 74% to be able to cope better with family, hobbies and work and 66% expected an improvement of their psychological state, namely depression and anxiety. By the end of the program, 66% of the patients expected to have minimal or no symptoms. When asked to identify any lifestyle changes which could help, 30.2% mentioned a better work-life balance, 12.8% starting an exercise routine, 10.5% weight loss, 11.6% a mixture of house adaptations while 34.9% could not come up with any suggestions.

Conclusions: Expectations of fibromyalgia patients were high in all domains. This study highlights the need for multidimensional assessment and a personalised treatment approach in managing fibromyalgia. Moreover, it is very important to assess patients' expectations in order to guide interventions and set realistic achievable goals which are acceptable to both patients and clinicians. Patients' expectations are an important patient reported outcome measure, which need to be assessed.

References:

[1] Goffaux P, De Souza J, Potvin S, Marchand S(2009) Research papers: Pain relief through expectation supersedes descending inhibitory deficits in fibromyalgia patients. Pain 145:18–23.

[2] Hamnes B, Hauge M, Kjeken I, Hagen K (2011) ' I have come here to learn how to cope with my illness, not to be cured': A Qualitative Study of Patient Expectations Prior to a One-Week Self-Management Programme. Musculoskeletal Care 9(4):200–210.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1599

SAT0753-HPR AWARENESS OF POSSIBLE SIDE EFFECTS OF NSAIDS AMONG THE ALBANIAN PATIENT POPULATION

E. Pistja, A. Themeli. *Continuing Education, Medical Training Center Santa Maria, Lezhe, Albania*

Background: No official published figures are available regarding the annual use of NSAIDs in Albania. Nonsteroidal anti-inflammatory drugs are used primarily to manage different pain conditions, less commonly they are used for their antipyretic effect. Although generally well tolerated, conventional NSAIDs have been associated with a wide range of adverse effects. The most common of which are gastrointestinal tract (GIT) side effects like: dyspepsia, abdominal pain, heartburn, and the most serious life–threatening gastrointestinal (GI) ulceration.
Objectives: To investigate patient awareness of the proper use and frequency of side effects in nonsteroidal anti-inflammatory drugs (NSAIDs) patients in Albania.
Methods: This study was a prospective 15 question interview of patients purchasing medications, during randomized 1 hour/day pharmacy visits over a one month study period (May 2015).
The study was conducted in 4 community pharmacies located in the city of Tirana (capital of Albania). Two hundred and ten patients were included in this study.
Results: Overall NSAIDs use during last year was 63%: Ibuprofene and diclofenac was the most used NSAIDs.
The majority of patients (58%) reported having side effects upon NSAIDs-use; gastrointestinal upset was the most frequently reported side effect.
Patients' awareness regarding proper NSAIDs use was poor, and pharmacist role in counseling was inadequate.
However, user ability to discover the most common side effect to the drug seemed not to be affected.
Conclusions: Nonsteroidal anti-inflammatory drugs use awareness and knowledge of probable serious side effects and how to handle them was not adequate. This probably reflected on high incidence of side effects. Nonsteroidal anti-inflammatory drugs are available on prescription as well as over the counter drugs.
Pharmacist involvement in education of patients using them is highly recommended and much needed to help decrease frequency of side effects.
However this is a small scale study and further studies need to be done.
References:
[1] Langman MJ. Risks of anti-inflammatory drug-associated damage. Inflamm Res 1999; 48: 236–238.
[2] Garcia Rodriquez LA, Jick H. Risk of upper gastrointestinal bleeding and perforation associated with individual non-steroidal anti-inflammatory drugs. Lancet 1994; 343: 769–772.
[3] Kay EA, Barker AR. Rheumatoid arthritis andosteoarthritis. In: Walker R, Edward C, editor. Clinicalpharmacy and therapeutics. Edinburgh (UK): Churchill Livingstone; 2002. p. 779–795.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1089

SAT0754-HPR "A NECESSARY INVESTMENT IN FUTURE HEALTH". PERCEPTIONS OF PHYSICAL ACTIVITY MAINTENANCE AMONG PEOPLE WITH RA PARTICIPATING IN AN OUTSOURCED HEALTH-ENHANCING PHYSICAL ACTIVITY PROGRAM

E. Swärdh[1,2], B. Nordgren[1,2], C.H. Opava[1,3], I. Demmelmaier[1]. *[1]Department of Neurobiology, Care sciences and Society, Division of Physiotherapy, Karolinska Institutet; [2]Functional Area Occupational Therapy & Physiotherapy, Allied Health Professionals' Function, Karolinska University Hospital, Huddinge; [3]Department of Rheumatology, Karolinska University Hospital, Solna, Sweden*

Background: Health-enhancing physical activity (HEPA) is an active treatment in rheumatoid arthritis (RA) that may be difficult for patients to maintain over time. A two-year HEPA program including twice-weekly circuit training at public gyms and 150 weekly minutes of moderately intense aerobic exercise was conducted in Sweden between 2011 and 2013. Regular peer support sessions were held to guide adoption and maintenance of HEPA. Patient perceptions on maintained physical activity in RA have been minimally explored.
Objectives: To describe perceptions of physical activity maintenance during the second year of an outsourced 2-year HEPA-program among people with RA
Methods: A descriptive design with a qualitative inductive approach was used. Interviews were conducted with 18 participants with RA, including men and women differing in age, disease duration, activity limitation, perceived pain, levels of physical activity, training centers and peer support groups. Qualitative content analysis was used, and a pattern of theme, subthemes, categories, and subcategories was constructed based on the participants' perceptions of the phenomenon.
Results: A main overarching theme and three subthemes were established, called '*A necessary investment in future health* through *dedication*, *affinity* and *awareness'*, which described participants' experiences of maintenance during the second year of an outsourced 2-year HEPA-program. This was further described in eight categories with 16 subcategories. The categories described the participants'; '*mindsets, habits, commitments, social support, PA contexts, monitoring, insights in PA, and health gains'*.
Conclusions: The findings are partly in line with the theoretically derived explanations for maintenance of behavior change formulated to date, such as maintenance motives (self-determination and identity), self-regulation (skills and processes, lapse, relapse and coping) habits, resources (psychological and physical) as well as environmental and social influences. The results of this study could also be transferable to similar groups of people with RA in similar settings and useful in designing future HEPA interventions to facilitate maintenance of behavior change.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6219

SAT0755-HPR VARIATION IN SLE-RELATED PAIN: A SEVEN YEAR FOLLOW-UP STUDY

E. Waldheim[1], S. Ajeganova[1], S. Bergman[2], J. Frostegård[1], E. Welin Henriksson[3]. *[1]Karolinska Institutet, Stockholm; [2]University of Gothenburg, Gothenburg; [3]Linköping Universitet, Linköping, Sweden*

Background: In a previous study we have shown that 24% of patients with SLE in our cohort reported high level of SLE-related pain, ≥40 mm on VAS (0–100 mm).[1] These patients with high pain level also reported significantly more fatigue, anxiety and depression and reduced health-related quality of life compared to the SLE patients with low pain level, ≤39 mm on VAS.[2]
Objectives: To investigate the variation in self-reported SLE-related pain and its association with presence of chronic widespread pain (CWP) and patient-related outcomes after seven years of follow-up.
Methods: 64 of 84 patients agreed to participate in the 7-year follow-up and answered questionnaires on pain (VAS/mm), fatigue (MAF), HRQoL (SF-36), anxiety and depression (HADS) and, in case of remaining pain > three months, marked painful body regions on a pain-drawing. Disease activity and damage (SLAM, SLEDAI, SLICC) were also captured. Nonparametric statistics were used to compare the different groups. Difference in measures (diff) between inclusion and follow-up was calculated.
Results: For the patients with low degree of SLE-related pain the previous week (≤39 mm on VAS) at inclusion, n=50, there were no significant difference at 7 years follow-up in pain, fatigue, anxiety, depression and all dimensions of SF-36, except for deterioration in physical function median diff (IQR) 0 (-10 to 5), p=0.024. Of these patients with low level of pain, 26% indicated chronic widespread pain on the pain drawing.
Among patients with high degree of pain (≥40 mm on VAS) at inclusion, n=14, half of the patients reported significantly decreased pain, diff (IQR) 45 (35 to 65), p=0.021, fatigue, 8 (8 to 17), p=0.018, anxiety, 4 (1 to 4), p=0.035 and depression, 4 (2 to 5), p=0.018 and improvements in all dimensions of SF-36 except for role emotional and social function at follow-up, $p<0.05$.
However, half of the patients with high degree of pain at inclusion reported no significant changes at follow up regarding pain, median diff (IQR) -13 (-20 to 28), fatigue, 5 (-0.3 to 6), anxiety, 2 (-1 to 3) and depression, 0 (-3 to 2). These patients reported significantly deterioration in vitality in SF-36, diff (IQR) 20 (15 to 35), p=0.0018 but no significant changes in the other dimensions of SF-36. All patients with high levels of remaining pain indicated chronic widespread pain on the pain drawing. These patients with remaining pain had significantly higher SLAM at follow-up compared to the patients with decreased pain at follow-up, p=0.017 and the patients with low levels of pain at inclusion, p=0.006. No significant differences were found regarding SLEDAI and disease damage.
Conclusions: Self-reported level of disease-related pain remain low in most patients and in some patients also significantly reduced. However, half of the patients with high level of pain at inclusion still experienced high level of pain and pain-related problems including widespread pain after 7 years of follow-up. These results suggest a transition from SLE-related pain to chronic widespread pain, which requires different pain management.
References:
[1] Waldheim,E.,et al.(2013).Lupus 22:136–143.
[2] Waldheim,E.,et al.(2013).Lupus 22:1118–1127.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1446

SAT0756-HPR EFFECT OF NSAID INTAKE ON KINESIOPHOBIA IN PATIENTS WITH ANKYLOSING SPONDYLITIS

G.I. Kinikli[1], S. Karahan[2], A. Ates[3], M. Turgay[3], G. Kinikli[3]. *[1]Department of Physiotherapy and Rehabilitation, Hacettepe University Faculty of Health Sciences; [2]Department of Biostatistics, Hacettepe University Faculty of Medicine; [3]Department of Rheumatology, Ankara University Faculty of Medicine, Ankara, Turkey*

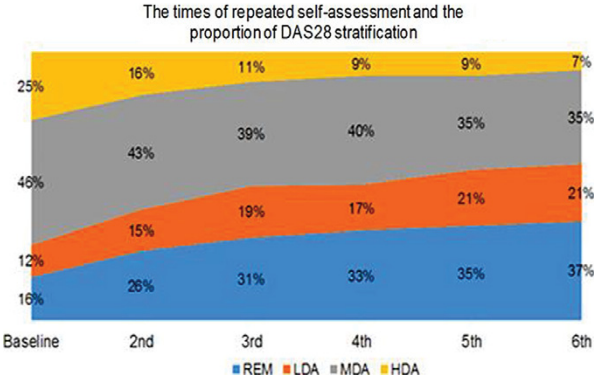
Background: Spinal stiffness and loss of spinal mobility, explained byspinal inflammation and structural damage due to extensive osteoproliferation, are characteristics of Ankylosing Spondylitis (AS). AS usually disables a person with severe back pain and, in later stages, remarkable spinal kyphotic deformity.The deformity eventually may necessitate a major corrective procedure. Therefore, controlling the symptoms and progression of AS in early stages by effective medication is the main step in the management of AS.
Objectives: The aim of this study was to investigate the effectiveness of DMARD therapies on NSAID intake and kinesiophobia in patients with AS.

Methods: A total of 74 patients, diagnosed according to the modified New York criteria for AS, were enrolled. Patients were assessed to measure disease activity using the Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]. Fear of movement was assessed with the Tampa Scale for Kinesiophobia [TSK]. To calculate NSAID intake and the type of NSAID, dose, percentage of days with intake were recorded, along with DMARD therapy, age, body mass index (BMI), and disease duration. The NSAID equivalent scoring was calculated according to recommendations from longitudinal clinical studies. The drug therapy groups were compared using the Kruskal-Wallis test and the Chi-square test. Correlation analysis was evaluated by Spearman's correlation coefficient.
Results: Seventy-four patients (36 women, 38 men; mean age: 43.81±10.18 years; mean disease duration: 9.89±8.50 years; BMI: 28.20±5.07) treated with four types of DMARDs (adalimumab+golimumab =17; infliximab =19; etanercept =13; sulfasalazine =25) were included. There were no drug group differences in terms of age (p=0.179), sex (p=0.886), or BMI (p=0.821). BASDAI scores (mean: 3.9±2.4) and NSAID intake (mean: 68.1±76.1; p=0.003) were significantly higher in the sulfasalazine therapy (ST) group compared to other drug groups. BASDAI scores were not correlated with age (p=0.103), disease duration (p=0.131), BMI (p=0.641) or the TSK scores (p=0.376). Different NSAID intake groups (p=0.089) had similar TSK scores.
Conclusions: Patients with AS had fear of movement independent of age, BMI or disease duration, even when they experienced positive results from drug therapies and concomitant therapy with a single oral dose of NSAID or oral corticosteroids in stable dosages.
References:
[1] Braun J, Baraliakos X, Heldmann F, et al. Tumor necrosis factor alpha antagonists in the treatment of axial spondyloarthritis. Expert Opin Investig Drugs. 2014;23:647–659.
[2] Rohekar S, Chan J, Tse SM, et al. 2014 update of the Canadian Rheumatology Association/Spondyloarthritis Research Consortium of Canada treatment recommendations for the management of spondy- loarthritis. Part I: principles of the management of spondyloarthritis in Canada. J Rheumatol. 2015;42:654–664.
[3] Rohekar S, Chan J, Tse SM, et al. 2014 update of the Canadian Rheumatology Association/Spondyloarthritis Research Consortium of Canada treatment recommendations for the management of spondy- loarthritis. Part II: specific management recommendations. J Rheu- matol. 2015;42:665–681.
Acknowledgements: We would like to thank Rheumatology Nurse Ayten Yuksek in our department for monitoring and documenting of the data, and our patients for assistance with their valuable participation to our study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1389

SAT0757-HPR SIGNIFICANT IMPROVEMENT OF RHEUMATOID ARTHRITIS (RA) OUTCOME WITH REPEATED SELF-ASSESSMENT APPLYING SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILES TOOLS: A COHORT STUDY OF RA PATIENTS IN CHINA

J. Yang[1], Y. Wang[2], F. Li[3], H. Wei[4], J. Xue[5], H. Wang[6], J. Ru[7], R. Mu[8], J. Huang[9], X. Zuo[10], X. Xin[11], F. He[12], X. Shi[13], Z. Li[14], F. Xiao[15], H. Xiao[15], Y. Liu[15], Y. Jia[15], Z. Li[8]. *[1]Department of Rheumatology, Central Hospital of MianYang, Sichuan, Mianyang; [2]Department of Rheumatology, The First Affiliated Hospital of BaoTou Medical College, Baotou; [3]Department of Rheumatology and Immunology, The Second Xiangya Hospital of Central South University, Changsha; [4]Department of Rheumatology, Northern Jiangsu People's Hospital, Yangzhou; [5]Department of Rheumatology and Immunology, The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou; [6]Department of Rheumatology and Immunology, JiaXing First Hospital, Zhejiang, Jiaxing; [7]Dept.of Rheumatology, The 264th Hospital of the PLA, Taiyuan; [8]Department of Rheumatology and Immunology, People's Hospital, Beijing University Medical School, Beijing; [9]Department of Rheumatology and Immunology, The sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou; [10]Department of Rheumatology and Immunology, Xiangya Hospital Centeral South University, Changsha; [11]Ningbo First Hospital, Zhejiang, Ningbo; [12]Department of Rheumatology, Suining Central Hospital, Suining; [13]Department of Rheumatology and Immunology, The First Affiliated Hospital of Henan University of Science and Technology, Luoyang; [14]Department of rheumatology, The First Affiliated Hospital of Bengbu Medical College, Bengbu; [15]Medical Department, Shanghai Gothic Internet Technology Co., Ltd., Shanghai, China*

Background: There are more than 5 million RA patients in China, but only 5,000 rheumatologists. Treat-to-Target (T2T) strategy are critical for the treatment of RA, but the Chinese rheumatologists can hardly provide patients with a complete assessment in the clinic due to limited time. The SSDM includes interfaces of both physicians' and patients' application. After entering the data of lab test records, treatment regiments, and executing DAS28 assessment by patients themselves, all data can be synchronized automatically to the authorized physicians' mobile tool. The rheumatologists can adjust treatment regiments base on patients' profile. Our previous study showed that patients in China can master the application of SSDM for accurately evaluating DAS28 and health assessment questionnaire (HAQ) after training.
Objectives: The purpose of this study is to explore the effectiveness of applying SSDM in improvement of disease activity after repeated self-assessment in Chinese RA patients.
Methods: Patients were educated to assess DAS28 with SSDM and asked to repeat the self-assessment once a month. Descriptive statistics were performed for patient and disease characteristics. According to DAS28 scores, disease activity was divided into four groups: remission (Rem), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA).
Results: From Aug 2014 to Jan 2017, a total of 11,867 RA patients from 459 centers in China participated in the study. The mean age was 49.27±14.35 (18 to 99) years and the median disease duration was 11.43 months. All patients performed self-assessment of DAS28, HAQ and morning stiffness time for 20,376 times. Proportion of patients in Rem, LDA, MDA and HDA was 16%, 12%, 46% and 25% respectively at baseline. Of which, 3,472 patients performed repeated assessment for 8,509 times. Proportion of patients in Rem, LDA, MDA and HDA changed into 34%, 18%, 38% and 10% at the last assessment. The proportion of T2T (DAS28 <3.2) at the last assessment was higher than that of baseline significantly (P<0.001). According to the assessments, the rate of T2T from baseline to 6 times were 28%, 41%, 49%, 51%, 56% and 58% (see Figure 1).With the increase of the times of self-assessment, the T2T rate was significantly improved (p<0.001).

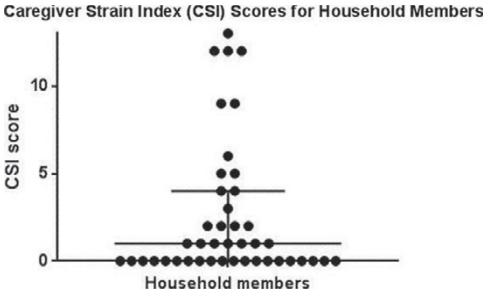


Conclusions: Under repeated self-assessment of DAS28 using SSDM, RA patients can achieve better T2T result. SSDM can assist rheumatologist to rationally adjust treatment for RA patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5042

SAT0758-HPR DEPRESSION BUT NOT CORE SYMPTOMS PREDICT CAREGIVER STRAIN IN ADULTS SHARING A HOME WITH PRIMARY SJÖGREN'S SYNDROME PATIENTS

K. Hackett[1], D. Lendrem[1], T. Rapley[1], V. Deary[2], K. Deane[3], J. Newton[1], W.-F. Ng[1]. *[1]Newcastle University; [2]Northumbria University, Newcastle Upon Tyne; [3]University of East Anglia, Norwich, United Kingdom*

Background: Patients with primary Sjögren's syndrome (PSS) experience a range of symptoms including dryness, fatigue, pain and low mood. The impact of these symptoms upon the people with whom they live, is unknown. The caregiver strain index (CSI) is a thirteen item questionnaire which measures strain in caregivers (Robinson 1983).
Objectives: To determine whether adults living in the same household as a person with PSS experience caregiver strain and to examine the relationship between caregiver strain and other factors.
Methods: We collected age, Carer Strain Index (CSI) and quality of life (QOL) (SF-36) scores from 62 adults who shared a home with a PSS patient. We also collected various measures from the PSS patients that they lived with. The patient measures included; age, time since diagnosis, fatigue, dryness, pain, QOL, depression, anxiety, and physical function (Improved HAQ). We conducted Spearman correlations to compare the relationship between the carers' CSI and SF-36 scores as well as the measures from the patients they lived with. We performed multivariate analyses on factors that significantly correlated with CSI scores.
Results: The caregiver strain scores are shown in the Figure. Although a median CSI score of 1 demonstrates that most AHM participants experienced very little caregiver strain, 14% of AHM participants did experience high levels (indicated with a CSI score ≥7).
Age and PSS disease duration negatively correlated with carer strain. Increased pain, fatigue, mental fatigue, physical functioning, anxiety, depression in the patients and SF-36 physical component scores in the household members all significantly correlated with increased carer strain. There was no relationship between dryness scores and age of the PSS patient and CSI scores.
Multivariate analysis suggests the main predictor of increased carer strain was depression in the PSS patient and younger age of the household member.
Conclusions: Caregiver strain is evident in a proportion of adults sharing a home with a person with PSS. Caregivers of patients with high depression scores are particularly susceptible and may benefit from additional support.



References:
[1] Robinson BC Validation of a Caregiver Strain Index. J Gerontol 1983; 38: 344–48.
Acknowledgements: Arthritis Research UK (grant 20169) and the United Kingdom Occupational Therapy Research Foundation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4996

SAT0760-HPR PSYCHOLOGICAL VARIABLES PREDICTIVE OF DISORDERS OF SLEEP IN PATIENTS WITH SPONDYLARTHRITIS AND PSORIATIC ARTRTITS. PRELIMINARY MULTICENTER STUDY

L. Cano Garcia[1], M.D. Hernandez-Sanchez[2], R. Segura-Ruiz[3], C. Dominguez-Quesada[4], M.J. Peña-Vallejo[4], N. Mena-Vázquez[1], E. Vilchez-Ocaña[1], A. Fernandez-Nebro[1]. *[1]Rheumatology, Hospital Regional Universitario de Málaga, Malaga; [2]Rheumatology, Complejo Hospitalario de Jaen, Jaen; [3]Rheumatology, Hospital Reina Sofia, Cordoba; [4]Rheumatology, Hospital Virgen Macarena, Sevilla, Spain*

Objectives: To study the psychological variables associated with the severity of insomnia and hypersomnia according to the Oviedo sleep questionnaire (COS) in patients with spondylarthritis (SPA) and psoriatic arthritis (PA), including the disease activity BASDAI and DAS28.
Methods: Design. Cross-sectional descriptive study. Patients: Patients with consecutive SPA or PA were selected by consecutive sampling in follow-up in rheumatology units of 4 Spanish hospitals. Inclusion criteria: Adults (age $\geq$16 years) with SPA (ASAS criteria) or PA (CASPAR criteria) capable of understanding and willing to perform questionnaires. Exclusion criteria: other rheumatic diseases, age $<$16 years. Protocol: Upon arriving at the consultation, he was offered to participate in the study, he was explained and the patient was given the battery of questionnaires; His physician performed the evaluation of disease activity and recorded the comorbidities and current medication. Main outcomes: the 3 dimensions of COS: (1) Subjective satisfaction with sleep, (2) Insomnia and (3) Hyperinsomnia. The COS is a semi-structured interview to aid the diagnosis of insomnia and hypersomnia according to the diagnostic criteria ICD-10 and DSM-IV. Other variables: current medication for SPA or PA, comorbidities, use of sleeping pills and/or CPAP according to COS questionnaire (insomnia was divided into mild $<$15 and moderate-severe $\geq$15), disease activity: AD BASDAI) and APs (DAS28); Health-related quality of life (HRQL) using SF-36; Pain perception (Brief Pain Inventory BPI questionnaire), SPA (BASDAI) and PA (DAS28, BASDAI) and FACIT fatigue, TMMS emotional intelligence, Resilience with resilience questionnaire, anxiety and depression sceening using HADs.Statistical analysis: descriptive, bivariate analysis using T-Student, Mann-Whitney and $\chi 2$; Followed by binary logistic regression (BLR) (Vd: moderate/severe insomnia).
Results: A total of 126 patients participated: 65 patients with SPA (33.8% women, 49.92±10.92 years) and 61 patients with PA (60.7% women, 49.4±9.5 years) with an average of 8.4±6.8 years of disease. They used biological therapy SPA 29 (23%) and PA 28 (45.9%). The most common comorbidity were in SPA and PA: disc disease 33 (50.8%) and 18 (29.5%). 16 (24.6%). Both patients with SPA and PA were dissatisfied with their sleep (3.42±1.39). We did not find correlation of the COS variables with the HRQoL, the fatigue or the pain. There were no differences in COS scale according to biological treatment and/or FAME. Logistic regression analysis demonstrated an association between insomnia and TMMS repair, resilience and anxiety in PA. Insomnia in SPA showed an association with depression and BASDAI
Conclusions: Insomnia is a common health problem in these diseases. Moderate-intense insomnia in patients with SPA was associated with an increase in BASDAI and depression. Also in patients with PA, the insomnia was associated with TMMS repair, resilience and anxiety. The patient assumes the slepp dissorder as part of this chronic illness, this jutifies the good evaluations of resilience and emotional inteligence of the evaluated patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2544

SAT0761-HPR IDENTIFICATION OF FACTORS THAT CONTRIBUTE TO SUCCESSFUL ONLINE MONITORING OF DISEASE ACTIVITY: EXPERIENCES FROM PATIENTS WITH RHEUMATOID ARTHRITIS

L. Renskers[1], S.A.A. Rongen[1,2], A.M.P. Huis[1], M.E.J.L. Hulscher[1], P.L.C.M. van Riel[1,2]. *[1]IQ Healthcare, Radboud Institute for Health Sciences, Radboud university medical center, Nijmegen; [2]Rheumatology, Bernhoven, Uden, Netherlands*

Background: In order to encourage patients to take an active role in their disease management and to enhance the dialogue between patients and healthcare providers, iMonitor was developed.[1] iMonitor is a Software Medical Device developed and funded by Pfizer. Patients can complete patient-reported outcome measures (PROMs) in this online system. This allows for monitoring of disease activity in between visits, identification of patients who need medical attention in between visits, and it may lead to reduction of consultations for patients with stable disease activity. Moreover, completion of a PROM might help a patient to prepare for his or her consultation and might improve the communication between physician and patient.
Objectives: This study aims to identify factors that contribute to adequate online monitoring of disease activity, by collecting experiences from patients with RA with iMonitor.
Methods: Patients were recruited at Bernhoven (Uden, the Netherlands) by an announcement of the study on the hospital website, leaflets and by specific meetings. Four instruction classes were organised in which two researchers gave live instructions about the programme. Patients received log-in codes and chose their PROM-preference(s) and PROM-frequency. After nine months a focus group interview was performed and three telephone interviews were held. Questions were semi-structured using a topic list based on Flottorp[2]. Data will be transcribed, coded and grouped.
Results: Currently 33 patients with RA are using iMonitor. Of these patients 17 (52%) attended the instruction classes and six patients (18%) attended the focus group discussion. Preliminary results reveal six themes (Technological aspects, Patient factors, Need for getting feedback, Incentives and resources, Reduction of consults and Security aspects). The Flottorp domain "Patient factors" provided most rich information. Most patients said they developed more knowledge about their disease activity and that they felt more aware about their disease activity. Additionally, iMonitor supported them in taking actions such as adjustments in lifestyle and becoming more prudent when noticing a flare. Some patients felt more prepared for a consultation and less dependent from their rheumatologist. With regard to the domain "Capacity for organisational change", patients were confident that iMonitor could contribute to reduction of consultations, but contacting the outpatient clinic when feeling worried should be required.
Conclusions: Patients' experiences with an online remote monitoring system were mainly positive. Instruction classes helped patients to get familiar with the programme. Patients experienced to have more control over their disease and to have developed more knowledge. This may result in enhanced self-management, which is important with regard to retain control over disease.
References:
[1] Medical and Educational Goods and Services (MEGS): iMonitor. 2014; Available from: http://www.pfizer.co.uk/content/medical-and-educational-goods-and-services-megs-imonitor.
[2] Flottorp, S.A., et al., A checklist for identifying determinants of practice: a systematic review and synthesis of frameworks and taxonomies of factors that prevent or enable improvements in healthcare professional practice. Implementation Science, 2013. 8(1): p. 1.
Disclosure of Interest: L. Renskers Grant/research support from: Pfizer, S. Rongen: None declared, A. Huis: None declared, M. Hulscher: None declared, P. van Riel Grant/research support from: Pfizer
DOI: 10.1136/annrheumdis-2017-eular.2294

SAT0762-HPR THE ACCESSIBILITY AND USABILITY OF AN AUSTRALIAN WEB-BASED SELF-MANAGEMENT PROGRAMME (MYJOINTPAIN) FOR PEOPLE WITH LOWER HEALTH LITERACY AND JOINT PAIN IN THE UK

L.B. Parsons[1], J. Adams[1,2]. *[1]Faculty of Health Sciences; [2]Arthritis Research UK Centre for Sport Exercise and Osteoarthritis, University of Southampton, Southampton, United Kingdom*

Background: Osteoarthritis (OA) is disproportionately prevalent in people from lower socio economic groups (1). People from lower socio economic groups are also more likely to have lower health literacy. Health literacy influences people's ability to access, understand and use health information. Currently, health professionals over estimate patients' health literacy (2), potentially reducing the impact of OA self-management interventions that rely on educational approaches (3). As internet usage increases, online OA self-management resources are an option for delivering patient education. Currently, there is no evidence as to whether online education resources are suitable and accessible for people with joint pain and lower health literacy.
Objectives: To identify facilitators and barriers experienced by people with joint pain and low health literacy to access and utilise information available on the MyJointPain website. (https://www.myjointpain.org.au).

Methods: A qualitative interview study was conducted. Participants were invited to use the website for two weeks and then participated in semi-structured interviews. The interview topic guide had been developed in line with current literature. The interviews were audio recorded and transcribed verbatim. Thematic analysis was used by the main researcher (with independent verification) to interrogate the data and identify themes.
Results: Six people with low health literacy (S-TOFHLA 17±3) were recruited from community groups from an inner-city area with a high index for social deprivation. Four key themes were identified. 1) Dealing with technical issues, where participants demonstrated that they could persevere with technical problems in using online resources; 2) Information overprovision, here participants found there was too much complex health information provided, that hindered usability; 3) Motivation for information seeking, where participants discussed that it was pain that encouraged resource use but motivation to self-manage was influenced by personal beliefs; 4) Specific professional input, the participants whilst willing to use and engage with the website recalled that they also want to have access to a health professional and felt the website could supplement but not replace this contact. *"I think you have it from the health care where the healthcare are telling you and explaining to you".*
Conclusions: Digital online OA self-management presented by MyJointPain showed potential for use by people with joint pain and lower health literacy levels. This is important as outcomes for this group are poor (1). Text volume, detail and image use should be carefully considered when designing new online resources and involvement of people with lower health literacy when designing online tools will help to ensure information is accessible and useful to all OA patients. Clinicians should consider their patients' health literacy level, computer literacy and readiness to change behaviour before prescribing web based self-management tools.
References:
[1] Luoung et al (2012) Aging health. 8(4): 413–437. doi:10.2217/ahe.12.43.
[2] Wallace L (2006) Annals of Family Medicine 4:85–86.
[3] Adams J et al (2016) Rheumatology 55 (S1):i8-i9.
Acknowledgements: Prof D. Hunter, A. Cahill and C. Dickson from Arthritis Australia.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1529

SAT0763-HPR FUNCTIONAL OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS ON THE BACKGROUND CORRECTION OF PROGESTERONE INSUFFICIENCY

M. Salokhiddinov[1], H. Ahmedov[2]. *[1]Tashkent Medical Academy; [2]General practicioner, Tashkent Medical Academy, Tashkent, Uzbekistan*

Background: It is known that one of the main demands of the health system is to improve preventive measures. In particular, issues of optimizing secondary prevention are very important, as it gives an opportunity to reduce the progression of the disease and complications, as well as improve the quality of life of patients. Therefore, the study values the correction of progesterone deficiency on the background of preventive and rehabilitation interventions in a general medical practice in patients with RA is of practical interest.
Objectives: Studying the role of progesterone deficiency correction efficiency to optimize secondary prevention in patients with RA in a general medical practice.
Methods: Study involved 180 RA patients aged 35,6±3,9 years. The study group (group 1) consisted of 80 patients with RA, the second 50 (group 2) and third and 50 (group 3). 1 group was carried preventive and curative interventions, based on an integrated approach with the inclusion of preventive and rehabilitation interventions on the background correction of progesterone deficiency (Duphaston) in a general medical practice. Group 2 is the same, but without the correction of progesterone deficiency, and the third group only took pathogenetic treatment. Group 3 as opposed to the 1 and 2 had displays of progesterone deficiency. For an objective assessment of the effectiveness of using EULAR recommendations, assessing the improvement in %, according to the ACR, and to assess the functional status - health status index questionnaire Stanford Health Assessment Questionnaire (HAQ)
Results: The impact of interventions carried out by us on the functional outcome showed some differences between groups. Thus, according to ACR 50 criteria dynamics between groups were significant difference at 24 months, since improvement was noted in 52% of group 1 and 32% in group 2 (p=0.032).By the end of 3 months of intervention minimal effect on performance within the HAQ $0,22 \leq \Delta HAQ \leq 0,36$ was observed in 80% of group 1, 78% in 2nd group and 76% in group 3 ($p > 0.05$), while not a single case was fixed not satisfactory or pronounced effect. By the end of 12 months, the dynamics of functional status was noticeable and patients in group 1 have prevailed a satisfactory effect within $0,36 \leq \Delta HAQ < 0.80$ - 48.75% (p=0.043 and p=0.048, respectively), so a marked effect within $\Delta HAQ \geq 0,80$ functional status - 15% (p=0.001; p=0.011, respectively). This trend continued and by the end of 24 and 36 months, as the group 1 compared with group 2 is almost 8 times (p=0.001) and group 3 2 times (p. =0.045) greater $\Delta HAQ \geq 0,80$ a marked effect.
Conclusions: The preventive and therapeutic interventions on the background correction of progesterone deficiency in RA patients in a general practice reliably delivers stable ACR 50 response (64%) and significantly improves the functionality of the joints in RA.
References:
[1] Akunts K.B. Menopause. M., Triada-H, 2004.
[2] Nasonov E.L. Rheumatology. Clinical recommendations. Moscow: GEOTAR-Media; 2010.
[1] Smolen J.S. Aletaha D, Bijlsma J.W, et.al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis. 2010.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1067

SAT0764-HPR RETROSPECTIVE STUDY ABOUT ASSOCIATION OF MENTAL AND SLEEP DISORDERS AMONG ADULTS WITH PAINFUL MUSCULOSKELETAL CONDITIONS

S. Abdul Latif[1], A. Abdel Zaher[2], K. Al Hassanein[3], M. Zaghloul[1], M.H. Salama[4], E. Barakat[1], E. Mohamed[3], A. Shaky[3]. *[1]Rheumatology, Saudi German hospital, Jeddah; [2]Rheumatology, Saudi German hospital, Medinah; [3]Rheumatology, Saudi German hospital, Riyadh, Saudi Arabia; [4]Rheumatology, Thumby Hospital, Dubai, United Arab Emirates*

Background: Chronic pain is a common condition that affects one-third of the population, accounting for a large number of medical consultations and a significant proportion of health care costs.
Evidence suggests that anxiety and depression are associated with increased pain sensitivity and pain-related disability, co-morbid states that are more disabling than either condition alone.
Likewise, sleep disorders have also been linked with chronic pain, and people who experience pain-related sleep disturbances are significantly more disabled than those who do not.
Objectives: The objective of this study was to determine the prevalence of anxiety, depression, and sleep disorders, painful musculoskeletal conditions in a sample of adults with disabilities.
Methods: This cross-sectional study analyzed data of 1692 adults aged 18 or older who have disabilities over 10 years (2005 to 2014). We examined the following chronic conditions, in which pain is a key symptom and forms part of the diagnosis, and organized them into 3 groups. Group 1 consisted of (rheumatic diseases), arthritis, osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis; group 2 consisted of muscular dystrophy; and group 3 consisted of neck or back pain;
The prevalence (95% confidence interval) of painful musculoskeletal conditions was determined according to the diagnosis. Factors associated with these painful conditions were analyzed separately for men and women by using a logistic regression model.
Results: The prevalence of painful musculoskeletal conditions was 66.9% (95% CI, 66%–67.5%). Factors associated with these conditions in both men and women included older age, a sleep disorder, and concomitant chronic anxiety and/or depression was 23.5% (95% CI, 22.5%–24%), all of which were higher in women than in men. Of the 1692 adults with disability included in the study, 65% were women. The average age was 50.5 (standard deviation, 12.5 y), and 65% of participants were 50.5 or older. In addition, 48% of participants were married. Of the participants, 16% had been diagnosed with chronic anxiety and 22% with chronic depression; and 32% with sleep disorder (sleeping 6 hours or less per day. Prevalence of Painful Conditions in Adults with Disabilities, by Group of Conditions and by Sex, Differences between men and women were significant at $P < .001$ (for all groups of conditions, except muscular dystrophy.
Conclusions: The prevalence of painful musculoskeletal conditions associated with depression, anxiety, and/or a sleep disorder, is high in people with disability, especially in women. To design plan for rehabilitation and improving the quality of life of adults with disability and painful conditions; treatments for depression, anxiety and/or sleep disorders should be considered in addition to conventional treatments.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3353

SAT0765-HPR CRITERION AND CONCURRENT VALIDITY OF THE AMERICAN-ENGLISH VERSION OF THE FLARE QUESTIONNAIRE TO DETECT AND MEASURE FLARES IN RHEUMATOID ARTHRITIS

N. Barroso[1], T.G. Woodworth[1], F. Guillemin[2], D.E. Furst[1], J. Brook[1], S. Kafaja[1], N. Borazan[1], D.A. Elashoff[1], B.J. Fautrel[3], V.K. Ranganath[1]. *[1]Medicine, UCLA, Los Angeles, United States; [2]Université de Lorraine, Paris Descartes University, APEMAC, EA 4360; [3]Pitié Salpêtrière Hospital, Paris, France*

Background: Despite advances in rheumatoid arthritis (RA) therapeutic agents, difficulty in managing RA flares persists, and remission or the *persistent* absence of inflammation remains challenging to achieve. The French FLARE (F-FLARE) was developed to facilitate and standardize detection and measurement of RA flares between clinic visits.[1,2] We have previously reported the cognitive debrief for the published British English version, which determined that revision of wording and presentation of items was required. Here we report validation of the American English version of FLARE (Am-E FLARE-RA).[3]
Objectives: To assess whether the Am-E FLARE questionnaire performs comparably to the French version of FLARE in detecting RA flare in an American English-speaking clinic population.

Methods: We enrolled patients attending UCLA rheumatology clinics. After informed consent, patients completed a questionnaire to collect demographics, Am-E FLARE, RAPID3, patient global visual analog scale (VAS), and self-reported flare at time of visit or between visits (yes/no). Questionnaires were provided to patients without specific instruction. From the electronic medical records, we extracted MD global VAS, MD-reported flare, seropositivity, disease duration, swollen/tender joint counts (SJC/TJC), and calculated the clinical disease activity index (CDAI). Analyses included Wilcoxon rank sum tests and Spearman correlations to assess criterion and concurrent construct validity.

Results: Eighty-five RA patients diagnosed by the1987 American College of Rheumatology (ACR) criteria enrolled in our study. For the study population as a whole, mean age was about 50 years and most were female. Mean disease duration was about 10 years and about 65% were seropositive. (see Table). Am-E FLARE scores were significantly higher in patients' self-reporting flare compared to patients who reported no flare (p=0.005), and also for patients with MD-reported flare compared to those without flare (p=0.008) (see Table). Interestingly, there were no significant differences in SJC (p=0.82) and physician global (p=0.19) between patients who self-reported flare versus those who reported no flare. In addition, the Am-E FLARE scores correlated moderately with both CDAI (corr=0.46) and RAPID3 (corr=0.57).

Table 1. Patient and MD Assessment of Flare

	Patient-reported FLARE			MD-reported FLARE		
	No Flare Mean (SD)/ N (%) n=51	Flare Mean (SD)/ N (%) n=34	*p-value	No Flare Mean (SD)/ N (%) n=67	Flare Mean (SD)/ N (%) n=18	*p-value
Age	52.37(15.62)	47.15(16.29)	0.15	51.73(16.09)	44.89(14.87)	0.08
Female	46(90.20)	31(91.18)	0.88	60(89.55)	17(94.44)	0.53
Race#						
Asian	11(21.57)	5(14.71)		16(23.88)	0(0.00)	
Black	5(9.80)	5(14.71)		8(11.94)	2(11.11)	
Pac Island	1(1.96)	1(2.94)	0.79	1(1.49)	1(5.56)	0.22
Caucasian	32(62.75)	23(67.65)		40(59.70)	15(83.33)	
Other	2(3.92)	0(0.00)		2(2.98)	0(0.00)	
Seropositivity#	32(62.75)	23(67.65)	0.64	42(62.69)	13(72.22)	0.45
Disease duration	9.63(9.07)	11.88(10.98)	0.41	11.06(10.21)	8.56(8.50)	0.32
RAPID3	9.24(6.23)	14.64(5.79)	0.0001	9.67(6.03)	17.63(4.38)	<.0001
CDAI	17.49(13.48)	22.88(13.03)	0.03	16.74(11.54)	30.11(15.19)	0.0003
TJC	6.29(6.67)	8.91(7.24)	0.04	6.25(6.36)	11.39(7.85)	0.005
SJC	4.67(4.94)	4.56(3.96)	0.82	3.96(3.88)	7.11(5.94)	0.005
Patient Global	3.33(2.39)	5.15(2.33)	0.001	3.45(2.32)	6.22(2.02)	<.0001
Physician Global	3.20(2.08)	3.85(2.24)	0.19	2.94(1.92)	5.39(1.91)	<.0001
FLARE Total	4.80(3.32)	6.88(2.01)	0.005	5.18(3.07)	7.31(2.27)	0.008
FLARE Physical	5.11(3.47)	7.28(2.02)	0.008	5.49(3.21)	7.81(2.10)	0.005
FLARE Emotional	4.48(3.47)	6.49(2.61)	0.007	4.88(3.33)	6.81(2.71)	0.03

CDAI = Clinical Disease Activity Index; RAPID3 = Routine Assessment of Patient Index Data; TJC = Tender Joint Count; SJC = Swollen Joint Count; Seropositivity = either CCP+ or RF+; *Wilcoxon rank sum test; #Race and Seropositivity are presented as frequencies and present and p-values are calculated using Chi-square test

Conclusions: The Am-E FLARE is feasible for use in clinic, and shows good criterion validity, with scores significantly higher in patients who self-report flare. In addition, Am-E FLARE shows good discriminant validity, distinguishing patients who are flaring according to MD or patient self-report from those who are not. Finally, Am-E FLARE demonstrates construct validity comparable to that of the original French version of FLARE.

References:

[1] Jean-Marie Berthelot, Michel De Bandt, Jacques Morel, et al. A tool to identify recent or present rheumatoid arthritis flare from both patient and physician perspectives: The "FLARE" instrument. Ann Rheum Dis 2012;71:1110–1116.
[2] Fautrel B, Morel J, Berthelot JM, et al. Validation of FLARE-RA, a self-administered tool to detect recent or current rheumatoid arthritis flare. Arthritis Rheumatol. 2016 Sep. 16.
[3] EULAR14-SCIE-4820.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3329

SAT0766-HPR THE FACTORS AFFECTING FUNCTIONAL ABILITIES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

E. Tarakci[1], N. Arman[1], O. Kasapcopur[2]. [1]*Division of Physiotherapy and Rehabilitation, Faculty of Health Science;* [2]*Department of Pediatric Rheumatology, Medical Faculty of Cerrahpasa, Istanbul University, Istanbil, Turkey*

Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in pediatric population and is characterized by a heterogeneous group of diseases that include chronic arthritis of unknown origin, which begins before 16 years of age (1). Patients with JIA commonly experience acute and chronic pain, decreased mobility, and joint stiffness leading to restrictions on functional ability and isolation from their peers (2).

Objectives: The aim of this study was to assess relationship between clinical features and functional ability and determine the factors affecting functional abilities in patients with JIA.

Methods: 172 (aged 5–18 years) with JIA were included in this study. Socio-demographic data, clinical features (duration of disease, subtype of JIA, and number of involved joint) and functional ability were assessed with Childhood Health Assessment Questionnaire (CHAQ). Pain and overall well-being were measured using a Visual Analog Scale (VAS). Relations between the factors affecting functional abilities in JIA were assessed by multiple linear regression analysis

Results: The mean age was 10.71±3.47 and the mean disease duration was 5.41±3.53 years. Score of CHAQ was affected by number of involved joint (β=0.18, $p<0.05$), subtypes of JIA (β=- 2.75, $p<0.01$) and pain (β=0.15, $p<0.05$), but were not affected by age (β=-0.03, $p>0.05$), gender (β=-0.03, $p>0.05$) and disease duration (β=0.03, $p>0.05$). In addition to, significant difference was found between all CHAQ subscores (except of "walking") of polyarticular and oligoarticular JIA ($p<0.001$). Functional abilities of patients with polyarticular JIA were lower than functional abilities of patients with oligoarticular JIA.

Conclusions: In the literature, it reported that functional activities were adversely affected in patients with JIA, when they compared with healthy subjects. In our study, we found that functional abilities were affected by subtypes of JIA, number of involved joint, and pain. But, these were not affected by age, gender, and disease duration in JIA. We suggest that subtypes of JIA, number of involved joint, and pain should be considered, when patients with JIA are directed to physical therapy program to encourage functional abilities.

References:

[1] Prakken B, Albani S, Martini A (2011) Juvenile idiopathic arthritis. Lancet 377:2138–2149.
[2] Tarakci, E., Yeldan, I., Mutlu, E. K., Baydogan, S. N., & Kasapcopur, O. (2011). The relationship between physical activity level, anxiety, depression, and functional ability in children and adolescents with juvenile idiopathic arthritis. Clinical rheumatology, 30(11), 1415.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4923

SAT0767-HPR PHYSICAL ACTIVITY MAINTENANCE AND DIGITAL HEALTH INTERVENTIONS IN PEOPLE WITH RHEUMATOID ARTHRITIS: PATIENT AND HEALTHCARE PROFESSIONALS' PERSPECTIVES

R. Simmons[1], H. Lempp[2], J. Galloway[2], L. Bearne[1]. [1]*Division of Health and Social Care Research, Kings College London University;* [2]*The Academic Department of Rheumatology, Kings College London, London, United Kingdom*

Background: Physical Activity (PA) improves health and function in people with Rheumatoid Arthritis (RA) but people with RA commonly fail to meet recommended PA levels. Digital Health Interventions (DHIs) are delivered through digital media to facilitate behaviour change, such as maintaining PA. To date, little is known about the perceptions of people who have RA or their healthcare professionals (HCPs) about the factors that influence PA and the desirability and perceived suitability of using DHI to support PA maintenance.

Objectives: To explore RA patients' and HCPs' perceptions of the factors that influence PA maintenance as well as their views on the use of DHIs to support sustained PA.

Methods: Adults aged >18 years with established RA were recruited from two inner-city NHS hospitals. Semi-structured interviews, using a topic guide developed a priori, were conducted by one researcher either face-to-face or by telephone until data saturation of themes was reached. HCPs working at one NHS inner-city hospital, who self-reported >3 months experience managing RA patients attended one semi-structured focus group, facilitated by two researchers and informed by a topic guide.

The interviews and focus group were audio-recorded, transcribed verbatim and the data analysed thematically. Themes were corroborated by a sample of participants and an independent researcher.

Results: 11 patients were recruited between January-May 2016 (five females; mean age 58 years [standard deviation 17 years]). Five themes were identified from the interviews: 1) Balancing the benefits of activity with the costs; 2) Gaining knowledge about safe and effective PA; 3) Disease control; 4) The environment matters; and 5) Interaction of person, disease and DHI.

Patient participants were largely aware of the benefits of PA but wanted more information about safe PA. Ongoing PA was informed by participants balancing the benefits of PA with concerns about aggravating symptoms. Good symptoms control facilitated PA but severe and unpredictable symptoms and unsuitability of exercise facilities were perceived as barriers to PA maintenance. Patient participants mostly stated that DHIs were a desirable and acceptable adjunct to supporting PA maintenance.

The focus group was conducted with six HCPs (two physiotherapists, two rheumatologists, one podiatrist and one medical student). Two themes were identified 1) Inactivity demands a proactive response by HCPs and 2) DHIs have potential to support PA, but "there is no panacea".

HCP participants universally agreed that PA was beneficial and that it was important to support ongoing PA through education and multimodal interventions, including DHIs.

Conclusions: Disease control, knowledge and environmental factors influence PA maintenance in people with RA, who balance the perceived benefits with the potential costs of PA. HCPs recognise the need to proactively support PA maintenance. DHIs offer a potentially useful and acceptable tool to support PA maintenance.

Disclosure of Interest: R. Simmons Grant/research support from: NIHR MRes fellowship, H. Lempp: None declared, J. Galloway: None declared, L. Bearne: None declared

DOI: 10.1136/annrheumdis-2017-eular.1695

SAT0768-HPR SUBJECTIVE COGNITIVE DYSFUNCTION AND COMPUTERIZED NEUROPSYCHOLOGICAL PERFORMANCE IN KOREAN ADULTS WITH RHEUMATOID ARTHRITIS

S.Y. Shin[1], J.H. Lee[2], B.Y. Yoon[2]. *[1]Department of Nursing, College of Medicine, Inje University; [2]Division of Rheumatology, College of Medicine, Inje University, Ilsan Paik Hospital, Busan, Korea, Republic Of*

Background: There is an increased appreciation of the burden of cognitive impairment in persons with rheumatoid arthritis (RA). Research shows a gap between subjective and objective measures of cognitive impairment in persons with chronic diseases.
Objectives: This study explored the relationship between subjective cognitive dysfunction and computerized neuropsychological performance in Korean older adults with RA.
Methods: Individuals with RA were recruited by their rheumatologists during follow-up visits at one university hospital in Korea. After getting signed consents, a trained research nurse assessed participants with a range of physical, psychosocial, and biological metrics. Subjective cognitive dysfunction was assessed using the Perceived Deficits Questionnaire (PDQ; range 0–20, higher score=greater impairment). Objective cognitive impairment was assessed using a set of 6 computerized neurocognitive tests yielding 18 indices covering a range of cognitive domains. Subjects were classified as "impaired" if they performed 1 *SD* below age-based population norms on each test [1]. A total cognitive impairment score was calculated by summing the transformed scores (range: 0–18, higher score=greater impairment). Multiple regression analysis controlling for education, disease severity, and depression was conducted to identify the relationship between objective and subjective cognitive measures.
Results: Fifty four subjects with a mean (±*SD*) age of 63.6 (±10.5) years were included in the final analyses. 85% were female and 87% were married. Mean educational level was 10.2 (±4.9) years and mean disease duration was 8.9 (±8.5) years. 25.9% had depression and 55.6% had sleep problem. Mean PDQ score was 11.8 (±4.5, range 5–25) and mean total cognitive impairment score was 11.0 (±4.1, range=2–18). 92% were classified as cognitively impaired on five or more test indices. There was no significant correlation between PDQ score and total cognitive function score (r=.260, p=.068). However, psychological factors including depression (r=.621, $p<.001$) and sleep problem (r=.577, $p<.001$) were significantly correlated with PDQ score. In the multivariate analysis, there was no significant relationship between PDQ score and total cognitive impairment score. However, functional limitations and depression (=0.317, p=0.048; =0.334, p=0.019) were significantly associated with the PDQ score.
Conclusions: There was no significant relationship between subjective cognitive dysfunction and computerized neuropsychological performance in this cohort. Functional limitations and depression were significantly associated with perceived cognitive dysfunction. Findings emphasize the gap between subjective and objective measures of cognitive impairment and the importance of considering psychological factors in the context of cognitive complaints in clinical settings.
References:
[1] Kozora, E., Ellison, M. C., & West, S. (2004). Reliability and validity of the proposed American College of Rheumatology neuropsychological battery for systemic lupus erythematosus. Arthritis Care & Research, 51(5), 810–818.
Acknowledgements: This research was supported by the 2015 Inje University research grant (No.20151092).
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1299

SAT0769-HPR DO PATIENTS RECALL PHYSICAL ACTIVITY ADVICE? INTERVIEWS WITH UK INFLAMMATORY ARTHRITIS PATIENTS TO EXPLORE EXPERIENCES OF PHYSICAL ACTIVITY COMMUNICATION

V. Salmon[1], N. Walsh[2], E. Dures[2], A. Haase[3], M. Urban[4], F. Cramp[2]. *[1]University of Exeter, Exeter; [2]University of the West of England; [3]University of Bristol; [4]University Hospitals Bristol NHS Foundation Trust, Bristol, United Kingdom*

Background: Guidelines for managing inflammatory arthritis (IA) indicate that patients should be encouraged to be physically active. Patient perceptions of physical activity (PA) communication during routine rheumatology consultations, or whether they recall or understand PA information, are not known.
Objectives: 1. To explore patients' short-term recollection and interpretation of communication relating to PA during consultation with a rheumatology doctor or nurse
2. To explore patients' needs for effective PA communication
Methods: Adults with IA took part in semi-structured telephone interviews 2 to 3 days after their consultation with a rheumatology doctor or nurse. Transcripts were analysed using thematic analysis.
Results: 26 patients took part (18 female; age 35–83 years; disease duration 0.25–40 years). Preliminary analysis suggests five themes:
Patients recall little communication about PA: Few patients recalled PA communication during their appointment, although some discussed general lifestyle and some recalled discussions about PA or exercise in previous consultations.
Appointments focus on medical management: Patients mainly recalled discussing medical management of IA. Some were asked about general health and support needs, but assumed health professionals were interested in disease status and medication rather than lifestyle and wellbeing.
Patients are uncertain as to what constitutes PA: Some patients seemed confused by what constituted discussion about PA. Different interpretations were reported, with many participants referring to condition specific exercises rather than lifestyle PA. Few patients described PA as general movement or everyday activity.
Patients would like to discuss PA: Few patients initiated conversation about PA, but many would welcome PA communication from any health professional with appropriate knowledge. Several patients felt most comfortable discussing PA with a member of their rheumatology team rather than a non-specialist. A small number felt the rheumatologist's role related to medical management rather than lifestyle advice. Preferences for communication style included a direct, honest approach using lay language. It was felt that health professionals could do more to ask about and encourage PA, reassure about PA safety, and offer individualized support to enable appropriate PA.
Perceived barriers to undertaking PA must be considered: Some patients perceived barriers to PA, such as lack of knowledge and skills for PA, lack of time, work commitments and IA flares. It was felt important to acknowledge that it can be difficult to apply lifestyle changes in practice.
Conclusions: IA patients recalled little discussion about PA in routine rheumatology consultations. Patients may interpret questions about general health and exercise as relating to their disease status and joint function rather than to lifestyle or PA. Health professionals should ask direct questions about lifestyle PA and offer non-didactic, individualized advice and support. Further research is needed to understand PA communication from the perspective of rheumatology health professionals, including identification of opportunities and challenges for implementing effective communication.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6866

SAT0770-HPR IS THE DUAL – TASK TRAINING BENEFICIAL ON THE CLINICAL OUTCOMES OF ELDERLY?

Y. Aydoğdu[1], O. Aydoğdu[2], S.H. İnal[3]. *[1]Department of Physiotherapy and Rehabilitation, Haydarpaşa Numune Hospital; [2]Department of Physiotherapy and Rehabilitation, Health Sciences Faculty, Marmara University; [3]Department of Physiotherapy and Rehabilitation, Health Sciences Faculty, Bahcesehir University, Istanbul, Turkey*

Background: The difficulties of elderly in performing two different tasks have been well documented (1). It has been reported that aging is associated with a decline in attention abilities and dual-task performances. Improving the ability to perform two different tasks simultaneously could therefore have significant impacts in the prevention of adverse outcomes associated with aging (2).
Objectives: Regarding specific dual-task training, recent studies have demonstrated its efficacy in various populations such as the elderly and individuals with neurological diseases, with the most notable improvements in gait. However, there is no evidence in the literature on the effects of this training on balance and clinical outcomes evaluated independently among elderly. Thus, considering the positive results of specific dual-task training obtained in other populations, we conducted a randomized trial to study the efficacy of an eight – week dual-task training program adjunct to conventional physiotherapy compared to a conventional physiotherapy program on balance, mobility, functional independence, fear of falling, functional capacity in elder individuals.
We hypothesized that, dual-task training is more effective at improving balance and clinical outcomes than conventional physiotherapy in elder individuals.
Methods: Fifty-five elderly were participated in our study. Balance, mobility, functional independence, fear of falling was measured with Berg Balance Scale, Rivermead Mobility Index, Functional Independence Measurement, and Fall Efficacy Scale-International, respectively. Functional capacity was assessed with Timed Up&Go, Chair Sit&Stand. Cases were divided into two different groups. Conventional Physiotherapy was applied in control group, and besides the same protocol, dual–task training was applied 5 days for 8 weeks in the intervention group. The dual–task training consisting of the cognitive activities included digit span, spelling words, stroop test, image description, counting, description of daily activities and routines was applied during the gait exercises. All of the assessments procedures were performed again after the treatment.
Results: There were statistically significant improvements in measures of balance, mobility, functional independence, fear of falling, and functional capacity between pre- and post – treatment in both groups ($p<0.05$). A significant difference was found in balance and mobility in favour of the intervention group (p=0.028).
Conclusions: Based on our findings, we found that dual–task training applied as an adjunct to conventional physiotherapy was superior to conventional physiotherapy on balance and mobility parameters. From this point of view, dual-task training should be considered as part of the rehabilitation process of elderly, although until now no guidelines have been defined for this type of intervention.
References:
[1] Bherer L, Kramer AF, Peterson MS, Colcombe S, Erickson K, Becic E. Transfer

effects in task-set cost and dual-task cost after dual-task training in older and younger adults: further evidence for cognitive plasticity in attentional control in late adulthood. Exp Aging Res. 2008 Jul-Sep;34(3):188–219.
[2] Lussier M, Gagnon C, Bherer L. An investigation of response and stimulus modality transfer effects after dual-task training in younger and older. Front Hum Neurosci. 2012 May 18;6:129.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6809

Abstracts Accepted for Publication

HPR measuring health (development and measurement properties of PROs, tests, devices) —

AB1195-HPR PSORIATIC ARTHRITIS PATIENTS INITIATED ON APREMILAST: A RETROSPECTIVE ANALYSIS OF PATIENT OUTCOMES FROM A WEST LONDON TEACHING HOSPITAL

C. Astbury. *Pharmacy, Imperial College NHS Healthcare Trust, London, United Kingdom*

Background: Apremilast is an oral phosphodiesterase 4 (PDE-4) inhibitor that reduces disease activity in psoriatic arthritis (PsA) by modulating the expression of inflammatroy cytokines. In December 2015, apremilast received a negative National Institute of Clinical Excellence (NICE) appraisal for its use in PsA, owing to a lack of robust evidence on its long-term impact on patient outcomes and efficacy in improving radiographic progression (TA372).
The role of the drug in the PsA treatment pathway remains uncertain. We present a retrospective analysis of the use of apremilast in 14 patients with PsA within our hospital trust.
Methods: Pharmcay funding applications and medication dispensing records were used to identify suitable patients. All patients commenced on apremilast at Imperial College NHS Healthcare Trust (ICHT) for PsA were included in the analysis.
Results: A total of 14 patients were initiated on apremilast between June 2015 and September 2016 (table1). Of these patients 9 (64%) achieved an adequate response to treatment, defined by NICE as an improvement in at least 2 of the 4 PsA response criteria (PsARC) scores, with no worsening in any of the four criteria.
Of the 5 patients not achieving response, 3 patients discontinued treatment prior to assessment due to intolerable side effects, whilst 2 further patients didnt acheive the appropriate therapeutic response (primary failure).
From the 9 patients that achieved an adequate response only 5 are currently taking therapy, with intolerable side effects causing discontinuation in a further 4. This gives an overall discontinuation rate of 65% (9 out of 14). In the 5 patients remaining on therapy, one patient needed to reduce the drug dose due to side effects, whilst one continued treatment despite tolerable side effects. Of our 14 patients only 3 remained on treatment in the absence of any side effects.
The most common side effects causing discontinuation were nausea and vomiting (3patients, 21%) and mood changes (2 patients, 14%).

Table 1. Patient demographics for all PsA patients initiated on apremilast (n=14). Median time to stopping treatment 4 months.

	Duration (years)	Erosive	Age	Sex	Psoriasis	Previous treatment		Concomitant csDMARD	Duration of treatment (months)	Side effects
						2x csDMARD	bDMARDs			
1	4	N	34	M	Y	Y	Y	Nil	14	Continues N+V but tolerable
2	13	Y	55	F	Y	Y	Y	SSC / HCQ	7	Stopped- primary failure
3	6	N	37	M	N	Y	Y	LEF	4	Stopped- N+V + hangover feeling
4	3	N	42	F	Y	Y	Y	SSZ	2	Responded but Stopped- N+V
5	12	Y	49	F	Y	Y	Y	HCQ / Pred	9	Responded but Stopped- Mood changes
6	22	Y	59	F	Y	Y	Y	MTX / SSC	6	Responded but Stopped- mood changes
7	9	Y	58	F	Y	Y	N	MTX	16	Continues
8	8	Y	62	F	Y	Y	Y	MTX	14	Continues
9	7	N	62	F	Y	Y	Y	SSZ	14	Continues - dose reduced
10	11	N	75	F	Y	Y	Y	MTX	1	Stopped- shingles
11	10	N	56	F	Y	Y	Y	MTX/SSZ	11	Continues
12	10	Y	77	F	N	Y	Y	LEF / Pred	1	Stopped- nausea
13	26	Y	44	F	N	Y	N	MTX	6	Stopped- primary failure
14	17	N	41	M	Y	Y	N	Nil	2	Responded but Stopped- Dizziness

Conclusions: Apremilast was poorly tolerated in our population with only 3 patients continuing the drug with response and without ongoing side effects. Discontinuation rates within ICHT were found to be much higher than those in the original trial data (65% versus 15%). Patients who have continued the medication and tolerated side effects, however have shown a good response to treatment.
References:
[1] Drugs and therapeutics bulletin. Apremilast for psoriasis and psoriatic arthritis. British Medical Journal , 2015: 105–108.
[2] Kavanaugh, Arthur, and Philip et al Mease. Treatment of psoriatic arthritis in a phase 3 randomised, placebo-controlled trial with apremilast, an oral phosphodiesterase 4 inhibitor. Annal of Rheumatic disease, no. 73 (2014): 1020–1026.
[3] National Institute for Health and Care Excellence. Apremilast for treating active psoriatic arthritis (TA372). 2015. https://www.nice.org.uk/guidance/ta372/resources/apremilast-for-treating-active-psoriatic-arthritis-82602785881285.

Acknowledgements: Dr Benjamin Ellis, consultant Rheumatologist, Imperial college NHS Healthcare trust. Dr Matthew Pickering, consultant Rheumatologist, Imperial college NHS healthcare trust
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3220

AB1196-HPR A COMPARISON OF PATIENT PREFERENCE AND USABILITY BETWEEN TWO ELECTRONIC GONIOMETRIC GLOVES IN THE MEASUREMENT OF JOINT MOVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

D. Small[1], P.V. Gardiner[1], J. Connolly[2], J. Condell[2], K. Curran[2], A. O'Neill[1], R. Friel[1]. *[1]Rheumatology, WHSCT; [2]School of Computing, Ulster University, Londonderry, United Kingdom*

Background: Patients with Rheumatoid arthritis suffer from pain, stiffness and reduced mobility of their finger joints. Instrumented electronic goniometric gloves have been developed which can enable dynamic measurements to be made with accuracy and efficiency [1]. This technology could be employed in assessing patients with rheumatoid arthritis and could also be used as an aid to rehabilitation. However, pain and swelling in the joints might limit the applicability of these measurement devices as to date they have not been tested in this patient group.
Objectives: The purpose of this pilot study was to establish the usability of two different electronic gloves in patients with mild to moderate Rheumatoid arthritis. We wished to establish if patients experienced difficulty donning or doffing either glove or if carrying out a series of measurements with the gloves on caused a change in pain and stiffness. We also investigated differences in the usability and preference between the two Datagloves.
Methods: We compared a commercially available electronic glove (the 5DT dataglove 14 Ultra) with a bespoke IMU based electronic glove produced to our specifications by Tyndall National Institute, University College Cork (Figure). We developed a programming interface for both devices to facilitate calibration and detailed evaluation of joint movement. Nine patients with mild to moderate rheumatoid arthritis who were experiencing significant but not severe pain and early morning stiffness in their hands were recruited. After calibration, the patients worked through a protocol of finger flexion and extension movements, which were repeated for each glove and again to test repeatability. The patients completed questionnaires before and after using the gloves on their pain and stiffness levels and at the end of the session on glove donning and doffing usability and preference between the two gloves.
Results: All nine patients were able to don and doff the IMU glove without any difficulty compared to 4/9 for the 5DT glove. Seven of 9 patients expressed a preference for the IMU glove. In 2/9 patients, joint stiffness increased after using the gloves and 4/9 patients reported an increase in pain. Seven out of nine patients were not able to complete the fourth set of movement tests because of discomfort.

Table of Change in Stiffness and Pain after glove use and subject glove preference

Subject	Hand stiffness		Change in in stiffness (VAS)	Hand pain		Change in in pain (VAS)	Preferred Glove IMU or 5DT
	Pre Study (VAS)	Post study (VAS)		Pre study (VAS)	Post study (VAS)		
S1	15	22	NC	27	33	NC	IMU
S2	59	40	–	51	73	+++	IMU
S3	65	61	NC	71	79	NC	IMU
S4	28	28	NC	11	15	NC	5DT
S5	0	44	+++	0	49	+++	IMU
S6	26	77	+++	15	82	+++	IMU
S7	36	34	NC	16	33	+	IMU
S8	0	0	NC	0	0	NC	IMU
S9	25	15	NC	9	19	NC	5DT

+ >10mm increase in VAS; – >10mm decrease in VAS, NC <10mm change in VAS.



Conclusions: Electrogoniometric gloves are usable in patients with rheumatoid

arthritis, but patients cannot tolerate longer protocols without an increase in discomfort.

References:

[1] Dipietro L, et al. (2003). Evaluation of an instrumented glove for hand-movement acquisition. Journal of Rehabilitation Research and Development, 40(2), 179–89.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5020

AB1197-HPR VALIDITY AND RELIABILITY OF A SMARTPHONE GONIOMETER APPLICATION FOR MEASURING HIP RANGE OF MOTION IN PATIENTS WITH HIP OSTEOARTHRITIS: A PILOT STUDY

D.C. Sarac[1], G. Yalcinkaya[2], B. Unver[2]. *[1]Division of Physiotherapy and Rehabilitation, Katip Celebi University; [2]School of Physical Therapy and Rehabilitation, Dokuz Eylül University, Izmir, Turkey*

Background: Osteoarthritis (OA) of the hip affects the entire joint structure and function and leads joint capsular changes which result limitation in range of motion (ROM). Therefore, measuring ROM is an essential part of the hip assessment. Various measurement tools are available for determining the ROM such as universal goniometers (UG), digital inclinometers, motion analysis systems. Recently, smartphones equipped with suitable applications are able to measure ROM.

Objectives: The aim of this study was to determine the inter-rater and intra-rater reliability of a smartphone application "PT Goniometer© 2015 Mark Busman" (PTG) and investigate the agreement within PTG versus UG for active hip ROMs in patients with hip OA.

Methods: This study included eight people who were diagnosed with hip OA. Two physiotherapists performed the ROM measurements on affected hips by using PTG and UG. UG was employed as the reference standard. Hip ROM tests were performed in the following order; flexion, abduction, internal and external rotation. Intraclass correlation coefficient (ICC) models were used to determine the intra-rater and inter-rater reliability. The Spearman correlation coefficients were used to establish validity of PTG.

Results: The PTG smartphone application demonstrated good to excellent inter-rater and intra-rater reliability (ICCs >0.75) for all measured hip movements in patients with hip OA. ICC scores, minimum detectable change (MDC_{95}) and standart error of measurement (SEM) values were indicated in Table 1 and Table 2. Additionally,UG and PTG application methods demonstrated positive correlations for all hip movements ($p<0.05$).

Table 1. Inter-rater Reliability of the PT Goniometer Application

Movement	PT 1, PTG (Mean ± SD)	PT 2, PTG (Mean ± SD)	ICC (%95 CI)	SEM	MDC_{95}
Flexion	66.18°±28.87°	63.66°±30.74°	0.99 (0.94–1.00)	0.91	2.52
Abduction	27.98°±12.93°	29.58°±13.03°	0.99 (0.90–0.99)	0.4	1.1
IR	10.86°±10.66°	11°±10.67°	0.99 (0.99–1.00)	0.33	0.91
ER	20.12°±11.74°	21.06°±12.5°	0.99 (0.96–1.00)	0.33	0.91

PT1: Physiotherapist1, PTG: PT Goniometer application, PT2: Physiotherapist 2, ICC: Intraclass correlation coefficient, CI: Confidence Interval, SEM: Standard Error of Measurement, MDC_{95}: Minimum Detectable change at the %95 confidence level, SD: Standard deviation, IR: Internal rotation, ER: External rotation. Table 2. Intra-rater Reliability of PT Goniometer Application

Movement	PT 1, PTG (Mean ± SD)	PT1, RT PTG (Mean ± SD)	ICC (%95 CI)	SEM	MDC_{95}
Flexion	66.18°±28.87°	65.64°±28.58°	0.99 (0.97–0.99)	0.91	2.52
Abduction	27.98°±12.93°	28.58°±13.61°	0.99 (0.98–1.00)	0.4	1.1
IR	10.86°±10.66°	10.96°±10.73°	0.99 (0.99–1.00)	0.33	0.83
ER	20.12°±11.74°	20.46°±11.96°	0.99 (0.98–1.00)	0.37	1.02

PT 1: Physiotherapist 1, PTG: PT Goniometer Application, RT PTG: Retest PT goniometer application, ICC: Intraclass correlation coefficient, CI: Confidence Interval, SEM: Standard Error of Measurement, MDC_{95}: Minimum Detectable Change at the %95 confidence level, SD: Standard deviation, IR: Internal rotation, ER: External rotation.

Conclusions: High correlations obtained in this pilot study suggest that using a smartphone application might be a valid and a reliable method for measuring hip ROM in patients with hip OA and smartphone applications can be used in clinical settings. Studies with larger population are required for further investigation of smartphones' psychometric properties on measuring hip ROM.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5710

AB1198-HPR PRESENTATION OF A NEW SCALE ASSESSING THE BIOPSYCHOSOCIAL ASPECTS OF HEALING PROPERTIES IN RHEUMATIC PATIENTS

E. Ünal[1], P. Kısacık[1], G. Arin[1], E. Karabulut[2], D. Göksülük[2], N. Vardar Yağlı[1], D. Aydın Özcan[1], U. Berberoğlu[1], N.B. Karaca[1], A. Akdoğan[3], Ö. Karadağ[3], U. Kalyoncu[3], L. Kılıç[3], A. Erden[3], S. Apraş Bilgen[3], S. Kiraz[3], A.I. Ertenli[3], M. Çalgüneri[3]. *[1]Department of Physiotherapy and Rehabilitation, Hacettepe University Faculty of Health Science;[2]Department of Biostatistics; [3]Department of Internal Medicine, Rheumatology Subdivision, Hacettepe University, Ankara, Turkey*

Background: Exercise programs have been being provided in Hacettepe University for 12 years. The group exercises were transformed into a book named as "Bilişsel Egzersiz Terapi Yaklaşımı (BETY) (1)" in 2014 and were registered as a trademark by the Turkish Patent Institute in 2015. This approach includes cognitive processes in pain management, clinical pilates exercises and awareness of mood state via dance therapy (2).When rheumatic patients participating in BETY sessions, they are evaluated with appropriate scales for their diseases and it is stated that these scales do not express enough the healing properties they feel with BETY.

Objectives: The aim was to develop a new scale assessing the biopsychosocial aspects of healing properties in rheumatic patients.

Methods: After 12 years of treatment, cognitive beliefs about health perceptions were gathered from the patients who participates in the BETY group for at least 5 years, with the open-ended question "What kind of changes did you make in this group?". After elimination of similar sentences, 30 cognitive beliefs about different health perceptions were obtained. The newly developed scale was applied to 89 patients aged 18–69 years (42,94±12.85), who had different rheumatic diseases and were not included in the BETY group. Working questions were determined.

Results: The internal consistency was found to be 0.89. In this process, 5 items that didn't work and had the same meaning were removed from the scale. After this, "What kind of improvements did you make in Daily life by participating in the BETY group?" question was asked to the patients participated in BETY group to narrow the expressions and 5 new sentences are determined. The scale was sent to 24 rheumatologists and 2 physiatrists for expert opinion. 15 rheumatologists and 1 physiatrist were returned. When the survey items were examined on a question-based basis, the acceptance rate of all questions was 70.83%. According to this result, the scale was finalized. Structural validity of the created draft will be investigated in the subheadings of functional activity, pain, sexual life, fear of movement, mood.

Conclusions: As a result, an original scale which will assess the biopsychosocial aspects of healing properties in rheumatic patients is developed. Our future purpose is to investigate the validation of this scale in different rheumatic diseases.

References:

[1] E.Ünal (Ed.) Romatizmal Hastalıklarda Biyopsikososyal Model: Bilişsel Egzersiz Terapi Yaklaşımı (BETY), 2014, Pelikan Yayıncılık, Ankara. ISBN: 9786056474101.

[2] Kısacık,P. Ünal,E. Akman,Ü. Yapalı,G. Karabulut,E. Akdoğan,A. Investigatition the effects of a multidimensional exercise program on sypmtoms and antiinflammatory status in female patients with ankylosing spondylitis. Complementary Ther. Clin. Pract. 22(2016):38–43.

Acknowledgements: The authors declare that they have no conflict of interest.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6283

AB1199-HPR IMPROVING TRIAGE TO APPROPRIATE TREATMENT LEVEL BY USING A COMBINATION OF SCREENING TOOLS IN PATIENTS AT RISK OF DEVELOPING CHRONIC BACK PAIN

E. Haglund[1,2], C. Olsson[3], A. Bremander[1,2,4], S. Bergman[2,3,4]. *[1]School of Business, Engineering and Science, Halmstad Univeristy; [2]Spenshult Research and Development Center, Halmstad; [3]Primary Health Care Unit, Department of Public Health and Community Medicine, Institute of Medicine, The Sahlgrenska Academy, University of Gothenburg, Gothenburg; [4]Department of clinical Sciences, Lund, Section of rheumatology, Lund University, Lund, Sweden*

Background: The screening instrument STarT (Subgroups for Targeted Treatment) Back Screening Tool (SBST) identify patients at risk of developing chronic back pain in order to facilitate triage to appropriate treatment level. The SBST takes into account known risk factors such as activity limitations, kinesiophobia and psychological health. However, SBST does not consider pain distribution which is a known predictor of chronic widespread pain (CWP). According to evidenced clinical practice patients with CWP should be referred to multimodal rehabilitation (1).

Objectives: The purpose of the study was to compare screening by SBST with screening of multisite chronic widespread pain (MS-CWP) in a group of patients with back pain and to analyze to what extent the two screening methods identify the same patients at higher risk.

Methods: 73 individuals with a report of chronic back pain ($\geq$3 months during last year) age 40–70 years responded to both screening tools. The SBST stratify patients into low, medium or high risk groups. A pain mannequin was used to categorize patients into no chronic pain (NCP), chronic regional pain (CRP) or chronic widespread pain (CWP) and number of painful areas (0–18). A presence of a CWP in combination with $\geq$7 painful areas was stratified as MS-CWP. The outcome of the different screening tools was analyzed by cross tabulations. The Roland-Morris Disability Questionnaire (RMDQ, 0–24), health related quality of life (EQ5D, 0–1), Fear-Avoidance Beliefs Questionnaire about physical activity (FABQ-PA, 0–24) and work (FABQ-Work, 0–42), Hospital Anxiety (HAD-A, 0–21) and Depression scale (HAD-D, 0–21) were used to describe physical function, health related quality of life, kinesiophobia and mental health.

Results: The mean (SD) age was 59 (8) years, 63% were women. Self-reports of physical function (RMDQ) were 4.5 (4.8), health related quality of life (EQ5D) 0.71 (0.21), kinesiophobia (FABQ-PA and FABQ-Work) 8.3 (5.9) and 14.7 (11.1), and mental health (HAD-A and HAD-B) 8.8 (2.0) and 4.5 (1.7). Comparing the different screening methods, 5 patients (7%) were at high risk as captured by SBST while using the pain mannequin 38 (52%) patients had CWP and 22 (30%) had MS-CWP. No patients in the SBST high risk group had NCP, but 31 (50%) in the SBST low risk group reported CWP, and 16 (26%) reported MS-CWP. In the medium risk group 3 reported CWP, and 3 were also categorized as MS-CWP.

Table 1

Pain distribution groups	StarT Back Screening Tool		
	Low risk	Medium risk	High risk
No chronic pain (NCP)	7	1	0
Chronic regional pain (CRP)	24	2	1
Chronic widespread pain (CWP)	31	3	4
No multisite - CWP	46	3	2
Multisite - CWP (high risk)	16	3	3

Conclusions: SBST and the pain mannequin as screening tools partly capture different patients at high risk of developing chronic back pain. Using a combination of the two instruments may improve the ability to facilitate triage to appropriate treatment level.

References:

[1] Macfarlane GJ et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis. 2017;76(2):318–328.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6065

AB1200-HPR THE RELIABILITY OF ROMANIAN ROLAND MORRIS DISABILITY QUESTIONNAIRE IN PEOPLE WITH LOW BACK PAIN. A PRELIMINARY STUDY

E. Ilie, L. Rusu. *Faculty of Physical Education, Department of Sports Medicine and Kinesiology, University of Craiova, Craiova, Romania*

Background: Patient reported assessments are widely recommended by the clinical guidelines and an important part of a comprehensive assessment. Patient-reported questionnaires should be translated into local language accordingly and validated in the translated language (1). The clinicians in Romania suffer from lack of validated questionnaires in Romanian language. The Roland Morris Disability questionnaire is one of the most recommended questionnaires evaluating low back pain. Although, the Romanian translation was performed before, there is no effort regarding to its validation in Romanian language until now.

Objectives: To investigate the test-retest reliability Romanian version of the Roland Morris Disability Questionnaire (RMDQ-Ro) in people low back pain.

Methods: The permission to conduct such a study was asked to the original author Prof. Martin Roland, before starting to the study. The Romanian translated form of Roland Morris Disability Questionnaire which is provided on the web site "http://www.rmdq.org/" was used in the study. A total of 100 people with low back pain filled the RMDQ as well as Numeric Rating Scales for rest (NRS-R) and activity (NRS-A). Due to the lack of other validated measures such the Oswestry Disability Index in Romanian, these additional assessments (VAS-R and VAS-A) were performed for investigating convergent validity. For test-retest reliability 30 people filled the RMDQ-Ro after 3–14 days later as recommended. Test-rest reliability was assessed with intra-class coefficient correlation (ICC). Non-parametric tests were employed due to the heterogeneity of the data. Therefore, the Spearman correlation test was used for determining the relationship between RMDQ-Ro and VAS-R and VAS-A.

Results: The characteristics of the participants were shown at Table 1. The test-retest reliability of RMDQ-Ro was found at an excellent level (ICC: 0.95). Moderate positive correlations were determined between RMDQ-Ro and NRS-R (rho: 0.518, $p<0.001$), and NRS-A (rho: 0.484, $p<0.001$).

Table 1. Characteristics of the Participants

	Male (n: 52) Median (IQR 25/75)	Female (n: 48) Median (IQR 25/75)	Total (n: 100) Median (IQR 25/75)
Age (years)	32 (28.25/46.50)	35 (28.5/45.5)	34.5 (28.5/46)
Height (cm)	179.50 (175/183)	168 (163/170.5)	174 (168/180)
Weight (kg)	81 (72/90)	61 (55.5/61)	71 (61/81.5)
RMDQ-Ro (0–24)	6 (3/8)	4 (3/7)	5 (3/7)
NRS-R (0–10)	3.5 (2/5)	3.5 (2/5)	3.5 (2/5)
NRS-A (0–10)	2 (1/5)	3 (1/6)	2 (1/5)

IQR: Interquartile Range, RMDQ-Ro: Romanian Version of Roland Morris Disability Questionnaire, NRS-R: Numeric Rating Scale in Rest, NRS-A: Numeric Rating Scale in Activity.

Conclusions: RMDQ-Ro was found reliable regarding test-retest reliability. This questionnaire can be performed in the repeated measures for evaluating low back pain patients. However, more psychometric characteristics of RMDQ-Ro such as internal consistency and construct validity should be investigated in further studies.

References:

[1] Beaton DE, Bombardier C, Guillemin F, Ferraz MB.Guidelines for the process of cross-cultural adaptation of self-report measures. Spine (Phila Pa 1976). 2000;25(24):3186–91.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6249

AB1201-HPR THE VALIDITY AND TEST-RETEST RELIABILITY OF THE TURKISH PATIENT SPECIFIC FUNCTIONAL SCALE IN CHRONIC NECK PAIN PATIENTS. A PRELIMINARY REPORT

G. Yalcinkaya[1], B. Kara[1], M.N. Arda[2]. *[1]School of Physical Therapy and Rehabilitation; [2]Department of Neurosurgery, Dokuz Eylül University, Izmir, Turkey*

Background: Current clinical guidelines recommend to use both clinical and self-reported measurements for evaluation of chronic neck pain. Among the self-reported outcomes, Neck Disability Index (NDI) and Patient Specific Functional Scale (PSFS) are the most widely used and recommended instruments.[1] Although, NDI was validated in Turkish language before, no validation study related to the PSFS was detected in the literature.

Objectives: The aims of this study were to translate PSFS in Turkish language and to establish the test-retest reliability and validity of the PSFS-T in chronic neck pain patients.

Methods: The PSFS was translated into Turkish by using the "translation-backward translation" method as recommended in the guidelines.[2] The demographic information, PSFS-T and NDI were recorded at the first visit of the patients. Thirty patients were called by phone for the retest evaluation of PSFS-T. The construct validity of PSFS-T was determined by investigating the correlation between NDI and PSFS-T scores. The Cronbach's alpha was used for the internal consistency. Intra-class coefficient (ICC) was employed to determine the test-retest reliability.

Results: The final form was completed by 42 chronic neck pain patients (18 F) until now. The mean age was 42±14. The internal consistency was found as good (Cronbach's alpha:0.89). A positive moderate correlation was determined between NDI and PSFS-T scores ($p<0.05$;$r=0.405$). The ICC for test-retest reliability was determined in high level (ICC: 0.88).

Conclusions: The PSFS-T is a reliable and valid instrument for chronic neck pain patients. However,the preliminary results should be confirmed by completing the study.

References:

[1] Childs JD, Cleland JA, Elliott JM, Teyhen DS, Wainner RS, Whitman JM, Sopky BJ, Godges JJ, Flynn TW. Neck pain: Clinical practice guidelines linked to the International Classification of Functioning, Disability, and Health from the Orthopedic Section of the American Physical Therapy Association.JOrthop Sports Phys Ther. 2008;38(9):A1-A34.

[2] Beaton DE, Bombardier C, Guillemin F, Ferraz MB.Guidelines for the process of cross-cultural adaptation of self-report measures. Spine (Phila Pa 1976). 2000;25(24):3186–91.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5686

AB1202-HPR RELATIONSHIP OF WORK DISABILITY BETWEEN THE DISEASE ACTIVITY, DEPRESSION AND QUALITY OF LIFE IN HOUSEWIFE AND WORKING PATIENTS WITH RHEUMATOİD ARTHRITIS

S. Sağ, K. Nas, M.S. Sağ, I. Tekeoğlu, A. Kamanlı. *Department of Physical Medicine and Rehabilitation, Rheumatology, Faculty of Medicine, Sakarya University, Sakarya, Turkey, sakarya, Turkey*

Background: The aim of this study was to determine the work status in patients with rheumatoid arthritis (RA) while also defining the factors related to work disability.

Objectives: In this study, our objective was to determine the work productivity, work disability and difficulty in time-off daily activities of the housewife and working patients with rheumatoid arthritis (RA) and to investigate the relation of these parameters with disease activity, anxiety, depression and quality of life.

Methods: 82 patients with the diagnosis of RA (26 males, 56 females) and 29 healthy control subjects (5 males, 24 females) were included in the study. In patients with RA, DAS28 was used to evaluate the disease activity; Duruöz hand index was used to determine the functional status. In addition, HAQ (Heath assesment quality) and The Short Form (SF-36) Health Survey was used to evaluate the health status, Hospital Anxiety and Depression Scale (HADS) was used for the evaluation of depression and anxiety and Work Productivity and Activity Impairment Questionnaire: Specific Health Problem v2.0 (WPAI:SHP) was used to evaluate the work productivity.

Results: Demographic characteristics such as age and gender, were comparable in both patient and control groups ($p>0.05$). The difficulty in the time off daily activities were worse in the patient group compared with the control group ($p<0.05$). Anxiety, were significantly higher in housewife RA group ($p<0.05$). Difficulty in time-off daily activities was correlated with VAS-fatigue and DAS28,HAQ,Duruöz hand index was correlated. ($p<0.05$).

Conclusions: Even if they are not working in housewives, we have found that

as much as the least active RA patients, it is difficult for activities in daily life, that the quality of life associated with the illness is low, and that depression and anxiety are similar to employees. As a result, disease activity, quality of life and functional status control in RA patients are as important as those who are working as housewives. Particularly in increasing productivity and participation in everyday life, the mood is influential and physicians must examine their patients in this regard. There is a need for more extensive cohort studies on this topic.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4614

AB1203-HPR COMPARISON OF QUALITY OF LIFE OF PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND ANKILOSING SPONDILITIS WITH TREATMENT OR PRESCRIPTION OF BIOLOGIC DRUGS: RESULTS FROM THE CARA STUDY

L. Sinigaglia[1], L. Scalone[2,3], P. Sarzi-Puttini[4], C.M. Montecucco[5], R. Giacomelli[6], G. Lapadula[7], I. Olivieri[8], A. Giardino[9], G. Didoni[9], P. Cortesi[2,3], L.G. Mantovani[2,3], M. Mecchia[9] on behalf of CARA study working group. *[1]Rheumatology Unit, G. Pini Hospital; [2]CHARTA Foundation, Milano; [3]University of Milano Bicocca, Monza; [4]Rheumatology Unit, L. Sacco University Hospital, Milano; [5]University of Pavia School of Medicine, IRCCS Policlinico San Matteo Foundation, Pavia; [6]Rheumatology Unit School of Medicine, University of L'Aquila, L'Aquila; [7]Rheumatology Unit, University of Bari, Bari; [8]San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, and the Basilicata Ricerca Biomedica (BRB) Foundation, Italy, Potenza and Matera; [9]MSD Italia, Roma, Italy*

Background: Chronic rheumatic conditions such as rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriatic arthritis (PsA) are associated with severe morbidity and significant impairment of patients' health related quality of life (HRQoL). Several treatments are available but not all the patients respond positively to them. Biologic therapies such as anti-TNFα agents are shown to benefit who fail or have partial responses to standard DMARD therapy.
Objectives: Within a multicenter stated preferences study (CARA Study), we assessed HRQoL in patients with RA, AS and PsA, and estimated relationship of HRQOL with the different diagnoses, clinical characteristics and biological treatment experience.
Methods: Patients with RA, AS, or PsA, who at the time of enrollment were following a treatment (experienced) or received a first prescription (naïve) of treatment with biological drugs were enrolled. Together with preferences data, clinical and HRQOL information was reported. HRQoL was assessed with the recently developed and successfully validated version of the EQ-5D-5L, which allows to obtain a description of health (in 5 domains and 5 levels of severity each), a measure (EQ-VAS) and a valuation (utility) of health. Multiple linear regression analyses were conducted to assess the association between EQ-5D VAS score and the utility with age, sex, diagnosis, treatment experience, years from symptoms onset and years from diagnosis.
Results: 513 patients were enrolled (mean±SD =50.0±13.6, 42.5% female). As regards the diagnosis, 33.9% had RA, 34.9% PsA and 31.2% AS. The mean±SD time from the symptoms onset was 10.8±9.4 and from the diagnosis was 8.0±8.2 years. Almost half of the patients (47.4%) were naïve to the biological treatment. Patients reporting severe or extreme problems were: 7.1% in mobility, 3.6% in self-care, 10.3% in usual activities, 18.6% in pain/discomfort, 5.5% in anxiety/depression. The mean±SD of the VAS was 60.4±20.5 and of the utility was 0.773±0.116. From the regression model the VAS and utility are significantly ($p<0.05$) associated with age, sex and treatment experience (table 1). In particular, the patients being naïve to the treatment with biological drugs had on average significant worse levels of HRQoL than experienced patients, adjusting for the other variables included in the model.

Table 1. Results of the regression analyses

Varibles	EQ-5D VAS		EQ-5D UTILITY	
	Coeff. Regr	p-value	Coeff. regr	p-value
Constant	92.455	0.000	0.954	0.000
Age	-0.205	0.002	-0.001	0.013
Gender (Female)	-7.473	0.000	-0.055	0.000
Psoriatic arthritis	-3.986	0.063	-0.009	0.448
Ankylosing spondylitis	-4.236	0.076	-0.016	0.228
Naïve patients	-13.873	0.000	-0.074	0.000
Time from symptoms onset	-0.105	0.557	0.000	0.858
Time from diagnosis	0.061	0.768	0.000	0.815

Conclusions: Patients naïve to biological treatment have significat lower levels of HRQoL, suggesting that their current situation is not satisfactory and need to start with a more effective treatment.
Disclosure of Interest: L. Sinigaglia: None declared, L. Scalone: None declared, P. Sarzi-Puttini: None declared, C. Montecucco: None declared, R. Giacomelli Grant/research support from: MSD, G. Lapadula: None declared, I. Olivieri: None declared, A. Giardino Employee of: MSD Italia, G. Didoni Employee of: MSD Italia, P. Cortesi Grant/research support from: Gilead, L. Mantovani: None declared, M. Mecchia Employee of: MSD Italia
DOI: 10.1136/annrheumdis-2017-eular.4904

AB1204-HPR EVALUATION OF CARBOHYDRATE METABOLISM IN RHEUMATOLOGIC PATIENTS AFTER PULSE THERAPY WITH GLUCOCORTICOIDS

M. Salokhiddinov, A. Tulabaev. *Rheumatology, Tashkent Medical Academy, Tashkent, Uzbekistan*

Background: Chronic inflammation – the crucial pathogenic mechanism of rheumatoid arthritis is the main cause of accelerated atherosclerosis, insulin resistance and well-known consequences related to it. The conservative treatment of rheumatoid arthritis may provide a significant influence on glucose metabolism. When the duration of rheumatic diseases of administration and dosage of glucocorticoids (GC) are significant predictors of the development of impaired glucose tolerance and diabetes mellitus.
Objectives: To study the effect of pulse-therapy (PT) of the GC on the violation of carbohydrate metabolism in patients with rheumatic diseases
Methods: The study included 35 patients (7 men, 18 women) with a variety of rheumatic diseases (systemic lupus erythematosus - 23, systemic vasculitis - 12) between the ages of 18 to 68 years (mean age 42,3±14,43 years) and duration of disease from 6 months to 12 years (mean 3,55±3,36 years). Pulse-therapy of GK included intravenous prednisolone 600–1000 mg per day for 3 consecutive days (course dose of 1800–3000 mg). Oral glucose tolerance test (OGTT) was performed after the course.The first group included patients with a normal result of OGTT (glucose concentration of <7.8 mmol/L at 2 hours after taking 75 g of glucose). There were 23 patients in the first group at the age of 18 to 54 years (mean age 38.0±2.8 years). Patients of the second group level had OGTT was>7.8 mmol/L. This group included 12 people aged from 44 to 61 years (mean age 52,6±8,4 years). All patients underwent the measurement of blood glucose levels prior to PT, 2, 4, 6, 10, 24, 48 and 72 hours and after the PT
Results: All patients included in the study, after the PT session there was an increase in blood glucose levels with a peak at 4 hours after the start of administration - 12.2±0.82 in the first group, in the second to 21.95±0.25 mmol/l ($p<0,05$). Normalization of glucose levels in the first group of patients occurred within 1.75±0.18 days (1 to 3), whereas in the second - for 5,0±1,0 (3 to 5; $p<0,05$). During the OGTT the mean fasting blood glucose levels in patients with the first group was 4.49±0.12 mmol/l, and the second - 5,85±0,35 ($p<0,05$), after 2 hours - 6.0±0.21 and 10.0±1.5 mmol/l, respectively ($p<0,05$).
Conclusions: Application PT of GC in rheumatic patients causes blood glucose levels to change values, indicating the development of impaired glucose tolerance. Predictors of disorders of carbohydrate metabolism in these patients are high levels of glycemia during the PT more continuous glucose normalization indices after the course PT GC.
References:
[1] Alekseeva EI. Pulse therapy with glucocorticoids of systemic manifestations of rheumatoid arthritis in children. Questions of modern times. Pediatrician 2005;4(1)9–14.
[2] Lebets IS, Tolmacheva SR, Shevchenko NS. Modern approaches to the treatment of systemic lupus erythematosus in adolescents. Wedge. Pediatrician 2012;6:91–94.
[3] Omelchenko LI, Nikolaenko VB. Some aspects of improving glucocorticoid therapy in rheumatic diseases in children. Ukr. Rheumatology 2010;1:44–49.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1169

AB1205-HPR THE EFFECTS OF KINESIOTAPING ON JOINT POSITION SENSE AND POSTURAL STABILITY FOLLOWING FATIGUE PROTOCOL

O. Aydoğdu, Z. Sarı, U.S. Yurdalan. *Physiotherapy and Rehabilitation, Marmara University, Health Sciences Faculty, Istanbul, Turkey*

Background: Muscle fatigue is common in sports activities and has been shown to adversely alter proprioception, impair neuromuscular control, and increase the risk of injury. Kinesiotaping has recently gained popularity among sports professionals for its assumed injury prevention and performance enhancement (1). Two studies have reported conflicting findings with respect to the effects of KT on proprioception. Halseth et al reported that KT produced no significant change in the absolute error in ankle joint position sense (2). However, Chang et al reported that KT decreased the force sense error in grip strength measurements among 21 healthy college athletes (3). Thus, the current literature does not provide clear information about the effects of KT on proprioception. Although there are published articles about investigating KT on joint position sense and postural stability, the effects of KT is still unknown after muscle fatigue, to our knowledge.
Objectives: There is a lack of literature examining the KT on joint position sense and postural stability following fatigue protocol. Therefore, the aim of this study was to investigate the effects of KT on knee joint position sense and postural stability after muscle fatigue. It was hypothesized that KT applied on quadriceps femoris muscle would partially compensate for the proprioceptive and balance-related deficits caused by muscle fatigue.
Methods: Thirty – six healthy subjects were evaluated in the study. Knee joint position sense was assessed by Biodex System Pro 4 during active repositioning tests at the target angles of 30º, 50º and 70º of knee flexion in sagittal plane. Postural stability was assessed by Pedalo Sensamove® System in antero –

posterior and medio – lateral plane. Joint position sense and postural stability were assessed three times: during rest, following the fatigue protocol, and following the taping. The subjects were received a clinically-used fatigue protocol on a cycle ergometer. The Modified Borg's Rate of Perceived Exertion Scale has been used for fatigue determination.
Results: Joint position sense and postural stability were significantly decreased following fatigue compared to the condition during rest ($p<0.05$). However, no significant difference was found in terms of joint position sense and postural stability after taping compared to the condition following fatigue ($p>0.05$).
Conclusions: The hypothesis of this study, that KT could partially compensate for the proprioceptive and balance-related deficits induced by muscle fatigue, was not supported. According to the results of our study, we concluded that the subjects do not benefit from the use of KT for compensating joint position sense and postural stability in condition following fatigue.
References:
[1] Yeung SS, Yeung EW, Sakunkaruna Y, et al. Acute effects of kinesio taping on knee extensor peak torque and electromyographic activity after exhaustive isometric knee extension in healthy young adults. Clin J Sport Med. 2015 May;25(3):284–90.
[2] Halseth T, McChesney JW, DeBeliso M, et al. The effects of Kinesio taping on proprioception at the ankle. J Sports Sci Med. 2004;3:1–7.
[3] Chang HY, Chou KY, Lin JJ, et al. Immediate effect of forearm Kinesio taping on maximal grip strength and force sense in healthy collegiate athletes. Phys Ther Sport. 2010;11:122–127.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5688

AB1206-HPR ADAPTATION INTO SPANISH OF THE SCLERODERMA HEALTH ASSESMENT QUESTIONNAIRE (S-HAQ)

P. Quevedo[1], M.A. Rivero[1], N. Perez[2], H. Laborde[2], G. Earsman[1], M. Mayer[1], S. Papasidero[3], S. Julia[3], C. Zaffarana[4], R. Maldonado[5], M. Khoury[6], M. Lara[7], C. Castell[7], A. Curti[7], J.C. Barreira[1], V. Steen[8]. *[1]British Hospital; [2]Hospital de Clinicas José de San Martin; [3]Tornu Hospital; [4]Psychophysical Rehabilitation Institute (Irep), Buenos Aires; [5]Padilla Hospital, TUCUMAN; [6]Statistics, British Hospital, Buenos Aires; [7]Luis Lagomaggiore Hospital, MENDOZA, Argentina; [8]Georgetown University, Washington, United States*

Background: The *Health Assessment Questionnaire* (HAQ) is an instrument administered to patients to self-report functional status originally in rheumatoid arthritis (RA). In Argentina, it has been translated and validated for RA in 2004. For diffuse SSc, HAQ has been associated to morbidity and mortality.
Objectives: To adapt S-HAQ into Spanish and to assess its validity in SSc patients in Argentina.
Methods: S-HAQ was translated following a forward-backward translation procedure of the original English version, and transcultural adaptation was performed by a comprehension test reaching the final Spanish version. SSc patients that fulfilled ACR 80 criteria and early Systemic Sclerosis according to Le Roy and Medsger criteria were included. Patients with overlap were excluded. Cronbach's alpha and item-item item-total correlations were used to assess internal consistency. Construction validity was analyzed through factor analysis with Varimax rotation. Continuous variables were compared by t-test, Mann-Whitney or Kruskal-Wallis test, and categorical variables by chi-square or Fisher's test. A value of $p<0.05$ was considered significant.
Results: l9An adapted Argentine-Spanish version of S-HAQ was developed. One hundred patients were surveyed; 84% were female, mean age 54±12.8 years and disease duration 8.8±9.1 years. Limited SSc was more frequent (63%), followed by diffuse SSc (36%). Serologically, 89% were ANA positive, 27% had anti Scl 70 and 41% had anti centromere antibodies. Median Rodnan score (mRSS) was 9.8 (0–40.5) and median activity measured by EUSTAR was 1.25 (0–6). Median S-HAQ was 0.62 (0–2.5), Cronbach's alpha 0.89, and when removing questions one by one the coefficient decreased. Median VAS (visual analogue scale) was 0.57 (0–2.8). Factor analysis identified two factors for the S-HAQ: factor 1: dressing (0.61), arising (0.68), reach (0.63), and personal hygiene (0.70); factor 2: eating (0.68), grip (0.72), walking (0.49), usual activities (0.62). For questions, three factors were identified through VAS: factor 1: overall disease severity (0.63) and gastro-intestinal symptoms (0.57); factor 2: Raynaud's (0.66), digital ulcers (0.56); factor 3: respiratory symptoms (0.43). There was a statistically significant association between higher values of S-HAQ and higher values of mRSS (1.1±0.74 vs. 0.64±0.5 p=0.002) and also with seropositivity for anti-Scl 70 (p=0.003). Higher values of total VAS were associated to female gender (0.75±0.5 vs. 0.49±0.71, p=0.01). There was a significant association between S-HAQ and MEDSGER (p=0.04) and EUSTAR (p=0.03) scores; likewise, between VAS and MEDSGER (p=0.00) and EUSTAR (p=0.00) scores.
Conclusions: A Spanish version of S-HAQ was developed, showing an acceptable reliability and validity.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4025

AB1207-HPR PATIENT SATISFACTION IN A RHEUMATOID ARTHRITIS SPECIALIZED CENTER

S. Henao[1], F. Rodriguez[2], P. Santos-Moreno[3], L. Villarreal[4], M. Cabrera[5], A. Malpica[6], D. Buitrago-Garcia[6]. *[1]Patient service; [2]Patient Program; [3]Rheumatology; [4]Psychology and processes; [5]Engineer and processes; [6]Epidemiology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: According to the Beryl Institute's, patient experience (PX) is "the sum of all interactions, shaped by an organization's culture, that influence patient perceptions, across the continuum of care"; nowadays patient satisfaction is considered as one of the quality for performance in health systems (1). In order to provide a multidisciplinary quality care to patients with RA in centers of excellence (CoEs) under the coordination of a rheumatologist, provide comprehensive management of patients with this pathology, ensuring approachability to medical appointments and treatment, in order to get better clinical outcomes and improve patient safety and satisfaction of the health services provided.
Objectives: To measure levels of satisfaction of RA patients treated at a specialized center and to evaluate patient service.
Methods: In a RA specialized center during a 24 month period we performed a satisfaction survey in order to evaluate the health services provided. We evaluated the timing on attention, appointment assignment, information provided, the treatment received by the healthcare team, facilities among others. Patients evaluated the services provided in a scale from 1 to 4, were 1 was very bad, 2 regular, 3 good and 4 excellent. Descriptive epidemiology was performed for each variable presented.
Results: We collected 1125 surveys during 2015 and 2016, 45% considered to have a timely care, the mean of waiting time for an appointment was 9 min ± 8; regarding the appointment assignment 96% of the patients evaluated it as good or excellent (mean 3.5±0.7), 80% considered that the information provided was clear and useful, 90% reported to receive a kind and friendly treatment and to considered the facilities as good or excellent. When we evaluated the satisfaction regarding the health care team 50% of patients evaluated the rheumatologist, nurse, nutritionist, physical therapist, psychologist and physiatrist as good and 40% as excellent.
Conclusions: Although we found that our patients are highly satisfied, there is a large opportunity to improve our services. Also, this evidence can support further research projects in order to increase the patient's satisfaction.
References:
[1] Th VP. Creating the ideal patient experience. Journal of medicine and life. 2016;9(4):380–385.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5380

HPR epidemiology and public health (including prevention)

AB1208-HPR PSORIASIS INDUCED BY TNF ANTAGONIST THERAPY. ANALYSIS OF 13 CASES

À. Martinez-Ferrer[1], A. Mateu Puchades[2], C. Vergara Dangond[1], M. Aguliar Zamora[1], L. Montolio[1], S. Santos[2], È. Valls Pascual[1], D. Ybáñez García[1], J.J. Alegre Sancho[1]. *[1]Rheumatology; [2]Dermatology, Hospital Dr Peset, Valencia, Spain*

Background: Tumor necrosis factor (TNF) antagonist drugs have been shown to be effective in different inflammatory arthropathies and autoimmune pathologies, including psoriasis. However, an unexpected side effect has been observed: the new occurrence or worsening of psoriatic lesions.
Objectives: The aim of this study is to describe the cases of induction or worsening of psoriasis in patients treated with TNF antagonist therapy in our center.
Methods: Retrospective observational study, review of cases of new or worsening psoriasis in patients with TNF antagonist at the University Hospital Dr. Peset from October 2008 to November 2016. A total of 13 cases were obtained.
Results: Thirteen patients, 8 females and 5 males with mean age 46 years (± 16). 38% of patients received treatment for Crohn's disease, 31% for rheumatoid arthritis (RA), 31% for psoriatic arthropathy (APs), 8% for ankylosing spondylitis (AE) and another 8% for psoriasis. Two patients were diagnosed of more than one pathology: Crohn's disease associated with APs and Crohn's disease associated with RA. Sixty one percent had no known personal history of psoriasis, in one of them the family history of psoriasis was recorded. Infliximab was used in 38.5% of cases, followed by adalimumab and golimumab in 23% each and etanercept in 15.4%. The mean latency time since drug introduction was 9.3 months (2–26). There were 12 cases of psoriasis and 1 case of pityriasis lichenoides (histologically confirmed). Lesion morphology included pustular psoriasis in 91%, scalp psoriasis in 25%, guttate lesions in 25%, plaque psoriasis in 8%, and inverse psoriasis in 8%; 58% experienced lesions of more than one type. There were no cases of nail, mucosal or erythrodermic psoriasis. The psoriasiform lesions resolved without interruption of TNF antagonist therapy in 53.85%. Of the 6 patients who required discontinuation, 3 patients were switched to another anti-TNF drug (adalimumab,

golimumab and certolizumab) and all 3 had recurrence of the lesions, in 2 patients the anti-TNF was replaced by a non-anti-TNF biological. Topical treatment was used in all cases, one patient also required systemic treatment with methotrexate.
Conclusions: TNF antagonist induced psoriasis is a well-described adverse event. Pustular psoriasis is the most frequent presentation. In most cases there is no personal or family history of psoriasis. Topical therapy may be effective but some patients require discontinuation of the drug. Skin lesions can reappear when switching to another anti-TNF drug.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2877

AB1209-HPR THE PREVALENCE OF DENTAL AND SINUS INFECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS BEFORE BIOLOGIC THERAPY INITIATION: USEFULNESS OF A SYSTEMATIC SCREENING?

C. Tawil, E. Descamps, M. Forien, A. Gardette, E. Palazzo, S. Ottaviani, P. Dieudé. *Rheumatology Department, Bichat Hospital, Paris, France*

Background: Introduction of the biologic therapies has dramatically improved the outcome of severe rheumatoid arthritis (RA). Biologic therapies play a central role in the control of synovial inflammation. However they also decrease host defenses leading to an increased rate of infection. Because of their adverse effects, a careful assessment is needed before their initiation. A systematic assessment of dental or sinus infection before a biologic therapy is not required.
Objectives: The aim of our study was to assess the prevalence and the usefulness of a systematic screening of oral (dental and/or sinus) infection of RA patients before biologic therapy initiation.
Methods: This was a monocentric retrospective study. We included RA (ACR/EULAR 2010 criteria) patients with active disease despite disease-modifying anti-rheumatic drugs (DMARDs) and requiring biologic therapy initiation between 2010 and 2016. The following parameters were collected: demographic and disease characteristics, disease activity (C-reactive protein, disease activity score (DAS) 28), currents therapies (DMARDS, corticosteroids). Dental infection was assessed by stomatologist after clinical and panoramic dental X- ray evaluation. Sinusitis was defined on sinus computed tomography as partial or complete opacification of one or more sinus cavities. Factors associated with oral infections were analyzed in uni- and multivariate models.
Results: We included 223 RA patients (79.4% of female, mean ± SD disease duration of 8.9±8.6 years). The mean age was 54±10.9 years, 70.8% rheumatoid factor (RF) positive, 84.4% anti–citrullinated protein antibody (ACPA) positive and 68.1% had radiographic damages. The mean DAS 28 was 5.5±2.6; 71% of patients received corticosteroids (mean 7mg per day of equivalent prednisone) and 63% methotrexate (mean 17.8mg per week). No patient had pain or other sinus or dental symptoms. Before biologic agent initiation, systematic dental and sinus screening revealed an oral infection in 31.5% of patients (dental: 20.2% and sinus: 14.8%). In univariate analysis, active smoking was associated with a higher risk of oral infection (OR=2.16 [1.02–4.57], p=0.038) and methotrexate with a lower rate (OR=0.43 [0.23–0.81], p=0.006). Corticosteroid, disease duration, DAS 28, RF, ACPA and structural damages were not associated with oral infection. No significant association was confirmed with oral infection using multivariate analysis.
Conclusions: In our study, one third of RA patients requiring biologic agents had asymptomatic oral infection. The high prevalence of oral infection in RA patients suggests the usefulness of systematic dental and sinus screening before biologic therapy initiation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4037

AB1210-HPR MENDELIAN RANDOMIZATION ANALYSIS INDICATES SERUM URATE HAS A CONDITIONAL CAUSAL EFFECT ON SERUM CREATININE AND RENAL FUNCTION

J. Liu[1], H. Zhang[1], Z. Dong[1], J. Zhou[1], Y. Ma[1], Y. Li[1], Q. Qian[1], Y. Yang[1,2], X. Wang[1,2], H. Zou[3,4], L. Jin[1,2], J. Wang[1,2,4]. *[1]State Key Laboratory of Genetic Engineering, Collaborative Innovation Center for Genetics and Development, School of Life Sciences, Fudan university, Shanghai; [2]Fudan-Taizhou Institute of Health Sciences, Taizhou; [3]Division of Rheumatology, Huashan Hospital, Fudan University; [4]Institute of Rheumatology, Immunology and Allergy, Fudan university, Shanghai, China*

Background: Uric acid, the weak organic acid and the end product of purine nucleotide degradation, is excreted predominantly by the proximal tubules [1]. Although large numbers of epidemiological, molecular and animal studies have focused on various pathogenic effects of serum uric acid, incldng chronic kidney disease (CKD), metabolic syndrome, and coronary artery disease [2], whether the serum uric acid is an independent risk factor or has causal impact on serum creatinine (SCr) and renal function remains unclear.
Objectives: We aim to study the effect of serum uric acid on renal function by applying the method of Mendelian randomization.
Methods: The study was represented by estimated glomerular filtration rate (eGFR) with potential confounding factors in 3,734 Chinese subjects. Four genetic variants of uric acid transporter genes (*rs1481012 [ABCG2], rs16890979 [SLC2A9], rs2231137 [ABCG2]* and *rs3799352 (SLC17A1]*) were selected for this study as they had highest correlation with serum uric acid in Chinese population in our previous study. In this research, serum uric acid was selected as exposure, genetic risk score of uric acid transporters was selected as instrumental variable, and SCr and eGFR were selected as the outcomes.
Results: 1) The results of the analysis showed that increased serum uric acid has a causal effect on reducing estimated glomerular filtration rate in both female population and the subjects who were under 65 years old. Because of protective effects on renal function of ovarian hormones such as estrogen, we postulated that estrogen might be the cause leading to the difference between men and women. 2) We also found that increased serum uric acid led to the damage of renal function in the subjects with normal eGFR value. 3) In addition, the serum uric acid was a risk factor to renal function in the subjects with relative high level of fasting glucose or who were smoking currently. Because of metabolic defects in people affected by diabetes, renal glucose reabsorption was increased, thus further sustaining hyperglycemia in patients.
Conclusions: Serum urate has causal effects on renal dysfunction in either female or individuals of under 65, or normal eGFR, or high level of fasting glucose, or current smokers.
References:
[1] Pasalic D, Marinkovic N, Feher-Turkovic L. Biochem Medica 2012;22(1):63–75.
[2] Sakhaee K. J Nephrol 2014;27(3):241–5.
Acknowledgements: National Natural Science Foundation of China (31521003), Science and Technology Committee of Shanghai Municipality (11DJ1400102), International S&T Cooperation Program of China (2013DFA30870), Ministry of Science and Technology (2011BAI09B00), 111 Project (B13016), and Program for 2012 Outstanding Medical Academic Leader for Hejian Zou. Computational support was provided by the High-End Computing Center located at Fudan University.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5601

AB1211-HPR THE USE OF SUBCUTANEOUS METHOTREXATE IN POLISH PATIENTS WITH RHEUMATOID ARTHRITIS

M. Przygodzka[1], K. Sikorska-Siudek[1], R. Radomski[2], S. Bojanowski[2]. *[1]Mazovian Centre of Rheumatology and Osteoporosis; [2]iEHR.eu, Warsaw, Poland*

Background: Methotrexate (Mtx) should be the drug of the first choice in rheumatoid arthritis (RA) if there are no contraindications to use it. The efficacy of Mtx is measured by remission or low disease activity and depends on the dose taken. Higher doses (25–30 mg/week) are more effective, but intolerance is the main cause of discontinuation of oral treatment. Subcutaneous Mtx is efficient alternative in those cases.
Objectives: The aim of this study was to evaluate subcutaneous Mtx use frequency in Polish patients and change oral form for subcutaneous as well.
Methods: The disease activity was assessed by Disease Activity Score 28 (DAS 28) during the first visit (V1) and after 3 months therapy (V2) and compliance with therapy as well.
Results: There were 194 RA patients diagnosed by the ACR and 1997 and/or ACR/EULAR 2010 criteria. 144 patients were treated by oral Mtx (group A) and 50 patients (group B) by subcutaneous Mtx at the time of study enrolment (V1).37 patients of group A (26%) required changes in therapy during V2, 24 (17%) were switched to subcutaneous Mtx (group A1). 6 patients of group B (12%) required change of treatment during V2, including 2 patients (4%) with subcutaneous Mtx, who were switched to oral Mtx.The main cause of changing therapy from oral to subcutaneous was gastrointestinal intolerance of high dose of Mtx. 69 patients (12%) of group A required additional steroid therapy compared to 18 (36%) of group B. Average DAS 28 decreased by 0.58 in group A1 in oral treatment and during the subcutaneous treatment time decreased by next 0.23. In group A1 during oral treatment 14 (58%) patients used 25 mg/week and 20 patients (83%) used 25 mg/week during subcutaneous treatment time.
Conclusions: Patients treatment by oral Mtx often require modification of therapy in comparison to patients treated by subcutaneous Mtx, including more frequent use of steroids
The main cause of oral intolerance are ailments of the digestive system.
Change of oral to subcutaneous therapy allows administration of higher doses of Mtx and results in decrease of DAS28 in comparison to the patients continuing their oral treatment.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6963

AB1212-HPR DYNAMICS OF ARTICULAR SYNDROME IN RHEUMATOID ARTHRITIS AGAINST CORRECTION OF PROGESTERONE INSUFFICIENCY

M. Salokhiddinov, A. Ahmedov. *Rheumatology and Osteopathy, Tashkent Medical Academy, Tashkent, Uzbekistan*

Background: According to the literature, sex hormones manifest themselves as immune modulators that inhibit the ones and stimulate other immune functions. Studies have shown that patients with RA, decrease of estradiol and particularly

progesterone in the blood serum is found in the women of reproductive age. According to the literature, progesterone has a close relationship with T-cell immunity. A value of T-cell deficiency plays an important role in the cause of the autoimmune process

Objectives: To study of progesterone correction in RA patients.The aim of this study was to evaluate the effectiveness of progesterone deficiency correction in patients with rheumatoid arthritis based on the analysis of articular syndrome

Methods: The study involved 40 patients with a documented diagnosis of RA, women of reproductive age. The study group consisted of 30 patients who had correction of progesterone deficiency background in the pathogenetic therapy. The control group consisted of 10 female patients who are on the pathogenetic therapy. We used the following criteria: disease activity and severity of the articular syndrome with determining of the number of tender and swollen joints, indices of DAS and HAQ. Statistical analysis of the results of research used the method of parametrics of Student criterion

Results: Among the patients studied disease duration ranged from 3 months to 19 years (mean age 10±7,2 years), 20 patients (50%), from 5 to 10 years – 15 (37.5%), and more than 10 years – 5 patients (12.5%). X-ray picture of joint damage in the majority of patients corresponded to stage 2–3 – 87.5% (35 patients). Less common muscular disorders (7.5%), mainly in patients taking long-term GC, myalgia and muscle malnutrition were detected in 7.5% and 25% of patients, respectively. In addition to the articular syndrome, the most frequent complaints of general weakness (75%), irritability, sleep disorders and attention (50%), anxiety and anxiety (75%), low-grade temperature (10%)

Conclusions: Progesterone deficiency correction in RA patients against pathogenic therapy has improved performance of articular syndrome and improves quality of life, such as vitality, general health and social function as well as it contributes to the positive dynamics of mental health

References:

[1] McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis New Engl. J. Med. 2011;365:2205–19.
[2] Wells G et al. Validation of the 28-joint Disease Activity Score (DAS28) and European League Against Rheumatism response criteria based on C-reactive protein against disease progression in patients with rheumatoid arthritis, and comparison with the DAS28 based on erythrocyte sedimentation rate. Ann. Rheum. Dis. 2009;68:954–60.
[3] Ware JE, Sherbourne CD. The MOS 36-Item short-form health survey. Med. Care. Med Care. 1992;30(6):473–83.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1306

AB1213-HPR A NATIONAL RHEUMATOID ARTHRITIS REGISTRY SUPPORTED BY A PUBLIC POLICY AS A STRATEGY FOR DISEASE CONTROL AND RISK MANAGEMENT IN COLOMBIA

O. Valencia[1], P. Sánchez[1], L. Acuña[1], L. Soler[1], C.E. Toro[2]. *[1]Cuenta de Alto Costo; [2]Asociación Colombiana de Reumatología, Bogotá, Colombia*

Background: Rheumatoid arthritis (RA) is a chronic disease that implies high direct and indirect costs for the health system (1,2). According to the needs of the health care system, the clinical interests and the national regulatory framework, it was developed a national registry information of RA patients (3).

Objectives: To show how a registry of information that would meet the RA situation was developed and to present the results obtained from the analysis of the Registry on this first year.

Methods: A national RA Registry was created after a comprehensive literature review to identify the relevant variables to determine monitoring indicators used by health insurers and health services providers in the attention of patients with RA. Variables were selected and defined by an agreement with clinical experts, thematic and methodological experts and were evaluated by the Ministry of Health in order to review and approve the structure to gather the information.

Results: A structure of 89 variables contained was defined. All entities must report annually to the Registry all the patients with a diagnosis of RA, their clinical and demographic characteristics, and the process of care and costs (3). On its first year the Registry provided a baseline of the disease situation of 68.357 patients with RA. Prevalence, incidence, state of disease and drugs including synthetic and biologic DMARDs were analyzed (Table 1). Most important results were: mean age 57 years; relation women: men 5.2:1; age at onset of disease: 36 years, mean evolution time of disease: 7 years; population with DAS 28 measured 45.6%; mean DAS-28 2.8; percentage of the patient with DMARD therapy 78.9% and bDMARD 16.5%.

Table 1. Characteristics of the population

Variable	Obs	Mean/prop.	Std. Dev.	Min	Max
Age	68376	57.0	13.3	22	104
Age at onset of disease	13607	36.4	7.7	20	51
Evolution time of RA	37963	7.5	8.1	0	51
DAS28	30956	2.82	1.37	0	1
*Women	57461	84.04			
*Men	10914	15.96			
*bDMARD	11276	16.50			
*DMARD	53374	78.01			

Conclusions: A national Registry supported by an official policy, with data from the real world provided for healthcare insurers gives an opportunity to obtain a global vision and to identify failures and strengths in the attention process of RA, and to develop indicators to obtain better outcomes. In the future, through continuous efforts towards improving the quality of care provided, these will allow to monitoring and decreasing the burden of RA in the country and may serve as a model to other countries.

References:

[1] Muñetón GA, Quintana G. La epidemiología de la artritis reumatoide. Rev Colomb Reumatol. 2015 Sep [cited 2016 Jul 25];22(3):145–7. Available from: http://www.elsevier.es/es-revista-revista-colombiana-reumatologia-374-articulo-la-epidemiologia-artritis-reumatoide-S0121812315000845.
[2] Quintana G., Restrepo JP, Cáceres H, Rueda JD. Economic evaluation of the treatment of rheumatoid arthritis with anti-TNF biological therapy in Colombia. Acta Médica Colomb. 2011;36(1):24–9. Available from: http://www.scielo.org.co/pdf/amc/v36n1/v36n1a05.pdf.
[3] MSPS. Resolucion No. 1393. 2015. p. 14.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5017

AB1214-HPR SPINAL BRUCELLOSIS: A RETROSPECTIVE STUDY OF 30 CASES

S. Rekik, S. Boussaid, I. Abdelkafi, S. Hela, I. Cheour, M. Elleuch.
Rheumatology, la Rabta, Tunis, Tunisia

Background: Brucellosis is a major health problem in Mediterranean countries including Tunisia. The clinical presentation of this zoonosis varies considerable but osteoarticular involvement and spinal brucellosis particulary is the commonest complication.

Methods: This study was carried out between 2000 and 2015. One hundred and six patients with infectious spondylodicitis hospitalized in the department of rheumatology were analyzed. All patients were thoroughly interrogated subjected to a rigorous clinical examination and a battery of investigations including: complete blood count, urine analysis, blood culture, erythrocyte sedimentation rate, C - reactive protein (CRP) and serology for brucellosis. The imaging of spine ordered including: X-ray, bone scan and magnetic resonance imaging (MRI) with contrast enhancement.

Results: Thirty of the 106 patients (28%) proved to have spinal brucellosis. The mean age of these patients was 53 years (range 15–68 years) and female/men ratio at 1.5. The mean delay of diagnosis was 8 months. The following symptoms were observed: fever in 14 patients and back pain in all of patients. Other symptoms were less frequently observed, such as splenomegaly (2 patients), peripheral adenopathy (5 patients) and diarrhea (2 patients). Laboratory exams showed elevated erythrocyte sedimentation rate in 13 patients, high levels of CRP in all patients and leukocytosis in 11 cases. Wright serology was positive in 21 of the patients. Brucella melitensis was isolated in blood cultures in 2 cases. Standard X-rays were performed in all patients. They showed signs of spondylodiscitis in the lumbar spine in 20 cases, cervical in 2 cases and dorsal in 8 cases. Ct-scan and MRI confirms the diagnosis and showed associated epiduritis in 2 cases or abscess in 6 cases. Bone biopsy with histopathological examination was performed in 7 cases. A combination of cycline and rifampicin was given to all patients. The duration of therapy was between 6 and 8 weeks.

Conclusions: Brucellosis is present with various clinical signs in endemic areas and may simulate many diseases. The need for prompt diagnosis and treatment of spinal brucellosis is of utmost importance to prevent serious bone destruction and severe neurologic Sequelae.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6301

HPR interventions (educational, physical, social and psychological)

AB1215-HPR EFFECTS OF BEETROOT JUICE SUPPLEMENTATION N ENDOTHELIAL FUNCTION AND MARKERS OF INFLAMMATION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

A. Stavropoulos[1], E. Manthou[2], T. Nakopoulou[3], K. Georgakouli[2], A. Jamurtas[2]. *[1]Carnegie School of Sport, Leeds Beckett University, Leeds, United Kingdom; [2]School of Physical Education and Sports Science, University of Thessaly; [3]Radiology, General Hospital of Trikala, Trikala, Greece*

Background: Nitric oxide (NO) is central in the process of vasodilatation (1). Limited bioavailability of NO often associates with endothelial dysfunction, a precursor to atherogenesis (1). Such dysfunction is often observed in patients with chronic conditions such as Rheumatoid Arthritis (RA) (2) and Chronic Obstructive Pulmonary Disease (COPD) (3). Common therapies for this include the administration of nitrate-rich medication. However, in the general population beetroot juice supplementation has been shown to increase NO bioavailability (4). It could therefore have beneficial effects on endothelial function of these patients as well.

Objectives: To evaluate the effects of short-term beetroot juice supplementation on endothelial function in patients with RA and COPD.
Methods: A total of 28 patients, 9 with RA, 9 with COPD and 10 healthy controls participated in the study. Following consent, they were asked to report at the testing venue (Ultrasonography Laboratory, General Hospital of Trikala) early in the morning, following an overnight fast. Demographic and disease characteristics were recorded; height, weight, classical risk factor for cardiovascular disease and body composition were assessed. Endothelial function was assessed using flow mediated vasodilatation. They randomly received either beetroot (experimental leg) or blackcurrant juice (control leg), which they consumed daily for two weeks. Thereafter they were re-evaluated. Following a two-week washout period, they crossed over to the other leg of the study.
Results: There was no difference in pre-occlusion diameter between any of the time-points. Endothelial function was significantly improved following beetroot juice consumption for both patient groups (RA: 2.6% [0.9 – 6.2] vs 10.7% [6.2 – 11.7]; p=0.013. COPD: 3.4% [1.2 – 4.8] vs 7.8% [3.6 – 10.2]; p=0.034) while it remained relatively unaffected by blackcurrant consumption (Overall: 3.9% [0 – 5.1] vs 4.2% [2.3 – 6.1]; p=0.26).

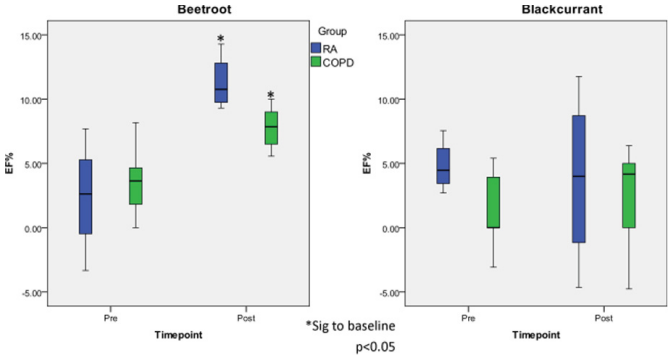


Figure 1

Conclusions: A two week consumption of beetroot juice seems to be able to improve endothelial function among patients with RA and COPD. This could elicit significant health benefits. Further research to investigate the benefits of longer-term use on endothelial function and related cardiovascular health, as well as disease symptoms, and quality of life is advocated.
References:
[1] Moncada, S. and Higgs, E.A. The discovery of nitric oxide and its role in vascular biology. British Journal of Pharmacology 2006, 147: S193–S201.
[2] Sandoo, A. et al. Vascular function and morphology in rheumatoid arthritis: a systematic review. Rheumatology 2011, 50 (11): 2125–2139.
[3] Clarenbach, C.F. Determinants of endothelial function in patients with COPD. European Respiratory Journal 2013, 42 (5): 1194–1204.
[4] Clifford, T. et al. The Potential Benefits of Red Beetroot Supplementation in Health and Disease. Nutrients 2015, 7.4: 2801–2822.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4519

AB1216-HPR THE EFFECTS OF APPLICATION OF IONTOPHORESIS AND PHONOPHORESIS IN PATIENTS WITH SUBACROMIAL IMPINGEMENT SYNDROME

A. Yildiz[1], E. Kusan[2]. *[1]Physiotherapy and Rehabilitation, Marmara University Health Sciences Faculty; [2]Physiotherapy and Rehabilitation, Kosuyolu Medipol Hospital, Istanbul, Turkey*

Background: Subacromial impingement syndrome (SIS) is defined as the mechanical compression of subacromial structures between the coraco-acromial arch and the humerus during active elevation of the arm above shoulder height.
Objectives: The aim of the study was to investigate the effects of applications of iontophoresis and phonophoresis, which has been used in addition to physiotherapy program on pain and disability level in patients with SIS.
Methods: The study was conducted with subjects (n=43) diagnosed with SIS. The subjects were divided into two groups randomly as iontophoresis group (IG) and phonophoresis group (PG). Diclofenac sodium iontophoresis was applied to the first group (n=22), diclofenac sodium phonophoresis was applied to the second group (n=21). In addition all of groups therapy program includes superficial heat, transcutaneous electrical nerve stimulation and exercise. The groups were evaluated before and after treatment in terms of pain and scores of shoulder disability. Visual analog scale was used to assess of pain (night pain, rest pain, pain with motion and pain in functional use), Shoulder Disability Questionnaire (SDQ) and Disabilities of the Arm Shoulder and Hand (DASH) were used to assess of shoulder disability.
Results: 43 patients with IS aged 18 to 65 years were recruited to the study. Demographic data were similar in the groups.
After treatments pain severity (night pain and pain in functional use) was significantly decreased in both groups (p<0,05) and in the scores of disability of shoulder (p<0,05) in both groups. Pain relief was similar in groups. SDQ and DASH scores were improved in two groups after treatments. But there was no difference between the groups in terms of functionality and disability scores.

Table 1. The level of pain, functionality and disability scores in groups

	IG		p	PG		p
	Before mean ± sd	After mean ± sd		Before mean ± sd	After mean ± sd	
Night pain severity	5,59±3,01	1,77±1,99	*	4,47±2,42	1,42±1,8	*
Severity of general pain	5,09±2,13	2,63±1,59	*	4,52±1,72	2,28±1,45	*
SDQ	48,00±20,75	22,36±20,41	*	50,12±21,18	19,35±15,84	*
DASH	38,90±14,74	19,63±9,37	*	41,57±9,53	22,64±10,37	*

IG: Iontophoresis group, PG: Phonophoresis group. *p<0,001.

Conclusions: This study shows that diclofenac sodium iontophoresis and phonophorosis that are used in patients with subacromial impingement syndrome have similar positive therapeutic effects on shoulder functions.
References:
[1] Kuhn JE. Exercise in the treatment of rotator cuff impingement: a systematic review and a synthesized evidence-based rehabilitation protocol. J Shoulder Elbow Surg. 2009 Apr;18(1):138–60.
[2] Sedeek SM et al. Subacromial impingement syndrome: review article. Hard Tissue 2013 Sep 28;2(4):39–43.
[3] Ozsahin M et al. Adaptation of the Shoulder Disability Questionnaire to the Turkish population, its reliability and validity. International Journal of Rehabilitation Research. 2008;31(3):241–45.
[4] Düger et al. Kol, omuz ve el sorunları anketi (Disabilities of the Arm, Shoulder and Hand – DASH) Türkçe uyarlamasının güvenirliği ve geçerliği. Fiyoter Rehabil. 2006;17(3):99–107.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4883

AB1217-HPR THE EFFCET OF ADDING WII FIT® GAMES TO TRADITIONAL REHABILITATION ON PAIN, QUALITY OF LIFE AND FUNCTIONALITY AFTER ACL RECONSTRUCTION

Z.B. Karakoç, T. Kuru Çolak, B. Kapşigay, Z. Sarı, M.G. Polat. *Physical Therapy and Rehabilitation, Marmara University Health Science Institute, Istanbul, Turkey*

Background: Wii Fit® games are widely used in the rehabilitation field due to their audiovisual feedback and motivating effect (1). Although it is well known that Wii Fit® games improve the quality of life in various groups (2, 3), there is no study on those who have undergone anterior cruciate ligament (ACL) arthroscopic surgery.
Objectives: The aim of this study was to determine the effect of Wii Fit® games on pain, quality of life and lower extremity functionality after ACL reconstruction.
Methods: Patients who underwent arthroscopic ACL reconstruction surgery in Kartal Dr. Lutfi Kırdar Training and Research Hospital were included in this study. Being volunteer for this study, not receiving any other treatment after surgery and being in the first 6 months after surgery were determined as inclusion criteria. Having any orthopaedic injury or congenital deformitiy and having vision, balance or neurologic problems were defined as exclusion criteria. After recording demographic data patients' pain, quality of life and lower extremity functionality were evaluated with "Visual Analog Scale (VAS)", Anterior Cruciate Ligament Quality of Life (ACL-QoL) Scale and "Lower Extremity Functionality Scale (LEFS)", respectively.
Patients received accelerated rehabilitation program 3 days per week, for 6 weeks. Wii Fit® games has added to accelerated program for 40 minutes in every treatment sessions in the last three weeks. Assessments were performed at the baseline 3th week and, end of the treatment. The SPSS v11.5 was used for data analysis.
Results: Twelve males with a mean age of 29±8,51 years were included in this study. Their average body mass index, time between injury and surgery and time between surgery and the beginning of rehabilitation were 25,82±2,85 kg/m^2, 374 days and 30±42,62 days, each seperately. Pain improved significantly during the treatment (p=0.012). The quality of life level increased significantly at the end of the study compared to the 3th assessment (p=0.041). Lower extremity functionality improved during the rehabilitation (p=0.003).
Conclusions: Patients participating in this study expressed Wii Fit® games as funny and easy method to utilize. Wii Fit® games are suitable for use in patients who have had ACL arthroscopic surgery.
References:
[1] Minyoung L, Dongwon S, Jaebum S, Jungjin K, Seon-Deok E, BumChul Y. Patient perspectives on virtual reality-based rehabilitation after knee surgery: importance of level of difficulty. Journal of Rehabilitation Research and Development. 2016; 53 (2): 239–52.
[2] Hammond, J., Jones, V., Hill, EL., Green, D., Male, I. An investigation of the impact of regular use of the Wii Fit to improve motor and psychosocial outcomes in children with movement difficulties: a pilot study. Child: care, health and development. 2014; 40 (2): 165–175.
[3] Plow, M., Finlayson, M. Potential benefits of Nintendo Wii Fit among people with multiple sclerosis: a longitudinal pilot study. International journal of MS care. 2011; 13 (1): 21–30.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6105

AB1218-HPR EFFECTIVENESS OF PLATELET-RICH PLASMA ON FUNCTION AND PERFORMANCE IN PATIENTS WITH KNEE OSTEOARTHRITIS: PRELIMINARY RESULTS

D.C. Sarac[1], B. Unver[2], S. Cekmece[2], M. Erduran[3]. *[1]Division of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Izmir Katip Celebi University; [2]School of Physiotherapy and Rehabilitation; [3]School of Medicine, Department of Orthopaedics, Dokuz Eylul University, Izmir, Turkey*

Background: Osteoarthritis is one of the most painful conditions and the most frequent cause of functional limitation and disability. There are variety of methods used in osteoarthritis (OA) treatment, including, physical therapy, exercise, intraarticular injections, surgery, etc. Platelet-rich Plasma (PRP) is a relatively new autologous biologic treatment that is used for stimulating cartilage healing process and improving the symptoms. Although the effects of PRP injection on pain and function investigated before, as to our knowledge there are no studies related to performance.
Objectives: Aim of this study was to investigate effectiveness of PRP on improving function and performance in patients with knee osteoarthritis.
Methods: This study included 28 patients (16 F, 12 M) who were affected by grade 1–3 bilateral knee OA according to Kellgren-Lawrence Scale. Patients received three injections of PRP that were performed at monthly intervals by the same doctor. All patients were evaluated before and six months after the first injection. Primary outcome measures were: Stair Climbing Test (SCT), 50-Foot Walk Test (50 FWT), 30-sec Chair Stand Test (30 CST) and Timed Up and Go Test (TUG), IOWA Score. Additionally, Hospital for Special Surgery Score (HSS) was also recorded as a secondary outcome measure. Wilcoxon signed-rank test is used for interpreting the differences between before and after the injections.
Results: All patients completed the study with no adverse effects. The mean age of the patients were 59±7.66 years. Improvements were determined for all outcome measures after 6 months regard to baseline results ($p<0.01$) (Table 1).

Table 1. Comparision of Primary and Secondary Outcomes at Baseline and After 6 months

	Before Median (IQR 25/75)	6 Months After Median (IQR 25/75)	P*
Stair Climbing Test	16 (10.55/19.75)	13.1 (9.25/16.75)	0.001
50-Foot Walk Test	29.5 (27.0/32.45)	27.26 (25.1/30.32)	0.001
30-sec Chair Stand Test	10.5 (9.25/14.0)	12.5 (10.1/15.75)	0.001
Timed Up and Go Test	9.25 (7.25/14.5)	8.1 (6.58/10.15)	0.001
IOWA Score	10.2 (8.92/12.87	9,9 (8.12/10.75)	0.008
HSS Right	63.5 (55.0/75.0)	75 (66.0/66.75)	0.001
HSS Left	66.5 (55.25/79.25)	78.5 (70.0/85.0)	0.001

Wilcoxon signed-rank test. IQR: Interquartile Range, HSS Right: Hospital for Special Surgery Score of right knee, HSS Left: Hospital for Special Surgery Score of left knee. *$p<0.05$.

Conclusions: Our preliminary findings show that PRP is safe and effective autologous biologic agent that might improve function and performance in patients with mild to moderate knee OA and; could be considered as a treatment option in patients with knee OA.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5952

AB1219-HPR EXPERIENCES OF SWEDISH "PAIN SCHOOL - COMPETENCE FOR LIFE" OF PATIENTS WITH CHRONIC WIDESPREAD PAIN - A QUALITATIVE INTERVIEW STUDY

C. Goksör[1,2], A. Bergenheim[1,3], K. Mannerkorpi[1]. *[1]Neuroscience and Physiology, Gothenburg University, Sahlgrenska Academy; [2]Närhälsan Frölunda Rehab, Gothenburg; [3]Närhälsan Uddevalla Rehab, Uddevalla, Sweden*

Background: Chronic pain is generally associated with low activity level, low work capability, and negative health consequences (1). Education and exercise have shown effective results for patients with chronic pain (2), and is according to EULAR 2016 recommendations first line interventions for patients with fibromyalgia (3). This educational program "Pain school - Competence for life" for patients with chronic pain was developed by the Swedish Rheumatoid Association together with health care professionals for use in primary health care, but is not previously evaluated. The pedagogy is based on a biopsychosocial perspective and self-efficacy with the purpose to provide knowledge, experience and skills within pain, balance of daily living and physical activity. The program comprises four educational group sessions and 10 weeks of physical activity.
Objectives: To gather deeper knowledge about how patients with chronic widespread pain experienced participation in the Pain school –Competence for life", with focus on changes in perception of pain and/or lifestyle.
Methods: 12 women (age 25–72 years) with chronic widespread pain were included in this qualitative interview study set in primary health care. Informed consent were signed by all participants. Semi-structured individual interviews were held 10 weeks after completion of four educational group sessions. Interviews were conducted by two authors and transcribed verbatim.
Results: One theme and four categories were identified. An overarching theme, describing the participants' experiences of the educational program, was *a meaningful learning process*. It covered four categories: *increased understanding of body and mind, new strategies and ways of thinking, experienced value of participation*, and *preconditions for change*. Participants described increased knowledge, awareness and acceptance relating to their symptoms and limitations. They expressed new strategies relating to managing pain, physical activity, and everyday life. Both individual and social value of participation was described, such as increased well-being, decreased anxiety and improved relationships. Group dynamics, structure of education and former knowledge was described to predispose change in perception of pain and lifestyle.
Conclusions: The results provide deeper knowledge about patients' experiences of the educational program Pain School Competence for life. The educational program appears to provide a meaningful and well-functioning structure for education for patients with chronic widespread pain in primary health care. Further, this can contribute to improve education and rehabilitation for patients with CWP provided by physiotherapists and occupational therapists in primary health care.
References:
[1] Harker J, Reid KJ, Bekkering GE, Kellen E, Bala MM, Riemsma B, et al. Epidemiology of chronic pain in denmark and sweden. Pain Res Treat. 2012; 1–30.
[2] Hassett AL, Williams DA. Non-pharmacological treatment of chronic widespread musculoskeletal pain. Best Pract Res Clin Rheumatol. 2011;25: 299–309.
[3] Macfarlane GJ, Kronisch C, Dean LE, Atzeni F, Häuser W, Fluß E, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis. 2016;0: 1–11.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4058

AB1220-HPR THE LEVEL OF ADHERENCE OF RHEUMATOLOGY PATIENTS IN SLOVENIA

D. Stanković, M. Pavic Nikolic, A. Hočevar. *Department of Rhematology, University Medical Centre Ljubljana, Ljubljana, Slovenia*

Background: Patient adherence is one of the central factors associated with the control of patient's symptoms, good functional ability and longevity. Health care professionals have significant role in their daily practice to improve the adherence to medications.
Objectives: We aimed to assess the adherence of patients treated at our secondary/tertiary rheumatology center.
Methods: Data were collected in a prospective manner. We investigated the level of self-reported adherence to treatment in 115 consecutive patients (81 women; mean age (SD) of 56.5±14.7 years) with systemic inflammatory diseases in December 2016. We used the 19-item questionnaire-Compliance-Rheumatology (CQR).
Results: We found optimal adherence in 52% of patients: the average (SD) adherence rate was 71.1±9.42. We didn't find any significant differences between adherent and nonadherent patients regarding patient age, gender, the diagnosis of rheumatic disease and disease duration time, however, patients with higher education level (at least graduate level) were more compliant than those without any formal education (p=0.006). In addition there was no association between adherence and the type of medication (csDMARD, bDMARD) (p=0.39). Patient data are presented in the table 1.

Table 1. The adherence according to the patient diagnosis

Diagnosis, n (%)		Disease duration, year	CQR total score, mean (SD)	CQR quartiles, n (%)			
				Least adherent n (%)		Most adherent n (%)	
				<64	64–71,9	71,9–87,9	87,9+
RA	65 (56%)	10,8	69,90 (9,56)	18 (28%)	19 (29%)	28 (43%)	0
PSA	14 (12%)	14,7	74,18 (10,62)	3 (22%)	1 (7%)	10 (71%)	0
AS	14 (12%)	9,7	73,43 (10,73)	2 (14%)	3 (22%)	9 (64%)	0
Other	22 (20%)	12	70,8 1 (11,59)	6 (27%)	3 (13%)	12 (55%)	1 (5%)

Conclusions: Our study showed lower adherence rate than expected. To improve patient adherence we should work more in the future on providing additional knowledge and support to patients.
Acknowledgements: Special thanks to our colleagues Tadeja Šušteršič and Albina Stanovnik.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3073

AB1221-HPR COMPARISON OF DMARD THERAPIES ON NSAID INTAKE, DISEASE ACTIVITY, FEAR OF MOVEMENT, AND QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

G.I. Kinikli[1], S. Karahan[2], A. Ates[3], M. Turgay[3], G. Kinikli[3]. *[1]Dept. of Physiotherapy and Rehabilitation, Hacettepe University Faculty of Health Sciences; [2]Dept. of Biostatistics, Hacettepe University Faculty of Medicine; [3]Dept, of Rheumatology, Ankara University Faculty of Medicine, Ankara, Turkey*

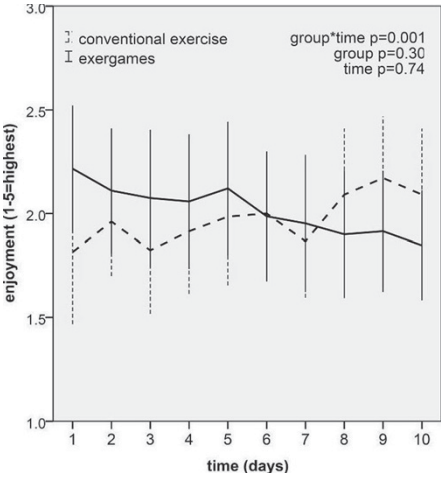
Background: Ankylosing Spondylitis (AS) may result in loss of mobility and function; therefore, patients can experience pain and stiffness with a loss of physical function in addition to severe impairment in their quality of life. Standard treatment of AS consists of nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy.

Objectives: The aim of this study was to compare the effectiveness of DMARD therapies on requirements for NSAIDs, disease activity, fear of movement, and quality of life in AS patients.
Methods: A total of 74 patients diagnosed according to the modified New York criteria for AS were enrolled. To calculate NSAID intake, the type of NSAID, dose, and percentage of days with intake were recorded in conjunction with DMARD therapy, age, body mass index (BMI), and disease duration. Patients were assessed to measure several parameters: 1) disease activity using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; 2), fear of movement as assessed by the Tampa Scale for Kinesiophobia (TSK); and 3) quality of life using the Ankylosing Spondylitis Quality of Life Scale (ASQoL) status from the patient's perspective.
Results: Seventy-four patients (36 women, 38 men; mean age: 43.81±10.18 years; mean disease duration: 9.89±8.50 years; BMI: 28.20±5.07) treated with four different DMARDs (Adalimumab+Golimumab [ADA+GO]=17; Infliximab [INFX]=19; Etanercept [ETA]=13; Sulphasalazine [ST]=25) were included. NSAID intake was significantly lower in the INFX therapy group (mean: 28.1±81.5) compared to the ADA+GO (mean: 33.3±76.0), ETA (mean: 33.5±58.2), and ST therapy groups (mean: 68.1±76.1) (p=0.003). BASDAI scores (mean: 3.9±2.4), NSAID intake (mean: 68.1±76.1; p=0.003), and AS-QoL scores (mean:10.2±7.4) were significantly higher in the ST group compared to the other drug groups. TSK scores were also similar between different NSAID intake groups (p=0.089).
Conclusions: According to our results, ST was not effective enough even with concomitant therapy consisting of a single oral dose of NSAID or standard doses of oral corticosteroids in terms of disease activity, fear of movement, and quality of life in AS patients.
References:
[1] Braun J, Baraliakos X, Heldmann F, et al. Tumor necrosis factor alpha antagonists in the treatment of axial spondyloarthritis. Expert Opin Investig Drugs. 2014;23:647–659.
[2] Rohekar S, Chan J, Tse SM, et al. 2014 update of the Canadian Rheumatology Association/Spondyloarthritis Research Consortium of Canada treatment recommendations for the management of spondy- loarthritis. Part I: principles of the management of spondyloarthritis in Canada. J Rheumatol. 2015;42:654–664.
[3] Rohekar S, Chan J, Tse SM, et al. 2014 update of the Canadian Rheumatology Association/Spondyloarthritis Research Consortium of Canada treatment recommendations for the management of spondy- loarthritis. Part II: specific management recommendations. J Rheu- matol. 2015;42:665–681.
Acknowledgements: We would like to thank Rheumatology Nurse Ayten Yuksek in our department for monitoring and documenting of the data, and our patients for assistance with their valuable participation to our study.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1391

AB1222-HPR EXERGAMES VERSUS SELF-REGULATED EXERCISES WITH INSTRUCTION LEAFLETS TO IMPROVE ADHERENCE IN GERIATRIC REHABILITATION: A RANDOMIZED CONTROLLED TRIAL

J. Kool[1], P. Oesch[1], L. Fernandez-Luque[2], E. Brox[3], G. Evertsen[3], A. Civit[4], R. Hilfiker[5], S. Bachmann[6,7]. *[1]Department of Physical Therapy, Kliniken Valens, Valens, Switzerland; [2]Qatar Computing Research Institute, Hamad Bin Khalifa University, Qatar Foundation, Doha, Qatar; [3]Norut, Tromsø, Norway; [4]Architecture and Computer Technology Department, University of Seville, Seville, Spain; [5]University of Applied Science HES-SO, Sion; [6]Department of Geriatrics, Inselspital, Bern University Hospital, University of Bern, Bern; [7]Department of Rheumatology, Kliniken Valens, Valens, Switzerland*

Background: Improving mobility in elderly persons is a primary goal in geriatric rehabilitation (Bachmann 2010). Self-regulated exercises with instruction leaflets are used to increase training volume but adherence is often low. Exergames may improve adherence. This study therefore compared exergames with self-regulated exercise using instruction leaflets.
Objectives: To evaluate short-term effects of exergames versus self-regulated exercise using instruction leaflets. Primary outcome was adherence. Secondary outcomes were enjoyment, motivation and balance.
Methods: Design: single center parallel group non-blinded randomized controlled trial with central stratified randomization (Hasselmann 2015). Setting: center for geriatric inpatient rehabilitation. Included were patients over 65 with mobility restrictions who were able to perform self-regulated exercise. Patients were assigned to self-regulated exercise using a) exergames on Windows Kinect® (exergame group EG) or b) instruction leaflets (conventional group CG). Physical therapists instructed self-regulated exercise to be conducted twice daily during thirty minutes during ten working days. Patients reported adherence (primary outcome), enjoyment and motivation daily. Balance during walking was measured blind with an accelerometer. Analysis was by intention to treat. Repeated measures mixed models and Cohen's d effect sizes (ES, moderate if >0.5, large if >0.8) were used to evaluate between-group effects over time.
Results: We evaluated 217 patients and included and 54, 26 in the EG and 28 in the CG. Adverse effects were observed in two patients in the EG who stopped because of pain during exercising. Adherence was comparable at day one (38 min. in the EG and 42 min. in the CG) and significantly higher in the CG at day 10 (54 min. in the CG while decreasing to 28 min. in the EG, p=0.007, ES 0.94, 0.39–0.151). Benefits favoring the CG were also observed for enjoyment (p=0.001, ES 0.88, 0.32 – 1.44) and motivation (p=0.046, ES 0.59, 0.05 -1.14)). There was no between-group effect in balance during walking.



Conclusions: Self-regulated exercise using instruction leaflets is superior to exergames regarding adherence, enjoyment and motivation in a geriatric inpatient rehabilitation setting. Effects were moderate to large. There was no between group difference in balance during walking.
References:
[1] Bachmann S, Finger C, Huss A, Egger M, Stuck AE, Clough-Gorr KM. Inpatient rehabilitation specifically designed for geriatric patients: systematic review and meta-analysis of randomised controlled trials. BMJ. 2010;340, c1718.
[2] Hasselmann V, Oesch P, Fernandez-Luque L, Bachmann S. Are exergames promoting mobility an attractive alternative to conventional self-regulated exercises for elderly people in a rehabilitation setting? Study protocol of a randomized controlled trial. BMC Geriatr. 2015;15;108.
Acknowledgements: The present study is part of the GameUp Project, focusing on game-based mobility training and motivation of elderly persons, and is co-funded by the European research and development joint program "Ambient Assisted Living" (AAL-2011–4-090). We thank Viviane Hasselman and Stine Staubach for data collection.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1176

AB1223-HPR BELIEFS AND ATTITUDES OF ITALIAN NURSES TOWARDS PLACEBO AND NOCEBO RESPONSES INDUCED BY CONTEXTUAL FACTORS IN CLINICAL PRACTICE

M. Testa[1], G. Rossettini[1], T. Geri[1], A. Viceconti[1], L. Colloca[2,3], A. Palese[4]. *[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova, Savona, Italy; [2]Department of Pain Translational Symptom Science, School of Nursing; [3]Department of Anesthesiology, School of Medicine, University of Maryland, Baltimore, United States; [4]Department of Medical and Biological Sciences, University of Udine, Udine, Italy*

Background: Placebo and nocebo represent psycho-neuro-immuno-endocrinological responses commonly encountered in nursing care (1,2). A new paradigm proposed the contextual factors (CF) as mediators and moderators of these responses (3). To date, the knowledge about the awareness of CF and their use in nursing is scant.
Objectives: The goal of this study was to examine frequency of use, beliefs and attitudes of Italian specialised nurses regarding the contextual factors.
Methods: In December 2016, through SurveyMonkey Software®, an online survey was conducted by sending a questionnaire to the members of four Italian Nursing Association, grouping nurses specialized in Neuroscience, Medical, Geriatric and Diabetic care. Behaviours, beliefs and attitudes of nurses about the implementation of CF in clinical practice were assessed by a 17 items questionnaire and resulting data were analysed by descriptive statistic.
Results: Of the 1411 members of the involved Nursing Associations invited to participate to the survey 425 responded (30.1%). An high number of respondent nurses adopts CF often in their practice (42%). They believe that CF can positively influence acute pain (47.5%), chronic pain (61%) and rheumatologic disorders (42%). 34% of responders consider the use of CF, if it can determine beneficial psychological effects, as ethically acceptable. 15.5% responders oppose to the adoption of CF when based on deception or if they undermines trust between nurses and patients. A relevant number of nurses (24%) do not communicate the use of CF to their patients and 19% implement CF as addition to other nursing interventions to optimize clinical responses. Nurses explain the power of CF through patient's expectation and psychological mechanism (11%).

Conclusions: The Italian specialised nurses use CF quite frequently and believe that their use has the capacity of positively influencing the clinical outcome. Larger surveys are needed to understand the proportion of use of CF by nurses in common clinical practice in Italy.

References:
[1] Miller LR, Miller FG. Understanding placebo effects: Implications for nursing practice. Nurs Outlook. 2015 Sep-Oct;63(5):601–6.
[2] Häuser W, Hansen E, Enck P. Nocebo phenomena in medicine: their relevance in everyday clinical practice. Dtsch Arztebl Int. 2012 Jun;109(26):459–65.
[3] Palese A, Rossettini G, Testa M. Placebo and nocebo responses in nursing practice: a discussion paper on the role of contextual factors. In revision at Nurs Inq.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4379

AB1224-HPR COULD WE USE THE LAY REFERRAL SYSTEM TO IMPROVE THE EARLY ARTHRITIS CLINIC EFFICIENCY?

M. Dobroiu[1], M. Trandafir[1], C. Ioan[1], D. Vasile[1], D. Predeteanu[2], R. Ionescu[2], F. Berghea[2] on behalf of RCRD. *[1]Rheumatology, Sf. Maria Hospital; [2]Rheumatology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania*

Background: The professional's monopoly on knowledge about disease and its treatment is something gone now, in the era of internet and patient consumerism. In addition, the interest of rheumatologists (and the interest of the society, too) shifted toward early recognition of the disease and early arthritis clinics. Education is definitely one of the solutions to increase the awareness of potential patients regarding rheumatic diseases. However most of rheumatic diseases are not very frequent in the population that raise the problem of cost efficacy of the education process. Per Eliot Freidson's view, the members of every community of whatever kind share some cultural understandings about disease, treatment, and cure. The lay community network could be considered an instrument for dissemination of proper knowledge regarding health and could help to earlier recognition of a sign of disease related to early arthritis.
Objectives: To identify the opportunity of using lay network for early arthritis referral. In addition, we intended to identify the most suitable vectors from this network to be used for education and dissemination of medical knowledge.
Methods: 48 rheumatic patients (mean age (SD): 50.8 (14,7)) consecutively admitted in one tertiary clinic have been invited to answer to a structured questionnaire. Sex ratio (M: F) was 1:2, average disease duration 7.7 (8.3) years.
Results: In 28.3% cases the first sign of disease was noticed not by the patient but by somebody else, for 36.7% a delay of several months to one year was declared between first sign of disease and professional examination, 71.7% use to discuss bout health problems with their lay network (often and very often), 76.1% consider them able to give pertinent advices regarding the disease they suffer from, 45,7% are ready to act as an education vector and 41,3% are ready to participate in additional education programs. They interest in such activity is not related to gender, education level or work status.
Conclusions: Lay network referral could be a powerful instrument to reduce the duration between onset of rheumatic symptoms and medical visit, to increase the awareness regarding rheumatic disease, to reduce the cost of health education. Health professionals should understand how to use these networks.

References:
[1] Freidson, Eliot. 1960. "Client Control and Medical Practice." American Journal of Sociology 65:374–82.
[2] Barley, Stephen R., and Gideon Kunda. 2004. Gurus, Hired Guns, and Warm Bodies: Itinerant Experts in a Knowledge Economy. Princeton, NJ: Princeton University Press.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4241

AB1225-HPR A PROGRAM BASED ON PSYCHOEDUCATION FOR RHEUMATOID ARTHRITIS PATIENTS

P. Osorio[1], L. Villarreal[2], P. Santos-Moreno[3], D. Buitrago-Garcia[4], G. Cajiao[5], A.M. Orozco[5]. *[1]Psychology; [2]Psychology and processes; [3]Rheumatology; [4]Epidemiology, Biomab, Center for Rheumatoid Arthritis, Bogota; [5]Psychology, El Bosque University, Bogota, Colombia*

Background: The National Institute of Arthritis and Musculoskeletal and Skin Diseases defines rheumatoid arthritis (RA) as a chronic disease that affects the joints, causing pain, swelling, stiffness, reduced mobility and affection of internal organs. In order for patients to be able to learn to accept and integrate the disease as a part of theirs daily life, it is important that they have enough information and knowledge about their health condition. The strategy of psychoeducation is important because it involves the patient actively and seeks to have specialist who provide relevant, clear, and comprehensive information. In this way, a change is generated at level of beliefs and myths on the disease, and suggests suggestions for coping with situations for the management of the disease's impact on the patient's life.
Objectives: To determine the effect of a psychoeducation program on the quality of life and commitment to the treatment of patients diagnosed with RA from an specialized center in Bogotá.
Methods: We conducted a quasi-experimental study with two independent groups, one experimental and one for control. The Inclusion Criteria was: patients with RA over 30 years old that knew how to write and read with mobility resources. We excluded patients with emotional stress, stroke, and diagnosed cognitive deficit or with patients with consumption of psychoactive substance. We applied the Analog Visual Scale (EVA), a Quality of Life Questionnaire - Specific for patients with Rheumatoid Arthritis (QOL-RA). Data Analysis: when performing the normality test, the QoL-RA results were parametric and the analysis was performed with Student's t test for independent measurements. On the other hand, the results of the EVA and CQR were non-parametric, for that reason we worked with the Mann Whitney U-test.
Results: We included 36 patients, men (4) and women (32), aged between 35 and 75 years, with diagnosis of RA, which belong to the integral model of RA specialized center. The subjects that patients preferred were: Disease management, changes in health condition, training in abilities for self-care among others. Statistical analysis showed that, when we evaluated quality of life T-student test did not showed any statistical differences between pre and post test results in both groups. The Man Wittney test showed statistical differences between groups (u=70,500, z=241,500, p=,004) regarding the compromise with the RA treatment, but it did not showed differences in regards of pain intensity between groups.
Conclusions: We recommend a strategy to facilitate the process of data collection in pre-test and post-test. For the next application of the program, it is suggested that the sample of patients must be increased, to increase the duration of each session and the number of sessions of the program. In order to achieve the patients' attendance at the program, maintain permanent communication (may be by telephone). To have printed or recorded material (Brochures, guides, CDs, etc.) is recommended with the most relevant to each session of the program.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6189

AB1226-HPR VACCINATION COMPLIANCE IN AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES (AIRDS): ROLE OF SPECIALIST NURSE

R.D. Thakran, S.S. Baghel, R. Rawat, C. Messi, S. Kapoor, S. Garg, A.N. Malaviya. *Rheumatology, Indian Spinal Injuries Centre, New Delhi, India*

Background: The patients with autoimmune inflammatory rheumatic diseases (AIRDs) have double the risk of infections as compared to the general population this may be due to highly inflammatory nature of the disease, the drug used, and the co-morbidities. In recent years, the efficacy of vaccinations has been proven in decreasing morbidities and mortality among these patients, hence, it reduces the cost of the treatment and improves the quality of life of the patients. However, low vaccination compliance is a global problem. Therefore, in this study, we tried to assess the effect of nursing counselling on vaccinations compliance.
Objectives: To assess the efficacy of counseling by the specialist rheumatology nurses in vaccination compliance among AIRDs patients.
Methods: - All the adult patients (>18yrs), suffering from AIRDs, were advised vaccinations between January to December 2016 were enrolled in this study. The basic demographic and disease-related data captured with details of vaccinations such as date of advice of vaccination and reasons for non-compliance were recorded. The patients were intensely counselled by specialist nurses about the importance and needs of vaccination, clarifying their doubts. Reinforcement of the same was carried out in the follow-up visits.
Results: A total of 506 patients (374 female, 73.9.2% and 132 male, 26%), with mean age 48 years, diagnoses; rheumatoid arthritis: 378 (74.75%), Spondyloarthropathy: 80 (15.81%) other autoimmune rheumatic disease 48 (9.48%). Co-morbidities status: 309 (61%) having multiple co-morbidities and 197 (38.9%) have no co-morbidities. The vaccination compliance outcome is shown in table.

Table 1

Vaccine	Patients	Compliant	Non-compliant	Same day	Within 3 months	Within 6–9 months
Pneumovac 23	506	456 (90.1%)	50 (9.9%)	306 (67.1%)	103 (22.5%)	43 (9.4%)
Prevnar 13	244	211 (86.4%)	33 (13.6%)	143 (58.6%)	61 (25.0%)	7 (3.3%)
Influvac	506	443 (87.5%)	63 (12.5%)			

Conclusions: The compliance rate of all vaccinations was highest on the same day when it was prescribed. This was despite the fact that the patients pay for their own vaccinations without any third party payment. However, the compliance decreases with increase in the period when it was prescribed with the passage of time. This suggests that intense counselling, availability of vaccines at premises (pharmacy) and administration of vaccination free of cost are a few of the contributory factors which can boost the compliance of the vaccination among patients with AIRDs

References:
[1] S.Shaffu, S.Mumtaz S, R.Neame: Vaccination in rheumatoid arthritis: Are your vaccinations up to date? Ann Rheum Dis 2013; 71:662.
[2] Gluck T. Vaccinate your immunocompromised patients. Rheumatology 2006:45:9–10.

Disclosure of Interest: R. Thakran: None declared, S. Baghel: None declared, R. Rawat: None declared, C. Messi: None declared, S. Kapoor Consultant for: Advisory board of Novartis,Pfizer, S. Garg Consultant for: Advisory board of Intas,

A. Malaviya Consultant for: Advisory board of IPCA, Janssen, Pfizer, Roche, BMS,Dr. Reddy's, Zydus
DOI: 10.1136/annrheumdis-2017-eular.2344

AB1227-HPR VALIDATION AND APPLICABILITY OF A NOVEL OSTEOMALACIA KNOWLEDGE BASED EDUCATIONAL INSTRUMENT (OKQ)

S. Robinson[1], R. Waxman[2], D. Walker[1], P. Helliwell[2], A. Adebajo[3]. *[1]Rheumatology, North Tynside General Hospital, North Shields; [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds; [3]Faculty of Medicine, Dentistry and Health, University of Sheffield, Sheffield, United Kingdom*

Background: Osteomalacia is caused by a deficiency of vitamin D and can be corrected by changes in diet, lifestyle and supplementation. Consequently, it is a condition where education has a primary role in prevention.
Objectives: If educational interventions are to be developed and evaluated, then an instrument for measuring knowledge is required. This has led us to develop a novel Osteomalacia Knowledge Questionnaire (OKQ).
Methods: Based on nominal group technique, a steering group of people who are knowledgeable about osteomalacia, educational theory and questionnaire development was convened. The group decided to use true and false questions. Important areas of knowledge of osteomalacia were first determined by the group and then relevant statements which were true or false were written and grouped into 8 sections of 5 questions, each covering the different areas of knowledge. This resulted in a knowledge instrument with 40 questions in all. The questions were tested for utility and ambiguity in the group and modified and replaced accordingly.
The questionnaire was then trialled in 37 people of South Asian origin (an osteomalacia susceptible population), in three groups. Participants were initially administered the OKQ and then received an educational intervention comprising a practitioner led education session on osteomalacia, including a presentation and written or electronic material. Participants were re tested with the OKQ after 6 weeks.
Although there is no "gold standard" for measuring knowledge about osteomalacia, if effective, increased knowledge should lead to an increase in vitamin D (Vit D) levels and a decrease in parathormone (Pth) levels. Vitamin D and Parathormone levels were measured alongside the OKQ in 2 of the groups before and after the educational intervention
Results: Baseline knowledge about osteomalacia was low pre education averaging only 12.7 out of 40 (range 0–29) (n=37).
A total of 30 participants (81%) attended for the follow up test. They averaged a score of 13.9 at baseline and 23.4 at follow up. This was statistically significant (p=0.002 Mann Whitney) and demonstrated sensitivity to change of the OKQ.
Knowledge at baseline was correlated with vit D and Pth blood levels for two of the groups (n=27). This showed correlation coeficients of 0.128 and -0.407 respectively. For change of knowledge and change of parathormone (n=21) the r value was -0.324 suggesting a relationship between knowledge and Pth that is worthy of confirmation through further studies.
Conclusions: A novel questionnaire has been developed that has face validity for testing knowledge about osteomalacia. It has proved feasible and shown sensitivity to change. It has also shown promising correlation with biochemical measures of osteomalacia.
Acknowledgements: This study was funded by Arthritis Research United Kingdom.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5280

AB1228-HPR IN ABSENCE OF SPECIFIC ADVICE, WHAT DO THEY EAT AND AVOID? DOES IT MATTER? DIET EVALUATION OF INDIAN (ASIAN) PATIENTS OF RA IN A COMMUNITY RHEUMATOLOGY CLINIC

T. Kianifard, M. Saluja, A. Chopra. *Rheumatology, Center for Rheumatic Diseases, Pune, India*

Background: Diet in RA is generally considered to be inadequate/inappropriate. Rheumatologists often neglect this important patient concern. ACR/EULAR guidelines do not provide adequate advice. Ayurveda (ancient India medicine system) with highly restricted diet is popular with Indian patients.
Objectives: To evaluate diet adequacy in patients of RA in our setting
Methods: 139 consenting patients (ACR 1987 classified)on long term supervised care and 165 unmatched healthy subjects (mean age 37.7 years) were interviewed in no particular order as per protocol; cross sectional design. A 10 day diet recall period and a-priori validated questionnaires was used. National (India) recommended daily allowance (RDA) and diet analysis (web based and food composition tables) methods were used.Standard CRF captured clinical data [mean pain VAS 4.6 cms,mean HAQ score (Indian version) 6.5]. Standard statistical analysis (SPSS) was done; significant $p<0.05$.
Results: Table 1 (women) and 2 (men) show average daily energy expenditure and consumption of selected food items, RDA and p values (on comparison: P (1) for patient versus control, P (2) for patient versus RDA: p by Mann Whitney). Compared to RDA, patient consumption was significantly higher for most of the items except K; includes calcium, phosphorus, zinc, iron, folic acid, vitamin B group (data not shown in Tables). When compared to healthy subjects, consumption was significantly lower for female patients but not different for men (except for K). Reduction in diet K in RA group was more pronounced for women. All patients tested normokalemic (mean serum K+ 4.37 mEq/l). No meaningful correlation between diet components and disease measures (data not shown).Food avoidance patterns identified a-priori did not seem to impact disease measures (data not shown). 44% RA and 77% controls consumed vegetarian diet (excluding eggs). Patient dependence for diet recall and measure was the important limiation.

Table 1. Women RA subjects and healthy control

Component	Patient (n=115)	Control (n=122)	RDA	P (1)	P (2)
Energy (kilocalorie)	2825	3436	2230	0.02	0.03
Carbohydrate (g/d)	457	532	NA	0.16	0.00
Protein (g/d)	94	127	55	0.00	0.00
Fat (g/d)	69	84	25	0.00	0.00
Sodium (mg/d)	3112	3221	1902	0.56	0.00
Potassium (mg/d)	1223	3393	3225	0.000	0.00

Table 2. Men RA subjects and healthy controls

Component	Patient (n=22)	Control (n=43)	RDA	P1	P2
Energy (Kcal)	2737	2829	2730	0.74	0.87
Carbohydrate (g/d)	439	425	NA	0.08	–
Protein (g/d)	92	109	60	0.33	0.07
Fat (g/d)	68	77	30	0.36	0.01
Sodium (mg/d)	3156	3180	2012	0.5	0.03
Potassium (mg/d)	1755	3562	3750	0.002	0.00

Conclusions: The diet of RA patients seemed adequate except for an intriguingly low K. We speculate that patients eat lesser vegetables and fruits that source K. K sub serves several physiological functions that may be deranged in RA and contribute to disease progression. This would need further investigation.
Acknowledgements: In contrary to our expectations and reassuringly, the diet of RA patients seemed adequate except for an intriguingly low potassium which should be investigated. We speculate that patients eat lesser vegetables and fruits that source potassium.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4335

AB1229-HPR EVALUATION OF RHEUMATOLOGY NURSE-LED CLINIC IN MANAGING PATIENTS WITH RHEUMATOID ARTHRITIS: A RETROSPECTIVE STUDY

Y.M.E. Leung[1], K.Y. Wong[2], L.S. Tam[1]. *[1]Department of Medicine and Therapeutics, Prince of Wales Hospital; [2]School of Nursing, Hong Kong Polytechnic University, Hong Kong, Hong Kong*

Background: Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease characterized by inflammation of the synovial joints. Management of RA patients are usually provided by rheumatologists only. Enhanced care provided by rheumatology nurses between rheumatologist consultations may have beneficial effects in terms of symptom control. In Hong Kong, whether rheumatology nurse care model can favor to patient outcomes remained uncertain.
Objectives: The aim of the study was to examine the clinical effectiveness of rheumatology nurse clinic in controlling disease activity as expressed in change of Disease Activity Score in 28 joints in RA patients compared with usual care led by rheumatologists only.
Methods: This was a retrospective study. Two historical groups of RA patients (30 patients at each group) were identified from attendance records between 1/1/2015 and 20/7/2015 at the rheumatology outpatient clinics. Group 1 comprised of patients who attended rheumatology nurse clinic in between the doctor clinic consultations. Patient education delivered by the rheumatology nurse included disease mechanism, treatment aim, pain management and checking medication adherence according to prescription. RA treatment could also be intensified if needed. Group 2 comprised of patients managed by rheumatologists only. Primary outcomes were changes in disease activity at follow-up visit after the doctor clinic and nurse clinic.
Results: The mean follow-up duration for the study cohort was 20 weeks (median: 22.5 weeks). Patient global assessment and DAS 28 were similar for both groups at baseline. At follow-up, patient global assessment and in the nurse group (Group 1) decreased from mean ± SD: 42±24.7 at baseline to 28.7±24.6 at follow-up, which was approaching the minimal clinically important improvement (MCII= -15). With regards to DAS28, there was a 8.2% decrease (absolute change: -0.38±1.14) in DAS28 in group 1 suggesting a trend of improvement (p=0.081). The corresponding decrease in group 2 was 1.2% (absolute change: -0.05±1.47) and such decrease was not significant (p=0.863). Changes in DAS28 did not exceed minimal clinically important improvement in both groups (MCII= -1.2).
Conclusions: This study demonstrates the short-term benefit of a nurse-led program on RA disease management. Future multi-center studies with a randomized controlled design and a larger sample will be required to confirm our findings.

Abstract AB1229-HPR – Table 1

Variables	Nurse clinic (n=30)			Doctor clinic (n=30)		
	Baseline	Follow-up	p-value	Baseline	Follow-up	p-value
Tender joint count	4 (2, 9)	2.5 (1, 8.25)	0.202	1.0 (0, 6.25)	1.5 (0, 5.00)	0.715
Swollen joint count	1 (0, 3)	0.5 (0, 3)	0.624	1.0 (0, 3.25)	1.0 (0, 4.25)	0.526
Patient global assessment	42.0±24.7	28.7±24.6	**0.009**	42.7±24.9	41.3±23.7	0.838
ESR, mm/hour	35.6±19.2	37.0±22.0	0.639	39.0±19.6	40.7±25.3	0.677
CRP, mg/L	4.6 (1.0, 12)	2.2 (0.7, 8.3)	0.808	2.95 (0.98, 7.00)	3.05 (1.30, 13.1)	0.274
DAS28 score	4.53±1.15	4.16±1.31	**0.081**	4.14±1.01	4.09±1.23	0.863

Acknowledgements: The author is very grateful to the supervisors from, Professor Wong Kam Yuet, Frances, Hong Kong Polytechnic University; Professor Tam Lai Shan and Dr Zhu Yaner, Tracy the Chinese University of Hong Kong. Lastly, the author would like to thank her parents and friends for their support.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6236

AB1230-HPR A SURVEY TO ESTABLISH CURRENT PRACTICE IN ADDRESSING WORK ISSUES AMONG PEOPLE WITH INFLAMMATORY ARTHRITIS IN THE IRISH CLINICAL SETTING

Y. Codd[1,2], T. Stapleton[1], R. Mullan[2,3], D. Kane[2,3]. *[1]Discipline of Occupational Therapy, Trinity College Dublin, Dublin; [2]Rheumatology Department, Naas General Hospital, Naas, Co. Kildare; [3]Rheumatology Department, Tallaght Hospital, Dublin, Ireland*

Background: Inflammatory arthritis strongly correlates with work disability. Treatment guidelines recommend work support but data are lacking on rheumatology clinicians' perspectives on work referral and extent of work support within current rheumatology services for this population.
Objectives: To scope the need for and patterns of work referral, and examine the extent and type of work support currently available in Irish rheumatology services for people with inflammatory arthritis. To identify factors that help or hinder employment-related service provision. To explore the role of occupational therapy in addressing work with this population from the perspectives of the other members of the rheumatology team and current practices and challenges.
Methods: A questionnaire concerning work support provision was distributed via online survey to doctors, nurses and physiotherapists working in clinical rheumatology in Ireland.
Results: Response rate of 22% was achieved and total sample of 73 analysed. Respondents indicated that 71% of service users were of working age and the majority of respondents (95%) agreed that addressing employment retention was within the remit of rheumatology services. Over half of respondent (55%) of respondents estimated that 25–49% of their caseload had work needs. Work was usually addressed if clients raised work concerns (94%), client reports work absenteeism (83%), client's work involved manual component (75%). Barriers to addressing work included limited time in clinical setting (92%); unfamiliarity with best practice for work support (91%); lack of perceived competency to assess work complexities (82%). Occupational therapy (OT) was identified as the most appropriate profession to address work (78%). However, 51% respondents reported not routinely referring to OT for work support due to limited availability of OT (13% of responders having no access to OT); uncertainty regarding optimum timing for work intervention, and uncertainty as to what OT could offer regarding work.
Conclusions: Addressing work was recognised as multifaceted and multidisciplinary. Work needs are addressed within current rheumatology services only when the client themselves initiate the issue. Opportunity exists to improve the quality of services to address work in line with guidelines by educating the multidisciplinary team about available work services and implementation of a clinical pathway for employment retention.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1107

HPR patients' perspectives, functioning and health (descriptive: qualitative or quantitative)

AB1231-HPR LIVING WITH RHEUMATOID ARTHRITIS IN SPAIN. A QUALITATIVE STUDY

A. Pedraz-Marcos[1], C. Hale[2], A. Palmar-Santos[1], J. Zarco-Colon[3], M. Ramasco-Gutierrez[4], T. Velasco-Ripoll[5], J. Martín-Alarcón[6], N. Sapena-Fortea[7] on behalf of Grupo de Investigación Cualitativa en Salud (GIQS-UAM). *[1]Surgery, University Autonoma of Madrid, Madrid, Spain; [2]University of Leeds, Leeds, United Kingdom; [3]Sociology, University Autonoma of Madrid; [4]Public Health, Regional Health Organization; [5]Rheumatology, Hospital la Princesa, Madrid; [6]Hospital Clinic Barcelona, Barcelona, Spain; [7]Rheumatology, Hospital Clinic Barcelona, Barcelona, Spain*

Background: The impact of rheumatoid arthritis (RA) on the lives of people is a constant in the studies explored. However, research shows the lack of impact that this has on clinical consultations, despite the influence it may have on the attitude of the person with RA towards treatment adherence. In the Spanish context, except for the study by Devillard & Otegui (1991), the experience of living with RA has scarcely been addressed.
Objectives: To explore the experience of living with RA in Spain.
Methods: In-depth interviews were conducted with a group of patients from two hospitals in the two main Spanish cities: Madrid and Barcelona. The interviews were conducted between April 2014 and February 2015. Thematic analysis was done, identifying the main themes and subthemes and organizing data in a coding framework that allows their interpretation
Results: Patients with disease activity moderate or severe (DAS28 >3.2), and already treated with DMARD, were aged 40–79, 15 were women and 4 men. Three main categories emerged from the discourses. (Table 1)

The symptoms and their management	Helplessness	*How do you live with this? Well, you have to know how to bear it because it is a life of always being tired. [...] You wake up with the body as if you had been beaten.* (EM7)
	Go along with	*When they come [the children], I pretend I'm not doing so badly. I make myself up, I dress up, for they wouldn't notice.* (EB3)
	Self-management	*You have to discover it by yourself, each person what their own experience teaches them.* (EB7)
Daily life	Home adapting	*I had a bath but now I have put a shower. We have set up single lever taps. I bought a step, because I cannot stand on tiptoe to reach something.* (EB8)
	Self image	*Of course, I have changed my shoes, I used to wear heels before, and now I use boots.* (EB8)
	Planning	*Always planning: you are not to improvise under any circumstances.* (EM9)
Therapeutic strategies	The DMARD miracle	*When I take this medicine, I totally revive.* (EM7)
	Ambivalent relation with health professionals	*I had an awful time ... The best thing is people. For me, my rheumatologist is like God.* (EB8) *I'm very frustrated... when they have been wrong with you a lot.* (EM1)

Conclusions: RA patients know well what is it like to get up in the morning, tired, stiff, sore and having to rethink their day. Prioritization and planning activities are key to the organization of the activity and rest. Families and external aid, in case they can afford it, are the most common supports on which the requested supports pivot.
The constant development of new therapeutic strategies and outbreaks of the disease determine the use of an important therapeutic arsenal, with unpleasant side effects, and that should be administered in a hospital setting. This need to rely on medical treatment also extends to doctors, as part of the therapeutic strategy. Nurses are absent from the speeches of our participants
RA patients in our study feel they are mainly on their own to cope with their disease. The new therapeutic strategies have improved the symptoms' control, but they feel they need more than drugs to cope with their daily life. Contrary to the variety of professionals, institutions and organizations that try to empower patients to self manage their disease in other countries, the Spanish attention pivot mainly in rheumatologists.
References:
[1] Devillard, Marie Jose; Otegui, Rosario; García, Pilar. La voz callada. Aproximaciones antropológico-social al enfermo de artritis reumatoide. Madrid: Comunidad de Madrid. Consejería de Salud; 1991.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3887

AB1232-HPR THE EFFECT OF THE DRAINAGE ON PROPRIOCEPTIVE ACUITY INPATIENTS WITH TOTAL KNEE PROSTHESIS

B. Ünver[1], M. Eymir[1], V. Karatosun[2]. *[1]School of Physical Therapy and Rehabilitation; [2]Faculty of Medicine Surgery Medicine Department of Orthopaedics and Traumatology, Dokuz Eylül University, Izmir, Turkey, Izmir, Turkey*

Background: With total knee replacement (TKR) surgery articular cartilage, meniscuses, articular ligaments are removed. Also articular effusion and

hematoma formation increase following surgery. Therefore, proprioceptive acuity decrease after TKR surgery (1). Drainage is a common procedure in TKR, but its effectiveness is controversial. Some studies have claimed that drainage decreases the risk of articular effusion and hematoma formation. However, some studies have demonstrated that drainage increases postoperative blood loss and does not improve the surgical result (2). Several studies have examined the effect of using drainage, but they have not involved improvement in proprioception for patients who had drains compared with those who did not after TKR.

Objectives: The aim of this study was to compare the effect of the drainage on proprioception acuity inpatients with total knee prosthesis.

Methods: The study group consisted of 60 patients (95 knees), who underwent primary TKR because of arthrosis were consecutively allocated to a drainage group (n=26 (41 knees), with median age; 66.23±8.63 years), and were allocated to a non-drainage group (n=34 (54 knees), with median age; 63.97±8.99 years). Patients were evaluated regarding knee proprioception (in knee joint angle 15°, 30° and 60°), knee function score (Hospital for Special Surgery (HSS) score), pain (Numeric Pain Rating Scale (NPRS)), knee circumference, knee range of motion. Functional activities were evaluated using the Iowa Level of Assistance Scale and walking speed was evaluated using the Iowa Ambulation Velocity Scale. Patients were evaluated preoperatively and at discharge. All patients underwent the same rehabilitation program.

Results: At baseline, demographic and anthropometric characteristics were similar in groups and there was no statistically difference between groups ($p>0.05$). When knee proprioceptive acuity measurements (in knee joint angle 15°, 30° and 60°) were compared before and after surgery, there was no statistical differences in proprioceptive acuity between groups ($p>0.05$). It was determined that; the drainage group had better results in terms of reduction of pain severity after surgery ($p<0.001$). When the HSS knee scores were compared there was statistically difference between groups ($p=0.001$) and the HSS knee scores were lower in non-drainage group after surgery. There were no statistical differences in knee circumference, knee range of motion, the IOWA help level score and IOWA walking speed score between groups after TKR ($p>0.05$).

Conclusions: According to our results, the use of drainage did not improve the knee proprioceptive acuity inpatients with TKR. But, it is suggested that using drainage decreases pain severity and improves the HSS knee score. Also the use of drains has no effect on patients' outcomes after TKR, in terms of improvements knee range of motion, knee circumference, functional activities and walking speed.

References:

[1] Pap G, Meyer M, Weiler H-T, et al. Proprioception after total knee arthroplasty: a comparison with clinical outcome. Acta Orthopaedica Scandinavica. 2000;71(2):153–9.

[2] Zhang QD, Guo WS, Zhang Q, et al. Comparison between closed suction drainage and nondrainage in total knee arthroplasty: a meta-analysis. The Journal of Arthroplasty. 2011;26(8):1265–1272.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5914

AB1233-HPR COGNITIVE COMPLAINTS IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS AND PAST NEUROPSYCHIATRIC SYMPTOMS

D. Usheva[1], D. Ivanova[2], J. Petrova[3]. *[1]MU Sofia, Sofia, Bulgaria; [2]Rheumatology, MU Sofia; [3]Neurology, University Hospital Alexandrovska, Sofia, Bulgaria*

Objectives: Cognitive complaints are common in patients with systemic lupus erythematosus (SLE). Their association with disease and non-disease related factors have been inconsistently reported. We studied their relation to disease related factors including disease activity, neuropsychiatric history and non-disease related factors such as anxiety or depression.

Methods: We used cognitive symptoms inventory (CSI) for measuring cognitive impairment at 3 time-points 12 months apart/2015–2016/ and Hospital Anxiety and Depression Scale (HADS)-HADS-A and D.Disease activity was measured by SLEDAI.

Results: 93 SLE patients were recruited at baseline (T0). Among them 59 had first re-evaluation (T1) and 34 had second re-evaluation (T2) at 12-month interval. Majority (72%, 24/34) of patients had stable CSI whereas 5.5% (2/34) of patients worsened CSI over 12 months. At T0, multivariate analysis revealed that higher CSI was associated with history of NPSLE ($p=0.005$) and psychiatric disease ($p=0.04$), higher HADS-A ($p<0.001$) and HADS-D ($p<0.001$) scores. CSI of active patients (SLEDAI>6) was not different from inactive patients. It did not change despite regression of disease activity in 12 months. There was no difference in CSI between T0 and T1 regardless of history of NPSLE, change in anxiety and depression at T1 (HADS-D>11 as cutoff).Multivariate linear regression analysis revealed change in HADS-A as the only significant predictive factor of change in CSI over time ($\beta=0.774$, 95% CI 0.43 – 1.12, $p<0.001$).

Conclusions: 11.5% of SLE patients reported persistent cognitive symptoms.CSI had worsened in patients with NPSLE and psychiatric illness, anxiety or depression.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5166

AB1234-HPR PHYSIOTHERAPY EFFECTS ON GAIT SPEED AND PAIN IN PATIENTS WITH KNEE OSTEOARTHRITIS THREE DAYS AFTER APPLYING KINESIOTAPE

K. Tani[1], I. Kola[2], F. Dhamaj[2], E. Qalliaj[1], K. Zallari[2]. *[1]University of Medicine, Tirana, Albania; [2]Faculty of Technical Medical Sciences, University of Medicine, Tirana, Albania*

Background: Knee osteoarthritis is a chronic degenerative disease, known as the most common cause of difficulty walking in older adults and subsequently is associated with slow walking, also one of the most main symptoms is a degenerative and mechanics type of pain. Pain is very noticeable while walking in rugged terrain, during ascent and descent of stairs, when changing from sitting to standing position as well as staying in one position for a long time. Many studies have shown that the strength of the quadriceps femoris muscle can affect gait, by improving or weakening it. Kinesiotape is a physiotherapeutic technique, which reduces pain and increases muscular strength by irritating the skin receptors

Objectives: The aims of this study was firstly to verify if the application of Kinesiotape on quadriceps femoris muscle increases gait speed in patients with knee osteoarthritis and secondly if applying Kinesiotape on quadriceps femoris muscle reduces pain while walking.

Methods: 73 patients with primary knee osteorathritis, aged 50–73 years, participated in this study. Firstly we observed the change of gait speed, while walking for 10 meters at normal speed for each patient, before and three days after the application of Kinesiotape on quadriceps femoris muscle, with the help of the 10-meter walk test. Secondly we observed the change of pain, while walking for 10 meters at normal speed for each patient, before and three days after the application, with the help of Numerical Pain Rating Scale-NRS.

Results: Our results indicated that there was a significant increase of gait speed while walking for 10 meters one day and also three days after application of Kinesiotape, also there was a significant change of pain. Before applying Kinesiotape on quadriceps muscle was shown that 41.1% chose score 6, 30.1% chose score 7 and 28.8% chose score 8 of the numerical pain rating scale. Three days after the application 15.1% chose score 2, 37% chose score 3 and 47.9% chose score 4 of numerical pain rating scale.

NRS	Number of patients before KT	%	Number of patients three days after KT	%
0				
1				
2			11	15.1
3			27	37
4			35	47.9
5				
6	30	41.1		
7	22	30.1		
8	21	28.8		
9				
10				

Conclusions: Our results indicated that there was a significant decrease of pain and increase of gait speed while walking for 10 meters. Kinesio-Tape can be used in patients with knee osteoarthritis, especially when changing walking stereotypes is a long term goal of the treatment.

References:

[1] Steultjens MP, Dekker J, van Baar ME, Oostendorp RA, Bijlsma JW. (2001). Muscle strength, pain and disability patients with osteoarthritis. Clin Rehabil 15:331–41.

[2] Slemenda C, Brandt KD, Heilman DK, Mazzuca S, Braunstein EM, Katz BP, et al. (1997). Quadriceps weakness and osteoarthritis of the knee. Ann Intern Med 127:97–104.

[3] Ayis S, Ebrahim S, Williams S, Juni P, Dieppe P. (2007). Determinants of reduced walking speed in people with musculoskeletal pain. J Rheumatol. 34(9):1905–12.

[4] Vercelli S, Sartorio F, Foti C, Colletto L, Virton D, Ronconi G, et al. (2012). Immediate effects of kinesiotaping on quadriceps muscle strength: a single-blind, placebo-controlled crossover trial. Clin J Sport Med. 22(4): 319–26.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3444

AB1235-HPR SEXUAL DISTURBANCES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND IT'S RELATION WITH DISEASE ACTIVITY

L. Villarreal[1], S. Henao[2], D. Buitrago-Garcia[3], P. Santos-Moreno[4]. *[1]Psychology and processes; [2]Patient service; [3]Epidemiology; [4]Rheumatology, Biomab, Center for Rheumatoid Arthritis, Bogota, Bogota, Colombia*

Background: Sexuality is an important dimension of personality and human body, therefore any involvement in this area should be considered as important. Sexual disturbances in rheumatoid arthritis (RA) patients are poorly described in literature. In other chronic conditions studies had shown that sexual disturbances can be common problem in but, sexual dysfunction has a high risk of under treatment because providers frequently do not initiate the conversation with the patient.

Objectives: The purpose of this study was to describe sexual disturbances in

population with RA and a possible correlation with disease activity in a specialized rheumatology center.
Methods: A descriptive cross-sectional study was performed in a specialized clinic dedicated to care patients with rheumatoid arthritis (RA). Data was collected during a two year period at a psychology consultation, through semi-structured interview. Descriptive epidemiology was applied for continuous variables, using measures of central tendency and dispersion for categorical and qualitative variables by averages and percentages. We analyzed bivariate association with Pearson's X^2.
Results: We included 1398 patients attending to our psychology consultation. Mean age was 55 years ± 8; 80% were female and 20% male. Mean DAS28 was 2.6±1.3, mean HAQ was 1.6±1.6; patients had the disease for an average of 12 years ± 8; 41% of patients had comorbidities associated with non-autoimmune disease, 14% comorbidities related to autoimmune disease; 35% of our patients did not report other comorbidities. Most of patients were married 60%, followed by divorced 19%, single 14% and widowed 7%. Regarding occupation 33% were employees, 25% were housekeepers or retired due to age, 12% were retired due to disabilities, and 3% unemployed. Of the total population 45% had elementary school, 32% high school, 8% college education, 7% graduate education and 7% were illiterate. 17% of patients lived alone. Concerning sexual disorders, 38% reported no to have any sexual activity, 32% reported to have a satisfactory sexual life, 11% dyspareunia,9% had an unsatisfactory sexual life, 5% loss of desire, 3% premature ejaculation and 2% orgasmic decrease. Regarding predisposing factors of sexual disorders 63% of our population did not present any, 11% had insecurity related to the sexual role, 10% inadequate information relating sexuality, 10% infidelity and 6% physical and biological predisposing factors. Regarding precipitant factors of sexual disorders 63% report no to have any, 19% had biological or physical factors, 12% infidelity, 3% inadequate information and 3% insecurity related to de sexual role. There was no statistical association between disease activity and predisposing or precipitant factors.
Conclusions: We found that a third of patients with AR have sexual disorders and a high percentage reported not having any sexual activity. Also, it is important to have a multidisciplinary care team for the patient with RA, including a psychologist and a sexologist for managing this kind of illness in order to improve the life quality of patients.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5635

AB1236-HPR CONNECTION BETWEEN FUNCTIONAL ABILITY AND SOCIO-DEMOGRAPHIC DATA IN PATIENTS WITH RA IN SLOVENIA

M. Pavic Nikolic, S. Kosir Jost. *Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia*

Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis, characterized by progressive, destructive course when left untreated, resulting in severe patient disability and significantly reduced quality of life. RA has an important impact on work ability and economic status of patients.
Objectives: In our study we were focused on specific consequences of arthritis in terms of functional ability and we were looking for correlation with socio-demographic data.
Methods: The study was conducted between January 2016 and May 2016 at the Department of Rheumatology, UMC Ljubljana and included patients with RA. Data were collected using Arthritis Impact Measurement Scales 2 (AIMS2) questionnaire.
Results: One hundred RA patients (76% women, mean age (SD) of 61.1±15.29 years) participated in the study. Disease duration was ± 5. 6 year. Most of our patients were married, retired with elementary education and lower incomes (Table1).

Table 1. Socio-demographic status of respondents

Married status/n		Education level/n		Working status/n		Monthly revenue/n	
Married	70	Primary school	40	Employed	27	up to 500€	32
Divorced	3	High school	27	Housekeeper	2	500€–900€	42
Single	6	University	27	Student	1	900€–1300€	19
Widowed	19	Master's degree	3	Unemployed	5	1300€–1700€	4
Separate life	2	Doctor's degree	3	Retired	65	1700€ and up	3

Respondents of our study described their functional ability good by the average of the entire sample 2.06. This value shows us a relatively good functional ability of patients most days or very often. Patients had some problems with function of hand and wrist in particular by opening jars (43%) and on area walking and bending with intensive activity (42%). Correlation between functional ability and socio-demographic data show us some statistical deviance in age group 41 to 50 year (p=0.94), in patients with higher education level (p=0.99) and in group of patients who monthly earns more then 900€ (p=0.96). But we didn't find any statistically significant difference in the entire sample including patients treated with biological drugs (functional ability patients on biologics p=0.91).
Conclusions: We found fairly good functional ability of patients; which might be explained by relatively short duration of RA. The most important functional-related issues from patient perspective were identified. Despite that we not find a statistically significant relationship between socio-demographic data and functional ability of patients, it is very important that we pay attention on socially unprivileged patients and we offer our support in managing disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2523

AB1237-HPR POSTURAL STABILITY AND ANKLE PROPRIOCEPTION IN DIFFERENT SUBGROUPS OF SUBJECTS WITH HALLUX VALGUS

O. Aydoğdu, Z. Sarı, G.M. Polat. *Physiotherapy and Rehabilitation, Marmara University, Health Sciences Faculty, Istanbul, Turkey*

Background: Hallux valgus (HV) is lateral deviation of the great toe towards the second with subluxation of the first metatarsophalangeal joint and medial deviation of the first metatarsal (1). Increasing HV severity has been shown to negatively impact on health-related quality of life and self-reported function, and HV has been linked to increased falls risk in older adults (2). HV, in particular, is associated with poorer performance during postural stability and functional testing in older adults (3).
Objectives: Despite the findings of impaired postural stability in older adults with hallux valgus, the links between functional status and postural stability, ankle proprioception are not well established in HV. One of clinical significance of this study was to determine whether impaired postural stability was caused by deficits in ankle proprioception and impaired functional status in HV subjects. Our purpose of this study was to assess postural stability and ankle proprioception in different subgroups of HV. In this study, we hypothesized that subjects with severe deformity would exhibit poorer postural stability and ankle proprioception performance compared to subjects with mild and moderate deformity in HV.
Methods: Thirty-five adults diagnosed with unilateral HV according to the Manchester Oxford Foot Questionnaire deformation grade 2 and on were participated in the study. They were distributed among three groups: Mild (grade 2), moderate (grade 3), and severe deformity (grade 4). Functional status was measured with a disease specific score (the hallux valgus scale of the American Orthopaedic Foot and Ankle Society). While postural stability was measured with Pedalo Sensamove® System, ankle proprioception was measured with Biodex Balance System Pro 4.
Results: Subjects in HV with severe deformity group showed poorer postural stability performance than those in HV with mild (p=0.024) and moderate (p=0.039) deformity groups. However, there was no significant difference between the groups in ankle proprioception. There was a significant correlation between postural stability and functional status ($p<0.05$, r=0.771) in all subjects with HV. In addition, it was found that ankle proprioception was not correlated to functional status and postural stability ($p>0.05$).
Conclusions: It has been concluded that HV with severe deformity affects postural stability according to the results of our study. On the other hand, ankle proprioception is not as an important predictor as postural stability for rehabilitation in different subgroups of HV. Therefore subjects in HV with severe deformity should be focused on stability exercises, in particular, in addition to home – based exercise programs, foot orthoses, footwear recommendations, and patient education in their rehabilitation.
References:
[1] Booth S, Bhosale A, Mustafa A, Shenoy R, Pillai A. Triple osteotomy for the correction of severe hallux valgus deformity: Patient reported outcomes and radiological evaluation. Foot (Edinb). 2016 Aug;28:30–35.
[2] Hurn SE, Vicenzino B, Smith MD. Functional impairments characterizing mild, moderate, and severe hallux valgus. Arthritis Care Res (Hoboken). 2015 Jan;67(1):80–8.
[3] Sadra S, Fleischer A, Klein E, Grewal GS, Knight J, Weil LS Sr, Weil L Jr, Najafi B. Hallux valgus surgery may produce early improvements in balance control: results of a cross-sectional pilot study. J Am Podiatr Med Assoc. 2013 Nov-Dec;103(6):489–97.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4669

AB1238-HPR PEOPLE'S PERCEPTIONS OF THEIR PHONE CALL WITH RHEUMA DIRECTLY, A RHEUMATIC DISEASES HELPLINE

S. Arvidsson[1,2], M. Nylander[2], S. Bergman[1,2,3]. *[1]School of Health and Welfare, Halmstad University; [2]Spenshult Research and Development Centre, Halmstad; [3]The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*

Background: Information on rheumatic diseases is often complex to understand or scary, and additional support is often necessary. Rheuma Directly (RD) is a helpline with specially trained nurses on rheumatic diseases, funded by the Swedish Rheumatism Association and Spenshult Research and Development Centre. Little is known of how people calling a helpline perceive the contact.
Objectives: To describe the variation in how people perceive the contact with the helpline RD.
Methods: The study had a descriptive, qualitative design with a phenomenographic approach and was carried out by means of 27 semi-structured telephone interviews. The informants were 22 female and 5 men, and their ages ranged from 22 to 89 years (mean 54 years).
Results: The informants called RD when they had problems getting answers

to their questions through the Internet or from healthcare professionals. Three different description categories emerged: Specific competence, Constructive dialogue, and Applicability. The informants' perceived Specific competence when the nurses were knowledgeable, the call was complementary to previously received information and when the informants had greater knowledge after the contact with RD. They perceived that it was a Constructive dialogue when they got someone to discuss with, a "sounding board", and perceived emotional support, felt reassured and were satisfied with the answer. The informants perceived Applicability because RD was available and they could make different choices according to their own desire; before (how and when they would contact RD), during (what to tell and what question they would ask) and after (how and what they would do after the contact with RD).

Conclusions: People calling RD perceived that the telephone call with the nurses meant meeting specific competence, gaining constructive dialogue and that the helpline was applicable. This knowledge ad to a fuller understanding of factors that from a caller's perspective, are important when calling a helpline with specially trained nurses on rheumatic diseases.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2466

AB1239-HPR FATIGUE AT DIAGNOSIS OF INFLAMMATORY JOINT DISEASES - A PREDICTOR OF FATIGUE DURING THE COURSE OF DISEASE DESPITE OF LOW DISEASE ACTIVITY

S.H. Jakobsen, A. Emamifar, I.M.J. Hansen. *Rheumatology, OUH, Svendborg Hospital, Svendborg, Denmark*

Background: Fatigue is a common symptom in patients suffering from inflammatory rheumatic diseases. Several patients still present with fatigue, although they are well treated with anti TNF-therapy (1).

Objectives: To investigate disease-related aspects of fatigue in patients with inflammatory rheumatic diseases using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) with the aim later to develop methods to improve the patients quality of life in a more specific way.

Methods: All patients with inflammatory diseases including Rheumatoid Arthritis (38) and Spondyloarthropathy (13) and Psoriatic arthritis (2) treated with Intravenous biologic from 15.10 until 31.12.16 were invited to fill out the FACIT-F questionnaire during intravenous (IV) infusion of the drugs in the rheumatology outpatient clinic. Furthermore hemoglobin and disease activity score were extracted from patients electronic records.

Results: Of 72 patients, 53 patients completed the questionnaire. 5 patients did not want to participate. In 11 patients treatment was discontinued during the study and 3 patients were not able to answer the questions.

Patients with a fatigue score of <30 had few problems with any of the subgroups within the FACIT-F questionnaire (A-E), whereas more than 30% of patients with a fatigue score of ≥ 30 had challenges in one of the FACIT-F subgroups (somewhat, quite a bit and very much) A. Physical well-being: lack of energy and troubles with meeting the needs of their family because of their physical condition. B. Social/family well-being: patients were not feeling close to their friends, not getting enough emotional support from their family and not satisfied with their sex life. C. Emotional well-being: patients worry if their conditions might get worse. D. Functional well-being: patients feel they are partly unable to work, not satisfied with their performance at work and they have sleeping and quality of life problems. E. Additional concerns: patients had problems with fatigue, weakness, tiredness, starting and finishing things because of tiredness, not having energy, not being able to do usual activities, frustration by being too tired to do the things they want to do as well as they want to limit social activities because of tiredness and they need to sleep during the day. Furthermore, there was a moderate correlation between fatigue at diagnosis and fatigue at time of data extraction ($r = 0.53$). The fatigue was not correlated with anemia or high disease activity.

Conclusions: Our results demonstrated that patients with a fatigue score of >30 had different challenges mentioned in the fatigue questionnaire. In addition, patients who experience fatigue at time of diagnosis, they often remain fatigue, provoking the thought that fatigue is not correlated with inflammatory joint disease. Maybe more explorative questions about fatigue at the consultation could be a part of improving the patients'quality of life.

References:

[1] Druce KL, et al. Most patients who reach disease remission following anti-TNF therapy continue to report fatigue: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. Rheumatology (Oxford). 2016;55:1786–1790.

[2] Webster K, Cella D, Yost K. The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: properties, applications, and interpretation. Health Qual Life Outcomes 2003;1:79.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.1885

AB1240-HPR PATIENTS' DOGMA, NUMBER OF SWOLLEN JOINTS AND PHYSICIANS' AND PATIENTS' AGE PREDICT NON-ADHERENCE TO MEDICINES AND NON-PHARMACOLOGICAL INTERVENTIONS IN RHEUMATOID ARTHRITIS – A MIXED METHODS STUDY

V. Ritschl[1], A. Lackner[2], C. Boström[3], M. Kundi[4], P. Studenic[5], J. Smolen[5], T. Stamm[1]. *[1]Institute of Outcomes Research, Center for Medical Statistics, Informatics, and Intelligent Systems, Medical University of Vienna, Vienna; [2]Department of Rheumatology, Medical University of Graz, Graz, Austria; [3]Department of Neurobiology, Karolinska Institute, Huddinge, Sweden; [4]Institute of Environmental Health, Center for Public Health; [5]Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Vienna, Austria*

Background: In rheumatoid arthritis (RA), up to 80% of patients were found to be non-adherent to prescribed medication and non-pharmacological recommendations. These patients do not achieve an optimal clinical outcome.

Objectives: In the present study, we therefore explored predictors that may lead to non-adherence to both medicines and/or non-pharmacological recommendations.

Methods: In a mixed methods study, retrospective observational data from patients meeting the ACR/EULAR criteria for RA who were non-attenders/missed the routine check up visits for at least 9 months to the rheumatology clinic and had had an initial DMARD therapy were queried of the databases of two rheumatology centers in Austria (Graz, Vienna). Subsequently, we invited all patients to take part in a qualitative semi-structured interview study with a meaning condensation data analysis. In the interviews, patients were assigned to the subgroups "adherent" (e.g. having regular rheumatology visits in another clinic) or "non-adherent" (e.g. having stopped taking the prescribed medication). Possible predictors derived from the qualitative analysis and the retrospective observational data were then tested in a logistic regression model.

Results: In total, data of 459 patients (346 [75.4%] females; mean age 63.0 [SD± 14.8]) were extracted out of the databases. 131 patients (109 [83.2%] females; mean age 64.8 [SD± 14.1]) participated in the qualitative interviews. In addition to already known themes, new topics arose from the analysis: (i) patient's dogma inhibited adherent behavior, in that patients felt that pain was an important part of life and attributed to having had a high manual workload during life of which patients were proud; (ii) patients had less trust in physicians when they were seeking support from other physicians, because they appeared to be "young or unexperienced"; (iii) Some patients did not feel properly understood if physicians only prescribed medication without giving advice on non-pharmacological aspects of treatment.

Two clinical variables were found to be predictors for non-adherent behavior (table 1): swollen joint count (patients with higher numbers of swollen joints were less adherent) and age (younger patients were less adherent).

Table 1. Logistic regression models. Odds ratios of relevant factors for non-adherent behavior in RA: results of the logistic regression analysis

Regression Model	Odds Ratio	CI 95%	Significance at 0.05 (p)
Age at the last visit	1.033	1.005 to 1.063	0.022
Swollen Joint Count using a 32 joint count form	0.876	0.767 to 1.000	0.050

Conclusions: In order to achieve a good clinical outcome, it is important to provide evidence based treatment recommendations, but also to ensure adherence to these. The predictors found in our study could be used to enhance patient adherence and therefore improve clinical outcome.

Acknowledgements: This project was partially funded by AbbVie Inc.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.5227

AB1241-HPR EVALUATION OF PATIENT COMPLIANCE WITH LONG TERM PRESCRIBED RHEUMATIC MEDICATION AT LOCAL LONDON HOSPITAL RHEUMATOLOGY UNIT

V. Sohdi, C.B. Colaço, M. Hoffman, J. Kirk on behalf of Central Middlesex Hospital Rheumatology (Patient) Support Group. *LNWHT, London, United Kingdom*

Background: Non-Compliance with Long term medication is reported as high 60% (1). Health belief model suggests four elements contribute to this problem. The Beliefs About Medicines Questionnaire (BMQ) is a tool for evaluating people's beliefs about medicines (1).

Objectives: A Service Evaluation of compliance with prescribed medication for Long Term Rheumatologic Conditions at Central Middlesex Hospital. This was conducted to assess any possible relationship between compliance with medicines and beliefs or concerns or patient's ethnicity.

Methods: The design was a voluntary self-reported, cross-sectional paper based questionnaire survey of people with Rheumatic Conditions. Twelve questions were grouped within three categories (healthcare utilisation, necessity beliefs and concern beliefs) to capture compliance behaviour for later analysis and comparison.

The Beliefs about Medicines Questionnaire was adapted from ref (1) to distinguish patients beliefs of 'necessity' or 'concerns'. In line with principles of PPP, the questionnaire was discussed prior to the audit with a sample focus group of 5

patients who contributed to the wording and the simplification of the questions re: ethnicity.
Questionnaires were offered to all patients attending the CMH Rheumatology Unit. The evaluation was discontinued when a target of 100 was reached (n=102). No questionnaires were excluded. And upto 5% of questions were unanswered. Data was analysed on SPSS.
Results: The Number of questionnaires returned for this service evaluation was 102.
- Most respondents (94%) showed compliance with rheumatic medication as prescribed.
- More than half the respondents (66%) agreed or strongly agreed that their arthritis medications are necessary for their health.
- 54% were concerned about potential adverse consequences.
- The overall necessity score (19.32 S.D. 3.17) was higher than the concerns score (13.48; S.D. 3.35; t =61.57, P<0.001).
- Concerns about the long term effect of rheumatic conditions correlate positively with perceptions of health in the future P<0.01 level (2-tailed Pearson).
- No significant correlation was found between compliance and patient's ethnicity/individuals demographics.

Conclusions: Most people with Rheumatic conditions have positive beliefs about the necessity of their medication. However, levels of concern are high, especially towards the long-term effects of the medication. This concurs with asimilar study in Rheumatoid Arthritis.(2). The service evaluation using the Beliefs about Medicines Questionnaire has helped to identify people at risk of poor compliance long term. This illustrates a need to discuss patients beliefs and concerns in targeted drug counseling sessions with specialist nurses. A post study patient focus group recognised the high level of compliance yet recommended a fixed weekly walk in session with a nurse and pharmacist to sustain this high quality outcome. Further methods of continued patient re-education will be explored.
References:
[1] Horne R, Weinman J, Hankins M. The Beliefs about Medicines Questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health 1999;14:1–24.
[2] Neame R, Hammond A Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis. Rheumatology (Oxford) 2005;44:762–7.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4738

HPR service developments, innovation and economics in healthcare

AB1242-HPR NUMERICAL PREDICTION OF THE OPTIMUM SHEET METAL THICKNESS IMPLANTED AS THE JOINT CARTILAGE

M. Moayedfar, A.M. Rani, H. Hanaei. *Mechanical Engineering, Universiti Teknologi Petronas, Bandar Seri Iskandar, Malaysia*

Background: The combination of computer-aided-design (CAD), digital image processing techniques and finite element method (FEM) has been successfully employed to create the customized distal condyle implants in human joints during arthroplasty surgery when the manufacturing method is incremental sheet forming (ISF) technique. However, due to the high time of process in the FEM analysing of human joints, finding the optimum material thickness with respect to the joint cartilage has been neglected.
Objectives: To apply a numerical investigation based on the FEM to predict and propose the sheet metal thickness for joint cartilage in the ISF process in a timely method for the human knee as a case study.
Methods: To reduce the expense of experiments and save the time of production, a numerical investigation method based on FEM is designed for the ISF. The user subroutine is employed to navigate the tool motion and material behaviour for reducing the time of simulation in the analysing tool. Hence, the sequence of FEM applied was as follow. 1) Create the solid model of the clamping system and sheet metal. 2) Choosing associated nodes together with Shell elements to increase the accuracy of the simulation and simplify the process. 3) Applying the specifications of every element. 4) Assign and render the material properties for sheet metal. 5) Apply the initial boundary conditions. 6) Assigning the asymmetric boundary conditions using the subroutine for time reduction purpose. 7) Apply the loads related to the complete FEM. Consequently, the proper thickness from MRI based on the previous study is sent to the CAD system for the mechanical and anatomical modification.
Sheet metal thickness and also material selection were based on the joint mechanical properties, shape and size. Therefore, by using the optimum pressure profile, the FEM can be performed to predict the sheet stretch and also shear failure to illuminate the optimum sheet thickness used in customized medical implants.
Results: The result of this study is based on the validation of predicted sheet thickness with the real patient cartilage thickness. This result showed a good agreement with the hospital data (for cartilage thickness of ~2.20mm) and simulation result (~2.23mm for sheet thickness). It was not possible to divide the model into some sections and only analyse one particular part as a sample. Therefore, the time of calculation was 23 hours for FEM when a high-performance computer was used. Regarding the same issue, the mesh was not uniform distributed so the time of analysing for each particular location was not the similar and predictable. The shear failure happens on the edge of design and also some locations that a turning point existed.
Conclusions: A numerical simulation is required to predict the material thickness replaced with the joint cartilage. Thus, the mathematical solution is investigated to predict the sheet thickness in the customized production process. Therefore, the result showed 98.5% similarity thickness of sheet metal with cartilage.
References:
[1] Moayedfar, M., Rani, A. A., & Kumar, D. (2015). An Integrated Manufacturing Method of Customized Medical Knee Implants Using Automated 3D Model Reconstruction and Prototyping Procedure. Annals of the Rheumatic Diseases, 74 (Suppl 2), 623–623.
Acknowledgements: The authors are thankful to the Ministry of Higher Education, Malaysia (MOHE) for supporting this research via FRGS/1/2014/TK01/UTP/02/8 research grant.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2046

AB1243-HPR USING INFORMATION-COMMUNICATION TECHNOLOGIES AND OPPORTUNITIES FOR TELEREHABILITATION IN OCCUPATIONAL THERAPY

B. Huzjan. *Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia*

Background: The use of information and communication technology (ICT) in occupational therapy should allow management of chronic diseases by providing support programs in education including the use of multimedia services.
Objectives: In order to determine the presence of information and communication technologies use in the options of telerehabilitation, a survey was conducted 224 newly diagnosed patients with rheumatoid arthritis (RA).
Methods: The quantitative research approach was used with the newly created detected patients with RA treated on Department of Rheumatology at the University Medical Centre Ljubljana. The questionnaire included basic demographic information and questions about the use extent and possibilities for using ICT. The population also accounted for patients with RA diagnosed between 1 January 2014 and 31 December 2015. The data obtained was statistically analysed with the SPSS program IMB 20. The total of 64 survey questionnaires were completed, which represents 28% of the selected population.
Results: 23.4% RA patients don't use internet. 48.4% RA patients use personal computers (PC), and 51.6% patients use smart phones. 35.3% of patients that use PC use it for e-mailing, searching health information (35.4%), video calls (13.3%) and sending messages (15%). Patients who use smart phones use them for calls (31.9%), texting and calls (26.7%), e-mailing (25%), searching health information (12.9%), and video calls (3.4%). There is a positive correlation between the use of modern ICT and the opinion that the interviewed patients would use telerehabilitation services during their rehabilitation. Pearson correlation coefficients are statistically significant with all the ICT. With using a PC (r =0.602) and smart phones (r =0.542) there is a medium strong positive correlation Positive coefficients indicate that the surveyed patients who are increasingly using ICT think they could help themselves with telerehabilitation. Increased frequency of ICT usage is associated with potentially greater possibility of using telerehabilitation.
Conclusions: The need for rapid access and exchange of information is the main reason for the use of information and communication technologies in healthcare, and is conditional for the development of e-health. Research provided answers questions about the possibilities of using information and communication technology and rehabilitation services at a distance – telerehabilitation in occupational therapy.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3728

AB1244-HPR GUIDED SELF-MANAGEMENT FOR PATIENTS WITH RHEUMATIC INFLAMMATORY DISEASES AND FATIGUE – A PILOT PROJECT

E. Fjerstad[1], R.H. Moe[2,3], S. Nymo[4], T. Berge[5]. *[1]Enhet for psykiske helsetjenester i somatikken, Diakonhjemmet Hospital, Oslo, Norway; [2]Rheumatology, NKRR, Diakonhjemmet Hospital, Oslo, Norway; [3]Rheumatology, NBRR, Diakonhjemmet Hospital, Oslo, Norway, Oslo; [4]Drammen Hospital, Dronninggata 28, 3004 Drammen, Drammen; [5]Enhet for psykiske helsetjenester i somatikken, Diakonhjemmet Hospital, Oslo, Norway*

Background: Fatigue is reported to be a common symptom in people with inflammatory rheumatic diseases. It is a complex symptom, characterized by an individual interplay of biopsychosocial factors that has been associated with factors like inflammation, deconditioning, sleep problems, decreased function, pain and psychosocial factors like depression.
Objectives: The main objective was to contribute to improved coping and quality of life in people with inflammatory rheumatic disease and fatigue. Cognitive therapy is one of the common psychological interventions used in the rehabilitation

of people with rheumatic diseases and fatigue. The current intervention was developed as a supplement to medical treatment to strengthen coping and quality of life, and reducing fatigue, depression and pain.
Methods: People with inflammatory rheumatic diseases and fatigue were recruited for 6–9 sessions of cognitive therapy sessions, in addition to treatment as usual at a rheumatology outpatient clinic in Norway. The intervention aimed at reducing fatigue, depression and pain, consisted of four main elements; understanding fatigue, assessment and activity planning, mental and cognitive self-help skills. The project was developed, and data collected at the rheumatology outpatient clinic at Diakonhjemmet Hospital in 2014–2016.
Results: This pilot project recruited 40 people with inflammatory rheumatic disease from a rheumatologic outpatient clinic in Norway. Participants had a disease duration of mean 14 years, they were mainly women (n=36) with a mean age of 45 (Standard Deviation =10) years (Table 1). Repeated ANOVA analyses and Paired t-tests showed promising statistically significant changes on a group level for fatigue and depression, not for pain (Table 2).

Table 1. Demographic data of included patients (n=40)

N=40	Mean values
Age (SD)	45 (10)
Women (men)	36 (4)
Disease duration (years)	14 (11)

Conclusions: This pilot project supports the idea of conducting a trial on the effectiveness of a brief cognitive therapy intervention for people with inflammatory rheumatic diseases and fatigue. ANOVA analyses and Paired t-tests showed promising statistically significant changes on a group level for fatigue and depression, but not for pain, whether these changes are clinically meaningful, and if there is a difference, compared to treatment as usual remains to be explored.
Acknowledgements: This project would not have been possible without the support from the national patient organization, through a grant from the Norwegian ExtraFoundation for Health and Rehabilitation. We acknowledge patients who contributed to this project and the staff at the rheumatological outpatient clinic at Diakonhjemmet Hospital.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6096

AB1245-HPR NEW HEALTH TECHNOLOGIES AND LIFESTYLE MANAGEMENT FOR PATIENTS WITH OSTEOARTHRITIS

M. Loiskandl[1], H. Ritschl[2], T. Stamm[1], G. Steiner[1], J. Smolen[1], D. Aletaha[1].
[1]Rheumatology, Medical University of Vienna, Vienna; [2]Joanneum, University of Applied Sciences, Graz, Austria

Background: Osteoarthritis (OA) is one of the most common chronic diseases of the elderly worldwide. It represents significant impairments in terms of quality of life [1]. It notably affects self-care-tasks, body-image, self-esteem, well-being, social-activities and relationships. A wide-ranged field of therapy concepts exist. Medication is often one part, but it cannot solve other existing problems due to OA [2]. The demographic trends combined with the growth of mobile devices among the older population suggest that using digital devices, as a platform for interventions in health, may be a viable way forward and open new opportunities in healthcare [2].
Objectives: To (A) analyse the literature to assistive devices and applications for OA patients and (B) to evaluate existing health applications.
Methods: We performed a systematic literature review on this topic and explored existing mobile and web-based apps. The app findings were classified into those categories of the Activities of Daily Living Model, which were related to the impairments of OA.
Results: We identified 6 studies, which contained relevant information. The main results showed, that there is interest and willingness to utilize mobile Health solutions [3]; a positive impact of web-based interventions; the benefit of online social support regarding the level of patient empowerment [4], self-management, lifestyle, physical activity [5] and self-efficacy [6].
The app exploration results in 16 web-based, 15 iOS and 9 Android applications. The areas most commonly found were disease- and treatment information (n=23), forum, report, self-help groups (n=16), self- and disease-management (n=11), as well as nutrition tips (n=8).
Conclusions: The recent years have seen a dramatic growth of digital applications. Also, the scientific interest has grown and numerous studies emphasise the power of these solutions to support OA patient in all areas of lifestyle management. Further research is necessary, to investigate the benefit of web-based or mobile applications for persons with OA.
References:
[1] T. Aigner, S. Söder, Typisierung, Graduierung und Stadieneinteilung der Osteoarthrose: Histopathologische Begutachtung der Gelenkdegeneration, Z. Für Rheumatol., 2008;67(1):32–40.
[2] J. Joe, G. Demiris, Older adults and mobile phones for health: A review, J. Biomed. Inform. 2013;46(5):947–954.
[3] S.J. Parker, S. Jessel, J.E. Richardson, M.C. Reid, Older adults are mobile too!Identifying the barriers and facilitators to older adults' use of mHealth for pain management, BMC Geriatr. 2013;13(1):43.
[4] A. Allam, Z. Kostova, K. Nakamoto, P. J. Schulz, The Effect of Social Support Features and Gamification on a Web-Based Intervention for Rheumatoid Arthritis Patients: Randomized Controlled Trial, J. Med. Internet Res. 2015;17(1):e14.
[5] H. Umapathy, K. Bennell, C. Dickson, F. Dobson, M. Fransen, G. Jones, D.J. Hunter, The Web-Based Osteoarthritis Management Resource My Joint Pain Improves Quality of Care: A Quasi-Experimental Study, J. Med. Internet Res. 2015;17(7):e167.
[6] K.R. Lorig, P.L. Ritter, D.D. Laurent, K. Plant, The internet-based arthritis self-management program: A one-year randomized trial for patients with arthritis or fibromyalgia, Arthritis Rheum. 2008;59(7):1009–1017.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6652

AB1246-HPR INTRA ARTICULAR OZONE OR HYALURONIC ACID INJECTION: WHICH ONE IS SUPERIOR IN PATIENTS WITH KNEE OSTEOARTHRITIS? A 6-MONTH RANDOMIZED CLINICAL TRIAL

S.A. Raeissadat[1], S.M. Rayegani[2], M. Moridnia[3], S. Rahimi Dehgolan[4].
[1]Physical Medicine and Rehabilitation Department, Shahid Modarres Hospital; [2]Physical Medicine and Rehabilitation Department, Shohadaye Tajrish Hospital; [3]Deputy of Education; [4]Physical Medicine and Rehabilitation Department, Shahid Beheshti University of Medical Sciences, Islamic Republic Of

Background: Knee osteoarthritis (OA) is a common disease with great burden through pain and decreased function (1). Except for knee replacement surgery as a definite treatment (2), there are many other therapeutic modalities including non-pharmacologic choices and some heterogeneous drugs like oral, topical and intra articular ones (3). Recent studies have showed promising results of ozone application in OA (2,4–5).
Objectives: The aim of this study was to compare the effects of ozone therapy versus hyaluronic acid (HA) intra articular injection in patients with knee OA.
Methods: This prospective RCT studied 174 patients in two random groups: ozone and HA. We performed three weekly injections of Hyalgan® versus 10 ml of ozone solution in moderate knee OA patients. Participants were primarily evaluated and 6 months after injection using pain, stiffness and function questionnaires.
Results: No major adverse events were noted in the study. Total WOMAC score decreased in the ozone group from 40.8±9.8 to 20.4±4.9 ($p<0.05$) and in the HA group from 38.5±7.9 to 17.1±4.2 ($p<0.05$). A similar trend was observed in pain improvement according to VAS (table 1). Pain, stiffness and function significantly improved in both groups but no differences were found between groups.
Conclusions: Although both ozone and HA can be effectively used for improving function and reducing pain in selected patients with knee OA, neither of the two showed no superiority at 6 months follow up.
References:
[1] Richmond J, Hunter D, Irrgang J, et al. American Academy of Orthopaedic Surgeons clinical practice guideline on the treatment of osteoarthritis (OA) of the knee. J Bone Joint Surg Am 2010; 92:990–993.
[2] Kr Mishra S, Pramanik R, Das P, Pratim Das Pl. Role of intra-articular ozone

Abstract AB1244-HPR – Table 2. Self-reported fatigue and depression at baseline, after treatment and at 6 months follow-up

Scale	Mean (SD) t1	Mean (SD) t2	Mean (SD) t3	P-value diff ANOVA	Paired t-test T1–3
BRAF fatigue[$]	13.89 (5.4)	10.85 (4.9)	9.46 (5.8)	p>0.001	Diff 4.57 (CI: 2.2/7.0) (p>0.001)**
PHQ[#]	25.13 (5.9)	20.67 (6.8)	18.25 (7.1)	p>0.001	Diff 6.44 (CI:4.0/8.9) (p>0.001)**
VAS pain[†]	45.54 (24.4)	39.08 (21.1)	36.9 (23.0)	p>0.241	Diff 7.64 (CI:-1.4/16.7) (p>0.096)

[$]BRAF (Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional questionnaire) fatigue global score (0–30), [#]PHQ-9 (Patient Health Questionnaire) depression score (0–70), [†]VAS pain (0–100).

Abstract AB1246-HPR – Table 1

Measure	Ozone Therapy (Mean ± SD)		Raw Mean Difference (SE) [95% CI]	HA Therapy (Mean ± SD)		Raw Mean Difference (SE) [95% CI]
	Before	After		Before	After	
VAS	7.6±2.8	2.6±2.0	-5.0 (0.2) [4.6–5.4]	7.1±3.2	3.0±2.4	-4.1 (0.15) [3.8–4.4]
WOMAC Pain	9.3±4.4	3.2±1.6	-6.1 (0.2) [5.7–6.5]	8.8±4.0	2.9±1.6	-5.9 (0.2) [5.5–6.3]
WOMAC Stiffness	2.3±2.4	1.1±1.6	-1.2 (0.05) [1.1–1.3]	2.1±1.6	1.1±0.8	-1.0 (0.05) [0.9–1.1]
WOMAC Function	29.2±7.0	16.1±4.2	-13.1 (0.15) [12.8–13.4]	27.6±6.6	13.1±3.2	-14.5 (0.3) [13.9–15.1]
WOMAC Total	40.8±9.0	20.4±5.0	-20.4 (0.2) [20.0–20.8]	38.5±8.0	17.1±4.2	-21.4 (0.2) [21.0–21.8]

in osteoarthritic knee for functional and symptomatic improvement. IJPMR 2011;22:65–69.
[3] Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Viscosupplementation for the treatment of osteoarthritis of the knee. Cochrane Database Syst Rev 2006;(2):CD005321.
[4] Sello Lebohang Manoto, Makwese Johaness Maepa, Shirley Keolebogile Motaung. Medical ozone therapy as a potential treatment modality for regeneration of damaged articular cartilage in osteoarthritis [Article in Press]. Saudi Journal of Biological Sciences (2016).
[5] Velio Alvaro Bocci. Scientific and Medical Aspects of Ozone Therapy: State of the Art. Archives of Medical Research 37 (2006) 425–435.
Disclosure of Interest: S. A. Raeissadat Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, S. M. Rayegani Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, M. Moridnia Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None, S. Rahimi Dehgolan Shareholder of: None, Grant/research support from: None, Consultant for: None, Employee of: None, Paid instructor for: None, Speakers bureau: None
DOI: 10.1136/annrheumdis-2017-eular.5484

HPR professional education, training and competencies

AB1247-HPR AN INTEGRATED APPROACH IN CUSTOMIZED MEDICAL FEMORAL COMPONENT PRODUCTION TO MINIMIZE THE CONDYLE CUT OFF DURING THE TKA

M. Moayedfar, A.M. Abdul Rani. *Mechanical Engineering, Universiti Teknologi Petronas, Bandar Seri Iskandar, Malaysia*

Background: To prepare the femoral component during the Total knee arthroplasty (TKA), it is needed to cut off the damaged condyle to a dimension matched with one of the available implant sizes in the market. Since there is a variety of humans' knee size and shape, therefore, some parts of the distal femoral are over cut. The solution to this problem is customisation of the implants via a cohesive procedure specifically designed for medical orthopaedic implant production.
Objectives: This research aims to provide a fully integrated system of digital image processing of Magnetic Resonance Imaging (MRI) data and Finite Element Method (FEM) for testing and analysing prior to manufacturing of customized medical femoral component.
Methods: An automatic algorithm to segment MR images from end-of-femur condyle is developed and employed for 3D reconstruction followed by computer-aided design (CAD) system, FEM and incremental sheet forming (ISF) process. In femur segmentation, multi-resolution edge detection is applied that extracts all the edges at bone surfaces. The edge detection process followed by the selection and extraction of strong edges with enhanced active contour technique that results in separation between femur and tibia components. Morphological processing is applied to extract the femur region as the segmented outcome. Consequential of segmentation, a surfaces rendering method is applied for the 3D structure that automatically converts the model into standard tessellation language (STL) format for later CAD system and rapid prototyping preparation. Generated STL file is applied for creating a solid part and solid body. The Proper femoral component is designed using region growing technique then exported to FEM system to calculate the best metal thickness and angles, regarding the normal cartilage, to bear the maximum load with the lighter material. The process of ISF that involves machining and sheet forming parameters is using to manufacture customized medical metal femoral component but in low surface quality which increases the risk of ion release at *in vivo* condition. Therefore, during this technique, optimum parameters using Design of Experiment method are applied to modify and enhance the sheet stretching of final parts.
Results: Applying this integrated system demonstrates a cohesive user-friendly system for creation of patients specific implants while it showed a substantial reduction in implant production time compares to the current manufacturing method. In ISF process optimum parameters are used to increase the rate of stretching together with the best sheet thickness ∼2.5 mm based on validated sheet stretching simulation. The results of this study also show that the high surface quality for femoral component up to ∼Ra 2.527 is achievable using this newly developed method.
Conclusions: An integrated system that combines computational method, CAD, FEM and ISF procedure is developed that shows its potential for manufacturing of customized medical femoral component. Flexibility in size and shape make this system prominent. The best sheet thickness with respect to the cartilage thickness is calculated and obtained with the optimum process parameters for manufacturing section.
Acknowledgements: The authors are thankful to the Ministry of Higher Education, Malaysia for supporting this research via FRGS/1/2014/TK01/UTP/02/8 research grant.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1351

AB1248-HPR THE ROLE OF PATIENT SUPPORT PROGRAMMES IN HEALTH LITERACY OF PATIENTS. RESULTS OF A 1.5-YEAR-LONG HUNGARIAN STUDY

A. Domján[1], Z. Szekanecz[1], J. Pilling[2], G. Purebl[2], Z. Szabo[1], P. Kakuk[3]. *[1]Department of Rheumatology, University of Debrecen Faculty of Medicine, Debrecen; [2]Institute of Behavioural Sciences, Semmelweis University, Budapest; [3]Institute of Behavioural Sciences, University of Debrecen, Faculty of Public Health, Debrecen, Hungary*

Background: Health literacy means our ability to find our way in health issues, to understand health information and how to utilize them, that is how we can understand and use health information. Unfortunately, every second person has serious deficit in this area in Hungary.
Objectives: We wished to determine the effectiveness of a specialized patient support program in Hungary.
Methods: The present study was conducted between August, 2015 and December, 2016 in Hungary. Altogether 24 health professionals in 15 investigational sites including rheumatology, gastroenterology and dermatology centres were involved. All participating health professionals was qualified and skilled in patient education. We tried to enrol mainly new patients with relatively little knowledge of their chronic illness. The participation was completely voluntary. The programme was based on 4 presentations on various but closely related topics, presented in small-group sessions by health professionals, and then discussed with the patients. The topics of the lectures were as follows: How to manage stress, associated with the disease? How to deal with the emotional burden of the disease? How to use social support when fighting a chronic disease? How should I tell? (physician-patient communication). The theoretical framework of the lectures was composed by 2 psychiatrists, proficient in the subject. The health professionals had also received extensive training before the programme. Altogether 1950 participants were present at least one of the lectures: Only those were carried forward and allowed to complete the questionnaire who participated in all 4 lectures of different topics. Thus, 480 patients completed the 8 questions of the questionnaire that evaluated the effectiveness of the programme.
Results: Among the 480 patients, who completed the study, 66% had joint and musculoskeletal complaints, 32% had inflammatory skin or gastrointestinal disease and 2% of them suffered from other chronic diseases. Altogether 24% was a member of a patient organization. Two-third of the patients felt better prepared for their consecutive doctor-patient or nurse-patient appointment after participating in the programme. In total, 49% of the responders found the doctor-patient communication lecture most helpful. In addition, 73% of them were able to successfully manage disease-related events and stress. Two-third of the patients wished to contact and/or keep in contact with a patient organization in order to take advantage of the opportunities of social support and 76% understood the place and role of patient organizations in the society. We wish to continue the programme in 2017 and we are aiming to target communication channels appropriate for the needs and opportunities of our age (e.g. Facebook).
Conclusions: The educational programme described above was successful among our patients. We think that appropriate health literacy can lead to the better understanding of the disease and maybe to the improvement of unfavourable health indicators.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1514

AB1249-HPR THE EFFECT OF TASK-ORIENTED TRAINING ON FUNCTIONALITY, DEXTERITY AND ADL PERFORMANCE IN RHEUMATOID ARTHRITIS

Ö.F. Özçelep[1], E.I. Üstün[2], Z.C. Algun[3]. *[1]Prosthetics Orthotics Research Center, Istanbul Medipol University; [2]Physical Therapy and Rehabilitation, Bağcılar Education and Research Hospital; [3]Orthotics and Prosthetics, Istanbul Medipol University, Istanbul, Turkey*

Background: Rheumatoid arthritis is the most common and most serious of the inflammatory arthritides, and it dominates clinical rheumatological practice (1).This inflammation leads gradually to a destruction of bone and cartilage, responsible for loss of function (2).The main goals of treatment for RA are to prevent or control joint damage, prevent loss of function, and decrease pain (3).
Objectives: The purpose of the study is to investigate the effect of task oriented training on functionality, dexterity and ADL performance in rheumatoic hands.Also the other goal of this study is to bring a new perspective to RA rehabilitation.
Methods: Thirty seven women (16 patients in control group and 17 patients in study group) performed therapy programme. Control group received hand exercise therapy (MCP, DIP, PIP mobilization, range of motion exercise, isometric exercise) and study group received both hand exercise therapy and task oriented training (fork use, drinking water with a glass, face washing, sit up-stand up and t-shirt wearing) twice a week for 5 weeks. Every therapy sessions took 40–45 minutes for study group and 20–25 minutes for control group. According to the patient's condition, the rest interval was given and it was said that the exercises should not be done too fast. The results were evaluated before and after the therapy program with Jamar Hand Dynamometer, Nine Hole Peg Test, Health Assessment Questionaire and Duruöz Hand Index.
Results: Age distribution of participants was 49, 57 ($p>0,005$) and were found to be homogeneously dispersed ($p=0$, 15). Hand grip strength was not statistically

significant, although it increased in both groups except left hand grip strenght which was decreased after the program (control group: =0,552 (right hand), p=0, 666 (left hand)/study group: p=0,136 (rigt hand), p=0,723 (left hand)).The NHP showed a decrease in the duration of the test within both groups, but this decrease was not statistically significant (control group: p=0,113 (right hand), p=0,265 (left hand) /study group: p=0,215 (right hand), p=0,291 (left hand). The HAQ showed a statistically significant decrease in both groups (control group: p=0,001/study group: p=0,01).Although DHI decreased in both groups, the decrease in the study group was not statistically significant (control group: p=0,003/ study group: p=0,440).Treatment efficacy between groups after treatment was evaluated by Independent-t test and change in parameters other than HAQ and DHI was not statistically significant.

Conclusions: Hand exercise program and task oriented training are safe methods that can be used to increase the grip strengths of patients with rheumatoid arthritis, daily life activities and hand skills.The statistical significance of the results may be due to the low number of patients.We assume that this study can be done in a larger sample, the effect of task-oriented training on patients with rheumatoid arthritis will be better.

References:

[1] Emery P. Pocket Reference to Early Rheumatoid Arthritis. Springer Healthcare; 2011.
[2] Bouysset M, Tourné Y, Tillmann K. Foot and ankle in rheumatoid arthritis.
[3] Christie A, Jamtvedt G, Dahm KT, Moe RH, Haavardsholm E a, Hagen KB. Effectiveness of nonpharmacological and nonsurgical interventions for patients with rheumatoid arthritis: an overview of systematic reviews. Phys Ther.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1065

People with Arthritis and Rheumatism in Europe
Abstracts

Poster Presentations

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Building patient led organisations

PARE0001 GROWING STRONGER TOGETHER: IMPLEMENTING EULAR YOUNG PARE'S STRATEGY

J. Andersen[1,2,3], P. Balazova[1,4,5], P. Boyd[1,6], W. Olsder[1,7], S. Ostuzzi[1,8], T. Papastavrou[1,4,9], S.R. Stones[1,10,11], T. Wilhelmer[1,12], L. Van Nieuwkoop[7], N. Caeyers[4,13], F. Klett[14]. *[1]EULAR Young PARE, Zurich, Switzerland; [2]Lupus Europe, Essex, United Kingdom; [3]Sle/Lupus Ung Dk, Gigtforeningen, Gentofte, Denmark; [4]EULAR Standing Committee of PARE, Zurich, Switzerland; [5]Slovak League Against Rheumatism, Piestany, Slovakia; [6]Arthritis Ireland, Dublin, Ireland; [7]Youth-R-Well.com, Lisse, Netherlands; [8]ANMAR Young, Rome, Italy; [9]ELEANA Hellenic League Against Rheumatism, Athens, Greece; [10]Fibromyalgia Action UK, Paisley, Renfrewshire, United Kingdom; [11]University of Leeds, Leeds, United Kingdom; [12]Österreichische Rheumaliga, Salzburg, Austria; [13]ReumaNet Jong & Reuma, Bresserdijk, Belgium; [14]EULAR, Zurich, Switzerland*

Background: In a recent European youth survey, 53% reported that rheumatic and musculoskeletal diseases (RMDs) affected their ability to work, while 75% reported that RMDs interrupted their education. Therefore, in 2017 and 2018, while continuing to achieve the objectives reached in 2015 and 2016, EULAR Young PARE will focus on two key points from EULAR Young PARE's strategic objectives: work and education.
Objectives: In 2017, in line with EULAR's efforts to raise awareness of the needs of people with RMDs among employers and other stakeholders, the specific and still unmet needs of young people with RMDs will be highlighted, so that employers and other stakeholders will be more aware of the needs of young people with RMDs and young people will receive better support to find a suitable job. In 2018, education for young people with RMDs will be in focus, so that educational institutions across Europe will be more flexible and assistive in supporting high quality education for young people with RMDs.
Methods: In 2017, we will support EULAR's lobbying activities by raising awareness among employers and other stakeholders about the needs of young people with RMDs. We will also provide information to support young people in finding suitable jobs and to be aware of their rights in the workplace. Best practices concerning ergonomics, support programmes, career counselling and suitable jobs will be collected and shared. In 2018, we will support educational institutions across Europe to be more flexible and assistive in providing high quality education for young people with RMDs by offering training and support to national youth leaders.
Results: Thanks to the results achieved in 2015 and 2016, it is anticipated that structures will be in place to continuously raise awareness among employers, medical staff in schools, teachers and unions about the competencies and limitations of young people with RMDs. These activities enable EULAR Young PARE to expand and strengthen the active network of youth groups across Europe. Every PARE organisation will have a PARE youth liaison person, who will be encouraged and supported to take active roles in their national organisations and in the EULAR community.
Conclusions: The objectives reached by EULAR Young PARE in 2015 and 2016 are closely related to its future aims and achievements, allowing EULAR Young PARE to grow stronger and continue its work by the side of young people with RMDs, in order to improve their quality of life.
References:
[1] EULAR Young PARE. Available from: http://www.youngpare.org [accessed on 30 January 2017].
Acknowledgements: Special thanks to EULAR and EULAR PARE for supporting the vision of EULAR Young PARE. EULAR Young PARE would also like to acknowledge all of the patient organisations that they continue to work with.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4891

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Arthritis research

PARE0002 CELEBRATING TEN YEARS OF SUCCESSFUL PATIENT INVOLVEMENT IN RESEARCH OF INFLAMMATORY CONDITIONS

A. Higginbottom[1], S. Blackburn[1], L. Campbell[1], C. Rhodes[1], R. Taylor[1], A. Machin[1], S. Hider[1,2], E. Roddy[1,2], C.A. Chew-Graham[1], K. Dziedzic[1]. *[1]Research Institute of Primary Care and Health Sciences, Keele University, Keele; [2]Haywood Academic Rheumatology Centre, Staffordshire and Stoke-on-Trent Partnership Trust, Stoke-On-Trent, United Kingdom*

Background: In 2016, the Research Institute (RI), Primary Care and Health Sciences, Keele University, UK, celebrated 10 years of Patient and Public Involvement and Engagement (PPIE) in research of musculoskeletal and other long term conditions. Our Research User Group (RUG) with over 90 members with a range of long-term conditions, actively work with research teams on studies. Many of whom have been involved in ten studies of different inflammatory conditions. We provide two case studies: 1) CONTACT: a trial comparing the effectiveness and side-effects of two commonly-used drugs (Naproxen and low-dose Colchicine) to treat acute gout in primary care; 2) A qualitative interview study with people with rheumatoid arthritis (RA) who had attended a nurse-led review clinic, which included identifying people at risk of anxiety and depression.
Objectives: To describe how PPIE helped shape the design and delivery of the CONTACT and qualitative interview studies.
Methods: 1) For the CONTACT trial, two RUG members with experience of gout joined the Trial Steering Committee. Another seven RUG members formed an advisory group to provide the patient perspective on trial procedures.
2) For the qualitative interview study, a group of eight people with RA from a local rheumatology centre (*Haywood User Group)* commented on the documents for the ethics application and met to discuss data analysis and dissemination.
Results: 1) In the CONTACT trial, RUG members made a difference by:
- Commenting on the trial design and acceptability of the drug intervention
- Helping to produce clear and user-friendly information sheets for participants in the trial.
- Provide practical advice regarding how participants were recruited

Future RUG involvement will include helping to interpret the trial findings planning further dissemination and discussing future research studies.
2) In the qualitative interview study, the PPIE group:
- Contributed to the development of readable patient questionnaires for use in the clinic
- Offered their perspectives on the interpretation of the qualitative data
- Helped develop a leaflet to inform patients about mood problems related to rheumatoid arthritis and where help could be sought
- Contributed to the establishment of an RA annual review clinic at the local hospital
- Advised on the dissemination of results to a lay audience
- Generated ideas for a study about the delivery of RA annual review clinics in primary care, supporting a related grant application

Conclusions: Both studies demonstrated the wide-ranging benefits of PPIE input throughout the research cycle of identification, designing, managing and disseminating research. The RI will continue to involve patients with long-term conditions in studies for the benefit of the wider patient community.
Acknowledgements: We thank all of our Research User Group members for their valuable time and contribution to the RI's research. CONTACT was funded by the NIHR School for Primary Care Research. The RA qualitative study was funded by the Scientific Foundation Board of the Royal College of General Practitioners and the Haywood Foundation. KD is part-funded by a NIHR Knowledge Mobilisation Research Fellowship (KMRF-2014–03–002). CCG is part funded by the NIHR Collaborations for Leadership in Applied Research and Care West Midlands.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3144

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Work and rehabilitation

PARE0003 ASSESSMENT OF PAIN AND IMPORTANCE OF EXERCISE IN HIP OSTEOARTHRITIS

A. Jurisic Skevin[1], V. Grbovic[2], A. Divjak[1], A. Tomic Lucic[1], M. Veselinovic[1], D. Pavlovic[3], J. Nurkovic[4]. *[1]Faculty of Medical Science; [2]Clinical center Kragujevac, Kragujevac; [3]Specialized Rehabilitation Hospital Bukovicka banja, Arandjelovac; [4]State University of Novi Pazar, Novi Pazar, Serbia*

Background: Osteoarthritis (OA) of the hip is a common condition which affects men and women of all ages. The cartilage becomes damaged. Stiffness and reduced range of movement are common. The pain experienced from OA of the hip may be felt in your lower back, buttocks and groin. You may also feel pain from your hip in your leg and down into your knee. This is called referred pain.The goals of OA treatment include alleviation of pain and improvement of functional status. Optimally, patients should receive a combination of nonpharmacologic and pharmacologic treatment. A physiatrist may help in formulating a nonpharmacologic management plan for the patient with OA.

Guidelines from Osteoarthritis Research Society International (OARSI) advise that nonpharmacologic treatment of hip and knee OA include the following: patient education; heat and cold; weight loss; exercise; physical therapy; occupational therapy; unloading in certain joints (eg, knee, hip).
Objectives: The aim of this study was to investigate the importance of exercise and TENS (Transcutaneous electrical nerve stimulation) therapy in patients with OA of the hip on the pain and functional status.
Methods: This was a prospective clinical study involving 20 patients with primary hip OA treated stationary at the Center for Physical Medicine and Rehabilitation during 2016. On receipt of all the respondents filled out the social survey, quantification of pain was conducted by visual analogue scale (VAS) and function was evaluated through measurement of the range of motionin hip joint. After that, they received physical therapy (exercise and TENS therapy) for 21 days. TENSwas applied once a day for 30 minnuteson both hip joints, with the frequency of 85 Hz and with short-term pulses (4 ms) (appliance TENS-2, Electronic Design Medical, Serbia). Exercisewas applied once a day for 30 minutes, according to individually customized protocol; active and active-assisted exercises were used to the point of pain for strengthening the muscles of the lower extremities and to increase range of motion in the hip joints.One month after the inspection we tested functional status and pain.
Results: There was 100% of women, mean age 64.15±4.06 years. The most represented were retirees, 60%, followed by workers and unemployed 10% and 30%.BMI was 27,3±4,22 kg/m^2. After a month there was a statistically significant reduction in pain measured by VAS (at the beginning it was 6,7; at the end 3,2; $p<0.001$). At the end of the study there was a statistically significant increasingrange of motion for active flexion ($p<0.05$) and active abduction ($p<0.0,5$), while there was no statistically significant increasing for active extension, adduction, internal and external rotation in the hip joint ($p>0.05$).
Conclusions: The ACR strongly recommends the following nonpharmacologic measures for patients with knee or hip OA: cardiovascular or resistance land-based exercise, aquatic exercise, weight loss, for overweight patients. TENS may be another treatment option for pain relief. Our study showed that exercise and TENS therapy led to a statistically significant reduction in pain as measured by VAS pain scale and improving range of motion in hip joint.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.3465

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Patient information and education

PARE0004 PATIENT REPORTED LONG TERM EFFECTS OF SIX WEEK PROGRESSIVE RESISTANCE TRAINING PROGRAMME FOR RHEUMATOID ARTHRITIS

R. Tekkatte[1], A. Suarez[1], B. Berntzen[2], D. Collins[1], E. Price[1], L. Williamson[1]. *[1]Rheumatology; [2]Physiotherapy, Great Western Hospital NHS Foundation Trust, Swindon, United Kingdom*

Background: We introduced six week physiotherapy led progressive resistance training (PRT) programme for Rheumatoid arthritis (RA) patients to improve physical function and prevent the muscle loss (rheumatoid cachexia). Six week data showed improvement in body composition, physical function and fatigue scores[1]. There is little published data about the longer term benefits of short exercise interventions and therefore we wished to study longer term effects on exercise behaviour in our patient group.
Methods: We surveyed 79 RA patients who had completed the six weeks PRT programme between 2013 and 2016 using two methods: Anonymous postal questionnaire; Direct telephone questionnaire. Patients were asked the same following questions: 1. Describe the best you feel at present following the exercise programme? Same/ Better/ Worse. 2. Have you continued with progressive resistance exercises? Yes/ No. 3. Do you feel the programme was worthwhile? Yes/No. 4. Did you feel the programme was too long, just right or too short?
Results:

Patient	Continued PRT 75% (27/36) (Postal)	Not continued PRT 25% (9/36) (Postal)	Continued PRT 51% (22/43) (Telephone)	Not continued PRT 49% (21/43) (Telephone)
Better	81% (22/27) (p=0.006)	33% (3/9)	77% (17/22) (p=0.009)	38% (8/21)
Same	15% (4/27)	56% (5/9)	18% (4/22)	19% (4/21)
Worse	4% (1/27)	11% (1/9)	5% (1/22)	43% (9/21)

Postal questionnaire: 45% (36/79) patients returned the postal questionnaire. Time from PRT programme completion to postal questionnaire was: range (mean) 12–36 (26) months. 69% (25/36) still felt better; 25% (9/36) felt the same; 3% (1/36) worse since the programme. 91% (33/36) felt the programme was worthwhile. 75% (27/36) continued PRT exercises. 81% (22/27) of these still felt better, compared with 33% (3/9) who have not continued PRT (p=0.006). The duration of the programme was just right for 69% (25/36) and too short for 30% (11/36).
Telephone questionnaire: 54% (43/79) patients were contactable by telephone. Time from PRT programme completion to telephone questionnaire was: range (mean) 14–38 (26) months. 58% (25/43) still felt better; 18% (8/43) felt the same; 23% (10/43) worse since the programme. 95% (41/43) felt the programme was worthwhile. 51% (22/43) continued PRT exercises. 77% (17/22) still felt better, compared with 38% (8/21) who have not continued PRT. (p=0.009). 49% (21/43) had not continued PRT exercises, of whom 43% feel worse at present. The duration of the programme was just right for 47% (20/43) and too short for 53% (23/43).
Conclusions: Over 90% of patients who responded found the six week PRT programme worthwhile. More than half (51–75%) of the patients continued a PRT exercise programme. Patients who continued exercises felt better compared with those who did not continue exercises.
References:
[1] Berntzen et al A Six-Week Progressive Resistance Training Class Improves Function and Fatigue in RA Patients: Annals of the Rheumatic Diseases 75 (S2):254 2016.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5840

PARE0005 EDUCATIONAL PROGRAM FOR OLDER ADULTS WITH KNEE OSTEOARTHRITIS

M.R. Espanha[1], P.P. Marconcin[1,2], P.L. Campos[2], F.G. Yázigi[3]. *[1]Portuguese League Against Rheumatic Diseases; [2]Department of Sports and Health; [3]Department of Sports & Health, Faculty of Human Kinetics, University of Lisbon, Lisboa, Portugal*

Background: Osteoarthritis is the commonest cause of disability at older ages and it is a huge burden on primary care (Peat, McCarney, & Croft, 2001). The knee joint is one of the most affected in elderly, influencing directly physical function and affecting physiological and social parameters. Therefore, it is imperative to development strategies that help individuals to change the way the disease affect their lives. International recommendations reinforce educational and exercise programs as the core of non-pharmacological approaches to enhance physical functional and relieve pain and others osteoarthritis symptoms.
Objectives: The purpose was to assess the effectiveness of three months educational program for older adults with knee osteoarthritis (KOA).
Methods: Participants recruitment was done in the community using various marketing strategies. Forty individuals with 60 years or more, bilateral or unilateral KOA diagnosed according to clinical and radiological criteria of the ACR (1) and independently mobile and literate participated in the program. Educational sessions regarding exercise and joint protection strategies were offered. Telephone calls were done 15 days after each educational session. Patients received a book (2), with a core exercise section. Patients in the first attendance session were taught to do registration in an exercise training diary. Self-reported measures were pain, other symptoms, activities of daily living (ADL), and quality of life assessed by Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire (3), Patient Global Impression of Change Scale (PGICS).
Results: Final sample included 32 adults (age: 67.8±5.3 years; bilateral KOA: 93.8%; female, 59.4%; BMI: 30.1±5.3 kg/m^2). Eight participants did not complete the program (3 due to health problems and 5 for personal reasons). KOOS pain improved 10% (p=.042), and other symptoms 8%. Improvement in KOOS ADL (-8.7±13.6) and quality of life (-8.2±18.0) were also observed. 47% of the participants reported significant changes (scores 5–7) after intervention and a decrease in medication use of 31.3%.
Conclusions: The educational program can be an effective and suitable way for osteoarthritis management and to improve pain and health-related quality of life, leading individuals with KOA to better control their pathology and consequently living better.
References:
[1] Altman, R., Asch, E., Bloch, D., Bole, G., Borenstein, D., Brandt, K., Brown C, Cooke TD, Daniel W, Feldman D, et al. (1986). Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum, 29(8), 1039–1049.
[2] Espanha, M., Priscila, M., Yázigi, F., Marques, A., Machado, M., Campos, P., & Carrão, L. (2015). Guia para viver em PLENO: com menos dor e mais qualidade de vida. Lisboa: FMH-ULisboa, Lab. de Biomecânica e Morfologia Funcional.
[2] Roos, E. M., & Lohmander, L. S. (2003). The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. Health and Quality of Life Outcomes, 1, 64–64. doi: 10.1186/1477–7525–1-64.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6642

PARE0006 PATIENT INVOLVEMENT IN BASIC RESEARCH: A PILOT STUDY

Y. Neijland[1], C. van den Ende[1], F. van den Hoogen[1], P. van der Kraan[2], F. van de Loo[2], M. Lieon[3]. *[1]Sint Maartenskliniek; [2]Experimental Rheumatology, Radboud University Medical Centre; [3]Patient Representative, Sint Maartenskliniek, Nijmegen, Netherlands*

Background: Although the potential value of patient involvement in clinical research has been recognized [1], involvement of patient representatives (PRs) in non-clinical research is uncommon.

Objectives:
- Mapping beliefs of researchers and PRs about the potential value of patient involvement in basic research.
- To document experiences of both patient representatives and researchers of a pilot project of PRs participating in basic research.

Methods: The method of participatory action research has been used. This is a research approach that emphasizes both participation and action [2]. In this case two working groups were involved. The coordinator participated in meetings of the working groups, made notes during these meetings about the nature and degree of participation, evaluated the meetings with the participants and kept a diary. At the start and at the end of the pilot 6 researchers of the working groups were interviewed by the coordinator. The findings of the interviews were categorized and summarized. During 6 months, 5 PRs were invited to attend once a month, in one of the working group meetings. In the first meeting expectations of both researchers and PRs were exchanged. In the following meetings one researcher presented a lay version summary of his/her work. There was room for PRs to ask questions.

Results: Prior to the pilot, some researchers had doubts about the added value of PRs, others were more positive and even curious. All PRs were open minded about the pilot, although none of them had experience with involvement in basic research.

At the end of the pilot, researchers expressed positive statements, such as: "(very) nice, good initiative and interesting discussions." Positive experiences included: exercise in explaining their work to lay persons; stimulation in developing a more holistic (helicopter) view of their research, and getting a better insight in problems in daily life that patients encounter.

The PRs experienced the atmosphere during meetings as open and pleasant; they felt that the degree of participation was limited, but worthwhile.

The coordinator observed that interaction between the researchers and PRs mainly consisted of asking questions for clarification. Besides, the coordinator observed after presentations exchanges between PRs and about research-related issues such as the availability of human tissues for research and conversations about personal experiences.

Critical comments were made about the difficulty in understanding the complex matter for PRs and the chosen method (researcher presents, PRs listened) that does not encourage interaction.

Conclusions: There is a potential value of patient involvement in basic research. A first result is that junior researchers develop a more holistic view of their research subject.

An open atmosphere and low expectations may contribute to success. Continuation of this pilot with modifications, including more research groups and PRs, are needed to finds ways to increase patient involvement in basic research.

References:

[1] Hsiao B., Fraenkel L., Incorporating the patient's perspective in outcomes research. Wolters Kluwer Health 2017 Number 00, volume 29.

[2] Wikipedia. https://en.wikipedia.org/wiki/Participatory_action_research.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4898

PARE0007 HOPES AND FEARS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN SPAIN. THE VALUE OF PATIENT OPINION: RESULTS FROM THE SPANISH ATLAS

M. Garrido-Cumbrera[1,2], P. Plazuelo-Ramos[2], A. Costa[3], O. Brace[1], J. Chacón-García[1], D. Gálvez-Ruiz[1]. *[1]Universidad de Sevilla, Seville; [2]CEADE, Madrid; [3]Novartis, Seville, Spain*

Background: Not much attention has been paid to listening to the opinions of patients in most scientific studies on Spondyloarthritis, despite their opinions playing an increasingly important role in decision-making alongside clinical and public health criteria.

Objectives: To assess the opinions of patients with Axial Spondyloarthritis (ax-SpA) using qualitative information.

Methods: A sample of 680 patients diagnosed with ax-SpA was interviewed during 2016 as part of the Spanish Atlas, which aims to promote early referral and improve healthcare and the use of effective treatments in patients with ax-SpA. The Atlas is a CEADE initiative (Spanish Coordinator of Patients with ax-SpA in Spain) developed by the University of Seville and Max Weber Institute in collaboration with GRESSER (Spanish Rheumatology Society spondyloarthritis study group). Responses to qualitative items about patients' hopes and fears for their disease and their personal aims regarding their treatment were analysed.

Results: 53% were females, mean age 46 years and 77.1% were HLA-B27+. The five main hopes of patients are: stopping the disease, dream of a cure, elimination of pain, improve their quality of life and live without limitations. Additionally, patients has expectations on the medical research outcomes. Thus, 81% of patients hope that the research will make possible to find the cause and a cure for ax-SpA, developing more efficient biologic therapies (11%), and finding new techniques or medication (8%).

The following stand out among drug treatment-related concerns: having more effective treatments (32%), sustaining the results of biologic therapies (29%), being able to start on biologics (8%), the public health system funding non-drug treatments for AS (8%), eliminating secondary effects (15%), reducing prices (4%), and correct use (4%).

With respect to their fears, patients stated that their main concern was mobility loss (31%), followed by loss of independence (23%), disability (22%), stiffness (12%), structural damage (3%), organ damage (3%), other illnesses and diseases related (3%), physical decline (3%), and sight loss (1%).

Patients who expressed fear regarding their disease listed their greatest concern was that they would not overcome or tolerate pain (56%), followed by the fear that the disease would develop (32%), along with apprehension about flare-ups (7%), and tiredness (5%).

With respect to patients' personal objectives in terms of their treatments, they highlighted the wish that their treatment would, first, help them to reduce and eliminate pain, increasing their in mobility, improved quality of life, the avoidance of structural damage and the disease eventually being cured.

Conclusions: Analysis of patient opinion using qualitative information has enabled the identification of important concerns for patients such as discovering the cause of the disease, reducing pain and structural damage, loss of self-sufficiency and disability.

Acknowledgements: This project has been supported by Novartis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6771

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Best practice campaigning

PARE0008 TRANSITION: PARTICULARLY DIFFICULT TIME FOR YOUNG PEOPLE WITH AR

U.G. Viora[1], E. Fusaro[2], S. Martino[3], D. Montin[3]. *[1]Anmar Italia; [2]SC Reumatologia; [3]SS Immunoreumatologia pediatrica, Città della salute e della scienza, Torino, Italy*

Background: Transition is a multifaceted process involving medical, psychosocial, educational needs of the teenager who must move from a pediatric care to adult care system.

The pediatric paradigm focuses on the family, it focuses on aspects of growth and development, often neglecting, to acknowledge the increasing independence and autonomy of the patient as an individual.

The culture of adult medicine implies to have as a partner a patient independent and autonomous in the management of the disease, including aspects of playing, ignoring the issues related to the growth, development and relations with the family.

Objectives: to drive the patient along the transition, getting him finding the new treating as a continued assistance, more mature and personalized in sharing issues related to the disease; to create a best practice of transition service.

Methods: promoted by AMaR Piemonte - regional expression of ANMAR - and thanks to the availability and sensitivity of the doctors of the Pediatric Rheumatology Service (responsible Prof. Silvana Martino) and the UOA Rheumatology (director dr. Enrico Fusaro), located in two different buildings of the same "Città della Salute e della Scienza di Torino" hospital, it was possible to organize a transition pathway for teenagers since eighteen, structured as follows:
- *first telephone contact between Pediatrician Rheumatologist and Rheumatologist*
- *sharing of clinical and personal information about the young patient*
- *introduction to the new care giver:* during the routine consultation Pediatrician Rheumatologist presents his colleague, anticipating the different types of examinations and departmental activities and highlighting the peculiarities and sensitivity of his colleague
- *meeting with parents:* on the fringes the two specialists meet parents, preparing them for their future role and announcing that in the next visit they will be excluded
- *transition examination:* directly scheduled, it is a joint examination by the two rheumatologists to the young patient, who is directly involved discussing his health state and the decisions to be taken to continue therapies or monitoring the disease (if in remission). A second one may be scheduled if the young patient shows severe psychological problems.
  A collegial meeting between patient, rheumatologists and physiatrist/rehabilitator will be programmed if a special rehabilitation is needed
- *taking care:* the new rheumatologist takes care of the young patient

All the pathway takes end in a period of time not exceeding one month, with a maximum of three consultations.

Results: 52 patients (79% female, 21% male) taken in care by "adult" rheumatology since 2012 to 2016. No patient reports he lived the transition as a trauma and 10%, even saying to have found in the new rheumatologist a sure and affordable referral, stay in contact with the pediatric rheumatologist "because of emotional issues". 58% remains under treatment with DMARDs and biologics; in 32% of patients an extra-articular manifestation occurs even in the absence of clinical parameters indicative of medium-high disease activity. The remaining 10%, in remission, continues the control.

Conclusions: Transition is an educational and therapeutic process, not an event; it requires collaboration between the teenager, family and caregivers.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3111

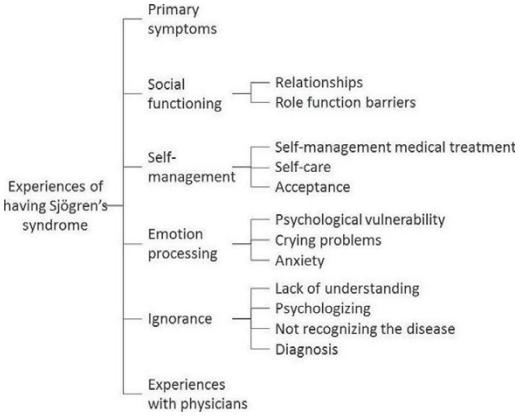
THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Psychosocial support

PARE0009 A TAXONOMY OF DISEASE EXPERIENCES OF WOMEN WITH SJÖGREN'S SYNDROME FROM THE PERSPECTIVE OF THE PATIENT

M.Y. Visser-Noordegraaf[1], V. Hiensch[2], G. Rojas-Alcayaga[3], R. Geenen[2]. *[1]NVSP, National Association Sjögren Patiënts, Maarssen; [2]Psychology, Utrecht University, Utrecht, Netherlands; [3]Faculty of Dentistry, Universidad de Chile, Santiago, Chile*

Background: In earlier studies of experiences of patients with Sjögren's Syndrome (SS), professionals interpreted the data and drew conclusions and implications. In the current study, patients had a major share in the interpretation and structuring of experiences, and a patient research partner was part of the research group in all phases of the study: planning, collecting data, organizing, analyzing, and reporting.
Objectives: The aim of this study was to examine the full spectrum of life experiences of women with SS in an integrated, hierarchical model, and to examine the degree to which the research participants experienced the sorted experiences themselves.
Methods: Patients structured and interpreted the data using a concept mapping technique. In a card-sorting task, 52 patients with SS from the Netherlands grouped 75 experiences in piles. These experiences came from previous in-depth interviews with Chilean patients [1]. Hierarchical cluster analysis yielded an integrated, hierarchical model of these sortings. The 52 patients indicated on a 4-point Likert scale whether they had had these experiences themselves: agree, agree a little, disagree a little, disagree.
Results: Hierarchical cluster analyses showed a main 6-category clustering of experiences with primary symptoms, emotional processing, social interaction, self-management, ignorance, and physicians. Four of these categories showed underlying clusters of experiences (see Figure). Patients generally agreed to have common experiences of "primary symptoms", "role functioning barriers", and "diagnosis" and they commonly disagreed with the "psychologizing" symptoms, while they differed in the degree to which they had individually experienced the other experiences.



Conclusions: Life experiences of women with SS were summarized in an integrated, hierarchical model consisting of 14 clusters in 6 overarching categories. The results may be colored by the cultural background of the participants. This year this concept mapping study will be extended to patients from Chile, which will increase the generalizability of the findings and allow cross-cultural comparison. The final hierarchical overview with life experiences from the patient's view can be used to improve screening in clinical consults, develop a questionnaire, give direction to future research, and enhance education and self-management support [cf. 2]. The method gives ample room to really incorporate the patient perspective in research.
References:
[1] Rojas-Alcayaga G et al. Illness Experiences in women with oral dryness as a result of Sjögren's syndrome: The patient point of view. Musculoskeletal Care 2016;14: 233–42.
[2] Ammerlaan JW et al. Building a tailored, patient-guided, web-based self-management intervention 'ReumaUitgedaagd!' for adults with a rheumatic disease. JMIR Res Protoc 2016;5:e113.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2923

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Arthritis research

PARE0010 SIGNIFICANCE OF FOOT PROBLEMS FOR PATIENTS WITH RHEUMATOID ARTHRITIS: A PATIENT-LED QUALITATIVE STUDY

S. de Souza, H. Lempp. *Academic Rheumatology, King's College London, London, United Kingdom*

Background: Patients with rheumatoid arthritis (RA) commonly report problems with their feet.[1] It is known that foot joint involvement begins early in the course of RA and even patients on biologic therapy and/or with low disease activity can still experience high levels of foot pain.[1–3] Current UK guidance states that "All people with RA and foot problems should have access to a podiatrist for assessment and periodic review of their foot health needs".[4]
Objectives: To understand how foot health problems affect patients with RA.
Methods: Adult patients, with a diagnosis of rheumatoid arthritis and ability to converse in English, were recruited by clinicians based at a London hospital rheumatology outpatient clinic to participate in two focus groups on foot health. These were conducted by the lead patient researcher and comprised 8 females and 1 male of diverse ethnicities, aged 27–68 years old with 4–46 years disease duration. The focus groups were audio-recorded and transcribed verbatim. Transcripts were verified for authenticity by a random sample of 4 participants, and were systematically coded with the assistance of qualitative data analysis computer software. Themes were generated and cross-checked by the co-researcher to negate any potential bias by the lead patient researcher.
Results: Four interlinked themes were identified: 1) dependence on feet, e.g. needed for standing and walking; 2) physical impact e.g. pain, swelling and deformities; 3) social impact e.g. hard to keep appointments and participate in leisure activities; 4) psychological impact e.g. low self-esteem, worry and using humour to cope. The sole male participant was unaffected by theme 4. One patient in the group had not experienced foot problems since diagnosis. No differences were identified across age, ethnicity or disease duration.
Conclusions: Foot problems can significantly lower quality of life for patients with RA. It is therefore essential that foot health is adequately addressed during rheumatology outpatient consultations with onward referral to podiatry services as necessary.
References:
[1] Grondal et al. The foot: still the most important reason for walking incapacity in rheumatoid arthritis: distribution of symptomatic joints in 1,000 RA patients. Acta Orthopaedica. 2008;79:257–61.
[2] Otter et al. Comparison of foot pain and foot care among rheumatoid arthritis patients taking and not taking anti-TNFα therapy: an epidemiological study. Rheumatol Int. 2011;31:1515–9.
[3] van der Leeden et al. Prevalence and course of forefoot impairments and walking disability in the first eight years of rheumatoid arthritis. Arthritis Rheum. 2008;59:1596–602.
[4] National Institute for Health and Care Excellence. Clinical Guideline 79, Rheumatoid arthritis: the management of rheumatoid arthritis in adults. 2009.
Acknowledgements: We thank James Galloway and Carron Congreve for patient recruitment, Patience Duffort for transcription services and the patient participants for sharing their experiences.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1400

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Best practice campaigning

PARE0011 ASK THE USERS - ESTABLISHING A DIGITAL USER PANEL

C.R. Ziegler[1,2]. *[1]Danish Rheumatism Association, Gentofte, Denmark; [2]Policy and Research, Danish Rheumatism Association, Gentofte, Denmark*

Background: A high level of user involvement is one way of assuring campaigns to be relevant to people with RMD's. This is true for all projects within the PARE organisations. The Danish Rheumatism Association would like to strengthen our political campaigning and we found this goal could be reached by establishing a representative digital user panel. A representative digital user panel would give us quicker, more relevant and high quality information about the opinion of the users and their experience within many different aspects of living with RMD's in Denmark.
Objectives: The Danish Rheumatism Association wanted to strengthen the impact of our political campaigning. We wanted to establish a representative user panel consisting of 1500 Danes with RMD's. A digital user panel was found to be a quick and efficient tool to secure real life experiences and knowledge from the users. The user panel would make us interact with our users in even better ways and through that we were able to strengthen our political campaigning.
Methods: In 2016 we tried to recruit participants among our members to assure that the panel was representative, but that was more difficult than we expected and we had to use other channels to recruit too. We wanted to ask the user panel about different themes 6–8 times each year. We investigated the collected data

and used them directly in our political campaigning and communicative work – without the time waster of making fancy reports.
Results: It turned out to be more difficult to establish a representative user panel than we thought. The barriers were various, but we succeeded in the end. The knowledge gained from the user panel has focused and strengthened our political work. This obtained influence would have been very difficult or even impossible to achieve without the experiences of the users. In our presentation we will go into details about the barriers of the establishing phase, share how we use the panel, give examples of how the answers are an added value and show how it helped us gain more political impact.
Conclusions: After overcoming several barriers it will possible to establish a digital user panel which can help organisations to improve their political campaigning.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2824

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Patient information and education

PARE0012 EDUCATING YOUNG CHILDREN, PARENTS AND DOCTORS THROUGH THE MEDIUM OF AN ILLUSTRATED CHILDREN'S BOOK

T. Egert[1], Y. Egert[2], R. Vitman[1], W. Costello[3]. *[1]4682, Efrat, Israel; [2]Netzach Yerushalayim 8, 4682, Efrat, Israel; [3]4682, Dublin, Ireland*

Background: Chronic illness in a child is a complex reality for all involved. *The child* often feels confused and afraid. He doesn't understand why he is sick and in pain, he worries about the doctor and hospital visits, as well as the medications and shots to which he is subjected. *Parents* are unsure how the illness will affect their child, and how to best prepare him for future challenges. Both parent and child are not always sure how to communicate to the *Doctor* their needs and concerns. Communication, however, between parent, doctor, child and health professional is critical for the effective treatment of the disease.
Objectives: This book attempts to open lines of communication between parent and child, to educate, give coping tools, and a voice to the young patient in a fun and optimistic manner. The book targets many of the children's challenges through identifying with Kipo, the young monkey who also has JIA.
The objectives: 1. To give the child strength and tools to deal with his illness. 2. Improve compliance through a better understanding of treatment.
Methods: A list of challenges young children with JIA face was compiled through meetings with parents, doctors and children. Next, a list of coping strategies was produced based on discussions with parents and health professionals. The story addresses the challenges and methods of dealing with them in a fun and optimistic manner through young Kipo's routine. Included are also messages addressed to the parent and doctor. To keep the child an active part of the story, thus allowing him to voice his concerns and discover coping skills, the story line requires active participation through "reading the pictures" which accompany the text. (The book includes a "how to read" guide). The back page includes a brief description of the illness, as well as other useful web addresses: parents associations, PRINTO, etc'.
Results: Working jointly with the illustrator an illustrated children's book in 3 different languages (Hebrew, English and Arabic) was published. The book addresses the challenges and difficulties of a young child with JIA through the story of Kipo the monkey who is also ill. Included are a visit to the doctor, getting an injection, going to the physiotherapist, etc. The book is distributed free of charge though the paediatric rheumatologists to the families, and is received very enthusiastically by parents, children and doctors. The children read and reread the book sharing it with family, friends and kindergarten classrooms. They use the terminology introduced in the book to describe their own physical and emotional feelings, and adopt coping strategies used by Kipo.
Conclusions: The success of the book motivated us to allow for a more international distribution. The illustrations and the text are available allowing it to be used by any national group.
Acknowledgements: Inbar, Mifrakim Zeerim, ENCA, Dror Adam (illustrator), anonymous unaffiliated donors, doctors, parents and translators.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.1687

PARE0013 BEHIND THE SMILE - RA AWARENESS VIDEOS - RAISING AWARENESS OF THE HIDDEN IMPACT OF RHEUMATOID ARTHRITIS

C.B. Jacklin, D. Saunders. *External Affairs, National Rheumatoid Arthritis Society, Maidenhead, United Kingdom*

Background: NRAS was approached by Lilly Pharmaceuticals to contribute to the design and production of a series of videos to raise awareness of the hidden impact of rheumatoid arthritis. As this clearly met the charity's own objectives of raising awareness to a variety of audiences NRAS gladly collaborated on this project.
Objectives: The key aim of developing these resources to be utilised in European countries was to raise awareness of the impact of RA on daily life to 1) the general public, 2) clinicians, 3) payers, 4) industry and 5) people living with RA and their families. The challenge was to capture, in a two minute video, key messages that would resonate with all these stakeholders.
Methods: NRAS worked with a PR agency to develop an appropriate script for the main Behind the Smile resource. The main character, Jane, who lives with RA, was to be in her mid 30s – to represent that RA is not associated with ageing; a school teacher – to represent that working is more than just a job for her and that she is a valued contributor to society; and a daughter, wife and mother – to represent how many other people depend on her and that she has commitments to.
We filmed with the support of Donna Saunders, NRAS Member & Volunteer, on hand to comment and ensure authenticity of how the actress moved and dealt with every day activities. The final scene shows the character of Jane attending her clinic appointment with her rheumatologist and even then putting on a brave face and hiding behind the smile of the typical response "I'm fine".
In addition, Donna who lives with RA, was filmed giving her personal comments on the awareness film and insights into her personal struggles. Finally, Prof. Iain McInnes, was filmed giving the clinicians perspective and offering advice as to how health care professionals need to keep at the forefront of their minds that patients are people and to be truly effective as physicians they should always make the time to open the dialogue on how the individual is truly "feeling"
Results: The films were released on World Arthritis Day 2016 via Lilly and NRAS social media channels in the UK. To date the "Jane" clip has been viewed in access of 200,000 times. The feedback from patients has been overwhelmingly that it has truly captured their "story". Physicians and industry staff have been left speechless and moved by the emotive film. NRAS and Lilly continue to utilise the films at health care professional training, staff and patient events.
Conclusions: Plans for 2017 is to develop more similar awareness raising videos as it is evident that using social media with video has impact and reach.
Acknowledgements: Acknowledge the support of Lilly Pharmaceuticals for the funding to develop these resources. The invaluable support of Prof.Iain McInnes and patient Donna Saunders
Disclosure of Interest: C. Jacklin Grant/research support from: Lilly Pharmaceuticals, D. Saunders: None declared
DOI: 10.1136/annrheumdis-2017-eular.1909

PARE0014 EXPLORING THE ADDED VALUE OF A BOOSTER SESSION AFTER COMPLETING THE DUTCH SELF-MANAGEMENT TRAINING "CHALLENGING ARTHRITIS"

M. Vos[1], R. Van den Brink[2], S. de Jong[2], J. Ammerlaan[3]. *[1]Expert Patient/Psychologist, Purmerend; [2]Dutch Arthritis Foundation, Amsterdam; [3]Rheumatology & Clinical Immunology, University Medical Centre Utrecht, Utrecht, Netherlands*

Background: In the Netherlands, the peer-guided self-management training "Challenging Arthritis" exists for over 15 years and is being organized by the Dutch Arthritis Foundation and the University Medical Center Utrecht. The training is based on the "Arthritis Self-Management Program"[1] but has recently gone through several updates, improvements and extensions[2]. The goal of the training is to improve self-management skills of patients and thereby improving their physical and emotional health and quality of life. Evaluations show that participants highly appreciate the training, but some of them have suggested that they would like to have an extra moment of training, (i.e., a booster session) after the ending of the regular program. Research shows that self-management programs are effective but mostly in the short term[3]. The effects of "Challenging Arthritis" may be enhanced and prolonged by organizing booster sessions.
Objectives: Aim of this research is to make recommendations about organizing booster sessions based on 1) a literature search and 2) a needs assessment among former participants and peer trainers.
Methods: A literature search was performed in databases like Google Scholar, PubMed and Science Direct, focusing on articles about the use of boosters in self-management interventions, limited to the years 2000–2016. Next to that, a needs assessment was conducted among participants and trainers on needs and preferences, using two separate online surveys. The survey for the participants, who followed a live training between 2012 and 2015, included items on the need for a booster and on preferences regarding its form, content and frequency. The survey for peer trainers addressed the perceived usefulness and the trainers' willingness to provide booster sessions. The resulting data were analyzed using SPSS and thematic analysis.
Results: The literature search yielded 27 articles describing health interventions with aspects of self-management, including one or more booster sessions. From a theoretical perspective, boosters are a way to maintain new behavior over an extended period of time. As of yet, there is little evidence that the use of boosters lead to better outcomes in terms of health or health behavior, but it has been suggested that tailoring may lead to better results[4,5]. Regarding the needs assessment, 124 participants and 34 trainers completed the survey. Results showed that almost half of the participants (47,5%) expressed a need for a booster, while the other half (52,5%) expressed little or no need. Participants who prefer a booster want to share experiences, learn how to stay active with self-management and how to cope with setbacks. Trainers think boosters are very useful for the participants to stay active with self-management and maintain behavior and they are unanimously willing to provide booster sessions.
Conclusions: Boosters may contribute to the maintenance of newly acquired health behavior, although more research is needed on this subject. A substantial

part of the participants expresses the need for a booster and trainers are highly motivated to provide it. Therefore, we think it's worthwhile to start experimenting with organizing booster sessions on a small scale and, depending on the outcomes, consider further implementation.

References:

[1] References can be obtained from the first author.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6171

PARE0015 THE IMPORTANCE OF FACE-TO-FACE NETWORKS: FINDINGS FROM THE 2ND EULAR YOUNG PARE CONFERENCE, "CHANGE THE FUTURE"

J. Andersen[1,2], P. Balazova[3,4], W. Olsder[5], S. Ostuzzi[6], D. Papastavrou[4,7], S. Stones[8,9], T. Wilhelmer[10], P. Boyd[11] on behalf of EULAR Young PARE. *[1]5sle/Lupus Ung Dk, Gigtforeningen, Gentofte, Denmark, Gentofte, Denmark; [2]Lupus Europe, Essex, United Kingdom, Essex, United Kingdom; [3]Slovak League Against Rheumatism, Piestany, Slovakia, Piestany, Slovakia; [4]EULAR Standing Committee of PARE, Zurich, Switzerland, Zurich, Switzerland; [5]Youth-R-Well.com, Lisse, The Netherlands, Lisse, Netherlands; [6]ANMAR Young, Rome, Italy, Rome, Italy; [7]ELEANA Hellenic League Against Rheumatism, Athens, Greece, Athens, Greece; [8]School of Healthcare, University of Leeds, Leeds, United Kingdom, Leeds; [9]Fibromyalgia Action UK, Paisley, Renfrewshire, United Kingdom, Paisley, United Kingdom; [10]Österreichische Rheumaliga, Salzburg, Austria, Salzburg, Austria; [11]Arthritis Ireland, Dublin, Ireland, Dublin, Ireland*

Background: EULAR Young PARE's strategy for 2020 is to establish and strengthen groups for young people with rheumatic and musculoskeletal diseases (RMDs) across Europe, by developing a collaborative network. We aim to empower youth leaders to ensure the voice of young people with RMDs is heard. To facilitate this, the 2nd EULAR Young PARE Conference was held in Retie, Belgium in October 2016.

Objectives: To empower and educate EULAR Young PARE youth liaisons, focusing on developing academic and interpersonal skills to best support young people across Europe living with RMDs. This was achieved through a series of practical, skills-based workshops and plenary sessions.

Methods: The EULAR Young PARE working group reflected on the conference during a debrief meeting. A post-conference evaluation was completed by liaisons. A five-point Likert scale (1= very bad, 5= very good) was used alongside open questions. In addition, there was an informal meeting to generate discussions and receive input from participants regarding the future direction and focus of EULAR Young PARE in 2017 and 2018.

Results: The conference was attended by 22 youth liaisons from 20 organisations. The programme was well received with the face-to-face interactions favoured to establish and grow collaborative networks. Through a series of digital poster presentations, each liaison had the opportunity to share recent work in their national organisations. This session was evaluated positively and encouraged liaisons to identify opportunities for collaboration and new national activities, using the VKC as a platform for the sharing of best practices. Workshops were delivered in collaboration with EMEUNET and a EULAR member organisation representative and we piloted a series of six walk-in workshops. While these workshops were evaluated positively, a lack of structure and the need for time constraints was a consistent finding.

Conclusions: The "Change the Future" conference was a successful meeting of youth liaisons from across Europe, who were highly satisfied with the programme and mechanism of delivery. Meeting in person facilitated the growth and continued involvement within the EULAR Young PARE network. The activities of EULAR, and specifically the Standing Committee of PARE, were shared with liaisons, encouraging liaisons to become involved in a wider number of EULAR activities. Theoretical and practical skills were developed, while best practices and experiences were shared and highly valued. Furthermore, in future conferences, bitesize workshops will replace walk-in workshops for structure and clarity. Despite living in a digitally connected world, face-to-face interactions cannot be replaced. Learning can be enhanced and actions implemented when motivated individuals are physically united, demonstrating the need for the use of multiple meeting methods to drive innovation. Following the conference, everyone felt inspired, empowered and motivated to implement concrete and tangible steps to inform ongoing and future work. Together, we can change the future for young people living with RMDs.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3203

PARE0016 KEEP CALM AND TELL ME YOUR STORY!: A NARRATIVE MEDICINE PILOT PROJECT FOR ITALIAN YOUNG PEOPLE LIVING WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

U.G. Viora[1], S. Ostuzzi[2,3] on behalf of ANMAR Italia - ANMAR Young. *[1]Anmar Italia, Torino; [2]Anmar Young, Anmar Italia, Rome, Italy; [3]Eular Young Pare, Zurich, Switzerland*

Background: The 7th point of EULAR Young PARE's Youth Strategy states that "By 2020, every European country has an active national youth group for young people with rheumatic and musculoskeletal diseases (RMDs)". On this basis, ANMAR – Italian national association for people with RMDs – has engaged in the creation of a youth group dedicated to Italian young people (aged 18–35) living with RMDs: ANMAR Young was born in 2015, through EULAR's Knowledge Transfer Programme. During its first year of activities, ANMAR Young has launched the pilot project of a narrative medicine campaign called *Keep Calm and Tell Me Your Story!*

Objectives: *Keep Calm and Tell Me Your Story!* was designed to make sure that the voice of young Italian people living with RMDs is heard, spread, and listened to. In its pilot phase, the project aimed to consult, engage, involve young rheumatic patients while building an Italian network. A major pilot phase's objective was, as well, the launch of a booklet presenting the collected stories on World Arthritis Day 2016.

Methods: The ANMAR Young task force has drafted the four different writing traces to compose the campaign, investigating some crucial issues, such as: the impact of RMDs on young people's personal life, working life and education; the experience of transitioning from pediatric to adult rheumatology care services; young rheumatic patients' unmet needs and priorities. The criteria for inclusion of participants were deliberately simple: every Italian person living with any RMDs and aged from 18 to 35 could take part in the campaign. Texts have been collected anonymously exclusively through an online form, promoted and disseminated mostly through social media. The pilot project campaign has lasted one month, from the end of July 2016 until the end of August 2016.

Results: From the end of July 2016 to the end of August 2016 21 stories have been submitted by 20 female respondents and 1 male respondent coming from 11 different Italian regions, suffering from different RMDs (among which the condition reported more often is Juvenile Idiopathic Arthritis). The collection has become the subject of a booklet, published in an edition of about 5,000 copies and officially launched in October 2016 in Rome, on World Arthritis Day. The campaign spread online, allowing ANMAR Young to gather different experiences, expand its network, contribute in the process of empowerment and engagement of Italian young rheumatic patients.

Conclusions: The campaign *Keep Calm and Tell Me Your Story!* has proved to be a valuable, peer-to-peer, economically sustainable, easily manageable and repeatable (also abroad) engaging tool for raising awareness about the impact of RMDs on the quality of life of young people. We intend to further develop this narrative medicine experience by keeping collecting new stories, by sharing them weekly through social media, by promoting our printed booklet. We intend to further analyze in detail the collected texts, in order to read them not only as personal experiences but also as a qualitative mapping of Italian young people with RMDs' unmet needs and priorities.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6175

PARE0017 EMPOWERING PATIENTS WITH OSTEOARTHRITIS WITH NON-PHARMACOLOGICAL MEASURES

J. Vergés[1], J. Monfort[2], M. Bibas[1], M.T. Vergés[1]. *[1]Osteoarthritis Foundation International; [2]Hospital del Mar, Barcelona, Spain*

Background: Osteoarthritis (OA) and other joint pains are generally seen as ailments that affect people with age. With the increase in life expectancy over recent decades, the prevalence of people with OA is drastically growing. Estimates suggest that there are 242M people with OA in the world[1]; 30M live in Europe[2]. The most commonly affected joint at the present time is the knee, followed by hips and shoulders[3].

Objectives: To run an educational program that will provide elderly people with tools to tackle their problems of joints so that they can improve their quality of life by adopting non-pharmacological measures. A well-informed patient knows how to address their disease. Thus, they can improve their quality of life.

Methods: The method is based on the capacity of a motivated patient to positively influence others also worried by their health situation by sharing their experiences and awareness of the disease.

Stage I. Preparatory actions:

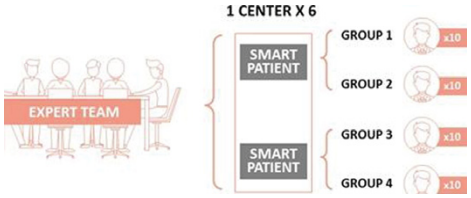
1. Elaboration of contents: An expert team (psychologist, nurse, rheumatologist, family doctor, physiotherapist and rehabilitator) elaborates the content: Knowledge, Weight control, Doing the right exercise, Dealing with the disease
2. Engagement of the target group: "La Caixa" Banking Foundation is supporting this study by giving access to its 63 senior centers in Catalonia (Spain)
3. Selection of senior centers: The educational program is planned to be run in 6 centers. Currently, 20 centers are conducting initial presentations to evaluate interest and ensure the selection of 6 final centers
4. Enrollment of smart seniors: 12 people will be selected (2 per center), called hereafter, "smart patients", through a survey so we can assess interest of enrolling and quality of the presentation

Stage II. Training and implementation:

5. Training of smart patients: Train selected smart patients during 9 sessions, 90 minutes each
6. Training groups of patients: Every smart patient will train 2 groups of 10 people also interested in joint health. A nurse will be in every session, giving support only if necessary
7. Evaluation and follow-up: Improvement of participants in the course will be assessed (anticipated sample size 240 people) by surveying level of satisfaction

(ARTS questionnaire), improvement of pain and functionality (WOMAC), improvement in perceived quality of life (EuroQuol 5), improvement of the degree of self-care to achieve a good management of the disease (IC, MPOC and TAC programs), improvement in therapeutic compliance

Results: Stage I initial presentations have been conducted at 8 out of 20 centers in urban and semi-rural areas to account for different social, economic, education and lifestyle demographics. Participants surveyed: 305; Interest in being a smart patient: 76; Interest in participating in the program: 193; No interest: 36; Level of satisfaction: >90% reporting good or very good.



Conclusions: Based on results to date, after the 20 sessions the team expects to collect 763 surveys and identify 190 potential smart patients and 483 people willing to participate in the program. There is a clear interest or concern for OA disease in elderly people and they want to take more responsibility for their disease and age with quality of life.

References:

[1] Global Burden of Disease Study 2013 Collaborators, The lancet, June 8, 2015.
[2] Osteoarthritis - An Overview, Frost & Sullivan, May 17th 2007.
[3] EPISER STUDY 2001, Spanish Rheumatology Society.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3180

PARE0018 WE DO THE IMPOSSIBLE, BECAUSE THE POSSIBLE EVERYONE CAN DO WAD AWARENESS CAMPAIGN

H. Bankova, B. Ivkov, S. Bozhinova, B. Boteva. *BOPRD, Sofia, Bulgaria*

Background: One of the main priorities that Bulgarian organization for people with rheumatic diseases follows is dissemination of knowledge and information about RMD'S and their impact on people's life and to the society.

The WAD awareness campaign is the culmination of the organization's activities during the whole year.

Objectives: The main goal of the 2016 WAD awareness campaign was to:

- Inform the society and BOPRD's members about the social importance of RMD's.
- To inform BOPRD's members what are their rights as people with long term chronic condition.
- To inform the society about RMD's and the challenges that people with RMD's face.
- To challenge the people with RMD's to look into their inner world and to define what are their strengths and weaknesses.
- To make the informing process more attractive, by visualizing the key features of life with an RMD.

Methods: In 2016 BOPRD organized an awareness campaign - "We do the impossible, because the possible everyone can do"

The start of our campaign was on 1st of October and lasted for more than two weeks till the World arthritis day and ended on 16th of October. Informative and motivating pictures, with information about different RMD's, were published every day on the official BOPRD's Facebook page and were shared in the closed group for people with rheumatic diseases as well.

A social experiment among the members of the organization was made. They were asked to explain what the disease means to them, like they are telling the story to a person who do not know anything about it.

The aim of this experiment was to identify the meaning and significance which people with rheumatic diseases give to their condition, as well as the basic problems result from the illness.

Based on the social experiment and analysis of 33 small biographical narratives 17 basic characteristics of the rheumatic diseases are identified. These characteristics form the problematic areas for people with RMD's and bases for their study.

The main characteristics are life with chronic pain, the process of disabling, life in continuous compliance with the environment and the high degree of uncertainty and ambiguity, imposed by chronic illness.

An e-booklet, containing the results of the social experiment was published on BOPRD's Facebook page and website on 12th October. On the same day we published the WAD video, of the PARE WAD campaign: "The future is in your hands".

At the end of the awareness campaign we published an online booklet, which contained translated articles about RMD's and the different aspects of life with a chronic condition.

Results:

- The total number of all publications is 22.
- The publications were seen from over 3 000 people.
- The WAD video was seen by 1000 people.
- The results of the social experiment were seen by 1500 people.
- The most popular were those pictures that managed to touch people's feelings.



Conclusions: Main common characteristics of rheumatic diseases were identified and can help patients in getting the right diagnosis.

The most popular were the posts that were related to emotions and experience of life with a chronic condition.

By publishing the results of the social experiment we managed to help those who read the narratives get the feeling that they are not alone.

The results of the social experiment will be used as a basis in developing a manual for the main symptoms of RMD's (the patient perspective)

Acknowledgements: Miglena Ivanova
Cveta Apostolova

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3095

PARE0019 ADHERENCE TO THERAPY: A COMPARISON BETWEEN THREE PATIENTS POPULATIONS WITH AUTOIMMUNE INFLAMMATORY DISEASES

U.G. Viora[1], R. Giannelli[2], M.G. Pisu[3], G. Voltan[4] on behalf of ANMAR Italia.
[1]Anmar Italia, Torino; [2]Anmar Italia, Firenze; [3]Anmar Italia, Milano; [4]Anmar Italia, Roma, Italy

Background: Non-adherence to therapy is one of the main obstacles achieving the goals of care in chronic autoimmune inflammatory diseases, including Rheumatic diseases (RMDs). In the " MOSAICO" study, ANMAR along with two other associations of Italian patients (AMICI chronic inflammatory bowel diseases (IBD) and ANAP - psoriasis (PSO) and chronic dermatological diseases) wanted to compare the adherence to therapies for IBD, RMDs and PSO and identify key problems that can affect it positively or negatively. This paper presents the results related to adherence to treatment, the obstacles that are disadvantageous and to the factors that, conversely, favor adherence and persistence.

Objectives: to fix the degree of adherence to therapy - with DMARDs and biological indifferently - in the three different pathologies; to identify obstacles and factors predisposing good adherence and persistence by patients; to compare the three different populations, highlighting similarities and significant differences

Methods: a 72 questions questionnaire - about 50% of which were dedicated to adherence and persistence to therapy and the predisposing factors and impediments - prepared in collaboration with Doxapharma was administered to patients with RMDS, IBD, PSO via web and by volunteers of the three associations. The evaluation of adherence to therapy ("degree in which a person's behavior in taking medication, following a diet and/or change the lifestyle, corresponds to the specific recommendations made in agreement with the Medical") was assessed by Morisky Medication Adherence Scale - 8 items (MMAS-8)

Results: 1.017 patients - 233 with RMDs (AR e SA), 449 with IBD (Crohn and ulcerative colitis), 273 with PSO and 62 APs –answered to the questionnaire useful for the purpose of the study.

Non-adherence varies in a range from 50% of dermatological patients, to 44% of them with IBDs, to 40% of patients with APs, to 36% of them with RMDs. Only 74.8% of adherent people is persistent (83% in biologic therapy; 76% in DMARDS) and non-persistent patients does not ask and/or inform their doctors.

Patients with Psoriasis take therapies more discontinuously and inaccurately then all the others.

Promote adherence:

- good support from doctors and health professionals
- satisfaciton with information received
- the best QOL
- easiness and lack of problems in taking drugs
- satisfaction with the therapy
- biologic therapies (even for the best QoL ensured)

Promote discontinuity and non-adherence:

- dissatisfaction with the relationship with doctors and health professionals (33% ÷ 70% of patients is dissatisfied)

Conclusions: Our study shows that patients who enjoy a better health state, both physically and psychologically, are more likely to follow the treatment prescribed by their doctor, according to the mode and the specified time, especially if properly informed and well supported in choices, shared by medical and health professional staff.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3102

THURSDAY, 15 JUNE TO SATURDAY, 17 JUNE 2017

Building patient led organisations

PARE0020 25 YEARS OF PATIENTS' ASSOCIATIONS OF ANKYLOSING SPONDYLITIS IN SPAIN: ACEADE

J.L. Garrido-Castro[1], C. Gonzalez-Navas[2], J. De La Haza[1], P. Plazuelo[3], E. Collantes-Estevez[4]. *[1]ACEADE. AS Patient Association of Cordoba; [2]CEADE. National Coordinator of AS Patient Associations, Cordoba; [3]CEADE. National Coordinator of AS Patient Associations, Madrid; [4]Reina Sofia University Hospital, Cordoba, Spain*

Background: Patients' associations can provide to the ankylosing spondylitis (AS) patient all the information and support that his/her rheumatologist cannot give and that is necessary to fight against the disease having a greater quality of life (1). Patients' and families' knowledge about AS is fundamental and Patients' associations play an important role in education on disease (2). In 1991, the first association dedicated to AS in Spain, was born: ACEADE (Asociacion Cordobesa de Enfermos Afectados de Espondilitis). The Rheumatologist, Dr Eduardo Collantes, after having spent some years in several countries, brings together several patients affected by this disease, in the city of Cordoba, to create the first Patients Association dedicated to this disease in Spain. There were some associations of this kind in the UK and France, and they decided to create their own association to promote the knowledge about AS and to help the AS patients. 25 years later, there are many AS patient associations in Spain that were created following the example of ACEADE, and with the help of this pioneering association.
Objectives: The aims of ACEADE during these 25 years has been:
1) Disseminate the knowledge of the disease.
2) Collaborate with medical researchers.
3) Improve the quality of life of the AS patient.
4) Organize and participate in scientific meetings, congresses and specialized courses.
5) Advise the patients in socio-labor aspects.
6) Inform associates of the advances related to the disease.
Methods: Several activities are being carried out in the Association, some of them were exposed previously (3): educational seminars, rehabilitation courses, patient guides, social events, legal advice, employment bureau, newsletter, web page, ... In order to develop these activities, we have several sources for fundraising: donations, local and regional governments, pharmaceuticals, foundations, ...
Results: ACEADE is formed by 415 members distributed in the province of Cordoba (Spain), although some of them are from outside this city (11%). 67% of them are men and the average age of the members is 53 years. Of these, 32% have a recognized legal disability. After ACEADE, up to 18 patient associations have been created in Spain. There is also a national organization of AS patient associations: CEADE.
Conclusions: ACEADE was the pioneering AS Association in Spain and has been the "mother" of others that have been appearing. Today there are associations of AS in virtually all territories of Spain, helping patients to have a better quality of life. The next 25 years appear, for our association, full of illusions, ideas and a lot of work ahead, to help in the fight against AS.
References:
[1] J.L. Garrido-Castro, E. Collantes, J. Blancat, J. Roman. Fighting against spondylitis from inside: what could do a patients' association. Ann Rheum Dis 2008;67(Suppl II):683.
[2] J. L. Garrido-Castro, E. Collantes-Estevez, C. Gonzalez-Navas, L. Carmona. What is the knowledge level that ankylosing spondylitis patients have about their own disease? Ann Rheum Dis 2013;72(Suppl3):141.
[3] J.L. Garrido-Castro, B. Martos, E. Collantes, J. Blancat. Rheumatic patients' associations in spain: organization, fundraising, activities and relationship with health professionals. Ann Rheum Dis 2010;69(Suppl3):754.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4754

PARE0021 PUBLIC AND PATIENT INVOLVEMENT AT ARTHRITIS RESEARCH UK: ENSURING BENEFIT FOR ALL

C. Macdonald. *Arthritis Research UK, London, United Kingdom*

Background: Since 2008, Arthritis Research UK have utilised the valuable experience and perspective of people with arthritis to review and evaluate the research applications we receive, through the USER stakeholder committee. The world of public and patient involvement (PPI) has developed and progressed hugely in that time. So too has Arthritis Research UK, becoming an insight-led charity that can now genuinely say that people with arthritis are at the centre of everything we do, helping those people to be in control, independent and recognised. As such, our approach to PPI must not only meet the new high standards of meaningful PPI set by the research community but also serve to anchor our research activities and the work that we fund in genuine relevance and patient benefit.
Objectives: To present our new approach to involving people with arthritis in the decision-making processes of research and the wider charity.
Methods: We carried out a UK-wide scoping exercise, consisting of questionnaires and one-to-one interviews, of key stakeholder groups and PPI leaders. This included: our funded researchers and centres of excellence; medical research charities; and people with arthritis including ex- and current USER members. The findings were written up in to a report.
Results: The findings of the report highlighted to us that we need to 1) scale up our PPI activities in order to ensure that insight of people with arthritis can be integrated at all stages of the research cycle 2) improve the quality of our PPI ensuring that all the things we do are carried out with clear purpose, that they are meaningful and add mutual value to all involved 3) increase the numbers of people with arthritis in our PPI group to help realise this vision, whilst improving our support, training and guidance processes for those people 4) recognise and support the already excellent PPI activities going on in the musculoskeletal community, and providing resources and training for those also wishing to start or improve PPI activities.
Conclusions: After implementing this new approach for over a 18 months, we are now confident that our research activities and the research we fund, have the utmost relevance and potential benefit to people with arthritis.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2475

PARE0022 ORGANIZATION OF GROUP EXERCISE THERAPY (GET) FOR PATIENTS WITH AXIAL SPONDYLOARTRITIS (AXSPA) IN THE NETHERLANDS; A NATIONWIDE SURVEY

F. Van Der Giesen[1,2], S. Van Weelij[1], N. Lopuhaa[3], T. Vliet Vlieland[1]. *[1]Orthopedics, Leiden University Medical Center, Leiden; [2]Rheumatology, Haga Teaching Hospital, The Hague; [3]Dutch Arthritis Foundation, Amsterdam, Netherlands*

Background: Exercise therapy is recommended for people with axSpA [1]. In the Netherlands GET specifically for patients with axSpA is usually organized by local rheumatology patient organizations. New scientific insights into the delivery of GET have emerged over the past years and structural reimbursement from the basic health insurance was terminated. To ensure the quality and continuity of the delivery of GET it is necessary first to determine their current structure and processes.
Objectives: To describe the structure and processes of group exercise therapy specifically for patients with axSpA in the Netherlands.
Methods: Using the database of the Dutch Arthritis Foundation in 2016 a pen-and-paper questionnaire was sent to the coordinators of all 82 local patient organizations who could potentially be involved in the delivery of AxSpA GET. The questionnaire comprised 18 questions on the numbers of groups and participating patients, organizational and financial responsibilities, recruitment methods for participants and supervisors, the type of exercise therapy provided (land based, hydrotherapy or a combination of both) and the perceived threats for future continuation.
Results: The questionnaire was returned by 66 of the 82 coordinators of whom17 stated their organization was involved in the delivery of axSpA specific GET (45 group therapy classes: 1 only land exercises; 13 only hydrotherapy; 31 combination) for 496 patients (estimated number of patients with axSpA in the Netherlands in 2016: 61.200 [2]). 15/17 local patient organisations have organisational as well as financial responsibilities. The most often used recruitment methods for participants were: via the rheumatologist/rheumatology nurses (n=17), physical therapists (n=8), or advertisement in local patient organisations' own media (n=8). Recruitment of supervisors was most often done by asking around within their own network (n=14) or asking the leaving supervisor for replacement (n=8). Regular evaluation of the delivery of care with the supervisors and participants was performed by 10 and 12 local patient organizations, respectively. Three had an agreement with health insurance companies regarding reimbursement of GET. In 6 regions the number of participants had been declining over the past 5 years. The most mentioned threats for continuity by coordinators were financial difficulties (n=7) and recruiting participants (n=9).
Conclusions: 17 local rheumatology patient organizations involved in the delivery of GET specifically for patients with axSpA in the Netherlands were identified. The large majority played an active role in the organization and reimbursement and regular evaluation of care delivery was done by two-thirds of them. Future challenges are the recruitment of new participants and reimbursement. As only a small minority of AxSpA patients appears to take part in group exercise therapy, more insight into the needs and preferences among the larger population is needed.
References:
[1] Van der Heijde D, Ramiro S, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis 2017 Jan 13.
[2] Stolwijk C, van Onna M, et al. Global Prevalence of Spondyloarthritis: A Systematic Review and Meta-Regression Analysis. Arthritis care & research. 2016;6:1320–31.
Acknowledgements: This study was funded by the Dutch Arthritis Foundation.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4197

Abstracts Accepted for Publication

Patient information and education

AB1250-PARE LOVE YOUR HEART – AN INTERACTIVE ON-LINE EDUCATION PROGRAMME TO ENABLE PEOPLE WITH RHEUMATOID ARTHRITIS TO ASSESS THEIR CARDIOVASCULAR RISK AND SET PERSONAL GOALS TO IMPROVE THEIR CARDIOVASCULAR HEALTH

H. John[1], A. Bosworth[2]. [1]*Rheumatology, The Dudley Group NHS Foundation Trust, Dudley;* [2]*CEO, National Rheumatoid Arthritis Society, Maidenhead, United Kingdom*

Background: Rheumatoid arthritis (RA) is associated with an increased risk of cardiovascular disease, akin to type 2 diabetes. However, screening for, management of, and education about co-morbidities is not always adequate and as a result, the co-morbid risks may be overlooked by the general public, some health professionals and policymakers alike. Dr. John originally developed and piloted a programme in group format in Dudley to educate RA patients about their cardiovascular risk and help them change their lifestyle to improve their health; it achieved promising results. The format however limited the number of people who could access it and NRAS wanted to make it as widely available as possible. The sad reality is that it is not unusual to meet someone with RA who does not realise that they are at an increased risk of heart disease, so they are far less likely to address factors such as smoking, weight and diet which are firmly within their control.
Objectives: Our aim was to create an engaging and interactive online programme to educate people with RA about heart disease and atherosclerosis. This programme should; explain in simple terms why they are at increased risk; include the opportunity to determine individual risk factors thereby allowing a QRISK2 score to be performed; provide a cognitive-behavioural framework to empower people to change their behaviours and achieve a healthier lifestyle, thereby reducing risk of premature death from heart disease.
Methods: The participant manual created for the group programme and working closely with Dr. John and other health professionals in Dudley (exercise physiologist, smoking cessation nurse, dietician, health psychologist) and patients who had attended the programme, we explored with our creative film production team the best way to adapt this to create a really engaging on-line experience which would allow participants to undertake the programme over time whilst working through the behaviour change goal-setting process. Two days of filming were done in Dudley and Maidenhead followed by a period of editing, additional recording and review. Beta testing of the programme will be conducted in February, piloting in March and launch anticipated for April 2017.
Results: Evaluation of both the programme and the potential to change health behaviours will be measured on completion of the programme and actual behaviour change will be measured at 6 months.
Quote from a patient who participated in the face to face programme: "*Before I did this programme I thought that I was doing pretty well in terms of diet and exercise but it showed me that there was a lot I wasn't aware of, that my knowledge of lifestyle factors wasn't adequate and I needed to do more to help myself. I found it a valuable and life-changing experience to do this programme.*"
Conclusions: We are very excited about the launch of this programme as it is an important new resource addressing the major co-morbidity which shortens the lives of those with RA. It is unique in that not only does it provide patient education, but it also provides a structure through which patient can change their behaviour. Furthermore, it also illustrates what can be achieved when patient-led charity organisations work alongside healthcare professionals; we are hugely excited by its potential.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6299

AB1251-PARE THE NEEDS AND PRIORITIES OF YOUNG PEOPLE LIVING WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES IN ITALY: A SUB-ANALYSIS OF THE PARE YOUTH RESEARCH PROJECT

U.G. Viora[1], S. Ostuzzi[2], A. Alunno[3,4] on behalf of ANMAR Italia - ANMAR Young - EULAR Young PARE. [1]*Anmar Italia, Torino;* [2]*ANMAR Young, Anmar Italia, Rome;* [3]*Rheumatology unit -depy. of Medicine, University of Perugia, Perugia, Italy;* [4]*Eular Young Pare, Zurich, Switzerland*

Background: In 2014 EULAR Young PARE conducted a research (PARE Youth Research) to gather information about how young people (aged 18–35) living with rheumatic and musculoskeletal diseases (RMDs) are organized in different European countries and to explore their specific needs, obstacles, preferences and priorities. The research was developed through a survey launched in countries with EULAR members organizations and a total of 2,329 validated responses from the target population were obtained. In 2015 ANMAR Young, Italian National Association for people with RMDs' (ANMAR) youth group, was born aimed to create a network of young people with RMDs living in this country.
Objectives: Taken the socio-economical and cultural differences across countries, as well as the need to tailor interventions, activities and projects of national youth groups accordingly, the purpose of this study was to map out specific insights about Italian young people living with RMDs.
Methods: Data from Italian responders to the survey of the PARE Youth Research Project survey were extrapolated and answers were encoded to be analyzed using SPSS 21.0 software. Descriptive statistics were calculated in the whole group as well in subgroups of subjects as needed.
Results: 81 young Italian people living with RMDs responded to the survey: 75 females and 6 males. The conditions reported most often are rheumatoid arthritis (36%), juvenile idiopathic arthritis (23%), ankylosing spondylitis (15%). The work on PARE Youth Research's Italian data shows some important insights, among which we highlight that 84% report a delay in their studies due to the rheumatic condition, 92% report that the condition has affected their ability to work; 90% report the impact of RMD on social life, 70% report an impact on sexual life and 83% on mental health. Focusing on mental health issues, we highlight that 69% express the need for psychological support while only 43% have the possibility to access psychological support. Although all patients reported that after being diagnosed with an RMD they have access to a rheumatologist for regular follow-up visits, an average 3-year diagnostic delay is reported.
Conclusions: The results from the analysis of Italian responders to the survey represent a crucial starting point to put in light the unmet needs of Italian young people living with RMDs. These findings will be of great help to develop a fruitful national network of young people with RMDs on one hand and a focused collaboration with patient representatives, physicians, and health professionals (HPs) on the other. We believe that the awareness of physicians and HPs working in the field of rheumatology about the needs and priorities of young people with RMDs will ensure a better management of the disease and therefore lead to the reduction of the RMD burden in this subgroup of patients.
References:
[1] EULAR Young PARE - Final Report PARE Youth Research Project (2014).
[2] http://www.youngpare.org/wp-content/uploads/2015/05/Final-report_PARE_Youth.pdf.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6190

Best practice campaigning

AB1252-PARE TO RAISE AWARENESS OF RHEUMATIC AND MUSCULOSKELETAL DISEASES AND TO PROVIDE THE OPPORTUNITY TO THE FINANCIALLY LESS ABLE TO RECEIVE TIMELY DIAGNOSIS AND INTERVENTION IN RMDS

A. Stara, R. Stara, K. Koutsogianni, J. Papadakis, M. Chatziioannou, L. Papadaki, M. Sfakianaki, M. Agapitou. *Arthritis Crete, Heraklion, Crete, Greece*

Background: The timely and accurate diagnosis in most rheumatic diseases is still a big issue for patients as the choice of the appropriate doctor's specialty is still at the discretion of the patient, mainly due to the poor organized health care services. Furthermore, the success of our campaign two years ago, when we gave the opportunity to people suspecting they might have an RMD but who could not afford a rheumatologist to be examined for free, prompted our organization to offer not only free consultations but free lab tests as well.
Objectives: To raise awareness of RMDs and at the same time to enable people of lower income who may have the early warning signs of rheumatic diseases to be examined by a rheumatologist and have lab tests done at no cost.
Methods: Firstly, we found a sponsor who embraced our initiative and was willing to cover the cost of the whole campaign. Secondly, we contacted various medical laboratories to give us low estimates on the RMD tests and then we chose to collaborate with the ones offering us the lowest prices. Then we came into contact with all the rheumatologists in all the prefectures of the island and asked them to offer consultations free of charge according to their availability. On WAD, 12 October, we erected four stands in four central locations of our island with our logo, a banner, informative leaflets and a large number of well-informed volunteers to answer queries. Prior to WAD we had promoted this special event in the mass and social media. A lot of people visited our stands, told us their problem and their signs and we wrote down the names and phone numbers of those we deemed needed a rheumatologist. As last time, there were people who had already been seeing a rheumatologist who wanted to take advantage

of this opportunity; we had to reject them as this was only available to people who had not been diagnosed previously. The following two days our office made an appointment for these people with a rheumatologist in their area. The doctors prescribed the necessary laboratory tests and gave a free voucher for the tests to those that needed them. The cost of the lab tests was covered by our association. Our office received a large number of calls from people who wanted to be tested and unfortunately, we could not accommodate all of them as our budget was limited.

Results: More than 267 people visited our stands and 209 people phoned our office asking to be tested. We made appointments for 123 people of whom 111 showed up for their appointments. The rheumatologists gave vouchers and prescribed lab tests for 89 of them. 12 rheumatologists volunteered their services gratis and more than 40 volunteers took part in the campaign.

Conclusions: People's awareness of RMDs is growing but there are still undiagnosed people due to financial constraints, inadequate health insurance coverage and lack of information. Since the demand for free testing is very high we will make every effort to be able to provide this opportunity to undiagnozed people again in the future!

Acknowledgements: BMS
Disclosure of Interest: A. Stara Grant/research support from: BMS
DOI: 10.1136/annrheumdis-2017-eular.2625

AB1253-PARE KID'S GET ARTHRITIS TOO - EXPANSION OF TARGET GROUPS

M. Ekroth. *The Finnish Rheumatism Association, Helsinki, Finland*

Background: The Finnish Rheumatism Association is generally perceived as a very strong alliance of older people. However in Finland there are more than 2000 children and youth suffering JIA and around 250 new ones get diagnosis yearly. Children will have their whole lives ahead with rheumatic disease, so they and their families also need information, support and friends.

Objectives: Support children and families living with JIA in different ways
To provide the accurate and latest information on JIA
Get in touch with families, understand what their needs are, provide them with the correct information and promote their interests
Bring new energy into the families' challenging lives affected by illness
Build a supporting network for the families and increase mental well-being
Rejuvenate the brand of our association

Methods: Ordered international top photographer to photograph the JIA children and families. Created an entirely new high-quality imagery and expression to all Rheumatism Association children communications.
Created the "Puppana" bunny soft toy and the mascot costume.
Have the rheumatism-week campaign: Kids Get Arthritis Too: one week nation wide big radio campaign with a child's voice, a poster campaign in hospitals, our local associations and public spaces.
First aid packet with information of JIA, some toys, and the Puppana mascot. Packets were delivered to all Finnish hospitals, juvenile rheumatoid arthritis units. The rheumatologist gives a packet for a child who receives a diagnosis.
Introduced the action program of two annual nationwide large children's events Joy of Life.
New juvenile rheumatoid arthritis sites for children and families on our new website.
Support the activities of local associations directed for children and families.
Create a new web portal support activities "Reumanakanssa.fi".
International Trials Organisation) in co-operation. Translated into Finnish and added to the new websitewhere we built ABC for JIA.

Results: The brand of the Finnish Rheumatism Association has become more modern and wider.
People have experienced an eye opening campaign, the children suffer from rheumatism–arthritis can be a disease at all ages
Families with children have been reached more, they have joined our social media groups, the event attracted more than 250 children and their families, new families with children have joined the association, some of the local association has begun to organize groups of juvenile rheumatoid arthritis
Fund-raising, it was very easy to find sponsors for children activities and it also helped in common fundraising.
Children suffering from rheumatoid have experienced a positive campaign, it feels better when people's attitudes change, and no longer think that they're suffering from "a disease of the elderly".
Cooperation with arthritis professionals has intensified and improved. Their want to do more co-operation and they guide patients to more actively explore the Finnish Rheumatism Association activities.



Conclusions: Operation for JIA children and their families are needed.
Children's powerful vision of the activities have a positive impact on the brand and fundraising organization
The positivity of this type of cooperation with arthritis professionals to approximate intervals and supported by more co-operation
It's relatively easy to receive sponsor funds for the development of children's activities
Children and families inclusion will bring new energy and confidence in the future among local associations

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2724

Author Index

Aaløkken, T., 106 (OP0129)
Aaløkken, T.M., 55 (OP0013), 765 (FRI0725), 1043 (SAT0709)
Aalto, K., 401 (THU0515)
Aaltonen, K., 341 (THU0361), 686 (FRI0518), 1027 (SAT0669)
Aamir RashediBonab, M., 1431 (AB1076)
Aarabi, M., 1137 (AB0254)
Aarbiou, J., 621 (FRI0356)
Abad, M.Á., 918 (SAT0387), 1307 (AB0723)
Abad, M.A., 685 (FRI0515), 954 (SAT0474)
Abad, S., 1175 (AB0362)
Abad-Sanchez, S., 1174 (AB0361)
Abal, F., 803 (SAT0093)
Abalos, M.C., 194 (OP0336), 492 (FRI0035), 504 (FRI0069), 1078 (AB0092)
Ábalos-Aguilera, M., 1082 (AB0104)
Ábalos-Aguilera, M.C., 648 (FRI0429), 649 (FRI0431)
Abalos-Aguilera, M.C., 497 (FRI0048), 622 (FRI0360), 1091 (AB0127, AB0128)
Abalos-aguilera, M.C., 287 (THU0218)
Abas, N., 1168 (AB0342)
Abásolo, L., 320 (THU0309), 520 (FRI0107)
Abbas, K., 1403 (AB0997)
Abbas, R., 187 (OP0319)
Abd alrazaq, F.K., 1000 (SAT0597)
Abd El Baki, N., 874 (SAT0265)
Abd El Hady, E.S.A., 1000 (SAT0596)
Abd El Samad Elhawala, T., 1000 (SAT0596)
Abd El-Khalik, D.M., 1224 (AB0495)
Abd El-Rahman, M.A., 1145 (AB0276)
Abd ElHamid, S.M., 1259 (AB0594)
Abd elkareem, M.I., 1216 (AB0474)
Abdel Moneim, G., 1047 (AB0002)
Abdel salam, R., 734 (FRI0647)
Abdel Wahab, S., 1048 (AB0006)
Abdel Zaher, A., 1526 (SAT0764-HPR)
Abdel-Hamid, M.S., 1047 (AB0002)
Abdel-Razek, R., 1168 (AB0342)
Abdel-Salam, G.M., 1047 (AB0002)
Abdelati, A.A., 1073 (AB0076)
Abdelatif, S., 670 (FRI0482)
Abdelaziz, A., 670 (FRI0482)
Abdelaziz, M., 1235 (AB0527), 1308 (AB0726)
Abdelghani, K., 1348 (AB0831), 1349 (AB0834)
Abdelhady, M., 1113 (AB0190)
Abdelhady Abdelsadek, N., 1171 (AB0351)
Abdelkader, A., 1275 (AB0637)
Abdelkafi, I., 995 (SAT0580), 1377 (AB0920), 1536 (AB1214-HPR)
Abdelkarem, D., 1384 (AB0940)
Abdelmoula, L., 347 (THU0373), 1073 (AB0077), 1297 (AB0697), 1306 (AB0720), 1373 (AB0906, AB0907, AB0908), 1377 (AB0919)
Abdelnabi, H.H., 404 (THU0524)
Abdelrahman, F.I., 733 (FRI0644)
Abdelzaher, A., 1216 (AB0473)
Abdesalam, A., 1174 (AB0360)
Abdessemed, A., 1009 (SAT0623), 1405 (AB1001, AB1002)
Abdi, B.A., 140 (OP0213)
Abdilla, M., 330 (THU0336)
Abdolahi, N., 1137 (AB0254), 1354 (AB0850)
Abdollahi-Roodsaz, S., 191 (OP0329), 504 (FRI0072)
AbdRahman, W., 874 (SAT0265)
Abdul Latif, S., 1526 (SAT0764-HPR)
Abdul Rani, A.M., 1548 (AB1247-HPR)
Abdul Sultan, A., 751 (FRI0690), 1028 (SAT0672)
Abdulahad, W., 647 (FRI0424)
Abdulazim, E., 1113 (AB0190)
Abdulganieva, D., 273 (THU0188), 1311 (AB0735)
Abdulhadi, R., 740 (FRI0663), 1420 (AB1044)
Abdulhakiem, S., 670 (FRI0482)
Abdulrahman, M.A., 307 (THU0272)
Abdulrazaq, S., 1444 (AB1111)
Abdul_Sattar, A.B., 733 (FRI0644)
Abe, A., 229 (THU0079), 809 (SAT0106), 853 (SAT0214), 1124 (AB0219), 1177 (AB0371)
Abe, K., 282 (THU0208)
Abe, S., 95 (OP0104), 800 (SAT0084)
Abe, T., 641 (FRI0408)
Abello-Banfi, M., 824 (SAT0146)
Aberer, E., 1106 (AB0169), 1110 (AB0181)
Abheiden, C., 184 (OP0310)
Abhishek, A., 38 (SP0158), 167 (OP0268), 383 (THU0464)
Abi Karam, G., 1159 (AB0317)
Abi karam, G., 762 (FRI0718)
Abignano, G., 455 (THU0659), 627 (FRI0370), 635 (FRI0390), 734 (FRI0646), 915 (SAT0380), 1057 (AB0029)
Abit Kocaman, A., 1518 (SAT0741-HPR)
Abitbol, V., 831 (SAT0163)
Ablin, J., 1095 (AB0138)
Abobului, M., 881 (SAT0288), 1278 (AB0647), 1460 (AB1158)
Abogamal, A., 670 (FRI0482), 962 (SAT0495)
Abou Dahab, M.H., 1150 (AB0291)
Abraham, D., 140 (OP0213), 892 (SAT0318), 1104 (AB0166)
Abraham, S., 668 (FRI0479)
Abrahamowicz, M., 825 (SAT0149)
Abrahamsson, A., 382 (THU0461)
Abrami, E., 1468 (AB1178)
Abramkin, A., 249 (THU0127)
Abramov, D.D., 1128 (AB0230)
Abrams, K., 683 (FRI0511)
Abramsky, S., 277 (THU0197)
Abreu, J.P., 902 (SAT0346)
Abreu-Arbaje, N., 877 (SAT0276)
Abril, A., 318 (THU0301), 1276 (AB0639)
Absher, D., 290 (THU0227), 776 (SAT0022)
Abu Al-Fadl, E.M., 1150 (AB0291)
Abu Nahya, N., 1309 (AB0728)
Abu-Zaid, M.H., 404 (THU0524), 1469 (AB1181)
Abud-Mendoza, C., 395 (THU0501), 586 (FRI0264), 760 (FRI0714), 774 (SAT0016), 1164 (AB0331), 1345 (AB0820), 1397 (AB0978)
Abujam, B., 588 (FRI0270)
Abusoglu, S., 931 (SAT0422)
Abutaha, N., 1284 (AB0662)
Acar-Denizli, N., 311 (THU0284), 464 (THU0681), 886 (SAT0302)
Acari, C., 1387 (AB0949)
Acasuso-Pardo de Vera, B., 936 (SAT0435)
Accioly, J.P.E., 397 (THU0505)
Accogli, S., 731 (FRI0640)
Accortt, N.A., 114 (OP0148), 239 (THU0102)
Acevedo, N., 1395 (AB0974)
Aceves-Avila, F.J., 1452 (AB1136)
Achenbach, S.J., 444 (THU0630)
Achit, H., 970 (SAT0513)
Achniotou, G., 1473 (AB1194)
Achtleitner, M., 461 (THU0674)
Acosta, C., 1339 (AB0805)
Acosta, I., 1396 (AB0975)
Acosta, M.E., 1455 (AB1142)
Acosta Colman, I., 1455 (AB1142)
Acosta Felquer, M.L., 1333 (AB0789)
Acosta Fernández, O., 1424 (AB1057)
Acosta-Hernández, I., 586 (FRI0264)
Acosta-Manzano, P., 1499 (FRI0743-HPR)
Acuña, L., 1536 (AB1213-HPR)
Adachi, J., 54 (OP0010), 71 (OP0048)
Adam, I., 1070 (AB0068)
Adami, G., 1124 (AB0216)
Adamichou, C., 297 (THU0246), 300 (THU0254), 574 (FRI0236), 577 (FRI0244), 850 (SAT0204), 1204 (AB0442)
Adams, D.H., 135 (OP0201), 679 (FRI0502), 937 (SAT0437), 941 (SAT0446)
Adams, H.R., 125 (OP0178)
Adams, J., 1508 (FRI0767-HPR), 1525 (SAT0762-HPR)
Adamsbaum, C., 56 (OP0014)
Adán, A., 75 (OP0059), 326 (THU0326), 718 (FRI0607)
Adan, A., 350 (THU0381), 405 (THU0526), 420 (THU0567), 421 (THU0569)
Addimanda, O., 248 (THU0123)
Addya, S., 91 (OP0096)
Adebajo, A., 1541 (AB1227-HPR)
Adeeb, F., 1036 (SAT0689)
Adejoro, O., 346 (THU0371), 945 (SAT0456)
Aderinto, J., 959 (SAT0485)
Adinolfi, A., 383 (THU0465), 730 (FRI0637), 1010 (SAT0625), 1013 (SAT0631)
Adnan, S., 821 (SAT0140)
Adolph, S.M.M., 1478 (THU0728-HPR)
Adrianto, I., 1096 (AB0143)
Adrosy, T.I., 1426 (AB1062)
Adrovic, A., 394 (THU0498), 1389 (AB0957), 1402 (AB0994)
Adzerikho, I., 153 (LB0002)
Aelion, J.A., 143 (OP0219)
Aeschlimann, A., 475 (THU0708), 478 (THU0718), 479 (THU0719), 1463 (AB1165)
af Forselles, K., 127 (OP0182)
af Klint, E., 726 (FRI0626), 785 (SAT0048)
Afeltra, A., 151 (OP0233), 304 (THU0267), 437 (THU0611), 876 (SAT0273), 1439 (AB1099)
Affandi, A.J., 1065 (AB0054), 1104 (AB0165)
Afonso, C., 607 (FRI0318), 612 (FRI0330), 637 (FRI0394), 736 (FRI0652), 1011 (SAT0627), 1015 (SAT0637), 1254 (AB0581), 1275 (AB0636)
Aga, A.-B., 176 (OP0289), 522 (FRI0111), 526 (FRI0121), 538 (FRI0151), 1017 (SAT0642)
Agafonova, E., 660 (FRI0458), 920 (SAT0394), 1294 (AB0688), 1411 (AB1017)
Agapitou, M., 1560 (AB1252-PARE)
Agar, V., 1459 (AB1154)
Agard, C., 778 (SAT0029)
Agarwal, M., 1385 (AB0944)
Agarwal, P., 563 (FRI0214), 580 (FRI0251)
Agarwal, V., 415 (THU0551), 913 (SAT0375)
Agelopoulos, M., 293 (THU0237)
Agewall, S., 1309 (AB0730)
Aggarwal, A., 388 (THU0481)
Aggarwal, A.K., 1346 (AB0825)
Aggarwal, N., 1346 (AB0825)
Aghaei, M., 1137 (AB0254), 1354 (AB0850)
Agorastos, A., 643 (FRI0412), 723 (FRI0619)
Agrawal, I., 1295 (AB0690)
Aguado, P., 416 (THU0553), 501 (FRI0062)
Agudelo, C.A., 1158 (AB0313)
Agudo, M., 594 (FRI0286), 1229 (AB0511), 1230 (AB0512)
Agudo-Bilbao, M., 1116 (AB0197)
Águeda, A., 1461 (AB1161)
Agüero, S., 440 (THU0619)
Agueusop, I., 195 (OP0339)
Aguiar, F., 468 (THU0690, THU0691), 852 (SAT0211), 1142 (AB0268)
Aguiar, M.G., 397 (THU0505)
Aguiar, R., 466 (THU0685)
Aguila Maldonado, R., 1263 (AB0606)

Aguilar-Arreola, J., 806 (SAT0100), 1075 (AB0083), 1164 (AB0330)
Aguilar-Hurtado, C., 261 (THU0160)
Aguilar-Rodríguez, M., 1380 (AB0929)
Aguilar-Salinas, C., 1225 (AB0499)
Aguilar-Zamora, M., 258 (THU0153), 1168 (AB0344), 1316 (AB0746), 1410 (AB1016), 1415 (AB1032)
Aguilera, C., 843 (SAT0191)
Aguilera, S., 1102 (AB0158)
Aguilera Barragán-Pickens, G., 1397 (AB0978)
Aguilera Barragan-Pickens, G., 395 (THU0501)
Aguilera Cros, C., 713 (FRI0592)
Aguilera-Barragán Pickens, G., 760 (FRI0714)
Aguirre, M., 1082 (AB0104)
Aguirre, M.A., 287 (THU0218), 622 (FRI0360), 1091 (AB0127, AB0128)
Aguirre-Valencia, D., 1225 (AB0498)
Aguirre-Zamorano, M.A., 290 (THU0227)
Aguliar Zamora, M., 1534 (AB1208-HPR)
Ahadieh, S., 277 (THU0196), 284 (THU0211)
Aharoni, D., 355 (THU0392)
Ahijado, P., 350 (THU0381)
Ahijón Lana, M., 698 (FRI0549)
Ahlsen, B., 384 (THU0468)
Ahluwalia, V., 194 (OP0337-HPR)
Ahmad, A., 596 (FRI0291)
Ahmad, H., 174 (OP0284), 233 (THU0089), 240 (THU0104), 687 (FRI0520), 782 (SAT0041), 842 (SAT0188), 951 (SAT0468)
Ahmad, M.S., 444 (THU0631)
Ahmad, N., 1309 (AB0729)
Ahmad, Z., 103 (OP0122)
Ahmed, A., 743 (FRI0669)
Ahmed, D., 696 (FRI0543)
Ahmed, K.A., 1219 (AB0481)
Ahmed, S., 388 (THU0481), 913 (SAT0375), 1044 (SAT0713), 1460 (AB1157)
Ahmed, U., 1025 (SAT0663)
Ahmed Abdi, B., 898 (SAT0334, SAT0335)
Ahmed Yahia, S., 188 (OP0323)
Ahmed-Abdi, B., 1104 (AB0166)
Ahmedov, A., 1535 (AB1212-HPR)
Ahmedov, H., 1526 (SAT0763-HPR)
Ahn, E.Y., 1053 (AB0020)
Ahn, G.Y., 882 (SAT0290), 1045 (SAT0714), 1061 (AB0040)
Ahn, J.K., 612 (FRI0331), 749 (FRI0685)
Ahn, S.S., 383 (THU0467)
Aiewruengsurat, D., 1378 (AB0922)
Aikawa, N.E., 76 (OP0061)
Aikman, L., 670 (FRI0484), 939 (SAT0441), 947 (SAT0461)
Ailioaie, C., 395 (THU0500)
Ailioaie, L.M., 395 (THU0500)
Aimo, C., 571 (FRI0229)
Ainola, M., 1080 (AB0097)
Ainon, M.-M., 1512 (SAT0722-HPR)
Airó, P., 909 (SAT0366), 1047 (AB0003)
Airò, P., 579 (FRI0249), 1214 (AB0468), 1225 (AB0497)
Airo, P., 202 (THU0006)
Airoldi, A., 52 (OP0006)
Aissi, K., 753 (FRI0696)
Aissoug, A., 982 (SAT0545)
Aitken, D., 193 (OP0334), 471 (THU0699), 962 (SAT0493)
Aiwu Li, A., 759 (FRI0710)
Aizaki, Y., 188 (OP0322)
Aizawa, T., 795 (SAT0071), 1178 (AB0372), 1182 (AB0382), 1426 (AB1063)
Ajeganova, S., 227 (THU0074), 1050 (AB0012), 1096 (AB0142), 1523 (SAT0755-HPR)
Ajmone Marsan, N., 903 (SAT0350), 907 (SAT0359)
Ak, S., 1035 (SAT0687), 1412 (AB1023)
Akai, Y., 282 (THU0207)
Akar, S., 102 (OP0120), 296 (THU0245), 354 (THU0389), 661 (FRI0462), 921 (SAT0395), 1170 (AB0349)
Akasaka, D., 507 (FRI0079)
Akasbi, M., 410 (THU0539), 597 (FRI0293), 721 (FRI0615), 1042 (SAT0706)
Akashi, K., 115 (OP0152), 282 (THU0207), 422 (THU0571), 487 (FRI0022), 507 (FRI0080), 699 (FRI0553)
Akashi, Y.J., 910 (SAT0369)
Akay, M., 254 (THU0141)
Akcay, B., 477 (THU0714)
Akdemir, G., 516 (FRI0097), 793 (SAT0067)
Akdeniz, S., 1162 (AB0324)
Akdeniz Leblebicier, M., 1405 (AB1003)
Akdoğan, A., 448 (THU0642), 1035 (SAT0687), 1412 (AB1023), 1531 (AB1198-HPR)
Akdogan, A., 250 (THU0131), 256 (THU0147), 402 (THU0518), 414 (THU0548), 534 (FRI0140), 616 (FRI0342), 637 (FRI0397), 720 (FRI0612), 854 (SAT0216), 1113 (AB0189), 1127 (AB0226), 1175 (AB0363), 1194 (AB0414), 1256 (AB0586), 1262 (AB0604), 1300 (AB0706)
Akdogan, B., 720 (FRI0612)
Akduman, V., 997 (SAT0586), 1003 (SAT0606)
Akerkar, S.M., 269 (THU0178)
Åkesson, K., 72 (OP0050)
Akesson, K., 7 (SP0025)
Akgün, K., 353 (THU0387), 1380 (AB0927)
Akhtyamov, I., 1203 (AB0438), 1300 (AB0704)
Akhverdyan, Y., 699 (FRI0554), 1149 (AB0288)
Akihiko Nakamura, A., 1471 (AB1187)
Akil, M., 847 (SAT0198)
Akıncı Tan, A., 1122 (AB0213)
Akiyama, M., 623 (FRI0361), 712 (FRI0590, FRI0591)
Akkoc, N., 1282 (AB0658)
Akl, E., 418 (THU0561)
Akman, S., 1392 (AB0965)
Akpinar, P., 999 (SAT0592, SAT0595)
Akrout, R., 1311 (AB0734), 1377 (AB0921)
Akrout, W., 1301 (AB0708)
Aksenova, T., 1311 (AB0736)
Aksoy, A., 644 (FRI0416), 1310 (AB0731)
Aksoy Kasapoğlu, M., 974 (SAT0525)
Aksu, K., 327 (THU0329)
Aktaou, S., 1358 (AB0862), 1365 (AB0883, AB0884, AB0885), 1418 (AB1041)
Aktaş, I., 1380 (AB0927)
Aktas, I., 735 (FRI0648), 999 (SAT0592, SAT0595), 1058 (AB0034)
Akuthota, P., 107 (OP0130)
Akyol, L., 327 (THU0329)
Al Araby, S., 1113 (AB0190)
Al Emadi, S., 1504 (FRI0758-HPR)
Al Ghafri, A.S., 1243 (AB0549)
Al Hassanein, K., 1526 (SAT0764-HPR)
Al Hinai, S., 127 (OP0182)
Al Kaffas, M., 1048 (AB0006)
Al Sawah-Folian, S., 1330 (AB0783)
Al Sherbeni, H.H., 734 (FRI0647)
Al Wahshi, H., 1243 (AB0549)
Al-Abadi, E., 409 (THU0536), 1395 (AB0972)
Al-Ali, S., 92 (OP0097), 295 (THU0242)
Al-Allaf, A.-W., 1420 (AB1044)
Al-Allaf, A.W., 740 (FRI0663)
Al-Ani, H., 1436 (AB1090)
Al-awamy, A., 1168 (AB0342)
Al-Hosni, R., 221 (THU0060)
Al-johi, A., 1168 (AB0342)
Al-Maini, M., 1284 (AB0662)
Al-Mashari, H., 1284 (AB0662)
Al-Mossawi, H., 419 (THU0562)
Al-Qadir, A.Z., 1460 (AB1157)
Al-qadir, A.Z., 1044 (SAT0713)
Al-Saleh, J., 1350 (AB0839)
Al-Sarraj, S., 64 (OP0032)
Al-Sayed, E., 1309 (AB0728)
Al-Sharqi, A., 1087 (AB0115)
Al-Soudi, A., 601 (FRI0303)
Alabarse, P.V.G., 1508 (FRI0768-HPR)
Alam, F., 1504 (FRI0758-HPR)
Alam, H., 333 (THU0344)
Alam, J., 228 (THU0078), 244 (THU0114), 511 (FRI0089), 1130 (AB0235)
Alanis, G., 1161 (AB0321)
Alaoui, F.-Z., 613 (FRI0333)
Alaoui, F.Z., 322 (THU0313)
Alarcón, G., 875 (SAT0269)
Alarcon-Riquelme, M., 492 (FRI0035)
Alase, A., 91 (OP0095)
Alasti, F., 445 (THU0633), 472 (THU0701), 520 (FRI0108), 560 (FRI0207), 1124 (AB0217)
Alawamy, A., 1384 (AB0940)
Alaya, Z., 926 (SAT0409), 927 (SAT0411)
Alba, M., 1252 (AB0575)
Alba, M.I., 1129 (AB0232)
Alba, P.B., 1220 (AB0484, AB0485)
Alba, R., 610 (FRI0324)
Alba-Barton, J.L., 1432 (AB1079)
Alba-Fériz, R., 877 (SAT0276, SAT0277)
Albayda, J., 67 (OP0038)
Albeer, M.R., 1000 (SAT0597)
Albertini, R., 995 (SAT0582)
Albiero, A., 1220 (AB0484, AB0485)
Albiero, E.H., 1220 (AB0484, AB0485)
Albina, S., 996 (SAT0584)
Albornoz, N., 1102 (AB0158)
Albrecht, K., 801 (SAT0087), 899 (SAT0337)
Albulescu, M.G., 867 (SAT0249)
Albulescu^, M., 564 (FRI0216)
Albuquerque, C., 1160 (AB0320)
Alcaide, L., 1472 (AB1192)
Alcalde, M., 718 (FRI0607)
Alcañiz Escandell, C., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1349 (AB0837), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Alcañiz Escandell, C.P., 441 (THU0623)
Alcaraz, M.J., 485 (FRI0014)
Alcino, S., 607 (FRI0318), 1011 (SAT0627)
Alcocer-Varela, J., 586 (FRI0264), 774 (SAT0016)
Aldana, C., 1158 (AB0313)
Alegre de Miguel, C., 1472 (AB1192)
Alegre Sancho, J.J., 1534 (AB1208-HPR)
Alegre-Sancho, J.J., 258 (THU0153), 1168 (AB0344), 1316 (AB0746), 1410 (AB1016), 1415 (AB1032), 1490 (THU0761-HPR)
Aleixo, J., 1254 (AB0581)
Alejandre, R., 1184 (AB0388)
Alekberova, Z., 616 (FRI0343)
Alekhina, I.Y., 1218 (AB0479)
Aleksandrov, A.V., 1218 (AB0479)
Aleksandrov, V.A., 1218 (AB0479)
Aleksandrova, E., 640 (FRI0403), 776 (SAT0024), 1283 (AB0659), 1404 (AB0998), 1411 (AB1018)
Aleksandrova, E.N., 861 (SAT0232)
Aleksandrova, N.V., 1218 (AB0479)
Aleksankin, A.A., 776 (SAT0024)
Aleksankin, A.P., 861 (SAT0232)
Alekseev, D., 1389 (AB0955)
Alekseeva, L., 169 (OP0272), 968 (SAT0509, SAT0510), 978 (SAT0534)
Alekseeva, L.I., 1337 (AB0799), 1347 (AB0828)
Aleksic, I., 1240 (AB0540)
Alemán-Ávila, I., 1133 (AB0242)
Alemany, X., 1041 (SAT0703), 1458 (AB1150)
Alemao, E., 75 (OP0058), 568 (FRI0223), 571 (FRI0230), 572 (FRI0232), 677 (FRI0499), 687 (FRI0520), 782 (SAT0041), 846 (SAT0197), 1120 (AB0207, AB0208), 1188 (AB0397), 1192 (AB0408), 1455 (AB1143), 1477 (THU0725-HPR)
Alende, V., 712 (FRI0589)
Alenius, G.-M., 444 (THU0632), 947 (SAT0460)
AleSaeidi, S., 1272 (AB0628)
Alessandri, C., 180 (OP0299), 204 (THU0013), 329 (THU0334), 463 (THU0678), 470 (THU0696), 489 (FRI0027), 490 (FRI0028), 496 (FRI0045), 757 (FRI0705), 860 (SAT0228), 864 (SAT0241), 872 (SAT0260), 879 (SAT0281), 880 (SAT0283), 1007 (SAT0615), 1059 (AB0036), 1093 (AB0132), 1094 (AB0135, AB0136), 1099 (AB0150), 1449 (AB1125), 1465 (AB1170)
Alessandri, E., 66 (OP0037), 641 (FRI0407), 704 (FRI0569), 897 (SAT0331), 915 (SAT0381)
Alessandro, R., 131 (OP0193), 183 (OP0309), 291 (THU0231), 777 (SAT0025)
Aletaha, D., 83 (OP0076), 97 (OP0108), 158 (OP0247), 224 (THU0070), 239 (THU0103),

242 (THU0110), 272 (THU0186), 445 (THU0633), 472 (THU0701), 520 (FRI0108), 528 (FRI0125), 560 (FRI0207), 563 (FRI0214), 580 (FRI0251), 677 (FRI0498), 845 (SAT0194), 971 (SAT0515), 1124 (AB0217), 1547 (AB1245-HPR)
Alexander, G.C., 859 (SAT0227)
Alexander, T., 446 (THU0637), 899 (SAT0337)
Alexander, Y., 1023 (SAT0657)
Alexandra, J.-F., 78 (OP0065)
Alexandrova, E., 254 (THU0142), 576 (FRI0241), 599 (FRI0299), 811 (SAT0113)
Alexandrova, E.N., 251 (THU0132), 1128 (AB0230), 1226 (AB0500)
Alexeeva, E., 186 (OP0316), 539 (FRI0154), 1082 (AB0105), 1387 (AB0950, AB0951), 1389 (AB0957)
Alexiou, I., 680 (FRI0504)
Alexopoulou, E., 293 (THU0237)
Alfaro-Lozano, J., 875 (SAT0269), 1142 (AB0269)
Alfonso-Cristancho, R., 857 (SAT0223)
Alfredsson, L., 228 (THU0077), 248 (THU0124), 1037 (SAT0692), 1038 (SAT0694), 1511 (SAT0721-HPR), 1512 (SAT0722-HPR)
Alguacil, A., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Algun, Z.C., 1548 (AB1249-HPR)
Alhefny, A.E.-A.M., 1145 (AB0276)
Ali, M., 988 (SAT0559)
Alía Jiménez, A., 587 (FRI0266)
Alia Jimenez, A., 1394 (AB0970)
Alibaz-Öner, F., 1310 (AB0731)
Alibaz-Oner, F., 315 (THU0295), 417 (THU0557), 609 (FRI0322)
Alivernini, S., 138 (OP0208), 154 (OP0239), 787 (SAT0052), 792 (SAT0066)
Aljohee, A., 1281 (AB0654)
Alkaabi, S., 1309 (AB0728)
Alkan, Z.B., 1004 (SAT0608)
Alkan Melikoglu, M., 387 (THU0477), 1340 (AB0809)
Alkin, A., 1173 (AB0357)
Allaart, C., 158 (OP0247), 434 (THU0604)
Allaart, C.F., 146 (OP0224), 160 (OP0252), 516 (FRI0097), 793 (SAT0067), 976 (SAT0529), 1076 (AB0084)
Allali, F., 1136 (AB0252), 1168 (AB0343), 1358 (AB0862), 1365 (AB0883, AB0884, AB0885), 1418 (AB1041)
Allande, M.J., 555 (FRI0195)
Allande-López-Linares, M., 1001 (SAT0600)
Allanore, Y., 65 (OP0035), 85 (OP0081), 195 (OP0339), 202 (THU0006), 635 (FRI0390), 831 (SAT0163), 909 (SAT0366), 915 (SAT0380), 1049 (AB0007), 1271 (AB0627), 1286 (AB0669)
Allen, N., 318 (THU0301)
Allen Jr, J.C., 1026 (SAT0666)
Allen-Redpath, K., 208 (THU0025)
Allende, I., 1459 (AB1154)
Allia, J., 707 (FRI0578)
Alliot Launois, F., 171 (OP0278-PARE)
Allotta, A., 901 (SAT0341)
Almaz, E., 652 (FRI0439)
Almeda-Valdés, P., 1225 (AB0499)
Almehed, K., 1513 (SAT0725-HPR)
Almeida, C., 110 (OP0139-HPR), 728 (FRI0631), 1018 (SAT0643)
Almeida, I., 902 (SAT0346)
Almeida, L., 1062 (AB0043)
Almendrales, L., 1239 (AB0538)
Almodóvar, R., 660 (FRI0459), 908 (SAT0363)
Almodovar, R., 452 (THU0651), 633 (FRI0385), 718 (FRI0607), 1270 (AB0625)
Almonte-Becerril, M., 502 (FRI0063)
Alonso, C., 1305 (AB0717)
Alonso, F., 873 (SAT0263)
Alonso Blanco Morales, E., 1333 (AB0788)
Alonso Blanco-Morales, E., 917 (SAT0385)
Alonso-Castro, S., 803 (SAT0093)
Alonso-Ruiz, A., 553 (FRI0189)
Alonso-Vila, S., 1262 (AB0603)
Alosami, M.H., 1000 (SAT0597)
Aloush, V., 1095 (AB0138)
Alparslan, Z.N., 905 (SAT0355)
Alpay Kanıtez, N., 1360 (AB0868)
Alpay-Kanıtez, N., 716 (FRI0600), 1170 (AB0350)
Alperi-López, M., 803 (SAT0093), 1079 (AB0093)
Alpizar-Rodriguez, D., 755 (FRI0701)
Alqadi, R., 826 (SAT0151)
Alrashed, F., 219 (THU0053)
Alric, L., 776 (SAT0023), 1376 (AB0916)
Alsaed, O., 1420 (AB1044)
AlSalmi, I., 545 (FRI0169), 818 (SAT0131)
Alsalmi, I., 1043 (SAT0710)
Alshevskaya, A.A., 1056 (AB0027)
Altaie, A., 480 (FRI0001)
Altan, L., 974 (SAT0525), 1380 (AB0927)
Altawil, R., 1037 (SAT0692)
Altay, D., 1121 (AB0209)
Alten, R., 59 (OP0021), 92 (OP0098), 96 (OP0107), 159 (OP0249), 230 (THU0081), 267 (THU0173), 470 (THU0695), 516 (FRI0098), 529 (FRI0128), 565 (FRI0217), 577 (FRI0245), 818 (SAT0132), 831 (SAT0161), 1141 (AB0267), 1193 (AB0412)
Altoé, R., 163 (OP0259-HPR)
Altug-Gucenmez, O., 53 (OP0009-HPR), 1387 (AB0949), 1522 (SAT0751-HPR)
Altuner, M.S., 327 (THU0329)
Alunno, A., 69 (OP0044), 305 (THU0268), 464 (THU0681), 873 (SAT0262), 880 (SAT0284), 1113 (AB0191), 1560 (AB1251-PARE)
Alvarado, J.D., 1351 (AB0840)
Alvarellos, A., 205 (THU0017), 206 (THU0018), 313 (THU0289), 670 (FRI0483), 995 (SAT0582)
Alvarellos, T., 205 (THU0017), 206 (THU0018), 313 (THU0289), 670 (FRI0483), 995 (SAT0582)
Alvarez, A., 1220 (AB0484, AB0485)
Alvárez, B., 826 (SAT0150)
Alvarez, B., 843 (SAT0191)
Álvarez, C., 213 (THU0037)
Alvarez, D., 571 (FRI0229)
Álvarez Castro, C., 719 (FRI0608), 1232 (AB0518)
Alvarez del Buergo, M., 1166 (AB0337)
Alvarez Grijalva, A.L., 1357 (AB0861)
Alvarez Hernandez, E., 363 (THU0411), 365 (THU0417)
Álvarez-Gallardo, I.C., 1499 (FRI0743-HPR)
Alvarez-Hernandez, E., 1362 (AB0873)
Alvarez-Nemegyei, J., 1453 (AB1137)
Alves, H., 1058 (AB0033)
Aly, H., 962 (SAT0495)
Alzate, M.A., 594 (FRI0287), 658 (FRI0453), 927 (SAT0413), 928 (SAT0414), 1286 (AB0667)
Amano, H., 141 (OP0215), 1095 (AB0139, AB0140)
Amano, K., 265 (THU0170), 279 (THU0199), 424 (THU0577), 544 (FRI0168), 1399 (AB0984)
Amantini, D., 126 (OP0180)
Amara, K., 1051 (AB0015)
Amaral, J., 1051 (AB0013), 1094 (AB0134)
Amaral Silva, M., 1382 (AB0935)
Amarilla Vallejo, A.D., 806 (SAT0099)
Amati, A., 639 (FRI0400)
Amato, G., 829 (SAT0158)
Ambler, N., 110 (OP0139-HPR)
Ambrosi, A., 316 (THU0299)
Ambrósio, C., 1314 (AB0741)
Ambrosioni, E., 366 (THU0420)
Ambrožič, A., 1143 (AB0272)
Amengual, O., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Amer, E.R., 1138 (AB0256)
Amess, B., 529 (FRI0128)
Ametzazurra, A., 555 (FRI0195)
Amezcua, L., 884 (SAT0295)
Amhaz-Escanlar, S., 494 (FRI0040)
Amiaud, J., 128 (OP0184)
Amigo, N., 312 (THU0287)
Amin, S., 705 (FRI0572)
Amine, B., 1136 (AB0252), 1163 (AB0327, AB0328), 1168 (AB0343)
Aminov, K., 1017 (SAT0641), 1351 (AB0842)
Amirdjanova, V., 464 (THU0680)
Amital, D., 297 (THU0248)
Amital, H., 84 (OP0078), 169 (OP0273), 297 (THU0248), 319 (THU0304), 332 (THU0342), 619 (FRI0350), 796 (SAT0074), 886 (SAT0300)
Ammerlaan, J., 1482 (THU0737-HPR), 1556 (PARE0014)
Ammitsbøll-Danielsen, M., 1409 (AB1013)
Ammitzbøll-Danielsen, M., 174 (OP0286), 726 (FRI0628)
Amorim, R., 1160 (AB0320)
Amosov, V.I., 810 (SAT0111)
Amosova, N.A., 810 (SAT0111)
Amoura, Z., 151 (OP0234), 426 (THU0584)
Amri, E.Z., 967 (SAT0507)
Amri, R., 1397 (AB0980)
Amris, K., 98 (OP0112)
Amselem, S., 1049 (AB0007)
Amuro, H., 115 (OP0152), 282 (THU0207)
An, Y., 285 (THU0215)
Anan, R., 1234 (AB0525)
Anand, A., 694 (FRI0538)
Ananieva, L., 640 (FRI0403), 1283 (AB0659)
Ananyeva, L.P., 1287 (AB0670)
Anaparti, V., 178 (OP0295)
Anchugina, D.A., 273 (THU0187)
Ancuta, C., 632 (FRI0383), 825 (SAT0148), 1151 (AB0294), 1269 (AB0620)
Ancuta, E., 825 (SAT0148), 1269 (AB0620)
Ancuta, I., 1032 (SAT0681), 1151 (AB0294)
Andani Cervera, J., 441 (THU0623)
Andersen, B.L., 553 (FRI0190)
Andersen, G.N., 456 (THU0660)
Andersen, J., 18 (SP0072), 172 (OP0280-PARE), 1552 (PARE0001), 1557 (PARE0015)
Andersen, J.R., 120 (OP0165)
Andersen, L., 73 (OP0055-HPR), 1512 (SAT0723-HPR)
Andersen, L.S., 553 (FRI0190)
Andersen, M., 456 (THU0660)
Andersen, M.S., 477 (THU0715)
Andersen, P., 1088 (AB0119)
Andersen, S., 621 (FRI0356), 769 (SAT0001)
Andersen, V., 775 (SAT0020)
Anderson, A.E., 200 (THU0003)
Anderson, F., 72 (OP0051)
Anderson, J., 758 (FRI0708)
Anderson, J.K., 156 (OP0243), 353 (THU0388), 654 (FRI0444), 829 (SAT0159), 1487 (THU0753-HPR)
Andersson, E., 626 (FRI0367)
Andersson, K.M., 777 (SAT0026), 779 (SAT0033)
Andersson, M., 340 (THU0359), 683 (FRI0511), 1513 (SAT0726-HPR)
Andersson, M.L., 812 (SAT0116), 1136 (AB0251)
Andrade, C.A., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Andrade, M.V., 522 (FRI0112)
Andrade, M.V.M., 1056 (AB0028)
Andrade, N., 814 (SAT0121)
Andras, L., 335 (THU0349)
André, B., 736 (FRI0650)
Andreasen, R.A., 660 (FRI0460), 990 (SAT0565)
Andreassen, A.K., 630 (FRI0376)
Andreassen, O., 1478 (THU0726-HPR)
Andréasson, K., 655 (FRI0445)
Andreoli, L., 28 (SP0114), 70 (OP0046), 245 (THU0116), 437 (THU0611), 867 (SAT0248), 1209 (AB0456), 1214 (AB0467, AB0468), 1225 (AB0497), 1439 (AB1099), 1468 (AB1178)
Andreou, A., 205 (THU0015)
Andrés, M., 361 (THU0406), 372 (THU0437), 374 (THU0441), 705 (FRI0570, FRI0571), 1367 (AB0890)
Andres, M., 383 (THU0464)
Andres Cerezo, L., 220 (THU0058), 243 (THU0113)
Andretto, L., 216 (THU0047)
Andreu, J.L., 290 (THU0227), 885 (SAT0299), 1232 (AB0519), 1406 (AB1004)
Andreu Sanchez, J.L., 1399 (AB0986)
Andrews, J., 238 (THU0101), 268 (THU0175)
Andrews, P., 1505 (FRI0761-HPR)
Andrews, S., 1514 (SAT0728-HPR)
Andrianakos, A., 559 (FRI0205)
Andronache, I.-T., 1162 (AB0325)
Aneja, R., 1284 (AB0662)

Anelli, M.G., 254 (THU0143), 521 (FRI0110), 1135 (AB0250), 1268 (AB0618), 1327 (AB0773)
Ang, B.-H., 364 (THU0415)
Angarita, J.-I., 201 (THU0005), 218 (THU0052), 752 (FRI0694), 993 (SAT0573, SAT0574, SAT0575), 994 (SAT0576), 1375 (AB0913)
Angarita, J.I., 1132 (AB0239)
Angeles, U., 860 (SAT0229)
Angeles-Angeles, A., 417 (THU0556)
Angeletti, A., 1189 (AB0400)
Angelina, M., 206 (THU0018), 313 (THU0289)
Angelini, F., 1077 (AB0088)
Angelo A, M., 1055 (AB0025)
Angerås, O., 375 (THU0443)
Angin, S., 477 (THU0714)
Angioni, M.M., 975 (SAT0528)
Angst, F., 475 (THU0708), 478 (THU0718), 479 (THU0719), 1463 (AB1165)
Angst, J., 1463 (AB1165)
Angulo, J., 1339 (AB0805)
Angulo-Gonzalez, A.G., 1255 (AB0585)
Anić, B., 592 (FRI0282), 883 (SAT0291)
Anic, B., 1055 (AB0026)
Ankaralı, H., 977 (SAT0532), 1340 (AB0808)
Annamalai, S., 572 (FRI0232)
Annapureddy, N., 378 (THU0450)
Anno, S., 1023 (SAT0658)
Anolik, J., 181 (OP0304)
Añón Oñate, I., 1228 (AB0506), 1321 (AB0760)
Anouk, M., 747 (FRI0679)
Ansell, R., 344 (THU0368)
Ansola, L., 241 (THU0109)
Anthi, A., 643 (FRI0414)
Antic, M., 65 (OP0034)
Antinozzi, C., 1057 (AB0029, AB0030)
Antivalle, M., 1008 (SAT0620), 1376 (AB0917), 1380 (AB0928)
Antohe, M., 1269 (AB0620)
Anton, J., 75 (OP0058), 77 (OP0063), 396 (THU0503), 399 (THU0511), 407 (THU0530), 1389 (AB0957), 1390 (AB0958), 1393 (AB0967)
Antonatou, K., 321 (THU0310), 1376 (AB0915)
Antończak, P., 1502 (FRI0752-HPR)
Antoniadou, A., 428 (THU0587)
Antony, B., 122 (OP0169), 960 (SAT0489)
Antony, B.E., 962 (SAT0493)
Antony, G., 423 (THU0575)
Antonyan, A., 787 (SAT0051)
Anupindi, V., 572 (FRI0232), 677 (FRI0499)
Anyfanti, P., 542 (FRI0161)
Anzini, M., 1343 (AB0816)
Aoki, A., 1150 (AB0292)
Aoki, I., 1150 (AB0292)
Aoki, N., 573 (FRI0233), 806 (SAT0101)
Aonuma, H., 1178 (AB0372), 1182 (AB0382), 1426 (AB1063)
Aouba, A., 330 (THU0337), 617 (FRI0345), 1256 (AB0587, AB0588)
Aouidane, S., 982 (SAT0545)
Aoyama, N., 418 (THU0559)
Apanaviciene, I., 367 (THU0423)
Apaolaza, I., 944 (SAT0453)
Aparicio, C., 1371 (AB0900)
Aparicio, V.A., 1499 (FRI0743-HPR)
Aparkina, A., 924 (SAT0403)
Apáthy, Á., 1104 (AB0164), 1149 (AB0290), 1252 (AB0577), 1283 (AB0660), 1312 (AB0737), 1328 (AB0777)
Apolinar, L.M., 1286 (AB0668)
Apostolopoulos, D., 876 (SAT0272)
Apparao, S., 561 (FRI0209)
Appels, C., 676 (FRI0497), 1306 (AB0722), 1308 (AB0725)
Appels, C.W.Y., 1325 (AB0770)
Apraş Bilgen, S., 448 (THU0642), 1035 (SAT0687), 1412 (AB1023), 1531 (AB1198-HPR)
Apras Bilgen, S., 250 (THU0131), 256 (THU0147), 402 (THU0518), 534 (FRI0140), 854 (SAT0216), 1127 (AB0226), 1175 (AB0363), 1194 (AB0414), 1212 (AB0463), 1300 (AB0706)
Aquilani, A., 399 (THU0511)
Arabi, A., 1042 (SAT0705)
Arad, U., 1095 (AB0138), 1118 (AB0203)
Arafa, S.G., 1219 (AB0481)
Aragón, A., 685 (FRI0515)
Aragona, C.O., 1312 (AB0738)
Arai, S., 531 (FRI0134), 1291 (AB0681)
Arakaki, J.S., 1508 (FRI0769-HPR)
Araki, Y., 188 (OP0322)
Aramă, V., 1032 (SAT0681)
Aramburu, F., 1275 (AB0637), 1338 (AB0801)
Arana-Guajardo, A.C., 425 (THU0581), 1054 (AB0023), 1410 (AB1015), 1448 (AB1122)
Aranda-Arreola, E., 1362 (AB0873)
Aranda-Pereira, P., 515 (FRI0095)
Aranda-Valera, C., 919 (SAT0391)
Arape, R., 1339 (AB0805), 1342 (AB0813)
Aras, I., 1496 (FRI0734-HPR)
Aras, U., 859 (SAT0226)
Araujo, E.G., 142 (OP0217)
Araújo, F., 830 (SAT0160)
Araujo, F., 784 (SAT0046)
Arbaje-Khoury, M., 877 (SAT0276)
Arboleya, L., 843 (SAT0191)
Archer, S., 213 (THU0038)
Archimandriti, D., 1217 (AB0476)
Archimandriti, D.T., 1193 (AB0411)
Arcila Durán, M., 713 (FRI0592)
Arciniega, I.M., 1286 (AB0668)
Arcos, H., 1351 (AB0840)
Arcuri, C., 901 (SAT0341)
Arda, M.N., 1532 (AB1201-HPR)
Arden, N., 966 (SAT0504)
Ardoin, S., 1099 (AB0151)
Arellano-Martinez, A., 117 (OP0158), 1446 (AB1116)
Arenas, M.D., 361 (THU0406), 374 (THU0441)
Arends, S., 67 (OP0040), 591 (FRI0277), 647 (FRI0424), 649 (FRI0430), 650 (FRI0433), 928 (SAT0416), 1007 (SAT0617)
Areti, M., 836 (SAT0176)
Arevalo, M., 926 (SAT0410)
Arévalo Ruales, K., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1349 (AB0837), 1374 (AB0912), 1433 (AB1080), 1434 (AB1084)
Arévalo Ruales, K.R., 441 (THU0623)
Arfa, A., 1348 (AB0830), 1362 (AB0876), 1383 (AB0937)
Argibay, A., 595 (FRI0289), 1252 (AB0576), 1400 (AB0988)
Argiento, P., 630 (FRI0378)
Argolini, L.M., 132 (OP0195)
Ariani, A., 1022 (SAT0653)
Arias, I., 1117 (AB0201)
Arias, S., 1132 (AB0239)
Arias de la Rosa, I., 194 (OP0336), 497 (FRI0048), 504 (FRI0069), 1078 (AB0092), 1082 (AB0104)
Arias Saavedra, M., 571 (FRI0229)
Arias-de la Rosa, I., 287 (THU0218), 622 (FRI0360), 648 (FRI0429), 649 (FRI0431), 1091 (AB0127, AB0128)
Arici, S.Z., 616 (FRI0342)
Arıcı, Z.S., 1515 (SAT0730-HPR)
Arida, A., 602 (FRI0306)
Arienzo, F., 888 (SAT0305)
Ariff, B., 316 (THU0299)
Arik, A., 1468 (AB1179)
Arima, M., 531 (FRI0134), 1291 (AB0681)
Arin, G., 1515 (SAT0730-HPR), 1531 (AB1198-HPR)
Aringer, M., 4 (SP0010), 50 (OP0002), 107 (OP0131), 461 (THU0674), 560 (FRI0207), 565 (FRI0217), 844 (SAT0193), 1187 (AB0396), 1200 (AB0430)
Arkachaisri, T., 401 (THU0517)
Arlettaz, L., 626 (FRI0369)
Armağan, B., 1035 (SAT0687), 1412 (AB1023)
Armagan, B., 250 (THU0131), 256 (THU0147), 329 (THU0333), 402 (THU0518), 414 (THU0548), 448 (THU0642), 534 (FRI0140), 637 (FRI0397), 720 (FRI0612), 854 (SAT0216), 1113 (AB0189), 1127 (AB0226), 1175 (AB0363), 1194 (AB0414), 1215 (AB0471), 1256 (AB0586), 1262 (AB0604), 1300 (AB0706)
Arman, N., 1527 (SAT0766-HPR)
Arman, S.N., 1500 (FRI0745-HPR, FRI0746-HPR)
Armas, E., 121 (OP0166), 985 (SAT0552)
Armata, I., 428 (THU0587)
Armbrecht, G., 1172 (AB0355)
Armesto, S., 742 (FRI0666)
Armingeat, T., 335 (THU0349)
Armstrong, A.W., 1330 (AB0783)
Armstrong, R., 933 (SAT0426)
Armuzzi, A., 154 (OP0239)
Arnalich, F., 873 (SAT0264), 1245 (AB0555), 1266 (AB0614), 1289 (AB0676)
Arnalich, V., 740 (FRI0661)
Arnaud, L., 611 (FRI0329), 726 (FRI0626)
Arnesen, S., 1491 (THU0763-HPR)
Arnold, G.E., 151 (OP0234)
Arnoldi, C., 1406 (AB1006)
Aroca, G., 1239 (AB0538)
Aronova, E., 576 (FRI0241)
Arora, R., 491 (FRI0032)
Arora, S., 172 (OP0279-PARE)
Arora, V., 228 (THU0078), 244 (THU0114), 517 (FRI0099)
Arozenius, H., 891 (SAT0314)
Arreba, M.P., 555 (FRI0195)
Arredondo-López, M., 350 (THU0380)
Arrona-Rios, K., 806 (SAT0100), 1075 (AB0083)
Arroyo, C., 1091 (AB0126), 1098 (AB0149)
Arroyo Prado, I., 1450 (AB1128)
Arsenyeva, S., 1389 (AB0955)
Arslan, E.K., 102 (OP0120)
Arslan Taş, D., 902 (SAT0344)
Arslan Tas, D., 921 (SAT0396)
Arteaga, M., 439 (THU0617), 556 (FRI0197), 736 (FRI0651)
Artemeva, A., 560 (FRI0208)
Artieda, M., 178 (OP0294)
Artsymovych, A.G., 1392 (AB0964)
Artukovic, M., 1055 (AB0026)
Arturi, P., 1143 (AB0271)
Arturi, V., 1263 (AB0606)
Artusi, C., 132 (OP0195), 1406 (AB1006)
Arvidsson, S., 1544 (AB1238-HPR)
Arvizu-Rivera, R.I., 253 (THU0140), 534 (FRI0141), 1118 (AB0204), 1119 (AB0205), 1156 (AB0309), 1157 (AB0310)
Asai, K., 1062 (AB0044)
Asai, N., 835 (SAT0174), 1195 (AB0415)
Asai, S., 708 (FRI0579), 1195 (AB0415)
Asako, K., 314 (THU0294), 1248 (AB0566)
Asami, Y., 645 (FRI0419), 1195 (AB0416)
Asano, Y., 88 (OP0087), 138 (OP0207), 202 (THU0006), 1274 (AB0635), 1484 (THU0744-HPR)
Asari, Y., 910 (SAT0369)
Ascherman, D., 1464 (AB1167)
Aşçı, E., 716 (FRI0600)
Ascone, G., 497 (FRI0049)
Aseeva, E.A., 861 (SAT0232), 1226 (AB0500)
Asghari Kaleibar, S., 1347 (AB0827)
Ashbeck, E., 964 (SAT0500)
Ashcroft, J., 201 (THU0004)
Ashour, M.M., 1465 (AB1171)
Ashraf, S., 127 (OP0183)
Ashton, D., 167 (OP0268)
Ashton, J., 1434 (AB1083), 1493 (THU0767-HPR), 1521 (SAT0748-HPR)
Asikainen, J., 784 (SAT0044)
Asimakopoulos, D., 1217 (AB0476)
Asker, A.M., 887 (SAT0304)
Askling, J., 57 (OP0016), 93 (OP0100), 114 (OP0149), 134 (OP0200), 154 (OP0240), 183 (OP0308), 341 (THU0361), 452 (THU0652), 537 (FRI0149), 563 (FRI0213), 567 (FRI0221), 656 (FRI0450), 686 (FRI0518), 1027 (SAT0669)
Aslan, S., 1137 (AB0255)
Aslan Tas, D., 640 (FRI0404)
Aslanidis, S., 542 (FRI0161)
Aslanyan, D., 1379 (AB0926)
Asmar, F., 286 (THU0217)
Asmawidjaja, P., 1088 (AB0118)
Asmawidjaja, P.S., 1058 (AB0033)
Asmussen, H., 1444 (AB1113)

Asmussen Andreasen, R., 246 (THU0118), 533 (FRI0137, FRI0139)
Assassi, S., 87 (OP0086), 624 (FRI0363)
Assmann, G., 1060 (AB0039)
Assudani, D., 553 (FRI0189)
Astbury, C., 1530 (AB1195-HPR)
Astesana, P., 440 (THU0619)
Astorri, D., 603 (FRI0308), 1123 (AB0215)
Astorri, E., 180 (OP0300)
Astrup, A., 196 (OP0340)
Astudillo Andrade, J.J., 571 (FRI0229)
Astudillo-Angel, M., 1225 (AB0499)
Asukai, Y., 599 (FRI0298), 857 (SAT0223)
Atagündüz, P., 644 (FRI0416), 821 (SAT0139), 889 (SAT0310), 910 (SAT0367), 1013 (SAT0633), 1310 (AB0731)
Ataman, S., 1321 (AB0762)
Atan, T., 1428 (AB1066)
Atanasio, S., 805 (SAT0097)
Atanes, A., 75 (OP0059), 405 (THU0526), 420 (THU0567), 718 (FRI0607)
Atencio, P., 128 (OP0186)
Aterido, A., 177 (OP0292), 290 (THU0227), 946 (SAT0458)
Ateş, A., 606 (FRI0315), 1124 (AB0218), 1244 (AB0554)
Ates, A., 1488 (THU0756-HPR), 1523 (SAT0756-HPR), 1538 (AB1221-HPR)
Athanassiades, T., 1076 (AB0085)
Athanassiou, P., 559 (FRI0205)
Atienza, B., 742 (FRI0666)
Atienza-Mateo, B., 1116 (AB0197)
Atiqi, S., 680 (FRI0505)
Atkinson, E., 705 (FRI0572)
Atkinson, J., 1125 (AB0220)
Atreya, R., 655 (FRI0446)
Atsumi, T., 202 (THU0006), 598 (FRI0295), 624 (FRI0364), 1200 (AB0431), 1453 (AB1139)
Atta, A., 176 (OP0290)
Atta, A.M., 1412 (AB1021)
Attipoe, L., 1024 (SAT0659)
Atyasova, E., 324 (THU0319)
Atzeni, F., 52 (OP0006), 263 (THU0164), 311 (THU0284), 343 (THU0366), 464 (THU0681), 564 (FRI0215), 886 (SAT0302), 1008 (SAT0620), 1294 (AB0689)
Aubailly, M., 701 (FRI0561)
Aubert, R., 945 (SAT0455)
Auberval, M., 118 (OP0161)
Aubourg, B., 775 (SAT0018)
Auclair, C., 1477 (THU0724-HPR)
Audisio, M.J., 1417 (AB1037)
Audureau, E., 188 (OP0323)
Auger, I., 523 (FRI0114)
Auger-Sarrazin, A., 1229 (AB0509)
Augustin, M., 1314 (AB0743)
Aung, T., 609 (FRI0321), 1238 (AB0535)
Aure, M.A., 1025 (SAT0662)
Aurichio, R.A.O., 443 (THU0627)
Aurrecoechea, E., 326 (THU0326), 420 (THU0567), 614 (FRI0336), 718 (FRI0607)
Aurrecoechea Aguinaga, E., 1374 (AB0910)
Ausili, M., 1358 (AB0863)
Austad, C., 52 (OP0005)
Austin, L., 547 (FRI0175), 1438 (AB1097)
Avanzini, R., 1468 (AB1178)
Avcin, T., 1389 (AB0957)
Avdeeva, A., 266 (THU0171), 776 (SAT0024)
Avdeeva, A.S., 1128 (AB0230)
Averkieva, J.V., 1351 (AB0841)
Avgoustidis, N., 574 (FRI0236), 577 (FRI0244), 850 (SAT0204), 896 (SAT0330)
Avid, E., 590 (FRI0276)
Avila, G., 1396 (AB0975)
Avila, M., 201 (THU0005), 218 (THU0052)
Avila Pedretti, G., 1455 (AB1142)
Avila-Armengol, H., 1075 (AB0083)
Avila-Zapata, F., 141 (OP0216)
Avina-Zubieta, J.A., 68 (OP0041), 373 (THU0440), 916 (SAT0384)
Avouac, J., 85 (OP0081), 635 (FRI0390), 831 (SAT0163), 915 (SAT0380)
Avrameas, A., 886 (SAT0301), 1229 (AB0509)
Avramut, M.C., 774 (SAT0015)
Avvedimento, E., 64 (OP0031)
Awisat, A., 653 (FRI0441), 926 (SAT0407)
Axelsen, M., 454 (THU0657)
Axelsen, M.B., 732 (FRI0641), 1419 (AB1042)
Ayabe, K., 1203 (AB0439)
Ayadi, I., 809 (SAT0108)
Aydin, S., 290 (THU0228)
Aydin, S.Z., 791 (SAT0063), 932 (SAT0424)
Aydın Özcan, D., 1531 (AB1198-HPR)
Aydoğan, I., 1297 (AB0698)
Aydoğdu, O., 1509 (FRI0770-HPR, FRI0771-HPR), 1519 (SAT0743-HPR), 1528 (SAT0770-HPR), 1533 (AB1205-HPR), 1544 (AB1237-HPR)
Aydoğdu, Y., 1528 (SAT0770-HPR)
Ayedi, F., 1311 (AB0734)
Ayhan, A.S., 720 (FRI0612)
Ayhan, F.F., 439 (THU0618), 1137 (AB0255), 1197 (AB0420)
Aykut, M., 1137 (AB0255)
Ayuzawa, N., 202 (THU0006)
Ayyildiz, M.O., 637 (FRI0396)
Azaryan, A., 870 (SAT0255)
Azeka, E.A.K., 443 (THU0627)
Azevedo, V.F., 135 (OP0202), 676 (FRI0496), 938 (SAT0439)
Azizi, H., 734 (FRI0647)
Azmat, O., 668 (FRI0478)
Azmillah, R., 1512 (SAT0722-HPR)
Aznar Sanchez, J.J., 1121 (AB0211), 1122 (AB0212)
Azoulay, D., 169 (OP0274), 385 (THU0470)
Azpiri-López, J.R., 253 (THU0140), 534 (FRI0141), 1156 (AB0309), 1157 (AB0310)
Azpiri-Lopez, J.R., 1118 (AB0204), 1119 (AB0205)
Azuma, N., 1288 (AB0674)
Azzabi, S., 1251 (AB0574)
Azzolini, V., 270 (THU0181)
Azzouz, D.F., 523 (FRI0114)

Baas, F., 123 (OP0172), 124 (OP0173)
Babaeva, A., 273 (THU0188)
Babaoglu, H., 608 (FRI0320), 1216 (AB0472)
Babbington, M., 1303 (AB0711)
Baboolal, T., 127 (OP0182)
Baboolal, T.G., 480 (FRI0001)
Babushkin, I.E., 273 (THU0187)
Bacalao, E., 1125 (AB0220)
Bacchelli, S., 366 (THU0420)
Baccouche, K., 543 (FRI0165), 926 (SAT0409), 927 (SAT0411)
Bachali, A., 1373 (AB0907)
Bachelez, H., 945 (SAT0455)
Bacherini, D., 411 (THU0540), 711 (FRI0586)
Bachiller, J., 452 (THU0651)
Bachiller-Corral, J., 1272 (AB0630)
Bachmann, S., 1539 (AB1222-HPR)
Bachta, A., 175 (OP0288)
Backhaus, M., 131 (OP0192), 400 (THU0512), 565 (FRI0217), 583 (FRI0256), 1008 (SAT0618), 1425 (AB1058)
Backlund, J., 499 (FRI0055)
Backman, C., 438 (THU0615)
Bacon, P., 316 (THU0298)
Bacon, P.A., 320 (THU0307)
Bacri, J.-L., 152 (OP0236)
Badaracco, A., 1445 (AB1114)
Baddoura, R.M., 1042 (SAT0705)
Bader-Meunier, B., 56 (OP0014)
Badley, E.M., 1035 (SAT0688), 1504 (FRI0757-HPR)
Badr, F.M., 1216 (AB0473)
Badra, B., 1001 (SAT0599)
Badreh, S., 172 (OP0280-PARE)
Bae, E.-K., 646 (FRI0422)
Bae, G.B., 422 (THU0572), 514 (FRI0093), 783 (SAT0042)
Bae, J.H., 1083 (AB0107)
Bae, S.-C., 882 (SAT0290), 1045 (SAT0714)
Bae, Y.J., 548 (FRI0178)
Baecklund, E., 134 (OP0200)
Baek, H.J., 369 (THU0427)
Baek, I.-W., 890 (SAT0311)
Baek, J.M., 482 (FRI0007)
Baenas, D., 670 (FRI0483), 933 (SAT0427)
Baer, A., 67 (OP0040)
Baerlecken, N., 666 (FRI0475)
Baerwald, C., 240 (THU0105), 308 (THU0277), 442 (THU0626)
Baeten, D., 118 (OP0159), 183 (OP0309), 213 (THU0038), 724 (FRI0623)
Baeten, D.L., 662 (FRI0464), 666 (FRI0475), 680 (FRI0505), 949 (SAT0464), 1086 (AB0114)
Baffie, C., 843 (SAT0189), 1186 (AB0395)
Baganz, L., 530 (FRI0130), 801 (SAT0087)
Bagcivan, G., 1297 (AB0698)
Bager, C., 1114 (AB0192)
Bagga, H., 429 (THU0591)
Baghel, S.S., 1506 (FRI0762-HPR), 1540 (AB1226-HPR)
Bagriy, M., 328 (THU0332), 616 (FRI0341)
Bahadur, S., 938 (SAT0438)
Baharuddin, H., 256 (THU0146), 596 (FRI0291)
Bahgat, D.M.R., 1237 (AB0533)
Bahha, J., 1136 (AB0252), 1163 (AB0327, AB0328), 1168 (AB0343)
Bahiri, R., 1136 (AB0252), 1163 (AB0327, AB0328), 1168 (AB0343), 1358 (AB0862), 1365 (AB0883, AB0884, AB0885), 1418 (AB1041)
Bahrami, M.H., 700 (FRI0557)
Bai, R., 1254 (AB0580)
Bai-Papoudou, A., 1243 (AB0551)
Baildem, E., 1390 (AB0958)
Bailón, L., 1245 (AB0555), 1266 (AB0614)
Bajema, I., 871 (SAT0258)
Bajnok, A., 780 (SAT0034)
Baker, J., 174 (OP0284), 240 (THU0104)
Baker, J.F., 732 (FRI0641)
Baker, M.C., 774 (SAT0017)
Bakırcı Üreyen, S., 327 (THU0329)
Bakker, J.A., 181 (OP0302), 903 (SAT0350)
Bakland, G., 647 (FRI0426), 1029 (SAT0673)
Baklouti, S., 1311 (AB0734), 1377 (AB0921)
Bakry, R., 406 (THU0529)
Bal, A., 733 (FRI0643)
Bala, V., 1520 (SAT0746-HPR)
Balan, M., 667 (FRI0477)
Balandraud, N., 523 (FRI0114), 811 (SAT0112)
Balanescu, A., 304 (THU0266), 416 (THU0555), 423 (THU0574), 435 (THU0606), 876 (SAT0271), 881 (SAT0288), 1025 (SAT0664), 1208 (AB0450), 1221 (AB0487), 1278 (AB0646, AB0647), 1333 (AB0790), 1428 (AB1068), 1460 (AB1158)
Balarini, G.M., 1102 (AB0160)
Balatska, N., 1177 (AB0369), 1469 (AB1182)
Balazova, P., 1552 (PARE0001), 1557 (PARE0015)
Balbi, G., 299 (THU0253), 312 (THU0286), 887 (SAT0303)
Balbir-Gurman, A., 333 (THU0343), 355 (THU0392), 910 (SAT0368), 1462 (AB1163)
Balcazar-Vargas, M.F., 311 (THU0283)
Balcıoğlu, H., 387 (THU0478)
Balcune, I., 245 (THU0116)
Baldi, C., 92 (OP0099)
Baldini, C., 67 (OP0040), 305 (THU0268), 311 (THU0284), 320 (THU0308), 446 (THU0636), 464 (THU0681), 584 (FRI0260), 589 (FRI0272), 617 (FRI0344), 875 (SAT0268), 886 (SAT0302)
Baldini, M., 328 (THU0331)
Baldisera, E., 328 (THU0331)
Baldissera, E., 437 (THU0611), 610 (FRI0325), 1439 (AB1099)
Baldovino, S., 761 (FRI0716), 1410 (AB1014)
Balduzzi, S., 1257 (AB0589)
Baleeiro, C., 176 (OP0290), 1412 (AB1021)
Balestri, F., 731 (FRI0640)
Bálint, B.L., 1094 (AB0137)
Bálint, P.V., 1428 (AB1067)
Balint, P.V., 175 (OP0288), 742 (FRI0668)
Baliu, C., 1434 (AB1085)
Balkarli, A., 609 (FRI0322)
Balkarlı, A., 327 (THU0329)
Ballak, D., 90 (OP0092)
Ballard, K., 1057 (AB0029)
Ballegaard, C., 96 (OP0106)

Ballesteros, G., 266 (THU0172), 529 (FRI0127), 852 (SAT0210), 1441 (AB1103)
Ballesteros, J.G., 1132 (AB0239)
Ballesteros Muñoz, J.G., 752 (FRI0694)
Ballina-García, F.J., 803 (SAT0093), 1079 (AB0093)
Balog, A., 780 (SAT0034), 1105 (AB0167)
Balsa, A., 357 (THU0396), 416 (THU0553), 452 (THU0651), 456 (THU0661), 501 (FRI0062), 510 (FRI0086), 551 (FRI0186), 554 (FRI0192), 555 (FRI0194, FRI0195), 559 (FRI0204), 822 (SAT0141), 833 (SAT0168), 1014 (SAT0634), 1116 (AB0198), 1179 (AB0374, AB0375), 1293 (AB0686), 1294 (AB0687), 1303 (AB0713), 1304 (AB0714)
Balsa Criado, A., 824 (SAT0145)
Balueva, O., 1421 (AB1048)
Balzan, D., 439 (THU0616), 1435 (AB1088)
Balzaretti, G., 123 (OP0172)
Bambara, L.M., 909 (SAT0366)
Bamberger, S., 1060 (AB0039)
Bamias, G., 1088 (AB0117)
Bananis, E., 272 (THU0186)
Bandinelli, F., 646 (FRI0423)
Bandyopadhyay, S., 1300 (AB0705)
Banefelt, J., 72 (OP0050)
Banerjee, S., 75 (OP0058), 93 (OP0101), 145 (OP0223), 174 (OP0284), 240 (THU0104), 687 (FRI0520), 837 (SAT0177), 951 (SAT0468)
Bang, H., 242 (THU0111), 528 (FRI0125), 848 (SAT0201)
Baniaamam, M., 1087 (AB0116)
Baniandres Rodriguez, O., 1414 (AB1029)
Bankova, H., 1558 (PARE0018)
Bannert, B., 92 (OP0099), 240 (THU0105)
Bannwarth, B., 710 (FRI0584)
Bañol-Giraldo, A.M., 514 (FRI0094)
Bansback, N., 443 (THU0629), 453 (THU0653)
Bantleon, F.I., 1463 (AB1166)
Banville, F., 1520 (SAT0745-HPR)
Banyai, M., 626 (FRI0369)
Banzo, J.I., 1255 (AB0583, AB0584)
Baquero, J.L., 520 (FRI0106), 1472 (AB1192)
Bar-On, Y., 169 (OP0273)
Bara, C., 626 (FRI0368)
Barabanova, O., 413 (THU0547)
Baraf, H.S., 1360 (AB0867)
Barahona-Correa, J.E., 1250 (AB0570)
Barajas-Ochoa, A., 1452 (AB1136)
Baraka, E., 781 (SAT0038)
Barakat, A.F., 1174 (AB0360)
Barakat, E., 1526 (SAT0764-HPR)
Baraliakos, X., 60 (OP0023), 100 (OP0114), 130 (OP0189), 337 (THU0352), 340 (THU0359), 356 (THU0394), 357 (THU0397), 358 (THU0398), 663 (FRI0466), 666 (FRI0474), 667 (FRI0476), 669 (FRI0480), 934 (SAT0429)
Baranauskaite, A., 367 (THU0423), 1306 (AB0719)
Baranda-Cándido, L., 774 (SAT0016)
Baranov, A., 273 (THU0188)
Baranov, E.V., 1128 (AB0228)
Baras, A., 570 (FRI0228), 838 (SAT0179)
Barbadillo, C., 633 (FRI0385), 908 (SAT0363), 1270 (AB0625)
Barbadillo Mateos, C., 1399 (AB0986)
Barbarash, O., 693 (FRI0536)
Barbarash, O.L., 1346 (AB0823, AB0824)
Barbarossa, S., 1154 (AB0301)
Barbarroja, N., 194 (OP0336), 287 (THU0218), 492 (FRI0035), 497 (FRI0048), 504 (FRI0069), 622 (FRI0360), 648 (FRI0429), 649 (FRI0431), 1078 (AB0092), 1082 (AB0104), 1091 (AB0127, AB0128)
Barbati, C., 463 (THU0678), 489 (FRI0027), 490 (FRI0028), 860 (SAT0228), 1093 (AB0132), 1094 (AB0135, AB0136), 1099 (AB0150), 1465 (AB1170)
Barber, B., 1396 (AB0976)
Barber, X., 1296 (AB0693), 1351 (AB0840)
Barber-Vallés, X., 1016 (SAT0638)
Barbero, A., 1069 (AB0064)
Barbero, C., 1476 (THU0720-HPR)
Barbey, C., 857 (SAT0222), 862 (SAT0235)
Barbic, S.P., 818 (SAT0132)
Barbieri, F., 728 (FRI0632)
Barbosa, M., 1177 (AB0368), 1466 (AB1172)
Barbosa-Bouças, S., 1508 (FRI0767-HPR)
Barbosa-Cobos, R.E., 1133 (AB0242)
Barcelos, A., 1314 (AB0741), 1461 (AB1161)
Barcelos, F., 464 (THU0679), 929 (SAT0418), 1051 (AB0013), 1094 (AB0134), 1163 (AB0329), 1464 (AB1168)
Barchiesi, S., 906 (SAT0356)
Barchuk, W., 142 (OP0218)
Barclay, C., 167 (OP0268)
Barclay, M., 1415 (AB1031)
Barczyk-Kahlert, K., 223 (THU0067)
Bardelli, M., 92 (OP0099), 1010 (SAT0625), 1318 (AB0753)
Bardin, T., 258 (THU0152), 359 (THU0401), 367 (THU0424), 382 (THU0461, THU0463), 811 (SAT0112), 1371 (AB0900)
Bårdsen, K., 184 (OP0312)
Barile Fabris, L., 1211 (AB0460)
Barington, T., 745 (FRI0675), 1024 (SAT0660)
Barini, A., 394 (THU0499)
Barinov, A., 169 (OP0272)
Barker, J.N., 201 (THU0004)
Barkovskaya, M., 206 (THU0019)
Barmaki, M., 388 (THU0480)
Barmakoudi, M., 1279 (AB0648)
Barnabe, C., 231 (THU0085)
Barnes, P.W., 1315 (AB0744)
Barnetche, T., 343 (THU0364), 701 (FRI0561), 804 (SAT0094), 866 (SAT0246), 1299 (AB0703)
Barnewitz, D., 485 (FRI0015)
Barnidge, D., 187 (OP0320)
Baron, D., 388 (THU0480)
Baron, G., 170 (LB0001)
Baron, M., 202 (THU0006), 770 (SAT0006)
Barone, F., 67 (OP0040), 302 (THU0259)
Barone, M., 1135 (AB0250)
Barra, G., 621 (FRI0355)
Barral, C., 58 (OP0018)
Barrasa, J.I., 504 (FRI0071)
Barratt, P., 1508 (FRI0767-HPR)
Barreira, B., 892 (SAT0316)
Barreira, J.C., 440 (THU0619), 1534 (AB1206-HPR)
Barrera, M.-J., 1102 (AB0158)
Barrera-Vargas, A., 586 (FRI0264)
Barrick, T., 976 (SAT0530)
Barrientos, S., 740 (FRI0663), 1420 (AB1044)
Barrio Nogal, L., 908 (SAT0363)
Barrios, B., 440 (THU0619)
Barrios, Y., 1037 (SAT0691), 1115 (AB0195)
Barroga, C., 984 (SAT0549)
Barros, C., 474 (THU0706)
Barros, R., 746 (FRI0678)
Barroso, N., 1526 (SAT0765-HPR)
Barsotti, S., 617 (FRI0344), 1272 (AB0630)
Bart, G., 90 (OP0093)
Bartels, E.M., 196 (OP0340), 332 (THU0340), 1332 (AB0786), 1412 (AB1020)
Bartels, L., 1020 (SAT0649)
Bartholdy, C., 161 (OP0254-HPR), 1481 (THU0734-HPR)
Bartlett, S., 231 (THU0085), 781 (SAT0039)
Bartlett, S.J., 470 (THU0695), 545 (FRI0171), 815 (SAT0122), 818 (SAT0132), 1176 (AB0366)
Bartoloni, E., 305 (THU0268), 311 (THU0284), 886 (SAT0302), 1113 (AB0191)
Bartoloni Bocci, E., 56 (OP0015), 1272 (AB0630)
Bartoloni-Bocci, E., 437 (THU0611), 1209 (AB0456), 1439 (AB1099)
Bartolovic, D., 640 (FRI0405)
Barton, A., 90 (OP0094), 98 (OP0110), 146 (OP0225), 179 (OP0298), 200 (THU0001, THU0002, THU0003), 201 (THU0004), 551 (FRI0185), 765 (FRI0724), 1087 (AB0115)
Bartosiewicz, I., 496 (FRI0045)
Barut, K., 394 (THU0498), 1402 (AB0994)
Bas, M., 303 (THU0262)
Baş Aslan, U., 1484 (THU0745-HPR)
Bas Aslan, U., 1514 (SAT0727-HPR)
Başak, K., 1232 (AB0520)
Basakci Calik, B., 1514 (SAT0727-HPR)
Basar, S., 1004 (SAT0608)
Basaric, M.M., 1020 (SAT0648)
Bashi, T., 502 (FRI0065)
Bashlakova, N.A., 1063 (AB0048)
Basoski, N., 1497 (FRI0739-HPR)
Bass, D., 861 (SAT0231)
Bassi, M., 493 (FRI0038)
Bassi Andreasi, R., 207 (THU0022)
Bassiouni, H., 986 (SAT0553)
Basta, F., 304 (THU0267), 876 (SAT0273)
Bastiaansen-Jenniskens, Y., 769 (SAT0001)
Bastida, C., 840 (SAT0184)
Basu, M., 491 (FRI0032)
Basualto-Alarcón, C., 1108 (AB0176)
Bathon, J.M., 1125 (AB0220)
Batista, F., 293 (THU0236)
Batkaev, E., 1334 (AB0791)
Batkaeva, N., 1334 (AB0791)
Batlle, E., 439 (THU0617)
Battagliotti, C., 440 (THU0619), 1389 (AB0957)
Batten, R.L., 1470 (AB1186)
Batteux, F., 182 (OP0307)
Batticciotto, A., 1008 (SAT0620), 1184 (AB0389), 1194 (AB0413), 1376 (AB0917), 1380 (AB0928)
Batu, E.D., 329 (THU0333), 414 (THU0548), 616 (FRI0342), 1515 (SAT0730-HPR)
Batuca, J.R., 293 (THU0236), 1053 (AB0019)
Batún Garrido, J.A.D.J., 1132 (AB0240, AB0241)
Baucells, A., 914 (SAT0379)
Baudouin, C., 152 (OP0237)
Bauer, A., 219 (THU0053)
Bauer, L., 60 (OP0023), 1316 (AB0747)
Bäuerle, T., 247 (THU0122)
Baumberger, H., 929 (SAT0417)
Baumgartner, S., 166 (OP0266), 380 (THU0457), 763 (FRI0720)
Bautista, W., 252 (THU0137)
Bautista Aguilar, L., 258 (THU0151), 700 (FRI0555), 975 (SAT0527)
Bautista-Aguilar, L., 942 (SAT0447), 1268 (AB0619)
Bautista-Molano, W., 1117 (AB0201)
Bax, D.E., 431 (THU0596)
Bax, N.D.S., 431 (THU0596)
Bay Nielsen, H., 1114 (AB0192)
Bay-Jensen, A.-C., 66 (OP0036), 94 (OP0103), 480 (FRI0003), 625 (FRI0365), 892 (SAT0317), 986 (SAT0554), 1068 (AB0062), 1109 (AB0179, AB0180)
Bay-Jensen, A.-C.S., 916 (SAT0383)
Bay-Jensen, A.C., 120 (OP0165), 966 (SAT0504), 1114 (AB0192)
Baydar, D.E., 720 (FRI0612)
Bayındır, Ö., 327 (THU0329)
Baykal, M., 1035 (SAT0687), 1412 (AB1023)
Bayrakci Tunay, V., 1468 (AB1179)
Bayrakcı Tunay, V., 1485 (THU0747-HPR)
Bayraktar, D., 53 (OP0009-HPR), 1522 (SAT0751-HPR)
Bazilio, A.P., 443 (THU0627)
Bazin, D., 1364 (AB0882)
Bazzan, M., 761 (FRI0716), 1410 (AB1014)
Bazzani, C., 564 (FRI0215)
Bazzani, P.V., 693 (FRI0535)
Beak, H.J., 1185 (AB0392)
Bearne, L., 1527 (SAT0767-HPR)
Beaton, D., 467 (THU0689)
Beaton, D.E., 471 (THU0698)
Beatrice, B., 549 (FRI0180)
Beattie, S., 511 (FRI0089), 527 (FRI0124)
Beaudreuil, J., 170 (LB0001)
Beaumel, A., 1385 (AB0945)
Beaumont, J., 448 (THU0643), 449 (THU0645)
Beauvais, C., 78 (OP0064), 258 (THU0152), 265 (THU0169), 271 (THU0184), 425 (THU0580), 427 (THU0586), 428 (THU0588, THU0589), 811 (SAT0112), 1299 (AB0702), 1470 (AB1185)
Becciolini, A., 343 (THU0365), 829 (SAT0158)
Bécède, M., 520 (FRI0108)
Becerra, E., 495 (FRI0042)
Becerra, S., 119 (OP0162-PARE)
Becerril-Mendoza, L.T., 1133 (AB0242), 1330 (AB0782)
Bechman, K., 1030 (SAT0676)

Beck, M., 400 (THU0512)
Becker, I., 74 (OP0057), 132 (OP0196)
Becker, M., 1286 (AB0669)
Becker, M.A., 375 (THU0444)
Beckmann, D., 486 (FRI0018)
Bečvář, R., 1285 (AB0665)
Becvar, R., 638 (FRI0399), 906 (SAT0358), 1280 (AB0653), 1287 (AB0671)
Bedina, S., 1361 (AB0872)
Bedoya, E., 440 (THU0619)
Beek, K., 347 (THU0374)
Beerends, G.A., 1279 (AB0650)
Beermann, M., 173 (OP0282-PARE)
Beermann, S., 489 (FRI0025), 493 (FRI0037)
Beers-Tas, M.V., 523 (FRI0113)
Beevor, C., 1490 (THU0760-HPR)
Beggio, M., 1111 (AB0184)
Beglaryan, A., 1398 (AB0983)
Begum, J., 199 (OP0347-HPR), 1484 (THU0746-HPR)
Begum, N., 1354 (AB0851)
Béhé, M., 621 (FRI0358)
Behlouli, H., 825 (SAT0149)
Behrens, F., 135 (OP0202), 565 (FRI0217), 1319 (AB0756), 1322 (AB0763)
Behrens, J., 1322 (AB0763)
Bei, D., 859 (SAT0226)
Beiki, H., 1338 (AB0803)
Bejerano-Herrería, M., 936 (SAT0435)
Bejia, I., 1353 (AB0848, AB0849), 1362 (AB0876), 1383 (AB0937)
Bekker, C.P., 182 (OP0306)
Bel Hadj, N., 1348 (AB0831, AB0832, AB0833), 1349 (AB0834)
Belai Beyene, N., 270 (THU0181)
Belakova, G., 1449 (AB1126)
Belendiuk, K.A., 593 (FRI0285)
Belenguer, R., 761 (FRI0715), 1456 (AB1146, AB1147)
Belghali, S., 347 (THU0373), 543 (FRI0165), 927 (SAT0411)
Belhadj, L., 1251 (AB0574)
Belhasan, B., 1311 (AB0734)
Belhassen, M., 434 (THU0605), 754 (FRI0699), 1033 (SAT0684), 1034 (SAT0685)
Belini, M.A., 1202 (AB0434)
Belinska, A., 1469 (AB1182)
Belkacemi, M., 231 (THU0084)
Belkhir, R., 51 (OP0004), 965 (SAT0501)
Belkina, G., 1115 (AB0196)
Bellando Randone, S., 631 (FRI0380)
Bellando-Randone, S., 623 (FRI0362), 628 (FRI0372), 633 (FRI0384), 915 (SAT0380), 1269 (AB0622), 1270 (AB0623)
Bellavia, S., 1013 (SAT0631)
Beller, C., 754 (FRI0697)
Bellier, B., 776 (SAT0023)
Bellis, E., 236 (THU0095)
Bellis, K., 518 (FRI0101), 1031 (SAT0678), 1155 (AB0306)
Bello, I., 900 (SAT0339)
Bello, J., 266 (THU0172), 529 (FRI0127), 852 (SAT0210), 1441 (AB1103)
Bello, N., 173 (OP0283), 233 (THU0088)
Bello-Gualtero, J., 252 (THU0137)
Bello-Gualtero, J.M., 1117 (AB0201)
Bellocchi, C., 624 (FRI0363)
Bellucci, E., 633 (FRI0384)
Belluzzi, E., 216 (THU0047)
Belmonte, A., 1174 (AB0361), 1175 (AB0362), 1443 (AB1109)
Belmonte, M.Á., 955 (SAT0475), 1333 (AB0788)
Belmonte-Serrano, M.A., 1472 (AB1191)
Belot, A., 432 (THU0599)
Belov, B., 464 (THU0680), 720 (FRI0611)
Belov, B.S., 251 (THU0132), 1226 (AB0500)
Beltrán, E., 307 (THU0273), 326 (THU0326), 420 (THU0567), 718 (FRI0607), 1166 (AB0337)
Beltran, E., 1181 (AB0381)
Beltran, L.M., 1004 (SAT0609), 1413 (AB1024)
Bély, M., 1104 (AB0164), 1149 (AB0290), 1252 (AB0577), 1283 (AB0660), 1312 (AB0737), 1328 (AB0777)
Belyaeva, I., 611 (FRI0328)
Belz, D., 1106 (AB0169)
Belzunegui, J., 826 (SAT0150)
Ben Abdelghani, K., 1306 (AB0720), 1371 (AB0902), 1394 (AB0969), 1417 (AB1038)
Ben Ahmed, I., 1397 (AB0980)
Ben Alaya, T., 1353 (AB0848, AB0849)
Ben Allouch, F., 1478 (THU0727-HPR)
Ben Chaaben, I., 885 (SAT0298)
Ben Ghorbel, I., 313 (THU0291), 596 (FRI0290), 599 (FRI0300), 889 (SAT0308), 1238 (AB0536), 1239 (AB0537)
Ben Hammouda, S., 1000 (SAT0598), 1169 (AB0346, AB0347), 1170 (AB0348)
Ben Hassine, L., 1251 (AB0574)
Ben Khelifa, M., 1353 (AB0848, AB0849)
Ben Mami, N., 1346 (AB0826)
Ben Nasr, M., 1258 (AB0592)
Ben Nejma, H., 1348 (AB0832)
Ben Ouhiba, A., 347 (THU0373)
Ben Salem, T., 313 (THU0291), 599 (FRI0300), 889 (SAT0308), 1238 (AB0536), 1239 (AB0537)
Ben Tekaya, A., 1073 (AB0077)
Ben-Ami Shor, D., 169 (OP0273)
Ben-Chetrit, E., 77 (OP0063)
Ben-Shlomo, N., 703 (FRI0564)
Benabdoune, H.A., 221 (THU0061)
Benaglio, F., 237 (THU0099), 787 (SAT0053), 790 (SAT0060), 1123 (AB0214)
Benavent, D., 1014 (SAT0634)
Benavent, M., 312 (THU0287)
Benavides-González, M.A., 253 (THU0140), 534 (FRI0141)
Benaziez, R., 1192 (AB0409)
Bencheikh, S., 1009 (SAT0623), 1405 (AB1001, AB1002)
Benchimol, R., 170 (LB0001)
Bendahan, D., 744 (FRI0671)
Bender, T.T.A., 423 (THU0576)
Benderdour, M., 126 (OP0181), 221 (THU0061), 483 (FRI0009)
Benderitter, F., 195 (OP0339)
Bendstrup, E., 546 (FRI0174)
Bene, F., 238 (THU0100), 511 (FRI0088)
Benedetti, M.G., 111 (OP0141-HPR)
Benešová, M., 86 (OP0083)
Benfaremo, D., 1189 (AB0400)
Bengana, B., 1359 (AB0866)
Bengtsson, A., 302 (THU0260), 861 (SAT0233)
Bengtsson, C., 248 (THU0124), 537 (FRI0149), 1512 (SAT0722-HPR)
Bengtsson, K., 134 (OP0200), 154 (OP0240)
Benhamou, Y., 108 (OP0134)
Benichou, O., 679 (FRI0502), 941 (SAT0446), 1334 (AB0793)
Benini, C., 363 (THU0412), 671 (FRI0485), 940 (SAT0445), 1314 (AB0742)
Benitez, A., 440 (THU0619)
Benito, P., 1181 (AB0381)
Benito-Miguel, M., 501 (FRI0062)
Benkhalifa, S., 1330 (AB0781)
Bennejma, H., 1348 (AB0833)
Bennett, L.A., 55 (OP0012-PARE)
Bennett, S., 933 (SAT0426), 1180 (AB0377)
Bennike, T.B., 775 (SAT0020)
Bennink, M.B., 493 (FRI0037)
Bensaber, O., 1467 (AB1177)
Benseler, S., 398 (THU0509)
Bensen, W., 656 (FRI0449)
Benson, H.A., 960 (SAT0487)
Bentin, J., 736 (FRI0650)
Bentivenga, C., 366 (THU0420)
Bentow, C., 911 (SAT0372), 1025 (SAT0662)
Benucci, M., 646 (FRI0423), 829 (SAT0158), 1272 (AB0630)
Benveniste, O., 912 (SAT0374)
Benvenuto, R., 792 (SAT0066)
Benz, T., 475 (THU0708), 478 (THU0718), 479 (THU0719)
Benzaquen, N.R., 313 (THU0289)
Béra-Louville, A., 170 (LB0001)
Bera-Louville, A., 815 (SAT0123)
Berardi, G., 197 (OP0343)
Berardicurti, O., 721 (FRI0613), 880 (SAT0284), 891 (SAT0313)
Berastegui, C., 900 (SAT0339)
Berber, E., 95 (OP0105), 579 (FRI0248)
Berberoğlu, U., 1531 (AB1198-HPR)
Berdal, G., 161 (OP0255-HPR)
Bereczki, D., 1027 (SAT0668)
Berenbaum, F., 38 (SP0157), 122 (OP0168), 171 (OP0278-PARE), 334 (THU0346), 339 (THU0356, THU0357), 388 (THU0482), 389 (THU0483), 461 (THU0675), 665 (FRI0472), 965 (SAT0501), 1050 (AB0012), 1072 (AB0073), 1296 (AB0694), 1299 (AB0702)
Berendsen, D., 240 (THU0106)
Beresford, M.W., 9 (SP0034)
Bereswill, M., 405 (THU0525)
Beretta, L., 1047 (AB0003), 1108 (AB0177), 1109 (AB0178)
Berg, I.J., 156 (OP0244), 666 (FRI0475)
Berg, J.K., 371 (THU0433)
Bergamini, A., 484 (FRI0012)
Bergaoui, N., 1348 (AB0830), 1353 (AB0848, AB0849), 1362 (AB0876), 1383 (AB0937)
Bergé, E., 965 (SAT0501)
Berge, T., 1546 (AB1244-HPR)
Bergeal, E., 1191 (AB0406)
Bergenheim, A., 1487 (THU0754-HPR), 1503 (FRI0753-HPR), 1538 (AB1219-HPR)
Berger, F., 718 (FRI0606)
Berghea, F., 304 (THU0266), 881 (SAT0288), 1026 (SAT0665), 1221 (AB0487), 1278 (AB0646, AB0647), 1460 (AB1158), 1540 (AB1224-HPR)
Berglind, A., 50 (OP0001), 870 (SAT0254)
Bergman, G.J., 831 (SAT0161)
Bergman, M., 233 (THU0089)
Bergman, M.J., 1129 (AB0232), 1130 (AB0233)
Bergman, S., 651 (FRI0436), 922 (SAT0397), 1495 (FRI0733-HPR), 1515 (SAT0731-HPR), 1523 (SAT0755-HPR), 1531 (AB1199-HPR), 1544 (AB1238-HPR)
Bergmann, C., 892 (SAT0318)
Bergner, R., 597 (FRI0294), 721 (FRI0614)
Bergquist, M., 779 (SAT0031)
Bergsmark, K., 1029 (SAT0673)
Bergsten, U., 360 (THU0404), 1512 (SAT0724-HPR), 1513 (SAT0725-HPR)
Bergstra, S.A., 146 (OP0224), 160 (OP0252), 567 (FRI0221), 793 (SAT0067), 907 (SAT0359), 976 (SAT0529)
Bergström, B., 117 (OP0156)
Bergström, M., 1518 (SAT0740-HPR)
Berjawi, A., 1400 (AB0989)
Berkhout, L., 758 (FRI0707)
Berking, C., 718 (FRI0606)
Berlin, A., 1011 (SAT0628)
Berman, A., 670 (FRI0483)
Berman, H., 670 (FRI0483)
Berman, J., 467 (THU0687)
Berman, M., 1328 (AB0776)
Bermúdez, A., 685 (FRI0515)
Bermudez, C.C., 878 (SAT0280)
Bermudez Torrente, A., 1041 (SAT0704)
Bermudez-Bermejo, P., 597 (FRI0292), 878 (SAT0278)
Berna, T., 1172 (AB0353)
Bernabeu, P., 1472 (AB1191)
Bernabeu Vicens, E., 1349 (AB0837)
Bernal, J., 843 (SAT0191), 1107 (AB0173)
Bernal, J.A., 374 (THU0441), 557 (FRI0199)
Bernard, M., 744 (FRI0671)
Bernard Medina, A., 1276 (AB0641)
Bernardes, M., 245 (THU0116), 468 (THU0690, THU0691), 852 (SAT0211), 1142 (AB0268), 1177 (AB0368), 1466 (AB1172)
Bernardi, L., 1123 (AB0215)
Bernardin, G., 991 (SAT0569)
Bernardino, V.R., 1429 (AB1070)
Bernardo, A., 468 (THU0690, THU0691), 852 (SAT0211), 1142 (AB0268), 1177 (AB0368), 1466 (AB1172)
Bernardo, J., 400 (THU0513), 1096 (AB0144)
Bernardo, P., 633 (FRI0384)
Bernardos, I., 691 (FRI0530), 694 (FRI0539)

Bernasconi, A., 403 (THU0521)
Bernasconi, C., 847 (SAT0199)
Bernatsky, S., 749 (FRI0684), 825 (SAT0149)
Bernelot Moens, H., 147 (OP0227), 240 (THU0106), 274 (THU0190)
Berner, C., 1154 (AB0302)
Bernhard, J., 130 (OP0189), 335 (THU0347)
Bernini, F., 1309 (AB0730)
Bernini, S.K., 1064 (AB0050)
Berntzen, B., 1553 (PARE0004)
Beron, A.M., 729 (FRI0635), 991 (SAT0568), 1217 (AB0478)
Beron, J., 626 (FRI0369)
Berrian, J., 817 (SAT0129)
Berrocal, V., 912 (SAT0373)
Berta, A., 1273 (AB0632)
Bertalan, Z., 1423 (AB1053)
Berthelot, J.-M., 549 (FRI0180)
Berthelot, J.M., 428 (THU0588, THU0589)
Berti, A., 604 (FRI0310), 605 (FRI0314), 614 (FRI0337), 1257 (AB0589)
Bertin, P., 388 (THU0480), 815 (SAT0123), 1299 (AB0701)
Bertolazzi, C., 739 (FRI0660), 1006 (SAT0613)
Bertoldo, E., 899 (SAT0336)
Bertoldo, F., 693 (FRI0535), 1200 (AB0429)
Bertoli, A., 440 (THU0619)
Bertoli, A.M., 1417 (AB1037)
Bértolo, M., 1160 (AB0320)
Bertouch, J.V., 447 (THU0639)
Bertrand, J., 14 (SP0057)
Bertsias, G., 192 (OP0332), 297 (THU0246), 300 (THU0254), 574 (FRI0236), 577 (FRI0244), 850 (SAT0204), 896 (SAT0330), 1204 (AB0442)
Bertulis, J., 642 (FRI0411)
Berwanger, D.D., 1438 (AB1096)
Berzi, A., 1184 (AB0389)
Bes, C., 609 (FRI0322), 716 (FRI0600), 1170 (AB0350), 1360 (AB0868)
Besselink, N., 741 (FRI0664), 978 (SAT0536), 1020 (SAT0649)
Besselink, N.J., 1344 (AB0818)
Bessette, L., 58 (OP0019), 349 (THU0378), 571 (FRI0230), 656 (FRI0449), 845 (SAT0195), 1188 (AB0397), 1303 (AB0712)
Bessonova, I.N., 1392 (AB0963)
Best, J., 846 (SAT0196), 1191 (AB0407)
Best, J.H., 264 (THU0167)
Betancourt, J., 1386 (AB0948)
Betenstehl, N., 195 (OP0338)
Bethencourt, J.J., 1390 (AB0959)
Bethencourt Baute, J.J., 955 (SAT0475), 1333 (AB0788)
Betteridge, Z., 912 (SAT0374)
Betts, K.A., 1487 (THU0753-HPR)
Beukenhorst, A., 1446 (AB1118)
Bevilacqua, J., 1108 (AB0176)
Beyaert, R., 125 (OP0176)
Beylot-Barry, M., 710 (FRI0584)
Bezerra, M.C., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Bhadu, D., 1006 (SAT0614)
Bhama, M., 989 (SAT0563)
Bharadwaj, A., 271 (THU0183)
Bharucha, K., 396 (THU0503)
Bhat, H.R., 1072 (AB0075)
Bhatnagar, A., 994 (SAT0577)
Bhattoa, H.P., 697 (FRI0547), 1027 (SAT0668)
Bhosekar, V., 688 (FRI0521), 1293 (AB0685)
Bi, X., 1085 (AB0111)
Bianchi, G., 270 (THU0181)
Bianchi, M., 621 (FRI0357)
Bianchini, E., 617 (FRI0344)
Biancone, L., 667 (FRI0477)
Biard, L., 108 (OP0134)
Biasi, D., 1388 (AB0953)
Biavasco, R., 126 (OP0179)
Bibas, M., 1557 (PARE0017)
Bica, B., 399 (THU0511), 875 (SAT0270)
Bıcakcı, F., 1514 (SAT0727-HPR)
Bielinska, A., 1470 (AB1184)
Bienvenu, B., 617 (FRI0345), 1256 (AB0588)
Bierma-Zeinstra, S., 961 (SAT0492), 973 (SAT0523), 1343 (AB0817)
Bierma-Zeinstra, S.M., 973 (SAT0522)
Bierman, W.F., 1007 (SAT0617)
Biersack, M., 253 (THU0139)
Biggers, S.R., 363 (THU0413), 1359 (AB0865)
Biggioggero, M., 343 (THU0365), 564 (FRI0215), 829 (SAT0158)
Bighea, A.C., 379 (THU0454), 478 (THU0717)
Bihlet, A., 120 (OP0165)
Bijlsma, H.W., 3 (SP0007)
Bijlsma, J., 478 (THU0716), 973 (SAT0523)
Bijlsma, J.W., 21 (SP0083), 41 (SP0169), 177 (OP0293), 855 (SAT0218)
Bijlsma, J.W.J., 968 (SAT0508)
Biko, D.M., 469 (THU0693), 471 (THU0697)
Bilbao-González, A., 1001 (SAT0600)
Bilberg, A., 674 (FRI0492)
Bilge, U., 387 (THU0478)
Bilgen, S.A., 414 (THU0548), 616 (FRI0342), 720 (FRI0612), 1113 (AB0189)
Bilgici, A., 1172 (AB0353)
Bilgin, E., 414 (THU0548), 616 (FRI0342), 1215 (AB0471), 1300 (AB0706)
Bilgin, M., 254 (THU0141)
Bilginer, Y., 1515 (SAT0730-HPR)
Biliavska, I.V., 399 (THU0510)
Billet, S., 901 (SAT0342)
Bindels, P., 961 (SAT0492)
Bindoli, S., 1066 (AB0055)
Bindroo, M., 1247 (AB0561, AB0562)
Bindroo, M.A., 1253 (AB0579)
Bineta, L., 182 (OP0307)
Bingham, C.O., 1176 (AB0366)
Bingham III, C., 1521 (SAT0750-HPR)
Bingham III, C.O., 460 (THU0672), 545 (FRI0171)
Biniecka, M., 221 (THU0059), 487 (FRI0020), 646 (FRI0421)
Binkley, N., 690 (FRI0525), 739 (FRI0658)
Biočina Lukenda, D., 1283 (AB0661)
Birbara, C.A., 672 (FRI0487), 942 (SAT0448)
Birchwood, C., 95 (OP0105), 567 (FRI0222), 581 (FRI0253)
Bird, P., 727 (FRI0629), 1010 (SAT0624)
Birkelund, S., 775 (SAT0020)
Birlik, A.M., 477 (THU0714)
Birlik, B., 1170 (AB0349)
Birlik, M., 306 (THU0271), 322 (THU0314), 1105 (AB0168), 1282 (AB0658)
Biro, I.A., 1440 (AB1101)
Birolo, C., 27 (SP0109)
Birra, D., 608 (FRI0319)
Birt, J., 932 (SAT0425), 941 (SAT0446), 1334 (AB0793)
Birtane, M., 1380 (AB0927)
Biscetti, F., 1077 (AB0088)
Bischof, A., 319 (THU0306)
Bisgaard, S.M., 732 (FRI0641)
Bishop-Bailey, A., 786 (SAT0049)
Bisoendial, R., 1058 (AB0033), 1088 (AB0118)
Bissell, L.-A., 635 (FRI0390)
Bistoni, O., 69 (OP0044), 305 (THU0268), 873 (SAT0262), 1113 (AB0191)
Biswas, P., 148 (OP0230), 676 (FRI0496), 938 (SAT0439)
Bitik, B., 992 (SAT0570)
Bitoun, S., 508 (FRI0081), 549 (FRI0180)
Björk, M., 10 (SP0041), 112 (OP0143-HPR), 1518 (SAT0740-HPR)
Björkman, L., 364 (THU0414)
Bjørn, M.E., 1075 (AB0081)
Bjørneboe, O., 81 (OP0071), 756 (FRI0702), 1030 (SAT0675)
Black, C.M., 447 (THU0640)
Black, S., 460 (THU0672)
Blackburn, S., 96 (OP0107), 1343 (AB0817), 1552 (PARE0002)
Blaginina, I., 675 (FRI0495)
Blagodarenko, A., 1115 (AB0196)
Blagojevic, J., 631 (FRI0380), 635 (FRI0390), 915 (SAT0380)
Blagojevic-Bucknall, M., 751 (FRI0690), 1028 (SAT0672), 1442 (AB1107)
Blair, P., 110 (OP0139-HPR)
Blake, C., 1493 (THU0767-HPR)
Blakley, M., 1390 (AB0958)
Blanc, A., 621 (FRI0358)
Blanch, J., 178 (OP0294)
Blanch Mur, C., 658 (FRI0452)
Blanch-Mur, C., 927 (SAT0412)
Blanchard, F., 90 (OP0093), 128 (OP0184), 130 (OP0190)
Blanchard-Delaunay, C., 1256 (AB0588)
Blanco, A., 75 (OP0059), 326 (THU0326), 350 (THU0381), 718 (FRI0607), 1166 (AB0337)
Blanco, F., 1067 (AB0059)
Blanco, F.J., 53 (OP0008), 203 (THU0009), 481 (FRI0005), 502 (FRI0063), 672 (FRI0487), 978 (SAT0535), 980 (SAT0539), 1135 (AB0249), 1343 (AB0816), 1466 (AB1174)
Blanco, J., 837 (SAT0178), 843 (SAT0191)
Blanco, R., 75 (OP0059), 108 (OP0135), 135 (OP0202), 251 (THU0134), 290 (THU0227), 326 (THU0326), 345 (THU0369), 350 (THU0381), 405 (THU0526), 420 (THU0567), 569 (FRI0226), 614 (FRI0336), 718 (FRI0607), 742 (FRI0666), 794 (SAT0070), 843 (SAT0191), 946 (SAT0458), 1084 (AB0108), 1116 (AB0197), 1166 (AB0337), 1255 (AB0583, AB0584)
Blanco Morales, E.A., 955 (SAT0475)
Blanco-Alonso, R., 1244 (AB0553)
Blanco-García, F.J., 936 (SAT0435)
Blanco-Madrigal, J., 1001 (SAT0600)
Blanco-Perez, J.J., 740 (FRI0661)
Blaney Davidson, E., 1057 (AB0031)
Blaney-Davidson, E.N., 211 (THU0032)
Blank, M., 502 (FRI0065)
Blank, N., 1106 (AB0169), 1110 (AB0181)
Blanqué, R., 126 (OP0180), 648 (FRI0428)
Blanquer, M., 487 (FRI0021)
Blas, R., 1064 (AB0051)
Blas Hernadez, P., 1401 (AB0991)
Blasco, A.J., 452 (THU0651)
Blasco-Blasco, M., 657 (FRI0451), 1307 (AB0724)
Blavnsfeldt, A.-B.G., 248 (THU0126)
Blay, G., 76 (OP0061)
Blázquez, M.A., 1471 (AB1189)
Blazquez, M.A., 1394 (AB0970)
Blázquez Cañamero, M.Á., 1391 (AB0961)
Bleil, J., 647 (FRI0425)
Bliddal, H., 196 (OP0340), 737 (FRI0654), 1412 (AB1020), 1419 (AB1042)
Blighe, K., 506 (FRI0076)
Blijdorp, I.C.J., 1086 (AB0114)
Blinova, E., 206 (THU0019)
Blizzard, L., 962 (SAT0493)
Block, J., 303 (THU0264), 1219 (AB0483), 1307 (AB0724)
Block, J.A., 318 (THU0301), 385 (THU0472), 971 (SAT0516), 1129 (AB0231), 1130 (AB0233), 1451 (AB1132), 1466 (AB1173)
Blockmans, D., 107 (OP0131), 636 (FRI0393), 1005 (SAT0612)
Bloem, K., 61 (OP0025)
Blokland, S.L., 181 (OP0303), 288 (THU0223), 292 (THU0234), 295 (THU0241), 1089 (AB0121)
Blom, A., 193 (OP0335), 772 (SAT0012)
Blom, A.B., 207 (THU0020), 211 (THU0032)
Blomberg, B.B., 775 (SAT0018)
Blomjous, B., 184 (OP0310)
Bludova, N., 249 (THU0128), 675 (FRI0495)
Blueml, S., 488 (FRI0024), 502 (FRI0064)
Blüml, S., 492 (FRI0033), 528 (FRI0125)
Blüthner, M., 461 (THU0673)
Blyszczuk, P., 86 (OP0084)
Błyszczuk, P., 88 (OP0088)
Bø, I., 161 (OP0255-HPR)
Bobirca, A., 1151 (AB0294)
Bobirca, F., 1151 (AB0294)
Boccassini, L., 1294 (AB0689)
Bocchino, M., 630 (FRI0378)
Bock, C., 499 (FRI0055)
Bodaghi, B., 77 (OP0062), 408 (THU0532)
Boddi, M., 1269 (AB0622), 1270 (AB0623)

Bode, C., 1478 (THU0727-HPR), 1515 (SAT0732-HPR)
Bode, C.S., 710 (FRI0583)
Boden, B., 724 (FRI0623)
Bodewes, I., 92 (OP0097)
Bódis, B., 1267 (AB0617)
Bodur, H., 235 (THU0092), 535 (FRI0144), 652 (FRI0439), 818 (SAT0130), 1114 (AB0193), 1122 (AB0213)
Boehncke, W.-H., 142 (OP0218)
Boer, A.C., 473 (THU0704)
Boerrigter, G.W.M., 907 (SAT0359)
Boers, M., 15 (SP0059), 23 (SP0091), 41 (SP0168), 111 (OP0141-HPR), 463 (THU0677), 473 (THU0703), 476 (THU0712), 604 (FRI0309), 811 (SAT0114), 817 (SAT0127), 837 (SAT0177)
Boes, M., 1065 (AB0054)
Boesen, M., 1021 (SAT0651), 1419 (AB1042)
Boeters, D., 215 (THU0042), 473 (THU0702), 530 (FRI0131), 1050 (AB0012)
Bogas, P., 551 (FRI0186), 559 (FRI0204), 833 (SAT0168), 1116 (AB0198), 1304 (AB0714)
Bogdanos, D.P., 680 (FRI0504), 903 (SAT0348), 1271 (AB0626), 1279 (AB0648)
Boggioni, I., 1154 (AB0301)
Bogmat, L.F., 399 (THU0510), 1392 (AB0963)
Bogomolov, A., 206 (THU0019)
Bohgaki, T., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Bohl-Bühler, M., 558 (FRI0203)
Bohnsack, J., 405 (THU0525)
Bohr, A., 440 (THU0619)
Boiardi, L., 323 (THU0316), 609 (FRI0323), 1247 (AB0563)
Boileau, C., 1049 (AB0007)
Boire, G., 131 (OP0192), 231 (THU0085), 496 (FRI0047), 769 (SAT0002), 781 (SAT0039), 815 (SAT0122)
Boisrame, S., 1215 (AB0469)
Boisrame-Gastrin, S., 309 (THU0278)
Boisseau, N., 1477 (THU0724-HPR)
Boissier, M.-C., 1049 (AB0007)
Boitier, E., 195 (OP0339)
Bojanowski, S., 1199 (AB0425), 1535 (AB1211-HPR)
Bojincă, M., 435 (THU0607), 1264 (AB0608)
Bojinca, M., 467 (THU0689), 626 (FRI0368), 745 (FRI0676), 983 (SAT0547), 1032 (SAT0681), 1151 (AB0294), 1179 (AB0376)
Bojinca, V., 304 (THU0266), 416 (THU0555), 423 (THU0574), 435 (THU0606), 881 (SAT0288), 1025 (SAT0664), 1208 (AB0450), 1221 (AB0487), 1278 (AB0646), 1333 (AB0790), 1428 (AB1068), 1429 (AB1069), 1460 (AB1158)
Bokarewa, M.I., 38 (SP0159), 777 (SAT0026), 779 (SAT0033)
Boki, K., 836 (SAT0176)
Bolaños-Chamorro, F., 1199 (AB0427)
Bolanowski, M., 1112 (AB0187)
Bolce, R.J., 232 (THU0087), 517 (FRI0100), 1121 (AB0210)
Bolek, E.C., 616 (FRI0342), 720 (FRI0612)
Bolstad, N., 338 (THU0354), 472 (THU0700), 549 (FRI0182)
Bombardier, C., 194 (OP0337-HPR), 531 (FRI0132)
Bombardieri, M., 125 (OP0175), 180 (OP0300), 238 (THU0100), 311 (THU0284), 464 (THU0681), 506 (FRI0076), 511 (FRI0088), 886 (SAT0302), 1205 (AB0444)
Bõmer, N., 207 (THU0020)
Bonaci Nikolic, B., 307 (THU0274)
Bonacini, M., 212 (THU0035), 1054 (AB0022)
Bonali, C., 1022 (SAT0654), 1152 (AB0295), 1412 (AB1022)
Bonali, C.F., 742 (FRI0667)
Bondanza, A., 126 (OP0179)
Bondarovich, N.A., 1073 (AB0078)
Bondermann, D., 65 (OP0034)
Bondor, C.I., 260 (THU0156)
Bondt, A., 509 (FRI0083), 775 (SAT0019)
Bonek, K., 1310 (AB0733)
Bonella, F., 1110 (AB0181)
Bonelli, M., 488 (FRI0024), 492 (FRI0033), 499 (FRI0055), 502 (FRI0064)
Bonet, M., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Bonfá, E., 76 (OP0061)
Bonfiglioli, K., 1160 (AB0320)
Bong, D., 175 (OP0288), 742 (FRI0668), 1428 (AB1067)
Bong, D.A., 19 (SP0076)
Bongiorno, G.K., 167 (OP0269)
Bongiovanni, S., 1294 (AB0689)
Bonifazi, M., 905 (SAT0353)
Bonilla, C., 406 (THU0527)
Bonilla, G., 456 (THU0661), 551 (FRI0186), 559 (FRI0204), 833 (SAT0168), 843 (SAT0191)
Bonilla, M.G., 1116 (AB0198), 1293 (AB0686)
Bonilla Arjona, A., 1424 (AB1057)
Bonilla Hernan, G., 824 (SAT0145)
Bonilla-Hernán, M.-G., 501 (FRI0062)
Bonin, R., 337 (THU0353), 350 (THU0382)
Bonini, M., 230 (THU0082)
Bonisconti, F., 205 (THU0017), 995 (SAT0582)
Bonnet, D., 1376 (AB0916)
Bonnet, I., 945 (SAT0455)
Bonvini, E., 777 (SAT0027)
Boocock, J., 165 (OP0263)
Boogaard, J., 111 (OP0141-HPR)
Book, C., 252 (THU0135)
Boone, C., 347 (THU0375)
Boonen, A., 80 (OP0070), 134 (OP0199-PARE), 157 (OP0245), 433 (THU0602, THU0603), 467 (THU0689), 539 (FRI0152), 649 (FRI0430), 763 (FRI0722), 977 (SAT0531), 1293 (AB0685)
Boonstra, M., 621 (FRI0356), 903 (SAT0350), 907 (SAT0359), 1279 (AB0650)
Boots, A., 647 (FRI0424)
Bootsma, H., 67 (OP0040), 308 (THU0276), 311 (THU0284), 464 (THU0681), 591 (FRI0277), 625 (FRI0366), 630 (FRI0377), 875 (SAT0270), 928 (SAT0416), 1007 (SAT0617), 1265 (AB0610)
Bootz, F., 92 (OP0099)
Boracchi, P., 643 (FRI0413), 746 (FRI0677), 908 (SAT0364)
Borangiu, A., 304 (THU0266), 416 (THU0555), 423 (THU0574), 435 (THU0606), 876 (SAT0271), 881 (SAT0288), 1208 (AB0450), 1221 (AB0487), 1278 (AB0646, AB0647), 1460 (AB1158)
Boraschi, D., 222 (THU0063)
Borazan, N., 1526 (SAT0765-HPR)
Bordy, R., 493 (FRI0039), 495 (FRI0044)
Borg, A., 1514 (SAT0729-HPR)
Borg, A.A., 439 (THU0616), 1234 (AB0524), 1435 (AB1088), 1522 (SAT0752-HPR)
Borges, J., 464 (THU0679), 929 (SAT0418), 1163 (AB0329), 1464 (AB1168)
Borges-Cosic, M., 1499 (FRI0743-HPR)
Borghi, C., 366 (THU0420)
Borghi, M.O., 1022 (SAT0655)
Borgiani, P., 204 (THU0013), 1007 (SAT0615)
Borgonovi, M., 118 (OP0161)
Borić, K., 1283 (AB0661)
Borie, R., 1049 (AB0007)
Borisov, S., 1157 (AB0311)
Borisova, M.A., 576 (FRI0241)
Borja, A., 1276 (AB0639)
Bork, D., 386 (THU0473)
Borlenghi, C., 670 (FRI0483)
Borm, M.E., 177 (OP0293), 855 (SAT0218)
Borman, P., 439 (THU0618)
Borodina, J., 61 (OP0024)
Borok, S., 747 (FRI0679)
Borona-Carvajal, R., 477 (THU0713)
Borrego, L.M., 1051 (AB0013), 1094 (AB0134)
Borrell, H., 663 (FRI0468)
Borresen, S., 332 (THU0340)
Bort-Martí, S., 557 (FRI0199)
Bortkevych, O.P., 399 (THU0510)
Bortolotti, R., 1200 (AB0429)
Bortoluzzi, A., 562 (FRI0212), 582 (FRI0255), 828 (SAT0156), 1111 (AB0186), 1207 (AB0448), 1209 (AB0456)
Bos, K., 375 (THU0444), 379 (THU0455), 961 (SAT0492)
Bos, N., 607 (FRI0317)
Bos, R., 928 (SAT0416)
Boschetti, G., 1315 (AB0745)
Bosello, S., 635 (FRI0390)
Bosello, S.L., 197 (OP0343), 608 (FRI0319)
Bossini-Castillo, L., 1047 (AB0003)
Bossuyt, X., 636 (FRI0393)
Boström, C., 162 (OP0256-HPR), 1545 (AB1240-HPR)
Bosworth, A., 140 (OP0211-PARE), 186 (OP0317-PARE), 433 (THU0602), 763 (FRI0722), 1560 (AB1250-PARE)
Bosworth, A.M., 11 (SP0045)
Bosycot, A., 1301 (AB0708)
Bot, J., 724 (FRI0623)
Boteanu, A., 400 (THU0514), 1391 (AB0961), 1394 (AB0970), 1396 (AB0977), 1471 (AB1189)
Boteanu, A.L., 392 (THU0491)
Botello Corzo, D.A., 1396 (AB0977)
Boteva, B., 1558 (PARE0018)
Botez, I., 126 (OP0180)
Both, T., 92 (OP0097)
Botman, J., 1476 (THU0721-HPR)
Botsios, C., 1123 (AB0215)
Botticella, G., 695 (FRI0540)
Bottini, A., 474 (THU0705)
Bou, R., 1393 (AB0967)
Bou Torrent, R., 407 (THU0530)
Bouajina, E., 543 (FRI0165), 926 (SAT0409), 927 (SAT0411)
Bouaziz, M., 1146 (AB0278)
Boudaoud, S., 182 (OP0307), 289 (THU0225)
Bouden, S., 1188 (AB0398), 1371 (AB0902)
Boudersa, N., 334 (THU0346), 339 (THU0356, THU0357), 388 (THU0482), 389 (THU0483), 665 (FRI0472), 1296 (AB0694)
Bouhoula, M., 926 (SAT0409)
Bouissar, W., 613 (FRI0333)
Boujenane, Y., 1136 (AB0252), 1163 (AB0327, AB0328), 1168 (AB0343)
Boujut, E., 1470 (AB1185)
Boukhris, I., 1251 (AB0574)
Bouleau, L., 476 (THU0711)
Boulman, N., 926 (SAT0407)
Bouma, G., 292 (THU0234)
Boumpas, D., 50 (OP0002), 192 (OP0332), 297 (THU0246), 300 (THU0254), 560 (FRI0207), 588 (FRI0269), 836 (SAT0176), 1204 (AB0442), 1215 (AB0471)
Boumpas, D.T., 574 (FRI0236), 850 (SAT0204)
Bounas, A., 559 (FRI0205)
Bounecer, H., 982 (SAT0545)
Boura, P., 569 (FRI0224), 1047 (AB0001), 1261 (AB0601)
Bourdaim, S.H., 430 (THU0593)
Bournazos, I., 836 (SAT0176)
Bournia, V.-K., 210 (THU0028), 642 (FRI0410), 643 (FRI0414)
Bournia, V.K., 908 (SAT0361)
Bouroncle Alaluna, C., 1396 (AB0977)
Boussaid, S., 995 (SAT0580), 1146 (AB0280), 1377 (AB0920), 1536 (AB1214-HPR)
Boutemy, J., 617 (FRI0345)
Boutet, M.-A., 90 (OP0093)
Boutin, S., 754 (FRI0698)
Boutron, I., 170 (LB0001)
Boutron-Ruault, M.C., 160 (OP0253)
Boutry-Bacle, M.-A., 549 (FRI0180)
Bouvard, B., 989 (SAT0561), 1191 (AB0406)
Bouwens, H., 1482 (THU0737-HPR)
Bouwer, E., 928 (SAT0416)
Bouwstra, J.D.V., 1047 (AB0003)
Bové, F., 1434 (AB1085)
Boveda, M.D., 494 (FRI0040)
Boveda-Ruiz, D., 740 (FRI0661), 1409 (AB1012)
Bovée, J.B., 207 (THU0020)
Bowers, E., 498 (FRI0053)
Bowes, J., 177 (OP0291), 201 (THU0004)
Bowes, M.A., 119 (OP0164), 268 (THU0175), 1010 (SAT0624)

Bowman, S., 67 (OP0040), 92 (OP0097), 295 (THU0242), 302 (THU0259), 1103 (AB0162)
Bowman, S.J., 4 (SP0011), 1205 (AB0444)
Boy, M., 277 (THU0196), 1034 (SAT0686)
Boyadzhieva, V., 245 (THU0116), 1233 (AB0521)
Boyadzhieva, V.V., 1147 (AB0283), 1148 (AB0284)
Boyapati, A., 570 (FRI0227, FRI0228), 838 (SAT0179), 844 (SAT0192)
Boyd, P., 1552 (PARE0001), 1557 (PARE0015)
Boyer, J.-F., 770 (SAT0006)
Bøyesen, P., 1030 (SAT0675)
Boyko, Y.E., 399 (THU0510)
Boyle, J.J., 219 (THU0053)
Boyle, K., 90 (OP0092)
Boyman, O., 191 (OP0330)
Bozán, M.F., 1108 (AB0176)
Bozan, T., 637 (FRI0396)
Bozec, A., 848 (SAT0201), 892 (SAT0318), 1063 (AB0046)
Bozhinova, S., 1558 (PARE0018)
Bozios, P., 1013 (SAT0631)
Bozzalla, E., 410 (THU0538)
Bozzalla Cassione, E., 1399 (AB0985)
Bozzano, G., 1459 (AB1154)
Bozzao, F., 1318 (AB0753)
Bozzolo, E., 410 (THU0538), 1399 (AB0985)
Bozzolo, E.P., 725 (FRI0624)
Brabant, M.-J., 558 (FRI0201), 832 (SAT0165)
Braçe, O., 658 (FRI0452)
Brace, O., 927 (SAT0412), 1554 (PARE0007)
Bradbury, L., 383 (THU0464)
Bradford, M.C., 409 (THU0537)
Bradley, J., 513 (FRI0092)
Bradley, J.D., 158 (OP0248), 794 (SAT0069)
Bradley, L.A., 971 (SAT0516)
Bradley, S., 1508 (FRI0767-HPR)
Bradunaite, R., 622 (FRI0359)
Bragagna, E., 1173 (AB0357)
Bragazzi, N.L., 319 (THU0304)
Brahe, C.H., 234 (THU0091), 437 (THU0612), 726 (FRI0628)
Brahem, M., 1000 (SAT0598), 1169 (AB0346, AB0347), 1170 (AB0348), 1353 (AB0848, AB0849)
Brahim, M., 1383 (AB0937)
Brahimi, N., 1009 (SAT0623), 1405 (AB1001, AB1002)
Braillard-Poccard, A., 590 (FRI0276)
Braña-Cardeñosa, A., 78 (OP0066)
Branch, W., 152 (OP0236)
Branco, J., 186 (OP0315), 902 (SAT0345), 1254 (AB0581)
Branco, J.C., 441 (THU0622), 466 (THU0685), 1051 (AB0013), 1052 (AB0016), 1094 (AB0134), 1153 (AB0300)
Brandi, M.L., 178 (OP0294)
Brandon, T.G., 469 (THU0693), 471 (THU0697)
Brands, R., 1075 (AB0082)
Brandt, A., 892 (SAT0318)
Brar, T., 826 (SAT0151)
Braschi, F., 628 (FRI0372)
Brasseur, J.-P., 736 (FRI0650)
Bratasz, A., 222 (THU0062)
Bratus, A., 190 (OP0326)
Braults, Y., 1330 (AB0781)
Braun, J., 13 (SP0054), 60 (OP0023), 87 (OP0085), 100 (OP0114), 356 (THU0394), 357 (THU0397), 663 (FRI0466), 669 (FRI0480), 934 (SAT0429)
Braun, M., 910 (SAT0368)
Braun, T., 253 (THU0139)
Braun-Moscovici, Y., 333 (THU0343), 355 (THU0392), 910 (SAT0368)
Braunewell, V., 844 (SAT0193), 1187 (AB0396)
Bravenboer, N., 724 (FRI0623)
Bravo, B., 75 (OP0059), 405 (THU0526)
Bravo, S.B., 503 (FRI0068)
Bravo Gallego, L.Y., 456 (THU0661), 555 (FRI0194)
Bravo-Oro, A., 395 (THU0501)
Brebion, F., 126 (OP0180)
Breda, S., 891 (SAT0315)
Brede, C., 184 (OP0312)
Bredemeier, M., 167 (OP0269), 628 (FRI0371)
Bredewold, O.W., 871 (SAT0258)
Breedveld, F., 560 (FRI0207)
Breen, K., 1097 (AB0147)
Breen, R., 1434 (AB1083), 1493 (THU0767-HPR), 1521 (SAT0748-HPR)
Bremander, A., 651 (FRI0436), 922 (SAT0397), 1488 (THU0757-HPR), 1495 (FRI0733-HPR), 1513 (SAT0726-HPR), 1515 (SAT0731-HPR), 1531 (AB1199-HPR)
Brennan, A., 1434 (AB1083), 1493 (THU0767-HPR), 1521 (SAT0748-HPR)
Brenol, C., 814 (SAT0121), 1160 (AB0320)
Brenol, C.V., 246 (THU0119), 1446 (AB1117)
Bressollette, C., 778 (SAT0029)
Breton, S., 56 (OP0014)
Brett, A., 119 (OP0164)
Breuil, V., 707 (FRI0578), 851 (SAT0207), 967 (SAT0507)
Brevet, P., 758 (FRI0707)
Briceño, I., 201 (THU0005), 218 (THU0052)
Bridges, A., 691 (FRI0528)
Bridges, S.L., 1125 (AB0220)
Brière-Bellier, C., 617 (FRI0345)
Brigante, A., 440 (THU0619)
Briggs, W., 714 (FRI0595)
Brill, G., 544 (FRI0167), 802 (SAT0089)
Brink, M., 792 (SAT0065)
Brinkmann, G.H., 1030 (SAT0675)
Brinks, R., 789 (SAT0056), 1449 (AB1127)
Brion, R., 90 (OP0093)
Brioschi, R., 478 (THU0718)
Briot, K., 73 (OP0054)
Brisacier, A., 844 (SAT0192)
Brisslert, M., 779 (SAT0033)
Brites, L., 694 (FRI0537), 700 (FRI0558), 702 (FRI0562)
Brito, I., 186 (OP0315), 400 (THU0513), 468 (THU0691), 1096 (AB0144)
Brito-Zerón, P., 311 (THU0284), 410 (THU0539), 464 (THU0681), 597 (FRI0293), 721 (FRI0615), 886 (SAT0302), 1042 (SAT0706)
Brito-Zeron, P., 67 (OP0040)
Britton, J., 1019 (SAT0647)
Brizzolara, R., 140 (OP0212), 378 (THU0451), 1110 (AB0182, AB0183), 1111 (AB0185)
Brock, M., 87 (OP0086), 117 (OP0157)
Broder, A., 297 (THU0247)
Broen, J.C., 288 (THU0223)
Brogan, P., 393 (THU0495)
Brohawn, P., 180 (OP0301), 865 (SAT0243)
Brokstad, K.A., 1102 (AB0160)
Brom, M., 1231 (AB0516), 1333 (AB0789)
Bromilow, L., 1494 (THU0771-HPR)
Bronsard, N., 707 (FRI0578)
Brook, J., 1526 (SAT0765-HPR)
Brooks, A., 1494 (THU0769-HPR)
Brooks, D., 531 (FRI0133), 816 (SAT0126)
Brooks, P.M., 463 (THU0677)
Broqua, P., 85 (OP0081)
Brouard, S., 778 (SAT0029)
Brouwer, E., 107 (OP0131), 607 (FRI0317), 647 (FRI0424)
Brouwer, J., 532 (FRI0136), 537 (FRI0147)
Brown, D., 965 (SAT0502)
Brown, E., 104 (OP0123)
Brown, G., 253 (THU0138)
Brown, J., 107 (OP0130)
Brown, K., 581 (FRI0252), 845 (SAT0194)
Brown, M., 118 (OP0160), 337 (THU0352), 383 (THU0464)
Brown, R., 983 (SAT0548)
Brox, E., 1539 (AB1222-HPR)
Broyde, A., 747 (FRI0679), 1118 (AB0203)
Brucato, A., 437 (THU0611), 1439 (AB1099)
Bruce, I., 803 (SAT0092), 1023 (SAT0657)
Brudniewski, J., 443 (THU0627)
Bruijnen, S., 724 (FRI0623), 1020 (SAT0650)
Brulhardt, L., 816 (SAT0125)
Brulhart, L., 168 (OP0271)
Brun, J.G., 875 (SAT0270), 1102 (AB0160)
Brunekreef, T., 147 (OP0227)
Brunetta, P., 187 (OP0320), 318 (THU0301), 857 (SAT0221), 865 (SAT0242), 868 (SAT0250)
Bruni, C., 628 (FRI0372), 631 (FRI0380), 633 (FRI0384), 1269 (AB0622), 1270 (AB0623)
Brunner, H., 75 (OP0058), 396 (THU0503), 405 (THU0525)
Brunner, J., 132 (OP0196), 1389 (AB0957)
Brunner, M., 86 (OP0083)
Brunori, G., 604 (FRI0310), 614 (FRI0337), 1257 (AB0589)
Bruschi, E., 270 (THU0181)
Bruschi, M., 954 (SAT0473)
Brussel, M.V., 478 (THU0716)
Bruyn, G., 583 (FRI0256), 1013 (SAT0631), 1015 (SAT0636)
Bruyn, G.A., 175 (OP0288)
Brzezińska-Pawłowska, O., 1458 (AB1152, AB1153)
Brzosko, M., 1005 (SAT0611)
Bublikov, D.S., 273 (THU0187), 1317 (AB0748)
Bucchia, M., 778 (SAT0029)
Bucci, R., 808 (SAT0105), 1327 (AB0773)
Buch, M., 786 (SAT0049)
Buch, M.H., 238 (THU0101), 635 (FRI0390), 987 (SAT0556), 1016 (SAT0639)
Buchanan, R., 383 (THU0464)
Buchanan, R.R.C., 377 (THU0447), 1367 (AB0889)
Bucka, J., 1470 (AB1184)
Buckely, C., 238 (THU0100), 511 (FRI0088)
Buckens, S.C., 1423 (AB1052)
Buckley, C., 242 (THU0111)
Buckley, C.D., 125 (OP0178), 190 (OP0326), 1125 (AB0220)
Budde, P., 193 (OP0333), 886 (SAT0301), 893 (SAT0319), 911 (SAT0372), 1007 (SAT0616)
Buder, T., 1011 (SAT0628)
Budzik, J.-F., 359 (THU0402)
Buehring, B., 690 (FRI0525), 691 (FRI0528)
Buendía Luca, M.A., 1221 (AB0486)
Bueno, A., 660 (FRI0459)
Bugatti, S., 237 (THU0099), 458 (THU0667), 787 (SAT0053), 790 (SAT0060), 1123 (AB0214)
Buglova, A.E., 1063 (AB0048)
Bugni, V., 76 (OP0061)
Bugrova, O., 153 (LB0002)
Buhanova, D.V., 251 (THU0132)
Bui, L., 154 (OP0239), 792 (SAT0066)
Buitelaar, H., 111 (OP0141-HPR)
Buitrago-Garcia, D., 162 (OP0257-HPR), 266 (THU0172), 427 (THU0585), 529 (FRI0127), 538 (FRI0150), 852 (SAT0210), 963 (SAT0496), 1208 (AB0453), 1441 (AB1103), 1479 (THU0729-HPR), 1502 (FRI0751-HPR), 1534 (AB1207-HPR), 1540 (AB1225-HPR), 1543 (AB1235-HPR)
Bujak, M., 276 (THU0194)
Bujakowska, O., 1152 (AB0297)
Bujan, S., 324 (THU0320)
Bujor, O., 1199 (AB0426)
Bukhari, M., 694 (FRI0538), 696 (FRI0543), 701 (FRI0560), 703 (FRI0565), 1139 (AB0260)
Bukowski, J.F., 337 (THU0353), 350 (THU0382)
Bulanov, N., 617 (FRI0346)
Bulanova, M., 617 (FRI0346)
Bulfoni, M., 1101 (AB0156)
Bull, S., 119 (OP0162-PARE)
Bulleri, A., 584 (FRI0260)
Bultink, I., 184 (OP0310)
Bultink, I.E., 67 (OP0039), 114 (OP0150)
Bulut, N., 261 (THU0159)
Bulut, Y., 921 (SAT0396)
Bumbăcea, D., 1032 (SAT0681)
Bumbea, A.M., 478 (THU0717)
Bungartz, C., 302 (THU0261)
Buño, A., 416 (THU0553)
Burakowski, T., 216 (THU0045)
Burbano, C., 1092 (AB0129)
Burden, A., 347 (THU0375)
Burenchev, D., 616 (FRI0343)
Burger, K., 1445 (AB1115)
Burgers, L.E., 82 (OP0073), 473 (THU0704)
Burges, R., 121 (OP0167)
Burghardt, A.J., 58 (OP0020)
Burgos Vargas, R., 365 (THU0417)
Burgos-Vargas, R., 363 (THU0411), 758 (FRI0709), 1362 (AB0873), 1450 (AB1129), 1453 (AB1137)

Burianov, O.A., 974 (SAT0526)
Burja, B., 219 (THU0054)
Burke, T., 186 (OP0317-PARE)
Burket, J., 467 (THU0687)
Burkhardt, H., 565 (FRI0217)
Burlakov, V., 413 (THU0547)
Burlison, J., 1010 (SAT0624)
Burls, A., 557 (FRI0199)
Burlui, A., 1261 (AB0600), 1411 (AB1019)
Burmester, G., 124 (OP0174), 131 (OP0192), 184 (OP0311), 244 (THU0114), 271 (THU0185), 560 (FRI0207), 564 (FRI0216), 565 (FRI0217), 581 (FRI0253), 676 (FRI0496), 769 (SAT0004), 773 (SAT0014), 938 (SAT0439), 1081 (AB0101)
Burmester, G.-R., 253 (THU0139), 486 (FRI0019), 530 (FRI0130), 1008 (SAT0618)
Burmester, G.R., 94 (OP0102), 356 (THU0394), 446 (THU0637), 558 (FRI0203), 838 (SAT0180), 849 (SAT0202), 853 (SAT0212)
Burnham, J.M., 391 (THU0490)
Burns, L., 677 (FRI0499), 1120 (AB0208)
Burrell, L.M., 377 (THU0447)
Burska, A., 159 (OP0250)
Burska, A.N., 1085 (AB0112)
Burston, J., 127 (OP0183)
Busato, F., 286 (THU0217)
Busca, C., 873 (SAT0264), 1245 (AB0555), 1266 (AB0614), 1289 (AB0676)
Buscetta, G., 496 (FRI0046)
Busger op Vollenbroek, F., 274 (THU0190)
Bush, J., 867 (SAT0249)
Busquets, N., 1289 (AB0675)
Busquets-Pérez, N., 344 (THU0368)
Bustabad, M., 556 (FRI0197)
Bustabad, S., 1037 (SAT0691), 1390 (AB0959), 1397 (AB0979)
Bustabad Reyes, S., 955 (SAT0475), 1333 (AB0788), 1424 (AB1057)
Bustamante, R., 1091 (AB0126), 1098 (AB0149)
Bustamante-González, R., 591 (FRI0279)
Bustamente, L., 851 (SAT0207)
Butrimiene, I., 245 (THU0116)
Buttgereit, F., 129 (OP0187), 446 (THU0637), 480 (FRI0002), 485 (FRI0015), 486 (FRI0019), 897 (SAT0333), 1067 (AB0060), 1199 (AB0428)
Buyuktepe, Y., 1476 (THU0722-HPR)
Buzatu, C., 423 (THU0574)
Buzatu, C.G., 416 (THU0555)
Byalik, E., 269 (THU0179)
Byelyaeva, L., 398 (THU0508), 1389 (AB0956)
Bykerk, V., 231 (THU0085), 781 (SAT0039)
Bykerk, V.P., 470 (THU0695), 815 (SAT0122), 818 (SAT0132)
Bylander, B., 437 (THU0612)
Byng-Maddick, R., 115 (OP0153), 753 (FRI0695)
Byrjalsen, I., 120 (OP0165)
Byrne, E., 847 (SAT0198)
Byrne, R., 486 (FRI0018)
Byun, S.-J., 383 (THU0467)
Bzarova, T., 186 (OP0316), 539 (FRI0154), 1387 (AB0950, AB0951)

Caballero, C., 1342 (AB0813)
Caballero, C.V., 1339 (AB0805)
Cabañas-Perianes, V., 487 (FRI0021)
Cabanes, C.A., 480 (FRI0003)
Cabanillas Salazar, G.M., 692 (FRI0531)
Cabanski, M., 1229 (AB0509)
Cabello, A., 128 (OP0186)
Cabello, J.B., 557 (FRI0199)
Cabello Fernandez, Y., 1183 (AB0385)
Cábez, A., 685 (FRI0515), 954 (SAT0474)
Cabral, A.R., 597 (FRI0292)
Cabral-Marques, O., 772 (SAT0011), 1108 (AB0175)
Cabrera, M., 427 (THU0585), 1479 (THU0729-HPR), 1534 (AB1207-HPR)
Cabrera, N., 432 (THU0599)
Cabrera, S., 1396 (AB0975)
Caccamo, N., 777 (SAT0025)
Cacciapaglia, F., 254 (THU0143), 521 (FRI0110), 639 (FRI0400), 1135 (AB0250), 1268 (AB0618), 1461 (AB1160)
Cacoub, P., 108 (OP0134), 776 (SAT0023), 1247 (AB0563)
Cadavid, A.P., 308 (THU0275)
Cadena Bonfanti, A.A., 1239 (AB0538)
Cadoni, M.L., 496 (FRI0046), 535 (FRI0143)
Cadzow, M., 165 (OP0263), 383 (THU0464)
Caeiro, F., 313 (THU0289), 995 (SAT0582)
Caeiro, J.P., 995 (SAT0582)
Caeiro, J.R., 1071 (AB0070)
Caetano, J., 902 (SAT0345), 1131 (AB0238)
Caetano-Lopes, J., 1080 (AB0097)
Caeyers, N., 1552 (PARE0001)
Cafaro, G., 69 (OP0044), 873 (SAT0262)
Cagliyan, H., 999 (SAT0592)
Cagnotto, G., 1272 (AB0630)
Cai, G., 621 (FRI0356)
Cai, Y., 1141 (AB0266)
Cai, Z., 524 (FRI0116)
Cai-Hong, W., 839 (SAT0181)
Caicedo, C., 427 (THU0585), 1479 (THU0729-HPR)
Caimmi, C., 693 (FRI0535), 899 (SAT0336), 1124 (AB0216)
Cainan, L., 738 (FRI0657)
Caínzos, T., 712 (FRI0589)
Cairns, A., 1477 (THU0723-HPR)
Cairo, V., 1312 (AB0738)
Cajiao, G., 1540 (AB1225-HPR)
Cakalagaoglu, F., 296 (THU0245)
Cakci, A., 733 (FRI0643)
Cakit, B., 1137 (AB0255)
Calabrese, C., 51 (OP0003), 713 (FRI0594)
Calabrese, E., 667 (FRI0477)
Calabrese, L., 27 (SP0108), 33 (SP0132), 51 (OP0003), 373 (THU0438)
Calabuig Muñoz, E., 1374 (AB0912)
Calamia, V., 53 (OP0008), 980 (SAT0539), 1135 (AB0249), 1343 (AB0816), 1466 (AB1174)
Calay, D., 219 (THU0053)
Calcagnile, F., 1483 (THU0743-HPR)
Calderan, L., 891 (SAT0315)
Calderón-Goercke, M., 1255 (AB0583, AB0584)
Calderón-Goerckel, M., 1116 (AB0197)
Caldonazzi, F., 1388 (AB0953)
Çalgüneri, M., 1531 (AB1198-HPR)
Calhoun, D.A., 363 (THU0413)
Calis, M., 659 (FRI0457)
Caliskan Uckun, A., 1114 (AB0193)
Caliz, R., 452 (THU0651)
Cáliz Cáliz, R., 1228 (AB0506), 1321 (AB0760)
Calizaya, G., 1429 (AB1071)
Callebaut, I., 1049 (AB0007)
Callegaro, D., 614 (FRI0335)
Callejas, J., 718 (FRI0607)
Callejas, J.L., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Callejas Moragas, E., 900 (SAT0340), 1262 (AB0602)
Callejas-Moraga, E.L., 1262 (AB0603)
Callejas-Rubio, J.L., 1047 (AB0003)
Calò, E., 212 (THU0035), 1054 (AB0022)
Calugi, S., 693 (FRI0535)
Calvo, C., 406 (THU0527)
Calvo, E., 201 (THU0005), 218 (THU0052), 330 (THU0336), 410 (THU0539), 721 (FRI0615), 1275 (AB0637), 1338 (AB0801)
Calvo, I., 75 (OP0059), 77 (OP0063), 405 (THU0526), 420 (THU0567), 837 (SAT0178)
Calvo, J., 194 (OP0336), 504 (FRI0069), 587 (FRI0267), 873 (SAT0263), 1107 (AB0173), 1184 (AB0388)
Calvo, M., 439 (THU0617)
Calvo, V., 350 (THU0381)
Calvo Alén, J., 685 (FRI0515), 1374 (AB0910)
Calvo Gutierrez, J., 1143 (AB0270)
Calvo Penades, I., 133 (OP0197)
Calvo-Alén, J., 550 (FRI0184), 556 (FRI0197), 614 (FRI0336)
Calvo-Gutiérrez, J., 650 (FRI0434), 1268 (AB0619)
Calvo-Gutierrez, J., 350 (THU0380)
Calvo-Río, V., 75 (OP0059), 326 (THU0326), 405 (THU0526), 420 (THU0567), 614 (FRI0336), 718 (FRI0607), 1166 (AB0337), 1244 (AB0553), 1255 (AB0583, AB0584)
Calvo-Rio, V., 251 (THU0134), 1116 (AB0197)
Calvo-Torres, L.F., 514 (FRI0094)
Calvo-Zorrilla, I., 1001 (SAT0600)
Calzada, J., 1393 (AB0967)
Calzada-Hernández, J., 407 (THU0530)
Calzavara Pinton, P., 585 (FRI0261)
Camacho, M., 980 (SAT0539)
Camacho-Encina, M., 1135 (AB0249), 1466 (AB1174)
Camara, N.O.S., 26 (SP0105)
Cambridge, G., 495 (FRI0042), 1090 (AB0124), 1205 (AB0443)
Cameron, J., 1051 (AB0015)
Cameron, N., 111 (OP0142-HPR)
Cameselle-Tejeiro, J.M., 415 (THU0550)
Camilleri, F., 1442 (AB1106)
Camilleri, L., 1234 (AB0524)
Camins, J., 988 (SAT0560), 1236 (AB0529), 1241 (AB0544)
Camisa, B., 126 (OP0179)
Camp, H., 280 (THU0203)
Campanilho-Marques, R., 186 (OP0315), 929 (SAT0418), 1080 (AB0097), 1163 (AB0329)
Campbell, J., 121 (OP0167)
Campbell, K., 94 (OP0103), 577 (FRI0243)
Campbell, L., 1343 (AB0817), 1552 (PARE0002)
Campbell, S., 448 (THU0641)
Campillo-Davó, D., 1047 (AB0003)
Campillo-Gimenez, L., 212 (THU0034), 216 (THU0046)
Campo, V., 1107 (AB0173)
Campochiaro, C., 437 (THU0611), 898 (SAT0335), 1269 (AB0621)
Campomori, F., 1267 (AB0616)
Camporeale, A., 983 (SAT0548)
Campos, J., 645 (FRI0420), 925 (SAT0405)
Campos, L.M.A., 76 (OP0061)
Campos, P.L., 1553 (PARE0005)
Campos Esteban, J., 1399 (AB0986)
Can, G., 306 (THU0271), 322 (THU0314), 1156 (AB0308), 1282 (AB0658)
Can, M., 1504 (FRI0756-HPR)
Can-Sandıkçı, S., 1170 (AB0350)
Canas da Silva, J., 436 (THU0610), 467 (THU0689), 533 (FRI0138), 1254 (AB0581)
Canavan, M., 203 (THU0011), 646 (FRI0421), 773 (SAT0013)
Candelas, G., 452 (THU0651), 990 (SAT0564)
Candelieri, M., 872 (SAT0260)
Cândido, V.B., 163 (OP0259-HPR)
Cañellas, J., 988 (SAT0560), 1241 (AB0544)
Caneparo, V., 1113 (AB0191)
Canestrari, G.B., 197 (OP0343)
Cañete, J., 817 (SAT0128)
Cañete, J.D., 128 (OP0185), 177 (OP0292), 685 (FRI0515), 688 (FRI0521), 946 (SAT0458), 954 (SAT0474), 1133 (AB0243)
Cañete, J.D.D., 1318 (AB0752)
Canevari, C., 1399 (AB0985)
Cangemi, I., 535 (FRI0143)
Canhão, H., 186 (OP0315), 498 (FRI0051), 834 (SAT0170), 1080 (AB0097, AB0098), 1254 (AB0581), 1317 (AB0750)
Cannegieter, S.C., 1040 (SAT0701)
Cannon, G.W., 239 (THU0102), 1435 (AB1089)
Cano, C., 1016 (SAT0638), 1296 (AB0693), 1351 (AB0840)
Cano Garcia, L., 1492 (THU0766-HPR), 1525 (SAT0760-HPR)
Cano-Bermuedez, M.A., 252 (THU0137)
Cano-García, L., 1443 (AB1109)
Cano-Garcia, L., 391 (THU0489), 1174 (AB0361), 1175 (AB0362)
Canofari, C., 667 (FRI0477)
Cánovas Olmos, I., 291 (THU0229), 441 (THU0623), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1349 (AB0837), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Cantagrel, A., 77 (OP0062), 231 (THU0084), 343 (THU0364), 428 (THU0588, THU0589), 770 (SAT0006), 843 (SAT0189), 1299 (AB0703)

Cantarini, L., 259 (THU0155), 395 (THU0502), 411 (THU0540, THU0541), 711 (FRI0586), 1059 (AB0037), 1461 (AB1160)
Cantatore, F.P., 263 (THU0164), 437 (THU0611), 629 (FRI0373, FRI0374), 895 (SAT0325), 1106 (AB0171), 1439 (AB1099)
Canti, V., 328 (THU0331), 1055 (AB0025), 1214 (AB0467)
Canuet, M., 106 (OP0128)
Canzoni, M., 742 (FRI0667), 1022 (SAT0654), 1152 (AB0295), 1412 (AB1022)
Cao, H., 1369 (AB0894), 1370 (AB0899)
Cao, J., 366 (THU0421), 1158 (AB0312), 1295 (AB0691)
Cao, J.P., 1266 (AB0612)
Cao, S., 351 (THU0384), 665 (FRI0471), 934 (SAT0431)
Capaci, K., 1499 (FRI0744-HPR)
Capalbo, G., 470 (THU0696), 879 (SAT0281)
Caparbo, V., 1448 (AB1124)
Caparros-Ruiz, R., 391 (THU0489), 1174 (AB0361)
Capecchi, R., 222 (THU0063)
Capel, F., 213 (THU0039)
Capellino, S., 1071 (AB0069)
Capillas, S., 1514 (SAT0728-HPR)
Capkin, E., 1121 (AB0209)
Capocotta, D., 763 (FRI0721)
Capone, L., 778 (SAT0028), 780 (SAT0035)
Caporali, R., 56 (OP0015), 237 (THU0099), 437 (THU0611), 564 (FRI0215), 614 (FRI0337), 787 (SAT0053), 790 (SAT0060), 847 (SAT0199), 1123 (AB0214), 1257 (AB0589), 1272 (AB0630), 1439 (AB1099)
Capozzi, A., 180 (OP0299), 490 (FRI0028)
Cappuccio, A.M., 440 (THU0619)
Caprioli, M., 620 (FRI0353)
Capuano, R., 484 (FRI0012)
Capucci, R., 828 (SAT0156)
Caputo, V., 906 (SAT0357)
Caraba, A., 1217 (AB0477)
Caracuel, M., 326 (THU0326), 504 (FRI0069), 718 (FRI0607)
Caracuel Ruiz, M.Á., 975 (SAT0527)
Caramaschi, P., 202 (THU0006), 899 (SAT0336)
Caramella, D., 731 (FRI0640)
Carames, B., 53 (OP0008), 481 (FRI0005)
Carapellucci, A., 933 (SAT0428)
Carati, D., 1483 (THU0743-HPR)
Caravia-Durán, D., 597 (FRI0293)
Carballo, V., 995 (SAT0582)
Carbo, M.J., 928 (SAT0416)
Carbone, J., 593 (FRI0283)
Carbone, L., 1507 (FRI0764-HPR)
Carbonell, J., 307 (THU0273)
Carcaud, C., 866 (SAT0246)
Cárdenas, C., 1108 (AB0176)
Cardenas, M., 1184 (AB0388)
Cárdenas-de la Garza, J.A., 253 (THU0140), 534 (FRI0141), 1156 (AB0309), 1157 (AB0310)
Cardenas-de la Garza, J.A., 1118 (AB0204), 1119 (AB0205)
Cardenas-Hernandez, M.L., 1330 (AB0782)
Cardillo, T.E., 527 (FRI0124)
Cardona, D., 1161 (AB0321)
Cardona, E., 1161 (AB0321), 1276 (AB0641)
Cardona-Müller, D., 1155 (AB0304)
Cardona-Muñoz, E., 1155 (AB0304)
Cardona-Muñoz, E.G., 262 (THU0161)
Cardoneanu, A., 1261 (AB0600), 1411 (AB1019)
Cardoso, A., 464 (THU0679), 929 (SAT0418), 1163 (AB0329), 1464 (AB1168)
Caricchio, R., 1407 (AB1007)
Carijn, S., 753 (FRI0696)
Carini, C., 437 (THU0611), 1439 (AB1099)
Carletti, L., 163 (OP0259-HPR)
Carletto, A., 343 (THU0365, THU0366), 829 (SAT0158), 854 (SAT0215)
Carlevaris, L., 440 (THU0619)
Carli, L., 457 (THU0664), 731 (FRI0640)
Carlino, G., 808 (SAT0105), 1327 (AB0773)
Carlsten, H., 117 (OP0156), 916 (SAT0382)
Carlströmer-Berthén, N., 861 (SAT0233)
Carmack, T., 513 (FRI0092)
Carmona, F.D., 1047 (AB0003)
Carmona, L., 196 (OP0340), 414 (THU0549), 520 (FRI0106), 735 (FRI0649), 736 (FRI0651), 918 (SAT0387), 925 (SAT0406), 1305 (AB0718), 1307 (AB0723)
Carmona, R., 933 (SAT0428)
Carmona, S., 1264 (AB0607)
Carnet, D., 425 (THU0580)
Caro Hernández, C., 1228 (AB0506), 1321 (AB0760)
Carotti, M., 1281 (AB0655)
Carpenter, L., 782 (SAT0040)
Carr, A., 1205 (AB0444)
Carr, B., 89 (OP0089)
Carranza Muleiro, R.A., 1286 (AB0668)
Carranza-Muleiro, A., 1282 (AB0657)
Carrara, C., 403 (THU0521)
Carrara, G., 236 (THU0095), 316 (THU0297), 562 (FRI0212), 730 (FRI0637), 1013 (SAT0631)
Carrasco, C., 326 (THU0326), 718 (FRI0607)
Carrasco Cubero, C., 1121 (AB0211), 1122 (AB0212)
Carrasco-Cubero, M., 569 (FRI0226)
Carreira, P., 290 (THU0227), 843 (SAT0191), 1047 (AB0003), 1286 (AB0669)
Carreira Roca, F.J., 187 (OP0318-PARE)
Carreiro, F., 715 (FRI0598)
Carreño, L., 1009 (SAT0621)
Carreras, E., 1386 (AB0948)
Carreto, P., 926 (SAT0410), 1184 (AB0388)
Carretta, R., 1076 (AB0086), 1318 (AB0753)
Carrié, D., 901 (SAT0342)
Carrier, M., 418 (THU0561)
Carrier, N., 496 (FRI0047)
Carriero, A., 895 (SAT0325)
Carrillo, S.M., 1343 (AB0815)
Carrillo-Vázquez, S.-M., 498 (FRI0052)
Carrión, I., 1181 (AB0381)
Carrión, M., 1128 (AB0229)
Carrion, O., 1275 (AB0637)
Carrión-Barberà, I., 307 (THU0273)
Carron, P., 62 (OP0026), 653 (FRI0440), 736 (FRI0650), 1305 (AB0716)
Carruthers, D., 409 (THU0536)
Carsons, S.E., 886 (SAT0302)
Carton, L., 425 (THU0580), 1470 (AB1185)
Carubbi, F., 69 (OP0044), 305 (THU0268), 721 (FRI0613), 873 (SAT0262), 880 (SAT0284), 891 (SAT0313)
Carvajal, P., 1102 (AB0158)
Carvajal Alegria, G., 1013 (SAT0632)
Carvalheiro, T., 894 (SAT0324)
Carvalho, F., 590 (FRI0274), 1206 (AB0445)
Carvalho, L.M., 76 (OP0061)
Carvalho, P., 1510 (SAT0718-HPR)
Carvalho, P.D., 528 (FRI0126)
Carvalho, S., 186 (OP0315)
Carvalho, T., 1080 (AB0096)
Casabella, A., 695 (FRI0540), 704 (FRI0569)
Casademont, J., 904 (SAT0351), 1386 (AB0948)
Casado, G., 440 (THU0619)
Casado Osorio, J.L., 696 (FRI0545), 697 (FRI0546), 701 (FRI0559)
Casado-Díaz, A., 1071 (AB0070)
Casal Moura, M., 1252 (AB0575)
Casal-Dominguez, M., 67 (OP0038)
Casale, R., 52 (OP0006)
Casanovas, A., 597 (FRI0293)
Cascão, R., 498 (FRI0051), 1080 (AB0096, AB0098)
Casciaro, E., 704 (FRI0568)
Casciaro, S., 704 (FRI0568), 1353 (AB0847)
Cascino, M., 187 (OP0320)
Cascino, M.D., 318 (THU0301), 593 (FRI0285), 857 (SAT0221), 865 (SAT0242), 868 (SAT0250)
Caselli, G., 1064 (AB0050)
Casey, K.A., 856 (SAT0220)
Casillas, M., 510 (FRI0087)
Casilli, O., 808 (SAT0105), 1327 (AB0773), 1483 (THU0743-HPR)
Casilli, O.E., 702 (FRI0563)
Caspi, D., 1095 (AB0138), 1118 (AB0203)
Cassone, G., 248 (THU0123), 1267 (AB0615, AB0616)
Castagné, B., 1297 (AB0696)
Castaneda, O., 1339 (AB0805)
Castañeda, S., 108 (OP0135), 139 (OP0209-HPR), 614 (FRI0336), 843 (SAT0191), 892 (SAT0316), 918 (SAT0387), 925 (SAT0406), 946 (SAT0458), 1084 (AB0108), 1107 (AB0172), 1305 (AB0718), 1307 (AB0723)
Castaneda, S., 1272 (AB0630)
Castañeda Sanz, S., 1472 (AB1192)
Castaneda-Sanchez, J.J., 1452 (AB1136)
Castañeda-Sanz, S., 251 (THU0134)
Castaño, A., 761 (FRI0715), 1456 (AB1146, AB1147)
Castaño, D., 1092 (AB0129)
Castaño, G., 1225 (AB0498)
Castaño, J., 1082 (AB0104), 1091 (AB0128)
Castaño, J.P., 648 (FRI0429)
Castelão, W., 1254 (AB0581)
Castelar-Pinheiro, G., 1160 (AB0320)
Castelino, M., 1087 (AB0115)
Castell, C., 1534 (AB1206-HPR)
Castell, S., 307 (THU0273), 1181 (AB0381)
Castellani, P., 1245 (AB0556)
Castellano Cuesta, J.A., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 1223 (AB0493), 1224 (AB0494), 1490 (THU0761-HPR)
Castellano-Cuesta, J.A., 1472 (AB1191)
Castellanos-Moreira, R.A., 817 (SAT0128), 1393 (AB0967)
Castelli, G., 670 (FRI0483)
Castellví, I., 1014 (SAT0635), 1047 (AB0003), 1305 (AB0717)
Castellvi, I., 914 (SAT0379), 1414 (AB1027)
Castiglioni, M.T., 1055 (AB0025)
Castillo, D., 904 (SAT0351), 1117 (AB0201), 1414 (AB1027)
Castillo, E., 266 (THU0172), 529 (FRI0127), 852 (SAT0210), 1441 (AB1103)
Castillo, M., 317 (THU0300), 330 (THU0336)
Castillo, R., 1213 (AB0466)
Castillo Dayer, P., 1041 (SAT0704)
Castillo-Ortiz, J.D., 1452 (AB1136)
Castrejón, I., 657 (FRI0451), 1307 (AB0724)
Castrejon, I., 385 (THU0472), 810 (SAT0109), 971 (SAT0516), 1129 (AB0231, AB0232), 1130 (AB0233), 1451 (AB1132), 1466 (AB1173)
Castro, A., 312 (THU0287), 1156 (AB0307)
Castro, F., 307 (THU0273), 1181 (AB0381)
Castro, I., 1102 (AB0158)
Castro, M., 504 (FRI0069), 926 (SAT0410)
Castro, M.C., 648 (FRI0429), 1184 (AB0388)
Castro, T.C.M., 76 (OP0061)
Castro Villegas, M.C., 975 (SAT0527)
Castro-Lopes, J., 1062 (AB0043)
Castro-Salomo, A., 1208 (AB0451)
Castro-Villegas, M.C., 350 (THU0380), 649 (FRI0431), 650 (FRI0434), 1268 (AB0619)
Catak, O., 455 (THU0658), 1462 (AB1162)
Catal, S., 1002 (SAT0601)
Catalano, N., 901 (SAT0341)
Catanoso, M., 323 (THU0316)
Catellvi, I., 904 (SAT0351)
Catlett, I., 859 (SAT0226)
Catoggio, L.J., 1333 (AB0789)
Catoni, M., 879 (SAT0282)
Catrina, A., 26 (SP0106), 212 (THU0036), 523 (FRI0113), 785 (SAT0048)
Catrina, A.I., 482 (FRI0006), 484 (FRI0013), 517 (FRI0100), 522 (FRI0111)
Catrina, F.M., 10 (SP0042)
Catrina, S.B., 484 (FRI0013)
Cattelaens, K., 198 (OP0345-PARE)
Cattelain-Lopez, E., 1448 (AB1123)
Cattoir, L., 763 (FRI0719)
Cauli, A., 535 (FRI0143), 975 (SAT0528)
Cauquil, C., 549 (FRI0180)
Cauvet, A., 85 (OP0081), 202 (THU0006)
Cauvin, A., 118 (OP0161), 648 (FRI0428)
Cavaco, M., 784 (SAT0046)
Cavagna, L., 305 (THU0268), 1272 (AB0630), 1281 (AB0656)
Cavagnoli, R., 1064 (AB0050)
Cavalcanti, N.G., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)

Cavallaro, A., 655 (FRI0446)
Cavalli, G., 90 (OP0092), 610 (FRI0325)
Cavazza, A., 131 (OP0193), 1248 (AB0564)
Cavazzana, I., 585 (FRI0261), 1207 (AB0448), 1225 (AB0497), 1272 (AB0630)
Cavill, C., 939 (SAT0442)
Cavillon, E., 440 (THU0619)
Çavuşoğlu, M., 1066 (AB0057)
Cawthon, P.M., 690 (FRI0525)
Cazalets, C., 1261 (AB0599)
Cazemier, L., 1482 (THU0737-HPR)
Cazenave, T., 1013 (SAT0631), 1425 (AB1060)
Cea-Calvo, L., 439 (THU0617), 550 (FRI0184), 556 (FRI0197), 736 (FRI0651)
Cebanu, M., 309 (THU0279), 884 (SAT0296), 1284 (AB0664)
Ceccarelli, F., 180 (OP0299), 204 (THU0013), 463 (THU0678), 470 (THU0696), 489 (FRI0027), 490 (FRI0028), 496 (FRI0045), 757 (FRI0705), 829 (SAT0158), 860 (SAT0228), 864 (SAT0241), 872 (SAT0260), 879 (SAT0281), 880 (SAT0283), 1007 (SAT0615), 1059 (AB0036), 1093 (AB0132), 1094 (AB0135, AB0136), 1099 (AB0150), 1209 (AB0456), 1214 (AB0467), 1449 (AB1125)
Cecchi, I., 194 (OP0336), 497 (FRI0048), 761 (FRI0716), 1450 (AB1130)
Cederlund, I., 172 (OP0281-PARE)
Cedola, F., 667 (FRI0477)
Cefai, E., 439 (THU0616), 1435 (AB1088)
Çefle, A., 327 (THU0329)
Cefle, A., 354 (THU0389), 598 (FRI0296), 634 (FRI0386)
Cekic, S., 722 (FRI0616)
Cekmece, S., 1496 (FRI0736-HPR), 1538 (AB1218-HPR)
Célia, H., 293 (THU0236)
Celik, A.F., 331 (THU0339), 618 (FRI0348)
Celik, A.M., 323 (THU0317), 618 (FRI0348)
Çelik, S., 716 (FRI0600), 1170 (AB0350), 1360 (AB0868)
Çeliker, R., 1380 (AB0927)
Celis, R., 128 (OP0185), 1133 (AB0243)
Cengiz Elcioglu, B., 1420 (AB1046)
Cepek, P., 179 (OP0297)
Cerbelli, B., 888 (SAT0305), 1465 (AB1170)
Cercas, M.J., 441 (THU0622)
Cerchiaro, M., 327 (THU0328)
Cerdà, D., 1005 (SAT0610)
Cerda, O., 440 (THU0619)
Ceribelli, A., 620 (FRI0353)
Cerinic, M., 1284 (AB0662)
Cerón, C., 1190 (AB0404)
Ceron-Gutierrez, L., 215 (THU0043)
Cerovec, M., 592 (FRI0282), 883 (SAT0291)
Cerpa Cruz, S., 1276 (AB0641), 1450 (AB1128)
Cerpa-Cruz, S., 117 (OP0158), 500 (FRI0058), 1199 (AB0427), 1446 (AB1116)
Cerqueira, M., 607 (FRI0318), 637 (FRI0394), 736 (FRI0652), 1011 (SAT0627), 1015 (SAT0637), 1275 (AB0636)
Cerri, S., 248 (THU0123)
Cervantes, E., 843 (SAT0191)
Cervantes Pérez, E.C., 1159 (AB0316)
Cervera, R., 150 (OP0231), 418 (THU0561), 426 (THU0584)
Cesak, M., 906 (SAT0358)
Cesak, P., 638 (FRI0399), 906 (SAT0358), 1280 (AB0653), 1287 (AB0671)
Cesana, D., 126 (OP0179)
Cesselli, D., 1101 (AB0156)
Cesta, A., 194 (OP0337-HPR), 531 (FRI0132)
Cetin, P., 322 (THU0314)
Cevik, R., 637 (FRI0396), 1317 (AB0751), 1320 (AB0757), 1324 (AB0767)
Ceylan, S., 1215 (AB0471)
Cha, H.-S., 612 (FRI0331), 646 (FRI0422), 749 (FRI0685), 1371 (AB0901)
Cha, S.J., 430 (THU0594), 1473 (AB1193)
Chaabani, I., 1353 (AB0848)
Chaabouni, D., 1353 (AB0849)
Chaabouni, H., 1346 (AB0826)
Chabrand, P., 744 (FRI0671)
Chacon, R., 1342 (AB0813)
Chacón-Díaz, R., 1339 (AB0805)
Chacón-García, J., 927 (SAT0412), 1554 (PARE0007)
Chadha-Boreham, H., 65 (OP0034)
Chadli, L., 621 (FRI0356)
Chadwick, L., 1251 (AB0573)
Chakera, A., 1241 (AB0542)
Chakr, R., 1107 (AB0174), 1278 (AB0645)
Chakr, R.M.D.S., 628 (FRI0371), 1508 (FRI0768-HPR)
Chakravarty, E., 57 (OP0017)
Chakravarty, S.D., 944 (SAT0453), 950 (SAT0465)
Chalcarz, I., 777 (SAT0025)
Chalem, P., 252 (THU0137)
Chales, G., 258 (THU0152), 811 (SAT0112)
Chalmeta Verdejo, I., 291 (THU0229), 441 (THU0623), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1349 (AB0837), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Chalom, E., 405 (THU0525)
Chalouhi El Khouri, E., 824 (SAT0146)
Chaltsev, B., 1237 (AB0531)
Chamizo-Carmona, E., 1121 (AB0211), 1122 (AB0212)
Chammakhi, M., 1417 (AB1038)
Chamorro, A.J., 597 (FRI0293)
Chamorro Fernández, J., 897 (SAT0332)
Champlin, R.E., 82 (OP0075)
Champsaur, P., 744 (FRI0671), 1442 (AB1108)
Chamurlieva, M., 956 (SAT0478), 1327 (AB0775)
Chan, C.C., 152 (OP0237)
Chan, C.M., 1493 (THU0768-HPR)
Chan, C.W.S., 919 (SAT0390)
Chan, D.W., 1055 (AB0024)
Chan, E., 780 (SAT0036)
Chan, E.K., 341 (THU0360), 1295 (AB0692)
Chan, J., 916 (SAT0384), 933 (SAT0428)
Chan, K., 303 (THU0263)
Chanakya, K., 1277 (AB0644)
Chanchek, N., 58 (OP0020)
Chandra, P., 1309 (AB0728)
Chandran, V., 98 (OP0111), 688 (FRI0522), 957 (SAT0481)
Chandrupatla, D.M.S.H., 494 (FRI0041), 1075 (AB0082)
Chang, H.-D., 21 (SP0086), 37 (SP0154)
Chang, P., 856 (SAT0219), 863 (SAT0236)
Chang, S.H., 1185 (AB0392)
Chang, Y.-L., 87 (OP0085)
Chang, Y.-S., 631 (FRI0381), 889 (SAT0309)
Chang, Y.J., 1437 (AB1094)
Chanroux, L., 1505 (FRI0760-HPR)
Chanson, N., 1256 (AB0588)
Chanson, P., 289 (THU0225)
Chanudet, E., 118 (OP0161)
Chao, W.-C., 82 (OP0074), 751 (FRI0691)
Chaplin, N., 541 (FRI0159)
Chapman, D., 268 (THU0175)
Chapman, M.J., 852 (SAT0209)
Chapman, V., 127 (OP0183)
Chapurlat, R., 7 (SP0026), 54 (OP0010), 178 (OP0294)
Chara, B., 1470 (AB1184)
Chara, J., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Charalampidis, M., 643 (FRI0412), 723 (FRI0619)
Charbonneau, M., 481 (FRI0004)
Charland, K., 349 (THU0378), 558 (FRI0201)
Charles, B., 1330 (AB0781)
Charles, J., 624 (FRI0363)
Charles-Schoeman, C., 271 (THU0185), 1034 (SAT0686)
Charlet, A., 172 (OP0280-PARE)
Charlton, R., 685 (FRI0514)
Charpentier, A., 417 (THU0558)
Charrier, C., 128 (OP0184)
Chartier, M., 577 (FRI0245), 1141 (AB0267), 1193 (AB0412)
Chary-Valckenaere, I., 258 (THU0152), 583 (FRI0256), 811 (SAT0112), 1383 (AB0938)
Chast, F., 831 (SAT0163)
Chastek, B., 346 (THU0371), 945 (SAT0456)
Chatelus, E., 106 (OP0128)
Chatham, W., 150 (OP0232)
Chatzidionysiou, K., 69 (OP0045), 341 (THU0361), 517 (FRI0100), 567 (FRI0221), 686 (FRI0518), 1027 (SAT0669)
Chatziioannou, M., 1560 (AB1252-PARE)
Chatzimichailidou, S., 542 (FRI0161)
Chaudhari, P., 1074 (AB0079)
Chaudier, B., 753 (FRI0696)
Chaudry, O., 247 (THU0122)
Chauhan, K., 378 (THU0450)
Chaurasia, S., 320 (THU0307)
Chaussade, S., 831 (SAT0163)
Chauveau, D., 188 (OP0321)
Chauveheid, M.-P., 187 (OP0319)
Chauvin, N.A., 469 (THU0693), 471 (THU0697)
Chauvin, P., 461 (THU0675)
Chavarria-Avila, E., 806 (SAT0100), 1075 (AB0083), 1169 (AB0345)
Chavez-Corrales, J., 824 (SAT0146)
Chawla, R., 491 (FRI0032)
Che, H., 701 (FRI0561)
Cheah, B., 151 (OP0234)
Cheah, C.K., 1140 (AB0262)
Chebil, E., 1353 (AB0848, AB0849)
Checchio, T., 277 (THU0196)
Chehab, G., 442 (THU0625), 1449 (AB1127)
Chehab, S., 931 (SAT0423)
Cheikh, M., 1348 (AB0831, AB0832, AB0833), 1349 (AB0834)
Cheikhrouhou, S., 1377 (AB0919)
Chekili, S., 1371 (AB0902), 1394 (AB0969), 1417 (AB1038)
Cheleschi, S., 966 (SAT0503), 1343 (AB0816)
Chen, B., 192 (OP0331)
Chen, C., 94 (OP0102), 575 (FRI0240), 1092 (AB0130)
Chen, C.-H., 1408 (AB1009)
Chen, C.-W., 892 (SAT0318)
Chen, D., 298 (THU0250), 1222 (AB0490)
Chen, D.-Y., 82 (OP0074), 751 (FRI0691), 1036 (SAT0690), 1503 (FRI0755-HPR)
Chen, F.Y., 810 (SAT0110), 1372 (AB0905)
Chen, G., 116 (OP0155), 250 (THU0130), 1226 (AB0502)
Chen, H., 324 (THU0318), 543 (FRI0163), 748 (FRI0681), 1141 (AB0266)
Chen, H.-C., 1408 (AB1009)
Chen, H.-H., 82 (OP0074), 751 (FRI0691), 1036 (SAT0690)
Chen, J., 69 (OP0043), 509 (FRI0084), 872 (SAT0261), 1144 (AB0274), 1464 (AB1167)
Chen, J.-Q., 1094 (AB0137)
Chen, J.-S., 360 (THU0403), 366 (THU0419)
Chen, K., 1081 (AB0100)
Chen, L., 158 (OP0248), 512 (FRI0090), 513 (FRI0092), 527 (FRI0124), 670 (FRI0484), 1335 (AB0794)
Chen, L.-X., 373 (THU0439)
Chen, M., 217 (THU0048), 268 (THU0176)
Chen, N., 829 (SAT0159), 855 (SAT0217)
Chen, P., 1260 (AB0596)
Chen, Q., 63 (OP0028), 108 (OP0132), 494 (FRI0041), 947 (SAT0459), 1020 (SAT0650)
Chen, R., 1314 (AB0743), 1325 (AB0771)
Chen, S., 122 (OP0168), 654 (FRI0444), 682 (FRI0510), 759 (FRI0710), 822 (SAT0142), 1081 (AB0099), 1230 (AB0513), 1234 (AB0523), 1241 (AB0543)
Chen, W., 324 (THU0318), 777 (SAT0027), 1103 (AB0163)
Chen, W.-S., 631 (FRI0381)
Chen, W.J., 1084 (AB0109)
Chen, X., 777 (SAT0027), 797 (SAT0077), 1081 (AB0099), 1148 (AB0286), 1219 (AB0482)
Chen, Y.-C., 690 (FRI0526), 708 (FRI0580), 709 (FRI0581), 1356 (AB0859)
Chen, Y.-L., 279 (THU0201)
Chen, Y.-M., 82 (OP0074), 751 (FRI0691)
Chen, Z., 123 (OP0171), 543 (FRI0163)
Chenevier-Gobeaux, C., 187 (OP0319)

Cheng, B., 845 (SAT0194)
Cheng, C.W., 589 (FRI0271)
Cheng, J., 555 (FRI0194), 998 (SAT0591)
Cheng, L.E., 151 (OP0234)
Cheng, M., 769 (SAT0003)
Cheng, T.H., 689 (FRI0524), 796 (SAT0073), 956 (SAT0479)
Cheng, Y.-W., 713 (FRI0594)
Cheon, Y.-H., 1454 (AB1140)
Cheong, S.Y., 136 (OP0203), 137 (OP0204), 834 (SAT0169)
Cheour, I., 1536 (AB1214-HPR)
Chereau, C., 182 (OP0307)
Cherian, S., 423 (THU0575)
Cherif, E., 1251 (AB0574)
Cherkasova, M., 254 (THU0142), 1404 (AB0998)
Cherkasova, M.V., 251 (THU0132), 1226 (AB0500)
Chernajovsky, Y., 214 (THU0041)
Chernoff, D., 232 (THU0087), 517 (FRI0100)
Chernyaeva, E., 560 (FRI0208)
Chernykh, E., 771 (SAT0008)
Chessa, D., 945 (SAT0454), 954 (SAT0473)
Chetcuti Zammit, S., 419 (THU0564)
Cheu, M., 187 (OP0320)
Cheung, B.M.Y., 936 (SAT0434)
Cheung, P., 816 (SAT0124), 1447 (AB1119)
Cheung, S., 1023 (SAT0657)
Cheung, T.T., 936 (SAT0434)
Cheung, Y.S., 1493 (THU0768-HPR)
Chevaisrakul, P., 1298 (AB0700)
Chevalier, N., 1100 (AB0153)
Chevalier, P., 380 (THU0456)
Chevalier, X., 43 (SP0180), 965 (SAT0501)
Chevalier, X.-J., 188 (OP0323)
Chew, L.C., 1026 (SAT0666)
Chew Graham, C.A., 438 (THU0614)
Chew-Graham, C.A., 973 (SAT0521), 1174 (AB0359), 1433 (AB1081), 1552 (PARE0002)
Chhabra, A., 939 (SAT0441), 947 (SAT0461)
Chhibar, P.S., 421 (THU0570), 1354 (AB0852)
Chialà, A., 1268 (AB0618)
Chiarlitti, N., 545 (FRI0171), 1176 (AB0366)
Chiba, A., 141 (OP0214), 1060 (AB0038), 1090 (AB0125), 1095 (AB0139)
Chiba, K., 738 (FRI0656), 1097 (AB0146)
Chicco, D., 621 (FRI0358)
Chiche, L., 108 (OP0134)
Chieffo, R., 1118 (AB0202)
Chighizola, C.B., 70 (OP0046), 437 (THU0611), 1439 (AB1099)
Chijiwa, T., 536 (FRI0145), 809 (SAT0107), 1127 (AB0225), 1349 (AB0835)
Chikina, M., 1019 (SAT0646)
Chikuda, H., 493 (FRI0036), 1203 (AB0439)
Chila-M., L., 252 (THU0137)
Chimenti, M.S., 484 (FRI0012), 667 (FRI0477), 1193 (AB0410)
Chinchilla, S.P., 368 (THU0426), 381 (THU0458), 1363 (AB0878)
Chino, K., 424 (THU0577), 1399 (AB0984)
Chinoy, H., 98 (OP0110), 912 (SAT0374)
Chiostri, M., 633 (FRI0384), 1269 (AB0622), 1270 (AB0623)
Chiowchanwisawakit, P., 930 (SAT0420), 1298 (AB0700)
Chipping, J., 803 (SAT0092)
Chipping, J.R., 243 (THU0112)
Chirico, C., 86 (OP0082), 894 (SAT0323)
Chirieac, R., 825 (SAT0148), 1269 (AB0620)
Chisholm, D., 59 (OP0021)
Chisholm, M., 241 (THU0107)
Chislari, L., 1199 (AB0426)
Chitale, S., 786 (SAT0049)
Chizh, K., 1240 (AB0541)
Chizzolini, C., 21 (SP0084), 626 (FRI0369)
Cho, C.-S., 890 (SAT0311)
Cho, J., 369 (THU0427)
Cho, N.H., 999 (SAT0593)
Cho, S., 1100 (AB0152)
Cho, S.-K., 430 (THU0594), 1045 (SAT0714), 1447 (AB1121), 1473 (AB1193)
Chodick, G., 169 (OP0273), 796 (SAT0074)
Choe, H., 1165 (AB0334), 1166 (AB0335)
Choe, J.-Y., 301 (THU0257), 552 (FRI0187), 1162 (AB0326), 1229 (AB0508)
Choe, J.Y., 1185 (AB0392)
Choi, D., 1315 (AB0744)
Choi, E.-H., 1131 (AB0236)
Choi, H., 165 (OP0263), 374 (THU0442), 383 (THU0464)
Choi, H.J., 58 (OP0020), 369 (THU0427)
Choi, H.K., 165 (OP0264), 166 (OP0266), 360 (THU0405), 362 (THU0410), 373 (THU0440), 381 (THU0460)
Choi, I.A., 877 (SAT0274)
Choi, J.-E., 518 (FRI0103)
Choi, J.R., 1406 (AB1005), 1437 (AB1092)
Choi, K., 1355 (AB0854)
Choi, M., 217 (THU0049), 911 (SAT0372)
Choi, S., 381 (THU0460), 858 (SAT0225), 870 (SAT0255)
Choi, S.J., 604 (FRI0311), 1037 (SAT0693), 1130 (AB0234), 1452 (AB1134)
Choi, S.T., 385 (THU0471), 692 (FRI0533), 1355 (AB0855), 1413 (AB1025)
Choi, S.W., 1222 (AB0491)
Choi, Y.Y., 1447 (AB1121)
Chollet, T., 901 (SAT0342)
Chong, G., 348 (THU0377)
Chopra, A., 146 (OP0224), 1510 (SAT0718-HPR), 1541 (AB1228-HPR)
Chopyak, V., 1290 (AB0677)
Choquette, D., 571 (FRI0230), 845 (SAT0195), 931 (SAT0423), 1188 (AB0397)
Chotard, E., 367 (THU0424)
Chou, B., 1432 (AB1077)
Chouc, P.-Y., 753 (FRI0696)
Chouk, M., 959 (SAT0486)
Chouri, E., 1089 (AB0121)
Chouri, E.C., 1109 (AB0178)
Chouvardas, P., 500 (FRI0059)
Chow, V., 1181 (AB0380)
Chowalloor, P., 960 (SAT0487)
Chowdry, A.M., 1453 (AB1138)
Choy, E., 31 (SP0125), 110 (OP0139-HPR), 269 (THU0180), 470 (THU0695), 525 (FRI0118), 818 (SAT0132), 847 (SAT0199), 957 (SAT0480), 1050 (AB0011), 1301 (AB0707)
Choy, E.H., 148 (OP0230)
Choy, E.H.S., 208 (THU0025), 1173 (AB0358)
Chretien, P., 508 (FRI0081)
Christ, L.A., 718 (FRI0606)
Christensen, K.R., 1068 (AB0061)
Christensen, R., 161 (OP0254-HPR), 166 (OP0267), 173 (OP0283), 196 (OP0340), 456 (THU0662), 463 (THU0677), 470 (THU0695), 660 (FRI0460), 737 (FRI0654), 818 (SAT0132), 1332 (AB0786)
Christensen, R.D., 433 (THU0601)
Christensen, T.G., 1068 (AB0062)
Christiansen, C.H., 120 (OP0165)
Christodoulou, C., 1437 (AB1093)
Christophe, T., 126 (OP0180)
Christopher-Stine, L., 67 (OP0038)
Christopoulos, P.F., 210 (THU0028), 1088 (AB0117)
Chrysidis, S., 553 (FRI0190), 583 (FRI0256)
Chtourou, M., 1311 (AB0734)
Chu, S.-J., 1408 (AB1009)
Chu Miow Lin, D., 1448 (AB1123)
Chua, C., 1447 (AB1119)
Chua, I., 637 (FRI0395)
Chua, J., 971 (SAT0516), 1129 (AB0231), 1466 (AB1173)
Chudek, J., 1502 (FRI0752-HPR)
Chudinov, A., 611 (FRI0328)
Chumasova, O., 771 (SAT0008), 1056 (AB0027)
Chun, G., 346 (THU0371), 348 (THU0376), 678 (FRI0501), 945 (SAT0456)
Chung, H.W., 718 (FRI0605)
Chung, H.Y., 919 (SAT0390)
Chung, J.B., 151 (OP0234)
Chung, L., 105 (OP0126)
Chung, M.K., 977 (SAT0533)
Chung, V., 998 (SAT0591)
Chung, W.T., 1083 (AB0107)
Church, J., 9 (SP0033)
Churchman, S.M., 959 (SAT0485)
Chyzheuskaya, I., 398 (THU0508), 1389 (AB0956)
Ciabatti, E., 320 (THU0308)
Ciancio, G., 954 (SAT0473), 1127 (AB0227)
Ciarka, A., 1275 (AB0638)
Ciccacci, C., 204 (THU0013), 1007 (SAT0615)
Ciccarese, M., 704 (FRI0568)
Ciccia, F., 131 (OP0193), 180 (OP0299), 183 (OP0309), 291 (THU0231), 721 (FRI0613), 777 (SAT0025)
Ciciarello, F., 329 (THU0334)
Cicuttini, F., 122 (OP0169), 193 (OP0334), 450 (THU0647), 471 (THU0699), 960 (SAT0489), 962 (SAT0493), 986 (SAT0555)
Cid, M., 1252 (AB0575)
Cid, M.C., 27 (SP0110), 107 (OP0130, OP0131), 610 (FRI0324)
Cidon, M., 448 (THU0641)
Ciechomska, M., 489 (FRI0026)
Cieślak, D., 141 (OP0216)
Cifani, N., 879 (SAT0282)
Cifrian-Martinez, J., 1116 (AB0197)
Ciftci, V., 640 (FRI0404), 902 (SAT0344)
Cijevschi Prelipcean, C., 1411 (AB1019)
Cikes, N., 431 (THU0596)
Cılesızoglu, N., 1121 (AB0209)
Cillero-Pastor, B., 977 (SAT0531)
Cimaz, R., 77 (OP0062), 1389 (AB0957)
Cimino, L., 212 (THU0035), 411 (THU0540), 1054 (AB0022), 1248 (AB0564)
Cimmino, M.A., 378 (THU0451), 728 (FRI0632)
Cinar, F.I., 352 (THU0385), 412 (THU0544), 1297 (AB0698)
Cinar, M., 352 (THU0385), 354 (THU0389), 412 (THU0544), 1297 (AB0698)
Ciobanu, G., 309 (THU0279)
Cioffi, E., 446 (THU0636)
Cioffi, G., 805 (SAT0097)
Ciofu, C., 1032 (SAT0681), 1179 (AB0376)
Cipinova, Z., 1379 (AB0926)
Cipolletta, E., 1358 (AB0863)
Cipriani, P., 291 (THU0231), 721 (FRI0613), 777 (SAT0025), 880 (SAT0284), 891 (SAT0313)
Cipriano, E., 204 (THU0013), 470 (THU0696), 757 (FRI0705), 879 (SAT0281), 1007 (SAT0615), 1449 (AB1125)
Cîrciumaru, A., 212 (THU0036)
Cirone, C., 1012 (SAT0630)
Ciurea, A., 130 (OP0189), 267 (THU0174), 335 (THU0347), 816 (SAT0125)
Ciurtin, C., 253 (THU0138), 726 (FRI0627), 1024 (SAT0659), 1100 (AB0152)
Civit, A., 1539 (AB1222-HPR)
Claassen, A., 1476 (THU0721-HPR)
Claes, K., 1481 (THU0735-HPR)
Claeys, K., 636 (FRI0393)
Clair, W.St., 187 (OP0320)
Clanchy, F., 770 (SAT0005)
Clarimundo, V.S., 502 (FRI0066)
Clark, A.R., 125 (OP0178)
Clark, K.E.N., 401 (THU0516)
Clark, P., 1343 (AB0815)
Clarke, C., 1477 (THU0723-HPR)
Clarke, F., 178 (OP0296)
Clarke, S., 288 (THU0222)
Clarke-Cornwell, A.M., 7 (SP0023)
Clarkson, K., 1442 (AB1107)
Claudepierre, P., 334 (THU0346), 337 (THU0353), 339 (THU0356, THU0357), 350 (THU0382), 388 (THU0482), 389 (THU0483), 662 (FRI0465), 665 (FRI0472), 917 (SAT0386), 945 (SAT0455), 1013 (SAT0632), 1296 (AB0694), 1301 (AB0708), 1303 (AB0712), 1330 (AB0781)
Clausen, J., 119 (OP0163-PARE)
Clauson, V., 370 (THU0432)
Clavijo-Cornejo, D., 205 (THU0016), 1067 (AB0059)
Clay, E., 1051 (AB0015)
Clayton, K.V., 449 (THU0645)
Clayton, P., 933 (SAT0426), 1180 (AB0377)
Clément, A., 754 (FRI0699), 1033 (SAT0684), 1034 (SAT0685), 1049 (AB0007)
Clement-Lacroix, P., 118 (OP0161), 126 (OP0180), 648 (FRI0428)

Clemente, D., 400 (THU0514), 1386 (AB0947)
Clemente, G., 76 (OP0061)
Clements, P.J., 87 (OP0085), 104 (OP0124)
Clerson, P., 382 (THU0461, THU0463)
Cleveland, J., 370 (THU0431), 752 (FRI0692), 1452 (AB1135)
Clifton, B.I.O., 470 (THU0695), 818 (SAT0132)
Close, D., 192 (OP0331), 564 (FRI0216)
Clowse, M.E.B., 540 (FRI0157), 548 (FRI0179), 813 (SAT0119), 950 (SAT0466)
Cluxton, D., 773 (SAT0013)
Cluzel, P., 108 (OP0134)
Coady, D., 1470 (AB1186)
Coates, L., 98 (OP0112)
Coates, L.C., 35 (SP0143), 97 (OP0108), 668 (FRI0479), 679 (FRI0502, FRI0503), 682 (FRI0509), 688 (FRI0521), 939 (SAT0441), 947 (SAT0461), 948 (SAT0462), 949 (SAT0464), 951 (SAT0469), 1326 (AB0772)
Coban, S., 321 (THU0311)
Cobanoglu, E., 791 (SAT0063)
Cobb, J., 177 (OP0291)
Cobeta, J.C., 685 (FRI0515)
Cobilinschi, C., 457 (THU0665), 1278 (AB0647), 1433 (AB1082), 1447 (AB1120)
Cobo, T., 633 (FRI0385), 1270 (AB0625)
Cobo-Ibáñez, T., 908 (SAT0363), 1244 (AB0553)
Cocchiara, E., 634 (FRI0388), 1272 (AB0629)
Cochener, B., 309 (THU0278)
Cochet, C., 171 (OP0278-PARE)
Cochran, S., 181 (OP0304)
Cochrane, A., 1434 (AB1083), 1521 (SAT0748-HPR)
Cockell, S., 295 (THU0242)
Codd, Y., 1542 (AB1230-HPR)
Codina Guinó, O., 1418 (AB1039)
Codreanu, C., 567 (FRI0221), 850 (SAT0206), 1018 (SAT0644), 1180 (AB0378)
Codullo, V., 891 (SAT0315), 1272 (AB0630), 1281 (AB0656)
Coeck, C., 642 (FRI0411)
Coeleveld, K., 482 (FRI0008), 483 (FRI0010), 968 (SAT0508), 1068 (AB0061)
Coello, C., 1420 (AB1045)
Coghlan, G., 65 (OP0034), 898 (SAT0334), 1266 (AB0613)
Cogliano, A., 1002 (SAT0602)
Cogolludo, Á., 892 (SAT0316)
Cohen, A., 84 (OP0078), 297 (THU0248), 886 (SAT0300)
Cohen, A.D., 332 (THU0342), 619 (FRI0350)
Cohen, C., 845 (SAT0194)
Cohen, I.R., 1407 (AB1007), 1462 (AB1163)
Cohen, M., 345 (THU0369), 523 (FRI0115)
Cohen, O., 355 (THU0392)
Cohen, S., 553 (FRI0189), 834 (SAT0171)
Cohen-Solal, M., 53 (OP0007), 212 (THU0034), 216 (THU0046)
Coiffier, G., 1261 (AB0599)
Coimbra, I., 1339 (AB0805)
Coksevim, N.H., 1298 (AB0699)
Colaci, M., 634 (FRI0388), 1267 (AB0615), 1272 (AB0629)
Colaço, C.B., 1545 (AB1241-HPR)
Colafrancesco, S., 411 (THU0541), 888 (SAT0305), 1465 (AB1170)
Colasanti, T., 180 (OP0299), 470 (THU0696), 489 (FRI0027), 490 (FRI0028), 860 (SAT0228), 880 (SAT0283), 1093 (AB0132), 1099 (AB0150), 1465 (AB1170)
Coldivar, A., 1161 (AB0321)
Coletto, L.A., 725 (FRI0624)
Colia, R., 629 (FRI0373, FRI0374), 895 (SAT0325)
Collado, M.V., 440 (THU0619), 1018 (SAT0645)
Collado, P., 24 (SP0096), 400 (THU0514), 406 (THU0527), 583 (FRI0256), 1015 (SAT0636)
Collado Ramos, P., 735 (FRI0649)
Collantes, E., 194 (OP0336), 492 (FRI0035), 504 (FRI0069), 736 (FRI0651), 918 (SAT0387), 926 (SAT0410), 1078 (AB0092), 1082 (AB0104), 1091 (AB0128), 1184 (AB0388), 1307 (AB0723)
Collantes Estévez, E., 917 (SAT0385), 975 (SAT0527)
Collantes Estevez, E., 258 (THU0151), 700 (FRI0555), 1143 (AB0270)
Collantes-Estévez, E., 350 (THU0380), 650 (FRI0434), 942 (SAT0447), 1268 (AB0619)
Collantes-Estevez, E., 153 (OP0238), 287 (THU0218), 441 (THU0624), 497 (FRI0048), 622 (FRI0360), 648 (FRI0429), 649 (FRI0431), 658 (FRI0452), 919 (SAT0391), 927 (SAT0412), 1091 (AB0127), 1559 (PARE0020)
Collee, G., 793 (SAT0067)
Collier, A., 474 (THU0707)
Collier, D., 239 (THU0102)
Collins, D., 1553 (PARE0004)
Collins, E.C., 983 (SAT0548)
Collins, M.P., 319 (THU0306)
Collinson, N., 107 (OP0131)
Colloca, L., 1539 (AB1223-HPR)
Colombo, B.M., 641 (FRI0407)
Colombo, E., 496 (FRI0046)
Colombo, M., 891 (SAT0315)
Colombres, F., 670 (FRI0483), 933 (SAT0427)
Colquechambi, A.M., 1434 (AB1085)
Colunga Argüelles, D., 639 (FRI0402)
Colunga-Pedraza, I., 586 (FRI0264)
Colunga-Pedraza, I.J., 253 (THU0140), 534 (FRI0141), 1118 (AB0204), 1119 (AB0205), 1156 (AB0309), 1157 (AB0310)
Çomak, E., 1392 (AB0965)
Comak, E., 397 (THU0506)
Comaneshter, D., 84 (OP0078), 297 (THU0248), 332 (THU0342), 619 (FRI0350), 886 (SAT0300)
Comarmond, C., 108 (OP0134), 776 (SAT0023), 1247 (AB0563)
Comas, D., 126 (OP0180)
Combalia, A., 706 (FRI0573)
Combe, B., 113 (OP0146), 131 (OP0192), 135 (OP0201), 158 (OP0247), 231 (THU0084), 235 (THU0093), 428 (THU0588, THU0589), 510 (FRI0086), 701 (FRI0561), 786 (SAT0050), 804 (SAT0094), 843 (SAT0189), 1159 (AB0315), 1186 (AB0395)
Combes, C., 212 (THU0034), 216 (THU0046)
Combier, A., 130 (OP0191)
Cometi, L., 915 (SAT0380)
Comsa, C., 1151 (AB0294)
Conaghan, P., 159 (OP0250), 174 (OP0284), 240 (THU0104)
Conaghan, P.G., 96 (OP0107), 119 (OP0164), 268 (THU0175), 355 (THU0393), 727 (FRI0630), 949 (SAT0463), 1010 (SAT0624), 1026 (SAT0666), 1293 (AB0685)
Concannon, T., 449 (THU0644)
Concepcion, A., 1020 (SAT0649)
Concha, A., 502 (FRI0063)
Conde, C., 503 (FRI0068)
Conde, M., 186 (OP0315)
Condé Da Silva Fraga, E., 1186 (AB0395)
Condell, J., 460 (THU0671), 1530 (AB1196-HPR)
Conesa, F.M., 128 (OP0186)
Conesa, M., 330 (THU0336)
Conforti, M.L., 633 (FRI0384)
Cong, L., 738 (FRI0657)
Conigliaro, P., 437 (THU0611), 484 (FRI0012), 667 (FRI0477), 1193 (AB0410), 1439 (AB1099)
Conijn, N.F.L., 1421 (AB1047)
Conklin, J., 1025 (SAT0662)
Connell, C.A., 272 (THU0186)
Connolly, J., 460 (THU0671), 1530 (AB1196-HPR)
Connolly, S., 566 (FRI0219), 1135 (AB0248), 1192 (AB0408), 1455 (AB1143)
Conort, O., 831 (SAT0163)
Conrad, K., 461 (THU0674)
Conrozier, T., 388 (THU0480)
Consolaro, A., 17 (SP0068)
Cônsolo, R.T., 386 (THU0476)
Consortium, G.M.C., 500 (FRI0059)
Constantin, A., 343 (THU0364), 530 (FRI0131), 770 (SAT0006), 1299 (AB0703)
Constantin, T., 133 (OP0197), 1390 (AB0958)
Constantine, S., 105 (OP0126)
Constantinescu, C., 304 (THU0266), 876 (SAT0271), 881 (SAT0288), 1025 (SAT0664), 1221 (AB0487), 1278 (AB0646, AB0647), 1428 (AB1068), 1460 (AB1158)
Constantinescu, T., 626 (FRI0368), 1264 (AB0608)
Contero, C., 372 (THU0437)
Conti, F., 180 (OP0299), 204 (THU0013), 329 (THU0334), 463 (THU0678), 470 (THU0696), 489 (FRI0027), 490 (FRI0028), 496 (FRI0045), 757 (FRI0705), 829 (SAT0158), 860 (SAT0228), 864 (SAT0241), 867 (SAT0248), 872 (SAT0260), 879 (SAT0281), 880 (SAT0283), 1007 (SAT0615), 1059 (AB0036), 1093 (AB0132), 1094 (AB0135, AB0136), 1099 (AB0150), 1209 (AB0456), 1214 (AB0467), 1449 (AB1125)
Contini, P., 1110 (AB0183)
Contreras-Yáñez, I., 1117 (AB0200), 1147 (AB0282)
Contreras-Yañez, I., 1155 (AB0305)
Conversano, F., 704 (FRI0568), 1353 (AB0847)
Convery, H., 773 (SAT0013)
Conway, R., 321 (THU0312)
Cook, R., 98 (OP0111), 688 (FRI0522)
Cooles, F.A.H., 1470 (AB1186)
Cooper, C., 760 (FRI0713), 933 (SAT0426), 1440 (AB1102)
Cooper, R.G., 912 (SAT0374)
Cooper, V., 1433 (AB1081)
Cope, A.P., 178 (OP0296)
Coq, M., 1463 (AB1164)
Coquerelle, P., 334 (THU0346), 339 (THU0356, THU0357), 388 (THU0482), 389 (THU0483), 665 (FRI0472), 1296 (AB0694)
Coral Cristado, C., 991 (SAT0568)
Corallo, C., 86 (OP0082), 894 (SAT0323), 1111 (AB0185)
Corander, J., 765 (FRI0725), 1043 (SAT0709)
Çorba, B.S., 327 (THU0329)
Corbanese, S., 270 (THU0181)
Corbera-Bellalta, M., 610 (FRI0324)
Corcoran, O., 1434 (AB1083), 1521 (SAT0748-HPR)
Cordeiro, A., 533 (FRI0138), 1254 (AB0581), 1264 (AB0607)
Cordeiro, I., 1254 (AB0581), 1264 (AB0607)
Cordeiro, J.V., 441 (THU0622)
Cordell, H.J., 200 (THU0003)
Cordero, M., 414 (THU0549), 420 (THU0567)
Cordero Coma, M., 75 (OP0059)
Cordero-Coma, M., 326 (THU0326), 717 (FRI0602)
Cordingley, L., 265 (THU0168), 275 (THU0192), 519 (FRI0105)
Cordtz, R., 96 (OP0106), 159 (OP0251)
Cordtz, R.L., 226 (THU0072)
Coret, V., 1175 (AB0362), 1443 (AB1109)
Corinaldesi, C., 1057 (AB0029, AB0030)
Cormier, G., 335 (THU0349)
Cornec, D., 67 (OP0040), 109 (OP0137), 187 (OP0320), 309 (THU0278), 591 (FRI0278), 605 (FRI0314), 881 (SAT0286), 1215 (AB0469)
Cornillet, M., 509 (FRI0085), 792 (SAT0065)
Cornish, G.H., 178 (OP0296)
Corominas, H., 946 (SAT0458), 1005 (SAT0610), 1014 (SAT0635)
Corona-Meraz, F., 806 (SAT0100), 1075 (AB0083), 1169 (AB0345)
Corona-Meraz, F.-I., 1164 (AB0330)
Corona-Sanchez, E., 1155 (AB0304)
Corr, M., 757 (FRI0706)
Corrado, A., 437 (THU0611), 629 (FRI0373, FRI0374), 895 (SAT0325), 1106 (AB0171), 1439 (AB1099)
Corrales, A., 614 (FRI0336), 742 (FRI0666), 1084 (AB0108)
Corrales-Martinez, A., 1116 (AB0197)
Corrao, S., 901 (SAT0341)
Correale, M., 895 (SAT0325)
Correia, R.M., 988 (SAT0558), 990 (SAT0566), 991 (SAT0567), 1372 (AB0903)
Correyero, M., 748 (FRI0683), 1276 (AB0640), 1297 (AB0695)
Correyero Plaza, M., 656 (FRI0448)
Correyero-Plaza, M., 462 (THU0676)
Corsiero, E., 125 (OP0175)
Corstjens, P., 215 (THU0042)
Cortés-Amador, S., 1380 (AB0929)

Cortés-Hernández, J., 286 (THU0216), 1208 (AB0451)
Cortes-Pereira, E., 203 (THU0009), 978 (SAT0535)
Cortesi, P., 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Cortesi, P.A., 445 (THU0634)
Corvaglia, S., 366 (THU0420)
Corzo, P., 307 (THU0273), 1181 (AB0381)
Corzo Dominguez, E., 365 (THU0417)
Cosentino, E.R., 366 (THU0420)
Coskun, B.N., 1196 (AB0418), 1434 (AB1086)
Cossío Jimenez, P.J., 1121 (AB0211)
Cossio Jimenez, P.J., 1122 (AB0212)
Cosso, C., 66 (OP0037)
Cossu, D., 496 (FRI0046)
Cossu, M., 1065 (AB0054), 1108 (AB0177), 1109 (AB0178)
Cost, C., 237 (THU0097)
Costa, A., 1554 (PARE0007)
Costa, C., 1381 (AB0930)
Costa, J., 612 (FRI0330)
Costa, L., 468 (THU0690), 852 (SAT0211), 1142 (AB0268), 1177 (AB0368), 1254 (AB0581), 1466 (AB1172)
Costa, L.H.A., 397 (THU0505)
Costa, M., 1052 (AB0016)
Costa, S., 309 (THU0278)
Costa, T., 1052 (AB0016), 1153 (AB0300)
Costa Reis, P., 391 (THU0490), 1390 (AB0958)
Costanza, D., 704 (FRI0568)
Costanzo, P., 761 (FRI0716)
Coste, J., 169 (OP0274), 385 (THU0470)
Costedoat-Chalumeau, N., 152 (OP0236)
Costello, W., 1556 (PARE0012)
Costenbader, K., 50 (OP0002)
Costi, A.C., 1202 (AB0434), 1263 (AB0606)
Costi, C., 440 (THU0619), 1245 (AB0556)
Costopoulos, M., 776 (SAT0023)
Cotten, A., 170 (LB0001)
Cottereaux, C., 126 (OP0180)
Cotti, R., 465 (THU0683)
Cottin, V., 1049 (AB0007)
Cotton, A., 253 (THU0138)
Coudenys, J., 490 (FRI0029)
Couderc, M., 638 (FRI0398), 813 (SAT0117), 1033 (SAT0682), 1297 (AB0696), 1384 (AB0942)
Coudeyre, E., 1477 (THU0724-HPR)
Coupal, L., 571 (FRI0230), 845 (SAT0195), 931 (SAT0423), 1188 (AB0397)
Courbebaisse, M., 1364 (AB0882)
Couret, M., 1385 (AB0945)
Courties, A., 1072 (AB0073)
Courvoisier, D., 168 (OP0271), 523 (FRI0113), 567 (FRI0221), 755 (FRI0701)
Courvoisier, D.S., 850 (SAT0206)
Coury, F., 1385 (AB0945)
Coustet, B., 1049 (AB0007)
Coutant, F., 1059 (AB0035)
Couto, S., 194 (OP0337-HPR), 531 (FRI0132)
Couto-Luvie, E., 993 (SAT0573)
Couvaras, L., 1454 (AB1141)
Couzy, L., 866 (SAT0246)
Cova, E., 891 (SAT0315)
Covarrubias-Cobos, J.A., 682 (FRI0509), 1335 (AB0794)
Coyle, P.V., 1372 (AB0904)
Cozma, F., 1245 (AB0557)
Cozmuta, R., 453 (THU0654, THU0655), 1441 (AB1105)
Cozos, A.I., 1440 (AB1101)
Cozzi, F., 603 (FRI0308), 634 (FRI0387), 1111 (AB0184)
Craig, G., 572 (FRI0232)
Cramp, F., 1528 (SAT0769-HPR)
Craven, A., 319 (THU0306), 605 (FRI0312)
Creevey, K., 204 (THU0014)
Cremers, N., 772 (SAT0012)
Cremin, K., 383 (THU0464)
Cren, J.B., 989 (SAT0561), 1191 (AB0406)
Crepaldi, G., 237 (THU0099), 433 (THU0602), 1123 (AB0214)
Crescentini, F., 1247 (AB0563)
Crescioli, C., 1057 (AB0029, AB0030)
Crespo Amaya, G., 933 (SAT0427)
Crespo Golmar, A., 719 (FRI0608), 1232 (AB0518)
Cresswell, K., 190 (OP0327-PARE)
Crestani, B., 1049 (AB0007)
Crins, M.H., 476 (THU0712)
Crisafulli, F., 1207 (AB0448)
Crisan, V., 1217 (AB0477)
Crisostomo, N., 1098 (AB0148)
Crisostomo, S., 171 (OP0276-PARE)
Cristiano, A., 52 (OP0006)
Cristofani, L., 875 (SAT0268)
Criswell, L., 289 (THU0225)
Criswell, L.A., 432 (THU0600)
Critchley, H.D., 1379 (AB0926)
Crnkic Kapetanovic, M., 823 (SAT0143)
Croca, S., 1092 (AB0131)
Croci, S., 212 (THU0035), 1054 (AB0022), 1247 (AB0563)
Croia, C., 180 (OP0300)
Cronstein, B., 128 (OP0186)
Crooks, J., 543 (FRI0164)
Cross, A., 852 (SAT0209)
Cross, M., 960 (SAT0489)
Crow, Y.J., 406 (THU0528)
Crow-Hercher, R., 448 (THU0643)
Crowley, J., 672 (FRI0487)
Crowley, T., 125 (OP0178)
Crowson, C., 591 (FRI0278), 881 (SAT0286), 1207 (AB0449)
Crowson, C.S., 444 (THU0630), 512 (FRI0091), 609 (FRI0323), 613 (FRI0332)
Crowther, M., 418 (THU0561)
Cruces Moreno, M.T., 1270 (AB0624)
Crucet, M., 500 (FRI0059)
Cruickshank, S.M., 139 (OP0210-PARE)
Cruz, A.P., 1419 (AB1043)
Cruz, E., 406 (THU0527), 466 (THU0685), 739 (FRI0660), 1006 (SAT0613)
Cruz, G., 721 (FRI0615), 1042 (SAT0706)
Cruz, J., 75 (OP0059)
Cruz Bautista, I., 1225 (AB0499)
Cruz González, D.D.J., 774 (SAT0016)
Cruz-Caparrós, G., 410 (THU0539)
Cruz-Domínguez, M.D.P., 1286 (AB0668)
Cruz-Dominguez, M.D.P., 421 (THU0568), 1282 (AB0657)
Cruz-Reyes, C.V., 860 (SAT0229)
Cruz-Rojas, Y., 877 (SAT0276, SAT0277)
Cseuz, R., 230 (THU0081), 267 (THU0173)
Csonka, V., 1267 (AB0617)
Csumita, M., 1049 (AB0009)
Cuadrado, M., 761 (FRI0716)
Cuadrado, M.J., 287 (THU0218), 1091 (AB0127, AB0128), 1450 (AB1130)
Cubería, M., 594 (FRI0286), 1229 (AB0511), 1230 (AB0512)
Cubero, R., 925 (SAT0406)
Cubides, H., 201 (THU0005), 218 (THU0052)
Cucchi, D., 506 (FRI0076)
Cuccioloni, M., 64 (OP0031)
Cuce, E., 659 (FRI0457)
Cuce, I., 659 (FRI0457)
Cucho-Venegas, J., 875 (SAT0269), 1142 (AB0269)
Čučnik, S., 219 (THU0054), 325 (THU0324)
Cucnik, S., 1243 (AB0552)
Cucurell, M., 1434 (AB1085)
Cuda, C.M., 1125 (AB0220)
Cuéllar Calàbria, H., 900 (SAT0340)
Cuervo, A., 817 (SAT0128), 1133 (AB0243)
Cuervo Aguilera, A., 128 (OP0185)
Cugno, M., 1022 (SAT0655)
Cui, B., 1218 (AB0480)
Cui, L., 748 (FRI0681)
Cui, Y., 358 (THU0399), 799 (SAT0080), 1230 (AB0513), 1234 (AB0523), 1241 (AB0543), 1338 (AB0802)
Cuitino, L., 1098 (AB0148)
Cukierman, G., 461 (THU0675), 786 (SAT0050)
Culfear, K., 271 (THU0183)
Cullen, E., 685 (FRI0514)
Cummings, S.R., 690 (FRI0525)
Cunha, B., 474 (THU0706)
Cunha, M.F., 1160 (AB0320)
Cunha-Miranda, L., 436 (THU0610), 464 (THU0679), 1163 (AB0329), 1464 (AB1168)
Cunningham, C., 1493 (THU0767-HPR)
Cuomo, G., 237 (THU0098), 635 (FRI0389), 923 (SAT0401)
Cup, E., 1492 (THU0764-HPR)
Cuquet-Pedragosa, J., 1208 (AB0451)
Cur, S., 1462 (AB1162)
Curbelo, R., 736 (FRI0651), 918 (SAT0387), 1305 (AB0718), 1307 (AB0723)
Curhan, G.C., 360 (THU0405)
Curiale, C., 831 (SAT0161), 1181 (AB0379)
Curiel-Quiroz, D., 1343 (AB0815)
Curram, J., 1271 (AB0627)
Curran, K., 460 (THU0671), 1530 (AB1196-HPR)
Curran, M., 250 (THU0130), 1390 (AB0958)
Curran-Fàbregas, A., 636 (FRI0392)
Curti, A., 1534 (AB1206-HPR)
Curtis, J., 72 (OP0051), 244 (THU0114), 1313 (AB0739), 1521 (SAT0750-HPR)
Curtis, J.R., 83 (OP0077), 232 (THU0087), 234 (THU0091), 426 (THU0583), 448 (THU0643), 449 (THU0645), 460 (THU0672), 511 (FRI0089), 654 (FRI0444), 676 (FRI0496), 825 (SAT0149), 1130 (AB0235)
Cusa, A., 906 (SAT0357)
Cusa, F., 906 (SAT0357)
Custers, R.J., 1344 (AB0818)
Cuthbert, R.J., 648 (FRI0427)
Cutolo, M., 25 (SP0099), 29 (SP0116), 42 (SP0176), 56 (OP0015), 65 (OP0035), 66 (OP0037), 86 (OP0082), 140 (OP0212), 245 (THU0116), 299 (THU0252), 378 (THU0451), 437 (THU0611), 560 (FRI0207), 595 (FRI0288), 641 (FRI0407), 695 (FRI0540), 704 (FRI0569), 728 (FRI0632), 867 (SAT0247), 894 (SAT0323), 897 (SAT0331), 914 (SAT0377), 915 (SAT0381), 942 (SAT0448), 1110 (AB0182, AB0183), 1111 (AB0185), 1221 (AB0488), 1263 (AB0605), 1390 (AB0958), 1439 (AB1099)
Cuttica, R., 133 (OP0197), 396 (THU0503)
Cuzdan Coskun, N., 640 (FRI0404), 902 (SAT0344), 905 (SAT0355)
Cypers, H., 62 (OP0026), 118 (OP0160)
Czarlewski, W., 428 (THU0588, THU0589)
Czibula, Á., 1090 (AB0123)
Czirják, L., 104 (OP0123), 909 (SAT0366), 915 (SAT0380), 1267 (AB0617)
Czirjak, L., 1286 (AB0669)

D'Abbicco, D., 639 (FRI0400)
D'Abrosca, V., 1118 (AB0202)
D'Agostino, M.-A., 103 (OP0121), 174 (OP0286), 175 (OP0288), 196 (OP0341), 518 (FRI0102), 583 (FRI0256), 663 (FRI0467), 726 (FRI0626), 727 (FRI0630), 736 (FRI0650), 1013 (SAT0631), 1015 (SAT0636)
D'Aguanno, G., 901 (SAT0341)
D'Alberti, V., 621 (FRI0357)
D'Alessandro, A., 90 (OP0092)
D'Alto, M., 630 (FRI0378)
D'Amati, G., 888 (SAT0305)
D'Andrea, A., 630 (FRI0378)
D'Andrea, G., 721 (FRI0613), 891 (SAT0313)
D'Angelo, S., 343 (THU0365), 437 (THU0611), 1439 (AB1099)
D'Aniello, D., 731 (FRI0640)
D'Oliveira, I., 247 (THU0122), 725 (FRI0625)
D'Onofrio, F., 263 (THU0164), 808 (SAT0105), 1327 (AB0773)
D'Souza, B., 1140 (AB0262)
Da, Z., 1370 (AB0897, AB0898)
da Fonte, C.A., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
da Rocha Jr, L.F., 988 (SAT0558), 990 (SAT0566), 991 (SAT0567), 1372 (AB0903)
Da Silva, F., 1378 (AB0923)
da Silva, J., 137 (OP0206), 528 (FRI0126), 1314 (AB0741)
da Silva, J.A., 894 (SAT0324)
da Silva, J.A.P., 112 (OP0144-HPR), 702 (FRI0562), 1501 (FRI0748-HPR), 1510 (SAT0718-HPR)

da Silva, R.V.T., 1478 (THU0728-HPR)
Daas, S., 1373 (AB0909)
Dadashova, R., 131 (OP0192)
Dadhaniya, N., 1292 (AB0683)
Dadlani, S., 695 (FRI0541), 1037 (SAT0691), 1115 (AB0195)
Dadoun, S., 433 (THU0602), 465 (THU0684), 763 (FRI0722)
Daga, S., 577 (FRI0243)
Dager, T.N., 161 (OP0255-HPR)
Dagfinrud, H., 22 (SP0089), 111 (OP0141-HPR), 161 (OP0255-HPR), 164 (OP0261-HPR), 466 (THU0686), 1517 (SAT0737-HPR)
Dagher, R., 406 (THU0528)
Dagli, A.F., 455 (THU0658)
Dagli, A.Z., 1317 (AB0751), 1320 (AB0757)
Dagna, L., 90 (OP0092), 126 (OP0179), 410 (THU0538), 610 (FRI0325), 1399 (AB0985)
Dagnelie, P.C., 433 (THU0603)
Dahab, S., 480 (FRI0003)
Dahan, S., 169 (OP0273)
Dahlbäck, B., 302 (THU0260)
Dahlberg, L., 1501 (FRI0749-HPR)
Dahle, C., 461 (THU0673)
Dahlui, M., 446 (THU0638)
Dahou Makhloufi, C., 1192 (AB0409)
Dai, L., 279 (THU0201), 373 (THU0439), 488 (FRI0023), 798 (SAT0078)
Daia, S., 881 (SAT0288)
Daia-Iliescu, S., 423 (THU0574), 1208 (AB0450)
Daia-Iliescu, S.E., 416 (THU0555)
Daien, C., 573 (FRI0234)
Daikeler, T., 319 (THU0306)
Daikh, D., 50 (OP0002)
Daita, R., 901 (SAT0341)
Daizadeh, N., 54 (OP0010)
Daker, L., 1228 (AB0505)
Dalal, D., 826 (SAT0151)
Dalbeni, A., 805 (SAT0097)
Dalbeth, N., 166 (OP0265, OP0266, OP0267), 383 (THU0464)
Dale, N., 1174 (AB0359)
Dalén, J., 447 (THU0640)
Dalgaard, E.B., 553 (FRI0190)
Dalkilic, E., 1434 (AB1086)
Dalkılıc, E., 1196 (AB0418)
Dall'Ara, F., 245 (THU0116), 437 (THU0611), 1214 (AB0468), 1439 (AB1099)
Dall'ara, F., 1225 (AB0497)
Dall'Era, M., 432 (THU0600), 857 (SAT0221), 865 (SAT0242), 868 (SAT0250)
Dallagiacoma, G., 1388 (AB0953)
Dalle Grave, R., 693 (FRI0535)
Dalmao-Fernandez, A., 203 (THU0009)
Dalmau, R., 918 (SAT0387), 1307 (AB0723)
Dalpke, A., 754 (FRI0698)
Dalwigk, K., 486 (FRI0018)
Daly, N., 401 (THU0516)
Damask, A., 570 (FRI0228), 838 (SAT0179), 844 (SAT0192)
Damen, P.-J., 967 (SAT0506)
Damerau, A., 480 (FRI0002)
Damgaard, D., 493 (FRI0038), 501 (FRI0061), 775 (SAT0020), 1075 (AB0081)
Damian, L., 170 (OP0275), 260 (THU0156), 880 (SAT0285), 1245 (AB0557), 1285 (AB0666)
Damiani, A., 646 (FRI0423)
Damjanov, N., 314 (THU0292), 730 (FRI0637), 792 (SAT0064), 914 (SAT0378), 1013 (SAT0631), 1015 (SAT0636), 1020 (SAT0648)
Damjanov, N.S., 559 (FRI0206), 1457 (AB1149)
Damjanovska-Krstikj, L., 280 (THU0202)
Damman, W., 197 (OP0342), 969 (SAT0512)
Dan, X., 348 (THU0377)
Danaci, E.S., 1434 (AB1086)
Dand, N., 201 (THU0004)
Danda, D., 311 (THU0284), 316 (THU0298), 325 (THU0322), 328 (THU0330), 464 (THU0681), 727 (FRI0629), 886 (SAT0302), 1061 (AB0042)
Dandreo, K.J., 60 (OP0022)
Danebod, K., 553 (FRI0190)
Dani, L., 896 (SAT0329)
Daniel, A., 455 (THU0659), 694 (FRI0537), 700 (FRI0558), 702 (FRI0562)
Danieli, M.G., 912 (SAT0374), 1189 (AB0400)
Danielsen, M.A., 19 (SP0075)
Danila, M., 72 (OP0051)
Danilin, S., 1463 (AB1164)
Danilko, K.V., 1049 (AB0008)
Dankaerts, W., 1501 (FRI0750-HPR)
Dankó, K., 911 (SAT0371), 912 (SAT0374)
Danneskiold-Samsøe, B., 1412 (AB1020)
Danoff, S.K., 67 (OP0038)
Dantas, A.T., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Dantu, A., 1378 (AB0923)
Dare, J., 405 (THU0525)
Daroca, G., 594 (FRI0286), 1229 (AB0511), 1230 (AB0512)
Darre, S., 1478 (THU0726-HPR)
Darrieutort-Laffite, C., 130 (OP0190), 430 (THU0593), 731 (FRI0638)
Dartevel, A., 1256 (AB0588)
Darvish-Zargar, M., 152 (OP0237)
Das, L., 401 (THU0517)
Das, S., 987 (SAT0556)
Das, S.K., 1006 (SAT0614)
Dasgupta, B., 94 (OP0103), 107 (OP0131), 316 (THU0297), 318 (THU0302), 577 (FRI0243), 609 (FRI0321)
Dash, R., 437 (THU0612)
Dash, S., 1300 (AB0705)
Dastmalchi, M., 896 (SAT0329)
Daudon, M., 1364 (AB0882)
Dauth, S., 565 (FRI0217)
Davelaar, N., 1058 (AB0033), 1088 (AB0118)
Davey, J.R., 1035 (SAT0688)
David, C., 648 (FRI0428)
Davidson, B., 933 (SAT0426)
Davies, K., 289 (THU0224)
Davies, K.A., 1205 (AB0444), 1379 (AB0926)
Davies, O., 60 (OP0023)
Davies, R., 146 (OP0225), 208 (THU0025), 1050 (AB0011), 1173 (AB0358)
Davies, U., 1246 (AB0559)
Davignon, J.-L., 770 (SAT0006)
Davis, A., 685 (FRI0514)
Davis, M., 83 (OP0076)
Davis III, J.M., 512 (FRI0091)
Dawar, R., 1292 (AB0683)
Dawczynski, C., 115 (OP0151)
De Abreu, P., 1396 (AB0975)
De Agustin, J.J., 583 (FRI0256)
De Andrea, M., 1113 (AB0191)
De Angelis, R., 867 (SAT0248), 1209 (AB0456)
De Aysa, C., 555 (FRI0195)
De Baillou, H., 753 (FRI0696)
De Bandt, M., 56 (OP0014)
De Benedetti, F., 77 (OP0063), 396 (THU0503), 398 (THU0509)
De Beuf, K., 92 (OP0098), 575 (FRI0239)
De Bleecker, J., 912 (SAT0374)
de Boer, M., 184 (OP0310)
de Boer, S., 817 (SAT0127)
de Boer, T.N., 968 (SAT0508)
de Boysson, H., 1256 (AB0588)
de Bree, G., 1221 (AB0488)
de Bruin, F., 100 (OP0114), 662 (FRI0465), 669 (FRI0480), 1013 (SAT0632)
De Brum Fernandes, A.J., 496 (FRI0047)
de Carlan, M., 1261 (AB0599)
De Ceuninck, F., 126 (OP0180)
de Chalus, T., 461 (THU0675)
De Cock, D., 147 (OP0226), 555 (FRI0196)
De Dios, J.R., 826 (SAT0150)
De Escalante, B., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
De Fátima Carvalho, M., 1382 (AB0935)
De Franceschi, L., 1062 (AB0045)
de Gendt, E.E., 1423 (AB1052)
De Gennaro, F., 270 (THU0181)
De Giorgio, C., 234 (THU0090), 1127 (AB0227)
De Groef, A., 1488 (THU0757-HPR)
De Groot, J., 621 (FRI0356)
de Groot, K., 721 (FRI0614)
de Guzman, E., 383 (THU0464)
De Haes, P., 636 (FRI0393)
de Hair, M., 123 (OP0172), 124 (OP0173)
De Hair, M.J., 1199 (AB0428)
De Hooge, M., 100 (OP0115, OP0116)
de Hooge, M., 130 (OP0189), 337 (THU0353), 350 (THU0382), 653 (FRI0440), 1305 (AB0716)
de Inocencio, J., 399 (THU0511)
de Jager, W., 16 (SP0067), 89 (OP0091), 181 (OP0303)
de Jong, A., 769 (SAT0001)
de Jong, H.M., 1086 (AB0114)
de Jong, P.A., 1423 (AB1052)
de Jong, S., 1556 (PARE0014)
de Jonge, A.V., 114 (OP0150)
De Keyser, F., 299 (THU0252)
de Koning, A., 100 (OP0114), 155 (OP0241)
De la Calle, F., 1014 (SAT0634)
De la Casa-Resino, C., 78 (OP0066)
De La Cruz Rodríguez, K., 1276 (AB0641)
De La Cruz-Castillejos, J.C., 1133 (AB0242)
De La Fuente, J., 313 (THU0289)
De la Fuente, J.L., 206 (THU0018)
de la Fuente-Fernández, M., 892 (SAT0316)
De la Garza-Ramos, M.-A., 498 (FRI0052)
De La Haza, J., 1559 (PARE0020)
De la Hera, M., 1472 (AB1192)
de la Nuez, F., 694 (FRI0539)
De la Puente Bujidos, C., 1396 (AB0977)
de la Puente Bujidos, C., 642 (FRI0409)
de la Red, G., 410 (THU0539), 597 (FRI0293), 721 (FRI0615), 1042 (SAT0706)
de la Sota, M., 440 (THU0619)
De la Torre, I., 233 (THU0088)
de la Torre, I., 228 (THU0078), 495 (FRI0042), 512 (FRI0090)
De la Torre Cisneros, J., 68 (OP0042)
De Lamotte, G., 1454 (AB1141)
de Lange-Brokaar, B., 769 (SAT0001)
De Langhe, E., 636 (FRI0393), 1275 (AB0638)
De Leeuw, K., 308 (THU0276)
De Leonardis, F., 230 (THU0081)
de Lima, H.D., 990 (SAT0566), 991 (SAT0567), 1372 (AB0903)
De Llobet, J.M., 904 (SAT0351), 1305 (AB0717), 1414 (AB1027)
De Lorenzis, E., 197 (OP0343)
De Lucia, O., 403 (THU0522), 643 (FRI0413), 746 (FRI0677), 908 (SAT0364)
De Maertelaer, V., 736 (FRI0650)
De Marchi, G., 1209 (AB0456)
De Marco, T., 1353 (AB0847)
De Mattei, C., 100 (OP0115, OP0116)
de Mattos, A.G.L., 990 (SAT0566), 991 (SAT0567)
de Melo, P.R.S., 990 (SAT0566), 991 (SAT0567), 1372 (AB0903)
De Miguel, E., 1004 (SAT0609), 1011 (SAT0626), 1014 (SAT0634), 1303 (AB0713), 1408 (AB1011), 1413 (AB1024)
de Miguel, E., 357 (THU0396), 930 (SAT0419)
de Miguel Mendieta, E., 917 (SAT0385)
De Mits, S., 653 (FRI0440), 1305 (AB0716)
de Moel, E.C., 1076 (AB0084)
de Moor, C., 127 (OP0183)
de Mutsert, R., 123 (OP0170)
De Muynck, A., 490 (FRI0029)
De Nardo, D., 1076 (AB0086)
de Oliveira, A.F.R., 990 (SAT0566), 1372 (AB0903)
de Oliveira, F.H., 1508 (FRI0768-HPR)
de Oliveira, W.L.M., 991 (SAT0567)
de Oliveira Pena, J., 1271 (AB0627)
De Paepe, B., 912 (SAT0374)
De Palma, A., 966 (SAT0503), 1343 (AB0816)
De Palma, R., 621 (FRI0355)
de Paulis, A., 490 (FRI0030)
De Peretti, F., 707 (FRI0578)
de Peyrecave, N., 60 (OP0023)
De Pouilly, A., 573 (FRI0234)
de Rooij, E., 871 (SAT0258)
De Rooij, M., 22 (SP0090)
De Rook, S., 940 (SAT0444)
de Ru, A., 778 (SAT0030)

De Santis, M., 620 (FRI0353)
De Socio, A., 756 (FRI0703), 1319 (AB0754)
de Souza, S., 1555 (PARE0010)
De Stefani, E., 828 (SAT0156)
De Thurah, A., 3 (SP0008)
de Thurah, A., 248 (THU0126), 1517 (SAT0738-HPR)
de Thurah, A.L., 84 (OP0079)
de Toro, F., 439 (THU0617)
de Torre, I., 510 (FRI0086)
De Vera, M.A., 374 (THU0442), 381 (THU0460)
de Vera-González, A., 802 (SAT0088), 804 (SAT0095)
de Vet, H.C., 476 (THU0712)
de Vet, R., 111 (OP0141-HPR)
De Vicente, M., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
De Vita, S., 67 (OP0040), 305 (THU0268), 585 (FRI0263), 867 (SAT0248), 940 (SAT0443), 1101 (AB0156), 1209 (AB0456)
de Vlam, K., 347 (THU0375), 1310 (AB0732), 1335 (AB0794), 1501 (FRI0750-HPR)
de Vries, A., 335 (THU0349)
de Vries, F., 67 (OP0039), 433 (THU0603)
de Vries, J., 184 (OP0310)
de Vries, N., 123 (OP0172), 124 (OP0173), 601 (FRI0303), 781 (SAT0037)
De Vries-Bouwstra, J., 621 (FRI0356)
de Vries-Bouwstra, J.K., 903 (SAT0350), 907 (SAT0359), 1279 (AB0650)
De Wilde, K., 490 (FRI0029)
de Winter, J.J., 666 (FRI0475)
De Wit, M., 34 (SP0138), 1343 (AB0817)
de Wit, M., 134 (OP0199-PARE), 1332 (AB0786)
De Zordo, T., 587 (FRI0268)
de Zoysa, J., 383 (THU0464)
de Zwart, A.H., 1488 (THU0755-HPR)
De-Avila, J., 252 (THU0137)
Deaconu, C., 20 (SP0080)
Deane, K., 1517 (SAT0736-HPR), 1524 (SAT0758-HPR)
Deane, K.D., 36 (SP0147), 498 (FRI0053), 757 (FRI0706)
Deary, V., 1517 (SAT0736-HPR), 1524 (SAT0758-HPR)
Debrach, A.-C., 1385 (AB0945)
Debray, M.-P., 1049 (AB0007)
Debusschere, K., 118 (OP0160)
Decaria, J., 1002 (SAT0603)
Dechant, C., 718 (FRI0606)
Decousser, J.-W., 188 (OP0323)
Decruze, A., 1002 (SAT0602, SAT0603)
Decuman, S., 299 (THU0252)
Deeg, M., 983 (SAT0548)
Deepak, S., 407 (THU0531)
Dees, C., 191 (OP0330), 892 (SAT0318)
Deflandre, E., 736 (FRI0650)
Degani, D., 1388 (AB0953)
Degauque, N., 778 (SAT0029)
Degboe, Y., 343 (THU0364), 770 (SAT0006), 1299 (AB0703)
Degli Esposti, D., 366 (THU0420)
Dehlin, M., 57 (OP0016), 154 (OP0240), 360 (THU0404), 361 (THU0408), 364 (THU0414), 563 (FRI0213)
Dehlin, M.I., 164 (OP0262), 375 (THU0443)
Dehoux, M., 187 (OP0319)
Dejaco, C., 24 (SP0095), 175 (OP0288), 583 (FRI0256), 587 (FRI0268), 1495 (FRI0732-HPR)
Dekker, J., 476 (THU0712), 966 (SAT0505), 972 (SAT0517), 982 (SAT0544), 1486 (THU0750-HPR), 1488 (THU0755-HPR)
Dekkers, J., 778 (SAT0030)
Del Campo, V., 68 (OP0042)
del Campo Pérez, V., 300 (THU0256)
Del Caño Garrido, A., 1362 (AB0875)
Del Castillo, N., 1289 (AB0675)
Del Galdo, F., 455 (THU0659), 627 (FRI0370), 635 (FRI0390), 734 (FRI0646), 915 (SAT0380), 1057 (AB0029, AB0030)
Del Mastro, A., 237 (THU0098), 635 (FRI0389)
Del Porto, F., 879 (SAT0282)
del Río, C., 622 (FRI0360)
Del Rio, L., 739 (FRI0658)
del Rio, L., 691 (FRI0529)
del Río, T., 386 (THU0474), 656 (FRI0448), 1276 (AB0640)
del Rio, T., 1476 (THU0720-HPR)
del Río-Moreno, M., 648 (FRI0429), 1091 (AB0128)
del Rio-Moreno, M., 1082 (AB0104)
Del Ross, T., 70 (OP0046)
Delannoy, C., 1470 (AB1185)
Delaporte, E., 823 (SAT0144)
Delaunay, C., 171 (OP0278-PARE)
Delaurière, L., 555 (FRI0194)
Delev, N., 143 (OP0219), 672 (FRI0487), 870 (SAT0255), 936 (SAT0436)
Delgado, C., 843 (SAT0191)
Delgado Alves, J., 293 (THU0236), 902 (SAT0345), 1053 (AB0019), 1131 (AB0238)
Delgado-Fernández, M., 1499 (FRI0743-HPR)
Delicha, E.M., 145 (OP0222), 345 (THU0369), 357 (THU0397), 952 (SAT0470)
Delis, K., 836 (SAT0176)
Dell'Aniello, S., 529 (FRI0129)
Della Casa, G., 248 (THU0123)
Della Torre, E., 410 (THU0538)
Della-Torre, E., 1399 (AB0985)
Delle Sedie, A., 175 (OP0288), 446 (THU0636), 584 (FRI0260), 731 (FRI0640), 742 (FRI0667), 1013 (SAT0631), 1022 (SAT0654), 1152 (AB0295), 1412 (AB1022)
Delli, K., 591 (FRI0277), 1007 (SAT0617)
Delmas, C., 617 (FRI0345)
Deloire, L., 662 (FRI0465)
DeLozier, A.M., 517 (FRI0099), 788 (SAT0055)
DeMasi, R., 149 (LB0003), 275 (THU0193), 277 (THU0197), 284 (THU0211), 1034 (SAT0686)
Demetrio-Pablo, R., 75 (OP0059), 326 (THU0326), 405 (THU0526), 718 (FRI0607)
Demidov, R., 1172 (AB0354), 1356 (AB0857)
Demidova, N., 256 (THU0148), 273 (THU0188), 572 (FRI0231), 1204 (AB0441)
Demidova, N.V., 1128 (AB0230)
Demina, A., 660 (FRI0458), 920 (SAT0394), 1294 (AB0688)
Deminger, A., 916 (SAT0382)
Demir, S., 414 (THU0548)
Demirbüken, I., 1509 (FRI0770-HPR)
Demirbuken, I., 997 (SAT0586), 1003 (SAT0606)
Demirkıran, N.D., 1340 (AB0807)
Demmelmaier, I., 1523 (SAT0754-HPR)
Demoruelle, M.K., 498 (FRI0053)
Demougeot, C., 493 (FRI0039), 495 (FRI0044)
Demoulin, N., 290 (THU0228)
Demoux, A.L., 753 (FRI0696)
den Braanker, H., 1058 (AB0033)
den Broeder, A., 470 (THU0695), 568 (FRI0223), 818 (SAT0132)
Den Broeder, A.A., 35 (SP0144)
den Broeder, A.A., 193 (OP0335), 519 (FRI0104), 526 (FRI0120), 557 (FRI0200)
Den Broeder, N., 526 (FRI0120)
den Broeder, N., 519 (FRI0104)
den Hollander, W., 207 (THU0020)
den Hoogen, F., 489 (FRI0025)
Denaxas, K., 908 (SAT0361)
Deng, C., 1084 (AB0109)
Deng, K., 509 (FRI0084)
Deng, W., 203 (THU0010), 934 (SAT0430)
Deng, X., 934 (SAT0429)
Deng, Z., 1338 (AB0802)
Denis, M.C., 500 (FRI0059)
Denisov, L., 256 (THU0148), 560 (FRI0208), 572 (FRI0231), 944 (SAT0452), 956 (SAT0478), 1337 (AB0797, AB0798)
Denisov, L.N., 1317 (AB0749)
Denisova, R., 186 (OP0316), 539 (FRI0154), 1387 (AB0950, AB0951)
Dennison, E., 933 (SAT0426)
Dennison, E.M., 1030 (SAT0676), 1039 (SAT0699)
Denotti, A., 975 (SAT0528)
Denova-Gutierrez, E., 1343 (AB0815)
Dent, S., 973 (SAT0521)
Dentali, F., 418 (THU0561)
Denton, C., 104 (OP0123), 140 (OP0213), 635 (FRI0390), 898 (SAT0334), 912 (SAT0373), 915 (SAT0380), 1104 (AB0166), 1271 (AB0627), 1286 (AB0669), 1390 (AB0958)
Denton, C.P., 27 (SP0107), 34 (SP0136), 43 (SP0177), 65 (OP0034), 195 (OP0339), 628 (FRI0372), 898 (SAT0335), 1266 (AB0613), 1269 (AB0621)
Denyschych, L., 1230 (AB0514)
Deodati, F., 1004 (SAT0609), 1413 (AB1024)
Deodhar, A., 142 (OP0218), 335 (THU0348), 337 (THU0352), 340 (THU0359), 341 (THU0360), 349 (THU0379), 355 (THU0393), 357 (THU0397), 1293 (AB0685), 1295 (AB0692), 1315 (AB0744), 1316 (AB0747)
Depinoy, T., 1215 (AB0469)
Deprez, P., 126 (OP0180)
DeQuattro, K., 432 (THU0600)
Derakhshan, M.H., 659 (FRI0456), 1308 (AB0727)
Derin, M.E., 1400 (AB0987)
Derk, C.T., 896 (SAT0328)
Derksen, R., 184 (OP0310)
Derksen, V.F.A.M., 1076 (AB0084)
Dermentzoglou, V., 909 (SAT0365)
Dermitzakis, E., 192 (OP0332)
Dernis, E., 258 (THU0152), 335 (THU0349), 428 (THU0588, THU0589), 549 (FRI0180), 811 (SAT0112)
Derrett-Smith, E., 1269 (AB0621), 1421 (AB1049)
Dervieux, T., 1025 (SAT0662)
Desai, R., 802 (SAT0089)
Desai, R.J., 544 (FRI0167)
Desbois, A.-C., 776 (SAT0023)
Descamps, E., 1535 (AB1209-HPR)
Deschepper, E., 299 (THU0252), 914 (SAT0377)
Deshayes, S., 330 (THU0337), 617 (FRI0345), 1256 (AB0587, AB0588)
Deshmukh, V., 984 (SAT0549), 1003 (SAT0607)
Deshpande, G., 631 (FRI0379)
Desinova, O., 640 (FRI0403), 1283 (AB0659)
Desinova, O.V., 1287 (AB0670)
Deslandre, C., 56 (OP0014)
Desmond, D., 1434 (AB1083), 1521 (SAT0748-HPR)
Desouches, S., 1299 (AB0702)
Dessein, P., 252 (THU0136), 545 (FRI0170)
Dessein, P.H., 245 (THU0117)
Dessì, M., 535 (FRI0143)
Desta, B., 859 (SAT0227)
Desthieux, C., 155 (OP0242), 428 (THU0589), 458 (THU0666), 665 (FRI0473), 1371 (AB0900)
Detert, J., 253 (THU0139)
deToro-Santos, F., 587 (FRI0267)
Devarasetti, P.K., 1277 (AB0644)
Devauchelle, A.M., 63 (OP0029)
Devauchelle-Pensec, V., 56 (OP0014), 67 (OP0040), 309 (THU0278), 311 (THU0284), 335 (THU0349), 464 (THU0681), 886 (SAT0302), 1215 (AB0469)
Devers, B., 95 (OP0104), 800 (SAT0084)
Devoe, D., 463 (THU0677)
DeVries, A.C., 222 (THU0062)
Dey, M., 703 (FRI0565)
Deyab, G., 1309 (AB0730)
Dhahri, R., 998 (SAT0589, SAT0590)
Dhakad, U., 1006 (SAT0614)
Dhamaj, F., 1543 (AB1234-HPR)
Dharmanand, B.G., 862 (SAT0234)
Dhiman, K., 960 (SAT0488)
Dhir, V., 1273 (AB0633)
Dhooria, A., 301 (THU0258)
Di Bartolomeo, S., 880 (SAT0284), 891 (SAT0313)
Di Bello, S., 321 (THU0312), 629 (FRI0374)
Di Benedetto, P., 721 (FRI0613), 880 (SAT0284), 891 (SAT0313)
Di Biase, M., 895 (SAT0325)
Di Carlo, M., 247 (THU0121), 259 (THU0155), 521 (FRI0109), 1281 (AB0655)
Di Ceglie, I., 497 (FRI0049)
Di Cristo, L., 1085 (AB0111)
Di Franco, M., 230 (THU0082), 329 (THU0334), 496 (FRI0045), 1378 (AB0924), 1379 (AB0925)

Di Genaro, M.S., 1064 (AB0051)
Di Giuseppe, D., 57 (OP0016), 134 (OP0200), 444 (THU0632), 452 (THU0652), 563 (FRI0213), 686 (FRI0518)
Di Lascio, N., 617 (FRI0344)
Di Liberto, D., 291 (THU0231)
Di Mario, C., 394 (THU0499), 787 (SAT0052), 792 (SAT0066)
Di Matteo, A., 247 (THU0121), 521 (FRI0109), 1209 (AB0456), 1358 (AB0863)
Di Natale, C., 484 (FRI0012)
Di Paola, M., 704 (FRI0568)
Di Paolo, M., 230 (THU0082)
Di Rosa, R., 879 (SAT0282)
Di Sabatino, V., 1010 (SAT0625), 1013 (SAT0631)
Di Sante, G., 138 (OP0208), 535 (FRI0143), 787 (SAT0052), 792 (SAT0066)
Di Stefano, I., 630 (FRI0378)
Diab, A., 717 (FRI0604)
Diacinti, D., 230 (THU0082)
Diamantopoulos, A., 318 (THU0302)
Diamantopoulos, A.P., 315 (THU0296)
Diamond, B., 50 (OP0002)
Diana, D., 1279 (AB0649)
Diao, T., 24 (SP0094)
Dias, L.H., 163 (OP0259-HPR)
Diaz, A., 775 (SAT0018)
Diaz, C., 1414 (AB1027)
Díaz, T., 1395 (AB0974)
Diaz Cortes, M.E., 1013 (SAT0631)
Diaz del Campo, P., 357 (THU0396), 554 (FRI0192)
Díaz González, F., 1037 (SAT0691), 1115 (AB0195)
Díaz Muñoz, J.A., 761 (FRI0715), 1456 (AB1146, AB1147)
Diaz Torne, C., 914 (SAT0379)
Díaz-Cordovés, G., 405 (THU0526)
Diaz-Cordoves, G., 261 (THU0160), 1175 (AB0362), 1443 (AB1109)
Díaz-Cordovés Rego, G., 1393 (AB0968)
Diaz-Cordoves Rego, G., 391 (THU0489)
Diaz-Delgado, R., 406 (THU0527)
Díaz-González, F., 656 (FRI0450), 802 (SAT0088), 1244 (AB0553)
Díaz-Llopis, M., 326 (THU0326)
Díaz-Miguel, C., 550 (FRI0184)
Diaz-Rubio, G.-I., 806 (SAT0100), 1164 (AB0330)
Díaz-Soriano, G., 75 (OP0059), 420 (THU0567)
Díaz-Torné, C., 946 (SAT0458), 1305 (AB0717)
Diaz-Torné, C., 904 (SAT0351)
Díaz-Valle, D., 75 (OP0059), 326 (THU0326), 420 (THU0567), 718 (FRI0607), 1166 (AB0337)
Dickson, C., 513 (FRI0092), 517 (FRI0099)
Dickson, C.L., 158 (OP0248)
DIdoni, G., 445 (THU0634)
Didoni, G., 1533 (AB1203-HPR)
Diederichsen, L.P., 64 (OP0033), 912 (SAT0374)
Diego, C., 824 (SAT0145), 1179 (AB0375)
Dieli, F., 291 (THU0231), 777 (SAT0025)
Dieperink, S., 553 (FRI0190)
Dietzel, R., 1172 (AB0355)
Dieudé, P., 130 (OP0191), 289 (THU0225), 359 (THU0401), 1049 (AB0007), 1535 (AB1209-HPR)
Dieude, P., 202 (THU0006)
Díez, E., 213 (THU0037), 290 (THU0227), 614 (FRI0336)
Díez Álvarez, E., 1232 (AB0518)
Diez Álvarez, E., 719 (FRI0608)
DiFrancesco, A., 121 (OP0166), 985 (SAT0552)
DiGiandomenico, A., 192 (OP0331)
Dijkstra, G., 87 (OP0086)
Dikranian, A., 670 (FRI0484)
Dileepan, K., 1061 (AB0041)
Dillaerts, D., 636 (FRI0393)
Dilleen, M.A., 347 (THU0375)
Diller, A., 313 (THU0289)
Dilley, A., 1459 (AB1156)
Dillinger, L., 1442 (AB1108)
Dima, A., 435 (THU0606), 1278 (AB0647)
Dimai, H.-P., 1423 (AB1053)
Dimitriadis, P., 643 (FRI0412), 723 (FRI0619)
Dimitroulas, T., 546 (FRI0173), 836 (SAT0176)
Dimonaco, S., 107 (OP0131)
Dimopoulou, D., 1204 (AB0442)
Dimopoulou, D.G., 205 (THU0015)
Dinarello, C., 1057 (AB0031)
Dinarello, C.A., 89 (OP0090), 90 (OP0092)
Dinçer, B., 606 (FRI0315)
Dinçes, E., 719 (FRI0610)
Dinçses, E., 1246 (AB0558)
Ding, C., 122 (OP0169), 123 (OP0171), 193 (OP0334), 450 (THU0647), 471 (THU0699), 960 (SAT0489), 962 (SAT0493), 986 (SAT0555)
Ding, H.J., 1237 (AB0532)
Ding, K., 948 (SAT0462), 1326 (AB0772)
Ding, X., 1206 (AB0447), 1338 (AB0802)
Dingsør, A., 161 (OP0255-HPR)
Dini, F., 484 (FRI0012)
Dinoia, L., 1268 (AB0618)
Direskeneli, H., 417 (THU0557), 609 (FRI0322), 644 (FRI0416), 821 (SAT0139), 889 (SAT0310), 910 (SAT0367), 1013 (SAT0633), 1310 (AB0731)
Dirven, L., 516 (FRI0097)
Dissanayake, U., 1355 (AB0853)
Distler, J., 87 (OP0086), 891 (SAT0315), 892 (SAT0318)
Distler, J.H., 104 (OP0123), 890 (SAT0312)
Distler, J.H.W., 191 (OP0330), 1106 (AB0169), 1110 (AB0181)
Distler, O., 65 (OP0034, OP0035), 86 (OP0083, OP0084), 87 (OP0086), 88 (OP0088), 104 (OP0123), 117 (OP0157), 190 (OP0326), 191 (OP0330), 195 (OP0339), 299 (THU0252), 621 (FRI0356, FRI0358), 625 (FRI0365), 626 (FRI0369), 635 (FRI0390), 890 (SAT0312), 892 (SAT0318), 909 (SAT0366), 915 (SAT0380), 1271 (AB0627), 1286 (AB0669)
Ditto, M.C., 1008 (SAT0620), 1184 (AB0389), 1194 (AB0413), 1376 (AB0917), 1380 (AB0928)
Dittrich, M., 115 (OP0151)
Divard, G., 187 (OP0319)
Divjak, A., 1552 (PARE0003)
Dixey, J., 782 (SAT0040)
Dixon, W., 519 (FRI0105), 547 (FRI0175), 1438 (AB1097)
Dixon, W.G., 1040 (SAT0700), 1446 (AB1118), 1453 (AB1138)
Diykanov, D.T., 266 (THU0171)
Djokovic, A., 751 (FRI0689), 1231 (AB0515)
Djuric, O., 307 (THU0274)
Djurovic, N., 640 (FRI0405)
Dobashi, H., 265 (THU0170), 283 (THU0209), 719 (FRI0609), 757 (FRI0704), 907 (SAT0360), 1213 (AB0465)
Dobloug, C., 904 (SAT0352)
Dobroiu, M., 1540 (AB1224-HPR)
Dobronravov, V., 153 (LB0002)
Dobrotă, R., 1032 (SAT0681)
Dobrota, R., 65 (OP0034), 87 (OP0086), 625 (FRI0365), 626 (FRI0368), 1264 (AB0608), 1286 (AB0669)
Docimo, L., 630 (FRI0378)
Doddoli, S., 706 (FRI0575)
Dodge, R., 1330 (AB0783)
Doelberg, M., 65 (OP0034)
Doerfler, A., 240 (THU0105)
Doffinger, R., 215 (THU0043)
Dogan, I., 1374 (AB0911)
Doğan, M.C., 902 (SAT0344)
Dogan, M.C., 640 (FRI0404)
Dogantekin, S., 387 (THU0477)
Doggen, C., 274 (THU0190)
Dogra, G., 467 (THU0688)
Dogru, M., 999 (SAT0594)
Doherty, M., 25 (SP0102), 167 (OP0268), 383 (THU0464), 752 (FRI0693), 973 (SAT0523), 1028 (SAT0670)
Døhn, U.M., 175 (OP0287)
Dolcini, G., 304 (THU0267), 876 (SAT0273)
Doleh, Y., 842 (SAT0188)
Dolhain, R., 478 (THU0716)
Dolhain, R.J., 509 (FRI0083), 532 (FRI0136), 537 (FRI0147)
Dolhain, R.J.E.M., 548 (FRI0179)
Dolman, C., 461 (THU0673)
Dolnikov, K., 910 (SAT0368)
Dolstra, H., 1109 (AB0178)
Doma, M., 958 (SAT0482)
Domakoski, A.C., 484 (FRI0012)
Dombrecht, E.J., 92 (OP0098), 575 (FRI0239)
Domènech, E., 177 (OP0292)
Domic, C., 261 (THU0160), 1174 (AB0361), 1175 (AB0362), 1443 (AB1109)
Domic-Bueno, C., 391 (THU0489), 1492 (THU0766-HPR)
Domiciano, D., 1448 (AB1124)
Domingues-Casas, L., 1116 (AB0197)
Dominguez, E., 481 (FRI0005)
Dominguez, S.T., 1125 (AB0220)
Domínguez Casas, L., 75 (OP0059)
Domínguez Casas, L.C., 718 (FRI0607)
Domínguez-Casas, L., 326 (THU0326), 405 (THU0526), 420 (THU0567), 742 (FRI0666), 1166 (AB0337)
Dominguez-Casas, L., 251 (THU0134), 569 (FRI0226)
Domínguez-Casas, L.C., 108 (OP0135), 614 (FRI0336), 1255 (AB0583)
Domínguez-González, M., 736 (FRI0651)
Dominguez-Quesada, C., 1525 (SAT0760-HPR)
Dominovic, M., 771 (SAT0009)
Domján, A., 767 (FRI0731), 1548 (AB1248-HPR)
Domsic, R., 105 (OP0126)
Don-Pedro, D., 82 (OP0075)
Donaldson, M., 471 (THU0698)
Donder, E., 1462 (AB1162)
Donepudi, K., 349 (THU0378)
Dong, B., 142 (OP0218)
Dong, J., 884 (SAT0294), 1081 (AB0100)
Dong, L., 724 (FRI0622)
Dong, Z., 1535 (AB1210-HPR)
Dongze, W., 689 (FRI0523)
Donnelly, S., 1432 (AB1078)
Doody, G., 314 (THU0293)
Dooley, M.A., 153 (LB0002)
Doorenspleet, M., 123 (OP0172), 601 (FRI0303)
Doorenspleet, M.E., 124 (OP0173)
Doornbos-van der Meer, B., 647 (FRI0424)
Doria, A., 305 (THU0268), 437 (THU0611), 603 (FRI0308), 861 (SAT0231), 867 (SAT0248), 1123 (AB0215), 1184 (AB0389), 1209 (AB0455, AB0456), 1214 (AB0467), 1272 (AB0630), 1439 (AB1099)
Dorjee, A., 202 (THU0008), 621 (FRI0356)
Dorleijn, D., 961 (SAT0492)
Dörner, T., 92 (OP0098), 184 (OP0311), 575 (FRI0239)
Dorner, T., 50 (OP0002), 67 (OP0040)
Dorner, T.E., 1154 (AB0302)
Dörtbaş, F., 397 (THU0506)
Dos Santos, T.A.F.G., 820 (SAT0135)
dos Santos, T.A.F.G., 1111 (AB0186)
Dosgilbert, A., 1059 (AB0035)
Doskas, T., 588 (FRI0269)
Dossier, A., 187 (OP0319), 883 (SAT0293)
Dostanko, N., 1240 (AB0541)
Dostanko, V., 1240 (AB0541)
Dou, Z., 1226 (AB0501)
Doualla, M.S., 368 (THU0425), 997 (SAT0587, SAT0588), 1362 (AB0874)
Doucet, J., 886 (SAT0301), 1229 (AB0509)
Dougados, M., 14 (SP0055), 63 (OP0030), 73 (OP0054), 80 (OP0070), 100 (OP0115, OP0116), 102 (OP0119), 129 (OP0188), 131 (OP0192), 155 (OP0241), 156 (OP0244), 158 (OP0248), 258 (THU0152), 260 (THU0158), 334 (THU0346), 336 (THU0350), 337 (THU0353), 339 (THU0356, THU0357), 349 (THU0379), 350 (THU0382), 388 (THU0482), 389 (THU0483), 428 (THU0588, THU0589), 510 (FRI0086), 515 (FRI0096), 524 (FRI0116), 569 (FRI0225), 649 (FRI0430), 650 (FRI0432), 665 (FRI0472), 811 (SAT0112), 831 (SAT0163), 917 (SAT0386), 996 (SAT0583), 1296 (AB0694), 1303 (AB0712)
Douglas, A., 1241 (AB0542)
Douglas, K., 546 (FRI0173), 632 (FRI0382), 1331 (AB0784)
Douma, S., 542 (FRI0161)

Dove, D., 118 (OP0160)
Dowell, S., 817 (SAT0129)
Doyle, R., 127 (OP0182)
Draganescu, C., 435 (THU0607)
Draghessi, A., 247 (THU0121)
Drago, F., 457 (THU0664)
Dragone, L., 593 (FRI0285), 857 (SAT0221), 865 (SAT0242), 868 (SAT0250)
Drake, M., 742 (FRI0666)
Drapé, J.-L., 170 (LB0001)
Dreinhöfer, K., 760 (FRI0713), 1440 (AB1102)
Dressler, F., 390 (THU0487)
Dreux, C., 171 (OP0278-PARE)
Drevets, W.C., 250 (THU0130)
Dreyer, L., 96 (OP0106), 98 (OP0112), 159 (OP0251), 226 (THU0072), 341 (THU0361), 451 (THU0649), 686 (FRI0518), 1332 (AB0786)
Driban, J., 384 (THU0469)
Drivelegka, P., 164 (OP0262), 360 (THU0404), 361 (THU0408), 364 (THU0414), 375 (THU0443)
Drljača, S., 1186 (AB0393)
Drobyshev, A., 1198 (AB0423)
Droitcourt, C., 1261 (AB0599)
Dromer, C., 1049 (AB0007)
Droogne, W., 1275 (AB0638)
Drosos, A., 559 (FRI0205), 836 (SAT0176)
Drosos, A.A., 1193 (AB0411), 1217 (AB0476), 1243 (AB0551), 1329 (AB0779)
Droz, N., 1401 (AB0990)
Druce, K., 758 (FRI0708)
Druce, K.L., 519 (FRI0105), 759 (FRI0712), 1453 (AB1138)
Druckmann, I., 747 (FRI0679)
Drumez, E., 152 (OP0236)
Dryglewska, M., 1273 (AB0631)
Drynda, A., 1072 (AB0074)
Drynda, S., 1072 (AB0074)
Du, J., 326 (THU0327)
Du, X., 1084 (AB0110)
Duan, X., 1491 (THU0762-HPR)
Duarte, A.C., 533 (FRI0138), 1264 (AB0607)
Duarte, A.L., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Duarte, A.L.B.P., 990 (SAT0566), 991 (SAT0567), 1372 (AB0903)
Duarte, C., 112 (OP0144-HPR), 186 (OP0315), 255 (THU0145), 1501 (FRI0748-HPR), 1510 (SAT0718-HPR)
Duarte, V., 670 (FRI0483)
Duarte, V.M., 933 (SAT0427)
Duarte-Millán, M.-A., 597 (FRI0293)
Dubey, D., 320 (THU0307), 913 (SAT0375)
Dubey, S., 988 (SAT0559)
Dubinina, T., 660 (FRI0458), 920 (SAT0394), 1198 (AB0423), 1294 (AB0688), 1411 (AB1017)
Dubinsky, D., 311 (THU0285), 590 (FRI0276), 729 (FRI0635), 991 (SAT0568), 1217 (AB0478)
Dubnovitsky, A., 779 (SAT0032)
Dubois, C., 481 (FRI0004)
Dubost, J.-J., 289 (THU0225), 813 (SAT0117), 1297 (AB0696), 1360 (AB0869), 1384 (AB0942)
Dubost, J.J., 1033 (SAT0682)
Duca, I., 1193 (AB0410)
Ducoulombier, V., 359 (THU0402)
Ducourau, E., 335 (THU0349)
Ducrot, M.-C., 265 (THU0169), 271 (THU0184)
Duda, J.L., 764 (FRI0723), 1044 (SAT0712)
Dudek, A., 267 (THU0173), 1419 (AB1042)
Dudenbostel, T., 363 (THU0413)
Dudler, J., 92 (OP0099), 267 (THU0174), 431 (THU0596), 1445 (AB1114)
Dufau, P., 866 (SAT0246)
Duffus, K., 179 (OP0298)
Dufour, A.B., 1032 (SAT0679)
Duftner, C., 175 (OP0288)
Duley, L., 167 (OP0268)
Dulgeroglu, D., 733 (FRI0643)
Dulic, S., 780 (SAT0034)
Dumitru, R.B., 635 (FRI0390)
Dumont, A., 1256 (AB0588)
Dumont, C., 1384 (AB0941)
Dumusc, A., 302 (THU0259)
Duncombe, P., 318 (THU0301)
Dundar, U., 475 (THU0709), 1162 (AB0324)
Dunkel, J., 786 (SAT0050)
Dunogeant, L., 51 (OP0004)
Dunsmuir, R., 648 (FRI0427)
Dupont, S., 118 (OP0161), 648 (FRI0428)
Duque, A.P., 176 (OP0290)
Duque, N., 1190 (AB0404)
Duque Botero, J., 308 (THU0275)
Duraj, V., 1033 (SAT0683)
Durán, A., 1098 (AB0149)
Durán, A.R., 1091 (AB0126)
Duran, J., 826 (SAT0151)
Duran-Barragan, S., 806 (SAT0100), 1075 (AB0083), 1164 (AB0330)
Durand, F., 510 (FRI0086), 788 (SAT0055)
Dures, E., 46 (SP0190), 110 (OP0139-HPR), 1528 (SAT0769-HPR)
Durez, P., 92 (OP0098), 174 (OP0284), 233 (THU0088)
Durigan, V., 387 (THU0479), 1429 (AB1071)
Durigutto, P., 1076 (AB0086)
Durmus, D., 1298 (AB0699)
Durnez, A., 728 (FRI0633)
Dursun, E., 1380 (AB0927)
Dursun, N., 1380 (AB0927)
Duruoz, T., 469 (THU0692), 715 (FRI0597)
Dutheil, F., 213 (THU0039)
Dutriaux, C., 710 (FRI0584)
Dutton, K., 1277 (AB0643)
Dutz, J., 937 (SAT0437)
Duval, M., 288 (THU0222)
Duymaz, T., 1381 (AB0931)
Dvorovkin, A., 1153 (AB0298)
Dwyer, T., 960 (SAT0489)
Dydykina, I.S., 1347 (AB0828)
Dyomina, A., 1411 (AB1017)
Dzerovych, N., 1469 (AB1182)
Dzhailobaeva, K., 1227 (AB0503)
Dzhetybaeva, M., 1227 (AB0503)
Dzhumakadyrova, A., 1227 (AB0503)
Dziedzic, K., 973 (SAT0523), 1343 (AB0817), 1552 (PARE0002)
Dziedzic, K.S., 1433 (AB1081)
Dziewiszek, W., 1112 (AB0187)

Ea, H.-K., 53 (OP0007), 212 (THU0034), 216 (THU0046), 359 (THU0401), 367 (THU0424), 1364 (AB0882), 1371 (AB0900)
Eaddy, M., 842 (SAT0188)
Earsman, G., 1534 (AB1206-HPR)
Eashwary, M., 1512 (SAT0722-HPR)
Eaton, S., 1459 (AB1156)
Ebata, S., 138 (OP0207)
Ebede, C., 82 (OP0075)
Ebeling, P.R., 71 (OP0048)
Ebener, W., 560 (FRI0207)
Eberhardt, K., 1513 (SAT0726-HPR)
Eberl, G., 1173 (AB0357)
Ebina, K., 115 (OP0152), 282 (THU0207)
Eccles, J.A., 1379 (AB0926)
Ecemis, S., 102 (OP0120)
Echchilali, K., 613 (FRI0333)
Echeverry, A., 1225 (AB0498)
Eck, S., 192 (OP0331)
Eder, L., 98 (OP0111), 688 (FRI0522)
Eder, R., 257 (THU0150)
Edlin, H., 803 (SAT0092)
Edugan, M., 748 (FRI0682)
Edwards, C.J., 672 (FRI0487), 684 (FRI0513), 933 (SAT0426), 942 (SAT0448), 1180 (AB0377), 1205 (AB0444)
Edwards, N.L., 377 (THU0448)
Eelsing, E., 607 (FRI0317)
Effat, L., 1047 (AB0002)
Efthimiou, P., 395 (THU0502), 714 (FRI0595)
Efthymiou, G., 1279 (AB0648)
Egea-Serrano, P., 1496 (FRI0735-HPR)
Egeberg, A., 98 (OP0112)
Egert, T., 1556 (PARE0012)
Egert, Y., 1556 (PARE0012)
Egila, S., 781 (SAT0038)
Egorova, O., 464 (THU0680), 720 (FRI0611)
Egsmose, E.L., 669 (FRI0481)
Egsmose, E.M., 1328 (AB0778)
Eguchi, K., 723 (FRI0620)
Ehkirch, F.-P., 1072 (AB0073)
Ehrbar, M., 88 (OP0088)
Ehresmann, G., 421 (THU0570), 1354 (AB0852)
Eichbauer-Sturm, G., 1455 (AB1144)
Eid, M.M., 1053 (AB0018)
Eide, R.E.M., 1478 (THU0726-HPR)
Eijsbouts, A., 112 (OP0145-HPR)
Eisenreich, M.A., 167 (OP0269)
Eissa, M., 874 (SAT0265), 1048 (AB0006)
Eisterhues, C., 530 (FRI0130)
Ejbjerg, B., 784 (SAT0045)
Ejbjerg, B.J., 732 (FRI0641)
Ekbote, G., 1253 (AB0579)
Ekbote, G.G., 1247 (AB0561, AB0562)
Eketjäll, S., 586 (FRI0265)
Ekinci, A., 637 (FRI0396)
Ekinci, G., 1013 (SAT0633)
Ekiz, E., 1499 (FRI0744-HPR)
Eklund, K., 341 (THU0361), 827 (SAT0152)
Eklund, K.K., 61 (OP0024)
Ekman, P., 61 (OP0024)
Ekroth, M., 171 (OP0277-PARE), 1561 (AB1253-PARE)
Ekström, G., 891 (SAT0314)
Ekvall Hansson, E., 1501 (FRI0749-HPR)
Ekwall, A.-K.H., 117 (OP0156)
El Amri, N., 926 (SAT0409), 927 (SAT0411)
El Arousi, N., 431 (THU0597), 821 (SAT0138), 1149 (AB0287)
EL Attar, E., 1332 (AB0787)
El Bakry, S.A., 1224 (AB0495)
El Binoune, I., 1136 (AB0252), 1163 (AB0327, AB0328), 1168 (AB0343)
El Dessouki, D., 1047 (AB0002)
El Gaafary, M., 431 (THU0597), 821 (SAT0138), 1149 (AB0287)
El Ghannudi, S., 106 (OP0128)
El Haddad, M., 523 (FRI0114)
El Hadidi, K., 874 (SAT0265)
El Hadidi, T., 874 (SAT0265)
El Maataoui, A., 697 (FRI0548), 1349 (AB0836)
El Mansouri, F., 483 (FRI0009)
El Miedany, Y., 431 (THU0597), 821 (SAT0138), 1149 (AB0287)
El morsy, S., 1469 (AB1181)
El Refai, R., 874 (SAT0265)
El Sammak, A.A., 733 (FRI0644)
El Zohri, M., 1235 (AB0527)
El-Azizi, N.O., 307 (THU0272), 1216 (AB0473)
El-Barbary, A.M., 404 (THU0524)
El-Fishawy, H.S., 1237 (AB0533)
El-Gabalawy, H., 178 (OP0295)
El-Gabalawy, H.S., 1117 (AB0199)
El-Gamal, S.M., 1465 (AB1171)
El-Gendy, H., 743 (FRI0669)
El-Gohary, R., 743 (FRI0669)
El-Hajj-Fuleihan, G., 1042 (SAT0705)
El-Hakeim, E., 1235 (AB0527)
El-Hewala, A.E.-S.I., 1404 (AB1000)
El-Jawhari, J., 159 (OP0250)
El-Jawhari, J.J., 1070 (AB0066)
El-Rabbat, S.M., 1045 (SAT0715)
EL-Saadany, H.A., 1138 (AB0256)
El-Sherbiny, Y., 91 (OP0095)
El-Sherbiny, Y.M., 152 (OP0235), 314 (THU0293), 771 (SAT0007), 869 (SAT0251)
El-sherbiny, Y.M., 1070 (AB0066)
El-Siri, O.M., 1151 (AB0293)
Elad Sfadia, G., 508 (FRI0082)
Elalouf, O., 1118 (AB0203)
Elamir, A., 1228 (AB0505)
Elamri, N., 543 (FRI0165)
Elashoff, D.A., 1526 (SAT0765-HPR)
Elashoff, R., 104 (OP0124)
ElBadawi, F.A., 1350 (AB0839)
Elbadri, M., 1309 (AB0728)
Elbæk, K.J., 456 (THU0660), 775 (SAT0020)
ElBakry, S.A., 1216 (AB0473)
Elbez, Y., 577 (FRI0245), 1141 (AB0267)

Elefante, E., 320 (THU0308), 446 (THU0636), 584 (FRI0260), 589 (FRI0272), 875 (SAT0268)
Eleftheriadis, G., 893 (SAT0320)
Eleftheriou, D., 74 (OP0056), 1389 (AB0957)
Elera-Fitzcarrald, C., 1142 (AB0269)
Elewa, E.A.K., 1465 (AB1171)
Elewaut, D., 62 (OP0026), 118 (OP0160), 125 (OP0176), 490 (FRI0029), 653 (FRI0440), 654 (FRI0444), 763 (FRI0719), 1305 (AB0716)
Elewski, B.E., 1319 (AB0756)
Elezoglou, A., 1204 (AB0442)
Elfering, A., 478 (THU0718)
Elfving, P., 61 (OP0024)
Elgohary, R., 1422 (AB1051)
Elgueta, S.F., 1257 (AB0590)
Eliasson, B., 674 (FRI0492)
Eliopoulos, E., 205 (THU0015)
Elisa, G., 343 (THU0366)
Eliseev, M., 1019 (SAT0646), 1369 (AB0895)
Eliseo, E., 657 (FRI0451)
Elizondo, L.J., 1196 (AB0419)
Elizondo-Riojas, G., 1118 (AB0204), 1119 (AB0205), 1156 (AB0309)
Elkabli, H., 613 (FRI0333)
Elkayam, O., 747 (FRI0679), 1095 (AB0138), 1118 (AB0203), 1328 (AB0776)
Elkhalifa, M., 740 (FRI0663), 1420 (AB1044)
Ellegaard, K., 161 (OP0254-HPR), 737 (FRI0654), 1481 (THU0734-HPR)
Elleuch, M., 1346 (AB0826), 1536 (AB1214-HPR)
Ellingsen, T., 168 (OP0270), 546 (FRI0174), 660 (FRI0460), 732 (FRI0641), 784 (SAT0045)
Ellins, E.A., 1173 (AB0358)
Ellis, L., 562 (FRI0211), 836 (SAT0175)
Ellmeier, W., 499 (FRI0055)
Ellul, P., 419 (THU0564)
Elmallah, R., 1332 (AB0787)
Elmesmari, A., 138 (OP0208)
Eloranta, M.-L., 182 (OP0305)
Elpek, G.Ö., 296 (THU0243)
Elsaman, A.M., 1008 (SAT0619), 1150 (AB0291)
Elsayad, E.S., 1000 (SAT0596)
Elsayed, A.M., 1216 (AB0473)
Elshabacy, F., 1138 (AB0256)
Elshanawany, A.T., 1404 (AB1000)
Elsharkawy, E., 1171 (AB0351)
Elshof, E., 1075 (AB0082)
Elting, L., 692 (FRI0531, FRI0532)
Elvan, A., 477 (THU0714)
Elvin, K., 885 (SAT0297)
Emamifar, A., 246 (THU0118), 533 (FRI0137, FRI0139), 1431 (AB1075), 1545 (AB1239-HPR)
Eman Abdulle, A., 625 (FRI0366), 1265 (AB0610)
Emans, P., 433 (THU0603), 977 (SAT0531)
Emery, P., 91 (OP0095), 137 (OP0204), 152 (OP0235), 159 (OP0250), 174 (OP0284), 196 (OP0341), 227 (THU0075), 238 (THU0101), 240 (THU0104), 242 (THU0110), 244 (THU0114), 314 (THU0293), 455 (THU0659), 510 (FRI0087), 518 (FRI0102), 527 (FRI0124), 566 (FRI0219), 627 (FRI0370), 635 (FRI0390), 727 (FRI0630), 771 (SAT0007), 785 (SAT0047), 786 (SAT0049), 794 (SAT0070), 834 (SAT0169), 869 (SAT0251), 987 (SAT0556), 1010 (SAT0624), 1016 (SAT0639), 1019 (SAT0647), 1085 (AB0112), 1205 (AB0444), 1329 (AB0780)
Emir, B., 670 (FRI0484)
Emiroglu, T., 1260 (AB0598)
Emkey, R., 54 (OP0010)
Emmi, G., 263 (THU0164), 411 (THU0540), 711 (FRI0586), 1209 (AB0456), 1272 (AB0630)
Emmi, L., 263 (THU0164), 867 (SAT0248), 1209 (AB0456)
Enache, L., 1018 (SAT0644)
Endo, H., 202 (THU0006)
Endo, Y., 1016 (SAT0640), 1200 (AB0431), 1416 (AB1035)
Eng, S., 455 (THU0659), 627 (FRI0370), 635 (FRI0390)
Engdahl, C., 775 (SAT0019), 848 (SAT0201)
Engel, R., 1070 (AB0067)
Engelbrecht, M., 1511 (SAT0719-HPR)
Engelke, K., 247 (THU0122), 1011 (SAT0628)
Engesser, M., 324 (THU0321)
Englbrecht, M., 73 (OP0052), 142 (OP0217), 159 (OP0249), 236 (THU0096), 240 (THU0105), 516 (FRI0098), 655 (FRI0446), 725 (FRI0625), 1011 (SAT0628)
Englund, M., 376 (THU0446)
Engström, M., 212 (THU0036), 484 (FRI0013)
Ennaifer, R., 1348 (AB0831, AB0832, AB0833), 1349 (AB0834)
Enriquez, F., 267 (THU0173)
Ensrud, K., 958 (SAT0484)
Ensrud, K.E., 690 (FRI0525)
Epis, O., 742 (FRI0667), 1152 (AB0295), 1412 (AB1022)
Epis, O.M., 1022 (SAT0654)
Eppeland, S., 161 (OP0255-HPR)
Er, G., 1156 (AB0308)
Er Gülbezer, E., 899 (SAT0338)
Erausquin, C., 1107 (AB0173)
Erba, G., 1154 (AB0301)
Erblang, F., 318 (THU0301)
Ercaliskan, A., 1243 (AB0550)
Ercan, I., 1380 (AB0927)
Erceg, M., 592 (FRI0282), 883 (SAT0291)
Erdat, E.C., 250 (THU0131), 534 (FRI0140), 1300 (AB0706)
Erden, A., 250 (THU0131), 256 (THU0147), 327 (THU0329), 329 (THU0333), 402 (THU0518), 414 (THU0548), 448 (THU0642), 534 (FRI0140), 588 (FRI0269), 616 (FRI0342), 637 (FRI0397), 720 (FRI0612), 854 (SAT0216), 1035 (SAT0687), 1113 (AB0189), 1127 (AB0226), 1175 (AB0363), 1194 (AB0414), 1204 (AB0442), 1215 (AB0471), 1256 (AB0586), 1262 (AB0604), 1300 (AB0706), 1412 (AB1023), 1531 (AB1198-HPR)
Erdes, S., 342 (THU0363), 660 (FRI0458), 920 (SAT0394), 1198 (AB0423), 1294 (AB0688), 1411 (AB1017)
Erdoğan, M., 719 (FRI0610), 1232 (AB0520)
Erdogan, M., 321 (THU0311)
Erdozain, J.-G., 593 (FRI0284)
Erduran, M., 999 (SAT0594), 1339 (AB0806), 1340 (AB0807), 1538 (AB1218-HPR)
Eremeeva, A., 560 (FRI0208)
Erer, B., 327 (THU0329)
Erez, Y., 1282 (AB0658)
Erfani fam, S., 1003 (SAT0604)
Ergelen, R., 417 (THU0557), 1013 (SAT0633)
Ergenç, I., 1013 (SAT0633)
Ergezen, B., 412 (THU0542), 714 (FRI0596)
Ergulu Esmen, S., 931 (SAT0422)
Ergun, G., 716 (FRI0600)
Ergun, T., 417 (THU0557)
Erhayiem, B., 238 (THU0101)
Ericsson, P., 770 (SAT0005)
Eriksson, F., 162 (OP0256-HPR)
Eriksson, L.R., 1500 (FRI0747-HPR)
Erkan, D., 150 (OP0231), 418 (THU0561)
Erken, E., 905 (SAT0355)
Erkorkmaz, U., 1320 (AB0757)
Erlacher, L., 1154 (AB0302)
Erlandsson, M., 777 (SAT0026), 779 (SAT0033)
Erler, A., 1200 (AB0430)
Erler, N.S., 532 (FRI0136)
Erman, F., 455 (THU0658)
Ermurat, S., 969 (SAT0511), 1196 (AB0418), 1434 (AB1086)
Ernberg, M., 163 (OP0260-HPR)
Ernestam, S., 341 (THU0361), 452 (THU0652)
Eröksüz, R., 974 (SAT0525)
Erra, A., 946 (SAT0458), 1351 (AB0843), 1469 (AB1183)
Erraoui, M., 1136 (AB0252), 1163 (AB0327, AB0328), 1168 (AB0343), 1358 (AB0862), 1365 (AB0883, AB0884, AB0885), 1418 (AB1041)
Erre, G.L., 496 (FRI0046), 535 (FRI0143)
Erten, S., 992 (SAT0570)
Ertenli, A.I., 402 (THU0518), 1531 (AB1198-HPR)
Ertenli, I., 250 (THU0131), 256 (THU0147), 329 (THU0333), 414 (THU0548), 448 (THU0642), 534 (FRI0140), 616 (FRI0342), 720 (FRI0612), 854 (SAT0216), 1035 (SAT0687), 1113 (AB0189), 1127 (AB0226), 1175 (AB0363), 1194 (AB0414), 1300 (AB0706), 1412 (AB1023)
Ertürk, Z., 644 (FRI0416), 889 (SAT0310), 910 (SAT0367), 1013 (SAT0633), 1310 (AB0731)
Erturk, Z., 417 (THU0557), 821 (SAT0139)
Ervin, J., 121 (OP0167)
Esatoglu, N.S., 323 (THU0317)
Esatoğlu, S.N., 719 (FRI0610), 1246 (AB0558)
Esatoglu, S.N., 208 (THU0024), 331 (THU0339), 618 (FRI0348), 1186 (AB0394)
Esbensen, B.A., 73 (OP0055-HPR), 1512 (SAT0723-HPR)
Esbesen, J., 553 (FRI0190)
Escalante, B., 330 (THU0336)
Escobar, A., 826 (SAT0150)
Escobar Martinez, A., 111 (OP0141-HPR)
Escoubet, B., 187 (OP0319)
Escudero, A., 492 (FRI0035), 497 (FRI0048), 504 (FRI0069), 648 (FRI0429), 840 (SAT0183), 1082 (AB0104)
Escudero Contreras, A., 258 (THU0151), 700 (FRI0555), 975 (SAT0527), 1143 (AB0270)
Escudero-Contreras, A., 194 (OP0336), 350 (THU0380), 441 (THU0624), 649 (FRI0431), 650 (FRI0434), 1078 (AB0092), 1268 (AB0619)
Esdaile, J., 373 (THU0440), 438 (THU0615)
Eshed, I., 32 (SP0128), 747 (FRI0679)
Eskitzis, A., 577 (FRI0244)
Esmaeilzadeh, S., 1347 (AB0827)
Espanha, M.R., 1553 (PARE0005)
Espartero-Santos, M., 1107 (AB0172)
Esparza-Holguin, H.E., 760 (FRI0714)
Espejo Pascencia, J.I., 1450 (AB1128)
Esperanza, N., 174 (OP0286)
Espí-lópez, G.V., 1380 (AB0929)
Espigol Frigole, G., 610 (FRI0324)
Espígol-Frigolé, G., 1252 (AB0575)
Espinosa, A., 182 (OP0305)
Espinosa, G., 150 (OP0231), 414 (THU0549), 418 (THU0561), 421 (THU0569), 716 (FRI0602)
Espinosa, M., 452 (THU0651)
Espinosa, R., 739 (FRI0660), 1006 (SAT0613), 1339 (AB0805)
Espinosa Malpartida, M., 1399 (AB0986)
Espinoza Martinez, J.E., 1164 (AB0331)
Espitia, O., 1256 (AB0588)
Esposito, C., 634 (FRI0388), 1267 (AB0615), 1272 (AB0629)
Esquivel Valerio, J.A., 1448 (AB1122)
Esquivel-Valerio, J.A., 425 (THU0581), 1054 (AB0023), 1410 (AB1015)
Essafi, F., 1306 (AB0720)
Esser, L., 1445 (AB1115)
Estañ-Capell, N., 1415 (AB1032)
Estanqueiro, P., 186 (OP0315)
Estévez, M., 595 (FRI0289), 1252 (AB0576), 1400 (AB0988)
Estevez, O., 884 (SAT0295)
Estévez-López, F., 45 (SP0187), 111 (OP0142-HPR), 1499 (FRI0743-HPR)
Estopiñan, L., 837 (SAT0178)
Estopiñán-Fortea, L., 1001 (SAT0600)
Estrada, E., 737 (FRI0653), 1276 (AB0640)
Estrada, P.V., 1005 (SAT0610)
Estrada-Y-Martin, R.M., 624 (FRI0363)
Esveldt, R., 601 (FRI0303)
Etchegaray-Morales, I., 311 (THU0283)
Etcheto, A., 73 (OP0054), 102 (OP0119), 334 (THU0346), 336 (THU0350), 339 (THU0356, THU0357), 388 (THU0482), 389 (THU0483), 665 (FRI0472), 917 (SAT0386), 1296 (AB0694), 1303 (AB0712)
Etzel, C.J., 953 (SAT0472), 1121 (AB0210), 1330 (AB0783)
Eudy, A.M., 540 (FRI0157), 813 (SAT0119), 950 (SAT0466)
Eugénio, G., 255 (THU0145)
Eugenio, G., 518 (FRI0102)
Euller Ziegler, L., 1438 (AB1095)
Euller-Ziegler, L., 258 (THU0152), 707 (FRI0578), 811 (SAT0112), 851 (SAT0207), 967 (SAT0507)

Eun, J.S., 422 (THU0572), 514 (FRI0093), 783 (SAT0042)
Eun, Y., 1371 (AB0901)
Eun, Y.H., 646 (FRI0422), 749 (FRI0685)
Eurico da Fonseca, J., 436 (THU0610)
Eurico Fonseca, J., 784 (SAT0046)
Eurico-Fonseca, J., 186 (OP0315)
Eusébio, M., 186 (OP0315), 1254 (AB0581)
Evangelatos, G., 836 (SAT0176)
Evans, A.L., 1433 (AB1081)
Evans, N., 1343 (AB0817)
Evans-Marin, H., 191 (OP0329), 504 (FRI0072)
Evennett, H., 1396 (AB0976)
Eveque-Mourroux, M., 977 (SAT0531)
Everett, C.C., 1205 (AB0444)
Evertsen, G., 1539 (AB1222-HPR)
Evrard, B., 1059 (AB0035)
Evstigneeva, L., 273 (THU0188)
Exarchou, S., 154 (OP0240)
Exeni, I., 440 (THU0619)
Exer, P., 130 (OP0189), 267 (THU0174), 335 (THU0347)
Expósito, L., 1390 (AB0959)
Exposito, R., 843 (SAT0191)
Expósito Pérez, L., 695 (FRI0541)
Expositor-Rodríguez, R., 477 (THU0713)
Eymard, F., 188 (OP0323)
Eymir, M., 1339 (AB0806), 1340 (AB0807), 1519 (SAT0742-HPR), 1542 (AB1232-HPR)
Eyre, S., 179 (OP0298), 200 (THU0003), 781 (SAT0037), 1087 (AB0115)
Ez-Zaitouni, Z., 156 (OP0244)
Ezzeddine, M., 1377 (AB0921)

F Cons Molina, F., 824 (SAT0146)
F-Carballido, C., 718 (FRI0607)
F-Cid, C., 718 (FRI0607)
F-Espartero, C., 718 (FRI0607)
Fabiani, C., 411 (THU0540), 711 (FRI0586), 1461 (AB1160)
Fabre, R., 851 (SAT0207)
Fabre, S., 382 (THU0461), 465 (THU0684)
Fabris, F., 1066 (AB0055)
Fabro, C., 585 (FRI0263), 1101 (AB0156)
Facchetti, R., 1154 (AB0301)
Facciolo, J., 966 (SAT0503)
Facio-Lince García, A., 905 (SAT0354)
Fadous Khalife, M.C., 406 (THU0528)
Fageli, K.M., 229 (THU0080), 938 (SAT0440)
Fagerli, K., 341 (THU0361), 686 (FRI0518)
Fagerli, K.M., 97 (OP0109), 334 (THU0345), 673 (FRI0490)
Faggioni, R., 867 (SAT0249)
Fagil, A., 1469 (AB1183)
Fagiuoli, S., 540 (FRI0155)
Fagnani, F., 786 (SAT0050)
Faguer, S., 188 (OP0321)
Fahmi, H., 126 (OP0181), 221 (THU0061), 483 (FRI0009)
Fahrleitner-Pammer, A., 1423 (AB1053)
Fairley, D., 1372 (AB0904)
Fais, S., 496 (FRI0045)
Fajardo, D., 586 (FRI0264)
Fajardo Hermosillo, L.D., 1210 (AB0457)
Fakharzadeh, S., 950 (SAT0465)
Fakhouri, F., 778 (SAT0029)
Falahee, M., 1511 (SAT0719-HPR)
Falappone, P.C.F., 808 (SAT0105), 1327 (AB0773)
Falcao, S., 1011 (SAT0626), 1408 (AB1011)
Falck, D., 509 (FRI0083)
Falco, A., 873 (SAT0262)
Falconi, M., 410 (THU0538), 1399 (AB0985)
Falenta-Hitnarowicz, M., 1470 (AB1184)
Faliti, C.E., 294 (THU0240)
Fallo, L., 1214 (AB0467)
Fallon, L., 670 (FRI0484)
Fan, A., 813 (SAT0117), 1033 (SAT0682), 1297 (AB0696)
Fan, F., 555 (FRI0194)
Fan, H., 275 (THU0193), 1202 (AB0436)
Fan, J., 63 (OP0028), 419 (THU0563), 947 (SAT0459), 1052 (AB0017), 1079 (AB0094)
Fan, W., 547 (FRI0176), 748 (FRI0681)
Fan, Y., 600 (FRI0302)
Fana, V., 726 (FRI0628)
Fang, C., 1219 (AB0482)
Fanizzi, R., 1135 (AB0250), 1268 (AB0618)
Fanlo, P., 421 (THU0569), 597 (FRI0293)
Fanouriakis, A., 192 (OP0332), 297 (THU0246), 300 (THU0254), 574 (FRI0236), 577 (FRI0244), 588 (FRI0269), 850 (SAT0204), 1204 (AB0442), 1215 (AB0471)
Farah, Z., 333 (THU0344), 431 (THU0595)
Fardellone, P., 388 (THU0480)
Farhat, A., 1383 (AB0937)
Farina, I., 234 (THU0090), 1127 (AB0227)
Fariñas-Padrón, L., 1244 (AB0553)
Farinon, M., 502 (FRI0066)
Farkas, F., 675 (FRI0493), 681 (FRI0507), 951 (SAT0467), 1319 (AB0755)
Farouk, A.S.M., 307 (THU0272)
Farouk, H.M., 307 (THU0272)
Farouk, S.M., 1138 (AB0256)
Farrag, D., 1332 (AB0787)
Farrell, J.F., 1290 (AB0678)
Farrell, W.E., 776 (SAT0022)
Faruch, M., 1018 (SAT0645)
Fasano, S., 151 (OP0233), 630 (FRI0378), 1118 (AB0202)
Fassio, A., 363 (THU0412), 671 (FRI0485), 693 (FRI0535), 940 (SAT0443, SAT0445), 1314 (AB0742)
Fasth, A.E., 250 (THU0129)
Fathi, N.A., 741 (FRI0665)
Fathy Mohammed, T., 1138 (AB0256)
Faugier, E., 1395 (AB0974)
Faundez, A., 168 (OP0271)
Faustini, F., 655 (FRI0446), 864 (SAT0239)
Faustino, A., 464 (THU0679), 929 (SAT0418), 1163 (AB0329), 1464 (AB1168)
Fautrel, B., 31 (SP0124), 54 (OP0011), 58 (OP0018), 155 (OP0242), 158 (OP0247), 230 (THU0081), 231 (THU0084), 395 (THU0502), 434 (THU0605), 436 (THU0609), 450 (THU0646), 458 (THU0666), 465 (THU0684), 467 (THU0689), 470 (THU0695), 665 (FRI0473), 686 (FRI0519), 709 (FRI0582), 754 (FRI0699), 755 (FRI0700), 788 (SAT0055), 818 (SAT0132), 847 (SAT0199), 970 (SAT0513), 1033 (SAT0684), 1034 (SAT0685), 1186 (AB0395), 1299 (AB0701)
Fautrel, B.J., 1526 (SAT0765-HPR)
Fava, C., 805 (SAT0097)
Favale, R., 1461 (AB1160)
Favalli, E.G., 343 (THU0365, THU0366), 564 (FRI0215), 829 (SAT0158)
Favaro, M., 437 (THU0611), 634 (FRI0387), 1439 (AB1099)
Favas, C., 293 (THU0236)
Favero, M., 216 (THU0047)
Favoino, E., 495 (FRI0043), 1106 (AB0171)
Fayad, F., 667 (FRI0476), 762 (FRI0718), 1001 (SAT0599), 1159 (AB0317)
Fayet, F., 258 (THU0152), 811 (SAT0112), 1515 (SAT0733-HPR)
Fazaa, A., 1371 (AB0902), 1394 (AB0969), 1417 (AB1038)
FdezNebro, A., 1107 (AB0173)
Fearon, U., 203 (THU0011), 221 (THU0059), 321 (THU0312), 487 (FRI0020), 646 (FRI0421), 773 (SAT0013), 776 (SAT0021)
Feced Olmos, C., 1349 (AB0837), 1382 (AB0933)
Feced Olmos, C.M., 291 (THU0229), 441 (THU0623), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1433 (AB1080), 1434 (AB1084)
Fechtenbaum, J., 73 (OP0054)
Fedele, A.L., 248 (THU0123), 535 (FRI0143), 787 (SAT0052), 792 (SAT0066)
Federico, F., 154 (OP0239), 792 (SAT0066)
Fedkov, D., 924 (SAT0404)
Fedorenko, E., 273 (THU0189)
Fedorov, E., 1389 (AB0955)
Fedorov, K., 663 (FRI0466)
Fedrigo, A., 1111 (AB0186)
Feelisch, M., 625 (FRI0366)
Feeney, M., 209 (THU0026)
Feghali, H., 406 (THU0528)
Feghali-Bostwick, C., 86 (OP0083), 87 (OP0086), 91 (OP0096)
Fehler, O., 1023 (SAT0656)
Fei, G., 785 (SAT0048)
Fei, J.Z., 957 (SAT0481)
Fei, K., 581 (FRI0252)
Fei, Y., 936 (SAT0434)
Feichtinger, J., 219 (THU0054)
Feig, D.I., 363 (THU0413)
Feijoo, C., 410 (THU0539), 1042 (SAT0706)
Feist, E., 36 (SP0149), 240 (THU0105), 395 (THU0502), 461 (THU0673), 565 (FRI0217), 709 (FRI0582)
Feitosa, A.R.X., 397 (THU0505)
Feki, A., 1311 (AB0734), 1377 (AB0921)
Feldt-Rasmussen, U., 332 (THU0340)
Felea, I., 170 (OP0275), 260 (THU0156), 1245 (AB0557), 1285 (AB0666)
Felicetti, M., 327 (THU0328), 603 (FRI0308), 604 (FRI0310), 614 (FRI0337), 1257 (AB0589)
Felipe-Díaz, O.J., 1190 (AB0404)
Felis-Giemza, A., 1470 (AB1184)
Fellous, S., 1136 (AB0252), 1163 (AB0327, AB0328), 1168 (AB0343)
Fellows, C., 964 (SAT0499)
Felsenberg, D., 1172 (AB0355)
Felson, D., 986 (SAT0554)
Feltelius, N., 57 (OP0016), 563 (FRI0213)
Feng, R., 1052 (AB0017)
Feng, R.-H., 291 (THU0232)
Feng, S., 983 (SAT0546)
Feng, X., 223 (THU0066), 600 (FRI0301), 1206 (AB0447), 1370 (AB0899), 1430 (AB1073)
Feng, Z., 1081 (AB0099)
Fennelly, O., 1493 (THU0767-HPR)
Fenstad, A.M., 783 (SAT0043)
Fenstad, M.H., 223 (THU0065)
Fent, G.J., 238 (THU0101)
Fenton, S.A.M., 764 (FRI0723), 1044 (SAT0712)
Fenzl, K.H., 1154 (AB0302)
Ferchichi, S., 543 (FRI0165)
Ferfar, Y., 108 (OP0134)
Ferlicot, S., 182 (OP0307)
Fernandes, A., 441 (THU0622)
Fernandes, A.D., 711 (FRI0588)
Fernandes, G.S., 752 (FRI0693), 1028 (SAT0670)
Fernandes, J.C., 221 (THU0061)
Fernandes, L.B., 443 (THU0627)
Fernandes, M., 1378 (AB0924)
Fernandes, M.A., 1429 (AB1070)
Fernandes, S., 64 (OP0032), 464 (THU0679), 929 (SAT0418), 1163 (AB0329), 1254 (AB0581), 1464 (AB1168)
Fernandes, T.A.P., 76 (OP0061)
Fernandes Das Neves, M., 293 (THU0236), 1053 (AB0019)
Fernandez, A., 1101 (AB0155)
FernÁNdez, B., 990 (SAT0564)
Fernández, B., 320 (THU0309)
Fernandez, B.O., 625 (FRI0366)
Fernandez, C., 1205 (AB0444)
Fernández, E., 177 (OP0292)
Fernandez, E., 1014 (SAT0634)
Fernández, J., 485 (FRI0016)
Fernández, M., 930 (SAT0419), 1422 (AB1050)
Fernández, O., 748 (FRI0683), 837 (SAT0178)
Fernández, S., 556 (FRI0197)
Fernandez Castro, M., 885 (SAT0299), 1232 (AB0519)
Fernández Codina, A., 900 (SAT0340)
Fernández Conde, S., 691 (FRI0530)
Fernández Matilla, M., 1490 (THU0761-HPR)
Fernandez Matilla, M., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 1223 (AB0493), 1224 (AB0494)
Fernandez Mestre, M.T., 1048 (AB0004)
Fernandez-Ahumada, L.M., 153 (OP0238)
Fernández-Ávila, D.G., 696 (FRI0544)

Fernandez-Berrizbeitia, O., 1001 (SAT0600)
Fernández-Carballido, C., 452 (THU0651)
Fernández-Cid, C., 75 (OP0059)
Fernández-Codina, A., 415 (THU0550), 629 (FRI0375)
Fernandez-Codina, A., 636 (FRI0392)
Fernandez-Cruz, E., 593 (FRI0283)
Fernández-Díaz, C., 75 (OP0059), 251 (THU0134), 326 (THU0326), 405 (THU0526), 420 (THU0567), 569 (FRI0226), 718 (FRI0607), 742 (FRI0666), 843 (SAT0191), 1116 (AB0197)
Fernandez-Dominguez, L., 946 (SAT0457), 1322 (AB0764)
Fernández-Guitiérrez, B., 177 (OP0292)
Fernández-Llanio, N., 291 (THU0229), 590 (FRI0275), 1223 (AB0493), 1224 (AB0494)
Fernandez-Llanio, N., 878 (SAT0279), 1472 (AB1191)
Fernández-Llanio Comella, N., 1490 (THU0761-HPR)
Fernandez-Lopez, C., 978 (SAT0535)
Fernandez-Lopez, J.C., 936 (SAT0435)
Fernandez-Luque, L., 1539 (AB1222-HPR)
Fernández-Martín, J., 595 (FRI0289), 1252 (AB0576)
Fernandez-Martín, J., 1400 (AB0988)
Fernández-Moreno, M., 203 (THU0009)
Fernandez-Moreno, M., 936 (SAT0435), 978 (SAT0535), 1067 (AB0059), 1343 (AB0816)
Fernández-Nebro, A., 177 (OP0292), 261 (THU0160), 873 (SAT0263), 946 (SAT0458), 1047 (AB0003), 1135 (AB0249), 1492 (THU0766-HPR)
Fernandez-Nebro, A., 290 (THU0227), 391 (THU0489), 1174 (AB0361), 1175 (AB0362), 1443 (AB1109), 1525 (SAT0760-HPR)
Fernández-Puente, P., 1135 (AB0249), 1466 (AB1174)
Fernandez-Puente, P., 980 (SAT0539)
Fernandez-Rodriguez, J.A., 502 (FRI0063)
Fernández-Torres, J., 291 (THU0230)
Fernandez-Torres, J., 205 (THU0016), 1067 (AB0059)
Ferraccioli, G., 56 (OP0015), 138 (OP0208), 154 (OP0239), 197 (OP0343), 343 (THU0366), 394 (THU0499), 535 (FRI0143), 608 (FRI0319), 635 (FRI0390), 787 (SAT0052), 792 (SAT0066), 1077 (AB0088), 1293 (AB0685)
Ferrandez, D., 1434 (AB1085)
Ferrándiz, C., 177 (OP0292)
Ferranti, M., 634 (FRI0387)
Ferrara, R., 763 (FRI0721)
Ferrari, M., 899 (SAT0336)
Ferrari, S., 178 (OP0294)
Ferraz-Amaro, I., 245 (THU0116), 592 (FRI0280), 802 (SAT0088), 804 (SAT0095), 882 (SAT0289)
Ferre, R., 1156 (AB0307)
Ferreira, A.C., 590 (FRI0274), 1206 (AB0445)
Ferreira, B., 474 (THU0706)
Ferreira, E.A.G., 386 (THU0475, THU0476)
Ferreira, G.V., 1102 (AB0160)
Ferreira, J.C., 76 (OP0061)
Ferreira, L.G.D.S., 1412 (AB1021)
Ferreira, M., 1264 (AB0607)
Ferreira, P.L., 1314 (AB0741)
Ferreira, R., 255 (THU0145), 468 (THU0690), 528 (FRI0126)
Ferreira, R.C., 443 (THU0627)
Ferreira, R.J.O., 47 (SP0195), 112 (OP0144-HPR), 1501 (FRI0748-HPR), 1510 (SAT0718-HPR)
Ferreira, R.M., 468 (THU0691), 852 (SAT0211), 1142 (AB0268)
Ferreira, T., 474 (THU0706)
Ferreira Dos Santos, G., 1382 (AB0935)
Ferreira-Gomes, J., 1062 (AB0043)
Ferrer González, M., 1321 (AB0760)
Ferrer González, M.Á., 1228 (AB0506)
Ferrero, S., 879 (SAT0282)
Ferreyra, L., 933 (SAT0427)
Ferreyra Garrott, L., 670 (FRI0483)
Ferreyra Garrott, L.G., 1333 (AB0789)
Ferri, C., 248 (THU0123), 634 (FRI0388), 1267 (AB0615, AB0616), 1272 (AB0629)
Ferri, L., 879 (SAT0282)
Ferrieres, L., 1376 (AB0916)
Ferro, C., 1160 (AB0318, AB0319)
Ferro, F., 320 (THU0308), 584 (FRI0260), 589 (FRI0272), 875 (SAT0268)
Ferruelo Magán, M., 1362 (AB0875)
Ferry, D., 204 (THU0014)
Fervenza, F., 187 (OP0320)
Fettiplace, J., 150 (OP0232)
Feuchtenberger, M., 159 (OP0249), 516 (FRI0098), 1440 (AB1100), 1444 (AB1112)
Fevang, B.-T.S., 522 (FRI0111), 783 (SAT0043)
Fevang, B.T., 1029 (SAT0673)
Feydi, A., 662 (FRI0465), 1013 (SAT0632)
Feydy, A., 170 (LB0001)
Fiehn, C., 1272 (AB0630)
Fielding, R., 384 (THU0469)
Fighera, T., 246 (THU0119)
Figueiredo, C., 247 (THU0122), 848 (SAT0201)
Figueiredo, C.P., 73 (OP0052), 655 (FRI0446), 1448 (AB1124)
Figuereido, C., 159 (OP0249), 236 (THU0096), 516 (FRI0098)
Figus, F., 1009 (SAT0621)
Filella, X., 369 (THU0429)
Filer, A., 125 (OP0178), 190 (OP0326), 458 (THU0667), 1051 (AB0015), 1125 (AB0220)
Filer, C., 1494 (THU0769-HPR)
Filhol, E., 113 (OP0146), 1159 (AB0315)
Filipescu, I., 170 (OP0275), 260 (THU0156)
Filippi, M., 725 (FRI0624)
Filippi, N., 235 (THU0093)
Filippin, L.I., 1438 (AB1096)
Filipponi, M., 702 (FRI0563)
Filippou, G., 10 (SP0037), 236 (THU0095), 383 (THU0465), 583 (FRI0256), 730 (FRI0637), 1010 (SAT0625), 1013 (SAT0631)
Filippucci, E., 175 (OP0288), 247 (THU0121), 521 (FRI0109), 742 (FRI0667), 1013 (SAT0631), 1022 (SAT0654), 1152 (AB0295), 1281 (AB0655), 1358 (AB0863), 1412 (AB1022)
Filkova, M., 806 (SAT0099)
Filonovich, R., 398 (THU0508), 1389 (AB0956)
Finch, R., 581 (FRI0253)
Finck, B., 144 (OP0220), 831 (SAT0162)
Finckh, A., 168 (OP0271), 267 (THU0174), 523 (FRI0113), 567 (FRI0221), 569 (FRI0225), 755 (FRI0701)
Finnes, H., 1044 (SAT0711)
Finney, A.G., 1433 (AB1081)
Finnilä, M., 498 (FRI0051), 1080 (AB0098)
Finucci, A., 489 (FRI0027), 490 (FRI0028), 1099 (AB0150)
Finzel, S., 92 (OP0099), 142 (OP0217), 159 (OP0249), 236 (THU0096), 516 (FRI0098), 583 (FRI0256), 1425 (AB1058)
Fioravanti, A., 966 (SAT0503), 1343 (AB0816)
Fiorella, M.L., 639 (FRI0400)
Fiorio, M., 1483 (THU0741-HPR)
Firat, E., 616 (FRI0342)
Fırat, E., 1256 (AB0586)
Firat, H., 1463 (AB1164)
Firat, T., 1489 (THU0759-HPR)
Firestein, G.S., 757 (FRI0706)
Fischer, A., 131 (OP0194)
Fischer-Betz, R., 28 (SP0113), 302 (THU0261), 1449 (AB1127)
Fischetti, A., 728 (FRI0632)
Fischetti, C., 305 (THU0268), 905 (SAT0353), 906 (SAT0356)
Fischetti, F., 1076 (AB0086), 1318 (AB0753)
Fisher, B., 67 (OP0040), 302 (THU0259)
Fisher, B.A., 1205 (AB0444)
Fisher, C., 74 (OP0056)
Fisher, M.J., 965 (SAT0502)
Fito, C., 843 (SAT0191)
Fitzcharles, M.-A., 523 (FRI0115)
FitzGerald, O., 131 (OP0192), 141 (OP0216), 145 (OP0223), 465 (THU0683), 656 (FRI0450), 675 (FRI0493), 676 (FRI0496), 681 (FRI0507, FRI0508), 688 (FRI0521), 938 (SAT0439), 940 (SAT0444), 951 (SAT0467, SAT0468), 1319 (AB0755), 1332 (AB0786), 1434 (AB1083), 1521 (SAT0748-HPR)
Fitzgerald, O., 948 (SAT0462), 1493 (THU0767-HPR)
Fjellstedt, E., 364 (THU0414)
Fjerstad, E., 1546 (AB1244-HPR)
Flacke, J.P., 844 (SAT0193), 1187 (AB0396)
Flaisler, F., 113 (OP0146), 1159 (AB0315)
Flato, B., 40 (SP0166)
Flatø, B., 55 (OP0013)
Fleck, M., 159 (OP0249), 516 (FRI0098)
Fleeming, E., 1031 (SAT0678)
Flegar, D., 1055 (AB0026)
Fleischmann, R., 122 (OP0168), 149 (LB0003), 233 (THU0088), 371 (THU0434), 673 (FRI0489), 681 (FRI0508), 782 (SAT0041), 789 (SAT0058), 838 (SAT0180), 853 (SAT0212), 951 (SAT0469), 1147 (AB0281), 1316 (AB0747), 1364 (AB0880), 1368 (AB0892)
Fleishaker, D., 337 (THU0352), 682 (FRI0509)
Fleming, D., 837 (SAT0177)
Flendrie, M., 369 (THU0428)
Fleri Soler, J., 1514 (SAT0729-HPR)
Fletcher, J., 773 (SAT0013)
Fletcher, J.M., 776 (SAT0021)
Fleury-Cappellesso, S., 1069 (AB0064)
Flex, A., 1077 (AB0088)
Fliedner, G., 844 (SAT0193), 1187 (AB0396)
Fligelstone, K., 104 (OP0123), 1286 (AB0669), 1390 (AB0958)
Flipo, R.-M., 57 (OP0017), 258 (THU0152), 265 (THU0169), 271 (THU0184), 413 (THU0546), 789 (SAT0057), 811 (SAT0112), 843 (SAT0189), 1049 (AB0007), 1186 (AB0395), 1299 (AB0701)
Flipo, R.M., 786 (SAT0050)
Flo, T.H., 223 (THU0065)
Florence, D.L.M., 1049 (AB0007)
Florentinus, S., 822 (SAT0142)
Flores, B., 736 (FRI0651)
Flores, R., 262 (THU0162)
Flores Robles, B.J., 1399 (AB0986)
Florez, H., 369 (THU0429)
Florez-Durante, O.I., 881 (SAT0287)
Floris, A., 315 (THU0296), 975 (SAT0528)
Flouri, I., 577 (FRI0244)
Flouri, I.D., 574 (FRI0236), 850 (SAT0204)
Flouzat-Lachaniette, C.H., 188 (OP0323)
Flurey, C., 73 (OP0055-HPR), 1512 (SAT0723-HPR)
Fluri, I.A., 680 (FRI0505), 1086 (AB0114)
Flusser, G., 747 (FRI0679)
Flynn, A., 57 (OP0017)
Flynn, T., 383 (THU0464)
Foà, R., 1099 (AB0150)
Focherini, M., 954 (SAT0473)
Foeldvari, I., 75 (OP0058), 76 (OP0060), 132 (OP0196), 195 (OP0338), 398 (THU0507), 399 (THU0511), 405 (THU0525), 448 (THU0641), 1389 (AB0957), 1390 (AB0958), 1394 (AB0971)
Fogagnolo Cobra, J., 159 (OP0249), 236 (THU0096), 516 (FRI0098)
Fogel, O., 77 (OP0062), 260 (THU0158), 289 (THU0225)
Foissac, F., 258 (THU0152), 811 (SAT0112)
Fokker, C., 817 (SAT0127)
Foley, C., 1507 (FRI0766-HPR)
Foley, J.R., 238 (THU0101)
Foley, R., 958 (SAT0484)
Follet, P., 1229 (AB0509)
Follonosa, A., 718 (FRI0607)
Foltz, V., 450 (THU0646), 755 (FRI0700)
Fomina, T., 1157 (AB0311)
Fong, B., 825 (SAT0147)
Fong, W., 918 (SAT0389)
Fonollosa Pla, V., 639 (FRI0402), 900 (SAT0340), 1262 (AB0602)
Fonollosa-Pla, V., 1262 (AB0603)
Fonseca, C., 1269 (AB0621)
Fonseca, E., 317 (THU0300), 330 (THU0336), 410 (THU0539), 597 (FRI0293), 721 (FRI0615), 1042 (SAT0706)
Fonseca, E.P.D., 1412 (AB1021)

Fonseca, J., 458 (THU0667), 498 (FRI0051), 1080 (AB0098)
Fonseca, J.E., 746 (FRI0678), 830 (SAT0160), 834 (SAT0170), 840 (SAT0183), 1080 (AB0096, AB0097), 1254 (AB0581), 1317 (AB0750)
Fonseca, R., 400 (THU0513), 468 (THU0690), 852 (SAT0211), 1096 (AB0144), 1142 (AB0268)
Fonseca-Aizpuru, E., 415 (THU0550)
Font, J., 320 (THU0309)
Font, P., 648 (FRI0429), 649 (FRI0431), 926 (SAT0410), 1184 (AB0388)
Font Ugalde, P., 258 (THU0151), 700 (FRI0555), 975 (SAT0527), 1143 (AB0270)
Font-Ugalde, P., 153 (OP0238), 350 (THU0380), 441 (THU0624), 650 (FRI0434), 919 (SAT0391), 1268 (AB0619)
Fontaine, H., 776 (SAT0023)
Fontana, L., 212 (THU0035), 1054 (AB0022)
Fontana, M., 227 (THU0076), 1427 (AB1064)
Fontas, E., 967 (SAT0507)
Foote, A.M., 1367 (AB0889)
Forcignanò, R., 704 (FRI0568)
Forejtova, S., 916 (SAT0383)
Forero, E., 752 (FRI0694), 1375 (AB0913)
Förger, F., 57 (OP0017), 548 (FRI0179), 755 (FRI0701), 1510 (SAT0717-HPR)
Forien, M., 130 (OP0191), 359 (THU0401), 1535 (AB1209-HPR)
Formsma, B., 1482 (THU0737-HPR)
Fornaro, M., 259 (THU0155), 808 (SAT0105), 1059 (AB0037), 1461 (AB1160)
Fornés Ferrer, V., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829)
Fornes Ferrer, V., 1349 (AB0837)
Forsblad, H., 775 (SAT0019)
Forsblad d'Elia, H., 375 (THU0443)
Forsblad-d'Elia, H., 134 (OP0200), 154 (OP0240), 444 (THU0632), 452 (THU0652), 916 (SAT0382)
Forslind, K., 227 (THU0074), 812 (SAT0116), 1136 (AB0251), 1513 (SAT0726-HPR), 1520 (SAT0746-HPR)
Fortin, I., 1520 (SAT0745-HPR)
Forton, E., 722 (FRI0618)
Foster, M., 127 (OP0182)
Foster, N.E., 973 (SAT0521)
Foster, P.A., 711 (FRI0588)
Foster, P.J., 363 (THU0413), 1359 (AB0865)
Foti, R., 343 (THU0366), 437 (THU0611), 829 (SAT0158), 1439 (AB1099)
Fouad, N.A., 1228 (AB0505)
Fourati, H., 1311 (AB0734), 1377 (AB0921)
Fouré, A., 744 (FRI0671)
Fournier, P., 901 (SAT0342)
Foutadakis, S., 293 (THU0237)
Fox, D., 1125 (AB0220)
Fox, N.L., 861 (SAT0231)
Fox, T., 340 (THU0359), 675 (FRI0494), 683 (FRI0511), 1301 (AB0707), 1322 (AB0765), 1323 (AB0766)
Fracassi, E., 854 (SAT0215), 1124 (AB0216)
Fraedrich, G., 615 (FRI0338)
Fraenkel, L., 453 (THU0654, THU0655), 1177 (AB0370), 1441 (AB1105)
Fraga, G., 1386 (AB0948)
Fraga, M.M., 76 (OP0061)
Fragiadaki, K., 602 (FRI0306), 836 (SAT0176), 1088 (AB0117)
Fragiadiaki, K., 642 (FRI0410)
Fragio Gil, J., 441 (THU0623), 1349 (AB0837)
Fragio Gil, J.J., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Fragkakis, E., 648 (FRI0427)
Fragoulis, G., 55 (OP0012-PARE)
Fragoulis, G.E., 323 (THU0315), 535 (FRI0142)
Fraile, G., 311 (THU0284), 317 (THU0300), 330 (THU0336), 464 (THU0681), 597 (FRI0293), 886 (SAT0302)
Fraile-Rodríguez, G., 415 (THU0550)
Francés, R., 980 (SAT0540)
Franceschini, F., 305 (THU0268), 585 (FRI0261), 1207 (AB0448), 1225 (AB0497)
Franceschini, R., 411 (THU0540), 711 (FRI0586)
Franchi, F., 474 (THU0705)
Franchimont, N., 857 (SAT0222), 862 (SAT0235)
Franchini, R., 704 (FRI0568)
Franchini, S., 621 (FRI0357)
Franci, D., 86 (OP0082)
Francisco, D.M., 1213 (AB0466)
Francisco, F., 718 (FRI0607)
Franco, L., 1342 (AB0813)
Franco, L.M., 1339 (AB0805)
Francois, C., 78 (OP0065)
Frank Bertoncelj, M., 190 (OP0326)
Frank-Bertoncelj, M., 87 (OP0086)
Franke, A., 465 (THU0682)
Franke, K., 710 (FRI0585)
Frankowski, M., 276 (THU0194)
Fransen, J., 369 (THU0428), 568 (FRI0223), 1280 (AB0651, AB0652), 1286 (AB0669)
Frasca, D., 775 (SAT0018)
Frasca, L., 903 (SAT0347)
Fraser, A., 1482 (THU0738-HPR)
Fraser, A.D., 1036 (SAT0689)
Fraser, P.A., 856 (SAT0219), 863 (SAT0236)
Frassanito, F., 52 (OP0006)
Frassi, M., 1225 (AB0497)
Fraticelli, P., 905 (SAT0353), 906 (SAT0356), 1189 (AB0400)
Frayssac, T., 813 (SAT0117), 1033 (SAT0682), 1297 (AB0696)
Frazier, A., 1049 (AB0007)
Frazier-Mironer, A., 963 (SAT0497)
Frech, A., 615 (FRI0338)
Frech, T., 105 (OP0126)
Fredberg, U., 168 (OP0270), 454 (THU0657)
Frederiksen, P., 98 (OP0112)
Fredi, M., 305 (THU0268), 585 (FRI0261), 1207 (AB0448), 1225 (AB0497)
Frediani, B., 383 (THU0465), 411 (THU0540), 711 (FRI0586), 730 (FRI0637), 1010 (SAT0625)
Freeman, D., 429 (THU0591)
Freeston, J., 159 (OP0250), 1010 (SAT0624), 1016 (SAT0639)
Freeston, J.E., 727 (FRI0630)
Freier, D., 253 (THU0139)
Freire, E., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Freire, M., 290 (THU0227), 595 (FRI0289), 740 (FRI0661), 1107 (AB0173), 1252 (AB0576), 1270 (AB0624), 1400 (AB0988)
Freire-Dapena, M., 1409 (AB1012)
Freitas, E.C., 1508 (FRI0768-HPR)
Freitas, M.R., 987 (SAT0557)
Freitas, M.R.D.A., 990 (SAT0566), 991 (SAT0567), 1372 (AB0903)
Freites Núñez, D., 320 (THU0309)
Frenkel, J., 77 (OP0063), 398 (THU0509)
Frerix, M., 915 (SAT0380)
Fresko, I., 603 (FRI0307), 618 (FRI0348), 1186 (AB0394), 1246 (AB0558), 1274 (AB0634)
Fretheim, H., 106 (OP0129)
Frey, D., 1445 (AB1114)
Frias, J.F., 761 (FRI0715), 1456 (AB1146, AB1147)
Fridkin, M., 502 (FRI0065)
Fridlund, B., 1520 (SAT0746-HPR)
Friedberger, A., 247 (THU0122)
Friedman, A., 855 (SAT0217)
Friedrich, S., 1008 (SAT0618)
Friel, R., 1530 (AB1196-HPR)
Friesen, R., 374 (THU0442)
Friguet, B., 1072 (AB0073)
Frisell, T., 57 (OP0016), 93 (OP0100), 134 (OP0200), 452 (THU0652), 563 (FRI0213), 1027 (SAT0669)
Friso, L., 603 (FRI0308), 1123 (AB0215)
Friswell, M., 399 (THU0511)
Frits, M., 846 (SAT0197), 1120 (AB0207)
Fritsch-Stork, R., 184 (OP0310)
Fritsch-Stork, R.D., 182 (OP0306)
Fritzler, M., 911 (SAT0372)
Frochot, V., 1364 (AB0882)
Frodlund, M., 861 (SAT0233)
Frommer, K., 220 (THU0056), 1070 (AB0067)
Frongillo, E., 237 (THU0098), 635 (FRI0389)
Frostegård, J., 1096 (AB0142), 1523 (SAT0755-HPR)
Frostegard, J., 289 (THU0226)
Frowd, N., 1028 (SAT0670)
Fu, A.-C., 435 (THU0608)
Fu, T., 1368 (AB0893), 1369 (AB0894), 1370 (AB0897, AB0898, AB0899)
Fu, W., 306 (THU0270)
Fu, X., 108 (OP0132)
Fuchs, H., 500 (FRI0059)
Fuego, C., 1174 (AB0361), 1175 (AB0362), 1443 (AB1109)
Fuego-Valera, C., 261 (THU0160)
Fuego-Varela, C., 391 (THU0489)
Fuegos-Varela, C., 1492 (THU0766-HPR)
Fuente Goig, M.T., 441 (THU0623)
Fuentes, R., 1286 (AB0667)
Fuentevilla, P., 742 (FRI0666), 1255 (AB0583)
Fügener, S., 1067 (AB0060)
Fügner, S., 446 (THU0637)
Fuji, H., 425 (THU0579)
Fujieda, Y., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Fujii, H., 711 (FRI0587), 722 (FRI0617), 1242 (AB0546)
Fujii, M., 707 (FRI0577), 1426 (AB1063)
Fujii, T., 527 (FRI0122), 744 (FRI0673), 1200 (AB0431)
Fujii, Y., 744 (FRI0673)
Fujikawa, K., 1016 (SAT0640), 1416 (AB1035)
Fujikawa, Y., 911 (SAT0370)
Fujimoto, K., 1403 (AB0995)
Fujimoto, M., 202 (THU0006)
Fujimoto, T., 282 (THU0207)
Fujimura, T., 115 (OP0152), 282 (THU0207)
Fujinaga, S., 392 (THU0492)
Fujioka, K., 537 (FRI0148)
Fujisawa, Y., 425 (THU0579), 711 (FRI0587), 722 (FRI0617), 995 (SAT0581), 1024 (SAT0661)
Fujita, K., 284 (THU0212), 605 (FRI0313), 1251 (AB0572), 1403 (AB0995)
Fukasawa, T., 138 (OP0207)
Fukaya, S., 1258 (AB0591)
Fuke, S., 644 (FRI0417)
Fukui, S., 318 (THU0303), 486 (FRI0017), 503 (FRI0067)
Funahashi, K., 1471 (AB1187)
Funaro, A., 64 (OP0031)
Fung, M., 166 (OP0266)
Fung, T.T., 360 (THU0405)
Furer, V., 747 (FRI0679), 1118 (AB0203)
Furfari, R., 1468 (AB1178)
Furie, R., 857 (SAT0222), 858 (SAT0225), 870 (SAT0255)
Furie, R.A., 150 (OP0232), 426 (THU0584)
Furini, F., 248 (THU0123), 1207 (AB0448), 1281 (AB0656)
Furlan, R., 52 (OP0006)
Furnback, W., 1511 (SAT0720-HPR)
Furnes, O.N., 783 (SAT0043)
Fursova, V., 1358 (AB0864)
Furst, D., 104 (OP0124), 105 (OP0126), 470 (THU0695), 818 (SAT0132), 912 (SAT0373)
Furst, D.E., 463 (THU0677), 566 (FRI0220), 628 (FRI0372), 631 (FRI0380), 1526 (SAT0765-HPR)
Furst, D.F., 1390 (AB0958)
Furtado, C., 186 (OP0315)
Furu, M., 115 (OP0152), 282 (THU0207), 527 (FRI0122), 744 (FRI0673)
Furugo, I., 1254 (AB0582)
Furukawa, H., 202 (THU0006)
Furukawa, K.-I., 95 (OP0104), 800 (SAT0084)
Furukawa, O., 409 (THU0535)
Furukawa, T., 210 (THU0030), 1288 (AB0674)
Furusawa, N., 1060 (AB0038)
Furuya, H., 222 (THU0064), 894 (SAT0322)
Fusama, M., 1484 (THU0744-HPR)
Fusaro, E., 564 (FRI0215), 829 (SAT0158), 1376 (AB0917), 1554 (PARE0008)

Fusco, H.C.S.C., 386 (THU0475)
Fusco, H.C.S.D.C., 386 (THU0476)
Fuster-Ortí, M., 477 (THU0713)
Fuwa, M., 537 (FRI0148)
Fuzibet, J.-G., 991 (SAT0569)

G-Aparicio, A., 326 (THU0326)
G-Serrano, J., 326 (THU0326), 718 (FRI0607)
Gaál, J., 767 (FRI0731), 911 (SAT0371)
Gabay, C., 90 (OP0093), 242 (THU0110), 267 (THU0174), 567 (FRI0221), 570 (FRI0227), 656 (FRI0450), 709 (FRI0582), 755 (FRI0701), 850 (SAT0206)
Gabcova, G., 970 (SAT0514), 1051 (AB0014)
Gaber, R.A., 404 (THU0524)
Gaber, T., 480 (FRI0002), 485 (FRI0015), 486 (FRI0019), 1067 (AB0060)
Gabilondo-Alvarez, G.A., 992 (SAT0571)
Gaboriau, L., 823 (SAT0144)
Gabrielli, A., 64 (OP0031), 305 (THU0268), 437 (THU0611), 621 (FRI0357), 905 (SAT0353), 906 (SAT0356), 1189 (AB0400), 1439 (AB1099), 1462 (AB1163)
Gábris, B., 1267 (AB0617)
Gabusi, E., 1069 (AB0064)
Gácserné, C., 1482 (THU0736-HPR)
Gademan, M., 1040 (SAT0701)
Gademan, M.G., 967 (SAT0506)
Gado, K., 743 (FRI0669)
Gaebelein-Wissing, N., 1106 (AB0169), 1110 (AB0181)
Gaetano, T., 349 (THU0378)
Gaffo, A., 166 (OP0265)
Gaffo, A.L., 363 (THU0413), 1359 (AB0865)
Gaich, C., 517 (FRI0099), 524 (FRI0116), 788 (SAT0055)
Gaich, C.L., 794 (SAT0069), 1511 (SAT0720-HPR)
Gaiduk, I., 424 (THU0578)
Gaigneux, E., 1299 (AB0702)
Gaillez, C., 358 (THU0398), 948 (SAT0462), 949 (SAT0463), 1058 (AB0033), 1322 (AB0765), 1323 (AB0766), 1326 (AB0772), 1329 (AB0780)
Gailus-Durner, V., 500 (FRI0059)
Gaisin, I.R., 1189 (AB0402)
Gajardo-Meneses, P., 1098 (AB0148)
Gal-Edd, N., 777 (SAT0027)
Galanopoulou, V., 1139 (AB0259)
Galarza-Delgado, D.Á., 253 (THU0140), 534 (FRI0141), 1156 (AB0309), 1157 (AB0310)
Galarza-Delgado, D.A., 1118 (AB0204), 1119 (AB0205)
Galbiati, V., 1406 (AB1006)
Gale, S., 95 (OP0105), 264 (THU0167), 579 (FRI0248)
Gale, S.L., 850 (SAT0206)
Galeazzi, M., 56 (OP0015), 92 (OP0099), 411 (THU0540, THU0541), 577 (FRI0245), 711 (FRI0586), 966 (SAT0503), 1010 (SAT0625), 1059 (AB0037), 1141 (AB0267), 1193 (AB0412), 1343 (AB0816), 1461 (AB1160)
Galeazzi, R., 690 (FRI0527)
Galeotti, C., 77 (OP0062)
Galien, R., 118 (OP0161), 270 (THU0182), 281 (THU0205, THU0206), 648 (FRI0428)
Galimberti, S., 320 (THU0308)
Galindez, E., 241 (THU0109), 837 (SAT0178)
Galíndez Agirregoikoa, E., 955 (SAT0475), 1333 (AB0788)
Galíndez-Aguirregoikoa, E., 1001 (SAT0600)
Galindo, L., 670 (FRI0483)
Galindo, M., 587 (FRI0267), 1107 (AB0173)
Galindo Zavala, R., 1393 (AB0968)
Galindo-Izquierdo, M., 68 (OP0042), 873 (SAT0263)
Galindo-Zavala, R., 391 (THU0489)
Galinier, M., 901 (SAT0342)
Galisteo, A.M., 919 (SAT0391)
Gallagher, P., 1434 (AB1083), 1521 (SAT0748-HPR)
Gallagher, S., 1482 (THU0738-HPR)
Gallego, R., 326 (THU0326)
Gallego-Rodriguez, P., 78 (OP0066)
Gallegos-Posada, A., 1345 (AB0820)
Gallina, P., 126 (OP0179)
Gallo, F., 1499 (FRI0742-HPR)
Gallo, G., 1288 (AB0673)
Gallo, J., 970 (SAT0514)
Galloway, J., 226 (THU0073), 805 (SAT0098), 806 (SAT0099), 1030 (SAT0676), 1039 (SAT0699), 1527 (SAT0767-HPR)
Galloway, J.B., 115 (OP0153), 753 (FRI0695)
Galluccio, F., 504 (FRI0070)
Galozzi, P., 210 (THU0029), 216 (THU0047), 634 (FRI0387), 1066 (AB0055)
Galuppi, E., 207 (THU0022), 234 (THU0090), 1127 (AB0227)
Galushko, E., 246 (THU0120)
Galvan, G., 1449 (AB1125)
Galvão, V., 176 (OP0290)
Gálvez-Romero, J., 974 (SAT0524)
Gálvez-Ruiz, D., 1554 (PARE0007)
Galvez-Ruiz, D., 658 (FRI0452), 927 (SAT0412)
Gamala, M., 376 (THU0445)
Gamallo, C., 892 (SAT0316)
Gambari, L., 1069 (AB0064)
Gamboa, R., 262 (THU0162)
Gamboa-Cárdenas, R., 875 (SAT0269), 1142 (AB0269)
Gamero, F., 326 (THU0326)
Gamez-Nava, J., 1155 (AB0304)
Gamez-Nava, J.I., 262 (THU0161)
Gámir, M.L., 400 (THU0514)
Gamir, M.L., 1394 (AB0970)
Gámir Gámir, M.L., 392 (THU0491), 1391 (AB0961)
Gan, K.-Y., 364 (THU0415)
Gan, W., 1494 (THU0771-HPR)
Gan, Y., 1065 (AB0052), 1144 (AB0274)
Ganapati, A., 325 (THU0322)
Gancheva, R.N., 379 (THU0453)
Gandhi, A., 1100 (AB0152)
Gandhi, K., 96 (OP0107), 355 (THU0393), 688 (FRI0521), 957 (SAT0480), 1293 (AB0685), 1301 (AB0707)
Gandhi, K.K., 675 (FRI0494), 1313 (AB0740)
Gandhi, R., 1035 (SAT0688)
Gandia, M., 326 (THU0326)
Gandino, I., 440 (THU0619)
Gandino, I.J., 716 (FRI0601), 1231 (AB0516)
Gandjbakhch, F., 174 (OP0286), 583 (FRI0256), 755 (FRI0700), 1013 (SAT0631)
Gandolfo, S., 585 (FRI0263), 1101 (AB0156)
Ganguli, A., 1503 (FRI0754-HPR)
Ganguly, R., 531 (FRI0133), 578 (FRI0246), 580 (FRI0251), 816 (SAT0126), 839 (SAT0182)
Gannon, B., 437 (THU0613), 1444 (AB1111)
Ganser, G., 132 (OP0196), 195 (OP0338), 398 (THU0507)
Ganz, F., 97 (OP0108), 677 (FRI0498), 682 (FRI0510)
Gao, A., 1117 (AB0199)
Gao, C., 63 (OP0028), 69 (OP0043), 108 (OP0132), 268 (THU0176), 853 (SAT0213), 869 (SAT0252), 872 (SAT0261), 947 (SAT0459), 1081 (AB0100), 1197 (AB0421), 1266 (AB0612), 1295 (AB0691)
Gao, D., 601 (FRI0304), 919 (SAT0392)
Gao, G., 344 (THU0367)
Gao, H.Y., 1266 (AB0612)
Gao, J., 419 (THU0563), 1079 (AB0094, AB0095), 1082 (AB0103)
Gao, L., 600 (FRI0302)
Gao, L.-L., 950 (SAT0465)
Gao, N., 1254 (AB0580)
Gao, W., 1290 (AB0679)
Gao, X., 1072 (AB0072)
Gao, X.C., 401 (THU0517)
Gaona, M., 906 (SAT0357)
Garabajiu, M., 884 (SAT0296)
Garaballu, C., 1476 (THU0720-HPR)
Garaiman, A., 1032 (SAT0681)
Garant, M.-P., 496 (FRI0047)
Garcés, E., 312 (THU0287)
García, A., 718 (FRI0607), 1351 (AB0840)
Garcia, A., 1339 (AB0805)
García, A.I., 1018 (SAT0645)
García, F., 1476 (THU0720-HPR)
García, J., 918 (SAT0387), 1307 (AB0723)
Garcia, J., 769 (SAT0001)
García, L., 748 (FRI0683)
García, M., 718 (FRI0607)
Garcia, M., 633 (FRI0385), 670 (FRI0483), 906 (SAT0357), 1245 (AB0556), 1270 (AB0625)
García, M.A., 1202 (AB0434), 1263 (AB0606)
García, M.L., 685 (FRI0515), 837 (SAT0178)
Garcia, M.M., 962 (SAT0494), 1062 (AB0043)
Garcia, M.V., 1115 (AB0194)
García, S., 416 (THU0553)
Garcia, S., 717 (FRI0604)
Garcia, Y., 1236 (AB0529)
García Aparicio, A., 1166 (AB0337)
Garcia Carrasco, M., 311 (THU0285), 590 (FRI0276), 729 (FRI0635), 1217 (AB0478), 1279 (AB0649)
García de la Peña, P., 1275 (AB0637)
Garcia de la Peña, P., 1338 (AB0801)
Garcia de la Pena, P., 633 (FRI0385), 1270 (AB0625)
García de Yébenes, M.J., 908 (SAT0363)
Garcia Diaz, S., 11 (SP0046)
Garcia Erauzkin, G., 1363 (AB0878)
García Fernández, A., 392 (THU0491)
García Gómez, J.A., 1016 (SAT0638)
García González, M., 695 (FRI0541)
García Hernández, A., 487 (FRI0021)
García Hernández, F.J., 1047 (AB0003)
García Hernández, S., 1424 (AB1057)
Garcia Montoya, L., 462 (THU0676), 656 (FRI0448)
Garcia Morillo, J.S., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
García Osuna, K., 1276 (AB0641)
García Ruíz de Morales, J.M., 414 (THU0549)
García Ruiz de Morales, J.M., 716 (FRI0602)
García Salinas, R., 1263 (AB0606)
Garcia Salinas, R., 1143 (AB0271)
García Var, L., 1263 (AB0606)
García Vicuña, R., 527 (FRI0123)
García Villanueva, M.J., 587 (FRI0266)
García-Aparicio, A., 452 (THU0651)
Garcia-Arellano, S., 500 (FRI0058)
Garcia-Betancurt, S., 514 (FRI0094)
Garcia-Bustuinduy, M., 1397 (AB0979)
García-Canale, S., 594 (FRI0286), 1229 (AB0511), 1230 (AB0512)
Garcia-Cardó, A., 1458 (AB1150)
Garcia-Cardo, A., 1041 (SAT0703)
García-Carrasco, M., 311 (THU0283), 1221 (AB0486), 1296 (AB0693)
Garcia-Cobian, T.A., 262 (THU0161)
García-Collinot, G., 591 (FRI0279), 1286 (AB0668)
Garcia-Collinot, G., 1282 (AB0657)
García-Colunga, J., 1156 (AB0309)
Garcia-Colunga, J.I., 1118 (AB0204), 1119 (AB0205)
García-García, C., 586 (FRI0264)
García-Garza, G., 591 (FRI0279)
Garcia-Guillén, A., 1305 (AB0717)
García-Lorenzo, E., 1107 (AB0172)
García-Magallón, B., 452 (THU0651)
Garcia-Mayor, S., 1486 (THU0751-HPR)
Garcia-Mira, Y., 988 (SAT0560), 1241 (AB0544)
García-Montoya, L., 1276 (AB0640), 1297 (AB0695)
Garcia-Osuna, K., 1446 (AB1116)
Garcia-Osuna, K.M., 117 (OP0158)
Garcia-Perez, S., 1104 (AB0165)
García-Planella, E., 177 (OP0292)
García-Porrúa, C., 946 (SAT0457), 1322 (AB0764)
García-Puig, J., 1004 (SAT0609), 1413 (AB1024)
García-Unzueta, M., 1229 (AB0511)
García-Vicuña, R., 452 (THU0651), 1128 (AB0229)
García-Vivar, M., 1001 (SAT0600)
Gard, C., 436 (THU0609), 450 (THU0646)
Gardette, A., 130 (OP0191), 1535 (AB1209-HPR)
Gardiner, D., 1103 (AB0162)
Gardiner, P., 460 (THU0671), 729 (FRI0634)
Gardiner, P.V., 1530 (AB1196-HPR)
Garen, T., 106 (OP0129), 630 (FRI0376)
Garg, J., 593 (FRI0285), 857 (SAT0221), 865 (SAT0242), 868 (SAT0250)
Garg, N., 340 (THU0358)
Garg, P., 238 (THU0101)
Garg, S., 1506 (FRI0762-HPR), 1540 (AB1226-HPR)
Garg, V., 83 (OP0076), 829 (SAT0159)
Garijo Buffort, M., 213 (THU0037)
Garijo Bufort, M., 719 (FRI0608), 1232 (AB0518)

Garip, Y., 652 (FRI0439), 1381 (AB0932)
Garıpoglu, M., 1121 (AB0209)
Garlaschi, G., 728 (FRI0632)
Garmish, O.O., 399 (THU0510), 541 (FRI0160)
Garnier Rodríguez, J.L., 695 (FRI0541), 1037 (SAT0691), 1115 (AB0195)
Garofalo, P., 1064 (AB0050)
Garraud, T., 130 (OP0190)
Garrido, J., 736 (FRI0651), 1009 (SAT0621)
Garrido, M., 776 (SAT0023)
Garrido-Castro, J.L., 153 (OP0238), 441 (THU0624), 650 (FRI0434), 919 (SAT0391), 1559 (PARE0020)
Garrido-Cumbrera, M., 658 (FRI0452), 927 (SAT0412), 1554 (PARE0007)
Garrigues, F., 662 (FRI0465), 1013 (SAT0632)
Garro, B., 1196 (AB0419)
Garrote, S., 1394 (AB0970)
Garrote Corral, S., 392 (THU0491)
Garyfallos, A., 205 (THU0015), 836 (SAT0176)
Garza-Elizondo, M., 1453 (AB1137)
Garza-Elizondo, M.A., 253 (THU0140), 425 (THU0581), 534 (FRI0141), 1054 (AB0023), 1156 (AB0309), 1410 (AB1015)
Garziera, G., 1446 (AB1117)
Garzya, M., 1483 (THU0743-HPR)
Gasink, C., 950 (SAT0465)
Gaspar, R., 1350 (AB0838)
Gasparini, S., 247 (THU0121), 905 (SAT0353)
Gašperšič, N., 1143 (AB0272)
Gatica, H., 1108 (AB0176)
Gatineau, F., 67 (OP0040)
Gato, A., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Gattamelata, A., 888 (SAT0305)
Gatterova, J., 916 (SAT0383)
Gatti, D., 363 (THU0412), 671 (FRI0485), 693 (FRI0535), 940 (SAT0443, SAT0445), 1062 (AB0045), 1124 (AB0216), 1200 (AB0429), 1314 (AB0742)
Gattinara, M., 403 (THU0522)
Gatto, M., 603 (FRI0308), 867 (SAT0248), 1209 (AB0455)
Gattorno, M., 77 (OP0063), 398 (THU0509)
Gaublomme, D., 490 (FRI0029)
Gaudin, P., 258 (THU0152), 1186 (AB0395)
Gaudy, A., 858 (SAT0225)
Gaujoux-Viala, C., 56 (OP0014), 113 (OP0146), 231 (THU0084), 530 (FRI0131), 789 (SAT0057), 804 (SAT0094), 1159 (AB0315)
Gaujoux-viala, C., 701 (FRI0561)
Gauthier Prieur, M., 1378 (AB0923)
Gautier, J.-F., 382 (THU0461)
Gautier, S., 823 (SAT0144)
Gavan, S., 551 (FRI0185)
Gavilán-Carrera, B., 1499 (FRI0743-HPR)
Gavrila, B.I., 1179 (AB0376)
Gay, C., 1477 (THU0724-HPR)
Gay, R.E., 116 (OP0154), 190 (OP0326)
Gay, S., 116 (OP0154), 117 (OP0157), 190 (OP0326)
Gaydukova, I.Z., 345 (THU0370), 924 (SAT0403)
Gayford, D., 609 (FRI0321)
Gaylis, N.B., 1139 (AB0261)
Gazaix-Fontaine, E., 1301 (AB0708)
Gazal, S., 1049 (AB0007)
Gazel, Ü., 821 (SAT0139)
Gazel, U., 644 (FRI0416)
Gazel, Ü.G., 1310 (AB0731)
Gazi, S., 836 (SAT0176)
Gcelu, A., 631 (FRI0379)
Ge, S., 1464 (AB1167)
Geborek, P., 542 (FRI0162), 823 (SAT0143)
Geenen, R., 110 (OP0138-HPR), 111 (OP0142-HPR), 1487 (THU0752-HPR), 1555 (PARE0009)
Géher, P., 767 (FRI0731)
Gehring, I., 1288 (AB0673)
Geier, J., 271 (THU0185), 277 (THU0196), 284 (THU0211)
Geiger, D., 343 (THU0364)
Geijer, M., 655 (FRI0445)
Geirsson, A.J., 341 (THU0361), 686 (FRI0518), 1027 (SAT0669)
Geisemeyer, N., 397 (THU0504)
Gelarden, T., 93 (OP0101)
Gelman, M.S., 1014 (SAT0635)
Geluk, A., 215 (THU0042)
Gemici, A., 1392 (AB0965)
Genant, H.K., 841 (SAT0186)
Genc, H., 1137 (AB0255)
Gendelman, O., 84 (OP0078), 297 (THU0248), 886 (SAT0300)
Gendi, N.S., 1205 (AB0444)
Generali, E., 437 (THU0611), 620 (FRI0353), 1439 (AB1099)
Generalov, I., 832 (SAT0166)
Genestet, S., 309 (THU0278)
Genevey, S., 168 (OP0271)
Geng, Z., 1319 (AB0756)
Genin, G., 78 (OP0064)
Genitori, C., 585 (FRI0261)
Genovese, M., 59 (OP0021), 136 (OP0203), 267 (THU0173), 283 (THU0210), 795 (SAT0072)
Genovese, M.C., 135 (OP0201), 158 (OP0248), 281 (THU0205), 576 (FRI0242), 838 (SAT0180)
Genre, F., 1084 (AB0108)
Gensler, L., 666 (FRI0474)
Gensler, L.S., 950 (SAT0465)
Gent, Y., 1020 (SAT0650)
Gentile, S., 1442 (AB1108)
Gentileschi, S., 259 (THU0155), 711 (FRI0586)
Gentner, B., 126 (OP0179)
Georgakouli, K., 1536 (AB1215-HPR)
Georganas, C., 836 (SAT0176)
Georgatzis, K., 1453 (AB1138)
George, E., 305 (THU0269)
George, R.E., 727 (FRI0629)
Georgel, P., 488 (FRI0024)
Georgiadou, A., 569 (FRI0224)
Georgiou, A., 923 (SAT0399), 1304 (AB0715)
Georgiou, P., 836 (SAT0176)
Georgopoulou, O., 1089 (AB0122)
Gerald, F., 78 (OP0064)
Geraldino-Pardilla, L., 305 (THU0269), 1125 (AB0220)
Gérard, C., 171 (OP0278-PARE)
Gerardi, M.C., 230 (THU0082), 1008 (SAT0620), 1194 (AB0413), 1376 (AB0917), 1379 (AB0925), 1380 (AB0928)
Gerards, A., 676 (FRI0497), 1308 (AB0725)
Gerards, A.H., 678 (FRI0500), 1324 (AB0769), 1325 (AB0770)
Gerasimova, E., 254 (THU0142), 776 (SAT0024)
Gerbaud, L., 1477 (THU0724-HPR)
Gerber, R.A., 60 (OP0022)
Gercik, O., 102 (OP0120), 296 (THU0245), 354 (THU0389), 661 (FRI0462), 1170 (AB0349)
Gerdle, B., 163 (OP0260-HPR)
Gergianaki, I., 192 (OP0332), 297 (THU0246), 300 (THU0254), 896 (SAT0330)
Gerhard Rogler, G., 87 (OP0086)
Geri, T., 1483 (THU0741-HPR), 1539 (AB1223-HPR)
Gerke, O., 64 (OP0033)
Gerlag, D., 123 (OP0172), 124 (OP0173), 781 (SAT0037)
Gerlag, D.M., 116 (OP0154)
Gerli, R., 69 (OP0044), 305 (THU0268), 437 (THU0611), 867 (SAT0248), 873 (SAT0262), 880 (SAT0284), 1113 (AB0191), 1209 (AB0456), 1439 (AB1099)
Gerloni, V., 403 (THU0522)
Germain, P., 106 (OP0128)
Germano, G., 1248 (AB0564)
Gerosa, M., 70 (OP0046), 294 (THU0240), 437 (THU0611), 1209 (AB0456), 1439 (AB1099)
Gerstner, C., 779 (SAT0032)
Gessl, I., 175 (OP0288), 292 (THU0233), 971 (SAT0515)
Geusens, P., 8 (SP0027), 32 (SP0130), 54 (OP0010), 71 (OP0048), 740 (FRI0662), 952 (SAT0470)
Geven, E., 211 (THU0033), 772 (SAT0012)
Geven, E.J.W., 211 (THU0032)
Ghadimy, S., 1137 (AB0254)
Ghafouri, M., 694 (FRI0538)
Ghaly, M.S., 1235 (AB0526)
Ghaname, W., 1159 (AB0317)
Ghanem, S., 962 (SAT0495)
Ghang, B., 549 (FRI0181), 606 (FRI0316)
Gharibdoost, F., 1272 (AB0628)
Gharsallah, I., 998 (SAT0589, SAT0590)
Ghazi, M., 697 (FRI0548), 1349 (AB0836)
Gheita, T.A., 464 (THU0681)
Gheita, T.A., 311 (THU0284), 886 (SAT0302), 1045 (SAT0715), 1237 (AB0533), 1259 (AB0594)
Gheith, R.E., 1237 (AB0533)
Gheorghe, M., 1429 (AB1069)
Gheorghiu, A., 1286 (AB0669)
Gheorghiu, A.M., 435 (THU0607), 626 (FRI0368), 1032 (SAT0681), 1264 (AB0608)
Gheysens, O., 1005 (SAT0612)
Ghib, L.-J., 260 (THU0156)
Ghib, L.J., 170 (OP0275)
Ghil, J., 136 (OP0203), 137 (OP0204), 556 (FRI0198), 834 (SAT0169)
Ghio, M., 66 (OP0037), 140 (OP0212), 641 (FRI0407), 704 (FRI0569), 915 (SAT0381), 1111 (AB0185), 1263 (AB0605)
Ghiti-Moghadam, M., 1140 (AB0263)
Ghiye, R., 406 (THU0528)
Ghizdavescu, A., 515 (FRI0096)
Ghoneim, S., 874 (SAT0265)
Ghorbani, R., 1338 (AB0803)
Ghosh, A., 1423 (AB1054)
Ghosh, P., 1423 (AB1054)
Ghozlani, I., 697 (FRI0548), 1349 (AB0836)
Ghrbel, A., 1311 (AB0734)
Giacomelli, R., 56 (OP0015), 69 (OP0044), 263 (THU0164), 291 (THU0231), 305 (THU0268), 311 (THU0284), 445 (THU0634), 464 (THU0681), 721 (FRI0613), 777 (SAT0025), 873 (SAT0262), 880 (SAT0284), 886 (SAT0302), 891 (SAT0313), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Giambelli, R., 1064 (AB0050)
Giannakou, I., 69 (OP0045)
Giannelli, R., 1558 (PARE0019)
Giannini, M., 254 (THU0143), 639 (FRI0400), 1135 (AB0250), 1461 (AB1160)
Giannitti, C., 966 (SAT0503)
Giannotta, M., 1135 (AB0250)
Giannotta, M.G., 254 (THU0143), 259 (THU0155)
Giannoudis, P., 648 (FRI0427)
Giannoudis, P.V., 959 (SAT0485), 1070 (AB0066)
Gianturco, L., 1294 (AB0689)
Giardino, A., 445 (THU0634), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Gibofsky, A., 121 (OP0166), 985 (SAT0552)
Gibor, G., 1095 (AB0138)
Gibson, K., 385 (THU0472)
Gibson, K.A., 810 (SAT0109), 1130 (AB0233)
Giera, M., 202 (THU0008), 220 (THU0057)
Gieseler, F., 1108 (AB0175)
Gifre, L., 691 (FRI0529), 988 (SAT0560), 1236 (AB0529), 1241 (AB0544)
Gigante, M.R., 394 (THU0499), 792 (SAT0066)
Giglioli, C., 633 (FRI0384)
Gignac, M., 438 (THU0615)
Gignac, M.A., 471 (THU0698)
Gijon-Nogueron, G., 1486 (THU0751-HPR)
Gikas, P., 221 (THU0060)
Gil, J., 415 (THU0550)
Gilbertson, J., 227 (THU0076)
Gilbertson, J.A., 1427 (AB1064)
Gilboe, I.-M., 1031 (SAT0677), 1032 (SAT0680)
Giles, I., 1092 (AB0131)
Giles, I.P., 1103 (AB0161)
Gilgil, E., 1382 (AB0934)
Gilis, E., 125 (OP0176)
Gill, D., 567 (FRI0222)
Gillen, M., 370 (THU0430, THU0432), 1366 (AB0886, AB0887)
Gillgren, P., 1096 (AB0142)
Gillmore, J.D., 227 (THU0076), 1427 (AB1064)
Gilmour, A., 242 (THU0111)
Gilmutdinov, I., 1203 (AB0438), 1300 (AB0704)

Gils, A., 20 (SP0082)
Gilson, M., 811 (SAT0112)
Gimena, B., 595 (FRI0289), 1252 (AB0576), 1400 (AB0988)
Gimenez, S., 761 (FRI0715), 1456 (AB1146, AB1147)
Gimenez Romero, D., 878 (SAT0279)
Gindzienska-Sieskiewicz, E., 1277 (AB0642)
Ginel, L., 1175 (AB0362)
Giner, E., 550 (FRI0184)
Ginies, P., 388 (THU0480)
Ginosyan, K., 1398 (AB0983)
Ginsberg, S., 448 (THU0643), 449 (THU0645), 926 (SAT0407)
Ginzler, E.M., 150 (OP0232)
Giollo, A., 363 (THU0412), 693 (FRI0535), 805 (SAT0097), 854 (SAT0215)
Giordano, C., 888 (SAT0305)
Giordano, N., 86 (OP0082), 894 (SAT0323), 1111 (AB0185)
Giorgi, R., 1160 (AB0320)
Giorgi, R.D.N., 1196 (AB0419)
Giraldo, R., 266 (THU0172), 529 (FRI0127), 752 (FRI0694), 852 (SAT0210), 1441 (AB1103)
Giraldo, S., 252 (THU0137)
Giraldo-Bustos, R., 1132 (AB0239)
Girard Bosch, M.P., 1143 (AB0271)
Giraud, C., 213 (THU0039)
Giraud, J., 171 (OP0278-PARE)
Giraudet-Le Quintrec, J.-S., 1470 (AB1185)
Girgis, I., 859 (SAT0226)
Girolamo, F., 639 (FRI0400)
Girschick, H., 400 (THU0512)
Gismondi, R., 641 (FRI0406)
Giuggioli, D., 634 (FRI0388), 1267 (AB0615), 1272 (AB0629)
Giusti, A., 270 (THU0181)
Gjeorgjieva, O., 280 (THU0202)
Gjertsson, I., 163 (OP0258-HPR), 779 (SAT0031)
Gkagkalis, A., 1139 (AB0259)
Gkaliagkousi, E., 542 (FRI0161)
Gkougkourelas, I., 569 (FRI0224), 1261 (AB0601)
Gkoutzourelas, A., 903 (SAT0348), 1271 (AB0626)
Gladman, D., 98 (OP0111), 145 (OP0223), 673 (FRI0489), 681 (FRI0508), 949 (SAT0463), 1332 (AB0786)
Gladman, D.D., 135 (OP0202), 677 (FRI0498), 682 (FRI0509), 688 (FRI0522), 936 (SAT0436), 942 (SAT0448), 948 (SAT0462), 957 (SAT0481), 1314 (AB0743), 1331 (AB0785), 1335 (AB0794)
Glanowski, C., 965 (SAT0501)
Glaser, C., 583 (FRI0256)
Glavac, D., 109 (OP0136)
Glazyrina, G.A., 1388 (AB0952)
Gleich, G., 107 (OP0130)
Glimm, A.-M., 400 (THU0512)
Glinatsi, D., 732 (FRI0641), 1409 (AB1013)
Glintborg, B., 341 (THU0361), 450 (THU0648), 451 (THU0649), 456 (THU0662), 553 (FRI0190), 686 (FRI0518)
Glossop, J.R., 776 (SAT0022)
Glott, T., 1497 (FRI0738-HPR)
Glover, J., 59 (OP0021)
Głowacka-Kulesz, M., 267 (THU0173)
Glukhova, S., 576 (FRI0241), 1369 (AB0895)
Glukhova, S.I., 943 (SAT0450), 1317 (AB0749), 1347 (AB0828)
Gluszko, P., 1310 (AB0733)
Gluzman, I., 1407 (AB1007), 1462 (AB1163)
Glynn-Servedio, B., 691 (FRI0528)
Go, D.J., 877 (SAT0274), 1053 (AB0020)
Gobbi, C.A., 1220 (AB0484, AB0485)
Göçer, M., 296 (THU0243)
Godart, C., 359 (THU0402)
Goday, S., 677 (FRI0499)
Goddard, N., 1427 (AB1064)
Godi, C., 316 (THU0299)
Godmer, P., 778 (SAT0029)
Godoy Tundidor, H., 1399 (AB0986)
Godoy-Navarrete, F.J., 1268 (AB0619)
Godwood, A., 564 (FRI0216), 867 (SAT0249)
Goeb, V., 1442 (AB1108)
Göecke, A., 1108 (AB0176)
Goecke, I., 1257 (AB0590)
Goekoop, R.J., 1076 (AB0084)
Goel, N., 463 (THU0677), 1332 (AB0786)
Goel, R., 316 (THU0298), 325 (THU0322), 328 (THU0330), 1061 (AB0042)
Goel, S., 662 (FRI0463)
Goeldner, I., 820 (SAT0135)
Goelela, V., 621 (FRI0356)
Goeschl, L., 502 (FRI0064)
Goetz, C., 426 (THU0582)
Goetze, K., 115 (OP0151)
Goffin, K., 1005 (SAT0612)
Goger, C., 579 (FRI0247)
Gogus, F., 321 (THU0311), 1223 (AB0492)
Goh, E.T., 226 (THU0073)
Goicoechea, C., 962 (SAT0494), 1062 (AB0043)
Gök, E.G., 1066 (AB0057)
Gökduman, A., 1310 (AB0731)
Goker, B., 608 (FRI0320), 1216 (AB0472), 1260 (AB0598)
Gökmen, E.A., 1002 (SAT0601)
Gokmen, E.A., 1382 (AB0934)
Goksör, C., 1538 (AB1219-HPR)
Göksülük, D., 1531 (AB1198-HPR)
Goldfarb, D.S., 379 (THU0455)
Goldmuntz, E., 104 (OP0124)
Goldscheider, I., 718 (FRI0606)
Goldstein, I., 508 (FRI0082)
Goldstein, N., 845 (SAT0194)
Goll, G.L., 338 (THU0354), 472 (THU0700), 549 (FRI0182)
Golovchenko, O., 1321 (AB0761)
Goltsev, A.N., 1073 (AB0078)
Goma, S., 1235 (AB0527)
Goma, S.H., 741 (FRI0665)
Gomaa, E., 1053 (AB0018)
Gomariz, R.P., 485 (FRI0016), 1128 (AB0229)
Gomes, J.L., 1052 (AB0016), 1153 (AB0300)
Gomes, K., 814 (SAT0121)
Gomes, R.K.S., 1441 (AB1104)
Gómez, A., 1406 (AB1004)
Gómez, C., 826 (SAT0150)
Gomez, D., 266 (THU0172), 529 (FRI0127), 852 (SAT0210), 1441 (AB1103)
Gomez, D.A., 153 (OP0238)
Gómez, G., 440 (THU0619)
Gómez, J., 1161 (AB0321)
Gómez, M.A., 695 (FRI0541)
Gomez, R., 1279 (AB0649)
Gomez, R.A., 311 (THU0285)
Gómez, S., 685 (FRI0515), 954 (SAT0474)
Gómez Cerezo, J.F., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Gómez De La Torre, R., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Gómez Gómez, A., 908 (SAT0363)
Gomez Gracia, I., 258 (THU0151), 700 (FRI0555)
Gómez López, C., 1276 (AB0641)
Gomez Lopez, C.E., 1450 (AB1128)
Gómez Lozano, A., 721 (FRI0615)
Gomez Mendez, L.M., 857 (SAT0221), 865 (SAT0242), 868 (SAT0250)
Gomez Ruiz, C., 363 (THU0411)
Gómez-Arango, C., 1001 (SAT0600)
Gomez-Bañuelos, E., 806 (SAT0100), 1075 (AB0083), 1164 (AB0330), 1169 (AB0345)
Gómez-Cano, C., 261 (THU0160), 1417 (AB1036)
Gomez-Cano, C., 1018 (SAT0643)
Gómez-Cárdenas, Ó.E., 1250 (AB0570)
Gomez-Centeno, A., 452 (THU0651)
Gómez-Gómez, A., 414 (THU0549)
Gómez-Martín, D., 586 (FRI0264)
Gomez-Martin, D., 774 (SAT0016)
Gómez-Puerta, J.A., 308 (THU0275), 1092 (AB0129), 1190 (AB0404), 1239 (AB0538)
Gómez-Quiroz, L.E., 205 (THU0016)
Gomez-Reino, J., 656 (FRI0450)
Gómez-Reino, J.J., 1159 (AB0316)
Gomez-Reino, J.J., 143 (OP0219), 277 (THU0196), 284 (THU0211), 936 (SAT0436), 942 (SAT0448), 951 (SAT0469), 1331 (AB0785)
Gomollón, F., 177 (OP0292)
Gömöri, E., 767 (FRI0731)
Gomulkiewicz, M.S., 276 (THU0194)
Gon, Y., 620 (FRI0352)
Goncalves, C., 614 (FRI0335)
Gonçalves, C.R., 1292 (AB0684)
Gonçalves, D.R., 852 (SAT0211), 1142 (AB0268)
Gonçalves, J., 830 (SAT0160)
Goncalves, J., 784 (SAT0046), 1080 (AB0096)
Gonçalves, L.M., 403 (THU0520), 1391 (AB0960)
Gonçalves, M., 1448 (AB1124)
Gonçalves, M.J., 834 (SAT0170)
Gonçalves, R.S., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Goncalves-Alves, E., 488 (FRI0024)
Goncharova, R.I., 389 (THU0485)
Gong, J., 58 (OP0020)
Gong, L.L., 730 (FRI0636)
Gong, Y., 77 (OP0063)
Gono, T., 618 (FRI0347)
Gontar, I.P., 459 (THU0670), 536 (FRI0146), 1128 (AB0228)
Gontarenko, N., 189 (OP0324)
Gonuguntla, S., 1284 (AB0662)
Gönüllü, E., 327 (THU0329)
Gonzalez, A., 494 (FRI0040), 500 (FRI0057)
González, C., 386 (THU0474), 439 (THU0617), 656 (FRI0448), 748 (FRI0683), 840 (SAT0183), 918 (SAT0387), 946 (SAT0458), 1307 (AB0723)
Gonzalez, C., 1276 (AB0640), 1414 (AB1029), 1476 (THU0720-HPR)
González, C.M., 462 (THU0676), 1297 (AB0695)
González, D., 1108 (AB0176)
González, E., 712 (FRI0589)
Gonzalez, G., 1259 (AB0595)
González, J., 1338 (AB0801)
González, L., 712 (FRI0589)
González, L.A., 308 (THU0275), 1190 (AB0404), 1239 (AB0538)
González, M., 1116 (AB0198)
González, M.-J., 1102 (AB0158)
Gonzalez, M.A., 456 (THU0661)
González, R., 748 (FRI0683), 1297 (AB0695)
González, S., 1102 (AB0158)
González Álvaro, I., 527 (FRI0123)
González Benítez, R., 386 (THU0474), 1276 (AB0640)
González Díaz, A., 695 (FRI0541)
González Díaz, V., 1276 (AB0641)
Gonzalez Diaz, V., 1450 (AB1128)
González Febles, J., 695 (FRI0541), 1037 (SAT0691), 1115 (AB0195)
González Fernández, C., 1362 (AB0875)
González García, A., 410 (THU0539), 413 (THU0545), 713 (FRI0593), 721 (FRI0615), 1042 (SAT0706)
Gonzalez Martin, J.J., 1275 (AB0637)
González Mazarío, R., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1349 (AB0837), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
González Mazario, R., 441 (THU0623)
Gonzalez Mazarío, R., 1374 (AB0912)
Gonzalez Nieto, I., 1262 (AB0602)
González Puig, L., 441 (THU0623), 1349 (AB0837)
Gonzalez Puig, L., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
González Utrilla, A., 1228 (AB0506), 1321 (AB0760)
González Vioque, E., 1399 (AB0986)
González-Acevedo, M., 1225 (AB0499)
González-Álvarez, I., 520 (FRI0107)
González-Álvaro, I., 485 (FRI0016), 1128 (AB0229)
Gonzalez-Alvaro, I., 1107 (AB0172)
Gonzalez-Alvaro, I., 452 (THU0651)
González-Amaro, R., 774 (SAT0016)
González-Benítez, R.D., 462 (THU0676)
González-Christen, J., 498 (FRI0052)
Gonzalez-Conejero, R., 287 (THU0218)
González-de-Garay-Sanzo, M., 1001 (SAT0600)

González-Delgado, A., 802 (SAT0088), 804 (SAT0095)
Gonzalez-Diaz, E., 117 (OP0158)
Gonzalez-Diaz, V., 117 (OP0158), 1446 (AB1116)
González-Fernández, M., 75 (OP0059), 405 (THU0526)
González-Gay, M., 75 (OP0059), 326 (THU0326), 405 (THU0526), 420 (THU0567), 718 (FRI0607), 742 (FRI0666), 1166 (AB0337)
Gonzalez-Gay, M., 251 (THU0134), 569 (FRI0226), 843 (SAT0191)
González-Gay, M.Á., 108 (OP0135), 614 (FRI0336), 803 (SAT0093), 1255 (AB0583, AB0584)
González-Gay, M.A., 802 (SAT0088), 804 (SAT0095), 1084 (AB0108)
Gonzalez-Gay, M.A., 139 (OP0209-HPR), 592 (FRI0280), 1116 (AB0197), 1272 (AB0630), 1472 (AB1192)
Gonzalez-Juanatey, C., 139 (OP0209-HPR)
Gonzalez-Lopez, L., 262 (THU0161), 1155 (AB0304)
González-Montagut Gómez, C., 1439 (AB1098)
González-Moreno, P., 728 (FRI0631), 1018 (SAT0643), 1417 (AB1036)
González-Navas, C., 153 (OP0238), 441 (THU0624), 919 (SAT0391)
Gonzalez-Navas, C., 1559 (PARE0020)
Gonzalez-Reyes, J.A., 1091 (AB0127)
González-Rodríguez, L., 1135 (AB0249), 1466 (AB1174)
Gonzalez-Rodriguez, L., 980 (SAT0539)
González-Rosas, L., 1075 (AB0083)
Gonzalez-Rosas, L., 806 (SAT0100)
González-Suárez, S., 718 (FRI0607)
González-Tajuelo, R., 892 (SAT0316), 1107 (AB0172)
González-Vela, C., 614 (FRI0336), 1255 (AB0583, AB0584)
González-Vela, J., 1084 (AB0108), 1255 (AB0584)
González-Vela, M., 75 (OP0059), 405 (THU0526), 718 (FRI0607)
Goodfield, M., 771 (SAT0007), 1019 (SAT0647), 1325 (AB0771)
Goodson, N., 852 (SAT0209), 1251 (AB0573)
Goodson, N.J., 659 (FRI0456), 1308 (AB0727)
Goossens, J., 53 (OP0007), 1364 (AB0882)
Gopaluni, S., 329 (THU0333)
Gorbunov, V., 1311 (AB0736)
Gordeev, A., 246 (THU0120)
Gordeev, I., 560 (FRI0208)
Gordon, D., 861 (SAT0231)
Gordon, J., 105 (OP0126)
Gordon, P., 64 (OP0032)
Gordon, P.A., 1265 (AB0611)
Gordon, S., 906 (SAT0357)
Górgolas, M., 128 (OP0186)
Goriachev, D., 169 (OP0272)
Gorla, R., 343 (THU0366), 564 (FRI0215), 1468 (AB1178)
Gorman, A., 693 (FRI0534), 871 (SAT0257)
Gormsen, L.C., 174 (OP0285), 329 (THU0335)
Gorodetskiy, V., 424 (THU0578)
Gorostiza, I., 826 (SAT0150)
Gorostiza, I., 241 (THU0109), 837 (SAT0178)
Górriz, L., 1196 (AB0419)
Goruroglu Ozturk, O., 921 (SAT0396)
Göschl, L., 499 (FRI0055)
Gosmini, R., 126 (OP0180)
Gossage, D., 89 (OP0089)
Gossec, L., 11 (SP0044), 18 (SP0074), 54 (OP0011), 94 (OP0102), 129 (OP0188), 155 (OP0242), 156 (OP0244), 258 (THU0152), 334 (THU0346), 339 (THU0356, THU0357), 355 (THU0393), 388 (THU0482), 389 (THU0483), 428 (THU0588, THU0589), 458 (THU0666), 461 (THU0675), 465 (THU0684), 549 (FRI0180), 575 (FRI0240), 650 (FRI0432), 662 (FRI0465), 665 (FRI0472, FRI0473), 686 (FRI0519), 755 (FRI0700), 811 (SAT0112), 949 (SAT0463), 1296 (AB0694), 1322 (AB0765), 1326 (AB0772), 1332 (AB0786), 1501 (FRI0748-HPR)
Gosselt, H., 241 (THU0107)
Gossens, L., 1482 (THU0737-HPR)
Gosset, M., 216 (THU0046)
Gossetti, B., 329 (THU0334)
Goswami, R.P., 1423 (AB1054)
Gota, C., 386 (THU0473), 1401 (AB0990)
Gotelli, E., 641 (FRI0407), 704 (FRI0569), 897 (SAT0331), 1263 (AB0605)
Gotla, S., 1010 (SAT0624)
Goto, D., 202 (THU0006)
Goto, H., 722 (FRI0618)
Gottenberg, J.-E., 218 (THU0051), 289 (THU0225), 311 (THU0284), 464 (THU0681), 567 (FRI0221), 886 (SAT0302)
Gottlieb, A., 142 (OP0218), 145 (OP0222, OP0223)
Gottlieb, A.B., 670 (FRI0484), 947 (SAT0461), 1313 (AB0740), 1334 (AB0793)
Gottschalk, P., 1233 (AB0522)
Gouda, W., 958 (SAT0482), 1395 (AB0973)
Gough, A., 1396 (AB0976)
Goulenok, T., 78 (OP0065), 883 (SAT0293)
Goulielmos, G.N., 205 (THU0015)
Goulvestre, C., 831 (SAT0163)
Goupille, P., 335 (THU0349), 1191 (AB0406), 1299 (AB0701), 1448 (AB1123)
Gouyette, N., 611 (FRI0329), 754 (FRI0699), 1033 (SAT0684), 1034 (SAT0685), 1299 (AB0701)
Govind, N., 146 (OP0224)
Govoni, M., 207 (THU0022), 234 (THU0090), 343 (THU0366), 437 (THU0611), 562 (FRI0212), 582 (FRI0255), 828 (SAT0156), 867 (SAT0248), 954 (SAT0473), 1127 (AB0227), 1207 (AB0448), 1209 (AB0456), 1439 (AB1099)
Gowri, M., 325 (THU0322)
Goyal, K., 562 (FRI0211), 836 (SAT0175)
Goyal, L., 270 (THU0182), 281 (THU0205, THU0206)
Goycochea-Robles, M.V., 1453 (AB1137)
Gozel, N., 455 (THU0658), 1462 (AB1162)
Gozzard, N., 221 (THU0060)
Gracia, B., 330 (THU0336)
Grados, D., 1434 (AB1085)
Graf, J., 58 (OP0020)
Graf, N., 790 (SAT0059), 1144 (AB0273)
Graham, D., 141 (OP0216), 1335 (AB0794)
Graham, N.M., 570 (FRI0227, FRI0228), 838 (SAT0179)
Grainger, A., 196 (OP0341), 518 (FRI0102), 727 (FRI0630)
Gran, S., 1023 (SAT0656)
Granada, S., 1190 (AB0403)
Granados, Y., 1453 (AB1137)
Granados-Sandoval, E., 1343 (AB0815)
Grandhomme, F., 617 (FRI0345)
Grandjean, A., 359 (THU0402)
Granel, A., 440 (THU0619)
Grange, L., 171 (OP0278-PARE), 425 (THU0580), 428 (THU0588, THU0589)
Graninger, W., 560 (FRI0207), 579 (FRI0247), 1495 (FRI0732-HPR)
Graninger, W.B., 587 (FRI0268)
Grant, E., 58 (OP0019), 192 (OP0331), 867 (SAT0249)
Grao Castellote, C., 1349 (AB0837)
Grapton, X., 1352 (AB0844)
Gras, P., 212 (THU0034)
Grassi, F., 294 (THU0240)
Grassi, G., 1154 (AB0301)
Grassi, W., 56 (OP0015), 247 (THU0121), 521 (FRI0109), 1281 (AB0655), 1358 (AB0863)
Gräßler, A., 461 (THU0674)
Gratacós, J., 177 (OP0292), 357 (THU0396), 926 (SAT0410), 946 (SAT0458)
Gratacos, J., 670 (FRI0484)
Gratacós-Masmitja, J., 658 (FRI0452)
Gratacos-Masmitja, J., 927 (SAT0412)
Gratal, P., 504 (FRI0071)
Grau, J.M., 1018 (SAT0645)
Grau García, E., 441 (THU0623), 1349 (AB0837)
Grau Garcia, E., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Grau Martin, A., 1418 (AB1039)
Grauer, A., 71 (OP0048)
Gravas, E.M.H., 1478 (THU0726-HPR)
Graveleau, J., 778 (SAT0029)
Graves, K., 847 (SAT0198)
Grazio, S., 245 (THU0116), 342 (THU0363)
Grbovic, V., 541 (FRI0158), 1552 (PARE0003)
Grcevic, D., 1055 (AB0026)
Greco, A., 1353 (AB0847)
Greco, D., 1309 (AB0730)
Green, A., 685 (FRI0514)
Green, L., 455 (THU0659), 627 (FRI0370), 1325 (AB0771)
Greenberg, J., 846 (SAT0196), 1313 (AB0739, AB0740)
Greenberg, J.D., 352 (THU0386), 953 (SAT0471, SAT0472), 1330 (AB0783)
Greenspan, S., 72 (OP0051)
Greenwald, M., 267 (THU0173)
Greenwood, J.P., 238 (THU0101)
Gregersen, P., 202 (THU0006)
Gregory, W., 104 (OP0123)
Gregson, J., 448 (THU0641)
Greidinger, E., 775 (SAT0018)
Grekhoff, R.A., 1483 (THU0739-HPR, THU0740-HPR)
Gremese, E., 56 (OP0015), 138 (OP0208), 154 (OP0239), 248 (THU0123), 394 (THU0499), 535 (FRI0143), 608 (FRI0319), 787 (SAT0052), 792 (SAT0066), 1077 (AB0088)
Grevich, S., 409 (THU0537)
Gridneva, G., 1204 (AB0441)
Grieco, A., 64 (OP0031)
Griep, E., 811 (SAT0114)
Griep-Wentink, H., 811 (SAT0114)
Griffini, S., 1022 (SAT0655)
Griffith, J., 552 (FRI0188), 827 (SAT0153), 828 (SAT0155), 1198 (AB0424), 1331 (AB0784), 1503 (FRI0754-HPR)
Griffith, S., 1246 (AB0559)
Griffiths, B., 92 (OP0097), 295 (THU0242), 1103 (AB0162)
Griffiths, J., 192 (OP0331)
Griffiths, M., 213 (THU0038)
Griger, Z., 911 (SAT0371)
Grika, E.P., 836 (SAT0176)
Grilo, A.C., 1429 (AB1070)
Grimaldi, A., 1353 (AB0847), 1483 (THU0743-HPR)
Grimm, A., 247 (THU0122)
Groark, J., 861 (SAT0231)
Grobelna, K., 916 (SAT0383)
Grobost, V., 1256 (AB0588)
Gröchenig, E., 626 (FRI0369)
Groh, M., 1256 (AB0588)
Groma, V., 1071 (AB0071)
Gromov, P., 1311 (AB0736)
Grøn, K.L., 451 (THU0649)
Grønbæk, K., 286 (THU0217)
Grondal, G., 341 (THU0361), 1027 (SAT0669)
Grønhaug, G., 1491 (THU0763-HPR)
Gronning, K., 1500 (FRI0747-HPR)
Grønning, K., 1480 (THU0733-HPR), 1492 (THU0765-HPR)
Grönwall, C., 1102 (AB0159)
Groppa, L., 1199 (AB0426)
Groseanu, L., 304 (THU0266), 423 (THU0574), 435 (THU0606), 876 (SAT0271), 881 (SAT0288), 1025 (SAT0664), 1208 (AB0450), 1221 (AB0487), 1278 (AB0646, AB0647), 1428 (AB1068), 1460 (AB1158)
Gross, W.L., 325 (THU0323)
Gross-Goupil, M., 710 (FRI0584)
Grossi, R., 320 (THU0308)
Grossi, V., 646 (FRI0423)
Grossman, J., 1238 (AB0535)
Grosso, V., 564 (FRI0215)
Grotti, A., 1064 (AB0050)
Grotto, S., 77 (OP0062)
Grotts, J., 628 (FRI0372)
Grouteau, E., 77 (OP0062)
Grovetti, E., 1022 (SAT0655)

Grøvle, L., 1030 (SAT0675)
Gruben, D., 60 (OP0022)
Gruber, J., 1173 (AB0357)
Grubisic, F., 1055 (AB0026)
Grünig, E., 65 (OP0034)
Gruppe, T., 1322 (AB0763)
Grydehøj, J., 553 (FRI0190)
Gsell, U., 465 (THU0682)
Gu, J., 351 (THU0384), 366 (THU0421), 664 (FRI0469, FRI0470), 665 (FRI0471), 934 (SAT0431), 1086 (AB0113), 1158 (AB0312), 1208 (AB0452), 1516 (SAT0734-HPR)
Gu, X., 1158 (AB0312)
Gu, Z., 293 (THU0235), 1097 (AB0145), 1230 (AB0513), 1234 (AB0523), 1241 (AB0543), 1368 (AB0893), 1369 (AB0894), 1370 (AB0897, AB0898, AB0899)
Gualillo, O., 39 (SP0162)
Gualtierotti, R., 294 (THU0240), 1022 (SAT0655)
Guan, Z., 601 (FRI0304)
Guañabens, N., 369 (THU0429), 691 (FRI0529), 706 (FRI0573)
Gubar, E., 660 (FRI0458)
Gubar, E.E., 674 (FRI0491), 943 (SAT0450), 1317 (AB0749)
Gubbins, S., 871 (SAT0257)
Gucenmez, S., 296 (THU0245), 1170 (AB0349)
Gudbergsen, H., 98 (OP0112), 196 (OP0340), 456 (THU0662), 1444 (AB1113)
Gudbjornsson, B., 341 (THU0361), 1027 (SAT0669)
Gudbjørnsson, B., 656 (FRI0450)
Guddorf, L., 1515 (SAT0732-HPR)
Guðbjörnsson, B., 686 (FRI0518)
Gudu, T., 416 (THU0555), 767 (FRI0729), 1208 (AB0450), 1278 (AB0647), 1333 (AB0790), 1460 (AB1158)
Guedes, K., 121 (OP0167)
Guedes, M., 186 (OP0315)
Guellec, D., 309 (THU0278), 1215 (AB0469)
Guenoun, D., 744 (FRI0671)
Guérette, B., 97 (OP0108)
Guérin, J., 169 (OP0274), 385 (THU0470)
Guermazi, A., 964 (SAT0500)
Guerra, M., 152 (OP0236), 1419 (AB1043)
Guerra-Vazquez, L., 946 (SAT0457), 1322 (AB0764)
Guerrero, E., 837 (SAT0178)
Guerrero, R., 734 (FRI0645), 1160 (AB0318, AB0319)
Guerrero-Basterretxea, E., 1001 (SAT0600)
Guerriero, S., 411 (THU0540), 711 (FRI0586), 1461 (AB1160)
Guettrot-Imbert, G., 152 (OP0236)
Guevara-Pacheco, S., 1453 (AB1137)
Guggino, G., 131 (OP0193), 183 (OP0309), 291 (THU0231), 721 (FRI0613), 777 (SAT0025)
Gui, Y., 496 (FRI0047), 1009 (SAT0622)
Guichard, I., 638 (FRI0398)
Guidelli, G.M., 620 (FRI0353)
Guidi, L., 154 (OP0239)
Guiducci, S., 504 (FRI0070), 623 (FRI0362), 628 (FRI0372), 631 (FRI0380), 633 (FRI0384), 915 (SAT0380), 1269 (AB0622), 1270 (AB0623)
Guignabert, C., 85 (OP0081)
Guigonis, V., 1364 (AB0882)
Guillard, G., 119 (OP0164), 268 (THU0175), 1010 (SAT0624)
Guillaume Czitrom, S., 408 (THU0532), 1015 (SAT0636)
Guillemin, F., 111 (OP0141-HPR), 134 (OP0199-PARE), 436 (THU0609), 470 (THU0695), 818 (SAT0132), 970 (SAT0513), 1457 (AB1149), 1526 (SAT0765-HPR)
Guillen, I., 485 (FRI0014)
Guillén del Castillo, A., 639 (FRI0402), 900 (SAT0340), 1262 (AB0602)
Guillen-Astete, C.A., 78 (OP0066), 298 (THU0249), 695 (FRI0542), 731 (FRI0639), 992 (SAT0571, SAT0572), 996 (SAT0585), 1432 (AB1079)
Guillén-Del Castillo, A., 1262 (AB0603)
Guillet, G., 1319 (AB0756)
Guillonneau, S., 94 (OP0102), 575 (FRI0240)
Guillot, X., 417 (THU0558), 959 (SAT0486)
Guimarães, H., 400 (THU0513), 1096 (AB0144)
Guimarães, M., 400 (THU0513), 1096 (AB0144)
Guimarães, M.F., 814 (SAT0121), 1160 (AB0320)
Guinard, J., 989 (SAT0561)
Guinto, J., 253 (THU0138)
Guis, S., 258 (THU0152), 744 (FRI0671), 1442 (AB1108)
Guisado Vasco, P., 1022 (SAT0653)
Guisado-Vasco, P., 597 (FRI0293)
Gül, A., 77 (OP0063), 276 (THU0195), 327 (THU0329)
Gul, H., 1196 (AB0417)
Gulati, M., 333 (THU0344)
Guldberg-Møller, J., 98 (OP0112), 737 (FRI0654)
Guler, T., 1381 (AB0932)
Guleria, A., 320 (THU0307)
Guleria, S., 287 (THU0219)
Gülfe, A., 157 (OP0246)
Gulko, P.S., 502 (FRI0066)
Gullick, N., 1154 (AB0303)
Gullstrand, B., 302 (THU0260)
Gulseth, H.C., 1029 (SAT0673)
Gültekin, S., 1400 (AB0987)
Gulyás, K., 697 (FRI0547)
Gumbley, E., 637 (FRI0395)
Gumus, Z.Z., 296 (THU0245)
Gümüştepe, A., 1197 (AB0420)
Gun, S.C., 1140 (AB0262), 1512 (SAT0722-HPR)
Gun Atak, P., 1420 (AB1046)
Gun'ko, Y., 1085 (AB0111)
Gunal, E.K., 791 (SAT0063)
Günaydın, Ö.E., 1485 (THU0747-HPR)
Gunderson, J., 81 (OP0072-PARE)
Günendi, Z., 1428 (AB1066)
Guner Akdogan, G., 1105 (AB0168)
Guney, H., 1488 (THU0756-HPR)
Gunnarsson, I., 162 (OP0256-HPR), 586 (FRI0265), 861 (SAT0233), 864 (SAT0239), 885 (SAT0297), 1102 (AB0159)
Gunnarsson, K., 896 (SAT0329)
Gunnarsson, R., 765 (FRI0725), 1043 (SAT0709)
Gunsior, M., 867 (SAT0249)
Gunter, S., 245 (THU0117), 252 (THU0136), 545 (FRI0170)
Gunther, C., 1106 (AB0169), 1110 (AB0181)
Guntupova, L., 1157 (AB0311)
Gunturk, I., 659 (FRI0457)
Guo, L., 621 (FRI0358)
Guo, R., 1083 (AB0106)
Guo, X., 203 (THU0010), 366 (THU0421)
Guo, Y., 203 (THU0011), 869 (SAT0252)
Guo, Z., 408 (THU0534), 677 (FRI0499), 846 (SAT0197), 1120 (AB0207, AB0208), 1491 (THU0762-HPR)
Gupta, A., 287 (THU0219), 392 (THU0493), 393 (THU0496), 394 (THU0497), 432 (THU0598), 727 (FRI0629), 1386 (AB0946), 1471 (AB1188)
Gupta, N., 328 (THU0330), 994 (SAT0577), 1236 (AB0530)
Gupta, R., 1236 (AB0530), 1247 (AB0561, AB0562), 1253 (AB0579), 1377 (AB0918)
Gupta, S., 960 (SAT0488), 1055 (AB0024)
Gupta, S.J., 1292 (AB0683)
Gupta, V., 1100 (AB0152)
Gür Kabul, E., 1514 (SAT0727-HPR)
Gürbüz Uçar, Ü., 1321 (AB0759)
Gurer, G., 1162 (AB0324)
Gurler, F., 1215 (AB0471)
Guruparan, T., 943 (SAT0449)
Gusetu, G., 880 (SAT0285)
Guseva, I., 640 (FRI0403), 1128 (AB0230)
Gushikem, A., 474 (THU0706)
Gustafsson, J.T., 885 (SAT0297)
Gustavsson, P., 248 (THU0124)
Gusto, G., 160 (OP0253)
Gutermann, L., 831 (SAT0163)
Guthrie, L.C., 1129 (AB0232)
Gutiérrez, J.M., 696 (FRI0544)
Gutíerrez, M., 1117 (AB0200)
Gutierrez, M., 739 (FRI0660), 1006 (SAT0613), 1011 (SAT0626), 1013 (SAT0631), 1067 (AB0059), 1155 (AB0305), 1408 (AB1011)
Gutiérrez Ureña, S., 1276 (AB0641)
Gutierrez Ureña, S., 1450 (AB1128)
Gutiérrez-Cañas, I., 485 (FRI0016)
Gutierrez-Gonzalez, L.A., 1048 (AB0004)
Gutiérrez-Leonard, A., 1417 (AB1036)
Gutierrez-Leonard, A., 728 (FRI0631)
Gutiérrez-Ruíz, M.C., 205 (THU0016)
Gutierrez-Ureña, S., 1446 (AB1116)
Gutierrez-Ureña, S.R., 117 (OP0158)
Gutoiu, G., 1018 (SAT0644)
Guven, D., 1262 (AB0604)
Guven, D.C., 1300 (AB0706)
Guven, S.C., 608 (FRI0320), 1216 (AB0472)
Güzelant, G., 719 (FRI0610)
Guzelant, G., 1274 (AB0634)
Gúzman, G., 1289 (AB0676)
Guzman, R., 194 (OP0336)
Guzman-Sanchez, I., 515 (FRI0095)
Guzzo, M.P., 230 (THU0082), 1378 (AB0924), 1379 (AB0925)
Gwinnutt, J., 803 (SAT0092)
Gwinnutt, J.M., 243 (THU0112)
Gysi-Klaus, F., 479 (THU0719)

H-Grafella, M., 326 (THU0326), 718 (FRI0607)
Haagsma, C., 240 (THU0106)
Haas, J.P., 132 (OP0196), 398 (THU0507)
Haase, A., 1528 (SAT0769-HPR)
Haavardsholm, E.A., 176 (OP0289), 224 (THU0070), 338 (THU0354), 361 (THU0407), 472 (THU0700), 522 (FRI0111), 526 (FRI0121), 538 (FRI0151), 549 (FRI0182), 797 (SAT0075), 1017 (SAT0642)
Habets, K., 202 (THU0008)
Hablas, S.A., 1469 (AB1181)
Habouri, L., 126 (OP0181), 483 (FRI0009)
Hacein-Bey, S., 182 (OP0307)
Hachfi, H., 1000 (SAT0598), 1169 (AB0346, AB0347), 1170 (AB0348)
Hachulla, E., 77 (OP0062), 108 (OP0134), 152 (OP0236), 202 (THU0006), 709 (FRI0582), 909 (SAT0366)
Hacioglu, A., 412 (THU0542), 1186 (AB0394)
Hackett, K., 1524 (SAT0758-HPR)
Hackett, K.L., 1236 (AB0528), 1517 (SAT0736-HPR)
Haddada, I., 1000 (SAT0598), 1169 (AB0346, AB0347), 1170 (AB0348)
Hadden, R.D.M., 319 (THU0306)
Haddouche, A., 1009 (SAT0623), 1405 (AB1001, AB1002)
Hadjicostas, P., 1345 (AB0821)
Hadjiroussos, V., 1437 (AB1093)
Hadrian, E., 355 (THU0392)
Hadziyannis, E., 1376 (AB0915)
Hafez, E.A., 1224 (AB0495)
Hafirassou, H., 1192 (AB0409)
Hafkenscheid, L., 125 (OP0177), 509 (FRI0083)
Hafström, I., 227 (THU0074)
Haftner, T., 1423 (AB1053)
Hagel, S., 252 (THU0135), 433 (THU0602), 763 (FRI0722)
Hagell, P., 1520 (SAT0746-HPR)
Hagen, K., 161 (OP0255-HPR)
Hagen, K.B., 1497 (FRI0738-HPR)
Hagen, M., 159 (OP0249), 236 (THU0096), 516 (FRI0098)
Hagfors, J., 161 (OP0255-HPR)
Hägglund, P., 501 (FRI0061), 1068 (AB0062)
Hagino, N., 278 (THU0198)
Hagiwara, T., 793 (SAT0068)
Haglund, E., 1495 (FRI0733-HPR), 1515 (SAT0731-HPR), 1531 (AB1199-HPR)
Hagoug, R., 1021 (SAT0651)
Hähnlein, J., 116 (OP0154)
Haibel, H., 101 (OP0118), 651 (FRI0435)
Haid, S., 1009 (SAT0623), 1405 (AB1001, AB1002)
Haidmayer, A., 587 (FRI0268)
Haiduk, P., 479 (THU0719)
Haigh, R., 1164 (AB0332)
Haines, C., 41 (SP0170)
Hajage, D., 58 (OP0018)
Hajj-Ali, R., 1167 (AB0338)
Hajjaj-Hassouni, N., 1358 (AB0862), 1365 (AB0883, AB0884, AB0885), 1418 (AB1041)

Hak, L., 1221 (AB0488)
Hakami, N., 103 (OP0122)
Häkkinen, A., 22 (SP0088)
Hakroush, S., 1402 (AB0992)
Halaby, G., 1042 (SAT0705)
Haladyj, E., 204 (THU0012)
Haładyj, E.N., 1224 (AB0496)
Halász, V., 1428 (AB1067)
Halbout, P., 760 (FRI0713), 1440 (AB1102)
Halcox, J.P., 1173 (AB0358)
Hale, C., 1542 (AB1231-HPR)
Hale, T.W., 548 (FRI0179)
Hall, F.C., 1205 (AB0444)
Hall, J., 370 (THU0430, THU0432), 371 (THU0433, THU0434, THU0435), 1364 (AB0880)
Hall, M., 752 (FRI0693), 1028 (SAT0670)
Hall, S., 141 (OP0216), 149 (LB0003), 683 (FRI0512), 684 (FRI0513), 936 (SAT0436), 952 (SAT0470), 1331 (AB0785)
Hall, S.A., 1459 (AB1156)
Halladay, C., 826 (SAT0151)
Halliday, A., 960 (SAT0489)
Halsaa, V., 52 (OP0005)
Hamad, G., 781 (SAT0038)
Hamada, N., 645 (FRI0419), 1195 (AB0416)
Hamaguchi, Y., 1464 (AB1169)
Hämäläinen, M., 893 (SAT0321)
Hamann, D., 461 (THU0673)
Hamano, H., 505 (FRI0075)
Hamano, Y., 1467 (AB1176)
Hamar, A., 469 (THU0694)
Hambardzumyan, K., 234 (THU0091)
Hamdi, W., 347 (THU0373), 1146 (AB0278), 1188 (AB0398), 1297 (AB0697), 1306 (AB0720)
Hamdulay, S., 333 (THU0344)
Hamdy, A.A., 1053 (AB0018)
Hamdy El Gobashy, N., 874 (SAT0265)
Häme, A., 1404 (AB0999)
Hamed, M., 1113 (AB0190)
Hameed, M., 376 (THU0446)
Hameetman, M., 155 (OP0241)
Hamidou, M., 778 (SAT0029)
Hamidou, M.A., 709 (FRI0582)
Hamilton, J.D., 570 (FRI0228), 838 (SAT0179)
Hammami, S., 885 (SAT0298), 1176 (AB0365), 1231 (AB0517), 1258 (AB0592), 1384 (AB0941)
Hammenfors, D., 67 (OP0040), 311 (THU0284), 464 (THU0681), 886 (SAT0302)
Hammenfors, D.S., 875 (SAT0270)
Hammer, A., 861 (SAT0231)
Hammer, H., 131 (OP0192)
Hammer, H.B., 26 (SP0103), 52 (OP0005), 97 (OP0109), 175 (OP0288), 176 (OP0289), 229 (THU0080), 361 (THU0407), 526 (FRI0121), 538 (FRI0151), 726 (FRI0626), 742 (FRI0668), 938 (SAT0440), 1011 (SAT0626), 1017 (SAT0642), 1408 (AB1011)
Hammer, N.M., 73 (OP0055-HPR), 1512 (SAT0723-HPR)
Hammerfors, D., 583 (FRI0256)
Hammond, A., 1075 (AB0082)
Hammond, E., 859 (SAT0227)
Hammoudeh, M., 1309 (AB0728), 1504 (FRI0758-HPR)
Hammoudeh, S., 1309 (AB0728)
Hamnes, B., 161 (OP0255-HPR)
Hamon, S., 570 (FRI0228), 838 (SAT0179)
Hamoud, H.S., 1426 (AB1062)
Hamuryudan, V., 323 (THU0317), 603 (FRI0307), 618 (FRI0348), 1186 (AB0394), 1246 (AB0558), 1274 (AB0634)
Hamza, S.A., 1224 (AB0495)
Han, C., 341 (THU0360), 1295 (AB0692)
Han, S.H., 762 (FRI0717)
Han, W., 122 (OP0169), 450 (THU0647), 962 (SAT0493), 986 (SAT0555)
Hanaei, H., 1546 (AB1242-HPR)
Hanafy, M.I., 1426 (AB1062)
Hanami, K., 257 (THU0149), 791 (SAT0062)
Hanaoka, H., 635 (FRI0391), 872 (SAT0259), 1260 (AB0597)
Handa, R., 1292 (AB0683)
Handel, I., 939 (SAT0442)
Handrich, A., 454 (THU0656)
Hands, R., 238 (THU0100), 458 (THU0667), 511 (FRI0088)
Hanlon, M.M., 221 (THU0059)
Hannan, M.T., 1032 (SAT0679)
Hannawi, S., 545 (FRI0169), 818 (SAT0131), 1043 (SAT0710)
Hanni, F., 1192 (AB0409)
Hannigan, A., 110 (OP0140-HPR)
Hannon, M.J., 123 (OP0171)
Hannonen, P., 784 (SAT0044)
Hanova, P., 583 (FRI0256)
Hansen, I., 732 (FRI0641)
Hansen, I.M.J., 553 (FRI0190), 660 (FRI0460), 745 (FRI0675), 990 (SAT0565), 1024 (SAT0660), 1519 (SAT0744-HPR), 1545 (AB1239-HPR)
Hansen, I.S., 161 (OP0254-HPR)
Hansen, I.T., 174 (OP0285), 329 (THU0335)
Hansen, K., 691 (FRI0528)
Hansen, K.E., 690 (FRI0525)
Hansen, L., 168 (OP0270)
Hansen, L.B., 168 (OP0270)
Hansen, M.S., 1419 (AB1042)
Hanson, P., 121 (OP0167)
Hansson, M., 509 (FRI0085), 522 (FRI0111), 773 (SAT0014), 785 (SAT0048), 792 (SAT0065)
Hao, M., 69 (OP0043), 872 (SAT0261)
Hao, Y., 600 (FRI0302)
Hao, Z., 869 (SAT0252)
Happe, A., 1448 (AB1123)
Haq, S.A., 153 (LB0002), 1044 (SAT0713), 1460 (AB1157)
Hara, N., 1134 (AB0247)
Hara, R., 115 (OP0152), 282 (THU0207), 923 (SAT0400)
Hara, S., 425 (THU0579), 711 (FRI0587), 722 (FRI0617)
Hara, Y., 800 (SAT0083)
Harada, Y., 1058 (AB0032)
Haraoui, B., 58 (OP0019), 231 (THU0085), 529 (FRI0128), 571 (FRI0230), 656 (FRI0449), 781 (SAT0039), 795 (SAT0072), 815 (SAT0122), 845 (SAT0195), 1188 (AB0397), 1303 (AB0712)
Harden, E., 449 (THU0644)
Härdfeldt, J., 254 (THU0143)
Hardt, U., 1102 (AB0159)
Harel, L., 1389 (AB0957)
Hargreaves, B., 1236 (AB0528)
Harigai, M., 158 (OP0248), 264 (THU0166), 265 (THU0170), 513 (FRI0092), 581 (FRI0252), 845 (SAT0194), 1200 (AB0431)
Harigane, K., 1165 (AB0334), 1166 (AB0335)
Hariz, A., 1251 (AB0574)
Harlaar, J., 111 (OP0141-HPR)
Harman, H., 1306 (AB0721)
Harmancı, D., 1105 (AB0168)
Haro-Martínez, A.C., 1496 (FRI0735-HPR)
Haroon, M., 1487 (THU0753-HPR)
Haroyan, A., 1403 (AB0996)
Harre, U., 775 (SAT0019)
Harris, E., 613 (FRI0334)
Harris, K., 673 (FRI0489)
Harrison, D.D., 335 (THU0348), 341 (THU0360), 671 (FRI0486), 1295 (AB0692)
Harrison, M., 443 (THU0629), 453 (THU0653)
Harrison, N.A., 1379 (AB0926)
Harrison, P., 148 (OP0229), 267 (THU0173), 270 (THU0182), 281 (THU0205, THU0206)
Harrison, R.W., 552 (FRI0188)
Harrison, S.R., 1085 (AB0112)
Harrold, L., 1192 (AB0408), 1313 (AB0739), 1455 (AB1143), 1521 (SAT0750-HPR)
Harrold, L.R., 808 (SAT0104), 1191 (AB0407)
Hársfalvi, J., 1273 (AB0632)
Hart, D., 966 (SAT0504)
Hartevioglu, H., 999 (SAT0595)
Hartgring, S.A., 1206 (AB0446)
Hartshorne, L., 973 (SAT0521)
Harutyunyan, R., 787 (SAT0051)
Harvey, B.P., 492 (FRI0034)
Harvey, H., 1028 (SAT0670)
Harvey, N., 933 (SAT0426)
Harvey, W., 384 (THU0469)
Hasan, A.S., 1350 (AB0839)
Hasan, M., 1101 (AB0155)
Hasan, T., 1404 (AB0999)
Hasanreisoglu, M., 321 (THU0311)
Haschka, J., 73 (OP0052), 159 (OP0249), 236 (THU0096), 516 (FRI0098), 655 (FRI0446), 1011 (SAT0628)
Hasegawa, M., 202 (THU0006)
Hasegawa, T., 699 (FRI0552)
Hashemi, M., 700 (FRI0557)
Hashemzadeh, K., 1341 (AB0811)
Hashimoto, M., 115 (OP0152), 220 (THU0057), 282 (THU0207), 527 (FRI0122), 744 (FRI0673), 1452 (AB1133)
Hashimoto, N., 105 (OP0127), 499 (FRI0054)
Hashimoto, T., 105 (OP0127), 499 (FRI0054)
Hashiramoto, A., 499 (FRI0054)
Hasırcı, Y., 1504 (FRI0756-HPR)
Haskard, D.O., 219 (THU0053)
Haslacher, H., 528 (FRI0125)
Hasler, P., 267 (THU0174)
Hasmann, S., 718 (FRI0606)
Hassan, D., 874 (SAT0265)
Hassan, R.M., 1145 (AB0276)
Hassan, W.A., 985 (SAT0551), 1148 (AB0285)
Hassanien, M., 1168 (AB0342), 1281 (AB0654), 1339 (AB0804), 1384 (AB0940)
Hasseb, A., 1403 (AB0997)
Hassoba, H.M., 887 (SAT0304)
Hassouns, P., 202 (THU0006)
Hatano, M., 800 (SAT0085), 1274 (AB0635)
Hatemi, G., 331 (THU0339), 354 (THU0389), 603 (FRI0307), 618 (FRI0348), 619 (FRI0351), 719 (FRI0610), 1186 (AB0394), 1246 (AB0558), 1274 (AB0634)
Hatemi, I., 331 (THU0339)
Hatron, P.-Y., 152 (OP0236), 413 (THU0546)
Hatta, K., 279 (THU0199)
Hattori, Y., 835 (SAT0174)
Hatzara, C., 1376 (AB0915)
Haug, M., 223 (THU0065)
Hauge, E., 248 (THU0126), 656 (FRI0450)
Hauge, E.-M., 174 (OP0285), 329 (THU0335)
Haugeberg, G., 97 (OP0109), 229 (THU0080), 938 (SAT0440), 1029 (SAT0673)
Haugen, A.J., 1030 (SAT0675)
Haugen, I.K., 122 (OP0168)
Häupl, T., 124 (OP0174)
Haupt, L., 520 (FRI0108)
Hautin-Monteil, V., 265 (THU0169), 271 (THU0184)
Hauzeur, J.-P., 736 (FRI0650)
Havana, M., 827 (SAT0152)
Haviv, Y., 319 (THU0304)
Havryliuk, H., 974 (SAT0526)
Hawkins, N., 939 (SAT0442)
Hawkins, P.N., 227 (THU0076), 710 (FRI0585), 1427 (AB1064)
Hawley, S., 159 (OP0251)
Hax, V., 246 (THU0119), 628 (FRI0371), 1107 (AB0174), 1278 (AB0645)
Haÿ, E., 53 (OP0007)
Hay, E.M., 973 (SAT0521)
Hayashi, M., 835 (SAT0174)
Hayashi, N., 1024 (SAT0661)
Hayashi, T., 800 (SAT0085)
Hayata, A.L., 443 (THU0627)
Haydar, A.A., 1400 (AB0989)
Haye Salinas, M.J., 206 (THU0018), 313 (THU0289), 995 (SAT0582)
Hayem, G., 1470 (AB1185)
Hayer, S., 488 (FRI0024), 502 (FRI0064)
Hayevska, V., 1290 (AB0677)
Hayevskyy, V., 1290 (AB0677)
Hays, S., 272 (THU0186)
Hayward, R., 958 (SAT0483)
Hazel, S., 449 (THU0645)
Hazes, J., 478 (THU0716), 1088 (AB0118), 1306 (AB0722)
Hazes, J.M., 509 (FRI0083), 532 (FRI0136), 537 (FRI0147), 1058 (AB0033)
Hazes, J.M.W., 678 (FRI0500), 1324 (AB0769), 1325 (AB0770), 1421 (AB1047)

Hazes, M., 241 (THU0107), 676 (FRI0497), 1308 (AB0725)
Hazirolan, T., 720 (FRI0612)
Hazlewood, G., 231 (THU0085)
Haznedaroglu, S., 608 (FRI0320), 1216 (AB0472), 1260 (AB0598)
He, D., 459 (THU0669)
He, F., 1524 (SAT0757-HPR)
He, H.-N., 798 (SAT0078)
He, J., 509 (FRI0084), 1065 (AB0052), 1096 (AB0141), 1144 (AB0274), 1197 (AB0421), 1295 (AB0691)
He, L., 459 (THU0669)
He, Y., 120 (OP0165), 986 (SAT0554)
Healey, E., 973 (SAT0521)
Healey, E.L., 438 (THU0614), 1433 (AB1081)
Heaney, A., 1461 (AB1161)
Heath, A., 150 (OP0232)
Heaton, R., 1494 (THU0769-HPR)
Hebeisen, M., 335 (THU0347)
Hebing, R., 550 (FRI0183)
Hecker, R., 257 (THU0150)
Hedlund, M., 182 (OP0305)
Hedström, A.K., 1511 (SAT0721-HPR)
Heegaard, N.H.H., 457 (THU0663)
Heeren, R., 977 (SAT0531)
Heffernan, E.J., 321 (THU0312)
Hegen, M., 778 (SAT0030)
Heggelman, B., 376 (THU0445)
Heiberg, T., 1286 (AB0669)
Heidari Almasi, M., 700 (FRI0556)
Heidecke, H., 772 (SAT0011), 1108 (AB0175)
Heijink, M., 202 (THU0008)
Heil, S., 241 (THU0107)
Heilmeier, U., 58 (OP0020)
Heitzmann, J., 1193 (AB0412)
Hejbøl, E.K., 745 (FRI0675), 1024 (SAT0660)
Hekayem, L., 707 (FRI0578)
Hela, S., 995 (SAT0580), 1377 (AB0920), 1536 (AB1214-HPR)
Helal, A., 1171 (AB0351)
Helliwell, P., 679 (FRI0502), 1332 (AB0786), 1541 (AB1227-HPR)
Helliwell, P.S., 953 (SAT0472)
Helliwell, T., 751 (FRI0690), 1028 (SAT0672), 1043 (SAT0708)
Hellmich, B., 709 (FRI0582)
Hellstrom, C., 626 (FRI0367)
Helmer, E., 57 (OP0017), 287 (THU0220)
Helmick, C.G., 432 (THU0600)
Helmus, N., 399 (THU0511), 1389 (AB0957)
Helsen, M., 211 (THU0033)
Helt, C., 228 (THU0078)
Henao, S., 162 (OP0257-HPR), 538 (FRI0150), 1479 (THU0729-HPR), 1534 (AB1207-HPR), 1543 (AB1235-HPR)
Henckaerts, L., 1005 (SAT0612)
Hendricks, O., 553 (FRI0190)
Hendrikx, T., 135 (OP0202), 141 (OP0216), 337 (THU0352), 676 (FRI0496), 682 (FRI0509), 951 (SAT0469), 1335 (AB0794)
Henes, J., 86 (OP0084), 88 (OP0088), 159 (OP0249), 516 (FRI0098), 899 (SAT0337), 1106 (AB0169), 1110 (AB0181)
Hennessey, A., 1090 (AB0124), 1205 (AB0443)
Henrickson, M., 396 (THU0503)
Henriksen, M., 45 (SP0185), 161 (OP0254-HPR), 196 (OP0340), 1481 (THU0734-HPR)
Henriques, C., 137 (OP0206)
Henriques, M., 112 (OP0144-HPR)
Hensor, E., 91 (OP0095), 152 (OP0235), 196 (OP0341), 314 (THU0293)
Hensor, E.M., 987 (SAT0556), 1019 (SAT0647)
Hensor, E.M.A., 227 (THU0075)
Hensvold, A., 523 (FRI0113), 785 (SAT0048)
Hensvold, A.H., 484 (FRI0013), 517 (FRI0100), 522 (FRI0111)
Hepguler, S., 475 (THU0709)
Heppt, M., 718 (FRI0606)
Heras, H., 421 (THU0569)
Heras, M., 312 (THU0287)
Herath, G., 1177 (AB0370)
Herb-van Toorn, L., 769 (SAT0001)
Herbette, M., 662 (FRI0465), 989 (SAT0561), 1191 (AB0406)
Herbst, R., 192 (OP0331)
Heredia, S., 1005 (SAT0610), 1014 (SAT0635), 1236 (AB0529), 1241 (AB0544)
Herlin, T., 1015 (SAT0636)
Herlyn, K., 325 (THU0323)
Herman-Demars, H., 789 (SAT0057)
Hermann, J., 587 (FRI0268), 1495 (FRI0732-HPR)
Hermann, K.G., 60 (OP0023)
Hermann, S., 446 (THU0637), 1023 (SAT0656)
Hermann, W., 25 (SP0100)
Hermida-Carballo, L., 502 (FRI0063)
Hermida-Gomez, T., 203 (THU0009)
Hermosa, J.C., 918 (SAT0387), 1307 (AB0723)
Hern, S., 1396 (AB0976)
Hernández, A., 308 (THU0275)
Hernández, A.M., 555 (FRI0195)
Hernández, B., 1116 (AB0198), 1422 (AB1050)
Hernandez, B., 551 (FRI0186), 559 (FRI0204), 833 (SAT0168), 843 (SAT0191), 940 (SAT0444)
Hernandez, C., 739 (FRI0660)
Hernández, D., 748 (FRI0683)
Hernandez, E., 237 (THU0097)
Hernández, Í., 614 (FRI0336)
Hernández, J., 75 (OP0059), 405 (THU0526), 420 (THU0567)
Hernandez, J., 843 (SAT0191)
Hernández, J.I., 1351 (AB0840)
Hernández, J.L., 108 (OP0135), 614 (FRI0336), 802 (SAT0088), 804 (SAT0095), 1229 (AB0511), 1255 (AB0583, AB0584)
Hernández, M., 75 (OP0059), 405 (THU0526), 420 (THU0567), 1351 (AB0840)
Hernandez, M., 326 (THU0326), 718 (FRI0607)
Hernández, M.V., 128 (OP0185), 350 (THU0381), 918 (SAT0387), 1133 (AB0243), 1307 (AB0723)
Hernandez, R., 1182 (AB0384)
Hernández, V., 452 (THU0651)
Hernandez, V., 567 (FRI0221), 850 (SAT0206)
Hernández Carballo, C., 691 (FRI0530)
Hernández Díaz, C., 1357 (AB0861)
Hernandez Diaz, C., 175 (OP0288)
Hernández Flórez, D., 386 (THU0474)
Hernández Flórez, D.C., 633 (FRI0385), 1270 (AB0625)
Hernández Miguel, M., 656 (FRI0450)
Hernández Núñez, É., 1132 (AB0240, AB0241)
Hernández-Baldizón, S., 407 (THU0530)
Hernández-Breijo, B., 822 (SAT0141)
Hernandez-Breijo, B., 456 (THU0661), 555 (FRI0194), 1179 (AB0375)
Hernández-Briano, P.L.R., 1397 (AB0978)
Hernandez-Cuervo, P., 1155 (AB0304)
Hernández-Díaz, C., 1408 (AB1010)
Hernandez-Diaz, C., 583 (FRI0256), 1015 (SAT0636)
Hernández-Flórez, D., 462 (THU0676), 656 (FRI0448), 1276 (AB0640)
Hernández-Grafella, M., 420 (THU0567)
Hernandez-Illas, M., 371 (THU0434), 1364 (AB0880)
Hernandez-Miguel, M.V., 817 (SAT0128)
Hernandez-Molina, G., 291 (THU0230), 311 (THU0284), 417 (THU0556), 464 (THU0681), 597 (FRI0292), 878 (SAT0278), 886 (SAT0302), 1225 (AB0499)
Hernandez-Palma, L.A., 500 (FRI0058), 1199 (AB0427)
Hernandez-Parra, D., 594 (FRI0287), 658 (FRI0453), 927 (SAT0413), 928 (SAT0414), 1286 (AB0667)
Hernandez-Ramirez, D.F., 597 (FRI0292)
Hernández-Rodríguez, J., 1252 (AB0575)
Hernandez-Rodriguez, J., 610 (FRI0324)
Hernandez-Sanchez, M.D., 1525 (SAT0760-HPR)
Herold, M., 1455 (AB1144)
Herrera, D., 1117 (AB0201)
Herrera, F., 1048 (AB0004)
Herrera, J.M., 414 (THU0549)
Herrera, S., 1386 (AB0948)
Herreras, J., 326 (THU0326), 718 (FRI0607)
Herreras, J.M., 717 (FRI0602)
Herrero, M., 178 (OP0294), 980 (SAT0540), 1466 (AB1174)
Herrero Barbero, M., 761 (FRI0715), 1456 (AB1146, AB1147)
Herrero-Beaumont, G., 128 (OP0186), 504 (FRI0071)
Herrick, A., 104 (OP0123), 1047 (AB0003)
Herrick, A.L., 5 (SP0016)
Herrings, I., 678 (FRI0500), 1324 (AB0769)
Herrmann, K.H., 442 (THU0626)
Herrmann, M., 34 (SP0137)
Hervás Marín, D., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080)
Hervert-Cavazos, F., 253 (THU0140)
Herzer, P., 1029 (SAT0674)
Herzog, L., 267 (THU0174)
Heselynn, H., 1512 (SAT0722-HPR)
Heslinga, M., 259 (THU0154), 811 (SAT0114)
Heslinga, S., 1087 (AB0116)
Hess, A., 240 (THU0105)
Hesselstrand, R., 104 (OP0123), 1286 (AB0669)
Hetland, M., 567 (FRI0221)
Hetland, M.L., 234 (THU0091), 341 (THU0361), 450 (THU0648), 451 (THU0649), 456 (THU0662), 553 (FRI0190), 656 (FRI0450), 686 (FRI0518), 726 (FRI0628), 732 (FRI0641), 784 (SAT0045)
Hetland Brinkmann, G., 81 (OP0071), 756 (FRI0702)
Hetlevik, S.O., 55 (OP0013)
Heuft, L., 157 (OP0245)
Hewlett, S., 110 (OP0139-HPR), 470 (THU0695), 818 (SAT0132), 1501 (FRI0748-HPR)
Hickmann, S., 167 (OP0269)
Hicks, L., 371 (THU0434), 1364 (AB0880)
Hidaka, N., 260 (THU0157), 1178 (AB0373)
Hidaka, T., 265 (THU0170)
Hidaka, Y., 1403 (AB0995)
Hidalgo, A., 15 (SP0061)
Hidalgo, V., 1303 (AB0713)
Hider, S., 751 (FRI0690), 1028 (SAT0672), 1552 (PARE0002)
Hider, S.L., 1043 (SAT0708), 1174 (AB0359), 1442 (AB1107)
Hiensch, V., 1555 (PARE0009)
Hiepe, F., 151 (OP0234)
Higa, S., 800 (SAT0083)
Higashi, K., 1484 (THU0744-HPR)
Higginbottom, A., 1552 (PARE0002)
Higgins, N.M., 1434 (AB1083)
Higgs, B., 180 (OP0301)
Higham, J., 302 (THU0259)
Higuchi, T., 644 (FRI0417), 1026 (SAT0667)
Hijab, A., 1000 (SAT0596)
Hilberdink, S., 1485 (THU0749-HPR)
Hilberg, O., 546 (FRI0174)
Hilfiker, R., 47 (SP0194), 1539 (AB1222-HPR)
Hilkens, A., 156 (OP0244)
Hill, C., 383 (THU0464)
Hill, J., 3 (SP0006), 430 (THU0594)
Hillen, M.R., 181 (OP0303), 288 (THU0223), 295 (THU0241), 1089 (AB0121)
Hilliquin, S., 54 (OP0011)
Hillis, C., 418 (THU0561)
Hilsted, L., 332 (THU0340)
Hiltunen, J., 61 (OP0024)
Hinks, A., 177 (OP0291)
Hinrichs, B., 1390 (AB0958)
Hinrichs, M.J., 192 (OP0331)
Hinton, M., 1021 (SAT0651)
Hirabayashi, M., 88 (OP0087)
Hirahara, K., 499 (FRI0055)
Hirai, Y., 318 (THU0303)
Hiramatsu, M., 1251 (AB0572)
Hirano, T., 115 (OP0152), 282 (THU0207)
Hirano, Y., 285 (THU0214), 582 (FRI0254), 708 (FRI0579), 1357 (AB0860)
Hiraoka, D., 1424 (AB1056)
Hirasawa, T., 1484 (THU0744-HPR)
Hirata, A., 995 (SAT0581), 1024 (SAT0661)
Hirata, M., 1251 (AB0572)
Hirata, S., 791 (SAT0062), 1009 (SAT0622), 1460 (AB1159)
Hiratsuka, S., 505 (FRI0075)

Hirohata, S., 314 (THU0294), 598 (FRI0297), 610 (FRI0326)
Hirose, J., 476 (THU0710)
Hirose, S., 141 (OP0215), 1095 (AB0140)
Hirose, T., 274 (THU0191), 1200 (AB0431)
Hirschmann, S., 655 (FRI0446)
Hisada, R., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Hislop Lennie, K., 1508 (FRI0767-HPR)
Hitchon, C., 131 (OP0192), 231 (THU0085), 781 (SAT0039), 815 (SAT0122), 1117 (AB0199)
Hitzelhammer, E., 750 (FRI0688)
Hivernat, H., 991 (SAT0569)
Hjelle, A., 184 (OP0312)
Hjeltnes, G., 1309 (AB0730)
Hjøllund, N.H.I., 454 (THU0657)
Hmila, S., 926 (SAT0409)
Ho, C., 416 (THU0554)
Ho, C.H., 589 (FRI0273), 898 (SAT0334)
Ho, D., 827 (SAT0152)
Ho, L.Y., 303 (THU0263), 583 (FRI0257), 825 (SAT0147), 874 (SAT0266, SAT0267)
Ho, P., 201 (THU0004), 1087 (AB0115)
Ho, T.-Y., 1408 (AB1009)
Hočevar, A., 108 (OP0133), 219 (THU0054), 325 (THU0324), 1143 (AB0272), 1186 (AB0393), 1291 (AB0682), 1538 (AB1220-HPR)
Hocevar, A., 109 (OP0136), 583 (FRI0256), 1243 (AB0552)
Hochberg, M., 837 (SAT0177)
Hochberg, M.C., 121 (OP0166)
Hochberg, S., 817 (SAT0129)
Hock, B., 1415 (AB1031)
Hodge, J., 148 (OP0230), 831 (SAT0162)
Hodgson, R., 727 (FRI0630), 1010 (SAT0624)
Hodkinson, B., 631 (FRI0379)
Hodosi, K., 1027 (SAT0668)
Hodson, J., 546 (FRI0173)
Hoehne-Zimmer, V., 253 (THU0139)
Hoekstra, M., 225 (THU0071)
Hoekstra, O., 724 (FRI0623), 1020 (SAT0650)
Hoekstra, O.S., 732 (FRI0642)
Hoekstra, T., 604 (FRI0309)
Hoepken, B., 60 (OP0023), 681 (FRI0508), 1316 (AB0747)
Hoepken, S., 142 (OP0217)
Hofauer, B., 303 (THU0262), 311 (THU0284), 464 (THU0681), 886 (SAT0302)
Hofer, M., 393 (THU0495), 398 (THU0509)
Hoff, P., 486 (FRI0019), 1067 (AB0060)
Hoffman, E., 543 (FRI0164)
Hoffman, G., 187 (OP0320)
Hoffman, G.S., 605 (FRI0314)
Hoffman, H.M., 77 (OP0063), 398 (THU0509)
Hoffman, M., 1545 (AB1241-HPR)
Hoffmann, F., 934 (SAT0429)
Hoffmann, H.M., 710 (FRI0585)
Hoffmann-Vold, A.-M., 87 (OP0085), 106 (OP0129), 630 (FRI0376), 1047 (AB0003)
Hoffmueller, U., 292 (THU0234)
Hoffstetter, C., 433 (THU0602), 467 (THU0689)
Hofilena, B., 1003 (SAT0607)
Hofman, A., 1088 (AB0118)
Hofmann, M., 488 (FRI0024)
Hofmann, M.W., 844 (SAT0193), 1187 (AB0396)
Hofstedt, O.E., 444 (THU0632)
Hogan, S., 41 (SP0167)
Hoh, S.F., 401 (THU0517)
Hohl, K., 1478 (THU0727-HPR)
Hoi, A., 876 (SAT0272)
Hoielt, S., 986 (SAT0554)
Høilund-Carlsen, P.F., 64 (OP0033)
Højgaard, P., 96 (OP0106), 98 (OP0112), 1332 (AB0786)
Hojnik, M., 97 (OP0108), 342 (THU0363), 349 (THU0379), 651 (FRI0435), 654 (FRI0444), 921 (SAT0395), 1180 (AB0378)
Hojo, S., 842 (SAT0187)
Hokstad, I., 1309 (AB0730)
Holers, V.M., 498 (FRI0053), 757 (FRI0706)
Holgado, S., 988 (SAT0560), 1236 (AB0529), 1241 (AB0544), 1424 (AB1055)
Holinka, J., 486 (FRI0018)
Holl-Wieden, A., 397 (THU0504)
Hollan, I., 1309 (AB0730)
Holland, E.J., 152 (OP0237)
Holland, R., 685 (FRI0514)
Hollingworth, W., 110 (OP0139-HPR)
Holmdahl, R., 779 (SAT0031), 792 (SAT0065)
Holmqvist, M., 114 (OP0149), 904 (SAT0352)
Holmsted, K., 1332 (AB0786)
Holmström, M., 805 (SAT0096)
Holobyn, T., 691 (FRI0528)
Holroyd, C., 933 (SAT0426), 1180 (AB0377)
Holtrop, M., 1497 (FRI0739-HPR)
Holz, A., 1050 (AB0010)
Homan, P., 1125 (AB0220)
Homey, B., 295 (THU0241)
Homik, J., 131 (OP0192)
Hon, A., 1152 (AB0296)
Honczarenko, M., 859 (SAT0226)
Honda, O., 1467 (AB1176)
Honda, Z.-I., 1248 (AB0566)
Hong, C., 918 (SAT0389)
Hong, E.E., 136 (OP0203), 137 (OP0204), 834 (SAT0169)
Hong, H.C., 1140 (AB0262)
Hong, J.-I., 217 (THU0050)
Hong, L.C., 82 (OP0075)
Hong, S., 1093 (AB0133), 1222 (AB0491)
Hong, S.-J., 482 (FRI0007)
Hong, S.J., 1185 (AB0392)
Hong, Y.S., 926 (SAT0408)
Hong-Qing, N., 839 (SAT0181)
Honold, L., 1023 (SAT0656)
Hoogland, W., 523 (FRI0113)
Hope, H.F., 265 (THU0168), 275 (THU0192)
Höpfl, P., 1288 (AB0673)
Hopp, E., 630 (FRI0376)
Horai, Y., 117 (OP0157)
Horák, P., 440 (THU0621), 451 (THU0650), 1183 (AB0387), 1264 (AB0609)
Horak, P., 1051 (AB0014)
Horcada, L., 1107 (AB0173)
Horga, J.F., 980 (SAT0540)
Horinkova, J., 916 (SAT0383)
Horita, N., 1191 (AB0405)
Horita, T., 202 (THU0006)
Horiuchi, H., 1249 (AB0567)
Horiuchi, T., 1254 (AB0582)
Horn, H.C., 660 (FRI0460)
Horn, T., 239 (THU0103), 1124 (AB0217), 1414 (AB1026)
Horne, R., 352 (THU0385)
Horneff, G., 74 (OP0057), 132 (OP0196), 195 (OP0338), 390 (THU0487), 398 (THU0507), 400 (THU0512), 405 (THU0525), 406 (THU0529), 448 (THU0641)
Hornung, Á., 1090 (AB0123)
Hørslev-Petersen, K., 433 (THU0601), 477 (THU0715), 732 (FRI0641), 784 (SAT0045)
Horta, S., 894 (SAT0324)
Horta Baas, G., 1211 (AB0460)
Horton, L., 518 (FRI0102)
Horváth, Á., 469 (THU0694), 697 (FRI0547)
Horváth, B., 650 (FRI0433)
Hoshino, S., 409 (THU0535)
Hoshino, T., 1403 (AB0995)
Hoshino-Negishi, K., 211 (THU0031)
Hosmane, B., 1201 (AB0432)
Hosoi, F., 507 (FRI0079)
Hospach, A., 398 (THU0507)
Hospach, T., 76 (OP0060)
Hospodarskyy, I., 824 (SAT0146)
Hossain, M.N., 1367 (AB0889)
Hossein, M., 553 (FRI0190)
Hou, J., 1079 (AB0094)
Houard, X., 1072 (AB0073)
Houben, E., 604 (FRI0309)
Hough, D., 858 (SAT0225), 870 (SAT0255)
Houman, M.H., 313 (THU0291), 596 (FRI0290), 599 (FRI0300), 889 (SAT0308), 1238 (AB0536), 1239 (AB0537)
Hourdille, A., 188 (OP0323)
Hourmant, M., 778 (SAT0029)
Houssiau, F., 153 (LB0002)
Houssiau, F.A., 290 (THU0228), 863 (SAT0238)
Houssien, A., 805 (SAT0098)
Houvenagel, E., 359 (THU0402), 549 (FRI0180)
Hov, J., 87 (OP0085)
Howard-Tripp, N., 1103 (AB0162)
Howe, D., 867 (SAT0249)
Howe, F., 976 (SAT0530)
Howren, A., 374 (THU0442)
Hoxha, A., 99 (OP0113), 1214 (AB0467), 1315 (AB0745)
Hrabě de Angelis, M., 500 (FRI0059)
Hrušková, V., 209 (THU0027)
Hrycaj, P., 824 (SAT0146), 853 (SAT0212)
Hsia, E., 142 (OP0218), 335 (THU0348), 341 (THU0360), 950 (SAT0465), 1295 (AB0692)
Hsia, E.C., 671 (FRI0486), 944 (SAT0453)
Hsu, B., 250 (THU0130), 577 (FRI0243), 581 (FRI0252), 845 (SAT0194)
Hsu, H.-C., 252 (THU0136)
Hsu, J., 133 (OP0197), 396 (THU0503)
Htut, E.E.P., 215 (THU0043), 943 (SAT0449)
Hu, C., 942 (SAT0448)
Hu, F., 1082 (AB0102), 1352 (AB0845)
Hu, J., 166 (OP0266), 375 (THU0444), 379 (THU0455)
Hua, B., 592 (FRI0281), 1430 (AB1073)
Hua, C., 113 (OP0146), 804 (SAT0094), 1159 (AB0315)
Hua, D., 1331 (AB0784)
Hua, W., 1192 (AB0408), 1455 (AB1143)
Huang, A., 749 (FRI0684)
Huang, C.-Y., 1503 (FRI0755-HPR)
Huang, F., 601 (FRI0304), 919 (SAT0392), 934 (SAT0429), 935 (SAT0432)
Huang, G.-S., 1408 (AB1009)
Huang, I.-S., 770 (SAT0005)
Huang, J., 547 (FRI0176), 1516 (SAT0734-HPR), 1524 (SAT0757-HPR)
Huang, J.-L., 1077 (AB0087)
Huang, L., 1219 (AB0482)
Huang, L.-H., 85 (OP0080)
Huang, Q., 294 (THU0239), 497 (FRI0050)
Huang, R., 191 (OP0330)
Huang, S., 1092 (AB0130)
Huang, W., 67 (OP0038)
Huang, Y., 203 (THU0010), 724 (FRI0622), 759 (FRI0710), 934 (SAT0430)
Huang, Z., 203 (THU0010), 934 (SAT0430)
Huart, A., 188 (OP0321)
Hubáčková, L., 1264 (AB0609)
Hübenthal, M., 465 (THU0682)
Huber, J.L., 409 (THU0537)
Hucke, M., 750 (FRI0688)
Hudry, C., 434 (THU0605), 461 (THU0675), 465 (THU0684), 754 (FRI0699), 755 (FRI0700), 789 (SAT0057), 1033 (SAT0684), 1034 (SAT0685)
Hudson, M., 202 (THU0006), 443 (THU0629), 453 (THU0653), 911 (SAT0372)
Hueber, A., 142 (OP0217), 159 (OP0249), 240 (THU0105), 516 (FRI0098), 1511 (SAT0719-HPR)
Hueber, A.J., 725 (FRI0625), 1011 (SAT0628)
Huerta Barberá, S., 1173 (AB0356)
Hughes, C., 938 (SAT0438)
Hughes, C.D., 1154 (AB0303)
Hughes, G., 382 (THU0461)
Hughes, L.B., 1125 (AB0220)
Hughes, M., 5 (SP0015)
Hughes, T.R., 208 (THU0025)
Hughes-Austin, J.M., 757 (FRI0706)
Hügle, T., 1427 (AB1065)
Hugues, B., 54 (OP0011)
Huguet, D., 731 (FRI0638)
Huis, A.M.P., 1525 (SAT0761-HPR)
Huiskes, V.J.B., 557 (FRI0200)
Huisman, A.M., 968 (SAT0508)
Huisman, C.C., 630 (FRI0377)
Huisman, M., 1020 (SAT0650)
Huizinga, R., 153 (LB0002)
Huizinga, T., 202 (THU0008), 240 (THU0104), 383 (THU0464), 560 (FRI0207), 566 (FRI0219),

569 (FRI0225), 621 (FRI0356), 778 (SAT0030), 1050 (AB0012), 1135 (AB0248), 1463 (AB1164)
Huizinga, T.W., 146 (OP0224), 160 (OP0252), 181 (OP0302), 234 (THU0091), 445 (THU0635), 473 (THU0704), 516 (FRI0097), 576 (FRI0242), 871 (SAT0258), 903 (SAT0350)
Huizinga, T.W.J., 512 (FRI0090), 907 (SAT0359), 1076 (AB0084)
Hulejová, H., 220 (THU0058)
Hulejova, H., 243 (THU0113)
Hulme, C.T., 1205 (AB0444)
Hulscher, M., 1505 (FRI0759-HPR)
Hulscher, M.E.J.L., 1498 (FRI0740-HPR), 1525 (SAT0761-HPR)
Hülser, M.-L., 1063 (AB0046)
Humbert, L., 691 (FRI0529)
Humbert, S., 1256 (AB0588)
Humbría, A., 614 (FRI0336)
Humby, F., 238 (THU0100), 458 (THU0667), 490 (FRI0030), 511 (FRI0088)
Hummel, A., 109 (OP0137), 187 (OP0320)
Hummers, L., 105 (OP0126)
Humrich, J.Y., 33 (SP0134), 44 (SP0183)
Huneault, L., 96 (OP0107)
Hunt, B.J., 1097 (AB0147)
Hunt, L., 238 (THU0101)
Hunter, A., 1246 (AB0559)
Hunter, D.J., 123 (OP0171)
Hunter, T.M., 932 (SAT0425)
Hunyh, D.H., 953 (SAT0471)
Hunzelmann, N., 202 (THU0006), 893 (SAT0319), 1047 (AB0003), 1106 (AB0169), 1110 (AB0181)
Huot-Marchand, P., 786 (SAT0050)
Huppertz, H.I., 133 (OP0197)
Hur, E.M., 780 (SAT0035)
Hur, J.-W., 827 (SAT0154)
Hurnakova, J., 243 (THU0113)
Husakova, M., 916 (SAT0383), 1468 (AB1180)
Huscher, D., 801 (SAT0087), 899 (SAT0337), 915 (SAT0380)
Husmark, T., 835 (SAT0173)
Husni, M.E., 671 (FRI0486), 679 (FRI0502)
Hussain, H., 446 (THU0638)
Hussain, S., 726 (FRI0627), 1024 (SAT0659)
Hussein, H., 1144 (AB0275)
Hussein, H.A., 1228 (AB0505)
Hussein, M., 1432 (AB1078)
Hussein, N., 1171 (AB0351)
Hussein, S.Y., 741 (FRI0665)
Hussein Gazar, Y., 986 (SAT0553)
Hussell, T., 90 (OP0094)
Huster, W.J., 1330 (AB0783)
Hutchings, A., 316 (THU0297), 318 (THU0302)
Hutchings, E., 131 (OP0192)
Hutchinson, D., 518 (FRI0101), 1031 (SAT0678), 1085 (AB0111), 1155 (AB0306)
Hutchinson, M., 635 (FRI0390)
Hutse, V., 763 (FRI0719)
Hutt, D., 1427 (AB1064)
Huzjan, B., 1546 (AB1243-HPR)
Hvidsten, S., 64 (OP0033)
Hviid Larsen, R., 246 (THU0118), 533 (FRI0137, FRI0139)
Hwang, C., 548 (FRI0179)
Hwang, C.C., 232 (THU0087), 517 (FRI0100)
Hwang, H.S., 217 (THU0049, THU0050)
Hwang, J., 612 (FRI0331), 749 (FRI0685)
Hwang, L., 1034 (SAT0686)
Hwu, P., 717 (FRI0604)
Hyldgaard, C., 546 (FRI0174)
Hymabaccus, B., 1215 (AB0471)
Hyrich, K., 177 (OP0291), 200 (THU0002), 265 (THU0168), 275 (THU0192), 753 (FRI0695), 765 (FRI0724), 806 (SAT0099)
Hyrich, K.L., 146 (OP0225), 200 (THU0001), 391 (THU0488), 408 (THU0533), 555 (FRI0196)
Hyslop, D., 513 (FRI0092)
Hyslop, D.L., 158 (OP0248)

Iaccarino, L., 867 (SAT0248), 1209 (AB0455, AB0456)
Iacono, D., 263 (THU0164), 1118 (AB0202)
Iagnocco, A., 10 (SP0039), 174 (OP0286), 175 (OP0288), 236 (THU0095), 583 (FRI0256), 730 (FRI0637), 742 (FRI0667), 1009 (SAT0621), 1013 (SAT0631), 1015 (SAT0636), 1022 (SAT0654), 1152 (AB0295), 1412 (AB1022)
Iannaccone, C., 846 (SAT0197), 1120 (AB0207)
Iannone, F., 248 (THU0123), 254 (THU0143), 259 (THU0155), 343 (THU0366), 411 (THU0540), 521 (FRI0110), 639 (FRI0400), 656 (FRI0450), 711 (FRI0586), 808 (SAT0105), 850 (SAT0206), 1059 (AB0037), 1135 (AB0250), 1268 (AB0618), 1272 (AB0630), 1327 (AB0773), 1461 (AB1160)
Iannuccelli, C., 56 (OP0015), 230 (THU0082), 1378 (AB0924), 1379 (AB0925)
Iaremenko, K., 615 (FRI0340), 924 (SAT0404)
Iaremenko, O., 235 (THU0094), 615 (FRI0340), 924 (SAT0404)
Ibañez, J., 1107 (AB0173)
Ibanez, M., 984 (SAT0549), 1003 (SAT0607)
Ibáñez Vodnizza, S.E., 661 (FRI0461), 931 (SAT0421), 1146 (AB0279), 1459 (AB1154)
Ibarguengoitia, O., 837 (SAT0178)
Ibarguengoitia-Barrena, O., 1001 (SAT0600)
Ibarra, C., 1025 (SAT0662)
Ibarreche, D., 312 (THU0287)
Ibba-Manneschi, L., 504 (FRI0070), 623 (FRI0362)
Ibero, I., 705 (FRI0570, FRI0571)
Ibrahim, S., 474 (THU0707)
Ibrahim, S.I., 1216 (AB0473), 1224 (AB0495)
İçağasıoğlu, A., 652 (FRI0437)
Ice, J.A., 1096 (AB0143)
Ichikawa, S., 699 (FRI0553)
Ichimura, Y., 88 (OP0087), 1026 (SAT0667)
Ichinose, K., 318 (THU0303), 503 (FRI0067), 723 (FRI0620)
Ichise, Y., 115 (OP0152), 487 (FRI0022), 507 (FRI0080), 699 (FRI0553)
Icke, K., 960 (SAT0488)
Ida, H., 1403 (AB0995)
Idborg, H., 586 (FRI0265), 626 (FRI0367)
Idier, I., 843 (SAT0189)
Idolazzi, L., 363 (THU0412), 671 (FRI0485), 693 (FRI0535), 854 (SAT0215), 940 (SAT0443, SAT0445), 1062 (AB0045), 1124 (AB0216), 1200 (AB0429), 1314 (AB0742)
Ifticene, M.A., 1192 (AB0409)
Igarashi, T., 800 (SAT0083)
Iglesias, A., 1239 (AB0538)
Iglesias, E., 407 (THU0530), 1393 (AB0967)
Iguchi, S., 507 (FRI0079)
Ihata, A., 602 (FRI0305)
Ihn, H., 202 (THU0006)
Iida, H., 635 (FRI0391), 872 (SAT0259), 1260 (AB0597)
Ijaz, U.Z., 1087 (AB0115)
Ikari, K., 263 (THU0165), 280 (THU0204), 524 (FRI0117), 798 (SAT0079), 799 (SAT0082), 814 (SAT0120), 1063 (AB0047)
Ikari, Y., 800 (SAT0085), 801 (SAT0086)
Ikdahl, E., 802 (SAT0090), 1029 (SAT0673)
Ike, R., 1125 (AB0220)
Ikeda, K., 77 (OP0062), 175 (OP0288), 738 (FRI0655), 1452 (AB1133)
Ikeda, W., 211 (THU0031)
Ikic Matijasevic, M., 1055 (AB0026)
Ikumi, N., 675 (FRI0493), 681 (FRI0507), 951 (SAT0467), 1319 (AB0755)
Ikuta, K., 1062 (AB0044)
Ilar, A., 248 (THU0124)
Ilas, D.C., 959 (SAT0485)
Ilashchuk, T., 1167 (AB0340)
İlcin, N., 1522 (SAT0751-HPR)
Ilcin, N., 53 (OP0009-HPR)
Ilhem, C., 995 (SAT0580), 1377 (AB0920)
Ilie, E., 1532 (AB1200-HPR)
Iliescu, M.G., 996 (SAT0584)
Iliopoulos, A., 659 (FRI0455), 836 (SAT0176), 928 (SAT0415)
Iliou, C., 1193 (AB0411)
Ilivanova, E., 560 (FRI0208)
Illeez, O.G., 1058 (AB0034)
Illei, G., 50 (OP0001), 180 (OP0301), 856 (SAT0220), 865 (SAT0243)
Illiano, S., 195 (OP0339)
Imai, T., 211 (THU0031), 842 (SAT0187)
Imamura, H., 799 (SAT0082), 1063 (AB0047)
Imamura, M., 1024 (SAT0661)
Imboden, J.B., 58 (OP0020)
İmeryüz, N., 1013 (SAT0633)
Imkamp, M., 649 (FRI0430)
Impellizzieri, D., 191 (OP0330)
Imura, Y., 220 (THU0057), 527 (FRI0122), 618 (FRI0349), 1452 (AB1133)
Inaba, T., 1274 (AB0635)
Inaba, Y., 1165 (AB0334), 1166 (AB0335)
Inagaki, M., 744 (FRI0673)
İnal, S.H., 1528 (SAT0770-HPR)
Inamova, O., 611 (FRI0328), 1153 (AB0298)
İnanç, N., 644 (FRI0416), 821 (SAT0139), 889 (SAT0310), 1013 (SAT0633), 1310 (AB0731)
Inanç, N., 910 (SAT0367)
Inceer, M., 545 (FRI0171), 1176 (AB0366)
Inchaurbe, A., 837 (SAT0178)
Inciarte-Mundo, J., 128 (OP0185)
Incorvaia, A., 247 (THU0121)
Inderjeeth, C., 767 (FRI0730), 1045 (SAT0716)
Inês, L., 137 (OP0206)
Inês, L.S., 342 (THU0362)
Infantino, M., 646 (FRI0423)
Ingegnoli, F., 41 (SP0171), 299 (THU0252), 643 (FRI0413), 746 (FRI0677), 908 (SAT0364), 1022 (SAT0655), 1390 (AB0958)
Inghilleri, S., 891 (SAT0315)
Iñiguez, C., 213 (THU0037)
Iñiguez Ubiaga, C., 719 (FRI0608), 1232 (AB0518)
Inman, R., 353 (THU0388)
Inman, R.D., 651 (FRI0435), 921 (SAT0395)
Inoo, M., 265 (THU0170), 283 (THU0209)
Inoue, E., 263 (THU0165), 280 (THU0204), 524 (FRI0117), 798 (SAT0079), 814 (SAT0120)
Inoue, H., 1203 (AB0439), 1254 (AB0582)
Inoue, K., 738 (FRI0655), 924 (SAT0402)
Inoue, M., 1203 (AB0439)
Inoue, Y., 747 (FRI0680), 1254 (AB0582)
Insua, S., 718 (FRI0607)
Intxaurbe-Pellejero, A., 1001 (SAT0600)
Inui, K., 540 (FRI0156), 955 (SAT0477), 1023 (SAT0658), 1134 (AB0245), 1324 (AB0768), 1426 (AB1061)
Inversetti, A., 1214 (AB0467)
Ioan, C., 1540 (AB1224-HPR)
Ioan-Facsinay, A., 39 (SP0161), 220 (THU0057), 769 (SAT0001), 778 (SAT0030)
Ioana, A., 1384 (AB0941)
Ioannou, Y., 74 (OP0056), 304 (THU0265), 389 (THU0484), 401 (THU0516)
Ionescu, C., 495 (FRI0043), 1429 (AB1069)
Ionescu, E.V., 996 (SAT0584)
Ionescu, R., 245 (THU0116), 304 (THU0266), 416 (THU0555), 423 (THU0574), 435 (THU0606), 457 (THU0665), 672 (FRI0488), 767 (FRI0729), 876 (SAT0271), 881 (SAT0288), 1025 (SAT0664), 1026 (SAT0665), 1208 (AB0450), 1221 (AB0487), 1278 (AB0646, AB0647), 1333 (AB0790), 1428 (AB1068), 1429 (AB1069), 1433 (AB1082), 1447 (AB1120), 1460 (AB1158), 1540 (AB1224-HPR)
Iordache, C., 1269 (AB0620)
Iorgoveanu, V., 1007 (SAT0615), 1026 (SAT0665)
Iorgoveanu, V.C., 1025 (SAT0664), 1428 (AB1068), 1429 (AB1069)
Iorio, A., 418 (THU0561)
Iosub, L., 342 (THU0363)
İpekci, S.H., 931 (SAT0422)
Iraheta, I., 1339 (AB0805)
Irigoyen, M.V., 1175 (AB0362), 1443 (AB1109)
Irigoyen-Oyarzábal, M.V., 261 (THU0160)
Irigoyen-Oyarzabal, M.V., 1492 (THU0766-HPR)
Irlapati, R.V.P., 1277 (AB0644)
Irure-Ventura, J., 1084 (AB0108)
Isaacs, J., 200 (THU0002)
Isaacs, J.D., 22 (SP0087), 200 (THU0001, THU0003)

Isaeva, K., 186 (OP0316), 539 (FRI0154), 1387 (AB0950, AB0951)
Isailovic, N., 620 (FRI0353)
Isaka, Y., 513 (FRI0092)
Isayama, T., 1009 (SAT0622)
Isenberg, D., 153 (LB0002), 300 (THU0256), 856 (SAT0219), 863 (SAT0236), 886 (SAT0302), 1090 (AB0124), 1205 (AB0443)
Isenberg, D.A., 37 (SP0152), 1100 (AB0152), 1265 (AB0611)
Ishchenko, D., 616 (FRI0343)
Ishida, M., 524 (FRI0116)
Ishida, Y., 800 (SAT0083)
Ishigatsubo, Y., 610 (FRI0326)
Ishigooka, N., 527 (FRI0122)
Ishiguro, N., 582 (FRI0254), 708 (FRI0579), 799 (SAT0081), 809 (SAT0106), 835 (SAT0174), 1124 (AB0219), 1177 (AB0371), 1195 (AB0415), 1357 (AB0860)
Ishii, K., 1165 (AB0334), 1166 (AB0335)
Ishii, M., 1344 (AB0819)
Ishii, N., 211 (THU0031)
Ishii, S., 222 (THU0064), 894 (SAT0322), 1149 (AB0289)
Ishii, T., 510 (FRI0087)
Ishikawa, H., 229 (THU0079), 809 (SAT0106), 853 (SAT0214), 1124 (AB0219), 1177 (AB0371)
Ishikawa, O., 202 (THU0006)
Ishimori, K., 872 (SAT0259), 1260 (AB0597)
Ishitoku, M., 1460 (AB1159)
Ishizuka, T., 537 (FRI0148)
Işıksoy, S., 863 (SAT0237)
Isil, U., 1156 (AB0308)
Isıyel, E., 397 (THU0506)
Islak, C., 603 (FRI0307)
Islam, J., 1021 (SAT0651)
Isleten, B., 475 (THU0709)
Ismaiel, B., 1348 (AB0830)
Ismail, A., 1494 (THU0769-HPR)
Ismail, M., 958 (SAT0482), 1308 (AB0726)
Ismail, S., 1113 (AB0190)
Isomäki, P., 61 (OP0024)
Isono, M., 285 (THU0214)
Isozaki, T., 222 (THU0064), 800 (SAT0085), 894 (SAT0322)
Issa, M., 512 (FRI0090), 789 (SAT0058), 1147 (AB0281)
Issaoui, D., 1346 (AB0826)
Italiani, P., 222 (THU0063)
Itescu, S., 566 (FRI0220)
Ito, H., 527 (FRI0122), 744 (FRI0673), 995 (SAT0581), 1024 (SAT0661)
Ito, J., 1344 (AB0819)
Ito, K., 425 (THU0579), 711 (FRI0587), 722 (FRI0617)
Ito, S., 809 (SAT0106), 853 (SAT0214), 1124 (AB0219), 1177 (AB0371)
Iturzaeta, J.M., 416 (THU0553)
Iuliano, A., 1281 (AB0656)
Ivanchenko, M., 182 (OP0305)
Ivanov, D., 269 (THU0179)
Ivanov, R., 560 (FRI0208)
Ivanova, D., 1543 (AB1233-HPR)
Ivanova, L.V., 1189 (AB0402)
Ivanova, M., 379 (THU0453), 584 (FRI0259), 888 (SAT0306), 1147 (AB0283), 1148 (AB0284)
Ivanova, O., 273 (THU0188)
Ivanova Goycheva, M., 1048 (AB0005)
Ivanova-Todorova, E., 1106 (AB0170)
Ivanovic, J., 443 (THU0628), 558 (FRI0201), 832 (SAT0165)
Ivashhenko, N., 1311 (AB0736)
Ivcevic, S., 1055 (AB0026)
Iversen, L., 892 (SAT0317), 1109 (AB0179)
Iversen, M.B., 505 (FRI0074)
Ivkov, B., 1558 (PARE0018)
Ivorra, J., 614 (FRI0336)
Ivorra Cortés, J., 441 (THU0623), 1349 (AB0837)
Ivorra Cortes, J., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Iwakura, Y., 2 (SP0003)
Iwamoto, K., 1403 (AB0995)
Iwamoto, N., 318 (THU0303), 486 (FRI0017), 503 (FRI0067), 723 (FRI0620), 738 (FRI0656)
Iwao, K., 1054 (AB0021)
Iwasaki, N., 505 (FRI0075)
Iwasaki, T., 105 (OP0127), 210 (THU0030)
Iwasawa, Y., 507 (FRI0079)
Iwata, S., 137 (OP0205), 257 (THU0149)
Ix, J.H., 757 (FRI0706)
Izawa, N., 476 (THU0710)
Izumi, K., 326 (THU0325), 699 (FRI0552), 995 (SAT0581)
Izumi, M., 282 (THU0208)
Izumikawa, M., 283 (THU0209), 719 (FRI0609), 757 (FRI0704), 907 (SAT0360), 1213 (AB0465)

Jacklin, C., 186 (OP0317-PARE)
Jacklin, C.B., 42 (SP0172), 172 (OP0279-PARE), 1556 (PARE0013)
Jackson, E., 426 (THU0583)
Jacky, S., 1095 (AB0138)
Jacob, I., 186 (OP0317-PARE)
Jacobs, B., 292 (THU0233)
Jacobs, J., 87 (OP0085), 376 (THU0445), 741 (FRI0664)
Jacobs, J.W., 177 (OP0293), 855 (SAT0218), 1199 (AB0428)
Jacobsen, S., 50 (OP0002), 64 (OP0033), 286 (THU0217), 457 (THU0663), 784 (SAT0045)
Jacobson, A., 426 (THU0584)
Jacobssen, L.T.H., 1419 (AB1042)
Jacobsson, L., 341 (THU0361), 360 (THU0404), 364 (THU0414), 376 (THU0446), 686 (FRI0518), 1513 (SAT0725-HPR)
Jacobsson, L.T., 154 (OP0240), 164 (OP0262), 252 (THU0135), 361 (THU0408), 375 (THU0443), 750 (FRI0686, FRI0687), 916 (SAT0382)
Jacquemin, C., 465 (THU0684), 755 (FRI0700)
Jacques, C., 1072 (AB0073)
Jacques, P., 118 (OP0160), 763 (FRI0719), 1481 (THU0735-HPR)
Jacquot, F., 1448 (AB1123)
Jadon, D.R., 943 (SAT0449)
Jadoul, M., 290 (THU0228)
Jae Hyun, J., 1452 (AB1134)
Jaeger, V.K., 319 (THU0306), 626 (FRI0369), 710 (FRI0585), 909 (SAT0366), 915 (SAT0380), 1445 (AB1114)
Jaffeux, P., 1033 (SAT0682)
Jafri, K., 759 (FRI0711)
Jagemann, L., 125 (OP0175)
Jahangir, A., 510 (FRI0086)
Jaheris, A., 912 (SAT0373)
Jahnsen, J., 338 (THU0354), 472 (THU0700), 549 (FRI0182)
Jahreis, G., 115 (OP0151)
Jaimes-Hernandez, J., 515 (FRI0095)
Jain, A., 320 (THU0307), 415 (THU0551)
Jain, D., 1346 (AB0825)
Jain, S., 1273 (AB0633)
Jaisson, S., 1072 (AB0073)
Jajic, Z., 1055 (AB0026)
Jakobi, K., 1407 (AB1007)
Jakobi-Brook, K., 1462 (AB1163)
Jakobsen, M., 710 (FRI0583)
Jakobsen, S.H., 1545 (AB1239-HPR)
Jakobsson, K., 750 (FRI0686, FRI0687)
Jakobsson, P.-J., 626 (FRI0367)
Jakovljevic, V., 541 (FRI0158)
Jakubaszek, M., 489 (FRI0026)
Jalal, D., 379 (THU0455)
James, E.A., 779 (SAT0032)
James, J.A., 1217 (AB0475)
James, K., 295 (THU0242)
James-Belin, E., 170 (LB0001)
Jameson, G., 776 (SAT0021)
Jamin, C., 492 (FRI0035)
Jamoul, C., 148 (OP0229), 270 (THU0182), 281 (THU0205, THU0206)
Jamurtas, A., 1536 (AB1215-HPR)
Janardhana, R., 325 (THU0322)
Janarthanan, M., 1389 (AB0957)
Jandric, S.D., 354 (THU0390), 1356 (AB0856)
Jani, M., 98 (OP0110), 1040 (SAT0700)
Janiaud, P., 432 (THU0599)
Jankovic, K., 640 (FRI0405)
Jannetto, P., 874 (SAT0267)
Janowska, I., 324 (THU0321)
Jansen, D., 566 (FRI0219)
Jansen, G., 494 (FRI0041), 1020 (SAT0650), 1075 (AB0082)
Jansen, T., 383 (THU0464)
Jansen, T.L., 365 (THU0418), 1140 (AB0263)
Janssen, C.A., 365 (THU0418)
Janssen, G., 778 (SAT0030)
Janssen, M., 369 (THU0428), 383 (THU0464), 781 (SAT0037)
Janssens, H., 369 (THU0428)
Janssens, R., 274 (THU0190)
Janta, I., 386 (THU0474), 462 (THU0676), 656 (FRI0448), 735 (FRI0649), 748 (FRI0683), 1009 (SAT0621), 1276 (AB0640), 1414 (AB1029), 1476 (THU0720-HPR)
Jaquet, J.-B., 1088 (AB0118)
Jara, D., 1102 (AB0158)
Jara, L., 1098 (AB0149)
Jara, L.J., 421 (THU0568), 591 (FRI0279), 860 (SAT0229), 881 (SAT0287), 1091 (AB0126), 1282 (AB0657), 1401 (AB0991)
Jara-Quezada, L.J., 1286 (AB0668)
Jaremko, J.L., 469 (THU0693), 471 (THU0697)
Jaries, N., 926 (SAT0407)
Jarjour, W., 222 (THU0062), 1099 (AB0151)
Jarošová, K., 420 (THU0565)
Jarret, G., 1479 (THU0731-HPR)
Jaspers, J.E., 1344 (AB0818)
Jasso-Ávila, F., 1345 (AB0820)
Jauregui, E.A., 1158 (AB0313)
Javier, R.-M., 815 (SAT0123)
Jaworski, J., 824 (SAT0146)
Jayakumar, K., 782 (SAT0040)
Jayaseelan, L., 316 (THU0298)
Jayawardena, S., 576 (FRI0242), 838 (SAT0180), 853 (SAT0212)
Jayne, D., 107 (OP0130), 329 (THU0333)
Jayseelan, V., 316 (THU0298)
Jazi, R., 1397 (AB0980)
Jedidi, M., 1239 (AB0537)
Jędrzejuk, D., 1112 (AB0187)
Jeffries, M., 961 (SAT0490)
Jégo, P., 1261 (AB0599)
Jeka, S., 824 (SAT0146)
Jemaa, R., 596 (FRI0290)
Jemseby, E., 626 (FRI0367)
Jenkins, W., 167 (OP0268)
Jenning, M., 769 (SAT0004), 1081 (AB0101)
Jennings, F.M., 1508 (FRI0769-HPR)
Jensen, A.C.B., 501 (FRI0061)
Jensen, B., 332 (THU0340), 745 (FRI0674)
Jensen, D.V., 456 (THU0662), 553 (FRI0190)
Jensen, K., 144 (OP0220)
Jensen, K.V., 73 (OP0055-HPR), 1512 (SAT0723-HPR)
Jensen Hansen, I.M., 246 (THU0118), 533 (FRI0137, FRI0139), 1431 (AB1075)
Jeon, Y.L., 1425 (AB1059)
Jeong, H., 646 (FRI0422), 1371 (AB0901)
Jeong, H.-J., 1061 (AB0040)
Jeong, H.S., 1130 (AB0234)
Jeong, W.S., 1126 (AB0223)
Jeremiasse, B., 963 (SAT0498), 964 (SAT0499)
Jeremic, I., 307 (THU0274)
Ješe, R., 219 (THU0054), 325 (THU0324)
Jese, R., 108 (OP0133), 1143 (AB0272), 1243 (AB0552)
Jesus, D., 137 (OP0206)
Jeucken, K.C., 1064 (AB0049)
Jguirim, M., 1000 (SAT0598), 1169 (AB0346, AB0347), 1170 (AB0348), 1348 (AB0830), 1353 (AB0848, AB0849), 1362 (AB0876), 1383 (AB0937)
Ji, B., 150 (OP0232)

Ji, J., 293 (THU0235), 1097 (AB0145), 1370 (AB0897, AB0898)
Jia, E., 759 (FRI0710)
Jia, R., 853 (SAT0213), 1197 (AB0421), 1295 (AB0691)
Jia, Y., 547 (FRI0176), 1491 (THU0762-HPR), 1516 (SAT0734-HPR), 1524 (SAT0757-HPR)
Jiang, F., 1491 (THU0762-HPR)
Jiang, M., 1418 (AB1040)
Jiang, P., 1201 (AB0432)
Jiang, Y., 664 (FRI0470), 665 (FRI0471), 689 (FRI0523), 934 (SAT0431)
Jibri, Z., 668 (FRI0478)
Jiménez, J.J., 1351 (AB0840)
Jimenez, S.A., 91 (OP0096)
Jiménez de Aberásturi, J.R.D.D., 350 (THU0381)
Jiménez Díaz, J.J., 761 (FRI0715), 1456 (AB1146, AB1147)
Jiménez Gasco, R., 975 (SAT0527), 1143 (AB0270)
Jimenez Gasco, R., 258 (THU0151), 700 (FRI0555)
Jimenez Palop, M., 1399 (AB0986)
Jiménez-Borreguero, L.J., 892 (SAT0316)
Jimenez-Gomez, Y., 194 (OP0336), 287 (THU0218), 492 (FRI0035), 497 (FRI0048), 504 (FRI0069), 622 (FRI0360), 648 (FRI0429), 649 (FRI0431), 1078 (AB0092), 1082 (AB0104), 1091 (AB0127, AB0128)
Jiménez-Heredia, I., 597 (FRI0293)
Jiménez-Herrera, E.A., 311 (THU0283)
Jiménez-Núñez, F.G., 261 (THU0160), 1174 (AB0361), 1492 (THU0766-HPR)
Jimenez-Nuñez, F.G., 1175 (AB0362), 1443 (AB1109)
Jin, D., 89 (OP0089)
Jin, H.S., 208 (THU0025), 1173 (AB0358)
Jin, L., 1535 (AB1210-HPR)
Jin, X., 962 (SAT0493)
Jin, Y., 509 (FRI0084), 544 (FRI0167), 983 (SAT0548), 1144 (AB0274)
Jin, Y.P., 802 (SAT0089)
Jindal, A., 1386 (AB0946)
Jing, J., 488 (FRI0023)
Jing, X., 69 (OP0043), 872 (SAT0261)
Jinks, C., 438 (THU0614), 973 (SAT0521), 1433 (AB1081)
Jinnan, F., 348 (THU0377)
Jinnin, M., 202 (THU0006)
Jo, M.-J., 820 (SAT0137)
Jo, S., 1089 (AB0120)
Joachims, M., 1096 (AB0143)
Jobanputra, P., 1421 (AB1049)
Jochems, A., 456 (THU0661), 555 (FRI0194), 822 (SAT0141), 1179 (AB0375), 1293 (AB0686), 1294 (AB0687)
Joelsson, M., 1487 (THU0754-HPR), 1503 (FRI0753-HPR)
Joensuu, J., 341 (THU0361), 686 (FRI0518)
Joffres, L., 989 (SAT0561), 1191 (AB0406)
Johal, S., 1477 (THU0725-HPR)
Johannes, E., 382 (THU0462), 1369 (AB0896)
Johannesson, S., 1487 (THU0754-HPR), 1503 (FRI0753-HPR)
Johansen, I., 1497 (FRI0738-HPR)
Johansen, M.B., 84 (OP0079)
Johansson, T., 79 (OP0068)
John, H., 1560 (AB1250-PARE)
Johnsen, A., 145 (OP0223), 687 (FRI0520), 951 (SAT0468), 1135 (AB0248)
Johnsen, S., 647 (FRI0426)
Johnson, B., 448 (THU0643)
Johnson, B.J., 448 (THU0643)
Johnson, K., 605 (FRI0314)
Johnson, S., 50 (OP0002), 83 (OP0076), 777 (SAT0027)
Johnson, S.R., 103 (OP0122)
Johnston, A., 1096 (AB0143)
Johnston, G.I., 287 (THU0220)
Johnston, J., 429 (THU0591)
Johnston, L., 367 (THU0422)
Jokar, M., 1341 (AB0811)
Jokiranta, S., 61 (OP0024), 827 (SAT0152)
Jolliffe, V., 1514 (SAT0728-HPR)
Jolly, M., 303 (THU0264), 1219 (AB0483)
Joly, J., 147 (OP0226), 765 (FRI0726)
Jones, A., 253 (THU0138)
Jones, C., 1514 (SAT0728-HPR)
Jones, C.J., 437 (THU0613)
Jones, E., 127 (OP0182), 480 (FRI0001), 648 (FRI0427), 959 (SAT0485), 1070 (AB0066)
Jones, G., 122 (OP0169), 193 (OP0334), 450 (THU0647), 471 (THU0699), 960 (SAT0489), 962 (SAT0493), 986 (SAT0555), 1050 (AB0011)
Jones, G.T., 656 (FRI0450)
Jones, G.W., 208 (THU0025)
Jones, H., 167 (OP0268), 337 (THU0353), 350 (THU0382), 443 (THU0628), 558 (FRI0201), 831 (SAT0161), 832 (SAT0164, SAT0165), 1181 (AB0379)
Jones, H.E., 666 (FRI0474)
Jones, M., 545 (FRI0171), 1176 (AB0366)
Jones, S.A., 208 (THU0025)
Jones, T., 938 (SAT0439)
Jonge, R.D., 241 (THU0107)
Jonkman, M., 308 (THU0276)
Jonsdottir, K., 184 (OP0312)
Jönsen, A., 302 (THU0260), 861 (SAT0233)
Jonsson, H., 341 (THU0361)
Jonsson, I.-M., 777 (SAT0026)
Jonsson, M., 67 (OP0040)
Jonsson, M.K., 522 (FRI0111)
Jonsson, M.V., 875 (SAT0270)
Jonsson, R., 875 (SAT0270), 1102 (AB0160)
Jönsson, T.S.J., 1501 (FRI0749-HPR)
Joo, Y.B., 882 (SAT0290)
Joos, R., 133 (OP0197)
Joosten, L., 383 (THU0464)
Joosten, L.A., 89 (OP0090), 90 (OP0092)
Joosten, L.A.B., 519 (FRI0104)
Jordan, C., 178 (OP0296)
Jordan, P., 912 (SAT0374)
Jordan, S., 625 (FRI0365), 635 (FRI0390)
Jorge, A.M., 165 (OP0264)
Jørgensen, K.K., 338 (THU0354), 472 (THU0700), 549 (FRI0182)
Jørgensen, S.H., 101 (OP0117)
Jørgensen, T.S., 96 (OP0106), 98 (OP0112), 341 (THU0361), 686 (FRI0518), 1444 (AB1113)
Jorquera, C., 826 (SAT0150)
Joseph, G., 316 (THU0298)
Joseph, J., 428 (THU0587), 1437 (AB1093)
Joseph, P.-A., 171 (OP0278-PARE)
Josephs, F., 304 (THU0265), 401 (THU0516)
Joshi, A.D., 1487 (THU0753-HPR)
Joshi, R., 531 (FRI0132)
Joshua, V., 212 (THU0036), 482 (FRI0006), 484 (FRI0013), 785 (SAT0048)
Jost, C.R., 774 (SAT0015)
Joubert, J.M., 428 (THU0588, THU0589), 461 (THU0675), 786 (SAT0050)
Jouenne, R., 883 (SAT0293)
Jourdy, J.C., 1033 (SAT0682)
Jousse-Joulin, S., 67 (OP0040), 309 (THU0278), 583 (FRI0256), 1215 (AB0469)
Jovaní, V., 657 (FRI0451), 1307 (AB0724)
Jovani, V., 718 (FRI0607)
Jovaní-Casado, V., 1472 (AB1191)
Jovanovic, J., 914 (SAT0378), 1240 (AB0540)
Joven, B., 633 (FRI0385), 908 (SAT0363), 1270 (AB0625)
Jover, J., 320 (THU0309)
Jover, J.Á., 520 (FRI0107), 990 (SAT0564)
Ju, J.H., 926 (SAT0408), 977 (SAT0533), 1458 (AB1151)
Juan Mas, A., 917 (SAT0385), 1166 (AB0337)
Juan-Mas, A., 1472 (AB1192)
Juanola, X., 663 (FRI0468), 1014 (SAT0635), 1375 (AB0914)
Juanola Roura, X., 917 (SAT0385)
Juarez, C., 914 (SAT0379)
Juarez, M., 287 (THU0220)
Juárez, P., 663 (FRI0468)
Juárez Rojop, I.E., 1132 (AB0240, AB0241)
Juarranz, Y., 485 (FRI0016), 1128 (AB0229)
Juche, A., 1106 (AB0169), 1110 (AB0181)
Judas, T., 1264 (AB0607)
Juday, T., 835 (SAT0172)
Judez, E., 350 (THU0381)
Juge, P.-A., 1049 (AB0007)
Jugl, S., 96 (OP0107), 355 (THU0393), 675 (FRI0494), 688 (FRI0521), 949 (SAT0463), 957 (SAT0480), 1293 (AB0685), 1301 (AB0707), 1313 (AB0740), 1322 (AB0765), 1323 (AB0766), 1326 (AB0772)
Juha, A., 61 (OP0024)
Juhl, P., 66 (OP0036), 625 (FRI0365), 892 (SAT0317), 1109 (AB0179, AB0180)
Julià, A., 177 (OP0292), 290 (THU0227), 776 (SAT0022), 946 (SAT0458), 1135 (AB0249)
Julia, S., 1534 (AB1206-HPR)
Julian-Santiago, F., 1453 (AB1137)
Julsrud Haugen, A., 81 (OP0071), 756 (FRI0702)
Jun, J.-B., 1414 (AB1028)
Jun, J.K., 922 (SAT0398)
Juneblad, K., 947 (SAT0460)
Jung, J., 1437 (AB1092)
Jung, J.-Y., 692 (FRI0533), 1355 (AB0855)
Jung, J.H., 604 (FRI0311), 1037 (SAT0693), 1130 (AB0234)
Jung, K.-H., 820 (SAT0137)
Jung, S., 1437 (AB1092)
Jung, S.M., 372 (THU0436), 383 (THU0467)
Junge, G., 77 (OP0063), 710 (FRI0585)
Jüngel, A., 890 (SAT0312)
Jungel, A., 117 (OP0157)
Junien, J.L., 85 (OP0081)
Junker, P., 710 (FRI0583), 732 (FRI0641), 784 (SAT0045)
Junyent Vilanova, E., 1418 (AB1039)
Jurado, C., 728 (FRI0631), 1018 (SAT0643)
Jurcut, R., 1264 (AB0608)
Jurik, A.G., 101 (OP0117), 732 (FRI0641)
Jurisic Skevin, A., 1552 (PARE0003)
Jury, E.C., 1053 (AB0019), 1100 (AB0152)
Just, G.-W., 74 (OP0057)
Just, S.A., 745 (FRI0675), 1024 (SAT0660)
Justet, A., 1049 (AB0007)
Justice, J.J., 90 (OP0092)
Juszkiewicz, A., 1152 (AB0297), 1398 (AB0982)

Kaabachi, N., 596 (FRI0290)
Kabadi, S., 766 (FRI0728)
Kabasakal, Y., 899 (SAT0338)
Kabat, B., 187 (OP0320), 605 (FRI0314)
Kabeer Doss, J., 328 (THU0330)
Kabeerdoss, J., 1061 (AB0042)
Kabouraki, E., 577 (FRI0244)
Kachakova, D., 208 (THU0023)
Kachroo, S., 447 (THU0640)
Kadir, B., 110 (OP0139-HPR)
Kadisa, A., 1071 (AB0071)
Kadono, Y., 476 (THU0710)
Kadowaki, N., 283 (THU0209), 719 (FRI0609), 757 (FRI0704), 907 (SAT0360), 1213 (AB0465)
Kadva, A.K., 396 (THU0503)
Kafaja, S., 566 (FRI0220), 1526 (SAT0765-HPR)
Kaffel, D., 1146 (AB0278), 1188 (AB0398), 1346 (AB0826)
Kafka, S., 460 (THU0672), 944 (SAT0453)
Kageyama, G., 459 (THU0668), 699 (FRI0553)
Kagwiria, R., 892 (SAT0318)
Kahan, A., 831 (SAT0163)
Kahlon, A., 988 (SAT0559)
Kahn, J.-E., 108 (OP0134), 1256 (AB0588)
Kahraman, M., 1066 (AB0057)
Kai, K., 1383 (AB0939)
Kaieda, S., 1403 (AB0995)
Kaili, Q., 348 (THU0377)
Kaine, J., 275 (THU0193)
Kaipiainen-Seppänen, O., 61 (OP0024)
Kaiser, M.-J., 736 (FRI0650)
Kaiser, S., 1229 (AB0509)
Kajekar, R., 145 (OP0222)
Kakehasi, A., 522 (FRI0112)
Kakehasi, A.M., 814 (SAT0121), 1056 (AB0028)
Kakuk, P., 1548 (AB1248-HPR)
Kalabic, J., 405 (THU0525), 829 (SAT0159)
Kaleda, M., 1389 (AB0955)
Kalergis, A.M., 1098 (AB0148)

Kalinova, D., 1106 (AB0170)
Kalish, R., 384 (THU0469)
Kaliyaperumal, A., 1181 (AB0380)
Kalkan, A.T., 1170 (AB0349)
Kalkancı, A., 321 (THU0311)
Kalla, A.A., 631 (FRI0379)
Kallan, M., 474 (THU0707)
Kallel, A., 596 (FRI0290)
Kallel-Sellami, M., 809 (SAT0108)
Kallenberg, C., 187 (OP0320)
Kallenberg, C.G., 605 (FRI0314)
Kallinich, T., 1389 (AB0957)
Kálmán, E., 1267 (AB0617)
Kalstad, S., 334 (THU0345), 673 (FRI0490)
Kaltenberger, R., 445 (THU0633)
Kaltsonoudis, E., 836 (SAT0176), 1243 (AB0551)
Kalunian, K., 864 (SAT0240)
Kaly, L., 926 (SAT0407)
Kalyoncu, U., 250 (THU0131), 256 (THU0147), 327 (THU0329), 354 (THU0389), 402 (THU0518), 414 (THU0548), 448 (THU0642), 534 (FRI0140), 720 (FRI0612), 854 (SAT0216), 932 (SAT0424), 1035 (SAT0687), 1113 (AB0189), 1127 (AB0226), 1175 (AB0363), 1194 (AB0414), 1215 (AB0471), 1300 (AB0706), 1412 (AB1023), 1531 (AB1198-HPR)
Kalyvas, C., 957 (SAT0480), 1301 (AB0707)
Kam, P.-S., 892 (SAT0318)
Kamada, K., 793 (SAT0068), 1424 (AB1056)
Kamanli, A., 1317 (AB0751), 1320 (AB0757)
Kamanlı, A., 241 (THU0108), 637 (FRI0396), 1182 (AB0383), 1532 (AB1202-HPR)
Kamath, S., 1188 (AB0399)
Kamble, P., 1074 (AB0079)
Kamdem, F., 1362 (AB0874)
Kameda, H., 440 (THU0620), 995 (SAT0581), 1024 (SAT0661)
Kameda, T., 283 (THU0209), 719 (FRI0609), 757 (FRI0704), 907 (SAT0360), 1213 (AB0465)
Kamei, R., 298 (THU0251), 788 (SAT0054)
Kamei, S., 810 (SAT0110), 1372 (AB0905)
Kamei, Y., 911 (SAT0370)
Kamen, D., 50 (OP0002)
Kamerling, S.W., 181 (OP0302), 774 (SAT0015), 871 (SAT0258)
Kamiya, M., 1137 (AB0253)
Kamiyama, R., 645 (FRI0419), 1195 (AB0416)
Kamp, O., 1087 (AB0116)
Kamp, P., 1217 (AB0475)
Kamp, S., 1217 (AB0475)
Kamphausen, E., 1229 (AB0509)
Kampman, W., 576 (FRI0242)
Kampouraki, E., 574 (FRI0236), 850 (SAT0204)
Kampylafka, E., 725 (FRI0625)
Kan, H., 859 (SAT0227)
Kanaan, S., 523 (FRI0114)
Kanatli, U., 1004 (SAT0608)
Kanayama, Y., 284 (THU0212), 582 (FRI0254), 708 (FRI0579), 835 (SAT0174), 1357 (AB0860)
Kanazawa, T., 279 (THU0199)
Kanda, M., 1258 (AB0591)
Kane, D., 175 (OP0288), 1542 (AB1230-HPR)
Kaneda, M., 1009 (SAT0622)
Kaneko, A., 835 (SAT0174)
Kaneko, H., 298 (THU0251), 788 (SAT0054), 1288 (AB0672)
Kaneko, R., 507 (FRI0079)
Kaneko, T., 1203 (AB0439)
Kaneko, Y., 326 (THU0325), 418 (THU0560), 529 (FRI0128), 547 (FRI0177), 699 (FRI0552), 712 (FRI0590, FRI0591), 747 (FRI0680), 1227 (AB0504), 1234 (AB0525)
Kanenishi, K., 757 (FRI0704)
Kaneshiro, K., 499 (FRI0054)
Kaneva, R., 208 (THU0023)
Kang, A., 1241 (AB0542)
Kang, E.H., 544 (FRI0167), 802 (SAT0089)
Kang, J.-H., 312 (THU0288), 791 (SAT0061), 877 (SAT0275), 972 (SAT0518, SAT0519)
Kang, J.W., 514 (FRI0093), 783 (SAT0042)
Kang, J.Y., 514 (FRI0093), 783 (SAT0042)
Kang, K.Y., 655 (FRI0447), 926 (SAT0408)
Kang, M.J., 877 (SAT0274)
Kang, S., 1061 (AB0040)
Kang, S.E., 1053 (AB0020)
Kang, S.W., 888 (SAT0307), 1259 (AB0593)
Kang, S.Y., 1425 (AB1059)
Kang, Y.M., 422 (THU0572), 514 (FRI0093), 783 (SAT0042)
Kania, G., 86 (OP0084), 87 (OP0086), 88 (OP0088), 191 (OP0330), 890 (SAT0312)
Kania-Pudło, M., 1398 (AB0982)
Kanik, K., 938 (SAT0439)
Kanik, K.S., 135 (OP0202), 141 (OP0216), 337 (THU0352), 676 (FRI0496), 682 (FRI0509), 951 (SAT0469)
Kanis, J.A., 29 (SP0117)
Kanitkar, M., 821 (SAT0140)
Kankam, M., 370 (THU0432)
Kannengiesser, C., 1049 (AB0007)
Kao, A., 856 (SAT0219), 862 (SAT0235), 863 (SAT0236)
Kao, S.-Y., 1408 (AB1009)
Kaouk, S., 386 (THU0473)
Kapetanovic, M.C., 376 (THU0446), 542 (FRI0162)
Kaplan, C., 1503 (FRI0754-HPR)
Kaplan, M., 498 (FRI0053)
Kaplan, M.J., 1055 (AB0024)
Kaplan, Y.C., 102 (OP0120)
Kapoor, B., 1303 (AB0711)
Kapoor, S., 1506 (FRI0762-HPR), 1540 (AB1226-HPR)
Kappes, L., 772 (SAT0011)
Kappes, L.M., 1108 (AB0175)
Kapranov, P., 202 (THU0007)
Kapşigay, B., 1431 (AB1076), 1496 (FRI0734-HPR), 1537 (AB1217-HPR)
Kapsogeorgou, E.K., 288 (THU0221)
Kaptijn, H.H., 967 (SAT0506)
Kara, B., 1532 (AB1201-HPR)
Karaagac Akyol, T., 1212 (AB0463)
Karaahmetoglu, S., 637 (FRI0397)
Karabulut, E., 1531 (AB1198-HPR)
Karabulut, G., 899 (SAT0338)
Karaca, G., 661 (FRI0462)
Karaca, N.B., 1515 (SAT0730-HPR), 1531 (AB1198-HPR)
Karacan, I., 208 (THU0024), 1101 (AB0157)
Karadağ, Ö., 448 (THU0642), 1035 (SAT0687), 1412 (AB1023), 1531 (AB1198-HPR)
Karadag, Ö., 402 (THU0518)
Karadag, O., 250 (THU0131), 256 (THU0147), 329 (THU0333), 354 (THU0389), 414 (THU0548), 534 (FRI0140), 609 (FRI0322), 616 (FRI0342), 720 (FRI0612), 854 (SAT0216), 1113 (AB0189), 1127 (AB0226), 1194 (AB0414), 1212 (AB0463), 1215 (AB0471), 1256 (AB0586), 1300 (AB0706)
Karageorgas, T., 588 (FRI0269)
Karagianni, K., 836 (SAT0176)
Karagianni, N., 500 (FRI0059)
Karagöz, A., 439 (THU0618), 1197 (AB0420)
Karagoz, A., 1137 (AB0255)
Karahan, S., 1066 (AB0057), 1488 (THU0756-HPR), 1523 (SAT0756-HPR), 1538 (AB1221-HPR)
Karahan Yesil, N., 992 (SAT0570)
Karakan, T., 321 (THU0311)
Karakas, F., 634 (FRI0386)
Karakas, S., 1431 (AB1076)
Karakoç, B., 1509 (FRI0771-HPR)
Karakoç, Z.B., 1537 (AB1217-HPR)
Karakoc, Z.B., 1431 (AB1076)
Karakota, M., 558 (FRI0202)
Karali, D., 715 (FRI0597)
Karamanlioglu, D., 999 (SAT0595)
Karamanolis, G., 908 (SAT0361)
Karamichali, E., 1089 (AB0122)
Karaogullarindan, U., 921 (SAT0396)
Karapetyan, L., 787 (SAT0051)
Karapinar, M., 1489 (THU0759-HPR), 1518 (SAT0741-HPR)
Karaseva, A., 186 (OP0316), 539 (FRI0154), 1387 (AB0950, AB0951)
Karatas, A., 455 (THU0658), 1462 (AB1162)
Karataş, Ö., 1002 (SAT0601)
Karatas, O., 1382 (AB0934)
Karateev, A., 189 (OP0324)
Karateev, D., 256 (THU0148), 273 (THU0188, THU0189), 572 (FRI0231), 943 (SAT0451), 944 (SAT0452), 956 (SAT0478), 1157 (AB0311), 1180 (AB0378), 1204 (AB0441), 1404 (AB0998)
Karateev, D.E., 251 (THU0132), 576 (FRI0241), 674 (FRI0491), 1128 (AB0230)
Karateev, D.K., 776 (SAT0024)
Karatemiz, G., 719 (FRI0610)
Karatosun, V., 1496 (FRI0736-HPR), 1519 (SAT0742-HPR), 1542 (AB1232-HPR)
Kardos, Z., 1027 (SAT0668)
Karela, M., 923 (SAT0399), 1304 (AB0715)
Karellis, A., 523 (FRI0115), 679 (FRI0503)
Kargozar, E., 1012 (SAT0629)
Karim, E., 82 (OP0075)
Karimova, E., 1227 (AB0503)
Karimzadeh, A., 1003 (SAT0604)
Karki, C., 352 (THU0386), 552 (FRI0188), 827 (SAT0153), 953 (SAT0471, SAT0472), 1313 (AB0740), 1331 (AB0784)
Karlsmark, T., 892 (SAT0317), 1109 (AB0179)
Karlson, J., 467 (THU0689)
Karlsson, A., 785 (SAT0048)
Karlsson, L., 72 (OP0050)
Karóczi, C.K., 1482 (THU0736-HPR)
Karoliussen, L.F., 361 (THU0407)
Karonitsch, T., 486 (FRI0018)
Karouzakis, E., 116 (OP0154), 190 (OP0326)
Karp, K., 248 (THU0125), 250 (THU0129)
Karpec, D., 622 (FRI0359)
Karpouzas, G., 237 (THU0097), 1432 (AB1077)
Karsdal, M., 94 (OP0103), 892 (SAT0317), 986 (SAT0554), 1109 (AB0179, AB0180)
Karsdal, M.A., 66 (OP0036), 120 (OP0165), 480 (FRI0003), 625 (FRI0365), 916 (SAT0383), 966 (SAT0504), 1068 (AB0062), 1114 (AB0192)
Karyekar, C., 395 (THU0502)
Karyekar, C.S., 398 (THU0509)
Kasai, S., 264 (THU0166)
Kasama, T., 222 (THU0064), 800 (SAT0085), 894 (SAT0322), 1149 (AB0289)
Kasapçopur, O., 1389 (AB0957)
Kasapcopur, O., 77 (OP0063), 394 (THU0498), 1402 (AB0994), 1500 (FRI0745-HPR, FRI0746-HPR), 1527 (SAT0766-HPR)
Kasavkar, G., 1188 (AB0399)
Kashchenko, E., 186 (OP0316), 539 (FRI0154), 1387 (AB0950, AB0951)
Kashevarova, N., 978 (SAT0534)
Kashevarova, N.G., 1337 (AB0799)
Kashiwagura, T., 707 (FRI0577), 795 (SAT0071), 1178 (AB0372), 1182 (AB0382), 1426 (AB1063)
Kashnikova, L., 860 (SAT0230)
Kashyap, V., 1506 (FRI0762-HPR)
Kaşifoğlu, T., 254 (THU0141), 327 (THU0329), 387 (THU0478)
Kasimos, D., 836 (SAT0176)
Kassab, S., 1371 (AB0902), 1394 (AB0969), 1417 (AB1038)
Kassai, B., 432 (THU0599)
Kassara, D., 588 (FRI0269)
Kastbom, A., 57 (OP0016), 563 (FRI0213), 947 (SAT0460)
Kastelein, J., 259 (THU0154)
Kästner, P., 844 (SAT0193), 1187 (AB0396)
Kasturi, S., 467 (THU0687)
Kasturiangan, S., 192 (OP0331)
Kaszuba, A., 135 (OP0202)
Katagiri, T., 1024 (SAT0661)
Katayama, K., 1471 (AB1187)
Katayama, M., 115 (OP0152), 282 (THU0207)
Katchamart, W., 930 (SAT0420), 1298 (AB0700)
Kathy, K., 330 (THU0337), 617 (FRI0345)
Kato, M., 598 (FRI0295), 624 (FRI0364), 719 (FRI0609), 1453 (AB1139)
Kato, S., 543 (FRI0166), 703 (FRI0566)
Kato, T., 835 (SAT0174)
Kato, Y., 1467 (AB1176)
Katsiari, C.G., 903 (SAT0348)
Katsicas, M., 403 (THU0521), 1389 (AB0957)
Katsifis, G., 836 (SAT0176)

Katsimbri, P., 588 (FRI0269), 836 (SAT0176)
Katsumata, Y., 280 (THU0204), 1026 (SAT0667)
Katz, P., 759 (FRI0711)
Katz, P.P., 432 (THU0600)
Kauer, J., 474 (THU0706)
Kaufman, I., 747 (FRI0679), 1095 (AB0138), 1118 (AB0203)
Kaufmann, J., 1029 (SAT0674)
Kaul, N.-C., 1070 (AB0068)
Kaul, P., 766 (FRI0727)
Kauppi, M., 61 (OP0024)
Kaur, K., 958 (SAT0483)
Kaur, P., 1181 (AB0380)
Kaur, S., 819 (SAT0133)
Kaushik, V., 561 (FRI0209)
Kautiainen, H., 61 (OP0024), 262 (THU0163), 401 (THU0515), 404 (THU0523)
Kavanaugh, A., 148 (OP0229), 228 (THU0078), 242 (THU0110), 267 (THU0173), 270 (THU0182), 373 (THU0438), 511 (FRI0089), 671 (FRI0486), 681 (FRI0508), 785 (SAT0047), 822 (SAT0142), 936 (SAT0436), 941 (SAT0446), 942 (SAT0448), 944 (SAT0453), 948 (SAT0462), 952 (SAT0470), 953 (SAT0471), 1130 (AB0235), 1313 (AB0739), 1314 (AB0743), 1331 (AB0785)
Kavlak, B., 1496 (FRI0734-HPR)
Kawabe, A., 491 (FRI0031)
Kawachi, I., 610 (FRI0326)
Kawaguchi, T., 202 (THU0006)
Kawaguchi, Y., 202 (THU0006), 280 (THU0204), 1026 (SAT0667), 1062 (AB0044)
Kawaji, H., 1344 (AB0819)
Kawakami, A., 318 (THU0303), 486 (FRI0017), 503 (FRI0067), 723 (FRI0620), 738 (FRI0656), 1016 (SAT0640), 1416 (AB1035)
Kawakubo, M., 842 (SAT0187)
Kawamoto, K., 800 (SAT0083)
Kawano, A., 1054 (AB0021)
Kawano, M., 425 (THU0579), 711 (FRI0587), 722 (FRI0617), 814 (SAT0120), 1242 (AB0546)
Kawano, S., 1095 (AB0140)
Kawano, T., 842 (SAT0187)
Kawano, Y., 392 (THU0492)
Kawasaki, A., 202 (THU0006)
Kawasaki, Y., 499 (FRI0054)
Kawashiri, S.-Y., 318 (THU0303), 503 (FRI0067), 723 (FRI0620)
Kawato, R., 871 (SAT0256)
Kay, J., 136 (OP0203), 513 (FRI0092), 1368 (AB0892)
Kaya, T., 748 (FRI0682)
Kaya Aksoy, G., 1392 (AB0965)
Kayalar, D., 86 (OP0084)
Kayhan, M., 387 (THU0478)
Kaymakcalan, Z., 492 (FRI0034)
Kaymaz, S., 644 (FRI0416), 910 (SAT0367), 1310 (AB0731)
Kazár-Tóth, K., 1482 (THU0736-HPR)
Kazi, S., 79 (OP0068)
Kazimir, M., 371 (THU0433)
Kazma, R., 886 (SAT0301), 1229 (AB0509)
Kc, S., 984 (SAT0549)
Kchir, H., 1346 (AB0826)
Kchir, M., 347 (THU0373), 1297 (AB0697)
Kchir, M.M., 1146 (AB0278), 1188 (AB0398), 1306 (AB0720), 1346 (AB0826)
Kchondkaryan, E., 924 (SAT0403)
Keating, P., 637 (FRI0395), 1415 (AB1031)
Kebapcılar, L., 931 (SAT0422)
Kechaou, I., 1251 (AB0574)
Kechida, M., 885 (SAT0298), 1176 (AB0365), 1231 (AB0517), 1258 (AB0592)
Keebler, D., 593 (FRI0285)
Keeling, S., 933 (SAT0428)
Keeling, S.O., 766 (FRI0727)
Keen, H., 175 (OP0288), 744 (FRI0672), 767 (FRI0730), 1045 (SAT0716)
Keenan, R.T., 375 (THU0444)
Kefi, A., 1239 (AB0537)
Kehler, T., 771 (SAT0009)
Keidar, Z., 910 (SAT0368)
Keir, G., 1266 (AB0613)
Kekow, J., 1072 (AB0074)
Keleşoğlu Dinçer, A.B., 1124 (AB0218), 1244 (AB0554)
Keller, K.K., 174 (OP0285), 329 (THU0335)
Keller, S.F., 165 (OP0264), 360 (THU0405)
Kelley, N., 1101 (AB0155)
Kellner, H., 565 (FRI0217), 844 (SAT0193), 1187 (AB0396), 1436 (AB1091)
Kelly, S., 203 (THU0011), 238 (THU0100), 458 (THU0667), 511 (FRI0088), 1125 (AB0220), 1192 (AB0408)
Kelsen, J., 1088 (AB0119)
Kelton, K.A., 599 (FRI0298)
Keltsev, V., 75 (OP0058)
Kemény-Beke, Á., 1273 (AB0632)
Kemp, B., 192 (OP0331)
Kemta Lekpa, F., 368 (THU0425), 997 (SAT0587, SAT0588), 1362 (AB0874)
Kenar, G., 306 (THU0271), 322 (THU0314), 477 (THU0714), 1282 (AB0658)
Kennedy, A., 1286 (AB0669)
Kennedy, B., 646 (FRI0421)
Kennedy, D., 447 (THU0639)
Kennedy, N., 1482 (THU0738-HPR)
Kenngott, E.E., 647 (FRI0425)
Kent, J., 1360 (AB0867)
Kerekes, G., 1027 (SAT0668)
Kermani, T.A., 609 (FRI0323)
Kerr, G., 817 (SAT0129)
Kerr, L., 679 (FRI0502), 937 (SAT0437)
Kerr, L.N., 135 (OP0201)
Kerschbaumer, A., 445 (THU0633), 472 (THU0701), 520 (FRI0108), 971 (SAT0515)
Kerstens, P., 516 (FRI0097)
Kerstens, P.J., 976 (SAT0529)
Kerstens, T., 568 (FRI0223)
Kerzberg, E., 440 (THU0619)
Kerzberg, E.M., 571 (FRI0229)
Kerzoncuf, M., 476 (THU0711)
Keser, G., 327 (THU0329), 354 (THU0389), 899 (SAT0338)
Keshishian, A., 835 (SAT0172)
Keskin, E.D., 1122 (AB0213)
Keskin, H., 791 (SAT0063)
Kessler, C.S., 960 (SAT0488)
Keyes-Elstein, L., 104 (OP0124)
Keystone, E., 136 (OP0203), 137 (OP0204), 230 (THU0083), 231 (THU0085), 233 (THU0089), 513 (FRI0092), 552 (FRI0187), 781 (SAT0039), 815 (SAT0122), 834 (SAT0169)
Keystone, E.C., 828 (SAT0155)
Khairy, M., 1403 (AB0997)
Khalfallah, N., 1251 (AB0574)
Khalfallah, R., 1373 (AB0906, AB0908)
Khalid, S., 847 (SAT0198)
Khalifa, W.A., 1384 (AB0940)
Khalil, A., 743 (FRI0669), 1422 (AB1051)
Khalil, M., 781 (SAT0038)
Khalili, A., 700 (FRI0556)
Khamashta, M., 37 (SP0153), 418 (THU0561), 1350 (AB0839)
Khamashta, M.A., 1400 (AB0989)
Khambir, T., 1341 (AB0812)
Khan, A., 821 (SAT0140), 1010 (SAT0624), 1309 (AB0729), 1354 (AB0851)
Khan, F., 884 (SAT0294)
Khan, H.A., 491 (FRI0032)
Khan, M.A., 929 (SAT0417)
Khan, M.F.J., 207 (THU0022)
Khan, S., 693 (FRI0534), 871 (SAT0257), 1509 (FRI0772-HPR)
Khan, T., 1284 (AB0662)
Khanna, D., 65 (OP0034), 104 (OP0124), 195 (OP0339), 912 (SAT0373), 1271 (AB0627), 1390 (AB0958), 1445 (AB1115)
Khanna, P., 377 (THU0449), 1368 (AB0892)
Khanna, P.P., 375 (THU0444)
Kharchenko, S.A., 1483 (THU0740-HPR)
Khare, M., 1302 (AB0710)
Khawaja, A., 1103 (AB0161)
Khawaja, K., 1284 (AB0662)
Khemis, M., 1353 (AB0849)
Khemiss, M., 1353 (AB0848)
Kherrab, A., 697 (FRI0548), 1349 (AB0836)
Khezami, A., 998 (SAT0589, SAT0590)
Khidir, S.J.H., 907 (SAT0359)
Khimion, L.V., 974 (SAT0526), 1167 (AB0339)
Khmel, O.S., 979 (SAT0537)
Khmelinskii, N., 1254 (AB0581)
Khochtali, I., 885 (SAT0298), 1231 (AB0517)
Kholoussi, N., 1047 (AB0002)
Khorbi, A., 1373 (AB0909)
Khosla, S., 705 (FRI0572)
Khoury, B., 762 (FRI0718)
Khoury, M., 1534 (AB1206-HPR)
Khoury, P., 107 (OP0130)
Khoy, K., 1256 (AB0587)
Khraishi, M., 443 (THU0628), 539 (FRI0153), 558 (FRI0201), 656 (FRI0449), 680 (FRI0506), 812 (SAT0115), 832 (SAT0165)
Khraishi, Z., 680 (FRI0506)
Khramov, A., 269 (THU0179)
Kianifard, T., 1541 (AB1228-HPR)
Kickham, L., 1085 (AB0111)
Kida, H., 1467 (AB1176)
Kido, A., 282 (THU0207)
Kielbik, Z., 1470 (AB1184)
Kiely, P., 782 (SAT0040), 1028 (SAT0671)
Kienast, A., 1390 (AB0958)
Kiener, H., 486 (FRI0018)
Kiener, H.P., 488 (FRI0024), 1414 (AB1026)
Kihara, M., 265 (THU0170)
Kihlberg, J., 779 (SAT0031)
Kikuchi, E., 573 (FRI0233), 806 (SAT0101)
Kikuchi, H., 314 (THU0294), 610 (FRI0326), 1137 (AB0253), 1248 (AB0566)
Kikuchi, J., 418 (THU0560), 1097 (AB0146), 1234 (AB0525)
Kikuchi-Taura, A., 1058 (AB0032)
Kilding, R., 847 (SAT0198)
Kilic, E., 1317 (AB0751), 1320 (AB0757)
Kilic, G., 1317 (AB0751), 1320 (AB0757)
Kilic, L., 250 (THU0131), 256 (THU0147), 402 (THU0518), 414 (THU0548), 534 (FRI0140), 616 (FRI0342), 637 (FRI0397), 720 (FRI0612), 854 (SAT0216), 1113 (AB0189), 1127 (AB0226), 1175 (AB0363), 1194 (AB0414), 1212 (AB0463), 1215 (AB0471), 1256 (AB0586), 1262 (AB0604), 1300 (AB0706)
Kılıç, L., 448 (THU0642), 1035 (SAT0687), 1412 (AB1023), 1531 (AB1198-HPR)
Kilic, S.S., 722 (FRI0616)
Kılıçarslan, A., 235 (THU0092)
Kilinc Kamaci, G., 535 (FRI0144), 818 (SAT0130)
Kilinckaya, M., 637 (FRI0397)
Killeen, O.G., 1507 (FRI0766-HPR)
Killeen, R.P., 321 (THU0312)
Killick, K., 773 (SAT0013)
Kiltz, U., 356 (THU0394, THU0395), 466 (THU0685), 663 (FRI0466), 933 (SAT0427)
Kim, B.R., 1341 (AB0810)
Kim, B.Y., 1406 (AB1005)
Kim, D., 430 (THU0594), 1045 (SAT0714), 1447 (AB1121), 1473 (AB1193)
Kim, D.-W., 827 (SAT0154)
Kim, G., 1364 (AB0881)
Kim, G.-T., 255 (THU0144), 585 (FRI0262), 698 (FRI0550)
Kim, H., 1045 (SAT0714), 1061 (AB0040), 1371 (AB0901)
Kim, H.-A., 692 (FRI0533), 1355 (AB0855)
Kim, H.-O., 585 (FRI0262)
Kim, H.-R., 718 (FRI0605), 1078 (AB0090), 1166 (AB0336)
Kim, H.-S., 1406 (AB1005), 1437 (AB1092)
Kim, H.A., 217 (THU0049, THU0050), 518 (FRI0103), 999 (SAT0593)
Kim, H.J., 1250 (AB0571)
Kim, H.O., 1364 (AB0881)
Kim, H.R., 1185 (AB0392)
Kim, H.S., 1185 (AB0392)
Kim, H.W., 762 (FRI0717)
Kim, H.Y., 882 (SAT0290)
Kim, I.Y., 646 (FRI0422), 1371 (AB0901)
Kim, J., 359 (THU0400), 692 (FRI0531), 888 (SAT0307), 1126 (AB0223), 1259 (AB0593)

Kim, J.-E., 312 (THU0288), 791 (SAT0061), 877 (SAT0275), 972 (SAT0518, SAT0519)
Kim, J.-H., 604 (FRI0311), 1037 (SAT0693), 1130 (AB0234), 1452 (AB1134)
Kim, J.-M., 692 (FRI0533), 1355 (AB0855)
Kim, J.-W., 1162 (AB0326)
Kim, J.-Y., 482 (FRI0007)
Kim, J.H., 514 (FRI0093), 783 (SAT0042)
Kim, J.N., 301 (THU0257), 1162 (AB0326), 1229 (AB0508)
Kim, K.-J., 890 (SAT0311)
Kim, K.J., 1185 (AB0392)
Kim, L., 335 (THU0348), 341 (THU0360), 671 (FRI0486), 1295 (AB0692)
Kim, M.H., 1425 (AB1059)
Kim, M.J., 346 (THU0372), 351 (THU0383), 652 (FRI0438), 882 (SAT0290), 1045 (SAT0714), 1061 (AB0040)
Kim, N.R., 514 (FRI0093), 783 (SAT0042)
Kim, S., 89 (OP0089), 1413 (AB1025), 1425 (AB1059), 1437 (AB1092)
Kim, S.-H., 255 (THU0144), 430 (THU0594), 692 (FRI0533), 1355 (AB0855), 1473 (AB1193)
Kim, S.-J., 653 (FRI0442)
Kim, S.-K., 301 (THU0257), 1162 (AB0326), 1229 (AB0508)
Kim, S.-S., 692 (FRI0533), 1355 (AB0855)
Kim, S.A., 1131 (AB0236)
Kim, S.B., 381 (THU0459)
Kim, S.C., 544 (FRI0167), 802 (SAT0089)
Kim, S.H., 827 (SAT0154), 1185 (AB0392)
Kim, S.M., 888 (SAT0307), 1259 (AB0593)
Kim, S.S., 1406 (AB1005)
Kim, S.T., 717 (FRI0604)
Kim, T.-H., 827 (SAT0154), 1089 (AB0120), 1166 (AB0336)
Kim, W.-U., 890 (SAT0311)
Kim, Y., 585 (FRI0262), 888 (SAT0307)
Kim, Y.-G., 549 (FRI0181), 606 (FRI0316), 1093 (AB0133), 1222 (AB0491)
Kim, Y.-K., 255 (THU0144), 698 (FRI0550)
Kim, Y.S., 827 (SAT0154), 1185 (AB0392)
Kimoto, Y., 1254 (AB0582)
Kimura, J., 561 (FRI0210)
Kimura, T., 94 (OP0102), 575 (FRI0240), 849 (SAT0202)
Kimura, Y., 133 (OP0197), 448 (THU0641), 707 (FRI0577), 1426 (AB1063)
King, J., 140 (OP0213)
Kingsbury, D., 75 (OP0058), 405 (THU0525)
Kinikli, G., 354 (THU0389), 1488 (THU0756-HPR), 1523 (SAT0756-HPR), 1538 (AB1221-HPR)
Kınıklı, G., 606 (FRI0315), 1124 (AB0218), 1244 (AB0554)
Kinikli, G.I., 1488 (THU0756-HPR), 1523 (SAT0756-HPR), 1538 (AB1221-HPR)
Kinjo, M., 279 (THU0200)
Kiprianos, A., 219 (THU0053)
Kira, T., 282 (THU0207)
Kiran, R., 1295 (AB0690)
Kiraz, S., 250 (THU0131), 256 (THU0147), 402 (THU0518), 414 (THU0548), 448 (THU0642), 534 (FRI0140), 616 (FRI0342), 720 (FRI0612), 854 (SAT0216), 1035 (SAT0687), 1113 (AB0189), 1127 (AB0226), 1175 (AB0363), 1194 (AB0414), 1215 (AB0471), 1300 (AB0706), 1412 (AB1023), 1531 (AB1198-HPR)
Kirby, B., 675 (FRI0493), 681 (FRI0507), 951 (SAT0467), 1319 (AB0755)
Kirchgesner, T., 728 (FRI0633)
Kirchner, E., 51 (OP0003)
Kirdaite, G., 622 (FRI0359)
Kirdi, N., 1489 (THU0759-HPR), 1518 (SAT0741-HPR)
Kirillova, I., 572 (FRI0231), 811 (SAT0113), 944 (SAT0452)
Kirillova, I.G., 256 (THU0148)
Kirino, Y., 602 (FRI0305), 645 (FRI0419), 1195 (AB0416)
Kirk, J., 1545 (AB1241-HPR)
Kirkham, B., 135 (OP0201), 145 (OP0222), 230 (THU0081), 675 (FRI0494), 938 (SAT0438)
Kirkham, B.W., 780 (SAT0036)
Kirmayr, K., 440 (THU0619)
Kirochristos, D., 1243 (AB0551)
Kirou, K., 467 (THU0687)
Kirsanova, T., 1238 (AB0534)
Kirwan, J., 110 (OP0139-HPR)
Kirwan, P., 9 (SP0032)
Kiryttopoulos, P., 643 (FRI0412), 723 (FRI0619)
Kisacik, B., 354 (THU0389)
Kısacık, B., 327 (THU0329)
Kısacık, P., 1515 (SAT0730-HPR), 1531 (AB1198-HPR)
Kisaki, W., 246 (THU0119)
Kishi, T., 913 (SAT0376)
Kishimoto, D., 645 (FRI0419), 1195 (AB0416)
Kishimoto, M., 574 (FRI0235), 813 (SAT0118), 871 (SAT0256)
Kishimoto, T.K., 367 (THU0422)
Kisiel, B., 1152 (AB0297)
Kisluk, B., 440 (THU0619)
Kissling, R., 130 (OP0189)
Kisten, Y., 726 (FRI0626), 785 (SAT0048)
Kitahara, Y., 842 (SAT0187)
Kitano, M., 105 (OP0127), 641 (FRI0408), 1288 (AB0674)
Kitano, S., 210 (THU0030)
Kitaori, T., 1453 (AB1139)
Kitas, G., 546 (FRI0173)
Kitas, G.D., 764 (FRI0723), 836 (SAT0176), 1044 (SAT0712)
Kitchen, J., 541 (FRI0159), 1309 (AB0729)
Kitsiou, V., 1076 (AB0085)
Kivistö, S., 805 (SAT0096)
Kivitz, A., 144 (OP0220), 149 (LB0003), 232 (THU0087), 272 (THU0186), 367 (THU0422), 581 (FRI0253), 831 (SAT0162), 834 (SAT0171)
Kivitz, A.J., 345 (THU0369), 357 (THU0397), 682 (FRI0509), 983 (SAT0548)
Kiyokawa, S., 1471 (AB1187)
Kiyokawa, T., 635 (FRI0391), 872 (SAT0259), 1260 (AB0597)
Kjeken, I., 161 (OP0255-HPR), 1478 (THU0726-HPR), 1497 (FRI0738-HPR)
Kjeldgaard, A.H., 433 (THU0601)
Kjelgaard-Hansen, M., 1068 (AB0061)
Kjelgaard-Petersen, C.F., 1068 (AB0062)
Klaasen, R., 376 (THU0445)
Klaasen, R.A., 472 (THU0700)
Klagou, A., 1204 (AB0442)
Klar, R., 510 (FRI0087), 515 (FRI0096), 795 (SAT0072)
Klarenbeek, P., 123 (OP0172), 124 (OP0173), 601 (FRI0303)
Klareskog, L., 228 (THU0077), 244 (THU0114), 248 (THU0124), 781 (SAT0037), 792 (SAT0065), 1037 (SAT0692), 1038 (SAT0694), 1511 (SAT0721-HPR), 1512 (SAT0722-HPR)
Klatzmann, D., 776 (SAT0023)
Klavdianou, K., 321 (THU0310), 1376 (AB0915)
Klearman, M., 107 (OP0131)
Kleftouris, G., 1070 (AB0066)
Klein, A., 74 (OP0057), 398 (THU0507)
Klein, A.B., 380 (THU0456)
Klein, K., 190 (OP0326)
Klein, M., 209 (THU0027), 220 (THU0058), 906 (SAT0358), 1280 (AB0653), 1287 (AB0671)
Klein Gitelman, M., 391 (THU0490)
Klein-Wieringa, I., 769 (SAT0001)
Kleinert, S., 159 (OP0249), 516 (FRI0098), 1440 (AB1100), 1444 (AB1112)
Kleinmann, J.-F., 611 (FRI0329)
Kleoudis, C., 861 (SAT0231)
Klersy, C., 56 (OP0015)
Klett, F., 1552 (PARE0001)
Kleyer, A., 73 (OP0052), 159 (OP0249), 240 (THU0105), 516 (FRI0098), 655 (FRI0446), 725 (FRI0625), 1011 (SAT0628)
Klii, R., 885 (SAT0298), 1176 (AB0365), 1231 (AB0517), 1258 (AB0592)
Klimenchenko, N., 1238 (AB0534)
Klimiuk, P.A., 553 (FRI0189)
Klimowicz, A., 118 (OP0160)
Klingberg, E., 154 (OP0240), 674 (FRI0492), 916 (SAT0382)
Klingel, K., 86 (OP0084), 88 (OP0088)
Klion, A., 107 (OP0130)
Klokker, L., 463 (THU0677), 1332 (AB0786), 1444 (AB1113)
Klokkereide, A., 1478 (THU0726-HPR)
Klokkerud, M., 1497 (FRI0738-HPR)
Klonizakis, P., 569 (FRI0224)
Kloog, Y., 508 (FRI0082)
Klooster, P.M.T., 1140 (AB0263)
Kloppenburg, M., 122 (OP0168), 123 (OP0170), 197 (OP0342), 769 (SAT0001), 961 (SAT0492), 969 (SAT0511, SAT0512), 976 (SAT0529)
Klopsch, T., 1029 (SAT0674)
Klotsche, J., 76 (OP0060), 195 (OP0338), 400 (THU0512), 1389 (AB0957)
Klukvina, N.G., 1226 (AB0500)
Kluzek, S., 966 (SAT0504)
Klymas, I.V., 1167 (AB0339)
Kmyta, V.S.S.U., 820 (SAT0136)
Knaapen, H., 1280 (AB0651, AB0652)
Knapp, K., 572 (FRI0232)
Knapp, S., 499 (FRI0055)
Knauer, N., 206 (THU0019)
Knevel, R., 445 (THU0635)
Knezevic-Apostolski, S., 640 (FRI0405)
Knight, A., 509 (FRI0085)
Knight, H., 492 (FRI0034)
Knoop, J., 972 (SAT0517)
Knop, F.K., 196 (OP0340)
Knopf, A., 303 (THU0262)
Knudsen, L.R., 16 (SP0066), 1517 (SAT0738-HPR)
Knyazeva, A., 249 (THU0128)
Ko, C.-H., 690 (FRI0526), 708 (FRI0580), 709 (FRI0581), 1356 (AB0859)
Koarada, S., 895 (SAT0326)
Kobak, S., 327 (THU0329), 422 (THU0573), 955 (SAT0476), 1402 (AB0993)
Kobalava, Z., 807 (SAT0103), 1158 (AB0314), 1175 (AB0364)
Kobayashi, D., 853 (SAT0214)
Kobayashi, K., 645 (FRI0418), 1134 (AB0246), 1191 (AB0405)
Kobayashi, M., 1062 (AB0044), 1178 (AB0372), 1182 (AB0382), 1426 (AB1063)
Kobayashi, S., 810 (SAT0110)
Koblowski, J., 1398 (AB0982)
Kobza, A., 471 (THU0698)
Koca, S.S., 327 (THU0329), 455 (THU0658), 1462 (AB1162)
Kocak, A., 1105 (AB0168)
Koçak Ulucaköy, R., 652 (FRI0439)
Kocer, N., 603 (FRI0307)
Koch, A.E., 794 (SAT0069)
Kochbati, S., 1146 (AB0280)
Kocher, A., 1489 (THU0758-HPR)
Kochtali, I., 1176 (AB0365), 1258 (AB0592)
Kocijan, R., 73 (OP0052), 655 (FRI0446)
Koeberle, A., 115 (OP0151)
Koehn, C., 443 (THU0629), 453 (THU0653)
Koenders, M., 191 (OP0329), 492 (FRI0033), 504 (FRI0072)
Koenders, M.I., 89 (OP0090), 488 (FRI0024), 489 (FRI0025), 493 (FRI0037)
Koenig, A., 268 (THU0175)
Koenig, M.J., 737 (FRI0654)
Koening, C.L., 318 (THU0301)
Koes, B., 1306 (AB0722)
Koëter, S., 1476 (THU0721-HPR)
Koetter, I., 709 (FRI0582), 1106 (AB0169), 1110 (AB0181)
Koga, K., 1021 (SAT0652)
Koga, T., 318 (THU0303), 503 (FRI0067), 723 (FRI0620), 1403 (AB0995)
Kogata, Y., 115 (OP0152), 422 (THU0571)
Koh, E.-M., 612 (FRI0331), 646 (FRI0422), 749 (FRI0685), 1371 (AB0901)
Köhm, M., 565 (FRI0217)
Kohsaka, H., 265 (THU0170)
Koike, T., 540 (FRI0156), 698 (FRI0551), 955 (SAT0477), 1023 (SAT0658), 1134 (AB0245), 1324 (AB0768), 1426 (AB1061)

Koilubaeva, G., 1227 (AB0503)
Koivuniemi, R., 805 (SAT0096)
Kojima, M., 809 (SAT0106), 1124 (AB0219), 1177 (AB0371)
Kojima, T., 582 (FRI0254), 708 (FRI0579), 799 (SAT0081), 809 (SAT0106), 835 (SAT0174), 1124 (AB0219), 1177 (AB0371), 1195 (AB0415), 1357 (AB0860)
Kok, M., 676 (FRI0497), 1088 (AB0118), 1308 (AB0725)
Kok, M.D., 1497 (FRI0739-HPR)
KoK, M.R., 1421 (AB1047)
Kok, M.R., 1325 (AB0770)
Kokosadze, N., 424 (THU0578), 723 (FRI0621)
Kokov, A.N., 693 (FRI0536), 1346 (AB0823, AB0824)
Koksvik, H., 1480 (THU0733-HPR)
Kokubo, T., 1200 (AB0431)
Kola, I., 1543 (AB1234-HPR)
Kolarov, Z., 208 (THU0023), 379 (THU0453)
Kolbeck, R., 192 (OP0331)
Kolbinger, F., 1058 (AB0033)
Koldingsnes, W., 319 (THU0305)
Koletsos, N., 542 (FRI0161)
Koliakos, G., 558 (FRI0202)
Kollcaku, A., 1033 (SAT0683)
Kollcaku, J., 1033 (SAT0683)
Koller, M., 244 (THU0115)
Kollias, G., 500 (FRI0059)
Kolling, C., 190 (OP0326)
Kolnikova, V., 1350 (AB0838)
Kolta, S., 260 (THU0158)
Koltakova, A., 943 (SAT0451), 956 (SAT0478)
Koltsova, E., 848 (SAT0200)
Kolyadina, N.A., 1388 (AB0952)
Kolyvanova, A., 1238 (AB0534)
Komarc, M., 243 (THU0113)
Komarova, E., 1115 (AB0196)
Komiya, A., 525 (FRI0119)
Kommer-Wichers, C.G., 288 (THU0223)
Komura, M., 1054 (AB0021)
Komuro, I., 1274 (AB0635)
Kondo, A., 283 (THU0209), 719 (FRI0609), 757 (FRI0704), 1213 (AB0465)
Kondo, T., 424 (THU0577), 1399 (AB0984)
Kondo, Y., 747 (FRI0680), 1021 (SAT0652)
Kondo-Ishikawa, S., 527 (FRI0122)
Kondou, A., 907 (SAT0360)
Kondratyeva, L., 811 (SAT0113)
Koné-Paut, I., 77 (OP0063)
Kone-Paut, I., 398 (THU0509)
Konenkova, L., 771 (SAT0008)
Konerth, L., 240 (THU0105)
Koneva, O., 640 (FRI0403), 1283 (AB0659)
Koneva, O.A., 1287 (AB0670)
Kong, Q., 351 (THU0384)
Kong, X., 293 (THU0235), 1097 (AB0145)
Koning, M.T., 125 (OP0177)
Konings, T., 1087 (AB0116)
Kono, H., 314 (THU0294), 1248 (AB0566)
Kono, M., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Konovalova, N., 640 (FRI0403)
Konrad, M., 492 (FRI0034)
Konsta, M., 659 (FRI0455), 928 (SAT0415)
Konsta, S., 1204 (AB0442)
Konstantinidou, E., 1139 (AB0259)
Konstantinova, I., 85 (OP0081)
Konstantonis, D., 643 (FRI0414)
Konstantonis, G., 642 (FRI0410)
Konstantopoulou, P., 1204 (AB0442)
Konthur, Z., 124 (OP0174)
Kontny, E., 1310 (AB0733)
Kontush, A., 213 (THU0039)
Kontzias, A., 51 (OP0003), 713 (FRI0594)
Koo, B.S., 1414 (AB1028)
Koo, J.H., 548 (FRI0178)
Koo, N., 977 (SAT0533), 1458 (AB1151)
Kool, J., 1539 (AB1222-HPR)
Kool, M.B., 111 (OP0142-HPR)
Kopacek, C., 403 (THU0520)
Kopchak, O., 1391 (AB0962)
Kopchev, A., 685 (FRI0516), 686 (FRI0517)
Kopec-Harding, K., 1040 (SAT0700)
Kopec-Medrek, M., 1470 (AB1184)
Korb-Pap, A., 486 (FRI0018)
Korendowych, E., 939 (SAT0442)
Korenskaya, E.G., 459 (THU0670)
Korish, S., 858 (SAT0225), 870 (SAT0255)
Korkmaz, C., 254 (THU0141), 863 (SAT0237)
Korkmaz, M., 1499 (FRI0744-HPR)
Korkosz, M., 1470 (AB1184)
Korkou, C., 1076 (AB0085)
Koroglu, F., 1431 (AB1076)
Korolev, M.A., 1067 (AB0058)
Köröskényi, K., 1273 (AB0632)
Korotaeva, T., 943 (SAT0451), 944 (SAT0452), 956 (SAT0478), 1327 (AB0775), 1334 (AB0791)
Korotaeva, T.V., 674 (FRI0491), 943 (SAT0450), 1317 (AB0749)
Korsten, P., 721 (FRI0614), 1100 (AB0154), 1402 (AB0992)
Korswagen, L.-A., 676 (FRI0497), 1308 (AB0725), 1325 (AB0770)
Kortekaas, M., 969 (SAT0511)
Korver, A., 1306 (AB0722)
Kosai, K., 486 (FRI0017)
Kosanovic, M., 42 (SP0173)
Kosek, E., 6 (SP0021), 163 (OP0260-HPR)
Kosek, J., 778 (SAT0028), 780 (SAT0035)
Koseki, M., 501 (FRI0060), 620 (FRI0354)
Kosheleva, N., 807 (SAT0102)
Kosinski, M., 531 (FRI0133), 816 (SAT0126)
Kosir Jost, S., 1544 (AB1236-HPR)
Koskas, F., 108 (OP0134)
Kossomtini, W., 1383 (AB0936)
Kostareva, O., 1389 (AB0955)
Koster, A.J., 774 (SAT0015)
Koster, M.J., 609 (FRI0323), 613 (FRI0332)
Kostik, M., 1389 (AB0957)
Kostik, M.M., 1391 (AB0962)
Kostov, B., 410 (THU0539), 597 (FRI0293), 721 (FRI0615), 1042 (SAT0706)
Kostyál, L., 1027 (SAT0668)
Kosuva Ozturk, Z., 306 (THU0271)
Kotek, J., 691 (FRI0528)
Kottschade, L., 1044 (SAT0711)
Kotulska, A.T., 1470 (AB1184)
Kotyla, P., 1502 (FRI0752-HPR)
Kougas, N., 574 (FRI0236), 850 (SAT0204)
Kougkas, N., 577 (FRI0244), 896 (SAT0330)
Koulas, I., 1047 (AB0001), 1261 (AB0601)
Kouniaki, D., 1076 (AB0085)
Kountouri, A., 896 (SAT0330)
Koutsianas, C., 321 (THU0310), 632 (FRI0382), 1376 (AB0915)
Koutsogianni, K., 40 (SP0164), 1560 (AB1252-PARE)
Koutsoviti, S., 1204 (AB0442)
Kovács, A., 767 (FRI0731)
Kovács, D., 1267 (AB0617)
Kovács, É., 1482 (THU0736-HPR)
Kovács, L., 767 (FRI0731), 780 (SAT0034), 1090 (AB0123), 1105 (AB0167)
Kovalenko, V., 541 (FRI0160)
Kovalenko, V.M., 399 (THU0510)
Kovalevskaya, O., 249 (THU0127), 616 (FRI0343)
Kővári, E., 175 (OP0288)
Kovrigina, A., 424 (THU0578), 723 (FRI0621)
Kow, N.Y., 730 (FRI0636)
Kowal-Bielecka, O., 65 (OP0035), 1286 (AB0669)
Kowalska-Majka, J., 1470 (AB1184)
Kowalski, M.L., 1458 (AB1153)
Kowalski, M.R., 477 (THU0715)
Koyama, Y., 644 (FRI0417)
Koyun, M., 1392 (AB0965)
Koyun, O.N., 1374 (AB0911)
Kozaci, D., 354 (THU0389), 1170 (AB0349)
Kozakova, D., 829 (SAT0157)
Kozijn, A., 483 (FRI0010)
Kozlov, V., 206 (THU0019)
Kozlova, A., 413 (THU0547), 890 (SAT0312)
Kraaij, T., 181 (OP0302), 774 (SAT0015), 871 (SAT0258)
Kraan, M.C., 1199 (AB0428)
Krabbe, S., 175 (OP0287), 726 (FRI0628), 745 (FRI0674)
Kraev, V., 691 (FRI0530)
Krafft, V., 185 (OP0314-HPR)
Kragstrup, T.W., 125 (OP0178), 189 (OP0325), 505 (FRI0074), 1088 (AB0119)
Krampe, S., 814 (SAT0121)
Krasimirova, E., 1106 (AB0170)
Krasnenko, S., 660 (FRI0458), 920 (SAT0394), 1294 (AB0688), 1411 (AB1017)
Krasnokutsky Samuels, S., 766 (FRI0728)
Kräuchi, S., 1463 (AB1166)
Kraus, S., 1425 (AB1058)
Kraus, V.B., 215 (THU0044)
Krause, A., 1239 (AB0539)
Krause, T., 1222 (AB0489)
Kravchenko, D., 423 (THU0576)
Kravtcov, V., 699 (FRI0554)
Kreis, S., 465 (THU0684)
Kreiselová, S., 1264 (AB0609)
Kremer, J., 271 (THU0185), 283 (THU0210), 512 (FRI0090), 564 (FRI0216), 567 (FRI0222), 1192 (AB0408), 1313 (AB0739), 1455 (AB1143), 1521 (SAT0750-HPR)
Kremer, J.M., 60 (OP0022), 552 (FRI0188), 808 (SAT0104), 827 (SAT0153), 828 (SAT0155), 1191 (AB0407)
Krenn, V., 128 (OP0184)
Krennert, T., 445 (THU0633)
Kreuter, A., 1047 (AB0003), 1106 (AB0169), 1110 (AB0181)
Kreuter, M., 1110 (AB0181)
Krieckaert, C., 550 (FRI0183)
Krieg, T., 1106 (AB0169), 1110 (AB0181)
Kriegová, E., 970 (SAT0514)
Kriegova, E., 1051 (AB0014)
Krienke, S., 1070 (AB0068)
Krishan, P., 340 (THU0358)
Krishnamurthy, A., 212 (THU0036), 482 (FRI0006), 484 (FRI0013)
Krishnan, E., 834 (SAT0171), 1181 (AB0380)
Krishnaswami, S., 149 (LB0003), 271 (THU0185), 277 (THU0196), 284 (THU0211)
Kristensen, L.-E., 157 (OP0246), 651 (FRI0436), 655 (FRI0445)
Kristensen, L.E., 96 (OP0106), 98 (OP0112), 159 (OP0251), 196 (OP0340), 226 (THU0072), 341 (THU0361), 660 (FRI0460), 686 (FRI0518), 937 (SAT0437), 1332 (AB0786), 1412 (AB1020), 1444 (AB1113)
Kristensen, S., 553 (FRI0190)
Kristianslund, E., 341 (THU0361)
Kristianslund, E.K., 97 (OP0109), 224 (THU0070), 229 (THU0080), 334 (THU0345), 673 (FRI0490), 686 (FRI0518), 797 (SAT0075), 938 (SAT0440)
Kroegler, B., 1193 (AB0410)
Kroenke, G., 492 (FRI0033)
Kroese, F.G.M., 591 (FRI0277)
Kroese, S., 184 (OP0310)
Kröger, L., 827 (SAT0152)
Krogh, N.S., 451 (THU0649), 456 (THU0662), 553 (FRI0190), 784 (SAT0045), 912 (SAT0374)
Krogh, T.P., 168 (OP0270)
Krøll, F., 334 (THU0345), 673 (FRI0490)
Kron, M., 722 (FRI0618)
Krönke, G., 15 (SP0062), 775 (SAT0019)
Kroon, F., 122 (OP0168), 123 (OP0170), 969 (SAT0511, SAT0512)
Kroon, F.P., 197 (OP0342), 976 (SAT0529)
Krošel, M., 1291 (AB0682)
Krueger, D., 739 (FRI0658)
Krueger, K., 159 (OP0249), 516 (FRI0098)
Krüger, K., 257 (THU0150), 356 (THU0394), 558 (FRI0203), 565 (FRI0217)
Kruize, A., 478 (THU0716), 1482 (THU0737-HPR)
Kruize, A.A., 181 (OP0303), 288 (THU0223), 292 (THU0234), 295 (THU0241), 311 (THU0284), 464 (THU0681), 886 (SAT0302), 1089 (AB0121), 1206 (AB0446)
Krylov, M., 640 (FRI0403), 1283 (AB0659)
Krylov, M.Y., 1128 (AB0230)
Krylova, A., 1341 (AB0812)
Krzysiek, R., 182 (OP0307)
Ksibi, I., 998 (SAT0589, SAT0590), 1383 (AB0936)
Kubassova, O., 1021 (SAT0651)

Kubinova, K., 906 (SAT0358), 1280 (AB0653), 1287 (AB0671), 1416 (AB1034)
Kubo, K., 1054 (AB0021)
Kubo, S., 66 (OP0036), 137 (OP0205), 257 (THU0149)
Kuboi, Y., 211 (THU0031)
Kubota, T., 1389 (AB0954)
Kuca-Warnawin, E., 216 (THU0045), 489 (FRI0026)
Kucharski, D., 163 (OP0258-HPR)
Kucharz, E., 1502 (FRI0752-HPR)
Kucharz, E.J., 1470 (AB1184)
Kucharzewka, P., 1064 (AB0049)
Kuchi, A.A., 1153 (AB0299)
Kuchroo, V., 36 (SP0150)
Küçük, A., 327 (THU0329)
Küçük, H., 327 (THU0329), 1216 (AB0472), 1260 (AB0598)
Kucuk, H., 608 (FRI0320)
Küçükşahin, O., 327 (THU0329)
Kucuksahin, O., 992 (SAT0570)
Kudinsky, D., 1019 (SAT0646)
Kudlacz, E., 135 (OP0202), 682 (FRI0509), 1335 (AB0794)
Kudo-Tanaka, E., 1058 (AB0032)
Kudriavtseva, G., 1077 (AB0089)
Kudriavtseva, G.V., 507 (FRI0078)
Kuemmerle-Deschner, J., 393 (THU0495), 710 (FRI0585)
Kuemmerle-Deschner, J.B., 398 (THU0509)
Kuester, R., 405 (THU0525)
Kuet, K.-P., 847 (SAT0198)
Kugasia, A., 1466 (AB1173)
Kuhlencord, M., 772 (SAT0010)
Kuhn, C., 1440 (AB1100), 1444 (AB1112)
Kuhr, K., 1106 (AB0169), 1110 (AB0181)
Kuijper, T., 1306 (AB0722)
Kuijper, T.M., 509 (FRI0083), 1421 (AB1047)
Kuijpers, T., 1221 (AB0488)
Kuipers, J.G., 244 (THU0115)
Kujime, R., 1024 (SAT0661)
Kul, A., 1340 (AB0809)
Kul, O., 394 (THU0498)
Kullamaa, L., 17 (SP0071)
Kumagai, K., 1165 (AB0334), 1166 (AB0335)
Kumagai, S., 282 (THU0208)
Kumanogoh, A., 1467 (AB1176)
Kumar, A., 393 (THU0496), 960 (SAT0488)
Kumar, D., 320 (THU0307), 913 (SAT0375)
Kumar, K., 23 (SP0093), 40 (SP0165)
Kumar, P., 662 (FRI0463)
Kumar, S., 316 (THU0298), 320 (THU0307)
Kumar, U., 320 (THU0307)
Kume, K., 279 (THU0199)
Kummen, M., 87 (OP0085)
Kümmerle-Deschner, J., 76 (OP0060)
Kun, E.W.L., 689 (FRI0524)
Kunder, E., 560 (FRI0208)
Kundi, M., 1545 (AB1240-HPR)
Kundurdjiev, A., 379 (THU0453)
Kundurzhiev, T., 379 (THU0453)
Kundzer, A., 832 (SAT0166)
Kunishita, Y., 602 (FRI0305), 645 (FRI0419), 1195 (AB0416)
Kunnathully, V., 1062 (AB0045)
Kuo, C.-F., 85 (OP0080), 360 (THU0403), 366 (THU0419)
Kuperus, J.S., 1423 (AB1052)
Kupper, H., 405 (THU0525)
Kur-Zalewska, J., 1152 (AB0297)
Kuramoto, N., 220 (THU0057), 1452 (AB1133)
Kuranobu, T., 1460 (AB1159)
Kurasawa, K., 531 (FRI0134), 1291 (AB0681)
Kurasawa, T., 424 (THU0577), 1399 (AB0984)
Kurata, N., 283 (THU0209)
Kuret, T., 219 (THU0054), 325 (THU0324)
Kurita, T., 1258 (AB0591)
Kuriya, B., 531 (FRI0132)
Kurochkina, Y., 771 (SAT0008)
Kuroda, T., 313 (THU0290)
Kurowska, W., 216 (THU0045), 489 (FRI0026)
Kurowska-Stolarska, M., 138 (OP0208)
Kurrasch, R., 563 (FRI0214), 580 (FRI0251)
Kurreeman, F., 155 (OP0241), 202 (THU0008), 383 (THU0464), 621 (FRI0356)
Kurt, E.A., 603 (FRI0307)
Kurtinecz, M., 857 (SAT0223)
Kuru, O., 1172 (AB0353), 1298 (AB0699)
Kuru Çolak, T., 1537 (AB1217-HPR)
Kuryta, O., 1171 (AB0352)
Kusan, E., 1537 (AB1216-HPR)
Kusche, Y., 223 (THU0067), 772 (SAT0010)
Kushimoto, K., 1424 (AB1056)
Kusunoki, S., 610 (FRI0326)
Kutlubay, Z., 619 (FRI0351), 1246 (AB0558)
Kuuliala, A., 805 (SAT0096)
Kuvikova, I., 1228 (AB0507)
Kuwabara, A., 1452 (AB1133)
Kuwana, M., 202 (THU0006), 610 (FRI0326), 620 (FRI0354), 624 (FRI0363), 901 (SAT0343), 1200 (AB0431)
Kuyucu, E., 1484 (THU0745-HPR)
Kuzenko, A., 70 (OP0046)
Kuzhir, T.D., 389 (THU0485)
Kuzikyants, K., 843 (SAT0190)
Kuzmenko, N., 413 (THU0547)
Kuznetsov, A., 1198 (AB0423)
Kuznetsova, A., 843 (SAT0190)
Kuznetsova, E., 617 (FRI0346)
Kuzu Okur, H., 735 (FRI0648)
Kvarnström, M., 309 (THU0280), 311 (THU0284), 464 (THU0681), 885 (SAT0297), 886 (SAT0302)
Kvien, T., 341 (THU0361), 1029 (SAT0673)
Kvien, T.K., 52 (OP0005), 81 (OP0071), 97 (OP0109), 176 (OP0289), 224 (THU0070), 229 (THU0080), 334 (THU0345), 338 (THU0354), 355 (THU0393), 361 (THU0407), 472 (THU0700), 526 (FRI0121), 538 (FRI0151), 549 (FRI0182), 567 (FRI0221), 656 (FRI0450), 673 (FRI0490), 756 (FRI0702), 794 (SAT0070), 797 (SAT0075), 938 (SAT0440), 949 (SAT0463), 1017 (SAT0642), 1030 (SAT0675), 1323 (AB0766), 1326 (AB0772), 1334 (AB0793)
Kvistgaard Olsen, J., 651 (FRI0436), 1412 (AB1020)
Kwan, Y.H., 918 (SAT0389)
Kwekkeboom, J., 769 (SAT0001)
Kweon, S.-M., 585 (FRI0262), 698 (FRI0550)
Kwiatkowska, B., 489 (FRI0026)
Kwiatkowska, J., 1112 (AB0187)
Kwoh, C., 123 (OP0171)
Kwoh, C.K., 964 (SAT0500)
Kwok, F.Y.H., 432 (THU0598)
Kwok, K., 277 (THU0197), 285 (THU0215)
Kwok, K.Y., 796 (SAT0073), 1520 (SAT0747-HPR)
Kwok, S.-K., 977 (SAT0533), 1458 (AB1151)
Kwok, W., 779 (SAT0032)
Kwon, H., 296 (THU0244)
Kwon, H.H., 882 (SAT0290), 1045 (SAT0714), 1414 (AB1028)
Kwon, H.M., 1053 (AB0020)
Kwon, O.C., 1093 (AB0133)
Kwon, S.-R., 692 (FRI0533), 820 (SAT0137), 1355 (AB0855)
Kwon, S.R., 827 (SAT0154), 1185 (AB0392)
Kyburz, D., 267 (THU0174)
Kydd, A., 374 (THU0442)
Kyfonidou, P., 574 (FRI0236), 577 (FRI0244), 850 (SAT0204)
Kyle, S., 519 (FRI0105)
Kyllonen, M., 404 (THU0523)
Kyriakidis, N., 182 (OP0305)
Kyurkchiev, D., 1106 (AB0170)

L'Ami, M., 550 (FRI0183)
L'Amour, C., 450 (THU0646)
L-Longo, F., 718 (FRI0607)
La Paglia, G.M.C., 1113 (AB0191)
La Torre, G., 329 (THU0334)
Laadhar, L., 809 (SAT0108)
Laar, M.V.D., 1140 (AB0263)
Laatar, A., 1348 (AB0831), 1349 (AB0834), 1371 (AB0902), 1417 (AB1038)
Laater, A., 1394 (AB0969)
Labeeb, A.A.E.-A., 1404 (AB1000)
Labetoulle, M., 408 (THU0532)
Laborde, H., 729 (FRI0635), 1534 (AB1206-HPR)
Labrador Sánchez, E., 291 (THU0229), 441 (THU0623), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1349 (AB0837), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Lacaille, D., 373 (THU0440), 433 (THU0602), 438 (THU0615), 467 (THU0689), 471 (THU0698), 763 (FRI0722)
Lachmann, H., 77 (OP0063), 398 (THU0509)
Lachmann, H.J., 227 (THU0076), 1427 (AB1064)
Lachnish, J., 502 (FRI0065)
Lackner, A., 1495 (FRI0732-HPR), 1545 (AB1240-HPR)
Laclau, S., 1299 (AB0703)
LaCroix, A., 72 (OP0051)
Lacy-Niebla, R.M., 1330 (AB0782)
Ladehesa Pineda, M.L., 258 (THU0151), 700 (FRI0555), 975 (SAT0527)
Ladehesa-Pineda, L., 942 (SAT0447), 1268 (AB0619)
Ladjouze, A., 1009 (SAT0623), 1359 (AB0866), 1405 (AB1001, AB1002)
Ladjouze-Rezig, A., 982 (SAT0545)
Lafarge, D., 425 (THU0580)
Lafaurie, G., 252 (THU0137)
Lafeber, F., 433 (THU0603), 483 (FRI0010), 741 (FRI0664), 978 (SAT0536), 1020 (SAT0649)
Lafeber, F.J.P.G., 968 (SAT0508)
Lafeber, F.P., 177 (OP0293), 482 (FRI0008), 855 (SAT0218), 963 (SAT0498), 964 (SAT0499), 1068 (AB0061), 1344 (AB0818)
Laffont, M., 904 (SAT0351)
Lafforgue, P., 58 (OP0018), 706 (FRI0575), 1454 (AB1141)
Lafourcade, A., 425 (THU0580)
Lagishetty, V., 87 (OP0085)
Lagvilava, L., 1352 (AB0846)
Lahfa, M., 1330 (AB0781)
Lahiri, D., 1423 (AB1054)
Lahiri, M., 816 (SAT0124)
Lai, C.-C., 631 (FRI0381), 1334 (AB0792)
Lai, L., 613 (FRI0334)
Lairez, O., 901 (SAT0342)
Laiz, A., 904 (SAT0351), 914 (SAT0379), 1305 (AB0717), 1414 (AB1027)
Laiz Alonso, A., 955 (SAT0475), 1333 (AB0788)
Lajili, F., 998 (SAT0589, SAT0590)
Lajnef, I., 998 (SAT0589, SAT0590)
Lakhani, A., 826 (SAT0151)
Lakota, K., 219 (THU0054), 325 (THU0324)
Lakshminarayana, R., 1453 (AB1138)
Lakshminarayanan, S., 1213 (AB0466)
Lal, A., 301 (THU0258)
Lalanne, C., 481 (FRI0004)
Laliberté, M.-C., 349 (THU0378)
Lalmohamed, A., 67 (OP0039)
Lam, C.K., 1493 (THU0768-HPR)
Lam, H.M., 1125 (AB0221)
Lamana, A., 1128 (AB0229)
Lamb, J.A., 912 (SAT0374)
Lamberg, T., 61 (OP0024)
Lambers, W., 308 (THU0276)
Lambert, G., 259 (THU0154)
Lambert, M., 108 (OP0134), 152 (OP0236), 823 (SAT0144)
Lambert, N.C., 523 (FRI0114)
Lambert, R.G., 103 (OP0121), 337 (THU0353), 350 (THU0382), 469 (THU0693), 471 (THU0697), 663 (FRI0467), 668 (FRI0478), 933 (SAT0428)
Lambotte, O., 51 (OP0004)
Lamerato, L., 842 (SAT0188)
Lamers-Karnebeek, F., 1140 (AB0263)
Lamezec, L., 434 (THU0605)
Lamloum, M., 313 (THU0291), 599 (FRI0300), 889 (SAT0308), 1238 (AB0536), 1239 (AB0537)
Lammertsma, A., 724 (FRI0623), 1020 (SAT0650)
Lammertsma, A.A., 494 (FRI0041), 1075 (AB0082)
Lammoglia-Ordiales, L., 1330 (AB0782)
LaMoreaux, B., 1360 (AB0867)
Lampa, J., 1037 (SAT0692), 1038 (SAT0694)

Lampl, K., 581 (FRI0253)
Lamprecht, P., 44 (SP0184), 709 (FRI0582), 772 (SAT0011), 1108 (AB0175)
Lamprecht, T., 1154 (AB0302)
Lanata, C., 432 (THU0600)
Lande, K., 1497 (FRI0738-HPR)
Landesmann, U., 445 (THU0633), 520 (FRI0108)
LandewÉ, R., 100 (OP0115, OP0116)
Landewé, R., 60 (OP0023), 63 (OP0030), 80 (OP0070), 97 (OP0108), 129 (OP0188), 130 (OP0189), 131 (OP0192), 156 (OP0243, OP0244), 336 (THU0350), 353 (THU0388), 434 (THU0604), 473 (THU0702, THU0703), 528 (FRI0126), 649 (FRI0430), 650 (FRI0432)
Landewe, R., 8 (SP0029), 28 (SP0111), 337 (THU0353), 350 (THU0382), 560 (FRI0207)
Landewé, R.B., 82 (OP0073), 146 (OP0224), 160 (OP0252), 793 (SAT0067)
Landgren, A.J., 360 (THU0404), 364 (THU0414)
Landolfo, S., 1113 (AB0191)
Landsmeer, M., 973 (SAT0522)
Landwójtowicz, M., 1112 (AB0187)
Lane, N.E., 121 (OP0166), 690 (FRI0525), 985 (SAT0552)
Lane, T., 227 (THU0076), 1427 (AB1064)
Lang, A., 480 (FRI0002), 485 (FRI0015), 1067 (AB0060)
Langdahl, B., 248 (THU0126)
Lange, E., 163 (OP0258-HPR)
Lange, T., 772 (SAT0011)
Lange, U., 220 (THU0056)
Langer, H.-E., 74 (OP0057)
Langford, C., 107 (OP0130), 187 (OP0320)
Langford, C.A., 318 (THU0301), 605 (FRI0314)
Langley, R.G.B., 1325 (AB0771)
Langsetmo, L., 958 (SAT0484)
Lanni, S., 1015 (SAT0636)
Lanyon, P.C., 1205 (AB0444)
Lanzillotta, M., 410 (THU0538), 1399 (AB0985)
Lao, V.W.-N., 1520 (SAT0747-HPR)
Lao, V.W.N., 796 (SAT0073)
Lapadula, G., 259 (THU0155), 343 (THU0366), 445 (THU0634), 521 (FRI0110), 1059 (AB0037), 1135 (AB0250), 1268 (AB0618), 1461 (AB1160), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Lapeyre-Mestre, M., 1248 (AB0565)
Lapin, S., 611 (FRI0328)
Lapshina, S., 1172 (AB0354), 1203 (AB0437, AB0438), 1300 (AB0704), 1311 (AB0735)
Lapunzina, P., 416 (THU0553)
Lara, M., 1534 (AB1206-HPR)
Lara-Mejía, A., 860 (SAT0229)
Larbre, J.-P., 1385 (AB0945)
Larché, M., 131 (OP0192)
Larcher, T., 508 (FRI0081)
Laredo, J.-D., 170 (LB0001)
Larena, C., 633 (FRI0385), 1270 (AB0625)
Largo, R., 128 (OP0186), 504 (FRI0071)
Larkin, L., 1482 (THU0738-HPR)
Larkman, N., 727 (FRI0630)
Larmore, C.J., 794 (SAT0069)
Laroche, F., 169 (OP0274), 385 (THU0470)
Laroche, M., 1376 (AB0916)
Larosa, M., 437 (THU0611), 1209 (AB0455, AB0456), 1214 (AB0467)
Larrañaga-Vera, A., 504 (FRI0071)
Larrea, M., 1351 (AB0843)
Larrosa, M., 926 (SAT0410)
Larroude, M.S., 440 (THU0619)
Larsen, E., 101 (OP0117)
Larsen, M., 1497 (FRI0738-HPR)
Larssen, E., 184 (OP0312)
Larsson, A., 163 (OP0260-HPR), 509 (FRI0085), 1102 (AB0159)
Larsson, E., 794 (SAT0070)
Larsson, I., 674 (FRI0492), 1488 (THU0757-HPR)
Larsson Ranada, Å., 1518 (SAT0740-HPR)
Las Alas, A., 1284 (AB0662)
Laselva, G., 521 (FRI0110), 1268 (AB0618), 1461 (AB1160)
Laskari, A., 602 (FRI0306)
Laskari, K., 1133 (AB0244)
Laskarin, G., 771 (SAT0009)
Laskin, C.A., 152 (OP0236)
Laslett, L., 960 (SAT0489)
Laslett, L.L., 122 (OP0169)
Lasso, J., 330 (THU0336)
Lataoui, S., 543 (FRI0165), 927 (SAT0411)
Latini, A., 204 (THU0013)
Latorre, M., 320 (THU0308)
Latorre, M.C., 1472 (AB1190)
Latour, M., 349 (THU0378)
Latourte, A., 53 (OP0007)
Latteur, V., 1384 (AB0941)
Latuhihin, T.E., 1086 (AB0114)
Lau, C.-S., 416 (THU0554)
Lau, C.S., 525 (FRI0118), 936 (SAT0434)
Lau, I.S., 256 (THU0146), 446 (THU0638), 1512 (SAT0722-HPR)
Lau, S.L., 706 (FRI0576)
Lau, X.S.L., 1520 (SAT0747-HPR)
Laudes, M., 465 (THU0682)
Launay, D., 152 (OP0236)
Launay, J.-M., 382 (THU0461)
Lauper, K., 850 (SAT0206)
Laura, Y., 262 (THU0162)
Laurberg, T.B., 454 (THU0657)
Laurent III, G.St., 202 (THU0007)
Lauri, J., 1514 (SAT0729-HPR)
Lauri, M.A., 1514 (SAT0729-HPR)
Laurindo, I.M.M., 443 (THU0627), 1516 (SAT0735-HPR)
Laursen, T., 332 (THU0340)
Laustsen, J., 1088 (AB0119)
Lauwerys, B., 36 (SP0148), 75 (OP0058), 290 (THU0228), 393 (THU0495)
LaValley, M.P., 1032 (SAT0679)
Lavazais, S., 118 (OP0161)
Laven, J.S., 532 (FRI0136), 537 (FRI0147)
Lavielle, M., 996 (SAT0583)
Lavoie, R.R., 481 (FRI0004)
Lawrence, A., 388 (THU0481)
Laws, P., 734 (FRI0646)
Lawton, S., 1433 (AB1081)
Laxer, R., 393 (THU0495)
Laxminarayan, R., 1355 (AB0853)
Laynez, P., 691 (FRI0530)
Layrolle, P., 90 (OP0093), 130 (OP0190)
Lazaretti-Castro, M., 71 (OP0048)
Lazariciu, I., 148 (OP0230)
Lazarini, A., 321 (THU0310), 1376 (AB0915)
Lazaro, E., 866 (SAT0246)
Lazaro, M., 906 (SAT0357)
Lazaro, P., 452 (THU0651)
Lazovskis, J., 58 (OP0019)
Lazure, T., 182 (OP0307)
Lazzaroni, M.G., 70 (OP0046), 437 (THU0611), 1439 (AB1099)
Le, B., 1507 (FRI0764-HPR)
Le, L., 789 (SAT0056)
Le Bars, M., 566 (FRI0219), 577 (FRI0245), 1141 (AB0267), 1193 (AB0412)
Le Berre, R., 309 (THU0278)
Le Burel, S., 51 (OP0004)
le Cessie, S., 123 (OP0170)
Le Corroller, T., 744 (FRI0671)
Le Gallou, T., 1256 (AB0588)
Le Garff-Tavernier, M., 776 (SAT0023)
Le Goff, B., 90 (OP0093), 128 (OP0184), 130 (OP0190), 335 (THU0349), 430 (THU0593), 731 (FRI0638)
Le Goff, M., 309 (THU0278)
Le Goux, P., 996 (SAT0583)
Le Grand, R., 508 (FRI0081)
Le Guenno, G., 1059 (AB0035)
Le Guern, V., 152 (OP0236), 289 (THU0225)
Le Guilchard, F., 335 (THU0349)
Le Jeunne, C., 831 (SAT0163)
Le Marshall, K., 1418 (AB1040)
Leal, G.N., 76 (OP0061)
Leal, S., 1279 (AB0649)
Leandro, M., 1090 (AB0124), 1205 (AB0443)
Leandro, M.J., 495 (FRI0042)
Leary, A., 51 (OP0004)
Lebedeva, V., 1204 (AB0441)
Lebkowska, U., 1277 (AB0642)
Leboime, A., 78 (OP0064)
Lebughe, P., 1310 (AB0732)
Lebwohl, M., 953 (SAT0472)
Lecauchois, S., 1442 (AB1108)
Leccese, I., 757 (FRI0705), 872 (SAT0260), 1449 (AB1125)
Leceta, J., 485 (FRI0016)
Lechiu, C.N., 397 (THU0505)
Lecorney, J., 959 (SAT0486)
Lecouvet, F., 728 (FRI0633)
Ledingham, J., 1490 (THU0760-HPR)
Ledingham, J.M., 1030 (SAT0676), 1039 (SAT0699)
Lee, A., 1444 (AB1113)
Lee, A.P.-W., 1520 (SAT0747-HPR)
Lee, A.P.W., 689 (FRI0524), 956 (SAT0479)
Lee, A.S., 318 (THU0301)
Lee, B.W., 977 (SAT0533), 1458 (AB1151)
Lee, C., 144 (OP0221), 371 (THU0433), 1131 (AB0237)
Lee, C.-H., 482 (FRI0007), 1511 (SAT0720-HPR)
Lee, C.-K., 1093 (AB0133), 1222 (AB0491)
Lee, C.H., 135 (OP0201)
Lee, C.U., 1162 (AB0326), 1229 (AB0508)
Lee, E., 553 (FRI0189)
Lee, E.-J., 1093 (AB0133)
Lee, E.B., 83 (OP0077), 277 (THU0197), 296 (THU0244), 346 (THU0372), 351 (THU0383), 652 (FRI0438), 849 (SAT0202), 877 (SAT0274), 922 (SAT0398), 1053 (AB0020)
Lee, E.E., 80 (OP0069), 351 (THU0383), 652 (FRI0438)
Lee, E.S., 514 (FRI0093), 783 (SAT0042)
Lee, E.Y., 80 (OP0069), 83 (OP0077), 346 (THU0372), 351 (THU0383), 422 (THU0572), 652 (FRI0438), 827 (SAT0154), 877 (SAT0274), 1053 (AB0020)
Lee, G.Y., 1413 (AB1025)
Lee, H., 1162 (AB0326)
Lee, H.-S., 827 (SAT0154)
Lee, H.Y., 80 (OP0069), 1126 (AB0223)
Lee, J., 646 (FRI0422), 749 (FRI0685), 977 (SAT0533), 1045 (SAT0714), 1371 (AB0901), 1385 (AB0943), 1458 (AB1151)
Lee, J.-H., 255 (THU0144)
Lee, J.-W., 255 (THU0144), 585 (FRI0262), 698 (FRI0550)
Lee, J.H., 1185 (AB0392), 1528 (SAT0768-HPR)
Lee, J.S., 80 (OP0069)
Lee, J.W., 1364 (AB0881)
Lee, J.Y., 877 (SAT0274)
Lee, K.-A., 1078 (AB0090)
Lee, K.-E., 312 (THU0288), 791 (SAT0061), 877 (SAT0275), 972 (SAT0518, SAT0519)
Lee, K.A., 718 (FRI0605), 1166 (AB0336)
Lee, K.L., 412 (THU0543), 644 (FRI0415), 706 (FRI0576), 715 (FRI0599)
Lee, K.W., 412 (THU0543), 715 (FRI0599)
Lee, K.Y., 383 (THU0467)
Lee, L., 1437 (AB1094)
Lee, L.H., 432 (THU0598), 1471 (AB1188)
Lee, M., 181 (OP0304)
Lee, M.-S., 482 (FRI0007)
Lee, M.H., 217 (THU0050)
Lee, P.F., 1493 (THU0768-HPR)
Lee, S., 552 (FRI0187), 1185 (AB0392), 1364 (AB0881), 1414 (AB1028)
Lee, S.-G., 255 (THU0144), 585 (FRI0262), 698 (FRI0550)
Lee, S.-H., 718 (FRI0605), 1078 (AB0090), 1166 (AB0336)
Lee, S.-S., 312 (THU0288), 791 (SAT0061), 877 (SAT0275), 972 (SAT0518, SAT0519)
Lee, S.-W., 372 (THU0436), 383 (THU0467), 1250 (AB0571)
Lee, S.-Y., 1355 (AB0855)
Lee, S.H., 381 (THU0459), 827 (SAT0154), 1074 (AB0080)
Lee, S.I., 1185 (AB0392)
Lee, S.J., 422 (THU0572), 514 (FRI0093), 548 (FRI0178), 783 (SAT0042), 824 (SAT0146), 827 (SAT0154), 1053 (AB0020)
Lee, S.K., 1131 (AB0236)
Lee, S.M., 922 (SAT0398)

Lee, S.S., 1185 (AB0392)
Lee, S.W., 1083 (AB0107)
Lee, S.Y., 518 (FRI0103), 824 (SAT0146), 1083 (AB0107)
Lee, T.S.-H., 1408 (AB1009)
Lee, W.I., 1425 (AB1059)
Lee, Y., 552 (FRI0187), 556 (FRI0198)
Lee, Y.H., 285 (THU0213), 604 (FRI0311), 1037 (SAT0693), 1242 (AB0548)
Lee, Y.J., 296 (THU0244), 346 (THU0372)
Lee, Y.L., 1140 (AB0262)
Leeb, B.F., 1455 (AB1144)
Leeden van der, M., 1486 (THU0750-HPR)
Leeming, D., 1109 (AB0179, AB0180)
Lefèvre-Colau, M.-M., 170 (LB0001)
Lefkir-Tafiani, S., 1359 (AB0866)
Lefrandt, J.D., 625 (FRI0366)
Lega, J.-C., 432 (THU0599)
Legány, N., 1105 (AB0167)
Legault, K., 418 (THU0561)
Legeler, C., 356 (THU0395)
Legerton, C.W., 345 (THU0369)
Leggett, S., 433 (THU0602), 467 (THU0689), 763 (FRI0722), 765 (FRI0724)
Legoupil, N., 1470 (AB1185)
Lehman, A.J., 679 (FRI0503)
Lehman, T., 687 (FRI0520), 1389 (AB0957)
Lehmann, S., 475 (THU0708), 478 (THU0718), 479 (THU0719)
Lei, G., 1338 (AB0802)
Leichtenberg, C., 966 (SAT0505), 967 (SAT0506)
Leipe, J., 718 (FRI0606)
Leirisalo-Repo, M., 805 (SAT0096)
Leirisalo-repo, M., 61 (OP0024)
Leiss, H., 292 (THU0233), 492 (FRI0033)
Leitão, R., 929 (SAT0418), 1163 (AB0329)
Leite de Oliveira, F., 1111 (AB0184)
Leite Silva, J., 637 (FRI0394), 736 (FRI0652), 1015 (SAT0637), 1275 (AB0636)
Leith, M., 1372 (AB0904)
Leiva, J.P., 1459 (AB1154)
Lejon, K., 250 (THU0129)
Lelann, L., 492 (FRI0035)
Lely, A., 184 (OP0310)
Lemal, R., 1059 (AB0035)
Lemay, C.A., 1521 (SAT0750-HPR)
Lemelle, I., 56 (OP0014)
Lemesle, P., 1352 (AB0844)
Lemeunier, L., 1299 (AB0702)
Lempp, H., 13 (SP0052), 1527 (SAT0767-HPR), 1555 (PARE0010)
Lems, W., 54 (OP0010), 347 (THU0374), 811 (SAT0114), 1038 (SAT0695)
Lems, W.F., 114 (OP0150), 516 (FRI0097), 661 (FRI0461), 817 (SAT0127), 931 (SAT0421), 972 (SAT0517), 976 (SAT0529), 982 (SAT0544), 1145 (AB0277), 1488 (THU0755-HPR)
Lenaerts, J., 636 (FRI0393), 1275 (AB0638)
Lendrem, D., 92 (OP0097), 163 (OP0259-HPR), 1103 (AB0162), 1524 (SAT0758-HPR)
Lendrem, D.W., 200 (THU0003)
Leng, J.C., 1437 (AB1094)
Lennerová, T., 209 (THU0027)
Lennerova, T., 220 (THU0058)
Lentas, A., 1458 (AB1153)
Lenzi, A., 1057 (AB0029, AB0030)
León, C., 320 (THU0309)
Leon, K., 395 (THU0502)
León, L., 320 (THU0309), 918 (SAT0387), 1307 (AB0723), 1471 (AB1189)
León Luque, M., 713 (FRI0592)
Leon Vazquez, F., 1362 (AB0875)
Leon Vazquez, M.D.L.L., 1221 (AB0486)
León-Idougourram, S., 942 (SAT0447)
León-Vázquez, J., 311 (THU0283)
Leonardi, C., 144 (OP0220)
Leonaviciene, L., 622 (FRI0359)
Leonchik, K., 1361 (AB0871)
Leong, A., 470 (THU0695), 605 (FRI0312), 818 (SAT0132)
Leong, A.L., 463 (THU0677)
Lepescheux, L., 118 (OP0161), 126 (OP0180)
Lepiarz-Rusek, W., 1470 (AB1184)
Leplina, O., 771 (SAT0008)
Leppänen, T., 893 (SAT0321)
Lepri, G., 631 (FRI0380)
Lepse, N., 180 (OP0300)
Lepus, C.M., 189 (OP0325)
Lequerre, T., 63 (OP0029), 1378 (AB0923)
Lerchen, V., 725 (FRI0625)
Lerma, S., 1471 (AB1189)
Lerner, P.G., 443 (THU0627)
Lerstrøm, K., 172 (OP0280-PARE)
Lertratanakul, A., 156 (OP0243)
Lertthanaphok, S., 908 (SAT0362)
Lesch, J., 789 (SAT0056)
Lescoat, A., 1261 (AB0599)
Lesperance, T., 114 (OP0148)
Lespesailles, E., 1299 (AB0701)
Lespessailles, E., 335 (THU0349), 679 (FRI0502), 683 (FRI0512), 684 (FRI0513), 936 (SAT0436), 942 (SAT0448), 1314 (AB0743), 1331 (AB0785), 1448 (AB1123)
Lessard, C.J., 1096 (AB0143)
Lestan, B., 1143 (AB0272)
Lester, S., 383 (THU0464)
Leszczynski, P., 1209 (AB0454), 1229 (AB0510), 1470 (AB1184)
Letarouilly, J.-G., 413 (THU0546)
Letyagina, E.A., 1067 (AB0058)
Leung, A.M.H., 589 (FRI0273)
Leung, M.-H.A., 525 (FRI0118)
Leung, M.C., 1493 (THU0768-HPR)
Leung, Y.M.E., 1541 (AB1229-HPR)
Leung, Y.Y., 1332 (AB0786)
Levartovsky, D., 747 (FRI0679), 1118 (AB0203), 1328 (AB0776)
Levchenko, V., 541 (FRI0160)
Levesque, M.C., 122 (OP0168), 983 (SAT0546)
Levet-Labry, R., 1301 (AB0708)
Levi, E., 1325 (AB0771)
Levine, A., 467 (THU0687)
Levitova, A., 1468 (AB1180)
Levy, G., 122 (OP0168)
Levy, J., 398 (THU0509)
Levy, P., 945 (SAT0455)
Levy, R.A., 299 (THU0253), 312 (THU0286), 887 (SAT0303)
Levy-Bachelot, L., 434 (THU0605)
Levy-Neto, M., 614 (FRI0335)
Lewandowicz, J., 1470 (AB1184)
Lewandowska-Polak, A., 1458 (AB1152)
Lewey, J.P., 802 (SAT0089)
Lewis, A., 539 (FRI0153), 812 (SAT0115)
Lewis, A.M., 680 (FRI0506)
Lewis, B.L., 690 (FRI0525)
Lewis, M., 238 (THU0100), 511 (FRI0088), 1433 (AB1081)
Lexberg, Å., 1029 (SAT0673)
Leyens, J., 423 (THU0576)
Leyton, C., 1102 (AB0158)
Lezcano, J.M., 520 (FRI0107)
Lheritier, K., 395 (THU0502)
Lhomme, M., 213 (THU0039)
Li, A., 438 (THU0615)
Li, B., 1290 (AB0679)
Li, C., 1144 (AB0274), 1226 (AB0502)
Li, D., 337 (THU0352)
Li, E.K., 1198 (AB0424)
Li, E.K.-M., 1520 (SAT0747-HPR)
Li, E.K.M., 689 (FRI0524), 796 (SAT0073), 956 (SAT0479)
Li, F., 1084 (AB0109), 1246 (AB0560), 1524 (SAT0757-HPR)
Li, G., 285 (THU0215)
Li, H., 272 (THU0186), 777 (SAT0027), 1112 (AB0188), 1189 (AB0401), 1338 (AB0802)
Li, J., 108 (OP0132), 375 (THU0444), 379 (THU0455), 393 (THU0494), 509 (FRI0084), 759 (FRI0710), 867 (SAT0249), 1081 (AB0099), 1096 (AB0141), 1144 (AB0274), 1295 (AB0691), 1338 (AB0802), 1352 (AB0845), 1416 (AB1033)
Li, K., 748 (FRI0681), 919 (SAT0392)
Li, K.-J., 1511 (SAT0720-HPR)
Li, L., 373 (THU0440), 438 (THU0615), 492 (FRI0034), 1230 (AB0513), 1234 (AB0523), 1241 (AB0543), 1368 (AB0893), 1369 (AB0894), 1370 (AB0897, AB0898, AB0899), 1459 (AB1156)
Li, M., 310 (THU0281), 583 (FRI0258), 600 (FRI0302), 689 (FRI0524), 796 (SAT0073), 858 (SAT0224), 883 (SAT0292), 1198 (AB0424)
Li, N., 341 (THU0360), 578 (FRI0246), 580 (FRI0251), 839 (SAT0182), 1295 (AB0692)
Li, P., 363 (THU0413), 1359 (AB0865)
Li, P.H., 416 (THU0554)
Li, Q., 664 (FRI0470)
Li, Q.-H., 373 (THU0439)
Li, R., 748 (FRI0681)
Li, S., 1084 (AB0109), 1516 (SAT0734-HPR)
Li, T., 203 (THU0010), 934 (SAT0430)
Li, T.-H., 889 (SAT0309), 1334 (AB0792)
Li, T.K., 1198 (AB0424)
Li, T.K.Y., 689 (FRI0524)
Li, W., 270 (THU0182), 281 (THU0205, THU0206), 1103 (AB0163)
Li, W.-C., 291 (THU0232)
Li, X., 58 (OP0020), 63 (OP0028), 69 (OP0043), 108 (OP0132), 194 (OP0337-HPR), 268 (THU0176), 311 (THU0284), 464 (THU0681), 531 (FRI0132), 543 (FRI0163), 547 (FRI0176), 853 (SAT0213), 869 (SAT0252), 872 (SAT0261), 886 (SAT0302), 947 (SAT0459), 1036 (SAT0689), 1081 (AB0100), 1141 (AB0266), 1197 (AB0421, AB0422), 1226 (AB0501), 1295 (AB0691), 1516 (SAT0734-HPR)
Li, X.F., 1266 (AB0612)
Li, Y., 283 (THU0210), 344 (THU0367), 348 (THU0376), 678 (FRI0501), 748 (FRI0681), 1229 (AB0509), 1535 (AB1210-HPR)
Li, Y.-H., 373 (THU0439)
Li, Z., 268 (THU0176), 285 (THU0215), 344 (THU0367), 509 (FRI0084), 515 (FRI0096), 621 (FRI0356), 1065 (AB0052), 1096 (AB0141), 1144 (AB0274), 1197 (AB0421), 1524 (SAT0757-HPR)
Li Gobbi, F., 646 (FRI0423)
Lia, A., 639 (FRI0400)
Liakouli, V., 721 (FRI0613), 880 (SAT0284), 891 (SAT0313)
Lian, F., 336 (THU0351)
Liang, J., 592 (FRI0281), 1092 (AB0130)
Liang, J.-J., 373 (THU0439), 798 (SAT0078)
Liang, L., 336 (THU0351)
Liang, N., 1138 (AB0257)
Liang, P., 496 (FRI0047)
Liang, R., 892 (SAT0318)
Liang, Z., 69 (OP0043), 872 (SAT0261)
Liao, H., 326 (THU0327)
Liao, K., 202 (THU0006), 445 (THU0635)
Liao, T.-L., 82 (OP0074)
Liao, Z., 351 (THU0384), 664 (FRI0470), 665 (FRI0471)
Liaskos, C., 903 (SAT0348), 1271 (AB0626), 1279 (AB0648)
Libanati, C., 71 (OP0048), 72 (OP0050)
Licciardi, F., 1012 (SAT0630)
Liddle, J., 1433 (AB1081)
Lie, E., 81 (OP0071), 97 (OP0109), 154 (OP0240), 229 (THU0080), 334 (THU0345), 341 (THU0361), 538 (FRI0151), 673 (FRI0490), 686 (FRI0518), 756 (FRI0702), 797 (SAT0075), 938 (SAT0440), 1017 (SAT0642), 1030 (SAT0675)
Liedert, B., 1185 (AB0391)
Liedgens, H., 382 (THU0462), 1369 (AB0896)
Liedmann, I., 76 (OP0060)
Liendo, V., 1339 (AB0805)
Lieon, M., 1553 (PARE0006)
Liew, D., 1367 (AB0889)
Ligeiro, D., 1052 (AB0016)
Lihua, Z., 1480 (THU0732-HPR)
Lijun, W., 738 (FRI0657), 1407 (AB1008)
Lila, A., 560 (FRI0208)
Lilleby, V., 55 (OP0013), 875 (SAT0270)
Lillegraven, S., 81 (OP0071), 176 (OP0289), 522 (FRI0111), 526 (FRI0121), 538 (FRI0151), 1017 (SAT0642)

Lilleker, J.B., 912 (SAT0374)
Lim, A., 1447 (AB1119)
Lim, D.-H., 549 (FRI0181), 606 (FRI0316), 1093 (AB0133)
Lim, D.H., 1222 (AB0491)
Lim, K., 1418 (AB1040)
Lim, M., 1131 (AB0236)
Lim, M.-J., 820 (SAT0137)
Lim, M.K., 1185 (AB0392)
Lim, S.H., 999 (SAT0593)
Lim, S.H.L., 781 (SAT0039)
Lima, A., 1052 (AB0016)
Lima, G., 291 (THU0230)
Lima, H.D., 989 (SAT0562)
Lima Passos, V., 649 (FRI0430)
Limam, K., 543 (FRI0165)
LiMin, L., 1241 (AB0545)
Limonta, M., 540 (FRI0155), 595 (FRI0288), 867 (SAT0247)
Lin, C., 912 (SAT0373)
Lin, C.-H., 82 (OP0074)
Lin, C.-Y., 144 (OP0221), 941 (SAT0446), 1334 (AB0793)
Lin, D.F., 366 (THU0421), 1158 (AB0312)
Lin, D.H., 859 (SAT0227)
Lin, J., 280 (THU0203), 855 (SAT0217)
Lin, L., 1219 (AB0482)
Lin, Q., 1095 (AB0140)
Lin, Y., 94 (OP0102), 849 (SAT0202), 853 (SAT0212)
Lin, Z., 351 (THU0384), 664 (FRI0470), 665 (FRI0471), 934 (SAT0431)
Linares, L., 420 (THU0567), 718 (FRI0607)
LInares Ferrando, L.F., 1041 (SAT0704)
Linares-Ferrando, L., 487 (FRI0021)
Linares-Ferrando, L.F., 658 (FRI0454), 739 (FRI0659)
Linauskas, A., 84 (OP0079), 553 (FRI0190)
Linda, M., 927 (SAT0411)
Linde, T., 824 (SAT0146)
Lindegaard, H., 226 (THU0072), 553 (FRI0190), 784 (SAT0045)
Lindegaard, H.M., 732 (FRI0641), 745 (FRI0675), 1024 (SAT0660)
Lindqvist, E., 452 (THU0652), 651 (FRI0436), 655 (FRI0445), 823 (SAT0143), 922 (SAT0397), 1050 (AB0012)
Lindqvist, J., 1038 (SAT0694)
Lindström, U., 154 (OP0240), 364 (THU0414), 452 (THU0652)
Ling, J.E.S., 1038 (SAT0695)
Ling, L.H., 730 (FRI0636)
Lingampalli, N., 774 (SAT0017)
Link, T.M., 58 (OP0020)
Linke, A.T., 579 (FRI0248)
Linn-Rasker, S., 376 (THU0445)
Lins, C., 176 (OP0290), 1412 (AB1021)
Lins, O., 990 (SAT0566)
Linz, C., 725 (FRI0625)
Lionaki, S., 323 (THU0315)
Lioté, F., 212 (THU0034), 216 (THU0046), 359 (THU0401), 367 (THU0424), 431 (THU0596), 1186 (AB0395), 1364 (AB0882), 1371 (AB0900)
Liote, F., 383 (THU0464)
Lioté, H., 1049 (AB0007)
Lipovskiy, L., 308 (THU0277)
Lipsky, P., 365 (THU0416), 373 (THU0438), 377 (THU0448, THU0449), 560 (FRI0207), 1368 (AB0892)
Lipsky, P.E., 38 (SP0156)
Lisbona Muñoz, M., 713 (FRI0592)
Lisignoli, G., 1069 (AB0064)
Lisitsyna, T., 249 (THU0127), 616 (FRI0343)
Lisney, A.R., 184 (OP0311)
Lisse, J.R., 789 (SAT0058), 1330 (AB0783)
Listing, J., 101 (OP0118), 530 (FRI0130), 1029 (SAT0674)
Listing, M., 76 (OP0060)
Litman, H., 1192 (AB0408), 1455 (AB1143)
Litman, H.J., 1331 (AB0784)
Litovchenko, I., 1321 (AB0761)
Little, C., 126 (OP0180)
Little, E.M., 409 (THU0537)
Little, R., 1023 (SAT0657)
Litviakov, A., 1497 (FRI0737-HPR)
Litvitskiy, P., 1082 (AB0105)
Litvyakov, A., 1430 (AB1072, AB1074)
Liu, A., 289 (THU0226), 1096 (AB0142)
Liu, B., 778 (SAT0030)
Liu, C., 291 (THU0232)
Liu, D., 1464 (AB1167)
Liu, F., 1077 (AB0087)
Liu, F.-C., 1408 (AB1009)
Liu, H., 180 (OP0301), 1082 (AB0102)
Liu, J., 324 (THU0318), 637 (FRI0395), 1260 (AB0596), 1415 (AB1031), 1535 (AB1210-HPR)
Liu, L., 600 (FRI0301), 1206 (AB0447)
Liu, M., 352 (THU0386), 953 (SAT0471)
Liu, N., 1083 (AB0106)
Liu, P., 965 (SAT0502)
Liu, R., 197 (OP0342), 969 (SAT0512), 1226 (AB0501)
Liu, S., 370 (THU0432), 371 (THU0434, THU0435)
Liu, W., 122 (OP0168)
Liu, X., 69 (OP0043), 348 (THU0376), 678 (FRI0501), 872 (SAT0261), 1082 (AB0102), 1121 (AB0210), 1226 (AB0502), 1260 (AB0596)
Liu, Y., 212 (THU0036), 286 (THU0217), 459 (THU0669), 484 (FRI0013), 859 (SAT0226), 1204 (AB0440), 1218 (AB0480), 1295 (AB0691), 1464 (AB1167), 1467 (AB1175), 1524 (SAT0757-HPR)
Liu, Z., 288 (THU0222)
Liu-Leage, S.S., 794 (SAT0070)
Liuzza, S., 901 (SAT0341)
Lizzi, A., 891 (SAT0313)
Lizzi, A.R., 721 (FRI0613)
Ljuhar, D., 1423 (AB1053)
Ljuhar, R., 1423 (AB1053)
Ljung, L., 114 (OP0149), 444 (THU0632)
Ljunggren, Ö., 72 (OP0050)
Llado, A.C., 1429 (AB1070)
Llamas, P., 128 (OP0186)
Llano Hernández, K., 990 (SAT0564)
Llanos, C., 1098 (AB0148)
Llinares, T., 1351 (AB0840)
Llinares-Tello, F., 1016 (SAT0638), 1296 (AB0693)
Llinas, H., 365 (THU0417)
Lliso-Ribera, G., 238 (THU0100), 511 (FRI0088)
Llisterri, J.L., 761 (FRI0715), 1456 (AB1146, AB1147)
Llobet, J.M., 914 (SAT0379)
Llop Vilaltella, M., 642 (FRI0409)
Llop Vilatella, M., 701 (FRI0559), 1391 (AB0961)
Llorca, J., 139 (OP0209-HPR), 1084 (AB0108)
Llorens, V., 350 (THU0381)
Llorente, I., 633 (FRI0385), 908 (SAT0363), 1270 (AB0625)
Llorente, L., 1147 (AB0282)
Lloves, N., 933 (SAT0427)
Lloves Schenone, N.M., 387 (THU0479)
Lloyd, M., 1396 (AB0976)
Lluch, J., 663 (FRI0468), 1375 (AB0914)
Lluch, P., 614 (FRI0336)
Lo, K.H., 335 (THU0348), 341 (THU0360), 671 (FRI0486), 1295 (AB0692)
Lo, L.Y.T., 589 (FRI0271)
Lo Gullo, A., 1312 (AB0738)
Lo Monaco, A., 829 (SAT0158)
Lo Monaco, M., 901 (SAT0341)
Lo Pizzo, M., 291 (THU0231)
Lo Vullo, M., 876 (SAT0273)
Loarce-Martos, J., 698 (FRI0549)
Lobato Faria, P., 441 (THU0622)
Lobbedez, T., 330 (THU0337), 1256 (AB0587)
Lobosco, S., 932 (SAT0425)
Locht, H., 332 (THU0340)
Loef, M., 976 (SAT0529)
Loeffen, D., 740 (FRI0662)
Loeuille, D., 103 (OP0121), 662 (FRI0465), 663 (FRI0467), 1013 (SAT0632)
Löffler, C., 597 (FRI0294)
Loft, A.G., 553 (FRI0190)
Logeart, I., 337 (THU0353), 350 (THU0382)
Loghin-Oprea, N., 309 (THU0279), 1284 (AB0664)
Loginova, E., 943 (SAT0451), 944 (SAT0452), 956 (SAT0478), 1327 (AB0775)
Loginova, E.Y., 674 (FRI0491), 943 (SAT0450), 1317 (AB0749)
Lohmander, L., 973 (SAT0523)
Lohmann, C.H., 1072 (AB0074)
Lohr, J., 777 (SAT0027)
Lohse, A., 56 (OP0014)
Loi, A., 975 (SAT0528)
Lois-Iglesias, A., 587 (FRI0267), 1107 (AB0173)
Loiskandl, M., 1547 (AB1245-HPR)
Lojacono, A., 70 (OP0046), 1214 (AB0467)
Lojo, L., 633 (FRI0385), 908 (SAT0363), 1270 (AB0625)
Løkke, A., 546 (FRI0174)
Lomakina, O., 186 (OP0316), 539 (FRI0154), 1387 (AB0950, AB0951)
Lomax, K.G., 448 (THU0641)
Lomborg, K., 454 (THU0657), 1517 (SAT0738-HPR)
Lomborg, N., 710 (FRI0583)
Lomholt, S., 505 (FRI0074), 1088 (AB0119)
Londoño, J., 1453 (AB1137)
Londono, J., 201 (THU0005), 218 (THU0052), 252 (THU0137), 752 (FRI0694), 993 (SAT0573, SAT0574, SAT0575), 994 (SAT0576), 1132 (AB0239), 1375 (AB0913)
Londono Jimenez, A., 297 (THU0247)
Longo, D., 1483 (THU0743-HPR)
Longo, F.J.L., 1297 (AB0695)
Longu, M.G., 496 (FRI0046), 535 (FRI0143)
Loni, E., 1012 (SAT0629)
Lönnblom, E., 779 (SAT0031)
Lood, C., 302 (THU0260)
Lopalco, A., 1059 (AB0037)
Lopalco, G., 56 (OP0015), 411 (THU0540), 521 (FRI0110), 711 (FRI0586), 1059 (AB0037), 1461 (AB1160)
Lopatnikova, J., 1056 (AB0027)
Lopes, A.P., 1089 (AB0121)
Lopes, C., 1052 (AB0016), 1153 (AB0300)
Lopes, C.D., 441 (THU0622)
Lopes, I., 498 (FRI0051), 1080 (AB0098)
Lopes, J.B., 1448 (AB1124)
Lopes, L.M., 167 (OP0269)
Lopes, T., 1051 (AB0013), 1094 (AB0134)
Lopes Barreto, D., 1421 (AB1047), 1497 (FRI0739-HPR)
López, A., 213 (THU0037), 748 (FRI0683), 974 (SAT0524), 1297 (AB0695)
Lopez, A., 570 (FRI0228), 838 (SAT0179)
Lopez, B., 64 (OP0032), 1265 (AB0611)
López, C., 415 (THU0550), 1351 (AB0840)
Lopez, J., 1384 (AB0942)
López, L., 1351 (AB0843), 1469 (AB1183)
Lopez, M., 843 (SAT0191)
López, M.D., 1351 (AB0840)
López, P., 803 (SAT0093), 1079 (AB0093)
Lopez, P., 1233 (AB0522)
Lopez, R., 1397 (AB0979)
Lopez Chozas, J.M., 574 (FRI0237)
López de Figueroa, P., 53 (OP0008)
López de Recalde, M., 663 (FRI0468), 1375 (AB0914)
Lopez Dupla, M., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
López Esteban, A., 1476 (THU0720-HPR)
López Flores, A.P., 1357 (AB0861)
López Gutiérrez, F., 696 (FRI0545), 697 (FRI0546)
Lopez Longo, J., 1414 (AB1029), 1476 (THU0720-HPR)
Lopez Lopez, C.O., 363 (THU0411), 365 (THU0417)
Lopez Macay, A., 1357 (AB0861)
López Medina, C., 975 (SAT0527)
Lopez Medina, E.C., 258 (THU0151), 700 (FRI0555)
López Robles, A., 719 (FRI0608), 1232 (AB0518)
Lopez Suarez, J.M., 574 (FRI0237)
Lopez-Armada, M.J., 502 (FRI0063)
López-Carrasco, G., 1225 (AB0499)
López-Cerón, A., 1276 (AB0640)
López-Chicheri, I., 111 (OP0142-HPR)
López-Corbeto, M., 290 (THU0227), 900 (SAT0339), 946 (SAT0458)
Lopez-Dupla, M., 597 (FRI0293)

López-González, R., 1166 (AB0337)
Lopez-Gonzalez, R., 139 (OP0209-HPR)
López-Hoyos, M., 594 (FRI0286), 1229 (AB0511), 1230 (AB0512)
López-Isac, E., 1047 (AB0003)
López-Lasanta, M., 177 (OP0292), 290 (THU0227), 776 (SAT0022), 946 (SAT0458)
López-Longo, F., 326 (THU0326), 1107 (AB0173)
Lopez-Longo, F., 633 (FRI0385), 1270 (AB0625)
López-Longo, F.J., 290 (THU0227), 386 (THU0474), 462 (THU0676), 656 (FRI0448), 737 (FRI0653), 748 (FRI0683), 908 (SAT0363), 1276 (AB0640)
Lopez-Longo, F.J., 1272 (AB0630)
López-Longo, J., 68 (OP0042), 587 (FRI0267), 873 (SAT0263)
López-Medina, A., 1001 (SAT0600)
LóPez-Medina, C., 1268 (AB0619)
López-Medina, C., 650 (FRI0434), 942 (SAT0447)
Lopez-Medina, C., 649 (FRI0431)
López-Medina, E.C., 350 (THU0380)
López-Mejías, R., 803 (SAT0093), 804 (SAT0095), 1084 (AB0108)
López-Montesinos, B., 75 (OP0059), 405 (THU0526)
López-Montilla, M.D., 942 (SAT0447)
Lopez-Montilla, M.D., 649 (FRI0431)
López-Morales, P., 993 (SAT0574)
Lopez-Olivo, M.A., 851 (SAT0208)
López-Ortega, J.M., 1410 (AB1016), 1415 (AB1032)
López-Otín, C., 53 (OP0008)
Lopez-Pedrera, C., 194 (OP0336), 287 (THU0218), 492 (FRI0035), 497 (FRI0048), 504 (FRI0069), 622 (FRI0360), 648 (FRI0429), 649 (FRI0431), 1078 (AB0092), 1082 (AB0104), 1091 (AB0127, AB0128), 1450 (AB1130)
López-Reyes, A., 205 (THU0016), 291 (THU0230)
Lopez-Reyes, A., 216 (THU0047)
Lopez-Reyes, A.G., 1067 (AB0059)
López-Robledillo, J.C., 400 (THU0514), 1386 (AB0947)
López-Rodriguez, W., 974 (SAT0524)
López-Romero, P., 794 (SAT0070)
Lopez-Romero, P., 233 (THU0088)
Lopez-Salguero, S., 705 (FRI0570, FRI0571)
Lopriore, S., 521 (FRI0110), 1268 (AB0618)
Lopuhaa, N., 1479 (THU0730-HPR), 1485 (THU0748-HPR), 1559 (PARE0022)
Lora, P., 1391 (AB0960)
Lóránd, V., 915 (SAT0380)
Lorente, M., 1016 (SAT0638), 1296 (AB0693), 1351 (AB0840)
Lorentzen, M., 338 (THU0354), 472 (THU0700), 549 (FRI0182)
Lorentzon, M., 916 (SAT0382)
Lorenz, H.-M., 159 (OP0249), 516 (FRI0098), 577 (FRI0245), 754 (FRI0698), 1070 (AB0068), 1141 (AB0267), 1193 (AB0412)
Lorenzetti, R., 615 (FRI0339)
Lorenzin, M., 99 (OP0113), 1315 (AB0745)
Lorenzo, N., 885 (SAT0298), 1231 (AB0517)
Lorenzo, R., 712 (FRI0589), 1252 (AB0576), 1400 (AB0988)
Lorenzo-Castro, R., 1409 (AB1012)
Lorenzoni, V., 457 (THU0664)
Loricera, J., 108 (OP0135), 405 (THU0526), 614 (FRI0336), 1255 (AB0583, AB0584)
Lories, R., 3 (SP0009), 19 (SP0079)
Lorkowski, S., 115 (OP0151)
Lorusso, O., 1135 (AB0250)
Losina, E., 1032 (SAT0679)
Lotfy, N.M., 307 (THU0272), 1216 (AB0473)
Lottenburger, T., 732 (FRI0641)
Lotz, M., 53 (OP0008)
Louati, K., 1299 (AB0702)
Loughrey, A., 1372 (AB0904)
Louka, P., 1021 (SAT0651)
Loukina, G., 273 (THU0188), 1157 (AB0311)
Loureiro, J., 324 (THU0320), 1071 (AB0070)
Loureiro, M.J., 1264 (AB0607)
Lourido, L., 980 (SAT0539), 1135 (AB0249)
Louthrenoo, W., 1298 (AB0700)
Louw, I., 75 (OP0058), 831 (SAT0162)
Louzada Jr., P., 1160 (AB0320)
Louzir, B., 998 (SAT0590)
Love, T.J., 686 (FRI0518)
Lovell, D., 75 (OP0058), 396 (THU0503), 405 (THU0525)
Lovisi, B., 1520 (SAT0745-HPR)
Lovy, M., 703 (FRI0564), 1366 (AB0888)
Low, P., 1020 (SAT0650)
Low, P.S., 494 (FRI0041)
Loyo, E., 1233 (AB0522), 1456 (AB1145)
Loza, E., 414 (THU0549), 1318 (AB0752)
Loza, M., 577 (FRI0243)
Loza, M.I., 481 (FRI0005)
Loza, M.J., 94 (OP0103)
Lozada, A.C., 739 (FRI0660), 1006 (SAT0613)
Lozada, C., 739 (FRI0660), 1006 (SAT0613)
Lozano, L., 1041 (SAT0703), 1458 (AB1150)
Lozano, N., 1041 (SAT0704)
Lozano Cardenas, A., 1357 (AB0861)
Lozano-Herrero, J., 287 (THU0218)
Lozano-Rivas, N., 487 (FRI0021), 550 (FRI0184)
Lozano-Saez, A., 1472 (AB1191)
Lu, C., 1295 (AB0691)
Lu, C.-C., 1408 (AB1009)
Lu, H., 82 (OP0075)
Lu, H.-F., 692 (FRI0532)
Lu, L., 344 (THU0367)
Lu, N., 165 (OP0264), 360 (THU0405), 362 (THU0410)
Lu, X., 217 (THU0048)
Lubberts, E., 1058 (AB0033), 1088 (AB0118)
Luberda, B., 1470 (AB1184)
Lubrano, E., 756 (FRI0703), 1319 (AB0754)
Lucas, C., 989 (SAT0561), 1191 (AB0406)
Lucas, P., 436 (THU0610), 645 (FRI0420)
Lucas, R., 1177 (AB0368), 1466 (AB1172)
Lucas López, M.D., 487 (FRI0021)
Luccarini, J.M., 85 (OP0081)
Lucchese, L., 831 (SAT0161)
Lucchesi, D., 180 (OP0300)
Lucchetti, R., 496 (FRI0045)
Lucchino, B., 230 (THU0082), 1379 (AB0925)
Lucena, I.R.S., 403 (THU0520)
Lucherini, O.M., 1059 (AB0037)
Luchetti, M., 183 (OP0309)
Luchetti, M.M., 1189 (AB0400)
Luchihina, E., 1404 (AB0998)
Luchihina, E.L., 576 (FRI0241)
Luchikhina, E., 256 (THU0148), 572 (FRI0231), 1157 (AB0311), 1204 (AB0441)
Luchikhina, E.L., 251 (THU0132), 273 (THU0188), 1128 (AB0230)
Luciano, N., 584 (FRI0260), 589 (FRI0272), 875 (SAT0268)
Lucidi, F., 1378 (AB0924)
Lucila, G., 1245 (AB0556)
Łuczak, A., 1458 (AB1153)
Łuczak, J., 1119 (AB0206)
Lüders, S., 1008 (SAT0618)
Lugo-Zamudio, G.E., 1133 (AB0242)
Luijsterburg, P., 961 (SAT0492)
Luime, J., 157 (OP0245), 676 (FRI0497), 1308 (AB0725)
Luime, J.J., 678 (FRI0500), 1324 (AB0769), 1325 (AB0770)
Luís, R., 746 (FRI0678)
Luisa Pinto Correia, A., 795 (SAT0072)
Luisetto, R., 210 (THU0029), 1111 (AB0184)
Luissi, A., 1115 (AB0194)
Luján, S., 520 (FRI0106)
Lukas, C., 113 (OP0146), 235 (THU0093), 573 (FRI0234), 701 (FRI0561), 804 (SAT0094), 1159 (AB0315)
Lukawska, J., 1205 (AB0443)
Lukic, T., 276 (THU0195), 1202 (AB0436)
Lukina, G., 273 (THU0189), 843 (SAT0190), 848 (SAT0200), 850 (SAT0206)
Lukina, G.V., 576 (FRI0241)
Lukinov, V., 1056 (AB0027)
Lumetti, F., 634 (FRI0388), 1267 (AB0615), 1272 (AB0629)
Luna, M.S., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Luna-Zúñiga, T.A., 395 (THU0501), 1397 (AB0978)
Lunardi, C., 621 (FRI0357), 1047 (AB0003)
Lund, H., 794 (SAT0070)
Lund, M.B., 55 (OP0013), 106 (OP0129), 765 (FRI0725), 1043 (SAT0709)
Lundberg, I., 904 (SAT0352)
Lundberg, I.E., 626 (FRI0367), 896 (SAT0329), 912 (SAT0374)
Lundin, K.E.A., 472 (THU0700)
Lundström, E., 248 (THU0125)
Lundström, S., 1096 (AB0142)
Lunt, L., 190 (OP0327-PARE)
Lunt, M., 104 (OP0123), 146 (OP0225), 243 (THU0112), 519 (FRI0105), 765 (FRI0724), 1040 (SAT0700)
Luo, J., 108 (OP0132), 268 (THU0176), 1197 (AB0421), 1295 (AB0691)
Luo, S.-F., 85 (OP0080), 366 (THU0419)
Luo, T., 1219 (AB0482)
Luo, X., 1467 (AB1175)
Luo, Y., 848 (SAT0201), 986 (SAT0554), 1063 (AB0046)
Luo, Z., 149 (LB0003)
Luong, S.-N., 447 (THU0639)
Luosujärvi, R., 401 (THU0515), 1404 (AB0999)
Lupi, E., 540 (FRI0155)
Luppi, F., 248 (THU0123)
Luqmani, R., 107 (OP0130), 315 (THU0296), 316 (THU0297), 319 (THU0306), 605 (FRI0312)
Luqmani, R.A., 13 (SP0053), 33 (SP0133), 45 (SP0189), 318 (THU0302), 1254 (AB0581)
Luque, R.M., 648 (FRI0429), 1082 (AB0104), 1091 (AB0128)
Luque Pinilla, J.M., 1022 (SAT0653)
Luraschi, H., 359 (THU0402)
Lüscher, T.F., 500 (FRI0059)
Lustberg, M., 222 (THU0062)
Lusynets, T., 1171 (AB0352)
Lutfi, A., 587 (FRI0268)
Lüthke, K., 461 (THU0674)
Lutsenko, E.D., 1073 (AB0078)
Lutz, T., 397 (THU0504)
Lv, J., 294 (THU0238)
Lv, Q., 665 (FRI0471), 1086 (AB0113)
Ly, B., 289 (THU0225)
Lydersen, S., 1031 (SAT0677), 1032 (SAT0680), 1039 (SAT0698)
Lye, W.K., 1026 (SAT0666)
Lyn Shue, K.A., 884 (SAT0294)
Lyngvær, E.K., 1492 (THU0765-HPR)
Lysholm, J., 509 (FRI0085)
Lytton, S.D., 898 (SAT0335)
Lyu, S.-Y., 1408 (AB1009)

M-Costa, L., 326 (THU0326), 718 (FRI0607)
Ma, D., 419 (THU0563), 920 (SAT0393), 1079 (AB0094)
Ma, H., 884 (SAT0294)
Ma, H.-J., 291 (THU0232)
Ma, J.-D., 279 (THU0201), 488 (FRI0023), 798 (SAT0078)
Ma, L., 1506 (FRI0763-HPR)
Ma, X., 1430 (AB1073)
Ma, Y., 1535 (AB1210-HPR)
Maamouri, N., 1346 (AB0826)
Maaoui, R., 998 (SAT0589, SAT0590), 1383 (AB0936)
Maas, F., 928 (SAT0416)
Maat, B., 523 (FRI0113)
Maat, G.J., 1423 (AB1052)
Maatallah, K., 347 (THU0373), 1297 (AB0697), 1306 (AB0720)
Mabrook, A., 1216 (AB0474)
Mac Carter, D., 583 (FRI0256)
Macaluso, F., 263 (THU0164)
Macarron, P., 990 (SAT0564)
Macartney-Coxson, D., 383 (THU0464)
MacCarter, D., 1013 (SAT0631)
Macchioni, P., 323 (THU0316), 742 (FRI0667), 945 (SAT0454), 954 (SAT0473), 1022 (SAT0654), 1152 (AB0295), 1412 (AB1022)
Macchioni, P.L., 1248 (AB0564)
MacDermott, E.J., 1507 (FRI0766-HPR)
Macdonald, C., 1559 (PARE0021)

Macdonald, J., 529 (FRI0128)
Macedo, C.G., 443 (THU0627)
Macedo, R.B.V., 1056 (AB0028)
Maceiras, F., 556 (FRI0197)
Maceiras-Pan, F.J., 946 (SAT0457), 1322 (AB0764)
Macfarlane, G.J., 656 (FRI0450)
MacGregor, A., 803 (SAT0092)
MacGregor, A.J., 243 (THU0112)
Macgregor, A.J., 1030 (SAT0676), 1039 (SAT0699)
Machado, C., 814 (SAT0121)
Machado, C.R.L., 1056 (AB0028)
Machado, J.D.M., 802 (SAT0088)
Machado, L.G., 1448 (AB1124)
Machado, M.A., 825 (SAT0149)
Machado, P., 1510 (SAT0718-HPR)
Machado, P.M., 60 (OP0023), 466 (THU0685), 528 (FRI0126)
Machado, S.H., 403 (THU0520), 1391 (AB0960)
Machado-Alba, J.E., 514 (FRI0094), 1190 (AB0403)
Machado-Duque, M.E., 1190 (AB0403)
Machicado, V., 176 (OP0290), 1412 (AB1021)
Machin, A., 1174 (AB0359), 1552 (PARE0002)
Machold, K., 560 (FRI0207), 750 (FRI0688)
Macía, C., 1011 (SAT0626), 1408 (AB1011)
Macía Villa, C., 701 (FRI0559)
Macía Villa, C.C., 1439 (AB1098)
Macía-Díaz, M., 802 (SAT0088)
Macias, W., 513 (FRI0092), 1147 (AB0281)
Macías Chumacera, A., 1276 (AB0641)
Macieira, C., 436 (THU0610), 1254 (AB0581)
Maciejewski, A., 776 (SAT0023)
Maciel, G., 591 (FRI0278), 881 (SAT0286)
Mackay, C., 43 (SP0178)
Mackay, F., 182 (OP0307)
Mackerness, C., 609 (FRI0321)
Mackie, S.L., 613 (FRI0334)
Mackiewicz, Z., 622 (FRI0359)
Macovei, L., 435 (THU0607), 626 (FRI0368), 1032 (SAT0681)
Madariaga, A., 262 (THU0162)
Madariaga, H., 1196 (AB0419)
Madden, S., 384 (THU0468)
Madeira, N., 464 (THU0679), 929 (SAT0418), 1163 (AB0329)
Madelaine-Bonjour, C., 1489 (THU0758-HPR)
Mader, R., 1423 (AB1052)
Madrigal-Santillan, E.O., 1282 (AB0657)
Madrisotti, F., 427 (THU0586)
Madroñero, A.B., 1047 (AB0003)
Madroñero Vuelta, A.B., 1042 (SAT0706)
Madroñero-Vuelta:, B., 897 (SAT0332)
Madsen, O.R., 669 (FRI0481), 745 (FRI0674), 1328 (AB0778)
Madureira, P., 1254 (AB0581)
Maeda, K., 800 (SAT0083)
Maestripieri, V., 1269 (AB0622), 1270 (AB0623)
Maezawa, R., 531 (FRI0134), 1291 (AB0681)
Magalhães, C.S., 76 (OP0061)
Magallares, B., 914 (SAT0379), 1305 (AB0717), 1414 (AB1027)
Magallares, B.P., 904 (SAT0351)
Magallares López, B., 1386 (AB0948)
Magazzino, O., 254 (THU0143), 1135 (AB0250)
Magda, S., 626 (FRI0368), 1264 (AB0608)
Magder, L., 69 (OP0045)
Magder, L.S., 300 (THU0255), 1211 (AB0461), 1212 (AB0462)
Maged, L., 874 (SAT0265)
Maggi, E., 623 (FRI0362)
Maggi, L., 446 (THU0636)
Magnat, E., 382 (THU0463)
Magner, R., 846 (SAT0196)
Magni-Manzoni, S., 1015 (SAT0636)
Magnussen, A.S., 1492 (THU0765-HPR)
Magrey, M., 156 (OP0243)
Magri, G., 366 (THU0420)
Magri, S., 1143 (AB0271)
Magro, R., 1234 (AB0524), 1442 (AB1106)
Maguire, A., 939 (SAT0442)
Maguire, N., 1010 (SAT0624)
Maguire, P., 886 (SAT0301), 1229 (AB0509)
Magyar, M., 587 (FRI0268)
Mahadeva, S., 446 (THU0638)
Mahdi, A.M., 1358 (AB0862)
Mahdi, M.A., 1365 (AB0883, AB0884, AB0885), 1418 (AB1041)
Mahfoudhi, A., 1397 (AB0980)
Mahgoub, E., 832 (SAT0164)
Mahler, M., 461 (THU0674), 911 (SAT0372), 1025 (SAT0662)
Mahlich, J., 440 (THU0620), 547 (FRI0177)
Mahmood, S., 227 (THU0076), 434 (THU0604), 473 (THU0703)
Mahmoud, E., 670 (FRI0482)
Mahmoud, I., 347 (THU0373), 1073 (AB0077), 1297 (AB0697), 1306 (AB0720), 1373 (AB0906, AB0907, AB0908), 1377 (AB0919)
Mahmoud, N.K., 1045 (SAT0715)
Mahmutović, E., 1327 (AB0774)
Mahomed, N., 1035 (SAT0688)
Mahran, S.A., 1339 (AB0804)
Maier, A., 437 (THU0611), 1439 (AB1099)
Maier, R., 647 (FRI0425)
Maier-Peuschel, M., 356 (THU0395)
Maigné, G., 617 (FRI0345)
Maijer, K., 781 (SAT0037)
Maillere, B., 20 (SP0081)
Maillet, J., 53 (OP0007)
Maindet-Dominici, C., 388 (THU0480)
Mainero Mendoza, S., 918 (SAT0388)
Maini, P., 428 (THU0587)
Maíz, O., 75 (OP0059), 326 (THU0326), 405 (THU0526), 718 (FRI0607), 1166 (AB0337)
Maiz, O., 350 (THU0381), 843 (SAT0191)
Majdan, M., 251 (THU0133), 1273 (AB0631), 1470 (AB1184)
Majewski, M., 1470 (AB1184)
Majumdar, A., 1074 (AB0079)
Mak, A., 730 (FRI0636)
Mak, W.Y., 796 (SAT0073), 1520 (SAT0747-HPR)
Makadsi, R., 1246 (AB0559)
Makarov, E., 617 (FRI0346)
Makarov, S., 269 (THU0179)
Makay, B., 53 (OP0009-HPR), 1387 (AB0949), 1522 (SAT0751-HPR)
Makdissi, J., 1205 (AB0444)
Makhloufi, M., 1359 (AB0866)
Makhloufi, M.M., 982 (SAT0545)
Makhzoum, A., 71 (OP0049)
Maki, H., 1274 (AB0635)
Mäkinen, H., 1404 (AB0999)
Makowka, A., 897 (SAT0333)
Makowska, J., 1458 (AB1152, AB1153)
Makris, A., 1376 (AB0915)
Maksymowych, W., 60 (OP0023), 131 (OP0192), 1301 (AB0707)
Maksymowych, W.P., 103 (OP0121), 337 (THU0352, THU0353), 350 (THU0382), 469 (THU0693), 471 (THU0697), 496 (FRI0047), 663 (FRI0467), 668 (FRI0478), 933 (SAT0428), 1009 (SAT0622)
Malagon, M., 194 (OP0336)
Malamet, R., 375 (THU0444), 379 (THU0455)
Malatesta, M., 891 (SAT0315)
Malatestinic, W., 1330 (AB0783)
Malattia, C., 1015 (SAT0636)
Malaviya, A.N., 1506 (FRI0762-HPR), 1540 (AB1226-HPR)
Malavolta, N., 366 (THU0420), 437 (THU0611), 954 (SAT0473), 1200 (AB0429), 1439 (AB1099)
Malcata, A., 1254 (AB0581)
Malcolm, S., 965 (SAT0502)
Maldonado, G., 734 (FRI0645), 1160 (AB0318, AB0319)
Maldonado, M., 782 (SAT0041), 1135 (AB0248), 1408 (AB1010)
Maldonado, R., 1395 (AB0974), 1534 (AB1206-HPR)
Maldonado, V., 908 (SAT0363)
Maldonado Cocco, J.A., 670 (FRI0483), 933 (SAT0427)
Maldonado Ficco, H., 933 (SAT0427)
Maldonado Romero, L.V., 698 (FRI0549)
Maleh, H., 641 (FRI0406)
Maleitzke, T., 129 (OP0187)
Malemba, J.-J., 1310 (AB0732)
Malenkov, Y.A., 507 (FRI0078), 1077 (AB0089)
Malézieux-Picard, A., 991 (SAT0569)
Małgorzewicz, S., 895 (SAT0327)
Malievsky, V.A., 1049 (AB0008)
Malik, F., 1421 (AB1049)
Malik, V., 318 (THU0301)
Malitchi, R., 1429 (AB1069)
Mallaci Bocchio, R., 901 (SAT0341)
Mallak, I., 667 (FRI0476)
Mallalieu, N.L., 107 (OP0131), 133 (OP0197), 396 (THU0503)
Mallano, T., 892 (SAT0318)
Mallen, C., 751 (FRI0690), 1028 (SAT0672), 1442 (AB1107)
Mallen, C.D., 8 (SP0031), 1043 (SAT0708), 1433 (AB1081)
Mallett, S., 107 (OP0130)
Mallia, L., 1378 (AB0924)
Malmström, V., 212 (THU0036), 482 (FRI0006), 484 (FRI0013), 779 (SAT0032), 1051 (AB0015)
Maloberti, A., 1154 (AB0301)
Malochet-Guinamand, S., 813 (SAT0117), 1033 (SAT0682), 1297 (AB0696), 1360 (AB0869), 1384 (AB0942)
Malouf Sierra, J., 1386 (AB0948)
Malpica, A., 963 (SAT0496), 1502 (FRI0751-HPR), 1534 (AB1207-HPR)
Malumbres, S., 1424 (AB1055)
Malviya, S., 1236 (AB0530)
Mamani, M., 387 (THU0479), 906 (SAT0357), 933 (SAT0427), 1429 (AB1071)
Mameli, G., 496 (FRI0046)
Mammadov, E., 1310 (AB0731)
Mammen, A., 913 (SAT0376)
Mammen, A.L., 67 (OP0038)
Mamoto, K., 540 (FRI0156), 955 (SAT0477), 1023 (SAT0658), 1134 (AB0245), 1324 (AB0768), 1426 (AB1061)
Manabe, Y., 800 (SAT0083)
Manara, M., 270 (THU0181)
Manci, E., 53 (OP0009-HPR), 1522 (SAT0751-HPR)
Mancini, R., 470 (THU0696), 880 (SAT0283)
Mancuso, P., 323 (THU0316)
Mandai, K., 260 (THU0157), 1178 (AB0373)
Mandegaran, R., 938 (SAT0438)
Mandelikova, S., 369 (THU0429)
Mandelin, A.M., 1125 (AB0220)
Mandell, B., 365 (THU0416), 1368 (AB0892)
Mandhair, H., 1420 (AB1045)
Mandl, L.A., 467 (THU0687), 1437 (AB1094)
Mandl, P., 10 (SP0038), 25 (SP0101), 175 (OP0288), 445 (THU0633), 742 (FRI0668), 971 (SAT0515), 1428 (AB1067)
Mandl, T., 311 (THU0284), 464 (THU0681), 542 (FRI0162), 886 (SAT0302)
Mandraffino, G., 1312 (AB0738)
Maneiro, J.R., 1159 (AB0316)
Manero, J., 326 (THU0326)
Manetti, M., 504 (FRI0070), 623 (FRI0362)
Manferdini, C., 1069 (AB0064)
Manfredi, A., 248 (THU0123), 621 (FRI0357), 1267 (AB0616), 1272 (AB0630), 1281 (AB0656)
Manfredi, A.A., 316 (THU0299), 328 (THU0331), 725 (FRI0624)
Manfredi, L., 1189 (AB0400)
Manfredi, M., 646 (FRI0423)
Mangan, E., 94 (OP0102), 575 (FRI0240)
Mangan, E.K., 838 (SAT0180), 849 (SAT0202), 853 (SAT0212)
Manganelli, V., 490 (FRI0028)
Manger, B., 159 (OP0249), 516 (FRI0098), 530 (FRI0130)
Manger, K., 159 (OP0249), 516 (FRI0098)
Mangnus, L., 473 (THU0704), 743 (FRI0670), 1050 (AB0012)
Mani, L., 926 (SAT0409)
Manilo, N., 553 (FRI0190)
Manivel, V.A., 228 (THU0077)
Manivet, P., 1371 (AB0900)
Manka, V., 1449 (AB1126)
Mankia, K., 518 (FRI0102)
Mankia, K.S., 238 (THU0101), 727 (FRI0630)
Mann, C., 356 (THU0395)
Mann, H., 209 (THU0027), 243 (THU0113),

638 (FRI0399), 656 (FRI0450), 906 (SAT0358), 1280 (AB0653), 1287 (AB0671), 1416 (AB1034)
Mann, H.F., 220 (THU0058)
Mannerkorpi, K., 163 (OP0258-HPR, OP0260-HPR), 1487 (THU0754-HPR), 1503 (FRI0753-HPR), 1538 (AB1219-HPR)
Manocha, S., 82 (OP0075)
Manolova, I., 1048 (AB0005)
Manounah, L., 1369 (AB0896)
Manoussakis, M.N., 1089 (AB0122)
Manrique-Arija, S., 261 (THU0160), 391 (THU0489), 1174 (AB0361), 1175 (AB0362), 1443 (AB1109), 1492 (THU0766-HPR)
Mansiz Kaplan, B., 1405 (AB1003)
Mansmann, U., 789 (SAT0056)
Mansour, A.I., 985 (SAT0551), 1148 (AB0285)
Mansour, H.E., 1219 (AB0481)
Mansour, H.E.S., 307 (THU0272)
Mansour, N., 303 (THU0262)
Mansueto, N., 895 (SAT0325)
Manthou, E., 1536 (AB1215-HPR)
Mantilla, R.D., 575 (FRI0238), 850 (SAT0205), 1196 (AB0419), 1250 (AB0570)
Mantovani, L.G., 445 (THU0634), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Manukyan, G., 970 (SAT0514)
Manwani, R., 227 (THU0076), 1427 (AB1064)
Manzano Fernandez, S., 1041 (SAT0704)
Manzo, A., 237 (THU0099), 458 (THU0667), 787 (SAT0053), 790 (SAT0060)
Mao, R., 981 (SAT0541)
Mapplebeck, S., 609 (FRI0321)
Marabelle, A., 5 (SP0018), 51 (OP0004)
Maracle, C.X., 1064 (AB0049)
Marampon, F., 1057 (AB0029, AB0030)
Marang-van de Mheen, P.J., 1040 (SAT0701)
Maraoui, M., 1000 (SAT0598), 1169 (AB0346, AB0347), 1170 (AB0348)
Marbury, T.C., 371 (THU0433)
Marcaida, P.M., 906 (SAT0357)
March, C., 897 (SAT0333)
March, L., 470 (THU0695), 760 (FRI0713), 818 (SAT0132), 960 (SAT0489), 1440 (AB1102)
Marchand-Adam, S., 1049 (AB0007)
Marchesoni, A., 56 (OP0015), 343 (THU0365, THU0366), 564 (FRI0215)
Marchetta, A., 945 (SAT0454)
Marchetti, C., 89 (OP0090)
Marco Mingot, M., 1016 (SAT0638)
Marco-Mingot, M., 1296 (AB0693), 1351 (AB0840)
Marconcin, P.P., 1553 (PARE0005)
Marcondes, N., 1107 (AB0174), 1278 (AB0645)
Marcos, J., 1202 (AB0434), 1263 (AB0606)
Marcoval, J., 1375 (AB0914)
Marcu, I.R., 478 (THU0717)
Marcu, R.I., 379 (THU0454)
Marcu-Malina, V., 508 (FRI0082)
Mardanyan, S., 787 (SAT0051)
Mardenly, G., 583 (FRI0256)
Marecek, O., 1287 (AB0671)
Marenco, J.L., 728 (FRI0631), 1018 (SAT0643), 1182 (AB0384), 1417 (AB1036)
Marenco de la Fuente, J.L., 290 (THU0227), 1210 (AB0458), 1211 (AB0459)
Margarita, D., 1455 (AB1142)
Margiotta, D., 151 (OP0233)
Margiotta, D.P.E., 263 (THU0164), 304 (THU0267), 876 (SAT0273)
Marhadour, T., 258 (THU0152), 309 (THU0278), 662 (FRI0465), 811 (SAT0112), 1013 (SAT0632), 1215 (AB0469)
Marí Alfonso, B., 897 (SAT0332)
Maria, N.I., 92 (OP0097)
María Celina, D.L.V., 440 (THU0619)
Maribo, T., 454 (THU0657)
Marie, K., 710 (FRI0584)
Mariette, X., 51 (OP0004), 57 (OP0017), 67 (OP0040), 160 (OP0253), 182 (OP0307), 258 (THU0152), 289 (THU0225), 311 (THU0284), 464 (THU0681), 508 (FRI0081), 549 (FRI0180), 567 (FRI0221), 577 (FRI0245), 811 (SAT0112), 886 (SAT0302), 965 (SAT0501), 1141 (AB0267), 1193 (AB0412)
Marijnissen, A., 741 (FRI0664)
Marijnissen, A.K., 1020 (SAT0649), 1344 (AB0818)
Marijnissen, W.-J.C., 967 (SAT0506)
Marin, A., 1386 (AB0948)
Marin, G., 235 (THU0093)
Marin, J., 1333 (AB0789)
Marín-Ballvé, A., 897 (SAT0332)
Marinez Angosto, F.A., 1041 (SAT0704)
Marinho, A., 902 (SAT0346)
Marini, R., 76 (OP0061)
Marinsek, N., 448 (THU0641)
Mariotte, D., 330 (THU0337), 617 (FRI0345), 1256 (AB0587)
Mark, P., 847 (SAT0198)
Markatseli, T.E., 1329 (AB0779)
Markelova, E., 256 (THU0148), 572 (FRI0231), 944 (SAT0452)
Marklein, B., 769 (SAT0004), 773 (SAT0014), 1081 (AB0101)
Markomichelakis, N., 602 (FRI0306)
Markova, G.A., 1337 (AB0799)
Markovic, S., 1044 (SAT0711)
Markovits, D., 333 (THU0343), 910 (SAT0368)
Markusse, I.M., 516 (FRI0097)
Marois, I., 769 (SAT0002)
Marone, G., 490 (FRI0030)
Maroof, A., 213 (THU0038), 221 (THU0060)
Maróstica, P.J.C., 403 (THU0520), 1391 (AB0960)
Marotta, A., 481 (FRI0004), 496 (FRI0047), 791 (SAT0062), 1009 (SAT0622)
Marotte, H., 218 (THU0051)
Marou, E., 1271 (AB0626), 1279 (AB0648)
Marquardt, K., 193 (OP0333)
Marquart, K., 893 (SAT0319)
Marques, A., 112 (OP0144-HPR), 694 (FRI0537), 700 (FRI0558), 702 (FRI0562)
Marques, A.A., 30 (SP0119)
Marques, A.P., 386 (THU0475)
Marques, C.D.L., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562), 990 (SAT0566), 991 (SAT0567), 1372 (AB0903)
Marques, E., 1382 (AB0935)
Marques, M., 700 (FRI0558)
Marques, M.L., 694 (FRI0537), 702 (FRI0562)
Marques, O.C., 44 (SP0181)
Marques, R., 464 (THU0679), 1090 (AB0124), 1464 (AB1168)
Marques, V.B., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Márquez Fernández, V., 1289 (AB0676)
Marrache, A.M., 554 (FRI0191)
Marras, C., 550 (FRI0184), 556 (FRI0197)
Marras Fernández-Cid, C., 487 (FRI0021)
Marsais, F., 118 (OP0161)
Marsal, J., 655 (FRI0445)
Marsal, S., 177 (OP0292), 290 (THU0227), 776 (SAT0022), 946 (SAT0458), 1135 (AB0249)
Marsal Barril, S., 139 (OP0209-HPR)
Marschner, G., 772 (SAT0011), 1108 (AB0175)
Marshall, D., 89 (OP0089)
Marshall, L., 402 (THU0519), 832 (SAT0164), 1028 (SAT0670)
Marshall, T., 243 (THU0112)
Marsico, A., 808 (SAT0105), 1327 (AB0773)
Marsman, A.F., 61 (OP0025)
Marta, D., 626 (FRI0368)
Marteau, P., 56 (OP0014)
Martel-Pelletier, J., 126 (OP0181), 483 (FRI0009)
Mårtensson, I.-L., 779 (SAT0031)
Marti, M., 1041 (SAT0703), 1458 (AB1150)
Martin, A., 334 (THU0346), 335 (THU0349), 339 (THU0356, THU0357), 388 (THU0482), 389 (THU0483), 665 (FRI0472), 1032 (SAT0681), 1296 (AB0694)
Martin, D., 862 (SAT0235)
Martin, F., 710 (FRI0584)
Martín, J., 1084 (AB0108)
Martin, J., 1047 (AB0003)
Martin, K.R., 140 (OP0211-PARE)
Martin, L., 933 (SAT0428)
Martín, M., 213 (THU0037)
Martin, M., 523 (FRI0114)
Martin, M.A., 1406 (AB1004)
Martin, P., 179 (OP0298)
Martin, R.S., 864 (SAT0240)
Martin, T., 106 (OP0128), 709 (FRI0582)
Martín Garrido, I., 1022 (SAT0653)
Martín Martínez, M., 719 (FRI0608), 1232 (AB0518)
Martin Martinez, M.A., 139 (OP0209-HPR)
Martín Mola, E., 840 (SAT0183)
Martín Pedraz, L., 1393 (AB0968)
Martin Segarra, O., 1022 (SAT0653)
Martin Silva, N., 330 (THU0337), 617 (FRI0345), 1256 (AB0587)
Martín-Alarcón, J., 1542 (AB1231-HPR)
Martín-Arranz, M.D., 918 (SAT0387), 1307 (AB0723)
Martín-López, M., 251 (THU0134)
Martin-Lopez, M., 569 (FRI0226)
Martin-Marquez, B.-T., 1169 (AB0345)
Martin-Martin, L.S., 270 (THU0181)
Martín-Martínez, M.A., 873 (SAT0263)
Martin-Mola, E., 501 (FRI0062)
Martin-Nares, E., 417 (THU0556), 878 (SAT0278)
Martín-Varillas, J., 742 (FRI0666)
Martin-Varillas, J., 1116 (AB0197)
Martinelli, E., 484 (FRI0012)
Martínez, A., 178 (OP0294), 555 (FRI0195), 826 (SAT0150), 1293 (AB0686), 1294 (AB0687)
Martinez, A., 551 (FRI0186), 559 (FRI0204), 833 (SAT0168), 1498 (FRI0741-HPR)
Martínez, C., 1128 (AB0229)
Martinez, C., 287 (THU0218)
Mártínez, E., 1289 (AB0676)
Martínez, E., 873 (SAT0264), 1245 (AB0555)
Martínez, F., 324 (THU0320)
Martínez, H., 178 (OP0294), 980 (SAT0540), 1466 (AB1174)
Martinez, H., 761 (FRI0715), 1456 (AB1146, AB1147)
Martinez, J., 633 (FRI0385), 1270 (AB0625)
Martinez, L., 914 (SAT0379)
Martinez, M., 202 (THU0006)
Martinez, M.A., 914 (SAT0379)
Martinez, M.T., 1455 (AB1142)
Martínez, R., 1422 (AB1050)
Martinez, S., 1014 (SAT0635)
Martínez Barrio, J., 386 (THU0474), 656 (FRI0448)
Martinez Barrio, J., 1414 (AB1029)
Martínez Bonilla, G., 1276 (AB0641)
Martinez Bonilla, G., 1450 (AB1128)
Martínez Cordellat, I., 291 (THU0229), 441 (THU0623), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1349 (AB0837), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Martinez Feito, A., 824 (SAT0145)
Martínez Ferrín, J., 487 (FRI0021)
Martinez Ferrin, J., 1041 (SAT0704)
Martínez Jañez, N., 698 (FRI0549)
Martinez MArtinez, M.U., 1164 (AB0331)
Martinez Martinez, M.U., 760 (FRI0714)
Martinez Perez, J.M., 716 (FRI0601)
Martínez Sanchez, I.R., 153 (OP0238)
Martínez Taboada, V., 885 (SAT0299), 1232 (AB0519)
Martínez Valle, F., 900 (SAT0340), 1262 (AB0602)
Martínez-Angosto, F.A., 487 (FRI0021)
Martinez-Arroyo, A.M., 1490 (THU0761-HPR)
Martínez-Barrio, J., 462 (THU0676), 748 (FRI0683), 1276 (AB0640)
Martinez-Bonilla, G.E., 117 (OP0158), 1446 (AB1116)
Martínez-Cáceres, E., 1236 (AB0529)
Martínez-Costa, L., 420 (THU0567), 1166 (AB0337)
Martínez-Cristóbal, A., 1490 (THU0761-HPR)
Martinez-Feito, A., 456 (THU0661), 555 (FRI0194), 822 (SAT0141), 1179 (AB0375)
Martínez-Ferrer, Á., 1316 (AB0746), 1410 (AB1016)
Martínez-Ferrer, À., 1415 (AB1032)
Martínez-Ferrer, A., 258 (THU0153), 1168 (AB0344)
Martinez-Ferrer, À., 1534 (AB1208-HPR)
Martínez-Flores, G., 395 (THU0501), 1397 (AB0978)
Martínez-Flores, K., 205 (THU0016)
Martinez-Flores, K., 1067 (AB0059)
Martínez-Galla, D., 760 (FRI0714)

Martínez-Lavin, M., 1006 (SAT0613)
Martínez-Martínez, M., 586 (FRI0264)
Martínez-Martínez, M.U., 1345 (AB0820)
Martínez-Moreno, A., 253 (THU0140), 534 (FRI0141), 1156 (AB0309), 1157 (AB0310)
Martinez-Moreno, A., 1118 (AB0204), 1119 (AB0205)
Martínez-Morillo, M., 988 (SAT0560), 1241 (AB0544), 1424 (AB1055)
Martinez-Morillo, M., 1236 (AB0529)
Martinez-Nava, G., 1067 (AB0059)
Martínez-Nava, G.A., 205 (THU0016), 291 (THU0230)
Martinez-Osuna, P., 789 (SAT0058)
Martínez-Prada, C., 990 (SAT0564)
Martínez-Quintanilla, L., 527 (FRI0123)
Martínez-Rivera, J.-I., 498 (FRI0052)
Martínez-Rodríguez, I., 1255 (AB0583, AB0584)
Martinez-Rodriguez, N., 201 (THU0005), 218 (THU0052)
Martínez-Taboada, V., 594 (FRI0286), 1229 (AB0511), 1230 (AB0512)
Martínez-Taboada, V.M., 177 (OP0292)
Martínez-Valle, F., 415 (THU0550)
Martinez-Valle, F., 317 (THU0300)
Martinez-Zapico, A., 330 (THU0336)
Martini, A., 75 (OP0058), 396 (THU0503), 405 (THU0525)
Martinis, F., 343 (THU0365)
Martino, E., 496 (FRI0045)
Martino, S., 1012 (SAT0630), 1554 (PARE0008)
Martinović Kaliterna, D., 1283 (AB0661)
Martins, C., 1051 (AB0013), 1094 (AB0134)
Martins, F., 186 (OP0315), 1254 (AB0581)
Martins, N., 834 (SAT0170)
Martins Rocha, T., 468 (THU0690), 1177 (AB0368), 1466 (AB1172)
Martins-Rocha, T., 468 (THU0691)
Martiradonna, A., 623 (FRI0362)
Martire, M.V., 1143 (AB0271), 1425 (AB1060)
Martire, V., 906 (SAT0357)
Martis, N., 991 (SAT0569)
Maruo, Y., 409 (THU0535)
Maruotti, N., 808 (SAT0105), 1327 (AB0773)
Marushko, T.V., 399 (THU0510)
Marut, W., 1104 (AB0165)
Maruyama, A., 895 (SAT0326)
Maruyama, K., 1251 (AB0572)
Marx, C., 1427 (AB1065)
Marynych, L., 1230 (AB0514)
Marzan, K., 405 (THU0525)
Marzo-Ortega, H., 159 (OP0250), 340 (THU0359), 344 (THU0368), 345 (THU0369), 659 (FRI0456), 683 (FRI0512), 734 (FRI0646), 1085 (AB0112), 1308 (AB0727)
Mas, L., 313 (THU0289)
Mas, L.A., 205 (THU0017), 206 (THU0018)
Masala, I.F., 1294 (AB0689)
Masana, L., 1156 (AB0307)
Masaryk, P., 245 (THU0116)
Mascella, F., 954 (SAT0473)
Maschio, M., 1388 (AB0953)
Mascia, M.T., 474 (THU0705)
Masenko, V., 693 (FRI0536)
Masenko, V.L., 1346 (AB0823, AB0824)
Masetto, A., 496 (FRI0047), 933 (SAT0428)
Maslakova, L.A., 536 (FRI0146), 1128 (AB0228)
Maslinski, W., 216 (THU0045), 489 (FRI0026)
Masolini, P., 1101 (AB0156)
Mason, A., 1490 (THU0760-HPR)
Mason, J., 316 (THU0299)
Mason, J.C., 219 (THU0053)
Mason, M., 1313 (AB0740)
Masood, A., 1196 (AB0417)
Massaro, L., 470 (THU0696), 757 (FRI0705), 860 (SAT0228), 864 (SAT0241), 879 (SAT0281), 1093 (AB0132), 1099 (AB0150), 1449 (AB1125)
Massenburg, D., 1222 (AB0489)
Massey, J., 200 (THU0003)
Massicotte, F., 571 (FRI0230), 845 (SAT0195), 1188 (AB0397)
Massol, J., 786 (SAT0050)
Masson Behar, V., 1371 (AB0900)
Mastaglio, C., 1406 (AB1006)
Mastbergen, S., 483 (FRI0010), 978 (SAT0536), 1020 (SAT0649)
Mastbergen, S.C., 482 (FRI0008), 968 (SAT0508), 1068 (AB0061), 1344 (AB0818)
Masuda, I., 1069 (AB0065)
Masuko, K., 1165 (AB0333)
Masuyama, R., 486 (FRI0017)
Masyan, H., 323 (THU0317)
Mat, C., 619 (FRI0351), 1246 (AB0558)
Mata-Perdigon, F.J., 153 (OP0238)
Matallah, K., 1146 (AB0278)
Matcham, F., 805 (SAT0098)
Matchanov, S.X., 1202 (AB0435)
Matei, D., 379 (THU0454), 478 (THU0717)
Mateo, L., 988 (SAT0560), 1236 (AB0529), 1241 (AB0544), 1424 (AB1055)
Mateu Puchades, A., 1534 (AB1208-HPR)
Mateus, E.F., 12 (SP0051), 171 (OP0276-PARE)
Mateus, M., 1052 (AB0016), 1153 (AB0300)
Matheou, M., 333 (THU0344)
Mathew, A.J., 325 (THU0322), 727 (FRI0629)
Mathew, J., 325 (THU0322)
Mathias, P., 499 (FRI0055)
Mathieson, H., 344 (THU0368)
Mathieu, A., 535 (FRI0143)
Mathieu, S., 813 (SAT0117), 1033 (SAT0682), 1297 (AB0696), 1384 (AB0942), 1515 (SAT0733-HPR)
Mathijssen, E., 112 (OP0145-HPR), 1488 (THU0757-HPR)
Mathson-Alm, L., 792 (SAT0065)
Mathsson Alm, L., 509 (FRI0085)
Mathsson-Alm, L., 522 (FRI0111), 785 (SAT0048)
Mathur, A., 1074 (AB0079)
Matianova, E., 807 (SAT0102)
Matias-Carmona, M., 1133 (AB0242)
Matos, A., 137 (OP0206)
Matos, A.R., 171 (OP0276-PARE)
Matre, K.H., 1478 (THU0726-HPR)
Matsubara, T., 1471 (AB1187)
Matsuda, F., 202 (THU0006)
Matsuda, M., 1054 (AB0021)
Matsueda, Y., 598 (FRI0297)
Matsui, K., 210 (THU0030), 641 (FRI0408), 1288 (AB0674)
Matsui, T., 1165 (AB0333)
Matsumoto, A., 834 (SAT0171)
Matsumoto, K., 326 (THU0325)
Matsumoto, T., 476 (THU0710), 1195 (AB0415)
Matsunaga, N., 59 (OP0021)
Matsuno, H., 1200 (AB0431)
Matsuo, H., 383 (THU0464)
Matsuoka, H., 1058 (AB0032)
Matsushita, M., 1058 (AB0032), 1203 (AB0439)
Matsushita, T., 1464 (AB1169)
Matsuura, I., 727 (FRI0630)
Matsuyama, Y., 224 (THU0069), 532 (FRI0135), 841 (SAT0185)
Mattè, A., 1062 (AB0045)
Mattei, J.-P., 1442 (AB1108)
Mattei, J.P., 744 (FRI0671)
Mattera Iacono, A., 630 (FRI0378)
Matteson, E., 591 (FRI0278), 881 (SAT0286)
Matteson, E.L., 444 (THU0630), 512 (FRI0091), 609 (FRI0323), 750 (FRI0686, FRI0687), 1125 (AB0220)
Mattioli, M., 905 (SAT0353)
Mattsson, C., 626 (FRI0367)
Matucci Cerinic, M., 56 (OP0015), 631 (FRI0380), 1286 (AB0669)
Matucci-Cerinic, M., 65 (OP0035), 202 (THU0006), 504 (FRI0070), 623 (FRI0362), 628 (FRI0372), 633 (FRI0384), 635 (FRI0390), 909 (SAT0366), 915 (SAT0380), 1269 (AB0622), 1270 (AB0623), 1271 (AB0627)
Matusevich, A., 851 (SAT0208)
Matuszewska, A., 1112 (AB0187)
Matz, H., 747 (FRI0679)
Matziolis, G., 486 (FRI0019)
Maugars, Y., 430 (THU0593), 1191 (AB0406)
Maugeri, N., 328 (THU0331), 621 (FRI0357), 1055 (AB0025)
Maure, B., 597 (FRI0293)
Maurer, B., 86 (OP0083), 88 (OP0088), 621 (FRI0358), 625 (FRI0365), 890 (SAT0312), 912 (SAT0374), 915 (SAT0380)
Maurer, K., 391 (THU0490)
Mauri-Plana, M., 1208 (AB0451)
Mauricio, E., 1337 (AB0800)
Maurier, F., 638 (FRI0398), 1272 (AB0630)
Mauro, C., 506 (FRI0076)
Mauro, D., 490 (FRI0030)
Mauro, F.R., 1099 (AB0150)
Mavragani, C.P., 210 (THU0028)
Mavragani, K., 836 (SAT0176)
Mavromatis, C., 836 (SAT0176)
Mavropoulos, A., 680 (FRI0504), 903 (SAT0348)
Maxim, R., 632 (FRI0383), 825 (SAT0148)
Maximov, N.I., 1189 (AB0402)
Maxwell, J., 847 (SAT0198)
Maya, J.J., 1276 (AB0639)
Maya Gutierrez, A., 363 (THU0411)
Mayán, M.D., 1071 (AB0070)
Mayansky, N., 1082 (AB0105)
Mayer, E., 87 (OP0085)
Mayer, M., 592 (FRI0282), 883 (SAT0291), 1534 (AB1206-HPR)
Mayes, M., 105 (OP0126), 624 (FRI0363)
Mayordomo, L., 728 (FRI0631), 1018 (SAT0643), 1417 (AB1036)
Mayosi, B., 631 (FRI0379)
Mayr, M., 750 (FRI0688)
Maz, M., 1061 (AB0041)
Mazilu, D., 304 (THU0266), 435 (THU0606), 876 (SAT0271), 881 (SAT0288), 1025 (SAT0664), 1221 (AB0487), 1278 (AB0646, AB0647), 1428 (AB1068)
Mazodier, K., 1256 (AB0588)
Mazor, K., 1521 (SAT0750-HPR)
Mazur, L., 309 (THU0279)
Mazur, M., 267 (THU0173), 309 (THU0279), 884 (SAT0296), 1284 (AB0664)
Mazur-Nicorici, L., 884 (SAT0296), 1284 (AB0664)
Mazurov, V., 273 (THU0188), 560 (FRI0208), 611 (FRI0328)
Mazzuca, C., 304 (THU0267)
Mazzucchelli, R., 736 (FRI0651)
Mboge, F., 1505 (FRI0760-HPR)
Mbuyi-Muamba, J.-M., 1310 (AB0732)
Mc Ardle, A.F., 940 (SAT0444)
Mc Carthy, M., 7 (SP0024)
Mc Gonagle, D., 945 (SAT0454)
McAlindon, T., 384 (THU0469), 973 (SAT0523)
McAlindon, T.E., 121 (OP0166), 985 (SAT0552)
Mcallister, M., 18 (SP0073)
McBeth, J., 438 (THU0614), 519 (FRI0105), 758 (FRI0708), 759 (FRI0712), 973 (SAT0521), 1446 (AB1118), 1453 (AB1138)
Mccaffrey, T., 202 (THU0007)
McCardell, E., 426 (THU0583)
McCarthy, C., 1432 (AB1078)
McCarthy, G., 383 (THU0464), 1432 (AB1078)
McCarthy, G.M., 321 (THU0312)
McCarthy, J.E., 1085 (AB0111)
McCarthy-Fruin, K., 512 (FRI0091)
McCormick, D., 729 (FRI0634)
McCormick, H., 1372 (AB0904)
McCormick, N., 373 (THU0440)
McCormick, S., 383 (THU0464)
McCorry, L., 1372 (AB0904)
McCune, W., 50 (OP0002)
McCune, W.J., 150 (OP0232)
McDaniel, G., 540 (FRI0157), 813 (SAT0119), 950 (SAT0466)
Mcdermott, E., 407 (THU0531)
McDonagh, J.E., 190 (OP0327-PARE), 391 (THU0488), 408 (THU0533)
Mcdonald, J., 1164 (AB0332)
McDonnell, T., 1092 (AB0131)
McElvaney, O., 1432 (AB1078)
McElvenny, D., 987 (SAT0556)
McGarry, T., 203 (THU0011), 221 (THU0059), 646 (FRI0421), 773 (SAT0013), 776 (SAT0021)
Mcgarry, T., 487 (FRI0020)
McGonagle, D., 127 (OP0182), 196 (OP0341),

344 (THU0368), 480 (FRI0001), 648 (FRI0427), 734 (FRI0646), 771 (SAT0007)
McGonnagle, D., 959 (SAT0485)
McGovern, A., 179 (OP0298)
Mcgwin, G., 1363 (AB0879)
McHugh, N., 201 (THU0004), 685 (FRI0514), 912 (SAT0374), 939 (SAT0442)
McIlraith, M., 672 (FRI0487), 683 (FRI0512), 684 (FRI0513), 936 (SAT0436), 942 (SAT0448)
McInnes, I., 238 (THU0100), 242 (THU0111), 511 (FRI0088), 944 (SAT0453), 951 (SAT0468), 957 (SAT0480), 1147 (AB0281)
McInnes, I.B., 55 (OP0012-PARE), 138 (OP0208), 145 (OP0222), 535 (FRI0142), 564 (FRI0216), 675 (FRI0494), 683 (FRI0511), 1034 (SAT0686), 1322 (AB0765), 1323 (AB0766), 1329 (AB0780)
McKay, J., 150 (OP0232)
McKenna, J., 1372 (AB0904)
McKenna, S., 1314 (AB0741)
McKenna, S.P., 1461 (AB1161)
McKinnon, A., 81 (OP0072-PARE)
McKnight, J., 1477 (THU0723-HPR)
McLaughlin, V.V., 65 (OP0034)
Mclean-Tooke, A., 467 (THU0688)
McMahon, M., 1238 (AB0535)
McNally, J., 541 (FRI0159)
McNamee, K., 770 (SAT0005)
Mcnearney, T.A., 983 (SAT0548)
McQuarrie, K., 578 (FRI0246), 839 (SAT0182)
McQuillan, M., 1432 (AB1078)
McRae, B., 288 (THU0222)
McWilliams, D.F., 782 (SAT0040)
Md Yusof, M.Y., 91 (OP0095), 152 (OP0235), 314 (THU0293), 869 (SAT0251), 987 (SAT0556), 1019 (SAT0647)
Meah, N., 1139 (AB0260)
Meara, A., 1099 (AB0151)
Mease, P., 144 (OP0221), 145 (OP0223), 679 (FRI0502), 687 (FRI0520), 949 (SAT0463), 951 (SAT0468), 957 (SAT0480), 1313 (AB0739), 1332 (AB0786)
Mease, P.J., 141 (OP0216), 145 (OP0222), 352 (THU0386), 668 (FRI0479), 673 (FRI0489), 675 (FRI0494), 682 (FRI0509, FRI0510), 683 (FRI0511, FRI0512), 684 (FRI0513), 936 (SAT0436), 942 (SAT0448), 952 (SAT0470), 953 (SAT0471, SAT0472), 1313 (AB0740), 1316 (AB0747), 1329 (AB0780), 1330 (AB0783), 1331 (AB0784, AB0785), 1335 (AB0794)
Meccariello, L., 702 (FRI0563)
Mecchia, M., 445 (THU0634), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Mechid, F., 1192 (AB0409)
Meda-Lara, R.M., 1199 (AB0427)
Medeiros, C., 255 (THU0145)
Medeiros, D., 929 (SAT0418), 1163 (AB0329)
Medeiros, M.M., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Medema, J., 122 (OP0168)
Medeot, M., 995 (SAT0582)
Medhat, B., 874 (SAT0265)
Mediero, A., 128 (OP0186)
Medina, F., 685 (FRI0515)
Medina, G., 421 (THU0568), 729 (FRI0635), 881 (SAT0287), 991 (SAT0568), 1091 (AB0126), 1098 (AB0149), 1217 (AB0478)
Medina, J., 1011 (SAT0626), 1408 (AB1011)
Medina, J.F., 201 (THU0005), 218 (THU0052)
Medina, L.F., 1196 (AB0419)
Medina, M., 875 (SAT0269)
Medina Luezas, J., 1439 (AB1098)
Medina Quiñones, C., 701 (FRI0559)
Medina-Chinchòn, M., 1142 (AB0269)
Medina-Garcia, G., 1282 (AB0657)
Medina-Luna, D., 1067 (AB0059)
Medina-Rodriguez, F., 824 (SAT0146)
Medrano-Rodriguez, G., 421 (THU0568)
Meehan, R., 543 (FRI0164)
Meerpohl, J., 418 (THU0561)
Meerwein, S., 855 (SAT0217)
Meesters, J., 1343 (AB0817)
Meesters, J.J., 966 (SAT0505)
Megallaa, M.H., 310 (THU0282)
Meghnathi, B., 102 (OP0119), 650 (FRI0432), 917 (SAT0386)
Mehdi, M., 1463 (AB1164)
Mehnert, F., 451 (THU0649)
Mehrotra, S., 239 (THU0102), 1435 (AB1089)
Mehsen-Cetre, N., 710 (FRI0584)
Mehta, B., 714 (FRI0595)
Mehta, V.R., 1290 (AB0678)
Meichtry, A., 185 (OP0314-HPR)
Meijboom, L.J., 732 (FRI0642)
Meijer, P., 741 (FRI0664)
Meissner, Y., 801 (SAT0087)
Mejri, I., 1397 (AB0980)
Mekinian, A., 108 (OP0134)
Melac-Ducamp, S., 549 (FRI0180)
Melchers, I., 202 (THU0006)
Melchior, J., 103 (OP0121)
Mele, A., 629 (FRI0373, FRI0374), 895 (SAT0325)
Melendez-Mercado, C.I., 515 (FRI0095)
Melero, R., 1107 (AB0173)
Melikoğlu, M., 1246 (AB0558)
Melikoglu, M., 603 (FRI0307), 618 (FRI0348), 1186 (AB0394), 1274 (AB0634)
Mellado, M., 645 (FRI0420)
Mellblom Bengtsson, M., 252 (THU0135)
Mellemkjaer, A., 505 (FRI0074)
Meller, S., 295 (THU0241)
Melo, A.K.G., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Melo, F., 440 (THU0619), 906 (SAT0357)
Melo, M., 1455 (AB1142)
Melo, P.R., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Melo-Gomes, J., 186 (OP0315)
Meloni, F., 891 (SAT0315)
Melsens, K., 299 (THU0252), 914 (SAT0377), 1221 (AB0488)
Memeti, N., 280 (THU0202)
Memi, T.-E., 1329 (AB0779)
Mena, N., 843 (SAT0191)
Mena Vazquez, N., 391 (THU0489)
Mena-Vázquez, N., 1175 (AB0362), 1525 (SAT0760-HPR)
Mena-Vazquez, N., 261 (THU0160), 1174 (AB0361), 1443 (AB1109), 1492 (THU0766-HPR)
Ménard, C., 1049 (AB0007)
Mendez, K., 963 (SAT0496), 1208 (AB0453), 1502 (FRI0751-HPR)
Mendiratta, N., 1247 (AB0561, AB0562), 1253 (AB0579), 1377 (AB0918)
Mendonça, J.A., 1516 (SAT0735-HPR)
Mendoza, F.A., 91 (OP0096)
Mendoza Pinto, C., 311 (THU0283), 1221 (AB0486)
Mendoza-Fuentes, A., 515 (FRI0095)
Menegatti, E., 1410 (AB1014)
Menegatti, S., 1086 (AB0114)
Meng, L., 1480 (THU0732-HPR)
Meng, T., 831 (SAT0161), 960 (SAT0489)
Meng, X., 178 (OP0295), 1117 (AB0199)
Mengru, Y., 903 (SAT0349)
Mengshoel, A.M., 384 (THU0468)
Menon, S., 135 (OP0202), 141 (OP0216), 149 (LB0003), 277 (THU0196), 284 (THU0211), 676 (FRI0496), 682 (FRI0509), 938 (SAT0439)
Menor Almagro, R., 1422 (AB1050)
Mentesidou, L., 1139 (AB0259)
Menz, H.B., 1032 (SAT0679)
Mera, A., 108 (OP0135), 503 (FRI0068), 614 (FRI0336)
Mera Varela, J.A., 1159 (AB0316)
Mera-Varela, A., 494 (FRI0040), 500 (FRI0057)
Merashli, M., 344 (THU0368)
Merayo-Chalico, J., 586 (FRI0264)
Mercedes-Núñez, I., 877 (SAT0276)
Mercedes-Nuñez, I., 877 (SAT0277)
Mercer, L., 1494 (THU0769-HPR)
Mercieca, C., 439 (THU0616), 1435 (AB1088), 1514 (SAT0729-HPR), 1522 (SAT0752-HPR)
Merciris, D., 118 (OP0161)
Merheb, G., 667 (FRI0476), 762 (FRI0718)
Merino Argumanez, C., 1399 (AB0986)
Merino-Meléndez, L., 1472 (AB1192)
Merkel, P., 187 (OP0320)
Merkel, P.A., 107 (OP0130), 318 (THU0301), 605 (FRI0312, FRI0314)
Merola, J.F., 98 (OP0112), 141 (OP0216), 857 (SAT0222), 937 (SAT0437), 947 (SAT0461)
Meroni, M., 437 (THU0611), 540 (FRI0155), 595 (FRI0288), 867 (SAT0247), 1439 (AB1099)
Meroni, P.L., 4 (SP0012), 70 (OP0046), 132 (OP0195), 294 (THU0240), 403 (THU0522), 437 (THU0611), 461 (THU0673), 643 (FRI0413), 746 (FRI0677), 908 (SAT0364), 1022 (SAT0655), 1209 (AB0456), 1406 (AB1006), 1439 (AB1099)
Merrigan, S., 646 (FRI0421)
Merrill, J., 864 (SAT0240)
Merrill, J.T., 150 (OP0232), 151 (OP0234), 856 (SAT0219), 863 (SAT0236), 1217 (AB0475)
Merrill, P.T., 722 (FRI0618)
Merriman, M., 383 (THU0464)
Merriman, T.R., 165 (OP0263), 383 (THU0464)
Merschon, F., 995 (SAT0582)
Mert, E., 1137 (AB0255)
Mertz, L.E., 318 (THU0301)
Mesa-Navas, M.A., 905 (SAT0354)
Mesci, E., 652 (FRI0437)
Mesci, N., 652 (FRI0437)
Meshcheryakova, T., 249 (THU0128)
Mesnyankina, A.A., 861 (SAT0232)
Mesquida, M., 75 (OP0059), 326 (THU0326), 350 (THU0381), 405 (THU0526), 420 (THU0567), 718 (FRI0607)
Messaoud, N., 1467 (AB1177)
Messas, E., 108 (OP0134)
Messemaker, T., 202 (THU0008), 621 (FRI0356)
Messenger, M., 635 (FRI0390)
Messi, C., 1506 (FRI0762-HPR), 1540 (AB1226-HPR)
Messias-Reason, I.J.T., 820 (SAT0135)
Messina, O., 54 (OP0010)
Mestre, J., 330 (THU0336)
Mestre, Y., 556 (FRI0197)
Mestre Torres, J., 324 (THU0320)
Meszaros, G., 233 (THU0088), 510 (FRI0087)
Metawie, S., 734 (FRI0647)
Metcalfe, A., 988 (SAT0559)
Mete, E., 997 (SAT0586), 1003 (SAT0606)
Mete, O., 1302 (AB0709)
Metola Gómez, M., 1362 (AB0875)
Metoui, L., 998 (SAT0589, SAT0590)
Metsios, G.S., 764 (FRI0723), 1044 (SAT0712)
Meulenbelt, I., 207 (THU0020)
Meuleners, L., 267 (THU0173)
Meunier, I., 769 (SAT0002)
Meurisse, S., 126 (OP0180)
Meyer, A., 638 (FRI0398)
Meyer, B., 131 (OP0194)
Meyer, M.K., 456 (THU0660), 775 (SAT0020)
Meyer, W., 1271 (AB0626), 1279 (AB0648)
Mezcúa, A., 822 (SAT0141)
Mezcua, A., 555 (FRI0194)
Meziani, A., 1384 (AB0941)
Mhenni, A., 1383 (AB0937)
Mia, S.M., 212 (THU0036)
Mian, M., 377 (THU0447), 1367 (AB0889)
Miao, H., 748 (FRI0681), 1249 (AB0568), 1363 (AB0877)
Miao, M., 839 (SAT0181), 869 (SAT0252)
Miao, Y., 724 (FRI0622)
Miceli, C., 289 (THU0225)
Miceli-Richard, C., 77 (OP0062), 260 (THU0158), 549 (FRI0180)
Micelli, C., 155 (OP0241)
Michaelides, M., 1437 (AB1093)
Michaelidou, M., 1437 (AB1093)
Michaels, M.A., 564 (FRI0216)
Michailidis, T., 643 (FRI0412), 723 (FRI0619)
Michalik, R., 1502 (FRI0752-HPR)
Michalsen, A., 960 (SAT0488)
Michalska, M., 95 (OP0105), 567 (FRI0222)
Michaud, J., 1378 (AB0923)
Michaud, K., 517 (FRI0099), 580 (FRI0250)
Michel, B.A., 479 (THU0719)
Michel, G., 1177 (AB0370)
Michelena, X., 663 (FRI0468), 1375 (AB0914)
Michelin, P., 63 (OP0029)

Michelsen, B., 97 (OP0109), 229 (THU0080), 938 (SAT0440)
Micheroli, R., 130 (OP0189), 335 (THU0347), 816 (SAT0125)
Michienzi, S., 496 (FRI0047)
Michou, L., 1303 (AB0712)
Micu, M., 1013 (SAT0631), 1151 (AB0294)
Miday, R., 867 (SAT0249)
Middleton, K., 564 (FRI0216)
Midtvedt, Ø., 87 (OP0085), 106 (OP0129), 630 (FRI0376)
Mielnik, P., 334 (THU0345), 673 (FRI0490)
Migas-Kukla, T., 1470 (AB1184)
Migita, K., 723 (FRI0620)
Migkos, M.P., 1329 (AB0779)
Miglio, C., 831 (SAT0161)
Migliorini, P., 222 (THU0063), 1113 (AB0191)
Migone, S., 728 (FRI0632)
Miguel, C., 464 (THU0679), 929 (SAT0418), 1163 (AB0329), 1464 (AB1168)
Miguel, M., 742 (FRI0668)
Mihai, C., 65 (OP0034), 433 (THU0602), 435 (THU0607), 626 (FRI0368), 763 (FRI0722), 1032 (SAT0681), 1151 (AB0294), 1179 (AB0376), 1264 (AB0608), 1286 (AB0669)
Mihai, C.M., 745 (FRI0676), 983 (SAT0547)
Mihailova, A., 1071 (AB0071)
Mijares, V., 1084 (AB0108)
Mikhnevich, E., 1361 (AB0870, AB0871)
Mikkers, H., 621 (FRI0356)
Mikó, I., 1482 (THU0736-HPR)
Mikulets, L., 1167 (AB0340)
Mikulkova, Z., 970 (SAT0514), 1051 (AB0014)
Miladi, S., 1146 (AB0278)
Milanez, F.M., 1292 (AB0684)
Milani, R., 410 (THU0538)
Milatz, F., 397 (THU0504)
Milbers, K., 443 (THU0629), 453 (THU0653)
Milchert, M., 1005 (SAT0611)
Milenkovic, S., 914 (SAT0378), 1240 (AB0540)
Miler, E., 609 (FRI0321)
Milewski, R., 1277 (AB0642)
Milic, V., 67 (OP0040), 314 (THU0292)
Milicescu, M., 435 (THU0607), 745 (FRI0676), 983 (SAT0547), 1032 (SAT0681)
Miligan, G., 932 (SAT0425)
Milini, C., 1468 (AB1178)
Milisenda, J.C., 1018 (SAT0645)
Militianu, D., 653 (FRI0441)
Millán, C., 1303 (AB0713)
Millán, M., 1305 (AB0717)
Millan, M., 904 (SAT0351), 1414 (AB1027)
Millan, P., 1414 (AB1027)
Millan Arciniegas, A.M., 914 (SAT0379)
Millen, A., 252 (THU0136), 545 (FRI0170)
Millen, A.M., 245 (THU0117)
Miller, F.W., 913 (SAT0376)
Miller, G., 1432 (AB1077)
Milleret, V., 88 (OP0088)
Milling, S., 183 (OP0309)
Mills, J., 187 (OP0320)
Millson, B., 349 (THU0378), 443 (THU0628), 558 (FRI0201), 832 (SAT0165)
Millstone, D., 1504 (FRI0757-HPR)
Milmont, C.J., 71 (OP0048)
Milo, J., 911 (SAT0372)
Milojevic, D., 133 (OP0197), 405 (THU0525)
Mimori, A., 298 (THU0251)
Mimori, T., 202 (THU0006), 220 (THU0057), 527 (FRI0122), 561 (FRI0210), 618 (FRI0349), 620 (FRI0352), 744 (FRI0673), 1200 (AB0431), 1452 (AB1133)
Mimura, T., 188 (OP0322)
Min, J.K., 1185 (AB0392)
Min, S.-H., 1166 (AB0336)
Min, W., 1491 (THU0762-HPR)
Mina, E., 1437 (AB1093)
Minami, M., 1134 (AB0247)
Minartz, C., 442 (THU0626)
Minas, K., 1241 (AB0542)
Minatsuki, S., 1274 (AB0635)
Minden, K., 16 (SP0065), 74 (OP0057), 76 (OP0060), 132 (OP0196), 195 (OP0338), 390 (THU0487), 396 (THU0503), 397 (THU0504), 398 (THU0507), 400 (THU0512), 405 (THU0525), 1389 (AB0957)
Mine, M., 1016 (SAT0640), 1416 (AB1035)
Minegishi, K., 602 (FRI0305), 645 (FRI0418, FRI0419), 1134 (AB0246)
Minegishi, K.M., 1191 (AB0405)
Miner, J.N., 382 (THU0461), 1364 (AB0880), 1366 (AB0886, AB0887)
Mingolla, S., 199 (OP0346-PARE)
Minguez, E., 326 (THU0326), 718 (FRI0607)
Minguez, S., 988 (SAT0560)
Minisola, G., 437 (THU0611), 1439 (AB1099)
MinLi, Q., 1291 (AB0680)
Minnion, M., 625 (FRI0366)
Minniti, A., 464 (THU0681), 888 (SAT0305)
Minten, M.J., 193 (OP0335)
Mir, A., 1101 (AB0155)
Mira-Avendaño, I., 1276 (AB0639)
Miraglia, F., 1438 (AB1096)
Miranda, F., 180 (OP0299), 489 (FRI0027), 757 (FRI0705), 864 (SAT0241), 872 (SAT0260), 879 (SAT0281), 880 (SAT0283), 1093 (AB0132), 1094 (AB0135, AB0136), 1099 (AB0150)
Miranda, G., 1459 (AB1154)
Miranda, L., 929 (SAT0418)
Miranda, P., 564 (FRI0216), 824 (SAT0146)
Miranda Carus, M.E., 501 (FRI0062)
Miranda-Filloy, J., 569 (FRI0226)
Miranda-Hernández, D., 591 (FRI0279), 860 (SAT0229)
Mirault, T., 108 (OP0134)
Mirete-Bachiller, S., 1409 (AB1012)
Mirfeizi, Z., 1341 (AB0811)
Mirjafari, H., 803 (SAT0092)
Mirovich, O., 1019 (SAT0646)
Misa, K., 1109 (AB0180)
Misaki, K., 738 (FRI0655)
Misasi, R., 490 (FRI0028)
Misevska Percinkova, S., 1153 (AB0299)
Mishra, S.K., 320 (THU0307)
Misiyuk, A., 256 (THU0148), 273 (THU0188), 572 (FRI0231)
Misra, D.P., 320 (THU0307), 913 (SAT0375)
Misra, R., 320 (THU0307)
Missaykeh, J., 762 (FRI0718)
Mitchell, K., 500 (FRI0059)
Mitchell, S., 382 (THU0462), 1369 (AB0896)
Miteva, L., 1048 (AB0005)
Mithal, A., 70 (OP0047), 169 (OP0272), 362 (THU0409), 672 (FRI0488)
Mitic, B., 1240 (AB0540)
Mitis, G., 1473 (AB1194)
Mitrovic, S., 54 (OP0011), 686 (FRI0519), 755 (FRI0700)
Mitsugi, N., 1165 (AB0334), 1166 (AB0335)
Mitsuka, T., 1471 (AB1187)
Mitsuyama, K., 1403 (AB0995)
Mittal, S., 1385 (AB0944)
Mitton, D., 409 (THU0536)
Mittwede, M., 960 (SAT0488)
Mitu, F., 632 (FRI0383)
Miura, N., 1061 (AB0041)
Miura, S., 88 (OP0087)
Miura, Y., 800 (SAT0085), 1242 (AB0547)
Miwa, Y., 800 (SAT0085), 801 (SAT0086), 1138 (AB0258), 1149 (AB0289)
Miyachi, F., 284 (THU0212)
Miyagawa, I., 137 (OP0205), 257 (THU0149)
Miyagawa, T., 88 (OP0087)
Miyahara, H., 1383 (AB0939)
Miyake, K., 1254 (AB0582)
Miyake, N., 1471 (AB1187)
Miyake, S., 141 (OP0214), 1060 (AB0038), 1090 (AB0125), 1095 (AB0139)
MIyakoshi, N., 795 (SAT0071)
Miyakoshi, N., 707 (FRI0577), 1178 (AB0372), 1182 (AB0382), 1426 (AB1063)
Miyamae, Y., 1165 (AB0334), 1166 (AB0335)
Miyamoto, S.T., 163 (OP0259-HPR)
Miyamura, G., 703 (FRI0566)
Miyamura, T., 1254 (AB0582)
Miyasaka, N., 264 (THU0166), 265 (THU0170)
Miyauchi, A., 71 (OP0048)
Miyauchi, S., 1054 (AB0021)
Miyazaki, Y., 137 (OP0205)
Mizokami, A., 1016 (SAT0640), 1416 (AB1035)
Mizukami, Y., 1165 (AB0333)
Mizuki, S., 1424 (AB1056)
Mizuki, S.-I., 565 (FRI0218)
Mizushima, I., 425 (THU0579), 711 (FRI0587), 722 (FRI0617)
Mizushina, K., 1024 (SAT0661)
Mjaavatten, M.D., 81 (OP0071), 756 (FRI0702), 1030 (SAT0675)
Mkoh, A.S., 997 (SAT0588)
Mkrtumyan, A., 968 (SAT0509)
Mo, L., 1491 (THU0762-HPR)
Mo, Y.-Q., 279 (THU0201), 373 (THU0439), 488 (FRI0023), 798 (SAT0078)
Moal, L., 408 (THU0532)
Moat, J., 1087 (AB0115)
Moawad, S., 1383 (AB0938)
Moayedfar, M., 1546 (AB1242-HPR), 1548 (AB1247-HPR)
Mobasher, S.A., 1145 (AB0276)
Mobeen, M., 222 (THU0062), 1099 (AB0151)
Mocarzel, L.O., 641 (FRI0406)
Mochida, Y., 1165 (AB0334), 1166 (AB0335)
Mochizuki, H., 610 (FRI0326)
Mociran, A., 170 (OP0275), 260 (THU0156), 880 (SAT0285), 1285 (AB0666)
Moder, K.G., 1207 (AB0449)
Modesto, C., 75 (OP0059), 405 (THU0526), 420 (THU0567)
Modi, K., 1065 (AB0053)
Moe, R.H., 1546 (AB1244-HPR)
Moed, M., 678 (FRI0500), 1324 (AB0769)
Moeller, B., 267 (THU0174)
Moeller-Doehn, U., 175 (OP0288)
Moens, H., 434 (THU0604)
Moffat, K., 418 (THU0561)
Mogard, E., 651 (FRI0436), 655 (FRI0445), 922 (SAT0397)
Mogensen, M., 892 (SAT0317), 1109 (AB0179)
Moghaddam, B., 68 (OP0041)
Moghimi, J., 1338 (AB0803)
Moghimy, N., 1284 (AB0663)
Mogosan, C., 1018 (SAT0644)
Mohamad, S., 1350 (AB0839)
Mohamad, S.R., 1228 (AB0505)
Mohamed, A., 91 (OP0095), 1395 (AB0973)
Mohamed, E., 995 (SAT0580), 1377 (AB0920), 1526 (SAT0764-HPR)
Mohamed, F., 583 (FRI0257)
Mohamed, K., 1113 (AB0190)
Mohamed, M.-E.F., 268 (THU0177), 1201 (AB0432)
Mohamed, N.A., 1339 (AB0804)
Mohammad, A., 871 (SAT0257), 1509 (FRI0772-HPR)
Mohammad, A.J., 750 (FRI0686, FRI0687)
Mohammed, A., 693 (FRI0534)
Mohammed, F.I., 583 (FRI0257)
Mohammed, N.A., 741 (FRI0665)
Mohammed, R.H.A., 981 (SAT0542, SAT0543)
Mohan, C., 583 (FRI0257)
Mohan, H., 328 (THU0330), 1061 (AB0042)
Mohan, S., 95 (OP0105)
Mohannad, N., 310 (THU0282)
Mohanty, B., 1074 (AB0079)
Mohapatra, S.R., 1070 (AB0068)
Mohd Isa, L., 446 (THU0638)
Mohd Jamid, N., 1140 (AB0262)
Mohd Noor, N., 1140 (AB0262)
Mohd Yusoof, H., 256 (THU0146)
Mohd Zain, M., 596 (FRI0291)
Mohd-Shahrir, M.S., 1512 (SAT0722-HPR)
Moilanen, E., 6 (SP0022), 893 (SAT0321)
Moinzadeh, P., 1106 (AB0169), 1110 (AB0181)
Moiola, L., 725 (FRI0624)
Moise, C., 672 (FRI0488)
Moiseev, S., 331 (THU0338), 617 (FRI0346)
Moita, L.F., 1080 (AB0096)
Mojcik, C., 149 (LB0003)
Mojcik, C.F., 148 (OP0230)
Mok, C.C., 303 (THU0263, THU0264),

583 (FRI0257), 589 (FRI0271), 644 (FRI0415), 825 (SAT0147), 874 (SAT0266, SAT0267), 1219 (AB0483)
Mokhort, T., 1356 (AB0858)
Mokotedi, L., 245 (THU0117)
Mokry, M., 177 (OP0293)
Moksnes, T.S., 223 (THU0065)
Molano-González, N., 575 (FRI0238)
Molano-Gonzàlez, N., 850 (SAT0205)
Molberg, O., 1272 (AB0630)
Molberg, Ø., 87 (OP0085), 106 (OP0129), 164 (OP0261-HPR), 630 (FRI0376), 765 (FRI0725), 912 (SAT0374), 1043 (SAT0709), 1517 (SAT0737-HPR)
Mole, E.N., 1076 (AB0085)
Molfetta, L., 695 (FRI0540), 704 (FRI0569)
Molica Colella, A.B., 270 (THU0181)
Molina, A., 694 (FRI0539)
Molina, C., 1102 (AB0158)
Molina, J., 1016 (SAT0638), 1296 (AB0693)
Molina, J.F., 1339 (AB0805)
Molina, M., 906 (SAT0357)
Molina-Aguilar, R., 881 (SAT0287)
Molinari, B.C., 76 (OP0061)
Molinari, N., 235 (THU0093)
Molinero, L.M., 660 (FRI0459)
Molinos, A.M., 1351 (AB0840)
Moll, C., 614 (FRI0336)
Moll, M., 1389 (AB0957)
Mollat, P., 126 (OP0180)
Möller, B., 248 (THU0125), 335 (THU0347), 569 (FRI0225), 816 (SAT0125)
Möller, I., 10 (SP0040), 24 (SP0097), 174 (OP0286), 742 (FRI0668), 1428 (AB1067)
Moller, I., 1013 (SAT0631)
Møller, J., 745 (FRI0674)
Møller, J.M., 732 (FRI0641)
Møller Døhn, U., 726 (FRI0628)
Mollerach, F.B., 1333 (AB0789)
Molloy, E.S., 321 (THU0312)
Molnar, C., 130 (OP0189)
Molokhia, M., 806 (SAT0099)
Molta, C., 539 (FRI0153), 680 (FRI0506), 812 (SAT0115)
Molthoff, C., 1020 (SAT0650)
Molthoff, C.F.M., 494 (FRI0041), 1075 (AB0082)
Moltó, A., 57 (OP0017), 63 (OP0030), 80 (OP0070), 102 (OP0119), 129 (OP0188), 334 (THU0346), 339 (THU0356, THU0357), 388 (THU0482), 389 (THU0483), 429 (THU0590), 650 (FRI0432), 665 (FRI0472), 917 (SAT0386), 996 (SAT0583), 1296 (AB0694)
Molto, A., 73 (OP0054), 100 (OP0115, OP0116), 260 (THU0158), 336 (THU0350), 337 (THU0353), 350 (THU0382), 659 (FRI0456), 665 (FRI0473), 755 (FRI0700), 831 (SAT0163), 1303 (AB0712), 1308 (AB0727)
Momohara, S., 1069 (AB0065), 1200 (AB0431)
Momoki, N., 1251 (AB0572)
Monach, P., 187 (OP0320)
Monach, P.A., 318 (THU0301), 605 (FRI0314)
Monaghan, J., 1477 (THU0723-HPR)
Mönch, S., 718 (FRI0606)
Mondal, S., 1300 (AB0705)
Monegal, A., 369 (THU0429), 691 (FRI0529), 706 (FRI0573)
Monek, B., 1482 (THU0736-HPR)
Monfort, J., 1557 (PARE0017)
Monjardet, A., 118 (OP0161)
Monjo, I., 416 (THU0553), 456 (THU0661), 822 (SAT0141), 1004 (SAT0609), 1293 (AB0686), 1304 (AB0714), 1413 (AB1024)
Monjo Henry, I., 1014 (SAT0634)
Mönkemöller, K., 76 (OP0060)
Monogioudi, E., 461 (THU0673)
Monostori, É., 1090 (AB0123)
Monov, S., 208 (THU0023), 584 (FRI0259), 685 (FRI0516), 686 (FRI0517), 888 (SAT0306)
Monova, D., 685 (FRI0516), 888 (SAT0306)
Monova, D.V., 584 (FRI0259)
Monroy Calero, A., 1424 (AB1057)
Monsiváis-Urenda, A.E., 774 (SAT0016)
Montagna, P., 140 (OP0212), 378 (THU0451), 1110 (AB0182, AB0183), 1111 (AB0185)
Montagu, G., 425 (THU0580), 427 (THU0586)
Montaguti, L., 954 (SAT0473)
Montañana, J., 1041 (SAT0703), 1458 (AB1150)
Monteagudo, I., 386 (THU0474), 400 (THU0514), 462 (THU0676), 550 (FRI0184), 556 (FRI0197), 656 (FRI0448), 748 (FRI0683), 1276 (AB0640), 1297 (AB0695), 1386 (AB0947), 1414 (AB1029), 1476 (THU0720-HPR)
Monteagudo, M., 330 (THU0336)
Montecucco, C., 56 (OP0015), 237 (THU0099), 305 (THU0268), 458 (THU0667), 787 (SAT0053), 790 (SAT0060), 891 (SAT0315), 1123 (AB0214), 1214 (AB0467), 1439 (AB1099)
Montecucco, C.M., 437 (THU0611), 445 (THU0634), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Monteleone, G., 667 (FRI0477)
Montell, E., 215 (THU0044)
Montella, A., 86 (OP0082), 894 (SAT0323)
Montero, Á., 1338 (AB0801)
Montes, A., 494 (FRI0040), 500 (FRI0057)
Montes-Castillo, M.D.L.L., 365 (THU0417)
Montes-Cortes, D.H., 1282 (AB0657)
Montgomery, C., 1096 (AB0143)
Monti, S., 315 (THU0296), 316 (THU0297), 318 (THU0302), 605 (FRI0312), 614 (FRI0337), 1257 (AB0589)
Montiel Cervantes, L., 881 (SAT0287)
Montiel Jarquin, A., 1221 (AB0486)
Montiel-Hernandez, J.-L., 498 (FRI0052)
Montieth, D., 983 (SAT0548)
Montilla, C., 685 (FRI0515), 946 (SAT0458), 954 (SAT0474)
Montilla Morales, C., 955 (SAT0475), 1333 (AB0788)
Montin, D., 1012 (SAT0630), 1554 (PARE0008)
Montini, E., 126 (OP0179)
Montolio, L., 1534 (AB1208-HPR)
Montolio-Chiva, L., 258 (THU0153), 1168 (AB0344), 1316 (AB0746), 1410 (AB1016), 1415 (AB1032)
Montoro, M., 685 (FRI0515)
Montoya, S., 906 (SAT0357)
Montvida, O., 264 (THU0167)
Mony, U., 423 (THU0575)
Mooe, T., 113 (OP0147)
Mookherjee, N., 178 (OP0295)
Moon, J., 83 (OP0077)
Moon, R., 932 (SAT0425)
Moore, P.A., 777 (SAT0027)
Moore, S., 519 (FRI0105)
Moorthy, A., 662 (FRI0463), 1302 (AB0710), 1303 (AB0711), 1436 (AB1090)
Moosig, F., 107 (OP0130)
Moosmann, T.M., 615 (FRI0338)
Moots, R., 149 (LB0003), 852 (SAT0209), 1181 (AB0379), 1251 (AB0573)
Moots, R.J., 1205 (AB0444)
Mora, V., 843 (SAT0191)
Morad, C.S., 1219 (AB0481), 1224 (AB0495)
Moradkhan, E., 1272 (AB0628)
Morado, C., 990 (SAT0564)
Morado, I., 320 (THU0309)
Moraes, J.C.B., 1292 (AB0684)
Moraes-Fontes, M.F., 715 (FRI0598), 1429 (AB1070)
Moral, E., 551 (FRI0186), 559 (FRI0204), 833 (SAT0168), 1116 (AB0198), 1304 (AB0714)
Moraleda, J.M., 487 (FRI0021)
Morales, A., 617 (FRI0344)
Morales, I., 663 (FRI0468)
Morales Garrido, P., 1228 (AB0506), 1321 (AB0760)
Morales-Asencio, J.M., 1486 (THU0751-HPR)
Morales-Cano, D., 892 (SAT0316)
Morales-Padilla, S., 586 (FRI0264)
Moran, B., 773 (SAT0013)
Morand, E., 50 (OP0001), 876 (SAT0272)
Morandi, A., 960 (SAT0488)
Morante Bolado, I., 1374 (AB0910)
Morcillo, C., 410 (THU0539), 597 (FRI0293), 721 (FRI0615), 1042 (SAT0706)
Morehouse, C., 180 (OP0301)
Moreira, L., 474 (THU0706)
Morel, J., 113 (OP0146), 235 (THU0093), 260 (THU0158), 311 (THU0284), 464 (THU0681), 567 (FRI0221), 701 (FRI0561), 709 (FRI0582), 804 (SAT0094), 886 (SAT0302), 1050 (AB0012), 1159 (AB0315)
Morel, N., 152 (OP0236)
Morel, Z., 1396 (AB0975)
Moreland, L.W., 318 (THU0301)
Morell Hita, J.L., 413 (THU0545), 713 (FRI0593)
Morelli, F., 1449 (AB1125)
Morello, F., 860 (SAT0228), 864 (SAT0241)
Moreno, J., 1006 (SAT0613)
Moreno, J.V., 1406 (AB1004)
Moreno, M., 843 (SAT0191), 884 (SAT0295), 926 (SAT0410), 1014 (SAT0635), 1160 (AB0319), 1498 (FRI0741-HPR)
Moreno Fresneda, P., 527 (FRI0123)
Moreno-Fresneda, P., 1084 (AB0108)
Moreno-Martínez, M.J., 739 (FRI0659)
Moreno-Martinez, M.J., 658 (FRI0454)
Moreno-Montoya, J., 758 (FRI0709), 1450 (AB1129), 1453 (AB1137)
Moreno-Ramos, M.J., 658 (FRI0454), 739 (FRI0659)
Morera-Morales, L., 897 (SAT0332)
Moret, F.M., 292 (THU0234)
Moretto, J., 493 (FRI0039)
Morgan, A., 200 (THU0002), 1010 (SAT0624)
Morgan, A.W., 200 (THU0001), 227 (THU0075)
Morgan, G.J., 944 (SAT0453)
Mori, I., 537 (FRI0148)
Mori, M., 1345 (AB0822)
Moriano, C., 213 (THU0037), 614 (FRI0336)
Moriano Morales, C., 719 (FRI0608), 1232 (AB0518)
Moridnia, M., 1547 (AB1246-HPR)
Morillon, M., 166 (OP0267)
Morinobu, A., 115 (OP0152), 422 (THU0571), 459 (THU0668), 487 (FRI0022), 507 (FRI0080), 699 (FRI0553)
Morishima, Y., 274 (THU0191), 1200 (AB0431)
Morita, K., 561 (FRI0210)
Morita, R., 1021 (SAT0652)
Mørk, C., 338 (THU0354), 472 (THU0700), 549 (FRI0182)
Morlock, R., 380 (THU0456, THU0457), 763 (FRI0720), 766 (FRI0728)
Moro, A.L.D., 246 (THU0119), 628 (FRI0371)
Moroncini, G., 64 (OP0031), 1189 (AB0400)
Morovic-Vergles, J., 245 (THU0116)
Morris, J., 939 (SAT0442)
Morris, V., 253 (THU0138)
Morsch, A.L.B., 1446 (AB1117)
Mortada, M., 583 (FRI0256)
Mortada, M.A., 733 (FRI0644), 1000 (SAT0596), 1013 (SAT0631), 1138 (AB0256)
Morton, A., 1360 (AB0867)
Morton, F., 242 (THU0111)
Moruno, H., 633 (FRI0385), 1270 (AB0625)
Mosad, E., 741 (FRI0665)
Mosallam, A., 1308 (AB0726)
Mosca, M., 50 (OP0002), 305 (THU0268), 320 (THU0308), 437 (THU0611), 446 (THU0636), 457 (THU0664), 584 (FRI0260), 589 (FRI0272), 617 (FRI0344), 731 (FRI0640), 867 (SAT0248), 875 (SAT0268), 1209 (AB0456), 1439 (AB1099)
Moschetta, A., 254 (THU0143)
Moschetti, V., 1185 (AB0391)
Mosher, D., 933 (SAT0428)
Moshrif, A., 1308 (AB0726)
Moskalev, A., 1056 (AB0027)
Mosor, E., 523 (FRI0113), 1511 (SAT0719-HPR)
Mosquera, J.A., 946 (SAT0458)
Mosquera, J.M., 1393 (AB0967)
Mosquera, N., 503 (FRI0068)
Mosquera-Martínez, J.A., 946 (SAT0457), 1322 (AB0764)
Moss, P., 960 (SAT0487)
Mossel, E., 591 (FRI0277), 875 (SAT0270)
Mostafa, E.S., 1008 (SAT0619)
Mota, L.M.H., 1160 (AB0320)
Motte, M., 359 (THU0402)
Mou, Y., 543 (FRI0163), 1141 (AB0266)
Mouanaa, H., 1348 (AB0830), 1362 (AB0876), 1383 (AB0937)

Moudatir, M., 322 (THU0313), 613 (FRI0333), 1253 (AB0578)
Mouhli, N., 1383 (AB0936)
Moulis, G., 1248 (AB0565)
Mounie, M., 1248 (AB0565)
Mount, D., 165 (OP0263)
Mountian, I., 1444 (AB1113)
Moura, C.S., 825 (SAT0149)
Moura, R.A., 834 (SAT0170)
Mourão, A.F., 186 (OP0315)
Mourguet, M., 188 (OP0321)
Mouriño, C., 1107 (AB0173)
Mourot Cottet, R., 1256 (AB0588)
Mousavi, S.M., 1431 (AB1075)
Mouterde, G., 51 (OP0004), 235 (THU0093), 258 (THU0152), 359 (THU0401), 811 (SAT0112), 1013 (SAT0631)
Mouthon, L., 104 (OP0123)
Moutschen, M., 77 (OP0063)
Moutsopoulos, H.M., 323 (THU0315)
Movahedi, M., 194 (OP0337-HPR), 531 (FRI0132)
Movia, D., 1085 (AB0111)
Mowinckel, P., 161 (OP0255-HPR)
Mowrey, W.B., 297 (THU0247)
Moya, P., 904 (SAT0351), 914 (SAT0379), 1305 (AB0717), 1414 (AB1027)
Moya Herraiz, A., 1347 (AB0829)
Moya Nájera, D., 1347 (AB0829)
Moyano, S., 1231 (AB0516), 1333 (AB0789)
Mozgovaya, E., 1361 (AB0872)
Mozzani, F., 1022 (SAT0653)
Mozzicafreddo, M., 64 (OP0031)
Mpektsis, T., 723 (FRI0619)
Mpofu, S., 145 (OP0222), 952 (SAT0470)
Mrazek, F., 1051 (AB0014)
Mroue, K., 762 (FRI0718)
Msihid, J., 570 (FRI0227), 844 (SAT0192)
Mtibaa, M., 571 (FRI0230), 1188 (AB0397)
Mu, F., 1487 (THU0753-HPR)
Mu, R., 1524 (SAT0757-HPR)
Mu, Y., 1081 (AB0100)
Mücke, M., 423 (THU0576)
Muda, A., 728 (FRI0632)
Mueller, A., 772 (SAT0011)
Mueller, K., 244 (THU0115)
Mueller, R., 267 (THU0174), 579 (FRI0247), 790 (SAT0059), 1144 (AB0273)
Mueller, R.B., 626 (FRI0369)
Mueller-Ladner, U., 1106 (AB0169), 1110 (AB0181)
Muenzer, K., 769 (SAT0004)
Mughal, F., 939 (SAT0442)
Muhaini, O., 1512 (SAT0722-HPR)
Muilu, P., 262 (THU0163)
Mukoyama, H., 422 (THU0571), 1398 (AB0981)
Mukuchyan, V.N., 1403 (AB0996)
Mulder, D.J., 625 (FRI0366), 630 (FRI0377), 1265 (AB0610)
Mulero, J., 645 (FRI0420), 736 (FRI0651), 925 (SAT0405)
Mulero Mendoza, J., 1399 (AB0986)
Mulhearn, B., 90 (OP0094)
Mullan, R., 773 (SAT0013), 1542 (AB1230-HPR)
Mullazehi, M., 228 (THU0077)
Mulleman, D., 335 (THU0349), 1448 (AB1123)
Müller, A., 1108 (AB0175)
Müller, C., 86 (OP0083), 257 (THU0150)
Müller, F., 1445 (AB1114)
Müller, G.A., 721 (FRI0614), 834 (SAT0171)
Müller, J., 1085 (AB0111)
Muller, S., 751 (FRI0690), 1028 (SAT0672), 1043 (SAT0708), 1442 (AB1107)
Müller-Gerbl, M., 1427 (AB1065)
Müller-Ladner, U., 65 (OP0034), 220 (THU0056), 299 (THU0252), 565 (FRI0217), 915 (SAT0380), 1063 (AB0046), 1070 (AB0067), 1071 (AB0069), 1286 (AB0669)
Mulvey, M., 758 (FRI0708)
Mumcu, G., 889 (SAT0310)
Munakata, M., 1109 (AB0180)
Munarriz, A., 1064 (AB0051)
Mundula, N., 496 (FRI0046)
Munguía-Realpozo, P., 311 (THU0283)
Muñiz-Gomez, M.L., 1363 (AB0878)
Muñoz, C.H., 308 (THU0275), 1092 (AB0129), 1239 (AB0538)
Muñoz, E., 622 (FRI0360)
Muñoz, M.C., 555 (FRI0195)
Muñoz, P., 594 (FRI0286), 1229 (AB0511), 1230 (AB0512)
Muñoz, S., 326 (THU0326)
Muñoz, Y.A., 1158 (AB0313)
Muñoz Cantos, N., 906 (SAT0357)
Muñoz Martínez de Salinas, C., 1362 (AB0875)
Muñoz-Fernández, S., 414 (THU0549), 520 (FRI0106), 921 (SAT0395), 946 (SAT0458)
Muñoz-Fernandez, S., 716 (FRI0602)
Muñoz-Louis, R., 877 (SAT0277)
Munoz-Louis, R., 877 (SAT0276)
Muñoz-Valle, J.F., 500 (FRI0058), 1199 (AB0427)
Munro, S., 443 (THU0629)
Muntean, L., 170 (OP0275), 260 (THU0156), 1245 (AB0557)
Muntner, P., 363 (THU0413)
Mura, S., 496 (FRI0046), 535 (FRI0143)
Murage, M.J., 1330 (AB0783)
Murakami, A., 1467 (AB1176)
Murakami, I., 220 (THU0057), 1452 (AB1133)
Murakami, K., 220 (THU0057), 527 (FRI0122), 618 (FRI0349), 620 (FRI0352), 1452 (AB1133)
Muram, D., 228 (THU0078), 244 (THU0114), 511 (FRI0089), 513 (FRI0092), 543 (FRI0164), 1130 (AB0235)
Muram, T., 1330 (AB0783)
Muramatsu, T., 923 (SAT0400)
Murasawa, A., 809 (SAT0106), 853 (SAT0214), 1124 (AB0219), 1177 (AB0371)
Murata, O., 1021 (SAT0652)
Muratore, F., 609 (FRI0323), 1247 (AB0563), 1248 (AB0564)
Muratore, M., 702 (FRI0563), 704 (FRI0568), 1353 (AB0847), 1483 (THU0743-HPR)
Muratti, E., 233 (THU0089), 571 (FRI0230), 1188 (AB0397)
Muraviev, Y., 1204 (AB0441)
Muravyev, Y.V., 251 (THU0132)
Murayama, G., 141 (OP0214), 1060 (AB0038), 1090 (AB0125), 1095 (AB0139)
Murayama, T., 543 (FRI0166)
Muresan, G.M., 1440 (AB1101)
Murgia, G., 1252 (AB0575)
Murgo, A., 643 (FRI0413), 746 (FRI0677), 908 (SAT0364)
Murillo-Vazquez, J., 1155 (AB0304)
Murimi, I.B., 859 (SAT0227)
Murovska, M., 1071 (AB0071)
Murphy, C.-L.M., 1092 (AB0131)
Murphy, C.C., 321 (THU0312)
Murphy, C.L., 401 (THU0516)
Murphy, D., 518 (FRI0101), 1031 (SAT0678), 1155 (AB0306), 1164 (AB0332)
Murphy, J., 195 (OP0339)
Murphy, M., 1069 (AB0064)
Murphy, R., 383 (THU0464)
Murphy Jr., W.A., 82 (OP0075)
Murray, C.W., 276 (THU0195)
Murray, D., 187 (OP0320)
Murray-Brown, W., 180 (OP0300)
Murt, A., 1243 (AB0550)
Murthy, B., 859 (SAT0226)
Mus, A., 1088 (AB0118)
Muschitz, C., 73 (OP0052), 655 (FRI0446)
Musellim, B., 1274 (AB0634)
Musetescu, A., 1151 (AB0294)
Museyko, O., 247 (THU0122)
Mushkin, A., 1391 (AB0962)
Mussano, E., 440 (THU0619)
Musselli, C., 857 (SAT0222), 862 (SAT0235), 1459 (AB1156)
Musset, L., 776 (SAT0023)
Mussetto, I., 728 (FRI0632)
Mustienes, R., 406 (THU0527)
Musto, A., 394 (THU0499)
Muth, J., 777 (SAT0027)
Mutis, A., 417 (THU0557)
Mutti, A., 1380 (AB0928)
Muxi, A., 691 (FRI0529)
Myasoedova, E., 512 (FRI0091)
Myasoutova, L., 1172 (AB0354), 1203 (AB0437, AB0438), 1300 (AB0704), 1311 (AB0735)
Mydel, P.M., 1102 (AB0160)
Myers, R.M., 290 (THU0227), 776 (SAT0022)
Mykytenko, G., 235 (THU0094)
Mysler, E., 149 (LB0003), 1181 (AB0379)
Myslinski, R., 79 (OP0068)
Mytilinaiou, M., 569 (FRI0224)
Mytnik, E., 1361 (AB0870, AB0871)

Na, S., 118 (OP0159)
Nab, H., 859 (SAT0227)
Nabozny, G., 118 (OP0160)
Naceur, I., 313 (THU0291), 599 (FRI0300), 889 (SAT0308), 1238 (AB0536)
Nachman, P.H., 318 (THU0301)
Nacır, B., 1197 (AB0420)
Nadali, M., 777 (SAT0026)
Naden, R., 50 (OP0002)
Nadin, T.G., 933 (SAT0426)
Nadkarni, G., 378 (THU0450)
Nadon, V., 1303 (AB0712)
Naegeli, A., 1334 (AB0793)
Næsborg-Andersen, K., 477 (THU0715)
Naffaa, M.E., 796 (SAT0074)
Nagafuchi, H., 1260 (AB0597)
Nagai, H., 645 (FRI0419), 1195 (AB0416)
Nagai, K., 115 (OP0152), 282 (THU0207)
Nagamine, R., 1342 (AB0814)
Nagamoto, T., 422 (THU0571), 1398 (AB0981)
Nagano, S., 1254 (AB0582)
Naganuma, Y., 1344 (AB0819)
Nagao, N., 703 (FRI0566)
Nagaoka, A., 1165 (AB0334), 1166 (AB0335)
Nagasaka, H., 284 (THU0212)
Nagata, A., 284 (THU0212)
Nagatomo, Y., 1054 (AB0021)
Nagel, J., 542 (FRI0162)
Naghdi, M., 1354 (AB0850)
Nagore, D., 555 (FRI0195), 826 (SAT0150)
Nagpal, S., 203 (THU0011)
Nagua, V., 1263 (AB0606)
Nagy, K., 767 (FRI0731)
Nagy, L., 1049 (AB0009)
Nagy, O., 342 (THU0363)
Nah, S.S., 1185 (AB0392)
Nahir, M.A., 333 (THU0343)
Nahman, N.S., 1507 (FRI0764-HPR)
Naidu, G., 1273 (AB0633)
Nair, A., 316 (THU0298)
Nair, J., 1251 (AB0573)
Nair, N., 200 (THU0001, THU0003)
Naishtetik, I.M., 1167 (AB0339)
Naito, M., 476 (THU0710)
Naito, Y., 703 (FRI0566)
Nájera Herranz, C., 291 (THU0229), 441 (THU0623), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1349 (AB0837), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Najm, A., 90 (OP0093), 128 (OP0184), 130 (OP0190)
Naka, I., 115 (OP0152), 487 (FRI0022), 507 (FRI0080), 699 (FRI0553)
Nakabo, S., 744 (FRI0673)
Nakachi, Y., 507 (FRI0079)
Nakagawa, N., 499 (FRI0054)
Nakahara, H., 800 (SAT0083), 1484 (THU0744-HPR)
Nakai, A., 499 (FRI0054)
Nakajima, A., 263 (THU0165), 280 (THU0204), 524 (FRI0117), 798 (SAT0079), 814 (SAT0120)
Nakajima, H., 602 (FRI0305), 645 (FRI0418, FRI0419), 1134 (AB0246), 1195 (AB0416)
Nakajima, H.N., 1191 (AB0405)
Nakajima, R., 561 (FRI0210)
Nakajima, T., 618 (FRI0349), 620 (FRI0352), 744 (FRI0673)
Nakamura, H., 318 (THU0303), 503 (FRI0067), 540 (FRI0156), 598 (FRI0295), 624 (FRI0364), 723 (FRI0620), 955 (SAT0477),

1023 (SAT0658), 1134 (AB0245), 1324 (AB0768), 1426 (AB1061), 1453 (AB1139)
Nakamura, K., 88 (OP0087)
Nakamura, S., 1134 (AB0247)
Nakamura, T., 67 (OP0040), 311 (THU0284), 464 (THU0681), 886 (SAT0302)
Nakamura, Y., 95 (OP0104), 422 (THU0571), 800 (SAT0084), 1398 (AB0981)
Nakanishi, K., 279 (THU0200)
Nakano, H., 645 (FRI0419), 1195 (AB0416)
Nakano, K., 66 (OP0036), 137 (OP0205), 257 (THU0149)
Nakano, M., 298 (THU0251), 313 (THU0290), 788 (SAT0054)
Nakashima, H., 1254 (AB0582)
Nakashima, R., 220 (THU0057), 527 (FRI0122), 618 (FRI0349), 620 (FRI0352), 1452 (AB1133)
Nakashima, S., 283 (THU0209), 719 (FRI0609), 757 (FRI0704), 831 (SAT0162), 907 (SAT0360), 1213 (AB0465)
Nakashima, Y., 1251 (AB0572)
Nakatani, T., 211 (THU0031)
Nakatsue, T., 313 (THU0290)
Nakayama, M., 799 (SAT0082), 1063 (AB0047)
Nakayama, Y., 778 (SAT0028)
Nakayamada, S., 66 (OP0036), 137 (OP0205), 257 (THU0149), 491 (FRI0031)
Nakazaki, S., 543 (FRI0166)
Nakazawa, T., 105 (OP0127), 911 (SAT0370)
Nakazono, K., 853 (SAT0214)
Naknao, K., 491 (FRI0031)
Nakopoulou, T., 1536 (AB1215-HPR)
Nalawade, A.B., 269 (THU0178)
Nalli, C., 437 (THU0611), 1468 (AB1178)
Nalotto, L., 305 (THU0268), 1209 (AB0455)
Nam, E.J., 422 (THU0572), 514 (FRI0093), 783 (SAT0042)
Nam, J., 518 (FRI0102), 1016 (SAT0639)
Namane, N., 359 (THU0402)
Namiki, Y., 531 (FRI0134), 1291 (AB0681)
Namme Luma, H., 368 (THU0425), 997 (SAT0587, SAT0588)
Namura, N., 793 (SAT0068)
Nanda, K., 405 (THU0525)
Nandagudi, A., 271 (THU0183), 1354 (AB0851)
Nanki, T., 842 (SAT0187)
Nantel, F., 554 (FRI0191), 679 (FRI0503)
Nantz, E., 233 (THU0088)
Naorem, S., 1295 (AB0690)
Naraghi, K., 1016 (SAT0639)
Narangoda, K., 1355 (AB0853)
Naranjo, A., 691 (FRI0530), 694 (FRI0539), 1016 (SAT0638)
Narayan, N., 1420 (AB1045)
Narayan R, V., 984 (SAT0550)
Narayanan, R.P., 852 (SAT0209)
Naredo, E., 173 (OP0283), 175 (OP0288), 233 (THU0088), 400 (THU0514), 583 (FRI0256), 735 (FRI0649), 737 (FRI0653), 742 (FRI0668), 1009 (SAT0621), 1013 (SAT0631), 1015 (SAT0636), 1414 (AB1029), 1428 (AB1067)
Naretto, C., 1410 (AB1014)
Narin, S., 999 (SAT0594), 1519 (SAT0742-HPR)
Narita, A., 1344 (AB0819)
Narita, I., 313 (THU0290), 853 (SAT0214)
Narongroeknawin, P., 1298 (AB0700)
Narváez, J., 614 (FRI0336)
Narvaez, J., 843 (SAT0191)
Narvaez-García, J., 251 (THU0134)
Naryshkin, E., 269 (THU0179)
Nas, K., 241 (THU0108), 637 (FRI0396), 1182 (AB0383), 1306 (AB0721), 1317 (AB0751), 1320 (AB0757), 1324 (AB0767), 1532 (AB1202-HPR)
Nascimento, D., 1062 (AB0043)
Nascimento, V.C., 1056 (AB0028)
Nasef, S.I., 887 (SAT0304), 1235 (AB0526)
Nash, P., 135 (OP0201), 143 (OP0219), 682 (FRI0509), 683 (FRI0511), 941 (SAT0446), 948 (SAT0462), 951 (SAT0469), 957 (SAT0480), 1326 (AB0772)
Nasim, A., 1196 (AB0417)
Nasonov, E., 169 (OP0272), 249 (THU0127), 273 (THU0188), 576 (FRI0241), 599 (FRI0299), 616 (FRI0343), 811 (SAT0113), 860 (SAT0230), 956 (SAT0478), 1337 (AB0797, AB0798)
Nasonov, E.L., 266 (THU0171), 861 (SAT0232), 1128 (AB0230), 1347 (AB0828)
Nasr, A., 1149 (AB0287)
Nasr, M., 1176 (AB0365)
Nasralla, J., 1494 (THU0769-HPR)
Nassar-Sheikh-Rashid, A., 1221 (AB0488)
Nassr, M.H., 1053 (AB0018)
Nasswetter, G., 311 (THU0285), 590 (FRI0276), 729 (FRI0635), 991 (SAT0568), 1217 (AB0478)
Nasswetter, G.G., 1279 (AB0649)
Nataf, H., 428 (THU0588, THU0589)
Natalello, G., 197 (OP0343)
Natalia, M., 1041 (SAT0702)
Natalucci, F., 470 (THU0696), 879 (SAT0281)
Natella, L.L., 707 (FRI0578)
Nathan, N., 1049 (AB0007)
Natoli, G., 901 (SAT0341)
Natour, J., 163 (OP0259-HPR), 1478 (THU0728-HPR), 1508 (FRI0769-HPR)
Natsumeda, M., 1484 (THU0744-HPR)
Natuzzi, D., 1059 (AB0037)
Naumenko, E., 1356 (AB0858)
Nava-Valdivia, C.A., 1155 (AB0304)
Nava-Zavala, A., 262 (THU0161)
Navales, I., 324 (THU0320)
Navarini, L., 151 (OP0233), 263 (THU0164), 304 (THU0267)
Navarro, A., 312 (THU0287)
Navarro, D., 590 (FRI0274), 1206 (AB0445)
Navarro, F., 577 (FRI0245), 1141 (AB0267), 1193 (AB0412)
Navarro, J.P., 593 (FRI0283)
Navarro, P., 728 (FRI0633)
Navarro, V., 1005 (SAT0610), 1304 (AB0714)
Navarro Compan, V., 100 (OP0115, OP0116), 824 (SAT0145)
Navarro-Blasco, F., 1472 (AB1191)
Navarro-Compán, V., 357 (THU0396), 429 (THU0590), 917 (SAT0385), 930 (SAT0419), 933 (SAT0427), 1293 (AB0686), 1294 (AB0687)
Navarro-Compan, V., 658 (FRI0452), 927 (SAT0412)
Navarro-Hernández, R.-E., 1164 (AB0330)
Navarro-Hernandez, R.-E., 806 (SAT0100), 1075 (AB0083), 1169 (AB0345)
Naveau, C., 736 (FRI0650)
Naveh, N., 654 (FRI0444)
Nawata, A., 257 (THU0149)
Nawrot, J., 539 (FRI0152)
Nazarova, L.S., 1049 (AB0008)
Nazligul, T., 735 (FRI0648), 999 (SAT0592)
Ndosi, M., 112 (OP0144-HPR), 430 (THU0594), 1473 (AB1193), 1495 (FRI0733-HPR), 1501 (FRI0748-HPR), 1510 (SAT0718-HPR)
Nduaka, C., 148 (OP0230), 277 (THU0197)
Neagu, A., 1208 (AB0450)
Nealon Lennox, N., 110 (OP0140-HPR)
Nebesky, J.M., 579 (FRI0248)
Nedovic, J., 914 (SAT0378)
Needell, S., 1139 (AB0261)
Néel, A., 778 (SAT0029)
Néel, M., 778 (SAT0029)
Negalur, N., 1247 (AB0561, AB0562)
Negm, A.A., 1113 (AB0190), 1403 (AB0997), 1426 (AB1062)
Negrin, M., 694 (FRI0539)
Negru, M.M., 1278 (AB0647), 1460 (AB1158)
Negueroles Albuixec, R., 1349 (AB0837)
Negueroles Albuixech, R., 291 (THU0229), 441 (THU0623), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Nehrer, S., 1423 (AB1053)
Neidhart, M., 117 (OP0157)
Neifar, M., 1311 (AB0734)
Neijland, Y., 1553 (PARE0006)
Neiman, M., 626 (FRI0367)
Nelissen, R., 769 (SAT0001)
Nelissen, R.G., 207 (THU0020), 966 (SAT0505), 967 (SAT0506), 1040 (SAT0701)
Nell-Duxneuer, V., 750 (FRI0688)
Nell-Duxneuner, V., 1494 (THU0770-HPR)
Nelson, C., 474 (THU0707)
Nematollahi, N., 1137 (AB0254)
Němcova, D., 1390 (AB0958)
Nemcova, D., 1389 (AB0957)
Nemeskéri, Á., 1428 (AB1067)
Nenasheva, N.V., 536 (FRI0146), 1218 (AB0479)
Neovius, M., 157 (OP0246)
Neregård, P., 831 (SAT0161)
Neri, D., 92 (OP0099)
Neri, R., 617 (FRI0344)
Nero, P., 35 (SP0142), 436 (THU0610)
Nerviani, A., 238 (THU0100), 490 (FRI0030), 511 (FRI0088)
Nesbitt, A., 554 (FRI0193)
Neseem, N.O., 1151 (AB0293)
Nesmeyanova, O., 560 (FRI0208)
Nesterovich, I.I., 810 (SAT0111)
Neto, F., 1062 (AB0043)
Neubauer, A.S., 442 (THU0626)
Neubauer, R., 896 (SAT0328)
Neumann, A., 73 (OP0052)
Neumann, E., 220 (THU0056), 1063 (AB0046), 1070 (AB0067), 1071 (AB0069)
Neumann, F., 1060 (AB0039)
Neumann, T., 115 (OP0151)
Neurath, M.F., 655 (FRI0446)
Nevin, K., 209 (THU0026)
New, P., 912 (SAT0374)
Newton, J., 1524 (SAT0758-HPR)
Newton, J.L., 966 (SAT0504), 1517 (SAT0736-HPR)
Neylander, M., 172 (OP0281-PARE)
Nezos, A., 210 (THU0028)
Nezzer, J., 121 (OP0167)
Ng, C.T., 446 (THU0638)
Ng, W.-F., 67 (OP0040), 92 (OP0097), 163 (OP0259-HPR), 295 (THU0242), 1103 (AB0162), 1205 (AB0444), 1236 (AB0528), 1517 (SAT0736-HPR), 1524 (SAT0758-HPR)
Ng, W.L., 412 (THU0543), 715 (FRI0599), 1493 (THU0768-HPR)
Ngahane Mbatchou, H.B., 997 (SAT0588)
Ngcozana, T., 628 (FRI0372)
Nguyen, C., 170 (LB0001)
Nguyen, D., 143 (OP0219), 684 (FRI0513)
Niamane, R., 697 (FRI0548), 1349 (AB0836)
Niazy, M., 1047 (AB0002)
Nicco, C., 182 (OP0307)
Nichitean, R., 1285 (AB0666)
Nicholls, E., 973 (SAT0521), 1433 (AB1081)
Nichols, K.K., 152 (OP0237)
Nicklin, J.K., 1501 (FRI0748-HPR)
Nicolaou, S., 166 (OP0266)
Nicolas, G., 406 (THU0528)
Niebrzydowski, J., 556 (FRI0198)
Niedermann, K., 185 (OP0314-HPR), 1489 (THU0758-HPR)
Niederreiter, B., 131 (OP0194), 486 (FRI0018), 502 (FRI0064)
Nielen, J.T.H., 433 (THU0603)
Nielsen, B.D., 174 (OP0285), 329 (THU0335)
Nielsen, C., 745 (FRI0675), 1024 (SAT0660)
Nielsen, C.H., 493 (FRI0038), 501 (FRI0061), 775 (SAT0020), 1075 (AB0081)
Nielsen, C.T., 457 (THU0663)
Nielsen, M., 161 (OP0255-HPR)
Nielsen, S., 1389 (AB0957)
Nielsen, S.M., 196 (OP0340), 737 (FRI0654)
Niemczynsky, P., 171 (OP0278-PARE)
Nieto, E., 1339 (AB0805)
Nieto, J., 593 (FRI0284)
Nieto, J.-C., 175 (OP0288)
Nieto, J.C., 386 (THU0474), 462 (THU0676), 656 (FRI0448), 748 (FRI0683), 918 (SAT0387), 1297 (AB0695), 1305 (AB0718), 1307 (AB0723)
Nieto Gonzales, J.C., 1015 (SAT0636)
Nieto Gonzalez, J.C., 1276 (AB0640), 1414 (AB1029), 1476 (THU0720-HPR)
Nieto-González, J.C., 400 (THU0514),

737 (FRI0653), 875 (SAT0270), 925 (SAT0406), 1386 (AB0947)
Nieuwenhuis, W., 473 (THU0702)
Nieuwenhuis, W.P., 473 (THU0704)
Nieuwland-Husson, S., 863 (SAT0238)
Nieves, J., 72 (OP0051)
Nieves, Y., 121 (OP0167)
Niewerth, M., 76 (OP0060), 397 (THU0504)
Nightingale, A., 685 (FRI0514)
Nihtyanova, S., 898 (SAT0334), 915 (SAT0380)
Nii, T., 1058 (AB0032)
Niiro, H., 1254 (AB0582)
Nijhof, M.W., 110 (OP0138-HPR), 1487 (THU0752-HPR)
Nijhuis-van der Sanden, R., 1492 (THU0764-HPR)
Nijjar, J., 242 (THU0111)
Nijjar, J.S., 55 (OP0012-PARE)
Nikaido, T., 1109 (AB0180)
Niki, Y., 1063 (AB0047)
Nikiforou, D., 1437 (AB1093)
Nikiphorou, E., 63 (OP0030), 80 (OP0070), 226 (THU0073), 429 (THU0590), 782 (SAT0040), 805 (SAT0098), 806 (SAT0099), 1028 (SAT0671)
Nikishina, I., 1389 (AB0955)
Nikitchenko, N.V., 389 (THU0485)
Nikitina, N.M., 546 (FRI0172), 819 (SAT0134)
Nikitinskaya, O., 704 (FRI0567)
Nikonova, V.V., 1392 (AB0963)
Nikulenkova, N., 267 (THU0173)
Niles, J., 318 (THU0301)
Nilsen, A.T., 319 (THU0305)
Nilsen, M.M., 184 (OP0312)
Nilssen, I.R., 1480 (THU0733-HPR)
Nilsson, J., 779 (SAT0031)
Nilsson, P., 626 (FRI0367)
Ninaber, M.K., 903 (SAT0350), 907 (SAT0359)
Ning, Y., 1352 (AB0845)
Nisar, M.K., 199 (OP0347-HPR), 430 (THU0592), 1484 (THU0746-HPR)
Nishida, M., 282 (THU0208)
Nishikawa, A., 158 (OP0248)
Nishikawa, H., 418 (THU0559), 717 (FRI0603), 924 (SAT0402)
Nishikawa, K., 1095 (AB0140)
Nishikomori, R., 1403 (AB0995)
Nishimi, A., 222 (THU0064), 894 (SAT0322), 1149 (AB0289)
Nishimi, S., 222 (THU0064), 894 (SAT0322), 1149 (AB0289)
Nishimoto, N., 1471 (AB1187)
Nishimura, H., 141 (OP0215)
Nishimura, K., 422 (THU0571), 699 (FRI0553), 1398 (AB0981)
Nishina, K., 618 (FRI0347)
Nishina, N., 418 (THU0560)
Nishino, A., 318 (THU0303)
Nishino, J., 278 (THU0198), 476 (THU0710), 525 (FRI0119)
Nishio, Y., 1134 (AB0247)
Nishioka, A., 641 (FRI0408)
Nishishinya, M.B., 554 (FRI0192)
Nishizaka, H., 1254 (AB0582)
Nisihara, R., 820 (SAT0135), 1111 (AB0186)
Nissen, M., 130 (OP0189)
Nissen, M.J., 168 (OP0271), 335 (THU0347), 656 (FRI0450)
Nissim, A., 483 (FRI0011), 646 (FRI0423)
Nititham, J., 289 (THU0225)
Nitsche, A., 906 (SAT0357)
Nitta, T., 841 (SAT0186)
Niu, H., 268 (THU0176), 1197 (AB0421), 1295 (AB0691)
Nived, P., 542 (FRI0162)
Nivuori, M., 254 (THU0143), 521 (FRI0110), 1268 (AB0618), 1461 (AB1160)
Nix, M., 376 (THU0445)
Nizard, J., 388 (THU0480)
Nkhoma, E., 93 (OP0101)
Noblejas, A., 873 (SAT0264), 1245 (AB0555), 1266 (AB0614), 1289 (AB0676)
Nobre, M.R.C., 1441 (AB1104)
Nobuhara, Y., 911 (SAT0370)
Nochevnaya, K.V., 810 (SAT0111)
Nock, G., 786 (SAT0049)
Nocturne, G., 182 (OP0307), 289 (THU0225), 508 (FRI0081)
Noda, Y., 282 (THU0208)
Nograles, K., 1325 (AB0771)
Nogueira-Recalde, U., 53 (OP0008), 481 (FRI0005)
Nogues, E., 1434 (AB1085)
Noirez, V., 426 (THU0582)
Nojima, T., 1460 (AB1159)
Nolasco, F., 590 (FRI0274), 1206 (AB0445)
Nolla, J., 326 (THU0326)
Nolla, J.-M., 663 (FRI0468)
Nolla, J.M., 290 (THU0227)
Nolte, J., 453 (THU0654, THU0655)
Nomura, A., 1090 (AB0125), 1095 (AB0139)
Nomura, H., 1054 (AB0021)
Nomura, Y., 809 (SAT0106), 853 (SAT0214), 1124 (AB0219), 1177 (AB0371), 1251 (AB0572)
Nonaka, F., 723 (FRI0620)
Nonaka, K., 1251 (AB0572)
Noort-van der Laan, W., 1476 (THU0721-HPR)
Noppakun, K., 908 (SAT0362)
Nör, C., 502 (FRI0066)
Nor-Shuhaila, S., 1512 (SAT0722-HPR)
Norberciak, L., 359 (THU0402)
Nordal, E.B., 55 (OP0013)
Nordberg, L.B., 538 (FRI0151), 1017 (SAT0642)
Nordeman, L., 1487 (THU0754-HPR), 1503 (FRI0753-HPR)
Nordgren, B., 1523 (SAT0754-HPR)
Nordin, H., 553 (FRI0190)
Nordlund, K., 173 (OP0282-PARE)
Nordmark, G., 311 (THU0284), 464 (THU0681), 886 (SAT0302)
Nordström, D., 341 (THU0361), 686 (FRI0518), 1027 (SAT0669)
Nordstrom, D., 656 (FRI0450)
Nordström, D.C., 850 (SAT0206)
Norelli, M., 126 (OP0179)
Nørgaard, M., 451 (THU0649)
Norheim, K.B., 184 (OP0312)
Norheim, P., 802 (SAT0090)
Norkuviene, E., 359 (THU0401), 367 (THU0423)
Norli, E.S., 81 (OP0071), 756 (FRI0702), 1030 (SAT0675)
Norling, L., 483 (FRI0011)
Norman, K., 897 (SAT0333)
Norris, J.M., 498 (FRI0053), 757 (FRI0706)
Norton, G., 252 (THU0136), 545 (FRI0170)
Norton, G.R., 245 (THU0117)
Norton, S., 63 (OP0030), 226 (THU0073), 782 (SAT0040), 805 (SAT0098), 806 (SAT0099), 1028 (SAT0671), 1030 (SAT0676), 1039 (SAT0699)
Norvang, V., 224 (THU0070), 797 (SAT0075)
Nossent, E.J., 732 (FRI0642)
Nossent, J., 467 (THU0688), 647 (FRI0426), 767 (FRI0730), 1045 (SAT0716), 1241 (AB0542)
Nossum, R., 1478 (THU0726-HPR)
Notario, I., 452 (THU0651)
Notario Ferreira, I., 1228 (AB0506), 1321 (AB0760)
Notarnicola, A., 626 (FRI0367), 896 (SAT0329)
Nothnagl, T., 1455 (AB1144)
Notopoulos, A., 1047 (AB0001)
Nour El-Din, A.M., 1237 (AB0533)
Noureldine, M.H.A., 1400 (AB0989)
Nourisson, C., 1360 (AB0869)
Novak, G., 76 (OP0061)
Novelli, G., 204 (THU0013), 1007 (SAT0615)
Novelli, L., 463 (THU0678), 489 (FRI0027)
Novikov, A., 576 (FRI0241), 640 (FRI0403), 811 (SAT0113), 1283 (AB0659), 1404 (AB0998), 1411 (AB1018)
Novikov, A.A., 251 (THU0132), 861 (SAT0232), 1128 (AB0230), 1226 (AB0500)
Novikov, A.N., 776 (SAT0024)
Novikov, P., 324 (THU0319), 331 (THU0338), 617 (FRI0346)
Novikova, D., 256 (THU0148), 572 (FRI0231), 599 (FRI0299), 811 (SAT0113), 944 (SAT0452), 1404 (AB0998)
Novkovic, S., 706 (FRI0574)
Novokov, A., 254 (THU0142)
Nowak, B., 1112 (AB0187)
Nowak, E., 67 (OP0040)
Nowell, W.B., 448 (THU0643), 449 (THU0644, THU0645), 1177 (AB0370), 1521 (SAT0750-HPR)
Nozaka, K., 707 (FRI0577)
Nozal, P., 456 (THU0661), 555 (FRI0194), 822 (SAT0141), 1179 (AB0375)
Ntali, S., 1204 (AB0442)
Ntari, L., 500 (FRI0059)
Nuccetelli, Y., 1245 (AB0556)
Nuesslein, H., 159 (OP0249), 516 (FRI0098)
Nugaliyadde, A., 271 (THU0183)
Numajiri, H., 138 (OP0207)
Nunes, G., 1051 (AB0013), 1094 (AB0134)
Nunes, H., 1049 (AB0007)
Nuñez, E., 1041 (SAT0703), 1458 (AB1150)
Nuñez, M., 1041 (SAT0703), 1458 (AB1150)
Núñez, M.J., 873 (SAT0264)
Nuñez Beltran, M., 990 (SAT0564)
Núñez Cuadros, E., 1393 (AB0968)
Núñez-Alvarez, C.A., 597 (FRI0292)
Nuñez-Cuadros, E., 391 (THU0489)
Núñez-Fernández, M.J., 415 (THU0550)
Núñez-Monje, V., 258 (THU0153), 1316 (AB0746)
Nuñez-Monje, V., 1168 (AB0344)
Nuño, L., 551 (FRI0186), 559 (FRI0204), 833 (SAT0168), 908 (SAT0363), 1116 (AB0198), 1179 (AB0375), 1294 (AB0687)
Nuno, L., 633 (FRI0385), 1270 (AB0625)
Nuño Nuño, L., 824 (SAT0145)
Nunokawa, T., 1176 (AB0367)
Nurkovic, J., 1552 (PARE0003)
Nurminen, T., 60 (OP0023)
Nurmohamed, M., 259 (THU0154), 280 (THU0203), 347 (THU0374), 550 (FRI0183), 758 (FRI0707), 811 (SAT0114), 935 (SAT0433), 1038 (SAT0695), 1087 (AB0116)
Nurmohamed, M.T., 32 (SP0127), 61 (OP0025), 354 (THU0391), 659 (FRI0455), 661 (FRI0461), 817 (SAT0127), 928 (SAT0415), 931 (SAT0421)
Nurul Aain, A.F., 1512 (SAT0722-HPR)
Nurullina, G., 1161 (AB0322, AB0323)
Nüßlein, H., 577 (FRI0245), 1141 (AB0267), 1193 (AB0412)
Nuti, R., 86 (OP0082), 894 (SAT0323)
Nutz, A., 113 (OP0146), 1159 (AB0315)
Nygaard, H., 81 (OP0071), 756 (FRI0702), 1030 (SAT0675)
Nylander, M., 1544 (AB1238-HPR)
Nymo, S., 1546 (AB1244-HPR)
Nyren, S., 896 (SAT0329)
Nys, E., 763 (FRI0719)
Nys, M., 75 (OP0058), 145 (OP0223)
Nystad, T.W., 783 (SAT0043)
Nzeusseu Toukap, A., 728 (FRI0633)

O'Brien, S., 418 (THU0561)
O'Connor, J., 1023 (SAT0657)
O'Dell, J., 144 (OP0220), 831 (SAT0162)
O'donnell, J., 637 (FRI0395)
O'donnell, J.L., 1415 (AB1031)
O'Dywer, J.L., 1205 (AB0444)
O'Mahony, A., 269 (THU0180)
O'Malley, T., 1025 (SAT0662)
O'Neil, J.D., 125 (OP0178)
O'Neil, K., 391 (THU0490)
O'Neill, A., 729 (FRI0634), 1530 (AB1196-HPR)
O'Neill, C., 140 (OP0211-PARE)
O'neill, C.H., 1372 (AB0904)
O'Neill, L., 321 (THU0312)
O'Neill, S., 110 (OP0140-HPR)
O'Neill, T., 1444 (AB1111)
O'Reilly, D., 786 (SAT0049)
O'Rourke, K., 693 (FRI0534), 871 (SAT0257)
O'Rourke, K.P., 1509 (FRI0772-HPR)
O'Shea, F., 656 (FRI0450)
O'Sullivan, M., 803 (SAT0092)
Oates, M., 71 (OP0048)
Obaya, J.C., 918 (SAT0387), 1307 (AB0723)
Obreque, J., 1098 (AB0148)
Obrien, R., 407 (THU0531)

Ocaña, A.M., 1472 (AB1190)
Océa, R.A., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Ocejo-Vinyals, G., 1084 (AB0108)
Ochiai, M., 263 (THU0165), 524 (FRI0117), 798 (SAT0079), 814 (SAT0120)
Ochiel, R., 104 (OP0123)
Ochoa Grullon, J., 990 (SAT0564)
Ochs, W., 159 (OP0249), 516 (FRI0098)
Ocsovszki, I., 1105 (AB0167)
Odgaard, A., 159 (OP0251), 226 (THU0072)
Odin, V., 1153 (AB0298)
Oelke, K., 276 (THU0195), 348 (THU0376), 678 (FRI0501)
Oelzner, P., 115 (OP0151)
Oesch, P., 46 (SP0191), 1539 (AB1222-HPR)
Offroy, M.-A., 963 (SAT0497)
Ogata, A., 800 (SAT0083)
Ogawa, M., 810 (SAT0110), 1372 (AB0905)
Ogawa, Y., 799 (SAT0081)
Ogbomo, A., 562 (FRI0211), 836 (SAT0175)
Ogbonnaya, A., 842 (SAT0188)
Ogdie, A., 759 (FRI0711), 1313 (AB0739), 1332 (AB0786)
Oger, E., 1448 (AB1123)
Ognenovski, V., 1445 (AB1115)
Ognibeni, F., 805 (SAT0097)
Ogren, G., 997 (SAT0586), 1003 (SAT0606)
Ogrič, M., 325 (THU0324)
Oguchi, Y., 1248 (AB0566)
Oguni, S., 1251 (AB0572)
Ogura, T., 995 (SAT0581), 1024 (SAT0661)
Oguri, Y., 1062 (AB0044)
Oguro, E., 1058 (AB0032)
Oguro, N., 1138 (AB0258)
Oh, D.-S., 381 (THU0459), 1074 (AB0080)
Oh, J.S., 1222 (AB0491)
Oh, Y.-J., 383 (THU0467)
Ohashi, S., 476 (THU0710)
Ohashi, T., 833 (SAT0167), 1183 (AB0386)
Ohde, S., 813 (SAT0118)
Ohishi, A., 282 (THU0208)
Ohkuro, M., 211 (THU0031)
Ohmura, K., 202 (THU0006), 220 (THU0057), 527 (FRI0122), 598 (FRI0295), 618 (FRI0349), 620 (FRI0352), 624 (FRI0364), 1452 (AB1133), 1453 (AB1139)
Ohnesorge, N., 646 (FRI0421)
Ohnishi, N., 598 (FRI0295)
Ohno, N., 1061 (AB0041)
Ohno, S., 645 (FRI0418, FRI0419), 1134 (AB0246), 1191 (AB0405)
Ohrndorf, S., 131 (OP0192), 400 (THU0512), 583 (FRI0256), 1008 (SAT0618), 1409 (AB1013)
Ohsfeldt, R.L., 599 (FRI0298)
Ohshima, S., 1058 (AB0032)
Ohson, K., 143 (OP0219)
Ohta, S., 1254 (AB0582)
Ohtsuji, M., 141 (OP0215)
Oishi, Y., 285 (THU0214), 582 (FRI0254)
Ojeda, C., 843 (SAT0191)
Ojeda, F., 307 (THU0273)
Ojeda, F.A., 1181 (AB0381)
Ojeda, I., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Ojeda, S., 691 (FRI0530), 694 (FRI0539)
Oka, A., 202 (THU0006)
Oka, H., 476 (THU0710), 1150 (AB0292)
Okada, H., 531 (FRI0134), 1291 (AB0681)
Okada, K., 1069 (AB0065)
Okada, M., 135 (OP0201), 144 (OP0221), 574 (FRI0235), 610 (FRI0326), 813 (SAT0118), 871 (SAT0256)
Okada, N., 1137 (AB0253)
Okada, Y., 165 (OP0263), 285 (THU0214), 424 (THU0577), 1248 (AB0566), 1399 (AB0984)
Okai, T., 573 (FRI0233), 806 (SAT0101)
Okamoto, N., 409 (THU0535)
Okamura, K., 493 (FRI0036), 1203 (AB0439)
Okano, T., 115 (OP0152), 487 (FRI0022), 507 (FRI0080), 540 (FRI0156), 699 (FRI0553), 955 (SAT0477), 1023 (SAT0658), 1134 (AB0245), 1324 (AB0768), 1426 (AB1061)
Okatan, E., 606 (FRI0315)
Okatan, I.E., 1124 (AB0218), 1244 (AB0554)
Okayama, A., 1054 (AB0021)
Okazaki, T., 635 (FRI0391), 872 (SAT0259), 910 (SAT0369), 1260 (AB0597)
Oke, V., 885 (SAT0297)
Oki, H., 1344 (AB0819)
Okita, Y., 1058 (AB0032)
ÖkmenMetin, B., 974 (SAT0525)
Okoye, R., 213 (THU0038)
Oksuz, M.F., 609 (FRI0322)
Oku, K., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Okubo, N., 841 (SAT0186)
Okura, C., 493 (FRI0036), 1203 (AB0439)
Okuyama, A., 424 (THU0577), 1399 (AB0984)
Oláh, C., 1027 (SAT0668)
Olán, F., 1132 (AB0240, AB0241)
Olariaga, E., 555 (FRI0194)
Oldenberg, J., 1222 (AB0489)
Oldham, J., 1444 (AB1111)
OLeary, G., 133 (OP0198-PARE)
Olech, E., 276 (THU0195)
Olejárová, M., 420 (THU0565)
Olek, S., 292 (THU0234)
Olesińska, M., 1224 (AB0496)
Olesinska, M., 204 (THU0012), 1470 (AB1184)
Oliffe, M., 429 (THU0591)
Olivares, B., 1006 (SAT0613)
Olivares González, L., 291 (THU0229)
Olivares-Martínez, E., 597 (FRI0292)
Olivari, D., 1189 (AB0400)
Olivas, O., 793 (SAT0067)
Olivé, A., 290 (THU0227), 843 (SAT0191), 873 (SAT0263), 1107 (AB0173), 1236 (AB0529), 1241 (AB0544)
Olive, A., 326 (THU0326), 885 (SAT0299), 988 (SAT0560), 1232 (AB0519), 1424 (AB1055)
Oliveira, E., 361 (THU0406)
Oliveira, I., 176 (OP0290)
Oliveira, I.S.D., 1412 (AB1021)
Oliveira, P.G., 502 (FRI0066)
Oliveira, S., 902 (SAT0345), 1131 (AB0238)
Oliveira-Ramos, F., 186 (OP0315)
Oliver, A., 1507 (FRI0764-HPR)
Oliver, J., 200 (THU0002)
Oliver, S., 886 (SAT0301), 1229 (AB0509)
Oliviera, N.C., 1438 (AB1096)
Olivieri, I., 343 (THU0365), 437 (THU0611), 445 (THU0634), 1439 (AB1099), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Olivieri, M., 496 (FRI0045)
Olivieri, S., 1468 (AB1178)
Oliviero, F., 99 (OP0113), 210 (THU0029), 216 (THU0047), 1111 (AB0184)
Olivos-Meza, A., 1067 (AB0059)
Oller Rodríguez, J.E., 441 (THU0623), 1349 (AB0837)
Oller Rodriguez, J.E., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Ollier, W.E., 912 (SAT0374)
Olmez, M.O., 791 (SAT0063)
Olmos, J.M., 802 (SAT0088), 804 (SAT0095)
Olofsson, T., 157 (OP0246), 651 (FRI0436), 655 (FRI0445)
Olsder, W., 16 (SP0064), 1552 (PARE0001), 1557 (PARE0015)
Olsen, I., 1029 (SAT0673)
Olsen, I.C., 176 (OP0289), 224 (THU0070), 334 (THU0345), 338 (THU0354), 472 (THU0700), 526 (FRI0121), 538 (FRI0151), 549 (FRI0182), 673 (FRI0490), 686 (FRI0518), 797 (SAT0075), 1017 (SAT0642)
Olsen, M., 1478 (THU0726-HPR)
Olsson, C., 1531 (AB1199-HPR)
Olsson, H., 1064 (AB0049)
Olstad, D.S., 466 (THU0686)
Olszewska, M., 216 (THU0045)
Olteanu, O., 435 (THU0607)
Olvera-Soto, M.G., 1343 (AB0815)
Omair, M., 1367 (AB0889)
Omar, H.H., 887 (SAT0304), 1235 (AB0526)
Omar, M.A.-B., 1151 (AB0293)
Ombe, T., 1251 (AB0572)
Omdal, R., 184 (OP0312)
Omelchenko, L.I., 399 (THU0510)
Omelchenko, T., 974 (SAT0526)
Omelchenko, V.O., 1067 (AB0058)
Ömercikoğlu, Z., 1462 (AB1162)
Omercikoglu, Z., 455 (THU0658)
Ometto, F., 603 (FRI0308), 1123 (AB0215), 1209 (AB0455)
Omma, A., 327 (THU0329), 609 (FRI0322), 1170 (AB0350)
Omorou, A.Y., 970 (SAT0513)
Omoumi, P., 14 (SP0058)
Omura, F., 443 (THU0627)
Onal, S., 1468 (AB1179)
Onali, S., 667 (FRI0477)
Onat, A.M., 327 (THU0329)
Oneata, R., 435 (THU0607), 1032 (SAT0681), 1264 (AB0608)
Onen, F., 306 (THU0271), 322 (THU0314), 1282 (AB0658)
Onen, S., 1381 (AB0932)
Oner, F.C., 1423 (AB1052)
Ong, S.G., 1237 (AB0532)
Ong, V., 635 (FRI0390), 1104 (AB0166)
Ong, V.H., 898 (SAT0334, SAT0335), 1269 (AB0621)
Ongenaert, M., 648 (FRI0428)
Onishi, A., 115 (OP0152), 422 (THU0571), 459 (THU0668), 487 (FRI0022), 507 (FRI0080), 699 (FRI0553)
Onishi, I., 283 (THU0209)
Onishi, T., 282 (THU0207)
Onizuka, N., 958 (SAT0484)
Önnheim, K., 779 (SAT0031)
Ono, K., 476 (THU0710)
Ono, N., 895 (SAT0326), 1254 (AB0582)
Ono, S., 923 (SAT0400)
Onstenk, R., 967 (SAT0506)
Onuma, K., 189 (OP0325), 981 (SAT0541)
Oommen, P., 74 (OP0057)
Oostveen, J., 1306 (AB0722)
Oparil, S., 363 (THU0413)
Opava, C.H., 1523 (SAT0754-HPR)
Opitz, C.A., 1070 (AB0068)
Opris, D., 876 (SAT0271), 881 (SAT0288), 1025 (SAT0664), 1208 (AB0450), 1333 (AB0790), 1428 (AB1068)
Opris-Belinski, D., 304 (THU0266), 342 (THU0363), 416 (THU0555), 423 (THU0574), 435 (THU0606), 457 (THU0665), 1221 (AB0487), 1278 (AB0646, AB0647), 1433 (AB1082), 1447 (AB1120), 1460 (AB1158)
Ora, J., 359 (THU0401)
Oral, A., 1347 (AB0827)
Orbai, A.-M., 12 (SP0050), 1332 (AB0786)
Ordi-Ros, J., 286 (THU0216), 1208 (AB0451)
Ordoñez, J.C., 705 (FRI0570, FRI0571)
Ordoñez, S., 843 (SAT0191), 1014 (SAT0635)
Ordoñez-Cañizares, M.C., 1174 (AB0361), 1175 (AB0362), 1443 (AB1109)
Orefice, V., 860 (SAT0228), 864 (SAT0241)
Oreiro-Villar, N., 936 (SAT0435), 978 (SAT0535)
Orejuela, J., 1092 (AB0129)
Orenius, T., 401 (THU0515)
Orenti, A., 643 (FRI0413), 746 (FRI0677), 908 (SAT0364)
Oreska, S., 638 (FRI0399), 906 (SAT0358), 1280 (AB0653), 1287 (AB0671)
Orfanos, S., 643 (FRI0414)
Oribe, M., 1471 (AB1187)
Origuchi, T., 318 (THU0303), 723 (FRI0620)
Origuchu, T., 503 (FRI0067)
Orita, K., 698 (FRI0551), 1134 (AB0245)
Orlando, I., 411 (THU0540)
Orlando, V., 777 (SAT0025)
Orman, M., 422 (THU0573), 955 (SAT0476), 1402 (AB0993)
Ormseth, S., 237 (THU0097)
Ørnbjerg, L., 732 (FRI0641)

Orozco, A.M., 1540 (AB1225-HPR)
Orozco, C., 933 (SAT0427)
Orozco, G., 179 (OP0298), 200 (THU0002)
Orozco, M.C., 670 (FRI0483)
Orpana, A., 1479 (THU0731-HPR)
Orr, C., 203 (THU0011), 487 (FRI0020), 773 (SAT0013), 1432 (AB1078)
Orrù, G., 496 (FRI0045)
Orsolini, G., 805 (SAT0097), 854 (SAT0215), 1062 (AB0045), 1124 (AB0216), 1200 (AB0429), 1207 (AB0449)
Ortega, R., 492 (FRI0035), 497 (FRI0048), 504 (FRI0069), 1184 (AB0388)
Ortega Castro, R., 975 (SAT0527), 1143 (AB0270)
Ortega-Castro, R., 350 (THU0380), 622 (FRI0360), 650 (FRI0434), 1082 (AB0104), 1268 (AB0619)
Ortego, N., 326 (THU0326), 718 (FRI0607)
Ortego Centeno, N., 1270 (AB0624), 1272 (AB0630)
Ortiz, A., 670 (FRI0483)
Ortiz, A.M., 452 (THU0651), 527 (FRI0123)
Ortiz, J., 555 (FRI0195)
Ortiz, V., 1429 (AB1071)
Ortiz Sanjuán, F., 1349 (AB0837)
Ortiz Sanjuan, F., 441 (THU0623)
Ortiz-Lopez, R., 425 (THU0581), 1054 (AB0023)
Ortiz-Reyes, B., 1239 (AB0538)
Ortiz-Salazar, P., 594 (FRI0287), 658 (FRI0453), 927 (SAT0413), 928 (SAT0414), 1286 (AB0667)
Ortiz-Sanjuán, F., 614 (FRI0336)
Ortiz-Sanjuan, F.M., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Ortiz-Santamaría, V., 1014 (SAT0635)
Ortiz-Santamaria, V., 1208 (AB0451), 1289 (AB0675)
Ortmann, R., 510 (FRI0087), 515 (FRI0096)
Ortolan, A., 99 (OP0113), 1315 (AB0745)
Ortsäter, G., 72 (OP0050)
Oryoji, K., 565 (FRI0218), 1254 (AB0582), 1424 (AB1056)
Osaki, M., 738 (FRI0656)
Osborne, B., 679 (FRI0503)
Oshikawa, H., 278 (THU0198)
Oshima, H., 995 (SAT0581)
Oshlyanska, O.A., 399 (THU0510), 1392 (AB0964)
Osiri, M., 1298 (AB0700)
Oskay, D., 1302 (AB0709)
Osorio, F.G., 53 (OP0008)
Osorio, P., 1540 (AB1225-HPR)
Ospelt, C., 116 (OP0154), 190 (OP0326), 484 (FRI0013)
Ostanin, A., 771 (SAT0008)
Ostankov, M.V., 1073 (AB0078)
Ostendorf, B., 789 (SAT0056)
Østensen, M., 1510 (SAT0717-HPR)
Ostensen, M., 28 (SP0112)
Østerås, N., 1343 (AB0817)
Osteras, N., 1478 (THU0726-HPR)
Østergaard, M., 19 (SP0078), 32 (SP0129), 131 (OP0192), 173 (OP0283), 174 (OP0284, OP0286), 175 (OP0287), 233 (THU0088), 240 (THU0104), 268 (THU0175), 355 (THU0393), 451 (THU0649), 656 (FRI0450), 726 (FRI0628), 732 (FRI0641), 745 (FRI0674), 784 (SAT0045), 949 (SAT0463), 1409 (AB1013), 1419 (AB1042)
Ostergaard, M., 234 (THU0091)
Ostermann, T., 960 (SAT0488)
Ostertag, A., 1371 (AB0900)
Östlund, G., 112 (OP0143-HPR), 1518 (SAT0740-HPR)
Ostojic, P., 640 (FRI0405)
Ostor, A., 829 (SAT0159)
Ostuzzi, S., 1552 (PARE0001), 1557 (PARE0015, PARE0016), 1560 (AB1251-PARE)
Ota, M., 505 (FRI0075)
Otaduy, C., 1220 (AB0484, AB0485)
Otani, H., 853 (SAT0214)
Otawa, S., 795 (SAT0072)
Otesbelgue, F., 1446 (AB1117)
Othman, A.A., 268 (THU0177), 1201 (AB0432)
Othmani, S., 998 (SAT0589, SAT0590)
Otón, T., 520 (FRI0106), 918 (SAT0387), 1307 (AB0723)
Otsa, K., 245 (THU0116)
Otsuka, K., 1203 (AB0439)
Otsuka, T., 1062 (AB0044)
Ottaviani, S., 130 (OP0191), 359 (THU0401), 1049 (AB0007), 1535 (AB1209-HPR)
Otten-Mus, A.-M., 1058 (AB0033)
Ouaniche, J., 1299 (AB0701)
Oude Voshaar, M.A., 365 (THU0418)
Oueniche, K., 1371 (AB0902)
Ouenniche, K., 1394 (AB0969)
Ouhaddi, Y., 126 (OP0181), 483 (FRI0009)
Ouichka, R., 1383 (AB0938)
Ovalles, J.G., 1414 (AB1029)
Ovalles B, J.G., 656 (FRI0448)
Ovalles B., J.G., 386 (THU0474)
Ovalles-Bonilla, J.G., 462 (THU0676), 748 (FRI0683), 1276 (AB0640)
Ovcharov, P., 616 (FRI0343)
Overgaard, S., 159 (OP0251), 226 (THU0072)
Overton, J., 570 (FRI0228), 838 (SAT0179)
Overvad, K., 84 (OP0079)
Ovsaynnikova, O., 640 (FRI0403), 1283 (AB0659)
Ovsyannikova, O.B., 1287 (AB0670)
Owada, T., 531 (FRI0134), 1291 (AB0681)
Owczarek, A.J., 1502 (FRI0752-HPR)
Owen, C.E., 1367 (AB0889)
Oygen, S., 1066 (AB0057)
Öz, B., 1462 (AB1162)
Oz, B., 455 (THU0658)
Öz, H.E., 1321 (AB0759)
Ozaki, H., 283 (THU0209), 719 (FRI0609), 757 (FRI0704), 907 (SAT0360), 1213 (AB0465)
Ozaki, S., 635 (FRI0391), 872 (SAT0259), 910 (SAT0369), 1260 (AB0597)
Ozbalkan, Z., 748 (FRI0682)
Özçakar, L., 1122 (AB0213)
Ozcebe, O.I., 1212 (AB0463)
Özçelep, Ö.F., 1548 (AB1249-HPR)
Özdem İnan, Y., 1360 (AB0868)
Ozdemir, O., 1297 (AB0698)
Ozdemir Işik, O., 634 (FRI0386)
Ozdemir Isik, O., 598 (FRI0296)
Ozdemirel, A.E., 1321 (AB0762)
Özdoğan, H., 719 (FRI0610)
Ozdogan, H., 412 (THU0542), 415 (THU0552), 618 (FRI0348), 714 (FRI0596), 1101 (AB0157), 1186 (AB0394), 1402 (AB0994)
Özdolap, S., 1380 (AB0927)
Ozel, S., 535 (FRI0144), 818 (SAT0130)
Ozen, N., 1297 (AB0698)
Özen, S., 1515 (SAT0730-HPR)
Ozen, S., 77 (OP0063), 329 (THU0333), 398 (THU0509), 402 (THU0518), 414 (THU0548), 616 (FRI0342)
Ozer Yaman, S., 1121 (AB0209)
Özgen, M., 327 (THU0329)
Özgül, B., 1504 (FRI0756-HPR)
Özgüler, Y., 719 (FRI0610)
Ozguler, Y., 331 (THU0339), 354 (THU0389), 603 (FRI0307), 619 (FRI0351), 1186 (AB0394)
Ozmen, M., 296 (THU0245), 354 (THU0389), 661 (FRI0462), 1170 (AB0349), 1282 (AB0658)
Özmen, Y., 1310 (AB0731)
Özsoy, T., 821 (SAT0139)
Ozturk, A.B., 791 (SAT0063)
Öztürk, M.A., 1216 (AB0472), 1260 (AB0598)
Özturk, M.A., 608 (FRI0320)
Özyazgan, Y., 1246 (AB0558)
Ozyazgan, Y., 603 (FRI0307)

Paalanen, K., 61 (OP0024), 784 (SAT0044)
Pablos, J.L., 834 (SAT0171)
Paccard, C., 570 (FRI0227, FRI0228), 838 (SAT0179), 844 (SAT0192)
Pace, S., 115 (OP0151)
Pacheco-Tena, C., 252 (THU0137), 1453 (AB1137)
Pachera, E., 86 (OP0084), 87 (OP0086), 117 (OP0157), 890 (SAT0312)
Packham, J., 659 (FRI0456), 1308 (AB0727)
Pacucci, V.A., 872 (SAT0260), 1059 (AB0036)
Padalko, E., 763 (FRI0719)
Padilla-Ortíz, D., 586 (FRI0264)
Padín-Martín, M., 261 (THU0160)
Padjen, I., 592 (FRI0282), 883 (SAT0291)
Padoan, R., 327 (THU0328), 603 (FRI0308), 604 (FRI0310), 614 (FRI0337), 1257 (AB0589)
Padovan, M., 437 (THU0611), 582 (FRI0255), 828 (SAT0156), 1439 (AB1099)
Padyukov, L., 228 (THU0077), 1512 (SAT0722-HPR)
Pagani, S., 490 (FRI0030)
Pagés, F., 718 (FRI0607)
Pagnotelli, B., 631 (FRI0380)
Paik, J.J., 67 (OP0038)
Pain, C., 1390 (AB0958)
Paira, S., 440 (THU0619), 670 (FRI0483)
Pais, S., 1343 (AB0817)
Paisal, V., 409 (THU0536), 1395 (AB0972)
Paiva, A., 894 (SAT0324)
Pajak, A., 117 (OP0157)
Pajot, C., 77 (OP0062)
Pak, K., 67 (OP0038)
Pakkala, T., 171 (OP0277-PARE)
Pala, O., 775 (SAT0018), 808 (SAT0104)
Palacios, F.A., 443 (THU0627)
Palacios, S., 178 (OP0294)
Palamar, D., 353 (THU0387), 1156 (AB0308)
Palange, P., 230 (THU0082)
Palau, N., 177 (OP0292), 290 (THU0227), 776 (SAT0022), 946 (SAT0458)
Palazzo, C., 170 (LB0001), 476 (THU0711)
Palazzo, E., 130 (OP0191), 1535 (AB1209-HPR)
Palazzo, R., 903 (SAT0347)
Palese, A., 1483 (THU0741-HPR), 1539 (AB1223-HPR)
Palhuyeva, H., 1497 (FRI0737-HPR)
Palladini, A., 197 (OP0343)
Pallarés, L., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Palma, D., 843 (SAT0191)
Palma-Sánchez, D., 1496 (FRI0735-HPR)
Palmar-Santos, A., 1542 (AB1231-HPR)
Palmer, D., 821 (SAT0138)
Palmer, J.B., 678 (FRI0501), 945 (SAT0456), 953 (SAT0471, SAT0472)
Palmer, L., 1313 (AB0739)
Palmer-Lourenco, G., 90 (OP0093)
Palmetto, N., 676 (FRI0496), 938 (SAT0439)
Palmou, N., 1166 (AB0337)
Palmou-Fontana, N., 75 (OP0059), 405 (THU0526), 420 (THU0567), 1116 (AB0197)
Palomino, E.V., 205 (THU0017), 206 (THU0018)
Palominos, P.E., 1446 (AB1117)
Palshina, S., 723 (FRI0621), 1237 (AB0531)
Palstam, A., 163 (OP0260-HPR)
Pamfil, C., 192 (OP0332), 290 (THU0228), 880 (SAT0285)
Pan, F., 193 (OP0334), 471 (THU0699)
Pan, L., 326 (THU0327), 884 (SAT0294)
Pan, W., 600 (FRI0301), 1206 (AB0447)
Pan, X., 104 (OP0123)
Pan, Y., 270 (THU0182), 281 (THU0205, THU0206), 1158 (AB0312)
Pan, Y.-F., 1077 (AB0087)
Panaccione, R., 83 (OP0076)
Panafidina, T., 599 (FRI0299), 1411 (AB1018)
Panagopoulos, P., 542 (FRI0161)
Panaitescu, E., 1179 (AB0376)
Panarra, A., 1429 (AB1070)
Panasyuk, E., 1337 (AB0797)
Pancaldi, F., 248 (THU0123)
Pandey, B.D., 269 (THU0178)
Pandit, A., 181 (OP0303), 182 (OP0306)
Pandurengan, R., 352 (THU0386), 953 (SAT0471)
Pandya, N., 777 (SAT0027)
Panelius, J., 1404 (AB0999)
Panero-Lamothe, B., 1174 (AB0361)
Panetta, V., 343 (THU0366)
Pang, H.T., 796 (SAT0073), 1520 (SAT0747-HPR)
Pangan, A.L., 353 (THU0388), 668 (FRI0479)
Paniagua Díaz, N., 1357 (AB0861)
Paniego, F., 1279 (AB0649)
Paniego, F.M., 311 (THU0285)

Pannacciulli, N., 54 (OP0010)
Panopoulos, S., 602 (FRI0306), 642 (FRI0410), 643 (FRI0414), 908 (SAT0361)
Paños Iniesta, A., 1041 (SAT0704)
Panousis, N., 192 (OP0332)
Pantano, I., 151 (OP0233), 1118 (AB0202)
Pantazi, L., 836 (SAT0176)
Paolazzi, G., 437 (THU0611), 604 (FRI0310), 614 (FRI0337), 1257 (AB0589), 1439 (AB1099)
Paolella, F., 1069 (AB0064)
Paolesse, R., 484 (FRI0012)
Paolini, C., 64 (OP0031)
Paolini, L., 905 (SAT0353)
Paolino, S., 66 (OP0037), 140 (OP0212), 641 (FRI0407), 695 (FRI0540), 704 (FRI0569), 728 (FRI0632), 897 (SAT0331), 915 (SAT0381), 1111 (AB0185), 1263 (AB0605)
Pap, T., 2 (SP0001), 33 (SP0135), 486 (FRI0018)
Papadaki, L., 1560 (AB1252-PARE)
Papadakis, J., 1560 (AB1252-PARE)
Papadopoulos, N., 1139 (AB0259)
Papadopoulou, E., 680 (FRI0504)
Papageorgiou, A., 288 (THU0221)
Papalopoulos, I., 574 (FRI0236), 577 (FRI0244), 836 (SAT0176), 850 (SAT0204)
Papasidero, S., 1339 (AB0805), 1534 (AB1206-HPR)
Papastavrou, D., 1557 (PARE0015)
Papastavrou, T., 1552 (PARE0001)
Papathanasiou, M., 588 (FRI0269)
Papchianou, E., 643 (FRI0412), 723 (FRI0619)
Papo, T., 78 (OP0065), 187 (OP0319), 883 (SAT0293)
Papp, G., 1094 (AB0137)
Papp, K., 144 (OP0220)
Papp, K.A., 951 (SAT0469), 1314 (AB0743)
Pappas, D., 552 (FRI0188), 827 (SAT0153), 1121 (AB0210)
Pappas, D.A., 846 (SAT0196)
Paradkar, S., 1074 (AB0079)
Paradowska-Gorycka, A., 204 (THU0012)
Paramalingam, S., 467 (THU0688), 744 (FRI0672)
Paramonova, O.V., 536 (FRI0146), 1128 (AB0228)
Paran, D., 747 (FRI0679), 1095 (AB0138), 1118 (AB0203), 1328 (AB0776)
Parat, K., 1283 (AB0661)
Pardo, N., 1386 (AB0948)
Pardo-Hidalgo, R., 1064 (AB0051)
Pardos-Gea, J., 415 (THU0550)
Paredes, C., 734 (FRI0645), 1160 (AB0318, AB0319)
Paredes, M.B., 1179 (AB0374)
Paredes, S., 1156 (AB0307)
Parent, I., 118 (OP0161)
Parenti, D., 460 (THU0672), 562 (FRI0211), 836 (SAT0175), 950 (SAT0465)
Parés, A., 706 (FRI0573)
Paris, G., 170 (LB0001)
Paris, M., 672 (FRI0487), 936 (SAT0436), 1314 (AB0743), 1331 (AB0785)
Pariser, D.M., 1314 (AB0743)
Parisi, F., 197 (OP0343)
Parisi, S., 829 (SAT0158), 1272 (AB0630), 1376 (AB0917)
Park, C., 548 (FRI0178)
Park, D.-J., 312 (THU0288), 791 (SAT0061), 877 (SAT0275), 972 (SAT0518, SAT0519)
Park, E.-J., 646 (FRI0422), 749 (FRI0685), 1126 (AB0223), 1371 (AB0901)
Park, E.-K., 255 (THU0144), 585 (FRI0262), 698 (FRI0550)
Park, E.H., 922 (SAT0398)
Park, E.S., 383 (THU0467)
Park, G., 1074 (AB0080)
Park, H.-R., 1447 (AB1121)
Park, H.S., 904 (SAT0351), 914 (SAT0379), 955 (SAT0475), 1305 (AB0717), 1333 (AB0788), 1414 (AB1027)
Park, I.Y., 217 (THU0049)
Park, J., 1131 (AB0237)
Park, J.-H., 255 (THU0144), 585 (FRI0262), 692 (FRI0533), 698 (FRI0550)
Park, J.-S., 359 (THU0400), 1385 (AB0943)
Park, J.K., 83 (OP0077), 346 (THU0372), 1053 (AB0020)
Park, J.W., 83 (OP0077), 346 (THU0372)
Park, K.S., 1185 (AB0392), 1454 (AB1140)
Park, M.-C., 762 (FRI0717)
Park, S.-G., 820 (SAT0137)
Park, S.-H., 311 (THU0284), 464 (THU0681), 886 (SAT0302), 926 (SAT0408), 977 (SAT0533), 1162 (AB0326)
Park, S.E., 1355 (AB0854)
Park, S.H., 1185 (AB0392), 1458 (AB1151)
Park, S.Y., 1083 (AB0107)
Park, W., 548 (FRI0178), 820 (SAT0137), 824 (SAT0146)
Park, Y., 346 (THU0371), 348 (THU0376), 352 (THU0386)
Park, Y.-B., 372 (THU0436), 383 (THU0467), 827 (SAT0154)
Park, Y.-J., 890 (SAT0311)
Park, Y.-S., 359 (THU0400), 1089 (AB0120), 1385 (AB0943)
Parker, G., 1023 (SAT0657)
Parker, G.J., 1010 (SAT0624)
Parks, C., 67 (OP0038)
Parks, D., 857 (SAT0223), 1125 (AB0220)
Parlak, S., 748 (FRI0682)
Parma, A., 446 (THU0636)
Parmanne, P., 61 (OP0024), 1404 (AB0999)
Parmar, K., 1097 (AB0147)
Parmeggiani, M., 212 (THU0035), 1054 (AB0022)
Parodis, I., 861 (SAT0233), 864 (SAT0239)
Paroni Sterbini, F., 197 (OP0343)
Parra, S., 312 (THU0287), 1208 (AB0451)
Parra, V., 201 (THU0005), 218 (THU0052)
Parrino, J., 570 (FRI0228), 838 (SAT0179)
Parslew, R., 1087 (AB0115)
Parsons, L.B., 1525 (SAT0762-HPR)
Parsons, S., 190 (OP0327-PARE)
Parthasarathy, S., 964 (SAT0500)
Parvu, M., 1440 (AB1101)
Pasali, M., 309 (THU0279)
Pasaoglu, H., 1260 (AB0598)
Pasaoglu, O.T., 1260 (AB0598)
Pascal, M., 840 (SAT0184)
Pascale, M., 873 (SAT0262)
Pascale, P., 952 (SAT0470)
Pascarelli, N.A., 966 (SAT0503)
Pascart, T., 359 (THU0402)
Pascaud, J., 182 (OP0307)
Paschke, J., 103 (OP0121), 131 (OP0192), 469 (THU0693), 471 (THU0697), 663 (FRI0467), 933 (SAT0428)
Pascual, D., 962 (SAT0494)
Pascual, E., 361 (THU0406), 374 (THU0441), 1307 (AB0724)
Pascual, M., 663 (FRI0468)
Pascual, V., 1117 (AB0200)
Pascual Ramos, V., 1147 (AB0282)
Pascual Salcedo, D., 1304 (AB0714)
Pascual-Ramos, V., 1155 (AB0305)
Pascual-Salcedo, D., 456 (THU0661), 551 (FRI0186), 555 (FRI0194, FRI0195), 559 (FRI0204), 824 (SAT0145), 833 (SAT0168), 1116 (AB0198), 1179 (AB0374, AB0375), 1293 (AB0686), 1294 (AB0687)
Pascual-Salcedo, M.D., 822 (SAT0141)
Pashayev, T., 1300 (AB0706)
Pasker-de Jong, P., 376 (THU0445)
Paskins, Z., 751 (FRI0690), 1028 (SAT0672)
Pasoto, S.G., 311 (THU0284), 464 (THU0681), 875 (SAT0270), 886 (SAT0302)
Pasquale, G., 621 (FRI0355)
Pasquau, F., 317 (THU0300)
Passiu, G., 496 (FRI0046), 535 (FRI0143)
Pastor Perez, F.J., 1041 (SAT0704)
Pastor-Asurza, C., 875 (SAT0269), 1142 (AB0269)
Pataka, A., 1261 (AB0601)
Patanè, M., 641 (FRI0407)
Patel, D., 448 (THU0641)
Patel, H., 788 (SAT0055)
Patel, N., 794 (SAT0069), 1432 (AB1077)
Patel, P.S., 711 (FRI0588)
Patel, S.K., 377 (THU0447)
Paterson, C., 242 (THU0111)
Paterson, J.M., 749 (FRI0684)
Pathai, S., 722 (FRI0618)
Patier de la Peña, J.L., 413 (THU0545), 713 (FRI0593)
Patil, A., 1292 (AB0683)
Pato, E., 326 (THU0326), 718 (FRI0607)
Patorno, E.P., 802 (SAT0089)
Patru, S., 379 (THU0454), 478 (THU0717)
Patsouras, M., 210 (THU0028)
Patsouras, M.D., 293 (THU0237)
Pau, D., 1186 (AB0395)
Paudyal, S., 1507 (FRI0764-HPR)
Paul, M., 1301 (AB0708)
Paul, S., 218 (THU0051), 1044 (SAT0713)
Paul, S.K., 264 (THU0167)
Paulding, C., 570 (FRI0228), 838 (SAT0179), 844 (SAT0192)
Pauling, J., 5 (SP0014)
Pauly, V., 744 (FRI0671)
Pavan, T.R., 628 (FRI0371)
Pavelcova, K., 179 (OP0297)
Pavelka, K., 73 (OP0053), 179 (OP0297), 209 (THU0027), 220 (THU0058), 243 (THU0113), 358 (THU0398), 383 (THU0464), 440 (THU0621), 451 (THU0650), 567 (FRI0221), 638 (FRI0399), 656 (FRI0450), 850 (SAT0206), 906 (SAT0358), 916 (SAT0383), 979 (SAT0538), 1183 (AB0387), 1280 (AB0653), 1287 (AB0671), 1468 (AB1180)
Pavía, P.X., 1375 (AB0913)
Pavič Nikolič, M., 1143 (AB0272)
Pavic Nikolic, M., 1538 (AB1220-HPR), 1544 (AB1236-HPR)
Pavlov, V., 269 (THU0179)
Pavlovic, D., 1552 (PARE0003)
Pavlovich, T., 1361 (AB0870)
Pavlovskaya, A., 424 (THU0578)
Pawlak-Bus, K., 1209 (AB0454), 1229 (AB0510), 1470 (AB1184)
Pawlik, A., 204 (THU0012)
Payne, A., 287 (THU0220)
Payne, K., 437 (THU0613), 551 (FRI0185)
Pazmino, S., 147 (OP0226), 765 (FRI0726)
Pazzola, G., 437 (THU0611), 1209 (AB0456), 1247 (AB0563), 1439 (AB1099)
Peall, A., 1514 (SAT0728-HPR)
Pease, C.T., 1205 (AB0444)
Pecani, A., 880 (SAT0283), 1465 (AB1170)
Peccarisi, M., 1353 (AB0847)
Peccatori, S., 437 (THU0611), 1439 (AB1099)
Peckham, H., 389 (THU0484)
Pedersen, A.B., 546 (FRI0174)
Pedersen, D.D., 553 (FRI0190)
Pedersen, R., 337 (THU0353), 350 (THU0382), 832 (SAT0164)
Pedersen, S.B., 505 (FRI0074)
Pedersen, S.J., 175 (OP0287), 745 (FRI0674)
Pedersen, T.T., 223 (THU0065)
Pedó, R.T., 502 (FRI0066)
Pedraz-Marcos, A., 1542 (AB1231-HPR)
Pedraza-Arévalo, S., 648 (FRI0429), 1091 (AB0128)
Pedraza-Arevalo, S., 1082 (AB0104)
Pedreira, A., 176 (OP0290)
Pedreira, A.L., 1412 (AB1021)
Pedro, S.A., 580 (FRI0250)
Pedro-Martínez, A.J., 395 (THU0501), 1397 (AB0978)
Pedrosa, T., 1254 (AB0581)
Peelen, D.M., 732 (FRI0642)
Peeters, R., 539 (FRI0152)
Pego, J.M., 290 (THU0227)
Pego-Reigosa, J., 68 (OP0042), 300 (THU0256), 587 (FRI0267), 1107 (AB0173)
Pego-Reigosa, J.M., 873 (SAT0263)
Pehlivan, E., 394 (THU0498)
Pehlivan, Ö., 1170 (AB0350)
Pei, J., 95 (OP0105), 567 (FRI0222), 581 (FRI0253)
Peikert, T., 109 (OP0137), 318 (THU0301)
Peinado-Villén, P., 1268 (AB0619)
Peiró, E., 556 (FRI0197), 614 (FRI0336)
Peitado, D., 718 (FRI0607)
Peiteado, D., 456 (THU0661), 501 (FRI0062),

551 (FRI0186), 559 (FRI0204), 833 (SAT0168), 1116 (AB0198), 1179 (AB0375), 1294 (AB0687), 1303 (AB0713), 1304 (AB0714)
Peiteado Lopez, D., 824 (SAT0145)
Peitz, J., 397 (THU0504)
Peixoto, D., 607 (FRI0318), 612 (FRI0330), 1011 (SAT0627), 1254 (AB0581), 1381 (AB0930)
Pekesen Kurtça, M., 1484 (THU0745-HPR)
Pel, S., 1118 (AB0203)
Peláez Ballestas, I., 363 (THU0411), 365 (THU0417)
Peláez-Ballestas, I., 1452 (AB1136)
Pelaez-Ballestas, I., 752 (FRI0694), 758 (FRI0709), 993 (SAT0573, SAT0574, SAT0575), 994 (SAT0576), 1362 (AB0873), 1375 (AB0913), 1450 (AB1129), 1453 (AB1137)
Pelechas, E., 1193 (AB0411), 1217 (AB0476)
Pellecchia, L., 621 (FRI0355)
Pellerito, R., 564 (FRI0215)
Pelletier, J.-P., 126 (OP0181), 483 (FRI0009), 571 (FRI0230), 845 (SAT0195), 1188 (AB0397)
Pelt, P.V., 478 (THU0716)
Peltea, A., 1333 (AB0790), 1460 (AB1158)
Peltomaa, R., 61 (OP0024), 1404 (AB0999)
Peluso, G., 608 (FRI0319)
Pena, C., 906 (SAT0357), 1263 (AB0606)
Pena, C.E., 1245 (AB0556)
Peña, P., 201 (THU0005), 218 (THU0052)
Peña, S., 350 (THU0381)
Peña Montelongo, S., 1424 (AB1057)
Peña-Amaro, J., 919 (SAT0391)
Peña-Blanco, R., 877 (SAT0276, SAT0277)
Peña-Vallejo, M.J., 1525 (SAT0760-HPR)
Penadés, M., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Pendleton, A., 1372 (AB0904)
Pendolino, M., 470 (THU0696), 490 (FRI0028), 880 (SAT0283)
Peneva, E., 584 (FRI0259)
Pengo, V., 70 (OP0046), 418 (THU0561)
Penn, J., 570 (FRI0228), 838 (SAT0179)
Penne, E.L., 604 (FRI0309)
Pennington, S.R., 465 (THU0683), 940 (SAT0444)
Pensa, C., 1099 (AB0150)
Pentazos, G., 602 (FRI0306), 1133 (AB0244)
Pentony, P., 1212 (AB0464)
Pera, M., 1245 (AB0556), 1263 (AB0606)
Peracchi, O.A.B., 76 (OP0061)
Peral, E., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Perdan Pirkmajer, K., 1143 (AB0272)
Perdomo-Ramirez, M., 877 (SAT0277)
Perdriger, A., 335 (THU0349), 428 (THU0588, THU0589), 989 (SAT0561), 1191 (AB0406), 1261 (AB0599)
Perebetiuk, L., 654 (FRI0443)
Pereda, C.A., 554 (FRI0192)
Peredo, R., 1290 (AB0678)
Pereira, B., 213 (THU0039), 573 (FRI0234), 813 (SAT0117), 1297 (AB0696), 1360 (AB0869)
Pereira, C., 315 (THU0296)
Pereira, D., 440 (THU0619)
Pereira, I., 1160 (AB0320)
Pereira, R.M., 875 (SAT0270)
Pereira, R.M.R., 76 (OP0061), 1448 (AB1124)
Pereira da Silva, J., 700 (FRI0558)
Pereira da Silva, J.A., 694 (FRI0537), 1254 (AB0581), 1272 (AB0630), 1381 (AB0930)
Pereira Gillion, C., 1191 (AB0406)
Perera, S., 1506 (FRI0763-HPR)
Peretz, A.S.R., 457 (THU0663)
Perez, A.J., 163 (OP0259-HPR)
Pérez, C., 307 (THU0273), 324 (THU0320)
Perez, C., 837 (SAT0178)
Pérez, C.E., 826 (SAT0150)
Pérez, F., 1161 (AB0321)
Perez, L.F., 884 (SAT0295), 1498 (FRI0741-HPR)
Perez, N., 590 (FRI0276), 1279 (AB0649), 1534 (AB1206-HPR)
Perez, P., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Pérez Albaladejo, L., 1228 (AB0506)
Perez Albaladejo, L., 1321 (AB0760)
Pérez Baos, S., 504 (FRI0071)
Pérez Cristóbal, M., 1211 (AB0460)
Perez del Caz, M.D., 485 (FRI0014)
Pérez Martín, L., 1424 (AB1057)
Perez Nino, C.A., 71 (OP0048)
Perez Romera, M.V., 1183 (AB0385)
Pérez Sánchez, L., 975 (SAT0527)
Perez Sanchez, L., 258 (THU0151), 700 (FRI0555)
Pérez Sandoval, T., 213 (THU0037), 719 (FRI0608)
Perez Sandoval, T., 1232 (AB0518)
Perez Venegas, J.J., 1183 (AB0385)
Pérez-Alvarez, R., 410 (THU0539), 597 (FRI0293), 721 (FRI0615), 1042 (SAT0706)
Perez-Conesa, M., 1208 (AB0451)
Pérez-Frías, A., 1107 (AB0172)
Pérez-García, C., 1181 (AB0381)
Pérez-García, S., 485 (FRI0016)
Pérez-Gisbert, J., 177 (OP0292)
Perez-Gomez, N., 1272 (AB0630)
Perez-Gonzalez, A., 740 (FRI0661)
Perez-Guerrero, E., 1155 (AB0304)
Perez-Guerrero, E.E., 262 (THU0161)
Perez-Guijo, V.C., 153 (OP0238)
Pérez-Hernández, N., 291 (THU0230)
Pérez-Pampín, E., 108 (OP0135), 614 (FRI0336)
Perez-Pampin, E., 494 (FRI0040), 500 (FRI0057)
Perez-Recio, T., 305 (THU0269)
Pérez-Ruiz, F., 1363 (AB0878)
Perez-Ruiz, F., 196 (OP0340), 368 (THU0426), 381 (THU0458), 383 (THU0464)
Pérez-Sánchez, C., 492 (FRI0035)
Perez-Sanchez, C., 194 (OP0336), 287 (THU0218), 497 (FRI0048), 504 (FRI0069), 622 (FRI0360), 648 (FRI0429), 649 (FRI0431), 1078 (AB0092), 1082 (AB0104), 1091 (AB0127, AB0128), 1450 (AB1130)
Perez-Sandoval, T., 843 (SAT0191)
Perez-Vazquez, F.D.J., 806 (SAT0100), 1164 (AB0330)
Pérez-Velásquez, C., 1001 (SAT0600)
Pérez-Venegas, J.J., 290 (THU0227), 946 (SAT0458)
Pérez-Vizcaíno, F., 892 (SAT0316)
Perich-Campos, R., 875 (SAT0269), 1142 (AB0269)
Perico, G.V., 1292 (AB0684)
Periculeous, C., 1092 (AB0131)
Peris, K., 1314 (AB0743)
Peris, P., 369 (THU0429), 691 (FRI0529), 706 (FRI0573)
Periyasamy, K., 1303 (AB0711)
Perkmann, T., 528 (FRI0125), 750 (FRI0688), 1124 (AB0217), 1414 (AB1026)
Perković, D., 1283 (AB0661)
Perlman, H., 1125 (AB0220)
Perniola, S., 254 (THU0143), 521 (FRI0110)
Perocheau, D., 770 (SAT0005)
Perosa, F., 263 (THU0164), 495 (FRI0043), 1106 (AB0171)
Perovaara, M., 1404 (AB0999)
Perper, S., 288 (THU0222)
Perpétuo, I.P., 1080 (AB0097)
Perrella, M., 1064 (AB0050)
Perricone, C., 204 (THU0013), 463 (THU0678), 470 (THU0696), 489 (FRI0027), 490 (FRI0028), 496 (FRI0045), 757 (FRI0705), 864 (SAT0241), 872 (SAT0260), 879 (SAT0281), 880 (SAT0283), 1007 (SAT0615), 1059 (AB0036), 1099 (AB0150), 1449 (AB1125)
Perricone, R., 437 (THU0611), 463 (THU0678), 484 (FRI0012), 667 (FRI0477), 1193 (AB0410), 1439 (AB1099)
Perrier-Cornet, J., 1383 (AB0938)
Perrin, F., 778 (SAT0029)
Perrone, G., 872 (SAT0260)
Perrot, S., 169 (OP0274), 334 (THU0346), 339 (THU0356, THU0357), 385 (THU0470), 388 (THU0482), 389 (THU0483), 665 (FRI0472), 754 (FRI0697), 815 (SAT0123), 1296 (AB0694)
Perrotta, F.M., 756 (FRI0703), 1319 (AB0754)
Perrotti, P.P., 177 (OP0292)
Perruccio, A., 957 (SAT0481)
Perruccio, A.V., 1035 (SAT0688), 1504 (FRI0757-HPR)
Pers, J.-O., 109 (OP0137), 309 (THU0278)
Pers, J.O., 492 (FRI0035), 1215 (AB0469)
Persic, V., 771 (SAT0009)
Persuitte, G., 846 (SAT0196), 1191 (AB0407)
Pertega, S., 978 (SAT0535)
Pertuiset, E., 51 (OP0004), 465 (THU0684)
Peruffo, A., 1111 (AB0184)
Perugino, C.A., 711 (FRI0588)
Pervakova, M., 611 (FRI0328)
Pesonen, A., 173 (OP0283)
Pessoa, C.V., 342 (THU0362)
Pestaña Fernández, M., 639 (FRI0402)
Petelytska, L., 615 (FRI0340)
Peter, N., 553 (FRI0189), 1185 (AB0391)
Peter, W., 111 (OP0141-HPR)
Peterfy, C., 122 (OP0168)
Peters, G.-J.Y., 1485 (THU0749-HPR)
Peters, M., 740 (FRI0662), 811 (SAT0114)
Petersel, D., 1181 (AB0379)
Petersen, D., 121 (OP0167)
Petersen, S.K., 990 (SAT0565)
Peterson, L., 673 (FRI0489), 681 (FRI0508), 1316 (AB0747)
Peterson, S., 341 (THU0360), 580 (FRI0251), 1295 (AB0692)
Pethö-Schramm, A., 177 (OP0293), 847 (SAT0199), 855 (SAT0218)
Pethoe-Schramm, A., 264 (THU0167), 850 (SAT0206)
Petisco, R., 820 (SAT0135)
Petitpain, N., 823 (SAT0144)
Petkovic, I., 440 (THU0619)
Petrackova, A., 1051 (AB0014)
Petraitis, M., 359 (THU0401), 367 (THU0423)
Petrariu, L., 825 (SAT0148)
Petrasca, A., 776 (SAT0021)
Petrella, R., 1002 (SAT0602, SAT0603)
Petri, M., 69 (OP0045), 150 (OP0232), 300 (THU0255), 306 (THU0270), 391 (THU0490), 1211 (AB0461), 1212 (AB0462), 1407 (AB1007)
Petricca, L., 138 (OP0208), 154 (OP0239), 787 (SAT0052), 792 (SAT0066)
Petrikkou, E., 559 (FRI0205)
Petrini, I., 320 (THU0308)
Petrini, M., 320 (THU0308)
Petriw, L., 71 (OP0049)
Petrov, A., 339 (THU0355), 1358 (AB0864)
Petrova, J., 1543 (AB1233-HPR)
Petrovich, D., 832 (SAT0166)
Petru, L., 179 (OP0297)
Petruzziello, C., 667 (FRI0477)
Pettersson, L., 891 (SAT0314)
Pettersson, S., 162 (OP0256-HPR), 586 (FRI0265)
Peytrignet, S., 104 (OP0123)
Pezet, S., 85 (OP0081)
Pfeiffenberger, M., 480 (FRI0002), 485 (FRI0015)
Pfeiffer, C., 1106 (AB0169), 1110 (AB0181)
Pfeiffer-Jensen, M., 454 (THU0657)
Pfeifle, R., 492 (FRI0033), 775 (SAT0019)
Pfister, S.S., 1101 (AB0155)
Pfreundschuh, M., 1060 (AB0039)
Pham, T., 58 (OP0018), 425 (THU0580), 427 (THU0586), 476 (THU0711), 706 (FRI0575), 1454 (AB1141)
Pham-Ledard, A., 710 (FRI0584)
Philipson, R., 107 (OP0130)
Phillips, K., 835 (SAT0172)
Phipps-Green, A., 383 (THU0464)
Phoka Charalambous, A., 172 (OP0281-PARE)
Piacarelli, G., 1465 (AB1170)
Piacentini, A., 1069 (AB0064)
Piacentini, G., 1388 (AB0953)
Piantoni, S., 579 (FRI0249), 1214 (AB0468)
Piaserico, S., 99 (OP0113)
Piazza, I., 829 (SAT0158)
Picard, C., 523 (FRI0114)
Picarelli, G., 305 (THU0268), 888 (SAT0305)
Picerno, V., 383 (THU0465), 730 (FRI0637), 1010 (SAT0625), 1013 (SAT0631)
Pichierri, P., 702 (FRI0563)
Pichler, L., 1445 (AB1114)
Pickney, A., 104 (OP0124)

Piera-Velazquez, S., 91 (OP0096)
Pieren, A., 996 (SAT0583), 1179 (AB0374), 1303 (AB0713)
Pieringer, H., 1173 (AB0357)
Pierini, F., 716 (FRI0601)
Pierini, F.S., 1115 (AB0194)
Pieropan, S., 1388 (AB0953)
Pierro, L., 151 (OP0233)
Piette, Y., 299 (THU0252)
Piga, M., 535 (FRI0143), 975 (SAT0528), 1272 (AB0630)
Pigatto, E., 634 (FRI0387), 1111 (AB0184)
Piggott, L., 45 (SP0188)
Pignataro, F., 304 (THU0267)
Pijnenburg, L., 638 (FRI0398)
Pijoan, J.-I., 593 (FRI0284)
Pijoán-Moratalla, C., 695 (FRI0542)
Pikwer, M., 437 (THU0612)
Pilipenko, A., 1341 (AB0812)
Pilkington, C., 1389 (AB0957), 1390 (AB0958)
Pillet, P., 56 (OP0014)
Pilling, J., 1548 (AB1248-HPR)
Pilling, M., 1444 (AB1111)
Pillinger, M., 379 (THU0455), 766 (FRI0728)
Pilloni, A., 496 (FRI0045)
Pimanov, S., 560 (FRI0208)
Pimenta, E., 176 (OP0290)
Pimenta, S., 852 (SAT0211), 1142 (AB0268), 1177 (AB0368), 1466 (AB1172)
Pimentel-Quiroz, V., 1142 (AB0269)
Pimentel-Santos, F., 1052 (AB0016), 1153 (AB0300)
Pimentel-Santos, F.M., 80 (OP0070), 441 (THU0622), 466 (THU0685)
Pina, T., 1084 (AB0108)
Pinal-Fernández, I., 415 (THU0550)
Pinal-Fernandez, I., 67 (OP0038), 636 (FRI0392), 913 (SAT0376)
Pincus, T., 385 (THU0472), 794 (SAT0069), 810 (SAT0109), 973 (SAT0521), 1129 (AB0231, AB0232), 1130 (AB0233), 1307 (AB0724), 1451 (AB1132), 1466 (AB1173)
Pineda, C., 175 (OP0288), 205 (THU0016), 739 (FRI0660), 1006 (SAT0613), 1013 (SAT0631), 1067 (AB0059)
Pineda, R., 594 (FRI0287), 658 (FRI0453), 927 (SAT0413), 928 (SAT0414), 1286 (AB0667)
Pinheiro, M., 1196 (AB0419)
Pinilla, B., 410 (THU0539), 415 (THU0550), 597 (FRI0293), 721 (FRI0615), 1042 (SAT0706)
Pinkston, O., 1044 (SAT0711)
Pinna, S., 975 (SAT0528)
Pinney, J., 227 (THU0076)
Pinta, A., 1186 (AB0395)
Pintilie, S., 1032 (SAT0681)
Pinto, A.L.R., 342 (THU0362)
Pinto, J.A., 946 (SAT0458)
Pinto, M.R., 522 (FRI0112)
Pinto, P., 1419 (AB1043)
Pinto Correia, A.L., 228 (THU0078)
Pinto Tasende, J.A., 955 (SAT0475), 1333 (AB0788)
Pinto-Tasende, J., 936 (SAT0435), 946 (SAT0457), 1322 (AB0764)
Pinto-Tasende, J.A., 139 (OP0209-HPR)
Pinzon, C., 1375 (AB0913)
Pinzón, D., 696 (FRI0544)
Piotrowski, M., 251 (THU0133), 824 (SAT0146)
Pipitone, N., 912 (SAT0374), 1247 (AB0563), 1272 (AB0630)
Piram, M., 398 (THU0509)
Piras, A., 496 (FRI0046), 535 (FRI0143)
Pirilä, L., 61 (OP0024)
Pirola, J.P., 205 (THU0017), 206 (THU0018), 313 (THU0289)
Pirro, L., 237 (THU0098), 635 (FRI0389)
Pisani, A.M., 906 (SAT0356)
Pisani, P., 704 (FRI0568), 1353 (AB0847)
Pisanti, N., 320 (THU0308)
Pisetsky, D., 12 (SP0049), 560 (FRI0207)
Pistja, E., 1523 (SAT0753-HPR)
Pistone, G., 901 (SAT0341)
Pisu, M.G., 1558 (PARE0019)
Pitann, S., 772 (SAT0011), 1108 (AB0175)
Pithioux, M., 744 (FRI0671)
Pitrez, E.H., 628 (FRI0371)
Pitzalis, C., 125 (OP0175), 180 (OP0300), 203 (THU0011), 238 (THU0100), 458 (THU0667), 490 (FRI0030), 506 (FRI0076), 511 (FRI0088), 1125 (AB0220), 1205 (AB0444)
Pivanova, A.V., 843 (SAT0190)
Piver, E., 335 (THU0349)
Pizem, J., 109 (OP0136)
Pizzi, N., 900 (SAT0340), 1262 (AB0602)
Pizzorni, C., 66 (OP0037), 140 (OP0212), 595 (FRI0288), 641 (FRI0407), 704 (FRI0569), 897 (SAT0331), 914 (SAT0377), 915 (SAT0381), 1111 (AB0185), 1263 (AB0605)
Pla Salas, X., 897 (SAT0332)
Plaksina, T., 560 (FRI0208)
Plana, C., 1406 (AB1004)
Planas-Rigol, E., 610 (FRI0324)
Plant, D., 200 (THU0001, THU0002)
Plant, T., 1421 (AB1049)
Plasencia, C., 416 (THU0553), 452 (THU0651), 456 (THU0661), 551 (FRI0186), 555 (FRI0194, FRI0195), 559 (FRI0204), 822 (SAT0141), 833 (SAT0168), 1116 (AB0198), 1179 (AB0374, AB0375), 1293 (AB0686), 1294 (AB0687), 1304 (AB0714)
Plasencia Rodriguez, C., 824 (SAT0145)
Plasqui, G., 157 (OP0245)
Platt, A., 382 (THU0461)
Plattfaut, C., 1108 (AB0175)
Plaza Aulestia, N., 1210 (AB0458), 1211 (AB0459)
Plazuelo, P., 1559 (PARE0020)
Plazuelo-Ramos, P., 1554 (PARE0007)
Plein, S., 238 (THU0101)
Plešivčnik Novljan, M., 1143 (AB0272)
Pluma, A., 776 (SAT0022), 946 (SAT0458)
Plummer, Z., 110 (OP0139-HPR)
Poddubnyy, D., 101 (OP0118), 651 (FRI0435), 921 (SAT0395)
Pødenphant, J., 784 (SAT0045)
Poder, A., 683 (FRI0512)
Podolinskay, N., 1497 (FRI0737-HPR)
Podovšovnik, A., 1186 (AB0393)
Podryadnova, M., 1411 (AB1017)
Poduval, M., 984 (SAT0550)
Podvorotova, M.M., 1347 (AB0828)
Poesen, K., 636 (FRI0393)
Pohl, C., 529 (FRI0128)
Poindron, V., 106 (OP0128)
Poiraudeau, S., 170 (LB0001)
Poivret, D., 426 (THU0582), 1470 (AB1185)
Pok, S.L., 446 (THU0638)
Pokryshka, I., 1115 (AB0196)
Polachek, A., 98 (OP0111)
Polak, A.A., 968 (SAT0508)
Polanco Cruz, J., 1276 (AB0641)
Polanco-Soriano, K., 877 (SAT0277)
Polanova, M., 829 (SAT0157)
Polat, G.M., 1509 (FRI0770-HPR), 1519 (SAT0743-HPR), 1544 (AB1237-HPR)
Polat, M.G., 1504 (FRI0756-HPR), 1537 (AB1217-HPR)
Poli, F., 1062 (AB0045)
Polido-Pereira, J., 746 (FRI0678), 834 (SAT0170)
Polimeni, A., 496 (FRI0045)
Polino, L., 307 (THU0273), 1181 (AB0381)
Póliska, S., 1094 (AB0137)
Poliska, S., 1049 (AB0009)
Polistena, B., 667 (FRI0477)
Politi, C., 204 (THU0013)
Polito, P., 603 (FRI0308), 634 (FRI0387)
Pollock, J., 110 (OP0139-HPR)
Polo y La Borda, J., 645 (FRI0420), 925 (SAT0405)
Polyakova, J., 1149 (AB0288)
Polyakova, Y., 699 (FRI0554)
Pomirleanu, C., 632 (FRI0383), 825 (SAT0148)
Pompermayer, L.E., 1231 (AB0516), 1333 (AB0789)
Pomponio, G., 1189 (AB0400)
Ponce, A., 1289 (AB0675), 1443 (AB1109)
Ponce, J., 705 (FRI0570, FRI0571)
Ponce, L., 267 (THU0173)
Ponce de Leon, D., 1196 (AB0419)
Ponce-Guarneros, J., 1155 (AB0304)
Ponce-Guarneros, M., 262 (THU0161)
Ponchel, F., 159 (OP0250), 1085 (AB0112)
Pongratz, G., 789 (SAT0056)
Ponomarev, I., 485 (FRI0015)
Pons, A., 1016 (SAT0638), 1296 (AB0693), 1351 (AB0840)
Pons, E., 108 (OP0135)
Pons-Estel, B., 1453 (AB1137)
Pontarini, E., 180 (OP0300)
Ponte, C., 315 (THU0296), 316 (THU0297), 1080 (AB0097), 1254 (AB0581)
Ponte, C.B., 318 (THU0302)
Pontes Filho, M.A.G., 386 (THU0475, THU0476)
Pontikaki, I., 132 (OP0195)
Ponzoni, M., 126 (OP0179)
Poojary, P., 378 (THU0450)
Poole, J., 35 (SP0140)
Poolman, R., 111 (OP0141-HPR)
Poon, K.S., 589 (FRI0271)
Poór, G., 1482 (THU0736-HPR)
Pop, D., 880 (SAT0285)
Pope, J., 58 (OP0019), 231 (THU0085), 781 (SAT0039), 815 (SAT0122), 1271 (AB0627)
Pope, J.E., 65 (OP0034), 629 (FRI0375)
Pope, R., 1125 (AB0220)
Popescu, C., 1018 (SAT0644)
Popescu, M., 1026 (SAT0665)
Popik, S., 563 (FRI0214), 580 (FRI0251), 581 (FRI0252)
Popkova, T., 254 (THU0142), 256 (THU0148), 572 (FRI0231), 599 (FRI0299), 776 (SAT0024), 811 (SAT0113), 1404 (AB0998), 1411 (AB1018)
Popkova, T.V., 266 (THU0171), 1226 (AB0500)
Popov-Celeketic, J., 482 (FRI0008)
Popoviciu, H.V., 1440 (AB1101)
Popp, D., 89 (OP0091)
Porcheret, M., 1433 (AB1081)
Porretti, L., 1109 (AB0178)
Porta, F., 1013 (SAT0631)
Portela Hernández, M., 1211 (AB0460)
Portell, E., 691 (FRI0529)
Porter, B., 340 (THU0359), 355 (THU0393), 357 (THU0397), 358 (THU0398), 1293 (AB0685)
Porter, D., 242 (THU0111), 535 (FRI0142)
Portilla, V., 742 (FRI0666), 1084 (AB0108)
Portilla-Gonzalez, V., 1116 (AB0197)
Ports, W.C., 951 (SAT0469)
Posso-Osorio, I., 1225 (AB0498)
Posta, E., 767 (FRI0731)
Postema, R., 442 (THU0626), 568 (FRI0223), 571 (FRI0230), 1188 (AB0397)
Posteraro, B., 197 (OP0343)
Postlethwaite, A., 1503 (FRI0754-HPR)
Potarniche, D., 304 (THU0266), 876 (SAT0271), 1221 (AB0487)
Poudroux, J., 218 (THU0051)
Poulain, L., 1352 (AB0844)
Poulsen, T.B.G., 775 (SAT0020)
Pouplin, S., 258 (THU0152), 811 (SAT0112), 815 (SAT0123), 1378 (AB0923), 1470 (AB1185)
Poursac, N., 638 (FRI0398)
Pouw, R.A.M., 982 (SAT0544)
Poveda, A., 302 (THU0259)
Povedano, J., 1422 (AB1050)
Povedano Gomez, J., 713 (FRI0592)
Povoroznyuk, R., 1469 (AB1182)
Povoroznyuk, V., 1177 (AB0369), 1469 (AB1182)
Powell, N., 1099 (AB0151)
Powell, S., 409 (THU0536)
Power, J.D., 1035 (SAT0688)
Poynard, T., 776 (SAT0023)
Pozniak, E., 426 (THU0584)
Pozzi, M.R., 270 (THU0181), 1154 (AB0301)
Pozzilli, P., 646 (FRI0423)
Pracon, G., 216 (THU0045)
Prade, J., 240 (THU0105)
Pradel, V., 1454 (AB1141)
Pradier, C., 851 (SAT0207)
Prado, L.L., 614 (FRI0335)
Prados, A., 500 (FRI0059)
Prados-Ojeda, J.L., 441 (THU0624)
Praino, E., 1135 (AB0250), 1268 (AB0618)
Praprotnik, S., 311 (THU0284), 464 (THU0681),

886 (SAT0302), 1143 (AB0272), 1186 (AB0393), 1291 (AB0682)
Prasad, P., 862 (SAT0235)
Pratesi, F., 222 (THU0063), 1113 (AB0191)
Pratesi, S., 623 (FRI0362)
Prati, C., 417 (THU0558), 493 (FRI0039), 495 (FRI0044), 959 (SAT0486)
Prato, G., 1008 (SAT0620)
Pratsidou-Gkertsi, P., 205 (THU0015)
Pratt, A.G., 200 (THU0003)
Predeteanu, D., 304 (THU0266), 416 (THU0555), 423 (THU0574), 435 (THU0606), 876 (SAT0271), 881 (SAT0288), 1025 (SAT0664), 1026 (SAT0665), 1221 (AB0487), 1278 (AB0646, AB0647), 1333 (AB0790), 1428 (AB1068), 1460 (AB1158), 1540 (AB1224-HPR)
Prediletto, E., 125 (OP0175)
Preen, D., 767 (FRI0730), 1045 (SAT0716)
Preglej, T., 499 (FRI0055)
Preijers, F., 1109 (AB0178)
Preis, E., 897 (SAT0333)
Preiss, P., 754 (FRI0697)
Prekas, K., 1133 (AB0244)
Prens, E., 1088 (AB0118)
Presberg, Y., 450 (THU0646)
Prete, M., 263 (THU0164), 1106 (AB0171)
Prevete, I., 437 (THU0611), 1439 (AB1099)
Prévot, G., 901 (SAT0342)
Prey, S., 710 (FRI0584)
Preziosa, P., 725 (FRI0624)
Price, E., 1553 (PARE0004)
Price, E.J., 1205 (AB0444)
Price, K., 677 (FRI0499), 842 (SAT0188), 1192 (AB0408), 1455 (AB1143)
Price, L.L., 384 (THU0469)
Pricop, L., 145 (OP0222), 675 (FRI0494), 688 (FRI0521), 949 (SAT0463), 952 (SAT0470), 957 (SAT0480), 1322 (AB0765), 1323 (AB0766), 1326 (AB0772), 1329 (AB0780)
Pricorp, L., 683 (FRI0511), 948 (SAT0462)
Prieto-Alhambra, D., 159 (OP0251), 760 (FRI0713), 1440 (AB1102)
Prieto-González, S., 415 (THU0550), 1252 (AB0575)
Prieto-Gonzalez, S., 610 (FRI0324)
Prieto-Peña, D., 1255 (AB0583, AB0584)
Prieto-Potin, I., 504 (FRI0071)
Primdahl, J., 433 (THU0601)
Prina-Mello, A., 1085 (AB0111)
Prior, A., 1236 (AB0529)
Prior, J., 1043 (SAT0708)
Prior, Y., 11 (SP0043)
Prior-Español, A., 988 (SAT0560), 1241 (AB0544)
Priori, R., 305 (THU0268), 311 (THU0284), 329 (THU0334), 411 (THU0541), 496 (FRI0045), 886 (SAT0302), 888 (SAT0305), 1465 (AB1170)
Prisco, E., 56 (OP0015)
Priyanka, K., 301 (THU0258)
Probatova, N., 424 (THU0578)
Proctor, J., 438 (THU0614)
Prodanovic, S.Z., 792 (SAT0064)
Proietta, M., 879 (SAT0282)
Prono, V., 728 (FRI0632)
Propato, M.L., 1220 (AB0484, AB0485)
Pros, A., 1181 (AB0381)
Prosperi, D., 891 (SAT0315)
Protaschik, Y., 1372 (AB0904)
Protheroe, S., 409 (THU0536)
Protopopov, M., 101 (OP0118)
Proudfoot, C., 94 (OP0102), 575 (FRI0240)
Proudman, S.M., 203 (THU0011)
Proulx, L., 81 (OP0072-PARE)
Provan, S.A., 52 (OP0005), 466 (THU0686)
Prystupa, L., 820 (SAT0136)
Przygodzka, M., 1199 (AB0425), 1535 (AB1211-HPR)
Psachoulia, E., 454 (THU0656)
Psaradellis, E., 554 (FRI0191), 679 (FRI0503)
Psarellis, S., 1437 (AB1093)
Psarras, A., 91 (OP0095), 314 (THU0293)
Puato, M., 1315 (AB0745)
Puchner, A., 292 (THU0233), 488 (FRI0024), 492 (FRI0033), 502 (FRI0064)
Puchner, R., 1173 (AB0357), 1455 (AB1144)
Pucino, V., 506 (FRI0076)
Pugliese, D., 154 (OP0239)
Pugnet, G., 188 (OP0321), 901 (SAT0342), 1248 (AB0565)
Puhakka, A., 1404 (AB0999)
Puig, J., 383 (THU0464)
Puig-Kröger, A., 501 (FRI0062)
Pulikool, S., 325 (THU0322)
Pulles, A.E., 1068 (AB0061)
Punceviciene, E., 245 (THU0116)
Pundak, S., 1118 (AB0203)
Pundole, X., 82 (OP0075)
Puntana, S., 908 (SAT0362)
Punwaney, R., 1506 (FRI0763-HPR)
Punzi, L., 56 (OP0015), 77 (OP0062), 99 (OP0113), 210 (THU0029), 216 (THU0047), 327 (THU0328), 383 (THU0465), 411 (THU0541), 603 (FRI0308), 634 (FRI0387), 730 (FRI0637), 1066 (AB0055), 1111 (AB0184), 1123 (AB0215), 1315 (AB0745)
Puolakka, K., 262 (THU0163), 404 (THU0523)
Purebl, G., 1548 (AB1248-HPR)
Purmalek, M., 498 (FRI0053)
Purvis, H., 178 (OP0296)
Pusey, C.D., 774 (SAT0015)
Puszczewicz, M., 1470 (AB1184)
Pusztai, A., 469 (THU0694)
Putrik, P., 31 (SP0123), 80 (OP0070), 134 (OP0199-PARE)
Putterman, C., 1407 (AB1007), 1462 (AB1163)
Puxeddu, I., 222 (THU0063), 1113 (AB0191)
Puyraimond-Zemmour, D., 155 (OP0242), 458 (THU0666)
Py, G.E., 1417 (AB1037)
Pyo, J.Y., 372 (THU0436), 383 (THU0467)

Qalliaj, E., 1543 (AB1234-HPR)
Qi, J., 665 (FRI0471), 1208 (AB0452)
Qian, J., 583 (FRI0258), 600 (FRI0302), 858 (SAT0224)
Qian, L., 1516 (SAT0734-HPR)
Qian, Q., 1535 (AB1210-HPR)
Qianqian, C., 348 (THU0377)
Qiao, L., 393 (THU0494)
Qiao, Y., 872 (SAT0261)
Qie, D., 393 (THU0494)
Qin, J., 509 (FRI0084)
Qin, K., 63 (OP0028), 947 (SAT0459), 1081 (AB0100)
Qin, L., 689 (FRI0524), 1198 (AB0424)
Qingshun, L., 141 (OP0215)
Qiu, M., 1208 (AB0452)
Qiu, Q., 298 (THU0250)
Quaresma, C., 834 (SAT0170)
Quarta, C.C., 227 (THU0076), 1427 (AB1064)
Quarta, E., 702 (FRI0563), 704 (FRI0568), 1353 (AB0847), 1483 (THU0743-HPR)
Quarta, L., 702 (FRI0563), 704 (FRI0568), 808 (SAT0105), 1327 (AB0773), 1353 (AB0847), 1483 (THU0743-HPR)
Quartier, P., 31 (SP0122), 77 (OP0063), 395 (THU0502), 405 (THU0525), 448 (THU0641)
Quartuccio, L., 305 (THU0268), 311 (THU0284), 464 (THU0681), 585 (FRI0263), 829 (SAT0158), 886 (SAT0302), 940 (SAT0443), 1101 (AB0156), 1272 (AB0630)
Quebe, A., 524 (FRI0116)
Queiró, R., 946 (SAT0458)
Queiro, R., 685 (FRI0515), 954 (SAT0474), 955 (SAT0475), 1333 (AB0788)
Quesada, E., 962 (SAT0494), 1062 (AB0043)
Quesada-Gómez, J.M., 1071 (AB0070)
Quevedo, J.C., 1397 (AB0979)
Quevedo, P., 1534 (AB1206-HPR)
Quevedo Abeledo, J.C., 917 (SAT0385)
Queyrel, V., 991 (SAT0569)
Quilis, N., 1367 (AB0890)
Quince, C., 1087 (AB0115)
Quinones, M., 817 (SAT0129)
Quiñones-Torres, J.R., 695 (FRI0542), 996 (SAT0585)
Quintana, R., 440 (THU0619), 1453 (AB1137)
Quintero, M., 1342 (AB0813)
Quintero, M.J., 1339 (AB0805)
Quinteros, A., 440 (THU0619)
Quirant, B., 1236 (AB0529)

R-Moreno, O., 326 (THU0326)
Raaschou, P., 183 (OP0308)
Rabah, D., 857 (SAT0222), 862 (SAT0235)
Rabbani, N., 1025 (SAT0663)
Rabea, R.E., 1259 (AB0594)
Rabelink, A.J., 774 (SAT0015)
Rabelink, T.J., 181 (OP0302), 871 (SAT0258)
Rabelo Jr., C.N., 397 (THU0505)
Rabik, Y.D., 810 (SAT0111)
Rabinovich, C., 405 (THU0525)
Racay, P., 1449 (AB1126)
Raczkiewicz, A., 1152 (AB0297)
Radak Perovic, M., 1020 (SAT0648)
Radak-Perovic, M.M., 1457 (AB1149)
Radić, M., 1283 (AB0661)
Radin, M., 761 (FRI0716), 1410 (AB1014), 1443 (AB1110), 1450 (AB1130), 1457 (AB1148)
Radmore, R., 1100 (AB0152)
Radner, H., 750 (FRI0688)
Radominski, S., 1160 (AB0320)
Radomski, R., 1199 (AB0425), 1535 (AB1211-HPR)
Radovanovic, D., 52 (OP0006)
Radrigan, F., 1339 (AB0805)
Radstake, T., 383 (THU0464)
Radstake, T.R., 181 (OP0303), 182 (OP0306), 288 (THU0223), 292 (THU0234), 295 (THU0241), 894 (SAT0324), 1065 (AB0054), 1089 (AB0121), 1206 (AB0446)
Radstake, T.R.D.J., 1047 (AB0003), 1104 (AB0165), 1108 (AB0177), 1109 (AB0178)
Radu, A., 1032 (SAT0681), 1264 (AB0608)
Radunovic, G., 314 (THU0292), 792 (SAT0064), 1020 (SAT0648)
Radwan, A.R., 1008 (SAT0619), 1150 (AB0291)
Radzikowska, A., 216 (THU0045), 489 (FRI0026)
Radziszewska, A., 389 (THU0484)
Raeissadat, S.A., 700 (FRI0556, FRI0557), 1003 (SAT0604, SAT0605), 1012 (SAT0629), 1547 (AB1246-HPR)
Raffeiner, B., 1123 (AB0215)
Raftakis, I., 1133 (AB0244)
Ragab, G., 1422 (AB1051)
Ragheb, M., 1246 (AB0559)
Rahal, F., 1359 (AB0866)
Rahali, H., 998 (SAT0589, SAT0590), 1383 (AB0936)
Rahimi Dehgolan, S., 1012 (SAT0629), 1547 (AB1246-HPR)
Rahm, M., 701 (FRI0560)
Rahman, A., 300 (THU0256), 304 (THU0265), 1092 (AB0131), 1103 (AB0161)
Rahman, M., 1096 (AB0142)
Rahman, M.M., 1044 (SAT0713)
Rahman, P., 135 (OP0201), 145 (OP0222), 679 (FRI0503)
Rahmouni, S., 1394 (AB0969)
Rahn, E.J., 363 (THU0413), 1359 (AB0865)
Rai, M.K., 913 (SAT0375)
Rai, S.K., 165 (OP0264), 360 (THU0405), 381 (THU0460)
Raijmakers, P., 724 (FRI0623)
Raikina, E., 413 (THU0547)
Raimondo, M.-G., 70 (OP0046)
Raimondo, M.G., 343 (THU0365)
Raimondo, S., 131 (OP0193)
Raimondo, V., 1272 (AB0629)
Rajalingam, S., 1144 (AB0275)
Rajalingham, S., 1144 (AB0275)
Rajasekhar, L., 1277 (AB0644)
Rallidis, L., 643 (FRI0414)
Ralston, E., 1055 (AB0024)
Ramachandran, S., 599 (FRI0298), 857 (SAT0223), 1506 (FRI0763-HPR)
Ramadan, H., 740 (FRI0663), 1420 (AB1044)
Ramael, S., 1185 (AB0391)
Ramanan, A., 448 (THU0641)
Ramanan, A.V., 396 (THU0503)
Ramasco-Gutierrez, M., 1542 (AB1231-HPR)

Ramazan, A.-M., 996 (SAT0584)
Ramazzotto, F., 70 (OP0046)
Ramil-Gomez, O., 502 (FRI0063)
Ramír, J., 955 (SAT0475), 1333 (AB0788)
Ramirez, F., 658 (FRI0453), 927 (SAT0413), 928 (SAT0414)
Ramirez, G., 621 (FRI0357)
Ramirez, G.A., 328 (THU0331), 725 (FRI0624)
Ramírez, J., 128 (OP0185), 918 (SAT0387), 925 (SAT0406), 946 (SAT0458), 1307 (AB0723)
Ramirez, J., 752 (FRI0694), 817 (SAT0128)
Ramirez, Y., 1395 (AB0974)
Ramírez García, J., 1133 (AB0243), 1305 (AB0718)
Ramírez-Bello, J., 1133 (AB0242)
Ramirez-Gomez, A., 1452 (AB1136)
Ramiro, S., 8 (SP0028), 63 (OP0030), 80 (OP0070), 100 (OP0114, OP0115, OP0116), 131 (OP0192), 134 (OP0199-PARE), 429 (THU0590), 433 (THU0602), 466 (THU0685), 649 (FRI0430), 668 (FRI0479), 763 (FRI0722), 1052 (AB0016)
Ramkhelawon, M., 1483 (THU0739-HPR, THU0740-HPR)
Ramming, A., 892 (SAT0318)
Ramonda, R., 99 (OP0113), 156 (OP0244), 210 (THU0029), 216 (THU0047), 343 (THU0366), 666 (FRI0475), 1315 (AB0745)
Ramoni, V., 437 (THU0611), 867 (SAT0247), 1214 (AB0467), 1439 (AB1099)
Ramos, C., 452 (THU0651), 1161 (AB0321)
Ramos, R., 641 (FRI0406)
Ramos, V.C., 76 (OP0061)
Ramos, Y.F., 207 (THU0020)
Ramos Becerra, C., 1276 (AB0641)
Ramos Giraldez, C., 1399 (AB0986)
Ramos-Bello, D., 395 (THU0501), 1345 (AB0820), 1397 (AB0978)
Ramos-Casals, M., 67 (OP0040), 311 (THU0284), 410 (THU0539), 464 (THU0681), 597 (FRI0293), 721 (FRI0615), 886 (SAT0302), 1042 (SAT0706)
Ramos-Cázares, R.E., 253 (THU0140), 534 (FRI0141), 1156 (AB0309), 1157 (AB0310)
Ramos-Cazares, R.E., 1118 (AB0204), 1119 (AB0205)
Ramos-Petersen, L., 1486 (THU0751-HPR)
Ramos-Remus, C., 1452 (AB1136)
Rampakakis, E., 58 (OP0019), 194 (OP0337-HPR), 523 (FRI0115), 531 (FRI0132), 539 (FRI0153), 554 (FRI0191), 679 (FRI0503)
Rampersaud, Y.R., 1035 (SAT0688)
Ramsey-Goldman, R., 50 (OP0002)
Ramwadhdoebe, T., 781 (SAT0037)
Ranade, K., 180 (OP0301)
Rancea, R., 1245 (AB0557)
Rancourt, J., 513 (FRI0092)
Rand, J., 418 (THU0561)
Randazzo, B., 950 (SAT0465)
Ranganath, V.K., 1526 (SAT0765-HPR)
Rangaraj, S., 407 (THU0531)
Rangel-Botello, A.N., 395 (THU0501), 1345 (AB0820), 1397 (AB0978)
Rangel-Charqueño, M.G., 1397 (AB0978)
Rangel-Moreno, J., 181 (OP0304)
Rani, A.M., 1546 (AB1242-HPR)
Ranieri, L., 372 (THU0437), 705 (FRI0570, FRI0571)
Rannio, T., 61 (OP0024), 784 (SAT0044)
Rannou, F., 170 (LB0001), 171 (OP0278-PARE)
Rantalaiho, V., 262 (THU0163)
Rantapää Dahlqvist, S., 113 (OP0147)
Rantapää-Dahlqvist, S., 82 (OP0073), 248 (THU0125), 792 (SAT0065), 947 (SAT0460), 1050 (AB0012)
Ranzolin, A., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562), 990 (SAT0566), 991 (SAT0567), 1372 (AB0903)
Rao, R., 581 (FRI0252), 845 (SAT0194)
Rao, V.K., 1295 (AB0690)
Rapaccini, G.L., 154 (OP0239)
Rapecki, S., 778 (SAT0030)
Rapley, T., 1517 (SAT0736-HPR), 1524 (SAT0758-HPR)
Raposo, A., 736 (FRI0652), 1015 (SAT0637)
Rasch, L., 1145 (AB0277)
Rascón, F.-J., 597 (FRI0293)
Rascón, J., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Rasero, L., 631 (FRI0380)
Rashad, S., 1281 (AB0654)
Rashed, L., 1048 (AB0006)
Rashid, A., 758 (FRI0708)
Rashkov, R., 208 (THU0023), 1106 (AB0170), 1148 (AB0284), 1233 (AB0521)
Raskina, T., 1351 (AB0841)
Raskina, T.A., 1346 (AB0823, AB0824)
Raslan, H., 1113 (AB0190)
Rasmussen, A., 67 (OP0040), 193 (OP0333), 311 (THU0284), 464 (THU0681), 886 (SAT0302), 1096 (AB0143)
Rasmussen, N.S., 457 (THU0663)
Rasouliyan, L., 948 (SAT0462), 949 (SAT0463), 1323 (AB0766), 1326 (AB0772)
Rat, A.-.-C., 436 (THU0609)
Rat, A.-C., 970 (SAT0513), 1470 (AB1185)
Raterman, H., 1038 (SAT0695)
Rathmann, S., 144 (OP0221)
Rathouska, A., 638 (FRI0399), 1280 (AB0653)
Ratsimbazafy, V., 1364 (AB0882)
Ratzinger, G., 615 (FRI0338)
Rauch, C., 577 (FRI0245), 1141 (AB0267), 1193 (AB0412)
Raufer, J., 775 (SAT0019)
Raun, J.L., 553 (FRI0190)
Rauwel, B., 770 (SAT0006)
Rauz, S., 302 (THU0259)
Ravagnan, G., 216 (THU0047)
Ravagnani, V., 1012 (SAT0630), 1015 (SAT0636), 1388 (AB0953)
Raval, D., 1253 (AB0579)
Ravaud, P., 170 (LB0001)
Rawal, D., 1377 (AB0918)
Rawat, A., 287 (THU0219), 320 (THU0307), 392 (THU0493), 394 (THU0497), 913 (SAT0375)
Rawat, R., 1506 (FRI0762-HPR), 1540 (AB1226-HPR)
Rawlings, C., 1050 (AB0011)
Rawlings, D., 178 (OP0296)
Rawstron, A., 152 (OP0235)
Rawstron, A.C., 869 (SAT0251)
Ray, A., 1295 (AB0690), 1300 (AB0705)
Ray, N., 408 (THU0534)
Raya, E., 550 (FRI0184), 556 (FRI0197), 718 (FRI0607)
Raya Álvarez, E., 1228 (AB0506), 1321 (AB0760)
Rayan, M.M., 1216 (AB0474)
Raychaudhuri, A., 152 (OP0237)
Raychaudhuri, S., 202 (THU0006), 445 (THU0635)
Rayegani, S.M., 700 (FRI0557), 1012 (SAT0629), 1547 (AB1246-HPR)
Rayeuneva, T., 1361 (AB0871)
Raymond, W.D., 767 (FRI0730), 1045 (SAT0716), 1241 (AB0542)
Raynal, M., 103 (OP0121), 663 (FRI0467)
Raynauld, J.-P., 571 (FRI0230), 845 (SAT0195), 1188 (AB0397)
Raza, K., 242 (THU0111), 523 (FRI0113), 1043 (SAT0708), 1051 (AB0015), 1511 (SAT0719-HPR)
Reaney, M., 94 (OP0102), 575 (FRI0240)
Reasner, D.S., 435 (THU0608)
Reategui-Sokolova, C., 875 (SAT0269)
Reàtegui-Solokova, C., 1142 (AB0269)
Rebane, K., 401 (THU0515)
Rebello, S., 1192 (AB0408), 1330 (AB0783), 1455 (AB1143)
Rebrov, A., 345 (THU0370), 924 (SAT0403)
Rebrov, A.P., 546 (FRI0172), 819 (SAT0134)
Rebrov, B., 1115 (AB0196)
Rebrova, O., 249 (THU0128), 675 (FRI0495)
Recalde, X., 555 (FRI0195)
Rech, J., 73 (OP0052), 107 (OP0131), 142 (OP0217), 159 (OP0249), 236 (THU0096), 240 (THU0105), 247 (THU0122), 516 (FRI0098), 655 (FRI0446), 709 (FRI0582), 725 (FRI0625), 952 (SAT0470), 1011 (SAT0628), 1324 (AB0767)
Reckless, J., 127 (OP0182)
Redden, D.T., 363 (THU0413)
Redlich, K., 488 (FRI0024), 492 (FRI0033)
Redmond, A., 34 (SP0139)
Rednic, D., 1245 (AB0557)
Rednic, S., 170 (OP0275), 260 (THU0156), 880 (SAT0285), 1245 (AB0557), 1285 (AB0666)
Redondo, C., 1293 (AB0686), 1294 (AB0687)
Redondo-Benito, A., 636 (FRI0392)
Reece, C., 81 (OP0072-PARE)
Reed, G.W., 60 (OP0022), 808 (SAT0104), 846 (SAT0196), 953 (SAT0472), 1191 (AB0407)
Rees, D., 1514 (SAT0728-HPR)
Rees, J., 215 (THU0043)
Rees, W., 180 (OP0301)
Regan, E.A., 1423 (AB1052)
Reggia, R., 1209 (AB0456), 1214 (AB0467), 1439 (AB1099)
Reginato, A., 1339 (AB0805)
Reginato, A.M., 1013 (SAT0631)
Registry, U., 295 (THU0242)
Rego-Pérez, I., 1466 (AB1174)
Rego-Perez, I., 203 (THU0009), 978 (SAT0535)
Regola, F., 579 (FRI0249), 1214 (AB0468)
Regueiro, C., 494 (FRI0040), 500 (FRI0057)
Rehart, S., 220 (THU0056), 1070 (AB0067), 1071 (AB0069)
Reich, K., 683 (FRI0511), 1325 (AB0771)
Reichardt, B., 1494 (THU0770-HPR)
Reid, J., 570 (FRI0228), 838 (SAT0179)
Reid, K., 384 (THU0469)
Reid, W.D., 1103 (AB0162)
Reiding, D., 982 (SAT0544)
Reifman, G., 355 (THU0392)
Reijman, M., 961 (SAT0492)
Reijnierse, M., 100 (OP0114), 473 (THU0702, THU0704), 662 (FRI0465), 669 (FRI0480), 969 (SAT0511, SAT0512), 1013 (SAT0632)
Reimold, A., 952 (SAT0470)
Rein, C., 465 (THU0684)
Reina, D., 1005 (SAT0610)
Reina-Sanz, D., 569 (FRI0226)
Reinbolt, R., 222 (THU0062)
Reinhold-Keller, E., 325 (THU0323)
Reiser, M., 159 (OP0249), 240 (THU0105), 516 (FRI0098)
Reiseter, S., 765 (FRI0725), 1043 (SAT0709)
Reiss, W., 567 (FRI0222)
Reitblat, T., 355 (THU0392)
Reiter, G., 1494 (THU0770-HPR)
Reiter, K., 184 (OP0311)
Rejaibi, S., 1417 (AB1038)
Rekik, S., 1536 (AB1214-HPR)
Relaño, S., 978 (SAT0535)
Relaño-Fernandez, S., 203 (THU0009)
Relas, H., 61 (OP0024), 401 (THU0515)
Rell-Bakalarska, M., 1419 (AB1042)
Rémillard, M.-A., 571 (FRI0230), 845 (SAT0195), 1188 (AB0397)
Rempenault, C., 804 (SAT0094)
Remple, V., 349 (THU0378)
Remple, V.P., 656 (FRI0449)
Remuzgo-Martínez, S., 1084 (AB0108)
Ren, H., 294 (THU0239), 497 (FRI0050)
Ren, L., 1082 (AB0102)
Ren, Q., 870 (SAT0253), 994 (SAT0578)
Renaudin, F., 212 (THU0034), 216 (THU0046)
Renaudineau, Y., 309 (THU0278)
Rendas-Baum, R., 531 (FRI0133), 816 (SAT0126)
Rengers, P., 1007 (SAT0616)
Renner, N., 1011 (SAT0628)
Renoux, F., 86 (OP0084), 191 (OP0330), 890 (SAT0312)
Rensen, W., 741 (FRI0664)
Renskers, L., 1498 (FRI0740-HPR), 1525 (SAT0761-HPR)
Renson, T., 653 (FRI0440), 1305 (AB0716)
Rentka, A., 1273 (AB0632)
Repa, A., 574 (FRI0236), 577 (FRI0244), 850 (SAT0204), 896 (SAT0330)
Resch, H., 73 (OP0052), 655 (FRI0446)
Resche-Rigon, M., 108 (OP0134)
Resende, G.G., 1056 (AB0028)
Reséndiz-Albor, A.A., 1286 (AB0668)
Reshetnyak, T., 269 (THU0179), 860 (SAT0230)

Resnick, D., 1423 (AB1052)
Restuccia, G., 323 (THU0316), 609 (FRI0323)
Retamero, A., 1434 (AB1085)
Retamozo, S., 205 (THU0017), 206 (THU0018), 311 (THU0284), 313 (THU0289), 440 (THU0619), 464 (THU0681), 886 (SAT0302), 995 (SAT0582)
Réthi, B., 482 (FRI0006)
Rethi, B., 212 (THU0036), 484 (FRI0013)
Retuerto, M., 843 (SAT0191)
Retuerto Guerrero, M., 213 (THU0037), 719 (FRI0608), 1232 (AB0518)
Reveille, J.D., 335 (THU0348), 341 (THU0360), 1295 (AB0692)
Revenga, M., 326 (THU0326)
Revenga-Martinez, M., 298 (THU0249)
Revy, P., 1049 (AB0007)
Rey, F., 406 (THU0527)
Reyes, G., 1339 (AB0805)
Reyes, J., 1456 (AB1145)
Reyes Rueda, J., 1276 (AB0641)
Reyes Servin, O., 1319 (AB0756)
Reyes-Maldonado, E., 881 (SAT0287)
Reyes-Rueda, J., 117 (OP0158), 1446 (AB1116)
Reygaerts, T., 686 (FRI0519)
Reyna, V., 453 (THU0654, THU0655)
Reyna-De la Garza, R., 586 (FRI0264)
Reynard, L., 200 (THU0003)
Reyner, P., 1014 (SAT0635)
Reynolds, J.C., 1217 (AB0475)
Reynolds, T.L., 857 (SAT0222)
Rezaei, H., 726 (FRI0626), 785 (SAT0048)
Rezende, R.P., 641 (FRI0406)
Rezk, T., 227 (THU0076), 1427 (AB1064)
Rezus, E., 1261 (AB0600), 1411 (AB1019)
Rezvani, A., 1380 (AB0927)
Rho, Y.H., 552 (FRI0187)
Rhodes, C., 1343 (AB0817), 1552 (PARE0002)
Rhys, H., 483 (FRI0011)
Riancho-Zarrabeitia, L., 594 (FRI0286), 1229 (AB0511), 1230 (AB0512)
Ribbens, C., 736 (FRI0650)
Ribeiro, D.L.D.S., 1412 (AB1021)
Ribeiro, D.S., 176 (OP0290)
Ribes, D., 188 (OP0321)
Ricaño Rocha, R., 1211 (AB0460)
Ricard, E., 989 (SAT0561), 1191 (AB0406)
Riccardi, A., 151 (OP0233), 630 (FRI0378)
Ricci Iamino, I., 366 (THU0420)
Ricci Larrea, L., 1257 (AB0590)
Riccieri, V., 202 (THU0006), 299 (THU0252), 329 (THU0334), 496 (FRI0045), 903 (SAT0347), 1057 (AB0029, AB0030)
Rich, P., 937 (SAT0437)
Rich, P.A., 1319 (AB0756)
Rich-Garg, N., 1315 (AB0744)
Richards, A., 302 (THU0259)
Richards, D.P., 81 (OP0072-PARE)
Richards, H., 345 (THU0369)
Richards, T., 304 (THU0265)
Richardson, H., 167 (OP0268), 1028 (SAT0670)
Richebé, P., 1330 (AB0781)
Riches, P., 383 (THU0464)
Richette, P., 53 (OP0007), 73 (OP0054), 171 (OP0278-PARE), 258 (THU0152), 359 (THU0401), 382 (THU0461, THU0463), 811 (SAT0112), 1049 (AB0007), 1364 (AB0882), 1371 (AB0900)
Richez, C., 549 (FRI0180), 573 (FRI0234), 710 (FRI0584), 815 (SAT0123), 866 (SAT0246), 1049 (AB0007)
Richter, A., 530 (FRI0130), 801 (SAT0087), 1029 (SAT0674), 1421 (AB1049)
Richter, J., 302 (THU0261), 899 (SAT0337)
Richter, J.G., 442 (THU0625), 1449 (AB1127)
Richter, M., 769 (SAT0002)
Richter, M.D., 444 (THU0630)
Rickert, M., 220 (THU0056)
Rider, L.G., 913 (SAT0376)
Rieker, R., 892 (SAT0318)
Riel, P.V., 1140 (AB0263)
Riemekasten, G., 202 (THU0006), 772 (SAT0011), 893 (SAT0320), 897 (SAT0333), 915 (SAT0380), 1008 (SAT0618), 1047 (AB0003), 1106 (AB0169), 1108 (AB0175), 1110 (AB0181)
Rienzi, L., 879 (SAT0282)
Riera, H., 1339 (AB0805), 1342 (AB0813)
Riera Mestre, A., 1208 (AB0451)
Riesco, M., 685 (FRI0515)
Rietschel, C., 397 (THU0504)
Rifbjerg, S., 161 (OP0254-HPR)
Rifbjerg-Madsen, S., 98 (OP0112)
Rigamonti, F., 1376 (AB0917), 1380 (AB0928)
Rigby, W., 567 (FRI0222)
Rigby, W.F.C., 135 (OP0202), 148 (OP0230), 676 (FRI0496), 938 (SAT0439), 1202 (AB0436)
Righetti, G., 521 (FRI0110), 1268 (AB0618)
Rigon, A., 876 (SAT0273)
Riis, B.J., 120 (OP0165)
Rijen, M.V., 483 (FRI0010)
Rijnen, W., 1476 (THU0721-HPR)
Rillo, O., 440 (THU0619), 670 (FRI0483), 1339 (AB0805)
Rimar, D., 653 (FRI0441), 926 (SAT0407)
Rimbert, M., 778 (SAT0029)
Rinaldi, A., 521 (FRI0110)
Rincón-Riaño, D.N., 696 (FRI0544)
Ringheim, G.E., 778 (SAT0028), 780 (SAT0035)
Rinkin, C., 736 (FRI0650)
Rinollo, C., 901 (SAT0341)
Rintelen, B., 1455 (AB1144)
Ríos, C., 734 (FRI0645)
Rios, C., 1160 (AB0318, AB0319)
Rios, J., 317 (THU0300)
Ríos, J.J., 873 (SAT0264), 1245 (AB0555), 1266 (AB0614), 1289 (AB0676)
Ríos-Martin, I., 1490 (THU0761-HPR)
Ripoll, M., 597 (FRI0293)
Ripoll-Nunez, V., 1092 (AB0131)
Ripoll-Nunez, V.M., 1103 (AB0161)
Rischmueller, M., 311 (THU0284), 383 (THU0464), 464 (THU0681), 886 (SAT0302)
Riskowski, J., 1505 (FRI0761-HPR)
Risoli, M., 1200 (AB0429)
Rispens, T., 61 (OP0025), 125 (OP0177), 335 (THU0349), 758 (FRI0707), 935 (SAT0433)
Rist, S., 1186 (AB0395)
Ristolainen, L., 401 (THU0515)
Ristori, D., 1499 (FRI0742-HPR)
Risum, K., 164 (OP0261-HPR), 1517 (SAT0737-HPR)
Ritchlin, C., 145 (OP0222)
Ritchlin, C.T., 97 (OP0108), 953 (SAT0471)
Ritschl, H., 1547 (AB1245-HPR)
Ritschl, V., 1545 (AB1240-HPR)
Ritsema, W., 1075 (AB0082)
Riva, M., 1154 (AB0301)
Rivas, A., 961 (SAT0490)
Riveiro-Naveira, R.R., 502 (FRI0063)
Riveline, J.-P., 382 (THU0461)
Rivellese, F., 490 (FRI0030)
Rivera, A., 595 (FRI0289), 1252 (AB0576), 1400 (AB0988)
Rivera, N., 555 (FRI0195), 837 (SAT0178)
Rivera-Gallego, A., 1409 (AB1012)
Rivera-García, N., 1001 (SAT0600)
Rivero, M.A., 1534 (AB1206-HPR)
Riveros, A., 1236 (AB0529), 1434 (AB1085)
Rivett, A., 1030 (SAT0676), 1039 (SAT0699)
Rivière, E., 289 (THU0225), 336 (THU0350)
Riyazi, N., 793 (SAT0067)
Rizzi, M., 52 (OP0006), 324 (THU0321), 615 (FRI0339)
Rizzo, A., 131 (OP0193), 180 (OP0299), 183 (OP0309)
Rizzoli, R., 178 (OP0294)
Rkain, H., 1358 (AB0862), 1365 (AB0883, AB0884, AB0885), 1418 (AB1041)
Roa Perez, L., 440 (THU0619)
Roa Prerez, L.O., 1279 (AB0649)
Robaina Sindin, J., 1259 (AB0595)
Röber, N., 461 (THU0674)
Roberts, C., 1010 (SAT0624)
Roberts, J., 1202 (AB0436)
Roberts, S., 221 (THU0060)
Roberts, W.N., 884 (SAT0294)
Robertson, N., 81 (OP0072-PARE)
Robertson-Plouch, C., 965 (SAT0502)
Robin-Jagerschmidt, C., 118 (OP0161), 648 (FRI0428)
Robineau, F., 188 (OP0323)
Robinson, C., 245 (THU0117), 252 (THU0136), 545 (FRI0170)
Robinson, G., 1266 (AB0613)
Robinson, H., 1514 (SAT0728-HPR)
Robinson, S., 1541 (AB1227-HPR)
Robinson, W., 498 (FRI0053), 774 (SAT0017)
Robinson, W.H., 189 (OP0325), 981 (SAT0541)
Robles, Á., 1245 (AB0555), 1266 (AB0614)
Robles, A., 410 (THU0539), 721 (FRI0615), 873 (SAT0264), 1042 (SAT0706), 1289 (AB0676)
Robles, B., 843 (SAT0191)
Robles Flores, B.J., 645 (FRI0420)
Robson, J., 605 (FRI0312)
Robustillo-Villarino, M., 258 (THU0153), 1168 (AB0344), 1316 (AB0746)
Rocca, M.A., 725 (FRI0624)
Roccatello, D., 761 (FRI0716), 1410 (AB1014), 1450 (AB1130)
Rocha, F.A.C., 397 (THU0505)
Rocha, H.A.L., 397 (THU0505)
Rocha, L.N., 397 (THU0505)
Rocha, T.M., 852 (SAT0211), 1142 (AB0268)
Rocha Junior, L.F., 987 (SAT0557), 989 (SAT0562)
Rochefort, S.V., 1520 (SAT0745-HPR)
Rocher, C., 195 (OP0339)
Rocher, V., 238 (THU0100), 458 (THU0667), 511 (FRI0088)
Roddy, E., 383 (THU0464), 751 (FRI0690), 1028 (SAT0672), 1552 (PARE0002)
Rodere, M., 1515 (SAT0733-HPR)
Rødevand, E., 334 (THU0345), 673 (FRI0490), 1492 (THU0765-HPR)
Rodionova, E., 1237 (AB0531)
Rodionova, V.V., 979 (SAT0537)
Rodionovskaya, S., 1389 (AB0955)
Rodrígez-Ramírez, A.-M., 1169 (AB0345)
Rodrigo Nicolás, R., 291 (THU0229)
Rodrigues, A., 186 (OP0315)
Rodrigues, A.C., 1429 (AB1070)
Rodrigues, A.M., 1080 (AB0097)
Rodrigues, C., 814 (SAT0121)
Rodrigues, J., 612 (FRI0330)
Rodrigues, J.C., 76 (OP0061)
Rodrigues, J.R., 607 (FRI0318), 1011 (SAT0627)
Rodrigues, M., 137 (OP0206), 437 (THU0611), 1254 (AB0581), 1439 (AB1099)
Rodrigues Ferreira, W.H., 1516 (SAT0735-HPR)
Rodrigues Manica, S., 80 (OP0070), 466 (THU0685)
Rodríguez, A., 400 (THU0514), 1091 (AB0126)
Rodriguez, A., 175 (OP0288), 1098 (AB0149)
Rodriguez, F., 427 (THU0585), 1479 (THU0729-HPR), 1534 (AB1207-HPR)
Rodriguez, F.J., 685 (FRI0515)
Rodriguez, G., 739 (FRI0660)
Rodríguez, I., 691 (FRI0530)
Rodriguez, I., 843 (SAT0191)
Rodríguez, J., 946 (SAT0458)
Rodriguez, L., 595 (FRI0289), 1252 (AB0576)
Rodriguez, M., 843 (SAT0191)
Rodríguez, S., 691 (FRI0530), 712 (FRI0589), 930 (SAT0419)
Rodriguez, S., 694 (FRI0539), 843 (SAT0191)
Rodriguez Araya, T.L., 1122 (AB0212)
Rodriguez Bellido, Z., 1142 (AB0269)
Rodríguez Caballeira, M., 1270 (AB0624)
Rodríguez de Cossío, Á., 761 (FRI0715), 1456 (AB1146, AB1147)
Rodríguez De La Peña, A., 990 (SAT0564)
Rodríguez Fernández, S., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Rodríguez Frías, E., 990 (SAT0564)
Rodriguez Henriquez, P., 1330 (AB0782)
Rodríguez Lozano, B., 1037 (SAT0691)
Rodriguez Montero, S., 1210 (AB0458), 1211 (AB0459)
Rodriguez Pinto, I., 418 (THU0561)
Rodriguez Portal, J.A., 713 (FRI0592)

Rodríguez Roca, G., 761 (FRI0715), 1456 (AB1146, AB1147)
Rodriguez Valls, M.J., 1183 (AB0385)
Rodríguez–Bautista, E., 877 (SAT0277)
Rodriguez-Amado, J., 758 (FRI0709), 1450 (AB1129)
Rodríguez-Bautista, E., 877 (SAT0276)
Rodríguez-Bellido, Z., 875 (SAT0269)
Rodriguez-Carballeira, M., 317 (THU0300)
Rodríguez-Carrio, J., 803 (SAT0093), 1079 (AB0093)
Rodríguez-Castellano, E., 873 (SAT0264)
Rodriguez-Cuenca, S., 194 (OP0336), 1078 (AB0092)
Rodríguez-Frade, J.M., 645 (FRI0420)
Rodriguez-García, S.C., 817 (SAT0128)
Rodriguez-Garcia, S.C., 1393 (AB0967)
Rodríguez-Jiménez, M., 575 (FRI0238), 850 (SAT0205)
Rodriguez-Jimenez, N.A., 262 (THU0161)
Rodríguez-Lozano, B., 695 (FRI0541), 1115 (AB0195), 1424 (AB1057)
Rodriguez-Lozano, B., 1397 (AB0979)
Rodriguez-Lozano, C., 1397 (AB0979)
Rodriguez-Martinez, L., 500 (FRI0057)
Rodríguez-Muguruza, S., 1424 (AB1055)
Rodríguez-Padilla, L.M., 905 (SAT0354)
Rodríguez-Pérez, J.M., 291 (THU0230)
Rodriguez-Perez, M., 1443 (AB1109)
Rodríguez-Pintó, I., 150 (OP0231)
Rodriguez-Reyna, T.S., 878 (SAT0278)
Rodríguez-Rodríguez, L., 177 (OP0292), 320 (THU0309), 1047 (AB0003)
Rodriguez-Rodriguez, L., 520 (FRI0107)
Rodriguez-Romo, R.M., 515 (FRI0095)
Rodríguez-Trillo, Á., 503 (FRI0068)
Røe, R., 1500 (FRI0747-HPR)
Roeleveld, D., 191 (OP0329)
Roemer, F.W., 964 (SAT0500)
Roepstorff, K., 1068 (AB0061)
Roffler, M., 1489 (THU0758-HPR)
Rogai, V., 510 (FRI0086)
Rogatkina, T., 1149 (AB0288)
Rogers, M., 419 (THU0564), 1442 (AB1106)
Rogers, P., 438 (THU0615)
Rogier, R., 191 (OP0329), 504 (FRI0072)
Rogoznica, M., 771 (SAT0009)
Röhner, E., 486 (FRI0019)
Rohrer, S., 345 (THU0369)
Roia, D., 521 (FRI0109)
Roig, D., 946 (SAT0458), 1005 (SAT0610)
Rojas, M., 1092 (AB0129)
Rojas Herrera, S.M., 1121 (AB0211), 1122 (AB0212)
Rojas-Alcayaga, G., 1555 (PARE0009)
Rojas-Giménez, M., 261 (THU0160), 1174 (AB0361)
Rojas-Gimenez, M., 391 (THU0489), 1175 (AB0362), 1443 (AB1109), 1492 (THU0766-HPR)
Rojas-Martínez, A., 1054 (AB0023)
Rojas-Serrano, J., 1272 (AB0630)
Rojkovich, B., 134 (OP0199-PARE), 1180 (AB0378)
Rojo, R., 676 (FRI0496), 938 (SAT0439)
Rokutanda, R., 871 (SAT0256)
Rolland, C., 1181 (AB0379)
Rollefstad, S., 802 (SAT0090), 1029 (SAT0673)
Rollo, G., 702 (FRI0563)
Román, A., 900 (SAT0339)
Román, L., 1455 (AB1142)
Román Ivorra, J.A., 291 (THU0229), 441 (THU0623), 590 (FRI0275), 685 (FRI0515), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1349 (AB0837), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Romanelli, G., 906 (SAT0356)
Romanini, F., 670 (FRI0483)
Romanini, F.E., 387 (THU0479), 1429 (AB1071)
Romano, C., 237 (THU0098), 635 (FRI0389)
Romano, E., 504 (FRI0070), 623 (FRI0362)
Romano, M., 403 (THU0522), 923 (SAT0401)
Romano, M.S., 633 (FRI0384)
Romano, N., 728 (FRI0632)
Romanova, T.A., 546 (FRI0172), 819 (SAT0134)
Romanowska-Prochnicka, K., 204 (THU0012)
Romanowski, W., 1470 (AB1184)
Romao, V., 458 (THU0667)
Romão, V.C., 834 (SAT0170)
Romao, V.C., 746 (FRI0678)
Rombouts, Y., 509 (FRI0083)
Romdhane, H., 1348 (AB0831, AB0832, AB0833), 1349 (AB0834)
Romeo, E., 630 (FRI0378)
Romeo, N., 270 (THU0181), 437 (THU0611), 1439 (AB1099)
Romera-Baures, M., 139 (OP0209-HPR)
Romero, F., 718 (FRI0607)
Romero, M., 685 (FRI0515), 1184 (AB0388)
Romero, S., 843 (SAT0191)
Romero Pazos, V., 187 (OP0318-PARE)
Romero-Barco, C.M., 1443 (AB1109)
Romero-Díaz, J., 1147 (AB0282)
Romero-Gomez, M., 350 (THU0380)
Romero-Sanchez, C., 252 (THU0137), 1117 (AB0201)
Romu, M., 61 (OP0024)
Ronda, N., 1309 (AB0730)
Rondaan, C., 607 (FRI0317)
Rondags, A., 650 (FRI0433)
Rondon, G., 82 (OP0075)
Rondon, P., 221 (THU0061)
Rondoni, A., 1499 (FRI0742-HPR)
Rones, R., 384 (THU0469)
Rongen, S., 434 (THU0604)
Rongen, S.A.A., 1498 (FRI0740-HPR), 1525 (SAT0761-HPR)
Rongen-van Dartel, S., 1505 (FRI0759-HPR)
Rönnblom, L., 11 (SP0047), 182 (OP0305)
Ronneberger, M., 159 (OP0249), 516 (FRI0098)
Rönnelid, J., 228 (THU0077), 461 (THU0673), 509 (FRI0085), 792 (SAT0065), 861 (SAT0233), 885 (SAT0297)
Rooke, C., 110 (OP0139-HPR)
Rooney, T., 789 (SAT0058), 795 (SAT0072), 1147 (AB0281)
Rooney, T.P., 527 (FRI0124)
Roorda, L., 111 (OP0141-HPR)
Roorda, L.D., 476 (THU0712), 972 (SAT0517), 982 (SAT0544), 1486 (THU0750-HPR), 1488 (THU0755-HPR)
Roos, E., 111 (OP0141-HPR), 1343 (AB0817)
Røpke, A., 161 (OP0254-HPR)
Roque Pérez, A., 900 (SAT0340)
Roquelaure, Y., 945 (SAT0455)
Roques, C., 171 (OP0278-PARE)
Roques, P., 508 (FRI0081)
Rosa, G., 176 (OP0290), 1412 (AB1021)
Rosa, I., 504 (FRI0070), 623 (FRI0362)
Rosa, J.E., 1115 (AB0194), 1333 (AB0789)
Rosa, M.L., 641 (FRI0406)
Rosa-Gonçalves, D., 468 (THU0691)
Rosa-Goncalves, D., 468 (THU0690)
Rosales, Z., 320 (THU0309)
Rosario, M.P., 414 (THU0549)
Rosario, V., 877 (SAT0276, SAT0277)
Rosas, J., 556 (FRI0197), 885 (SAT0299), 1232 (AB0519), 1296 (AB0693), 1351 (AB0840)
Rosas Gómez de Salazar, J., 1016 (SAT0638)
Rosas Gomez-Salazar, J., 1472 (AB1191)
Rosato, E., 909 (SAT0366)
Rösch, J., 240 (THU0105)
Rose, A., 186 (OP0317-PARE)
Rose, D., 30 (SP0120)
Rose, S., 859 (SAT0226)
Rose, T., 184 (OP0311)
Rose-John, S., 208 (THU0025)
Roseman, C., 823 (SAT0143)
Rosemffet, M., 1425 (AB1060)
Rosen, A., 5 (SP0017)
Rosenbaum, D., 1337 (AB0800)
Rosenberg, D.M., 65 (OP0034)
Rosenberg, V., 796 (SAT0074)
Rosendaal, F., 123 (OP0170)
Rosenkranz, M., 133 (OP0197)
Rosenzwajg, M., 776 (SAT0023)
Roshak, K., 402 (THU0519)
Roskos, L., 865 (SAT0243), 867 (SAT0249)
Rosman, A., 446 (THU0638), 596 (FRI0291)
Rosmus-Kuczia, I., 1470 (AB1184)
Rosner, I., 653 (FRI0441), 926 (SAT0407)
Rossato, M., 182 (OP0306), 1089 (AB0121), 1108 (AB0177), 1109 (AB0178)
Rossettini, G., 1483 (THU0741-HPR), 1499 (FRI0742-HPR), 1539 (AB1223-HPR)
Rossi, C., 1339 (AB0805)
Rossi, D., 1410 (AB1014)
Rossi, J., 403 (THU0521)
Rossi, P., 753 (FRI0696)
Rossi, R., 690 (FRI0527)
Rossi-Semerano, L., 56 (OP0014)
Rossini, M., 343 (THU0365), 363 (THU0412), 671 (FRI0485), 693 (FRI0535), 805 (SAT0097), 854 (SAT0215), 899 (SAT0336), 940 (SAT0443, SAT0445), 1062 (AB0045), 1124 (AB0216), 1200 (AB0429), 1207 (AB0449), 1314 (AB0742), 1388 (AB0953)
Rossini, T., 270 (THU0181)
Rossinyol, T., 415 (THU0550)
Rossmanith, T., 565 (FRI0217)
Rotar, Ž., 108 (OP0133), 219 (THU0054), 325 (THU0324), 1143 (AB0272), 1186 (AB0393), 1291 (AB0682)
Rotar, Z., 656 (FRI0450), 850 (SAT0206), 1243 (AB0552)
Roth, D., 150 (OP0232), 861 (SAT0231)
Roth, J., 89 (OP0091), 223 (THU0067), 772 (SAT0010), 1023 (SAT0656)
Roth, M., 104 (OP0124)
Rothwell, C.J., 1434 (AB1083), 1521 (SAT0748-HPR)
Rotondo, C., 521 (FRI0110), 1135 (AB0250), 1268 (AB0618)
Rotte, M.D., 241 (THU0107)
Rouchon, B., 382 (THU0463)
Roudier, J., 523 (FRI0114)
Rougelot, A., 1385 (AB0945)
Roulland, S., 182 (OP0307)
Rouse, P.C., 764 (FRI0723)
Rouse, T., 870 (SAT0254)
Roussaki-Schulze, A.-V., 680 (FRI0504)
Rousseau, A., 408 (THU0532)
Roussou, E., 923 (SAT0399), 1205 (AB0444), 1304 (AB0715)
Rout, J., 1205 (AB0444)
Roux, C., 73 (OP0054), 831 (SAT0163), 851 (SAT0207), 996 (SAT0583)
Roux, C.H., 967 (SAT0507)
Roux, N., 334 (THU0346), 339 (THU0356, THU0357), 388 (THU0482), 389 (THU0483), 665 (FRI0472), 1296 (AB0694)
Rouxel, L., 710 (FRI0584)
Rouzaire, P., 1059 (AB0035)
Rovati, L., 410 (THU0538), 1399 (AB0985)
Rovati, L.C., 1064 (AB0050)
Rovere Querini, P., 621 (FRI0357), 1214 (AB0467)
Rovere-Querini, P., 15 (SP0063), 328 (THU0331), 725 (FRI0624), 1055 (AB0025)
Rovina, M., 1318 (AB0753)
Rowczenio, D., 1427 (AB1064)
Roy, A.N., 1295 (AB0690)
Roy, M., 152 (OP0237)
Roy Ariño, G., 1396 (AB0977)
Royo, A., 520 (FRI0106)
Royuela, A., 645 (FRI0420)
Rozenbaum, M., 926 (SAT0407)
Rozendaal, R., 973 (SAT0523)
Rozin, A., 333 (THU0343), 910 (SAT0368)
Rozwadowski, G., 1470 (AB1184)
Ru, J., 1524 (SAT0757-HPR)
Rua, C., 308 (THU0275)
Rúa-Figueroa, I., 300 (THU0256)
Rua-Figueroa, I., 68 (OP0042), 587 (FRI0267), 873 (SAT0263), 1107 (AB0173)
Ruacho, G., 885 (SAT0297)
Ruaro, B., 66 (OP0037), 641 (FRI0407), 695 (FRI0540), 704 (FRI0569), 897 (SAT0331), 915 (SAT0381), 1110 (AB0182, AB0183)
Rubbert-Roth, A., 565 (FRI0217), 794 (SAT0070)
Rubin de Celis, T., 262 (THU0162)
Rubini, M., 207 (THU0022)
Rubio, A., 406 (THU0527)

Rubio, C., 1338 (AB0801)
Rubio, E., 946 (SAT0458), 1422 (AB1050)
Rubio Rivas, M., 639 (FRI0402), 1047 (AB0003)
Rubio Romero, E., 574 (FRI0237)
Rubio-Muñoz, P., 251 (THU0134), 569 (FRI0226)
Rubio-Romero, E., 326 (THU0326), 1166 (AB0337)
Rubtsov, N., 206 (THU0019)
Rubtsov, Y.P., 266 (THU0171)
Ruddock, S.P., 1205 (AB0444)
Ruderman, E., 1521 (SAT0750-HPR)
Ruderman, E.M., 1125 (AB0220)
Rudnik, M., 86 (OP0084), 88 (OP0088), 890 (SAT0312)
Rudolph, J., 826 (SAT0151)
Rudolph, S., 461 (THU0674)
Rudwaleit, M., 101 (OP0118)
Rudys, R., 622 (FRI0359)
Rueda, J.C., 201 (THU0005), 218 (THU0052), 752 (FRI0694), 993 (SAT0573, SAT0574, SAT0575), 994 (SAT0576), 1375 (AB0913)
Rueda, J.M., 1375 (AB0913)
Rueda-Gotor, J., 742 (FRI0666), 1116 (AB0197)
Rueda-Sanchez, J.C., 1132 (AB0239)
Rueffer, J.U., 244 (THU0115)
Ruffa, A., 667 (FRI0477)
Ruffatti, A., 70 (OP0046), 437 (THU0611), 1214 (AB0467), 1439 (AB1099)
Rufibach, K., 101 (OP0117)
Rufini, S., 204 (THU0013), 1007 (SAT0615)
Rugiene, R., 622 (FRI0359)
Rühle, F., 89 (OP0091)
Ruibal, A., 826 (SAT0150), 843 (SAT0191)
Ruiz, D., 926 (SAT0410), 1184 (AB0388)
Ruíz, E., 837 (SAT0178)
Ruiz, E., 555 (FRI0195)
Ruiz, L., 633 (FRI0385), 908 (SAT0363), 1270 (AB0625)
Ruiz del Agua, A., 826 (SAT0150)
Ruiz García, V., 557 (FRI0199)
Ruiz Giraldo, S., 308 (THU0275)
Ruiz Jimeno, T., 1374 (AB0910)
Ruiz Moreno, O., 75 (OP0059)
Ruiz Román, A., 713 (FRI0592)
Ruiz Sara, J., 1041 (SAT0704)
Ruiz-Arruza, I., 593 (FRI0284)
Ruiz-Cantero, M., 657 (FRI0451), 1307 (AB0724)
Ruíz-Esquide, V., 128 (OP0185)
Ruiz-Esquide, V., 840 (SAT0184), 1133 (AB0243)
Ruiz-Gaspà, S., 706 (FRI0573)
Ruiz-Irastorza, G., 50 (OP0002), 593 (FRI0284)
Ruiz-Limón, P., 1091 (AB0128)
Ruiz-Limon, P., 194 (OP0336), 287 (THU0218), 492 (FRI0035), 497 (FRI0048), 504 (FRI0069), 622 (FRI0360), 648 (FRI0429), 649 (FRI0431), 1078 (AB0092), 1082 (AB0104), 1091 (AB0127)
Ruíz-Lucea, E., 1001 (SAT0600)
Ruiz-Romero, C., 980 (SAT0539), 1135 (AB0249), 1466 (AB1174)
Rukavina, D., 771 (SAT0009)
Rumi, F., 316 (THU0297)
Rumiantceva, D., 660 (FRI0458), 920 (SAT0394), 1294 (AB0688), 1411 (AB1017)
Rumiantceva, O., 1411 (AB1017)
Rumyantseva, O., 660 (FRI0458), 920 (SAT0394), 1294 (AB0688)
Runhaar, J., 973 (SAT0522, SAT0523)
Ruoff, P., 184 (OP0312)
Ruperto, N., 75 (OP0058), 396 (THU0503), 405 (THU0525)
Rusanova, O.A., 536 (FRI0146)
Rusch, E., 1448 (AB1123)
Ruscitti, P., 263 (THU0164), 291 (THU0231), 721 (FRI0613), 777 (SAT0025), 880 (SAT0284), 891 (SAT0313)
Rush, J.S., 1101 (AB0155)
Rushton, S., 1103 (AB0162)
Rusman, T., 354 (THU0391)
Russ, F., 162 (OP0256-HPR)
Russ, I., 388 (THU0480)
Russell, M., 976 (SAT0530)
Russi, S., 1101 (AB0156)
Russi, V., 702 (FRI0563)
Russo, M.G., 630 (FRI0378)
Russo, R., 403 (THU0521)
Russo-Marie, F., 461 (THU0675)
Russu, E., 1199 (AB0426)
Rusu, L., 1532 (AB1200-HPR)
Ruta, D., 635 (FRI0389)
Ruta, S., 716 (FRI0601)
Rutherford, A., 806 (SAT0099), 1030 (SAT0676)
Rutherford, A.I., 115 (OP0153), 753 (FRI0695)
Rutigliano, I.M., 329 (THU0334), 864 (SAT0241), 1009 (SAT0621)
Rutka, K., 1277 (AB0642)
Rutkowski, R., 1119 (AB0206)
Ruwaard, J., 61 (OP0025), 758 (FRI0707), 935 (SAT0433)
Ruyssen-Witrand, A., 155 (OP0242), 258 (THU0152), 343 (THU0364), 458 (THU0666), 573 (FRI0234), 811 (SAT0112), 1299 (AB0703)
Ruzek, M., 492 (FRI0034)
Ruzickova, O., 73 (OP0053), 638 (FRI0399), 906 (SAT0358), 979 (SAT0538), 1280 (AB0653), 1287 (AB0671)
Ryan, D., 1036 (SAT0689)
Ryan, S., 1174 (AB0359)
Rybar, I., 829 (SAT0157), 1350 (AB0838)
Rybnikov, A., 269 (THU0179)
Rydholm, U., 437 (THU0612)
Rygg, M., 55 (OP0013)
Ryter, N., 465 (THU0683)
Ryu, H.J., 369 (THU0427)
Rzepka, R., 1100 (AB0153)

S-Andrade, A., 718 (FRI0607)
S-Bursón, J., 326 (THU0326), 718 (FRI0607)
Saad, C.G.S., 614 (FRI0335), 1292 (AB0684)
Saad, H., 962 (SAT0495)
Saad, Y., 1384 (AB0940)
Saadoun, C., 78 (OP0064)
Saadoun, D., 108 (OP0134), 776 (SAT0023), 1247 (AB0563)
Saag, K., 54 (OP0010), 72 (OP0051), 166 (OP0265), 379 (THU0455)
Saag, K.G., 363 (THU0413), 1359 (AB0865)
Saaibi, D.L., 1375 (AB0913)
Saarakkala, S., 498 (FRI0051), 1080 (AB0098)
Saavedra, M.Á., 1091 (AB0126)
Saavedra, M.A., 591 (FRI0279), 860 (SAT0229), 1098 (AB0149)
Saavedra, S., 1108 (AB0176)
Saba, P.S., 535 (FRI0143)
Sabaliauskiene, J., 1306 (AB0719)
Sabbadini, M.G., 437 (THU0611), 621 (FRI0357)
Sabbah, F., 910 (SAT0368)
Sabokbar, A., 1420 (AB1045)
Sabugo, M.F., 1108 (AB0176)
Sacchetti, S.B., 76 (OP0061)
Saccomani, C., 118 (OP0161), 648 (FRI0428)
Sachchithanantham, S., 227 (THU0076)
Sachdev, S., 1074 (AB0079)
Sacks, S., 419 (THU0562)
Sackstein, R., 487 (FRI0021)
Sacré, K., 1256 (AB0588)
Sacre, K., 78 (OP0065), 187 (OP0319), 883 (SAT0293)
Sacre, S., 289 (THU0224)
Sada, K.-E., 1242 (AB0547)
Sadanaga, Y., 895 (SAT0326)
Sadarani, B., 1074 (AB0079)
Saddekni, M.B., 363 (THU0413), 1359 (AB0865)
Sadik, C., 893 (SAT0320)
Sadoine, J., 85 (OP0081)
Sadovici, V., 309 (THU0279)
Sadovici-Bobeica, V., 884 (SAT0296)
Sadri, S., 716 (FRI0600)
Saegusa, J., 115 (OP0152), 422 (THU0571), 459 (THU0668), 487 (FRI0022), 507 (FRI0080), 699 (FRI0553)
Saeidi, A., 1284 (AB0663)
Saeki, Y., 1058 (AB0032)
Sáenz, C., 748 (FRI0683)
Saenz, C., 1297 (AB0695)
Sáenz Tenorio, C., 386 (THU0474), 1276 (AB0640)
Sáenz-Tenorio, C.N., 462 (THU0676)
Saevarsdottir, S., 158 (OP0247), 228 (THU0077), 234 (THU0091), 517 (FRI0100), 537 (FRI0149)
Saez, L., 317 (THU0300)
Sáez Comet, L., 1270 (AB0624)
Saez-Comet, L., 1208 (AB0451)
Safaa, B., 926 (SAT0409)
Safer, P., 1407 (AB1007), 1462 (AB1163)
Saferding, V., 488 (FRI0024), 492 (FRI0033), 499 (FRI0055)
Safonova, T., 424 (THU0578), 723 (FRI0621), 1237 (AB0531)
Safonova, Y., 1507 (FRI0765-HPR)
Safy, M., 781 (SAT0037), 1199 (AB0428)
Sağ, M.S., 241 (THU0108), 1182 (AB0383), 1532 (AB1202-HPR)
Sağ, S., 241 (THU0108), 1182 (AB0383), 1532 (AB1202-HPR)
Sag, S., 1317 (AB0751), 1320 (AB0757)
Sagawa, A., 1471 (AB1187)
Sagliani, J., 1139 (AB0261)
Saha, A., 378 (THU0450)
Sahakian, L., 1238 (AB0535)
Şahin, A., 327 (THU0329), 1400 (AB0987)
Sahin, G., 977 (SAT0532), 1340 (AB0808)
Sahin, K., 455 (THU0658)
Şahin, M., 1400 (AB0987)
Sahin, S., 394 (THU0498), 1402 (AB0994)
Sahin, T., 1420 (AB1046)
Sahingoz, E., 1137 (AB0255)
Sahli, H., 1073 (AB0077), 1346 (AB0826), 1373 (AB0906, AB0907, AB0908, AB0909), 1397 (AB0980)
Sahli, M., 1297 (AB0697), 1373 (AB0906, AB0908)
Sahlmann, C.O., 1402 (AB0992)
Sahuguet, J., 73 (OP0054)
Said, M.S., 446 (THU0638)
Saidane, O., 1073 (AB0077), 1297 (AB0697), 1306 (AB0720), 1373 (AB0906, AB0907, AB0908), 1377 (AB0919)
Saidenberg, N., 1049 (AB0007)
Saidi, S., 1371 (AB0902)
SAieva, L., 777 (SAT0025)
Saieva, L., 291 (THU0231)
Saifan, C.G., 512 (FRI0090)
Saigusa, R., 88 (OP0087)
Saiki, O., 849 (SAT0203)
Säilä, H., 401 (THU0515)
Sailler, L., 188 (OP0321), 1248 (AB0565)
Saillot, C., 1191 (AB0406)
Sainsbury, I., 242 (THU0110), 785 (SAT0047)
Sainz, F., 1275 (AB0637)
Sainz de la Maza, M., 350 (THU0381)
Saip, S., 603 (FRI0307)
Saito, K., 137 (OP0205), 257 (THU0149), 1248 (AB0566)
Saito, M., 1242 (AB0547)
Saito, R., 422 (THU0571), 1398 (AB0981)
Saito, S., 544 (FRI0168), 1097 (AB0146), 1234 (AB0525)
Saito, T., 1165 (AB0334), 1166 (AB0335)
Saitta, A., 1312 (AB0738)
Sakai, M., 895 (SAT0326)
Sakai, R., 264 (THU0166), 265 (THU0170)
Sakai, Y., 499 (FRI0054)
Sakamoto, A.P., 76 (OP0061)
Sakamoto, Y., 1345 (AB0822)
Sakata, K., 491 (FRI0031), 501 (FRI0060), 620 (FRI0354), 747 (FRI0680)
Sakellariou, G., 236 (THU0095), 237 (THU0099), 763 (FRI0722), 787 (SAT0053), 790 (SAT0060), 1123 (AB0214)
Sakharov, V., 1082 (AB0105)
Sakınç Toprak, G., 1381 (AB0931)
Sakkas, L., 1271 (AB0626), 1279 (AB0648)
Sakkas, L.I., 680 (FRI0504), 836 (SAT0176), 903 (SAT0348)
Sakkou, M., 500 (FRI0059)
Sakr, B.R., 1259 (AB0594)
Sakr, H.M., 1145 (AB0276)
Sakuma, Y., 799 (SAT0082), 1063 (AB0047)
Sakuraba, K., 1383 (AB0939)
Sala Gomez, M., 1418 (AB1039)
Salaffi, F., 245 (THU0116), 259 (THU0155),

343 (THU0366), 521 (FRI0109), 829 (SAT0158), 1281 (AB0655)
Salah, N., 1350 (AB0839)
Salama, M.H., 1526 (SAT0764-HPR)
Salaru, V., 309 (THU0279), 884 (SAT0296), 1284 (AB0664)
Salas, A., 670 (FRI0483), 1196 (AB0419), 1263 (AB0606)
Salas, A.P., 1202 (AB0434)
Salas, E., 1296 (AB0693), 1351 (AB0840)
Salas, J., 1339 (AB0805)
Salas Magaña, M., 1132 (AB0240, AB0241)
Salas-Cuesta, F., 1117 (AB0201)
Salas-Heredia, E., 1016 (SAT0638)
Salavert Lleti, M., 1374 (AB0912)
Salazar, F., 520 (FRI0107)
Salazar, G., 87 (OP0086), 624 (FRI0363)
Salazar-Paramo, M., 262 (THU0161), 1155 (AB0304)
Salazar-Uribe, J.C., 594 (FRI0287), 658 (FRI0453), 927 (SAT0413), 928 (SAT0414), 1286 (AB0667)
Salberg, A., 1029 (SAT0673)
Salcion, A., 831 (SAT0163)
Saldaña-Cruz, A., 1155 (AB0304)
Saldaña-Millan, A., 806 (SAT0100), 1075 (AB0083), 1164 (AB0330)
Saldarriaga, E.-L., 201 (THU0005), 218 (THU0052), 752 (FRI0694), 993 (SAT0573, SAT0574, SAT0575), 994 (SAT0576), 1375 (AB0913)
Saldarriaga, E.L., 1132 (AB0239)
Saldarriaga, M., 1190 (AB0404)
Saleem, A., 1420 (AB1045)
Saleh, S., 740 (FRI0663), 1420 (AB1044)
Salford, L., 770 (SAT0005)
Salgado, A., 740 (FRI0661)
Salgado, M., 186 (OP0315)
Salim, B., 1196 (AB0417)
Salliot, C., 989 (SAT0561)
Salman-Monte, T., 307 (THU0273), 550 (FRI0184), 1181 (AB0381)
Salmon, J.-H., 436 (THU0609)
Salmon, J.E., 152 (OP0236)
Salmon, V., 1528 (SAT0769-HPR)
Salmoral Chamizo, A., 258 (THU0151), 700 (FRI0555)
Salokhiddinov, M., 1526 (SAT0763-HPR), 1533 (AB1204-HPR), 1535 (AB1212-HPR)
Salom, D., 326 (THU0326)
Salomon-Escoto, K., 528 (FRI0126), 1510 (SAT0718-HPR)
Salomone, O., 995 (SAT0582)
Salsabil, S., 1512 (SAT0722-HPR)
Saluja, M., 1541 (AB1228-HPR)
Salvador, G., 550 (FRI0184), 556 (FRI0197), 946 (SAT0458)
Salvador, M.J., 894 (SAT0324)
Salvador-Cervelló, G., 415 (THU0550)
Salvarani, C., 107 (OP0131), 131 (OP0193), 212 (THU0035), 323 (THU0316), 411 (THU0540), 437 (THU0611), 609 (FRI0323), 867 (SAT0248), 1054 (AB0022), 1209 (AB0456), 1247 (AB0563), 1248 (AB0564), 1439 (AB1099)
Salvatierra, J., 685 (FRI0515)
Salvesen, K.Å., 1031 (SAT0677), 1032 (SAT0680)
Salvucci, S., 64 (OP0031)
Salzer, U., 332 (THU0341), 615 (FRI0339)
Samaha, D., 1332 (AB0787)
Samanci, N., 1002 (SAT0601)
Samarkina, E., 1283 (AB0659)
Samarkina, E.Y., 1128 (AB0230)
Sambalino, C., 1269 (AB0622), 1270 (AB0623)
Samborski, W., 1119 (AB0206)
Sammaritano, L., 467 (THU0687)
Sammaritano, L.R., 152 (OP0236)
Sampaio-barros, P.D., 1292 (AB0684)
Sampalis, J., 194 (OP0337-HPR), 531 (FRI0132)
Sampalis, J.S., 58 (OP0019), 523 (FRI0115)
Sampath, S., 177 (OP0291)
Samreen, S., 1196 (AB0417)
Samson, M., 1256 (AB0588)
Samuelli, G., 1064 (AB0050)
Sanada, K., 800 (SAT0085)
Sanal Top, C., 469 (THU0692)
Sánchez, A., 591 (FRI0279), 860 (SAT0229), 925 (SAT0405), 1091 (AB0126)
Sanchez, A., 995 (SAT0582), 1098 (AB0149)
Sanchez, K., 170 (LB0001)
Sánchez, L., 761 (FRI0715), 1456 (AB1146, AB1147)
Sánchez, M.A., 645 (FRI0420)
Sánchez, P., 1536 (AB1213-HPR)
Sánchez Alonso, F., 1037 (SAT0691), 1115 (AB0195)
Sanchez Andia, C., 440 (THU0619)
Sanchez Cano, D., 1270 (AB0624)
Sanchez Chapul, L., 1357 (AB0861)
Sánchez González, M.D., 1439 (AB1098)
Sánchez Huerta, J.M., 974 (SAT0524)
Sanchez Manubens, J., 407 (THU0530)
Sánchez Pérez, H., 1424 (AB1057)
Sanchez Ramón, S., 990 (SAT0564)
Sanchez Serrano, J.P., 713 (FRI0592)
Sanchez-Alonso, F., 139 (OP0209-HPR)
Sánchez-Andrade, A., 614 (FRI0336)
Sánchez-Berná, I., 597 (FRI0293)
Sanchez-Blanco, C., 178 (OP0296)
Sanchez-Bringas, G., 1408 (AB1010)
Sanchez-Dopico, M.J., 203 (THU0009)
Sánchez-Fernández, P., 1225 (AB0499)
Sánchez-Fernández, S., 946 (SAT0458)
Sanchez-Gonzalez, M.D., 139 (OP0209-HPR)
Sánchez-Herrero, Á., 1415 (AB1032)
Sánchez-Mateos, P., 501 (FRI0062)
Sánchez-Pérez, H., 592 (FRI0280), 882 (SAT0289)
Sánchez-Piedra, C., 452 (THU0651)
Sanchez-Piedra, C., 885 (SAT0299), 1232 (AB0519)
Sanchez-Riera, L., 760 (FRI0713), 1440 (AB1102)
Sánchez-Rodríguez, A., 1401 (AB0991)
Sanchís-Selfa, M., 1296 (AB0693), 1351 (AB0840)
Sand, J., 1109 (AB0179, AB0180)
Sand, O., 1049 (AB0007)
Sand-Svartrud, A.-L., 161 (OP0255-HPR)
Sanders, C., 547 (FRI0175), 1438 (AB1097), 1453 (AB1138)
Sandıkci, S.C., 748 (FRI0682)
Sandoo, A., 546 (FRI0173), 1044 (SAT0712)
Sandoval, D., 932 (SAT0425)
Sandoval-Cruz, H., 1221 (AB0486)
Sandoval-García, F., 1169 (AB0345)
Sandqvist, G., 1286 (AB0669)
Sandri, G., 248 (THU0123), 474 (THU0705), 954 (SAT0473)
Sands, E., 367 (THU0422)
Sandström, T.Z., 364 (THU0414)
Sanduzzi, A., 630 (FRI0378)
Sangiovanni, L., 540 (FRI0155)
Sanguinetti, M., 197 (OP0343)
Sanjuan, M.A., 856 (SAT0220)
Sanmartí, R., 128 (OP0185), 177 (OP0292), 350 (THU0381), 452 (THU0651), 840 (SAT0184), 1133 (AB0243)
Sanmarti, R., 840 (SAT0183), 847 (SAT0199)
Sanmarti-Sala, R., 817 (SAT0128)
Sanna, C., 975 (SAT0528)
Sanner, H., 164 (OP0261-HPR), 1517 (SAT0737-HPR)
Sano, H., 210 (THU0030), 641 (FRI0408), 1288 (AB0674)
Sanpaolo, E., 629 (FRI0373)
Sansinanea, P., 1202 (AB0434), 1263 (AB0606)
Santana, F.M., 1448 (AB1124)
Santaniello, A., 1047 (AB0003)
Santarelli, F., 1012 (SAT0630)
Santarelli, M., 167 (OP0268)
Santiago, L., 870 (SAT0254)
Santiago, L.C., 865 (SAT0243)
Santiago, M., 176 (OP0290), 700 (FRI0558), 894 (SAT0324)
Santiago, M.B., 1412 (AB1021)
Santiago, T.L., 1381 (AB0930)
Santillán-Guerrero, E., 1397 (AB0978)
Santilli, D., 1022 (SAT0653)
Santo, L., 808 (SAT0105), 1327 (AB0773)
Santo, P., 1014 (SAT0635)
Santo, R.C.E., 246 (THU0119)
Santos, A.M., 201 (THU0005), 218 (THU0052), 752 (FRI0694), 993 (SAT0573, SAT0574, SAT0575), 994 (SAT0576), 1132 (AB0239), 1375 (AB0913)
Santos, H., 464 (THU0679), 929 (SAT0418), 1163 (AB0329), 1464 (AB1168)
Santos, J., 1264 (AB0607)
Santos, M., 171 (OP0276-PARE), 656 (FRI0450)
Santos, M.A., 1456 (AB1145)
Santos, M.J., 186 (OP0315), 533 (FRI0138), 567 (FRI0221), 850 (SAT0206), 1254 (AB0581), 1264 (AB0607), 1389 (AB0957)
Santos, P.R., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Santos, S., 1534 (AB1208-HPR)
Santos, W., 176 (OP0290)
Santos, W.G.D., 1412 (AB1021)
Santos Gómez, M., 1244 (AB0553)
Santos-Faria, D., 607 (FRI0318), 612 (FRI0330), 637 (FRI0394), 736 (FRI0652), 1011 (SAT0627), 1015 (SAT0637), 1275 (AB0636)
Santos-Gómez, M., 405 (THU0526), 1374 (AB0910)
Santos-Granados, A.M., 1453 (AB1137)
Santos-Moreno, P., 162 (OP0257-HPR), 266 (THU0172), 427 (THU0585), 529 (FRI0127), 538 (FRI0150), 852 (SAT0210), 963 (SAT0496), 1208 (AB0453), 1342 (AB0813), 1441 (AB1103), 1479 (THU0729-HPR), 1502 (FRI0751-HPR), 1534 (AB1207-HPR), 1540 (AB1225-HPR), 1543 (AB1235-HPR)
Santos-Rey, J., 139 (OP0209-HPR)
Santos-Soler, G., 1016 (SAT0638), 1296 (AB0693), 1351 (AB0840)
Santosa, A., 1447 (AB1119)
Santucci, A., 1010 (SAT0625)
Santus, P., 52 (OP0006)
Sanz, J., 452 (THU0651), 645 (FRI0420), 685 (FRI0515), 925 (SAT0405)
Sanz Alonso, M., 1037 (SAT0691), 1115 (AB0195)
Sanz Pérez, I., 900 (SAT0340), 1262 (AB0602)
Sanz Rodrigo, C., 1362 (AB0875)
Sanz Sanz, J., 1399 (AB0986)
Saoussen, Z., 1348 (AB0830), 1362 (AB0876), 1383 (AB0937)
Sapag Duran, A.M., 991 (SAT0568), 1217 (AB0478)
Sapag Duran, S., 991 (SAT0568), 1217 (AB0478)
Sapag duran, S., 729 (FRI0635)
Sapena-Fortea, N., 1542 (AB1231-HPR)
Sarac, D.C., 1496 (FRI0736-HPR), 1531 (AB1197-HPR), 1538 (AB1218-HPR)
Saraiva, F., 746 (FRI0678)
Sarano, J., 906 (SAT0357)
Sarantopoulos, A., 569 (FRI0224), 1047 (AB0001), 1261 (AB0601)
Sarapulova, A., 1421 (AB1048)
Saraux, A., 67 (OP0040), 102 (OP0119), 131 (OP0192), 309 (THU0278), 436 (THU0609), 461 (THU0675), 662 (FRI0465), 665 (FRI0473), 786 (SAT0050), 843 (SAT0189), 989 (SAT0561), 1013 (SAT0632), 1191 (AB0406), 1215 (AB0469)
Sarbagil-Maman, H., 747 (FRI0679)
Sardemberg, W.M., 1102 (AB0160)
Sárdy, M., 1106 (AB0169), 1110 (AB0181)
Sareila, O., 779 (SAT0031)
Sargin, G., 354 (THU0389)
Sari, A., 250 (THU0131), 256 (THU0147), 329 (THU0333), 402 (THU0518), 414 (THU0548), 534 (FRI0140), 637 (FRI0397), 720 (FRI0612), 854 (SAT0216), 1113 (AB0189), 1127 (AB0226), 1175 (AB0363), 1194 (AB0414), 1215 (AB0471), 1256 (AB0586), 1262 (AB0604), 1300 (AB0706)
Sarı, A., 448 (THU0642), 609 (FRI0322), 1035 (SAT0687), 1412 (AB1023)
Sarı, H., 353 (THU0387)
Sarı, Y.E., 387 (THU0478)
Sari, Z., 1496 (FRI0734-HPR)
Sarı, Z., 1431 (AB1076), 1509 (FRI0770-HPR, FRI0771-HPR), 1519 (SAT0743-HPR), 1533 (AB1205-HPR), 1537 (AB1217-HPR), 1544 (AB1237-HPR)
Saridogan, M., 1156 (AB0308)
Sarıkaya, S., 1380 (AB0927)

Sarioglu, S., 1105 (AB0168)
Sarkar, R.N., 1295 (AB0690), 1300 (AB0705)
Sarmanova, A., 167 (OP0268), 752 (FRI0693), 1028 (SAT0670)
Sarmiento, E., 593 (FRI0283)
Sarmiento Monroy, J.C., 1250 (AB0570)
Sarmiento-Monroy, J.C., 575 (FRI0238), 850 (SAT0205), 1196 (AB0419)
Sarmiento-Velasquez, O., 1142 (AB0269)
Sarpel, T., 905 (SAT0355)
Sarsour, K., 264 (THU0167), 850 (SAT0206)
Sarti, M., 477 (THU0713)
Sartori, M., 940 (SAT0443)
Sarzi Puttini, P., 92 (OP0099), 564 (FRI0215), 1184 (AB0389), 1194 (AB0413), 1376 (AB0917)
Sarzi-Puttini, P., 52 (OP0006), 263 (THU0164), 343 (THU0366), 445 (THU0634), 510 (FRI0086), 1008 (SAT0620), 1294 (AB0689), 1380 (AB0928), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Sas, A., 1027 (SAT0668)
Sasaki, E., 507 (FRI0079)
Sasaki, K., 1344 (AB0819)
Sasaki, T., 712 (FRI0590, FRI0591)
Sassi, N., 1176 (AB0365)
Sasso, E., 1140 (AB0263)
Sasso, E.H., 234 (THU0091), 1121 (AB0210)
Sastre, S., 1041 (SAT0703), 1458 (AB1150)
Sasu, M., 435 (THU0607), 1032 (SAT0681)
Satake, A., 210 (THU0030)
Satamaria-Olmedo, M., 1067 (AB0059)
Sato, H., 313 (THU0290)
Sato, K., 188 (OP0322)
Sato, M., 833 (SAT0167), 1183 (AB0386)
Sato, S., 88 (OP0087), 138 (OP0207), 202 (THU0006), 392 (THU0492), 1274 (AB0635)
Sato, T., 409 (THU0535)
Sato, Y., 644 (FRI0417), 645 (FRI0418), 1109 (AB0180)
Sattin, M., 71 (OP0049)
Sattler, H., 597 (FRI0294)
Satulu, I., 745 (FRI0676), 983 (SAT0547), 1013 (SAT0631)
Satybaldyev, A., 1157 (AB0311)
Satybaldyeva, M.A., 860 (SAT0230)
Sauer, B.C., 239 (THU0102), 1435 (AB1089)
Sauleau, E., 611 (FRI0329)
Saulescu, I., 304 (THU0266), 416 (THU0555), 423 (THU0574), 876 (SAT0271), 881 (SAT0288), 1025 (SAT0664), 1208 (AB0450), 1221 (AB0487), 1278 (AB0646, AB0647), 1428 (AB1068), 1460 (AB1158)
Saulot, V., 461 (THU0675)
Saunders, D., 1556 (PARE0013)
Saurit, V., 205 (THU0017), 206 (THU0018), 313 (THU0289), 995 (SAT0582)
Sautner, J., 1173 (AB0357)
Sauvageau, D., 571 (FRI0230), 845 (SAT0195), 1188 (AB0397)
Savage, E., 729 (FRI0634)
Savage, L., 771 (SAT0007)
Savchenko, O., 820 (SAT0136)
Savci, S., 53 (OP0009-HPR), 1522 (SAT0751-HPR)
Savel, C., 1515 (SAT0733-HPR)
Savic, S., 987 (SAT0556)
Savill, J., 481 (FRI0004), 496 (FRI0047)
Savina, N.V., 389 (THU0485)
Saviola, G., 1200 (AB0429)
Savu, A., 766 (FRI0727)
Savushkina, N., 464 (THU0680), 720 (FRI0611)
Sawabe, T., 1254 (AB0582)
Sawada, H., 574 (FRI0235)
Sawada, T., 610 (FRI0326)
Sawhney, S., 1385 (AB0944)
Saxne, T., 376 (THU0446), 542 (FRI0162)
Sayarlıoğlu, M., 327 (THU0329)
Sayed, N., 1355 (AB0853)
Sayed, S., 1235 (AB0527)
Sayer, J., 1415 (AB1030)
Saylisoy, S., 748 (FRI0682)
Sayre, E.C., 68 (OP0041), 373 (THU0440), 916 (SAT0384)
Sazonova, O., 1336 (AB0795, AB0796)
Sbai, M.A., 1373 (AB0909)
Scabini, S., 1110 (AB0182)
Scalbert, C., 823 (SAT0144)
Scalone, L., 445 (THU0634), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Scanu, A., 210 (THU0029), 216 (THU0047), 383 (THU0465), 730 (FRI0637), 1111 (AB0184)
Scarafia, S., 387 (THU0479), 906 (SAT0357)
Scarano, M., 875 (SAT0268)
Scarpato, S., 1272 (AB0630)
Scarsi, M., 579 (FRI0249), 1214 (AB0468)
Scendoni, P., 690 (FRI0527)
Schaardenburg, D.V., 523 (FRI0113)
Schaeffler, A., 39 (SP0160)
Schaeverbeke, T., 258 (THU0152), 709 (FRI0582), 710 (FRI0584), 811 (SAT0112), 1049 (AB0007), 1186 (AB0395)
Schafer, P., 858 (SAT0225)
Schafer, P.H., 778 (SAT0028), 780 (SAT0035), 870 (SAT0255)
Schäfer, V.S., 1239 (AB0539)
Schäfers, M., 1023 (SAT0656)
Schäffler, A., 220 (THU0056)
Schagat, T., 555 (FRI0194)
Schaible, A.M., 115 (OP0151)
Schanberg, L., 391 (THU0490)
Scharmga, A., 740 (FRI0662)
Scheel-Toellner, D., 1051 (AB0015)
Scheinberg, M., 861 (SAT0231), 864 (SAT0240)
Scheinecker, C., 499 (FRI0055), 502 (FRI0064)
Schelin, M.E., 1037 (SAT0692)
Schenker, H., 240 (THU0105)
Scheper, T., 1271 (AB0626), 1279 (AB0648)
Scher, J., 191 (OP0329), 504 (FRI0072)
Scherer, A., 130 (OP0189), 267 (THU0174)
Scherer, H.U., 44 (SP0182), 125 (OP0177), 774 (SAT0015), 775 (SAT0019), 1279 (AB0650)
Scherlinger, M., 866 (SAT0246)
Scherrer, A., 335 (THU0347), 816 (SAT0125)
Schers, H., 1476 (THU0721-HPR)
Schers, H.J., 110 (OP0138-HPR), 1487 (THU0752-HPR)
Schett, G., 73 (OP0052), 107 (OP0131), 142 (OP0217), 159 (OP0249), 233 (THU0088), 236 (THU0096), 240 (THU0105), 247 (THU0122), 516 (FRI0098), 560 (FRI0207), 655 (FRI0446), 675 (FRI0494), 725 (FRI0625), 775 (SAT0019), 848 (SAT0201), 892 (SAT0318), 936 (SAT0436), 942 (SAT0448), 1011 (SAT0628), 1063 (AB0046), 1324 (AB0767), 1331 (AB0785), 1425 (AB1058), 1511 (SAT0719-HPR)
Schiavon, F., 327 (THU0328), 603 (FRI0308), 604 (FRI0310), 614 (FRI0337), 1257 (AB0589)
Schibli, R., 86 (OP0083), 621 (FRI0358)
Schieir, O., 231 (THU0085), 781 (SAT0039), 815 (SAT0122)
Schiff, M., 283 (THU0210), 358 (THU0398), 510 (FRI0087), 581 (FRI0252), 782 (SAT0041), 789 (SAT0058), 845 (SAT0194), 1147 (AB0281), 1329 (AB0780)
Schiffer, P., 1445 (AB1114)
Schiffrin, E., 709 (FRI0582)
Schikler, K., 133 (OP0197)
Schindler, T., 857 (SAT0221)
Schioldan, C., 101 (OP0117)
Schioppo, T., 643 (FRI0413), 746 (FRI0677), 908 (SAT0364), 1022 (SAT0655)
Schiphof, D., 1343 (AB0817)
Schirmer, M., 615 (FRI0338)
Schlacher, C.A., 552 (FRI0188), 827 (SAT0153)
Schlattmann, P., 115 (OP0151)
Schleich, C., 789 (SAT0056)
Schlesinger, N., 362 (THU0410), 377 (THU0449)
Schlichting, D., 233 (THU0088), 788 (SAT0055), 789 (SAT0058), 1147 (AB0281)
Schlichting, D.E., 527 (FRI0124)
Schlinker, A., 1303 (AB0713)
Schlitt, T., 1101 (AB0155)
Schmajuk, G., 759 (FRI0711)
Schmalzing, M., 1106 (AB0169), 1110 (AB0181)
Schmeiser, T., 1106 (AB0169), 1110 (AB0181)
Schmeling, H., 396 (THU0503)
Schmid, C., 384 (THU0469)
Schmidt, E., 848 (SAT0200)
Schmidt, J., 912 (SAT0374)
Schmidt, R.E., 1050 (AB0010)
Schmidt, W., 583 (FRI0256)
Schmidt, W.A., 175 (OP0288), 315 (THU0296), 318 (THU0302), 1004 (SAT0609), 1013 (SAT0631), 1239 (AB0539), 1413 (AB1024)
Schmidt-Bleek, K., 1067 (AB0060)
Schmidt-Olsen, S., 101 (OP0117)
Schmitt-Haendle, M., 159 (OP0249), 516 (FRI0098)
Schmukler, J., 1466 (AB1173)
Schneeberger, E., 670 (FRI0483)
Schneeberger, E.E., 933 (SAT0427), 1196 (AB0419)
Schneider, L., 1107 (AB0174), 1278 (AB0645)
Schneider, M., 21 (SP0085), 50 (OP0002), 193 (OP0333), 302 (THU0261), 442 (THU0625), 789 (SAT0056), 801 (SAT0087), 893 (SAT0319), 1007 (SAT0616), 1449 (AB1127), 1463 (AB1166)
Schneider, R., 395 (THU0502)
Schniering, J., 86 (OP0083), 621 (FRI0358)
Schnitzer, T.J., 983 (SAT0548)
Schoen, P., 92 (OP0098), 575 (FRI0239)
Schofield, J.P., 609 (FRI0321)
Scholtes, V., 111 (OP0141-HPR)
Scholz, C., 184 (OP0311)
Scholz, G., 569 (FRI0225)
Schönbeck, K., 486 (FRI0019)
Schonenberg-Meinema, D., 1221 (AB0488)
Schonkeren, J., 202 (THU0008)
Schoonmade, L., 473 (THU0703)
Schordan, E., 1463 (AB1164)
Schormann, C., 1060 (AB0039)
Schorpion, A., 896 (SAT0328)
Schougaard, L.M.V., 454 (THU0657)
Schreiber, B., 898 (SAT0334)
Schreiber, B.E., 1266 (AB0613)
Schreiber, K., 437 (THU0612), 761 (FRI0716), 1097 (AB0147), 1450 (AB1130)
Schreiber, S., 465 (THU0682)
Schreiyäck, C., 1063 (AB0046)
Schreurs, K., 1515 (SAT0732-HPR)
Schreurs, M.W., 92 (OP0097)
Schroder, D., 605 (FRI0314)
Schrøder, H.D., 745 (FRI0675), 1024 (SAT0660)
Schröder, J.O., 465 (THU0682)
Schroeder, D., 187 (OP0320)
Schubertova, M., 1051 (AB0014)
Schuch, F., 159 (OP0249), 516 (FRI0098), 1440 (AB1100), 1444 (AB1112)
Schulte-Pelkum, J., 911 (SAT0372), 1007 (SAT0616)
Schultz, C.M.A., 214 (THU0041)
Schultz, D., 1446 (AB1118)
Schultz, D.M., 1453 (AB1138)
Schultze-Koops, H., 709 (FRI0582)
Schulz-Knappe, P., 886 (SAT0301), 893 (SAT0319), 1007 (SAT0616)
Schulz-Knappe, P.K., 193 (OP0333)
Schulze-Koops, H., 107 (OP0131), 560 (FRI0207), 718 (FRI0606), 790 (SAT0059), 1144 (AB0273)
Schumacher, M., 1463 (AB1164)
Schumacher, R., 580 (FRI0250)
Schunemann, H., 418 (THU0561)
Schurder, J., 883 (SAT0293)
Schuster, L., 73 (OP0052)
Schuster, T.B., 1463 (AB1166)
Schutgens, R.E., 1068 (AB0061)
Schwarting, A., 861 (SAT0231), 1272 (AB0630), 1281 (AB0656)
Schwartzman, S., 1202 (AB0436)
Schwarz, H., 730 (FRI0636)
Schwarze, I., 844 (SAT0193), 1187 (AB0396), 1322 (AB0763)
Schwarzwald, C., 500 (FRI0059)
Schwenke, H., 1322 (AB0763)
Sciandrone, M., 1449 (AB1125)
Sciarra, I., 903 (SAT0347)
Sciascia, S., 497 (FRI0048), 761 (FRI0716), 1410 (AB1014), 1443 (AB1110), 1450 (AB1130), 1457 (AB1148)
Scioscia, C., 521 (FRI0110), 1268 (AB0618)

Scirè, C., 562 (FRI0212)
Scirè, C.A., 234 (THU0090), 236 (THU0095), 383 (THU0465), 582 (FRI0255), 730 (FRI0637), 1013 (SAT0631)
Scire, C.A., 1272 (AB0630)
Scire', C.A., 1127 (AB0227)
Scirocco, C., 1009 (SAT0621), 1059 (AB0036)
Scleroderma Group, S., 1047 (AB0003)
Scolnik, M., 716 (FRI0601), 1115 (AB0194), 1231 (AB0516), 1333 (AB0789)
Scotece, M., 893 (SAT0321)
Scouppe, L., 573 (FRI0234)
Scoutellas, V., 1473 (AB1194)
Scoville, C., 230 (THU0083)
Scrivo, R., 329 (THU0334), 489 (FRI0027), 490 (FRI0028), 496 (FRI0045)
Seabra, L., 406 (THU0528)
Seagal, J., 288 (THU0222)
Sebastian, A., 311 (THU0284), 886 (SAT0302)
Sebastiani, G., 92 (OP0099), 437 (THU0611)
Sebastiani, G.D., 1439 (AB1099)
Sebastiani, M., 248 (THU0123), 343 (THU0366), 1267 (AB0616), 1281 (AB0656)
Sebbar, H., 1214 (AB0467)
Sebedio, J.L., 213 (THU0039)
Seccia, V., 875 (SAT0268)
Secco, A., 387 (THU0479), 906 (SAT0357), 1429 (AB1071)
Secher, A.E., 456 (THU0662)
Sechi, L.A., 496 (FRI0046)
Sedighipour, L., 700 (FRI0556, FRI0557), 1003 (SAT0604, SAT0605)
Seewordova, L., 1149 (AB0288)
Sefik-Bukilica, M., 559 (FRI0206), 792 (SAT0064)
Segal, K.R., 566 (FRI0220)
Segaud, N., 413 (THU0546)
Segeda, I., 1228 (AB0507)
Seghieri, C., 589 (FRI0272)
Segui, P., 492 (FRI0035), 1082 (AB0104), 1091 (AB0127, AB0128)
Segur, J.M., 1041 (SAT0703), 1458 (AB1150)
Segura, B., 804 (SAT0095)
Segura, V., 1041 (SAT0703), 1458 (AB1150)
Segura-Jiménez, V., 1499 (FRI0743-HPR)
Segura-Ruiz, R., 441 (THU0624), 1525 (SAT0760-HPR)
Sehgal, M., 70 (OP0047)
Sehimi, A., 1467 (AB1177)
Seibel, M., 129 (OP0187)
Seibert, J., 710 (FRI0585)
Seibold, J.R., 65 (OP0034)
Seidel, M.F., 185 (OP0313), 423 (THU0576)
Seifert, O., 308 (THU0277)
Seilheimer, B., 202 (THU0007)
Seipelt, E., 195 (OP0338)
Seiser, C., 499 (FRI0055)
Sekiguti, M., 1288 (AB0674)
Selby, D.A., 1453 (AB1138)
Sell, A., 1222 (AB0489)
Sellam, J., 425 (THU0580), 427 (THU0586), 638 (FRI0398), 755 (FRI0700), 965 (SAT0501), 1072 (AB0073), 1299 (AB0702)
Sellami, I., 1377 (AB0921)
Sellami, M., 1377 (AB0919)
Sellas, A., 326 (THU0326), 685 (FRI0515), 718 (FRI0607)
Selmani, M., 477 (THU0714)
Selmi, C., 437 (THU0611), 620 (FRI0353), 1439 (AB1099)
Selten, E.M., 110 (OP0138-HPR), 1487 (THU0752-HPR)
Selva O'Callaghan, A., 1272 (AB0630), 1281 (AB0656)
Selva-O'Callaghan, A., 636 (FRI0392), 900 (SAT0339), 1262 (AB0603)
Selvaag, A.M., 164 (OP0261-HPR), 1517 (SAT0737-HPR)
Selvaskandan, H., 1436 (AB1090)
Selvi, E., 92 (OP0099), 1010 (SAT0625)
Semagina, O., 273 (THU0188)
Semb, A.G., 802 (SAT0090), 1029 (SAT0673)
Semenov, S., 693 (FRI0536)
Semenov, S.E., 1346 (AB0823, AB0824)
Semeraro, A., 808 (SAT0105), 829 (SAT0158), 1327 (AB0773)
Semiz, H., 422 (THU0573), 1402 (AB0993)
Semmelink, J.F., 116 (OP0154)
Sempere-Rubio, N., 1380 (AB0929)
Sen, D., 74 (OP0056), 401 (THU0516)
Senabre Gallego, J.M., 1016 (SAT0638)
Senabre-Gallego, J.M., 1296 (AB0693), 1351 (AB0840)
Senbel, E., 1186 (AB0395)
Sendo, S., 115 (OP0152), 282 (THU0208), 487 (FRI0022), 507 (FRI0080), 699 (FRI0553)
Sene, D., 311 (THU0284), 464 (THU0681), 886 (SAT0302)
Sener, Y.Z., 1215 (AB0471)
Seneschal, J., 866 (SAT0246)
Seneviratne, A., 219 (THU0053)
Sengewein, R., 789 (SAT0056)
Sengupta, R., 659 (FRI0456), 1308 (AB0727)
Sennikov, S., 1056 (AB0027)
Šenolt, L., 209 (THU0027), 220 (THU0058), 342 (THU0363)
Senolt, L., 73 (OP0053), 243 (THU0113), 501 (FRI0061), 638 (FRI0399), 906 (SAT0358), 979 (SAT0538), 1280 (AB0653), 1287 (AB0671)
Sensky, T., 529 (FRI0128)
Senturk, T., 354 (THU0389)
Seo, M.R., 369 (THU0427)
Seo, P., 187 (OP0320), 605 (FRI0314)
Seo, T., 984 (SAT0549), 1003 (SAT0607)
Seo, W.-J., 1093 (AB0133)
Seo, W.J., 549 (FRI0181), 606 (FRI0316)
Seo, Y.H., 285 (THU0213), 1130 (AB0234), 1242 (AB0548), 1452 (AB1134)
Seo, Y.I., 518 (FRI0103)
Seoane, I.V., 1128 (AB0229)
Sepici Dincel, A., 1223 (AB0492)
Sepriano, A., 80 (OP0070), 100 (OP0115, OP0116), 131 (OP0192), 466 (THU0685), 560 (FRI0207), 1052 (AB0016)
Sepsi, M., 1027 (SAT0668)
Sepúlveda, C., 715 (FRI0598)
Sepulveda Delgado, J., 421 (THU0568)
Sepulveda-Delgado, J., 1255 (AB0585)
Sequeira, G., 186 (OP0315), 571 (FRI0229), 1254 (AB0581)
Serapioni, M., 171 (OP0276-PARE)
Seravina, O., 249 (THU0127), 616 (FRI0343)
Serban, T., 745 (FRI0676), 983 (SAT0547), 1013 (SAT0631)
Serce, A., 733 (FRI0643)
Seredavkina, N., 860 (SAT0230)
Sergeant, J., 1446 (AB1118)
Sergeant, J.C., 1453 (AB1138)
Sergeeva, M., 240 (THU0105)
Sergeeva, M.S., 251 (THU0132), 1226 (AB0500)
Serguera, C., 508 (FRI0081)
Seric, S., 792 (SAT0064)
Seriolo, C., 695 (FRI0540), 704 (FRI0569)
Seror, R., 67 (OP0040), 160 (OP0253), 182 (OP0307), 289 (THU0225), 311 (THU0284), 464 (THU0681), 549 (FRI0180), 886 (SAT0302), 965 (SAT0501)
Serpen, B., 1387 (AB0949)
Serra, S., 1254 (AB0581)
Serra-Añó, P., 1380 (AB0929)
Serrano, B., 386 (THU0474), 462 (THU0676), 656 (FRI0448), 748 (FRI0683), 1276 (AB0640)
Serrano, É.V., 163 (OP0259-HPR), 1102 (AB0160)
Serrano, P., 930 (SAT0419)
Serrano-Benavente, B., 1386 (AB0947)
Serre, G., 508 (FRI0081), 509 (FRI0085), 792 (SAT0065)
Serre, J., 78 (OP0065)
Sert, Ö., 1392 (AB0965)
Servy, H., 428 (THU0588, THU0589), 755 (FRI0700)
Sessa, P., 329 (THU0334)
Seta, N., 639 (FRI0401)
Seth, R., 933 (SAT0426)
Seto, N.L., 498 (FRI0053)
Setoguchi, K., 810 (SAT0110), 1372 (AB0905)
Settas, L., 558 (FRI0202)
Sève, P., 77 (OP0062)
Sevelda, F., 486 (FRI0018)
Seven, S., 175 (OP0287)
Sever, F., 422 (THU0573), 1402 (AB0993)
Severino, A., 270 (THU0181)
Severinova, M., 1019 (SAT0646)
Sevim, S., 977 (SAT0532)
Sevinc, C., 1468 (AB1179)
Sewerin, P., 789 (SAT0056)
Sexton, J., 522 (FRI0111)
Seyahi, E., 208 (THU0024), 323 (THU0317), 603 (FRI0307), 618 (FRI0348), 719 (FRI0610), 1186 (AB0394), 1246 (AB0558), 1274 (AB0634)
Şeyhoğlu, E., 1035 (SAT0687), 1412 (AB1023)
Seyhoglu, E., 414 (THU0548), 448 (THU0642), 616 (FRI0342)
Sezgin, M., 977 (SAT0532), 1340 (AB0808)
Sfakianaki, M., 1560 (AB1252-PARE)
Sfikakis, P.P., 210 (THU0028), 602 (FRI0306), 642 (FRI0410), 643 (FRI0414), 659 (FRI0455), 836 (SAT0176), 908 (SAT0361), 928 (SAT0415), 1088 (AB0117), 1133 (AB0244)
Sfontouris, C., 1076 (AB0085)
Sfrenţ-Cornăţeanu, R., 1264 (AB0608)
Sfrent-Cornateanu, R., 626 (FRI0368)
Sfriso, P., 77 (OP0062), 395 (THU0502), 411 (THU0541), 1066 (AB0055), 1111 (AB0184)
Sgambato, D., 923 (SAT0401)
Sghir, M., 1383 (AB0936)
Shabaan, M., 874 (SAT0265)
Shabaruddin, F.H., 446 (THU0638)
Shacham, S., 181 (OP0304)
Shadick, N., 846 (SAT0197), 1120 (AB0207)
Shah, M., 221 (THU0060)
Shah, R., 1246 (AB0559)
Shah, S., 821 (SAT0140)
Shahin, A., 1460 (AB1157)
Shahin, D., 1174 (AB0360)
Shahnaz, M., 1512 (SAT0722-HPR)
Shahraeeni, S., 1003 (SAT0605)
Shaikh, M., 1168 (AB0341)
Shajpal, A., 1302 (AB0710)
Shakoor, N., 971 (SAT0516), 1451 (AB1132)
Shaky, A., 1526 (SAT0764-HPR)
Shalev, V., 169 (OP0273), 796 (SAT0074)
Shamil, M., 1295 (AB0690)
Shan, Y., 60 (OP0022), 552 (FRI0188), 827 (SAT0153)
Shanahan, W.R., 864 (SAT0240)
Shang, L.L., 1266 (AB0612)
Shang, Q., 689 (FRI0524), 796 (SAT0073), 956 (SAT0479), 1520 (SAT0747-HPR)
Shankar, S., 777 (SAT0027)
Shapiro, L.S., 1290 (AB0678)
Shapoval, I., 654 (FRI0443), 1038 (SAT0696)
Shapovalenko, A., 1389 (AB0955)
Sharabi, A., 1095 (AB0138)
Sharapova, E.P., 1337 (AB0799)
Sharma, A., 287 (THU0219), 301 (THU0258), 392 (THU0493), 1386 (AB0946)
Sharma, J., 222 (THU0062), 1099 (AB0151)
Sharma, M., 501 (FRI0061), 1309 (AB0728)
Sharma, S.K., 1273 (AB0633)
Sharoyan, S., 787 (SAT0051)
Sharples, L.D., 1205 (AB0444)
Shattles, W., 1246 (AB0559)
Shaughnessy, L., 57 (OP0017), 548 (FRI0179)
Shaw, D., 869 (SAT0251)
Shaw, S., 213 (THU0038), 221 (THU0060)
Shayakhmetova, R.U., 1287 (AB0670)
Shazzad, N., 1460 (AB1157)
Shcherbina, A., 413 (THU0547)
Sheahan, A., 1459 (AB1155)
Shedid, N.H., 1145 (AB0276)
Sheeehy, C., 1509 (FRI0772-HPR)
Sheen, D., 1131 (AB0236)
Sheeran, T., 786 (SAT0049)
Shen, M., 420 (THU0566)
Shen, S., 1329 (AB0780)
Shen, X.-D., 1084 (AB0110)
Shen, Z., 371 (THU0435), 1366 (AB0886)
Sheng-Xiao, Z., 839 (SAT0181)
Shenin, M., 896 (SAT0328)
Shenoi, S., 448 (THU0641)

Shenoy, P., 423 (THU0575)
Sheridan, J., 1099 (AB0151)
Sherif, A.M., 1150 (AB0291)
Sherlock, S.P., 337 (THU0352)
Shesternya, P., 824 (SAT0146)
Shevchenko, N.S., 399 (THU0510), 1392 (AB0963)
Shevchuk, O., 1228 (AB0507)
Shevchuk, S., 1228 (AB0507), 1230 (AB0514)
Sheytanova, T., 50 (OP0001)
Shi, B., 692 (FRI0531)
Shi, G., 351 (THU0384)
Shi, L., 393 (THU0494), 1198 (AB0424), 1352 (AB0845)
Shi, M., 116 (OP0155)
Shi, Q., 221 (THU0061), 1511 (SAT0720-HPR)
Shi, X., 1524 (SAT0757-HPR)
Shi, Y., 223 (THU0066)
Shi Wen, X., 1104 (AB0166)
Shibanuma, N., 499 (FRI0054)
Shibata, A., 424 (THU0577), 1399 (AB0984)
Shiboski, C., 67 (OP0040)
Shibutou, N., 605 (FRI0313), 1251 (AB0572)
Shiels, P., 1047 (AB0003)
Shigematsu, K., 849 (SAT0203)
Shigesaka, M., 1058 (AB0032)
Shih, H.-C., 842 (SAT0188)
Shihkin, V.I., 507 (FRI0078)
Shilova, L.N., 459 (THU0670)
Shim, S.-C., 888 (SAT0307), 1259 (AB0593)
Shim, S.C., 548 (FRI0178), 824 (SAT0146)
Shimabuco, A.Y., 1292 (AB0684)
Shimada, H., 283 (THU0209), 719 (FRI0609), 757 (FRI0704), 907 (SAT0360), 1213 (AB0465)
Shimada, K., 525 (FRI0119), 1176 (AB0367)
Shimada, Y., 707 (FRI0577), 795 (SAT0071), 1178 (AB0372), 1182 (AB0382), 1426 (AB1063)
Shimamura, S., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Shimizu, T., 58 (OP0020), 318 (THU0303), 505 (FRI0075), 1058 (AB0032)
Shimizu, Y., 263 (THU0165), 524 (FRI0117), 798 (SAT0079), 814 (SAT0120)
Shimmyo, N., 282 (THU0207)
Shimotake, M., 284 (THU0212)
Shimoyama, S., 1258 (AB0591)
Shin, S.H., 385 (THU0471)
Shin, S.Y., 1528 (SAT0768-HPR)
Shinohara, M., 282 (THU0208)
Shir, Y., 523 (FRI0115)
Shirai, T., 699 (FRI0553)
Shirai, Y., 901 (SAT0343)
Shiraishi, A., 278 (THU0198)
Shiramoto, M., 371 (THU0435)
Shirinsky, I., 961 (SAT0491)
Shirinsky, V., 961 (SAT0491)
Shishkin, V.I., 1077 (AB0089)
Shishkin, V.V., 507 (FRI0078), 1077 (AB0089)
Shivpuri, A., 1385 (AB0944)
Shkaruba, N., 1056 (AB0027)
Shmagel, A., 958 (SAT0484)
Shoenfeld, Y., 150 (OP0231), 319 (THU0304), 332 (THU0342), 502 (FRI0065), 886 (SAT0300)
Shojaei, A., 152 (OP0237)
Shojania, K., 374 (THU0442)
Shoop-Worrall, S.J.W., 391 (THU0488), 408 (THU0533)
Short, V., 519 (FRI0105)
Shovman, O., 319 (THU0304)
Shpigelman, A., 653 (FRI0441)
Shrivastava, J.K., 1072 (AB0075)
Shtefiuk, O., 1201 (AB0433)
Shtokalo, D., 202 (THU0007)
Shuba, N., 1341 (AB0812)
Shuldiner, A.R., 570 (FRI0228), 838 (SAT0179)
Shuler, C.L., 135 (OP0201), 144 (OP0221)
Shumnalieva, R., 208 (THU0023), 685 (FRI0516)
Shynkaruk, I., 924 (SAT0404)
Shynkovski, V., 1497 (FRI0737-HPR)
Si Ahmed, S.N., 776 (SAT0023)
Siao-Pin, S., 1285 (AB0666)
Sibilia, J., 77 (OP0062), 258 (THU0152), 611 (FRI0329), 638 (FRI0398), 1049 (AB0007)
Sica, A., 26 (SP0104)
Sid Mohand, D., 1330 (AB0781)
Sidiropoulos, P., 297 (THU0246), 300 (THU0254), 559 (FRI0205), 574 (FRI0236), 577 (FRI0244), 579 (FRI0247), 836 (SAT0176), 850 (SAT0204), 896 (SAT0330), 1204 (AB0442)
Siebert, S., 55 (OP0012-PARE), 535 (FRI0142), 659 (FRI0456), 1308 (AB0727)
Siebuhr, A.S., 66 (OP0036), 120 (OP0165), 480 (FRI0003), 625 (FRI0365), 892 (SAT0317), 916 (SAT0383), 986 (SAT0554), 1109 (AB0179, AB0180), 1114 (AB0192)
Sieburg, M., 844 (SAT0193), 1187 (AB0396)
Siegel, J., 912 (SAT0373)
Siegert, E., 897 (SAT0333), 909 (SAT0366), 915 (SAT0380), 1106 (AB0169), 1110 (AB0181)
Sieghart, D., 239 (THU0103), 528 (FRI0125), 1124 (AB0217)
Sieper, J., 101 (OP0118), 156 (OP0243), 340 (THU0359), 345 (THU0369), 349 (THU0379), 353 (THU0388), 647 (FRI0425), 651 (FRI0435), 921 (SAT0395)
Sierakowski, S., 1277 (AB0642)
Sierra Herranz, L., 1232 (AB0518)
Sifuentes, C., 1117 (AB0200)
Sifuentes Giraldo, W.A., 392 (THU0491), 413 (THU0545), 587 (FRI0266), 696 (FRI0545), 697 (FRI0546), 698 (FRI0549), 701 (FRI0559), 713 (FRI0593), 1391 (AB0961)
Sifuentes Giraldo, W.A.A., 642 (FRI0409)
Sifuentes-Cantu, C., 1155 (AB0305)
Sifuentes-Giraldo, W.-A., 1389 (AB0957)
Sigidin, Y., 273 (THU0189), 576 (FRI0241), 843 (SAT0190)
Siglinsky, E., 739 (FRI0658)
Signorelli, F., 299 (THU0253), 312 (THU0286), 887 (SAT0303)
Signorini, V., 437 (THU0611)
Sigurdardottir, V., 164 (OP0262), 360 (THU0404), 361 (THU0408), 364 (THU0414), 375 (THU0443), 835 (SAT0173)
Sikorska, D., 1119 (AB0206)
Sikorska-Siudek, K., 1199 (AB0425), 1535 (AB1211-HPR)
Sili Scavalli, A., 496 (FRI0045)
Siljehult, F., 82 (OP0073)
Silman, A., 104 (OP0123)
Silva, A., 748 (FRI0683), 1276 (AB0640)
Silva, C., 255 (THU0145), 464 (THU0679), 929 (SAT0418), 1163 (AB0329), 1464 (AB1168)
Silva, C.A., 76 (OP0061), 875 (SAT0270)
Silva, D.R., 1446 (AB1117)
Silva, F., 1146 (AB0279)
Silva, F.C., 1478 (THU0728-HPR)
Silva, J., 554 (FRI0193)
Silva, J.A.P., 255 (THU0145)
Silva, J.L., 607 (FRI0318), 612 (FRI0330), 1011 (SAT0627)
Silva, J.M.D.S., 1508 (FRI0768-HPR)
Silva, J.P.C.G.D., 1412 (AB1021)
Silva, M., 1022 (SAT0653)
Silva, M.F.C.D., 397 (THU0505)
Silva, T.P., 1056 (AB0028)
Silva Cardoso, S.C., 1104 (AB0165)
Silva-Cardoso, S.C., 1065 (AB0054)
Silva-Ortiz, J.A., 534 (FRI0141)
Silvagni, E., 562 (FRI0212), 582 (FRI0255)
Silván, J., 892 (SAT0316), 1107 (AB0172)
Silveira, L., 1498 (FRI0741-HPR)
Silveira, L.H., 739 (FRI0660), 884 (SAT0295), 1006 (SAT0613)
Silverfield, J., 277 (THU0197)
Silverman, G.J., 1102 (AB0159)
Silverman, S., 72 (OP0051)
Silvestre, A., 485 (FRI0014)
Silvestri, V., 329 (THU0334)
Silvia, R., 1338 (AB0801)
Sim, J., 384 (THU0468)
Sim, M., 104 (OP0124)
Sime, K., 208 (THU0025)
Simeón, C.P., 1047 (AB0003)
Simeón Aznar, C., 897 (SAT0332), 1270 (AB0624)
Simeón Aznar, C.P., 639 (FRI0402), 900 (SAT0340), 1262 (AB0602)
Simeón-Aznar, C.P., 1262 (AB0603)
Simic, B., 500 (FRI0059)
Simic Pasalic, K., 245 (THU0116)
Simic-Pasalic, K., 792 (SAT0064)
Simmons, R., 1527 (SAT0767-HPR)
Simms, R., 105 (OP0126)
Simó, M., 324 (THU0320)
Simon, A., 662 (FRI0465), 1013 (SAT0632)
Simon, D., 655 (FRI0446), 1011 (SAT0628)
Simon, G., 1318 (AB0753)
Simon, L.S., 463 (THU0677)
Simon, S.-P., 170 (OP0275), 260 (THU0156), 1245 (AB0557)
Simon, T., 93 (OP0101), 408 (THU0534), 529 (FRI0129), 837 (SAT0177)
Simons, G., 642 (FRI0411), 1511 (SAT0719-HPR)
Simons, S., 1280 (AB0651)
Simonsen, J., 64 (OP0033)
Simonsen, M.B., 477 (THU0715)
Simopoulou, T., 1271 (AB0626), 1279 (AB0648)
Simpson, C., 213 (THU0038)
Simpson, J., 57 (OP0017), 548 (FRI0179)
Sims, G., 192 (OP0331)
Sims, M., 94 (OP0103)
Simsek, C., 1300 (AB0706)
Simsek, I., 562 (FRI0211), 836 (SAT0175)
Simsek, I.E., 477 (THU0714)
Sin, F.E., 1246 (AB0559)
Sinbaldi, D., 856 (SAT0220)
Sindel, D., 1347 (AB0827)
Singal, V., 1247 (AB0561, AB0562), 1253 (AB0579)
Singer, N., 567 (FRI0222)
Singh, E., 443 (THU0628), 558 (FRI0201), 831 (SAT0161), 832 (SAT0165), 1181 (AB0379)
Singh, G., 70 (OP0047), 169 (OP0272), 362 (THU0409), 672 (FRI0488)
Singh, J., 166 (OP0265, OP0267), 370 (THU0431), 377 (THU0448), 752 (FRI0692), 1363 (AB0879), 1452 (AB1135)
Singh, J.A., 196 (OP0340)
Singh, R., 874 (SAT0267), 1331 (AB0784)
Singh, S., 287 (THU0219), 301 (THU0258), 318 (THU0302), 320 (THU0307), 392 (THU0493), 393 (THU0496), 394 (THU0497), 588 (FRI0270), 1386 (AB0946)
Singh, U.P., 1072 (AB0075)
Singhal, S., 408 (THU0534)
Sinha, R., 1139 (AB0260)
Sinigaglia, L., 270 (THU0181), 437 (THU0611), 445 (THU0634), 1439 (AB1099), 1518 (SAT0739-HPR), 1533 (AB1203-HPR)
Siores, E., 1133 (AB0244)
Šipek Dolničar, A., 1143 (AB0272)
Sipetic-Grujicic, S.B., 1457 (AB1149)
Sippl, N., 1051 (AB0015)
Sireci, G., 291 (THU0231)
Sirenko, O., 1171 (AB0352)
Sirois, A., 81 (OP0072-PARE), 545 (FRI0171), 1176 (AB0366)
Sirotka, U., 1430 (AB1072, AB1074)
Sirotka, V., 1430 (AB1072, AB1074)
Situnayake, D., 409 (THU0536)
Siva, A., 603 (FRI0307)
Sivakumaran, P., 726 (FRI0627), 1024 (SAT0659)
Sivera, F., 134 (OP0199-PARE), 429 (THU0590)
Sivils, K., 193 (OP0333), 1096 (AB0143)
Sivordova, L., 699 (FRI0554)
Sizikov, A., 206 (THU0019), 273 (THU0188), 771 (SAT0008), 1056 (AB0027)
Sjö, A.-S., 1512 (SAT0724-HPR)
Sjogren, H.-O., 770 (SAT0005)
Sjölander, S., 1288 (AB0673)
Sjöwall, C., 452 (THU0652), 457 (THU0663), 861 (SAT0233)
Skácelová, M., 1183 (AB0387)
Skacelova, M., 1051 (AB0014)
Skaggs, B., 1238 (AB0535)
Skakić, V., 1327 (AB0774)
Skalska, U., 489 (FRI0026)
Skapenko, A., 718 (FRI0606)
Skare, T., 820 (SAT0135), 1111 (AB0186)
Skattum, L., 542 (FRI0162)
Skelton, A., 200 (THU0003), 295 (THU0242)

Skelton, D., 1444 (AB1111)
Skeoch, S., 803 (SAT0092), 1023 (SAT0657)
Skerrett, D., 566 (FRI0220)
Skielta, M., 113 (OP0147)
Skjødt, H., 784 (SAT0045)
Skoczynska, M., 276 (THU0194)
Skomsvoll, J., 1039 (SAT0698)
Skorpen, A.C.G., 1031 (SAT0677), 1032 (SAT0680)
Skougaard, M., 96 (OP0106), 98 (OP0112), 456 (THU0662), 1444 (AB1113)
Skoutellas, V., 1437 (AB1093)
Skrepnik, N., 121 (OP0166), 985 (SAT0552)
Skriner, K., 124 (OP0174), 509 (FRI0085), 769 (SAT0004), 773 (SAT0014), 792 (SAT0065), 1081 (AB0101)
Skuja, S., 1071 (AB0071)
Skup, M., 83 (OP0076), 1487 (THU0753-HPR)
Sleep, D., 140 (OP0213)
Sleglova, O., 73 (OP0053), 979 (SAT0538)
Sleight, A., 709 (FRI0582)
Sleptsova, T., 186 (OP0316)
Sliepen, M., 1337 (AB0800)
Slimani, S., 982 (SAT0545), 1009 (SAT0623), 1359 (AB0866), 1405 (AB1001, AB1002)
Slimani, Y., 1467 (AB1177)
Sloan, V.S., 1459 (AB1155)
Slobodin, G., 653 (FRI0441), 926 (SAT0407)
Słodkowski, K., 1458 (AB1152)
Sloetjes, A., 211 (THU0033)
Sloetjes, A.W., 211 (THU0032)
Slot, L.M., 125 (OP0177)
Slot, O., 1368 (AB0891)
Slováková, A., 1285 (AB0665)
Slowinska, I., 216 (THU0045)
Slungaard, B., 161 (OP0255-HPR)
Small, D., 460 (THU0671), 729 (FRI0634), 1530 (AB1196-HPR)
Smallie, T., 213 (THU0038)
Smedby, T., 248 (THU0125)
Smedslund, G., 466 (THU0686)
Smerilli, G., 247 (THU0121)
Smichowski, A., 440 (THU0619)
Smirnakis, K., 857 (SAT0222), 862 (SAT0235)
Smirnov, A., 843 (SAT0190), 920 (SAT0394), 943 (SAT0451), 1019 (SAT0646), 1369 (AB0895)
Smirnov, A.V., 943 (SAT0450), 1317 (AB0749), 1347 (AB0828)
Smirnova, E., 1180 (AB0378)
Smit, A.J., 625 (FRI0366), 630 (FRI0377), 1265 (AB0610)
Smith, C., 983 (SAT0548)
Smith, C.H., 201 (THU0004)
Smith, D., 1061 (AB0041)
Smith, J., 506 (FRI0076), 546 (FRI0173)
Smith, L., 1427 (AB1064)
Smith, M., 383 (THU0464)
Smith, M.A., 856 (SAT0220)
Smith, M.D., 203 (THU0011)
Smith, S.L., 177 (OP0291)
Smith, T., 670 (FRI0484)
Smith, V., 24 (SP0098), 65 (OP0035), 89 (OP0089), 140 (OP0212), 299 (THU0252), 914 (SAT0377), 1110 (AB0182, AB0183), 1111 (AB0185), 1221 (AB0488), 1263 (AB0605), 1389 (AB0957), 1390 (AB0958)
Smith, W.B., 371 (THU0433)
Smith, Y., 1118 (AB0203)
Smithson, G.M., 295 (THU0241)
Smitienko, I., 324 (THU0319)
Smolen, J., 50 (OP0002), 149 (LB0003), 158 (OP0247), 224 (THU0070), 239 (THU0103), 242 (THU0110), 292 (THU0233), 486 (FRI0018), 492 (FRI0033), 520 (FRI0108), 560 (FRI0207), 566 (FRI0219), 677 (FRI0498), 750 (FRI0688), 971 (SAT0515), 1511 (SAT0719-HPR), 1545 (AB1240-HPR), 1547 (AB1245-HPR)
Smolen, J.S., 272 (THU0186), 445 (THU0633), 472 (THU0701), 488 (FRI0024), 502 (FRI0064), 511 (FRI0089), 515 (FRI0096), 517 (FRI0099), 527 (FRI0124), 528 (FRI0125), 552 (FRI0187), 785 (SAT0047), 795 (SAT0072), 822 (SAT0142), 832 (SAT0164), 1124 (AB0217), 1130 (AB0235), 1322 (AB0765), 1323 (AB0766)
Smolewska, E., 390 (THU0486)
Smolik, I., 178 (OP0295)
Smolik, K., 1470 (AB1184)
Smolina, L.O., 974 (SAT0526)
Smržová, A., 1183 (AB0387), 1264 (AB0609)
Smrzova, A., 1051 (AB0014)
Smucrova, H., 638 (FRI0399)
Smulders, Y., 811 (SAT0114)
Snijders, G.F., 193 (OP0335)
Snoad, B., 222 (THU0062), 1099 (AB0151)
Snowden, N., 1030 (SAT0676), 1039 (SAT0699)
Snyder, M., 187 (OP0320), 275 (THU0193), 1202 (AB0436)
So, A., 378 (THU0452), 383 (THU0464)
So, A.C.L., 916 (SAT0384)
So, H., 998 (SAT0591)
Soare, A., 626 (FRI0368), 1032 (SAT0681), 1264 (AB0608)
Soares-Santeugini, M.J., 994 (SAT0576)
Soaures de Souza, S., 440 (THU0619)
Sobhy, N., 874 (SAT0265)
Sobue, Y., 1195 (AB0415)
Sochocka-Bykowska, M., 1470 (AB1184)
Sockalingam, S., 446 (THU0638)
Soden, M., 1277 (AB0643)
Söder, F., 864 (SAT0239)
Södergren, A., 248 (THU0125), 250 (THU0129)
Söderkvist, P., 947 (SAT0460)
Söderling, J., 183 (OP0308)
Söderling, J.K., 157 (OP0246)
Söderström, L., 113 (OP0147)
Sodin-Šemrl, S., 219 (THU0054), 325 (THU0324)
Soejima, Y., 645 (FRI0419), 1195 (AB0416)
Soen, S., 841 (SAT0186), 1137 (AB0253)
Soepnel, A., 637 (FRI0395)
Sofat, N., 976 (SAT0530)
Sohdi, V., 1545 (AB1241-HPR)
Sohn, D.H., 189 (OP0325), 585 (FRI0262), 698 (FRI0550)
Sohn, I.W., 1061 (AB0040)
Sohrabi, Y., 140 (OP0213)
Sohrabian, A., 509 (FRI0085), 861 (SAT0233)
Sokhova, M., 599 (FRI0299)
Sokka, T., 134 (OP0199-PARE), 784 (SAT0044)
Sokka-Isler, T., 61 (OP0024)
Sokol, E., 723 (FRI0621), 1237 (AB0531)
Sokolove, J., 189 (OP0325), 283 (THU0210)
Solanich, X., 317 (THU0300)
Solans, R., 311 (THU0284), 324 (THU0320), 464 (THU0681), 886 (SAT0302)
Solans Laque, R., 1262 (AB0602)
Solans-Laqué, R., 317 (THU0300), 330 (THU0336)
Solans-Laque, R., 415 (THU0550)
Solau Gervais, E., 1191 (AB0406)
Solau-Gervais, E., 56 (OP0014), 335 (THU0349), 989 (SAT0561)
Solberg, E.E., 466 (THU0686)
Soldal, D., 1029 (SAT0673)
Soldano, S., 86 (OP0082), 140 (OP0212), 245 (THU0116), 378 (THU0451), 894 (SAT0323), 1110 (AB0182, AB0183), 1111 (AB0185)
Solé-Marcé, C., 286 (THU0216)
Soler, C., 410 (THU0539), 1042 (SAT0706)
Soler, L., 1536 (AB1213-HPR)
Soler Bas, B., 1039 (SAT0697)
Solfietti, L., 1410 (AB1014)
Soliman, S., 583 (FRI0257)
Soliman, S.G., 1404 (AB1000)
Solmaz, D., 102 (OP0120), 296 (THU0245), 354 (THU0389), 661 (FRI0462), 1170 (AB0349), 1282 (AB0658)
Solomon, A., 252 (THU0136)
Solomon, D., 1313 (AB0739)
Solomon, D.H., 114 (OP0148)
Solomon, J., 543 (FRI0164)
Solomons, N., 153 (LB0002)
Solonos, M., 1437 (AB1093)
Soloshenko, M., 186 (OP0316), 539 (FRI0154), 1387 (AB0950, AB0951)
Solovic, I., 829 (SAT0157)
Soloviev, S.K., 861 (SAT0232), 1226 (AB0500)
Solovyova, I., 968 (SAT0509)
Soma, K., 148 (OP0230), 149 (LB0003), 268 (THU0175), 271 (THU0185), 1034 (SAT0686)
Somani, S., 1065 (AB0053)
Somma, L., 440 (THU0619)
Sommer, C., 6 (SP0020)
Sommerlatte, S., 772 (SAT0011), 1108 (AB0175)
Somura, J., 409 (THU0535)
Son, C.-N., 827 (SAT0154)
Son, C.N., 1185 (AB0392)
Son, K.M., 217 (THU0049, THU0050), 518 (FRI0103), 999 (SAT0593)
Son, Y., 115 (OP0152), 282 (THU0207)
Sondag, M., 417 (THU0558)
Sonderegger, I., 553 (FRI0189), 1185 (AB0391)
Søndergaard, J., 433 (THU0601)
Sondes, A., 1258 (AB0592)
Sonesson, S.-E., 182 (OP0305)
Song, G.G., 285 (THU0213), 604 (FRI0311), 1037 (SAT0693), 1130 (AB0234), 1452 (AB1134)
Song, H., 1516 (SAT0734-HPR)
Song, I.-H., 268 (THU0177), 668 (FRI0479)
Song, I.H., 855 (SAT0217)
Song, J.-S., 385 (THU0471), 1413 (AB1025)
Song, J.J., 372 (THU0436), 383 (THU0467)
Song, M., 944 (SAT0453)
Song, S., 1464 (AB1167)
Song, Y., 358 (THU0399), 1414 (AB1028)
Song, Y.W., 80 (OP0069), 83 (OP0077), 346 (THU0372), 351 (THU0383), 422 (THU0572), 652 (FRI0438), 877 (SAT0274), 922 (SAT0398), 1053 (AB0020)
Sonia, R., 995 (SAT0580), 1377 (AB0920)
Sönmez, E., 1515 (SAT0730-HPR)
Sonmez, H.E., 414 (THU0548), 616 (FRI0342)
Soo, A.J.X., 226 (THU0073)
Soonasra, A., 272 (THU0186)
Sopczynski, J.M., 402 (THU0519)
Sopeña, B., 712 (FRI0589)
Sordet, C., 56 (OP0014), 78 (OP0064), 549 (FRI0180), 811 (SAT0112)
Sorek, R., 1407 (AB1007), 1462 (AB1163)
Sørensen, I.J., 175 (OP0287), 456 (THU0662), 553 (FRI0190), 745 (FRI0674)
Sørensen, J., 450 (THU0648)
Soriano, A., 212 (THU0035), 411 (THU0540), 1054 (AB0022)
Soriano, E., 670 (FRI0483), 933 (SAT0427)
Soriano, E.R., 716 (FRI0601), 1115 (AB0194), 1231 (AB0516), 1333 (AB0789)
Soriano, R., 361 (THU0406)
Sorice, M., 180 (OP0299), 490 (FRI0028)
Sormani de Fonseca, M.L., 1429 (AB1071)
Soroka, N., 560 (FRI0208)
Sorotskaya, V., 273 (THU0188)
Sotlar, K., 86 (OP0084), 88 (OP0088)
Soto, C., 1245 (AB0555), 1289 (AB0676)
Soto, M.J., 452 (THU0651)
Soto Pino, M.J., 1228 (AB0506)
Soto-Peleteiro, A., 1409 (AB1012)
Sotomayor, M., 586 (FRI0264)
Soubrier, M., 213 (THU0039), 258 (THU0152), 334 (THU0346), 339 (THU0356, THU0357), 388 (THU0482), 389 (THU0483), 428 (THU0588, THU0589), 665 (FRI0472), 811 (SAT0112), 813 (SAT0117), 815 (SAT0123), 1033 (SAT0682), 1049 (AB0007), 1059 (AB0035), 1296 (AB0694), 1297 (AB0696), 1360 (AB0869), 1384 (AB0942), 1515 (SAT0733-HPR)
Soudah, E., 520 (FRI0107)
Soufleros, K., 1076 (AB0085)
Souissi, M., 1373 (AB0909)
Soule, B., 837 (SAT0177)
Sousa, S., 466 (THU0685), 533 (FRI0138), 1254 (AB0581)
Sousa-Neves, J., 607 (FRI0318), 612 (FRI0330), 637 (FRI0394), 736 (FRI0652), 1011 (SAT0627), 1015 (SAT0637), 1275 (AB0636)
Souter, S.T., 1236 (AB0528)
Southwood, T., 409 (THU0536), 1395 (AB0972)
Souto, R., 1339 (AB0805)

Souto Vilas, A., 1159 (AB0316)
Souverijns, G., 653 (FRI0440), 1305 (AB0716)
Souza, A.P.M.D., 1412 (AB1021)
Souza, D., 118 (OP0160)
Souza, E., 458 (THU0667)
Soy, D., 840 (SAT0184)
Soypacaci, Z., 296 (THU0245)
Soyuoz, A., 1212 (AB0463)
Sozlu, U., 1004 (SAT0608)
Sozmen, M.K., 1387 (AB0949)
Spaggiari, L., 1247 (AB0563)
Spähtling-Mestekemper, S., 1440 (AB1100)
Spalek, M., 1229 (AB0510)
Spandonaro, F., 667 (FRI0477)
Spångéus, A., 72 (OP0050)
Sparks, J.A., 114 (OP0148)
Sparsa, L., 334 (THU0346), 339 (THU0356, THU0357), 388 (THU0482), 389 (THU0483), 665 (FRI0472), 1296 (AB0694)
Späthling-Mestekemper, S., 1444 (AB1112)
Specker, C., 92 (OP0099), 844 (SAT0193), 1187 (AB0396)
Specks, U., 107 (OP0130), 109 (OP0137), 187 (OP0320), 605 (FRI0314)
Spector, T., 966 (SAT0504)
Spel, L., 1065 (AB0054)
Spellerberg, M., 637 (FRI0395), 1415 (AB1031)
Spellitz, P., 1455 (AB1144)
Speranskaya, A.A., 810 (SAT0111)
Speriatu, M., 435 (THU0607)
Spertini, F., 626 (FRI0369), 709 (FRI0582)
Speyer, I., 1076 (AB0084)
Speziale, A., 393 (THU0495), 395 (THU0502), 710 (FRI0585)
Spicer, V., 1117 (AB0199)
Spiera, R., 105 (OP0126), 107 (OP0131), 187 (OP0320), 605 (FRI0314)
Spiera, R.F., 318 (THU0301)
Spies, C., 129 (OP0187)
Spijkervet, F.K.L., 591 (FRI0277), 1007 (SAT0617)
Spindler, A., 267 (THU0173), 670 (FRI0483)
Spindler, W., 670 (FRI0483)
Spinella, A., 634 (FRI0388), 954 (SAT0473), 1272 (AB0629)
Spinella, P., 216 (THU0047)
Spinelli, F., 1465 (AB1170)
Spinelli, F.R., 180 (OP0299), 204 (THU0013), 463 (THU0678), 470 (THU0696), 489 (FRI0027), 490 (FRI0028), 757 (FRI0705), 860 (SAT0228), 864 (SAT0241), 872 (SAT0260), 879 (SAT0281), 880 (SAT0283), 1007 (SAT0615), 1093 (AB0132), 1094 (AB0135, AB0136), 1099 (AB0150), 1449 (AB1125)
Spiritovic, M., 638 (FRI0399), 906 (SAT0358), 1280 (AB0653), 1287 (AB0671), 1468 (AB1180)
Spivey, C.A., 1503 (FRI0754-HPR)
Spoo, M., 960 (SAT0488)
Spooner, L., 443 (THU0629), 453 (THU0653)
Spoorenberg, A., 157 (OP0245), 647 (FRI0424), 649 (FRI0430), 650 (FRI0433), 928 (SAT0416)
Spoorenberg, J., 1306 (AB0722)
Spotwood, H., 912 (SAT0373)
Springer, J.M., 1061 (AB0041)
Spruijt, S., 978 (SAT0536)
Spyrou, G., 297 (THU0246), 300 (THU0254), 896 (SAT0330)
Sreenath, S., 423 (THU0575)
Sridharan, R., 1144 (AB0275)
Srinonprasert, V., 930 (SAT0420)
Srivastava, P.M., 377 (THU0447)
Srour, F., 171 (OP0278-PARE)
Sruamsiri, R., 440 (THU0620), 547 (FRI0177)
Ssymank, S., 42 (SP0174)
St Clair, E.W., 605 (FRI0314)
Staal, B., 1492 (THU0764-HPR)
Staal, J., 125 (OP0176)
Stabler, T.V., 215 (THU0044)
Stack, A.G., 1036 (SAT0689)
Stack, R.J., 1511 (SAT0719-HPR)
Stadler, B., 820 (SAT0135)
Stagnaro, C., 446 (THU0636), 457 (THU0664), 617 (FRI0344), 731 (FRI0640)
Stahl, E., 165 (OP0263), 383 (THU0464)
Ståhl-Hallengren, C., 437 (THU0612)
Stalmach, D., 1458 (AB1153)
Stamenkovic, B., 914 (SAT0378), 1240 (AB0540)
Stamm, T., 750 (FRI0688), 1494 (THU0770-HPR), 1495 (FRI0732-HPR), 1511 (SAT0719-HPR), 1545 (AB1240-HPR), 1547 (AB1245-HPR)
Stamm, T.A., 560 (FRI0207)
Stamp, L., 166 (OP0267), 383 (THU0464), 1415 (AB1031)
Stanevicha, V., 1389 (AB0957)
Stanilova, S., 1048 (AB0005)
Stanisavljevic, N., 751 (FRI0689), 1231 (AB0515)
Stanislavchuk, M., 267 (THU0173), 654 (FRI0443)
Stanislavhuk, M., 1038 (SAT0696)
Stankovic, A., 914 (SAT0378)
Stanković, D., 1538 (AB1220-HPR)
Stanmore, E.K., 1444 (AB1111)
Stanojevic, G., 706 (FRI0574)
Stanopoulos, I., 1261 (AB0601)
Stanyer, N., 1174 (AB0359)
Stapelfeldt, E., 960 (SAT0488)
Stapleton, T., 1542 (AB1230-HPR)
Stara, A., 1560 (AB1252-PARE)
Stara, R., 1560 (AB1252-PARE)
Starba, A., 276 (THU0194)
Stark, M., 747 (FRI0679)
Starkova, A., 1411 (AB1017)
Starmans, M., 539 (FRI0152)
Starmans-Kool, M., 781 (SAT0037)
Starodubtseva, I., 1451 (AB1131)
Starovoitova, M.N., 1287 (AB0670)
Starovoytova, M., 640 (FRI0403), 1283 (AB0659)
Starr, M., 523 (FRI0115)
Statti, B., 1351 (AB0840)
Stattin, N., 444 (THU0632)
Staub, F.L., 1446 (AB1117)
Stausbo, T.V., 456 (THU0660)
Stavrakis, S., 1217 (AB0475)
Stavropoulos, A., 1536 (AB1215-HPR)
Stawski, L., 209 (THU0026)
Ste-Marie, P., 523 (FRI0115)
Steel, K.J.A., 780 (SAT0036)
Steen, J., 482 (FRI0006), 484 (FRI0013), 871 (SAT0257)
Steen, V., 1534 (AB1206-HPR)
Steengaard-Pedersen, K., 454 (THU0657)
Steenwijk, E.C., 92 (OP0097)
Stefanantoni, K., 903 (SAT0347)
Stefanek, J., 1419 (AB1042)
Stefanović, L., 1327 (AB0774)
Steffensen, M.A., 493 (FRI0038)
Steigelman, H., 1099 (AB0151)
Stein, A., 268 (THU0175)
Steiner, G., 131 (OP0194), 239 (THU0103), 486 (FRI0018), 488 (FRI0024), 499 (FRI0055), 528 (FRI0125), 750 (FRI0688), 773 (SAT0014), 1124 (AB0217), 1414 (AB1026), 1511 (SAT0719-HPR), 1547 (AB1245-HPR)
Steinfeld, J., 107 (OP0130)
Steingrimsdottir, L., 1027 (SAT0669)
Steiniche, T., 329 (THU0335)
Steinmeyer, J., 220 (THU0056)
Steinsbekk, A., 1480 (THU0733-HPR)
Stel, A.J., 591 (FRI0277), 630 (FRI0377), 1007 (SAT0617), 1265 (AB0610)
Stellato, M., 86 (OP0084), 88 (OP0088), 191 (OP0330)
Stemmler, F., 1011 (SAT0628)
Stengaard-Pedersen, K., 84 (OP0079), 732 (FRI0641)
Stengaard-Petersen, K., 784 (SAT0045)
Stensballe, A., 456 (THU0660), 775 (SAT0020)
Stenström, B., 112 (OP0143-HPR)
Stephenson, S., 30 (SP0118), 1415 (AB1030)
Steuer, J., 1096 (AB0142)
Steultjens, M., 111 (OP0141-HPR), 1505 (FRI0761-HPR)
Steunebrink, L.M., 225 (THU0071)
Stevanović, R., 592 (FRI0282), 883 (SAT0291)
Stevens, A., 1389 (AB0957)
Stevens, A.M., 409 (THU0537)
Stevens, R., 121 (OP0167)
Stevenson, L., 857 (SAT0222), 862 (SAT0235)
Stevenson, M., 167 (OP0268)
Stewart, J., 1003 (SAT0607), 1470 (AB1186)
Stiburkova, B., 179 (OP0297), 383 (THU0464)
Stieber, C., 423 (THU0576)
Stilgren, L., 533 (FRI0139)
Stille, J.R., 965 (SAT0502)
Stimmer, L., 182 (OP0307)
Stober, C., 943 (SAT0449)
Stöcker, J.K., 1492 (THU0764-HPR)
Stocks, J., 1028 (SAT0670)
Stoenoiu, M.S., 173 (OP0283), 728 (FRI0633)
Stoffer, M., 1511 (SAT0719-HPR)
Stohl, W., 150 (OP0232), 861 (SAT0231)
Stoica, V., 435 (THU0607), 626 (FRI0368), 1032 (SAT0681), 1151 (AB0294), 1179 (AB0376), 1264 (AB0608)
Stoilov, N., 1148 (AB0284), 1233 (AB0521)
Stoilov, N.R., 1147 (AB0283)
Stoilov, R., 1048 (AB0005), 1147 (AB0283), 1148 (AB0284)
Stojan, G., 306 (THU0270)
Stojanovic, R.M., 1457 (AB1149)
Stojanovic, S., 914 (SAT0378)
Stojanovic-Susulic, V., 769 (SAT0001)
Stojanovich, L., 751 (FRI0689), 1231 (AB0515)
Stojic, B., 640 (FRI0405)
Stone, J., 187 (OP0320)
Stone, J.H., 107 (OP0131), 605 (FRI0314), 711 (FRI0588)
Stones, S., 190 (OP0327-PARE), 1557 (PARE0015)
Stones, S.R., 119 (OP0162-PARE), 139 (OP0210-PARE), 1552 (PARE0001)
Stoop, J., 778 (SAT0030)
Štork, J., 1285 (AB0665)
Storkanova, H., 638 (FRI0399), 906 (SAT0358), 1280 (AB0653), 1287 (AB0671)
Stouten, V., 147 (OP0226), 765 (FRI0726)
Stoye, C., 826 (SAT0150)
Stoykov, I., 524 (FRI0116), 789 (SAT0058)
Stradner, M., 1495 (FRI0732-HPR)
Stradner, M.H., 587 (FRI0268)
Strand, V., 17 (SP0070), 94 (OP0102), 96 (OP0107), 283 (THU0210), 284 (THU0211), 355 (THU0393), 463 (THU0677), 531 (FRI0133), 575 (FRI0240), 578 (FRI0246), 581 (FRI0253), 675 (FRI0494), 687 (FRI0520), 688 (FRI0521), 816 (SAT0126), 839 (SAT0182), 855 (SAT0217), 951 (SAT0468), 957 (SAT0480), 1293 (AB0685), 1313 (AB0740), 1322 (AB0765), 1326 (AB0772), 1332 (AB0786), 1334 (AB0793), 1335 (AB0794)
Strangfeld, A., 302 (THU0261), 530 (FRI0130), 801 (SAT0087), 1029 (SAT0674)
Stratta, E., 1110 (AB0182)
Stratton, R., 140 (OP0213)
Straub, R.H., 29 (SP0115)
Strebkova, E., 968 (SAT0509, SAT0510)
Strehl, C., 486 (FRI0019)
Streicher, K., 180 (OP0301)
Strengholt, S., 271 (THU0185)
Strobe, M., 1499 (FRI0742-HPR)
Stroes, E.S.G., 662 (FRI0464)
Strollo, R., 646 (FRI0423)
Ström, O., 72 (OP0050)
Strotz, V., 1352 (AB0844)
Strugariu, G., 825 (SAT0148)
Struik, T., 1344 (AB0818)
Stubbs, R., 383 (THU0464)
Studenic, P., 175 (OP0288), 239 (THU0103), 528 (FRI0125), 971 (SAT0515), 1124 (AB0217), 1545 (AB1240-HPR)
Stummvoll, G., 292 (THU0233)
Stutz, M., 539 (FRI0153)
Stypinska, B., 204 (THU0012)
Su, Y., 1082 (AB0102)
Suárez, A., 803 (SAT0093), 1079 (AB0093)
Suarez, A., 5 (SP0013), 1553 (PARE0004)
Suárez, C., 918 (SAT0387), 1307 (AB0723)
Suarez-Almazor, M., 692 (FRI0532)
Suarez-Almazor, M.E., 463 (THU0677), 692 (FRI0531), 851 (SAT0208)
Subasinghe, S., 632 (FRI0382)
Subesinghe, S., 115 (OP0153), 753 (FRI0695), 938 (SAT0438)

Suboticki, J., 230 (THU0083), 785 (SAT0047), 828 (SAT0155)
Suboticki, J.L., 552 (FRI0188), 822 (SAT0142)
Subramaniam, A., 191 (OP0330)
Subtil, A.M., 163 (OP0259-HPR)
Sucur, A., 1055 (AB0026)
Suda, M., 574 (FRI0235), 813 (SAT0118)
Sudo, A., 703 (FRI0566)
Sudol-Szopinska, I., 216 (THU0045)
Suehiro, R.M., 402 (THU0519)
Suffield, L., 304 (THU0265)
Suga, K., 298 (THU0251), 788 (SAT0054)
Sugahara, K., 219 (THU0055), 1097 (AB0146)
Suganuma, E., 392 (THU0492)
Sugawara, E., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Sugihara, T., 265 (THU0170)
Sugii, S., 525 (FRI0119), 1176 (AB0367)
Sugimoto, N., 263 (THU0165), 524 (FRI0117), 798 (SAT0079), 814 (SAT0120)
Sugimura, Y., 1178 (AB0372), 1182 (AB0382), 1426 (AB1063)
Sugioka, Y., 540 (FRI0156), 955 (SAT0477), 1023 (SAT0658), 1134 (AB0245), 1324 (AB0768), 1426 (AB1061)
Sugitani, N., 618 (FRI0347)
Sugiura, H., 1021 (SAT0652)
Sugiura-Ogasawara, M., 1453 (AB1139)
Sugiyama, E., 1460 (AB1159)
Sugiyama, N., 274 (THU0191), 1200 (AB0431)
Sugiyama, Y., 645 (FRI0419), 1195 (AB0416)
Suh, C.-H., 692 (FRI0533), 824 (SAT0146), 1355 (AB0855)
Suh, C.H., 548 (FRI0178), 1185 (AB0392)
Suh, H.J., 385 (THU0471)
Suh, J., 1185 (AB0392)
Suh, M.J., 1341 (AB0810)
Suh, Y.-S., 585 (FRI0262)
Suhial, O., 740 (FRI0663)
Suin, V., 763 (FRI0719)
Suissa, S., 529 (FRI0129)
Sukalo, A.V., 389 (THU0485)
Sukumaran, S., 821 (SAT0140)
Suleyman, E., 1306 (AB0721)
Suleymanova, G., 1483 (THU0739-HPR, THU0740-HPR)
Suliman, Y.A., 628 (FRI0372)
Sulli, A., 66 (OP0037), 140 (OP0212), 245 (THU0116), 595 (FRI0288), 641 (FRI0407), 695 (FRI0540), 704 (FRI0569), 897 (SAT0331), 914 (SAT0377), 915 (SAT0381), 1110 (AB0182, AB0183), 1111 (AB0185), 1263 (AB0605)
Sullivan, B.A., 151 (OP0234)
Sullivan, C., 656 (FRI0450)
Sullivan, E., 96 (OP0107)
Sullivan, K., 104 (OP0124)
Sullivan, K.E., 391 (THU0490)
Sullivan, V., 693 (FRI0534)
Sultan, M., 1101 (AB0155)
Sultanova, M., 1152 (AB0296)
Sulutian, A., 771 (SAT0008)
Šumová, B., 220 (THU0058)
Sun, H., 192 (OP0331), 547 (FRI0176), 1516 (SAT0734-HPR)
Sun, J., 289 (THU0226), 1096 (AB0142)
Sun, K., 1437 (AB1094)
Sun, L., 592 (FRI0281), 600 (FRI0301), 866 (SAT0244, SAT0245), 1052 (AB0017), 1092 (AB0130), 1103 (AB0163), 1206 (AB0447), 1430 (AB1073)
Sun, L.-Y., 291 (THU0232)
Sun, M., 212 (THU0036), 482 (FRI0006), 484 (FRI0013)
Sun, X., 1065 (AB0052), 1096 (AB0141), 1295 (AB0691)
Sun, Y., 250 (THU0130), 883 (SAT0292)
Sunar, I., 1321 (AB0762)
Sunderkoetter, C., 1106 (AB0169), 1110 (AB0181)
Sundlisater, N.P., 176 (OP0289), 526 (FRI0121)
Sundman-Engberg, B., 1419 (AB1042)
Sundstedt, A., 770 (SAT0005)
Suñe, P., 1208 (AB0451)
Sung, I., 653 (FRI0442)
Sung, I.-H., 1089 (AB0120)
Sung, Y.-K., 430 (THU0594), 1045 (SAT0714), 1414 (AB1028), 1447 (AB1121), 1473 (AB1193)
Sungur, U., 1162 (AB0324)
Sunkureddi, P., 1202 (AB0436)
Suntharalingam, J., 1266 (AB0613)
Suponitskaya, E., 776 (SAT0024)
Suponitskaya, E.V., 861 (SAT0232)
Supp, G., 175 (OP0288), 520 (FRI0108), 971 (SAT0515)
Supp, G.M., 445 (THU0633)
Suppiah, R., 319 (THU0306)
Šuput Skvarča, D., 1143 (AB0272)
Suri, D., 287 (THU0219), 392 (THU0493), 393 (THU0496), 394 (THU0497), 1386 (AB0946)
Surico, G., 704 (FRI0568)
Surís, X., 1289 (AB0675)
Sürmeli, Z.S., 1321 (AB0762)
Suruki, R., 1459 (AB1155)
Susic, G., 1015 (SAT0636)
Suskind, D.L., 409 (THU0537)
Susok, L., 1106 (AB0169), 1110 (AB0181)
Suta, M., 1162 (AB0325)
Suta, V.C., 1162 (AB0325)
Sutcliffe, N., 180 (OP0300), 1205 (AB0444)
Suto, T., 493 (FRI0036), 1203 (AB0439)
Suurmond, J., 202 (THU0008)
Suyu, L., 82 (OP0075)
Suzaki, M., 1484 (THU0744-HPR)
Suzuki, A., 1345 (AB0822)
Suzuki, F., 425 (THU0579), 711 (FRI0587), 722 (FRI0617)
Suzuki, K., 219 (THU0055), 499 (FRI0054), 544 (FRI0168), 639 (FRI0401), 712 (FRI0590, FRI0591), 747 (FRI0680), 910 (SAT0369), 1021 (SAT0652), 1134 (AB0247)
Suzuki, M., 224 (THU0069), 532 (FRI0135), 841 (SAT0185)
Suzuki, S., 923 (SAT0400)
Suzuki, Y., 311 (THU0284), 464 (THU0681), 886 (SAT0302), 1242 (AB0546)
Svärd, A., 164 (OP0262), 361 (THU0408), 835 (SAT0173)
Svedbom, A., 447 (THU0640)
Svedlund, S., 163 (OP0258-HPR)
Svendsen, A.J., 286 (THU0217)
Svensson, B., 227 (THU0074), 501 (FRI0061), 812 (SAT0116), 1050 (AB0012), 1136 (AB0251), 1520 (SAT0746-HPR)
Svensson, J., 904 (SAT0352)
Svensson, K., 163 (OP0258-HPR)
Svensson, M.N., 777 (SAT0026)
Svenungsson, E., 162 (OP0256-HPR), 586 (FRI0265), 864 (SAT0239), 885 (SAT0297), 1102 (AB0159)
Sverker, A., 112 (OP0143-HPR), 1518 (SAT0740-HPR)
Sverzelatti, N., 1266 (AB0613)
Sverzellati, N., 1022 (SAT0653)
Sverzut, J.M., 367 (THU0424)
Svetlana, K., 1041 (SAT0702)
Swales, C., 529 (FRI0128)
Swärdh, E., 1523 (SAT0754-HPR)
Swart, J.F., 30 (SP0121)
Swartzwelter, B., 89 (OP0090)
Swearingen, C., 817 (SAT0129)
Swearingen, C.J., 121 (OP0166), 985 (SAT0552)
Sweet, K., 94 (OP0103), 577 (FRI0243)
Świdrowska-Jaros, J., 390 (THU0486)
Swierkot, J., 276 (THU0194)
Swikszcz-Gniadek, J., 1470 (AB1184)
Swiniarski, S., 1288 (AB0673)
Swinnen, T.W., 1501 (FRI0750-HPR)
Swoboda, P.P., 238 (THU0101)
Syed, K., 1035 (SAT0688)
Sylvain, H., 1520 (SAT0745-HPR)
Symeonidou, S., 1437 (AB1093)
Symmons, D., 803 (SAT0092)
Symmons, D.P.M., 243 (THU0112)
Synenky, O., 1177 (AB0369)
Syngle, A., 340 (THU0358), 819 (SAT0133)
Syngle, T., 819 (SAT0133)
Syrbe, U., 647 (FRI0425)
Szabó, E., 1090 (AB0123)
Szabo, I., 1285 (AB0666)
Szabó, K., 911 (SAT0371), 1094 (AB0137)
Szabo, S., 931 (SAT0423)
Szabo, Z., 1548 (AB1248-HPR)
Szalay, B., 780 (SAT0034)
Szamosi, S., 697 (FRI0547), 1049 (AB0009)
Szántó, S., 342 (THU0363), 469 (THU0694), 1049 (AB0009)
Szarecka, M., 1470 (AB1184)
Szasz, S., 1440 (AB1101)
Szczuková, L., 1183 (AB0387)
Szczukova, L., 440 (THU0621), 451 (THU0650)
Szekanecz, Z., 31 (SP0126), 33 (SP0131), 469 (THU0694), 697 (FRI0547), 767 (FRI0731), 1027 (SAT0668), 1049 (AB0009), 1273 (AB0632), 1548 (AB1248-HPR)
Szeląg, A., 1112 (AB0187)
Szelag, E., 1112 (AB0187)
Szelinski, F., 184 (OP0311)
Szentpetery, A., 465 (THU0683), 675 (FRI0493), 681 (FRI0507), 940 (SAT0444), 951 (SAT0467), 1319 (AB0755)
Szeto, C.C., 956 (SAT0479)
Szodoray, P., 630 (FRI0376), 1094 (AB0137), 1273 (AB0632)
Szombati, I., 267 (THU0173)
Sztajnbok, F., 1389 (AB0957)
Sztanka, A., 1458 (AB1152)
Szücs, G., 469 (THU0694), 697 (FRI0547), 767 (FRI0731), 1049 (AB0009), 1273 (AB0632)
Szumski, A., 337 (THU0353), 350 (THU0382), 666 (FRI0474), 939 (SAT0441), 947 (SAT0461)
Szymczak-Bartz, L., 1470 (AB1184)
Szymialis, A., 842 (SAT0188)
Szymonifka, J., 467 (THU0687)

Taal, E., 1478 (THU0727-HPR), 1515 (SAT0732-HPR)
Taams, L.S., 780 (SAT0036)
Tachibana, M., 493 (FRI0036), 1203 (AB0439)
Tackett, M., 202 (THU0007)
Tada, M., 260 (THU0157), 540 (FRI0156), 1134 (AB0245), 1178 (AB0373), 1324 (AB0768)
Tada, Y., 895 (SAT0326), 1254 (AB0582)
Tadesse, K., 61 (OP0024)
Tadiotto, G., 99 (OP0113)
Tag, H.-S., 255 (THU0144), 698 (FRI0550)
Tagetti, A., 805 (SAT0097)
Taggart, P., 1477 (THU0723-HPR)
Tago, F., 842 (SAT0187)
Taher, A.T., 1400 (AB0989)
Tahir, H., 952 (SAT0470)
Tahir Turanli, E., 1101 (AB0157)
Tahir Turanlı, E., 208 (THU0024)
Tahiri, L., 1136 (AB0252), 1168 (AB0343), 1358 (AB0862), 1365 (AB0883, AB0884, AB0885), 1418 (AB1041)
Tajali, A., 1060 (AB0039)
Tajima, R., 611 (FRI0329)
Tak, P.-P., 124 (OP0173), 781 (SAT0037)
Tak, P.P., 116 (OP0154), 123 (OP0172), 560 (FRI0207), 563 (FRI0214)
Takagi, M., 1344 (AB0819)
Takahashi, C., 747 (FRI0680)
Takahashi, H., 202 (THU0006)
Takahashi, N., 582 (FRI0254), 708 (FRI0579), 799 (SAT0081), 835 (SAT0174), 1195 (AB0415), 1357 (AB0860)
Takahashi, R., 800 (SAT0085)
Takahashi, S., 115 (OP0152), 487 (FRI0022), 507 (FRI0080), 699 (FRI0553)
Takahashi, Y., 298 (THU0251), 788 (SAT0054), 1288 (AB0672)
Takahata, M., 505 (FRI0075)
Takai, C., 853 (SAT0214)
Takajo, I., 1054 (AB0021)
Takakubo, Y., 1344 (AB0819)
Takakuwa, Y., 635 (FRI0391), 872 (SAT0259), 1260 (AB0597)
Takamatsu, H., 1467 (AB1176)
Takano, T., 392 (THU0492)
Takasaki, Y., 141 (OP0214)

Takashima, L., 1429 (AB1071)
Takayama, L., 1448 (AB1124)
Takehara, K., 202 (THU0006), 1464 (AB1169)
Takei, H., 424 (THU0577), 1227 (AB0504), 1399 (AB0984)
Takei, S., 1200 (AB0431), 1389 (AB0954)
Takemoto, H., 95 (OP0104), 800 (SAT0084)
Takemoto, M., 1484 (THU0744-HPR)
Takemoto, Y., 1254 (AB0582)
Takemura, M., 833 (SAT0167)
Takenaka, S., 995 (SAT0581), 1024 (SAT0661)
Takeno, M., 610 (FRI0326)
Takeshita, M., 747 (FRI0680), 1021 (SAT0652)
Takeuchi, A., 1248 (AB0566)
Takeuchi, K., 1203 (AB0439)
Takeuchi, T., 219 (THU0055), 274 (THU0191), 326 (THU0325), 418 (THU0560), 501 (FRI0060), 544 (FRI0168), 561 (FRI0210), 581 (FRI0252), 620 (FRI0354), 623 (FRI0361), 639 (FRI0401), 699 (FRI0552), 712 (FRI0590, FRI0591), 747 (FRI0680), 789 (SAT0058), 795 (SAT0072), 831 (SAT0162), 841 (SAT0186), 842 (SAT0187), 901 (SAT0343), 1021 (SAT0652), 1078 (AB0091), 1097 (AB0146), 1147 (AB0281), 1227 (AB0504), 1234 (AB0525)
Takiya, L., 60 (OP0022), 149 (LB0003), 275 (THU0193), 276 (THU0195), 1202 (AB0436)
Takken, T., 478 (THU0716)
Talaat, F., 874 (SAT0265)
Talarico, R., 617 (FRI0344)
Talarico, S., 446 (THU0636)
Talbot, J., 983 (SAT0548)
Talli, C., 433 (THU0602)
Talli, S., 467 (THU0689), 763 (FRI0722)
Talloczy, Z., 357 (THU0397)
Talotta, R., 1008 (SAT0620), 1184 (AB0389), 1194 (AB0413), 1376 (AB0917), 1380 (AB0928)
Tam, A., 140 (OP0213), 1104 (AB0166)
Tam, L.-S., 505 (FRI0073), 689 (FRI0523), 706 (FRI0576), 1198 (AB0424)
Tam, L.H.P., 1520 (SAT0747-HPR)
Tam, L.S., 689 (FRI0524), 796 (SAT0073), 956 (SAT0479), 1125 (AB0221), 1520 (SAT0747-HPR), 1541 (AB1229-HPR)
Tamai, H., 418 (THU0560)
Tamai, M., 318 (THU0303), 503 (FRI0067), 723 (FRI0620)
Tamas, M.M., 170 (OP0275), 260 (THU0156), 1245 (AB0557)
Tamashiro, H., 1064 (AB0051)
Tamashiro, J.C., 1508 (FRI0769-HPR)
Tamási, L., 767 (FRI0731), 1027 (SAT0668)
Tamayo, D., 262 (THU0162)
Tambiah, J.R., 121 (OP0166), 985 (SAT0552)
Tamborrini, G., 130 (OP0189), 335 (THU0347), 583 (FRI0256), 816 (SAT0125), 1427 (AB1065)
Tamir, S., 181 (OP0304)
Tamirou, F., 863 (SAT0238)
Tampe, B., 1100 (AB0154)
Tamura, M., 645 (FRI0419)
Tamura, N., 141 (OP0214), 1060 (AB0038), 1095 (AB0139, AB0140), 1200 (AB0431)
Tamura, Y., 901 (SAT0343), 1203 (AB0439)
Tan, A.L., 159 (OP0250), 196 (OP0341), 786 (SAT0049)
Tan, J.H.T., 401 (THU0517)
Tan, L.K., 1512 (SAT0722-HPR)
Tan, V.A., 1433 (AB1081)
Tan, W., 223 (THU0066)
Tan, Y.K., 1026 (SAT0666)
Tanabe, N., 313 (THU0290)
Tanaka, A., 531 (FRI0134), 1291 (AB0681)
Tanaka, E., 263 (THU0165), 280 (THU0204), 524 (FRI0117), 798 (SAT0079), 814 (SAT0120)
Tanaka, K., 507 (FRI0079), 1452 (AB1133)
Tanaka, M., 58 (OP0020), 527 (FRI0122), 744 (FRI0673), 1452 (AB1133)
Tanaka, S., 476 (THU0710), 841 (SAT0186)
Tanaka, Y., 66 (OP0036), 137 (OP0205), 257 (THU0149), 274 (THU0191), 282 (THU0207), 491 (FRI0031), 510 (FRI0087), 527 (FRI0124), 561 (FRI0210), 563 (FRI0214), 580 (FRI0251), 581 (FRI0252), 791 (SAT0062), 831 (SAT0162), 841 (SAT0186), 842 (SAT0187), 1009 (SAT0622)
Taneja, V., 506 (FRI0077)
Tang, A.C., 524 (FRI0116)
Tang, C.-H., 1503 (FRI0755-HPR), 1511 (SAT0720-HPR)
Tang, C.P., 412 (THU0543), 715 (FRI0599)
Tang, H., 144 (OP0220), 831 (SAT0162)
Tang, X., 1052 (AB0017), 1103 (AB0163)
Tang, Y., 1491 (THU0762-HPR)
Tangiku, M., 537 (FRI0148)
Tanhan, A., 1496 (FRI0734-HPR)
Tani, C., 437 (THU0611), 446 (THU0636), 457 (THU0664), 617 (FRI0344), 731 (FRI0640), 1209 (AB0456), 1439 (AB1099)
Tani, K., 1543 (AB1234-HPR)
Tani, T., 833 (SAT0167), 1183 (AB0386)
Taniguchi, A., 263 (THU0165), 280 (THU0204), 524 (FRI0117), 798 (SAT0079), 814 (SAT0120)
Taniguchi, T., 88 (OP0087)
Taniguchi, Y., 418 (THU0559), 717 (FRI0603), 924 (SAT0402)
Tanimura, K., 1484 (THU0744-HPR)
Tanimura, S., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Tanino, Y., 1109 (AB0180)
Tanure, L.V., 1102 (AB0160)
Tanwar, A., 491 (FRI0032)
Tao, J., 769 (SAT0003)
Tao, Y., 351 (THU0384), 1066 (AB0056)
Tappuni, A., 180 (OP0300)
Taraborelli, M., 585 (FRI0261), 1225 (AB0497)
Tarakci, E., 1500 (FRI0745-HPR, FRI0746-HPR), 1527 (SAT0766-HPR)
Tarasova, G.M., 251 (THU0132), 1226 (AB0500)
Tarasova, N., 482 (FRI0006)
Tarasovs, M., 1071 (AB0071)
Tarassi, K., 1076 (AB0085)
Taravati, S., 475 (THU0709)
Tardella, M., 1281 (AB0655)
Targoff, I.N., 913 (SAT0376)
Targonska-Stepniak, B., 251 (THU0133)
Tari, S., 722 (FRI0618)
Tarn, J., 92 (OP0097), 295 (THU0242)
Tarn, J.R., 1103 (AB0162)
Tarp, S., 96 (OP0106), 248 (THU0126)
Tarparelli, R., 704 (FRI0568)
Tarr, T., 1094 (AB0137)
Tarrant, J., 270 (THU0182), 281 (THU0205, THU0206)
Tarrini, G., 320 (THU0308)
Tas, S., 11 (SP0048), 601 (FRI0303), 781 (SAT0037)
Tas, S.W., 1064 (AB0049)
Tas Kilic, D., 637 (FRI0397)
Tascı, M., 1514 (SAT0727-HPR)
Tascilar, K., 619 (FRI0351)
Taser, B., 439 (THU0618)
Tashkin, D.P., 104 (OP0124)
Tasias Pitarch, M., 1374 (AB0912)
Taskın, H., 1514 (SAT0727-HPR)
Taskina, E., 978 (SAT0534)
Taskina, E.A., 1337 (AB0799), 1347 (AB0828)
Tasset, C., 148 (OP0229), 267 (THU0173), 270 (THU0182), 281 (THU0205, THU0206)
Taştekin, N., 1380 (AB0927)
Tatar, Z., 813 (SAT0117), 1033 (SAT0682), 1059 (AB0035), 1297 (AB0696), 1384 (AB0942)
Tataru, C., 1151 (AB0294)
Tatematsu, N., 1062 (AB0044)
Tatsis, S., 195 (OP0338), 1394 (AB0971)
Tatulych, S., 149 (LB0003)
Tauber, J., 152 (OP0237)
Taulaigo, A.V., 715 (FRI0598)
Taurog, J., 118 (OP0159)
Tausche, A.-K., 383 (THU0464)
Tauveron, P., 1448 (AB1123)
Tavares-Costa, J., 186 (OP0315), 607 (FRI0318), 1011 (SAT0627)
Tavera, E., 1456 (AB1145)
Taverner, D., 1156 (AB0307)
Tavoni, A., 222 (THU0063)
Tavor, Y., 333 (THU0343), 910 (SAT0368)
Tawfik, O., 1061 (AB0041)
Tawil, C., 1535 (AB1209-HPR)
Tay, S.H., 730 (FRI0636)
Tayar, J., 717 (FRI0604)
Tayel, M., 310 (THU0282)
Taylor, A., 744 (FRI0672)
Taylor, D.C., 380 (THU0457), 435 (THU0608), 763 (FRI0720), 766 (FRI0728)
Taylor, K., 289 (THU0225)
Taylor, P., 230 (THU0081), 238 (THU0100), 281 (THU0206), 511 (FRI0088), 788 (SAT0055), 1420 (AB1045)
Taylor, P.C., 529 (FRI0128), 1459 (AB1155)
Taylor, R., 1552 (PARE0002)
Taylor, W., 166 (OP0265, OP0267), 196 (OP0340)
Tchetina, E.V., 1337 (AB0799)
Tchetverikov, I., 676 (FRI0497), 678 (FRI0500), 1306 (AB0722), 1308 (AB0725), 1324 (AB0769), 1325 (AB0770)
Tchitchko, A.M., 389 (THU0485)
te Velthuis, H., 61 (OP0025)
Tebenkova, A.A., 1189 (AB0402)
Tebib, J., 843 (SAT0189)
Tecer, D., 321 (THU0311), 608 (FRI0320), 1216 (AB0472), 1223 (AB0492)
Tedeschi, S., 50 (OP0002)
Teeple, A., 562 (FRI0211), 836 (SAT0175)
Teerenstra, S., 1498 (FRI0740-HPR)
Teil, M., 57 (OP0017), 548 (FRI0179)
Teitsma, X.M., 177 (OP0293), 855 (SAT0218)
Teixeira, C., 1052 (AB0016)
Teixeira, F., 607 (FRI0318), 637 (FRI0394), 736 (FRI0652), 1011 (SAT0627), 1015 (SAT0637), 1275 (AB0636)
Teixeira, L., 1254 (AB0581)
Teixeira, V., 1254 (AB0581)
Teixeira, V.D.O.N., 1508 (FRI0768-HPR)
Teixeira, V.O.N., 502 (FRI0066), 1438 (AB1096)
Tejada, R., 1233 (AB0522)
Tejada-Reyes, E., 877 (SAT0276, SAT0277)
Tejedor, D., 178 (OP0294)
Tejera, B., 452 (THU0651)
Tejera Segura, B., 300 (THU0256), 592 (FRI0280), 802 (SAT0088)
Tejera-Segura, B., 882 (SAT0289)
Tejón, P., 350 (THU0381)
Tejón Menéndez, P., 955 (SAT0475), 1333 (AB0788)
Tejón-Menendez, P., 1472 (AB1191)
Tekaya, R., 347 (THU0373), 1073 (AB0077), 1297 (AB0697), 1306 (AB0720), 1373 (AB0906, AB0907, AB0908), 1377 (AB0919)
Tekeoğlu, I., 241 (THU0108), 1182 (AB0383), 1532 (AB1202-HPR)
Tekeoglu, I., 637 (FRI0396), 1317 (AB0751), 1320 (AB0757)
Tekeoglu, S., 598 (FRI0296), 634 (FRI0386)
Tekgoz, E., 352 (THU0385), 412 (THU0544), 1297 (AB0698)
Tekkatte, R., 1553 (PARE0004)
Tektonidou, M., 192 (OP0332), 602 (FRI0306), 836 (SAT0176), 1088 (AB0117)
Tektonidou, M.G., 642 (FRI0410)
Telli Atalay, O., 1514 (SAT0727-HPR)
Tellier, S., 77 (OP0062)
Temiz Karadag, D., 598 (FRI0296), 634 (FRI0386)
Ten Brinck, R.M., 224 (THU0068), 473 (THU0704), 743 (FRI0670), 803 (SAT0091)
ten Brinck, R.M., 79 (OP0067), 82 (OP0073)
ten Klooster, P.M., 225 (THU0071)
Teng, C.-C., 239 (THU0102)
Teng, G.G., 1447 (AB1119)
Teng, J.Y., 446 (THU0638)
Teng, L., 143 (OP0219), 672 (FRI0487), 683 (FRI0512), 684 (FRI0513), 936 (SAT0436), 1331 (AB0785)
Teng, Y.K., 181 (OP0302), 774 (SAT0015), 871 (SAT0258)
Teniente-Serra, A., 1236 (AB0529)
Tennant, A., 227 (THU0075)
Tenorio, J., 416 (THU0553)
Tenten-Diepenmaat, M., 1486 (THU0750-HPR)
Teplyakova, O., 1421 (AB1048)
Ter Wee, M., 523 (FRI0113), 1038 (SAT0695)
ter Wee, M.M., 114 (OP0150), 1145 (AB0277)

Terada, Y., 418 (THU0559), 717 (FRI0603), 924 (SAT0402)
Terai, C., 618 (FRI0347)
Terán Tinedo, M.A., 1391 (AB0961)
Terán-Tinedo, M., 992 (SAT0572)
Teran-Tinedo, M., 731 (FRI0639)
Terao, C., 202 (THU0006), 618 (FRI0349), 620 (FRI0352)
terAvest, A., 240 (THU0106)
Terazawa, T., 1062 (AB0044)
Terenas, M., 610 (FRI0324)
Terenzi, R., 504 (FRI0070)
Teresa-Herranz, M., 287 (THU0218)
Terizaki, M., 574 (FRI0236), 850 (SAT0204)
Terkeltaub, R., 379 (THU0455)
Terlemez, R., 353 (THU0387), 1156 (AB0308)
Ternant, D., 335 (THU0349)
Terrades, N., 610 (FRI0324)
Terreri, M.T., 76 (OP0061), 1389 (AB0957)
Terry, K., 277 (THU0197)
Terry, O., 421 (THU0569)
Terslev, L., 131 (OP0192), 173 (OP0283), 174 (OP0286), 175 (OP0287, OP0288), 583 (FRI0256), 726 (FRI0626, FRI0628), 737 (FRI0654), 1013 (SAT0631), 1015 (SAT0636), 1409 (AB1013)
Terwee, C., 111 (OP0141-HPR), 1332 (AB0786)
Terwee, C.B., 463 (THU0677), 476 (THU0712)
Terzioğlu, M.E., 296 (THU0243), 1066 (AB0057)
Tesei, G., 1269 (AB0622), 1270 (AB0623)
Teshigawara, S., 1058 (AB0032)
Tesser, J., 272 (THU0186), 275 (THU0193), 276 (THU0195)
Testa, M., 1483 (THU0741-HPR), 1499 (FRI0742-HPR), 1539 (AB1223-HPR)
Testas, K., 1359 (AB0866)
Testi, A., 1263 (AB0606)
Tetsu Oyama, T., 1471 (AB1187)
Tetu, L., 901 (SAT0342)
Teuchner, B., 615 (FRI0338)
Tezcan, M.E., 261 (THU0159), 1232 (AB0520)
Thabah, M.M., 984 (SAT0550)
Thabut, G., 1049 (AB0007)
Thakran, R.D., 1506 (FRI0762-HPR), 1540 (AB1226-HPR)
Thakur, K., 454 (THU0656)
Thalayasingam, N., 200 (THU0003)
Thallinger, G., 219 (THU0054)
Thalmann, R., 790 (SAT0059), 1144 (AB0273)
Thanarajasingam, U., 1044 (SAT0711)
Thanos, D., 293 (THU0237)
Thanou, A., 1217 (AB0475)
Tharwat, S., 1174 (AB0360)
Thayer, S., 960 (SAT0489)
Thebault, S., 1376 (AB0916)
Thedrez, A., 259 (THU0154)
Themeli, A., 1523 (SAT0753-HPR)
Theodorou, I., 1047 (AB0001)
Théophile, H., 823 (SAT0144)
Therapontos, A., 1437 (AB1093)
Therkildsen, P., 174 (OP0285), 329 (THU0335)
Thevissen, K., 299 (THU0252)
Thiel, J., 324 (THU0321), 332 (THU0341), 615 (FRI0339)
Thiele, R., 175 (OP0288), 583 (FRI0256)
Thøgersen, K.F., 64 (OP0033)
Thom, H., 957 (SAT0480), 1301 (AB0707)
Thom, L., 418 (THU0561)
Thomas, E., 222 (THU0062), 1099 (AB0151)
Thomas, G., 85 (OP0081)
Thomas, K., 321 (THU0310), 836 (SAT0176), 1376 (AB0915)
Thomas, L., 115 (OP0151)
Thomas, M.H., 356 (THU0394), 558 (FRI0203)
Thomas, R., 193 (OP0333)
Thompson, C.R., 208 (THU0025), 1173 (AB0358)
Thompson, N., 1100 (AB0152)
Thomsen, H.S., 732 (FRI0641)
Thomsen, L.M., 190 (OP0328-PARE)
Thomsen, M.D., 248 (THU0126)
Thomson, M., 287 (THU0220)
Thomson, W., 177 (OP0291), 190 (OP0327-PARE), 391 (THU0488), 408 (THU0533)
Thon, A., 390 (THU0487)
Thong, B.Y., 364 (THU0415)
Thong, D., 1251 (AB0573)
Thorlacius, G.E., 182 (OP0305)
Thorn, J., 110 (OP0139-HPR)
Thornalley, P.J., 1025 (SAT0663)
Thorne, C., 231 (THU0085), 349 (THU0378), 781 (SAT0039), 815 (SAT0122), 845 (SAT0194)
Thornton, C.C., 219 (THU0053)
Thorp, J., 548 (FRI0179)
Thorpe, S.J., 461 (THU0673)
Thorstensson, C.A., 1501 (FRI0749-HPR)
Thudium, C.S., 120 (OP0165), 480 (FRI0003), 966 (SAT0504), 1068 (AB0062)
Thumboo, J., 1026 (SAT0666)
Thunem, C., 81 (OP0071), 756 (FRI0702), 1030 (SAT0675)
Thurah, A., 454 (THU0657)
Thurlings, R.M., 519 (FRI0104), 526 (FRI0120)
Thuy, N.T.P., 912 (SAT0374)
Thwaites, R., 289 (THU0224)
Thyberg, I., 112 (OP0143-HPR), 1518 (SAT0740-HPR)
Tiabut, T., 831 (SAT0162)
Tian, H., 96 (OP0107), 1437 (AB1094)
Tian, J., 193 (OP0334), 471 (THU0699)
Tian, M., 1082 (AB0103)
Tian, Z., 583 (FRI0258), 858 (SAT0224)
Tianwang, L., 1480 (THU0732-HPR)
Tiengo, G., 634 (FRI0388)
Tierce, J., 859 (SAT0227)
Tikhonova, M., 771 (SAT0008)
Tikly, M., 631 (FRI0379)
Tillett, W., 668 (FRI0479), 682 (FRI0510), 939 (SAT0442), 1332 (AB0786)
Tilleul, P., 450 (THU0646)
Tillisch, K., 87 (OP0085)
Tilly, G., 778 (SAT0029)
Tilson, H., 710 (FRI0585)
Timurtas, E., 1504 (FRI0756-HPR)
Tin, D., 231 (THU0085), 781 (SAT0039), 815 (SAT0122)
Tinazzi, I., 945 (SAT0454)
Tincani, A., 70 (OP0046), 245 (THU0116), 437 (THU0611), 579 (FRI0249), 585 (FRI0261), 867 (SAT0248), 1207 (AB0448), 1209 (AB0456), 1214 (AB0467, AB0468), 1225 (AB0497), 1439 (AB1099), 1468 (AB1178)
Tineke, A., 448 (THU0641)
Tineo, C., 1233 (AB0522), 1456 (AB1145)
Tiniakou, E., 67 (OP0038)
Tinone, G., 614 (FRI0335)
Tiosano, S., 84 (OP0078), 297 (THU0248), 332 (THU0342), 619 (FRI0350), 796 (SAT0074), 886 (SAT0300)
Tipa, P., 1468 (AB1178)
Tirri, R., 56 (OP0015), 763 (FRI0721)
Tissier, M., 260 (THU0158)
Titah, C., 408 (THU0532)
Tjensvoll, A.B., 184 (OP0312)
Tjon Kon Fat, E., 215 (THU0042)
Tkaczyk, C., 679 (FRI0503), 1303 (AB0712)
Tlustochowicz, M., 245 (THU0116), 1470 (AB1184)
Tłustochowicz, M., 1152 (AB0297)
Tlustochowicz, W., 1398 (AB0982)
Tłustochowicz, W., 1152 (AB0297)
To, C.H., 825 (SAT0147)
Tobimatsu, H., 799 (SAT0082), 1063 (AB0047)
Tobón, G., 1225 (AB0498)
Tochihara, M., 280 (THU0204), 1026 (SAT0667)
Tochimoto, A., 202 (THU0006), 1026 (SAT0667)
Todd, C., 1444 (AB1111)
Todlí Parra, J.A., 1270 (AB0624)
Toes, R., 35 (SP0145), 37 (SP0155), 202 (THU0008), 566 (FRI0219), 621 (FRI0356), 769 (SAT0001), 778 (SAT0030), 1050 (AB0012), 1135 (AB0248)
Toes, R.E., 125 (OP0177), 224 (THU0068)
Toes, R.E.M., 1076 (AB0084)
Toffolo, S.R., 1508 (FRI0769-HPR)
Tofiño-Vian, M., 485 (FRI0014)
Toftegaard, P., 1519 (SAT0744-HPR)
Togawa, R., 1109 (AB0180)
Tohma, S., 202 (THU0006), 278 (THU0198), 476 (THU0710), 525 (FRI0119), 1165 (AB0333)
Tokairin, T., 1248 (AB0566)
Tokuhira, M., 544 (FRI0168)
Tokunaga, K., 278 (THU0198)
Tokunaga, T., 222 (THU0064), 894 (SAT0322), 1149 (AB0289), 1460 (AB1159)
Toldi, G., 780 (SAT0034), 1105 (AB0167)
Toledano, K., 333 (THU0343), 910 (SAT0368)
Toledo Coello, M.D., 1183 (AB0385)
Tolone, S., 630 (FRI0378)
Tolosa, C., 721 (FRI0615)
Tolosa Vilella, C., 639 (FRI0402)
Tolosa-Vilella, C., 897 (SAT0332)
Tolun, A., 208 (THU0024), 1101 (AB0157)
Tolusso, B., 138 (OP0208), 154 (OP0239), 394 (THU0499), 535 (FRI0143), 787 (SAT0052), 792 (SAT0066), 1077 (AB0088)
Toma, I., 202 (THU0007)
Tomak, L., 1172 (AB0353)
Tomás, X., 1018 (SAT0645)
Tomatis, V., 704 (FRI0569), 728 (FRI0632), 915 (SAT0381)
Tombetti, E., 316 (THU0299), 328 (THU0331), 621 (FRI0357), 725 (FRI0624)
Tomčík, M., 209 (THU0027), 1285 (AB0665)
Tomcik, M., 638 (FRI0399), 906 (SAT0358), 916 (SAT0383), 1280 (AB0653), 1287 (AB0671)
Tomelleri, A., 610 (FRI0325)
Tomero, E., 68 (OP0042), 527 (FRI0123), 1107 (AB0173)
Tomi, A.-L., 965 (SAT0501)
Tomic Lucic, A., 1552 (PARE0003)
Tomic-Lucic, A., 541 (FRI0158)
Tomietto, P., 1272 (AB0630)
Tomiyama, N., 1467 (AB1176)
Tomohiko Yoshida, T., 1471 (AB1187)
Tomšič, M., 108 (OP0133), 219 (THU0054), 325 (THU0324), 1143 (AB0272), 1186 (AB0393), 1291 (AB0682)
Tomsic, M., 109 (OP0136), 656 (FRI0450), 1243 (AB0552)
Tonello, M., 634 (FRI0387)
Tong, L., 89 (OP0089)
Tonga, E., 1504 (FRI0756-HPR)
Tonini, J.F.V., 1102 (AB0160)
Tonnini, C., 64 (OP0031)
Tontini, C., 1189 (AB0400)
Tony, H.-P., 159 (OP0249), 356 (THU0395), 510 (FRI0086), 516 (FRI0098), 565 (FRI0217), 844 (SAT0193), 1187 (AB0396)
Too, C.L., 1512 (SAT0722-HPR)
Tooze, R., 314 (THU0293)
Topal, F.E., 661 (FRI0462)
Topless, R., 165 (OP0263), 383 (THU0464)
Toporkov, M., 1153 (AB0298)
Topping, L.M., 483 (FRI0011)
Toprak, U., 748 (FRI0682)
Torbeyns, A., 837 (SAT0177)
Torell, A., 1515 (SAT0731-HPR)
Torfing, T., 732 (FRI0641)
Torgutalp, M., 606 (FRI0315), 1124 (AB0218), 1244 (AB0554)
Torii, M., 1452 (AB1133)
Torikai, E., 224 (THU0069), 532 (FRI0135), 841 (SAT0185)
Tornero, C., 416 (THU0553), 551 (FRI0186), 559 (FRI0204), 833 (SAT0168), 1116 (AB0198), 1304 (AB0714)
Tornero, J., 177 (OP0292), 946 (SAT0458), 1135 (AB0249), 1318 (AB0752)
Tornero-Molina, J., 139 (OP0209-HPR)
Toro, C., 752 (FRI0694)
Toro, C.E., 1536 (AB1213-HPR)
Torok, K., 1389 (AB0957)
Toroptsova, N., 245 (THU0116), 704 (FRI0567)
Torp-Pedersen, A., 737 (FRI0654)
Torp-Pedersen, S., 737 (FRI0654)
Torralba, A.I., 1472 (AB1192)
Torralba Collados, F., 1349 (AB0837)
Torre, I., 326 (THU0326), 718 (FRI0607), 837 (SAT0178)
Torre Alonso, J.C., 685 (FRI0515)

Torre-Alonso, J.C., 918 (SAT0387), 946 (SAT0458), 1307 (AB0723)
Torre-Salaberri, I., 1001 (SAT0600)
Torrent, M., 1386 (AB0948)
Torrente, V., 1005 (SAT0610)
Torrente-Segarra, V., 407 (THU0530), 550 (FRI0184), 1472 (AB1192)
Torres, A., 1098 (AB0148)
Torres, C., 694 (FRI0537)
Torres, N., 555 (FRI0195)
Torres, R., 383 (THU0464)
Torres Hernández, L., 691 (FRI0530)
Torres-Oliva, N.E., 421 (THU0568)
Torres-Quintanilla, F.J., 253 (THU0140), 534 (FRI0141), 1118 (AB0204), 1119 (AB0205), 1156 (AB0309), 1157 (AB0310)
Torres-Salido, M., 286 (THU0216)
Tortosa, R., 177 (OP0292), 290 (THU0227), 946 (SAT0458)
Toscano, C., 730 (FRI0637), 1010 (SAT0625), 1013 (SAT0631)
Tosi, G.M., 711 (FRI0586)
Tost, J., 286 (THU0217)
Tosun, A., 661 (FRI0462)
Tosun, O., 661 (FRI0462)
Tóth, E., 767 (FRI0731)
Toth, E., 72 (OP0050)
Toth, M., 405 (THU0525)
Toth, P., 443 (THU0627)
Totoson, P., 493 (FRI0039), 495 (FRI0044)
Totsuka, S., 1161 (AB0321)
Toublanc, N., 548 (FRI0179)
Touchais, S., 90 (OP0093)
Tougorti, M., 313 (THU0291), 596 (FRI0290), 599 (FRI0300), 1238 (AB0536)
Touitou, I., 77 (OP0062)
Tournadre, A., 213 (THU0039), 573 (FRI0234), 813 (SAT0117), 1033 (SAT0682), 1297 (AB0696), 1360 (AB0869), 1384 (AB0942)
Tournier-Nappey, M., 493 (FRI0039)
Tournilhac, O., 1059 (AB0035)
Touzi, M., 1348 (AB0830), 1353 (AB0848, AB0849), 1362 (AB0876), 1383 (AB0937)
Tovar, J., 550 (FRI0184), 556 (FRI0197)
Tovar Sugreñes, E., 1224 (AB0494)
Towheed, T., 71 (OP0049)
Townsend, A., 381 (THU0460)
Toyoizumi, S., 274 (THU0191)
Toyos-SMiera, F., 326 (THU0326)
Töyrä Silfverswärd, S., 777 (SAT0026), 779 (SAT0033)
Toz, B., 327 (THU0329)
Trabattoni, D., 1184 (AB0389)
Tracey, G., 1320 (AB0758)
Trachana, M., 192 (OP0332), 205 (THU0015)
Trallero, E., 290 (THU0227)
Trallero Araguas, E., 1272 (AB0630)
Trallero-Araguás, E., 636 (FRI0392), 900 (SAT0339)
Tramontano, G., 343 (THU0365)
Tran, C.L., 486 (FRI0019)
Tran, D., 739 (FRI0658)
Tran, T.A., 56 (OP0014)
Trancho, Z., 826 (SAT0150)
Trandafir, M., 1540 (AB1224-HPR)
Tranquilino Batres, E.G., 1357 (AB0861)
Trapiella Martinez, L., 639 (FRI0402)
Trauzeddel, R., 398 (THU0507), 400 (THU0512)
Través, P.G., 489 (FRI0025)
Treede, R.-D., 6 (SP0019)
Trellu, S., 1072 (AB0073)
Trenell, M., 163 (OP0259-HPR)
Trenkler, A., 1173 (AB0357)
Trenkmann, M., 204 (THU0014)
Trespidi, L., 70 (OP0046)
Treuer, T., 1511 (SAT0720-HPR)
Trevisani, M., 248 (THU0123), 437 (THU0611), 1439 (AB1099)
Trevisani, V., 311 (THU0284), 464 (THU0681), 886 (SAT0302)
Triantafyllias, K., 1272 (AB0630), 1281 (AB0656)
Triantafyllou, A., 542 (FRI0161)
Triantafyllou, G., 542 (FRI0161)
Trichet, V., 90 (OP0093)
Trickey, J., 1514 (SAT0728-HPR)
Trifonova, E., 1336 (AB0795, AB0796)
Triggianese, P., 667 (FRI0477), 1193 (AB0410)
Trigo, C., 361 (THU0406)
Trigo, E., 1014 (SAT0634)
Trijau, S., 1454 (AB1141)
Trinca, R., 464 (THU0679), 929 (SAT0418), 1163 (AB0329), 1464 (AB1168)
Trindade, H., 894 (SAT0324)
Trindade, L., 1391 (AB0960)
Trinh, H., 593 (FRI0285)
Triolo, G., 56 (OP0015), 131 (OP0193), 180 (OP0299), 183 (OP0309), 263 (THU0164), 291 (THU0231), 721 (FRI0613), 777 (SAT0025)
Trofimenko, A., 1361 (AB0872)
Trofimenko, A.S., 459 (THU0670), 536 (FRI0146), 1128 (AB0228)
Trofimov, D.Y., 1128 (AB0230)
Trofimov, V.I., 810 (SAT0111)
Troilo, A., 324 (THU0321), 615 (FRI0339)
Troisi, F., 115 (OP0151)
Troitskaya, E., 807 (SAT0103), 1158 (AB0314), 1175 (AB0364)
Trojanowska, M., 209 (THU0026)
Trombetta, A.C., 66 (OP0037), 140 (OP0212), 914 (SAT0377), 915 (SAT0381), 1110 (AB0182, AB0183), 1111 (AB0185), 1263 (AB0605)
Trombetta, E., 1109 (AB0178)
Troncoso, J.A., 1245 (AB0555), 1266 (AB0614)
Tropé, S., 425 (THU0580), 427 (THU0586)
Tropea, S., 742 (FRI0667), 1022 (SAT0654), 1152 (AB0295), 1412 (AB1022)
Troplini, S., 854 (SAT0215)
Trotta, A., 629 (FRI0374)
Troum, O., 377 (THU0448)
Trouvin, A.-P., 754 (FRI0697)
Trouw, L., 778 (SAT0030), 1050 (AB0012), 1135 (AB0248)
Trouw, L.A., 224 (THU0068), 1076 (AB0084)
Truchetet, M.E., 866 (SAT0246)
Truchon, M., 529 (FRI0128)
Truglia, S., 180 (OP0299), 757 (FRI0705), 864 (SAT0241), 872 (SAT0260), 879 (SAT0281), 880 (SAT0283), 1094 (AB0135, AB0136), 1099 (AB0150)
Trujillo, E., 695 (FRI0541), 1397 (AB0979)
Trukchina, A.A., 1189 (AB0402)
Trupin, L., 432 (THU0600), 1435 (AB1087)
Tryfonidou, M.A., 482 (FRI0008)
Tsai, C.-Y., 889 (SAT0309)
Tsai, C.-Y.T., 1334 (AB0792)
Tsai, C.Y., 1215 (AB0470)
Tsai, P.-H., 85 (OP0080)
Tsai, T.Y.-E., 1212 (AB0464)
Tsalapaki, C., 321 (THU0310), 1204 (AB0442), 1376 (AB0915)
Tsamados, S., 1427 (AB1064)
Tsang, L., 245 (THU0117), 252 (THU0136), 545 (FRI0170)
Tsangaris, I., 643 (FRI0414)
Tsao, N., 374 (THU0442), 443 (THU0629)
Tsao, Y.-P., 631 (FRI0381)
Tsao, Y.P., 1215 (AB0470)
Tsarenok, S., 1311 (AB0736)
Tsatsani, P., 836 (SAT0176)
Tse, S.M., 303 (THU0263), 874 (SAT0266)
Tseng, W., 770 (SAT0005)
Tseronis, D., 588 (FRI0269)
Tsiklauri, L., 1070 (AB0067)
Tsinti, M., 909 (SAT0365)
Tsirogianni, A., 1076 (AB0085), 1345 (AB0821), 1437 (AB1093)
Tsirves, G., 1217 (AB0476)
Tsitsami, E., 909 (SAT0365)
Tsoi, M.F., 936 (SAT0434)
Tsuchida, K., 910 (SAT0369)
Tsuchida, N., 645 (FRI0419), 1195 (AB0416)
Tsuchiya, N., 202 (THU0006)
Tsuda, K., 115 (OP0152)
Tsuda, T., 813 (SAT0118)
Tsuge, S., 425 (THU0579), 711 (FRI0587), 722 (FRI0617)
Tsuji, G., 282 (THU0208)
Tsuji, H., 744 (FRI0673)
Tsuji, S., 1058 (AB0032)
Tsuji, W.H., 151 (OP0234)
Tsuji, Y., 744 (FRI0673)
Tsukamoto, M., 639 (FRI0401)
Tsunoda, S., 641 (FRI0408)
Tsurgan, A., 189 (OP0324)
Tsurko, V., 1507 (FRI0765-HPR)
Tsuru, T., 1484 (THU0744-HPR)
Tsutsumino, M., 264 (THU0166), 265 (THU0170)
Tsvetkova, E., 1337 (AB0797, AB0798)
Tu, J., 129 (OP0187)
Tu, L., 85 (OP0081)
Tubach, F., 58 (OP0018), 425 (THU0580), 427 (THU0586), 434 (THU0605), 754 (FRI0699), 1033 (SAT0684), 1034 (SAT0685), 1299 (AB0701)
Tucker, L., 419 (THU0562)
Tuckwell, K., 107 (OP0131), 581 (FRI0253)
Tufan, A., 608 (FRI0320), 1216 (AB0472), 1260 (AB0598), 1302 (AB0709)
Tufan, A.N., 327 (THU0329), 1434 (AB1086)
Tugwell, P., 463 (THU0677)
Tukmacheva, A.A., 1189 (AB0402)
Tulabaev, A., 1533 (AB1204-HPR)
Tumangelova-Yuzeir, K., 1106 (AB0170)
Tummala, R., 50 (OP0001), 870 (SAT0254)
Tuna, S., 1321 (AB0759)
Tuncer, O.B., 1381 (AB0932)
Tundia, N., 855 (SAT0217)
Tuompo, R., 61 (OP0024)
Tural, R., 1223 (AB0492)
Turanli, E.T., 1402 (AB0994)
Turchetti, G., 457 (THU0664)
Turcotte, A., 571 (FRI0230), 845 (SAT0195), 1188 (AB0397)
Turesson, C., 57 (OP0016), 252 (THU0135), 563 (FRI0213), 567 (FRI0221), 750 (FRI0686, FRI0687)
Turgay, M., 606 (FRI0315), 1488 (THU0756-HPR), 1523 (SAT0756-HPR), 1538 (AB1221-HPR)
Turgay, T.M., 1124 (AB0218), 1244 (AB0554)
Turhan, T., 637 (FRI0397)
Turiel, M., 1294 (AB0689)
Türk, I., 902 (SAT0344)
Turk, I., 640 (FRI0404), 905 (SAT0355)
Türk, S., 254 (THU0141)
Turk, S.A., 817 (SAT0127), 1145 (AB0277)
Turki, M., 1311 (AB0734)
Turkiewicz, A., 376 (THU0446)
Turkkila, M., 779 (SAT0033)
Turkmen, I., 1170 (AB0349)
Turman, S., 192 (OP0331)
Tutino, M., 1087 (AB0115)
Tutkak, H., 1321 (AB0762)
Tweehuysen, L., 519 (FRI0104), 526 (FRI0120), 557 (FRI0200), 568 (FRI0223)
Twigg, S., 227 (THU0075)
Twisk, J., 473 (THU0703)
Tyabut, T.D., 1063 (AB0048)
Tyack, L., 1241 (AB0542)
Tydén, H., 302 (THU0260)
Tykocinski, L.-O., 1070 (AB0068)
Tyrenko, V., 1153 (AB0298)
Tyrinova, T., 771 (SAT0008)
Tzallas, A.T., 1193 (AB0411)
Tzaribachev, N., 75 (OP0058), 1015 (SAT0636), 1021 (SAT0651)
Tzatzagou, G., 1139 (AB0259)
Tzioufas, A.G., 288 (THU0221), 293 (THU0237), 323 (THU0315)

Ubaldi, F.M., 879 (SAT0282)
Ubilla, B., 804 (SAT0095), 1084 (AB0108)
Uçar, D., 1246 (AB0558)
Ucar, D., 603 (FRI0307), 618 (FRI0348)
Ucar, E., 826 (SAT0150)
Uçar, I., 1066 (AB0057)
Uceda, J., 1182 (AB0384)
Ucer, M., 1420 (AB1046)
Uchtenhagen, H., 779 (SAT0032)
Uçkun, A., 652 (FRI0439)
Uda, H., 849 (SAT0203)

Udachkina, H., 256 (THU0148), 572 (FRI0231)
Udayakumar, A.A., 1036 (SAT0689)
Uder, M., 247 (THU0122)
Udkoff, J., 703 (FRI0564)
Udrea, G., 1179 (AB0376)
Uebelhack, R., 253 (THU0139)
Ueda, K., 1467 (AB1176)
Ueda, N., 1254 (AB0582)
Ueda, Y., 115 (OP0152), 459 (THU0668), 487 (FRI0022), 507 (FRI0080), 699 (FRI0553)
Ueffing, H., 754 (FRI0698)
Uejima, Y., 392 (THU0492)
Ueki, N., 1254 (AB0582)
Ueland, P.M., 1102 (AB0160)
Uemura, M., 717 (FRI0604), 1429 (AB1071)
Uemura, Y., 282 (THU0208)
Ueno, A., 605 (FRI0313), 1251 (AB0572)
Ugarte-Gil, M., 875 (SAT0269), 1142 (AB0269)
Ughi, N., 299 (THU0252)
Uğurlu, S., 719 (FRI0610)
Ugurlu, S., 412 (THU0542), 415 (THU0552), 603 (FRI0307), 618 (FRI0348), 714 (FRI0596), 1101 (AB0157), 1186 (AB0394), 1274 (AB0634), 1402 (AB0994)
Uguztemur, E., 716 (FRI0600)
Uhlig, T., 52 (OP0005), 176 (OP0289), 224 (THU0070), 361 (THU0407), 526 (FRI0121), 538 (FRI0151), 797 (SAT0075), 1017 (SAT0642)
Ulff-Møller, C.J., 286 (THU0217)
Ulrichsen, S.P., 546 (FRI0174)
Ulus, Y., 1172 (AB0353)
Ulutaş, F., 1196 (AB0418)
Ulutatar, F., 715 (FRI0597)
Umeda, M., 318 (THU0303), 723 (FRI0620)
Umehara, H., 842 (SAT0187)
Umekita, K., 1054 (AB0021)
ÜNal, A.U., 910 (SAT0367)
Ünal, A.U., 327 (THU0329), 644 (FRI0416), 1013 (SAT0633), 1310 (AB0731)
Unal, A.U., 889 (SAT0310)
Ünal, B., 296 (THU0243)
Ünal, E., 1515 (SAT0730-HPR), 1531 (AB1198-HPR)
Unal, I., 640 (FRI0404), 902 (SAT0344)
Unal Ertekin, C., 469 (THU0692), 715 (FRI0597)
Unger, B., 587 (FRI0268)
Unger, J., 1495 (FRI0732-HPR)
Unger, L., 461 (THU0674)
Unizony, S.H., 107 (OP0131)
Ünlü, A., 931 (SAT0422)
Unlu Ozkan, F., 735 (FRI0648), 999 (SAT0592, SAT0595), 1058 (AB0034)
Ünlüoğlu, I., 387 (THU0478)
Unsal, S.E., 53 (OP0009-HPR), 1387 (AB0949), 1522 (SAT0751-HPR)
Unsal Delialioglu, S., 535 (FRI0144), 818 (SAT0130)
Untas, A., 1470 (AB1185)
Ünver, B., 1339 (AB0806), 1340 (AB0807), 1542 (AB1232-HPR)
Unver, B., 1496 (FRI0736-HPR), 1521 (SAT0749-HPR), 1531 (AB1197-HPR), 1538 (AB1218-HPR)
Unver, F., 1521 (SAT0749-HPR)
Upadhyaya, S.K., 1292 (AB0683)
Upegui-Arango, L.D., 1362 (AB0873)
Upmanyu, R., 396 (THU0503)
Upton, M., 1087 (AB0115)
Uranga, J.A., 962 (SAT0494)
Urano, F., 923 (SAT0400)
Urata, Y., 95 (OP0104), 800 (SAT0084)
Urayama, M., 1182 (AB0382), 1426 (AB1063)
Urban, M., 1528 (SAT0769-HPR)
Urbaniak, P., 1427 (AB1065)
Urbanova, M., 916 (SAT0383)
Urda Cardona, A.L., 1393 (AB0968)
Ureña, I., 1175 (AB0362), 1443 (AB1109)
Ureña-Garnica, I., 261 (THU0160), 1174 (AB0361), 1492 (THU0766-HPR)
Ureyen, S., 609 (FRI0322)
Ureyen, S.B., 791 (SAT0063)
Uriarte, E., 68 (OP0042), 1107 (AB0173)
Uriarte-Hernández, C., 586 (FRI0264)
Uriarte-Isacelaya, E., 587 (FRI0267)
Uribe Botero, L., 1190 (AB0404)
Urionagüena, I., 368 (THU0426), 381 (THU0458), 1363 (AB0878)
Urioste, L., 1339 (AB0805)
Urowitz, M., 50 (OP0002)
Urowitz, M.B., 599 (FRI0298)
Urra, F., 1108 (AB0176)
Urrego, J., 1208 (AB0453)
Urrego, T., 308 (THU0275), 1239 (AB0538)
Urruticoechea, A., 350 (THU0381), 685 (FRI0515), 843 (SAT0191)
Urruticoechea-Arana, A., 569 (FRI0226), 873 (SAT0263), 918 (SAT0387), 1244 (AB0553), 1307 (AB0723)
Ursani, M.A., 692 (FRI0532)
Ursin, K., 1039 (SAT0698)
Urumova, M., 1411 (AB1017)
Urzainqui, A., 892 (SAT0316), 1107 (AB0172)
Urzúa, U., 1102 (AB0158)
Usheva, D., 1543 (AB1233-HPR)
Ushikubo, M., 1097 (AB0146), 1234 (AB0525)
Uskova, Y., 246 (THU0120)
Üsküdar Cansu, D., 254 (THU0141), 327 (THU0329), 863 (SAT0237)
Uskudar Cansu, D., 609 (FRI0322)
Üsküdar Teke, H., 254 (THU0141), 863 (SAT0237)
Uslu, E., 606 (FRI0315)
Uslu Yurteri, E., 1124 (AB0218), 1244 (AB0554)
Üstün, E.I., 1548 (AB1249-HPR)
Üstüner, E., 1321 (AB0762)
Usui, T., 220 (THU0057), 1452 (AB1133)
Uthman, I., 1400 (AB0989)
Utiyama, S., 820 (SAT0135)
Utsugi, T., 507 (FRI0079)
Uutela, T., 61 (OP0024)
Uy, P.P., 1213 (AB0466)
Uyaroglu, A.O., 616 (FRI0342)
Uyaroğlu, O.A., 1035 (SAT0687), 1412 (AB1023)
Uyaroglu, O.A., 448 (THU0642)
Uygunoglu, U., 603 (FRI0307)
Uziel, Y., 1389 (AB0957)
Uzun, H., 331 (THU0339)

V-Pascual, E., 326 (THU0326)
Vaccaro, F., 230 (THU0082)
Vacchi, C., 634 (FRI0388), 1267 (AB0615, AB0616)
Vadacca, M., 304 (THU0267), 437 (THU0611), 876 (SAT0273), 1439 (AB1099)
Vagelli, R., 446 (THU0636), 457 (THU0664), 731 (FRI0640)
Vaggers, S., 315 (THU0296)
Vagnani, S., 446 (THU0636)
Vahasalo, P., 404 (THU0523)
Vaillancourt, J., 554 (FRI0191)
Vaishnav, B., 1292 (AB0683)
Vakrakou, A.G., 1089 (AB0122)
Valadares, L.D., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Valadares, M.L.D., 987 (SAT0557), 988 (SAT0558), 989 (SAT0562)
Valcov, R., 378 (THU0452)
Valdes, A., 1028 (SAT0670)
Valdes, A.M., 752 (FRI0693)
Valdez, H., 1034 (SAT0686)
Valdez, S., 371 (THU0434), 1364 (AB0880), 1366 (AB0887)
Valdez-Lorie, T., 877 (SAT0276, SAT0277)
Valdovinos-Bañuelos, A., 253 (THU0140), 534 (FRI0141), 1118 (AB0204), 1119 (AB0205), 1156 (AB0309), 1157 (AB0310)
Valen, P., 958 (SAT0484)
Valena, C.A., 1154 (AB0301)
Valencia, O., 1536 (AB1213-HPR)
Valencia-Quiñones, K.R., 1147 (AB0282)
Valentin, M.-A., 886 (SAT0301), 1229 (AB0509)
Valentini, E., 69 (OP0044)
Valentini, G., 151 (OP0233), 202 (THU0006), 263 (THU0164), 621 (FRI0355), 630 (FRI0378), 909 (SAT0366), 915 (SAT0380), 1106 (AB0171), 1118 (AB0202)
Valentini, V., 873 (SAT0262)
Valenzuela, G., 272 (THU0186)
Valenzuela, O., 1146 (AB0279), 1459 (AB1154)
Valero, L., 1132 (AB0239)
Valero, M., 1338 (AB0801), 1406 (AB1004)
Valero, O., 1424 (AB1055)
Valesini, G., 180 (OP0299), 204 (THU0013), 230 (THU0082), 305 (THU0268), 329 (THU0334), 411 (THU0541), 463 (THU0678), 470 (THU0696), 489 (FRI0027), 490 (FRI0028), 496 (FRI0045), 757 (FRI0705), 860 (SAT0228), 864 (SAT0241), 872 (SAT0260), 879 (SAT0281), 880 (SAT0283), 888 (SAT0305), 903 (SAT0347), 1007 (SAT0615), 1057 (AB0029, AB0030), 1059 (AB0036), 1093 (AB0132), 1094 (AB0135, AB0136), 1099 (AB0150), 1214 (AB0467), 1379 (AB0925), 1449 (AB1125), 1465 (AB1170)
Valeyre, D., 1049 (AB0007)
Valiente, G., 1099 (AB0151)
Valieva, S., 186 (OP0316), 539 (FRI0154), 1387 (AB0950, AB0951)
Valikovics, A., 1027 (SAT0668)
Valim, V., 163 (OP0259-HPR), 311 (THU0284), 464 (THU0681), 875 (SAT0270), 886 (SAT0302), 1102 (AB0160)
Vallarino Reyes, E., 1357 (AB0861)
Valle, A.G., 213 (THU0037)
Valle-Oñate, R., 252 (THU0137), 1117 (AB0201)
Valleala, H., 61 (OP0024)
Vallejo, C., 1160 (AB0319)
Vallejo Pascual, E., 719 (FRI0608)
Vallín-Orozco, C., 760 (FRI0714)
Valls, E., 420 (THU0567), 718 (FRI0607)
Valls Pascual, È., 1534 (AB1208-HPR)
Valls Roc, M., 1418 (AB1039)
Valls-Pascual, E., 258 (THU0153), 1168 (AB0344), 1316 (AB0746), 1410 (AB1016), 1415 (AB1032)
Vallve, J.C., 1156 (AB0307)
Valor, L., 386 (THU0474), 462 (THU0676), 633 (FRI0385), 656 (FRI0448), 748 (FRI0683), 1009 (SAT0621), 1270 (AB0625), 1276 (AB0640), 1414 (AB1029)
Valtanen, S., 827 (SAT0152)
Valtersson, E., 112 (OP0143-HPR), 1518 (SAT0740-HPR)
van Adelsberg, J., 94 (OP0102), 570 (FRI0228), 838 (SAT0179)
van As, B., 438 (THU0615)
van Baarsen, L.G., 116 (OP0154)
van Beers-Tas, M., 124 (OP0173)
van Beest, S., 197 (OP0342), 969 (SAT0512)
Van Beneden, K., 92 (OP0098), 575 (FRI0239)
van Beuningen, H., 1057 (AB0031)
van Bijnen, S.T.A., 1109 (AB0178)
van Bon, L., 1108 (AB0177), 1109 (AB0178)
van Caam, A., 1057 (AB0031)
Van Cleemput, J., 1275 (AB0638)
van Daele, P.L., 871 (SAT0258)
van Daele, P.L.A., 92 (OP0097)
van Dalen, S., 211 (THU0033)
Van Dam, L.S., 774 (SAT0015)
van de Laar, M., 157 (OP0245), 230 (THU0081), 1515 (SAT0732-HPR)
van de Laar, M.A., 225 (THU0071), 365 (THU0418)
van de Loo, F., 1553 (PARE0006)
van de Loo, F.A.J., 489 (FRI0025), 493 (FRI0037)
van de Sande, M., 123 (OP0172), 656 (FRI0450)
van de Sande, M.G., 666 (FRI0475), 1086 (AB0114)
van de Sande, M.G.H., 680 (FRI0505)
van de Ven, P., 724 (FRI0623)
van Delft, D., 769 (SAT0001)
van Delft, M.A., 224 (THU0068)
van den Bemt, B., 112 (OP0145-HPR), 433 (THU0603)
van den Bemt, B.J.F., 557 (FRI0200)
Van Den Berg, R., 100 (OP0115, OP0116)
van den Berg, R., 100 (OP0114), 146 (OP0224), 434 (THU0604), 669 (FRI0480)
van den Berg, W., 504 (FRI0072)
Van den Berge, M., 1007 (SAT0617)
van den Bergh, J., 740 (FRI0662)
Van den Bosch, F., 62 (OP0026), 80 (OP0070), 118 (OP0160), 336 (THU0350), 653 (FRI0440), 683 (FRI0512), 684 (FRI0513), 829 (SAT0159), 1293 (AB0685), 1305 (AB0716)

van den Bosch, F., 63 (OP0030), 649 (FRI0430)
van den Bosch, M., 207 (THU0020), 497 (FRI0049), 772 (SAT0012)
van den Brandt, S., 1510 (SAT0717-HPR)
Van den Brink, R., 1556 (PARE0014)
van den Broek, M., 516 (FRI0097)
van den Eeden, S., 215 (THU0042)
van den Ende, C., 198 (OP0344-HPR), 568 (FRI0223), 1476 (THU0721-HPR), 1553 (PARE0006)
van den Ende, C.H., 110 (OP0138-HPR), 193 (OP0335), 1487 (THU0752-HPR)
van den Ende, E., 1492 (THU0764-HPR)
van den Hombergh, W., 1280 (AB0651, AB0652)
van den Hoogen, F., 493 (FRI0037), 568 (FRI0223), 1280 (AB0651, AB0652), 1306 (AB0722), 1492 (THU0764-HPR), 1553 (PARE0006)
van den Hoogen, F.H., 110 (OP0138-HPR), 193 (OP0335)
van den Hoogen, F.H.J., 519 (FRI0104), 526 (FRI0120), 557 (FRI0200)
Van Den Hoogen, L.L., 182 (OP0306)
van den Oever, I., 811 (SAT0114)
van Denderen, C., 347 (THU0374), 724 (FRI0623)
van Denderen, J,C., 659 (FRI0455)
van Denderen, J.C., 354 (THU0391), 661 (FRI0461), 928 (SAT0415), 931 (SAT0421)
Van der Aa, A., 148 (OP0229), 267 (THU0173), 270 (THU0182), 281 (THU0205, THU0206)
van der Aar, E., 126 (OP0180)
Van Der Elst, K., 765 (FRI0726)
Van der Elst, K., 147 (OP0226), 1488 (THU0757-HPR)
van der Esch, M., 966 (SAT0505), 972 (SAT0517), 982 (SAT0544), 1488 (THU0755-HPR)
van der Geest, K., 607 (FRI0317)
Van der Geest, S., 230 (THU0081)
Van Der Giesen, F., 1479 (THU0730-HPR), 1559 (PARE0022)
van der Giesen, F., 1485 (THU0748-HPR)
van der Graaff, W., 1325 (AB0770)
Van der Haegen, M.-C., 78 (OP0065)
van der Heide, H., 769 (SAT0001)
Van Der Heijde, D., 14 (SP0056), 100 (OP0115, OP0116)
Van der Heijde, D., 336 (THU0350)
van der Heijde, D., 60 (OP0023), 63 (OP0030), 80 (OP0070), 100 (OP0114), 122 (OP0168), 129 (OP0188), 130 (OP0189), 131 (OP0192), 141 (OP0216), 144 (OP0221), 145 (OP0223), 155 (OP0241), 156 (OP0244), 157 (OP0245), 176 (OP0289), 233 (THU0088), 242 (THU0111), 337 (THU0352, THU0353), 350 (THU0382), 352 (THU0386), 473 (THU0703), 510 (FRI0087), 511 (FRI0089), 526 (FRI0121), 538 (FRI0151), 560 (FRI0207), 649 (FRI0430), 650 (FRI0432), 662 (FRI0465), 666 (FRI0475), 669 (FRI0480), 841 (SAT0186), 1013 (SAT0632), 1017 (SAT0642), 1030 (SAT0675), 1130 (AB0235), 1316 (AB0747), 1510 (SAT0718-HPR)
van der Heijden, E.H., 1206 (AB0446)
van der Heijden, J.W., 604 (FRI0309)
van der Helm van Mil, A.H., 473 (THU0704)
van der Helm-van Mil, A., 215 (THU0042), 473 (THU0702), 530 (FRI0131), 1043 (SAT0708), 1050 (AB0012)
van der Helm-van Mil, A.H., 79 (OP0067), 82 (OP0073), 224 (THU0068), 743 (FRI0670), 803 (SAT0091)
van der Horst-Bruinsma, I., 347 (THU0374), 724 (FRI0623), 1087 (AB0116)
van der Horst-Bruinsma, I.E., 354 (THU0391), 656 (FRI0450), 659 (FRI0455), 928 (SAT0415), 931 (SAT0421)
van der horst-Bruinsma, I.E., 661 (FRI0461)
van der Kooij, J., 1421 (AB1047)
van der Kraan, P., 193 (OP0335), 497 (FRI0049), 504 (FRI0072), 772 (SAT0012), 1057 (AB0031), 1553 (PARE0006)
van der Kraan, P.M., 489 (FRI0025), 493 (FRI0037)
van der Kroef, M., 1109 (AB0178)
van der Laan, W.H., 110 (OP0138-HPR), 1487 (THU0752-HPR)
van der Laken, C., 724 (FRI0623), 1020 (SAT0650)
van der Laken, C.J., 494 (FRI0041), 732 (FRI0642), 1075 (AB0082)
van der Leeden, M., 972 (SAT0517), 982 (SAT0544), 1488 (THU0755-HPR)
van der Linden-van der Zwaag, H.M., 967 (SAT0506)
van der Meijde, P., 741 (FRI0664)
van der Merwe, A.E., 1423 (AB1052)
van der Meulen-Dilling, R.G., 110 (OP0138-HPR), 1487 (THU0752-HPR)
van der Pol, J.A., 516 (FRI0097), 976 (SAT0529)
van der Poll, T., 710 (FRI0585)
van der Steen, M., 1421 (AB1047)
van der Veer, E., 928 (SAT0416)
Van Der Veer, S., 547 (FRI0175)
van der Veer, S.N., 1453 (AB1138)
van der Vlugt, E., 758 (FRI0707), 935 (SAT0433)
van der Weijden, M., 347 (THU0374)
Van Der Woude, D., 36 (SP0146)
van der Woude, D., 1076 (AB0084)
van der Woude, J., 978 (SAT0536)
van Dijk, B.T., 79 (OP0067)
van Duivenvoorde, L., 118 (OP0159), 724 (FRI0623)
Van Eijk-Hustings, Y., 1494 (THU0772-HPR)
van Eijk-Hustings, Y., 1488 (THU0757-HPR)
van Gaalen, F., 156 (OP0244), 669 (FRI0480), 1485 (THU0748-HPR)
van Gaalen, F.A., 100 (OP0114), 155 (OP0241), 666 (FRI0475)
Van Ganse, E., 434 (THU0605), 754 (FRI0699), 1033 (SAT0684), 1034 (SAT0685)
Van Geffen, E., 1057 (AB0031)
van Genderen, S., 157 (OP0245)
van Goor, H., 625 (FRI0366)
van Groenendaal, H., 1308 (AB0725)
van Groenendael, H., 676 (FRI0497)
Van Groenendael, J.H., 793 (SAT0067)
van Groenendael, J.H.L.M., 1325 (AB0770)
Van Gucht, S., 763 (FRI0719)
van Gysel, D., 883 (SAT0293)
van Haaften, T., 87 (OP0086)
van Hamburg, J.P., 1058 (AB0033), 1064 (AB0049)
Van Hecke, A., 1481 (THU0735-HPR)
van Heerwaarden, R., 978 (SAT0536)
van Helden, C.G., 92 (OP0097)
Van Helvoort, E.M., 482 (FRI0008), 968 (SAT0508)
van Herwaarden, N., 526 (FRI0120)
Van Hoeven, L., 1306 (AB0722)
van Hoogstraten, H., 94 (OP0102), 575 (FRI0240), 576 (FRI0242), 838 (SAT0180), 849 (SAT0202), 853 (SAT0212)
van Hooij, A., 215 (THU0042)
van Kampen, A., 123 (OP0172), 124 (OP0173)
van Kooij, R., 494 (FRI0041)
van Kooten, C., 181 (OP0302), 774 (SAT0015), 871 (SAT0258)
van Kuijk, A.W.R., 662 (FRI0464), 680 (FRI0505), 949 (SAT0464), 1086 (AB0114)
van Laar, J., 184 (OP0310), 376 (THU0445), 741 (FRI0664), 1482 (THU0737-HPR)
van Laar, J.M., 177 (OP0293), 855 (SAT0218), 968 (SAT0508), 1199 (AB0428)
van Lent, P., 211 (THU0033), 497 (FRI0049), 772 (SAT0012)
van Lent, P.L.E.M., 211 (THU0032), 489 (FRI0025), 493 (FRI0037)
van Maurik, A., 292 (THU0234)
Van Mens, L.J.J., 662 (FRI0464), 680 (FRI0505), 949 (SAT0464), 1086 (AB0114)
van Middelkoop, M., 973 (SAT0522, SAT0523)
Van Nie, L., 1071 (AB0069)
Van Nieuwkoop, L., 1552 (PARE0001)
Van Nimwegen, J.F., 591 (FRI0277), 1007 (SAT0617)
Van Onna, M., 429 (THU0590), 539 (FRI0152)
van Onna, M., 1221 (AB0488)
van Oosterhout, M., 1306 (AB0722)
van Osch, G., 769 (SAT0001)
Van Praet, L., 62 (OP0026)
van Riel, P., 434 (THU0604), 794 (SAT0070), 1505 (FRI0759-HPR)
van Riel, P.L.C.M., 1498 (FRI0740-HPR), 1525 (SAT0761-HPR)
van Rietbergen, B., 740 (FRI0662)
Van Roon, A.M., 625 (FRI0366), 630 (FRI0377), 1265 (AB0610)
van Roon, A.M., 625 (FRI0366), 630 (FRI0377), 1265 (AB0610)
van Roon, J.A., 181 (OP0303), 182 (OP0306), 288 (THU0223), 292 (THU0234), 295 (THU0241), 894 (SAT0324), 1089 (AB0121), 1206 (AB0446)
van Roon, J.A.G., 1104 (AB0165)
Van Royen-Kerkhof, A., 9 (SP0036)
van Schaardenburg, D., 124 (OP0173), 434 (THU0604), 811 (SAT0114), 817 (SAT0127), 1043 (SAT0708), 1145 (AB0277)
van Schaik, B., 123 (OP0172)
van Spil, W., 978 (SAT0536)
Van Spil, W.E., 963 (SAT0498), 964 (SAT0499)
van Spil, W.E., 433 (THU0603)
van Steenbergen, H., 473 (THU0702)
Van Steenbergen, H.W., 473 (THU0704)
van Steenbergen, H.W., 79 (OP0067), 82 (OP0073), 224 (THU0068), 743 (FRI0670), 803 (SAT0091)
van Steenbergen, L.N., 1040 (SAT0701)
Van Tok, M., 118 (OP0159)
van Tubergen, A., 57 (OP0017), 548 (FRI0179), 649 (FRI0430), 740 (FRI0662), 781 (SAT0037)
van Tunen, J., 972 (SAT0517)
van Tuyl, L., 434 (THU0604), 473 (THU0703), 1145 (AB0277)
van Veelen, P., 778 (SAT0030)
Van Vollenhoven, R., 15 (SP0060), 158 (OP0247), 567 (FRI0221)
van Vollenhoven, R., 69 (OP0045), 228 (THU0078), 601 (FRI0303)
van Vollenhoven, R.F., 822 (SAT0142), 864 (SAT0239)
van Voorthuizen, M., 637 (FRI0395)
Van Weelij, S., 1559 (PARE0022)
Van Weely, S., 1479 (THU0730-HPR)
van Weely, S., 1485 (THU0748-HPR)
Van Welden, S., 490 (FRI0029)
Váncsa, A., 1049 (AB0009)
Vandame, D., 78 (OP0064)
Vande Berg, B., 728 (FRI0633)
Vandecandelaere, M., 359 (THU0402)
Vandecasteele, E., 299 (THU0252)
VanderLugt, J.T., 370 (THU0430)
Vanderschueren, S., 1005 (SAT0612)
Vandervoort, N., 126 (OP0180)
Vanegas-García, A., 1092 (AB0129)
Vanegas-García, A.L., 308 (THU0275), 1239 (AB0538)
Vanesa, D., 906 (SAT0357)
Vanhoof, L., 157 (OP0245)
Vanier, A., 158 (OP0247)
Vanni, S., 52 (OP0006)
Vannozzi, L., 411 (THU0540), 711 (FRI0586)
Vantaggiato, E., 363 (THU0412), 671 (FRI0485), 940 (SAT0445), 1314 (AB0742)
Varan, Ö., 1216 (AB0472), 1260 (AB0598)
Varan, O., 608 (FRI0320)
Vardanyan, V., 1398 (AB0983)
Vardar Yağlı, N., 1531 (AB1198-HPR)
Varela Eirin, M., 1071 (AB0070)
Varga, E., 767 (FRI0731)
Varga, J., 202 (THU0006)
Vargas, A., 739 (FRI0660)
Vargas, D., 1257 (AB0590)
Vargas, F., 658 (FRI0453), 927 (SAT0413), 928 (SAT0414), 1286 (AB0667)
Vargas, J.I., 849 (SAT0202)
Vargas-Osorio, K., 1244 (AB0553)
Vargas-Santos, A.B., 1160 (AB0320)
Varjú, C., 1267 (AB0617)
Varkas, G., 62 (OP0026), 653 (FRI0440), 1305 (AB0716)
Varlamov, D., 640 (FRI0403)
Varlamova, T., 413 (THU0547)
Varna, A., 680 (FRI0504)
Varney, F., 265 (THU0168)
Vásárhelyi, Z., 780 (SAT0034)

Vasconcelos, C., 902 (SAT0346)
Vasile, D., 1540 (AB1224-HPR)
Vasile, M., 903 (SAT0347), 1057 (AB0029, AB0030)
Vasilev, G., 1048 (AB0005)
Vasiliev, V., 1237 (AB0531)
Vasiljeva, N., 1389 (AB0956)
Vasilkova, V., 1356 (AB0858)
Vasilyev, V., 424 (THU0578), 723 (FRI0621)
Vasireddy, S., 1494 (THU0771-HPR)
Vasques, J.I., 397 (THU0505)
Vasques, M., 826 (SAT0150)
Vasquez, A., 1132 (AB0239)
Vásquez, G., 308 (THU0275), 1239 (AB0538)
Vasquez, G., 1092 (AB0129)
Vasquez-Colon, R., 1233 (AB0522)
Vassilopoulos, D., 321 (THU0310), 559 (FRI0205), 836 (SAT0176), 1204 (AB0442), 1376 (AB0915)
Vastesaeger, N., 158 (OP0247)
Vaughan, D., 138 (OP0208), 972 (SAT0520)
Vax, E., 508 (FRI0082)
Vaz Patto, J., 1051 (AB0013), 1094 (AB0134)
Vazirpanah, N., 1109 (AB0178)
Vázquez, J., 326 (THU0326)
Vázquez, M., 1471 (AB1189)
Vazquez, V., 1259 (AB0595)
Vázquez del Mercado, M., 1161 (AB0321)
Vázquez Díaz, M., 642 (FRI0409), 696 (FRI0545), 697 (FRI0546), 698 (FRI0549), 701 (FRI0559), 1391 (AB0961)
Vázquez Lojo, A.I., 187 (OP0318-PARE)
Vazquez Mateo, C., 856 (SAT0219)
Vazquez Mellado, J., 363 (THU0411)
Vázquez-Del Mercado, M., 806 (SAT0100), 1075 (AB0083), 1164 (AB0330), 1169 (AB0345)
Vazquez-Del Mercado, M., 912 (SAT0374)
Vázquez-Martínez, A.L., 1286 (AB0668)
Vazquez-Mellado, J., 365 (THU0417), 1362 (AB0873)
Vazquez-Mosquera, M.E., 203 (THU0009), 936 (SAT0435), 978 (SAT0535)
Vazquez-Murillo, G., 1199 (AB0427)
Vázquez-Rodríguez, R., 586 (FRI0264)
Vázquez-Rodríguez, T., 556 (FRI0197)
Vázquez-Rodriguez, T., 550 (FRI0184)
Vázquez-Triñanes, C., 712 (FRI0589), 1252 (AB0576), 1400 (AB0988)
vd Berg, M., 1221 (AB0488)
vd Graaff, W., 676 (FRI0497)
Veale, D., 221 (THU0059)
Veale, D.J., 203 (THU0011), 321 (THU0312), 487 (FRI0020), 528 (FRI0126), 646 (FRI0421), 773 (SAT0013), 776 (SAT0021), 840 (SAT0183)
Vedin Balcı, N., 1321 (AB0759)
Veelken, H., 125 (OP0177)
Veenbrink, A., 123 (OP0170)
Vega, D., 1510 (SAT0718-HPR)
Vega, O., 262 (THU0162)
Vega-Cornejo, G., 75 (OP0058)
Vega-Hinojosa, O., 1453 (AB1137)
Vega-Morales, D., 425 (THU0581), 528 (FRI0126), 1054 (AB0023), 1410 (AB1015), 1448 (AB1122)
Vegas-Revenga, N., 75 (OP0059), 108 (OP0135), 251 (THU0134), 326 (THU0326), 405 (THU0526), 420 (THU0567), 569 (FRI0226), 718 (FRI0607), 742 (FRI0666), 1255 (AB0583, AB0584)
Vegas-revenga, N., 1116 (AB0197)
Végh, E., 469 (THU0694), 1049 (AB0009)
Vehmeijer, S.B., 967 (SAT0506)
Veillette, C., 1035 (SAT0688)
Veillon, R., 710 (FRI0584)
Veit, J.A., 356 (THU0395)
Vela, P., 68 (OP0042), 290 (THU0227), 550 (FRI0184), 556 (FRI0197), 557 (FRI0199), 614 (FRI0336), 843 (SAT0191), 946 (SAT0458)
Vela-Anero, A., 502 (FRI0063)
Velarde Ruiz Velasco, J.A., 1450 (AB1128)
Velasco-Ripoll, T., 1542 (AB1231-HPR)
Velásquez-Franco, C.J., 905 (SAT0354)
Velázquez, M., 308 (THU0275)
Velázquez Arce, C., 698 (FRI0549)
Velcheti, V., 51 (OP0003)
Veldhuijzen van Zanten, J.J., 764 (FRI0723), 1044 (SAT0712)
Velikova, T., 1106 (AB0170)
Velilla, J., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Velipaşalar, Ö., 716 (FRI0600)
Veljković, D., 1327 (AB0774)
Velloso, M.L., 728 (FRI0631), 1018 (SAT0643), 1417 (AB1036)
Velloso Feijoo, M.L., 1210 (AB0458), 1211 (AB0459)
Velmakin, S., 807 (SAT0103), 1158 (AB0314), 1175 (AB0364)
Velozo, E., 440 (THU0619)
Veltishchev, D., 249 (THU0127), 616 (FRI0343)
Venalis, A., 622 (FRI0359)
Vencovský, J., 209 (THU0027), 220 (THU0058), 564 (FRI0216), 1183 (AB0387)
Vencovsky, J., 137 (OP0204), 243 (THU0113), 440 (THU0621), 451 (THU0650), 638 (FRI0399), 834 (SAT0169), 906 (SAT0358), 912 (SAT0374), 1280 (AB0653), 1287 (AB0671), 1416 (AB1034)
Vender, R., 941 (SAT0446)
Venerito, V., 248 (THU0123), 1059 (AB0037), 1461 (AB1160)
Venetsanopoulou, A., 323 (THU0315)
Venhoff, A., 615 (FRI0339)
Venhoff, A.C., 332 (THU0341)
Venhoff, N., 324 (THU0321), 332 (THU0341), 615 (FRI0339)
Venkatachalam, S., 449 (THU0644)
Venn, A., 960 (SAT0489)
Ventura, D., 1194 (AB0413)
Ventura, F., 366 (THU0420)
Ventura, L., 739 (FRI0660)
Ventura Ríos, L., 1357 (AB0861)
Ventura-Rios, L., 1408 (AB1010)
Venturini, A., 899 (SAT0336)
Vera, M., 1339 (AB0805)
Vera Lastra, O., 421 (THU0568)
Vera-Lastra, O., 1255 (AB0585), 1282 (AB0657), 1401 (AB0991)
Vera-Navarrete, E.Y., 262 (THU0161)
Vera-Pineda, R., 253 (THU0140), 534 (FRI0141), 1118 (AB0204), 1156 (AB0309), 1157 (AB0310)
Veraar, C., 615 (FRI0338)
Verbeek, J.S., 497 (FRI0049)
Verbeek, S.J., 141 (OP0215)
Verde, M., 923 (SAT0401)
Verdegaal, S.H., 967 (SAT0506)
Verdet, M., 1378 (AB0923)
Verduci, E., 954 (SAT0473)
Vergara, F., 1115 (AB0194)
Vergara, J., 761 (FRI0715), 1456 (AB1146, AB1147)
Vergara Dangond, C., 1534 (AB1208-HPR)
Vergara-Dangond, C., 258 (THU0153), 1168 (AB0344), 1316 (AB0746), 1410 (AB1016), 1415 (AB1032)
Vergés, J., 178 (OP0294), 980 (SAT0540), 1557 (PARE0017)
Vergés, M.T., 1557 (PARE0017)
Vergés Milano, J., 761 (FRI0715), 1456 (AB1146, AB1147)
Vergne-Salle, P., 573 (FRI0234), 815 (SAT0123)
Vergroesen, R.D., 125 (OP0177)
Verhaar, J., 961 (SAT0492)
Verhelst, X., 763 (FRI0719)
Verheugen, E., 763 (FRI0719)
Verheul, M., 778 (SAT0030)
Verheul, M.K., 224 (THU0068)
Verhoeven, F., 417 (THU0558), 493 (FRI0039), 495 (FRI0044), 959 (SAT0486)
Veris, J., 676 (FRI0497), 1308 (AB0725)
Veris-van Dieren, J.J., 1325 (AB0770)
Verizhnikova, Z., 1411 (AB1018)
Verlaan, J.-J., 1423 (AB1052)
Verlaan, M., 494 (FRI0041), 1075 (AB0082)
Verma, A., 1072 (AB0075)
Verma, I., 301 (THU0258), 819 (SAT0133)
Verma, N., 1085 (AB0111)
Vernerová, L., 209 (THU0027)
Vernerova, L., 906 (SAT0358), 1280 (AB0653), 1287 (AB0671)
Vernier, N., 638 (FRI0398)
Vernuccio, A., 304 (THU0267)
Veroz Gonzalez, R., 1121 (AB0211), 1122 (AB0212)
Verra, M.L., 475 (THU0708)
Verschueren, P., 147 (OP0226), 158 (OP0247), 765 (FRI0726)
Versini, M., 1256 (AB0588)
Versnel, M.A., 92 (OP0097)
Verstappen, S., 186 (OP0317-PARE), 433 (THU0602), 437 (THU0613), 467 (THU0689), 763 (FRI0722), 803 (SAT0092)
Verstappen, S.M., 200 (THU0001), 265 (THU0168), 275 (THU0192), 391 (THU0488), 408 (THU0533), 765 (FRI0724)
Verstappen, S.M.M., 139 (OP0210-PARE), 146 (OP0225), 243 (THU0112)
Versteeg, G.A., 225 (THU0071)
Verstuyft, C., 549 (FRI0180)
Vervoort, V., 198 (OP0344-HPR)
Verweij, N., 724 (FRI0623), 1020 (SAT0650)
Verweij, S.L., 662 (FRI0464)
Veselinovic, M., 541 (FRI0158), 1552 (PARE0003)
Vesely, R., 17 (SP0069)
Vestergaard, A., 732 (FRI0641), 784 (SAT0045)
Vetrila, S., 1284 (AB0664)
Vettori, S., 621 (FRI0355), 915 (SAT0380), 1106 (AB0171)
Vial, G., 573 (FRI0234)
Viana, H., 590 (FRI0274), 1206 (AB0445)
Viapiana, O., 92 (OP0099), 363 (THU0412), 671 (FRI0485), 693 (FRI0535), 805 (SAT0097), 854 (SAT0215), 940 (SAT0445), 1062 (AB0045), 1124 (AB0216), 1200 (AB0429), 1207 (AB0449), 1314 (AB0742)
Viatte, S., 90 (OP0094)
Viceconti, A., 1483 (THU0741-HPR), 1539 (AB1223-HPR)
Vicedomini, L., 621 (FRI0355)
Vicens Bernabéu, E., 441 (THU0623)
Vicens Bernabeu, E., 291 (THU0229), 590 (FRI0275), 878 (SAT0279), 918 (SAT0388), 1039 (SAT0697), 1173 (AB0356), 1223 (AB0493), 1224 (AB0494), 1347 (AB0829), 1374 (AB0912), 1382 (AB0933), 1433 (AB1080), 1434 (AB1084)
Vicente, A., 1393 (AB0967)
Vicente, E.F., 1472 (AB1192)
Vicente, L.N., 1449 (AB1125)
Vicente, M., 1429 (AB1070)
Vicente-Rabaneda, E., 892 (SAT0316), 1107 (AB0172)
Victorino, G., 441 (THU0622)
Vidal, A., 1496 (FRI0735-HPR)
Vidal, B., 498 (FRI0051), 1080 (AB0098)
Vidal, J., 691 (FRI0529)
Vidal, M., 286 (THU0216)
Vidal-Puig, A., 194 (OP0336), 1078 (AB0092)
Vidal-Trecan, T., 382 (THU0461)
Videira, T., 1419 (AB1043)
Vidgen, B., 1453 (AB1138)
Vidqvist, K.-L., 1404 (AB0999)
Vieira, A.R., 834 (SAT0170)
Vieira, F.G.T., 991 (SAT0567)
Vieira, M.V., 628 (FRI0371)
Vieira, R., 1254 (AB0581), 1419 (AB1043)
Vieira-Sousa, E., 746 (FRI0678), 1317 (AB0750)
Viggiani, M.T., 1135 (AB0250)
Viktorova, T.V., 1049 (AB0008)
Vilas-Pio, B., 1409 (AB1012)
Vilchez-Ocaña, E., 1492 (THU0766-HPR), 1525 (SAT0760-HPR)
Viles I Lladó, E., 761 (FRI0715), 1456 (AB1146, AB1147)
Viljanen, J., 779 (SAT0031)
Villa, I., 843 (SAT0191)
Villa, P., 1154 (AB0301)
Villa Alcazar, L.F., 1399 (AB0986)
Villa Blanco, I., 1374 (AB0910)
Villa-Calderón, C., 1345 (AB0820)
Villalba, A., 501 (FRI0062), 551 (FRI0186), 559 (FRI0204), 822 (SAT0141), 833 (SAT0168), 1116 (AB0198), 1179 (AB0375), 1294 (AB0687), 1304 (AB0714)
Villalba, J.M., 1091 (AB0127)

Villalba Yllan, A., 824 (SAT0145)
Villalobos Sánchez, L., 587 (FRI0266)
Villanueva-Romero, R., 485 (FRI0016)
Villar, I., 593 (FRI0284)
Villar, M.J., 1146 (AB0279)
Villar-Gomez, A., 636 (FRI0392)
Villares, R., 645 (FRI0420)
Villarreal, A.V., 1395 (AB0974)
Villarreal, L., 162 (OP0257-HPR), 266 (THU0172), 427 (THU0585), 529 (FRI0127), 538 (FRI0150), 852 (SAT0210), 963 (SAT0496), 1441 (AB1103), 1479 (THU0729-HPR), 1534 (AB1207-HPR), 1540 (AB1225-HPR), 1543 (AB1235-HPR)
Villarreal-Alarcón, M.A., 1054 (AB0023)
Villaverde, I., 1252 (AB0576)
Villaverde García, V., 1244 (AB0553)
Villeneuve, É., 571 (FRI0230), 845 (SAT0195), 1188 (AB0397)
Villevalde, S., 807 (SAT0103), 1158 (AB0314), 1175 (AB0364)
Villiger, P., 626 (FRI0369)
Villiger, P.M., 569 (FRI0225), 1510 (SAT0717-HPR)
Villota Bello, A., 1347 (AB0829)
Vina, E.R., 474 (THU0707)
Vinall, L., 192 (OP0331)
Viñas, S., 502 (FRI0063)
Vinatzer, A., 971 (SAT0515)
Vincent, F., 63 (OP0029), 182 (OP0307)
Vincent, G.R., 119 (OP0164)
Vinci, C., 646 (FRI0423)
Vincken, K., 1020 (SAT0649)
Vincze, A., 911 (SAT0371)
Vinderslev Iversen, L., 1288 (AB0673)
Vinogradova, M., 1238 (AB0534)
Viola, D., 75 (OP0058)
Violani, C., 1378 (AB0924)
Viora, U.G., 1554 (PARE0008), 1557 (PARE0016), 1558 (PARE0019), 1560 (AB1251-PARE)
Vioulac, C., 1470 (AB1185)
Virasoro, B., 440 (THU0619)
Virta, L., 262 (THU0163)
Virviciute, D., 367 (THU0423)
Vis, M., 676 (FRI0497), 678 (FRI0500), 1058 (AB0033), 1308 (AB0725), 1324 (AB0769), 1325 (AB0770)
Visalli, E., 437 (THU0611), 1439 (AB1099)
Viscondi, J.Y.K., 1441 (AB1104)
Visman, I., 354 (THU0391), 659 (FRI0455), 928 (SAT0415)
Visman, I.M., 661 (FRI0461), 931 (SAT0421)
Visser, H.D., 483 (FRI0010)
Visser, J.A., 532 (FRI0136), 537 (FRI0147)
Visser, K., 8 (SP0030), 158 (OP0247)
Visser, M., 1488 (THU0755-HPR)
Visser, W., 123 (OP0170)
Visser-Noordegraaf, M.Y., 1555 (PARE0009)
Vissink, A., 67 (OP0040), 591 (FRI0277), 886 (SAT0302), 1007 (SAT0617)
Vital, E.M., 91 (OP0095), 152 (OP0235), 314 (THU0293), 869 (SAT0251), 987 (SAT0556), 1010 (SAT0624), 1019 (SAT0647)
Vitale, A., 411 (THU0540), 711 (FRI0586), 722 (FRI0618), 1461 (AB1160)
Vitaliti, A., 886 (SAT0301), 1229 (AB0509)
Vitiello, M., 1062 (AB0045), 1200 (AB0429)
Vitman, R., 1556 (PARE0012)
Vitolo, B., 56 (OP0015), 787 (SAT0053)
Vitorino, E., 746 (FRI0678)
Vittecoq, O., 63 (OP0029), 1186 (AB0395), 1378 (AB0923)
Vitters, E., 1057 (AB0031)
Vitters, E.L., 211 (THU0032)
Vivaldelli, E., 437 (THU0611), 1439 (AB1099)
Vivekanantham, A., 988 (SAT0559)
Vives, I., 1245 (AB0555), 1266 (AB0614)
Vives, M.J., 410 (THU0539), 721 (FRI0615), 1042 (SAT0706)
Vlachogiannis, N.I., 210 (THU0028), 1088 (AB0117)
Vlachoyiannopoulos, P.G., 210 (THU0028), 293 (THU0237), 323 (THU0315), 836 (SAT0176)
Vlad, V., 304 (THU0266), 876 (SAT0271), 881 (SAT0288), 1013 (SAT0631), 1025 (SAT0664), 1026 (SAT0665), 1221 (AB0487), 1278 (AB0647), 1428 (AB1068), 1460 (AB1158)
Vladimirov, S., 1019 (SAT0646), 1369 (AB0895)
Vlahos, B., 337 (THU0353), 350 (THU0382)
Vlasov, T.D., 810 (SAT0111)
Vliet Vlieland, T., 2 (SP0005), 46 (SP0192), 1343 (AB0817), 1479 (THU0730-HPR), 1485 (THU0748-HPR), 1486 (THU0750-HPR), 1559 (PARE0022)
Vliet Vlieland, T.P., 966 (SAT0505), 967 (SAT0506)
Vo, T., 958 (SAT0484)
Voelker, S., 115 (OP0151)
Vogelzang, E., 550 (FRI0183)
Vogetseder, A., 191 (OP0330)
Vogl, T., 89 (OP0091), 519 (FRI0104), 526 (FRI0120), 772 (SAT0010), 1023 (SAT0656)
Voicu, G., 881 (SAT0288)
Voidazan, S., 1440 (AB1101)
Voirin-Hertz, M., 1013 (SAT0632)
Voisin, A.-L., 51 (OP0004)
Vojinovic, J., 19 (SP0077), 245 (THU0116), 735 (FRI0649), 1015 (SAT0636)
Vojinovic, T., 1016 (SAT0639)
Volberg, C., 844 (SAT0193), 1187 (AB0396)
Volkava, M., 832 (SAT0166)
Volkmann, E., 106 (OP0129)
Volkmann, E.R., 87 (OP0085), 104 (OP0124)
Volkov, A., 256 (THU0148), 572 (FRI0231)
Volkov, Y., 1085 (AB0111)
Volkova, Y.A., 1189 (AB0402)
Voll, R., 92 (OP0099), 615 (FRI0339), 1100 (AB0153), 1425 (AB1058)
Voll, R.E., 240 (THU0105), 324 (THU0321), 332 (THU0341)
Vollenveider, C., 311 (THU0284), 464 (THU0681), 886 (SAT0302)
Volman, O., 675 (FRI0495)
Volpi, N., 86 (OP0082)
Voltan, G., 1558 (PARE0019)
Vomero, M., 489 (FRI0027), 490 (FRI0028), 496 (FRI0045), 1093 (AB0132), 1099 (AB0150), 1465 (AB1170)
von Bülow, C., 161 (OP0254-HPR)
von Kempis, J., 579 (FRI0247), 790 (SAT0059), 1144 (AB0273)
von Muehlenen, I., 267 (THU0174)
von Scheven, E., 391 (THU0490)
Vonk, M., 104 (OP0123), 1280 (AB0651, AB0652), 1286 (AB0669), 1492 (THU0764-HPR)
Vonk, M.C., 65 (OP0034), 1047 (AB0003), 1109 (AB0178)
Vonkeman, H., 1140 (AB0263), 1478 (THU0727-HPR)
Vonkeman, H.E., 225 (THU0071), 365 (THU0418)
Voogt-van der Harst, E.M., 907 (SAT0359)
Voorneveld-Nieuwenhuis, J.E., 1497 (FRI0739-HPR)
Vordenbäumen, S., 789 (SAT0056)
Voronova, T., 1341 (AB0812)
Vos, M., 1556 (PARE0014)
Vos, R., 494 (FRI0041), 1075 (AB0082)
Voskuyl, A., 184 (OP0310), 724 (FRI0623), 811 (SAT0114), 1020 (SAT0650)
Voskuyl, A.E., 604 (FRI0309), 732 (FRI0642), 1047 (AB0003)
Voulgarelis, M., 288 (THU0221)
Voulgari, P., 1243 (AB0551)
Voulgari, P.V., 1193 (AB0411), 1217 (AB0476), 1329 (AB0779)
Voumvourakis, K., 588 (FRI0269)
Vounotrypidis, P., 836 (SAT0176)
Vousden, K., 192 (OP0331)
Vrancianu, C., 435 (THU0607)
Vreju, F., 1013 (SAT0631)
Vriezekolk, J., 112 (OP0145-HPR), 198 (OP0344-HPR), 1488 (THU0757-HPR)
Vriezekolk, J.E., 39 (SP0163), 46 (SP0193), 110 (OP0138-HPR), 1487 (THU0752-HPR)
Vritzali, E., 77 (OP0063), 710 (FRI0585)
Vukatana, G., 366 (THU0420), 954 (SAT0473)
Vulcano, A., 1202 (AB0434), 1263 (AB0606)
Vullo, F., 230 (THU0082)
Vulsteke, J.-B., 636 (FRI0393)
Vural, N., 999 (SAT0595)
Vutcanu, O., 745 (FRI0676), 983 (SAT0547)
Vyatkin, Y., 202 (THU0007)

Wada, Y., 313 (THU0290)
Wade, S., 221 (THU0059), 487 (FRI0020), 646 (FRI0421), 773 (SAT0013)
Wadiwalla, A., 1505 (FRI0760-HPR)
Wadsack, D., 597 (FRI0294)
Wadström, H., 93 (OP0100)
Waehrens, E., 161 (OP0254-HPR)
Wæhrens, E., 1481 (THU0734-HPR)
Wagman, R.B., 54 (OP0010)
Waguri-Nagaya, Y., 1062 (AB0044)
Wahab, A.A., 1144 (AB0275)
Wähämaa, H., 212 (THU0036), 482 (FRI0006), 484 (FRI0013)
Wahinuddin, S., 1512 (SAT0722-HPR)
Wahlin, B., 250 (THU0129)
Wahren, M., 182 (OP0305)
Wahren-Herlenius, M., 309 (THU0280)
Wai, B., 377 (THU0447)
Waimann, C., 1425 (AB1060)
Waisberg, M.G., 1292 (AB0684)
Waite Jones, L., 776 (SAT0022)
Wakabayashi, H., 703 (FRI0566)
Wakabayashi, I., 707 (FRI0577), 1426 (AB1063)
Wakabayashi, K., 222 (THU0064), 894 (SAT0322)
Wakefield, R., 159 (OP0250), 518 (FRI0102)
Wakefield, R.J., 1016 (SAT0639)
Wakhlu, A., 1006 (SAT0614)
Waki, D., 115 (OP0152), 699 (FRI0553)
Wakiguchi, H., 1389 (AB0954)
Wakiya, R., 283 (THU0209), 719 (FRI0609), 757 (FRI0704), 907 (SAT0360), 1213 (AB0465)
Waldenlind, K., 537 (FRI0149)
Walder, M., 1445 (AB1114)
Waldheim, E., 1523 (SAT0755-HPR)
Walgreen, B., 211 (THU0032, THU0033)
Walitt, B., 45 (SP0186)
Walker, D., 515 (FRI0096), 1541 (AB1227-HPR)
Walker, K.M., 629 (FRI0375)
Walker, R., 383 (THU0464)
Walker, S., 370 (THU0432), 371 (THU0433)
Walker, U., 909 (SAT0366), 915 (SAT0380)
Walker, U.A., 626 (FRI0369), 710 (FRI0585), 1445 (AB1114)
Walker-Bone, K., 765 (FRI0724)
Walker-Bone, K.E., 933 (SAT0426)
Wall, O., 480 (FRI0001)
Wallace, D., 318 (THU0301)
Wallace, D.J., 150 (OP0232), 856 (SAT0219), 863 (SAT0236)
Wallace, J.L., 972 (SAT0520)
Wallace, S., 1407 (AB1007), 1462 (AB1163)
Wallace, Z.S., 711 (FRI0588)
Wallaert, B., 413 (THU0546), 1049 (AB0007)
Wållberg Jonsson, S., 113 (OP0147)
Wållberg-Jonsson, S., 248 (THU0125), 250 (THU0129)
Wallenius, M., 223 (THU0065), 1031 (SAT0677), 1032 (SAT0680), 1039 (SAT0698)
Wallenstein, G.V., 60 (OP0022)
Waller, J., 1507 (FRI0764-HPR)
Wallis, D., 933 (SAT0426), 1180 (AB0377)
Wallman, J., 1095 (AB0138)
Wallman, J.K., 157 (OP0246), 651 (FRI0436), 655 (FRI0445), 686 (FRI0518)
Walls, C.D., 512 (FRI0090)
Walsh, A.M., 203 (THU0011)
Walsh, D., 1028 (SAT0670)
Walsh, D.A., 752 (FRI0693), 782 (SAT0040)
Walsh, J., 143 (OP0219), 1301 (AB0707)
Walsh, J.A., 346 (THU0371), 688 (FRI0521), 945 (SAT0456)
Walsh, N., 1528 (SAT0769-HPR)
Wan, M.C., 412 (THU0543), 715 (FRI0599), 1125 (AB0221)
Wang, B., 865 (SAT0243)
Wang, B.C., 1511 (SAT0720-HPR)
Wang, C., 135 (OP0202), 141 (OP0216), 268 (THU0176), 384 (THU0469), 459 (THU0669), 676 (FRI0496), 682 (FRI0509), 724 (FRI0622), 829 (SAT0159), 853 (SAT0213),

938 (SAT0439), 947 (SAT0459), 951 (SAT0469), 995 (SAT0579), 1081 (AB0100), 1197 (AB0421)
Wang, D., 250 (THU0130), 866 (SAT0244, SAT0245), 1103 (AB0163), 1198 (AB0424)
Wang, F., 223 (THU0066), 1206 (AB0447)
Wang, G., 912 (SAT0374), 935 (SAT0432), 1226 (AB0501)
Wang, H., 834 (SAT0171), 1430 (AB1073), 1524 (SAT0757-HPR)
Wang, J., 69 (OP0043), 579 (FRI0248), 872 (SAT0261), 1503 (FRI0754-HPR), 1535 (AB1210-HPR)
Wang, K., 123 (OP0171), 133 (OP0197), 450 (THU0647)
Wang, L., 122 (OP0168), 148 (OP0230), 275 (THU0193), 277 (THU0197), 285 (THU0215), 324 (THU0318), 856 (SAT0220), 865 (SAT0243), 884 (SAT0294)
Wang, M., 57 (OP0017), 277 (THU0197), 294 (THU0238), 548 (FRI0179), 1516 (SAT0734-HPR)
Wang, Q., 189 (OP0325), 294 (THU0238), 581 (FRI0252), 583 (FRI0258), 858 (SAT0224), 883 (SAT0292), 981 (SAT0541), 995 (SAT0579), 1052 (AB0017), 1103 (AB0163)
Wang, R., 89 (OP0089)
Wang, S., 192 (OP0331), 1206 (AB0447)
Wang, W., 857 (SAT0222), 862 (SAT0235), 1226 (AB0501)
Wang, X., 156 (OP0243), 232 (THU0087), 234 (THU0091), 351 (THU0384), 353 (THU0388), 517 (FRI0100), 668 (FRI0479), 785 (SAT0047), 859 (SAT0227), 962 (SAT0493), 1109 (AB0180), 1226 (AB0502), 1535 (AB1210-HPR)
Wang, X.-Q., 1084 (AB0110)
Wang, Y., 142 (OP0218), 310 (THU0281), 336 (THU0351), 460 (THU0672), 547 (FRI0176), 601 (FRI0304), 919 (SAT0392), 934 (SAT0429), 1524 (SAT0757-HPR)
Wang, Y.Y., 935 (SAT0432)
Wang, Z., 310 (THU0281), 1329 (AB0780)
Wangkaew, S., 908 (SAT0362)
Wannick, M., 893 (SAT0320)
Ward, M.M., 1129 (AB0232)
Ware, M., 523 (FRI0115)
Warner, M., 965 (SAT0502)
Warner, R., 605 (FRI0314)
Warner, S., 1028 (SAT0670)
Warren, D.J., 472 (THU0700)
Warren, R.B., 201 (THU0004), 1087 (AB0115)
Warrier, K., 407 (THU0531)
Warrington, K.J., 609 (FRI0323), 613 (FRI0332), 750 (FRI0686, FRI0687)
Wasén, C., 779 (SAT0033)
Wassenberg, S., 356 (THU0394), 530 (FRI0130), 558 (FRI0203), 565 (FRI0217), 829 (SAT0159)
Wassmer, E., 1395 (AB0972)
Watad, A., 84 (OP0078), 319 (THU0304), 332 (THU0342), 619 (FRI0350)
Watanabe, E., 618 (FRI0347)
Watanabe, S., 618 (FRI0347)
Watanabe, T., 1195 (AB0415)
Waterborg, C.E.J., 489 (FRI0025), 493 (FRI0037)
Waterton, J., 1023 (SAT0657)
Watfeh, R., 1358 (AB0862), 1365 (AB0883, AB0884, AB0885)
Watson, K., 555 (FRI0196)
Watson, Y., 1023 (SAT0657)
Watts, N., 72 (OP0051)
Watts, R., 605 (FRI0312)
Watts, R.A., 319 (THU0305)
Wautier, S., 863 (SAT0238)
Wax, S., 863 (SAT0236)
Waxman, R., 1541 (AB1227-HPR)
Webb, K., 389 (THU0484)
Webber, S., 1320 (AB0758)
Weber, J.M., 465 (THU0683), 1463 (AB1166)
Weber, U., 101 (OP0117), 130 (OP0189)
Webers, C., 157 (OP0245)
Wechalekar, A., 227 (THU0076)
Wechalekar, M., 458 (THU0667)
Wechalekar, M.D., 203 (THU0011)
Wechsler, M.E., 107 (OP0130)
Wedderburn, L., 177 (OP0291)
Wedderburn, L.R., 912 (SAT0374)
Weel, A., 1306 (AB0722)
Weel, A.E.A.M., 1421 (AB1047)
Wegdan, A.A., 1053 (AB0018)
Wei, H., 547 (FRI0176), 1206 (AB0447), 1524 (SAT0757-HPR)
Wei, J., 1338 (AB0802)
Wei, J.C., 357 (THU0397)
Wei, P., 207 (THU0021), 1141 (AB0264)
Wei, Q., 664 (FRI0469), 665 (FRI0471), 934 (SAT0431)
Wei, W., 769 (SAT0001)
Wei, X., 393 (THU0495)
Wei, X.-N., 279 (THU0201), 373 (THU0439)
Weigt, G., 1200 (AB0430)
Weijers, J., 1505 (FRI0759-HPR)
Weijers, R., 740 (FRI0662)
Weinans, H., 483 (FRI0010)
Weinberg, S., 1466 (AB1173)
Weinblatt, M., 92 (OP0098), 136 (OP0203), 575 (FRI0239), 782 (SAT0041), 846 (SAT0197), 1120 (AB0207)
Weinblatt^, M., 564 (FRI0216)
Weinstein, A., 150 (OP0232)
Weiß, A., 302 (THU0261)
Weiss, J., 448 (THU0641)
Weiss, J.E., 396 (THU0503)
Weiss, K., 1445 (AB1115)
Weiß, K., 1239 (AB0539)
Weiss, P.F., 469 (THU0693), 471 (THU0697)
Weiswasser, M., 858 (SAT0225), 870 (SAT0255)
Weitoft, T., 509 (FRI0085)
Weitzman, D., 169 (OP0273)
Welcker, M., 1440 (AB1100), 1444 (AB1112)
Welin Henriksson, E., 1523 (SAT0755-HPR)
Welle, S., 185 (OP0313)
Weller, H., 430 (THU0592)
Weller, P.F., 107 (OP0130)
Weller-Heinemann, F., 398 (THU0507)
Wells, A., 684 (FRI0513)
Wells, A.F., 1222 (AB0489)
Wells, A.U., 1266 (AB0613)
Wells, C., 133 (OP0197)
Welsing, P., 433 (THU0603)
Welsing, P.M., 855 (SAT0218), 964 (SAT0499)
Welting, T., 977 (SAT0531)
Welzel, A., 115 (OP0151)
Wemeau-Stervinou, L., 1049 (AB0007)
Wen, H., 1197 (AB0422)
Wen, H.Y., 1204 (AB0440)
Wen, Y., 499 (FRI0056), 1241 (AB0545), 1291 (AB0680)
Wendler, J., 159 (OP0249), 516 (FRI0098), 1322 (AB0763)
Wendling, D., 417 (THU0558), 428 (THU0588, THU0589), 495 (FRI0044), 959 (SAT0486), 1303 (AB0712)
Wenglén, C., 891 (SAT0314)
Wenisch, S., 1070 (AB0067)
Wermeling, F., 864 (SAT0239)
Wermuth, P., 91 (OP0096)
Werneburg, B., 857 (SAT0222)
Werner, D., 1011 (SAT0628)
Werner, J., 1070 (AB0067)
Werner, S., 400 (THU0512), 1008 (SAT0618)
Werner, S.G., 74 (OP0057)
Werth, V., 858 (SAT0225)
Werth, V.P., 857 (SAT0222), 870 (SAT0255)
Wervers, K., 676 (FRI0497), 678 (FRI0500), 1308 (AB0725), 1324 (AB0769), 1325 (AB0770)
Werz, O., 115 (OP0151)
West, R., 1070 (AB0066)
West, R.M., 613 (FRI0334)
Westbrook, S., 127 (OP0182)
Westerlind, H., 228 (THU0077), 1037 (SAT0692), 1038 (SAT0694)
Westhovens, R., 147 (OP0226), 148 (OP0229), 267 (THU0173), 281 (THU0206), 476 (THU0712), 566 (FRI0219), 636 (FRI0393), 765 (FRI0726), 1275 (AB0638), 1310 (AB0732), 1488 (THU0757-HPR), 1501 (FRI0750-HPR)
Westmoreland, S., 288 (THU0222), 492 (FRI0034)
Westra, J., 308 (THU0276), 607 (FRI0317)
Whallett, M., 518 (FRI0101)
Wheeler, K.H., 172 (OP0280-PARE)
Whelan, C., 227 (THU0076), 1427 (AB1064)
Whist, J.E., 1309 (AB0730)
White, B., 105 (OP0126)
White, P., 1508 (FRI0767-HPR)
White, W., 856 (SAT0220)
White, W.B., 375 (THU0444)
Whitfield, M., 621 (FRI0356)
Whittle, R., 751 (FRI0690), 1028 (SAT0672)
Wiatr, T., 663 (FRI0466)
Wibetoe, G., 802 (SAT0090), 1029 (SAT0673)
Wibowo, T., 800 (SAT0083)
Wichers, C.G.K., 1109 (AB0178)
Widdifield, J., 749 (FRI0684)
Widmer, A., 358 (THU0398)
Wiebe, E., 129 (OP0187), 446 (THU0637)
Wiebe, S., 1185 (AB0391)
Wiebert, P., 248 (THU0124)
Wieczorek, A., 1224 (AB0496)
Wieczorek, M., 970 (SAT0513)
Wiedmeyer, C., 448 (THU0643), 449 (THU0645), 1177 (AB0370)
Wiegant, K., 978 (SAT0536)
Wielage, R., 599 (FRI0298)
Wielosz, E., 1273 (AB0631)
Wiemkes, M., 124 (OP0174)
Wierød, A., 334 (THU0345), 673 (FRI0490)
Wiesenhutter, C., 232 (THU0086)
Wigers, S., 161 (OP0255-HPR)
Wigginton, J., 777 (SAT0027)
Wigler, I., 747 (FRI0679)
Wijeysundera, D.N., 103 (OP0122)
Wijnant, S., 299 (THU0252)
Wiland, P., 464 (THU0681), 824 (SAT0146), 1470 (AB1184)
Wilburn, J., 1314 (AB0741)
Wilcke, C., 426 (THU0582)
Wilder, T., 128 (OP0186)
Wildi, L., 130 (OP0189), 335 (THU0347), 625 (FRI0365)
Wilding, J., 852 (SAT0209)
Wilhelm, L., 81 (OP0072-PARE)
Wilhelmer, T., 1552 (PARE0001), 1557 (PARE0015)
Wilhelms, E., 453 (THU0654, THU0655)
Wilke, W.S., 386 (THU0473)
Wilkes, S., 265 (THU0168)
Wilkie, R., 958 (SAT0483)
Wilkins, J., 1117 (AB0199)
Wilkinson, B., 268 (THU0175)
Will, R., 960 (SAT0487)
Willemijns, S., 1501 (FRI0750-HPR)
Willemze, A., 35 (SP0141)
Williams, A., 1050 (AB0011)
Williams, A.S., 208 (THU0025), 1173 (AB0358)
Williams, G., 938 (SAT0439)
Williams, J.O., 208 (THU0025)
Williams, N., 355 (THU0393), 675 (FRI0494)
Williams, R.O., 770 (SAT0005)
Williamson, L., 1553 (PARE0004)
Williamson, P., 463 (THU0677)
Willig, J., 448 (THU0643), 449 (THU0645)
Willisch-Domínguez, A., 946 (SAT0458)
Wilson, A.G., 200 (THU0001, THU0002), 204 (THU0014)
Wilson, L., 609 (FRI0321)
Wilson, N., 760 (FRI0713), 1440 (AB1102)
Wimalasundera, S., 133 (OP0197), 396 (THU0503)
Wincup, C., 304 (THU0265)
Wind, S., 642 (FRI0411)
Windels, F., 490 (FRI0029)
Windhorst, A., 1020 (SAT0650)
Windhorst, A.D., 494 (FRI0041)
Windschall, D., 175 (OP0288), 1015 (SAT0636)
Wink, F., 649 (FRI0430), 650 (FRI0433), 928 (SAT0416)
Winkle, P., 371 (THU0434), 1364 (AB0880)
Winkler-Rohlfing, B., 1449 (AB1127)
Winteler, B., 475 (THU0708)
Winter, D.R., 1125 (AB0220)

Winthrop, K., 93 (OP0101), 267 (THU0173), 676 (FRI0496), 938 (SAT0439)
Winthrop, K.L., 148 (OP0230), 158 (OP0248)
Winzenberg, T., 450 (THU0647), 962 (SAT0493), 986 (SAT0555)
Wipff, J., 56 (OP0014)
Wirtz, D., 193 (OP0333), 911 (SAT0372)
Wirtz, D.S., 893 (SAT0319), 1007 (SAT0616)
Wise, B., 1338 (AB0802)
Wisniacki, N., 209 (THU0026)
Witowski, J., 1119 (AB0206)
Witt, C., 960 (SAT0488)
Witt, S., 510 (FRI0086)
Witt, S.L., 512 (FRI0090)
Witte, T., 193 (OP0333), 666 (FRI0475), 667 (FRI0476), 1007 (SAT0616), 1047 (AB0003), 1050 (AB0010)
Wittenberg, G.M., 250 (THU0130)
Wittmann, M., 91 (OP0095), 152 (OP0235), 314 (THU0293), 771 (SAT0007), 1019 (SAT0647)
Wittoek, R., 43 (SP0179), 736 (FRI0650)
Wluka, A., 962 (SAT0493)
Wofsy, D., 50 (OP0002), 864 (SAT0240)
Wohlfahrt, T., 892 (SAT0318)
Wojtala, P., 276 (THU0194)
Wojteczek, A., 895 (SAT0327)
Wolbink, G., 550 (FRI0183)
Wolbink, G.J., 61 (OP0025), 758 (FRI0707), 935 (SAT0433)
Wolf, A.M., 185 (OP0313)
Wolfe, B.A., 822 (SAT0142)
Wolff, B., 754 (FRI0698)
Wolff, D., 754 (FRI0698)
Wollenhaupt, J., 92 (OP0099), 275 (THU0193), 277 (THU0197), 683 (FRI0512), 684 (FRI0513), 936 (SAT0436), 942 (SAT0448), 1316 (AB0747), 1331 (AB0785)
Wollman, J., 747 (FRI0679), 1118 (AB0203), 1328 (AB0776)
Won, S., 882 (SAT0290)
Wong, B., 1241 (AB0542)
Wong, D., 1241 (AB0542)
Wong, H., 981 (SAT0541)
Wong, K.T., 956 (SAT0479)
Wong, K.Y., 1541 (AB1229-HPR)
Wong, P., 1198 (AB0424)
Wong, P.C.H., 689 (FRI0524), 796 (SAT0073), 1520 (SAT0747-HPR)
Wong, P.K., 429 (THU0591)
Wong, R., 75 (OP0058)
Wood, J., 1514 (SAT0728-HPR)
Woodiwiss, A., 252 (THU0136), 545 (FRI0170)
Woodiwiss, A.J., 245 (THU0117)
Woodworth, T., 463 (THU0677), 470 (THU0695), 818 (SAT0132)
Woodworth, T.G., 1526 (SAT0765-HPR)
Woolcott, J., 443 (THU0628), 558 (FRI0201), 832 (SAT0165)
Woolf, A., 134 (OP0199-PARE), 760 (FRI0713), 1440 (AB1102)
Worm, M., 1106 (AB0169), 1110 (AB0181)
Woronoff, M.-C., 434 (THU0605), 754 (FRI0699), 1033 (SAT0684), 1034 (SAT0685)
Worthington, J., 179 (OP0298), 1047 (AB0003)
Wouters, A., 148 (OP0230)
Wouters, C., 75 (OP0058), 133 (OP0197)
Wraith, D.C., 36 (SP0151)
Wright, A., 960 (SAT0487)
Wright, K., 1125 (AB0220)
Wright, S., 691 (FRI0528)
Wu, B., 1516 (SAT0734-HPR)
Wu, D., 420 (THU0566)
Wu, H., 217 (THU0048), 1491 (THU0762-HPR), 1516 (SAT0734-HPR)
Wu, J., 951 (SAT0469), 1335 (AB0794)
Wu, M., 600 (FRI0301), 624 (FRI0363), 1206 (AB0447)
Wu, Q., 285 (THU0215)
Wu, R., 547 (FRI0176), 1042 (SAT0707), 1185 (AB0390), 1516 (SAT0734-HPR)
Wu, T., 668 (FRI0479)
Wu, W.-S., 1511 (SAT0720-HPR)
Wu, X., 69 (OP0043), 724 (FRI0622), 869 (SAT0252), 1086 (AB0113), 1260 (AB0596)
Wu, Y., 293 (THU0235), 366 (THU0421), 1097 (AB0145)
Wu, Z., 459 (THU0669), 547 (FRI0176)
Wuhrer, M., 509 (FRI0083)
Wulffraat, N., 448 (THU0641), 478 (THU0716)
Wulffraat, N.M., 42 (SP0175)
Wunderlin, A., 87 (OP0086)
Wurmann, P., 1108 (AB0176), 1257 (AB0590)

Xavier, R., 847 (SAT0199)
Xavier, R.M., 246 (THU0119), 403 (THU0520), 502 (FRI0066), 628 (FRI0371), 1107 (AB0174), 1278 (AB0645), 1391 (AB0960), 1508 (FRI0768-HPR)
Xhaxho, D., 1514 (SAT0729-HPR), 1522 (SAT0752-HPR)
Xia, P., 1480 (THU0732-HPR)
Xia, Y., 1370 (AB0897, AB0898)
Xiao, C., 1516 (SAT0734-HPR)
Xiao, F., 543 (FRI0163), 547 (FRI0176), 1141 (AB0266), 1491 (THU0762-HPR), 1516 (SAT0734-HPR), 1524 (SAT0757-HPR)
Xiao, H., 547 (FRI0176), 1491 (THU0762-HPR), 1516 (SAT0734-HPR), 1524 (SAT0757-HPR)
Xiao, X., 759 (FRI0710)
Xiao-Feng, L., 839 (SAT0181)
Xiao-Qing, L., 839 (SAT0181)
Xiao-Wen, M., 839 (SAT0181)
Xiao-Yan, W., 839 (SAT0181)
Xiaofeng, L., 348 (THU0377)
Xiaomei, C., 738 (FRI0657), 1407 (AB1008)
Xiaoyan, Y., 1480 (THU0732-HPR)
Xibillé, D.X., 1343 (AB0815)
Xibillé-Friedmann, D.-X., 498 (FRI0052)
Xie, H., 373 (THU0440)
Xie, J., 1226 (AB0502), 1295 (AB0691)
Xie, L., 510 (FRI0087), 515 (FRI0096), 562 (FRI0211), 789 (SAT0058), 795 (SAT0072), 836 (SAT0175)
Xie, Z., 268 (THU0175)
Xin, X., 1524 (SAT0757-HPR)
Xiong, X., 192 (OP0331)
Xu, B., 779 (SAT0031)
Xu, D., 63 (OP0028), 869 (SAT0252), 947 (SAT0459)
Xu, H., 116 (OP0155), 336 (THU0351), 459 (THU0669)
Xu, J., 748 (FRI0681), 759 (FRI0710), 1081 (AB0099), 1198 (AB0424)
Xu, K., 419 (THU0563), 748 (FRI0681), 1079 (AB0094), 1082 (AB0103), 1138 (AB0257), 1249 (AB0568), 1290 (AB0679), 1363 (AB0877)
Xu, L., 1082 (AB0102)
Xu, S., 460 (THU0672)
Xu, X., 1058 (AB0033), 1491 (THU0762-HPR)
Xu, X.L., 142 (OP0218)
Xuan, W., 223 (THU0066)
Xue, J., 1524 (SAT0757-HPR)
Xue, Z., 770 (SAT0005)
Xuechan, H., 1480 (THU0732-HPR)
Xumian, L., 1480 (THU0732-HPR)

Yabe, H., 618 (FRI0347)
Yabe, Y., 582 (FRI0254)
Yaga, M., 800 (SAT0083)
Yağcı, I., 821 (SAT0139)
Yagci, I., 1405 (AB1003)
Yaghi, N.A., 1042 (SAT0705)
Yagi, N., 1464 (AB1169)
Yagız, B., 1434 (AB1086)
Yagüe, J., 840 (SAT0184)
Yagur, V., 1240 (AB0541)
Yajima, N., 800 (SAT0085), 801 (SAT0086), 1138 (AB0258), 1242 (AB0547)
Yakupova, S., 1356 (AB0857)
Yalcin, A.G., 1297 (AB0698)
Yalçin, A.P., 1321 (AB0762)
Yalcın, B., 1162 (AB0324)
Yalcinbayir, O., 722 (FRI0616)
Yalcinkaya, G., 1531 (AB1197-HPR), 1532 (AB1201-HPR)
Yalçınkaya, Y., 644 (FRI0416), 821 (SAT0139), 889 (SAT0310), 910 (SAT0367), 1013 (SAT0633), 1310 (AB0731)
Yaliman, A., 1347 (AB0827)
Yamada, H., 115 (OP0152), 487 (FRI0022), 507 (FRI0080), 635 (FRI0391), 699 (FRI0553), 910 (SAT0369)
Yamada, K., 425 (THU0579), 711 (FRI0587), 722 (FRI0617), 1242 (AB0546)
Yamada, S., 279 (THU0199), 298 (THU0251), 788 (SAT0054), 1288 (AB0672)
Yamada, Y., 260 (THU0157), 1178 (AB0373)
Yamagami, T., 1062 (AB0044)
Yamagata, K., 491 (FRI0031)
Yamaguchi, R., 263 (THU0165), 524 (FRI0117), 798 (SAT0079), 814 (SAT0120)
Yamaguchi, Y., 800 (SAT0083)
Yamaji, K., 141 (OP0214), 1060 (AB0038), 1095 (AB0139, AB0140)
Yamamoto, A., 371 (THU0433)
Yamamoto, K., 2 (SP0004), 383 (THU0464), 1200 (AB0431)
Yamamoto, T., 202 (THU0006)
Yamamoto, W., 115 (OP0152), 282 (THU0207)
Yamamoto, Y., 699 (FRI0553)
Yamamura, M., 605 (FRI0313), 1251 (AB0572)
Yamamura, Y., 605 (FRI0313), 1251 (AB0572)
Yamanaka, H., 263 (THU0165), 264 (THU0166), 274 (THU0191), 280 (THU0204), 524 (FRI0117), 561 (FRI0210), 798 (SAT0079), 814 (SAT0120), 841 (SAT0186), 1026 (SAT0667), 1069 (AB0065)
Yamaoka, K., 326 (THU0325), 501 (FRI0060), 544 (FRI0168), 712 (FRI0590, FRI0591), 747 (FRI0680), 1021 (SAT0652), 1078 (AB0091), 1097 (AB0146)
Yamasaki, H., 1424 (AB1056)
Yamasaki, Y., 910 (SAT0369)
Yamashita, H., 298 (THU0251), 788 (SAT0054), 1288 (AB0672)
Yamashita, N., 1024 (SAT0661)
Yamashita, T., 88 (OP0087)
Yamauchi, T., 211 (THU0031)
Yamazaki, R., 531 (FRI0134), 1291 (AB0681)
Yamei, S., 738 (FRI0657)
Yan, L., 499 (FRI0056), 903 (SAT0349), 1241 (AB0545), 1291 (AB0680)
Yan, M., 1290 (AB0679)
Yan, T., 488 (FRI0023)
Yan, X., 371 (THU0434), 1364 (AB0880)
Yanagawa, M., 1467 (AB1176)
Yanagida, H., 202 (THU0006)
Yanagida, T., 314 (THU0294), 598 (FRI0297)
Yanagihara, K., 486 (FRI0017)
Yancey, S.W., 107 (OP0130)
Yang, H.I., 1185 (AB0392)
Yang, J., 1524 (SAT0757-HPR)
Yang, J.S., 935 (SAT0432)
Yang, M., 294 (THU0239), 459 (THU0669), 497 (FRI0050), 664 (FRI0470), 665 (FRI0471), 692 (FRI0532), 934 (SAT0431), 1467 (AB1175)
Yang, S., 448 (THU0643), 449 (THU0645)
Yang, T., 1338 (AB0802)
Yang, X., 104 (OP0125), 336 (THU0351), 370 (THU0430, THU0432)
Yang, Y., 298 (THU0250), 1290 (AB0679), 1338 (AB0802), 1535 (AB1210-HPR)
Yang, Z.-H., 798 (SAT0078)
Yano, K., 799 (SAT0082), 1063 (AB0047)
Yao, G., 1052 (AB0017), 1092 (AB0130), 1103 (AB0163)
Yao, H., 268 (THU0176)
Yao, T., 1480 (THU0732-HPR)
Yao, X.-T., 777 (SAT0027)
Yao, Z., 1271 (AB0627)
Yaowmaneerat, T., 1378 (AB0922)
Yap, E.M.L., 878 (SAT0280)
Yap, M., 778 (SAT0029)
Yargucu, F., 354 (THU0389)
Yargucu Zihni, F., 899 (SAT0338)
Yarkan, H., 322 (THU0314)
Yarkan Tugsal, H., 306 (THU0271), 1282 (AB0658)
Yarwood, A., 177 (OP0291), 179 (OP0298)
Yaşar Bilge, N.S., 387 (THU0478)
Yaseen, K., 386 (THU0473)

Yashima, A., 298 (THU0251), 788 (SAT0054)
Yasuda, N., 211 (THU0031), 842 (SAT0187)
Yasuda, S., 598 (FRI0295), 624 (FRI0364), 1453 (AB1139)
Yasumura, M., 923 (SAT0400)
Yasuoka, H., 501 (FRI0060), 620 (FRI0354), 623 (FRI0361), 712 (FRI0590, FRI0591), 901 (SAT0343), 1021 (SAT0652), 1078 (AB0091)
Yates, M., 1030 (SAT0676), 1039 (SAT0699)
Yatskiu, H.A., 389 (THU0485)
Yatsyshyn, R., 1201 (AB0433)
Yavne, Y., 332 (THU0342), 619 (FRI0350)
Yavuz, S., 1420 (AB1046)
Yayla, E., 606 (FRI0315)
Yayla, M.E., 1124 (AB0218), 1244 (AB0554)
Yazdany, J., 79 (OP0068), 432 (THU0600), 759 (FRI0711), 1435 (AB1087)
Yazici, A., 598 (FRI0296), 634 (FRI0386)
Yazıcı, A., 327 (THU0329)
Yazici, C., 659 (FRI0457)
Yazici, H., 331 (THU0339), 603 (FRI0307), 618 (FRI0348), 619 (FRI0351), 1243 (AB0550)
Yazıcı, H., 323 (THU0317)
Yazici, Y., 121 (OP0166), 233 (THU0089), 562 (FRI0211), 836 (SAT0175), 971 (SAT0516), 984 (SAT0549), 985 (SAT0552), 1003 (SAT0607), 1130 (AB0233), 1301 (AB0707)
Yázigi, F.G., 1553 (PARE0005)
Yazisiz, V., 1066 (AB0057)
Yazısız, V., 296 (THU0243)
Ybáñez García, D., 1490 (THU0761-HPR), 1534 (AB1208-HPR)
Ybáñez-García, A., 1316 (AB0746)
Ybañez-Garcia, A., 1472 (AB1191)
Ybáñez-García, D., 258 (THU0153), 1410 (AB1016), 1415 (AB1032)
Ybañez-Garcia, D., 1168 (AB0344)
Ybañez-García, M., 477 (THU0713)
Ye, J., 174 (OP0284), 233 (THU0089), 240 (THU0104), 566 (FRI0219), 782 (SAT0041), 951 (SAT0468), 1135 (AB0248)
Ye, S., 621 (FRI0358)
Ye, W., 943 (SAT0449)
Ye, X., 797 (SAT0076)
Ye, Y., 858 (SAT0225), 957 (SAT0481)
Yedimenko, J., 1099 (AB0151)
Yeker, R., 913 (SAT0376)
Yelin, E., 1435 (AB1087)
Yelin, E.H., 432 (THU0600)
Yelnik, C.M., 152 (OP0236), 823 (SAT0144)
Yeo, A., 365 (THU0416), 373 (THU0438), 377 (THU0448, THU0449), 1368 (AB0892)
Yeremenko, N.G., 1086 (AB0114)
Yeruva, K., 613 (FRI0332)
Yesil, H., 475 (THU0709), 992 (SAT0570), 1162 (AB0324)
Yeşildal, E., 977 (SAT0532), 1340 (AB0808)
Yesim, A., 1172 (AB0353)
Yeter, H.G., 791 (SAT0063)
Yetterberg, J., 1081 (AB0101)
Yeung, C., 418 (THU0561)
Yeung, J., 933 (SAT0428)
Yeung, W.Y., 644 (FRI0415)
Yi, E., 877 (SAT0274)
Yiğit, M., 327 (THU0329)
Yıldırım Çetin, G., 327 (THU0329)
Yildiz, A., 1476 (THU0722-HPR), 1537 (AB1216-HPR)
Yıldız, A.I., 1514 (SAT0727-HPR)
Yildiz, F., 609 (FRI0322)
Yildiz, I., 1324 (AB0767)
Yilmaz, D.D., 1274 (AB0634)
Yilmaz, G., 1321 (AB0762)
Yilmaz, H., 1521 (SAT0749-HPR)
Yilmaz, N., 1420 (AB1046)
Yilmaz, S., 352 (THU0385), 354 (THU0389), 412 (THU0544), 609 (FRI0322), 1297 (AB0698)
Yılmaz, S., 931 (SAT0422)
Yilmaz Kaysin, M., 999 (SAT0595)
Yılmaz Öner, S., 327 (THU0329), 1360 (AB0868)
Yılmaz-Öner, S., 716 (FRI0600), 1170 (AB0350)
Yim, I.C.-W., 1520 (SAT0747-HPR)
Yim, I.C.W., 796 (SAT0073)
Yin, R., 1368 (AB0893), 1369 (AB0894), 1370 (AB0897, AB0898, AB0899)
Yin, X., 203 (THU0011)
Ying, J., 624 (FRI0363)
Yip, C., 1035 (SAT0688)
Yip, M.L., 706 (FRI0576), 998 (SAT0591), 1520 (SAT0747-HPR)
Yixuan, C., 214 (THU0040), 1069 (AB0063)
Yli-Kerttula, T., 61 (OP0024)
Yokogawa, N., 525 (FRI0119), 1176 (AB0367)
Yokota, E., 1424 (AB1056)
Yokota, T., 422 (THU0571), 1398 (AB0981)
Yokoyama, Y., 210 (THU0030), 1288 (AB0674)
Yoldi, B., 1406 (AB1004)
Yoneda, K., 282 (THU0208)
Yoneda, T., 841 (SAT0186)
Yonekura, K., 507 (FRI0079)
Yonemoto, Y., 493 (FRI0036), 1203 (AB0439)
Yoo, B., 549 (FRI0181), 606 (FRI0316), 1093 (AB0133), 1222 (AB0491)
Yoo, D., 430 (THU0594), 1473 (AB1193)
Yoo, D.H., 548 (FRI0178), 824 (SAT0146), 1061 (AB0040)
Yoo, J., 1131 (AB0236)
Yoo, S.-J., 888 (SAT0307), 1259 (AB0593)
Yoo, W.-H., 482 (FRI0007)
Yoon, B.Y., 1528 (SAT0768-HPR)
Yoong, P., 1309 (AB0729)
Yorio, M.A., 1220 (AB0484, AB0485)
Yoshida, A., 220 (THU0057), 1452 (AB1133)
Yoshida, K., 499 (FRI0054), 565 (FRI0218), 1424 (AB1056)
Yoshida, M., 1345 (AB0822)
Yoshida, S., 115 (OP0152), 282 (THU0207)
Yoshida, Y., 1460 (AB1159)
Yoshifuji, H., 202 (THU0006), 220 (THU0057), 527 (FRI0122), 618 (FRI0349), 620 (FRI0352), 1452 (AB1133)
Yoshiga, Y., 507 (FRI0079)
Yoshii, I., 536 (FRI0145), 809 (SAT0107), 1126 (AB0224), 1127 (AB0225), 1349 (AB0835)
Yoshii, N., 274 (THU0191), 1200 (AB0431)
Yoshikawa, M., 137 (OP0205), 257 (THU0149)
Yoshimi, R., 265 (THU0170), 602 (FRI0305), 645 (FRI0419), 1195 (AB0416)
Yoshimine, Y., 800 (SAT0083)
Yoshimoto, K., 219 (THU0055), 501 (FRI0060), 620 (FRI0354), 623 (FRI0361), 1078 (AB0091)
Yoshimura, A., 1021 (SAT0652)
Yoshimura, H., 955 (SAT0477), 1324 (AB0768)
Yoshinaga, Y., 924 (SAT0402)
Yoshio, T., 598 (FRI0297)
Yoshioka, T., 573 (FRI0233), 806 (SAT0101)
Yoshitama, T., 1471 (AB1187)
Yoshizaki, A., 88 (OP0087), 138 (OP0207)
Yoshizawa, K., 581 (FRI0252)
Yoshizawa, S., 1254 (AB0582)
You, J., 1250 (AB0571)
You, Y., 944 (SAT0453)
Younes, M., 1000 (SAT0598), 1169 (AB0346, AB0347), 1170 (AB0348), 1353 (AB0848, AB0849)
Young, A., 782 (SAT0040), 1028 (SAT0671)
Young, D., 295 (THU0242)
Young, J., 831 (SAT0161)
Young, N.A., 222 (THU0062), 1099 (AB0151)
Youngstein, T.A.-B., 227 (THU0076), 1427 (AB1064)
Younis, G., 1171 (AB0351)
Yourish, J., 95 (OP0105)
Yousri, A., 874 (SAT0265)
Youssef, A.A.-R., 1151 (AB0293)
Youssef, S.S., 431 (THU0597), 821 (SAT0138), 1149 (AB0287)
Ytterberg, J., 482 (FRI0006)
Ytterberg, S., 187 (OP0320)
Yu, C.-A., 764 (FRI0723)
Yu, C.M., 1520 (SAT0747-HPR)
Yu, D., 1096 (AB0141)
Yu, F., 1503 (FRI0755-HPR)
Yu, K.-H., 366 (THU0419)
Yu, P., 748 (FRI0681)
Yu, S., 505 (FRI0073), 1066 (AB0056)
Yu, X., 2 (SP0002)
Yuan, C., 294 (THU0239)
Yuan, Q., 1072 (AB0072)
Yuan, X., 1103 (AB0163)
Yue, J., 1198 (AB0424)
Yuen, K.Y., 412 (THU0543), 715 (FRI0599)
Yukai, H., 1480 (THU0732-HPR)
Yun, H., 448 (THU0643), 449 (THU0645), 676 (FRI0496)
Yunfeng, P., 903 (SAT0349)
Yunqing, W., 1480 (THU0732-HPR)
Yurdakul, F., 535 (FRI0144), 818 (SAT0130)
Yurdakul, F.G., 235 (THU0092), 652 (FRI0439), 1114 (AB0193), 1122 (AB0213)
Yurdakul, S., 603 (FRI0307), 618 (FRI0348), 1186 (AB0394), 1246 (AB0558)
Yurdalan, U.S., 1509 (FRI0770-HPR, FRI0771-HPR), 1519 (SAT0743-HPR), 1533 (AB1205-HPR)
Yurttas, B., 415 (THU0552)

Zaal, K.J., 1055 (AB0024)
Zabotti, A., 940 (SAT0443), 954 (SAT0473), 1314 (AB0742)
Zacarías-Crovato, A., 407 (THU0530)
Zacariaz, J.B., 1196 (AB0419)
Zack, D.J., 711 (FRI0588)
Zaenker, M., 23 (SP0092)
Zafar, A.-S., 821 (SAT0140)
Zaffarana, C., 1534 (AB1206-HPR)
Zafiriou, E., 680 (FRI0504)
Zaghloul, M., 1526 (SAT0764-HPR)
Zagvozdkina, E., 331 (THU0338)
Zaheer, Q., 1506 (FRI0762-HPR)
Zahiroglu, Y., 1172 (AB0353)
Zahuczky, G., 1049 (AB0009)
Zaia, A., 690 (FRI0527)
Zaichko, K., 654 (FRI0443), 1038 (SAT0696)
Zainudin, N., 256 (THU0146), 596 (FRI0291)
Zajdel, J., 1470 (AB1184)
Zajtseva, L., 398 (THU0508), 1389 (AB0956)
Zakalka, M., 558 (FRI0202)
Zakharova, A.Y., 246 (THU0120)
Zakirov, R., 1082 (AB0105)
Zalazar, M., 670 (FRI0483)
Zaldivar-Castaño, B., 993 (SAT0575)
Zallari, K., 1543 (AB1234-HPR)
Zámečník, J., 220 (THU0058)
Zamora, M., 597 (FRI0293)
Zamora-Legoff, J.A., 444 (THU0630)
Zamora-Legoff, V., 597 (FRI0292), 878 (SAT0278), 1225 (AB0499)
Zamorano-Serrano, M., 78 (OP0066)
Zamoyska, R., 178 (OP0296)
Zamudio-Cuevas, Y., 205 (THU0016), 216 (THU0047), 1067 (AB0059)
Zanatta, E., 634 (FRI0387), 1111 (AB0184)
Zandonade, E., 1102 (AB0160)
Zandonella Callegher, S., 585 (FRI0263)
Zanelli, T., 1064 (AB0050)
Zanetti, M., 1468 (AB1178)
Zanframundo, G., 790 (SAT0060), 1123 (AB0214)
Zangi, H.A., 1500 (FRI0747-HPR)
Zannettou, N., 1437 (AB1093)
Zannini, I., 872 (SAT0260)
Zanova, E., 829 (SAT0157), 1449 (AB1126)
Zanwar, A., 320 (THU0307)
Zapata-Castellanos, A.L., 905 (SAT0354)
Zapater, P., 980 (SAT0540)
Zapletalová, J., 1264 (AB0609)
Zappia, M., 923 (SAT0401)
Zarco, P., 660 (FRI0459), 736 (FRI0651), 930 (SAT0419), 946 (SAT0458)
Zarco-Colon, J., 1542 (AB1231-HPR)
Zarco-Montejo, P., 658 (FRI0452), 927 (SAT0412)
Zarei, H., 1341 (AB0811)
Zaremba-Pechmann, L., 794 (SAT0070)
Zaslavskiy, I., 1198 (AB0423)
Zateri, C., 1380 (AB0927)
Zatti, S., 70 (OP0046)
Zauner, M., 971 (SAT0515)
Závada, J., 1183 (AB0387)
Zavada, J., 179 (OP0297), 243 (THU0113), 440 (THU0621), 451 (THU0650)

Zavareh, A., 938 (SAT0438)
Zavodovsky, B., 699 (FRI0554), 1149 (AB0288)
Zayaeva, H., 339 (THU0355)
Zayoud, M., 508 (FRI0082)
Zbinden, A., 1510 (SAT0717-HPR)
Zborovskaya, I., 1149 (AB0288), 1361 (AB0872)
Zborovskaya, I.A., 459 (THU0670)
Zdravkovic, M., 751 (FRI0689), 1231 (AB0515)
Zdrenghea, D., 880 (SAT0285)
Zdrojewski, Z., 895 (SAT0327), 1470 (AB1184)
Zduniak, K., 1112 (AB0187)
Zea, A., 290 (THU0227)
Zea Mendoza, A., 392 (THU0491), 587 (FRI0266)
Zea-Mendoza, A., 298 (THU0249), 587 (FRI0267)
Zeft, A., 77 (OP0063), 448 (THU0641)
Zegarra Mondragón, S., 642 (FRI0409)
Zegers, I., 461 (THU0673)
Zeglaoui, H., 543 (FRI0165), 926 (SAT0409), 927 (SAT0411)
Zegzulkova, K., 916 (SAT0383)
Zeher, M., 311 (THU0284), 464 (THU0681), 886 (SAT0302), 1094 (AB0137)
Zeidler, G., 1106 (AB0169), 1110 (AB0181)
Zejden, A., 101 (OP0117)
Zelarney, P., 543 (FRI0164)
Zeldin, R.K., 92 (OP0098), 575 (FRI0239)
Zemah, R., 747 (FRI0679)
Zeman, F., 244 (THU0115)
Zen, M., 327 (THU0328), 1209 (AB0455, AB0456)
Zeng, C., 1338 (AB0802)
Zeng, H., 207 (THU0021), 358 (THU0399), 611 (FRI0327), 797 (SAT0077), 799 (SAT0080), 870 (SAT0253), 994 (SAT0578), 1112 (AB0188), 1126 (AB0222), 1141 (AB0264, AB0265), 1148 (AB0286), 1189 (AB0401), 1246 (AB0560), 1249 (AB0569), 1393 (AB0966)
Zeng, J., 268 (THU0177), 1201 (AB0432)
Zeng, P., 294 (THU0238), 1141 (AB0265), 1393 (AB0966)
Zeng, X., 310 (THU0281), 420 (THU0566), 583 (FRI0258), 600 (FRI0302), 858 (SAT0224), 883 (SAT0292), 1260 (AB0596)
Zeng, Y., 358 (THU0399)
Zengin, B., 306 (THU0271), 322 (THU0314), 1282 (AB0658)
Zengin, O., 327 (THU0329)
Zenker, S., 772 (SAT0010), 1023 (SAT0656)
Zerbini, A., 212 (THU0035), 1054 (AB0022)
Zerbini, C.A., 789 (SAT0058)
Zerkak, D., 450 (THU0646)
Zervou, M.I., 205 (THU0015)
Zeuner, R., 465 (THU0682)
Zevallos, F., 875 (SAT0269)
Zevallos-Miranda, F., 1142 (AB0269)
Zgolii, R., 1346 (AB0826)
Zhan, Z., 298 (THU0250), 1222 (AB0490)
Zhang, B., 1096 (AB0142), 1266 (AB0612)
Zhang, C., 276 (THU0195)
Zhang, D., 630 (FRI0377)
Zhang, F., 324 (THU0318), 1491 (THU0762-HPR)
Zhang, G., 419 (THU0563), 748 (FRI0681), 1079 (AB0094), 1083 (AB0106), 1249 (AB0568), 1290 (AB0679), 1363 (AB0877)
Zhang, H., 592 (FRI0281), 785 (SAT0047), 1535 (AB1210-HPR)
Zhang, J., 601 (FRI0304), 919 (SAT0392)
Zhang, L., 419 (THU0563), 748 (FRI0681), 920 (SAT0393), 1079 (AB0094, AB0095), 1082 (AB0103), 1083 (AB0106), 1138 (AB0257), 1249 (AB0568), 1260 (AB0596), 1290 (AB0679), 1363 (AB0877), 1368 (AB0893), 1369 (AB0894), 1370 (AB0897, AB0898, AB0899)
Zhang, M., 223 (THU0066), 547 (FRI0176), 1061 (AB0041)
Zhang, N., 1181 (AB0380)
Zhang, P., 543 (FRI0163), 883 (SAT0292), 1141 (AB0266)
Zhang, Q., 835 (SAT0172), 1368 (AB0893), 1369 (AB0894), 1370 (AB0897, AB0898, AB0899)
Zhang, R., 149 (LB0003), 271 (THU0185), 1065 (AB0052), 1096 (AB0141), 1144 (AB0274)
Zhang, S., 869 (SAT0252)
Zhang, W., 167 (OP0268), 752 (FRI0693), 973 (SAT0523), 1028 (SAT0670), 1206 (AB0447)
Zhang, X., 358 (THU0399), 583 (FRI0258), 788 (SAT0055), 869 (SAT0252), 1352 (AB0845)
Zhang, X.-Y., 1084 (AB0110)
Zhang, Y., 97 (OP0108), 129 (OP0187), 165 (OP0264), 242 (THU0110), 280 (THU0203), 324 (THU0318), 349 (THU0379), 443 (THU0628), 459 (THU0669), 558 (FRI0201), 664 (FRI0470), 665 (FRI0471), 677 (FRI0498), 828 (SAT0155), 832 (SAT0165), 892 (SAT0318), 1338 (AB0802)
Zhang, Z., 293 (THU0235), 547 (FRI0176), 600 (FRI0302), 797 (SAT0076), 1092 (AB0130), 1097 (AB0145), 1103 (AB0163), 1416 (AB1033), 1491 (THU0762-HPR), 1516 (SAT0734-HPR)
Zhang, Z.-Y., 291 (THU0232)
Zhao, C., 547 (FRI0176)
Zhao, H., 692 (FRI0531, FRI0532)
Zhao, J., 497 (FRI0050), 583 (FRI0258), 797 (SAT0076), 858 (SAT0224), 883 (SAT0292)
Zhao, L., 884 (SAT0294), 1260 (AB0596)
Zhao, M., 351 (THU0384)
Zhao, Q., 1230 (AB0513), 1234 (AB0523), 1241 (AB0543)
Zhao, X., 1081 (AB0100)
Zhao, Y., 409 (THU0537), 1260 (AB0596), 1491 (THU0762-HPR), 1516 (SAT0734-HPR)
Zhao, Z., 935 (SAT0432)
Zhelyabina, O., 1019 (SAT0646), 1369 (AB0895)
Zheng, D.-H., 279 (THU0201), 373 (THU0439)
Zheng, S., 203 (THU0010), 450 (THU0647), 934 (SAT0430), 962 (SAT0493), 986 (SAT0555)
Zheng, W., 324 (THU0318), 1260 (AB0596)
Zheng, X., 664 (FRI0469)
Zhengping, H., 1480 (THU0732-HPR)
Zhilyaev, E., 848 (SAT0200)
Zhixiang, H., 1480 (THU0732-HPR)
Zhong, J., 510 (FRI0086)
Zhong, S., 156 (OP0243), 230 (THU0083)
Zhou, C., 1234 (AB0523)
Zhou, G., 294 (THU0238)
Zhou, H., 129 (OP0187)
Zhou, J., 202 (THU0007), 336 (THU0351), 1535 (AB1210-HPR)
Zhou, L., 151 (OP0234)
Zhou, M., 93 (OP0101)
Zhou, W., 688 (FRI0522)
Zhou, Y., 759 (FRI0710)
Zhu, B., 230 (THU0081), 517 (FRI0099), 524 (FRI0116), 788 (SAT0055), 794 (SAT0069)
Zhu, H., 1082 (AB0102)
Zhu, J., 601 (FRI0304), 759 (FRI0710), 919 (SAT0392), 935 (SAT0432), 1081 (AB0099)
Zhu, L., 1082 (AB0102)
Zhu, S.-L., 1077 (AB0087)
Zhu, T.Y., 689 (FRI0524), 1198 (AB0424)
Zhu, X., 1370 (AB0897, AB0898)
Zhu, Z., 122 (OP0169), 450 (THU0647), 962 (SAT0493), 986 (SAT0555)
Ziade, N., 1159 (AB0317)
Ziade, N.R., 667 (FRI0476), 762 (FRI0718), 1001 (SAT0599)
Zickert, A., 861 (SAT0233), 885 (SAT0297)
Zickuhr, L., 1167 (AB0338)
Ziegler, C.R., 1555 (PARE0011)
Zielińska, A., 556 (FRI0198)
Zierhut, M., 722 (FRI0618)
Ziętkiewicz, M., 895 (SAT0327)
Žigon, P., 219 (THU0054), 325 (THU0324)
Zigon, P., 1243 (AB0552)
Zilber, K., 926 (SAT0407)
Zilberstein, M., 570 (FRI0227), 844 (SAT0192)
Zimanova, T., 1350 (AB0838)
Zimba, O., 328 (THU0332), 616 (FRI0341)
Zimin, S., 413 (THU0547)
Zimmermann, J., 655 (FRI0446)
Zindel, B., 185 (OP0314-HPR)
Zink, A., 134 (OP0199-PARE), 302 (THU0261), 530 (FRI0130), 801 (SAT0087), 899 (SAT0337), 1029 (SAT0674)
Zinke, S., 1029 (SAT0674)
Zinovieva, E., 789 (SAT0057)
Zioupos, P., 498 (FRI0051), 1080 (AB0098)
Ziouzina, O., 933 (SAT0428)
Zisman, D., 1328 (AB0776)
Ziswiler, H., 816 (SAT0125)
Zivkovic, V., 914 (SAT0378), 1240 (AB0540)
Zivojinovic, S.M., 559 (FRI0206)
Zlatanovic, M., 792 (SAT0064)
Zlatkovic-Svenda, M.I., 1457 (AB1149)
Zleik, N., 1507 (FRI0764-HPR)
Zlotnick, S., 846 (SAT0196), 1191 (AB0407)
Zmailik, M., 1356 (AB0858)
Zoghbi, M., 762 (FRI0718)
Zoli, A., 608 (FRI0319)
Zolotnitskaya, V.P., 810 (SAT0111)
Zonova, E., 560 (FRI0208), 1336 (AB0795, AB0796)
Zorbala, A., 908 (SAT0361)
Zou, H., 1535 (AB1210-HPR)
Zou, Y., 1065 (AB0052), 1206 (AB0447)
Zouch, I., 1146 (AB0278)
Zrida, S., 1383 (AB0936)
Zrour, S., 1353 (AB0848, AB0849)
Zubarev, R., 1096 (AB0142)
Zuccaro, C., 808 (SAT0105), 1327 (AB0773)
Zucht, H.-D., 193 (OP0333), 886 (SAT0301), 893 (SAT0319), 911 (SAT0372), 1007 (SAT0616)
Zuckerman, S., 1147 (AB0281)
Zufferey, P., 130 (OP0189), 267 (THU0174), 335 (THU0347), 378 (THU0452), 816 (SAT0125), 1013 (SAT0631), 1445 (AB1114)
Zulian, F., 9 (SP0035)
Zuliani, F., 940 (SAT0443), 954 (SAT0473)
Zuliani, L., 437 (THU0611), 1439 (AB1099)
Zuo, X., 1524 (SAT0757-HPR)
Zurita, E., 1098 (AB0149)
Zurita, E.J., 1091 (AB0126)
Zuurmond, A.-M., 769 (SAT0001)
Zverkova Sandström, T., 360 (THU0404)
Zwezerijnen, B., 732 (FRI0642)
Zwinderman, K., 781 (SAT0037)
Zwolak, R., 251 (THU0133)
Zytoon, A.A., 1404 (AB1000)